Manipulation of Steroid Core and Side Chain:

Methodology for the Synthesis of Steroid Natural Products Strophasterol A–D and Glaucoposterol A

Inaugural-Dissertation
to obtain the academic degree
Doctor rerum naturalium (Dr. rer. nat.)

submitted to the Department of Biology, Chemistry and Pharmacy
Freie Universität Berlin

submitted by

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from Berlin

May 2019

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Florian Noack, Berlin, den 27.05.2019.

Diese Arbeit wurde im Zeitraum von Januar 2016 bis Februar 2019 im Fachbereich Biologie, Chemie, Pharmazie der Freien Universität Berlin angefertigt.

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Disputation am: 28. November 2019

Parts of this thesis have been published:

F. Noack, B. Hartmayer, P. Heretsch, *Synthesis* **2018**, *50*, 809−820.

F. Noack, R.C. Heinze, P. Heretsch, *Synthesis* **2019**, *51*, 2039−2057.

Contents

I. Danksagung

Wie es wohl Tradition bei der Anfertigung solcher Arbeiten ist, war dies auch bei mir ohne die Hilfe vieler Menschen nicht möglich. Ich danke allen von Herzen und werde es nie vergessen!

Lieber Philipp, bei dir möchte ich mich für die Aufnahme in deine Arbeitsgruppe, den gemeinsamen Weg sowie das fordernde und interessante Thema bedanken. Durch die drei lehrreichen Jahre konnte ich mich nicht nur fachlich entwickeln, sondern auch persönlich. Ohne den Platz in deiner Gruppe hätte ich die wertvollsten Dinge meines jetzigen Lebens wahrscheinlich nicht gefunden. Dafür werde ich dir für immer dankbar sein!

Besonderer Dank gilt auch der Familie Krieger, die mir mit Ihrer großzügigen Unterstützung überhaupt erst ermöglicht haben zu promovieren! Ich hoffe Sie wissen, dass ich Ihnen für immer zutiefst verbunden bin. Ich danke Ihnen vor allem auch für das Vertrauen, dass Sie mir stets entgegengebracht haben. Ich hatte immer viel Spaß an der Arbeit mit Konrad und habe mich immer herzlich bei Ihnen willkommen gefühlt. Ich wünsche Ihnen und auch Konrad von Herzen nur das Beste für den weiteren Weg, ein erfolgreiches Studium und ein erfülltes und gesundes Leben.

Ohne dich, Louisa, wäre diese Arbeit ganz sicher nicht möglich gewesen. Deine Liebe und Unterstützung ist der wertvollste und wichtigste Bestandteil in meinem Leben.

Auch dir lieber Geerd möchte ich für die tatkräftige Unterstützung während der gesamten Zeit danken, ob nun finanzieller oder seelischer Natur, ich bin sehr froh, dass ich dich und Rüdiger in meinem Leben habe.

Ebenfalls Prof. Dr. Matthew Hopkinson möchte ich für die freundliche Übernahme der Zweitgutachtens danken, gleiches gilt auch für die restlichen Mitglieder der Prüfungskommission.

Besonderer Dank gilt Bence und Merlin für die ständigen Diskussionen, Ratschläge, Korrekturen und auch den Spaß, den wir zusammen hatten.

Timme, dir möchte ich besonders für die Freundschaft und die bedingungslose Loyalität und Unterstützung in der gesamten Zeit danken! Auch bei Lia, Alex, Brian und Nico möchte ich mich für das immer offene Ohr und die Ratschläge bedanken.

Selbstverständlich möchte ich mich bei allen herzlichst bedanken, die durch ihre Korrekturen zur Qualität dieser Arbeit beigetragen haben: Merlin, Bence, Caro, Alex, Franzi und Fenja.

Ohne meine Familie, insbesondere meine Mutter und Oma wäre diese Arbeit sicher auch nicht zum Erfolg gekommen. Aber auch dem Rest, dem alten und auch dem neuen Teil der Familie, danke ich für die liebevolle Unterstützung.

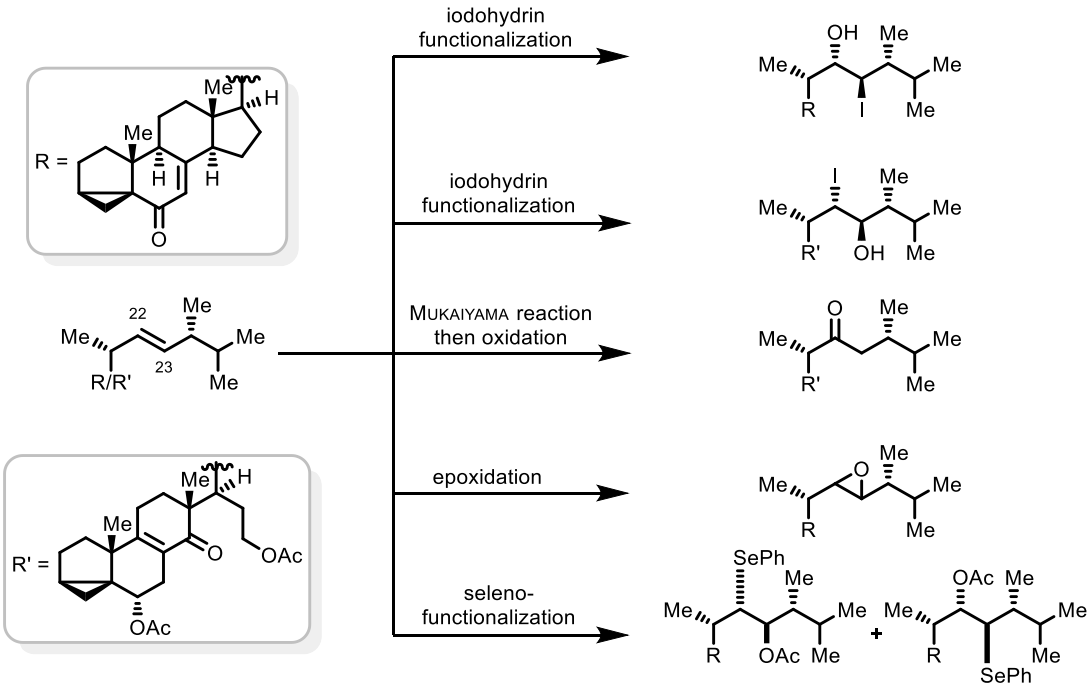
Vielen Dank auch an Herrn Prof. Christmann und seine Arbeitsgruppe für die nette Zusammenarbeit und jegliche Unterstützung in den letzten drei Jahren. Gleiches gilt auch für alle weiteren Mitarbeiter des Instituts. Besonderer Dank gilt hierbei Hr. Dr. Schäfer und dem gesamten Team der Analytik.

Ich danke allen, die immer an mich geglaubt haben!

II. Abstract

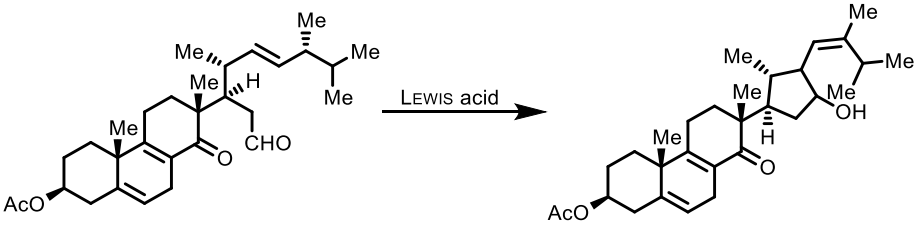
The first part of this thesis deals with studies on the synthesis of a platform for the targeted synthesis of the natural product class of strophasterols. The second part describes the development of a method for access to abeo steroids.

The strophasterols are four rearranged steroids that were isolated in 2012. Strophasterols A and B were synthesized by HERETSCH et al. and KUWAHARA et al. in 2016 and 2017, respectively, whereas strophasterols C and D still lack synthetic access. In addition, the absolute stereo configuration of strophasterols C and D is unknown and should be elucidated. Based on the synthesis of strophasterol A by HERETSCH et al., known and new methods for the oxidative functionalization of the ergosterol side chain were tested in order to introduce the required oxidation state at position C23.



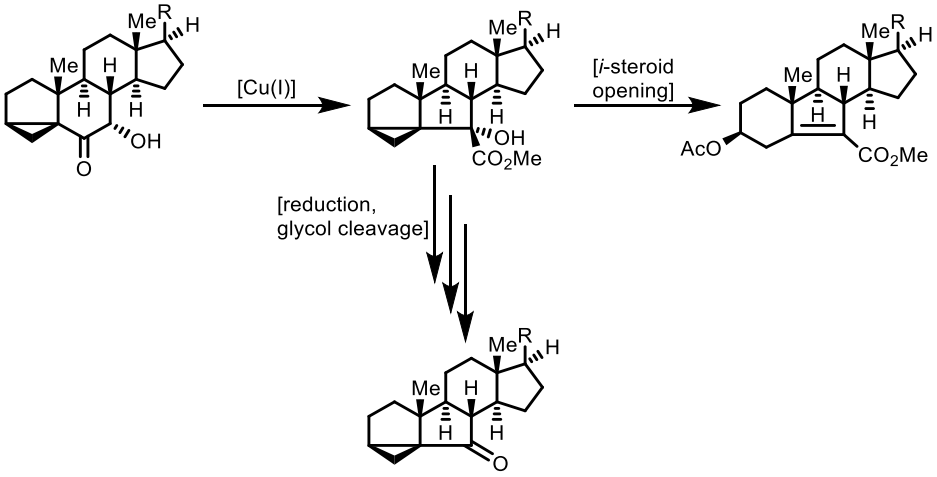
En route towards the required platform, known methods for the functionalization of the ergosterol side chain were applied and evaluated. Due to low yields or undesired regioselectivity, no suitable method for the targeted installation of the required oxidation state at C23 could be identified. Nevertheless, valuable results for the general and improved functionalization of ergostane and other steroidal systems could be generated.

The application of an intramolecular, LEWIS acid mediated carbonyl-ene reaction made a significant contribution to the generation of the desired platform.



On the basis of these results, an elegant, efficient and selective access to each member of the natural product class of strophasterols can be envisioned.

The second part of the thesis deals with the development of a method for contraction of the B-ring of steroidal systems based on α-hydroxy ketones. Conventional methods often have the disadvantage of poor yields, low reproducibility or difficult accessible starting materials. A mild and effective alternative with a high tolerance for functional groups was developed on the basis of benzilic acid rearrangement, thus enabling the synthesis of abeo steroids. In addition, access to B-nor ketones has been developed without the use of harmful reagents such as lead(IV) acetate.

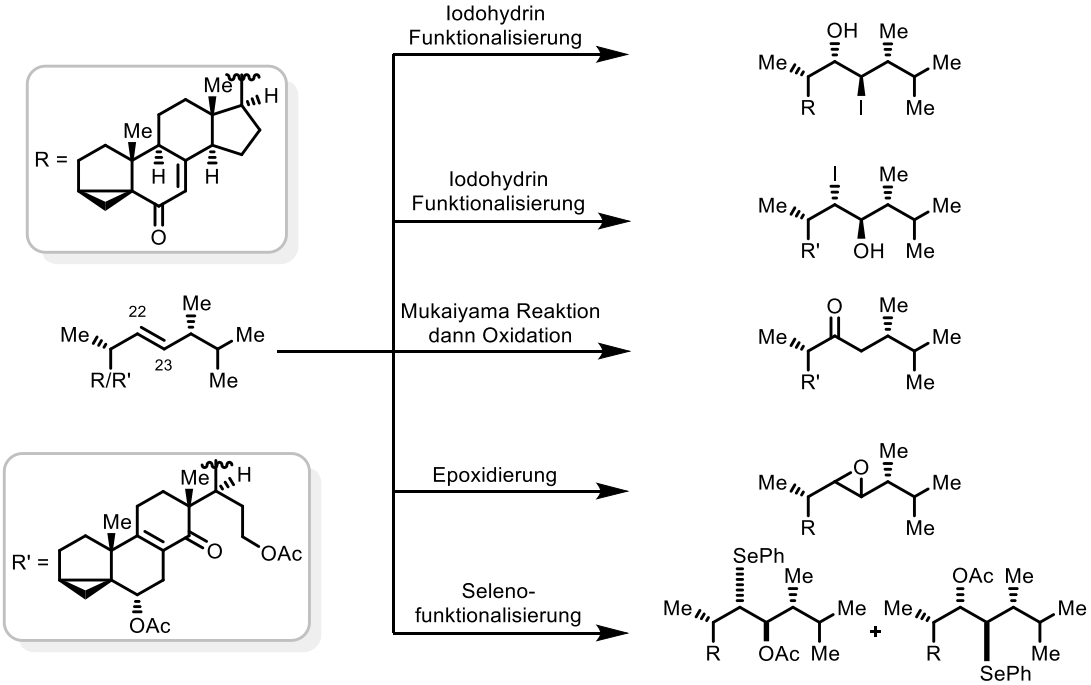


This way, the developed method provides advanced and reliable access to the described class of substances, enabling future work on biologically relevant compounds.

III. Kurzzusammenfassung

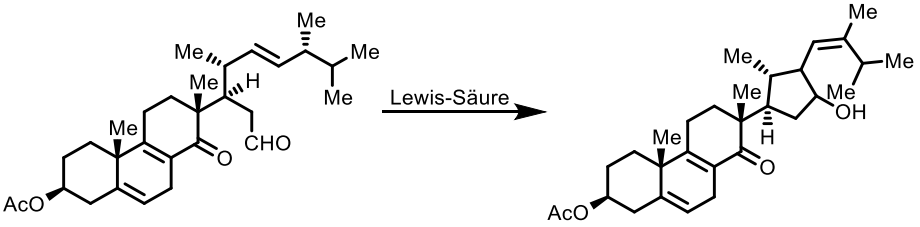
Die vorliegende Arbeit befasst sich im ersten Teil mit Studien zur Synthese einer Plattform, die für die gezielte Synthese der Naturstoffklasse der Strophasterole verwendet werden soll. Im zweiten Teil wird die Entwicklung einer Methode zum Zugang zu *abeo*-Steroiden beschrieben.

Die Strophasterole sind vier im Jahr 2012 isolierte, umgelagerte Steroide. Die Strophasterole A und B wurden bereits 2016 bzw. 2017 von den Arbeitsgruppen HERETSCH und KUWAHARA synthetisiert, wohingegen zu den Strophasterolen C und D bis heute ein synthetischer Zugang fehlt. Zusätzlich ist die absolute Stereokonfiguration der bisher nicht synthetisch zugänglichen Strophasterole C und D unbekannt und soll aufgeklärt werden. Auf Grundlage der Synthese von Strophasterol A von HERETSCH et al. wurden bekannte und neue Methoden zur oxidativen Funktionalisierung der Ergosterolseitenkette erprobt, um gezielt den benötigten Oxidationszustand an Position C23 einzuführen.



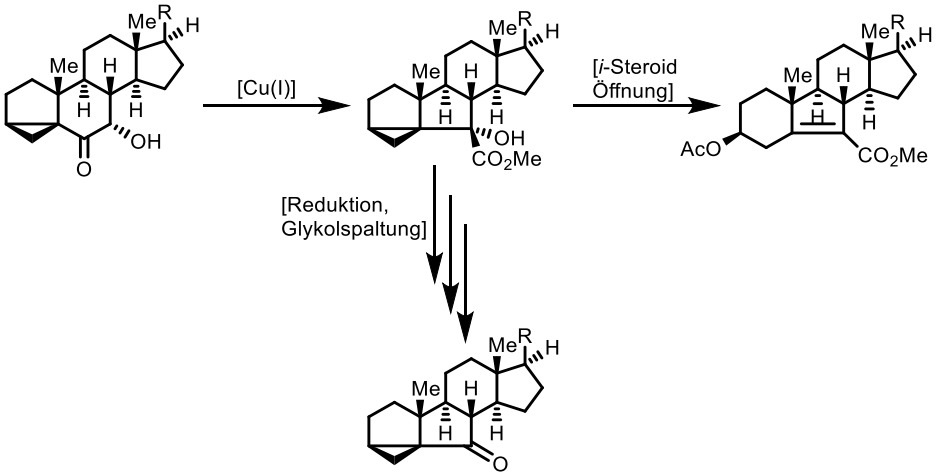
Auf dem Weg zu der erwünschten Plattform wurden bekannte Methoden zur Funktionalisierung von Olefinen auf die Ergosterolseitenkette angewendet und evaluiert. Durch die oftmals geringen Ausbeuten oder unerwünschte Regioselektivität konnte keine passende Methode zur gezielten Installation des benötigten Oxidationszustands an C23 identifiziert werden. Dennoch konnten wertvolle Ergebnisse für die allgemeine und verbesserte Funktionalisierung von Ergosterol-artigen und anderen steroidalen Systemen generiert werden.

Durch die Anwendung einer intramolekularen, Lewis Säure mediierten Carbonyl-En Reaktion wurde ein entscheidender Beitrag zur Generierung der gewünschten Plattform geleistet.



Auf Grundlage dieser Ergebnisse kann so ein eleganter, effizienter und selektiver Zugang zu jedem Mitglied der Naturstoffklasse der Strophasterole erschlossen werden.

Der zweite Teil der Arbeit behandelt die Entwicklung einer Methode zur Kontraktion des B-Rings steroidaler Systeme ausgehend von α-Hydroxy Ketonen. Gängige Methoden haben den Nachteil oft schlechte Ausbeuten zu liefern, schwer reproduzierbar zu sein oder von schwer zugänglichen Verbindungen auszugehen. Auf Grundlage der Benzilsäureumlagerung konnte eine milde und effektive Alternative mit hoher Toleranz für funktionelle Gruppen entwickelt und so die Synthese von *abeo*-Steroiden ermöglicht werden. Darüber hinaus wurde ein Zugang zu B-nor-Ketonen erschlossen, der ohne die Verwendung schädlicher Reagenzien wie Blei(IV) acetat auskommt.



Auf diese Weise liefert die entwickelte Methode einen fortschrittlichen und verlässlichen Zugang zu der beschriebenen Substanzklasse, sodass ein zukünftiges Arbeiten an biologisch relevanten Verbindungen ermöglicht wird.

IV. List of Abbreviations

2D	two dimensional	Ac	acetyl
acac	acetylacetonate	Å	Ångström 10^{-10} m
BPO	benzoylperoxide	d	duplett
DBDMH	1,3-dibrom-5,5-dimethylhydantoin	DCE	1,2-dichloroethane
DIAD	diisopropyl azodicarboxylate	4-DMAP	*N*,*N*-dimethylamino-pyridine
DMF	*N*,*N*-dimemthylformamide	DMP	DESS-MARTIN periodinane
DMSO	dimethylsulfoxide	d.r.	diasteromeric ratio
et al.	and others	*epi*	epimer
equiv.	equivalents	HMBC	heteronuclear multiple-bond correlation spectroscopy
h	hour	HMQC	heteronuclear multiple-quantum correlation spectroscopy
HRMS	high resolution mass spectroscopy	Hz	Hertz (s^{-1})
FT-IR	Fourier transform infrared spectroscopy	IBX	2-iodoxybenzoic acid
J	coupling constant	KHMDS	potassium bis(trimethysilyl) amide
L	liter	L	Ligand
LDA	lithium diisoproylamide	LG	leaving group
m	multiplett	Me	methyl
min	minute	mg	milligram (10^{-3} g)
M	molar (mol/L)	mmol	millimole (10^{-3} mol)
m.p.	melting point	mL	milliliter (10^{-3} L)
MS	molecular sieves	NMR	nuclear magnetic resonance
NBS	*N*-bromosuccinimide	*m*-CPBA	*meta*-chloroperoxybenzoic acid
NIS	*N*-iodosuccinimide	nOe	nuclear OVERHAUSER effect

Pd/C	palladium on charcoal	Ph	Phenyl
PCC	pyridinium chlorochromate	PDC	pyridinium dichromate
quant.	quantitative	ppm	parts per million
TBS	*tert*-butyldimethylsilyl	THF	tetrahydrofuran
TES	triethylsilyl	PinB	pinacolatoboran
py	pyridine	PhMe	toluene

1. The Chemistry of Steroids

1.1 Biosynthesis and Synthetic Strategies

Owing to their structural diversity and often valuable biological activity, the natural product class of steroids plays an essential role in chemical, pharmaceutical, and medicinal research.[1–3] Landmarks in the synthetic organic chemistry such as the first syntheses of equilenin (**1**, 1939 by BACHMANN et al., *Figure 1*), lanosterol (**2**, 1952 by WOODWARD et al.) or progesterone (**3**, 1971 by JOHNSON et al.) had a major influence on the field.[4–7] They inspired the development of new synthetic methods and pushed the advances in medicinal, pharmaceutical and organic chemistry.

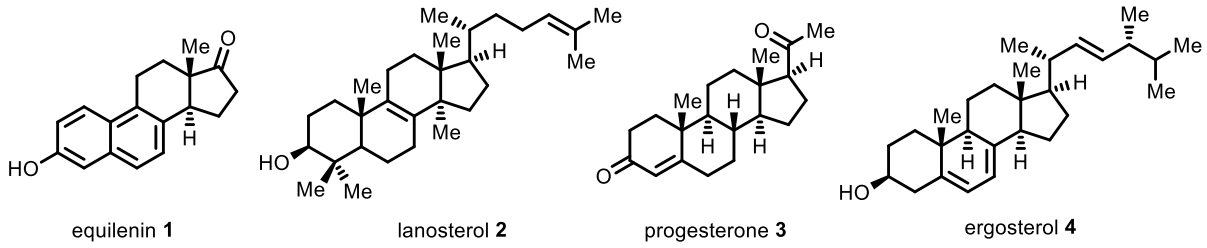
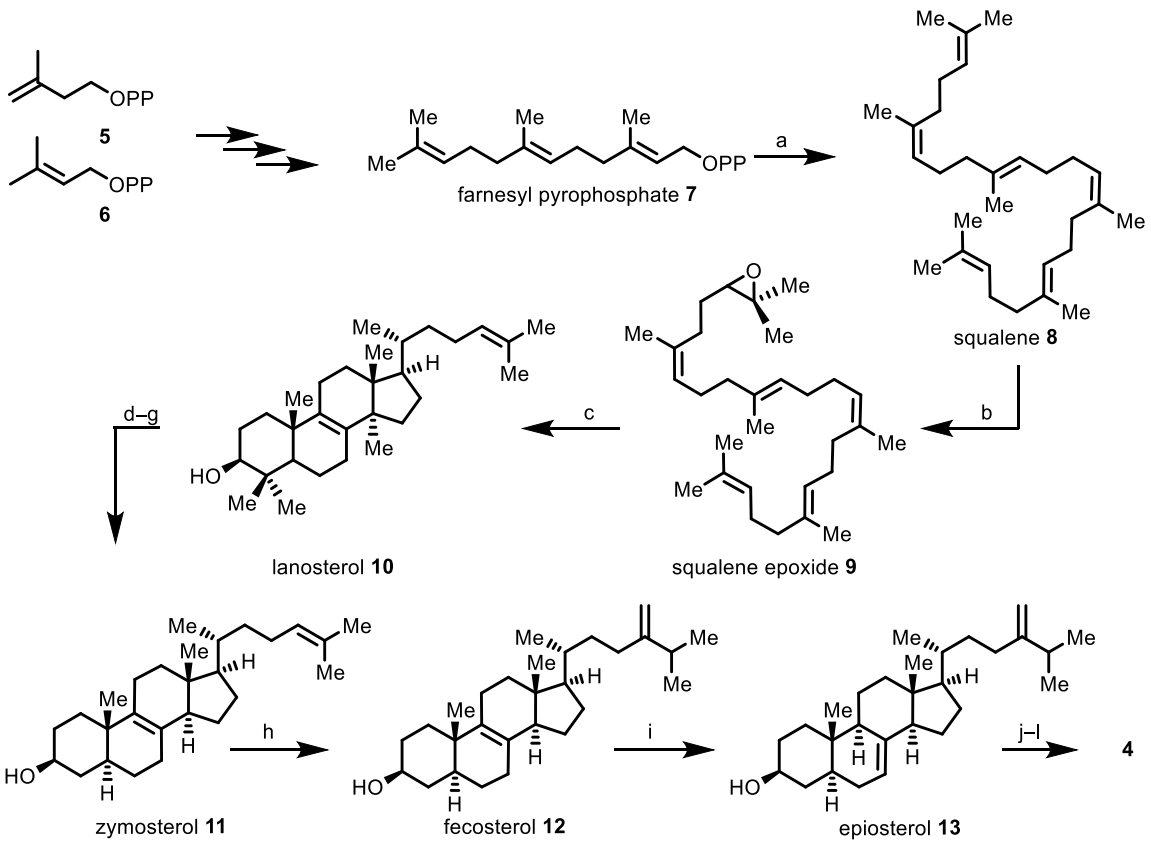


Figure 1: Structures of equilenin, lanosterol, progesterone, and ergosterol

One remarkable steroid that is also subject to modern research is ergosterol **4**. It is one of nature's most abundant steroids and is primarily found in the membranes of fungal cells where it is responsible for the membrane's fluidity and integrity. Due to its facile isolation from plant sources, ergosterol is commercially available and can readily be used as a starting point for natural product synthesis. Commercialization of ergosterol began early on *via* yeast fermentation and can be obtained through isolation of the complete sterol content of the fermentation followed by separation of the compounds.[8] The biosynthesis of **4** starts with the synthesis of the triterpene squalene **8** from dimethylallyl pyrophosphate **5** and isopentenyl pyrophosphate **6** (*Scheme 1*). After enzymatic epoxidation to squalene epoxide **9** and pre-folding in the lanosterol synthase, intermediate **10** is formed by cation-polyene cyclization and 1,2-methyl and -hydride shifts. It delivers the steroidal frame and demethylation and adjustment of the oxidation states finally forms ergosterol **4** in few steps.



Scheme 1: Biosynthetic pathway to ergosterol. Enzymes: a) squalene synthase; b) squalene epoxidase; c) lanosterol synthase; d) lanosterol demethylase; e) C14 reductase; f) C3 dehydrogenase; g) C3 keto reductase; h) C24 methyl transferase; i) C8 isomerase; j) C5 desaturase; k) C3 desaturase; l) C24 reductase.

Ergosterol is not only an abundant starting material for the industrial synthesis of ergocalciferol (vitamin D2) and other synthetic endeavors but also subject to pharmaceutical research itself. As it is a crucial part of the fungal cell membrane, various antimycotic compounds like amphotericin B **14** were developed to interact with the ergosterol in the membrane by binding to it (*Figure 2*).

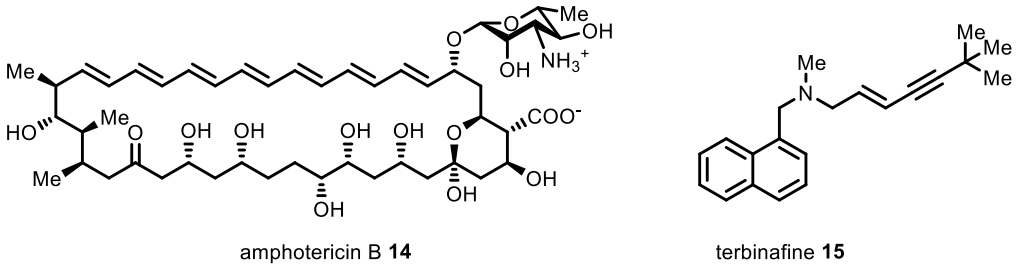
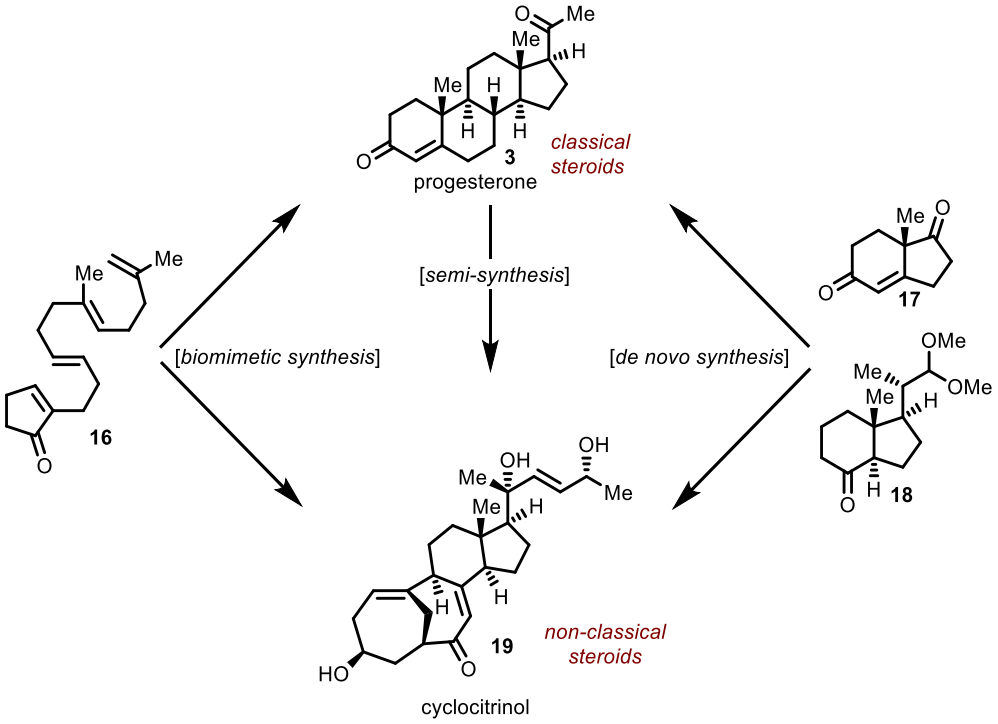


Figure 2: Antimycotic pharmaceuticals amphotericin B **14** and terbinafine **15**.

This way, the cell membrane's integrity is damaged, resulting in a leakage of ions (e.g., K^+, Na^+, Cl^-) and small organic molecules, eventually resulting in cell death.[9] Other antimycotic agents like terbinafine **15** directly intercept in the biosynthesis of ergosterol and disturb the process, also leading to cell death.[10]

From a chemists point of view, an advantage of this class of natural products that is also used today for most pharmaceutically relevant steroids is that they can be derived by semi-synthesis *via* modification of abundant natural products, e.g., ergosterol.[11] In general, there are three established strategies for the synthesis of steroidal natural products: biomimetic, *de novo* and the semi-synthetic approach (*Scheme 2*). A breakthrough for the synthesis of classic steroids, the term classic should thereby refer to compounds with the intact 6/6/6/5 steroid frame, was the development of the biomimetic strategy. It is based on polyene ring closure cascades developed by JOHNSON et al. during their work towards the total synthesis of progesterone.[12,13]

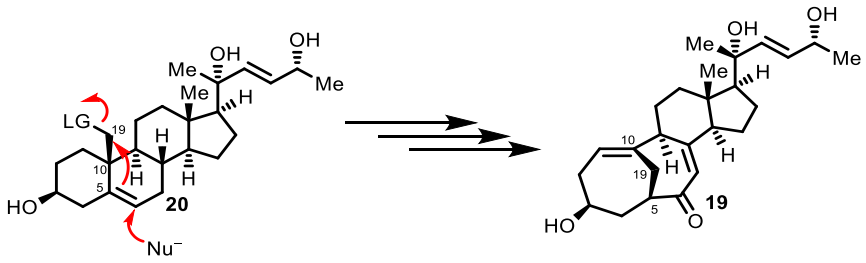


Scheme 2: Synthetic strategies toward classical and non-classical steroids.

This strategy can be used for efficient and quick access to the steroidal frame from readily available starting materials. On the other hand, the *de novo* strategy starts from simply accessible starting materials such as the HAJOS-WIECHERT ketone **17** or commercially available ketone **18**. This strategy allows for diversification on numerous synthetic stages with the drawback of often requiring many synthetic steps towards the target.[14] The semisynthesis as the third strategy starts from abundant natural products such as pregnenolone or prednisone allowing for more concise and scalable syntheses.[15]

1.2 Rearranged Steroids

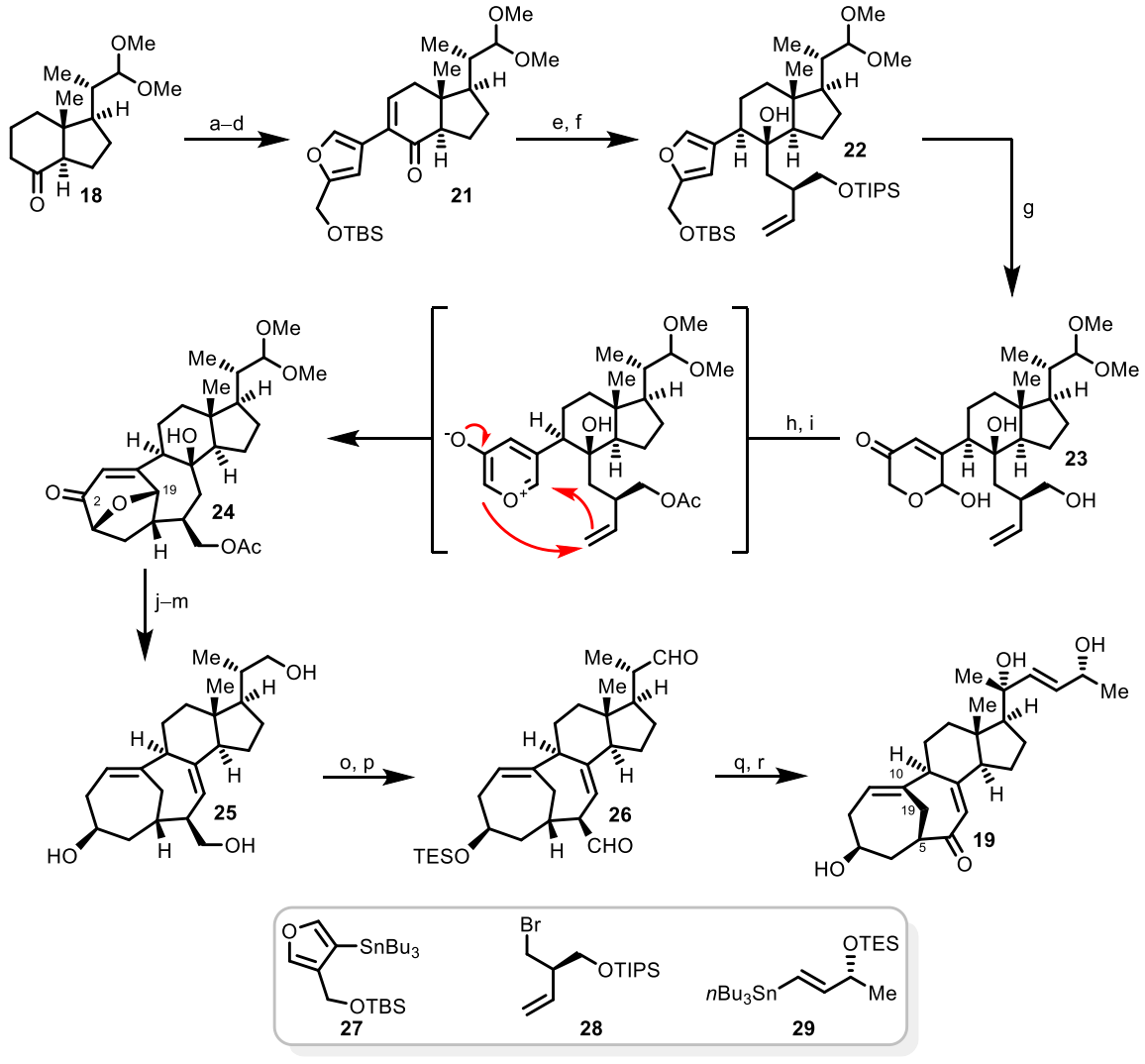
Although steroid chemistry experienced a slight decrease in efforts towards new total syntheses in the early 2000s there has been a renaissance lately. This might be due to an increasing number of rearranged steroids, referred to as seco- or *abeo*-steroids that have recently been isolated and partly synthesized by means of the established strategies.[3,16,17] Secosteroids are molecular entities where a bond at any position of the typical tetracyclic steroid frame is broken. The term "*abeo*" is used, when one or multiple bond migrations have occurred, e.g., as in cyclocitrinol **19** where C5 is no longer bound to C10 but to C19 instead (*Scheme 3*). Thus, **19** is referred to as a 5(10→19)*abeo* steroid, indicating the bond migration from C5−C10 to C5−C19.[18]



Scheme 3: Simplified representation of the bond migration in cyclocitrinol.

Cyclocitrinol **19** was recently synthesized by the groups of LI and GUI in 2018 and allows for a comparison between two synthetic strategies.[14,15] While LI et al. completed their enantioselective synthesis in a *de novo* approach, while GUI et al. used a biomimetic approach to furnish the target molecule (*Scheme 4* and *Scheme 5*). LI's synthesis started form commercially available ketone **18** that was transformed into an enone by oxidation of the corresponding silyl ether with 2-iodoxybenzoic acid (*Scheme 4*). Subsequent α-Iodination of the enone and subsequent STILLE coupling with stannane **27** in *N*-methyl-2-pyrrolidone in presence of tetrakis(triphenylphosphine)palladium(0), copper(I) thiophene carboxylate and lithium acetate gave **21** in 46% yield over four steps. Reduction of the enone to the ketone with nickel(II) chloride in presence of sodium borohydride followed by 1,2-addition of lithiated **28** to the ketone gave tertiary alcohol **22** in 55% yield over two steps. Desilylation and ACHMATOWICZ rearrangement to lactol **23** gave the precursor for the key step of the synthesis. Acetylation and type II intramolecular [5+2] bipolar cycloaddition furnished the desired bicyclo[4.4.1]undecane ring system **24** in 68% yield over two steps. Due to the influence of the C2 carbonyl on the cleavage of the allyic C19–O bond, the C2 carbonyl was removed in a three step sequence consisting of 1,2-reduction, methyl carbodithioate formation and radical

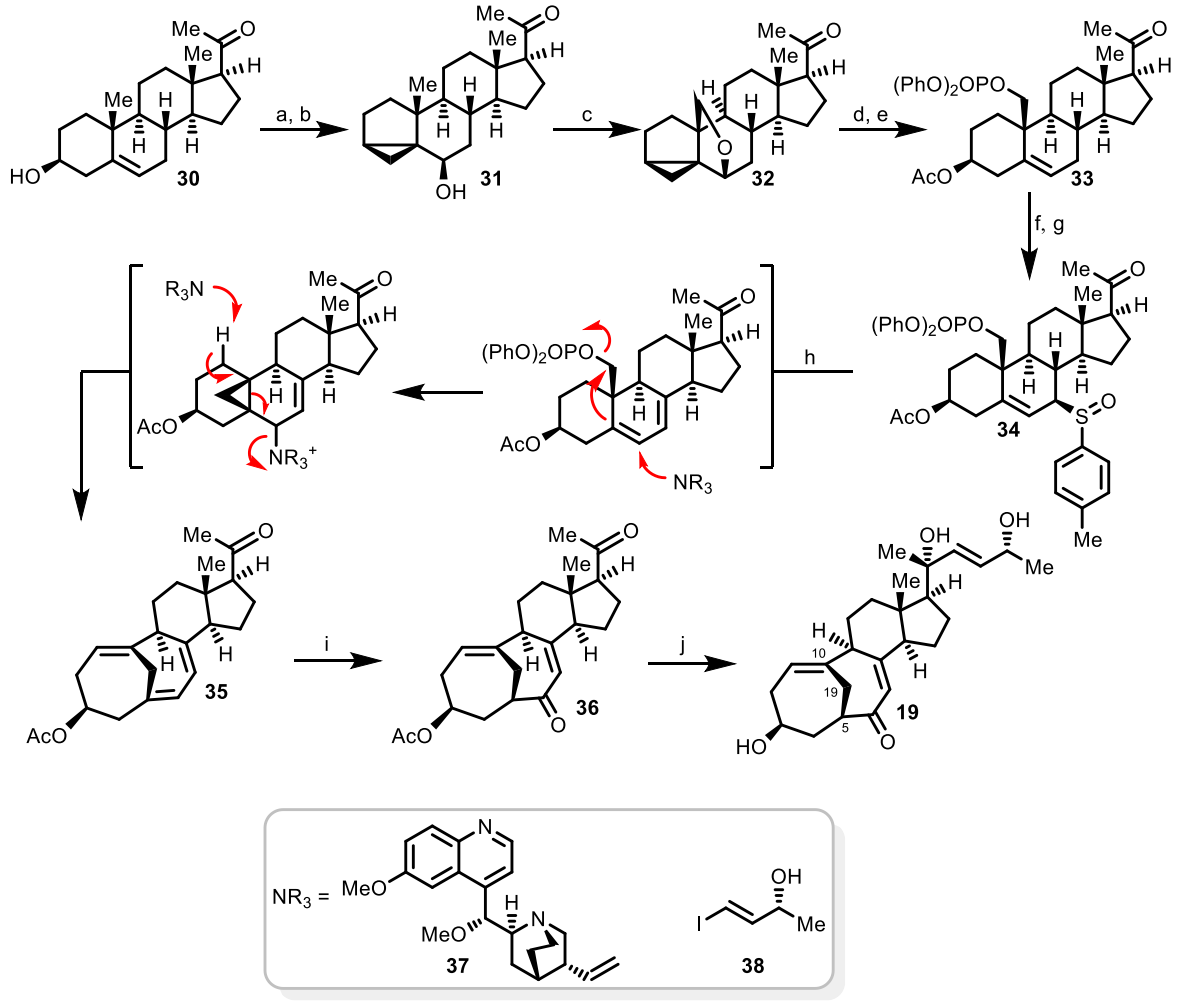
reductive scission. Removal of the C8 hydroxy group *via* elimination of the corresponding sulfurochloridite and selective cleavage of the C18–O bond with lithium in ethyl amine gave **25** in 21% over five steps. For the final steps of the synthesis, both primary alcohols were chemoselectively oxidized to the corresponding aldehydes with 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO) and *N*-chlorosuccinimide (NCS) in presence of *n*-tetrabutylammonium chloride. Subsequent silylation of the secondary alcohol gave **26** in 60% yield over two steps. The final steps included the challenging oxidative deformylation of both aldehydes corresponding ketones with potassium *t*-butoxide in presence of oxygen to give the diketone (structure not shown).



Scheme 4: L1 synthesis of cyclocitrinol. Conditions: a) LDA, TMSCl, THF; −78 °C; b) IBX, DMSO, 25 °C, 80% over two steps; c) $TMSN_3$, I_2, CH_2Cl_2/py, 0 °C→25 °C, 70%; d) **27**, $Pd(PPh_3)_4$, CuTC, LiOAc, NMP, 25 °C, 83%; e) $NaBH_4$, $NiCl_2$, MeOH, −78 °C→25 °C, 67%; f) **28**, *t*-BuLi, Et_2O, −78 °C, 83%; g) TBAF, THF; then H_2O, NBS, NaOAc, $NaHCO_3$, 25 °C, h) TMP, Ac_2O, DMAP, CH_2Cl_2, 25 °C; i) TMP, CH_3CN, 155 °C, 68% over three steps; j) $NaBH_4$, THF/H_2O, 0 °C; k) KHMDS, CS_2, MeI, THF, −78 °C; l) AIBN, *n*-Bu_3SnH, PhMe, 80 °C, 41% over three steps; m) $SOCl_2$, py, CH_2Cl_2, 0 °C; n) Li, $EtNH_2$, 25 °C, 51% over two steps; o) TBACl, TEMPO, NCS, CH_2Cl_2-buffer, 70%; p) TESOTf, 2,6-lutidine, CH_2Cl_2, −78 °C, 86%; q) *t*-BuOK, O_2, *t*-BuOH, 25 °C, 56%; r) **29**, *n*-BuLi, THF, −78 °C; then TBAF, 84%.

Addition of lithiated **29** followed by desilylation then gave cyclocitrinol **19** in 47% over two steps.

In contrast to LI's synthesis, GUI's synthetic endeavor started from commercially available pregnenolone **30** (*Scheme 5*). Starting with the tosylation of the C3 hydroxy group and *i*-sterol formation under basic aqueous conditions gave **31** in 84% yield over two steps. Oxidation of the C19-methyl group with lead(IV) acetate gave tetrahydrofuran **32**, which after opening of the *i*-steroid and cleavage of the tetrahydrofuran delivered **33** in 49% yield over two steps. Phosphorylation of the C19 hydroxy group followed by allylic bromination of C7 gave after S_N2 replacement with *p*-thiocresol and oxidation to the sulfoxide **34** in 74% over three steps. Submission of **34** to *O*-methylquinine **37** delivered triene *via* a sequence of intramolecular cyclopropanation and fragmentation in 54% yield.



Scheme 5: GUI synthesis of cyclocitrinol. Conditions: a) TsCl, DMAP, py, 23 °C; b) K_2CO_3, Me_2CO/H_2O, 85 °C, 84% over two steps; c) $Pb(OAc)_4$, BPO, $CaCO_3$, PhH, 80 °C; d) $BF_3{\cdot}Et_2O$, AcOH, 23 °C, 49% over two steps; e) $(PhO)_2POCl$, DMAP, CH_2Cl_2, 23 °C, 93%; f) DBDMH, $NaHCO_3$, PhH/hexanes; then TBAB; then NEt_3, *p*-toluenethiol, 23 °C, 80%; g) *m*CPBA, EtOAc, 0 °C; h) *O*-methylquinine, PhMe, 130 °C, 54% over two steps; i)$BH_3{\cdot}Me_2S$, H_2O, $NaBO_3{\cdot}H_2O$; then JONES' reagent, 74%; j) **38**, *n*-BuLi, THF; then K_2CO_3, MeOH, 73%.

Triene **35** was then transformed to enone **36** by hydroboration and oxidation. Final addition of lithiated **38** gave cyclocitrinol in 54% over two steps.

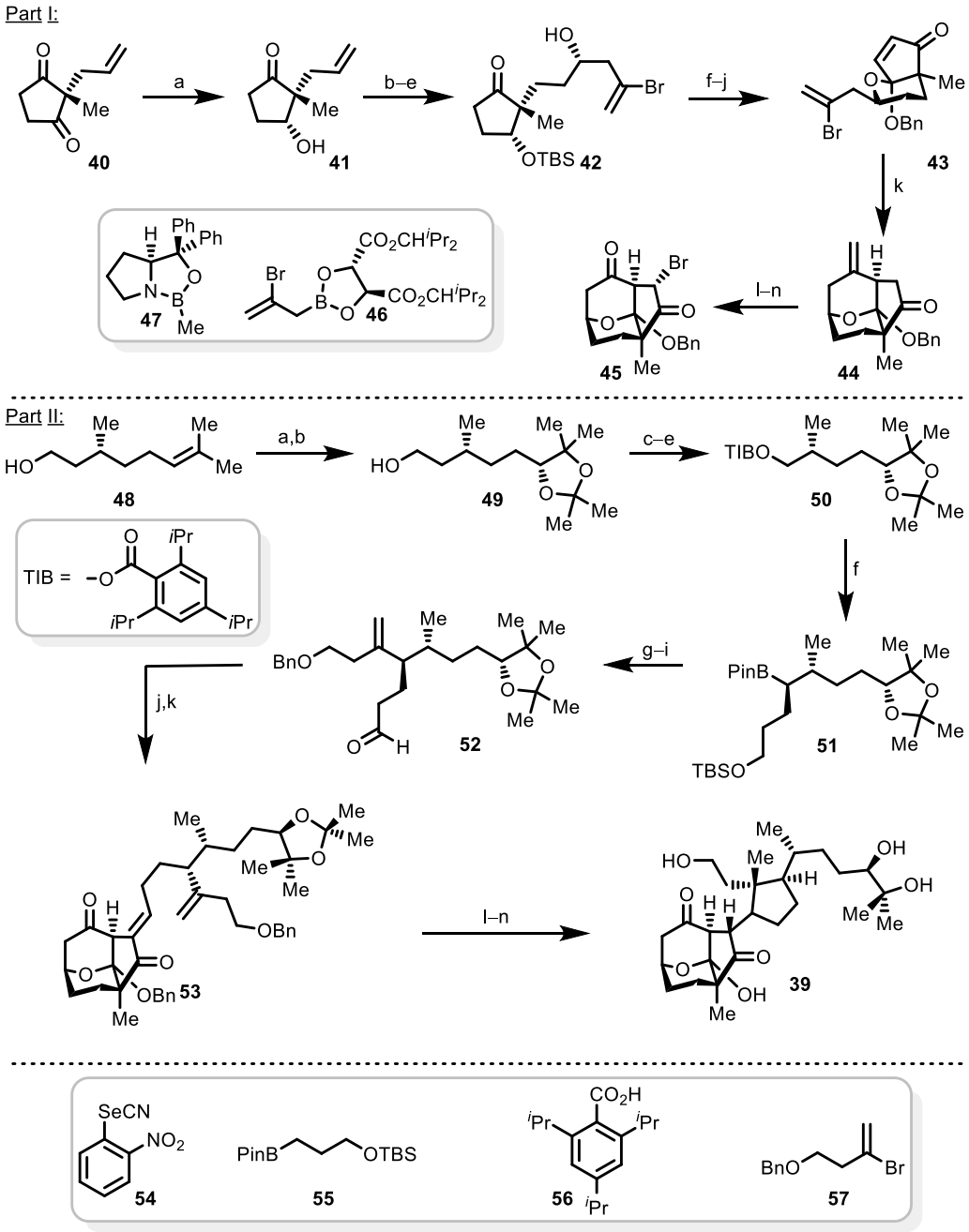
Table 1: Comparison of LI's and GUI's syntheses of cyclocitrinol.

	LI TOTAL SYNTHESIS	GUI SEMI SYNTHESIS
total steps	18	10
overall yield	1%	8.9%
redox manipulations	6	1
C–C bond formations	4	-
protection/deprotection steps	2	-

Comparing both syntheses, one quickly becomes aware of the power of the semi-synthetic strategy. By using a naturally occurring steroid, no C–C bond formations are necessary. The synthesis also manages with a minimal number of redox manipulations and can avoid the use of protecting groups. In total, this results in a halving of the required steps and a total yield that is almost nine times higher compared to the *de novo* approach. However, the *de novo* strategy offers a greater possibility for the synthesis of derivatives, which is of great importance for the discovery of new pharmaceuticals.

To date, many of the isolated, rearranged steroids show interesting structural features and valuable biological activities, explaining the recently growing interest in this class of natural products. Another example of such an impressive structure, where the steroidal origin is not readily seen, is aplysiasecosterol A **39**. This natural product is a 5(4→7),6(5→4)di*abeo*-9,11-secosteroid featuring an unprecedented and cage-like, tricyclic γ-diketone. This fascinating natural product was recently synthesized by LI et al. in a *de novo* convergent approach (*Scheme 6*).

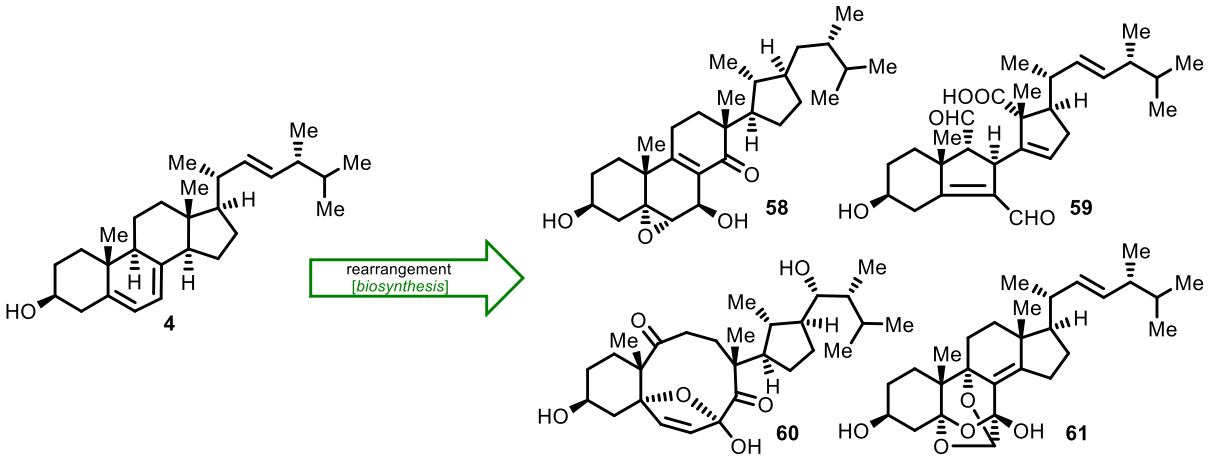
Starting from cyclopentadione **40**, COREY-BAKSHI-SHIBATA (CBS) reduction gave β-hydroxy ketone **41,** which was elaborated into bicyclic compound **43** in nine steps (*Scheme 6*). Radical generation and intramolecular, conjugate addition to the enone gave cage-like **44** which was further converted into the left-hand fragment **45**. The synthesis of the right-hand fragment started with the dihydroxylation under SHARPLESS conditions of (+)-citronellol **48** with concomitant acetonide formation. Degradation of the alcohol in a sequence of GRIECO elimination, ozonolysis, and MITSUNOBU reaction gave ester **50** as the precursor for a diastereoselective lithiation with *s*-butyl lithium and (+)-sparteine, followed by coupling with borane **55**. The lithium-halogen exchange of vinyl bromide **57** initiated a ZWEIFEL-EVANS olefination with borane **51**. The coupling product was further converted to the right-hand frag-



Scheme 6: Li's total synthesis of aplysiasecosterol A. Conditions: Part I a) **47**, catecholborane, *N*,*N*-diethylaniline, PhMe, −78 °C, 72%; b) imid., TBSCl, DMF, 22 °C; c) cyclohexene, BH_3·THF, THF, 0 °C; then $NaBO_3$·H_2O, 22 °C; d) DMP, CH_2Cl_2, 22 °C, 74% over three steps; e) **46**, PhMe/pentane, −95 °C, 88%; f) HF, MeCN, 22 °C; g) BnOH, CSA, 4 Å MS, CH_2Cl_2, 22 °C; h) DMP, CH_2Cl_2, 22 °C, 72% over three steps; i) NEt_3, TMSOTf, CH_2Cl_2, 0 °C; j) IBX, MPO, DMSO, 22 °C, 82% over two steps; k) 1,1'-azobis(cyclohexanecarbonitrile), TMS_3SiH, PhMe, 22 °C, 78%; l) KHMDS, TMSCl, THF, −78 °C; m) NBS, CH_2Cl_2, 0 °C; n) O_3, MeOH/ CH_2Cl_2, −78 °C; then Me_2S, 22 °C, 91% over three steps. Part II a) AD-mix-β *t*-BuOH/H_2O, $MsNH_2$, 0 °C; b) acetone, TsOH·H_2O, CH_2Cl_2, 22 °C, 92% over two steps; c) **54**, *n*-Bu_3P, CH_2Cl_2; then *m*CPBA, NEt_3, d) O_3, MeOH/ CH_2Cl_2, −78 °C; then $NaBH_4$, 0 °C, 85% over two steps, e) **56**, PPh_3, DIAD, THF, 22 °C, 98%, f) (+)-sparteine, **55**, *s*-BuLi, Et_2O, −78 °C→22 °C, 93%; g) **53**, *t*-BuLi, −78 °C; then NaOMe, I_2, 22 °C, 93%; h) AcOH, TBAF, THF, 22 °C; i) $NaHCO_3$, DMP, CH_2Cl_2, 22 °C, 82% over two steps; j) **57**, *n*-Bu_3SnH, Et_3B, O_2, PhMe, 22 °C, 70%; k) Burgess' reagent, PhMe, 50 °C, 83%; l) $Fe(dpm)_3$, Ph(*i*-PrO)SiH_2, EtOH/DCE/$(CH_2OH)_2$, 60 °C, 56%; m) $HClO_4$, THF, 22 °C; $Pd(OH)_2$/C, H_2, 22 °C, 92% over two steps.

ment **52** that was then coupled with left-hand fragment **45** under OSHIMA conditions.[19] Elimination under BURGESS' conditions followed by the key step of the synthesis, a hydrogen atom transfer (HAT) radical cyclization to furnish the final ring of the target gave the desired product **53** in 56% yield.[20] Global deprotection then gave aplysiasecosterol A in 92 % yield over two steps. This synthesis shows that also intimidating steroidal architectures as those of **39** can be readily synthesized in the laboratory.

Interestingly, many of the lately isolated and characterized non-classical steroids like strophasterol A **58**, solanioic acid **59**, tricholumin A **60** and eringiacetal B **61** may have their biosynthetic origin in ergosterol **4** (*Scheme 7*).[21–24]



Scheme 7: Natural products with biosynthetic origin from ergosterol.

This plethora of ergostane-type steroids is structurally intriguing and biologically relevant.[17] Due to these current findings and developments in the field of rearranged steroids, this thesis will explore the efficient synthesis of relevant natural products, as well as the development of a new methodology to further access *abeo*-steroids.

Especially the strophasterols A−D (see **58**, *Scheme 7*) are of interest because of their unprecedented molecular structure and biological activity. The first part of this thesis focuses on studies towards a platform for a unified synthetic access to the entire strophasterol family.

In order to access natural products like solanioic acid **59** from abundant starting material such as ergosterol **4**, the development of a method for the contraction of steroidal B-rings is investigated in the second part.

Part One

2. Introduction - The Strophasterols

The strophasterols are a class of *abeo*-steroids isolated from the edible mushroom *stropharia rugosoannulata* in 2012 by KAWAGISHI et al. (*Figure 4*). The authors were screening extracts of various mushrooms for anti-endoplasmatic-reticulum stress (ER) and anti-methicillin-resistant *Staphylococcus aureus* (MRSA) effects and found activity in the extracts of this mushroom.[25] Strophasterols A−D are four 15(14→22)*abeo* steroids, that can biosynthetically be traced back to the steroid ergosterol (*Figure 4*). These natural products feature a relatively dense oxidation pattern in the A and B ring, including two alcohols and an epoxide, while the D ring underwent an oxidative scission and is reconnected to the ergostane side chain to form a cyclopentane moiety. Strophasterol A and B are epimers with respect to the C22 stereoconfiguration, while strophasterol C and D feature an additional oxo functionality at C23. While the complete stereoconfiguration of both **58** and **62** were determined by X-ray crystallographic analysis, the absolute stereoconfiguration of the two other strophasterols has not been confirmed to date.[26]

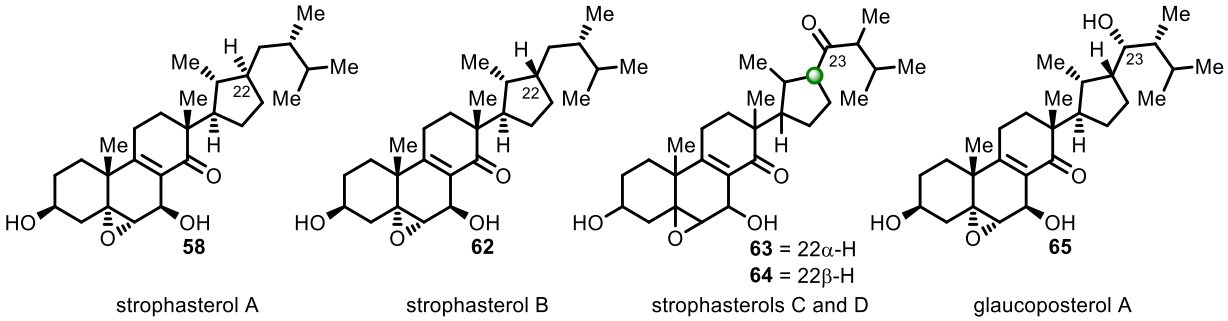
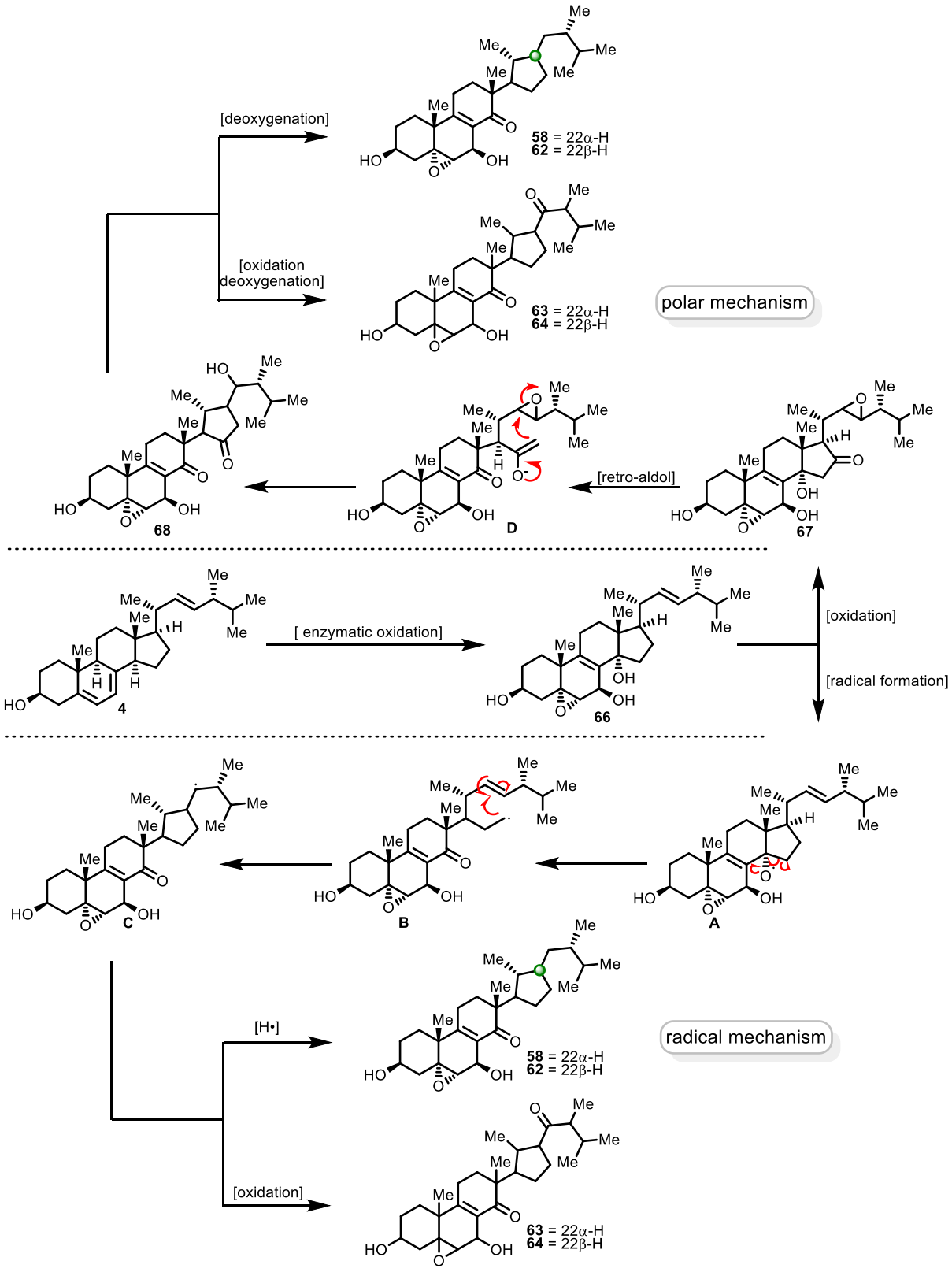


Figure 4: Structures of ergosterol, strophasterols A-D and glaucoposterol A. The green dot indicates the proposal, that the strophasterols C and D are epimers with regard to the C22 stereocenter.

Recently, AUNG et al. were able to isolate strophasterol C from the fruiting body of *Cortinarius glaucopus* along with glaucoposterol A **65** and were furthermore able to show that the absolute configurations of strophasterol C and glaucoposterol A are identical with exception of the C23 stereocenter.[27] As those findings were based on the respective NOESY spectra and biosynthetic considerations, they can only attempt to suggest the respective configurations of **63** and **64**. They still lack the required proof as the determination of the configuration of conformationally flexible five-membered rings is to date challenging to achieve *via* NOESY spectroscopy.[28]

Biosynthetically, the strophasterols are thought to be derived from ergosterol in several steps. KAWAGISHI et al. proposed two possible pathways, where one is based on a polar and the other

on a radical mechanism. First, the A- and B-ring are enzymatically oxidized to compound **66** (*Scheme 8*). The polar path then proceeds with further oxidation of the ergostane side chain as well as C16 to the corresponding oxo-compound **67**.



Scheme 8: Proposed biosynthetic pathways for the synthesis of **58**, **62**–**64**, in a polar approach (top) and based on a radical approach (bottom).

Scission of the 14,15-bond in a retro-aldol process followed by the nucleophilic opening of the epoxide by the intermediate enolate then furnishes cyclopentanone **68**. Deoxygenation of the

C16 ketone and subsequent oxidation of the C23-alcohol give strophasterol C and D while a second deoxygenation of the C23-alcohol give strophasterol A and B.

The radical pathway starts by the generation of the C14 alkoxy radical and homolytic fragmentation of the C14,15 bond. Addition of the primary radical to the double bond in a 5-*exo*-trig cyclization gives secondary radical **C** that gives strophasterols A and B *via* reductive quench with a hydrogen atom or strophasterols C and D by an oxidative quench (*Scheme 8*, bottom). Both proposed pathways show a reasonable construction of the target molecules. Following both biosynthetic suggestions one might assume strophasterol C and D of probably having the identical stereoconfiguration as A and B, respectively.

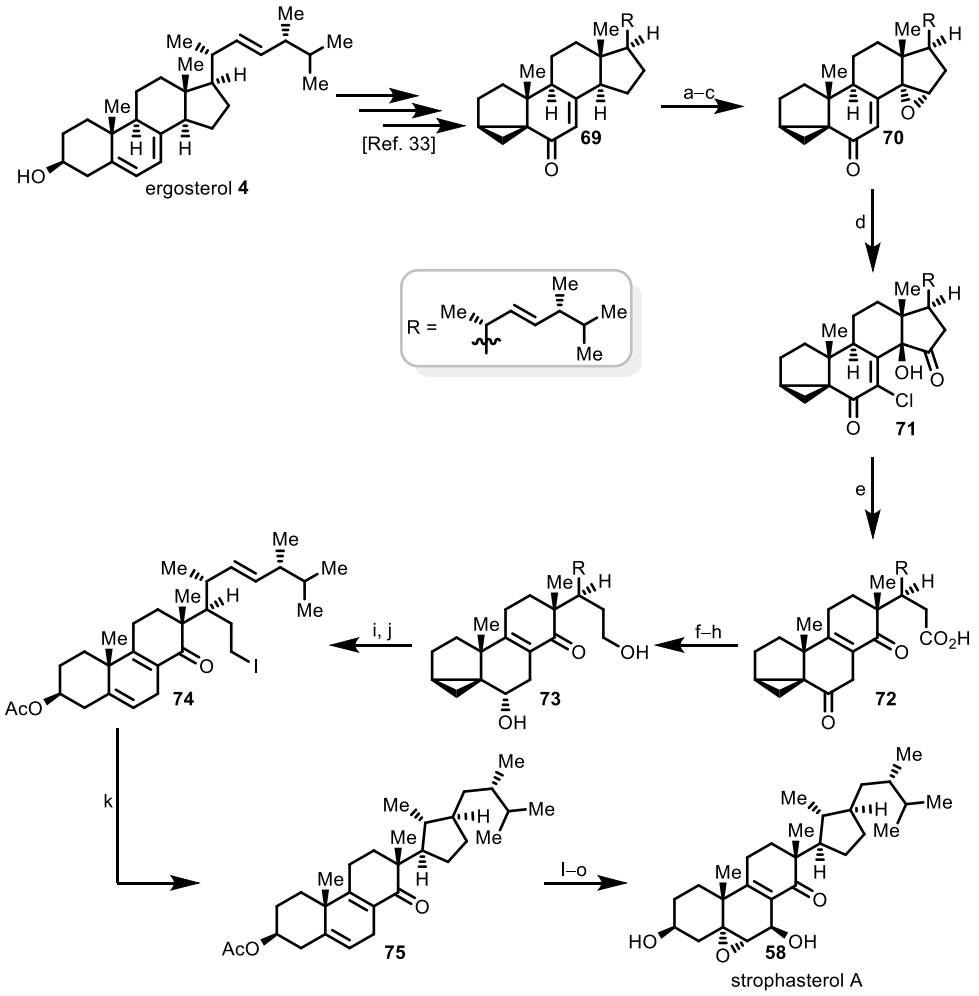
Due to their structural features, strophasterols A−D are interesting for a chemical synthesis but also for their biological activity. While strophasterol A showed only weak effects against MRSA, it also showed activity against ER stress-dependent cell death. The ER fulfills multiple cellular functions, such as the oxidative formation of disulfide bonds as well as the proper folding of proteins that are destined for excretion or deployment on the cell surface. The ER stress can be caused by tunicamycin (TM) or thapsigargin (TG). TM as an inhibitor of N-glycosylation of glycoproteins may cause misfolding of proteins. Also, TG may cause misfolding as it acts as an inhibitor of the Ca^{2+}-ATPase, thus being able to disrupt the homeostatic balance of the Ca^{2+} concentration in the ER. Disruption in the normal functions of the ER leads to an evolutionarily conserved cell stress response, the unfolded protein response (UPR). Initially, this response was aimed at compensating for damage but can eventually trigger cell death if ER dysfunction is severe or prolonged.[29] The stress of the ER can be associated with a range of diseases, including neurodegeneration, diabetes, amyotrophic lateral sclerosis, and HUNTINGTON's disease making ER stress a probable incendiary of pathological cell death and misfunction.[30]

To investigate the biological properties of this natural product family, as well as to enable the construction of these unprecedented structural motifs, the synthetic access is desirable and was, for strophasterols A and B, enabled by HERETSCH et al. in 2016 and KUWAHARA et al. in 2017, respectively.[31,32]

2.1 Syntheses of Strophasterols A and B

2.1.1 The HERETSCH Synthesis of Strophasterol A

The first synthesis of strophasterol A was published in 2016 by HERETSCH et al. and featured a semi-synthetic approach to the target with a biomimetic radical cyclization as one of the key steps.[31] The synthesis commenced from commercially available ergosterol **4** by transformation into the literature-known *i*-steroid enone **69** (*Scheme 9*).[33] Allylic oxidation at C14 under RILEY conditions followed by syn-elimination with BURGESS' reagent gave after chemoselective epoxidation of the Δ^{14} bond with magnesium monoperoxyphthalate (MMPP), gave the desired epoxide **70** for the planned oxidative cleavage of the C14,15 bond.



Scheme 9: The HERETSCH synthesis of strophasterol A. Conditions: a) SeO_2, TBHP, CH_2Cl_2, 60 °C; b) Burgess' reagent, PhMe, 60 °C; c) MMPP, MeOH, 24 °C, (49% over 3 steps); d) PCC, 4-Cl-Py·HCl, CH_2Cl_2, 24 °C, 68%; e) KOH, *t*-BuOH, 50 °C, quant.; f) EtSH, EDC·HCl, 4-DMAP, CH_2Cl_2, 24 °C; g) Et_3SiH, Pd/C, Me_2CO, 24 °C; h) $NaBH_4$, MeOH, 0 °C (75% over 3 steps); i) AcOH, $BF_3{\cdot}Et_2O$, Et_2O, 24 °C; j) I_2, PPh_3, imid., MeCN/Et_2O, 0 °C (82% over 2 steps); k) Et_3B, O_2, *n*-Bu_3SnH, PhMe, 0 °C, 80%; l) MMPP, CH_2Cl_2, 24 °C, m) PDC, TBHP, PhH, 24 °C; n) $NaBH_4$, MeOH, −15 °C; o) KOH, MeOH, 24 °C (41% over 4 steps).

Under various conditions for the cleavage of epoxide **70** (e.g., periodic acid, sodium periodate, lead tetraacetate), only decomposition was observed. Thus, a stepwise procedure was

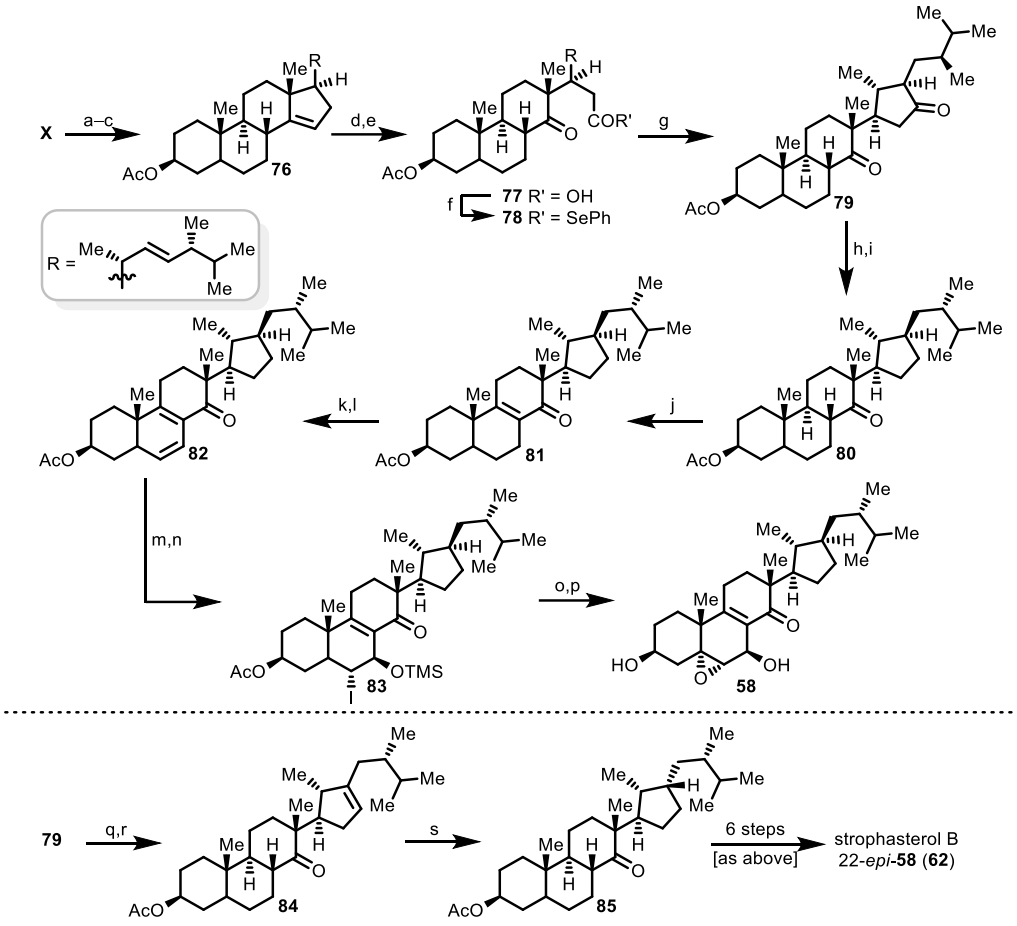
envisioned to access a more suitable structural motif for the oxidative cleavage. Epoxide **70** was treated with pyridinium chlorochromate initiating an oxidative cleavage to yield the corresponding α-hydroxy ketone. The reaction did not provide the desired product but gave the densely functionalized α-chloro γ-hydroxy keto enone **71**. Upon treatment of this highly functionalized compound with potassium hydroxide in *t*-butanol, the quantitative rearrangement to keto acid **72** was observed, presumably *via* a vinylogous ketol rearrangement or retro-DIECKMANN reaction. A sequence of three steps (thioester formation, FUKUYAMA reduction, and reduction with sodium borohydride) delivered diol **73** in 75% yield over three steps. Opening of the *i*-sterol motif under acidic conditions (boron trifluoride etherate, acetic acid) gave, after transformation under APPEL conditions, iodide **74** as the precursor for the biomimetic radical cyclization. Treatment of iodide **74** with triethylborane, *n*-tributyltin hydride and oxygen led to the formation of cyclopentane **75** as a single diastereomer. For the adjustments of the oxidation state of the B-ring, the Δ^5 olefin was epoxidized with MMPP, followed by allylic oxidation of C7 with pyridinium dichromate and *t*-butyl hydroperoxide and immediate reduction of the intermediary, instable diketone with sodium borohydride to yield the C7 alcohol. Saponification of the acetate then gave strophasterol A **58** in 41% yield over four steps. This synthesis gave a thorough insight into the reactivity of highly functionalized ergostane derivatives and showed unprecedented reactivity such as the highly efficient α-ketol rearrangement of chloroenone **71**. Also, the synthetic route offers many valuable synthetic intermediates for further studies on the chemistry of ergostanes and possible access to strophasterols B, C, and D as well as glaucoposterol A.

2.1.2 The KUWAHARA Synthesis of Strophasterol A and B

One year later, KUWAHARA et al. published the synthesis of strophasterol A and also of strophasterol B. As the HERETSCH synthesis of **58**, this synthesis started with commercially available ergosterol **4**.[32] In the first step, the conjugated diene of **4** was reduced under BIRCH conditions followed by acetylation of the secondary alcohol. Treatment of the obtained material with hydrochloric acid at −78 °C led to isomerization of the double bond to give a separable 5:2 mixture of the desired Δ^{14} isomer **76** and the undesired $\Delta^{8(14)}$ isomer, which after resubmission to the reaction conditions gave another 14% of **76** to give a combined yield of 82% over three steps (*Scheme 10*, top). Epoxidation of the Δ^{14} bond with MMPP followed by oxidative cleavage under JONES conditions gave keto carboxylic acid **77** that was further elaborated into the corresponding selenoester **78** upon treatment with *n*-tributyl phosphine and phenylselenyl chloride. Generation of the corresponding acyl radical under BOGER's conditions leads to the formation of cyclopentanone **79** in 61% yield over two steps as a single diastereomer. This ketone was then further converted into strophasterols A and B, respectively with a stereodivergent strategy.

Formation of the corresponding 1,3-dithiane at −40 °C to suppress C22 epimerization followed by hydrogenation with RANEY nickel gave **80** in 66% yield. Next, the remaining ketone was transformed into an enone by α-bromination using trimethylphenyl ammonium tribromide and subsequent elimination with diazabicyclo[5.4.0]undec-7-ene (DBU). For the adjustment of the B-ring oxidation state, **81** was submitted to allylic bromination conditions using *N*-bromosuccinimide and 2,2'-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70) followed by conversion into the corresponding selenide and oxidation to the selenoxide to overcome the formation of undesired isomers. Iodohydrin formation with *N*-iodosuccinimide gave a 5.5:1 diastereomeric ratio favoring the desired isomer **83** after silylation with trimethylsilyl triflate. Oxidation with *meta*-chloroperbenzoic acid to the iodoso compound initiated a *syn*-elimination to provide the Δ^5 olefin that was subsequently epoxidized by excess *meta*-chloroperbenzoic acid. After global deprotection with potassium hydroxide strophasterol A was obtained in 62% yield over two steps.

On the other hand, the formation of the thio enol ether of **79** (*Scheme 10*, bottom) and desulfurization with RANEY nickel under an atmosphere of hydrogen gave the $\Delta^{15,22}$ olefin **84**. Hydrogenation of this olefin using CRABTREE's catalyst gave a 54% yield of 22-*epi*-**58** along with 34% of **58**. The identical synthetic sequence as for **58** starting from **85** consequently gave strophasterol B **62** in a similar yield over six steps.



Scheme 10: KUWAHARA's synthesis of strophasterol A (top) and B (bottom). Conditions: a) Li, 2-methyl-2-butanol, THF, liq. NH_3, −78 °C, 99%; b) AcCl, pyridine, 24 °C, 98%; c) HCl, CH_2Cl_2, −78 °C, 71% (85%, based on a single separation/re-equilibration cycle); d) MMPP, EtOH/CH_2Cl_2, 24 °C, 82%; e) CrO_3, H_2SO_4, acetone, 24 °C, 77%; f) PhSeCl, *n*-Bu_3P, Et_3N, THF, 24 °C, 94%; g) *n*-Bu_3SnH, AIBN, PhH, 80 °C, 65%; h) $HS(CH_2)_3SH$, $BF_3{\cdot}Et_2O$, CH_2Cl_2, −40 °C to −20 °C, 94%; i) H_2, RANEY Ni, THF, EtOH, 66%; j) $PhNMe_3{\cdot}Br_3$,THF, 50 °C, then DBU, 50 °C, 89%; k) NBS, V-70, CCl_4, 40 °C, 50%; l) PhSeSePh, $NaBH_4$, THF, 24 °C, then 30% H_2O_2, 24 °C, 74%; m) NIS, H_2O, acetone, 24 °C; n) TMSOTf, 2,6-lutidine, 24 °C, 48% for two steps; o) *m*CPBA, $NaHCO_3$,CH_2Cl_2, 24 °C, 78%; p) KOH, MeOH, 24 °C, 80%. q) EtSH, TMSCl, CH_2Cl_2, 24 °C, 88%; r) H_2, RANEY Ni, EtOH, 60 °C, 83%; s) H_2, CRABTREE's catalyst, CH_2Cl_2, 24 °C, 58% (+ 34% **58**).

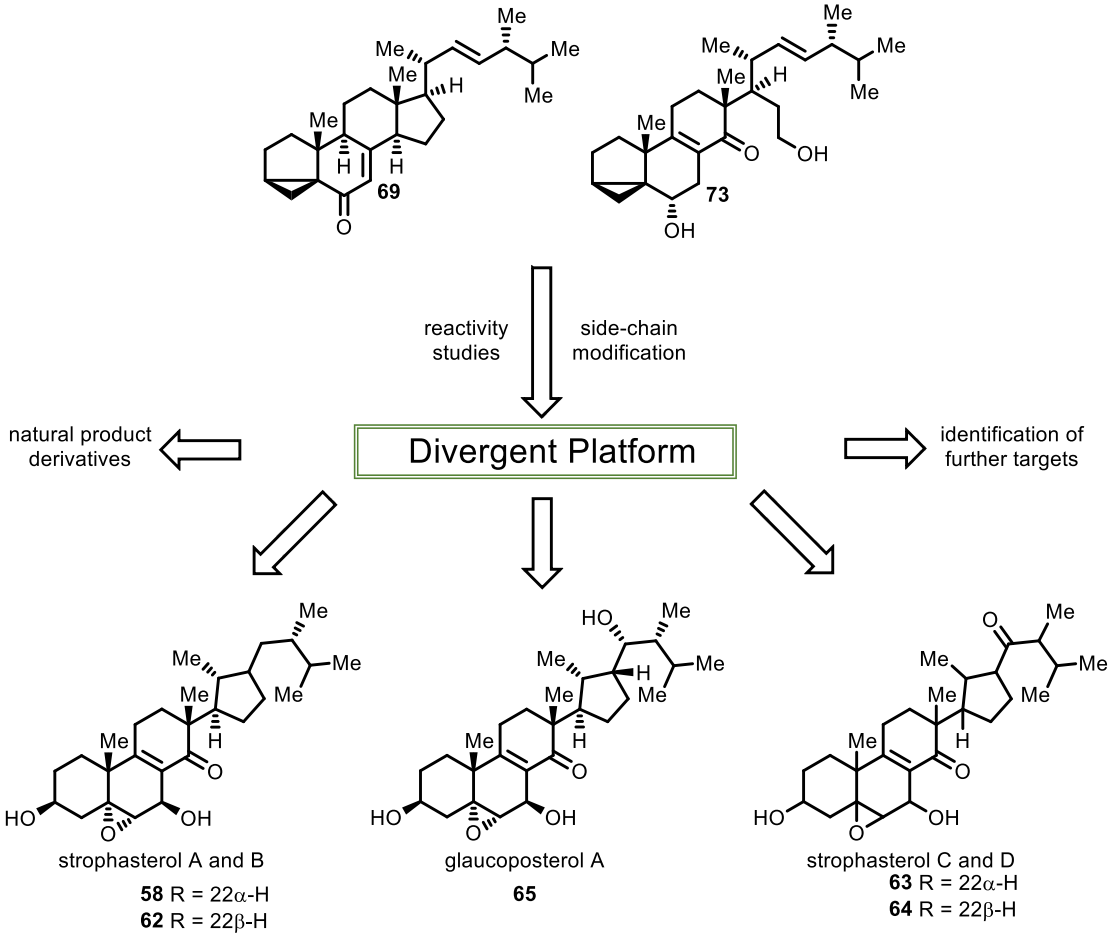
The two syntheses presented show some similarities, but nevertheless pursue a different core idea for reaching the target structures. The most important common feature of both syntheses strategies is the approach of oxidative cleavage of the D-ring *via* an epoxide. In HERETSCH's synthesis, the D-ring was cleaved by rearrangement of a highly functionalized chloroenone, whereas KUWAHARA's synthesis relied on oxidative cleavage under JONES conditions. Probably the most important difference between the two syntheses is the formation of the cyclopentane motif. While in the synthesis of HERETSCH the 5-exo-trig radical cyclization of an alkyl radical leads to only strophasterol A, KUWAHARA et al. realized the cyclization *via* an acyl radical. This gave the authors the opportunity to produce the $\Delta^{14(22)}$ olefin, which could be used for the divergent synthesis of strophasterol A and B. However, the synthesis of Kuwahara had the disadvantage of requiring a relatively large number of redox manipulations in order to

generate the oxidation pattern of strophasterols A and B. Here HERETSCH's synthesis was much more efficient and was able to generate strophasterol A after epoxidation and allylic oxidation.

3. Motivation and Objective

3.1 Towards a Unified Synthetic Approach to Strophasterol A – D and Glaucoposterol A

The synthetic access to strophasterol A and B was provided as shown in chapter 1.3. Access to the remaining members of the strophasterol family, C and D as well as to glaucoposterol A, has not been achieved to date.[31,32] Hence, finding a reliable and divergent approach to synthesize all members of the strophasterols selectively *via* a common intermediate is desirable. First, the synthesis of strophasterol C and D would enable the final elucidation of their respective absolute stereo configurations and provide additional material for extensive testing of their respective biological properties. Second, a platform to access all these natural products would also allow for the efficient synthesis of derivatives of all family members for potential structure-activity studies (SAR) to identify compounds with a superior biological profile.

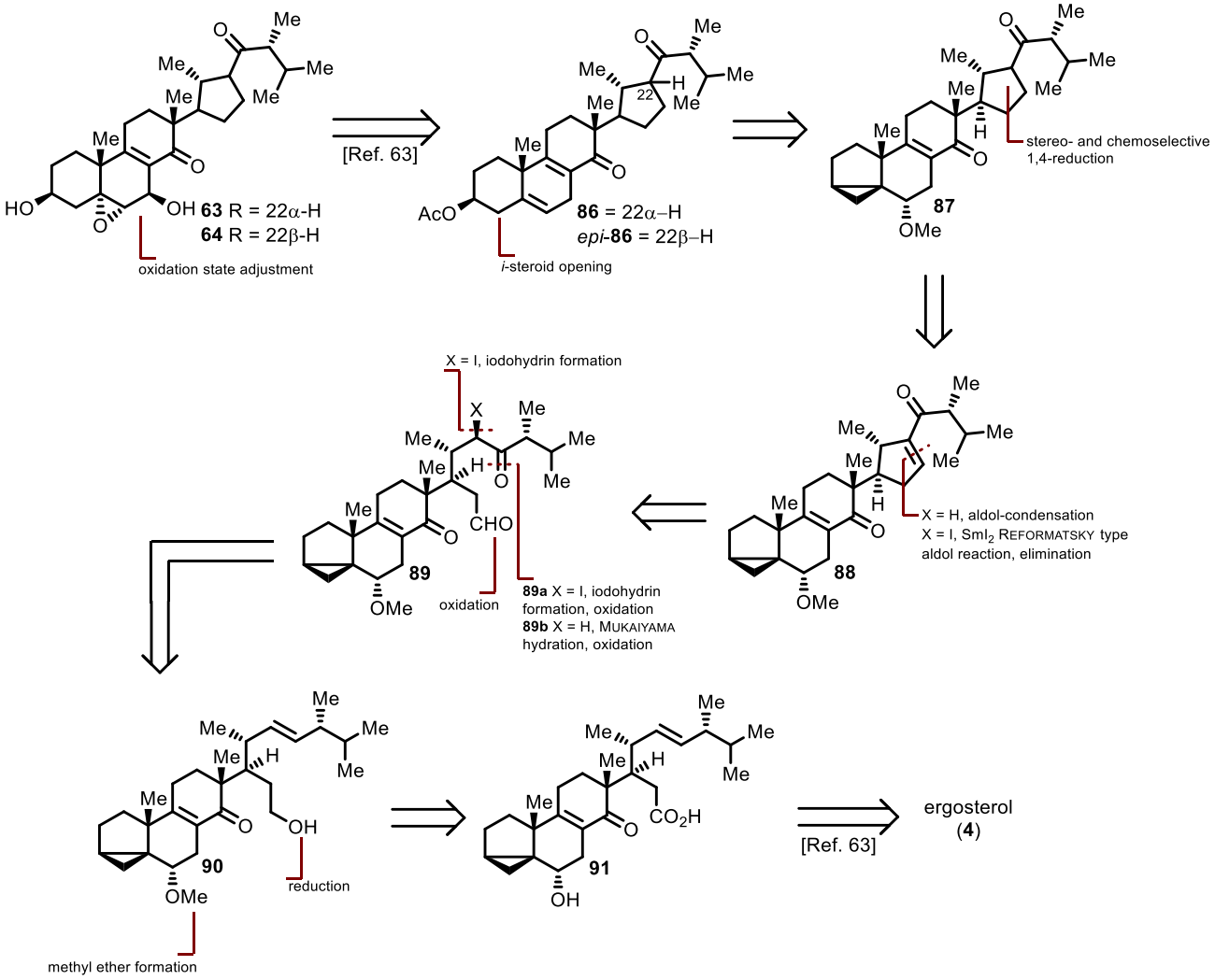


Scheme 11: General strategy for the identification of a unified approach to strophasterols A−D and glaucoposterol A based on literature known compounds **69** and **73**.

The identification of a suitable platform for the selective synthesis of either of the targeted natural products required the oxidative manipulation of the ergostane sidechain. As not many regio- and stereoselective methods for such modifications are known, a thorough investigation of known procedures was necessary (*Scheme 11*).[34–36] Additionally, the development of new methods was desirable, as techniques for the selective manipulation of ergostane type sidechains are scarce. Starting, e.g., from known intermediates like **69** or **73**, studies on their respective reactivity as well as the identification of methods for the oxidative manipulation of the side chain were planned. Identification of transformations with the appropriate selectivity should help to access a platform for the divergent synthesis of the target molecules, derivatives and eventually newly identified targets.

3.2 Retrosynthetic Analysis

To access the target natural products *via* a divergent platform, a multitude of different synthetic strategies should be feasible. As the adjustments of the oxidation states of the A and B rings, as well as the scission of the C14,15 bond have been elaborated, implementation of this strategy is envisioned (*Scheme 12*).



Scheme 12: Retrosynthetic analysis of strophasterols C and D.

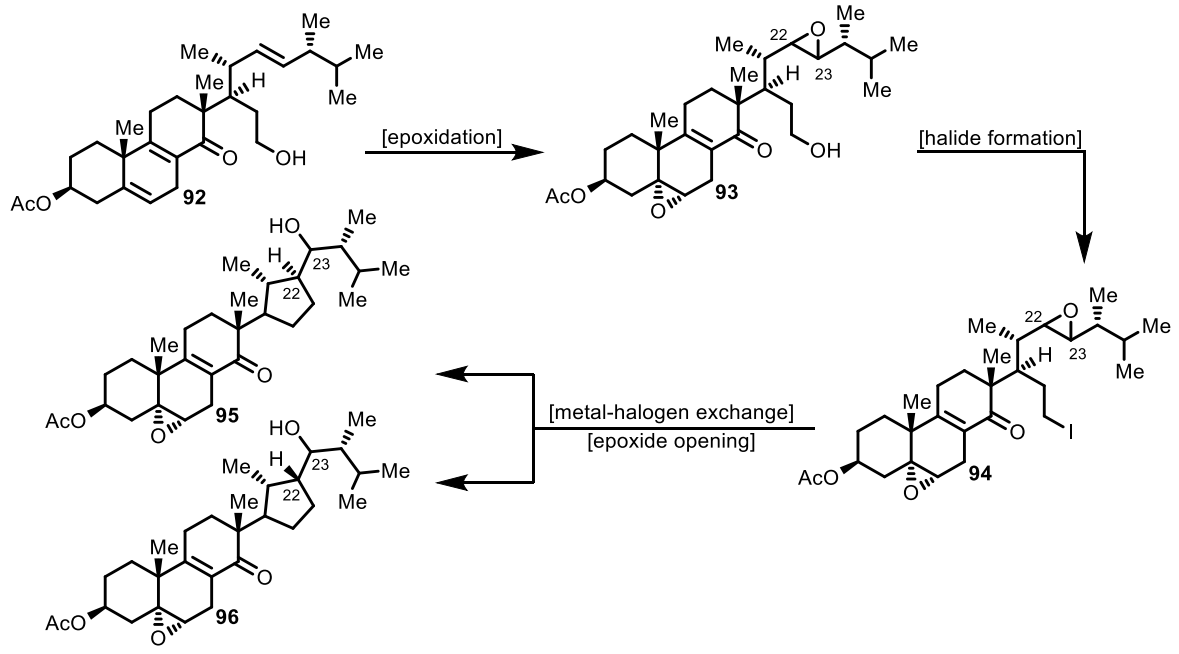
The selective access to strophasterol C and D is planned *via* oxidative adjustment of the A and B ring of either **86** or 22-*epi*-**86** accessible by opening of the *i*-steroid motif of **87**. Cyclopentenone **87** is planned to be accessed by diastereoselective 1,4-reduction of enone **88**. Selective 1,4-reduction of the cyclopentenone over the second C14 enone is envisioned due to the steric hindrance. Hence sterically demanding reagents like STRYKER's reagent are planned to induce the required selectivity. The cyclopentenone should be constructed by aldol condensation of keto-aldehyde **89b** or by samarium(II) iodide mediated aldol reaction of α-

iodo ketone **89a** and subsequent elimination of the hydroxy group. Oxidation of the side chain is planned to be achieved either by iodo hydroxylation or by regioselective MUKAIYAMA hydration and subsequent oxidation. Methyl ether **90** can be traced back to carboxylic acid **91**. Hydroxy acid **91**, as a known intermediate of the synthetic endeavor towards strophasterol A, can be traced back to commercially available ergosterol.[31]

4. Results and Discussion

4.1 First Synthetic Strategy: Epoxidation of the Sidechain

The first synthetic strategy towards strophasterol C and D aimed for the opening of an epoxide by a C-centered nucleophile. The epoxidation of the ergostane sidechain is one of the most prominent examples for its oxidative manipulation. It is well known that using *meta*-chloroperbenzoic acid (*m*CPBA) gives an approximate 2:1 mixture of diastereomers.[35–37] It was planned to use this formation of diastereomers to gain access to both, the 22(*S*) and the 22(*R*) isomers **95** and **96**, of the strophasterol C and D upon the opening of the respective epoxide **94** (*Scheme 13*).



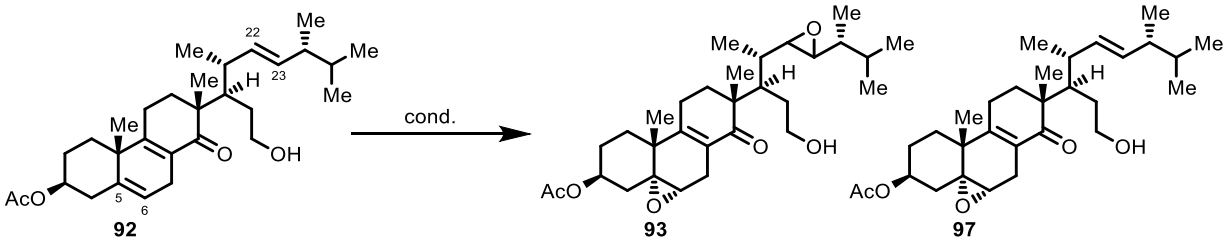
Scheme 13: Concept of the first synthetic strategy towards strophasterols C and D.

Although this synthetic concept showed a relatively simple way to access the desired platform intermediate, some potential difficulties had to be considered. The lithium-halogen exchange and the opening of the epoxide need to be performed chemoselectively in the presence of an α,β-unsaturated ketone. Furthermore, it was necessary to selectively form the cyclopentane ring upon opening of the epoxide at C22 over the six-membered isomer formed upon nucleophilic attack at C23. A classical approach to overcome chemoselectivity issues is the transmetalation to a suitable metal. E.g., the transmetalation of a lithiated species to copper should enhance the selectivity towards the addition of the nucleophile to the epoxide over the competing 1,2-addition. The common approach would be a lithium-halogen exchange, followed by transmetalation to the desired metal and addition of the electrophile. However, in this case the

sensitive functional groups are present at all times. Thus, transmetallation of the intermediary organolithium species is difficult. As found by HOUPIS et al., the lithiated species were relatively stable in presence of epoxides at −78 °C but rapidly cyclized upon warming to ambient temperature, allowing for the transmetalation and selective ring formation.[38]

Additionally, investigations of RIEKE et al. revealed that the use of highly reactive copper(0), generated in situ from lithium naphthalide and copper(I) iodide, allows the selective cyclization to a cyclopentane ring in the presence of bromoepoxides depending on the solvent and phosphine ligand used.[39–41] Supported by the literature precedent, the epoxidation of **92** was investigated. First, a one-pot procedure to oxidize the Δ^5- and Δ^{22}-olefins in the same reaction was tested.

Table 2: Conditions for the epoxidation of **92**.



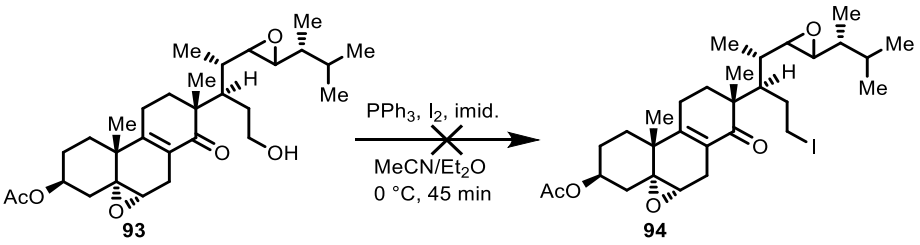
Entry	Conditions	Temp.	Time	Yield	Product
1	MMPP, H_2O, CH_2Cl_2	23 °C	18 h	80%	**97**
2	DMDO, $CHCl_3$	23 °C	4 h	10%	**97**
3	MTO/UHP, py, Et_2O	23 °C	1 h	-	complex mixture
4	MTO/H_2O_2, CH_2Cl_2	23 °C	2 h	-	no conversion
5[a]	*m*CPBA, $NaHCO_3$	0 °C→17 °C	48 h	74% (59% over 2 steps)	**93**

MTO = Methyltrioxorhenium, UHP = urea hydrogen peroxide complex; [a)] 5,6-epoxide already in SM

Using an excess of magnesium monoperoxyphthalate (MMPP) in dichloromethane resulted only in the oxidation of the Δ^5-olefin to give **97** in 80% yield without any oxidation of the Δ^{22}-olefin (*Table* **2**, entry 1). Other oxidative conditions, e.g., dimethyldioxirane also led to the epoxidation of the Δ^5-olefin albeit in a much lower yield of 10%. The use of methyltrioxorhenium (MTO) in the presence of hydrogen peroxide or urea hydrogen peroxide complex (UHP) gave either a complex mixture or no conversion.[42,43] As the use of *m*CPBA for the epoxidation of the Δ^5-olefin gives inconsistent results in the literature regarding its facial

selectivity of the Δ^5 olefin, it was decided to elaborate a two-step procedure, first installing the 5,6-epoxide with MMPP, followed by second oxidation with *m*CPBA, thus providing the desired epoxide **93** in 59% over two steps (*Table 2*, entry 5).[44–46] Nevertheless, the formation of **93** was still somewhat problematic as the R_f values of starting material and product were identical, and consumption of the starting material had to be observed by ^{1}H NMR.

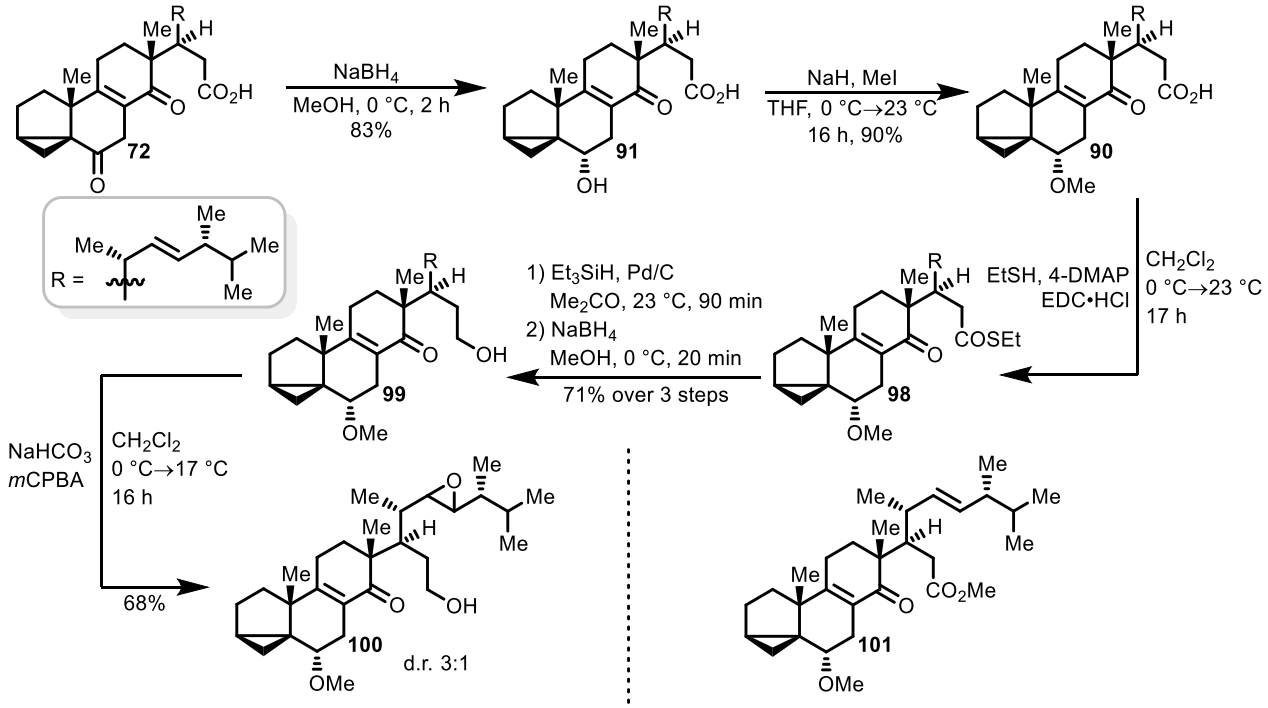
With the desired epoxide **93** in hand, the transformation of the primary alcohol into the corresponding iodide was investigated. As the formation of the primary iodide was already part of the synthetic route towards strophasterol A, the same conditions were applied to **93** (*Scheme* 14).[31]



Scheme 14: APPEL reaction of diepoxide **93.**

Submission of diepoxide **93** to APPEL conditions led to the decomposition of the starting material, as indicated by TLC. The desired product could be isolated only in traces. It was found, that the submission of trisubstituted steroidal epoxides to APPEL conditions leads to deoxygenation to the corresponding olefins.[47,48]

As diepoxide **93** was not compatible with the required reaction conditions and to gain access to the desired iodide, modification of the route was undertaken.



Scheme 15: Synthesis of substrate **100** for the epoxide opening strategy.

To avoid the installation of the 5,6-epoxide, the C6 alcohol was strategically protected as the corresponding methyl ether, for the opening of the *i*-steroid on a later stage. The methyl ether was chosen as a protecting group, as opening of *i*-steroids from the respective methyl ethers is a well-known process. Thus, no formal deprotection would be needed.[15,34] Reduction of the C6-ketone gave literature-known alcohol **91**, which was transformed into the corresponding methyl ether **90** upon treatment with sodium hydride and methyl iodide in excellent yield with minor formation of methyl ester **101** as side product (*Scheme 15*). A sequence of thioester formation, FUKUYAMA reduction, and sodium borohydride reduction provided alcohol **99** in 71% yield over three steps.[31] Epoxidation with *m*CPBA went smoothly and gave the desired epoxide **100** in 68% yield as a 3:1 mixture of diastereomers. Again, the focus was set on the synthesis of the corresponding iodide, whose formation once more gave a complex mixture. Various conditions were tested in order to obtain the respective halide (*Table 3*). Using standard protocols, only a small amount of the desired product could be isolated accompanied by the formation of numerous side products (entries 1 and 2). The yield slightly increased when iodine and triphenylphosphine were mixed prior to the addition of epoxide **100**, but again, extensive decomposition of the reactant was observed (entry 3).

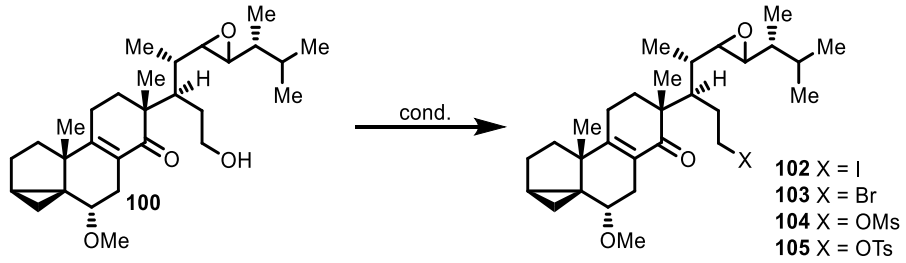


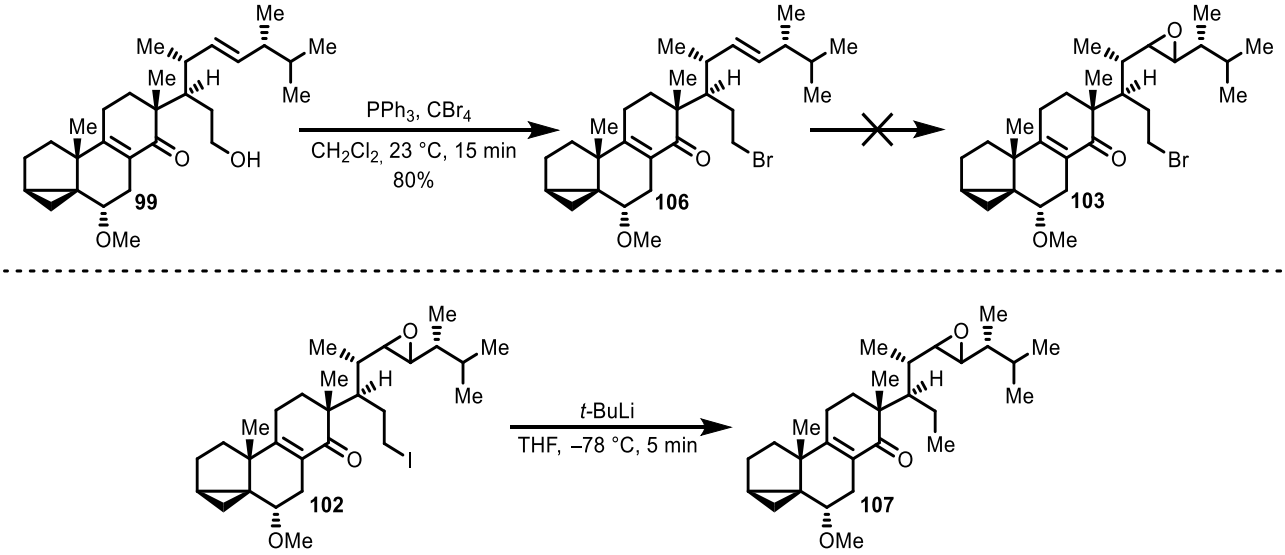
Table 3: Screening conditions for the formation of alkyl halides **102** or **103**.

Entry	Reagents	Solvent	Temp.	Yield
1	PPh_3, I_2, imid.	MeCN/Et_2O	0 °C	complex mixture
2	PPh_3, I_2, imid.	THF	0 °C	8% (**102**)
3	PPh_3, I_2, imid.[a]	THF	0 °C	28% (**102**)
4	CBr_4, PPh_3	CH_2Cl_2	0 °C	12% (**103**)
5	MsCl	pyridine	0 °C	decomposition
6	TsCl	pyridine	23 °C	decomposition
7	MsCl then NaI	pyridine, then Me_2CO	23 °C	decomposition
8	TsCl then NaI	pyridine, then Me_2CO	23 °C	decomposition

[a] PPh_3 and I_2 were allowed to react prior addition of the starting material.

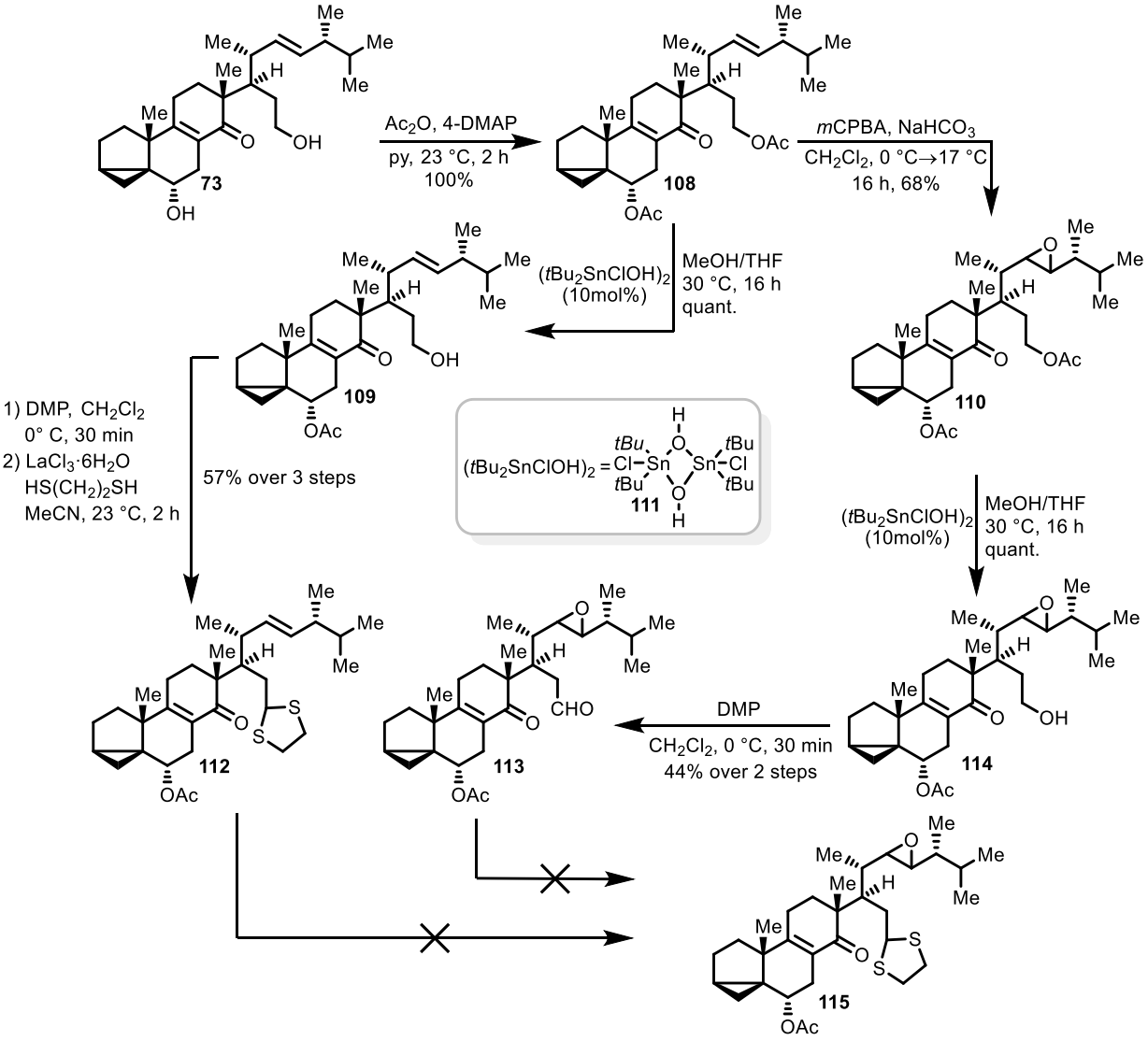
The substitution of iodine with carbon tetrabromide for the formation of the corresponding bromide gave similar results (entry 4). Next, a two-step procedure by first forming the corresponding mesylate and tosylate followed by nucleophilic substitution with sodium iodide was tested. The formation of the corresponding mesylate and tosylate was observed *via* TLC and indicated the clean formation of the desired product. Any attempts to isolate either the mesylate or the tosylate resulted in decomposition of the material. Thus, only the exchange of the solvent and direct conversion into the iodide was tested with the same result and no detectable product (entries 5−8). The formation of bromide **106** from **99** gave the corresponding product in 80% yield. Epoxidation of the obtained bromide led to the decomposition of the starting material as previously observed (*Scheme 16*, top).

The small amount of the obtained iodide **102** was treated with two equivalents of *t*-butyl lithium in tetrahydrofuran at −78 °C to test the cyclization, but only dehalogenation was observed, probably due to the small scale of the reaction and traces of water in the solvent (*Scheme 16*, bottom).



Scheme 16: Formation of bromide **106** and attempted epoxidation (*top*) and attempted cyclization of iodide **102** by halogen-metal exchange (*bottom*).

To avoid installation of the halide in presence of the epoxide, the COREY−SEEBACH approach seemed reasonable, as the C-centered nucleophile is generated from a thioacetal, accessible from the corresponding aldehydes (*Scheme 17*).[49]

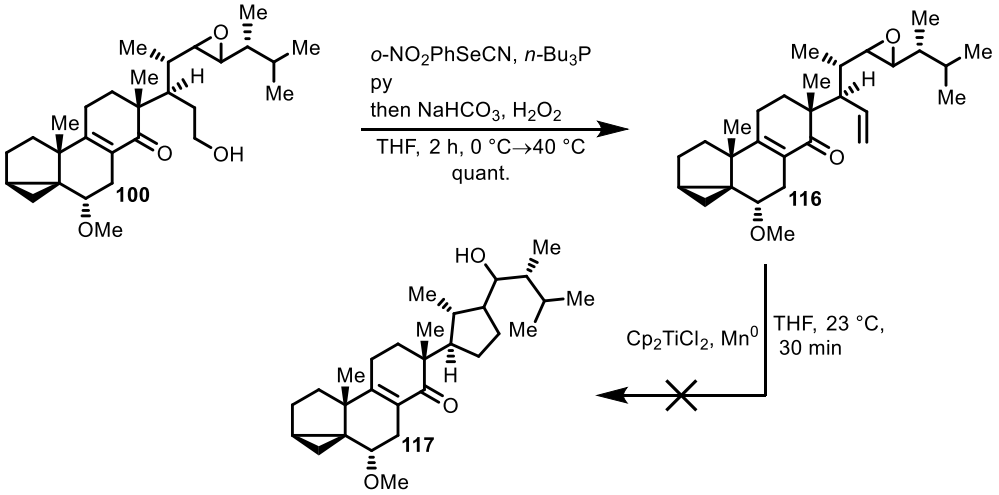


Scheme 17: COREY−SEEBACH approach from diacetate **108**.

For further experiments, the starting material was changed to diacetate **108**, as this system offered more experimental freedom and enhanced accessibility. Treating diol **73** with acetic anhydride in the presence of 4-dimethylamino pyridine (4-DMAP) in pyridine gave diacetate **108** in quantitative yield. Epoxidation of diacetate **108** with *m*CPBA gave epoxide **110** that was further treated with tin compound **111** for the selective saponification of the primary acetate.[50–52] Oxidation of **114** with DESS−MARTIN periodinane (DMP) then gave epoxy aldehyde **113** in 44% yield over two steps. Treatment of aldehyde **113** with lanthanum(III) chloride in acetonitrile in the presence of 1,2-ethanedithiol led to the formation of a complex mixture, albeit dithiolane **115** could be identified by high resolution mass spectroscopy

(HRMS).[53] To avoid the somewhat fragile nature of the side-chain epoxide, it was attempted to introduce it as late as possible. Thus, diacetate **108** was treated with tin compound **111** to give alcohol **109**. Oxidation and formation of the respective thioacetal with lanthanum(III) chloride and 1,2-ethanedithiol gave 1,3-dithiolane **112** in 57% yield over three steps. Treatment of this dithiolane under the epoxidation conditions again lead to the formation of a complex mixture, and none of the desired product **115** could be isolated. Under these oxidative conditions, also the oxidation of the sulfur to the sulfoxide or sulfone is imaginable, possibly leading to unstable products. Although it is reported, that 1,3-dithiolanes undergo rearrangement to ethene and the corresponding dithiocarboxylates, attempts for the synthesis of **115** were made .[49,54] As the synthesis of **115** was not possible, further studies on the synthesis of the respective 1,3-dithiane were not conducted.

The primary alcohol of **100** was eliminated under GRIECO conditions to yield the terminal olefin **116** in quantitative yield (*Scheme 18*).[55]



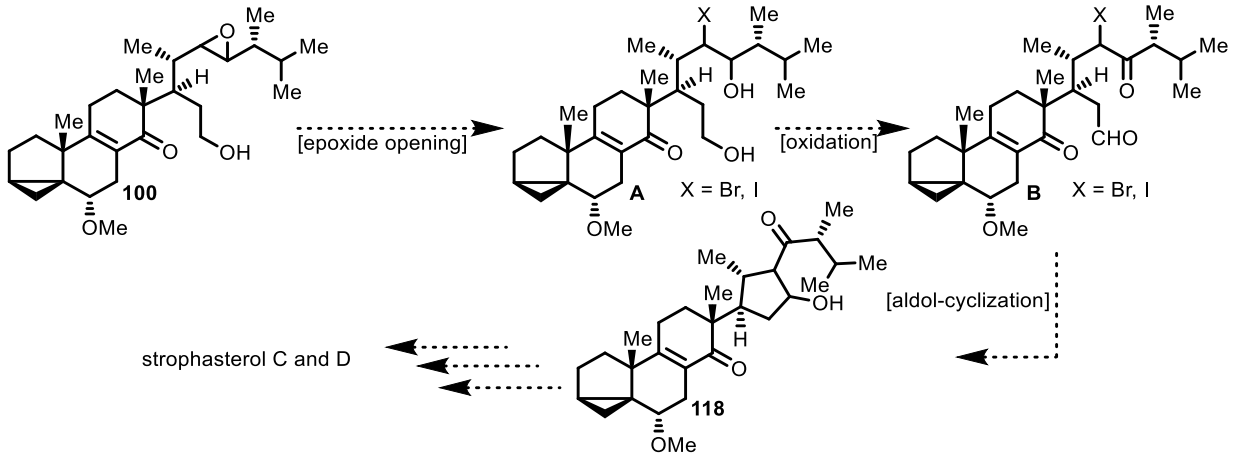
Scheme 18: GRIECO elimination and attempted radical cyclization.

Titanocene(III) species, generated from titanium(IV) compounds by in situ reduction, have been introduced by NUGENT and RAJAN-BABU as radical generating metal complexes for the opening of epoxides *via* electron transfer.[56–58] However, taking a closer look at the desired transformation, the reaction would proceed as a 5-endo-*trig* cyclization, which is disfavored by BALDWIN's rules. Only a few examples of anti-BALDWIN cyclizations of this type have been reported to date.[59,60] Generation of the sensitive titanocene(III) chloride by reduction of titanocene(IV) chloride with manganese(0) was observed through the characteristic lime green color of the complex in solution. Yet, addition of olefin **116** resulted in no reaction, and only the starting material was reisolated.

To summarize, the planned opening of an epoxide with a C-centered nucleophile was not possible, as the installation of a suitable nucleophilic precursor into the system failed. Also, the radical approach was not feasible as the epoxide opening using titanocene(III) chloride failed to generate the required secondary radical.

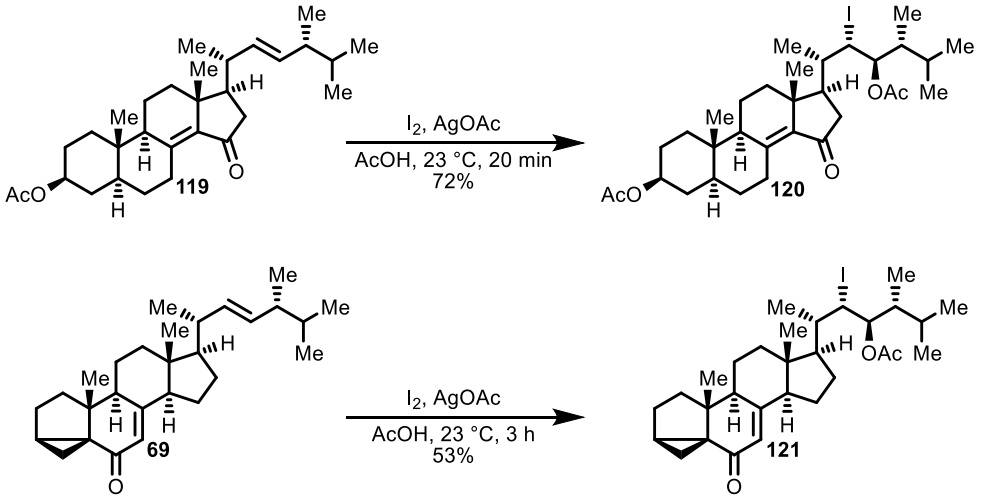
4.2 Second Synthetic Strategy: Regioselective Halo Functionalization

As the intramolecular opening of the epoxides was not possible, an intermolecular approach was envisioned. The opening of epoxides by various nucleophiles is a well-studied reaction, that can introduce a variety of nucleophiles to give α-substituted alcohols (**A**, *Scheme 20*).[61–64] A regioselective opening of the epoxide with a halide to yield an α-halo ketone **B** after oxidation, would be especially interesting. This structural motif could be used to close the desired cyclopentane **118** in a REFORMATSKY-type aldol reaction using, e.g., samarium(II) iodide (*Scheme 19*).[65–67]



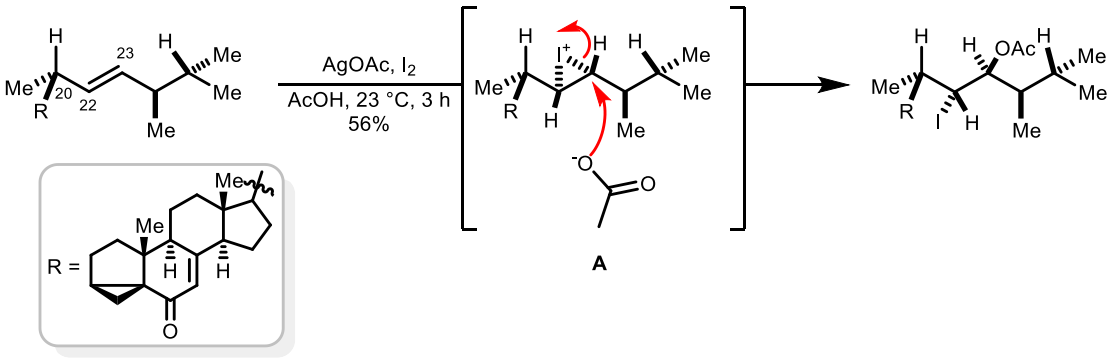
Scheme 19: Potential synthetic pathway involving a regioselective epoxide opening and a SmI_2-mediated intramolecular REFORMATSKY reaction.

Similar structural motifs are known and the direct oxidative conversion of the Δ^{22} olefin of ergostane type steroids to the corresponding iodo acetates was already developed (*Scheme 20*).[68–71]



Scheme 20: Iodo acetoxylation of the ergostane sidechain by MEHTIEV et al. (top) and by BARTON et al. (bottom).

During their synthesis of the insect moulting hormone ecdysone starting from ergosterol, BARTON et al. found, that treatment of 3α,5α-cycloergosta-7,22-diene-6-one (**69**) with iodine and silver acetate in glacial acetic acid selectively gave **121** as a single regio- and diastereomer in 53% yield.[68] The authors concluded, that this selectivity results as a combination of a preferred orientation and opening of the intermediary iodonium ion and based their suggestions on the X-ray structure analysis of ergocalciferol 4-iodo-3-nitrobenzoate. It was assumed that the bulk of the steroidal core shields the 22β-side of the olefin, thus approach of the electrophile is more facile from the 22α-side (**A**, *Scheme 21*). The attack of the nucleophile would again occur from the more accessible position at C23 away from the bulk of the steroid skeleton. Various authors confirmed the adaption of this concept as a general rule to predict the regio- and stereochemical outcome of related reactions during their synthetic endeavors.[72–75]

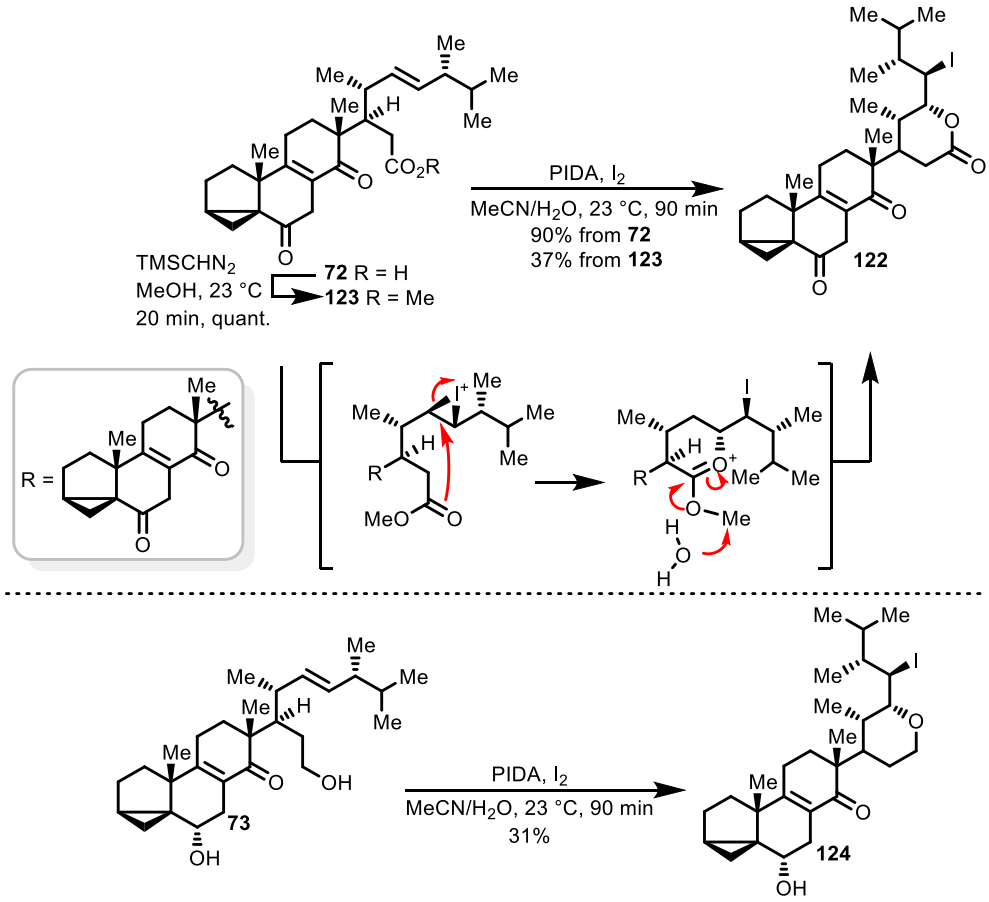


Scheme 21: Defined orientation of the iodonium ion and attack of the acetate according to BARTON et al.

Starting from *i*-steroid ketone **69**, which is also part of the synthetic route to strophasterol C and D, it was possible to reproduce the results by BARTON et al. as a single diastereoisomer albeit with a much lower yield of 22%.

For efficient synthetic access, the functionalization of the sidechain was planned after the D-ring scission. Substituting water with acetic acid as the nucleophile was necessary to avoid the saponification of the acetate. As BARTON's conditions are quite harsh, other methods for the generation of iodonium ions were investigated, and a method reported by VINOD et al. employing hypervalent iodine(III) reagents was identified as the most promising.[76] Starting from carboxylic acid **72**, the iodohydroxylation was attempted with iodobenzene diacetate (PIDA) and iodine in a 4:1 mixture of acetonitrile and water but gave only the corresponding iodolactonization product **122** in 90% yield (*Scheme 22*). Transformation of the carboxylic acid to the non-nucleophilic methyl ester with trimethylsilyl diazomethane gave the desired ester **123** in quantitative yield. Submission of **123** to the reaction conditions gave the identical iodolactone **122** as before in 37% yield but no traces of the desired iodohydrin. The reaction

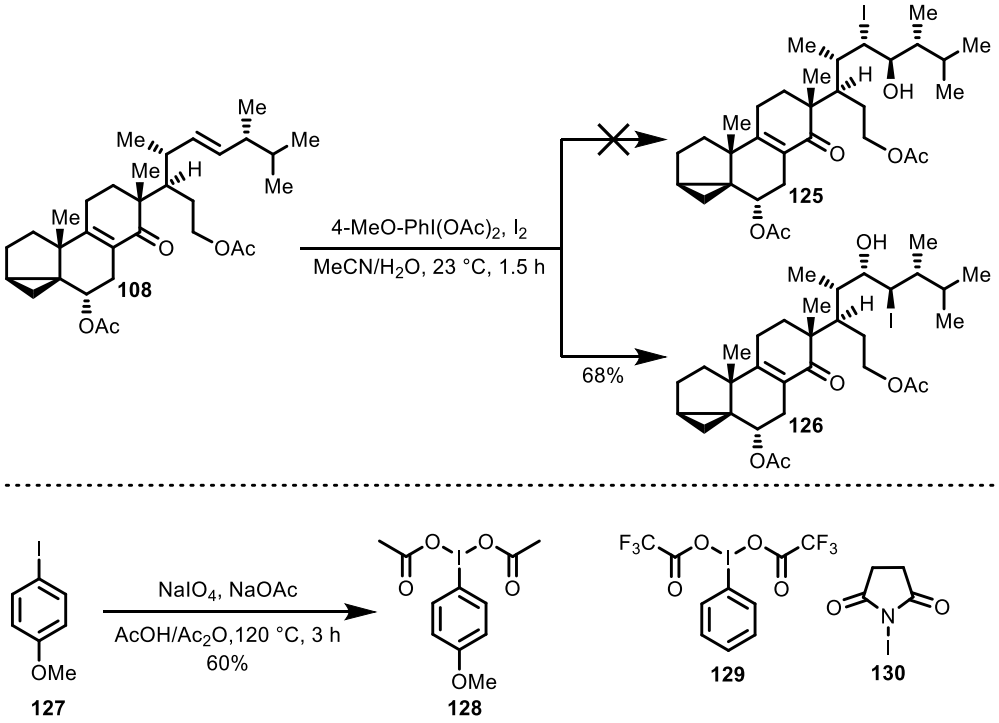
proceeds probably *via* opening of the formed iodonium ion by the carbonyl oxygen (*Scheme* 22, top). Nucleophilic attack of water and elimination of methanol then gives lactone **122**.



Scheme 22: Reactivity of carboxylic acid **72** and methyl ester **123** and proposed mechanism (top) and iodoetherification of diol **73** (bottom).

Moving to diol **73**, the reaction gave the expected product of iodo etherification **124** in 31% yield under identical conditions (*Scheme 22*, bottom). As the intramolecular nucleophilicity was quite problematic, a suitable protection group was introduced. To avoid the additional reduction and protection step needed to introduce methyl ether **99**, diacetate **108** was employed. A selective deprotection of the primary alcohol was necessary to avoid the non-strategic oxidation of the secondary alcohol during the generation of the required C15 aldehyde. Again, tin compound **111** was used for this chemoselective transformation.[50–52] Additionally, later saponification of the secondary acetate would not be needed, as the opening of *i*-sterols from their corresponding acetates is reported in the literature.[77,78] Submission of **108** to iodobenzene diacetate and iodine in a 4:1 mixture of acetonitrile and water gave a single product that was isolated (*Scheme 23*, top). Analysis of the ^{1}H NMR and HRMS indicated the diastereo- and regioselective formation of an iodohydrin. However, further analysis of the 2D NMR spectra revealed that the obtained product was not the desired iodohydrin **126**, but the undesired

regioisomer **125** (*Scheme 23*, top). The regio- and diastereoselectivity was further confirmed by X-ray crystallographic analysis of the product (*Figure 1*). It is to note that the quality of the crystallographic data was not suitable for publication but confirmed the structure confirmation in combination with 2D NMR analysis.



Scheme 23: Functionalization of diacetate **108** (top) and synthesis of hypervalent iodine reagent **128**. Related reagents for iodofunctionalization **129** and **130** (bottom).

Under various conditions, the product was formed without any traces of additional isomers, as initially anticipated by the results of BARTON et al., however under complete inversion of the desired regioselectivity (*Scheme 23*, top). The highest yield of 68% was obtained by using the more electron rich *para*-methoxy-iodobenzene diacetate (**128**, 4-MeO-PIDA), readily available from 4-methoxyphenyl iodide (**127**), in a 4:1 ratio of acetonitrile and water (*Table 4*, entry 1). Other reagents such iodobenzene bis(trifluoroacetate) (**129**, PIFA) or *N*-iodosuccinimide (**130**, NIS) gave the product only in low yields or showed no reactivity at all (*Scheme 23*, bottom).[79]

Table 4: Optimization of the iodohydrin formation.

Entry	Reagents	Solvent	Temp.	Yield (126)
1	4-MeO-PIDA, I_2	MeCN/H_2O 4:1	23 °C	65%
2	PIDA, I_2	MeCN/H_2O 4:1	23 °C	45%
3	PIDA, I_2	MeCN/H_2O 20:1	23 °C	26%
4	PIFA, I_2	MeCN/H_2O 4:1	−15 °C	35%
5	NIS	DME/H_2O 2:1	−20 °C	no reaction

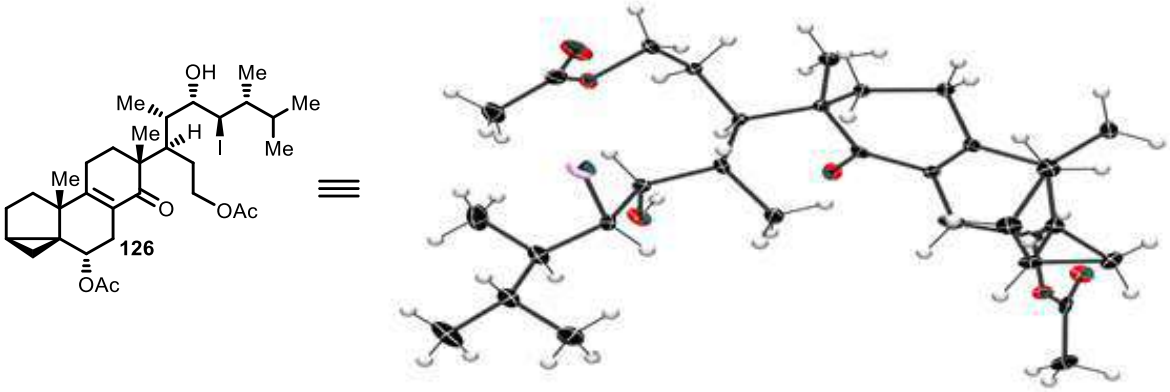


Figure 1: ORTEP of **126**. Ellipsoids are shown at a 50% probability level.

To understand the inversion of the regioselectivity, it was necessary to evaluate all available data to find a conclusive hypothesis for the observed inversion. Most apparent was the difference between the system on which BARTON et al. based their hypothesis and diacetate **108**. While BARTON's theoretical approach is based on the X-ray crystal structure analysis of ergocalciferol 4-iodo-3-nitrobenzoate, it might only apply to steroids with an intact D-ring. The scission of the 14,15-bond introduces an additional degree of rotational freedom (*Figure 2*, highlighted in green), that probably arranges for C22 to be the most accessible position for the nucleophile. The fact that only one diastereoisomer suggests either a defined iodonium ion transition state or one of the iodonium transition states is attacked selectively.

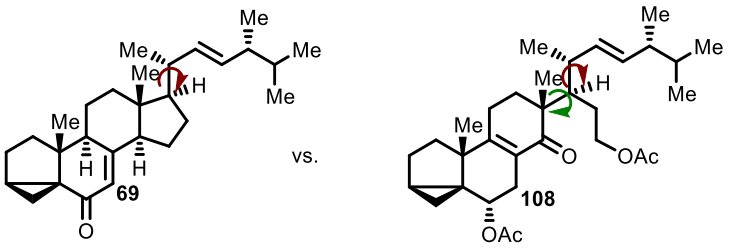
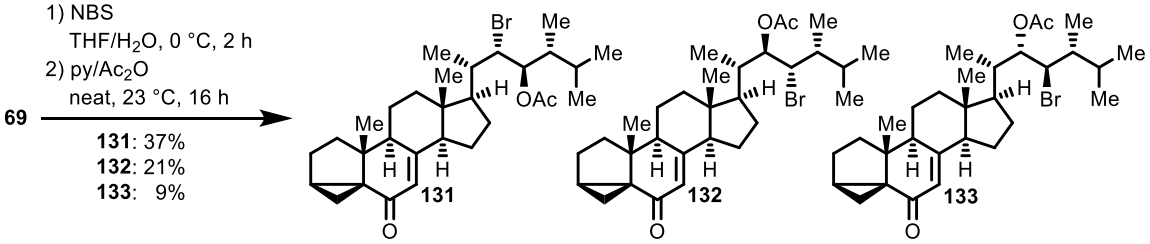


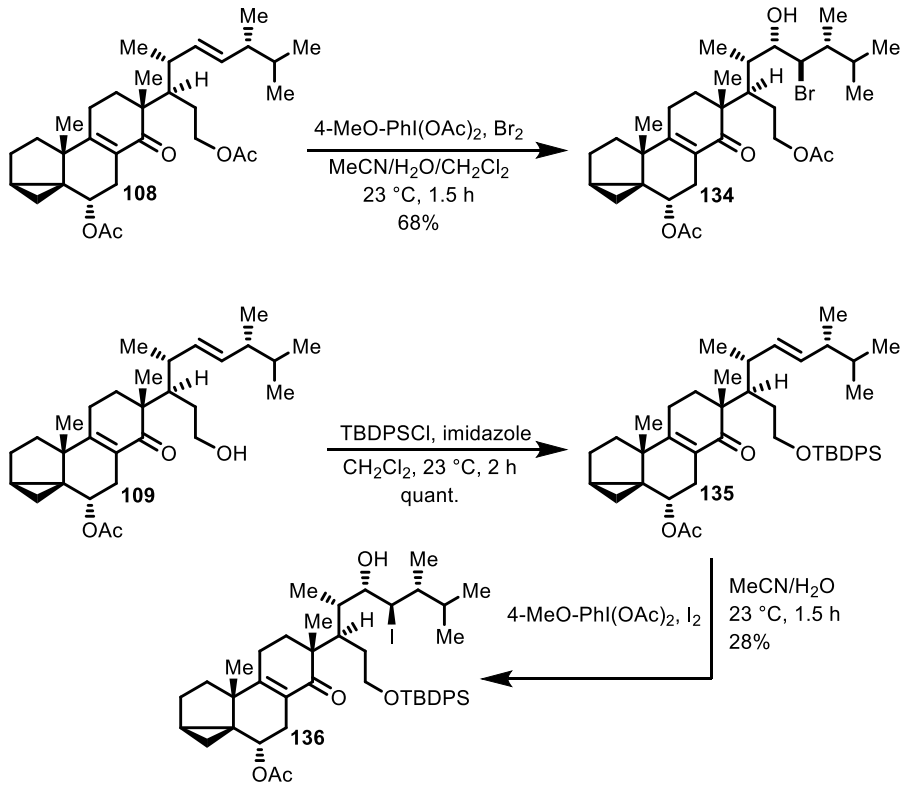
Figure 2: Rotational freedom of the sidechain of **69** and **108**.

In order to gain access to the desired isomer, it was necessary to find conditions to change the preferred point of the nucleophilic attack. BARTON et al. found that the size of the nucleophile plays a crucial role for the regioselectivity. Since water is a small nucleophile, choosing a bigger nucleophile would not change the outcome of the reaction, as the bigger nucleophile would show an even higher selectivity towards the more accessible C22. Also, the formation of three out of four possible isomers in a 9:4:1 ratio was observed by BARTON et al. while treating enone **69** with *N*-bromosuccinimide (NBS) under aqueous conditions and subsequent acetylation (*Scheme 24*). It was reasoned, that water is capable of opening the respective halonium ion at C23.[68] As no additional isomers were observed in the functionalization of diacetate **108**, it suggests a highly distinct difference in the accessibility of C22 towards C23.



Scheme 24: Bromoacetoxylation on enone **69** as reported by BARTON et al.

Another option was the use of a different halogen source, as the size of the formed halonium ion might influence the conformation of the 14,15-seco system. This could eventually enable the reversion of the regioselectivity to some extent. Thus, diacetate **108** was treated with 4-MeO-PIDA and the dropwise addition of a bromine solution. The isolated product **134** was investigated by 2D NMR spectroscopy and revealed the undesired regioselectivity, again. Remarkably, once more, only a single regio- and diastereomer could be found. This unexpected high preference for the nucleophilic attack of the respective halonium ion, seems to be not influenced by the particular halogen used.



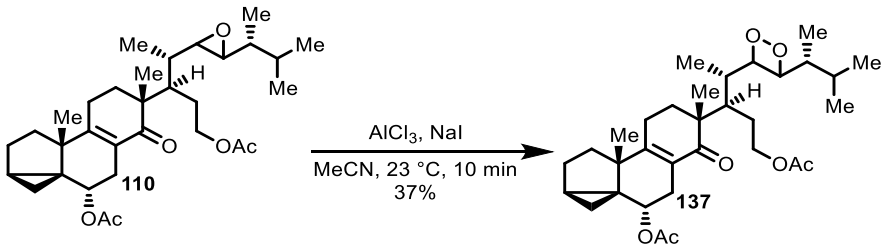
Scheme 25: Bromohydrin formation (top) and iodohydrin formation with sterically demanding TBDPS ether **133**.

A promising alternative was the influence of the protecting group on the primary alcohol, as very large substituents might have a distinct influence on the conformation of the molecule. Thus, the primary alcohol of **109** was transformed into the sterically demanding *t*-butyl-diphenyl silyl ether **135** and treated under the conditions for the iodo hydroxylation (*Scheme 25*). As before, the structural analysis showed the formation of undesired regioisomer **136** in a low yield of 28% without any additional products. Desilylation due to the formation of hypoiodous acid might be accountable for the reduced yield. This experiment showed that the manipulation of the system towards the desired regioisomer seems impossible on this stage.

Although the regioselectivity of the iodohydrin formation was not invertible, the strong preference for the nucleophile to attack at C22 opened new vistas and opportunities.

An adjustment of the order in which the functionality is introduced to the system should render the problem solvable. By first transforming the Δ^{22} olefin into the corresponding epoxide and then opening this epoxide with a suitable nucleophile, e.g., an iodide, the better accessibility of C22 should give the desired regioisomer.

Accordingly, epoxide **108** was treated with aluminum(III) chloride in acetonitrile in the presence of sodium iodide (*Scheme 26*). After consumption of the starting material and isolation of a more polar compound, a first analysis of the ^{1}H NMR indicated the success of the reaction, as the obtained spectral data were very similar to the known iodohydrin but not identical. While analyzing the 2D spectra to confirm the supposed structure, the implementation of a second heteroatom could be confirmed in the ^{13}C NMR spectrum.



Scheme 26: Oxidation of epoxide **110** to 1,2-dioxetane **137** under aerobic conditions.

The shift of the C-atom attached to the new heteroatom at 73.0 ppm was contrary to the expected shift of a secondary alkyl iodide and indicated the implementation of a chlorine atom or a second oxygen atom. The analysis of the high-resolution mass spectrum showed a mass difference between starting material and product of a single oxygen atom (Δ = 15.9949), ruling out a chlorine atom. As also other reaction conditions, without any possible sources of chlorine, gave the same compound, 1,2-dioxetane **137** was proposed as the structure of the obtained product (*Table 5*, entry 2).

Table 5: Conditions for the attempted opening of epoxide **110**.

Entry	Reagents	Temp.	Time	Product (yield%)
1	$AlCl_3$, NaI; MeCN	0 °C	15 min	**137** (37)
2	$BF_3{\cdot}OEt_2$, MgI_2; MeCN	23 °C	10 min	**137** (10)
3	AcOH, LiI; MeCN	23 °C	24 h	**138** (42)
4[a]	$In(OTf)_3$, NaI; MeCN	23 °C	5 h	**138** (62)

[a] Reaction performed after degassing of the solvent.

A close look on the NMR spectra of starting material and product indicates a strong structural relation and both the analysis of the 2D spectra as well as analysis of the mass spectra strongly indicate the formation of dioxetane **137** (*Figure 5*).

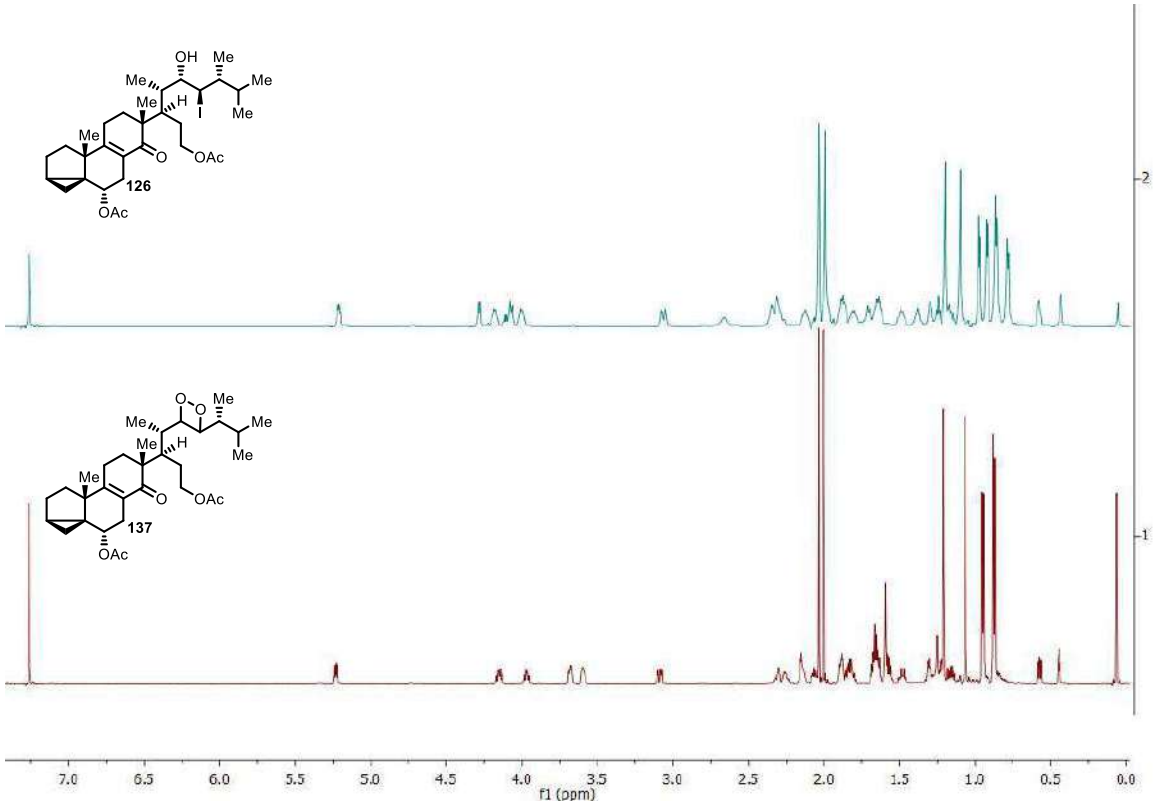
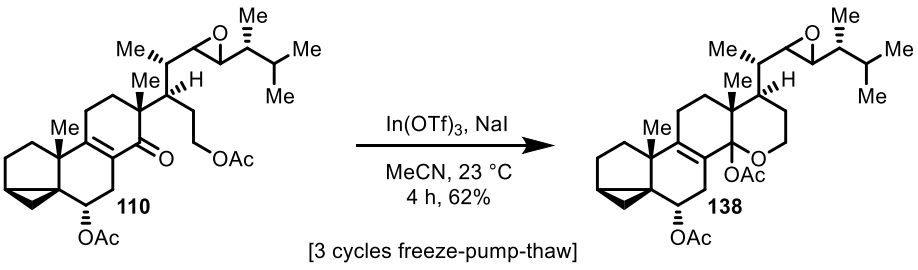


Figure 3: ^{1}H NMR spectra of iodohydrin **126** (top) and proposed 1,2-dioxetane **137** (bottom).

This reactivity is unprecedented, and the mechanism of the reaction remains elusive. Imaginable would be the activation of the epoxide followed by the LEWIS acid mediated opening with traces of oxygen present in the solvent. Intramolecular substitution of a LEWIS acid oxygen adduct could in principle close the 1,2-dioxetane. While the oxidation of carbanions, organometallic species or carbon-centered radicals is a well-known reactivity, the formal oxidation of carbocations has not been described. Another possibility that cannot be ruled out is that the reaction proceeds *via* a radical mechanism.

Interestingly, the exclusion of oxygen from the reaction mixture suppressed the formation of **137** but still gave no formation of the desired product, as the formation of acetal **138** was observed (*Scheme* 27).

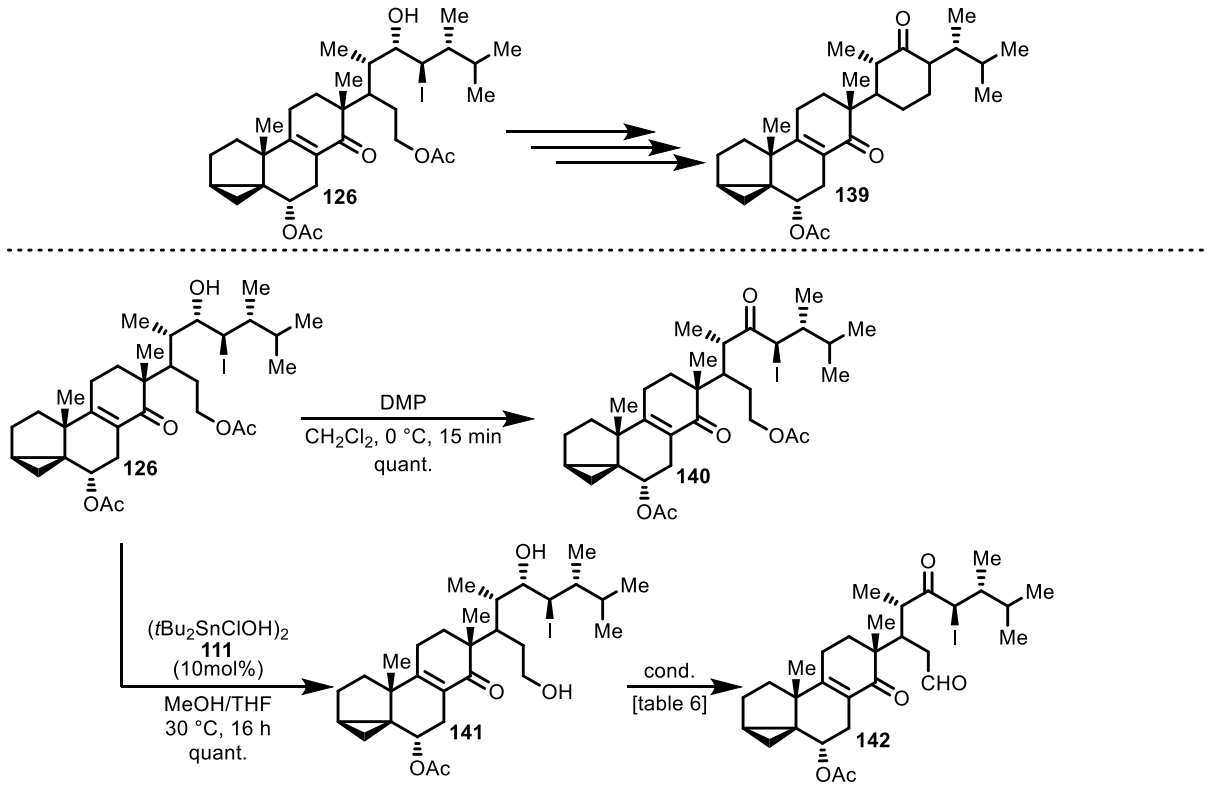


Scheme 27: Acetal formation from epoxide **110**.

Epoxide **110** showed an increased sensitivity towards acidic conditions as the substrate readily forms an acetal as the primary side product under LEWIS acidic conditions. This reaction pathway seemed to be favored over the desired opening of the epoxide.

Remarkably, the acetalization only occurred after the installation of the epoxide from **110**. The 2D NMR spectra also indicate that the acetate shifts from the primary to the tertiary alcohol upon cyclization. Structural change is imaginable due to the strained epoxide in the sidechain, that might lead to the closer proximity of the respective alcohol (or acetate) to the enone facilitating the acetal formation under acidic conditions. Other protecting groups on the primary alcohol than the acetate were not tested, although the use of a tosylate as the protecting group might have been a valuable system for this transformation.[80]

Although access to the target natural products was still missing at this point, valuable insight into the behavior of the system and its unprecedented reactivity was discovered. As the development of synthetic routes that bear the potential for diversification on various points is desirable, the regioselective oxidation of diacetate **108** can be regarded as a versatile intermediate for the generation of derivatives of strophasterols A−D. To evaluate this hypothesis, a small study was realized in order to access possible cyclohexane derivatives of strophasterol C and D (*Scheme* 28, top).

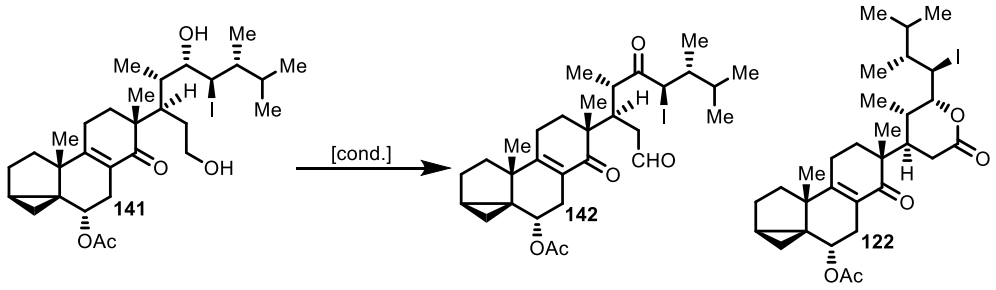


Scheme 28: Potential elaboration of **126** into derivative **139** (top) and sequence towards **142** (bottom).

Iodohydrin **126** was treated with tin compound **111** for the saponification of the primary acetate to give diol **141** in quantitative yield. Starting from here, the oxidation of both, the primary and secondary alcohol to the corresponding keto-aldehyde **142** was investigated. Due to the proximity of both alcohols, and the faster oxidation rate of the primary alcohols to the aldehyde, the formation of the corresponding lactone *via* oxidation of the formed hemiacetal was observed under most conditions (*Table 6*, entries 1−3).

To circumvent this reactivity, the PARIKH-DOERING and the SWERN oxidations were tested, as both alcohols are trapped as an alkoxysulfonium salt prior to the addition of base and final product formation.[81–84] While the PARIKH-DOERING oxidation showed only the decomposition of the starting material, the SWERN oxidation gave a small amount of the desired product, accompanied by the formation of various other compounds (*Table 5*, entries 4,5 and 7).

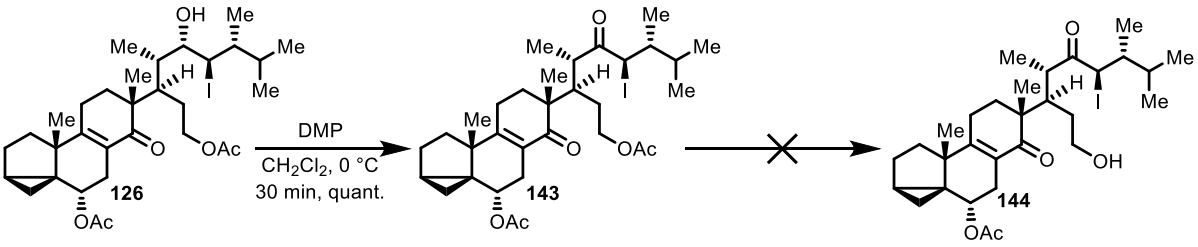
Table 6: Conditions for the oxidation of diol **141** to keto-aldehyde **142**.



Entry	Conditions	Temp.	Yield	Comments
1	DMP, CH_2Cl_2	0 °C	-	lactone formation
2	PCC, CH_2Cl_2	23 °C	-	lactone formation
3	IBX, DMSO	60 °C	-	lactone formation
4	$Py{\cdot}SO_3$, then NEt_3, CH_2Cl_2	23 °C	-	decomposition
5	TPAP, NMO, 4 Å MS, MeCN	23 °C	-	complex mixture
6[a]	DMSO, $(COCl)_2$, then NEt_3, CH_2Cl_2	−78 °C	19%	-
7[b]	DMSO, $(COCl)_2$, then NEt_3, CH_2Cl_2	−78 °C	-	-

[a] The reaction was stirred at −78 °C for 20 min, and gradually warmed to 0 °C after addition of the base. [b] The reaction was stirred at −60 °C for two hours prior to the addition of triethylamine.

On the other hand, oxidation of the iodohydrin **126** to the α-iodo ketone **143** went smoothly employing the DESS−MARTIN reagent as the oxidant (*Scheme 29*). Further saponification of the primary acetate was met with failure, as only the formation of a complex mixture was observed.



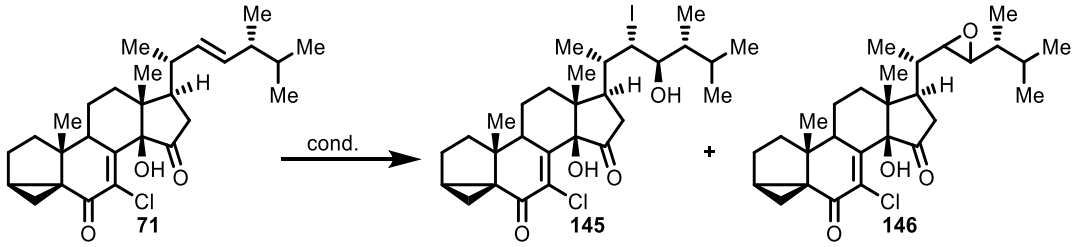
Scheme 29: Oxidation of iodohydrin **126** to the corresponding iodoketone.

As the synthesis of derivatives was not a crucial part of this work, further attempts were discontinued. Nevertheless, the discovered selectivity still bears the potential to synthesize a pool of derivatives under the right conditions.

4.2.1 Functionalization of the Ergostane Sidechain

As the synthesis of the desired iodohydrin resulted in the formation of the undesired regio-isomer, the results indicated the additional degree of rotational freedom as the main reason. Thus, chloroenone **71** was chosen for the functionalization, as it is the last compound prior to the D-ring scission (*Table 7*).

Table 7: Screening of reaction conditions for the functionalization of chloroenone **71**.

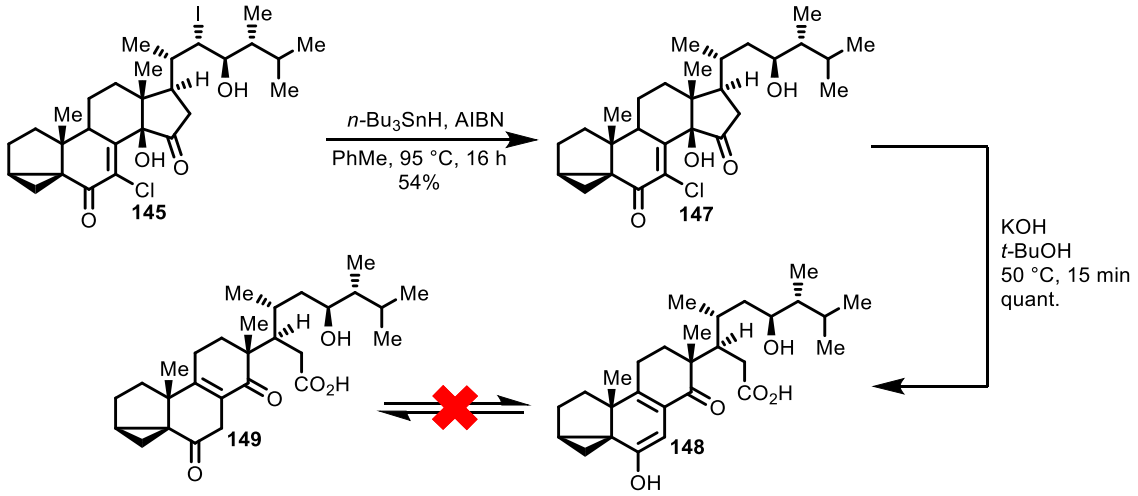


Entry	Conditions	Temperature	Time	Yield [141]	Comments
1	MeO-PIDA, I_2, AcOH; MeCN/water	23 °C	1.5 h	19%	54% **146**
2	PIFA, I_2; MeCN/water	0 °C	1.5 h	-	decomposition
3	PIDA, I_2, AcOH; MeCN/water	23 °C	2 h	18%	42% **146**
4	ICl; wet CH_2Cl_2	23 °C	24 h	-	no conversion
5	$[I(py)_2BF_4]$; dioxane/water	23 °C	24 h	-	no conversion
6	NBS; MeCN/water	23 °C	3 h	-	37% **146**
7	NIS; MeCN/water	23 °C	16 h	-	complex mixture
8	$Hg(OAc)_2$; THF/water	23 °C–50 °C	24 h	-	no conversion
	BH_3·THF; THF	66 °C	16 h	-	no conversion

Under the established conditions using iodine and hypervalent iodine reagent **128**, chloroenone **71** reacted smoothly but gave epoxide **146** as the main product in 52% yield and the desired iodohydrin **144** in 19% yield (*Table 7*, entry 1). Various conditions were tested such as different

sources of hypervalent iodine that all either showed the primary formation of the undesired epoxide or decomposition of the starting material (*Table 7*, entries 1−3). Bis(pyridine)iodo(I) tetrafluoroborate developed by BARLUENGA et al. and iodine monochloride were tested but did not show any conversion of the starting material.[85–88] The use of NBS showed the exclusive formation of the epoxide while *N*-iodosuccinimide gave only a very slow conversion and after a reaction time of 16 h resulted a complex mixture of starting material and various other compounds was detected by TLC (entries 6,7).

Radical scission of the iodine from **145** was carried out with *n*-tributyltin hydride and azobis(isobutyronitril) (AIBN) in refluxing toluene and gave the desired dehalogenated product **147** in 54% yield (*Scheme 30*). The submission of **147** to the conditions for the α-ketol rearrangement seemed to give the desired transformation, but due to the small scale of the reaction, the product formed the assumed enol compound **148** during the workup. Any attempts to re-equilibrate the material towards the desired ketone **149** failed.



Scheme 30: Dehalogenation and attempted α-ketol rearrangement of 23-OH-chloroenone **147**.

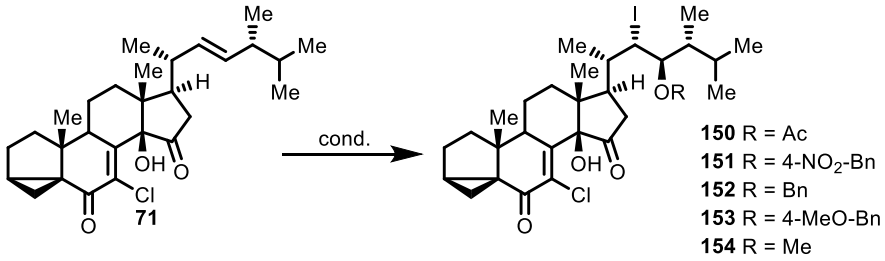
As the yield of **145** as the required precursor for the rearrangement to carboxylic acid **149** was not sufficient to continue the synthesis towards the desired platform, alternatives were investigated.

Employing mercury(II) acetate or borane tetrahydrofuran complex gave no reaction, not even under prolonged reaction times, elevated temperature or increased concentration. As the spatial arrangement in the sidechain seem to favor the formation of epoxide **146**, the installation of a group that would suppress the epoxide formation, e.g., an acetate, was required.

Thus, water was exchanged for acetic acid as the nucleophile. Initial attempts using different sources of hypervalent iodine and iodine in acetic acid gave the desired product as the single diastereomer **150** in yields between 21−32% (*Table 8*, entries 1−3). Also, applying the

conditions reported by BARTON et al. using silver acetate and iodine did not improve the yield and gave the desired product in 32% yield. As the desired product **146** was the only compound detected by TLC, and as no further compounds were isolable, it was difficult to investigate, what happened to the missing material, as ~70% of the deployed mass was missing, also after variation of the work-up procedure. The TLC indicated a clean conversion of the starting material and also using different TLC stains or washing the column with ethyl acetate did not give any identifiable side-products.

Table 8: Conditions for the iodo acetoxylation of chloroenone **71**.

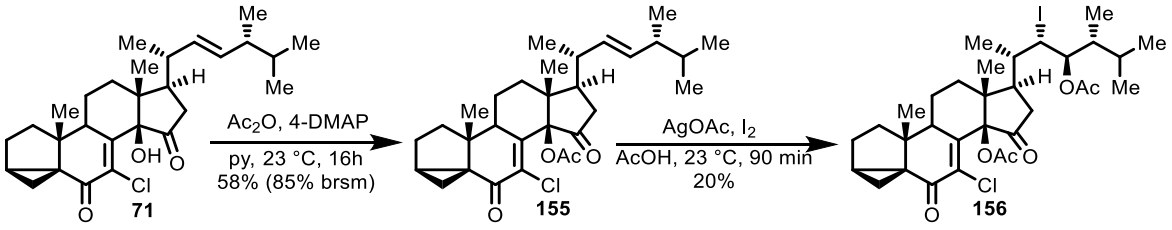


Entry	Reagents[a]	Time	Yield	Comments	R
1	PIDA, I_2, AcOH	45 min	32%	-	Ac
2	MeO-PIDA, I_2, AcOH	45 min	21%	-	Ac
3[b]	AgOAc, I_2, H_2O; AcOH	30 min	32%	-	Ac
4	Oxone®, I_2, AcOH, Ac_2O	23 h	-	no conversion	Ac
5	NIS, AcOH	3.5 h	-	no conversion	Ac
6	Me_3SI, PIDA, AcOH	24 h	-	no conversion	Ac
7	MeO-PIDA, I_2, AcOH	90 min	16%	-	Ac
8	*p*-NO_2-BnOH, MeO-PIDA, I_2; MeCN	90 min	-	complex mixture	*p*-NO_2-Bn
9	BnOH, MeO-PIDA, I_2; MeCN	90 min	-	complex mixture	Bn
10	*p*-MeO-BnOH, MeO-PIDA, I_2; MeCN	90 min	-	complex mixture	*p*-MeO-Bn
11	MeOH, MeO-PIDA, I_2; MeCN	90 min	-	complex mixture	Me

[a]All reactions were performed at 23 °C on a 0.05 mmol scale at 0.1 M concentration. [b]0.05 M concentration

Other conditions such as the use of trimethylsulfonium iodide in the presence of diacetoxy iodobenzene as developed by REDDY et al. or the generation of hypoiodous acetate from iodine and Oxone® in acetic acid as reported by WIRTH et al. did gave no conversion at all.[89,90] As the use of potentially milder sources of I^+ did not show any effect on the yield, various other

nucleophiles were tested to assess the impact of the respective nucleophile on the outcome of the reaction. The use of benzyl alcohol and substituted derivatives or methanol lead to the formation of complex mixtures (*Table 8*, entries 8−11). Since the source of the synthetic problems was still not identifiable, modifications on the chloroenone were tested. The chloroenone is a densely functionalized system at which the high level of functionality may be the origin of undesired side reactions. For example, the PIDA/iodine system is well known for the generation of alkoxy radicals, whose reactivity in such a densely functionalized system is hard to anticipate. Even though, generation of radicals under these conditions requires the irradiation with light for the homolytic cleavage of the formed O−I bond, the tertiary hydroxy group was transformed into the corresponding acetate.[91–93] Treating **71** with acetic anhydride in pyridine in the presence of 4-dimethylamino pyridine gave tertiary acetate **155** in 57% yield along with 23% of reisolated **71** (*Scheme 31*). Treatment of acetate **155** under the highest yielding conditions for chloroenone **71** (silver acetate, iodine, acetic acid) gave the desired iodo diacetate **156** in 20% yield.

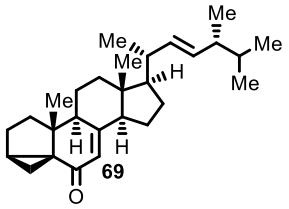
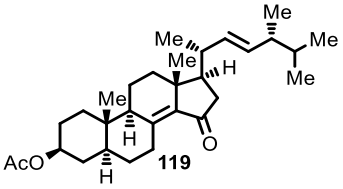
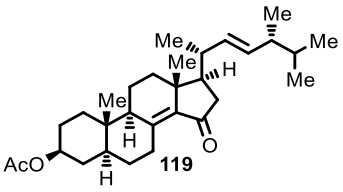


Scheme 31: Acetate protection of chloroenone **71** and iodoacetoxylation of acetate **155**.

Next, reduction of the α-hydroxy ketone to the corresponding diol was considered, as the rates for the enolization of cyclic ketones under acidic conditions is considerably faster than for comparable dialkyl ketones.[94] The enolization might enable side-reactions, but as earlier studies on chloroenone **71** en route to strophasterol A showed, reduction of the ketone is not possible.[1] Since no improvement was found under the tested conditions, the reactivity of enone **69** was reviewed, as BARTON et al., MEHTIEV et al., and FLEGENTOV et al. reported yields between 53% to 72% (*Table 9*).[68,70,71] After careful evaluation of their publications, it was found that all authors used different conditions. While BARTON et al. reported the optimal conditions to be anhydrous, MEHTIEV et al., and FLEGENTOV et al. stated that the addition of water is crucial for the success of the reaction.

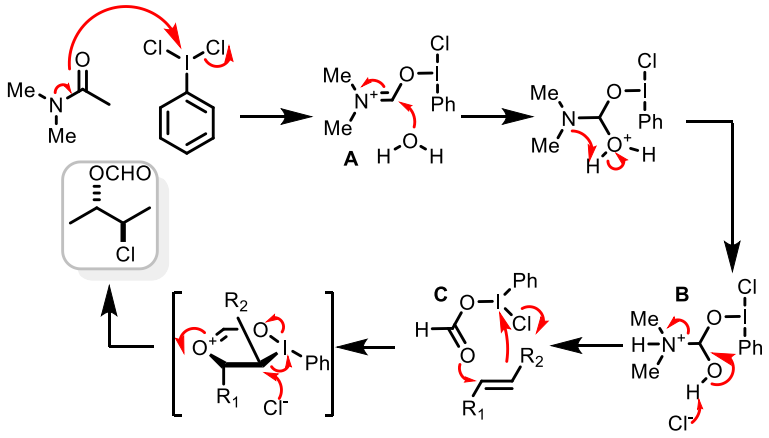
[1] Dissertation Dr. R. Heinze, Berlin 2018

Table 9: Literature conditions for the iodo acetoxylation of ergostane sidechains.

Author	System	Conditions	Yield
BARTON et al.	 **69**	glacial AcOH, AgOAc in portions addition of powdered iodine during 15 min (3 h reaction time)	53%
MEHTIEV et al.	 **119**	95:5 AcOH/H_2O, AgOAc in portions addition of powdered iodine during 20 min (20 min reaction time)	72%
FLEGENTOV et al.	 **119**	95:5 AcOH/H_2O, AgOAc, dropwise addition of 45 °C sol. of I_2 in AcOH (20 min reaction time)	70%

After extensive experimentation and exact reproduction of the reported conditions, the yield of the iodo acetate remained between 15−32% (*Table 9*). Variation of other reaction parameters such as the concentration of the reaction, the temperature, the rate of the iodine addition or changing the system from silver acetate/iodine to PIDA/iodine did not increase the yield.

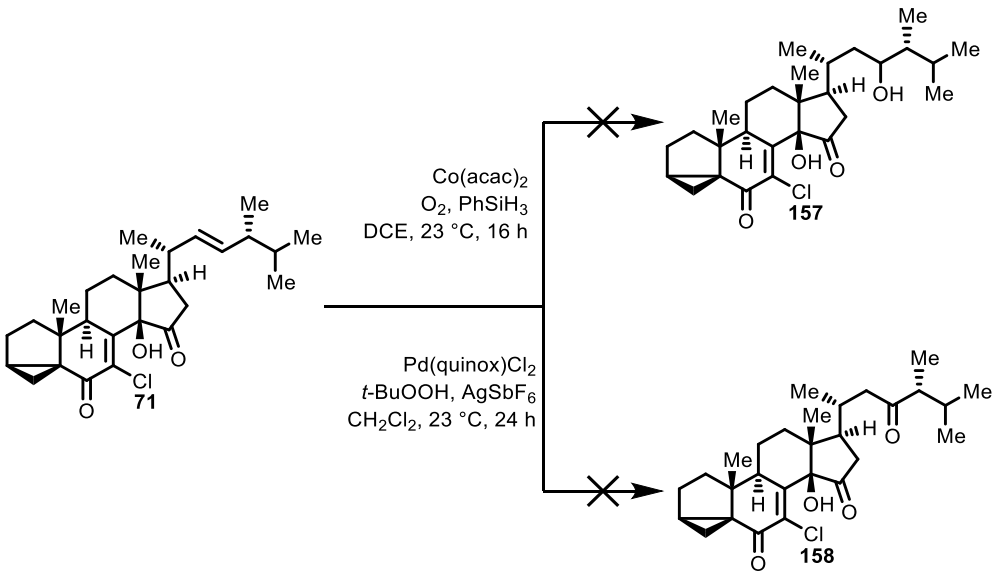
The introduction of the required functionality to the sidechain was successful so far, albeit with too low yields on an early stage for efficient synthetic access to proceed with this strategy. Since the success of the synthetic endeavor was not dependent on the installation of the halohydrin motif but only dependent on the selective oxygenation of the C23 position, other possibilities to functionalize the sidechain were investigated. First, the chloroformyloxylation reported by LUI et al. using iodobenzene dichloride and wet dimethylformamide was tested.[95] Mechanistically, this transformation is thought to proceed *via* the mechanism depicted in *Scheme 32* and is initiated by displacement of one chlorine ligand by dimethylformamide followed by addition of water to the iminium ion (**A**). Deprotonation by a chloride ion and elimination of dimethylamine (**B**) gives the reactive hypervalent iodine reagent (**C**).



Scheme 32: Proposed reaction mechanism for the chloroformyloxylation of olefins.

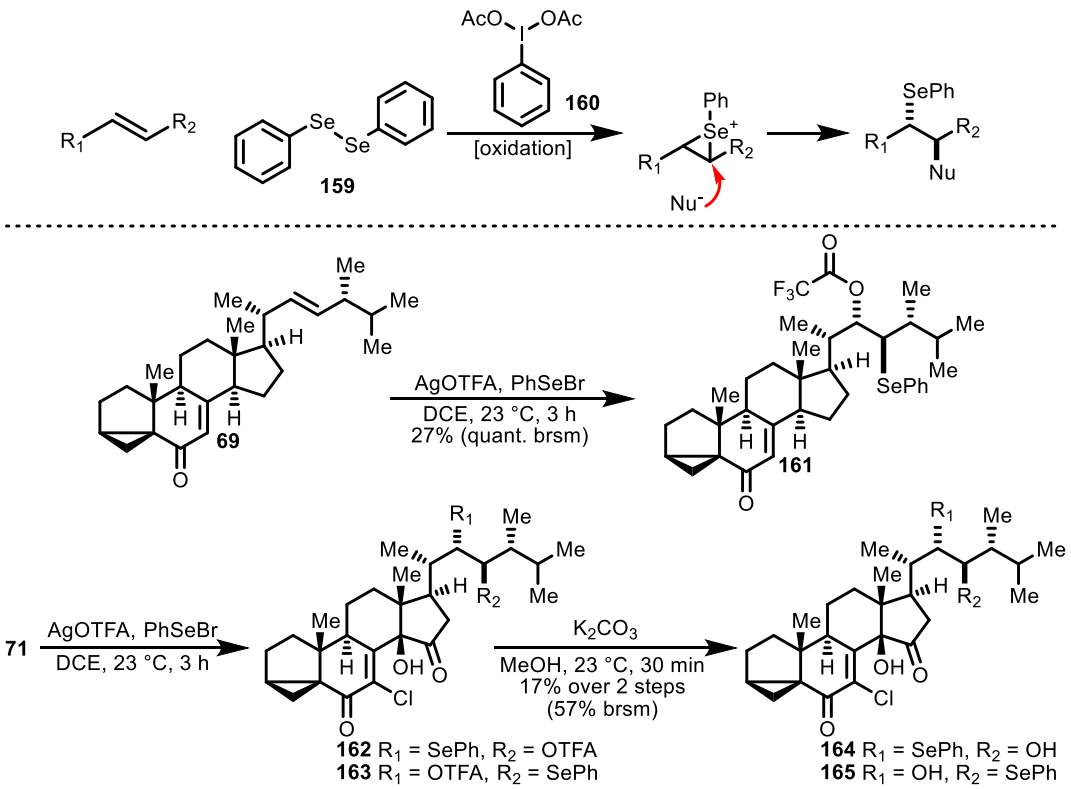
As the reactive intermediate differs from the previously employed halo-functionalization method as no halonium ion is formed, this reaction presented an attractive alternative. Nevertheless, treating chloroenone **71** under the reported conditions resulted in no conversion of the starting material.

Other known oxidative methods for the manipulation of olefins such as the MUKAIYAMA hydration and the WACKER oxidation also resulted either in no conversion or the decomposition of the starting material (*Scheme 33*).[96–98]



Scheme 33: Attempted MUKAIYAMA hydration and WACKER oxidation of chloroenone **71**.

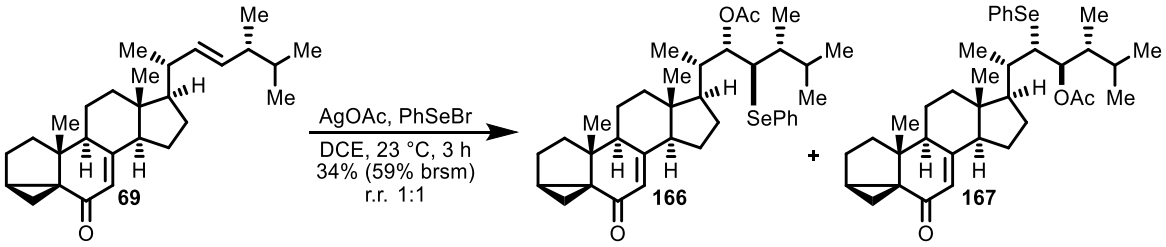
TINGOLI et al. found that hypervalent iodine reagents such as diacetoxy iodobenzene can oxidatively cleave Se−Se bonds to generate a very reactive, electrophilic selenium species in situ. In absence of a suitable nucleophile, the authors observed that the acetoxy ligands of the iodine(III) species can trap the cationic intermediate to give products of seleno acetoxylation (*Scheme 34*, top).



Scheme 34: Oxidative generation of electrophilic selenium (top) and seleno trifluoroacetoxylation of chloroenone **71** (bottom).

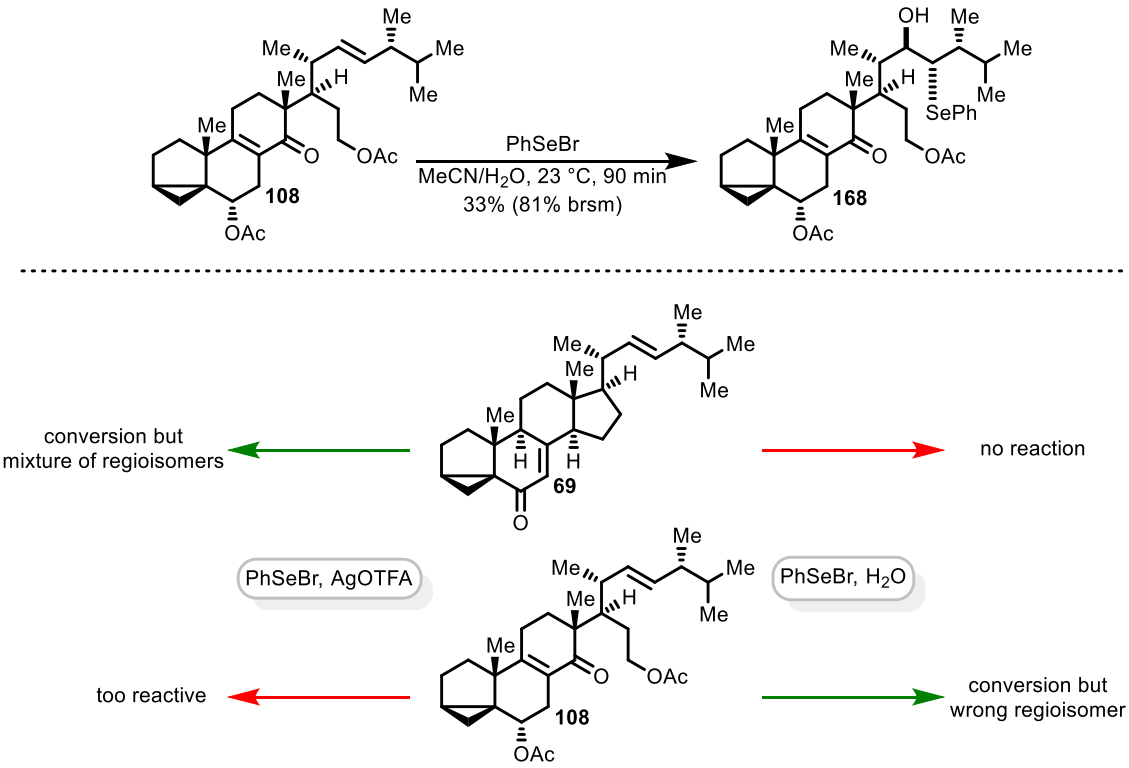
Treating chloroenone **71** under the reported conditions gave no conversion. Since in many experiments no conversion of the starting material could be observed, it was assumed that the reagents employed were not reactive enough. In 1973, CLIVE et al. reported that the combination of phenylselenyl chloride and silver trifluoroacetate generates a "super-electrophilic" selenium species. REICH et al. and SEEBACH et al. further investigated this reagent and found among others application in the total synthesis of the tricyclic skeleton of natural *Celastraceae* sesquiterpenoids.[99–102] The phenylselenyl trifluoroacetate was generated by the dropwise addition of a 1,2-dichloroethane solution of phenylselenyl bromide to a suspension of silver trifluoroacetate (*Scheme 34*, bottom). Submission of enone **69** to the in situ generated reagent showed the formation of two new compounds on thin layer chromatography of which only the more polar was isolable by column chromatography in 27% yield along with 73% of unreacted starting material, as it seemed that the seleno trifluoroacetate rapidly decomposed to give enone **69**. The isolated trifluoroacetate **161** proved to be very labile and decomposed in deuterated chloroform. All attempts for the saponification of the trifluoroacetate (treatment with methanol, potassium carbonate in methanol or sodium methoxide) failed, as in all cases an insoluble, yellow colored solid was formed without any traces of the desired product. Submission of chloroenone **71** to the same conditions followed

by saponification with potassium carbonate in methanol yielded α-hydroxy selenides **164** and **165** in an approximate 1:1 ratio (*Scheme 34*, bottom). As the saponification suffered from low reproducibility and was thus impractical, alternatives were investigated. The use of phenylselenyl bromide in a mixture of acetonitrile and water gave no conversion, but it turned out that substituting silver trifluoroacetate with silver acetate gave the corresponding seleno acetates as stable products. Submitting enone **69** to the reaction conditions gave a separable 1:1 mixture of seleno acetates **166** and **167** in 34% combined yield along with 25% of re-isolated starting material **69** (*Scheme 35*).



Scheme 35: Selenoacetoxylation of enone **69**.

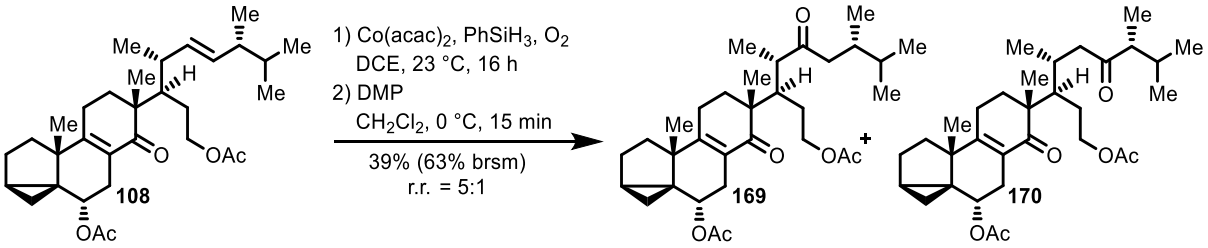
Finding conditions for the complete consumption of starting material proved to be challenging, as, e.g., increasing the equivalents of silver acetate and phenylselenyl bromide, prolonging the reaction time or increasing the temperature showed no effect. Even though in all cases an approximate 1:1 ratio of regioisomers was isolated, this reactivity was applied to diacetate **108**. The potential generation of 50% of the correct regioisomer on a 14,15-seco intermediate would generate sufficient material to finish the synthetic endeavor and would therefore be desirable. Submission of diacetate **108** to the reaction conditions, however, showed the decomposition of the starting material, indicating too harsh conditions for the system (*Scheme 36*). Using the less reactive phenylselenyl bromide under aqueous conditions, in contrast, gave rise to the seleno hydroxylated product, albeit as the undesired regioisomer **168** in 35% yield with 46% reisolated starting material **108**.



Scheme 36: Selenohydroxylation of diacetate **108** (*top*) and observed reactivity of enone **69** and diacetate **108** with different electrophiles (*bottom*).

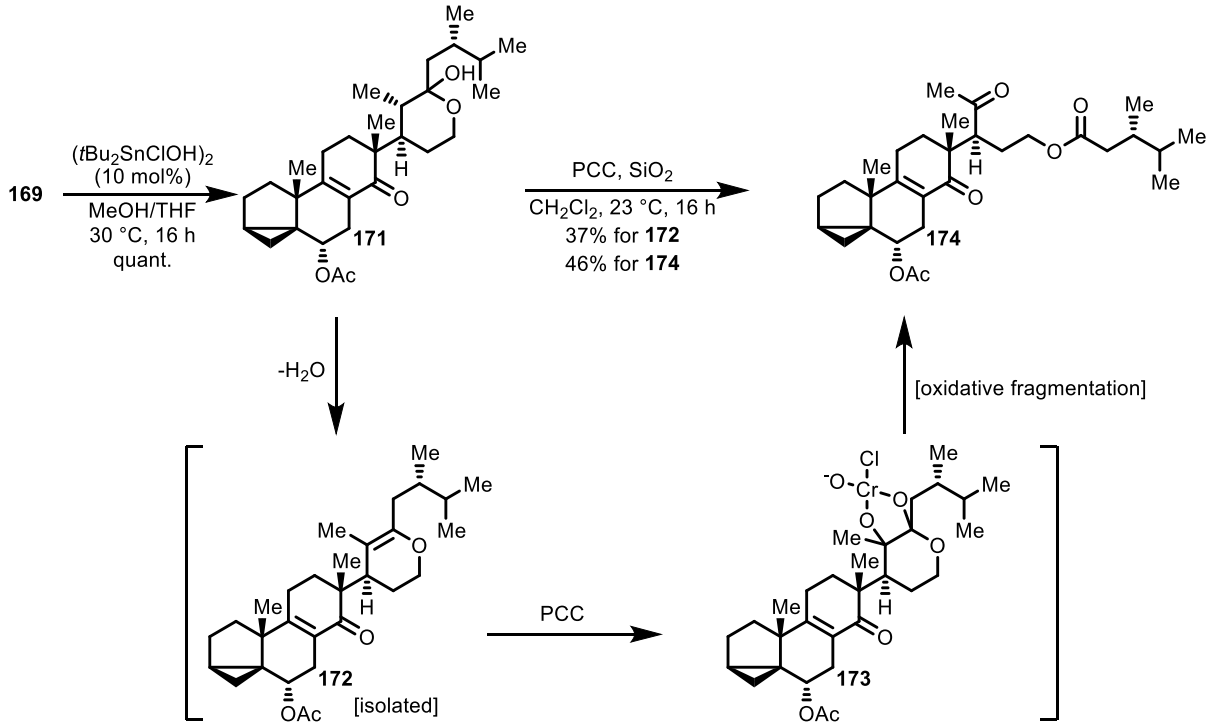
Interestingly, conditions that led to the decomposition of enone **69** and chloroenone **71** were suitable for diacetate **108**. This finding pointed towards the necessary reevaluation of methods, that were considered inapplicable previously, e.g., the MUKAIYAMA hydration.

Submission of diacetate **108** to the MUKAIYAMA hydration reaction showed the formation of all four possible isomeric alcohols. After oxidation employing DESS–MARTIN periodinane, the alcohols converged in an inseparable 5:1 mixture of C22 and C23 ketones **169** and **170** in 39% yield (*Scheme 37*).



Scheme 37: Mukaiyama hydration of diacetate **108** and subsequent oxidation.

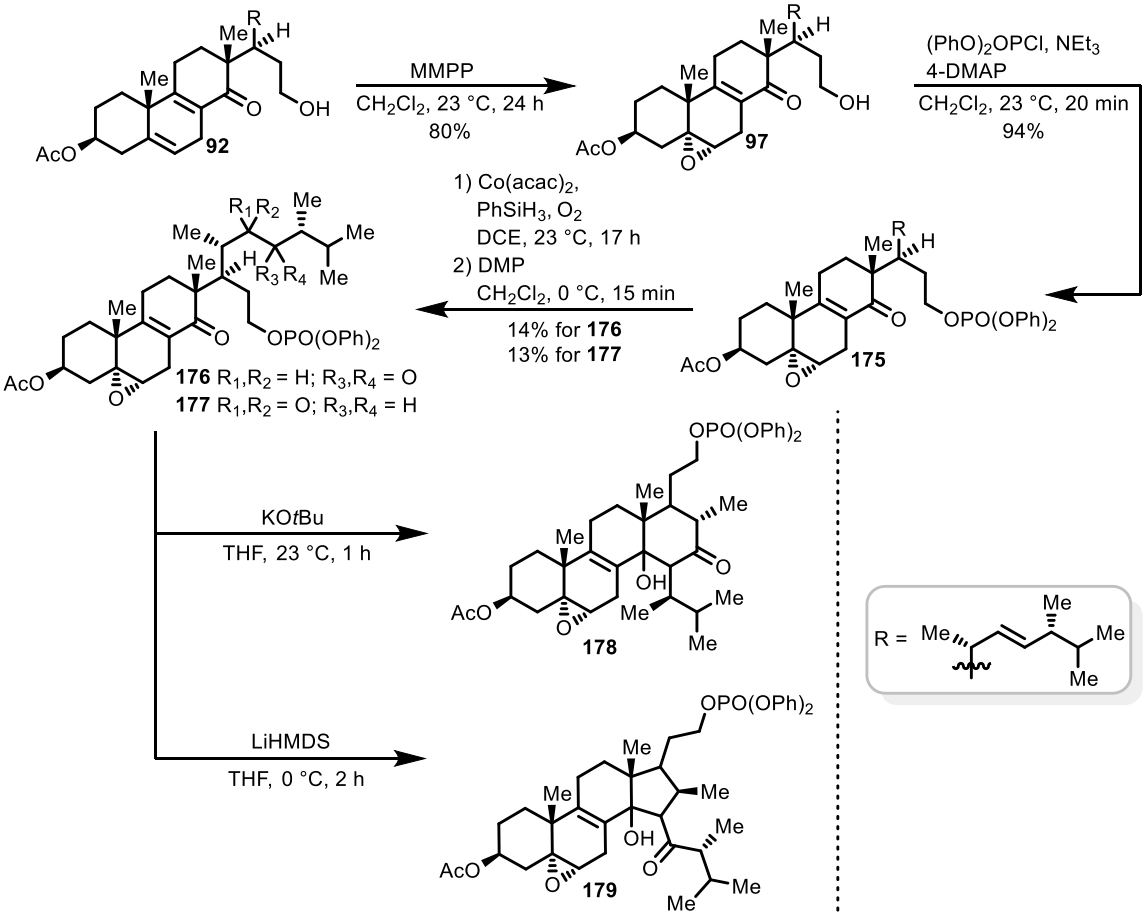
Saponification of the primary acetate with tin compound **111** gave the hemiacetal **171** and a small portion of the assumed δ-hydroxy alcohol that was not isolable. Treating hemiacetal **171** with pyridinium chlorochromate (PCC) and silica in dichloromethane gave two products that were identified by high resolution mass spectroscopy and 2D NMR analysis (*Scheme 38*). Compound **172** seemed to be an intermediate on the reaction pathway from acetal **171** to **174**.



Scheme 38: Saponification of ketone **169** and rearrangement to secopregnane **174** under oxidative conditions.

Formation of secopregnane **174** is believed to proceed upon elimination of the C22 hydroxy group to yield enol ether **172**.[103,104] Addition of chlorochromate to the olefin leads to unstable intermediate **173**. Oxidative fragmentation then gives the observed secopregnane **174** in 46% isolated yield.

As the MUKAIYAMA hydration again gave the undesired regioisomer of ketone **169**, it was attempted to influence the regioselectivity was made with a sterically demanding substituent on the C15 alcohol. Diphenyl phosphate **175**, readily available upon phosphorylation of the C15-alcohol can serve for two purposes. First, its steric demand should have a substantial impact on the conformation of the molecule and second it might be used as a leaving group in an enol-alkylation to furnish the desired cyclopentane ring. Starting from acetate **92**, epoxidation of the Δ^5 olefin with magnesium monoperoxyphthalate gave the corresponding epoxide **97** in 80% yield. Phosphorylation of the obtained epoxide gave phosphate **175** in 93%, which was submitted to the MUKAIYAMA conditions (*Scheme 39*).



Scheme 39: Synthesis of the phosphorylated alcohol **175** and subsequent oxidation and cyclization.

As anticipated, the reaction gave a separable 1:1 mixture of the C22 and C23 ketones **176** and **177** after oxidation, albeit in low yields of 14% and 13% over two steps respectively. Nevertheless, this showed that the size of the respective group on the alcohol indeed influences the molecule's conformation and thus the accessibility of C22 and C23. Submission of both regioisomers to basic conditions using potassium *t*-butoxide or lithium bis(trimethylsilyl)amide (LiHMDS) presumably led to the formation of **178** and **179**, respectively, as the electrophilicity of the C14-enone seems to outmatch that of the phosphate.

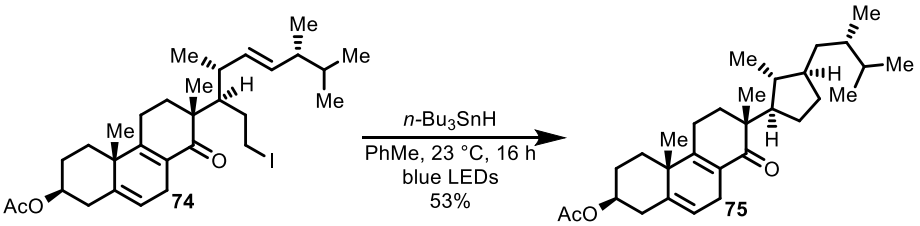
Although most methods showed interesting and valuable results for the field of steroid derivatization and functionalization and gave insights into the reactivity of manipulated steroidal compounds, they did not give efficient and selective access to the desired platform. Thus, a change in strategy towards a radical based, biomimetic approach was investigated.

4.3 Third Synthetic Strategy: Biomimetic Strategy

In contrast to all the strategies pursued so far, the biomimetic approach has not been considered to be an attractive strategy. In the biosynthesis of strophasterol C and D, the C23 oxidation state is proposed to be installed by an oxidative quench of a secondary radical. Such transformations are only rarely reported literature and as they are non-trivial. To mimic this transformation, it is required to install a suitable radical precursor, perform the cyclization and quench the resulting secondary radical with a suitable oxidizing agent. Although few examples of such transformations are reported, a common problem is the solubility of oxygen and the fragile nature of the intermediate radicals.[105,106] Triplet oxygen is reported to combine with radicals at diffusion rates, but the solubility and thus effective concentration of oxygen in most organic solvents is too low to be of general synthetic use.[107] Another crucial fact for the success of such a transformation is the generation of the alkyl radicals itself. Most common protocols for the radical generation include a radical initiator such as triethylborane and oxygen or azobis(isobutyronitril) and a tin compound, e.g., *n*-tributyltin hydride. To solve the issue of oxygen availability in the reaction as well as potential substitution of any tin compounds, as a tin hydride would reductively quench the alkyl radical, the use of perfluorinated solvents as well as the use of visible light for the homolytic cleavage of the carbon-halide bond was intended.

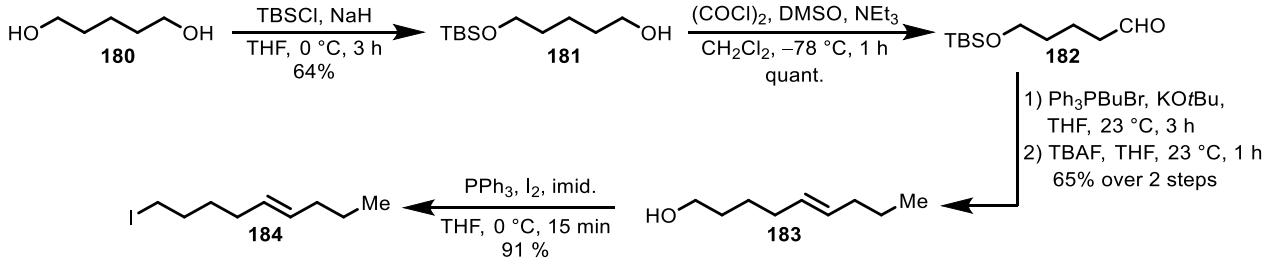
Perfluorinated solvents undergo only weak VAN-DER-WAALS interactions due to the low polarizability of the electrons of a C−F bond and modest availability of the lone-pair of fluorine. Therefore, the replacement of a perfluoroalkane by another molecule costs only a small amount of energy. Those properties lead to high solubility of gases in perfluorinated solvents, especially oxygen with an excellent solubility of up to 57 mL in 100 mL perfluoro heptane.[108,109]

Irradiation with visible light as was intended to cleave the C−I bond for the generation of the primary alkyl radical. Accordingly, iodide **74** was treated with *n*-tributyltin hydride in toluene and irradiated with blue LEDs for 16 h to give cyclopentane **75** in 53% yield (*Scheme 40*).



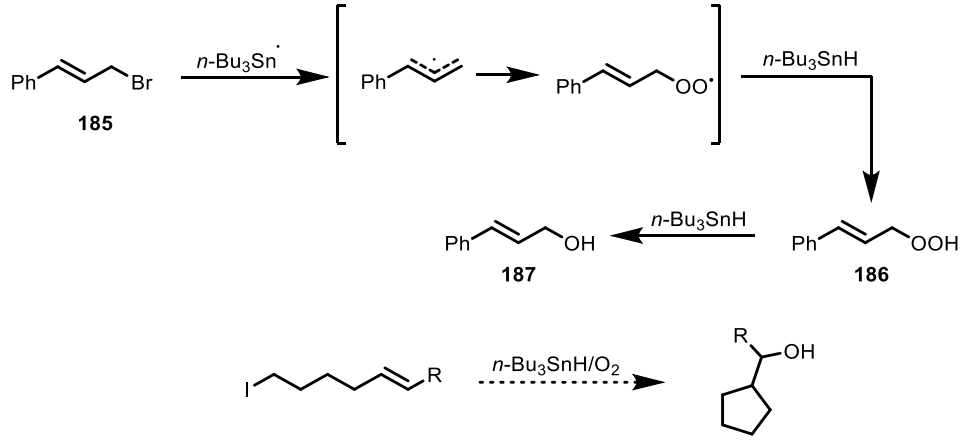
Scheme 40: Activation of iodide **70** with visible light and formation of cyclopentane **71**.

A test system for the planned transformations was synthesized in five steps from 1,5-pentanediol **180**. Protection of one alcohol as the *t*-butyl dimethyl silyl ether gave the desired product **181** in 64% yield. SWERN oxidation to aldehyde **182** followed by WITTIG olefination and desilylation with *n*-tetrabutylammonium fluoride gave non-5-ene-1-ol **183** in 65% over three steps. Formation of the primary alkyl iodide using the APPEL reaction gave test substrate **184** in 91% yield (*Scheme 41*).



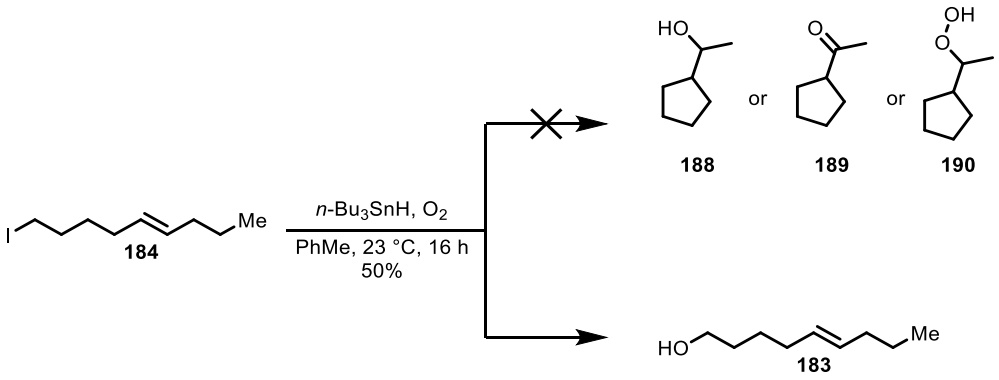
Scheme 41: Synthetic sequence for the preparation of iodide **184**.

In 1991, NAKAMURA et al. reported the aerobic conversion of halides to alcohols in a tin hydride mediated reaction.[106] The reaction proceeds by the reductive cleavage of the carbon halide bond of **185** followed by aerobic oxidation of the intermediate allylic radical to the corresponding peroxoradical (*Scheme 42*). Formation of hydroperoxide **186** and subsequent reduction to alcohol **187** by another equivalent of tin hydride gives the alcohol. The authors also proposed the possibility for a cyclization to occur prior to the oxidation.



Scheme 42: NAKAMURA's aerobic conversion of alkyl halides to alcohols.

Submission of iodide **184** to the reported reaction conditions gave alcohol **183** as the only product. The aerobic oxidation occurred under NAKAMURA's conditions but did not undergo the desired cyclization. This makes a radical mechanism unlikely, as the cyclization to the corresponding cyclopentane due to an intramolecular process should be faster than the oxidation of the primary radical by oxygen (*Scheme 43*).

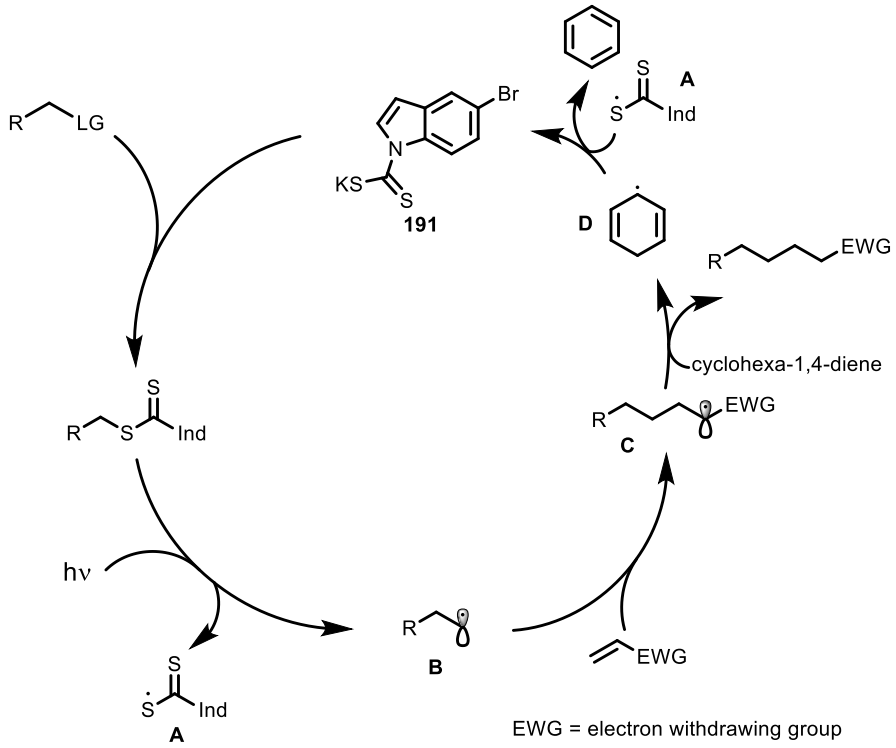


Scheme 43: Desired transformation of iodide **184** with possible products alcohol **188**, ketone **189** and hydroperoxide **190** and observed formation of alcohol **183**.

For an alternative generation of the required radical, iodide **184** was dissolved in perfluoro benzene for an enhanced presence of oxygen and irradiated with blue LEDs for 16 h. TLC indicated the formation of a complex mixture, and it was found that perfluoro benzene itself reacts, due to its extreme electron poverty, with the substrate during the reaction. Substituting perfluoro benzene with perfluoro hexane suppressed side reactions with the solvent but also showed the formation of a biphasic mixture, as **184** was insoluble in perfluoro hexane. Also, the addition of 10 equivalents of hexafluoro isopropanol as additive did not result in a better solubility. Irradiation of the reactions with blue LEDs or 365 nm UV LEDs did not result in any observable conversion of the starting material. This indicated two significant problems, first the solubility of the substrate in the perfluorinated solvents and second the generation of the primary radical by irradiation with light. It seemed that the success of the transformation of iodide **74** to cyclopentane **75** is somehow affiliated with the tin hydride.[106] Thus, the addition of *n*-hexabutyl distannane as potential radical initiator was tested but resulted in no conversion of the starting material.

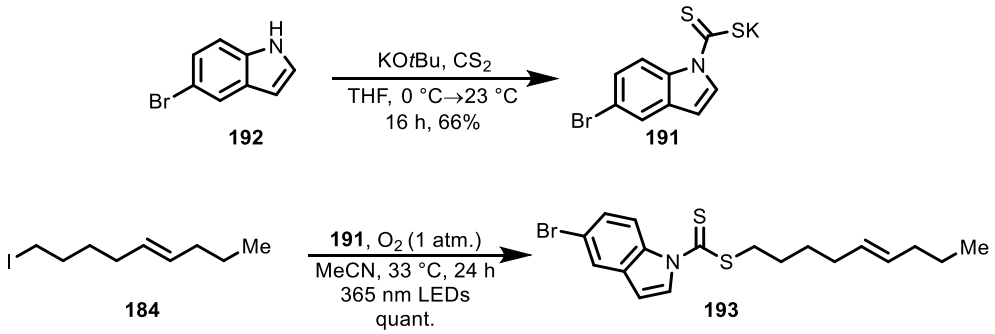
Other methods for the generation of radicals such as photoredox catalysis is strongly dependent on the redox properties and the bond dissociation energy of the target, making the use of activated halides necessary.[110–112]

An new method for the photochemical generation of radicals from alkyl electrophiles was introduced by MELCHIORRE et al. using a nucleophilic dithionyl catalyst.[113] The reaction takes advantage of the electrophilic nature of the catalyst and the resulting weak C−S-bond that can be readily cleaved homolytically by irradiation with light of an appropriate wavelength. As the authors found the reaction to be inert towards moisture and air, this methodology became valuable for the planned transformation.



Scheme 44: Catalytic cycle of the photochemical generation of alkyl radicals.

The reaction starts with the S_N2 displacement of the leaving group by catalyst **191** (*Scheme 44*). Irradiation with visible light leads to the homolytic cleavage of the C−S-bond and generates radicals **A** and **B**. The C−C-bond formation then occurs between radical **B** and a suitable olefin, H-atom transfer from cyclohexadiene gives the product, and electron transfer between **A** and **D** closes the catalytic cycle. Imaginable is the substitution of cyclohexadiene by an appropriate source of oxygen or even a halide to quench radical **C** oxidatively.



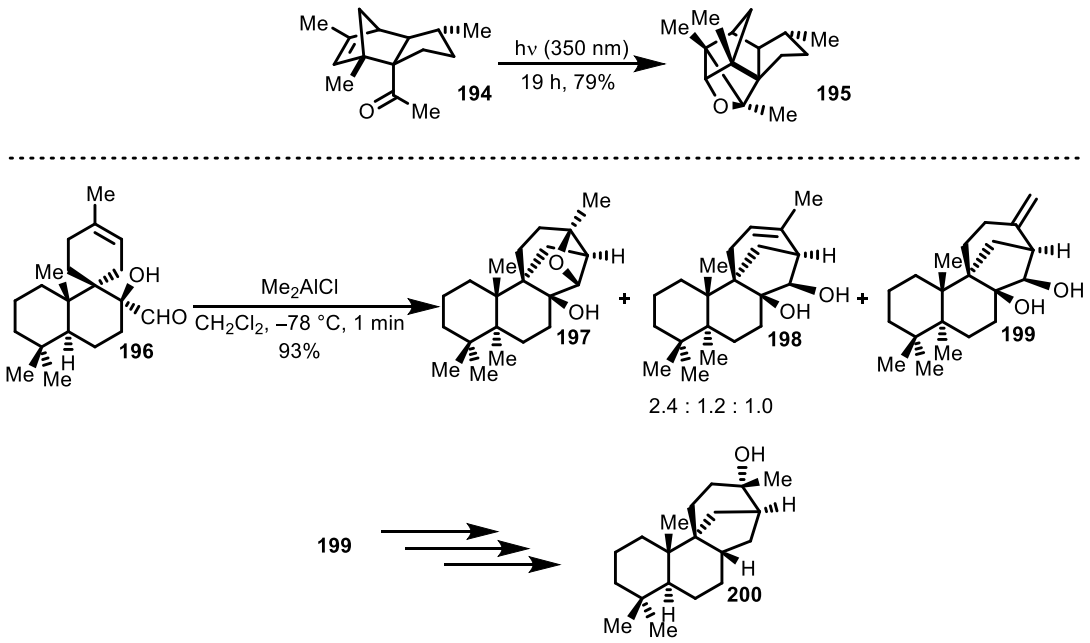
Scheme 45: Synthesis of thiocarbonyl **191** (top) and S_N2-displacement of iodide **184**.

In a first attempt, iodide **184** was dissolved in acetonitrile, and thiocarbonyl **191** was added (*Scheme 45*). The reaction vessel was evacuated and backfilled with oxygen, and the mixture was irradiated with 365 nm UV light for 24 h. Complete consumption of the starting material was observed, and isolation and characterization revealed the quantitative formation of

dithiocarbonyl **193**. No C−S-bond cleavage was achieved. Also using different light sources gave no conversion of the starting material.

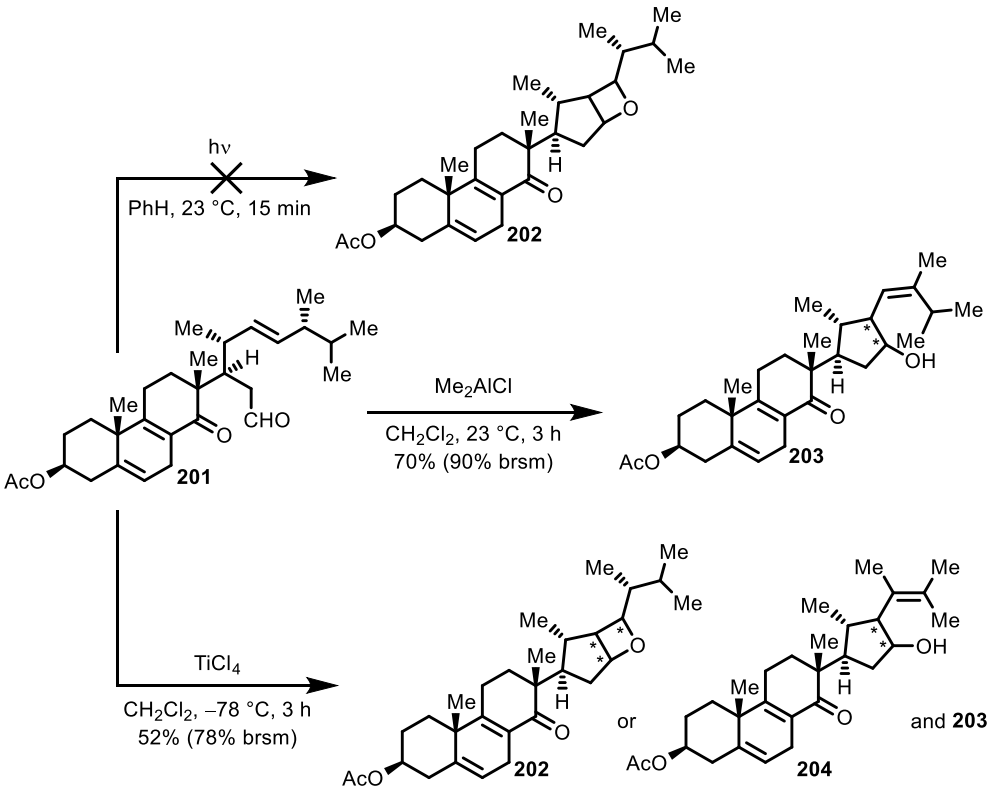
4.4 Final Synthetic Strategy: Carbonyl-Ene Approach

Another radical based organic transformation that came to mind while working on the biomimetic approach is the PATERNO–BÜCHI reaction. Seminal contributions by E. PATERNO and G. CHIEFFI, reported in 1909, showed the [2+2] cycloaddition of benzaldehyde with 2-methyl-2-butene upon exposure to sunlight.[114–116] The reaction found application in total synthesis of (±)-oxosilphiperfol-6-ene and was used for the construction of the cage-like motiv of **195** (*Scheme 46*, top).[117] In 1987, WHITE et al. found during their synthesis of (±)-2-desoxystemodinone, that submission of aldehyde **196** to dimethylaluminum chloride led to the formation of oxetane **197** along with the isomeric olefins **198** and **199** (*Scheme 46*, bottom). The LEWIS acid activated carbonyl-ene reaction provides a valuable alternative for substrates that might not withstand the harsh conditions of irradiation with UV light or bare multiple functional groups that can be activated by light.[118]



Scheme 46: Application of the PATERNO–BÜCHI reaction in the synthesis of synthesis of (±)-oxosilphiperfol-6-ene (top) and LEWIS acid enabled carbonyl-ene reaction for the construction of oxetane **197** (bottom).

Application of the PATERNO–BÜCHI reaction is of great interest, as it would form the required cyclopentane ring and install the desired oxidation state in a single step. As the carbonyl functionality is the energy absorbing component in the reaction and aldehyde **201** possesses two of those, irradiation with UV light led to the formation of a complex mixture (*Scheme 47*, top).



Scheme 47: Attempted PATERNO–BÜCHI approach starting from aldehyde **201** and carbonyl-ene cyclization.

The alternative approach to oxetane **202** using milder conditions is the before mentioned LEWIS acid mediated carbonyl-ene reaction as observed by WHITE et al..[118] Applying the reported conditions and using dimethyl aluminum chloride, aldehyde **201** gave no reaction at −78 °C. Upon warming to room temperature, the formation of new compounds was observable (*Scheme* 47, middle). The reaction gave a mixture of all four possible diastereomers of homoallylic alcohol **203** in 70% combined yield along with 20% of unreacted starting material. Using titanium(IV) chloride, the reaction already proceeded at −78 °C and in turn gave either the desired oxetane **202** or triene **204** as a mixture of diastereomers, however a distinct verification which of the two compounds was formed was not possible (*Scheme 47*, bottom). A minor side product of the reaction was one diastereomer of the beforementioned homoallylic alcohol **203** (*Figure 4*, cf. purple frames). Analysis of the ^{13}C NMR of the obtained mixture still allowed for no conclusive correlation to either of the assumed structures **202** or **204**. The corresponding ^{1}H NMR spectra show a possible indication for quaternary olefin **204**, as only one proton with a matching shift for an alcohol is identified in the ^{1}H NMR (*Figure 4*, bottom, orange frame). Nevertheless, an absolute assignment to **204** is not possible and further experiments are necessary. This could be achieved by e.g., using a chiral LEWIS acid to reduce the number of formed diastereomers.

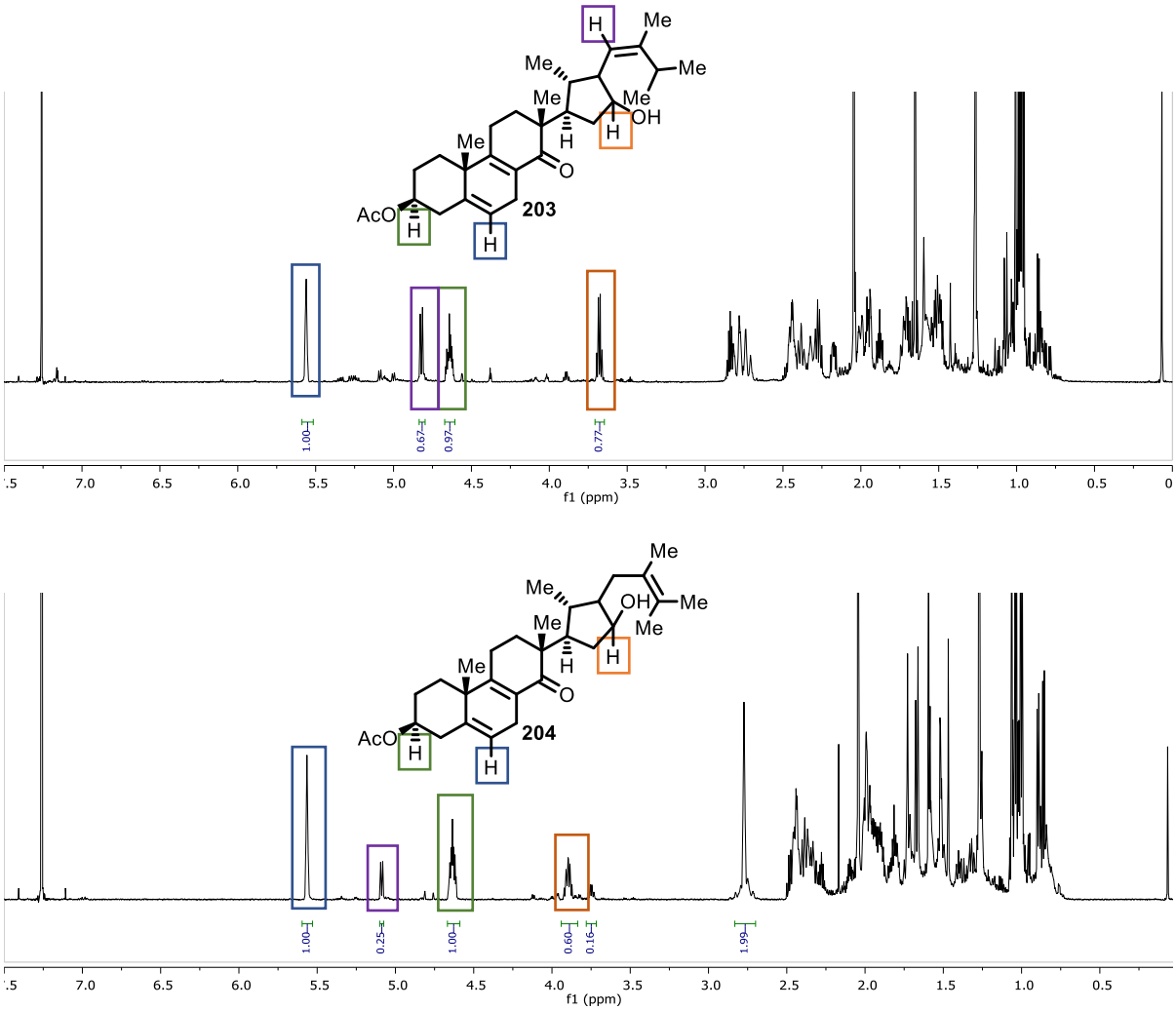
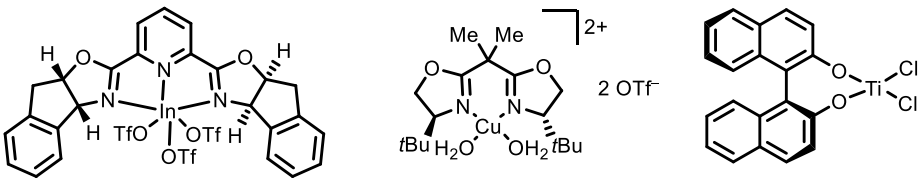


Figure 4: ^{1}H NMR spectra of homoallylic alcohol **203** and possible quaternary olefin **204**. *Note*: The respective signals in the bottom spectrum with integrals of 0.25 and 0.16 can be assigned to one isomer of **203**.

The asymmetric carbonyl-ene reaction is a well-studied process, and prominent examples include EVAN's C_2-symmetric copper(II) complex **205** and LOH's indium(III) pybox complex **206** or 1,1'-bi-2-naphtol based titanium(IV) complexes **207** (*Figure 5*).[119–122] Both reaction pathways, the one leading to homoallylic alcohol **203** and the other giving non assigned compounds **202** or **204** could be optimized this way.



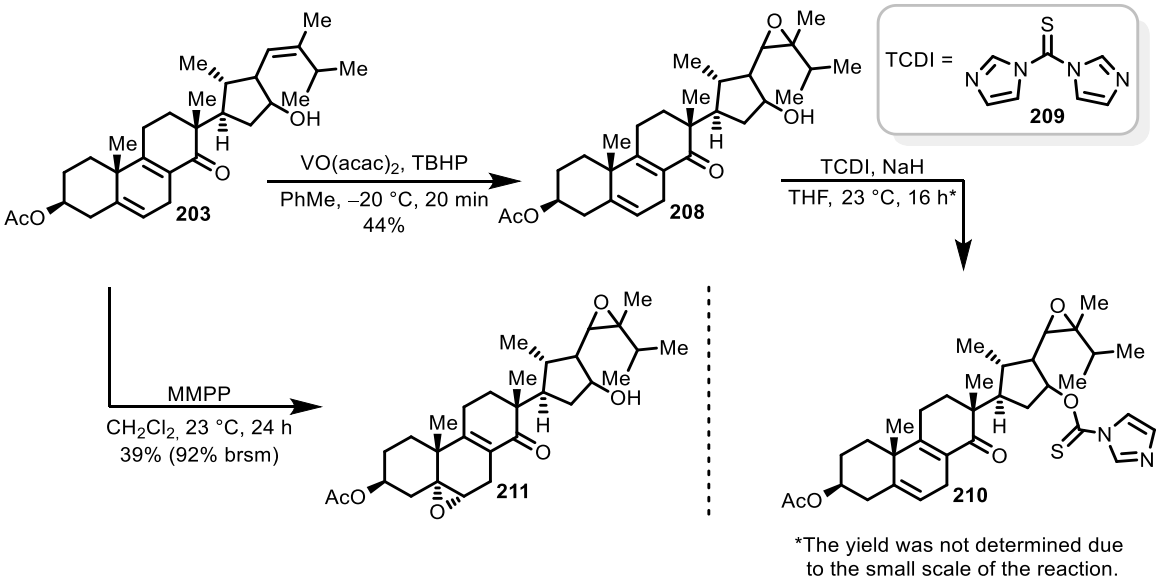
205 **206** **207**

Figure 5: Chiral LEWIS acids as reported by LOH and EVANS.

Having homoallylic alcohol **203** in hand, the desired platform to generate selective access to all strophasterols should be approachable. Although the stereo information of the C24 methyl

group was lost during the formation of the cyclopentanol, the reintroduction of the stereocenter should in principle be possible, as many methods for the asymmetric introduction of epoxides are known.[123–125]

Starting from one isomer of **203**, submission to vanadyl acetylacetonate and *tert*-butyl hydroperoxide gave the chemoselective homoallylic epoxidation product **208** as a mixture of diastereomers in 44% yield (*Scheme 48*).

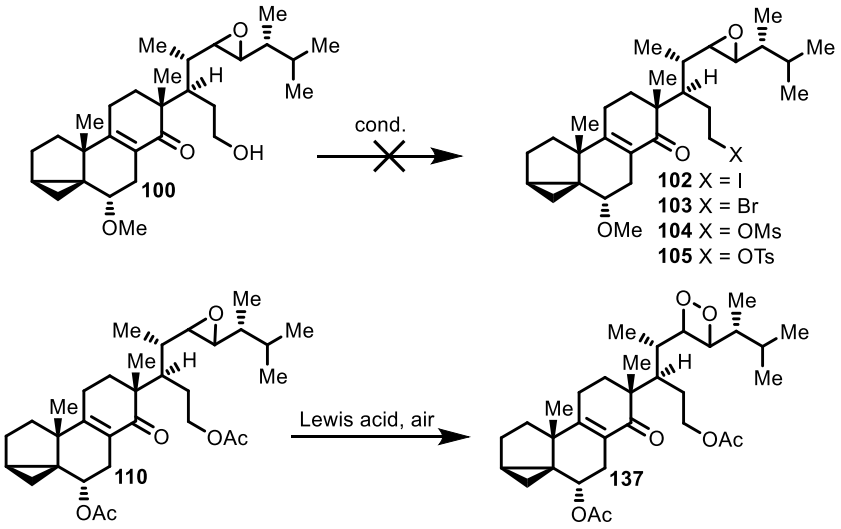


Scheme 48: Directed epoxidation of homoallylic alcohol **203** and epoxidation with MMPP.

Treatment of epoxide with thiocarbonyldiimidazole (**209**, TCDI) gave the corresponding thiooxoester **210** on analytical scale that was detected by HRMS but accompanied by the formation of numerous side products. Thus, to remove the hydroxy group at C15, the formation of the corresponding mesylate and base induced elimination or using BURGESS' reagent might be more efficient. On the other hand, using MMPP as epoxidizing agent gave, a mixture of diepoxidized compound **211** in 39% yield and 53% of reisolated starting material **203** This indicates that the chemoselective epoxidation of the Δ^5 olefin is no longer an option on this stage. Due to time limitations, no further experiments were conducted.

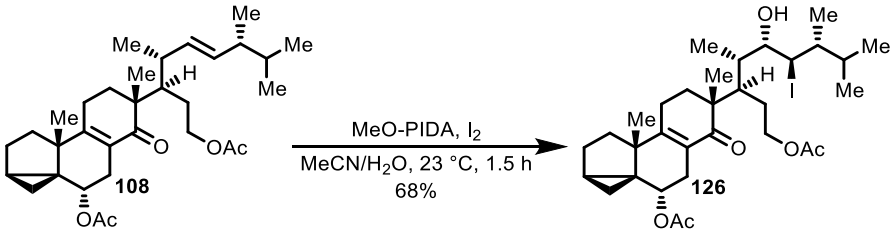
5. Summary

Although the synthesis of the desired natural products was not accomplished, many valuable intermediates, reactivity, and methods were observed en route. The presented work opens up new opportunities and possibilities for the functionalization of ergostane type side chains and with that the potential development of compounds with superior biological activities and pharmacological profile. Additionally, crucial transformations for the synthesis of the targeted platform were identified.



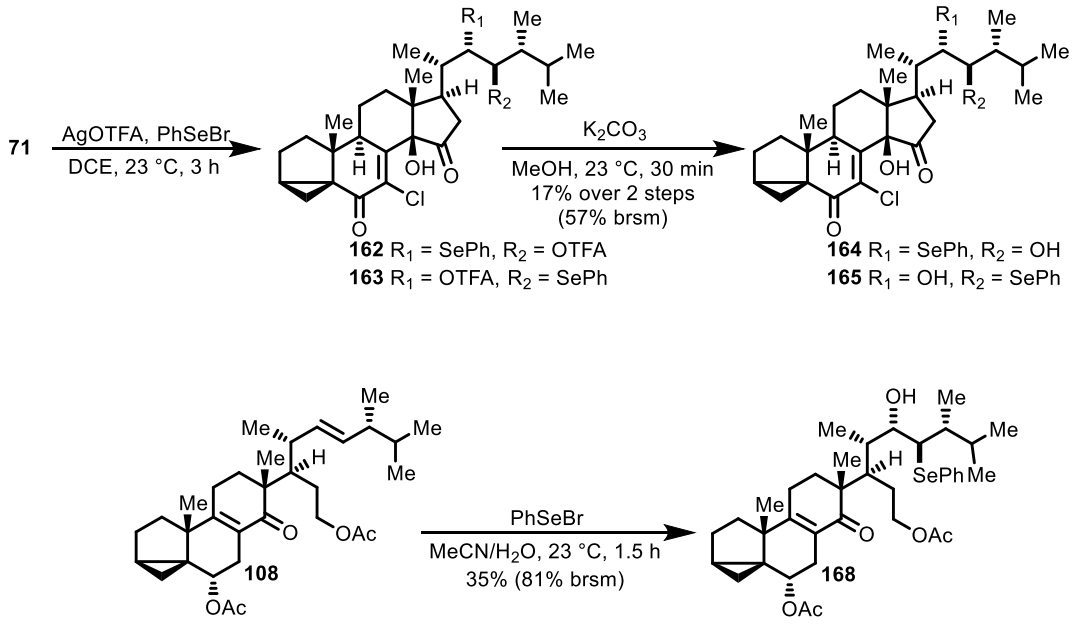
Scheme 49: Attempted formation of a C15 electrophile and formation of oxetane **138** under aerobic conditions.

The epoxidation of the ergostane side chain and subsequent opening of the epoxide with a C-centered nucleophile was not possible, as no suitable and stable precursor for a metal-halogen exchange could be synthesized and isolated. Attempted LEWIS acid mediated opening of the epoxide with a nucleophile lead to the formation of unprecedented dioxetane **137** under aerobic conditions (*Scheme 49*). The direct iodoacetoxylation of enone **69** published by BARTON et al. was not reproducible in terms of the reported yield but showed the described regio- and diastereoselectivity.



Scheme 50: Iodohydroxylation of diacetate **107**.

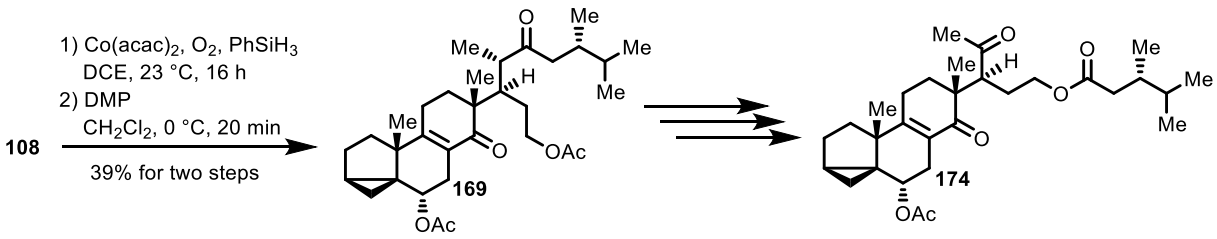
The functionalization of diacetate **108** *via* iodohydroxylation under VINOD's conditions gave a good yield of the functionalized system albeit with the undesired regioselectivity (*Scheme 52*). Any attempts for the inversion of the regioselectivity towards the desired regioisomer failed due to the superior accessibility of C22. The observed inversion probably results from additional degrees of rotational freedom upon scission of the C14,15 bond. Functionalization of earlier synthetic intermediates such as enone **69** or chloroenone **71** gave the desired products but were not optimizable to synthetically useful yields.



Scheme 51: Seleno functionalization of diacetate **108** and chloroenone **71**.

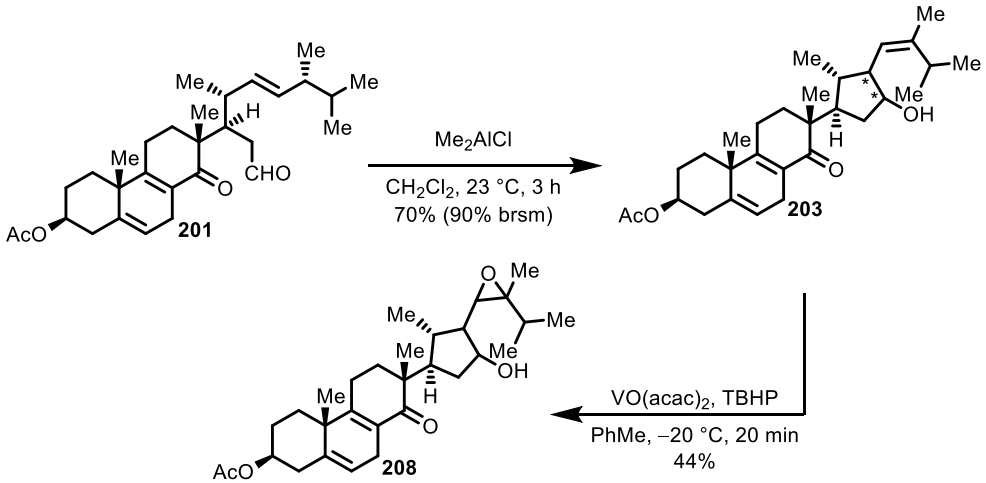
The seleno functionalization was developed as a new method for the functionalization of ergostane side chains but gave a mixture of regioisomers when applied to chloroenone **71** or the undesired regioisomer when applied to diacetate **108**, respectively (*Scheme 51*). Nevertheless, the seleno functionalization offers a relatively mild method for the stereo- and regioselective hydroxylation of the ergostane side chain. So far, the oxidation of the ergostane side chain is limited to either the epoxidation and successive opening of the epoxide under harsh conditions (lithium aluminum hydride, reflux) or its dihydroxylation.[126] Thus, the compatibility towards functional groups, especially those labile under reductive conditions is very limited. The selenohydroxylation offers more operational freedom as the introduction as well as the removal of the selenophenyl group can be achieved under very mild conditions. The regioisomers are readily separable and diasteromerically pure. Of interest would also be the use of trifluoromethylselenyl halides as trifluoromethylselenylated compounds are new compounds with interesting physicochemical properties.[127,128]

Furthermore, the method revealed, that the behavior of **108** and **71** towards various reactions conditions was different. While the MUKAIYAMA hydration reaction led to the decomposition of **71** it readily oxidized **108** and gave after oxidation with DMP ketone **169**. Saponification of the primary acetate gave a hemiacetal that rearranged to secopregnane **174** under oxidative conditions (*Scheme 52*).



Scheme 52: MUKAIYAMA hydration/oxidation sequence to ketone **169** and subsequent rearrangement to secopregnane **174**.

A biomimetic approach was then considered to install the required C23 oxidation state in a radical cyclization with subsequent oxidative quench of an intermediary secondary alkyl radical. Various methods for the generation of alkyl radicals were tested but no suitable conditions were found.

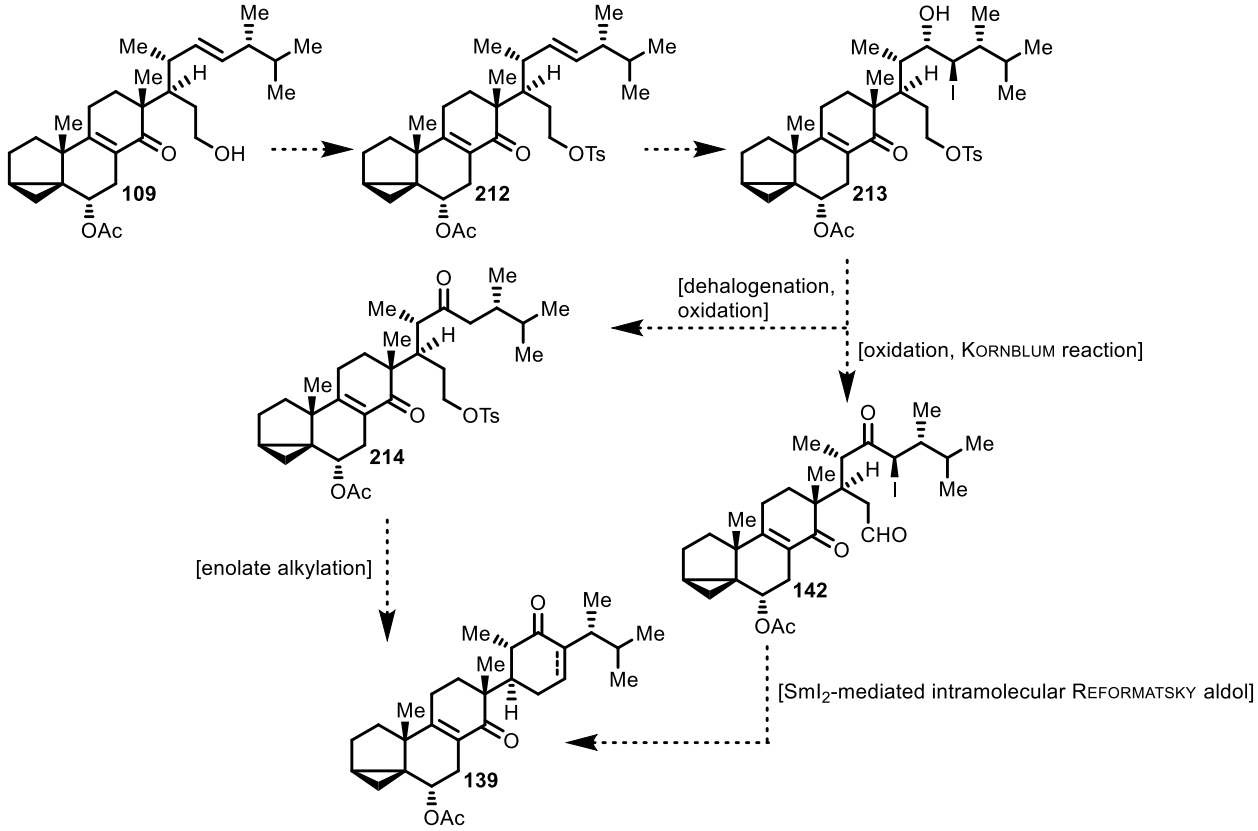


Scheme 53: Carbonyl-Ene cyclization of aldehyde **201** and chemoselective epoxidation to epoxide **208**.

Finally, aldehyde **201** was submitted to LEWIS acidic conditions and gave homoallylic cyclopentanole **203**. Further experiments gave epoxide **208** as a starting point for the synthesis of the desired platform (*Scheme 53*).

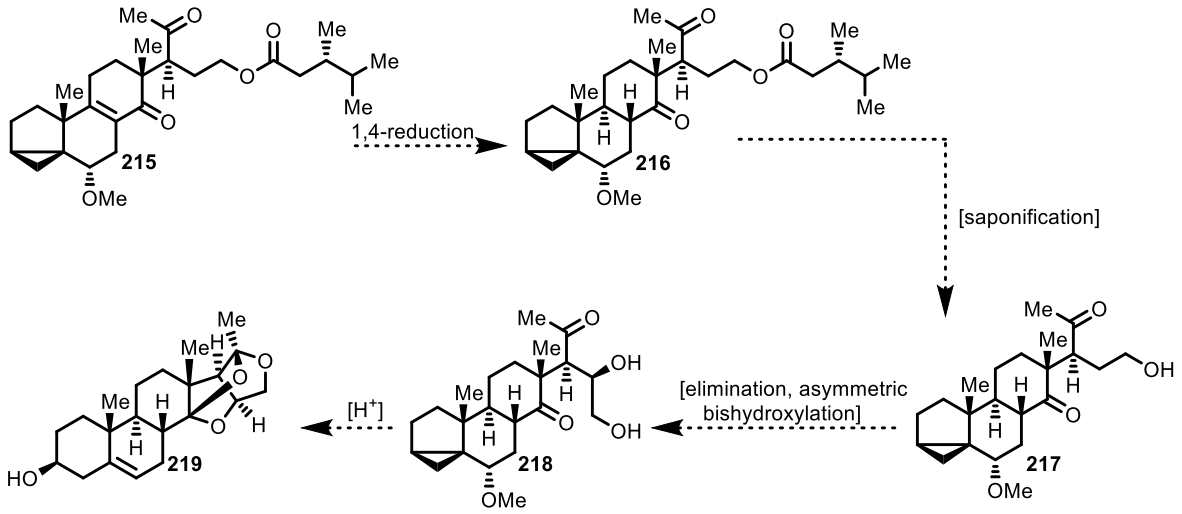
6. Outlook

The observed regioselectivity of the iodohydrin formation on acetate **108** bears the potential for the synthesis of derivatives of strophasterol C and D. Various options are possible to access the respective compounds (*Scheme 54*). The first is based on the tosylation of the primary alcohol **109** followed by the introduction of iodohydrin **213**. This would enable, after dehalogenation and oxidation to ketone **214**, a ring closure *via* enolate alkylation.[80,129] A second approach could feature the oxidation of iodohydrin **213** to the corresponding α-iodo ketone followed by the introduction of aldehyde **142** *via* KORNBLUM oxidation, as it is known, that sterically hindered halides do not react or only very slow while primary tosylates readily give the corresponding aldehydes.[130–132]



Scheme 54: Two alternative proposals for the synthesis of cyclohexanone **139**.

Interestingly, ester **170**, obtained from the oxidative rearrangement of hemiacetal **167** can be elaborated into the argeloside aglycon, a highly oxygenated secopregnane (*Scheme 55*). More than ten glycosides of argeloside aglycon have been isolated of which some show antiproliferative activity in vascular endothelial growth factor (VEGF)-induced Kaposi's sarcoma cells.

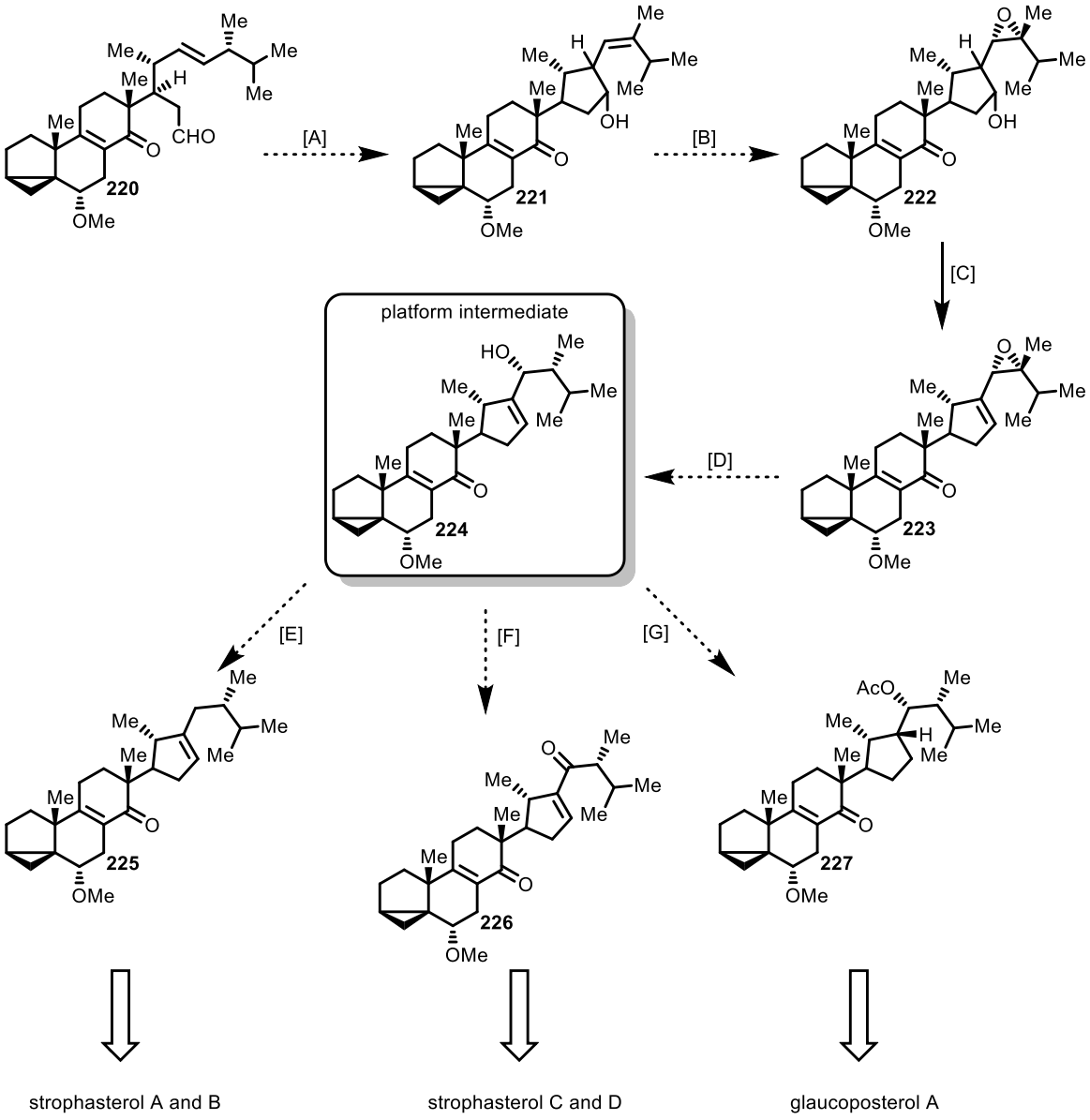


Scheme 55: Possible elaboration of **174** into the argeloside aglycon **178**.

Starting with from methyl ether **215** the 1,4-reduction of enone should give corresponding ketone **216** (*Scheme 55*). Saponification would give γ-ketol **217**. Elimination under GRIECO conditions and dihydroxylation as literature known transformations on a similar substrate to **217** should give, after treatment under aqueous, acidic conditions the desired natural product **219** *via* diol **218** in a formal synthesis.[133–136]

The formation of dioxetane **137** is an unprecedented transformation, investigations on the respective reaction mechanisms are of interest. Furthermore, identification of a potential application in chemical synthesis as well as studies on the pharmacological profile of **137** is desirable.

To achieve the synthesis of the desired platform **224**, the use of chiral LEWIS acids needs to be investigated [**A**] to preferably generate a defined relationship of the C15 hydroxy group and the C22 proton (*Scheme 56*). This way, either a *syn*-elimination under BURGESS' conditions or an E2-type elimination *via* a corresponding leaving group, e.g., mesylate or tosylate could give the $\Delta^{15(22)}$ olefin. Next, diastereoselective homoallylic epoxidation, e.g., under YAMAMOTO's conditions should give access to epoxide **222** [**B**].[123,137,138]



Scheme 56: Possible synthetic route to allylic alcohol **218**.

Elimination of the C15 alcohol under BURGESS' or related conditions should give allylic epoxide **223** that could be transformed into allylic alcohol **224** upon treatment with boron trifluoride etherate and sodium cyanoborohydride [**C**,**D**].[139,140] Allylic alcohol **224** shows all

the features of the desired platform for the synthesis of all strophasterols and glaucoposterol A. For example, the deoxygenation of **224** should give cyclopentene **225** that could be hydrogenated under different conditions. This has already been done by KUWAHARA et al. in their synthesis of strophasterol A and B to selectively generate **58** or **62** [**E**]. Opening of the *i*-steroid and adjustment of the oxidation states of the A and B ring under known conditions should furnish both epimers.[31] By oxidation of the allylic alcohol **224** to enone **226**, the missing two members of the strophasterols should be accessible by again opening of the *i*-steroid and adjustment of the oxidation states of the A and B ring [**F**]. Then, 1,4-reduction of the cyclopentanone under different conditions could give selective access to either **63** or **64**.

Finally, protection of the alcohol as the corresponding acetate **227** and stereoselective hydrogenation of the $\Delta^{15,22}$ olefin followed by the opening of the *i*-steroid and oxidation state adjustments should give, after global saponification glaucoposterol A **65** [**G**].

Part Two

7. Introduction

As modern medicine faces threats like the growing resistance of bacteria against established antibiotics, the development of new pharmaceuticals is an ongoing process. A study found that curing all types of cancer would add an average total of two years to the life expectancy of Americans, while the introduction of antibiotics added an average of ten years.[141,142] As the methicillin-resistant *Staphylococcus aureus* (MRSA) is resistant to almost all available β-lactam antibiotics, it became a serious, worldwide threat in hospitals and various types of care facilities. *Staphylococcus aureus* was identified to be the most commonly isolated human bacterial pathogen. It causes uncomplicated skin and soft-tissue infections as well as invasive infections, such as pneumonia, endocarditis, and sepsis.[143] Deaths related to MRSA infections exceed the number of HIV related deaths each year in the United States, highlighting the urgent need for new and efficient antibiotics.[144]

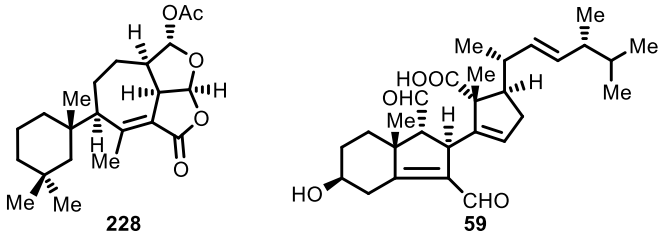


Figure 6: Structures of anti-MRSA active (+)-darwinolide and solanioic acid.

Several natural products like (+)-darwinolide **228**, a rearranged spongian diterpenoid from the Antarctic sponge *Dendrilla membranosa* isolated in 2016 and recently synthesized by CHRISTMANN et al. show the required antibiotic properties (*Figure 6*).[145,146] Other natural products that have not been synthesized to date like the rearranged steroid solanioic acid **59**, also show promising in vitro activity against MRSA and thus are valuable synthetic targets.[24] Continuous research in the field of alternative antibiotics is of great importance to cope with the increasing resistance of bacteria against established antibiotics.

8. Motivation and Objective

The 5(6→7)*abeo*-steroids are a rather small subgroup with a few reported examples such as isolated natural products and semisynthetic analogs and display an interesting class of rearranged steroids (*Figure 7*). Solanioic acid is a 5(6→7)*abeo*-11,12-secosteroid that was isolated from extracts of laboratory cultures of the fungus *Rhizoctonia solani* in 2015 by ANDERSEN et al.

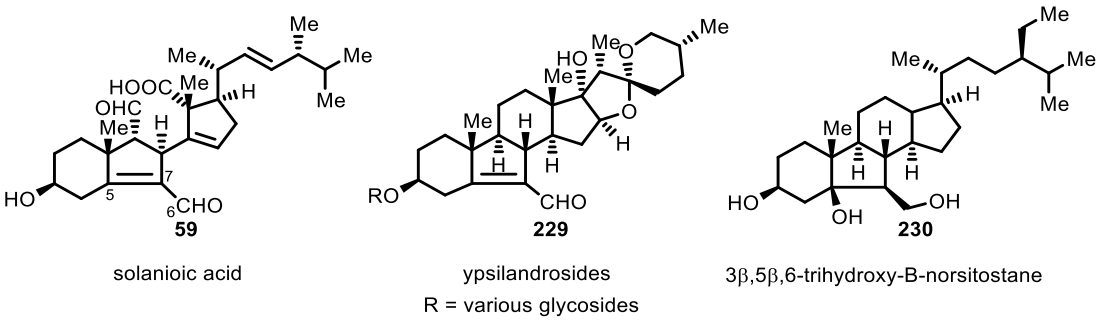
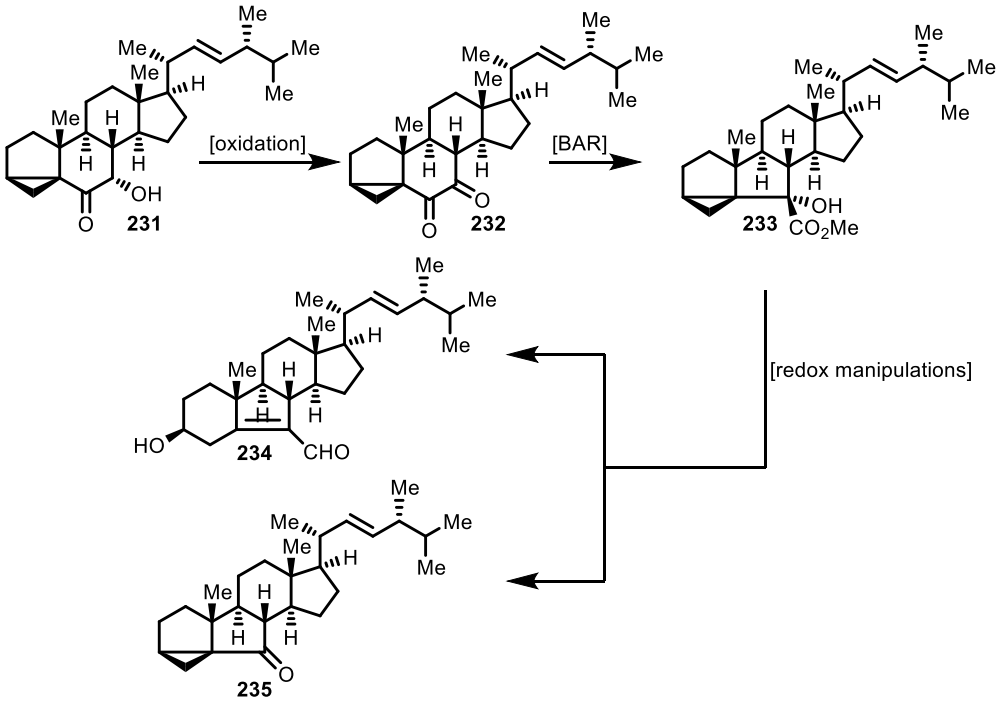


Figure 7: Examples for 5(6→7)abeo-steroids.

Determination of the in vitro antimicrobial activity showed a minimal inhibitory concentration of 1 µg/mL against Gram-positive bacteria including MRSA and *Bacillus subtilis*. Structure elucidation of **59** by X-ray crystallography revealed a dense oxidation pattern, including two aldehydes, an alcohol and an acid.



Scheme 57: Concept of the targeted methodology: oxidation to diketone **232**, benzilic acid rearrangement (BAR) and further redox manipulations.

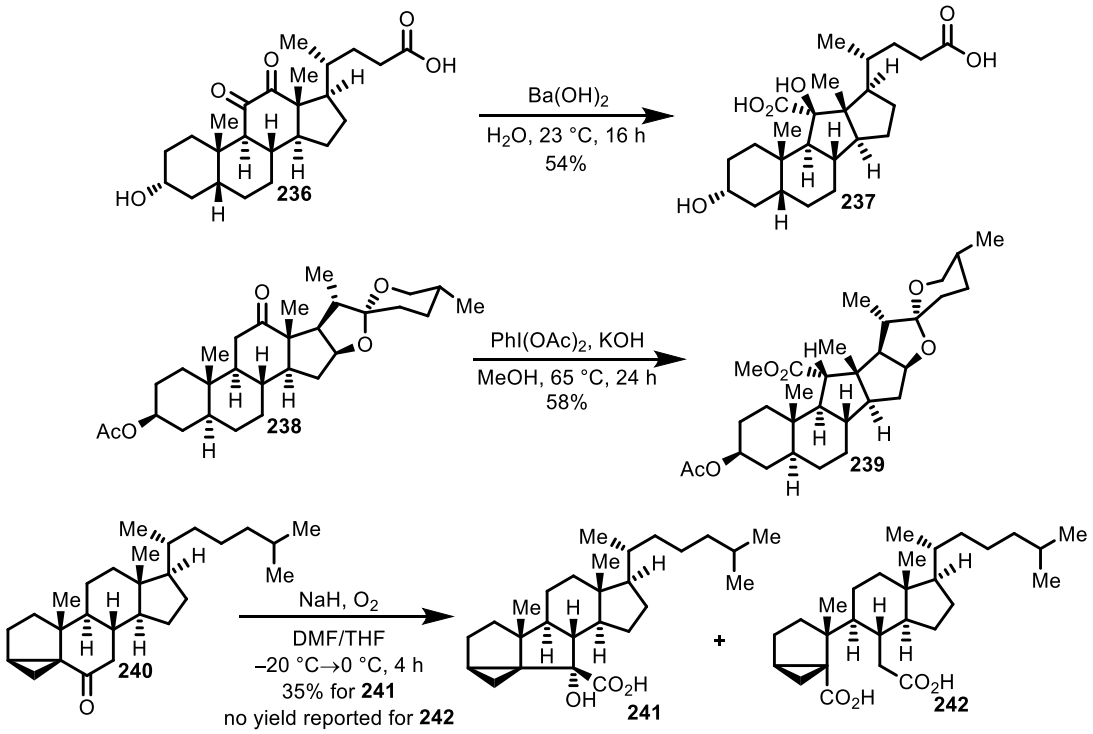
Methods for the synthetic access to B-nor-steroids are scarce and often involve a sequence of ozonolysis and aldol reaction limiting the functional group tolerance. Other methods suffer from low yields, poor reproducibility or harsh conditions.[147–149]

The goal was to develop a reliable and mild alternative to build the critical structural feature of natural products such as solanioic acid **59** or the ypsilandrosides **229** with a high degree of functional group tolerance. For an efficient access to the desired motifs, the contraction of the B-ring should proceed from readily available precursors. To achieve this, the benzilic acid rearrangement was identified as a powerful transformation, starting from the respective 6,7-diketo compounds Additionally, it was aimed to develop an improved method for the synthesis of B-nor-7-oxo steroids without the requirement for harmful and toxic reagents such as lead(IV) acetate (**235**, *Scheme 57*).[150]

9. Results and Discussion

The benzilic acid rearrangement was first observed in 1838 by VON LIEBIG and since has been subject to extensive mechanistic studies and application in synthesis.[151–154] The reaction proceeds through a base-catalyzed rearrangement of a 1,2-dicarbonyl compound to yield α-hydroxy acids or esters depending on the utilized nucleophile.

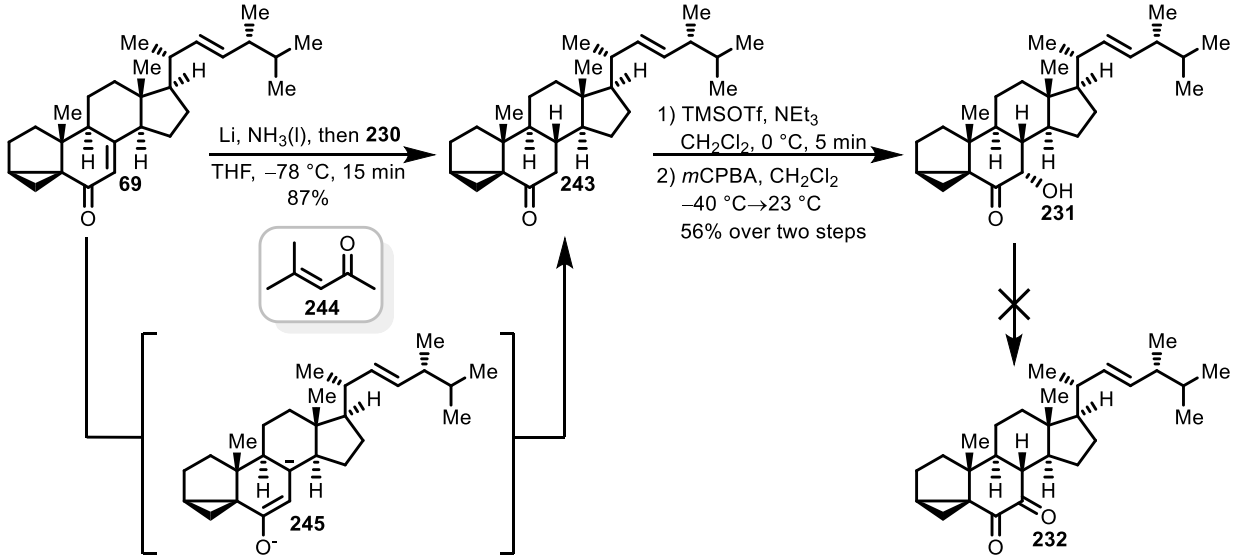
The use of this transformation to access nor-steroids was already reported in 1964 by WINTER et al. to obtain C-nor-steroids. The authors synthesized the respective 11,12-diones and initiated the benzilic acid rearrangement by the addition of barium hydroxide (*Scheme 58*, top). The methodology was then again used by MITSUHASHI et al. for the C-ring contraction and subsequent introduction of nitrogen *via* BECKMANN rearrangement. Novel access to C-nor-methyl esters without the hydroxy substituent in the α-position was provided by SÁNCHEZ-FLORES et al. who reported the access from the corresponding 12-oxo steroids using diacetoxy iodobenzene (*Scheme 58*, middle).[155–158]



Scheme 58: Known methods for the formation of C-nor steroids.

Also, the contraction of the B-ring relying on the benzilic acid rearrangement has been observed by LIANG et al. but suffered from several drawbacks: First, the generation of 6,7-diones is not trivial as they are transient species that could not be accessed or isolated in pure form.[159] Thus, they had to be synthesized in situ by autoxidation of 6-oxo steroids under strongly basic conditions (sodium hydride, oxygen) for extended reaction times (*Scheme 58*,

bottom). The formation of hydroxide ions from trace amounts of water in the solvent then initiates the benzilic acid rearrangement to give the α-hydroxy acid in a low yield of 35%.[159] To improve access to this structural motif, α-hydroxy ketone **231** was considered to be an ideal starting point, as the oxidation and direct benzilic acid rearrangement of α-ketols have been published on non-steroidal systems by STOLTZ et al.[160] Thus, starting from *i*-steroid enone **69**, α-hydroxy ketone **231** was synthesized in a sequence of BIRCH reduction and RUBOTTOM oxidation (*Scheme 59*).[161,162] Although this was a literature known sequence, some optimization was necessary, as the reported yields were not reproducible.[163] The BIRCH reduction was reported to yield 93% of the desired ketone, but the first experiment gave a low yield of 53% accompanied by the formation of undesired side products. WENDEBORN et al. optimized the transformation as they met the same problems of low yields and side-product formation.[164] It was found that the quenching of the intermediate carbanion was the most crucial part of the reaction. The addition of ammonium chloride, reported in the original publication, led to a faster protonation of the formed dianionic species **239** compared to the quenching of the excess of electrons. Ketone **238** would then be formed in a strongly reducing environment, allowing the further reaction to undesired side-products during the quenching procedure. The optimized conditions, first quenching the electrons by the addition of mesityl oxide (**240**) followed by protonation with ammonium chloride gave the desired product in 87% yield without the formation of undesired side-products.



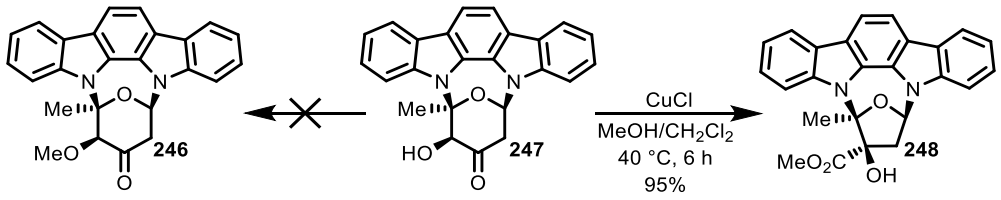
Scheme 59: Reaction sequence from enone **69** to α-ketol **231**.

Also, the α-oxidation *via* the RUBOTTOM procedure was reported to give a good yield of 87% over two steps.[163] These conditions gave the desired α-ketol, albeit in much lower yields of 42%. Attempts to optimize this transformation were made by using different reagents for the

oxidation of the silyl enol ether. Using dimethyl dioxirane, DAVIES' oxaziridine or MMPP as the oxidizing agent did not result in any improvement on the yield of α-ketol **231**.

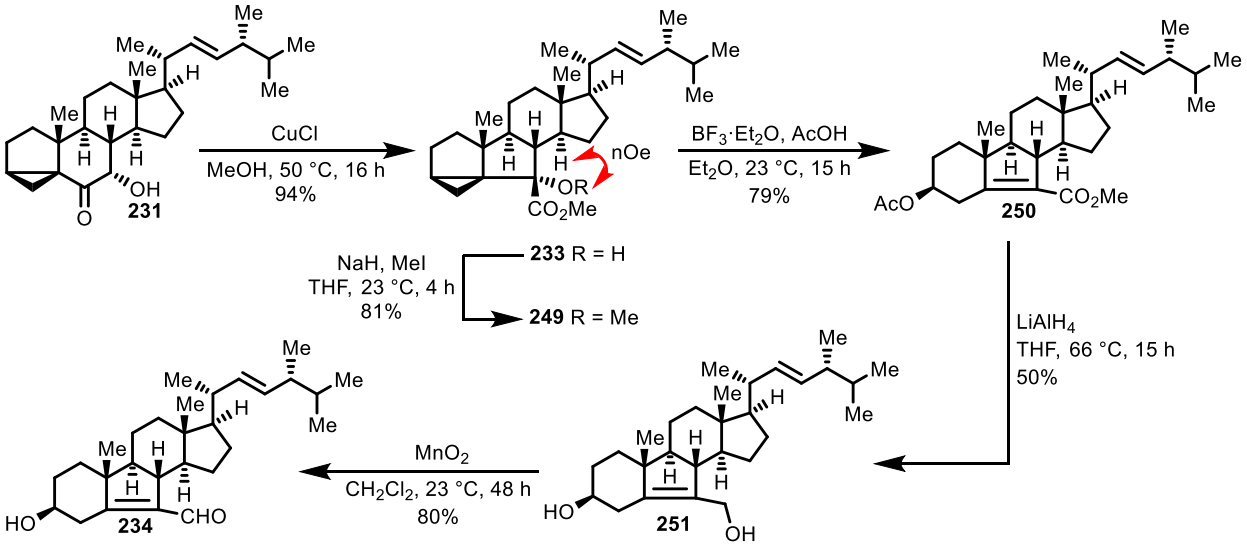
With compound **231** in hand, the direct oxidation to the corresponding dione **232** was tested under various conditions. Using pyridinium chlorochromate in dichloromethane as well as trichlorooxyvanadium under aerobic conditions did not result in the formation of the desired products probably due to the instability of the product (*Scheme 59*).[165]

Encountering these problems, the in situ oxidation to the dione followed by the direct rearrangement was envisioned. MARQUES et al. described the one pot oxidation/rearrangement of α-ketols to the corresponding α-hydroxy esters using copper(II) acetate in methanol at room temperature.[166] Applying these conditions to ketol **231** gave no observable conversion, not even at elevated temperatures or longer reaction times. A very similar reaction was described by STOLTZ et al. in 1996 while conducting experiments towards the K252a carbohydrate moiety (*Scheme 60*). Trying to find suitable conditions for the methylation of an α-hydroxy ketone, the authors applied VOWINKEL's conditions to their system and observed the clean formation of α-hydroxy ester **248** rather than the desired methoxy ketone **246**.[160,167]



Scheme 60: Desired transformation by STOLTZ et al. and observed reactivity of the system.

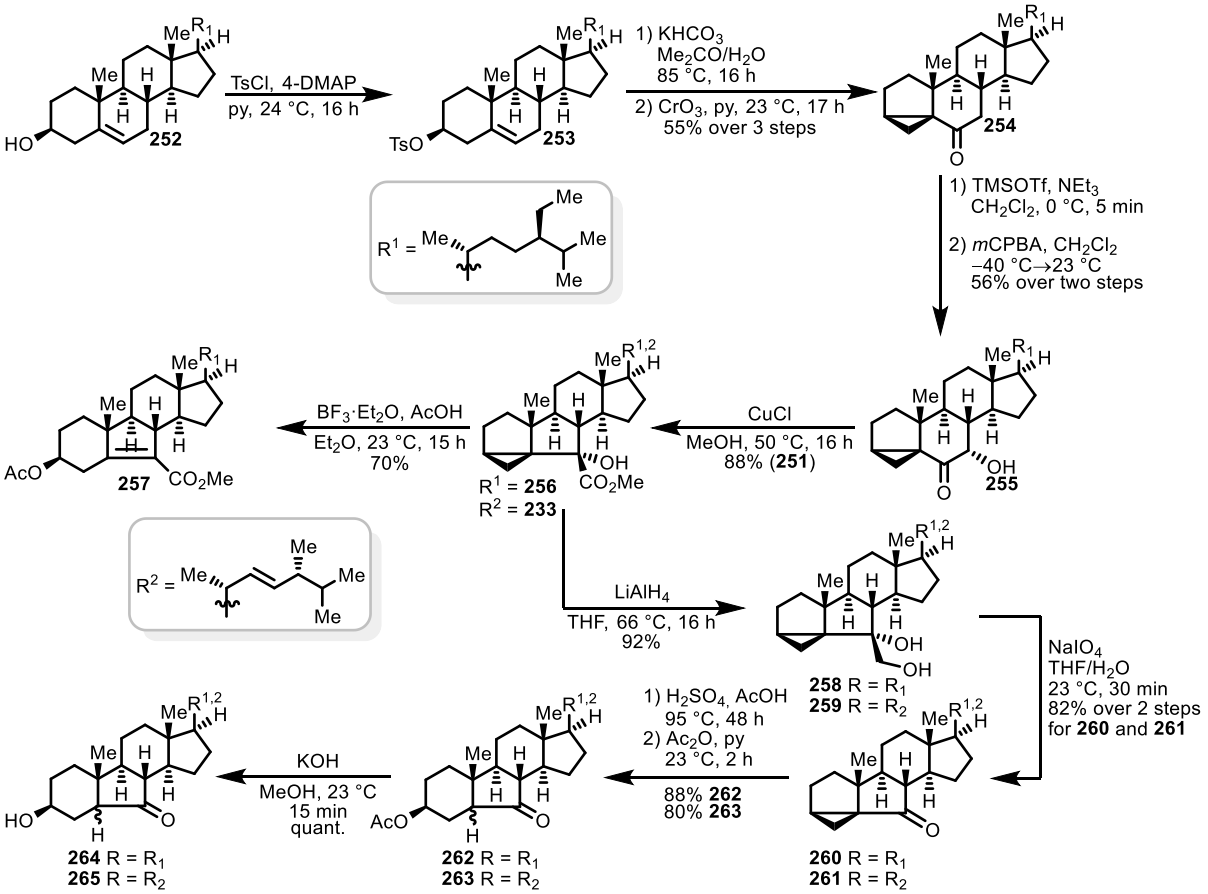
Thus, under STOLTZ' reported conditions, α-ketol **231** gave the clean formation of the desired α-hydroxy methyl ester **233** (*Scheme 61*). Formation of the corresponding methyl ether **249** and analysis of the nuclear OVERHAUSER effect (nOe) showed the cross peak between the methoxy group at C7 and H14 assigning the absolute conformation at C7 as *S*. Upon treatment of ester **233** with boron trifluoride etherate in acetic acid, the cyclopropyl moiety underwent C−C-cleavage by nucleophilic attack of the acetate on C3 and elimination of the C7-alcohol to obtain acrylic ester **250**.



Scheme 61: Synthesis of the AB-ring mimic of solanioic acid.

Attempts for the direct conversion of acrylic ester **250** to the corresponding aldehyde with diisobutyl aluminum hydride at −78 °C in toluene resulted in the reisolation of the starting material. Treating **250** with lithium aluminum hydride in refluxing tetrahydrofuran gave allylic alcohol **251** in 50% yield. Chemoselective oxidation with manganese dioxide in dichloromethane gave aldehyde **234** in 80% yield, completing the synthesis of the A, B-ring mimic of solanioic acid **59**.

Next, the substrate scope of the method was investigated starting with β-sitosterol by preparing the corresponding α-hydroxy ketone **255** (*Scheme 62*). In the same procedure as compound **231**, α-ketol **255** was synthesized and submitted to the rearrangement conditions to give α-hydroxy ester **256** in 88% yield. Subsequent opening of the *i*-steroid gave acrylic ester **257** in 70% yield. This efficient sequence provided the acrylic esters in good yields, and only three column chromatography steps were required for six synthetic transformations.

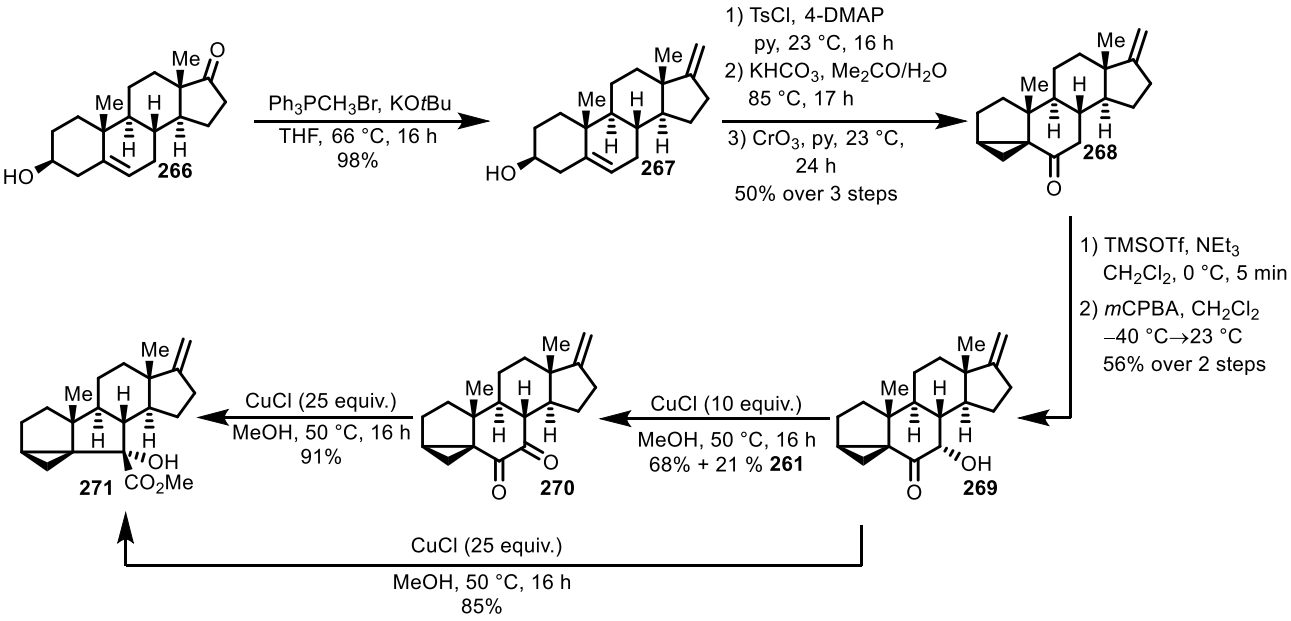


Scheme 62: Synthesis of B-nor-acrylic acids and 7-keto B-nor-steroids.

Recently, B-nor-steroids have been reported as positive modulators of γ-aminobutyric acid ($GABA_A$) receptors in the brain.[168] The 7-oxo derivatives of those B-nor-steroids were synthesized and showed a better solubility and bioavailability under physiological conditions thus making the substrates potentially more useful as positive modulators of the $GABA_A$ receptor. The syntheses of the reported compounds suffer from the same drawbacks as the previous methods for the synthesis of B-nor-steroids. To improve the synthesis of those compounds, the application of the newly developed method was envisioned. Established methods rely on the oxidative decarboxylation of the corresponding α-hydroxy-acids with lead tetraacetate and copper(II) acetate. Attempts to saponify the obtained methyl esters **233** and **256** failed under all conditions. Thus, the reduction with lithium aluminum hydride to diols **258** and **259** followed by glycol cleavage with sodium periodate gave rise to the desired ketones **260** and **261** in a good yield of 82% over two steps, with no required purification for diols **260** and **261**. Additionally, the use of toxic lead(IV) acetate was no longer a requirement, making the methods more attractive for the pharmaceutical industry. Opening of the respective *i*-steroids was realized with 2.5 N sulfuric acid in AcOH followed by acetylation of the deacetylated part of the product. Saponification with potassium hydroxide in methanol gave

the 7-oxo-B-nor sterols as an approximate 4:1 mixture of C5 diastereomers in 88% yield for **264** and 80% yield for **265** over two steps.

Next, the general applicability of the developed method was tested on several substrates (*Scheme 63*). Starting from dehydroepiandrosterone (DHEA, **266**), WITTIG olefination gave methylene derivative **267** in 98% yield in a modified, improved literature procedure.[169] Tosylation, *i*-steroid formation, and oxidation gave *i*-steroid ketone **268** in 50% yield over three steps. RUBOTTOM oxidation under the established conditions gave 38% yield of the desired α-ketol alongside with 44% of the recovered starting material, and the following rearrangement of **269** gave α-hydroxy methyl ester **271** in 85% yield.

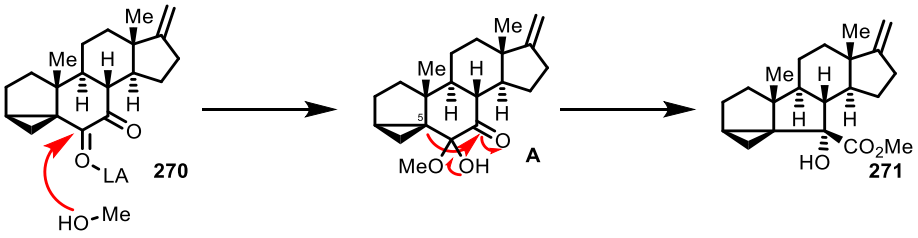


Scheme 63: Synthesis of 17-methylene substrate **268**, dione **270**, and α-hydroxymethyl ester **271**.

Interestingly, while lowering the equivalents of the copper(I) chloride in the rearrangement step, the formation of a new compound was observed. While the yield of the desired product dropped to 21%, the major product of the reaction was identified as the assumed intermediary dione **270**. For this substrate, the dione was stable and could be isolated by column chromatography. It was found to reenter the reaction path when resubmitting it to the original conditions to give α-hydroxy methyl ester **271**.

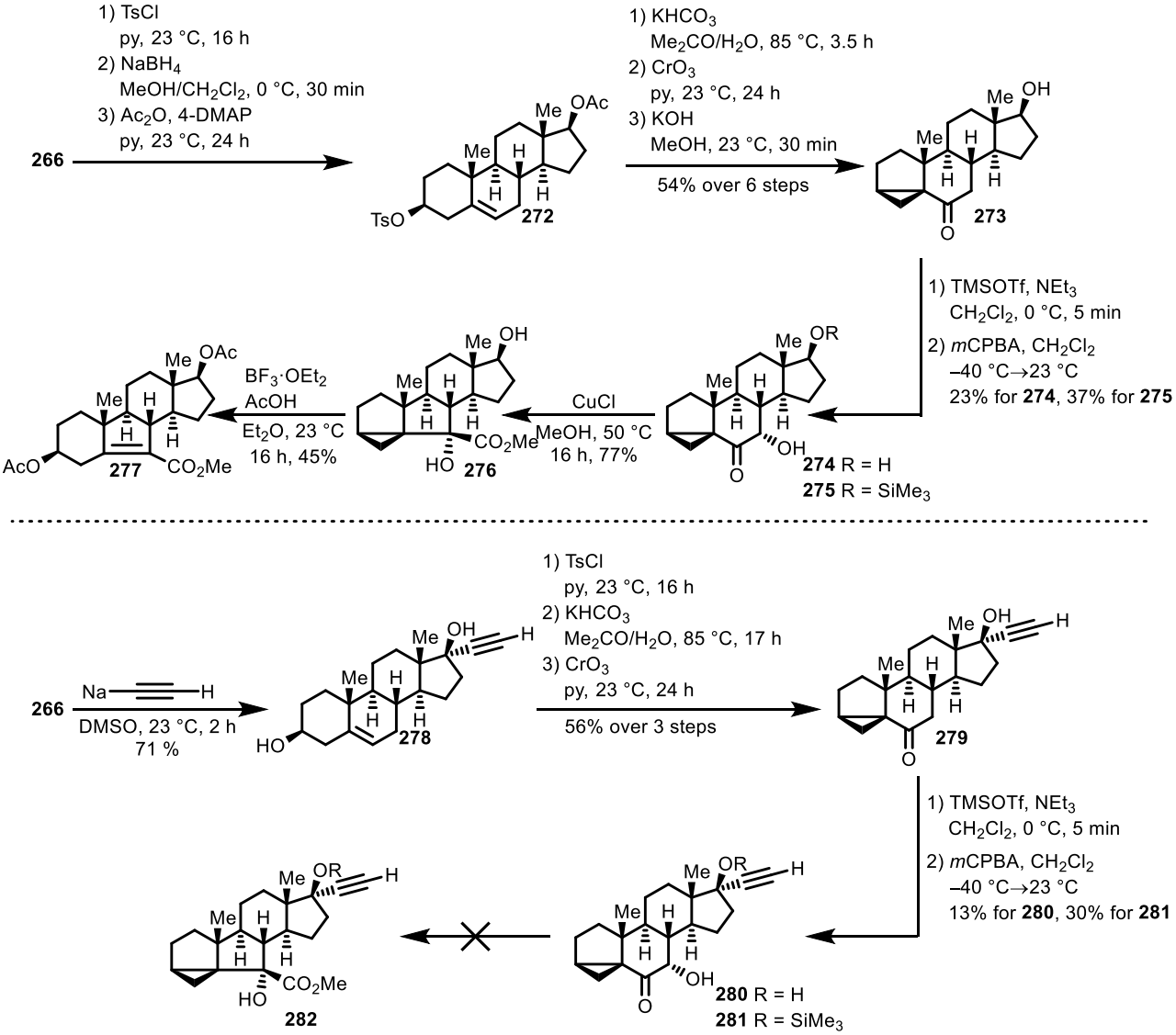
The reaction could in principle proceed *via* two mechanistic pathways, first a ring contractive α-ketol rearrangement with subsequent oxidation event, or the initially proposed benzilic acid rearrangement (*Scheme 64*). Activation of dione **270** followed by the addition of methanol gives hemiacetal **A**. Shift of C5 to C7 then gives the desired α-hydroxymethyl ester **271**. The isolated dione **270** and the transformation of it to the desired product under the reaction conditions strongly support the benzilic acid rearrangement. Also, substituting methanol with

non-nucleophilic dichloromethane resulted in the recovery of starting material and no formation of either **270** or **271**.



Scheme 64: Proposed mechanism of the benzilic acid rearrangement.

It was found that **271** failed to undergo the opening of the *i*-steroid, likely due to isomerization of the *exo* methylene group under the LEWIS acidic conditions or the occurrence of WAGNER–MEERWEIN type rearrangements.



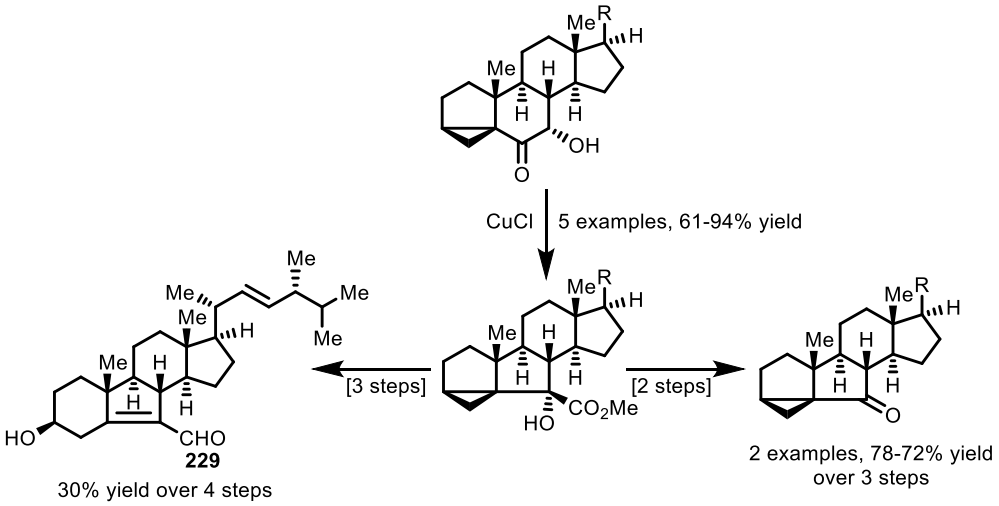
Scheme 65: Synthesis and rearrangement of 17-ethyne and 17-hydroxy sterols **274** and **280**.

Further substrates were readily accessible starting from **266** in eight and six synthetic steps respectively (*Scheme 65*, top). Substrate **273** was synthesized starting with the tosylation of the C3 alcohol, followed by reduction with sodium borohydride of the 17-oxo functionality. Acetylation, *i*-steroid formation and subsequent oxidation with chromium(VI) oxide in pyridine gave, after saponification of the C17 acetate the corresponding ketone. RUBOTTOM oxidation gave a mixture of the desired product **274** and the corresponding C17-trimethylsilyl ether **275**. The desilylation of the C17-alcohol was problematic as the silyl ether proved to be very stable. Submission of both **274** and **275** to the rearrangement conditions gave the identical product **276** in 61% and 77% yield respectively**,** as the silyl ether was cleaved at elevated temperatures under LEWIS acidic conditions. Finally, opening of the *i*-steroid gave B-nor-acrylic ester **277** in 45% yield.

The synthesis of the last substrate started with the addition of sodium acetylide to DHEA **266** followed by the same reaction sequence as before (tosylation, *i*-sterol formation, oxidation, RUBOTTOM oxidation) to give a mixture of tertiary alcohol **280** and tertiary trimethylsilyl ether **281** in 43% combined yield (*Scheme 65*, bottom). Submission of **280** to the reaction conditions resulted in the formation of a complex mixture. For substrate **281**, the TLC showed the same pattern as for the transformation of the 17-methylene substrate, indicating the formation of the desired α-hydroxy methyl ester and the corresponding dione. Elongation of the reaction time lead to the decomposition of the material with no isolation of any product. Probably, upon desilylation of the tertiary alcohol, it can act in the proximity of the alkyne in a MYER−SCHUSTER or RUPE type rearrangement.[170–172] Thus, probably by using a suitable, under the reaction conditions stable protecting group, a derivative of **280** should undergo the desired rearrangement.

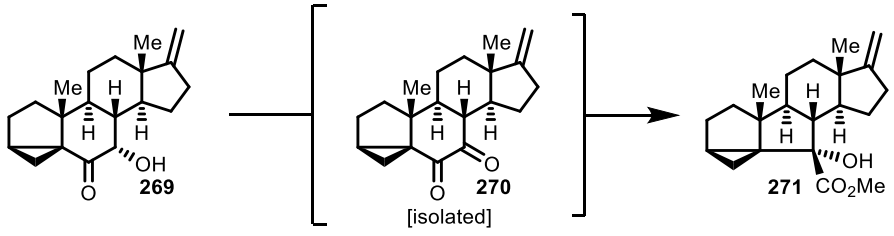
10. Summary

The developed method provides access to valuable B-nor-steroids in good to excellent yields from readily available α-hydroxy ketones. Also, due to the mild reaction conditions, a broad scope of functional groups is tolerated, most importantly additional olefinic moieties. Although alkyne substrate **280** did not give the desired rearranged product, the experimental results point towards the propargylic alcohol and competitive rearrangements, e.g., MYER-SCHUSTER or RUPE-type, as the reason. Thus, employing an appropriate protecting group substrate **280** should undergo the rearrangement (*Scheme 66*).



Scheme 66: Rearrangement of steroidal α-ketols to the respective abeo-steroids and further elaboration to α,β-unsaturated aldehyde **234** and 7-oxo-B-nor steroids.

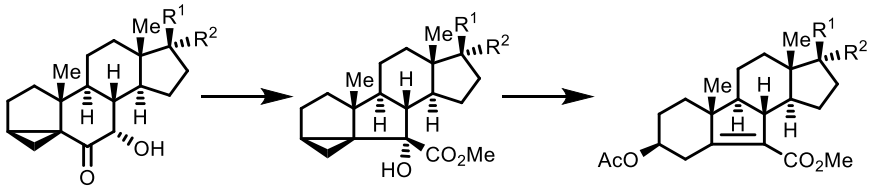
A broad scope of substrates with additional olefinic moieties smoothly underwent the rearrangement and gave the desired products in good to excellent yields (*Scheme 66, Table 10*). Additionally, isolation of diketone **270** evidentiary supported the benzilic acid rearrangement as the mechanistic proposal (*Scheme 67*).

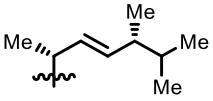
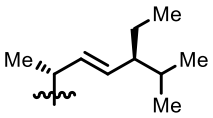
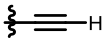
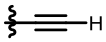


Scheme 67: Isolation of the intermediary diketone **270**.

The synthesis of B-nor-7-oxo compounds is now possible without the need for toxic reagents such as lead(IV) acetate and gives the desired compounds in good overall yields with few required chromatographic steps and from abundant starting materials (*Table 10*).

Table 10: Summary of the rearranged systems and *i*-steroid opening and the respective yields.



Entry	R^1	R^2	Yield [%] for the rearrangement	Yield [%] for the *i*-steroid opening
1		H	94	79
2		H	88	70
3	OH	H	61	42
4	OTMS	H	83	-
5	OH		-	-
6	OTMS		-	-
7		-	85	-

11. Outlook

The mild access to B-nor-steroids should enable the synthetic access to several natural products like solanioic acid **59** or 3β,5β,6-trihydroxy-B-norsitostane **230**, a recently isolated compound (*Figure 8*).[173]

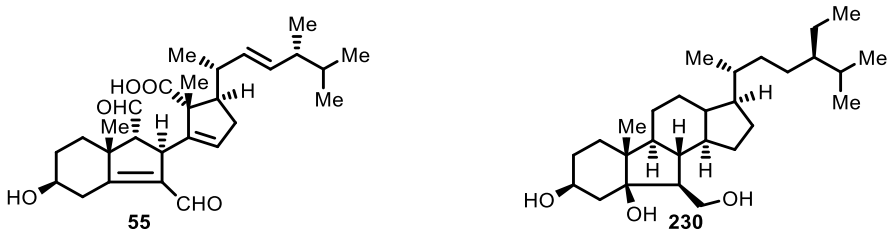
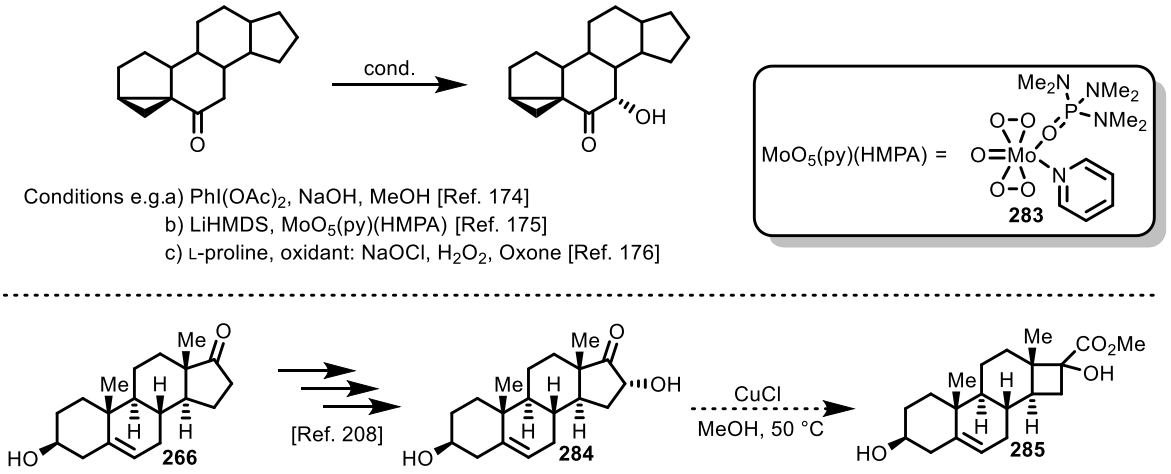


Figure 8: Potentially accessible natural products **59** and **230**.

For further improvement, a higher yielding access to the corresponding α-hydroxy ketones needs to be found, as the application of the RUBOTTOM oxidation is only giving acceptable yields. Other methods for the α-hydroxylation of ketones, e.g., hypervalent iodine(III) reagents (a), VEDEJS' reagent **283** (b) or the organocatalytic α-oxidation (c) that have not been tested so far need to be evaluated (*Scheme 68*, top).[174–176]



Scheme 68: Possible improvement for the α-ketol formation (*top*) and desired application of the method for the synthesis of D-abeo-steroids (*bottom*).

Furthermore, advancements in the synthesis of D-nor-steroids should be made as current methods require multiple steps and suffer from low yields.[177–179] Also, studies on the biological activity of D-nor-steroids need to be undertaken as their evaluation is scarce. Starting from **266**, the respective compounds should be accessible in a few synthetic steps (*Scheme 68*, bottom).[180]

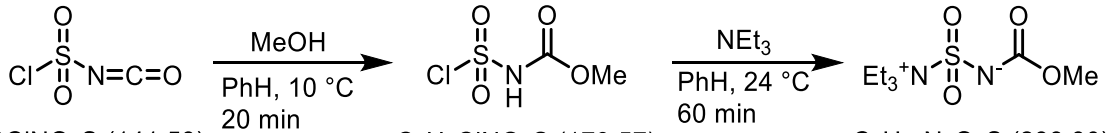
Experimental Part

12. General Information

All reactions sensitive to moisture and/or air were carried out using heat-gun dried glassware, an argon atmosphere, and anhydrous solvents. Anhydrous dichloromethane and diethyl ether were prepared by an M. Braun GmbH MB SPS-800 solvent purification system. Anhydrous toluene and methanol were purchased from Acros (extra dry quality). Ethyl acetate and *n*-hexane were purified by distillation on a rotary evaporator. All other solvents and commercially available reagents were used without further purification unless otherwise stated. Reactions were monitored by TLC carried out on Merck Silica Gel 50 F245 plates and visualized by fluorescence quenching under UV light, or an aqueous solution of cerium sulfate and phosphomolybdic acid, or ceric ammonium molybdate (CAM), or an acidic methanolic solution of vanillin and heat as the developing agent. Column chromatographic purifications were performed on Macherey-Nagel Silica Gel 60 M (40–60μm) and preparative TLC was performed on Merck Silica Gel 50 F245-plates. Concentration under reduced pressure was performed by rotary evaporation at 40 °C and the appropriate pressure and subsequent exposure to vacuum (1 x 10^{-3} mbar) at 25 °C. NMR spectra were recorded on either a Jeol ECX400 (400 MHz), a Jeol ECP500 (500 MHz), a BrukerAVANCE III 500 (500 MHz), a Varian INOVA 600 (600 MHz) or a BrukerAVANCE III 700 (700 MHz,with CryoProbe) spectrometer. Chemical shifts were calibrated by using the residual un-deuterated solvent signals ($CDCl_3$: ^1H, $\delta = 7.26$; ^{13}C, $\delta = 77.16$; CD_3OD: ^1H, $\delta = 3.31$; ^{13}C, $\delta = 49.00$) as internal reference at 298 K and are reported in ppm. The given multiplicities are phenomenological; thus the actual appearance of the signals is stated and not the theoretically expected one. In case no multiplicity could be identified, the chemical shift range of the signal is given. IR spectra were measured on a Jasco FT/IR-4100 Type A spectrometer with a TGS detector. HRMS was carried out by using an Agilent 6210 ESI-TOF or an Ionspec QFT-7 ESI-TOF spectrometer. Optical rotations were measured on a JASCO P-2000 polarimeter at 589 nm by using 100 mm cells; the solvent and concentration (g/100 mL) are indicated. Melting points were measured on a Stuart SMP30 melting point apparatus and are uncorrected.

13. Synthesis of Reagents

BURGESS' reagent



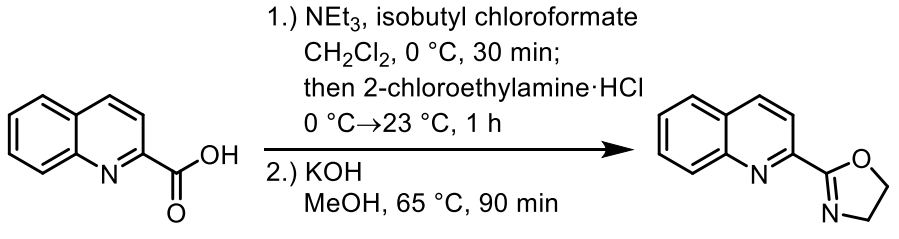
$CClNO_3S$ (141.53) **286** | $C_2H_4ClNO_4S$ (173.57) **287** | $C_8H_{18}N_2O_4S$ (238.30) **288**

To chlorosulfonyl isocyanate (3.0 mL, 35 mmol, 1.0 equiv.) in benzene (19 mL) was added MeOH (2.2 mL, 55 mmol, 1.6 equiv.) in benzene (3 mL) dropwise while cooling in a water bath. After 20 min, the solvent was removed under reduced pressure to yield methyl (chlorosulfonyl)carbamate as a colorless solid that was immediately dissolved in benzene (75 mL). The solution of the carbamate was then added dropwise to a solution of triethylamine (11 mL, 76 mmol, 2.2 equiv.) in benzene (19 mL) over 60 min at 24 °C. The precipitate of triethylamine hydrochloride was removed by filtration, and the solvent was removed under reduced pressure to yield BURGESS' reagent (6.0 g, 25 mmol, 73%) as a colorless solid that was used without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ [ppm] = 3.68 – 3.65 (m, 3H), 3.45 (qt, *J* = 7.3, 1.5 Hz, 6H), 1.39 (tt, *J* = 7.3, 1.7 Hz, 9H).

The spectroscopic data match those reported in the literature.[181]

2-(Quinolin-2-yl)-4,5-dihydrooxazole



$C_{10}H_7NO_2$ (173.17) **289** | $C_{12}H_{10}N_2O$ (198.23) **290**

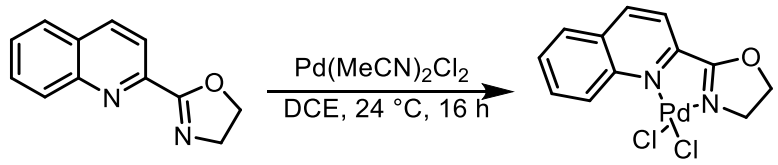
4-Methoxyquinaldic acid (0.33 g, 1.6 mmol, 1.0 equiv.) in CH_2Cl_2 (16 mL) was cooled to 0 °C in an ice bath. Triethylamine (0.62 mL, 4.4 mmol, 2.75 equiv.), followed by isobutyl chloroformate (0.24 mL, 1.8 mmol, 1.15 equiv.), were added dropwise to the mixture and stirred at 0 °C for 30 min when 2-chloroethylamine hydrochloride (0.22 g, 1.9 mmol, 1.15 equiv.) was added in one portion. The solution stirred for an additional 10 min at 0 °C, warmed to room temperature and monitored for consumption of starting material. Once all

the starting material was consumed, most of the dichloromethane was removed under reduced pressure. Methanol (10 mL) was added, along with potassium hydroxide pellets (0.45 g, 8.0 mmol, 5.0 equiv.). The solution was heated to 65 °C for 90 min, cooled to room temperature and CH_2Cl_2 (20 mL) was added. The organic phase was washed with water (20 mL) and the aq. phase was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phases were washed with sat. aq. NH_4Cl (25 mL), sat. aq. NaCl (25 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, CH_2Cl_2/MeOH 95:5) to yield quinox ligand **290** (322 mg, 1.62 mmol, 86%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ [ppm] = 8.25 (ddd, *J* = 16.1, 8.5, 0.9 Hz, 2H), 8.16 (d, *J* = 8.6 Hz, 1H), 7.84 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.75 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.60 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 4.60 (t, *J* = 9.4 Hz, 2H), 4.19 (t, *J* = 9.6 Hz, 2H).

The spectroscopic data match those reported in the literature.[98]

Pd(Quinox)Cl_2

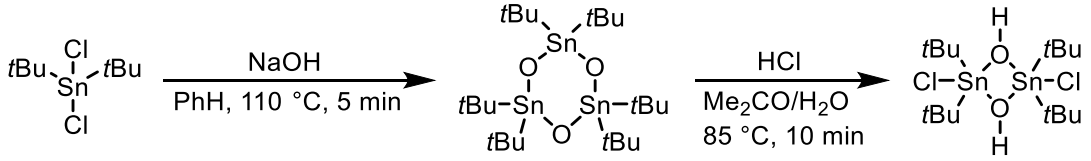


$C_{12}H_{10}N_2O$ (198.23)
290

$C_{12}H_{10}Cl_2N_2OPd$ (375.55)
291

Quinoline-2-oxazoline (0.10 g, 0.52 mmol, 1.04 equiv.) was dissolved in dichloroethane (3.5 mL) and $Pd(CH_3CN)_2Cl_2$ (0.13 g, 0.50 mmol, 1.0 equiv.) was added. The reaction mixture was allowed to stir for 16 h at 24 °C. The formed precipitate was filtered off and dried under vacuum to yield Pd(quinox)Cl_2 (0.18 g, 0.48 mmol, 99%) as an orange powder. The complex was used without further analysis.

Dichlorotetrakis(1,1-dimethylethyl)di-μ-hydroxyditin



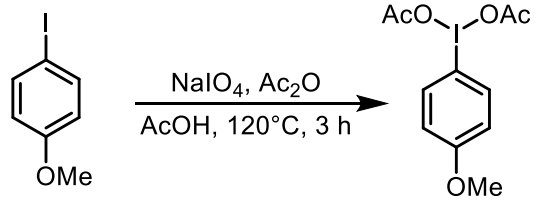
$C_8H_{18}Cl_2Sn$ (303.84) **292** | $C_{24}H_{54}O_3Sn_3$ (746.82) **293** | $C_{16}H_{38}Cl_2O_2Sn_2$ (570.80) **111**

Di-*tert*-butyldichlorostannane (500 mg, 1.6 mmol, 1.0 equiv.) was dissolved in toluene (10 mL) and heated to 110 °C. At this temperature, sodium hydroxide (700 µL, 5.0 M, 2.2 equiv.) was added dropwise and the mixture was allowed to stir at the same temperature for 5 min. The mixture was cooled to r.t. and water (3 mL) was added. The organic phase was separated and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was recrystallized from toluene to yield 2,2,4,4,6,6-hexa-*tert*-butyl-1,3,5,2,4,6-trioxatristanninane **293** (307 mg, 0.411 mmol, 62%) as a crystalline, colorless solid.

293 (307 mg, 0.411 mmol, 1.0 equiv.) was dissolved in acetone (10.2 mL) and water (1.02 mL) was added. The mixture was heated to 85 °C and hydrochloric acid (100 µL, 37%) was added and the mixture was allowed to stir at the same temperature for 10 min. The mixture was cooled to ambient temperature to yield colorless crystals. The solid was removed by filtration and recrystallized from acetone to give catalyst **111** (100 mg, 0.18 mmol, 29%) as a colorless crystalline solid.

The compound was used without further characterization as obtained. It was synthesized as described in the literature.[50]

p-(diacetoxyiodo)-Anisole



C_7H_7IO (234.04) **127** | $C_{11}H_{13}IO_5$ (352.12) **128**

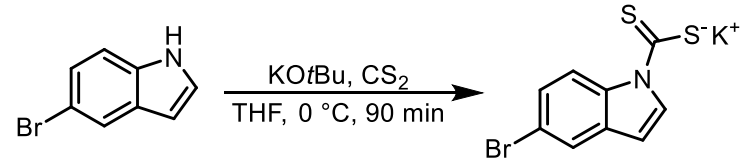
A stirred suspension of $NaIO_4$ (1.1 g, 5.1 mmol, 1.0 equiv.) and sodium acetate (0.90 g, 10 mmol, 2.0 equiv.) in glacial acetic acid (7.5 mL) and acetic anhydride (0.76 g, 7.4 mmol, 1.5 equiv.) at 23 °C was treated with 4-iodoanisole (1.2 g, 5.0 mmol, 1.0 eq). The resulting mixture was heated to 120 °C for 3 h. After cooling to 24 °C, water (20 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried

over $MgSO_4$ and concentrated under reduced pressure. The residue was treated with a mixture of hexane (30 mL) and glacial acetic acid (0.1 mL). After 30 min of sonication, the solid was filtered and dried under vacuum to obtain *p*-(diacetoxyiodo)-anisole **128** (1.1 g, 3.0 mmol, 60%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ [ppm] = 8.05 – 7.97 (m, 2H), 6.99 – 6.93 (m, 2H), 3.86 (s, 3H), 1.99 (s, 6H).

The spectroscopic data match those reported in the literature.[182]

Potassium 5-bromo-1*H*-indole-1-carbodithioate



C_8H_6BrN (196.05) **192** → $C_9H_5BrKNS_2$ (310.27) **191**

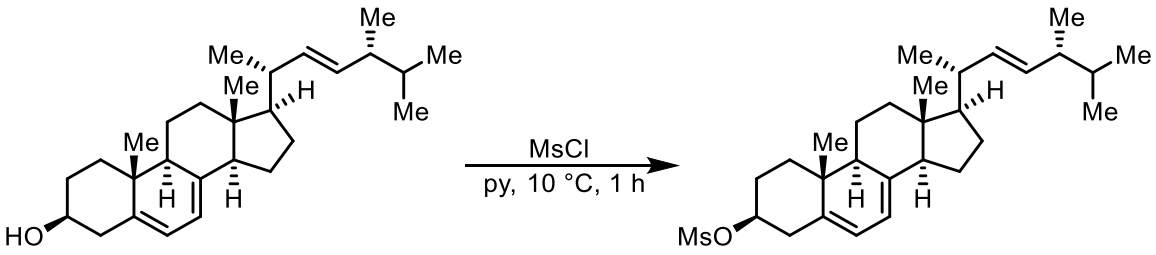
To 5-bromoindole (500 mg, 2.55 mmol, 1.0 equiv.) in THF (5 mL) was added potassium *tert*-butoxide (315 mg, 2.81 mmol, 1.1 equiv.) at 0 °C. After stirring at the same temperature for 60 min, carbon disulfide (231 µL, 3.83 mmol, 1.5 equiv.) was added dropwise. The resulting mixture was allowed to stir at the same temperature for 60 min. After warming to ambient temperature, the THF was removed under reduced pressure to obtain a thick slurry. Toluene (3 mL) was added and removed under reduced pressure to obtain a yellowish solid. The so-obtained solid was suspended in a 1:1 mixture of pentane/diethyl ether (5 mL) and stirred vigorously to generate a fine suspension. The suspension was filtered, washed with pentane/diethyl ether and dried under vacuum overnight to obtain **191** (523 mg, 1.69 mmol, 66%) as a yellow powder.

^{1}H NMR (500 MHz, DMSO-*d6*) δ [ppm] = 9.27 (d, *J* = 9.0 Hz, 1H), 8.68 (d, *J* = 3.6 Hz, 1H), 7.67 (d, *J* = 2.1 Hz, 1H), 7.24 (dd, *J* = 9.0, 2.2 Hz, 1H), 6.37 (dd, *J* = 3.6, 0.8 Hz 1H).

The spectroscopic data match those reported in literature.[113]

14. Part One

Ergosterol mesylate



$C_{28}H_{44}O$ (396.66)
4

$C_{29}H_{46}O_3S$ (474.74)
294

Ergosterol (15.0 g, 37.8 mmol, 1.0 equiv.) was dissolved in pyridine (300 mL) at 10 °C. Mesyl chloride (14.6 mL, 190 mmol, 5.0 equiv.) was added dropwise and the mixture was stirred for 1 h at the same temperature. The resulting precipitate of pyridinium hydrochloride was filtered off and the filtrate was added to ice/water (500 mL). The precipitate was filtered in a Büchner funnel and washed with water (3 x 100 mL). The filter cake was compressed into the funnel using a syringe stamp to obtain a dense and smooth surface. The cake was then washed with water (5 x 200 mL) and dried to yield **294** (17.6 g, 43.7 mmol, 98%) as a colorless solid which was used in the next step without further purification.

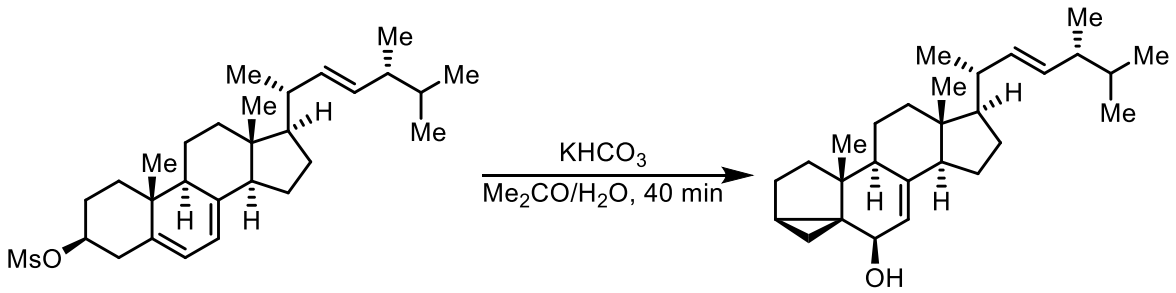
NOTE!: It is crucial for the success of the following reaction to remove all traces of Py·HCl from the mesylate, as it decomposes the starting material even in traces. Measure a ^{1}H NMR (30 mg, 64 scans) to make sure no Py·HCl* is left.

^{1}H NMR (500 MHz, $CDCl_3$) δ [ppm] = 5.60 (dd, *J* = 5.7, 2.3Hz, 1H), 5.39 (dt, *J* = 5.3, 2.6 Hz, 1H), 5.23 (dd, *J* = 15.2, 7.1 Hz, 1H), 5.17 (dd, *J* = 15.2, 7.8 Hz, 1H), 4.63 (tt, *J* = 11.4, 4.7 Hz, 1H), 3.02 (s, 3H), 2.65 (ddd, *J* = 14.4, 5.1, 2.4 Hz, 1H), 2.62 – 2.50 (m, 1H), 2.15 – 1.21 (m, 18H), 1.03 (d, *J* = 6.6 Hz,3H), 0.95 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.62 (s, 3H).

^{1}H NMR* Py·HCl (500 MHz, $CDCl_3$) δ [ppm] = 9.01 – 8.91 (m, 2H), 8.54 – 8.46 (m, 1H), 8.05 – 7.98 (m, 2H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-3*α*,5-Cyclo-5*α*-ergosta-7,22-dien-6β-ol



$C_{29}H_{46}O_3S$ (474.74)
295

$C_{28}H_{44}O$ (396.66)
296

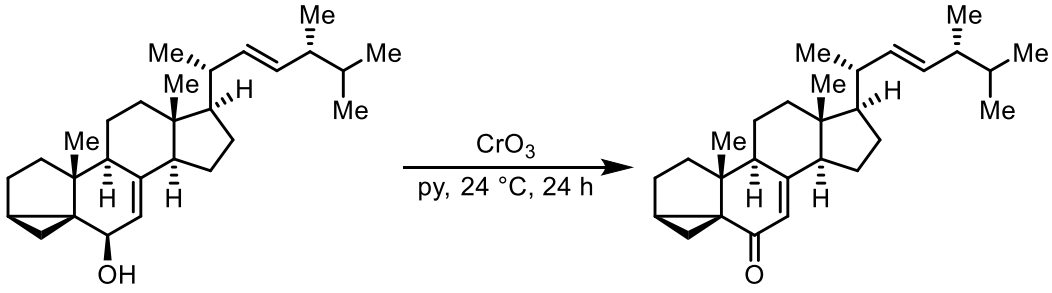
Mesylate **295** (9.40 g, 19.8 mmol, 1.0 equiv.) was added in portions to a refluxing solution of potassium hydrogen carbonate (1.98 g, 19.8 mmol, 1.0 equiv.) in Me_2CO/H_2O (287 mL). After stirring for 40 min under reflux, water (170 mL) was added and the mixture was cooled to 0 °C. The precipitate was filtered off and washed with water (100 mL) and dried under vacuum to yield *i*-sterol **296** (7.70 g, 19.5 mmol, 98%) as a brownish solid which was used in the next step without further purification.

NOTE!: It is essential for the success of the reaction to meet the exact concentration and equivalents. Mesylate that sticks to the flask needs to be rinsed into the reaction with the minimal amount of Me_2CO/H_2O (4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ [ppm] = 5.52 – 5.42 (m, 1H), 5.23 (dd, *J* = 15.2, 7.3 Hz, 1H), 5.17 (dd, *J* = 15.3, 8.1 Hz, 1H), 3.42 (s, 1H), 2.10 – 1.18 (m, 20H), 1.08 (s, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.66 – 0.60 (m, 4H), 0.48 (dd, *J* = 7.9, 5.0 Hz, 1H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-3*α*,5-Cyclo-5*α*-ergosta-7,22-dien-6-one



$C_{28}H_{44}O$ (396.66) **296**

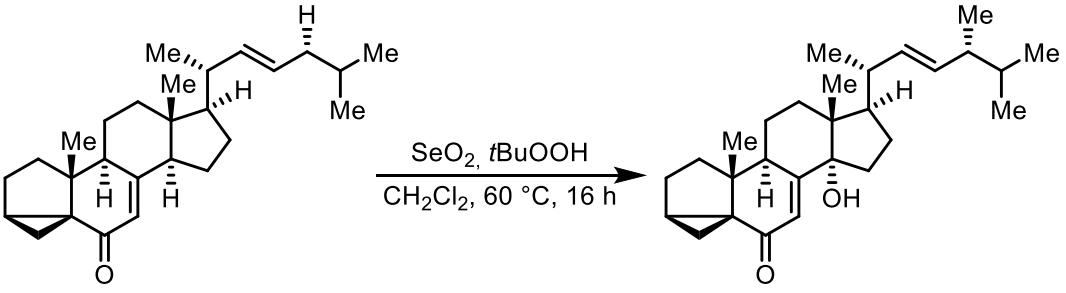
$C_{28}H_{42}O$ (394.64) **69**

CrO_3 (8.50 g, 85.5 mmol, 4.0 equiv.) was added in portions to pyridine (85 mL) cooled by a water bath. The resulting yellow solution was added to *i*-sterol **296** (8.50 g, 21.4 mmol, 1.0 equiv.) in pyridine (85 mL) *via* Teflon tube. After stirring at 24 °C for 24 h, Et_2O (280 mL) was added and the resulting mixture was filtered over Celite® and rinsed with Et_2O (3 x 150 mL). The filtrate was washed with water (2 x 100 mL), sat. aq. NaCl (150 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue recrystallized form acetone. The residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1) to give enone **69** (5.02 g, 12.7 mmol, 60%) as a crystalline solid.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.82 (t, *J* = 2.2 Hz, 1H), 5.27 (dd, *J* = 15.3,7.6 Hz, 1H), 5.20 (dd, *J* = 15.7, 8.3 Hz, 1H), 2.28 (ddd, *J* = 11.7, 7.2, 2.3 Hz, 1H), 2.19 – 2.05(m, 3H), 2.00 (tdd, *J* = 12.3, 8.0, 4.4 Hz, 1H), 1.93 – 1.85 (m, 1H), 1.84 – 1.64 (m, 8H), 1.58 –1.47 (m, 2H), 1.47 – 1.33 (m, 3H), 1.19 – 1.13 (m, 1H), 1.12 (s, 3H), 1.07 (d, *J* = 6.6 Hz, 3H),0.95 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* =6.8 Hz, 3H), 0.85 (d, *J* =6.7 Hz, 3H), 0.78 (t, *J* =4.6 Hz,1H), 0.71 (s, 3H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-14*α*-Hydroxy-3*α*,5-cyclo-5*α*-ergosta-7,22-dien-6-one



$C_{28}H_{42}O$ (394.64)
69

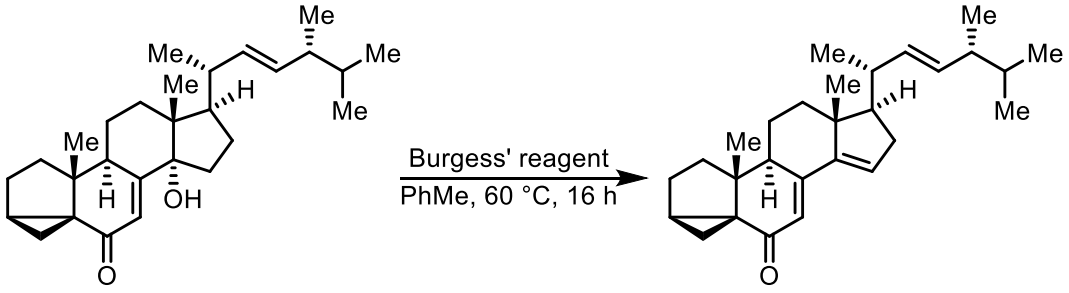
$C_{28}H_{42}O_2$ (410.64)
297

In a pressure tube, SeO_2 (830 mg, 7.40 mmol, 0.5 equiv.) was suspended at 0 °C in CH_2Cl_2 (13 mL) and *tert*-butyl hydroperoxide (70% aq., 8.30 mL, 59.7 mmol, 4.0 equiv.) was added dropwise. After stirring at 24 °C for 15 min, enone **69** (5.90 g, 14.9 mmol, 1.0 equiv.) in CH_2Cl_2 (16 mL) was added. The tube was sealed and stirred at 60 °C for 16 h. The mixture was allowed to cool to ambient temperature and was slowly added to $NaHSO_3$ (10% aq., 150 mL) at 0 °C. The mixture was extracted with EtOAc (2 x 200 mL) and the organic phase was washed with sat. aq. $NaHCO_3$ (200 mL), sat. aq. NaCl (200 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure, the residue was adsorbed to silica gel (50 g) and submitted to column chromatography (SiO_2, *n*hexane/EtOAc 5:1) to give γ-hydroxy enone **297** (4.61 g, 11.2 mmol, 75%) as a yellowish solid.

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.97 (d, *J* = 2.7 Hz, 1H), 5.27 (dd, *J* = 15.2, 7.6 Hz, 1H), 5.20 (ddd, *J* = 15.2, 8.5, 0.9 Hz, 1H), 2.79 – 2.75 (m, 1H), 2.13 – 1.84 (m, 7H), 1.80 (dt, *J* = 8.8, 4.6 Hz, 1H), 1.75 – 1.65 (m, 6H), 1.55 (ddd, *J* = 13.7, 9.8, 5.1 Hz, 1H), 1.48 (qd, *J* = 6.8, 5.7 Hz, 1H), 1.43 (s, 1H), 1.43 – 1.37 (m, 1H), 1.15 – 1.11 (m, 1H), 1.10 (s, 3H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.79 (t, *J* = 4.7 Hz, 1H), 0.76 (s, 3H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-3*α*,5-Cyclo-5*α*-ergosta-7,14,22-trien-6-one



$C_{28}H_{42}O_2$ (410.64)
297

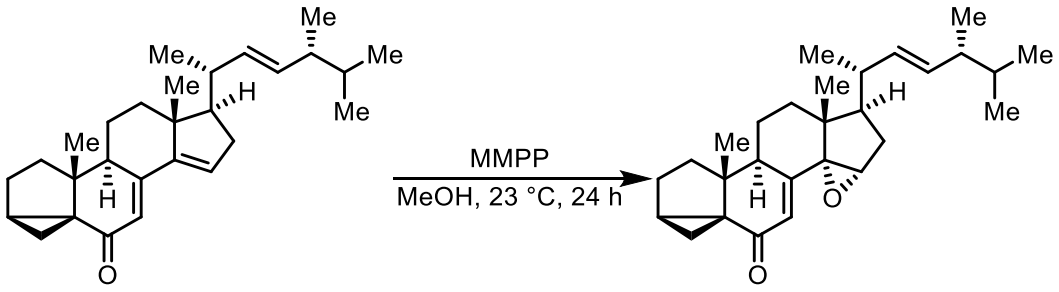
$C_{28}H_{40}O$ (392.63)
298

To a solution of γ-hydroxy enone **297** (4.61 g, 11.2 mmol, 1.0 equiv.) in toluene (110 mL) was added Burgess' reagent (3.72 g, 15.5 mmol, 1.4 equiv.). After stirring at 60 °C for 16 h, the mixture was allowed to cool to ambient temperature, diluted with EtOAc (150 mL) and washed with sat. aq. $NaHCO_3$ (200 mL). The aqueous phase was extracted with EtOAc (2 x 100 mL) and the combined organic phases were washed with sat. aq. NaCl (200 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1) to yield dienone **298** (3.90 g, 9.90 mmol, 90%) as a colorless, crystalline solid.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 6.27 (d, *J* = 2.8 Hz, 1H), 6.07 (dd, *J* = 3.7, 2.2 Hz, 1H), 5.32 (dd, *J* = 15.2, 7.7 Hz, 1H), 5.23 (dd, *J* = 15.2, 8.2 Hz, 1H), 2.39 (ddd, *J* = 12.3, 6.0, 2.7 Hz, 1H), 2.36 – 2.25 (m, 2H), 2.13 (dt, *J* = 13.1, 3.5 Hz, 1H), 2.11 – 1.96 (m, 2H), 1.95 – 1.87 (m, 1H), 1.86 – 1.69 (m, 7H), 1.59 – 1.42 (m, 2H), 1.20 – 1.14 (m, 1H), 1.12 (s, 3H), 1.08 (d, *J* = 6.6 Hz, 3H), 1.00 (s, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 7.1 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.80 (t, *J* = 4.7 Hz, 1H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-14,15α-Epoxy-3α,5-cyclo-5α-ergosta-7,22-dien-6-one



$C_{28}H_{40}O$ (392.63)
298

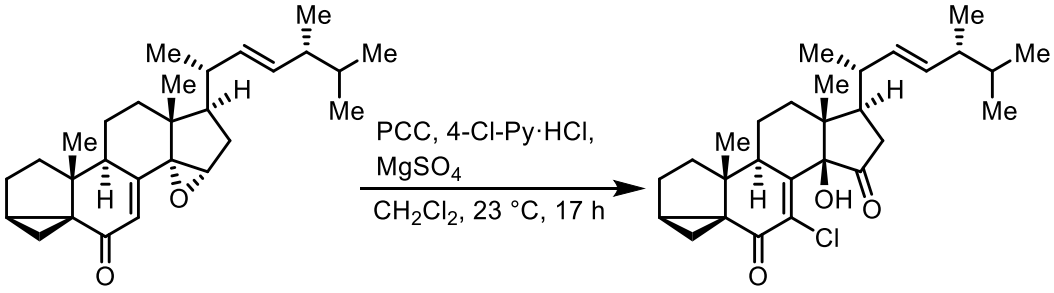
$C_{28}H_{40}O_2$ (408.63)
70

To a suspension of **298** (2.92 g, 7.44 mmol, 1.0 equiv.) in MeOH (300 mL) was added magnesium monoperoxyphthalate (80%, 4.50 g, 9.30 mmol, 1.1 equiv.). After stirring at 23 °C for 24 h, water (70 mL) was added and the methanol was removed under reduced pressure. The residue was added to sat. aq. $NaHCO_3$ (50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic phases were sequentially washed with sat. aq. $NaHCO_3$ (100 mL), sat. aq. NaCl (100 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1→6:1) to yield epoxide **70** (2.20 g, 5.44 mmol, 72%) as a colorless, crystalline solid and recovered dienone **298** (450 mg, 1.15 mmol, 15%).

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.91 (d, *J* = 2.8 Hz, 1H), 5.24 (dd, J = 15.3, 7.8 Hz, 1H), 5.11 (dd, J = 15.2, 8.7 Hz, 1H), 3.79 (s, 1H), 2.61 – 2.54 (m, 1H), 2.07 – 1.93 (m, 4H), 1.90 – 1.66 (m, 8H), 1.47 (qd, J = 6.8, 5.8 Hz, 1H), 1.40 – 1.27 (m, 2H), 1.18 – 1.09 (m, 1H), 1.13 (s, 3H), 0.99 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H), 0.85 (s, 3H), 0.83 (d, J = 6.8 Hz, 3H), 0.82 (d, J = 6.8 Hz, 3H), 0.78 (t, J = 4.8 Hz, 1H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-7-Chloro-14β-hydroxy-3*α*,5-cyclo-5*α*-ergosta-7,22-diene-6,15-dione



$C_{28}H_{40}O_2$ (408.63)
70

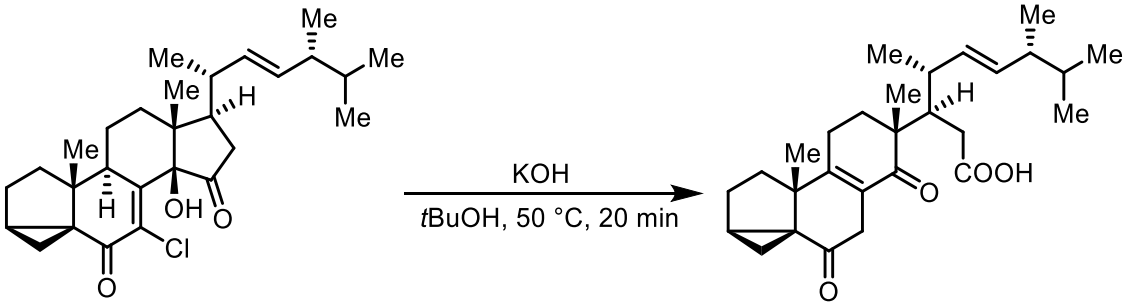
$C_{28}H_{39}ClO_3$ (459.07)
71

Epoxide **70** (2.55 g, 6.24 mmol, 1.0 equiv.) in CH_2Cl_2 (19 mL) was added to a suspension of pyridinium chlorochromate (5.38 g, 25.0 mmol, 4.0 equiv.), magnesium sulfate (5.41 g) and 4-chloropyridine hydrochloride (5.62 g, 37.4 mmol, 6.0 equiv.) in CH_2Cl_2 (42 mL). After stirring at 23 °C for 16 h, Et_2O (150 mL) was added and the resulting mixture was filtered over Celite® and rinsed with Et_2O (2 x 50 mL). The filtrate was concentrated under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield **71** (2.86 g, 4.61 mmol, 73%) as a yellowish foam.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.30 (dd, *J* = 15.2, 7.8Hz, 1H), 5.17 (dd, *J* = 15.3, 8.6Hz, 1H), 3.07 (dd, *J* = 11.2, 6.7Hz, 1H), 2.51 (dd, *J* = 18.7, 6.8Hz, 1H), 2.28 (dd, *J* = 18.7, 11.2Hz, 1H), 2.23 – 2.08 (m, 4H), 2.00 (tdd, *J* = 12.2, 7.8, 4.3Hz, 1H), 1.94 – 1.73 (m, 7H), 1.64 (dd, *J* = 13.6, 7.7Hz, 1H), 1.49 (qd, *J* = 6.8, 6.5Hz, 1H), 1.15 (ddd, *J* = 13.5, 11.5, 7.5Hz, 1H), 1.09 (s, 3H), 1.08 (d, *J* = 6.5Hz, 3H), 1.04 (s, 3H), 0.92 (d, *J* = 6.8Hz, 3H), 0.84 (d, *J* = 6.7Hz, 3H), 0.83 (d, *J* = 6.5Hz, 3H), 0.81 (t, *J* = 4.8Hz, 1H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-6,14-Dioxo-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dien-15-oic acid



$C_{28}H_{39}ClO_3$ (459.07)
71

$C_{28}H_{40}O_4$ (440.62)
72

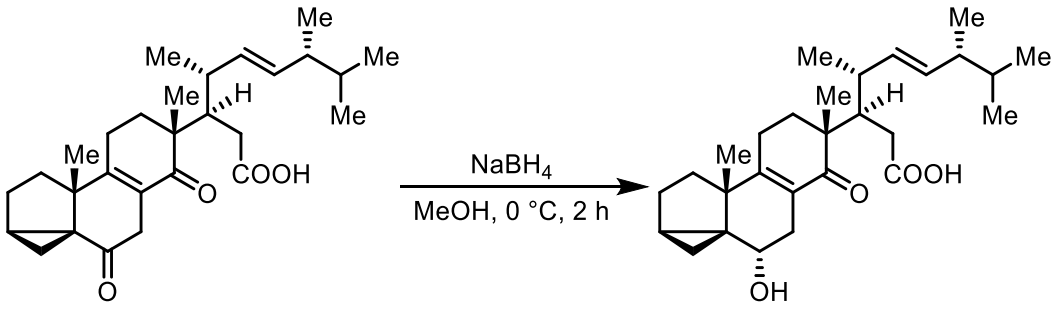
Finely ground potassium hydroxide (1.75 g, 31.1 mmol, 5.0 equiv.) in *t*-butanol (42.3 mL) was heated to 50 °C. After 10 min at that temperature chloroenone **71** (2.86 g, 6.23 mmol, 1.0 equiv.) was added. Stirring was continued for 20 min at 50 °C. The mixture was allowed to cool to ambient temperature and water (50 mL) was added. The pH was adjusted to 3 with aq. HCl (1 M) and more water (200 mL) was added. The aq. phase was extracted with EtOAc (2 x 100 mL) and the combined organic extracts were washed with sat. aq. NaCl (150 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield carboxylic acid **72** (2.75 g, 6.23 mmol, quant.) as a yellow foam which was used without further purification.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.32 – 5.24 (m, 2H), 3.39 (dd, *J* = 21.1, 1.2 Hz, 1H), 2.81 (dt, *J* = 21.1, 3.3 Hz, 1H), 2.61 – 2.53 (m, 1H), 2.52 – 2.44 (m, 1H), 2.44 – 2.38 (m, 1H), 2.37 – 2.32 (m, 1H), 2.31 – 2.24 (m, 3H), 2.10 (dd, *J* = 14.1, 7.0 Hz, 1H), 1.88 – 1.66 (m, 6H), 1.46 (qd, *J* = 6.8, 6.4 Hz, 1H), 1.24 – 1.19 (m, 1H), 1.18 (s, 3H), 1.03 (d, *J* = 7.0 Hz, 3H), 1.01 (s, 3H), 0.99 – 0.97 (m, 1H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H).

The spectroscopic data match those reported in literature.[31]

NOTE!: It is essential for the success of the reaction to completely precipitate the product by addition of water before extraction, otherwise the product forms an enol and cannot be used further.

(22*E*)-6*α*-Hydroxy-14-oxo-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dien-15-oic acid



$C_{28}H_{40}O_4$ (440.62)
72

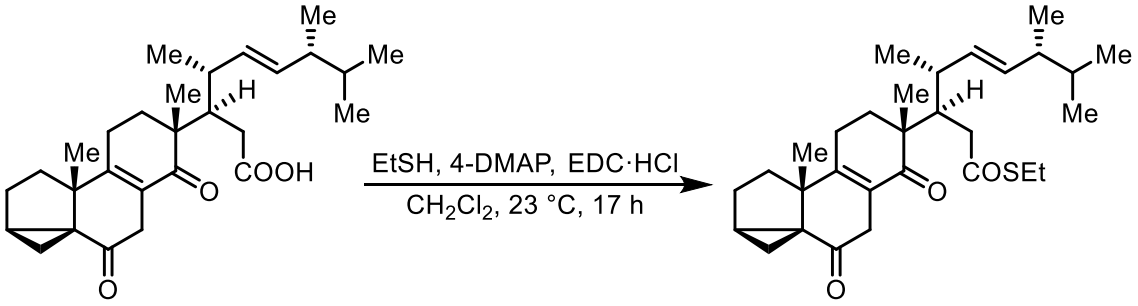
$C_{28}H_{42}O_4$ (442.64)
91

To carboxylic acid **72** (624 mg, 1.42 mmol, 1.0 equiv.) in MeOH (14 mL) at 0 °C was added sodium borohydride (536 mg, 14.2 mmol, 10.0 equiv.) in portions. After stirring at 0 °C for 2 h, the pH was adjusted to 3 by addition of aq. HCl (1 M). Water (100 mL) was added and the aq. phase was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with sat. aq. NaCl (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; CH_2Cl_2/MeOH 19:1) to yield 6-hydroxy carboxylic acid **91** (522 mg, 1.18 mmol, 83%) as a colorless, crystalline solid.

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.28 (dd, *J* = 15.3, 7.9 Hz, 1H), 5.22 (dd, *J* = 15.4, 7.7 Hz, 1H), 4.07 (dd, *J* = 10.3, 5.7 Hz, 1H), 3.06 (dd, *J* = 16.5, 5.6 Hz, 1H), 2.59 (p, *J* = 7.4 Hz, 1H), 2.47 (dd, *J* = 17.9, 9.3 Hz, 1H), 2.41 – 2.34 (m, 1H), 2.31 (d, *J* = 9.3 Hz, 1H), 2.26 – 2.12 (m, 3H), 1.90 – 1.76 (m, 3H), 1.71 (td, *J* = 13.2, 4.4 Hz, 1H), 1.67 – 1.55 (m, 2H), 1.52 – 1.44 (m, 2H), 1.26 (s, 1H), 1.22 (s, 3H), 1.20 – 1.11 (m, 1H), 1.07 – 0.99 (m, 4H), 0.97 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.40 (t, *J* = 4.3 Hz, 1H).

The spectroscopic data match those reported in literature.[31]

_S_-Ethyl (22_E_)-6,14-dioxo-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-diene-15-thioate



$C_{28}H_{40}O_4$ (440.62)
72

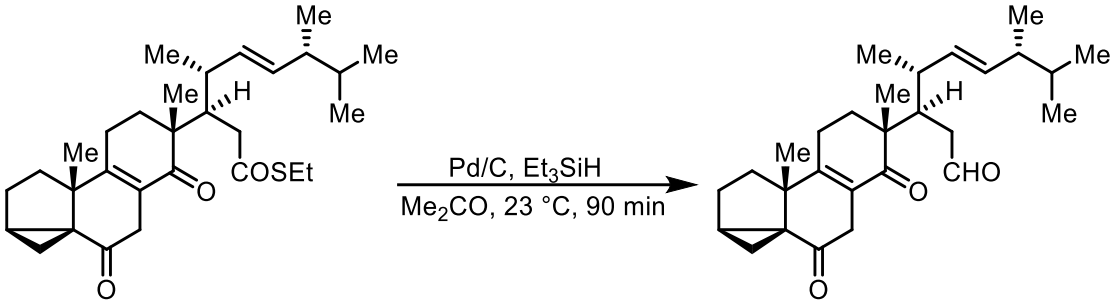
$C_{30}H_{44}O_3S$ (484.74)
299

To carboxylic acid **72** (1.8 g, 4.2 mmol, 1.0 equiv.) in CH_2Cl_2 (21 mL) was added 4-dimethylaminopyridine (51 mg, 0.42 mmol, 0.1 equiv.) and ethanethiol (1.2 mL, 17 mmol, 4.0 equiv.). *N*-(3-Dimethylaminopropyl)-*N'*-ethyl carbodiimide hydrochloride (1.2 g, 6.2 mmol, 1.5 equiv.) was added in portions at 0 °C. After all solids dissolved, the reaction mixture was allowed to warm to 23 °C and stirred for 17 h. The mixture was diluted with CH_2Cl_2 (40 mL) and added to aq. sat. NH_4Cl (40 mL). The aq. phase was extracted with CH_2Cl_2 (2 x 40 mL) and the combined organic phases were sequentially washed with aq. sat. NH_4Cl (40 mL), water (40 mL), sat. aq. NaCl (40 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield thioester **299** (2.0 g, 4.2 mmol, quant.) as a yellow oil, which was used without further purification.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.36 – 5.24 (m, 2H), 3.39 (dd, *J* = 21.0, 1.6 Hz, 1H), 2.82 (dt, *J* = 20.9, 3.4 Hz, 1H), 2.73 (q, *J* = 7.4 Hz, 2H), 2.60 – 2.55 (m, 2H), 2.54 – 2.45 (m, 3H), 2.37 – 2.25 (m, 2H), 2.16 – 2.08 (m, 1H), 1.93 – 1.86 (m, 2H), 1.83 – 1.75 (m, 4H), 1.48 (qd, *J* = 6.7, 6.4 Hz, 1H), 1.25 – 1.21 (m, 1H), 1.19 (s, 3H), 1.16 (t, *J* = 7.4 Hz, 3H), 1.05 – 0.98 (m, 7H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-6,14-Dioxo-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dien-15-al



$C_{30}H_{44}O_3S$ (484.74)
299

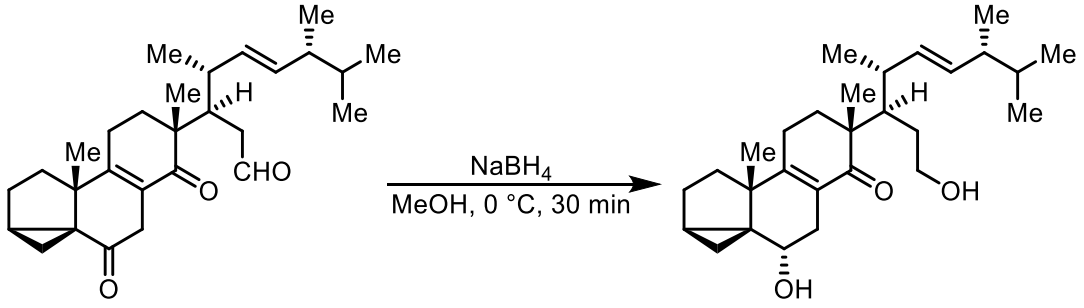
$C_{28}H_{40}O_3$ (424.63)
300

Thioester **299** (2.01 g, 4.15 mmol, 1.0 equiv.) was dissolved in acetone (21 mL) and Pd/C (440 mg, 0.415 mmol, 0.1 equiv., 10%) was added. Triethyl silane (2.60 mL, 16.6 mmol, 4.0 equiv.) was added and the resulting mixture was allowed to stir for 90 min at 23 °C. The mixture was diluted with acetone (25 mL) and filtered over Celite® and rinsed with acetone (2 x 20 mL). The solvent was removed under reduced pressure to yield aldehyde **300** (1.76 g, 4.15 mmol, quant.) as a yellow oil, which was used without further purification.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 9.55 (t, *J* = 1.0 Hz, 1H), 5.31 – 5.21 (m, 2H), 3.34 (dd, *J* = 21.1, 1.6 Hz, 1H), 2.79 (dt, *J* = 21.1, 3.4 Hz, 1H), 2.64 – 2.45 (m, 4H), 2.40 – 2.24 (m, 3H), 2.17 – 2.08 (m, 1H), 1.96 – 1.84 (m, 2H), 1.83 – 1.74 (m, 4H), 1.46 (qd, *J* = 6.8, 6.5 Hz, 1H), 1.26 – 1.20 (m, 1H), 1.19 (s, 3H), 1.02 – 0.99 (m, 4H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.82 (s, 3H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-6*α*,15-Dihydroxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dien-14-one



$C_{28}H_{40}O_3$ (424.63)
300

$C_{28}H_{44}O_3$ (428.66)
73

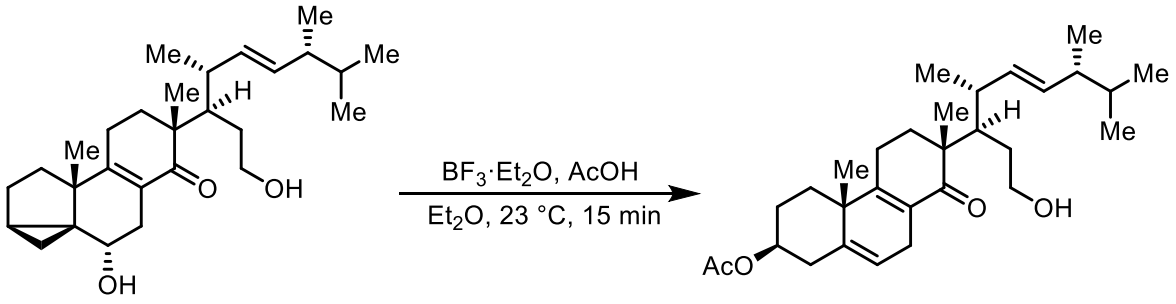
Aldehyde **300** (1.76 g, 4.15 mmol, 1.0 equiv.) was dissolved in MeOH (42 mL) and cooled to 0 °C. Sodium borohydride (785 mg, 20.6 mmol, 5.0 equiv.) was added in portions. After

stirring at 0 °C for 20 min, aq. HCl (1 M, 15 mL) was carefully added, the resulting mixture was allowed to warm to ambient temperature and diluted with water (20 mL). The mixture was extracted with EtOAc (3 x 40 mL), the combined organic phases were washed with sat. aq. NaCl (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1→1:1) to yield diol **73** (1.25 g, 2.91 mmol, 70% over 4 steps) as a colorless foam.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.35 (dd, *J* = 15.3, 8.2 Hz, 1H), 5.22 (dd, *J* = 15.3, 8.1 Hz, 1H), 4.10 (dd, *J* = 10.2, 5.5 Hz, 1H), 3.42 (ddd, *J* = 10.3, 9.0, 6.0 Hz, 1H), 3.34 – 3.23 (m, 1H), 3.09 (dd, *J* = 16.5, 5.5 Hz, 1H), 2.45 – 2.25 (m, 2H), 2.25 – 2.07 (m, 4H), 1.92 – 1.73 (m, 3H), 1.71 – 1.55 (m, 4H), 1.54 – 1.39 (m, 3H), 1.33 – 1.25 (m, 1H), 1.18 (s, 3H), 1.16 – 1.09 (m, 1H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.99 (s, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.86 – 0.83 (m, 1H), 0.82 (d, *J* = 7.0 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H), 0.41 (t, *J* = 4.4 Hz, 1H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-15-Hydroxy-14,15-secoergosta-5,8,22-trien-14-on-3β-yl acetate



$C_{28}H_{44}O_3$ (428.66)
73

$C_{30}H_{46}O_4$ (470.69)
92

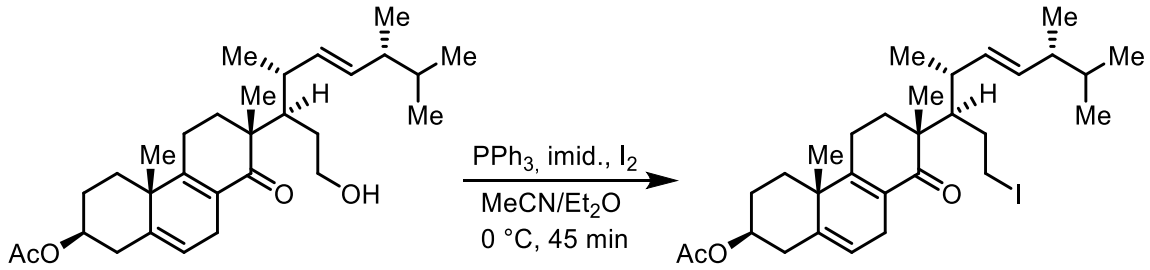
To diol **73** (0.24 g, 0.56 mmol, 1.0 equiv.) in Et_2O (10 mL) was added acetic acid (5.7 mL) and $BF_3{\cdot}Et_2O$ (5.7 mL, 45 mmol, 80.0 equiv.). After stirring at 24 °C for 15 min, the mixture was diluted with EtOAc (20 mL) and carefully added to aq. sat. $NaHCO_3$ (40 mL). The aq. phase was extracted with EtOAc (3 x 20 mL). The combined organic phases were sequentially washed with aq. $NaHCO_3$ (5%, 2 x 40 mL) and sat. aq. NaCl (40 mL). The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 4:1→2:1) to give acetate **92** (0.21 g, 0.45 mmol, 81%) as a colorless foam.

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.56 (p, *J* = 2.2 Hz, 1H), 5.36 (dd, *J* = 15.3, 8.1 Hz, 1H), 5.24 (dd, *J* = 15.3, 8.1 Hz,1H), 4.63 (tt, *J* = 11.6, 4.8 Hz, 1H), 3.49 (td, *J* =

9.4, 6.0 Hz, 1H), 3.37 (td, *J* = 9.4, 6.5 Hz, 1H), 2.82 (dt, *J* = 22.7, 3.0 Hz, 1H), 2.75 – 2.68 (m, 1H), 2.44 (ddd, *J* = 12.8, 5.1, 2.1 Hz, 1H), 2.42 – 2.33 (m, 3H), 2.33 – 2.26 (m, 1H), 2.18 (dt, *J* = 13.8, 5.3Hz, 1H), 2.05 (s, 3H), 1.99 (dt, *J* = 12.1, 3.2 Hz, 1H), 1.94 (dt, *J* = 13.2, 3.7 Hz, 1H), 1.88 (qd, *J* = 6.8, 6.6 Hz, 1H), 1.80 (td, *J* = 5.2, 2.7 Hz, 1H), 1.77 – 1.67 (m, 2H), 1.64 – 1.44 (m, 5H), 1.26 (s, 3H), 1.03 (s, 3H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H).

The spectroscopic data match those reported in literature.[31]

(22*E*)-15-Iodo-14,15-secoergosta-5,8,22-trien-14-on-3β-yl acetate



$C_{30}H_{46}O_4$ (470.69)
92

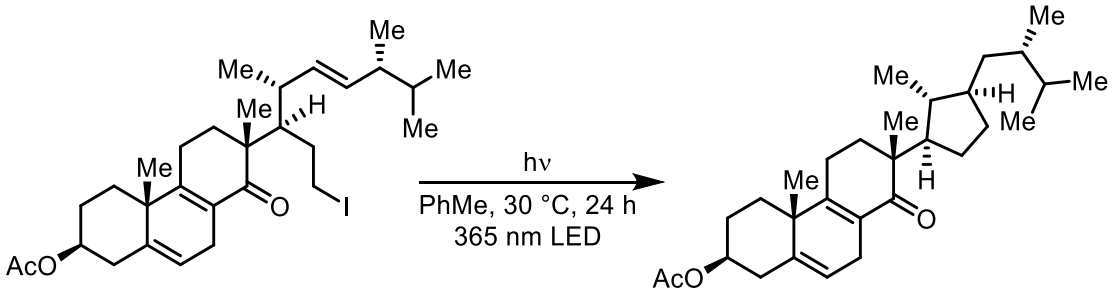
$C_{30}H_{45}IO_3$ (580.59)
74

Acetate **92** (18 mg, 38 µmol, 1.0 equiv.) was dissolved in Et_2O/MeCN (5:3, 0.38 mL). Triphenylphosphine (14 mg, 54 µmol, 1.4 equiv.) and imidazole (3.9 mg, 57 µmol, 1.5 equiv.) were added and the resulting mixture was cooled to 0 °C. Iodine (15 mg, 57 µmol, 1.5 equiv.) was added in portions in darkness. The resulting mixture was allowed to stir for 45 min in the dark at the same temperature, then Et_2O (2 mL) was added and the mixture was added to sat. aq. $Na_2S_2O_3$ (3 mL). The aq. phase was extracted with Et_2O (2 x 3 mL) and the combined organic phases were sequentially washed with aq. $CuSO_4$ (10%, 5 mL), water (5 mL), sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 12:1→9:1) to give iodide **74** (17 mg, 29 µmol, 77%) as a colorless oil.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.56 (p, *J* = 2.4 Hz, 1H), 5.31 (dd, *J* = 15.4, 7.2 Hz, 1H), 5.25 (dd, *J* = 15.4, 7.6 Hz, 1H), 4.62 (tt, *J* = 11.3, 4.9 Hz, 1H), 3.10 – 3.00 (m, 2H), 2.83 (dt, *J* = 22.3, 2.4 Hz, 1H), 2.77 – 2.65 (m, 1H), 2.49 – 2.26 (m, 5H), 2.20 – 2.09 (m, 1H), 2.04 (s, 3H), 1.97 – 1.66 (m, 8H), 1.55 (td, *J* = 13.5, 3.8 Hz, 1H), 1.47 (qd, *J* = 6.9, 6.5 Hz, 1H), 1.27 (s, 3H), 1.05 (d, *J* = 7.1 Hz, 3H), 1.02 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H).

The spectroscopic data match those reported in literature.[31]

(22*R*)-15,22-Cyclo-14,15-secoergosta-5,8-dien-14-on-3β-yl acetate



$C_{30}H_{45}IO_3$ (580.59)
74

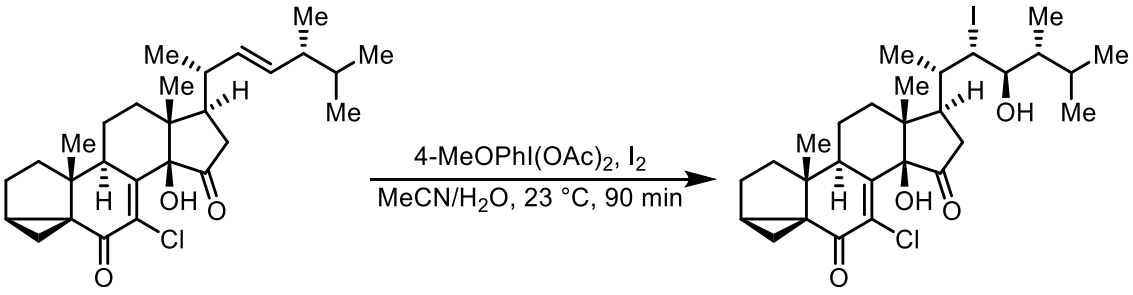
$C_{30}H_{46}O_3$ (454.70)
75

To iodide **74** (7.7 mg, 13 µmol, 1.0 equiv.) in toluene (1 mL) was added *n*-tributyltin hydride (12 µL, 46 µmol, 3.5 equiv.). The solution was irradiated with light (365 nm UV LED strips) for 24 h at 35 °C. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield cyclopentane **75** (3.1 mg, 6.7 µmol, 53%) as a colorless oil.

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.55 (p, *J*= 2.3 Hz, 1H), 4.63 (tt, *J*= 11.4, 4.8 Hz,1H), 2.81 (dt, *J*= 22.6, 2.7 Hz, 1H), 2.76 – 2.64 (m, 1H), 2.50 – 2.35 (m, 3H), 2.34 – 2.23 (m, 1H), 2.04 (s, 3H), 2.01 – 1.89 (m, 4H), 1.75 – 1.59 (m, 4H), 1.55 – 1.33 (m, 6H), 1.32 – 1.27(m, 1H), 1.25 (s, 3H), 1.11 – 1.03 (m, 1H), 0.98 (s, 3H), 0.97 (d, *J*= 6.6 Hz, 3H), 0.90 – 0.86(m, 1H),0.85(d, *J*= 6.9 Hz, 3H), 0.76 (d, *J*= 6.8 Hz, 3H), 0.74 (d, *J*= 6.9 Hz, 3H)

The spectroscopic data match those reported in literature.[31]

22(*S*)-Iodo-7-Chloro-14β,23(*R*)-dihydroxy-3*α*,5-cyclo-5*α*-ergosta-7-ene-6,15-dione



$C_{28}H_{40}O_3$ (424.63)
71

$C_{28}H_{40}ClIO_4$ (602.98)
145

To chloroenone **71** (100 mg, 0.220 mmol, 1.0 equiv.) in MeCN/H_2O (4:1, 2.2 mL) was added 4-methoxyiodobenzene diacetate (115 mg, 0.320 mmol, 1.5 equiv.) and iodine (41.0 mg,

0.160 mmol, 0.75 equiv.). The resulting mixture was allowed to stir for 90 min at 25 °C, diluted with Et_2O (15 mL) and added to sat. aq. $Na_2S_2O_3$ (10 mL). The aqueous phase was extracted with Et_2O (3 x 5 mL) and the combined organic phases were washed with sat. aq. NaCl (10 mL). The solvents were removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 5:1→3:1→1:1) to yield iodohydrin **145** (31 mg, 50 µmol, 24%) as a colorless solid and single diastereomer. Additionally, chloroenone **71** (14 mg, 30 µmol, 14%) as well as epoxide **146** (37 mg, 80 µmol, 37%; approx. 1:1 mixture of diastereomers) were isolated as colorless oils.

R_f : 0.47 (*n*hexane/EtOAc 3:1, CAM [*blue*, UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 4.08 (dd, *J* = 9.8, 2.2 Hz, 1H), 4.00 (dd, *J* = 9.7, 2.1 Hz, 1H), 3.09 (dd, *J* = 11.2, 6.6 Hz, 1H), 2.69 (dd, *J* = 17.7, 6.9 Hz, 1H), 2.33 (td, *J* = 10.7, 6.8 Hz, 1H), 2.28 – 2.21 (m, 2H), 2.03 – 1.97 (m, 1H), 1.92 (dt, *J* = 8.7, 4.4 Hz, 1H), 1.88 – 1.83 (m, 2H), 1.81 – 1.73 (m, 3H), 1.64 (dd, *J* = 13.6, 7.7 Hz, 1H), 1.59 (dq, *J* = 13.8, 6.9 Hz, 1H), 1.48 (dqd, *J* = 12.3, 6.2, 1.9 Hz, 1H), 1.25 (t, *J* = 3.5 Hz, 1H), 1.18 – 1.14 (m, 1H), 1.11 (s, 3H), 1.09 (s, 3H), 1.04 (d, *J* = 6.2 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.81 (s, 1H).

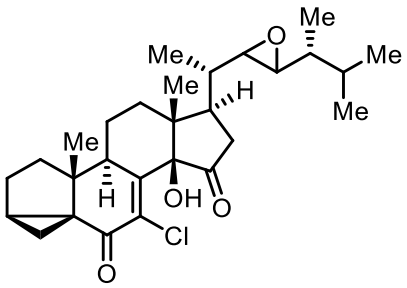
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 208.9, 189.5, 151.3, 127.6, 83.7, 73.3, 50.4, 48.4, 47.7, 43.5, 43.0, 42.9, 42.2, 40.8, 35.6, 35.5, 35.3, 31.6, 31.3, 27.1, 25.6, 20.8, 20.5, 20.3, 17.3, 14.9, 13.9, 9.4.

FTIR: (neat) [cm^{-1}] = 2961 (m), 2872 (w), 2360 (m), 2341 (w), 1740 (s), 1672 (s), 1597 (w) 1455 (m), 1366 (s), 1264 (m), 1227 (s), 1085 (s), 1016 (m), 733 (s), 701 (m)

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{40}ClINaO_4^+$: 625.1552; found: 625.1556

$[\alpha]_D^{23}$: +175.8 (c= 1.00; $CHCl_3$)

22,23-Epoxy-7-Chloro-14β-hydroxy-3α,5-cyclo-5α-ergosta-7-ene-6,15-dione



$C_{28}H_{39}ClO_4$ (475.07)

146

R_f : 0.52 (*n*hexane/EtOAc 3:1, CAM [*blue*, UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 4.05 (dd, *J*=10.7, 2.8, 1H), 3.65 (dd, *J*=10.2, 2.1, 1H), 3.21 (d, *J*=10.2, 1H), 3.07 (ddt, *J*=10.9, 8.8, 3.3, 4H), 2.81 (dd, *J*=17.8, 7.0, 1H), 2.67 – 2.57 (m, 2H), 2.57 – 2.41 (m, 4H), 2.36 – 2.13 (m, 6H), 2.06 – 1.96 (m, 3H), 1.92 (p, *J*=4.7, 3H), 1.90 – 1.81 (m, 4H), 1.82 – 1.69 (m, 6H), 1.64 (dd, *J*=13.6, 7.7, 3H), 1.45 (p, *J*=6.9, 1H), 1.42 (s, 3H), 1.34 (d, *J*=6.8, 3H), 1.19 (s, 4H), 1.18 (s, 3H), 1.11 (d, *J*=6.2, 4H), 1.01 (dd, *J*=6.8, 5.6, 6H), 0.98 (d, *J*=7.0, 5H), 0.97 (d, *J*=7.1, 4H), 0.97 – 0.90 (m, 2H), 0.90 – 0.76 (m, 4H).

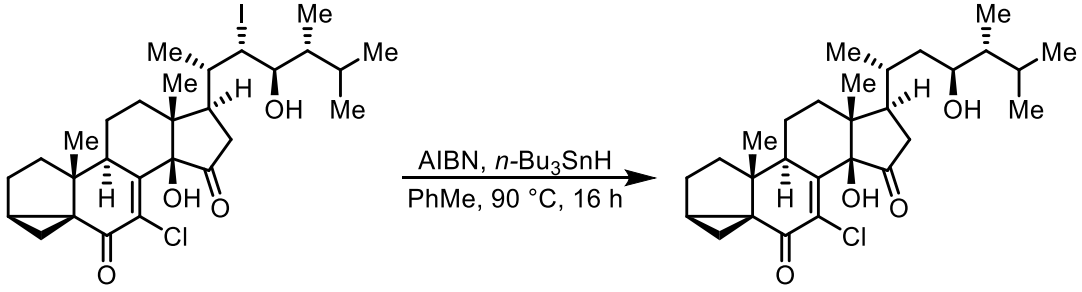
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 208.3, 208.1, 189.5(2xC), 151.3, 151.0, 127.7, 127.7, 83.6, 83.2, 66.9, 64.8, 64.1, 62.4, 48.7, 48.2, 47.2, 45.5, 43.5, 43.4, 43.0, 42.9, 42.0, 40.8, 40.7, 36.9, 36.5, 36.5, 35.6, 35.5, 35.5, 31.5, 31.3, 31.1, 30.7, 27.1, 27.0, 25.5, 25.4, 20.3, 18.8, 18.8, 18.6, 17.7, 17.6, 17.3, 17.2, 17.0, 14.7, 14.3, 14.0, 13.6, 13.4, 13.0, 11.7, 11.3.

FTIR: (neat) [cm^{-1}] = 2961 (m), 2872 (w), 2360 (m), 2341 (w), 1747 (s), 1672 (s), 1597 (m), 1455 (m), 1365 (s), 1265 (m), 1137 (m), 1084 (s), 1049 (m), 897 (s), 850 (m), 734 (s), 702 (s), 657 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{39}ClKO_4^+$: 513.2168; found: 513.2168.

$[\alpha]_D^{23}$: +143.9 (c= 1.00; $CHCl_3$)

7-Chloro-14β,23(*R*)-dihydroxy-3*α*,5-cyclo-5*α*-ergosta-7-en-6,15-dione



$C_{28}H_{40}ClIO_4$ (602.98)
146

$C_{28}H_{41}ClO_4$ (477.08)
147

Iodohydrin **146** (10 mg, 17 µmol, 1.0 equiv.) was dissolved in toluene (0.17 mL) and *n*-tributyltin hydride (13 µL, 50 µmol, 3.0 equiv.) was added followed by the addition of AIBN (0.30 mg, 1.7 µmol, 0.1 equiv.). The mixture was stirred at 90 °C for 16 h, cooled to ambient temperature and concentrated under reduced pressure. The residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1) to yield diol **147** (4.3 mg, 9.0 µmol, 54%) as a colorless oil.

R_f : 0.29 (*n*hexane/EtOAc 3:1, CAM [*blue*, UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 3.75 – 3.71 (m, 1H), 3.07 (dd, *J* = 11.1, 6.7 Hz, 1H), 2.68 (dd, *J* = 18.3, 6.9 Hz, 1H), 2.37 – 2.31 (m, 1H), 2.21 – 2.14 (m, 1H), 2.09 (td, *J* = 10.7, 7.0 Hz, 1H), 2.04 – 1.97 (m, 1H), 1.91 (ddd, *J* = 17.5, 9.0, 5.0 Hz, 3H), 1.81 – 1.73 (m, 2H), 1.69 (dt, *J* = 13.1, 6.6 Hz, 1H), 1.64 (ddd, *J* = 15.7, 8.0, 4.9 Hz, 1H), 1.49 (ddd, *J* = 13.4, 10.5, 2.5 Hz, 1H), 1.37 (ddt, *J* = 22.9, 15.5, 8.2 Hz, 1H), 1.31 – 1.28 (m, 2H), 1.21 – 1.17 (m, 1H), 1.17 – 1.11 (m, 1H), 1.09 (s, 3H), 1.06 (s, 3H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.82 (t, *J* = 4.8 Hz, 1H).

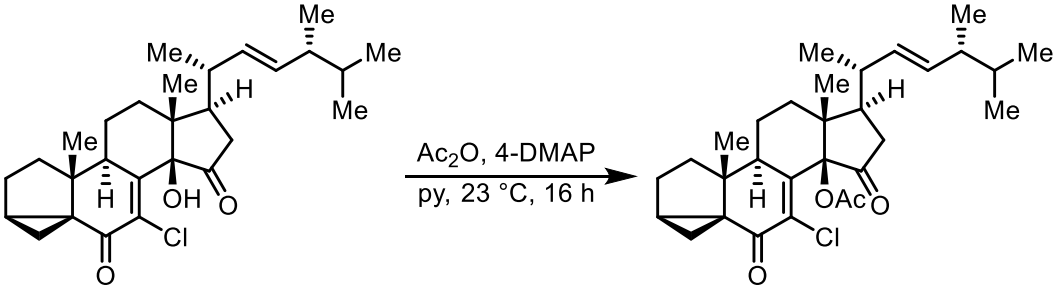
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 209.7, 189.5, 151.5, 127.6, 83.8, 70.7, 48.6, 47.6, 45.5, 43.5, 43.1, 42.9, 42.1, 42.0, 35.6, 35.4, 31.7, 31.3, 29.8, 28.0, 27.1, 25.5, 21.6, 20.3, 19.1, 18.6, 13.8, 10.0.

FTIR: (neat) [cm^{-1}] = 2966 (m), 2874 (w), 2358 (m), 2343 (w), 1740 (s), 1675 (s), 1371 (m), 1086 (m), 1026 (m), 1011 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{27}H_{39}ClNaO_4^+$: 499.2586; found: 499.2601.

$[\alpha]_D^{23}$: +202.7 (c= 1.00; $CHCl_3$)

(22*E*)-7-Chloro-14β-acetoxy-3α,5-cyclo-5α-ergosta-7,22-dien-6,15-dione



$C_{28}H_{39}ClO_3$ (459.07)
67

$C_{30}H_{41}ClO_4$ (501.10)
155

Chloroenone **71** (75 mg, 0.16 mmol, 1.0 equiv.) was dissolved in pyridine (1.6 mL) and 4-dimethylaminopyridine (6.0 mg, 50 µmol, 0.3 equiv.) was added. Acetic anhydride (77 µL, 0.82 mmol, 5.0 equiv.) was added dropwise and the resulting mixture was allowed to stir for 16 h at 24 °C. Water (5 mL) was added and extracted with EtOAc (3 x 4 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was re-dissolved in toluene and concentrated under reduced pressure. The residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1→5:1) to yield acetate **155** (48 mg, 0.10 mmol, 58%) as a colorless oil. Additionally, unreacted **71** (21 mg, 40 µmol, 27%) was reisolated.

R_f : 0.26 (*n*hexane/EtOAc 4:1, CAM [*blue*, UV])

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.30 (dd, *J* = 15.2, 7.9 Hz, 1H), 5.16 (ddd, *J* = 15.3, 8.8, 0.9 Hz, 1H), 2.53 (dd, *J* = 19.4, 7.4 Hz, 1H), 2.40 – 2.34 (m, 1H), 2.27 – 2.22 (m, 1H), 2.21 – 2.07 (m, 2H), 2.05 (s, 3H), 1.93 – 1.79 (m, 6H), 1.73 – 1.68 (m, 3H), 1.62 – 1.51 (m, 1H), 1.48 (dt, *J* = 12.8, 6.4 Hz, 1H), 1.26 – 1.12 (m, 1H), 1.09 (d, *J* = 6.5 Hz, 3H), 1.08 (s, 3H) 1.07 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 7.0 Hz, 3H), 0.75 (t, *J* = 4.8 Hz, 1H).

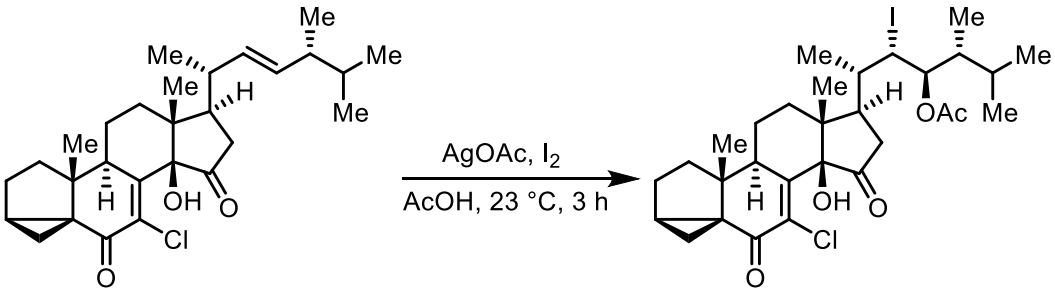
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 202.1, 189.0, 167.4, 148.2, 134.3, 133.9, 128.6, 90.8, 50.0, 46.5, 44.9, 43.0, 42.9, 42.5, 42.3, 39.6, 36.8, 34.4, 33.1, 31.9, 27.2, 27.0, 21.6, 21.5, 20.5, 20.1, 19.8, 17.7, 13.5, 12.9.

FTIR: (neat) [cm^{-1}] = 2957 (m), 2926 (w), 2870 (w), 2359 (m) 2341 (w), 1765 (s), 1674 (s), 1603 (w), 1455 (m), 1367 (s), 1263 (w), 1208 (s), 1087 (m), 975 (m), 835 (w), 730 (s), 701 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{41}ClNaO_4^+$: 523.2586; found: 523.2599.

$[\alpha]_D^{24}$: +188.6 (c= 1.00; $CHCl_3$)

22(*S*)-Iodo-7-Chloro-14β-hydroxy-23(*R*)-acetoxy-3*α*,5-cyclo-5*α*-ergosta-7-ene-6,15-dione



$C_{28}H_{39}ClO_3$ (459.07)
71

$C_{30}H_{42}ClIO_5$ (645.02)
150

Chloroenone **71** (25 mg, 50 µmol, 1.0 equiv.) was dissolved in AcOH (0.54 mL) and silver acetate (22 mg, 0.13 mmol, 2.2 equiv.) was suspended in the mixture. Iodine (17 mg, 60 µmol, 1.2 equiv.) was added in portions in the dark. After stirring for 3 h at 24 °C, the mixture was diluted with Et_2O (5 mL), filtered over a plug of Celite® and rinsed with Et_2O (2 x 5 mL). The filtrate was washed with sat. aq. $Na_2S_2O_3$ (10 mL) and the aq. phase was extracted with Et_2O (2 x 3 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (3 x 5 mL), sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography

(SiO_2, *n*hexane/EtOAc 5:1) to yield iodo acetate **150** (10 mg, 16 µmol, 28%) as a colorless oil.

R_f : 0.59 (*n*hexane/EtOAc 3:1, CAM [*blue*, UV])

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.47 (dd, *J* = 10.2, 2.1 Hz, 1H), 4.08 – 4.05 (m, 1H), 3.08 (dd, *J* = 10.7, 6.9 Hz, 1H), 2.68 (dd, *J* = 17.6, 6.8 Hz, 1H), 2.42 (d, *J* = 2.1 Hz, 1H), 2.36 – 2.16 (m, 4H), 2.08 (s, 3H), 1.93 (dt, *J* = 8.6, 4.4 Hz, 1H), 1.84 – 1.74 (m, 4H), 1.64 (dd, *J* = 13.7, 7.8 Hz, 2H), 1.27 – 1.11 (m, 3H), 1.08 (s, 3H), 1.06 (s, 3H), 1.02 (d, *J* = 6.1 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.82 (t, *J* = 4.7 Hz, 1H).

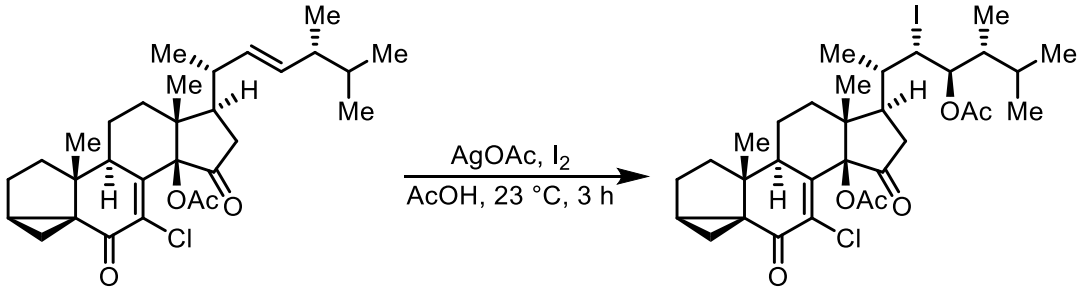
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 208.2, 189.4, 169.9, 151.1, 127.7, 83.6, 74.3, 48.2, 47.3, 45.5, 43.5, 43.4, 43.0, 42.9, 42.6, 40.8, 35.6, 35.6, 35.5, 31.5, 30.7, 27.1, 25.5, 21.2, 21.0, 20.3, 18.3, 14.7, 13.9, 10.4.

FTIR: (neat) [cm^{-1}] = 2961 (m), 2872 (w), 2360 (m), 2341 (w), 1740 (s), 1672 (s), 1366 (m), 1085 (m), 1016 (m), 957 (m), 896 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{44}ClINaO_5^+$: 679.2466; found: 679.2482.

$[\alpha]_D^{24}$: +128.8 (c= 1.00; $CHCl_3$)

22(*S*)-Iodo-7-Chloro-14β,23(*R*)-diacetoxy-3*α*,5-cyclo-5*α*-ergosta-7-en-6,15-dione



$C_{30}H_{41}ClO_4$ (501.10)
155

$C_{32}H_{44}ClIO_6$ (687.05)
156

Acetate **155** (74 mg, 0.15 mmol, 1.0 equiv.) was dissolved in acetic acid (2.9 mL) and water (0.14 mL) was added. Silver acetate (74 mg, 0.45 mmol, 3.0 equiv.) was suspended in the mixture and iodine (75 mg, 0.30 mmol, 2.0 equiv.) was added in portions in the dark. After stirring for 3 h at 23 °C, the mixture was diluted with Et_2O (5 mL), filtered over a plug of Celite® and rinsed with Et_2O (2 x 5 mL). The filtrate was washed with sat. aq. $Na_2S_2O_3$ (10 mL) and the aq. phase was extracted with Et_2O (2 x 3 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL) dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography

(SiO_2, *n*hexane/EtOAc 5:1→2:1) to yield iodoacetate **156** (20 mg, 30 µmol, 20%) as a colorless oil.

R_f : 0.45 (2:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (600 MHz, $CDCl_3$) δ [ppm] = 5.47 (dd, *J* = 10.1, 2.1, 1H), 4.06 (dd, *J* = 10.0, 1.8, 1H), 2.71 (dd, *J* = 18.3, 7.6, 1H), 2.38 (dd, *J* = 11.3, 6.7, 1H), 2.32 (td, *J* = 10.5, 7.6, 1H), 2.20 – 2.11 (m, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 1.93 – 1.81 (m, 1H), 1.75 – 1.68 (m, 1H), 1.59 , 1.55 (dd, *J* = 13.4, 7.5, 1H), 1.45 – 1.36 (m, 4H), 1.27 – 1.23 (m, 4H), 1.20 – 1.11 (m, 2H), 1.09 (s, 3H), 1.07 (s, 3H), 1.03 (d, *J* = 6.1, 3H), 0.97 (d, *J* = 6.6, 3H), 0.90 (d, *J* = 6.7, 3H), 0.84 (d, *J* = 6.9, 3H), 0.76 (td, *J* = 4.9, 2.2, 1H).

^{13}C NMR: (151 MHz, $CDCl_3$) δ [ppm] = 200.5, 189.0, 169.9, 167.3, 147.7, 128.8, 90.3, 74.2, 49.9, 47.1, 45.6, 44.9, 42.9, 42.6, 42.5, 40.6, 36.8, 35.7, 34.5, 32.2, 30.6, 27.2, 27.0, 21.6, 21.2, 21.0, 20.5, 20.3, 18.2, 14.4, 13.0, 10.4.

FTIR: (neat) [cm^{-1}] = 2958 (s), 2926 (s), 2871 (w), 2360 (s), 2341 (m), 1767 (s), 1750 (m), 1676 (s), 1455 (w), 1366 (m), 1294 (w), 1209 (s), 1047 (w), 915 (w).

HRMS: *m/z* $[M+K]^+$ calcd for $C_{32}H_{44}ClIKO_6^+$: 725.1503; found: 725.1537.

$[\alpha]_D^{25}$: +172.9 (c= 1.00; $CHCl_3$)

15-Methyl (22*E*)-6,14-dioxo-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dieneoate

$C_{28}H_{40}O_4$ (440.62)
72

$C_{29}H_{42}O_4$ (454.65)
123

To carboxylic acid **72** (25 mg, 0.57 mmol, 1.0 equiv.) in MeOH (0.57 mL) was added trimethylsilyl diazomethane (19 mg, 0.17 mmol, 3.0 equiv., 85 µL, 2.0 M in hexanes) dropwise at 0 °C. After stirring for 15 min, AcOH (glacial, 3 drops) was added and the solvent was removed under reduced pressure. The residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 5:1) to give methyl ester **123** (25 mg, 0.54 mmol, 95%) as a colorless oil.

R_f : 0.53 (*n*hexane/EtOAc 3:1, CAM [*blue*, UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.31 – 5.25 (m, 2H), 3.52 (s, 3H), 3.38 (dd, *J* = 20.9, 1.5 Hz, 1H), 2.82 (dt, *J* = 20.9, 3.5 Hz, 1H), 2.59 (ddt, *J* = 7.1, 4.6, 2.3 Hz, 1H), 2.54 – 2.47 (m, 1H), 2.44 (ddd, *J* = 6.6, 4.9, 2.3 Hz, 1H), 2.33 (ddt, *J* = 18.8, 5.2, 3.0 Hz, 1H), 2.28 (ddd, *J* = 14.1, 4.7, 3.0 Hz, 1H), 2.22 (t, *J* = 5.3 Hz, 2H), 2.14 – 2.10 (m, 1H), 1.90 – 1.86 (m, 4H), 1.82 – 1.72 (m, 4H), 1.47 (dq, *J* = 13.3, 6.6 Hz, 1H), 1.19 (s, 3H), 1.02 (d, *J* = 7.3 Hz, 3H), 1.01 (s, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H).

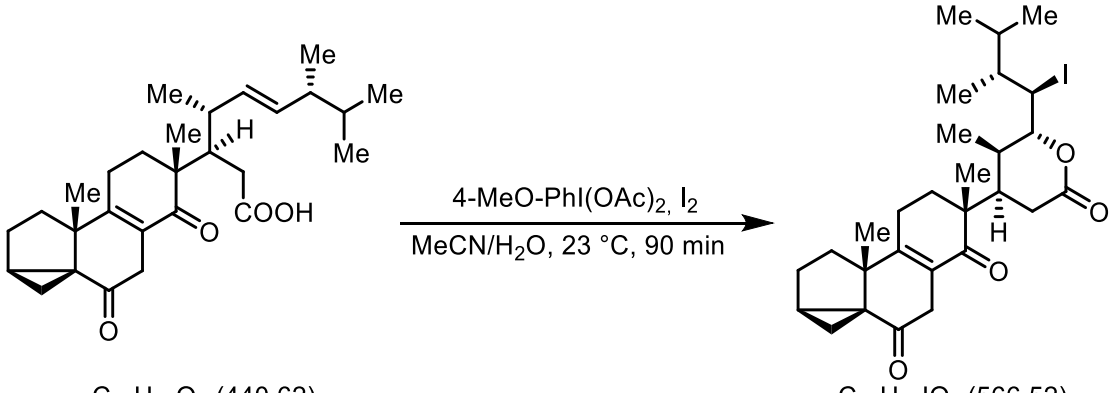
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 208.0, 202.4, 173.9, 158.5, 135.4, 131.6, 127.8, 51.6, 48.0, 47.0, 43.3, 43.0, 40.5, 36.9, 36.8, 36.7, 33.1, 32.8, 32.5, 30.3, 26.3, 23.3, 22.4, 22.2, 20.1, 19.7, 18.9, 17.5, 14.2.

FTIR: (neat) [cm^{-1}] = 2959 (s), 2871 (m), 2354 (w), 1736 (s), 1670 (m), 1454 (m), 1373 (m), 1234 (m), 1166 (w), 1096 (w), 1026 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{42}NaO_4^+$:477.2975 ; found: 477.2998.

$[\alpha]_D^{24}$: +103.1 (c= 1.00; $CHCl_3$)

23-Iodo-6,14-dioxo-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en-15,22-carbolactone



$C_{28}H_{40}O_4$ (440.62)
72

$C_{28}H_{39}IO_4$ (566.52)
122

Carboxylic acid **72** (15 mg, 34 µmol, 1.0 equiv.) was dissolved in MeCN (0.34 mL) and water (6.1 µL, 0.34 mmol, 10.0 equiv.) was added. Iodobenzene diacetate (16 mg, 51 µmol, 1.5 equiv.) and iodine (6.5 mg, 26 µmol, 0.75 equiv.) were added in one portion and the resulting red solution was allowed to stir at 23 °C for 3 h. The solution was diluted with Et_2O (1.5 mL) and added to sat. aq. $Na_2S_2O_3$ (4 mL). The aqueous phase was extracted with Et_2O (3 x 2 mL) and the combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1) to yield iodo lactone **122** (19 mg, 32 µmol, 94%) as a colorless oil.

Starting from methyl ester **123**, the reaction gave the same product in 41% yield.

R_f : 0.23 (*n*hexane/EtOAc 3:1, CAM [*blue*, UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 4.33 (s, 2H), 3.54 (dd, *J* = 21.3, 1.6 Hz, 1H), 2.88 (dt, *J* = 21.3, 3.4 Hz, 1H), 2.68 (q, *J* = 7.3 Hz, 1H), 2.54 – 2.37 (m, 4H), 2.22 – 2.00 (m, 4H), 1.89 (tt, *J* = 9.7, 5.3 Hz, 2H), 1.83 (dd, *J* = 8.3, 4.9 Hz, 1H), 1.76 (dd, *J* = 13.1, 7.2 Hz, 1H), 1.62 (tdd, *J* = 12.8, 7.5, 4.7 Hz, 1H), 1.41 – 1.36 (m, 1H), 1.27 – 1.24 (m, 1H), 1.22 (s, 3H), 1.15 (s, 3H), 1.03 (t, *J* = 5.0 Hz, 1H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.88 – 0.87 (m, 3H).

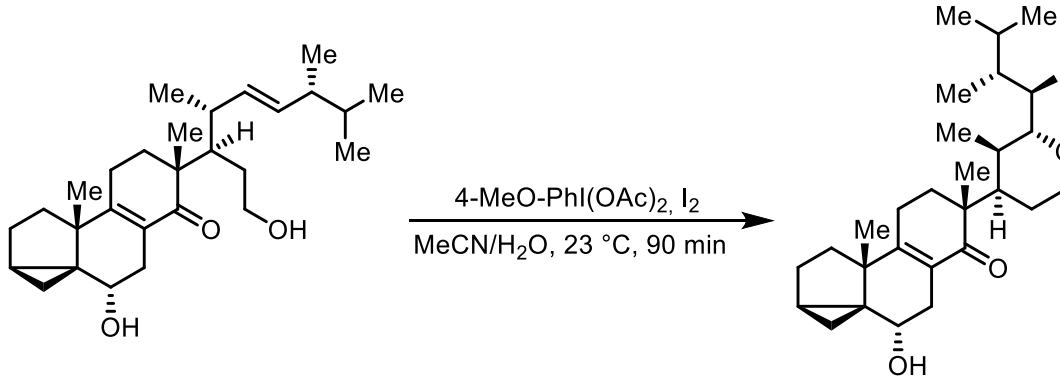
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 206.1, 200.1, 172.5, 160.3, 128.1, 79.4, 48.5, 47.1, 43.3, 42.7, 40.4, 39.5, 37.1, 36.6, 33.9, 33.0, 32.8, 31.3, 29.4, 26.3, 23.2, 23.1, 20.8, 20.3, 18.6, 15.4, 15.1, 14.6, .

FTIR: (neat) [cm^{-1}] = 2964 (s), 2955 (m), 1742 (s), 1672 (m), 1456 (m), 1369 (m), 1232 (m), 1167 (w), 1096 (w), 1029 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{39}INaO_4^+$: 589.1785 ; found: 589.1812.

$[\alpha]_D^{24}$: +37.8 (c= 1.00; $CHCl_3$)

23-Iodo-6α-hydroxy-15,22-oxane-3α,5-cyclo-14,15-seco-5α-ergosta-8-en-14-one



$C_{28}H_{44}O_3$ (428.66)
73

$C_{28}H_{43}IO_3$ (554.55)
124

To diol **73** (25 mg, 60 µmol, 1.0 equiv.) in MeCN/water (0.60 mL; 4:1) was added *p*-(diacetoxyiodo)-anisole (32 mg, 90 µmol, 1.5 equiv.) and iodine (11 mg, 45 µmol, 0.75 equiv.) in one portion. After stirring at 23 °C for 90 min, sat. aq. NaCl (1.5 mL) was added and extracted with Et_2O (3 x 2 mL). The combined organic phases were washed with sat. aq. $Na_2S_2O_3$ (1.5 mL), sat. aq. NaCl (1.5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue submitted to column chromatography

(SiO_2, *n*hexane/EtOAc 5:1→3:1) to give iodoether **124** (12 mg, 22 µmol, 36%) as a colorless oil.

R_f: 0.29 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 4.31 (dd, *J* = 10.3, 2.2 Hz, 1H), 4.11 (dd, *J* = 10.3, 1.3 Hz, 1H), 4.08 (dd, *J* = 10.2, 5.2 Hz, 1H), 3.78 (ddd, *J* = 10.3, 5.9, 4.6 Hz, 1H), 3.60 (td, *J* = 9.5, 5.3 Hz, 1H), 3.10 (ddd, *J* = 16.2, 5.3, 1.9 Hz, 1H), 2.35 (dtd, *J* = 17.9, 5.0, 1.9 Hz, 1H), 2.27 (ddd, *J* = 23.8, 13.8, 4.9 Hz, 2H), 2.13 – 2.06 (m, 2H), 1.89 (dd, *J* = 13.8, 7.8 Hz, 1H), 1.77 (dddd, *J* = 16.0, 10.3, 3.4, 2.2 Hz, 1H), 1.73 – 1.68 (m, 2H), 1.68 – 1.63 (m, 1H), 1.63 – 1.56 (m, 2H), 1.49 (tdd, *J* = 12.3, 7.8, 4.2 Hz, 1H), 1.43 – 1.37 (m, 1H), 1.30 – 1.25 (m, 2H), 1.17 (s, 3H), 1.09 (s, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.1 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.87 – 0.83 (m, 1H), 0.78 (d, *J* = 7.2 Hz, 3H), 0.43 (t, *J* = 4.6 Hz, 1H).

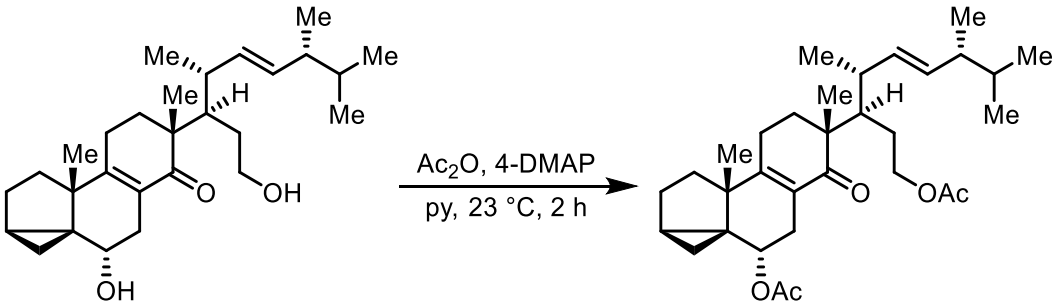
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 203.2, 159.0, 129.4, 72.2, 64.1, 63.6, 51.2, 50.0, 48.1, 43.5, 40.3, 38.8, 37.7, 34.0, 33.4, 31.7, 30.2, 29.3, 26.2, 22.7, 22.5, 21.3, 20.9, 20.4, 18.1, 15.5, 12.6, 7.1.

FTIR: (neat) [cm^{-1}] = 2958 (m), 2361 (s), 1648 (m), 1457 (s), 1048 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{43}INaO_3^+$: 555.2330; found: 555.2343.

$[\alpha]_D^{24}$: +107.1 (c= 1.00; $CHCl_3$)

(22*E*)-6*α*,15-Diacetoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dien-14-one



$C_{28}H_{44}O_3$ (428.66)
73

$C_{32}H_{48}O_5$ (512.73)
108

Diol **73** (0.37 g, 0.87 mmol, 1.0 equiv.) was dissolved in pyridine (8.7 mL) and 4-dimethylaminopyridine (11 mg, 90 µmol, 0.1 equiv.) was added. Acetic anhydride (0.41 mL, 4.3 mmol, 5.0 equiv.) was added dropwise to the solution at 23 °C. The resulting mixture was allowed to stir at the same temperature for 2 h. The solution was cooled to 0 °C and water (30 mL) was added. The mixture was extracted with EtOAc (3 x 25 mL), the combined organic phases were washed with sat. aq. NaCl (25 mL), dried over $MgSO_4$ and filtered. The

solvent was removed under reduced pressure and the residue was dissolved in toluene (2 x 10 mL). The toluene was removed under reduced pressure to yield diacetate **108** (0.44 g, 0.87 mmol, 100%) as a colorless oil.

R_f : 0.44 (5:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.34 (dd, *J* = 15.3, 8.1 Hz, 1H), 5.31 – 5.21 (m, 2H), 3.93 – 3.80 (m, 2H), 3.10 (dd, *J* = 16.2, 5.2 Hz, 1H), 2.42 – 2.18 (m, 3H), 2.14 (ddd, *J* = 13.8, 6.7, 4.6 Hz, 1H), 2.01 (s, 3H), 2.00 (s, 3H), 1.94 – 1.78 (m, 2H), 1.71 – 1.58 (m, 2H), 1.55 (s, 3H), 1.52 – 1.40 (m, 2H), 1.37 – 1.24 (m, 2H), 1.22 (s, 3H), 1.19 – 1.11 (m, 1H), 1.02 (s, 3H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H) 0.82 (d, *J* = 6.7 Hz, 3H), 0.56 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.45 (t, *J* = 4.8 Hz, 1H).

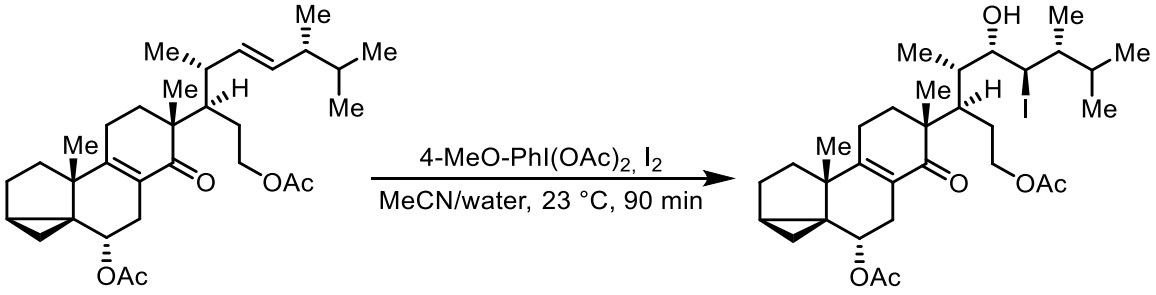
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 202.7, 171.0, 170.3, 158.5, 135.0, 132.3, 129.0, 66.2, 64.9, 49.8, 47.6, 43.3, 42.3, 38.1, 35.2, 33.1, 32.8, 31.0, 28.5, 25.9, 24.8, 23.0, 22.4, 22.4, 21.1, 21.0, 20.1, 20.1, 19.7, 18.4, 17.5, 7.3.

FTIR: (neat) [cm^{-1}] = 1743 (s), 1716 (m), 1660 (m), 1388 (m), 1363 (w), 1247 (s), 1204 (w), 1137 (w), 1031 (s), 979 (m), 865 (m), 663 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{48}NaO_5^+$: 535.3394; found: 535.3427.

$[\alpha]_D^{24}$: +152.8 (c= 1.00; $CHCl_3$)

23(*R*)-Iodo-22(*S*)-hydroxy-6*α*,15-diacetoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en-14-one



$C_{32}H_{48}O_5$ (512.73)
108

$C_{32}H_{49}IO_6$ (656.64)
126

To diacetate **108** (0.15 g, 0.29 mmol, 1.0 equiv.) in MeCN/H_2O (4:1, 2.9 mL) was added *p*-(diacetoxyiodo)anisole (0.16 g, 0.44 mmol, 1.5 equiv.) and iodine (56 mg, 0.16 mmol, 0.75 equiv.). The resulting mixture was allowed to stir for 90 min at 23 °C, diluted with Et_2O (20 mL) and added to sat. aq. $Na_2S_2O_3$ (10 mL). The aq. phase was extracted with Et_2O (3 x 5 mL) and the combined organic phases were washed with sat. aq. NaCl (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue

was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1) to yield iodohydrin **126** (0.12 g, 0.18 mmol, 63%) as a colorless solid and single diastereomer.

R_f : 0.34 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.21 (dd, *J* = 10.2, 5.4 Hz, 1H), 4.28 (dd, *J* = 10.2, 2.2 Hz, 1H), 4.21 – 4.15 (m, 1H), 4.07 (d, *J* = 10.5 Hz, 1H), 4.03 – 3.97 (m, 1H), 3.06 (dd, *J* = 16.4, 5.4 Hz, 1H), 2.66 (s, 1H), 2.37 – 2.26 (m, 3H), 2.16 – 2.09 (m, 1H), 2.04 (s, 3H), 1.99 (s, 3H), 1.92 – 1.85 (m, 2H), 1.85 – 1.77 (m, 1H), 1.70 (dt, *J* = 13.3, 4.7 Hz, 1H), 1.65 – 1.61 (m, 3H), 1.52 – 1.45 (m, 1H), 1.38 (m, 2H), 1.32 – 1.27 (m, 2H), 1.20 (s, 3H), 1.10 (s, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.2 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 7.2 Hz, 3H), 0.58 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.43 (t, 1H).

^{13}C NMR: (700 MHz, $CDCl_3$) δ [ppm] = 202.7, 171.4, 170.4, 158.9, 129.2, 72.8, 66.4, 65.6, 60.5, 50.9, 50.3, 48.1, 43.5, 40.3, 38.7, 35.4, 34.1, 33.2, 28.5, 27.1, 26.3, 22.7, 22.6, 21.2 (2C), 20.9, 20.5, 18.8, 15.7, 14.3, 13.2, 7.7.

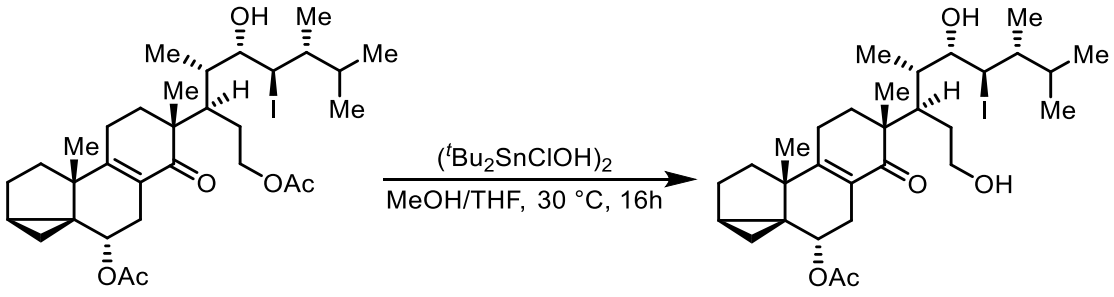
FTIR: (neat) [cm^{-1}] = 2958 (m), 1743 (s), 1716 (s), 1363 (m), 1247 (w), 1073(m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{49}IO_6Na^+$: 679.2466; found: 679.2482.

$[\alpha]_D^{24}$: +110.0 (c= 1.00; $CHCl_3$)

MP 145 °C (EtOAc, decomp.)

23(*R*)-Iodo-22(*S*),15-dihydroxy-6*α*-acetoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en-14-one



$C_{32}H_{49}IO_6$ (656.64)
126

$C_{30}H_{47}IO_5$ (614.61)
141

Iodohydrin **126** (0.10 g, 0.15 mmol, 1.0 equiv.) was dissolved in MeOH/THF (1:1, 1.5 mL) and tin compound **111** (4.4 mg, 7.7 µmol, 0.05 equiv.) was added. The mixture was allowed to stir at 30 °C for 16 h. The mixture was diluted with EtOAc (5 mL) and filtered over a plug of silica. The solvent was removed under reduced pressure to give diol **141** (95 mg, 0.16 mmol, quant.) as a colorless oil.

R_f : 0.24 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.22 (ddt, *J* = 10.3, 5.4, 1.1 Hz, 1H), 4.31 (dd, *J* = 10.3, 2.1 Hz, 1H), 4.10 (dd, *J* = 10.3, 1.3 Hz, 1H), 3.82 – 3.76 (m, 1H), 3.61 (td, *J* = 9.5, 5.3 Hz, 1H), 3.09 (ddd, *J* = 16.3, 5.5, 1.9 Hz, 1H), 2.38 – 2.23 (m, 3H), 2.14 – 2.07 (m, 2H), 2.00 (s, 3H), 1.92 – 1.83 (m, 2H), 1.75 – 1.68 (m, 1H), 1.67 – 1.56 (m, 3H), 1.52 (tdd, *J* = 12.3, 7.9, 4.2 Hz, 1H), 1.39 (dp, *J* = 8.9, 6.5 Hz, 1H), 1.31 (dt, *J* = 8.3, 4.1 Hz, 1H), 1.25 (d, *J* = 1.8 Hz, 1H), 1.21 (s, 3H), 1.20 – 1.15 (m, 1H), 1.08 (s, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.1 Hz, 3H), 0.88 (d, *J* = 6.5 Hz, 3H), 0.78 (d, *J* = 7.2 Hz, 3H), 0.59 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.48 – 0.42 (m, 1H).

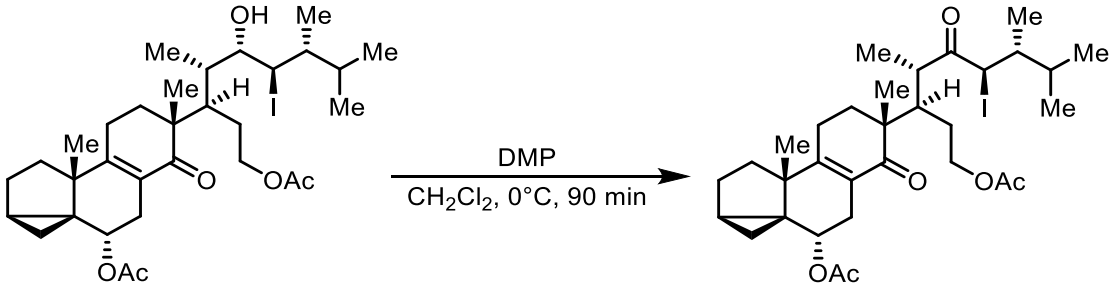
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 202.8, 170.4, 158.8, 129.2, 72.3, 66.5, 64.2, 51.4, 50.3, 48.3, 43.9, 40.4, 39.0, 35.5, 34.2, 33.3, 30.1, 29.4, 28.5, 26.4, 22.7, 22.6, 21.5, 21.2, 21.0, 20.5, 18.9, 15.6, 12.8, 7.8.

FTIR: (neat) [cm^{-1}] = 2958 (s), 2933 (m), 2873 (w), 1733 (s), 1654 (s), 1457 (m), 1375 (m), 1131 (w), 1032 (s), 977 (w), 735 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{47}INaO_5^+$: 637.2360; found: 637.2397.

$[\alpha]_D^{23}$: +129.6 (c= 1.00; $CHCl_3$)

23(*R*)-Iodo-6*α*,15-diacetoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en-22,14-dione



$C_{32}H_{49}IO_6$ (656.64)
126

$C_{32}H_{47}IO_6$ (654.63)
143

To iodohydrin **126** (18.3 mg, 27.9 µmol, 1.0 equiv.) in CH_2Cl_2 (280 µL) was added Dess-Martin periodinane (23.6 mg, 55.7 µmol, 2.0 equiv.) at 0 °C. The mixture was allowed to stir for 90 min at the same temperature. After warming to ambient temperature, sat. aq. $NaHCO_3$ (2 mL) was added and the phases were separated. The aq. phase was extracted with CH_2Cl_2 (2 x 3 mL) and the combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1) to yield α-iodo ketone **143** (18.1 mg, 27.2 mmol, 99%) as a colorless oil.

R_f : 0.42 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.24 – 5.20 (m, 1H), 4.72 (d, *J* = 7.3 Hz, 1H), 4.07 (ddd, *J* = 10.6, 8.9, 5.9 Hz, 1H), 3.95 (ddd, *J* = 10.7, 8.6, 6.8 Hz, 1H), 3.13 (qd, *J* = 7.4, 4.8 Hz, 1H), 3.06 (ddt, *J* = 16.2, 5.4, 1.1 Hz, 1H), 2.29 (dtd, *J* = 20.5, 5.3, 3.3 Hz, 3H), 2.09 – 2.04 (m, 1H), 2.03 (s, 3H), 2.00 (s, 3H), 1.89 (tdd, *J* = 13.5, 5.9, 3.1 Hz, 3H), 1.81 – 1.75 (m, 2H), 1.66 – 1.61 (m, 1H), 1.55 – 1.46 (m, 3H), 1.30 (dt, *J* = 8.2, 4.1 Hz, 1H), 1.20 (s, 3H), 1.19 – 1.14 (m, 1H), 1.11 (d, *J* = 7.4 Hz, 3H), 1.10 (s, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.5 Hz, 3H), 0.58 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.45 – 0.41 (m, 1H).

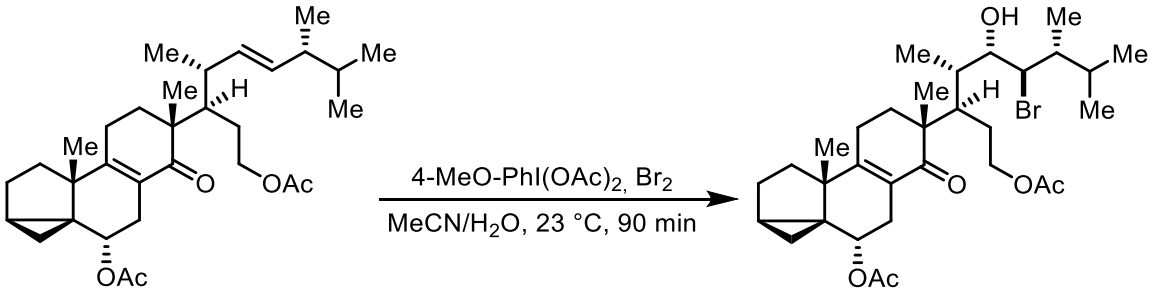
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 206.1, 201.7, 171.1, 170.4, 159.4, 129.1, 66.4, 65.7, 50.4, 47.5, 44.6, 44.0, 42.5, 40.2, 35.5, 33.3, 30.5, 29.2, 28.5, 26.5, 25.8, 22.9, 22.7, 22.1, 21.8, 21.2, 21.2, 18.9, 18.9, 17.3, 16.5, 7.9.

FTIR: (neat) [cm^{-1}] = 2963 (m), 2933 (m), 2872 (w), 2360 (s), 2341 (s), 1735 (s), 1659 (m), 1618 (w), 1456 (w), 1367 (m), 1240 (s), 1033 (m), 916 (w), 732 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{47}INaO_6^+$: 677.2310; found: 677.2346.

$[\alpha]_D^{24}$: +29.2 (c= 0.80; $CHCl_3$)

23(*R*)-Bromo-22(*S*)-hydroxy-6*α*,15-diacetoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en-14-one



$C_{32}H_{48}O_5$ (512.73)
108

$C_{32}H_{49}BrO_6$ (609.64)
134

To diacetate **108** (20 mg, 39 mmol, 1.0 equiv.) in $MeCN/H_2O$ (4:1, 0.39 mL) was added *p*-(diacetoxyiodo)anisole (21 mg, 59 µmol, 1.5 equiv.). Bromine (29 µL, 1 M in CH_2Cl_2, 0.75 equiv.) was added dropwise at 23 °C. The resulting mixture was allowed to stir for 1 h at the same temperature, diluted with Et_2O (5 mL) and added to sat. aq. $Na_2S_2O_3$ (5 mL). The aq. phase was extracted with Et_2O (3 x 3 mL) and the combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2;

*n*hexane/EtOAc 3:1) to yield bromohydrine **134** (16 mg, 26 µmol, 68%) as a colorless oil and single diastereomer.

R_f : 0.27 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.26 – 5.19 (m, 1H), 4.22 (ddd, *J* = 10.7, 8.7, 6.4 Hz, 1H), 4.18 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.04 – 4.00 (m, 1H), 4.00 – 3.96 (m, 1H), 3.08 (ddd, *J* = 16.3, 5.5, 1.8 Hz, 1H), 2.64 (d, *J* = 5.1 Hz, 1H), 2.30 (qdd, *J* = 19.0, 9.1, 4.1 Hz, 2H), 2.19 – 2.08 (m, 1H), 2.05 (s, 3H), 2.00 (s, 3H), 1.98 – 1.95 (m, 2H), 1.93 – 1.85 (m, 2H), 1.81 (dt, *J* = 14.6, 7.3 Hz, 1H), 1.73 – 1.61 (m, 2H), 1.57 – 1.46 (m, 2H), 1.35 – 1.23 (m, 1H), 1.20 (s, 3H), 1.19 – 1.12 (m, 2H), 1.10 (s, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 6.6 Hz 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 7.2 Hz, 3H), 0.59 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.44 (dd, *J* = 5.5, 4.0 Hz, 1H).

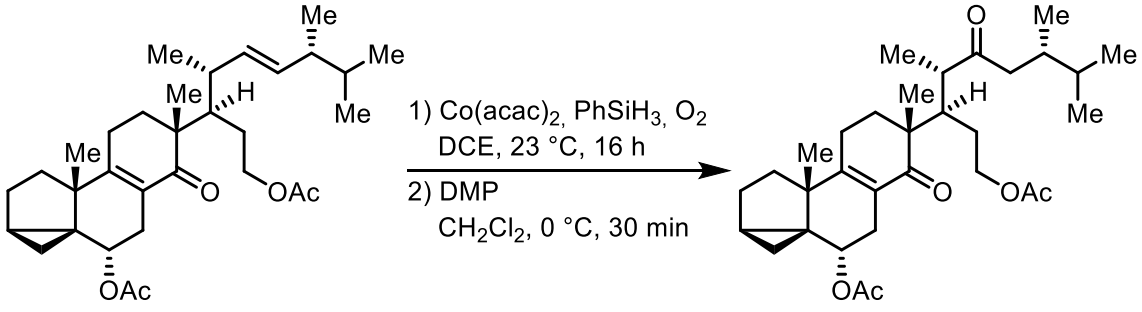
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 202.7, 171.6, 170.4, 159.0, 129.2, 72.5, 66.5, 65.6, 63.7, 50.3, 48.3, 43.4, 40.3, 37.1, 35.4, 33.2, 32.1, 30.1, 29.8, 28.6, 27.0, 26.2, 22.7, 22.6, 21.3, 21.2 (2C), 20.6, 18.8, 13.7, 12.9, 7.8.

FTIR: (neat) [cm^{-1}] = 3496 (br), 2961 (m), 2932 (m), 2360 (w), 1736 (s), 1660 (m), 1620 (w), 1455 (m), 1370 (s), 1305 (w), 1238 (s), 1032 (s), 869 (w), 755 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{47}INaO_5^+$: 637.2360; found:

$[\alpha]_D^{23}$: +67.7 (c= 0.60; $CHCl_3$)

6α,15-Diacetoxy-14,22-dioxo-3α,5-cyclo-14,15-seco-5α-ergosta-8-en



$C_{32}H_{48}O_5$ (512.73)
108

$C_{32}H_{48}O_6$ (528.73)
169

Diacetate **108** (62 mg, 0.12 mmol, 1.0 equiv.) was dissolved in dichloroethane (1.2 mL) and $Co(acac)_2$ (7.8 mg, 30 µmol, 0.25 equiv.) was added followed by phenyl silane (37 µL, 0.30 mmol, 2.5 equiv.). The resulting mixture was evacuated and backfilled with oxygen (three cycles) and stirred under an atmosphere of oxygen at 23 °C for 16 h. The resulting, green solution was filtered over a small plug of silica, washed with sat. aq. $Na_2S_2O_3$ (1 mL)

and the aq. phase was extracted with EtOAc (3 x 1 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure, the obtained residue was dissolved in CH_2Cl_2 (1.2 mL) and cooled to 0 °C. DESS-MARTIN periodinane (62 mg, 0.15 mmol, 1.2 equiv.) was added and the mixture was allowed to stir at 0 °C for 30 min. The mixture was allowed to warm to ambient temperature and sat. aq. $NaHCO_3$ (2 mL) was added. The phases were separated, and the aq. phase was extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 5:1) to yield ketone **169** (25 mg, 50 µmol, 39% over two steps) as a colorless oil as well as unreacted acetate **108** (15 mg, 30 µmol, 24%).

R_f: 0.61 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.23 (dd, *J* = 10.2, 5.6 Hz, 1H), 4.02 (ddd, *J* = 10.8, 8.5, 6.1 Hz, 1H), 3.94 – 3.85 (m, 1H), 3.13 – 3.04 (m, 1H), 2.62 – 2.56 (m, 1H), 2.50 (dd, *J* = 17.0, 4.3 Hz, 1H), 2.35 (t, *J* = 7.6 Hz, 1H), 2.32 – 2.23 (m, 2H), 2.16 (dd, *J* = 17.0, 8.9 Hz, 1H), 2.02 (s, 3H), 2.01 (s, 3H), 1.93 – 1.44 (m, 12H), 1.21 (s, 3H), 1.03 (s, 3H), 1.03 (d, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H), 0.59 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.45 (t, *J* = 4.7 Hz, 1H).

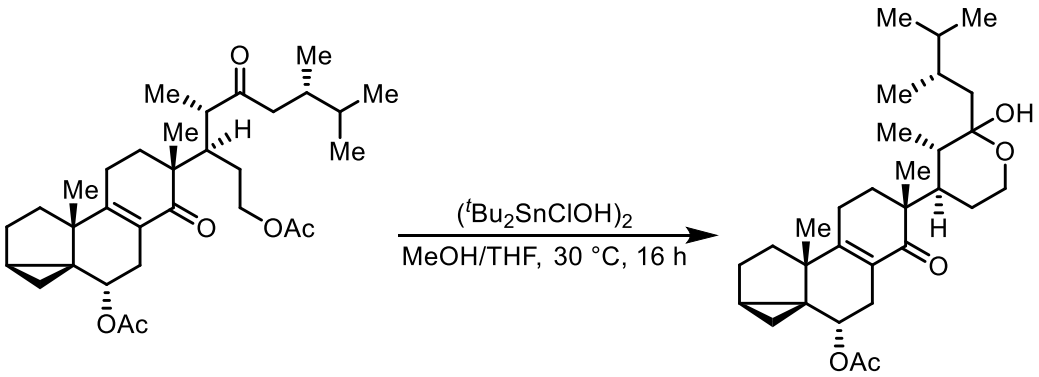
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 214.0, 201.6, 171.1, 170.4, 159.1, 129.3, 66.3, 65.0, 50.3, 47.8, 47.6, 47.3, 42.5, 35.4, 33.9, 33.1, 32.2, 30.5, 29.8, 28.6, 26.3, 26.2, 22.6, 22.6, 21.3, 21.2, 20.1, 18.7, 18.3, 18.1, 15.9, 7.7.

FTIR: (neat) [cm^{-1}] = 2959 (m), 2932 (w), 2871 (w), 2359 (w), 2342 (w), 1735 (s), 1712 (m), 1620 (w), 1455 (m), 1367 (s), 1235 (s), 1095 (m), 1031 (s), 735 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{48}NaO_6^+$:551.3343; found: 551.3367.

$[\alpha]_D^{23}$: +136.9 (c= 1.00; $CHCl_3$)

6α-Acetoxy-22-hydroxy-15,22-oxane-3α,5-cyclo-14,15-seco-5α-ergosta-8-en-14-one



$C_{32}H_{48}O_6$ (528.73)
169

$C_{30}H_{46}O_5$ (486.69)
171

Ketone **169** (14 mg, 27 µmol, 1.0 equiv.) was dissolved in MeOH/THF (1:1, 0.27 mL) and tin compound **111** (1.4 mg, 2.7 µmol, 0.1 equiv.) was added. The mixture was allowed to stir at 30 °C for 16 h. The mixture was diluted with EtOAc (3 mL) and filtered over a plug of silica. The solvent was removed under reduced pressure to give acetal **171** (13 mg, 27 µmol, 100%) as a colorless oil.

R_f: 0.61 (5:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.28 – 5.18 (m, 1H), 3.66 – 3.52 (m, 2H), 3.14 (s, 2H), 2.60 (td, *J* = 11.9, 10.7, 3.3 Hz, 1H), 2.37 – 2.32 (m, 1H), 2.29 – 2.19 (m, 1H), 2.00 (s, 3H), 1.93 – 1.89 (m, 1H), 1.86 – 1.74 (m, 2H), 1.71 (dd, *J* = 14.3, 6.1 Hz, 1H), 1.69 – 1.58 (m, 4H), 1.56 – 1.49 (m, 2H), 1.40 – 1.26 (m, 4H), 1.19 (s, 3H), 0.98 (s, 3H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H), 0.60 (d, *J* = 6.8 Hz, 3H), 0.60 – 0.56 (m, 1H), 0.45 (t, *J* = 4.7 Hz, 1H).

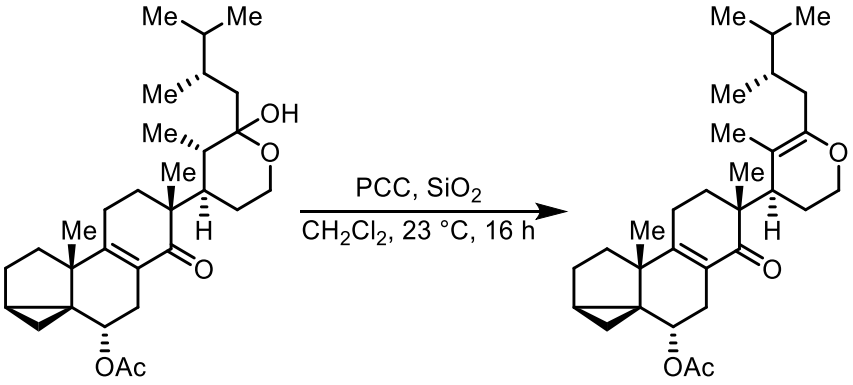
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 201.7, 170.4, 157.7, 129.2, 102.3, 66.6, 61.1, 50.3, 46.9, 45.4, 38.8, 38.7, 38.5, 35.5, 33.6, 33.2, 31.6, 28.6, 27.0, 26.2, 22.6, 22.6, 21.5, 21.2, 21.0, 18.8, 16.4, 16.1, 15.0, 7.8.

FTIR: (neat) [cm^{-1}] = 2956 (m), 2872 (w), 2360 (s), 2341 (s), 1738 (m), 1663 (m), 1456 (w), 1372 (w), 1239 (m), 1033 (w), 916 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{46}NaO_5$: 509.3237 found: 509.3240.

$[\alpha]_D^{23}$: +82.1 (c= 0.71; $CHCl_3$)

6α-Axetoxy-15,22-oxane-3α,5-cyclo-14,15-seco-5α-ergosta-8,21-dien-14-one



$C_{30}H_{46}O_5$ (486.69)
171

$C_{30}H_{44}O_4$ (468.68)
172

To hemiacetal **171**(12 mg, 25 µmol, 1.0 equiv.) in CH_2Cl_2 (0.3 mL) was added SiO_2 (19 mg, 1 mg/mg PCC) and pyridinium chlorochromate (19 mg, 86 µmol, 3.0 equiv.) at 23 °C. The resulting mixture was allowed to stir at the same temperature for 16 h and diluted with Et_2O. The mixture was filtered over a plug of Celite® and rinsed with Et_2O. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 5:1) to give alkyl enol ether **172** (4.3 mg, 9.2 µmol, 37%) as a colorless oil and rearranged ester **174** (5.7 mg, 11 µmol, 46%) as a colorless oil.

R_f: 0.59 (5:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.23 (ddt, *J* = 10.4, 5.4, 1.1 Hz, 1H), 3.97 (ddd, *J* = 10.4, 4.8, 3.8 Hz, 1H), 3.76 (td, *J* = 10.4, 2.5 Hz, 1H), 3.17 – 3.13 (m, 1H), 3.04 (t, *J* = 8.2 Hz, 1H), 2.31 (dtd, *J* = 17.2, 4.5, 1.6 Hz, 1H), 2.27 – 2.15 (m, 1H), 2.09 – 2.03 (m, 1H), 2.00 (s, 3H), 1.90 – 1.84 (m, 2H), 1.79 (dddd, *J* = 13.6, 7.3, 4.8, 2.5 Hz, 1H), 1.71 – 1.63 (m, 4H), 1.60 – 1.47 (m, 4H), 1.35 – 1.29 (m, 1H), 1.24 (d, *J* = 0.9 Hz, 3H), 1.19 (s, 3H), 1.19 – 1.14 (m, 1H), 1.03 (s, 3H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H), 0.60 (dd, *J* = 8.2, 5.4 Hz, 1H), 0.46 – 0.44 (m, 1H).

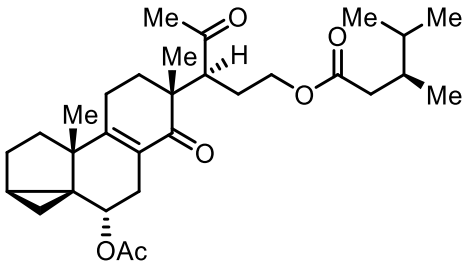
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 202.2, 170.4, 158.7, 151.9, 129.5, 104.6, 66.6, 65.1, 50.5, 46.1, 40.3, 37.4, 35.8, 35.4, 33.2, 32.1, 28.7, 28.7, 26.3, 26.0, 22.6, 22.4, 21.7, 21.2, 20.4, 18.8, 18.1, 17.5, 15.1, 7.8.

FTIR: (neat) [cm^{-1}] = 2958 (s), 2930 (m), 2868 (w), 2360 (s), 2341 (m), 1736 (s), 1658 (s), 1455 (m), 1371 (m), 1308 (w), 1237 (s), 1210 (m), 1032 (s), 916 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_4$: 491.3132; found: 491.3140

$[\alpha]_D^{23}$: +78.2 (c= 1.00; $CHCl_3$)

6α-Acetoxy-14,20-dioxo-3α,5-cyclo-14,15-seco-5α-progest-8-en-15-(*S*)-3,4-dimethylpentanoate



$C_{30}H_{44}O_6$ (500.68)

174

R_f: 0.45 (5:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.21 (ddt, *J* = 10.2, 5.5, 1.0 Hz, 1H), 4.09 – 4.00 (m, 2H), 3.14 (dd, *J* = 11.0, 3.0 Hz, 1H), 2.99 – 2.90 (m, 1H), 2.38 (tdd, *J* = 11.0, 6.7, 4.4 Hz, 1H), 2.33 (dd, *J* = 14.8, 5.2 Hz, 1H), 2.25 (dd, *J* = 11.1, 1.8 Hz, 2H), 2.21 (s, 3H), 2.06 (dd, *J* = 14.8, 9.2 Hz, 1H), 2.00 (s, 3H), 1.97 – 1.84 (m, 3H), 1.82 – 1.75 (m, 1H), 1.73 – 1.69 (m, 1H), 1.65 – 1.60 (m, 1H), 1.61 – 1.54 (m, 3H), 1.31 (dt, *J* = 8.2, 4.2 Hz, 1H), 1.20 (s, 3H), 1.19 – 1.13 (m, 1H), 1.12 (s, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.59 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.45 – 0.41 (m, 1H).

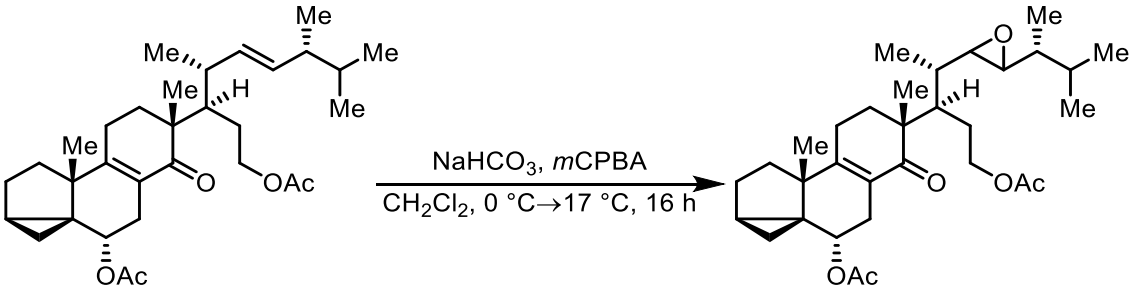
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 212.9, 201.8, 173.7, 170.5, 160.2, 128.8, 66.5, 62.9, 53.2, 50.4, 47.3, 39.2, 36.0, 35.3, 33.2, 33.1, 32.2, 30.2, 28.7, 26.8, 26.0, 22.9, 22.8, 21.5, 21.2, 20.0, 18.9, 18.4, 16.0, 7.7.

FTIR: (neat) [cm^{-1}] = 2960 (s), 2932 (m), 2871 (w), 2360 (s), 2341 (m), 1734 (s), 1708 (m), 1658 (m), 1620 (w), 1369 (m), 1272 (w), 1238 (s), 1167 (m), 1032 (m), 918 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_6^+$: 523.3030; found: 523.3048.

$[\alpha]_D^{23}$: +120.5 (c= 1.00; $CHCl_3$)

22,23-Epoxy-6*α*,15-diacetoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en-14-one



$C_{32}H_{48}O_5$ (512.73)
108

$C_{32}H_{48}O_6$ (528.73)
110

To diacetate **108** (60 mg, 0.12 mmol, 1.0 equiv.) in CH_2Cl_2 (1.2 mL) at 0 °C was added $NaHCO_3$ (25 mg, 0.29 mmol, 2.5 equiv.) followed by *meta*-chloroperbenzoic acid (28 mg, 0.16 mmol, 1.4 equiv.). The mixture was allowed to slowly warm to 17 °C over night by melting of the ice. The mixture was diluted with EtOAc (3 mL) and added to sat. aq. $NaHCO_3$ (3 mL). The aqueous phase was extracted with EtOAc (2 x 2 mL) and the combined organic phases were washed with sat. aq. $NaHCO_3$ (3 mL) and sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 5:1) to yield epoxide **110** (53 mg, 0.10 mmol, 85%) as a colorless oil in a 3:1 ratio of diastereomers as well as unreacted **108** (3.4 mg, 6.6 µmol, 6%) as a colorless oil. Signals of the minor diastereomer are marked with * as identifiable in the respective ^{1}H and ^{13}C NMR spectra.

R_f : 0.27 (5:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.23 (ddt, *J* = 10.3, 5.7, 1.0 Hz, 1H), 4.03 – 3.92 (m, 2H), 3.11 – 3.04 (m, 1H), 2.63 (dd, *J* = 8.0, 2.2 Hz, 1H), 2.62 – 2.58 (m, 1H), 2.44 (dd, *J* = 8.0, 2.2 Hz, 1H), 2.30 – 2.24 (m, 1H), 2.22 – 2.16 (m, 1H), 2.10 (ddd, *J* = 13.1, 8.2, 4.6 Hz, 1H), 2.03 (s, 3H), 2.02* (s, 1H), 2.00* (s, 1H), 2.00 (s, 3H), 1.98 – 1.95 (m, 1H), 1.91 – 1.81 (m, 1H), 1.78 (qd, *J* = 7.6, 2.2 Hz, 2H), 1.75 – 1.68 (m, 1H), 1.64 (tdd, *J* = 12.4, 6.3, 2.6 Hz, 1H), 1.55 – 1.44 (m, 1H), 1.30 (tt, *J* = 8.1, 3.9 Hz, 2H), 1.21* (s, 1H), 1.20 (s, 3H), 1.17 – 1.13 (m, 2H), 1.12 (s, 3H), 1.06* (s, 1H), 1.02 (d, *J* = 7.3 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 11.1 Hz, 1H), 0.57 (td, *J* = 8.6, 5.5 Hz, 1H), 0.44 (dd, *J* = 5.5, 3.9 Hz, 1H).

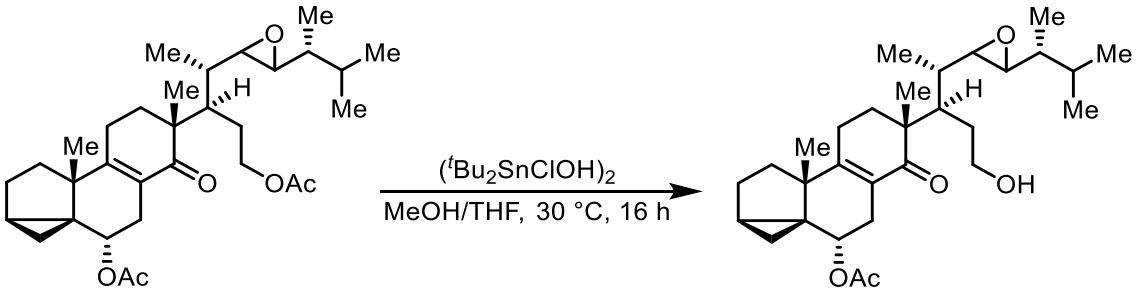
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 202.6, 202.0*, 171.1, 171.0*, 170.4*, 170.4, 159.0, 158.7*, 129.4*, 129.1, 66.4, 66.3*, 64.9, 64.6*, 62.6, 62.6*, 60.6, 59.9*, 50.1, 50.0*, 47.6*, 47.4, 43.6, 42.6*, 42.4, 42.1*, 38.5, 36.2*, 35.4, 33.0*, 33.0, 31.2*,

31.1, 31.0*, 30.4*, 28.6, 26.1*, 26.0, 25.7*, 25.1, 22.6, 22.6*, 22.5, 21.2, 21.2, 21.1*, 20.8*, 20.7, 20.5, 20.4*, 19.5, 19.4, 18.6, 18.6, 18.2*, 13.5, 12.5*, 7.5.

FTIR: (neat) [cm^{-1}] = 2961 (m), 2933 (w), 2359 (m), 2341 (w), 1737 (s), 1660 (m), 1621 (m), 1457 (w), 1368 (m), 1238 (s), 1033 (m), 904 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{48}NaO_6^+$: 551.3343; found: 551.3345.

22,23-Epoxy-6α-acetoxy-15-hydroxy-3α,5-cyclo-14,15-seco-5α-ergosta-8-en-14-one



$C_{32}H_{48}O_6$ (528.73)
110

$C_{30}H_{46}O_5$ (486.69)
114

Epoxide **110** (12 mg, 23 µmol, 1.0 equiv.) was dissolved in MeOH/THF (1:1, 0.23 mL) and **111** (2.7 mg, 4.7 µmol, 0.2 equiv.) was added. The resulting mixture was allowed to stir at 30 °C for 16 h and diluted with EtOAc (1 mL). The resulting mixture was filtered over a plug of silica and the solvent was removed to yield epoxy alcohol **114** (12 mg, 23 µmol, 99%) as a colorless oil. Signals of the minor diastereomer are marked with * as identifiable in the respective ^{1}H and ^{13}C NMR spectra.

R_f : 0.22 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.23 (ddt, *J* = 10.2, 5.6, 1.1 Hz, 1H), 3.63 – 3.55 (m, 1H), 3.55 – 3.47 (m, 1H), 3.09 – 3.02 (m, 1H), 2.65 (dd, *J* = 8.0, 2.3 Hz, 1H), 2.64 – 2.60 (m, 1H), 2.46 (dd, *J* = 8.0, 2.3 Hz, 1H), 2.34 – 2.18 (m, 2H), 2.09 (ddd, *J* = 13.7, 7.9, 4.7 Hz, 1H), 2.00 (s, 1H), 2.00 (s, 3H), 1.92 – 1.58 (m, 5H), 1.46 (s, 3H), 1.33 (ddt, *J* = 43.5, 8.3, 4.1 Hz, 2H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.13 (s, 3H), 1.11 – 1.04 (m, 1H), 1.00 (d, *J* = 7.3 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.90 – 0.87 (m, 1H), 0.56 (dd, *J* = 8.1, 5.4 Hz, 1H), 0.44 (dd, *J* = 5.5, 3.9 Hz, 1H).

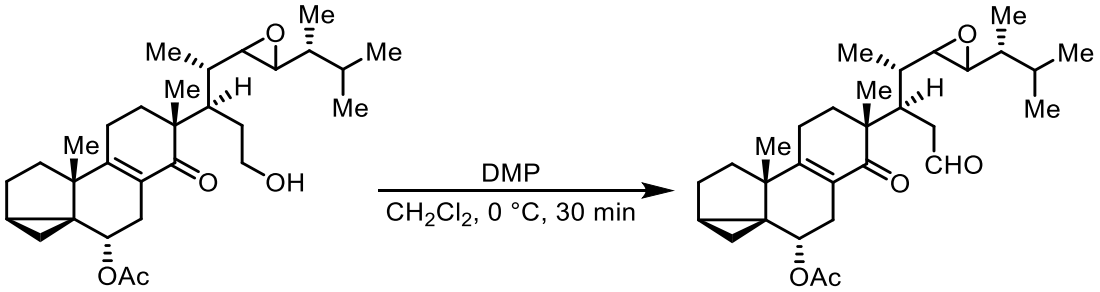
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.3,202.5*, 170.4, 158.9, 158.6*, 129.4*, 129.0, 66.5, 66.3*, 63.5, 63.1, 62.9*, 62.7, 62.4*, 60.0, 59.9*, 50.0, 47.6*, 47.3, 43.1, 42.4, 42.2, 42.0*, 38.6, 36.1, 36.0*, 35.4, 33.1, 33.0*, 31.3, 31.2*, 31.1, 31.0,

30.6*, 29.9, 29.8*, 29.5*, 29.4, 28.7, 26.0, 22.6, 22.5, 21.2, 20.7, 20.6*, 20.4, 20.3, 20.2*, 19.5, 19.3, 18.7, 18.6, 18.3*, 13.6, 12.6, 12.4*, 7.5.

FTIR: (neat) [cm^{-1}] = 3462 (br), 2960 (m), 2931 (m), 2873 (w), 2360 (s), 2341 (s), 1737 (m), 1659 (m), 1622 (w), 1456 (w), 1371 (m), 1240 (s), 1033 (m), 904 (w), 668 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{46}NaO_5^+$: 535.3394; found: 535.3403.

22,23-Epoxy-6α-acetoxy-15-hydroxy-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien-15-al-14-one



$C_{30}H_{46}O_5$ (486.69)
114

$C_{30}H_{44}O_5$ (484.68)
113

To alcohol **114** (12 mg, 25 µmol, 1.0 equiv.) in CH_2Cl_2 (0.25 mL) was added DESS-MARTIN periodinane (14 mg, 32 µmol, 1.3 equiv.) at 0 °C. The resulting mixture was allowed to stir at the same temperature for 30 min. Sat. aq. $NaHCO_3$ (1 mL) was added and the phases were separated. The aq. phase was extracted with EtOAc (3 x 2 mL) and the combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 5:1) to give epoxy aldehyde **113** (5.3 mg, 11 µmol, 44%) as a colorless oil. Signals of the minor diastereomer are marked with * as identifiable in the respective ^1H and ^{13}C NMR spectra.

R_f : 0.33 (5:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^1H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = δ 9.73 (t, *J* = 1.4 Hz, 1H), 5.23 (dd, *J* = 10.3, 5.5 Hz, 1H), 3.02 – 2.96 (m, 1H), 2.77 – 2.73 (m, 1H), 2.68 (ddd, *J* = 18.1, 5.2, 1.3 Hz, 1H), 2.58 – 2.53 (m, 1H), 2.50 (dd, *J* = 8.1, 2.3 Hz, 1H), 2.45 (dd, *J* = 8.0, 2.2 Hz, 1H), 2.35 – 2.28 (m, 1H), 2.22 (dddt, *J* = 17.8, 7.2, 4.8, 2.5 Hz, 1H), 2.12 – 2.06 (m, 1H), 2.00 (d, *J* = 1.4 Hz, 3H), 1.87 – 1.81 (m, 2H), 1.73 (dddd, *J* = 33.9, 13.8, 7.4, 5.0 Hz, 1H), 1.67 – 1.61 (m, 3H), 1.44 – 1.38 (m, 1H), 1.35 (dd, *J* = 7.7, 3.6 Hz, 1H), 1.22 (s, 3H), 1.19 – 1.11 (m, 1H), 1.10 (s, 3H), 1.08 – 1.04 (m, 1H), 0.98

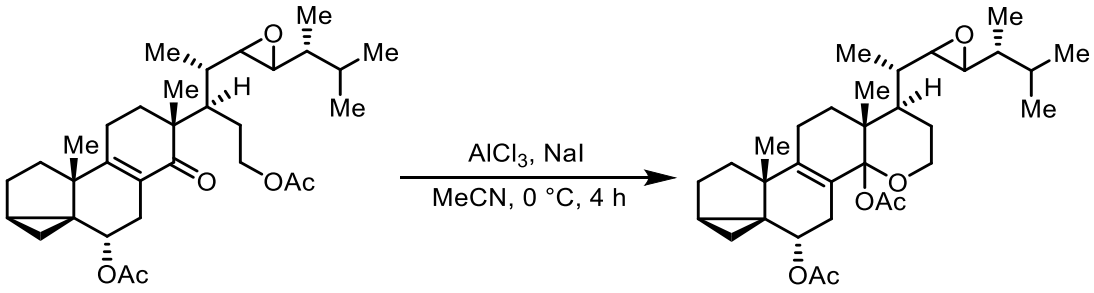
(d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.58 – 0.55 (m, 1H), 0.45 (dd, *J* = 5.4, 4.0 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 202.5, 202.1*, 201.7, 202.2*, 170.5*, 170.4, 158.9, 158.8*, 129.6*, 129.2, 66.5, 66.4*, 62.7, 61.6*, 60.8, 59.6*, 50.0, 49.9*, 46.9, 46.7, 42.3, 42.1*, 41.3, 39.9*, 38.6*, 38.0, 35.3, 35.0*, 33.1*, 33.1, 32.1*, 31.7*, 31.1, 31.1*, 30.9*, 30.9, 29.9*, 28.6, 26.0, 25.9*, 22.6, 22.6*, 22.5, 22.5*, 21.2, 20.9*, 20.6, 20.4*, 20.3, 19.4, 18.8*, 18.8, 18.7*, 18.7, 17.2*, 12.7*, 13.6, 7.5, 7.4*.

FTIR: (neat) [cm^{-1}] = 2961 (m), 2930 (w), 2360 (s), 2341 (s), 1735 (m), 1656 (m), 1457 (w), 1372 (m), 1240 (s), 1033 (m), 905 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_5^+$: 507.3081; found: 507.3102.

22,23-Epoxy-14,15-Oxane-6*α*,14-diacetoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en



$C_{32}H_{48}O_6$ (528.73)
110

$C_{32}H_{48}O_6$ (528.73)
138

To epoxide **110** (20 mg, 38 µmol, 1.0 equiv.) in MeCN (0.38 mL) was added sodium iodide (15 mg, 0.10 mmol, 2.7 equiv.). The mixture was degassed by three cycles of freeze-pump-thaw and cooled to 0 °C. Aluminum trichloride (6.6 mg, 49 µmol, 1.3 equiv.) was added in two portions and the resulting mixture was allowed to stir at the same temperature for 15 min. Sat. aq. $NaHCO_3$ (1 mL) was carefully added and the mixture was extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 3:1) to yield hemiacetal **138** (20 mg, 38 µmol, quant.) as a colorless oil and 1:2 of diastereomers. Signals of the minor diastereomer are marked with * as identifiable in the respective ^{1}H and ^{13}C NMR spectra.

R_f : 0.26 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (500 MHz, $CDCl_3$) δ [ppm] = 5.26 (dd, *J* = 10.4, 5.4, 1H), 4.19 – 4.08 (m, 1H), 4.03 – 3.94 (m, 1H), 3.85 (dt, *J* = 10.6, 7.8, 1H), 3.62 (dd, *J* = 11.9, 3.0, 1H), 2.93 – 2.72 (m, 1H), 2.30 – 2.14 (m, 1H), 2.05 (s, 3H), 1.99 (s, 3H), 1.95 – 1.17 (m,

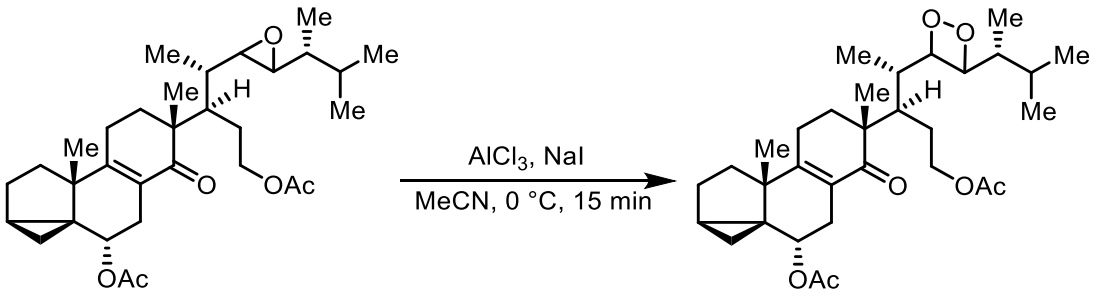
18H), 1.11 (s, 3H), 1.06 (s, 3H), 1.03 (d, *J* = 7.8, 3H), 0.91 (d, *J* = 6.9, 3H), 0.78 (d, *J* = 6.8, 3H), 0.47 (dd, *J* = 8.1, 5.3, 1H), 0.40 – 0.36 (m, 1H).

^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 171.4, 171.3*, 170.5*, 170.4, 139.6*, 138.5, 127.1, 126.4*, 108.6*, 106.5, 84.6, 82.5*, 81.1*, 80.9, 67.5, 67.2*, 66.9, 62.9*, 49.0, 48.9*, 44.0, 44.0*, 40.0, 39.7*, 38.0*, 37.5*, 37.2, 35.9*, 35.7, 33.9, 33.0, 32.7*, 29.8, 29.3*, 28.9*, 28.9, 27.5*, 27.1, 26.9*, 26.0, 25.9*, 25.8, 25.0*, 23.9, 23.4*, 23.4, 22.2*, 21.9, 21.7, 21.3, 21.2, 21.1*, 20.5*, 20.2*, 18.9, 18.7*, 16.6*, 15.6, 15.5*, 15.4, 11.3*, 10.6, 7.8, 7.7*.

FTIR: (neat) [cm^{-1}] = 2959 (m), 2874 (w), 2360 (m), 2342 (w), 1456 (w), 1368 (m), 1237 (s), 1032 (s) 737 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{48}NaO_6^+$: 551.3343; found: 551.3348.

22,23-Dioxetan-6α,15-diacetoxy-3α,5-cyclo-14,15-seco-5α-ergosta-8-en-14-one



$C_{32}H_{48}O_6$ (528.73)
110

$C_{32}H_{48}O_7$ (544.73)
137

To epoxide **110** (20 mg, 38 µmol, 1.0 equiv.) in MeCN (0.38 mL) was added sodium iodide (15 mg, 0.10 mmol, 2.7 equiv.) at 0 °C. Aluminum trichloride (6.6 mg, 49 µmol, 1.3 equiv.) was added in two portions and the resulting mixture was allowed to stir at the same temperature for 15 min. Sat. aq. $NaHCO_3$ (1 mL) was carefully added and the mixture was extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 3:1→2:1) to yield dioxetane **137** (9.2 mg, 17 µmol, 45%) as a colorless oil.

R_f : 0.20 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: (700 MHz, $CDCl_3$) δ [ppm] = 5.23 (dd, *J* = 10.3, 5.5 Hz, 1H), 4.15 (ddd, *J* = 10.7, 8.7, 6.5 Hz, 1H), 3.97 (ddd, *J* = 10.5, 8.4, 6.1 Hz, 1H), 3.68 (dd, *J* = 9.1, 5.0 Hz, 1H), 3.61 – 3.58 (m, 1H), 3.09 (dd, *J* = 16.5, 3.8 Hz, 1H), 2.35 – 2.22 (m, 2H), 2.18 – 2.12 (m, 2H), 2.04 (s, 3H), 2.00 (s, 3H), 1.91 – 1.87 (m, 1H), 1.87 – 1.79

(m, 2H), 1.70 – 1.62 (m, 3H), 1.61 – 1.56 (m, 1H), 1.48 (tdd, *J* = 12.3, 7.8, 4.2 Hz, 1H), 1.31 (dt, *J* = 8.2, 4.1 Hz, 1H), 1.28 – 1.22 (m, 2H), 1.21 (s, 3H), 1.19 – 1.13 (m, 1H), 1.06 (s, 3H), 0.97 – 0.94 (m, 6H), 0.89 – 0.85 (m, 6H), 0.57 (dd, *J* = 8.2, 5.5 Hz, 1H), 0.44 (t, *J* = 4.7 Hz, 1H).

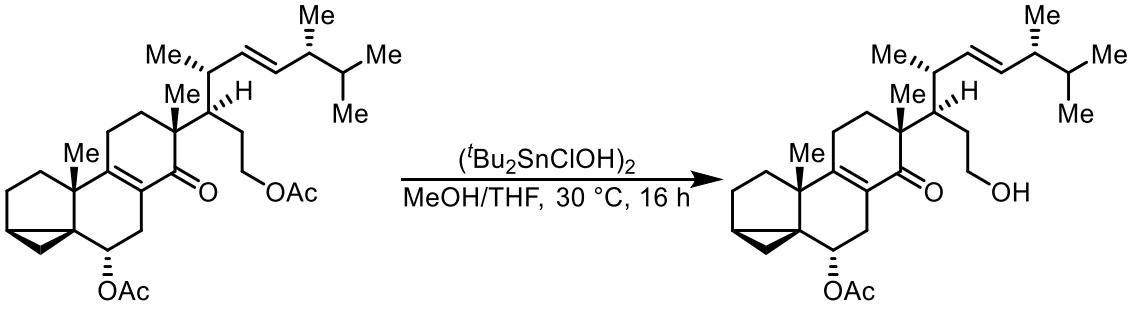
^{13}C NMR: (176 MHz, $CDCl_3$) δ [ppm] = 203.0, 171.5, 170.4, 158.7, 129.2, 73.2, 72.4, 66.4, 65.5, 50.1, 48.0, 42.8, 39.4, 35.4, 34.7, 33.1, 31.2, 30.6, 29.8, 28.6, 27.0, 26.1, 22.7, 22.6, 21.2, 21.0, 20.8, 18.7, 14.2, 9.5, 7.6, 1.2.

FTIR: (neat) [cm^{-1}] = 2959 (m), 2932 (w), 2363 (s), 2337 (s), 1740 (m), 1657 (m), 1333 (w), 1371 (m), 1240 (s), 1043 (m), 907 (w), 872 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{48}NaO_7^+$: 567.6292; found: 567.6319

$[\alpha]_D^{23}$: +143.3 (c= 1.00; $CHCl_3$)

(22*E*)-15-Hydroxy-6α-acetoxy-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien-14-one



$C_{32}H_{48}O_5$ (512.73)
108

$C_{30}H_{46}O_4$ (470.69)
109

Diacetate **108** (0.40 g, 0.78 mmol, 1.0 equiv.) was dissolved in MeOH/THF (1:1, 7.8 mL) and tin compound **111** (44 mg, 78 µmol, 0.05 equiv.) was added. The mixture was allowed to stir at 30 °C for 16 h. The mixture was diluted with EtOAc (25 mL) and filtered over a plug of silica. The solvent was removed under reduced pressure to give alcohol **109** (0.36g, 0.78 mmol, quant.) as a colorless oil.

R_f: 0.16 (4:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.35 (ddd, *J* = 15.3, 8.2, 0.9 Hz, 1H), 5.26 – 5.22 (m, 2H), 3.48 (ddd, *J* = 10.4, 8.4, 6.2 Hz, 1H), 3.38 (ddd, *J* = 10.4, 8.3, 6.6 Hz, 1H), 3.12 – 3.07 (m, 1H), 2.39 – 2.28 (m, 2H), 2.22 (dddt, *J* = 18.0, 6.9, 4.7, 2.4 Hz, 1H), 2.13 (ddd, *J* = 13.7, 6.3, 4.6 Hz, 1H), 2.00 (s, 3H), 1.92 – 1.85 (m, 2H), 1.81 (dd, *J* = 13.8, 7.6 Hz, 1H), 1.76 (td, *J* = 5.2, 2.7 Hz, 1H), 1.70 – 1.63 (m, 2H), 1.62 – 1.49 (m, 3H), 1.48 – 1.43 (m, 1H), 1.31 (dt, *J* = 8.2, 4.1 Hz, 1H), 1.22 (s,

3H), 1.18 – 1.10 (m, 1H), 1.01 (s, 3H), 1.00 (d, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.56 (dd, *J* = 8.1, 5.5 Hz, 1H), 0.46 – 0.43 (m, 1H).

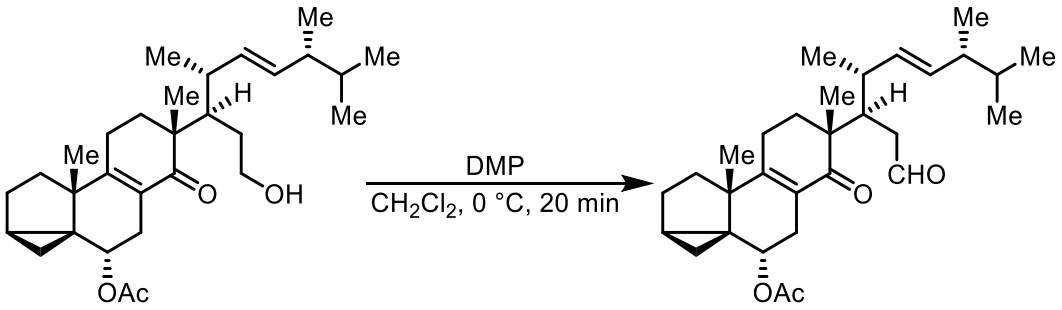
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 203.3, 170.4, 158.6, 134.9, 132.6, 129.1, 66.4, 63.7, 49.8, 47.7, 43.4, 42.1, 38.4, 35.4, 33.3, 33.0, 31.4, 29.2, 28.7, 26.1, 23.1, 22.6 (2C), 21.2, 20.2, 20.2, 19.8, 18.6, 17.7, 7.5.

FTIR: (neat) [cm^{-1}] = 2958 (m), 2870 (w), 2359 (s), 2341 (s), 1740 (m), 1653 (m), 1622 (w), 1456 (m), 1372 (m), 1239 (m), 1034 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{46}NaO_4^+$: 493.3288; found: 493.3296.

$[\alpha]_D^{23}$: +151.8 (c= 1.00; $CHCl_3$)

(22*E*)-6α-acetoxy-14-oxo-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien-15-al



$C_{30}H_{46}O_4$ (470.69)
109

$C_{30}H_{44}O_4$ (468.68)
301

To alcohol **109** (37 mg, 80 µmol, 1.0 equiv.) in CH_2Cl_2 (0.79 mL) was added at 0 °C Dess-Martin periodinane (40 mg, 90 µmol, 1.2 equiv.). After stirring at the same temperature for 20 min, sat. aq. $NaHCO_3$ (1 mL) was added. The phases were separated, and the aq. phase was extracted with EtOAc (3 x 1 mL). The combined organic phases were washed with sat. aq. NaCl (1 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 5:1) to yield aldehyde **301** (37 mg, 80 µmol, quant.) as a colorless oil.

R_f: 0.44 (5:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 9.63 (s, 1H), 5.27 – 5.21 (m, 3H), 2.98 (dd, *J* = 16.5, 5.6 Hz, 1H), 2.59 (q, *J* = 3.5, 3.0 Hz, 1H), 2.57 – 2.52 (m, 1H), 2.44 (d, *J* = 7.3 Hz, 1H), 2.40 – 2.29 (m, 2H), 2.24 (d, *J* = 18.0 Hz, 1H), 2.15 (dt, *J* = 13.4, 5.1 Hz, 1H), 1.99 (d, *J* = 1.5 Hz, 3H), 1.88 (q, *J* = 6.3 Hz, 1H), 1.85 – 1.80 (m, 2H), 1.75 – 1.65 (m, 3H), 1.58 (s, 1H), 1.46 (h, *J* = 6.7 Hz, 1H), 1.38 (dt, *J* = 8.2, 4.0 Hz, 1H), 1.24 – 1.22 (m, 3H), 1.15 (td, *J* = 13.2, 7.5 Hz, 1H), 1.00 – 0.97 (m, 3H), 0.94 – 0.93

(m, 3H), 0.93 – 0.91 (m, 3H), 0.84 – 0.83 (m, 3H), 0.82 – 0.80 (m, 3H), 0.56 (t, *J* = 6.8 Hz, 1H), 0.45 (d, *J* = 4.7 Hz, 1H).

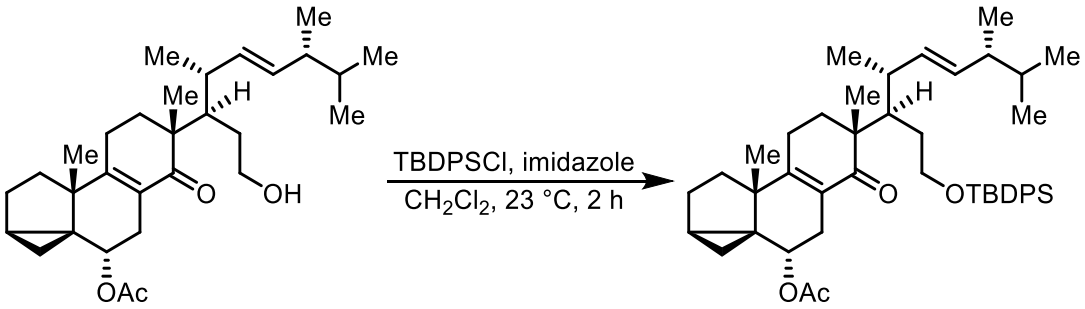
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 202.6, 201.9, 170.4, 158.7, 135.6, 132.2, 129.3, 66.4, 49.8, 47.0, 43.4, 41.1, 38.9, 37.7, 35.3, 33.2, 33.0, 31.6, 28.7, 25.9, 22.6, 22.5, 22.4, 21.2, 20.3, 20.2, 19.8, 18.7, 17.6, 7.4.

FTIR: (neat) [cm^{-1}] = 2958 (m), 2929 (w), 2868 (w), 2360 (s), 2341 (m), 1725 (s), 1655 (s), 1622 (w), 1455 (m), 1368 (m), 1238 (s), 1211 (s), 1031 (s), 983 (w), 870 (w), 754 (s), 667 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_4^+$: 491.3132; found: 491.3119.

$[\alpha]_D^{21}$: +152.9 (c= 1.00; $CHCl_3$)

(22*E*)-6α-Acetoxy-15-(*tert*-butyldiphenylsilyl)oxy-14-oxo-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien



$C_{30}H_{46}O_4$ (470.69)
109

$C_{46}H_{64}O_4Si$ (709.10)
135

To alcohol **109** (360 mg, 0.760 mmol, 1.0 equiv.) in CH_2Cl_2 (7.6 mL) was added 4-dimethylaminopyridine (19.0 mg, 0.150 mmol, 0.2 equiv.) and imidazole (78.1 mg, 1.15 mmol, 1.5 equiv.). At 23 °C, *tert*-butyldiphenylsilyl chloride (275 µL, 1.07 mmol, 1.4 equiv.) was added and the resulting mixture was allowed to stir at the same temperature for 2 h. Sat. aq. $NaHCO_3$ (20 mL) was added and the phases were separated. The aq. phase was extracted with EtOAc (3 x 10 mL) and washed with sat. aq. NaCl (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1) to yield silyl ether **135** (542 mg, 0.760 mmol, quant.).

R_f: 0.42 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.42 – 7.36 (m, 10H), 5.29 (ddd, *J* = 15.3, 8.2, 0.9 Hz, 1H), 5.21 – 5.15 (m, 2H), 3.43 (t, *J* = 7.8 Hz, 2H), 3.07 – 3.01 (m, 1H), 2.26 – 2.21 (m, 2H), 2.16 (dddt, *J* = 15.0, 9.6, 4.6, 2.3 Hz, 1H), 2.09 (ddd, *J* = 13.6, 7.2,

4.5 Hz, 1H), 2.01 (s, 3H), 1.86 (dtt, *J* = 8.2, 7.2, 6.3 Hz, 1H), 1.78 – 1.70 (m, 2H), 1.66 (td, *J* = 5.2, 2.7 Hz, 1H), 1.62 – 1.55 (m, 4H), 1.55 – 1.52 (m, 1H), 1.49 – 1.41 (m, 1H), 1.36 (dtt, *J* = 16.6, 7.9, 4.3 Hz, 1H), 1.18 (s, 3H), 1.13 (td, *J* = 9.4, 8.7, 4.7 Hz, 1H), 1.04 (s, 9H), 0.93 (s, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 7.1 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.52 (dd, *J* = 8.1, 5.4 Hz, 1H), 0.40 (dd, *J* = 5.4, 4.0 Hz, 1H).

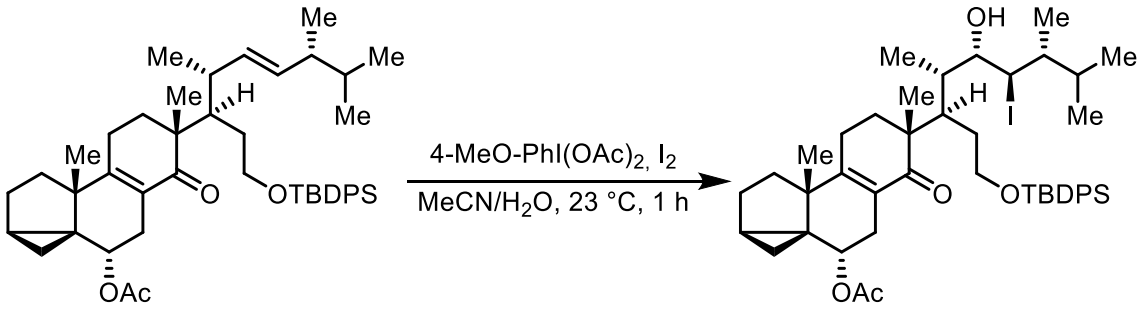
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 202.8, 170.3, 158.3, 135.7, 135.7, 135.3, 134.9, 134.6 , 134.2, 133.1, 129.8, 129.6, 129.1, 127.9, 127.7, 127.0, 66.4, 65.0, 49.9, 47.8, 43.4, 42.6, 38.6, 35.3, 33.3, 33.0, 30.9, 29.0, 28.5, 28.3, 27.1, 27.0, 26.7, 26.1, 23.2, 22.6, 22.5, 21.2, 20.6, 20.3, 19.8, 19.3, 19.2, 18.5, 17.8, 7.5.

FTIR: (neat) [cm^{-1}] = 2957 (s), 2931 (m), 2857 (w), 2359 (s), 2341 (m), 1740 (m), 1661 (m), 1428 (m), 1371 (w), 1240 (s), 1111 (s), 1032 (m), 821 (w), 740 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{46}H_{64}NaO_4Si^+$: 731.4466; found: 731.4470.

$[\alpha]_D^{23}$: +90.3 (c= 1.00; $CHCl_3$)

23(*R*)-Iodo-6*α*-Acetoxy-15-(*tert*-butyldiphenylsilyl)oxy-22(*S*)-hydroxy-14-oxo-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8-en



$C_{46}H_{64}O_4Si$ (709.10)
135

$C_{46}H_{65}IO_5Si$ (853.01)
136

Silyl ether **135** (71 mg, 0.10 mmol, 1.0 equiv.) was dissolved in MeCN/H_2O (4:1, 1.0 mL) at 23 °C. *p*-(diacetoxyiodo)anisole (53 mg, 0.15 mmol, 1.5 equiv.) and iodine (19 mg, 0.75 mmol, 0.75 equiv.) were added and the resulting mixture was allowed to stir at the same temperature for 1 h. The mixture was diluted with Et_2O (5 mL) and added to sat. aq. $Na_2S_2O_3$ (10 mL). The aq. phase was extracted with Et_2O (2 x 5 mL), the combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 5:1) to yield iodohydrin **136** (32 mg, 38 µmol, 38%) as a colorless oil.

R_f: 0.28 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.68 (dq, *J* = 6.7, 1.3 Hz, 4H), 7.44 – 7.36 (m, 6H), 5.22 – 5.18 (m, 1H), 4.24 (dd, *J* = 10.2, 2.0 Hz, 1H), 4.02 (ddd, *J* = 10.2, 4.3, 1.3 Hz, 1H), 3.76 – 3.64 (m, 2H), 3.09 – 3.03 (m, 1H), 2.90 (d, *J* = 4.3 Hz, 1H), 2.32 – 2.24 (m, 2H), 2.09 – 2.01 (m, 2H), 2.00 (s, 3H), 1.91 – 1.82 (m, 2H), 1.77 – 1.70 (m, 1H), 1.69 – 1.65 (m, 1H), 1.64 – 1.59 (m, 3H), 1.52 – 1.44 (m, 1H), 1.37 (dp, *J* = 8.7, 6.6 Hz, 1H), 1.29 – 1.25 (m, 2H), 1.19 (s, 3H), 1.18 – 1.14 (m, 1H), 1.06 (s, 9H), 1.02 (s, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.88 – 0.85 (m, 6H), 0.71 (d, *J* = 7.2 Hz, 3H), 0.58 (dd, *J* = 8.2, 5.4 Hz, 1H), 0.44 – 0.41 (m, 1H).

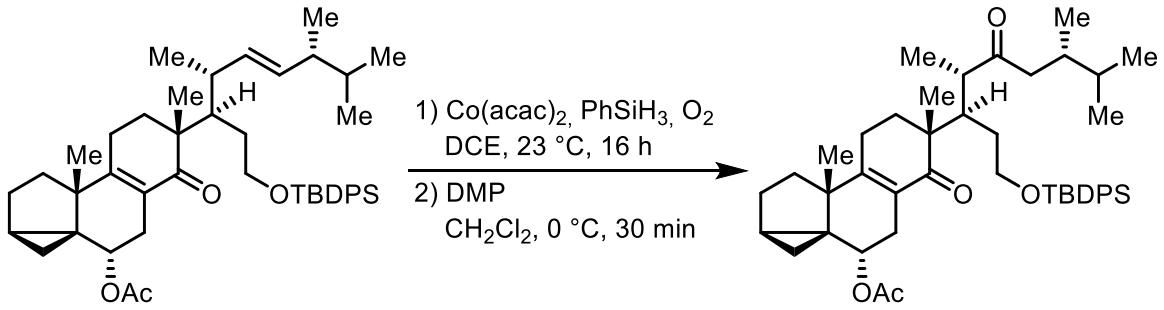
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 203.2, 170.4, 158.8, 135.8 (4C), 133.8, 133.7, 129.8, 129.8, 129.3, 127.8 (3C), 127.8, 73.1, 66.5, 65.2, 51.3, 50.4, 47.9, 43.7, 40.2, 35.4, 34.1, 33.3, 31.7, 28.6, 27.1 (3C), 25.4, 22.7, 22.6, 22.0, 21.2, 21.0, 20.5, 19.3, 18.9, 15.9, 15.8, 12.4, 11.6, 7.8.

FTIR: (neat) [cm^{-1}] = 2959 (m), 2929 (m), 2857 (w), 2360 (s), 2341 (m), 1735 (m), 1652 (m), 1619 (w), 1456 (w), 1373 (w), 1239 (s), 1109 (s), 1030 (s), 736 (s), 701 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{46}H_{65}INaO_5Si^+$: 875.3538; found: 875.3548.

$[\alpha]_D^{23}$: +76.5 (c= 1.00; $CHCl_3$)

6α-Acetoxy-15-(*tert*-butyldiphenylsilyl)oxy-14,22-dioxo-3α,5-cyclo-14,15-seco-5α-ergosta-8-en



$C_{46}H_{64}O_4Si$ (709.10)
135

$C_{46}H_{64}O_5Si$ (725.10)
302

Silyl ether **135** (87 mg, 0.12 mmol, 1.0 equiv.) was dissolved in dichloroethane (1.2 mL) and $Co(acac)_2$ (6.3 mg, 25 µmol, 0.20 equiv.) was added followed by phenyl silane (45 µL, 0.37 mmol, 3.0 equiv.). The resulting mixture was evacuated and backfilled with oxygen (three cycles) and stirred under an atmosphere of oxygen at 23 °C for 16 h. The resulting, green solution was filtered over a small plug of silica, washed with sat. aq. $Na_2S_2O_3$ (1 mL) and the aq. phase was extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed

under reduced pressure and the obtained residue was dissolved in CH_2Cl_2 (1.2 mL) and cooled to 0 °C. Dess-Martin periodinane (62 mg, 0.15 mmol, 1.2 equiv.) was added and the mixture was allowed to stir at 0 °C for 45 min. The mixture was allowed to warm to ambient temperature and sat. aq. $NaHCO_3$ (2 mL) was added. The phases were separated, and the aq. phase was extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1) to yield ketone **302** (19 mg, 26 µmol, 19%) as a colorless oil.

R_f: 0.61 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.65 (d, *J* = 6.7 Hz, 4H), 7.39 (dd, *J* = 17.7, 7.3 Hz, 6H), 5.18 (dd, *J* = 10.1, 5.4 Hz, 1H), 3.55 (t, J = 7.5 Hz, 2H), 3.03 (dd, *J* = 16.3, 4.8 Hz, 1H), 2.53 – 2.49 (m, 1H), 2.43 (dd, *J* = 16.7, 4.1 Hz, 1H), 2.26 – 2.11 (m, 5H), 2.00 (s, 3H), 1.88 (d, *J* = 6.7 Hz, 1H), 1.83 – 1.69 (m, 5H), 1.68 – 1.56 (m, 4H), 1.54 – 1.21 (m, 6H), 1.18 (s, 3H), 1.03 (s, 5H), 0.93 (d, *J* = 7.2 Hz, 3H), 0.89 (s, 3H), 0.83 (d, *J* = 6.8 Hz, 2H), 0.78 (d, *J* = 3.8 Hz, 3H), 0.77 (d, *J* = 3.7 Hz, 3H), 0.56 (dd, *J* = 8.0, 5.6 Hz, 1H), 0.43 – 0.40 (m, 1H).

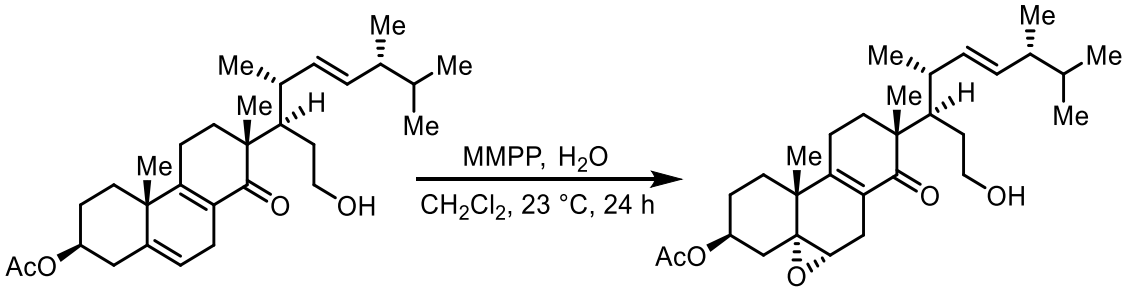
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 214.1, 201.7, 170.3, 158.8, 135.7, 134.9, 134.1, 134.0, 129.7, 129.3, 127.8, 66.4, 64.6, 50.3, 48.5, 47.2, 47.1, 42.0, 35.3, 34.0, 33.1, 32.1, 30.7, 30.2, 28.5, 27.0, 26.2, 22.6, 21.5, 21.2, 20.1, 19.3, 18.7, 18.3, 17.6, 15.9, 7.7.

FTIR: (neat) [cm^{-1}] = 2959 (s), 2931 (m), 2858 (w), 2360 (s), 2341 (s), 1737 (s), 1715 (w), 1661 (m), 1621 (w), 1457 (m), 1371 (m), 1240 (s), 1111 (s), 1033 (m), 822 (w), 703 (s), 669 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{46}H_{64}NaO_5Si^+$: 747.4415; found: 747.4424.

$[\alpha]_D^{23}$: +84.4 (c= 1.00; $CHCl_3$)

5,6*α*-Epoxy-(22*E*)-15-hydroxy-14,15-secoergosta-8,22-dien-14-on-3β-yl acetate



$C_{30}H_{46}O_4$ (470.69)
92

$C_{30}H_{46}O_5$ (486.69)
97

Acetate **92** (30 mg, 64 µmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (1.3 mL) and H_2O (20 µL) and magnesium monoperoxyphthalate (80%, 86 mg, 0.14 mmol, 2.2 equiv.) were added. After stirring at 23 °C for 24 h, the mixture was diluted with CH_2Cl_2 (3 mL) and added to aq. $NaHSO_3$ (10%, 5 mL). The aq. phase was extracted with CH_2Cl_2 (3 x 3 mL) and the combined organic phases were sequentially washed with sat. aq. $NaHCO_3$ (5 mL) and sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 2:1→1:1) to yield epoxide **97** (26 mg, 51 µmol, 80%) as a colorless oil.

R_f: 0.52 (2:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.35 (dd, *J* = 15.3, 7.7, 1H), 5.24 (dd, *J* = 15.3, 8.1, 1H), 4.96 (td, *J* = 11.4, 5.7, 1H), 3.42 – 3.32 (m, 1H), 3.24 – 3.19 (m, 1H), 3.20 – 3.11 (m, 1H), 3.04 – 2.93 (m, 1H), 2.48 (q, *J* = 7.7, 7.2, 1H), 2.39 (d, *J* = 18.9, 1H), 2.25 (dd, *J* = 13.1, 11.8, 1H), 2.22 – 2.04 (m, 2H), 2.03 (s, 3H), 1.92 – 1.76 (m, 4H), 1.72 – 1.53 (m, 5H), 1.53 – 1.40 (m, 2H), 1.38 – 1.23 (m, 2H), 1.21 (s, 3H), 1.05 (d, *J* = 7.0, 3H), 0.97 (s, 3H), 0.91 (d, *J* = 6.8, 3H), 0.83 (d, *J* = 6.8, 3H), 0.81 (d, *J* = 6.8, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 204.9, 170.3, 156.7, 134.7, 132.6, 124.3, 70.6, 63.3, 61.6, 58.6, 47.3, 43.5, 39.8, 39.7, 37.2, 35.4, 33.3, 32.4, 29.4, 28.3, 26.8, 23.9, 22.9, 22.5, 21.4, 20.2, 20.0, 19.8, 19.1, 17.7.

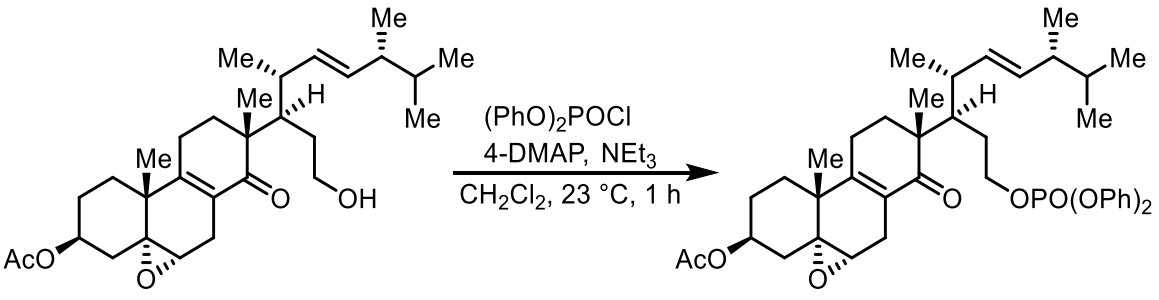
FTIR: (neat) [cm^{-1}] = 2956 (m), 2871 (w), 2360 (s), 2341 (m), 1732 (s), 1659 (s), 1456 (m), 1376 (m), 1365 (m), 1240 (s); 1159 (w), 1041 (s), 975 (w), 913 (m), 731 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{46}NaO_5^+$: 509.3237; found: 509.3243.

$[\alpha]_D^{23}$: −4.6 (c= 0.64; $CHCl_3$)

MP 105.7-106.9 °C ($CHCl_3$)

5,6*α*-Epoxy-(22*E*)-3β-acetoxy-15-(diphenoxy)oxy-14,15-secoergosta-8,22-dien-14-on-phosphate



$C_{30}H_{46}O_5$ (486.69)
97

$C_{42}H_{55}O_8P$ (718.87)
175

To epoxide **97** (74 mg, 0.15 mmol, 1.0 equiv.) in CH_2Cl_2 (0.51 mL) was sequentially added 4-dimethylaminopyridine (1.9 mg, 15.0 µmol, 0.1 equiv.) and triethylamine (84 µL, 0.61 mmol, 4.0 equiv.). Diphenyl phosphorochloridate (63 µL, 0.30 mmol, 2.0 equiv.) was added and the resulting mixture was allowed to stir at 23 °C for 1 h. The reaction was quenched by the addition of sat. aq. $NaHCO_3$ (3 mL) and extracted with CH_2Cl_2 (3 x 3 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1→2:1) to give **175** (0.10g, 0.14 mmol, 93%) as a colorless, crystalline solid.

R_f: 0.30 (2:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.35 – 7.31 (m, 4H), 7.24 (dp, *J* = 7.8, 1.1 Hz, 4H), 7.18 – 7.15 (m, 2H), 5.30 – 5.21 (m, 2H), 4.98 (tt, *J* = 11.7, 4.9 Hz, 1H), 4.06 (ddt, *J* = 10.0, 8.2, 5.1 Hz, 1H), 3.99 – 3.94 (m, 1H), 3.11 (dd, *J* = 2.5, 1.6 Hz, 1H), 2.98 (dt, *J* = 18.9, 1.9 Hz, 1H), 2.39 – 2.30 (m, 2H), 2.30 – 2.21 (m, 2H), 2.17 – 2.07 (m, 3H), 2.03 (s, 3H), 1.88 – 1.83 (m, 2H), 1.80 (td, *J* = 13.2, 3.9 Hz, 1H), 1.74 – 1.71 (m, 2H), 1.71 – 1.64 (m, 2H), 1.59 (td, *J* = 7.7, 6.8, 4.2 Hz, 1H), 1.49 – 1.42 (m, 2H), 1.19 (s, 3H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.95 (s, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.5, 170.3, 157.0,150.8, 150.8, 135.2, 132.0, 129.8 (3C), 125.3 (2C), 124.6, 120.3 (2C), 120.3 (2C), 70.7, 69.6, 62.5, 58.0, 47.3, 43.4, 41.7, 39.9, 38.0, 35.5, 33.2, 30.9, 29.5, 26.9, 26.8, 26.8, 23.9, 23.0, 21.8, 21.4, 20.6, 20.2, 20.1, 19.9, 17.6.

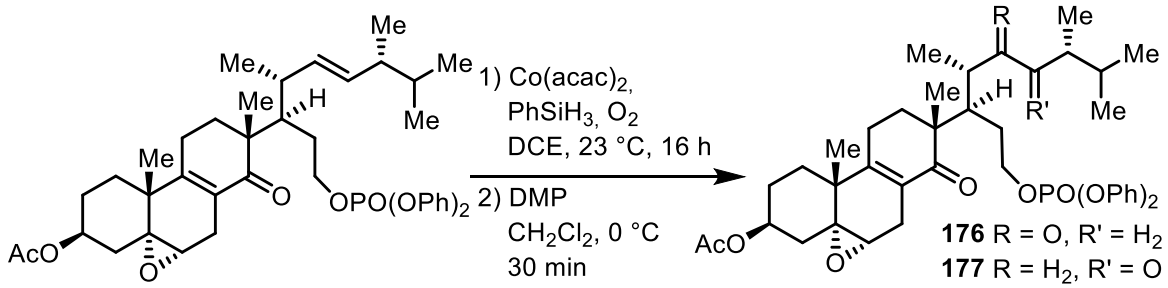
FTIR: (neat) [cm^{-1}] = 2956 (w), 2871 (w), 2360 (s), 2341 (s), 1732 (m), 1658 (m), 1591 (w), 1488 (m), 1456 (w), 1240 (s), 1190 (s), 1024 (s), 948 (s), 768 (m), 689 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{42}H_{55}NaO_8P^+$: 741.3527; found:.

$[\alpha]_D^{23}$: −44.6 (c= 1.00; $CHCl_3$)

MP 157.7-158.9 °C ($CHCl_3$)

5,6*α*-Epoxy-3β-acetoxy-15-(diphenoxy)oxy-14,15-secoergosta-8-en-14,22-dion-phosphate
and
5,6*α*-Epoxy-3β-acetoxy-15-(diphenoxy)oxy-14,15-secoergosta-8-en-14,23-dion-phosphate



$C_{42}H_{55}O_8P$ (718.87)
175

$C_{42}H_{55}O_9P$ (734.87)

Phosphate **175** (50 mg, 70 µmol, 1.0 equiv.) was dissolved in dichloroethane (0.75 mL) and $Co(acac)_2$ (3.6 mg, 14 µmol, 0.20 equiv.) was added, followed by phenyl silane (43 µL, 0.35 mmol, 5.0 equiv.). The resulting mixture was evacuated and backfilled with oxygen (three cycles) and stirred under an atmosphere of oxygen at 23 °C for 16 h. The resulting, green solution was filtered over a small plug of silica, washed with aq. sat. $Na_2S_2O_3$ (1 mL) and the aq. phase was extracted with EtOAc (3x 1 mL). The combined organic phases were washed with NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the obtained residue was dissolved in CH_2Cl_2 (0.75 mL) and cooled to 0 °C. Dess-Martin periodinane (38 mg, 90 µmol, 1.3 equiv.) was added and the mixture was allowed to stir at 0 °C for 45 min. The mixture was allowed to warm to 24 °C and aq. sat. $NaHCO_3$ (2 mL) was added. The phases were separated and the aq. phase was extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1→2:1) to yield C22-ketone **176** (7.3 mg, 9.9 µmol, 14%) as a colorless oil as well as C23-ketone **177** (6.8 mg, 9.3 µmol, 13%) as a colorless oil.

176

R_f: 0.25 (2:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.34 (d, *J* = 7.1, 4H), 7.25 – 7.16 (m, 6H), 4.97 (ddd, *J* = 15.9, 10.6, 4.9, 1H), 3.99 – 3.90 (m, 2H), 3.13 – 3.07 (m, 1H), 2.99 – 2.89 (m, 1H), 2.38 (m, 2H), 2.25 – 2.07 (m, 4H), 2.03 (s, 3H), 1.92 – 1.24 (m,

13H), 1.19 (s, 3H), 0.96 (d, *J* = 7.0, 3H), 0.89 – 0.86 (m, 9H), 0.83 (d, *J* = 6.6, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 213.7, 203.8, 170.3, 157.4, 150.7, 141.9, 133.6, 133.3, 131.9, 129.9, 128.1, 125.3, 124.5, 120.4, 120.3, 120.3, 120.2, 70.7, 69.5, 62.3, 58.0, 53.3, 47.3, 46.2, 40.6, 40.0, 35.4, 32.2, 30.2, 29.3, 27.4, 27.0, 26.8, 23.9, 23.0, 22.3, 21.5, 21.4, 20.2, 19.3, 18.8, 12.9.

FTIR: (neat) [cm^{-1}] = 2960 (w), 2869 (w), 2365 (s), 2343 (s), 1731 (m), 1658 (m), 1590 (w), 1030 (s), 946 (s), 761 (m), 689 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{42}H_{55}NaO_8P^+$: 757.3476; found: 757.3442.

$[\alpha]_D^{23}$: −26.8 (c= 0.73; $CHCl_3$)

177

R_f: 0.16 (2:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.35 – 7.30 (m, 4H), 7.25 – 7.21 (m, 4H), 7.19 – 7.15 (m, 2H), 4.97 (tt, *J* = 11.7, 5.4 Hz, 1H), 4.23 – 4.08 (m, 2H), 3.13 (s, 1H), 3.02 (d, *J* = 18.8 Hz, 1H), 2.55 (d, *J* = 7.1 Hz, 1H), 2.49 (dd, *J* = 17.3, 4.6 Hz, 1H), 2.41 – 2.26 (m, 3H), 2.26 – 2.09 (m, 5H), 2.04 (s, 3H), 1.84 (s, 5H), 1.67 (d, *J* = 12.8 Hz, 2H), 1.55 – 1.43 (m, 2H), 1.19 (d, *J* = 5.1 Hz, 3H), 0.99 (d, *J* = 7.2 Hz, 3H), 0.94 (s, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.80 – 0.76 (m, 6H).

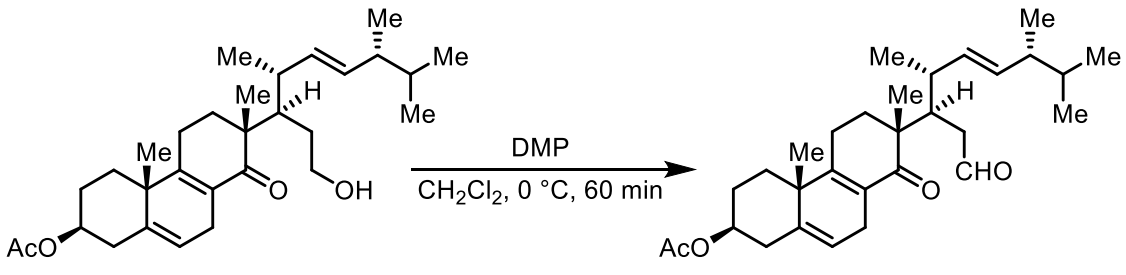
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 213.9, 202.4, 170.3, 157.1, 150.7, 141.9, 133.3, 131.9, 129.9 (3C), 128.1, 125.3, 125.0, 120.3 (3C), 70.6, 69.6, 62.7, 57.9, 48.1, 47.7, 46.5, 41.4, 39.8, 35.5, 33.8, 32.0, 30.2, 29.9, 29.1, 28.6, 27.0, 24.1, 21.4, 21.2, 21.1, 20.1, 18.4, 18.2, 15.9.

FTIR: (neat) [cm^{-1}] = 2962 (w), 2358 (s), 2340 (s), 1733 (m), 1651 (m), 1587 (w), 1491 (m), 1455 (w), 1241 (s), 1192 (s), 1026 (s), 942 (s), 763 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{42}H_{55}NaO_8P^+$: 757.3476; found: 757.3439.

$[\alpha]_D^{23}$: −36.2 (c= 1.00; $CHCl_3$)

(22*E*)-5,6α-Epoxy-3β-acetoxy-14,15-secoergosta-8,22-dien-14-on-15-al



$C_{30}H_{46}O_4$ (470.69)
92

$C_{30}H_{44}O_4$ (468.68)
201

To alcohol **92** (37 mg, 80 µmol, 1.0 equiv.) in CH_2Cl_2 (0.79 mL) was added at 0 °C Dess-Martin periodinane (40 mg, 90 µmol, 1.2 equiv.). After stirring at the same temperature for 20 min, sat. aq. $NaHCO_3$ (1 mL) was added. The phases were separated, and the aq. phase was extracted with EtOAc (3 x 1 mL). The combined organic phases were washed with sat. aq. NaCl (1 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 5:1) to yield aldehyde **201** (37 mg, 80 µmol, quant.) as a colorless oil.

R_f: 0.33 (6:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 9.63 (t, *J* = 1.8 Hz, 1H), 5.56 (d, *J* = 4.4 Hz, 1H), 5.25 (dd, *J* = 4.9, 2.3 Hz, 2H), 4.66 (tt, *J* = 11.5, 4.9 Hz, 1H), 2.73 (t, *J* = 22.0 Hz, 3H), 2.64 (td, *J* = 5.6, 3.3 Hz, 1H), 2.49 – 2.28 (m, 4H), 2.19 (ddd, *J* = 13.6, 6.5, 4.5 Hz, 1H), 2.07 – 2.02 (m, 3H), 2.02 – 1.93 (m, 1H), 1.90 – 1.84 (m, 2H), 1.72 (dtt, *J* = 18.9, 13.7, 8.8 Hz, 3H), 1.61 – 1.41 (m, 3H), 1.27 (s, 3H), 1.00 (s, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H).

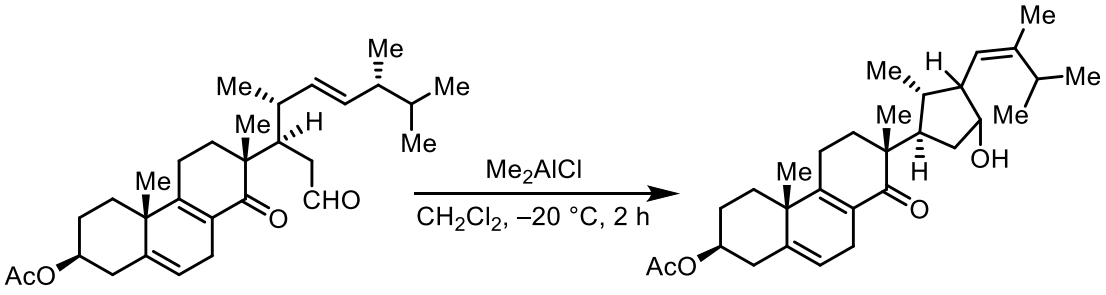
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.3, 202.4, 170.5, 157.6, 135.6, 135.1, 132.2, 127.4, 121.0, 73.1, 47.2, 43.4, 41.4, 39.7, 39.4, 38.1, 37.9, 34.5, 33.2, 31.4, 27.8, 25.0, 22.5 (2C), 21.5, 21.3, 20.5, 20.2, 19.9, 17.6.

FTIR: (neat) [cm^{-1}] = 2957 (s), 2871 (m), 2359 (m), 2341 (w), 1730 (s), 1659 (s), 1628 (w), 1456 (w); 1374 (m), 1240 (s), 1030 (m), 816 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_4^+$: 491.3132; found: 491.3148.

$[\alpha]_D^{23}$: +39.0 (c=1.00; $CHCl_3$)

15,22-Cyclo-15-hydroxy-14,15-secoergosta-5,8,23-trien-14-on-3β-yl acetate



$C_{30}H_{44}O_4$ (468.68)
201

$C_{30}H_{44}O_4$ (468.68)
203

To aldehyde **201** (42.0 mg, 90 µmol, 1.0 equiv.) in CH_2Cl_2 (0.9 mL) at −20 °C was added dimethylaluminum chloride (0.22 mL, 0.22 mmol, 2.5 equiv., 1.0 M in hexane) dropwise. The resulting mixture was allowed to warm to −10 °C over 2 h when sat. aq. $NaHCO_3$ (2 mL) was added. The mixture was allowed to warm to ambient temperature, the phases were separated and the aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 4:1→2:1) to give unreacted aldehyde **201** (8.4 mg, 0.02 mmol, 20%), a fraction of a 1:1 mixture of two diastereomers **203a** (9.7 mg, 0.02 mmol, 23%) as a colorless foam, a fraction of a pure diastereomer of **203b** (6.8 mg, 0.015 mmol, 16%) as a colorless oil and a fraction of a pure diastereomer of **203c** (13 mg, 0.03 mmol, 31%) as a colorless foam.

203a

R_f: 0.27 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.56 (d, *J* = 1.9, 2H), 5.28 (d, *J* = 9.8, 1H), 5.00 (d, *J* = 8.7, 1H), 4.71 – 4.59 (m, 1H), 4.14 – 3.98 (m, 1H), 2.82 – 2.67 (m, 2H), 2.50 – 2.40 (m, 3H), 2.40 – 2.25 (m, 4H), 2.05 (s, 6H), 2.03 – 1.96 (m, 2H), 1.78 – 1.68 (m, 4H), 1.67 (d, *J* = 1.0, 3H), 1.60 (d, *J* = 1.1, 3H), 1.56 – 1.39 (m, 4H), 1.26 – 1.24 (m, 12H), 1.08 (s, 3H), 1.03 (s, 3H), 1.03 (s, 3H), 1.02 (d, *J* = 6.8, 3H), 1.00 (d, *J* = 7.1, 3H), 0.98 (d, 3H), 0.96 (d, *J* = 6.9, 3H), 0.94 – 0.88 (m, 3H), 0.86 (d, *J* = 6.6, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 210.3, 203.3, 173.5, 159.1, 145.8, 130.0, 117.5, 75.9, 72.5, 57.1, 49.9, 48.0, 47.8, 45.8, 37.5, 36.6, 36.0, 32.9, 32.0, 28.2, 26.2, 22.9, 22.8, 21.9, 21.8, 21.7, 21.0, 20.0, 19.6, 18.9, 14.2, 7.1.

FTIR: (neat) [cm^{-1}] = 2962 (s), 2872 (m), 2360 (m), 1732 (s), 1661 (s), 1383 (s), 1256 (s), 1032 (m), 915 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_4^+$: 491.3132; found: 491.3134.

203b

R_f: 0.21 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.57 (td, *J* = 3.6, 1.6 Hz, 1H), 5.09 (dt, *J* = 9.5, 1.3 Hz, 1H), 4.68 – 4.60 (m, 1H), 3.89 (td, *J* = 8.9, 6.4 Hz, 1H), 2.77 (dt, *J* = 4.0, 2.4 Hz, 2H), 2.52 – 2.33 (m, 5H), 2.30 – 2.26 (m, 1H), 2.13 – 2.08 (m, 1H), 2.05 (s, 3H), 2.03 – 1.93 (m, 2H), 1.90 (ddd, *J* = 12.9, 8.7, 6.4 Hz, 2H), 1.82 (ddd, *J* = 13.0, 7.4, 5.0 Hz, 1H), 1.76 – 1.67 (m, 1H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.54 – 1.49 (m, 2H), 1.42 – 1.37 (m, 1H), 1.27 (s, 3H), 1.06 (s, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.3, 170.6, 157.3, 145.1, 135.3, 128.0, 121.0, 120.7, 76.5, 73.1, 50.5, 47.0, 46.1, 39.3, 37.9, 37.2, 36.0, 35.0, 34.5, 31.1, 27.9, 25.1, 22.6, 21.9, 21.7, 21.5, 21.5, 19.9, 18.9, 14.3.

FTIR: (neat) [cm^{-1}] = 2958 (s), 2869 (m), 2824 (w), 2360 (m), 2337 (w), 1732 (s), 1659 (s), 1627 (m), 1455 (m), 1375 (s), 1243 (s), 1030 (m), 911 (m), 761 (w), 702 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_4^+$: 491.3132; found: 491.3135.

$[\alpha]_D^{23}$: +16.6 (c=0.52; $CHCl_3$)

203c

R_f: 0.17 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.56 (s, 1H), 4.82 (d, *J* = 9.6, 1H), 4.68 – 4.59 (m, 1H), 3.68 (q, *J* = 8.1, 1H), 2.84 (dt, *J* = 13.9, 6.9, 2H), 2.79 – 2.72 (m, 1H), 2.49 – 2.25 (m, 2H), 2.20 – 2.15 (m, 1H), 2.05 (s, 3H), 2.03 – 1.92 (m, 2H), 1.88 (ddd, *J* = 13.4, 7.7, 5.5, 2H), 1.77 – 1.67 (m, 3H), 1.65 (d, *J* = 1.2, 3H), 1.61 – 1.46 (m, 3H), 1.28 – 1.24 (m, 3H), 1.08 – 1.02 (m, 2H), 1.01 (s, 3H), 0.99 – 0.98 (m, 3H), 0.97 (s, 3H), 0.96 (d, *J* = 6.7, 3H), 0.89 – 0.86 (m, 1H).

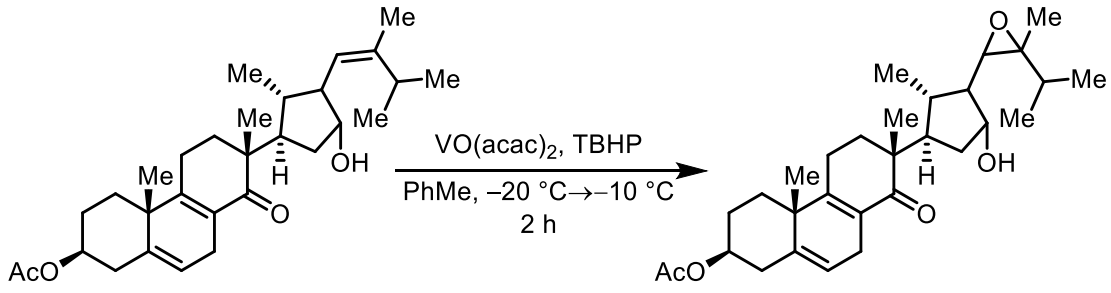
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.5 , 170.5 , 157.3 , 144.9 , 135.3 , 127.8 , 125.5 , 121.0 , 77.3 , 73.1 , 55.7 , 45.9 , 45.8 , 39.9 , 39.3 , 37.9 , 34.9 , 34.4 , 32.0 , 29.1 , 27.8 , 25.1 , 22.5 , 21.7 , 21.5 (2C) , 21.2 , 20.2 , 20.0 , 18.4.

FTIR: (neat) [cm^{-1}] = 2960 (s), 2865 (m), 2827 (w), 2361 (m), 1733 (s), 1672 (s), 1630 (m), 1456 (m), 1371 (s), 1238 (s), 1031 (m), 934 (m), 766 (w), 706 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_4^+$: 491.3132; found: 491.3128.

$[\alpha]_D^{23}$: +9.6 (c=0.63; $CHCl_3$)

23,24-Epoxy-15,22-cyclo-15-hydroxy-14,15-secoergosta-5,8-dien-14-on-3β-yl acetate



$C_{30}H_{44}O_4$ (468.68)
203

$C_{30}H_{44}O_5$ (484.68)
208

To homoallylic alcohol **203** (7.5 mg, 16 µmol, 1.0 equiv.) in toluene (0.16 mL) at −20 °C was added vanadyl acetylacetonate (0.20 mg, 0.80 µmol, 0.05 equiv.) followed by the dropwise addition of *tert*-butyl hydroperoxide (4.0 µL, 19 µmol, 1.2 equiv. 5-6 M in decane). The resulting mixture was allowed to warm to −10 °C over 2 h. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 1:1) to give epoxide **208** (3.4 mg, 7.0 µmol, 44%) as a colorless oil and 1:1 mixture of diastereomers.

R_f: 0.33 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

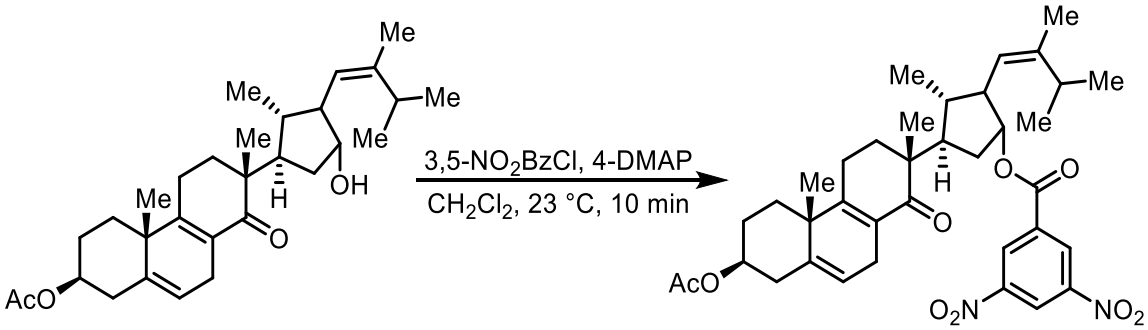
^{1}H NMR: ($CDCl_3$, 600 MHz): δ [ppm] = 5.57 (td, *J* = 3.6, 1.6 Hz, 1H), 4.63 (tt, *J* = 11.4, 4.7 Hz, 1H), 4.27 (q, *J* = 8.0 Hz, 1H), 2.79 – 2.77 (m, 2H), 2.75 (d, *J* = 9.4 Hz, 1H), 2.47 – 2.33 (m, 3H), 2.28 (s, 1H), 2.21 – 2.16 (m, 1H), 2.05 (s, 3H), 2.02 – 1.96 (m, 2H), 1.89 – 1.68 (m, 3H), 1.61 – 1.49 (m, 3H), 1.47 – 1.35 (m, 2H), 1.27 (s, 2H), 1.26 – 1.23 (m, 2H), 1.19 (s, 3H), 1.04 (s, 3H), 1.01 (d, *J* = 4.6 Hz, 3H), 1.00 (d, *J* = 5.0 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.0 (2C), 170.6 (2C), 157.5 (2C), 135.2 (2C), 128.0 (2C), 120.9 (2C), 76.0, 76.0, 73.1 (2C), 64.3, 64.2, 63.5 (2C), 49.9, 49.9, 48.3 (2C), 46.0 (2C), 39.4 (2C), 37.9 (2C), 36.4 (2C), 35.1, 35.1, 34.6, 34.4, 34.3, 30.4, 30.3, 29.9, 27.9, 26.6, 25.1, 25.1, 25.1, 22.6, 22.6, 21.5, 21.5, 21.3, 20.5 (2C), 18.8 (2C), 18.6 (2C), 17.9 (2C), 12.8 (2C).

FTIR: (neat) [cm^{-1}] = 2962 (m), 2360 (s), 2341 (s), 1771 (w), 1732 (m), 1653 (m), 1456 (m), 1375 (m), 1242 (m), 1028 (w), 750 (m), 669 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_5^+$: 507.3081; found: 507.3096.

15,22-Cyclo-3β-acetoxy-15-(3,5-dinitro)-14,15-secoergosta-5,8,23-trien-14-on benzoate



$C_{30}H_{44}O_4$ (468.68)
203

$C_{37}H_{46}N_2O_{10}$ (678.78)
303

To homoallylic alcohol **203** (6.8 mg, 15 µmol, 1.0 equiv.) in CH_2Cl_2 (0.15 mL) was added 4-dimethylamino pyridine (18 mg, 0.15 mmol, 10.0 equiv.) at 0 °C. 3,5-dinitrobenzoyl chloride (8.5 mg, 36 µmol, 2.5 equiv.) was added and the mixture was allowed to stir at the same temperature for 10 min. Sat. aq. NH_4Cl (1 mL) was added and the resulting mixture was allowed to warm to ambient temperature. The phases were separated, and the aq. phase was extracted with EtOAc (3 x 1 mL). The combined organic phases were washed with sat. aq. NaCl (1 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 4:1) to give dinitro benzoate **303** (9.6 mg, 15 µmol, quant.) as a colorless foam.

R_f: 0.44 (4:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 9.21 (t, *J* = 2.2 Hz, 1H), 9.10 (d, *J* = 2.2 Hz, 2H), 5.57 (td, *J* = 3.6, 1.7 Hz, 1H), 5.16 (td, *J* = 8.0, 6.5 Hz, 1H), 5.10 (dt, *J* = 9.4, 1.2 Hz, 1H), 4.65 (tt, *J* = 11.6, 4.8 Hz, 1H), 2.97 (dt, *J* = 9.5, 8.2 Hz, 1H), 2.78 (q, *J* = 4.5, 3.7 Hz, 2H), 2.51 – 2.45 (m, 2H), 2.42 – 2.35 (m, 2H), 2.30 – 2.23 (m, 2H), 2.20 – 2.13 (m, 2H), 2.05 (s, 3H), 2.04 – 1.95 (m, 2H), 1.85 (ddd, *J* = 13.3, 8.1, 5.0 Hz, 1H), 1.78 – 1.70 (m, 1H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.58 – 1.51 (m, 1H), 1.29 (s, 3H), 1.12 (s, 3H), 0.97 – 0.95 (m, 6H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.89 – 0.81 (m, 2H).

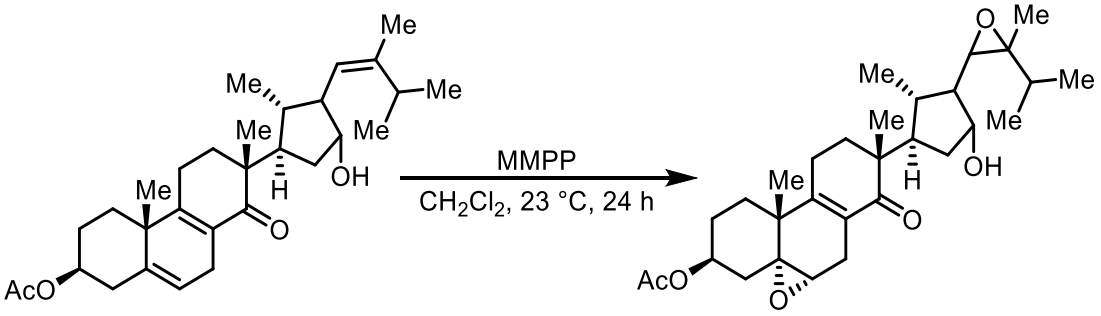
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 202.8, 170.5, 162.4, 157.7, 148.8, 145.4, 135.3, 134.5, 129.5, 127.9, 122.3, 120.9, 119.0, 81.4, 73.0, 47.9, 46.4, 45.8, 39.4, 37.9, 37.2, 35.4, 34.4, 32.3, 31.5, 29.8, 27.8, 25.0, 22.6, 21.7, 21.6, 21.5, 21.5, 19.7, 18.5, 14.1, 1.2.

FTIR: (neat) [cm^{-1}] = 2958 (m), 2928 (w), 2360 (s), 2341 (s), 1732 (m), 1661 (w), 1627 (w), 1546 (s), 1457 (w), 1344 (s), 1277 (m), 1170 (m), 1029 (w), 721 (m), 669 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{37}H_{46}N_2NaO_9^+$: 685.7692; found: 685.7688.

$[\alpha]_D^{23}$: +12.4 (c=0.82; $CHCl_3$)

15,22-Cyclo-3β-acetoxy-5,6α,23,24-diepoxy-15-hydroxy-14,15-secoergosta-8-trien-14-on



$C_{30}H_{44}O_4$ (468.68)
203

$C_{30}H_{44}O_6$ (500.68)
211

To homoallylic alcohol **203** (9.8 mg, 21 µmol, 1.0 equiv.) in CH_2Cl_2 (0.42 mL) was added MMPP (8.9 mg, 23 µmol, 1.1 equiv., 80%). The resulting mixture was allowed to stir at 23 °C for 24 h. The mixture was diluted with EtOAc (3 mL) and washed with sat. aq. $NaHCO_3$ (5 mL). The aqueous phase was extracted with EtOAc (2 x 3 mL) and the combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 2:1→1:1) to yield diepoxide **211** (4.1 mg, 8.2 µmol, 39%) as a colorless oil and approximate 2:1 mixture of diastereomers along with unreacted **203** (2.3 mg, 4.9 µmol, 23%) as a colorless oil.

R_f: 0.28 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

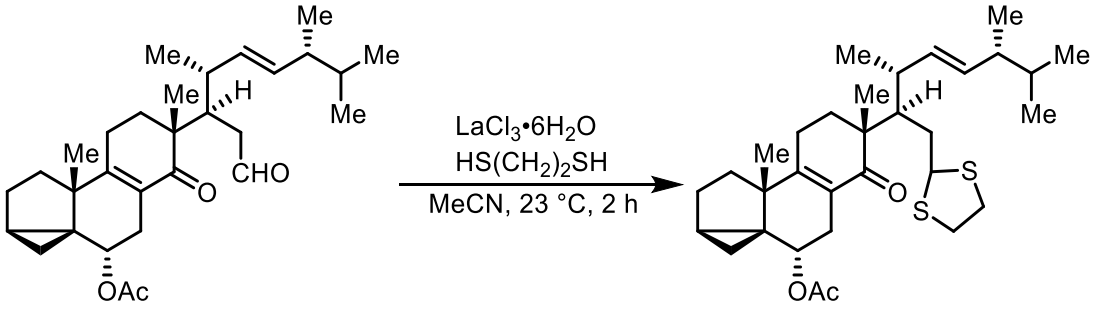
^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 4.98 (tt, *J*=11.6, 4.9, 1H), 4.34 (td, *J*=3.8, 1.4, 1H), 3.19 – 3.15 (m, 1H), 3.07 (dt, *J*=19.0, 2.1, 1H), 3.02 (d, *J*=8.8, 1H), 2.44 – 2.32 (m, 2H), 2.30 – 2.15 (m, 1H), 2.14 – 2.05 (m, 2H), 2.03 (d, *J*=0.4, 3H), 1.97 – 1.81 (m, 4H), 1.74 – 1.38 (m, 5H), 1.22 (d, *J*=1.0, 3H), 1.21 (s, 3H), 1.20 (s, 3H), 1.18 (d, *J*=7.3, 3H), 1.02 (d, *J*=6.9, 3H), 0.97 (d, *J*=7.0, 3H), 0.96 (s, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.2*, 202.7, 170.1*, 170.1, 156.8*, 156.8, 125.0*, 124.9, 75.5, 73.0*, 70.5*, 70.5, 66.2, 64.9*, 64.8*, 64.2, 62.7, 61.0, 58.1, 58.1*, 50.2, 48.4, 47.7*, 47.5, 45.3, 44.5*, 39.8, 39.8*, 36.5, 36.4, 35.5*, 35.4*, 35.4, 35.0, 31.7, 30.4, 30.4*, 29.7*, 29.7, 29.4*, 29.2, 26.8*, 26.7, 23.9, 23.7, 21.9, 21.8*, 21.3, 20.7, 20.7*, 20.7, 20.1, 19.7*, 19.4, 18.4, 18.4*, 17.9, 17.8*, 16.7*, 12.7.

FTIR: (neat) [cm^{-1}] = 2963 (m), 2359 (s), 2343 (s), 1769 (w), 1733 (m), 1654 (m), 1457 (m), 1375 (m), 1233 (m), 1018 (w), 751 (m), 670 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{44}NaO_6^+$: 523.3030; found: 523.3042.

(22*E*)-14-(1,3-dithiolan-15-yl)-6α-acetoxy-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien-14-one



$C_{30}H_{44}O_4$ (468.68)
301

$C_{32}H_{48}O_3S_2$ (544.85)
112

Aldehyde **301** (37 mg, 80 µmol, 1.0 equiv.) was dissolved in MeCN (0.8 mL) and ethane-1,2-dithiol (20 µL, 0.24 mmol, 3.0 equiv.) was added followed by $LaCl_3 \cdot 6H_2O$ (28 mg, 80 µmol, 1.0 equiv.). The mixture was allowed to stir at 23 °C for 2 h when water (2 mL) was added. The mixture was extracted with EtOAc (3 x 2 mL), the combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 7:1) to give 1,3-dithiolane **112** (25 mg, 50 µmol, 57%) as a colorless oil.

R_f: 0.30 (7:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.35 (dd, *J* = 15.3, 8.0, 1H), 5.29 – 5.19 (m, 2H), 4.35 (dd, *J* = 9.0, 6.4, 1H), 3.20 (dt, *J*=9.6, 5.7, 1H), 3.16 – 3.06 (m, 3H), 2.45 (h, *J* = 7.8, 7.1, 1H), 2.33 (ddt, *J* = 14.1, 9.0, 4.3, 1H), 2.20 (dtt, *J* = 18.1, 4.7, 2.2, 1H), 2.13 (dt, *J* = 13.9, 4.5, 1H), 2.00 (s, 3H), 1.90 (tdd, *J* = 13.9, 7.8, 4.4, 3H), 1.82 (dt, *J* = 13.5, 6.8, 2H), 1.78 – 1.60 (m, 3H), 1.46 (hept, *J* = 6.7, 1H), 1.30 (dq, *J* = 9.5, 5.5, 4.7, 1H), 1.22 (s, 3H), 1.13 (dt, *J* = 12.9, 6.6, 3H), 1.09 (d, *J* = 7.1, 3H), 0.99 (s, 3H), 0.92 (d, *J* = 6.8, 3H), 0.84 (d, *J* = 6.8, 3H), 0.81 (d, *J* = 6.8, 3H), 0.53 (dd, *J* = 8.1, 5.4, 1H), 0.43 (t, *J* = 4.7, 1H).

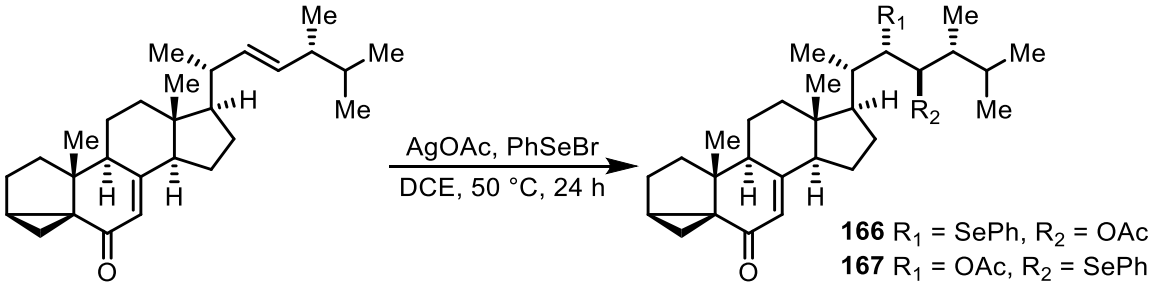
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.2, 170.4, 158.2, 135.1, 132.4, 129.1, 66.4, 54.0, 49.7, 47.8, 44.9, 43.5, 38.2, 37.9, 37.7, 36.6, 35.4, 33.3, 32.9, 32.6, 28.7, 26.0, 23.6, 22.7, 22.6, 21.2, 20.2, 19.9, 19.7, 18.6, 17.7, 7.3.

FTIR: (neat) [cm^{-1}] = 2957 (m), 2926 (m), 2867 (w), 2359 (m), 2342 (w), 1737, (s), 1658 (s), 1621 (w), 1455 (m), 1368 (m), 1238 (s), 1209 (m), 1031 (s), 983 (m), 910 (m), 730 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{48}NaO_3S_2^+$: 567.2937; found: 567.2953.

$[\alpha]_D^{25}$: +143.8 (c= 1.00; $CHCl_3$)

22-Phenylselanyl-23-acetoxy-3α,5-Cyclo-5α-ergosta-7-en-6-one and 22-Acetoxy-23-phenylselanyl-3α,5-Cyclo-5α-ergosta-7-en-6-one



$C_{28}H_{42}O$ (394.64)
69

$C_{36}H_{50}O_3Se$ (609.75)

Silver acetate (63 mg, 0.38 mmol, 3.0 equiv.) was suspended in dichloroethane (1.3 mL) and a solution of phenylselenyl bromide (90 mg, 0.38 mmol, 3.0 equiv.) in dichloroethane (0.50 mL) was added dropwise at 24 °C. After 5 min, enone **69** (50 mg, 0.13 mmol, 1.0 equiv.) was added in one portion and the mixture was allowed to stir at 50 °C for 24 h. EtOAc (5 mL) was added and the mixture was filtered over a plug of Celite® and rinsed with EtOAc (2 x 2 mL). The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to give unreacted enone 63 (13 mg, 30 µmol, 25%), isomer **166** (11 mg, 20 µmol, 15%) as a colorless oil and isomer **167** (15 mg, 30 µmol, 19%) as a colorless oil.

166

R_f: 0.23 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.60 – 7.58 (m, 2H), 7.27 – 7.26 (m, 3H), 5.80 (t, *J* = 2.3 Hz, 1H), 5.37 (dd, *J* = 8.6, 3.7 Hz, 1H), 3.33 (dd, *J* = 8.6, 1.7 Hz, 1H), 2.27 (ddd, *J* = 11.7, 7.0, 2.4 Hz, 1H), 2.16 (dq, *J* = 11.4, 3.7, 3.0 Hz, 2H), 2.06 (s, 3H), 2.04 – 1.97 (m, 1H), 1.91 (ddt, *J* = 10.6, 6.9, 4.0 Hz, 2H), 1.81 – 1.68 (m, 8H), 1.53 (m, 3H), 1.44 – 1.37 (m, 1H), 1.33 – 1.23 (m, 2H), 1.09 (s, 3H), 1.07 (d, *J* = 6.6

Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.76 (t, *J* = 4.7 Hz, 1H), 0.71 – 0.68 (m, 6H), 0.58 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 197.3, 170.4, 163.9, 135.0, 130.1 (2C), 129.3, 127.8 (2C), 123.9, 76.5, 56.2, 55.3, 54.0, 45.2, 44.6, 43.8, 42.1, 40.7, 39.2, 36.6, 35.1, 33.9, 30.3, 28.1, 26.9, 23.3, 22.9, 21.4, 21.2, 19.6, 19.0, 16.2, 13.3, 12.9, 10.6.

FTIR: (neat) [cm^{-1}] = 2958 (s), 2872 (w), 2360 (m), 2340 (w), 1737 (s), 1653 (s), 1474 (w), 1380 (m), 1297 (w), 1020 (s), 988 (m), 739 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{36}H_{50}NaO_3Se^+$: 633.2817; found: 633.2848.

$[\alpha]_D^{25}$: +1.1 (c= 1.00; $CHCl_3$)

167

R_f: 0.18 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.56 (dd, *J* = 6.5, 3.0 Hz, 2H), 7.26 – 7.23 (m, 3H), 5.79 (t, *J* = 2.3 Hz, 1H), 5.36 (d, *J* = 10.9 Hz, 1H), 3.55 (dd, *J* = 10.9, 1.9 Hz, 1H), 2.25 – 2.15 (m, 3H), 2.06 (s, 3H), 2.05 – 2.00 (m, 2H), 1.94 (dq, *J* = 12.5, 4.1 Hz, 2H), 1.78 (dt, *J* = 8.7, 4.5 Hz, 1H), 1.70 (dq, *J* = 16.3, 5.9, 4.2 Hz, 4H), 1.67 – 1.52 (m, 3H), 1.33 – 1.20 (m, 4H), 1.07 (s, 3H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.89 – 0.82 (m, 1H), 0.74 (t, *J* = 4.7 Hz, 1H), 0.52 (s, 3H), 0.50 (d, *J* = 6.7 Hz, 3H).

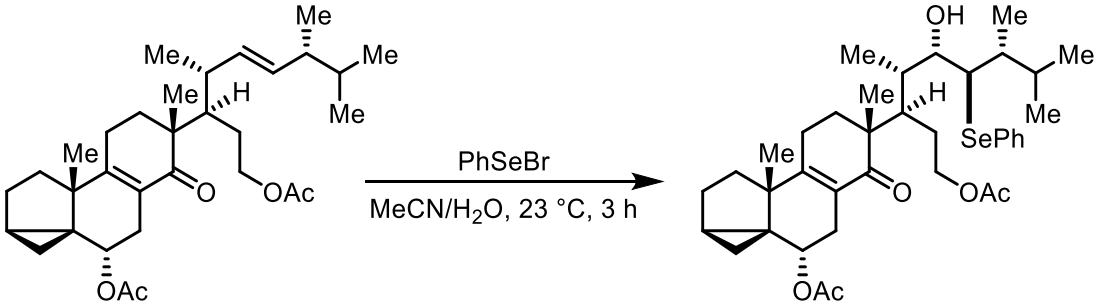
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 197.2, 170.4, 164.0, 134.6, 130.6 (2C), 129.3, 127.5, 123.9 (2C), 77.2, 56.2, 53.8, 53.5, 45.2, 44.5, 43.8, 42.1, 40.4, 39.1, 38.1, 35.0, 33.9, 31.3, 27.7, 26.9, 23.2, 22.9, 21.9, 21.2, 21.1, 19.6, 14.3, 13.3, 13.1, 12.5.

FTIR: (neat) [cm^{-1}] = 2959 (m), 2872 (w), 2360 (s), 2341 (s), 1734 (s), 1653 (s), 1474 (w), 1380 (m), 1298 (w), 1234 (s), 1174 (w), 1018 (w), 737 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{36}H_{50}NaO_3Se^+$: 633.2817; found: 633.2844.

$[\alpha]_D^{25}$: −15.2 (c= 1.00; $CHCl_3$)

22-Hydroxy-23-phenylselanyl-6α,15-diacetoxy-14-oxo-3α,5-cyclo-14,15-seco-5α-ergosta-8-en



$C_{32}H_{48}O_5$ (512.73)
108

$C_{38}H_{54}O_6Se$ (685.80)
168

To diacetate **108** (23 mg, 47 µmol, 1.0 equiv.) in a mixture of MeCN/H_2O (4:1, 0.46 mL) was added phenylselenyl bromide (38 mg, 0.16 mmol, 3.5 equiv.) at 23 °C. The mixture was allowed to stir for 3 hours at 23 °C. The mixture was diluted with Et_2O (3 mL) and washed with sat. aq. $NaHCO_3$ (2 mL). The aqueous phase was extracted with Et2O (3 x 2 mL), the combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 3:1) to yield **168** (10 mg, 15 µmol, 33%) as a colorless oil and diacetate **108** (11 mg, 22 µmol, 48%) as a colorless oil.

R_f : 0.18 (3:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.51 – 7.46 (m, 2H), 7.25 – 7.20 (m, 3H), 5.22 (dd, *J*=10.3, 5.4, 1H), 4.27 – 4.19 (m, 1H), 4.18 (dd, *J*=10.0, 2.0, 1H), 4.02 (d, *J*=10.1, 1H), 4.01 – 3.95 (m, 1H), 3.08 (dd, *J*=16.2, 5.4, 1H), 2.33 – 2.24 (m, 2H), 2.18 – 2.06 (m, 2H), 2.05 (s, 2H), 2.00 (s, 2H), 1.95 – 1.23 (m, 14H), 1.20 (s, 3H), 1.10 (s, 3H), 0.97 (d, *J*=6.5, 3H), 0.96 (d, *J*=6.7, 3H), 0.91 (d, *J*=6.5, 3H), 0.84 (d, *J*=7.3, 2H), 0.59 (dd, *J*=8.2, 5.5, 1H), 0.46 – 0.42 (m, 1H).

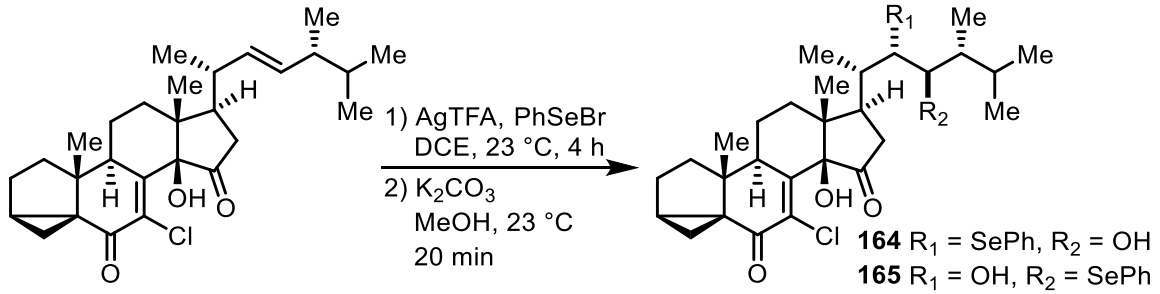
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 202.6, 171.4, 170.3, 158.8, 134.5, 130.1, 129.1, 129.1, 129.0, 128.2, 127.4, 72.4, 66.3, 65.5, 63.6, 50.2, 48.1, 43.3, 40.2, 39.8, 35.3, 33.1, 31.6, 28.4, 26.1, 22.6, 22.3, 21.5, 21.1, 21.1, 21.0, 20.3, 18.7, 18.5, 14.5, 13.6, 12.7, 7.6.

FTIR: (neat) [cm^{-1}] = 2956 (s), 2924 (s), 2869 (m), 2359 (w), 2345 (s), 1728 (s), 1640 (s), 1373 (m), 1188 (w), 1020 (m), 737 (m) 721 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{38}H_{54}NaO_6Se^+$: 709.2978; found: 709.2977.

$[\alpha]_D^{25}$: +72.1 (c= 1.00; $CHCl_3$)

7-Chloro-14β,22-dihydroxy-23-phenylselanyl-3α,5-cyclo-5α-ergosta-7-en-6,15-dione
and
7-Chloro-22-phenylselanyl-14β,23-dihydroxy-3α,5-cyclo-5α-ergosta-7-en-6,15-dione



$C_{28}H_{39}ClO_3$ (459.07)
71

$C_{34}H_{45}ClO_4Se$ (632.14)

Silver trifluoroacetate (12 mg, 54 µmol, 1.0 equiv.) was suspended in dichloroethane (0.34 mL) and a solution of phenylselenyl bromide (13 mg, 54 µmol, 1.0 equiv.) in dichloroethane (0.20 mL) was added dropwise with the formation of silver bromide. After the addition, chloroenone **71** (25 mg, 54 µmol, 1.0 equiv.) was added in one portion. The resulting mixture was allowed to stir at 25 °C for 4 h and filtered over a plug of Celite®. The solvent was removed under reduced pressure and the obtained residue was immediately dissolved in MeOH (0.54 mL) and K_2CO_3 (11 mg, 81 µmol, 1.5 equiv.) was added. After stirring at 25 °C for 1.5 h, water (3 mL) was added and the mixture was extracted with EtOAc (3 x 3 mL). The combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 5:1→3:1) to yield unreacted chloroenone **71** (9.8 mg, 21 µmol, 40%), isomer **164** (6.4 mg, 10 µmol, 19%) as a colorless oil and isomer **165** (5.8 mg, 9.2 µmol, 17%) as a colorless oil.

164

R_f: 0.47 (2:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.57 – 7.55 (m, 2H), 7.30 – 7.23 (m, 3H), 3.77 (dd, *J* = 7.4, 4.9 Hz, 1H), 3.15 (dd, *J* = 7.3, 2.0 Hz, 1H), 3.09 (dd, *J* = 11.4, 6.7 Hz, 1H), 2.78 (td, *J* = 10.9, 7.1 Hz, 1H), 2.51 (dd, *J* = 17.9, 7.0 Hz, 1H), 2.35 – 2.19 (m, 4H), 2.04 – 1.96 (m, 1H), 1.95 – 1.86 (m, 3H), 1.83 – 1.74 (m, 3H), 1.66 (dd, *J* = 13.6, 7.7 Hz, 1H), 1.58 (dt, *J* = 13.1, 6.6 Hz, 1H), 1.37 – 1.24 (m, 3H), 1.15 (d, *J* = 6.6 Hz, 3H), 1.09 (s, 3H), 1.07 (s, 3H), 0.94 (dd, *J* = 6.8, 1.3 Hz, 3H), 0.74 – 0.71 (m, 6H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 209.0, 189.4, 151.3, 135.1, 129.5 (2C), 129.2, 128.1, 127.7 (2C), 83.9, 74.3, 58.2, 48.5, 45.5, 43.5, 43.2, 43.0, 42.9, 41.8, 40.5, 35.6, 35.4, 35.4, 31.5, 30.1, 27.1, 21.3, 20.3, 18.3, 16.6, 14.0, 13.9, 10.0.

FTIR: (neat) [cm^{-1}] = 2958 (s), 2872 (w), 2360 (m), 2340 (w), 1737 (s), 1653 (s), 1474 (w), 1380 (m), 1297 (w), 1020 (s), 988 (m), 739 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{34}H_{45}ClNaO_4Se^+$: 655.2064; found: 655.2058.

$[\alpha]_D^{25}$: +42.3 (c= 1.00; $CHCl_3$)

165

R_f: 0.29 (2:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 7.59 – 7.53 (m, 2H), 7.26 – 7.25 (m, 3H), 3.85 (d, *J* = 10.0 Hz, 1H), 3.48 (dd, *J* = 10.3, 2.5 Hz, 1H), 3.05 (dd, *J* = 11.7, 6.7 Hz, 1H), 2.71 (dd, *J* = 14.7, 8.8 Hz, 1H), 2.44 – 2.37 (m, 4H), 2.24 (t, *J* = 8.0 Hz, 1H), 2.12 (td, *J* = 12.9, 5.3 Hz, 1H), 2.03 – 1.97 (m, 2H), 1.92 (dt, *J* = 8.6, 4.5 Hz, 1H), 1.84 – 1.59 (m, 7H), 1.18 – 1.13 (m, 1H), 1.07 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 5.6 Hz, 3H), 0.88 (s, 3H), 0.81 (t, *J* = 4.8 Hz, 1H), 0.55 (d, *J* = 5.2 Hz, 3H).

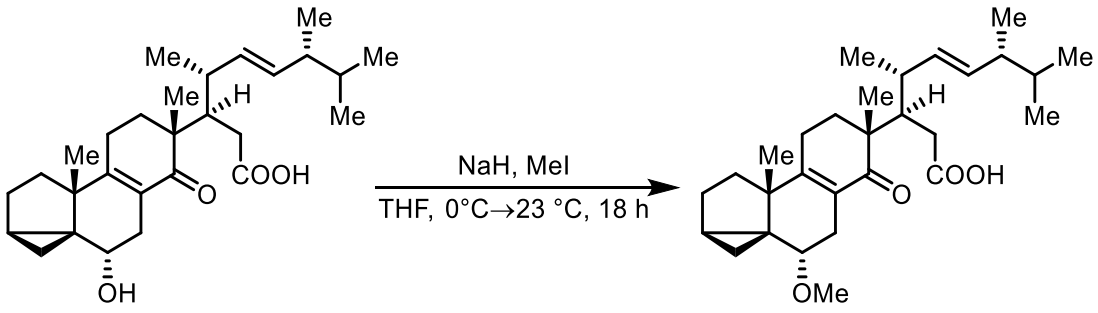
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 209.4, 189.5, 151.5, 134.4 (2C), 130.7, 129.3, 127.5 (2C), 83.7, 75.4, 55.8, 48.4, 44.5, 43.5, 43.0, 42.9, 41.6, 39.9, 36.8, 35.6, 35.4, 31.4, 31.3, 27.1, 25.5, 21.7, 21.0, 20.3, 14.1, 13.9, 13.6, 12.4, 1.2.

FTIR: (neat) [cm^{-1}] = 2960 (s), 2874 (w), 1739 (m), 1671 (s), 1463 (m), 1374 (m), 1023 (w) 909 (w), 735 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{34}H_{45}ClNaO_4Se^+$: 655.2064; found:655.2067.

$[\alpha]_D^{25}$: +25.7 (c= 0.44; $CHCl_3$)

(22*E*)-6*α*-Methoxy-14-oxo-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dien-15-oic acid



$C_{28}H_{42}O_4$ (442.64)
91

$C_{29}H_{44}O_4$ (456.67)
90

To carboxylic acid **91** (238 mg, 0.540 mmol, 1.0 equiv.) in THF (5.3 mL) was added sodium hydride (130 mg, 3.23 mmol, 60% in mineral oil, 6.0 equiv.) at 0 °C. After 5 minutes, methyl iodide (135 µL, 2.15 mmol, 4.0 equiv.) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 16 hours. The mixture was diluted with water (5 mL) and acidified (pH = 3) with aq. HCl (1 M). The solution was extracted with EtOAc (3 x5 mL), the combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield methyl ether **90** (246 mg, 0.540 mmol, quant.) as a colorless foam that was used in the next step without further purification.

R_f : 0.37 (19:1; CH_2Cl_2/MeOH [CAM, *blue*]; UV])

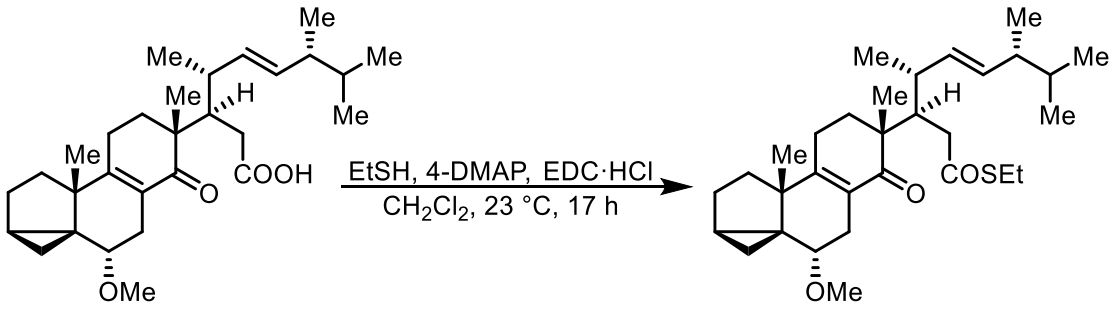
^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.33 – 5.22 (m, 2H), 3.53 (dd, *J* = 10.2, 5.1 Hz, 1H), 3.33 (s, 3H), 3.13 (dd, *J* = 16.3, 5.2 Hz, 1H), 2.49 – 2.40 (m, 2H), 2.32 (dd, *J* = 9.9, 5.5 Hz, 2H), 2.26 – 2.09 (m, 2H), 1.88 (h, *J* = 6.8 Hz, 1H), 1.78 (dd, *J* = 13.7, 6.7 Hz, 1H), 1.68 (dddd, *J* = 13.1, 10.4, 6.7, 3.7 Hz, 2H), 1.58 (dd, *J* = 14.9, 7.6 Hz, 2H), 1.47 (dq, *J* = 13.3, 6.7 Hz, 1H), 1.27 (dd, *J* = 9.9, 5.5 Hz, 2H), 1.19 (s, 3H), 1.15 – 1.08 (m, 1H), 1.01 (s, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.86 – 0.84 (m, 1H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.37 (t, *J* = 4.4 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 203.2, 178.6, 158.8, 135.5, 132.1, 129.6, 72.4, 57.0, 49.8, 47.2, 43.4, 41.7, 38.1, 36.5, 33.2, 33.1, 31.4, 30.8, 28.2, 26.0, 22.7, 22.5, 22.4, 20.2, 19.9, 19.8, 18.9, 17.6, 7.1.

FTIR: (neat) [cm^{-1}] = 2956 (s), 2924 (s), 2869 (m), 2359 (w), 1736 (w), 1705 (s), 1660 (m), 1622 (w), 1455 (m), 1371 (m), 1104 (s), 1017 (m), 911 (w), 831 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{44}NaO_4^+$: 479.3132; found: 479.3150.

S-Ethyl (22*E*)-14-Oxo-6*α*-methoxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-diene-15-thioate



$C_{29}H_{44}O_4$ (456.67)
90

$C_{31}H_{48}O_3S$ (500.78)
98

To carboxylic acid **90** (0.26 g, 0.57 mmol, 1.0 equiv.) in CH_2Cl_2 (2.9 mL) was added 4-dimethylaminopyridine (7.0 mg, 0.060 mmol, 0.1 equiv.) and ethanethiol (0.17 mL, 2.3 mmol, 4.0 equiv.). *N*-(3-Dimethylaminopropyl)-*N'*-ethyl carbodiimide hydrochloride (0.16 g, 0.85 mmol, 1.5 equiv.) was added in portions at 0 °C. After all solids dissolved, the reaction mixture was allowed to warm to ambient temperature and stirred for 17 h. The mixture was diluted with CH_2Cl_2 (5 mL) and added to sat. aq. NH_4Cl (5 mL). The aq. phase was extracted with CH_2Cl_2 (2 x 5 mL) and the combined organic phases were sequentially washed with sat. aq. NH_4Cl (5 mL), water (5 mL), sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield thioester **98** (0.29 g, 0.57 mmol, quant.) as a yellow oil, which was used without further purification.

R_f : 0.56 (4:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.29 (dd, *J* = 15.3, 8.2 Hz, 1H), 5.22 (dd, *J* = 15.3, 8.0 Hz, 1H), 3.51 (ddd, *J* = 10.2, 5.2, 1.1 Hz, 1H), 3.31 (s, 3H), 3.14 – 3.10 (m, 1H), 2.80 (ttd, *J* = 7.4, 3.7, 1.0 Hz, 2H), 2.57 (dd, *J* = 5.4, 2.9 Hz, 2H), 2.51 (dd, *J* = 5.6, 2.6 Hz, 2H), 2.41 (td, *J* = 7.5, 2.9 Hz, 1H), 2.36 – 2.28 (m, 2H), 2.19 (dddd, *J* = 15.8, 6.2, 4.7, 2.3 Hz, 2H), 2.14 – 2.10 (m, 1H), 1.88 – 1.84 (m, 1H), 1.77 (dd, *J* = 13.6, 7.4 Hz, 1H), 1.70 – 1.62 (m, 2H), 1.60 (dd, *J* = 12.4, 7.3 Hz, 1H), 1.48 – 1.41 (m, 1H), 1.19 (t, *J* = 7.4 Hz, 3H), 1.16 (s, 3H), 1.10 (ddd, *J* = 13.7, 12.3, 7.5 Hz, 1H), 0.96 – 0.95 (m, 2H), 0.94 (d, *J* = 7.1 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.87 – 0.82 (m, 1H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.36 (t, *J* = 4.4 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 202.9, 199.3, 158.6, 135.4, 132.1, 129.5, 72.4, 57.0, 49.7, 47.3, 43.3, 41.6, 41.2, 38.2, 36.5, 33.2, 33.0, 31.7, 28.2, 26.0, 23.4, 22.7, 22.5, 22.5, 20.2, 20.0, 19.8, 18.9, 17.5, 14.8, 7.0.

FTIR: (neat) [cm^{-1}] = 2957 (s), 2926 (s), 2869 (m), 2359 (m), 2341 (w), 1690 (s), 1660 (s), 1622 (m), 1455 (s), 1306 (w), 1198 (m), 1103 (s), 1016 (s), 911(m), 833 (w), 766 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{31}H_{49}NaO_3S^+$: 523.3216; found: 523.3217.

$[\alpha]_D^{23}$: +122.3 (c=1.00; $CHCl_3$)

(22*E*)-14-Oxo-6α-methoxy-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien-15-al

$C_{31}H_{48}O_3S$ (500.78)
98

$C_{29}H_{44}O_3$ (440.67)
304

Thioester **98** (0.39 g, 0.78 mmol, 1.0 equiv.) was dissolved in acetone (4.0 mL) and Pd/C (83 mg, 80 µmol, 0.10 equiv., 10 wt.%) was added. Triethylsilane (0.50 mL, 3.1 mmol, 4.0 equiv.) was added and the resulting mixture was allowed to stir for 90 min. The mixture was diluted with acetone (10 mL) and filtered over Celite® and rinsed with acetone (2 x 10 mL). The solvent was removed under reduced pressure to yield aldehyde **304** (0.34 g, 0.78 mmol, quant.) as a yellow oil, which was used without further purification.

R_f : 0.51 (6:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 9.63 (t, *J* = 1.6 Hz, 1H), 5.28 – 5.18 (m, 2H), 3.55 – 3.51 (m, 1H), 3.33 (d, *J* = 0.5 Hz, 3H), 3.14 – 3.08 (m, 1H), 2.62 (ddd, *J* = 6.0, 5.1, 3.3 Hz, 1H), 2.49 (ddd, *J* = 17.8, 6.1, 1.7 Hz, 1H), 2.44 – 2.32 (m, 3H), 2.28 – 2.19 (m, 1H), 2.18 – 2.11 (m, 1H), 1.87 (qdd, *J* = 6.7, 4.5, 1.6 Hz, 1H), 1.84 – 1.78 (m, 1H), 1.72 – 1.55 (m, 4H), 1.49 – 1.44 (m, 1H), 1.31 – 1.24 (m, 2H), 1.19 (s, 3H), 0.99 (s, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.89 – 0.84 (m, 1H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.38 (t, *J* = 4.4 Hz, 1H).

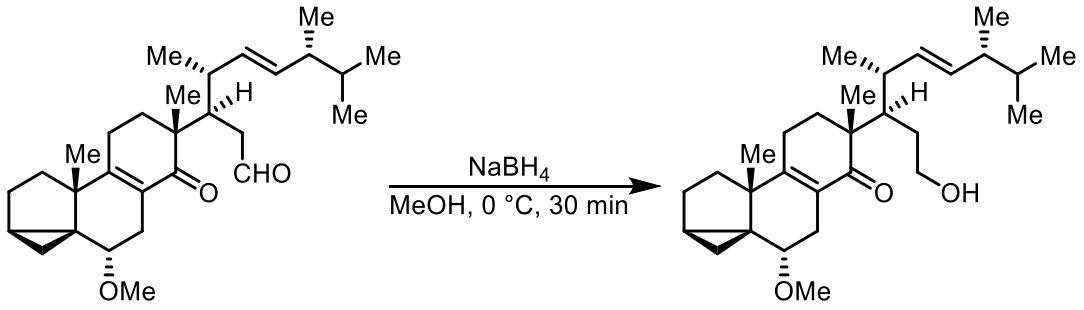
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.1, 202.1, 159.3, 135.6, 132.3, 129.6, 72.4, 57.0, 49.9, 47.2, 43.4, 41.3, 39.6, 38.1, 36.5, 33.2, 33.1, 31.3, 28.2, 26.1, 22.8, 22.5, 22.5, 20.6, 20.2, 19.8, 19.0, 17.6, 7.1.

FTIR: (neat) [cm^{-1}] = 2957 (s), 2869 (m), 2360 (s), 2341 (m), 1725 (s), 1656 (s), 1455 (m), 1370 (m), 1275 (w), 1199 (m), 1103 (s), 984 (w), 868 (w), 669 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{44}NaO_3^+$: 463.3183; found: 463.3198.

$[\alpha]_D^{23}$: +151.3 (c= 0.94; $CHCl_3$)

(22*E*)-6α-Methoxy-15-hydroxy-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien-14-one



$C_{29}H_{44}O_3$ (440.67)
304

$C_{29}H_{46}O_3$ (442.68)
99

Aldehyde **304** (0.13 g, 0.30 mmol, 1.0 eq. was dissolved in MeOH (3.0 mL) and cooled to 0 °C. Sodium borohydride (46 mg, 1.2 mmol, 4.0 eq.) was added in portions. The resulting mixture was allowed to stir at the same temperature for 30 min when aq. HCl (1 mL, 1.0 M) was carefully added and the mixture was allowed to warm to ambient temperature. Water (3 mL) was added and the mixture was extracted with EtOAc (3 x 5 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 4:1) to yield alcohol **100** (86 mg, 0.19 mmol, 64% over 4 steps) as a colorless oil. Additionally, methyl ester **101** (19 mg, 40 µmol, 10% over 4 steps) was isolated as a colorless oil.

R_f: 0.25 (4:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.35 (dd, *J* = 15.3, 8.2 Hz, 1H), 5.23 (dd, *J* = 15.3, 8.1 Hz, 1H), 3.54 (dd, *J* = 10.1, 5.2 Hz, 1H), 3.46 (ddd, *J* = 10.3, 8.6, 6.1 Hz, 1H), 3.38 (ddd, *J* = 10.3, 8.6, 6.4 Hz, 1H), 3.33 (s, 3H), 3.19 (dd, *J* = 16.5, 5.2 Hz, 1H), 2.35 (td, *J* = 7.5, 2.4 Hz, 1H), 2.30 (ddd, *J* = 16.8, 8.3, 3.9 Hz, 1H), 2.23 – 2.17 (m, 1H), 2.12 (ddd, *J* = 13.7, 6.4, 4.4 Hz, 1H), 1.87 (dq, *J* = 13.8, 6.6 Hz, 1H), 1.80 – 1.73 (m, 2H), 1.71 – 1.50 (m, 6H), 1.49 – 1.42 (m, 2H), 1.24 (dt, *J* = 8.0, 4.0 Hz, 1H), 1.17 (s, 3H), 1.11 (ddt, *J* = 15.3, 12.3, 7.8 Hz, 1H), 1.01 (s, 3H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H), 0.38 (t, *J* = 4.4 Hz, 1H).

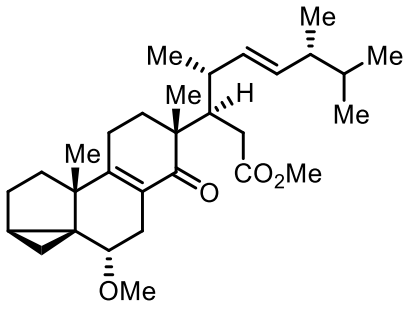
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 204.1, 159.0, 134.8, 132.7, 129.5, 72.4, 63.6, 57.0, 49.7, 47.8, 43.4, 42.2, 38.3, 36.6, 33.2, 33.1, 31.4, 29.2, 26.2, 23.2, 22.7, 22.6, 22.4, 20.2 (2C), 19.8, 18.8, 17.7, 7.2.

FTIR: (neat) [cm^{-1}] = 2957 (s), 2929 (m), 2869 (w), 2359 (m), 2341 (w), 1654 (s), 1619 (m), 1455 (s), 1370 (s), 1275 (w), 1212 (m), 1198 (m), 1103 (s), 910 (m), 730 (s), 685 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{46}NaO_3^+$: 465.3339; found: 465.3345.

$[\alpha]_D^{23}$: +203.8 (c= 1.00; $CHCl_3$)

(22*E*)-6α-Methoxy-14-oxo-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-diene-15-methyl ester



$C_{30}H_{46}O_4$ (470.69)

101

R_f : 0.60 (4:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.30 (dd, *J* = 15.3, 7.6 Hz, 1H), 5.24 (dd, *J* = 15.3, 7.4 Hz, 1H), 3.60 (s, 3H), 3.53 (dd, *J* = 10.2, 5.2 Hz, 1H), 3.34 (s, 3H), 3.18 – 3.10 (m, 1H), 2.46 (tdd, *J* = 10.0, 6.5, 2.9 Hz, 1H), 2.38 – 2.12 (m, 5H), 1.87 (td, *J* = 7.1, 6.0 Hz, 1H), 1.82 – 1.75 (m, 1H), 1.73 – 1.60 (m, 6H), 1.50 – 1.40 (m, 1H), 1.31 – 1.22 (m, 2H), 1.19 (s, 3H), 0.98 (s, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.38 (t, *J* = 4.4 Hz, 1H).

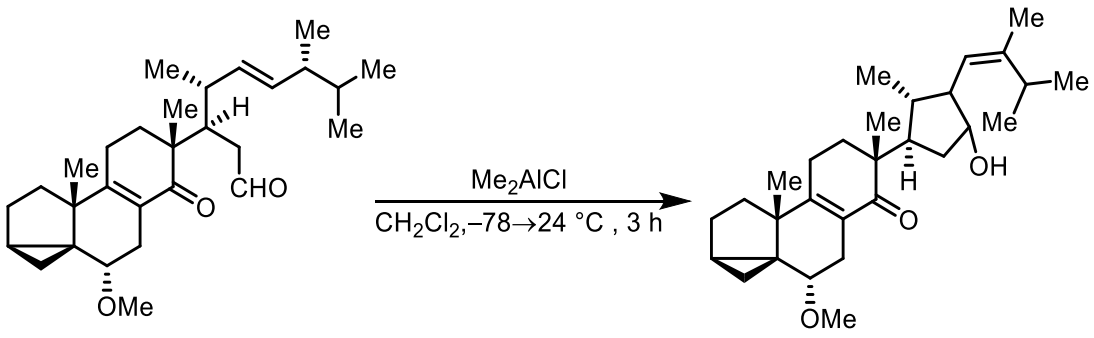
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 203.2, 174.4, 158.6, 135.4, 132.2, 129.6, 72.5, 57.1, 51.7, 49.7, 47.3, 43.4, 41.8, 38.0, 36.5, 33.2, 33.1, 31.6, 31.0, 28.3, 27.1, 26.0, 22.7, 22.5, 20.2 (2C), 19.8, 18.9, 17.6, 7.0.

FTIR: (neat) [cm^{-1}] = 2957 (s), 2928 (m), 2870 (w), 2359 (s), 2341 (m), 1737 (s), 1659 (s), 1622 (w), 1455 (m), 1434 (m), 1371 (m), 1197 (m), 1172 (m), 1103 (s), 1016 (m), 733 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{46}NaO_4^+$: 493.3288; found: 493.3317.

$[\alpha]_D^{23}$: +161.8 (*c* = 1.00, $CHCl_3$)

15,22-Cyclo-6*α*-Methoxy-15-hydroxy-3*α*,5-cyclo-14,15-seco-5*α*-ergosta-8,22-dien-14-one



$C_{29}H_{44}O_3$ (440.67)
304

$C_{29}H_{44}O_3$ (440.67)
305

To aldehyde **304** (9.0 mg, 21 µmol, 1.0 equiv.) in CH_2Cl_2 (0.4 mL) was added dimethylaluminum chloride (20 µL, 20 µmol, 1.0 equiv., 1.0 M in hexane) at −78 °C. The mixture was allowed to warm to ambient temperature over 3 h when sat. aq. $NaHCO_3$ (1 mL) was added. The phases were separated, and the aq. phase was extracted with EtOAc (3 x 1 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was purified by preparative TLC (SiO_2; *n*hexane/EtOAc 2:1) to give homoallylic alcohol **305** (3.6 mg, 8.2 µmol, 40%) as colorless oil along with unreacted **304** (1.8 mg, 4.2 µmol, 20%) as a colorless oil.

R_f : 0.32 (4:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.26 (dt, *J* = 9.8, 1.2 Hz, 1H), 4.09 (q, *J* = 4.7 Hz, 1H), 3.56 – 3.53 (m, 1H), 3.34 (s, 3H), 3.20 – 3.16 (m, 1H), 2.75 – 2.71 (m, 1H), 2.42 – 2.20 (m, 3H), 2.06 – 2.02 (m, 1H), 1.90 (ddd, *J* = 13.5, 6.7, 4.7 Hz, 1H), 1.80 (dd, *J* = 13.7, 7.7 Hz, 1H), 1.74 – 1.66 (m, 3H), 1.60 (s, 3H), 1.30 – 1.23 (m, 4H), 1.19 (s, 3H), 1.08 (d, *J* = 1.7 Hz, 1H), 1.04 – 1.01 (m, 9H), 0.96 (d, *J* = 7.2 Hz, 3H), 0.90 – 0.80 (m, 3H), 0.38 (t, *J* = 4.4 Hz, 1H).

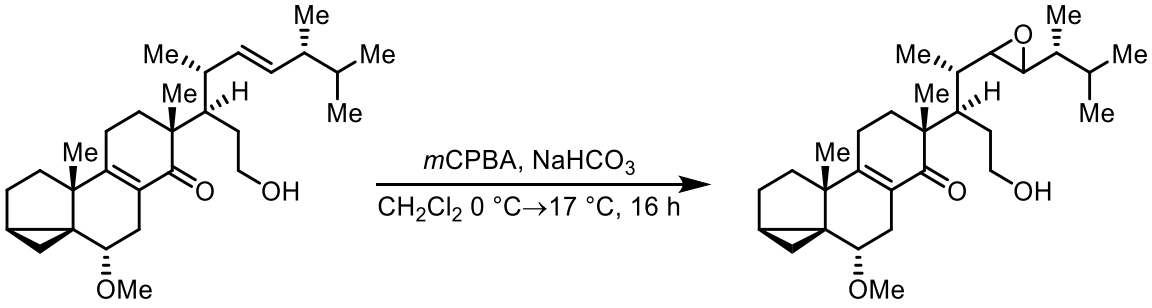
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.3, 159.1, 145.8, 130.0, 117.5, 75.9, 72.5, 57.1, 49.9, 48.0, 47.8, 45.8, 37.5, 36.6, 36.0, 32.9, 32.0, 28.2, 26.2, 24.2, 22.9, 22.8, 21.9, 21.8, 20.0, 19.6, 18.9, 14.2, 7.1.

FTIR: (neat) [cm^{-1}] = 2958 (s), 2929 (m), 2869 (w), 2359 (s), 2341 (m), 1770 (m), 1654 (m), 1456 (w), 1213 (w), 913 (w), 668 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{44}NaO_3^+$: 463.3183; found: 463.3204.

$[\alpha]_D^{24}$: +21.3 (*c* = 0.12, $CHCl_3$)

22,23-Epoxy-6α-methoxy-15-hydroxy-3α,5-cyclo-14,15-seco-5α-ergosta-8-en-14-on



$C_{29}H_{46}O_3$ (442.68)
99

$C_{29}H_{46}O_4$ (458.68)
100

To alcohol **99** (30 mg, 68 µmol, 1.0 equiv.) in CH_2Cl_2 (0.68 mL) at 0 °C was added $NaHCO_3$ (6.3 mg, 75 µmol, 1.1 equiv.) followed by *meta*-chloroperbenzoic acid (16 mg, 95 µmol, 1.4 equiv.). The mixture was allowed to slowly warm to 17 °C over night by melting of the ice. The mixture was diluted with EtOAc (3 mL) and added to sat. aq. $NaHCO_3$ (3 mL). The aqueous phase was extracted with EtOAc (2 x 2 mL) and the combined organic phases were washed with sat. aq. $NaHCO_3$ (3 mL) and sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 2:1) to yield epoxide **100** (21 mg, 46 µmol, 68%) as a colorless oil and an approximate 7:3 mixture of diastereomers.

R_f : 0.30 (2:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

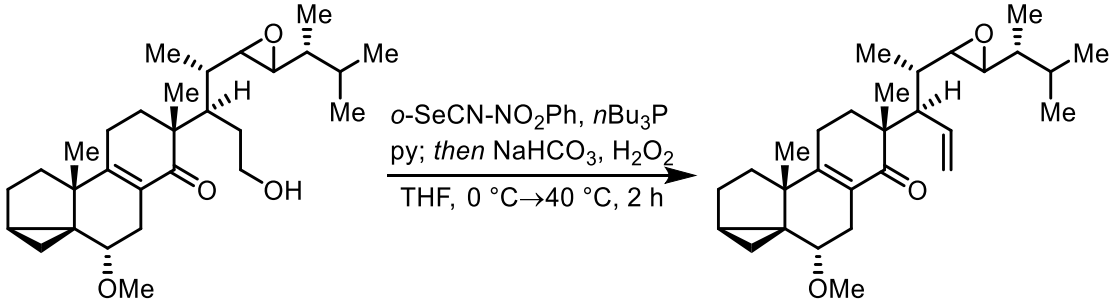
^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 3.59 – 3.49 (m, 3H), 3.34 (s, 3H), 3.20 – 3.15 (m, 1H), 2.66 (dd, *J* = 7.9, 2.3 Hz, 1H), 2.46 (dd, *J* = 8.0, 2.3 Hz, 1H), 2.31 – 2.15 (m, 2H), 2.07 (ddd, *J* = 19.7, 9.6, 5.6 Hz, 1H), 2.00 (q, *J* = 4.6 Hz, 1H), 1.84 – 1.58 (m, 5H), 1.47 (tdd, *J* = 12.2, 7.7, 4.1 Hz, 1H), 1.37 (ddt, *J* = 11.2, 7.3, 4.0 Hz, 1H), 1.24 (ddd, *J* = 12.2, 6.1, 3.3 Hz, 2H), 1.17 (s, 3H), 1.13 (s, 3H), 1.00 (d, *J* = 7.3 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 6H), 0.84 (dd, *J* = 8.2, 4.7 Hz, 1H), 0.38 (t, *J* = 4.5 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 204.0, 203.4*, 159.3, 159.1*, 129.8, 129.8*, 72.5, 72.5*, 63.4, 63.0*, 62.7, 62.5*, 60.0, 57.2*, 57.1, 49.9*, 49.9, 47.7*, 47.3, 43.2, 42.4* 42.4, 42.3*, 42.2*, 38.6, 36.6, 36.0*, 33.2*, 33.2, 33.1, 31.4*, 31.1, 31.0*, 30.6, 30.0*, 29.6, 28.2, 28.2*, 26.2, 22.7*, 22.7, 22.6*, 22.6, 20.8*, 20.6, 20.5*, 20.4, 19.5, 19.3, 18.9*, 18.9, 18.6*, 18.3*, 13.6, 16.6*, 12.6*, 7.3*, 7.3.

FTIR: (neat) [cm^{-1}] = 2959 (w), 2930 (w), 2873 (w), 2360 (s), 2341 (s), 1792 (m), 1683 (m), 1653 (m), 1456 (w), 1213 (w), 1022 (m), 905 (w), 802 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{46}NaO_4^+$: 481.3288; found: 481.3290.

22,23-Epoxy-6α-methoxy-3α,5-cyclo-14,15-seco-5α-ergosta-8,15-dien-14-on



$C_{29}H_{46}O_4$ (458.68)
100

$C_{29}H_{44}O_3$ (440.67)
116

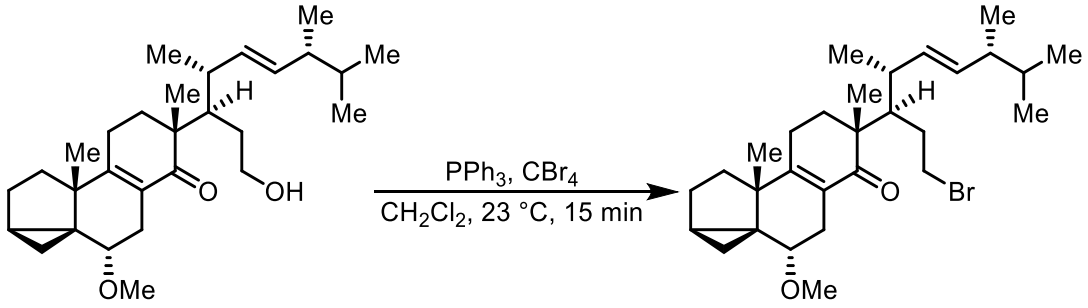
To alcohol **100** (11 mg, 24 µmol, 1.0 equiv.) and *o*-nitrophenyl selenocyanate (21 mg, 93 µmol, 4.0 equiv.) in THF (1.5 mL) were added pyridine (7.5 µL, 93 µmol, 4.0 equiv.) and *n*-tributylphosphine (23 µL, 93 µmol, 4.0 equiv.) at 23 °C. The resulting mixture was stirred at the same temperature for 1 h and cooled to 0 °C. Sodium hydrogen carbonate (7.6 mg, 93 µmol, 4.0 equiv.) and hydrogen peroxide (0.38 mL, mmol? 30% aq.) were added and the resulting mixture was heated to 40 °C and stirred at that temperature for 1 h. The mixture was allowed to cool to ambient temperature, diluted with Et_2O (5 mL) and sequentially washed with water (3 mL), sat. aq. Na_2CO_3 (3 mL), sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 19:1) to give alkene **116** (5.0 mg, 11 µmol, 49%) as a colorless oil and mixture of diastereomers as well as pure alkene **116** (5.3 mg, 12 µmol, 51%) as a colorless oil.

R_f : 0.30 (19:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.78 (dt, *J* = 16.9, 10.4 Hz, 1H), 5.18 (dd, *J* = 10.1, 2.2 Hz, 1H), 5.07 (dd, *J* = 16.9, 2.3 Hz, 1H), 3.52 (dd, *J* = 10.2, 5.1 Hz, 1H), 3.34 (s, 3H), 3.17 (ddd, *J* = 16.1, 5.5, 1.5 Hz, 1H), 2.62 (dd, *J* = 10.8, 4.0 Hz, 1H), 2.57 (dd, *J* = 8.1, 2.3 Hz, 1H), 2.43 – 2.38 (m, 1H), 2.35 – 2.27 (m, 1H), 2.28 – 2.10 (m, 2H), 1.87 (dd, *J* = 13.7, 7.7 Hz, 1H), 1.65 (dd, *J* = 13.0, 6.7 Hz, 4H), 1.57 – 1.46 (m, 2H), 1.33 – 1.20 (m, 3H), 1.16 (s, 3H), 1.03 (s, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 0.86 (dd, *J* = 8.1, 4.9 Hz, 1H), 0.38 (t, *J* = 4.5 Hz, 1H).

Only the ^{1}H NMR was measured.

(22*E*)-6α-Methoxy-15-bromo-3α,5-cyclo-14,15-seco-5α-ergosta-8,22-dien-14-one



$C_{29}H_{46}O_3$ (442.68)
99

$C_{29}H_{45}BrO_2$ (505.58)
106

To a solution of alcohol **99** (10 mg, 23 µmol, 1.0 equiv.) in CH_2Cl_2 (0.23 mL) was added triphenylphosphine (8.9 mg, 34 µmol, 1.5 equiv.) and carbon tetrabromide (9.7 mg, 29 µmol, 1.3 equiv.). The resulting mixture was allowed to stir at 24 °C for 15 min. The mixture was diluted with Et_2O (2 mL) and added to sat. aq. $Na_2S_2O_3$ (3 mL). The phases were separated, and the aq. phase was extracted with Et_2O (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield bromide **106** (9.3 mg, 18 µmol, 80%) as a colorless oil.

R_f : 0.48 (9:1; *n*hexane/EtOAc [CAM, *blue*]; UV])

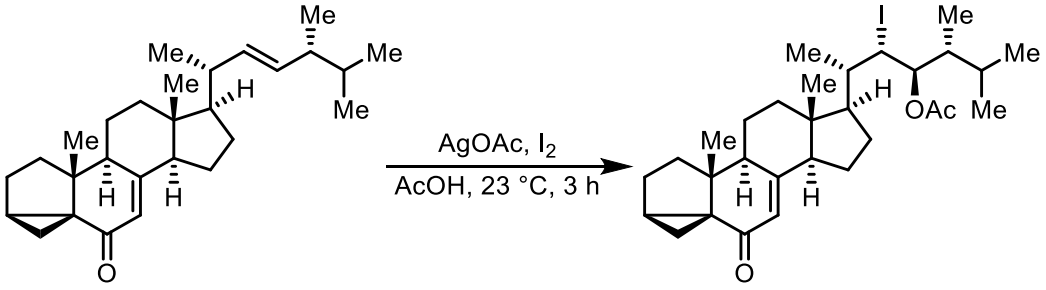
^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.31 (dd, *J* = 15.3, 7.5 Hz, 1H), 5.25 (dd, *J* = 15.3, 8.1 Hz, 1H), 3.55 (dd, *J* = 10.1, 5.3 Hz, 1H), 3.35 (s, 3H), 3.32 – 3.27 (m, 1H), 3.25 – 3.21 (m, 2H), 2.38 – 2.30 (m, 2H), 2.22 (tt, *J* = 4.7, 2.3 Hz, 1H), 2.20 (td, *J* = 4.4, 2.2 Hz, 1H), 2.12 (ddd, *J* = 13.7, 6.4, 4.4 Hz, 1H), 1.93 (td, *J* = 5.3, 2.7 Hz, 1H), 1.91 – 1.83 (m, 1H), 1.79 (dd, *J* = 13.8, 7.1 Hz, 1H), 1.72 – 1.57 (m, 4H), 1.55 (s, 3H), 1.50 – 1.44 (m, 1H), 1.19 (s, 3H), 1.16 – 1.08 (m, 1H), 1.04 (d, *J* = 7.0 Hz, 3H), 1.02 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.38 (t, *J* = 4.4 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 203.7, 159.1, 135.3, 132.3, 129.5, 72.4, 57.1, 49.8, 47.8, 44.5, 43.5, 37.9, 36.6, 34.4, 33.2, 33.0, 31.7, 30.2, 28.2, 26.2, 23.0, 22.9, 22.6, 20.3, 20.2, 19.9, 18.9, 17.8, 7.1.

FTIR: (neat) [cm^{-1}] = 2958 (s(, 2927 (m), 2870 (w), 2360 (s), 2341 (s), 1733 (w), 1661 (s), 1457 (m), 1371 (m), 1213 (w), 1103 (m), 983 (w), 669 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{45}BrNaO_2^+$: 527.2495; found: 527.2495.

22*S*-Iodo-3*α*,5-Cyclo-5*α*-ergosta-7,22-dien-6-one-23*R*-yl acetate



$C_{28}H_{42}O$ (394.64)
69

$C_{30}H_{45}IO_3$ (580.59)
121

To enone **69** (204 mg, 517 µmol, 1.0 equiv.) in acetic acid (5.2 mL) was added silver acetate (207 mg, 1.24 mmol, 2.4 equiv.) at 23 °C. Finely ground iodine (157 mg, 620 µmol, 1.2 equiv.) was added in portions over 15 min. The resulting mixture was allowed to stir for 3 h in the dark. Benzene (15 mL) was added and the resulting mixture was filtered over a plug of Celite® and rinsed with benzene (2 x 5 mL). The filtrate was carefully washed with sat. aq. $NaHCO_3$ (3 x 10 mL), sat. aq. $Na_2S_2O_3$ (10 mL), sat. aq. NaCl (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield iodoacetate **121** (55.0 mg, 95.1 µmol, 18%) as a colorless solid.

R_f : 0.20 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.79 (t, *J* = 2.4 Hz, 1H), 5.46 (dd, *J* = 10.1, 2.2 Hz, 1H), 4.27 (dd, *J* = 10.1, 1.8 Hz, 1H), 2.26 (ddd, *J* = 10.9, 7.5, 2.3 Hz, 1H), 2.17 – 2.07 (m, 2H), 2.06 (s, 3H), 2.02 – 1.93 (m, 2H), 1.82 – 1.66 (m, 7H), 1.60 – 1.50 (m, 2H), 1.50 – 1.38 (m, 2H), 1.34 – 1.10 (m, 4H), 1.08 (s, 3H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.77 – 0.73 (m, 1H), 0.71 (s, 3H).

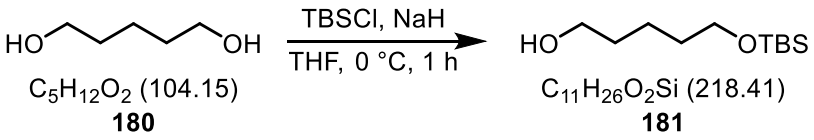
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 197.2, 170.0, 163.6, 123.9, 74.4, 56.2, 55.9, 47.3, 45.2, 44.4, 43.8, 42.6, 42.1, 39.1, 36.9, 35.1, 33.9, 30.6, 26.9, 25.4, 23.3, 22.6, 21.3, 21.0, 20.2, 19.5, 18.3, 13.5, 13.3, 10.4.

FTIR: (neat) [cm^{-1}] = 2960 (s), 2873 (w), 2360 (m), 2340 (w), 1740 (s), 1654 (s), 1479 (w), 1381 (m), 1280 (w), 1020 (s), 987 (m), 724 (m), 668 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{43}INaO_3^+$: 589.2149; found: 589.2151.

$[\alpha]_D^{23}$: +24.6 (c= 1.00; $CHCl_3$)

5-((*tert*-butyldimethylsilyl)oxy)pentan-1-ol



$C_5H_{12}O_2$ (104.15)
180

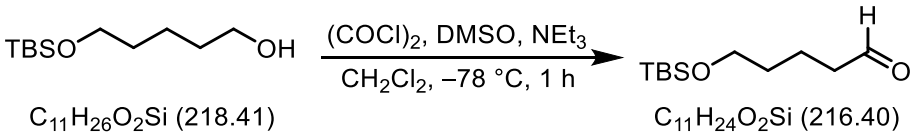
$C_{11}H_{26}O_2Si$ (218.41)
181

To 1,5-pentanediol **180** (1.62 g, 15.6 mmol, 1.0 equiv.) in THF (31 mL) at 0 °C was added sodium hydride (680 mg, 17.1 mmol, 1.1 equiv.) and *tert*-butyldimethylsilyl chloride (2.58 g, 17.1 mmol, 1.1 equiv.). The resulting mixture was allowed to stir at the same temperature for 1 h. The mixture was allowed to warm to ambient temperature and sat. aq. NH_4Cl (20 mL) was added and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with sat. aq. NaCl (20 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 4:1) to give silyl ether **181** (2.20 g, 10.1 mmol, 64%) as a colorless liquid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.65 (t, *J* =6.6, 2H), 3.62 (t, *J* =6.5, 2H), 1.63 – 1.51 (m, 2H), 1.47 – 1.37 (m, 4H), 0.89 (s, 9H), 0.05 (s, 6H).

The spectroscopic data match those reported in literature.[183]

5-((*tert*-butyldimethylsilyl)oxy)pentanal



$C_{11}H_{26}O_2Si$ (218.41)
181

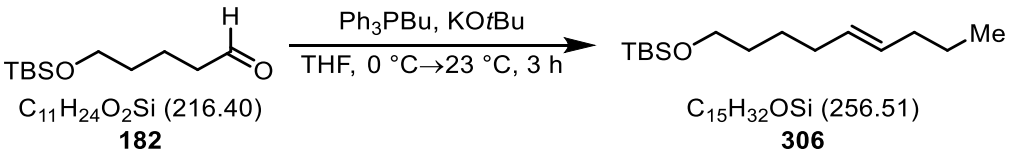
$C_{11}H_{24}O_2Si$ (216.40)
182

To dimethyl sulfoxide (0.73 mL, 10 mmol, 2.0 equiv.) in CH_2Cl_2 (52 mL) at −78 °C was added oxalyl chloride (0.54 mL, 6.2 mmol, 1.2 equiv.) dropwise. After 15 min, a solution of silyl ether **181** (1.1 g, 5.1 mmol, 1.0 equiv.) in CH_2Cl_2 (9.7 mL) was added dropwise and the resulting mixture was allowed to stir at the same temperature for 1 h. Triethylamine (2.8 mL, 21 mmol, 4.0 equiv.) was added and the mixture was allowed to warm to ambient temperature. Water (100 mL) was added to the solution and the phases were separated. The aq. phase was extracted with Et_2O (3 x 20 mL) and the combined organic phases were washed with NaCl (25 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 4:1) to give aldehyde **182** (1.1 g, 5.1 mmol, quant.) as a colorless oil.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 9.76 (t, *J* = 2.0 Hz, 1H), 3.61 (t, *J* = 6.5 Hz, 2H), 2.44 (dt, *J* = 2.0, 7.5 Hz, 2H), 1.72-1.66 (m, 2H), 1.57-1.51 (m, 2H), 1.88 (s, 9 H), 0.03 (s, 6H).

The spectroscopic data match those reported in literature.[184]

(*E*)-*tert*-butyldimethyl(non-5-en-1-yloxy)silane



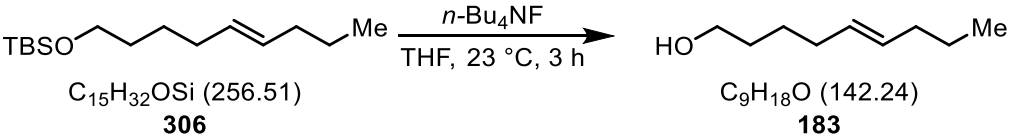
$C_{11}H_{24}O_2Si$ (216.40) **182** — $C_{15}H_{32}OSi$ (256.51) **306**

To butyltriphenylphosphonium bromide (2.5 g, 6.2 mmol, 1.2 equiv.) in THF (17 mL) at 0 °C was added potassium *tert*-butoxide (3.5 mL, 5.6 mmol, 1.1 equiv., 1.6 M in THF). After stirring for 20 min, aldehyde **182** (1.1 g, 5.1 mmol, 1.0 equiv.) in THF (4 mL) dropwise. The resulting mixture was allowed to warm to ambient temperature and stirred for 3 h. Sat. aq. NH_4Cl (10 mL) was added and the resulting mixture was extracted with Et_2O (3 x 10 mL) and the combined organic extracts were washed with NaCl (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 19:1) to yield silyl ether **306** (1.3 g, 5.1 mmol, 100%) as a colorless oil.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.48-5.36 (m, 2H), 3.63 (t, *J* = 6.4 Hz, 2H), 2.11-1.98 (m, 4H), 1.60-1.51 (m, 4H), 1.46-1.35 (m, 5H), 0.93-0.89 (m, 9H), 0.08 (s, 6H).

The spectroscopic data match those reported in literature.[185]

(*E*)-non-5-en-1-ol



$C_{15}H_{32}OSi$ (256.51) **306** — $C_9H_{18}O$ (142.24) **183**

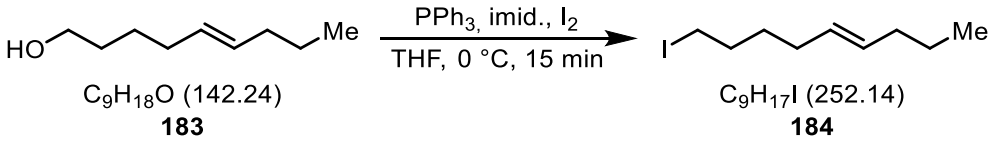
To silyl ether **306** (1.3 g, 5.1 mmol, 1.0 equiv.) in THF (19 mL) at 23 °C was added *n*-tetrabutyl ammonium fluoride (6.0 mL, 6.2 mmol, 1.2 equiv.). The resulting mixture was allowed to stir at the same temperature for 3 h when sat. aq. NH_4Cl (20 mL) was added. The resulting mixture was extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with NaCl (20 mL), dried over $MgSO_4$ and filtered. The solvent was removed under

reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 4:1) to give alcohol **183** (2.2 g, 10 mmol, 64%) as a colorless liquid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.44 – 5.30 (m, 2H), 3.65 (t, *J*=6.6, 2H), 2.09 – 2.03 (m, 2H), 2.00 (ddd, *J*=8.7, 7.2, 6.0, 2H), 1.59 (dddd, *J*=9.6, 8.5, 7.1, 5.2, 2H), 1.45 – 1.33 (m, 4H), 0.91 (dt, *J*=10.4, 7.4, 3H).

The spectroscopic data match those reported in literature.[186]

(*E*)-9-iodonon-4-ene



$C_9H_{18}O$ (142.24)
183

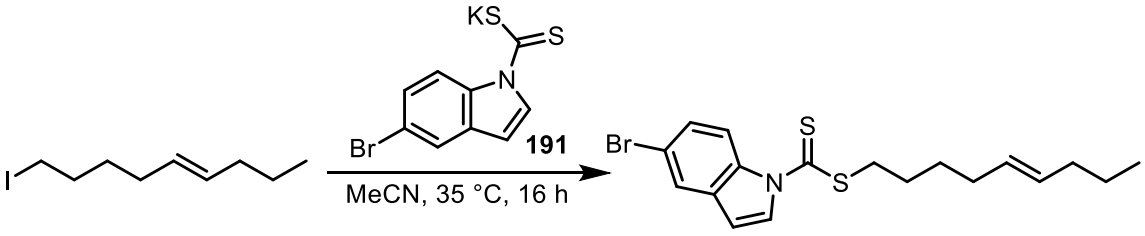
$C_9H_{17}I$ (252.14)
184

To alcohol **183** (165 mg, 1.16 mmol, 1.0 equiv.) in THF (12 mL) at 0 °C was added triphenyl phosphine (456 mg, 1.74 mmol, 1.5 equiv.) and imidazole (118 mg, 1.74 mmol, 1.5 equiv.). Iodine (297 mg, 1.17 mmol, 1.01 equiv.) was added in portions and the resulting mixture was allowed to stir for 15 min at the same temperature. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane) to give iodide **184** (288 mg, 1.14 mmol, 99%) as a colorless liquid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.45 – 5.29 (m, 2H), 3.19 (t, *J*=7.0, 2H), 2.06 (dddd, *J*=8.1, 7.4, 6.6, 0.9, 2H), 2.03 – 1.97 (m, 2H), 1.88 – 1.80 (m, 2H), 1.50 – 1.42 (m, 2H), 1.36 (dt, *J*=14.6, 7.3, 2H), 0.93 – 0.86 (m, 3H).

The spectroscopic data match those reported in literature.[187]

(*E*)-non-5-en-1-yl 5-bromo-1*H*-indole-1-carbodithioate



$C_9H_{17}I$ (252.14)
184

$C_{18}H_{22}BrNS_2$ (396.41)
193

To iodide **184** (32 mg, 0.13 mmol, 1.0 equiv.) in MeCN (2.6 mL) was added 2,6-lutidine (19 µL, 0.17 mmol, 1.3 equiv.). Carbodithioate **191** (44 mg, 0.14 mmol, 1.1 equiv.) was added and the resulting mixture was placed near a blue LED (365 nm) and stirred at 35 °C for 16 h. The solvent was removed under reduced pressure and the residue was submitted to

column chromatography (SiO_2, *n*hexane) to give **193** (50 mg, 0.13 mmol, 98%) as a yellow oil.

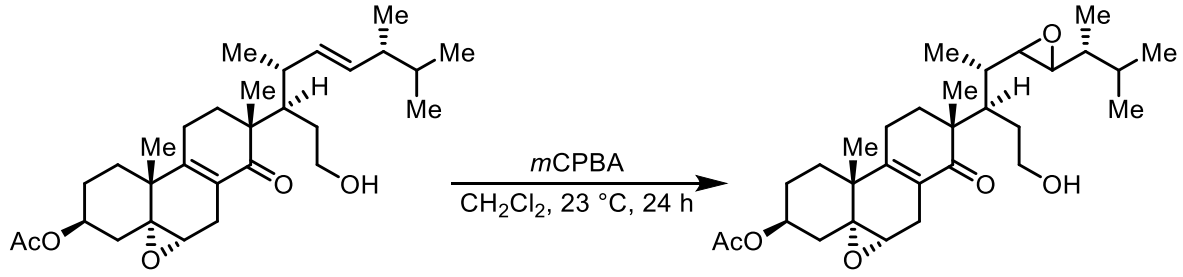
^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 8.86 (dt, *J*=8.9, 0.6, 1H), 8.11 (d, *J*=3.8, 1H), 7.69 (d, *J*=2.0, 1H), 7.47 – 7.39 (m, 1H), 6.60 (dd, *J*=3.8, 0.8, 1H), 5.44 – 5.33 (m, 2H), 3.44 – 3.32 (m, 2H), 2.12 (tdd, *J*=7.4, 6.6, 1.1, 2H), 2.05 – 2.00 (m, 2H), 1.82 (tt, *J*=8.6, 6.9, 2H), 1.58 – 1.52 (m, 2H), 1.38 (h, *J*=7.3, 2H), 0.91 (t, *J*=7.4, 3H).

^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 199.0, 135.9, 133.8, 130.7, 129.1, 128.4, 128.0, 124.0, 118.4, 117.3, 108.5, 37.1, 29.5, 29.2, 27.4, 26.9, 23.0, 14.0.

FTIR: (neat) [cm^{-1}] = 3004 (w), 2954 (w), 2925 (w), 2360 (w), 2342 (w), 1438 (s), 1364 (s), 1296 (s), 1272 (m), 1224 (m), 1185 (s), 1034 (m), 811 (s), 710 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{18}H_{22}BrNNaS_2^+$: 418.0269; found: 418.0271.

5,6α,22,23-Diepoxy-3β-acetoxy-15-hydroxy-14,15-secoergosta-8-en-14-on



$C_{30}H_{46}O_5$ (486.69)
97

$C_{30}H_{46}O_6$ (502.69)
93

To a solution of Δ^5-epoxide **97** (41 mg, 84 µmol, 1.0 equiv.) in CH_2Cl_2 (0.64 mL) was added *m*CPBA (16 mg, 92 µmol, 1.1 equiv.) at 0 °C. The resulting mixture was allowed to warm to 23 °C and stirred at that temperature for 24 h. A second portion of *m*CPBA (8.0 mg, 46 µmol 0.55 equiv.) was added and the mixture was allowed to stir for further 24 h. The consumption of the starting material was monitored by ^{1}H NMR. Upon complete consumption of the starting material, sat. aq. $NaHCO_3$ (3 mL) was added and the phases were separated. The aq. phase was extracted with CH_2Cl_2 (3 x 4 mL) and the combined organic phases were sequentially washed with sat. aq. $NaHCO_3$ (5 mL), sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, CH_2Cl_2/MeOH 19:1) to give diepoxide **93** (32 mg, 63 µmol, 75%) as a colorless oil.

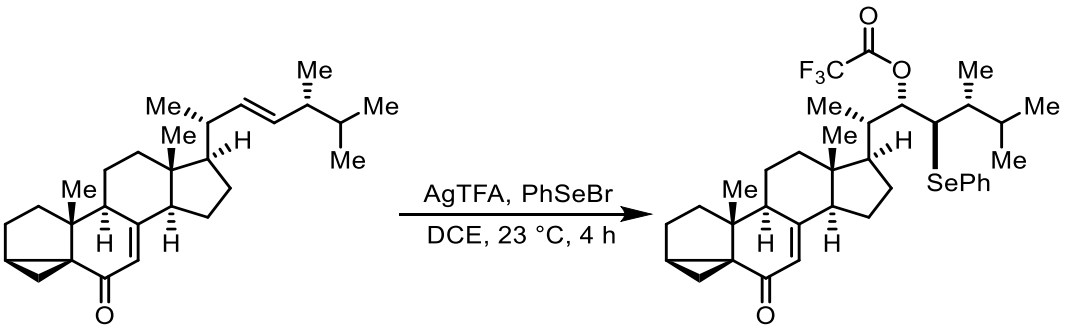
R_f : 0.36 (CH_2Cl_2/MeOH 19:1 [CAM, *blue*, UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.95 (ddt, *J*=11.4, 7.0, 4.7, 1H), 4.67 (d, *J*=2.2, 0H), 3.44 (ddd, *J*=11.9, 6.9, 5.6, 1H), 3.27 (ddd, *J*=11.3, 7.9, 6.1, 1H), 3.21 – 3.18 (m,

1H), 2.99 (dt, *J*=18.8, 2.2, 1H), 2.63 (td, *J*=7.5, 2.4, 1H), 2.53 (dd, *J*=7.9, 2.3, 1H), 2.42 – 2.34 (m, 1H), 2.24 (ddd, *J*=14.0, 11.9, 2.2, 1H), 2.02 (s, 3H), 1.92 – 1.23 (m, 16H), 1.20 (s, 3H), 1.11 (s, 3H), 1.05 (d, *J*=7.3, 3H), 0.96 (d, *J*=6.8, 3H), 0.93 (d, *J*=6.9, 3H), 0.91 (d, *J*=6.8, 3H).

Only the ^{1}H NMR was measured.

22-phenylselanyl-23-trifluoroacetoxy-3*α*,5-Cyclo-5*α*-ergosta-7-en-6-one



$C_{28}H_{42}O$ (394.64)
69

$C_{36}H_{47}F_3O_3Se$ (663.72)
161

Silver trifluoroacetate (14 mg, 63 µmol, 1.0 equiv.) was suspended in dichloroethane (0.40 mL) and a solution of phenylselenyl bromide (12 mg, 63 µmol, 1.0 equiv.) in dichloroethane (0.20 mL) was added dropwise. To the yellowish suspension, enone **69** (25 mg, 63 µmol, 1.0 equiv.) was added in one portion and allowed to stir at 23 °C for 4 h. The suspension was filtered over Celite® and rinsed with CH_2Cl_2 (2 x1 mL). The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to give trifluoroacetate **161** (11.2 mg, 17 µmol, 27%) as a colorless oil, as well as unreacted enone **69** (18.2 mg, 46 µmol, 73%).

R_f : 0.23 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

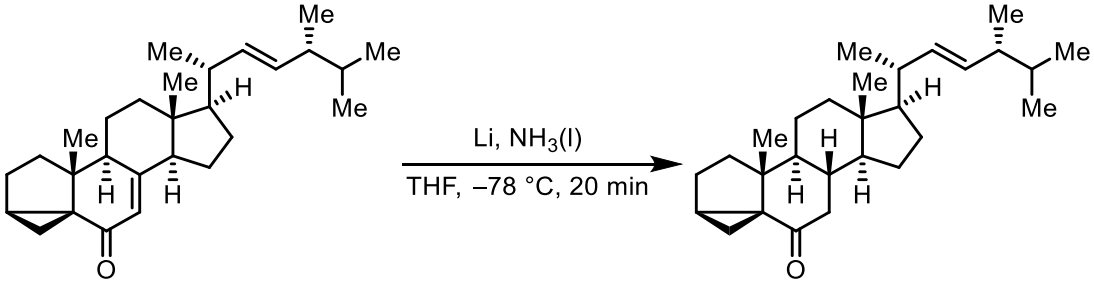
^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 7.62 – 7.52 (m, 2H), 7.37 – 7.25 (m, 3H), 5.81 (d, *J* = 2.5 Hz, 1H), 5.49 (dd, *J* = 8.3, 4.1 Hz, 1H), 3.42 (dd, *J* = 8.3, 1.7 Hz, 1H), 2.28 (ddd, *J* = 10.6, 7.6, 2.4 Hz, 1H), 2.22 – 1.88 (m, 6H), 1.83 – 1.66 (m, 8H), 1.63 – 1.38 (m, 3H), 1.35 – 1.11 (m, 3H), 1.10 (s, 3H), 1.07 (d, *J* = 6.6 Hz, 2H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.77 (t, *J* = 4.7 Hz, 1H), 0.70 (s, 3H), 0.69 (d, *J* = 6.9 Hz, 3H), 0.61 (d, *J* = 6.9 Hz, 3H).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{36}H_{47}F_3NaO_3Se^+$: 687.2535; found: 687.2529.

Due to the compounds instability, only the ^{1}H NMR and HRMS were measured

15. Part Two

(22*E*)-3*α*,5-Cyclo-5*α*-ergosta-22-en-6-one



$C_{28}H_{42}O$ (394.64)
69

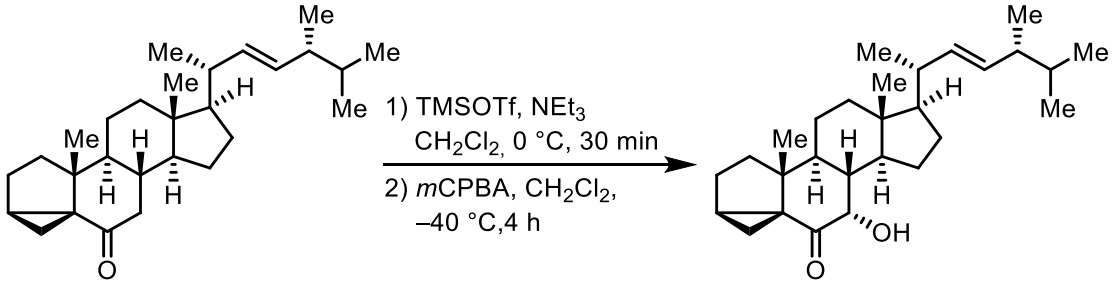
$C_{28}H_{44}O$ (396.66)
243

Lithium (61.5 mg, 8.87 mmol, 7.0 equiv.) was dissolved in ammonia (4 mL) at −78 °C. After stirring at the same temperature for 10 min, enone **69** (500 mg, 1.27 mmol, 1.0 equiv.) in THF (1 mL) was added dropwise. After 15 min, 4-methylpent-3-en-2-one (1.25 g, 12.7 mmol, 10 equiv.) was added dropwise at the same temperature. After fading of the blue color, solid ammonium chloride (500 mg) was added carefully. After evaporation of ammonia, water (10 mL) was added and the aq. phase was extracted with EtOAc (3 x5 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL) and dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 10:1) to yield ketone **243** (403 mg, 1.01 mmol, 80%) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = δ 5.22 (dd, *J* = 15.2, 7.3 Hz, 1H), 5.16 (dd, *J* = 15.3, 7.9 Hz, 1H), 2.45 – 2.40 (m, 1H), 2.06 – 2.01 (m, 2H), 1.97 – 1.76 (m, 5H), 1.72 – 1.67 (m, 4H), 1.61 – 1.44 (m, 5H), 1.31 – 1.05 (m, 4H), 1.02 (d, *J* = 6.6 Hz, 3H), 1.01 (s, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.73 (s, 3H), 0.71 (t, *J* = 4.9 Hz, 1H).

All spectroscopic data match those reported in literature.[163]

(22*E*)-7*α*-Hydroxy-3*α*,5-cyclo-5*α*-ergosta-22-en-6-one



$C_{28}H_{44}O$ (396.66)
243

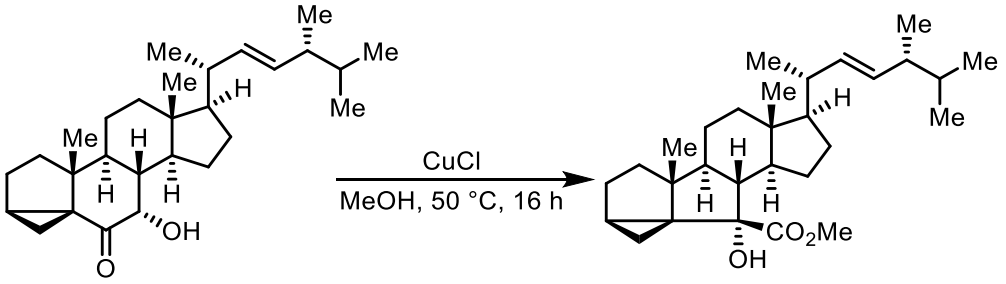
$C_{28}H_{44}O_2$ (412.66)
231

Ketone **243** (220 mg, 0.560 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (3.4 mL) and cooled to 0 °C. Triethylamine (0.28 mL) was added followed by the dropwise addition of trimethyl silyl triflate (205 µL, 1.05 mmol, 1.9 equiv.) over 20 min. The organic phase was washed with sat. aq. $NaHCO_3$ (3 mL) and dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The so-obtained silyl enol ether was dissolved in CH_2Cl_2 (5.6 mL) and cooled to −40 °C. Freshly purified *m*CPBA (106 mg, 0.611 mmol, 1.1 equiv.) in CH_2Cl_2 (6.1 mL) was added dropwise and the resulting mixture was allowed to stir for 2 h at the same temperature. Sat. aq. Na_2SO_3 (8 mL) was added and the mixture was stirred for 15 min at 25 °C. The organic phase was washed sequentially with sat. aq. $NaHCO_3$ (5 mL), aq. HCl (5 mL, 1.0 M), and sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2; *n*hexane/EtOAc 9:1→7:1) to yield α-ketol **231** (117 mg, 0.290 mmol, 51%) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.25 – 5.13 (m, 2H), 3.78 (t, *J* = 3.5 Hz, 1H), 2.05 – 2.01 (m, 4H), 1.90 – 1.61 (m, 8H), 1.62 – 1.56 (m, 3H), 1.53 – 1.42 (m, 2H), 1.34 – 1.19 (m, 3H), 1.11 – 1.06 (m, 2H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.98 (s, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.84 – 0.80 (m, 6H), 0.72 (s, 3H), 0.70 (t, *J* = 5.0 Hz, 1H).

All spectroscopic data match those reported in literature.[163]

(7*β*a)-Methyl (22*E*)-7*α*-hydroxy-3*α*,5-Cyclo-5*α*-5(6→7)*abeo* ergosta-22-en-oate



$C_{28}H_{44}O_2$ (412.66)
231

$C_{29}H_{46}O_3$ (442.68)
233

α-Ketol **231** (139 mg, 0.330 mmol, 1.0 equiv.) was dissolved in MeOH (8.4 mL) and CuCl (660 mg, 6.60 mmol, 20 equiv.) was added to the solution. The resulting suspension was allowed to stir for 17 h at 50 °C. After cooling to ambient temperature, the mixture was filtered over Celite®. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to give B-*nor*-*α*-hydroxy methyl ester **233** as a colorless oil (139 mg, 0.310 mmol, 94%).

R_f : 0.68 (*n*hexane/EtOAc 7:1, CAM [*blue*])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.21 – 5.14 (m, 2H), 3.76 (s, 3H), 2.87 (s, 1H), 2.29 (t, *J* = 11.5 Hz, 1H), 2.07 – 1.99 (m, 1H), 1.97 (dt, *J* = 12.5, 3.0 Hz, 1H), 1.84 (td, *J* = 6.9, 5.8 Hz, 1H), 1.74 – 1.56 (m, 5H), 1.52 – 1.43 (m, 4H), 1.40 – 1.33 (m, 3H), 1.27 – 1.12 (m, 4H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.93 (s, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.68 (s, 3H), 0.54 (t, *J* = 5.4 Hz, 1H), 0.50 (dd, *J* = 8.8, 5.5 Hz, 1H).

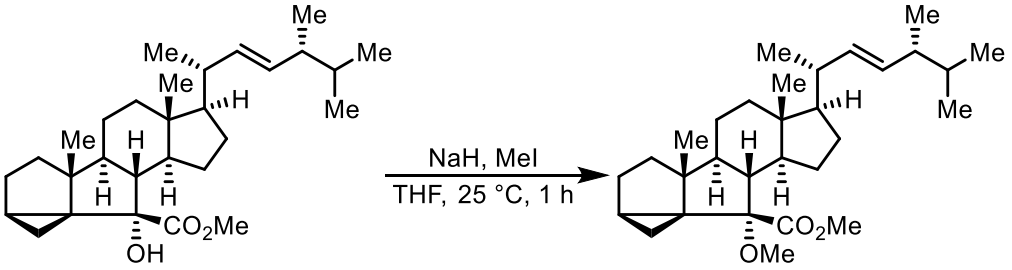
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 178.5, 136.0, 132.0, 80.5, 55.3, 53.0, 52.0, 50.7, 50.4, 50.3, 50.0, 44.7, 43.0, 40.1, 39.1, 34.2, 33.3, 28.9, 25.9, 24.0, 23.6, 21.8, 21.3, 20.1, 19.8, 18.5, 17.8, 12.9, 11.5.

FTIR: (neat) [cm^{-1}] = 3524 (w), 2951 (s), 2929 (m), 2866 (s), 1723 (s), 1455 (m), 1379 (m), 1270 (w), 1247 (s), 1215 (m), 1159 (s), 1107 (m), 1097 (m), 1072 (w), 1015 (w), 971 (m), 754 (w).

HRMS: *m/z* $[M+Na]^+$ calcd. for $C_{29}H_{46}NaO_3^+$: 465.3339; found: 465.3345.

$[\alpha]_D^{20}$: −19.2 (c= 1.00; $CHCl_3$)

(7*β*a)-Methyl (22*E*)-7*α*-methoxy-3*α*,5-cyclo-5*α*-5(6→7)*abeo* ergosta-22-en-oate



$C_{29}H_{46}O_3$ (442.68)
233

$C_{30}H_{48}O_3$ (456.71)
249

α-Hydroxy methyl ester **233** (16 mg, 0.036 mmol, 1.0 equiv.) was dissolved in THF (0.36 mL). NaH (5.8 mg, 0.14 mmol, 4.0 equiv.) was added and the resulting mixture was stirred for 5 min at 25 °C. MeI (16 µL, 0.25 mmol, 7.0 equiv.) was added and the mixture was stirred for 1 h at 25 °C. The mixture was cooled to 0 °C and quenched with sat. aq. NH_4Cl (2 mL) and warmed to ambient temperature. The mixture was then extracted with EtOAc (3 x 2 mL) and the combined organic phases were washed sequentially with H_2O (3 mL) and sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1) to yield *α*-methoxy methyl ester **249** (13 mg, 0.030 mmol, 81%) as a colorless oil.

R_f : 0.76 (*n*hexane/EtOAc 9:1, CAM [*orange*])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.21 – 5.16 (m, 2H), 3.72 (s, 3H), 3.20 (s, 3H), 2.11 (t, J = 11.6 Hz, 1H), 1.95 (dt, J = 12.9, 3.3 Hz, 1H), 1.92 – 1.82 (m, 2H), 1.75 – 1.63 (m, 4H), 1.57 – 1.37 (m, 7H), 1.19 – 1.03 (m, 3H), 1.01 (d, J = 6.6 Hz, 3H), 0.98 – 0.92 (m, 2H), 0.91 (d, J = 6.9 Hz, 3H), 0.89 (s, 3H), 0.83 (d, J = 6.8 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H), 0.74 (dd, J = 8.6, 5.9 Hz, 1H), 0.67 (d, J = 5.4 Hz, 1H), 0.65 (s, 3H).

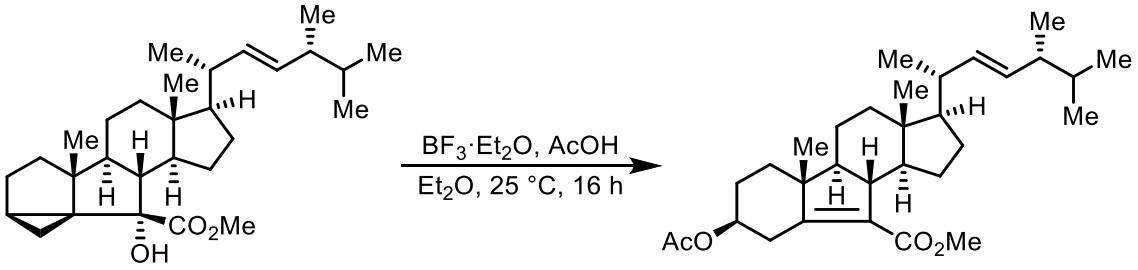
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 175.1, 135.9, 131.7, 87.8, 55.2, 55.1, 52.7, 51.8, 51.6, 51.4, 50.1, 49.6, 45.0, 42.8, 39.9, 39.0, 33.2, 33.1, 28.7, 25.7, 23.9, 23.8, 21.9, 21.1, 20.0, 19.6, 18.2, 17.6, 13.3, 12.6.

FTIR: (neat) [cm^{-1}] = 2951 (s), 2924 (s), 2866 (s), 2359 (w), 1740 (s), 1456 (m), 1379 (m), 1246 (m), 1215 (w), 1199 (w), 1152 (w), 1104 (m), 1053 (w), 970 (w), 793 (w).

HRMS: *m/z* $[M+Na]^+$ calcd. for $C_{30}H_{48}NaO_3^+$: 479.3496; found: 479.3497.

$[\alpha]_D^{20}$: −18.9 (c= 1.00; $CHCl_3$

(7a)-Methyl (22*E*)-3*β*-acetoxy-5(6→7)*abeo* ergosta-5,22-dien-oate



$C_{29}H_{46}O_3$ (442.68)
233

$C_{31}H_{48}O_4$ (484.72)
250

To α-hydroxy methyl ester **233** (94 mg, 0.21 mmol, 1.0 equiv.) in Et_2O (5.3 mL) were added acetic acid (2.6 mL, 21 mmol, 100 equiv.) and $BF_3{\cdot}Et_2O$ (2.6 mL, 17 mmol, 80.0 equiv.) and the resulting mixture was allowed to stir at 25 °C for 16 h. EtOAc (10 mL) was added and the solution was carefully added to sat. aq. $NaHCO_3$ (15 mL). The aq. phase was extracted with EtOAc (3 x 5 mL), the combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to give acrylic ester **250** (80 mg, 0.17 mmol, 79%) as a colorless oil.

R_f : 0.32 (*n*hexane/EtOAc 9:1, CAM [*blue*, UV])

^{1}H NMR: ($CDCl_3$, 700 MHz): δ [ppm] = 5.23 – 5.14 (m, 2H), 4.72 (tt, *J* = 11.5, 4.6 Hz, 1H), 3.68 (s, 3H), 3.26 (ddd, *J* = 13.9, 4.9, 2.1 Hz, 1H), 2.63 (td, *J* = 10.7, 4.4 Hz, 1H), 2.04 (s, 3H), 2.02 – 1.97 (m, 3H), 1.87 – 1.80 (m, 2H), 1.68 – 1.60 (m, 2H), 1.50 – 1.42 (m, 4H), 1.41 – 1.31 (m, 2H), 1.29 – 1.24 (m, 3H), 1.16 – 1.13 (m 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.92 (s, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.73 (s, 3H).

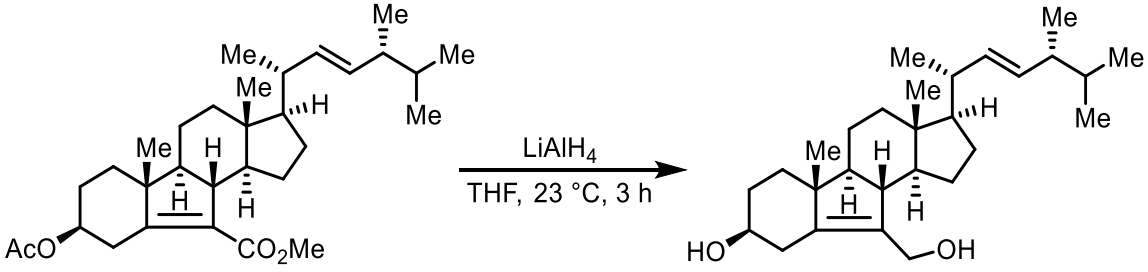
^{13}C NMR: ($CDCl_3$, 176 MHz): δ [ppm] = 170.4, 168.2, 156.4, 135.9, 132.0, 131.4, 72.9, 60.4, 55.3, 54.6, 51.0, 47.7, 45.9, 45.2, 43.0, 40.0, 39.9, 36.3, 33.3, 30.6, 28.9, 27.7, 25.3, 21.5, 21.4, 20.9, 20.1, 19.8, 17.7, 15.4, 12.9.

FTIR: (neat) [cm^{-1}] = 2953 (m), 2869 (w), 2360 (m) 1735 (m), 1716 (s), 1456 (m), 1370 (m), 1235 (s), 1035 (m), 971 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{31}H_{48}NaO_4^+$: 507.3445; found: 507.3451.

$[\alpha]_D^{23}$: −68.9 (c= 1.00; $CHCl_3$)

(22*E*)-3β,7a-dihydroxy-5(6→7)*abeo* ergosta-5,22-dien



$C_{31}H_{48}O_4$ (484.72)
250

$C_{28}H_{46}O_2$ (414.67)
251

B-*nor*-acrylic ester **250** (58 mg, 0.12 mmol, 1.0 equiv.) in THF (0.6 mL) was added dropwise to a suspension of lithium aluminum hydride (22 mg, 0.59 mmol, 4.0 equiv.) in THF (0.6 mL) at 25 °C. The resulting mixture was stirred at the same temperature for 3 h. A sat. aq. K/Na tartrate solution (2 mL) was added and the mixture was stirred for 15 min. The phases were separated and the aq. phase was extracted with EtOAc (2 x 3 mL). The combined organic extracts were washed with sat. aq. NaCl (4 mL) and dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 1:1→1:3) to give the corresponding B-*nor*-allylic alcohol **251** (25 mg, 0.060 mmol, 50%) as a colorless solid.

R_f: 0.26 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.24–5.14 (m, 2 H), 4.14 (d, J = 11.6 Hz,1 H), 4.06 (d, J = 11.6 Hz, 1 H), 3.53 (tt, J = 11.2, 4.4 Hz, 1 H), 2.80 (ddd, J = 13.7, 4.6, 2.0 Hz, 1 H), 2.37 (td, J = 10.8, 4.0 Hz, 1 H), 2.08–1.98 (m, 2 H), 1.93–1.82 (m, 4 H), 1.78 (dt, J = 13.2, 3.4 Hz, 2 H), 1.75–1.04 (m, 13 H), 1.02 (d, J = 6.6 Hz, 3 H), 0.91 (d, J = 6.8 Hz, 3 H), 0.87 (s, 3 H), 0.83 (d, J = 6.8 Hz, 3 H), 0.82 (d, J = 6.8 Hz, 3 H), 0.71 (s, 3 H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 145.9, 136.9, 136.0, 132.0, 71.7, 61.3, 57.5, 55.2, 54.1, 7.5, 45.3, 44.8, 43.0, 40.0, 39.9, 37.2, 33.5, 33.3, 32.0, 29.1, 24.9, 21.4, 21.0, 20.1, 19.8, 17.7, 15.3, 12.9.

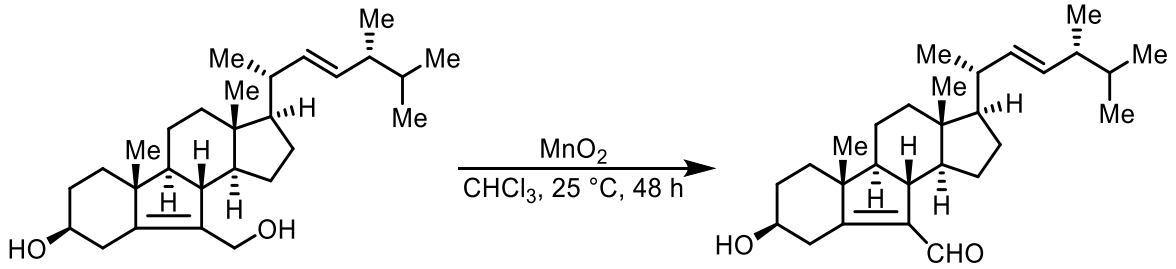
FTIR: (neat) [cm^{-1}] = 3275 (b), 2954 (m), 2926 (w), 2866 (w), 2360 (s), 2338 (s), 1457 (w), 1368 (m), 1273 (w), 1016 (w), 975 (m), 751 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{44}NaO_2^+$: 437.3390; found: 437.3398.

$[\alpha]_D^{23}$: −102.7 (c= 1.00; $CHCl_3$)

MP 183.5–184.5 °C ($CHCl_3$)

(22*E*)-3*β*-hydroxy-5(6→7)*abeo* ergosta-5,22-dien-7a-al



$C_{28}H_{46}O_2$ (414.67)
251

$C_{28}H_{44}O_2$ (412.66)
234

To allylic alcohol **251** thus obtained (25 mg, 0.060 mmol, 1.0 equiv.) was dissolved in $CHCl_3$ (1 mL) and MnO_2 (50 mg, 0.60 mmol, 10.0 equiv.) was added. The resulting dark suspension was allowed to stir for 48 h at 25 °C. The suspension was diluted with CH_2Cl_2 (2 mL) and filtered over a plug of Celite®. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 1:1) to give aldehyde **234** (20 mg, 0.050 mmol, 80%) as a colorless solid.

R_f: 0.51 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 9.96 (s, 1H), 5.26 – 5.12 (m, 2H), 3.70 (tt, *J* = 11.2, 4.5 Hz, 1H), 3.47 (ddd, *J* = 14.3, 4.6, 2.0 Hz, 1H), 2.56 (td, *J* = 10.8, 4.0 Hz, 1H), 2.14 – 1.99 (m, 3H), 1.97 – 1.10 (m, 17H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.94 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.82 (t, *J* = 6.6 Hz, 6H), 0.74 (s, 3H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 189.8, 169.0, 139.4, 135.8, 132.0, 71.0, 60.3, 55.4, 54.7, 46.4, 45.3, 43.0, 40.0, 36.3, 34.0, 33.3, 33.2, 31.4, 28.8, 26.7, 26.7, 21.4, 20.8, 20.1, 19.8, 17.7, 15.8, 12.9.

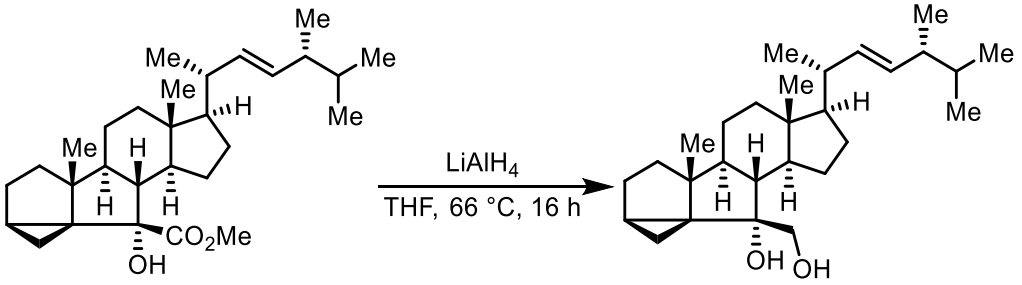
FTIR: (neat) [cm^{-1}] = 3321 (b), 2955 (s), 2928 (s), 2867 (s), 2359 (w), 1675 (s), 1596 (m), 1370 (w), 1239 (w), 1071 (m), 970 (m), 817 (w).

HRMS: *m/z* $[M+Na]^+$ calcd. for $C_{28}H_{42}NaO_2^+$: 437.3390; found: 437.3398.

$[\alpha]_D^{23}$: −58.4 (c= 0.47; $CHCl_3$)

MP 124–124.5 °C ($CHCl_3$)

(22*E*)-3*α*,5-Cyclo-5*α*-5(6→7)*abeo* ergosta-22-en-7*α*,7a-diol



$C_{29}H_{46}O_3$ (442.68)
233

$C_{28}H_{46}O_2$ (414.67)
259

To α-hydroxy methyl ester **233** (50 mg, 0.11 mmol, 1.0 equiv.) in THF (4 mL) at 0 °C was added lithium aluminum hydride (17 mg, 0.45 mmol, 4.0 equiv.). The resulting suspension was heated to 66 °C for 16 h. After cooling to ambient temperature, the reaction was quenched by addition of an sat. aq. K/Na tartrate solution (2.5 mL) and the mixture was stirred vigorously for 15 min. The phases were separated, and the aq. phase was extracted with EtOAc (2 x 5 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield diol **259** (42 mg, 0.10 mmol, 92%) as a colorless solid that was used in the next step without further purification.

R_f : 0.15 (*n*hexane/EtOAc 9:1, [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.24 – 5.15 (m, 2H), 3.41 (s, 2H), 2.09 – 2.03 (m, 1H), 2.00 (dt, *J* = 12.8, 3.1 Hz, 1H), 1.88 – 1.80 (m, 2H), 1.77 – 1.63 (m, 6H), 1.51 – 1.37 (m, 4H), 1.34 – 1.08 (m, 7H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.85 – 0.81 (m, 9H), 0.72 – 0.71 (m, 3H), 0.47 (t, *J* = 5.0 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 136.0, 132.0, 78.4, 69.3, 55.4, 51.8, 51.3, 50.1, 49.1, 47.4, 44.9, 43.0, 40.1, 39.5, 33.5, 33.3, 29.0, 25.8, 24.9, 21.8 (2C), 21.3, 20.1, 19.8, 18.5, 17.8, 13.1, 9.4.

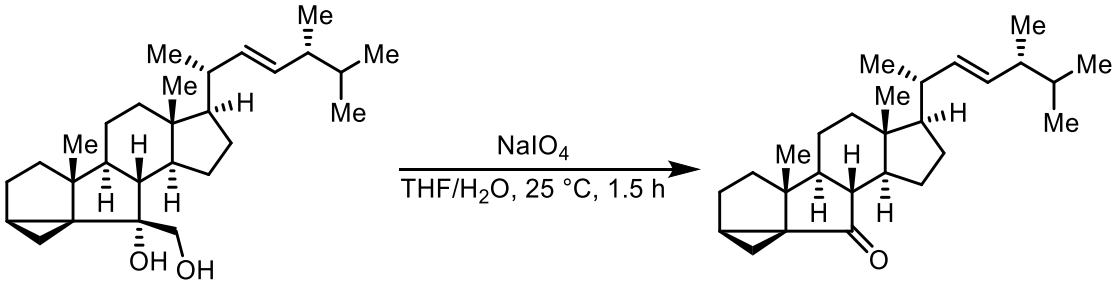
FTIR: (neat) [cm^{-1}] = 3394 (b), 2954 (s), 2866 (s), 2360 (s), 2342 (m), 1456 (m), 1371 (m), 1275 (m), 1262 (m), 1159 (w), 970 (m), 749 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{46}NaO_2^+$: 437.3390; found: 437.3398.

$[\alpha]_D^{20}$: −5.7 (c= 1.00; $CHCl_3$)

MP 88–90 °C ($CHCl_3$)

3*α*,5-Cyclo-5*α*-6-nor-ergosta-7-one



$C_{28}H_{46}O_2$ (414.67)
259

$C_{27}H_{42}O$ (382.63)
261

To diol **259** (40.1 mg, 0.101 mmol, 1.0 equiv.) in a mixture of THF (0.75 mL) and H_2O (0.25 mL) was added $NaIO_4$ (248 mg, 1.16 mmol, 5.0 equiv.). The resulting suspension was stirred at 25 °C for 1.5 h. H_2O (4 mL) was added and the resulting mixture was extracted with EtOAc (3 x 3 mL). The combined organic phases were washed with sat. aq. NaCl (3 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield B-*nor*-*i*-steroid ketone **261** (83.0 mg, 0.210 mmol, 90%) as a colorless solid.

R_f: 0.65 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.24 – 5.14 (m, 2H), 2.18 (dd, *J* = 12.6, 10.3 Hz, 1H), 2.09 – 2.00 (m, 3H), 1.96 – 1.81 (m, 3H), 1.78 – 1.69 (m, 2H), 1.65 – 1.53 (m, 3H), 1.51 – 1.41 (m, 2H), 1.40 – 1.24 (m, 4H), 1.23 – 1.11 (m, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.00 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 5.4 Hz, 1H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.69 (s, 3H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 217.0, 135.8, 132.1, 55.0, 51.8, 51.8, 50.7, 50.2, 48.1, 44.9, 43.0, 40.1, 39.4, 36.5, 35.0, 33.3, 29.2, 25.9, 23.9, 21.7, 21.4, 20.1, 19.8, 17.8, 17.7, 15.2, 12.6.

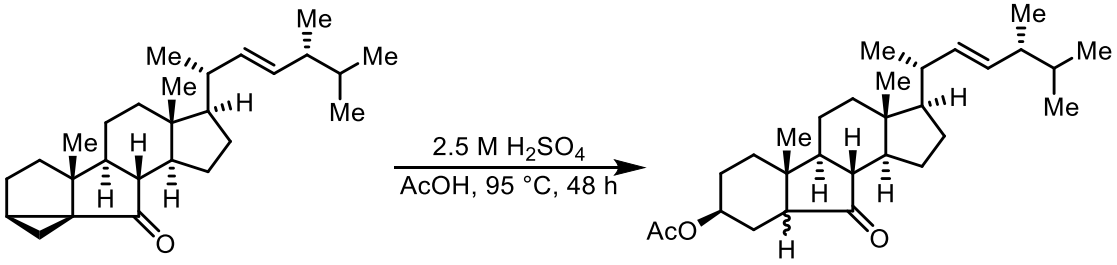
FTIR: (neat) [cm^{-1}] = 2961 (s), 2940 (s), 2361 (s), 2338 (s), 1780 (s), 1463 (m), 1366 (m), 988 (w), 755 (w).

HRMS: *m/z* $[M+Na]^+$ calcd. for $C_{27}H_{42}NaO^+$: 405.3128; found: 405.3148.

$[\alpha]_D^{23}$: −28.9 (c= 1.00; $CHCl_3$)

MP 133–134.5 °C (EtOAc)

6-*nor*-3*β*-Acetoxy-ergosta-7-one



$C_{27}H_{42}O$ (382.63)
261

$C_{29}H_{46}O_3$ (442.68)
263

B-*nor*-*i*-Steroid ketone **261** (24 mg, 0.060 mmol, 1.0 equiv.) was dissolved in acetic acid (glacial, 4.2 mL) and aq. H_2SO_4 (2.5 M, 1.1 mL) was added. The resulting solution was stirred at 95 °C for 48 h. After cooling to ambient temperature, the solution was neutralized with NaOH (25%, aq.) and extracted with Et_2O (3 x 5 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1→1:1) to yield 3-acetyl ketone **263** as a colorless solid (16 mg, 0.040 mmol, 60%, mixture of C5-epimers).

R_f: 0.44 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 401 MHz): δ [ppm] = 5.23 – 5.08 (m), 5.01 (t, *J* = 3.9 Hz), 4.35 (tq, *J* = 11.8, 4.4 Hz), 2.65 – 2.58 (m), 2.40 – 2.34 (m), 2.29 (ddt, *J* = 13.3, 4.3, 2.2 Hz), 2.23 – 2.16 (m), 2.16 – 2.04 (m), 2.02 (s), 1.99 (s), 1.98 – 1.20 (m), 1.17 (s), 1.04 – 1.02 (m), 1.03 (s), 1.01 (d, *J* = 6.6 Hz), 0.97 (d, *J* = 6.6 Hz), 0.90 (d, *J* = 6.8 Hz), 0.89 (d, *J* = 6.8 Hz), 0.82 (d, *J* = 6.9 Hz), 0.81 (d, *J* = 6.9 Hz), 0.80 (d, *J* = 6.8 Hz), 0.79 (d, *J* = 6.8 Hz), 0.65 (s), 0.51 (s).

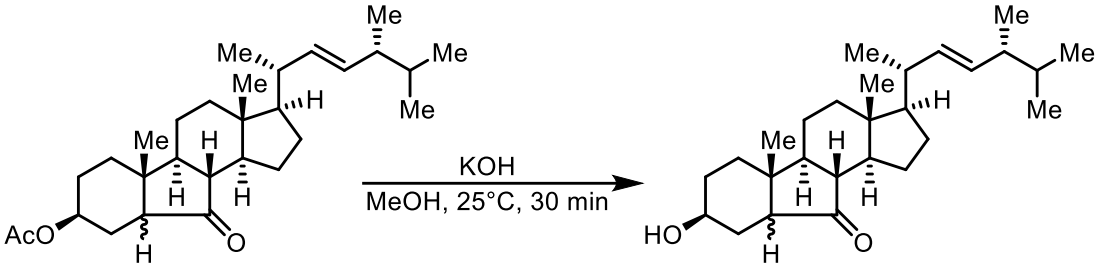
^{13}C NMR: ($CDCl_3$, 101 MHz): δ [ppm] = 207.6, 206.8, 170.2, 135.4, 132.0, 70.7, 68.4, 55.4, 54.8, 53.4, 52.2, 51.2, 50.4, 49.8, 47.6, 44.8, 44.1, 42.8, 42.8, 42.0, 40.2, 40.0, 39.2, 38.6, 38.0, 37.2, 33.1, 33.0, 32.8, 29.0, 27.9, 27.8, 27.1, 26.6, 25.0, 23.6, 23.6, 23.0, 21.8, 21.3, 21.3, 21.2, 21.1, 21.0, 20.7, 20.0, 19.9, 19.6, 17.6, 17.6, 17.6, 12.7, 12.4.

FTIR: (neat) [cm^{-1}] = 2943 (s), 2939 (m), 2830 (s), 2359 (s), 2341 (s), 1450 (m), 1417 (m), 1115 (w), 1022 (s), 839 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{46}NaO_3^+$: 465.3339; found: 465.3359.

MP 110.5–112 °C (EtOAc)

6-*nor*-3*β*-Hydroxy-ergosta-7-one



$C_{29}H_{46}O_3$ (442.68)
263

$C_{27}H_{44}O_2$ (400.65)
265

To acetate **263** (16 mg, 0.040 mmol, 1.0 equiv.) was added potassium hydroxide (1 mL, 5% in MeOH). The solution was allowed to stir at 25 °C for 30 min. Water (1 mL) was added, the solution was neutralized with aq. HCl (1 M) and extracted with EtOAc (3 x 2 mL). The combined organic phases were washed with sat. aq. NaCl (1 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield ketone **265** (16 mg, 0.040 mmol, 100%) as a colorless oil.

R_f: 0.59 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

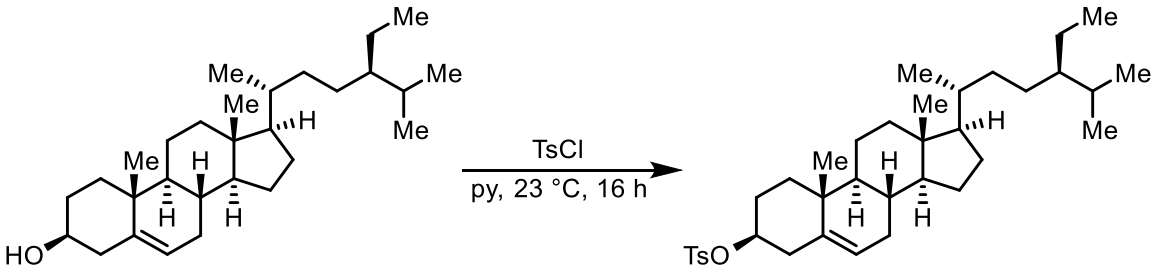
^{1}H NMR: ($CDCl_3$, 401 MHz): δ [ppm] = 5.26 – 5.08 (m), 4.10 – 4.05 (m), 3.39 – 3.28 (m), 2.64 – 2.57 (m), 2.38 – 1.22 (m), 1.17 (s), 1.03 (s), 1.02 (d, *J* = 6.6 Hz), 0.98 (d, *J* = 6.6 Hz), 0.91 (d, *J* = 6.8 Hz), 0.90 (d, *J* = 6.8 Hz), 0.84 (d, *J* = 1.6 Hz), 0.83 (d, *J* = 1.6 Hz), 0.82 (d, *J* = 1.6 Hz), 0.81 (d, *J* = 1.6 Hz), 0.66 (s), 0.53 (s).

^{13}C NMR: ($CDCl_3$, 101 MHz): δ [ppm] = 197.2, 195.2, 135.6, 132.2, 76.8, 68.3, 65.4, 55.6, 53.9, 52.5, 50.6, 47.8, 44.2, 43.0, 42.1, 40.3, 40.1, 38.8, 38.2, 33.4, 33.2, 30.8, 30.7, 28.0, 23.2, 22.0, 21.2, 20.9, 20.1, 19.8, 17.7, 17.7, 12.9.

FTIR: (neat) [cm^{-1}] = 3313 (b), 2947 (s), 2918 (m), 2359 (s), 2341 (s), 1711 (w), 1540 (m), 1507 (w), 1264 (m), 763 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{46}NaO^+$: 423.6362 found: 423.6354.

Stigmastane tosylate



$C_{29}H_{50}O$ (414.72)
252

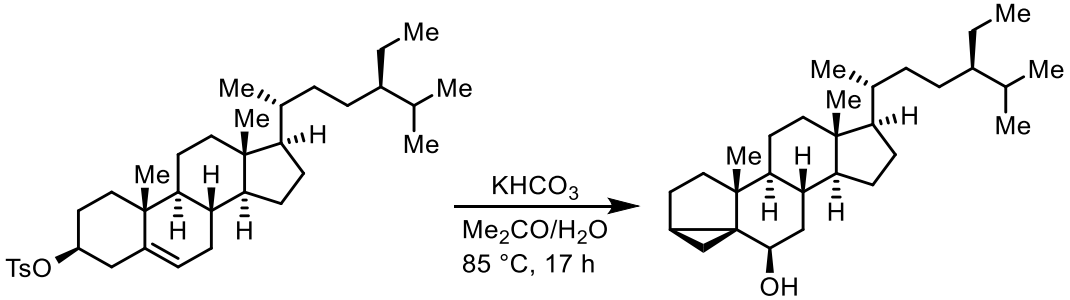
$C_{36}H_{56}O_3S$ (568.90)
253

To β-sitosterole **252** (2.5 g, 6.0 mmol, 1.0 equiv.) in pyridine (60 mL) was added 4-dimethylaminopyridine (72 mg, 0.60 mmol, 0.1 equiv.) and tosyl chloride (3.4 g, 1.8 mmol, 3.0 equiv.). After stirring at 25 °C for 16 h, the mixture was added to ice/water (200 mL) and extracted with Et_2O (3 x 65 mL). The combined organic phases were washed with sat. aq. NaCl (100 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield tosylate **253** (3.1 g, 5.5 mmol, 90%) as a colorless solid that was used in the next step without further purification.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 7.81 – 7.77 (m, 2H), 7.34 – 7.31 (m, 2H), 5.30 (dt, *J* = 5.5, 2.1 Hz, 1H), 4.32 (tt, *J* = 11.5, 4.7 Hz, 1H), 2.44 (s, 4H), 2.27 (ddd, *J* = 13.3, 5.2, 2.1 Hz, 1H), 2.03 – 1.92 (m, 2H), 1.87 – 1.77 (m, 3H), 1.74 – 1.62 (m, 3H), 1.61 – 1.48 (m, 3H), 1.47 – 1.38 (m, 4H), 1.35 – 0.99 (m, 11H), 0.97 (s, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.90 – 0.84 (m, 2H), 0.84 (d, *J* = 1.9 Hz, 3H), 0.83 (d, *J* = 1.3 Hz, 2H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.66 (s, 3H).

The spectroscopic data match those reported in literature.[188]

3*α*,5-Cyclo-5*α*-6*β*-hydroxy-stigmastane



$C_{36}H_{56}O_3S$ (568.90)
253

$C_{29}H_{50}O$ (414.72)
307

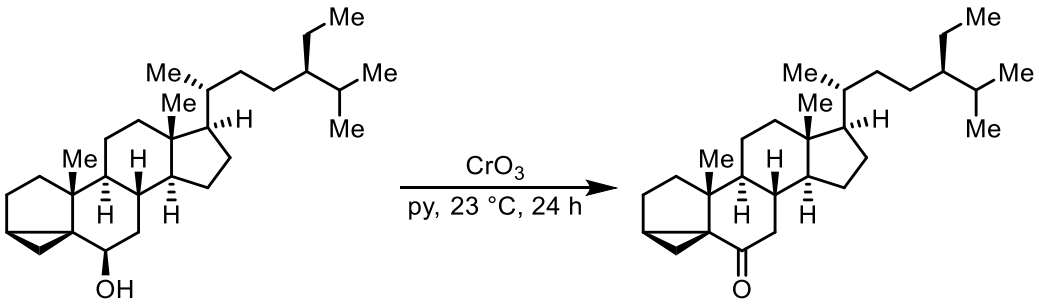
Tosylate **253** (3.0 g, 5.4 mmol, 1.0 equiv.) was suspended in Me_2CO/H_2O (4:1, 68 mL) in a pressure tube and $KHCO_3$ (2.6 g, 27 mmol, 5.0 equiv.) was added. The tube was sealed and

the mixture was stirred at 85 °C for 17 h. After cooling to ambient temperature, water (50 mL) was added and extracted with Et_2O (3 x 25 mL). The combined organic phases were washed with sat. aq. NaCl (30 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield *i*-sterol **307** (2.1 g, 5.0 mmol, 93%) as a colorless solid that was used in the next step without further purification.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.26 (t, *J* = 2.9 Hz, 1H), 2.63 (s, 1H), 2.00 (dt, *J* = 12.7, 3.5 Hz, 1H), 1.87 – 1.79 (m, 3H), 1.72 – 1.64 (m, 1H), 1.62 – 1.49 (m, 9H), 1.43 – 1.08 (m, 11H), 1.06 (s, 3H), 0.92 (d, *J* = 6.6 Hz, 4H), 0.85 (d, *J* = 7.4 Hz, 2H), 0.84 (d, *J* = 6.9 Hz, 4H), 0.81 (d, *J* = 6.9 Hz, 4H), 0.72 (s, 3H), 0.52 (dd, *J* = 4.9, 3.7 Hz, 1H), 0.29 (dd, *J* = 8.1, 4.9 Hz, 1H).

The spectroscopic data match those reported in literature.[188]

3α,5-Cyclo-5α-stigmast-6-one



$C_{29}H_{50}O$ (414.72)
307

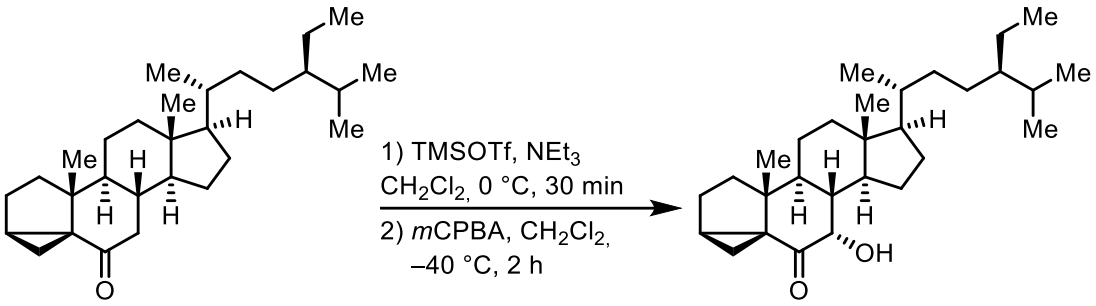
$C_{29}H_{48}O$ (412.70)
254

CrO_3 (1.8 g, 18 mmol, 4.0 equiv.) was added in portions to pyridine (18 mL) cooled by water bath. *i*-sterol **307** (2.1 g, 5.0 mmol, 1.0 equiv.) in pyridine (18 mL) was added to the resulting yellow suspension and the mixture was allowed to stir for 16 h at 23 °C. Et_2O (70 mL) was added and the mixture was filtered over Celite® and rinsed with Et_2O (2 x 25 mL). The filtrate was washed with water (3 x 100 mL), sat. aq. NaCl (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield ketone **254** (1.1 g, 2.7 mmol, 55% over 3 steps).

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 2.47 – 2.41 (m, 1H), 2.06 (dt, *J* = 12.8, 3.4 Hz, 1H), 1.95 – 1.84 (m, 4H), 1.80 (dd, *J* = 13.7, 8.0 Hz, 1H), 1.72 – 1.66 (m, 4H), 1.61 – 1.46 (m, 6H), 1.42 – 1.02 (m, 13H), 1.01 (s, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 7.5 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H), 0.72 (s, 3H).

The spectroscopic data match those reported in literature.[189]

3*α*,5-Cyclo-5*α*-7*α*-hydroxy-stigmast-6-one



$C_{29}H_{48}O$ (412.70)
254

$C_{29}H_{48}O_2$ (428.70)
255

Ketone **254** (480 mg, 1.16 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (12 mL) and cooled to 0 °C. triethylamine (0.660 mL, 4.65 mmol, 4.0 equiv.) was added followed by the dropwise addition of trimethyl silyl triflate (0.640 mL, 3.48 mmol, 3.0 equiv.) over 20 min. The organic phase was washed with sat. aq. $NaHCO_3$ (3 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The so-obtained silyl enol ether was dissolved in CH_2Cl_2 (5.6 mL) and cooled to −40 °C. Freshly purified *m*CPBA (219 mg, 1.27 mmol, 1.1 equiv.) in CH_2Cl_2 (12 mL) was added dropwise and the resulting mixture was allowed to stir for 2 h at the same temperature. Sat. aq. Na_2SO_3 (15 mL) was added and the mixture was stirred for 15 min at 25 °C. The organic phase was washed sequentially with sat. aq. $NaHCO_3$ (10 mL), aq. 1 M HCl (10 mL), and sat. aq. NaCl (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1→7:1) to yield α-ketol **255** (278 mg, 0.650 mmol, 56%) as a colorless solid.

R_f: 0.30 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.78 (s, 1H), 2.24 (s, 1H), 2.10 – 1.98 (m, 2H), 1.96 – 1.83 (m, 1H), 1.82 – 1.75 (m, 2H), 1.75 – 1.62 (m, 3H), 1.62 – 1.54 (m, 1H), 1.52 – 1.08 (m, 18H), 0.98 (s, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.86 – 0.83 (m, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.70 (s, 3H), 0.69 (m, 1H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 210.6, 73.2, 55.9, 49.5, 47.4, 46.0, 44.3, 39.5, 39.2, 37.7, 37.7, 36.3, 34.0, 33.8, 29.3, 28.4, 26.3, 26.1, 23.6, 23.2, 22.9, 20.0, 19.4, 19.2, 18.9, 12.1, 11.9, 10.8

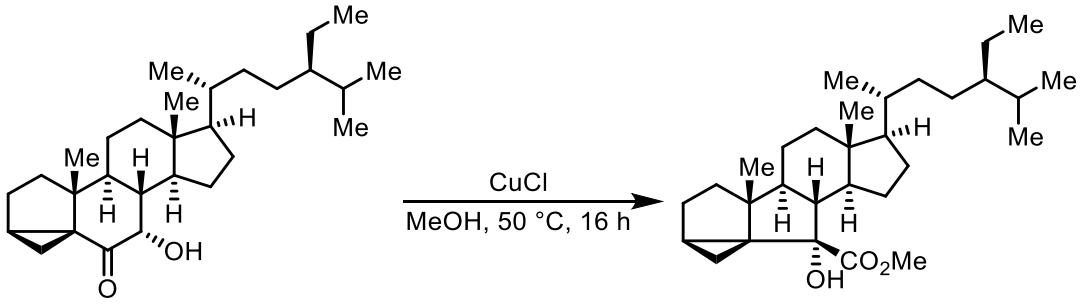
FTIR: (neat) [cm^{-1}] = 3398 (b), 2957 (m), 2869 (w), 2360 (s), 2341 (s), 1675 (w), 1376 (w), 1302 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{48}NaO_2^+$: 451.3547; found: 451.3556.

$[\alpha]_D^{24}$: +23.7 (c= 1.00; $CHCl_3$)

MP 152-154 °C ($CHCl_3$)

(7*β*a)-Methyl 7*α*-hydroxy-3*α*,5-Cyclo-5*α*-5(6→7)*abeo* stigmastaneoate



$C_{29}H_{48}O_2$ (428.70)
255

$C_{30}H_{50}O_3$ (458.73)
256

α-Ketol **255** (202 mg, 0.470 mmol, 1.0 equiv.) was dissolved in MeOH (12.0 mL) and CuCl (940 mg, 9.40 mmol, 20 equiv.) was added to the solution. The resulting suspension was allowed to stir for 17 h at 50 °C. After cooling to ambient temperature, the mixture was filtered over Celite®. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to give B-*nor*-*α*-hydroxy methyl ester **256** as a colorless oil (190 mg, 0.410 mmol, 88%).

R_f: 0.57 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.77 (s, 3H), 2.88 (s, 1H), 2.28 (t, *J* = 11.4 Hz, 1H), 2.01 (dt, *J* = 12.6, 3.0 Hz, 1H), 1.87 (dddd, J = 15.3, 13.3, 9.1, 5.7 Hz, 2H), 1.72 (dd, *J* = 14.0, 9.4 Hz, 1H), 1.69 – 1.61 (m, 3H), 1.56 (s, 1H), 1.52 – 1.44 (m, 3H), 1.39 – 1.30 (m, 3H), 1.30 – 1.20 (m, 3H), 1.19 – 1.10 (m, 3H), 1.07 – 0.95 (m, 2H), 0.94 – 0.92 (m, 8H), 0.84 – 0.80 (m, 6H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.67 (s, 3H), 0.54 (t, *J* = 5.4 Hz, 1H), 0.50 (dd, *J* = 8.8, 5.5 Hz, 1H).

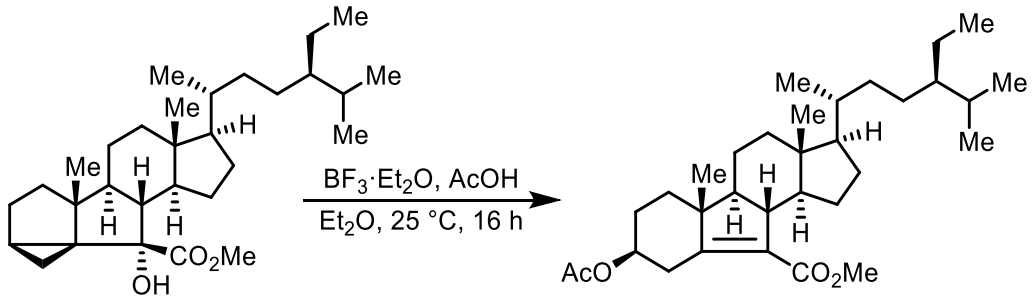
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 178.6, 80.5, 55.2, 53.0, 52.0, 50.7, 50.4, 50.2, 50.0, 46.0, 44.7, 39.2, 36.2, 34.2, 34.2, 29.3, 28.8, 26.2, 25.9, 24.0, 23.6, 23.2, 21.9, 19.9, 19.2, 19.0, 18.5, 12.6, 12.1, 11.5.

FTIR: (neat) [cm^{-1}] = 2950 (s), 2934 (s), 2865 (s), 1724 (s), 1462 (m), 1378 (m), 1271 (w), 1247 (s), 1215 (w), 1159 (m), 1108 (w), 1049 (w), 954 (m), 754 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{50}NaO_3^+$: 481.3652; found: 481.3659.

$[\alpha]_D^{24}$: +13.1 (c= 1.00; $CHCl_3$)

3*α*,5-Cyclo-5*α*-5(6→7)*abeo* stigmastane-7*α*,7a-diol



$C_{30}H_{50}O_3$ (458.73) **256**

$C_{32}H_{52}O_4$ (500.76) **257**

To α-hydroxy methyl ester **256** (78 mg, 0.17 mmol, 1.0 equiv.) in Et_2O (4.3 mL) were added acetic acid (2.1 mL, 17 mmol, 100 equiv.) and $BF_3{\cdot}Et_2O$ (2.1 mL, 13.6 mmol, 80.0 equiv.) and the resulting mixture was allowed to stir at 25 °C for 16 h. EtOAc (10 mL) was added and the solution was carefully added to sat. aq. $NaHCO_3$ (15 mL). The aq. phase was extracted with EtOAc (3 x 5 mL), the combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to give acrylic ester **257** (58 mg, 0.12 mmol, 70%) as a colorless oil.

R_f: 0.40 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.71 (tt, *J* = 11.5, 4.5 Hz, 1 H), 3.68 (s, 3 H), 3.25 (ddd, *J* = 13.9, 4.9, 2.0 Hz, 1 H), 2.63 (td, *J* = 10.7, 4.3 Hz, 1 H), 2.03 (s, 3 H), 1.97 (dd, *J* = 32.6, 12.2 Hz, 1 H), 1.81 (d, *J* = 13.4 Hz, 2 H), 1.70–1.58 (m, 1 H), 1.56–1.05 (m, 20 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 0.91 (s, 3 H), 0.85 (s, 1 H), 0.82 (d, *J* = 7.5 Hz, 3 H), 0.81 (s, 3 H), 0.80 (d, *J* = 6.8 Hz, 3 H), 0.72 (s, 3 H).

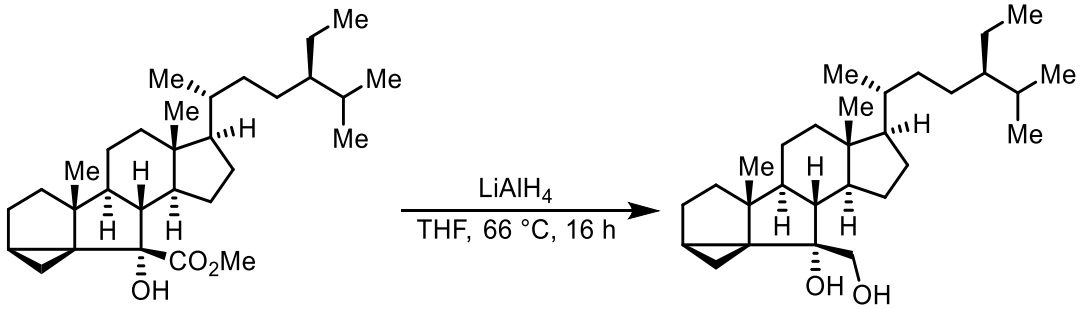
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 170.4, 168.2, 156.3, 131.4, 72.9, 60.3, 55.3, 54.5, 51.0, 47.7, 46.0, 45.9, 45.3, 40.0, 36.3, 36.1, 34.1, 30.6, 29.3, 28.8, 27.7, 26.3, 25.3, 23.2, 21.5, 20.9, 20.0, 19.2, 19.1, 15.3, 12.6, 12.1.

FTIR: (neat) [cm^{-1}] = 3 2955 (m), 2870 (w), 2360 (w), 2341 (w), 1730 (m), 1717 (s), 1456 (w), 1434 (w), 1376 (w), 1362 (w), 1238 (s), 1139 (w), 1078 (w), 1035 (m), 754 (s) cm^{-1}.

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{52}NaO_4^+$: 523.3758; found: 523.3764.

$[\alpha]_D^{20}$: −40.0 (c= 1.00; $CHCl_3$)

3*α*,5-Cyclo-5*α*-5(6→7)*abeo* stigmastane-7*α*,7a-diol



$C_{30}H_{50}O_3$ (458.73)
256

$C_{29}H_{50}O_2$ (430.72)
258

To α-hydroxy methyl ester **256** (190 mg, 0.410 mmol, 1.0 equiv.) in THF (4 mL) at 0 °C was added $LiAlH_4$ (63.0 mg, 1.65 mmol, 4.0 equiv.). The resulting suspension was heated to 66 °C for 16 h. After cooling to ambient temperature, the reaction was quenched by addition of an sat. aq. K/Na tartrate solution (6 mL) and the mixture was stirred vigorously for 15 min. The phases were separated, and the aq. phase was extracted with EtOAc (2 x 5 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield the corresponding diol **258** (164 mg, 0.380 mmol, 92%) as a colorless solid that was used in the next step without further purification.

R_f: 0.24 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.42 (d, *J* = 5.0 Hz, 2H), 2.03 (dt, *J* = 12.8, 3.0 Hz, 1H), 1.93 – 1.62 (m, 6H), 1.50 – 0.96 (m, 19H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 1H), 0.84 (d, *J* = 1.6 Hz, 3H), 0.83 – 0.82 (m, 6H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.70 (s, 3H), 0.47 (t, *J* = 5.0 Hz, 1H).

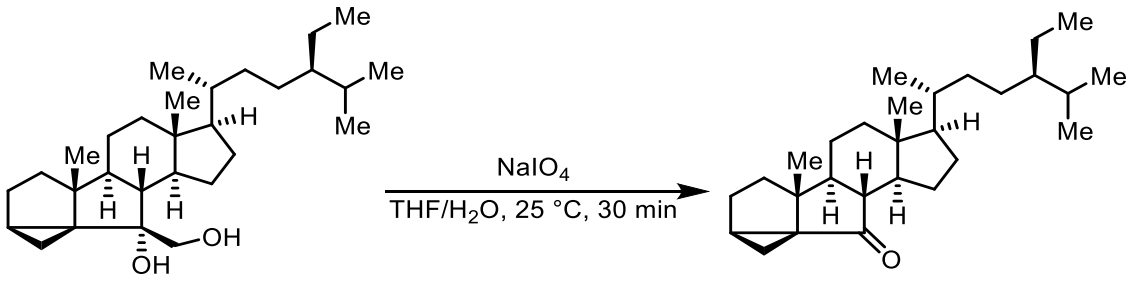
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 78.3, 69.3, 55.3, 51.7, 51.2, 50.0, 49.1, 47.4, 45.9, 45.0, 39.6, 36.1, 34.1, 33.5, 29.2, 28.8, 26.1, 25.7, 24.8, 23.1, 21.8, 21.7, 19.9, 19.1, 19.0, 18.4, 12.7, 12.1, 9.3.

FTIR: (neat) [cm^{-1}] = 3379 (b), 2965 (s), 2958 (s), 2864 (s), 2360 (m), 2341 (m), 1463 (m), 1376 (m), 1309 (w), 1266 (w), 1047 (w), 1020 (m), 747 (m) cm^{-1}.

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{50}NaO_2^+$: 453.3703; found: 453.3717.

$[\alpha]_D^{20}$: +28.9 (c= 1.00; $CHCl_3$)

3*α*,5-Cyclo-5*α*-6-nor-stigmast-7-one



$C_{29}H_{50}O_2$ (430.72)
258

$C_{28}H_{46}O$ (398.68)
260

To diol **258** (100 mg, 0.230 mmol, 1.0 equiv.) in a mixture of THF (2 mL) and H_2O (0.5 mL) was added sodium periodate (248 mg, 1.16 mmol, 5.0 equiv.). The resulting suspension was stirred at 25 °C for 30 min. H_2O (4 mL) was added and the resulting mixture was extracted with EtOAc (3x 3 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield B-*nor*-*i*-steroid ketone **260** (83.0 mg, 0.210 mmol, 90%) as a colorless solid.

R_f: 0.59 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 2.17 (dd, *J* = 12.4, 10.4 Hz, 1H), 2.11 – 2.03 (m, 2H), 1.96 – 1.79 (m, 2H), 1.74 (dd, *J* = 12.9, 8.8 Hz, 2H), 1.69 – 1.51 (m, 4H), 1.47 (dd, *J* = 12.7, 3.6 Hz, 1H), 1.43 – 1.08 (m, 15H), 0.99 (s, 3H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.89 (t, *J* = 5.3 Hz, 1H), 0.84 (d, *J* = 7.6 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H), 0.68 (s, 3H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 217.1, 55.1, 51.8, 51.7, 50.6, 50.2, 48.1, 46.0, 44.9, 39.6, 36.5, 36.3, 35.0, 34.2, 29.3, 29.0, 26.3, 25.9, 23.9, 23.2, 21.7, 19.9, 19.2, 19.1, 17.7, 15.1, 12.3, 12.1.

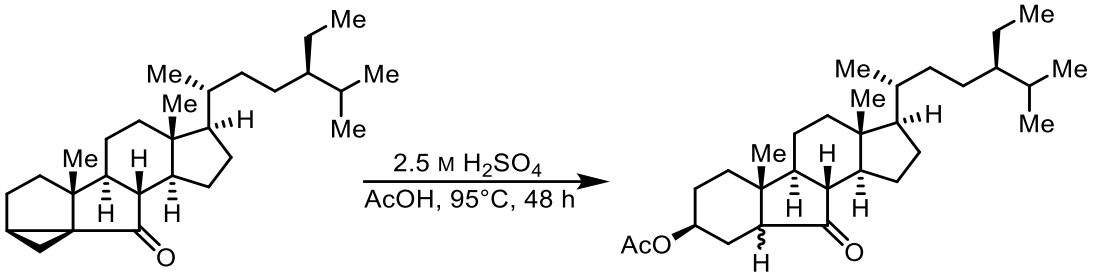
FTIR: (neat) [cm^{-1}] = 2953 (s), 2934 (s), 2867 (s), 2360 (s), 2341 (s), 1721 (s), 1540 (w), 1456 (m), 1383 (m), 1366 (m), 1290 (m), 1260 (m), 749 (s) cm^{-1}.

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{46}NaO^+$: 421.3441; found: 421.3454.

$[\alpha]_D^{20}$: +8.8 (c= 1.00; $CHCl_3$)

MP 75-76 °C ($CHCl_3$)

6-*nor*-3*β*-acetoxy-stigmast-7-one



$C_{28}H_{46}O$ (398.68)
260

$C_{30}H_{50}O_3$ (458.73)
262

B-*nor*-*i*-Steroid ketone **260** (82 mg, 0.20 mmol, 1.0 equiv.) was dissolved in acetic acid (glacial, 17 mL) and aq. H_2SO_4 (2.5 M, 4.2 mL) was added. The resulting solution was stirred at 95 °C for 48 h. After cooling to ambient temperature, the solution was neutralized with NaOH (25%, aq.) and extracted with Et_2O (3 x 5 mL). The combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1→1:1) to yield B-*nor*-3-acetyl ketone **262** as a colorless solid (59 mg, 0.13 mmol, 64%, mixture of C5-epimers). **262** was resubmitted to column chromatography (SiO_2, CH_2Cl_2/EtOAc/acetone 300:2:1) to yield an analytically pure sample of the less polar epimer.

mixture of C5 epimers

R_f: 0.40 (9:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.04 – 5.00 (m), 4.37 (tt, *J* = 11.5, 4.4 Hz), 2.63 (t, *J* = 6.7 Hz), 2.38 (dt, *J* = 6.5, 2.1 Hz), 2.34 – 2.19 (m), 2.04 (s), 2.01 (s), 1.96 – 1.79 (m), 1.83 (s), 1.78 – 1.68 (m), 1.71 – 1.31 (m), 1.33 (s), 1.34 – 1.18 (m), 1.18 (s), 1.17 – 1.05 (m), 1.04 (s), 0.93 (d, *J* = 6.5 Hz), 0.89 (d, *J* = 6.5 Hz), 0.87 – 0.82 (m), 0.81 (d, *J* = 6.8 Hz), 0.65 (s), 0.52 (s).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 219.9, 170.6, 170.3, 70.9, 68.5, 55.6, 55.0, 53.5, 52.3, 51.4, 50.5, 50.0, 47.8, 47.6, 46.0, 45.9, 45.1, 44.2, 42.2, 39.5, 38.8, 38.2, 37.4, 36.4, 36.2, 34.1, 33.9, 33.0, 29.3, 29.2, 29.0, 28.1, 28.0, 27.7, 27.3, 26.7, 26.3, 26.2, 25.2, 23.8, 23.2, 23.2, 23.1, 22.0, 21.5, 21.4, 21.3, 20.9, 20.0, 19.9, 19.2, 19.2, 19.0, 19.0, 12.6, 12.3, 12.1.

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{50}NaO_3^+$: 481.3652; found: 481.3675.

MP 115.5-116 °C ($CHCl_3$)

major, less polar epimer

R_f: 0.51 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.37 (tt, *J* = 11.4, 4.4 Hz, 1H), 2.62 (t, *J* = 6.7 Hz, 1H), 2.37 (dt, *J* = 6.3, 2.1 Hz, 1H), 2.30 (ddt, *J* = 12.9, 4.6, 2.3 Hz, 1H), 2.25 – 2.17 (m, 1H), 2.03 (t, *J* = 3.6 Hz, 1H), 2.00 (s, 3H), 1.89 – 1.79 (m, 2H), 1.73 (dt, *J* = 13.2, 6.9 Hz, 1H), 1.70 – 1.53 (m, 6H), 1.54 – 1.21 (m, 9H), 1.18 (s, 3H), 1.16 – 0.98 (m, 6H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.85 – 0.82 (m, 6H), 0.80 (d, *J* = 6.8 Hz, 2H), 0.51 (s, 3H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 219.9, 170.3, 70.9, 55.6, 53.5, 50.5, 47.8, 45.9, 44.2, 42.2, 38.9, 38.2, 36.4, 33.9, 33.0, 29.3, 27.7, 27.3, 26.7, 26.2, 23.2, 23.2, 22.0, 21.5, 20.9, 19.9, 19.2, 19.0, 12.6, 12.1

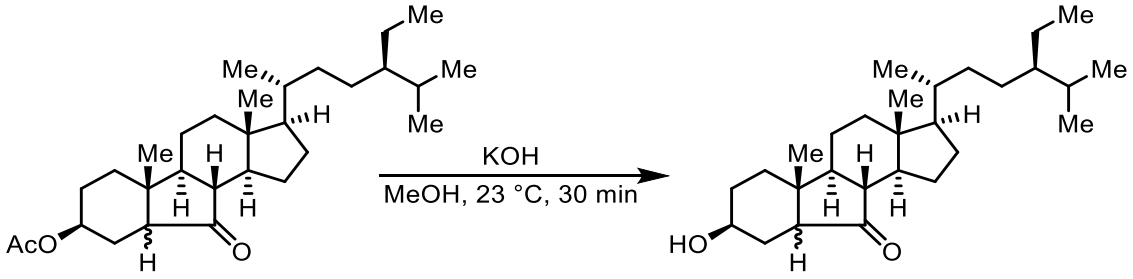
FTIR: 2954 (s), 2931 (s), 2869 (m), 2360 (w), 1733 (s), 1462 (m), 1375 (m), 1240 (s), 1140 (w), 1030 (m), 750 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{50}NaO_3^+$: 481.3652; found: 481.3675.

$[\alpha]_D^{20}$: −24.9 (c= 1.00; $CHCl_3$)

MP 122.5-123 °C ($CHCl_3$)

6-nor-3*β*-hydroxy-stigmast-7-one



$C_{30}H_{50}O_3$ (458.73)
262

$C_{28}H_{48}O_2$ (416.69)
264

To acetate **262** (50 mg, 0.11 mmol, 1.0 equiv.) was added potassium hydroxide (2 mL, 5% in MeOH). The solution was allowed to stir at 25 °C for 30 min. Water (2 mL) was added, the solution was neutralized with aq. HCl (1 M) and extracted with EtOAc (3 x 3 mL). The combined organic phases were washed with sat. aq. NaCl (2 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield ketone **264** (45 mg, 0.11 mmol, quant.) as a colorless oil.

R_f: 0.48 (1:1; *n*hexane/EtOAc [CAM, *blue*; UV])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.04 – 5.00 (m), 4.37 (tt, *J* = 11.5, 4.4 Hz), 2.63 (t, *J* = 6.7 Hz), 2.38 (dt, *J* = 6.5, 2.1 Hz), 2.34 – 2.19 (m), 2.04 (s), 2.01 (s), 1.96 – 1.79 (m), 1.83 (s), 1.78 – 1.68 (m), 1.71 – 1.31 (m), 1.33 (s), 1.34 – 1.18 (m), 1.18 (s), 1.17 – 1.05 (m), 1.04 (s), 0.93 (d, *J* = 6.5 Hz), 0.89 (d, *J* = 6.5 Hz), 0.87 – 0.82 (m), 0.81 (d, *J* = 6.8 Hz), 0.65 (s), 0.52 (s).

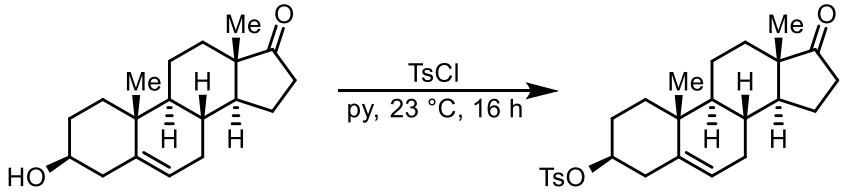
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 221.1, 68.3, 65.3, 55.6, 55.0, 53.9, 52.4, 51.2, 50.5, 50.0, 47.9, 45.9, 45.1, 44.1, 42.2, 38.9, 38.2, 37.4, 36.4, 36.2, 33.9, 33.4, 30.7, 30.7, 29.3, 27.7, 26.1, 23.9, 23.2, 22.0, 21.2, 20.9, 20.0, 19.2, 19.0, 12.6, 12.3, 12.1.

FTIR: (neat) [cm^{-1}] = 3389 (br), 2955 (s), 2932 (s), 2867 (s), 2360 (m), 2342 (m), 1729 (s), 1461 (m), 1379 (m), 1259 (m), 1204 (w), 1059 (m), 909 (m) cm^{-1}.

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{48}NaO_2^+$: 439.3547; found: 439.3550.

MP 115.5-116 °C ($CHCl_3$)

Dehydroepiandrosterone tosylate



$C_{19}H_{28}O_2$ (288.43)
266

$C_{26}H_{34}O_4S$ (442.61)
308

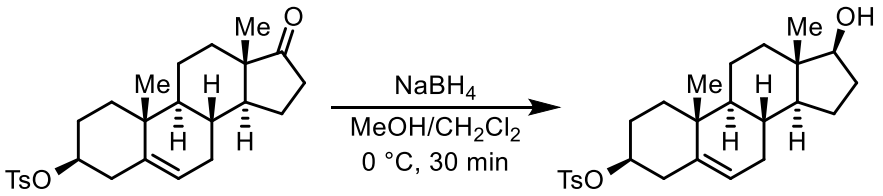
Dehydroepiandrosterone **266** (1.5 g, 5.2 mmol, 1.0 equiv.) was dissolved in pyridine (52 mL). 4-dimethylaminopyridine (0.64 g, 0.52 mmol, 0.1 equiv.) and tosyl chloride (4.9 g, 26 mmol, 5.0 equiv.) were added sequentially and the resulting mixture was allowed to stir at 24 °C for 17 h. The mixture was cooled to 0 °C and water (200 mL) was added. The aq. phase was extracted with EtOAc (3 x 100 mL) and the combined organic extracts were washed with water (2 x 150 mL), sat. aq. NaCl (2 x 100 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure, the residue was dissolved in toluene (3 x 100 mL) and evaporated to dryness to yield tosylate **308** (2.3 g, 5.1 mmol, 98%) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 7.83 – 7.73 (m, 2H), 7.33 (dt, *J* = 7.9, 0.8 Hz, 2H), 5.40 – 5.32 (m, 1H), 4.33 (tt, *J* = 11.5, 4.8 Hz, 1H), 2.48 – 2.46 (m, 1H), 2.45 (s, 3H), 2.33 (ddd, *J* = 13.3, 5.2, 2.2 Hz, 1H), 2.12 – 2.03 (m, 2H), 1.93 (ddd, *J* = 14.3, 8.6, 5.8 Hz, 1H), 1.86 – 1.80 (m, 4H), 1.74 – 1.66 (m, 1H), 1.66 – 1.57 (m, 3H),

1.53 – 1.40 (m, 2H), 1.26 (td, *J* = 12.9, 4.2 Hz, 2H), 1.05 (dd, *J* = 13.4, 3.8 Hz, 1H), 1.00 (s, 3H), 0.98 – 0.92 (m, 1H), 0.87 (s, 3H).

The spectroscopic data match those reported in literature.[190]

17-*β*-Hydroxy-dehydroandrostane tosylate



$C_{26}H_{34}O_4S$ (442.61)
308

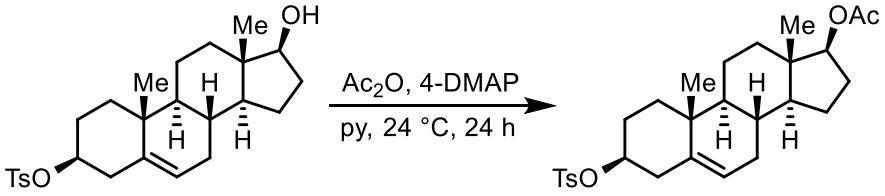
$C_{26}H_{36}O_4S$ (444.63)
309

Tosylate **308** (2.3 g, 5.1 mmol, 1.0 equiv.) was dissolved in MeOH/CH2Cl2 (2:1, 51 mL) and cooled to 0 °C. Sodium borohydride (0.76 g, 20 mmol, 4.0 equiv.) was added in portions. After stirring at the same temperature for 30 min, aq. HCl (1 M, 20 mL) was carefully added and the mixture was allowed to warm to ambient temperature. The mixture was extracted with EtOAc (3 x 10 mL) and the combined organic phases were washed with bNaCl (20 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield alcohol **309** (2.26 g, 5.08 mmol, quant.) as a colorless solid that was used in the next step without further purification.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 7.82 – 7.77 (m, 2H), 7.35 – 7.30 (m, 2H), 5.31 (dt, *J*=5.8, 1.9, 1H), 4.33 (tt, *J*=11.5, 4.7, 1H), 3.63 (t, *J*=8.5, 1H), 2.45 (s, 3H), 2.29 (ddd, *J*=13.2, 5.2, 2.2, 1H), 2.12 – 2.02 (m, 2H), 1.97 (ddd, *J*=12.6, 5.6, 3.0, 1H), 1.87 – 1.78 (m, 3H), 1.77 – 1.66 (m, 1H), 1.61 – 1.39 (m, 3H), 1.31 – 1.23 (m, 3H), 1.12 – 1.01 (m, 2H), 0.98 (s, 3H), 0.98 – 0.80 (m, 3H), 0.74 (s, 3H).

The spectroscopic data match those reported in literature.[191]

17-*β*-Acetoxy-dehydroandrostane tosylate



$C_{26}H_{36}O_4S$ (444.63)
309

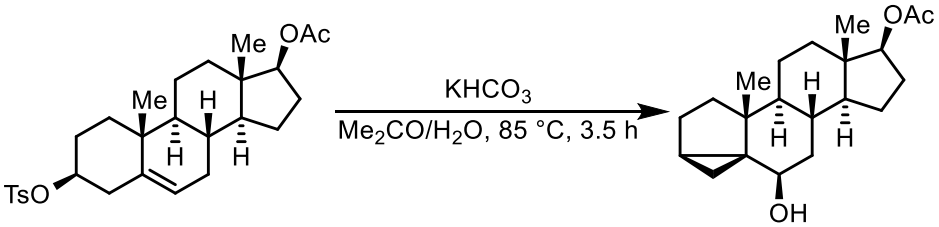
$C_{28}H_{38}O_5S$ (486.67)
272

Alcohol **309** (2.3 g, 5.1 mmol, 1.0 equiv.) was dissolved in pyridine (51 mL) and 4-dimethylaminopyridine (61 mg, 0.51 mmol, 0.10 equiv.) was added. Acetic anhydride (5.4 mL, 25 mmol, 5.0 equiv.) was added dropwise at 24 °C. After stirring at the same temperature for 24 h, water (150 mL) was carefully added and the mixture was extracted with EtOAc (3 x 25 mL) and the combined organic phases were washed with sat. aq. NaCl (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield acetate **272** (2.4 g, 4.9 mmol, 96%) as a colorless solid that was used in the next step without further purification.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 7.81 – 7.76 (m, 2H), 7.36 – 7.30 (m, 2H), 5.30 (dd, *J*=4.9, 2.6, 1H), 4.59 (dd, *J*=9.2, 7.8, 1H), 4.38 – 4.26 (m, 1H), 2.45 (s, 3H), 2.29 (ddd, *J*=13.3, 5.3, 2.1, 1H), 2.20 – 2.11 (m, 1H), 2.03 (s, 3H), 1.97 (ddd, *J*=12.7, 5.4, 2.9, 1H), 1.85 – 1.78 (m, 2H), 1.75 (dt, *J*=12.3, 3.3, 1H), 1.69 – 1.58 (m, 1H), 1.58 – 1.45 (m, 6H), 1.45 – 1.37 (m, 1H), 1.33 – 1.27 (m, 1H), 1.16 (td, *J*=12.9, 4.3, 1H), 1.02 (td, *J*=12.4, 11.2, 3.6, 2H), 0.98 (s, 3H), 0.93 – 0.87 (m, 1H), 0.78 (s, 3H).

The spectroscopic data match those reported in literature.[191]

3*α*,5-Cyclo-5*α*-6*β*-hydroxy-17*β*-acetoxy-androstane



$C_{28}H_{38}O_5S$ (486.67)
272

$C_{21}H_{32}O_3$ (332.48)
310

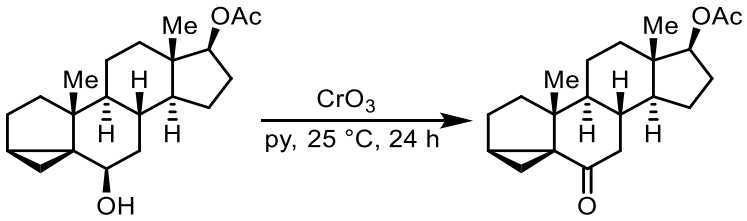
Tosylate **272** (2.37 g, 4.88 mmol, 1.0 equiv.) in a pressure tube was suspended in Me_2CO/H_2O (4:1, 61 mL) and $KHCO_3$ (2.40 g, 24.4 mmol, 5.0 equiv.) was added. The tube was sealed and heated to 85 °C for 3.5 h. After cooling to ambient temperature, water

(50 mL) was added and extracted with Et_2O (3 x 25 mL). The combined organic phases were washed with sat. aq. NaCl (25 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield *i*-sterol **310** (1.60 g, 4.83 mmol, 99%) as a colorless solid that was used in the next step without further purification.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.61 (dd, *J* = 9.2, 7.8 Hz, 1H), 3.27 (t, *J* = 3.0 Hz, 1H), 2.17 (dtd, *J* = 13.7, 9.4, 6.2 Hz, 1H), 2.04 (s, 3H), 1.95 – 1.82 (m, 2H), 1.76 (dt, *J* = 12.5, 3.6 Hz, 2H), 1.69 – 1.33 (m, 8H), 1.26 (t, *J* = 7.1 Hz, 1H), 1.20 – 1.09 (m, 3H), 1.07 (s, 3H), 0.92 – 0.86 (m, 1H), 0.85 (s, 3H), 0.55 – 0.52 (m, 1H), 0.30 (dd, *J* = 8.1, 4.8 Hz, 1H).

The spectroscopic data match those reported in literature.[192]

3*α*,5-Cyclo-5*α*-17*β*-acetoxy-androsta-6-one



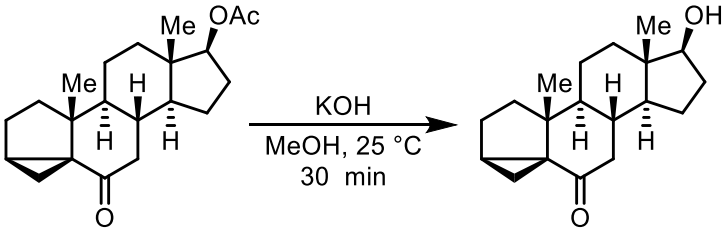
$C_{21}H_{32}O_3$ (332.48) **310** $C_{21}H_{30}O_3$ (330.47) **311**

CrO_3 (1.92 g, 19.2 mmol, 4.0 equiv.) was added in portions to pyridine (19.2 mL) cooled by a water bath. *i*-Sterol **310** (1.60 g, 4.81 mmol, 1.0 equiv.) in pyridine (19.2 mL) was added to the resulting yellow suspension *via* canula and allowed to stir at 25 °C for 24 h. Et_2O (50 mL) was added to the suspension and the resulting mixture was filtered over Celite® and rinsed with Et_2O (2 x 25 mL). The filtrate was washed with water (2 x 75 mL) and sat. aq. NaCl (75 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 7:1) to yield ketone **311** (1.38 g, 2.60 mmol, 54% over 5 steps) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.64 (dd, *J* = 9.2, 7.8 Hz, 1H), 2.44 (dd, *J* = 16.1, 4.0 Hz, 1H), 2.20 (dtd, *J* = 13.8, 9.4, 6.2 Hz, 1H), 2.05 (s, 3H), 2.02 – 1.86 (m, 3H), 1.85 – 1.77 (m, 2H), 1.70 (ddd, *J* = 8.8, 7.1, 5.8 Hz, 2H), 1.67 – 1.61 (m, 2H), 1.58 – 1.52 (m, 3H), 1.52 – 1.41 (m, 1H), 1.39 – 1.18 (m, 4H), 1.02 (s, 3H), 0.84 (d, *J* = 0.6 Hz, 3H), 0.73 (d, *J* = 4.9 Hz, 1H).

The spectroscopic data match those reported in literature.[193]

3α,5-Cyclo-5α-17β-hydroxy-androsta-6-one



$C_{21}H_{30}O_3$ (330.47)
310

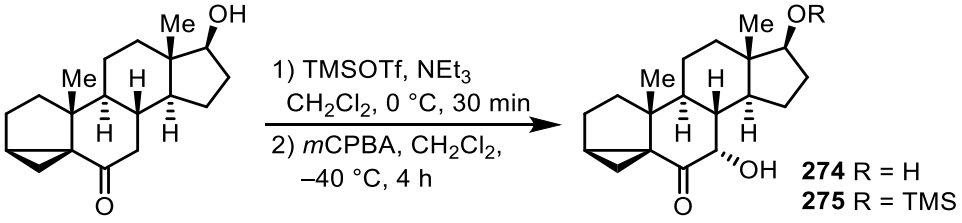
$C_{19}H_{28}O_2$ (288.43)
273

To acetate **310** (1.38 g, 2.60 mmol, 1.0 equiv.) was added potassium hydroxide (50 mL, 5% in MeOH). The solution was allowed to stir at 25 °C for 30 min. Water (100 mL) was added, the solution was neutralized with aq. HCl (1 M) and extracted with EtOAc (3x50 mL). The combined organic phases were washed with sat. aq. NaCl (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield ketone **273** (755 mg, 2.60 mmol, quant.) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.68 (t, *J* = 8.6 Hz, 1H), 2.44 (dd, *J* = 16.3, 4.1 Hz, 1H), 2.10 (dtd, *J* = 13.5, 9.3, 5.9 Hz, 1H), 2.03 – 1.86 (m, 3H), 1.85 – 1.79 (m, 1H), 1.73 – 1.67 (m, 2H), 1.67 – 1.43 (m, 4H), 1.35 – 1.24 (m, 4H), 1.21 – 1.10 (m, 2H), 1.04 (d, *J* = 7.8 Hz, 1H), 1.02 (s, 3H), 0.80 (s, 3H), 0.73 (t, *J* = 4.9 Hz, 1H).

The spectroscopic data match those reported in literature.[192]

3α,5-Cyclo-5α-7α,17β-dihydroxy-androsta-6-one
and
3α,5-Cyclo-5α-7α-hydroxy-17β-(trimethylsilyl)oxy-androsta-6-one



$C_{19}H_{28}O_2$ (288.43)
273

$C_{19}H_{28}O_3$ (304.43)
274

$C_{22}H_{36}O_3Si$ (376.61)
275

Ketone **273** (154 mg, 0.530 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (5.3 mL) and cooled to 0 °C. Triethylamine (0.31 mL, 2.1 mmol, 4.0 equiv.) was added followed by the dropwise addition of trimethyl silyl triflate (0.30 mL, 1.6 mmol, 3.0 equiv.) over 20 min. The organic

phase was washed with sat. aq. $NaHCO_3$ (3 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The so-obtained silyl enol ether was dissolved in CH_2Cl_2 (2.5 mL) and cooled to −40 °C. Freshly purified *m*CPBA (104 mg, 0.580 mmol, 1.1 equiv.) in CH_2Cl_2 (6 mL) was added dropwise and the resulting mixture was allowed to stir for 2 h at the same temperature. Sat. aq. Na_2SO_3 (10 mL) was added and the mixture was stirred for 15 min at 25 °C. The organic phase was washed sequentially with sat. aq. $NaHCO_3$ (5 mL), aq. 1 M HCl (5 mL), and sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 7:1→1:1) to yield α-ketol **275** (46 mg, 0.12 mmol, 23%) as a colorless solid and α-ketol **274** (59 mg, 0.20 mmol, 37%) as a colorless solid.

275

R_f: 0.47 (1:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.79 – 3.76 (m, 1H), 3.63 (t, *J* = 8.4 Hz, 1H), 2.34 (s, 1H), 2.03 (dtd, *J* = 17.0, 8.2, 4.1 Hz, 1H), 1.98 – 1.87 (m, 2H), 1.84 – 1.57 (m, 7H), 1.54 – 1.43 (m, 2H), 1.35 – 1.23 (m, 2H), 1.12 – 0.99 (m, 2H), 0.99 (s, 3H), 0.90 – 0.82 (m, 1H), 0.75 (s, 3H), 0.71 (t, *J* = 4.9 Hz, 1H), 0.08 (s, 9H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 210.6, 81.6, 72.6, 47.3, 44.4, 43.9, 43.1, 39.3, 38.1, 37.9, 36.6, 33.8, 30.8, 26.3, 22.9, 22.5, 19.5, 11.2, 11.0.

FTIR: (neat) [cm^{-1}] = 2969 (w), 2954 (w), 2359 (s), 2341 (m), 1737 (s), 1682 (w), 1372 (s), 1228 (m), 1216 (s), 840 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{21}H_{28}NaO_3Si^+$: 399.2326; found: 399.2344.

$[\alpha]_D^{20}$: +5.4 (c= 1.00; $CHCl_3$)

MP 93−94 °C ($CHCl_3$)

274

R_f: 0.55 (1:3; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: (CD_3OD, 500 MHz): δ [ppm] = 3.67 (d, *J* = 2.2 Hz, 1H), 3.64 (d, *J* = 8.7 Hz, 1H), 2.13 – 1.99 (m, 3H), 1.90 – 1.79 (m, 4H), 1.77 – 1.61 (m, 5H), 1.56 – 1.44 (m, 2H), 1.32 (td, *J* = 11.9, 5.9 Hz, 1H), 1.13 (td, *J* = 12.9, 4.1 Hz, 1H), 1.08 – 1.02 (m, 1H), 1.00 (s, 3H), 0.79 (s, 3H), 0.69 (t, *J* = 4.9 Hz, 1H).

^{13}C NMR: (CD_3OD, 126 MHz): δ [ppm] = 211.9, 82.3, 73.5, 45.4, 45.2, 44.3, 44.0, 41.1, 39.2, 37.6, 37.3, 34.6, 30.6, 27.1, 23.5, 23.5, 19.5, 11.4, 10.3.

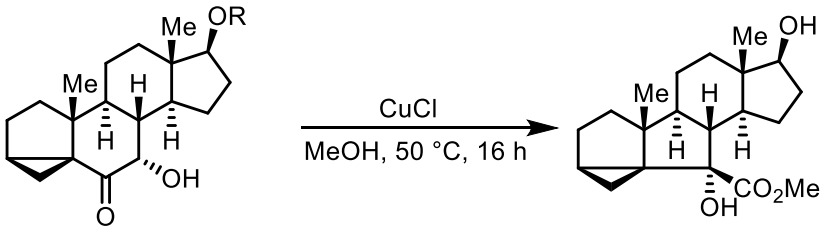
FTIR: (neat) [cm^{-1}] = 3393 (br), 2995 (m), 2870 (w), 2360 (s), 2341 (s), 1682 (s), 1455 (m), 1375 (m), 1046 (m), 1019 (m) 736 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{19}H_{28}NaO_3^+$: 327.1931; found: 327.1944.

$[\alpha]_D^{20}$: +6.4 (c= 1.00; $CHCl_3$)

MP 163−164 °C ($CHCl_3$)

(7βa)-Methyl 7α,17β-dihydroxy-3α,5-Cyclo-5α-5(6→7)*abeo* androstaneoate



$C_{19}H_{28}O_3$ (304.43) **274**
$C_{22}H_{36}O_3Si$ (376.61) **275**

274 R = H
275 R = TMS

$C_{20}H_{30}O_4$ (334.46) **276**

α-Ketol **275** (20 mg, 50 µmol, 1.0 equiv.) was dissolved in MeOH (1.4 mL) and CuCl (79 mg, 0.79 mmol, 15 equiv.) was added to the solution. The resulting suspension was allowed to stir for 16 h at 50 °C. After cooling to ambient temperature, the mixture was filtered over a plug of Celite®. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 1:1) to give B-*nor*-α-hydroxy methyl ester **276** (13.4 mg, 0.04 mmol, 77%) as a colorless oil. Starting from α-ketol **274** (38 mg, 0.12 mmol, 1.0 equiv.) the reaction gave the identical product (26 mg, 0.076 mmol, 61%).

R_f: 0.46 (1:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.78 (s, 3H), 3.71 (t, *J* = 8.5 Hz, 1H), 2.36 (t, *J* = 11.5 Hz, 1H), 2.07 (dtd, *J* = 13.6, 9.3, 6.0 Hz, 1H), 1.91 – 1.85 (m, 1H), 1.82 (dt, *J* = 12.6, 3.1 Hz, 1H), 1.75 – 1.70 (m, 1H), 1.70 – 1.63 (m, 2H), 1.58 – 1.35 (m, 7H), 1.17 (qd, *J* = 12.2, 6.0 Hz, 1H), 1.07 (td, *J* = 12.5, 4.1 Hz, 1H), 0.98 (ddd, *J* = 13.8, 10.8, 8.8 Hz, 1H), 0.94 (s, 3H), 0.77 (s, 3H), 0.55 (t, *J* = 5.5 Hz, 1H), 0.52 – 0.49 (m, 1H).

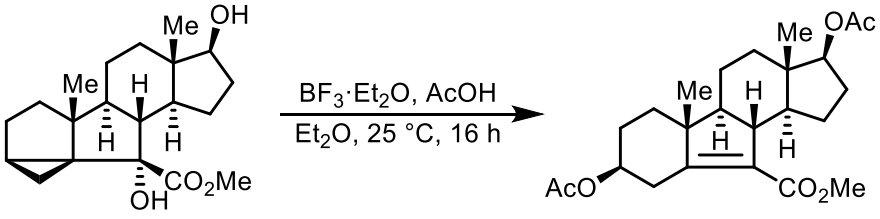
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 178.4, 81.3, 80.1, 53.1, 51.9, 50.4, 50.3, 50.2, 45.6, 45.1, 36.2, 34.2, 30.8, 25.8, 24.0, 23.1, 21.5, 18.5, 11.7, 11.4.

FTIR: (neat) [cm^{-1}] = 3481 (b), 2947 (w), 2865 (w), 2360 (s), 2341 (m), 1719 (s), 1455 (w), 1978 (w), 1274 (w), 1252 (s), 1160 (m), 1106 (m), 1096 (m), 1051 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{20}H_{30}NaO_4^+$: 357.2036; found: 357.2043.

$[\alpha]_D^{24}$: −4.4 (c= 1.00; $CHCl_3$)

(7a)-Methyl 3β,17β-diacetoxy-5(6→7)*abeo* androst-5-enoate



$C_{20}H_{30}O_4$ (334.46)
276

$C_{24}H_{34}O_6$ (418.53)
277

To α-hydroxy methyl ester **276** (14 mg, 41 µmol, 1.0 equiv.) in Et_2O (1.6 mL) were added acetic acid (0.51 mL, 4.1 mmol, 100 equiv.) and $BF_3{\cdot}Et_2O$ (0.51 mL, 3.3 mmol, 80.0 equiv.) and the resulting mixture was allowed to stir at 25 °C for 16 h. EtOAc (3 mL) was added and the solution was carefully added to sat. aq. $NaHCO_3$ (3 mL). The aq. phase was extracted with EtOAc (3 x 3 mL), the combined organic phases were washed with sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 4:1) to give acrylic ester **277** (6.7 mg, 18 µmol, 45%) as a colorless oil.

R_f: 0.81 (1:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.72 (tt, *J* = 11.5, 4.6 Hz, 1H), 4.62 (dd, *J* = 9.3, 7.8 Hz, 1H), 3.70 (s, 3H), 3.35 (ddd, *J* = 13.9, 4.8, 2.1 Hz, 1H), 2.70 (td, *J* = 10.9, 4.3 Hz, 1H), 2.18 – 2.09 (m, 1H), 2.04 (s, 3H), 2.03 (s, 3H) 2.02 – 1.92 (m, 1H), 1.83 (dt, *J* = 13.4, 3.5 Hz, 1H), 1.80 – 1.76 (m, 4H), 1.74 – 1.68 (m, 2H), 1.68 – 1.54 (m, 1H), 1.52 – 1.36 (m, 2H), 1.31 – 1.23 (m, 1H), 1.22 – 1.10 (m, 2H), 0.93 (s, 3H), 0.87 (s, 3H).

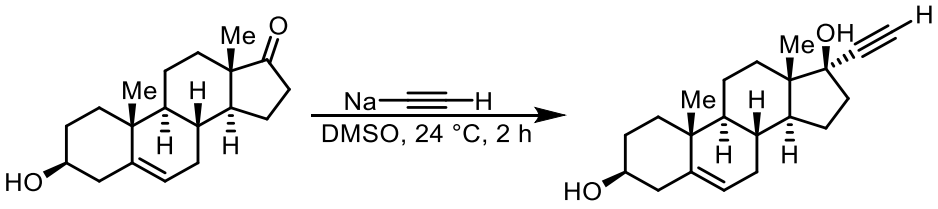
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 171.3, 170.4, 167.7, 157.9, 130.3, 82.3, 72.8, 60.3, 51.0, 49.2, 47.3, 45.9, 45.2, 37.1, 36.2, 30.7, 27.9, 27.6, 25.2, 24.2, 21.3, 20.3, 15.5, 12.6.

FTIR: (neat) [cm^{-1}] = 3734 (b), 2952 (m), 2860 (w), 2360 (s), 2341 (s), 1733 (m), 1716 (w), 1540 (m), 1507 (w), 1260 (m), 750 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{34}NaO_6^+$: 441.2248; found: 441.2250.

$[\alpha]_D^{24}$: −18.9 (c= 0.48, $CHCl_3$)

3β,17β-dihydroxy-androst-5-en-18α-yne



$C_{19}H_{28}O_2$ (288.43)
266

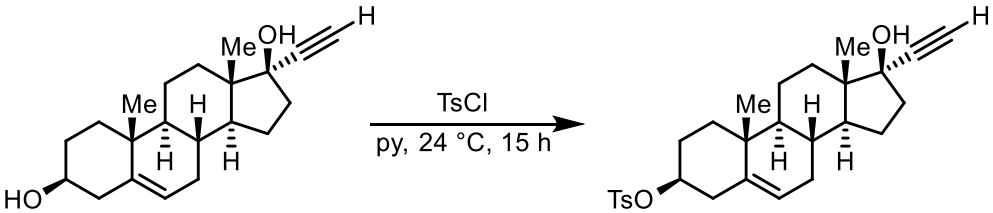
$C_{21}H_{30}O_2$ (314.47)
278

Dehydroepiandrosterone (**266**) (600 mg, 2.08 mmol, 1.0 equiv.) was dissolved in DMSO (16 mL). Sodium acetylide (8.0 mL, 18w% in xylene/mineral oil) was added dropwise to the solution at 24 °C. The mixture was allowed to stir at the same temperature for 2 h, then the solution was cooled to 0 °C. Cold, sat. aq. NH_4Cl (25 mL) was carefully added to the solution. The aq. phase was extracted with EtOAc (3 x 25 mL) and the combined organic phases were washed with H_2O (30 mL), sat. aq. NaCl (30 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1) to give alkyne **278** (464 mg, 1.48 mmol, 71%) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.35 (dt, *J* = 5.4, 2.0 Hz, 1H), 3.52 (tt, *J* = 11.1, 4.7 Hz, 1H), 2.56 (s, 1H), 2.34 – 2.21 (m, 3H), 2.00 (tdd, *J* = 11.9, 5.5, 3.3 Hz, 2H), 1.93 – 1.81 (m, 2H), 1.75 – 1.43 (m, 10H), 1.38 – 1.25 (m, 3H), 1.11 (dd, *J* = 13.3, 3.9 Hz, 1H), 1.03 (s, 3H), 0.86 (d, *J* = 0.6 Hz, 3H).

The spectroscopic data match those reported in literature.[194]

17β-Hydroxy-androst-5-en-18α-yne-3β-tosylate



$C_{21}H_{30}O_2$ (314.47)
278

$C_{28}H_{36}O_4S$ (468.65)
312

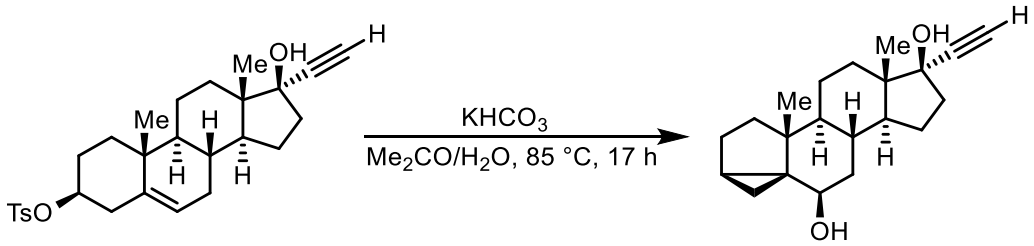
To alkyne **278** (370 mg, 1.20 mmol, 1.0 equiv.) in pyridine (12 mL) was added 4-dimethylaminopyridine (12.0 mg, 0.120 mmol, 0.1 equiv.) and tosyl chloride (1.12 g, 5.90 mmol, 5.0 equiv.). After stirring at 25 °C for 15 h, the mixture was added to ice/water

(50 mL) and extracted with Et_2O (3 x 25 mL). The combined organic phases were washed with sat. aq. NaCl (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield tosylate **312** (543 mg, 1.12 mmol, 93%) as a colorless solid that was used in the next step without further purification.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 7.80 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.31 (m, 2H), 5.31 (dt, *J* = 5.4, 2.1 Hz, 1H), 4.33 (tt, *J* = 11.5, 4.7 Hz, 1H), 2.56 (s, 1H), 2.45 (s, 4H), 2.32 – 2.24 (m, 2H), 1.99 (ddd, *J* = 13.8, 11.8, 3.9 Hz, 2H), 1.87 – 1.80 (m, 3H), 1.76 – 1.65 (m, 3H), 1.64 – 1.25 (m, 6H), 1.08 – 1.00 (m, 1H), 0.99 (s, 3H), 0.94 (ddd, *J* = 12.4, 10.0, 4.6 Hz, 1H), 0.84 (d, *J* = 0.6 Hz, 3H).

The spectroscopic data match those reported in literature.[195]

17β-hydroxy-3*α*,5-Cyclo-5*α*-androst-18-yne-3β-tosylate



$C_{28}H_{36}O_4S$ (468.65)
312

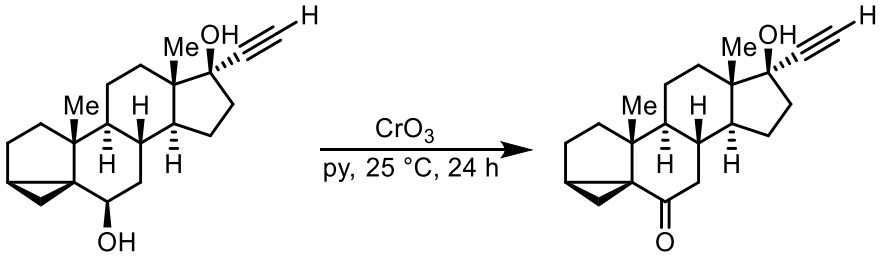
$C_{21}H_{30}O_2$ (314.47)
313

Tosylate **312** (479 mg, 1.02 mmol, 1.0 equiv.) was suspended in Me_2CO/H_2O (4:1, 12.7 mL) in a pressure tube and $KHCO_3$ (589 mg, 61.0 mmol, 5.0 equiv.) was added. The tube was sealed and the mixture was stirred at 85 °C for 17 h. After cooling to ambient temperature, water (25 mL) was added and extracted with Et_2O (3 x 10 mL). The combined organic phases were washed with NaCl (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to yield *i*-sterol **313** (302 mg, 0.96 mmol, 96%) as a colorless solid that was used in the next step without further purification.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.27 (t, *J* = 2.8 Hz, 1H), 2.57 (s, 1H), 2.29 (ddd, *J* = 13.8, 9.7, 5.6 Hz, 1H), 2.05 – 1.94 (m, 2H), 1.94 – 1.79 (m, 3H), 1.77 – 1.30 (m, 10H), 1.23 – 1.15 (m, 2H), 1.07 (s, 3H), 0.90 (s, 3H), 0.53 (dd, *J* = 4.9, 3.7 Hz, 1H), 0.30 (dd, *J* = 8.1, 4.8 Hz, 1H).

The spectroscopic data match those reported in literature.[195]

17β-hydroxy-3α,5-Cyclo-5α-androst-18-yn-6-one



$C_{21}H_{30}O_2$ (314.47)
313

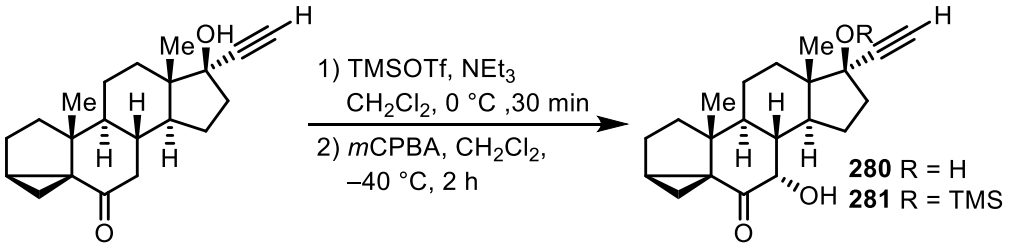
$C_{21}H_{28}O_2$ (312.45)
279

CrO_3 (400 mg, 4.00 mmol, 4.0 equiv.) was added in portions to pyridine (4 mL) cooled by a water bath. *i*-Sterol **313** (314 mg, 1.00 mmol, 1.0 equiv.) in pyridine (4 mL) was added to the resulting yellow suspension *via* canula and allowed to stir at 25 °C for 24 h. Et_2O (15 mL) was added to the suspension and the resulting mixture was filtered over Celite® and rinsed with Et_2O (2 x 10 mL). The filtrate was washed with water (2 x 20 mL) and sat. aq. NaCl (20 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 4:1) to yield ketone **279** (174 mg, 0.561 mmol, 56%) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 2.60 (s, 1H), 2.47 – 2.42 (m, 1H), 2.32 (ddd, *J* = 13.9, 9.5, 5.6 Hz, 1H), 2.02 – 1.40 (m, 16H), 1.41 – 1.28 (m, 2H), 1.03 (s, 3H), 0.90 (d, *J* = 0.7 Hz, 3H), 0.73 (t, *J* = 4.9 Hz, 1H).

The spectroscopic data match those reported in literature.[196]

17β-hydroxy-3α,5-Cyclo-5α-androst-18α-yn-6-one



$C_{21}H_{28}O_2$ (312.45)
279

$C_{21}H_{28}O_3$ (328.45)
280

$C_{24}H_{36}O_3Si$ (400.63)
281

Ketone **279** (116 mg, 0.370 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (3.7 mL) and cooled to 0 °C. Triethylamine (0.220 mL, 1.48 mmol, 4.0 equiv.) was added followed by the drop-wise addition of trimethyl silyl triflate (0.210 mL, 1.11 mmol, 3.0 equiv.) over 20 min. The

organic phase was washed with sat. aq. $NaHCO_3$ (3 mL) and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The so-obtained silyl enol ether was dissolved in CH_2Cl_2 (1.8 mL) and cooled to −40 °C. Freshly purified *m*CPBA (71.0 mg, 0.410 mmol, 1.1 equiv.) in CH_2Cl_2 (4.2 mL) was added dropwise and the resulting mixture was allowed to stir for 2 h at the same temperature. Sat. aq. Na_2SO_3 (5 mL) was added and the mixture was stirred for 15 min at 25 °C. The organic phase was washed sequentially with sat. aq. $NaHCO_3$ (5 mL), aq. 1 M HCl (5 mL), and sat. aq. NaCl (5 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 7:1→4:1) to yield α-ketol **281** (21.3 mg, 0.0500 mmol, 13%) as a colorless solid and α-ketol **280** (36.0 mg, 0.110 mmol, 30%) as a colorless solid.

281

R_f: 0.48 (7:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.77 (t, *J* = 3.2 Hz, 1H), 2.56 (s, 1H), 2.41 (d, *J* = 3.8 Hz, 1H), 2.27 (ddd, *J* = 13.5, 9.8, 5.4 Hz, 1H), 2.13 (td, *J* = 11.6, 7.6 Hz, 1H), 2.10 – 2.02 (m, 1H), 1.99 – 1.86 (m, 2H), 1.84 – 1.54 (m, 9H), 1.50 – 1.39 (m, 1H), 1.32 (qd, *J* = 12.1, 5.4 Hz, 1H), 1.05 – 1.00 (m, 1H), 0.99 (s, 3H), 0.81 (s, 3H), 0.70 (t, *J* = 5.0 Hz, 1H), 0.17 (s, 9H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 210.6, 87.8, 80.6, 75.1, 72.6, 47.7, 47.3, 44.4, 42.6, 40.4, 40.0, 37.8, 37.8, 33.8, 32.3, 26.6, 22.8, 22.6, 19.5, 12.7, 11.0.

FTIR: (neat) [cm^{-1}] = 3386 (b), 3307 (w), 2956 (s), 2872 (m), 2360 (w), 2340 (w), 1677 (s), 1378 (m), 1303 (w), 1248 (s), 1148 (m), 1137 (m), 1087 (s), 917 (m), 890 (m), 842 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{36}NaO_3Si^+$:423.2326; found: 423.2331.

$[\alpha]_D^{24}$: −24.3 (c= 1.00, $CHCl_3$)

MP 81–81.5 °C ($CHCl_3$)

280

R_f: 0.15 (1:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 3.77 (d, *J* = 3.3 Hz, 1H), 3.47 (s, 1H), 2.60 (s, 1H), 2.34 (ddd, *J* = 13.8, 9.8, 5.6 Hz, 1H), 2.17 (td, *J* = 11.8, 7.5 Hz, 1H), 1.91 (td, *J* = 11.3, 3.4 Hz, 1H), 1.86 – 1.77 (m, 5H), 1.74 – 1.72 (m, 4H), 1.65 – 1.58 (m, 1H),

1.46 (qd, *J* = 13.4, 4.1 Hz, 1H), 1.35 (qd, *J* = 12.1, 5.6 Hz, 1H), 1.06 – 1.01 (m, 1H), 0.99 (s, 3H), 0.89 (s, 3H), 0.71 (t, *J* = 5.0 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 210.7, 87.4, 79.8, 74.5, 72.4, 47.2, 46.9, 44.4, 43.7, 39.8, 39.0, 38.0, 37.7, 33.8, 32.4, 26.2, 22.6, 22.5, 19.5, 12.7, 11.1.

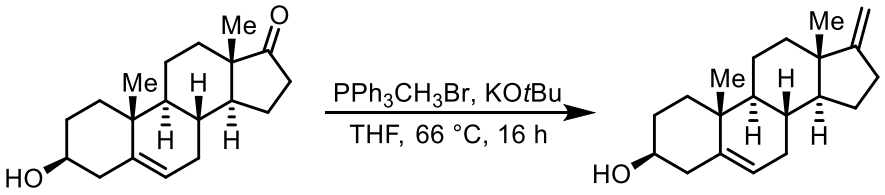
FTIR: (neat) [cm^{-1}] = 3420 (b), 3305 (m), 2956 (s), 2931 (s), 2871 (m), 2360 (s), 2341 (m), 1675 (s), 1376 (s), 1301 (m), 1252 (m), 1148 (m), 1046 (s), 754 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{22}H_{32}NaO_5^+$: 399.2141; found: 399.2137.

$[\alpha]_D^{24}$: −18.6 (c= 1.00, $CHCl_3$)

MP 163–164 °C ($CHCl_3$)

3β-Hydroxy-androst-5,17-dien



$C_{19}H_{28}O_2$ (288.43) **266**

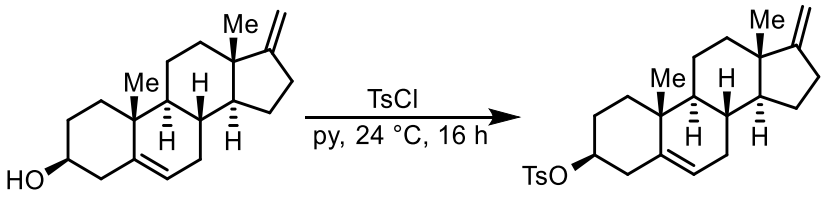
$C_{20}H_{30}O$ (286.46) **267**

To methyltriphenylphosphonium bromide (2.97 g, 8.32 mmol, 4.0 equiv.) in THF (10.4 mL) was added potassium *tert*-butoxide (5.20 mL, 8.32 mmol, 4.0 equiv., 1.6 M in THF). Dehydroepiandrosterone **266** (600 mg, 2.08 mmol, 1.0 equiv.) was dissolved in THF (5.20 mL) and added to the yellow solution of the phosphonium ylide. The resulting solution was heated to 66 °C for 16 h. After cooling to ambient temperature, water (25 mL) was added and the aq. phase was extracted with Et_2O (3 x 25 mL) and the combined organic phases were washed with sat. aq. NaCl (30 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 3:1) to give alkene **267** (587 mg, 2.03 mmol, 98%) as a colorless solid.

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 5.36 (dt, *J* = 5.5, 2.0 Hz, 1H), 4.67 – 4.61 (m, 2H), 3.53 (tt, *J* = 11.0, 4.6 Hz, 1H), 2.51 (ddq, *J* = 17.1, 10.0, 2.3 Hz, 1H), 2.35 – 2.20 (m, 3H), 2.04 (dddd, *J* = 14.7, 7.5, 4.9, 2.6 Hz, 1H), 1.91 – 1.82 (m, 3H), 1.75 – 1.57 (m, 3H), 1.56 – 1.43 (m, 4H), 1.35 – 1.20 (m, 2H), 1.10 (td, *J* = 14.7, 14.0, 4.2 Hz, 1H), 1.03 (s, 3H), 1.02 – 0.94 (m, 2H), 0.80 (s, 3H).

The spectroscopic data match those reported in literature.[169]

Androst-5,17-dien-3β-tosylate



$C_{20}H_{30}O$ (286.46)
267

$C_{27}H_{36}O_3S$ (440.64)
314

Alkene **267** (580 mg, 2.02 mmol, 1.0 equiv.) was dissolved in pyridine (20 mL) and 4-dimethylaminopyridine (24.0 mg, 0.200 mmol, 0.1 equiv.) was added. Tosyl chloride (1.93 g, 10.1 mmol, 5.0 equiv.) was added and the resulting mixture was stirred for 16 h at 24 °C. The solution was added to ice/water (70 mL) and extracted with Et_2O (3 x 25 mL). The organic phase was separated, washed sequentially with water (2 x 50 mL) and sat. aq. NaCl (100 mL). The organic phase was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The residue was dissolved in toluene (2 x 15 mL) and concentrated under reduced pressure to give tosylate **314** (781 mg, 1.77 mmol, 88%) as a colorless solid which was used in the next step without further purification.

R_f: 0.47 (9:1; *n*hexane/EtOAc [CAM, *blue*])

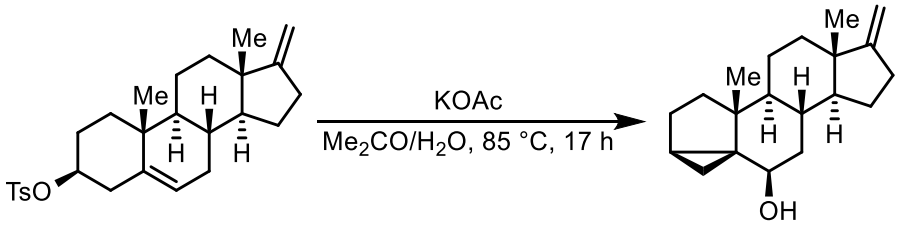
^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 7.80 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 7.7 Hz, 2H), 5.34 – 5.30 (m, 1H), 4.70 – 4.60 (m, 2H), 4.33 (tt, *J* = 11.5, 4.8 Hz, 1H), 2.57 – 2.45 (m, 1H), 2.45 (s, 3H), 2.34 – 2.17 (m, 3H), 2.06 – 1.99 (m, 1H), 1.86 – 1.79 (m, 3H), 1.76 – 1.65 (m, 2H), 1.62 – 1.42 (m, 4H), 1.34 – 1.17 (m, 2H), 1.07 – 1.00 (m, 1H), 0.99 (s, 3H), 0.98 – 0.87 (m, 2H), 0.78 (s, 3H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 161.7, 144.5, 139.1, 134.9, 129.9 (2C), 127.8 (2C), 123.5, 101.1, 82.4, 54.8, 50.3, 44.0, 39.0, 37.1, 36.6, 35.6, 31.8, 31.8, 29.5, 28.8, 24.4, 21.8, 21.1, 19.4, 18.4.

FTIR: (neat) [cm^{-1}] = 2944 (m), 2907 (w), 2360 (s), 2341 (m), 1716 (w), 1652 (w), 1455 (w), 1362 (s; 1187 (s), 1175 (s), 1098 (w), 939 (s), 888 (m), 864 (s), 813 (m), 667 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{27}H_{36}NaO_3S^+$: 463.2277; found: 463.2280.

6β-Hydroxy-3α,5-Cyclo-5α-androst-17-en



$C_{27}H_{36}O_3S$ (440.64)
314

$C_{20}H_{30}O$ (286.46)
315

Tosylate **314** (780 mg, 1.77 mmol, 1.0 equiv.) was suspended in Me_2CO/H_2O (4:1, 22.4 mL) in a pressure vessel and potassium acetate (694 mg, 7.08 mmol, 4.0 equiv.) was added. The resulting mixture was stirred for 17 h at 85 °C. After cooling to ambient temperature, water (15 mL) was added and the mixture was extracted with Et_2O (3 x 10 mL). The combined organic phases were washed with sat. aq. NaCl (10 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to give 6-hydroxy-*i*-steroid **21** (500 mg, 1.77 mmol, quant.) as a pale-yellow oil which was used in the next step without further purification. A small sample was purified by column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield pure 6-hydroxy-*i*-sterol **315** as a colorless oil.

R_f: 0.35 (9:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.66 – 4.59 (m, 2H), 3.27 (t, *J* = 2.9 Hz, 1H), 2.51 (ddq, *J* = 17.1, 10.1, 2.3 Hz, 1H), 2.24 (dtt, *J* = 17.4, 8.7, 2.0 Hz, 1H), 1.95 – 1.86 (m, 2H), 1.83 (ddd, *J* = 12.4, 3.9, 2.9 Hz, 1H), 1.80 – 1.69 (m, 2H), 1.61 – 1.52 (m, 4H), 1.52 – 1.31 (m, 3H), 1.22 (dtd, *J* = 14.1, 12.6, 3.5 Hz, 2H), 1.08 (s, 3H), 1.08 – 1.01 (m, 1H), 0.92 – 0.85 (m, 2H), 0.84 (s, 3H), 0.53 (dd, *J* = 4.8, 3.7 Hz, 1H), 0.32 – 0.28 (m, 1H).

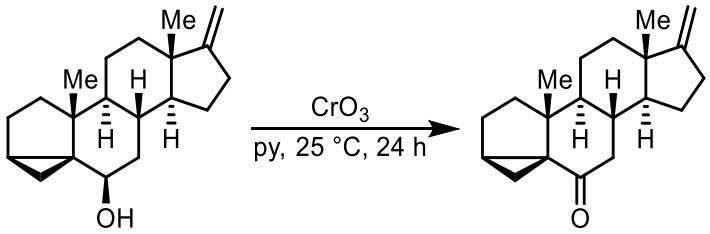
^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 162.1, 100.8, 73.9, 54.7, 48.1, 44.4, 43.2, 39.1, 37.1, 36.1, 33.4, 30.0, 29.6, 25.2, 24.4, 24.3, 22.7, 20.4, 18.8, 11.8.

FTIR: (neat) [cm^{-1}] = 2927 (s), 2865 (m), 2360 (s), 2341 (m), 1737 (s), 1653 (w), 1455 (m), 1373 (s), 1228 (m), 1216 (s), 1025 (m) 875 (m), 668 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{20}H_{30}NaO^+$: 309.2189; found: 309.2201.

$[\alpha]_D^{24}$: +40.7 (c= 1.00; $CHCl_3$)

3*α*,5-Cyclo-5*α*-androst-17-en-6-one



$C_{20}H_{30}O$ (286.46)
315

$C_{20}H_{28}O$ (284.44)
268

CrO_3 (1.42 g, 14.4 mmol, 4.0 equiv.) was added in portions to pyridine (15 mL) cooled by a water bath. Then, 6-hydroxy-*i*-steroid **315** (1.02 mg, 3.56 mmol, 1.0 equiv.), dissolved in pyridine (15 mL), was added *via* cannula to the yellow suspension. The resulting, dark solution was stirred for 15 h at 25 °C. Et_2O (60 mL) was added and the solution was filtered over Celite® and rinsed with Et_2O (2x 30 mL). The filtrate was washed sequentially with water (2 x 50 mL) and sat. aq. NaCl (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2; *n*hexane/EtOAc 9:1) to yield *i*-steroid ketone **268** (555 mg, 1.95 mmol, 55% over 2 steps) as a colorless solid.

R_f: 0.45 (9:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.69 – 4.65 (m, 2H), 2.58 – 2.46 (m, 2H), 2.32 – 2.23 (m, 1H), 2.06 – 1.92 (m, 2H), 1.89 (ddd, *J* = 12.6, 4.2, 3.1 Hz, 2H), 1.83 (dd, *J* = 13.7, 8.1 Hz, 1H), 1.74 – 1.68 (m, 4H), 1.59 – 1.49 (m, 2H), 1.37 – 1.27 (m, 3H), 1.19 (ddd, *J* = 12.8, 10.2, 6.4 Hz, 1H), 1.03 (s, 3H), 1.02 – 0.98 (m, 1H), 0.84 (s, 3H), 0.73 (t, *J* = 4.9 Hz, 1H)

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 209.5, 161.1, 101.4, 55.1, 47.0, 46.5, 46.5, 44.8, 44.4, 35.6, 35.5, 34.9, 33.6, 29.5, 26.0, 24.2, 22.9, 19.9, 18.6, 11.9.

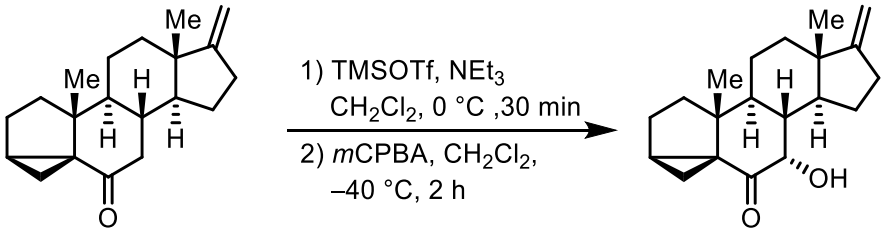
FTIR: (neat) [cm^{-1}] = 2946 (m), 2906 (m), 1680 (s), 1454 (w), 1372 (w), 1295 (w), 1161 (w), 875 (m), 809 (w), 737 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{20}H_{28}NaO^+$: 307.2032; found: 307.2047.

$[\alpha]_D^{24}$: +41.0 (c= 1.00; $CHCl_3$)

MP 176–177 °C ($CHCl_3$).

3α,5-Cyclo-5α-7β-hydroxy-androst-17-en-6-one



$C_{20}H_{28}O$ (284.44)
268

$C_{20}H_{28}O_2$ (300.44)
269

Ketone **268** (408 mg, 1.43 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 °C. Triethylamine (0.76 mL, 4.30 mmol, 4.0 equiv.) was added followed by the dropwise addition of trimethyl silyl triflate (0.82 mL, 5.72 mmol, 3.0 equiv.) over 20 min. The organic phase was washed with aq. sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the so-obtained silyl enol ether was dissolved in CH_2Cl_2 (15 mL) and cooled to −40 °C. Freshly purified *m*CPBA (271 mg, 1.57 mmol, 1.1 equiv.) in CH_2Cl_2 (16 mL) was added dropwise and the resulting mixture was allowed to stir for 2 h at the same temperature. Sat. aq. Na_2SO_3 (20 mL) was added and the mixture was stirred for 15 min at 25 °C. The organic phase was washed sequentially with sat. aq. $NaHCO_3$ (15 mL), aq. 1 M HCl (15 mL), and sat. aq. NaCl (15 mL), dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 15:1→7:1) to yield α-ketol **269** (165 mg, 0.550 mmol, 38%) as a colorless solid and recovered ketone **268** (180 mg, 0.630 mmol, 44%) as a colorless solid.

R_f: 0.38 (9:1; *n*hexane/EtOAc [CAM, *red*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.69 – 4.64 (m, 2H), 3.84 (t, *J* = 2.9 Hz, 1H), 2.59 – 2.50 (m, 1H), 2.49 – 2.44 (m, 1H), 2.36 – 2.26 (m, 1H), 2.04 (dtd, *J* = 17.1, 8.1, 4.0 Hz, 1H), 1.93 (td, *J* = 11.3, 3.3 Hz, 1H), 1.88 – 1.79 (m, 4H), 1.76 – 1.64 (m, 4H), 1.60 (dd, *J* = 8.3, 5.0 Hz, 1H), 1.52 (tdd, *J* = 13.6, 12.1, 4.1 Hz, 1H), 1.38 – 1.27 (m, 2H), 1.08 – 1.01 (m, 1H), 1.00 (s, 3H), 0.83 (s, 3H), 0.71 (t, *J* = 5.0 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 210.6, 161.0, 101.3, 73.0, 47.7, 47.3, 44.4, 44.1, 39.2, 38.0, 37.8, 35.3, 33.8, 29.5, 26.3, 23.7, 22.8, 19.5, 18.2, 11.0.

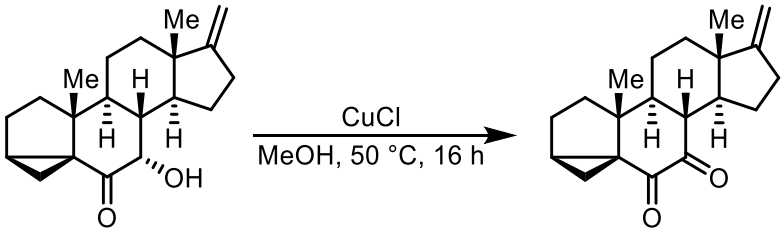
FTIR: (neat) [cm^{-1}] = 3304 (b), 2959 (s), 2872 (m), 1737 (m), 1693 (s), 1678 (s), 1655 (m), 1452 (w), 1373 (s), 1302 (w), 1216 (w), 1160 (w), 875 (m) 850 (w).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{20}H_{28}NaO_2^+$: 323.1982; found: 323.1997.

$[\alpha]_D^{24}$: −8.1 (c= 1.00; $CHCl_3$)

MP 63-64.5 °C ($CHCl_3$).

3α,5-Cyclo-5α-androst-17-en-6,7-dione



$C_{20}H_{28}O_2$ (300.44)
269

$C_{20}H_{26}O_2$ (298.43)
270

α-Hydroxy ketone **269** (45 mg, 0.15 mmol, 1.0 equiv.) was suspended in MeOH (3.8 mL) and CuCl (0.15 g, 1.5 mmol; 10.0 equiv.) was added. The resulting suspension was stirred at 50 °C for 16 h. After cooling to ambient temperature, the suspension was filtered through a plug of Celite®, the solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1) to give the *i*-steroid dione **270** (31 mg, 0.10 mmol, 68%) as a colorless solid along with B-*nor*-α-hydroxy methyl ester **271** (16 mg, 0.050 mmol, 21%).

R_f: 0.32 (9:1; *n*hexane/EtOAc [CAM, *green*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.70 (s, 1H), 4.66 (s, 1H), 2.77 (dd, *J* = 12.1, 10.4 Hz, 1H), 2.58 – 2.49 (m, 1H), 2.38 – 2.28 (m, 2H), 2.00 – 1.41 (m, 10H), 1.32 – 1.24 (m, 1H), 1.23 (s, 3H) 1.23 – 1.25 (m, 1H), 1.19 (t, *J* = 10.5 Hz, 1H), 1.10 (s, 1H), 0.85 (s, 3H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 198.2, 197.1, 159. 7, 101.7, 50.5, 50.3, 48.7, 45.7, 45.4, 44.6, 40.9, 34.8, 34.1, 29.5, 25.8, 25.4, 23.0, 19.4, 18.6, 15.9.

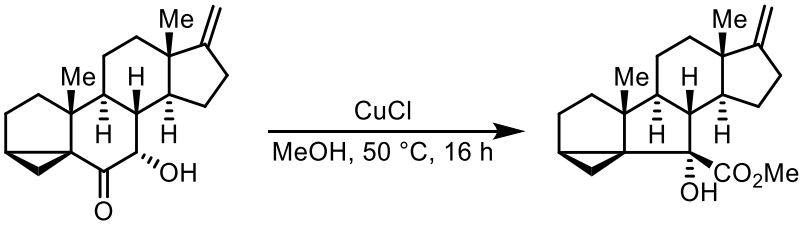
FTIR: (neat) [cm^{-1}] = 2963 (m), 2922 (m), 2359 (m), 2342 (w), 1720 (m), 1693 (s), 1654 (w), 1455 (w), 1365 (w), 1293 (m), 1141 (w), 1100 (w), 991 (w), 876 (m).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{20}H_{26}NaO_2^+$: 321.1825; found: 321.1811.

$[\alpha]_D^{24}$: −25.9 (c= 1.00; $CHCl_3$)

MP 87.5-88 °C ($CHCl_3$).

7α-hydroxy-3α,5-Cyclo-5α-5(6→7)*abeo*-androst-17-en-7βa-methyl ester



$C_{20}H_{28}O_2$ (300.44)
269

$C_{21}H_{30}O_3$ (330.47)
271

α-Hydroxy ketone **269** (80 mg, 0.26 mmol, 1.0 equiv.) was suspended in MeOH (6.8 mL) and CuCl (0.52 g, 5.2 mmol; 20.0 equiv.) was added. The resulting suspension was stirred at 50 °C for 3 h. After cooling to ambient temperature, the suspension was filtered through a plug of Celite®, the solvent was removed under reduced pressure and the residue was submitted to column chromatography (SiO_2, *n*hexane/EtOAc 9:1) to give α-hydroxy methyl ester **271** (73 mg, 0.22 mmol, 85%) as a colorless oil.

R_f: 0.64 (9:1; *n*hexane/EtOAc [CAM, *blue*])

^{1}H NMR: ($CDCl_3$, 500 MHz): δ [ppm] = 4.64 (ddt, *J* = 4.2, 2.1, 1.3 Hz, 2H), 3.78 (s, 3H), 2.89 (s, 1H), 2.46 (ddq, *J* = 17.1, 10.0, 2.2 Hz, 1H), 2.39 – 2.32 (m, 1H), 2.26 (dtt, *J* = 17.3, 8.8, 2.0 Hz, 1H), 1.94 – 1.80 (m, 2H), 1.79 – 1.70 (m, 2H), 1.67 – 1.58 (m, 2H), 1.55 – 1.44 (m, 2H), 1.42 – 1.37 (m, 1H), 1.28 – 1.13 (m, 2H), 1.03 – 0.97 (m, 1H), 0.95 (s, 3H), 0.80 (s, 3H), 0.56 (t, *J* = 5.5 Hz, 1H), 0.51 (dd, *J* = 8.9, 5.6 Hz, 1H).

^{13}C NMR: ($CDCl_3$, 126 MHz): δ [ppm] = 178.4, 160.5, 100.9, 80.2, 53.0, 51.9, 50.5, 50.4, 50.3, 48.6, 46.1, 35.1, 34.2, 29.7, 25.9, 24.0, 23.7, 21.6, 19.1, 18.5, 11.5.

FTIR: (neat) [cm^{-1}] = 2929 (m), 2864 (w), 2360 (s), 2341 (s), 1722 (m), 1653 (w), 1455 (w), 1375 (w), 1274 (m), 1260 (m), 1157 (w), 1091 (w), 875 (w), 764 (s), 750 (s).

HRMS: *m/z* $[M+Na]^+$ calcd for $C_{21}H_{30}NaO_3^+$: 353.2087; found: 353.2101.

$[\alpha]_D^{24}$: +13.8 (c= 1.00; $CHCl_3$)

MP 78-80 °C ($CHCl_3$)

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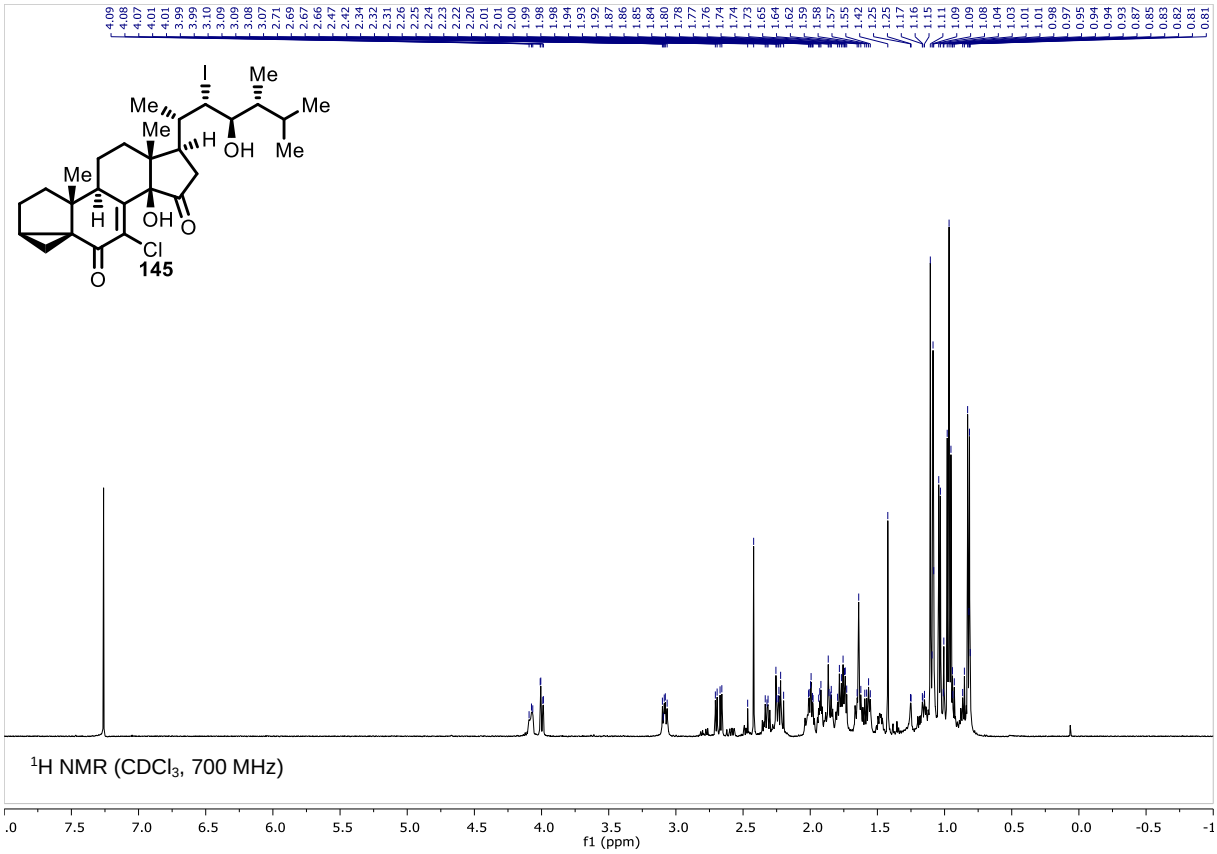
Appendix

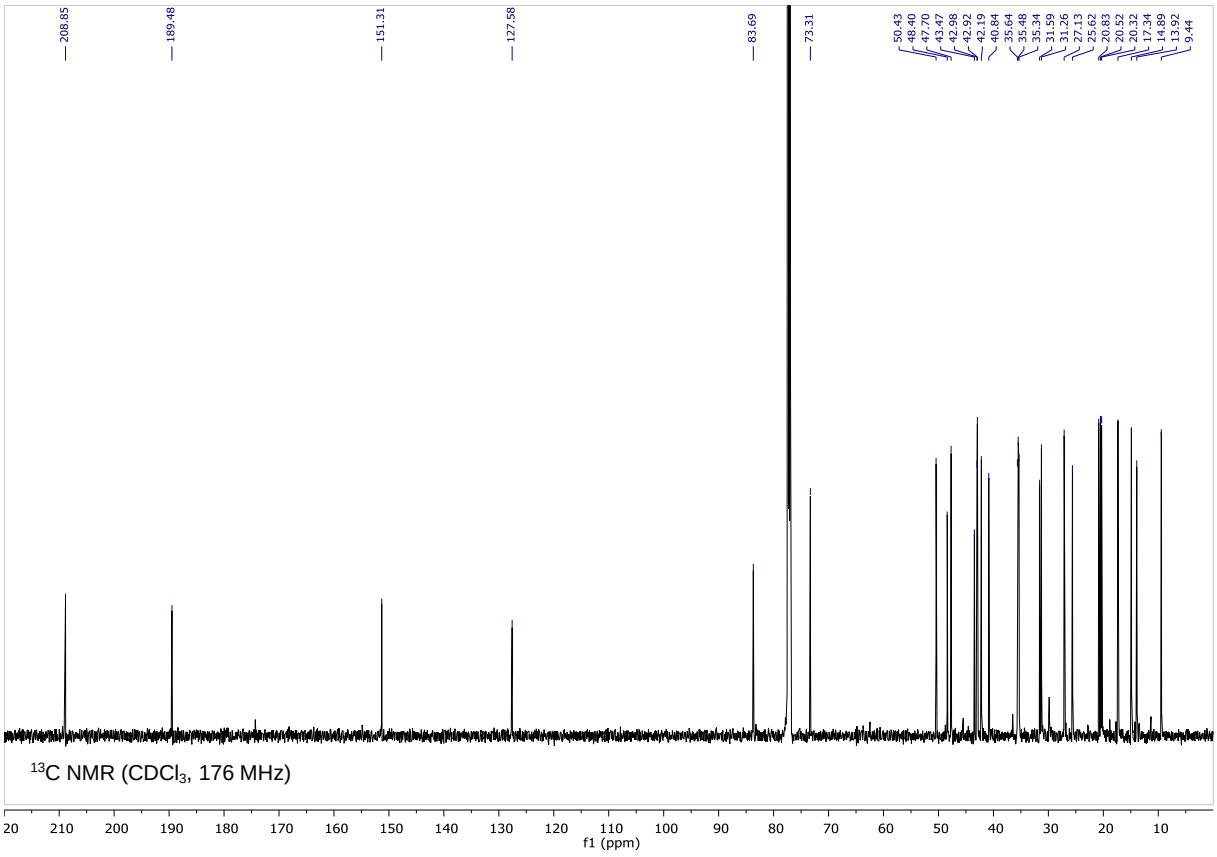
17. Appendix

Crystallographic data for compound **126**:

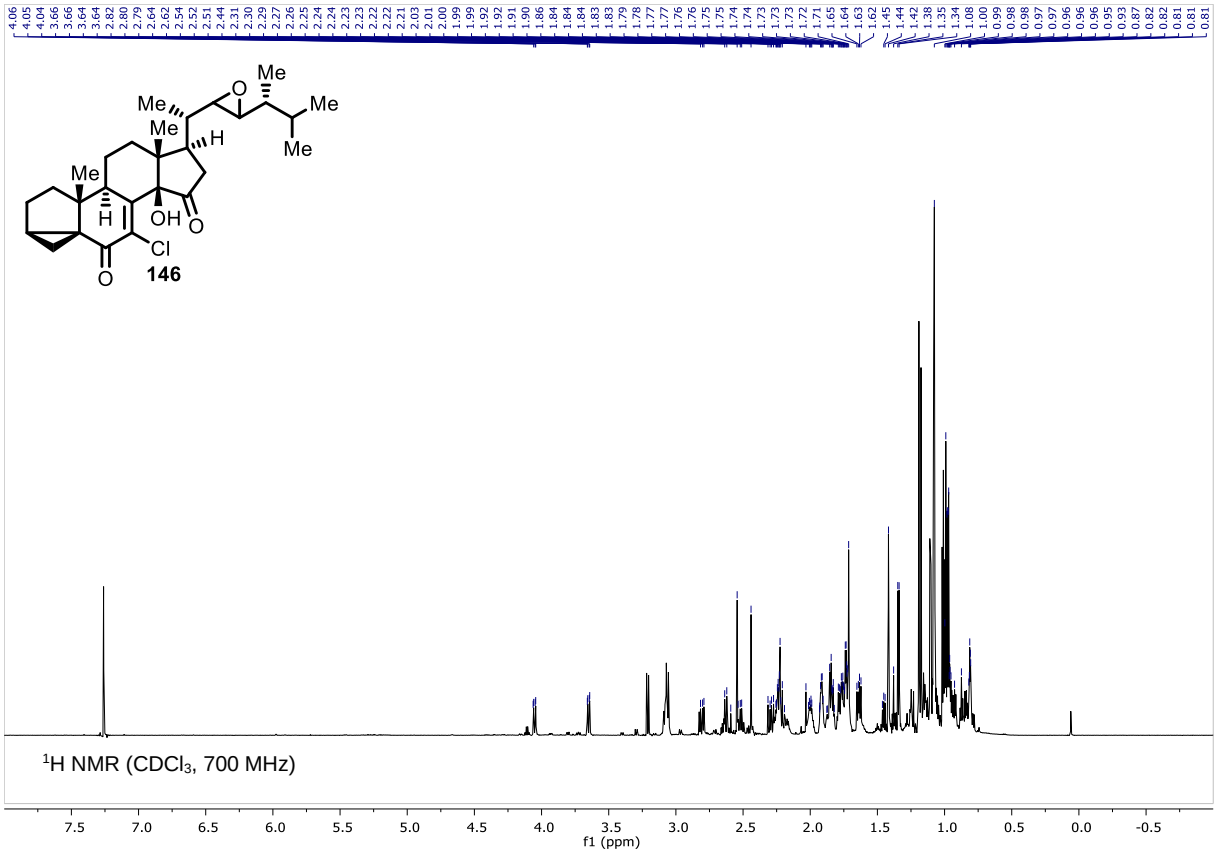
Molecular formula	$C_{32}H_{49}IO_6$
Molar mass [g/mol]	656.64
Crystal system	Monoclinic
Space group	P 2yb
Cell constant a [Å]	13.0260
Cell constant b [Å]	7.8663
Cell constant c [Å]	15.2826
Angle α [°]	90.00
Angle β [°]	92.27
Angle γ [°]	90.00



^{1}H NMR ($CDCl_3$, 700 MHz)



^{13}C NMR ($CDCl_3$, 176 MHz)



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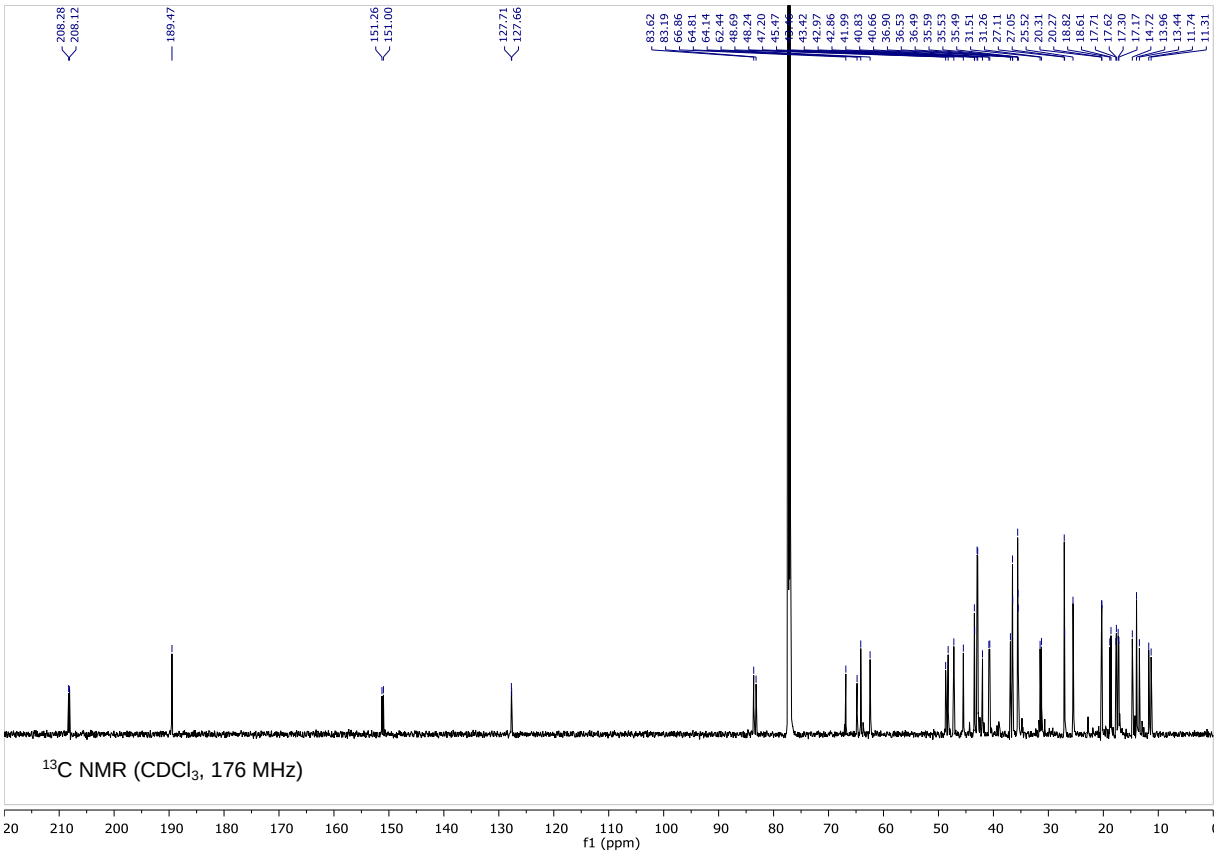

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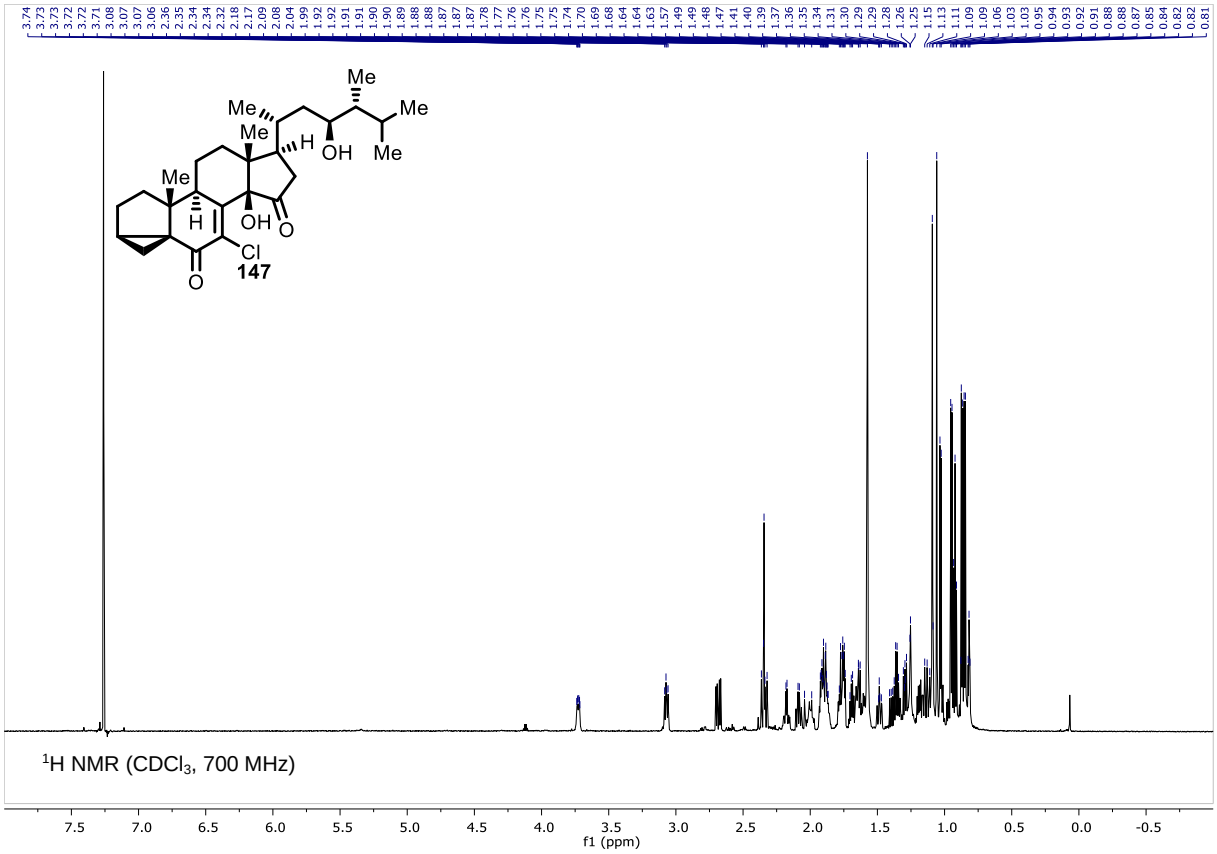
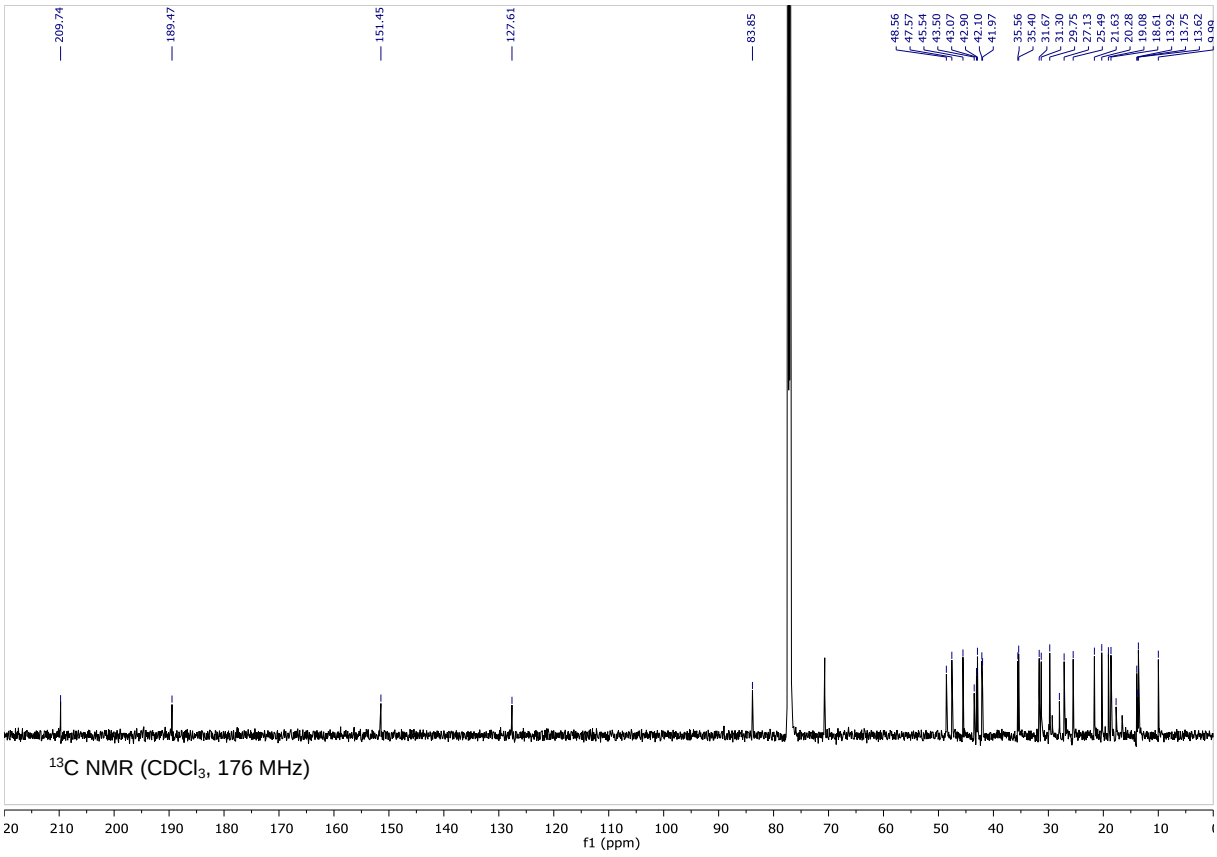


^{1}H NMR ($CDCl_3$, 700 MHz)



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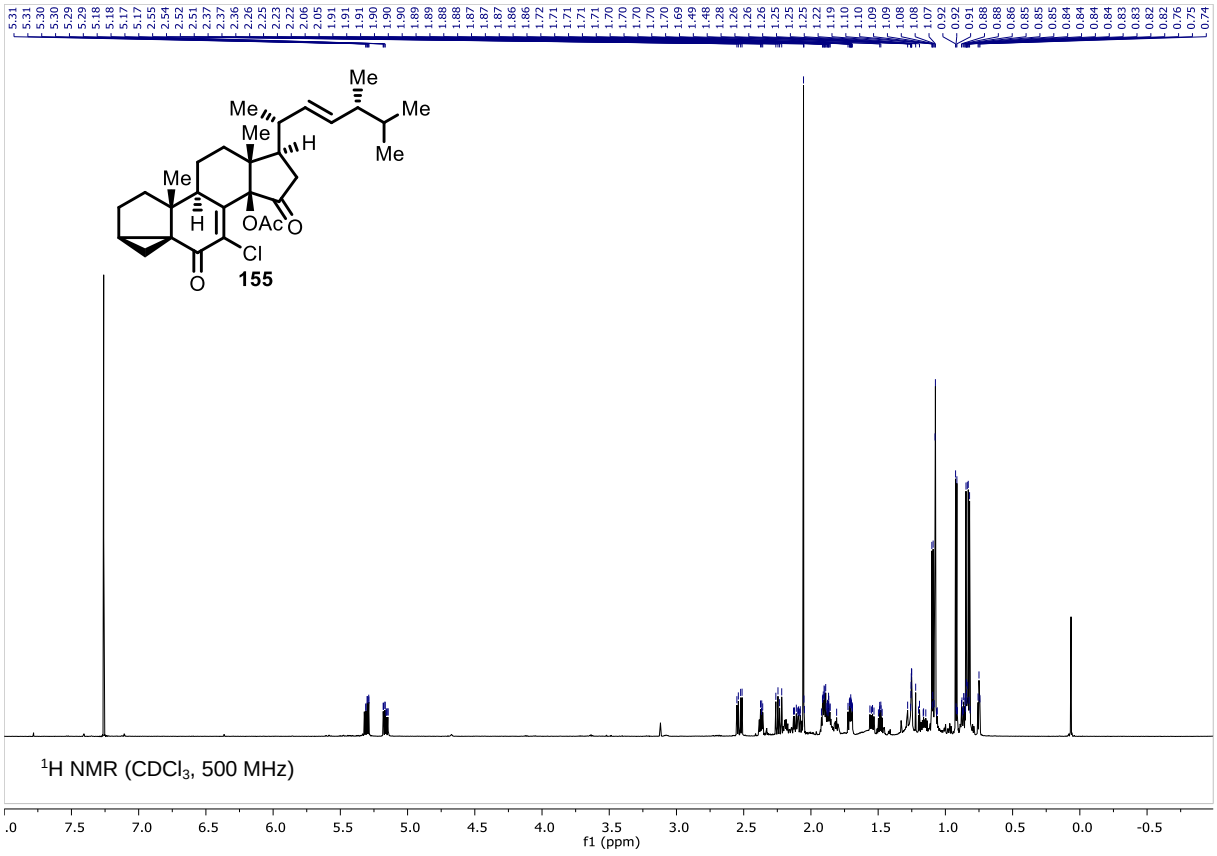

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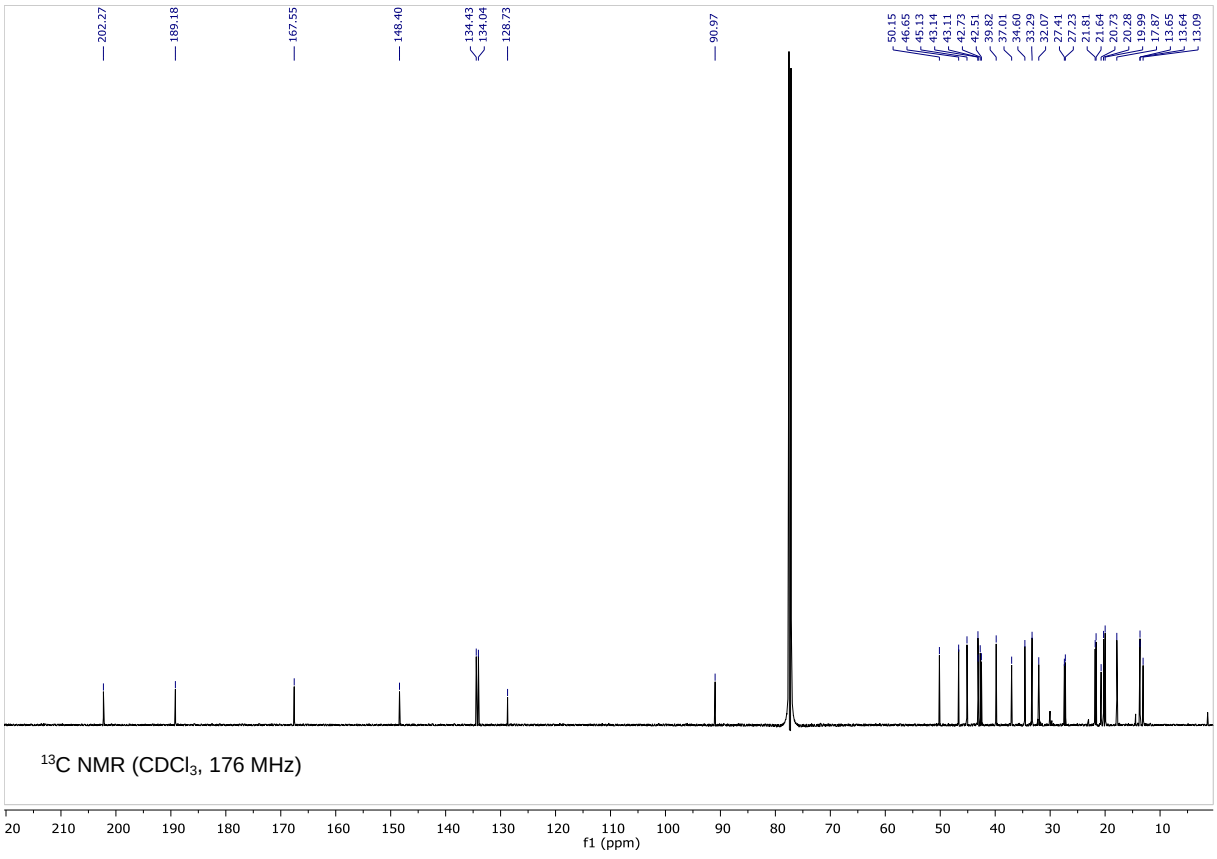

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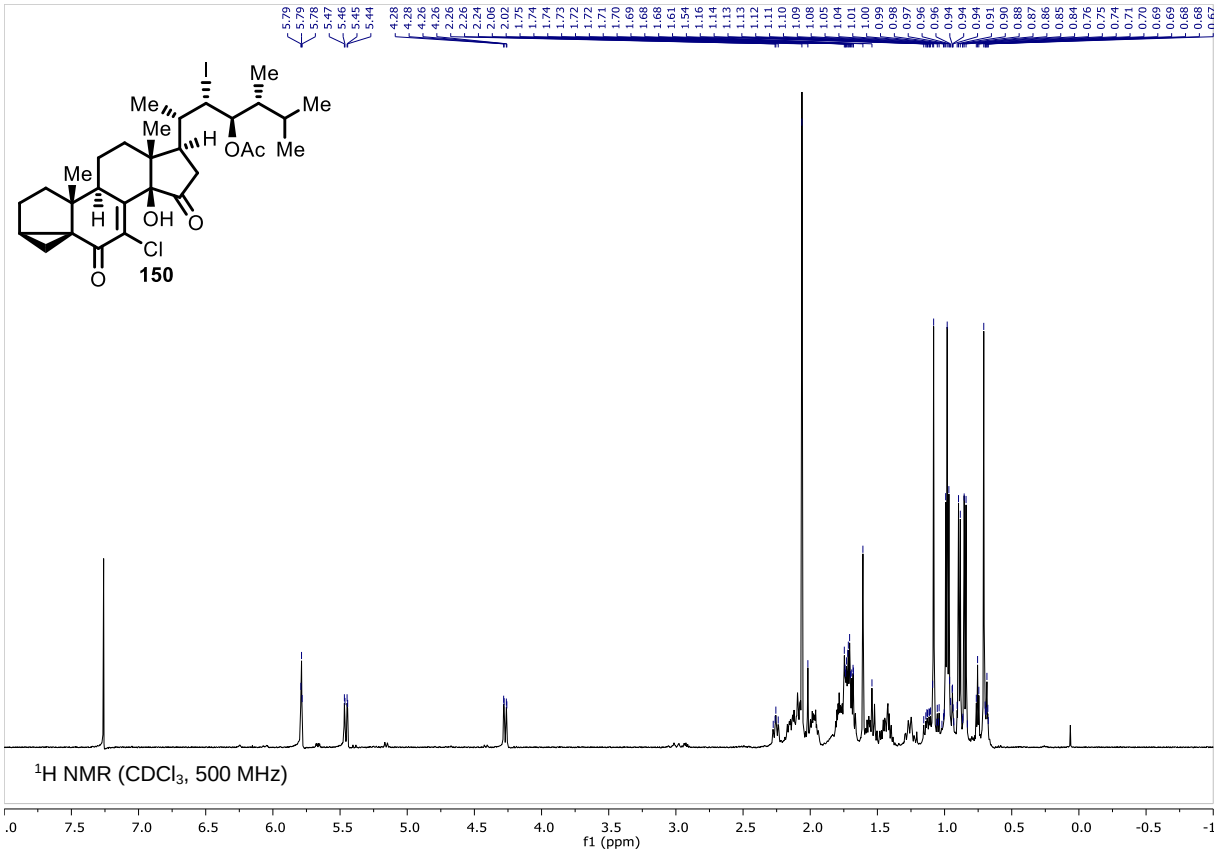
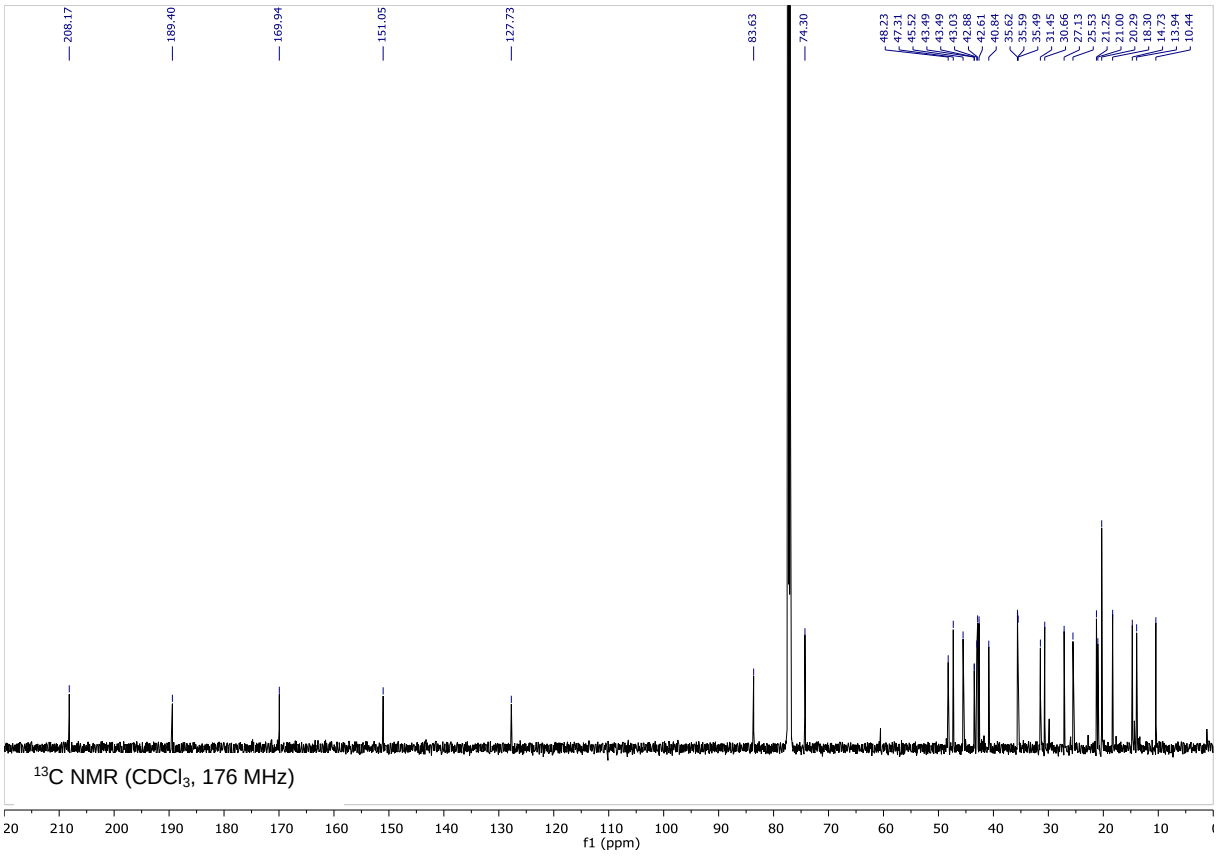

Me
I
Me
Me
Me
H
OAc
Me
Me
H
OH
O
Cl
O
150
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)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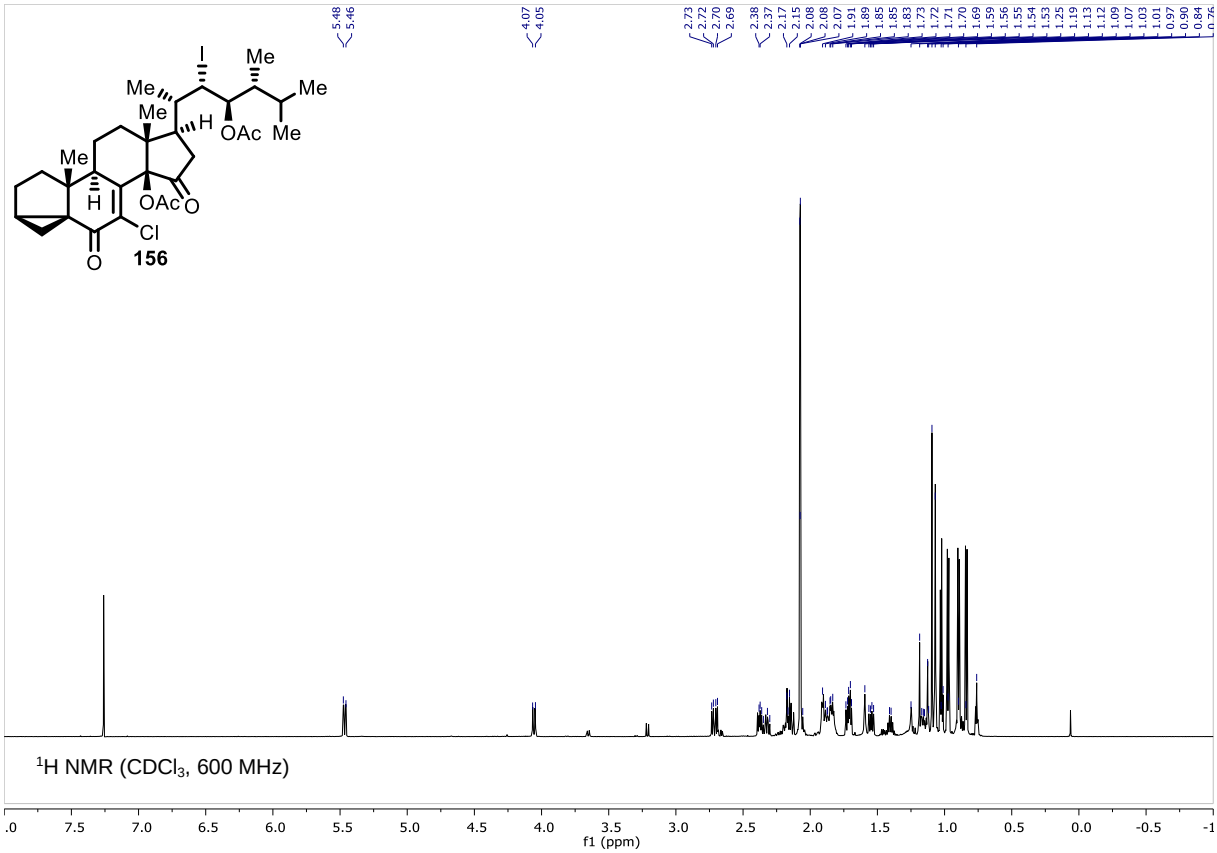
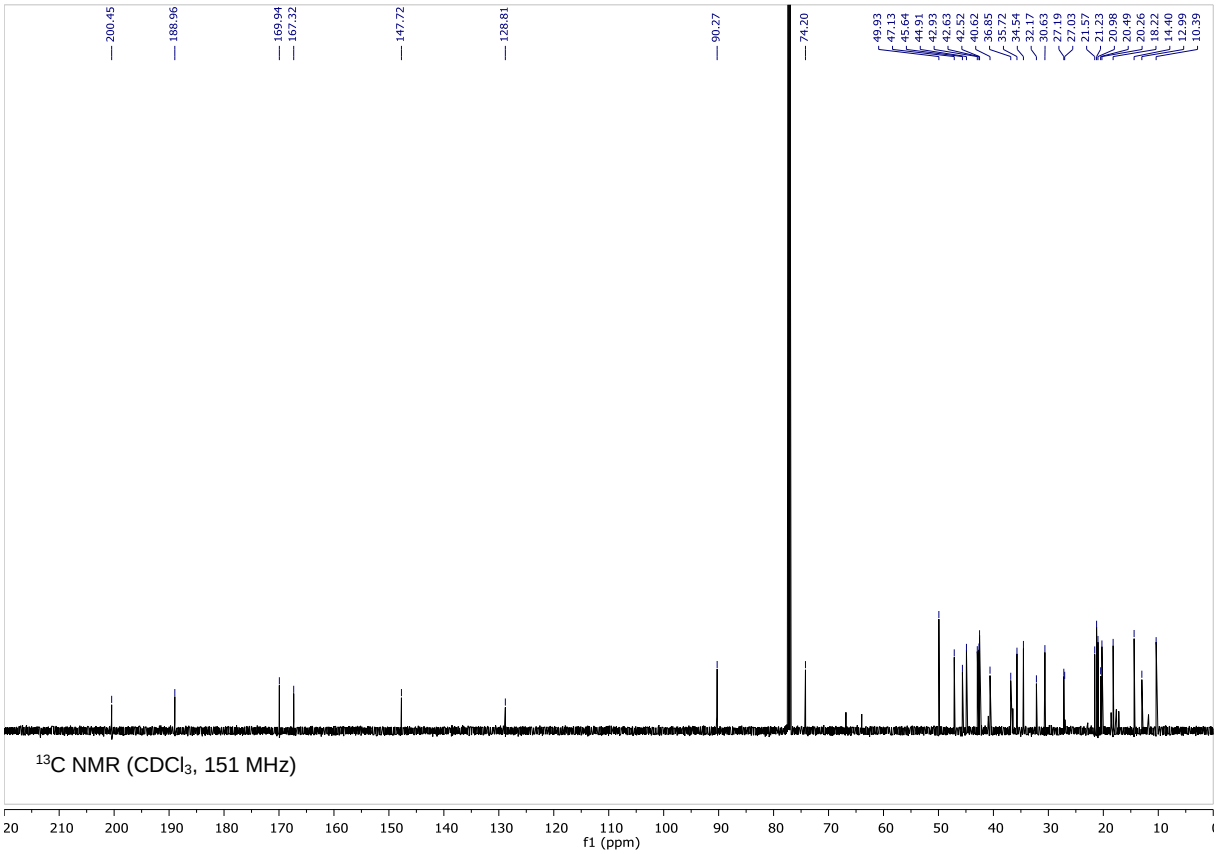
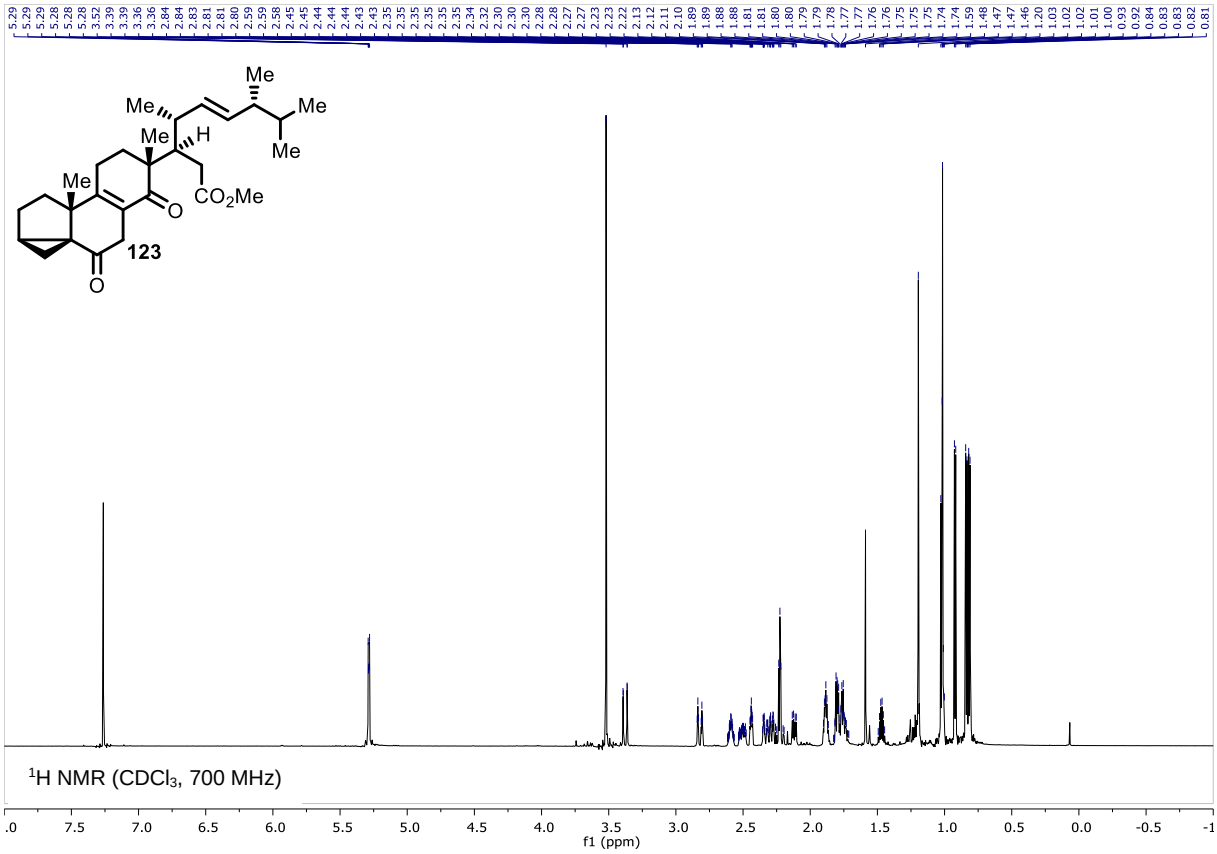
189.40
169.94
151.05
127.73
83.63
74.30
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)



^{1}H NMR ($CDCl_3$, 600 MHz)



^{13}C NMR ($CDCl_3$, 151 MHz)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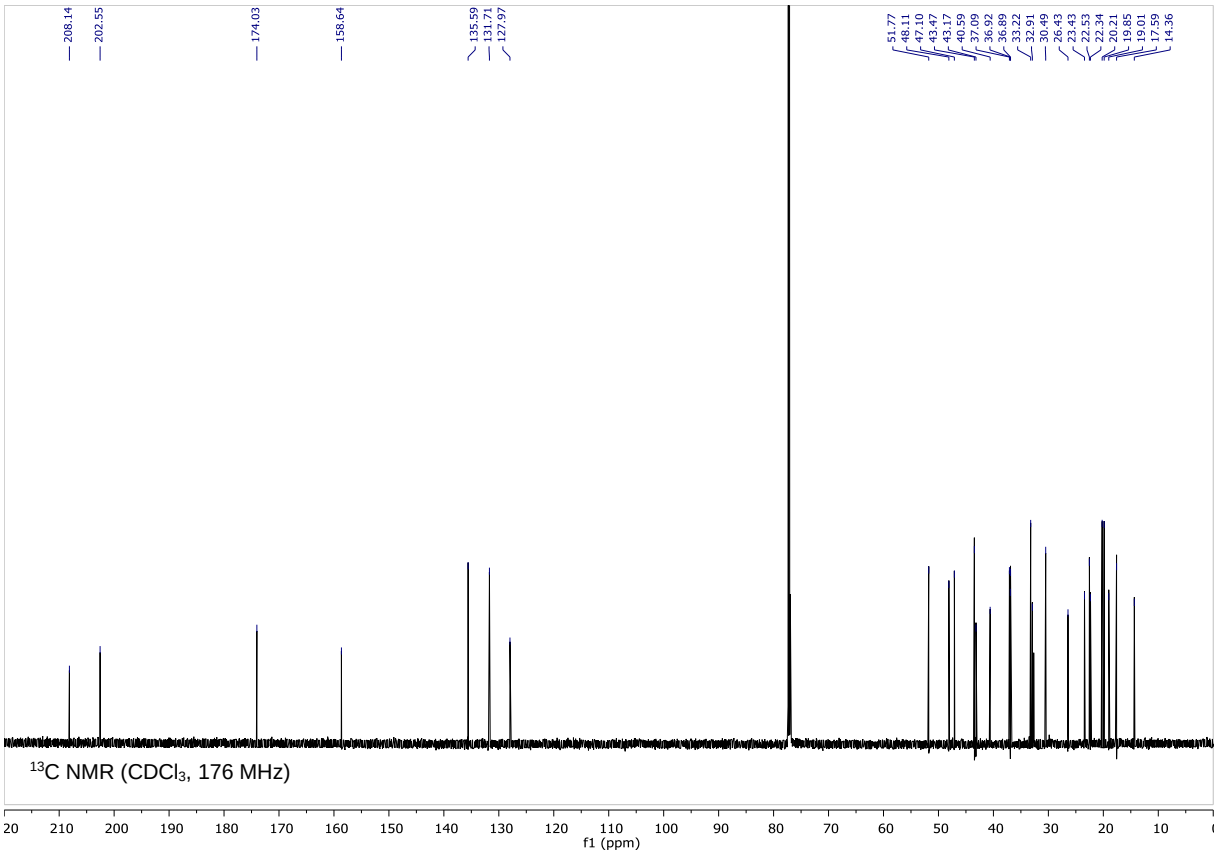
Me
Me
H
Me
Me
Me
CO2Me
O
123
O
1H NMR (CDCl3, 700 MHz)
f1 (ppm)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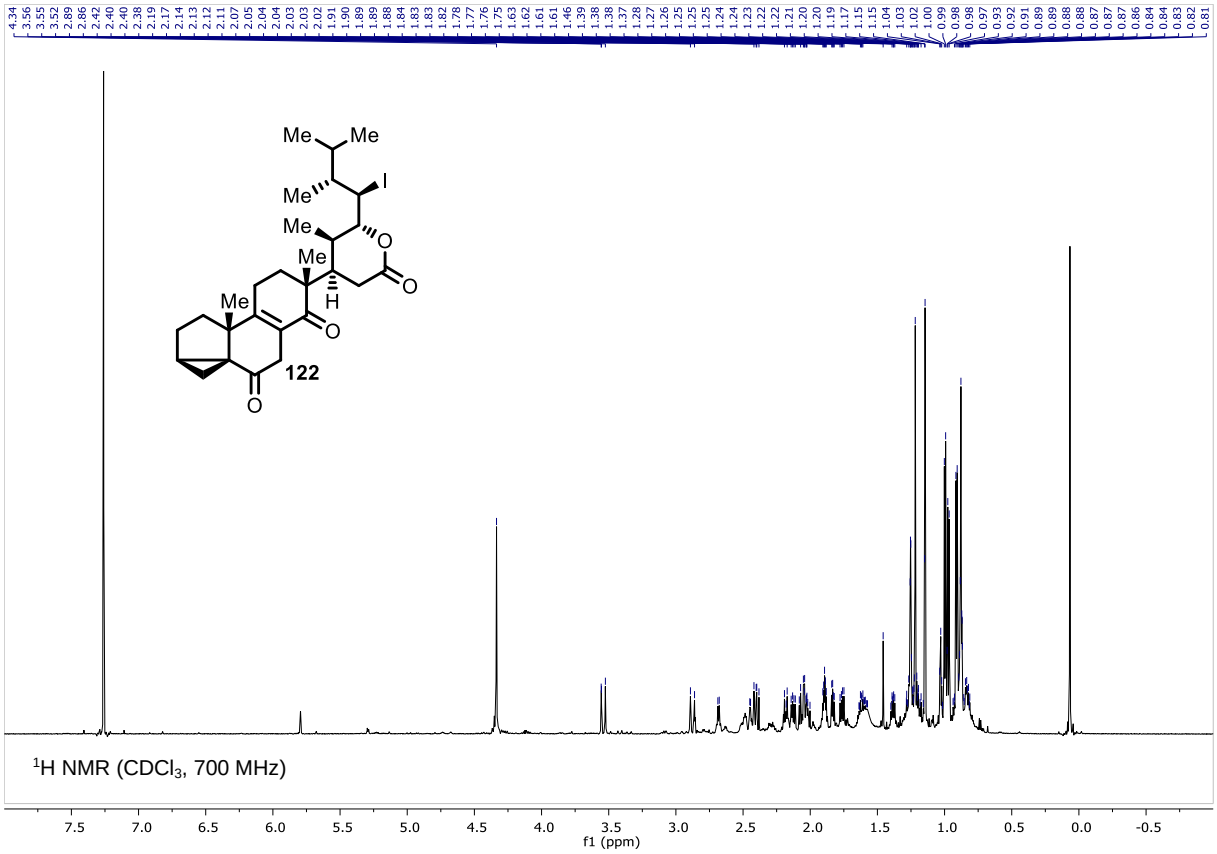
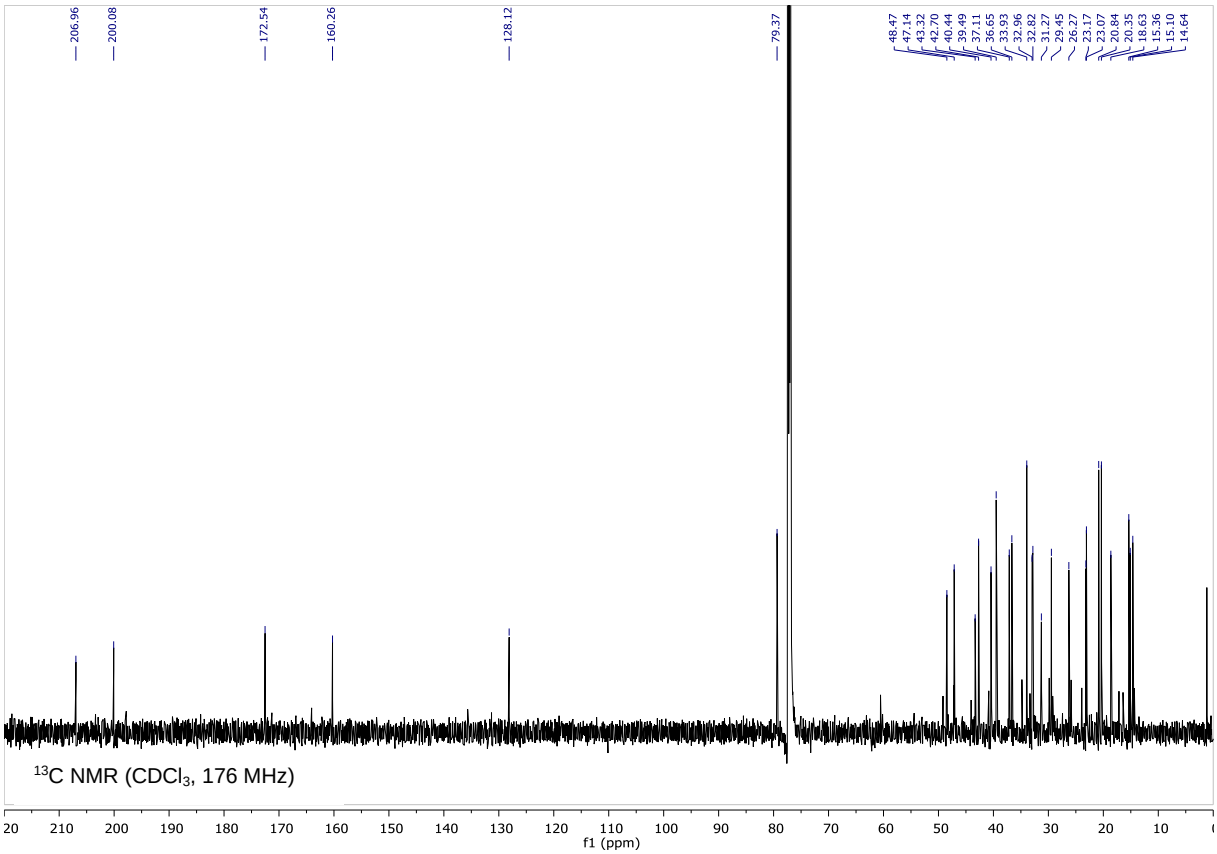
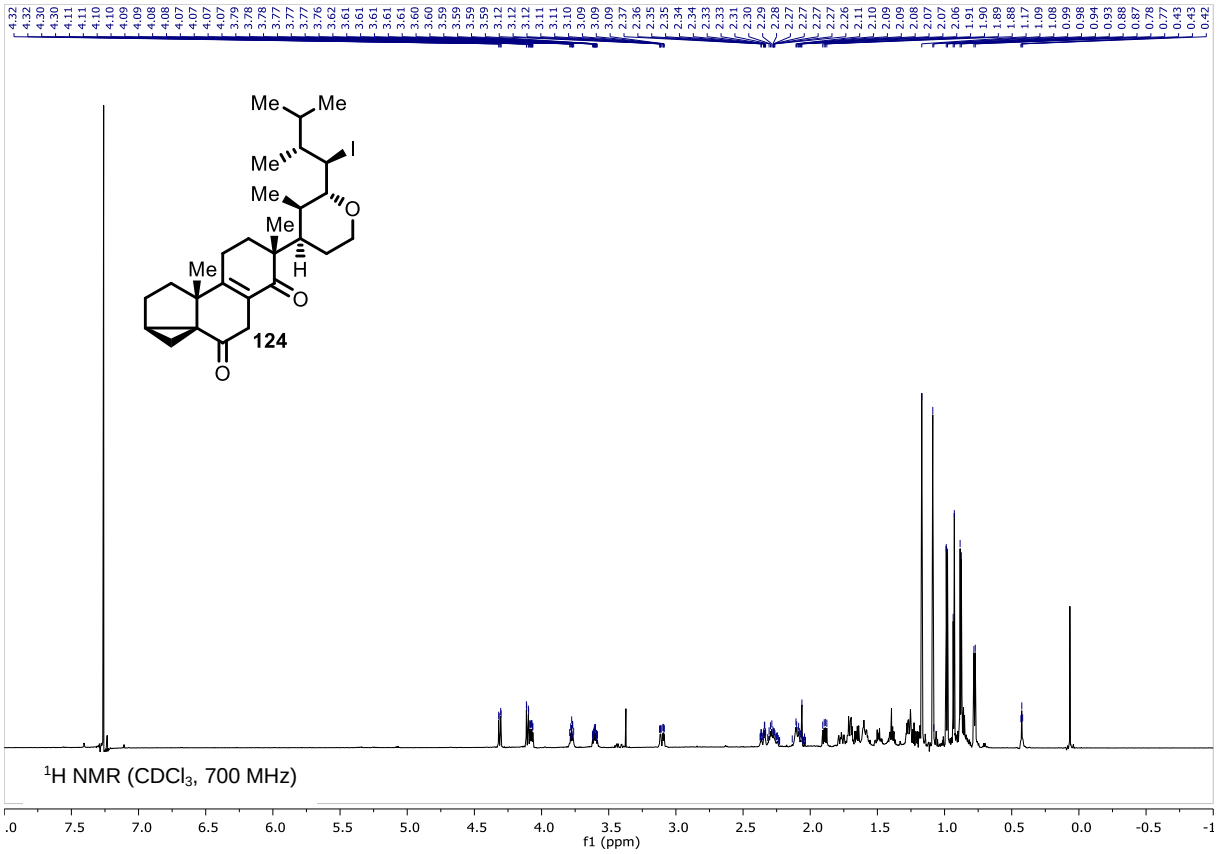
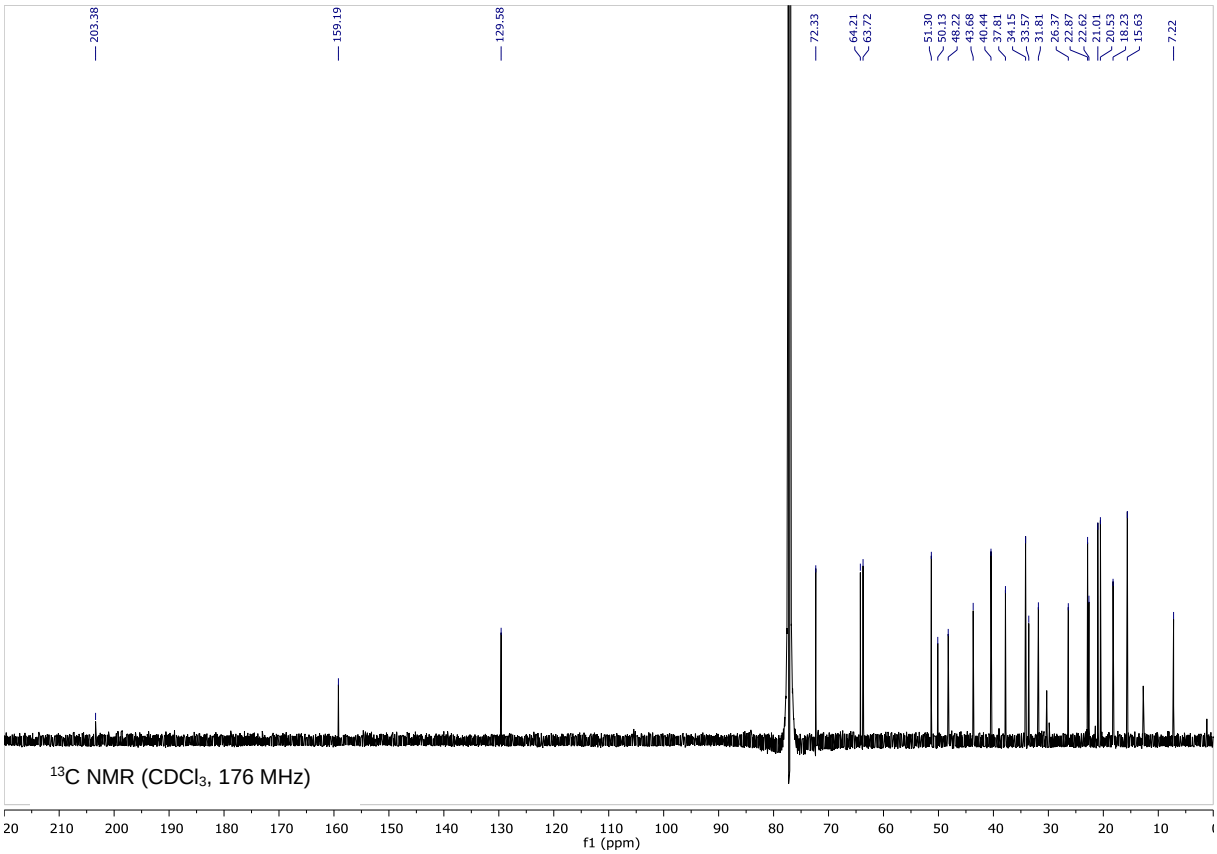
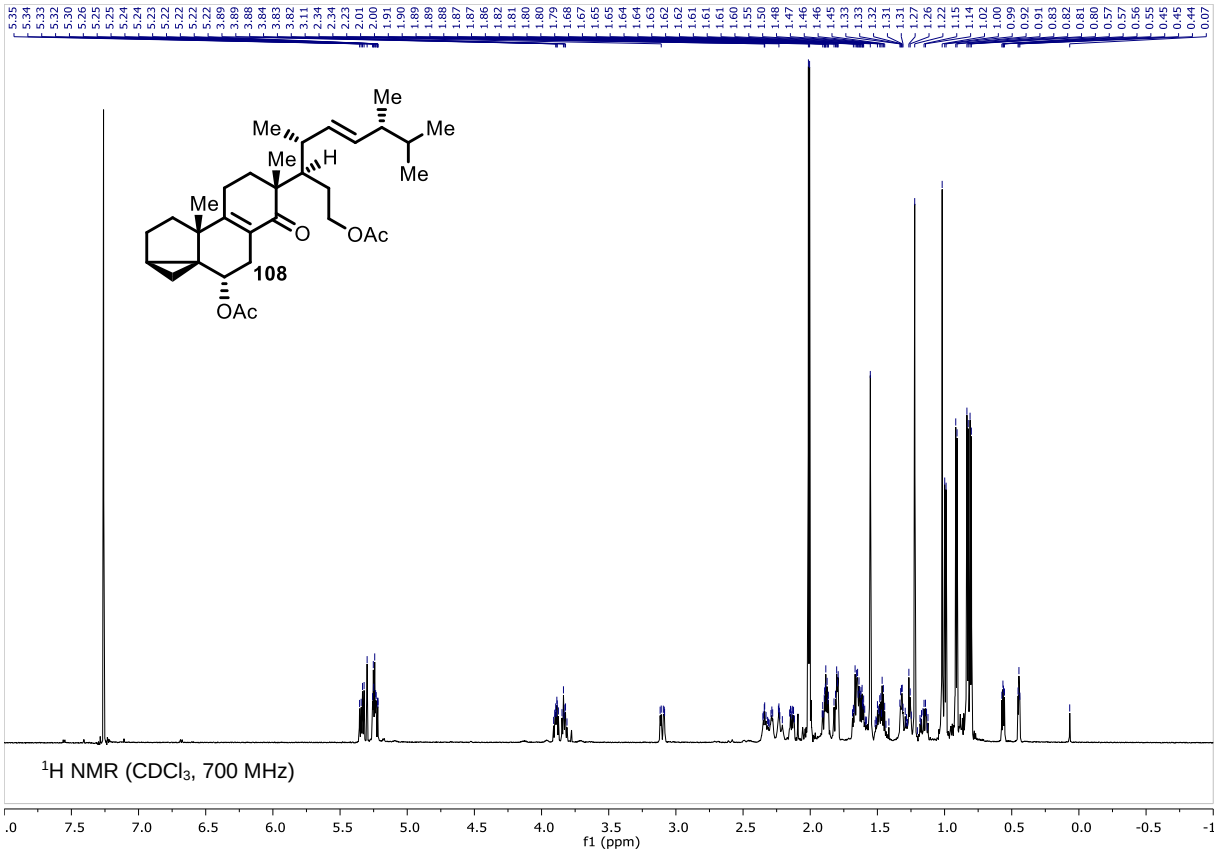
202.55
174.03
158.64
135.59
131.71
127.97
51.77
48.11
47.10
43.47
43.17
40.59
37.09
36.92
36.89
33.22
32.91
30.49
26.43
22.43
22.33
22.34
20.21
19.85
19.01
17.59
14.36
13C NMR (CDCl3, 176 MHz)
f1 (ppm)

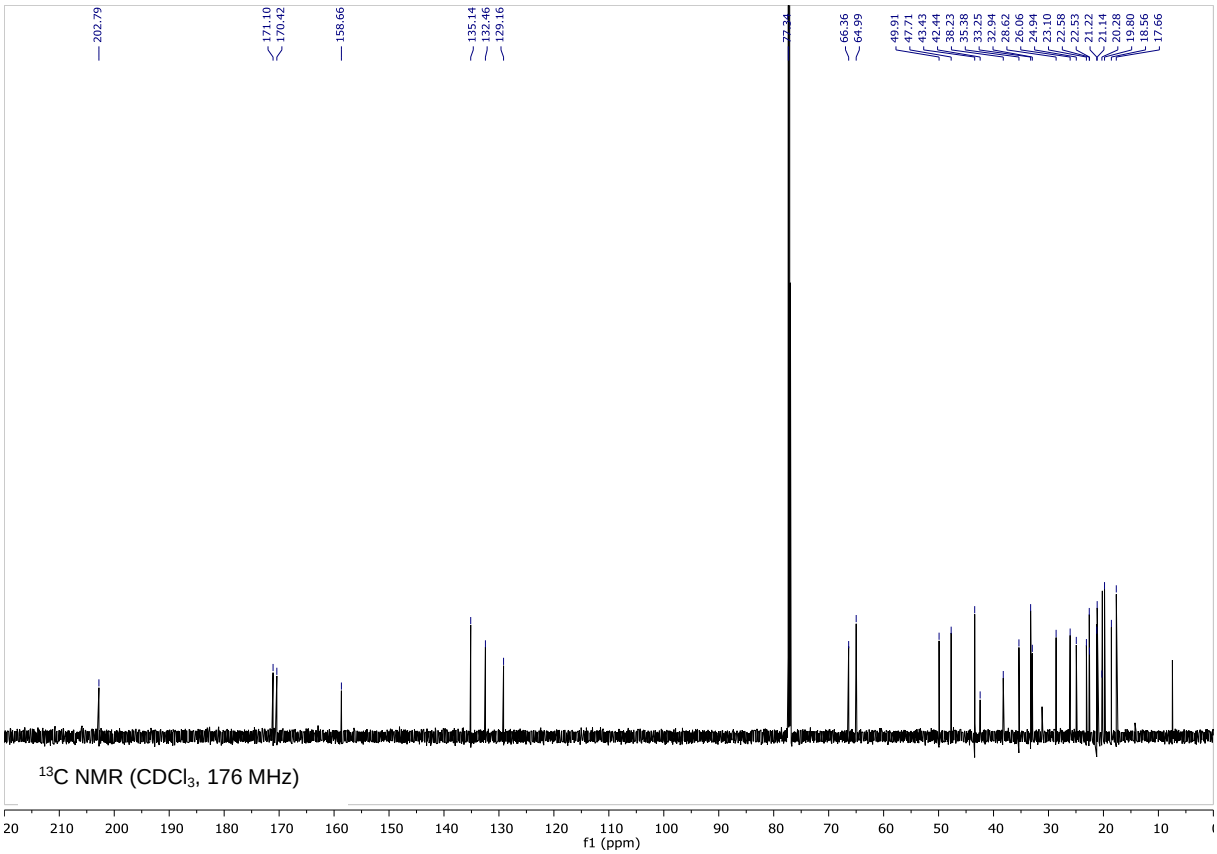

Me
Me
Me
I
Me
O
Me
O
Me
H
O
122
O
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)


206.96
200.08
172.54
160.26
128.12
79.37
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


Me
Me
Me
I
Me
O
Me
H
Me
O
O
124
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)


203.38
159.19
129.58
72.33
64.21
63.72
51.30
50.13
48.22
43.68
40.44
37.81
34.15
33.57
31.81
26.37
22.87
22.62
21.01
20.53
18.23
15.63
7.22
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


Me
Me
Me
Me
H
Me
Me
O
OAc
108
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)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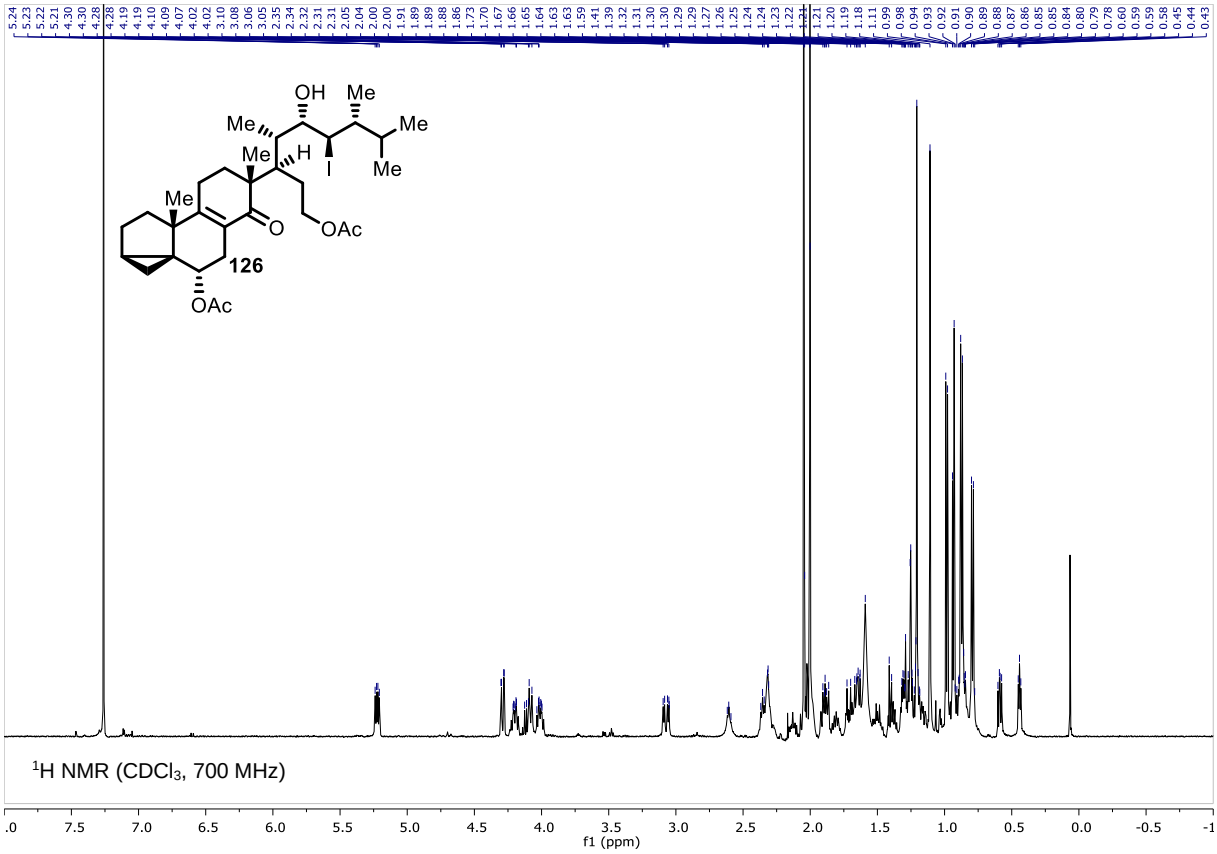
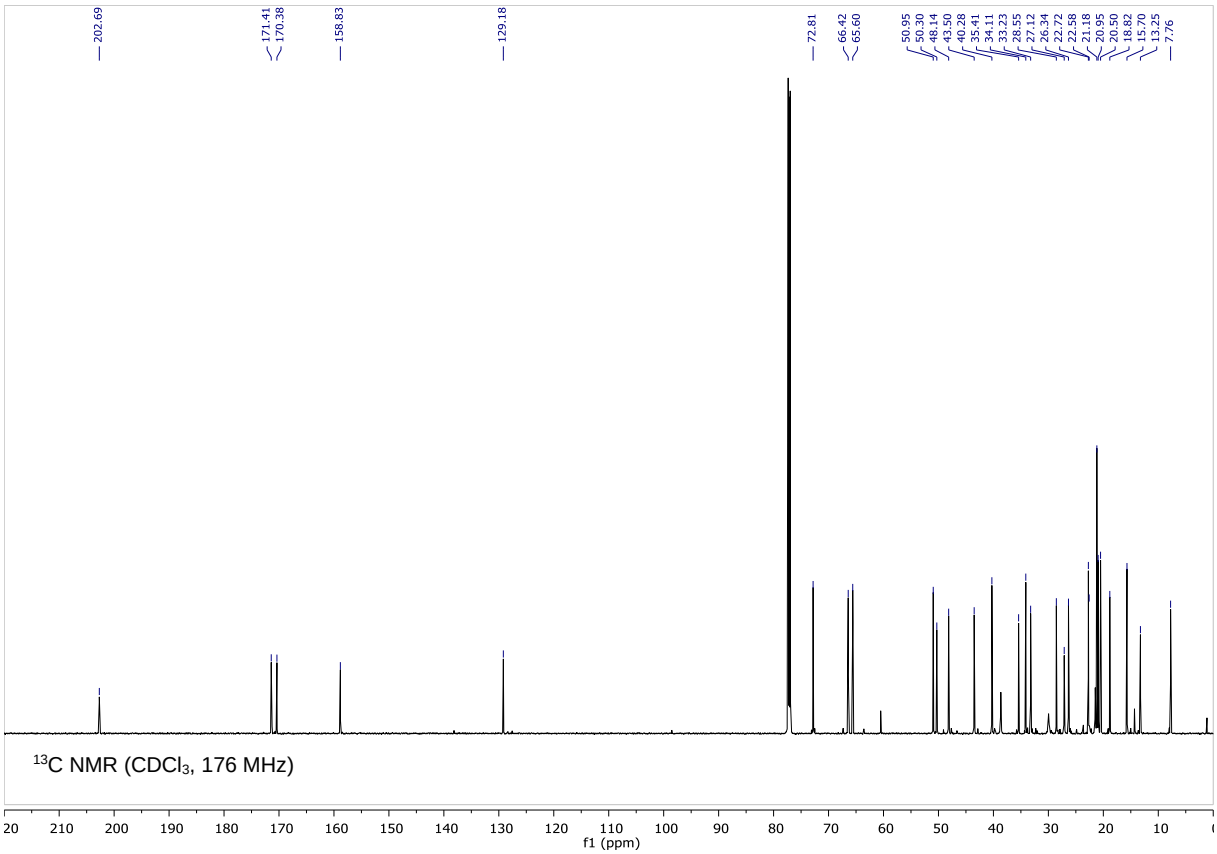
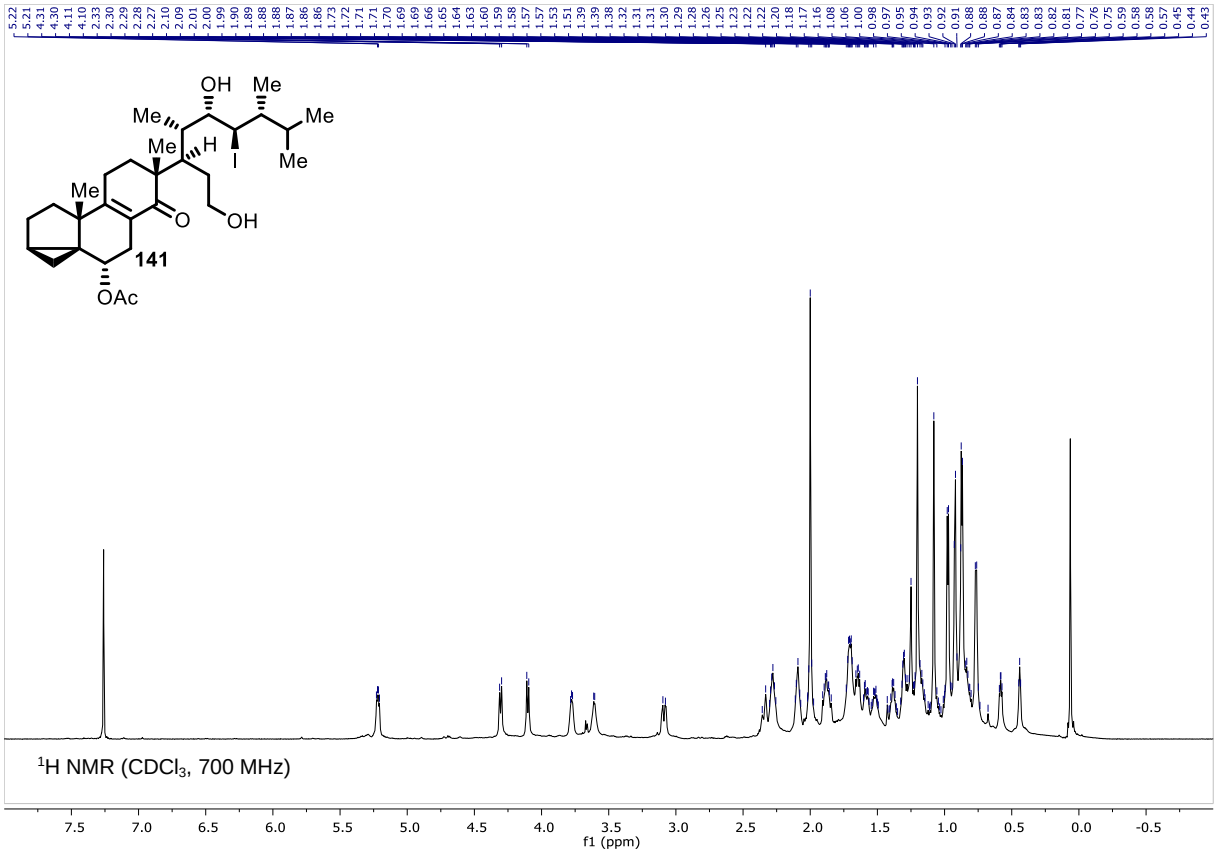
171.10
170.42
158.66
135.14
132.46
129.16
77.34
66.36
64.99
49.91
47.71
43.43
42.44
38.23
35.38
33.25
32.94
28.62
26.06
24.94
23.10
22.58
22.53
21.22
21.14
20.28
19.80
18.56
17.66
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

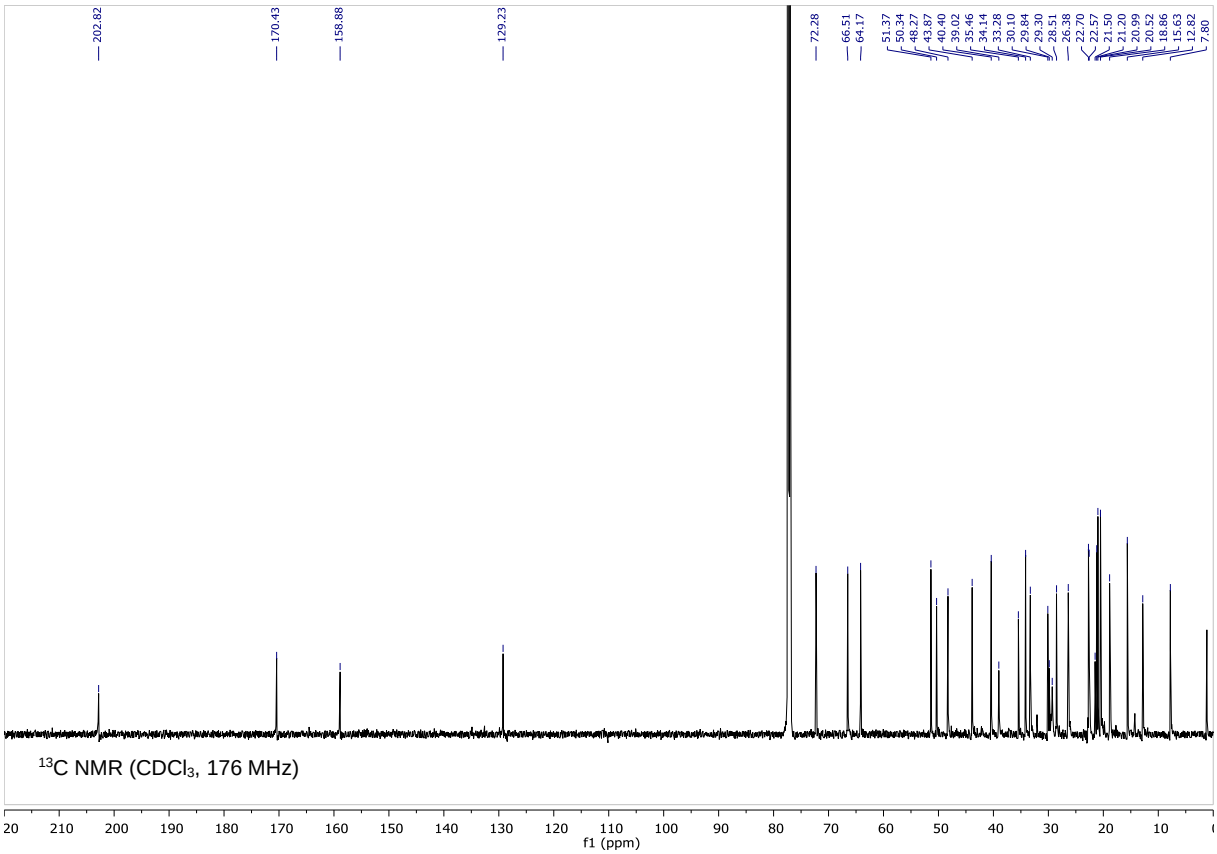


^{1}H NMR ($CDCl_3$, 700 MHz)



^{13}C NMR ($CDCl_3$, 176 MHz)


OH
Me
Me
Me
Me
H
I
Me
Me
O
OH
141
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)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158.88
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72.28
66.51
64.17
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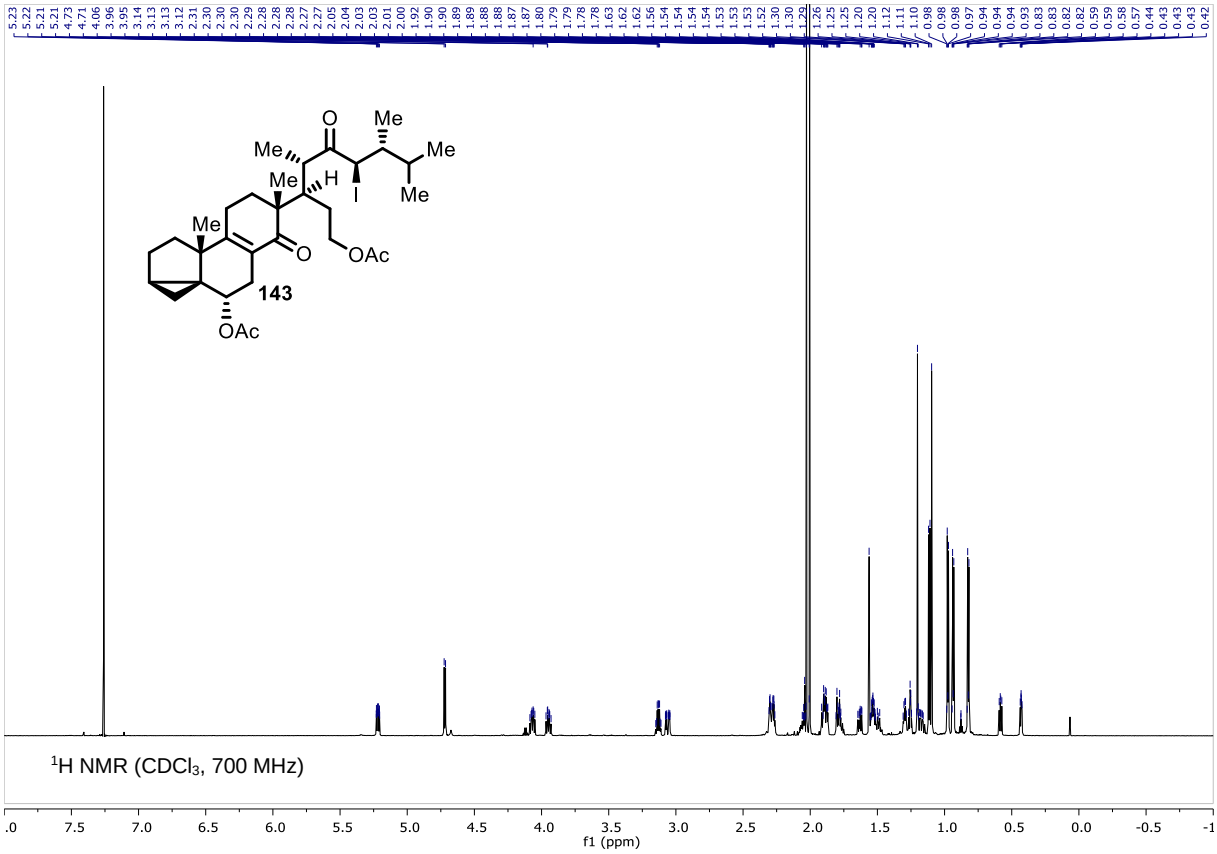
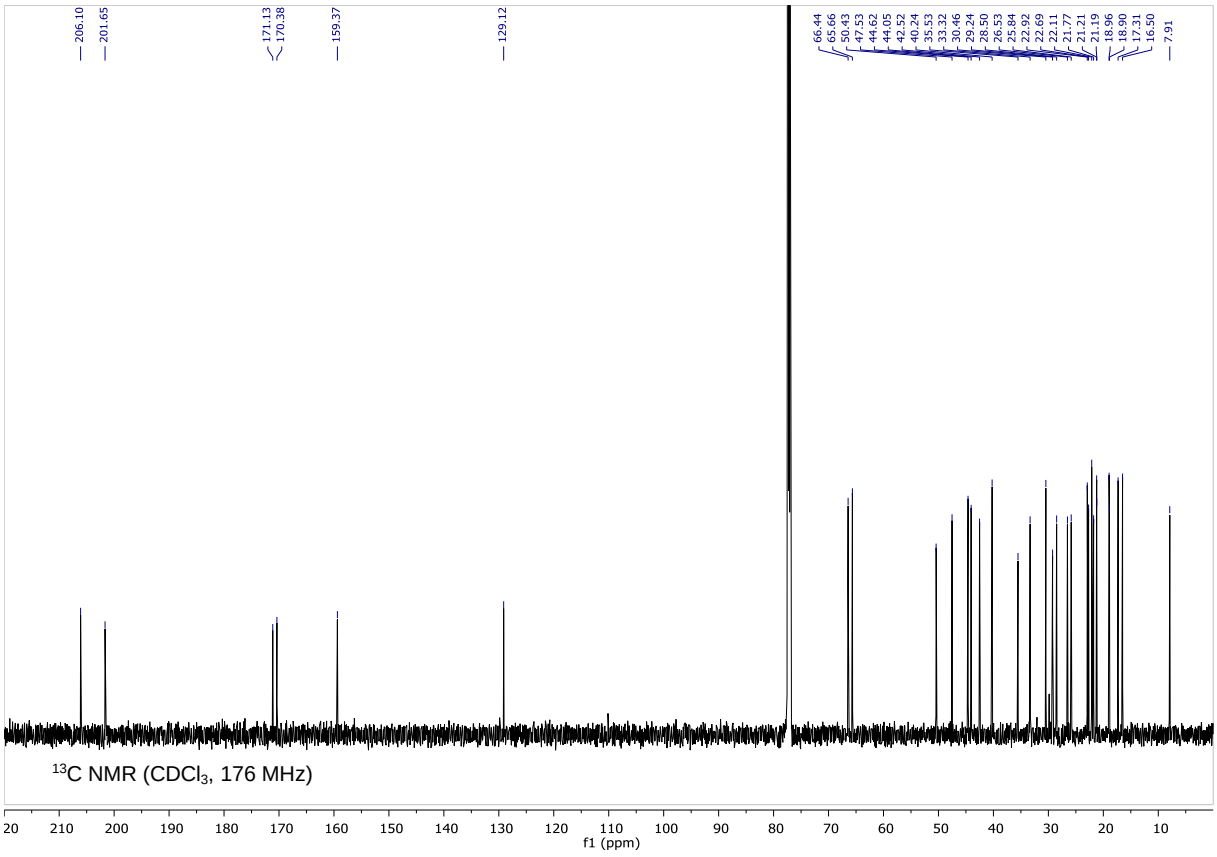
f1 (ppm)


Me
Me
Me
O
H
I
Me
Me
Me
O
OAc
143
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)


206.10
201.65
171.13
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159.37
129.12
66.44
65.66
50.43
47.53
44.62
44.05
42.52
40.24
35.53
33.32
30.46
29.24
28.50
26.53
25.84
22.92
22.69
22.11
21.77
21.21
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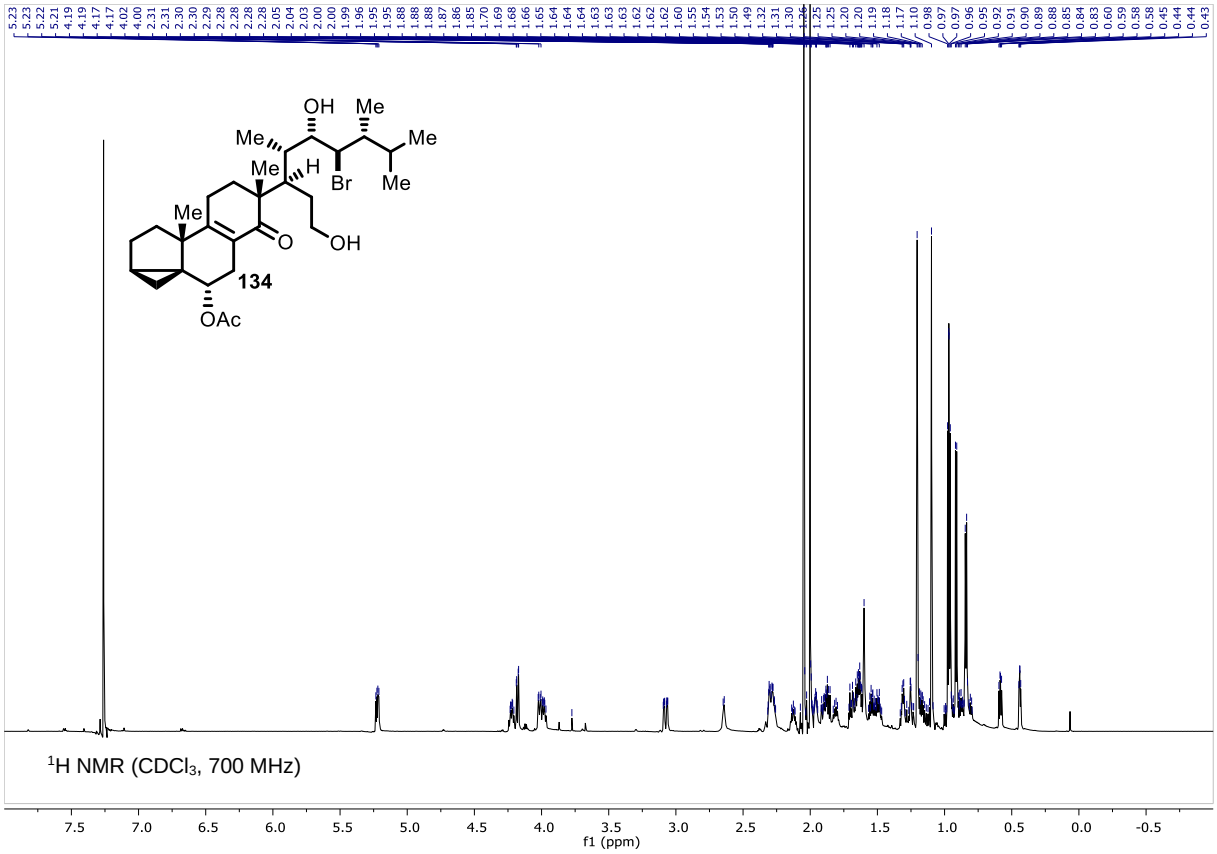
18.96
18.90
17.31
16.50
7.91
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)



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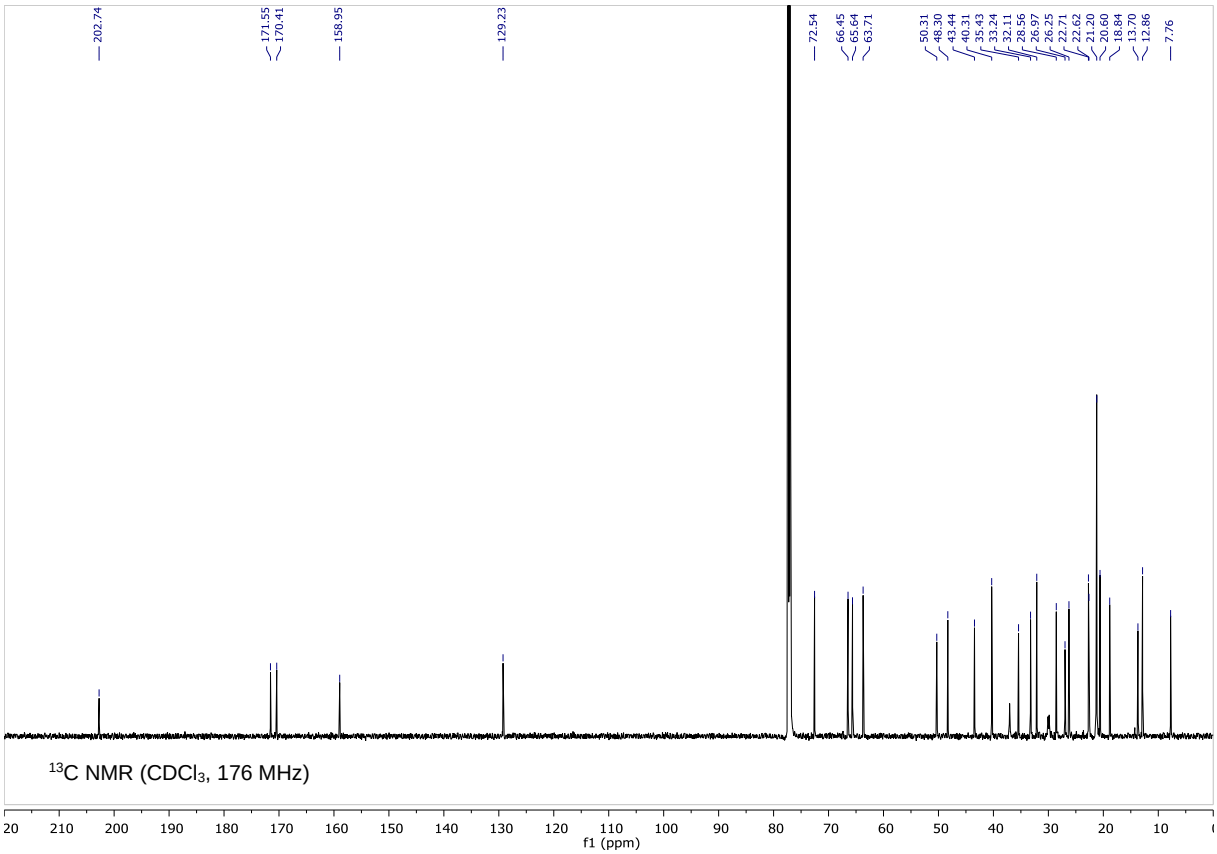
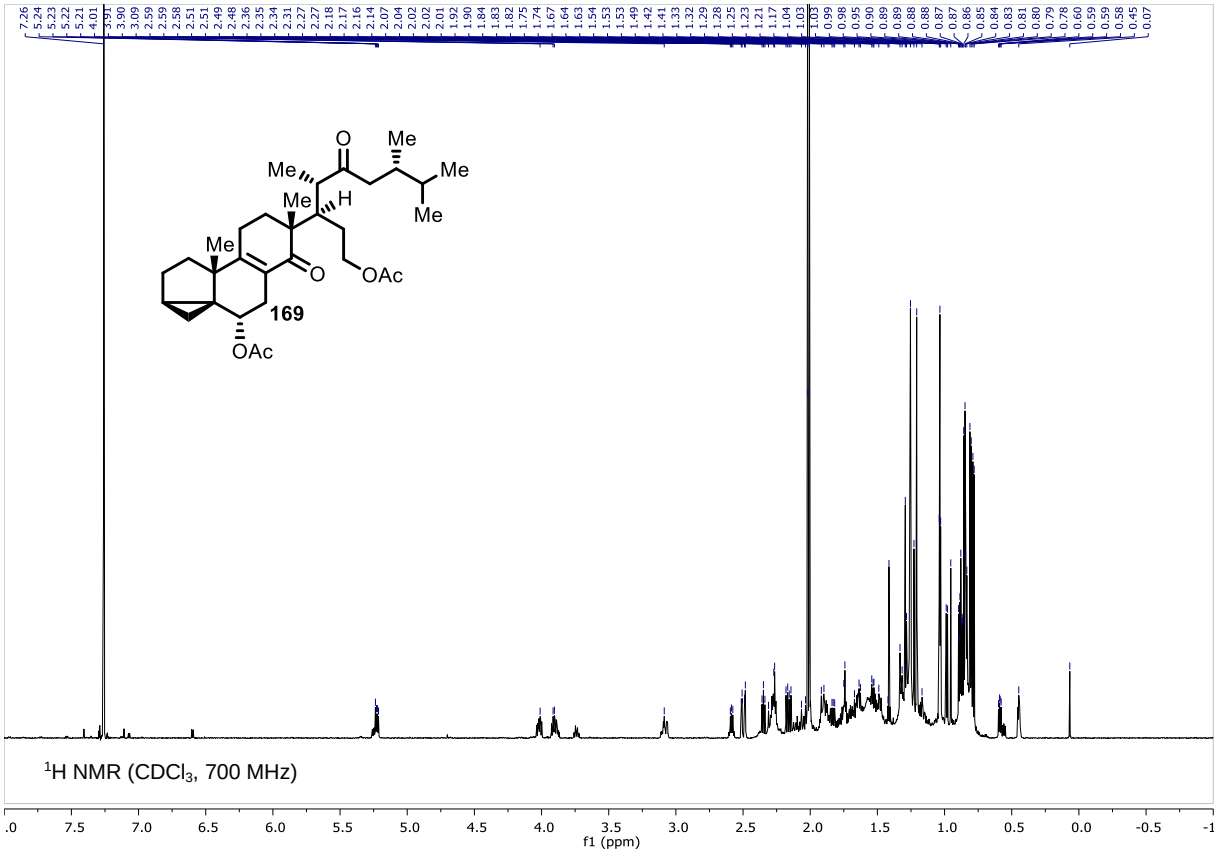
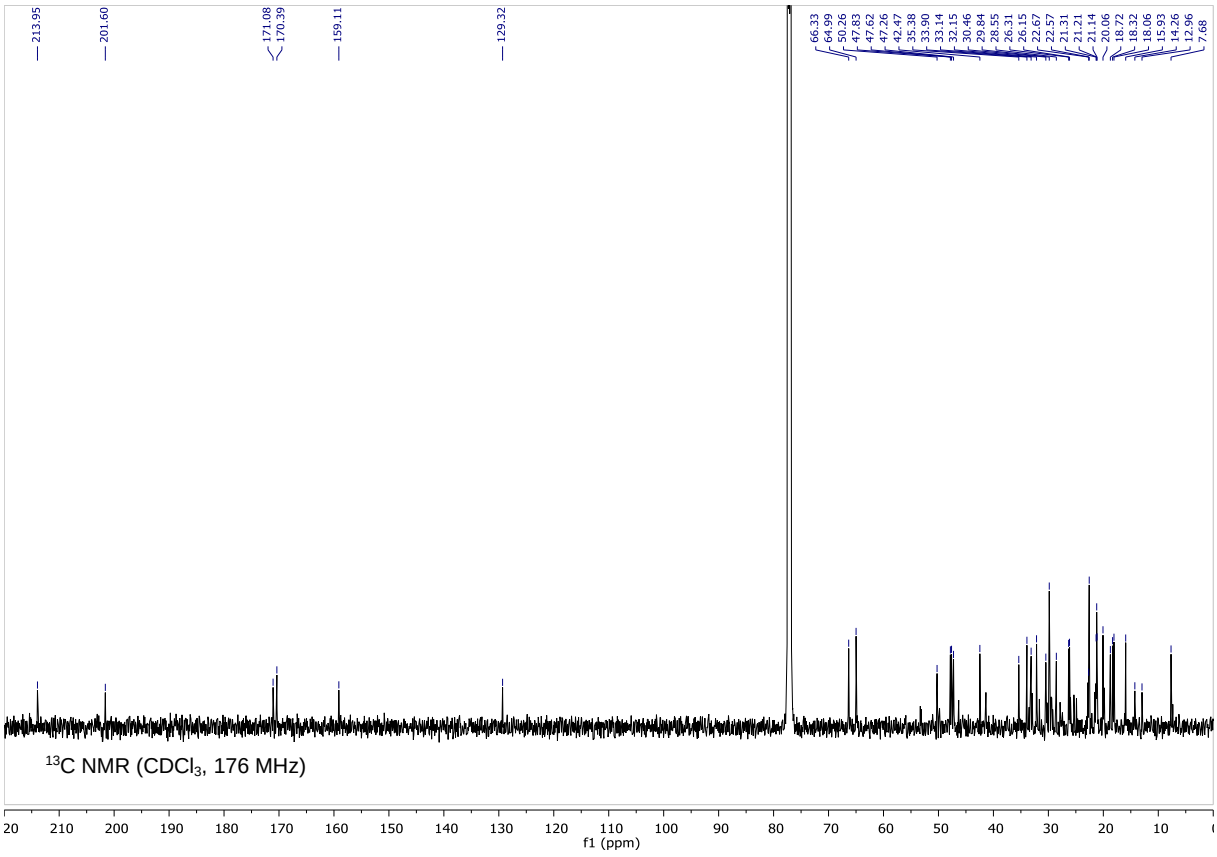
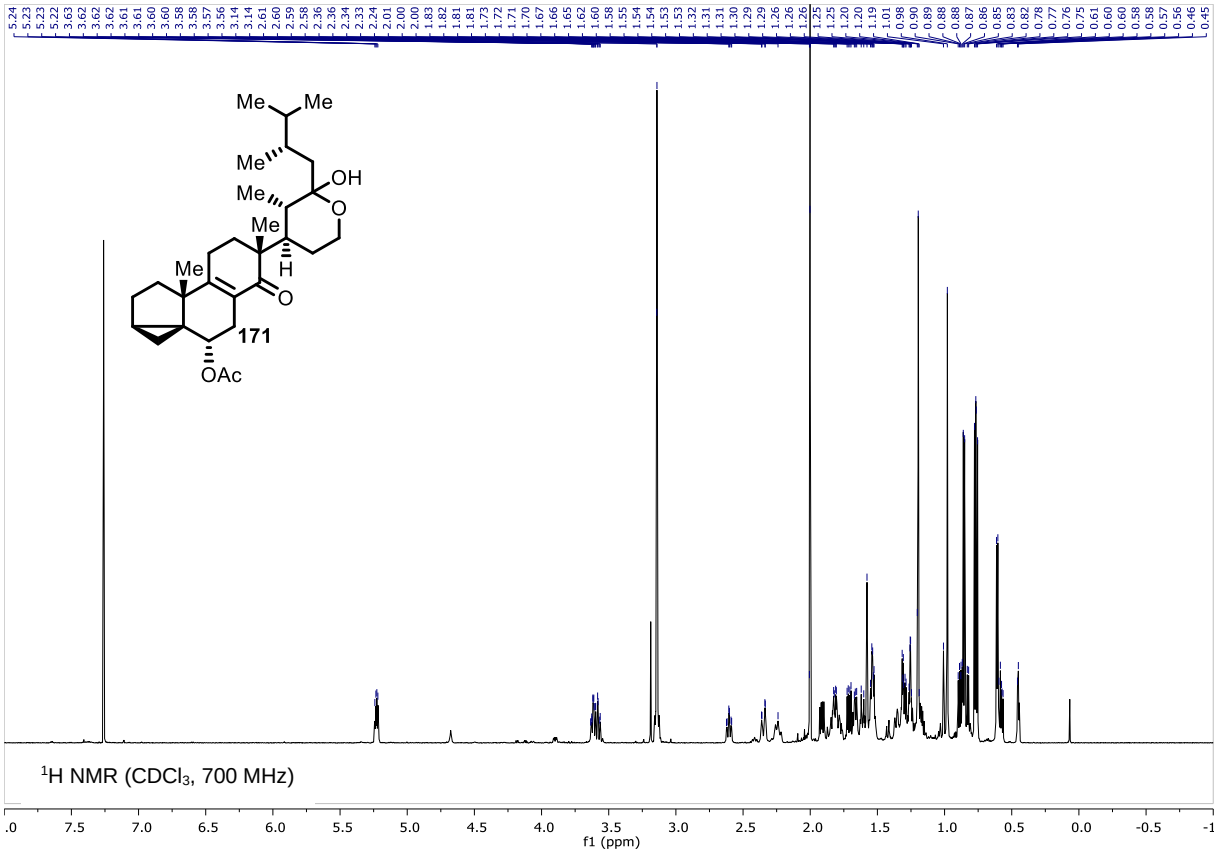


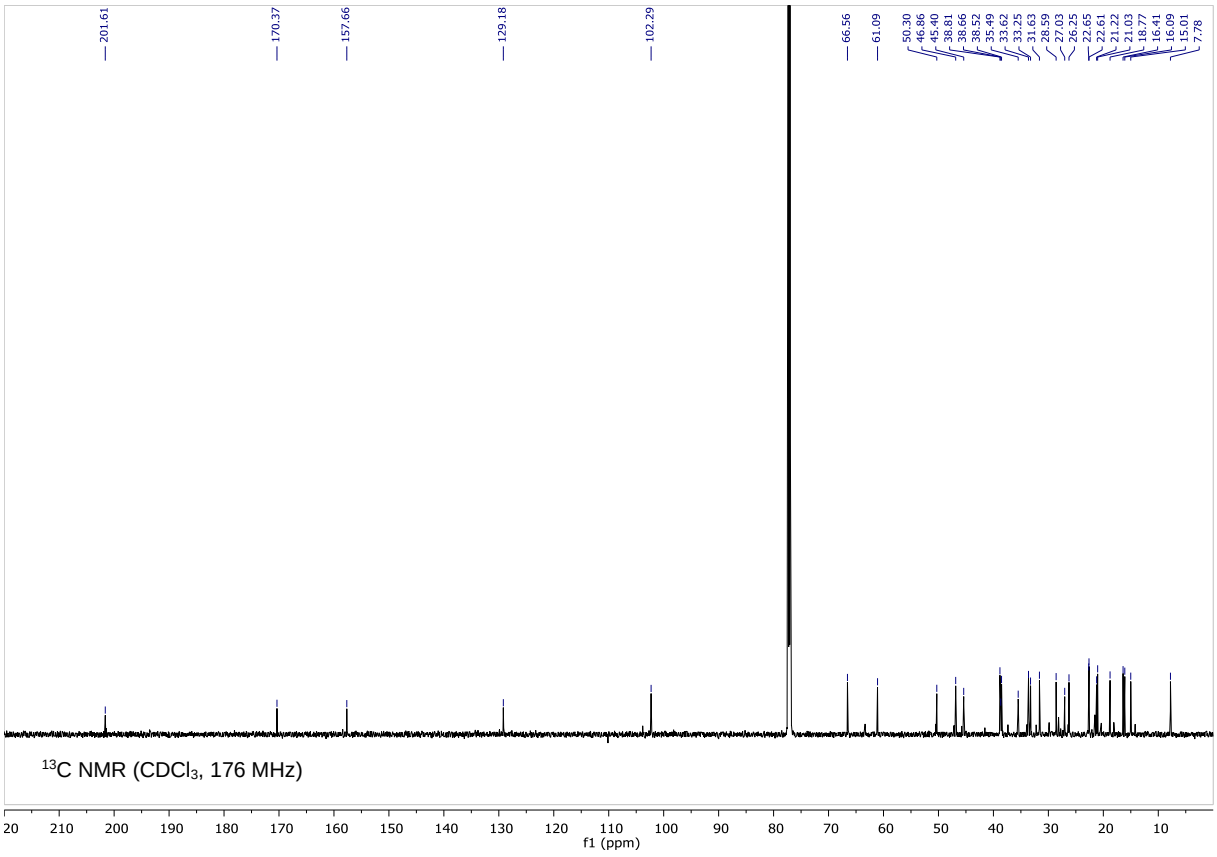
^{13}C NMR ($CDCl_3$, 176 MHz)


Me
Me
Me
Me
H
Me
O
O
OAc
169
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

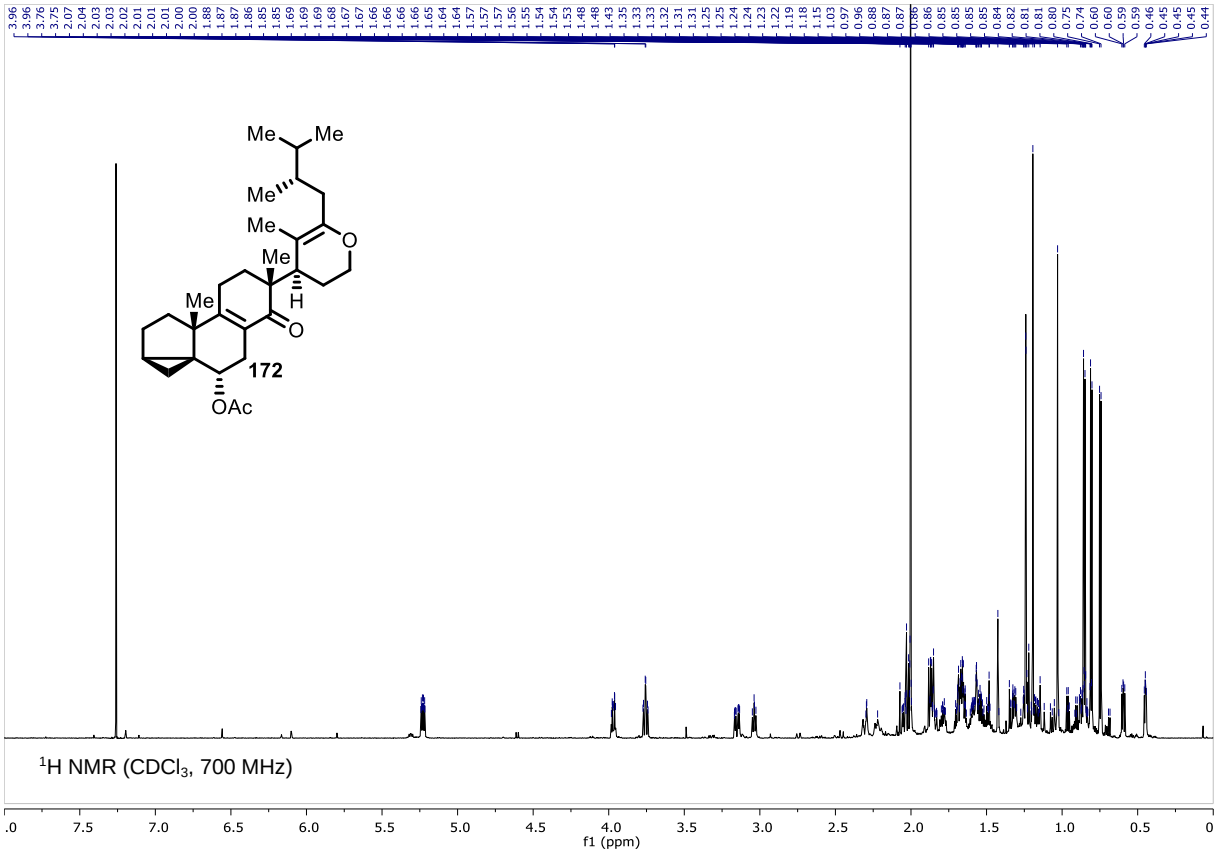

213.95
201.60
171.08
170.39
159.11
129.32
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)



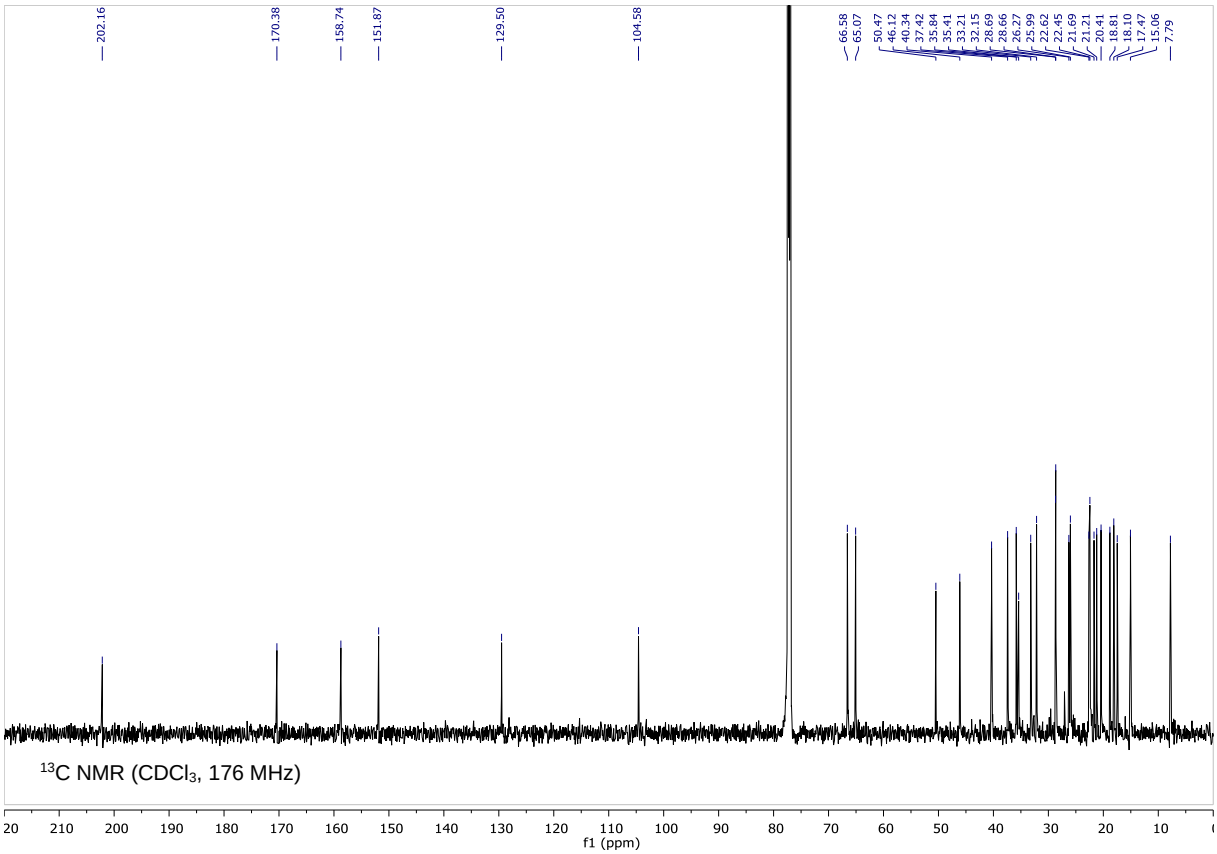
^{1}H NMR ($CDCl_3$, 700 MHz)



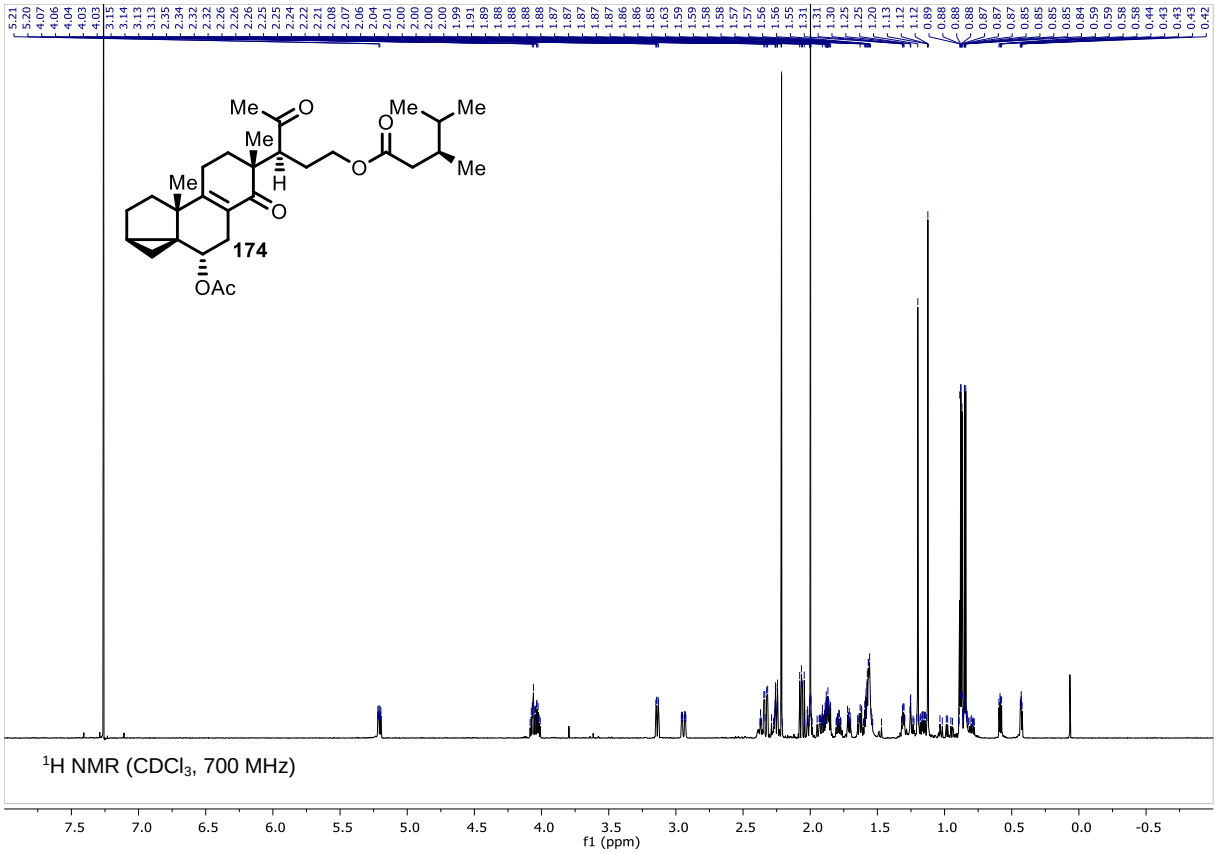
^{13}C NMR ($CDCl_3$, 176 MHz)



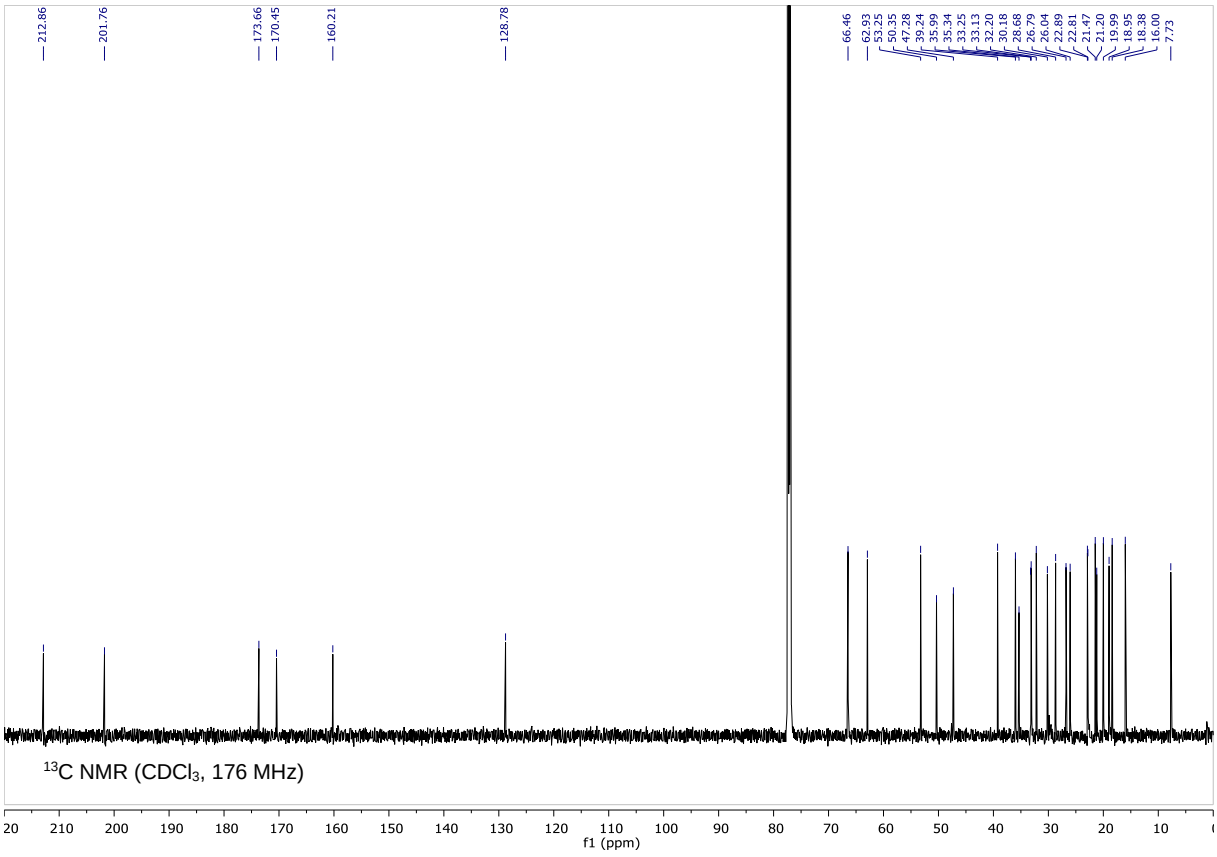
^{1}H NMR ($CDCl_3$, 700 MHz)



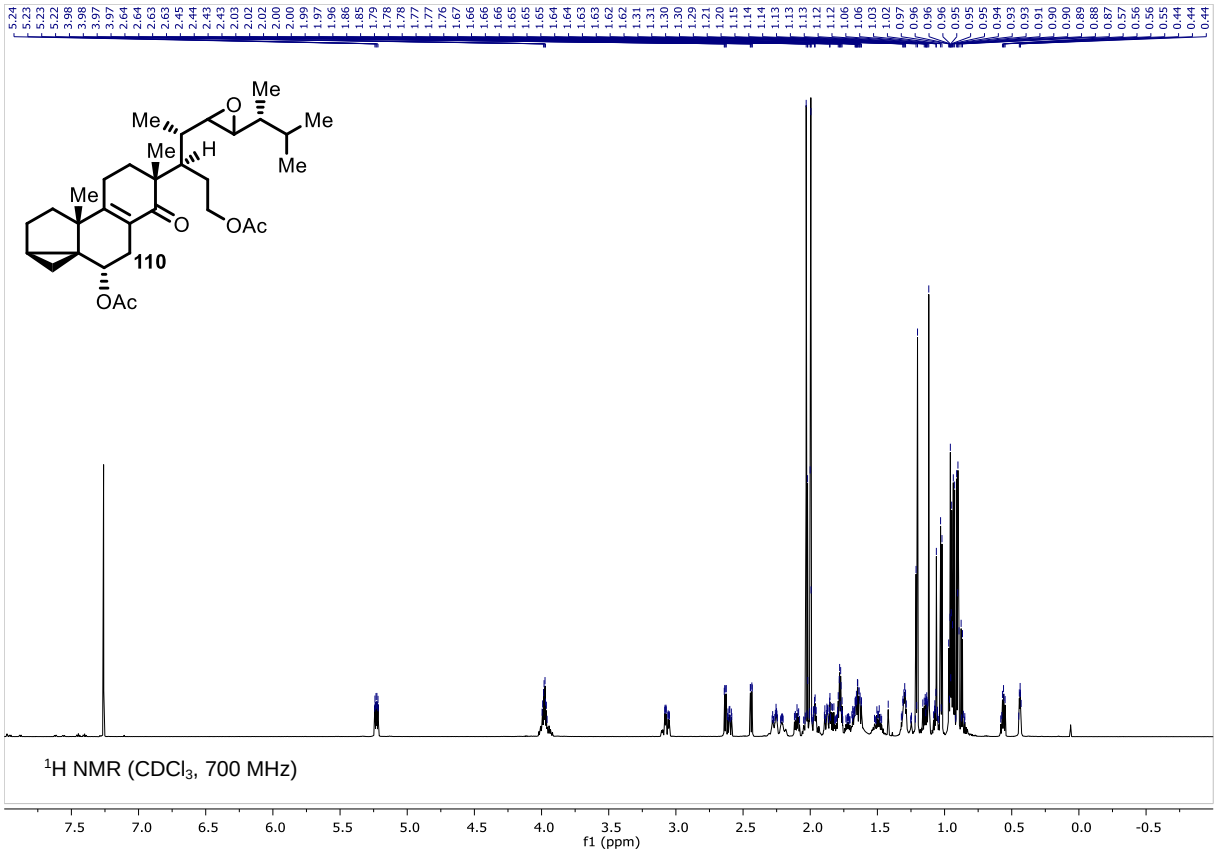
^{13}C NMR ($CDCl_3$, 176 MHz)

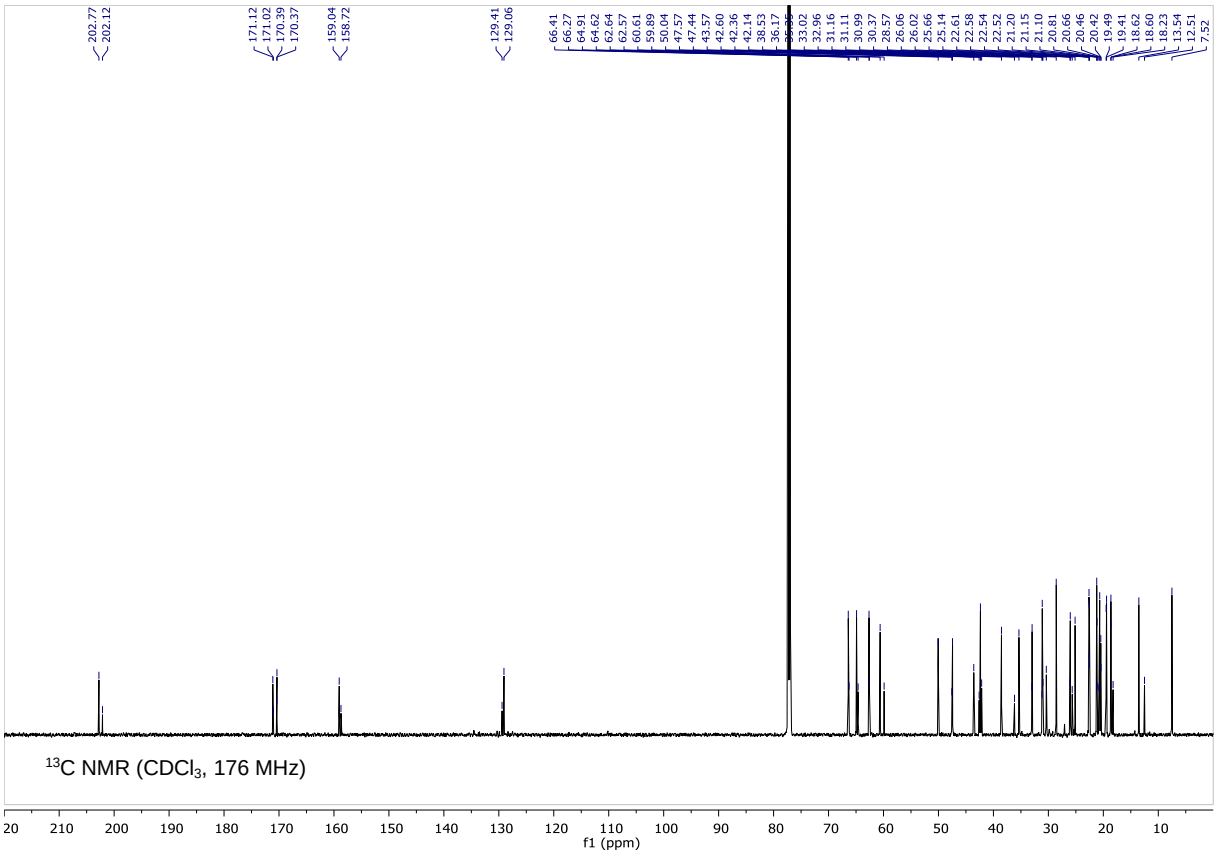


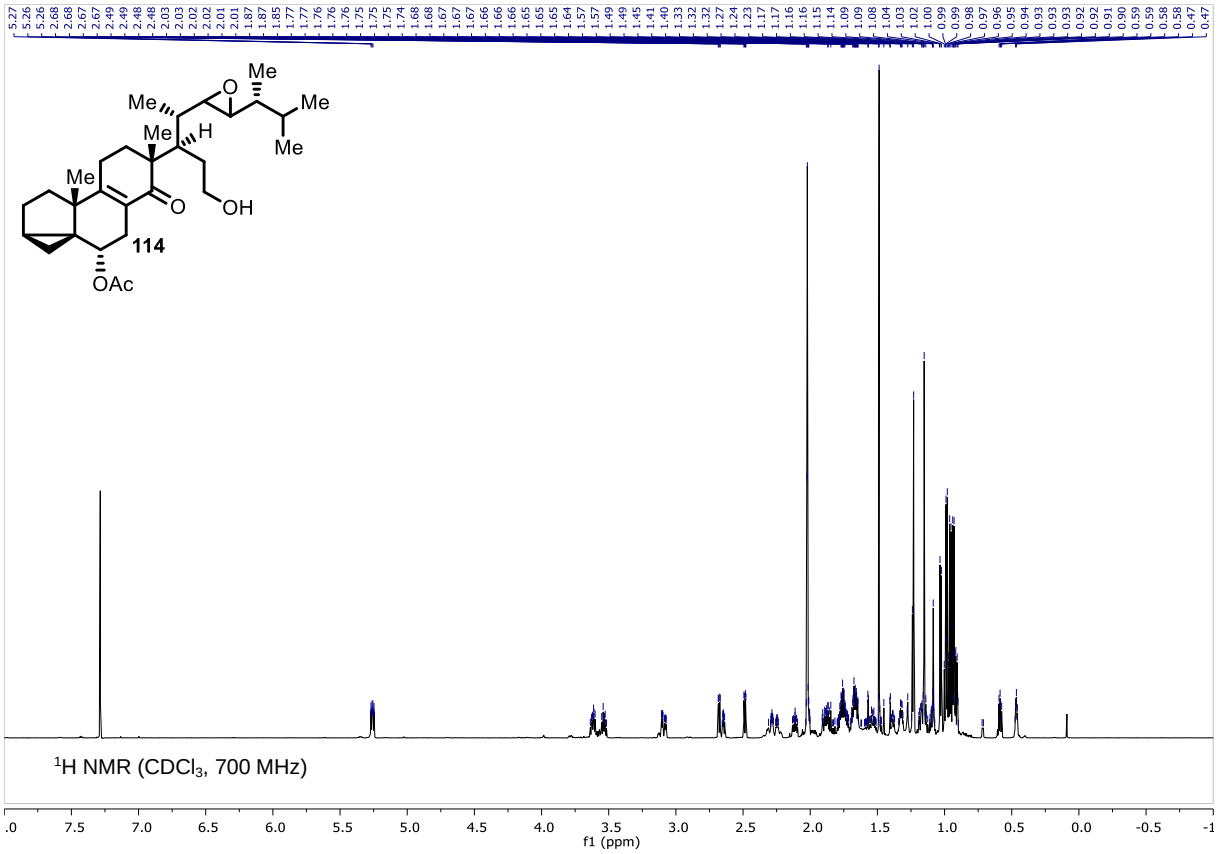
^{1}H NMR ($CDCl_3$, 700 MHz)

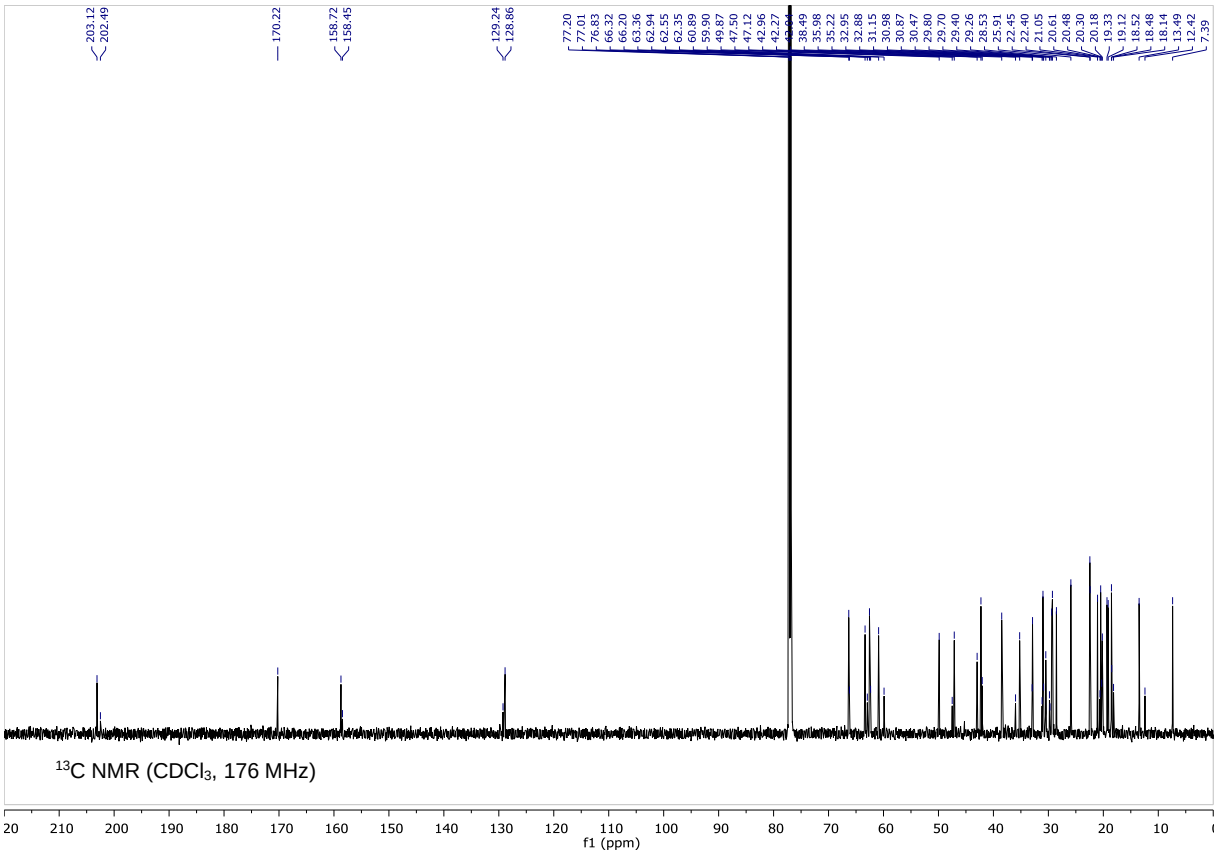


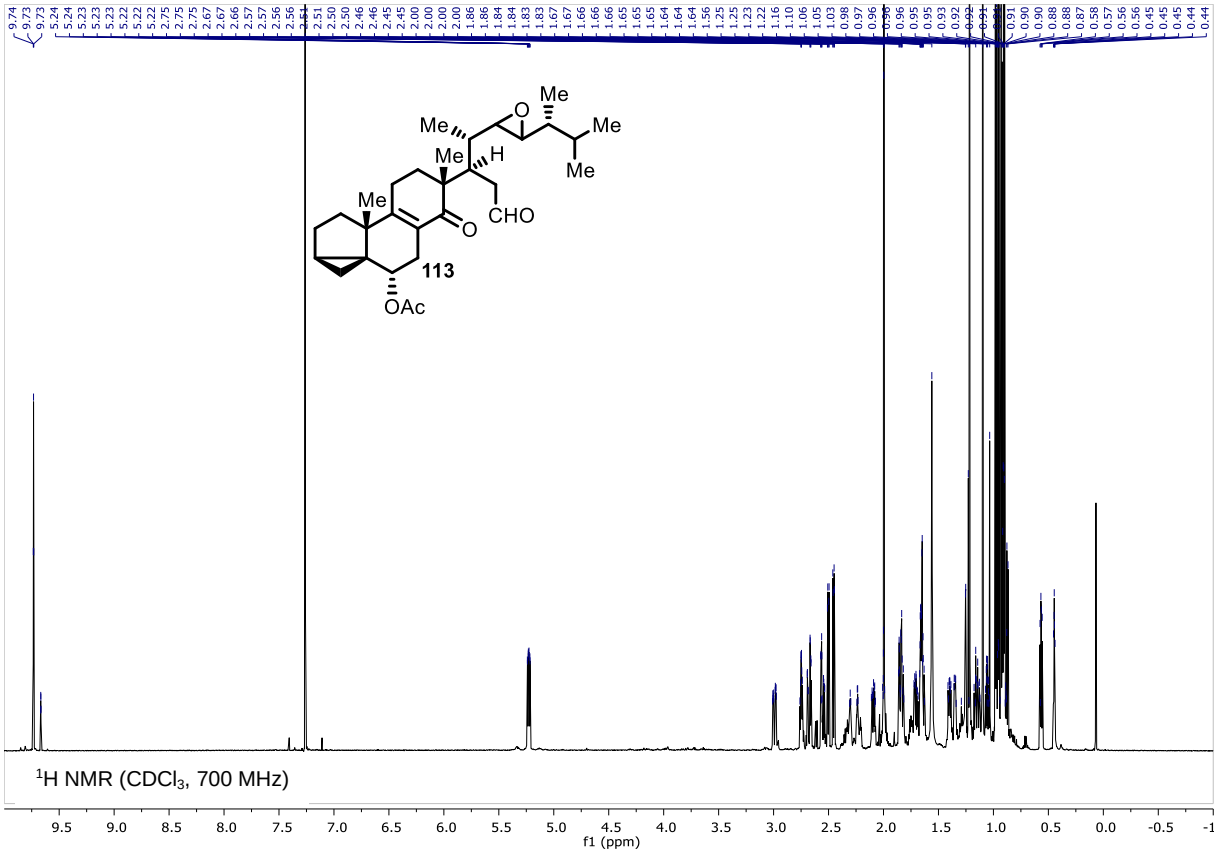
^{13}C NMR ($CDCl_3$, 176 MHz)

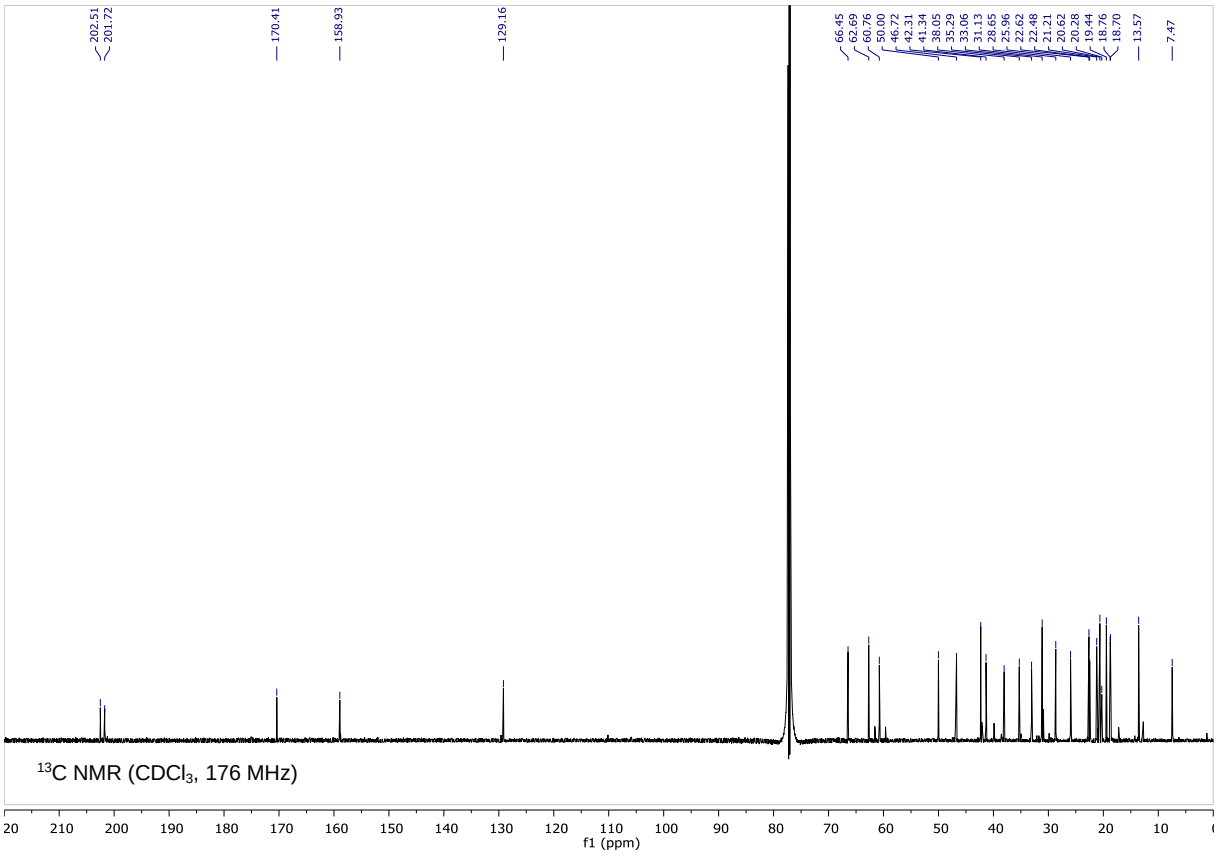

Me
O
Me
Me
Me
H
Me
Me
O
OAc
110
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

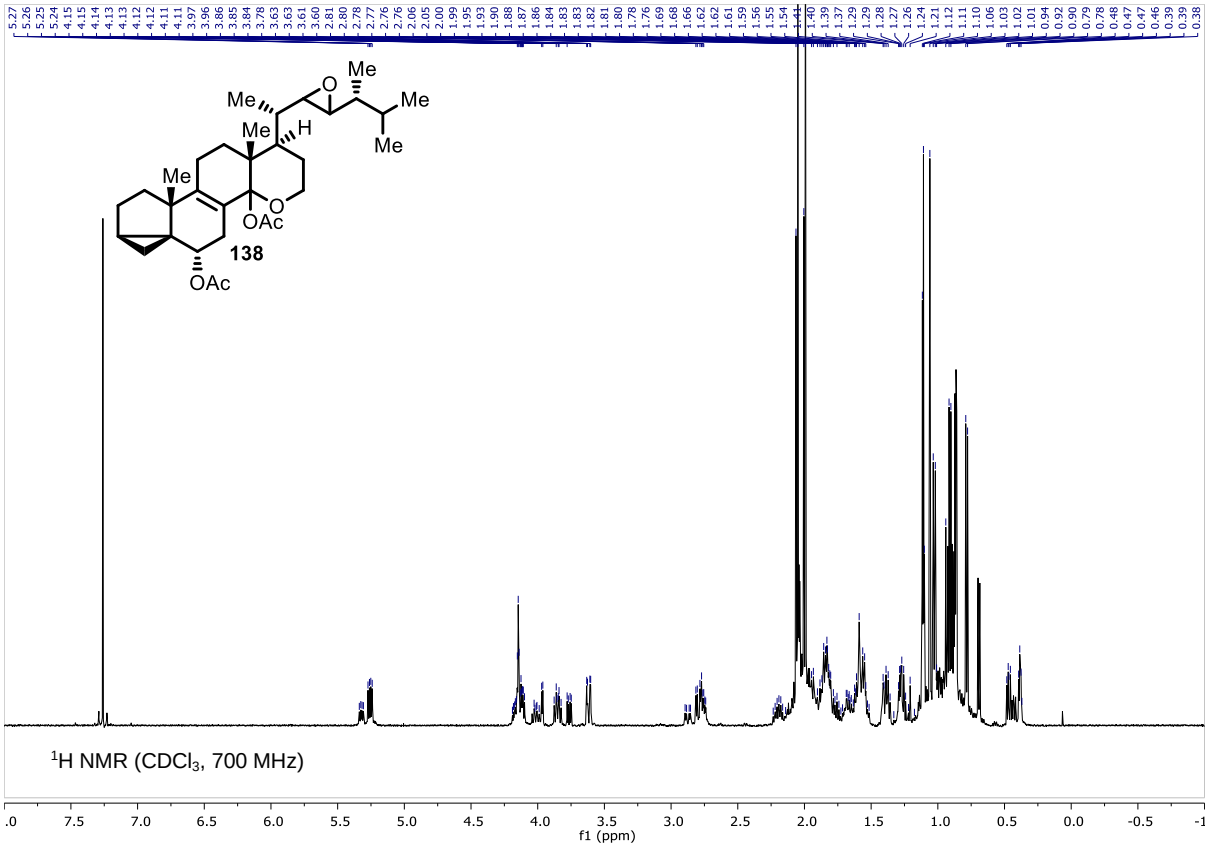

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


Me
Me
O
Me
Me
H
Me
Me
O
OH
114
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

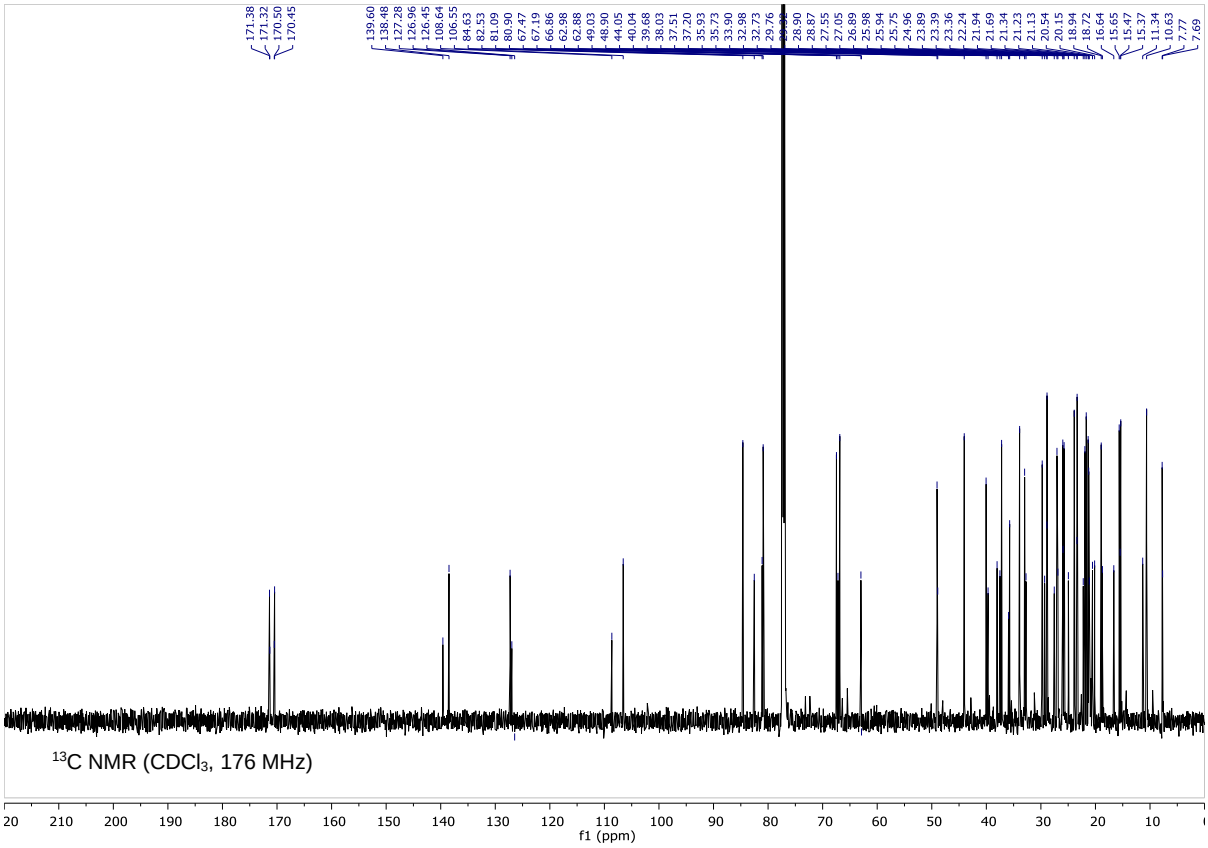

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


Me
O
Me
Me
Me
H
Me
Me
CHO
O
113
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

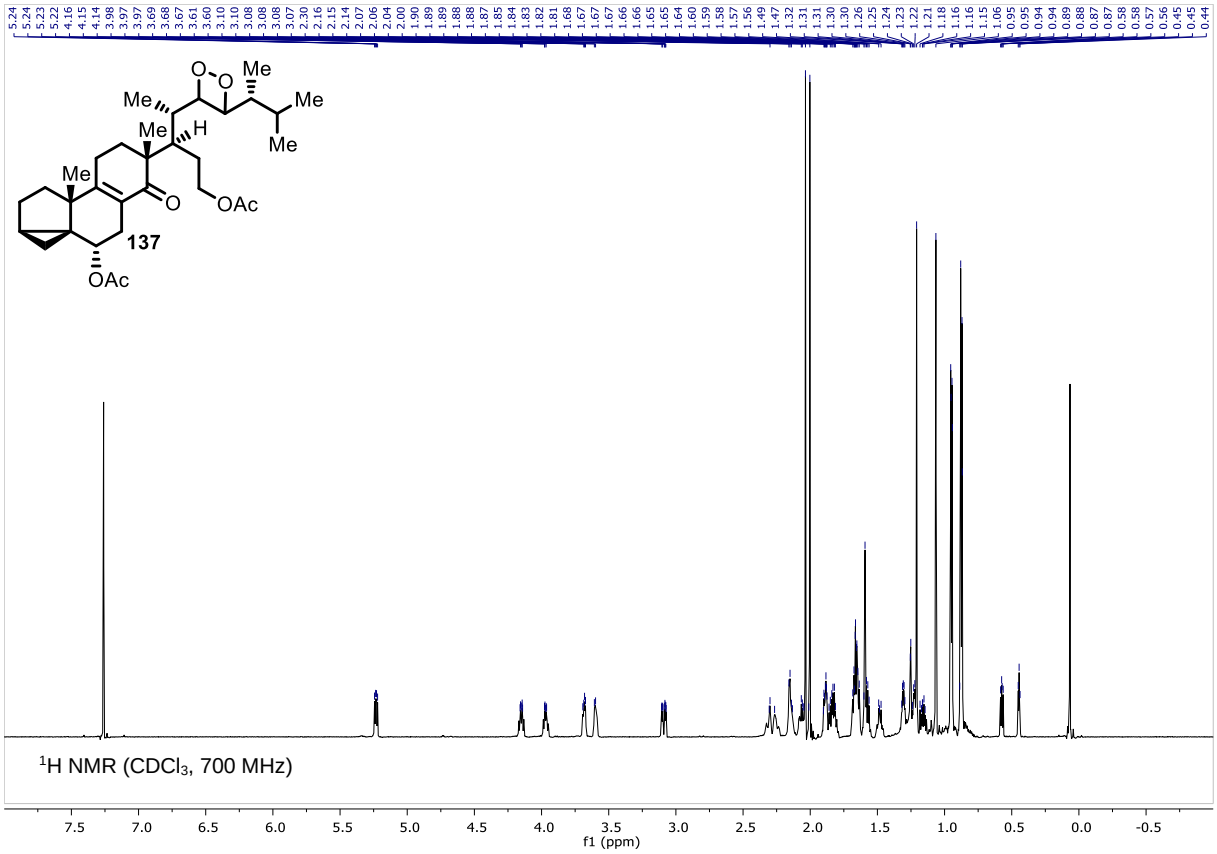

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

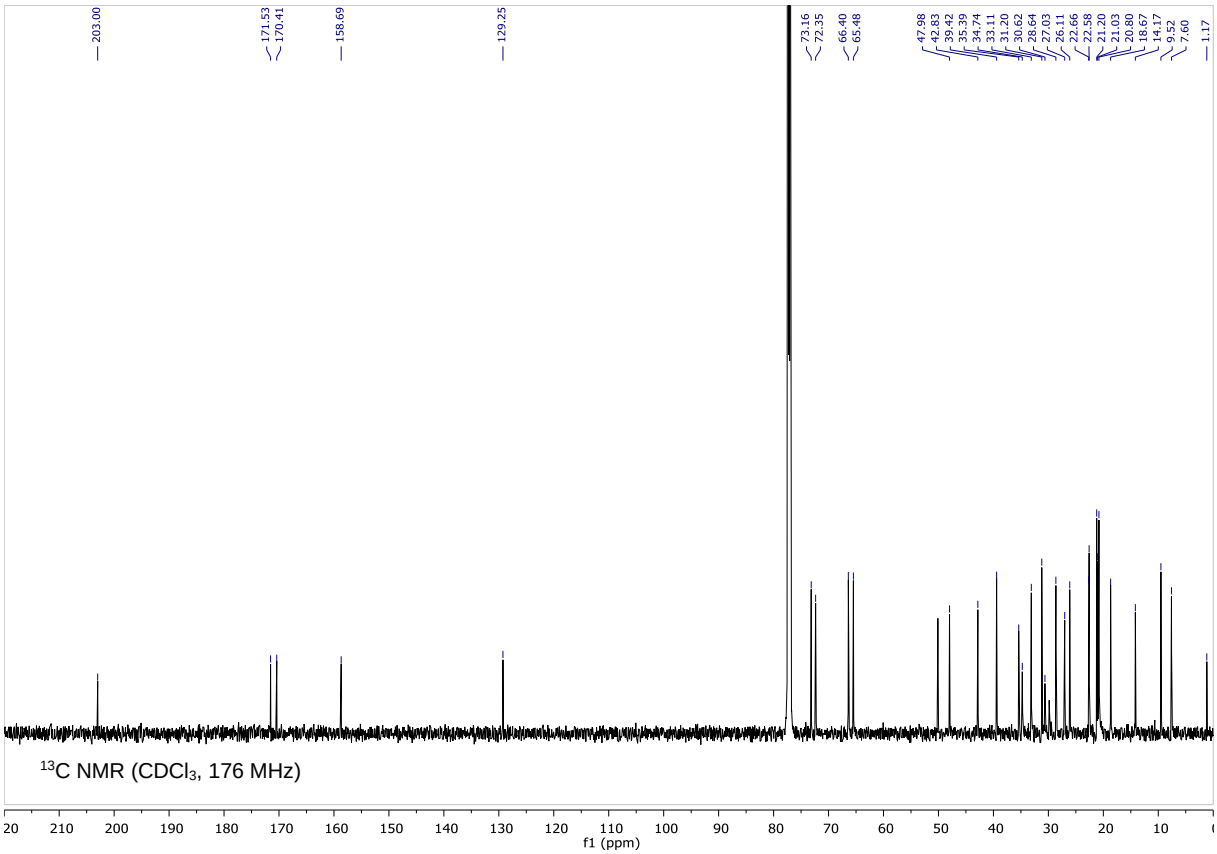


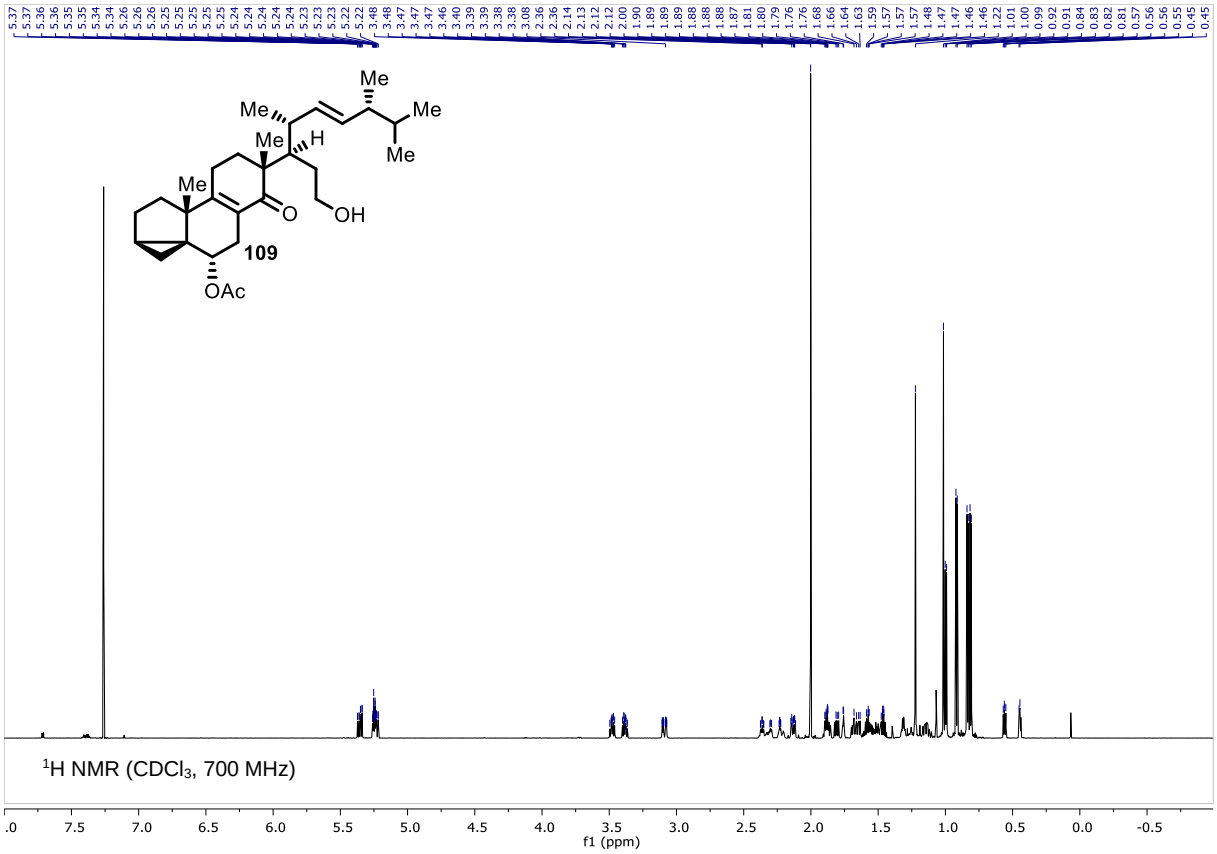
^{1}H NMR ($CDCl_3$, 700 MHz)



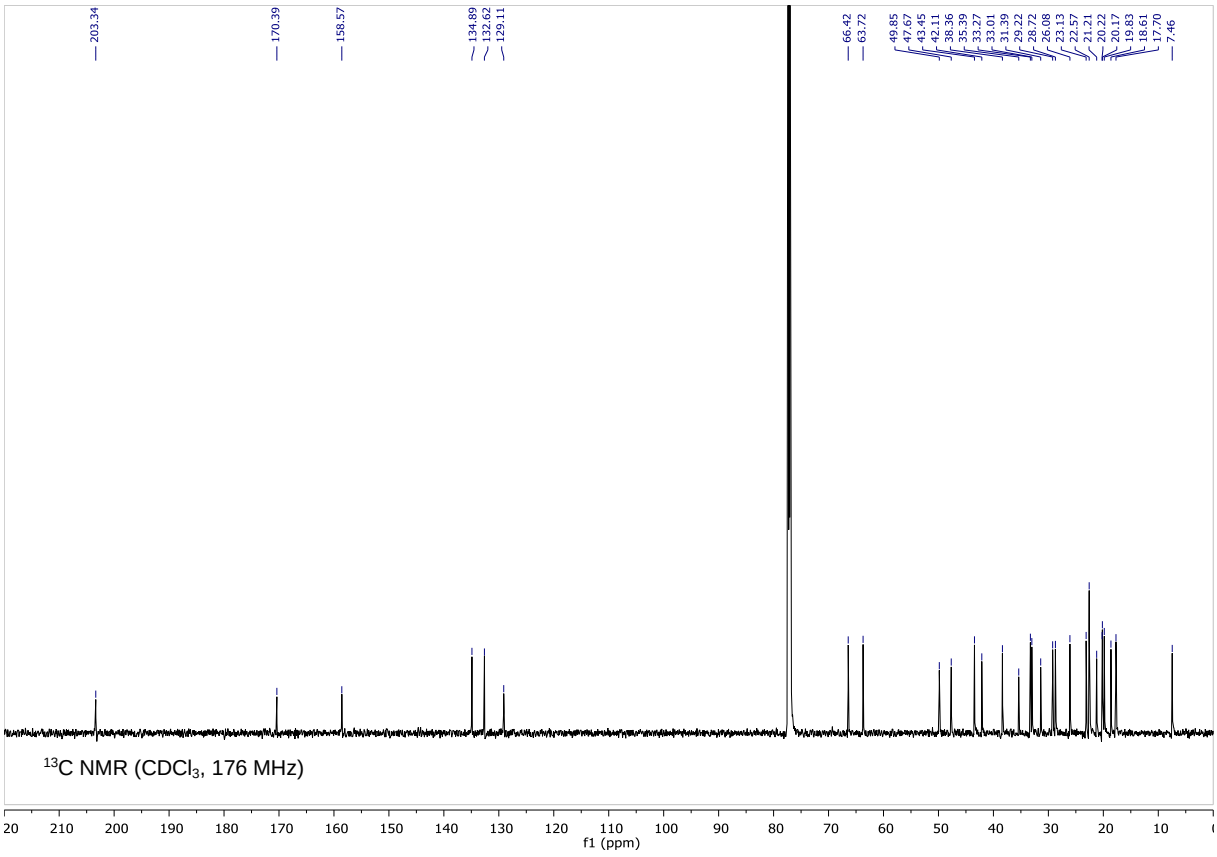
^{13}C NMR ($CDCl_3$, 176 MHz)


Me
O
O
Me
Me
Me
H
Me
Me
Me
O
OAc
137
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

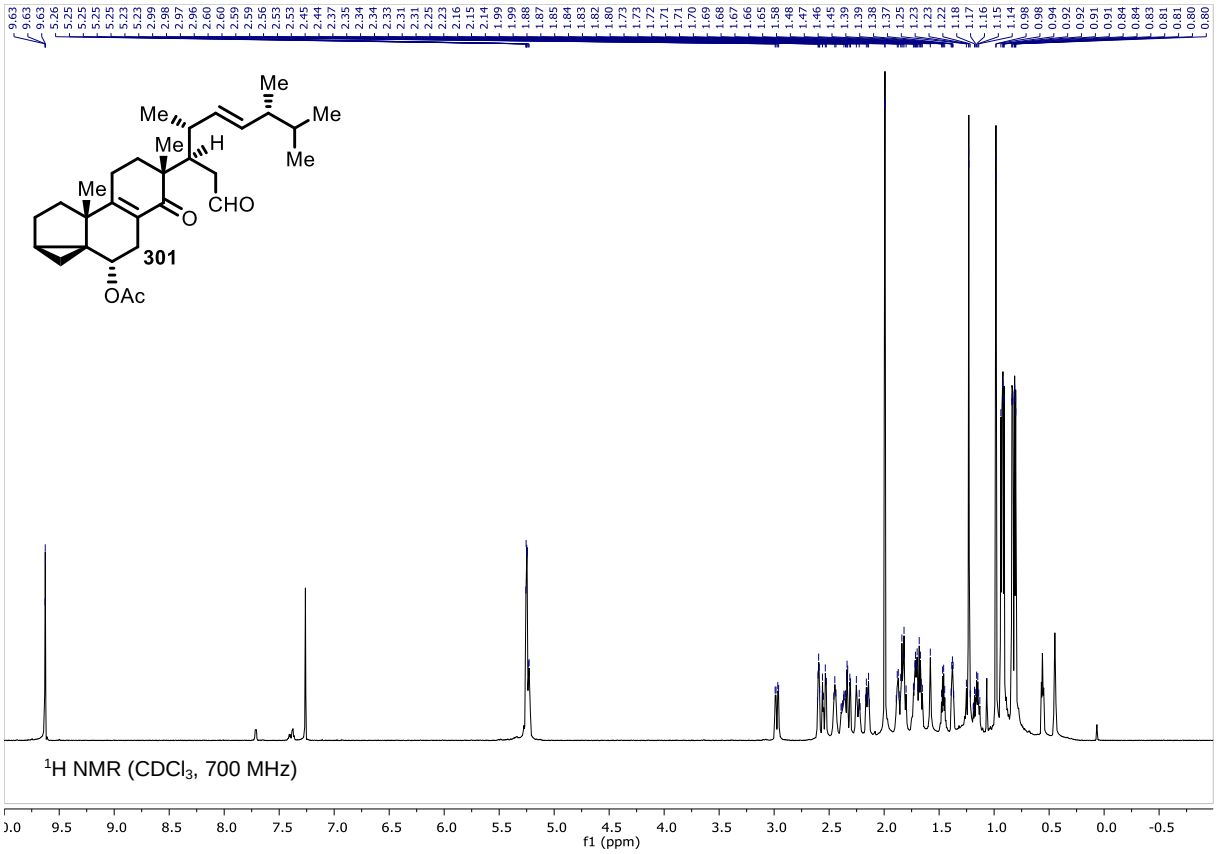

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

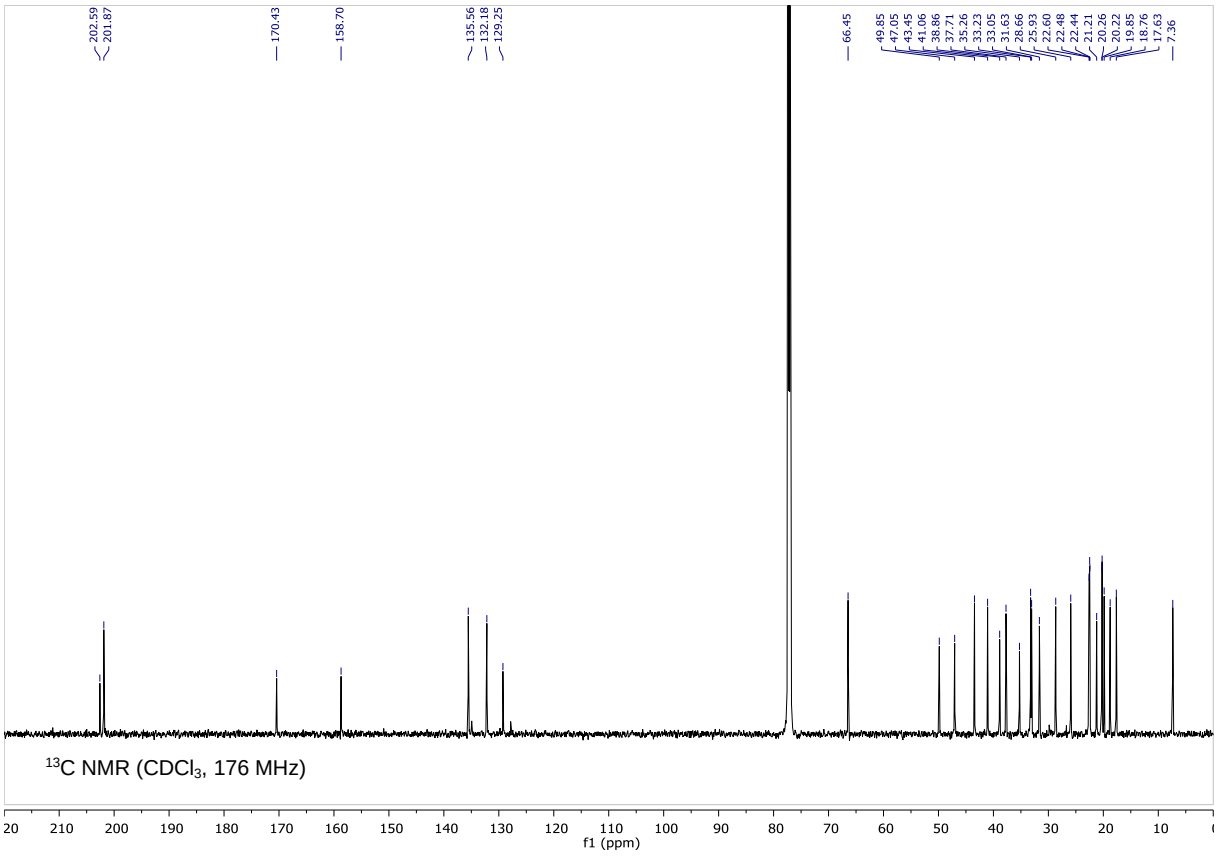


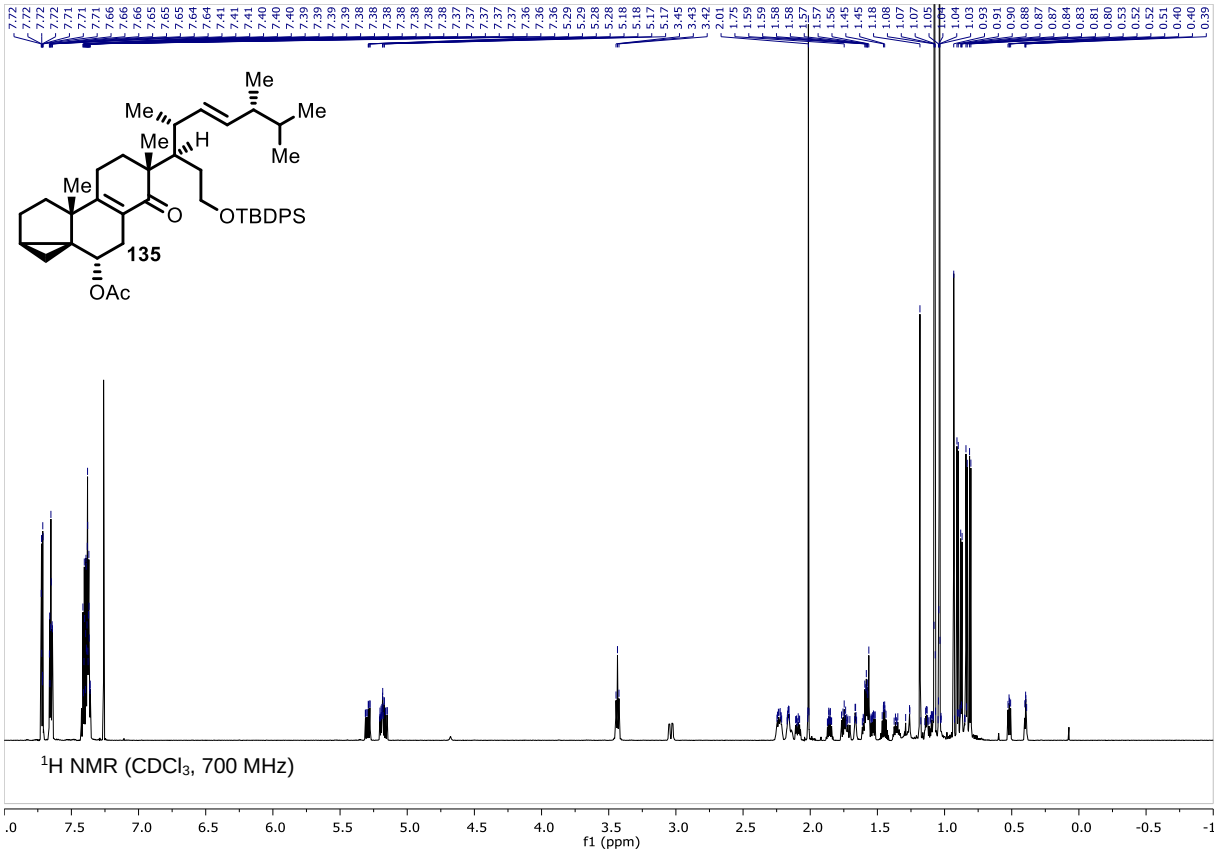
^{1}H NMR ($CDCl_3$, 700 MHz)

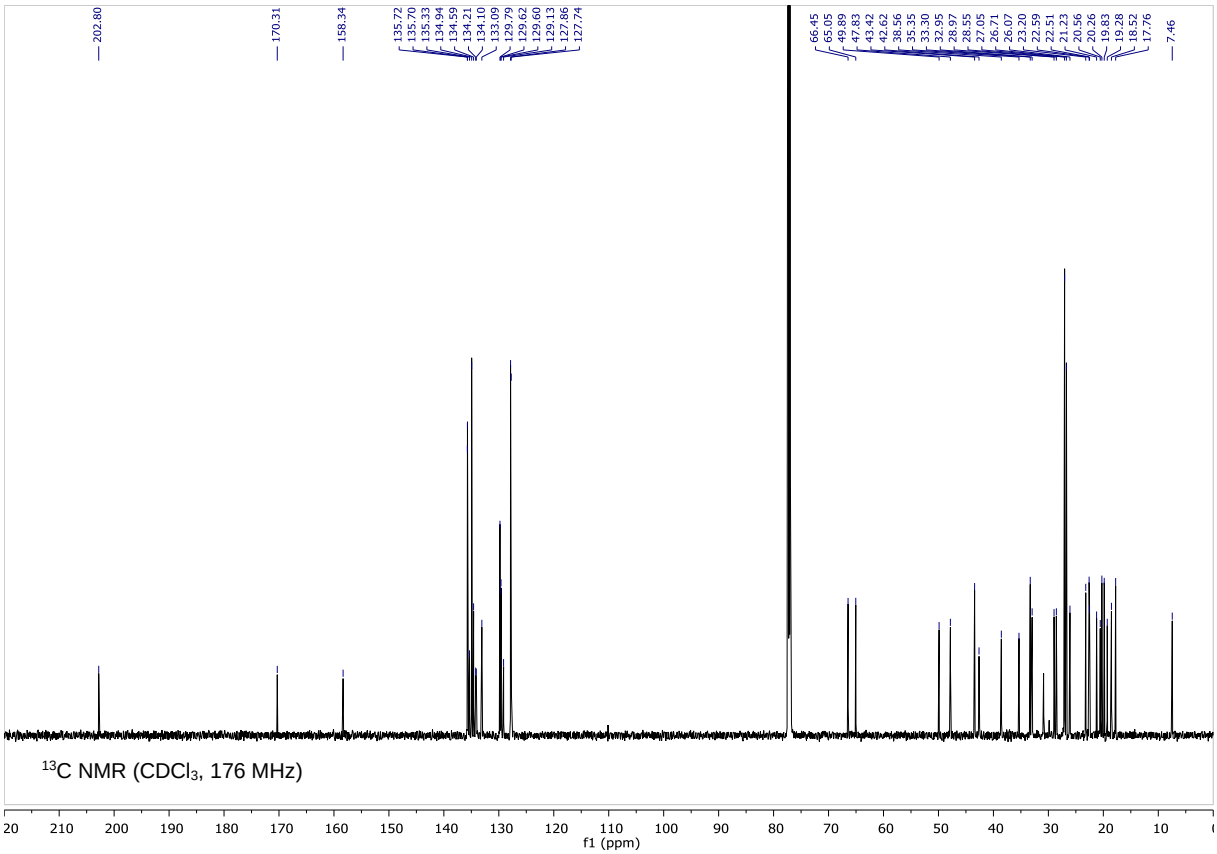


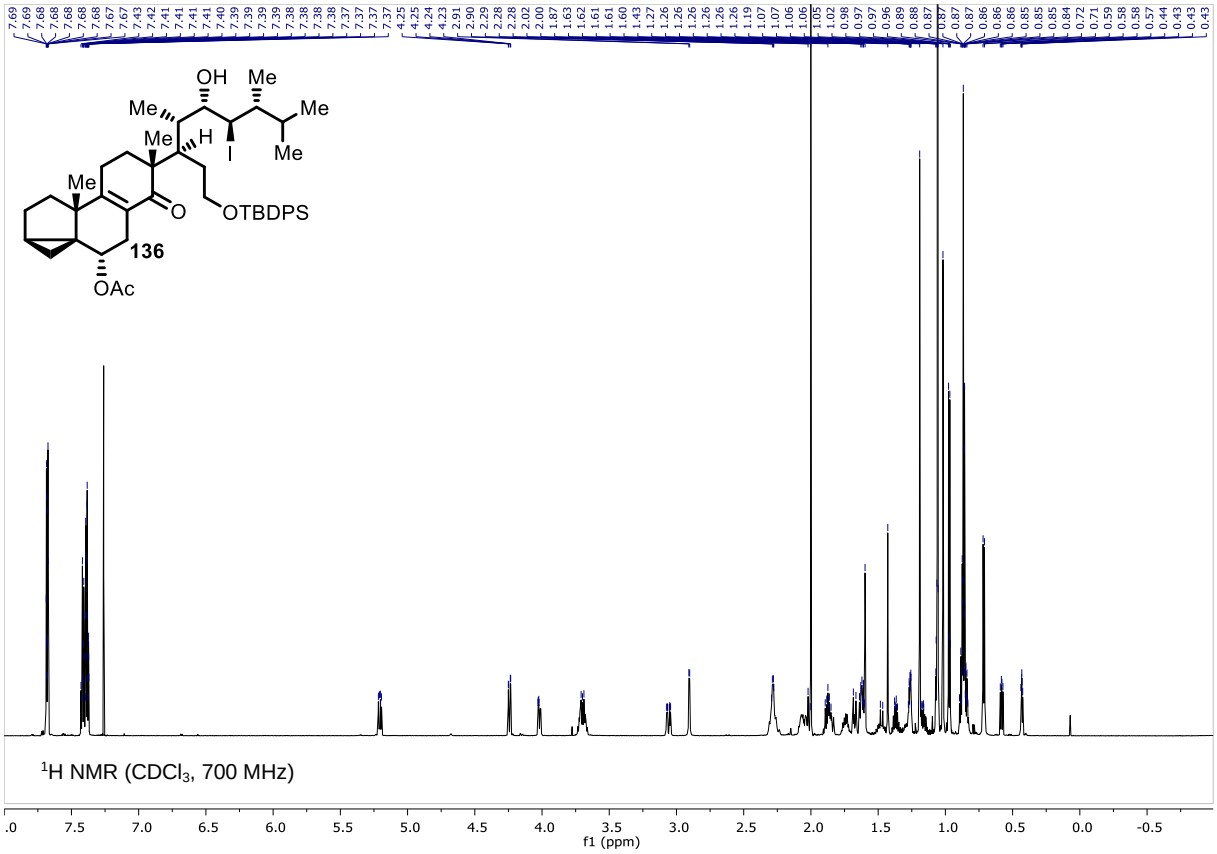
^{13}C NMR ($CDCl_3$, 176 MHz)

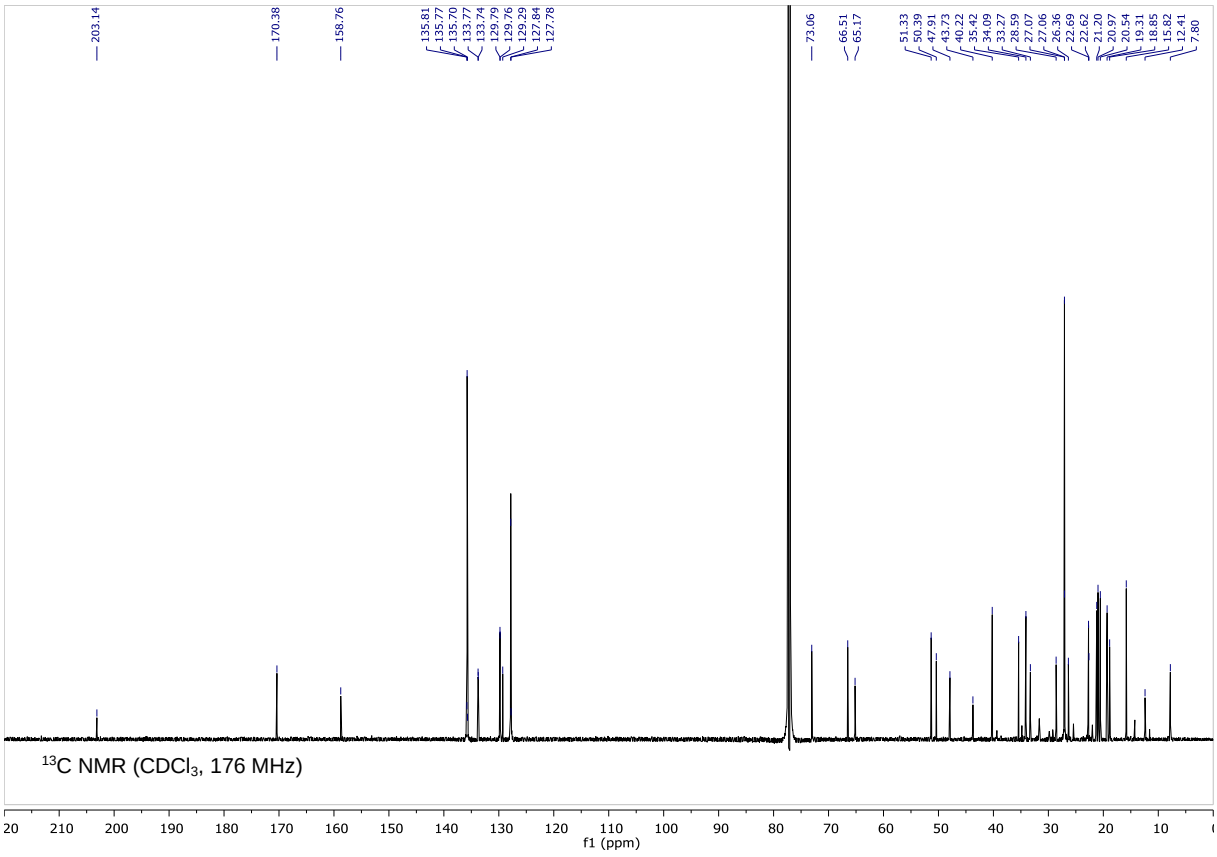

Me
Me
Me
H
Me
Me
Me
CHO
O
301
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

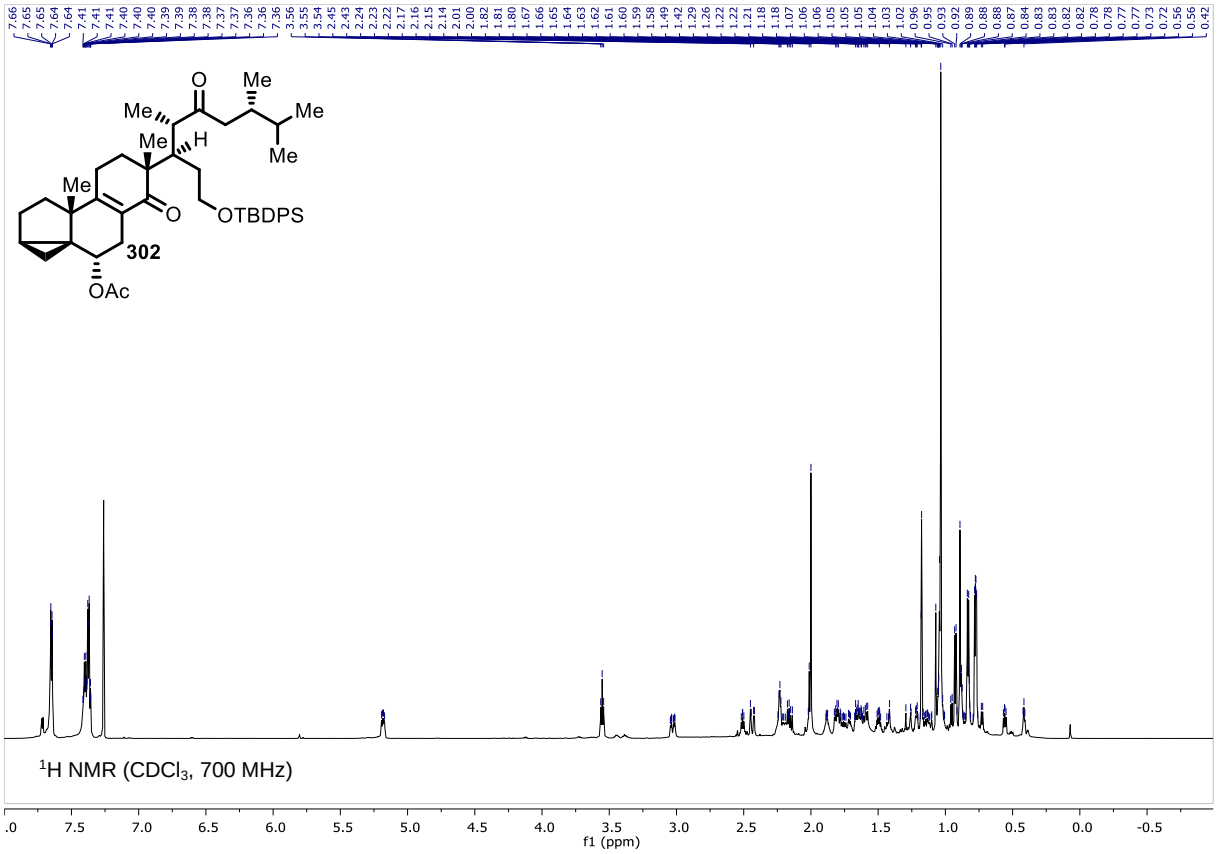

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

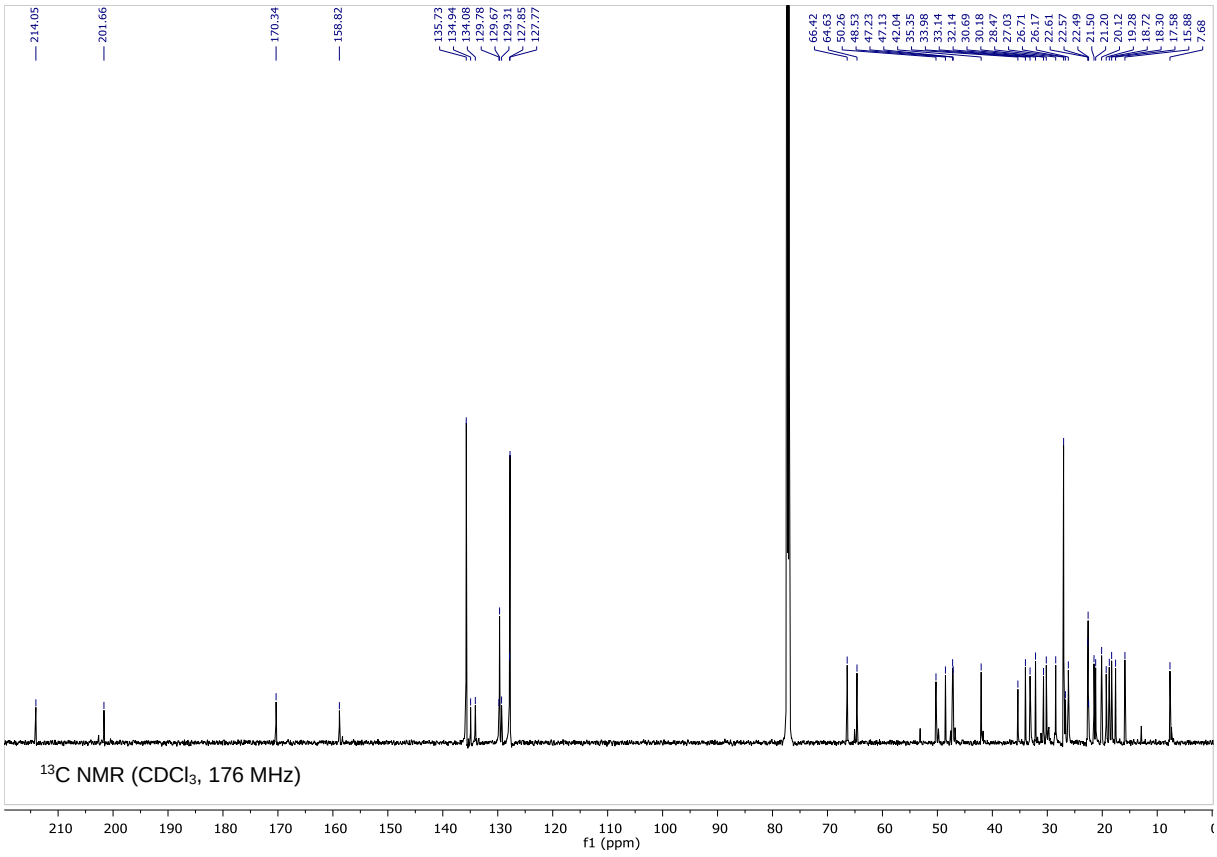

Me
Me
Me
H
Me
Me
Me
O
OTBDPS
135
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

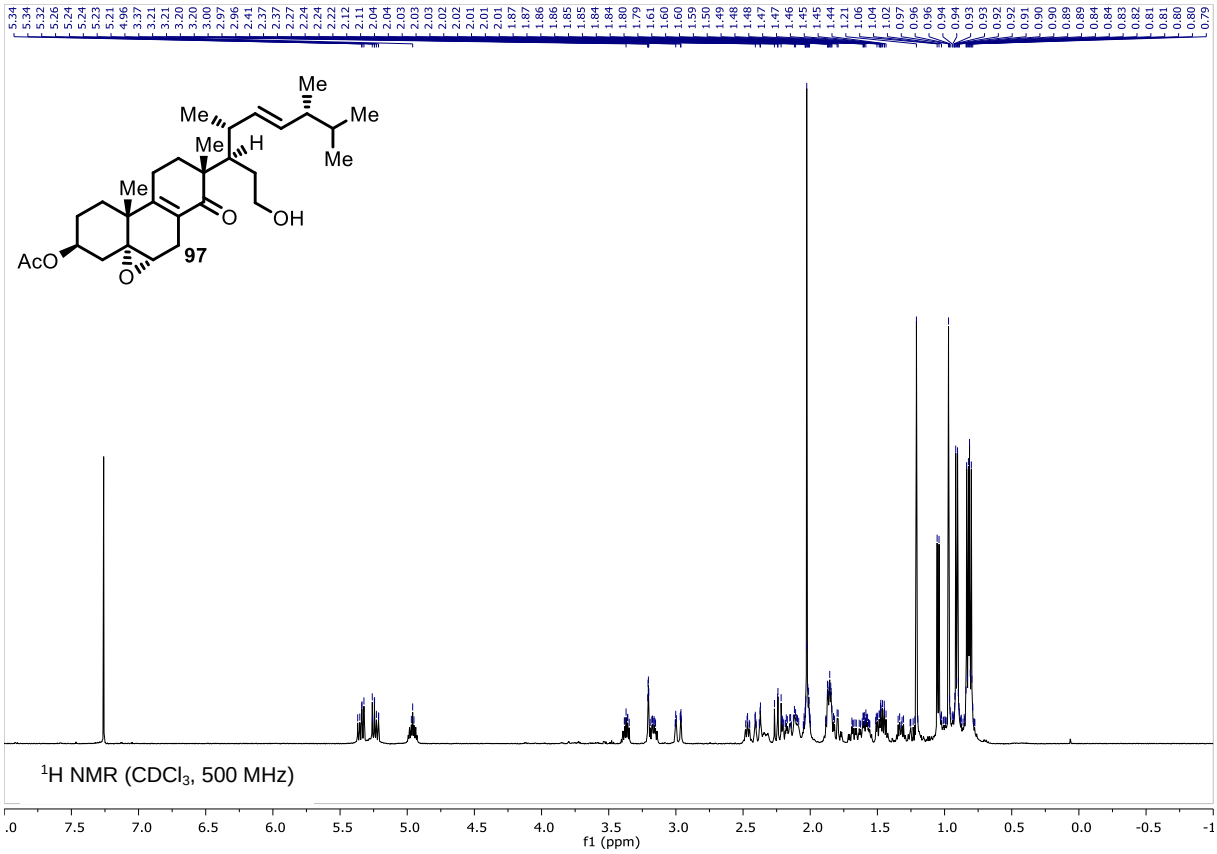

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


OH
Me
Me
Me
Me
H
I
Me
Me
O
OTBDPS
136
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

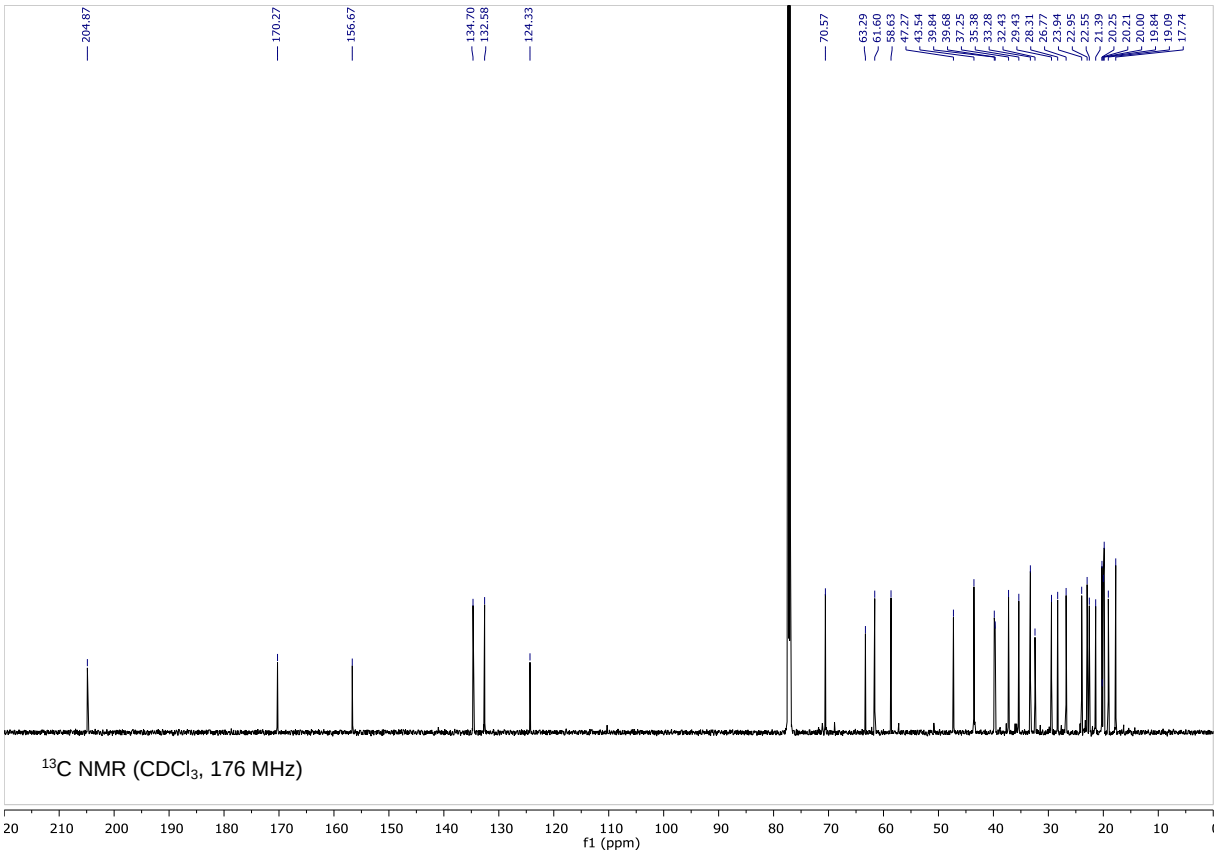

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


Me
O
Me
Me
H
Me
Me
Me
O
OTBDPS
302
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

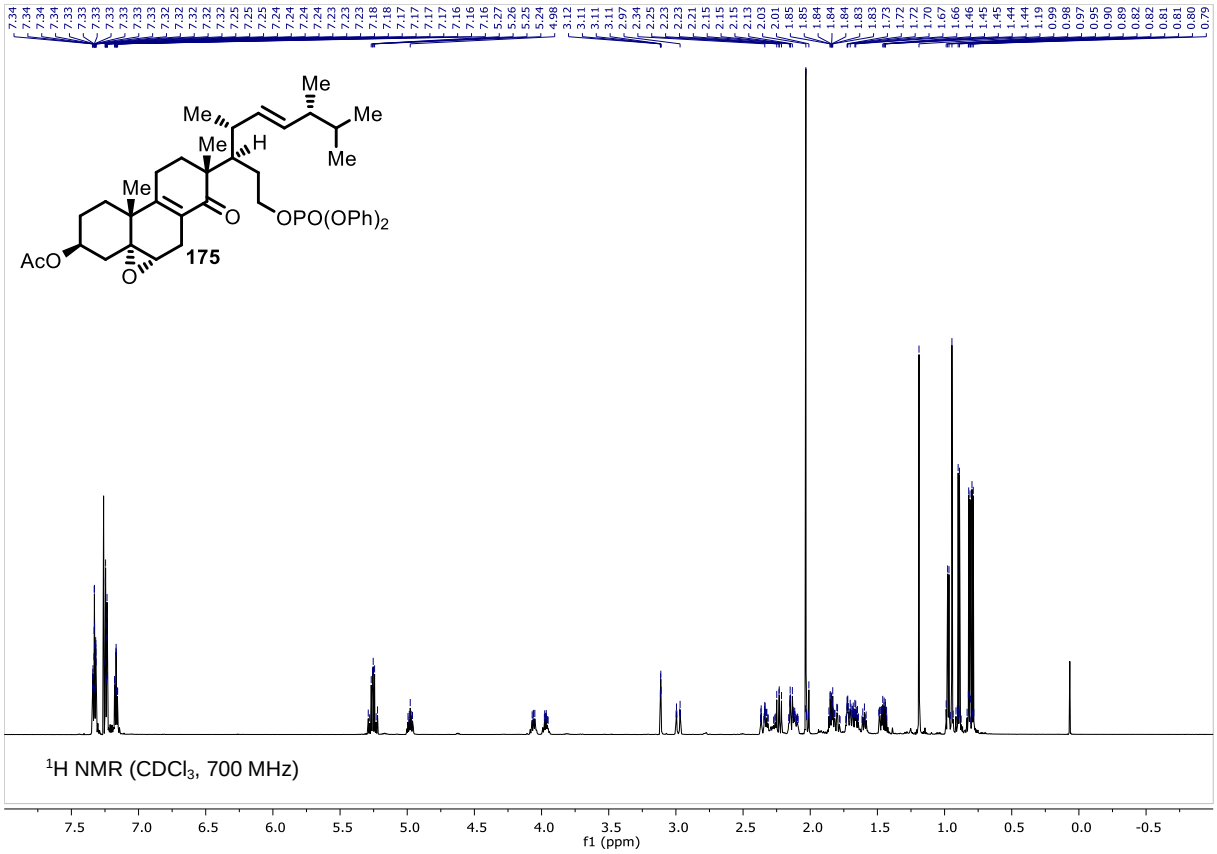

214.05
201.66
170.34
158.82
135.73
134.94
134.08
129.78
129.67
129.31
127.85
127.77
66.42
64.63
50.26
48.53
47.23
47.13
42.04
35.35
33.98
33.14
32.14
30.69
30.18
28.47
27.03
26.71
26.17
22.61
22.57
22.49
21.50
21.20
20.12
19.28
18.72
18.30
17.58
15.88
7.68
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

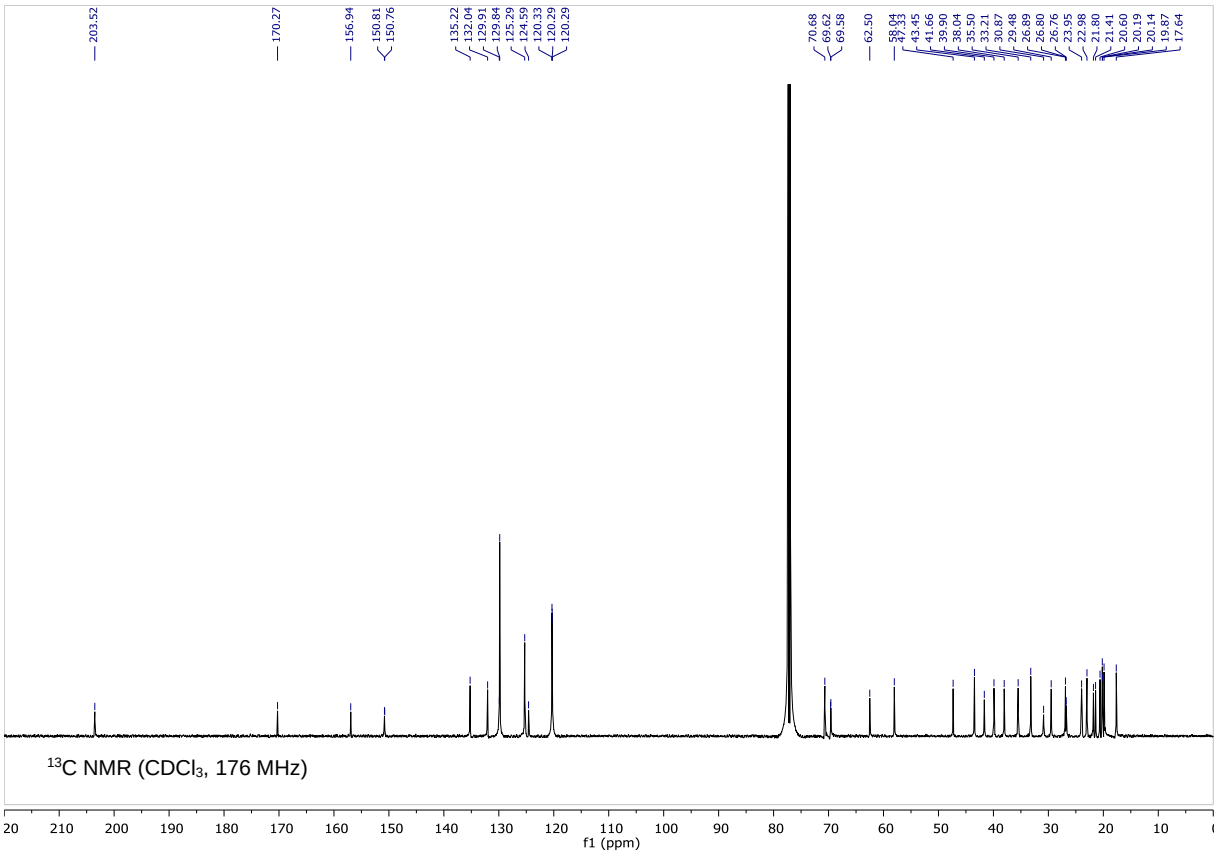


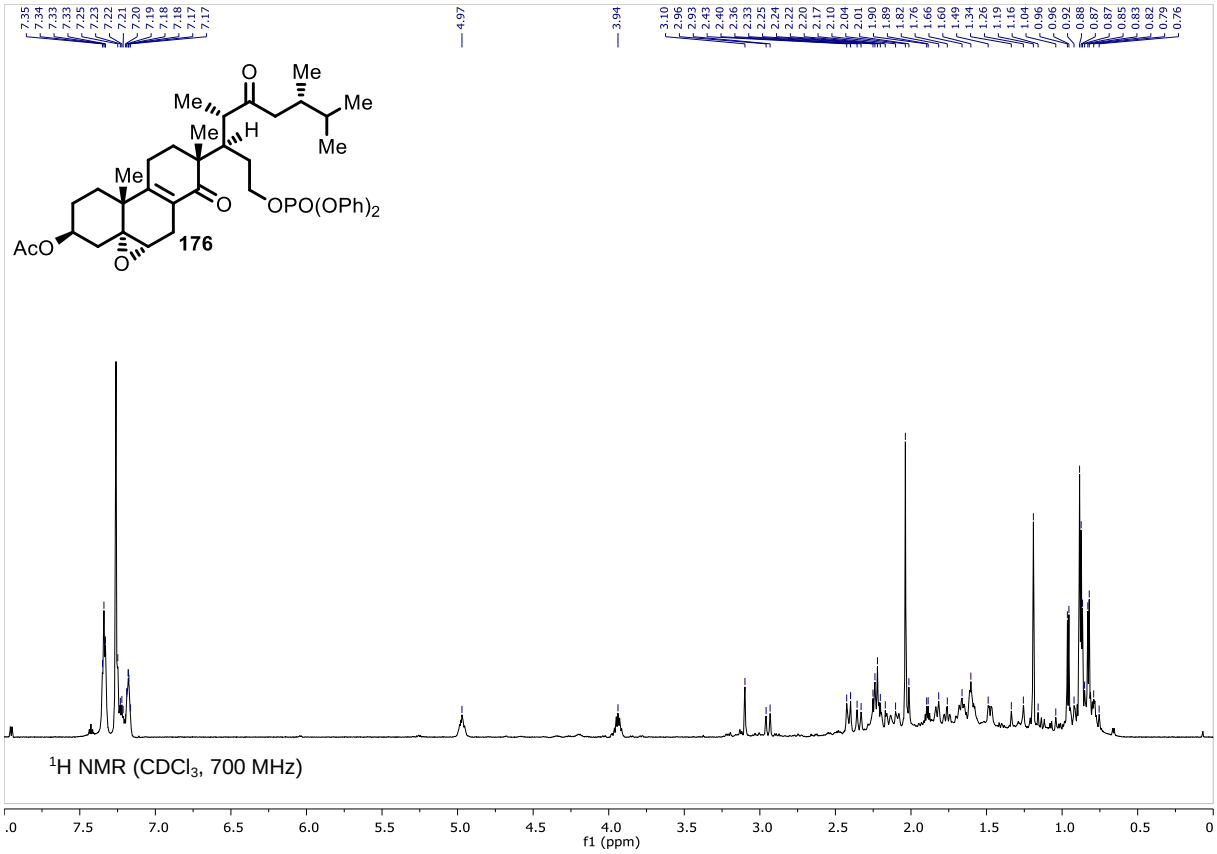
^{1}H NMR ($CDCl_3$, 500 MHz)



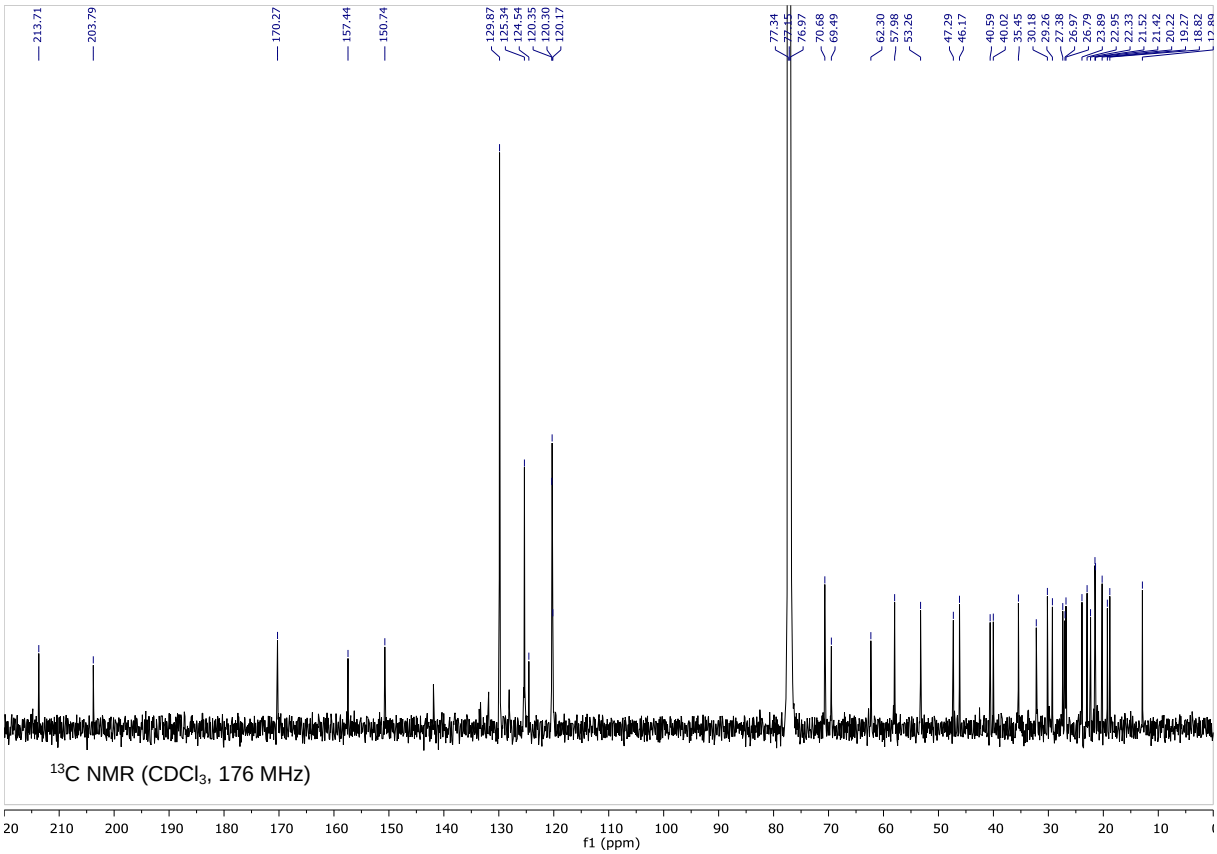
^{13}C NMR ($CDCl_3$, 176 MHz)


Me
Me
Me
Me
H
Me
Me
O
OPO(OPh)2
AcO
O
175
1H NMR (CDCl3, 700 MHz)
f1 (ppm)

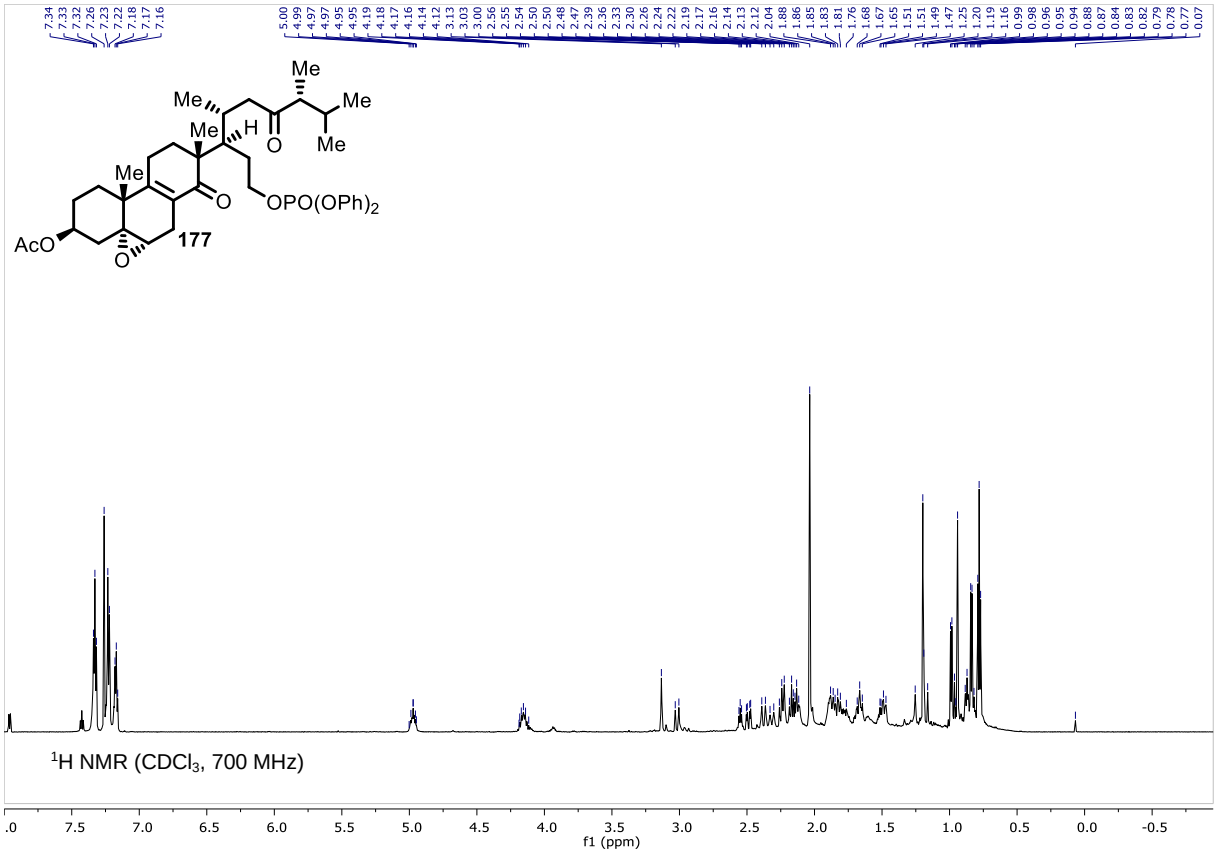

203.52
170.27
156.94
150.81
150.76
135.22
132.04
129.91
129.84
125.29
124.59
120.33
120.29
120.29
70.68
69.62
69.58
62.50
59.04
58.33
43.45
41.66
39.90
38.04
35.50
33.21
30.87
29.48
26.89
26.80
26.76
23.95
22.98
21.80
21.41
20.60
20.19
20.14
19.87
17.64
13C NMR (CDCl3, 176 MHz)
f1 (ppm)



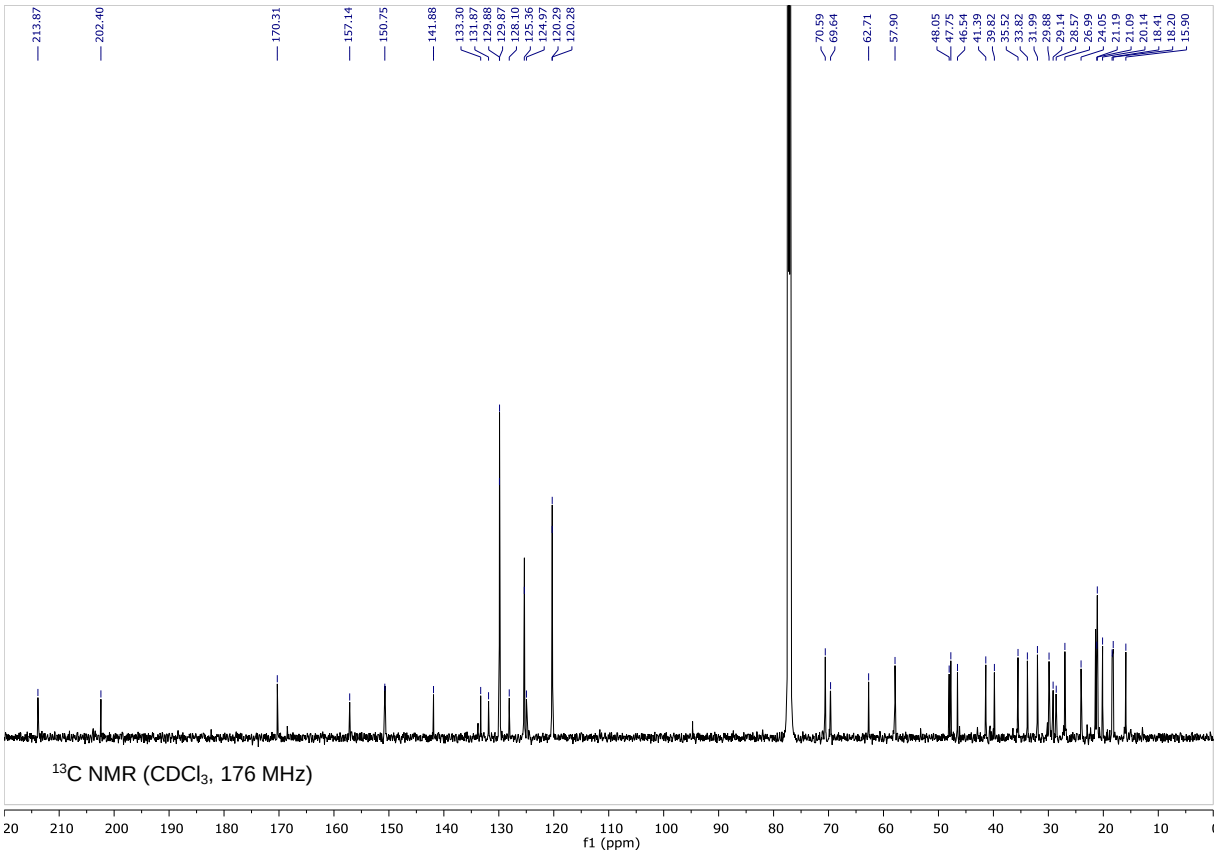
^{1}H NMR ($CDCl_3$, 700 MHz)



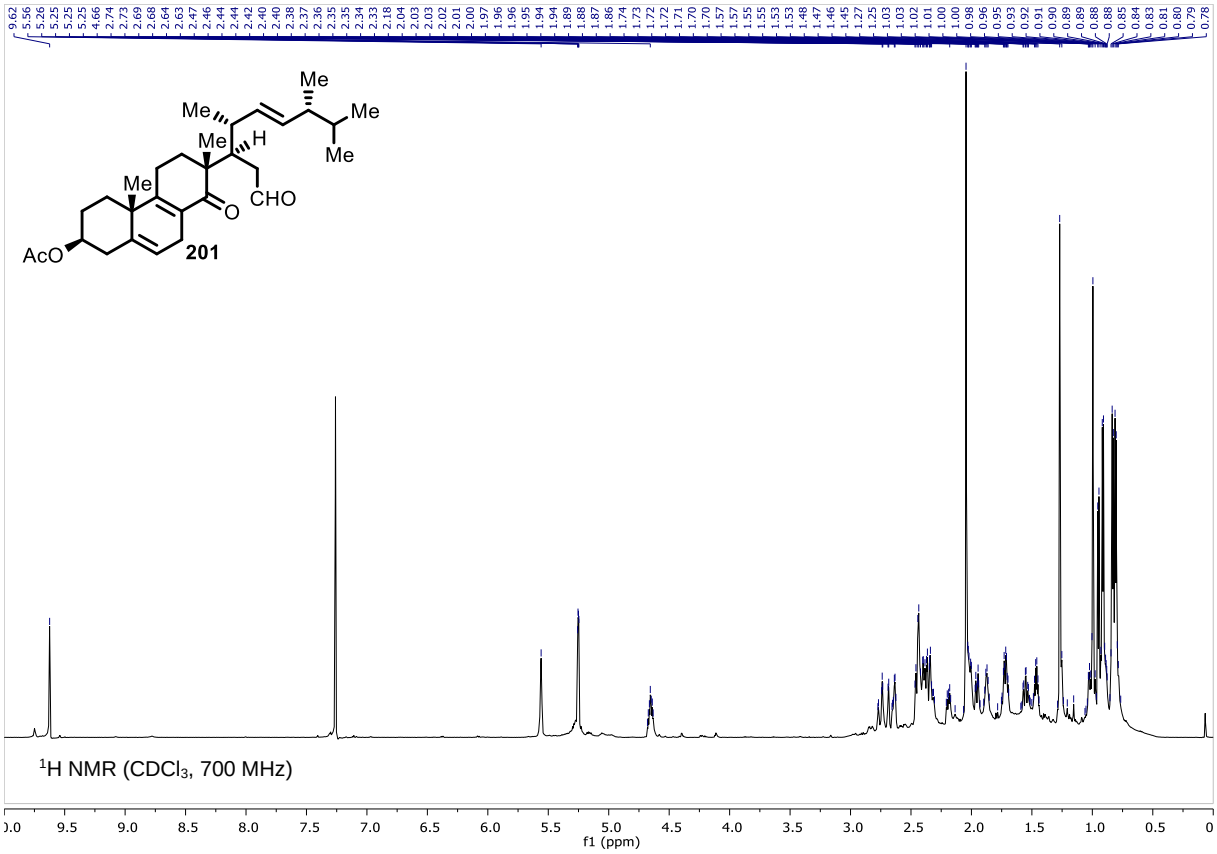
^{13}C NMR ($CDCl_3$, 176 MHz)

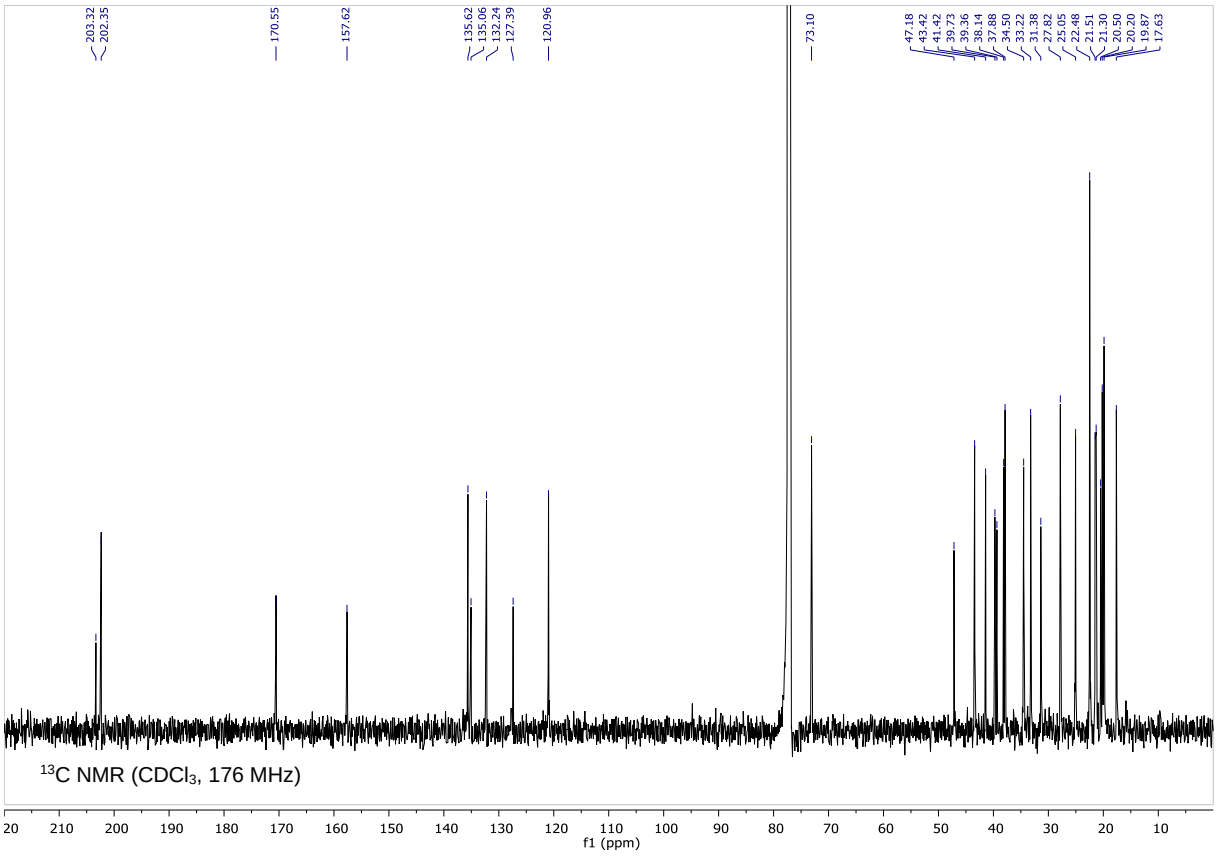


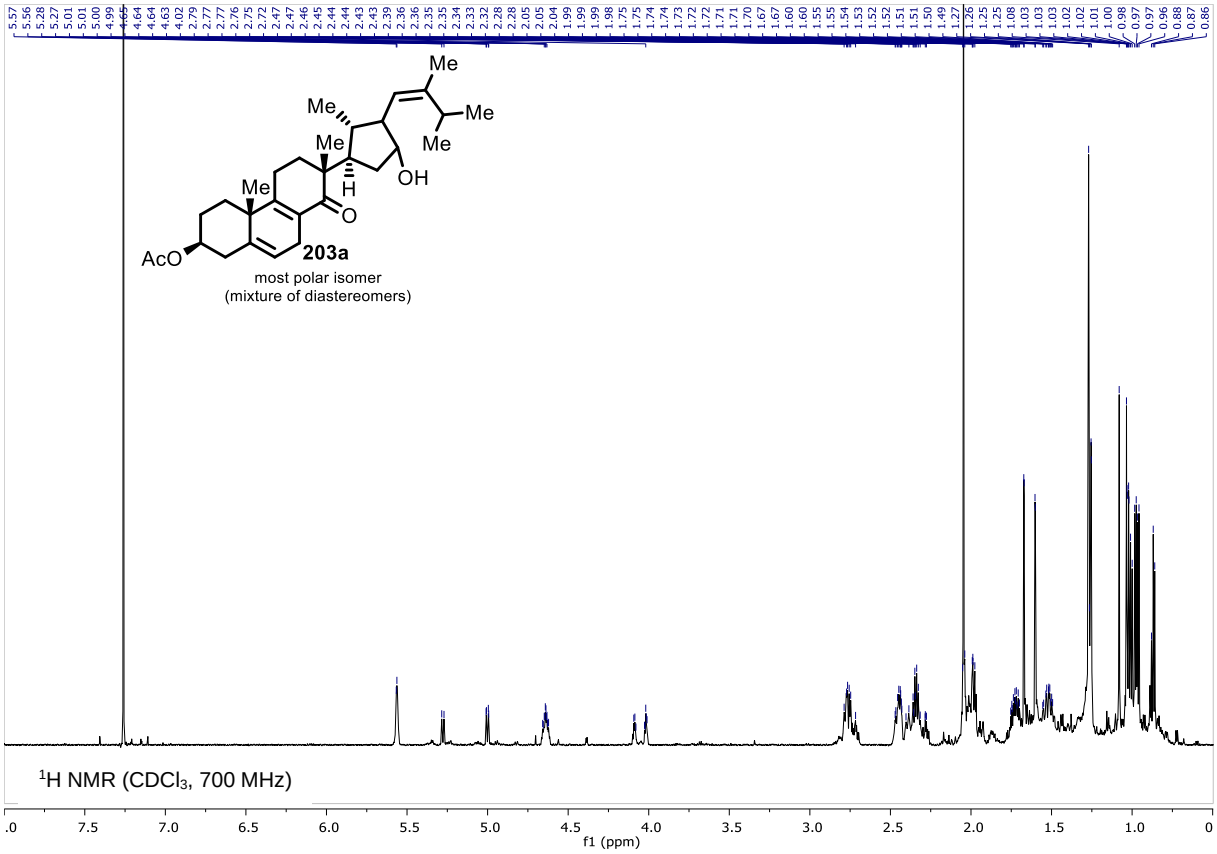
^{1}H NMR ($CDCl_3$, 700 MHz)

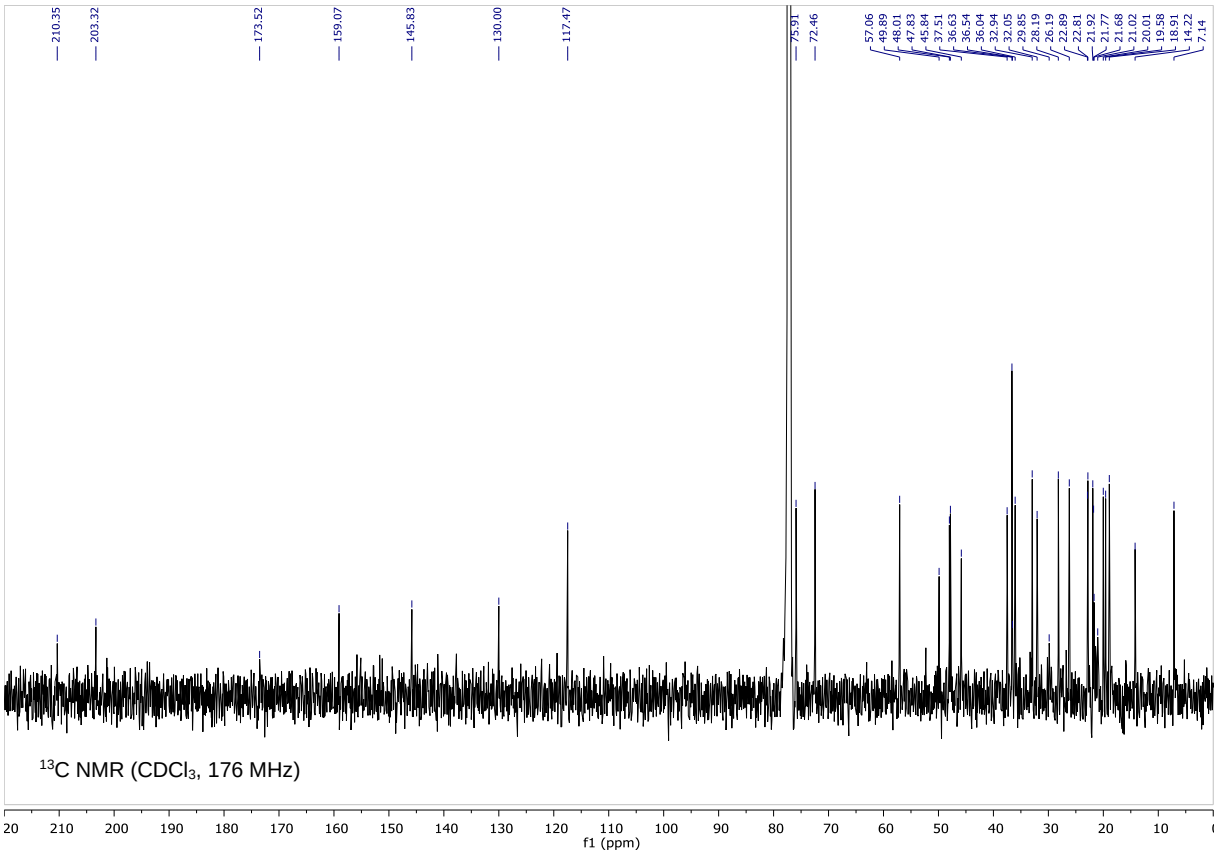


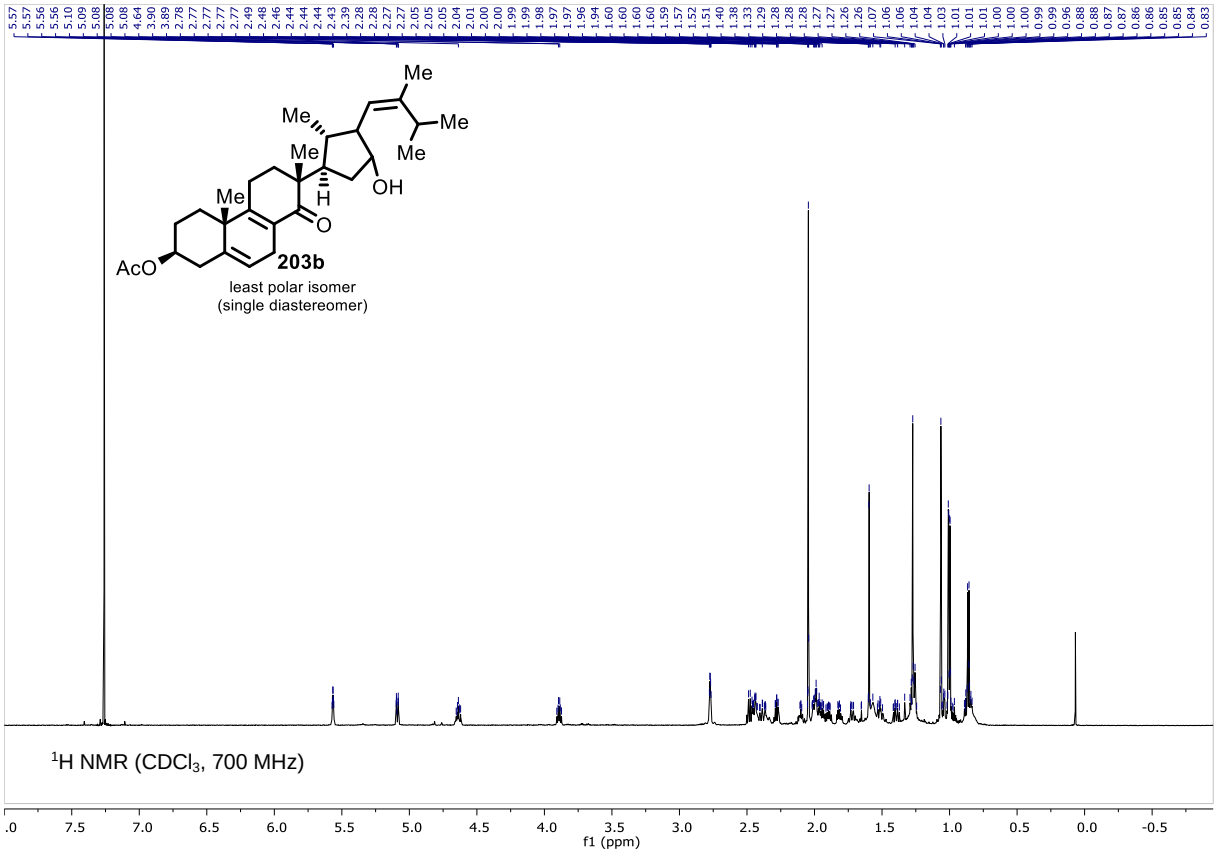
^{13}C NMR ($CDCl_3$, 176 MHz)


Me
Me
Me
H
Me
Me
Me
CHO
O
AcO
201
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

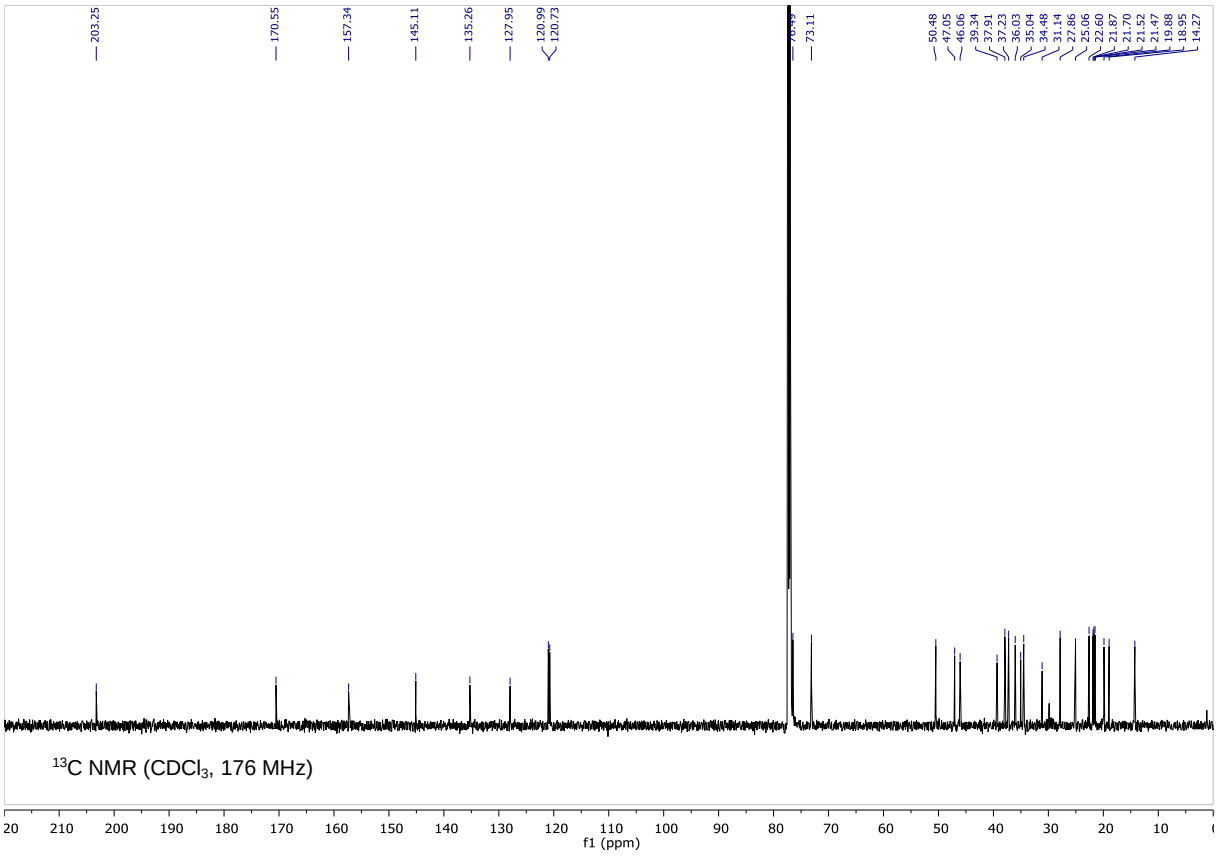

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


Me
Me
Me
Me
Me
OH
H
O
AcO
203a
most polar isomer
(mixture of diastereomers)
1H NMR (CDCl3, 700 MHz)
f1 (ppm)

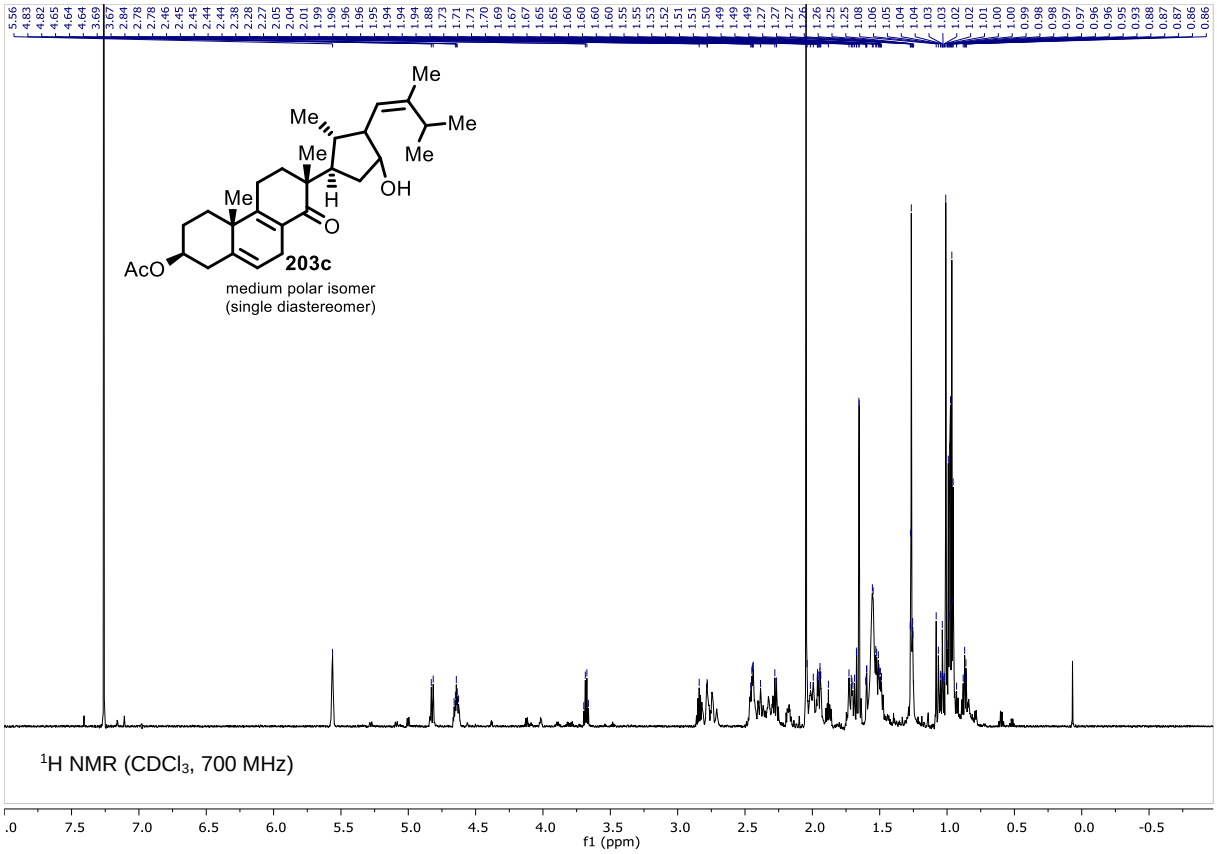

210.35
203.32
173.52
159.07
145.83
130.00
117.47
75.91
72.46
13C NMR (CDCl3, 176 MHz)
f1 (ppm)



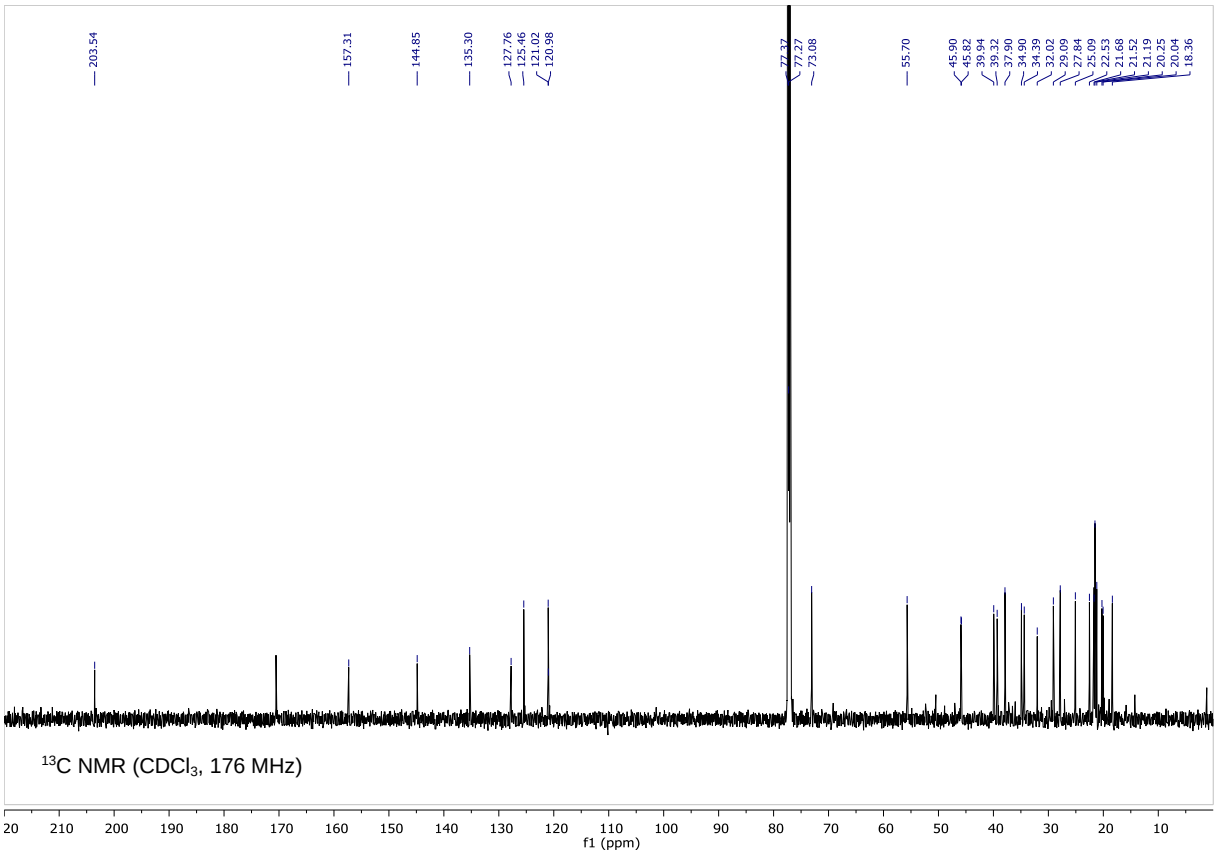
^{1}H NMR ($CDCl_3$, 700 MHz)



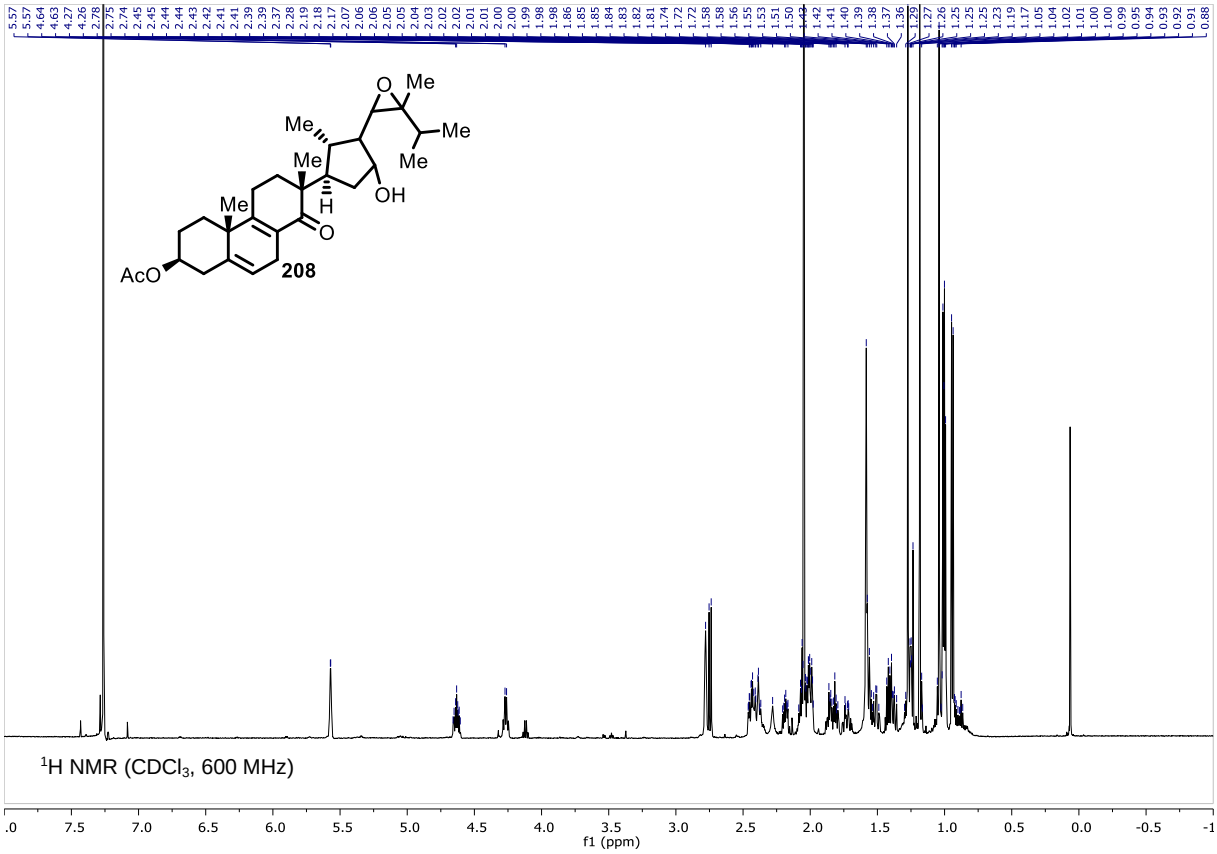
^{13}C NMR ($CDCl_3$, 176 MHz)

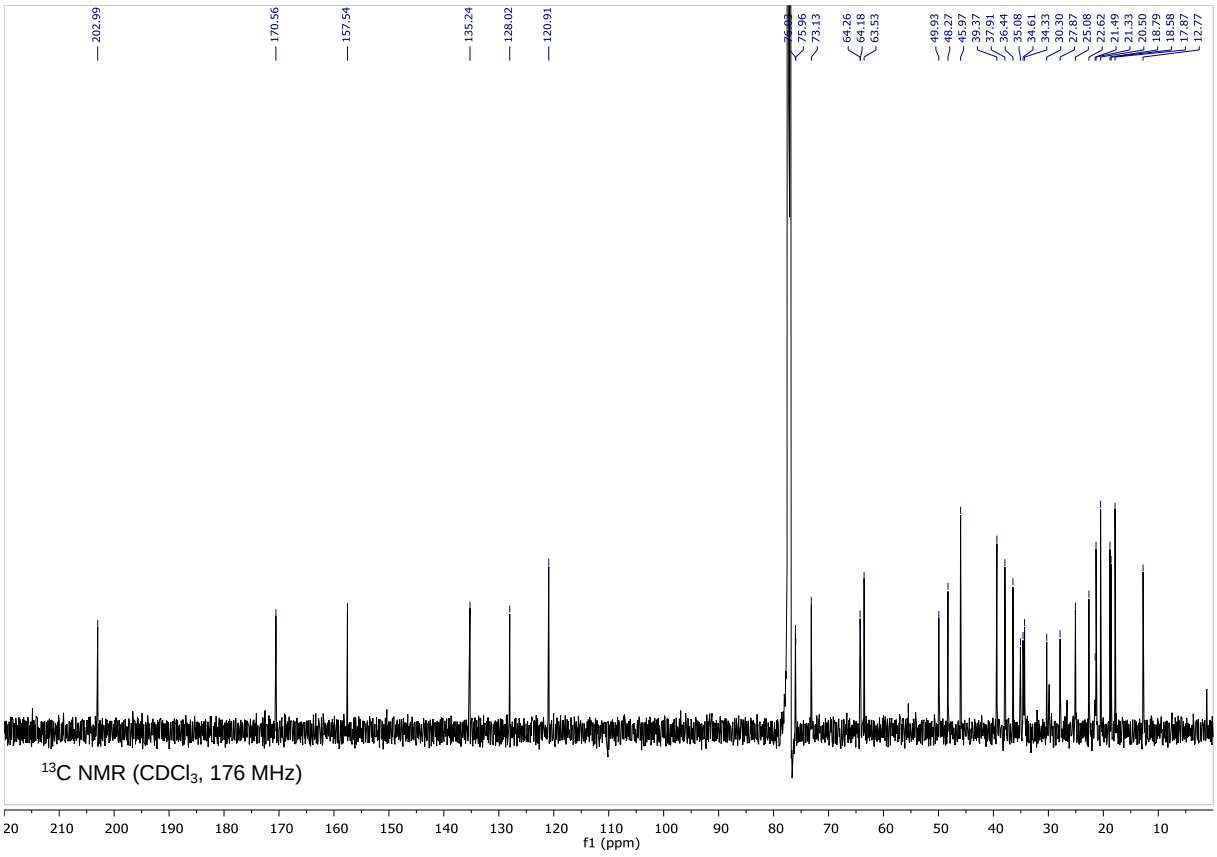


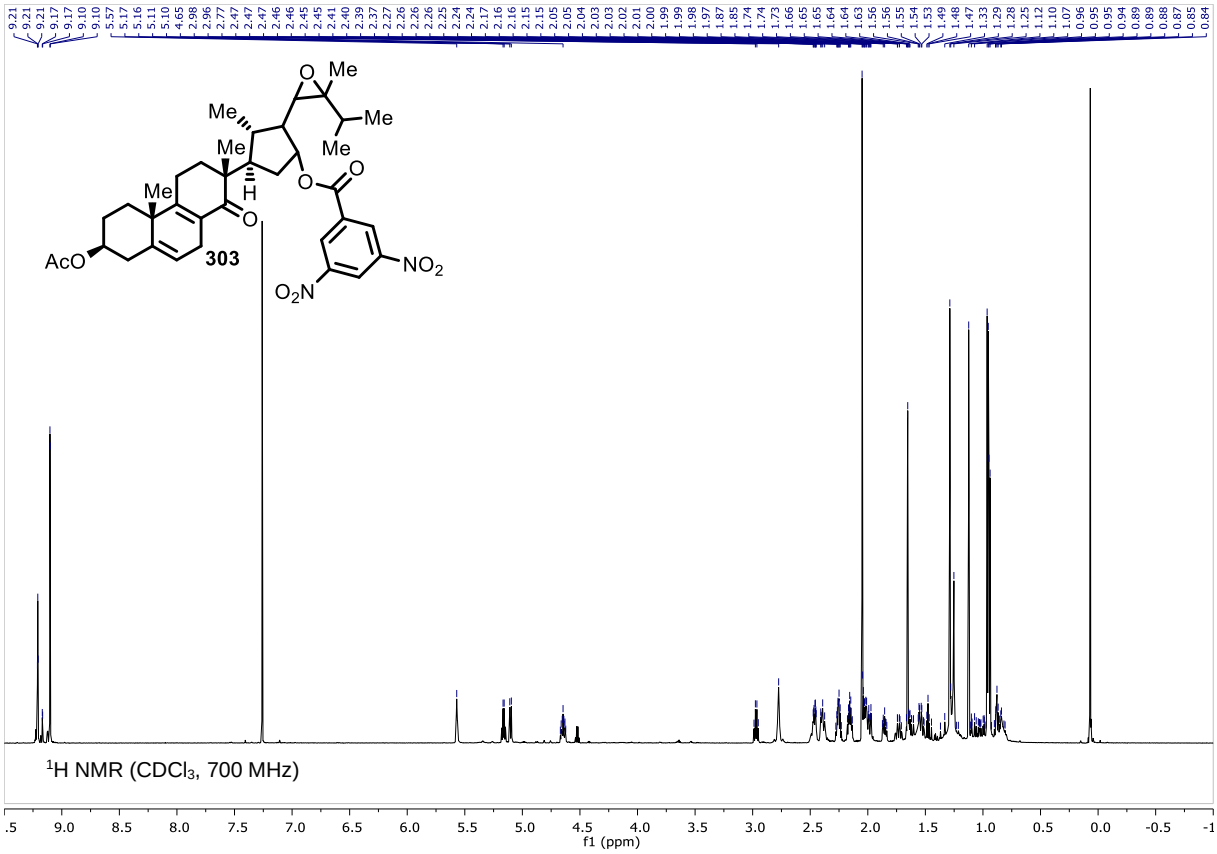
^{1}H NMR ($CDCl_3$, 700 MHz)

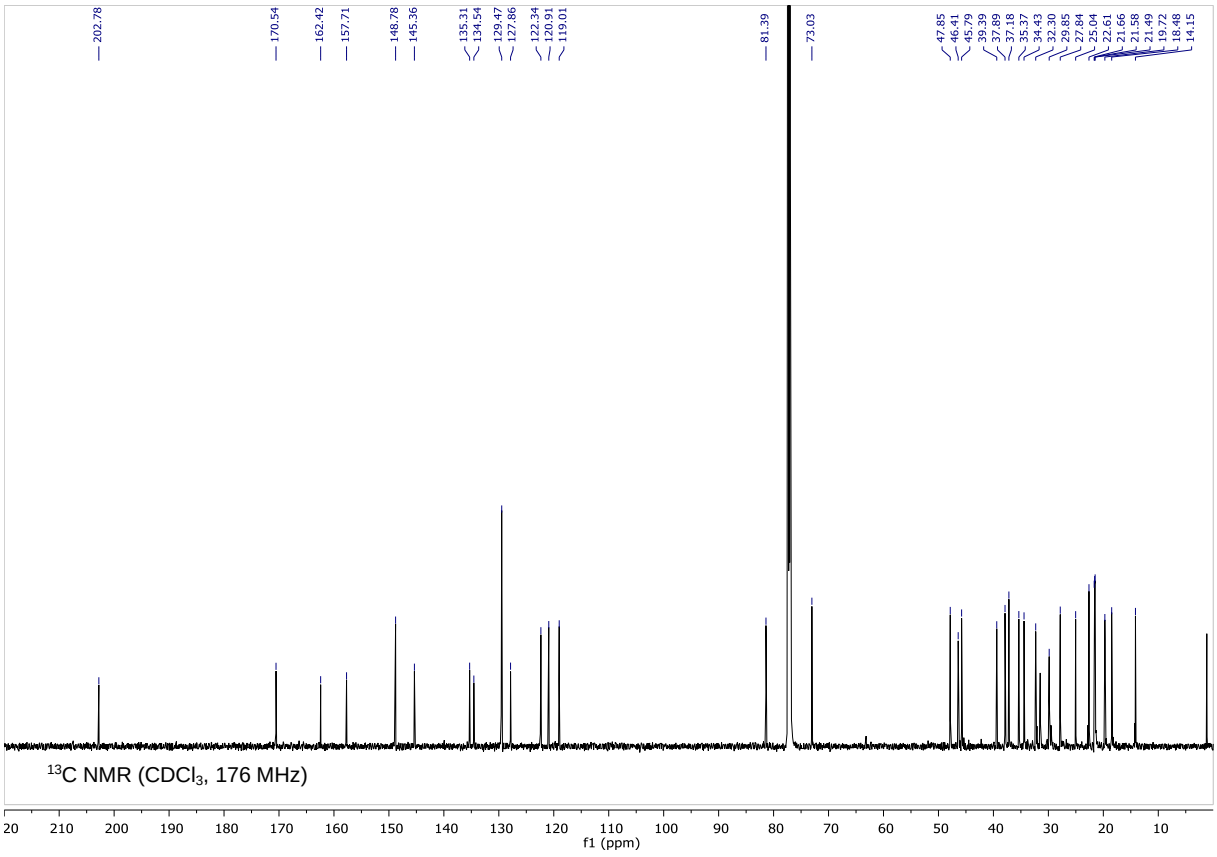


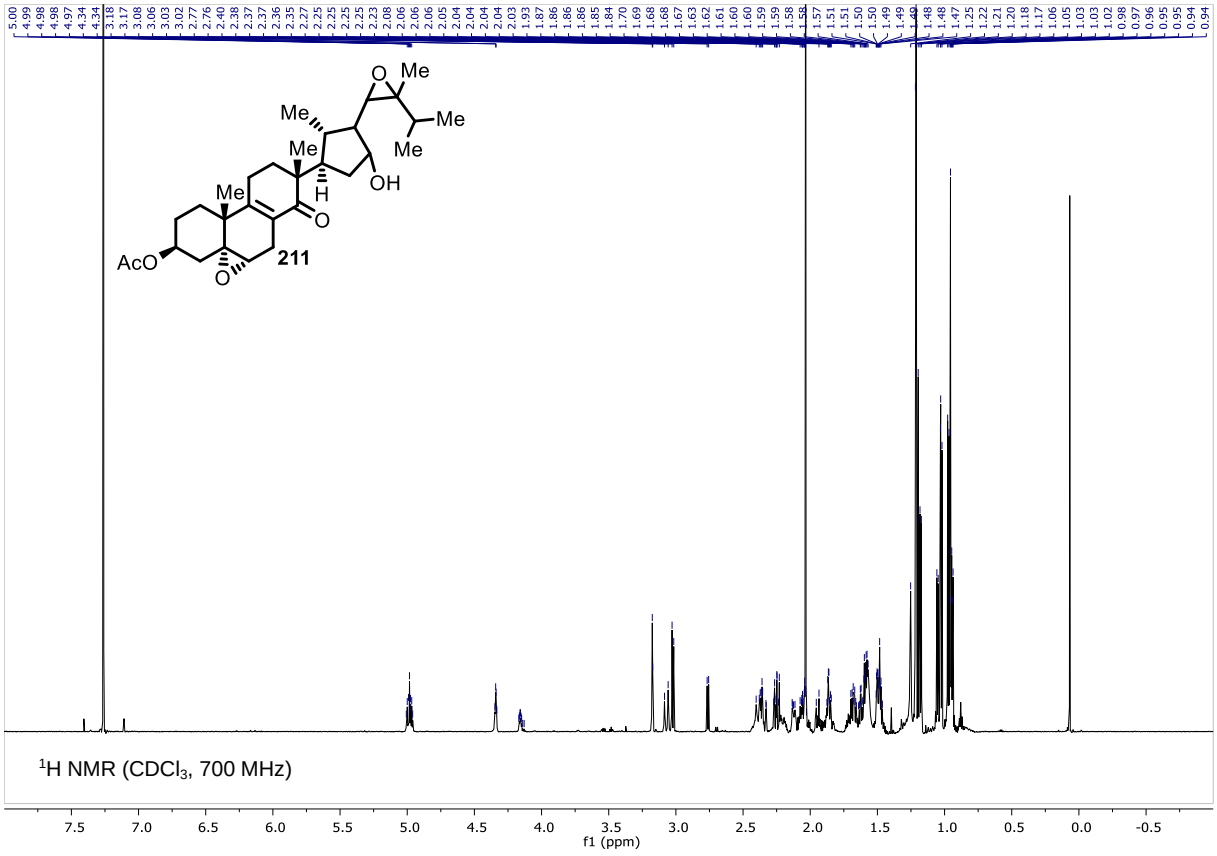
^{13}C NMR ($CDCl_3$, 176 MHz)


Me
O
Me
Me
Me
Me
OH
H
Me
O
AcO
208
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)

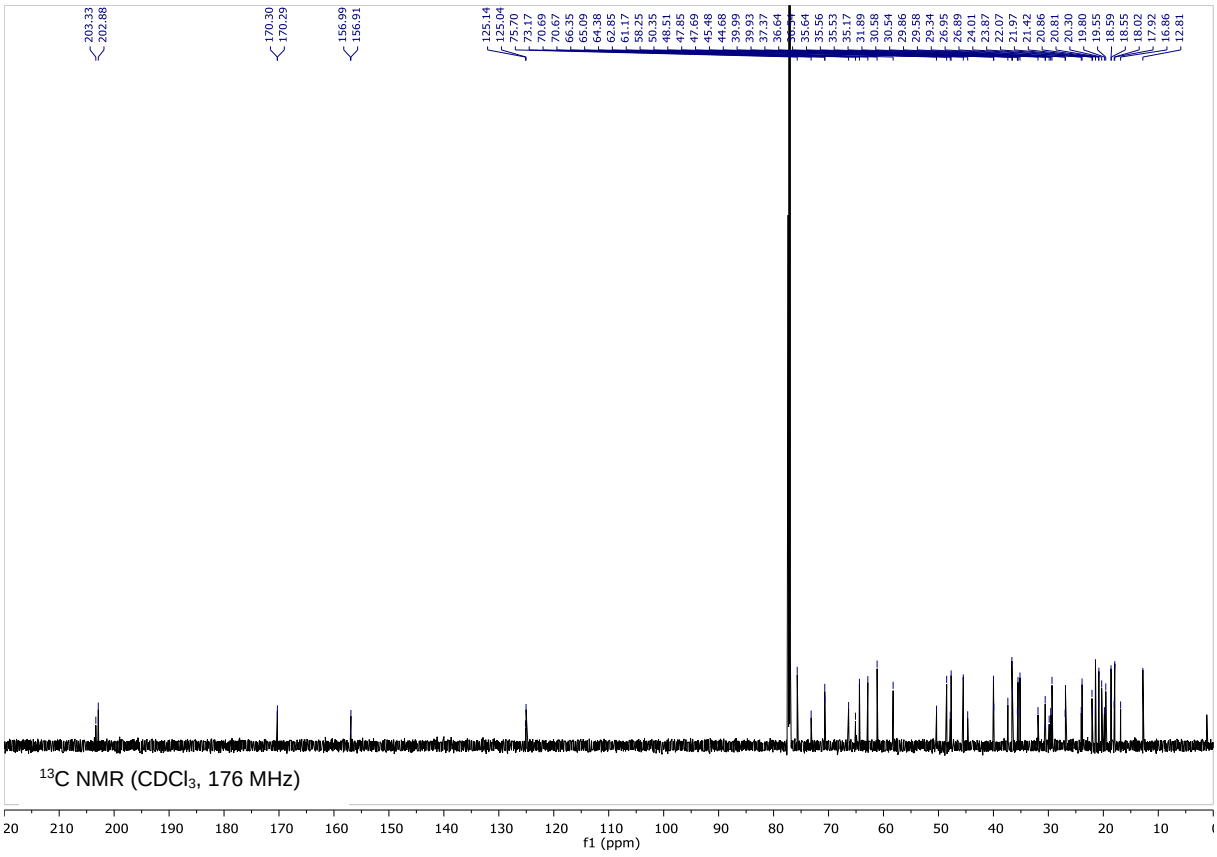

202.99
170.56
157.54
135.24
128.02
120.91
76.03
75.96
73.13
64.26
64.18
63.53
49.93
48.27
45.97
39.37
37.91
36.44
35.08
34.61
34.33
30.30
27.87
25.08
22.62
21.49
21.33
20.50
18.79
15.58
13.87
12.77
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


Me
Me
Me
Me
Me
O
O
O
H
AcO
303
NO2
O2N
1H NMR (CDCl3, 700 MHz)
f1 (ppm)

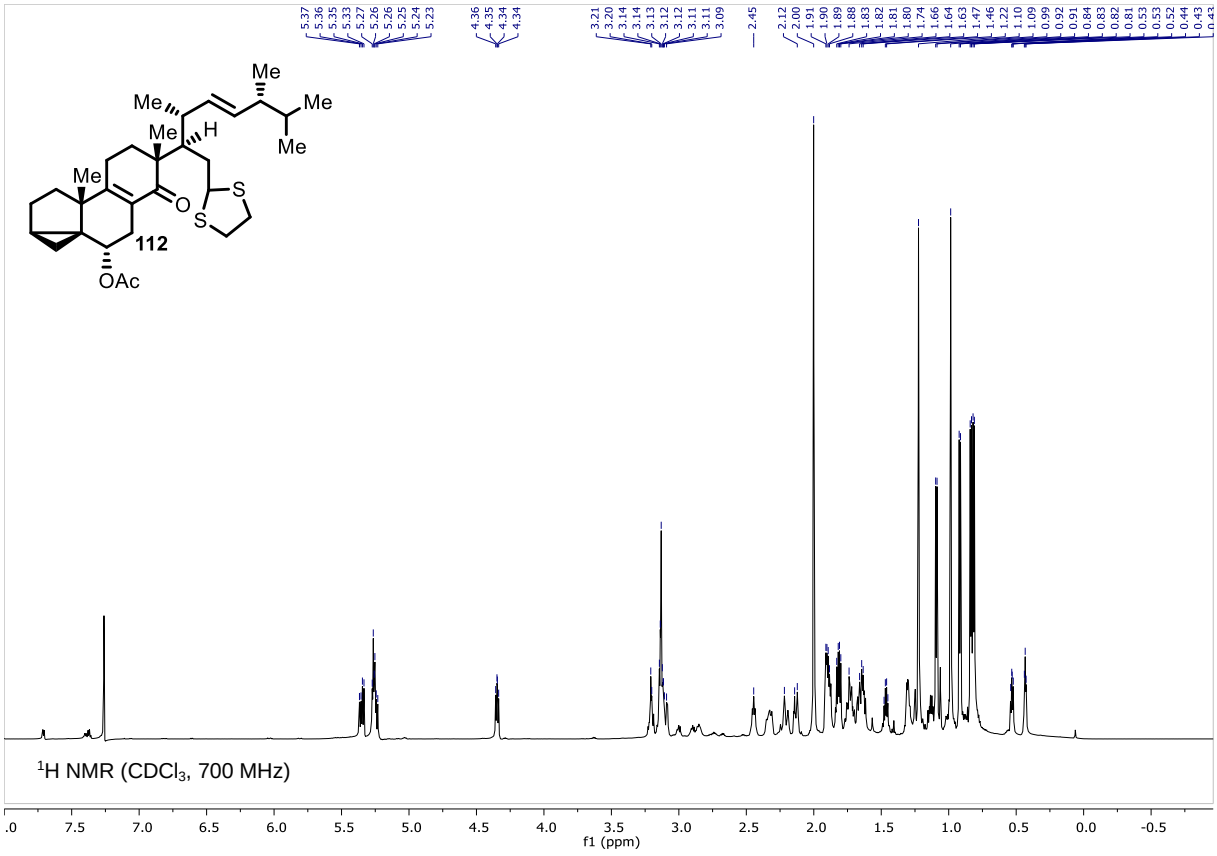

202.78
170.54
162.42
157.71
148.78
145.36
135.31
134.54
129.47
127.86
122.34
120.91
119.01
81.39
73.03
47.85
46.41
45.79
39.39
37.89
37.18
35.37
34.43
32.30
29.85
27.84
25.04
22.61
21.66
21.58
21.49
19.72
18.48
14.15
13C NMR (CDCl3, 176 MHz)
f1 (ppm)

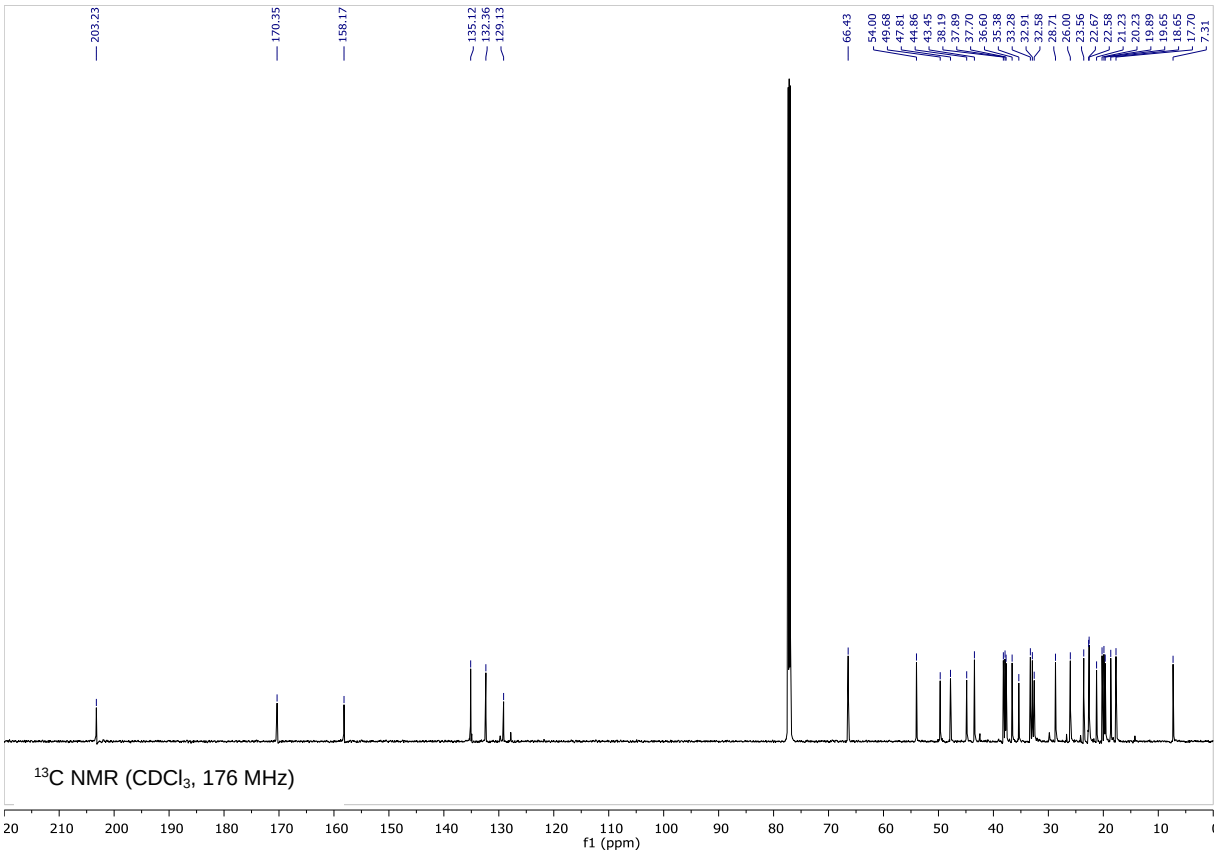


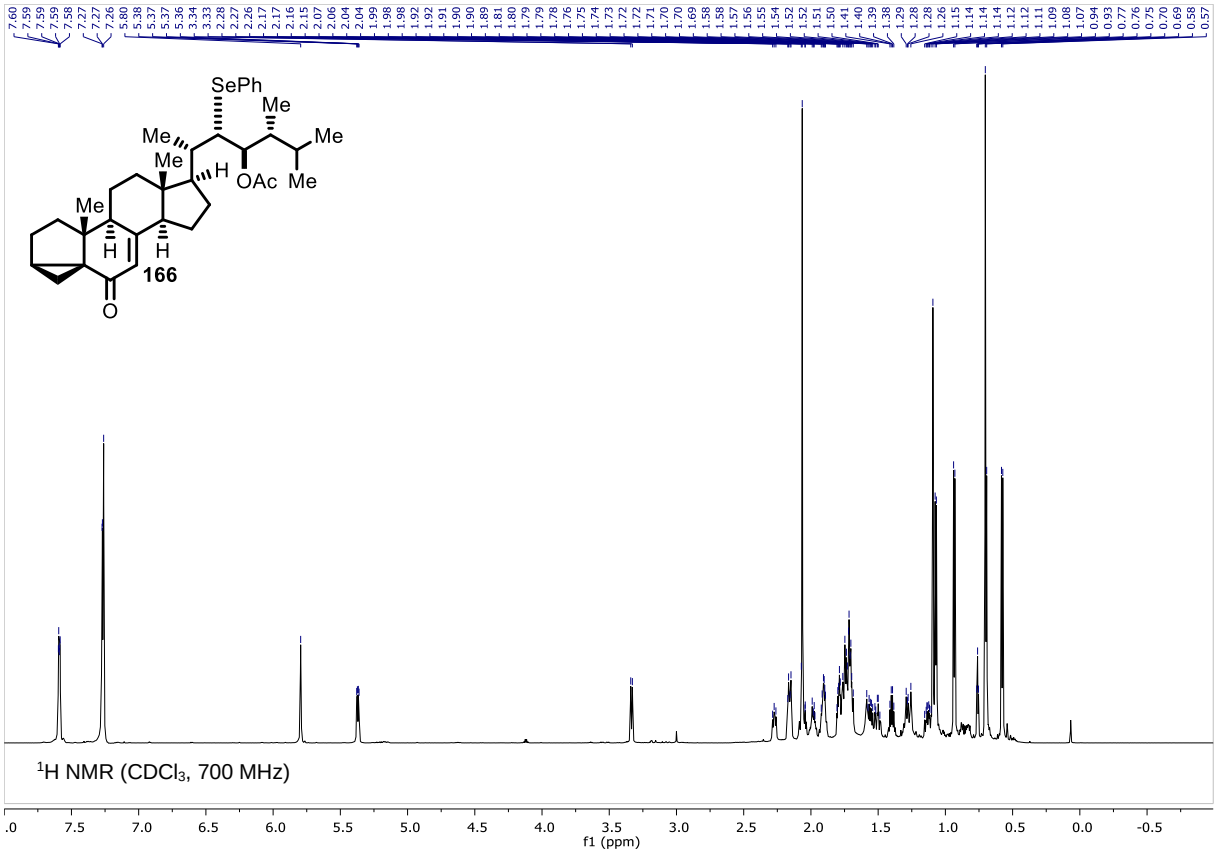
^{1}H NMR ($CDCl_3$, 700 MHz)



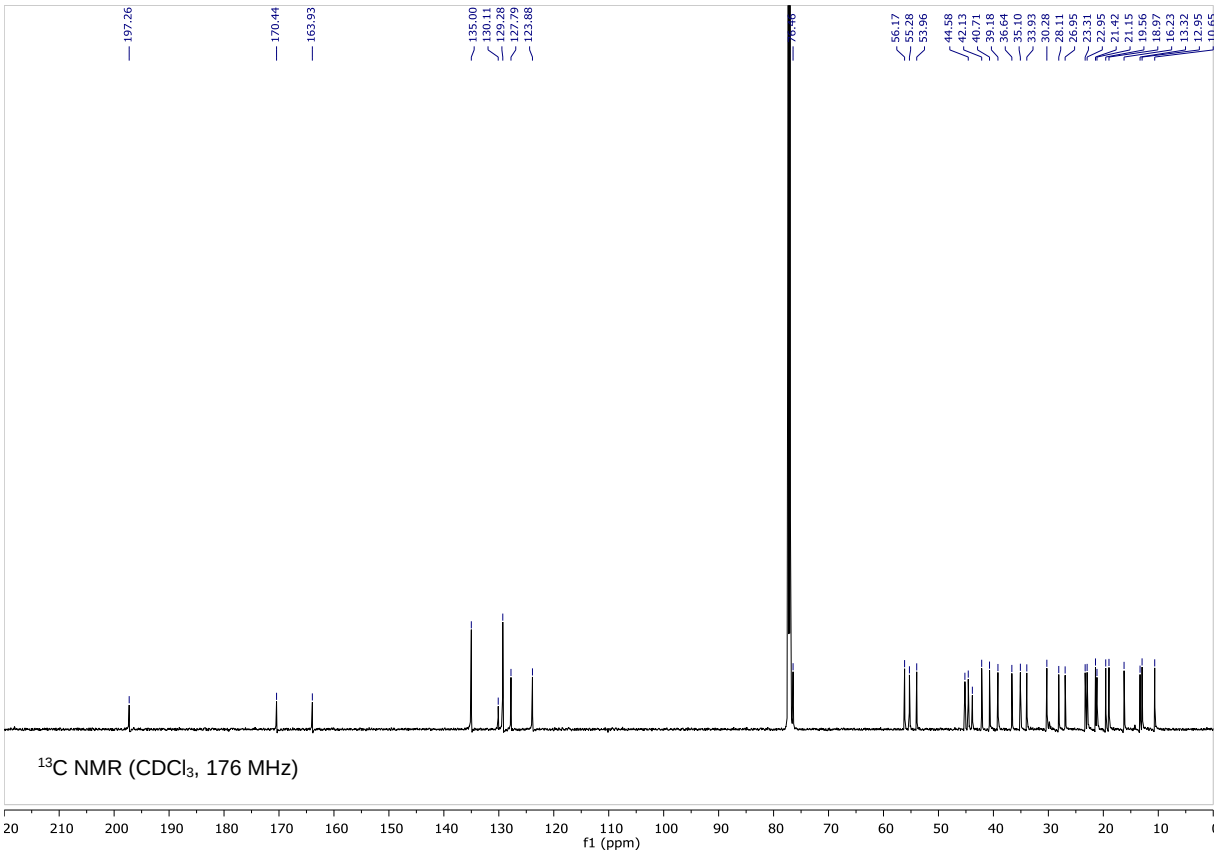
^{13}C NMR ($CDCl_3$, 176 MHz)


Me
Me
Me
H
Me
Me
Me
O
S
S
112
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

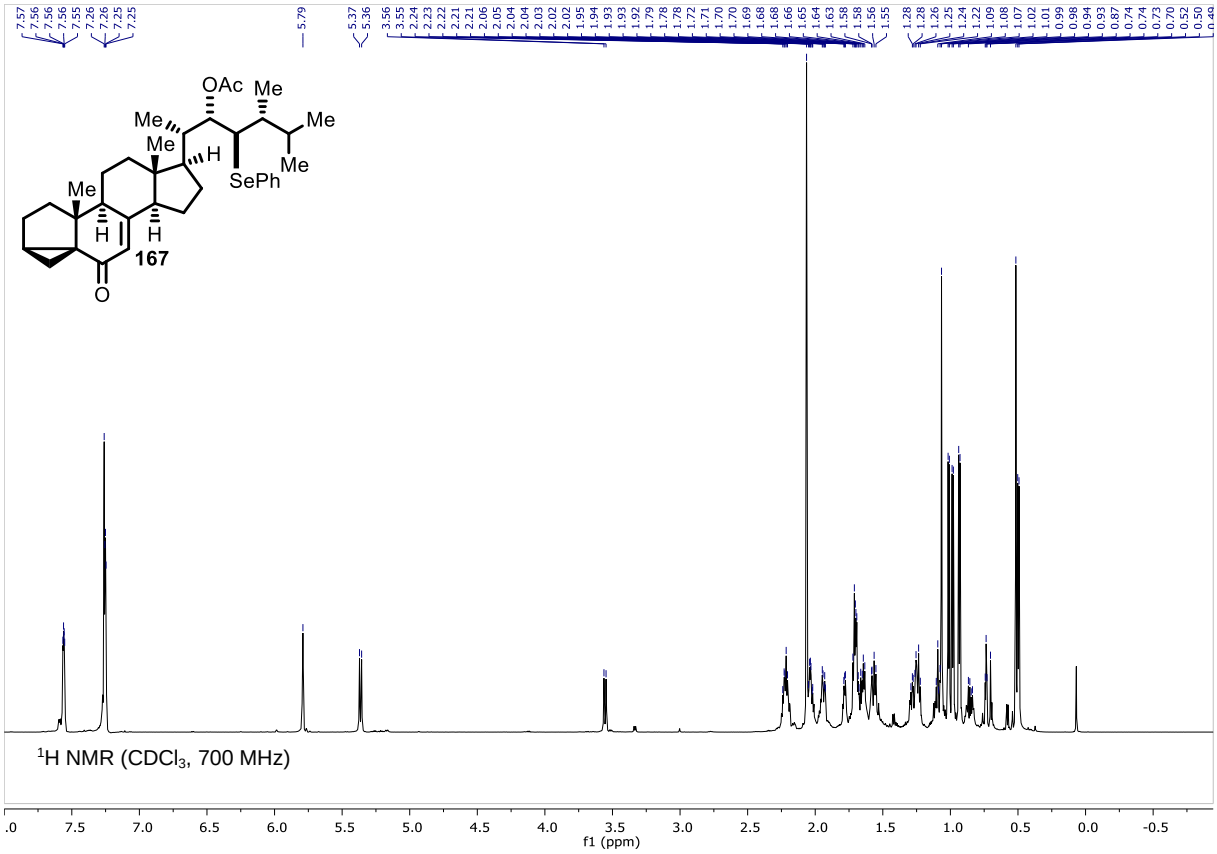

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

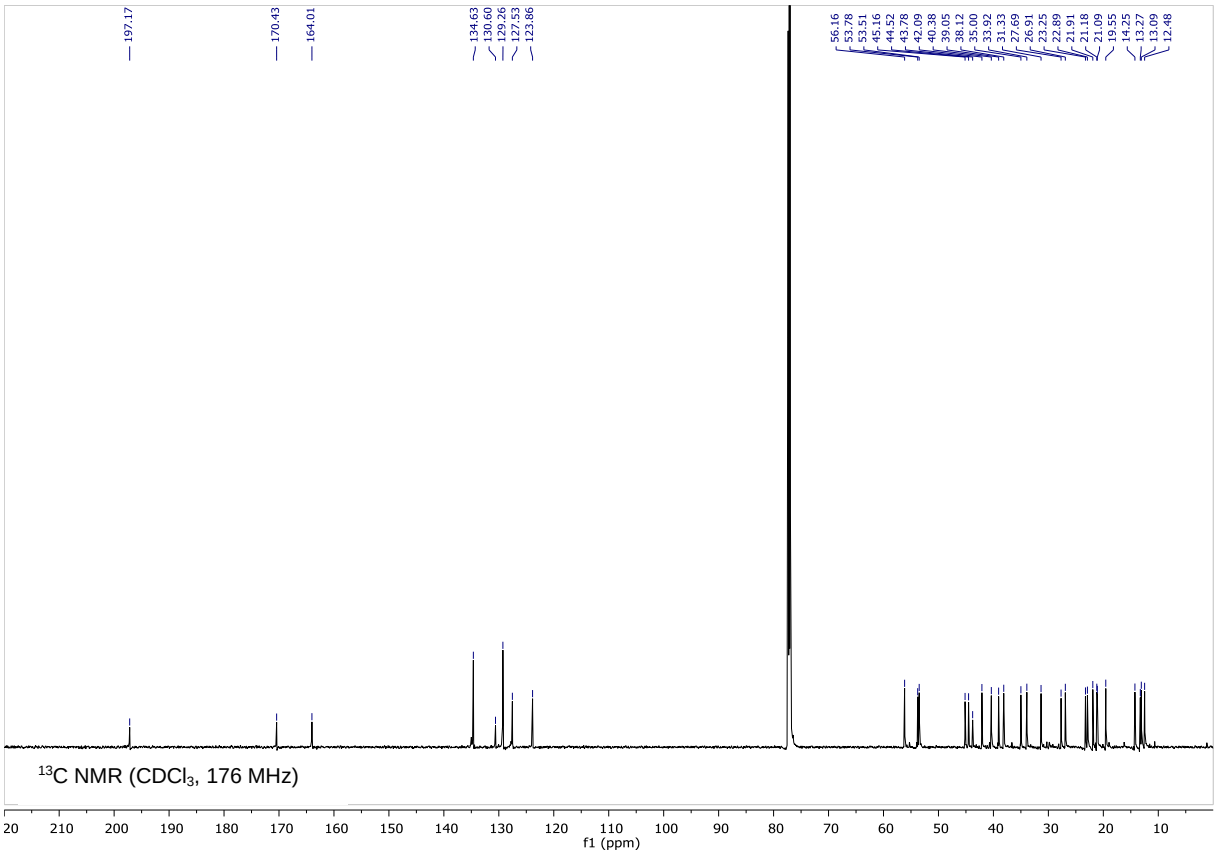


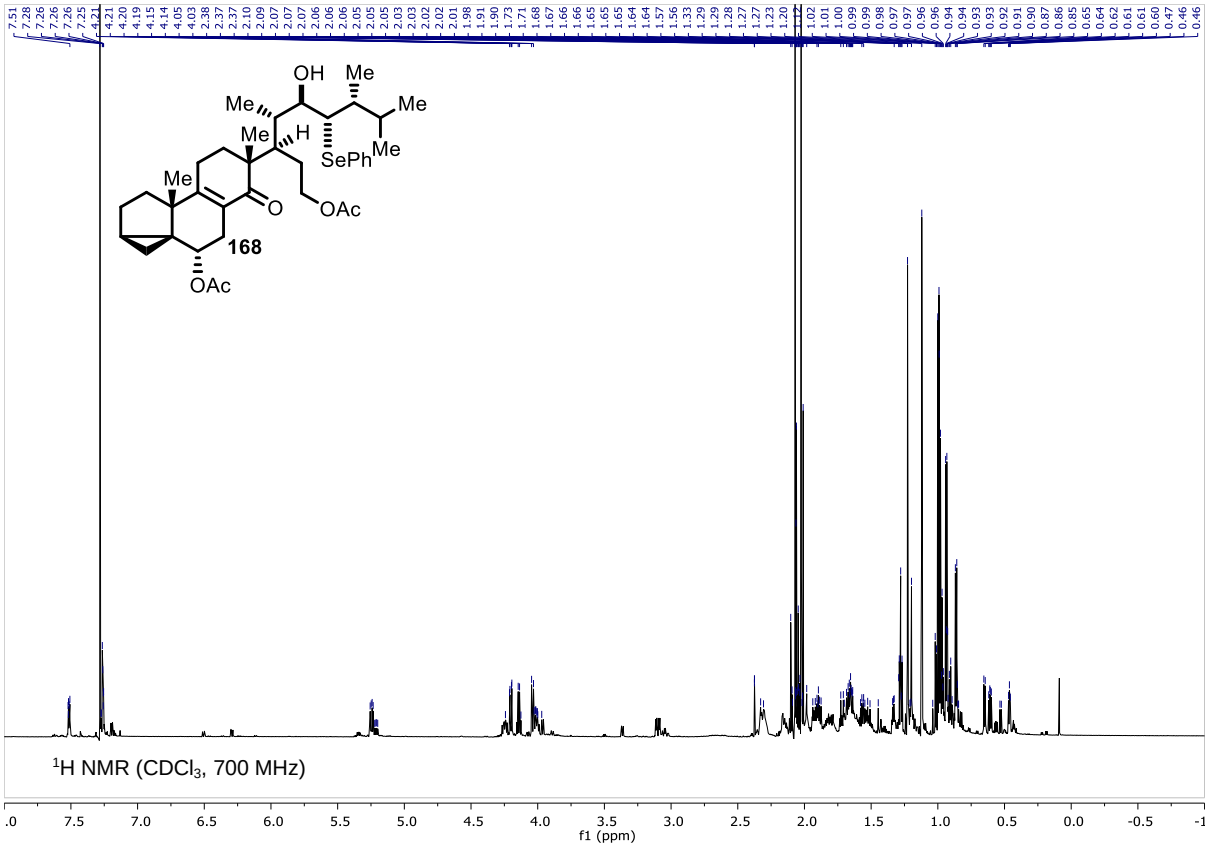
^{1}H NMR ($CDCl_3$, 700 MHz)

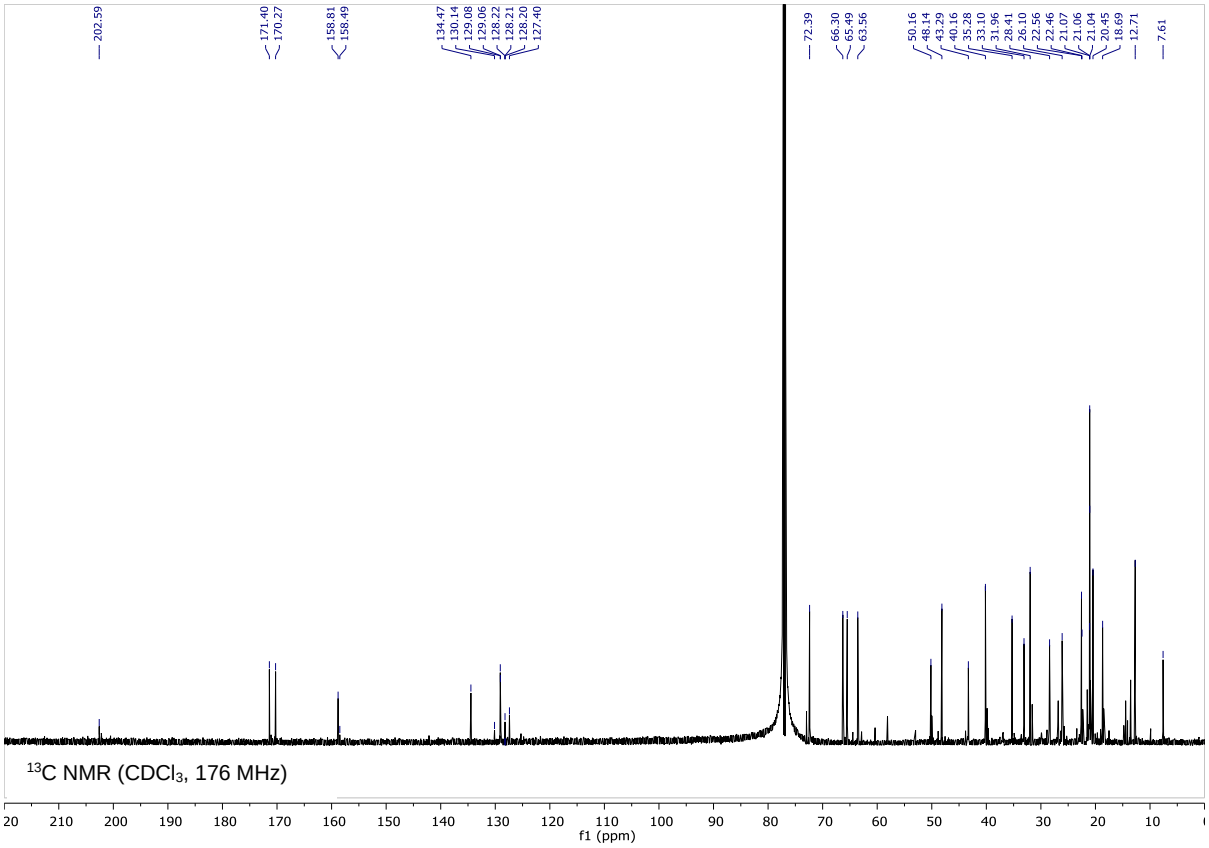


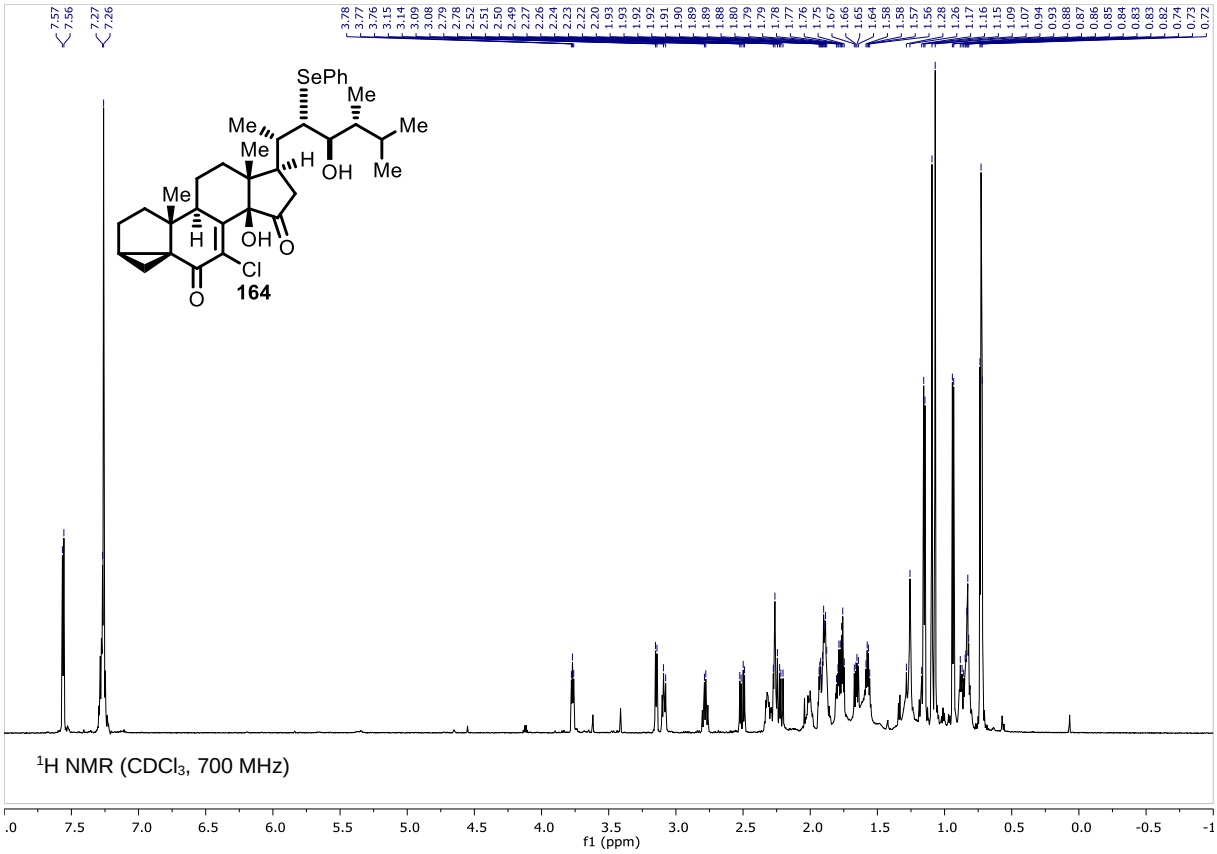
^{13}C NMR ($CDCl_3$, 176 MHz)

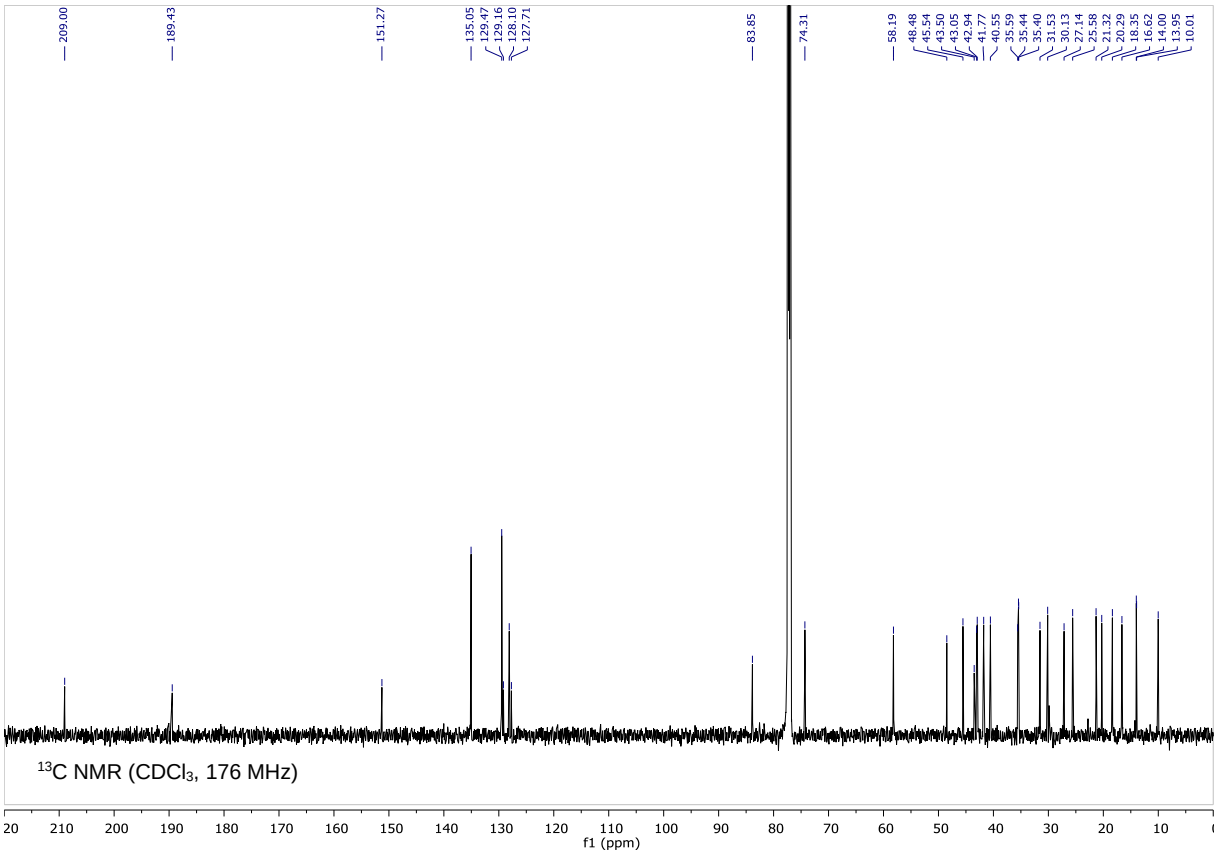

OAc
Me
Me
Me
Me
H
Me
SePh
Me
H
H
167
O
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

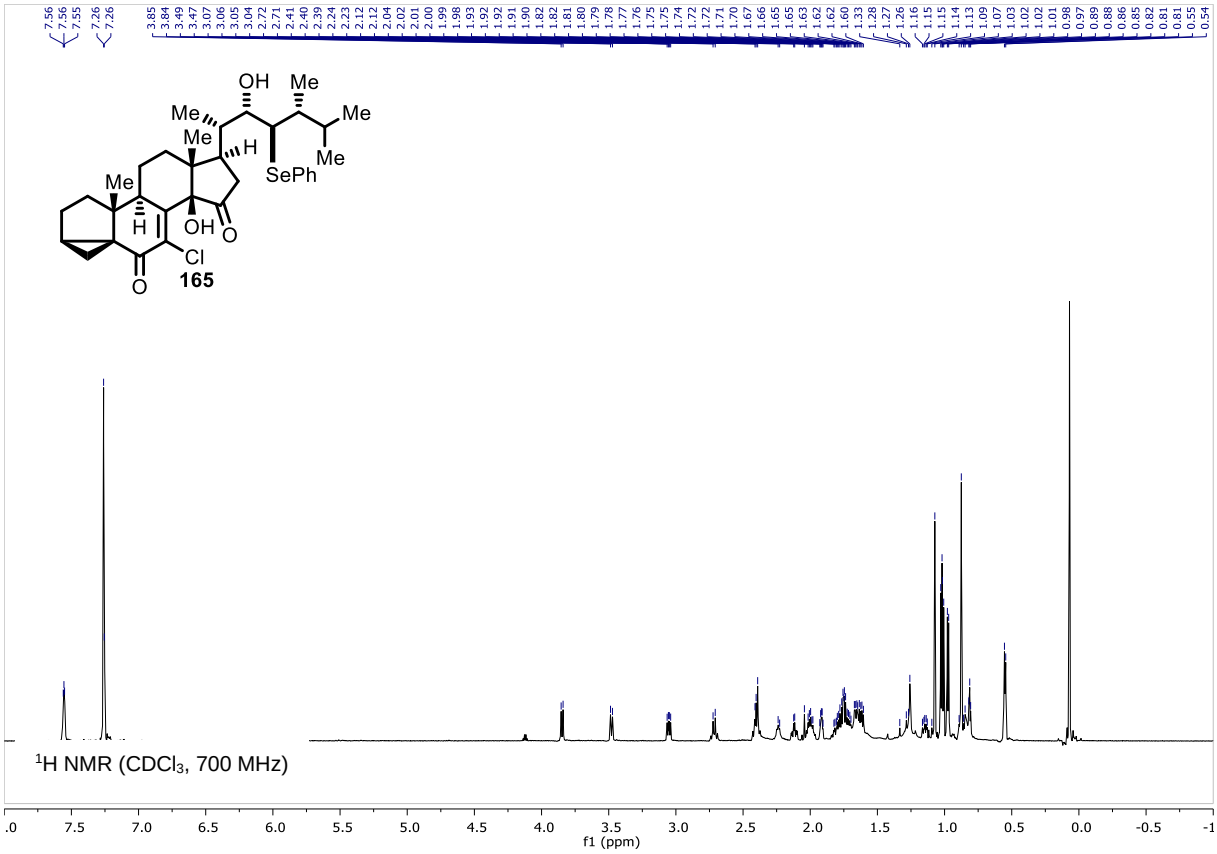

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

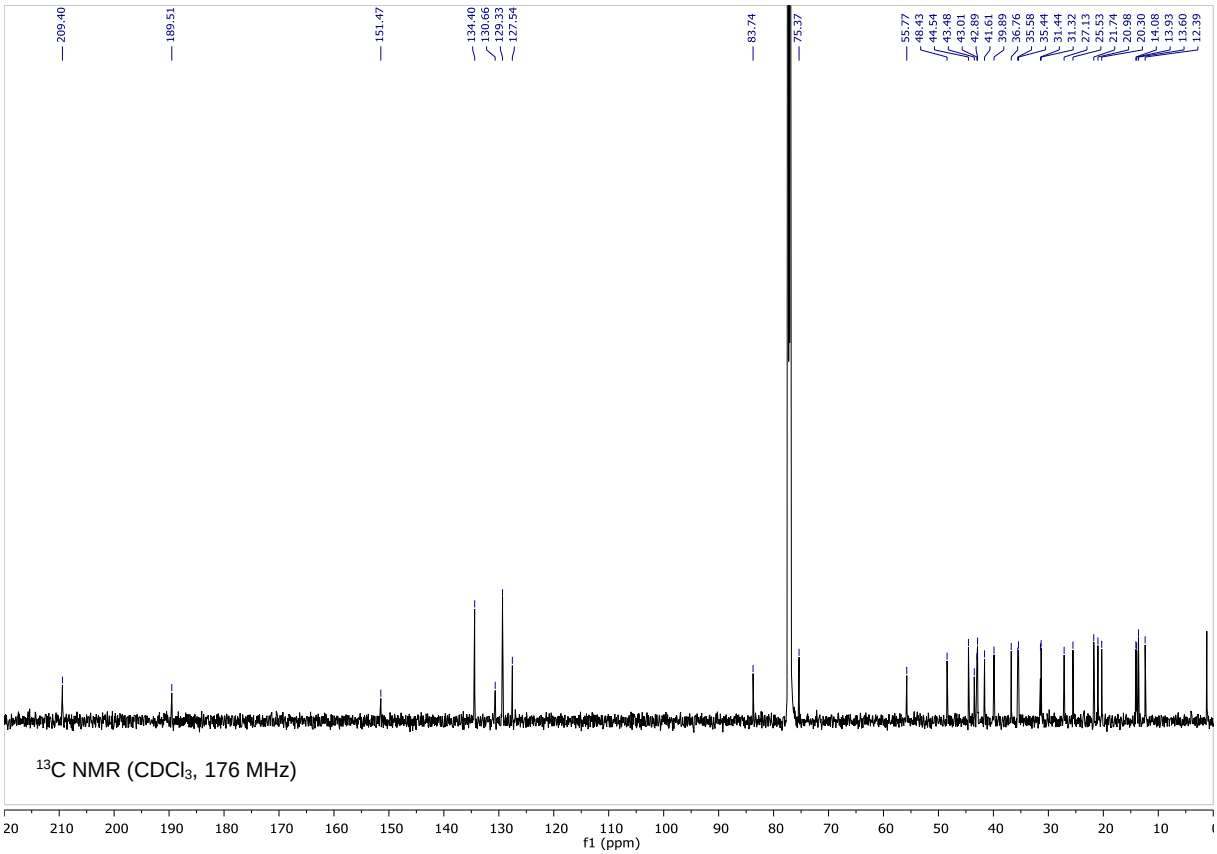

OH
Me
Me
Me
Me
H
SePh
Me
Me
O
OAc
168
OAc
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

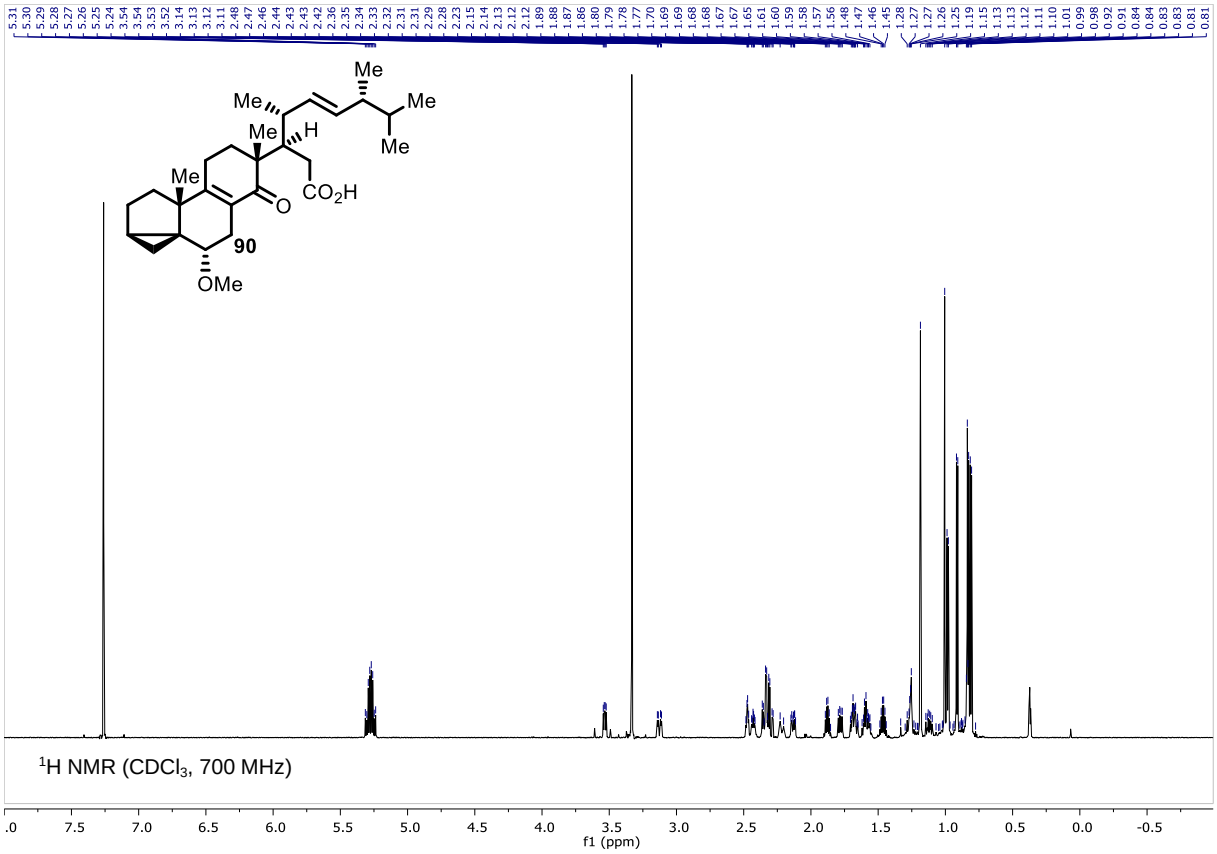

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


SePh
Me
Me
Me
Me
H
OH
Me
Me
H
OH
O
Cl
O
164
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

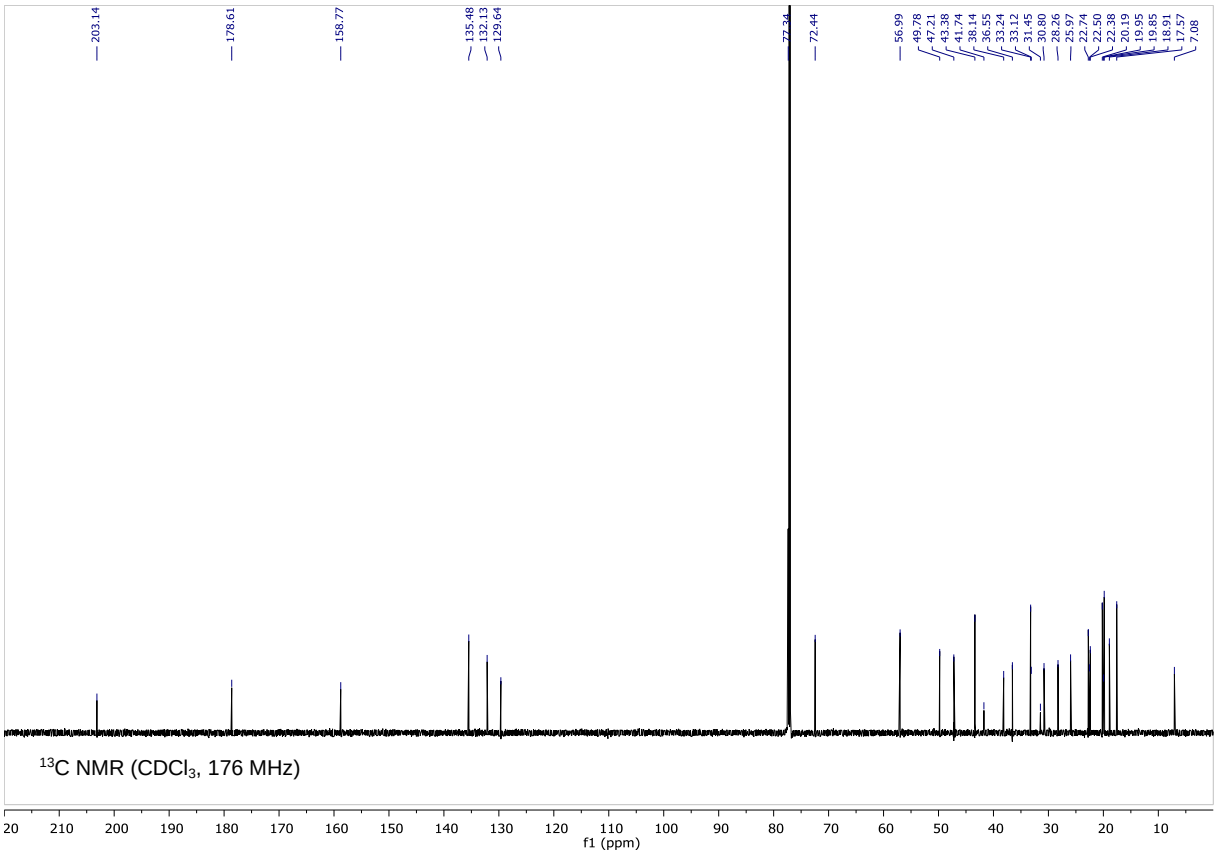

^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)


OH
Me
Me
Me
Me
H
SePh
Me
Me
H
OH
O
Cl
O
165
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

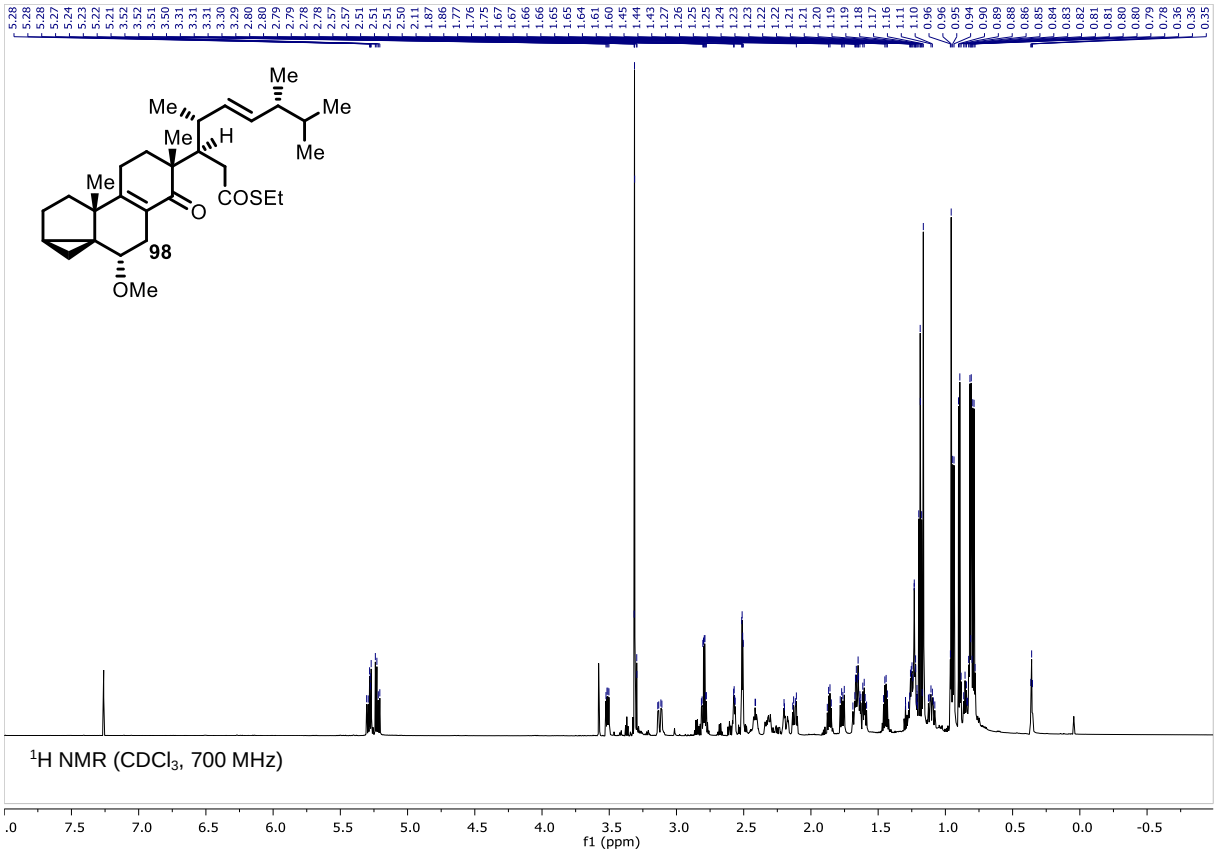

209.40
189.51
151.47
134.40
130.66
129.33
127.54
83.74
75.37
55.77
48.43
44.54
43.48
43.01
42.89
41.61
39.89
36.76
35.58
35.44
34.44
31.32
27.13
25.53
21.74
20.98
20.30
14.08
13.93
13.60
12.39
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)



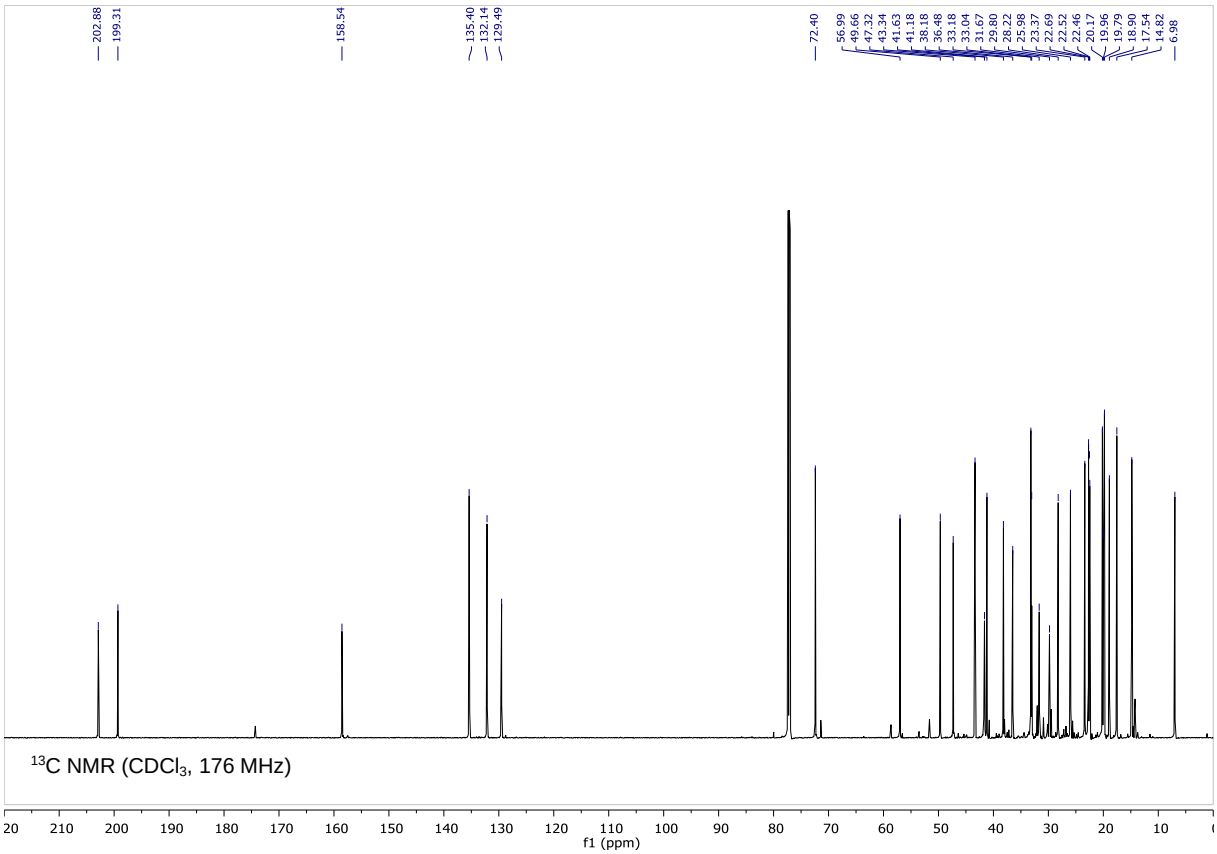
^{1}H NMR ($CDCl_3$, 700 MHz)



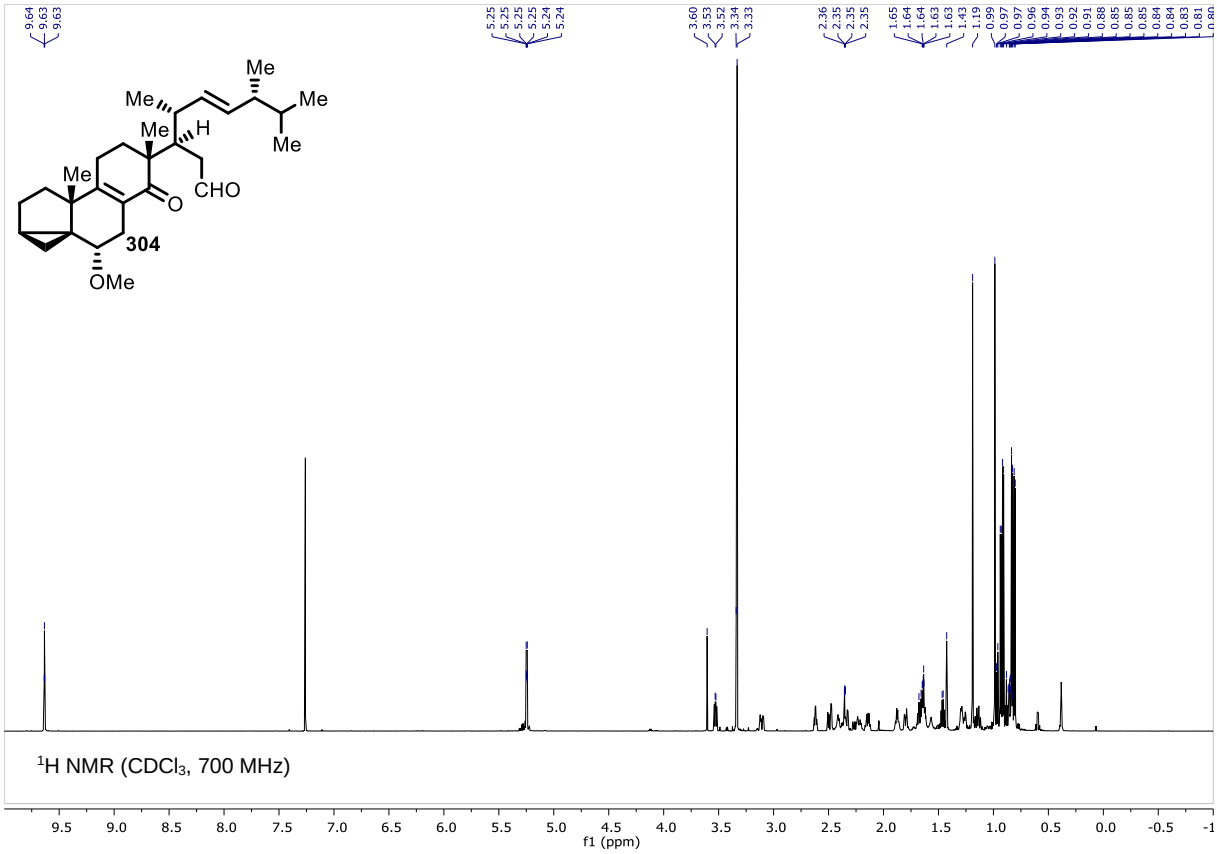
^{13}C NMR ($CDCl_3$, 176 MHz)



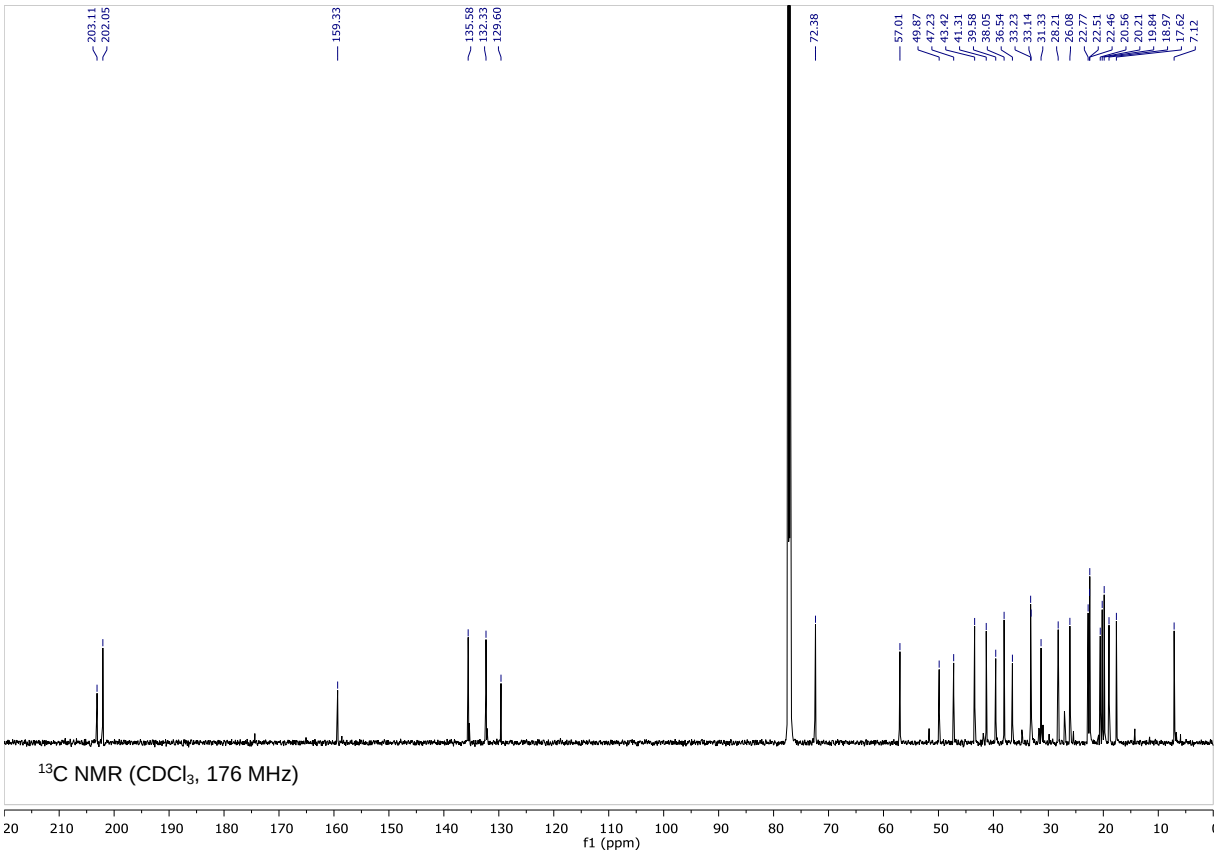
^{1}H NMR ($CDCl_3$, 700 MHz)



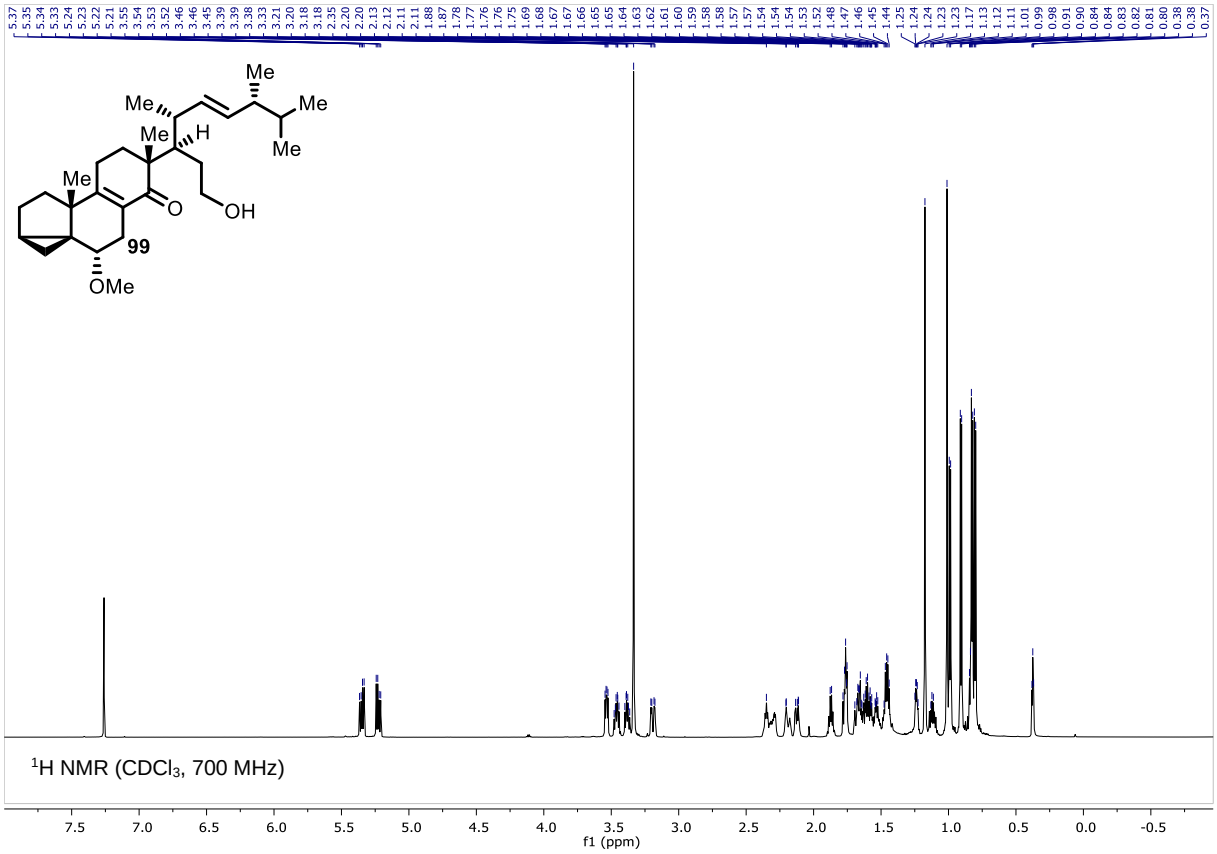
^{13}C NMR ($CDCl_3$, 176 MHz)

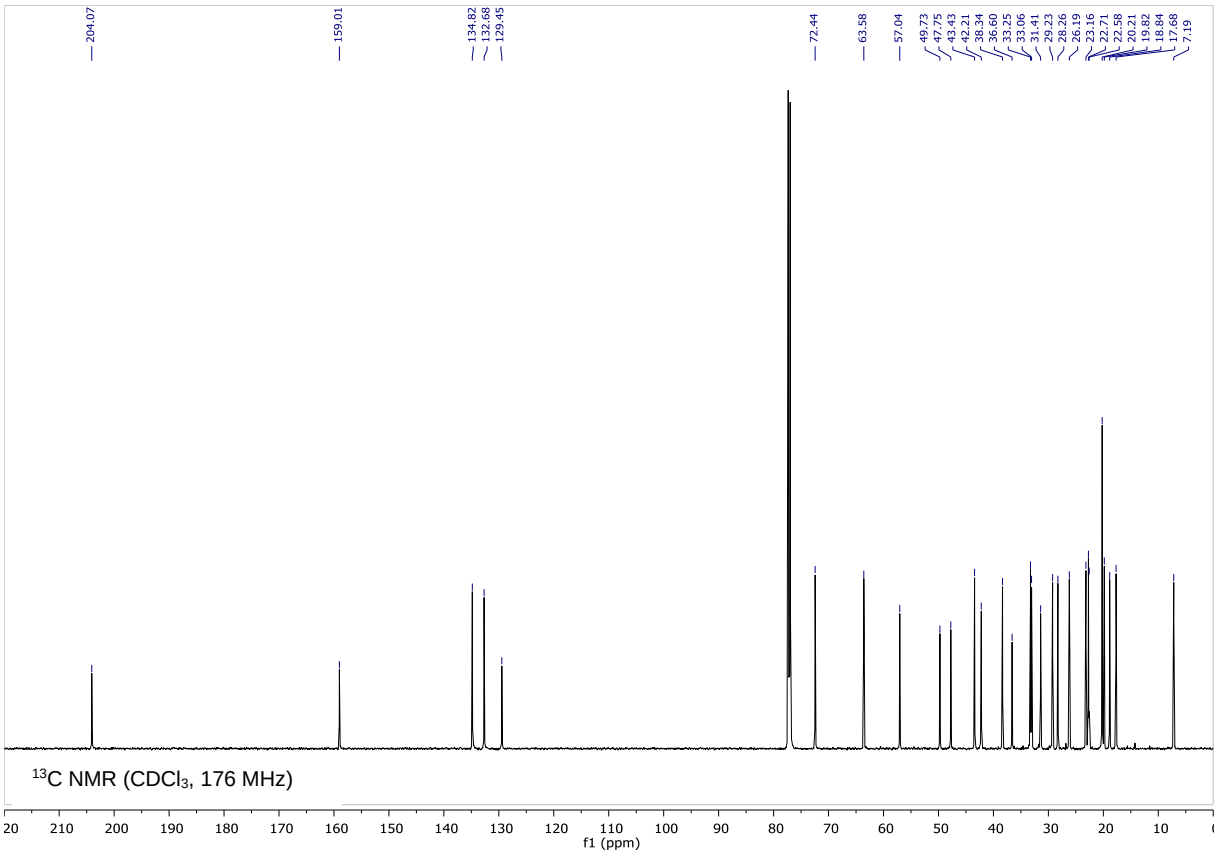


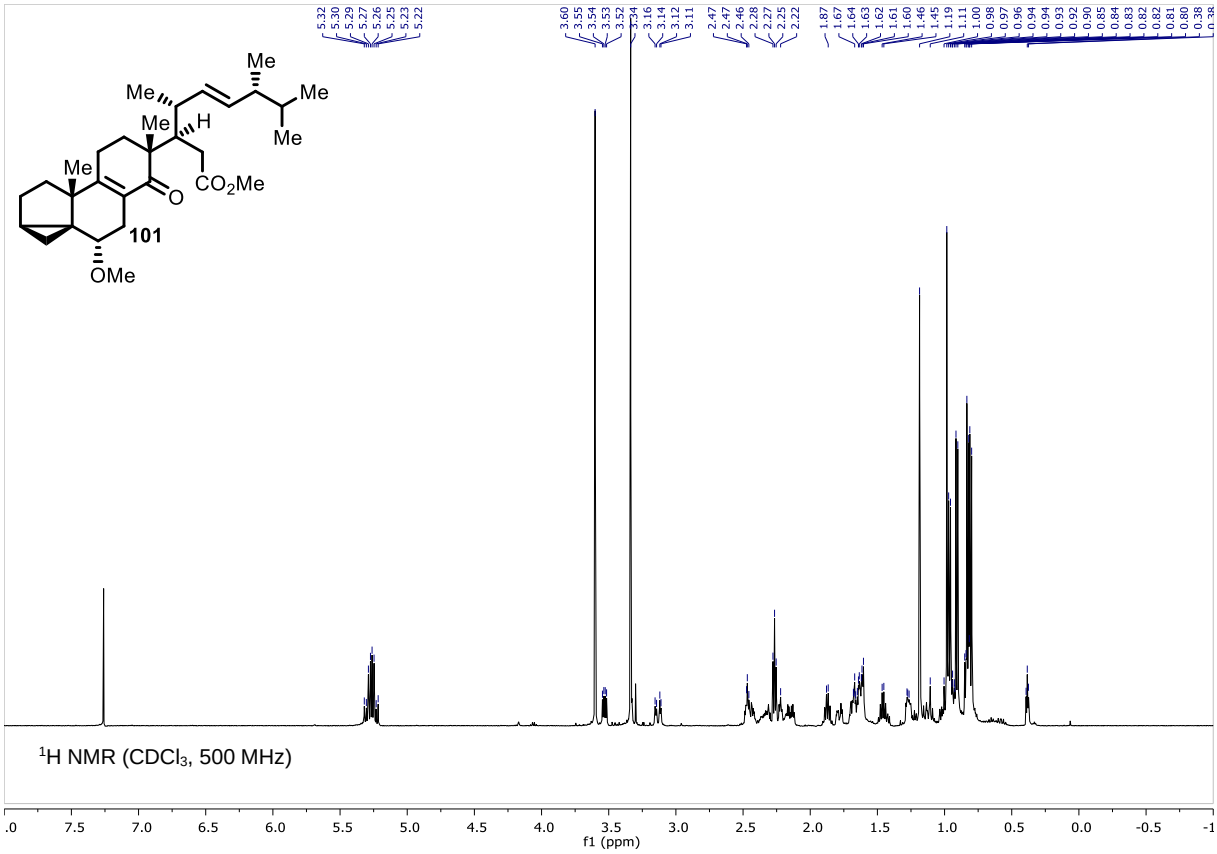
^{1}H NMR ($CDCl_3$, 700 MHz)



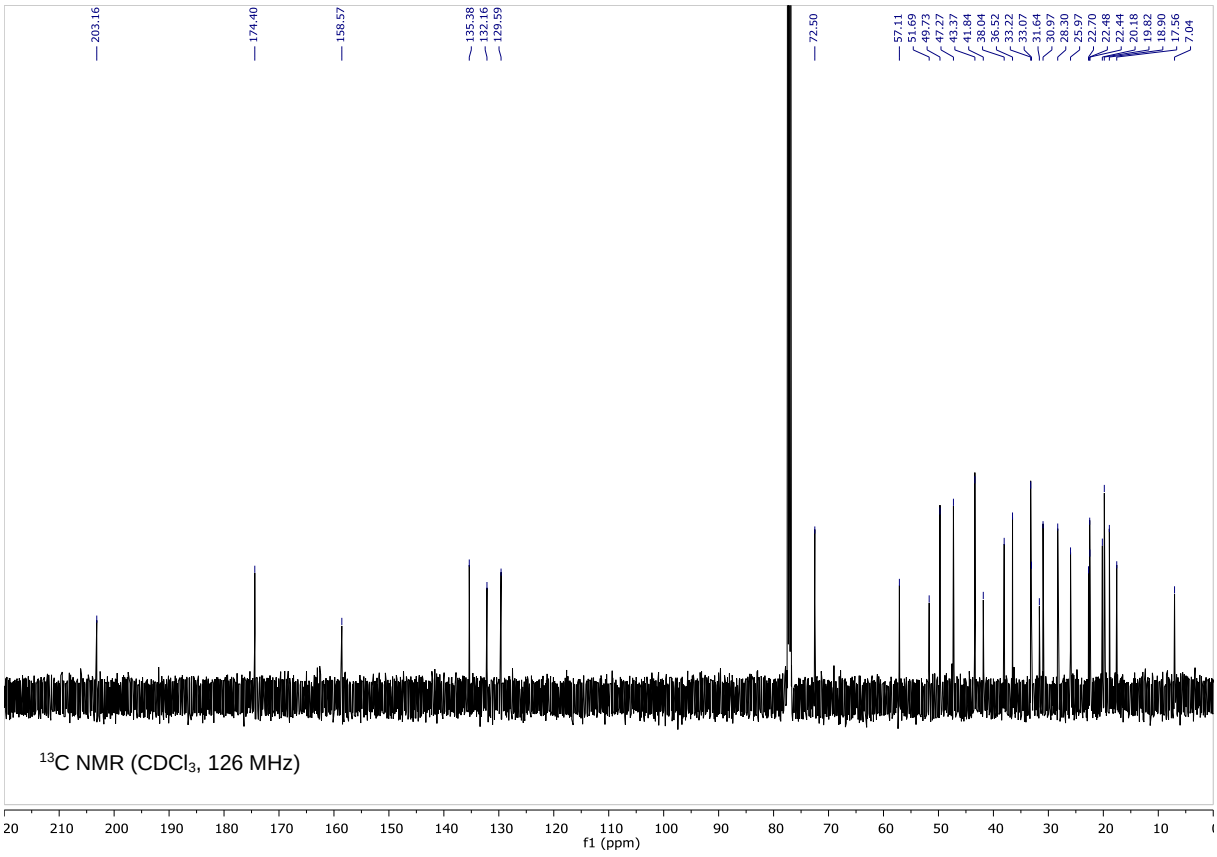
^{13}C NMR ($CDCl_3$, 176 MHz)


Me
Me
Me
Me
H
Me
Me
O
OH
99
OMe
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

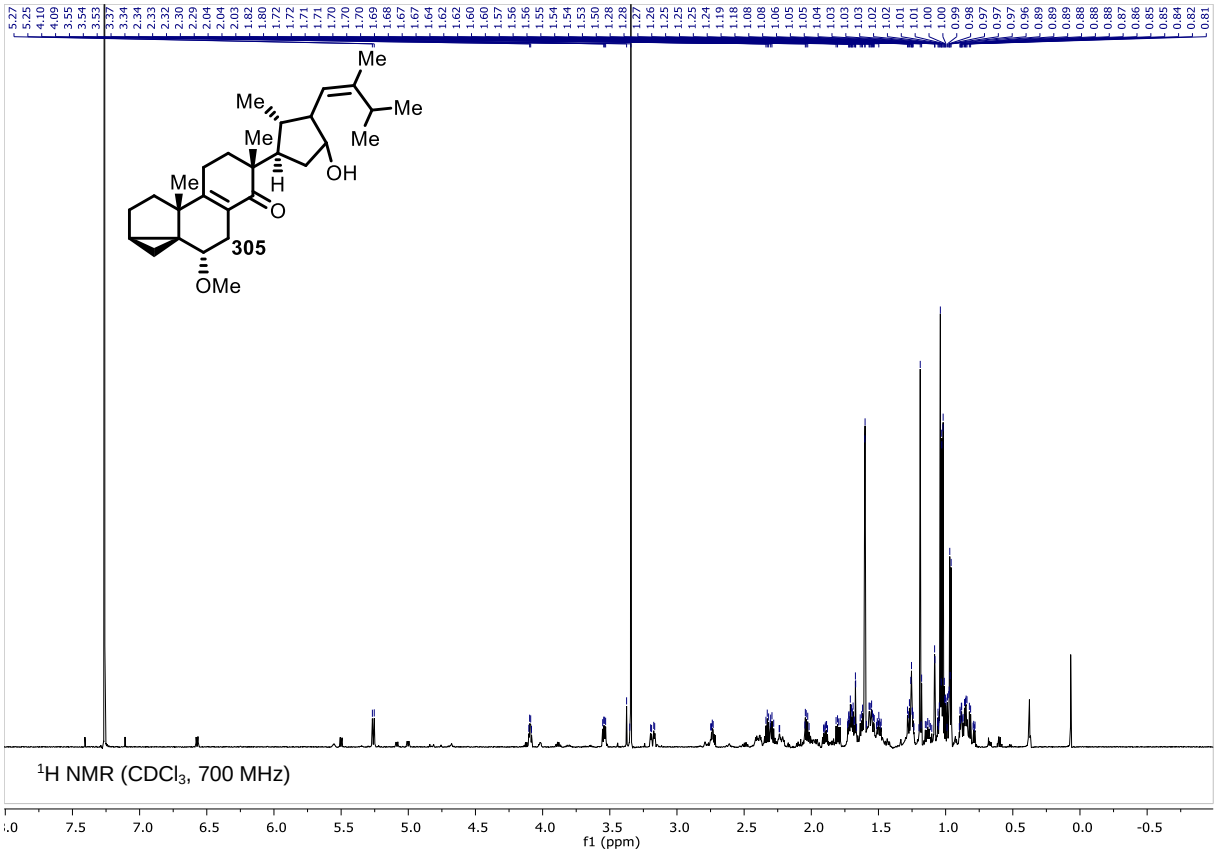

204.07
159.01
134.82
132.68
129.45
72.44
63.58
57.04
49.73
47.75
43.43
42.21
38.34
36.60
33.25
33.06
31.41
29.23
28.26
26.19
23.16
22.71
22.58
20.21
19.82
18.84
17.68
7.19
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

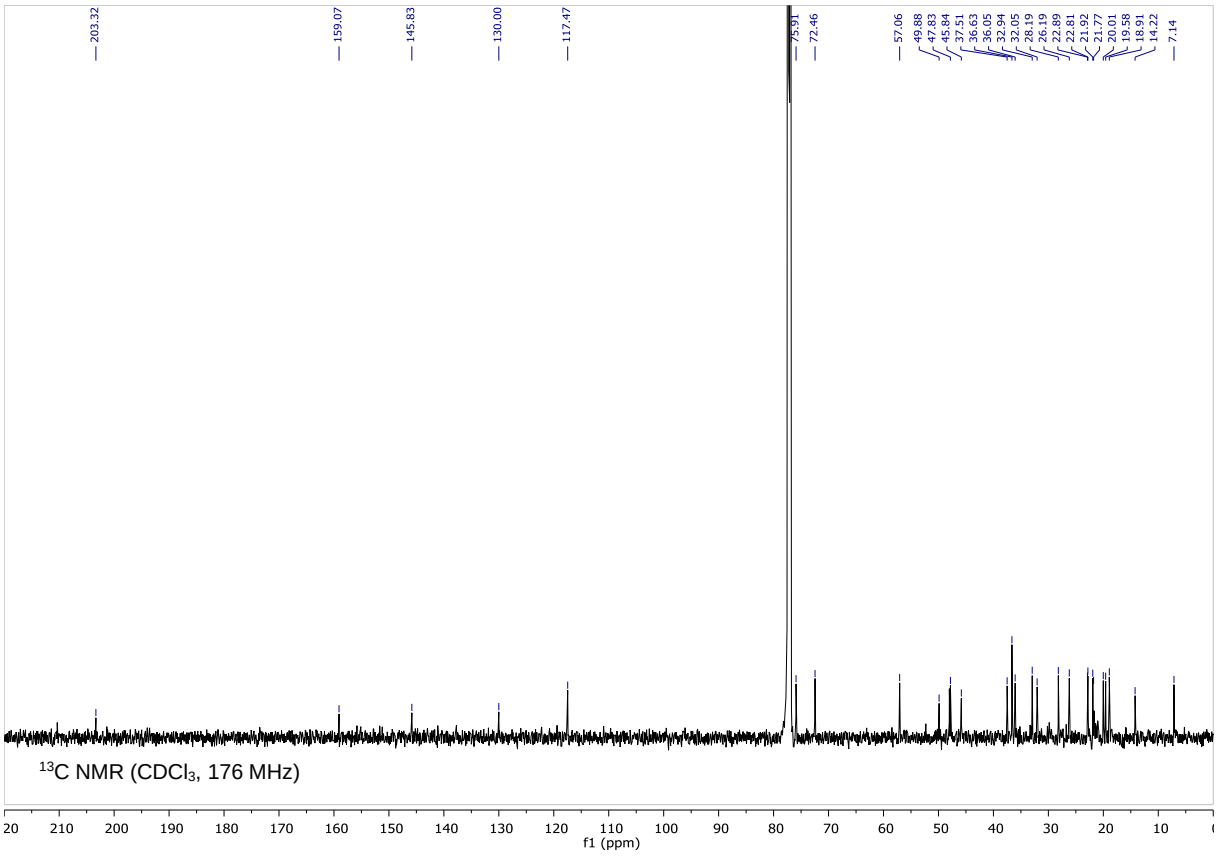


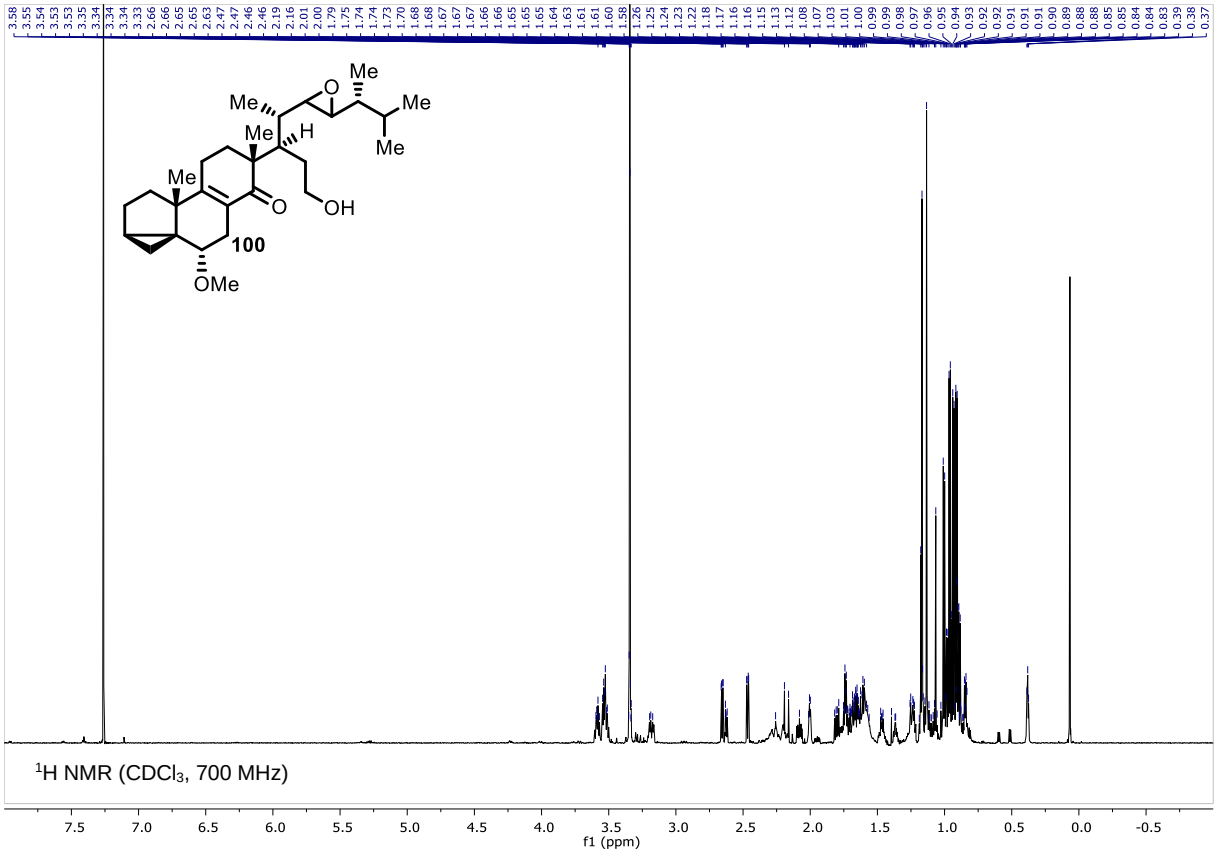
^{1}H NMR ($CDCl_3$, 500 MHz)



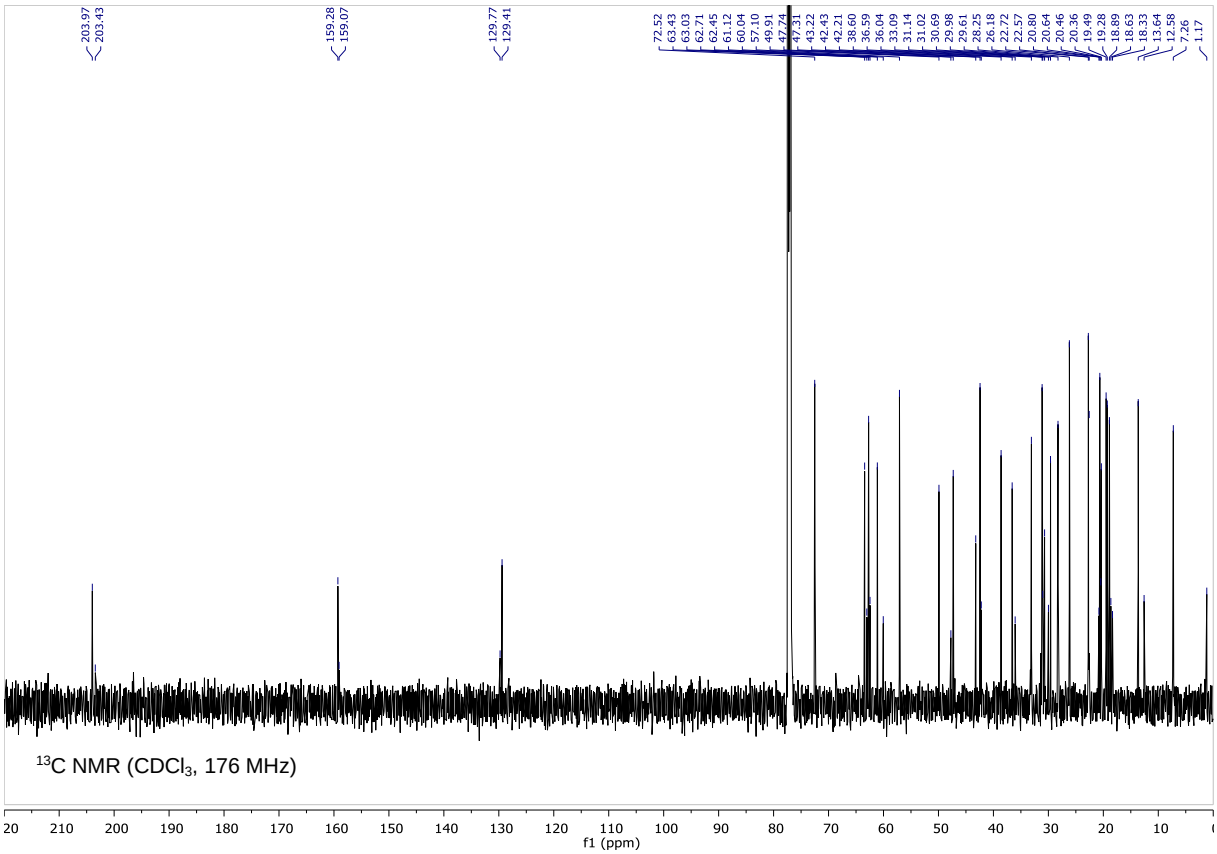
^{13}C NMR ($CDCl_3$, 126 MHz)


Me
Me
Me
Me
Me
OH
Me
H
O
305
OMe
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

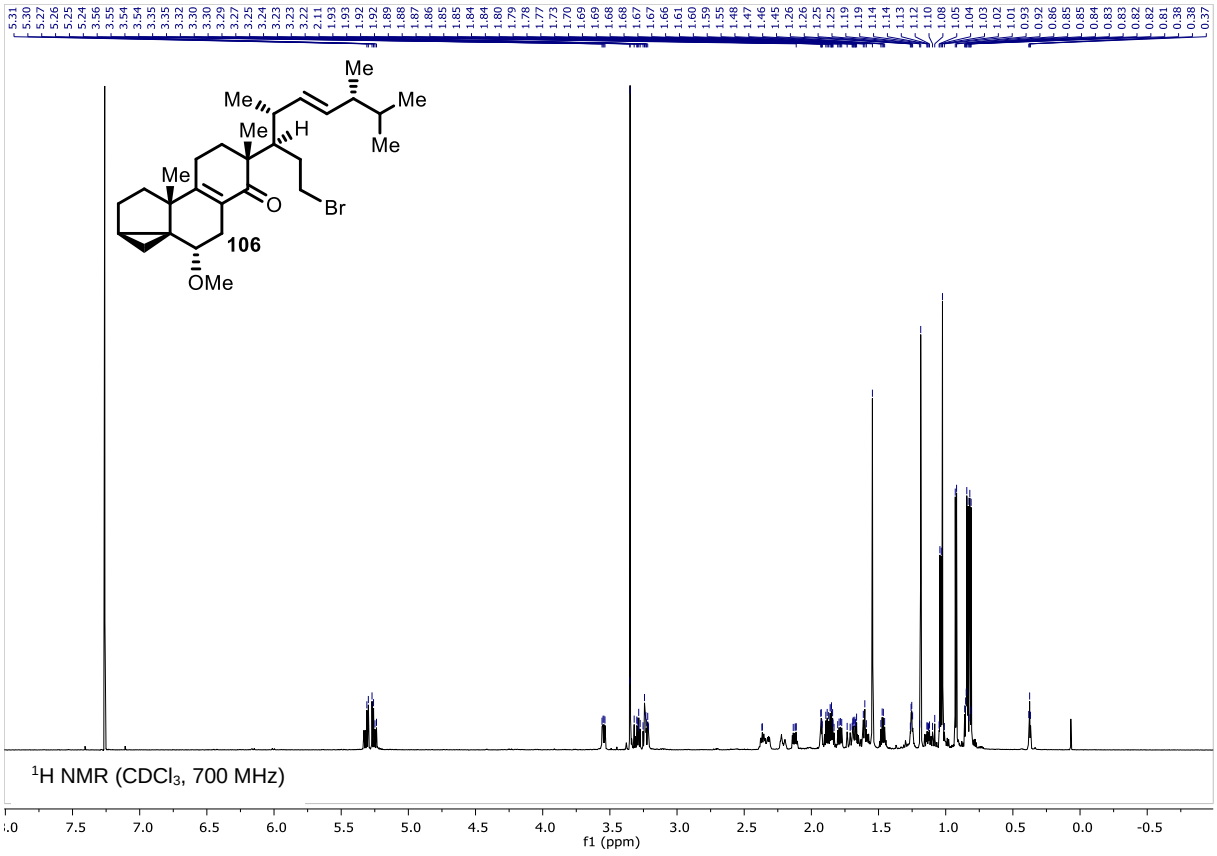

203.32
159.07
145.83
130.00
117.47
75.91
72.46
57.06
49.88
47.83
45.84
37.51
36.63
36.05
32.94
32.05
28.19
26.19
22.89
22.81
21.92
21.77
20.01
19.58
18.91
14.22
7.14
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

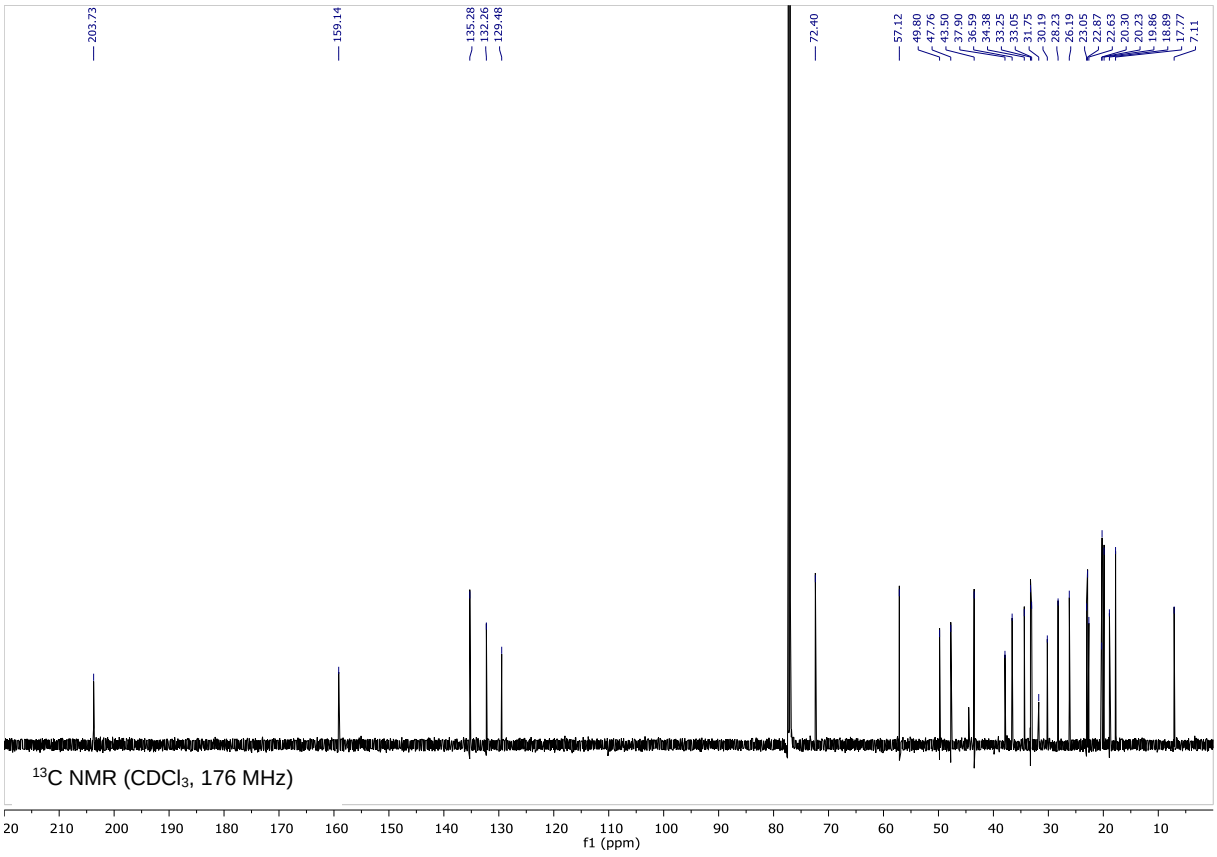


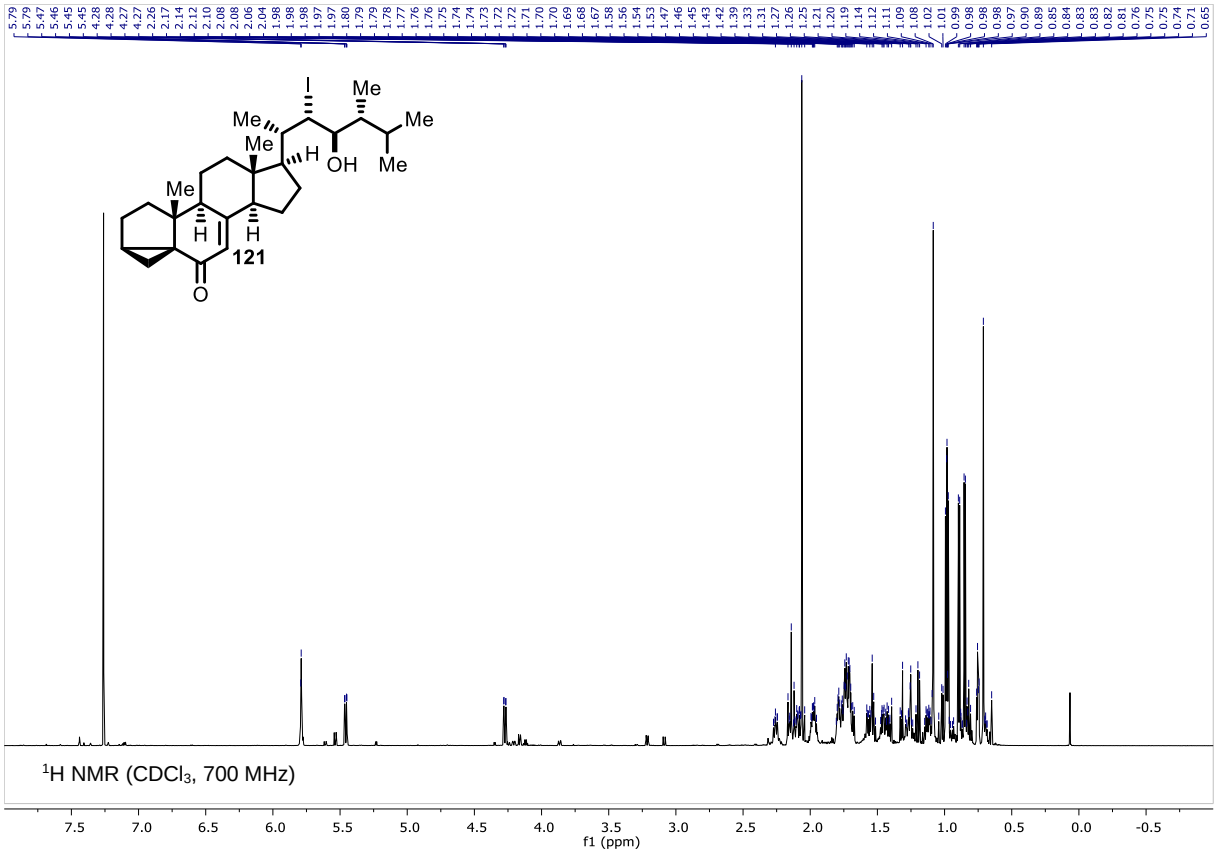
^{1}H NMR ($CDCl_3$, 700 MHz)

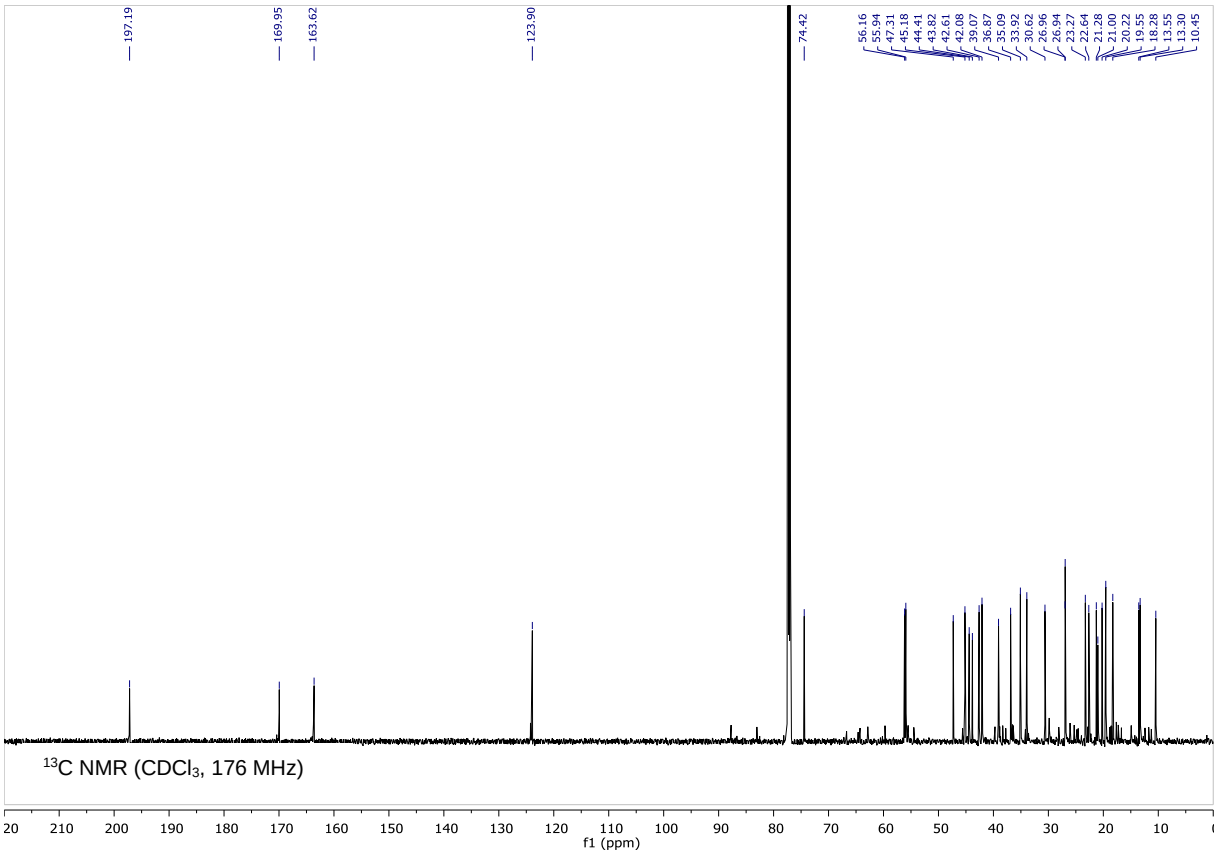


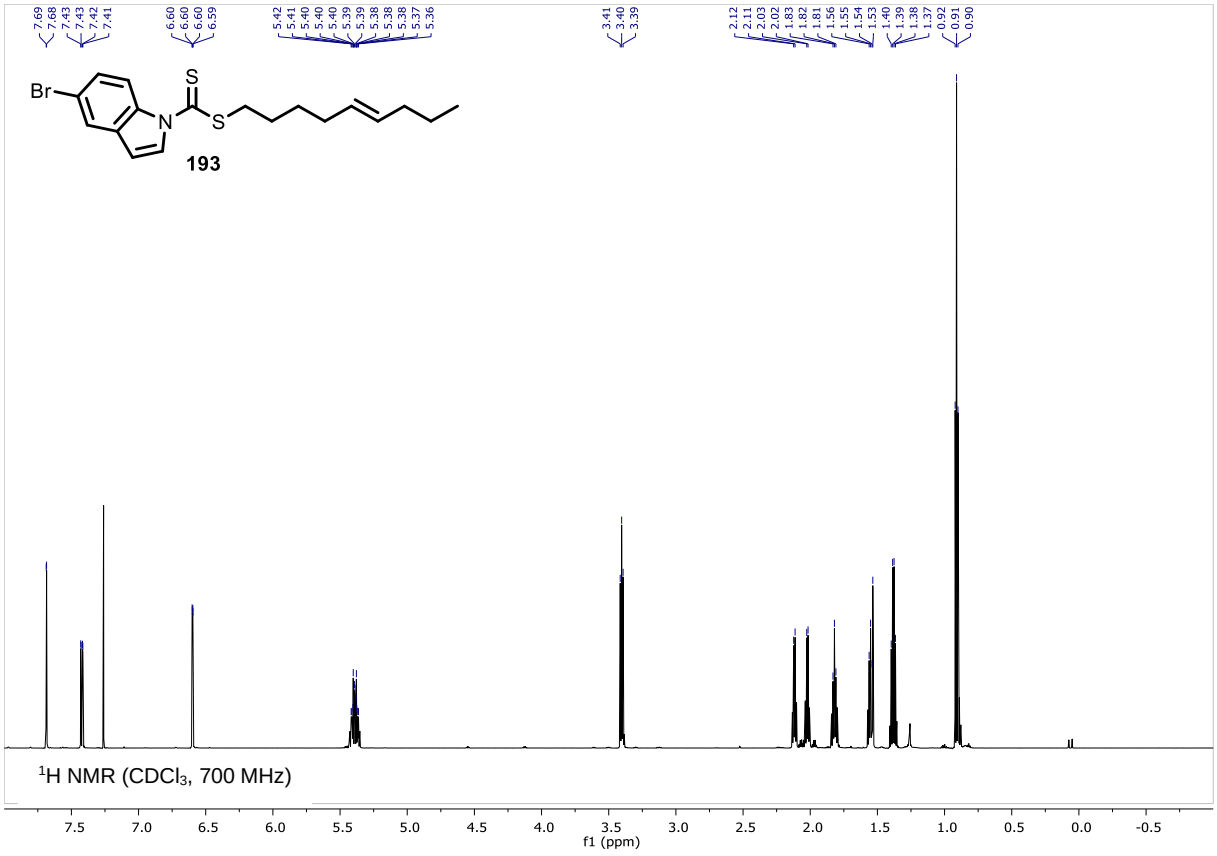
^{13}C NMR ($CDCl_3$, 176 MHz)

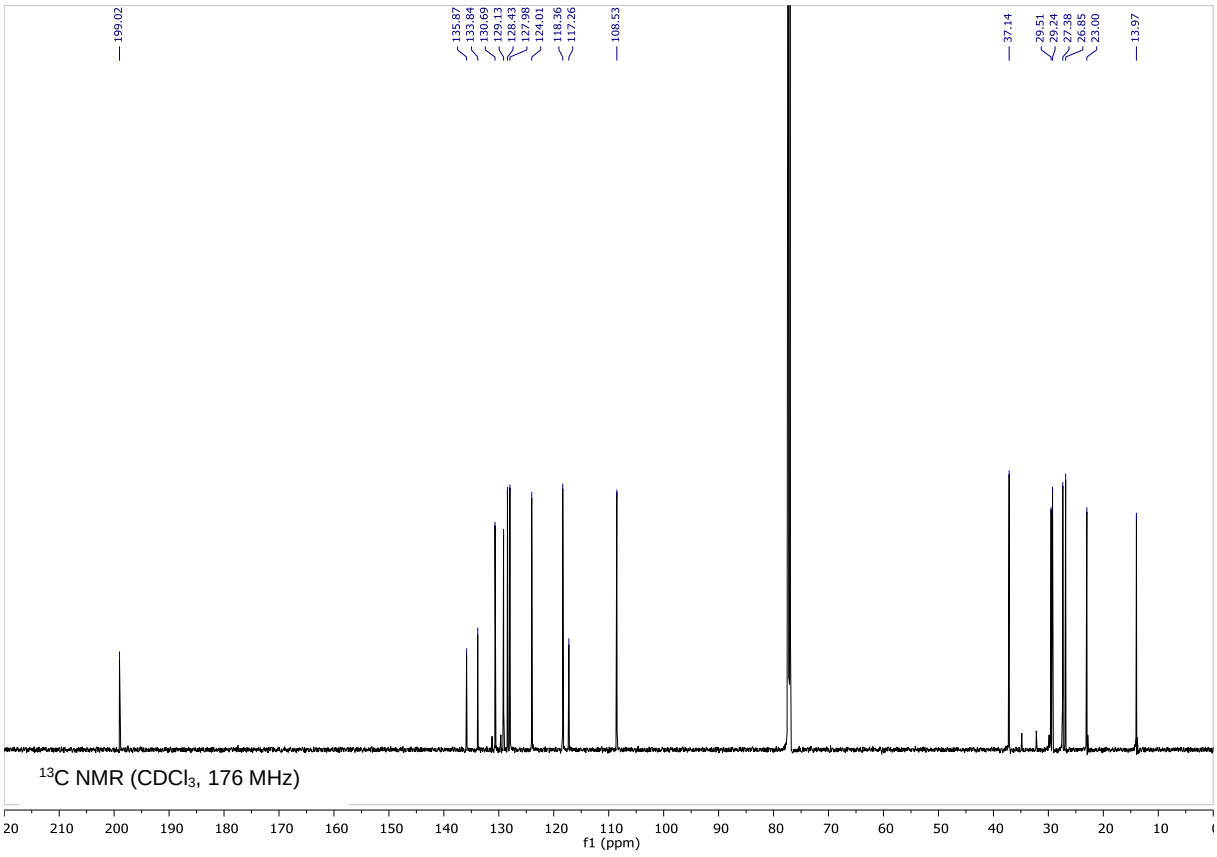

Me
Me
Me
Me
H
Me
Me
O
Br
106
OMe
^{1}H NMR ($CDCl_3$, 700 MHz)
f1 (ppm)

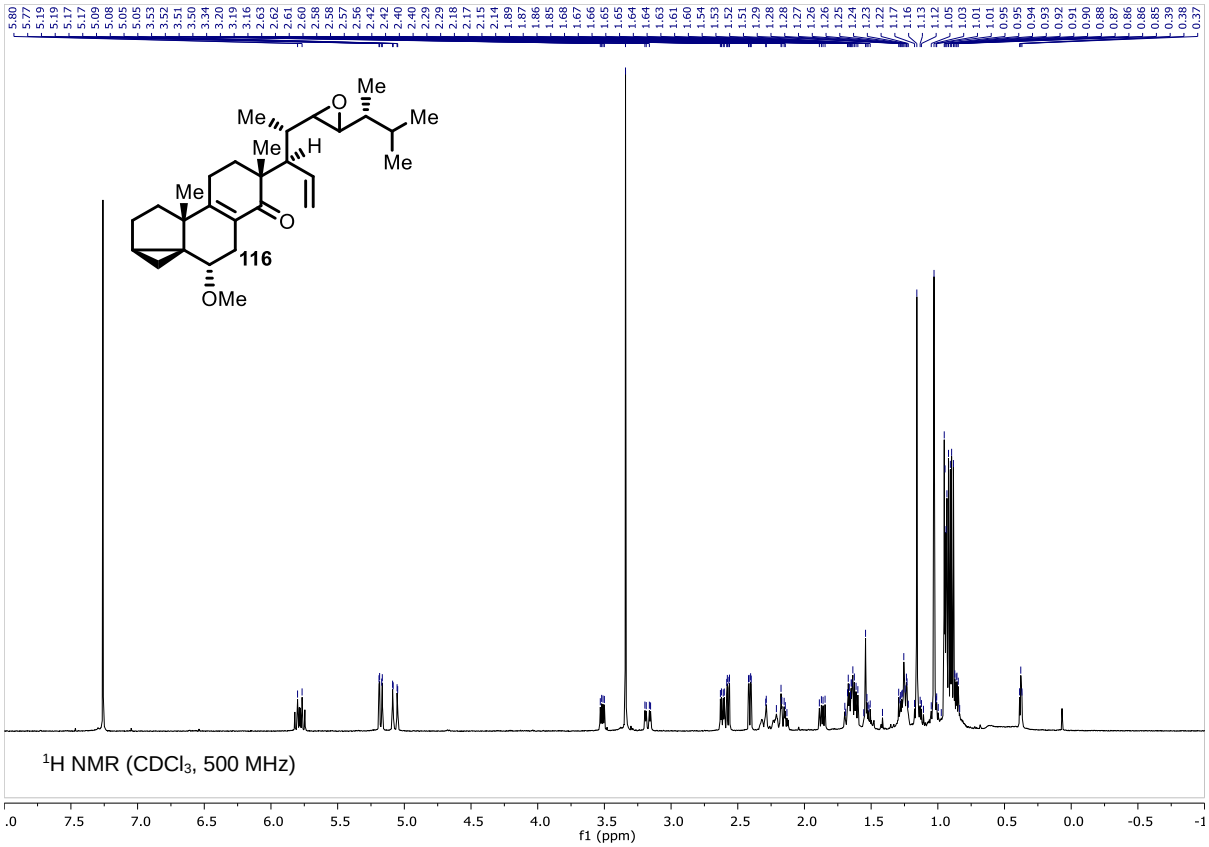

203.73
159.14
135.28
132.26
129.48
72.40
57.12
49.80
47.76
43.50
37.90
36.59
34.38
33.25
33.05
31.75
30.19
28.23
26.19
23.05
22.87
22.63
20.30
20.23
19.86
18.89
17.77
7.11
^{13}C NMR ($CDCl_3$, 176 MHz)
f1 (ppm)

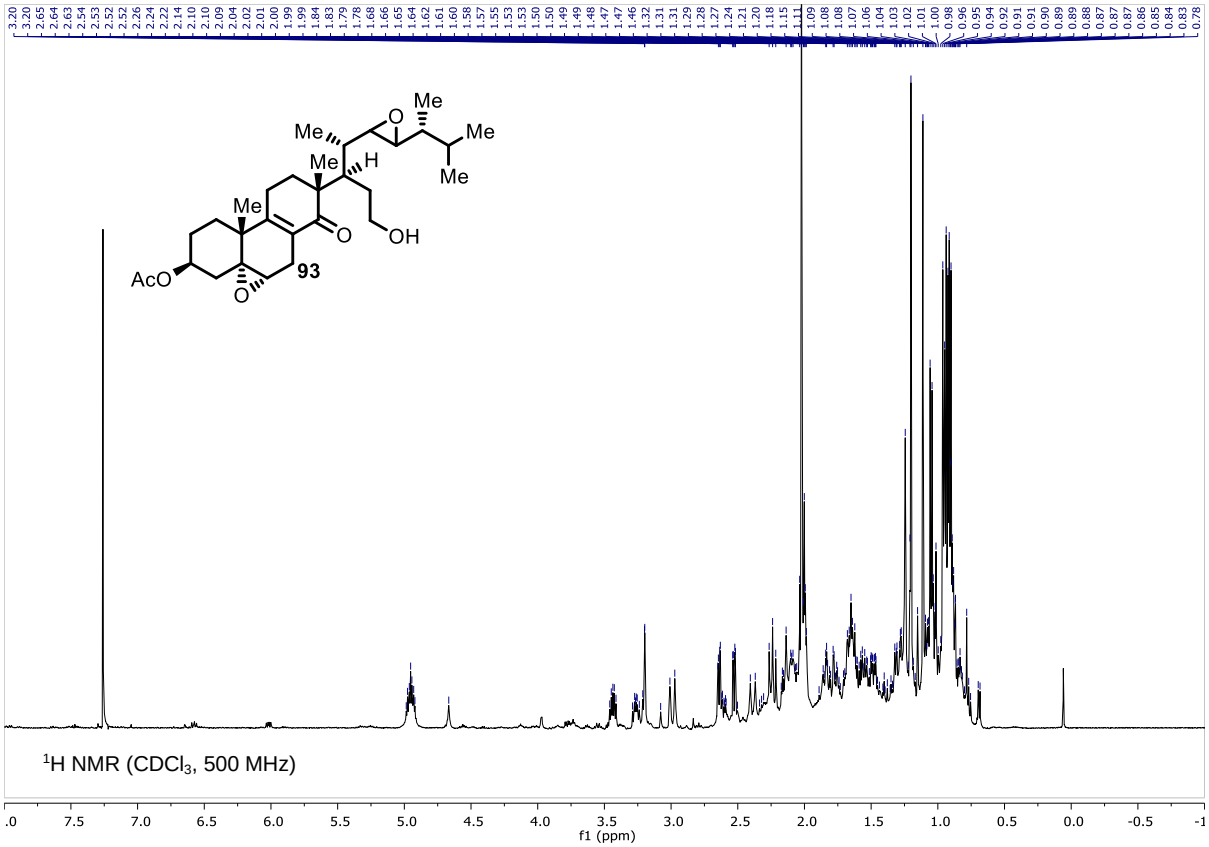

Me
Me
Me
Me
H
OH
Me
Me
H
H
121
O
^{1}H NMR (CDCl$_3$, 700 MHz)
f1 (ppm)

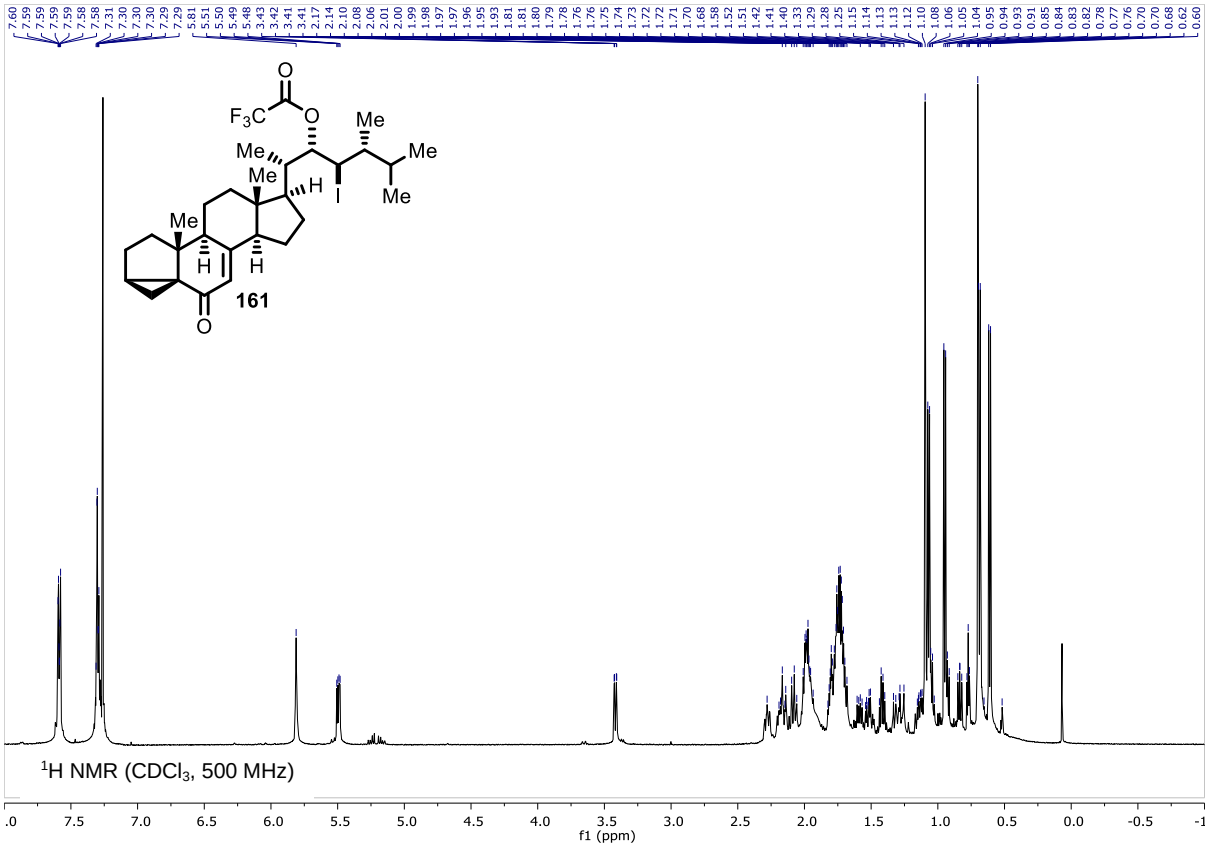

197.19
169.95
163.62
123.90
74.42
^{13}C NMR (CDCl$_3$, 176 MHz)
f1 (ppm)

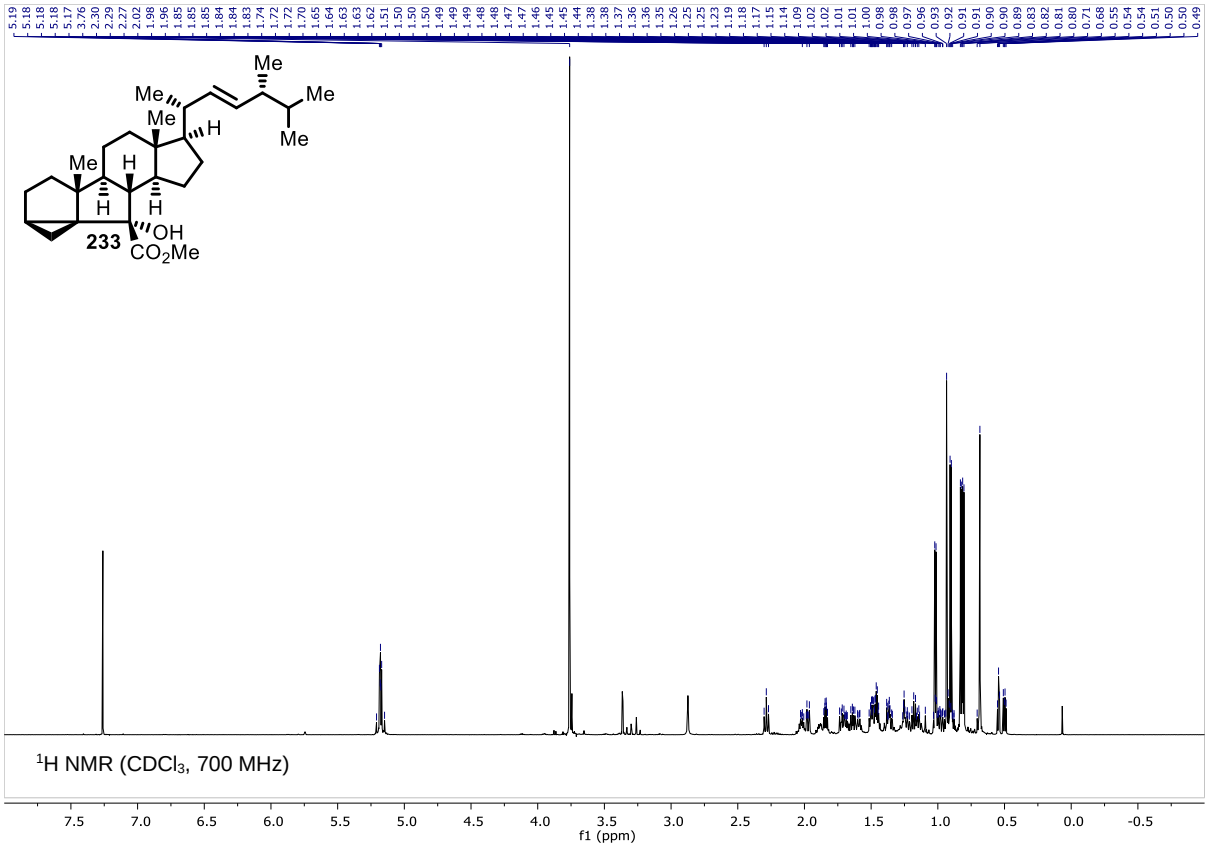

7.69
7.68
7.43
7.43
7.42
7.41
6.60
6.60
6.60
6.59
5.42
5.41
5.40
5.40
5.40
5.39
5.39
5.38
5.38
5.38
5.37
5.36
3.41
3.40
3.39
2.12
2.11
2.03
2.02
1.83
1.82
1.81
1.56
1.55
1.54
1.53
1.40
1.39
1.38
1.37
0.92
0.91
0.90
Br
S
N
S
193
^{1}H NMR ($CDCl_3$, 700 MHz)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

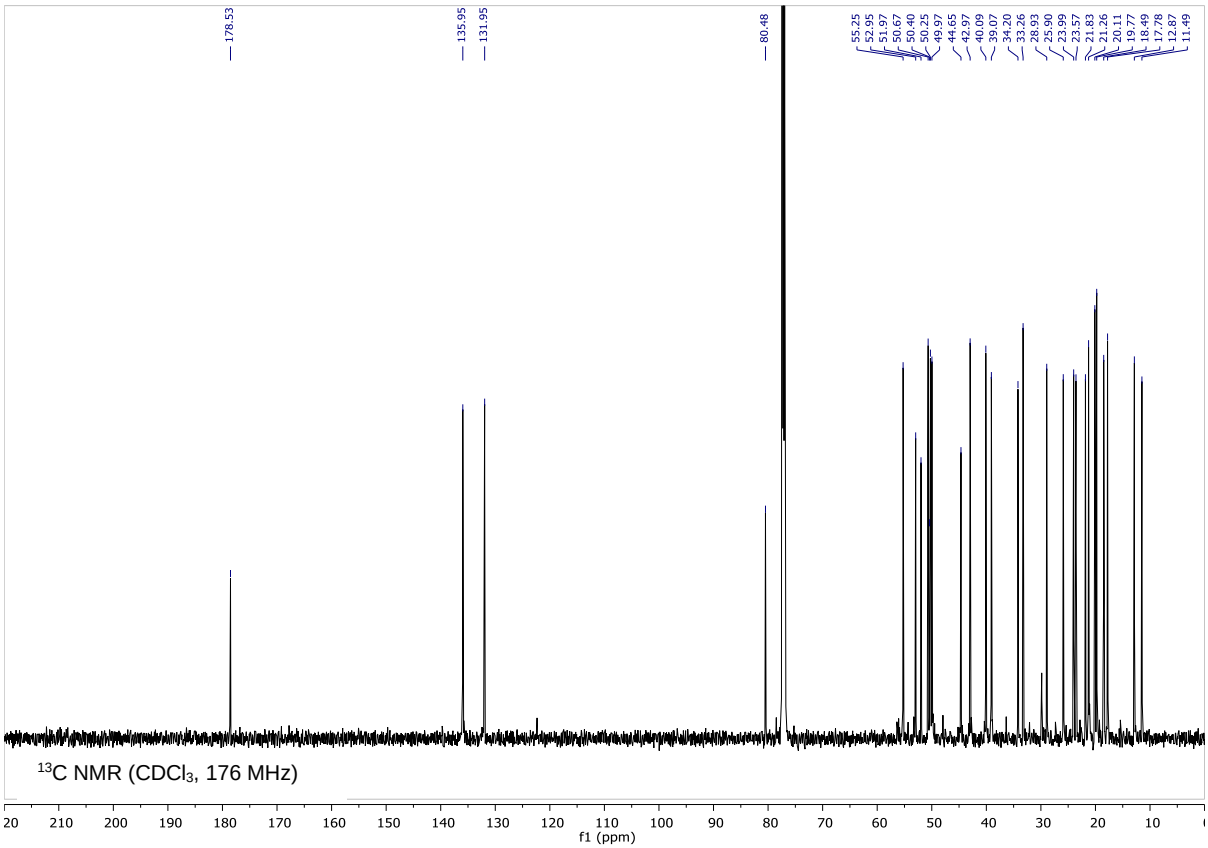

199.02
135.87
133.84
130.69
129.13
128.43
127.98
124.01
118.36
117.26
108.53
37.14
29.51
29.24
27.38
26.85
23.00
13.97
^{13}C NMR ($CDCl_3$, 176 MHz)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

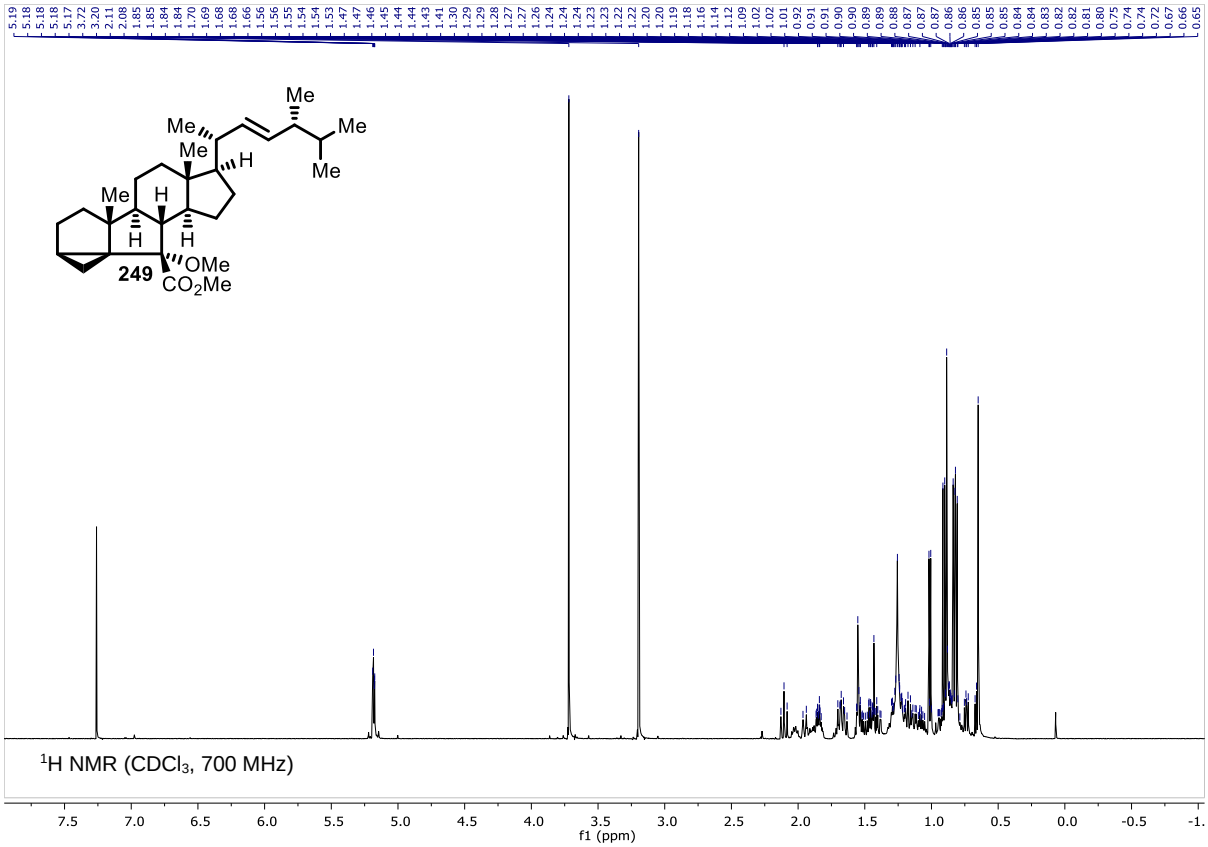

Me
Me
O
Me
Me
H
Me
Me
O
116
OMe
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

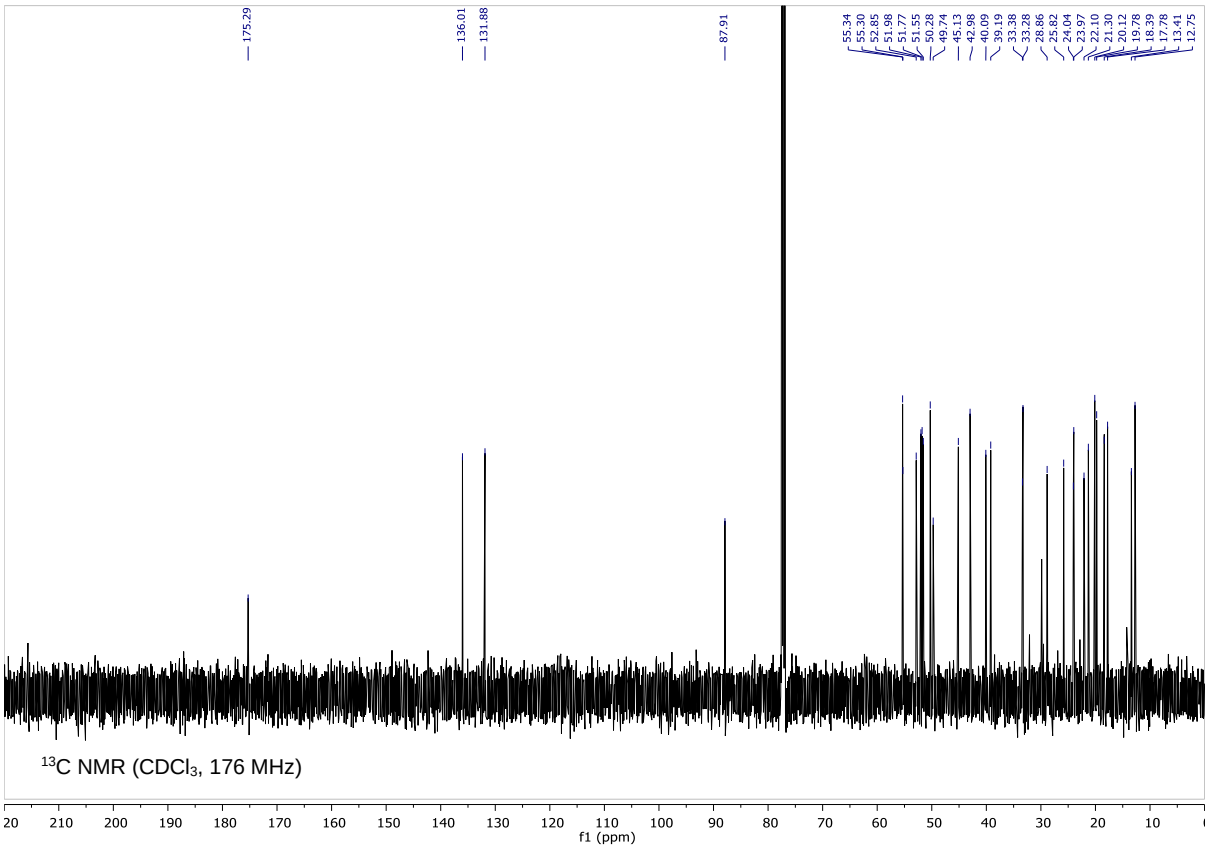

Me
Me
O
Me
Me
H
Me
Me
O
OH
AcO
O
93
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

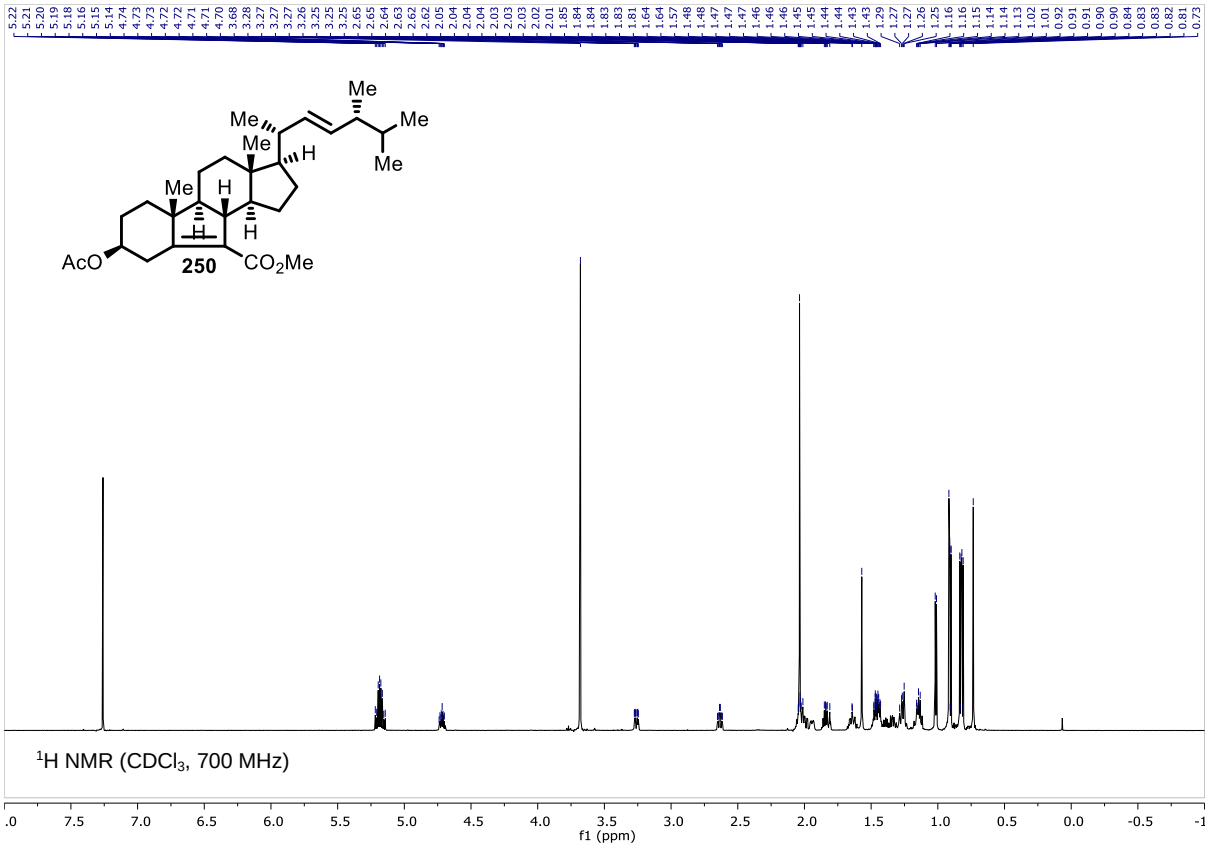

7.60 7.59 7.59 7.59 7.59 7.58 7.58 7.31 7.30 7.30 7.30 7.29 7.29 5.81 5.51 5.50 5.49 5.48 3.43 3.42 3.41 3.41 2.17 2.14 2.10 2.08 2.06 2.01 2.00 1.99 1.98 1.97 1.97 1.96 1.95 1.93 1.81 1.81 1.80 1.79 1.78 1.76 1.76 1.75 1.74 1.73 1.72 1.72 1.71 1.70 1.68 1.58 1.52 1.51 1.42 1.41 1.40 1.33 1.29 1.28 1.25 1.15 1.14 1.13 1.13 1.12 1.10 1.08 1.06 1.05 1.04 0.95 0.94 0.93 0.91 0.85 0.84 0.83 0.82 0.78 0.77 0.76 0.70 0.70 0.68 0.62 0.60
O
F3C
O
Me
Me
Me
Me
H
I
Me
Me
H
H
O
161
1H NMR (CDCl3, 500 MHz)
.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

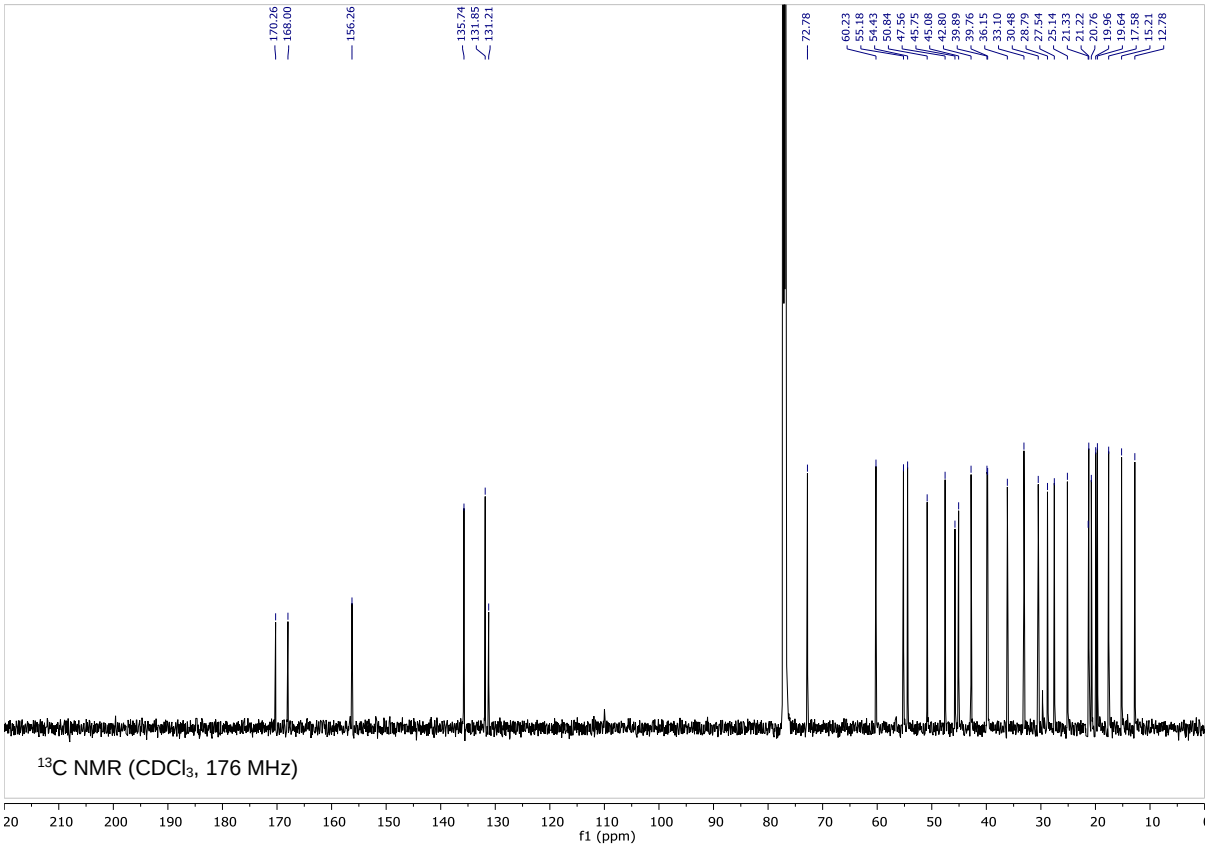

Me
Me
Me
Me
H
Me
H
H
H
233
OH
CO2Me
1H NMR (CDCl3, 700 MHz)
f1 (ppm)

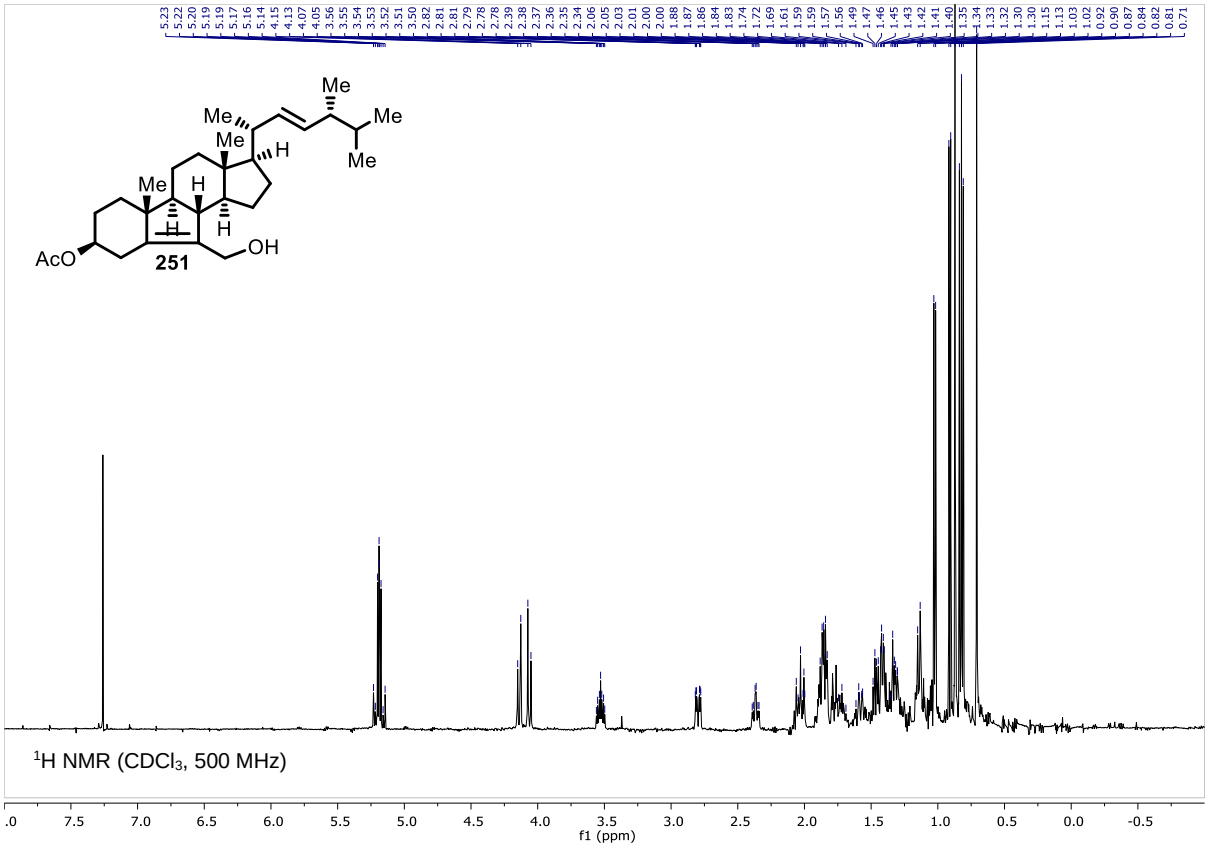

178.53
135.95
131.95
80.48
55.25
52.95
51.97
50.67
50.40
50.25
49.97
44.65
42.97
40.09
39.07
34.20
33.26
28.93
25.90
23.99
23.57
21.83
21.26
20.11
19.77
18.49
17.78
12.87
11.49
13C NMR (CDCl3, 176 MHz)
f1 (ppm)

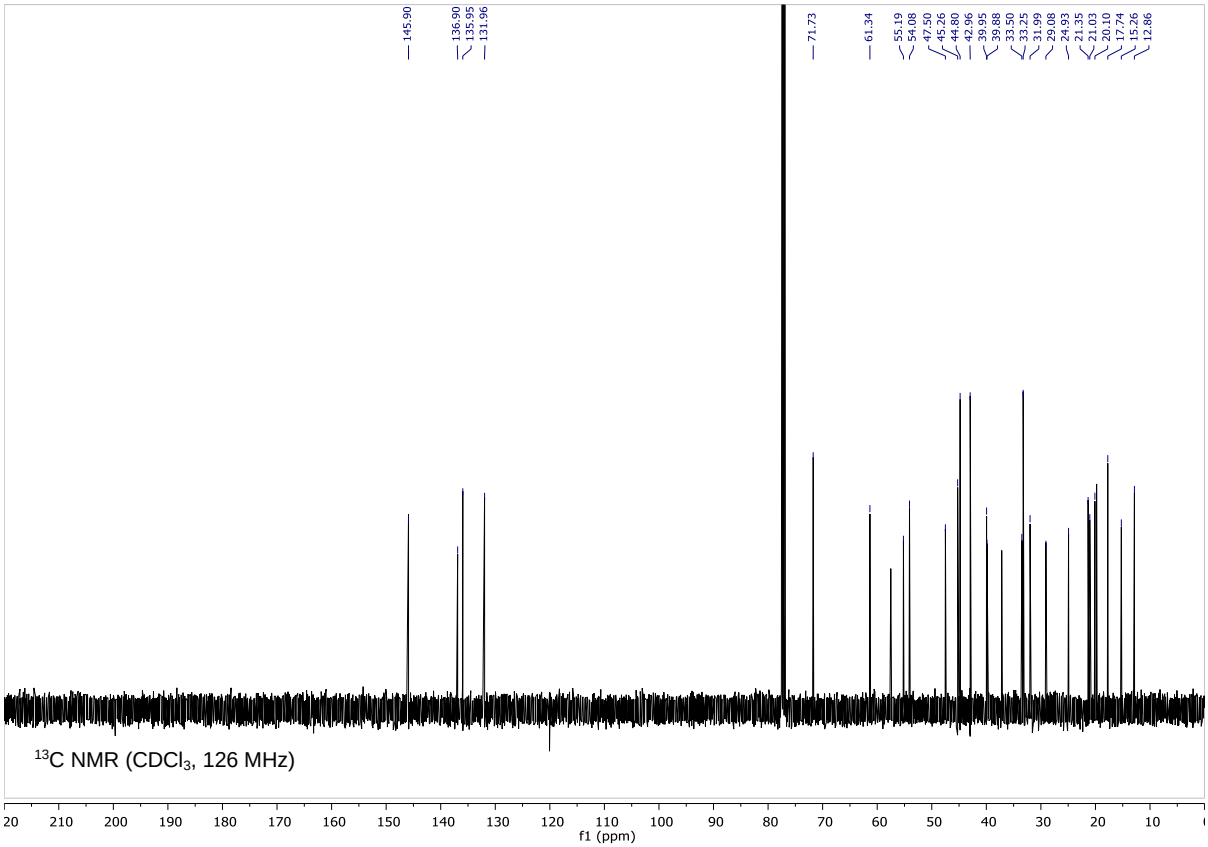

Me
Me
Me
Me
H
Me
H
Me
H
H
H
OMe
CO2Me
249
1H NMR (CDCl3, 700 MHz)
f1 (ppm)

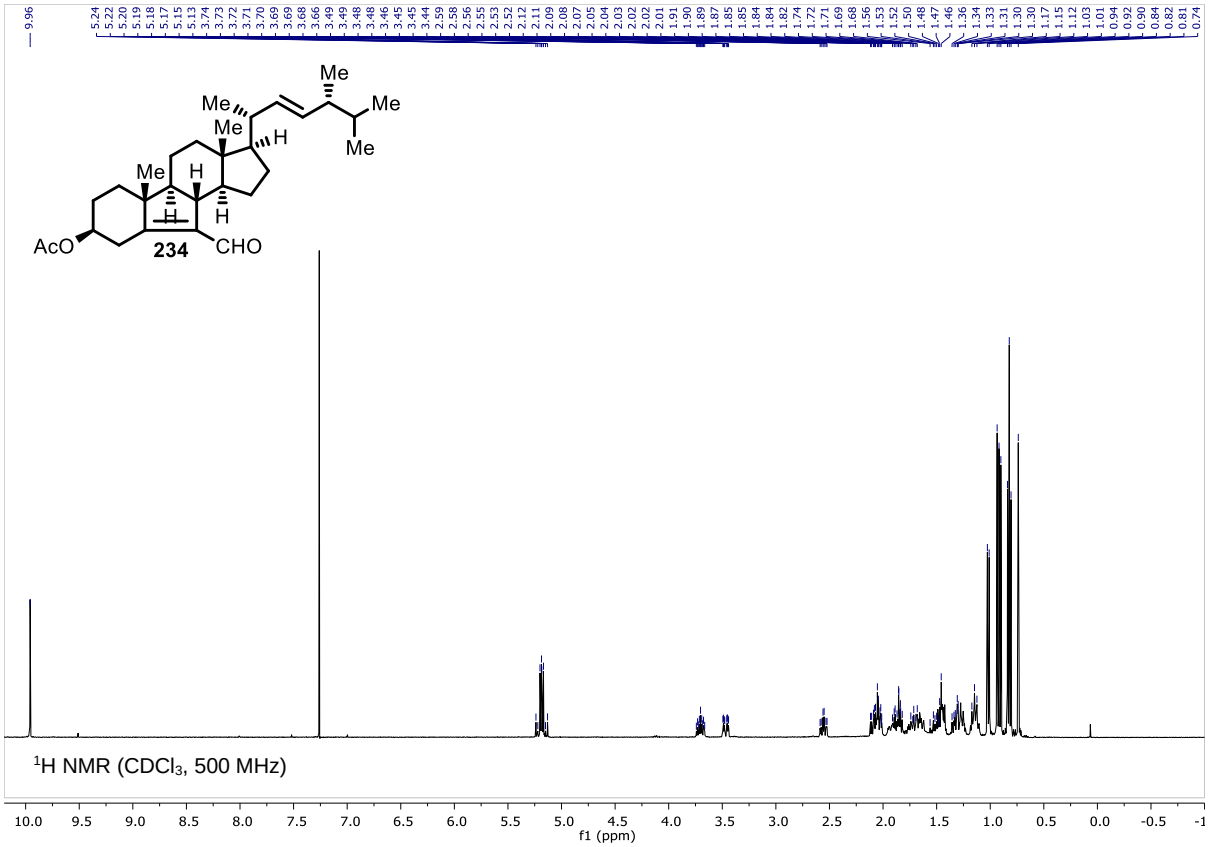

175.29
136.01
131.88
87.91
55.34
55.30
52.85
51.98
51.77
51.55
50.28
49.74
45.13
42.98
40.09
39.19
33.38
33.28
28.86
25.82
24.04
23.97
22.10
21.30
20.12
19.78
18.39
17.78
13.41
12.75
13C NMR (CDCl3, 176 MHz)
f1 (ppm)

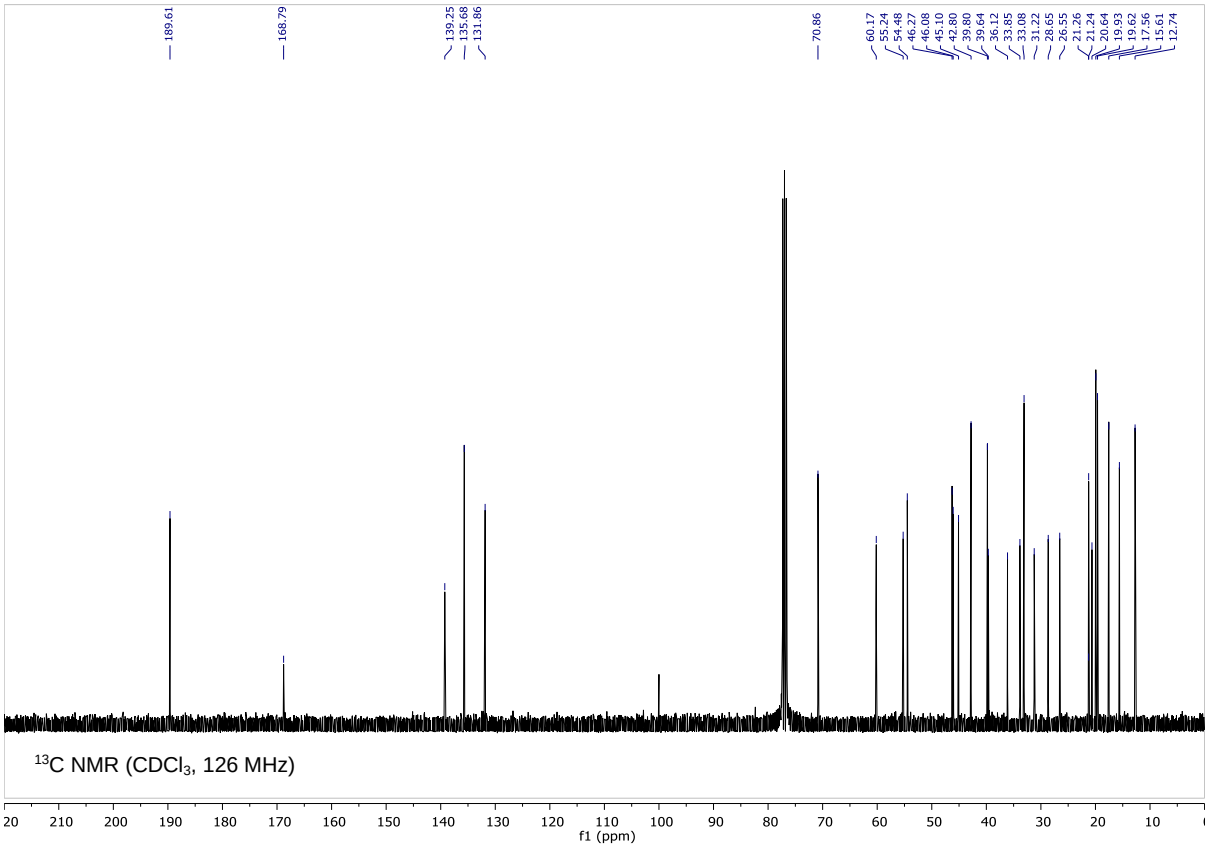

Me
Me
Me
Me
H
Me
H
H
H
AcO
250
CO2Me
1H NMR (CDCl3, 700 MHz)
f1 (ppm)

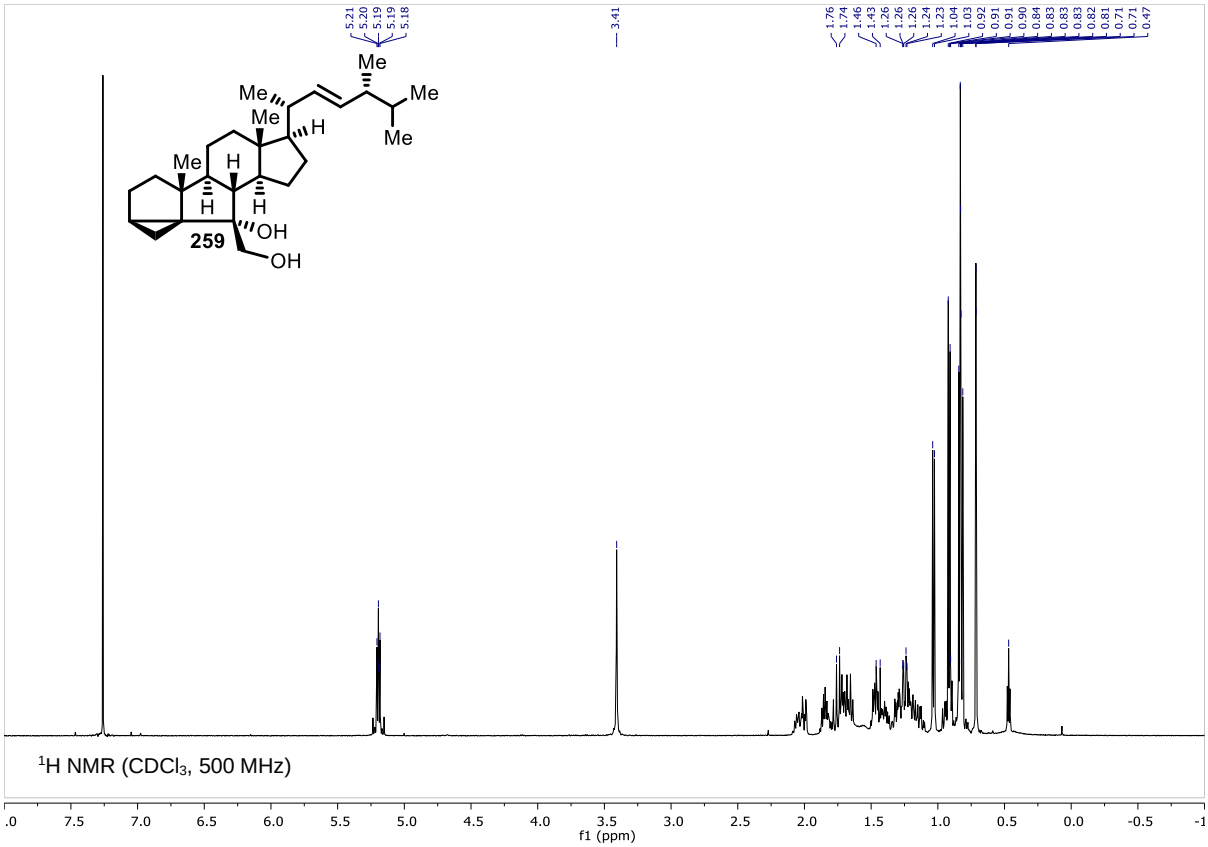

170.26
168.00
156.26
135.74
131.85
131.21
72.78
60.23
55.18
54.43
50.84
47.56
45.75
45.08
42.80
39.89
39.76
36.15
33.10
30.48
28.79
27.54
25.14
21.33
21.22
20.76
19.96
19.64
17.58
15.21
12.78
13C NMR (CDCl3, 176 MHz)
f1 (ppm)


Me
Me
Me
Me
H
Me
H
H
H
AcO
OH
251
1H NMR (CDCl3, 500 MHz)
f1 (ppm)

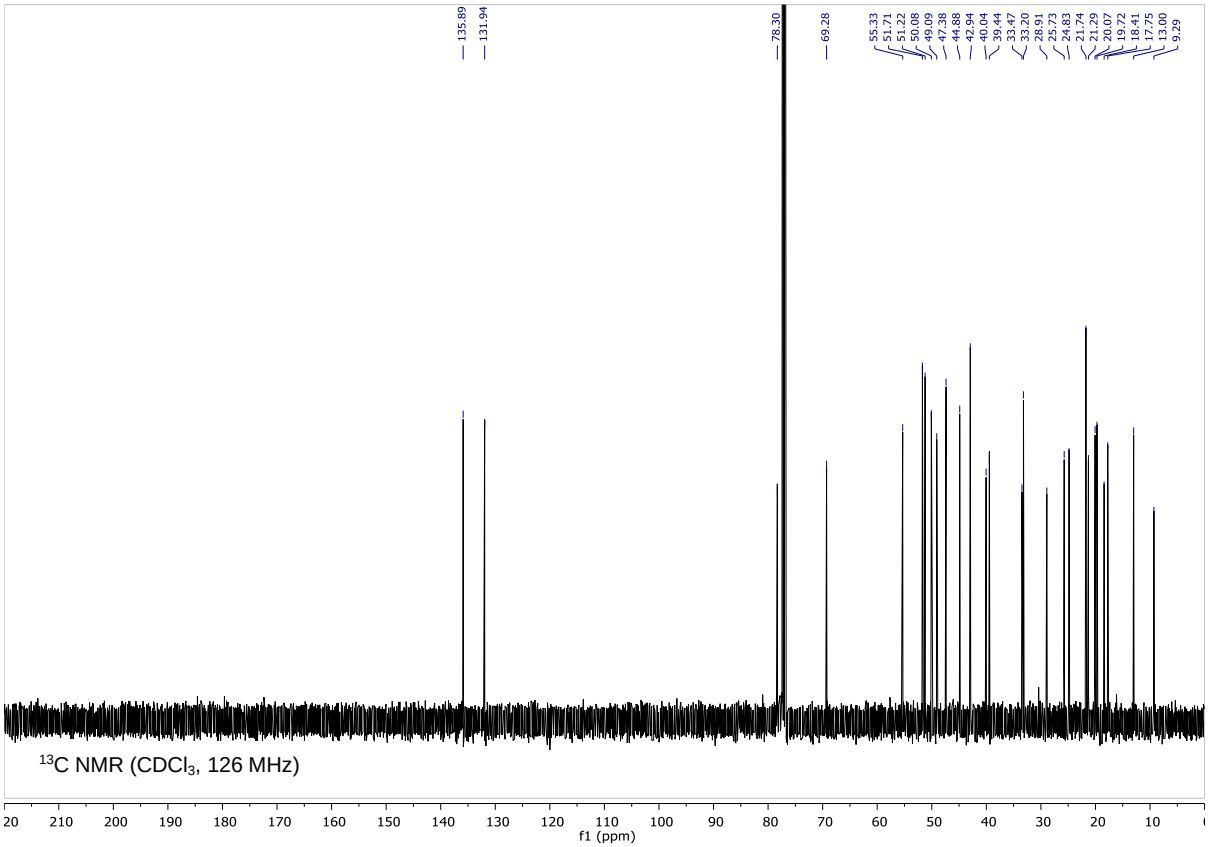

145.90
136.90
135.95
131.96
71.73
61.34
55.19
54.08
47.50
45.26
44.80
42.96
39.95
39.88
33.50
33.25
31.99
29.08
24.93
21.35
21.03
20.10
17.74
15.26
12.86
13C NMR (CDCl3, 126 MHz)
f1 (ppm)


Me
Me
Me
Me
H
Me
H
H
H
AcO
CHO
234
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

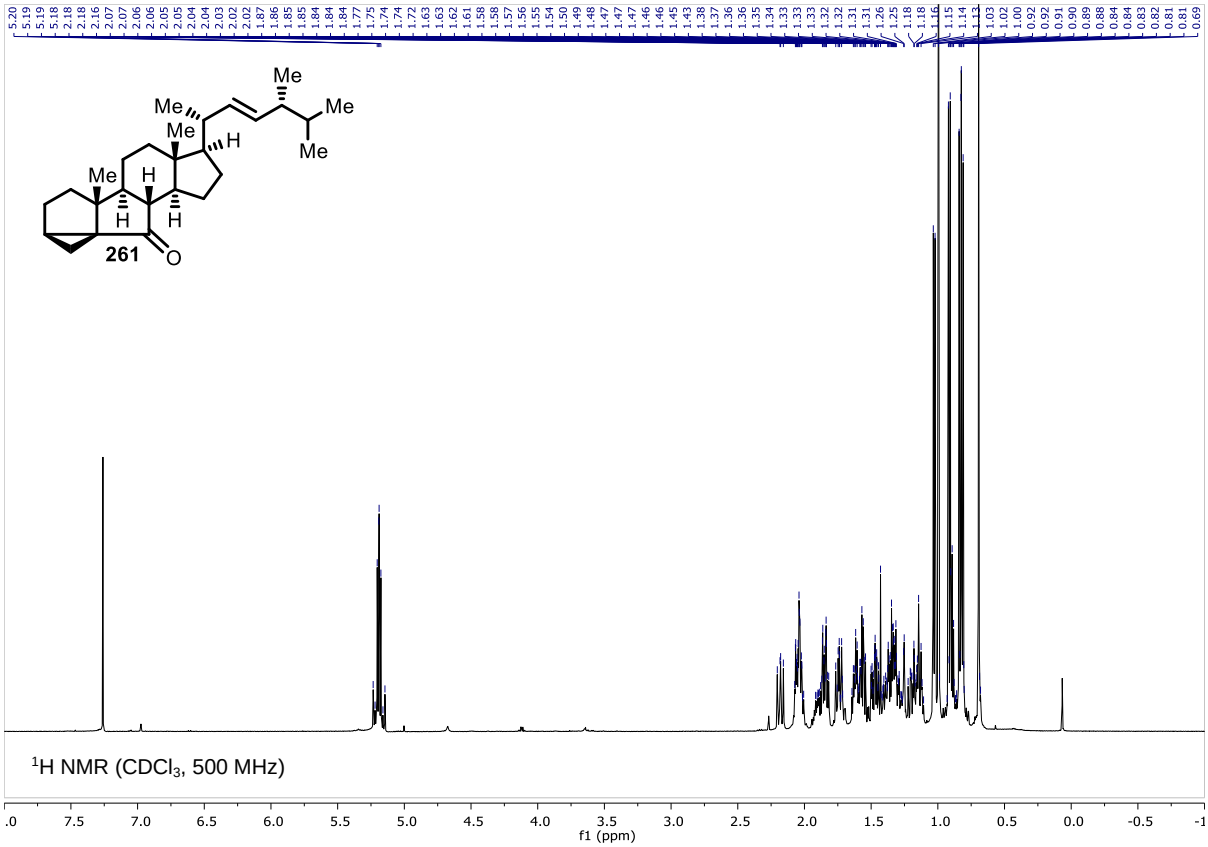

^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)

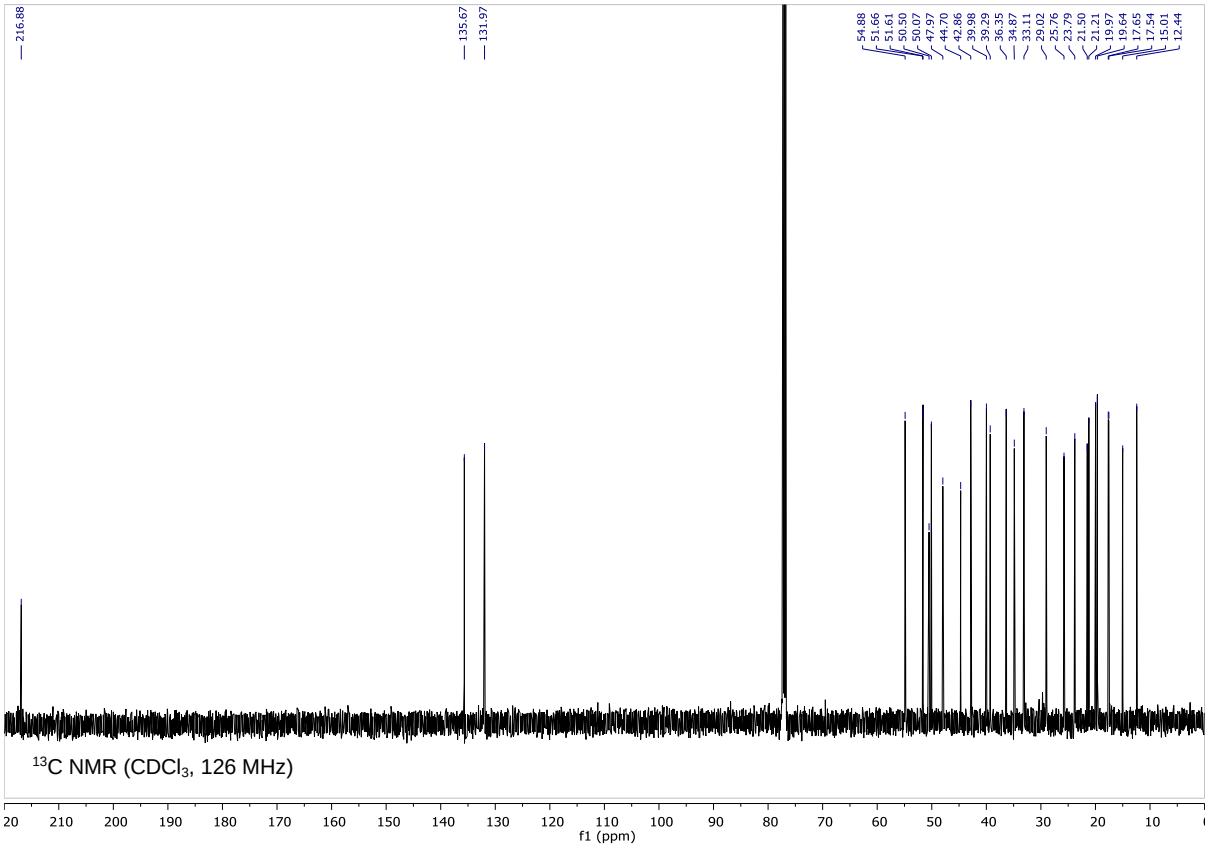


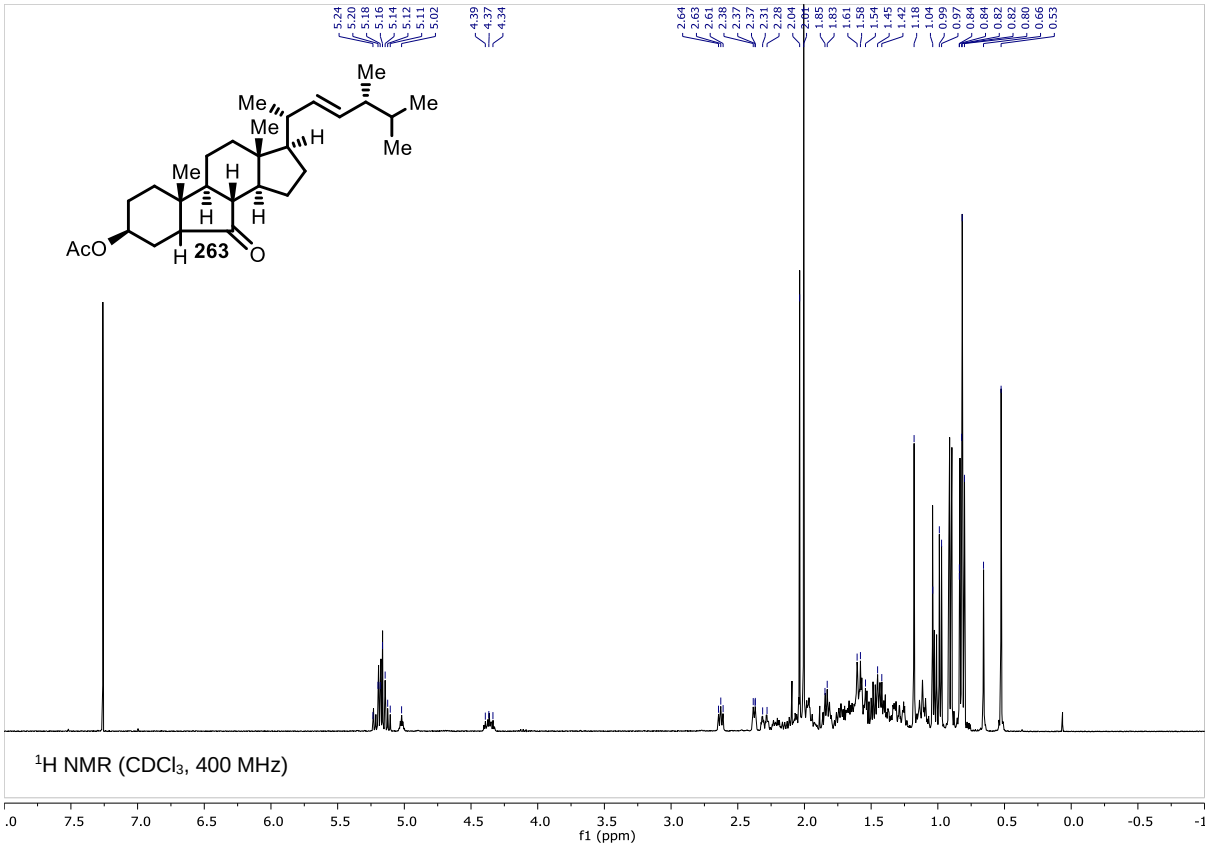
^{1}H NMR ($CDCl_3$, 500 MHz)



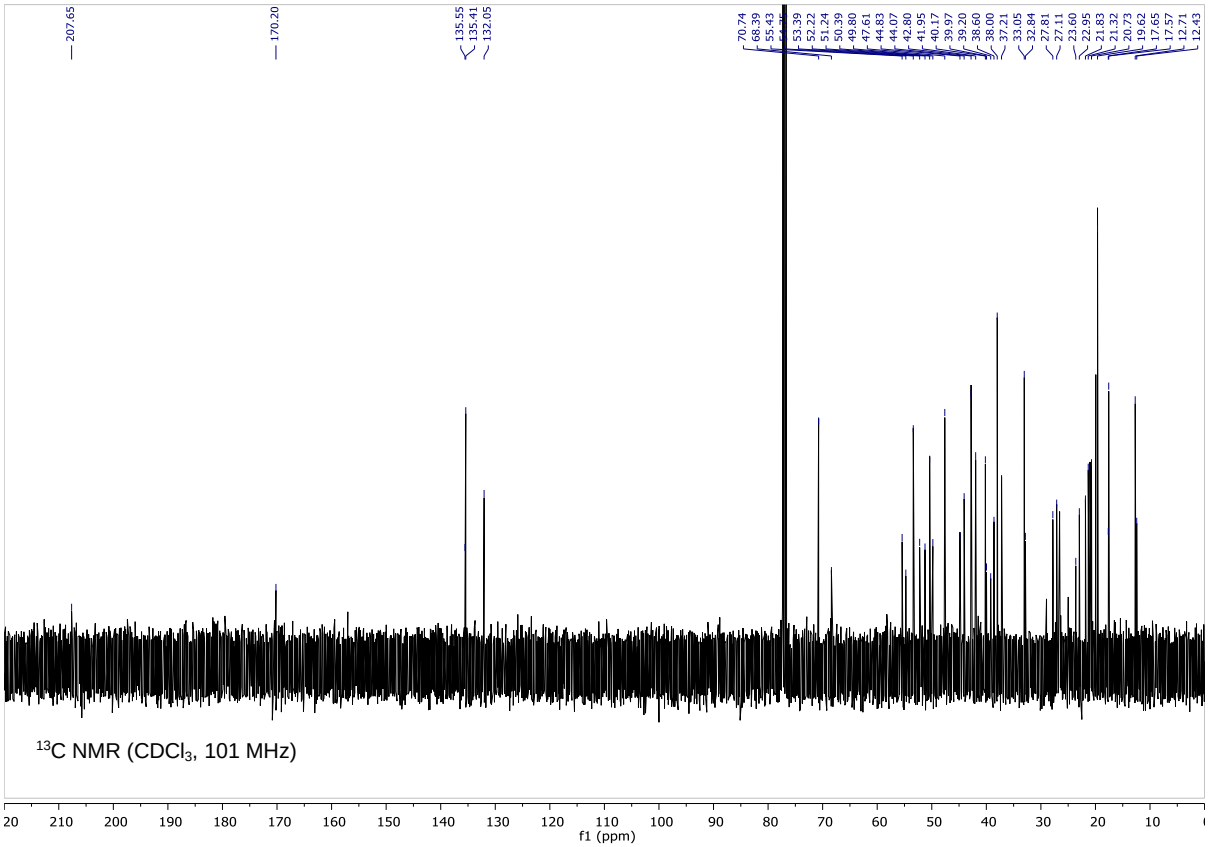
^{13}C NMR ($CDCl_3$, 126 MHz)


Me
Me
Me
Me
H
Me
H
H
H
261
O
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

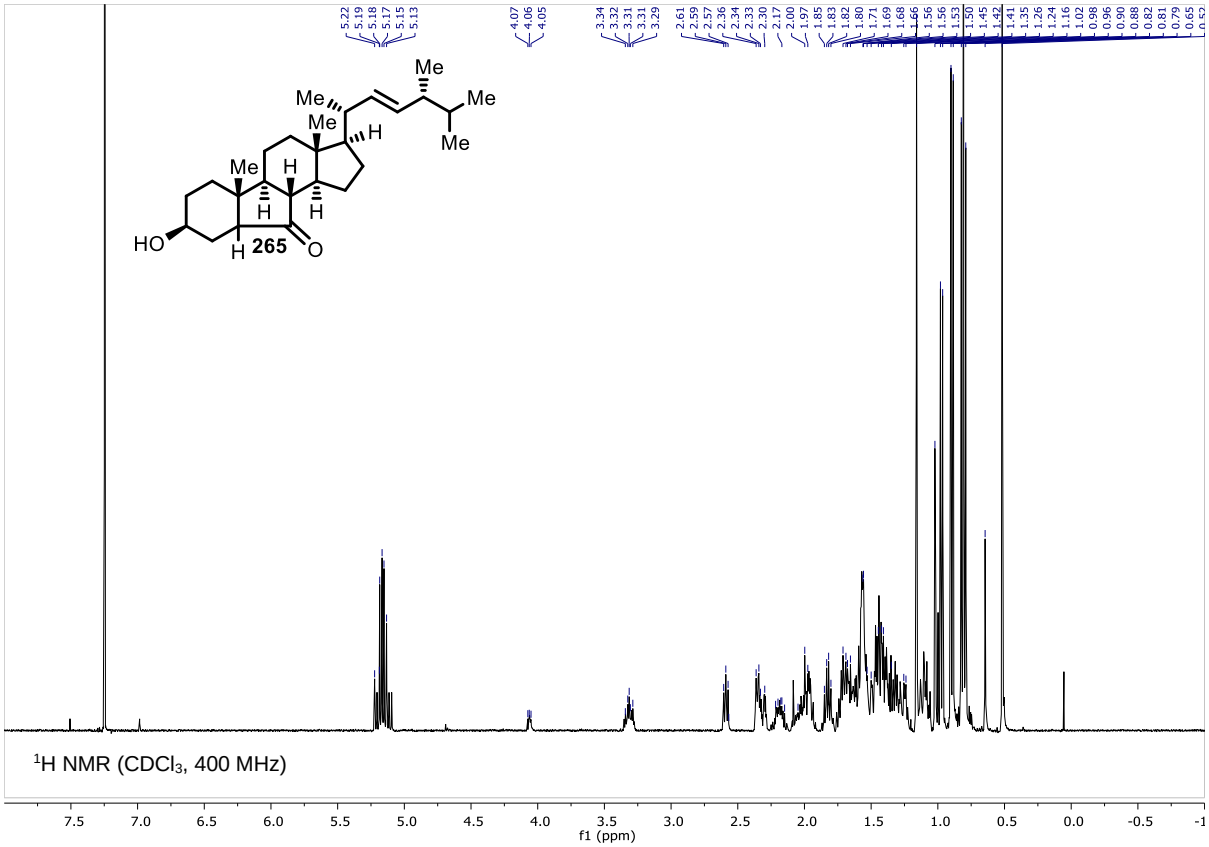

216.88
135.67
131.97
54.88
51.66
51.61
50.50
50.07
47.97
44.70
42.86
39.98
39.29
36.35
34.87
33.11
29.02
25.76
23.79
21.50
21.21
19.97
19.64
17.65
17.54
15.01
12.44
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)

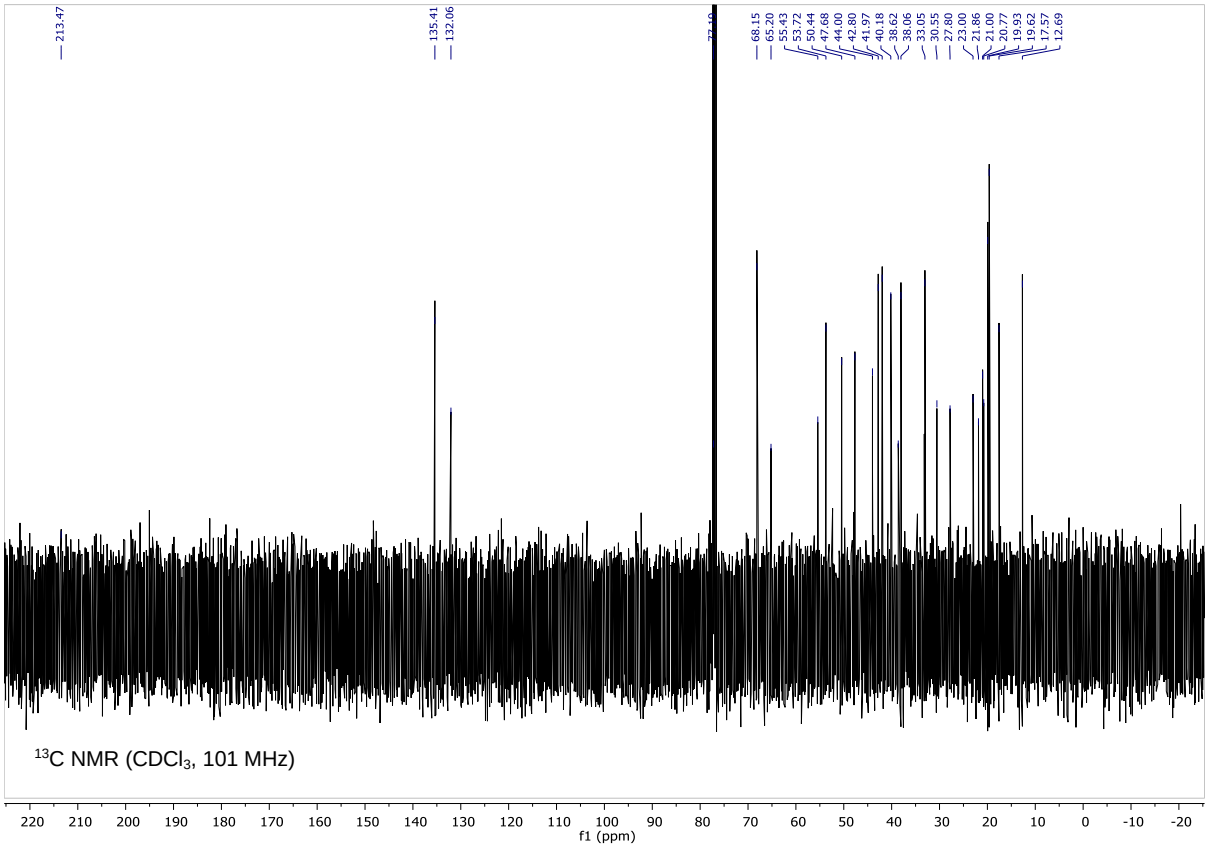


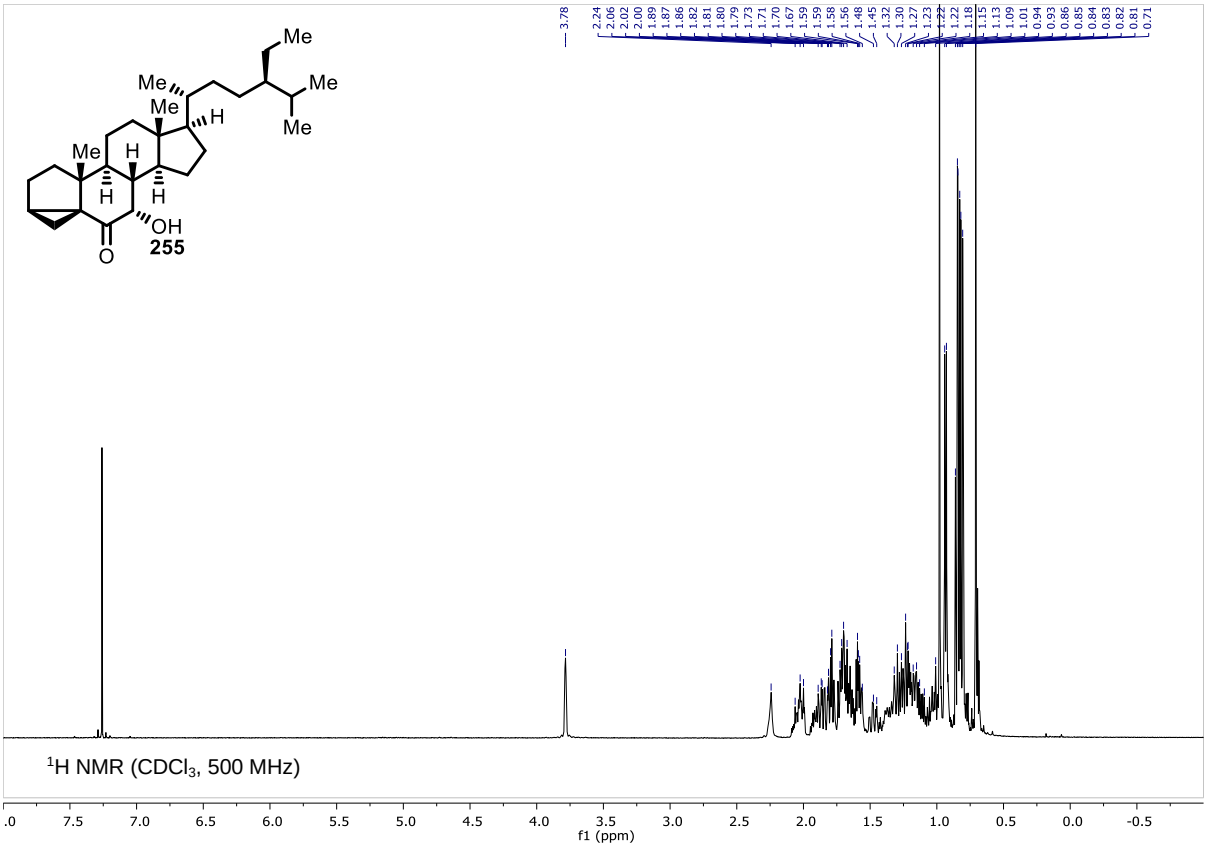
^{1}H NMR ($CDCl_3$, 400 MHz)

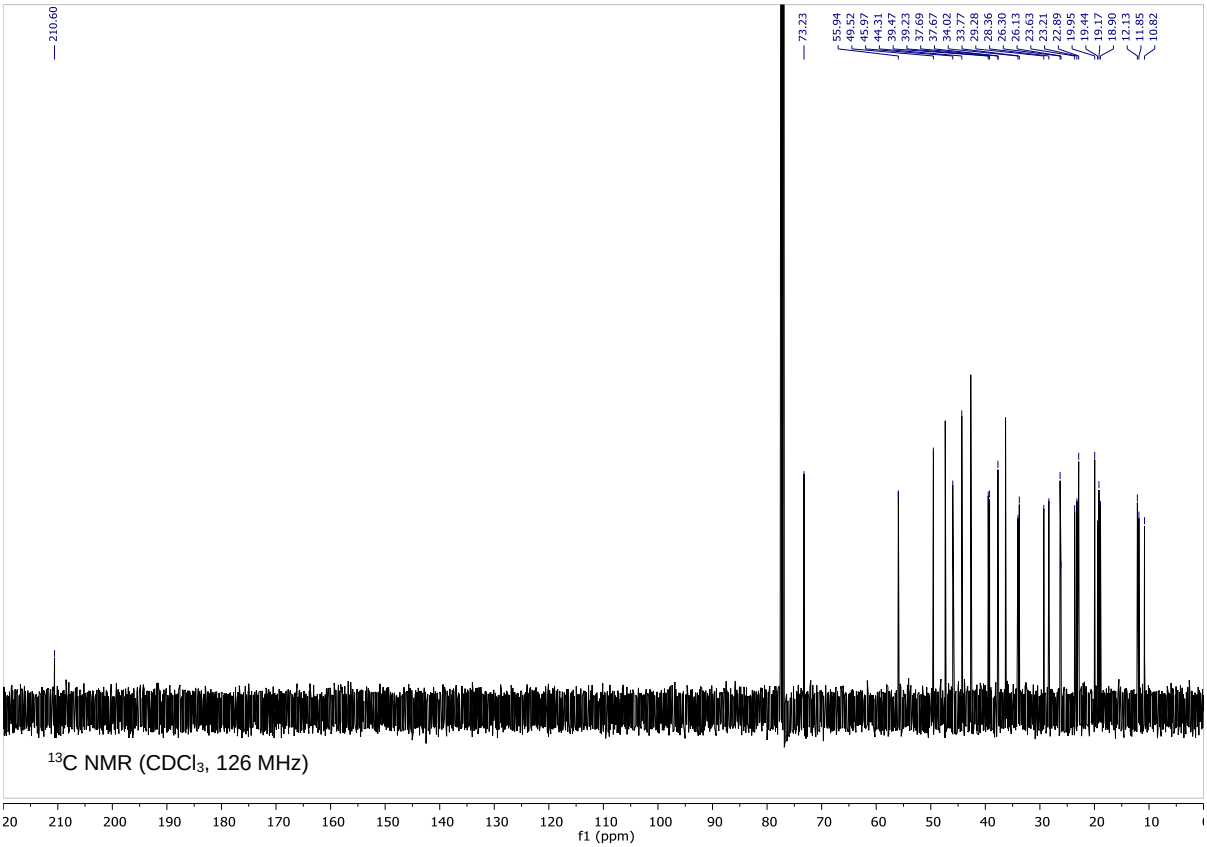


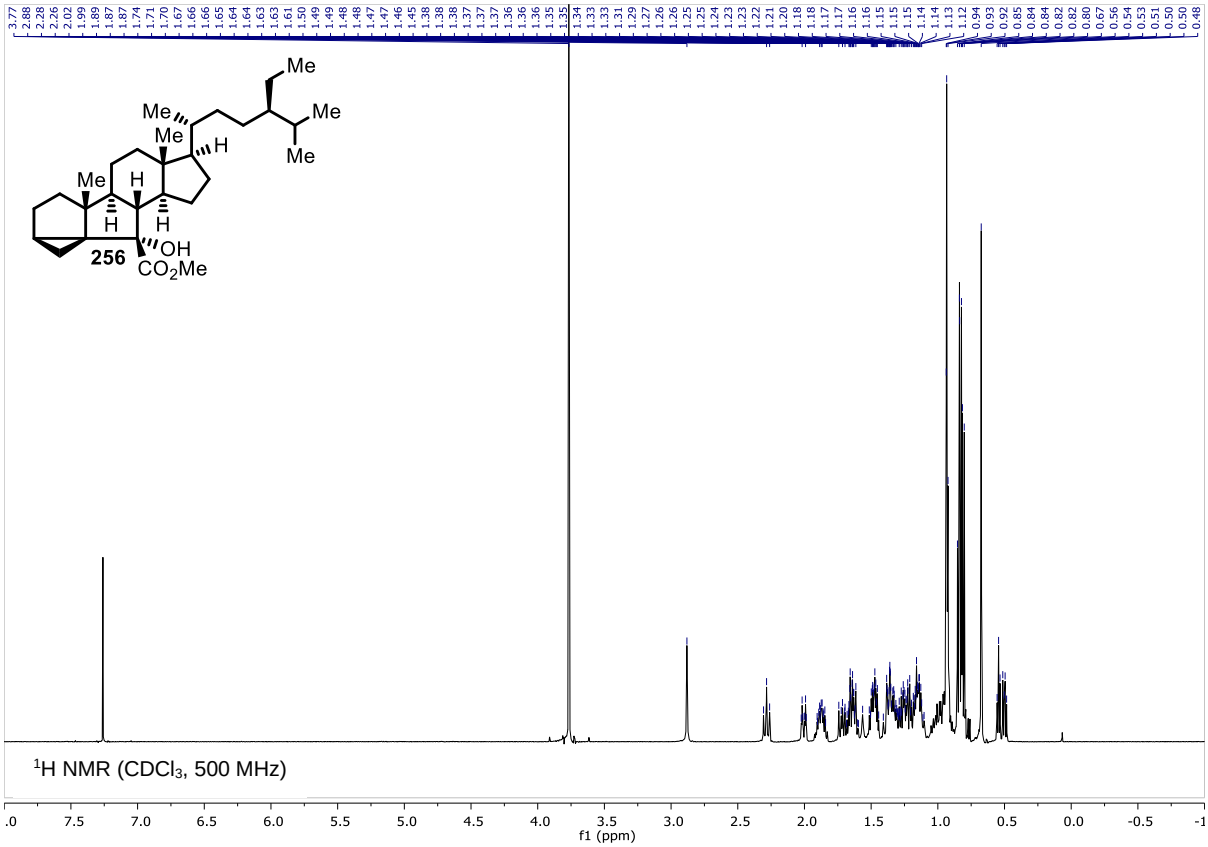
^{13}C NMR ($CDCl_3$, 101 MHz)


Me
Me
Me
Me
H
Me
H
H
H
HO
H
265
O
^{1}H NMR ($CDCl_3$, 400 MHz)
f1 (ppm)

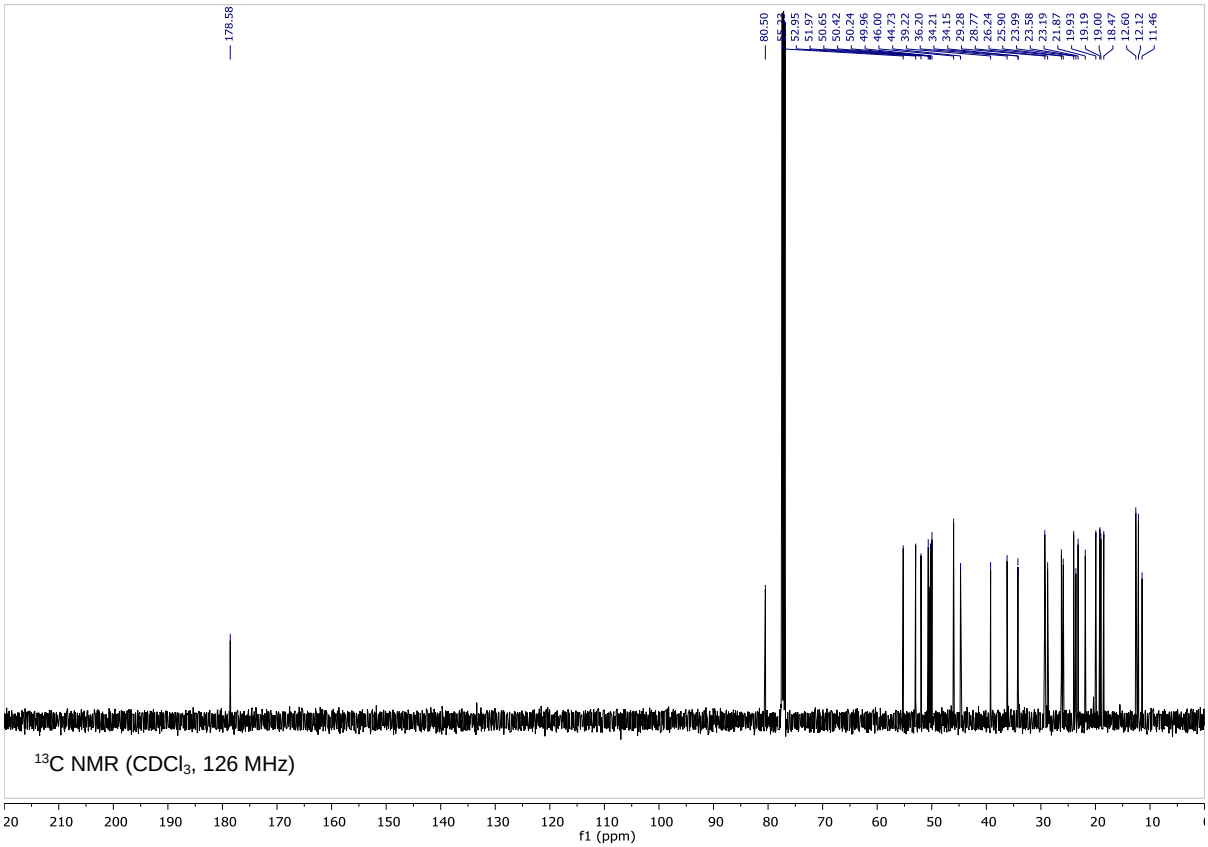

^{13}C NMR ($CDCl_3$, 101 MHz)
f1 (ppm)


Me
Me
Me
Me
H
Me
H
H
H
OH
O
255
3.78
2.24
2.06
2.02
2.00
1.89
1.87
1.86
1.82
1.81
1.80
1.79
1.73
1.71
1.70
1.67
1.59
1.59
1.58
1.56
1.48
1.45
1.32
1.30
1.27
1.23
1.22
1.22
1.18
1.15
1.13
1.09
1.01
0.94
0.93
0.86
0.85
0.84
0.83
0.82
0.81
0.71
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

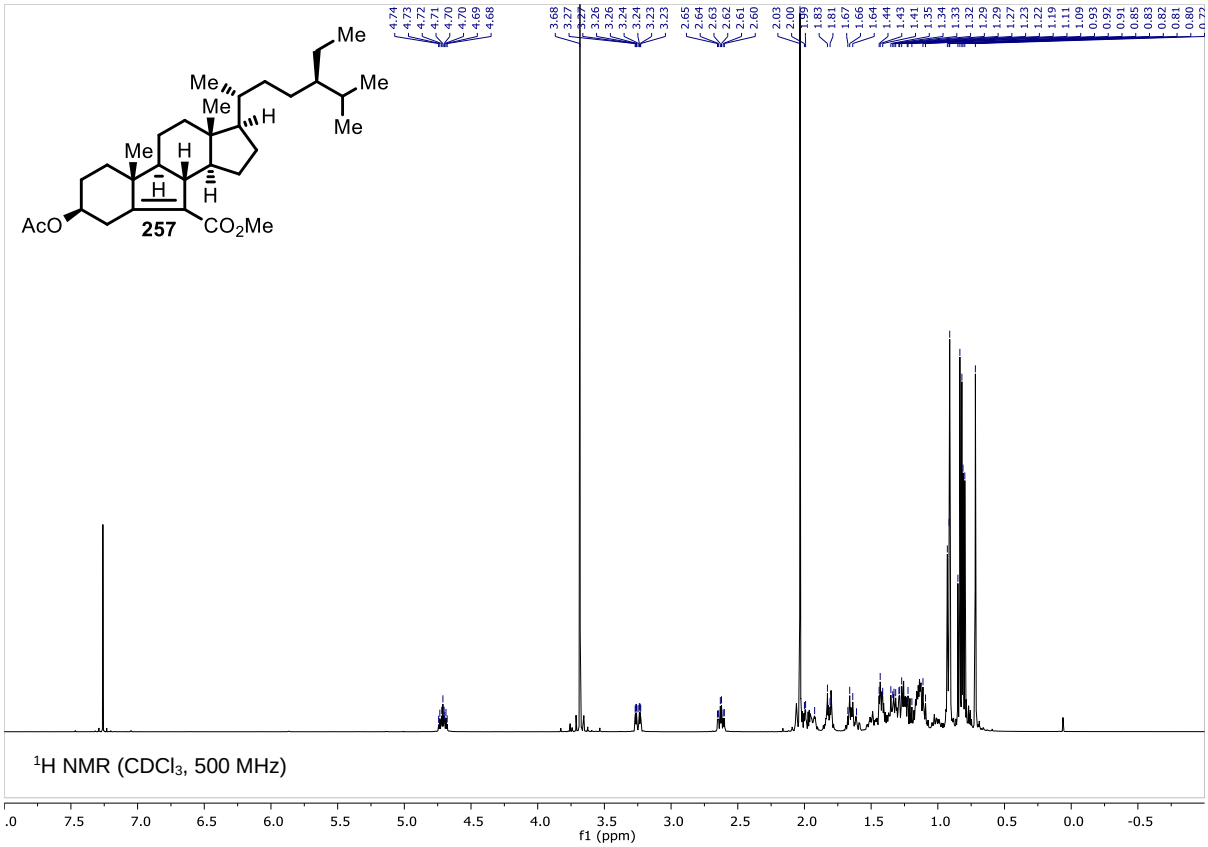

210.60
73.23
55.94
49.52
45.97
44.31
39.47
39.23
37.69
37.67
34.02
33.77
29.28
28.36
26.30
26.13
23.63
23.21
22.89
19.95
19.44
19.17
18.90
12.13
11.85
10.82
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)

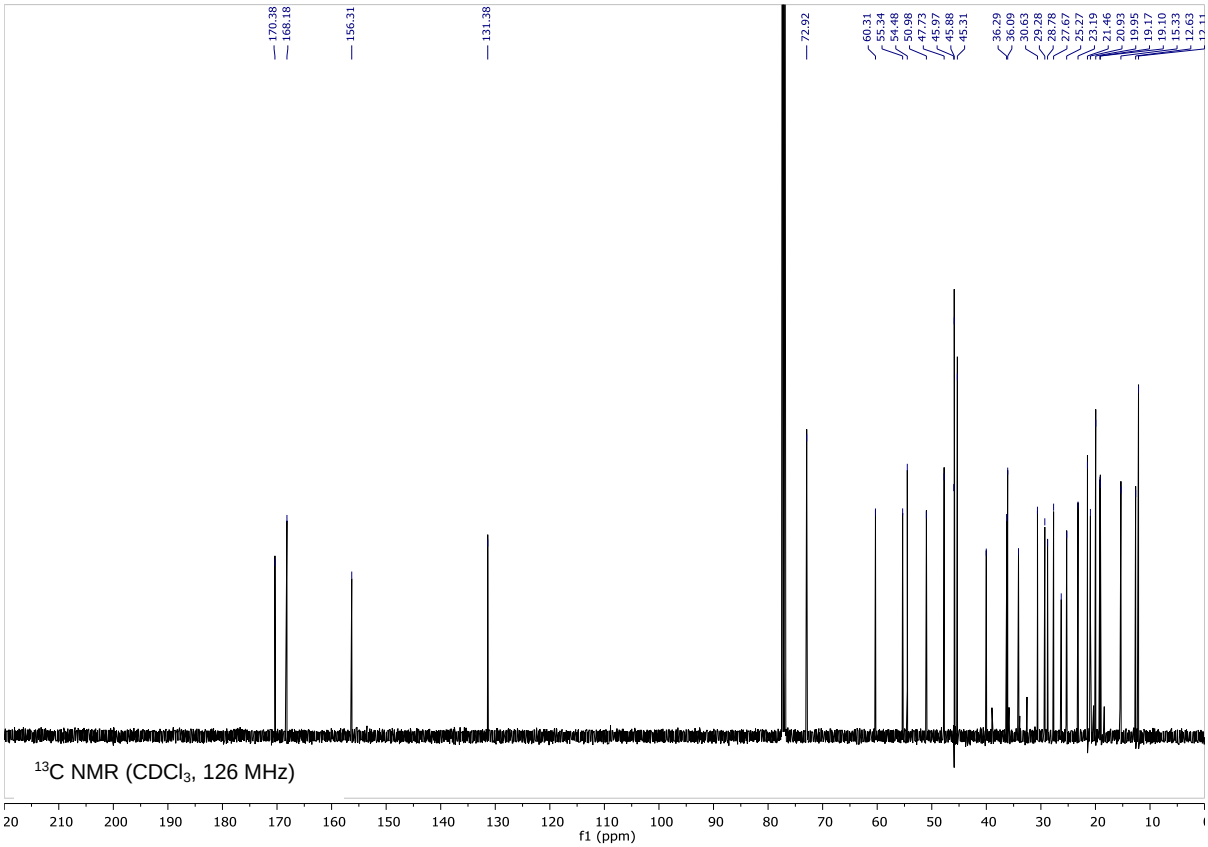


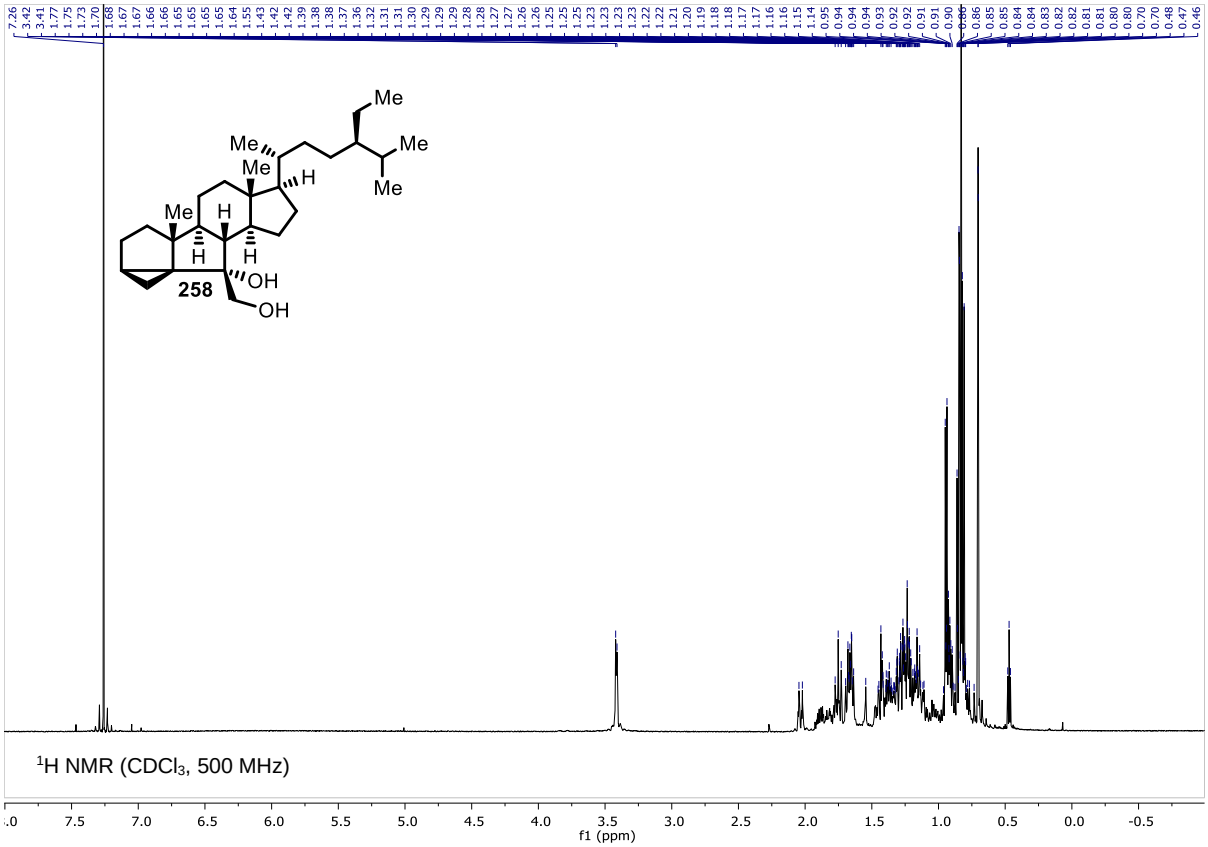
^{1}H NMR ($CDCl_3$, 500 MHz)



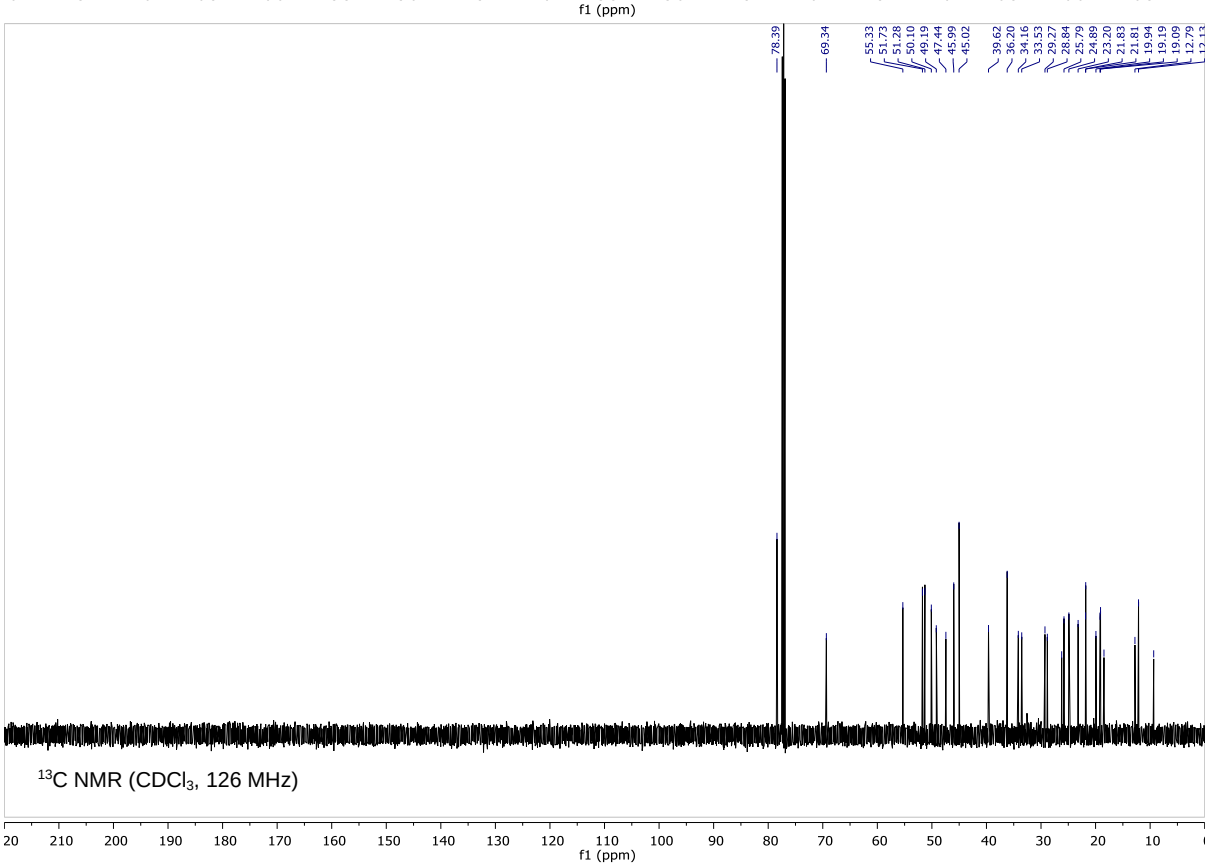
^{13}C NMR ($CDCl_3$, 126 MHz)


Me
Me
Me
Me
H
Me
H
H
H
AcO
257
CO2Me
4.74 4.73 4.72 4.71 4.70 4.70 4.69 4.68
3.68 3.27 3.26 3.26 3.24 3.24 3.23 3.23
2.65 2.64 2.63 2.62 2.61 2.60
2.03 2.00 1.99 1.83 1.81 1.67 1.66 1.64 1.44 1.43 1.41 1.35 1.34 1.33 1.32 1.29 1.29 1.27 1.23 1.22 1.19 1.11 1.09 0.93 0.92 0.91 0.85 0.83 0.82 0.81 0.80
1H NMR (CDCl3, 500 MHz)
.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

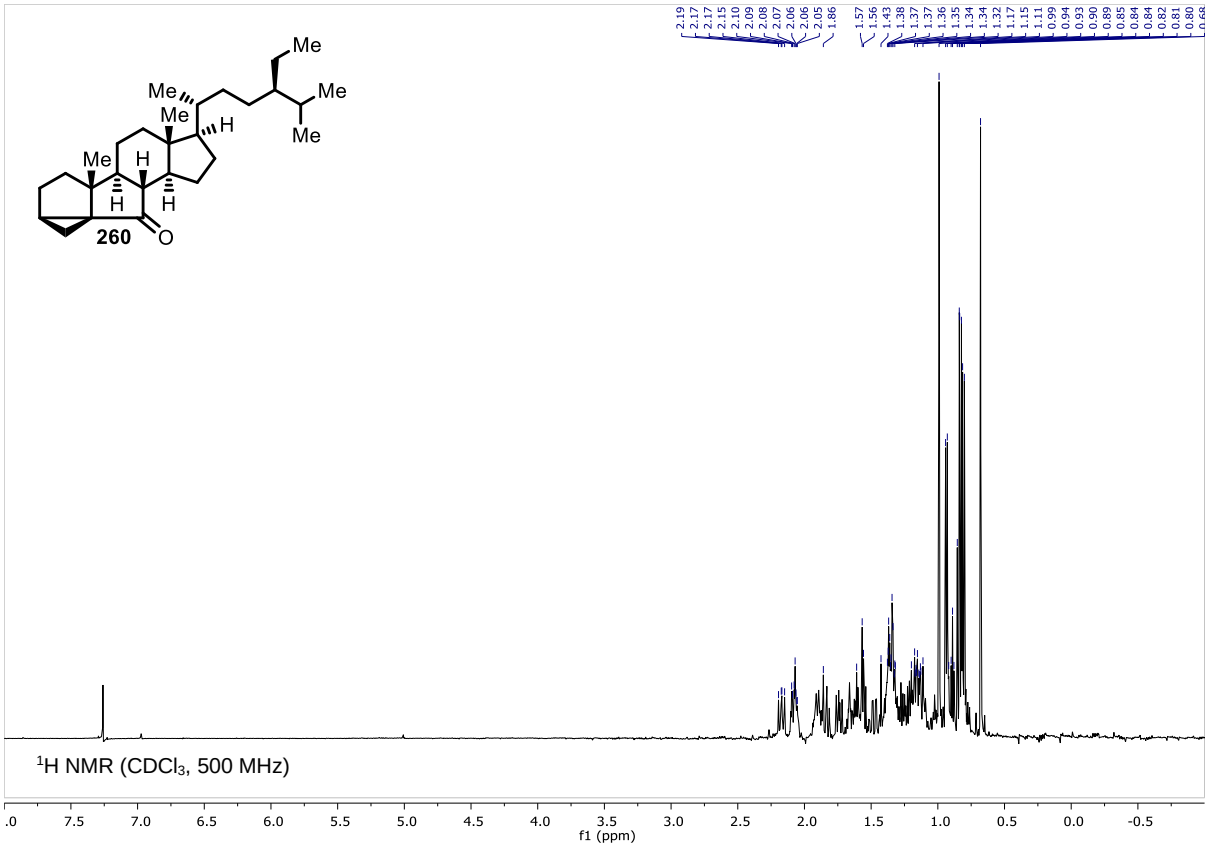

170.38
168.18
156.31
131.38
72.92
60.31
55.34
54.48
50.98
47.73
45.97
45.88
45.31
36.29
36.09
30.63
29.28
28.78
27.67
25.27
23.19
21.46
20.93
19.95
19.17
19.10
15.33
12.63
13C NMR (CDCl3, 126 MHz)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



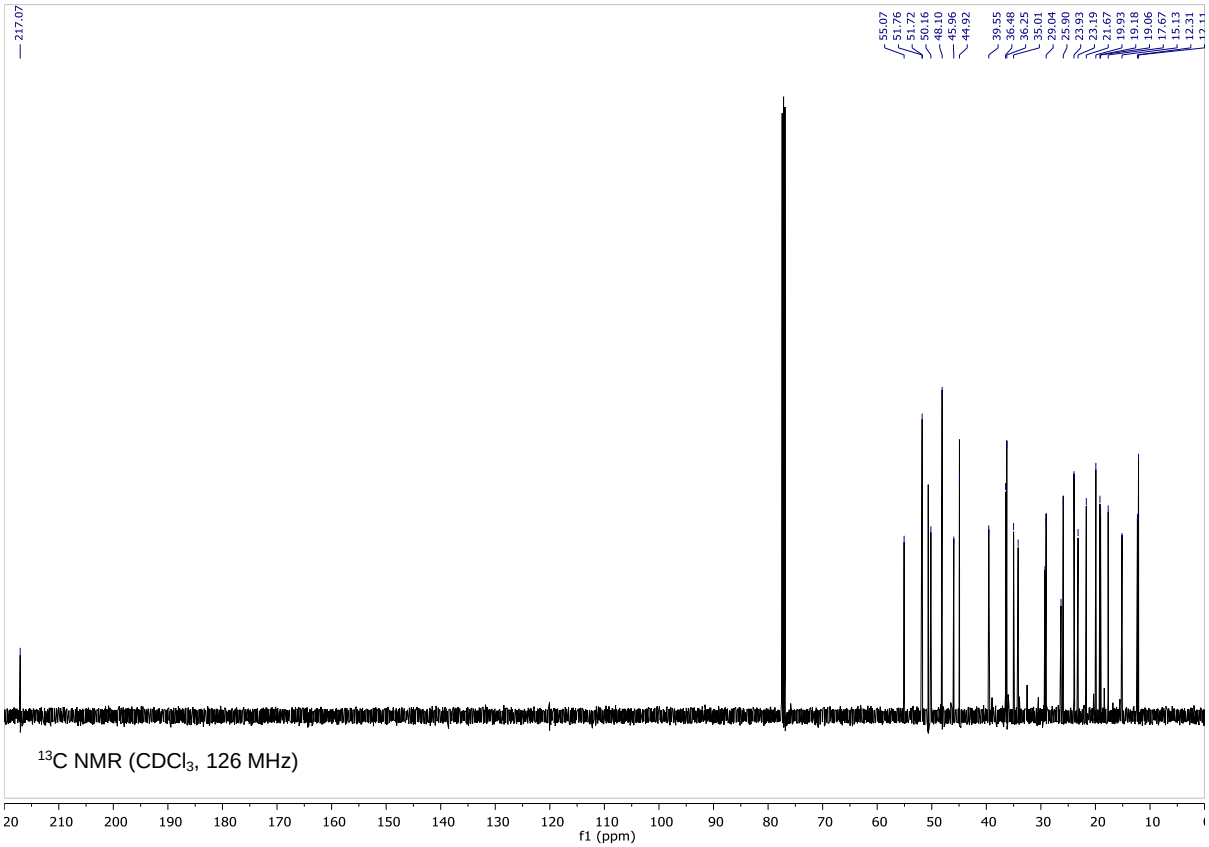
^{1}H NMR ($CDCl_3$, 500 MHz)



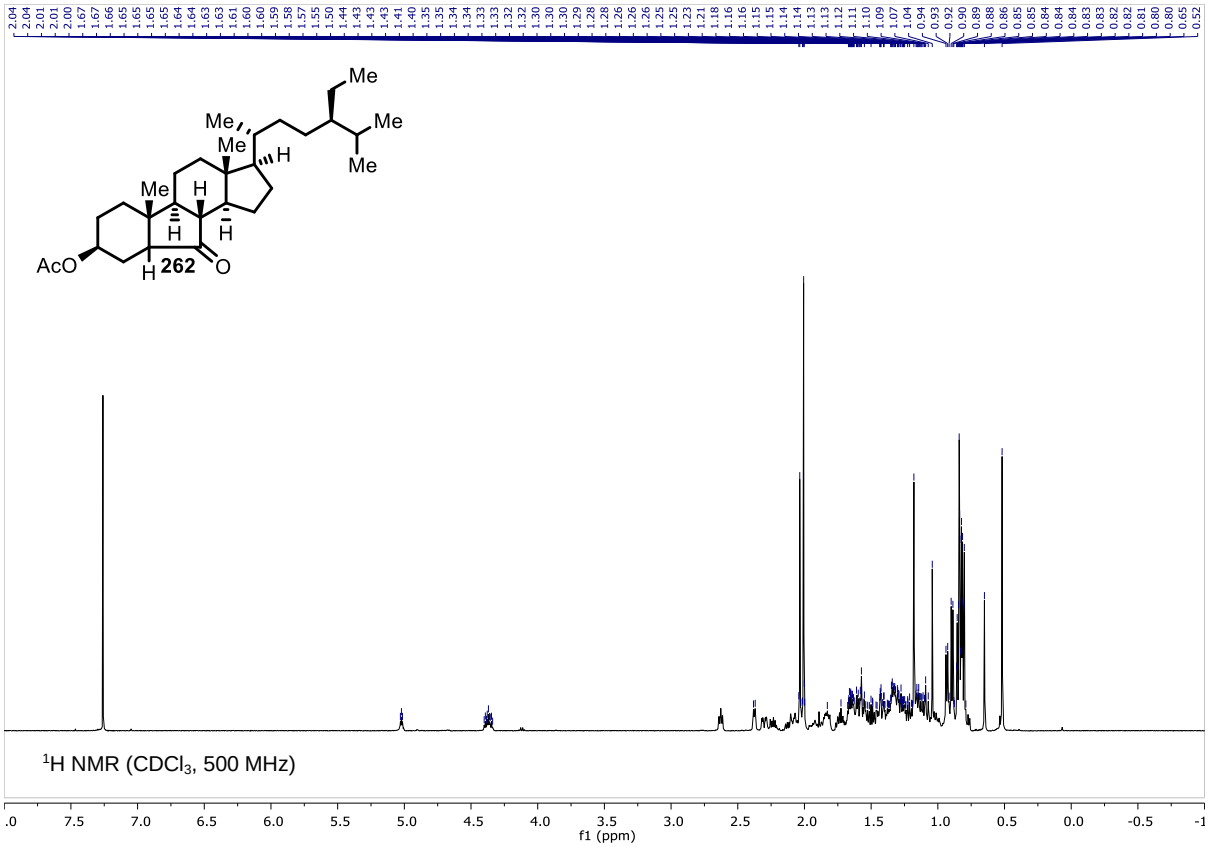
^{13}C NMR ($CDCl_3$, 126 MHz)

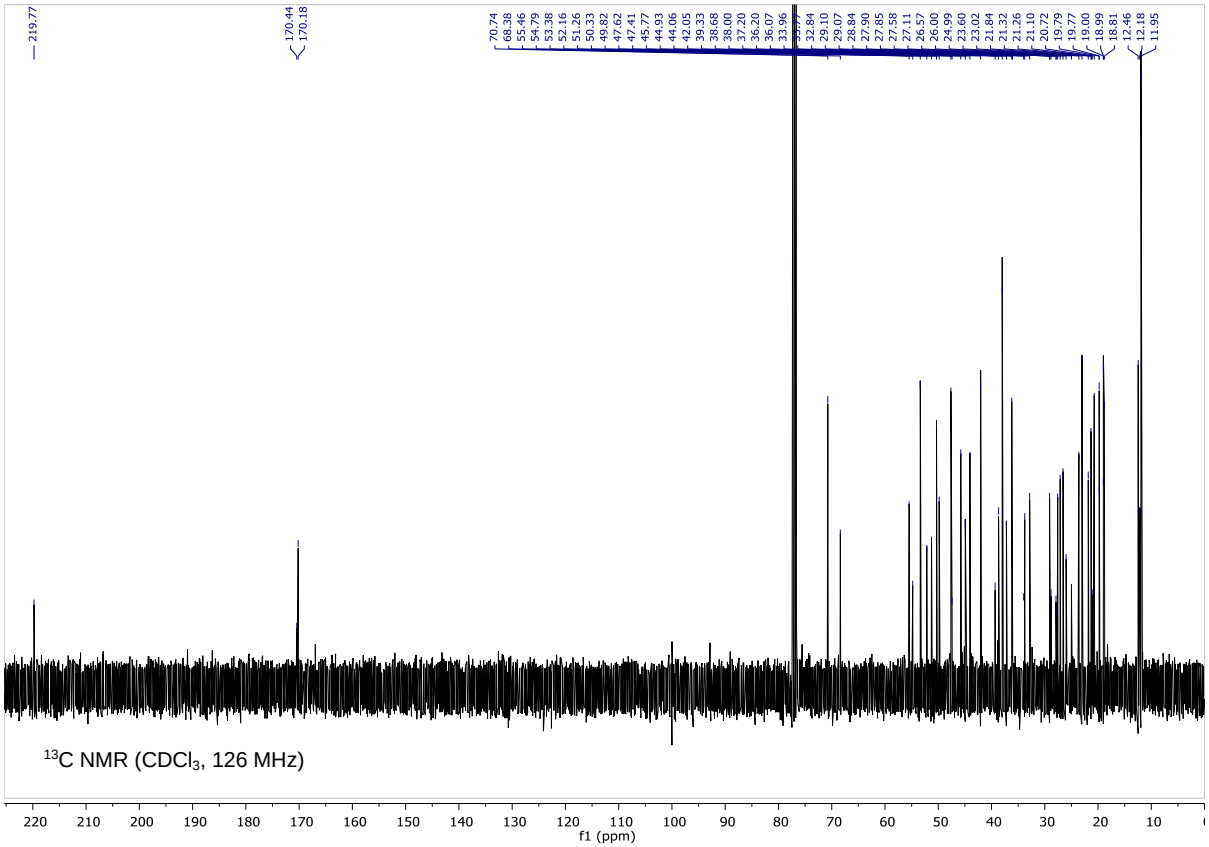


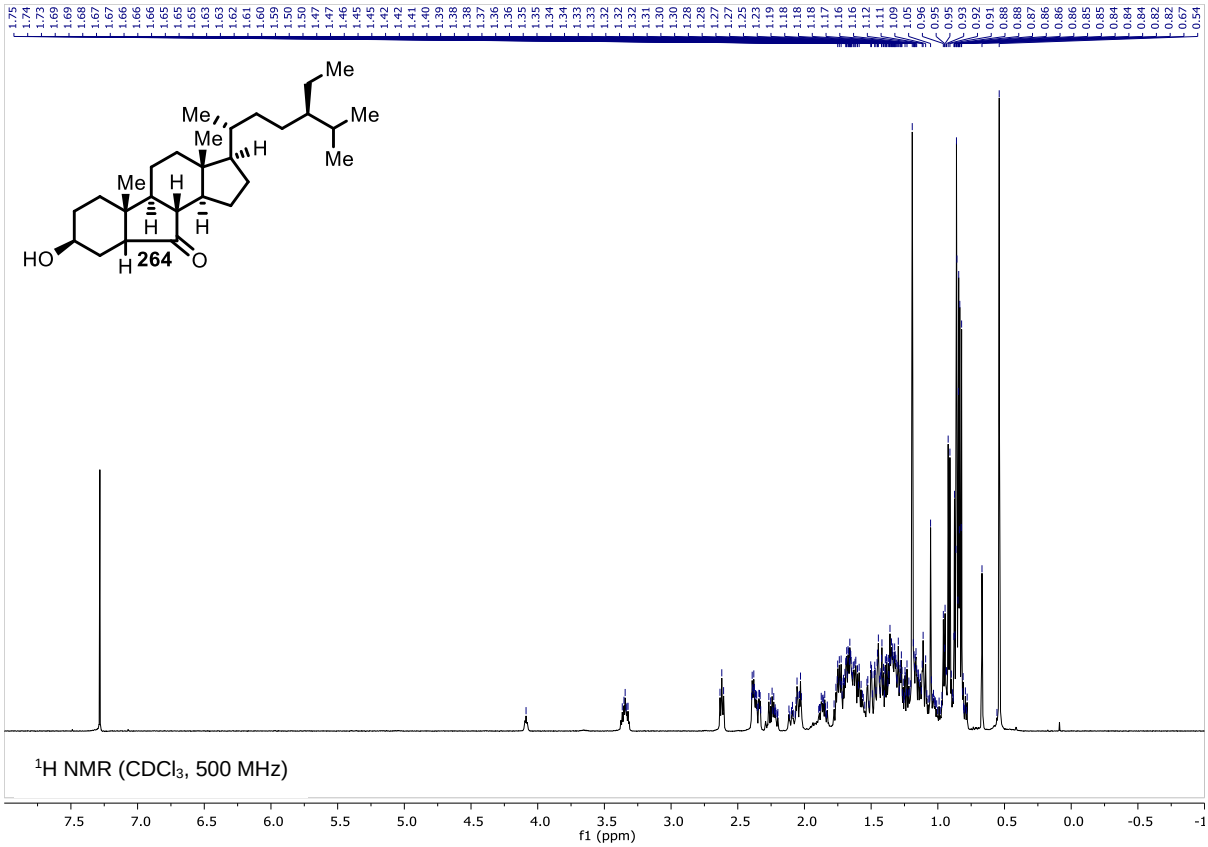
^{1}H NMR ($CDCl_3$, 500 MHz)



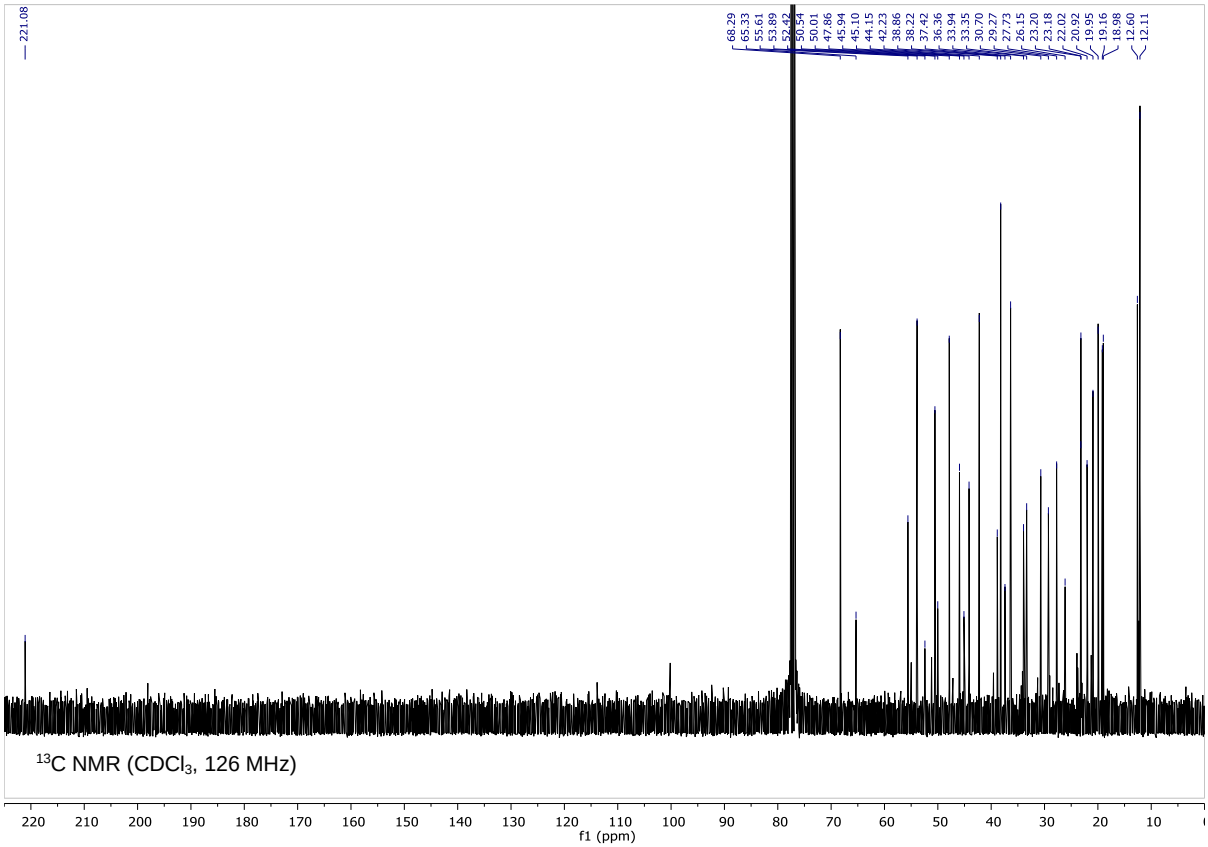
^{13}C NMR ($CDCl_3$, 126 MHz)


Me
Me
Me
Me
H
Me
H
H
H
AcO
H
262
O
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

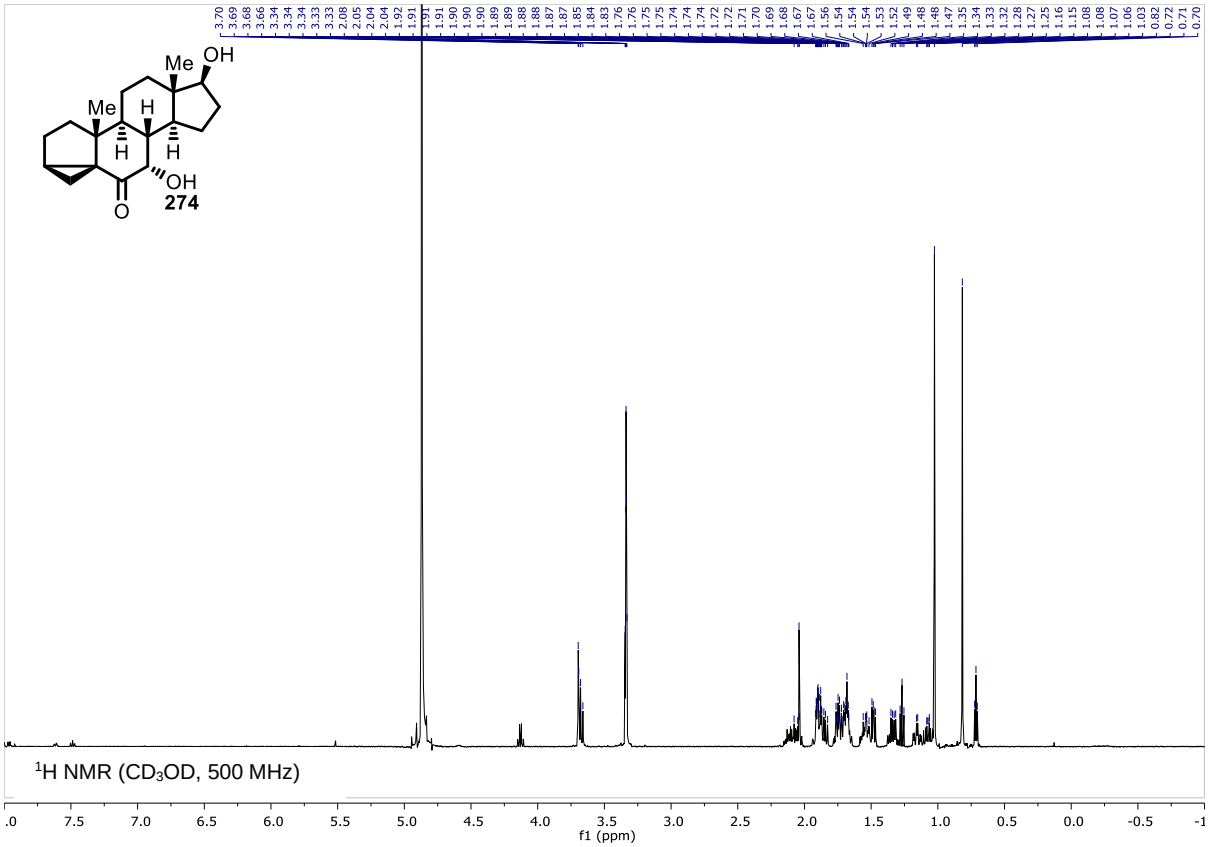

219.77
170.44
170.18
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)

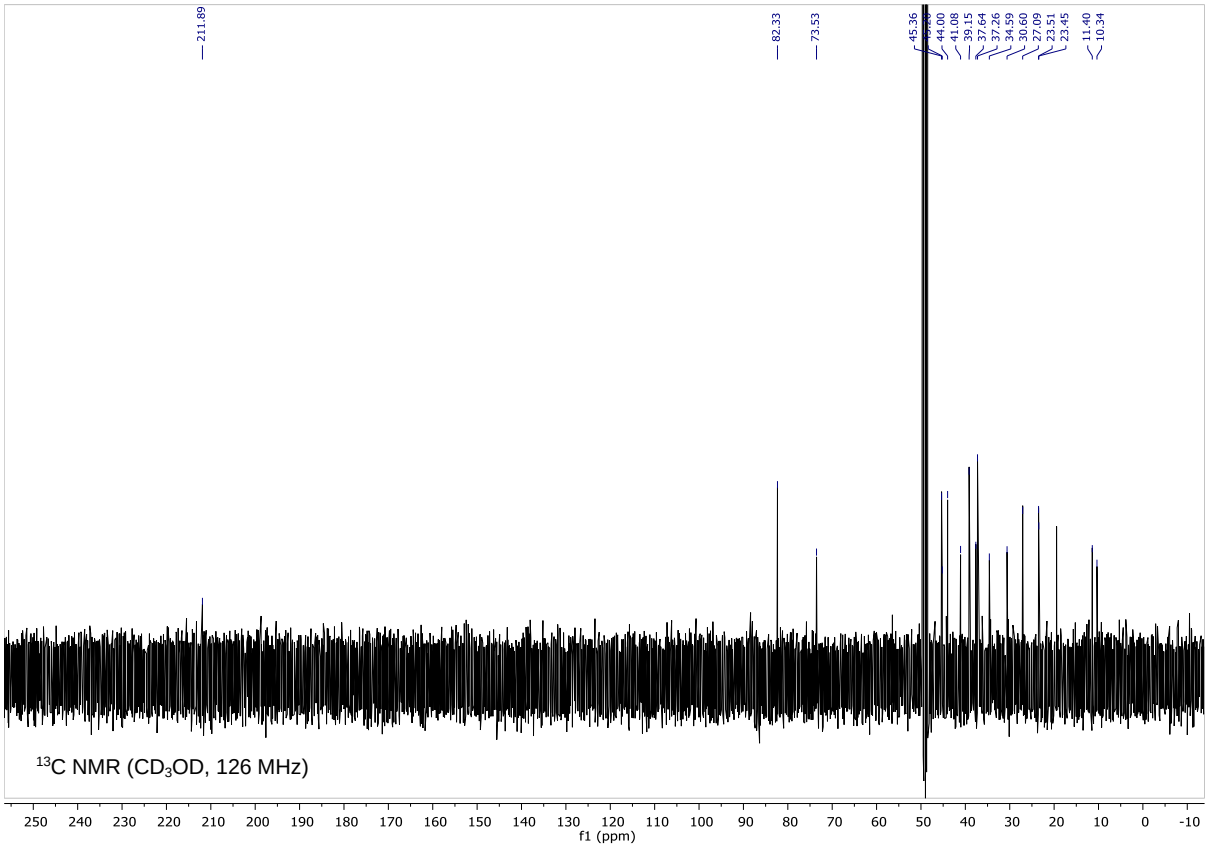


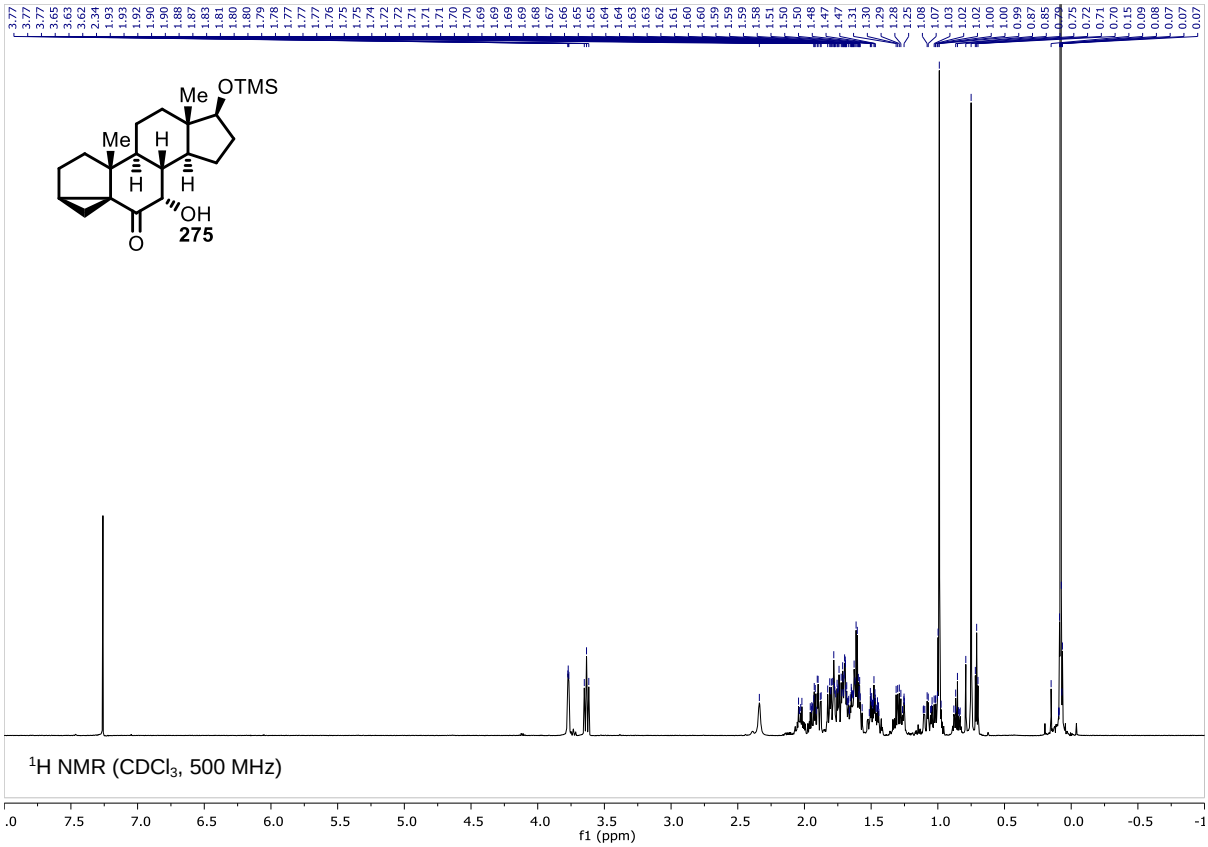
^{1}H NMR ($CDCl_3$, 500 MHz)



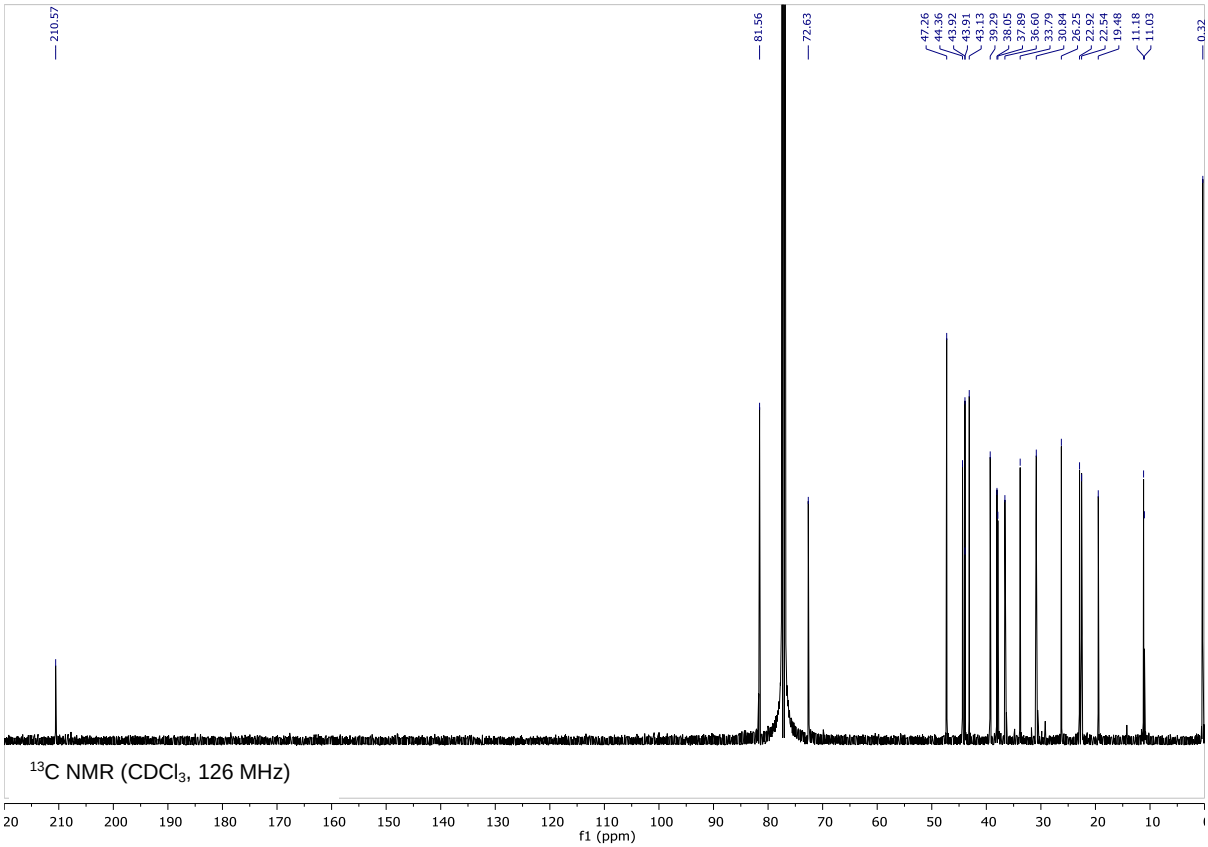
^{13}C NMR ($CDCl_3$, 126 MHz)


Me
OH
Me
H
H
H
OH
O
274
^{1}H NMR (CD_3OD, 500 MHz)
f1 (ppm)

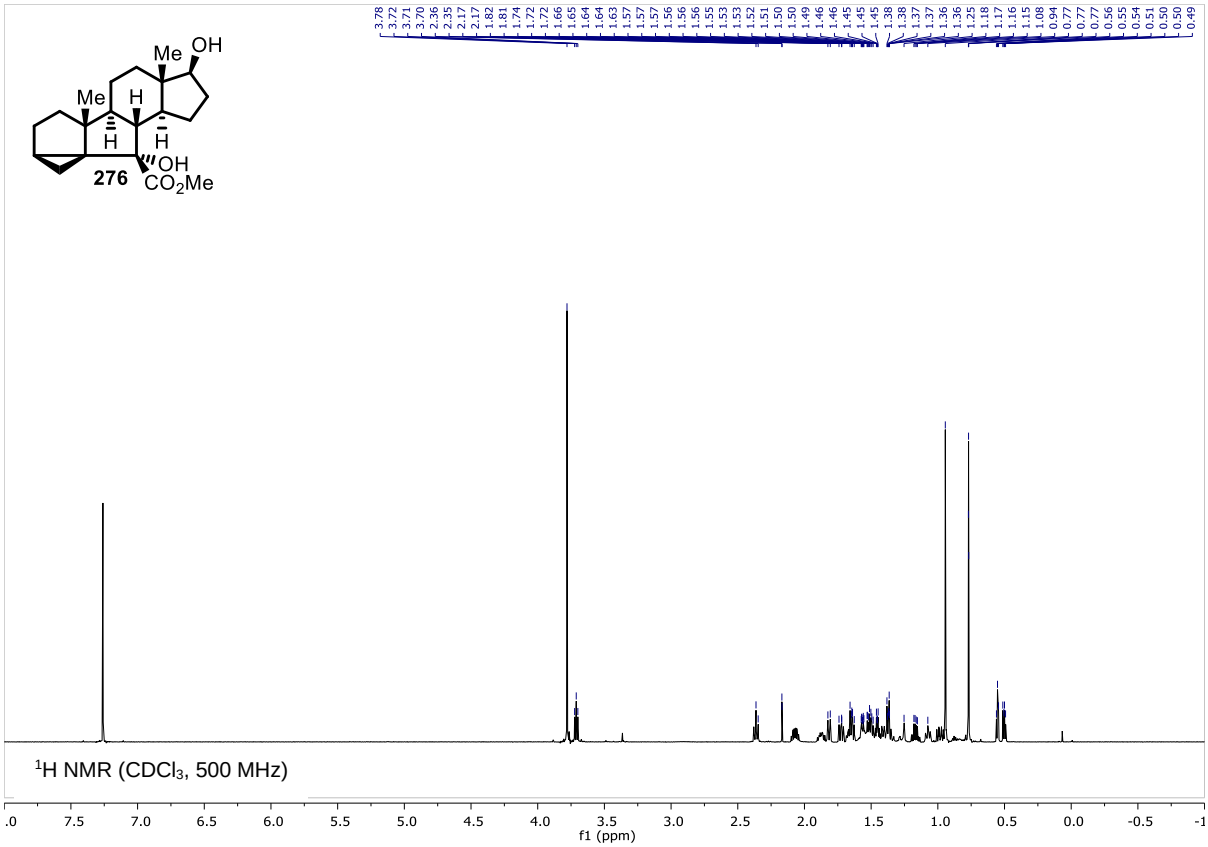

211.89
82.33
73.53
45.36
44.00
41.08
39.15
37.64
37.26
34.59
30.60
27.09
23.51
23.45
11.40
10.34
^{13}C NMR (CD_3OD, 126 MHz)
f1 (ppm)

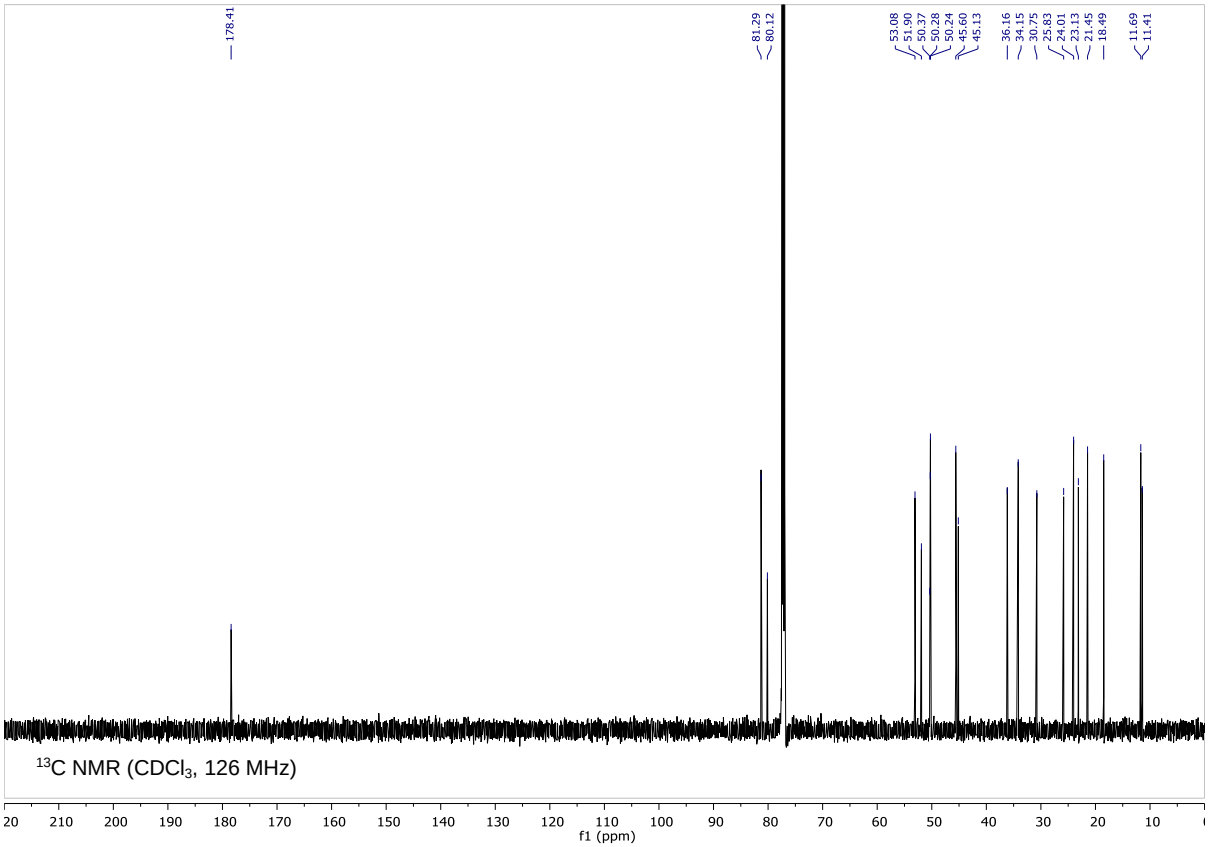


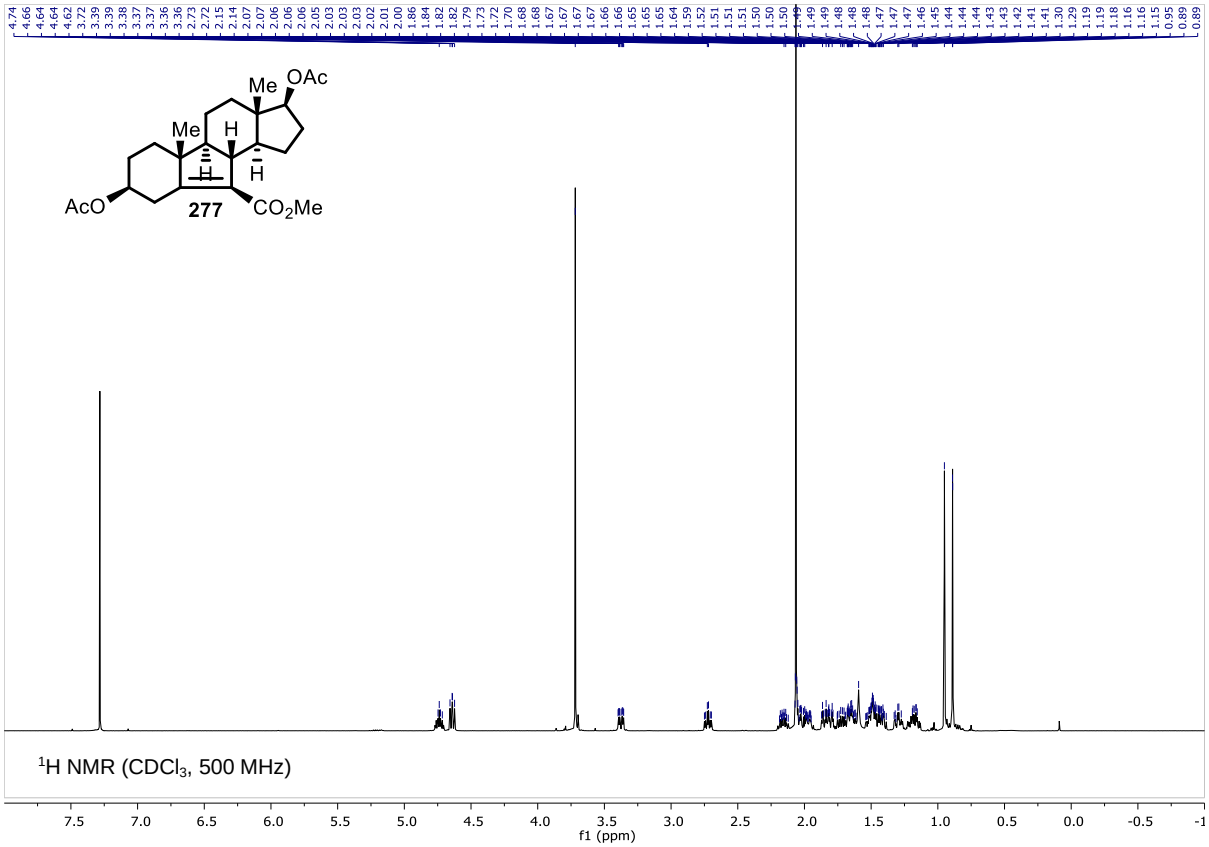
^{1}H NMR ($CDCl_3$, 500 MHz)

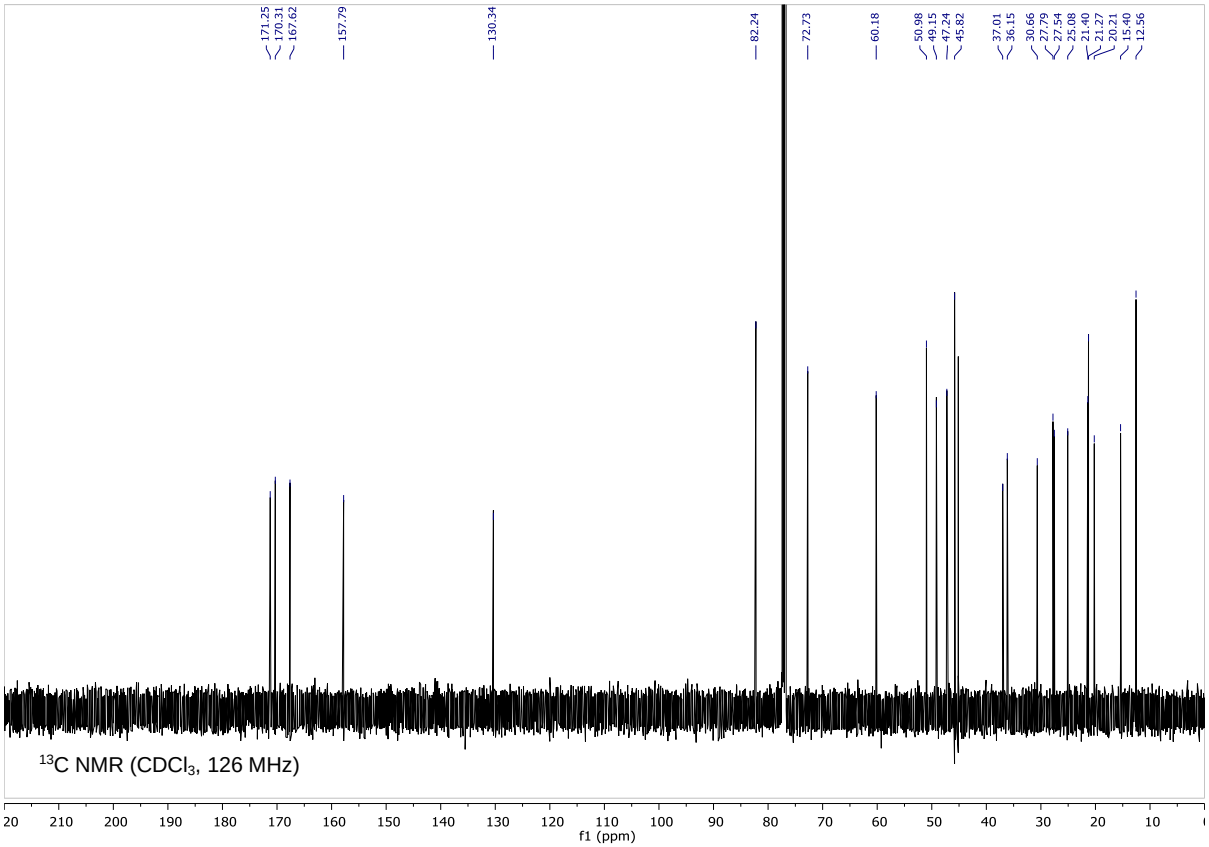


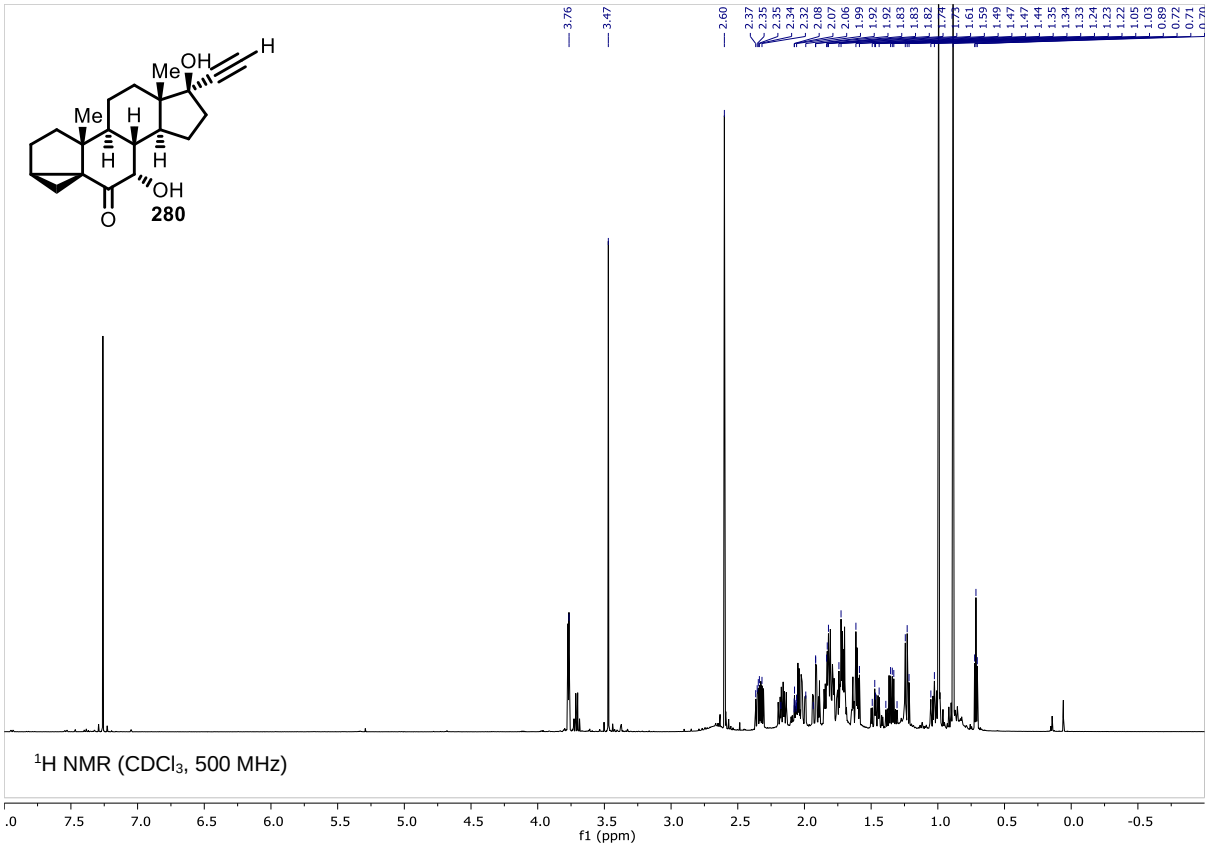
^{13}C NMR ($CDCl_3$, 126 MHz)


Me
OH
Me
H
H
H
OH
CO2Me
276
3.78 3.72 3.71 3.70 2.36 2.35 2.17 2.17 1.82 1.81 1.74 1.72 1.72 1.66 1.65 1.64 1.64 1.63 1.57 1.57 1.57 1.56 1.56 1.56 1.55 1.53 1.53 1.52 1.51 1.50 1.50 1.49 1.46 1.45 1.45 1.45 1.38 1.38 1.37 1.37 1.36 1.25 1.18 1.17 1.16 1.15 1.08 0.94 0.77 0.77 0.77 0.56 0.55 0.54 0.51 0.50 0.50 0.49
1H NMR (CDCl3, 500 MHz)
.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

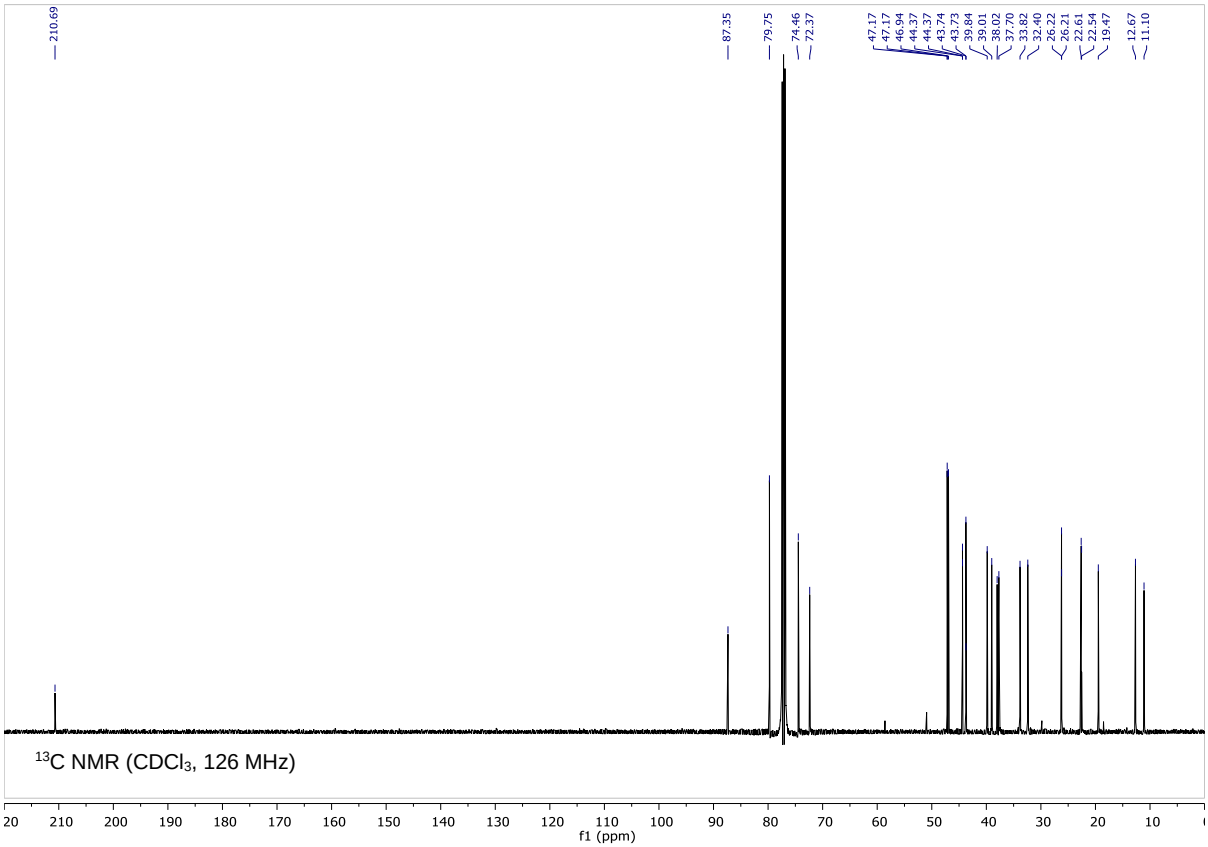

178.41
81.29
80.12
53.08
51.90
50.37
50.28
50.24
45.60
45.13
36.16
34.15
30.75
25.83
24.01
23.13
21.45
18.49
11.69
11.41
13C NMR (CDCl3, 126 MHz)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


Me
OAc
Me
H
H
H
AcO
277
CO2Me
1H NMR (CDCl3, 500 MHz)
f1 (ppm)

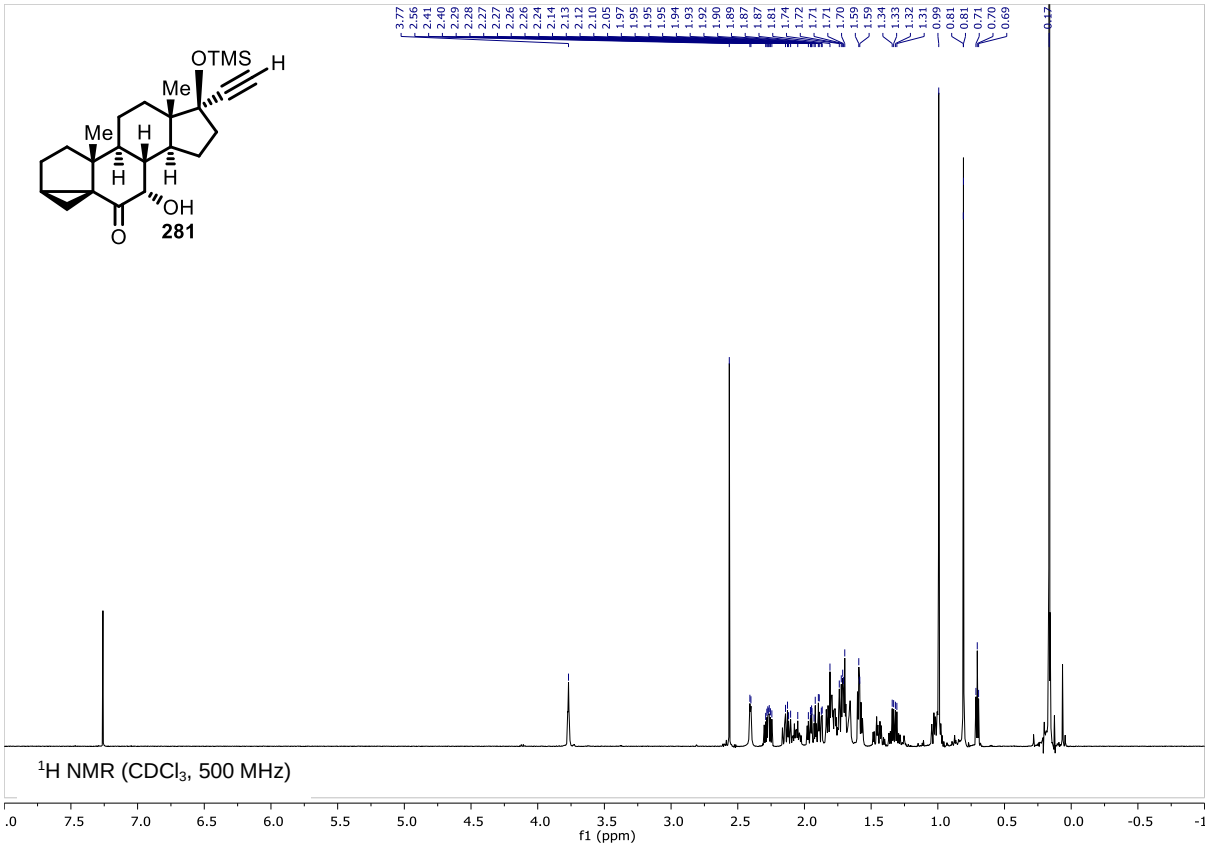

171.25
170.31
167.62
157.79
130.34
82.24
72.73
60.18
50.98
49.15
47.24
45.82
37.01
36.15
30.66
27.79
27.54
25.08
21.40
21.27
20.21
15.40
12.56
13C NMR (CDCl3, 126 MHz)
f1 (ppm)

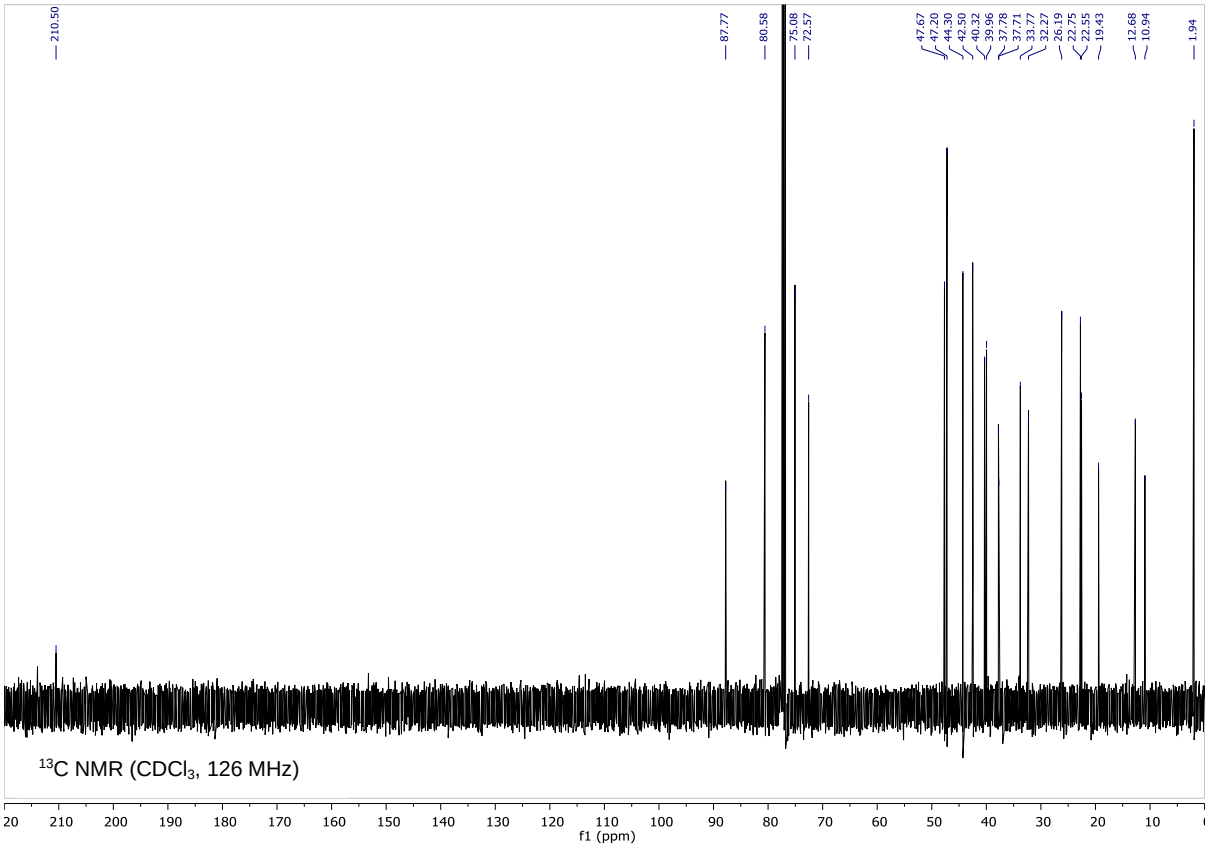


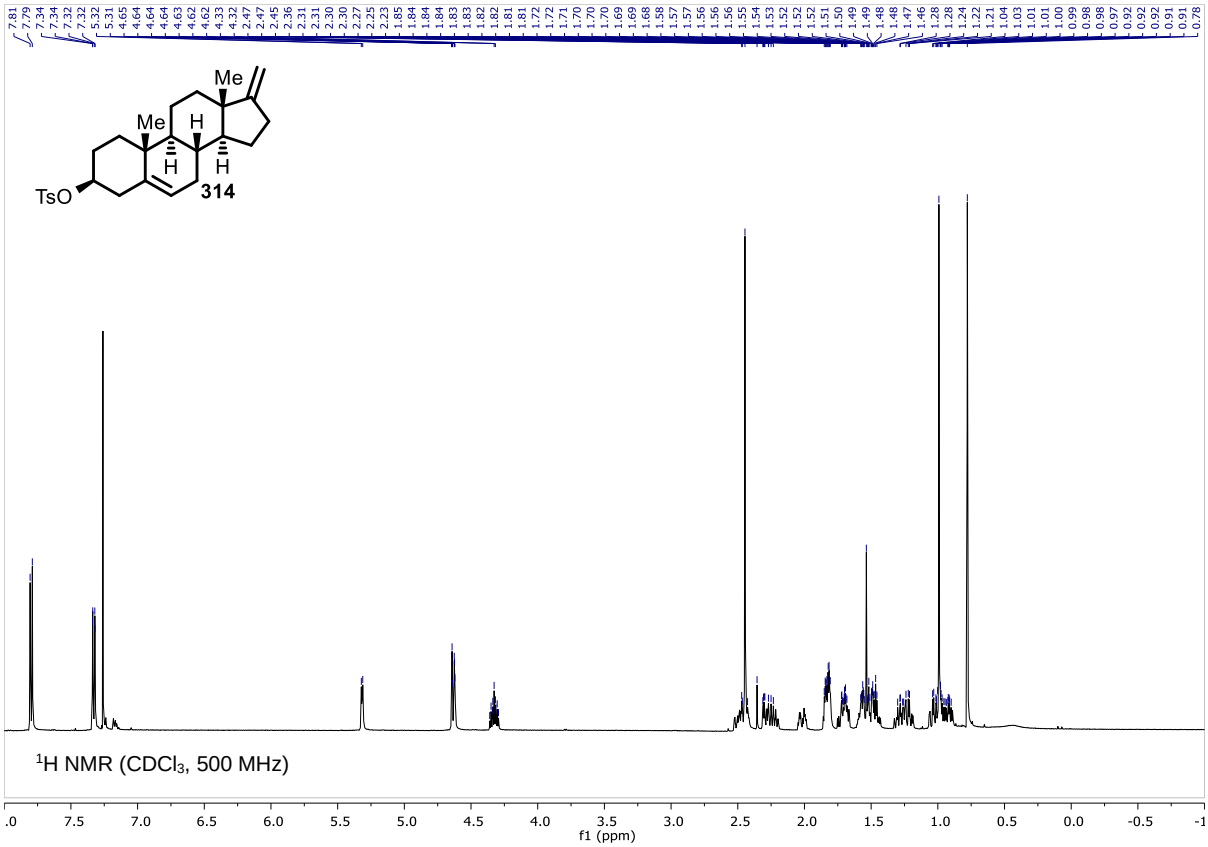
^{1}H NMR ($CDCl_3$, 500 MHz)

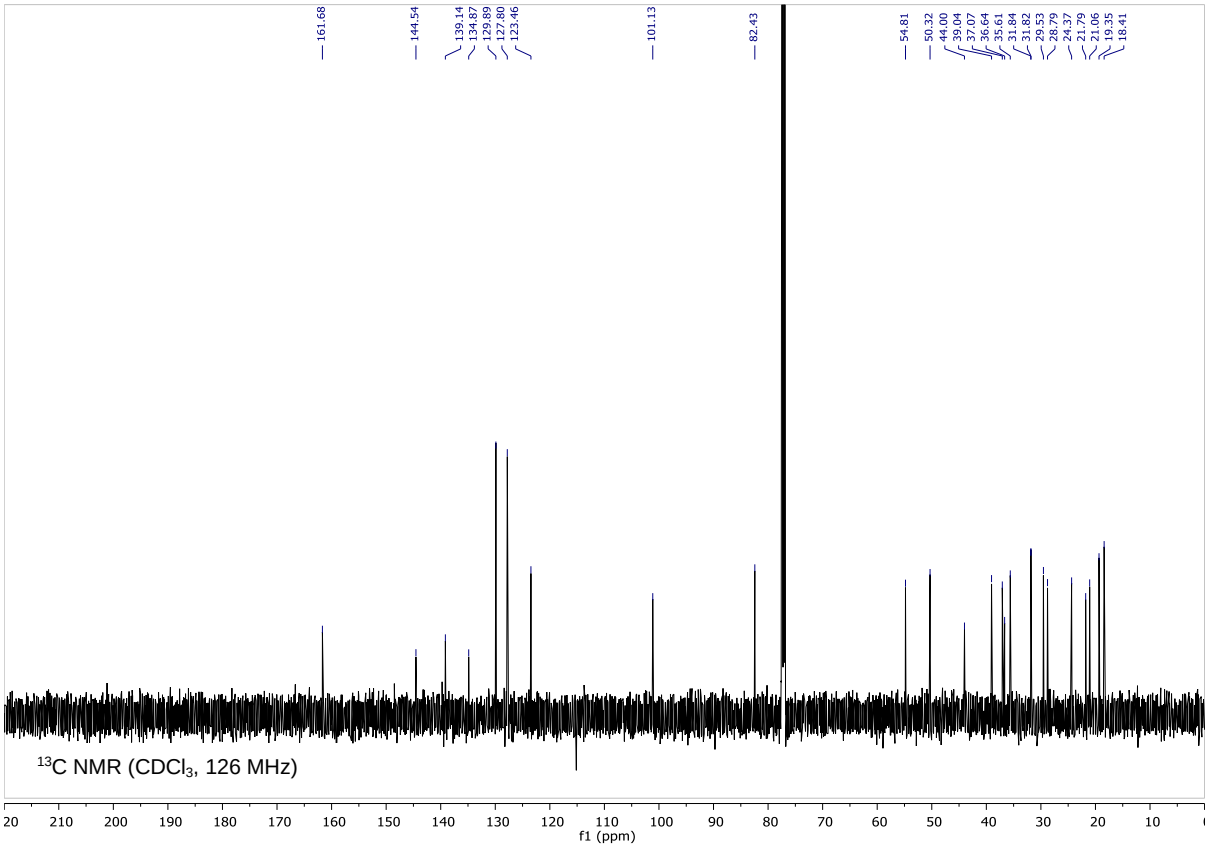


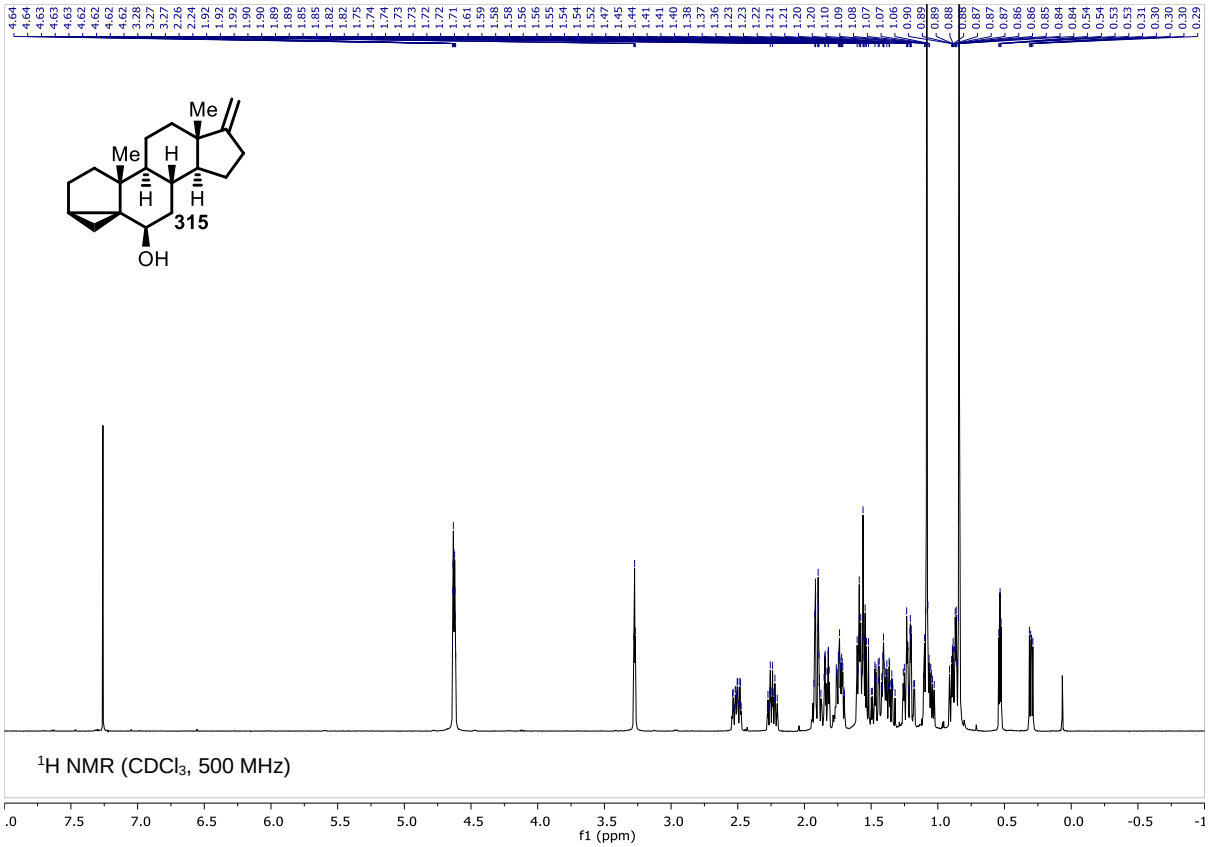
^{13}C NMR ($CDCl_3$, 126 MHz)

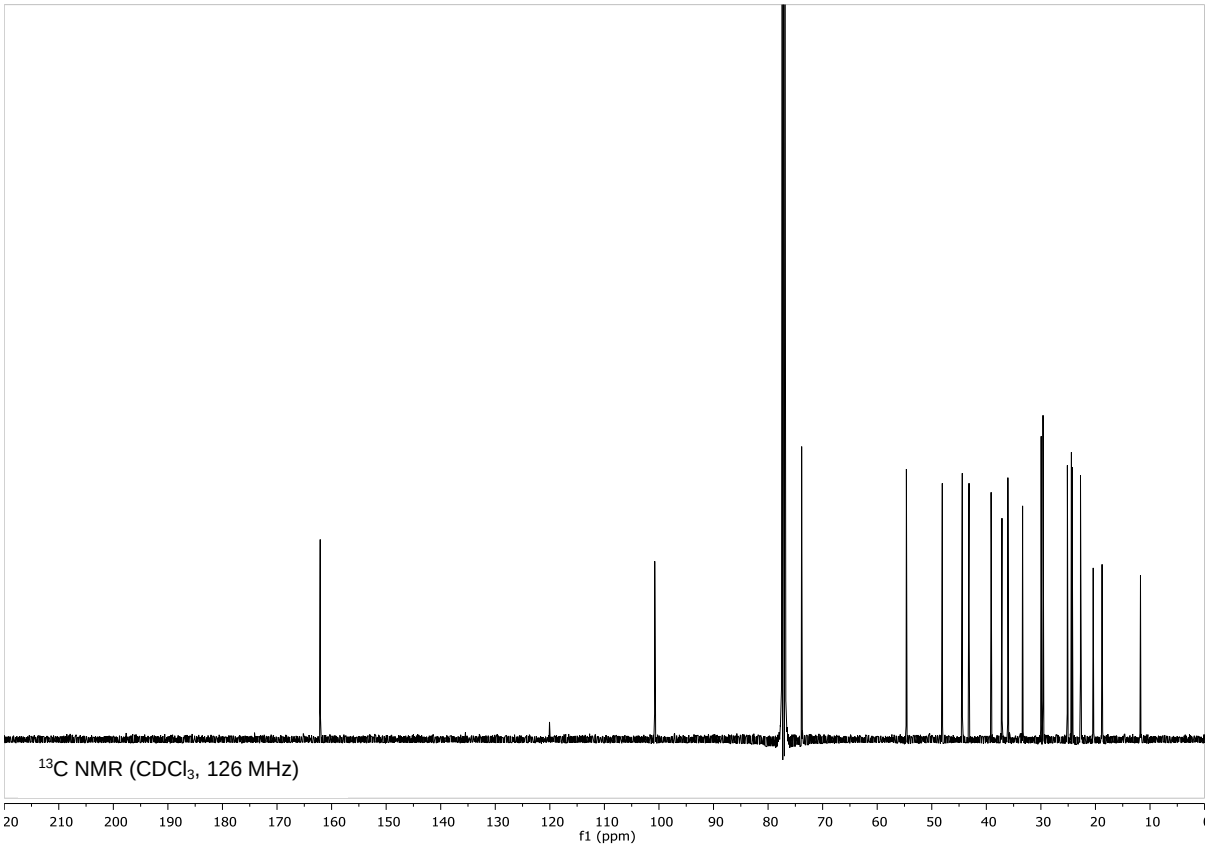

OTMS
H
Me
Me
H
H
H
OH
O
281
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

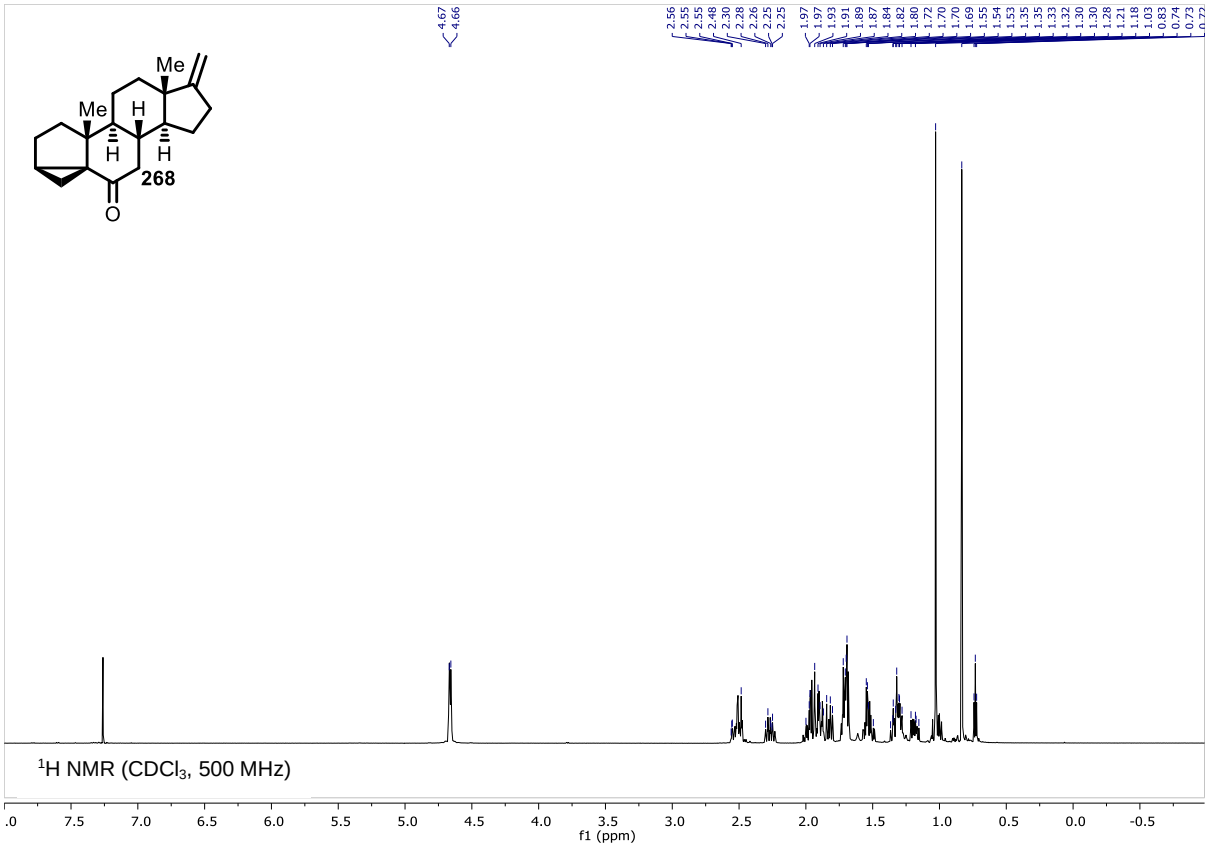

^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)


Me
Me
H
H
H
TsO
314
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)

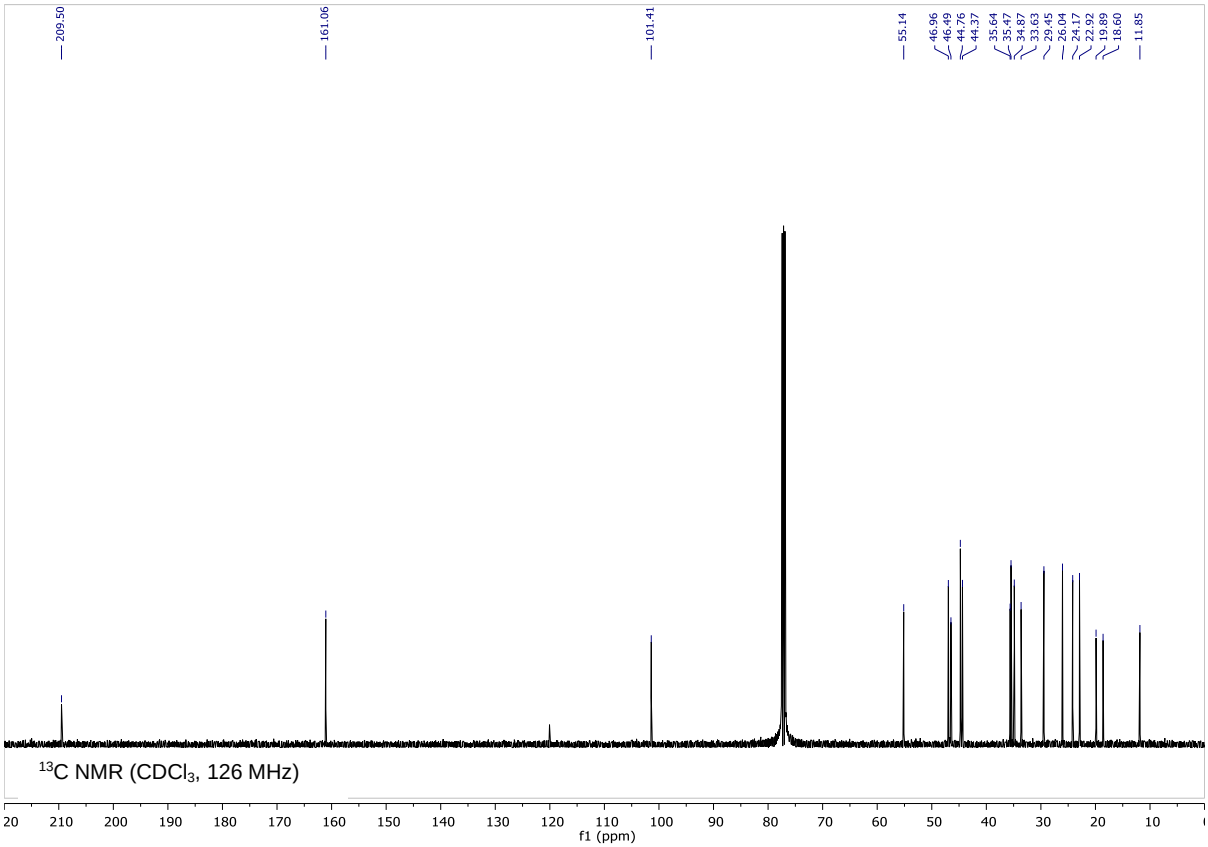

161.68
144.54
139.14
134.87
129.89
127.80
123.46
101.13
82.43
54.81
50.32
44.00
39.04
37.07
36.64
35.61
31.84
31.82
29.53
28.79
24.37
21.79
21.06
19.35
18.41
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)


Me
Me
H
H
H
315
OH
1H NMR (CDCl3, 500 MHz)
f1 (ppm)

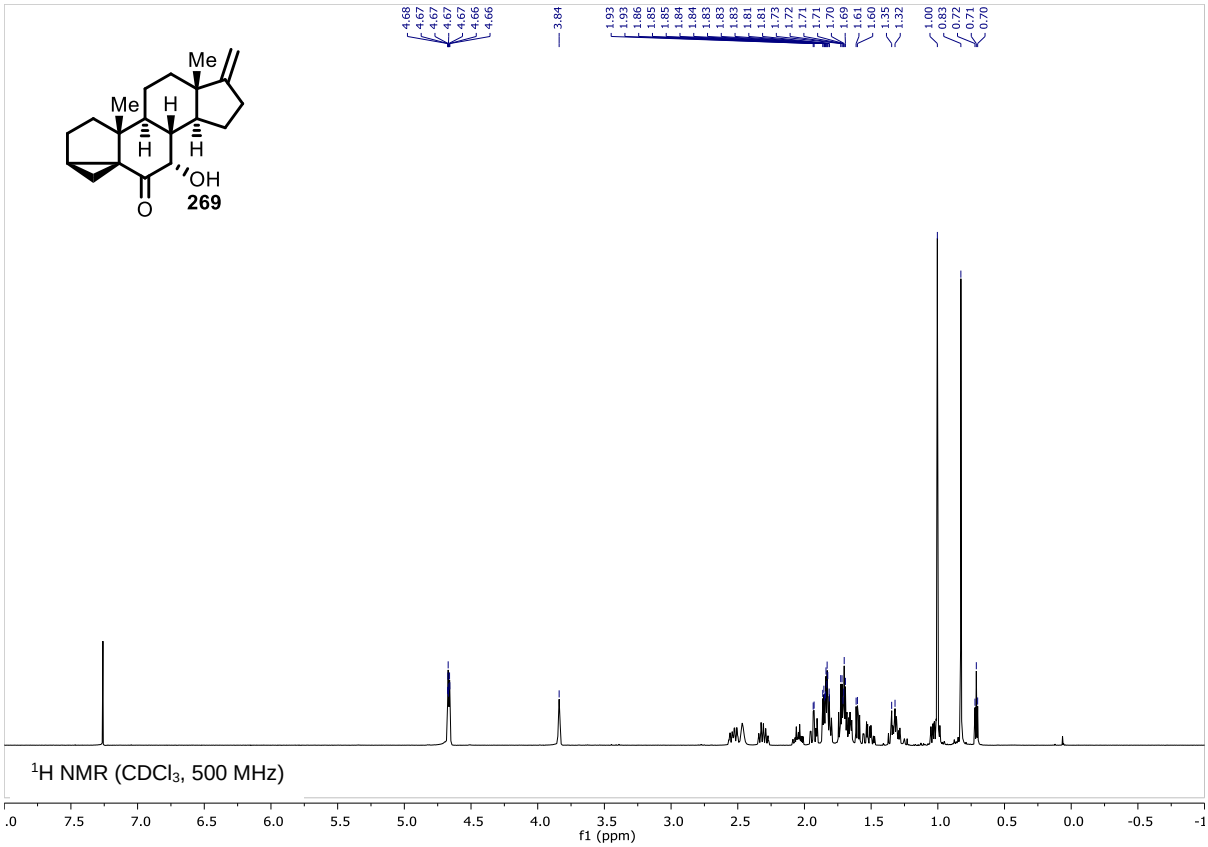

13C NMR (CDCl3, 126 MHz)
f1 (ppm)



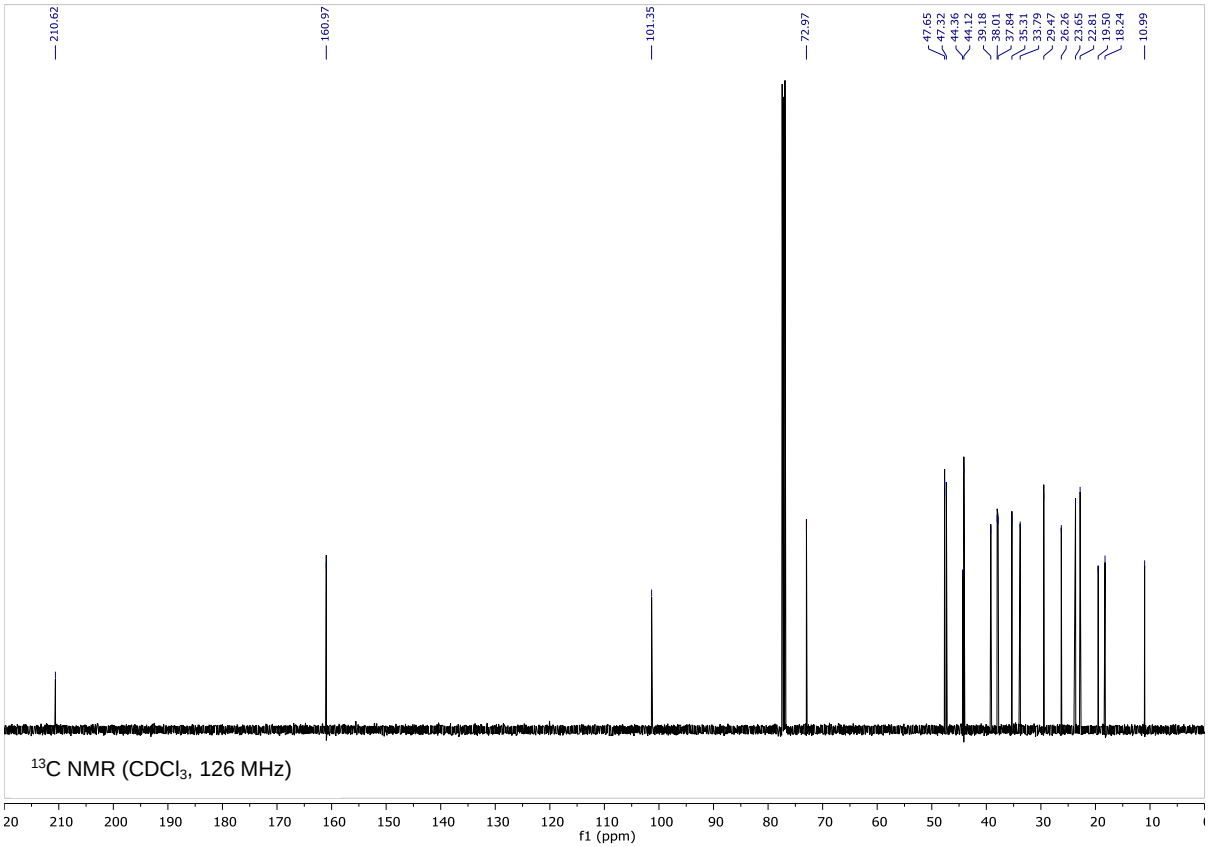
^{1}H NMR ($CDCl_3$, 500 MHz)



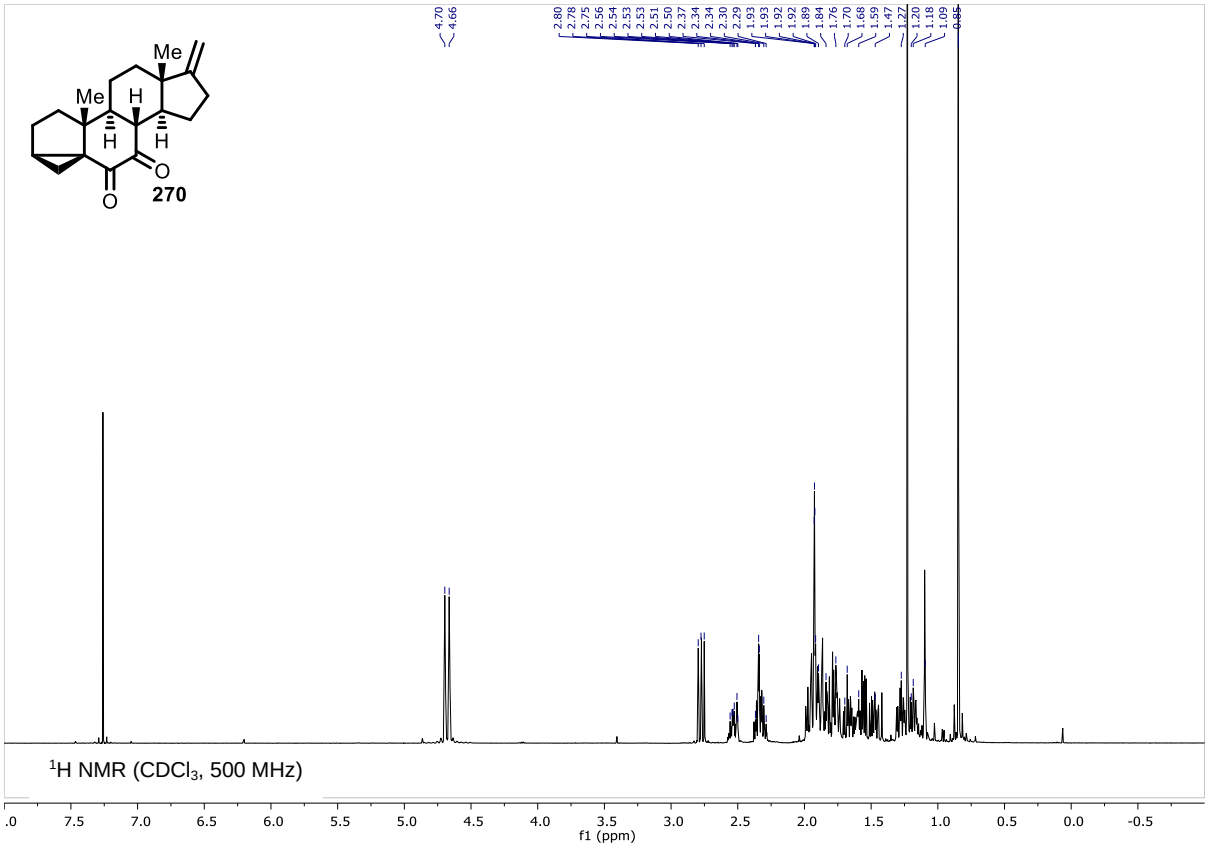
^{13}C NMR ($CDCl_3$, 126 MHz)

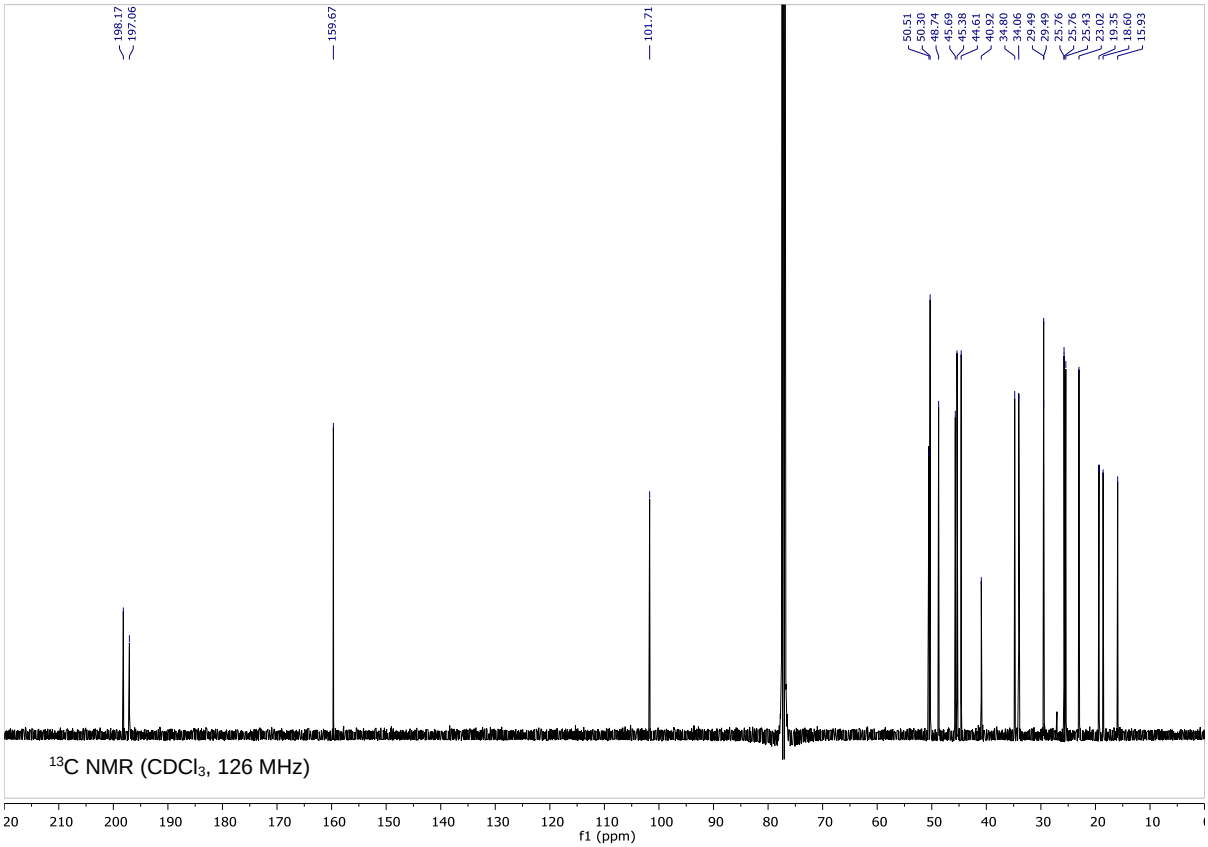


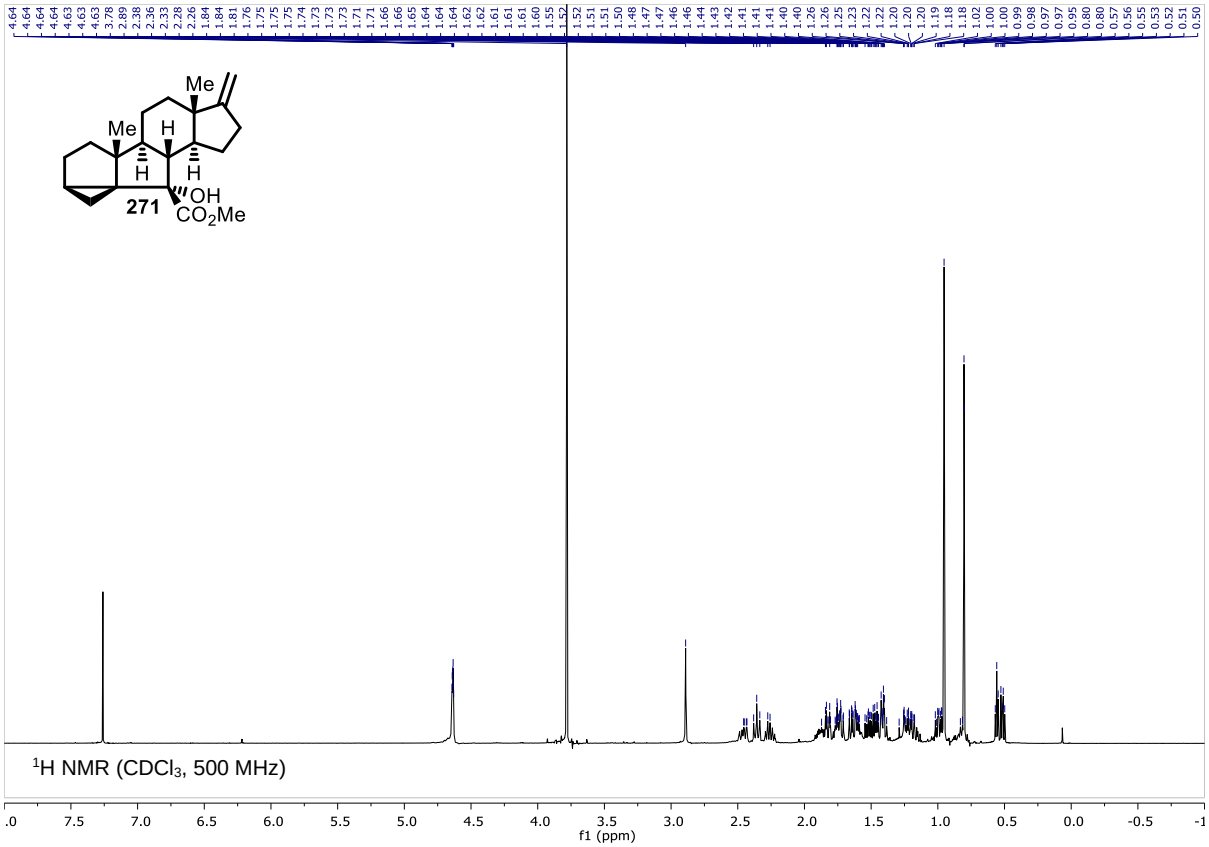
^{1}H NMR ($CDCl_3$, 500 MHz)

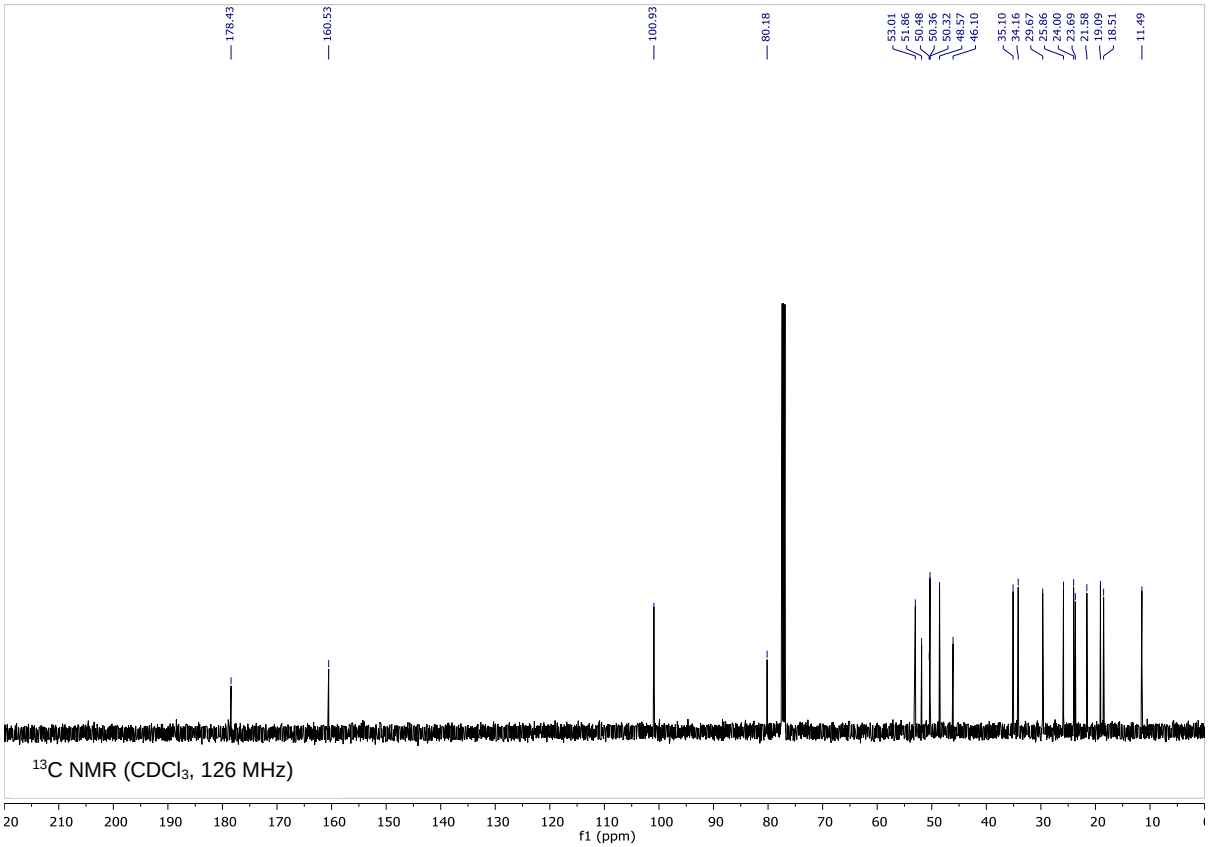


^{13}C NMR ($CDCl_3$, 126 MHz)


Me
Me
H
H
H
O
O
270
4.70
4.66
2.80
2.78
2.75
2.56
2.54
2.53
2.53
2.51
2.50
2.37
2.34
2.34
2.30
2.29
1.93
1.93
1.92
1.90
1.89
1.84
1.76
1.70
1.68
1.59
1.47
1.22
1.20
1.18
1.09
0.85
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)


198.17
197.06
159.67
101.71
50.51
50.30
48.74
45.69
45.38
44.61
40.92
34.80
34.06
29.49
29.49
25.76
25.76
25.43
23.02
19.35
18.60
15.93
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)


Me
Me
H
H
H
OH
CO2Me
271
1H NMR (CDCl3, 500 MHz)
f1 (ppm)


178.43
160.53
100.93
80.18
53.01
51.86
50.48
50.36
50.32
48.57
46.10
35.10
34.16
29.67
25.86
24.00
23.69
21.58
19.09
18.51
11.49
13C NMR (CDCl3, 126 MHz)
f1 (ppm)