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Catalyst-Free Trifluoromethoxylation of Silyl Enol Ethers and Allyl Silanes with Bis(trifluoromethyl)peroxide

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Abstract: Radical trifluoromethoxylation is an attractive approach to prepare compounds featuring the important OCF_3 group, however most existing methods have focused on aromatic substrates. Here, we report novel methodologies with alkenyl substrates employing bis(trifluoromethyl)peroxide (BTMP) as a practical and comparatively atom economical trifluoromethoxylating reagent. With silyl enol ether substrates, switching reaction solvent allows for the synthesis of either α-(trifluoromethoxy)ketone products or unprecedented alkenyl-OCF_3 species. Furthermore, allyl silanes have been employed as substrates for the first time, affording allyl(trifluoromethyl)ether products in good yields. In each case, the methods operate at room temperature without large excesses of the alkene substrate while, in contrast to previous radical trifluoromethoxylation reactions, no catalyst, light or other activators are required.

Introduction

The trifluoromethoxy (OCF_3) group and its introduction into organic molecules is of growing interest in several different fields, especially agro- and medicinal chemistry, due to its unique properties and good metabolic stability.[1] Often referred to as a "superhalogen", the OCF_3 group exhibits high lipophilicity ($\pi = 1.04$) and comparable electronegativity to an individual fluorine atom ($\chi^{OCF3} = 3.7$, $\chi^{F} = 4.0$), however its electron-withdrawing effect is somewhat lower than many other fluorinated groups.[2] The unique stereoelectronic requirements of OCF_3 moieties can also result in unconventional conformational preferences rarely encountered with alternative groups. Incorporating a trifluoromethoxy group onto a valuable molecule therefore can result in better fine tuning of its properties and an improved overall activity. Furthermore, with perfluoroalkyl substances (PFAS) currently attracting concern as so-called "forever chemicals", the comparatively lower environmental persistence of trifluoromethoxy moieties could make these motifs attractive alternatives to CF_3 and other fluorinated groups in pharmaceuticals, agrochemicals and materials.[3]

Despite this great potential, only a handful of OCF_3-containing molecules are currently employed commercially with only 0.01 % of the fluorinated pharmaceuticals on the market and 0.02 % of fluorinated agrochemicals being trifluoromethoxylated.[1e,g] A major contributing factor for this is the lack of practical methods for introducing OCF_3, especially at a late stage of a synthetic route. Compared to indirect approaches involving fluorination of pre-functionalised ether motifs[4] or trifluoromethylation of alcohols,[5] direct trifluoromethoxylation methods, wherein the whole OCF_3 moiety is attached in one step, are particularly attractive in this regard. The available methods can be categorised into nucleophilic and radical approaches, where nucleophilic methods can be challenging due to the instability of the $^{-}OCF_3$ anion towards β-fluoride elimination.[6] As a result, considerable attention has been devoted to the development of new radical trifluoromethoxylation reactions.[7] In 2018, the groups of Ngai and Togni both introduced bench stable reagents which release $^{\bullet}OCF_3$ radicals upon activation of an N–O bond.[8] These compounds represented a major breakthrough for the field that opened up novel synthetic routes towards OCF_3-substituted molecules directly from unfunctionalised aromatics.[7,9] In 2021, our groups explored bis(trifluoromethyl)peroxide (BTMP) as an alternative source of $^{\bullet}OCF_3$ radicals in related photocatalytic and TEMPO-induced reactions of arenes and heteroarenes.[10] First reported by Swarts in 1933[11] and reinvestigated by Cady in 1957,[12a] BTMP is a remarkably stable (no thermal decomposition below 200 °C) and easy to handle gas which can be synthesised on a large scale from the relatively inexpensive industrial chemicals CO and F_2.[13,14] In comparison to the previous reagents, which are themselves prepared from expensive electrophilic trifluoromethylating reagents and generate significant waste, BTMP offers promise as a practical and atom-economical alternative.

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While there have been a number of reports in recent years on the radical trifluoromethoxylation of arenes and, to a lesser extent, heteroarenes, applications for the synthesis of other important classes of OCF_3-containing molecules are scarce (Figure 1a). In particular, radical methodologies that afford products substituted with OCF_3 groups at sp^3-hybridised carbon atoms have been seldom reported. In 2021, a collaborative study between the Magnier, Dagousset and Dell'Amico groups investigated $^{\bullet}OCF_3$ radical addition to enol carbonate substrates using the Togni trifluoromethoxylating reagent (Figure 1b).[15] Although requiring 5 equivalents of the alkene substrates and employing photoredox catalysis conditions, the success of this process demonstrates the potential of radical trifluoromethoxylation to generate diverse OCF_3-containing products, delivering α-trifluoromethoxylated ketones in generally moderate yields.[16] Inspired by this report and by our previous work on the radical trifluoromethoxylation of aromatics,[10] we considered whether BTMP could be employed as a reagent for preparing a wider range of OCF_3-containing molecules. Here we report the results of this investigation, which not only led to efficient methods for preparing α-trifluoromethoxylated ketones and allyl(trifluoromethoxy)ethers from silyl enol ethers and allyl silanes, respectively, but also gave access to unprecedented alkenyl-OCF_3 products. Moreover, in addition to its practical and atom-economical nature, the use of BTMP also allowed for trifluoromethoxylation to be conducted under catalyst-free conditions without large excesses of the substrate and employing inexpensive potassium carbonate as the only additive (Figure 1c).

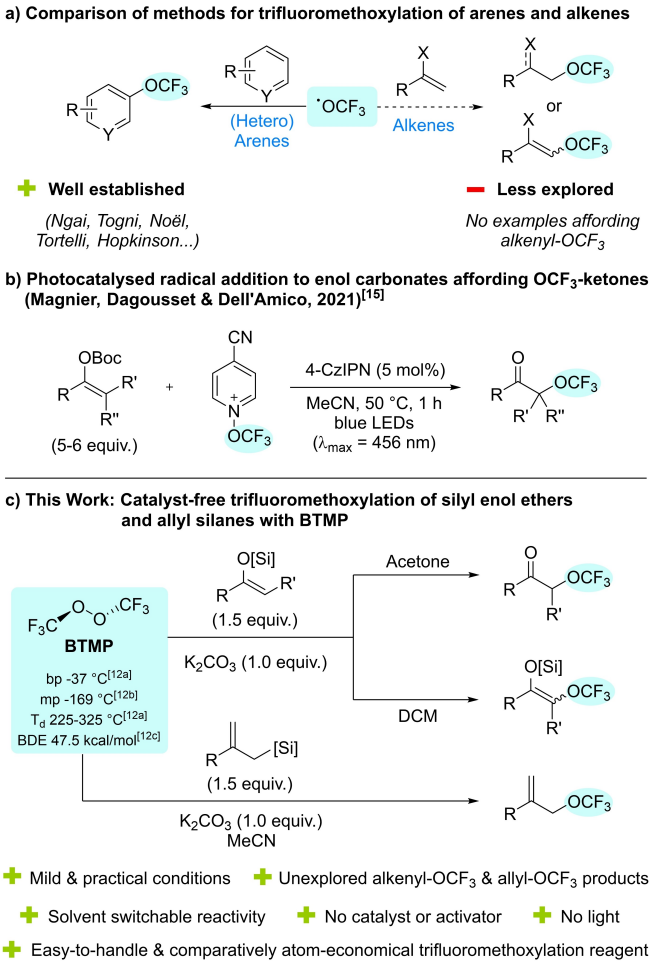
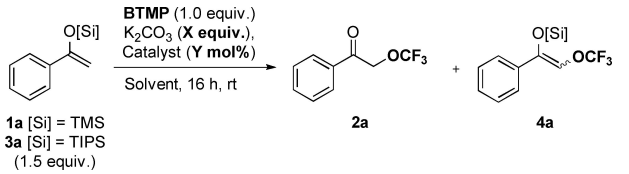


Figure 1. a) Radical trifluoromethoxylation of arenes and alkenes. b) Previous report on the photoredox catalysed trifluoromethoxylation of enol carbonates affording α-(trifluoromethoxy) ketones. c) This work: Catalyst-free trifluoromethoxylation of silyl enol ethers and allyl silanes with BTMP. 4-CzIPN: 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene, T_d: decomposition temperature.

Results and Discussion

At the beginning of the study, we investigated potential alkenyl substrates that could serve as acceptors of $^{\bullet}OCF_3$ radicals, and selected silyl enol ethers as representative substrates. To our delight, an initial test reaction employing the established photocatalytic conditions from our prior work with the trimethylsilyl enol ether of acetophenone (**1a**, 1.5 equiv.) provided the desired α-(trifluoromethoxy)ketone **2a** in a ^{19}F NMR yield of 16 % (internal standard: $PhCF_3$, Table 1, Entry 1).[17] Product **2a** was also generated in 6 % ^{19}F NMR yield when **1a** was reacted in the presence of BTMP, TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl, 25 mol %) and K_2CO_3 (1.0 equiv.) under conditions also developed in our previous study with (hetero)arene substrates (Table 1, Entry 2). In both cases, almost complete desilylation of **1a** was observed during the reaction suggesting the relatively low yields could result in part from undesired background hydrolysis of the trimethylsilyl enol ether. We therefore investigated the more hydrolytically stable compound **3a**, which features a sterically more demanding triisopropylsilyl (TIPS) group in place of the trimethylsilyl (TMS) motif. Pleasingly, under the TEMPO-mediated conditions, **3a** reacted smoothly to afford **2a** in an increased ^{19}F NMR yield of 44 %. Furthermore, analysis of the crude NMR spectra revealed the presence of small amounts of trifluoromethoxylated side-products, which could be assigned as the (*Z*) and (*E*) isomers of the silyl enol ether **4a** ((*Z*)-**4a**, 4 %; (*E*)-**4a**, 5 %, Table 1, Entry 3). To the best of our knowledge, products featuring an alkenyl OCF_3 group have not been obtained previously via radical trifluoromethoxylation. Silyl enol ethers of general structure **4** could serve as useful building blocks for the construction of diverse OCF_3-containing compounds. An investigation of the reaction stoichiometry revealed 1.5 equivalents of **3a** to be optimum with 1.0 or 2.0 equivalents leading to lower yields of **2a** (Table 1, Entries 4&5). Such a low loading of the alkene is remarkable and stands in contrast to other radical trifluoromethoxylation methodologies, which typically require 5 equivalents or more of the organic substrate. Reducing the TEMPO catalyst loading to 5 mol % suppressed the formation of silyl enol ethers **4a** and led to an increase in ^{19}F NMR yield of ketone product **2a** to 48 % (Table 1, Entry 6). Moreover, omitting the catalyst entirely did not lead to the expected suppression of reactivity but rather resulted in a further small increase in ^{19}F NMR yield

Table 1: Optimisation of the direct trifluoromethoxylation of silyl enol ethers using BTMP.



1a [Si] = TMS
3a [Si] = TIPS
(1.5 equiv.)

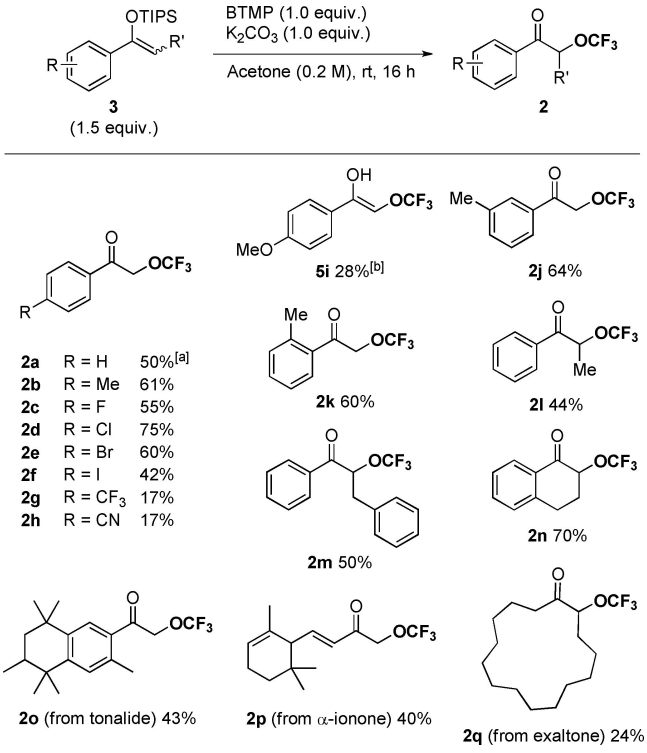
2a **4a**

Entry	[Si]	Catalyst (mol%)	K_2CO_3 (equiv.)	Solvent	Yield **2a**[a]	Yield **4a**[a] (*Z*/*E*)
1[b]	TMS	$[Ru(bpy)_3](PF_6)_2$ (4 mol%)	–	MeCN	16	–
2	TMS	TEMPO (25 mol%)	1.0	MeCN	6	–
3	TIPS	TEMPO (25 mol%)	1.0	MeCN	44	4:5
4[c]	TIPS	TEMPO (25 mol%)	1.0	MeCN	16	–
5[d]	TIPS	TEMPO (25 mol%)	1.0	MeCN	42	5:3
6	TIPS	TEMPO (5 mol%)	1.0	MeCN	48	–
7	TIPS	–	1.0	MeCN	50	–
8	TIPS	–	1.5	MeCN	50	–
9	TIPS	–	0.5	MeCN	31	–
10	TIPS	–	1.0	Acetone	55	–
11	TIPS	–	1.0	$MeNO_2$	12	49:6
12	TIPS	–	1.0	Et_2O	12	34:22
13	TIPS	–	1.0	DCM	5	57:12
14[e]	TIPS	–	1.5	Acetone	49	–
15[e]	TIPS	–	1.5	DCM	2	28:6

[a] ^{19}F NMR yields using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard. [b] Reaction was performed under irradiation from blue LEDs. [c] With **3a** (1.0 equiv.). [d] With **3a** (2.0 equiv.) [e] inverted stoichiometry: with **3a** (1.0 equiv.) and BTMP (1.5 equiv.). TMS = trimethylsilyl, bpy = 2,2′-bipyridine, TEMPO = 2,2,6,6-tetramethylpiperidin-1-yl)oxyl, TIPS = triisopropylsilyl. DCM = dichloromethane.

of **2a** to 50% (Table 1, Entry 7). This surprising result implies that independent activation of BTMP is not required for a successful reaction and that substrate **3a** may itself directly react with the peroxide. Increasing the amount of the K_2CO_3 additive did not influence the yield of **2a**, however reducing down to 0.5 equiv. resulted in a decreased yield of 31% (Table 1, Entries 8&9). K_2CO_3 likely serves to mop up any HF side-product generated under the reaction conditions. During the solvent screening, a solvent-dependent product distribution was observed. When acetone was used as the solvent, **2a** was selectively formed in a ^{19}F NMR yield of 55% (Table 1, Entry 10). However, when conducted in diethyl ether, nitromethane or dichloromethane (DCM), silyl enol ethers **4a** were generated as the major products of the reaction, with DCM leading to the highest yield (Table 1, Entries 11–13). Finally, both the DCM and acetone methods were tested using inverted stoichiometry using **3a** as the limiting reagent and maintaining a BTMP:K_2CO_3 ratio of 1:1 (Table 1, Entries 14 & 15). In acetone, the reaction proceeded with only a slight decrease in ^{19}F NMR yield of **2a** relative to the standard conditions, however, the reaction in DCM affording **4a** was considerably less efficient. In both reactions, increased formation of aromatic OCF_3 side-products was observed. For these reasons, the conditions from Table 1, entries 10 and 13 were used for further studies. Overall, the optimisation study led to the development of two practical sets of conditions for radical trifluoromethoxylation that employ only a slight excess of the alkenyl substrate, do not require any catalyst and proceed at room temperature with only K_2CO_3 as an additive.

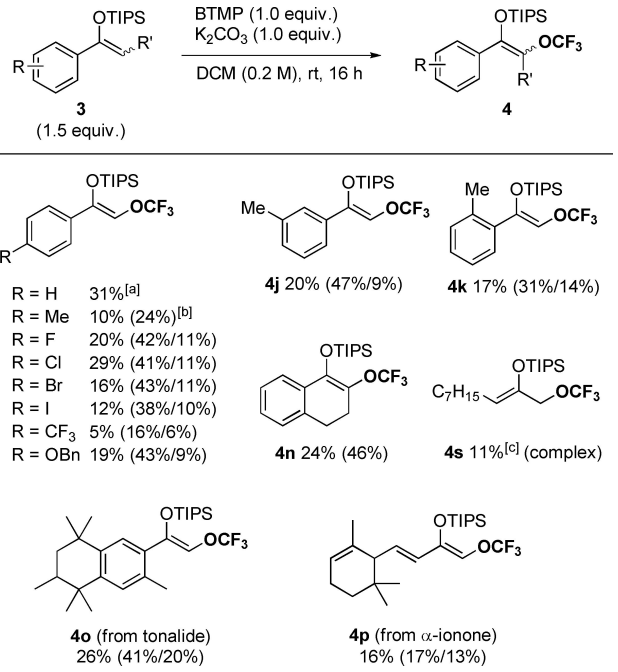
We next set out to evaluate the scope and limitations of the method affording α-(trifluoromethoxy)ketone products **2** (Scheme 1). To our delight, common substituents on the aromatic ring of acetophenone-derived silyl enol ethers such as alkyl moieties and halogens were well tolerated and afforded the corresponding products in moderate to good isolated yields up to 75%.[18] The halogenated products **2d–f** are particularly noteworthy as they offer the potential for further elaboration, for example through cross-coupling methodologies. The reactions with silyl enol ethers bearing strongly electron-withdrawing groups on the aromatic ring, on the other hand, showed reduced reactivity with the α-(trifluoromethoxy)ketones **2g** and **2h** being both obtained in 17% isolated yield. This observation is consistent with our findings in aromatic trifluoromethoxylation reactions with BTMP.[10] Interestingly, NMR analysis of the crude reaction mixture with the methoxy-substituted silyl enol ether **3i** revealed the formation of not only the desired



Scheme 1. Scope of the reaction of silyl enol ethers **3** with BTMP affording α-(trifluoromethoxy)ketones **2**. Isolated yields. [a] Reaction with DCM as the solvent. After reaction time, trifluoroacetic acid (TFA, 3.0 equiv.) was added and reaction mixture was stirred for an additional 4 h at rt. [b] Single diastereomer, configuration not determined.

ketone **2i** but also the corresponding enol **5i**. Two spots were observed by thin layer chromatography (TLC), however, upon purification by column chromatography, both isolated fractions exhibited NMR spectra in $CDCl_3$ consistent with **5i**, implying tautomerisation to the seemingly more stable enol form had occurred (total isolated yield = 28 %).[19,20] Products **2j** and **2k**, which feature substituents at the *ortho*- and *meta*- positions, as well as ketones **2l**–**n** derived from internal silyl enol ethers could also be obtained in good yields up to 70 %. The *ortho*-methyl-substituted product **2k** was a solid and allowed for confirmation of the structure by single crystal X-ray diffraction (Figure 2).[21] Overall, the yields are largely comparable with those obtained by Magnier, Dagousset and Dell'Amico employing the Togni trifluoromethoxylating reagent and enol carbonate substrates under photoredox catalysis conditions.[15] Moreover, in some ways, the two systems are complementary with the photocatalytic method working somewhat better for relatively electron-deficient substrates and the catalyst-free method with BTMP affording higher yields with more electron-rich derivatives. Finally, to evaluate the applicability of the method for late-stage functionalisation, a selection of silyl enol ethers derived from ketones used in the perfumery industry were tested. Product **2o** derived from the aromatic ketone tonalide was delivered in 43 % isolated yield while silyl enol ethers generated from α-ionone and exaltone also reacted smoothly indicating that alkenyl and aliphatic α-(trifluoromethoxy)ketone products are also readily accessible using BTMP (yield of **2p** = 40 %, yield of **2q** = 24 %).

After evaluating the method affording α-(trifluoromethoxy)ketones **2**, we next turned our attention to the synthesis of OCF_3-substituted silyl enol ethers **4**. Compounds that feature an OCF_3 group at an electron-rich alkene functionality have not been obtained previously as products of radical trifluoromethoxylation and we were therefore eager to investigate the efficiency of this process with a range of different substrates.[22] In each case, the crude yield and Z/E ratio was measured by ^{19}F NMR, and the major isomer was then isolated by preparative HPLC (Scheme 2). As for the reaction in acetone affording α-(trifluoromethoxy)ketones, the process in DCM showed good tolerance of common substituents and substitution patterns on the aryl ring of acetophenone-derived silyl enol ethers **3**. Substrates containing halogens and alkyl groups at the *para*-position reacted



Scheme 2. Scope of the reaction of silyl enol ethers **3** with BTMP affording trifluoromethoxylated silyl enol ethers **4**. Isolated yields of the major isomer. ^{19}F NMR yields of the (*Z*) and (*E*) products using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard are given in parentheses. [a] Reaction was performed on a 2.4 mmol scale. ^{19}F NMR yield not measured. [b] Minor diastereomer could not be unambiguously observed in the crude ^{19}F NMR. [c] Stereochemistry not determined.

smoothly while both electron-withdrawing groups such as CF_3 and electron-donating substituents such as OBn were tolerated. The isolated major isomer of the benzyloxy-substituted product **4r** was a solid which allowed for the configuration to be confirmed as *Z* by X-ray crystallography (Figure 3).[21] NOE analysis of the major isomer obtained from silyl enol ether **3a** was also consistent with a *Z*-configuration and, by analogy, we tentatively assume that the reaction is moderately selective for this isomer for all the substrates tested with diastereomeric ratios averaging around 4:1.[23] Methyl substitution at the *ortho*- and *meta*-positions of the aryl ring was also well tolerated with the

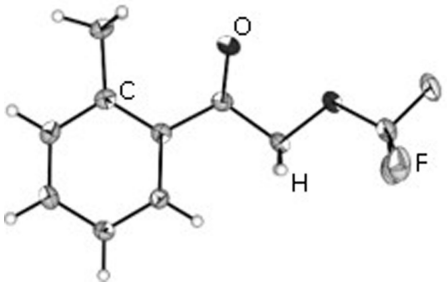


Figure 2. Molecular structure, determined by X-ray diffraction, of ketone **2k**. Thermal ellipsoids set at 50% probability.

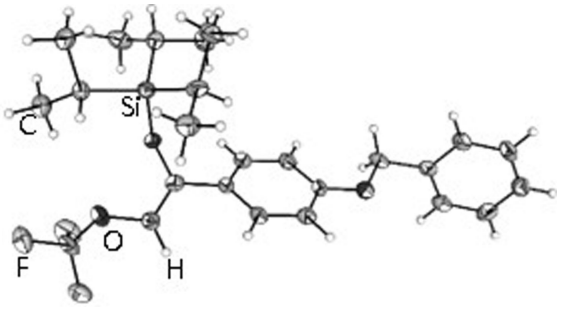


Figure 3. Molecular structure, determined by X-ray diffraction, of trifluoromethoxylated silyl enol ether (*Z*)-**4r**. Thermal ellipsoids set at 50% probability.

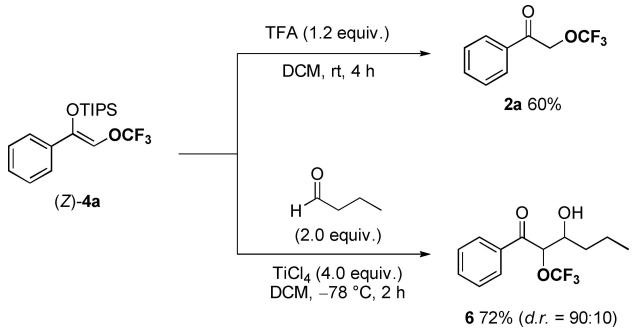
ortho-substituted product reacting with somewhat lower diastereoselectivity (^{19}F NMR yields of (*Z*)-**4k** and (*E*)-**4k** = 31 % and 14 %, respectively). While the silyl enol ether derived from α-tetralone reacted smoothly (^{19}F NMR yield of **4n** = 46 %), the reaction was found to be less successful with other internal alkene substrates with methyl or benzyl substitution at the 2-position suppressing product formation. Subjecting the aliphatic silyl enol ether substrate **3s** led to a complex reaction mixture with the major product isolated by preparative HPLC being the internal alkene product **4s** (isolated yield = 11 %). Finally, (trifluoromethoxy)silyl enol ethers of the compounds derived from tonalide (**4o**) and α-ionone (**4p**) could be obtained in moderate yields.

To probe the potential of trifluoromethoxylated silyl enol ethers **4** as useful OCF_3-containing building blocks, the benchmark compound (*Z*)-**4a** was synthesised on a 2.4 mmol scale and subjected to further transformations. Treatment with trifluoroacetic acid (TFA, 1.2 equiv.) in DCM resulted in smooth desilylation affording the corresponding α-(trifluoromethoxy)ketone **2a** in 60 % yield (Scheme 3).[24] Moreover, following a literature-known protocol,[25] product (*Z*)-**4a** could be successfully converted into the Mukaiyama aldol product **6** in 72 % yield (*d.r.* = 90 : 10) upon reaction with *n*-butanal and titanium chloride. In both reactions, no cleavage or elimination of the OCF_3 group was observed.

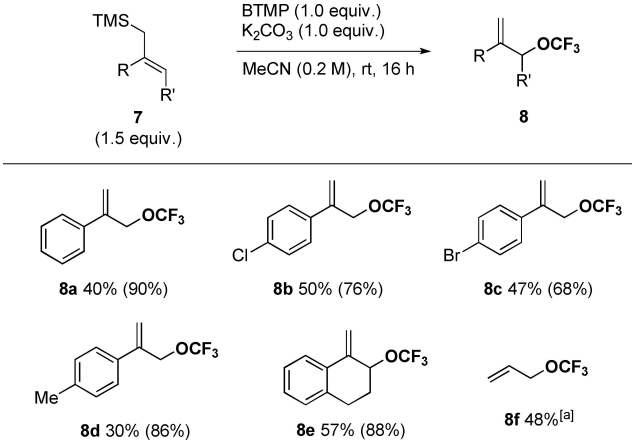
Having established silyl enol ethers as suitable substrates for catalyst-free radical trifluoromethoxylation with BTMP, we next sought to explore alternative potential classes of alkene reaction partner. By virtue of the silicon β-effect, allyl silanes are competent radical acceptors with subsequent desilylation affording functionalised allyl products. To the best of our knowledge, general methods for radical trifluoromethoxylation of alkenyl substrates other than enol ether derivatives have not been reported previously while the potential allyl(trifluoromethyl)ether products could serve as useful OCF_3-containing motifs that feature an alkene handle for further derivatisation. In an initial test reaction, trimethyl(2-phenylallyl)silane **7a** was reacted under the TEMPO-mediated reaction conditions developed in our previous study: TEMPO (25 mol %), K_2CO_3 (1.0 equiv.), MeCN, rt, 1 h. To our delight, smooth conversion to the desired product **8a** was observed with ^{19}F NMR analysis indicating a yield of 53 %. Moreover, switching to catalyst-free conditions without TEMPO led to a significant improvement in efficiency with **8a** being delivered in 90 % ^{19}F NMR yield.

A short scope and limitations study was then conducted with a selection of allyl silane structures **7** (Scheme 4). The *para*-substituted aryl derivatives **7b–d** all reacted efficiently in ^{19}F NMR yields greater than 68 % although product volatility had a detrimental effect on the isolated yields. The reaction with an internal allyl silane was also successful with allyl(trifluoromethyl)ether **8e** being generated in 88 % ^{19}F NMR yield (57 % isolated yield). With this unsymmetrical allyl substrate, selective installation of the OCF_3 group within the carbocyclic ring was observed, indicating that trifluoromethoxylation occurs at the alkenyl β-position and not at the carbon directly bonded to silicon. Finally, to fully probe the extent of suitable allyl silane substrates, the simplest unsubstituted derivative, allyl(trimethyl)silane **7f**, was tested. Radical trifluoromethoxylation proceeded very slowly in this case, however after 14 days at rt, allyl(trifluoromethyl)ether (**8f**) was observed in the crude mixture with distillation providing the gaseous product as an inseparable mixture with the TMS–F side-product (calculated isolated yield = 48 %).

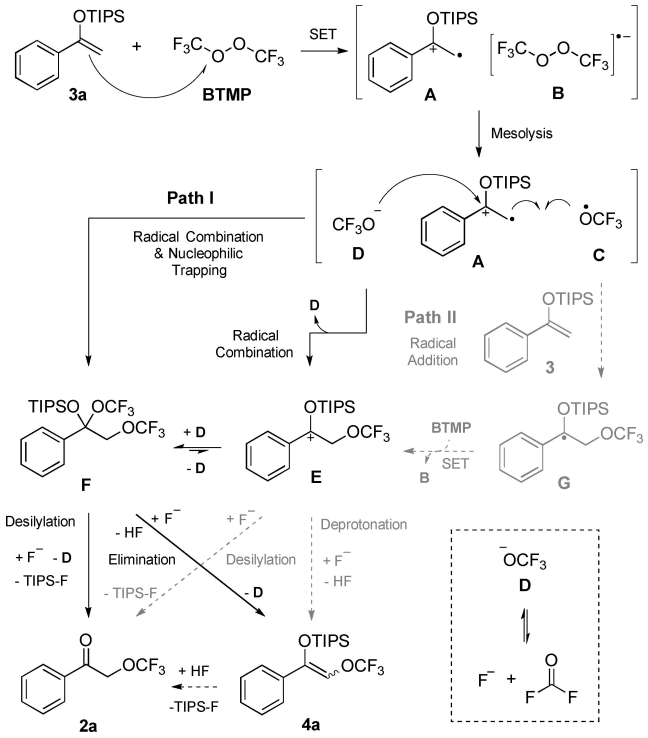
The success of the trifluoromethoxylation reactions under such simple conditions without a catalyst or other activators raises questions regarding the operating mechanism. To provide insight into the potential pathways, preliminary DFT calculations were conducted. A comparison of the computed ionisation energy of silyl enol ether **3a** and electron affinity of BTMP in acetone implies that single electron transfer affording the radical cation **A** and radical anion **B** is thermodynamically feasible ($\Delta G = -7.7$ kJ/mol at 298.15 K, Scheme 5).[26] Subsequent mesolysis of **B** would then provide an $^{\bullet}OCF_3$ radical **C** and an $^{-}OCF_3$ anion **D**. In principle, radical **C** could directly combine with the silyl



Scheme 3. Desilylation and Mukaiyama Aldol Reaction of trifluoromethoxylated silyl enol ether (*Z*)-**4a**. Isolated yields.



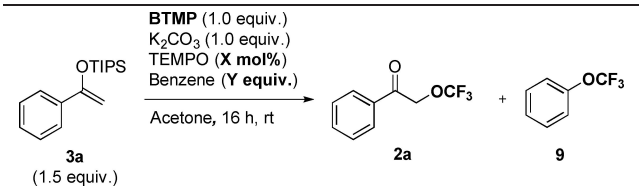
Scheme 4. Scope of the reaction of allyl silanes **7** with BTMP affording allyl(trifluoromethyl)ethers **8**. Isolated yields. ^{19}F NMR yields using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard are given in parentheses. [a] Reaction was performed on a 20 mmol scale over 14 days. Product **8f** was isolated as a 1 : 1 mixture with TMS–F. ^{19}F NMR yield not measured.



Scheme 5. Postulated mechanism for the catalyst-free trifluoromethoxylation of silyl enol ethers **3** with BTMP. SET = single electron transfer.

enol ether-derived radical cation **B** affording cation **E** (Path I, Scheme 5) or the 1,2-di(trifluoromethoxy) compound **F** upon additional trapping with $^{-}OCF_3$ (**D**). In an alternative pathway, $^{\bullet}OCF_3$ radical (**C**) could instead add to another molecule of the starting material affording radical species **G**, which could then be oxidised to cation **E** by BTMP as part of a radical chain mechanism (Path II, Scheme 5). To probe the involvement of such a radical chain mechanism, the standard reaction with **3a** in acetone was performed again in the presence of benzene (10 equiv., Table 2). As shown in our previous work,[10] benzene is a competent radical acceptor for free $^{\bullet}OCF_3$ radicals **C**, and it could be expected to provide competition to silyl enol ether **3a** if a radical chain mechanism of the type described above were operating. Analysis of the crude reaction mixture, however, did not indicate the formation of (trifluoromethoxy)benzene (**9**) as a side-product, suggesting that free $^{\bullet}OCF_3$ radicals that then engage with a second molecule of **3a** are not involved (Table 2, Entry 3). Interestingly, conducting the same experiment with additional TEMPO (25 mol%) as a catalyst did result in formation of **9**, implying free radicals **C** are involved in this case (Table 2, Entry 4).[27] In light of these results, we tentatively propose the mechanistic scenario shown as Path I in Scheme 5 where initial single electron reduction of BTMP by the electron-rich alkene substrate is followed by mesolysis and fast radical combination within the solvent cage. Finally, desilylative elimination from 1,2-di(trifluoromethoxy) compound **F** or cation **E** assisted by fluoride generated upon β-elimination from $^{-}OCF_3$ (**D**) would afford α-(trifluoromethoxy)ketones **2**, while α-deprotonation would lead to trifluoromethoxylated silyl enol ethers **4**.[28] Further studies would be required, however, to fully elucidate the reaction mechanism.

Table 2: Mechanistic experiments with benzene as a competing radical acceptor.



Entry	TEMPO (mol%)	Benzene (equiv.)	Yield **2a**[a]	Yield **9**[a]
1	–	–	50	–
2	25	–	44	–
3	–	10	44	–
4	25	10	40	9

[a] ^{19}F NMR yields using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard.

Conclusion

In conclusion, novel trifluoromethoxylation methodologies of alkene substrates have been developed using bis(trifluoromethyl)peroxide (BTMP). In contrast to previously developed radical trifluoromethoxylation approaches, these methods proceed under catalyst-free conditions without photoredox or any other activation, operate at room temperature with only a slight excess of the organic substrate and employ inexpensive potassium carbonate as the sole additive. With silyl enol ether substrates, judicious selection of the reaction solvent provides access either to α-(trifluoromethoxy)ketones or unprecedented alkenyl-OCF_3-containing silyl enol ether products, which can serve as useful trifluoromethoxylated building blocks. Moreover, allyl silanes have been employed as novel substrates for trifluoromethoxylation, delivering allyl(trifluoromethyl)ethers. Given the increasing importance of the OCF_3 group and the attractive features of BTMP as a practical and comparatively atom-economical reagent, we anticipate these methods will find applications in many areas of chemistry.

Supporting Information

The authors have cited additional references within the Supporting Information.[30–46]

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Conflict of Interest

The results underpinning this work have been protected in a patent application (EP23186390.3, submitted on 19.07.2023). Related use of BTMP for preparing (trifluoromethoxy)-arenes was previously protected in another patent application (EP2021-158495, submitted on 22.02.2021; WO2022-EP54181, submitted on Feb 21, 2022.).

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Allyl Silanes · Fluorine · Ketones · Silyl Enol Ethers · Trifluoromethoxylation

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[18] In some cases, the isolated yields were lowered due to the high volatility of the products (see also ref. [15]).

[19] An NMR spectrum in toluene-d_8 indicated an enol/ketone ratio of 95:5, suggesting the equilibrium position is influenced by the solvent.

[20] The increased stability of the enol form could potentially result from a favourable hyperconjugative interaction between the extended styrenyl π-system and the O–CF_3 σ* antibonding orbital in this electron rich compound. Similar hyperconjugative interactions are thought to lay behind the unconventional conformational preferences observed with (trifluoromethoxy)arenes (see ref. [1]).

[21] Deposition numbers 2306068 (for **2k**), 2306494 (for (*Z*)-**4r**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

[22] To the best of our knowledge, only one example of an OCF_3-substituted silyl enol ether has been reported previously in the literature. This (*tert*-butyl)dimethylsilyl (TBS)-containing species was synthesised from the corresponding α-(trifluoromethoxy)ketone. See: R. Zriba, E. Magnier, J.-C. Blazejewski, *Synlett* **2009**, *2009*, 1131.

[23] DFT calculations on (*Z*)- and (*E*)-**4a** revealed there is little difference in the thermodynamic stability of the isomers with (*Z*)-**4a** being only 0.1 kJ/mol more stable than (*E*)-**4a** in DCM at 298.15 K, which is within the systematic error of the method. This implies the moderate diastereoselectivity observed results from kinetic factors during the deprotonation step.

[24] Surprisingly, treatment of (*Z*)-**4a** with tetra-*n*-butylammonium fluoride (TBAF, 1.2 equiv.) in DCM at rt led to decomposition although desilylation reactivity was somewhat recovered employing potassium fluoride (^{19}F NMR yield of **2a** = 16 % after 16 h at 70 °C).

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[26] Cyclic voltammetry measurements of BTMP and silyl enol ether **3a** revealed reduction and oxidation peaks, respectively. The irreversibility of these redox events and the instability of the decomposition products, however, make it difficult to give a definitive statement about the reduction potentials, especially for BTMP.

[27] Alternative potential reaction pathways include direct nucleophilic attack of the silyl enol ether onto BTMP generating cation **E** directly or a formal [2+2]-cycloaddition generating the 1,2-di(trifluoromethoxy)alkene intermediate **F** (Scheme).

[28] In the presence of TEMPO, direct single electron transfer between the catalyst and BTMP could occur providing an $^{\bullet}OCF_3$ radical without concomitant formation of a reactive radical cation intermediate. In this case, radical addition to the silyl enol ether or, potentially, benzene starting materials as part of a radical chain seemingly occurs.

[29] The origin of the solvent-dependent switch in product distribution is not abundantly clear; however, the different solubility of the KF generated as a reaction side-product could play a role. The generation of a strong Si–F bond is likely a driving force behind the desilylation process and it could be expected that a higher effective fluoride concentration would favor the formation of ketones **2**. A test reaction conducted with $CaCO_3$ in place of K_2CO_3 was accordingly performed to test this hypothesis. In this reaction, the CaF_2 formed as side-product is essentially insoluble and, even in more polar solvents, the degree of desilylation would be expected to be lower. Indeed, under the standard conditions with **3a** in acetone, much less of the ketone **2a** (^{19}F NMR yield = 15 %) was observed with OCF_3-conatining alkene **4a** being obtained as the major product (10:32 %). For a more complete understanding of the likely much more complex influence of the solvent on the reaction outcomes, however, further detailed mechanistic studies would be required.

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