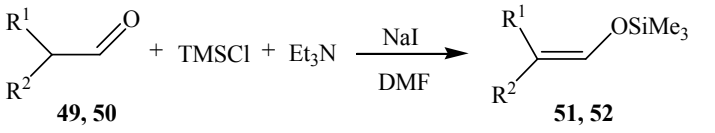
3 Synthesis of starting material

In numerous applications it was established that methyl 2-siloxycyclopropanecarboxylates may serve as equivalents of γ-oxocarboxylates, which are smoothly liberated under certain conditions of ring cleavage.[66, 67] This concept could be exploited in many one-pot reactions which are based on ring-opening and subsequent reactions without isolation of intermediate dicarbonyl compounds. Of particular synthetic value are cyclopropane derivatives which contain a hidden enone functionality[68-71] or aldehyde group[72-74], because the corresponding dicarbonyl compounds are often hardly accessible and occasionally very sensitive.

3.1 Syntheses of silyl enol ethers

Silyl enol ethers **51** and **52** for the syntheses of siloxycyclopropanes used in this work have been prepared from acetaldehyde **49** or *iso*-butyraldehyde **50**, which have been reacted with trimethylchlorosilane in the presence of triethylamine and sodium iodide in dimethylformamide (Scheme 22).[75] The relatively low yield of silyl enol ether **51** perhaps reflects its sensitivity (especially upon acidic workup) and unstable nature.



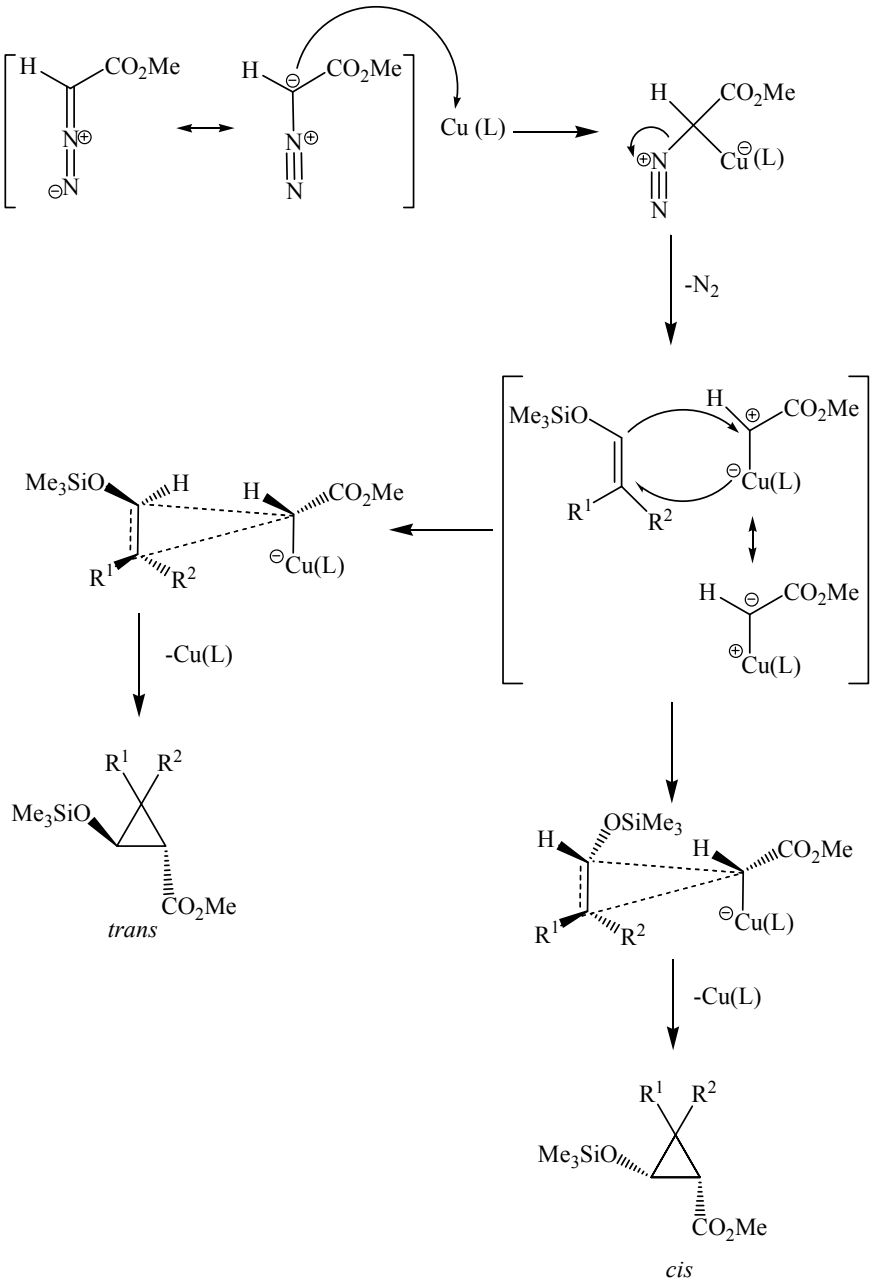
49, 50 **51, 52**

51: $R^1 = R^2 = H$ 35 %
52: $R^1 = R^2 = Me$ 89 %

Scheme 22. Synthesis of silyl enol ethers

3.2 Cyclopropanation reactions

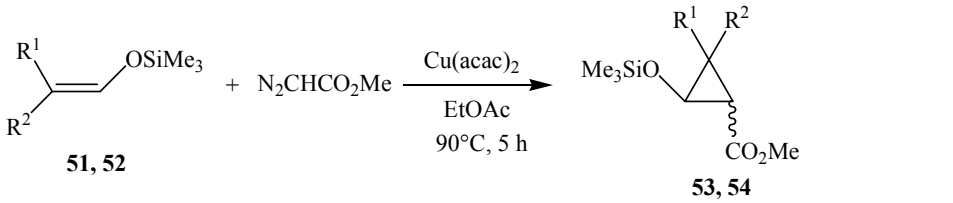
Direct [2+1]-cycloaddition reaction of electron rich olefins and acceptor-substituted carbenes proved to be one of the most efficient synthetic routes for generating donor-acceptor substituted cyclopropanes.[66] According to this, siloxycyclopropanes can be synthesized by reaction of silyl enol ethers with methyl diazoacetate which decomposes in the presence of a copper catalyst to furnish a carbenoid able to undergo smooth addition to olefins (Scheme 23).



Scheme 23. Mechanism of cyclopropanation reaction

This reaction is only very moderately stereoselective concerning the methoxycarbonyl group and *cis*/*trans* mixtures are obtained according to the mechanism depicted above.

Two known siloxycyclopropanes, **53** and **54**, employed in this work have been synthesized in very good yields starting from silyl enol ethers **51** and **52** (Scheme 24).[76]

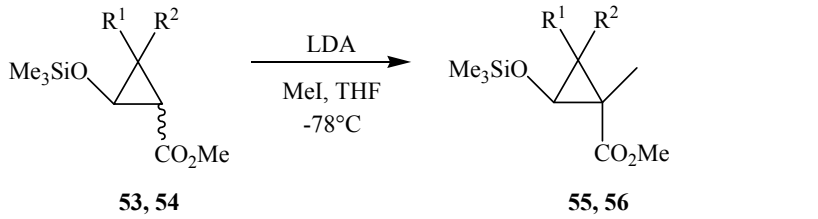


53: $R^1 = R^2 = H$ 77 % (*trans:cis* 70:30)
54: $R^1 = R^2 = Me$ 80 % (*trans:cis* 75:25)

Scheme 24. Synthesis of siloxycyclopropanes **53** and **54** by cyclopropanation with methyl diazoacetate in the presence of $Cu(acac)_2$

3.3 Alkylations of methyl 2-siloxycyclopropanecarboxylates

Alkylations of siloxycyclopropanes **53** and **54** in the presence of *in situ* generated LDA with methyl iodide furnished known 1-methyl siloxycyclopropanes **55** and **56** (Scheme 25).[77]



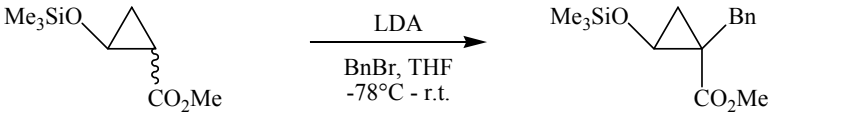
55: $R^1 = R^2 = H$ 35 % (*trans:cis* 90:10)
56: $R^1 = R^2 = Me$ 81 % (*trans:cis* 90:10)

Scheme 25. Alkylations of siloxycyclopropanes **53** and **54**

Regardless of the *cis*/*trans* ratio of the starting materials in THF as solvent the deprotonation/alkylation reaction afforded *trans*-configured products with high

preference. Alkylation of 3-unsubstituted siloxycyclopropane **53** proceeded with significantly lower yield than the alkylation reaction of 3,3-dimethyl substituted siloxycyclopropane **54**. Missing of steric hindrance in this case very likely causes considerable selfcondensation during enolate generation.

Similarly to the reaction depicted above, siloxycyclopropanecarboxylate **53** was reacted with benzyl bromide in the presence of LDA and yielded compound **57** in 65% yield (Scheme 26).[66]



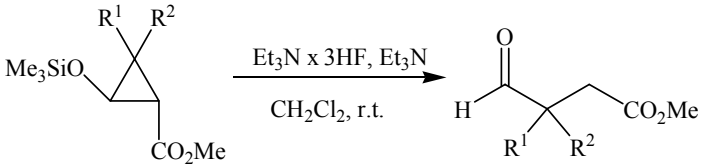
53 **57**

65% (*trans:cis* 95:5)

Scheme 26. Synthesis of methyl 1-benzyl-2-siloxycyclopropanecarboxylate **57**

3.4 Siloxycyclopropanes as masked carbonyl compounds

Siloxycyclopropanes can be cleaved under very mild conditions to give γ-oxocarboxylates. The ring cleavage can be achieved by acids or strong bases and most selectively by fluoride reagents. Easily accessible $NEt_3 \cdot xHF$ (x = 1-3) is the most effective reagent for this retro aldol type reaction. Siloxycyclopropanes **53** and **54** have been reacted with $NEt_3 \cdot 3HF$ in dichloromethane, in the presence of NEt_3, to give β-formylesters **58** and **59** in very good yields (Scheme 27).[78, 79]

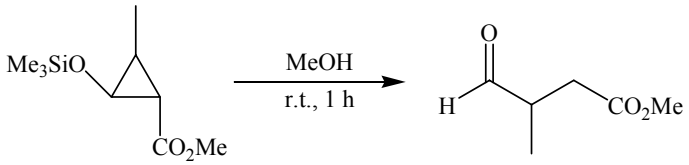


53, 54 **58, 59**

58: $R^1 = R^2 = H$ 87 %
59: $R^1 = R^2 = Me$ 88 %

Scheme 27. Ring-opening of siloxycyclopropanes in the presence of fluoride reagent

β-Formylesters obtained from siloxycyclopropanes **53** and **54** are achiral compounds. In some experiments siloxycyclopropane **60** was used as a starting material, which generated *in situ* chiral aldehyde **61** as a racemic mixture (Scheme 28).

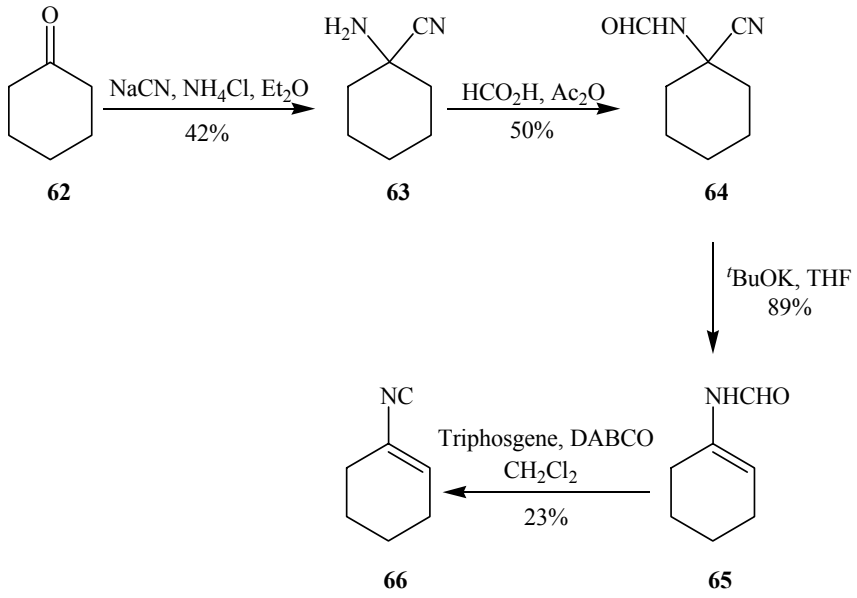


60 **61**

Scheme 28. Generation of aldehyde **61**

3.5 Synthesis of cyclohexenylisocyanide

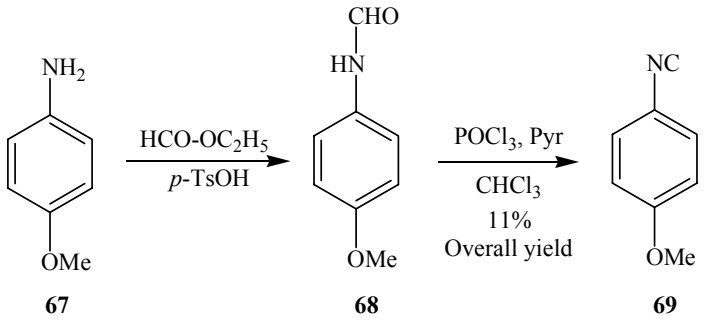
Cyclohexenylisocyanide (**66**) was synthesized according to the procedure described by Armstrong et al.[38] in overall yield of 4%. 1-Amino-1-cyanocyclohexane (**63**) was synthesized from cyclohexanone (**62**), and then converted into 1-cyano-1-formamidocyclohexane (**64**) in the presence of the mixed anhydride. Further reaction of **64** with anhydrous potassium *tert*-butoxide afforded 1-formamidocyclohexene (**65**) that yielded cyclohexenylisocyanide upon dehydration with triphosgene (Scheme 29). This procedure was modified comparing to Ugi's original procedure[80] only in that **64** was purified prior to dehydration and that triphosgene was used as the dehydrating agent in place of phosphorus oxychloride.



Scheme 29. Synthesis of cyclohexenylisocyanide

3.6 Synthesis of *p*-methoxyphenylisocyanide

p-Methoxyphenylisocyanide (**69**) was prepared utilizing the procedure described by Casanova et al.[39] in overall yield of 11% (Scheme 30).

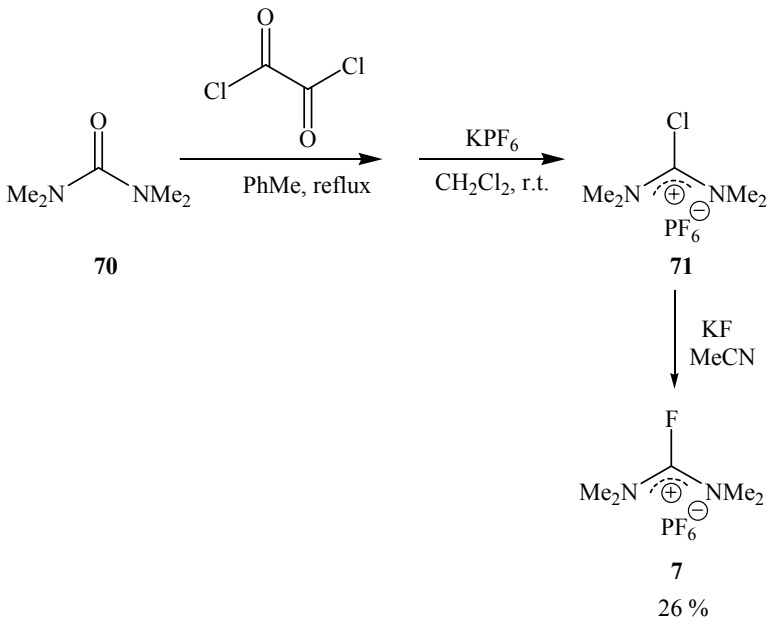


Scheme 30. Synthesis of *p*-methoxyphenylisocyanide **69**

p-Anisidine **67** was reacted with ethyl formate in the presence of traces of *p*-toluenesulfonic acid to afford *p*-methoxyformanilide **68** that gave *p*-methoxyphenylisocyanide (**69**) upon treatment with phosphorooxychloride in pyridine and chloroform.

3.7 Synthesis of tetramethyl fluoroformamidinium hexafluorophosphate (TFFH)

Tetramethyl fluoroformamidinium hexafluorophosphate (**7**) was obtained *via* reaction of tetramethyl chloroformamidinium hexafluorophosphate (**71**) with excess anhydrous potassium fluoride, which is synthesized from tetramethylurea **70**, oxalyl chloride and potassium hexafluorophosphate (Scheme 31).[10]



Scheme 31. Synthesis of TFFH **7** (experiment: E1)

TFFH **7** appeared to be unstable during longer periods of time. It should be stored in the refrigerator and under inert atmosphere.