Chiral Sulfoxides in the Enantioselective Allylation of Aldehydes with Allyltrichlorosilane: a Kinetic Study.

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SUPPORTING INFORMATION

General methods and materials

General remarks

All reactions were performed in oven-dried (140 °C) or flame-dried glassware under dry N_2. Dichloromethane was reagent grade and was dried and distilled immediately from CaH_2 before use. Column chromatographic purification of products was carried out using silica gel 60 (70–230 mesh, Merck). The reagents (Aldrich and Fluka) were used without further purification. The NMR spectra were recorded on Bruker DRX 400, 300, 250 spectrometers (400 MHz, 300 MHz, 250 MHz). Spectra were referenced to residual $CHCl_3$ (7.26 ppm, ^{1}H, 77.23 ppm, ^{13}C). Coupling constants J are reported in Hz. Yields are given for isolated products showing one spot on a TLC plate and no impurities detectable in the NMR spectrum. Elemental analyses were performed with FLASHEA 1112 series-Thermo Scientific for CHNS-O apparatus.

The enantiomeric excesses of alcohol **3** were determined by GC analysis, with Agilent 6850 equipment, using Supelco β-DEX 120; oven: 100° C for 2 min, then 0.5°C/min to 200°C, 10 min at that temperature. The chiral GC methods were calibrated with the corresponding racemic mixtures. The absolute configuration of the products was determined by comparison of their optical rotations (measured in $CHCl_3$ and their GC retention times with the literature data.

The enantiomeric excesses of sulfoxide **4** were determined by HPLC analysis, with Waters 2487, using OD-H column, 0.6 mL/min, in 90/10 hexane/i-PrOH mixture, 254nm. The chiral HPLC method was calibrated with the corresponding racemic mixtures. The absolute configuration of the products was determined by comparison with literature data.

The conductometric analysis was performed using a conductivity meter AMEL mod. 133 equipped with a standard electrode.

General procedure for allylation of aldehyde

In a flame dried two-necked round bottom flask, benzaldehyde **1** (0.40 mmol) was added to a solution of sulfoxide **2** (1, 2 or 3 equivalents), diisopropylethylamine (0.40 mmol) and allyltrichlorosilane (0.48 mmol), in dry CH_2Cl_2 (2.0 mL) at −78°C under argon. Then saturated aqueous $NaHCO_3$ (20 mL) and CH_2Cl_2 (30 mL) were added, the organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (2×40 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated at reduced pressure. The residue was purified by flash chromatography on silica gel with a petroleum ether–Et_2O mixture (from 95:5 to 90:10) to afford pure **3**, followed by AcOEt to recover the pure sulfoxide **4**.

Kinetic analysis

According to the procedure reported in ref.1, kinetic measurements were carried out by monitoring the formation of the product and plotting its concentration as a function of time. The product concentration was calculated by integrating the signals of the corresponding homoallylic alcohol and the internal standard, naphthalene (**N**) of the related gas-chromatogram, applying the relative response factor determined as shown below.

Determination of the relative response factor of 1-phenyl-but-3-en-1-ol (3) and naphthalene (std)

Stock solutions containing 1-phenyl-but-3-en-1-ol (**3**), (purity >99% was determined by ^{1}H-NMR, GC and elemental analysis), and naphthalene as internal standard (**std**) were used to prepare samples for GC analysis in the proportions shown in columns 1 and 3 in 4.0 mL of CH_2Cl_2 These samples were injected into the GC three times. The areas of each component are listed in columns 2 and 4. The resultant mass response factor R was calculated as

$$R = \frac{m_{alcohol} \times A_{std}}{m_{std} \times A_{alcohol}},$$ (S1)

where m_X and A_X are the mass and the chromatographic area of X.

GC conditions:
Chiral GC (Supelco β-DEX 120 column, oven: 100°C for 5 min, then 1°C/min to 138°C, then 5°C/min to 200°C and 10 min at that temperature)

t (**std**) = 22.10 min.
t ((R)-**3**) = 37.75 min.
t ((S)-**3**) = 38.15 min.

$m_{alcohol}$ (mg)	Area alcohol (%)	m_{std} (mg)	Area std	R
2.8	28.72	5.6	71.27	1,34
2.8	29.04	5.6	70.96	1,32
2.8	29.28	5.6	70.77	1,31
9.8	68.17	3.0	31.82	1,42
9.8	67.76	3.0	32.24	1,45
9.8	68.19	3.0	31.81	1,42
3.7	56,971	3.6	43,029	1,36
3.7	57,103	3.6	42,897	1,37
3.7	57,378	3.6	42,622	1,38

The average relative response factor is: $<R> = 1.37 \pm 0.05$.

The concentration of alcohol produced was obtained from Eq. (S1) and considering that the volume adopted was always 5.0 cm^3. Combined standard uncertainties $\tilde{\sigma}_i$ of the product concentrations were determined by considering that the individual source of error were normally distributed with standard deviation 0.05 (R) and $0.1 \cdot 3^{-1/2}$ mg (m_{std})[1]. The standard deviation of the $A_{alcohol}/A_{std}$ ratio was estimated from triplicate GC injections. In all cases, but those with smallest conversion, the triplicate GC analysis turned out to be redundant as the combined standard uncertainty was dominated by the relative error on the factor R.

General Procedure for the Kinetic Runs

In a flame dried two-necked round bottom flask, benzaldehyde **1** (X mmol) was added to a solution of sulfoxide **2** (Y mmol), naphthalene (10.3 mg, 0.0804 mmol), diisopropylethylamine (0.40 mmol) and allyltrichlorosilane (Z mmol), in dry CH_2Cl_2 (5.0 mL) at −78°C under argon. Then aliquots (50 μL) were taken after the time reported in the tables (see experiments 1-14). Each sample was quickly quenched with saturated aqueous $NaHCO_3$ (0.15 mL) and the resulting mixture was diluted with 1 mL of $CHCl_3$. Then, it was filtered through a short pad of silica gel on pipette Pasteur, and the plug was washed with $CHCl_3$ to adjust the total sample volume to 4 mL. The samples were injected into the GC three times.

Kinetic runs for determination of order in sulfoxide

Following the general procedure, several experiments were set up changing the amount of sulfoxide (0.5, 1.0, 2.0 and 3.0 eq), while concentrations of other reagents were kept constant. In the tables are reported the average concentrations with the related standard deviation.

```
EXPERIMENT  1. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080       0.080        0.040
t(min)  Conc(M)    sigma_Conc(M)
5        0.00136   0.00009
10       0.00168   0.00011
15       0.00227   0.00011
20       0.00258   0.00011
25       0.00316   0.00013
30       0.00325   0.00014
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EXPERIMENT  2. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080       0.080        0.080
t(min)  Conc(M)    sigma_Conc(M)
2        0.00170   0.00007
4        0.00265   0.00011
6        0.00398   0.00016
10       0.00558   0.00022
15       0.00662   0.00026
20       0.00770   0.00030
30       0.00866   0.00032
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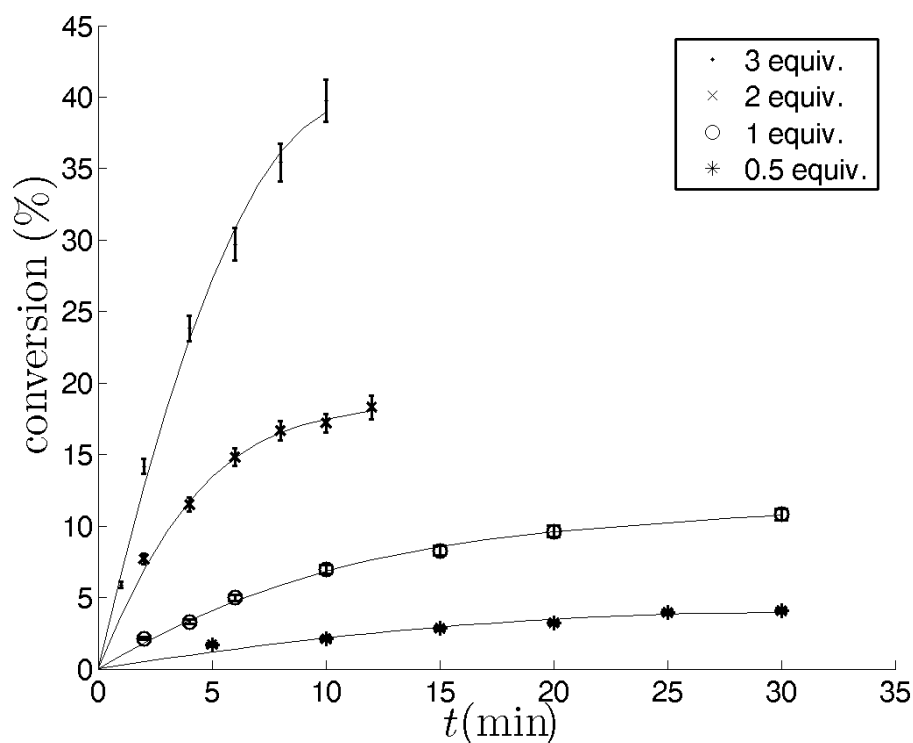
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EXPERIMENT  3. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080       0.080        0.160
t(min)  Conc(M)    sigma_Conc(M)
2        0.00616    0.00030
4        0.00920    0.00038
6        0.01185    0.00050
8        0.01334    0.00055
10       0.01377    0.00051
12       0.01465    0.00066
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EXPERIMENT  4. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080       0.080        0.240
t(min)  Conc(M)    sigma_Conc(M)
1        0.00471   0.00017
2        0.01134   0.00042
4        0.01907   0.00071
6        0.02376   0.00089
8        0.02834   0.00104
10       0.03180   0.00117
```

EXPERIMENT 5. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080   0.480   0.080
t(min)   Conc(M)   sigma_Conc(M)
1   0.00148   0.00008
2   0.00278   0.00012
4   0.00412   0.00016
6   0.00587   0.00022
8   0.00692   0.00026

EXPERIMENT 6. Molar Conc.of Aldehyde, Silane, Sulfoxide:
0.080   0.480   0.160
t(min)   Conc(M)   sigma_Conc(M)
1   0.00186   0.00009
2   0.00502   0.00019
4   0.00708   0.00027
6   0.00939   0.00035
8   0.01099   0.00041
10   0.01262   0.00047

Kinetic runs for determination of order in aldehyde

Following the general procedure, several experiments were set up changing the amount of benzaldehyde (0.5, 1.0, 2.0 and 9.0 eq), while concentrations of other reagents were kept constant. Kinetics at 9 eq of benzaldehyde were performed in the presence of 1 and 2 eq of sulfoxide (exp. 7 and 8 respectively). In the tables are reported the average concentrations with the related standard deviation.

EXPERIMENT 7. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.040   0.080   0.080
t(min)   Conc(M)   sigma_Conc(M)

2	0.00106	0.00005
4	0.00152	0.00006
6	0.00231	0.00010
8	0.00286	0.00011
10	0.00332	0.00014
12	0.00406	0.00015

EXPERIMENT 8. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.160   0.080   0.080

t(min)	Conc(M)	sigma_Conc(M)
2	0.00347	0.00014
4	0.00499	0.00020
6	0.00576	0.00022
8	0.00697	0.00031
10	0.00795	0.00029
12	0.00831	0.00032

EXPERIMENT 9. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.720   0.080   0.080

t(min)	Conc(M)	sigma_Conc(M)
2	0.0057	0.0012
4	0.0079	0.0003
6	0.0097	0.0004
8	0.0108	0.0004
10	0.0112	0.0004
12	0.0121	0.0005

EXPERIMENT 10. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.720   0.080   0.160

t(min)	Conc(M)	sigma_Conc(M)
1	0.0087	0.0003
2	0.0167	0.0007
4	0.0205	0.0008
6	0.0214	0.0008
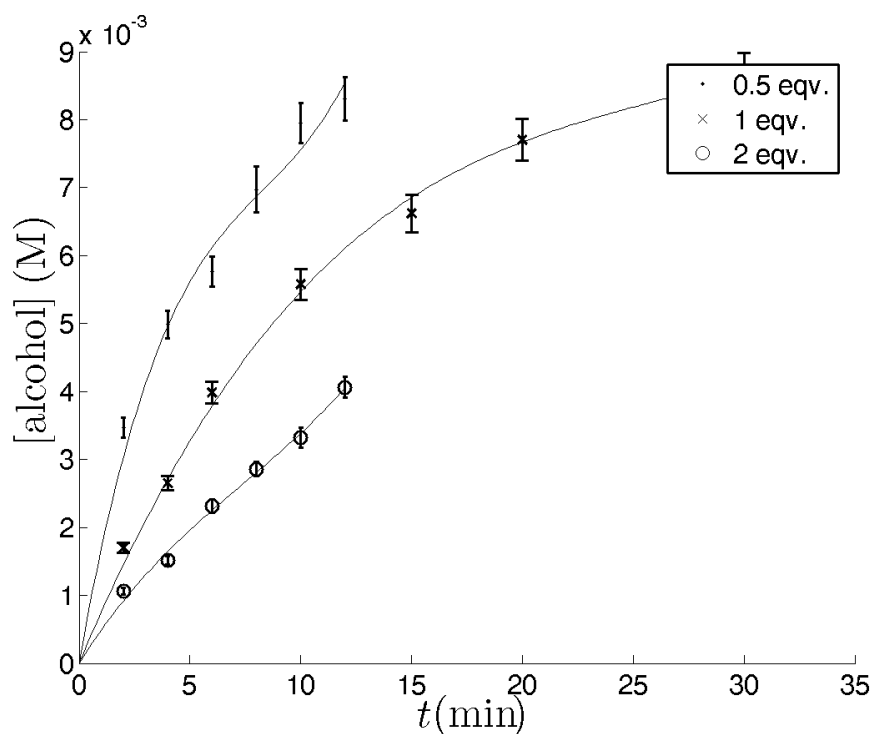
Kinetic runs for determination of order in allyltrichlorosilane

Following the general procedure, several experiments were set up changing the amount of silane (0.5, 1.0, 2.0, 3.0, 4.0, 5.0 and 6.0 eq), while concentrations of other reagents were kept constant. In the tables are reported the average concentrations with the related standard deviation.

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EXPERIMENT 11. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080       0.040       0.080
t(min)  Conc(M)    sigma_Conc(M)
4         0.00117    0.00006
6         0.00150    0.00008
8         0.00192    0.00008
12        0.00243    0.00013


EXPERIMENT  12. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080       0.160       0.080
t(min)  Conc(M)    sigma_Conc(M)
2       0.00217    0.00009
4       0.00356    0.00017
6       0.00532    0.00022
8       0.00652    0.00032
10      0.00708    0.00026
12      0.00727    0.00028


EXPERIMENT  13. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080       0.240       0.080
t(min)  Conc(M)    sigma_Conc(M)
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7

2	0.00313	0.00013
4	0.00554	0.00022
6	0.00703	0.00027
11	0.00984	0.00038
15	0.01150	0.00049
20	0.01199	0.00045

EXPERIMENT 14. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080   0.320   0.080

t(min)	Conc(M)	sigma_Conc(M)
2	0.00276	0.00011
4	0.00477	0.00020
6	0.00543	0.00021
10	0.00753	0.00029
15	0.00886	0.00033
20	0.00896	0.00033

EXPERIMENT 15. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080   0.400   0.080

t(min)	Conc(M)	sigma_Conc(M)
2	0.00308	0.00013
4	0.00469	0.00019
6	0.00640	0.00024
10	0.00723	0.00030
15	0.00893	0.00034
20	0.00908	0.00034

EXPERIMENT 16. Molar Conc. of Aldehyde, Silane, Sulfoxide:
0.080   0.480   0.080

t(min)	Conc(M)	sigma_Conc(M)
1	0.00148	0.00008
2	0.00278	0.00012
4	0.00412	0.00016
6	0.00587	0.00022
8	0.00692	0.00026
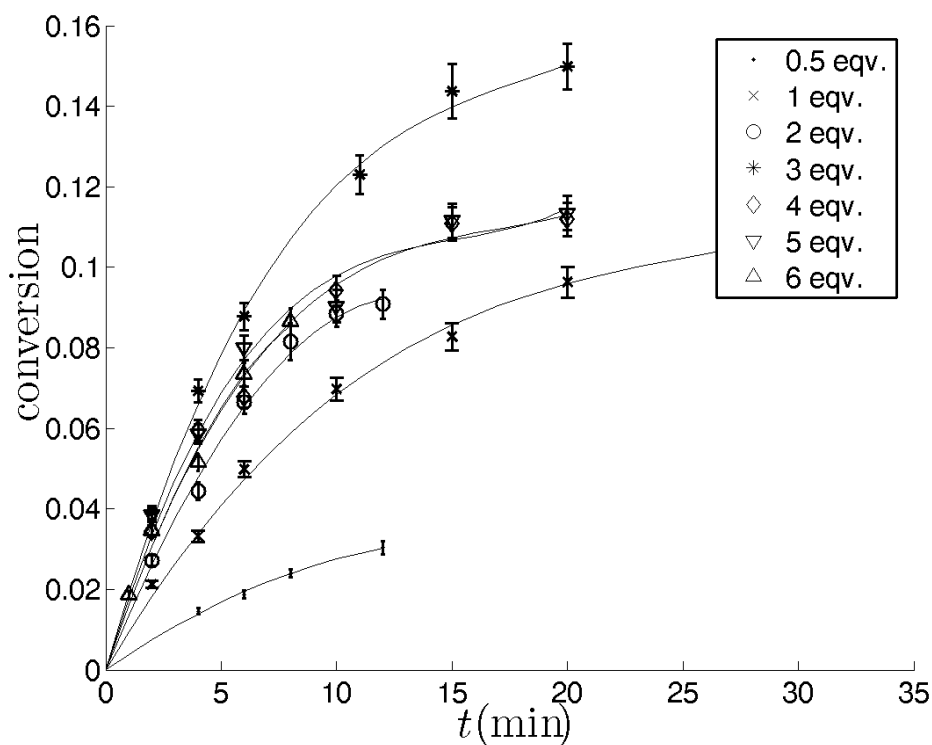
Conversions are given in molar ratio.

Determination of initial rates

Considering the practical set up of the timing and quenching a maximum error Δt on time of 20 seconds was considered. Therefore, in order to determine the initial rate v_0 for each kinetic run I, we performed the iteratively reweighted total least-squares method, minimizing the function

$$\chi^2 = \sum_{i \in I} \frac{\left([\mathbf{3}]_i - [\mathbf{3}]_{i,calc}\right)^2}{\tilde{\sigma}_i^2},$$

(S1)

where the sum is over all times considered in the kinetic run, $[\mathbf{3}]_i$ is the molar concentration of $\mathbf{3}$, $\tilde{\sigma}_i^2 = \sigma_i^2 + \left(\frac{d[\mathbf{3}]_{i,calc}}{dt} \frac{\Delta t}{3}\right)^2$ and the molar concentration was computed as $[\mathbf{3}]_{i,calc} = v_0 t_i + c t_i^2 + (d t_i^3)$, *i.e.* it was computed two times using both a quadratic and a cubic polynomial. The selection between the two polynomials was afforded according to the Bayesian information criterion,[2] *i.e.* selecting the model which gave smaller values of the function $\text{BIC} = \chi^2 + N_p \ln N_I$, where the number of parameters N_p is either 2 or 3, in our case.

One equivalent is 0.08 M. Last digits of initial rates have the estimated standard errors given in parentheses.

Equiv. of **4** / **2** /**1**	v_0 (10^3 M min^{-1})
1.0/0.5/1.0	0.20(2)
1.0/1.0/1.0	0.78(4)
1.0/2.0/1.0	3.3(2)
1.0/3.0/1.0	5.6(3)
0.5/1.0/1.0	0.52(7)
2.0/1.0/1.0	1.8(2)
1.0/1.0/0.5	0.318(14)
1.0/1.0/2.0	1.13(4)
1.0/1.0/3.0	1.62(8)
1.0/1.0/4.0	1.38(12)
1.0/1.0/5.0	1.52(13)
1.0/1.0/6.0	1.36(10)
1.0/2.0/6.0	2.7(3)
9.0/1.0/1.0	2.7(2)
9.0/2.0/1.0	10(2)

General procedure for conductometric measurements: data of table 2

Under nitrogen, the standard conductometric cell, fitted with a suitable rubber septum, was fixed to a previously flamed three-necked round bottom flask and all the equipment was submitted to a series of high vacuum-nitrogen cycles. Then the reagents, according to the order of addition reported in column 2 of table 2, were consecutively added to 15 mL of dry CH_2Cl_2 at $-78°C$. The conductimetric measurements were detected after 1 min of the addition of the last component. The quantities are those reported in brackets and refer to 0.40 mmol in 15 mL of dry CH_2Cl_2 for the limiting component. The used amounts of all the components can be easily calculated from the reported equivalents in brackets of column 2 of table 2.

**General procedure for dynamic conductometric measurements.**

The same equipment used for the experiments of table 2 was employed in the determination of conductimetric curves of Figure 4. In a typical experimental procedure, benzaldehyde **1** (0.40 mmol) was added to a solution of sulfoxide **2** (1, 2 or 3 equivalents), diisopropylethylamine (0.40 mmol) and allyltrichlorosilane (0.48 mmol), in dry CH_2Cl_2 (15.0 mL) at -78 °C under argon.

Quantum chemical calculations

All geometry optimizations were performed with Gaussian 09[3] at the B97(D)/6-31g(d,p) level. The energy of lowest energy conformers were then recomputed at a higher level and corrected for salvation as reported in the paper.

In the case of $Si(OR)Cl_3(OS)_2$ and $Si(OR)Cl_2(OS)_2^+$ (and to a minor extent of $SiallCl_3(OS)_2$ and $SiallCl_2(OS)_2^+$) several starting conformations were considered. The C-O bond of the alcoxy group turned out invariably coplanar with the benzyl ring. The following tables give the dihedrals defining the conformers considered, together with their energy.

Si(OR)Cl₃(OS)₂

$Si(OR)Cl_3(OS)_2$
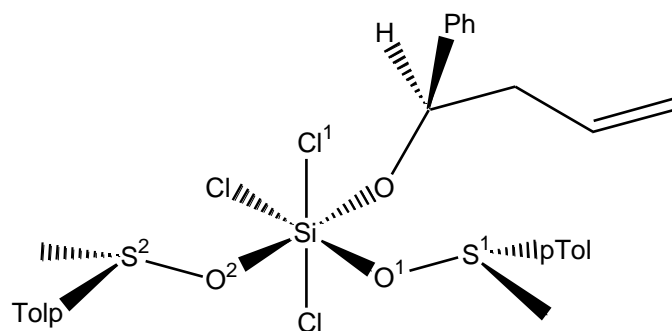
				RELEVANT DIHEDRALS AND ENERGIES		
conformer	ClSi(OS)₁	ClSi(OS)₂	(MeSO)₁Si	(MeSO)₂Si	Cl₁-Si-O-C-C-(C=C)	E (au)
1	-103.3	16.3	82.5	156.9	-134.1, -123.6, -63.7, 135.4	-3700.8263
2	-102.5	138.5	82.6	126.3	-133.3, -121.3, -67.1, -132.3	-3700.8232
3	-98.9	-0.6	95.3	83.7	-54.5, -104.7, 179.8, -110.4	-3700.8228
4	-21.8	136.0	129.2	179.4	-99.1, -88.1, -54.2, -118.2	-3700.8222
5	-114.8	-53.7	101.7	151.6	-132.9, -125.9, -64.1, -133.5	-3700.8215
6	-57.1	135.6	148.4	127.8	-127.5, -124.6, -66.5, -132.0	-3700.8213
7	-84.8	-52.7	151.3	161.6	-136.0, -130.5, -63.3, -143.2	-3700.8212
8	-84.8	-52.7	151.3	161.6	-136.0, -130.5, -63.3, -143.2	-3700.8210
9	-102.5	138.5	82.6	126.3	-133.3,-121.3,-67.1, -132.3	-3700.8207
10	123.8	37.3	124.3	137.3	173.7, -82.0, -54.2, -137.4	-3700.8206
11	137.6	11.6	158.8	82.3	177.3, -83.1,- 55.5, -136.8	-3700.8186
12	-59.9	-147.6	142.9	156.7	-133.9, -122.6, 64.4, -140.6	-3700.8183
13	59.2	17.8	106.2	161.5	-132.9,-106.8, -51.5, -99.2	-3700.8178
14	126.0	133.2	120.9	134.8	-177.8, -87.0,-52.6, -136.1	-3700.8149

A single non-hindered conformer with meridional chlorines and sulfoxides in trans was also considered and had an energy of -3700.8195 au.
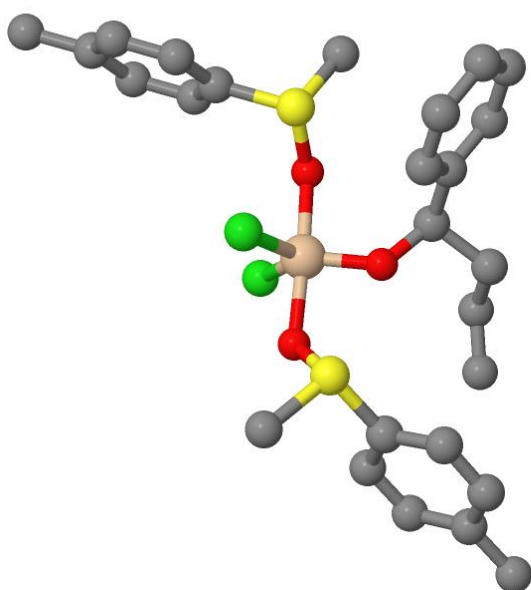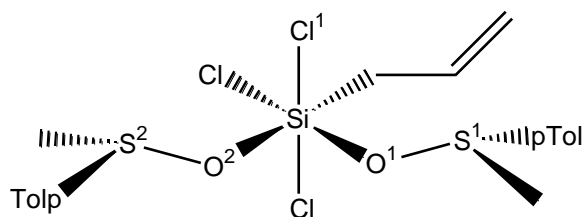

Conformer 1

$$Si(OR)Cl_2(OS)_2{}^+$$
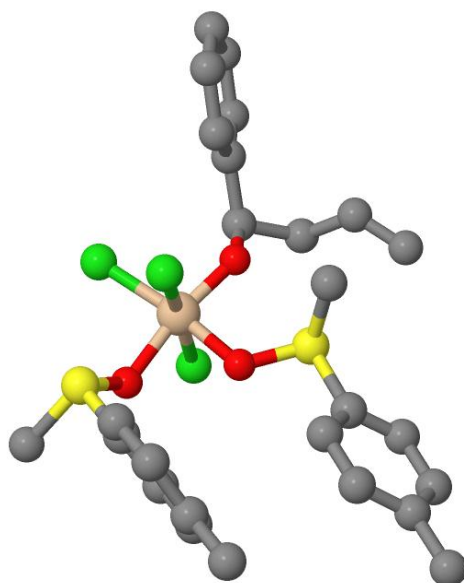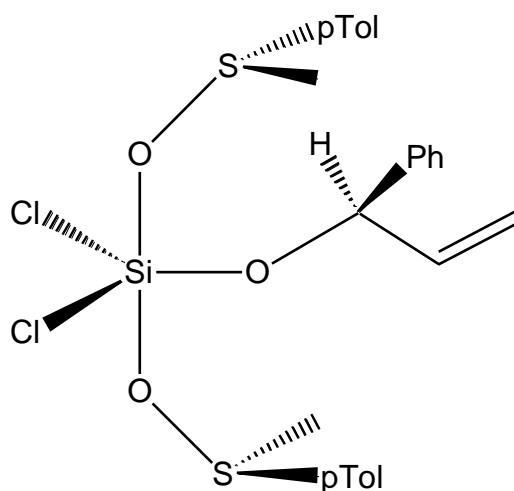
RELEVANT DIHEDRALS AND ENERGIES

Conf.	O_1SiOC_{alc}	$S_1O_1SiO_{eq}$	$S_2O_2SiO_{eq}$	$Me_1S_1O_1Si$	$Me_2S_2O_2Si$	$SiO_{eq}C_{alc}C-(C=C)$	E (au)
1	162.1	47.4	-98.1	138.6	156.5	-147.8, 67.7, -123.0	-3240.4234
2	166.5	61.5	86.3	-126.2	110.5	-156.3, 49.7, -135.5	-3240.4232
3	163.3	40.0	86.9	162.7	107.6	-159.4, 172.4, -110.6	-3240.4227
4	168.7	179.0	-165.1	120.6	113.4	-167.5, 61.1, -117.6	-3240.4209
5	178.7	-44.6	180.0	-1.8	124.0	-76.4, 179.3, -130.7	-3240.4208
6	-156.0	178.5	68.4	136.7	119.4	-175.1, 64.2, -112.2	-3240.4158
7	-162.1	-44.8	163.4	104.7	115.5	50.2, 163.3, -101.1	-3240.4149

A few conformers with a different disposition of substituents were also considered: 1 with apical alcoxy and sulfoxide (E = -3240.4100 au) and 2 with apical chlorine and sulfoxide (E = -3240.4098 au, -3240.4066).

Conformer 1

## SiallCl$_3$(OS)$_2$

RELEVANT DIHEDRALS AND ENERGIES						
Conformer	ClSiOS$_{cis}$	ClSiOS$_{trans}$	(MeSO)$_{cis}$Si	(MeSO)$_{trans}$Si	Cl-Si-C-C=C	E (au)
1	121.0	38.9	124.4	136.4	-170.5, 106.0	-3355.4456
2	126.5	126.1	170.1	115.6	-166.0, 104.2	-3355.4418
3	-23.8	46.8	102.2	127.1	-166.2, 106.1	-3355.4382
4	14.9	136.1	164.1	129.1	-173.4, 108.7	-3355.4366
5	-93.4	23.3	92.7	144.9	175.5, -122.7	-3355.4349

A single conformer with apical sulfoxides was also considered (E = -3355.4361 au).

Conformer 1

SiallCl$_2$(OS)$_2$$^+$
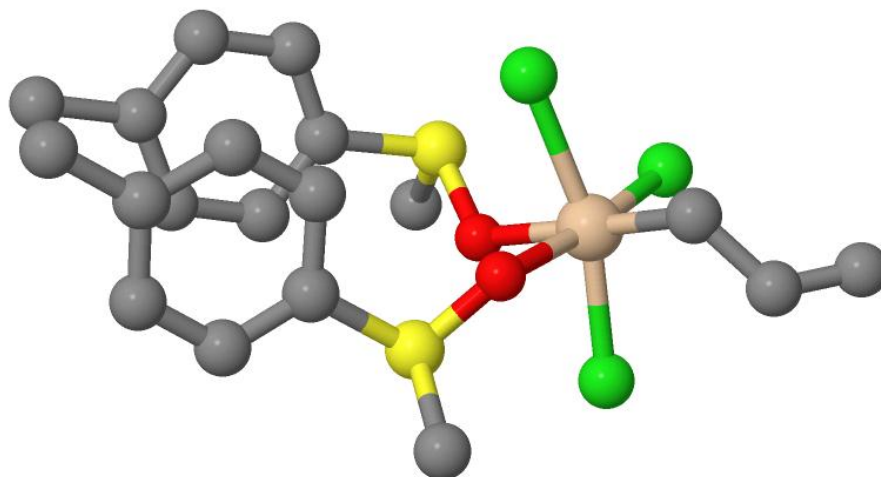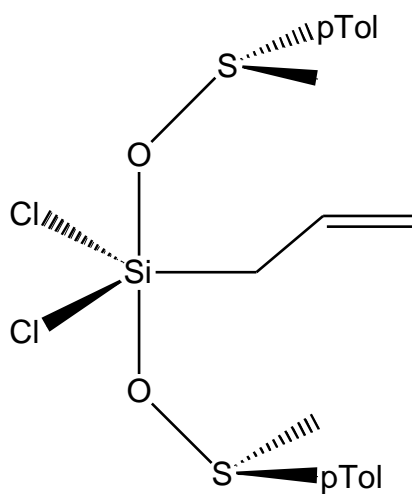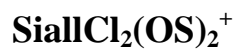
RELEVANT DIHEDRALS AND ENERGIES							
Conformer	O$_1$SiC$_1$C$_2$	S$_1$O$_1$SiC$_1$	S$_2$O$_2$SiC$_1$	Me$_1$S$_1$O$_1$Si	Me$_2$S$_2$O$_2$Si	C$_3$C$_2$C$_1$Si	E (au)
1	177.7	177.2	170.6	132.8	142.2	-111.2	-2895.0379
2	167.9	64.6	-169.7	133.6	146.0	-108.0	-2895.0354

A single conformer with apical allyl and sulfoxide was also considered (*E*=−2895.0261 au).
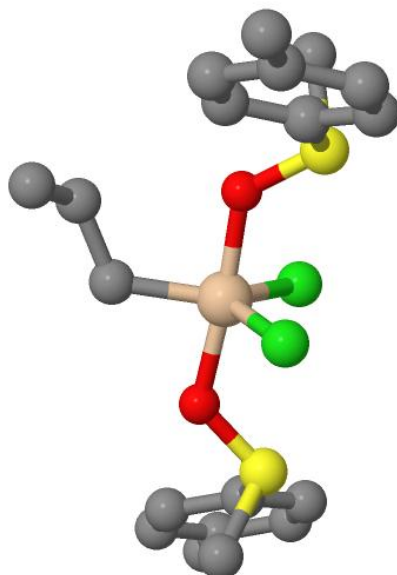
Conformer 1

SiORCl$_2$(OS)(OSCl)
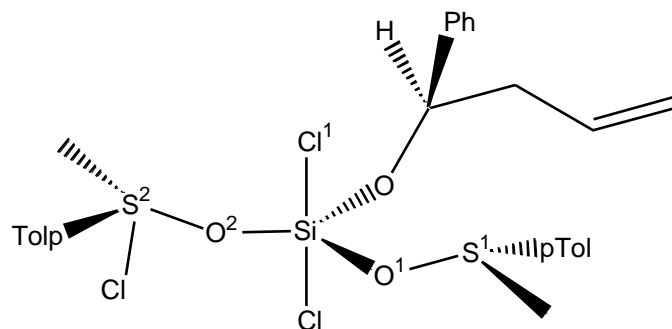
RELEVANT BOND LENGTHS (Å), VALENCE AND DIHEDRAL ANGLES (DEG.) AND ENERGIES

Conf.	Cl-Si-O-S-Me	Cl-Si-O-S-Me	S-O	S-Cl	O-S-Cl	Cl-Si-O-C-C-(C=C)	E (au)
1	162.1, -170.5	-34.0, 104.0	1.81	2.55	172.4	-128.3, -172.4, 179.4, -114.7	-3700.8313
2	29.0, 58.2	24.0, 56.5	1.89	2.48	176.3	147.9, -71.1, -179.4, -108.5	-3700.8142

A single conformer with two chlorines on the equatorial plane was also considered ($E=-3700.8272$ au).
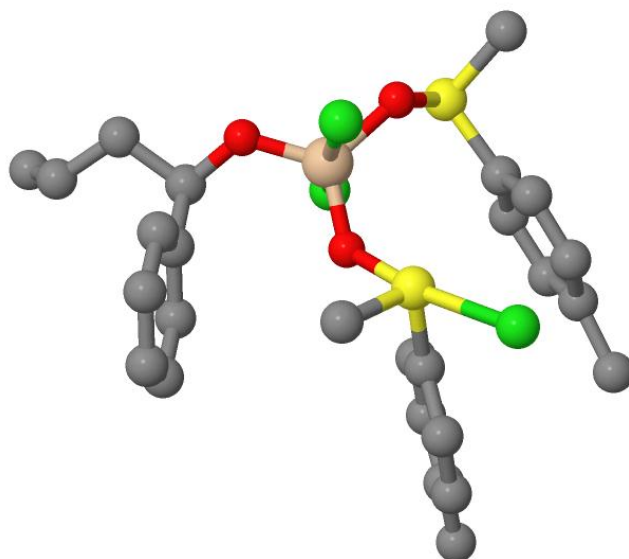
Conformer 1

[1] Instrumental errors have been treated according to the ISO-GUM method, see http://www.bipm.org/utils/common/documents/jcgm/JCGM_100_2008_E.pdf

[2] Schwarz G., *Ann. Statist.* **1978**, 5, 461.

[3] Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.