Diastereoselective Formation of Dithioacetal Oxides from Aliphatic Sulfines under Thermodynamic Control

Florence Corbin,[a] Carole Alayrac,*[a] and Patrick Metzner*[a]

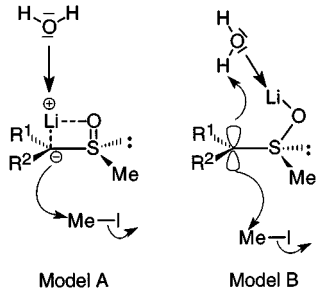
Keywords: Aliphatic sulfine / Organolithium, thiophilic addition of / Carbanions / Protonation / Stereoselectivity / Sulfur / Lithium

Protonation of α-sulfinyl carbanions **3**, resulting from the selective thiophilic addition of organolithium compounds to aliphatic sulfines **2**, provided dithioacetal oxides **4** (63–94% yield). The diastereomeric ratio ranged from 52:48 up to 100:0 with sterically hindered substituents. Thus, (1*S**,*SS**)-2,2-dimethyl-1-methylsulfanyl-1-methylsulfinylpropane (**4ca**) was obtained as a single isomer. The origin of the stereoselectivity is rationalized in terms of a thermodynamic equilibrium between the two diastereomers of α-sulfinyl carbanions **3**, at which protonation occurs under kinetic control and with retention of configuration with the assistance of the lithium cation. Moreover, the stereochemistry could be totally reversed by converting the lithiated anion intermediate into an aluminium "ate" complex. Thus, (1*R**,*SS**)-2,2-dimethyl-1-methylsulfanyl-1-methylsulfinylpropane (**4ca**) was selectively obtained by this method (*dr* = 0:100).

Introduction

α-Sulfinyl carbanions are important synthetic building blocks and their use in asymmetric synthesis has recently been reviewed.[1] To account for the origin of the stereoselectivity of the reactions of these stabilized carbanions with electrophiles, a considerable amount of effort has been focused on the elucidation of their structures.[2] However, this matter has still to be fully resolved. With reference to ^{1}H- and ^{13}C-NMR studies, Chassaing and Marquet[3] showed the metallated carbon of an α-phenylsulfinyl carbanion to be planar. In contrast, some authors have rationalized their results by invoking a tetrahedral species.[4][5] The position of the cation within the molecule has also been questioned. The most common representation is a four-centre chelate structure,[6] involving coordination of a lithium ion both to the carbon and to the sulfinyl oxygen atoms (Scheme 1, model A). However, this model was challenged by some experimental findings. ^{7}Li-, ^{17}O-, as well as ^{13}C-NMR analyses of anions derived from benzylic sulfoxides indicated that they were more closely related to oxylate anions than to carbanions.[7][8] Moreover, Boche[9] and coworkers have published the first crystal structure of a complex between an α-sulfinyl carbanion and TMEDA {[Ph(C)Me−PhSO]Li·2TMEDA}, which crystallizes as a dimer. They showed the C−Li bond length to be much longer (400 pm) than a classical C−Li bond length (< 250 pm). The presence of the O−Li bond (192 pm) was clearly established (Scheme 1, model B).

The nature of the electrophile is known to influence the stereochemical outcome of reactions with α-sulfinyl carbanions.[10] If the electrophile has the ability to coordinate to the lithium atom, for example water, the reaction will proceed with retention of configuration at the carbon atom (Scheme 1). On the other hand, the reaction with a nonchelating electrophile such as methyl iodide will occur with inversion of configuration at the carbon atom.



Scheme 1

In the course of our research program concerning the synthesis and reactivity of aliphatic sulfines (*S*-oxides),[11][12] we observed that the protonation of the α-sulfinyl carbanions generated by the thiophilic addition of organolithium compounds to the sulfines was diastereoselective. In a preliminary communication,[11] we presented experimental evidence showing that the process was not stereospecific with respect to the (*E*) or (*Z*) configuration of sulfines. In order to understand the origin of the stereoselectivity, we set out to further investigate the nature of the intermediate and to establish the configurations of the products. We report herein the findings of our studies and make conclusions concerning the stereoselectivity of dithioacetal oxide carbanions.

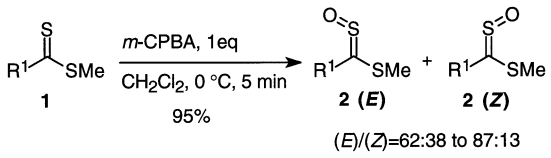
Results and Discussion

Three aliphatic sulfines **2** with varying degrees of steric hindrance (R^1 = cyclohexyl, *n*-nonyl and *tert*-butyl) were

[a] Laboratoire de Chimie Moléculaire et Thio-organique (Unité mixte CNRS), ISMRA − Université,
6 Boulevard du Maréchal Juin, F-14050 Caen, France
Fax: (internat.) + 33-2/31452877
E-mail: metzner@ismra.fr

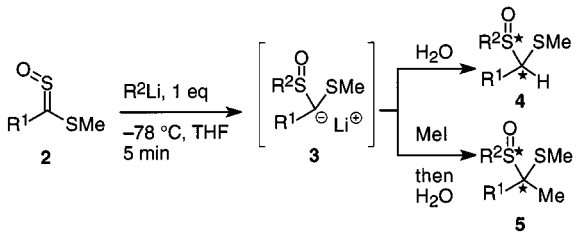
  1434−193X/99/1111−2859 $ 17.50+.50/0

chosen for this study. Their syntheses have been described previously.[13] They are prepared by the rapid oxidation of thiocarbonyl esters **1** with one equivalent of *m*−CPBA at 0 °C in CH_2Cl_2 (Scheme 2). Sulfines exist in isomeric (*E*) and (*Z*) forms according to the relative position of the methylsulfanyl group and the S=O bond. Assignments were made on the basis of ^{1}H-NMR analyses.



Scheme 2

As sulfines are moderately stable, they were directly subjected to a series of four organolithium compounds (R^2 = Me, *n*Bu, *t*Bu, Ph) at −78 °C in THF (Scheme 3). The reaction was rapid (5 min) and exclusively thiophilic: No carbophilic addition nor ene-thiolization reaction was observed. The resulting stabilized dithioacetal oxide carbanions **3** were subsequently treated with H_2O or MeI to afford dithioacetal oxides **4** and **5**, respectively.



Scheme 3

Compounds **4** were obtained in high yields ranging from 63 to 94% (Table 1). Alkylation of the dithioacetal oxide carbanions **3** was, however, not as straightforward. No reaction occurred with electrophiles such as benzaldehyde, benzyl bromide, or conjugated ketones. With methyl iodide as the electrophile, either the reaction did not take place, or the alkylated dithioacetal oxides were unstable. In the case of **3a** (R^1 = cyclohexyl, R^2 = Me), the expected dithioacetal oxide **5aa** was not observed but cyclohexyl methyl ketone was detected instead. Indeed, dithioacetal oxides are known to be readily transformed into aldehydes or ketones[14−16] simply by treatment with a mineral acid and even some examples of spontaneous rearrangement into ketones have been reported.[11][17] Finally, one substrate − **3b** (R^1 = nonyl, R^2 = Me) − was successfully alkylated with methyl iodide to afford compound **5ba** in 76% yield. The difficulties we encountered in the alkylation of the intermediates **3** reflect their low reactivities, which can probably be attributed to stabilization by both the methylsulfanyl and alkylsulfinyl groups. This is in agreement with the results described by Zwanenburg concerning the alkylation of carbanions resulting from the thiophilic addition of organolithium compounds to aromatic sulfines.[18] Their methylation was smooth but the resulting products were rather instable. With other electrophiles, the use of an additive such as HMPT, copper bromide, a crown ether, or triton B was required. No reaction occurred with Michael acceptors. In contrast, Schlessinger reported that the (ethylsulfanyl)(ethylsulfinyl)methane carbanion underwent mono- and dialkylation reactions with alkyl halides[14] and conjugated aldehydes and ketones[19] in high yields.

The dithioacetal oxides **4** and **5ba** contain two asymmetric centres, i.e. the carbon atom bearing the two sulfur atoms and the oxidized sulfur atom. The diastereomeric ratio was determined by integration of the ^{1}H-NMR signals relative to SMe (δ = 2.0 to 2.4). It ranged from 52:48 to 100:0 (Table 1). The diastereoselectivity increased with the bulkiness of R^1 so that dithioacetal oxide **4ca** (R^1 = *t*Bu) was obtained as a single isomer (entry 7). On the other hand, the selectivity decreased with increasing steric hindrance of R^2 (entries 1−3). Alkylation with methyl iodide showed little stereoselectivity (entry 6).

Compounds **4** and **5ba** are not sufficiently robust to allow their purification in satisfactory yield. Decomposition occurred on silica gel. Nevertheless, we attempted to separate the isomers for the purpose of obtaining spectroscopic data. Flash chromatography on alumina enabled us to isolate the minor isomer of **4ab** and the major isomer of **4ca** in yields of 8% and 41%, respectively. The major isomers of **4aa** and **4ad** could be isolated by precipitation with diethyl ether and pentane in yields of 22% and 50%, respectively. It should be noted that the dithioacetal oxides did not undergo isomerization on alumina or upon standing − neat or in solution − at room temperature. Thus, they appear to be configurationally stable.

The relative configuration of the major diastereomer of compound **4aa** (R^1 = cC$_6$H$_{11}$; R^2 = Me) was assigned as (1*S**,S*S**) by X-ray crystallography (Figure 1). In the Newman representation of the molecule in the solid state, the methylsulfanyl group (SMe) and the S=O bond are *anti*; moreover, the two bulkier substituents[20] − the methyl and cyclohexyl groups − are also *anti* to one another. Steric interactions and electronic repulsions are minimized in this conformation of the major diastereomer of **4aa**.

All dithioacetal oxides **4** other than **4ba** (R^1 = n-C$_9$H$_{19}$, R^2 = Me) showed similar trends in their ^{1}H-NMR spectra. The signal of the diastereomeric proton of the major isomer appeared downfield relative to that of the minor isomer. The chemical shift difference Δδ ranged from 0.08 to 0.42 ppm. In the case of **4ba**, the chemical shift was the same for both diastereoisomers.

On the basis of this observation, the same relative configuration was empirically assigned to the major isomers of all compounds **4**. We then proposed conformations for the major and minor diastereomers compatible with the ^{1}H-NMR analyses (Scheme 4). The diastereomeric proton of the minor isomer resides within the positive cone of the S=O bond (the shielding region), while the corresponding proton of the major isomer resides outside.

As mentioned previously, we found evidence for the configurational stability of compounds **4**. Protonation is a rapid process and, according to the Curtin−Hammett principle,[21][22] the diastereomeric ratio of dithioacetal oxides **4**

Table 1. Yields and diastereomeric ratios of dithioacetal oxides

Entry	R^1	R^2	Electrophile	Product	Yield[a] [%]	*dr*[b]
1	cC_6H_{11}	Me	H_2O	**4aa**	77	83:17
2	cC_6H_{11}	*n*Bu	H_2O	**4ab**	63	70:30
3	cC_6H_{11}	*t*Bu	H_2O	**4ac**	74	52:48
4	cC_6H_{11}	Ph	H_2O	**4ad**	94	67:33
5	nC_9H_{19}	Me	H_2O	**4ba**	73	57:43
6	nC_9H_{19}	Me	MeI	**5ba**	76	60:40
7	*t*Bu	Me	H_2O	**4ca**	73	100:0

[a] Crude yield; the purities of crude compounds **4** were generally in excess of 95% (as estimated by ^{1}H NMR). – [b] Diastereoisomeric ratio determined by ^{1}H NMR.

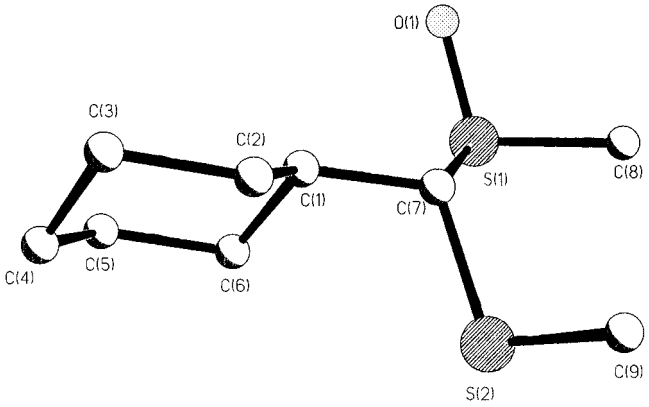
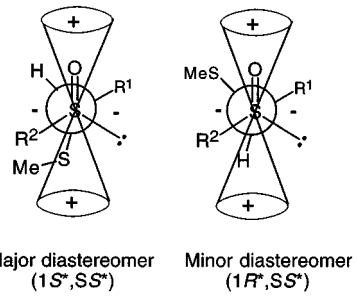


Figure 1. Crystal structure of (1*S**,S*S**)-**4aa** (R^1 = cC_6H_{11}; R^2 = Me); selected interatomic distances [Å], bond angles [°], and torsion angles [°]: S1–O1 1.4999(13), S1–C8 1.787(2), S1–C7 1.8413(14), S2–C9 1.791(2), S2–C7 1.8117(15), C1–C7 1.529(2); O1–S1–C8 105.53(9), O1–S1–C7 105.12(7), C8–S1–C7 98.93(8), C9–S2–C7 101.10(11), C6–C1–C7 113.76(13), C2–C1–C7 110.97(12), C1–C7–S2 113.69(10), C1–C7–S1 109.17(9), S2–C7–S1 109.23(7); C8–S1–C7–C1 169.06(11), O1–S1–C7–S2 –174.92(7)



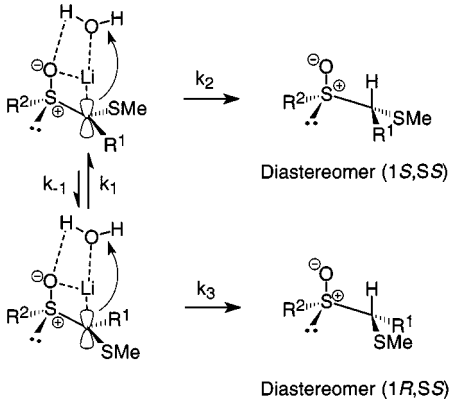
Scheme 4

should reflect the diastereomeric ratio of carbanions **3**. Sulfur-stabilized carbanions are known to be configurationally much less stable than those stabilized by oxygen or nitrogen.[23] We thus envisaged a thermodynamic equilibrium between the two isomers of **3**. In order to validate this hypothesis, we investigated the influence of the hydrolysis temperature on the diastereoselectivity. Methyllithium was added to a solution of sulfine **2a** (R^1 = cyclohexyl) at –78 °C and the reaction mixture was hydrolysed at different temperatures (–78 °C, –50 °C, and room temperature). It is worth noting that previous experiments had shown that the reaction time did not influence the diastereoselectivity. We observed that the diastereomeric ratio of dithioacetal oxide **4aa** (R^1 = cyclohexyl; R^2 = Me) was different at each hydrolysis temperature (Table 2).

Table 2. Effect of hydrolysis temperature on the diastereomeric ratio of **4**

Hydrolysis temperature [°C]	*dr*
–78	83:17
–50	77:23
20	64:36

On the basis of our results and the previously cited literature data, we propose a chelated model for the structure of the α-sulfanyl-α-sulfinyl carbanion. Here, the lithium atom is bound both to the oxygen atom of the sulfinyl group and to the carbon atom (Scheme 5). The protonation is directed by the initial coordination of water at the lithium atom and thus occurs with retention of configuration.



Scheme 5

Electronic repulsions and steric interactions are minimized in the carbanion, which leads to the major isomer of **4** as previously described for the model of the dithioacetal oxide (Scheme 4). Conversely, steric hindrance (between the two alkyl groups R^1 and R^2) and electronic repulsions (between the lone pairs on the two sulfur atoms) are greater in the carbanion, which leads to the minor isomer of **4**. The carbon atom bearing the two sulfur atoms has a hybridization between sp^2 and sp^3 and rotation about the sulfur–carbon bond enables interconversion of the two isomers.

Thus, a thermodynamic equilibrium exists between the two carbanions, with one of them being preferred. As protonation is *quasi* instantaneous, the diastereomeric ratio of **4** corresponds to the relative concentrations of the carbanions at the hydrolysis temperature. Analogous examples have been described in the literature, such as the diastereoselective functionalization of sulfides[24][25] or selenides[25][26] involving thermodynamic control of the configuration of the intermediate lithiated species.

In order to obtain further information, we decided to replace the lithium by another metal ion. Yamamoto[27] has shown that the protonolysis of α-lithiosulfinyl carbanions exhibits reversed stereoselectivity in the presence of $AlEt_3$ due to the formation of an intermediate aluminium "ate" complex. We thus investigated the effect of this Lewis acid on the protonolysis of the dithioacetal oxide carbanions **3**.

We carried out MeLi additions to sulfines **2a−c**, under the same conditions as described above, and subsequently added one equivalent of $AlEt_3$. Hydrolysis of the resulting aluminates afforded dithioacetals **4** in similar yields as obtained in the absence of $AlEt_3$. We were pleased to observe that the diastereoselectivity was completely inverted (Table 3). For the dithioacetal oxide **4ca** (R^1 = *t*Bu), the inversion was particularly spectacular: The lithium carbanion led to a 100:0 diastereomer ratio, whereas the aluminate led to the opposite selectivity (0:100).

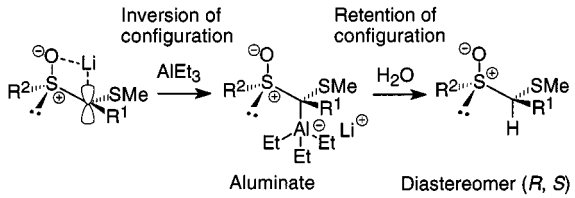
Table 3. Comparison of the diastereomeric ratios of **4** obtained in the presence and absence of $AlEt_3$

4	R^1	E	*dr* [Li][a]	*dr* [$AlEt_3$][b]
4aa	cC_6H_5	H	83:17	10:90
4ca	*t*Bu	H	100:0	0:100
4ba	nC_9H_{19}	H	57:43	35:65
4bb	nC_9H_{19}	Me	60:40	60:40

[a] Diastereoisomeric ratio obtained following a sequence of MeLi (1 equiv.), −78°C, THF, 5 min, then H_2O, −78°C. − [b] Diastereoisomeric ratio obtained following a sequence of MeLi (1 equiv.), −78°C, THF, 5 min, then $AlEt_3$ (1 equiv.), −78°C, 5 min, then H_2O.

The formation of an intermediate containing an oxygen−aluminium bond might be envisaged, but this would not explain the observed stereoselectivity. Rather, by analogy with the work of Yamamoto, our interpretation of these results is as follows (Scheme 6): The major lithium carbanion resulting from the thiophilic addition of MeLi to sulfine **2** is transformed into an aluminium "ate" complex with configurational inversion at the carbon atom since a Lewis acid cannot form a chelate with the lithium ion. Thermodynamic factors also need to be invoked: As the carbon−aluminium and the sulfur−oxygen bonds are positioned *anti*, the steric interactions and electronic repulsions are minimized. Aluminate hydrolysis occurs with retention of configuration.[27] The major diastereomer is thus the minor diastereomer from the classical thiophilic reaction in the absence of $AlEt_3$.

We were able to obtain single crystals of the minor isomer (formed as the major isomer through an aluminate intermediate) of **4ca** (R^1 = *t*Bu, R^2 = Me) suitable for X-ray diffraction analysis. From this, the (1*R**,S*S**) configuration could be assigned (Figure 2), which is consistent with our model of the α-sulfanyl-α-sulfinyl carbanion.



Scheme 6

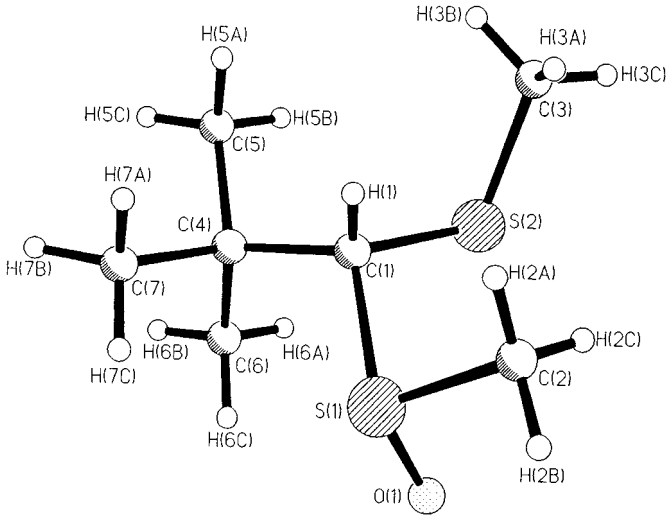
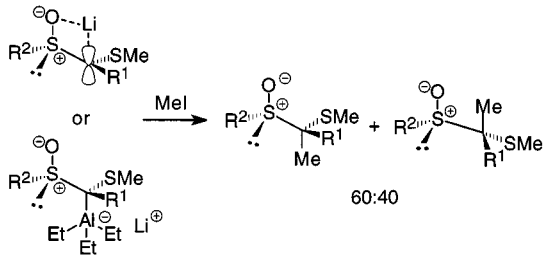


Figure 2. Crystal structure of (1*R**,S*S**)-**4ca** (R^1 = *t*Bu, R^2 = Me); selected interatomic distances [A], bond angles [°], and torsion angles [°]: S1−O1 1.497(2), S1−C2 1.780(3), S1−C1 1.840(2), S2−C3 1.805(3), S2−C1 1.815(2), C1−C4 1.543(3); O1−S1−C2 106.84(12), O1−S1−C1 108.88(8), C2−S1−C1 97.78(11), C3−S2−C1 100.35(11), C4−C1−S2 115.25(12), C4−C1−S1 111.59(11), S2−C1−S1 108.99(9), C6−C4−C1 112.3(2), C5−C4−C1 108.4(2), C7−C4−C1 109.2(2); C3−S2−C1−S1 −121.68(14), C2−S1−C1−C4 −162.97(15)

The hypothesis of chelation control was reinforced by the observation that the alkylation of **3b** with methyl iodide proceeded with poor stereoselectivity (*dr* = 60:40) both in the presence and absence of $AlEt_3$ (Scheme 7). We did not assign the configurations of the isomers of **5ba**. According to the literature,[10] attack of CH_3I preferentially occurs *trans* to the S=O bond, in order to avoid any interaction between the oxygen atom and the iodide ion extruded in the reaction. We envisaged the trapping of compounds **3** with methylating agents[10] capable of coordinating the lithium atom, such as $(MeO)_3P{=}O$. Unfortunately, attempts to alkylate **3** in this manner were unsuccessful.

Conclusion

In this study, we have investigated the stereochemical course of the reaction of electrophiles with α-sulfinyl carbanions **3** resulting from the thiophilic addition of organolithium compounds to aliphatic sulfines **2**. Carbanions stabil-



Scheme 7

ized by sulfur are known to be configurationally much less stable than those stabilized by other heteroatoms such as oxygen or nitrogen. Nevertheless, we observed the protonation of α-sulfinyl carbanions **3** to be diastereoselective. The selectivity was up to 100:0 in the case of **4ca** (R^1 = *t*Bu). Our experimental results can be rationalized in terms of a thermodynamic equilibrium between the two diastereomers of α-sulfinyl carbanions **3**. These undergo rapid interconversion and the subsequent reaction with water is faster than the equilibration. The protonation proceeds under kinetic control and with retention of configuration, with the assistance of the lithium cation. Therefore, the diastereomeric ratio of **4** corresponds to the carbanion ratio at the hydrolysis temperature. Moreover, reversal of the stereochemistry was achieved by the addition of $AlEt_3$ with subsequent formation of an aluminate intermediate. In this way, **4ca** (R^1 = *t*Bu) was obtained as a single isomer with opposite stereochemistry (*dr* = 0:100) to that observed previously. In several cases, we were able to prepare one isomer selectively by choosing the appropriate experimental conditions

Experimental Section

General: THF was distilled from sodium benzophenone. *meta*-Chloroperoxybenzoic acid (*m*-CPBA) was titrated using iodine/sodium thiosulfate.[28] Organolithium compounds were titrated according to literature methods.[29][30] − NMR: Bruker AC and DPX 250 spectrometers (250 MHz and 62 MHz, for ^1H and ^{13}C, respectively), chemical shifts are given relative to tetramethylsilane (δ = 0.00); $CDCl_3$ (δ_H = 7.27, δ_C = 77.00) was used as solvent. Isomeric ratios were determined from suitable ^1H-NMR integrals. − Melting points: Reichert melting-point apparatus. − IR spectra: Perkin−Elmer 16 PC FT-IR. − Mass spectra: Nermag apparatus, University of Caen, or courtesy of Professor C. Lange, IRCOF, University of Rouen. − Elemental analyses: University of Caen or CNRS at Vernaison or Gif-sur-Yvette. − The preparation of sulfines **2a−c** has been described in the literature.[13] All given yields of dithioacetal oxides **4** and **5ba** are overall yields based on dithioesters **1**.

Organolithium Addition to Sulfines (Method I): A solution of the appropriate alkyl- or aryllithium (1 equiv.) was added to a solution of sulfine **2** (1 equiv., 0.73 to 9.04 mmol) in anhydrous THF (10−100 mL) at −78°C under N_2. After stirring for 5 min, water (5 to 10 mL) or iodomethane (1.2 equiv.) was added. The organic layer was then extracted with CH_2Cl_2, washed with brine, and dried with magnesium sulfate. After concentration in vacuo, dithioacetal oxides were obtained in overall yields of 63−89% based on dithioesters **1**. Purification by flash chromatography on alumina resulted in low recovered yields owing to decomposition. Dithioacetal oxides can exist in two diastereomeric forms; ^1H-NMR analyses of all the major diastereomers showed that the signal of the proton attached to the asymmetric carbon centre was downfield shifted relative to that of the corresponding proton in the minor diastereomers.

Organolithium Addition to Sulfines with Addition of $AlEt_3$ (Method II): A solution of the appropriate alkyl- or aryllithium (1 equiv.) was added to a solution of sulfine **2** (1 equiv., 0.91 to 5.87 mmol) in anhydrous THF (15 to 80 mL) at −78°C under N_2. After stirring for 5 min, $AlEt_3$ (1 equiv.) was added. The temperature was kept at −78°C for 5 min, then water (5 to 10 mL) or iodomethane (1.2 equiv.) was added. The organic layer was extracted with CH_2Cl_2, washed with brine, and dried with magnesium sulfate. After concentration under reduced pressure, dithioacetal oxides were obtained in overall yields of 58−85% based on dithioesters **1**.

(1*S,S*S**)-Cyclohexyl(methylsulfanyl)(methylsulfinyl)methane (4aa):** Reaction of sulfine **2a** (858 mg, 4.51 mmol) and MeLi (1.6 M, 2.82 mL, 4.51 mmol) afforded compound **4aa** (755 mg, 77% yield) in an 83:17 diastereomeric ratio. By precipitation with diethyl ether (3 mL), the major diastereomer (200 mg, 0.97 mmol) was isolated (22% yield). Its (1*S**,S*S**) configuration was determined by an X-ray structure analysis. Colourless crystals; m.p. 99−100°C (pentane). − ^1H NMR ($CDCl_3$): δ = 1.15−1.45 [m, 4 H, $(CH_2)_2$], 1.56−1.87 [m, 6 H, $(CH_2)_3$], 2.19−2.33 (m, 1 H, CH of cyclohexyl), 2.26 (s, 3 H, SCH_3), 2.74 (s, 3 H, $CH_3S{=}O$), 3.28 (d, *J* = 3.8 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 18.7 (SCH_3), 25.7, 26.0, 26.1, 27.7, 30.7, 36.6, 37.2, 78.0 (CHS=O). − IR (KBr): $\tilde{\nu}$ = 1032 cm^{-1}, 2850, 2922. − MS (70 eV); *m/z* (%): 44 (100), 73 (15), 85 (14), 97 (12), 126 (3), 143 (1) [$M^+ - CH_3S{=}O$], 207 (2) [M^+ + H]. − $C_9H_{18}OS_2$ (206.36): calcd. C 52.41, H 8.80, O 7.76; found C 52.55, H 8.82, O 7.68.

(1*R,S*S**)-Cyclohexyl(methylsulfanyl)(methylsulfinyl)methane (4aa):** From sulfine **2a** (162 mg, 0.85 mmol), MeLi (1.6 M, 0.53 mL, 0.85 mmol), and $AlEt_3$ (0.85 mL, 0.85 mmol), the dithioacetal oxide **4aa** (157 mg, 85% yield) was obtained in a 10:90 diastereomeric ratio, i.e. the inverse of the ratio obtained using Method I. Recrystallization from pentane gave the minor isomer generated using Method I (59 mg, 33% yield). Its (1*R**,S*S**) configuration was deduced from that of the above isomer. White crystals; m.p. 68−70°C (pentane). − ^1H NMR ($CDCl_3$): δ = 1.15−1.45 [m, 4 H, $(CH_2)_2$], 1.56−1.87 [m, 6 H, $(CH_2)_3$], 2.19−2.33 (m, 1 H, CH of cyclohexyl), 2.32 (s, 3 H, SCH_3), 2.67 (s, 3 H, $CH_3S{=}O$), 3.10 (d, *J* = 6.4 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 16.4 (SCH_3), 26.1, 30.9, 32.0, 35.9, 37.6, 74.5 (CHS=O). − IR (KBr): $\tilde{\nu}$ = 1028 cm^{-1}, 2848, 2888, 2918. − MS (70 eV); *m/z* (%): 44 (100), 73 (15), 85 (14), 97 (12), 126 (3), 143 (1) [$M^+ - CH_3S{=}O$], 207 (2) [M^+ + H]. − $C_9H_{18}OS_2$ (206.36): calcd. C 52.41, H 8.80, O 7.76; found C 52.26, H 8.86, O 7.62.

(*n*-Butylsulfinyl)cyclohexyl(methylsulfanyl)methane (4ab): Reaction of sulfine **2a** (276 mg, 1.54 mmol) and *n*BuLi (1.15 M, 1.27 mL, 1.54 mmol) gave dithioacetal oxide **4ab** (279 mg, 63% yield) in a 70:30 diastereomeric ratio. The minor isomer (37 mg, 8% yield) was isolated by chromatography on alumina using petroleum ether/ethyl acetate (70:30) as eluent. Yellow oil. − **Major Isomer:** ^1H NMR ($CDCl_3$): δ = 0.98 (t, *J* = 7.3 Hz, 3 H, CH_3CH_2), 1.20−1.67 [m, 8 H, $(CH_2)_4$], 1.72−1.80 [m, 5 H, $(CH_2)_2$ and CH of cyclohexyl], 2.05−2.17 (m, 2 H, CH_2), 2.22 (s, 3 H, SCH_3), 2.73−2.98 (m, 2 H, $CH_2S{=}O$), 3.28 (d, *J* = 3.5 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 13.8 (CH_3CH_2), 18.5 (SCH_3), 22.1, 25.0, 25.6, 26.0, 26.1, 27.4, 30.5, 36.9 (*C*HCHS=O), 49.6 ($CH_2S{=}O$), 75.3 (CHS=O). − **Minor Isomer:** ^1H NMR ($CDCl_3$): δ = 0.98 (t, *J* = 7.3 Hz, 3 H, CH_3CH_2), 1.20−1.67 [m, 8 H, $(CH_2)_4$], 1.72−1.80 [m,

5 H, $(CH_2)_2$ and CH of cyclohexyl], 2.05−2.17 (m, 2 H, CH_2), 2.31 (s, 3 H, SCH_3), 2.73−2.98 (m, 2 H, $CH_2S{=}O$), 3.13 (d, J = 6.5 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 16.1 (CH_3CH_2), 18.5 (SCH_3), 22.2, 25.2, 25.6, 26.0, 30.9, 31.8, 37.9 (*C*HCHS=O), 49.8 ($CH_2S{=}O$), 73.0 (CHS=O).

Cyclohexyl(methylsulfanyl)[(1,1-dimethylethyl)sulfinyl]methane (4ac): Reaction of sulfine **2a** (504 mg, 2.65 mmol) and *t*BuLi (1.2 M, 2.2 mL, 2.65 mmol) gave dithioacetal oxide **4ac** (545 mg, 74% yield) in a 52:48 diastereomeric ratio. The ^{1}H-NMR spectrum showed additional signals besides those expected, which could not be assigned. By precipitation with pentane, a 72:28 mixture of the two diastereomers (148 mg, 20% yield) was isolated as a white solid. − **Major Isomer:** ^{1}H NMR ($CDCl_3$): δ = 1.25−2.00 [m, 11 H, $(CH_2)_5$ and CH of cyclohexyl], 1.28 (s, 9 H, *t*BuS=O), 2.21 (s, 3 H, SCH_3), 3.55 (d, J = 5.5 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 15.8 (SCH_3), 23.7 [$(CH_3)_3$], 26.2, 26.3, 26.4, 29.8, 31.4, 40.8 (CH of cyclohexyl), 54.8 [$C(CH_3)_3$], 69.7 (CHS=O). − **Minor Isomer:** ^{1}H NMR ($CDCl_3$): δ = 1.25−2.00 [m, 11 H, $(CH_2)_5$ and CH of cyclohexyl], 1.34 (s, 9 H, *t*BuS=O), 2.19 (s, 3 H, SCH_3), 3.38 (d, J = 3.7 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 16.3 (SCH_3), 24.1 [$(CH_3)_3$], 26.0, 26.3, 26.4, 28.9, 31.4, 37.4 (CH from cyclohexyl), 56.0 [$C(CH_3)_3$], 66.2 (CHS=O). − MS (70 eV); *m*/*z* (%): 41 (86), 57 (99) [*t*Bu$^+$], 61 (97), 95 (62), 143 (100) [M$^+$ − *t*BuS=O], 248 (1) [M$^+$].

Cyclohexyl(methylsulfanyl)(phenylsulfinyl)methane (4ad): Reaction of sulfine **2a** (1.72 g, 9.04 mmol) and PhLi (1.56 M, 5.8 mL, 9.04 mmol) gave dithioacetal oxide **4ad** (2.33 g, 94% yield) in a 67:33 diastereomeric ratio. The major diastereomer (1.24 g, 50% yield) was isolated as white crystals by precipitation with pentane. − **Major Isomer:** ^{1}H NMR ($CDCl_3$): δ = 0.90−1.90 [m, 11 H, $(CH_2)_5$ and CH of cyclohexyl], 2.02 (s, 3 H, SCH_3), 3.30 (d, J = 5.2 Hz, 1 H, CHS=O), 7.50 (m, 3 H, aromatic CH), 7.70 (m, 2 H, aromatic CH). − ^{13}C NMR ($CDCl_3$): δ = 17.4, 26.0, 26.1, 26.2, 30.1, 31.9, 38.9, 81.4 (CHS=O), 125.3, 128.9, 131.2, 143.0 (aromatic C). − **Minor Isomer:** ^{1}H NMR ($CDCl_3$): δ = 0.90−1.90 [m, 11 H, $(CH_2)_5$ and CH of cyclohexyl], 1.26 (s, 3 H, SCH_3), 3.22 (d, J = 2.7 Hz, 1 H, CHS=O), 7.50 (m, 3 H, aromatic CH), 7.70 (m, 2 H, aromatic CH). − ^{13}C NMR ($CDCl_3$): δ = 17.5, 25.8, 26.1, 26.9, 30.5, 36.9, 39.1, 81.2 (CHS=O), 126.9, 127.2, 129.4, 131.7 (aromatic C). − MS (70 eV); *m*/*z* (%): 95 (18), 125 (9) [PhS=O$^+$], 143 (98) [M$^+$ − PhS=O], 235 (27), 251 (100), 268 (1.5) [M$^+$], 269 (48).

1-Methylsulfanyl-1-methylsulfinyldecane (4ba): Reaction of sulfine **2b** (769 mg, 3.28 mmol) and MeLi (1.4 M, 2.32 mL, 3.28 mmol) afforded compound **4ba** (598 mg, 73% yield) in a 57:43 diastereomeric ratio. From sulfine **2b** (294 mg, 1.25 mmol), MeLi (1.6 M, 0.78 mL, 1.25 mmol), and $AlEt_3$ (1.25 mL, 1.25 mmol), the dithioacetal oxide **4ba** (184 mg, 58%) was obtained in a 35:65 ratio. Yellow oil. − **Major Isomer:** ^{1}H NMR ($CDCl_3$): δ = 0.88 (t, J = 6.8 Hz, 3 H, CH_3CH_2), 1.27 [m, 14 H, $(CH_2)_7$], 1.69 (m, 2 H, CH_2CHSCH_3), 2.17 (s, 3 H, SCH_3), 2.71 (s, 3 H, $CH_3S{=}O$), 3.47 (dd, J = 3.6 Hz, J = 10.8 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 13.2 (SCH_3), 14.1 [$CH_3(CH_2)_8$], 24.8, 26.5, 26.8, 27.3, 29.1, 29.2, 29.4, 36.5 ($CH_2CHSOCH_3$), 67.6 (*C*HSOCH$_3$). − **Minor Isomer:** ^{1}H NMR ($CDCl_3$): δ = 0.88 (t, J = 6.8 Hz, 3 H, CH_3CH_2), 1.27 [m, 14 H, $(CH_2)_7$], 1.69 (m, 2 H, CH_2CHSCH_3), 2.28 (s, 3 H, SCH_3), 2.55 (s, 3 H, $CH_3S{=}O$), 3.47 (dd, J = 3.6 Hz, J = 10.8 Hz, 1 H, CHS=O). − ^{13}C NMR ($CDCl_3$): δ = 15.6 (SCH_3), 14.1 [$CH_3(CH_2)_8$], 24.8, 26.5, 26.8, 27.3, 29.1, 29.3, 29.4, 32.0 ($CH_2CHSOCH_3$), 65.8 (*C*HSOCH$_3$). − IR (NaCl): $\tilde{\nu}$ = 1030 cm^{-1}, 1052, 1466, 2850, 2918. − MS (200 eV); *m*/*z* (%): 251 (20) [M$^+$ + 1], 187 (100) [M$^+$ − CH_3SOH], 85 (10).

2-Methylsulfanyl-2-methylsulfinylundecane (5ba): Reaction of sulfine **2b** (213 mg, 0.91 mmol), MeLi (1.6 M, 0.57 mL, 0.91 mmol), and MeI (0.07 mL, 1.09 mmol) afforded compound **5ba** (184 mg, 76% yield) in a 60:40 diastereomeric ratio. From sulfine **2b** (319 mg, 1.36 mmol), MeLi (1.6 M, 0.85 mL, 1.36 mmol), $AlEt_3$ (1.36 mL, 1.36 mmol), and MeI (0.1 mL, 1.6 mmol), the dithioacetal oxide **5ba** (280 mg, 78% yield) was obtained in the same 60:40 diastereomeric ratio. − **Major Isomer:** ^{1}H NMR ($CDCl_3$): δ = 0.88 (m, 3 H, CH_3CH_2), 1.27 [m, 14 H, $(CH_2)_7$], 1.47 [s, 3 H, $CH_2C(SCH_3)$], 1.53−1.71 (m, 2 H, CH_2), 2.18 (s, 3 H, SCH_3), 2.60 (s, 3 H, $CH_3S{=}O$). − ^{13}C NMR ($CDCl_3$): δ = 11.6 (SCH_3), 14.0 [$CH_3(CH_2)_8$], 19.0 [$CH_3C(SCH_3)$], 25.7, 28.9, 29.2, 29.5, 29.7, 31.6, 43.9, 65.3 (*C*SOCH$_3$). − **Minor Isomer:** ^{1}H NMR ($CDCl_3$): δ = 0.88 (m, 3 H, CH_3CH_2), 1.27 [m, 14 H, $(CH_2)_7$], 1.44 [s, 3 H, $CH_3C(SCH_3)$], 1.53−1.71 (m, 2 H, CH_2), 2.10 (s, 3 H, SCH_3), 2.61 (s, 3 H, $CH_3S{=}O$). − ^{13}C NMR ($CDCl_3$): δ = 11.9 (SCH_3), 14.0 [$CH_3(CH_2)_8$], 15.5 [$CH_3C(SCH_3)$], 25.6, 26.8, 29.0, 29.1, 29.3, 30.1, 40.8, 65.1 (*C*SOCH$_3$).

(1*S,S*S**)-2,2-Dimethyl-1-methylsulfanyl-1-methylsulfinylpropane (4ca):** Reaction of sulfine **2c** (965 mg, 5.87 mmol) and MeLi (1.6 M, 3.67 mL, 5.87 mmol) gave dithioacetal oxide **4ca** (773 mg, 73% yield) as a single isomer (*dr* = 100:0). Flash chromatography on alumina using petroleum ether/ethyl acetate (50:50) as eluent led to **4ca** (440 mg, 41% yield) as a colourless oil (*dr* = 100:0). The (1*S**,S*S**) relative configuration was assigned on the basis of that of the isomer prepared by Method II (as determined by an X-ray structure analysis). − ^{1}H NMR ($CDCl_3$): δ = 1.20 (s, 9 H, *t*Bu), 2.34 (s, 3 H, SCH_3), 2.78 (s, 3 H, $CH_3S{=}O$), 3.41 (s, 1 H, CH). − ^{13}C NMR ($CDCl_3$): δ = 18.9 (SCH_3), 28.0 (*t*Bu), 36.6 (*Ct*Bu), 37.2 ($CH_3S{=}O$), 82.5 (CH). − IR (KBr): $\tilde{\nu}$ = 1038 cm^{-1}, 2908, 2964. − MS (70 eV); *m*/*z* (%): 117 (57.5), 69 (100), 43 (70), 41 (74.5).

(1*R,S*S**)-2,2-Dimethyl-1-methylsulfanyl-1-methylsulfinylpropane (4ca):** From sulfine **2c** (208 mg, 1.27 mmol), MeLi (0.8 mL, 1.27 mmol), and $AlEt_3$ (1.27 mL, 1.27 mmol), dithioacetal oxide **4ca** (159 mg, 67% yield) was obtained as a single isomer, the configuration of which was opposite to that of the product obtained using Method I. Its (1*R**,S*S**) relative configuration was determined by an X-ray structure analysis. Colourless crystals; m.p. 148−149°C (pentane). − ^{1}H NMR ($CDCl_3$): δ = 1.22 (s, 9 H, *t*Bu), 2.34 (s, 3 H, SCH_3), 2.64 (s, 3 H, $CH_3S{=}O$), 2.99 (s, 1 H, CH). − ^{13}C NMR ($CDCl_3$): δ = 20.3 (SCH_3), 28.6 (*t*Bu), 38.2 ($CH_3S{=}O$), 38.7 (*Ct*Bu), 120.0 (CH). − IR (KBr): $\tilde{\nu}$ = 1038 cm^{-1}, 2908, 2964. − MS (70 eV); *m*/*z* (%): 117 (57.5), 69 (100), 43 (70), 41 (74.5). − $C_7H_{16}OS_2$ (180.32): calcd. C 46.65, H 8.96, O 8.88; found C 46.41, H 8.88, O 9.21.

X-ray Crystal Data of 4aa: $C_9H_{18}OS_2$, M_r = 206.35, triclinic, space group $P\bar{1}$ (No. 2), a = 6.3936(8), b = 9.6253(12), c = 9.6912(12) Å, α = 101.556(10), β = 102.078(10), γ = 98.379(10)°, V = 560.31(12) Å^3, F(000) = 224, Z = 2, $\rho_{calcd.}$ = 1.223 Mg/m^3. Data were collected with a Siemens P3/PC diffractometer, Mo-K_α radiation (highly oriented graphite-crystal monochromator, λ = 0.71073 Å). The structure was solved using Siemens SHELXTL and refined by the full-matrix least-squares method. μ(Mo-K_α) = 0.432 mm^{-1}, 2θ range 2.2−30.06°, scan type θ/2θ, T = 293(2) K, 2 standard reflections measured every 98 reflections, 3491 collected reflections, 3228 independent reflections, 2705 observed reflections, no absorption corrections applied, 181 refined parameters, R = 0.0422 (R_w = 0.1064). Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-179-113070.

X-ray Crystal Data of 4ca: $C_7H_{16}OS_2$, M_r = 180.32, monoclinic, space group $P2_1/c$ (No. 14), a = 12.216(3), b = 7.882(2), c = 10.407(3) Å, α = 90.00, β = 99.19(2), γ = 90.00°, V = 989.2(4) Å^3, $F(000)$ = 392, Z = 4, $\rho_{calcd.}$ = 1.211 Mg/m^3. Data were collected on a Siemens P3/PC diffractometer, Mo-K_α radiation (highly oriented graphite-crystal monochromator, λ = 0.71073 Å). The structure was solved using Siemens SHELXTL-PLUS (PC version) and refined by the full-matrix least-squares method. μ(Mo-K_α) = 0.480 mm^{-1}, 2θ range 3.09−29.05°, scan type θ/2θ, T = 298(2) K, 2 standard reflections measured every 98 reflections, 2775 collected reflections, 2637 independent reflections, 1655 observed reflections, no absorption corrections applied, 152 refined parameters, R = 0.0377 (R_w = 0.0865). Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-179-113071.

Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

[1] A. J. Walker, *Tetrahedron: Asymmetry* **1992**, *3*, 961−998.
[2] Reviews concerning the structure of α-sulfinyl carbanions: [2a] S. M. Allin, S. J. Shuttleworth, P. C. B. Page, *Organosulfur Chemistry − Synthetic and Stereochemical Aspects* (Ed.: P. C. B. Page), Academic Press, London, **1998**, vol. 2, pp. 97−155. − [2b] M. Mikolajczyk, J. Drabowicz, P. Kielbasinski, *Chiral Sulfur Reagents (Applications in Asymmetric and Stereoselective Synthesis)*, CRC Press, Boca Raton, **1997**. − [2c] G. Solladié, *Stereoselective Synthesis (Houben-Weyl)* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Georg Thieme, Stuttgart, **1996**, vol. E21, pp. 1056−1076. − [2d] G. Boche, *Angew. Chem.* **1989**, *101*, 286; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 277−297. − [2e] G. Solladié, *Synthesis* **1981**, 185−196.
[3] G. Chassaing, A. Marquet, *Tetrahedron* **1978**, *34*, 1399−1404.
[4] G. Posner in *The Chemistry of Sulphones and Sulphoxides − The Chemistry of Functional Groups* (Eds.: S. Patai, Z. Rappoport, C. Stirling), Wiley, Chichester, **1988**, p. 823−849.
[5] D. R. Williams, J. G. Phillips, F. H. White, J. C. Huffman, *Tetrahedron* **1986**, *42*, 3003−3011.
[6] J.-F. Biellmann, J. J. Vicens, *Tetrahedron Lett.* **1978**, *19*, 467−470.
[7] C. Najera, M. Yus, R. Hässig, D. Seebach, *Helv. Chim. Acta* **1984**, *67*, 1100−1103.
[8] M. Higaki, M. Goto, A. Ohno, *Heteroatom Chem.* **1990**, *1*, 181.
[9] M. Marsch, W. Massa, K. Harms, G. Baum, G. Boche, *Angew. Chem.* **1986**, *98*, 1004; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 1011−1012.
[10] G. Chassaing, R. Lett, A. Marquet, *Tetrahedron Lett.* **1978**, *19*, 471−474.
[11] C. Alayrac, F. Cerreta, F. Corbin, I. Chapron, P. Metzner, *Tetrahedron Lett.* **1996**, *37*, 4507−4510.
[12] C. Leriverend, P. Metzner, A. Capperucci, A. Degl′Innocenti, *Tetrahedron* **1997**, *53*, 1323−1342.
[13] F. Cerreta, A.-M. Le Nocher, C. Leriverend, P. Metzner, T. N. Pham, *Bull. Soc. Chim. Fr.* **1995**, *132*, 67−74.
[14] J. E. Richman, J. L. Herrmann, R. H. Schlessinger, *Tetrahedron Lett.* **1973**, *14*, 3267−3270.
[15] J. L. Herrmann, G. R. Kieczykowski, R. F. Romanet, R. H. Schlessinger, *Tetrahedron Lett.* **1973**, *14*, 4715−4718.
[16] K. Ogura, G.-i. Tsuchihashi, *Tetrahedron Lett.* **1971**, *12*, 3151−3154.
[17] C. Alayrac, F. Cerreta, F. Corbin, I. Chapron, P. Metzner, *Phosphorus Sulfur Silicon Relat. Elem.* **1997**, *120/121*, 321−322.
[18] G. E. Veenstra, B. Zwanenburg, *Tetrahedron* **1978**, *34*, 1585−1592.
[19] J. E. Richman, J. L. Herrmann, R. H. Schlessinger, *Tetrahedron Lett.* **1973**, *14*, 3271−3274.
[20] Steric hindrance effects of substituents compared to hydrogen, as determined from the conformational energies of the respective cyclohexane derivatives:[21] cC_6H_{11} (2.2 kcal/mol), Me (1.74 kcal/mol), SMe (1.04 kcal/mol).
[21] E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, John Wiley, New York, **1994**.
[22] J. I. Seeman, *Chem. Rev.* **1983**, *83*, 83−134.
[23] V. K. Aggarwal, *Angew. Chem.* **1994**, *106,* 185; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 175−177, and references cited therein.
[24] P. G. McDougal, B. D. Condon, M. D. Laffosse, A. M. Lauro, D. VanDeerveer, *Tetrahedron Lett.* **1988**, *29*, 2547−2550.
[25] M. D. Bowe, H. J. Reich, *J. Am. Chem. Soc.* **1990**, *112*, 8994−8995.
[26] R. Dress, W. Klute, R. W. Hoffmann, *J. Chem. Soc., Perkin Trans. 2* **1993**, 1409−1411.
[27] Y. Yamamoto, K. Maruyama, *J. Chem. Soc., Chem. Commun.* **1980**, 239−240.
[28] A. Ibbotson, A. C. Reduto dos Reis, S. P. Saberi, A. M. Z. Slawin, S. E. Thomas, G. J. Tustin, D. J. Williams, *J. Chem. Soc., Perkin Trans. 1* **1992**, 1251−1259.
[29] W. G. Kofron, L. M. Baclawski, *J. Org. Chem.* **1976**, *41*, 1879−1880.
[30] L. Duhamel, J.-C. Plaquevent, *J. Organomet. Chem.* **1993**, *44S*, 1−3.

Received February 4, 1999
[O99049]