DOI: 10.1002/ejoc.201000410

Enantioselective Synthesis, Configurational Stability, and Reactivity of Lithium α-*tert*-Butylsulfonyl Carbanion Salts

Roland Scholz,[a][‡] Gunther Hellmann,[a][‡‡] Susanne Rohs,[a][‡‡‡] Diana Özdemir,[a][‡‡‡‡] Gerhard Raabe,[a] Cornelia Vermeeren,[a] and Hans-Joachim Gais*[a]

Keywords: Chirality / Carbanions / Racemization / Enantioselectivity / Alkylation

The reactions of enantiopure *S*-*tert*-butyl sulfones of the type $R^1CH(R^2)SO_2tBu$ (≥99 % *ee*) with lithiumorganyl compounds gave the corresponding chiral α-sulfonyl carbanion salts $[R^1C(R^2)SO_2tBu]Li$ with ≥94 % *ee*. The enantioselectivity of the deprotonation of the phenyl- but not dialkyl-substituted sulfones is strongly dependent on the nature of the lithiumorganyl. Because of this observation and the strong decrease in enantioselectivity in the presence of TMEDA and HMPA, we propose an intramolecular proton transfer following complexation of the sulfone by RLi. Racemization of $[R^1C(R^2)SO_2tBu]Li$ follows first-order kinetics and seems to be mainly an enthalpic process with a small negative activation entropy, as revealed by polarimetric measurements at low temperatures. This is in accordance with C_α–S bond rotation as the rate-determining step. The salts $[R^1C(R^2)SO_2tBu]Li$ have half-lives of racemization in the order of several hours at –105 °C. The deuteriation of the salts at –105 °C with CF_3CO_2D proceeded with enantioselectivities of ≥94 % *ee*, the magnitude of which was not significantly affected by the presence of TMEDA and HMPA. The salts also reacted with carbon-based electrophiles at low temperatures with high enantioselectivity. The conversion of $R^1CH(R^2)SO_2tBu$ via $[R^1C(R^2)SO_2tBu]Li$ to $R^1C(R^2,E)SO_2tBu$, which involves the loss of stereogenicity at the α-stereogenic center and its re-establishment upon reaction of the chiral carbanion with electrophiles, occurred with high overall enantioselectivity. Electrophiles attack the anionic C atom of $[R^1C(R^2)SO_2tBu]Li$ with high selectivity on the side *syn* to the O atoms and *anti* to the *tert*-butyl group. The reactivity of the dialkyl-substituted salts $[R^1C(R^2)SO_2tBu]Li$ (R^1, R^2 = alkyl) is significantly higher than that of the benzylic salts $[RC(Ph)SO_2tBu]Li$ (R = alkyl) and the HMPA-coordinated SIPs of $[MeC(Ph)SO_2tBu]Li$ are significantly more reactive towards EtI than the corresponding O–Li contact ion pairs.

Introduction

We have described in the previous paper[1] the results of a study of the structures and enantiomerization dynamics of the racemic lithium α-*tert*-butylsulfonyl carbanion salts *rac*-**1**–**5**, which were prepared by deprotonation of the corresponding sulfones *rac*-**6**–**10** with *n*BuLi (Figure 1). Dynamic NMR (DNMR) spectroscopy of the salts *rac*-**2**, *rac*-**3**, and *rac*-**5** had indicated that the configurational stability of C_α-disubstituted *S*-*tert*-butylsulfonyl carbanions should be high enough at low temperatures to allow a study of their enantioselective synthesis and reactions and racemization dynamics. The enantiomerization barriers of the lithium *S*-*tert*-butylsulfonyl carbanion salts are identical to the C_α–S rotational barrier, which is determined by steric effects and the n_C–σ^*_{StBu} interaction.[1] Whereas the half-lives for the enantiomerization of the *S*-*tert*-butyl salts *rac*-**2**, *rac*-**3**, and *rac*-**5** at –105 °C are in the order of a few hours, those of the *S*-phenyl derivatives are only in the order of a few minutes.[1] The low enantiomerization barriers of the latter salts explain why all previous attempts to enantioselectively synthesize α-arylsulfonyl carbanions were unsuccessful.[2] We had previously observed that lithium *S*-trifluoromethylsulfonyl carbanion salts have an even higher enantiomerization barrier than their *S*-*tert*-butyl-substituted analogues.[3] Although this feature permitted both an enantioselective synthesis and investigation of the racemization dynamics, the strong stabilization of the *S*-trifluoromethylsulfonyl carbanions by electrostatic and n_C–σ^*_{SCF3} interactions strongly reduces their reactivity towards electrophiles at low temperatures.[3] In contrast, the *S*-*tert*-butyl-substituted salts **1**–**5** are expected to exhibit a much higher reactivity towards electrophiles at low temperatures because of the reduced stabilization of the negative charge by the alkylsulfonyl as compared with the trifluoromethylsulfonyl group. Basic structural features of the salts *rac*-**1**–**5** are (1) a

[a] Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, 52056 Aachen, Germany
Fax: +49-241-8092665
E-mail: gais@rwth-aachen.de
[‡] Current address: Kelheim Fibres, Regensburger Strasse 109, 93309 Kelheim, Germany
[‡‡] Current address: DSM Nutritional Products Ltd., Wurmisweg 576, 4002 Kaiseraugst, Switzerland
[‡‡‡] Current address: ICG-1: Stratosphäre, Forschungszentrum Jülich, 52425 Jülich, Germany
[‡‡‡‡] Current address: Lummus Novolen Technology GmbH, Gottlieb-Daimler-Strasse 8, 68165 Mannheim, Germany
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201000410.

 WILEY InterScience DISCOVER SOMETHING GREAT © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

C_α–S conformation in which the lone-pair orbital at the anionic C atom bisects the O–S–O angle, (2) a planar C_α atom in the C_α-phenyl-substituted salts *rac*-**1**–**4** and a most probably planar one in the C_α-dialkyl-substituted salt *rac*-**5**,[1] (3) a stabilization of the negative charge by electrostatic interaction and negative hyperconjugation (n_C–σ^*_{StBu}), and (4) a stabilization of *rac*-**1**–**3** by benzylic conjugation.[1] Although the racemic salts *rac*-**1**–**5** exist in THF solution as mixtures of rapidly equilibrating monomeric and dimeric contact ion pairs (CIPs) with O–Li bonds,[4] they form mixtures of solvent-separated ion pairs (SIPs) and CIPs in the presence of hexamethylphosphoric triamide (HMPA), as demonstrated in the case of *rac*-**1**.[1] In contrast to the intensively investigated and synthetically important chiral α-heteroatom-substituted lithiumorganyls,[5] the salts *rac*-**1**–**5** do not exhibit a C_α–Li bond.[1]

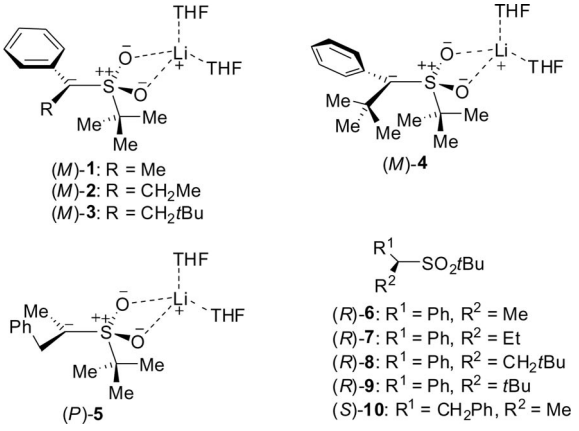
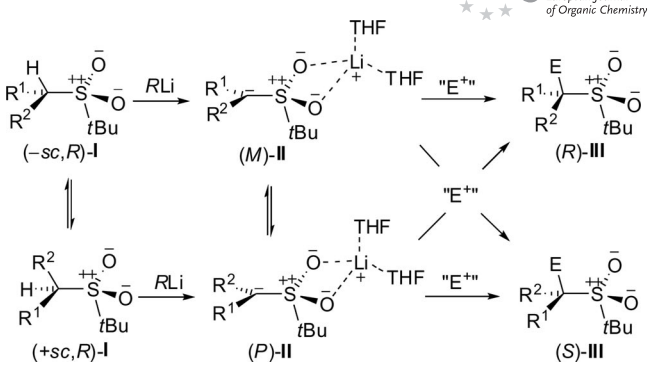


Figure 1. The chiral lithium α-*tert*-butylsulfonyl carbanion salts (*M*)-**1**–**4** and (*P*)-**5** and the sulfones (*R*)-**6**–**9** and (*S*)-**10**.

We envisioned an enantioselective synthesis of the salts (*M*)-**1**–**4** and (*P*)-**5** by deprotonation of the corresponding enantiopure sulfones (*R*)-**6**–**9** and (*S*)-**10** with a lithiumorganyl. In principle, the reaction of a sulfone of the type (*R*)-**I**, which has an α-stereogenic center, with RLi can give both enantiomeric salts (*M*)-**II** and (*P*)-**II**, which are endowed with a stereogenic axis (Scheme 1). Although deprotonation of rotamer (–*sc*,*R*)-**I** would yield the (*M*)-configured salt (*M*)-**II**, that of rotamer (+*sc*,*R*)-**I** could give the (*P*)-configured salt (*P*)-**II**. The reaction of a given enantiomer of salt **II** with an electrophile can in principle also lead to the formation of both enantiomers of the substituted sulfones **III**, as exemplified for (*M*)-**II** and its conversion into (*R*)-**III** and (*S*)-**III**. The key feature of the concept depicted in Scheme 1 is the use of chiral lithium α-sulfonyl carbanion salts **II**, which are configurationally stable and carry achiral ligands at the Li atom. This is in contrast to the realization of enantioselective reactions of chiral lithium α-sulfonyl carbanion salts coordinated by chiral ligands,[6] which follow a dynamic kinetic[6a] and dynamic thermodynamic resolution[6b,6c] pathway.[7]



Scheme 1. Enantioselective synthesis of lithium α-*tert*-butylsulfonyl carbanion salts from chiral sulfones and their reactions with electrophiles (priority: S > R^1 > R^2 > E).

To achieve a high overall enantioselectivity in the formation of **III**, the following points had to be addressed. First, is an enantioselective deprotonation of sulfones **6**–**10** with RLi feasible and what are the factors determining its selectivity? Secondly, what is the selectivity of the reactions of salts (*M*)-**1**–**4** and (*P*)-**5** with electrophiles? On the basis of the crystal structures of *rac*-**1**–**4** the salts are expected to react with electrophiles at the anionic C_α atom with high selectivity on the side *syn* to the O atoms because of the strong shielding of the opposite side by the *S*-*tert*-butyl group.[1] Thirdly, is the configurational stability of the salts (*M*)-**1**–**4** and (*P*)-**5** at low temperatures high enough that both the deprotonation of the corresponding sulfones (*R*)-**6**–**9** and (*S*)-**10** with RLi and the reactions of the salts with electrophiles can successfully compete with the racemization of the salts? Finally, sufficient configurational stability of the salts is also a prerequisite for an investigation of their racemization by physical measurements.

In this paper we describe the enantioselective synthesis of the salts (*M*)-**1**–**3** and (*P*)-**5** by the deprotonation of the corresponding enantiopure sulfones with lithiumorganyls. It will be shown that the enantioselectivity strongly depends on both the substituents of the sulfone and the nature of RLi. Furthermore, highly enantioselective reactions of the salts (*M*)-**1**–**3** and (*P*)-**5** with electrophiles are reported as well as the determination of the configurational stability of the salt (*P*)-**5** by polarimetry[8] and of the salts (*M*)-**1** and (*M*)-**2** by time-dependent deuteriation. The reactivity and enantioselectivity of the lithium *S*-*tert*-butylsulfonyl carbanion salts in these reactions are rationalized on the basis of the results of our previous investigation of their structures in solution and in the crystal form.[1] The enantioselective conversion of the chiral sulfone **I** via the corresponding chiral carbanion **II** to the substituted chiral sulfone **III** involves the loss of stereogenicity at the α-stereogenic center upon deprotonation and its re-establishment upon reaction of the chiral α-sulfonyl carbanion with an electrophile.[9] Although transformations of this type[10] are well documented for chiral enolates,[11] examples involving other chiral carbanions are very scarce.[12]

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Results and Discussion

Synthesis of Chiral *S*-*tert*-Butyl Sulfones

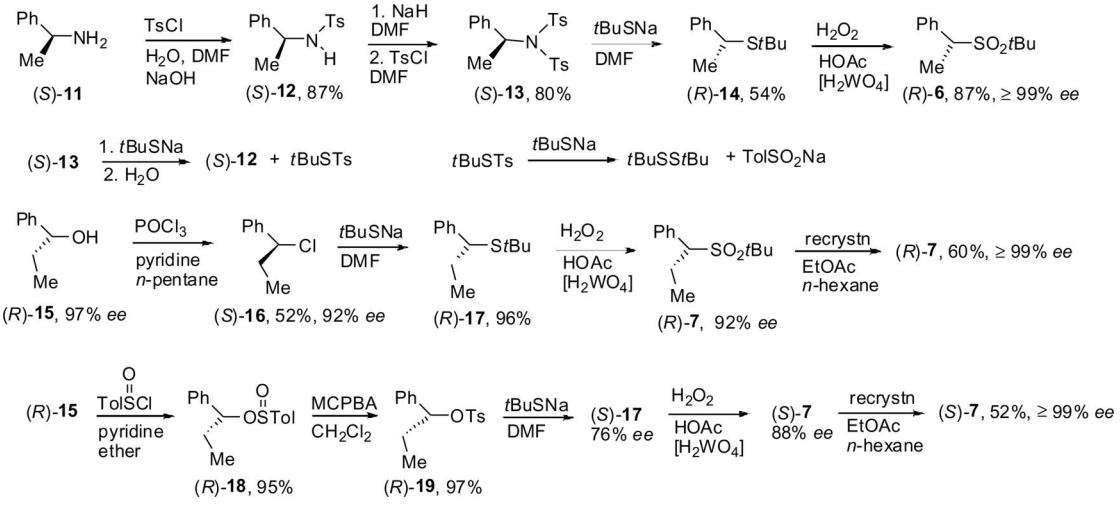
From Amines and Alcohols

The methyl-substituted sulfone (*R*)-**6** was synthesized starting from the enantiopure amine (*S*)-**11** in four steps, as shown in Scheme 2. Tosylation of amine (*S*)-**11** with ≥99% *ee* afforded sulfonamide (*S*)-**12** in 87% yield.[13] Deprotonation of (*S*)-**12** with sodium hydride and treatment of the corresponding sodium salt with TsCl gave bis-sulfonamide (*S*)-**13** in 80% yield.[13] The reaction of bis-sulfonamide (*S*)-**13** with NaS*t*Bu in DMF furnished sulfane (*R*)-**14**[14] in 54% yield. Sulfonamide (*S*)-**12** and 1,2-di-*tert*-butyldisulfane were isolated as side-products. Their formation is primarily due to a detosylation of (*S*)-**13** by the thiolate with the formation of (*S*)-**12** and *S*-*tert*-butyl tolylsulfonothioate, the latter of which reacts with the thiolate to form the disulfane and tolylsulfinate, as depicted in Scheme 2. Oxidation of sulfide (*R*)-**14** afforded sulfone (*R*)-**6** with ≥99% *ee* in 87% yield. The *ee* of (*R*)-**6** was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ using the *tert*-butyl signal and its ^{13}C satellites as an internal standard for the detection of (*S*)-**6**. This was confirmed by GC analysis of (*R*)-**6** and *rac*-**6** on a cyclodextrin phase.

The ethyl-substituted sulfone (*R*)-**7** was synthesized starting from alcohol (*R*)-**15** in three steps, as shown in Scheme 2. Alcohols (*R*)-**15** and (*S*)-**15** with 97 and 99% *ee* (GC, β- and γ-cyclodextrin phase), respectively, were obtained by application of a *Pseudomonas fluorescence* lipase catalyzed kinetic resolution of the corresponding racemic chloroacetate in 45 and 46% yields, respectively.[15] Treatment of (*R*)-**15** with POCl$_3$ in *n*-pentane in the presence of pyridine furnished chloride (*S*)-**16** with 92% *ee* (GC) in 52% yield.[16] β-Methylstyrene was formed as a side-product. In contrast, chlorination of alcohol (*R*)-**15** with SOCl$_2$ gave the (*R*)-configured chloride (*R*)-**16** with 32% *ee* and the reaction with TsCl in pyridine yielded (*S*)-**16** with only 71% *ee*. Treatment of chloride (*S*)-**16** (92% *ee*) with sodium *tert*-butylthiolate in DMF afforded sulfane (*R*)-**17** in 96% yield. Finally, oxidation of (*R*)-**17** furnished sulfone (*R*)-**7** with 92% *ee*. Recrystallization gave sulfone (*R*)-**7** with ≥99% *ee* in 60% yield. The *ee* of (*R*)-**7** was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ using the *tert*-butyl signal and its ^{13}C satellites as an internal standard for the detection of (*S*)-**7**.

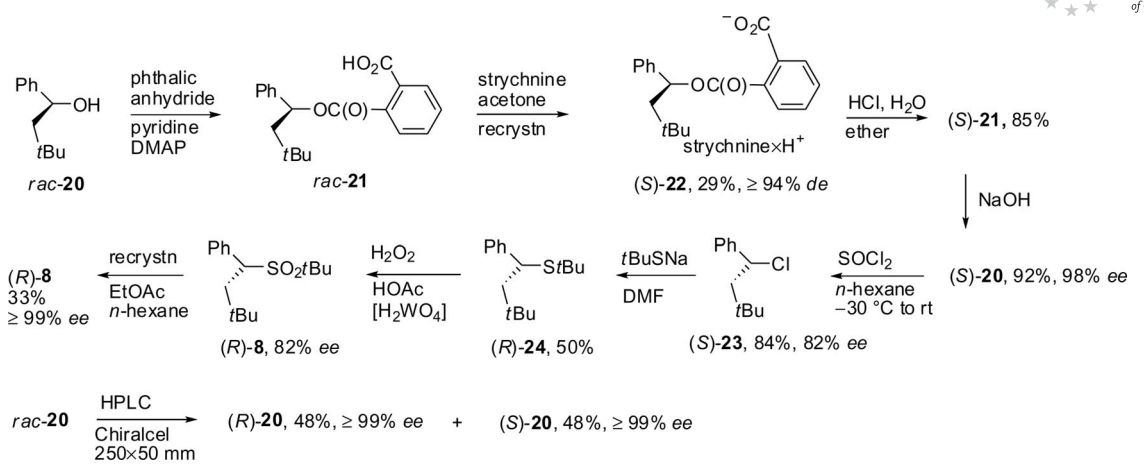
The synthesis of sulfone (*R*)-**7** involves two steps that proceed with an inversion of configuration. The omission of one of these steps could give access to the enantiomeric sulfone (*S*)-**7** provided, for example, tosylate (*R*)-**19** can be synthesized. Treatment of alcohol (*R*)-**15** with TsCl in pyridine did, however, not give tosylate (*R*)-**19** but chloride (*S*)-**16** with 71% *ee*. Therefore tosylate (*R*)-**19** was synthesized from alcohol (*R*)-**15** by a two-step procedure previously reported for the tosylation of tertiary alcohols.[17] Treatment of alcohol (*R*)-**15** (97% *ee*) with tolylsulfinyl chloride gave a mixture of the diastereomeric sulfinates (*R*)-**18** in 95% yield. Oxidation of (*R*)-**18** furnished the thermally labile tosylate (*R*)-**19** in 97% yield. Treatment of tosylate (*R*)-**19** with sodium *tert*-butylthiolate in DMF afforded sulfane (*S*)-**17** in 76% yield. Finally, oxidation of sulfane (*S*)-**17** gave sulfone (*S*)-**7** with 88% *ee*. Recrystallization afforded sulfone (*R*)-**7** with ≥99% *ee* in 52% yield.

The neopentyl-substituted sulfone (*R*)-**8** was synthesized starting from alcohol (*S*)-**20**, as shown in Scheme 3. Because the kinetic resolution of the chloroacetate of *rac*-**20** with enzymes including pig liver esterase, *Pseudomonas cepacia* lipase, *Pseudomonas fluorescence* lipase, lipase N, and lipase AK failed, a conventional resolution was carried out. Thus, the racemic alcohol *rac*-**20** was converted into the racemic phthalate *rac*-**21**, the resolution of which with various chiral amines including cinchonidine, cinchonine, brucine, strychnine, ephedrine, and 1-phenylethylamine was studied. The use of strychnine gave the salt (*S*)-**22** with ≥94% *de* (^{1}H NMR) in 29% yield. Cleavage of the salt (*S*)-**22** furnished the ester (*S*)-**21** in 85% yield, the hydrolysis of which afforded alcohol (*S*)-**20** with 98% *ee* (GC) in 92% yield. Alcohol (*S*)-**20** was converted into chloride (*S*)-**23** with 82%



Scheme 2. Synthesis of sulfones (*R*)-**6**, (*R*)-**7**, and (*S*)-**7**.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 3. Synthesis of sulfone (*R*)-**8**.

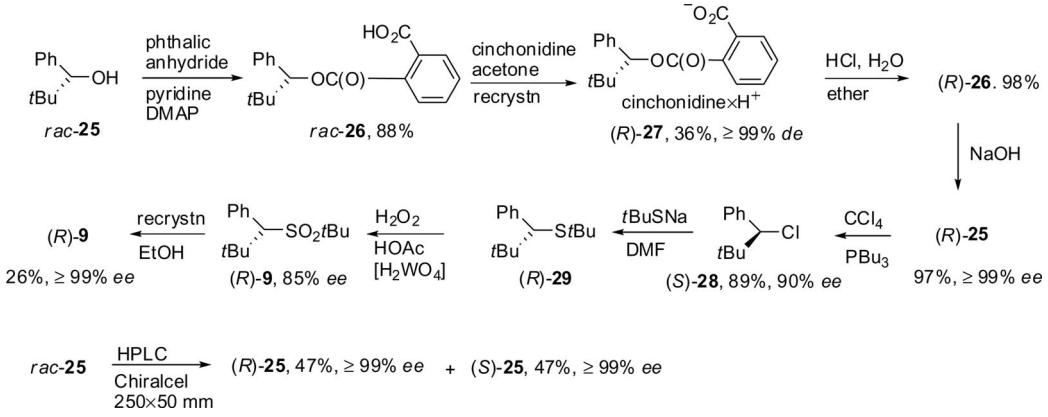
ee (GC) in 84% yield upon treatment with $SOCl_2$ at –30 °C to room temperature in *n*-hexane. The reaction conditions proved to be crucial for the attainment of chloride (*S*)-**23** with a reasonably high *ee* value. For example, reaction of (*S*)-**20** with neat $SOCl_2$ at –75 °C to room temperature afforded (*S*)-**23** with only 61% *ee*. Treatment of chloride (*S*)-**23** with sodium *tert*-butylthiolate gave sulfane (*R*)-**24** in 50% yield. In a competing reaction the chloride yielded β-*tert*-butylstyrene. Finally, oxidation of sulfane (*R*)-**24** furnished sulfone (*R*)-**8** with 82% *ee*. Recrystallization gave sulfone (*R*)-**8** with ≥99% *ee* in 33% yield. The *ee* of (*R*)-**8** was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ using the *tert*-butyl signal and its ^{13}C satellites as an internal standard for the detection of (*S*)-**8**. The configuration of (*R*)-**8** was assigned in analogy to that of (*R*)-**6** and (*R*)-**7** on the basis of both similar chiroptical properties and NMR spectroscopic behavior in the presence of Eu(hfc)$_3$.

The resolution of alcohol *rac*-**20** via the formation of the diastereomeric salts is cumbersome. Therefore *rac*-**20** was separated by preparative HPLC[18] on a Chiralcel column to give the enantiopure alcohols (*R*)-**20** and (*S*)-**20** in high yields.

The *tert*-butyl-substituted sulfone (*R*)-**9** was synthesized from alcohol (*R*)-**25**,[19] as outlined in Scheme 4. The alcohol was obtained by a conventional racemate separation. Thus, the racemic alcohol *rac*-**25** was converted into the racemic phthalate *rac*-**26** in 88% yield. Racemate separation of *rac*-**26** with cinchonidine afforded the salt (*R*)-**27** with ≥99% *de* in 36% yield.[19] Cleavage of the salt (*R*)-**27** gave the ester (*R*)-**26** in 98% yield, the hydrolysis of which furnished alcohol (*R*)-**25** with ≥99% *ee* (GC) in 97% yield. The chlorination of alcohol (*R*)-**25** with CCl_4/PBu_3 furnished the chloride (*S*)-**28** with 90% *ee* (GC) in 89% yield.[20] The chloride (*S*)-**28** was treated with sodium *tert*-butylthiolate in DMF to afford sulfane (*R*)-**29** in 90% yield. Finally, oxidation of sulfane (*R*)-**29** yielded sulfone (*R*)-**9** with 85% *ee*. Recrystallization gave sulfone (*R*)-**9** with ≥99% *ee* in 26% yield. The *ee* of (*R*)-**9** was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ using the *tert*-butyl signal and its ^{13}C satellites as an internal standard for the detection of (*S*)-**9**.

The resolution of alcohol *rac*-**25** via the formation of the diastereomeric salts is tedious. Therefore *rac*-**25** was separated by preparative HPLC on a Chiralcel column to give the enantiopure alcohols (*R*)-**25** and (*S*)-**25** in high yields.

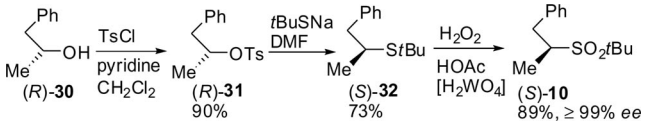
Finally, the methyl- and benzyl-substituted sulfone (*S*)-**10** was synthesized starting from alcohol (*R*)-**30** in three steps, as shown in Scheme 5. Alcohol (*R*)-**30** with 99% *ee* was obtained by application of a *Pseudomonas sp.* lipase



Scheme 4. Synthesis of sulfone (*R*)-**9**.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

catalyzed kinetic resolution of the corresponding racemic chloroacetate in 49% yield.[15] Treatment of tosylate (*R*)-**31**, which was prepared from alcohol (*R*)-**30** in 90% yield,[21] with sodium *tert*-butylthiolate in DMF afforded sulfane (*S*)-**32** in 73% yield. Oxidation of sulfane (*S*)-**32** furnished sulfone (*S*)-**10** with ≥99% *ee* in 89% yield. The *ee* of (*S*)-**10** was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ with the *tert*-butyl signal and its ^{13}C satellites as an internal standard for the determination of (*R*)-**10**.

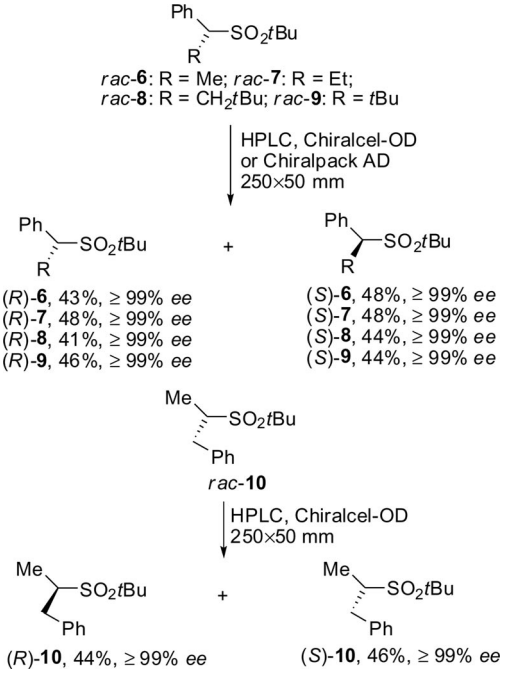


Scheme 5. Synthesis of sulfone (*S*)-**10**.

Through Chromatographic Resolution

The enantiopure sulfones **6**–**10** were synthesized by using a chiral starting material that was either commercially available or prepared by resolution. However, each synthesis included one or two crucial nucleophilic substitution steps involving the stereogenic center. On the other hand, the racemic sulfones *rac*-**6**–**10** are readily accessible starting either from the corresponding chlorides and/or by deprotonation/alkylation of the parent sulfones.[1] Thus, the preparative resolution of the racemic sulfones by HPLC on a chiral column was investigated as a perhaps attractive alternative for the attainment of the enantiopure sulfones.

Preparative HPLC of sulfones *rac*-**6**–**10** on a Chiralcel-OD column (250 mm × 50 mm) gave the corresponding sulfones (*R*)-**6**, (*S*)-**6**, (*R*)-**7**, (*S*)-**7**, (*R*)-**8**, (*S*)-**8**, (*R*)-**9**, (*S*)-**9**, (*R*)-**10**, and (*S*)-**10** all with ≥99% *ee* in high yields (Scheme 6). Because of the ready separation of the enantiomers, the attainment of the enantiopure sulfones on a multigram scale should pose no problems.



Scheme 6. Preparation of sulfones (*R*)-**6**, (*S*)-**6**, (*R*)-**7**, (*S*)-**7**, (*R*)-**8**, (*S*)-**8**, (*R*)-**9**, (*S*)-**9**, (*R*)-**10**, and (*S*)-**10** by chromatographic resolution.

Structures and Dynamics of the *S-tert*-Butyl Sulfones

X-Ray Crystal Structure Analysis

Because of the possible dependence of the selectivity of the deprotonation of the sulfones **6**–**10** upon their C_α–S conformation (cf. Scheme 1), information about the structures of *S-tert*-butyl sulfones of this type was desirable. Furthermore, knowledge of the bonding parameters of the sulfones was required to evaluate the changes that occur upon deprotonation to yield the corresponding salts.[1] Therefore an X-ray crystal structure analysis of the C_α-phenyl-substituted sulfones (*R*)-**9** and *rac*-**33** and C_α-dialkyl-substituted sulfone (*S*)-**10**, as representative examples, was carried out (see Figures 2, 3, and 4).[22] Sulfones (*R*)-**9**,

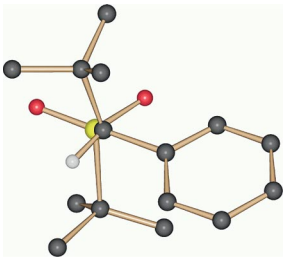


Figure 2. View of the crystal structure of sulfone (*R*)-**9** with H atoms and THF molecules omitted for clarity. Color code: C, black; S, yellow; O, red; H, grey.

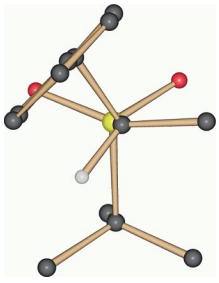


Figure 3. View of the crystal structure of sulfone (*S*)-**10** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red; H, grey.

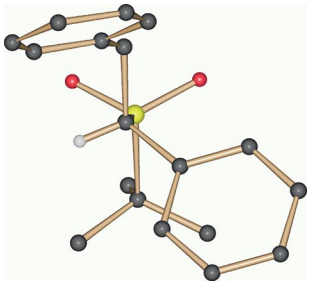
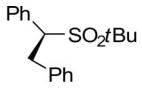


Figure 4. View of the crystal structure of sulfone *rac*-**33** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red; H, white [(*R*)-**33** is shown].

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(*S*)-**10**, and *rac*-**33** all adopt a similar C_α–S conformation in the crystal form in which (1) the benzyl and *tert*-butyl groups at the C_α atom are approximately antiperiplanar to the *S*-*tert*-butyl group, (2) the H atom at the C_α atom is approximately *gauche* to the *S*-*tert*-butyl group, and (3) the phenyl and methyl groups are also *gauche* to the *S*-*tert*-butyl group (Table 1). Although the bond lengths and angles of (*S*)-**10** and *rac*-**33** are similar, those of the C_α-*tert*-butyl-substituted sulfone (*R*)-**9** are significantly different. Presumably for steric reasons, the bonds of the C_α atom of (*R*)-**9** are longer and the S–C_α–*t*Bu bond angle is larger than the corresponding bonds and angles of (*S*)-**10** and *rac*-**33**.



rac-**33**

Table 1. Selected bond lengths, bond angles, and dihydral angles of sulfones (*R*)-**9**, (*S*)-**10**, and *rac*-**33**.

Parameter	(*R*)-**9**	(*S*)-**10**	*rac*-**33**
S–C_α [Å]	1.820(4)	1.821(3)	1.826(3)
S–*t*Bu [Å]	1.862(20)	1.828(3)	1.822(3)
S–O [Å]	1.433(17), 1.426(3)	1.445(2), 1.448(2)	1.454(2), 1.443(2)
C_α–Ci(Me) [Å]	1.528(18)	1.508(4)	1.507(4)
C_α–CH_2Ph(*t*Bu) [Å]	1.605(20)	1.534(4)	1.543(4)
*t*Bu–S–C_α [°]	105.7(2)	107.9(1)	110.7(1)
C_i(Me)–C_α–CH_2Ph(*t*Bu) [°]	115.1(6)	112.2(2)	114.2(2)
S–C_α–C_i(Me) [°]	111.7(9)	111.7(2)	113.8(2)
S–C_α–CH_2Ph(*t*Bu) [°]	113.4(9)	108.4(2)	104.8 (2)
*t*Bu–S–C_α–CH_2Ph(*t*Bu) [°]	–163.0(5)	–146.9(2)	180.0(2)

NMR Spectroscopy

Having obtained information about the structures of (*R*)-**9**, (*S*)-**10**, and *rac*-**33** in the crystal form, knowledge of the conformational behavior of *S*-*tert*-butyl sulfones of this type in solution was required. Therefore the C_α-phenyl-substituted sulfones *rac*-**6**–**9** were studied by NMR spectroscopy. In contrast to the methyl- and ethyl-substituted benzylic sulfones *rac*-**6** and *rac*-**7**, respectively, the ^{1}H and ^{13}C NMR spectra of the neopentyl- and *tert*-butyl-substituted benzylic sulfones *rac*-**8** and *rac*-**9**, respectively, in [D_6]-benzene indicated hindered rotation around the C_α–phenyl bond. Whereas the H_o and C_o signals of the neopentyl-substituted sulfone *rac*-**8** were very broad at room temperature, those of the C_α-*tert*-butyl-substituted sulfone *rac*-**9** were each split into two signals. High-temperature NMR spectroscopy of sulfone *rac*-**9** in [D_{14}]diglyme at 100 °C did not show any change in the shift difference between the H_o/$H_{o'}$ and C_o/$C_{o'}$ signals nor line-broadening. By assuming a coalescence temperature of 150 °C for the H_o/$H_{o'}$ signals of *rac*-**9**, the activation free energy for the C_α-phenyl rotation $\Delta G^{\ddagger}_{rot}$ is estimated[23] to be 19.5 kcal mol^{-1} at 423 K. The high C_α–Ph barrier is a reflection of the fixation of the phenyl group by the bulky *tert*-butyl and *tert*-butylsulfonyl groups.[24]

A first indication that sulfones *rac*-**6**–**9** preferentially adopt in solution a conformation similar to those attained by (*R*)-**9**, (*S*)-**10**, and *rac*-**33** in the crystal form is provided by the chemical shifts of the *S*-*tert*-butyl signals. Whereas the *S*-*tert*-butyl signals of the phenyl-substituted sulfones *rac*-**6**–**9** in $CDCl_3$ appeared at 1.11–1.21 ppm that of the C_α-dialkyl-substituted sulfone *rac*-**10** showed up at 1.40–1.50 ppm. The significant upfield shift of the *S*-*tert*-butyl signals of the C_α-phenyl-substituted sulfones can be attributed to the anisotropic effect of the phenyl group, which is *gauche* to the *S*-*tert*-butyl group.

^{1}H{^{1}H} NOE experiments on sulfones *rac*-**6**–**9** in [D_6]-benzene at room temperature gave further proof of the preferred conformation of the sulfones, which is characterized by the C_α-H atom and the phenyl group both being *gauche* to the *S*-*tert*-butyl group (Figure 5). Although strong NOEs were observed between the *S*-*tert*-butyl group and both the C_α-H atom and H_o of the phenyl group, no NOEs were recorded between the *S*-*tert*-butyl and C_α-methyl, C_α-ethyl, C_α-neopentyl, and C_α-*tert*-butyl groups, respectively.

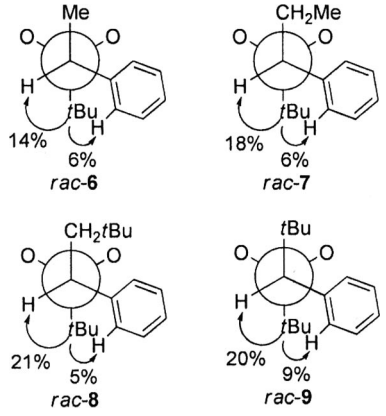


Figure 5. NOEs of sulfones *rac*-**6**–**9** (charges on the O and S atoms have been omitted for clarity) [(*R*) configuration is shown].

Ab Initio Calculations

NMR spectroscopy of sulfones *rac*-**6**–**9** at low temperatures gave no indication of the equilibria formed between different conformers. Therefore ab initio calculations on the C_α-methyl- and phenyl-substituted sulfone **6**[25] were carried out to obtain information about the relative energies of the conformers. Calculations at the ZPE+MP2/6-31+G*//MP2/6-31+G* level[26] identified the three conformers **6A**, **6B**, and **6C** (Figure 6) with relative energies of +3.23, 0.00, and +4.05 kcal mol^{-1}, respectively. Conformer **6B**, which has the lowest energy, has the phenyl group *gauche* to the *S*-*tert*-butyl group and the methyl group *gauche* to both O atoms. It thus resembles the conformation of *rac*-**6** in solution as revealed by NOE experiments and adopted by the C_α-benzyl-substituted sulfone *rac*-**33** in the crystal form. The calculated energy difference between the conformers correlates with the nonobservance of a conformational equilibrium for *rac*-**6**. In summary, all available evidence points to a preferred C_α–S conformation of the substituted benzylic *S*-*tert*-butyl sulfones in which the H atom and the phenyl group are *gauche*

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

to the *S*-*tert*-butyl group and the alkyl group is *gauche* to both O atoms. The dialkyl-substituted *S*-*tert*-butyl sulfones seem to preferentially adopt a C_α–S conformation in which the larger alkyl group is *gauche* to both O atoms.

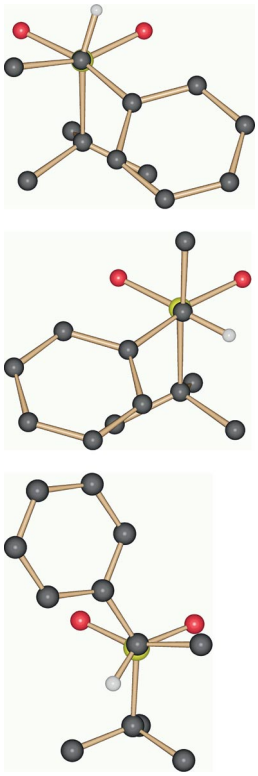


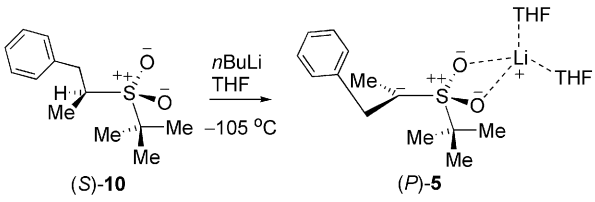
Figure 6. Views of the structures of conformers **6A** (top), **6B** (middle), and **6C** (bottom) of sulfone **6** determined by ab initio calculations. Color code: C, black; S, yellow; O, red; H, grey [(*R*)-configuration is shown].

Configurational Stability of Lithium α-*tert*-Butyl-Sulfonyl Carbanion Salts

DNMR spectroscopy of the salts *rac*-**2**, *rac*-**3**, and *rac*-**5** had given an estimate of the free energy of activation for their enantiomerization. The other activation parameters had not been ascertained by the DNMR experiments or are, because of a lack of diastereotopic H atoms, not accessible by this method. Therefore the enantioselective synthesis of salts (*M*)-**1**, (*M*)-**2**, and (*P*)-**5** was studied and the determination of their racemization dynamics attempted by two different methods, directly by polarimetry and indirectly by time-dependent deuteriation.

Determination by Polarimetry

DNMR spectroscopy of the dialkyl-substituted *S*-*tert*-butyl salt *rac*-**5** in [D_8]THF derived from sulfone *rac*-**10** revealed an activation free energy of enantiomerization $\Delta G^{\ddagger}_{enant}$ of 13.6 ± 0.2 kcal mol^{-1} at 288 K. Therefore the salt (*P*)-**5** was selected for polarimetric experiments at low temperatures. The reaction of sulfone (*S*)-**10** (≥99% *ee*) with *n*BuLi in THF at –105 °C proceeded enantioselectively and gave the nonracemic (*P*)-configured lithium salt (*P*)-**5** (see below) with an optical rotation $[\alpha]^{-86}_{546}$ of 16.0 (*c* = 2.08, THF) (Scheme 7). The optical rotation fell to zero within 20 min at –86 °C and quenching of the solution of the salt with CF_3CO_2D furnished the racemic sulfone *rac*-[D]**10** with a D content of ≥98% in 93% yield.



Scheme 7. Enantioselective synthesis of the salt (*P*)-**5**.

The observation of an optical rotation for (*P*)-**5** provided a tool for the determination of its racemization kinetics. Racemization of (*P*)-**5** in THF was polarimetrically monitored at –86 °C as a function of time by using a special polarimeter tube with a cooling jacket and vacuum windows made of quartz glass to prevent their icing. Furthermore, a stream of nitrogen was directed towards the windows during measurement. The salt (*P*)-**5** was prepared from sulfone (*S*)-**10** (≥99% *ee*) and *n*BuLi in THF at –105 °C and the solution of the salt was rapidly transferred to the tube through a steel cannula, which had been cooled to –100 °C in a liquid nitrogen/EtOH cooling bath. The temperature of the THF solution of the salt (*P*)-**5** was internally measured with a digital thermometer. A plot of $\ln \alpha_o/\alpha_t$ versus time for the salt showed a good linearity over four half-lives (Figure 7), which indicates that racemization follows first-order kinetics and the existence of a linear relationship between [*α*] and the concentration of (*P*)-**5**.

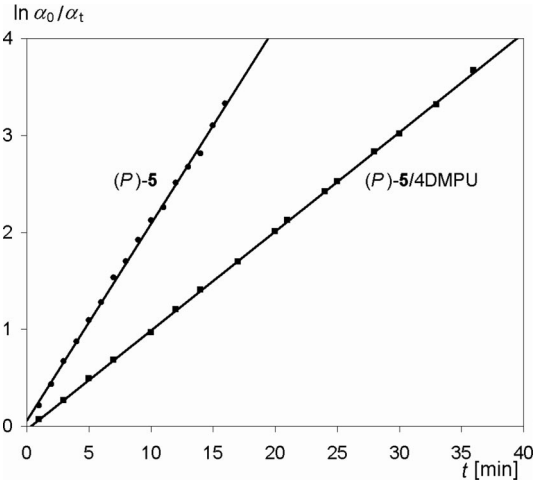


Figure 7. Polarimetric determination of the racemization of the salts (*P*)-**5** and (*P*)-**5**·4DMPU in THF at –86 °C.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

The macroscopically observable process of racemization is regarded as an irreversible transformation of the optically active species into the racemate according to Equation (1). The time-dependence of the optical rotation is described by Equation (2).

$$2\ (P)\text{-}\mathbf{5} \rightarrow (P)\text{-}\mathbf{5} + (M)\text{-}\mathbf{5} \quad (1)$$

$$\ln \alpha_o/\alpha_t = -k_{rac}t \quad (2)$$

From the slope of the plot of $\ln \alpha_o/\alpha_t$ versus t the rate constant for racemization k_{rac} was deduced to be $(3.42 \pm 0.2) \times 10^{-3}$ s^{-1} at 187 K. The half-life for the racemization $\tau_{½rac}$ of (*P*)-**5** is 3.4 ± 2 min at 187 K. The Eyring equation gave an activation free energy $\Delta G^{‡}_{rac}$ of 12.9 ± 0.1 kcal mol^{-1} for the racemization at 187 K. Because of the insufficient capacity of our cryostat for polarimetric experiments of (*P*)-**5** at temperatures below –90 °C, the temperature range for temperature-dependent measurements was too small. Thus, the racemization of (*P*)-**5** in THF in the presence of 4 equiv. of *N*,*N*-dimethylpropylurea (DMPU) was polarimetrically monitored at –86 °C as a function of time in the hope that the coordination of the lithium salt by DMPU would, as in the case of hexamethylphosphoric triamide (HMPA),[1] lead to an increase in the racemization barrier. A plot of $\ln \alpha_o/\alpha_t$ versus time showed good linearity over seven half-lives, which indicates that the racemization of the salt follows first-order kinetics. This gave the kinetic parameters for the racemization of (*P*)-**5**/4DMPU: $k_{rac} = (1.70 \pm 0.1) \times 10^{-3}$ s^{-1} at 187 K, $\tau_{½rac}$ = 6.8 ± 3 min, and $\Delta G^{‡}_{187}$ = 13.1 ± 0.1 kcal mol^{-1}. Thus, the rate constants for the racemization of (*P*)-**5**/4DMPU and (*P*)-**5** differ by a factor of two, which allowed temperature-dependent measurements in the range of –76.5 to –88.5 °C. The results of the measurements at six different temperatures are collected in Table 2.

Table 2. Rate constants (k_{rac}) and half-lives ($\tau_{½}$) for the racemization of the salt (*P*)-**5**·4DMPU in THF at low temperatures.

T [°C]	T^{-1} [10^{-3} K^{-1}]	k_{rac} [10^{-3} s^{-1}]	$\tau_{½}$ [min]
–76.6	5.085	11.1	1.0
–80.0	5.177	5.56	2.1
–81.5	5.218	4.59	2.5
–83.5	5.273	2.91	4.0
–86.5	5.358	1.70	6.8
–88.5	5.416	1.14	10.2

The Eyring plot of $\log(k_{rac}/T)$ versus $1/T$ showed good linearity (Figure 8). Calculation gave the activation parameters $\Delta H^{‡}_{rac}$ = 13.2 ± 0.3 kcal mol^{-1}, $\Delta S^{‡}_{rac}$ = 0.6 ± 1.2 cal mol^{-1} K^{-1}, and $\Delta G^{‡}_{rac}$ = 13.0 ± 0.3 kcal mol^{-1} at 298 K and $\Delta G^{‡}_{rac}$ = 13.1 ± 0.3 kcal mol^{-1} at 193 K. Because of the previous determination of the enantiomerization barrier for *rac*-**5** ($\Delta G^{‡}_{enant}$ = 13.6 ± 0.2 kcal mol^{-1} at 298 K) by DNMR spectroscopy,[1] the activation parameter $\Delta G^{‡}_{enant}$ for the enantiomerization ($k_{rac} = 2k_{enant}$) of *rac*-**5**·4DMPU was calculated to be 13.5 ± 0.3 kcal mol^{-1} at 298 K. The half-life for the racemization of the salt (*P*)-**5**·4DMPU is 6.8 ± 3 min at 187 K and 2.4 h at 168 K.

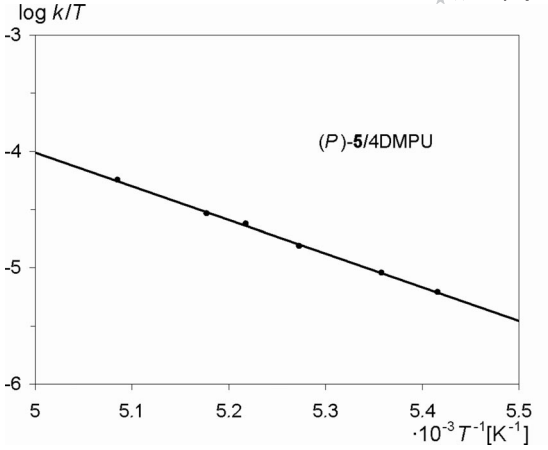
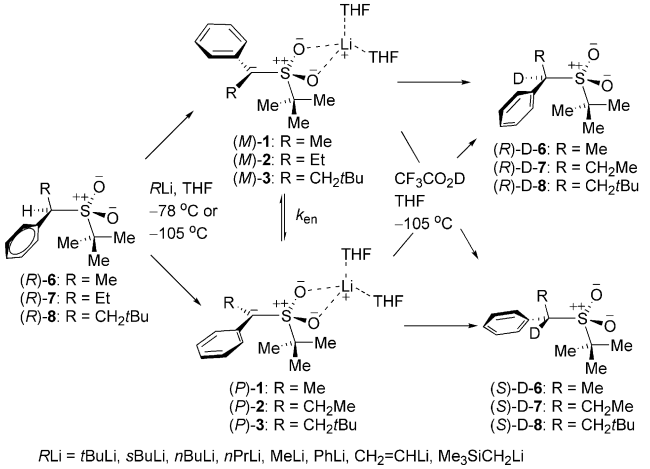


Figure 8. Eyring plot of the racemization of the salt (*P*)-**5**·4DMPU in THF.

Determination by Time-Dependent Deuteriation

The time-dependent deuteriation of the nonracemic salts provides an independent and less costly alternative means to obtain information about their racemization dynamics. To determine the racemization dynamics of the benzylic lithium *S*-*tert*-butylsulfonyl carbanion salts **1** and **2** by time-dependent deuteriation, the successive deprotonation of the enantiopure sulfones (*R*)-**6** and (*R*)-**7** and deuteriation of the corresponding salts after a given time with the formation of sulfones [D]**6** and [D]**7**, respectively, were studied (Scheme 8). Sulfones (*R*)-**6** and (*R*)-**7** were treated with *t*BuLi in THF at –105 °C and after 15 and 25 min, respectively, had elapsed the corresponding salts (*M*)-**1** and (*M*)-**2** were deuteriated at –105 °C with CF_3CO_2D, which gave the corresponding sulfones (*R*)-[D]**6** and (*R*)-[D]**7** with 86 and 93% *ee*, respectively, with a D content of ≥99%. Both reactions were performed under standard conditions and special experimental precautions were taken to ensure that the reactions were conducted at –105 °C. These results show that both deprotonation and deuteriation occurred with high selectivity and proceeded with an overall retention of



Scheme 8. Enantioselective synthesis and deuteriation of the salts (*M*)-**1**–**3**.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

configuration. Therefore it is proposed that deprotonation of the (*R*)-configured sulfones (*R*)-**6** and (*R*)-**7** with *t*BuLi gave with high selectivity the corresponding (*M*)-configured salts (*M*)-**1** and (*M*)-**2**, the deuteriation of which also proceeded with high selectivity to yield the corresponding sulfones (*R*)-[D]**6** and (*R*)-[D]**7** (see below). The isolation of sulfone (*R*)-[D]**7** with 93% *ee* implies that both the deprotonation of (*R*)-**7** and the deuteriation of (*M*)-**2** occurs, for example, with a calculated selectivity of 96% *ee*.

The *ee* values of the deuteriated sulfones (*R*)-[D]**6** and (*R*)-[D]**7** are a function of (1) the selectivity of the deprotonation of the corresponding sulfones (*R*)-**6** and (*R*)-**7**, (2) the selectivity of the deuteriation of the corresponding salts (*M*)-**1** and (*M*)-**2**, and (3) the extent of racemization of the salts. On the basis of these considerations the activation free energies for the enantiomerization/racemization of (*M*)-**1** and (*M*)-**2** were determined. Although the kinetic parameter for the enantiomerization of *rac*-**2** had already been estimated by DNMR spectroscopy,[1] that of the C_α-methyl-substituted salt *rac*-**1** is not accessible by this method. A series of deprotonation–deuteriation experiments was performed in which all experimental parameters, including those of deprotonation and deuteriation, were kept constant except the time that elapsed after the addition of *t*BuLi to the sulfones (*R*)-**6** and (*R*)-**7** and the beginning of the addition of CF_3CO_2D to the salts (*M*)-**1** and (*M*)-**2**, the racemization time t_{rac}. Under these conditions the enantioselectivities of deprotonation and deuteriation are constant and the decrease in the *ee* values for (*R*)-[D]**6** and (*R*)-[D]**7** only depends on t_{rac}. By assuming first-order kinetics for the racemization of (*M*)-**1** and (*M*)-**2**, the *ee* values for (*R*)-[D]**6** and (*R*)-[D]**7** can be described by Equation (3) and Equation (4).

$$ee_{D\text{–sulfone}}(t_{rac}) = ee_0 e^{-k_{rac}t_{rac}} \quad (3)$$

$$\ln ee_{D\text{–sulfone}}(t_{rac}) = \ln ee_0 - k_{rac}t_{rac} \quad (4)$$

However, it is not possible to give the exact time for the completion of the deprotonation of sulfones (*R*)-**6** and (*R*)-**7** and the deuteriation of (*M*)-**1** and (*M*)-**2** in these experiments. Deuteriation experiments had shown that the deprotonation of sulfones (*R*)-**6** and (*R*)-**7** with *t*BuLi in THF at –105 °C was complete after 10 min. The deuteriation of salts (*M*)-**1** and (*M*)-**2** is a fast process and the termination of the racemization of the salt is practically determined by the time required for the addition of the acid. Thus, t_{0rac} was set to 15 min, which included 5 min each for the addition of *t*BuLi and CF_3CO_2D and 5 min for the completion of the deprotonation. In further experiments the time for the addition of the base and the deuteriation reagent was kept constant and the time between the additions of both was increased. This leads to Equations (5) and (6), which allow the determination of k_{rac}. Four deprotonation–deuteriation experiments were performed with sulfones (*R*)-**6** and (*R*)-**7** with variation of the racemization time from 15 to 305 min (Table 3) under otherwise identical conditions for each sulfone.

$$ee_{D\text{–sulfone}}(t_{rac}) = ee(t_{0rac})e^{-k_{rac}(t_{rac} - t_{0rac})} \quad (5)$$

$$\ln ee_{D\text{–sulfone}}(t_{rac} - t_{0rac}) = \text{const} - k_{rac}(t_{rac} - t_{0rac}) \quad (6)$$

Table 3. Values of *ee* for the sulfones (*R*)-[D]**6** and (*R*)-[D]**7** and their dependence on the racemization time t_{rac} for the salts (*M*)-**1** and (*M*)-**2**.

(*R*)-[D]**6**			(*R*)-[D]**7**		
$t_{rac} - t_{0rac}$ [min]	t_{rac} [min]	*ee* [%]	$t_{rac} - t_{0rac}$ [min]	t_{rac} [min]	*ee* [%]
0	15	86	0	25	93
50	65	78	35	60	92
140	155	60	125	150	89
290	305	40	275	300	85

From the slope of the linear plot of $\ln ee_{D\text{–sulfone}}$ versus $t_{rac} - t_{0rac}$ (Figure 9) the rate constant k_{rac} was determined and the activation free energy at 168 K calculated with the aid of the Eyring equation (Table 4).

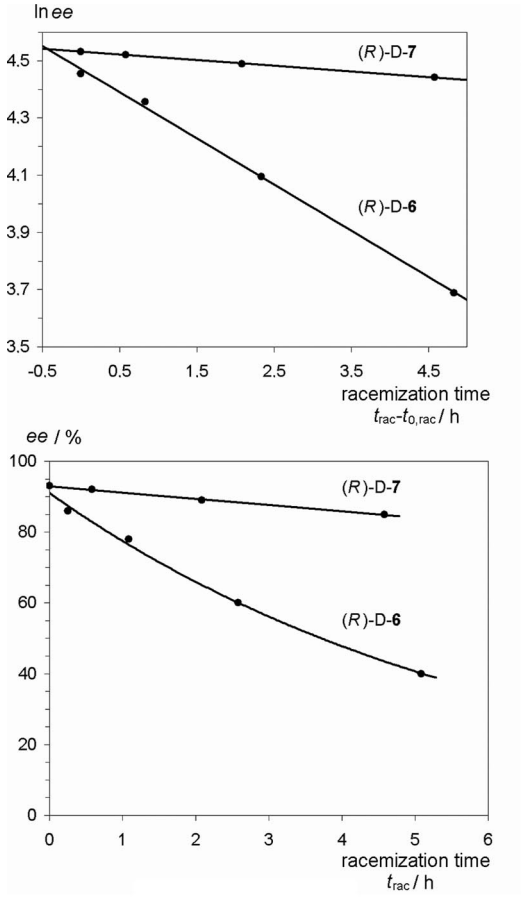


Figure 9. Plot of $\ln ee$ of sulfones [D]**6** and [D]**7** as a function of the racemization time $t_{rac} - t_{0rac}$ of the corresponding salts (*M*)-**1** and (*M*)-**2** in THF at –105 °C (top) and the plot of *ee* of sulfones [D]**6** and [D]**7** as a function of the racemization time t_{rac} of the corresponding salts (*M*)-**1** and (*M*)-**2** in THF at –105 °C (bottom).

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Table 4. Dynamic parameters for the racemization of the salts (*M*)-**1**, (*M*)-**2**, and (*P*)-**5**·4DMPU at 168 K.

Parameter	(*M*)-**1**	(*M*)-**2**	(*P*)-**5**·4DMPU
k_{rac} [s^{-1}]	4.48×10^{-5}	5.51×10^{-6}	7.61×10^{-5}
$\Delta G^{\ddagger}_{rac}$ [kcal mol^{-1}]	13.0 ± 0.2	13.7 ± 0.2	13.1 ± 0.3
$\tau_{½rac}$ [h]	4.3	34.9	2.4
$\Delta H^{\ddagger}_{rac}$ [kcal mol^{-1}]	–	–	13.2 ± 0.3
$\Delta S^{\ddagger}_{rac}$ [cal mol^{-1} K^{-1}]	–	–	0.6 ± 1.2

Whereas the enantiomerization barrier for the salt (*M*)-**2**, as derived from the time-dependent deuteriation experiments, is 13.9 ± 0.2 kcal mol^{-1} at 168 K, that obtained by DNMR spectroscopy of the racemic salt is 14.2 ± 0.3 kcal mol^{-1} at 295 K (that is, at different temperatures).[1] The significantly lower activation barrier for the methyl-substituted salt as compared to its ethyl-substituted analogue is in accordance with the results of the DNMR spectroscopic studies, which showed that the enantiomerization barriers for salts of the type [Ph-C(R_α)-SO_2*t*Bu]$^-$Li$^+$ increase with increasing steric demand of the substituent R_α.[1] This supports the notion that the enantiomerization of the salts (*M*)-**1** and (*M*)-**2** is mainly an enthalpic process with a small negative activation entropy, as is to be expected for a process in which C_α–S bond rotation is rate-determining. Insertion of the values of k_{rac} and *ee* (t_{0rac}) into Equation (5) gave the curves in Figure 9 (bottom) on the assumption that *ee* (t_{0rac}) = 87% for sulfone (*R*)-[D]**6** instead of the measured value of 86%. The calculated curves are in good agreement with the experimental data and support the notion of first-order racemization kinetics for the lithium salts. Extrapolation of the curves to t_{rac} = 0 shows that the stereoselectivities of the deprotonation and deuteriation are very high. Thus, the *ee* values for sulfones (*R*)-[D]**6** and (*R*)-[D]**7** in the absence of any racemization of the salts would be at least 91 and 94% *ee*, respectively.

Enantioselective Deprotonation of Sulfones and Deuteriation of C_α-Phenyl-Substituted Lithium α-*tert*-Butylsulfonyl Carbanion Salts

The experiments with the salts (*M*)-**1** and (*M*)-**2** revealed a relatively high configurational stability at low temperatures (<–100 °C) and the feasibility of their enantioselective synthesis. To obtain a more general picture, the following questions had to be addressed. First, what is the dependence of the enantioselectivity of the deprotonation of the enantiopure sulfones on both the structure of the sulfone and the nature of the lithiumorganyl used in the deprotonation? Secondly, what is the enantioselectivity of the reactions of the lithium salts with electrophiles? Thirdly, is the configurational stability of the salts sufficiently high with regard to the timescale of their reactions with C-electrophiles? Therefore sulfones (*R*)-**6–8**, which all carry a phenyl and an alkyl group at the C_α atom, were deprotonated with various lithiumorganyls followed by deuteriation of the corresponding salts **1**–**3** (cf. Scheme 8, Tables 5, 6, and 7). The deprotonation and deuteriation experiments were both carried out in a standardized fashion. The methyl- and ethyl-substituted sulfones (*R*)-**6** and (*R*)-**7** were deprotonated in THF at –105 °C and the neopentyl- and *tert*-butyl-substituted sulfones (*R*)-**8** and (*R*)-**9** at –78 °C. The metalation times t_{met} (time that elapses between the addition of the base and the deuteriation reagent) given in Tables 5–7 were specifically selected to ensure both complete deprotonation and maximum suppression of the racemization (≤1%) of the corresponding salts. Solutions of the lithiumorganyl and CF_3CO_2D were both slowly added under film-cooling (see the Supporting Information) to the solution of the sulfone and salt, respectively, to establish for both deprotonation and deuteriation a reaction temperature of –105 °C, which was internally measured by using a fast responding digital thermometer. The *ee* values of the deuteriated sulfones (*R*)-[D]**6–8** and [D]**9** were determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ using the *S*-*tert*-butyl signal. The degree of deuteriation of the sulfones was determined by ^{1}H NMR spectroscopy.

Table 5. Deprotonation of sulfone (*R*)-**6** with ≥99% *ee* with RLi in THF at –105 °C and deuteriation of the salt **1** with CF_3CO_2D.

Entry	RLi, solvent	t_{met}[a] [min]	Sulfone [D]**6** D content [%]/%	*ee* [%]	Conf.
1	*t*BuLi, *n*-pentane	15	≥98	87	*R*
2	*s*BuLi, cyclohexane	15	≥98	48	S
3	*n*BuLi, *n*-hexane	10	≥98	60	S
4	*n*PrLi, *n*-pentane	10	95	50	S
5	MeLi, THF	80	≥98	8	*R*
6	PhLi, Et_2O	45	≥98	72	*R*
7	CH_2=CHLi, Et_2O	90	84	57	*R*
8	Me_3SiCH_2Li, *n*-pentane	20	98	80	*R*
9	*t*BuLi, *n*-pentane	35	97	85	*R*

[a] Time elapsed between the beginning of the addition of RLi and CF_3CO_2D.

Table 6. Deprotonation of sulfone (*R*)-**7** with ≥99% *ee* with RLi in THF at –105 °C and deuteriation of the salt **2** with CF_3CO_2D.

Entry	RLi, solvent	t_{met}[a] [min]	Sulfone [D]**7** D content [%]	*ee* [%]	Conf.
1	*t*BuLi, *n*-pentane	25	99	93	*R*
2	*s*BuLi, cyclohexane	15	98	78	*R*
3	*n*BuLi, *n*-hexane	10	98	35	S
4	*n*PrLi, *n*-pentane	10	96	25	S
5	MeLi, THF	40[b]	95	0	–
6	PhLi, Et_2O	90	99	87	*R*
7	CH_2=CHLi, Et_2O	90	87	71	*R*
8	Me_3SiCH_2Li, *n*-pentane	20	0	–	–
9	*t*BuLi, *n*-pentane	–	–	–	–

[a] Time elapsed between the beginning of the addition of RLi and CF_3CO_2D. [b] Not optimized.

Tables 5–7 show that the time required for complete deprotonation of sulfones (*R*)-**6–8** with a given lithiumorganyl increases with increasing steric demand of the substituent R_α at the C_α atom. For example, whereas the deprotonation reactions of sulfones (*R*)-**6** and (*R*)-**7** with *n*BuLi at –105 °C were complete within 10 min (Table 5, entry 3 and Table 6, entry 3), the reaction of the neopentyl-substituted sulfone

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Table 7. Deprotonation of sulfone (*R*)-**8** with ≥99% *ee* with RLi in THF at –78 °C and deuteriation of the salt (*M*)-**3** with CF_3CO_2D.

Entry	RLi, solvent	t_{met}[a] [min]	Sulfone [D]**8**		
			D content [%]	*ee* [%]	Conf.
1	*n*BuLi, *n*-hexane	65	96	90	*R*
2	MeLi, THF	60	90	91[b]	*R*

[a] Time elapsed between the beginning of the addition of RLi and CF_3CO_2D. [b] Sulfone (*R*)-**8** with 66% *ee* was used and sulfone (*R*)-[D]**8** with 60% *ee* was isolated.

(*R*)-**8** required 65 min at –78 °C (Table 7, entry 1). This effect was even more pronounced with the use of Me_3SiCH_2Li. Whereas the methyl-substituted sulfone (*R*)-**6** reacted within 20 min (Table 5, entry 8), no deprotonation of the ethyl-substituted sulfone (*R*)-**7** was observed under these conditions (Table 6, entry 8). The metalation time also varied depending on the lithiumorganyl. Deprotonation of a given sulfone with *t*BuLi for example was slower than with *n*BuLi. Particularly noteworthy is the comparatively low rate of deprotonation of the sulfones with MeLi, PhLi, and vinyllithium. Whether this is due to a difference in the basicity of RLi[27] or aggregation (see below) is not clear.

The highest *ee* of the deuteriated sulfones (*R*)-[D]**6** and (*R*)-[D]**7** was recorded in the deprotonation of the corresponding sulfones (*R*)-**6** and (*R*)-**7** with *t*BuLi (Table 5, entry 1 and Table 6, entry 1). Sulfones (*R*)-[D]**6** and (*R*)-[D]**7** were obtained with retention of configuration. Thus, it is proposed that the deprotonation reactions of the (*R*)-configured sulfones (*R*)-**6** and (*R*)-**7** give the corresponding (*M*)-configured salts (*M*)-**1** and (*M*)-**2**, the deuteriation of which afforded the corresponding (*R*)-configured sulfones (*R*)-[D]**6** and (*R*)-[D]**7** (cf. Scheme 8). As already discussed above, the alternative stereochemical course involving deprotonation of sulfones (*R*)-**6** and (*R*)-**7** with the formation of the corresponding (*P*)-configured salts (*P*)-**1** and (*P*)-**2** and their subsequent deuteriation to give the corresponding (*R*)-configured sulfones (*R*)-[D]**6** and (*R*)-[D]**6** can be excluded. Although a (*P*)-selective deprotonation of the (*R*)-configured sulfones (*R*)-**6** and (*R*)-**7** is quite possible (see below), an (*R*)-selective deuteriation of the (*P*)-configured salts can be dismissed for steric reasons (see below). The *ee* values of (*R*)-[D]**6** and (*R*)-[D]**7** are a function of the selectivity of deprotonation and protonation and the degree of racemization. Racemization of the methyl-substituted salt **1** only amounts to 4% at –105 °C within 15 min according to the racemization barrier of $\Delta G^{\ddagger}_{rac} = 13.0 \pm 0.2$ kcal mol^{-1} at this temperature. Thus, the combined selectivity of generation and deuteriation of (*M*)-**1** is approximately 91% *ee*. Accordingly, the combined selectivity of the generation and deuteriation of the ethyl-substituted salt (*M*)-**2** is approximately 94% *ee* because only 1% racemization of this salt occurs at –105 °C within 25 min [$\Delta G^{\ddagger}_{rac}$ (–105 °C) = 13.7 ± 0.2 kcal mol^{-1}]. The combined selectivity of 94% *ee* translates into a deprotonation selectivity in the range of 95–99% *ee* and a deuteriation selectivity in the range of 99–95% *ee*. Deprotonation of the neopentyl-substituted sulfone (*R*)-**8** with *n*BuLi at –78 °C and deuteriation of the salt (*M*)-**3** gave sulfone (*R*)-[D]**8** with 90% *ee* (Table 7, entry 1). Again this equates to a 1% racemization of the salt (*M*)-**3** at –78 °C in 65 min [$\Delta G^{\ddagger}_{rac}$ (–78 °C) = 16.2 ± 0.5 kcal mol^{-1}]. Thus, the generation and deuteriation of this salt by using *n*BuLi also occurred with a combined selectivity of approximately 91% *ee* with retention of configuration. Most interestingly, Tables 5 and 6 reveal that not only the selectivity but also the stereochemical course of the deprotonation of the benzyl sulfones (*R*)-**6** and (*R*)-**7** is strongly dependent upon both the lithiumorganyl and the substituent R_α. It should be emphasized that the deprotonation of the sulfone and deuteriation of the corresponding salt were performed under similar reaction conditions for the series of bases *t*BuLi, *s*BuLi, *n*BuLi, *n*PrLi, and Me_3SiCH_2Li in hydrocarbon solution and MeLi, PhLi, and vinyllithium in ethereal solution. Furthermore, the extent of racemization and the selectivity of the deuteriation of the salt remained constant in the deprotonation–deuteriation sequence with the various lithiumorganyls and only the selectivity and stereochemical course of the deprotonation varied.

Deprotonation of the methyl-substituted sulfone (*R*)-**6** with *n*BuLi afforded preferentially the (*P*)-configured salt (*P*)-**1**, the deuteriation of which gave the (*S*)-configured sulfone (*S*)-[D]**6** with 60% *ee* (Table 5, entry 3). Because the deuteriation of (*P*)-**1** proceeded with a selectivity of at least 91% *ee*, the deprotonation of sulfone (*R*)-**6** with *n*BuLi had occurred with a selectivity of 60–66% *ee*. Deprotonation of (*R*)-**6** with *s*BuLi also afforded preferentially the (*P*)-configured salt (*P*)-**1**, the deuteriation of which gave the (*S*)-configured sulfone (*S*)-[D]**6** with 48% *ee* (Table 5, entry 2). In contrast, deprotonation of (*R*)-**6** with *t*BuLi gave the (*M*)-configured salt (*M*)-**1**, the deuteriation of which furnished the (*R*)-configured sulfone (*R*)-[D]**6** with 87% *ee* (Table 5, entry 1). In the case of the ethyl-substituted sulfone (*R*)-**7** a similar but less pronounced dependency of the selectivity of deprotonation on the structure of the lithiumorganyl was observed. Thus, deprotonation of (*R*)-**7** with *n*BuLi preferentially gave the (*P*)-configured salt (*P*)-**2**, the deuteriation of which afforded sulfone (*S*)-[D]**7** with 35% *ee* (Table 6, entry 3). In contrast, treatment of (*R*)-**7** with *s*BuLi yielded the (*M*)-configured salt (*M*)-**2**, the deuteriation of which afforded sulfone (*R*)-[D]**7** with 78% *ee* (Table 6, entry 2). Finally, the application of *t*BuLi in the deprotonation of sulfone (*R*)-[D]**7** also gave the (*M*)-configured salt (*M*)-**2**, the deuteriation of which afforded sulfone (*R*)-[D]**7** with 93% *ee* (Table 6, entry 1).

The results of the enantioselective deprotonation of the sulfone are graphically depicted in Figure 10. Whereas the lower figure summarizes and illustrates the dependency of the selectivity of deprotonation of sulfones (*R*)-**6** and (*R*)-**7** on the lithiumorganyl, the upper figure summarizes and shows the influence of the substituent R at the C_α atom of sulfones (*R*)-**6–8** upon the selectivity of deprotonation with *n*BuLi. The deprotonation of the methyl- and ethyl-substituted sulfones (*R*)-**6** and (*R*)-**7** with *n*BuLi preferentially yielded the corresponding (*P*)-configured salts (*P*)-**1** and (*P*)-**2** with decreasing selectivity, whereas deprotonation of

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

the neopentyl-substituted sulfone (*R*)-**8** preferentially gave the (*M*)-configured salt (*M*)-**3** with high selectivity (Table 7, entry 1).

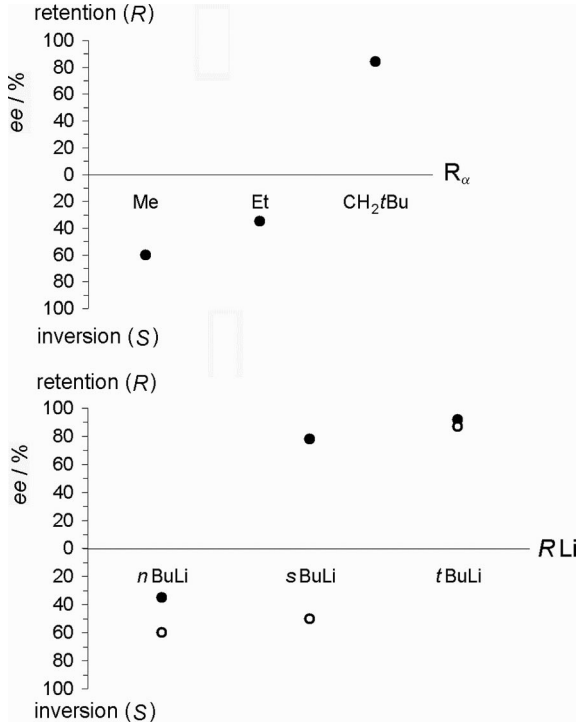
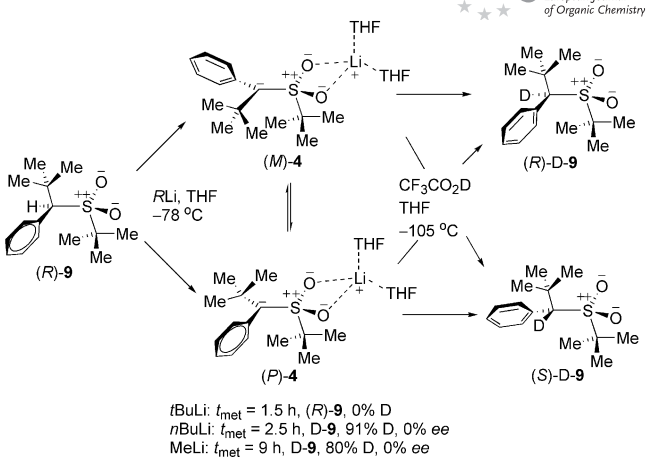


Figure 10. Top: *ee* values of the deuteriated sulfones [D]**6** (R_α = Me), [D]**7** (R_α = Et), and [D]**8** (R_α = CH_2tBu) obtained by deprotonation of the corresponding sulfones with *n*BuLi in THF at –105 °C. Bottom: *ee* values of the deuteriated sulfones [D]**6** (○) and [D]**7** (●) obtained by deprotonation of the corresponding sulfones with various RLi in THF at –105 °C (bottom).

Deprotonation of the C_α-*tert*-butyl-substituted sulfone (*R*)-**9** at –78 °C could only be achieved with *n*BuLi and MeLi (Scheme 9). However, deprotonation was incomplete even after a rather long metalation time (t_{met}) and most importantly sulfone *rac*-[D]**9** was isolated as a racemate. The long metalation time of (*R*)-**9** is a reflection of the extreme steric hindrance at the C_α atom. The isolation of the racemic deuteriated sulfone may be a reflection of (1) an unselective deprotonation of (*R*)-**9** with the formation of *rac*-**4**, (2) an unselective deuteriation of **4**, or (3) a low racemization barrier for **4**.[1]

Rationalization of the dependence of the enantioselectivity of deprotonation of the sulfones on the lithiumorganyl and the substituent R_α is hampered because of a lack of information about (1) the mechanism of deprotonation and (2) the structure of the reacting lithiumorganyl. Thus, the rationalization shown in Scheme 10 (and in Scheme 12, see below) represents only a crude picture with a number of speculative elements. We had previously rationalized the diastereoselectivity of the deprotonation of racemic bicyclic *S*-*tert*-butyl sulfones with lithiumorganyls in THF at low temperatures by assuming a prior complex formation between the sulfone and the base followed by an intramolecular proton transfer.[28] Carbanion formation by the prior complexation of a CH acid with a lithiumorganyl



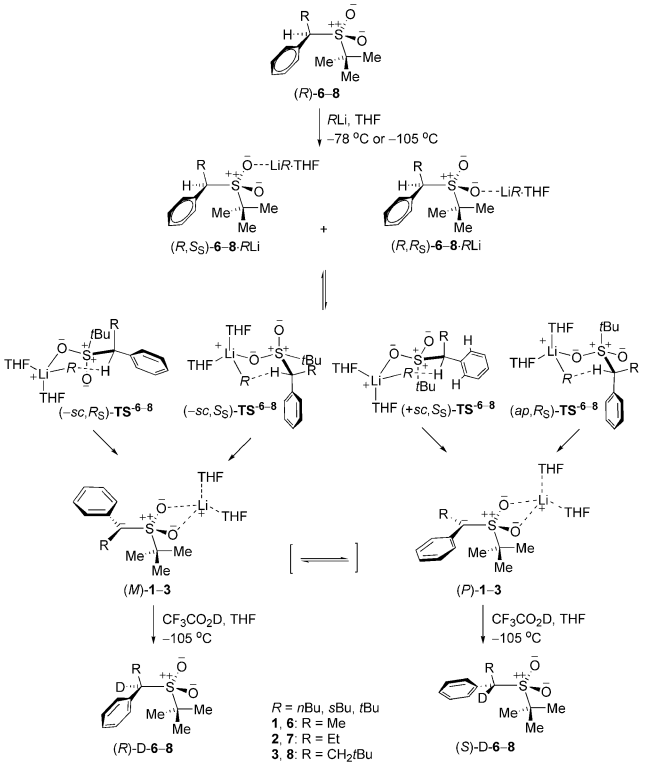
Scheme 9. Attempted enantioselective synthesis and deuteriation of salt **4**.

followed by an intramolecular proton transfer has frequently been proposed or even proven.[5f,29] The *tert*-butylsulfonyl group is one of the most powerful directing groups in the *ortho*-lithiation of aryl derivatives,[30] a reaction that is generally thought to involve a precomplexation of RLi by the substrate.[29] Thus, it is proposed that sulfones (*R*)-**6–8** react with the lithiumorganyl by a prior reversible coordination to one of the O atoms with the formation of the corresponding diastereomeric complexes (*R*,*S*$_S$)-**6–8**·RLi and (*R*,*R*$_S$)-**6–8**·RLi (Scheme 10). An intramolecular proton transfer of the complexes via the cyclic six-membered transition states (–*sc*,*R*$_S$)-**TS-6–8** and (–*sc*,*S*$_S$)-**TS-6–8** then leads to the corresponding (*M*)-configured salts (*M*)-**1**–**3**, whereas proton transfer via transition states (+*sc*,*S*$_S$)-**TS-6–8** and (*ap*,*R*$_S$)-**TS-6–8** gives the corresponding (*P*)-configured salts (*P*)-**1**–**3**. The negative charge of the α-sulfonyl carbanion is stabilized by (1) an electrostatic interaction, which is independent of the C_α–S and C_α–Ph conformation, (2) negative hyperconjugation, which depends on the C_α–S conformation, and (3) benzylic conjugation, which depends on the C_α–Ph conformation.[1] During the conversion from sulfones (*R*)-**6–8** into the corresponding lithium salts **1**–**3** a significant structural reorganization has to occur with regard to the conformation around the C_α–S and C_α–Ph bonds, the configuration of the C_α atom, and the lengths of the C_α–S and C_α–Ph bonds.[1] Although information about the structure and energy of the transition state of the deprotonation of a sulfone with RLi in THF solution, as derived from kinetic analysis or theoretical calculations, is not available,[31] it is assumed that the factors that stabilize the lithium salt are, to some extent, also effective in the stabilization of the corresponding transition state. The sulfones were deprotonated by the addition of solutions of $MeSi_3CH_2Li$, *n*PrLi, *n*BuLi, *s*BuLi, and *t*BuLi in hydrocarbons and MeLi, PhLi, and vinyllithium in diethyl ether to their solutions in THF. Whereas in hydrocarbons *n*BuLi, *s*BuLi, and *t*BuLi are highly aggregated, in THF *t*BuLi is a monomer,[32] *s*BuLi is a monomer–dimer equilibrium,[32a] and *n*BuLi is a dimer–tetramer mixture.[32] In THF MeLi is a tetramer[33] and PhLi a dimer.[32a,34] Thus, the questions

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

arise (1) as to what extent had the aggregate equilibrium of the various lithiumorganyls already been established under the reaction conditions and (2) which species of RLi is the most reactive one in the proposed complexation–deprotonation of sulfones? It is assumed that under the conditions employed (addition of RLi/hydrocarbon to sulfone/THF at –105 °C) the aggregate equilibrium had perhaps not fully been established (see below) and that the corresponding monomers and dimers of RLi are the most reactive bases.[5f,35] Transition states (*–sc*,R_S)-**TS-6–8** and (*–sc*,S_S)-**TS-6–8**, which lead to the (*M*)-configured salts, have a C_α–S conformation in which the H atom is *gauche* to both O atoms and the *S*-*tert*-butyl group is in a pseudo-equatorial position. Thus, these transition states should also be stabilized by n_C–σ^*_{StBu}-hyperconjugation.[1] Although transition states (+*sc*,S_S)-**TS-6–8** and (*ap*,R_S)-**TS-6–8**, which give the (*P*)-configured salts, are not stabilized by the n_C–σ^*_{StBu} interaction, the n_C–σ^*_{SO} interaction should provide stabilization. However, according to ab initio calculations on α-sulfonyl carbanions this interaction is significantly less stabilizing than the n_C–σ^*_{SR} interaction.[3d,36] All transition states should be stabilized by electrostatic interactions between the developing negative charge and the sulfonyl group and by benzylic conjugation. Sulfones carrying a phenyl group at the C_α atom are four to six pK_a-units more acidic than the corresponding alkyl-substituted sulfones in DMSO (K^+)[37a] and THF (Li^+).[37b] However, the benzylic conjugation in (+*sc*,S_S)-**TS-6–8** is perhaps reduced in comparison with the other transition states because of the steric interactions between the *t*Bu and Ph groups. Finally, steric interactions in the transition states around the C_α–S bond have to be considered. Ab initio calculations on the methyl-substituted sulfone **6** had revealed the three rotamers **6A**, **6B**, and **6C** (cf. Figure 6) with relative energies of +3.23, 0.00, and +4.05 kcal mol^{-1}, respectively. Whereas transition states (*–sc*,R_S)-**TS-6–8** and (*–sc*,S_S)-**TS-6–8** have a C_α–S conformation similar to that of **6A**, the transition states (+*sc*,S_S)-**TS-6–8** and (*ap*,R_S)-**TS-6–8** have a C_α–S conformation that resembles that of **6B** and **6C**, respectively. Thus, steric interactions around the C_α–S bond should be less in (+*sc*,S_S)-**TS-6–8** than in (*–sc*,R_S)-**TS-6–8**, (*–sc*,S_S)-**TS-6–8**, and (*ap*,R_S)-**TS-6–8**. Whereas the *tert*-butyl groups in transition states (*–sc*,R_S)-**TS-6–8** and (*–sc*,S_S)-**TS-6–8** are in a pseudo-equatorial position, those in (+*sc*,S_S)-**TS-6–8** and (*ap*,R_S)-**TS-6–8** are in a pseudo-axial position. On passing from the transition states (+*sc*,S_S)-**TS-6–8** and (*ap*,R_S)-**TS-6–8** to the corresponding (*P*)-configured salts the substituent R_α and the phenyl group, respectively, have to move past the O atom in an anticlockwise and clockwise fashion, respectively. In contrast, no C_α–S bond rotation was required on the way from transition states (*–sc*,R_S)-**TS-6–8** and (*–sc*,S_S)-**TS-6–8** to the (*M*)-configured salts.

The deprotonation experiments on (*R*)-**6** and (*R*)-**7** had revealed a reversal of the selectivity of deprotonation on going from *n*BuLi to *s*BuLi to *t*BuLi from (*P*)-selective to (*M*)-selective (cf. Figure 10, bottom). A similar inversion of selectivity was observed upon increasing the steric size of R_α of the sulfone in the deprotonation with *n*BuLi (cf. Figure 10, top). Based on the above discussion of the transition states it is thus proposed that the deprotonation reactions of the sulfones with *n*BuLi proceed in the case of a small substituent R_α preferentially through transition states (+*sc*,S_S)-**TS-6–8**. Although this transition state is not stabilized by the n_C–σ^*_{StBu} interaction, it is stabilized by benzylic conjugation, electrostatic interactions, and the n_C–σ^*_{SO} interaction, and it should have the least steric interaction around the C_α–S bond. With increasing steric size of RLi and R_α, the interaction between the residue, the lithiumorganyl, and the *S*-*tert*-butyl group of (+*sc*,S_S)-**TS-6–8** should become more and more destabilizing and the benzylic conjugation will be reduced because of steric interactions between the Ph, *t*Bu, and R_α groups. Thus, deprotonation now occurs preferentially via transition states (*–sc*,R_S)-**TS-6–8** despite the increasing steric interaction between R_α and *t*Bu because this transition state is stabilized by the n_C–σ^*_{StBu} interaction and benzylic conjugation, the latter of which is sterically unhindered.



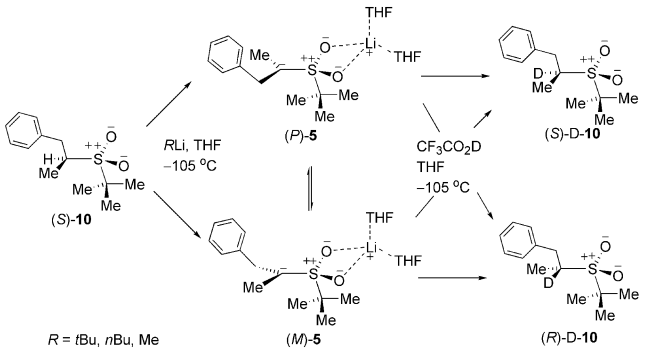
Scheme 10. Rationalization of the enantioselective deprotonation of sulfones (*R*)-**7**–**9** (aggregation of RLi and the degree of its solvation by THF are not considered; conformational descriptors refer to the C_α–S bond).

Enantioselective Deprotonation of Sulfones and Deuteriation of C_α-Dialkyl-Substituted Lithium α-*tert*-Butylsulfonyl Carbanion Salts

The reactions of the C_α-phenyl-substituted sulfones **6**–**8** with RLi are characterized by a strong dependency of the selectivity of deprotonation on the lithiumorganyl and the

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

second C_α substituent. It was therefore of interest to study the selectivity of the deprotonation of sulfone (*S*)-**10**, the C_α atom of which carries two alkyl groups (Scheme 11). The experiments with (*S*)-**10** were also carried out in a standardized fashion for both the deprotonation and deuteriation. Whereas the conditions for deprotonation were varied, those of protonation were kept constant. Deprotonation was performed in THF at –105 °C and the metalation time t_{met} given in Table 8 was specifically selected to ensure both complete deprotonation and maximum suppression of racemization (≤1%) of the salt (*P*)-**5** with the exceptions stated. Solutions of the lithiumorganyl and CF_3CO_2D were added under film-cooling to solutions of the sulfone and salt, respectively, to establish a reaction temperature of –105 °C, which was measured by using a fast responding digital thermometer. The *ee* of the deuteriated sulfone (*S*)-[D]**10** was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ by using the *S*-*tert*-butyl signal and the degree of deuteriation of the sulfones was also determined by ^{1}H NMR spectroscopy.



Scheme 11. Enantioselective synthesis and deuteriation of the salt (*P*)-**5**.

Table 8. Deprotonation of sulfone (*S*)-**10** with ≥99% *ee* in THF with RLi and deuteriation of the salt (*P*)-**5** with CF_3CO_2D.

Entry	RLi,solvent	t_{met}[a] [min]	Electrophile	Solvent	Sulfone [D]**10** D content [%]	*ee* [%]	Conf.
1	*n*BuLi, *n*-hexane	8	CF_3CO_2D	THF	≥98	89	*S*
2	*n*BuLi, *n*-hexane	10	CF_3CO_2D	THF	≥98	86	*S*
3	*n*BuLi, *n*-hexane	8	Me_2OHBF_4	THF	–	82	*S*
4	MeLi, Et_2O	8	CF_3CO_2D	THF	–	–	–
5	PhLi, Et_2O	15	CF_3CO_2D	THF	24	84	*S*
6	*t*BuLi, *n*-pentane	15	CF_3CO_2D	THF	34	93	*S*
7	*t*BuLi, THF	15	CF_3CO_2D	THF	67	92	*S*

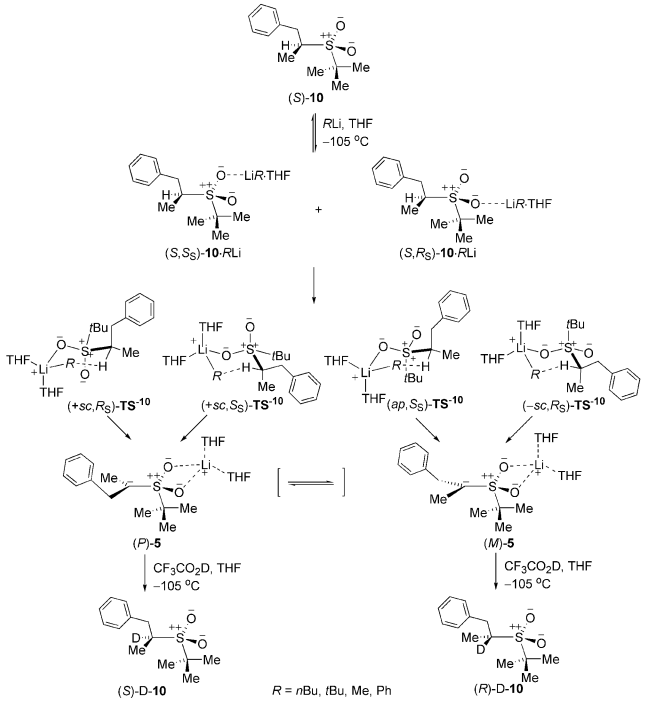
[a] Time elapsed between the beginning of the addition of RLi and the acid.

Deprotonation of (*S*)-**10** with *n*BuLi gave the (*P*)-configured salt (*P*)-**5**, the deuteriation of which afforded sulfone (*S*)-[D]**10** with 89% *ee* (Table 8, entry 1). The salt (*P*)-**5** has an activation free energy of racemization $\Delta G_{rac}^{\ddagger}$ (268 K) of 12.9 kcal mol^{-1} and a half-life of racemization $\tau_{½rac}$ of 3 h at –105 °C. Thus, racemization of (*P*)-**5** at –105 °C within 5 min is less than 2%. This is corroborated by the deprotonation of (*S*)-**10** under the same conditions except that the metalation time t_{met} was extended to 10 min, which gave sulfone (*S*)-[D]**10** with 86% *ee* (entry 2). These results show that (1) both the deprotonation of the dialkyl-substituted sulfone (*S*)-**10** by *n*BuLi and the deuteriation of the salt (*P*)-**5** with CF_3CO_2D are highly enantioselective and (2) the whole sequence proceeds with retention of configuration. Reaction of the salt (*P*)-**5** with CF_3CO_2D could in principle proceed by a prior coordination of the acid to the Li atom followed by an intramolecular transfer of the D atom. This could result in selectivity that is different to that of the intermolecular reaction. Therefore the protonation of (*P*)-**5** with $Me_2O{\cdot}HBF_4$, was studied, which is less capable of coordinating to the Li atom. The two-step transformation of (*S*)-**10** with *n*BuLi and this acid gave sulfone (*S*)-[D]**10** with 82% *ee* (entry 3). Surprisingly, deprotonation of sulfone (*S*)-**10** with MeLi could not be achieved under the conditions used (entry 4). Furthermore, deprotonation of (*S*)-**10** with PhLi was also very slow, as indicated by a conversion of only 24% after a time t_{met} of 15 min (entry 5). The selectivity was, however, high and sulfone (*S*)-[D]**10** with 84% *ee* and a D content of 24% was isolated. Similar results were obtained with *t*BuLi. Deprotonation of the sulfone was slow but the selectivity was higher (entry 6). Sulfone (*S*)-[D]**10** with 93% *ee* and a D content of only 34% was isolated. In this experiment a solution of *t*BuLi in *n*-pentane was added to a solution of the sulfone in THF. Although *t*BuLi is an aggregate in *n*-pentane, it is a monomer in THF,[32] which should be more reactive. Thus, the question arose as to whether the metalation with monomeric *t*BuLi in THF is faster than with the monomer/aggregate equilibrium mixture in THF/*n*-pentane. Indeed, deprotonation of sulfone (*S*)-**10** with *t*BuLi in THF was faster and gave sulfone (*S*)-[D]**10** with 92% *ee* and a D content of 67% after a time t_{met} of 15 min (entry 7). The deprotonation of (*S*)-**10** with *t*BuLi in *n*-pentane was much slower than that of sulfone (*R*)-**6** (cf. Table 5), which is perhaps a reflection of the lower acidity of the dialkyl-substituted sulfone.

Table 8 reveals that the deprotonation–deuteriation sequence starting with sulfone (*S*)-**10** gave sulfone (*S*)-[D]**10** irrespective of the lithiumorganyl used. Thus, deprotonation of (*S*)-**10** preferentially gave the (*P*)-configured salt (*P*)-**5** with medium-to-high selectivity, the deuteriation of which with CF_3CO_2D proceeded with high selectivity with the formation of the (*S*)-configured sulfone (*S*)-[D]**10**. It is proposed that sulfone (*S*)-**10** and RLi engage in a complexation similar to that of sulfones (*R*)-**6**–**8** (see above) with the formation of the (S_S)- and (R_S)-configured complexes (*S*)-**10**·RLi (Scheme 12). The intramolecular proton transfer preferentially proceeds through the transition states (+*sc*,R_S)-**TS-10** and (+*sc*,S_S)-**TS-10**, the developing negative charge of which should also be stabilized by electrostatic interactions and n_C–$\sigma^*_{S\,tBu}$ hyperconjugation. Within the framework of these model considerations the alternative transition states (*ap*,S_S)-**TS-10** and (–*sc*,R_S)-**TS-10** should

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

be higher in energy because of stabilization by the less efficient n_C–σ^*_{SO} interaction. The deprotonation reactions of the benzylic sulfones (*R*)-**6–8** by RLi are characterized by a selectivity reversal depending on the structure of the lithiumorganyl. The deprotonation of the dialkyl-substituted sulfone (*S*)-**10** with RLi lacks such a dependency. The reason for the differing behavior of the two types of sulfones, dialkyl- and phenyl,alkyl-substituted, may be seen in the lack of stabilization of the transition states (*ap*,S_S)-**TS-10** and (–*sc*,R_S)-**TS-10** by benzylic conjugation, which makes the transition states (+*sc*,R_S)-**TS-10** and (+*sc*,S_S)-**TS-10** more stable irrespective of the size of R.



Scheme 12. Rationalization of the enantioselective deprotonation of sulfone (*S*)-**10** (aggregation of RLi and the degree of its solvation by THF are not considered; conformational descriptors refer to the C_α–S bond).

Enantioselective Deprotonation of Sulfones and Deuteriation of C_α-Alkyl,Aryl and C_α-Dialkyl-Substituted Lithium α-*tert*-Butylsulfonyl Carbanion Salts in the Presence of Additives

In the Presence of HMPA

A key element of the reactivity–selectivity models depicted in Scheme 10 and Scheme 12 is the formation of a complex between the sulfone and RLi. Thus, the deprotonation reactions of sulfones (*R*)-**6** and (*S*)-**10** with *t*BuLi and *n*BuLi in the presence of HMPA were studied. In general, HMPA acts a strong binding ligand for RLi, breaking up aggregates and weakening any potential coordination of the lithiumorganyl with basic substrates.[34] The action of HMPA upon RLi establishes an equilibrium between HMPA-coordinated RLi, which should have a low complexation ability towards sulfone, and THF-coordinated RLi, which possesses a high complexation ability.[34] In addition, the selectivity of the deuteriation of the salts **1** and **5** in the presence of HMPA was investigated. The reactions of the salts **1** and **5** with HMPA in THF is expected to lead to the establishment of equilibria between the corresponding THF/HMPA-coordinated CIPs and HMPA-coordinated SIPs.[1,38]

Deprotonation of (*R*)-**6** with *t*BuLi at –105 °C followed by the deuteriation of the salt with CF_3CO_2D at the same temperature had given after a metalation time of 35 min sulfone (*R*)-[D]**6** with 85% *ee* (cf. Table 5, entry 9). The addition of 2 equiv. of HMPA to the sulfone before treatment with *t*BuLi did not significantly influence the selectivity of deprotonation (Table 9, entries 3 and 4). However, deprotonation of (*R*)-**6** in the presence of 5 and 10 equiv. of HMPA saw a significant decline in the selectivity of the deprotonation reaction and sulfone (*R*)-[D]**6** with only 84 and 66% *ee*, respectively, was isolated (entries 5 and 6). Control experiments in which 2 and 10 equiv. of HMPA were added after the completion of the deprotonation of the sulfone and before the addition of CF_3CO_2D showed that the selectivity of the deuteriation of the salt (*M*)-**1** is not affected by the presence of 2 or 10 equiv. of HMPA (entries 1 and 2).

Table 9. Deprotonation of sulfone (*R*)-**6** with ≥99% *ee* with *t*BuLi/*n*-pentane in THF and deuteriation of the salt (*M*)-**1** with CF_3CO_2D in the presence of HMPA at –105 °C.

Entry	Additive[a]	t_{me}[b] [min]	Sulfone [D]**6**		
			D content [%]	*ee* [%]	Conf.
1	HMPA (2)[c]	30	98	89	*R*
2	HMPA (10)[c]	30	≥98	89	*R*
3	HMPA (2)[d]	10	≥98	91	*R*
4	HMPA (2)[d]	35	96	87	*R*
5	HMPA (5)[d]	10	≥98	84	*R*
6	HMPA (10)[d]	30	≥98	66	*R*

[a] Number of equiv. in parentheses. [b] Time elapsed between the beginning of the addition of *t*BuLi and CF_3CO_2D. [c] Addition before the addition of CF_3CO_2D. [d] Addition before the addition of *t*BuLi.

Next the influence of the additive HMPA on the deprotonation of the dialkyl-substituted sulfone (*S*)-**10** was investigated. In three otherwise identical experiments sulfone (*S*)-**10** was treated with *n*BuLi in THF in the presence of 1, 5, and 10 equiv. of HMPA followed by deuteriation with CF_3CO_2D (Table 10, entries 2–4). In a last experiment sulfone (*S*)-**10** was treated with *n*BuLi in THF and 10 equiv. of HMPA were added before the addition of CF_3CO_2D (entry 1). Although HMPA had only a small influence on the selectivity of the deuteriation of the salt (*P*)-**5**, it exerted a strong influence on the selectivity of the deprotonation of the sulfone. With increasing amounts of HMPA, the selectivity of the deprotonation of sulfone (*S*)-**10** strongly decreased.

In summary, although HMPA has a negligible influence on the selectivity of the deuteriation of salts **1** and **5** with CF_3CO_2D, it exerts a strong effect on the deprotonation of the sulfones (*R*)-**6** and (*S*)-**10** with the lithiumorganyls depending on the amount of HMPA added. The minor in-

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

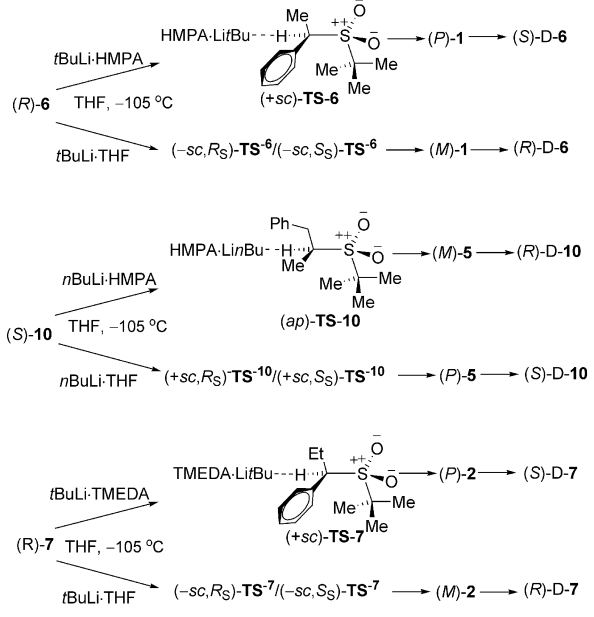
Table 10. Deprotonation of sulfone (*S*)-**10** with ≥99% *ee* with *n*BuLi/*n*-hexane in THF and deuteriation of the salt (*P*)-**5** with CF_3CO_2D in the presence of HMPA and DMPU at –105 °C.

Entry	Additive[a]	t_{met}[b] [min]	Sulfone [D]**10**		
			D content [%]	*ee* [%]	Conf.
1	HMPA (10)[c]	10	92	83	*S*
2	HMPA (1)[d]	10	≥98	70	*S*
3	HMPA (5)[d]	10	≥98	56	*S*
4	HMPA (10)[d]	10	≥98	36	*S*
5	DMPU (4)[c]	8	≥98	87	*S*
6	DMPU (4)[d]	8	≥98	82	*S*

[a] Number of equiv. in parentheses. [b] Time elapsed between the beginning of the addition of *n*BuLi and CF_3CO_2D. [c] Addition before the addition of CF_3CO_2D. [d] Addition before the addition of *n*BuLi.

fluence of HMPA on the deuteriation of **1** and **5** is not surprising. The anions of the THF-coordinated CIPs and the HMPA-coordinated SIPs have similar basic structural features, which should be expressed in similar enantioselectivities in reactions with electrophiles.

The decreasing selectivity of the deprotonation of sulfones (*R*)-**6** and (*S*)-**10** with RLi in THF in the presence of increasing amounts of HMPA may be rationalized by proposing the involvement of two competing deprotonation pathways of opposite selectivity (Scheme 13). The "cyclic pathway" features a deprotonation of the sulfone with THF-coordinated RLi, which proceeds via the six-membered cyclic transition states (–*sc*,R_S)-**TS-6**/(–*sc*,S_S)-**TS-6** and (+*sc*,R_S)-**TS-10**/(+*sc*,S_S)-**TS-10** (cf. Scheme 10 and Scheme 12) to give the corresponding salts (*M*)-**1** and (*P*)-**5**, respectively. The "acyclic pathway" entails a deprotonation of the sulfone with HMPA-coordinated RLi, which proceeds via the acyclic transition states (+*sc*)-**TS-6** and (*ap*)-**TS-10** to yield preferentially the salts (*P*)-**1** and (*M*)-**5**, respectively, with the opposite configuration. The acyclic transition states have a C_α–S conformation that is similar to that adopted by the sulfones (*R*)-**6** and (*S*)-**10** in the crystal and solution. The developing negative charge of (+*sc*)-**TS-6** and (*ap*)-**TS-10** should be stabilized by electrostatic and n_C–σ^*_{SO} interactions and (+*sc*)-**TS-6** also by benzylic conjugation. On proceeding from (+*sc*)-**TS-6** and (*ap*)-**TS-10** to the corresponding carbanions, C_α–S bond rotation has to occur in which only the methyl and benzyl group, respectively, have to pass a O atom.



Scheme 13. Rationalization of the enantioselective deprotonation of sulfones (*R*)-**6**, (*S*)-**10**, and (*R*)-**7** in the presence of HMPA and TMEDA (aggregation of RLi and the degree of its solvation by THF and HMPA are not considered; conformational descriptors refer to the C_α–S bond).

In the Presence of TMEDA and DMPU

Having observed a strong effect of HMPA on the selectivity of the deprotonation of sulfones (*R*)-**6** and (*S*)-**10**, the influence of DMPU and TMEDA on the deprotonation of sulfones (*R*)-**7** and (*S*)-**10** was studied (cf. Scheme 13). The reaction of sulfone (*S*)-**10** in THF with *n*BuLi in the presence of 4 equiv. of DMPU under the standard conditions and the subsequent deuteriation of (*P*)-**5** with CF_3CO_2D gave, after a metalation time of 8 min, sulfone (*S*)-[D]**10** with 82% *ee* (Table 10, entry 6). Similarly, deprotonation of sulfone (*S*)-**10** with *n*BuLi in THF followed by the addition of 4 equiv. of DMPU after a metalation time of 8 min and the subsequent deuteriation of the salt (*P*)-**5** with $CF_3CF_3CO_2D$ under the standard conditions afforded sulfone (*S*)-[D]**10** with 87% *ee* (entry 5). Thus, although the selectivity of the deprotonation of (*S*)-**10** was slightly reduced in the presence of DMPU, this ligand had only a small influence upon the selectivity of the deuteriation of (*P*)-**5**. A different situation was encountered with TMEDA in the case of sulfone (*R*)-**7**. The reaction of (*R*)-**7** in THF under the standard conditions with *t*BuLi in the presence of 2 equiv. of TMEDA followed by the deuteriation of the salt (*M*)-**2** with $CF_3CF_3CO_2D$ under the standard conditions gave after a metalation time of 20 min sulfone (*R*)-[D]-**7** with only 39% *ee*. Sulfone (*R*)-[D]**7** with 91% *ee* was obtained in a similar deprotonation–deuteriation experiment with (*R*)-**7** in which 2 equiv. of TMEDA were added to the salt **2** before deuteriation. Thus, although 2 equiv. of TMEDA strongly reduced the selectivity of the deprotonation of sulfone (*R*)-[D]**7**, its presence had no bearing upon the selectivity of the deuteriation of the salt (*M*)-**2**. The salt (*M*)-**2** most likely forms monomeric and dimeric TMEDA-coordinated CIPs, the selectivity of the deuteriation of which should be similar to that of the THF-coordinated CIPs because of a similar anion structure. The addition of TMEDA to *t*BuLi in THF at low temperatures is expected to establish an equilibrium between THF- and TMEDA-coordinated *t*BuLi,[34b,39] the latter having a reduced ability for the complexation of sulfone **7**. Thus, deprotonation of **7** with *t*BuLi/TMEDA could occur, as in the case of **6** in the presence of HMPA, by an "acyclic pathway" via (+sc)-**TS-7** to give (*P*)-**2** and by a "cyclic pathway" via (–*sc*,R_S)-**TS-7**/(–*sc*,S_S)-**TS-7** to yield (*M*)-**2**.

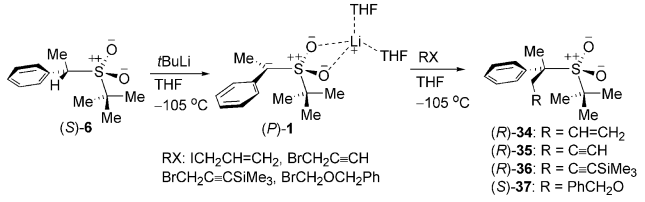
 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Enantioselective Reactions of C_α-Dialkyl- and C_α-Phenyl,Alkyl-Substituted Lithium α-Sulfonyl Carbanion Salts with C-Electrophiles

The appropriate choice of lithiumorganyl as base allows the highly enantioselective synthesis of the lithium salts **1**–**3** and **5** from the corresponding enantiopure sulfones. The salts showed high selectivity in their reactions with CF_3CO_2D. These observations led to a study of the reactions of the salts **1**, **2**, and **5** with carbon-based electrophiles to see whether C–C bond formation occurs with a similar high selectivity and the same stereochemical course as the deuteriation. Only reactive electrophiles were studied and used in excess because of the low reaction temperatures and the short reaction times that are required to suppress the racemization of the salt.

C_α-Phenyl-Substituted Carbanions

Treatment of the methyl-substituted salt (*P*)-**1**, which was generated with high selectivity by deprotonation of sulfone (*S*)-**6** with *t*BuLi, with 8 equiv. of allyl iodide at –105 °C gave sulfone (*R*)-**34** with 90% *ee* in 92% yield (Scheme 14 and Table 11, entry 1). The *ee* of (*R*)-**34** was determined by chiral HPLC using *rac*-**34** as reference and its absolute configuration was established by X-ray crystal structure analysis (Figure 11).[22] Because 4% racemization of the salt (*P*)-**1** at –105 °C occurs within 15 min, the overall selectivity of the deprotonation of sulfone (*S*)-**5** and the allylation of the salt is approximately 94% *ee*. Formation of the (*R*)-configured sulfone (*R*)-**34** shows that allyl iodide attacks the planar anionic C atom of salt (*P*)-**1** with high selectivity *syn* to the O atoms and *anti* to the *tert*-butyl group.



Scheme 14. Enantioselective reaction of the phenyl-substituted salt (*P*)-**1** with allyl iodide, propargylic bromides, and benzyloxymethyl bromide.

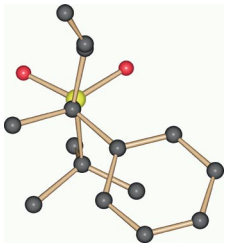


Figure 11. View of the crystal structure of sulfone (*R*)-**34** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red.

Similar treatment of the enantiomeric salt (*M*)-**1**, which was synthesized by deprotonation of sulfone (*S*)-**6** with *n*BuLi instead of *t*BuLi, with 8 equiv. of allyl iodide at –105 °C afforded the (*S*)-configured sulfone (*S*)-**34** with 59% *ee* in 90% yield (entry 2). Here, the low overall selectivity of the synthesis of sulfone (*S*)-**34** from sulfone (*S*)-**6** is primarily due to the low selectivity of the deprotonation of the latter.

Next the reactions of salt (*P*)-**1** with propargyl bromide, trimethylsilylpropargyl bromide, and benzyloxymethyl bromide were studied. Treatment of the salt (*P*)-**1**, which was obtained by deprotonation of sulfone (*S*)-**6** with *t*BuLi, with propargyl bromide at –105 °C gave the (*R*)-configured sulfone (*R*)-**35** with 87% *ee* in 77% yield (entry 3). The *ee* was determined by GC and ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ with *rac*-**35** as reference. An X-ray crystal structure analysis of (*R*)-**35** secured the (*R*) configuration of the sulfone (Figure 12).[22]

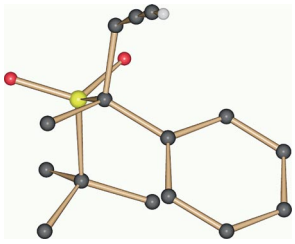


Figure 12. View of the crystal structure of sulfone (*R*)-**35** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red; H, grey.

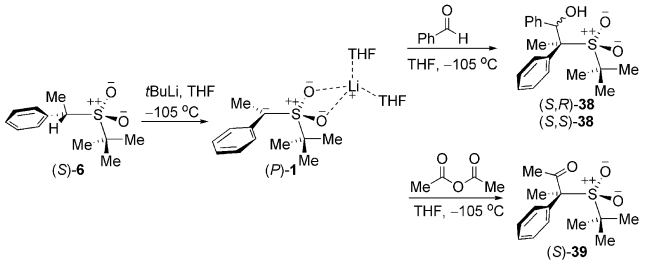
Table 11. Enantioselective reactions of the salts (*P*)-**1**, (*M*)-**1**, (*P*)-**2**, (*M*)-**2** and (*P*)-**5** with C-electrophiles at –105 °C.

Entry	Sulfone[a]	Base	t_{met} [min][b]	Salt	Electrophile[c]	t_{reac} [min][d]	Sulfone	Yield [%]	*ee* [%]
1	(*S*)-**6**	*t*BuLi	12	(*P*)-**1**	CH_2=$CHCH_2I$ (8)	20	(*R*)-**34**	92	90
2	(*S*)-**6**	*n*BuLi	12	(*M*)-**1**	CH_2=$CHCH_2I$ (8)	20	(*S*)-**34**	90	59
3	(*S*)-**6**	*t*BuLi	12	(*P*)-**1**	CH≡CCH_2Br (4)	15	(*R*)-**35**	77	87
4	(*S*)-**6**	*t*BuLi	12	(*P*)-**1**	Me_3SiC≡CCH_2Br (4)	15	(*S*)-**36**	84	94
5	(*S*)-**6**	*t*BuLi	12	(*P*)-**1**	$PhCH_2OCH_2Br$ (8)	15	(*R*)-**37**	72	95
6	(*S*)-**6**	*t*BuLi	12	(*P*)-**1**	PhCHO (8)	15	(*S*,*S*)-**38**/(*S*,*R*)-**38**[e]	65	94/95
7	(*S*)-**6**	*t*BuLi	12	(*P*)-**1**	$(MeCO)_2O$ (3)	15	(*S*)-**39**	69	94
8	(*R*)-**7**	*t*BuLi	12	(*M*)-**2**	MeI (8)	20	(*R*)-**40**/(*R*)-[D]**7**	24/71	94/91
9	(*R*)-**7**	*n*BuLi	12	(*P*)-**2**	MeI (8)	20	(*S*)-**40**/(*S*)-[D]**7**	32/65	33/28
10	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	CH_2=$CHCH_2I$ (5)	10	(*R*)-**41**	80	92
11	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	$PhCH_2OCH_2Br$ (5)	10	(*S*)-**42**	70	91

[a] Sulfone with ≥99% *ee* was used. [b] Time elapsed between the beginning of the addition of RLi and the electrophile. [c] Number of equiv. in parentheses. [d] Time elapsed between the beginning of the addition of the electrophile and CF_3CO_2D. [e] Ratio 71:29.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

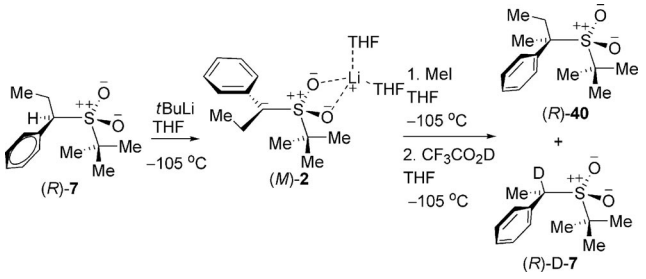
Treatment of the salt (*P*)-**1**, which was obtained by deprotonation of sulfone (*S*)-**6** with *t*BuLi, with trimethylsilylpropargyl bromide at –105 °C furnished the (*R*)-configured sulfone (*R*)-**36** with 94% *ee* in 84% yield (entry 4). The *ee* of the sulfone was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ with *rac*-**36** as reference. The absolute configuration of (*R*)-**36** was assigned by analogy to that of (*R*)-**35**. It is not clear what caused the difference in the overall selectivities of the synthesis of sulfones (*R*)-**35** and (*R*)-**36**. Finally, reaction of the salt (*P*)-**1**, which was obtained by deprotonation of sulfone (*S*)-**6** with *t*BuLi, with benzyloxymethyl bromide at –105 °C afforded the (*R*)-configured sulfone (*R*)-**37** with 95% *ee* in 72% yield (entry 5). The *ee* of the sulfone was determined by chiral GC and ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ with *rac*-**37** as reference. The absolute configuration of (*R*)-**37** was assigned by analogy to that of (*R*)-**35**. Having observed high selectivities in the alkylation of (*P*)-**1** with alkyl halides, the reactivity of the salt towards carbonyl derivatives was probed to obtain a somewhat more general picture. Reaction of the salt (*P*)-**1**, which was obtained by deprotonation of sulfone (*S*)-**6** with *t*BuLi, with benzaldehyde at –105 °C gave two diastereomeric hydroxy sulfones, (*S*,*S*)-**38** and (*S*,*R*)-**38**, the configurations of which were not determined, in a ratio of 71:29 in a combined yield of 65% (Table 11, entry 6, Scheme 15). One diastereomer had an *ee* of 94% and the other 95%. The *ee* values of the hydroxy sulfones were determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ or Pirkle alcohol[40] employing the racemic diastereomers as reference. The (*S*) configuration of the hydroxy sulfones at the C$_\alpha$ atom was assigned by analogy to that of (*R*)-**35**.



Scheme 15. Enantioselective reaction of the salt (*P*)-**1** with benzaldehyde and acetic anhydride.

In a further experiment the reaction of (*P*)-**1** with acetic anhydride was studied. Treatment of salt (*P*)-**1**, which was obtained by deprotonation of sulfone (*S*)-**6** with *t*BuLi, with acetic anhydride at –105 °C gave the keto sulfone (*S*)-**39** with 94% *ee* in 69% yield (entry 7). The *ee* of the sulfone was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ and by HPLC employing the racemic sulfone as reference. The (*S*) configuration of the sulfone was assigned by analogy to that of (*R*)-**35**.

Next the reactivity of the ethyl-substituted salt (*M*)-**2** towards C-electrophiles was investigated. Treatment of the salt (*M*)-**2**, which was obtained by deprotonation of sulfone (*R*)-**7** with *t*BuLi, with 8 equiv. of methyl iodide at –105 °C followed by the addition of CF_3CO_2D after t_{met} = 20 min and terminated after 20 min gave sulfone (*R*)-**40** with 94% *ee* in 24% yield and sulfone (*R*)-[D]**7** with 91% *ee* in 71% yield (Table 11, entry 8, Scheme 16). The *ee* of sulfone (*R*)-**40** was determined by chiral GC using the racemic sulfone as reference. The absolute configuration of the sulfone was determined by X-ray crystal structure analysis (Figure 13).[22] Then the salt (*P*)-**2** was prepared and treated with methyl iodide. Treatment of (*P*)-**2**, which was obtained from (*S*)-**7** and *t*BuLi, with 8 equiv. of methyl iodide at –105 °C after t_{met} = 35 min and a reaction time of 4 h gave sulfone (*S*)-**40** with 83% *ee* in 83% yield. Recrystallization afforded (*S*)-**40** with ≥98% *ee* in 48% yield. The *ee* of sulfone (*S*)-**40** was determined by chiral GC using the racemic sulfone as reference. In a final experiment the enantiomeric salt (*P*)-**2** was prepared by deprotonation of sulfone (*R*)-**7** with *n*BuLi and treated with 8 equiv. of methyl iodide at –105 °C followed by the addition of CF_3CO_2D after t_{met} = 20 min. This sequence afforded sulfone (*S*)-**40** with 33% *ee* in 32% yield and sulfone (*S*)-[D]**7** with 28% *ee* in 65% yield (entry 9). The steric size of the C_α-alkyl group of the C_α-phenyl-substituted salts **1**–**3** has a profound influence on the rate of the reaction with C-electrophiles. For example, although the methylation of the methyl-substituted salt **1** with 8 equiv. of methyl iodide at –105 °C was complete after 15 min, that of the ethyl-substituted salt **2** had only proceeded to an extent of 25%, and that of the neopentyl-substituted salt **3** had not occurred at all even after several hours. This is corroborated by an increasing steric shielding of the anionic C atom by the alkyl group on going from the methyl to the ethyl to the neopentyl derivative as revealed by the crystal structures of **1**–**3**.[1] However, deuteriation of the salts **1**–**3** with CF_3CO_2D in THF at –105 °C was fast in all cases.



Scheme 16. Reaction of the salt (*M*)-**2** with methyl iodide.

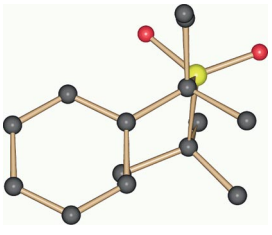
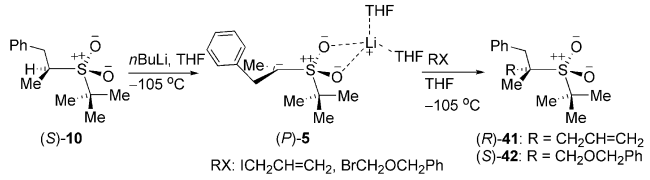


Figure 13. View of the crystal structure of sulfone (*S*)-**40** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

C_α-Dialkyl-Substituted Carbanion

Finally, having obtained information about the reactivity and selectivity of the benzylic salts **1**–**3**, which have a planar anionic C atom, it was of interest to study the reactions of the dialkyl-substituted salt **5**, which most likely also has a planar anionic C atom,[1] with C-electrophiles. Reaction of the salt (*P*)-**5**, which was synthesized by deprotonation of sulfone (*S*)-**10** with *n*BuLi, with allyl iodide at –105 °C gave sulfone (*R*)-**41** with 92% *ee* in 80% yield (Scheme 17, Table 12, entry 1). The *ee* of (*R*)-**41** was determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ employing the racemic sulfone as reference. The similar reaction of (*P*)-**5** with benzyloxymethyl bromide at –105 °C afforded sulfone (*S*)-**42** with 91% *ee* in 70% yield (entry 2). The *ee* of (*S*)-**42** was determined by ^{1}H NMR spectroscopy in the presence of Pr(tfc)$_3$ using the racemic sulfone as reference. The (*S*) configuration of (*S*)-**42** was assured by X-ray crystal structure analysis (Figure 14).[22] Because of the (*S*) configuration of (*S*)-**42**, the (*R*) configuration was assigned to (*R*)-**41**. These results reveal that the reactions of the salt (*P*)-**5** with alkyl halides at the most likely planar anionic C atom[1] occur with a similarly high selectivity to the planar salts (*P*)-**1** and (*M*)-**2**, *syn* to the O atoms and *anti* to the *tert*-butyl group.



Scheme 17. Enantioselective reactions of the salt (*P*)-**5** with allyl iodide and benzyloxymethyl bromide.

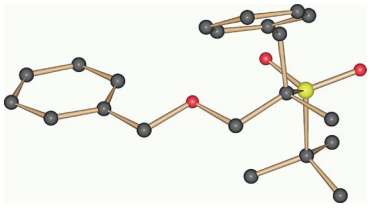
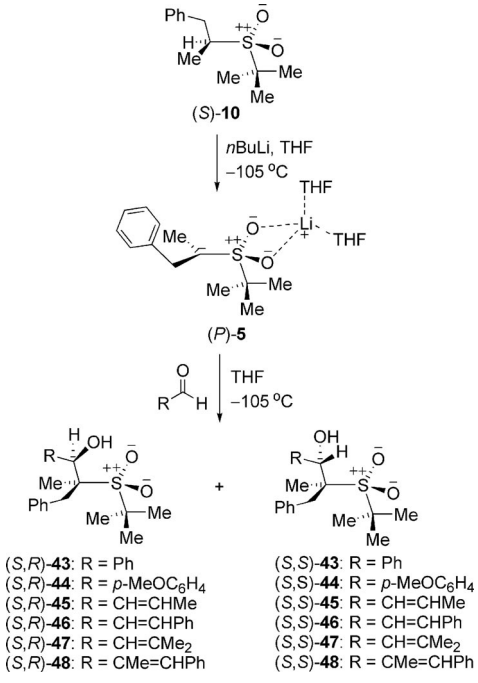


Figure 14. View of the crystal structure of sulfone (*S*)-**42** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red.

In a final series of experiments the reactivity of the salt (*P*)-**5** towards saturated and unsaturated aldehydes was investigated (Scheme 18). The reaction of (*P*)-**5** with benzaldehyde at –105 °C proceeded with high enantioselectivity but low diastereoselectivity and gave two diastereomeric hydroxy sulfones, (*S*,*S*)-**43** and (*S*,*R*)-**43**, in a combined yield of 84% (entry 3). The ratio of the two diastereomers was 60:40 and both had an *ee* of 92%. A similar situation was encountered in the reaction of (*P*)-**5** with *p*-methoxybenzaldehyde at –105 °C, which gave the two diastereomeric hydroxy sulfones (*S*,*S*)-**44** and (*S*,*R*)-**44** both with 95% *ee* in a ratio of 50:50 in a combined yield of 70% (entry 4). X-ray crystal structure analysis of (*S*,*S*)-**44** and (*S*,*R*)-**44** (Figures 15 and 16)[22] showed their C_α atoms to have the (*S*) configuration. Thus, the (*S*) configuration was also assigned to (*S*,*S*)-**43**, (*S*,*R*)-**43**, and all the hydroxy sulfones derived from (*P*)-**5** and the unsaturated aldehydes (see below). The *ee* values for (*S*,*S*)-**43**, (*S*,*R*)-**43**, (*S*,*S*)-**44**, (*S*,*R*)-**44**, and the hydroxy sulfones further derived from (*P*)-**5** and the unsatu-



Scheme 18. Enantioselective reactions of the salt (*P*)-**5** with aldehydes.

Table 12. Enantioselective reactions of the dialkyl-substituted salt (*P*)-**5** with C-electrophiles.

Entry	Sulfone[a]	Base	t_{met}[b] [min]	Salt	Electrophile[c]	t_{reac} [min][d]	Sulfone	Yield [%]	*ee* [%]
1	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	CH_2=$CHCH_2I$ (5)	10	(*R*)-**41**	80	92
2	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	$PhCH_2OCH_2Br$ (5)	10	(*S*)-**42**	70	91
3	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	PhCHO (5)	10	(*S*,*S*)-**43**/(*S*,*R*)-**43**[e]	84	92/92
4	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	*p*-$MeOC_6H_4CHO$ (5)	10	(*S*,*S*)-**44**/(*S*,*R*)-**44**[f]	70	95/95
5	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	MeCH=CHCHO (5)	10	(*S*,*S*)-**45**/(*S*,*R*)-**45**[f]	76	94/91
6	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	PhCH=CHCHO (5)	10	(*S*,*S*)-**46**/(*S*,*R*)-**46**[f]	69	93/91
7	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	Me_2C=CHCHO (5)	10	(*S*,*S*)-**47**/(*S*,*R*)-**47**[g]	81	90/95
8	(*S*)-**10**	*n*BuLi	10	(*P*)-**5**	PhCH=CMeCHO (5)	10	(*S*;*S*)-**48**/(*S*,*R*)-**48**[h]	87	91/91

[a] Sulfone with ≥99% *ee* was used. [b] Time elapsed between the beginning of the addition of RLi and the electrophile. [c] Number of equiv. in parentheses. [d] Time elapsed between the beginning of the addition of the electrophile and CF_3CO_2D. [e] Ratio 60:40. [f] Ratio 50:50. [g] Ratio 65:35. [h] Ratio 55:45.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

rated aldehydes were determined by ^{1}H NMR spectroscopy in the presence of Eu(tfc)$_3$ using the racemic diastereomers as reference. The configurations of the diastereomeric hydroxy sulfones at the C atom bearing the hydroxy group has, with the exception of (*S*,*S*)-**44** and (*S*,*R*)-**44**, not been determined.

The reaction of the salt (*P*)-**5** with crotonaldehyde at –105 °C furnished the hydroxy sulfones (*S*,*S*)-**45** and (*S*,*R*)-**45** in a ratio of 50:50 and a combined yield of 76% (entry 5). The hydroxy sulfones had *ee* values of 94 and 91%. With cinnamaldehyde as electrophile (*P*)-**5** gave at –105 °C the hydroxy sulfones (*S*,*S*)-**46** and (*S*,*R*)-**46** in a ratio of 50:50 and a combined yield of 69% (entry 6). The hydroxy sulfones had *ee* values of 93 and 91%. In both these reactions of (*P*)-**5**, the formation of derivatives derived from conjugate addition of the salt to the unsaturated aldehyde was not observed. The reactions of (*P*)-**5** with β-methylcrotonaldehyde and α-methylcinnamaldehyde at –105 °C also proceeded with high enantioselectivity and low diastereoselectivity (entries 7 and 8). The *ee* values of (*S*,*S*)-**47**, (*S*,*R*)-**47**, (*S*,*S*)-**48**, and (*S*,*R*)-**48** ranged from 90 to 95%.

Stereochemical Course of the Reactions with Electrophiles

The attack of the electrophile at the C$_\alpha$ atom of the salts **1**–**5** occurred with high selectivity *syn* to the O atoms and *anti* to the *tert*-butyl group. The crystal structures of the lithium *S*-*tert*-butylsulfonyl carbanion salts show strong steric shielding of the C$_\alpha$ atom of the anions by the *S*-*tert*-butyl group and only a minor shielding by the Li-coordinated O atoms. The monomeric and dimeric salts, which are the dominating species in THF solution, are in this regard similar. However, both sides of the C$_\alpha$ atom of the dimeric salts, being coordinated by four THF molecules, are severely shielded and not accessible to electrophiles.[1] Thus, of all the species that exist in THF solution the tetracoordinated dimeric lithium salt should have the lowest reactivity and the di(tri)-coordinated monomeric salt should have the highest reactivity.

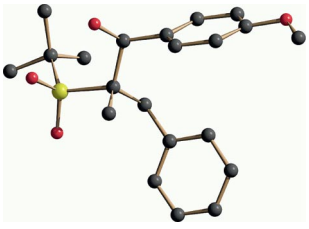
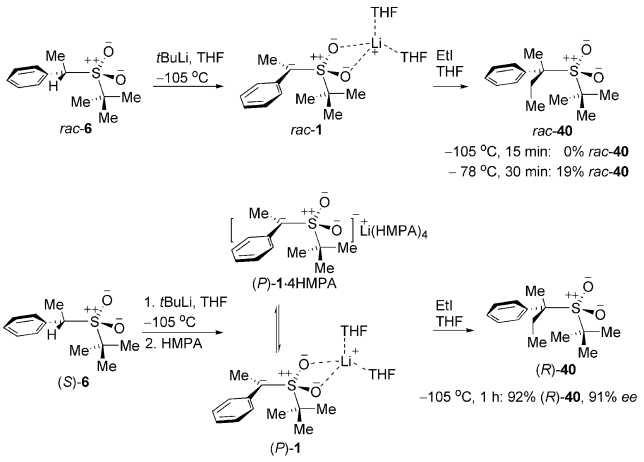


Figure 15. View of the crystal structure of sulfone (*S*,*S*)-**44** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red.

Figure 16. View of the crystal structure of sulfone (*S*,*R*)-**44** with H atoms omitted for clarity. Color code: C, black; S, yellow; O, red.

Reactivity of CIPs and SIPs

The study of the reactivity of the CIPs of salts **1**–**3** with alkyl halides in THF had revealed a significant influence of the size of the C_α-alkyl group upon the reaction rate. For example, no ethylation of the C_α-methyl-substituted CIP of *rac*-**1** with the formation of sulfone *rac*-**40** occurred upon treatment with ethyl iodide at –105 °C (Scheme 19). Quenching the mixture with CF_3CO_2D after 15 min gave the fully deuteriated sulfone *rac*-[D]**6** in quantitative yield. Raising the temperature of the mixture of *rac*-**1** and EtI to –78 °C resulted after 30 min in the formation of *rac*-**40** in only 19% yield.



Scheme 19. Reactions of the CIPs and SIPs of the salt (*P*)-**1** with ethyl iodide.

NMR spectroscopy of *rac*-**1** in THF in the presence of HMPA had revealed the formation of THF/HMPA-solvated CIPs and a HMPA-solvated SIP.[1] It was therefore of interest to see whether the SIP of (*P*)-**1** would show a higher reactivity in the ethylation. Treatment of the salt (*P*)-**1**, which was prepared by deprotonation of sulfone (*S*)-**5** with *t*BuLi at –105 °C in THF, with 13 equiv. of HMPA followed by the addition of 4 equiv. of ethyl iodide gave after a reaction time of 1 h sulfone (*S*)-**40** with 91% *ee* in 92% yield. This result impressively demonstrates that (1) the SIP of (*P*)-**1** has a significantly higher reactivity than the corresponding CIP[41] towards ethyl iodide and (2) both exhibit a similar high enantioselectivity in their reactions with electrophiles.

Conclusions

Enantiomerically highly enriched lithium *S*-*tert*-butylsulfonyl carbanion salts carrying a phenyl and alkyl group or two alkyl groups at the C$_\alpha$ atom are accessible by enantioselective deprotonation of the corresponding enantiopure sulfones with *t*BuLi and *n*BuLi, respectively, in THF at –105 °C. The synthesis of racemic *S*-*tert*-butyl sulfones and

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

their chromatographic resolution by chiral HPLC is an attractive route for their attainment in enantiopure form. There is evidence to suggest that the deprotonation of the sulfone with the lithiumorganyl follows an intramolecular pathway. The lithium *S*-*tert*-butylsulfonyl carbanion salts, which have a half-life of racemization of several hours at –105 °C, are configurationally stable on the timescale of their reactions with reactive electrophiles and structural investigation. The reactions of lithium *S*-*tert*-butylsulfonyl carbanion salts with acids and C-electrophiles proceed with high enantioselectivity *syn* to the O atoms, and the HMPA-solvated SIP has a significantly higher reactivity than the corresponding CIP. The conversion of the chiral sulfone into the corresponding substituted chiral sulfone, which involves the loss of stereogenicity at the α-stereogenic center upon deprotonation and its re-establishment upon reaction of the chiral α-sulfonyl carbanion with the electrophile, occurs with high overall enantioselectivity.

Experimental Section

General: All manipulations with the α-sulfonyl carbanion salts were performed under dry argon using Schlenk and syringe techniques in oven-dried glassware unless otherwise stated. Solvents were purified and dried prior to use by distillation from an appropriate drying agent under argon. Tetrahydrofuran (THF) was distilled from potassium benzophenone ketyl. Hexamethylphosphoric triamide (HMPA) was distilled from calcium hydride. Diethyl ether was distilled from sodium benzophenone ketyl. Starting materials were obtained from commercial sources and used without further purification unless otherwise stated. Solutions of *n*-butyllithium (*n*BuLi) in *n*-hexane, *tert*-butyllithium (*t*BuLi) in *n*-pentane, phenyllithium (PhLi) in diethyl ether, *sec*-butyllithium (*s*BuLi) in cyclohexane, *n*-propyllithium (*n*PrLi) in *n*-pentane, *sec*-butyllithium in *n*-pentane, methyllithium (MeLi) in diethyl ether, vinyllithium in diethyl ether and trimethylsilylmethyllithium (Me_3SiCH_2Li) in *n*-pentane were obtained from commercial sources and standardized by titration with diphenylacetic acid.[42] Analytical thin-layer chromatography (TLC) was performed on E. Merck precoated TLC plates (silica gel 60 F_{254}, layer thickness 0.2 mm). Column chromatography was performed with Merck silica gel 60 (70–230 mesh). Polarimetric measurements at low temperatures were conducted with Perkin–Elmer P141 and P241 instruments using a Colora Ultra-cryostat KT 290 S, a Lauda TP 10 digital thermometer with a Pt 82 thermosensor, and a Hellma (Müllheim) quartz glass polarimeter tube (5 mL) equipped with a cooling jacket and evacuated quartz glass windows. Melting points were determined by using a Büchi SMP-20 apparatus. ^1H and ^{13}C NMR spectra were recorded with Bruker AM 400, Bruker WM 300, Bruker WM 250, Varian Unity 500, Varian Inova 400, Varian VXR 300, and Varian Gemini 300 instruments. ^1H NMR chemical shifts of measurements in $CDCl_3$ are reported in ppm relative to Me_4Si (δ = 0.00 ppm) as internal standard. Splitting patterns are designated as follows: s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet; br., broad; ps, pseudo in the case that the apparent multiplicity is a result of the overlap of several multiplets or additional couplings are not resolved because of line-broadening; sh., shoulder; unsym., unsymmetrical; hn, hidden; app., apparent. ^{13}C NMR chemical shifts of measurements in $CDCl_3$ are reported in ppm relative to Me_4Si (δ = 0.00 ppm) as internal standard. Peaks in the ^{13}C NMR spectra are denoted as "u" for carbons with zero of two attached protons and as "d" for carbon atoms with one or three attached protons, as determined from the attached proton test (APT) pulse sequence. The following abbreviations are used to designate the peaks: br., broad; vbr., very broad; t, triplet. Low-resolution mass spectra were recorded with a Varian MAT 212 mass spectrometer. Only peaks of $m/z \geq 80$ and an intensity of ≥5%, except decisive ones, are listed. IR spectra were recorded with a Perkin–Elmer FT 1760 S and 1760 instruments. Only peaks of $\tilde{\nu} \geq 800\ cm^{-1}$ are listed. The following abbreviations are used to designate the peaks: vs, very strong; s, strong; m, medium; w, weak. GC analyses were performed with a Carlo–Erba HRGC 5300 Mega-Series instrument. MPLC was performed with a Kronwald Constakron 3 HPP instrument with a Knauer detector of variable wavelength and a Bischoff RI detector 8110 using Kronwald FHPLC columns filled with IMPAQ RG 1020 Si (16.2 μm) and Merck LiChoprep Si 60 (15–25 μm). Polarimetric measurements were performed with a Perkin–Elmer P241 instrument at approximately 22 °C unless otherwise stated using a micro-tube (l = 10 cm, V = 1 mL). Specific rotations are given in $deg\,cm^{-3}\,dm^{-1}\,g^{-1}$ and concentration c in $10^{-2}\,g\,cm^{-3}$. Elemental analyses were performed by the Institute of Organic Chemistry Microanalytical Laboratory.

General Procedure for the Enantioselective Synthesis of [*t*Bu-$SO_2C(R^1)(R^2)]^-Li^+$ and Their Reactions with Electrophiles (GP1): An oven-dried long-necked Schlenk flask, which was equipped with a Teflon™-coated magnetic stirring bar, was filled with argon. The flask was charged with the sulfone and closed with a rubber septum, which was fitted with a thermoelement reaching to 1 cm above the bottom of the flask. Temperatures were measured with a Kelvimat type 4321 precision thermometer (Burster Präzisionsmeßtechnik, Gernsbach, Germany), which had an accuracy of measurement of 10 mK and a reproducibility of ± 2 mK. A Pt-100 thermocouple of type 42943 (Burster Präzisionsmeßtechnik, Gernsbach, Germany) was used as the thermoelement, which was suitable for measurements in the range of –200 to +500 °C. Then the flask was evacuated three times and refilled with argon and charged with THF (33 mL/mmol sulfone) with a syringe. The solution was cooled under argon to the given temperature either in a dry ice/MeOH or liquid nitrogen/EtOH bath. Then the long-necked flask was immersed just below the joint into the cooling bath and the solution of RLi was added with a syringe under film-cooling (the solution was allowed to run down the cooled long neck) to the solution of the sulfone under rapid stirring. The solution of RLi was added at such a rate that both efficient film-cooling and temperature control were guaranteed. After the given metalation time, the mixture was treated with a solution of the electrophile under rapid stirring and film-cooling. Because of exothermic reactions, efficient cooling is required to achieve temperature control. Deuteriation and quenching of the reaction mixture after a given reaction time was carried out with a 2 M solution of CF_3CO_2D in THF unless otherwise stated. Then diethyl ether (20 mL) was added and the mixture was successively washed with saturated aqueous $NaHCO_3$, brine, and water. The organic phase was dried ($MgSO_4$) and concentrated in vacuo. A separate determination of the *ee* value of the deuteriated sulfone in the presence of the non-deuteriated sulfone was not possible. Therefore the *ee* value of the recovered sulfone was, in the case of incomplete deprotonation of the sulfone, calculated by correction of the experimental *ee* value of both sulfones by the degree of deuteriation.

General Procedure for the Enantioselective Synthesis of the Salt 5 and Its Polarimetric Measurement (GP2): Sulfone **10** (0.06 to 0.60 mmol) was dissolved in dry THF (5.0 mL) under argon in an oven-dried and argon-filled Schlenk flask. *n*BuLi (1.05–1.10 mmol

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

in *n*-hexane) was placed in the oven-dried and argon-filled long-necked Schlenk flask. Then the solvent was removed in vacuo whilst stirring and the residue was dried under high vacuum for 5 min. The flask was filled with argon and cooled to –90 °C. Then dry THF (1.0 mL) was slowly added under film-cooling and stirring. Stirring was continued at –90 °C until all of the oily *n*BuLi had dissolved. Then the cold solution of *n*BuLi in THF was added through a syringe whilst stirring and under argon to the homogeneous solution of the sulfone in THF at –105 °C under film-cooling. At the same time the polarimeter together with the tube were made ready for the measurement. The oven-dried and argon-filled tube was closed with a septum, placed in the polarimeter, and connected with the cryostat. Then a strong stream of dry nitrogen was directed towards the windows of the tube, which was continued throughout the measurement. The polarimeter compartment was closed and the tube was cooled to the given temperature for 10 min. Then the wavelength was adjusted and the setting was adjusted to zero. Then the cold solution of the salt **5** (–105 °C) was rapidly (1 min) transferred to the cold tube through a cold (–100 °C) steel cannula with application of argon pressure. The cannula was equipped with a cooling jacket made of plastic tubing filled with liquid nitrogen/EtOH. The tube compartment of the polarimeter was closed and the measurement was started. At the end of the measurement the salt solution was removed with a syringe and added to a solution of CF_3CO_2D (4 equiv.) in THF (3 mL) unless otherwise stated. Work-up gave the deuteriated sulfone, the D content of which was determined by ^1H MMR spectroscopy.

Special care was taken to address the following points. (1) *n*BuLi is at –90 °C a viscous oil which dissolves only slowly in THF. (2) The sulfone must be completely dissolved in THF at –105 °C before the addition of the solution of *n*BuLi in THF. (3) The addition of THF to *n*BuLi and the addition of the THF solution of *n*BuLi to the THF solution of the sulfone must be carried out under efficient film-cooling at –105 °C. (4) The solution of the salt in THF in the polarimeter tube must be free of argon bubbles, clear, and homogeneous. (5) Fogging of the windows of the polarimeter tube must be prevented. (6) The transfer of the cold solution of the salt to the polarimeter tube has to occur as rapidly as possible under efficient cooling of the cannula to –105 °C to avoid a warming of the solution ($\Delta T < 15$ K).

Preparative Racemate Separation of Sulfones *rac*-6–10

Sulfone *rac*-6: Chiralcel OD, 250 mm × 50 mm; SD-1 pump. UV-Prostar 320; RI detector Knaur; workstation Varian; *n*-hexane/*i*PrOH, 95:5; 40 mL min^{-1}, 400 kPa; 254 nm + RI, 30 mg mL^{-1}. Sulfone *rac*-**6** (270 mg) gave (*S*)-**6** (131 mg, 48%) with ≥99% *ee*, m.p. 138 °C, $[\alpha]_D$ = –57.8 (*c* = 3.75, THF) and (*R*)-**6** (117 mg, 44%) with ≥99% *ee*, m.p. 139 °C, $[\alpha]_D$ = +57.6 (*c* = 3.0, THF).

Sulfone *rac*-7: Chiralcel OD, 250 mm × 50 mm; SD-1 pump. UV-Prostar 320; RI detector Knaur; workstation Varian; *n*-hexane/*i*PrOH, 98:2; 40 mL min^{-1}, 400 kPa; 254 nm + RI, 25 mg mL^{-1}. Sulfone *rac*-**7** (130 mg) gave (*S*)-**7** (62 mg, 48%) with 99% *ee*, m.p. 120 °C, $[\alpha]_D$ = –39.04 (*c* = 2.8, THF) and (*R*)-**7** (62 mg, 48%) with ≥99% *ee*, m.p. 120 °C, $[\alpha]_D$ = +39.07 (*c* = 2.8, THF).

Sulfone *rac*-8: Chiralpack AD, 250 mm × 50 mm; SD-1 pump. UV-Prostar 320; RI detector Knaur; workstation Varian; *n*-hexane/*i*PrOH, 99.5:0.5; 50 mL min^{-1}, 600 kPa; 254 nm + RI, 25 mg mL^{-1}. Sulfone *rac*-**8** (34 mg) gave (*S*)-**8** (15 mg, 44%) ≥99% *ee*, m.p. 119 °C, $[\alpha]_D$ = –43.5 (*c* = 0.6, THF) and (*R*)-**8** (14 mg, 41%) with ≥99% *ee*, m.p. 120 °C, $[\alpha]_D$ = +42.7 (*c* = 0.6, THF).

Sulfone *rac*-9: Chiralcel OD, 250 mm × 50 mm; SD-1 pump. UV-Prostar 320; RI detector Knaur; workstation Varian; *n*-hexane/*i*PrOH, 99.5:0.5, 40 mL min^{-1}, 400 kPa; 254 nm + RI, 25 mg mL^{-1}. Sulfone *rac*-**9** (140 mg) gave (*R*)-**9** (64 mg, 46%) with ≥99% *ee*, m.p. 126 °C, $[\alpha]_D$ = +44.9 (*c* = 1.75, THF) and (*S*)-**9** (62 mg, 44%) with ≥99% *ee*, m.p. 126 °C, $[\alpha]_D$ = –45.1 (*c* = 1.75, THF).

Sulfone *rac*-10: Chiralcel OD, 250 mm × 50 mm; SD-1 pump. UV-Prostar 320; RI detector Knaur; workstation Varian; *n*-hexane/*i*PrOH, 1000:1.5, 40 mL min^{-1}, 400 kPa; 254 nm + RI, 25 mg mL^{-1}. Sulfone *rac*-**10** (80 mg) gave (*S*)-**10** (35 mg, 44%) with ≥99% *ee*, m.p. 82–83 °C, $[\alpha]_D$ = +26.0 (*c* = 0.175, diethyl ether), $[\alpha]_{365}$ = +88.6 (*c* = 0.17, diethyl ether) and (*R*)-**10** (37 mg, 46%) with ≥99% *ee*, m.p. 82 °C, $[\alpha]_D$ = –26.1 (*c* = 0.185, diethyl ether), $[\alpha]_{365}$ = –88.4 (*c* = 0.185, ether).

Synthesis of Lithium (*M*)-1-(*tert*-Butylsulfonyl)-1-phenylethan-1-ide [(*M*)-1]: The ethanide salt was synthesized by deprotonation of sulfone (*R*)-**6** with *t*BuLi and deuteriation with CF_3CO_2D. Following GP1, a solution of sulfone (*R*)-**6** (219 mg, 0.97 mmol, ≥99% *ee*) in THF (30 mL) was treated at –105 °C with *t*BuLi (0.80 mL of 1.60 M in *n*-pentane, 1.17 mmol) over 5 min. After stirring the mixture at –105 °C for 10 min, it was treated at –105 °C over 5 min with CF_3CO_2D (1.0 mL of 2 M in THF, 2 mmol). Work-up afforded sulfone (*R*)-[D]**6** (95%) with ≥98% D content [^1H NMR: δ = 4.39 ppm (H_α)] and 87% *ee* {^1H NMR [$CDCl_3$, 20 mol-% Eu(hfc)$_3$] and GC (permethyl-β-cyclodextrin)}, $[\alpha]_D$ = +50.4 (*c* = 1.1, THF).

Synthesis of Lithium (*M*)-1-(*tert*-Butylsulfonyl)-1-phenylpropan-1-ide [(*M*)-2]: The propanide salt was synthesized by deprotonation of sulfone (*R*)-**7** with *t*BuLi and deuteriation with CF_3CO_2D. Following GP1, a solution of sulfone (*R*)-**7** (202 mg, 0.84 mmol, ≥99% *ee*) in THF (30 mL) was treated at –105 °C over 5 min with *t*BuLi (0.66 mL of 1.52 M in *n*-pentane, 1.0 mmol). After stirring the mixture at –105 °C for 20 min, it was treated at –105 °C over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up afforded sulfone (*R*)-[D]**7** (98%) with ≥98% D content [^1H NMR: δ = 4.06 ppm (H_α)] and 93% *ee* {^1H NMR [300 MHz, 15 mol-% Eu(hfc)$_3$]}, $[\alpha]_D$ = +34.4 (*c* = 1.2, THF).

Synthesis of Lithium (*M*)-1-(*tert*-Butylsulfonyl)-1-phenylpropan-1-ide [(*M*)-2]: The propanide salt was synthesized by deprotonation of sulfone (*R*)-**7** with *t*BuLi/TMEDA and deuteriation with CF_3CO_2D. Following GP1, a mixture of sulfone (*R*)-**7** (203 mg, 0.84 mmol, ≥99% *ee*) in THF (22 mL) and TMEDA (0.84 mL of 2 M in THF, 1.68 mmol) was treated at –105 °C over 5 min with *t*BuLi (0.66 mL of 1.52 M in *n*-pentane, 1.10 mmol). After stirring the mixture at –105 °C for 15 min, it was treated at –105 °C over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Diethyl ether was added and the mixture was extracted with 2 M HCl. Work-up according to GP1 afforded sulfone (*R*)-[D]**7** (99%) with 93% D content [^1H NMR: δ = 4.06 ppm (H_α)] and 39% *ee* {^1H NMR [300 MHz, 15 mol-% Eu(hfc)$_3$]}, $[\alpha]_D$ = +12.9 (*c* = 1.5, THF).

Synthesis of Lithium (*M*)-1-(*tert*-Butylsulfonyl)-1-phenylpropan-1-ide [(*M*)-2]: The propanide salt was synthesized by deprotonation of sulfone (*R*)-**7** with *t*BuLi and subsequent addition of TMEDA and deuteriation with CF_3CO_2D. Following GP1, a mixture of sulfone (*R*)-**7** (200 mg, 0.83 mmol, ≥99% *ee*) in THF (30 mL) was treated at –105 °C over 5 min with *t*BuLi (0.66 mL of 1.50 M in *n*-pentane, 1.08 mmol). After stirring the mixture at –105 °C for 15 min, it was treated at –105 °C over 2 min with TMEDA (0.83 mL of 2 M in THF, 1.66 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C over 2 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up afforded sulfone (*R*)-[D]**7** (99%) with ≥98% D content [^1H NMR: δ = 4.06 ppm (H_α)] and 91% *ee* {^1H NMR [300 MHz, 15 mol-% Eu(hfc)$_3$]}, $[\alpha]_D$ = +32.4 (*c* = 1.5, THF).

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(*R*)-(–)-[2-(*tert*-Butylsulfonyl)pent-4-en-2-yl]benzene [(*R*)-34]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylethan-1-ide [(*P*)-**1**] was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi and treated with allyl iodide. Following GP1, a solution of sulfone (*S*)-**6** (1.025 g, 4.53 mmol, ≥99% *ee*) in THF (90 mL) was treated at –105 °C over 10 min with a solution of *t*BuLi (3.8 mL of 1.52 M in *n*-pentane, 5.93 mmol). After stirring the mixture at –105 °C for 15 min, it was treated at –105 °C over 5 min with allyl iodide (9.0 mL of 4 M in THF, 36.0 mmol). After stirring the mixture at –105 °C for 15 min, it was warmed to room temperature. Work-up gave sulfone (*R*)-**34** (1.175 g, 97%) with 90% *ee* {HPLC (*n*-hexane/*i*PrOH, 98:2, 0.5 mL min^{-1}, UV 254 nm; Chiracel OD-H with OD): t_R = 20.49 min [(*S*)-**34**], t_R = 21.33 min [(*R*)-34]}. GC (permethyl-β-cyclodextrin, 140 °C; 100 kPa H_2): t_R [(*S*)-**34**] = 32.3 min, t_R [(*R*)-**34**] 32.9 = min {^{1}H NMR [300 MHz, $CDCl_3$, 30 mol-% Eu(hfc)$_3$]: δ = 1.39 (S-*t*Bu) [(*S*)-**34**], 1.41 ppm (S-*t*Bu) [(*R*)-**34**]}, $[\alpha]_D$ = –22.2 (*c* = 1.8, THF).

Sulfone (*R*)-**34** (1.071 g) with 90% *ee* was heated at reflux for 20 min in *n*-hexane/EtOAc (20 mL, 8:1) and the solution was kept for 2 d at 2 °C. The resulting crystals were washed with cold *n*-hexane (2 × 5 mL) and dried to give sulfone (*R*)-**34** (490 mg, 44%), $[\alpha]_D$ = –24.6 (*c* = 1.5, THF), m.p. 85–90 °C. Recrystallization from *n*-hexane (8 mL) gave sulfone (*R*)-**34** (231 mg, 21%) with ≥99% *ee* as colorless plates and needles, m.p. 90–90.5 °C, $[\alpha]_D$ = –24.7 (*c* = 1.7, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (s, 9 H, S-*t*Bu), 1.90 (d, *J* = 0.7 Hz, 3 H, α-CH_3), 2.89 (dd, *J* = 13.8, *J* = 8.7 Hz, 1 H, CH_2), 3.42 (ddm, *J* = 13.8, *J* = 4.7 Hz, 1 H, CH_2), 5.04 (dm, *J* = 9.7 Hz, 1 H, =CH_2), 5.13 (dm, *J* = 17.1 Hz, 1 H, =CH_2), 5.32 (dddd, *J* = 17.1, *J* = 9.7, *J* = 8.7, *J* = 4.7 Hz, 1 H, =CH), 7.31–7.42 (m, 3 H, *m*-, *p*-Ph), 7.67–7.73 (m, 2 H, *o*-Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (α-Me, d), 25.6 (S-*t*Bu-CH_3, d), 40.7 (CH_2, u), 66.7, 71.4 (S-*t*Bu-*C*Me$_3$, C_α, u), 120.0 (u), 128.5, 128.8 (*o*-, *m*-Ph, d), 128.6 (*p*-Ph, d), 131.3 (d), 136.2 (*i*-Ph, u) ppm. IR (KBr): $\tilde{\nu}$ = 3448 (w br., H_2O), 3074 (w), 2988 (m), 2934 (m), 2873 (w), 2373 (w), 1980 (w), 1910 (w), 1854 (w), 1832 (w), 1655 (w), 1641 (w), 1582 (w), 1500 (m), 1482 (s), 1452 (s), 1421 (w), 1397 (m), 1383 (m), 1364 (w), 1290 (s), 1281 (s), 1269 (vs), 1215 (w), 1182 (m), 1111 (vs), 1084 (m), 1059 (s), 1029 (w), 1020 (w), 994 (w), 927 (s), 887 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 146 (14), 145 (100) [M – SO_2*t*Bu]$^+$, 144 (11), 129 (15), 128 (12), 117 (31), 115 (13), 105 (13), 91 (23), 77 (10), 57 (25), 41 (30), 39 (13). $C_{15}H_{22}O_2S$ (266.40): calcd. C 67.63, H 8.32; found C 67.73, H 8.33.

Synthesis of Lithium (*P*)-1-(*tert*-Butylsulfonyl)-1-phenylethan-1-ide [(*P*)-1]: The ethanide salt was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and a metalation time t_{met} of 30 min, addition of 2 equiv. of HMPA and deuteriation with CF_3CO_2D. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (33 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 25 min, it was first treated at –105 °C with HMPA (2 mL of 1 M in THF, 2 mmol) and then after over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up afforded sulfone (*R*)-[D]**6** (99%) with 98% D content [^{1}H NMR: δ = 4.39 ppm (H_α)] and 89% *ee* (^{1}H NMR, GC, HPLC).

The ethanide salt (*P*)-**1** was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and a metalation time t_{met} of 35 min, addition of 10 equiv. of HMPA before metalation and deuteriation with CF_3CO_2D. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) and HMPA (2.3 mL, 10 mmol) in THF (33 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 30 min, it was treated at –105 °C over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up afforded sulfone (*R*)-[D]**6** (99%) with ≥98% D content [^{1}H NMR: δ = 4.39 ppm (H_α)] and 66% *ee* (^{1}H NMR, GC, HPLC), $[\alpha]_D^{20}$ = –39.2 (*c* = 1.1, THF).

The ethanide salt (*P*)-**1** was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and a metalation time t_{met} of 30 min, addition of 2 equiv. of HMPA before deuteriation with CF_3CO_2D. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (26 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 5 min, it was first treated at –105 °C with HMPA (2 mL of 1 M in THF, 2 mmol) and then after 25 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up afforded sulfone (*R*)-[D]**6** (99%) with 98% D content [^{1}H NMR: δ = 4.39 ppm (H_α)] and 89% *ee* (^{1}H NMR, GC, HPLC), $[\alpha]_D^{20}$ = –47.4 (*c* = 1.1, THF).

The ethanide salt (*P*)-**1** was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and a metalation time t_{met} of 30 min, addition of 10 equiv. of HMPA, and deuteriation with CF_3CO_2D. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (26 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 25 min, it was first treated at –105 °C with HMPA (10 mL of 1 M in THF, 10 mmol) and then after 25 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up afforded sulfone (*R*)-[D]**6** (99%) with ≥98% D content [^{1}H NMR: δ = 4.39 ppm (H_α)] and 90% *ee* (^{1}H NMR, GC, HPLC), $[\alpha]_D^{20}$ = –51.7 (*c* = 1.0, THF).

(–)-[1-(Benzyloxy)-2-(*tert*-butylsulfonyl)propan-2-yl]benzene [(–)-37]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylethan-1-ide [(*P*)-**1**] was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and reaction with benzyloxymethyl bromide. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (26 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C with benzyloxymethyl bromide (2 mL of 1 M in THF, 2.0 mmol) and then after 15 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up and chromatography (*n*-hexane/EtOAc, 5:1) afforded sulfone **37** (250 mg, 72%) with 95% *ee* {^{1}H NMR [300 MHz, $CDCl_3$, 75 mol-% Eu(hfc)$_3$]: δ = 2.77 (Me) [(–)-**37**], 2.82 (Me) [(+)-**37**]}, R_f = 0.17 (*n*-hexane/EtOAc, 5:1), $[\alpha]_D^{20}$ = +8.80 (*c* = 0.9, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07 (s, 9 H, S-*t*Bu), 2.03 (s, 3 H, CH_3), 4.16 (d, *J* = 9.7 Hz, 1 H, α-CH_2), 4.29 (d, *J* = 9.4 Hz, 1 H, α-CH_2), 4.50 (d, *J* = 12.1 Hz, 1 H, $PhCH_2$), 4.59 (d, *J* = 12.4 Hz, 1 H, $PhCH_2$), 7.20–7.38 (m, 8 H, Ph), 7.66–7.70 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8 (d), 25.3 (d), 67.0, 72.5 (u), 72.6, 73.8 (u), 127.7, 127.7, 128.3, 128.4, 128.7, 128.8 (d, Ph), 135.5, 137.6 (u, *i*-Ph) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3089 (w), 3062 (w), 3026 (m), 2999 (m), 2976 (m), 2932 (m), 2871 (m), 1497 (m), 1480 (m), 1454 (s), 1396 (w), 1363 (m), 1281, 1214 (m), 1184 (m), 1148 (m), 1117, 1068, 1030 (m), 1018 (s), 925 (w) cm^{-1}. MS (70 eV): *m*/*z* (%) = 225 (13) [M – CH_2OCH_2Ph]$^+$, 118 (16), 92 (10), 91 (100), 57 (17). $C_{20}H_{26}O_3S$ (346.48): calcd. C 69.33, H 7.56; found C 69.36, H 7.71.

(–)-(*R*)-[2-(*tert*-Butylsulfonyl)pent-4-yn-2-yl]benzene [(*R*)-35]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylethan-1-ide [(*P*)-**1**] was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and reaction with propargyl bromide. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (26 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with propargyl bromide

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(0.45 mL of 80% in toluene, 4.0 mmol) and then after 15 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up and chromatography (petroleum ether/diethyl ether, 2:1) afforded sulfone (*R*)-**35** (204 mg, 77%) with 87% *ee*. ^{1}H NMR [300 MHz, $CDCl_3$, 75% Eu(hfc)$_3$]: δ = 2.86 (Me) [(*R*)-**35**], 2.90 ppm (Me) [(*S*)-**35**]. GC (permethyl-β-cyclodextrin): t_R [(*S*)-**35**] = 35.8 min, t_R [(*R*)-**35**] = 36.2 min. Recrystallization from cyclohexane/EtOAc gave single crystals of the sulfone as colorless blocks, m.p. 145–150 °C, R_f = 0.30 [petroleum ether (40–70)/Et_2O, 2:1], $[\alpha]_D^{20}$ = –38.54 (*c* = 1.0, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (s, 9 H, S-*t*Bu), 1.86 (t, *J* = 2.7 Hz, 1 H, ≡CH), 2.07 (d, *J* = 1.0 Hz, 3 H, CH_3), 3.14 (dd, *J* = 16.8, *J* = 2.7 Hz, 1 H, CH_2), 3.54 (ddd, *J* = 16.8, *J* = 2.7, *J* = 1.0 Hz, 1 H, CH_2), 7.35–7.44 (m, 3 H, Ph), 7.69–7.74 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (d), 25.4 (d), 27.4 (u), 66.8 (u), 70.9 (u), 71.9 (u), 78.5 (u), 128.5 (d), 128.7 (d), 128.9 (d) (Ph), 135.4 (u, *i*-Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3430 (w), 3273 (s), 2999 (m), 2981 (m), 2935 (m), 1499 (w), 1480 (m), 1452 (m), 1384 (m), 1368 (w), 1275, 1212 (w), 1181 (m), 1115, 1084 (m), 1063 (s), 1031 (w), 927 (w), 881 (w) cm^{-1}. MS (70 eV): *m*/*z* (%) = 143 (27) [M – SO_2tBu]$^+$, 128 (18), 57 (5). $C_{15}H_{20}O_2S$ (264.38): calcd. C 68.15, H 7.62; found C 68.25, H 7.78.

(–)-[4-(*tert*-Butylsulfonyl)-4-phenylpent-1-ynyl]trimethylsilane [(–)-36]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylethan-1-ide [(*P*)-**1**] was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and reaction with 3-(trimethylsilyl)propargyl bromide. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (26 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with trimethylsilylpropargyl bromide (1 mL of 4 M in THF, 4.0 mmol) and then after 30 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up and chromatography (*n*-hexane/EtOAc, 3:1) afforded sulfone (*R*)-**36** (283 mg, 84%) with 94% *ee* {^{1}H NMR [300 MHz, $CDCl_3$, 75 mol-% Eu(hfc)$_3$]: δ = 3.01 (Me) [(–)-**36**], 3.06 ppm (Me) [(+)-**37**]}, m.p. 66–67 °C, R_f = 0.17 (*n*-hexane/EtOAc, 5:1), $[\alpha]_D^{20}$ = –45.53 (*c* = 1.1, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.05 [s, 9 H, $Si(CH_3)_3$], 1.14 (s, 9 H, S-*t*Bu), 2.10 (d, *J* = 1.0 Hz, 3 H, CH_3), 3.14 (d, *J* = 16.8 Hz, 1 H, CH_2), 3.63 (dd, *J* = 16.8, *J* = 0.7 Hz, 1 H, CH_2), 7.37–7.47 (m, 3 H, Ph), 7.72–7.77 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.0 (d), 21.6 (d), 25.7 (d), 29.1 (u), 67.0 (u), 71.4 (u), 89.2 (u), 101.3 (u), 128.5 (d), 128.9 (d), 129.1 (d) (Ph), 135.9 (u) ppm. IR (KBr): $\tilde{\nu}$ = 3074 (w), 3058 (w), 3001 (m), 2990 (m), 2963 (m), 2951 (m), 2898 (m), 2181 (m), 1498 (m), 1482 (m), 1446 (m), 1396 (w), 1383 (m), 1366 (w), 1272 (s), 1254 (s), 1216 (w), 1185 (m), 1157 (w), 1114 (s), 1080 (m), 1072 (m), 1060 (s), 1041 (s), 1030 (m) cm^{-1}. MS (70 eV): *m*/*z* (%) = 215 (16) [M – SO_2tBu]$^+$, 73 (100), 57 (17). $C_{18}H_{28}O_2SSi$ (336.56): calcd. C 64.24, H 8.39; found C 64.06, H 8.43.

(–)-2-(*tert*-Butylsulfonyl)-1,2-diphenylpropan-1-ol [(–)-38]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylethan-1-ide [(*P*)-**1**] was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and reaction with benzaldehyde. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (26 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with benzaldehyde (2 mL of 4 M in THF, 8.0 mmol) and then after 15 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). The mixture was washed first with saturated aqueous $NaHCO_3$ (10 mL) and then with saturated aqueous Na_2SO_3 (2 × 20 mL). Work-up according to GP1 and purification by chromatography gave a mixture of alcohols **38A** and **38B** (266 mg, 80%) in a ratio of 63:21. Separation of the diastereomeric alcohols (70 mg) by MPLC (*n*-hexane/EtOAc, 5:1) gave diastereomer (–)-**38A** (51 mg) with 94% *ee* {^{1}H NMR (300 MHz, $CDCl_3$, 5 equiv. of Pirkle alcohol): δ = 6.06, 6.07 (CHOH), 4.15, 4.16 ppm (OH); ^{1}H NMR [30 MHz, $CDCl_3$, 7 mol-% Eu(hfc)$_3$]: δ = 1.31, 1.36, (S-*t*Bu), 2.72, 2.48 ppm (Me); HPLC (Chiralcel OD-H, *n*-hexane/*i*PrOH, 9:1, UV, 254 nm): t_R = 24.6, 25.9 min} and diastereomer (–)-**38B** (15 mg) with 95% *ee* {^{1}H NMR (300 MHz, $CDCl_3$, 5 equiv. of Pirkle alcohol): δ = 5.68, 5.70 (CHOH), 4.63, 4.65 (OH) ppm; ^{1}H NMR [300 MHz, $CDCl_3$, 7% Eu(hfc)$_3$]: δ = 2.02, 2.04 ppm (Me)} as colorless solids.

(–)-38A: R_f = 0.40 (*n*-hexane/EtOAc, 3:1), m.p. 98 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 9 H, S-*t*Bu), 1.99 (s, 3 H, CH_3), 4.20 (d, *J* = 1.3 Hz, 1 H, OH), 6.14 [br. s, 1 H, CH(OH)], 6.95–7.10 (m, 6 H, *m*-, *p*-Ph), 7.26–7.35 (m, 4 H, *o*-Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4 (d), 25.7 (d), 69.1, 75.9 (u), 71.1 (d), 125.4 (d), 127.1 (d), 127.5 (d), 128.4 (d), 129.0 (d), 129.7 (d) (Ph), 134.4 (u), 137.0 (u) (*i*-Ph) ppm. MS (70 eV): *m*/*z* (%) = 332 (0.1) [M]$^+$, 211 (5), 133 (4), 105 (21), 77 (8), 57 (9). $C_{19}H_{24}O_3S$ (332.46): calcd. C 68.64, H 7.28; found C 68.56, H 7.38.

(–)-38B: R_f = 0.44 (*n*-hexane/EtOAc, 3:1), m.p. 160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (s, 9 H, S-*t*Bu), 1.67 (s, 3 H, CH_3), 4.65 (d, *J* = 1.7 Hz, 1 H, OH), 5.74 [d, *J* = 1.3 Hz, 1 H, C*H*(OH)], 6.95–7.10 (m, 6 H, *m*-, *p*-Ph), 7.26–7.35 (m, 4 H, *o*-Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (d), 25.9 (d), 69.1, 74.1 (u), 78.5 (d), 123.6 (d), 124.7 (d), 126.4 (d), 127.5 (d), 128.0 (d), 128.3 (d), 129.1 (d), 129.4 (d) (Ph), 130.4 (u), 132.6 (u) (*i*-Ph) ppm.

(–)-3-(*tert*-Butylsulfonyl)-3-phenylbutan-2-one [(–)-39]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylethan-1-ide [(*P*)-**1**] was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and reaction with acetic anhydride. Following GP1, a solution of sulfone (*R*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (26 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with acetic anhydride (0.3 mL, 3.0 mmol) and then after 30 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up and purification by chromatography (*n*-hexane/EtOAc/THF, 8:1:0.1) have ketone **39** (184 mg, 69%) with 94% *ee* {^{1}H NMR [300 MHz, $CDCl_3$, 30 mol-% Eu(hfc)$_3$]: δ = 2.63, 2.65 ppm (CH_3); HPLC (Chiralcel OD-H, *n*-hexane/*i*PrOH, 98:2, UV 254 nm): t_R = 20.9, 23.8 min} as a colorless solid, m.p. 107–110 °C, R_f = 0.06 (*n*-hexane/EtOAc/THF, 8:1:0.1), $[\alpha]_D^{20}$ = –78.1 (*c* = 1.1, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (s, 9 H, S-*t*Bu), 2.16 (s, 3 H, CH_3), 2.44 (s, 3 H, CH_3), 7.38–7.43 (m, 3 H, Ph), 7.59–7.64 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (d), 25.6 (d), 28.3 (d), 69.2 (u), 82.7 (u), 128.5 (d), 129.4 (d), 129.7 (d), 133.2 (u), 201.4 (u) ppm. IR (KBr): $\tilde{\nu}$ = 3423 (w), 3064 (w), 3004 (m), 2977 (m), 2936 (w), 2875 (w), 1719 (vs), 1601 (w), 1582 (w), 1498 (m), 1479 (m), 1468 (s), 1450 (s), 1398 (m), 1383 (m), 1364 (m), 1351 (m), 1284 (s), 1175 (s), 1113 (vs), 1102 (s), 1069 (s), 1057 (s), 1034 (m), 1020 (m), 1003 (m), 958 (m), 932 (m), 835 (m), 802 (s) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%) = 268 (4) [M]$^+$, 189 (41), 148 (18), 147 (100), 129 (29), 57 (23). $C_{15}H_{20}O_3S$ (268.37): calcd. C 62.66, H 7.51; found C 62.46, H 7.46.

(*R*)-[2-(*tert*-Butylsulfonyl)butan-2-yl]benzene [(*R*)-40]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylethan-1-ide [(*P*)-**1**] was synthesized by deprotonation of sulfone (*S*)-**6** with *t*BuLi at –105 °C and reaction with ethyl iodide in the presence of 10 equiv. of HMPA (t_{rac} = 1 h, –105 °C). Following GP1, a solution of sulfone (*S*)-**6** (226 mg, 1.0 mmol, ≥99% *ee*) in THF (29 mL) was treated at –105 °C over 5 min with *t*BuLi (0.9 mL of 1.5 M in *n*-pentane, 1.3 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with HMPA (13 mL of 1 M in THF, 10 mmol), then with EtI (1 mL of 4 M in THF, 4 mmol), and then after 1 h over 5 min with

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up gave sulfone (*R*)-**40** (234 mg, 92%) with 91% *ee* {GC (permethyl-β-cyclodextrin): t_R [(*R*)-**40**] = 57.4 min, t_R [(*S*)-**40**] = 58.0 min}, m.p. 115 °C, $[\alpha]_D^{20}$ = +28.8 (*c* = 0.9, THF).

(*R*)-[2-(*tert*-Butylsulfonyl)-2-methylpent-4-enyl]benzene [(*R*)-41]: Lithium (*P*)-1-(*tert*-butylsulfonyl)-1-phenylpropan-2-ide [(*P*)-**5**] was synthesized by deprotonation of sulfone (*S*)-**10** with *n*BuLi at –105 °C and reaction with allyl iodide. Following GP1, a solution of sulfone (*S*)-**10** (400 mg, 1.67 mmol, ≥99% *ee*) in THF (20 mL) was treated at –105 °C over 5 min with *n*BuLi (2.1 mL of 1.5 M in *n*-hexane, 3.1 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with a solution of allyl iodide (0.2 mL, 3.7 mmol) in THF (1 mL) and then after 10 min over 5 min with a solution of CF_3CO_2D (0.3 mL, 3.4 mmol) in THF (1 mL). Work-up and purification first by chromatography (*n*-hexane/EtOAc, 4:1) and then by MPLC (cyclohexane/EtOAc, 8:1) gave sulfone (*R*)-**41** (368 mg, 80%) with 91% *ee* {^{1}H NMR [300 MHz, 41 mol-% Eu(hfc)$_3$, $CDCl_3$]: δ = 4.05 (s) and 4.03 (d, *J* = 11.8 Hz)/ 4.12 ppm (d, *J* = 11.8 Hz) ($PhCH_2$)} as a colorless oil, R_f = 0.41 (*n*-hexane/EtOAc, 2:1), $[\alpha]_{365}$ = +13.0 (*c* = 2.00, Et_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (s, 3 H, CH_3), 1.60 (s, 9 H, *t*Bu-CH_3), 2.54 (ddt, *J* = 1.4, *J* = 6.7, *J* = 15.3 Hz, 1 H, CH_2CH=CH_2), 2.66 (ddt, *J* = 7.0, *J* = 1.4, *J* = 15.3 Hz, 1 H, CH_2CH=CH_2), 3.29 (s, 2 H, CH_2Ph), 5.02 (dq, *J* = 17.1, *J* = 1.8 Hz, 1 H, CH_2CH=CH_2), 5.09 (dq, *J* = 10.2, *J* = 2.0 Hz, 1 H, CH_2CH=CH_2), 5.93 (m, 1 H, CH_2CH=CH_2), 7.21–7.24 (m, 2 H, *m*-Ph), 2.24–7.32 (m, 3 H, *p*-, *o*-Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0 (α-CH_3), 26.4 (*t*Bu-CH_3), 39.4 (CH_2), 40.9 (CH_2), 66.6 (*t*Bu-C), 72.1 (C_α), 118.6 (CH_2CH=CH_2), 127.1 (*p*-Ph), 128.2, 131.2 (*o*-, *m*-Ph), 133.2 (CH_2CH=CH_2), 135.4 (*i*-Ph) ppm. IR (CH_2Cl_2): ṽ = 2980 (m), 1640 (w), 1600 (w), 1460 (m), 1280 (s), 1180 (w), 1100 (s), 920 (m), 800 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 159 (25), 117 (15), 105 (13), 91 (100), 81 (44), 65 (10), 57 (82), 55 (23), 41 (28). $C_{16}H_{24}O_2S$ (280.41): calcd. C 68.53, H 8.63; found C 68.05, H 8.67.

(*S*)-(+)- and (*R*)-(–)-[3-(Benzyloxy)-2-(*tert*-butylsulfonyl)-2-methylpropyl]benzene [(*S*)-42 and (*R*)-42]: Compounds (*S*)-**42** and (*R*)-**42** were synthesized from lithium (*P*)- and (*M*)-2-(*tert*-butylsulfonyl)-1-phenylpropan-2-ide [(*P*)-**5** and (*M*)-**5**] by reaction with benzyloxymethyl bromide. Following GP1, a solution of sulfone (*S*)-**10** (200 mg, 0.83 mmol, ≥99% *ee*) in THF (20 mL) was treated at –105 °C over 5 min with *n*BuLi (1.08 mL of 1.37 M in *n*-hexane, 1.49 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with a solution of benzyloxymethyl bromide (0.6 mL, 4.15 mmol) and then after 20 min over 5 min with CF_3CO_2D (1 mL of 2 M in THF, 2 mmol). Work-up and purification first by chromatography (*n*-hexane/EtOAc, 4:1) and then by MPLC (cyclohexane/EtOAc, 8:1) gave sulfone (*S*)-**42** (209 mg, 70%) with 91% *ee* {^{1}H NMR [300 MHz, 69 mol-% Pr(thfc)$_3$, $CDCl_3$]: δ = 4.32, 4.41 ppm ($PhCH_2$)} as colorless needles, R_f = 0.54 (*n*-hexane/EtOAc, 2:1), $[\alpha]_D$ = +39.59 (*c* = 0.99, CH_2Cl_2), m.p. 68 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, CH_3), 1.54 (s, 9 H, *t*Bu-CH_3), 3.15 (d, *J* = 13.1 Hz, 1 H, CH_2Ph), 3.35 (d, *J* = 11.1 Hz, 1 H, CH_2Ph), 3.58 (d, *J* = 12.8 Hz, 1 H, CH_2OCH_2Ph), 3.77 (d, *J* = 11.1 Hz, 1 H, CH_2OCH_2Ph), 4.49 (d, *J* = 11.4 Hz, 1 H, OCH_2Ph), 4.56 (d, *J* = 11.4 Hz, 1 H, OCH_2Ph), 7.16–7.40 (m, 10 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.3 (CH_3), 25.2 (*tert*-Butyl-CH_3), 37.2 (CH_2Ph), 67.1 (*t*Bu-C), 69.8 (*C*H_2OCH_2Ph), 73.1 (OCH_2Ph), 73.5 (C_α), 126.9, 128.0, 128.1, 128.2, 128.5, 131.0 (*o*-, *m*-, *p*-Ph), 135.5, 136.9 (*i*-Ph) ppm. IR (KBr): ṽ = 3450 (m), 2980 (w), 2880 (w), 1750 (w), 1630 (w), 1600 (w), 1500 (m), 1475 (m), 1455 (m), 1370 (m), 1275 (s), 1140 (w), 1100 (s), 1020 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 132 (15), 131 (44), 92 (11), 91 (100), 57 (25). $C_{21}H_{28}O_3S$ (360.52): calcd. C 69.96, H 7.83; found C 69.92, H 7.72.

Following the above procedure, sulfone (*R*)-**10** (200 mg, 0.83 mmol) gave at –95 °C sulfone (*R*)-**42** (313 mg, 87%) with 84 *ee*, $[\alpha]_D$ = –35.05 (*c* = 0.53, CH_2Cl_2).

(1*R*,2*S*)- and (1*S*,2*S*)-2-(*tert*-Butylsulfonyl)-2-methyl-1,3-diphenylpropan-1-ol [(1*R*,2*S*)-43 and (1*S*,2*S*)-43]: Lithium (*P*)-2-(*tert*-butylsulfonyl)-1-phenylpropan-2-ide [(*P*)-**5**] was synthesized by deprotonation of sulfone (*S*)-**10** with *n*BuLi and reaction with benzaldehyde: According to GP1, a solution of *t*BuLi (3.040 mmol) in THF (12 mL) was treated at –105 °C over 5 min with a solution of sulfone (*S*)-**10** (242 mg, 1.007 mmol, ≥99% *ee*) in THF (1 mL). After stirring the mixture at –105 °C for 3 min, it was treated at –105 °C first with a solution of benzaldehyde (318 mg, 3.00 mmol) in THF (1 mL) and then after 10 min with a solution of CF_3CO_2D (0.2 mL, 2.6 mmol) in THF (1 mL). Work-up and MPLC (*n*-hexane/EtOAc, 8:1) gave a mixture of alcohols (2*S*)-**43A** with ≥95% *ee* and (2*S*)-**43B** with ≥95% *ee* (292 mg, 84%) in a ratio of 3:2 as a heavy oil, which crystallized upon standing, m.p. 75 °C, R_f = 0.22 (*n*-hexane/EtOAc, 4:1), $[\alpha]_{365}^{21}$ = +49.4 (*c* = 1.92, THF), ^{1}H NMR [250 MHz, 25 mol-% Eu(hfc)$_3$, $CDCl_3$]: major diastereomer: δ = 1.79, 1.83 ppm (S-*t*Bu); minor diastereomer: δ = 2.05, 2.08 ppm (S-*t*Bu); major diastereomer: δ = 2.32, 2.42 ppm (Me); minor diastereomer: δ = 2.28, 2.35 ppm (Me).

(2*S*)-43A: ^{1}H NMR (400 MHz. $CDCl_3$): δ = 1.46 (s, 3 H, α-CH_3), 1.53 (s, 9 H, *t*Bu-CH_3), 3.28 (d, *J* = 13.5 Hz, 1 H, CH_2), 3.44 (d, *J* = 13.5 Hz, 1 H, CH_2), 4.52 [s, 1 H, C*H*(Ph)OH], 4.85 (d, *J* = 7.4 Hz, 1 H, OH), 6.98–7.46 (m, 10 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (α-CH_3), 25.9 (*t*Bu-CH_3), 39.5 (CH_2), 68.7 (*t*Bu-C), 77.5 (C_α), 127.2 (*p*-Ph), 127.7 (Ph), 127.9 (Ph), 128.2 (Ph), 128.3 (Ph), 128.4 (Ph), 128.5 (Ph), 128.8 (Ph), 131.1 (Ph), 131.7 (Ph-C), 134.9 (Ph), 138.9 (*i*-Ph) ppm.

(2*S*)-43B: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (s, 3 H, α-CH_3), 1.62 (s, 9 H, *t*Bu-CH_3), 3.22 (d, *J* = 15.4 Hz, 1 H, CH_2), 3.74 (d, *J* = 15.4 Hz, 1 H, CH_2), 5.48 [s, 1 H, C*H*(Ph)OH], 4.81 (d, *J* = 7.4 Hz, 1 H, OH), 6.98–7.46 (m, 10 H, Ph) ppm. ^{13}C NMR (100 MHz. CDC13): δ = 21.1 (α-CH_3), 26.3 (*t*Bu-CH_3), 33.8 (CH_2), 68.4 (*t*Bu-C), 76.6 (C_α), 126.6 (*p*-Ph), 135.9 (*i*-Ph), 138.0 (*i*-Ph) ppm.

(2*S*)-43A/(2*S*)-43B: IR (KBr): ṽ = 3600–3200 (br s, OH), 3080, 3070, 3000 (w), 2975, 2940, 2880 (w), 1600 (w), 1490, 1450 (m), 1265 (s), 1103 (s), 1080, 1060, 1040 (m), 910, 890 (w), 760, 700, 680 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 346 (7) [M]$^+$, 240 (24), 225 (58), 208 (20), 207 (18), 193 (11), 184 (45), 167 (52), 117 (13), 115 (18), 107 (68), 105 (98), 92 (22), 91 (100), 79 (34), 77 (36), 71 (30), 65 (21), 57 (100), 43 (16), 41 (53), 39 (24). $C_{20}H_{26}O_3S$ (346.5): calcd. C 69.33, H 7.56; found C 69.37, H 7.60.

(2*S*,3*R*,*E*)- and (2*S*,3*S*,*E*)-2-(*tert*-Butylsulfonyl)-2-methyl-1-phenylhex-4-en-3-ol [(2*S*,3*S*,*E*)-45 and (2*S*,3*R*,*E*)-45]: The hexenols were synthesized from lithium (*P*)-(*tert*-butylsulfonyl)-1-phenylpropan-2-ide [(*P*)-**5**] by reaction with but-2-enal. Following GP1, a solution of sulfone (*S*)-**10** (600 mg, 2.5 mmol, ≥99% *ee*) in THF (50 mL) was treated at –105 °C over 5 min with *n*BuLi (3.3 mL of 1.4 M in *n*-hexane, 4.5 mmol). After stirring the mixture at –105 °C for 5 min, it was treated at –105 °C first with a solution of but-2-enal (1.05 mL, 12.5 mmol) and then after 10 min over 5 min with a solution of CF_3CO_2D (0.4 mL, 5.0 mmol) in THF (1 mL). Work-up and purification by chromatography (*n*-hexane/EtOAc, 2:1) gave a mixture of the diastereomeric alcohols (548 mg, 76%) in a ratio of 1:1. Separation by MPLC (cyclohexane/EtOAc, 2:1) gave diastereomer (2*S*)-**45A** (270 mg, 38%) with 94% *ee* {^{1}H NMR [300 MHz, 70 mol-% Eu(tfc)$_3$, $CDCl_3$]: δ = 1.72, 1.76 ppm (*t*Bu)}

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

and diastereomer (2*S*)-**45B** (267 mg, 37%) with 90% *ee* {^{1}H NMR [300 MHz, 68 mol-% Eu(tfc)$_3$, $CDCl_3$]: δ = 7.62, 7.65 ppm (Ph)} both as colorless needles.

(2*S*)-45A: $[\alpha]_D$ = –30.67 (*c* = 0.70, CH_2Cl_2), m.p. 118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 3 H, α-CH_3), 1.59 (s, 9 H, *t*Bu-CH_3), 1.62 (dd, *J* = 6.7, *J* = 1.2 Hz, 3 H, CH_3), 3.29 (d, *J* = 13.9 Hz, 1 H, CH_2), 3.49 (d, *J* = 13.9 Hz, 1 H, CH_2), 3.78 (d, *J* = 4.0 Hz, 1 H, OH), 4.54 (dd, *J* = 7.7, *J* = 4.0 Hz, 1 H, C*H*OH), 5.26 (dd, *J* = 7.7, *J* = 4.0 Hz, 1 H, C*H*CHCH$_3$), 5.72 (m, 1 H, CHC*H*CH$_3$), 7.23–7.34 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8 (α-CH_3), 19.9 (*C*H$_3$CHCH), 26.1 (*t*Bu-CH_3), 36.41 (CH_2), 68.1 (*t*Bu-C), 76.16 (CHOH), 76.62 (C_α), 127.0 (*p*-Ph), 128.1 (*m*-Ph), 128.3, 131.0 (C=C), 131.7 (*o*-Ph), 135.6 (Ph) ppm.

(2*S*)-45B: $[\alpha]_D$ = +21.54 (*c* = 0.65, CH_2Cl_2), m.p. 116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, α-CH_3), 1.59 (s, 9 H, *t*Bu-CH_3), 1.69 (dd, *J* = 6.4, *J* = 1.7 Hz, 3 H, CH_3), 3.12 (d, *J* = 12.1 Hz, 1 H, CH_2), 3.78 (t, *J* = 9.4 Hz, 1 H, C*H*OH), 3.81 (d, *J* = 12.4 Hz, 1 H, CH_2), 3.90 (d, *J* = 9.4 Hz, 1 H, CHO*H*), 5.25 (m, 1 H, CHC*H*CH$_3$), 5.90 (m, 1 H, C*H*CHCH$_3$), 7.26–7.42 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8 (α-CH_3), 19.4 (*C*H$_3$CHCH), 25.7 (*t*Bu-CH_3), 39.1 (CH_2), 68.1 (*t*Bu-C), 75.8 (C_α), 77.3 (CHOH), 127.3 (*p*-Ph), 128.3 (*m*-Ph), 129.1, 129.5 (C=C), 131.3 (*o*-Ph), 134.7 (Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3456 (w), 3054 (m), 3030 (m), 2962 (m), 2938 (m), 2883 (w), 1951 (w), 1750 (w), 1603 (m), 1456 (m), 1447 (m), 1397 (m), 1365 (s), 1266 (s), 1125 (s), 1089 (s), 967 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 240 (14), 189 (20), 184 (18), 167 (23), 143 (18), 119 (23), 91 (100), 71 (14), 57 (37), 43 (13), 41 (23). $C_{17}H_{26}O_3S$ (310.45): calcd. C 65.77, H 8.44; found C 65.91, H 8.44.

Synthesis of Lithium (*P*)-(+)-2-(*tert*-Butylsulfonyl)-1-phenylpropan-2-ide [(*P*)-5] and Polarimetric Investigation of the Racemization at –86 °C: Following GP1, a solution of sulfone (*S*)-**10** (166 mg, 0.69 mmol, ≥99% *ee*) in THF (7.5 mL) was treated at –105 °C over 5 min with *n*BuLi (0.48 mL of 1.6 M in *n*-hexane, 0.77 mmol). After stirring the mixture at –105 °C for 5 min, the solution (5 mL) was transferred under argon pressure through a cold (–100 °C) cannula to the polarimeter tube kept at –86.2 °C by a thermostat (*c* = 0.087 mol l^{-1}). The polarimeter was closed (*t* = 0). The optical rotation of α = 0.334° {$[\alpha]_{546}^{-86}$ = 16.0 (*c* = 2.08, THF)} at λ = 546 nm fell over 20 min to 0° (Table 13; *c* = 0.086 mol L^{-1}, T_{tube} = –86.2 °C, λ = 546 nm, α_0 = 0.334°, measurement time 4.4 × $\tau_{½}$). Treatment of the salt *rac*-**5** with CF_3CO_2D gave sulfone *rac*-**10** (96 mg, 93%) with ≥98% D content.

Table 13. Time-dependence of the optical rotation of the salt (*P*)-**5** at –86 °C.

t [min]	α [°]	ln α_0/α	*t* [min]	α [°]	ln α_0/α
1	0.270	0.213	9	0.049	1.919
2	0.216	0.435	10	0.040	2.122
3	0.171	0.669	11	0.035	2.256
4	0.139	0.876	12	0.027	2.515
5	0.112	1.093	13	0.023	2.677
6	0.093	1.279	14	0.020	2.815
7	0.072	1.534	15	0.015	3.103
8	0.061	1.700	16	0.012	3.326

Analysis of the data according to first-order kinetics gave k_{rac} (187 K) = (3.42 ± 0.2) × 10^{-3} s^{-1}, $\tau_{½}$ (187 K) = 3.4 ± 0.2 min, and $\Delta G^{\ddagger}_{187}$ = 12.9 ± 0.1 kcal mol^{-1}.

Synthesis of Lithium (*P*)-(+)-2-(*tert*-Butylsulfonyl)-1-phenylpropan-2-ide·4DMPU [(*P*)-5·4DMPU] and Polarimetric Investigation of the Racemization at –77 °C: Following GP1, a solution of sulfone (*S*)-**10** (183 mg, 0.76 mmol, ≥99% *ee*) and DMPU (391 mg, 3.05 mmol) in THF (7 mL) was treated at –105 °C over 5 min with *n*BuLi (0.51 mL of 1.6 M in *n*-hexane, 0.81 mmol). After stirring the mixture at –105 °C for 5 min, the solution (5 mL) was transferred under argon pressure through a cold (–100 °C) cannula to the polarimeter tube kept at –76.5 °C by a thermostat (Table 14; *c* = 0.095 mol L^{-1}, T_{tube} = –76.5 °C, λ = 546 nm, α_0 = 0.683°, measurement time 6.8 × $\tau_{½}$). Treatment of salt *rac*-**5** with CF_3CO_2D gave sulfone *rac*-**10** (96 mg, 93%) with ≥98% D content.

Table 14. Time-dependence of the optical rotation of the salt (*P*)-**5**·4DMPU at –77 °C.

t [min]	α [°]	ln α_0/α	*t* [min]	α [°]	ln α_0/α
0.5	0.611	0.111	4.0	0.049	2.635
1.0	0.360	0.640	4.5	0.036	2.943
1.5	0.259	0.970	5.0	0.026	3.268
2.0	0.186	0.876	5.5	0.019	3.582
2.5	0.133	1.301	6.0	0.013	3.962
3.0	0.096	1.962	6.5	0.010	4.224
3.5	0.067	2.322	7.00	0.007	4.581

Analysis of the data according to first-order kinetics gave k_{rac} (187 K) = (1.11 ± 0.1) × 10^{-2} s^{-1} and $\tau_{½}$ (187 K) = 1.0 ± 0.1 min.

Synthesis of Lithium (*P*)-(+)-2-(*tert*-Butylsulfonyl)-1-phenylpropan-2-ide·4DMPU [(*P*)-5·4DMPU] and Polarimetric Investigation of the Racemization at –80 °C: Following GP1, a solution of sulfone (*S*)-**10** (187 mg, 0.778 mmol, ≥99% *ee*) and DMPU (400 mg, 3.12 mmol) in THF (7 mL) was treated at –105 °C over 5 min with *n*BuLi (0.54 mL of 1.6 M in *n*-hexane, 0.86 mmol). After stirring the mixture at –105 °C for 5 min, the solution (5 mL) was transferred under argon pressure through a cold (–100 °C) cannula to the polarimeter tube kept at –80.0 °C (Table 15; *c* = 0.097 mol L^{-1}, T_{tube} = –80.0 °C, λ = 546 nm, α_0 = 1.078°, measurement time 7.1 × $\tau_{½}$). Treatment of salt *rac*-**5** with CF_3CO_2D gave sulfone *rac*-**10** (96 mg, 93%) with ≥98% D content.

Table 15. Time-dependence of the optical rotation of the salt (*P*)-**5**·4DMPU at –80 °C.

t [min]	α [°]	ln α_0/α	*t* [min]	α [°]	ln α_0/α
0.5	0.946	0.131	8.0	0.073	2.692
1.0	0.804	0.293	9.0	0.054	2.994
2.0	0.569	0.639	10.0	0.037	3.372
3.0	0.395	1.003	11.0	0.027	3.387
4.0	0.279	1.352	12.0	0.019	4.038
5.0	0.200	1.685	13.0	0.014	4.344
6.0	0.143	2.020	14.0	0.010	4.680
7.0	0.102	2.358	15.0	0.007	5.037

Analysis of the data according to first-order kinetics gave k_{rac} (193 K) = (5.56 ± 0.2) × 10^{-3} s^{-1} and $\tau_{½}$ (193 K) = 2.1 ± 0.1 min.

Synthesis of Lithium (*P*)-(+)-2-(*tert*-Butylsulfonyl)-1-phenylpropan-2-ide·4DMPU [(*P*)-5·4DMPU] and Polarimetric Investigation of the Racemization at –82 °C: Following GP1, a solution of sulfone (*S*)-**10** (156 mg, 0.65 mmol, ≥99% *ee*) and DMPU (333 mg, 2.60 mmol) in THF (7 mL) was treated at –105 °C over 5 min with *n*BuLi (0.44 mL of 1.6 M in *n*-hexane, 0.70 mmol). After stirring the mixture at –105 °C for 5 min, the solution (5 mL) was transferred under argon pressure through a cold (–100 °C) cannula into the polarimeter tube kept at –81.5 °C (Table 16; *c* = 0.081 mol L^{-1}, T_{tube} = –81.5 °C, λ = 546 nm, α_0 = 0.507°, measurement time 5.6 × $\tau_{½}$). Treatment of the salt *rac*-**5** with CF_3CO_2D gave sulfone *rac*-**10** (96 mg, 93%) with ≥98% D content.

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Table 16. Time-dependence of the optical rotation of the salt (*P*)-**5**·4DMPU at –82 °C.

t [min]	*α* [°]	ln *α*$_0$/*α*	*t* [min]	*α* [°]	ln *α*$_0$/*α*
0.5	0.452	0.115	8.0	0.056	2.203
1.0	0.399	0.240	9.0	0.043	2.467
2.0	0.297	0.535	10.0	0.033	2.732
3.0	0.224	0.817	11.0	0.025	3.010
4.0	0.168	1.105	12.0	0.019	3.284
5.0	0.126	1.392	13.0	0.014	3.589
6.0	0.097	1.654	14.0	0.011	3.831
7.0	0.073	1.938			

Analysis of the data according to first-order kinetics gave k_{rac} (192 K) = $(4.59 \pm 0.2) \times 10^{-3}$ s^{-1} and $\tau_{½}$ (192 K) = 2.5 ± 0.1 min.

Synthesis of Lithium (*P*)-(+)-2-(*tert*-Butylsulfonyl)-1-phenylpropan-2-ide·4DMPU (*P*-5·4DMPU) and Polarimetric Investigation of the Racemization at –84 °C: Following GP1, a solution of sulfone (*S*)-**10** (151 mg, 0.627 mmol, ≥99% *ee*) and DMPU (322 mg, 2.508 mmol) in THF (7 mL) was treated at –105 °C over 5 min with *n*BuLi (0.42 mL of 1.6 M in *n*-hexane, 0.67 mmol). After stirring the mixture at –105 °C for 5 min, the solution (5 mL) was transferred under argon pressure through a cold (–100 °C) cannula into the polarimeter tube kept at –83.5 °C (Table 17; c = 0.078 mol L^{-1}, T_{tube} = –83.5 °C, λ = 546 nm, α_0 = 0.543°, measurement time $5.8 \times \tau_{½}$). Treatment of the salt *rac*-**5** with CF_3CO_2D gave sulfone *rac*-**10** (96 mg, 93%) with ≥98% D content.

Table 17. Time-dependence of the optical rotation of the salt (*P*)-**5**·4DMPU at –84 °C.

t [min]	*α* [°]	ln *α*$_0$/*α*	*t* [min]	*α* [°]	ln *α*$_0$/*α*
1	0.463	0.159	10	0.099	1.702
2	0.394	0.321	12	0.070	2.049
3	0.331	0.495	14	0.050	2.385
4	0.276	0.677	16	0.034	2.771
5	0.231	0.855	18	0.024	3.119
6	0.195	1.024	20	0.017	3.464
8	0.140	1.355	23	0.010	3.995

Analysis of the data according to first-order kinetics gave k_{rac} (190 K) = $(2.91 \pm 0.2) \times 10^{-3}$ s^{-1} and $\tau_{½}$ (190 K) = 4.0 ± 0.2 min.

Synthesis of Lithium (*P*)-(+)-2-(*tert*-Butylsulfonyl)-1-phenylpropan-2-ide·4DMPU [(*P*)-5·4DMPU] and Polarimetric Investigation of the Racemization at –87 °C: Following GP1, a solution of sulfone (*S*)-**10** (152 mg, 0.630 mmol, ≥99% *ee*) and DMPU (323 mg, 2.520 mmol) in THF (7 mL) was treated at –105 °C over 5 min with *n*BuLi (0.42 mL of 1.6 M in *n*-hexane, 0.67 mmol). After stirring the mixture at –105 °C for 5 min, the solution (5 mL) was transferred under argon pressure through a cold (–100 °C) cannula into the polarimeter tube kept at –86.5 °C (Table 18; c = 0.079 mol L^{-1}, T_{tube} = –86.5 °C, λ = 546 nm, α_0 = 1.020°, measurement time $5.3 \times \tau_{½}$). Treatment of the salt *rac*-**5** with CF_3CO_2D gave sulfone *rac*-**10** (96 mg, 93%) with ≥98% D content.

Table 18. Time-dependence of the optical rotation of the salt (*P*)-**5**·4DMPU at –87 °C.

t [min]	*α* [°]	ln *α*$_0$/*α*	*t* [min]	*α* [°]	ln *α*$_0$/*α*
1	0.950	0.071	20	0.137	2.007
3	0.780	0.268	21	0.122	2.124
5	0.624	0.491	24	0.091	2.417
7	0.516	0.681	25	0.082	2.521
10	0.378	0.969	28	0.060	2.833
12	0.306	1.204	30	0.050	3.016
14	0.250	1.406	33	0.037	3.317
17	0.187	1.696	36	0.026	3.669

Analysis of the data according to first-order kinetics gave k_{rac} (187 K) = $(1.70 \pm 0.1) \times 10^{-3}$ s^{-1} and $\tau_{½}$ (187 K) = 6.8 ± 0.3 min.

Synthesis of Lithium (*P*)-(+)-2-(*tert*-Butylsulfonyl)-1-phenylpropan-2-ide·4DMPU [(*P*)-5·4DMPU] and Polarimetric Investigation of the Racemization at –89 °C: Following GP1, a solution of sulfone (*S*)-**10** (158 mg, 0.659 mmol, ≥99% *ee*) and DMPU (328 mg, 2.635 mmol) in THF (7 mL) was treated at –105 °C over 5 min with *n*BuLi (0.45 mL of 1.6 M in *n*-hexane, 0.72 mmol). After stirring the mixture at –105 °C for 5 min, the solution (5 mL) was transferred under argon pressure through a cold (–100 °C) cannula into the polarimeter tube kept at –88.5 °C (Table 19; c = 0.082 mol L^{-1}, T_{tube} = –88.5 °C, λ = 546 nm, α_0 = 1.174°, measurement time $5.3 \times \tau_{½}$). Treatment of the salt *rac*-**5** with CF_3CO_2D gave sulfone *rac*-**10** (96 mg, 93%) with ≥98% D content.

Table 19. Time-dependence of the optical rotation of the salt (*P*)-**5**·4DMPU at –89 °C.

t [min]	*α* [°]	ln *α*$_0$/*α*	*t* [min]	*α* [°]	ln *α*$_0$/*α*
2	1.020	0.141	25	0.137	2.148
5	0.780	0.409	28	0.122	2.264
7	0.624	0.632	30	0.091	2.557
10	0.516	0.822	35	0.082	2.661
13	0.378	1.133	40	0.060	2.974
15	0.306	1.345	45	0.050	3.156
20	0.250	1.547	50	0.037	3.457
24	0.187	1.837	55	0.026	3.810

Analysis of the data according to first-order kinetics gave k_{rac} (185 K) = $(1.14 \pm 0.1) \times 10^{-3}$ s^{-13} and $\tau_{½}$ (185 K) = 10.2 ± 0.9 min.

Determination of the Activation Parameters for the Racemization of (*P*)-5·4DMPU: To determine of the temperature dependence of k_{rac} only those data were considered for which complete deprotonation of the sulfone (*S*)-**10** was demonstrated by deuteriation of the salt (*P*)-**5** (Tables 20 and 21).

Table 20. Temperature of the solution of the salt (*P*)-**5**·4DMPU in the tube and temperature of the cryostat in the measurement of the optical rotations.[a]

T_{cry} [°C]	–78.0	–81.5	–83.0	–85.0	–88.0	–90.0
T_{tube} [°C]	–76.5	–80.0	–81.5	–83.5	–86.5	–88.5

[a] Error of measurement: ±0.3 K.

Table 21. Rate constants for the racemization of the salt (*P*)-**5**·4DMPU at different temperatures.

T [°C]	T^{-1} [10^{-3} K^{-1}]	k_{rac} [10^{-3} s^{-1}]	log(*k*/*T*)
–76.5	5.085	11.1	–4.248
–80.0	5.177	5.56	–4.536
–81.5	5.218	4.59	–4.624
–83.5	5.273	2.91	–4.814
–86.5	5.358	1.70	–5.041
–88.5	5.416	1.14	–5.210

Analysis of the data gave the Eyring equation (k_{rac}/*T*) = –2894/*T* + 10.46 and the activation parameters $\Delta H^{‡}$ = 13.2 ± 0.2 kcal mol^{-1}, $\Delta S^{‡}$ = 0.7 ± 1 cal mol^{-1} K^{-1}, $\Delta G^{‡}_{298}$ = 13.0 ± 0.2 kcal mol^{-1}, and $\Delta G^{‡}_{193}$ = 13.10 ± 0.05 kcal mol^{-1}.

Supporting Information (see also the footnote on the first page of this article): Experimental procedures and characterization data for

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(*S*)-**12**, (*R*)-**12**, (*S*)-**13**, (*R*)-**13**, (*S*)-**14**, (*R*)-**14**, (*S*)-**6**, (*R*)-**6**, (*S*)-**16**, (*R*)-**17**, (*R*)-**7**, (*R*)-**18**, (*R*)-**19**, (*S*)-**17**, (*S*)-**7**, *rac*-**21**, (*S*)-**22**, (*S*)-**21**, (*S*)-**20**, *rac*-**20**, (*R*)-**20**, (*S*)-**23**, (*R*)-**24**, (*R*)-**8**, (*R*)-**25**, (*S*)-**25**, (*S*)-**28**, (*R*)-**29**, (*R*)-**9**, (*R*)-**31**, (*S*)-**31**, (*S*)-**32**, (*R*)-**32**, (*S*)-**10**, (*R*)-**10**, *rac*-**33**, (*R*)-**30**, (*S*)-**30**, (*S*)-**32**, (*R*)-**32**, **49**, **50**, *rac*-**10**, *rac*-**6**, *rac*-**7**, (*S*)-**40**, *rac*-**40**, (2*S*,3*S*)-**47**, (2*S*,3*R*)-**47**, (1*R*,2*S*)-**44**, (1*S*,2*S*)-**47**, (3*R*,4*S*)-**46**, and (3*S*,4*S*)-**46**; scheme describing the synthesis of *rac*-**6**–**9**, **59**, and **50**; experimental procedures for the synthesis and reactions of the salts (*M*)-**1**, (*P*)-**1**, (*M*)-**2**, (*P*)-**2**, *rac*-**2**, (*P*)-**3**, (*M*)-**3**, *rac*-**4**, and (*P*)-**5**; tables containing the racemization data for (*P*)-**1** and (*M*)-**2**, tables containing the crystal data and experimental details of the structure determination of (*R*)-**9**, (*S*)-**10**, *rac*-**33**, (*R*)-**34**, (*R*)-**35**, (*S*)-**40**, (*S*)-42, (*S*,*R*)-**44**, and (*S*,*S*)-**44**.

Acknowledgments

This research was supported by the Deutsche Forschungsgemeinschaft (DFG), Volkswagen Foundation, and Fonds der Chemischen Industrie. We thank D. Wolters for his help with the graphics.

[1] R. Scholz, G. Hellmann, S. Rohs, G. Raabe, J. Runsink, D. Özdemir, O. Luche, T. Heß, A. W. Giesen, J. Atodiresei, H. J. Lindner, H.-J. Gais, *Eur. J. Org. Chem.* **2010**, 4559–4587, preceding contribution.

[2] a) N. S. Simpkins, *Chem. Ind.* **1988**, 387–389; b) P. J. Cox, N. S. Simpkins, *Tetrahedron: Asymmetry* **1991**, *2*, 1–26; c) H.-J. Gais, in: *Organosulfur Chemistry in Asymmetric Snythesis* (Eds.: T. Toru, C. Bolm), Wiley-VCH, Weinheim, **2008**, pp. 375–398.

[3] a) H.-J. Gais, G. Hellmann, H. Günther, F. Lopez, H. J. Lindner, S. Braun, *Angew. Chem.* **1989**, *101*, 1061–1064; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1025–1028; b) H.-J. Gais, G. Hellmann, H. J. Lindner, *Angew. Chem.* **1990**, *102*, 96–99; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 100–103; c) H.-J. Gais, G. Hellmann, *J. Am. Chem. Soc.* **1992**, *114*, 4439–4440; d) G. Raabe, H.-J. Gais, J. Fleischhauer, *J. Am. Chem. Soc.* **1996**, *118*, 4622–4630.

[4] For clarity lithium α-sulfonyl carbanion salts are represented throughout this paper only by the structural formula of their monomers. Although the monomers may have only one O–Li bond they are depicted with two bonds of this type; see ref.[1] According to NMR spectroscopic and cryoscopic analysis of the racemic salts the monomers are in equilibrium with the dimers, both of which are O–Li CIPs with similar basic structural features; see ref.[1] The monomer/dimer ratio of the racemic and enantiopure salts may differ, however, because of the lack of achiral dimers in the latter case.

[5] a) H. J. Reich, R. P. Dykstra, *Angew. Chem.* **1993**, *105*, 1489–1491; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1469–1470; b) H. J. Reich, R. P. Dykstra, *J. Am. Chem. Soc.* **1993**, *115*, 7041–7042; c) R. E. Gawley, *Curr. Org. Chem.* **1997**, *1*, 71–94; d) T. Toru, S. Nakamura, *Top. Organomet. Chem.* **2003**, *5*, 177–216; e) A. Basu, S. Thayumanavan, *Angew. Chem.* **2002**, *114*, 740–763; *Angew. Chem. Int. Ed.* **2002**, *41*, 716–738; f) J. Clayden, in: *Organolithiums: Selectivity for Synthesis* (Eds.: J. E. Baldwin, R. M. Williams), Elsevier, Oxford, **2002**; g) P. Beak, T. A. Johnson, D. D. Kim, S. H. Lim, *Top. Organomet. Chem.* **2003**, *5*, 139–176; h) D. Hoppe, F. Marr, M. Brueggemann, *Top. Organomet. Chem.* **2003**, *5*, 61–137; i) R. W. Hoffmann, *Chem. Soc. Rev.* **2003**, *32*, 225–230; j) R. E. Gawley, in: *Chemistry of Organolithium Compounds* (Eds.: Z. Rappoport, I. Marek), Wiley, Chichester, **2004**, vol. 2, pp. 997–1053; k) D. Hoppe, G. Christoph, in: *Chemistry of Organolithium Compounds* (Eds.: Z. Rappoport, I. Marek), Wiley, Chichester, **2004**, vol. 2, pp. 1055–1164.

[6] a) T. Akiyama, M. Shimizu, T. Mukaiyama, *Chem. Lett.* **1984**, 611–614; b) S. Nakamura, N. Hirata, T. Kita, R. Yamada, D. Nakane, N. Shibata, T. Toru, *Angew. Chem.* **2007**, *119*, 7792–7794; *Angew. Chem. Int. Ed.* **2007**, *46*, 7648–7650; c) S. Nakamura, N. Hirata, R. Yamada, T. Kita, N. Shibata, T. Toru, *Chem. Eur. J.* **2008**, *14*, 5519–5527.

[7] W. K. Lee, Y. S. Park, P. Beak, *Acc. Chem. Res.* **2009**, *42*, 224–234.

[8] C. Wolf, *Dynamic Stereochemistry of Chiral Compounds, Principles and Applications*, RSC, Cambridge, **2008**.

[9] For short communications, see ref.[3a,3c]

[10] The enantioselective conversion of the sulfone via the α-sulfonyl carbanion into the substituted sulfone may be regarded as an example of what has been termed "memory of chirality", see ref.[11a] However, the use of this term has been criticized, see: F. Cozzi, J. S. Siegel, *Org. Biomol. Chem.* **2005**, *3*, 4296–4298.

[11] a) T. Kawabata, K. Fuji, *Top. Stereochem.* **2003**, *23*, 175–205; b) H. Zhao, D. C. Hsu, P. R. Carlier, *Synthesis* **2005**, *1*, 1–16; c) T. Kawabata, J. Chen, H. Suzuki, K. Fuji, *Synthesis* **2005**, 1368–1377; d) A. G. Brewster, J. Jayatissa, M. B. Mitchell, A. Schofield, R. J. Stoodley, *Tetrahedron Lett.* **2002**, *43*, 3919–3922; e) M. A. Bonache, G. Gerona-Navarro, M. Martin-Martinez, M. T. Garcia-Lopez, P. Lopez, C. Cativiela, R. Gonzalez-Muniz, *Synlett* **2003**, 1007–1011; f) J. Clayden, C. C. Stimson, M. Keenan, *Synlett* **2005**, 1716–1720; g) P. C.-H. Lam, P. R. Carlier, *J. Org. Chem.* **2005**, *70*, 1530–1538.

[12] R. W. Baker, M. A. Foulkes, J. A. Taylor, *J. Chem. Soc. Perkin Trans. 1* **1998**, 1047–1057.

[13] a) P. J. DeChristopher, J. P. Adamek, G. D. Lyon, S. A. Klein, R. J. Baumgarten, *J. Org. Chem.* **1974**, *39*, 3525–3532; b) P. Müller, M. P. Nguyen-Thi, *Helv. Chim. Acta* **1980**, *63*, 2168–2172.

[14] J. Dupont, A. S. Gruber, G. S. Fonseca, A. L. Monteiro, G. Ebling, *Organometallics* **2001**, *20*, 171–176.

[15] K. Laumen, M. P. Schneider, *J. Chem. Soc., Chem. Commun.* **1988**, 598–600.

[16] H. L. Holland, F. M. Brown, B. Munoz, R. W. Ninniss, *J. Chem. Soc. Perkin Trans. 2* **1988**, 1557–1563.

[17] R. M. Coates, J. P. Chen, *Tetrahedron Lett.* **1969**, *10*, 2705–2708.

[18] T. Shibata, K. Iwahashi, T. Kawasaki, K. Soai, *Tetrahedron: Asymmetry* **2007**, *18*, 1759–1762.

[19] a) S. Winstein, B. K. Morse, *J. Am. Chem. Soc.* **1952**, *74*, 1133–1139; b) M. Falorni, L. Lardicci, C. Rosini, G. Giacomelli, *J. Org. Chem.* **1986**, *51*, 2030–2033; c) F. Toda, K. Tanaka, K. Koshiro, *Tetrahedron: Asymmetry* **1991**, *2*, 873–874.

[20] H. E. Zieger, D. A. Bright, H. Haubenstock, *J. Org. Chem.* **1986**, *51*, 1180–1184.

[21] C. L. Arcus, P. A. Hallgarten, *J. Chem. Soc.* **1956**, 2987–2991.

[22] CCDC-767751 [for (*R*)-**9**], -767753 [for (*S*)-**10**], -767752 (*rac*-**33**), -767750 [(*R*)-**34**], -767748 [for (*R*)-**35**], -767749 [for (*S*)-**40**], -767754 [for (*S*)-**42**], -767756 [for (*S*,*S*)-**44**], and -767755 [for (*S*,*R*)-**44**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.ac.uk/data_request/cif.

[23] a) R. J. Kurland, M. B. Rubin, W. B. Wise, *J. Chem. Phys.* **1964**, *40*, 2426–2427; b) G. Binsch, *Top. Stereochem.* **1968**, *3*, 97–192.

[24] M. Õki, *The Chemistry of Rotational Isomers*, Springer, Heidelberg, **1993**.

[25] O. Takahashi, Y. Gondoh, K. Saito, Y. Kohno, H. Suezawa, T. Yoshida, S. Ishihara, M. Nishio, *New J. Chem.* **2003**, *27*, 1639–1643.

[26] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pom-

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

elli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03*, *revision B.04*, Gaussian, Inc., Wallingford, CT, **2004**.

[27] C. Lambert, P. v. R. Schleyer, *Angew. Chem.* **1994**, *106*, 1187–1199; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1129–1140.

[28] a) H.-J. Gais, M. van Gumpel, G. Raabe, M. Müller, S. Braun, H. J. Lindner, S. Rohs, J. Runsink, *Eur. J. Org. Chem.* **1999**, 1627–1651; b) H.-J. Gais, M. van Gumpel, M. Schleusner, G. Raabe, J. Runsink, C. Vermeeren, *Eur. J. Org. Chem.* **2001**, 4275–4303.

[29] a) M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem.* **2004**, *116*, 2256–2276; *Angew. Chem. Int. Ed.* **2004**, *43*, 2206–2225; b) P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356–363; c) E.-U. Würthwein, D. Hoppe, *J. Org. Chem.* **2008**, *73*, 9055–9060.

[30] a) F. M. Stoyanovich, R. G. Karpenko, G. I. Gorushkina, Ya. L. Gol'dfarb, *Tetrahedron* **1972**, *28*, 5017–5023; b) M. Iwao, T. Iihama, K. K. Mahalanabis, H. Perrier, V. Snieckus, *J. Org. Chem.* **1989**, *54*, 26–28.

[31] a) S. Wodzinski, J. W. Bunting, *J. Am. Chem. Soc.* **1994**, *116*, 6910–6915; b) F. Terrier, E. Kizilian, R. Goumont, N. Faucher, C. Wakselman, *J. Am. Chem. Soc.* **1998**, *120*, 9496–9503.

[32] a) W. Bauer, W. R. Winchester, P. v. R. Schleyer, *Organometallics* **1987**, *6*, 2371–2379; b) D. Seebach, R. Hässig, J. Gabriel, *Helv. Chim. Acta* **1983**, *66*, 308–337.

[33] a) L. D. McKeever, R. Waack, M. A. Doran, E. B. Baker, *J. Am. Chem. Soc.* **1969**, *91*, 1057–1061; b) F. Paté, H. Oulyadi, A. Harrison-Marchand, J. Maddaluno, *Organometallics* **2008**, *27*, 3564–3569.

[34] a) H. J. Reich, J. P. Borst, R. R. Dykstra, P. D. Green, *J. Am. Chem. Soc.* **1993**, *115*, 8728–8741; b) H. J. Reich, D. P. Green, M. A. Medina, W. S. Goldenberg, B. Ö. Gudmundsson, R. R. Dykstra, N. H. Phillips, *J. Am. Chem. Soc.* **1998**, *120*, 7201–7210.

[35] A. C. Jones, A. W. Sanders, M. J. Bevan, H. J. Reich, *J. Am. Chem. Soc.* **2007**, *129*, 3492–3493.

[36] a) D. A. Bors, A. Streitwieser, *J. Am. Chem. Soc.* **1986**, *108*, 1397–1404; b) R. Koch, E. Anders, *J. Org. Chem.* **1994**, *59*, 4529–4534; c) E. D. Glendening, A. L. Shrout, *J. Phys. Chem. A* **2005**, *109*, 4966–4972.

[37] a) F. G. Bordwell, *Acc. Chem. Res.* **1988**, *21*, 456–463; b) A. Streitwieser, G. P. Wang, D. A. Bors, *Tetrahedron* **1997**, *53*, 10103–10112.

[38] a) H. J. Reich, J. P. Borst, *J. Am. Chem. Soc.* **1991**, *113*, 1835–1837; b) H. J. Reich, J. P. Borst, M. Bevan, unpublished results; c) H. J. Reich, personal communication, **2009**.

[39] a) D. Hoffmann, D. B. Collum, *J. Am. Chem. Soc.* **1998**, *120*, 5810–5811; b) M. A. Nichols, P. G. Williard, *J. Am. Chem. Soc.* **1993**, *115*, 1568–1572.

[40] W. H. Pirkle, S. D. Beare, *J. Am. Chem. Soc.* **1969**, *91*, 5150–5155.

[41] Kinetic studies of lithium *S*-phenylsulfonyl carbanions have also revealed a much greater reactivity towards alkyl halides in the presence of HMPA due to the formation of very reactive SIPs. H. J. Reich, personal communication, **2009**.

[42] W. G. Kofron, L. M. Baclawski, *J. Org. Chem.* **1976**, *41*, 1879–1880.

Received: March 26, 2010
Published Online: July 15, 2010

 © 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim