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Highly stereoselective additions of sulfur stabilized carbanions to [(S)*R*]-2-(*p*-tolylsulfinyl)cyclohexanones

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Abstract

We describe the addition reactions of α-thiocarbanions derived from sulfoxides, thioethers, and sulfones to 2-(*p*-tolylsulfinyl)cyclohexanones. The high stereoselectivity observed in the formation of the chiral hydroxylic carbon is controlled by the configuration of the sulfinyl group at the substrate, but it is modulated by the nature of the sulfur function at the reagent (SOTol>SO_2Ph>SPh). The highly stereoselective formation of the second stereogenic center generated in these reactions from prochiral anions is only achieved with sulfinylcarbanions, the configuration of which controls that of such a center.

1. Introduction

Recently our group has demonstrated the high efficiency of the sulfinyl group in the stereochemical control of the reduction,[1–5] alkylation,[6–9] and hydrocyanation[10–12] reactions on β-ketosulfoxides. The results obtained from substrates with an additional stereogenic center in the α-position have a special significance because the stereoselectivity at the hydroxylic center is controlled mainly by the configuration at sulfur and therefore their reactions can be carried out on the epimeric mixture at C-α. The reactions of the [(S)*R*]-2-(*p*-tolylsulfinyl)cyclohexanones **1** with lithium ester enolates[13,14] have special relevance because they are stereocontrolled aldol reactions using ketones as the electrophiles. Starting from prochiral nucleophiles, the control of the C-2 stereogenic center (Scheme 1) was only possible in reactions from lactone enolates.

The easy generation of sulfur-stabilized carbanions and their successful reactivity with a variety of electrophiles, along with the synthetic versatility of the sulfur functions,[15–17] determine that these reagents are valuable nucleophiles in C–C bond-forming reactions.[18,19] In this sense,

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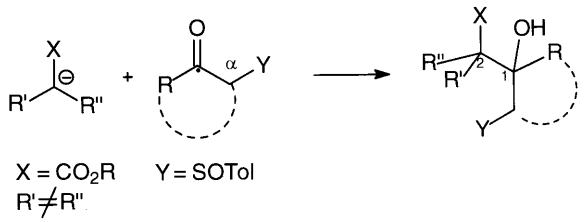


Scheme 1.

chiral sulfinyl carbanions are especially interesting because the sulfinyl group can act as a chiral auxiliary. However, it is well established that the addition of simple α-sulfinylcarbanions to ketones takes place with satisfactory 1,2-induction but a poor 1,3-induction is achieved,[19–23] which determines an efficient control of the stereogenic center next to the sulfinyl sulfur but a less efficient control of the hydroxylic stereogenic center.

On the basis of this assumption we reasoned that the use of a combined effect of the sulfinyl group at the electrophilic ketone and at the nucleophile would allow the simultaneous control of both stereogenic centers formed in reactions with prochiral carbanions. We have checked the efficiency of this combination in reactions involving *N*-sulfinylimines.[24] In this paper we report on the asymmetric addition of α-lithiated alkyl aryl sulfides, sulfoxides, and sulfones to the [(S)*R*]-2-(*p*-tolylsulfinyl)cyclohexanones **1** and some useful transformations of the obtained tertiary carbinols allowing their configurational assignment.

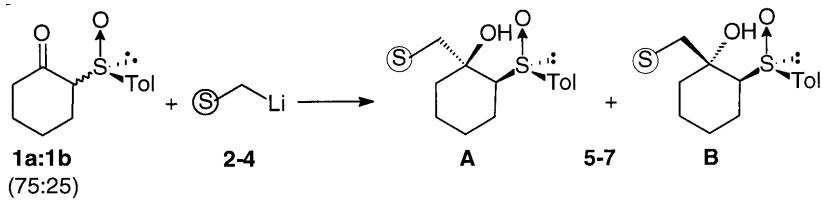
2. Results and discussion

Reactions with α-sulfinylcarbanions derived from enantiomerically pure [(S)*R*]-alkyl *p*-tolyl sulfoxide are especially significant because the double stereoselection allows the simultaneous control of three contiguous stereogenic centers. The stereochemical study is completed with the reactions of sulfide and sulfone carbanions. These reactions are a valuable reference to those of sulfoxide anions, besides the synthetic properties of the obtained adducts by themselves. The synthesis of the starting sulfinylcyclohexanone **1**, as a 75:25 mixture of epimers at C-2, was performed by sulfinylation of the cyclohexanone *N*-phenylimine, according to a previously reported method.[25] The results obtained in the reactions of this epimeric mixture with α-thiocarbanions **2**–**4** are collected in Table 1. In all cases the reactions were carried out by slow addition at −78°C of the epimeric mixture to a solution of the lithium anions (3.5 equiv.) derived from [(S)*R*]-methyl *p*-tolyl sulfoxide **2** or its corresponding thioether **3**‡ or sulfone **4**, which were prepared by deprotonation with LDA at the same temperature in THF.

The reaction of the sulfinylcarbanion **2** takes place with complete stereoselectivity affording hydroxy bis-sulfoxide **5A** as the only diastereoisomer in 84% yield. The reactions with carbanions derived from sulfone **3** and sulfide **4** were less stereoselective, a mixture of two diastereoisomers having been isolated (Table 1). A dynamic resolution of the C-2 stereogenic center is observed in all cases determining the exclusive formation of compounds which exhibit the (*S*) configuration at such a center. This suggests a much quicker evolution of [(S)*R*,2*S*]-**1a** and the easy epimerization of C-2 in the presence of the strongly basic thiocarbanions. The chemical

‡ The reaction with the sulfide anion required 6 molar equiv. and the use of *n*-BuLi as the base.

Table 1
Addition of α-thiocarbanions **2–4** to ketosulfoxides **1**



Entry	Nucleophile	Ⓢ	Adduct	**A**:**B**	Yield (%)[a]
1	**2**	[(S)*R*]-SOTol	**5**	100:0	84
2	**3**	SO_2Ph	**6**	96:4	65[b]
3	**4**	STol	**7**	85:15	51[c]

[a] Isolated yield of the major compounds **A**.
[b] 15% of **1** (as a 75:25 epimeric mixture) was recovered.
[c] 40% of **1** (75:25) was recovered.

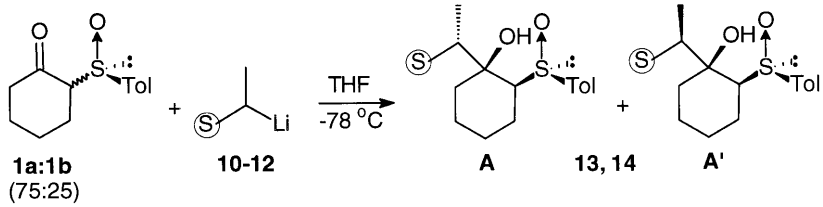
correlation of the major compounds **5A** and **7A** was carried out by their oxidation into the same bis-sulfone **9A**. The ^{1}H NMR spectrum of **8A**, obtained by oxidation of **6A**, is almost identical to that of **9A** (they only differ in the aromatic residue of the acyclic sulfone) thus suggesting that both sulfones must have the same stereochemistry. The [1*S*,2*S*,(S)*R*)] configuration was tentatively assigned to the major adducts **5A–7A** taking into account previous results obtained with sulfinylcyclohexanone **1** and lithium ester enolates.[13] The same criteria were applied to assign the minor compounds **6B** and **7B** (they could not be isolated in their diastereomerically pure form), as indicated in Table 1.

As a second stage of this research we investigated the reaction with prochiral α-thiocarbanions. The obtained results are collected in Table 2. Starting from ethyl *p*-tolyl sulfoxide [(S)*R*]-**10**, compound **13A** was obtained exclusively in 88% yield (no other diastereoisomer could be detected by ^{1}H NMR of the reaction crude). By contrast, the reaction with the sulfonylcarbanion **11** afforded a 55:45 diastereoisomeric mixture of two sulfinyl-sulfones **14A** and **14A′**, and sulfenylcarbanion **12** did not react.[§] The comparison between these results and those obtained from reactions of **1** with ester enolates[13] suggests that these exhibit a behavior similar to carbanions derived from sulfones. In both cases a quite efficient control of the configuration at the endocyclic stereogenic carbon but a quite poor control of that of the exocyclic one are observed. It allows us to assign tentatively the configurations depicted in Table 2 for compounds **14A** and **14A′**, which were confirmed by X-ray diffraction analysis for compound **14A** (Fig. 1).

The formation of only one diastereoisomer in reactions of **1** with **10** suggests that the sulfur configuration at the carbanion is responsible for the control of the stereoselective formation of the exocyclic stereogenic carbon. In order to verify this point we treated compound **1** with a carbanion derived from racemic (±)-**10**. The reaction afforded an almost equimolar mixture

[§] The strong basic character of the sulfenylcarbanion could enolizate the substrate, thus precluding its reaction with nucleophiles.

Table 2
Addition of α-thiocarbanions **10–12** to ketosulfoxides **1**



Entry	Nucleophile	Ⓢ	Adduct	**A**:**A**′[a]	Yield (%)[b]
1	**10**	[(S)*R*]-SOTol	**13**	100:0	88
2	**11**	SO_2Ph	**14**	55:45	**A** (38):**A**′ (28)
3	**12**	STol		No reaction[c]	–

[a] From the ^1H NMR spectra of the reaction crudes.
[b] Isolated yield.
[c] Unaltered **1** were recovered.

of two diastereoisomers, $\mathbf{13A}_R$ and $\mathbf{13A}'_S$, which must exhibit a different configuration at the exocyclic sulfinyl group. The chemical correlation of this mixture with the previously described [1*S*,2*S*,(S)*R*]-2-(*p*-tolylsulfinyl)-1-vinylcyclohexanol **16A**[7] by pyrolytic elimination of the exo-

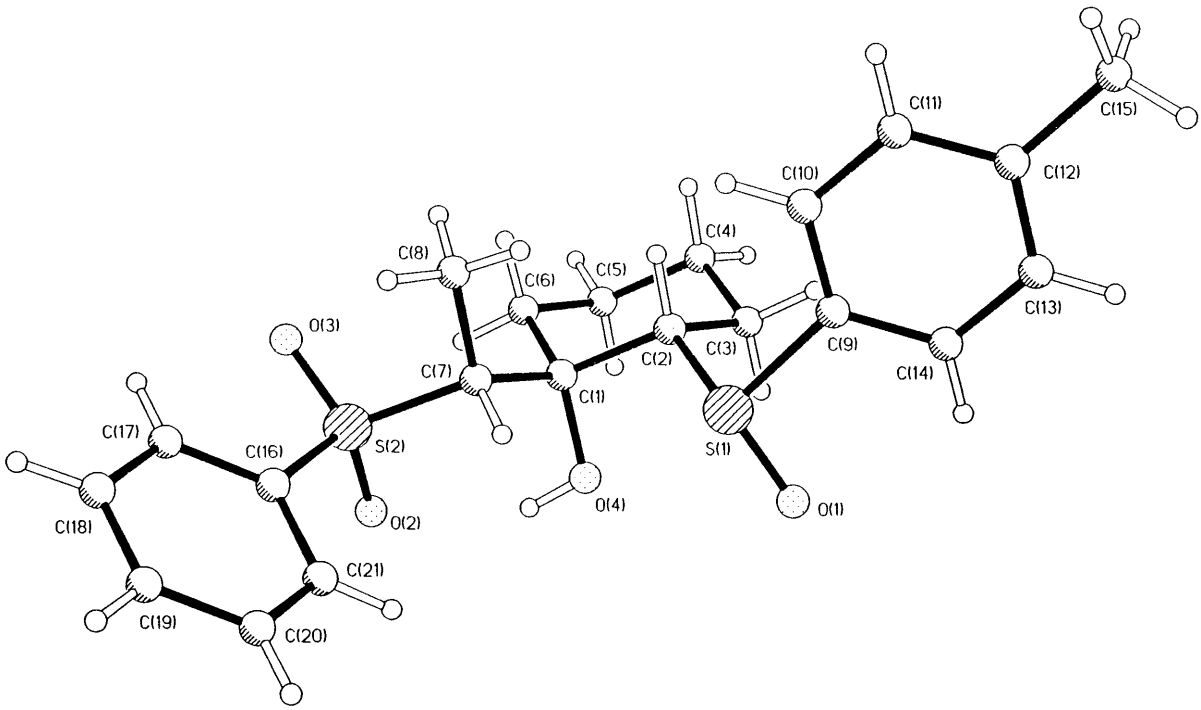
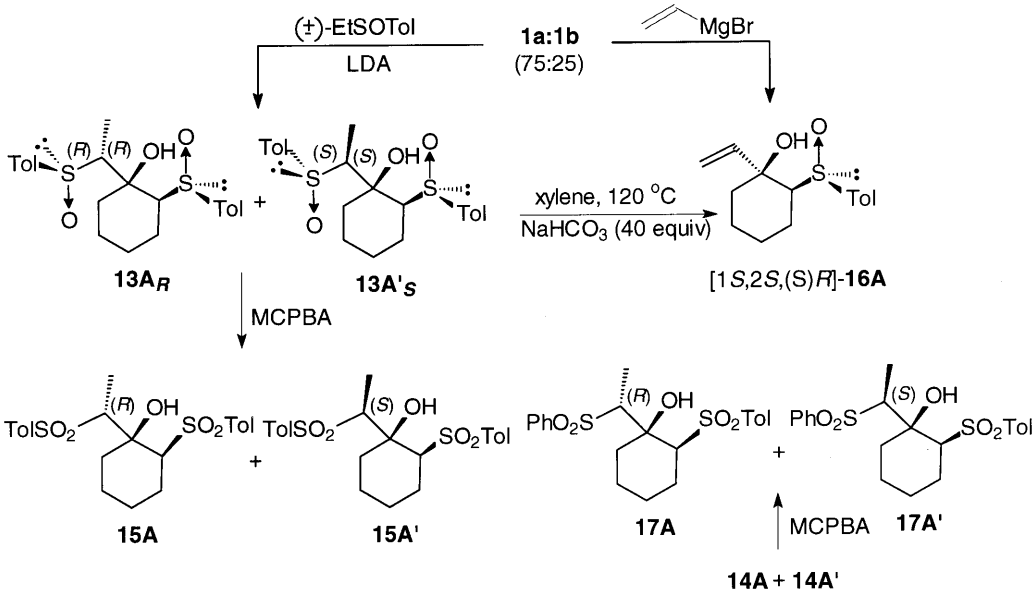


Figure 1. X-Ray structure for compound **14A**

cyclic sulfinyl group allowed us to state that $\mathbf{13A}_R$ and $\mathbf{13A'}_S$ have an identical configuration at the two stereogenic carbons of the cyclohexane ring. Additionally, the oxidation of the mixture of $\mathbf{13A}_R$ and $\mathbf{13A'}_S$ yielded a mixture of diastereomeric sulfones, **15A** and **15A′**, which must differ in the configurations at the exocyclic stereogenic carbon. All these reactions (Scheme 2) allowed us to assign unequivocally the configurations of the bis-sulfoxides $\mathbf{13A}_R$ and $\mathbf{13A'}_S$ and, therefore, to confirm the simultaneous control exerted by the sulfinyl groups at nucleophiles and electrophiles on the exocyclic and endocyclic new stereogenic carbons, respectively. Finally, the relative configuration assigned to **14A** and **14A′** is based on the fact that the MCPBA oxidation of a 55:45 mixture of both afforded a similar mixture of bis-sulfones **17A** and **17A′** with identical ^{1}H NMR spectra (except in the aromatic signals) to the mixture of **15A** and **15A′**.

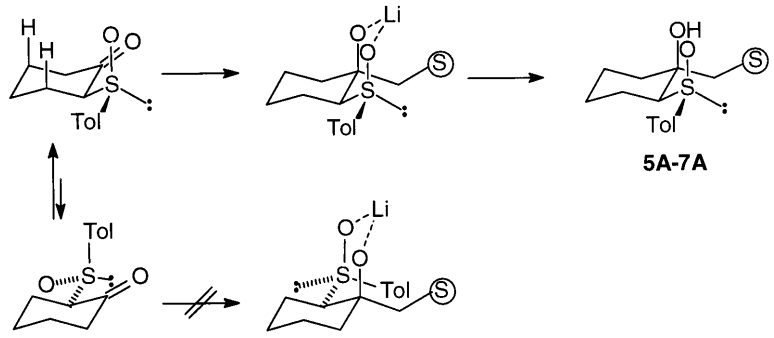


Scheme 2.

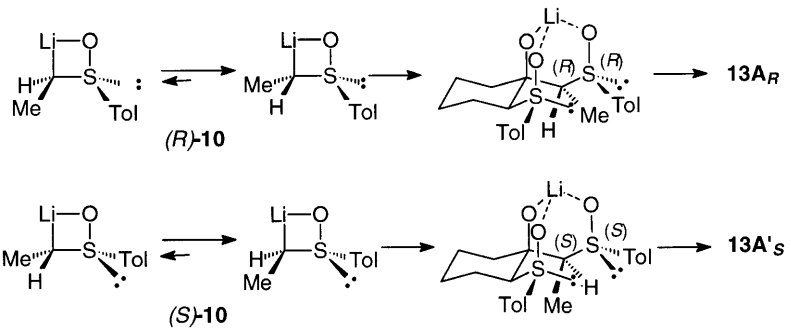
Therefore, the stereochemical course of the reaction should explain the following experimental facts: (a) the (*R*) configuration at sulfur in starting ketosulfoxide **1** induces the (*S*) configuration at hydroxylic carbon; (b) the reactivity of the [(S)*R*,2*S*]-**1** epimer is higher than that of the [(S)*R*,2*R*]-**1** one (kinetic resolution is observed); (c) the configuration of the sulfinyl group in the nucleophile controls the configuration of the exocyclic stereogenic carbon, but has no significant influence in that of the endocyclic hydroxylic carbon.

Taking into account the preference of nucleophiles for the equatorial attack on cyclohexanones to avoid steric interactions with the axial hydrogens at C-3 and C-5,[7,13] both the control of the sulfinyl group at **1** and the kinetic resolution observed in reactions with **2** are easily explained. As we can see in Scheme 3 the equatorial approach of the carbanions on [(S)*R*,2*S*]-**1** must be sterically favored with respect to a similar approach to [(S)*R*,2*R*]-**1**.

In order to rationalize the control of the sulfinyl group at nucleophiles on the configuration of the exocyclic stereogenic carbon it is necessary to assume that α-sulfinyl carbanions must be stabilized by the sulfinyl oxygen. In the case of compound **10** intermediates exhibiting *p*-tolyl and methyl groups in a *trans* arrangement in the four-membered ring will be clearly favored with respect to their *cis*-isomers (Scheme 4). If we assume that the nucleophilic attack takes place



Scheme 3.



Scheme 4.

with retention of the configuration of the stabilized carbanion, the experimental results (identical configuration at the above-mentioned sulfur and carbon atoms are favored) are easily explained. The contribution of the sulfinyl oxygen to the stabilization of the lithium could explain the higher reactivity and selectivity of these carbanions.

As a conclusion, we have demonstrated in this paper that the reactions of α-thiocarbanions with sulfinyl cyclohexanones take place with a total control of the stereoselectivity at the hydroxylic carbon. The best results are obtained with sulfinyl carbanions, which are also able to control the stereoselectivity of the exocyclic stereogenic carbons obtained from prochiral carbanions. We are currently interested in the synthetic transformations of the obtained products, mainly those with bis-sulfoxide structures, in order to obtain spiro-epoxides.

3. Experimental

Diastereoisomeric ratios were established by integration (^{1}H NMR) of well-separated signals of the diastereoisomers in the crude reaction mixtures. All reactions were monitored by TLC, which was performed on precoated sheets of silica gel 60 (F_{254}), and flash chromatography was effected with silica gel 60 (230–400 mesh). The vessels for inert atmospheric experiments were flame-dried in a stream of dry argon. THF was distilled from sodium/benzophenone under argon. Diisopropylamine was distilled from potassium hydroxide. *n*-Butyllithium (2.5 M solution in hexanes) was purchased from Aldrich.

The X-ray structure was refined by full-matrix least-squares (Sheldrick, G. M., SHELXL96, Program for Crystal Structure Refinement; University of Göttingen: Göttingen, 1996) on F^2. All non-hydrogen atoms were refined anisotropically.

3.1. Condensation of lithium alkyl aryl sulfoxides and keto sulfoxide **1**. General procedure

A solution of butyllithium (5.9 mL of a 2.5 M solution in hexanes, 14.9 mmol) was added dropwise to a cooled (−78°C) solution of diisopropylamine (2.2 mL, 15.7 mmol). After 20 min of stirring, a solution of the corresponding sulfoxide (14.9 mmol) in 5 mL of THF at rt was added via cannula. The mixture was maintained for 30 min at the same temperature and a solution of 2-(*p*-tolylsulfinyl)cyclohexanone (**1**, 1.01 g, 4.3 mmol) in 25 mL of THF was added via cannula. After 20 min at −78°C the reaction was quenched with a saturated solution of NH_4Cl (40 mL) and extracted with ethyl acetate (2×40 mL). The organic extracts were washed with brine (2×20 mL) and dried ($MgSO_4$). The solvent was removed under vacuum and the crude product purified by flash chromatography to afford the corresponding hydroxy sulfoxide.

3.1.1. *[(S′)*R,*1*S,*2*S,*(S)*R*]-1-[(*p-*Tolylsulfinyl)methyl]-2-(*p-*tolylsulfinyl)cyclohexanol **5A**

Compound **5A** was obtained as the sole diastereomer following the general procedure from (*R*)-methyl *p*-tolyl sulfoxide **2**. Column chromatography on silica gel (hexane–acetone, 3:1) and subsequent recrystallization (hexane–$CHCl_3$) afforded 3.46 g of pure **5A** (84%) as a white solid. $[\alpha]_D^{25}$ +195 (*c* 1, $CHCl_3$), mp 182–184°C (acetone). ^{1}H NMR δ 7.6 and 7.3 (8H, AA′BB′ system), 4.59 (1H, d, $J_{1,3}=1$ Hz), 3.47 and 3.38 (2H, AB system, $J_{AB}=13.6$ Hz), 3.42 (1H, dd, $J=13.6$ and 3.3 Hz), 2.44 (3H, s), 2.43 (3H, s), 2.20–1.00 (8H, bm). ^{13}C NMR δ 141.9, 141.5, 140.7, 136.6, 130.2 (2C), 130.1 (2C), 130.0 (2C), 124.3 (2C), 73.9, 68.4, 65.4, 38.7, 24.5, 21.4 (2C), 20.4, 16.7. IR ($CHCl_3$) 3390, 1705, 1170, 1020, 1010, 800. Anal. calcd for $C_{21}H_{26}O_3S_2$: C, 64.58; H, 6.71; S, 16.42. Found: C, 64.23; H, 6.82; S, 16.19.

3.1.2. *[(S′)*R,*1′*R,*1*S,*2*S,*(S)*R*]-1-[1′-(*p-*Tolylsulfinyl)ethyl]-2-*p-*tolylsulfinylcyclohexanol **13A**

Compound **13A** was obtained as a sole diastereomer from (*R*)-ethyl *p*-tolyl sulfoxide **10** following the general procedure. Purification was effected by crystallization ($CHCl_3$–hexane). Yield 88%. $[\alpha]_D^{25}$ +111 (*c* 1, $CHCl_3$), mp 193–195°C. ^{1}H NMR δ 7.52 and 7.32 (4H, AA′BB′ system), 7.44 and 7.36 (4H, AA′BB′ system), 4.28 (1H, d, $J=1.3$ Hz), 3.62 (1H, q, $J=6.9$ Hz), 3.37 (1H, dd, $J=12.0$ and 2.8 Hz,), 2.44 (3H, s) and 2.41 (3H, s), 2.3–1.0 (8H, m), 1.17 (3H, d, $J=6.9$ Hz). ^{13}C NMR δ 141.7, 141.1, 138.8, 135.5, 130.1 (2C), 129.9 (2C), 124.3 (2C), 124.0 (2C), 76.1, 66.5, 63.7, 33.0, 24.8, 21.4, 21.3, 20.1, 17.2, 2.0. Anal. calcd for $C_{22}H_{28}O_3S_2$: C, 65.31; H, 6.98; S, 15.85. Found: C, 65.12; H, 6.67; S, 15.72.

A 59:41 mixture of C-1′ epimers **13A**$_R$:**13A**′$_S$ was obtained from racemic ethyl *p*-tolyl sulfoxide (±)-**10**. Purification and separation of both epimers was effected by crystallization ($CHCl_3$–hexane) and subsequent column chromatography on silica gel (hexane–acetone, 3:1).

[(S′)*S*,1′*S*,1*S*,2*S*,(S)*R*]-**13A**′$_S$: ^{1}H NMR δ 7.70 and 7.30 (8H, m), 4.71 (1H, d, $J=1.8$ Hz), 3.94 (1H, q, $J=6.9$ Hz), 2.58 (1H, dd, $J=11.8$ and 3.1 Hz), 2.44 (3H, s), 2.41 (3H, s), 2.30–1.00 (8H, m), 1.21 (3H, d, $J=6.9$ Hz).

3.2. Condensation of lithium alkyl aryl thioether or sulfone and β-keto sulfoxides. General procedure

A solution of *n*-butyllithium (5.9 mL of a 2.5 M solution in hexanes, 14.9 mmol) was added dropwise to a cooled (−78°C) solution of the corresponding sulfur compound (14.9 mmol) in 5 mL of THF. The mixture was stirred for 30 min (at 0°C for sulfones and −20°C for thioethers) and then cooled at −78°C before the addition via cannula of a solution of 2-(*p*-tolylsulfinyl)cyclohexanone (**1**, 1.01 g, 4.3 mmol) in 25 mL of THF. After 5 min at −78°C, the reaction mixture was quenched with a saturated solution of NH_4Cl (40 mL) and extracted with ethyl acetate (2×40 mL). The organic extracts were washed with brine (2×20 mL) and dried ($MgSO_4$). The solvent was removed under vacuum and the crude product was purified by flash chromatography to afford the corresponding adducts.

3.2.1. 1-(Phenylsulfonyl methyl)-2-p-tolylsulfinylcyclohexanol **6**

Compound **6** was obtained following the general procedure from methyl phenyl sulfone **3** as a 96:4 mixture of C-1 epimers, **6A**:**6B**. Column chromatography on silica gel (CH_2Cl_2–acetone, 10:1) afforded pure **6A** (65%) as a white solid.

[1*S*,2*S*,(S)*R*]-**6A**: $[\alpha]_D^{25}$ +4 (*c* 1, $CHCl_3$), mp 100–102°C (hexane–ether). ^{1}H NMR δ 8.10 and 7.30 (9H), 4.74 (1H, d, $J_{1,3}=1.7$ Hz), 4.20 and 3.47 (2H, AB system, $J_{AB}=14.2$ Hz), 3.39 (1H, dd, $J=12.5$ and 3.5 Hz), 2.42 (3H, s), 2.40–0.70 (8H, m). ^{13}C NMR δ 141.4, 140.9, 135.9, 133.9, 129.9 (2C), 129.5 (2C), 127.5 (2C), 124.4 (2C), 74.7, 64.7, 63.9, 38.5, 24.4, 21.4, 20.3, 16.2. Anal. calcd for $C_{20}H_{24}O_4S_2$: C, 61.20; H, 6.16; S, 16.34. Found: C, 60.91; H, 6.25; S, 16.28.

3.2.2. 1-(p-Tolylthio)methyl-2-p-tolylsulfinylcyclohexanol **7**

Compound **7** was obtained following the general procedure from methyl *p*-tolyl sulfide **4** as an 85:15 mixture of C-1 epimers, **7A**:**7B** (global yield 67%). Column chromatography on silica gel (hexane–ethyl acetate, 4:1) of the mixture afforded **7A** which was further purified by crystallization (hexane–ethyl acetate) to yield the pure compound as a white solid (51%). Isolation of diastereomer **7B** has not been accomplished.

[1*S*,2*S*,(S)*R*]-**7A**: $[\alpha]_D^{25}$ −10 (*c* 1, $CHCl_3$). ^{1}H NMR δ 7.39 and 7.33 (4H, AA′BB′ system), 7.29 and 7.16 (4H, AA′BB′ system), 4.59 (1H, s,), 3.86 and 3.36 (2H, AB system, $J_{AB}=13.5$ Hz), 2.76 (1H, dd, $J=12.7$ and 3.8 Hz), 2.40 (3H, s), 2.30 (3H, s), 2.2–0.7 (8H, m). ^{13}C NMR δ 141.1, 136.7, 136.4, 132.5, 130.5 (2C), 129.8 (2C), 129.7 (2C), 124.2 (2C), 75.4, 63.0, 45.7, 37.1, 24.7, 21.3, 20.9, 20.4, 16.5. Anal. calcd for $C_{21}H_{26}O_2S_2$: C, 67.34; H, 7.00; S, 17.12. Found: C, 67.13; H, 6.85; S, 17.40.

3.2.3. 1-[1′-(Phenylsulfonyl)ethyl]-2-(p-tolylsulfinyl)cyclohexanol **14**

Compound **14** was obtained following the general procedure from ethyl phenyl sulfone **11** as a 55:45 mixture of C-1′ epimers, **14A**:**14A**′ (global yield: 75%). Purification and separation of both epimers was effected by column chromatography on silica gel (hexane–CH_2Cl_2–acetone, 5:1:1).

[1′*R*,1*R*,2*S*,(S)*R*]-**14A**: $[\alpha]_D^{25}$ −22 (*c* 1, $CHCl_3$). ^{1}H NMR δ 8.10–7.30 (9H, m), 4.55 (1H, d, $J=2.1$), 4.29 (1H, q, $J=6.9$ Hz), 3.85 (1H, dd, $J=12.7$ and 3.6 Hz), 2.43 (3H, s), 2.2–0.8 (8H, bm), 1.38 (3H, d, $J=6.9$ Hz). ^{13}C NMR δ 141.3, 139.3, 135.7, 133.7, 130.0 (2C), 129.2 (2C), 128.2 (2C), 124.4 (2C), 76.7, 64.9, 64.5, 32.8, 24.6, 21.4, 20.2, 16.8, 16.8, 10.6. Anal. calcd for $C_{21}H_{26}O_4S_2$: C, 62.04; H, 6.45; S, 15.77. Found: C, 61.73; H, 6.41; S, 15.38.

[1′*S*,1*R*,2*S*,(S)*R*]-**14A**′: $[\alpha]_D^{25}$ +30 (*c* 1, $CHCl_3$). ^{1}H NMR δ 8.10–7.30 (9H, m), 4.70 (1H, d, $J=1.3$), 4.02 (1H, q, $J=6.9$ Hz), 2.67 (1H, dd, $J=12.0$ and 3.5 Hz), 2.43 (3H, s), 2.30–1.00 (8H, bm), 1.50 (3H, d, $J=6.9$ Hz). ^{13}C NMR δ 139.7, 138.1, 137.0, 132.6, 128.6 (2C), 128.0 (2C), 127.3 (2C), 123.0 (2C), 76.9, 67.8, 66.3, 35.7, 25.6, 22.6, 21.6, 17.5, 13.4.

3.3. Sulfinyl group pyrolysis. General procedure

A 25 mL two-necked round bottomed flask, equipped with a stirrer and a reflux condenser and containing sodium bicarbonate (3.5 g, 40.6 mmol), was flame-dried in an N_2 stream. A solution of the corresponding hydroxysulfoxide (1.06 mmol) in *o*-xylene (10 mL) was added via cannula and the mixture was stirred vigorously and heated in an oil bath at the temperature indicated in each case. The mixture was cooled to room temperature and the crude was filtered over Celite® and washed with a saturated solution of NH_4Cl (20 mL). The organic layer was separated and the aqueous one was extracted with ethyl acetate (2×20 mL). The combined organic layers were finally washed with brine and dried ($MgSO_4$). To prevent any reaction product from evaporating, ethyl acetate was eliminated under reduced pressure without heating. Alkene isolation was effected by flash chromatography using successively hexane (to remove remaining *o*-xylene) and the eluent indicated in each case.

*3.3.1. [1*S,*2*S,*(S)*R*]-2-(*p-*Tolylsulfinyl)-1-vinylcyclohexanol* ***16A***

Compound **16A** was obtained from a 55:45 mixture of $\mathbf{13A}_R$:$\mathbf{13A}'_S$ diastereomers by heating the mixture for 4 h at 110°C. Chromatographic purification (ethyl acetate–hexane, 1:5) affords compound **16A** (68%) as a white solid. $[\alpha]_D^{25}$ +23 (*c* 1, $CHCl_3$), mp 92–93°C (acetone–hexane). ^{1}H NMR δ 7.34 (4H, m), 6.16 (1H, dd, $J=17.1$ and 10.4 Hz), 5.71 (1H, dd, $J=17.1$ and 1.5 Hz), 5.65 (1H, dd, $J=10.4$ and 1.5 Hz), 4.00 (1H, d, $J=2.2$ Hz, OH), 2.43 (3H, s), 2.20–0.80 (8H, m). ^{13}C NMR δ 143.8, 141.1, 136.7, 129.8, (2C), 124.3 (2C), 115.0, 74.7, 65.2, 39.2, 24.8, 21.3, 20.2, 16.5. Anal. calcd for $C_{15}H_{20}SO_2$: C, 68.15; H, 7.62; S, 12.13. Found: C, 68.05; H, 7.71; S, 12.10.

3.4. MCPBA oxidation of hydroxy sulfoxides. General procedure

A $CDCl_3$ solution of the corresponding hydroxy sulfoxides was added to an NMR tube containing a previously dried ($MgSO_4$) MCPBA solution in the same solvent. The bis-sulfones ratios and NMR signals were evaluated from the crude mixtures.

*3.4.1. [1′*R,*1*S,*2*S*]-1-[1′-(*p-*Tolylsulfonyl)ethyl]-2-(*p-*tolylsulfonyl)cyclohexanol* ***15A***

Compound **15A** was obtained from **13A** by MCPBA oxidation (5 molar equiv.). ^{1}H NMR δ 8.10–7.30 (8H), 4.96 (1H, q, $J=6.90$ Hz), 4.59 (1H, dd, $J=13.2$ and 2.6 Hz), 2.50 (3H, s), 2.48 (3H, s), 2.20–0.80 (8H, m), 1.36 (3H, d, $J=7.0$ Hz). ^{13}C NMR δ 145.4, 139.4, 135.2, 133.1, 129.8 (2C), 129.3 (2C), 128.9 (2C), 128.7 (2C), 75.7, 66.9, 64.2, 33.0, 25.2, 24.6 (2C), 21.5, 19.8, 10.2.

*3.4.2. 1-[1′-(Phenylsulfonyl)ethyl]-2-(*p-*tolylsulfonyl)cyclohexanol* ***17***

Compound **17** was obtained as a 75:25 diastereoisomeric mixture of **17A** and **17A**′ by MCPBA oxidation (3 molar equiv.) of a 75:25 mixture of **14A** and **14A**′.

[1′*R*,1*S*,2*S*]-**17A**: ^{1}H NMR δ 8.10–7.30 (9H), 4.97 (1H, c, $J=6.90$ Hz), 4.63 (1H, dd, $J=13.2$ and 2.5 Hz), 2.50 (3H, s, C*H*$_3$-Ar), 2.2–0.8 (8H, m), 1.37 (3H, d, $J=6.9$ Hz, C*H*$_3$CH). ^{13}C NMR δ 145.2, 139.8, 134.9, 133.4, 129.8 (2C), 129.3 (2C), 128.9 (2C), 128.7 (2C), 75.3, 66.3, 63.8, 33.1, 25.2, 24.6, 21.7, 19.8, 10.4.

[1′*S*,1*S*,2*S*]-**17A′**: ^{1}H NMR δ 8.10–7.30 (7H), 4.83 (1H, c, $J=7.1$ Hz), 3.17 (1H, dd, $J=10.2$ and 3.0 Hz), 2.48 (3H, s), 2.2–0.8 (8H, m), 1.51 (3H, d, $J=7.0$ Hz). ^{13}C NMR δ 144.5, 139.6, 135.8, 133.8, 129.5 (2C), 129.2 (2C), 128.5 (2C), 128.3 (2C), 76.8, 68.1, 65.2, 33.8, 25.0, 24.7, 21.7, 19.9, 12.2.

*3.4.3. (1*S*,2*S*)-1-(*p*-Tolylsulfonylmethyl)-2-(*p*-tolylsulfonyl)cyclohexanol **9A***

Compound **9A** was obtained from **5A** or **7A** by MCPBA oxidation (5 molar equiv. for **5A** and 3 molar equiv. for **7A**) following the general procedure. ^{1}H NMR δ 8.40–7.30 (8H), 4.35–3.38 (2H, AB system, $J=15$ Hz), 3.56 (1H, dd, $J=12.1$ and 2.7 Hz), 2.42 (3H, s), 2.20–1.00 (8H)

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