Highly Stereoselective Route to Dialkyl Sulfoxides Based upon the Sequential Displacement of Oxygen and Carbon Leaving Groups by Grignard Reagents on Sulfinyl Compounds

Maria Annunziata M. Capozzi, Cosimo Cardellicchio, Francesco Naso,* Giulia Spina, and Paolo Tortorella

Consiglio Nazionale delle Ricerche, Centro di Studio sulle Metodologie Innovative di Sintesi Organiche, Dipartimento di Chimica, Università di Bari, via Amendola 173, 70126 Bari, Italy

naso@area.ba.cnr.it

Received March 30, 2001

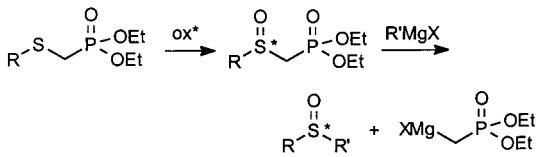
In recent work,[1−3] we have shown that the stereospecific displacement of a carbanionic leaving group[4] from suitable sulfinyl compounds by means of Grignard reagents represents a novel and versatile route to chiral nonracemic sulfoxides, a class of compounds which has always enjoyed a deserved popularity.[5,6]

Basically, we have set up a two-step procedure by subjecting sulfinyl derivatives, obtained by enantioselective oxidation of the corresponding sulfides, to the action of organometallic reagents.[1,2] In particular, as shown in Scheme 1, the oxidation of arylthio- or alkylthiomethylphosphonates in high enantiomeric purity (91 to >98%), followed by reaction with Grignard reagents, led to a variety of sulfoxides.[1]

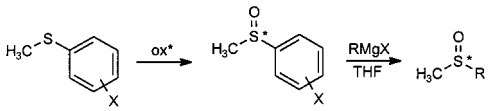
Particularly high ee values (>98%) were obtained in the synthesis of methyl alkyl sulfoxides, whereas ethyl or phenyl sulfoxides were prepared with lower ee values (91−94%).

An important improvement[2] in the synthesis of methyl sulfoxides with ee values >98% was brought about by reacting the Grignard reagent with aryl methyl sulfoxides, easily obtained by enantioselective cumene hydroperoxide oxidation of the corresponding sulfide, a process mediated by a diethyl (*R*,*R*)-tartrate/titanium complex (Scheme 2).

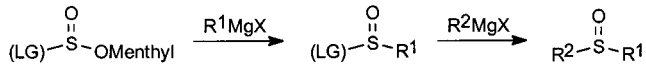
Scheme 1



Scheme 2



Scheme 3



Taking into account the yields, the stereochemical course of the reactions, and the availability of the substrates in high enantiomeric purity, it appeared that the best substrate was the *p*-bromophenyl methyl sulfoxide.[2] In this substrate, the whole *p*-bromophenyl moiety was displaced by Grignard reagents as a carbanionic leaving group with full inversion of configuration. Alkyl methyl sulfoxides were then obtained in good isolated yields (74−90%) and with high enantiomeric purity (ee > 98%).[2]

Our two-step strategy (enantioselective oxidation/enantiospecific displacement of a carbanionic leaving group, as depicted in Schemes 1 and 2) has allowed an easy access to dialkyl sulfoxides, a type of sulfoxide which has attracted considerable interest.[7−10] However, a structural limitation resulting from the application of our protocol to the synthesis of dialkyl sulfoxides was the fact that, in the first step, that is, the oxidation of the sulfides, good ee values were obtained only when either the methyl[1,2] or ethyl[1] group was present.

We reasoned that, in principle, this limitation could be circumvented by combining our carbanionic leaving group approach with the classical displacement[5] of the OMenthyl group from a suitable menthyl sulfinate according to Scheme 3, where (LG) is a carbanionic leaving group.

We report now our successful experimental efforts to transform Scheme 3 in a general procedure for the synthesis of dialkyl sulfoxides.

Results and Discussion

According to our experience in the field of carbanionic leaving groups, a good candidate for a two-step synthesis of chiral sulfoxides was represented by the menthyl

(1) Capozzi, M. A. M.; Cardellicchio, C.; Fracchiolla, G.; Naso, F.; Tortorella, P. *J. Am. Chem. Soc.* **1999**, *121*, 4708.

(2) Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Tortorella, P. *J. Org. Chem.* **2000**, *65*, 2843−2846.

(3) (a) Cardellicchio, C.; Fiandanese, V.; Naso, F. *J. Org. Chem.* **1992**, *57*, 1718−1722. (b) Cardellicchio, C.; Fiandanese, V.; Naso, F.; Scilimati, A. *Tetrahedron Lett.* **1992**, *33*, 5121−5124. (c) Cardellicchio, C.; Iacuone, A.; Naso, F.; Tortorella, P. *Tetrahedron Lett.* **1996**, *37*, 6017−6020. (d) Cardellicchio, C.; Fracchiolla, G.; Naso, F.; Tortorella, P. *Tetrahedron* **1999**, *55*, 525−532.

(4) For earlier work on the use of carbanionic leaving groups in sulfoxide chemistry see: (a) Durst, T.; LeBelle, M. J.; Van Der Elzen, R.; Tin, K.-C. *Can. J. Chem.* **1974**, *52*, 761−766. (b) Lockard, J. P.; Schroeck, C. W.; Johnson, C. R. *Synthesis* **1973**, 485−486. For work on the fate of carbanionic leaving groups see: (c) Hoffmann, R. W.; Nell, P. G.; Leo, R.; Harms, K. *Chem. Eur. J.* **2000**, *6*, 3359−3365.

(5) Drabowicz, J.; Kiełbasinski, P.; Mikołajczyk, M. Synthesis of Sulphoxides. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C., Eds.; John Wiley and Sons: New York, 1988; pp 233−378.

(6) (a) Solladié, G. Optically active β-ketosulfoxides in asymmetric synthesis. In *Advanced Asymmetric Synthesis*; Stephenson, G. R., Ed.; Chapman and Hall: London, 1996; pp 60−92. (b) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717−1760. (c) Walker, A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 961−998. (d) Solladié, G. *Synthesis* **1981**, 185−196.

(7) Alayrac, C.; Nowaczyk, S.; Lemarié, M.; Metzner, P. *Synthesis* **1999**, 669−675.

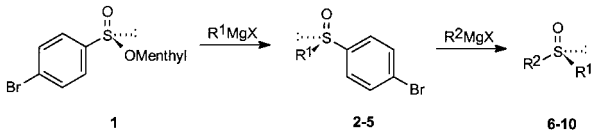
(8) Fernandez, I.; Khiar, N.; Llera, J. M.; Alcudia, F. *J. Org. Chem.* **1992**, *57*, 6789−6796.

(9) Colonna, S.; Gaggero, N.; Pasta, P.; Ottolina, G. *Chem. Commun.* **1997**, 439−440.

(10) (a) Rebiere, F.; Samuel, O.; Ricard, L.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 5991−5999. (b) Benson, S. C.; Snyder, J. K. *Tetrahedron Lett.* **1991**, *32*, 5885−5888. (c) Wudl, F.; Lee, T. B. K. *J. Am. Chem. Soc.* **1973**, *95*, 6349−6358.

10.1021/jo010334m CCC: $20.00
Published on Web 08/02/2001

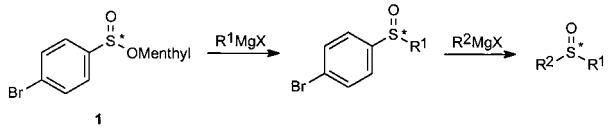
Table 1. Stereospecific Substitution of Leaving Groups by Grignard Reagents on Sulfinyl Compounds



entry	substrate (configuration)	R^1	R^2	solvent[a]	temp (°C)	RMgX/substrate ratio	product (configuration)	yield[b] (%)	ee (%)
1	**1** (*S*)	ethyl		benzene	5	1.1:1	**2** (*R*)[c]	88	>98[d]
2	**1** (*S*)	*n*-decyl		benzene	5	1.1:1	**3** (*R*)[c]	91	>98[d]
3	**1** (*S*)	*i*-propyl		benzene	5	1.1:1	**4** (*R*)[c]	83	>98[d]
4	**1** (*S*)	cyclohexyl		benzene	5	1.1:1	**5** (*R*)[c]	97	>98[d]
5	**2** (*R*)	ethyl	*n*-decyl	THF	−30	1.5:1	**6** (*S*)[e]	76	>98[d]
6	**2** (*R*)	ethyl	cyclohexyl	THF	−30	1.5:1	**7** (*S*)[e]	89	>98[d]
7	**3** (*R*)	*n*-decyl	ethyl	THF	−30	1.5:1	**6** (*R*)[e]	95	>98[d]
8	**3** (*R*)	*n*-decyl	*i*-propyl	THF	−30	1.5:1	**8** (*S*)[e]	97	>98[d]
9	**3** (*R*)	*n*-decyl	cyclohexyl	THF	−30	1.5:1	**9** (*S*)[e]	96	>98[f]
10	**4** (*R*)	*i*-propyl	cyclohexyl	THF	−30	1.5:1	**10**[g]	42	>98[d]
11	**5** (*R*)	cyclohexyl	ethyl	THF	−30	1.5:1	**7** (*R*)[e]	60	>98[d]

[a] Solvent for the substrate. Grignard reagents were prepared in THF. [b] Isolated yield. [c] Configuration expected on the basis of a stereochemical course occurring with inversion. [d] Determined by HPLC (see text). [e] Configuration expected on the basis of a stereochemical course occurring with inversion and confirmed by NMR upon addition of (*R*)-(methoxy)phenylacetic acid (see text). [f] Determined by NMR upon addition of (*R*)-(methoxy)phenylacetic acid. [g] The product should be (*S*), provided that also this reaction occurred with inversion of configuration.

Scheme 4



p-bromobenzenesulfinate (**1**). In preliminary experiments, we checked that this substrate actually reacted with Grignard reagents, undergoing a carbon for oxygen substitution, followed by a carbon for carbon substitution (Scheme 4).

First of all, the possibility of transforming this double displacement sequence into a convenient route to dialkyl sulfoxides was strictly dependent upon the availability of the starting material. Menthyl *p*-bromobenzenesulfinate (**1**) with the (*S*) configuration at the sulfur stereogenic center had been prepared starting from a sulfinic acid derivative.[11] However, this procedure did not seem to be adequate for the preparation of the substrate on a large scale. On the other hand, different menthyl sulfinates had been prepared by the reaction between (−)-menthol and sulfonyl chlorides, with the addition of trimethyl phosphite as a reducing agent.[12] By modifying this procedure, we were able to obtain substrate (*S*)-**1** on a scale of several grams. According to our protocol, menthyl *p*-bromobenzenesulfinate was prepared as a mixture of diastereomers, the predominant one being the stereoisomer with the (*S*) configuration at the sulfur stereogenic center (see Experimental Section). This diastereomer was separated by crystallization, and iteration of the procedure, after subjecting the mother liquors enriched in the (*R*)-stereoisomer to epimer equilibration by adding HCl, led to a 57% overall yield of (*S*)-**1**.

Menthyl (*S*)-*p*-bromobenzenesulfinate (**1**) in benzene was subjected to reactions with 1.1 equiv of alkyl Grignard reagents in THF at 5 °C (Table 1, entries 1−4). The formation of alkyl *p*-bromophenyl sulfoxides **2**−**5** was found to take place in high yield (83−97%). Under these reaction conditions, only the substitution of the menthoxide ion occurred. The enantiomeric purity of the obtained sulfoxides was determined by HPLC and was found to be >98%. Taking into account that the nucleophilic displacement of a menthoxide ion at a sulfur atom occurs with inversion, the configuration of the products **2**−**5** should be (*R*).

The second step of the procedure, that is, the carbon for carbon substitution on the alkyl *p*-bromophenyl sulfoxides **2**−**5**, was performed with alkyl Grignard reagents, yielding the target dialkyl sulfoxide in good yields and with the same enantiomeric purity of the starting material (ee > 98%). In particular, when an *n*-alkyl *p*-bromophenyl sulfoxide (Table 1, entries 5−9) was the substrate for the second step, dialkyl sulfoxides were obtained in high yields (76−97%). On the other hand, when a *sec*-alkyl *p*-bromophenyl sulfoxide was used, the yields were lower (Table 1, entries 10−11). As a consequence, an *n*-alkyl *sec*-alkyl sulfoxide could be obtained in better yields by reacting the secondary alkyl Grignard reagents with an *n*-alkyl *p*-bromophenyl sulfoxide.

A stereochemical course of inversion of configuration should be expected also in the carbon for carbon substitution.[1,2,3b−d] This type of stereochemical outcome has been observed in similar cases.[5]

The configuration of the sulfoxides **6**−**9** could be inferred also by using an NMR technique, according to a work of Buist et al.[13] Indeed, (methoxy)phenylacetic acid was reported to yield a complex with alkyl sulfoxides, and a distinction between the two possible diastereomeric complexes resulting from the interaction with (*R*)-(methoxy)phenylacetic acid could be made on the basis of the signals attributed to the methylene group bound to the sulfur atom. When this analysis was performed, the results were consistent with the configuration expected from a sequence requiring inversion in both steps. The determination of the configuration of **10** was not possible

(11) (a) Cooke, R. S.; Hammond, G. S. *J. Am. Chem. Soc.* **1970**, *92*, 2739−2745. (b) Nishide, K.; Nakayama, A.; Kusumoto, T.; Hiyama, T.; Takehara, S.; Shoji, T.; Osawa, M.; Kuriyama, T.; Nakamura, K.; Fujisawa, T. *Chem. Lett.* **1990**, 623−626.

(12) Klunder, J. M.; Sharpless, K. B. *J. Org. Chem.* **1987**, *52*, 2598−2602.

(13) Buist, P. H.; Marecak, D.; Holland, H. L.; Brown, F. M. *Tetrahedron: Asymmetry* **1995**, *6*, 7−11.

by NMR, because of the absence of methylene groups bound to the sulfur atom.

In conclusion, the present work extends the applications of carbanionic leaving groups to a simple and viable route to various types of dialkyl sulfoxides in high enantiomeric purity. A common precursor is prepared first, and the target sulfoxides are obtained in two consecutive displacements with the organometallic reagent. The simple control of the sequence of these displacements leads to the required configuration.

Our method compares favorably with other procedures, which are less general, each one being restricted to limited types of dialkyl sulfoxides or presenting other disadvantages.[7−10] For instance, the method of Kagan et al.[10a] requires in the first step a reaction of an organometallic reagent on a cyclic sulfite. This reaction is not always regioselective, and the ratio between the two resulting sulfinates depends on the organometallic reagent used. On the other hand, the work of Alcudia et al.[8] hinges on the availability of alkanesulfinates of diacetone-D-glucose (DAG), obtained by the crystallization or the chromatographic separation of mixtures of diastereomers. Depending on the type of sulfoxides needed, the appropriate type of DAG sulfinate has to be prepared.

At this point, it seems also appropriate to make a comparison between the use of Grignard reagents and the use of lithium alkyls in the second step of our procedure. In this respect, it is worth noting that a displacement of the aryl group has been reported by Johnson et al.[4b] in the reactions of phenyl or *p*-tolyl methyl sulfoxide with *n*-butyllithium, leading to *n*-butyl methyl sulfoxide with 87 or 93% optical purity, respectively.[14] However, the reaction appears to be of limited scope. Indeed, only unreacted material was recovered in the reaction between *p*-tolyl butyl sulfoxide and methyllithium. Therefore, if we take into account also the tendency of lithium alkyls to abstract a proton from alkyl sulfoxides,[6d] and the serious lack of reproducibility of results in terms of ee values and stereochemical course evidenced in a recent work of Drabowicz et al.[15] for the reaction between *tert*-butyllithium and *n*-butyl *p*-tolyl sulfoxide, one is led to the conclusion that the use of Grignard reagents associated with an appropriate substrate is by far to be preferred in the synthesis of dialkyl sulfoxides.

The ready availability of a variety of chiral nonracemic sulfoxides with primary and/or secondary alkyl groups should now promote their use in the important field of asymmetric synthesis or for novel applications.[16]

Finally, it is worth noting that in the present work our attention was focused on the synthesis of dialkyl sulfoxides because these represented a type of compounds for which there was much more need of a general route. However, in principle, by adopting the carbanionic leaving group strategy, it should be possible to prepare any type of sulfoxide, provided that appropriate substrates with suitable leaving groups are uncovered.

Experimental Section

The purified reaction products were characterized by their ^{1}H and ^{13}C NMR spectra, recorded in $CDCl_3$ at 500 and 125 MHz, respectively, and their mass spectra, determined by GC/MS analysis (SE30, 30 m, capillary columns and mass selective detector, 70 eV).

The de values of the diastereomeric mixture of menthyl *p*-bromobenzenesulfinate were determined by GC analysis (SE30, 30 m, capillary columns). The ee values of the sulfoxides **2**−**8** and **10** were determined by HPLC (Chiralcel OB-H or OD-H). The ee values of **9** were determined by NMR, after the addition of (*R*)-(methoxy)phenylacetic acid.

Racemic **2**−**10,** used as references in HPLC or NMR methods, were prepared starting from a mixture of (*R*)-**1** and (*S*)-**1** of low de, which resulted from the purification of (*S*)-**1**. The same compounds could also be obtained by treating acetone solutions containing small amounts of chiral nonracemic material with a drop of HCl. After the usual workup, a complete racemization of the starting sulfoxide was revealed.

Synthesis of Menthyl (*S*)-*p*-Bromobenzenesulfinate (1). Triethylamine (8.2 mL) was added under a nitrogen atmosphere to a solution of (1*R*,2*S*,5*R*)-(−)-menthol (6.1 g, 39 mmol) and *p*-bromobenzenesulfonyl chloride (15 g, 58.7 mmol) in 140 mL of methylene chloride. Trimethyl phosphite (9.3 mL) was then added, and the mixture was refluxed for 3 h. After this time, the mixture was cooled and quenched with a 1.2 N solution of HCl. The separated organic layer was washed twice with a 2 M solution of Na_2CO_3 and twice with brine, and the solvent was evaporated at a reduced pressure. The crude residue was heated in a Kugelrohr oven at 40 °C and at 10^{-3} mbar to remove some impurities (phosphorus compounds and traces of unreacted menthol). After this treatment, menthyl (*S*)-*p*-bromobenzenesulfinate (**1**) was found to be the predominant stereoisomer (de = 13%). The residue was treated with 60 mL of hexane, and 6.3 g of a white solid and a solution were obtained. The white crystalline solid was found to be highly enriched in menthyl (*S*)-*p*-bromobenzenesulfinate (**1**, de 89%). A simple recrystallization from acetone yielded 4.1 g of pure (*S*)-**1**. The hexane and acetone solutions were combined and evaporated to give a residue which was crystallized three times (acetone), yielding an additional 1.5 g of pure (*S*)-**1**. The mother liquors of these crystallizations were collected and evaporated. The residue, highly enriched in (*R*)-**1**, was dissolved in 60 mL of acetone and treated with 0.1 mL of 12 N HCl at room temperature for 2 h. After the usual workup, (*S*)-**1** and (*R*)-**1** were present in almost equal amounts. The crude mixture was heated in a Kugelrohr oven to evaporate a small amount of formed menthol. The diastereomeric couple was recrystallized twice (acetone), yielding an additional 2.1 g of pure (*S*)-**1**. From the combination of the two processes (production of menthyl (*S*)-*p*-bromobenzenesulfinate and separations of the diastereomers), a 57% overall yield of pure (*S*)-**1** was obtained.

Menthyl (*S*)-*p*-bromobenzenesulfinate (1) mp 120−121 °C (acetone) (lit.[11a] 108−113.5 °C; lit.[11b] 117−118 °C). $[\alpha]_D$ −156.5 (*c* 1, $CHCl_3$) (lit.[11a] $[\alpha]_D$ −159.8 (*c* 2.7, $CHCl_3$); lit.[11b] $[\alpha]_D$ −158 (*c* 1.11, MeOH)).

Reaction of Alkyl Grignard Reagents with Menthyl (*S*)-*p*-Bromobenzenesulfinate (1). A solution of 4.6 mmol of Grignard reagent in THF was added to a solution of 4.2 mmol of **1** in 25 mL of benzene at 5 °C and under N_2. After 1.5 h, the reaction mixture was quenched with a saturated solution of NH_4Cl. The usual workup yielded a residue which was purified by column chromatography and crystallization (hexane).

***(R)*-*p*-Bromophenyl ethyl sulfoxide (2)**[17] mp 53−55 °C (hexane). $[\alpha]_D$ +162.0 (*c* 1, $CHCl_3$). The ee value, measured by HPLC (Chiralcel OB-H, hexane−*i*-propanol 70:30), was >98%.

***(R)*-*p*-Bromophenyl *n*-decyl sulfoxide (3)** mp 51−52 °C (hexane). $[\alpha]_D$ +122.8 (*c* 1, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65−7.62 (m, 2H), 7.48−7.45 (m, 2H), 2.74 (t-like, J = 7.7 Hz, 2H), 1.74−1.67 (m, 1H), 1.59−1.54 (m, 1H), 1.42−1.31 (m, 2H), 1.30−1.22 (m, 12H), 0.85 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.28, 132.39, 125.64, 125.29, 57.33, 31.83, 29.44, 29.31, 29.22, 29.13, 28.63, 22.64, 21.99, 14.08. MS (70 eV): 330 (10), 328 (10), 190 (33), 188 (24), 55 (39), 43 (100). Anal.

(14) Values calculated on the basis of optical rotations taken in acetone: Johnson, C. R.; Kirchhoff, R. A.; Corkins, H. G. *J. Org. Chem.* **1974**, *39*, 2458−2459.

(15) Drabowicz, J.; Dudziński, B.; Mikołajczyk, M.; Wang, F.; Dehlavi, A.; Goring, J.; Park, M.; Rizzo, C. J.; Polavarapu, P. L.; Biscarini, P.; Wieczorek, M. W.; Majzner, W. R. *J. Org. Chem.* **2001**, *66*, 1122−1129.

(16) Fanizzi, F. P.; Alicino, V.; Cardellicchio, C.; Tortorella, P.; Rourke, J. P. *Chem. Commun.* **2000**, 673−674.

(17) Racemic **2**: Kim, Y. H.; Lee, H. K. *Chem. Lett.* **1987**, 1499−1502.

Calcd for $C_{16}H_{25}BrOS$: C, 55.65; H, 7.30. Found: C, 55.37; H, 7.20. The ee value, measured by HPLC (Chiralcel OD-H, hexane−*i*-propanol 90:10), was >98%.

***(R)-p*-Bromophenyl *i*-propyl sulfoxide (4)** mp 68−70 °C (hexane). $[\alpha]_D$ +160.8 (*c* 1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.66−7.63 (m, 2H), 7.47−7.44 (m, 2H), 2.80 (heptet, J = 6.9 Hz, 1H), 1.22 (d, J = 6.9 Hz, 3H), 1.11 (d, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.93, 132.06, 126.53, 125.39, 54.57, 15.73, 13.73. Anal. Calcd for $C_9H_{11}BrOS$: C, 43.74; H, 4.49. Found: C, 43.42; H, 4.57. The ee value, measured by HPLC (Chiralcel OB-H, hexane−*i*-propanol 70:30), was >98%.

***(R)-p*-Bromophenyl cyclohexyl sulfoxide (5)** mp 119−120 °C (hexane). $[\alpha]_D$ +156.3 (*c* 1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.64−7.62 (m, 2H), 7.45−7.42 (m, 2H), 2.55−2.49 (m, 1H), 1.85−1.62 (m, 5H), 1.43−1.31 (m, 2H), 1.28−1.14 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.01, 132.12, 126.57, 125.36, 63.25, 26.20, 25.58, 25.37, 25.28, 23.85. Anal. Calcd for $C_{12}H_{15}BrOS$: C, 50.18; H, 5.26. Found: C, 50.32; H, 5.34. The ee value, measured by HPLC (Chiralcel OB-H, hexane−*i*-propanol 80:20), was >98%.

Reaction of Alkyl Grignard Reagents with *p*-Bromophenyl Sulfoxides (2−5). A solution of 1.5 mmol of Grignard reagent in THF was added to a solution of 1 mmol of alkyl *p*-bromophenyl sulfoxide in 15 mL of THF at −30 °C and under N_2. After 1.5 h, the reaction mixture was quenched with a saturated solution of NH_4Cl. The usual workup yielded a residue, which was purified by column chromatography and crystallization (hexane) or distillation.

***n*-Decyl ethyl sulfoxide (6)**[18] mp 51−52 °C (hexane). $[\alpha]_D$ +26.0 (*c* 1, $CHCl_3$) for the (*S*) configuration; $[\alpha]_D$ −25.5 (*c* 1, $CHCl_3$) for the (*R*) configuration. The ee value, measured by HPLC (Chiralcel OB-H, hexane−*i*-propanol 95:5), was >98%. A further NMR control of the enantiomeric purity was performed by adding (*R*)-(methoxy)phenylacetic acid.

Cyclohexyl ethyl sulfoxide (7)[9,19] bp 60−65 °C, $p = 3 \times 10^{-4}$ Torr, Kugelrohr. $[\alpha]_D$ +2.9 (*c* 1, $CHCl_3$) for the (*R*) configuration; $[\alpha]_D$ −2.5 (*c* 1, $CHCl_3$) for the (*S*) configuration (lit.[19] $[\alpha]_D$ −27.2 (*c* 1, EtOH) for a 72% ee mixture). The ee value, measured by HPLC (Chiralcel OD-H, hexane−*i*-propanol 95:5), was >98%. A further NMR control of the enantiomeric purity was performed by adding (*R*)-(methoxy)phenylacetic acid.

***(S)-n*-Decyl *i*-propyl sulfoxide (8)** mp = 38−40 °C (pentane). $[\alpha]_D$ −42.8 (*c* 1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 2.76 (heptet, J = 7.0 Hz, 1H), 2.61 (ddd, J = 12.8, J = 9.2, J = 5.6 Hz, 1H), 2.56 (ddd, J = 12.8, J = 9.1, J = 7.2 Hz, 1H), 1.85−1.71 (m, 2H), 1.51−1.12 (m, 20H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 50.09, 48.73, 31.84, 29.48, 29.36, 29.25, 29.21, 28.96, 22.86, 22.64, 16.06, 14.62, 14.08. Anal. Calcd for $C_{13}H_{28}OS$: C, 67.18; H, 12.14. Found: C, 67.06; H, 11.95. The ee value, measured by HPLC (Chiralcel OD-H, hexane−*i*-propanol 97:3), was >98%. A further NMR control of the enantiomeric purity was performed by adding (*R*)-(methoxy)-phenylacetic acid.

***(S)*-Cyclohexyl *n*-decyl sulfoxide (9)** mp 69−70 °C (hexane). $[\alpha]_D$ −22.1 (*c* 1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 2.63 (ddd, J = 12.9, J = 8.9, J = 6.2 Hz, 1H), 2.60 (ddd, J = 12.9, J = 8.8, J = 7.4 Hz, 1H), 2.52 (tt, J = 11.6, J = 3.6 Hz, 1H), 2.12−2.08 (m, 1H), 1.93−1.62 (m, 7H), 1.51−1.21 (m, 18H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 58.84, 48.95, 31.87, 29.50, 29.39, 29.27, 29.23, 28.98, 26.48, 25.58, 25.50, 25.23, 24.83, 22.75, 22.67, 14.11. Anal. Calcd for $C_{16}H_{32}OS$: C, 70.52; H, 11.84. Found: C, 70.59; H, 11.92. The ee value, measured by NMR by addition of (*R*)-(methoxy)phenylacetic acid, was found to be >98%.

***(S)*-Cyclohexyl *i*-propyl sulfoxide (10)**[20] bp 60−65 °C, $p = 4 \times 10^{-4}$ Torr, Kugelrohr. $[\alpha]_D$ +20.5 (*c* 1, $CHCl_3$). The ee value, measured by HPLC (Chiralcel OD-H, hexane−*i*-propanol 95:5), was >98%.

Acknowledgment. This work was financially supported in part by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome (National Project "Stereoselezione in Sintesi Organica. Metodologie e Applicazioni"), and by the University of Bari.

Supporting Information Available: Relevant spectral data for compounds **1**−**10**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO010334M

(18) Racemic **6**: Novitskaya, N. N.; Chernikova, S. I. *Neftekhimiya* **1970**, *10*, 429−436; *Chem. Abstr.* **1970**, *73*, 76486*r*.

(19) Holland, H. L.; Brown, F. M.; Lakshmaiah, G.; Larsen, B. G.; Patel, M. *Tetrahedron: Asymmetry* **1997**, *8*, 683−698.

(20) Racemic **10**: Firouzabadi, H.; Iranpoor, N.; Zolfigol, M. A. *Synth. Commun.* **1998**, *28*, 1179−1187.