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Biotransformation of Organic Sulfides—IV. Formation of Chiral Benzyl Alkyl and Phenyl Alkyl Sulfoxides by *Helminthosporium* Species NRRL 4671†

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Abstract—The fungus *Helminthosporium* species NRRL 4671 has been used for the biotransformation of a series of phenyl alkyl sulfides with alkyl groups ranging from methyl to *n*-hexyl, and benzyl alkyl sulfides with alkyl groups from methyl to *n*-nonyl. Several 2-phenylethyl and 3-phenylpropyl sulfides have also been examined as substrates, together with cyclohexyl methyl sulfide and 1- and 2-naphthyl methyl sulfides. For the majority of substrates, sulfoxide formation occurred in moderate yield and with predominant (*S*) chirality at sulfur; lesser amounts of sulfone product were also obtained in some cases. The data so obtained have been used to define the preparatively useful limits of S-oxidation of phenyl alkyl sulfides and benzyl alkyl sulfides by biotransformation using *Helminthosporium*.

Introduction

In recent years, chiral sulfoxides have become increasingly available as a result of developments in asymmetric synthesis[1] and biotransformation.[2] Work to date has shown that the latter area has tremendous potential for the preparative scale production of chiral sulfoxides, but in spite of the continuing discovery of new organisms capable of performing asymmetric oxidation of prochiral sulfides,[3] and developments in the application of isolated oxidase enzyme methodology,[4–7] the overall scope and limitations of the reaction remain largely undefined. In an effort to address this problem, we have undertaken a systematic study of the oxidation of prochiral sulfides by the fungus *Helminthosporium* species NRRL 4671. We have chosen this organism for study for two reasons: firstly, it is known to carry out the asymmetric oxidation of a range of structurally different prochiral sulfides[8–10] and secondly it produces little or no sulfone product,[10] thus ensuring that stereochemical analyses of sulfoxides are not complicated by considerations of enantioselective oxidation of sulfoxide to sulfone, as is the case with some other organisms of biotransformation (e.g. *Aspergillus niger*).[11] In this paper, we present the results of biotransformation studies with phenyl alkyl sulfide and benzyl alkyl sulfide substrates. Later papers will describe the biotransformations of substituted benzyl alkyl sulfides, and discuss the nature and substrate specificity of the S-oxidizing enzymes of *Helminthosporium*.

Results and Discussion

The results of the biotransformations of substrates **1** to **31** are presented in the accompanying table in terms of isolated yields of sulfone and sulfoxide products, together with the enantiomeric excesses and predominant configuration of the latter, referred to as **1a** to **31a**, respectively, in the Experimental section (below). The absolute configurations of sulfoxide products were assigned by reference to literature rotation values (where known), and otherwise by correlation of rotation data for analogous compounds within a series [e.g. **16a–20a** (unknown configuration) compared with **10a**, **11a**, **12a** and **13a** (known configuration)]. The absolute configurations of sulfoxides thus derived (those of **16a–20a**, **22a**, **23a** and **25a–29a** were also suggested by analysis of their ^{1}H NMR spectra in the presence of the chiral shift reagents (*S*)-(+)-α-methoxyphenylacetic acid (MPAA)[12] or (*R*)-(−)-*N*-(3,5-dinitrobenzoyl)-α-methylbenzylamine (Kagan reagent).[13] Both reagents gave consistent chemical shift patterns which were enantiomer-dependent: presence of the Kagan reagent results in enantiomeric duplication of one or both halves of the AB quartet due to the benzylic CH_2 group of **10a** to **26a** in a consistent manner, and can also be used to generate resolvable signals from the protons α to sulfur in **1a** to **9a**, while MPAA produces splitting of the ^{1}H resonances α to sulfur in the entire series **1a** to **31a**. The latter reagent is particularly valuable in the assignment of absolute configuration using the model proposed by Buist and Marecak,[12] and a full analysis of its use in this capacity will be presented elsewhere.[14] In our experience with the series **1a** to **31a**, alkyl group protons α to sulfur in the (*S*) enantiomer appear consistently at higher field than those of the corresponding (*R*) enantiomer. For example, in **27**, the ^{1}H NMR methyl resonances in the presence of MPAA are at δ 2.590 and 2.602 ppm, the former being assigned to the (*S*) enantiomer by comparison with the methyl resonances of **10** ((±) at δ 2.466 and 2.482, and (*R*) at δ 2.482 ppm).

It is apparent from the data presented in the table that the predominant absolute stereochemistry and enantiomeric

†It is with great pleasure that we present this paper to honour the 60th birthday of Professor J. Bryan Jones, in celebration of his outstanding achievements in the area of biocatalysis.

Table 1.

Substrate	Sulfone (%)	Sulfoxide					
		yield (%)	config.	ee ($[\alpha]_D$)	ee (MPAA)	ee (Kagan)	ee (Euhfc$_3$)
1	nil	30	*S*	48			
2	nil	40	*S*	84			
3	nil	57	*S*	33			
4	nil	42	*R*	32			
5	2	39	*S*	16	15	14	
6	nil	1	*R*	15			
7	4	19	*S*		10		
8	1	7	*R*		25		
9	nil	22	*R*	45			
10*	nil	68	*S*	62	60	62	
11*	3	55	*S*	51	50	52	
12*	nil	12	*S*				10
13*	nil	22	-	0			
14*	nil	38	*S*	25	24	23	
15*	nil	5	*S*	7			
16	7	20	*S*		70	68	
17	2	22	*S*		82	78	
18	1	11	*S*		>95	>95	
19	2	8	*S*		8	6	
20	nil	1	*S*		4		
21	2	12	-		0		
22	1	61	*S*		23	25	
23	2	38	*S*		45	46	
24	nil	10	-				
25	nil	14	*S*			6	
26	1	11	*S*			10	
27	nil	72	*S*		30	#	
28	7	73	*S*		34	#	
29	nil	40	*S*		8	#	
30	nil	7	*S*	27			25
31	1	18	*S*	75			72

*values taken from reference 10.
#could not be determined by this method.

purity of sulfoxidation is dependent on the nature of the alkyl group for both the phenyl and benzyl alkyl substrates. In the phenyl series, the (*S*) enantiomer, presented in Figure 1, predominates in the case of saturated, small and unbranched alkyl substituents (**1a–3a**, **5a** and **7a**), but when the alkyl group is branched (e.g. **4a** and **6a**) or large (e.g. **8a**), then the opposite absolute configuration of product becomes predominant. The yield of sulfoxidation is also influenced by the nature of the alkyl group, becoming small in the case of *t*-butyl phenyl sulfoxide (**6a**), and the effect of unsaturation is evident from the sulfoxide **9a** obtained from ethenyl phenyl sulfide, which possesses predominantly the (*R*) absolute stereochemistry, but in moderate enantiomeric excess. A complete analysis of the effects which control the absolute stereochemistry of sulfoxidation of phenyl alkyl sulfides by *Helminthosporium* is not possible at the present time, but it is clear that, for efficient formation of (*S*) sulfoxides from phenyl alkyl sulfides, the alkyl group should be small and unbranched adjacent to sulfur. The (*S*)-stereoselectivity of this reaction is preserved in the case of naphthyl sulfides (**30** and **31**), and also for cyclohexyl methyl sulfide (**29**), but again the enantiomeric purities of the corresponding sulfoxides are disparate.

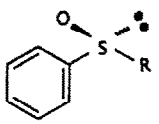

Figure 1. Predominant configuration of phenyl alkyl sulfoxides 1–3, 5, and 7.

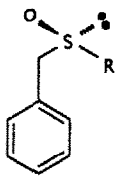

Figure 2. Predominant configuration of benzyl sulfoxides 10–12, 14, 16–23, 25 and 26.

In the case of the benzyl alkyl substrates **10** to **26**, however, the situation is amenable to closer analysis. For the *n*-alkyl benzyl sulfides it is clear that yield is approximately inversely dependent on chain length, being maximal for **10** and minimal for **20**. This phenomenon may be related to the aqueous solubility of the substrates concerned, or to a connected factor such as their ability to

form micelles under the conditions of the biotransformation. In any event, it is also clear that, having passed through a minimum at the C_4 chain length (**13**), enantiomeric purity rises consistently until, with benzyl *n*-heptyl sulfide, sulfoxide formation is enantioselective. Lower enantiomeric purities thereafter may reflect a contribution from non-stereoselective autooxidation at the low conversion levels concerned. In all cases, the predominant absolute stereochemistry is (*S*), presented in Figure 2. This state of affairs complements biotransformation of benzyl alkyl sulfides by *Mortierella isabellina*, in which the (*R*) sulfoxide is often formed,[10] and is perturbed during *Helminthosporium* biotransformation only when the alkyl group is branched directly adjacent to sulfur. In this latter eventuality, product is either racemic (as with **13a** and **21a**), or is formed with opposite configuration (as with **15a**, in which a reversal of priority assignment in the Cahn–Ingold–Prelog system unfortunately results in the same stereochemical descriptor).

These data confirm, as with those for biotransformation of phenyl alkyl sulfides, a susceptibility of the process to branching in the alkyl chain adjacent to sulfur. It is apparent, however, from the bioconversions of substrates **22** and **23**, which give rise to (*S*) sulfoxide with typical yields and enantiomeric purities, that this sensitivity to alkyl branching is not present if the branch is located remote from the site of oxidation. It is also clear from the yields and (*S*) stereochemistry of sulfoxides produced from **27** and **28** that the stereoselective formation of (*S*) sulfoxides is not restricted to phenyl and benzyl alkyl substrates, but can also be applicable to other substrates containing the aromatic ring.

The effect of a systematic variation in the nature and position of substitution in the aromatic ring of both phenyl and benzyl alkyl substrates remains to be examined, and will be the subject of a future study. At the present time, however, it can be concluded that the sulfoxidation reaction performed by *Helminthosporium* species NRRL 4671 gives predominantly (*S*) sulfoxide with a wide range of substrates; that this stereochemistry is perturbed by the presence of branched alkyl substituents, but only when the branch is located adjacent to sulfur; and that maximal stereoselectivities are obtained with phenyl ethyl sulfide and benzyl *n*-heptyl sulfide as substrates.

All of our experiments have been conducted with intact cells, and the results represent the combined metabolic action of all cellular enzymes to which the substrates are acceptable. Although this situation is not ideal from a mechanistic standpoint, it does permit the preparative scale formation of chiral sulfoxides in a cheap and convenient manner. Oxidase enzymes of the type responsible for the bioconversions reported herein are typically insoluble, membrane bound, multi-protein complex monooxygenases, which are not amenable to simple isolation. Some other isolated enzymes, notably chloroperoxidase,[15,16] cyclohexanone monooxygenase,[17] and horseradish peroxidase,[18] have been used for the production of chiral sulfoxides on a millimolar scale, complementing the present study, but at this time the prognosis for the preparative scale application of isolated fungal monooxygenases is poor and these enzymes will undoubtedly continue to be applied in whole cell bioconversions. The factors which control both the yield and stereoselectivity of prochiral sulfide oxidation by *Helminthosporium* will be further explored in future publications.

Experimental

Apparatus, materials and methods

Melting points were determined on a Kofler heating stage. Infrared spectra were recorded with an Analect 6260FX spectrometer. The NMR spectra were recorded at 200 MHz (routine ^1H) or 50 MHz (^{13}C) with a Bruker AC200 spectrometer using $CDCl_3$ as solvent and $CHCl_3$ as internal standard. Enantiomeric ratios were examined by ^1H NMR analysis at 500 MHz in the presence of (*S*)-(+)-α-methoxyphenylacetic acid (MPAA) or (*R*)-(–)-*N*-(3,5-dinitrobenzoyl)-α-methylbenzylamine (Kagan reagent),[13] or at 200 MHz using tris-[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III). Optical rotations were obtained in the stated solvent at ambient temperature with a Rudolph Autopol III polarimeter. Mass spectra were obtained with a Kratos 1S instrument operating in EI mode. Thin layer chromatography was performed on Merck silica gel 60F-254 and flash column chromatography used silica gel, 230–400 mesh.

Maintenance of microorganisms

Helminthosporium species NRRL 4671 was obtained from the U.S. Department of Agriculture, Northern Regional Research Laboratories, Peoria, IL, and was maintained on 4 % malt agar slopes, grown at 27 °C and stored at 4 °C.

Preparation of substrates

Substrates **1**, **2**, **9**, **10** and **24** were commercial samples. The remaining substrates were prepared as described below. All substrates gave satisfactory spectral data (^1H NMR, ^{13}C NMR, MS and IR).

Phenyl alkyl sulfides. Compounds **3**, **4**, **5**, and **7** were prepared by reaction of thiophenol (1 eq.), sodium ethoxide (1 eq.) and the corresponding alkyl halide (1 eq.) in ethanol in the standard manner, and gave the reported physical data.[19] *t*-Butyl phenyl sulfide (**6**) was prepared by addition of thiophenol to isobutene as described,[20] and phenyl *n*-hexyl sulfide (**8**) was prepared by alkylation of thiophenol and analyzed as reported.[21]

Benzyl alkyl sulfides. Compounds **11–15** have been described previously.[10] Substrates **16**,[22] **17**,[23] **18**, **19**,[23] **20**,[23] **21**,[22] **22**,[22] **23**,[22] **25**[24] and **26** were prepared by reaction of benzyl mercaptan (1 eq.), sodium ethoxide (1

eq.), and the corresponding alkyl halide (1 eq.) in ethanol in the standard manner. Hitherto unreported data are: benzyl *n*-heptyl sulfide (**18**); oil; ^{1}H NMR δ 0.85 (3H, t, CH_3), 1.1–1.65 (10H, m, CH_2's), 2.35 (2H, t, S-CH_2), 3.63 (2H, s, Ph-CH_2-S), and 7.15–7.30 (5H, m, aromatic H's) ppm; MS m/z (%) 222(18), 131(30), 91(100). Benzyl 3-phenylpropyl sulfide (**26**); oil, H NMR δ 1.75–2.05 (2H, m, CH_2), 2.45 (2H, t, CH_2), 2.70 (2H, t, CH_2), 3.68 (2H, s, Ph-CH_2-S) and 7.10–7.35 (5H, m, aromatic H's) ppm.

Methyl 2-phenylethyl sulfide (27)[25] and *methyl 3-phenylpropyl sulfide (28).* These were prepared by addition of 1-chloro-2-phenylethane and 1-chloro-3-phenylpropane, respectively (0.9 eq.) to a solution of sodium thiomethoxide (1 eq.) in ethanol at room temperature, followed by refluxing of the mixture for 4h and the usual work up. Methyl 3-phenylpropyl sulfide (**28**) (oil) had ^{1}H NMR δ 1.90 (2H, m, CH_2), 2.05 (3H, s, S-CH_3), 2.50 (2H, t, CH_2), 2.70 (2H, t, CH_2), and 7.20 (5H, s, aromatic H's) ppm.

Cyclohexyl methyl sulfide (29). This compound was prepared by reaction of cyclohexanethiol (1 eq.) and sodium ethoxide (1 eq.) with methyl iodide (1.1 eq.) and possessed the reported physical data.[26]

Methyl 1- and 2-naphthyl sulfides (30) and (31). These were prepared by alkylation of the corresponding naphthalenethiol with methyl iodide as described above for the preparation of phenyl alkyl sulfides, and gave the expected physical and spectral data. 1-Naphthalenethiol was prepared from 1-naphthol by the method of Newman and Karnes,[27] and 2-naphthalenethiol was a commercial sample.

Biotransformations with Helminthosporium *species*

These are summarized in the accompanying table. Two slopes of *Helminthosporium* species NRRL 4671 were used to inoculate 15 1 L Erlenmeyer flasks each containing 200 mL of an autoclaved medium composed of V-8 vegetable juice (200 mL) and calcium carbonate (3 g) per L of distilled water, adjusted to pH 7.2 prior to sterilization by the addition of 1 M sodium hydroxide. The flasks were allowed to stand overnight at 27 °C, then placed on a rotary shaker at 180 rpm, and growth continued for a further 72 h at 27 °C. The fungus was then harvested by vacuum filtration (Buchner funnel), and resuspended in 15 1 L Erlenmeyer flasks each containing 200 mL of distilled water. Substrate (1 g in 30 mL of 95 % ethanol) was then distributed among the flasks, which were replaced on the rotary shaker at 180 rpm, 27 °C for a further 48 h. The fungus and aqueous medium were then separated by filtration as before, the aqueous medium extracted with dichloromethane (continuous extraction, 72 h), and the fungus discarded. Concentration of the medium extract gave the crude product, which was treated as described below.

Isolation and characterization of products: The crude biotransformation extracts obtained as described above were examined by TLC, using ether or 10 % methanol/ether as solvent, and then submitted to flash chromatography using a benzene–ether 10 % stepwise gradient, followed by an ether–methanol 5 % stepwise gradient. The yields and *e.e.* values quoted in the table refer to isolated, purified, homogeneous material, and arise from the combination of (only) homogeneous column fractions without further purification (e.g. crystallization) that could lead to changes in stereochemical enrichment values. The balance of the material could be accounted for by unchanged substrate associated with the fungal mycelia. Products were identified by a combination of NMR, mass, and infrared spectral analysis. Spectral and optical rotation data for the sulfoxides obtained in this study are listed below. Sulfone products (where formed) were identified by MS and ^{1}H NMR data.

Methyl phenyl sulfoxide (1a). Oil; ^{1}H NMR δ 2.75 (3H, s), 7.25–7.75 (5H, m); ^{13}C NMR δ 43.9, 123.5, 129.4, 131.0, 145.7; MS m/z (%) 140(100), 125(95), 97(50), 77(52), 51(44); $[\alpha]_D$ –84.4 ° (c = 1.9, $CHCl_3$), (*S*) configuration, *e.e.* 48 % based on $[\alpha]_D$ +178 ° ($CHCl_3$) for the (*R*) enantiomer.[28]

Ethyl phenyl sulfoxide (2a). Oil; ^{1}H NMR δ 1.05–1.30 (3H, m), 2.5–3.0 (2H, m), 7.2–7.6 (5H, m); ^{13}C NMR δ 5.9, 50.3, 124.2, 129.1, 130.9, 144.0; MS m/z (%) 154(28), 138(10), 126(60), 78(100); $[\alpha]_D$ –153 ° (c = 0.425, $CHCl_3$), (*S*) configuration, *e.e.* 84% based on $[\alpha]_D$ +186 ° ($CHCl_3$) for the (*R*) enantiomer.[29]

n-*Propyl phenyl sulfoxide (3a).* Oil; ^{1}H NMR δ 1.04 (3H, d of t), 1.55–1.9 (2H, m), 2.6–2.85 (2H, m), 7.4–7.65 (5H, m); ^{13}C NMR δ 13.2, 15.9, 59.2, 124.0, 129.2, 130.7, 144.2; MS m/z (%) 168(30), 152(20), 126(100), 110(20), 78(27); $[\alpha]_D$ –62.4 ° (c = 1.225, $CHCl_3$), (*S*) configuration, *e.e.* 33 % based on $[\alpha]_D$ +192 ° ($CHCl_3$) for the (*R*) enantiomer.[30]

i-*Propyl phenyl sulfoxide (4a).* Oil; ^{1}H NMR δ 1.0–1.3 (6H, dd), 2.7–2.95 (1H, m), 7.2–7.65 (5H, m); ^{13}C NMR δ 13.8, 15.8, 54.4, 124.9, 128.7, 130.8, 143.0; MS m/z (%) 168(5), 152(5), 126(100), 110(18), 97(10), 78(80); $[\alpha]_D$ + 55.3 ° (c = 1.8, $CHCl_3$), (*R*) configuration, *e.e.* 32 % based on $[\alpha]_D$ +174.6 ° ($CHCl_3$) for the (*R*) enantiomer.[30]

n-*Butyl phenyl sulfoxide (5a).* Oil; ^{1}H NMR δ 0.85(3H, t), 1.25–1.8 (4H, m), 2.73 (2H, t), 7.40–7.65 (5H, m); ^{13}C NMR δ 13.6, 21.9, 24.1, 57.1, 124.0, 129.2, 130.9, 144.0; MS m/z (%) 182(18), 166(10), 126(100), 110(18), 78(54); $[\alpha]_D$ –31.8 ° (c = 1.84, $CHCl_3$), –30.4 ° (c = 1.68, acetone), (*S*) configuration, *e.e.* 16% based on $[\alpha]_D$ +193 ° (acetone) for the (*R*) enantiomer.[31]

t-*Butyl phenyl sulfoxide (6a).* Oil; ^{1}H NMR δ 1.17 (9H, s), 7.4–7.6 (5H, m); MS m/z (%) 182(2.2), 166(1.2), 126(100), 110(15), 97(12), 78(40); $[\alpha]_D$ +26.7 ° (c = 0.1, $CHCl_3$), (*R*) configuration, *e.e.* 15 % based on $[\alpha]_D$ +177 ° ($CHCl_3$) for the (*R*) enantiomer.[28]

n-*Pentyl phenyl sulfoxide (7a).* Oil; ^{1}H NMR δ 0.9 (3H, t), 1.3–2.0 (6H, m), 2.76 (2H, t), 7.5–7.8 (5H, m); ^{13}C

NMR δ 13.8, 21.1, 21.8, 57.0, 124.0, 128.9, 130.3, 144.1; MS m/z (%) 196(4), 179(23), 164(2), 126(100), 110(8), 78(40); $[\alpha]_D$ −13.6 ° (c = 0.425, $CHCl_3$).

n-*Hexyl phenyl sulfoxide (8a)*. Oil; ^1H NMR δ 0.85 (3H, t), 1.2–1.85 (8H, m), 2.78 (2H, t), 7.4–7.7 (5H, m); ^{13}C NMR δ 13.9, 22.1, 22.3, 29.5, 31.3, 57.4, 124.0, 129.1, 130.0, 144.0; MS m/z (%) 210(2), 193(30), 126(100), 110(22), 78(28); $[\alpha]_D$ +37.6 ° (c = 0.25, $CHCl_3$).

Ethenyl phenyl sulfoxide (9a). Oil; ^1H NMR δ 5.80 (1H, d), 6.10 (1H, d), 6.53 (1H, q), 7.35–7.65 (5H, m); ^{13}C NMR δ 120.5, 124.1, 129.5, 130.8, 142.5, 142.8; MS m/z (%) 152(20), 136(25), 135(32), 125(18), 109(38), 104(100); $[\alpha]_D$ + 211 ° (c = 0.66, acetone), (*R*) configuration, *e.e.* 45 % based on $[\alpha]_D$ + 474 ° (acetone) for the (*R*) enantiomer.[32]

Benzyl n-*pentyl sulfoxide (16a)*. Mp 55–57 °C; ^1H NMR δ 0.9 (3H, t), 1.25–1.5 (4H, m), 1.75–1.85 (2H, m), 2.5–2.65 (2H, m), 4.01 and 3.91 (2H, ABq), 7.25–7.4 (5H, m); ^{13}C NMR δ 13.8, 22.2(2C), 30.9, 50.8, 58.2, 128.4, 129.0, 130.0; MS m/z (%) 210(1), 194(0.5), 121(0.2), 91(100); $[\alpha]_D$ −100.0 ° (c = 0.985, $CHCl_3$).

Benzyl n-*hexyl sulfoxide (17a)*. Mp 60–62 °C (lit.[23] mp 62–63 °C); ^1H NMR δ 0.88 (3H, t), 1.25–1.55 (6H, m), 1.75–1.85 (2H, m), 2.45–2.6 (2H, m), 3.93 and 4.02 (2H, ABq), 7.25–7.4 (5H, m); ^{13}C NMR δ 13.9, 22.4(2C), 28.5, 31.3, 50.9, 58.2, 128.4, 129.0, 130.0; MS m/z (%) 224(1.1), 181(1), 117(1), 91(100); $[\alpha]_D$ −88.0 ° (c = 0.225, $CHCl_3$).

Benzyl n-*heptyl sulfoxide (18a)*. Oil; ^1H NMR δ 1.88 (3H, t), 1.2–1.5 (8H, m), 1.65–1.9 (2H, m), 2.5–2.7 (2H, m), 3.90 and 4.0 (2H, ABq), 7.25–7.5 (5H, m); MS m/z (%) 238(1), 222(0.5), 181(2), 91(100); $[\alpha]_D$ −99.7 ° (c = 0.95, $CHCl_3$), $[\alpha]_D$ −41.6 ° (c = 0.82, ethanol).

Benzyl n-*octyl sulfoxide (19a)*. Mp 56–58 °C; ^1H NMR δ 1.88 (3H, t), 1.2–1.5 (10H, m), 1.65–1.8 (2H, m), 2.5–2.7 (2H, m), 3.90 and 4.05 (2H, ABq), 7.25–7.5 (5H, m); MS m/z (%) 252(1), 236 (0.7), 181(1), 163(1.5), 145(2), 91(100); $[\alpha]_D$ −18.9 ° (c = 0.37, $CHCl_3$), $[\alpha]_D$ −17.9 ° (c = 0.27, ethanol).

Benzyl n-*nonyl sulfoxide (20a)*. Oil; ^1H NMR δ 1.88 (3H, t), 1.2–1.5 (12H, m), 1.65–1.8 (2H, m), 2.5–2.7 (2H, m), 3.92 and 4.05 (2H, ABq), 7.25–7.5 (5H, m); MS m/z (%) 266(1), 250(2), 179(3), 159(8), 91(100); $[\alpha]_D$ −13.2 ° (c = 0.44, ethanol).

Benzyl cyclohexyl sulfoxide (21a). Mp 74–76 °C; ^1H NMR δ 1.25–2.75 (11H, m), 3.93 and 3.98 (2H, ABq), 7.3–7.5 (5H, m); ^{13}C NMR δ 24.2, 25.4(2C), 26.9(2C), 54.4, 57.1, 128.3, 128.9, 130.0; MS m/z (%) 222(3), 206(2), 140(12), 91(100); $[\alpha]_D$ −1.7 ° ± 1.5 ° (c = 0.38, $CHCl_3$).

Benzyl 2-methylpropyl sulfoxide (22a). Mp 53–56 °C; ^1H NMR δ 1.0–1.1 (6H, dd), 2.20 (1H, m), 2.3 and 2.6 (2H, ABX), 3.93 and 4.05 (2H, ABq), 7.25–7.4 (5H, m); ^{13}C NMR δ 21.6, 22.9, 23.8, 58.9, 60.5, 128.3, 128.8, 130.0; MS m/z (%) 196(2.5), 180(0.5), 139(0.5), 121(0.5), 91(100); $[\alpha]_D$ −47.6 ° (c = 0.525, $CHCl_3$).

Benzyl 3-methylbutyl sulfoxide (23a). Mp 43–45 °C; ^1H NMR δ 0.9–1.0 (6H, dd), 1.5–1.7 (4H, m), 2.6–2.7 (1H, m), 3.95 and 4.03 (2H, ABq), 7.25–7.4 (5H, m); ^{13}C NMR δ 22.2, 22.4, 27.7, 30.7, 48.7, 58.0, 128.3, 129.0, 130.0; MS m/z (%) 210(1), 194(0.2), 181(0.2), 91(100); $[\alpha]_D$ −26.4 ° (c = 1.06, $CHCl_3$).

Dibenzyl sulfoxide (24a). Mp 132–134 °C, identified by comparison with an authentic sample of commercial material.

Benzyl 2-phenylethyl sulfoxide (25a). Mp 109–111 °C; ^1H NMR δ 2.85 (2H, t), 2.98–3.15 (2H, m), 3.93 and 4.05 (2H, ABq), 7.15–7.4 (10H, m); ^{13}C NMR δ 28.6, 52.2, 58.2, 126.8–130.0 (complex); MS m/z (%) 244(2), 228(7), 166(8), 137(7), 105(20), 91(100); $[\alpha]_D$ −15.9 ° (c = 0.64, $CHCl_3$).

Benzyl 3-phenylpropyl sulfoxide (26a). Mp 70–72 °C; ^1H NMR δ 2.0–2.15 (2H, m), 2.6 (2H, t), 2.7–2.85 (2H, m), 3.90 and 3.99 (2H, ABq), 7.1–7.4 (5H, m); ^{13}C NMR δ 24.0, 34.6, 49.9, 58.1, 126.3–130.0 (complex); MS m/z (%) 258(1), 242(1), 205(1), 180(2.5), 117(6), 105(4), 91(100); $[\alpha]_D$ −14.3 ° (c = 0.84, $CHCl_3$).

Methyl 2-phenylethyl sulfoxide (27a). Mp 42–44 °C; ^1H NMR δ 2.58 (3H, s), 2.9–3.18 (4H, m), 7.15–7.35 (5H, m); ^{13}C NMR δ 28.7, 38.6, 56.0, 126.6, 128.5, 128.8, 138.7; MS m/z (%) 152 (0.5), 135 (0.5), 105(100); $[\alpha]_D$ +59.0 ° (c = 1.03, $CHCl_3$).

Methyl 3-phenylpropyl sulfoxide (28a). Mp 42–44 °C; ^1H NMR δ 2.1–2.2 (2H, m), 2.55 (3H, s), 2.6–2.8 (4H, m), 7.1–7.3 (5H, m); ^{13}C NMR δ 24.1, 34.6, 38.5, 53.7, 126.3, 128.5, 128.6, 140.4; MS m/z (%) 182(5), 118(50), 103(5), 91(100); $[\alpha]_D$ +40.8 ° (c = 1.19, $CHCl_3$).

Cyclohexyl methyl sulfoxide (29a). Oil; ^1H NMR δ 1.2–1.95 (10H, m), 2.12 (1H, d), 2.49 (3H, s); ^{13}C NMR δ 24.8, 25.1, 25.9, 35.0, 60.7; MS m/z (%) 146(6), 130(2), 83(52), 55(100); $[\alpha]_D$ +5.7 ° (c = 1.225, $CHCl_3$).

Methyl 1-naphthyl sulfoxide (30a). Mp 55–57 °C; ^1H NMR δ 2.80 (3H, s), 7.5–8.25 (7H, m); ^{13}C NMR δ 42.9, 121.4–141.5 (complex); MS m/z (%) 190(55), 175(100), 159(12), 143(20), 127(24), 115(33); $[\alpha]_D$ −142.8 ° (c = 0.215, $CHCl_3$), $[\alpha]_D$ −124 ° (c = 0.16, ethanol), *e.e.* 27%, (*S*) configuration based on $[\alpha]_D$ −460 ° (ethanol) for the (*S*) enantiomer.[33]

Methyl 2-naphthyl sulfoxide (31a). Mp 82–84 °C; ^1H NMR δ 2.77 (3H, s), 7.4–8.25 (7H, m); ^{13}C NMR δ 43.7, 119.5, 124.1, 127.4, 127.8, 128.1, 128.5, 129.6, 133.0, 134.5, 142.7; $[\alpha]_D$ −106.3 ° (c = 0.3, $CHCl_3$), (*S*) configuration, *e.e.* 75% based on $[\alpha]_D$ +141 ° ($CHCl_3$) for the (*R*) enantiomer.[34]

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