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Biotransformation of β-ketosulfides to produce chiral β-hydroxysulfoxides

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Abstract The biotransformations of a series of substituted phenylthio-2-propanone and benzylthio-2-propanone were carried out using *Helminthosporium* sp. NRRL 4671, *Mortierella isabellina* ATCC 42613, or *Rhodococcus erythropolis* IGTS8. Several products gave microbial oxidation of sulfide to sulfoxide and reduction of carbonyl to secondary alcohol, producing β-hydroxysulfoxides in medium to high enantiomeric and diastereomeric purities. Fungal biotransformations using *Helminthosporium* sp. and *M. isabellina* resulted in the opposite sulfoxide configurations of various β-hydroxysulfoxide products.

Keywords Biocatalysis · Biotransformation · Carbonyl reduction · *Helminthosporium* sp. NRRL 4671 · *Mortierella isabellina* ATCC 42613 · *Rhodococcus erythropolis* IGTS8 · Sulfoxidation

Introduction

The ability of biocatalytic reactions to produce chiral products from non-chiral starting materials is a key reaction. Many common types of simple functional groups are subject to chiral conversions by biological catalysts including whole cells (fungi or bacteria), isolated enzymes, and plant cells. Of the reactions that can be simply produced in this way, perhaps the commonest are the conversion of carbonyl groups to secondary alcohols [26], Baeyer-Villiger oxidations [23], hydroxylations [13], the use of hydroxynitrile lyases [11], and the oxidation of sulfide to sulfoxide [14]. In comparison, the generation of more that one chiral centre from a non-chiral starting material is not common. Such reactions are known for the reduction of diketones to chiral diols [7], the use of dioxygenase enzymes to oxide aromatic rings to produce dihydrodiols [1], and by the conversion of ketones into chiral diols using a combination of carbonyl reduction and alkane hydroxylation reactions by the same microorganism [27].

These reactions can be carried out by two different enzymes, but analogous examples can also occur from the use of simple multiple reactions by single enzymes [2], and the dioxygenase from *Pseudomonas putida* has been reported to convert aryl sulfides to dihydrodiol sulfoxides [3, 4]. Biotransformation methods from chiral sulfoxide alcohols are typically involved with only one of two separate biotransformation reactions. Such products include, for example, the reduction of racemic β-keto sulfoxides by *Saccaromyces cervisiae* to give β-hydroxy sulfoxides, which can then be separated chemically into stereochemically defined products [6], and the separtion of racemic β-hydroxy sulfides by treating with *Humicola lanuginose*, to produce chiral β-hydroxy sulfides, followed by oxidation of the sulfide to give a chiral sulfoxide by chemical oxidation [29].

Research has been undertaken to focus on using single biocatalysts, either *Helminthosporium* sp. NRRL 4671 [15], *Mortiella isabellina* ATCC 42613 [16, 17], or *Rhodococcus erythropolis* IGTS8 [20], to examine the bioconversion of substrates that contain both sulfide and carbonyl functional groups. Our preliminary research of the use of *Helminthosporium* for the production of diastereomers from two β-hydroxysulfoxides from ketosulfides has been reported [18]. Here, a concomitant oxidation of sulfide to sulfoxide and reduction of carbonyl to a secondary alcohol, using a series of varied biocatalysts that can generate single products containing two new chiral centres, is discussed.

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Materials and methods

Melting points were determined on a Kofler hot stage (Reichert, Austria) and are uncorrected. The ^{1}H NMR spectra were recorded on a Bruker Avance series 300 spectrometer (Bruker, Milton,

Ontario) in $CDCl_3$ using residual $CHCl_3$ as the internal standard unless otherwise stated; chemical shifts are reported in ppm (δ) and the signals quoted as s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet). The ^{13}C NMR spectra were recorded at 75 mHz on the same spectrometer in $CDCl_3$ solution. Diastereomeric excess (D.e.) was determined by ^1H NMR analysis of C*H*(OH)CH_3 or CH(OH)C*H*$_3$ signals, or ^{13}C NMR analysis of signals α and β to sulfoxide or R*C*H(OH)R′. Chiral shift reagents were commercial samples of (*S*)-(+)-α-methoxyphenyl acetic acid (MPAA) and (*R*)-(−)-N-(3,5-dinitrobenzoyl)-α-methylbenzylamine (Kagan reagent). Mass spectra (MS) were obtained using a Kratos 1S spectrometer (Kratos, Chestnut Ridge, New York) operating under EI or FAB conditions, and MSis indicated, where possible, using absolute configuration data. Optical rotations were recorded at ambient temperature in $CHCl_3$ using a Rudolph Autopol 3 polarimeter (Rudolph Research Analytical, Flanders, New Jersey). Thin-layer chromatography (TLC) was carried out on Merck silica gel F_{254} plates (EM Science, Gibbstown, New Jersey), 0.2 mm, and column chromatography used Merck silica gel 9385, 230–400 mesh. *Helminthosporium* sp. NRRL 4671 and *Mortierella isabellina* ATCC 42613 were maintained on 4% malt agar slopes, grown at 27 °C and stored at 4 °C; *Rhodococcus erythropolis* IGTS8 BK053 was grown at 30 °C, collected by centrifugation and stored at −20 °C.

Preparation of substrates

Substrates **1–2** were all prepared by routine reaction of thiols (**1**–**6**) or benzyl thiols (**7**–**12**) with the appropriate α-chloroketones. A typical procedure, using the preparation of α-(*p*-bromophenylthio)acetophenone (**6**) as an example, is: 4-bromobenzenethiol (4.72 g, 0.025 mol) was dissolved in sodium hydroxide solution (52 ml, 0.85 M), and the solution was then treated by addition of α-chloroacetophenone (3.9 g, 0.0253 mol). The mixture was heated under reflux for 1 h, then cooled and extracted with ether (3×50 ml). The extract was washed (H_2O, sat. NaCl), then dried and evaporated to give α-(*p*.-bromophenylthio)acetophenone (6, 5.53 g, 72%). Solid products were crystallised (typically hexane) and liquid products dried under vacuum.

Physical information and spectral data of products **1**–**12** (^1H NMR, ^{13}C NMR, and MS) are listed below:

- 1-(phenylthio)-2-propanone (**1**): oil; ^1H NMR δ 2.28 (3H, s), 3.68 (2H, s), and 7.30 (5H, m) ppm; ^{13}C NMR δ 28.4, 45.1, 127.3, 129.6, 129.9, 135.1, and 203.9 ppm; MS NBA (M/z, %) 167(90), 166(M^+,100); M^+ 166.04570, ppm 2.81, $C_9H_{10}O_1S_1$.
- 1-(*p*.-methoxyphenylthio)-2-propanone (**2**): oil; ^1H NMR δ 3.79 (3H, s), 4.15 (2H, s), 6.83 (2H, d of ABq), 7.37 (2H, d of ABq), 7.48 (2H, m), 7.57 (1H, m) and 7.93 (2H, d of ABq) ppm; ^{13}C NMR δ 43.2, 55.7, 115.1, 125.0, 129.0, 129.1, 133.7, 135.0, 135.9, 160.1, and 194.7 ppm; MS NBA (M/z, %) 197(50), 196(M^+,100); M^+ 196.05564, ppm 0.81, $C_{10}H_{12}O_2S_1$.
- 1-(*p*.-bromophenylthio)-2-propanone (**3**): m.p. 63–65 °C ([22] m.p. 64–65 °C); ^1H NMR δ 2.30 (3H, s), 3.64 (2H, s), and 7.17/7.48 (4H, ABq) ppm; ^{13}C NMR δ 28.4, 44.9, 121.3, 129.8, 131.4, 134.3, and 203.4 ppm; MS NBA (M/z, %) 246/244(M^+,100/98).
- α-(phenylthio)acetophenone (**4**): m.p. 53–54 °C ([19] m.p. 53–54 °C); ^1H NMR δ 4.28 (2H, s), 7.23 (3H, m), 7.43 (4H, m), 7.60 (1H, m), and 7.92 (2H, d of ABq) ppm; ^{13}C NMR δ 41.6, 127.5, 129.1, 129.5, 130.9, 133.9, 135.3, 135.8, and 194.5 ppm; MS NBA (M/z, %) 457(2), 229(100), 228(M^+,70).
- α-(*p*.-methoxyphenylthio)acetophenone (**5**): oil; ^1H NMR δ 3.79 (3H, s), 4.15 (2H, s), 6.83 (2H, d of ABq), 7.36 (2H, d of ABq), 7.47 (2H, m), 7.57 (1H, m), and 7.93 (2H, d of ABq) ppm; ^{13}C NMR δ 43.2, 55.7, 115.1, 124.9, 129.0, 129.1, 133.7, 135.0, 135.8, 160.1, and 194.7 ppm; MS NBA (M/z, %) 517(2), 259(80), 258(M^+, 100); M^+ 258.07048, ppm 3.78, $C_{15}H_{14}O_2S_1$.
- α-(*p*.-bromophenylthio)acetophenone (**6**): m.p. 80–82 °C ([24] m.p. 82–83 °C); ^1H NMR δ 4.20 (2H, s), 7.21 (2H, d of ABq), 7.40 (2H, d of ABq), 7.50 (2H, m), 7.58 (1H, m) and 7.95 (2H, d of ABq) ppm; ^{13}C NMR δ 41.4, 121.6, 129.0, 129.1, 132.4, 132.5, 134.0, 134.3, 135.6, and 194.1 ppm; MS NBA (M/z, %) 615(4), 306/309(M^+ + 1, 68/55), 105(100).
- 1-(benzylthio)-2-propanone (**7**): oil; ^1H NMR δ 2.20 (3H, s), 3.11 (2H, s), 3.69 (2H, s), and 7.26 (5H, m) ppm; ^{13}C NMR δ 28.4, 36.4, 41.2, 127.7, 129.0, 129.6, 137.6, and 204.1 ppm; MS NBA (M/z, %) 181(36), 180(M^+, 24), 91(100); M^+ 180.06083, ppm 0.34, $C_{10}H_{12}O_1S_1$.
- 1-(*p*.-methoxybenzylthio)-2-propanone (**8**): oil; ^1H NMR δ 2.25 (3H, s), 3.12 (2H, s), 3.65 (2H, s), 3.80 (3H, s), and 6.82/7.20 (4H, ABq) ppm; ^{13}C NMR δ 28.4, 35.8, 41.0, 55.7, 114.3, 129.5, 130.7, 159.2, and 204.2 ppm; MS EI (M/z, %) 210(M^+, 18), 152(16), 121(100); M^+ 210.07112, ppm −1.57, $C_{11}H_{14}O_2S_1$.
- 1-(*p*.-bromobenzylthio)-2-propanone (**9**): oil; ^1H NMR δ 2.28 (3H, s), 3.10 (2H, s), 3.63 (2H, s), and 7.20/7.58 (4H, ABq); ^{13}C NMR δ 28.4, 35.6, 40.8, 121.6, 131.3, 132.0, 136.6 and 203.8 ppm; MS NBA (M/z, %) 258/261(M^+ + 1, 18/33), 171(98), 169(100); M^+ 257.97008, ppm 5.10, $C_{10}H_{11}O_1S_1Br_1$.
- α-(benzylthio)acetophenone (**10**): m.p. 86–88 °C ([10]) m.p. 87–89 °C); ^1H NMR δ 3.70 (2H, s), 3.80 (2H, s), 7.18–7.60 (8H, m), and 7.91 (2H, d of ABq) ppm; ^{13}C NMR δ 35.5, 35.7, 126.8, 128.1, 128.5, 128.9, 133.6, 136.9, and 194.0 ppm; MS NBA (M/z, %) 243(M^+ + 1,84), 91(100).
- α-(*p*.-methoxybenzylthio)acetophenone (**11**): m.p. 41–43 °C ([21] m.p. 40–41 °C); ^1H NMR δ 3.68 (2H, s), 3.74 (2H, s), 3.81 (3H, s), 6.86 (2H, d of ABq), 7.30 (2H, d of ABq), 7.47 (2H, m), 7.56 (1H, m) and 7.95 (2H, d of ABq) ppm; ^{13}C NMR δ 35.9, 36.1, 55.7, 114.3, 129.0, 129.1, 129.6, 130.8, 133.7, 135.8, 159.2 and 194.9 ppm; MS NBA (M/z, %) 273(8), 272(10, M^+), 121(100).
- α-(*p*.-bromobenzylthio)acetophenone (**12**): m.p. 80–81 °C; ^1H NMR δ 3.52 (2H, s), 3.61 (2H, s), 7.10–7.50 (7H, m), and 7.80 (2H, ABq) ppm; ^{13}C NMR δ 35.7, 36.0, 128.6, 129.0, 129.1, 131.4, 132.4, 133.7, 135.7, 136.7, and 194.7 ppm; MS NBA (M/z, %) 323/321(48/54, M^+ + 1), 171/169(68/66), 105(100); M^+ 319.98680, ppm 0.77, $C_{15}H_{13}O_1S_1Br_1$.

Biotransformation procedures

Helminthosporium sp. NRRL 4671

Two slopes of *Helminthosporium* were used to inoculate 15 1-l Erlenmeyer flasks each containing 200 ml of an autoclaved medium composed of V-8 vegetable (200 ml) juice and calcium carbonate (3 g) per l of tap water, adjusted to pH 7.2 by the addition of 1 M sodium hydroxide, then subject to sterilization. After sterilization, 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 fungal mycelia were then harvested by filtration 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 fungal mycelia and aqueous medium were separated by filtration as before, the aqueous medium was extracted with dichloromethane (continuous extraction, 72 h) and the fungus autoclaved prior to being discarded. Concentration of the medium extract gave the crude product, which was examined by TLC using ether or 5% methanol/ether as solvent, and then submitted to flash chromatography using a hexane/ethyl acetate or benzene/ether 10% stepwise gradient, followed by a ethyl acetate/methanol or ether/methanol in 5% stepwise gradient if necessary. The yields and e.e. values quoted in Table 1 refer to purified, homogenous materials and, unless otherwise stated, arise from the combination of (only) homogeneous column fractions without further purification (e.g. crystallization), which could lead to changes in stereochemical enrichment values [9]. Data from d.e. values were initially quoted in Table 1 from isolation without purification by separation and/or purification. Where appropriate, subsequent improvement in d.e. samples was obtained.

Mortierella isabellina ATCC 42613

Two slopes of *M. isabellina* were used to inoculate 15 1-l Erlenmeyer flasks each containing 200 ml of an autoclaved medium composed of glucose (40 g), yeast extract (5 g), sodium chloride (5 g), dibasic potassium phosphate (5 g), and soya flour (5 g) per l of distilled water. Subsequent manipulations were exactly as described for *Helminthosporium* sp. NRRL 4671, except that the fungal mycelia were harvested by centrifugation rather than filtration.

Rhodococcus erythropolis IGTS8 BK053.

This microorganism was obtained as frozen cell paste from The Energy BioSystems [25]. Concentrated frozen paste was resuspended in dibasic potassium phosphate/basic dipotassium phosphate buffer (pH 7, 100 mM) supplemented with glucose (2% w/v final concentration) to form a whole-cell preparation of the biocatalyst at a wet weight concentration of 2 g cells per 100 ml of buffer. The substrate was added with 95% ethanol to the cells to give a final concentration of 4 mM sulfide in 1% (v/v) ethanol, and the reaction shaken in an orbital shaker at 180 rpm, 30 °C, for 12–15 h. The cells were then centrifuged (3,000 rpm, 15 min) and the supernatant transferred for continuous extraction by dichloromethane. The extract was evaporated, examined by TLC using ether or 5% methanol/ether as solvent, and then submitted to flash chromatography using a hexane/ethyl acetate or benzene/ether 10% stepwise gradient, followed by an ethyl acetate/methanol or ether/methanol in a 5% stepwise gradient if necessary.

Physical and spectral data for biotransformation products

Physical information of products **13**–**59** (m.p. and optical rotation data where appropriate) and spectral data (^{1}H NMR, ^{13}C NMR, and MS and HRMS) are listed below. Related samples of products with only different optical purities are listed below.

- (S_SS_C)-1-(Phenylsulfinyl)-2-propanol (**13**) (recryst): m.p. 55–57 °C; ^{1}H NMR ($CDCl_3$) δ 1.32 (3H, d), 2.74 and 3.0 (2H, ABX, m), 3.63 (1H, br.s, OH), 4.45 (1H, m), 7.52 (3H, m) and 7.70 (2H,d) ppm; ^{13}C NMR ($CDCl_3$) δ 23.7, 64.1, 64.5, 124.2, 129.9, 131.9, and 144.0 ppm; MS EI (M/z, %) 184(M^+,14), 168(62), 126(90), 124(100); $[\alpha]_D$ 260 (c = 1.0, $CHCl_3$); M^+ 184.05566, ppm 0.75, $C_9H_{12}O_2S_1$.
- (S_SS_C)-1-(*p*.-Methoxyphenylsulfinyl)-2-propanol (**14**) (recryst): m.p. 84–86 °C; ^{1}H NMR ($CDCl_3$) δ 1.32 (3H, d), 2.73 and 3.0 (2H, ABX, m), 3.73 (1H, br.s, OH), 3.82 (3H, s), 4.45 (1H, m), and 7.02/7.58 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 23.7, 56.0, 64.1, 65.4, 115.4, 126.5, 134.8, and 162.7 ppm; MS EI (M/z, %) 214(M^+,11), 198(30), 155(100); $[\alpha]_D$ 267 (c = 1.0, $CHCl_3$); M^+ 214.06657, ppm 0.95, $C_{10}H_{14}O_3S_1$.
- (S_SS_C)-1-(*p*.-Bromophenylsulfinyl)-2-propanol (**15**) (recryst): m.p. 62–64 °C; ^{1}H NMR ($CDCl_3$) δ 1.30 (3H, d), 2.73 and 3.0 (2H, ABX, m), 4.0 (1H, br.s, OH), 4.30 (1H, m), and 7.4/7.5 (4H, ABq); ^{13}C NMR ($CDCl_3$) δ 23.6, 64.7, 65.0, 125.9, 126.2, 133.0, and 142.9 ppm; MS EI (M/z, %) 262/264(M^+,8), 246/248(18), 204/206(100/82); $[\alpha]_D$ −188 (c = 1.08, $CHCl_3$); M^+ 261.96522, ppm 4.17, $C_9H_{11}O_2S_1Br_1$.
- (R_SS_C)-1-(Phenylsulfinyl)-2-propanol (**16**) (d.e. 46%): m.p. 90–115 °C; ^{1}H NMR ($CDCl_3$) δ 1.20/1.30 (total 3H, each d), 2.7–2.03 (2H, m), 4.3/4.48 (total 1H, m), and 7.58–7.65 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 23.6, 63.3/63.9, 63.5/65.6, 124.2, 129.9, 131.5, 131.9, and 142.7 ppm; MS EI (M/z, %) 184(M^+, 13), 168(60), 126(80), 124(100); $[\alpha]_D$;

Table 1 Biotransformation of substrates **1**–**12**

Substrate	Biocatalyst								
	Helminthosporium sp.			*Mortierella isabellina*			*Rhodococcus erythropolis*		
	Product	Yield	Selectivity	Product	Yield	Selectivity	Product	Yield	Selectivity
1	**13**	90%	d.e. 89%	**16**	23%	d.e. 46%	**16**	51%	d.e. 30%
				19	62%	e.e. > 95%	**19**	12%	e.e. > 95%
2	**14**	70%	d.e. 85%	**17**	69%	d.e. 52%	**17**	54%	d.e. 80%
				20	25%	e.e. > 95%	**20**	21%	e.e. > 90%
							22	2%	e.e. > 90%
							24	6%	e.e. > 95%
3	**15**	30%	d.e. 86%	**18**	64%	d.e. 50%	**18**	16%	d.e. 86%
	21	8%	e.e. > 95%	**23**	4%	e.e. > 95%	**21**	35%	e.e. > 90%
							25	1%	e.e. > 95%
4	**29**	11%	e.e. > 90%	**27**	70%	d.e. 24%	**32**	32%	e.e. > 95%
5	**26**	6%	d.e. < 5%	**30**	5%	e.e. 95%	**33**	10%	e.e. 48%
				28	48%	d.e. 40%	**28**	3%	d.e. 0%
6	No detectable products			**31**	35%	e.e. 95%	**34**	8%	e.e. 0%
7	**35**	66%	d.e. 92%	**38**	48%	d.e. 40%	**38**	32%	d.e. 82%
				41	10%	e.e. > 95%	**41**	38%	e.e. > 95%
				44	3%	e.e. > 90%	**47**	3%	e.e. 80%
8	**36**	72%	d.e. > 95%	**39**	42%	d.e. 85%	**39**	12%	d.e. 86%
				45	29%	e.e. > 90%	**42**	9%	e.e. > 95%
							48	27%	e.e. 92%
9	**37**	72%	d.e. > 90%	**40**	37%	d.e. 40%	**40**	5%	d.e. 85%
				46	24%	e.e. > 90%	**43**	5%	e.e. 60%
							49	20%	e.e. > 95%
10	**57**	4%	e.e. 0%	**51**	75%	d.e. 20%	**57**	7%	e.e. 80%
				54	18%	e.e. > 90%			
11	**50**	16%	d.e. 26%	**52**	69%	d.e. 54%	**58**	12%	e.e. > 90%
	55	4%	e.e. 95%						
	58	2%	e.e. 8%						
12	No detectable products			**53**	25%	d.e. 28%	**59**	1%	e.e. > 90%
				56	23%	e.e. > 90%			

+172.7 (c = 0.62, $CHCl_3$) ([29] for (R_SS_C) $[\alpha]_D$ +369 (CH_2Cl_2)).

- (R_SS_C)-1-(*p*.-Methoxyphenylsulfinyl)-2-propanol (**17**): oil; ^{1}H NMR ($CDCl_3$) δ 1.20 (3H, d), 2.10 (1H, br.S, OH), 2.65/3.0 (2H, ABX, m), 3.82 (3H, s), 4.30 (1H, m), and 6.62/7.40 (4H, ABX) ppm; ^{13}C NMR ($CDCl_3$) δ 23.6, 55.9, 62.8, 64.8, 115.3, 126.4, 133.7, and 162.6 ppm; MS (NMA) (M/z, %) 215 ($M^+ + 1$, 18), 155(30), 59(100); $[\alpha]_D$ +233.0 (c = 0.7, $CHCl_3$); M^+ 214.06436, ppm 9.37, $C_{10}H_{14}O_3S_1$.
- (R_SS_C)-1-(*p*.-Bromophenylsulfinyl)-2-propanol (**18**): m.p. 112–114 °C; ^{1}H NMR ($CDCl_3$) δ 1.30 (3H, s), 2.68/2.92 (2H, ABX, m), 4.32 (1H, m), and 7.5/7.7 (4H, ABX) ppm; ^{13}C NMR ($CDCl_3$) δ 23.7, 62.8, 64.7, 125.9, 126.2, 133.0, and 142.5 ppm; MS NBA (M/z, %) 265/263 ($M^+ + 1$, 24) 205/207(5), 50(100); $[\alpha]_D$ +238.6 (c = 0.7, $CHCl_3$); M^+ 261.96589, ppm 1.61, $C_9H_{11}O_2S_1Br_1$.
- (*S*)-1-(Phenylthio)-2-propanol (**19**): oil; ^{1}H NMR ($CDCl_3$) δ 1.30 (3H, d), 1.90 (1H, br. S, OH), 2.80/3.11 (2H, ABX), 3.83 (1H, m), and 7.23 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 22.3, 44.0, 65.9, 127.0, 129.4, and 130.5 ppm; MS EI (M/z, %) 168(M^+, 78), 124(100); $[\alpha]_D$ +56.6 (c = 1.22, $CHCl_3$) ([6] +54.7 (c = 1.0, $CHCl_3$).
- (*S*)-1-(*p*.-Methoxyphenylthio)-2-propanol (**20**): oil; ^{1}H NMR ($CDCl_3$) δ 1.21 (3H, d), 2.68/2.98 (2H, ABX), 3.72 (1H, m), 3.75 (3H, s), and 6.81/7.38 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 22.1, 46.1, 55.7, 65.6, 115.1, 125.4, 134.3, and 159.7 ppm; MS EI (M/z, %) 198(100), 153(43), 139(62); $[\alpha]_D$ +70.4 (c = 1.4, $CHCl_3$); M^+ 198,07251, ppm 5.33, $C_{10}H_{14}O_2S_1$.
- (*S*)-1-(*p*.-Bromophenylthio)-2-propanol (**21**): oil; ^{1}H NMR ($CDCl_3$) δ 1.32 (3H, d), 2.40 (1H, br.S, OH), 2.82/3.02 (2H, ABq), 3.82 (1H, m), and 7.18/7.38 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 22.4, 43.9, 66.0, 120.8, 131.8, 132.4, and 135.0 ppm; MS NBA (M/z, %) 246/248(M^+, 100), 232/230(72/70); $[\alpha]_D$ +30.7 (c = 1.05, $CHCl_3$); M^+ 245.96989, ppm 6.13, $C_9H_{11}O_1S_1Br_1$.
- (*S*)-1-(*p*.-Methoxyphenylsulfonyl)-2-propanol (**22**); oil; ^{1}H NMR ($CDCl_3$) δ 1.25 (3H, d), 3.2 (2H, m), 3.90 (3H, s), 4.31 (1H, m), and 7.05/7.88 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) 22.8, 56.1, 62.8, 63.9, 115,0, 130.5, and 164.4 ppm; MS EI (M/z, %) 230 (4, M^+), 198(8), 171(2), 155(22), 123(28) and 108(100); $[\alpha]_D$ +4.3 (c = 0.6, $CHCl_3$).
- (*S*)-1-(*p*.-Bromophenylsulfonyl)-2-propanol (**23**); m.p. 73–75 °C; ^{1}H NMR ($CDCl_3$) δ 1.25 (3H, d), 3.2 (2H, m), 4.28 (1H, m), and 7.7 (4H, ABq) ppm; ^{13}C

NMR ($CDCl_3$) 23.0, 62.8, 63.8, 129.9, 133.2, and 138.6 ppm; MS EI (M/z, %) 278/280 (M^+, 6), 260/262(28), 236/238(45), 202/207(80), 155/157(92/100); $[\alpha]_D$ +10.9 (c = 1.05, $CHCl_3$); M^+ 277.96315, ppm 6.90, $C_9H_{11}O_3S_1Br_1$.

- (*R*)-1-(*p*.-Methoxyphenylsulfinyl)-2-propanone (**24**); m.p. 72–73 °C; ^1H NMR ($CDCl_3$) δ 2.21 (3H, s), 3.84 (2H, ABq), 3.89 (3H, s), and 7.03/7.60 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 32.5, 55.9, 69.2, 115.4, 126.4, 133.9, 162.8, and 200.0 ppm; MS EI (M/z, %) 212(M^+, 4), 196(5), 155(100); $[\alpha]_D$ +198.1 (c = 0.5, $CHCl_3$); M^+ 212.04886, ppm 8.76, $C_{10}H_{12}O_3S_1$.
- (*R*)-1-(*p*.-Bromophenylsulfinyl)-2-propanone (**25**); m.p. 78–81 °C; ^1H NMR (CDCl3) δ 2.18 (3H, s), 3.82 (2H, ABq), and 7.5/7.66 (4H, ABq) ppm; MS EI (M/z, %) 262/260 (M^+, 12), 244/246(20), 203(55), 121(45), 109(54), 43(100); $[\alpha]_D$ +127.8 (c = 0.2, $CHCl_3$); M^+ 259.95002, ppm −2.46, $C_9H_9O_2S_1Br_1$.
- (S_SR_C)-2-(*p*.-Methoxyphenylsulfinyl)-1-phenylethanol (**26**); oil; ^1H NMR ($CDCl_3$) δ 2.8/3.2 (2H, b), 3.85 (3H, s), 5.33 (1H, d), 7.11/7.68 (4H, ABq), and 7.33 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 56.1/56.2, 64.2/64.7, 69.0, 71.5, 115.3, 126.0, 126.3, 128.8, 129.0, 142.4, and 162.7 ppm; MS EI (M/z, %) 276(M^+ 1), 156(100), 139(30), 107(85); $[\alpha]_D$ +6.8 (c = 1.29, $CHCl_3$), sample close to racemic; M^+ 276.08175, ppm 0.98, $C_{15}H_{16}O_3S_1$.
- (R_SR_C)-2-(Phenylsulfinyl)-1-phenylethanol (**27**); d.e. ratio 24%; m.p. 80–88 °C; ^1H NMR ($CDCl_3$) δ 2.88/3.25 and 3.10 (2H, all m.), 5.08, 5.15 (1H, d), and 7.23–7.58 (10H, d.) ppm; ^{13}C NMR ($CDCl_3$) δ 65.4, 66.0, 68.4, 70.8, 124.3, 124.5, 128.9, 129.0, 129.8, 129.8, 131.8, 132.7, 142.7, 147.8, and 143.7 ppm; MS NBA (M/z, %) 247(M^+ + 1, 62), 141(30), 125(100); $[\alpha]_D$ +29.3 (c = 1.5, $CHCl_3$); M^+ 247.07837, ppm 3.66, $C_{14}H_{15}O_2S_1$.
- (R_SR_C)-2-(*p*.-Methoxyphenylsulfinyl)-1-phenylethanol (**28**); (d.e. ratio 90% >); m.p. 115–117 °C; ^1H NMR ($CDCl_3$) δ 2.81/3.22 (2H, all m.), 3.85 (3H, s), 5.33 (1H, s,), 7.1/7.68 (4H, ABq), and 7.24 (5H, s) ppm; ^{13}C NMR ($CDCl_3$) δ 56.0, 63.6, 69.3, 115.6, 126.0, 126.3, 128.4, 129.9, 132.7, 142.4, and 162.5 ppm; MS EI (M/z, %) 276(M^+, 1), 156(100), 139(28), 107(82); $[\alpha]_D$ +138 (c = 1.5, $CHCl_3$); M^+ 276.08193, ppm 0.33, $C_{15}H_{16}O_3S_1$.
- (*R*)-2-(Phenylthio)-1-phenylethanol (**29**); oil; ^1H NMR ($CDCl_3$) δ 3.1–3.3 (2H, m), 5.28 (1H, d), 7.4–7.45 (10H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 46.6, 71.7, 127.5, 129.1, 129.5, 130.9, 133.9, 135.2, and 135.8 ppm; MS NBA (M/z, %) 231 (M^+ + 1, 100), 123(28), 105(58); $[\alpha]_D$ +45.4 (c = 1.5, $CHCl_3$) (lit.. [30] +47.5 (1.13, EtOH).
- (*R*)-2-(*p*.-Methoxyphenylsulfonyl)-1-phenylethanol (**30**); oil; ^1H NMR ($CDCl_3$) δ 3.42 (2H, m), 3.90 (3H, s), 5.30 (1H, d), 7.0/785 (4H, ABq), and 7.50 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 65.1, 64.5, 68.9, 114.9, 126.2, 128.2, 128.7, 129.1, 129.9, 134.6, 142.5, and 164.5 ppm; MS EI (M/z, %) 274(M^+, -H_2O, 13), 246(10), 186(52), 155(82), 107(100); $[\alpha]_D$ +6.2 (c = 1.2, $CHCl_3$); M^+ 293.08296, ppm 6.14, $C_{15}H_{17}O_4S_1$.
- (*R*)-2-(*p*.-Bromophenylsulfonyl)-1-phenylethanol (**31**); oil, ^1H NMR ($CDCl_3$) δ 3.26/3.36 (2H, m), 5.3 (1H, m), and 7.26/7.66 (9H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 64.6, 71.4, 125.9, 126.0, 129.1, 130.5, 133.1, 133.9 ppm; MS NBA (M/z, %) 341/343(M^+ + 1, 60), 55(100); $[\alpha]_D$ +5.1 (c = 1.8, $CHCl_3$).
- (*R*)-2-(*p*.-Phenylsulfinyl)-1-acetophenone (**32**); m.p. 94–97 °C; ^1H NMR ($CDCl_3$) δ 4.13/4.40 (2H, ABq), and 7.30/7.70 (10H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 66.5, 124.7, 129.1, 129.2, 129.7, 132.0, 134.6, 136.4, 143.7, and 191.8 ppm; MS EI (M/z, %) 244(M^+, 22), 185(58), 125(52), 105(100); $[\alpha]_D$ 170.3 (c = 1.0, $CHCl_3$); M^+ 244.05446, ppm 5.49, $C_{14}H_{12}O_2S_1$.
- (*R*)-2-(*p*.-Methoxyphenylsulfinyl)-1-acetophenone (**33**); oil; ^1H NMR ($CDCl_3$) δ 3.81 (3H, s), 4.30/4.52 (2H, ABq), 7.0/7.88 (4H, ABq), and 7.40/7.62 (5H, m); ^{13}C NMR ($CDCl_3$) δ 55.9, 66.5, 115.7, 126.7, 129.2, 134.5, 136.4, 162.8, and 191.9 ppm ; MS EI (M/z, %) 274(M^+, 4), 258(28), 155(55), 140(40), 105(100); $[\alpha]_D$ 47.2 (e.e. 48%, c = 1.15, $CHCl_3$); M^+ 274.06609, ppm 1.03, $C_{15}H_{14}O_3S_1$.
- (*R*)-2-(*p*.-Bromophenylsulfinyl)-1-acetophenone (**34**); ^1H NMR ($CDCl_3$) δ 4.72/4.7 (2H, ABq), and 7.65/7.92 (9H, m); MS EI (M/z, %) 322/324(M^+,10), 203/205(40), 105(100); $[\alpha]_D$ zero (c = 1, $CHCl_3$); M^+ 321.94711, ppm 59.64, $C_{14}H_{11}O_2S_1Br_1$.
- (R_SS_C)-1-(Phenylmethylsulfinyl)-2-propanol (**35**); oil; ^1H NMR ($CDCl_3$) δ 1.20 (3H, d), 2.57/2.77 (2H, m), 4.0 (2H, ABq), 4.30 (1H, m), and 7.26 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 23.6, 58.4, 59.6, 63.6, 128.8, 129.5, 130.1, and 130.6 ppm; MS EI (M/z, %) 198(M^+, 1), 182(1), 91(100); $[\alpha]_D$ 92 (c = 1.3, $CHCl_3$); M^+ 198.07139, ppm 1.21, $C_{10}H_{14}O_2S_1$.
- (R_SS_C)-1-(*p*.-Methoxyphenylmethylsulfinyl)-2-propanol (**36**); m.p. 142–144 °C; ^1H NMR ($CDCl_3$) δ 1.20 (3H, d), 2.5/2.8 (2H, m), 3.64 (3H, s), 3.90 (2H, ABq), 4.35 (1H, m), and 6.75/7.18 (4H, ABq); ^{13}C NMR ($CDCl_3$) δ 23.6, 55.6, 57.5, 58.1, 63.7, 114.7, 121.7, 131.8, and 160.0 ppm; MS NBA (M/z, %) 229 (M^+ + 1, 19), 121(100); $[\alpha]_D$ 83.5 (c = 1.3, $CHCl_3$); M^+ 229.08946, ppm 1.66, $C_{11}H_{17}O_3S_1$.
- (R_SS_C)-1-(*p*.-Bromophenylmethylsulfinyl)-2-propanol (**37**); m.p. 84–86 °C; ^1H NMR ($CDCl_3$) δ 1.20 (3H, d), 2.56/2.8 (2H, m), 4.0 (2H, s), 4.41 (1H, m), and 7.15–7.48 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 23.8, 56.8, 58.6, 64.5, 123.3, 128.8, 132.1, and 132.6 ppm; MS EI (M/z, %) 264/262 (M^+, 3), 185(5), 169/171(100/96); $[\alpha]_D$ 47.5 (c = 1.2, $CHCl_3$); M^+ 275.98269, ppm 2.65, $C_{10}H_{13}O_2S_1Br_1$.
- (S_SS_C)-1-(Phenylmethylsulfinyl)-2-propanol (**38**); oil; ^1H NMR ($CDCl_3$) δ 1.30 (3H, d), 2.52/2.85 (2H, m), 4.0/4.14 (2H, ABq), 4.42 (1H, m), and 7.25–7.4 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 23.8, 57.5, 58.3, 62.9, 128.9, 129.0, 129.9, and 130.4 ppm; MS EI (M/z,

%) 198(M^+, 3), 182(1), 91(100); $[\alpha]_D$ +140.5 (c = 0.7, $CHCl_3$); M^+ 198.06861, ppm 14.35, $C_{1o}H_{14}O_2S_1$.

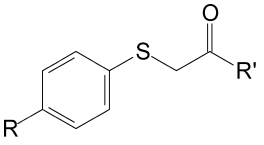
- (S_SS_C)-1-(*p*.-Methoxyphenylmethylsulfinyl)-2-propanol (**39**); m.p. 157–159 °C; ^1H NMR ($CDCl_3$) δ 1.29 (3H, d), 2.52/2.75 (2H, ABq), 3.73 (3H, s), 3.90/4.05 (2H, ABq), 4.4 (1H, m), and 6.82–7.16 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 23.8, 55.7, 57.2, 57.6, 63.0, 114.8, 121.7, 131.6, and 160.2 ppm; MS NBA (M/z, %) 229(M^+ + 1, 17), 121(100); $[\alpha]_D$ +172.2 (c = 0.7, $CHCl_3$); M^+ 228.08149, ppm 2.29, $C_{11}H_{16}O_3S_1$.
- (S_SS_C)-1-(*p*.-Bromophenylmethylsulfinyl)-2-propanol (**40**); m.p. 104–107 °C; ^1H NMR ($CDCl_3$) δ 1.30 (3H, d), 2.51/2.74(2H, ABq), 3.98 (2H, s), 4.4 (1H, m) and 7.15–7.5 (5H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 23.8, 57.6, 57.7, 63.1, 123.2, 129.0, 132.1, and 132.6 ppm; MS NBA (M/z, %) 227/229(M^+ + 1, 86/86), 169/171(100/95); $[\alpha]_D$ +143.9 (c = 0.5, $CHCl_3$); M^+ 275.98092, ppm 3.70, $C_{1o}H_{13}O_2S_1Br_1$.
- (S_C)-1-(Phenylmethylthio)-2-propanol (**41**); oil; ^1H NMR ($CDCl_3$) δ 1.30 (3H, d), 2.4/2.65 (2H, m), 3.81 (2H, s), 3.93 (1H, m), and 7.30 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 22.4, 36.4, 41.0, 65.8, 127.6, 129.0, 129.2, and 138.4 ppm; MS EI (M/z, %) 182(M^+, 12), 106(32), 91(100); $[\alpha]_D$ +67.5 (c = 2.4, $CHCl_3$); M^+ 182.07732, ppm 4.30, $C_{10}H_{14}O_1S_1$.
- (S_C)-1-(*p*.-Methoxyphenylmethylthio)-2-propanol (**42**); oil; ^1H NMR ($CDCl_3$) δ 1.30 (3H, d), 2.4/2.65 (2H, m), 3.7 (2H, s), 3.82 (4H, s + s superimposed), and 6.97/7.32 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 22.4, 36.9, 41.0, 55.7, 65.7, 114.4, 129.0, 130.3, and 159.1 ppm; MS NBA (M/z, %) 212 (M^+, 16), 121(100); $[\alpha]_D$ +38.2 (c = 1.1, $CHCl_3$); M^+ 212.08765, ppm 2.56, $C_{11}H_{16}O_2S_1$.
- (S_C)-1-(*p*.-Bromophenylmethylthio)-2-propanol (**43**); oil, ^1H NMR ($CDCl_3$) δ 1.30 (3H, d), 2.30/2.55 (2H, m), 3.61 (2H, s), 3.80 (1H, m), 7.3/7.56 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) 22.5, 36.0, 41.0, 65.9, 121.4, 130.9, 132.0, and 137.4 ppm; MS NBA (M/z, %) 260/262 (M^+ + 1), 243/245(30), 169/171(100/96); $[\alpha]_D$ +18.8 (c = 1.1, $CHCl_3$), e.e. = 60%; M^+ 259.98547, ppm 6.07, $C_{10}H_{13}O_1S_1Br_1$.
- (S_C)-1-(Phenylmethylsulfonyl)-2-propanol (**44**); oil; ^1H NMR ($CDCl_3$) δ 1.22 (3H, d), 2.82/3.02 (2H, m), 4.28 (2H, ABq), 4.38 (1H, m), and 7.41 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 23.3, 58.4, 61.3, 63.1, 128.2, 129.5, 129.5, and 131.2 ppm; MS NBA (M/z, %) 215(M^+ + 1, 100); $[\alpha]_D$ +7.7 (c = 1.4, $CHCl_3$) ([8] $[\alpha]_D$ +7.8 (c = 1.4, $CHCl_3$).
- (S_C)-1-(*p*.-Methoxyphenylmethylsulfonyl)-2-propanol (**45**); m.p. 90–92 °C; ^1H NMR ($CDCl_3$) δ 1.22 (3H, d), 2.82/2.99 (2H, m), 3.78 (3H, s), 4.42 (2H, ABq), 4.38 (1H, m) and 6.90/7.35 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 23.4, 55.7, 58.2, 60.6, 63.0, 114.9, 120.0, 132.5, and 160.6 ppm; MS NBA (M/z, %) 245(M^+ + 1, 6), 121 (100); $[\alpha]_D$ +5.4 (c = 1.0, $CHCl_3$); M^+ 245.08502, ppm 1.07, $C_{11}H_{17}O_4S_1$.
- (S_C)-1-(*p*.-Bromophenylmethylsulfonyl)-2-propanol (**46**); m.p. 99–102 °C, ^1H NMR ($CDCl_3$) δ 1.25 (3H, d), 2.8/3.0 (2H, m), 4.28 (2H, ABq), 4.45 (1H, m), and 7.30/7.52 (4H, ABQ) ppm; ^{13}C NMR ($CDCl_3$) δ 23.1, 58.2, 60.2, 62.9, 123.6, 126.8, 132.3, and 132.5 ppm; MS NBA (M/z, %) 292/294 (M^+ + 1, 24), 171/173 (100); $[\alpha]_D$ +6.7 (c = 1.6, $CHCl_3$); M^+ 275.98092, ppm 3.79, $C_{10}H_{13}O_2S_1Br_1$.
- (S_S)-1-(Phenylmethylsulfinyl)-2-propanone (**47**); m.p. 103–104 °C; ^1H NMR ($CDCl_3$) δ 2.30 (3H, s), 3.58 (2H, ABq), 4.14 (2H, ABq), and 7.30 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 33.0, 58.1, 60.8, 129.0, 129.4, 130.7, and 200.8; MS NBA (M/z, %) 197(M^+ + 1, 5), 99(28), 59(100); $[\alpha]_D$ +10.4 (c = 0.4, $CHCl_3$); M^+ 196.05490, ppm 4.59, $C_{10}H_{12}O_2S_1$.
- (S_S)-1-(*p*.-Methoxyphenylmethylsulfinyl)-2-propanone (**48**); m.p. 101–103 °C; ^1H NMR ($CDCl_3$) δ 2.24 (3H, s), 3.30 (2H, ABq), 3.71 (3H, s), 4.04 (2H, ABq), and 6.86/7.16 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 32.9, 55.7, 57.4, 60.7, 114.8, 121.2, 131.9, 160.3 and 210.2 ppm; MS NBA (M/z, %) 227(M^+ + 1, 10), 121(100); $[\alpha]_D$ +14.0 (c = 1.0, $CHCl_3$); M^+ 226.06676, ppm 1.73, $C_{11}H_{14}O_3S_1$.
- (S_S)-1-(*p*.-Bromophenylmethylsulfinyl)-2-propanone (**49**); m.p. 123–124 °C; ^1H NMR ($CDCl_3$) δ 2.28 (3H, s), 3.60 (2H, ABq), 4.09 (2H, ABq), and 7.15/7.46 (4H, ABq) ppm; ^{13}C NMR ($CDCl_3$) δ 33.0, 57.1, 60.7, 123.4, 128.5, 132.3, 132.6, and 201.0 ppm; MS NBA (M/z, %) 274/276(M^+ + 1, 65/60), 169/171(100/96); $[\alpha]_D$ 25.1 (c = 0.6, $CHCl_3$); M^+ 273.96581, ppm 1.85, $C_{10}H_{11}O_2S_1Br_1$.
- (R_SR_C)-2-(*p*.-Methoxyphenylmethylsulfinyl)-1-phenylethanol (**50**); d.e. purity 26%; m.p. 115–125 °C; ^1H NMR ($CDCl_3$) δ 2.8/3.01 (2H, m), 3.80 (3H, s), 4.12 (2H, m), 5.53 (1H, s), 6.87/7.20 (4H, m) and 7.06 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 55.7, 56.4/55.7, 58.9/57.6, 70.0/68.9, 114.9, 121.1, 126.1, 128.5, 129.1, 129.1, 131.7, and 131.8 ppm; MS NBA (M/z, %) 291(M^+ + 1, 22), 121 (100); $[\alpha]_D$ +24.7 (c = 0.6, $CHCl_3$); M^+ 291.09917, ppm 21.72, $C_{16}H_{19}O_3S_1$.
- (S_SR_C)-2-(Phenylmethylsulfinyl)-1-phenylethanol (**51**); d.e. 26%; m.p. 90–115 °C; ^1H NMR ($CDCl_3$) δ 2.8/3.01 (2H, m), 4.14 (2H, m), 5.32 (1H, d), and 7.28 (10H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 56.7/58.1, 58.6/59.7, 68.9/76.9, 126.0, 128.4, 128.5, 128.9, 129.0 129.2, 129.5, 129.8, 130.5, 130.6, and 142.6 ppm; MS NBA (M/z, %) 261(M^+ + 1, 64), 243(38), 139(26), 91(100); $[\alpha]_D$ 19.0 (c = 0.62, $CHCl_3$); M^+ 261.08931, ppm 21.53, $C_{15}H_{17}O_2S_1$.
- (S_SR_C)-2-(*p*.-Methoxyphenylmethylsulfinyl)-1-phenylethanol (**52**); d.e. 54%; m.p. 102–105 °C; ^1H NMR ($CDCl_3$) δ 2.7/2.9 (2H, m), 3.7 (3H, s), 3.95 (2H, m), 5.22 (1H, m), 6.8/7.1 (4H, ABq) and 7.26 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 55.7, 56.8/57.8, 58.3/59.3, 68.1/69.8, 114.8, 121.7, 126.3, 128.4, 129.0, 131.6, 143.1, and 160.1 ppm; MS NBA (M/z, %) 291(M^+ + 1, 17), 121(100); $[\alpha]_D$ 38.4 (c = 1.0, $CHCl_3$); M^+ 291.10427, ppm 4.20, $C_{16}H_{19}O_3S_1$.

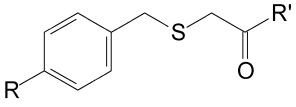
- (S_SR_C)-2-(*p*.-Bromophenylmethylsulfinyl)-1-phenylethanol (**53**); d.e. 28%; m.p. 149–159 °C; ^{1}H NMR ($CDCl_3$) δ 2.79/2.92 (2H, m), 4.0 (2H, m), 5.30 (1H, m), 7.08/7.40 (4H, ABq), and 7.22 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 56.7, 58.6, 70.3, 123.3, 126.1, 128.6, 129.2, 132.1, 132.6, and 142.5 pm; MS EI (M/z, %) 218(M^+, 18), 171/173(100); $[\alpha]_D$ 20.0 (c = 1.0, $CHCl_3$); M^+ 339.00578, ppm 1.01, $C_{15}H_{16}O_2S_1Br_1$.
- (R_C)-2-(Phenylmethylsulfonyl)-1-phenylethanol (**54**); m.p. 178–180 °C; ^{1}H NMR ($CDCl_3$) δ 2.97/3.3 (2H, m), 4.28/4.35 (2H, ABq), 5.38 (1H, d), and 7.34 (10H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 38.8, 61.6, 69.6, 126.0, 128.3, 129.0, 129.3, 129.5, 129.5 and 131.4 ppm; MS EI (M/z, %) 258(M^+, 2), 194(6), 91(100); $[\alpha]_D$ +3.6 (c = 1.0, $CHCl_3$); M^+ 277.09248, ppm 9.52, $C_{15}H_{17}O_3S_1$.
- (R_C)-2-(*p*.-Methoxyphenylmethylsulfonyl)-1-phenylethanol (**55**); m.p. 133–135 °C; ^{1}H NMR ($CDCl_3$) δ 2.85/3.20 (2H, m), 3.73 (3H, s), 4.12/4.30 (2H, ABq), 5.30 (1H, d), 6.84/7.35 (4H, ABq) and 7.32 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 55.7, 58.6, 60.9, 69.5, 114.9, 120.0, 126.0, 128.9, 129.3, 132.6, 141.3, and 160.7 ppm; MS NBA (M/z, %) 306(M^+, 5), 289(10), 121(100); $[\alpha]_D$ +7.3 (c = 0.26, $CHCl_3$); M^+ 307.09213, ppm 26.96, $C_{16}H_{19}O_4S_1$.
- (R_C)-2-(*p*.-Bromophenylmethylsulfonyl)-1-phenylethanol (**56**); m.p. 172–174 °C; ^{1}H NMR ($CDCl_3$) δ 2.91/3.32 (2H, m), 4.25/4.50 (2H, ABq), 5.32 (1H, d), and 7.32–7.6 (9H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 58.0, 60.1, 70.3, 123.3, 126.0, 126.2, 128.6, 129.2, 132.2, and 132.6 ppm; MS EI (M/z, %) 354/365 (M^+, 2), 169/170(100/95); $[\alpha]_D$ +5.5 (c = 1.16, $CHCl_3$).
- (S_S)-2-(Phenylmethylsulfinyl)-1-acetophenone (**57**); m.p. 94–96 °C; ^{1}H NMR ($CDCl_3$) δ 4.15/4.3 (4H, double ABq), 7.20–7.55 (8H, m) and 7.90 (2H, d) ppm; ^{13}C NMR ($CDCl_3$) δ 57.2, 58.1, 128.0, 128.4, 129.3, 129.5, 129.0, 129.9, 130.9, 133.8, 134.7, 192.1 ppm; MS NBA (M/z, %) 259 (M^+ + 1, 48), 91(100); $[\alpha]_D$ +41.2 (c = 0.34, $CHCl_3$); M^+ 258.071078, ppm 1.28, $C_{15}H_{14}O_2S_1$.
- (S_S)-2-(*p*.-Methoxyphenylmethylsulfinyl)-1-acetophenone (**58**); m.p. 128–130; ^{1}H NMR ($CDCl_3$) δ 3.39 (3H, s), 4.15 (4H, m), 6.85/7.25 (4H, ABq) and 7.45/7.60 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 55.7, 57.3, 57.9, 114.7, 121.2, 129.1, 129.3, 132.1, 134.7, 136.4, 160.3, and 193.1 ppm; MS EI (M/z, %) 151(12), 121(100); $[\alpha]_D$ +51.8 (c = 0.61, $CHCl_3$); M^+ 288.08072, ppm 4.49, $C_{16}H_{16}O_3S_1$.
- (S_S)-2-(*p*.-Bromophenylmethylsulfinyl)-1-acetophenone (**59**); m.p. 165–168 °C; ^{1}H NMR ($CDCl_3$) δ 4.13 (4H, m), 7.22–7.45 (9H, m) ppm; MS EI (M/z, %) 336/338(M^+, 1), 236(5), 220(100), 169/171(18); $[\alpha]_D$ +38.4 (c = 0.8, $CHCl_3$); M^+ 335.97991, ppm 6.12, $C_{15}H_{13}O_2S_1Br_1$.

Conversion of diastereomerics to enantiomers

Representative reactions are:

- 1. Conversion of sulfoxides to sulfones: (S_SS_C)-1-(*p*.-bromophenylsulfinyl)-2-propanol (**15**) (produced from **3** by *Helminthosporium* sp.) to (*S*)-1-(*p*.-bromophenylsulfonyl)-2-propanol (**23**). The sulfoxide alcohol (15, 64 mg) was dissolved in CH_2Cl_2 (5 ml), and then m.-chloroperoxybenzoic acid (100 mg, 1.2 eq. of 50%) added. The solution was stirred overnight at room temperature, then diluted by an addition 10 ml of CH_2Cl_2. The solution was washed with 5% NaOH (twice), water, then 5% NaCl. It was dried and evaporated to give 54 mg, m.p. 72–74 °C, $[\alpha]_D$ +11.2 (c = 1.0, $CHCl_3$) [compared with product **23**, m.p. 73–75 °C, $[\alpha]_D$ +10.9 (c = 1.5, $CHCl_3$)]. All spectral data (^{1}H NMR ($CDCl_3$), ^{13}C NMR ($CDCl_3$), and MS EI) were identical with those listed for product **23**, and ^{1}H NMR with Kagan and MPAA reagent was identical for both.
- 2. Conversion of hydroxy sulfoxides to keto sulfoxides: (R_SS_c)-1-(*p*.-methoxyphenylsulfinyl)-2-propanol (**17**), produced from **2** by *Rhodococcus erythropolis*, to (*R*)-1-(*p*.-methoxyphenylsulfinyl)-2-propanone (**24**). The sulfoxide alcohol (**17**, 60 mg) was dissolved in acetone (5 ml), and the mixture stirred at 0 °C. Jones reagent (ca. 15 ml) was added slowly via a syringe to maintain the orange colour, and the reagent was then stirred at 0 °C for 15 min. The reaction was worked up using isopropanol (5 min), and then by adding water (20 ml) and dichloromethanone (20 ml). After re-extraction with dichloromethanone, the total extract was washed (water, satd. NaCl), then dried and evaporated. The yield was 31 mg, m.p. 72–73 °C, $[\alpha]_D$ +151 (c = 1.0, $CHCl_3$), e.e. 76% (from product 24, m.p. 72–73 °C, $[\alpha]_D$ +198.1 (c = 1, $CHCl_3$), e.e. > 95%). All spectral data (^{1}H NMR ($CDCl_3$), ^{13}C NMR ($CDCl_3$), and MS EI) were identical with those listed for product **24**, and ^{1}H NMR with Kagan reagent and MPAA for the product with d.e. = 76% was comparable with the value for d.e. of the starting material **17** (d.e. = 80%).

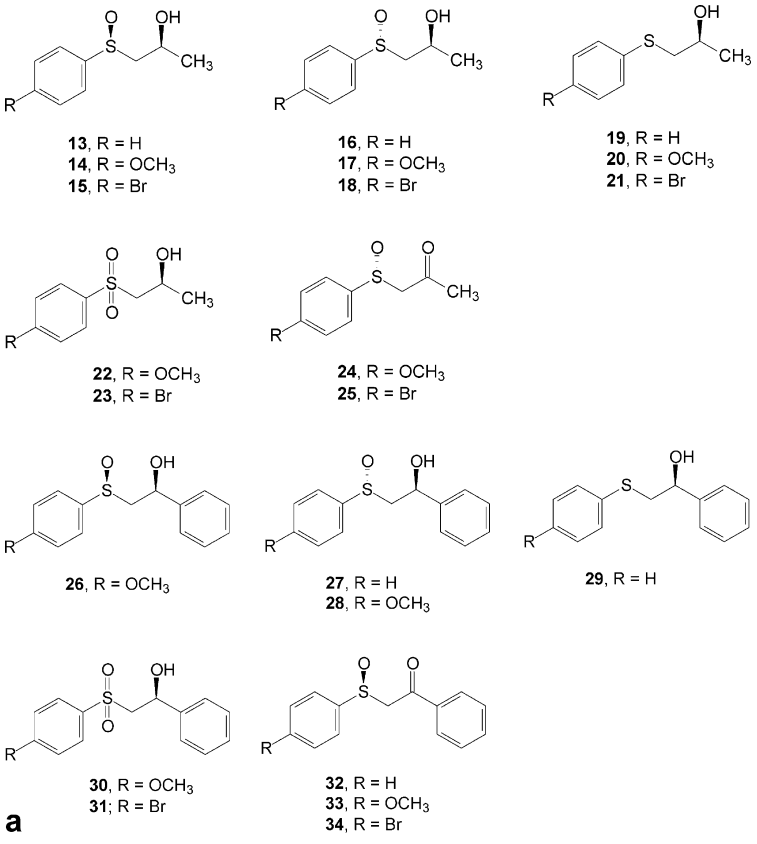




1, R = H, R' = CH_3
2, R = OCH_3, R' = CH_3
3, R = Br, R' = CH_3
4, R = H, R' = Ph
5, R = OCH_3, R' = Ph
6, R = Br, R' = Ph

7, R = H, R' = CH_3
8, R = OCH_3, R' = CH_3
9, R = Br, R' = CH_3
10, R = H, R' = Ph
11, R = OCH_3, R' = Ph
12, R = Br, R' = Ph

Fig. 1 Structures of substrates



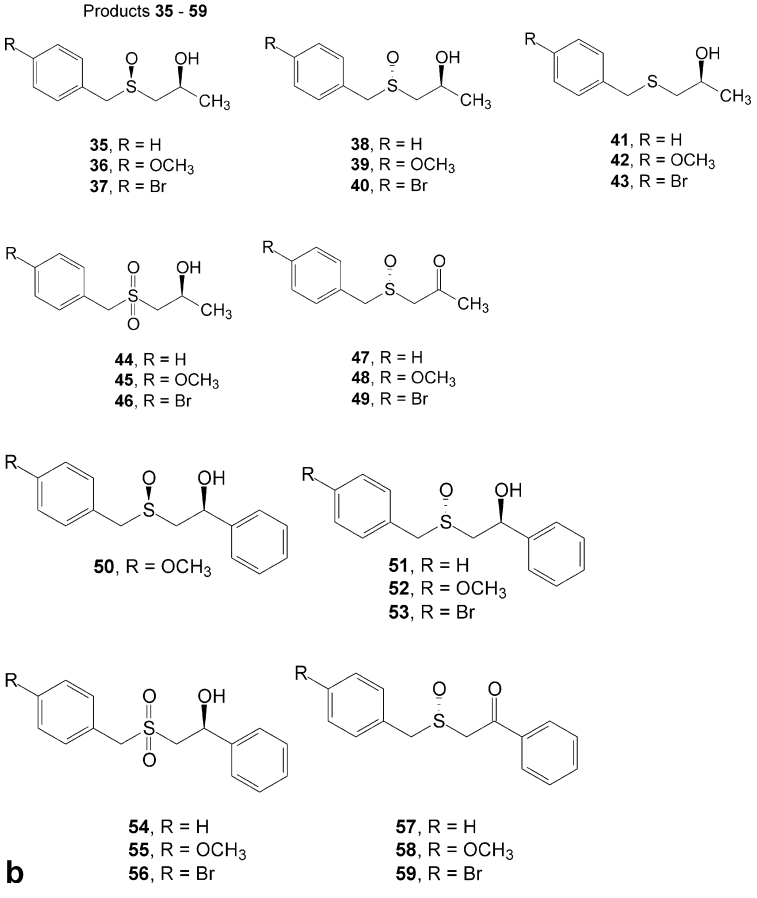


Fig. 2 **a** Products 13–34.
b Products 35–59

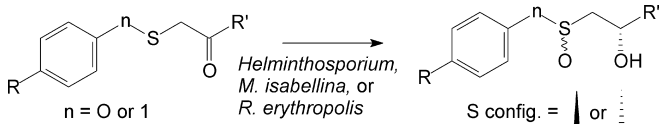


Fig. 3 Biotransformation of β-ketosulfides to produce chiral β-hydroxysulfoxides

Results and discussion

The substrates that have been studied in the present series, structures **1**–**12**, have the common features illustrated in Fig. 1.

Substrates **1**–**12** were all prepared by similar reactions, as described in Materials and methods, specifically for α-(*p*.-bromophenylthio)acetophenone (**6**). Physical information and spectral data of products **1**–**12** (^{1}H NMR, ^{13}C NMR, and MS) are also provided in Materials and methods. The results are summarized for the biotransformation products **13**–**59** (Table 1, Figs. 2, 3).

The configurations at carbon and sulfur in products **13** and **16**, from *Helminthosporium* sp. and *M. isabellina*, respectively, were determined independently by conversion of **13** and **16** to the sulfone alcohols and sulfoxide ketones. Optical rotations of the sulfone alcohols were identical with those reported for stereochemically pure versions produced by biotransformation of the corresponding sulfone ketones [6] and enantiomeric purity was confirmed at ≥95% by ^{1}H NMR analysis using Eu(thfc)$_3$ as a chiral reagent. This analysis was extended for the analogous products, **14**, **15**, **17**, and **18** in a similar manner to all the products in Table 1. Stereochemical analysis of the sulfoxides obtained by oxidation of the alcohol from products **13**–**16** was carried out by ^{1}H NMR analysis using the Kagan [8] and MPAA [5] chiral shift reagents. Chirality of the other products containing only a single chiral centre was determined by combination of optical rotations and by Kagan and MPAA chiral-shift reagents. Crystallisation of products **13**–**15**, from *Helminthosporium* sp., and **17** and **18**, from *R. erythropolis*, after original biotransformation gave hydroxy sulfoxides of d.e.≥95%. It is apparent from the stereochemical analysis of the above products that they arose from materials with a single configuration (*S*) at carbon and a mixed configuration (ca. 90:10) at sulfur. The configurations of all the sulfoxides obtained from *Helminthosporium* sp. and *M. isabellina* were consistent with those observed from over 100 other similar (but not identical) substrates [5]. *R. erythropolis* biotransformations were determined by comparison of the optical rotation values of the products with those of other biotransformation samples.

It is clear that only *M. isabellina* is capable of producing hydroxysulfoxides **27** and **28** from substrates **4**–**6**, but with low optical purities, and the sulfoxidation by *R. erythropolis* produces stereochemically useful material for only one sample (**32**, e.e. > 95%). The preferential substrate for sulfur oxidation by *R. erythropolis* is one containing two aromatic rings, typically a dibenzothiophene-type example, but it is now apparent that such substrates do not undergo sulfur oxidations when they contain *para*-substituents contained in at least one of the aromatic rings [12].

Regarding the products of substrates **7**–**9**, the structural combination of benzyl sulfide and methyl ketone turned out to be particularly effective for providing chiral products for a series of starting materials. Products from *Heminthosporium* sp. (**35**–**37**) and *R. erythropolis* (**38**–**40**) represent a series of diastereomeric purities that can be purified to > 95% d.e., although yields of products **38**–**40** are not high. The ketosulfoxides **47**–**49** are also produced in acceptably optical purity by *R. erythropolis*, but again the yields were not high. As in all these biotransformations, the optical purities of the simple thia-alcohols (**41**–**43**) were > 95%.

Biotransformation of substrates **10**–**12** results in benzyl-type sulfides, with phenyl substituents on the carbonyl groups. With the exception of products **57**–**59**, arising from *R. erythropolis* (and then in low yield), sulfoxide products are generally of low optical purity. The only other useful products of high optical purity (but low yield) from this series of biotransformations were the sulfone compounds **54**–**56**.

It is apparent from the biotransformation results that substrates for *Helminsporium* are useful for the formation of high optical purity sulfoxide hydroxides when the carbonyl group is substituted by methyl, not phenyl . In contrast, the use of *M. isabellina* can result in sulfoxide alcohols from substrates with phenyl carbonyls, but, with one exception (product **39**), the optical purities of sulfoxide alcohols from *M. isabellina* are only moderate.

The fact that the sulfoxide alcohols from *Helminthosporium* and *M. Isabellina* are uniformly of different sulfoxide configurations is not unusual, arising from the different enzymes used by these microorganisms and consistent with their models [14]. In contrast, the configuration of alcohols by the reduction of carbonyls are consistent in stereochemistry in all cases, which is entirely consistent with the regular reduction of ketosulfides to hydroxysulfides by other organisms (e.g. baker's yeast) that reduce such sulfide carbonyl substrates to chiral alcohols in the absence of any oxidation at sulfur [28]. The relatively common formation of ketosulfoxides by *R. erythropolis* by simple biotransformation of sulfides to sulfoxides, without a large extent of the associated carbonyl reduction, is consistent with this selectivity because the microorganism's oxidative enzyme activity for sulfoxidation has been significantly increased by gene selectivity [24].

The biotransformation of β-ketosulfides to produce chiral β-hydroxysulfoxides of different but defined configuration presents a new consistent method for the preparation of such compounds. This process is currently under investigation using a variety of such sub-

strates for microbial catalysis that are known to carry out both sulfide oxidation and carbonyl reduction when applied to different, independent substrates.

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