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Copper-Catalyzed Asymmetric Oxidation of Sulfides

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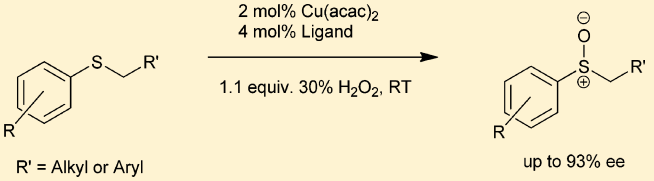
Supporting Information

ABSTRACT: Copper-catalyzed asymmetric sulfoxidation of aryl benzyl and aryl alkyl sulfides, using aqueous hydrogen peroxide as the oxidant, has been investigated. A relationship between the steric effects of the sulfide substituents and the enantioselectivity of the oxidation has been observed, with up to 93% ee for 2-naphthylmethyl phenyl sulfoxide, in modest yield in this instance (up to 30%). The influence of variation of solvent and ligand structure was examined, and the optimized conditions were then used to oxidize a number of aryl alkyl and aryl benzyl sulfides, producing sulfoxides in excellent yields in most cases (up to 92%), and good enantiopurities in certain cases (up to 84% ee).



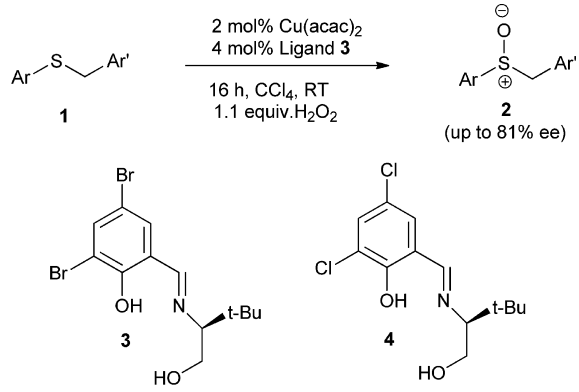
INTRODUCTION

Optically pure sulfoxides are widely used as building blocks and chiral auxiliaries in asymmetric synthesis.[1] The sulfinyl group has been shown to be an effective chiral auxiliary in a broad range of synthetic reactions from carbon−carbon bond-forming reactions[2] to cycloaddition reactions.[3−5] Enantiopure sulfoxides have also found use in the pharmaceutical industry due to their important biological activity; for example, esomeprazole, the (*S*)-enantiomer of omeprazole, has been one of the world's best-selling drugs since its launch in 2001. Modafinil is a psychostimulant agent that has been used for the treatment of narcolepsy; it is manufactured by Cephalon and is marketed in the racemic form as Provigil.[6]

Since the 1980s, metal-catalyzed asymmetric sulfide oxidation employing titanium, vanadium, and a number of other metal-based systems has developed rapidly as a route to enantiopure sulfoxides.[7] The initial breakthrough came in 1984 when the research groups of Kagan[8,9] and Modena[10] independently reported an efficient titanium-mediated sulfide oxidation based on the Sharpless asymmetric epoxidation procedure.[11] In 1995, Bolm reported a robust vanadium sulfoxidation procedure using a vanadium Schiff base complex.[12] The oxidation was carried out under mild conditions using hydrogen peroxide as the oxidant. A number of other metals, such as iron, manganese, aluminum, niobium, zirconium, tungsten, molybdenum, and osmium, have also been used to catalyze asymmetric oxidation of sulfides.[7]

However, there are disadvantages associated with the Kagan and Bolm procedures for asymmetric oxidation. The Kagan system is limited by its sensitivity to atmospheric moisture and low turnover numbers, and it utilizes a complex and expensive catalytic system.[13] Although the Bolm procedure is robust and operationally straightforward, the use of vanadium is not advantageous since vanadium is known to exert toxic, mutagenic, and genotoxic effects on a variety of biological systems.[14]

Scheme 1. Copper-Catalyzed Asymmetric Oxidation of Sulfides



Copper has received relatively little attention in metal-catalyzed asymmetric sulfoxidation. The research groups of Cross,[15] Kraemer,[16] Zhu,[17] and Alcon[18] have all used copper-based systems to asymmetrically oxidize sulfides, but with limited success (enantioselectivities of 0−30% ee). In an initial study, we demonstrated good enantiocontrol in copper-catalyzed asymmetric oxidation of aryl benzyl sulfides with up to 81% ee, albeit with modest yields (typically 20−30%, Scheme 1).[19] Herein, we wish to describe the expansion of this early investigation resulting in improved yields, while retaining good enantioselectivity through variation of reaction conditions. The influence of variation of solvent, ligand, and substrate structure has been examined, rendering this oxidation synthetically useful.

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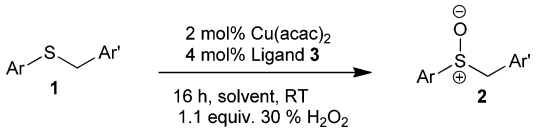
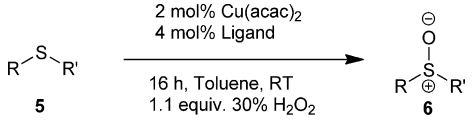
Table 1. Investigation of Solvent



				toluene				CCl_4[d]			
entry	1	Ar	Ar′	**1:2**[a]	**2**	% yield[b]	% ee (*R*)[c]	**1:2**[a]	% yield[b]	% ee (*R*)[c]	
1	**1a**	Ph	Ph	73:27	**2a**	21	58	74:26	27	61	
2	**1b**	2-$MeOC_6H_4$	Ph	74:26	**2b**	19	77	57:43	29	79	
3	**1c**	3-$MeOC_6H_4$	Ph	74:26	**2c**	18	73	68:32	24	69	
4	**1d**	4-$MeOC_6H_4$	Ph	54:46	**2d**	33	54	63:37	17	39	
5	**1e**	4-MeC_6H_4	Ph	78:22	**2e**	15	51	46:54	38	55	
6	**1f**	4-MeC_6H_4	4′-$MeOC_6H_4$	55:45	**2f**	30	46	47:53	42	27	
7	**1g**	4-FC_6H_4	Ph	75:25	**2g**	18	34	71:29	13	39	

[a]Ratio of **1**:**2** determined by ^{1}H NMR analysis of the crude product; no sulfone produced. [b]Yield of **2** after purification by column chromatography. [c]Determined by HPLC analysis on chiral column (Daicel Chiracel OD-H). Absolute configuration determined by comparison of specific rotation values for **2a** and **2e** to known literature values; for **2b**, **2c**, **2d**, **2f**, and **2g**, proposed configuration based on HPLC elution order and the direction of the specific rotations. [d]Results obtained by Kelly et al.[19]

Table 2. Influence of Steric and Electronic Effects



						no NMO			NMO[d]		
entry	sulfide **5**	R	R′	sulfoxide **6**	ligand	**5:6**[a]	% yield[b]	% ee (*R*)[c]	**5:6**[a,d]	% yield[b]	% ee (*R*)[c,d]
1	**5a**	Ph	$-CH_2C_6H_4$	**6a**	**3**	79:21	17	58	61:39	30	60
2	**5b**	4-MeC_6H_4	Me	**6b**	**3**	79:21	15	22	65:35	37	21
3	**5c**	4-MeC_6H_4	$-CH_2C{\equiv}CH$	**6c**	**3**	84:16	8	3	83:17	10	6
4	**5d**	Ph	Et	**6d**	**3**	80:20	12	40	60:40	39	49
5	**5e**	Ph	$-CH_2$-cyclohexyl	**6e**	**3**	86:14	23	54	78:22	20	60
6	**5b**	4-MeC_6H_4	Me	**6b**	**4**	81:19	11	19	64:36	36	16
7	**5c**	4-MeC_6H_4	$-CH_2C{\equiv}CH$	**6c**	**4**	81:19	4	5	78:22	14	4
8	**5d**	Ph	Et	**6d**	**4**	72:28	22	46	59:41	40	53
9	**5e**	Ph	$-CH_2$-cyclohexyl	**6e**	**4**	70:30	19	57	71:29	24	63
10	**5f**	Ph	*i*-Pr	**6f**	**4**	72:28	19	50	69:31	26	64
11	**5g**	Ph	$-CH_2CH(CH_3)_2$	**6g**	**3**	82:18	13	51	78:22	17	56
12	**5g**	Ph	$-CH_2CH(CH_3)_2$	**6g**	**4**	71:29	15	61	76:24	18	61
13	**5h**	Ph	$-CH_2C(CH_3)_3$	**6h**	**4**	80:20	15	71	72:28	28	71
14	**5i**	Ph	$-CH_2$-2′-naphthyl	**6i**	**4**	73:27	23	93	45:55	30	93

[a]Ratio of **5**:**6** determined by ^{1}H NMR analysis of the crude product; no sulfone produced. [b]Yield of **6** after purification by column chromatography. [c]Determined by HPLC analysis on chiral column (Daicel Chiracel OD-H). Absolute configuration determined by comparison of specific rotation values for **6a**, **6b**, **6d**, **6e**, **6f**, and **6g** to known literature values; for **6c**, **6h**, and **6i**, proposed configuration based on HPLC elution order and direction of specific rotations. [d]Results obtained when oxidation was carried out in the presence of 2.5 mol % NMO.

RESULTS AND DISCUSSION

The effects of varying sulfide substituents, Schiff base ligand, and solvent were investigated in an attempt to optimize the asymmetric oxidation and, in particular, to improve the efficiency of the transformation. An initial solvent study demonstrated that CCl_4 could be replaced with toluene as the solvent for copper-catalyzed asymmetric sulfoxidation with no significant loss in yield or enantioselectivity, as shown in Table 1.

We next examined the influence of steric and electronic effects on the efficiency and enantioselectivity of the oxidation. Since Schiff base ligands **3** and **4** had produced the best results in preliminary studies, these were used in this investigation, as shown in Table 2. The results indicate that the steric effect (Table 2, entries 5 and 9) of the R′ substituent has a much stronger influence on the enantioselectivity of the oxidation than the electronic effect (Table 2, entries 3 and 7). There is a direct trend between the size of R′ and the enantioselectivity of the oxidation; for example, substitution of a methyl group with an ethyl group in the R′ position results in a large increase in enantioselectivity (22% to 40% ee, Table 2, entries 2 and 4). A similar increase in enantioselectivity is observed on replacing an isobutyl with a neopentyl group in the R′ position (Table 2, entries 12 and 13). The oxidation of 2-naphthylmethyl phenyl sulfide produced the corresponding sulfoxide in 93% ee, the highest to date in copper-catalyzed asymmetric sulfide oxidation. We have previously shown that carrying out copper-catalyzed oxidations in the presence of NMO results in an improvement in the yield of sulfoxide.[19] Thus, the above experiments were repeated using NMO as an additive, and the

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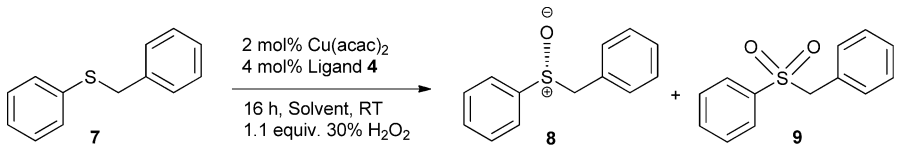
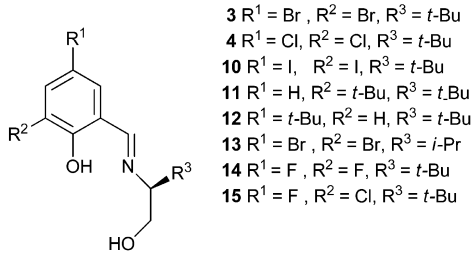
Table 3. Investigation of Solvent

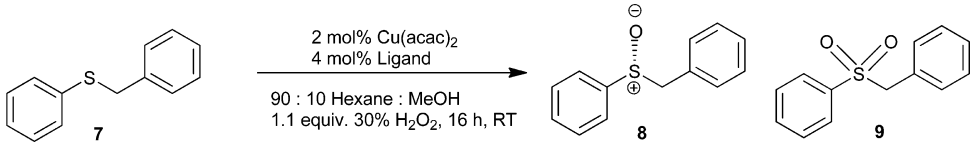


entry	solvent	7:8:9[a]	yield, 8 (%)[b]	% ee (*R*)[c]
1	ether	85:15:0	8	10
2	dioxane	69:31:0	25	1
3	toluene	79:21:0	17	58
4	CCl_4	65:35:0	27	61
5	benzene	66:34:0	26	69
6	hexane	100:0:0	0	
7	MeOH	40:60:0	50	24
8	MeOH[d]	19:81:0	73	29
9	50:50 toluene/MeOH	47:53:0	48	47
10	75:25 toluene/MeOH	46:54:0	47	47
11	90:10 toluene/MeOH	42:58:trace	52	49
12	95:5 toluene/MeOH	48:52:0	45	46
13	90:10 hexane/MeOH	3:96:1	87	80
14	90:10 hexane/EtOH	1:98:1	90	76
15	90:10 cyclohexane/MeOH	8:91:1	85	79
16	90:10 hexane/IPA	7:92:1	83	1
17	90:10 CCl_4/MeOH	21:76:3	70	62
18	90:10 CCl_4/MeOH[d]	9:89:2	82	63
19	90:10 hexane/benzyl alcohol	4:94:2	87	7
20	90:10 hexane/*t*-BuOH	45:55:trace	46	4
21	90:10 hexane/2-butanol	57:43:0	38	8

[a]Ratio of **7**:**8**:**9** determined by ^{1}H NMR analysis of the crude product. [b]Yield of **8** after purification by column chromatography. [c]Determined by HPLC analysis on chiral column (Daicel Chiracel OD-H). Absolute configuration determined by comparison of rotation values to literature values. [d]Was carried out in the presence of 2.5 mol % NMO.

Table 4. Investigation of Effect of Ligand Structure





entry	ligand	7:8:9[a]	yield, 8 (%)[b]	% ee (*R*)[c]
1	**3**	1:97:2	86	66
2	**4**	1:98:1	90	79
3	**10**	68:32:0	28	3
4	**11**	73:27:0	24	3
5	**12**	74:36:0	39	2
6	**13**	50:50:0	44	6
7	**14**	45:55:trace	47	37
8	**15**	3:96:1	87	58

[a]Ratio of **7**:**8**:**9** determined by ^{1}H NMR analysis of the crude product. [b]Yield of **8** after purification by column chromatography. [c]Determined by HPLC analysis on chiral column (Daicel Chiracel OD-H). Absolute configuration determined by comparison of rotation values to literature values.

results are shown in Table 2. We found that the addition of NMO (2.5 mol %) resulted in an improvement in yield in nearly all cases. The poor yields obtained were attributed to product inhibition of the oxidation, presumably through

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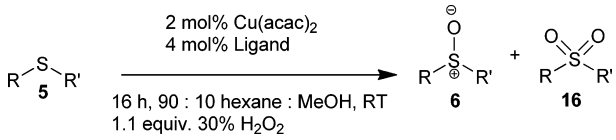
Table 5. Asymmetric Oxidation of Sulfides Using Optimized Conditions



entry	5	R	R′	ligand	5:6:16[a]	6	% yield[b]	% ee (*R*)[c]
1	**5a**	Ph	$-CH_2C_6H_4$	**4**	1:98:1	**6a**	90	79
2	**5a**	Ph	$-CH_2C_6H_4$	**15**	2:98:0	**6a**	91	58
3	**5b**	4-MeC_6H_4	Me	**4**	4:96:trace	**6b**	90	23
4	**5d**	Ph	Et	**4**	2:98:trace	**6d**	92	44
5	**5f**	Ph	*i*-Pr	**4**	19:81:trace	**6f**	74	60
6	**5g**	Ph	$-CH_2CH(CH_3)_2$	**4**	10:90:trace	**6g**	82	48
7	**5h**	Ph	$-CH_2C(CH_3)_3$	**4**	15:85:0	**6h**	79	71
8	**5i**	Ph	$-CH_2$-2′-naphthyl	**4**	100:0:0	**6i**		
9	**5j**	4-MeC_6H_4	$-CH_2C_6H_4$	**4**	2:97:1	**6j**	91	81
10	**5j**	4-MeC_6H_4	$-CH_2C_6H_4$	**15**	4:96:0	**6j**	90	84
11	**5k**	4-MeC_6H_4	4-$MeOC_6H_4$	**4**	2:97:1	**6k**	90	47
12	**5l**	2-$MeOC_6H_4$	$-CH_2C_6H_4$	**4**	8:92:trace	**6l**	85	29
13	**5m**	3-$MeOC_6H_4$	$-CH_2C_6H_4$	**4**	46:54:0	**6m**	47	21
14	**5n**	2-MeC_6H_4	$-CH_2C_6H_4$	**4**	1:98:1	**6n**	91	64
15	**5n**	2-MeC_6H_4	$-CH_2C_6H_4$	**15**	6:94:0	**6n**	88	71
16	**5o**	3-MeC_6H_4	$-CH_2C_6H_4$	**4**	11:89:0	**6o**	84	54
17	**5o**	3-MeC_6H_4	$-CH_2C_6H_4$	**15**	10:88:2	**6o**	83	69
18	**5p**	Ph	$-CH_2$-*p*-Tol	**4**	1:97:2	**6p**	89	55
19	**5q**	Ph	$-CH_2$-*m*-Tol	**4**	7:92:1	**6q**	83	50
20	**5q**	Ph	$-CH_2$-*m*-Tol	**15**	4:95:1	**6q**	90	46
21	**5r**	Ph	$-CH_2$-*o*-Tol	**4**	12:85:2	**6r**	80	47[d]

[a]Ratio of **5**:**6**:**16** determined by ^{1}H NMR analysis of the crude product. [b]Yield of **6** after purification by column chromatography. [c]Determined by HPLC analysis on chiral column (Daicel Chiracel OD-H for **6a**−**6q**, Chiracel As−H for **6r**). Absolute configuration determined by comparison of rotation values for **6a**, **6b**, **6d**, **6f**, and **6g** to known literature values; for **6h**, **6k**, **6l**, **6m**, **6n**, **6o**, **6p**, and **6q**, proposed configuration based on HPLC elution order and direction of specific rotations. [d]Configuration of **6r** not determined.

complexation of the sulfoxide to the copper catalyst. It is believed that NMO coordinates to the copper catalyst, removing sulfoxide, which results in an improvement in yield. Entries 10 and 12 demonstrate that the presence of a CH_2 group between the sulfur and the isopropyl group results in improved enantioselection. However, the opposite trend was observed when the oxidation was carried out in the presence of NMO.

The results of the NMO study indicated that the use of more polar solvents or solvent mixtures may overcome product inhibition by coordinating to the copper catalyst. Katsuki reported an enhancement in the enantioselectivity of the vanadium Schiff base-catalyzed oxidation of thioanisole in the presence of a small amount of methanol.[20] An initial solvent study indicated that low-polarity solvents, such as toluene, benzene, and CCl_4, produced the best results in terms of enantioselectivity, as we had described previously (Table 3).[19]

Depending on the solvent(s) employed, the oxidation system with aqueous hydrogen peroxide was either monophasic or biphasic. When the oxidation was carried out in methanol, there was a large increase in yield, but a decrease in enantioselectivity (Table 3, entry 7) in comparison to the low-polarity solvents. There was no sulfoxide produced when the oxidation was carried out in hexane (Table 3, entry 6). Carrying out the oxidation in a mixed solvent system of toluene−methanol resulted in improved yield, but with a reduced enantioselectivity (Table 3, entries 9−12). However, using a 90:10 hexane−methanol solvent mixture produced benzyl phenyl sulfoxide in excellent yield and good enantioselectivity (Table 3, entry 13). Similar results were achieved using solvent mixtures of hexane and ethanol, and cyclohexane and methanol (Table 3, entries 14 and 15). Interestingly, the use of a mixture of hexane and the bulky alcohol IPA afforded practically racemic sulfoxide (Table 3, entry 16). The use of hexane−methanol (partially miscible) and hexane−ethanol (miscible) solvent mixtures afforded sulfoxide in almost identical yield and enantioselectivity (Table 3, entries 13 and 14). The dramatic improvements in yields using solvent mixtures of methanol are further evidence for sulfoxide inhibition. Presumably, methanol can coordinate to the copper catalyst, thereby displacing the sulfoxide, which results in improved yields.

An extensive ligand study was then undertaken in an attempt to find the optimum ligand for this system (Table 4). The results indicate that ligands **3**, **4**, and **15** perform much better than the other Schiff bases in the oxidation of benzyl phenyl sulfide. Ligand **4** performed the best, producing the sulfoxide in 90% yield and 79% ee. Replacement of the *tert*-butyl with an isopropyl in the R^3 position of the ligand results in a significant reduction in yield and enantioselectivity (Table 4, entries 1 and 6). This indicates that the steric bulk at the R^3 position is crucial to maintaining the enantioselectivity of the oxidation. Interestingly, the diiodo and difluoro ligands **10** and **14** perform poorly in terms of both yield and enantioselectivity (Table 4, entries 3 and 7).

Having established the optimum ligand (ligand **4**) and solvent system (90:10 hexane/methanol), these conditions were then used in the asymmetric oxidation of a range of aryl benzyl and aryl alkyl sulfides, as shown in Table 5. Excellent

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yields and modest to good enantiopurities were obtained; for example, benzyl phenyl sulfoxide was obtained in 90% yield and 79% ee (Table 5, entry 1). Overoxidation to sulfone is either entirely absent or very minimal (no more than 2%) despite the dramatic improvements in oxidation efficiency using the optimized conditions. The formation of significant amounts of sulfone would have a detrimental effect on sulfoxide yield and would lead to difficulties in isolation of the desired product. A relationship between the steric bulk of the R′ substituent of the sulfide and the enantioselectivity of the oxidation was observed again. As R′ is changed from a methyl group to an ethyl group and then to an isopropyl and neopentyl group, there is an increase in enantioselectivity (Table 5, entries 3−7). Interestingly, in Table 5, it is evident that, with the different substrates, in some instances, the enantiopurity achieved was higher with ligand **4**, while in others, it was higher with ligand **15**, although differences are relatively modest in most cases. Thus, the optimum ligand appears to be substrate-specific. Sulfide **5l** did not fully dissolve in 1 mL of 90:10 hexane/methanol, and as a result, an increased amount of solvent was used. This may have resulted in reduced enantioselectivity, as previous work in the group had demonstrated that increasing dilution had a detrimental effect on the enantioselectivity of the oxidation.[21] Sulfide **5i** was insoluble in 9:1 hexane/methanol, and hence no oxidation was observed.

CONCLUSION

Efficient enantioselective sulfide oxidation is effected using copper−Schiff base catalysis. The procedure employed is clean, inexpensive, and is not air-sensitive, utilizing aqueous hydrogen peroxide as the oxidant. An important feature of this oxidation system is that the Schiff base ligand can be recovered after chromatography and can be reused without loss of activity. The use of copper as the transition metal offers significant safety benefits over other established methods, employing other toxic metals. Another important feature of this system is the absence or very limited amount of overoxidation to produce sulfones. Use of a hexane−methanol solvent mixture overcomes catalyst inhibition by the sulfoxide and thereby leads to excellent yields. Steric effects are significant in determining the enantioselectivity of the oxidation.

EXPERIMENTAL SECTION

General. Sulfides **5a**, **5b**, and **5d** were commercially available. For thin-layer chromatography (TLC), silica gel plates were used and compounds were visualized using UV. Solvents were distilled prior to use. ^{1}H (300 MHz), ^{1}H (400 MHz), and ^{13}C NMR (75 MHz) were recorded with spectrometers at 20 °C using $CDCl_3$ as the solvent. Chemical shifts are given in parts per million relative to TMS as the internal standard. Coupling constants (J) are reported in hertz. Chiral HPLC was performed using Chiralpak OD-H, OJ-H, and AS-H columns, eluting with *n*-hexane and 2-propanol. Specific rotations were recorded at 20 °C in the solvents indicated. The Sodium D line (589 nm) was used unless otherwise indicated. Samples were analyzed in a 1 mL dual-walled thermostatted glass cell of path length 10 cm. Sample temperature control was maintained using an immersion circulator. Absolute configurations were assigned by comparison of the specific rotations with the literature data for **6a**, **6b**, and **6d**−**6g**. Notably, the directions of the specific rotations were in complete agreement with literature values; however, the magnitudes varied somewhat. Racemic sulfoxides were prepared by treatment of the sulfide with 0.6 equiv of oxone in acetone at 0 °C. All reactions are carried out at room temperature unless otherwise indicated. Sulfoxides **6a**,[22] **6b**,[23] **6c**,[24] **6d**,[25] **6f**,[26] **6g**,[27] **6j**,[28] **6k**,[29] **6l**,[19] **6m**,[19] and **6p**[30] have been reported in enantioenriched form. Sulfoxides **6e**,[31] **6n**,[32] **6q**,[33] and **6r**[34] have been reported in racemic form only. Sulfoxides **6h**, **6i**, and **6o** have not been previously reported.

EXPERIMENTAL PROCEDURE FOR ASYMMETRIC SULFIDE OXIDATION

Copper(II) acetylacetonate (5.2 mg, 2.0 mol %) was added to a round-bottom flask containing Schiff base ligand **4** (11.6 mg, 4.0 mol %), and 9:1 hexane/MeOH (1 mL). The resulting solution was stirred at room temperature for 5 min, and then a solution of sulfide (1 mmol) in 9:1 hexane/MeOH (1 mL) was added. After 5 min of stirring at r.t., H_2O_2 (0.130 mL, 30%, 1.1 mmol) was added in one portion, dropwise, to the solution. The reaction mixture was stirred at room temperature for a further 16 h. H_2O (1 mL) and CH_2Cl_2 (1 mL) were then added and the phases separated; the organic layer was washed with water (2 × 5 mL) and brine (5 mL), dried, and concentrated under reduced pressure to give the crude product. The ratio of sulfide−sulfoxide−sulfone in the crude product was determined by ^{1}H NMR. The product was purified by column chromatography on silica gel (6:4 hexane/ethyl acetate). The Schiff base ligand can be recovered after chromatography and can be reused.

In experiments in which NMO was used (Table 2), NMO (2.5 mol %) was added 5 min after addition of the sulfide. The reaction mixture was then stirred for 5 min, followed by addition of H_2O_2 (0.130 mL, 30%, 1.1 mmol).

(*R*)-(+)-Benzyl Phenyl Sulfoxide (6a, Table 5, Entry 1).[22] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (1:98:1). Purification by chromatography afforded the product as a white solid (194 mg, 90%, 79% ee).

^{1}H NMR δ_H (300 MHz) 4.00 (1H, A of AB system, J = 12.5 Hz), 4.10 (1H, B of AB system, J = 12.5 Hz), 6.90−7.04 (2H, m), 7.19−7.32 (3H, m), 7.33−7.52 (5H, m); mp 125−126 °C (lit. mp 127 °C);[30] IR (KBr) ν = 2961, 1455, 1442, 1084, 1033, 746 cm^{-1}; HPLC t_R (*R*) = 17.1 min, t_R (*S*) = 21.3 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +146.5° (*c* 1.0, acetone) {ref 22, $[\alpha]_D^{20}$ = −169.8 (*c* 1.0, acetone) for (*S*) 79% ee}.

(*R*)-(+)-Methyl *p*-Tolyl Sulfoxide (6b, Table 5, Entry 3).[23] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (4:96:trace). Purification by chromatography afforded the product as a clear oil (138 mg, 90%, 23% ee).

^{1}H NMR δ_H (400 MHz) 2.42 (3H, s), 2.71 (3H, s), 7.34 (2H, d, J = 8.4 Hz), 7.54 (2H, d, J = 8.4 Hz); HRMS (ESI) exact mass calculated for $C_8H_{10}OS$ [(M + H)$^+$] 155.0531; found, 155.0526; HPLC t_R (*R*) = 20.1 min, t_R (*S*) = 23.8 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (95:5); 20 °C]; $[\alpha]_D^{20}$ = +43.6° (*c* 1.0, acetone) {ref 23, $[\alpha]_D^{20}$ = +150.4 (*c* 1.17, acetone) for (*R*) > 99% ee}.

(*R*)-(+)-Ethyl Phenyl Sulfoxide (6d, Table 5, Entry 4).[25] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (2:98:trace). Purification by chromatography afforded the product as a clear oil (142 mg, 92%, 44% ee).

^{1}H NMR δ_H (400 MHz) 1.20 (3H, t, J = 3.5 Hz), 2.70−3.00 (2H, m), 7.46−7.57 (3H, m), 7.58−7.66 (2H, m); IR (film) ν = 2935, 1479, 1444, 1087, 1021, 749 cm^{-1}; HRMS (ESI) exact mass calculated for $C_8H_{10}OS$ [(M + H)$^+$] 155.0531; found, 155.0532; HPLC t_R (*R*) = 8.1 min, t_R (*S*) = 9.8 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; = +96.1° (*c* 1.0, acetone) {ref 25, $[\alpha]_D^{20}$ = +185.6 (*c* 0.71, acetone) for (*R*) > 99% ee}.

(*R*)-(+)-Isopropyl Phenyl Sulfoxide (6f, Table 5, Entry 5).[26] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (19:81:trace). Purification by chromatography afforded the product as a clear oil (124 mg, 74%, 60% ee).

^{1}H NMR δ_H (400 MHz) 1.15 (3H, d, J = 6.6 Hz), 1.23 (3H, d, J = 6.6 Hz), 2.75−2.91 (1H, m), 7.44−7.62 (5H, m); ^{13}C NMR δ_C (75 MHz) 14.0, 15.9, 54.6, 125.0, 128.9, 131.0, 141.7; IR (KBr) ν = 2970, 1464, 1444, 1088, 1023 cm^{-1}; HPLC t_R (*R*) = 6.6 min, t_R (*S*) = 7.5 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +112.8 (*c* 1.0, $CHCl_3$).

(*R*)-(+)-Isobutyl Phenyl Sulfoxide (6g, Table 5, Entry 6).[27] Crude product contained a mixture of sulfide, sulfoxide, and sulfone

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(10:90:trace). Purification by chromatography afforded the product as a clear oil (149 mg, 82%, 48% ee).

^{1}H NMR δ_H (400 MHz) 1.07 (3H, d, J = 6.6 Hz), 1.17 (3H, d, J = 6.6 Hz), 2.14−2.33 (1H, m), 2.45 (1H, A of ABX system, J = 12.0 and 4.8 Hz), 2.82 (1H, B of ABX system, J = 12.0 and 4.8 Hz), 7.43−7.58 (3H, m), 7.59−7.69 (2H, m); ^{13}C NMR δ_C (75 MHz) 21.7, 22.8, 24.2, 67.6, 123.9, 129.3, 130.9, 144.7; HRMS (ESI) exact mass calculated for $C_{10}H_{14}SO$ [(M + H)$^+$] 183.0844; found, 183.0850; IR (KBr) ν = 2960, 1465, 1444, 1090, 1038, 750 cm^{-1}; HPLC t_R (R) = 5.9 min, t_R (S) = 6.7 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +129.0 (c 1.0, $CHCl_3$).

(*R*)-(+)-Neopentyl Phenyl Sulfoxide (6h, Table 5, Entry 7). Crude product contained a mixture of sulfide and sulfoxide (15:85). Purification by chromatography afforded the product as a clear oil (155 mg, 79%, 71% ee).

^{1}H NMR δ_H (300 MHz) 1.21 (9H, s), 2.54 (1H, A of AB system, J = 13.5 Hz), 2.81 (1H, B of AB system, J = 13.8 Hz), 7.43−7.56 (3H, m), 7.59−7.66 (2H, m); ^{13}C NMR δ_C (75 MHz) 29.8, 32.0, 73.9, 123.8, 129.2, 130.7, 145.6; (found C, 67.10; H, 8.37; S, 16.29; $C_{11}H_{16}OS$ requires C, 67.30; H, 8.22; S 16.33); IR (film) ν = 2958, 1474, 1448, 1084, 1045, 709 cm^{-1}; HPLC t_R (R) = 6.6 min, t_R (S) = 7.6 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +87.9 (c 1.0, $CHCl_3$).

(*R*)-(+)-Benzyl *p*-Tolyl Sulfoxide (6j, Table 5, Entry 8).[28] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (2:97:1). Purification by chromatography afforded the product as a white solid (209 mg, 91%, 81% ee).

^{1}H NMR δ_H (300 MHz) 2.40 (3H, s), 3.97 (1H, A of AB system, J = 12.6 Hz), 4.09 (1H, B of AB system, J = 12.6 Hz), 7.00 (2H, dd, J = 7.5 Hz and J = 1.5 Hz), 7.17−7.37 (7H, m); HRMS (ESI) exact mass calculated for $C_{14}H_{14}SO$ [(M + H)$^+$] 231.0844; found, 231.0839; IR (KBr) ν = 2912, 1494, 1456, 1083, 1014, 768 cm^{-1}; HPLC t_R (R) = 16.3 min, t_R (S) = 19.9 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +106.0 (c 1.0, acetone), {ref 30, $[\alpha]_D^{20}$ = −254.0 (c 0.7, acetone) for (S) > 99% ee}.

(*R*)-(+)-4-Methoxybenzyl 4′-Methylphenyl Sulfoxide (6k, Table 5, Entry 10).[29] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (2:97:1). Purification by chromatography afforded the product as a white solid (234 mg, 90%, 47% ee).

mp 123−124 °C; ^{1}H NMR δ_H (300 MHz) 2.40 (3H, s), 3.79 (3H, s), 3.93 (1H, A of AB system, J = 12.6 Hz), 4.03 (1H, B of AB system, J = 12.6 Hz), 6.75−6.81 (2H, m), 6.87−6.94 (2H, m), 7.19−7.32 (4H, m); ^{13}C NMR δ_C (75.5 MHz) 21.5, 55.3, 63.0, 113.9, 121.2, 124.5, 129.6, 131.6, 139.6, 141.5, 159.6; IR (KBr) ν = 2961, 1610, 1514, 1036, 809 cm^{-1}; HRMS (ESI) exact mass calculated for $C_{15}H_{16}SO_2$ [(M + H)$^+$] 261.0949; found, 261.0947; HPLC t_R (R) = 12.7 min, t_R (S) = 15.9 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +37.9 (c 1.0, $CHCl_3$), {ref 29, $[\alpha]_D^{20}$ = −87 (c 0.2, $CHCl_3$) for (S) > 99% ee}.

(*R*)-(+)-Benzyl 2-Methoxyphenyl Sulfoxide (6l, Table 5, Entry 11).[19] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (8:92:trace). Purification by chromatography afforded the product as a white solid (209 mg, 85%, 29% ee).

mp 31−33 °C; ^{1}H NMR δ_H (300 MHz) 3.87 (3H, s), 3.98 (1H, A of AB system, J = 12.0 Hz), 4.24 (1H, B of AB system, J = 12.0 Hz), 6.90 (1H, d, J = 7.8 Hz), 6.99−7.11 (3H, m), 7.17−7.30 (3H, m), 7.36−7.49 (2H, m); ^{13}C NMR δ_C (75.5 MHz) 55.8, 59.7, 110.3, 121.5, 125.8, 127.9, 128.2, 130.2, 130.3, 130.4, 132.0, 155.1; IR (KBr) ν = 2959, 1596, 1496, 1086, 1032, 697 cm^{-1}; HRMS (ESI) exact mass calculated for $C_{14}H_{14}SO_2$ [(M + H)$^+$] 247.0793; found, 247.0783; HPLC t_R (R) = 16.2 min, t_R (S) = 18.6 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +60.3 (c 1.0, acetone), {ref 19, $[\alpha]_D^{20}$ = +351 (c 0.32, $CHCl_3$) for (R) = 81% ee}.

(*R*)-(+)-Benzyl 3-Methoxyphenyl Sulfoxide (6m, Table 5, Entry 12).[19] Crude product contained a mixture of sulfide and sulfoxide (46:54). Purification by chromatography afforded the product as a clear oil (115 mg, 47%, 21% ee).

^{1}H NMR δ_H (300 MHz) 3.72 (3H, s), 4.00 (1H, A of AB system, J = 12.5 Hz), 4.07 (1H, B of AB system, J = 12.5 Hz) 6.87−7.03 (5H, m), 7.20−7.37 (4H, m); ^{13}C NMR δ_C (75 MHz) 55.5, 63.5, 108.4, 116.5, 118.1, 128.3, 128.5, 129.1, 129.8, 130.4, 144.0, 160.1; IR (KBr) ν = 2907, 1594, 1481, 1248, 1031, 697 cm^{-1}; HRMS (ESI) exact mass calculated for $C_{14}H_{14}SO_2$ [(M + H)$^+$] 247.0793; found, 247.0789; HPLC t_R (R) = 12.2 min, t_R (S) = 14.0 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +68.5 (c 1.0, acetone), {ref 19, $[\alpha]_D^{20}$ = +73.5 (c 0.17, acetone) for (R) = 69% ee}.

(*R*)-(+)-Benzyl *o*-Tolyl Sulfoxide (6n, Table 5, Entry 13).[32] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (1:98:1). Purification by chromatography afforded the product as a white solid (209 mg, 91%, 64% ee).

mp 69−71 °C; ^{1}H NMR δ_H (300 MHz) 2.06 (3H, s), 4.00 (1H, A of AB system, J = 12.3 Hz), 4.10 (1H, B of AB system, J = 12.6 Hz), 6.97 (2H, dd, J = 7.8 Hz and J = 1.3 Hz), 7.06−7.16 (1H, m), 7.19−7.41 (5H, m), 7.67−7.78 (1H, m); ^{13}C NMR δ_C (75.5 MHz) 18.0, 62.3, 124.2, 127.1, 128.3, 128.5, 129.3, 130.2, 130.4, 130.9, 135.6, 141.3; ESI-HRMS calcd for $C_{14}H_{14}OS$ [(M + H)$^+$] 231.0844; found, 231.0855 (found C, 73.06; H, 6.12; S, 14.20; $C_{14}H_{14}OS$ requires C, 73.01; H, 6.13; S 13.92); HPLC t_R (R) = 11.2 min, t_R (S) = 13.2 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +18.5 (c 1.0, $CHCl_3$).

(*R*)-(+)-Benzyl *m*-Tolyl Sulfoxide (6o, Table 5, Entry 15). Crude product contained a mixture of sulfide, sulfoxide, and sulfone (11:89:0). Purification by chromatography afforded the product as a clear oil (193 mg, 84%, 62% ee).

^{1}H NMR δ_H (300 MHz) 2.34 (3H, s) 3.97 (1H, A of AB system, J = 12.6 Hz), 4.08 (1H, B of AB system, J = 12.3 Hz), 7.00 (2H, dd, J = 7.8 Hz and J = 2.1 Hz), 7.10−7.34 (7H, m); ^{13}C NMR δ_C (75.5 MHz) 21.3, 63.7, 121.5, 124.7, 128.2, 128.4, 128.6, 129.3, 130.4, 131.9, 139.1, 142.7; IR (film) ν = 2919, 1454, 1038, 766 cm^{-1}; ESI-HRMS calcd for $C_{14}H_{14}OS$ [(M + H)$^+$] 231.0844; found, 231.0840 (found C, 72.96; H, 6.28; S, 14.0; $C_{14}H_{14}OS$ requires C, 73.01; H, 6.13; S 13.92); HPLC t_R (R) = 15.1 min, t_R (S) = 18.9 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +48.6 (c 1.0, $CHCl_3$).

(*R*)-(+)-4-Methylbenzyl Phenyl Sulfoxide (6p, Table 5, Entry 17).[30] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (1:97:2). Purification by chromatography afforded the product as a white solid (205 mg, 89%, 55% ee).

^{1}H NMR δ_H (300 MHz) 2.32 (3H, s), 3.96 (1H, A of AB system, J = 12.6 Hz), 4.07 (1H, B of AB system, J = 12.6 Hz), 6.87 (2H, d, J = 7.8 Hz), 7.06 (2H, d, J = 7.8 Hz), 7.36−7.51 (5H, m); IR (KBr) ν = 2959, 1512, 1442, 1043, 687 cm^{-1} (found C, 73.12; H, 6.33; S, 13.94; $C_{14}H_{14}OS$ requires C, 73.01; H, 6.13; S 13.92); HPLC t_R (R) = 12.7 min, t_R (S) = 14.3 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +42.2 (c 1.0, $CHCl_3$).

(*R*)-(+)-3-Methylbenzyl Phenyl Sulfoxide (6q, Table 5, Entry 18).[33] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (7:92:1). Purification by chromatography afforded the product as a clear oil (191 mg, 83%, 50% ee).

^{1}H NMR δ_H (300 MHz) 2.27 (3H, s), 3.94 (1H, A of AB system, J = 12.3 Hz), 4.08 (1H, B of AB system, J = 12.6 Hz), 6.80 (2H, d, J = 5.7 Hz), 7.06−7.19 (2H, m), 7.36−7.51 (5H, m); ^{13}C NMR δ_C (75 MHz) 21.3, 63.9, 124.5, 127.4, 128.4, 128.8, 129.0, 129.1, 131.1, 131.2, 138.2, 143.0; IR (KBr) ν = 2967, 1604, 1444, 1040, 736 cm^{-1}; ESI-HRMS calcd for $C_{14}H_{14}OS$ [(M + H)$^+$] 231.0844; found, 231.0846 (found C, 73.42; H, 6.13; S, 13.97; $C_{14}H_{14}OS$ requires C, 73.01; H, 6.13; S, 13.92); HPLC t_R (R) = 16.2 min, t_R (S) = 18.7 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +36.8 (c 1.0, $CHCl_3$).

(-)-2-Methylbenzyl Phenyl Sulfoxide (6r, Table 5, Entry 20).[34] Crude product contained a mixture of sulfide, sulfoxide, and sulfone (12:85:2). Purification by chromatography afforded the product as a clear oil (184 mg, 80%, 47% ee).

^{1}H NMR δ_H (300 MHz) 2.18 (3H, s), 3.99 (1H, A of AB system, J = 12.3 Hz), 4.27 (1H, B of AB system, J = 12.3 Hz), 6.85 (1H, d, J = 6.6 Hz), 7.02−7.25 (3H, m), 7.35−7.52 (5H, m); IR (KBr) ν = 2926, 1443, 1094, 1030, 750 cm^{-1} (found C, 73.19; H, 6.02; S, 13.85; $C_{14}H_{14}OS$ requires C, 73.01; H, 6.13; S, 13.92); HPLC t_R = 67.1 min, t_R = 85.3 min [Chiracel AS-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 20 °C]; $[\alpha]_D^{20}$ = −16.5 (c 1.0, $CHCl_3$).

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(*R*)-(+)-4-Methylphenyl prop-2′-ynyl Sulfoxide (6c, Table 2, Entry 7).[24] Crude product contained a mixture of sulfide and sulfoxide (78:22). Purification by chromatography afforded the product as a white solid (23 mg, 14%, 4% ee).

^{1}H NMR δ_H (300 MHz) 2.33 (1H, t, J = 2.7 Hz), 2.44 (3H, s), 3.59 (1H, A of ABX system, J_{AB} = 14.2 Hz, J_{AX} = 2.6 Hz), 3.67 (1H, B of ABX system, J_{AB} = 14.4 Hz, J_{BX} = 2.6 Hz) 7.35 (2H, d, J = 8.3 Hz), 7.61 (2H, d, J = 8.2 Hz); HPLC t_R (R) = 14.6 min, t_R (S) = 17.5 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 20 °C]; $[\alpha]_D^{20}$ = +5.2 (c 1.0, $CHCl_3$).

(*R*)-(+)-2-Naphthylmethyl Phenyl Sulfoxide (6i, Table 2, Entry 14). Crude product contained a mixture of sulfide and sulfoxide (45:55). Purification by chromatography afforded the product as a white solid (80 mg, 30%, 93% ee).

mp 85−87 °C; ^{1}H NMR δ_H (400 MHz) 4.15 (1H, A of AB system, J = 12.4 Hz), 4.26 (1H, B of AB system, J = 12.4 Hz), 7.08 (1H, dd, J = 8.6 Hz and J = 1.6 Hz), 7.31−7.53 (8H, m), 7.66−7.85 (3H, m); ^{13}C NMR δ_C (75 MHz) 64.0, 124.5, 126.3, 126.4, 126.7, 127.7, 127.75, 127.9, 128.1, 128.9, 129.8, 131.2, 132.9, 133.1, 142.9 (found C, 76.43; H, 5.58; S, 12.10; $C_{17}H_{14}OS$ requires C, 76.66; H, 5.30; S, 12.04); HPLC t_R (R) = 32.1 min, t_R (S) = 40.6 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 20 °C]; $[\alpha]_D^{20}$ = +75.4 (c 1.0, $CHCl_3$).

(*R*)-(+)-Benzyl 4-Methoxyphenyl Sulfoxide (2d, Table 1, Entry 4).[19,35] Crude product contained a mixture of sulfide and sulfoxide (54:46). Purification by chromatography afforded the product as a white solid (81 mg, 33%, 54% ee).

^{1}H NMR δ_H (300 MHz) 3.84 (3H, s), 3.95 (1H, A of AB system, J = 12.0 Hz), 4.11 (1H, B of AB system, J = 12.0 Hz), 6.89−7.02 (4H, m), 7.20−7.33 (5H, m), δ_C (75.5 MHz) 55.5, 63.8, 114.4, 126.4, 128.2, 128.5, 129.3, 130.4, 133.6, 162.0; HPLC t_R (R) = 15.5 min, t_R (S) = 18.4 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 40 °C]; $[\alpha]_D^{20}$ = +48.2 (c 1.0, acetone), {ref 19, $[\alpha]_D^{20}$ = +31.9 (c 0.28, acetone) for (R) = 44% ee}.

(*R*)-(+)-Cyclohexylmethyl Phenyl Sulfoxide (6e, Table 2, Entry 5).[31] Crude product contained a mixture of sulfide and sulfoxide (71:29). Purification by chromatography afforded the product as a clear oil that solidified to form a white solid (44 mg, 20%, 60% ee).

^{1}H NMR δ_H (300 MHz) 1.01−1.41 (5H, m), 1.60−1.83 (4H, m), 1.89−2.08 (1H, m), 2.09−2.17 (1H, m), 2.45−2.52 (1H, A of ABX system, J = 12.9 and 9.0 Hz), 2.76−2.82 (1H, B of ABX system, J = 12.9 and 4.8 Hz), 7.42−7.72 (5H, m); IR (KBr) ν = 2920, 1443, 1034, 752 cm^{-1}; HPLC t_R (R) = 17.3 min, t_R (S) = 20.3 min [Chiracel OD-H; flow rate = 1 mL min^{-1}; hexane-2-PrOH (90:10); 20 °C]; $[\alpha]_D^{20}$= +47.8 (c 1.0, $CHCl_3$).

EXPERIMENTAL PROCEDURE FOR SCHIFF BASE LIGAND SYNTHESIS

Commercially available salicylaldehyde (1 mmol) and sodium sulfate (0.5 g) were added to a solution of (*S*)-*tert*-leucinol (1 mmol) or L-valinol (1 mmol) in ethanol (20 mL). The reaction mixture was stirred under reflux for 16 h, filtered, and concentrated under reduced pressure. The reaction mixture was then dissolved in dichloromethane (10 mL) and washed with water (3 × 10 mL) and brine (15 mL). The organic layer was dried and concentrated under reduced pressure to leave the crude product, which was purified by column chromatography on silica gel (8:2 hexane/ethyl acetate) to yield the pure ligand.

(*S*)-2-(*N*-3′,5′-Dibromosalicylidene)-amino-3,3-dimethyl-1-butanol (3, Table 4):.[36,37] Yellow solid, 73%, mp 160−162 °C; ^{1}H NMR δ_H (300 MHz) 1.01 (9H, s), 3.10 (1H, dd, J = 9.5 and 2.4 Hz), 3.11 (1H, brs), 3.70 (1H, dd, J = 11.2 and 9.8 Hz), 3.98−4.08 (1H, brm), 7.35 (1H, d, J = 2.5 Hz), 7.58 (1H, d, J = 2.4 Hz), 8.12 (1H, s); ^{13}C NMR δ_C (75.5 MHz) 27.3, 33.4, 62.2, 79.2, 107.9, 114.8, 118.2, 133.8, 139.1, 162.9, 164.9; m/z (ESI) [(M + H)$^+$] 378; HRMS (ESI) exact mass calculated for $C_{13}H_{17}{}^{79}Br_2NO_2$ [(M + H)$^+$] 377.9704; found, 377.9710; $[\alpha]_D^{20}$ = −16.1 (c 1.0, acetone).

(*S*)-2-(*N*-3′,5′-Dichlorosalicylidene)-amino-3,3-dimethyl-1-butanol (4, Table 4): Yellow solid, 72%, mp 153−156 °C; ^{1}H NMR δ_H (300 MHz) 1.02 (9H, s), 3.11 (1H, dd, J = 9.5 and 2.4 Hz), 3.69 (1H, dd, J = 11.2 and 9.8 Hz), 3.82−4.10 (1H, brs), 3.96−4.06 (1H, brm), 7.04 (1H, d, J = 2.5 Hz), 7.27 (1H, d, J = 2.4 Hz), 8.12 (1H, s); ^{13}C NMR δ_C (75.5 MHz) 26.9, 32.9, 61.7, 78.5, 116.9, 120.2, 124.5, 129.6, 133.4, 162.3, 164.8; m/z (ESI) [(M + H)$^+$] 290; HRMS (ESI) exact mass calculated for $C_{13}H_{17}Cl_2NO_2$ [(M + H)$^+$] 290.0715; found, 290.0723; IR ν_{max}/cm^{-1} (KBr) 3322, 2971, 1645, 1502 1209, 1058 (found C, 54.07; H, 5.91; N, 4.64; $C_{13}H_{17}Cl_2NO_2$ requires C, 53.81; H, 5.90; N, 4.64); $[\alpha]_D^{20}$ = −23.6 (c 1.0, acetone).

(*S*)-2-(*N*-3,5-Diiodosalicylidene)-amino-3,3-dimethyl-1-butanol (10, Table 4):.[22,36] Yellow solid, 79%, mp 164−165 °C (lit. mp 163−164);[22] ^{1}H NMR δ_H (300 MHz) 1.00 (9H, s), 2.53 (1H, brs), 3.08 (1H, dd, J = 9.5 and 2.5 Hz), 3.68 (1H, dd, J = 11.1 and 9.8 Hz), 3.93−4.07 (1H, brm), 7.51 (1H, d, J = 2.1 Hz), 8.01 (1H, d, J = 2.1 Hz), 8.10 (1H, s); IR ν_{max}/cm^{-1} (KBr) 3320, 2965, 1638, 1479, 1217, 1060; $[\alpha]_D^{20}$ = −18.5 (c 0.1, acetone), lit.[22] $[\alpha]_D^{20}$ = −16.6 (c 1.0 for *S* in acetone).

(*S*)-2-(*N*-3′-*tert*-Butylsalicylidene)-amino-3,3-dimethyl-1-butanol (11, Table 4):.[37] Yellow oil, 88%; ^{1}H NMR δ_H (300 MHz) 0.99 (9H, s), 1.44 (9H, s), 2.93 (1H, dd, J = 9.4 and 2.7 Hz), 3.73 (1H, dd, J = 11.0 and 9.7 Hz), 3.90 (1H, dd, J = 11.1 and 2.8 Hz), 6.84 (1H, t, J = 7.5 Hz), 7.15 (1H, dd, J = 7.6 and 1.6 Hz), 7.35 (1H, dd, J = 7.6 and 1.6 Hz), 8.42 (1H, s); IR ν_{max}/cm^{-1} (film) 3367, 2959, 1633, 1458, 1436; $[\alpha]_D^{20}$ = −54.3 (c 0.3, acetone).

(*S*)-2-(*N*-5′-*tert*-Butylsalicylidene)-amino-3,3-dimethyl-1-butanol (12, Table 4).[38] Yellow solid, 82%, mp 119−120 °C; ^{1}H NMR δ_H (300 MHz) 0.96 (9H, s), 1.31 (9H, s), 1.62 (1H, brs), 2.93 (1H, dd, J = 9.5 and 2.8 Hz), 3.75 (1H, dd, J = 11.0 and 9.6 Hz), 3.92 (1H, dd, J = 11.1 and 2.8 Hz), 6.91 (1H, d, J = 8.6 Hz), 7.26−7.28 (1H, m), 7.36 (1H, dd, J = 8.6 and 2.5 Hz), 8.36 (1H, s); ^{13}C NMR δ_C (75.5 MHz) 27.0, 31.4, 33.2, 34.0, 62.5, 81.3, 116.5, 117.8, 128.0, 129.8, 141.5, 158.9, 166.4 (HC═N); IR ν_{max}/cm^{-1} (KBr) 3422, 2958, 1633, 1493 (found C, 73.31; H, 9.89; N, 5.12; $C_{17}H_{27}NO_2$ requires C, 73.61; H, 9.81; N, 5.05); $[\alpha]_D^{20}$ = −46.8 (c 0.3, acetone).

(*S*)-2-(*N*-3′,5′-Dibromosalicylidene)-amino-3-methyl-1-butanol (13, Table 4). Yellow solid, 76%, mp 136−138 °C; ^{1}H NMR δ_H (300 MHz) 0.99 (3H, d, J = 6.7 Hz), 1.01 (3H, d, J = 6.7 Hz), 1.88−2.07 (1H, m), 3.17−3.30 (1H, m), 3.65−3.80 (1H, m), 3.99 (1H, dd, J = 11.4 and 2.6 Hz), 7.25 (1H, d, J = 2.5 Hz), 7.60 (1H, d, J = 2.5 Hz) 8.14 (1H, s); ^{13}C NMR δ_C (75.5 MHz) 18.4, 19.8, 29.6, 64.0, 74.8, 107.2, 114.8, 117.6, 133.5, 138.8, 163.0, 164.6; m/z IR (KBr) ν_{max}/cm^{-1} 3259, 2965, 1645, 1497, 1212, 1043, 857, 690 (found C, 39.73; H, 4.14; N, 3.57; $C_{12}H_{15}Br_2NO_2$ requires C, 39.48; H, 4.14; N, 3.84); $[\alpha]_D^{20}$ = −9.1 (c 1.0, acetone).

(*S*)-2-(*N*-3′,5′-Difluorosalicylidene)-amino-3,3-dimethyl-1-butanol (14, Table 4). Yellow solid, 57%, mp 161−163 °C; ^{1}H NMR δ_H (300 MHz) 0.99 (9H, s), 2.08 (1H, brs), 3.01 (1H, dd, J = 9.6 and 2.7 Hz), 3.70 (1H, dd, seen as t, J = 9.9 and 9.9 Hz), 3.99 (1H, brd, J = 9.8 Hz), 6.75−6.82 (1H, m), 6.86−6.96 (1H, m), 8.26 (1H, s); ^{13}C NMR δ_C (75.5 MHz) 26.9, 33.1, 62.0, 80.4, 107.4−108.0 (m), 111.2−111.5 (m), 164.6; m/z (ESI) [(M + H)$^+$] 258; HRMS (ESI) exact mass calculated for $C_{13}H_{17}F_2NO_2$ [(M + H)$^+$] 258.1328; found, 258.1317; IR (KBr) ν_{max}/cm^{-1} 3308, 2966, 1638, 1479, 1215, 1059, 857; $[\alpha]_D^{20}$ = −35.6 (c 0.5, acetone).

(*S*)-2-(*N*-3′-Chloro-5′-fluorosalicylidene)-amino-3,3-dimethyl-1-butanol (15, Table 4). Yellow solid, 75%, mp 103−105 °C; ^{1}H NMR δ_H (300 MHz) 1.00 (9H, s), 2.81 (1H, bs), 3.06 (1H, dd, J = 9.6 and 2.4 Hz), 3.70 (1H, overlapping dd, J = 11.1 and 9.6 Hz), 3.99 (1H, dd, J = 11.4 and 2.7 Hz), 6.87 (1H, dd, J = 8.1 and 3.0 Hz), 7.14 (1H, dd, J = 8.1 and 3.0 Hz), 8.22 (1H, s); ^{13}C NMR δ_C (75.5 MHz) 26.9, 33.0, 61.9, 79.8, 115.2, 117.0 (d, $^3J_{CF}$ = 8 Hz), 121.0 (d, $^2J_{CF}$ = 26 Hz), 122.8 (d, $^3J_{CF}$ = 10 Hz), 153.4 (d, $^1J_{CF}$ = 239 Hz), 157.0, 164.6 (d, $^4J_{CF}$ = 3 Hz, HC═N); m/z (ESI) [(M + H)$^+$] 274; HRMS (ESI) exact mass calculated for $C_{13}H_{17}FClNO_2$ [(M + H)$^+$] 274.1010; found, 274.1006; IR (KBr) ν_{max}/cm^{-1} 3288, 2973, 1643, 1471, 1366, 1209, 1063, 803 (found C, 57.41; H, 6.30; N, 5.24; $C_{13}H_{17}ClFNO_2$ requires C, 57.04; H, 6.26; N, 5.12); $[\alpha]_D^{20}$ = −27.4 (c 1.0, acetone).

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EXPERIMENTAL PROCEDURE FOR SYNTHESIS OF SULFIDES

Method A.[39] This method was used for the synthesis of sulfides **5e**−**5g**, **5i**−**5r**, and **1d**.

The thiolate anion was first prepared by treatment of the thiol with an excess of sodium ethoxide. The thiolate anion was then treated with an equimolar amount of aryl or alkyl halide and stirred for 16 h at room temperature. Water (20 mL) and dichloromethane (20 mL) were added to the flask. The layers were separated, and the aqueous layer was extracted with dichloromethane (10 mL). The combined organic layers were washed with aqueous sodium hydroxide (2 M, 3 × 20 mL) and brine (20 mL), dried, filtered, and concentrated under reduced pressure to give the sulfides, which were purified by column chromatography.

Method B.[40] This method was used for the synthesis of neopentyl phenyl sulfide, **5h**.

1-Bromo-2,2-dimethyl propane (3.02 g, 20 mmol), aqueous benzenethiolate (20 mmol), and Aliquat 336 (0.033 mol equiv) were added to a 2-neck round-bottom flask under nitrogen. The mixture was heated at 70 °C with vigorous stirring for 16 h. After the mixture had cooled to room temperature, the organic layer was separated and the aqueous phase was extracted with two 20 mL portions of diethyl ether. The combined organic phases were washed with 20 mL of 10% aqueous sodium chloride and dried over magnesium sulfate. After removal of the solvent, the resulting residual oil was distilled using a Kugelrohr apparatus to give neopentyl phenyl sulfide, bp 145−147° (0.1 mm. Hg).

Method C.[41] This method was used for the synthesis of 4-methylphenyl prop-2′-ynyl sulfide, **5c**.

NaH (0.72 g of 67% dispersion in mineral oil, 20 mmol) was added to a two-neck flask under nitrogen. After washing with hexane (3 × 5 mL), dry dimethylformamide (DMF) (15 mL) was added to the flask and the mixture was stirred for 5 min. The reaction mixture was cooled to 0 °C, and 4-methylbenzene thiol (20 mmol, 2.48 g) was added slowly. After stirring for 5 min, a solution of propargyl bromide (20 mmol, 1.72 mL) in DMF (10 mL) was added. The mixture was removed from the ice bath, allowed to return to room temperature, and stirred for 16 h under nitrogen. HCl (2 M, 20 mL) and dichloromethane (20 mL) were added to the flask. The layers were separated, and the organic layers were washed with aqueous HCl (2 M, 3 × 20 mL) and brine (15 mL), dried, and concentrated under reduced pressure, to yield the crude product as a yellow oil. This was purified by column chromatography on silica gel (100% hexane) to yield the product.

4-Methylphenyl prop-2′-ynyl Sulfide[41] **(5c).** Clear oil, 47%; ^{1}H NMR δ_H (400 MHz) 2.23 (1H, t, J = 2.6 Hz), 2.34 (3H, s), 3.56 (2H, d, J = 2.6 Hz), 7.14 (2H, d, J = 8.5 Hz), 7.38 (2H, d, J = 8.5 Hz); IR (film) ν_{max}/cm^{-1} 2117, 1231, 643.

Cyclohexylmethyl Phenyl Sulfide[42] **(5e):** Clear oil, 95%; ^{1}H NMR δ_H (400 MHz) 0.89−1.08 (2H, m), 1.10−1.32 (3H, m), 1.45−1.80 (4H, m), 1.82−1.94 (2H, m), 2.80 (2H, d, J = 6.8 Hz) 7.09−7.18 (1H, m), 7.21−7.38 (4H, m); IR (film) ν_{max}/cm^{-1} 2924, 1584, 1480, 1448, 736.

Isopropyl Phenyl Sulfide[43] **(5f):** Clear oil, 70%; ^{1}H NMR δ_H (300 MHz) 1.29 (6H, d, J = 6.9 Hz), 3.30−3.45 (1H, m), 7.18−7.33 (3H, m), 7.38−7.42 (2H, m); ^{13}C NMR δ_C (75 MHz) 23.1, 38.2, 126.7, 128.8, 131.9, 135.5; IR (film) ν_{max}/cm^{-1} 2962, 2925, 1584, 1480, 1439, 1026, 741, 692.

Isobutyl Phenyl Sulfide[44] **(5g):** Clear oil, 97%; ^{1}H NMR δ_H (300 MHz) 1.03 (6H, d, J = 6.6 Hz), 1.79−1.94 (1H, m), 2.81 (2H, d, J = 6.6 Hz), 7.11−7.19 (1H, m), 7.22−7.35 (4H, m); ^{13}C NMR δ_C (75 MHz) 22.1, 28.3, 42.6, 125.6, 128.8, 128.8, 137.4; IR (film) ν_{max}/cm^{-1} 2958, 2927, 1586, 1481, 1438, 1026, 737, 690.

Neopentyl Phenyl Sulfide[40] **(5h):** Clear oil, 37%; ^{1}H NMR δ_H (300 MHz) 1.04 (9H, s), 2.90 (2H, s), 7.10−7.18 (1H, m), 7.21−7.30 (2H, m), 7.32−7.38 (2H, m); ^{13}C NMR δ_C (75 MHz) 29.1, 32.5, 48.6, 125.5, 128.8, 128.9, 138.5; IR (film) ν_{max}/cm^{-1} 2958, 2907, 1584, 1480, 1438, 1026, 736, 690.

2-Naphthylmethyl Phenyl Sulfide[45] **(5i):** White solid, 82%; ^{1}H NMR δ_H (300 MHz) 4.26 (2H, s), 7.11−7.27 (3H, m), 7.28−7.36 (2H, m), 7.38−7.51 (3H, m), 7.63−7.85 (4H, m); ^{13}C NMR δ_C (75 MHz) 39.5, 125.8, 126.1, 126.5, 127.0, 127.4, 127.7, 127.7, 128.3, 128.9, 130.1, 132.6, 133.3, 134.9, 136.3 ($C_{Ar(q)}$); IR (KBr) ν_{max}/cm^{-1} 3048, 2917, 1438, 832, 738.

Benzyl-(4-methylphenyl)-sulfide[39] **(5j):** White solid, 76%, mp 42−43 °C (lit. 45 °C);[8] ^{1}H NMR δ_H (300 MHz) 2.30 (3H, s), 4.06 (2H, s), 7.05 (2H, d, J = 8.2 Hz), 7.15−7.32 (7H, m); ^{13}C NMR δ_C (75.5 MHz) 21.0, 39.7, 127.1, 128.4, 128.8, 129.6, 130.7, 132.4, 136.5, 137.8; ν_{max}/cm^{-1} (KBr) 2921, 1494, 1454, 1265, 740, 697;

4-Methoxybenzyl-(4′-methylphenyl)-sulfide[39] **(5k):** White solid, 75%, mp 65−67 °C, (lit. 67 °C);[46] ^{1}H NMR δ_H (300 MHz) 2.30 (3H, s,), 3.78 (3H, s), 4.03 (2H, s), 6.76−6.84 (2H, m), 7.03−7.11 (2H, m), 7.13−7.28 (4H, m); ^{13}C NMR δ_C (75.5 MHz) 21.0, 39.2, 55.3, 113.9, 129.6, 129.8, 129.9, 130.7, 132.7, 136.5, 158.7; IR ν_{max}/cm^{-1} (KBr) 2958, 2833, 1609, 1510, 1492, 1241, 1174, 1030, 799; m/z (ESI) [(M + OH)$^+$] 261; HRMS (ESI) exact mass calculated for $C_{15}H_{16}OS$ [(M + OH)$^+$] 261.0949; found, 261.0937.

Benzyl-(2-methoxyphenyl)-sulfide[47,48] **(5l):** White solid, 55%, mp 68−70 °C; ^{1}H NMR δ_H (300 MHz) 3.88, 4.09 (2H, s), 6.79−6.91 (2H, m), 7.12−7.35 (7H, m); ^{13}C NMR δ_C (75.5 MHz) 37.3, 55.8, 110.5, 121.0, 124.5, 127.0, 127.6, 128.4, 128.9, 130.5, 137.5, 157.6; IR ν_{max}/cm^{-1} (KBr) 2934, 1577, 1476, 1245, 1071, 1025, 747; m/z (ESI) [(M + OH)$^+$] 247; HRMS (ESI) exact mass calculated for $C_{14}H_{14}OS$ [(M + OH)$^+$] 247.0793; found, 247.0799.

Benzyl-(3-methoxyphenyl)-sulfide[47] **(5m):** Clear oil, 83%; ^{1}H NMR δ_H (300 MHz) 3.73 (3H, s,), 4.12 (2H, s), 6.67−6.75 (1H, m), 6.80−6.85 (1H, m), 6.87−6.94 (1H, m), 7.12−7.35 (6H, m); ^{13}C NMR δ_C (75.5 MHz) 38.9, 55.2, 112.2, 114.8, 121.8, 127.2, 128.5, 128.8, 129.7, 137.4, 137.8, 159.7; IR ν_{max}/cm^{-1} (film) 3062, 3029, 2936, 1590, 1479, 1249, 1043, 769; m/z (ESI) [(M + OH)$^+$] 247; HRMS (ESI) exact mass calculated for $C_{14}H_{14}OS$ [(M + OH)$^+$] 247.0793; found, 247.0796.

Benzyl *o*-Tolyl Sulfide[49] **(5n):** Clear oil, 90%; ^{1}H NMR δ_H (300 MHz) 2.32 (3H, s), 4.08 (2H, s), 7.04−7.18 (3H, m), 7.19−7.33 (6H, m); ^{13}C NMR δ_C (75.5 MHz) 20.3, 38.3, 126.1, 126.4, 127.2, 128.5, 128.8, 128.9, 130.1, 135.8, 137.2, 137.9; IR (film) ν_{max}/cm^{-1} 3061, 3029, 1469, 1454, 1066, 744, 697 (found C, 78.50; H, 6.62; $C_{14}H_{14}S$ requires C, 78.46; H, 6.58); m/z (ESI) [(M + OH)$^+$] 231; HRMS (ESI) exact mass calculated for $C_{14}H_{14}S$ [(M + OH)$^+$] 231.0844; found, 231.0848.

Benzyl *m*-Tolyl Sulfide (5o): Clear oil, 91%; ^{1}H NMR δ_H (300 MHz) 2.29 (3H, s), 4.11 (2H, s), 6.95−7.02 (1H, m), 7.07−7.34 (8H, m); ^{13}C NMR δ_C (75.5 MHz) 21.4, 39.0, 126.7, 127.2, 128.5, 128.8, 128.9, 130.4, 136.2, 137.6, 138.6; IR (film) ν_{max}/cm^{-1} 3029, 2921, 1592, 1495, 1453, 770, 693 (found C, 78.55; H, 6.62; S, 14.93; $C_{14}H_{14}S$ requires C, 78.46; H, 6.58; S 14.96); m/z (ESI) [(M + OH)$^+$] 231; HRMS (ESI) exact mass calculated for $C_{14}H_{14}S$ [(M + OH)$^+$] 231.0844; found, 231.0843.

4-Methylbenzyl Phenyl Sulfide[50] **(5p):** White solid, 87%, mp 69−71 °C (lit. 63.5−64.4 °C);[50] ^{1}H NMR δ_H (300 MHz) 2.32 (3H, s), 4.09 (2H, s), 7.03−7.36 (9H, m); ^{13}C NMR δ_C (75.5 MHz) 21.1, 38.7, 126.2, 128.7, 128.8, 129.2, 129.6, 134.3, 136.7, 136.8; IR (film) ν_{max}/cm^{-1} 3058, 2918, 1582, 1479, 1435, 1090, 738, 690 (found C, 78.13; H, 6.59; S, 15.30; $C_{14}H_{14}S$ requires C, 78.46; H, 6.58; S 14.96); m/z (ESI) [(M + OH)$^+$] 231; HRMS (ESI) exact mass calculated for $C_{14}H_{14}S$ [(M + OH)$^+$] 231.0844; found, 231.0849.

3-Methylbenzyl Phenyl Sulfide (5q): Clear oil, 77%; ^{1}H NMR δ_H (300 MHz) 2.31 (3H, s), 4.09 (2H, s), 7.00−7.37 (9H, m); ^{13}C NMR δ_C (75.5 MHz) 21.3, 39.0, 125.9, 126.3, 128.0, 128.4, 128.8, 129.6, 129.7, 136.6, 137.3, 138.2; IR (film) ν_{max}/cm^{-1} 3057, 2920, 1584, 1480, 1438, 1089, 738, 690 (found C, 78.20; H, 6.51; S, 15.3; $C_{14}H_{14}S$ requires C, 78.46; H, 6.58; S 14.96); m/z (ESI) [(M + OH)$^+$] 231; HRMS (ESI) exact mass calculated for $C_{14}H_{14}S$ [(M + OH)$^+$] 231.0844; found, 231.0843.

2-Methylbenzyl Phenyl Sulfide (5r): Clear oil, 86%; ^{1}H NMR δ_H (300 MHz) 2.39 (3H, s), 4.10 (2H, s), 7.02−7.37 (9H, m); ^{13}C NMR δ_C (75.5 MHz) 19.2, 37.4, 126.0, 126.5, 127.5, 128.9, 129.8, 130.3, 130.5, 135.1, 136.7, 136.8; IR (film) ν_{max}/cm^{-1} 3060, 2929,

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1583, 1479, 1438, 737, 690 (found C, 78.61; H, 6.32; S, 15.02; $C_{14}H_{14}S$ requires C, 78.46; H, 6.58; S 14.96); *m/z* (ESI) [$(M + OH)^+$] 231; HRMS (ESI) exact mass calculated for $C_{14}H_{14}S$ [$(M + OH)^+$] 231.0844; found, 231.0844.

Benzyl-(4-methoxyphenyl)-sulfide[47,48] (1d): White solid, 95%, mp 47−49 °C (lit. 48−49 °C);[9] ^{1}H NMR δ_H (300 MHz) 3.77 (3H, s), 3.98 (2H, s), 6.73−6.83 (2H, m), 7.13−7.31 (7H, m); ^{13}C NMR δ_C (75.5 MHz) 41.2, 55.3, 114.4, 126.1, 127.0, 128.4, 128.9, 134.1, 138.1, 159.2; IR ν_{max}/cm^{-1} (KBr) 2920, 2834, 1595, 1493, 1288, 1246, 1179, 1026, 810.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR spectra are available for compounds **5o**, **5r**, **5q**, **6a**, **6b**, **6c**, **6d**, **6e**, **6f**, **6g**, **6h**, **6i**, **6j**, **6k**, **6l**, **6m**, **6n**, **6o**, **6p**, **6q**, **6r**, **2d**, **4**, **13**, **14**, and **15**. ^{13}C NMR spectra are available for compounds **5o**, **5r**, **5q**, **6h**, **6i**, **4**, **13**, **14**, and **15**. HPLC data are available for sulfoxides **6i** and **6h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Carreno, M. C.; Hernandez-Torres, G.; Ribagorda, M.; Urbano, A. *Chem. Commun.* **2009**, 6129.
(2) Sklute, G.; Amsallem, D.; Shabli, A.; Varghese, J. P.; Marek, I. *J. Am. Chem. Soc.* **2003**, *125*, 11776.
(3) García Ruano, J. L.; Cid de la Plata, B. *Top. Curr. Chem.* **1999**, *204*, 1.
(4) Lee, A. W. M.; Chan, W. H. *Top. Curr. Chem.* **1997**, *190*, 103.
(5) Arai, Y.; Koizumi, T. *Sulfur Rep.* **1993**, *15*, 41.
(6) Myrick, H.; Malcolm, R.; Taylor, B.; LaRowe, S. *Ann. Clin. Psychiatry* **2004**, *16*, 101.
(7) O'Mahony, G. E.; Kelly, P.; Lawrence, S. E.; Maguire, A. R. *ARKIVOC (Gainesville, FL, U.S.)* **2011**, *1*, 1.
(8) Pitchen, P.; Kagan, H. B. *Tetrahedron Lett.* **1984**, *25*, 1049.
(9) Pitchen, P.; Dunach, E.; Deshmukh, M. N.; Kagan, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 8188.
(10) Di, F. F.; Modena, G.; Seraglia, R. *Synthesis* **1984**, 325.
(11) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(12) Bolm, C.; Bienewald, F. *Angew. Chem., Int. Ed. Engl.* **1996**, *34*, 2640.
(13) Bryliakov, K. P.; Talsi, E. P. *Curr. Org. Chem.* **2008**, *12*, 386.
(14) Willsky, G. R. Vanadium in the Biosphere. In *Vanadium in Biological Systems: Physiology and Biochemstry*; Chasteen, N. D., Ed.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1990; pp 1−24.
(15) Bunce, S.; Cross, R. J.; Farrugia, L. J.; Kunchandy, S.; Meason, L. L.; Muir, K. W.; O'Donnell, M.; Peacock, R. D.; Stirling, D.; Teat, S. J. *Polyhedron* **1998**, *17*, 4179.
(16) Plitt, P.; Pritzkow, H.; Oeser, T.; Kraemer, R. *J. Inorg. Biochem.* **2005**, *99*, 1230.
(17) Zhu, H.-B.; Dai, Z.-Y.; Huang, W.; Cui, K.; Gou, S.-H.; Zhu, C.-J. *Polyhedron* **2004**, *23*, 1131.
(18) Alcon, M. J.; Corma, A.; Iglesias, M.; Sanchez, F. *J. Mol. Catal. A: Chem.* **2002**, *178*, 253.
(19) Kelly, P.; Lawrence, S. E.; Maguire, A. R. *Synlett* **2007**, 1501.
(20) Ohta, C.; Shimizu, H.; Kondo, A.; Katsuki, T. *Synlett* **2002**, 161.
(21) Kelly, P. Ph.D. Thesis, National University of Ireland, Cork, Cork, Ireland, 2008.
(22) Legros, J.; Bolm, C. *Chem.—Eur. J.* **2005**, *11*, 1086.
(23) Mancheno, O. G.; Dallimore, J.; Plant, A.; Bolm, C. *Org. Lett.* **2009**, *11*, 2429.
(24) Shimizu, M.; Shibuya, K.; Hayakawa, R. *Synlett* **2000**, 1437.
(25) Umemura, K.; Matsuyama, H.; Watanabe, N.; Kobayashi, M.; Kamigata, N. *J. Org. Chem.* **1989**, *54*, 2374.
(26) Benson, S. C.; Snyder, J. K. *Tetrahedron Lett.* **1991**, *32*, 5885.
(27) Duddeck, H.; Korek, U.; Rosenbaum, D.; Drabowicz, J. *Magn. Reson. Chem.* **1986**, *24*, 792.
(28) Davis, F. A.; Reddy, R. T.; Han, W.; Carroll, P. J. *J. Am. Chem. Soc.* **1992**, *114*, 1428.
(29) Kelly, P.; Lawrence, S. E.; Maguire, A. R. *Eur. J. Org. Chem.* **2006**, 4500.
(30) Guo, Y.; Jenks, W. S. *J. Org. Chem.* **1995**, *60*, 5480.
(31) King, J. F.; Coppen, M. J. *Can. J. Chem.* **1971**, *49*, 3714.
(32) Kwart, O. *J. Am. Chem. Soc.* **1971**, *93*, 7250.
(33) Samanta, R.; Antonchick, A. P. *Angew. Chem., Int. Ed.* **2011**, *50*, 5217.
(34) Rodríguez, N.; Cuenca, A.; Ramírez de Arellano, C.; Medio-Simón, M.; Asensio, G. *Org. Lett.* **2003**, *5*, 1705.
(35) Baciocchi, E.; Rol, C.; Scamosci, E.; Sebastiani, G. V. *J. Org. Chem.* **1991**, *56*, 5498.
(36) Pelotier, B.; Anson, M. S.; Campbell, I. B.; MacDonald, S. J. F.; Priem, G.; Jackson, R. F. W. *Synlett* **2002**, 1055.
(37) Cogan, D. A.; Liu, G.; Kim, K.; Backes, B. J.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 8011.
(38) Balcells, D.; Maseras, F.; Ujaque, G. *J. Am. Chem. Soc.* **2005**, *127*, 3624.
(39) Ding, Q.; Cao, B.; Yuan, J.; Liu, X.; Peng, Y. *Org. Biomol. Chem.* **2011**, *9*, 748.
(40) Landini, D.; Rolla, F. *Org. Synth.* **1978**, *58*, 143.
(41) Glaspy, P. E.; Hancock, R. A.; Thyagarajan, B. S. *Org. Mass Spectrom.* **1985**, *20*, 281.
(42) King, J. F.; Coppen, M. J. *Can. J. Chem.* **1971**, *49*, 3714.
(43) Jean, M.; Renault, J.; van der Weghe, P.; Asao, N. *Tetrahedron Lett.* **2010**, *51*, 378.
(44) Russell, G. A.; Ngoviwatchai, P.; Tashtoush, H. I.; Pla-Dalmau, A.; Khanna, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 3530.
(45) Chai, C. L. L.; Christen, D.; Halton, B.; Neidlein, R.; Starr, M. A. E. *Aust. J. Chem.* **1995**, *48*, 577.
(46) Lapkin, I. I.; Bogoslovskii, N. V.; Mozhova, N. F *Chem. Abstr.* **1966**, *64*, 11115.
(47) Ham, J.; Yang, I.; Kang, H. *J. Org. Chem.* **2004**, *69*, 3236.
(48) Barry, N.; Brondel, N.; Lawrence, S. E.; Maguire, A. R. *Tetrahedron* **2009**, *65*, 10660.
(49) Vowinkel, E. *Synthesis* **1974**, 430.
(50) Sakai, N.; Moritaka, K.; Konakahara, T. *Eur. J. Org. Chem.* **2009**, *24*, 4123.