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Asymmetric Synthesis of Aryl Benzyl Sulfoxides by Vanadium-Catalysed Oxidation: A Combination of Enantioselective Sulfide Oxidation and Kinetic Resolution in Sulfoxide Oxidation

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Enantioselective vanadium-catalysed oxidation of aryl benzyl sulfides using Bolm's procedure is accompanied by kinetic resolution in the oxidation of the resulting sulfoxides which enhances the enantiopurities of the sulfoxides recovered (typically >90% *ee*), albeit with an associated reduction in yield. The effects of ligand, solvent and reaction conditions are discussed in detail.

The development of novel methods to prepare enantiopure sulfoxides has attracted considerable attention over the last few years. Enantiopure sulfoxides are useful as both building blocks and chiral auxiliaries in organic synthesis.[1] There are two main routes used to prepare enantiopure sulfoxides, namely nucleophilic displacement and enantioselective sulfur oxidation.[2]

The Andersen synthesis, which involves the nucleophilic displacement of a leaving group from a diastereopure sulfinate ester, was first reported in the 1960s and is a very popular method for the preparation of enantiopure sulfoxides.[3] However, its utility is limited by the fact that only one diastereopure sulfinate ester is commercially available and the preparation of further diastereopure sulfinate esters is difficult. The use of a chiral auxiliary that could undergo two consecutive nucleophilic displacements to give an enantiopure sulfoxide has also been investigated, most recently by Ruano[4] and Senanayake[5] and their co-workers.

An attractive alternative to nucleophilic displacement is enantioselective sulfur oxidation.[2] This method is particularly attractive given that the prochiral sulfides are usually easily prepared. To date relatively few enantioselective sulfur oxidation methods have yielded enantiopure sulfoxides, though many have resulted in highly enantioenriched sulfoxides. One of the most widely used oxidation methods is the titanium-based Kagan oxidation method, which was first reported in the 1980s.[2] For example, the drug esomeprazole has been successfully prepared on a large scale by asymmetric oxidation using this method.[6] Among the Alimitations of this method is its sensitivity to moisture. Bolm and Bienewald reported a robust oxidation method based on vanadium in 1995.[7] This involved the in situ formation of a catalyst from vanadyl acetylacetonate and a Schiff base. The oxygen source for this method is hydrogen peroxide, the reaction is not moisture-sensitive and can be carried out in an open reaction vessel. This reaction method has attracted a lot of attention principally due to its ease of use.[8]

Of particular importance to this work is the fact that in the original paper by Bolm and Bienewald it was reported that the high enantioselectivity of the sulfoxide product was due exclusively to asymmetric oxidation of the sulfide to the sulfoxide and that kinetic resolution did not play a role.[7] This is backed up by the considerable amount of literature that has since been published on this oxidation method in which kinetic resolution has not been reported.[8]

Kinetic resolution of sulfoxides is the reaction of two enantiomeric sulfoxides at different rates.[9a] There are numerous examples of the oxidative kinetic resolution of sulfoxides to sulfones, most of which were discovered during the investigation of asymmetric sulfide oxidation.[9] In the early 1980s Davis and Billmers, using chiral 2-sulfonyloxaziridines as catalysts, reported that sulfoxides of up to 28% *ee* could be obtained using multistep oxidative kinetic resolution.[9a]

Uemura and co-workers reported kinetic resolution when carrying out sulfur oxidations using a titanium–binaphthol catalyst with aryl methyl sulfoxides of up >99% *ee* being obtained in 26% yield.[9b,9c] Recently Chan and co-workers optimised this and reported that carrying out the kinetic resolution step at 25 °C gave the best results, obtaining phenyl methyl sulfoxide in 29% yield and 95% *ee*.[9d] Scettri et al. reported that by carrying out a kinetic resolution ex-

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periment using the racemic sulfoxides as substrate and following the Modena procedure for asymmetric sulfur oxidation, aryl methyl sulfoxides could be obtained in 31% yield and 94% *ee*.[9e] Licini and co-workers reported that kinetic resolution accompanied a titanium–chiral-trialkanolamine-catalysed sulfur oxidation.[9f] The sulfoxide derived from phenyl benzyl sulfide, a poor substrate for titanium diethyl tartrate catalysed sulfur oxidations, was obtained with an enantiopurity of 84% *ee* along with 27% sulfone formation. Similarly Rosini and co-workers obtained *p*-tolyl benzyl sulfoxide in 65% yield with 98% *ee* using a titanium–diphenylethane-1,2-diol catalyst through a combination of asymmetric sulfur oxidation and kinetic resolution.[9g] Korb and co-workers, using a titanium–chiral-hydroperoxide complex and starting with the racemic sulfoxide, obtained methyl *p*-tolyl sulfoxide in 39% *ee* in a kinetic resolution experiment.[9h]

Katsuki and co-workers reported that a manganese–salen catalyst could be used to carry out the kinetic resolution of aryl methyl sulfoxides.[9i] However, the selectivity was low and methyl phenyl sulfoxide of 95% *ee* was recovered in just 5% yield. This indicated that kinetic resolution played only a very minor role in the asymmetric sulfide oxidation using the Katsuki catalyst. Thakur and Sudalai recently reported a tungsten–cinchona-alkaloid-catalysed kinetic resolution of aryl alkyl and aryl benzyl sulfoxides obtaining phenyl benzyl sulfoxide with 90% *ee* in 25% yield using the racemic sulfoxide as substrate.[9j] Zhu and co-workers reported in 2004 a vanadium–salen-catalysed kinetic resolution of aryl methyl and aryl benzyl sulfoxides.[9k] Here sulfoxides of up to 98% *ee* were obtained. Unusually, the selectivity of the kinetic resolution step here is opposite to that of the asymmetric sulfur oxidation step so unlike the other systems mentioned; asymmetric sulfur oxidation and kinetic resolution using a vanadium–salen catalyst cannot be used in combination as a route to enantioenriched sulfoxides.[9k]

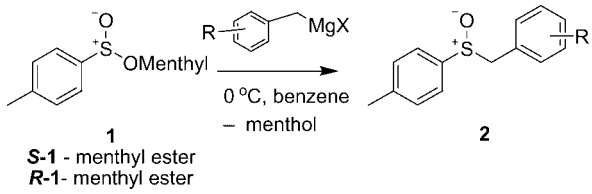
Up to quite recently there had been no report of kinetic resolution playing a role in the Bolm oxidation method. Jackson and co-workers have very recently reported kinetic resolution in the oxidation of aryl alkyl sulfoxides using this system.[10] It was found that the optimum solvent for kinetic resolution of aryl alkyl sulfoxides using this system was chloroform and the kinetic resolution was most efficient at 0 °C. Jackson and co-workers reported that through a combination of both asymmetric oxidation and kinetic resolution enantiopure aryl alkyl sulfoxides could be obtained in good yield. Interestingly Katsuki and co-workers carried out the Bolm oxidation under the same conditions as described by Jackson except using a different ligand.[8e] He obtained aryl methyl sulfoxides in about the same yield albeit with lower enantiopurity; sulfone formation was not reported. This indicates that the ligand used could play an important role in kinetic resolution.

We have recently investigated the enantioselective synthesis of aryl benzyl sulfoxides using the Bolm method and wish to report here our observations on both asymmetric sulfide oxidation and kinetic resolution in sulfoxide oxidation.[11] Furthermore these processes can be employed in combination to yield sulfoxides with high enantiopurity. Aryl benzyl sulfoxides are of particular interest due to their potential as chiral auxiliaries.[12]

Results and Discussion

At the outset of this work, the Andersen method was employed to prepare genuine samples of enantiopure sulfoxides (**2a**–**2d**) for analytical method development. Compound **2** was prepared by treating **1** with a freshly prepared Grignard reagent while stirring in benzene at 0 °C. The results are shown in Table 1.

Table 1. Preparation of enantiopure sulfoxides using the Andersen synthesis.



1
***S*-1** - menthyl ester
***R*-1**- menthyl ester

2

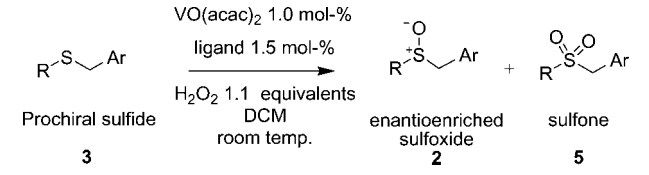
R	Sulfoxide	**2** Yield [%][a]	**2** *ee* [%][b]
4-F	**2a**	41	98 (*R*)
4-F	**2a**	62	96 (*S*)
4-H	**2b**	61	>99 (*R*)
4-H	**2b**	88	96 (*S*)
4-Cl	**2c**	43	98 (*R*)
4-Cl	**2c**	36	94 (*S*)
4-Me	**2d**	16	>99 (*R*)
4-Me	**2d**	13	*98* (*S*)

[a] Yield of **2** after purification by chromatography. [b] Determined by HPLC analysis on a chiral column (Daicel Chiracel OD-H). The absolute configuration was determined by choice of sulfinate ester for **2a**, **2c** and **2d**, which have previously been described only in racemic form. The absolute configuration of **2b** was determined by comparison of specific rotation values to known literature values (see the Expt. Sect.).

Initial work focused on using the Bolm oxidation method to enantioselectively oxidise an aryl benzyl sulfide **3** and good enantioselectivity was observed as shown in Table 2. A range of Schiff-base ligands **4a**–**4e** was employed throughout this work to explore the ligand effects on efficiency and enantioselectivity. These were prepared as described by Bolm.[13] During the oxidation of **3a**, using ligands **4a**–**4e** to form the catalyst, it was noticed that a considerable amount of sulfone was formed during these reactions. Notably the amount of over-oxidation to the sulfone depended strongly on the ligand structure.[14]

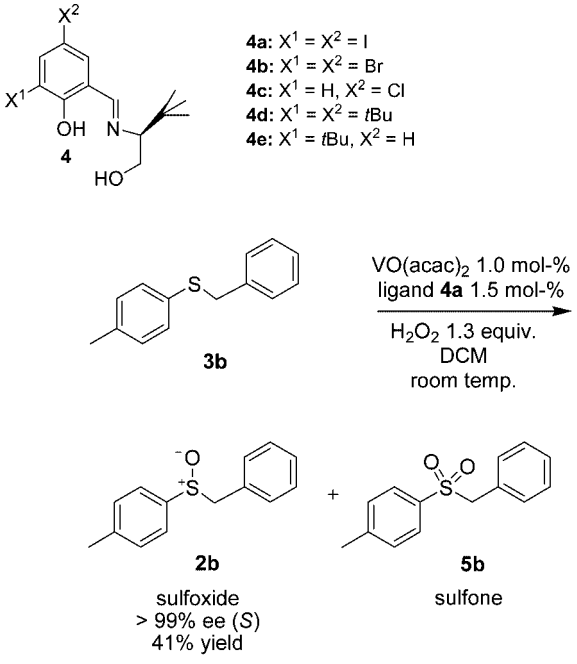
Taking yield and enantioselectivity into account, ligand **4a** was deemed to be the best ligand and it was used as the ligand of choice for the subsequent sulfur oxidations. Carrying out the reaction using **3b** as the substrate gave impressive results with **2b** being recovered in 41% yield and with >99% *ee* (Scheme 1).

Table 2. Asymmetric oxidation of aryl benzyl sulfide **3**.



3	R	Ar	Ligand	Ratio **2a**/**5a**[a]	**2a** Yield [%][b]	**2a** *ee* [%][c]
			4a	71:29	54	*71* (*S*)
			4b	78:22	56	61 (*S*)
3a	4-MeC_6H_4	4-FC_6H_5	**4c**	82:18	45	42 (*S*)
			4d	85:15	28	33 (*S*)
			4e	62:38	11	45 (*S*)

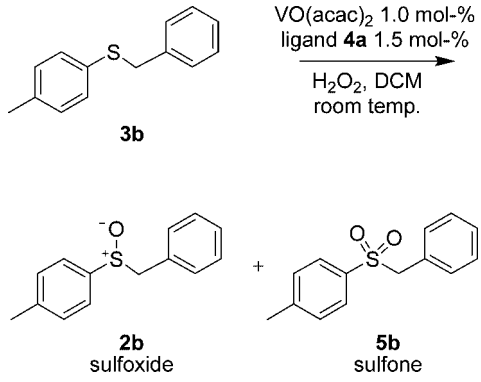
[a] The sulfoxide/sulfone ratio was determined by ^{1}H NMR spectroscopy of the crude product.[14] [b] Yield of **2** after purification by chromatography. [c] Determined by HPLC analysis on a chiral column (Daicel Chiracel OD-H). The absolute configuration was determined by comparing HPLC retention times with enantiopure sulfoxides prepared using the Andersen method.



Scheme 1.

The ratio of sulfoxide to sulfone in the crude product was 47:53.[14] This coupled with the high enantiopurity reported indicated that kinetic resolution was possibly taking place. Accordingly, an investigation was carried out to establish if there was a relationship between the extent of sulfone formation and enantiopurity. This was done by carrying out the reaction using varying equivalents of the oxidant. The results of these experiments are shown in Table 3 and Figure 1. The relationship between sulfone formation and the enantiopurity of the remaining sulfoxide can be clearly seen.

Table 3. Investigation of the relationship between the extent of sulfone formation and the enantiopurity of the remaining sulfoxide.



H_2O_2 [equiv.]	Ratio **3b**/**2b**/**5b**[a]	**2b** Yield [%][b]	**2b** *ee* [%][c]
0.25	73:27:0	20	62 (*S*)
0.5	46:54:0	26	58 (*S*)
0.75	35:59:6	45	72 (*S*)
1.1	0:72:28	48	94 (*S*)
1.3	0:47:53	41	>99 (*S*)

[a] The sulfide/sulfoxide/sulfone ratio was determined by ^{1}H NMR spectroscopy of the crude product.[14] [b] Yield of **2** after purification by chromatography. [c] Determined by HPLC analysis on a chiral column (Daicel Chiracel OD-H). The absolute configuration was determined by comparison of specific rotation values for **2b** with a known literature value (see the Expt. Sect.).

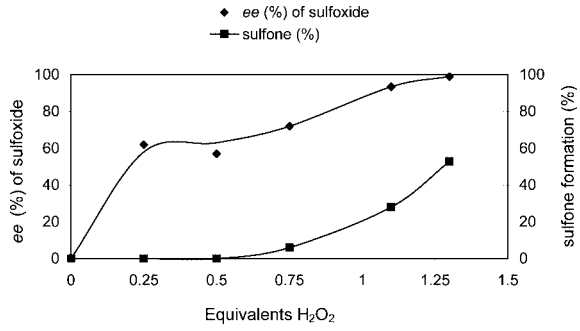
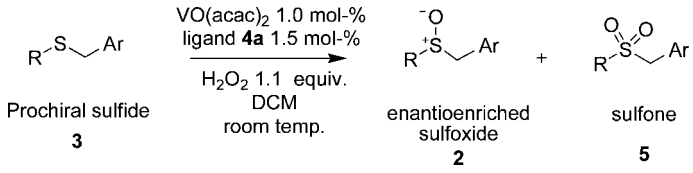


Figure 1. Relationship between the extent of sulfone formation and the enantiopurity of the sulfoxide.

Oxidation reactions using a range of aryl benzyl sulfides produced similar results, with significant sulfone formation and high enantiopurity of sulfoxides occurring together. The results of this work are shown in Table 4. Notably, each of the aryl benzyl sulfoxides **2a**–**h** were obtained with good enantiopurities (71–99% *ee*). However, the enantiopurities of the benzyl methyl and benzyl *tert*-butyl sulfoxides were much lower.

Based on the results obtained in the asymmetric sulfide oxidation reactions the next step was to investigate kinetic resolution in the oxidation of sulfoxide as substrate (see Table 5). Using the racemic sulfoxide **2b** as substrate and ligand (*S*)-**4a**, the (*S*) enantiomer of the sulfoxide was obtained in 94% *ee*, while with ligand (*R*)-**4a**, the (*R*) enantiomer of the sulfoxide was obtained in 98% *ee*. Enantioenriched samples of **2b** [both the (*R*) and (*S*) enantiomers]

Table 4. Asymmetric oxidation of aryl benzyl sulfides.



3	R	Ar	2	Ratio 2/5[a]	2 Yield [%][b]	2 *ee* [%][c]
3a	4-MeC_6H_4	4-FC_6H_4	**2a**	71:29	54	71 (*S*)
3b	4-MeC_6H_4	Ph	**2b**	72:28	48	94(*S*)
3c	4-MeC_6H_4	4-ClC_6H_4	**2c**	57:43	47.6	98 (*S*)
3d	4-MeC_6H_4	4-MeC_6H_4	**2d**	66:34	45	>99 (*S*)
3e	4-MeC_6H_4	2-$MeOC_6H_4$	**2e**	69:31	50	>99 (*R*)
3f	4-MeC_6H_4	4-$MeOC_6H_4$	**2f**	62:38	52	>99 (*S*)
3g	4-BrC_6H_4	Ph	**2g**	45:55	41	>99 (*S*)
3h	Ph	Ph	**2h**	70:30	51	91 (*S*)
3i	*t*Bu	Ph	**2i**	95:5	42	56.3 (*S*)
3j	Me	Ph	**2j**	83:17	76	10 (*S*)

[a] The sulfoxide/sulfone ratio was determined by ^{1}H NMR spectroscopy of the crude product.[14] [b] Yield of **2** after purification by chromatography. [c] Determined by HPLC analysis on a chiral column (Daicel Chiracel OD-H). The absolute configurations for **2a**, **2c** and **2d** were determined by comparing HPLC retention times with those of enantiopure sulfoxides prepared using the Andersen method. The absolute configurations for **2b**, **2g**, **2h**, **2i** and **2j** were determined by comparison of specific rotation values with known literature values (see the Expt. Sect.). For **2e** and **2f**, the proposed configuration was based on the HPLC elution order and the direction of the specific rotations.

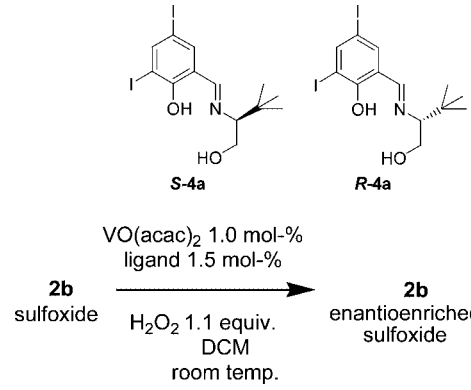
were prepared using the Andersen synthesis as described above (see Table 1). It was observed that when using ligand (*S*)-**4a** and the (*S*) enantiomer of **2b** as the substrate in the Bolm oxidation that very little sulfone was formed. Conversely when using ligand (*S*)-**4a** and the (*R*) enantiomer of **2b** under the same conditions significant sulfone formation occurred and the enantiopurity dropped. In the case of **2b** the (*R*) enantiomer is preferentially oxidised to the sulfone when using ligand (*S*)-**4a** while the (*S*) enantiomer is preferentially oxidised to the sulfone when ligand (*R*)-**4a** is used. Furthermore, there is very little oxidation when the ligand and sulfoxide are mismatched. Critically the enantiomer of the sulfoxide which is preferentially formed in the asymmetric sulfide oxidation process [(*S*)-**4a** ligand produces (*S*) sulfoxide] is complementary to that which is selectively oxidised in the sulfoxide oxidation step [the (*S*)-**4a** ligand selectively oxidises the (*R*) sulfoxide]; thereby the kinetic resolution reinforces the intrinsic enantioselectivity of the sulfide oxidation and results in excellent enantiopurities depending on the stage at which the oxidation/over-oxidation is stopped.

When using racemic sulfoxide as the substrate, in excess of 50% sulfone was detected and the remaining sulfoxide after the reaction was enantioenriched but not enantiopure, thus one enantiomer is preferentially but not exclusively oxidised to the sulfone.

No kinetic resolution was observed when carrying out the reaction in the absence of either vanadyl acetylacetonate or the Schiff-base ligand.

To extend this initial study, an investigation was carried out using a series of racemic aryl benzyl sulfoxides as substrate for the Bolm oxidation procedure. The resulting crude product was a mixture of enantioenriched sulfoxide and sulfone as shown in Table 6. Plotting the results (extent of sulfone formation vs. the enantiomeric purity of the remaining sulfoxide) in Figure 2 a direct relationship between conversion of sulfoxide to sulfone and enantiomeric excess of the remaining sulfoxide can be seen.

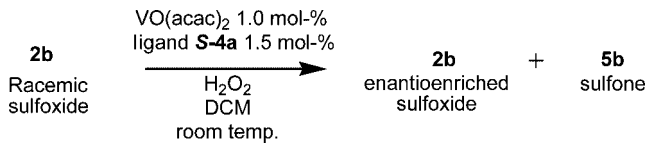
Table 5. Investigation of the selectivity of kinetic resolution.



Sulfoxide	Ligand	*ee* of **2b** before exp. [%][a]	Ratio **2b/5b**[b]	**2b** Yield [%][c]	**2b** *ee* after exp. [%][a]
2b	(*S*)-**4a**	0	34:66	18	94 (*S*)
2b	(*R*)-**4a**	0	31:69	25	98 (*R*)
2b	(*S*)-**4a**	96.5 (*S*)	94:06	74	98 (*S*)
2b	(*S*)-**4a**	92.3 (*R*)	06:94	4	55 (*R*)

[a] Determined by HPLC analysis on a chiral column (Daicel Chiracel OD-H). The absolute configuration was determined by comparison of specific rotation values with known literature values (see the Expt. Sect.). [b] The sulfoxide/sulfone ratio was determined by ^{1}H NMR spectroscopy of the crude product. [c] Yield of **2b** after purification by chromatography.

Table 6. Relationship between the extent of sulfone formation and the enantiopurity of the remaining sulfoxide.



Sulfoxide	H_2O_2 [equiv.]	Ratio **2b**/**5b**[a]	**2b** Yield [%][b]	**2b** *ee* [%][c]
2b	0	100:0	–	0
2b	0.2	85:15	48	11 (*S*)
2b	0.4	67:33	30	48 (*S*)
2b	0.6	44:56	41	60 (*S*)
2b	0.8	36:64	23	92 (*S*)

[a] The sulfoxide/sulfone ratio was determined by ^{1}H NMR spectroscopy of the crude product. [b] Yield of **2** after purification by chromatography. [c] Determined by HPLC analysis on a chiral column (Daicel Chiracel OD-H). The absolute configuration was determined by comparison of specific rotation values with known literature values (see the Expt. Sect.).

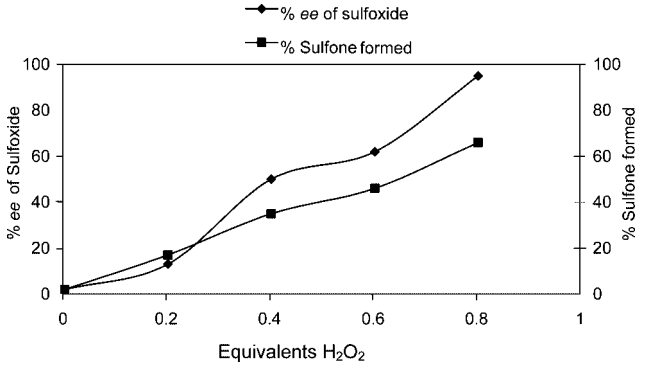


Figure 2. Relationship between sulfone formation and the *ee* of sulfoxide during the kinetic resolution experiment.

Using this series of experiments optimum conditions for the kinetic resolution of the racemic sulfoxide were found to be largely similar to those of the standard Bolm procedure except that only 0.8 equivalents of the oxidising agent were used and the oxidising agent was added portionwise over an extended period (70 minutes). This portionwise addition agrees with the report by Karpyshev et al. who found that the enantioselectivity of the Bolm oxidation reaction was enhanced when the oxidant was added over an extended period.[15]

It was found that the kinetic resolution experiments worked best when carried out at room temperature. Carrying out the reaction at either lower or higher temperatures (temperature range investigated –20 to +30 °C) resulted in a decrease in enantiopurity. At lower temperatures the enantioselectivity dropped to 63% *ee* for **2b**. Carrying out the experiments at higher temperatures resulted in a dramatic drop in enantioselectivity to 34% *ee* for **2b**. This agrees with research carried out by Jackson and co-workers who found that kinetic resolution was most efficient when carried out at room temperature when the solvent used was dichloromethane, although the optimum temperature is solvent dependent.[10] A moderate stirring rate as suggested by Bolm and Bienewald in the original paper was found to be best.[7] Carrying out the reaction at either a slower or faster stirring rate resulted in a drop in enantioselectivity to approximately 85% *ee*. When experiments were undertaken in the absence of any of the following: hydrogen peroxide, vanadium or ligand, no kinetic resolution was observed indicating that each of these components is necessary for the enantioselective oxidation.

The results obtained for the kinetic resolution experiments on various racemic sulfoxides are summarised in Table 7.

From the above data it can be concluded that aryl benzyl sulfoxides are very susceptible to kinetic resolution using this system. As stated earlier Bolm and Bienewald reported that kinetic resolution was not responsible for the high enantiopurity obtained when oxidising aryl methyl sulfides.[7] This has been confirmed by the work of other groups and indeed work carried out within this group in which kinetic resolution was not reported when using this system to oxidise aryl methyl sulfides.[8] Evidently subtle steric and electronic factors result in efficient kinetic resolution in the oxidation of aryl benzyl sulfoxides. Carrying out the Bolm oxidation with **3i** as substrate resulted in very little sulfone formation indicating that the bulky *tert*-butyl group of the sulfoxide may have impeded oxidation and kinetic resolution. This is further supported by the fact that when **2i** was used as substrate little sulfone formation was observed.

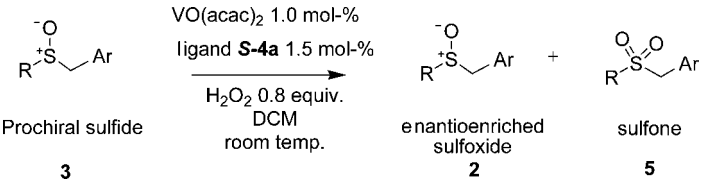
Note that when using **2j** as substrate, significant sulfone formation occurs but there is no significant increase in enantiopurity. Thus non-enantioselective oxidation of the sulfoxide leads to sulfone formation with the recovered sulfoxide product being effectively racemic. This indicates that the efficiency of kinetic resolution is strongly substrate-dependent.

Following the recent report by Jackson and co-workers that kinetic resolution of aryl alkyl sulfoxides was most efficient in chloroform, the oxidation of the aryl benzyl sulfoxide **2h** was undertaken using chloroform as the solvent.[10] Notably Jackson's procedure used just 0.6 equivalents of hydrogen peroxide added in one portion at 0 °C whereas our conditions employed 0.8 equivalents added portionwise at room temperature. As shown in Table 8 use of Jackson's protocol in DCM led to a poorer outcome than with the conditions developed in this work (entries 1 and 2). However use of chloroform with either 0.6 or 0.8 equivalents of H_2O_2 led to improved results (entries 3 and 4). The results agree with Jackson's observations that optimum kinetic resolution in chloroform is seen at 0 °C while room temperature is preferred for dichloromethane.

While oxidation of the complete series of aryl benzyl sulfoxides in chloroform was not investigated it is reasonable to assume that improved yields and enantioselectivity would ensue in chloroform as seen for **2h**.

The results shown in Tables 7 and 8 compare very favourably in terms of yield and enantioselectivity with the results of other published kinetic resolution methods. Most of the published studies focus on aryl methyl sulfoxides.

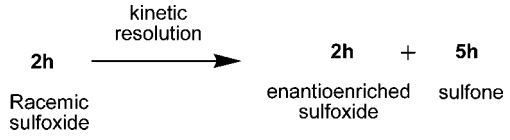
Table 7. Vanadium-catalysed kinetic resolution of aryl benzyl sulfoxides.



2	R	Ar	Ratio 2/5[a]	2 Yield [%][b]	2 *ee* [%][c]	Selectivity factor[d]
2a	4-MeC_6H_4	4-FC_6H_4	30:70	21	98.3 (*S*)	9.9
2b	4-MeC_6H_4	Ph	36:64	23	92 (*S*)	8.2
2c	4-MeC_6H_4	4-ClC_6H_4	20:80	14	97.3 (*S*)	6.7
2d	4-MeC_6H_4	4-MeC_6H_4	16:84	15	>99 (*S*)	5.6
2e	4-MeC_6H_4	2-$MeOC_6H_4$	33:67	25	>99 (*R*)	13.1
2f	4-MeC_6H_4	4-$MeOC_6H_4$	26:74	19	74 (*S*)	3.4
2g	4-BrC_6H_4	Ph	37:63	31	>99 (*S*)	17.6
2h	Ph	Ph	28:72	21	86 (*S*)	4.6
2i	*t*Bu	Ph	86:14	60	5.4 (*S*)	1.1
2j	Me	Ph	54:46	51	4 (*S*)	1.1

[a] The sulfoxide/sulfone ratio was determined by ^{1}H NMR spectroscopy of the crude product. [b] Yield of **2** after purification by chromatography. [c] Determined by HPLC analysis on a chiral column (Daicel Chiracel OD-H). The absolute configurations for **2a**, **2c** and **2d** were determined by comparing HPLC retention times with those of enantiopure sulfoxides prepared using the Andersen method. The absolute configurations for **2b**, **2g**, **2h**, **2i** and **2j** were determined by comparison of specific rotation values with known literature values (see the Expt. Sect.). For **2e** and **2f** the proposed configurations were based on the HPLC elution order and the direction of the specific rotations. [d] The selectivity factor was calculated using the formula of Kagan and Fiaud using ^{1}H NMR conversions.[16]

Table 8. Importance of solvent in the kinetic resolution of racemic **2h**.



Entry	H_2O_2 [equiv.]	Rate of H_2O_2 addition	Solvent	Temp. [°C]	Ratio 2h/5h[a]	2h Yield [%][b]	2h *ee* [%][c]	Selectivity factor [d]
1	0.8	portionwise	DCM	room temp.	28:72	21	86 (*S*)	4.6
2	0.6	single portion	DCM	0	46:54	23	44 (*S*)	3.3
3	0.6	single portion	$CHCl_3$	0	39:61	29	80 (*S*)	7.2
4	0.8	portionwise	$CHCl_3$	room temp.	38:62	33	78 (*S*)	5.8

[a] The sulfoxide/sulfone ratio was determined by ^{1}H NMR spectroscopy of the crude product. [b] Yield of **2h** after purification by chromatography. [c] Determined by HPLC analysis on chiral a column (Daicel Chiracel OD-H). The absolute configuration was determined by comparison of specific rotation values with known literature values (see the Expt. Sect.). [d] The selectivity factor was calculated using the formula of Kagan and Fiaud using ^{1}H NMR conversions.[15]

However, Sudalai (tungsten–cinchona-alkaloid catalyst) and Zhu (vanadium–salen catalyst) and their co-workers have reported kinetic resolution experiments using racemic aryl benzyl sulfoxides as substrates.[9j,9k] A comparison of the results for the kinetic resolution of **2b** and **2h** are summarised in Table 9. Interestingly the oxidant used in all these reactions is hydrogen peroxide. Notably Sudalai reported lower enantiopurities when starting from the sulfide, while as mentioned earlier Zhu's method is not amenable to the combination of asymmetric sulfide oxidation and kinetic resolution, highlighting the advantage of the current method in which a combination of asymmetric sulfide oxidation and kinetic resolution can result in high enantiopurities when starting from sulfides (see Table 4).[9j,9k]

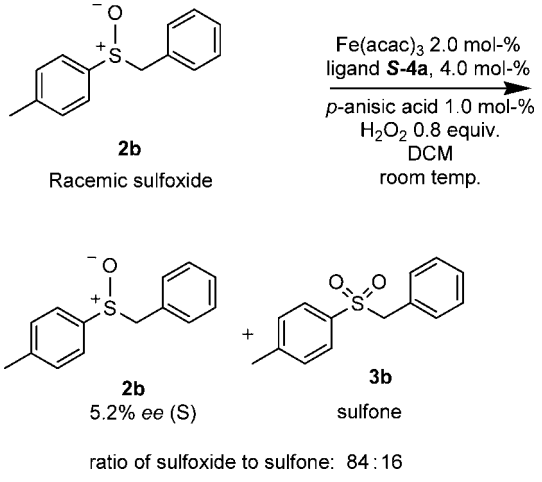
Table 9. Kinetic resolution of racemic sulfoxides using different methods.

Catalyst	**2b**: *ee* [%] (yield [%])	**2h**: *ee* [%] (yield [%])
Tungsten–cinchona alkaloid (Sudalai[9j])	90 (25)	82 (25)
Vanadium–salen (Zhu[9k])	91 (27)	93 (26)
Vanadium–Schiff base (this work)	92 (23)	86 (21)

Korb and co-workers investigated the mechanism of titanium–chiral-hydroperoxide-catalysed kinetic resolution and found evidence for coordination of the sulfoxide to the titanium complex.[9h] No kinetic resolution was observed when the reaction was carried out in 2-propanol in which case

coordination of the sulfoxide was inhibited through solvation. Based on this work the kinetic resolution of sulfoxide **2b** under the protocol described above in Table 7 was explored replacing dichloromethane with either 2-propanol or acetone as solvent. In both cases very little sulfone formation was observed which would be consistent with disruption of a sulfoxide–vanadium complex critical to the oxidation process.

Bolm and co-workers recently published the results of an iron-catalysed asymmetric sulfur oxidation reaction using among other sulfides phenyl benzyl sulfide.[17] In a footnote Bolm indicated that kinetic resolution may be taking place using this catalyst system.[17b] However, in a later report Legros and Bolm stated that the role of kinetic resolution in the enantioselectivity of sulfur oxidation is negligible.[17d] Accordingly, to place our work in context, we undertook some limited studies using this iron-based catalyst with sulfide **2b** (which had not been among the substrates studied by Bolm), which showed that while kinetic resolution occurs, it is to a much lesser extent than that described above using Bolm and co-workers' vanadium-based oxidation reaction (Scheme 2).



Scheme 2.

A recent paper reports high enantiopurities and yields in the oxidation of aryl benzyl sulfides using an alternative vanadium-based catalyst with a different ligand system.[18] Kinetic resolution in this context was not mentioned.

From this research it can be concluded that a combination of both kinetic resolution and asymmetric oxidation can occur in the preparation of enantioenriched aryl benzyl sulfoxides using the Bolm oxidation method.

Experimental Section

General: Chemicals and solvents were purchased from commercial suppliers. Sulfides **3a**–**3g** and **3i** were prepared in the laboratory by treatment of an excess of thiolate anion with the appropriate benzyl halide.[19] Sulfides **3h** and **3j** were purchased from Aldrich. For thin-layer chromatography (TLC), Merck 60 F254 silica gel plates were used and compounds were visualized using UV. Solvents were distilled before use. ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded with a Bruker AVANCE300 spectrometer at 20 °C using $CDCl_3$ as solvent. Chemical shifts are given in ppm relative to TMS as the internal standard. Coupling constants (J) are reported in Hz. Chiral HPLC was performed with a Waters 600E System Controller and a Waters 996 Photodiode Array Detector with a Chiralpak OD-H column from Daicel Chemical Industries Ltd., eluting with *n*-hexane and 2-propanol. Specific rotations were recorded on a Perkin–Elmer 341 polarimeter at 20 °C in the solvents indicated. The sodium D line (589 nm) was used unless otherwise indicated. Samples were analysed in a 1 mL dual-walled, thermostatted glass cell (PE part number: 631136) of path length 10 cm. Sample temperature control was maintained using a Julabo F25-MV immersion circulator. Results were processed on a Dell Optiplex GX260 PC using Bio Light Pol Winlab software (version number 1.00.01). The units of a are 10^{-1} deg cm^2 g^{-1}. Absolute configurations were assigned by comparison of the specific rotations with the literature data for **2b**, **2f**, **2g**, **2h** and **2i** or by comparison of HPLC retention times with enantiopure samples of known configuration for **2a**, **2c** and **2d**. Notably, the direction of the specific rotations were in complete agreement with literature values, however the magnitudes varied somewhat. Racemic sulfoxides **2a–2j** were prepared by treatment of the sulfide with 0.5 equiv. of Oxone® in acetone at 0 °C.[20] Melting points were determined with an Electrothermal 9100 apparatus and are not corrected. All reactions were carried out at room temperature unless otherwise indicated.

Sulfoxides **2a**, **2d**, **2e** and **2f** have been previously reported in racemic form only.[20] Sulfoxides **2b**, **2g**, **2h**, **2i** and **2j** have been reported in enantioenriched form.[17d,21,22] Sulfoxide **2c** has not been previously reported.

Preparation of Enantioenriched Sulfoxides by Sulfide Oxidation:[7] Vanadyl acetylacetonate (2.6 mg, 0.01 mmol) and the ligand (*S*)-**4a** (7.1 mg, 0.015 mmol) were stirred together in a 25 mL round-bottomed flask in dichloromethane (1 mL) for 5 min. Sulfide (1.0 mmol) in dichloromethane (1 mL) was then added and the reaction mixture was stirred for a further 5 min. Hydrogen peroxide (30% w/w, 1.1 mmol) was added in one portion dropwise. The reaction mixture was then stirred for 16 h. The reaction was quenched by the addition of water (5 mL). The layers were separated and the aqueous layer was washed with dichloromethane (3 mL). The combined organic layers were washed with brine (5 mL), dried and concentrated under reduced pressure. The ratio of sulfide/sulfoxide/sulfone in the crude product was determined by ^{1}H NMR spectroscopy. The product was purified by flash chromatography (6:4 hexane/ethyl acetate) on silica gel.

(*S*)-(–)-4-Fluorobenzyl 4′-Tolyl Sulfoxide (2a): The crude product contained a mixture of sulfoxide and sulfone (71:29). Purification by chromatography afforded the product as a white solid (134 mg, 54%, 71% *ee*). ^{1}H NMR (300 MHz): δ = 7.27–7.17 (m, 4 H, Ar-H), 6.96 (d, J = 7.6 Hz, 4 H, Ar-H), 3.99 (s, 2 H, SCH_2), 2.40 (s, 3 H, Ar-CH_3) ppm. ^{13}C NMR (75 MHz): δ = 162.70 (d, $J_{C,F}$ = 245.6 Hz), 141.75, 139.16, 132.04 (d, $J_{C,F}$ = 8.3 Hz), 129.63, 124.94, 124.40, 115.38 (d, $J_{C,F}$ = 21.7 Hz), 62.34, 21.45 ppm. $C_{14}H_{13}FOS$ (248.32): calcd. C 67.75, H 5.28, F 7.65, S 12.91; found C 67.80, H 5.30, F 7.46, S 13.16. M.p. 174.6–175.3 °C. HPLC: t_r (*R*) = 34.6 min, t_r (*S*) = 40.3 min (Chiracel OD-H; flow rate = 0.5 mL min^{-1}; hexane/2-propanol 93:7; 10 °C). $[a]_D^{20}$ = –109 (c = 0.4, $CHCl_3$).

(*S*)-(–)-Benzyl 4′-Tolyl Sulfoxide (2b):[21] The crude product contained a mixture of sulfoxide and sulfone (72:28). Purification by chromatography afforded the product as a white solid (111 mg, 48%, 94% *ee*). ^{1}H NMR (300 MHz): δ = 7.34–7.20 (m, 7 H, Ar-H), 7.02–6.98 (m, 2 H, Ar-H), 4.13–3.94 (ABq, J = 12.5 Hz, 2 H,

SCH_2), 2.40 (s, 3 H, Ar-CH_3) ppm. ^{13}C NMR (75 MHz): δ = 142.03, 139.93, 130.77, 129.96, 129.72, 128.85, 128.58, 124.86, 64.08, 21.86 ppm. M.p. 165.3–165.8 °C. HPLC: t_r (*R*) = 44.4 min, t_r (*S*) = 51.9 min (Chiracel OD-H; flow rate = 1.0 mL min^{-1}; hexane/2-propanol 98:2; 20 °C). $[\alpha]_D^{20}$ = –235.2 (*c* = 0.7, acetone) {ref.[20] $[\alpha]_D^{20}$ = –179.1 (*c* = 1.3, acetone) for (*S*) 94%*ee*}.

(*S*)-(–)-4-Chlorobenzyl 4′-Tolyl Sulfoxide (2c): The crude product contained a mixture of sulfoxide and sulfone (53:47). Purification by chromatography afforded the product as a white solid (124 mg, 48%, 98% *ee*). IR (KBr): $\tilde{\nu}$ = 2962, 2345, 1596, 1147, 1038, 802 cm^{-1}. ^1H NMR (300 MHz): δ = 7.28–7.20 (m, 6 H, Ar-H), 6.91 (d, *J* = 7.6 Hz, 2 H, Ar-H), 3.98 (s, 2 H, SCH_2), 2.40 (s, 3 H, Ar-CH_3) ppm. ^{13}C NMR (75 MHz): δ = 142.22, 139.52, 134.72, 132.06, 130.08, 128.97, 128.02, 124.79, 62.87, 21.87 ppm. $C_{14}H_{13}ClOS$ (264.77): calcd. C 63.51, H 4.95, Cl, 13.39, S 12.11; found C 63.66, H 4.99, Cl 13.15, S 12.18. M.p. 164.2–166.0 °C. HPLC: t_r (*R*) = 34.5 min, t_r (*S*) = 40.9 min (Chiracel OD-H; flow rate = 0.5 mL min^{-1}; hexane/2-propanol 93:7; 10 °C). $[\alpha]_D^{20}$ = –140 (*c* = 0.5, $CHCl_3$).

(*S*)-(–)-4-Methylbenzyl 4′-Tolyl Sulfoxide (2d): The crude product contained a mixture of sulfoxide and sulfone (66:34). Purification by chromatography afforded the product as a white solid (110 mg, 45%, >99% *ee*). ^1H NMR (300 MHz): δ = 7.32–7.17 (m, 4 H, Ar-H), 7.04 (d, *J* = 7.0 Hz, 2 H, Ar-H), 6.85 (d, *J* = 7.2 Hz, 2 H, Ar-H), 4.07–3.88 (ABq, *J* = 12.5 Hz, 2 H, SCH_2), 2.40 (s, 3 H, Ar-CH_3) ppm. ^{13}C NMR (75 MHz): δ = 141.93, 140.13, 138.43, 130.66, 129.95, 129.58, 126.62, 124.89, 63.91, 21.86, 21.61 ppm. $C_{14}H_{16}OS$ (244.35): calcd. C 73.73, H 6.55, S 13.12; found C 73.62, H 6.55, S 13.39. M.p. 140.2–140.9 °C. HPLC: t_r (*R*) = 75.6 min, t_r (*S*) = 83.0 min (Chiracel OD-H; flow rate = 1.0 mL min^{-1}; hexane/2-propanol 98:2; 0 °C). $[\alpha]_D^{20}$ = –43 (*c* = 0.5, $CHCl_3$).

(*R*)-(–)-2-Methoxybenzyl 4′-Tolyl Sulfoxide (3e): The crude product contained a mixture of sulfoxide and sulfone (69:31). Purification by chromatography afforded the product as a clear oil (130 mg, 50%, >99% *ee*). ^1H NMR (300 MHz): δ = 7.34–7.18 (m, 5 H, Ar-H), 6.97–6.91 (m, 1 H, Ar-H), 6.90–6.77 (m, 2 H, Ar-H), 4.14–3.93 (ABq, *J* = 12.7 Hz, 2 H, SCH_2), 3.73 (s, 3 H, Ar-OCH_3), 2.40 (s, 3 H, Ar-CH_3) ppm. ^{13}C NMR (75 MHz): δ = 158.03, 141.67, 140.96, 132.55, 130.18, 129.71, 124.85, 120.79, 118.64, 110.65, 59.37, 55.68, 21.82 ppm. $C_{14}H_{16}O_2S$ (260.35): calcd. C 69.20, H 6.19, S 12.32; found C 68.90, H 6.15, S 12.35. HPLC: t_r (*R*) = 79.0 min, t_r (*S*) = 116.0 min (Chiracel OD-H; flow rate = 0.5 mL min^{-1}; hexane/2-propanol 90:10; 10 °C). $[\alpha]_D^{20}$ = +30 (*c* = 1.1, $CHCl_3$).

(*S*)-(–)-4-Methoxybenzyl 4′-Tolyl Sulfoxide (2f): The crude product contained a mixture of sulfoxide and sulfone (62:38). Purification by chromatography afforded the product as a white solid (135 mg, 52%, >99% *ee*). ^1H NMR (300 MHz): δ = 7.37–7.17 (m, 5 H, Ar-H), 6.93–6.90 (m, 1 H, Ar-H), 6.88–6.77 (m, 2 H, Ar-H), 4.29–3.97 (ABq, *J* = 12.7 Hz, 2 H, SCH_2), 3.69 (s, 3 H, Ar-OCH_3), 2.39 (s, 3 H, Ar-CH_3) ppm. ^{13}C NMR (75 MHz): δ = 159.97, 141.93, 140.00, 131.97, 129.95, 124.91, 121.57, 114.27, 63.38, 55.66, 21.86 ppm. $C_{14}H_{16}O_2S$ (260.35): calcd. 69.20, H 6.19, S 12.32; found C 69.47, H 6.09, S 12.30 ppm. M.p. 124–125.1 °C. HPLC: t_r (*R*) = 33.4 min, t_r (*S*) = 41.0 min (Chiracel OD-H; flow rate = 0.5 mL min^{-1}; hexane/2-propanol 90:10; 10 °C). $[\alpha]_D^{20}$ = –87 (*c* = 0.2, $CHCl_3$).

(*S*)-(–)-Benzyl 4′-Bromophenyl Sulfoxide (2g):[22] The crude product contained a mixture of sulfoxide and sulfone (45:55). Purification by chromatography afforded the product as a white solid (121 mg, 41%, >99% *ee*). ^1H NMR (300 MHz): δ = 7.61–7.51 (m, 2 H, Ar-H), 7.35–7.15 (m, 5 H, Ar-H), 7.01–6.94 (m, 2 H, Ar-H), 4.22–3.95 (ABq, *J* = 12.6 Hz, 2 H, SCH_2) ppm. ^{13}C NMR (75 MHz): δ = 142.19, 132.42, 130.78, 128.97, 128.85, 128.73, 126.44, 126.04, 63.80 ppm. M.p. 166.6–167.6 °C. HPLC: t_r (*R*) = 44.4 min, t_r (*S*) = 50.1 min (Chiracel OD-H; flow rate = 0.5 mL min^{-1}; hexane/2-propanol 94:6; 10 °C). $[\alpha]_D^{20}$ = –65 (*c* = 0.2, $CHCl_3$) {ref.[21] $[\alpha]_D^{20}$ = –80 (*c* = 1.6, $CHCl_3$) for (*S*) >99% *ee*}.

(*S*)-(–)-Benzyl Phenyl Sulfoxide (2h):[17d] The crude product contained a mixture of sulfoxide and sulfone (70:30). Purification by chromatography afforded the product as a white solid (110 mg, 51%, 91% *ee*). ^1H NMR (300 MHz): δ = 7.58–7.21 (m, 6 H, Ar-H), 7.01–6.91 (m, 2 H, Ar-H), 4.15–3.95 (ABq, *J* = 12.6 Hz, 2 H, SCH_2) ppm. ^{13}C NMR (75 MHz): δ = 142.86, 131.16, 130.35, 129.10, 128.84, 128.44, 128.24, 124.42, 63.57 ppm. M.p. 137.6–138.9 °C. HPLC: t_r (*R*) = 28.0 min, t_r (*S*) = 34.6 min (Chiracel OD-H; flow rate = 1.0 mL min^{-1}; hexane/2-propanol 98:2; 20 °C). $[\alpha]_D^{20}$ = –135.9 (*c* = 0.49, acetone) {ref.[17d] $[\alpha]_D^{20}$ = –169.8 (*c* = 1.0, acetone) for (*S*) 79% *ee*}.

(*S*)-(–)-Benzyl *tert*-Butyl Sulfoxide (2i):[22] The crude product contained a mixture of sulfoxide and sulfone (95:5). Purification by chromatography afforded the product as a white solid with a low melting point (83 mg, 42%, 56% *ee*). ^1H NMR (300 MHz): δ = 7.41–7.25 (m, 5 H, Ar-H), 3.85–3.60 (ABq, *J* = 12.8 Hz, 2 H, SCH_2), 1.33 (s, 9 H, C–CH_3) ppm. ^{13}C NMR (75 MHz): δ = 134.08, 132.08, 130.92, 130.06, 55.77, 55.03, 25.13 ppm. M.p. 71.9–73.3 °C. HPLC: t_r (*R*) = 18.5 min, t_r (*S*) = 23.4 min (Chiracel OD-H; flow rate = 1.0 mL min^{-1}; hexane/2-propanol 96:4; 10 °C). $[\alpha]_D^{20}$ = –128 (*c* = 0.6, $CHCl_3$) {ref.[20] $[\alpha]_D^{20}$ = –220 (*c* = 1.7, $CHCl_3$) for (*S*) 94% *ee*}.

(*S*)-(–)-Benzyl Methyl Sulfoxide (2j):[21] The crude product contained a mixture of sulfoxide and sulfone (83:17). Purification by chromatography afforded the product as a clear oil (105 mg, 76%, 10% *ee*). ^1H NMR (300 MHz): δ = 7.43–7.21 (m, 5 H, Ar-H), 4.10–3.90 (ABq, *J* = 12.8 Hz, 2 H, SCH_2), 2.46 (s, 9 H, S–CH_3) ppm. ^{13}C NMR (75 MHz): δ = 130.43, 130.23, 129.39, 128.85, 60.64, 37.65 ppm. HPLC: t_r (*R*) = 51.3 min, t_r (*S*) = 58.3 min (Chiracel OD-H; flow rate = 1.0 mL min^{-1}; hexane/2-propanol 96:4; 0 °C). $[\alpha]_D^{20}$ = 5 (*c* = 0.5, $CHCl_3$) {ref.[20] = +19.5 (*c* = 4.6, EtOH) for (*S*) 19% *ee*}.

Kinetic Resolution. General Procedure: Vanadyl acetylacetonate (2.6 mg, 0.01 mmol) and the ligand (*S*)-**4a** (7.1 mg, 0.015 mmol) in dichloromethane were stirred in a 25 mL round-bottomed flask (1 mL) for 5 min. Racemic sulfoxide **2** (1.0 mmol) in dichloromethane (1 mL) was then added and the reaction mixture was stirred for a further 5 min. Hydrogen peroxide (30% w/w, 0.8 mmol) was added portionwise over 70 min. The reaction mixture was then stirred for a further 30 min. The reaction was quenched by the addition of water (5 mL). The layers were separated and the aqueous layer was washed with dichloromethane (3 mL). The combined organic layers were washed with brine (5 mL), dried and concentrated under reduced pressure. The ratio of sulfoxide/sulfone in the crude product was determined by ^1H NMR spectroscopy. The product was purified by flash chromatography on silica gel.

(*S*)-(–)-4-Fluorobenzyl 4′-Tolyl Sulfoxide (2a): The crude product contained a mixture of sulfoxide and sulfone (30:70). Purification by chromatography afforded the product as a white solid (52 mg, 21%, 98% *ee*). Analytical data as previously reported.

(*S*)- (–)-Benzyl 4′-Tolyl Sulfoxide (2b): The crude product contained a mixture of sulfoxide and sulfone (36:64). Purification by chromatography afforded the product as a white solid (54 mg, 23%, 92% *ee*). Analytical data as previously reported.

(*S*)-(–)-4-Chlorobenzyl 4′-Tolyl Sulfoxide (2c): The crude product contained a mixture of sulfoxide and sulfone (20:80). Purification

by chromatography afforded the product as a white solid (37 mg, 14%, 97% *ee*). Analytical data as previously reported.

(*S*)-(–)-4-Methylbenzyl 4′-Tolyl Sulfoxide (2d): The crude product contained a mixture of sulfoxide and sulfone (16:84). Purification by chromatography afforded the product as a clear oil (37 mg, 15%, >99% *ee*). Analytical data as previously reported.

(*R*)-(–)-2-Methoxybenzyl 4′-Tolyl Sulfoxide (3e): The crude product contained a mixture of sulfoxide and sulfone (33:67). Purification by chromatography afforded the product as a white solid (65 mg, 25%, >99% *ee*). Analytical data as previously reported.

(*S*)-(–)-4-Methoxybenzyl 4′-Tolyl Sulfoxide (2f): The crude product contained a mixture of sulfoxide and sulfone (26:74). Purification by chromatography afforded the product as a white solid (49 mg, 19%, 74% *ee*). Analytical data as previously reported.

(*S*)-(–)-Benzyl 4′-Bromophenyl Sulfoxide (2g): The crude product contained a mixture of sulfoxide and sulfone (37:63). Purification by chromatography afforded the product as a white solid (91 mg, 31%, >99% *ee*). Analytical data as previously reported.

(*S*)-(–)-Benzyl Phenyl Sulfoxide (2h): The crude product contained a mixture of sulfoxide and sulfone (28:72). Purification by chromatography afforded the product as a white solid (45 mg, 21%, 86% *ee*). Analytical data as previously reported.

(*S*)-(–)-Benzyl *tert*-Butyl Sulfoxide (2i): The crude product contained a mixture of sulfoxide and sulfone (86:14). Purification by chromatography afforded the product as a white solid (118 mg, 60%, 5% *ee*). Analytical data as previously reported.

(*S*)-(–)-Benzyl Methyl Sulfoxide (2j): The crude product contained a mixture of sulfoxide and sulfone (54:46). Purification by chromatography afforded the product as a clear oil (79 mg, 51%, 4% *ee*). Analytical data as previously reported.

Kinetic Resolution Using $CHCl_3$ and 0.8 mmol of H_2O_2 Added Portionwise − (*S*)-(–)-Benzyl Phenyl Sulfoxide (2h): Vanadyl acetylacetonate (2.6 mg, 0.01 mmol) and the ligand (*S*)-**4a** (7.1 mg, 0.015 mmol) in chloroform (1 mL) were stirred in a 25 mL round-bottomed flask for 5 min. Racemic sulfoxide **2h** (216 mg, 1.0 mmol) in chloroform (1 mL) was then added and the reaction mixture was stirred for a further 5 min. Hydrogen peroxide (30% w/w, 0.8 mmol) was added portionwise over 70 min. The reaction mixture was then stirred for a further 30 min. The reaction was quenched by the addition of water (5 mL). The layers were separated and the aqueous layer was washed with dichloromethane (3 mL). The combined organic layers were washed with brine (5 mL), dried and concentrated under reduced pressure. The crude product was a mixture of sulfoxide and sulfone (38:62) and was purified by flash chromatography on silica gel (72 mg, 33%, 78% *ee*). Analytical data as previously reported.

Kinetic Resolution Using Jackson's Method: $CHCl_3$[10] and 0.6 mmol of H_2O_2 Added in One Portion − (*S*)-(-)-Benzyl Phenyl Sulfoxide (2h): Vanadyl acetylacetonate (2.6 mg, 0.01 mmol) and the ligand (*S*)-**4a** (7.1 mg, 0.015 mmol) in chloroform (1 mL) were stirred together in a 25 mL round-bottomed flask at 0 °C for 5 min. Racemic sulfoxide **2h** (216 mg, 1.0 mmol) in chloroform (1 mL) was then added and the reaction mixture was stirred for a further 5 min at 0 °C. Hydrogen peroxide (30% w/w, 0.6 mmol) was added in one portion dropwise and the reaction mixture was then stirred for 16 h at 0 °C. The reaction was quenched by the addition of water (5 mL). The layers were separated and the aqueous layer was washed with dichloromethane (3 mL). The combined organic layers were washed with brine (5 mL), dried and concentrated under reduced pressure. The crude product was a mixture of sulfoxide and sulfone (39:61) and was purified by flash chromatography on silica gel (63 mg, 29%, 80% *ee*). Analytical data as previously reported.

Kinetic Resolution Using an Iron Catalyst:[17c] Iron acetylacetonate (7.1 mg, 0.02 mmol) and the ligand (*S*)-**4a** (18.9 mg, 0.04 mmol) in dichloromethane were stirred in a 25 mL round-bottomed flask (0.7 mL) for 5 min. The solution was then transferred to a 25 mL flask containing a suspension of 4-methoxybenzoic acid (1.5 mg, 0.01 mmol) in dichloromethane (0.5 mL). The resulting mixture was stirred for 10 min. Racemic sulfoxide **2b** (230 mg, 1.0 mmol) in dichloromethane (0.8 mL) was then added and the reaction mixture was stirred for a further 5 min. Hydrogen peroxide (30% w/w, 1.1 mmol) was added portionwise over 70 min. The reaction mixture was then stirred for a further 24 h. The reaction was quenched by the addition of water (5 mL). The layers were separated and the aqueous layer was washed with dichloromethane (3 mL). The combined organic layers were washed with brine (5 mL), dried and concentrated under reduced pressure. The crude product was a mixture of sulfoxide and sulfone (84:16) and was purified by flash chromatography on silica gel (171 mg, 74%, 5% *ee*). Analytical data as previously reported.

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