Asymmetric Synthesis of Protected α-Hydroxyaldehydes *via* Reduction of α-Arylthio-β-oxosulphoxides †

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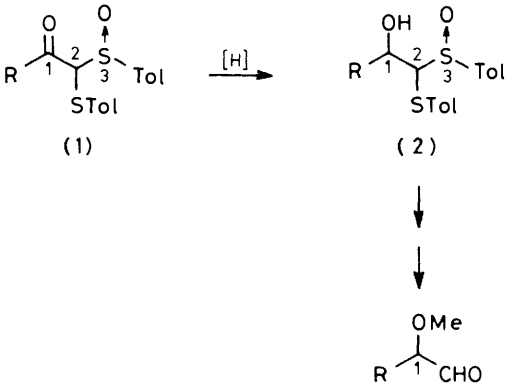
The complex metal hydride reduction of α-arylthio-β-oxosulphoxides to the corresponding alcohols is highly stereospecific. The stereochemical course of the reaction has been determined and a detailed examination of the factors responsible for the stereospecificity has been made. The asymmetric reduction has been used to synthesise protected α-hydroxyaldehydes in high optical purity starting from (+)-(*S*)-*p*-tolyl *p*-tolylthiomethyl sulphoxide and acyl chlorides.

The reduction of readily available β-oxosulphoxides is a suitable reaction for studying the transfer of chirality from sulphur to carbon moieties and a valuable tool for the synthesis of optically active non-sulphur compounds.[1] However, although various papers have appeared in this area,[1] the interest has been mainly focused on the problem of 1,3-asymmetric induction and little attention [2,3a] has been paid to ketones possessing a chiral α-carbon in addition to the β-sulphinyl function.

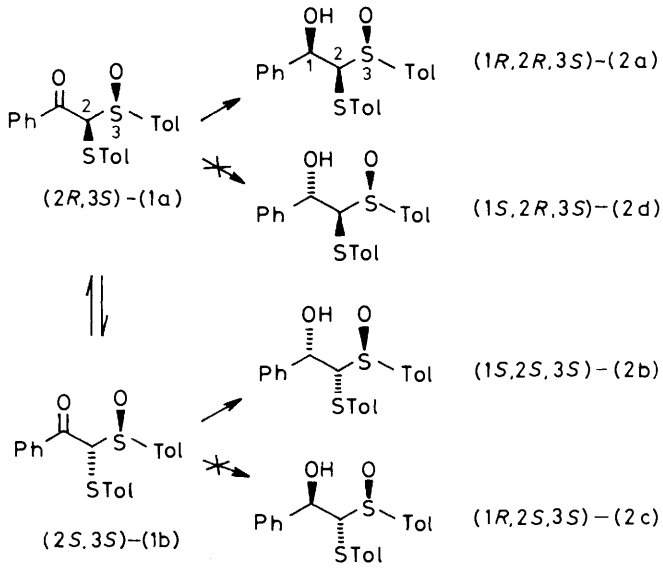
Recently we described a new method for obtaining protected α-hydroxyaldehydes with 100% optical purity.[3a] The key step of this procedure was the $LiAlH_4$ reduction at −78 °C in Et_2O–THF of α-arylthio-β-oxosulphoxides (Scheme 1) which proceeded with a sterospecificity >99 : 1. Since such a large asymmetric induction is not a usual result in acyclic substrates, we have examined this reaction in more detail and we report now the results collected in order to understand the reasons for the observed stereospecificity.

First we established the stereochemical course of the reaction (Scheme 2). Since compounds (1) and (2) have two and three chiral centres respectively, in principle we should expect two diastereoisomers for (1) and four diastereoisomers for (2). The absolute configurations of (1a) and (1b) and (2a—d) (R = Ph) were determined as follows. The configurations of centres 1 and 3 of (2a) and (2b) had already been established as 1*R*,3*S* and 1*S*,3*S* respectively.[3a] Optically active (2c) and (2d) were obtained, together with (2a) and (2b), by aldol condensation of benzaldehyde with (−)-(*S*)-*p*-tolyl *p*-tolylthiomethyl sulphoxide.[3b] After chromatographic separation and fractional crystallisation, the four diastereoisomers were separately reduced to α-hydroxydithioacetals: isomers (2a) and (2c) gave the (+)-dithioacetal, while (2b) and (2d) gave the (−)-dithioacetal. Moreover, the low J_{CHCH} values in $CDCl_3$ for (2a) and (2b), in contrast with those of (2c) and (2d) (see Table 1), show that they must have the *erythro* configuration ‡ at their centres 1 and 2, *i.e.* 1*R*,2*R* and 1*S*,2*S* respectively, on the reasonable assumption that their hydrogen-bonded conformations are preferred.[4] Since (1a) and (1b) gave respectively (2a) and (2b) upon $LiAlH_4$ reduction, the configurations of (1a) and (1b) are automatically assigned as 2*R*,3*S* and 2*S*,3*S*, respectively. The stereochemical course of the reaction is depicted in Scheme 2. Absolute configurations of (1a) and (1b) and (2a—d) when R = Bu^t and Me[CH_2]$_5$ (see Scheme 1) were not determined, but low J_{CHCH} values in (2a) and (2b) indicate that, as for R = Ph, the two major diastereoisomers always obtained in the reduction have the *erythro* configuration (1*S*,2*S*,3*S* or 1*R*,2*R*,3*S*) at C-1 and C-2.

Of the various models generally proposed to rationalise the stereochemistry of reduction of carbonyl compounds,



Scheme 1. R = Ph, Bu^t, Me$(CH_2)_5$, Tol = *p*-MeC_6H_4



Scheme 2. Tol = *p*-MeC_6H_4

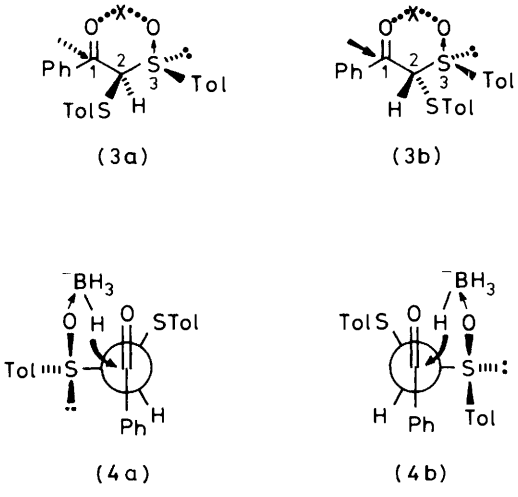
† Preliminary results have been presented at the XIII Convegno di Chimica Organica della Società Chimica Italiana (Milano, 2—6 October, 1982).

‡ We follow here the nomenclature proposed by Heathcock (H. H. Heathcock, C. T. White, J. J. Morrison, and D. VanDerveer, *J. Org. Chem.*, 1981, **46**, 1296).

Table 1. ^{1}H N.m.r. data (δ in $CDCl_3$) for α-arylthio-β-hydroxysulphoxides (2a—d) (*J*/Hz in parentheses)

R	Compd.	*p*-Me-C$_6$H$_4$S (s, 3 H)	*p*-Me-C$_6$H$_4$SO (s, 3 H)	C*H*(SAr)-SOAr (d, 1 H)	C*H*OH (1 H)	OH (d, 1 H) [a]	ArH (m)	Others
Ph	(2a)	2.21	2.40	3.99 (3.0)	5.56 (app. t, 3.0)	2.84 (3.0)	6.54—7.61 (13 H)	
Ph	(2b)	2.21	2.39	3.81 (1.7)	5.64 (dd, 1.7, 3.7)	4.17 (3.7)	6.48—7.60 (13 H)	
Ph	(2c)	2.18	2.40	4.05 [b]	5.14—5.30 [c] (total 2 H)		6.26—7.79 (13 H)	
Ph	(2d)	2.24	2.46	4.18 (9.5)	4.97 (dd, 1.9, 9.5)	5.34 (1.9)	6.53—7.83 (13 H)	
Bu^t	(2a)	2.35	2.37	3.84—3.97 [c,d] (total 2 H)		3.12 (4.1)	7.07—7.43 (8 H)	0.83 (s, 9 H, Bu^t)
Bu^t	(2b)	2.34	2.40	4.35 (0.7)	4.02 (dd, 0.7, 5.6)	1.09 (6.5)	7.06—7.85 (8 H)	0.98 (s, 9 H, Bu^t)
Bu^t	(2c)	2.30	2.37	3.80—4.20 (ABC, total 3 H, J_{CHCH} 6.2 Hz)			6.95—7.66 (8 H)	1.00 (s, 9 H, Bu^t)
Bu^t	(2d)	2.28	2.40	3.83—5.13 (ABC, total 3 H, J_{CHCH} 4.8 Hz)			7.03—7.68 (8 H)	1.02 (s, 9 H, Bu^t)
Hex [e]	(2a)	2.28	2.39	3.93 (2.6)	4.23—4.53 (m)	2.21 (3.8)	6.95—7.66 (8 H)	0.80—1.96 (m, 13 H, Hex)
Hex	(2b)	2.31	2.38	3.76 (1.4)	4.22—4.50 (m)	3.66 (4.7)	7.02—7.76 (8 H)	0.77—1.88 (m, 13 H, Hex)
Hex	(2c)	2.27	2.38	3.92 (8.0)	4.06—4.42 (m, total 2 H)		6.96—7.70 (8 H)	0.79—1.74 (m, 13 H, Hex)

[a] Exchangeable on shaking with D_2O. [b] X Part of an ABX system; J_{CHCH} 9.5 Hz. [c] AB Part of an ABX system. [d] J_{CHCH} 0.7 Hz. [e] Hex = Me[CH_2]$_5$.



Scheme 3. X = co-ordinating species (see text)

the cyclic model [5,6] [see (3a) and (3b) in Scheme 3, corresponding to (1a) ⟶ (2a) and (1b) ⟶ (2b)] seems to be the most suitable for explaining the observed stereospecificity * in the reduction of (1a) and (1b). The nature of the co-ordinating species (X), in principle, could be either the anionic part of the reducing agent [5] or, as seems more likely in the light of recent results on the reduction of β-oxoesters,[6] the lithium ion. To distinguish between these two possibilities and to gain more insight into the mechanism of the reaction we performed the experiments reported in Table 2 (entries 3—10). The immediate consideration which emerges from an examination of the data is that the cation does not seem to play any important role with regard to the stereochemical aspects of the reduction: in fact, the reaction also proceeds with a large degree of stereospecificity with $NaBH_4$ in EtOH,[7] either in the absence or in the presence of crown ether,[8]† and with Bu$^n_4$NBH_4 in tetrahydrofuran (THF).‡ Also the temperature and the solvent seem to have little effect on the (2a) : (2d) and (2b) : (2c) ratios. Therefore, in the light of these results, it is apparent that the observed high stereospecificity can be explained with a cyclic model only if it is the anionic part of the reducing agent that strongly co-ordinates the carbonyl and sulphinyl moieties (X = AlH_4^- or BH_4^-).

Another attractive explanation could be given [see (4a) and (4b) in Scheme 3, corresponding to the (1a) ⟶ (2a) and (1b) ⟶ (2b) conversions respectively] which involves a Felkin-type conformation [9] with an ' anti-Felkin ' attack due to intramolecular assistance of the sulphinyl group on the complex metal hydride attack.[10] It is noteworthy that, according to Ogura *et al.*,[2b] the observed stereochemistry could also be explained by a simple ' all-staggered ' open-chain model, with the sulphinyl group not directly involved in the hydride transfer. However, besides the observed large stereospecificity, which is not usual in open-chain flexible systems, some support for the direct participation of the sulphinyl group comes from the $LiAlH_4$ reduction of the α-arylthio-β-oxosulphone PhCOCH(SC$_6$H$_4$Me-*p*)SO$_2$C$_6$H$_4$-Me-*p* § which affords both diastereoisomeric alcohols with the *threo* diastereoisomer predominating (*threo* : *erythro*, 77 : 23).¶ In accordance with the strong polarity of the sulphonyl group and with its poor co-ordinating properties this result can be reasonably accounted for by a normal Felkin model.[9]

Finally, a more detailed examination of Table 2 reveals some further interesting features of the $NaBH_4$ reaction. Differing from $LiAlH_4$,[3a] the $NaBH_4$ reduction always affords a mixture of the two diastereoisomers (2a) and (2b), also starting from pure (1a). Moreover, the partial yields (1a) ⟶ (2a) and (1b) ⟶ (2b) are sensitive to change in the (1a) : (1b) ratio (see Table 2, entries 2—4). Since (2a) and (2b) do not epimerise under the reaction conditions, the most reasonable explanation is that during $NaBH_4$ reduction a competitive epimerisation (1a) ⇄ (1b) occurs. To confirm this hypothesis we reduced a diastereoisomeric mixture [(1a) : (1b) 8 : 2] in EtOD with a deficiency of $NaBH_4$ (0.3 equiv.) at −78 °C: the recovered substrate was partially deuteriated (about 40%) and the diastereoisomeric ratio (1a) : (1b) changed to 6 : 4.

* Other models, *e.g.* a five-membered cyclic model (involving *p*-tolylthio and carbonyl moieties) and open-chain Cram's, Karabatsos', and Felkin's models (ref. 9 and references therein) predict the wrong diastereoisomer.

† 15-Crown-5 is possibly too weak a chelating agent to disrupt the intramolecular co-ordination between sulphinyl and carbonyl moieties by the sodium cation (see G. Chassaing and A. Marquet, *Tetrahedron*, 1978, **34**, 1399).

‡ Tetra-alkylammonium ion should act as an alkaline metal cation complexed with a cryptate (see J. R. Boone and E. C. Ashby, in ' Topics in Stereochemistry,' eds. N. L. Allinger and E. L. Eliel, John Wiley and Sons, New York, 1979, vol. 11, p. 64).

§ More extensive data on this reaction are to be published.

¶ The J_{CHCH} values in $CDCl_3$ were 9.5 and 1.1 Hz for the *threo* and *erythro* diastereoisomers, respectively.

Table 2. Complex metal hydride reduction of α-arylthio-β-oxosulphoxides (1a) and (1b)

Entry	R	Hydride [molar ratio to (1)]	Solvent (v/v)	Additive [molar ratio to (1)]	T (°C)	(1a) : (1b) [a]	(2a) : (2b) : (2c) : (2d) [b,c]	Yield (%)
1 [d]	Ph	$LiAlH_4$ [2]	Et_2O–THF (70 : 30)		−78	>99 : 1	>99 : 1 : 0 : 0	76
2 [d]	Ph	$LiAlH_4$ [2]	Et_2O–THF (70 : 30)		−78	68 : 32	83 : 17 : 0 : 0	64
3	Ph	$NaBH_4$ [2]	abs. EtOH		−78	>99 : 1	94 : 6 : 0 : 0	79
4	Ph	$NaBH_4$ [2]	abs. EtOH		−78	68 : 32 [e]	75 : 25 : 0 : 0	70
5	Ph	$NaBH_4$ [2]	abs. EtOH		−78	37 : 63	54 : 46 : 0 : 0	68
6	Ph	$NaBH_4$ [2]	abs. EtOH	15-crown-5 [4]	−78	94 : 6	91 : 9 : 0 : 0	83
7	Ph	$Bu^n_4NBH_4$ [10]	THF		R.t.	68 : 32	79 : 21 : 0 : 0	72
8	Ph	$NaBH_4$ [2]	EtOH–H_2O (96 : 4)		R.t.	68 : 32	63 : 37 : 0 : 0	75
9	Ph	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)		R.t.	68 : 32	83 : 17 : 0 : 0	80
10	Ph	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)		−30	68 : 32	75 : 25 : 0 : 0	80
11	Ph	$NaBH_4$ [50]	EtOH–H_2O (96 : 4)		R.t.	68 : 32	90 : 10 : 0 : 0	73
12	Ph	$NaBH_4$ [50]	EtOH–H_2O (96 : 4)	NaOH [0.05]	R.t.	68 : 32	90 : 10 : 0 : 0	77
13	Ph	$NaBH_4$ [50]	EtOH–H_2O (96 : 4)	NaOH [0.05]	R.t.	94 : 6	90 : 10 : 0 : 0	74
14	Ph	$NaBH_4$ [50]	EtOH–H_2O (96 : 4)	Et_3N [1]	R.t.	68 : 32	91 : 9 : 0 : 0	74
15	Ph	$NaBH_4$ [2]	EtOH–H_2O (96 : 4)	NaOH [0.05]	R.t.	68 : 32	60 : 40 : 0 : 0	75
16	Ph	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)	NaOH [0.05]	R.t.	68 : 32	90 : 10 : 0 : 0	80
17	Ph [f]	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)	NaOH [0.05]	−30	68 : 32	72 : 28 : 0 : 0	76
18 [d]	Bu^t	$LiAlH_4$ [2]	Et_2O–THF (70 : 30)		−78	36 : 64	36 : 64 : 0 : 0	75
19	Bu^t	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)		R.t.	36 : 64 [e]	33 : 67 : 0 : 0	80
20	Bu^t	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)		−30	36 : 64	31 : 69 : 0 : 0	88
21	Bu^t	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)	NaOH [0.05]	−30	36 : 64	13 : 87 : 0 : 0	85
22	Bu^t	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)	NaOH [0.05]	−30	5 : 95	15 : 85 : 0 : 0	83
23	Bu^t	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)	NaOH [0.05]	R.t.	36 : 64	50 : 50 : 0 : 0	80
24 [d]	Hex [g]	$LiAlH_4$ [2]	Et_2O–THF (70 : 30)		−78	59 : 41	74 : 26 : 0 : 0	60
25	Hex	$NaBH_4$ [2]	abs. EtOH		R.t.	59 : 41 [e]	71 : 18 : 5 : 6	85
26	Hex	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)		R.t.	59 : 41	57 : 30 : 3 : 10	80
27	Hex	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)		−30	59 : 41	58 : 36 : 1 : 5	80
28	Hex	$NaBH_4$ [2]	abs. EtOH	EtONa [0.05]	R.t.	59 : 41	76 : 13 : 4 : 7	89
29	Hex	$NaBH_4$ [2]	abs. EtOH	EtONa [0.05]	R.t.	81 : 19	75 : 14 : 5 : 6	86
30	Hex	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)	NaOH [0.05]	R.t.	59 : 41	55 : 27 : 5 : 13	82
31	Hex	$NaBH_4$ [2]	EtOH–H_2O (70 : 30)	NaOH [0.05]	−30	59 : 41	66 : 26 : 2 : 6	81

[a] Determined by n.m.r.; (1a) is always the diastereoisomer with the higher chemical shift. [b] Determined by n.m.r. when R = Ph and Bu^t; (2c) and (2d) were never detectable in any experiment by this technique: h.p.l.c. analysis (eluant $CHCl_3$–Pr^i_2O, 55 : 45) revealed traces of (2c) and (2d), always less than 1% each. When R = Hex, n.m.r. was useless owing to the presence of appreciable amounts of (2c) and (2d) and final reaction mixtures were analysed by h.p.l.c. ($CHCl_3$–Pr^i_2O, 6 : 4). The order of h.p.l.c. elution is (2a), (2c), (2d), and (2b) when R = Ph; (2b), (2a), (2c), and (2d) when R = Bu^t; (2a), (2c), (2d), and (2b) when R = Hex. [c] Absolute configurations of (2a—d) (R = Ph) are given in Scheme 2. When R = Bu^t and Hex, (2a) and (2b) are the *erythro* diastereoisomers (see Text) derived from (1a) and (1b) respectively. The stability of each diastereoisomer under the reaction conditions was tested. [d] Ref. 3*a*. [e] (2a) : (2b) Ratios directly obtained by quenching the final acylation mixture at −78 °C (see Experimental section). [f] Other reaction conditions were tested on (1; R = Ph), *e.g.* $NaBH_4$ in EtONa–absolute EtOH, NaOH–70% aq. Pr^iOH, NaOH–70% aq. THF, phase-transfer conditions [CH_2Cl_2–40% Bu^n_4NOH, 7 : 3 (v/v)] and modified borohydrides ($NaBH_4$ plus equimolecular amounts of $MeCO_2H$ or $Me_2CHCH_2CO_2H$) (see D. J. Morrison, E. D. Grandbois, and S. I. Howard, *J. Am. Chem. Soc.*, 1980, **45**, 4229; H. Hirao, S. Nakahama, H. Mokizuki, S. Itsuno, and M. Yamakazi, *ibid.*, p. 4231) in NaOH–70% aq. Pr^iOH at room temperature afforded poorer results in the diastereoselectivity. Increasing the amount of water in EtOH (*e.g.*, operating with $NaBH_4$ in NaOH–50% aq. EtOH at room temperature) gave good diastereoselectivity [(2a) : (2b) *ca.* 9 : 1] but reactions were slowed by the extreme dilution caused by the low solubility of (1) in this medium. [g] Hex = $Me[CH_2]_5$.

In principle, this competition should be altered by varying the reaction conditions, and for this purpose the reaction was investigated in detail in order to find the most suitable conditions for a fast epimerisation and a highly stereoselective reduction. In fact, the ratio (2a) : (2b) changes with the solvent, temperature, molar ratio of reducing agent to substrate (1), and basic substances added in catalytic amounts. Some representative experiments are reported in Table 2 (entries 9—17). The examination of data shows that added bases under suitable conditions of solvent and temperature cause the diastereoisomeric ratio of the β-hydroxysulphoxides (2a) : (2b) to increase (up to 9 : 1) and to become independent of the starting (1a) : (1b) ratio. Thus, though the acylation of *p*-tolyl *p*-tolylthiomethyl sulphoxide is a reaction occurring with low diastereoselectivity [(1a) : (1b) = 68 : 32],[3a] this result suggests that it is still possible to achieve α-arylthio-β-hydroxysulphoxides with good overall diastereoselectivity through the acylation–reduction route if the mixture of (1a) and (1b), as obtained in the first stage, is reduced under conditions of fast equilibration of the reactants. The overall reaction represents therefore an example of the kinetic resolution of rapidly epimerising reactants.

An interpretation of the preferential formation of (2a) under equilibrating conditions can be given on the basis of the models previously described if the configuration at centre 3 is taken into account. In fact, an examination of models (Scheme 3) shows that the transition state [(3a) or (4a)] leading from (1a) to (2a) could be favoured over the one [(3b) or (4b)] leading from (1b) to (2d), both in cyclic and in Felkin-type models, owing to lower 1,3-interactions of substituents at chiral sulphur with either entering hydride [(3a)] or phenyl group [(4a)]. Thus the configuration at centre 3 seems to have little influence in determining the direction and the extent of asymmetric induction in the reduction of (1a) and (1b) separately, but it seems to play an important role in affecting the relative rates of reduction of the two diastereoisomers.

Table 3. ^{1}H N.m.r. data (δ in $CDCl_3$) for α-arylthio-β-oxosulphoxides (1a) and (1b)

		p-MeC_6H_4S (s, 3 H)	*p*-MeC_6H_4SO (s, 3 H)	CH (s, 1 H)	ArH (m)	Others
R = Ph	(1a)	2.29	2.34	5.47	6.96—7.94 (13 H)	
	(1b)	2.28	2.41	5.39	6.97—7.74 (13 H)	
R = Bu^t	(1a)	2.27	2.40	4.87	6.88—7.88 (8 H)	1.23 (s, 9 H, Bu^t)
	(1b)	2.36 [a]		4.70	7.12—7.62 (8 H)	0.81 (s, 9 H, Bu^t)
R = Hex [b]	(1a)	2.35	2.37	4.67	7.04—7.63 (8 H)	0.84—1.24 (m, 11 H, Me[CH_2]$_4$), 2.42 (t, 2 H, *J* 7.8 Hz, CH_2CO) [c]
	(1b)	2.29	2.37	4.48	7.03—7.63 (8 H)	0.84—1.24 (m, 11 H, Me[CH_2]$_4$), 2.62 (t, 2 H, *J* 6.7 Hz, CH_2CO)

[a] Overlapping s; total 6 H. [b] Hex = Me[CH_2]$_5$. [c] Partially overlapped with methyl group signals.

In order to investigate the generality of this result we examined two other substrates (1a) and (1b) (R = Bu^t and Me[CH_2]$_5$) (see entries 19—23 and 25—31 of Table 2). Also in these cases we found that added base causes an increase in the (2b) : (2a) ratio up to 87 : 13 when R = Bu^t, and in the (2a) : (2b) ratio up to 76 : 13 when R = Me[CH_2]$_5$.

Since as previously described [3] the α-arylthio-β-hydroxysulphoxides (2) can be easily transformed into *O*-protected α-hydroxyaldehydes, the $NaBH_4$ method herein described represents an alternative method to $LiAlH_4$ reduction [3a] of achieving optically active protected α-hydroxyaldehydes when optically active *p*-tolyl *p*-tolylthiomethyl sulphoxide is used. In fact, on starting from benzoyl chloride and optically pure (+)-(*S*)-*p*-tolyl *p*-tolylthiomethyl sulphoxide [3a] and reducing the mixture (1a) : (1b) = 68 : 32 under the conditions of entry 16 (Table 2), a mixture of (2a) and (2b) with an 80% diastereoisomeric excess of (2a) was obtained. At this stage the diastereoisomeric mixture (2a) and (2b) was directly worked up to give (−)-(*R*)-α-methoxyphenylacetaldehyde in 80% enantiomeric excess, or, more conveniently, (2a) and (2b) were separated by fast column chromatography and independently transformed into both (−)-(*R*)- and (+)-(*S*)-α-methoxyphenylacetaldehyde which were 100% optically pure.

Experimental

^{1}H N.m.r. spectra were recorded with a Varian FT-80 (80 MHz) instrument, using Me_4Si as internal standard. Optical rotations were measured at 25 °C on a Jasco DIP-181 digital polarimeter, using a 1-dm tube. H.p.l.c. analyses were run with a Varian 5000 instrument using a S_i-100 10 μm column (Brownlee Labs).

Organic extracts were dried (Na_2SO_4) and filtered, and the solvent then removed at <40 °C under reduced pressure. Chromatographic separations were performed either with a Jobin Yvon Chromatospac Prep column packed with Silica Gel 60 H or with a Lobar pre-packed column LiChroprep Si 60 (40—63 μm) (Merck).

Benzaldehyde was purified as described.[3b] Trimethylacetaldehyde and heptanal, as well as benzoyl, trimethylacetyl, and heptanoyl chlorides, were redistilled under reduced pressure just before use.

Reactions involving air-sensitive reagents were carried out as described.[3b]

Synthesis of the α-Arylthio-β-oxosulphoxides (1a) *and* (1b).—n-Butyl-lithium (11 mmol) in n-hexane was added at −78 °C to a solution of *p*-tolyl *p*-tolylthiomethyl sulphoxide (10 mmol) in dry THF (60 ml). After 10 min, the acyl chloride (5 mmol) was added. After stirring for 20 min, further portions of Bu^{n}Li (5.5 mmol) and of acyl chloride (2.5 mmol) were added following the same procedure. Similar additions were repeated three times, then the reaction was quenched (saturated aqueous NH_4Cl) and extracted with Et_2O. The crude product obtained from the usual work-up was chromatographed (n-hexane–ethyl acetate, 1 : 1) to give in each case a mixture of the two diastereoisomers (70%) (1a) : (1b) ratio 68 : 32 (R = Ph), 36 : 64 (R = Bu^t) and 59 : 41 (R = Me[CH_2]$_5$). ^{1}H N.m.r. data are reported in Table 3 and analytical data in Table 4. Pure (1a; R = Ph and Me[CH_2]$_5$) and (1b; R = Bu^t) could be obtained by successive crystallisations from Et_2O. Different (1a) : (1b) ratios reported in Table 1 were obtained by just one crystallisation from Et_2O. Diastereoisomeric (1a) : (1b) ratios were determined by the ratio of the intensities of methine proton signals.

Table 4. Analytical data for α-arylthio-β-oxosulphoxides (1)

	Found (%)			Requires (%)	
R	C	H	Formula	C	H
Ph	68.7	5.4	$C_{22}H_{20}O_2S_2$	69.4	5.3
Bu^t	66.6	6.8	$C_{20}H_{24}O_2S_2$	66.6	6.7
Hex [a]	68.2	7.4	$C_{22}H_{28}O_2S_2$	68.0	7.3

[a] Hex = Me[CH_2]$_5$.

$NaBH_4$ *Reduction of the α-Arylthio-β-oxosulphoxides* (1a) *and* (1b).—To a solution of $NaBH_4$ in the appropriate solvent (see Table 1) (7 ml per mmol of $NaBH_4$) a solution of compound (1) in the same solvent [1 ml per 10 mg of (1)] was added. The reaction was monitored by t.l.c. (CH_2Cl_2–Pr^iOH, 6 : 4). 4% Aqueous HCl was added until the solution was acidic, then the solvent was evaporated and the residue taken up with Et_2O–water and extracted with Et_2O. The crude final residue was directly analysed either by ^{1}H n.m.r. (by using the ratio of the intensities of the dithioacetal methine signals and/or t-butyl signals when R = Bu^t) or by h.p.l.c. (see Table 1).

$LiAlH_4$ *Reduction of the α-Arylthio-β-oxosulphoxide* (1a; R = Ph).—To a suspension of $LiAlH_4$ in dry Et_2O (40 ml) at −78 °C, a solution of (1a) (1 mmol) in dry THF (17 ml) was added. After 30 min the reaction was quenched (4% aqueous HCl) and extracted with Et_2O. The crude final residue was analysed as described for $NaBH_4$ reduction.

$Bu^n_4NBH_4$ *Reduction of the α-Arylthio-β-oxosulphoxides* (1a; R = Ph) *and* (1b; R = Ph).—To a solution of $Bu^n_4NBH_4$ (10 mmol) in dry THF (12 ml) at room temperature a solution of (1) (1 mmol) in dry THF (10 ml) was added. After 60 min, the reaction was quenched (4% aqueous HCl) and extracted

Table 5. Analytical data for α-arylthio-β-hydroxysulphoxides (2a—d)

R		M.p. (°C)	Found (%) C	Found (%) H	Formula	Requires (%) C	Requires (%) H
Ph	(2a)	119—120	69.3	5.7			
Ph	(2b)	141—142	68.9	5.8			
Ph	(2c)	134—135	69.0	5.8	$C_{22}H_{22}O_2S_2$	69.1	5.8
Ph	(2d)	143—145	69.0	5.7			
Bu^t	(2a)	134—135	66.0	7.3			
Bu^t	(2b)	134—135	66.6	7.1			
Bu^t	(2c)	136—137	66.4	7.1	$C_{20}H_{26}O_2S_2$	66.3	7.2
Bu^t	(2d)	97—99	65.9	7.2			
Hex[a]	(2a)	105—107	67.9	7.8			
Hex	(2b)	95—96	67.6	7.8			
Hex	(2c)	89—90	67.6	7.6	$C_{22}H_{30}O_2S_2$	67.65	7.7

[a] Hex = $Me[CH_2]_5$.

with Et_2O. The crude final residue was chromatographed (n-hexane–ethyl acetate 1 : 1) and analysed as described for $NaBH_4$ reduction.

Synthesis of the α-Arylthio-β-hydroxysulphoxides (2a—d).—The reaction between the lithium salt of *p*-tolyl *p*-tolylthiomethyl sulphoxide and benzaldehyde or trimethylacetaldehyde or heptanal was performed as previously described [3b] for benzaldehyde. The yields exceeded 90% in each case and a mixture of diastereoisomers was formed. By column chromatography (CH_2Cl_2–Et_2O, 7 : 3, CH_2Cl_2–ethyl acetate, 9 : 1, and CH_2Cl_2–ethyl acetate, 75 : 25 when R = Ph, Bu^t, and $Me[CH_2]_5$ respectively) and fractional crystallisation (from Et_2O or Et_2O–CH_2Cl_2) pure samples of (2a—d) (R = Ph and Bu^t) and (2a—c) (R = $Me[CH_2]_5$) were obtained; (2d; R = $Me[CH_2]_5$) was never obtained in significant amounts either from reduction of the β-oxosulphoxide or from addition to the aldehyde. ^{1}H N.m.r. data are reported in Table 1 and analytical data in Table 5.

Reduction of 1-Phenyl-2-p-tolylthio-2-p-tolylsulphinylethanol (2; R = Ph) *to 1-Phenyl-2,2-bis(p-tolylthio)ethanol.*—This reduction was performed according to the described procedure.[11] The crude product was chromatographed (n-hexane–ethyl acetate, 9 : 1) to yield $PhCH(OH)CH(SC_6H_4Me\text{-}p)_2$, m.p. 99—100 °C (from Et_2O–n-pentane) (Found: C, 72.2; H, 5.9. $C_{22}H_{22}OS_2$ requires C, 72.1; H, 6.05%); δ($CDCl_3$) 2.31 (s, 6 H, 2 × Me), 3.24 (d, 1 H, *J* 2.8 Hz, OH, exchangeable with D_2O), 4.44 [d, 1 H, *J* 4.9 Hz, C*H*$(SAr)_2$], 4.83 (dd, 1 H, *J* 2.8 and 4.9 Hz, C*H*OH), and 6.91—7.31 (m, 13 H, ArH). When the four diastereoisomers (2a—d) (R = Ph) obtained from optically pure (+)-(*S*)-*p*-tolyl *p*-tolylthiomethyl sulphoxide [3b] were separately subjected to this procedure, (+)-α-hydroxydithioacetal {$[\alpha]_D$ +200° and +211° (*c* 0.4 in acetone)} was obtained from (2a) and (2c), while (−)-α-hydroxydithioacetal {$[\alpha]_D$ −202° and −206° (*c* 0.4 in acetone)} was obtained from (2b) and (2d).

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