Asymmetric Induction in the Reduction of Optically Active N-Alkylidenesulphinamides by Metal Hydrides. A New, Efficient Enantioselective Route to Chiral Amines

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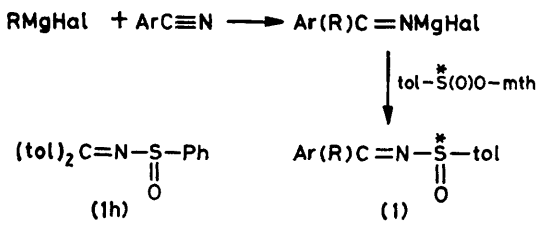
A series of racemic and optically active *N*-alkylidenesulphinamides has been prepared and their reduction by metal hydrides studied. The extent of asymmetric synthesis mainly depends on the nature of the reducing species; the best results (up to 92% of stereoselectivity) are obtained with alkoxy-lithium aluminium hydrides. A new, highly enantioselective synthesis of amines is described.

REACTIONS of optically active sulphur derivatives often result in high degrees of asymmetric induction, as shown by several recent reports.[1] Various classes of chiral compounds have been synthesized by exploiting transfer of chirality from sulphur to carbon. For this purpose, the sulphoxide is the most widely used optically active sulphur species, since it can be easily inserted into molecules bearing different functionalities, both by direct Andersen synthesis or by reaction of α-sulphinyl carbanions with suitable substrates.

The synthetic strategy to the functionalized optically active sulphoxide must account for two main factors in order to maximize the inducing ability of the sulphinyl group: (i) the centre that will undergo the asymmetric transformation should be close enough (α, β, or γ) to the chiral moiety; (ii) easy co-ordination between the reagent and the sulphinyl oxygen, which must be regarded as important, if not essential, to the success of the stereoselective process.

On the basis of these general ideas we have prepared,[2] with an easy, one-pot synthesis, a series of *N*-alkylidenesulphinamides in both optically active and racemic forms.[3] Our synthesis involves the reaction of an alkyl



a; R = Me, Ar = Ph
b; R = Et, Ar = Ph
c; R = Pr^{i}, Ar = Ph
d; R = naph, Ar = Ph
e; R = Bu^{t}, Ar = Ph
f; R = Ph, Ar = Ph
g; R = tol, Ar = tol

tol = *p*-tolyl; mth = menthyl; naph = α-naphthyl throughout this paper.

or an aryl Grignard reagent with an aromatic nitrile to give an imino-Grignard, which is allowed to react with a sulphinate ester. Starting from (−)-menthyl (*S*)-toluene-*p*-sulphinate the optically active *N*-alkylidenesulphinamides (1a)—(1g) were obtained in good yields.†

† Together with compound (1b) minor amounts of the tautomeric enamine were obtained (see Experimental section).

As in many analogous Andersen-type syntheses, the reactions proceed with a high stereospecificity and, as we have already pointed out,[2] the optically active *N*-alkylidenesulphinamides (1a)—(1g) thus obtained are enantiomerically pure. Furthermore, experimental evidence allowed us to assign the (*S*) absolute configuration to the sulphur atom of compounds (1a)—(1g). As far as the *E*–*Z* isomerism about the carbon–nitrogen double bond is concerned, we confirmed the results found by Davis *et al.*[4] who reported a barrier to planar inversion at nitrogen of ⩽17 kcal/mol (J = 4.184 cal) in similar

TABLE 1

Data for the *N*-alkylidenesulphinamides (1a)—(1g)

Compound	M.p./°C (n_D^{25})	$[\alpha]_D^{25}$/° [a]	$[\alpha]_{436}^{25}$/° [a]
(1a)	99—100	+98.0	+204.0
(1b)	(1.6170)	+26.2	+35.0
(1c)	74—75 [b]	−288.0	−696.0
(1d)	166—168 [c]	+7.1	+252.0
(1e)	(1.5751)	−174.3	−414.8
(1f)	143—144 [c]	−56.2	+61.0
(1g)	111—112 [b]	−61.0	+50.3

[a] *c* 1, In chloroform. [b] From bis(methylethyl) ether. [c] From ethanol.

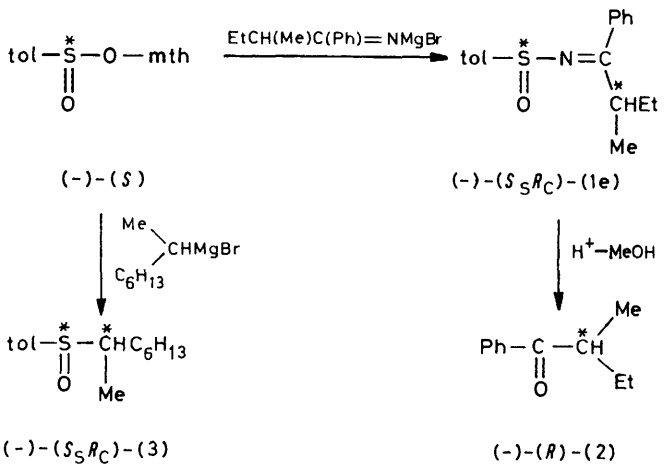
compounds. Indeed, the ^{13}C n.m.r. spectra of compounds (1a) and (1c) remained unchanged in the range −50—+50 °C, while for compound (1h) coalescence was observed at 28 °C with an estimated value of 15.0 ± 1 kcal/mol for the barrier.‡,§ Thus, compounds (1a)—(1h) exist as rapidly interconverting mixtures of *E*- and *Z*-isomers at room temperature.

An interesting situation was found in the case of compound (1e) which was obtained as a 3 : 2 mixture of diastereoisomers (by ^{1}H n.m.r. spectroscopy). The absolute configuration of the dominant isomer was established as (−)-(S_SR_C) by acid hydrolysis of compound (1e) to give (−)-(*R*)-2-methyl-1-phenylbutan-1-one (2).[5]

A useful comparison can be made between the extent of asymmetric induction from sulphur to carbon observed [6] in the synthesis of (−)-(S_SR_C)-1-methylheptyl *p*-tolyl sulphoxide (3), *ca.* 9%, and in the synthesis of compound (1e), *ca.* 20%; both reactions proceed *via* attack of

‡ $\Delta G^{\ddagger}$ obtained from $k_c = \Delta\gamma_\infty/2$ (T_c = 28.0 ± 2 °C; $\Delta\nu_\infty$ = 30.1 Hz) and the Eyring equation.

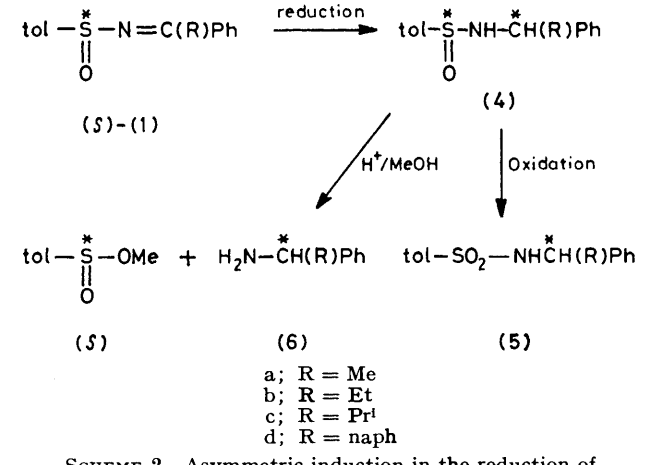
§ From the ^{13}C n.m.r. spectra of compound (1h), recorded in the range −20 °C to −50 °C, the ratio between *E*- and *Z*-isomers was estimated as *ca.* 1 : 1.



SCHEME 1 α- and γ-Asymmetric induction in the reaction of optically active sulphinate ester with Grignard reagents (the configuration of the dominant isomer is given)

Grignard reagents on the same optically active sulphinate ester. Rather surprisingly, in our method a γ-asymmetric induction turned out to be more efficient than an α-asymmetric induction, even though the chiral carbon atom in compound (1e) bears ligands which are more closely similar to each other than those of the chiral carbon atom in compound (3).

The *N*-alkylidenesulphinamides can easily be reduced to the corresponding sulphinamides in excellent yields by common metal hydrides such as sodium borohydride, lithium aluminium hydride,[7] and its alkoxy-derivatives. The reaction is stereoselective and the diastereoisomeric sulphinamides (4a)—(4d) were produced in unequal amounts.



SCHEME 2 Asymmetric induction in the reduction of *N*-alkylidenesulphinamides

The extent of asymmetric induction was determined directly by ^{1}H n.m.r. spectroscopy on the diastereoisomeric mixtures of the sulphinamides (4a)—(4d) and the values were checked by comparison with material of known optical purity and/or by conversion into the corresponding sulphonamides (5) and amines (6). The results were always in good agreement.

The reaction temperature does not seem to affect the selectivity of the process, since similar results were obtained in the range −30—+25 °C. More dramatic was the effect caused by changing the reducing species from $NaBH_4$ to $LiAlH_4$ (see Table 2).

TABLE 2

Reduction of the *N*-alkylidenesulphinamides (1a)—(1d) to the sulphinamides (4a)—(4d) by metal hydrides at 25 °C

		Sulphinamides		
Substrate	Reducing agent		$[\alpha]_D^{25}$/° [c]	Diastereoisomeric ratio
(1a)	$NaBH_4$ [a]	(4a)	+62.6	3 : 2
(1b)	$NaBH_4$ [a]	(4b)	+50.0	13 : 7
(1c)	$NaBH_4$ [a]	(4c)	+58.8	13 : 7
(1d)	$NaBH_4$ [a]	(4d)	+66.6	4 : 1
(1a)	$LiAlH_4$ [b]	(4a)	+42.3	9 : 1
(1b)	$LiAlH_4$ [b]	(4b)	+49.2	4 : 1
(1c)	$LiAlH_4$ [b]	(4c)	+55.0	4 : 1
(1d)	$LiAlH_4$ [b]	(4d)	+56.0	9 : 1

[a] In ethanol. [b] In diethyl ether. [c] *c* 1, In chloroform.

As shown in Table 2, lithium aluminium hydride always gave better results, transfer of chirality from sulphur to carbon being in the range 60—80%. Sodium borohydride reductions were less selective, with diastereoisomeric ratios in the range 20—60%. An analogous difference in selectivity has already been observed [8] in the reduction of β-oxosulphoxides by the same hydrides and therefore was expected.

The use of alkoxy-lithium aluminium hydrides [9] in the reduction of compounds (1) was also investigated and generally resulted in a marked increase in the stereoselectivity. A systematic study (see Table 3) was carried out on the easily obtained, racemic compound (1d), which allowed direct determination of the extent of asymmetric synthesis, by ^{1}H n.m.r. spectroscopy, on the produced sulphinamide (4d). Also, in this case, a decrease in the reaction temperature did not increase the extent of the stereoselectivity (see Expts. 1, 2, and 3). The stereoselectivity, however, increased when the monoalkoxy-derivatives of $LiAlH_4$ were used and then remained almost unchanged even when the steric requirements of the reducing agents become more demanding.

TABLE 3

Reduction of the racemic *N*-alkylidenesulphinamide (1d) to the sulphinamide (4d) by complex hydrides

Expt.	Reducing agent [a]	*T*/°C	Yield (%)	$[\alpha]_D^{25}$/° [b]	Diastereoisomeric ratio
1	$LiAlH_3$–A	+25 [c]	81		93 : 7
2	$LiAlH_3$–A	0 [c]	80	−1.0	87 : 13
3	$LiAlH_3$–A	−30 [c]	80	−2.1	87 : 13
4	$LiAlH_3$–B	+25 [d]	75		47 : 3
5	$LiAlH_2$–C	+25 [c]	57		19 : 1
6	$LiAlH_2$–A_2	+25 [c]	90		24 : 1
7	LiAlH–AE_2	+25 [e]	35	+4.4	24 : 1

[a] A = menthyloxy; B = bornyloxy; C = ephedrinyl; D = *N*-methylephedrinyl; E = xylyloxy. [b] *c* 1, In chloroform. [c] Reaction time 4 h. [d] Reaction time 15 h. [e] Reaction time 6 h.

The reduction of the racemic *N*-alkylidenesulphinamides by optically active hydrides can, in principle, lead to kinetic resolution and/or asymmetric induction. However, as shown in Table 3, only very low values, if any, of optical rotation were obtained even at a low degree of conversion of starting material (Expt. 7), thus showing that both kinetic resolution at the sulphur atom and asymmetric induction at the carbon atom are reasonably negligible processes. This result agrees well with previous observation.[8,10] The assignment of the absolute configuration to the dominant isomer of the compounds (4) has been achieved by two main routes, as shown in Scheme 2 and as previously described.[7]

TABLE 4

Asymmetric induction in the reduction of the compounds (*S*)-(1a)—(1d) by $LiAlH_4$

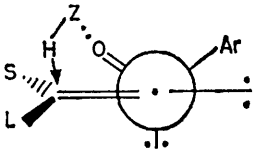
			Amine (6) [a]	
Substrate	Sulphinamide (4) [a]	Sulphonamide (5) [a] $[\alpha]_D^{25}$/°	$[\alpha]_D^{25}$/°	Optical purity (%)
(1a)	(S_SS_C)	−64.6,[b] (*S*)	−31.3,[d] (*S*)	78
(1b)	(S_SS_C)	−41.7,[c] (*S*)	−12.1,[d] (*S*)	57
(1c)	(S_SR_C)	+25.4,[c] (*R*)	+2.1,[d] (*R*)	[e]
(1d)	(S_SS_C)	+3.4,[c] (*S*)	+52.4,[b] (*S*)	80

[a] Absolute configuration of the dominant isomer. [b] *c* 1, In benzene. [c] *c* 1, In chloroform. [d] Neat. [e] Enantiomeric excess (e.e.) assumed to be 80% (see Experimental section).

The sulphur–nitrogen bond cleavage, performed according to the Mikolajczyk method,[11] while allowing the recovery of the amines (6) in unchanged enantiomeric excess, caused noticeable racemization at the sulphur chiral centre.[12] The enantiomeric excess of the recovered (*S*)-methyl toluene-*p*-sulphinate ranged from 30—60%, thus precluding the attractive possibility of recycling the inducing reagent in an enantiomerically pure form.

The sign and the values of the optical rotations of the amines (6) made possible the assignment of the absolute configuration to the dominant isomer of the compounds (4) and confirmed our n.m.r. evaluation of the degree of asymmetric induction in the reduction of compounds (1). The sulphinamide (4a) has been prepared [13] in both the (S_SR_C) and (S_SS_C) diastereoisomerically pure forms, starting from optically pure α-phenylethylamine. The sulphonamide (5a) has also been prepared [14] in the (*S*) enantiomerically pure form. A comparison of the values of optical rotation of compounds (4a) and (5a) obtained by us with those reported in the literature confirms both the assignment of absolute configuration and the extent of stereoselectivity.

Various factors must be taken into account in a tentative explanation of the stereochemistry of the process. As mentioned above, the *E*- and *Z*-isomers of the *N*-alkylidenesulphinamides (1) interconvert rapidly at the temperature of the reductions. However, inspection of molecular models shows that the *E*-isomer is less hindered than the Z-isomer, and that within the *E*-configuration the conformation shown in the Figure (viewed along the S–N bond axis) is least sterically crowded. Furthermore, the high degree of stereoselectivity can be rationalized only on the assumption that a major role is played by a cyclic transition state, derived by co-ordination of the reducing species (ZH) at the sulphinyl oxygen, which probably increases the steric requirements of the system. This should lead to the transition state depicted in the Figure, which is in agreement with the absolute configuration of the dominant isomers produced in the reaction.* (In the Figure, L and S are the large and the small group, respectively, the bulkiness order being Me < Et < Ph < Pr^i, α-naphthyl.)



FIGURE

On the bases of the results obtained in this work, the ready availability of the optically active *N*-alkylidenesulphinamides and the broad spectrum of reactivity of the imino-group indicate compounds (1) as potentially powerful tools for the asymmetric synthesis of various classes of compounds. Work is underway to test this hypothesis, especially with respect to asymmetric carbon–carbon bond formation.

EXPERIMENTAL

Light petroleum refers to the fraction of b.p. 40—60 °C. Diethyl ether was dried over and distilled from sodium. Extractions were performed with dichloromethane and the extracts were dried over sodium sulphate. I.r. spectra were recorded on a Perkin-Elmer 377 instrument and optical rotations were measured with a Perkin-Elmer 141 and/or 241 polarimeter. ^1H and ^{13}C N.m.r. spectra were recorded on a Varian A60 and/or a Varian XL100 instrument in $CDCl_3$ as solvent and with tetramethylsilane as internal standard. (−)-Menthyl (*S*)-toluene-*p*-sulphinate, $[\alpha]_D^{25}$ −202° (*c* 1, in acetone) {lit.,[15] $[\alpha]_D^{25}$ −202.5° (*c* 1, in acetone)}, methyl toluene-*p*-sulphinate, b.p. 127 °C at 10 mmHg, (lit.,[16] b.p. 135 °C at 14 mmHg), methyl benzenesulphinate, b.p. 62—63 °C at 0.03 mmHg, (lit.,[17] b.p. 63 °C at 0.03 mmHg), *N*-chlorobenzotriazole,[18] and the alkoxy-lithium hydrides [9] were prepared by literature methods. Benzonitrile and *p*-toluonitrile were distilled from P_2O_5 and stored over molecular sieves and trifluoroacetic acid was distilled and stored under nitrogen. Sodium borohydride was used as purchased and lithium aluminium hydride was used in *ca.* 1M ethereal solution. (−)-Menthol, $[\alpha]_D^{20}$ −49.5° (*c* 10, in EtOH); (−)-borneol, $[\alpha]_D^{25}$ −26.6° (*c* 5.3, in EtOH), and (−)-(1*R*,2*S*)-ephedrine, $[\alpha]_D^{25}$ −35.0° (*c* 4, in H_2O–HCl), were commercial products; (−)-(1*R*,2*S*)-*N*-methylephedrine, prepared by literature methods, had $[\alpha]_D^{20}$ −24° (*c* 1, in EtOH) {lit.,[19] $[\alpha]_D^{20}$ −24° (*c* 1, in EtOH)}.

Synthesis of the Optically Active N-*Alkylidenesulphinamides* (1a)—(1g).—The nitrile (20 mmol) in diethyl ether was added as drops to a stirred solution of Grignard reagent (20 mmol) in diethyl ether at 0 °C. The mixture was kept

* It must be noted that, starting from the *Z*-isomer, a similar reasoning would lead to the wrong absolute configurations being predicted for the products.

at room temperature for 2—6 h and then cooled to −40 °C. (−)-Menthyl (*S*)-toluene-*p*-sulphinate (10 mmol) was then added in one portion and the mixture was stirred overnight at room temperature. Work-up afforded a syrupy oil which was chromatographed (silica; diethyl ether–light petroleum) to give the products. Yields and analytical data are reported in Table 5.

As already pointed out,[2] compounds (1a) and (1b) were accompanied by two undesired, though easily separable, products. Together with the sulphinamide (1a) a compound, m.p. 132—133 °C, $[\alpha]_D^{25}$ +360.7° (*c* 1, in $CHCl_3$) (Found: C, 66.75; H, 5.3; N, 3.5. $C_{22}H_{21}NO_2S_2$ requires C, 66.81; H, 5.35; N, 3.54%) was obtained in 32% yield. This product, on the bases of i.r. and n.m.r. spectroscopy, was tentatively assigned the structure *p*-tolyl-S(O)N=C(Ph)CH_2S(O)-tolyl-*p*. Together with the sulphinamide (1b), a compound, m.p. 92—93 °C, $[\alpha]_D^{25}$ −17.0° (*c* 1, in $CHCl_3$) (C, 70.25; H, 6.4; N, 5.15. $C_{16}H_{17}NOS$ requires C, 70.80; H, 6.32; N, 5.17%) was obtained in 3% yield. This product, on the bases of i.r. and n.m.r spectroscopy, was assigned the structure of the tautomeric sulphinamide tolyl-S(O)NHC(Ph)=CHMe; ν 3 200—3 300 (NH) and 1 000—1 100 cm^{-1} (S=O); δ 1.85 (d, =CH*Me*), 2.40 (s, *p*-Me), 5.38 (q, =C*H*Me), 5.50br (s, NH), and 7.1—7.7 (m, ArH).

Synthesis of Racemic N-Alkylidenesulphinamides.—The reaction was carried out as in the case of the optically active compounds, but with methyl toluene-*p*-sulphinate as the sulphinate ester. The racemic compounds (1a), m.p. 109—111 °C, (1b), n_D^{19} 1.6249, (1c), m.p. 53—55 °C, (1d), m.p. 138—140 °C, and (1f), m.p. 112—114 °C were obtained in comparable yields and had n.m.r. spectra analogous to those of the optically active compounds. Starting from *p*-tolyl bromide, *p*-toluonitrile, and methyl benzenesulphinate, compound (1h) was obtained in 50% yield, m.p. 117—119 °C (Found: C, 75.7; H, 5.7; N, 4.1. $C_{21}H_{19}NOS$ requires C, 75.64; H, 5.74; N, 4.20%).

Reduction of the N-Alkylidenesulphinamides.—Method A. Sodium borohydride (1 mmol) was added to a stirred solution or suspension of the *N*-alkylidenesulphinamide (1 mmol) in absolute EtOH (10 ml). The reaction mixture was kept at room temperature for 10—15 h. Methanol (5 ml) was then added and solvent evaporated off under reduced pressure. Water and dichloromethane were added to the residue; the organic phase was dried and the solvent evaporated to give the crude product which was chromatographed (silica; diethyl ether–light petroleum) to give 90—100% yield of diastereoisomeric mixtures of the sulphinamides.

Method B. To a stirred solution of lithium aluminium hydride (1 mmol) in diethyl ether (5 ml) was added, as drops, the *N*-alkylidenesulphinamide (1 mmol) in diethyl ether (10 ml) at room temperature. The mixture was stirred for 10—15 h under nitrogen and then ethyl acetate (1 ml) was added. Work-up gave the crude product which was chromatographed (silica; diethyl ether–light petroleum) to give 80—90% yield of diastereoisomeric mixtures of the sulphinamides. Table 6 shows physical and analytical data for the optically active products obtained by $LiAlH_4$ reduction.

Reduction of the Racemic Compound (1d) *with Alkoxylithium Aluminium Hydrides.*—A solution of compound (1d) in diethyl ether (10 ml) was added under nitrogen to a stirred solution of the reducing species in diethyl ether. A 4 : 1 ratio between the active hydrogens of the reducing agent and compound (1d) was used. After the mixture had been stirred at room temperature, work-up as described above afforded a diastereoisomeric mixture of compound (4d) (see Table 3).

Oxidation of the Sulphinamides to the Sulphonamides (5).—*N*-Chlorobenzotriazole (1 mmol) in methanol (5 ml) was added as drops to a cold (0 °C) solution of the sulphinamide (1 mmol) in methanol (10 ml). The mixture was stirred at room temperature for 15 h after which time the solvent was evaporated off under reduced pressure. The residue was dissolved in dichloromethane and washed with 10% aqueous sodium carbonate. The organic phase was dried and the solvent evaporated off. The resulting crude product was chromatographed (silica; diethyl ether–light petroleum) to afford a 60—90% yield of the sulphonamide. Physical and analytical data of compounds (5) are reported in Table 7.

TABLE 5

Yields and analytical data for compounds (1a)—(1g)

		Found (%)				Requires (%)		
	Yield (%)	C	H	N	Formula	C	H	N
(1a)	20	70.0	5.85	5.35	$C_{15}H_{15}NOS$	70.00	5.88	5.44
(1b)	52	70.75	6.35	5.2	$C_{16}H_{17}NOS$	70.80	6.32	5.17
(1c)	27	71.05	6.8	4.9	$C_{17}H_{19}NOS$	71.54	6.71	4.91
(1d)	70	77.8	5.15	3.7	$C_{24}H_{19}NOS$	78.01	5.18	3.79
(1e)	15	72.1	7.05	4.7	$C_{18}H_{21}NOS$	72.20	7.07	4.68
(1f)	70	75.3	5.35	4.35	$C_{20}H_{17}NOS$	75.20	5.37	4.39
(1g)	68	76.3	6.2	4.0	$C_{22}H_{21}NOS$	76.04	6.09	4.03

TABLE 6

Physical and analytical data for compounds (4a)—(4d)

	M.p./°C (n_D^{20})	Found (%)				Requires (%)		
		C	H	N	Formula	C	H	N
(4a)	110—112		*b*		$C_{15}H_{17}NOS$			
(4b)	*a*	70.35	7.0	5.15	$C_{16}H_{19}NOS$	70.29	7.00	5.12
(4c)	(1.5605)	71.3	7.4	4.75	$C_{17}H_{21}NOS$	71.04	7.37	4.87
(4d)	48—50	77.3	5.8	3.85	$C_{24}H_{21}NOS$	77.59	5.69	3.77

[a] Waxy solid. [b] Lit. (ref. 13), m.p. 116.5—119.5 °C, $[\alpha]_D^{25}$ +37.2° ($CHCl_3$) for (S_SS_C) diastereomerically pure material.

TABLE 7

Physical and analytical data for compounds (5a)—(5d)

	M.p./°C	Found/% C	Found/% H	Found/% N	Formula	Requires/% C	Requires/% H	Requires/% N
(5a)	93—94		*a*		$C_{15}H_{17}NO_2S$			
(5b)	95—99	66.6	6.8	4.65	$C_{16}H_{19}NO_2S$	66.40	6.62	4.84
(5c)	143—144	67.05	7.1	4.65	$C_{17}H_{21}NO_2S$	67.29	6.98	4.62
(5d)	150 (decomp.)	74.45	5.35	3.55	$C_{24}H_{21}NO_2S$	74.39	5.46	3.61

[a] Lit. (ref. 14), m.p. 98—99 °C, $[\alpha]_D^{20}$ −79.3° (benzene) for the (*S*)-enantiomerically pure material.

Synthesis of (−)-(R)-2-*Methyl*-1-*phenylbutan*-1-*one* (2) *from Compound* (1e).—To a stirred solution of compound (1e) (186 mg, 0.62 mmol) in methanol (5 ml), 10% aqueous hydrochloric acid (2 ml) was added as drops at 0 °C, and the mixture was stirred overnight at room temperature. Methanol was then evaporated off, the residue taken into dichloromethane, washed twice with 5% aqueous sodium hydrogencarbonate, and the organic phase dried. The solvent was evaporated and the crude product chromatographed (silica; diethyl ether–light petroleum) to give 60 mg (60% yield) of compound (2) the structure of which was confirmed by i.r. and n.m.r. spectroscopy; $[\alpha]_D^{25}$ −2.6° (*c* 1, in $CHCl_3$). This value of optical rotation cannot be used for a determination of the diastereoisomeric ratio of compound (1e), since compound (2) has been shown to racemize in acidic medium.[5b]

Cleavage of the Nitrogen–Sulphur Bond in the Sulphinamides (4).—To a stirred solution of the sulphinamide (2 mmol) in methanol (7 ml), trifluoroacetic acid (0.3 ml, 4 mmol) in methanol (3 ml) was added at 0 °C. After the mixture had been stirred for 1 h at 0 °C the solvent was removed under reduced pressure and the residue taken into diethyl ether. The diethyl ether extracts were washed with 15% aqueous hydrochloric acid. The organic phase was separated off, washed with 5% aqueous sodium hydrogencarbonate (3 × 10 ml), dried, and evaporated to give a 70% yield of optically active (−)-methyl toluene-*p*-sulphinate (*c* 3, in ethanol). The acidic aqueous phase was added to 30% aqueous sodium hydroxide and the resulting basic solution was extracted with diethyl ether (3 × 20 ml). The organic phase was dried and the solvent evaporated off under reduced pressure to give a 60—70% yield of the amine (6); the structures of the compounds (6) were confirmed by i.r. and n.m.r. spectroscopy.

Determination of Enantiomeric Purities and of Diastereoisomeric Ratios.—N-*Alkylidenesulphinamides* (1). Despite several attempts, the enantiomeric purity of compound (1a) could only be determined with the aid of a chiral shift-reagent, $Eu(tfc)_3$.[2,20] The method previously [2] employed with compounds (1b), (1c), and (1d) gave analogous results with compounds (1f) and (1g). The diastereoisomeric ratio of compound (1e) was determined directly by ^1H n.m.r. spectroscopy (assuming an enantiomerically pure sulphur chiral centre), the ratio of intensities of the aliphatic methyl signals (two doublets centred at δ 1.4) being exploited.

Sulphinamides (4). The diastereoisomeric ratios were determined directly by ^1H n.m.r. spectroscopy through the ratio of intensities of the signals of the aromatic methyl group (two singlets at δ 2.4).

Amines (6). The enantiomeric excess was determined by comparison with the values of optical rotations reported in the literature for compounds (6b) [21] and (6d).[22] As far as compound (6c) is concerned no values are, unfortunately, available for material of known enantiomeric purity; [23] however, the good general agreement observed in the other cases leads us to consider as reliable the diastereoisomeric ratio determined by ^1H n.m.r. spectroscopy for compound (4c).

[1/729 *Received*, 8*th May*, 1981]

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