# Stereoselective Protonation and Reduction of β-Sulphinyl Enamines. X-Ray Molecular Structure of *N*-Benzyl-2-(*p*-tolylsulphinyl)propylamine

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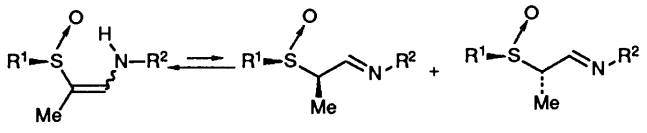
Reduction of β-substituted β-sulphinyl enamines by acyloxyborohydrides in the presence of carboxylic acids leads to β-sulphinyl amines in good chemical yield and diastereoisomeric excess (de) up to 92%. Two methods of reduction, differing by the introduction sequence of the acid, are examined. The stereoselectivity is enhanced with large proton donors and strong acids but is less dependent on the type of reducing agent and solvent used. A mechanism for the stereoselective protonation is proposed.

Optically active sulphoxides are applied with great success in stereoselective syntheses.[1,2] Enamines are also used in asymmetric synthesis,[3] mainly as alkylation targets. We tried to utilize both these functions, *i.e.* sulphinyl and enaminic, by using β-sulphinyl enamines in stereoselective reactions. In 1982 Cozzi and co-workers[4] published a convenient method for the synthesis of secondary β-sulphinyl enamines from the reaction of (−)-menthyl toluene-*p*-sulphinate and imines. In this publication, as well as in earlier work,[5] the *Z*-configuration at the double bond was postulated for these compounds, as being the result of stabilizing intramolecular hydrogen bonding. This latter parameter seems to be overestimated in the light of our recent investigations[6] showing that unsubstituted β-sulphinyl enamines appear, in benzene or chloroform solution, mainly as the *E*-isomers.



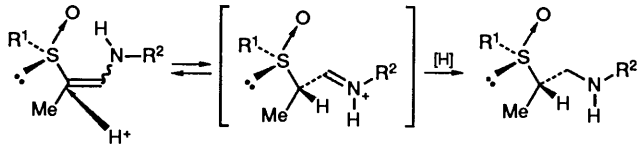
Scheme 1

Earlier we reported[7] that immediately after dissolution of β-substituted β-sulphinyl enamines in chloroform one diastereoisomer of the tautomeric imine predominated (Scheme 1). Our explanation of this process is that the $C^{\beta}$ atom was stereoselectively protonated. We expected that a similar protonation reaction and subsequent reduction would provide β-sulphinyl amines, that have recently been the subject of many investigations due to their synthetic utility in alkaloid syntheses.[8] The analogous reaction of kinetic protonation of enolates has been well examined[9] and distinguishes itself by its high stereoselectivity.

## Results and Discussion

Reduction of the β-sulphinyl enamines in aqueous ethanol solution results in formation of two diastereoisomers in nearly equal amounts. However, in the presence of acid a pronounced stereoselectivity is observed. As the iminium salt is the active form that is reduced, β-sulphinyl enamines are not reduced to amines under basic conditions (aq. NaOH, $NaBH_4$). We have examined the widely used borohydride–carboxylic acid system.[10] The results of reduction by method A (carboxylic acid was added to the suspension of borohydride in enamine solution) are given in Table 1.

Carboxylic acids used in excess react with borohydride to form a mixture of mono-, di- and tri-acyloxyborohydrides. It can be assumed that all these species take part in the reduction. At the same time the enamine is protonated at the $C^{\beta}$ atom (iminium salt) or the N atom (enammonium salt). We assume that the proton donor attacks the β-carbon atom from the sulphur lone-pair side which is sterically privileged (Scheme 2). As the first step of this reaction is reversible, only the reduction of the iminium salt shifts the equilibrium to the right. Recently Hua *et al.*[11] published a synthesis of yohimbanoid alkaloids in which one of the key steps was the reduction of a cyclic β-sulphinyl enamine. The excellent stereoselectivity was attributed to the stereoselective protonation.



**Scheme 2** **1 a**; $R^1$ = Me $R^2$ = $Bu^t$ *l*-**2a**
**b**; Ph $Bu^t$ *u*-**2b**
**c**; Tol $Bu^t$ *u*-**2c**
**d**; $Bu^t$ $Bu^t$ *u*-**2d**
**e**; Tol Bn *u*-**2e**

Tol = *p*-tolyl, Bn = benzyl

The majority of the experiments presented here were performed using sodium borohydride, but exchange of the cation by zinc or tetrabutylammonium cation did not result in an increase of stereoselectivity. Hua *et al.*[12] also examined reduction of cyclic α-sulphinyl enamines with zinc borohydride but the stereoselectivity in this reaction was poor.

In the case of tetrabutylammonium borohydride the reduction was carried out homogeneously. The results obtained with this reducing agent in dichloromethane and with the inverse introducing of reagents (method B: the acyloxyborohydride is generated before addition of the enamine) are presented in Table 2.

Equilibration between iminium and enammonium salt is the main factor that lowers the stereoselectivity. This is shown by the decrease in diastereoisomeric excess (de) in the case of a bulky substituent at sulphur (entry 4, Table 1). Such compounds require a longer reaction time. Another fact confirming this hypothesis was gained from the reduction of the enamine **1d** in a presence of deuteriated trifluoroacetic acid ([$^2$H]TFA) (entry 8, Table 2). The obtained amine **2d** was deuteriated at the $C^{\beta}$ atom in 66% yield. This confirms the significant contribution of the equilibration between iminium and enammonium salts to the observed low de (38%) in this case. On the other hand deuteriation on $C^{\beta}$ indicates that the iminium salt does undergo reduction. This is in agreement with

**Table 1** Reduction of β-sulphinyl enamines **1a–e** in THF by method A

| Entry | Enamine | Amine | $R^1$ | $R^2$ | Borohydride | Acid | Temp. (°C) | Chemical yield (%) | de (%)[a] | Major diastereo-isomer's configuration[b] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **1a** | **2a** | Me | Bu$^t$ | $NaBH_4$ | AcOH | 20 | 87 | 70 | *l*[c] |
| 2 | **1b** | **2b** | Ph | Bu$^t$ | $NaBH_4$ | AcOH | −5 | 92 | 42 | *u* |
| 3 | **1c** | **2c** | *p*-$MeC_6H_4$ | Bu$^t$ | $NaBH_4$ | AcOH | 20 | 98 | 62 | *u* |
| 4 | **1d** | **2d** | Bu$^t$ | Bu$^t$ | $NaBH_4$ | AcOH | 20 | 93 | 31 | *u* |
| 5 | **1e** | **2e** | *p*-$MeC_6H_4$ | Bn | $NaBH_4$ | AcOH | 20 | 90 | 54 | *l* |
| 6 | **1e** | **2e** | *p*-$MeC_6H_4$ | Bn | $NaBH_4$ | TFA | 0 | 48 | 22 | *u* |
| 7 | **1b** | **2b** | Ph | Bu$^t$ | $NaBH_4$ | TFA | −20 | 92 | 77 | *u* |
| 8 | (−)-**1c** | **2c** | *p*-$MeC_6H_4$ | Bu$^t$ | $NaBH_4$ | TFA | −20 | 64 | 92 | *u* |
| 9 | **1b** | **2b** | Ph | Bu$^t$ | $NaBH_4$ | $Ph_2CHCO_2H$ | 20 | 90 | 59 | *u* |
| 10 | **1e** | **2e** | *p*-$MeC_6H_4$ | Bn | $Zn(BH_4)_2$ | AcOH | −18 | 94 | 34 | *u* |
| 11 | **1e** | **2e** | *p*-$MeC_6H_4$ | Bn | $Bu_4NBH_4$ | AcOH | 20 | 75 | 30 | *u* |

[a] Diastereoisomeric ratio was established from integration of appropriate signals in the $^1H$ NMR spectrum. [b] The relative configuration of the major diastereoisomer of amine **2e** (entry 5) was found from X-ray analysis. The configuration of amines **2a–d** was assigned on the basis of $^1H$ NMR spectral comparison with the spectrum of amine **2e**. [c] Another relative configuration of amine **2a** is caused by the opposite configuration at sulphur (Me substituent).

**Table 2** Reduction of β-sulphinyl enamines with acyloxyborohydrides (method B)

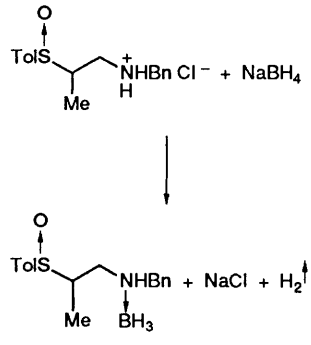
| Entry | Enamine | $R^1$ | $R^2$ | Borohydride | Acid | Solvent | Temp./°C | Chemical yield (%) | de (%)[a] | Major diastereo-isomer's configuration[b] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **1e** | *p*-$MeC_6H_4$ | Bn | $Bu_4NBH_4$ | AcOH | $CH_2Cl_2$ | 23 | 71 | 28 | *u* |
| 2 | **1e** | *p*-$MeC_6H_4$ | Bn | $Bu_4NBH_4$ | AcOH | $CH_2Cl_2$ | −15 | 68 | 32 | *u* |
| 3 | **1e** | *p*-$MeC_6H_4$ | Bn | $Bu_4NBH_4$ | AcOH | $CH_2Cl_2$ | −50 | 60 | 42 | *u* |
| 4 | **1b** | Ph | Bu$^t$ | $Bu_4NBH_4$ | AcOH | $CH_2Cl_2$ | −20 | 93 | 40 | *u* |
| 5 | **1e** | *p*-$MeC_6H_4$ | Bn | $NaBH_4$ | AcOH | THF | −15 | 68 | 32 | *u* |
| 6 | **1b** | Ph | Bu$^t$ | $NaBH_4$ | AcOH | THF | 0 | 92 | 35 | *u* |
| 7 | **1d** | Bu$^t$ | Bu$^t$ | $NaBH_4$ | AcOH | THF | 0 | 85 | 15 | *u* |
| 8 | **1d** | Bu$^t$ | Bu$^t$ | $NaBH_4$ | [$^2$H]TFA | THF | 0 | 78 | 38 | *u*[c] |
| 9 | **1b** | Ph | Bu$^t$ | $NaBH_4$ | Bu$^tCO_2H$ | THF | −20 | 90 | 26 | *u* |
| 10 | **1b** | Ph | Bu$^t$ | $NaBH_4$ | L-tartaric | THF | 20 | 89 | 12 | *u*[d] |

[a,b] See Table 1. [c] Deuteriation in 66%. [d] Product is not optically active.

Marshall's work[13] on reduction of enamines in an acidic environment, which suggested a protonation–hydride-transfer mechanism. However, compounds with an isolated double bond are known to undergo reduction under these conditions by a hydroboration pathway.[14,15] The main influence on reduction mechanism, with regard to the nature of the reduced species and the homogeneity of the reaction mixture, is concentration of the acid used. The use of equimolar (to the borohydride) amounts of acid is known to result in hydroboration.[15] In the above described experiments no derivatives of alkylboronic acids were observed that were characteristic for hydroboration of enamines.[16]

The size of the proton donor and the strength of the acid largely determine the de-value (entries 7, 9, Table 1). This is in agreement with the proposed reaction mechanism. A decrease in temperature only has a moderate effect and causes an increase in de. In both methods the relative configuration of the chiral centres in the major diastereoisomer was in agreement with the mechanism as depicted in Scheme 2. Only in the case of compound **1e** (entry 5, Table 1) was inversion of stereoselectivity observed. However, we characterized the complex of amine **2e** with borane as one of the products. This complex is formed in the reaction of the ammonium salt and sodium borohydride [eqn. (1)] and was thus identified.

Such a complex is able to reduce the C=C double bond as well as the C=N double bond[17] and therefore it may compete with the mechanism shown in Scheme 2. Strong acids such as TFA decompose this complex to amine and hydrogen. Formation of this complex is facilitated in the case of small substituents on the




(1)

nitrogen atom and by a high concentration of sodium borohydride (method A). Reduction of enamine **1e** by method B (entry 5, Table 2) gave mainly the *u*-diastereoisomer as in other cases.

The relative configuration of stereogenic centres in compound **2e** was determined from X-ray crystal-structure analysis of its picrate. As shown in Fig. 1, the (*R*)-configuration is assigned both to the S(1) and C(8) atoms. The relative configuration of stereogenic centres in other compounds was determined by comparison of their $^1H$ NMR spectra. In the *u*-diastereoisomer of the amine **2e** the vicinal coupling constants of hydrogens at C-1 are 5.4 and 8.4 Hz (for the signal at lower frequencies). The relative configation *u* was assigned for those amines, compounds **2a–d**, that have the same values of vicinal coupling constants (Table 4).

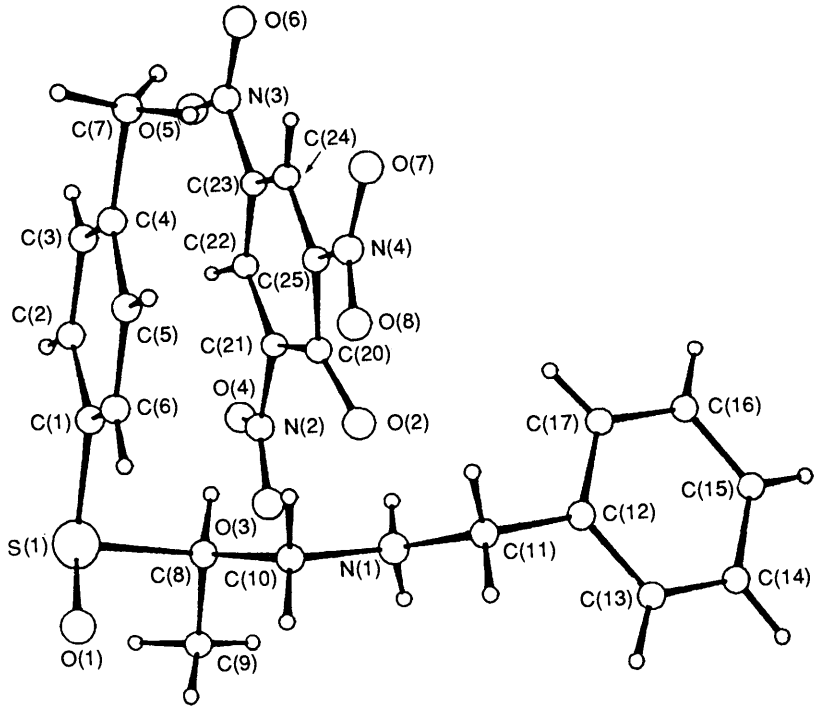
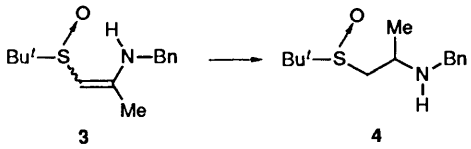



**Fig. 1** Three-dimensional picture of the X-ray molecular structure of amine (*l*)-**2e** picrate (atom numbering is taken from X-ray measurements)




**3** **4**

**Table 3** Reduction of enamine **3** to amine **4**

| Method | Boro-hydride | Acid | Solvent | Temp. /°C | Chemical yield (%) | de (%) |
|---|---|---|---|---|---|---|
| A | $NaBH_4$ | AcOH | THF | 20 | 62 | 32 |
| B | $Bu_4NBH_4$ | AcOH | $CH_2Cl_2$ | −18 | 85 | 46 |

The presence of a strong acid such as TFA does not cause any racemization at the sulphur atom. Optically pure β-sulphinyl enamine **1c** was converted (Table 1, entry 8) into optically active amine **2c** in 64% yield and 92% de.

In the case of α-substituted β-sulphinyl enamines the decisive stereoselection step is reduction but not protonation. The results of reduction of the α-substituted enamine **3** by methods A and B are presented in Table 3. They are similar to our previous results but the configuration of the product amine **4** was not determined.

The latter example shows that preferential reduction of one diastereoisomer of the iminium salt may have some contribution to the overall stereoselection results.

Although the reaction examined by us is a rather complicated case, because stereoselection occurs in an acyclic system, nevertheless during a systematic study we were able to determine the conditions leading to high stereoselectivity. The de appears to be strongly dependent on the nature of the acid used as well as on the size of the substituents at the sulphur and nitrogen atoms.

## Experimental

Unless stated otherwise, NMR spectra were recorded on a Bruker AM-500 spectrometer (500 MHz for $^1H$ and 125 MHz for $^{13}C$). *J*-Values are given in Hz. IR spectra were determined on a Beckman Acculab 1. Mass spectra were obtained on an LKB-2091 or a Finnigan MAT 8200 spectrometer at 70 eV. Optical rotations were measured on a Perkin-Elmer PE-141 apparatus. M.p.s were measured on a Kofler apparatus and are uncorrected.

*Materials.*—Anhydrous tetrahydrofuran (THF) was distilled from $LiAlH_4$, and dichloromethane from $CaH_2$. [$^2$H]TFA (99%) was obtained from Aldrich. Tetrabutylammonium borohydride was prepared from tetrabutylammonium hydrogen sulphate and sodium borohydride.[18] Zinc borohydride was obtained from $ZnCl_2$ and sodium borohydride[19] as a solution in THF. β-Sulphinyl enamines **1a–e** were prepared according to Cozzi's procedure[4] from propionaldehyde imine and the appropriate racemic sulphinate. Optically active enamine **1c** was obtained from (−)-menthyl toluene-*p*-sulphinate, and had m.p. 182–184 °C; $[\alpha]_D$ −221° (*c* 1, $CHCl_3$) {lit.,[4] m.p. 175–176 °C; $[\alpha]_D$ −226° (*c* 1, $CHCl_3$)}. All experiments were performed under nitrogen. The following enamines were prepared.

N-t-*Butyl*-2-*methylsulphinylprop*-1-*enamine* **1a** (68%), yellow crystals, m.p. 128–132 °C (from benzene) (Found: $M^+$, 175.1031. $C_8H_{17}NOS$ requires M, 175.1031); $\nu_{max}(CHCl_3)/cm^{-1}$ 1010 (S=O) and 1650 (C=C); $\delta_H(CDCl_3$; $Me_4Si)$ 1.25 (9 H, s, Bu$^t$), 1.80 (3 H, s, 2-Me), 2.64 (3 H, s, MeSO), 3.98 (1 H, br, d, *J* 13.5, NH) and 6.86 (1 H, d, *J* 13.5, 1-H); $\delta_C(CDCl_3$; $Me_4Si)$ 4.59 (2-*Me*), 30.06 ($CMe_3$), 38.01 (MeSO), 51.24 ($CMe_3$), 104.46 (C-2) and 137.89 (C-1).

N-t-*Butyl*-2-*phenylsulphinylprop*-1-*enamine* **1b** (63%), crystals, m.p. 160–162 °C (from benzene) (Found: $M^+$, 237.1187. $C_{13}H_{19}NOS$ requires M, 237.1187); $\nu_{max}(CHCl_3)/cm^{-1}$ 1020 (S=O) and 1650 (C=C); $\delta_H(CDCl_3$; $Me_4Si)$ 1.30 (9 H, s, Bu$^t$), 1.42 (3 H, d, *J* 1, Me), 3.98 (1 H, br d, *J* 13.6, NH), 7.08 (1 H, dq, *J* 13.6, *J'* 1, 1-H) and 7.4–7.6 (5 H, m, Ph); $\delta_C(CDCl_3$; $Me_4Si)$ 5.84 (2-*Me*), 30.20 ($CMe_3$), 51.53 ($CMe_3$), 105.93 (C-2), 124.86 (Ph-*o*), 128.51 (Ph-*m*), 129.30 (Ph-*p*), 140.15 (C-1) and 144.28 (Ph-*i*).

**Table 4** $^1$H NMR chemical shifts and coupling constants [a] (in parentheses) for amines **2a–e** in $C_6D_6$

| | $R^1$–S(O)–CH(Me)–$CH_AH_B$–NH–$R^2$ | | | | | | |
|---|---|---|---|---|---|---|---|
| Amine | $R^1$ | 2-Me | 2-H | $H_A$ | $H_B$ | NH | $R^2$ |
| *l*-**2a** | 1.97s | 0.81d (7.0) | 2.40m | 2.65dd (5.2v) (12.2g) | 2.75dd (6.2v) (12.2g) | 1.4br s | 0.97s |
| *u*-**2a** | 1.96s | 1.04d (6.9) | 2.05m | 2.43dd (5.4v) (12.3g) | 2.73dd (8.4v) (12.3g) | 1.4br s | 0.93s |
| *l*-**2b** | 7.6m | 0.98d (6.8) | 2.59m | 2.68dd (5.7v) (12.2g) | 2.75dd (5.5v) (12.2g) | 1.1br s | 0.95s |
| *u*-**2b** | 7.5m | 0.88d (6.8) | 2.31m | 2.52dd (5.3v) (12.4g) | 2.99dd (8.5v) (12.4g) | 1.1br s | 1.00s |
| *l*-**2c** | 2.01s, 7.2–7.7m | 0.99d (6.7) | | 2.8m | | 1.2br s | 0.97s |
| *u*-**2c** | 2.02, 7.2–7.7m | 0.93d (6.7) | 2.41m | 2.58dd (5.4v) (12.3g) | 3.02dd (8.4v) (12.3g) | 1.2br s | 1.01s |
| *l*-**2d** | 1.07s | 0.98d (6.7) | 2.71m | 2.74dd (4.0v) (12.1g) | 2.92dd (6.5v) (12.1g) | 1.23br s | 1.00s |
| *u*-**2d** | 1.02s | 1.15d (6.7) | 2.43m | 2.47dd (5.5v) (11.9g) | 2.69dd (7.8v) (11.9g) | 1.23br s | 0.93s |
| *l*-**2e** | 1.97s, 6.9–7.5m | 0.93d (6.8) | | 2.7m | | 1.38 br s | AB: 3.51, 3.48 (13.4) 6.85m |
| *u*-**2e** | 1.99s 6.9–7.5m | 0.85d (6.8) | 2.38m | 2.53dd (5.4v) (12.7g) | 2.98dd (8.4v) (12.7g) | 1.38 br s | AB: 3.53, 3.57 (13.4) 6.85m |

[a] v = vicinal, g = geminal coupling constant.

N-t-*Butyl*-2-(p-*tolylsulphinyl*)*prop*-1-*enamine* **1c** (76%), crystals, m.p. 155–162 °C (from benzene) (Found: C, 67.1; H, 8.6; N, 5.9; S, 12.6. $C_{14}H_{21}NOS$ requires C, 66.9; H, 8.4; N, 5.6; S, 12.75%); $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1010 (S=O) and 1650 (C=C); $\delta_H$(100 MHz; $CDCl_3$, $Me_4Si$) 1.28 (9 H, s, Bu$^t$), 1.41 (3 H, s, 2-*Me*), 2.39 (3 H, s, Ar*Me*), 3.98 (1 H, d, *J* 13.5, NH), 7.04 (1 H, d, *J* 13.5, 1-H) and 7.2–7.6 (4 H, m, ArH).

N-t-*Butyl*-2-(t-*butylsulphinyl*)*prop*-1-*enamine* **1d** (60%), crystals, m.p. 157–162 °C (decomp.) (from benzene) (Found: $M^+$, 217.1500. $C_{11}H_{23}NOS$ requires M, 217.1500); $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1010 (S=O) and 1640 (C=C); $\delta_H$($CDCl_3$; $Me_4Si$) 1.18 (9 H, s, Bu$^t$SO), 1.25 (9 H, s, NBu$^t$), 1.70 (3 H, d, *J* 1.1, 2-Me), 3.82 (1 H, br d, *J* 13.5, NH) and 6.68 (1 H, dq, *J* 13.5, *J'* 1.1, 1-H); $\delta_C$($CDCl_3$; $Me_4Si$) 7.43 (2-Me), 23.76 (SC*Me*$_3$), 29.99 (NC*Me*$_3$), 51.05 (N*C*Me$_3$), 55.33 (S*C*Me$_3$), 100.37 (C-2) and 138.26 (C-1).

N-*Benzyl*-2-(p-*tolylsulphinyl*)*prop*-1-*enamine* **1e** (82%), crystals, m.p. 130–131 °C (from benzene) (Found: C, 71.8; H, 6.7; N, 5.1; S, 11.25. $C_{17}H_{19}NOS$ requires C, 71.6; H, 6.7; N, 4.9; S, 11.2%); $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1010 (S=O) and 1650 (C=C); $\delta_H$($CDCl_3$; $Me_4Si$) 1.45 (3 H, d, *J* 1, 2-Me), 2.38 (3 H, s, Ar*Me*), 4.36 (2 H, m, $CH_2$), 4.40 (1 H, m, NH), 6.95 (1 H, dq, *J* 13.2, *J'* 1, 1-H) and 7.2–7.5 (9 H, m, ArH); $\delta_C$($CDCl_3$; $Me_4Si$) 6.08 (2-Me), 21.23 (Ar*Me*), 51.61 ($CH_2$), 106.74 (C-2), 124.87, 127.26, 127.62, 128.76, 129.36, 138.90, 139.60, 140.90 (Ar) and 144.19 (C-1).

Compound **3** was obtained from condensation of benzylamine with 1-*t*-butylsulphinylpropan-2-one in benzene according to the standard procedure.[13]

N-*Benzyl*-1-(t-*butylsulphinyl*)*prop*-1-*ene*-2-*amine* **3**.—Yield 82%, pink crystals, m.p. 114–117 °C (from benzene) [Found: *m/z*, 195.0718. $C_{10}H_{13}NOS$ requires (M − $C_4H_8$), 195.0718]; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1000 (S=O) and 1610 (C=C); $\delta_H$(100 MHz; $CDCl_3$; $Me_4Si$) enamine form (82%): 1.10 (9 H, s, Bu$^t$), 2.11 (3 H, s, Me), 4.24 (2 H, m, $CH_2$), 4.43 (1 H, br m, NH), 4.73 (1 H, s, CH) and 7.2–7.3 (5 H, m, Ph). Imine tautomer (18%): 1.29 (9 H, s, Bu$^t$), 2.17 (3 H, s, Me), 3.49 (2 H, m, $CH_2SO$), 4.58 (2 H, br s, $NCH_2$) and 7.2–7.4 (5 H, m, Ph); $\delta_C$(25 MHz; $CDCl_3$; $Me_4Si$) only enamine form: 18.34 (Me), 22.65 (C*Me*$_3$), 47.18 ($CH_2$), 55.46 (*C*Me$_3$), 91.20 (C-1), 127.16 (Ph-*m*), 127.22 (Ph-*p*), 128.50 (Ph-*o*), 137.38 (Ph-*i*) and 153.28 (C-2).

*General Procedure for Reduction of* β-*Sulphinyl Enamines* **1a–e** *and* **3** *to Amines* (*Method A*).—To a suspension of borohydride (8 mmol) in a solution of β-sulphinyl enamine (0.7 mmol) a carboxylic acid (33 mmol) was added very slowly at the temperature indicated in Table 1. A vigorous evolution of hydrogen was observed. The reaction mixture was stirred at the indicated temperature for 16 h and was then poured into aq. sodium hydroxide (2 g in 10 $cm^3$). After separation, the aq. layer was extracted twice with chloroform. All organic extracts were concentrated under reduced pressure (~10 $cm^3$) and extracted twice with hydrochloric acid (0.5 mol $dm^{-3}$). The acidic layer was washed with chloroform, made basic by addition of aq. NaOH, and extracted with diethyl ether. The extracts were dried over $MgSO_4$ and evaporated to give an amine **2** of good purity. For analytical purposes these products were chromatographed on silica gel ($CHCl_3$–MeOH; 15:1).

*General Procedure for Reduction of* β-*Sulphinyl Enamines to Amines* (*Method B*).—A carboxylic acid (17 mmol) was slowly added to a suspension of sodium borohydride (5 mmol) in THF (8 $cm^3$) at 10 °C. A vigorous evolution of the hydrogen was observed. The reaction mixture was stirred at room temperature for 1.5 h. After cooling to the temperature indicated in Table 2 the reaction mixture was treated dropwise with a solution of enamine (1.0 mmol) in THF (15 $cm^3$). The mixture was stirred for 6 h. After this time the reaction mixture was quenched with aq. sodium hydroxide (1.5 g in 10 $cm^3$). The work-up as described above gave amines **2**.

In the case of reduction with tetrabutylammonium boro-

**Table 5** Atomic fractional co-ordinates ($\times 10^4$) with esds in parentheses

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| S(1) | 8 511(0) | 4(1) | 3 687(0) |
| O(1) | 8 102(1) | −1 150(2) | 3 218(2) |
| N(1) | 7 965(1) | 2 794(2) | 1 189(2) |
| C(1) | 9 177(1) | −200(3) | 2 980(2) |
| C(2) | 9 675(1) | 528(3) | 3 379(2) |
| C(3) | 10 193(1) | 386(4) | 2 833(3) |
| C(4) | 10 224(1) | −474(4) | 1 906(3) |
| C(5) | 9 727(1) | −1 237(3) | 1 546(2) |
| C(6) | 9 202(1) | −1 112(3) | 2 079(2) |
| C(7) | 10 789(2) | −613(6) | 1 304(3) |
| C(8) | 8 232(1) | 1 652(3) | 3 038(2) |
| C(9) | 7 707(1) | 2 128(3) | 3 666(2) |
| C(10) | 8 095(1) | 1 417(3) | 1 785(2) |
| C(11) | 7 929(1) | 2 639(3) | −61(2) |
| C(12) | 7 842(1) | 4 048(3) | −633(2) |
| C(13) | 7 288(1) | 4 445(4) | −1 075(2) |
| C(14) | 7 205(2) | 5 766(5) | −1 586(3) |
| C(15) | 7 680(3) | 6 678(5) | −1 657(3) |
| C(16) | 8 225(2) | 6 285(5) | −1 232(4) |
| C(17) | 8 316(2) | 4 967(4) | −720(3) |
| O(2) | 8 674(1) | 4 797(2) | 2 274(2) |
| O(3) | 8 316(1) | 5 660(3) | 4 245(2) |
| O(4) | 8 876(1) | 7 164(3) | 5 151(2) |
| O(5) | 10 928(1) | 7 277(3) | 4 793(2) |
| O(6) | 11 308(1) | 6 352(3) | 3 370(3) |
| O(7) | 10 160(1) | 3 571(4) | 770(3) |
| O(8) | 9 284(1) | 2 947(3) | 1 067(2) |
| N(2) | 8 789(1) | 6 259(3) | 4 420(2) |
| N(3) | 10 891(1) | 6 594(3) | 3 917(2) |
| N(4) | 9 722(1) | 3 680(3) | 1 293(2) |
| C(20) | 9 177(1) | 5 062(3) | 2 704(2) |
| C(21) | 9 281(1) | 5 886(3) | 3 728(2) |
| C(22) | 9 824(1) | 6 371(3) | 4 106(2) |
| C(23) | 10 315(1) | 6 041(3) | 3 535(2) |
| C(24) | 10 273(1) | 5 155(3) | 2 605(2) |
| C(25) | 9 729(1) | 4 646(3) | 2 229(2) |

**Table 6** Selected bond lengths (Å) and bond angles (°) with esds in parentheses

| Atoms | Bond | Atoms | Bond |
|---|---|---|---|
| O(1)–S(1) | 1.509(2) | C(6)–C(5) | 1.388(3) |
| C(1)–S(1) | 1.784(2) | C(9)–C(8) | 1.512(3) |
| C(8)–S(1) | 1.823(3) | C(10)–C(8) | 1.523(3) |
| N(1)–C(10) | 1.494(3) | C(12)–C(11) | 1.494(4) |
| N(1)–C(11) | 1.495(3) | C(13)–C(12) | 1.381(3) |
| C(2)–C(1) | 1.377(3) | C(17)–C(12) | 1.385(5) |
| C(6)–C(1) | 1.377(4) | C(14)–C(13) | 1.388(6) |
| C(3)–C(2) | 1.384(4) | C(15)–C(14) | 1.381(8) |
| C(4)–C(3) | 1.374(5) | C(16)–C(15) | 1.356(8) |
| C(5)–C(4) | 1.379(4) | C(17)–C(16) | 1.388(6) |
| C(7)–C(4) | 1.512(5) | | |
| **Atoms** | **Angle** | **Atoms** | **Angle** |
| O(1)–S(1)–C(1) | 105.4(1) | C(3)–C(4)–C(5) | 118.2(2) |
| O(1)–S(1)–C(8) | 105.2(1) | C(3)–C(4)–C(7) | 121.4(3) |
| S(1)–C(1)–C(2) | 118.8(2) | C(4)–C(5)–C(6) | 121.3(3) |
| S(1)–C(1)–C(6) | 120.9(2) | C(5)–C(4)–C(7) | 120.4(3) |
| C(1)–S(1)–C(8) | 99.8(2) | C(9)–C(8)–C(10) | 114.3(2) |
| S(1)–C(8)–C(9) | 107.6(2) | C(11)–C(12)–C(13) | 120.2(2) |
| S(1)–C(8)–C(10) | 109.7(2) | C(11)–C(12)–C(17) | 120.2(2) |
| N(1)–C(10)–C(8) | 111.3(2) | C(12)–C(13)–C(14) | 120.2(3) |
| C(10)–N(1)–C(11) | 112.8(2) | C(13)–C(12)–C(17) | 119.6(3) |
| N(1)–C(11)–C(12) | 111.5(2) | C(12)–C(17)–C(16) | 119.5(4) |
| C(1)–C(2)–C(3) | 119.3(2) | C(13)–C(14)–C(15) | 119.7(4) |
| C(2)–C(1)–C(6) | 120.3(2) | C(14)–C(15)–C(16) | 120.2(4) |
| C(1)–C(6)–C(5) | 119.2(2) | C(15)–C(16)–C(17) | 120.9(4) |
| C(2)–C(3)–C(4) | 121.6(2) | | |

hydride in dichloromethane the proportions were as follows: acetic acid (17 mmol), $Bu_4NBH_4$ (1.9 mmol), $CH_2Cl_2$ (2 $cm^3$), enamine (0.6 mmol) in $CH_2Cl_2$ (2 $cm^3$). The reaction mixture was stirred at the appropriate temperature for 7 h and was then extracted with hydrochloric acid (0.5 mol $dm^{-3}$). The aq. layer was made basic with NaOH, then extracted with diethyl ether, and the extract was dried with $MgSO_4$ and evaporated. The oily residue was purified by column chromatography (silica gel; $CHCl_3$–MeOH; 15:1).

The $^1H$ NMR ($C_6D_6$; $Me_4Si$) spectral data for amines **2a–e** are presented in Table 4.

N-t-*Butyl*-2-(*methylsulphinyl*)*propylamine* **2a**. Oil, m.p. (picrate) 164–167 °C (from $CHCl_3$) [Found: C, 34.0; H, 4.5; N, 10.8; S, 6.25. $C_{15}H_{23}Cl_3N_4O_8S$ (amine picrate·$CHCl_3$) requires C, 34.25; H, 4.4; N, 10.7; S, 6.1%]; $\nu_{max}$(neat)/$cm^{-1}$ 1040 (S=O).

N-t-*Butyl*-2-(*phenylsulphinyl*)*propylamine* **2b**. Oil, m.p. (hydrochloride) 176–180 °C (from THF–$CH_2Cl_2$) [Found: C, 56.4; H, 8.0; N, 5.0. $C_{13}H_{22}ClNOS$ (hydrochloride) requires C, 56.6; H, 8.0; N, 5.1%]; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1040 (S=O).

N-t-*Butyl*-2-(p-*tolylsulphinyl*)*propylamine* **2c**. Crystals, m.p. (hydrochloride) 187–189 °C (from THF–$CH_2Cl_2$) [Found: C, 57.9; H, 8.5; N, 4.9. $C_{14}H_{24}ClNOS$ (hydrochloride) requires C, 58.0; H, 8.3; 6, 4.8%]; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1040 (S=O). Optically active amine **2c** cited in entry 8 (Table 1) had $[\alpha]_D$ +187.5°, $[\alpha]_{546}$ +231.2° (*c* 1.7, $Et_2O$). After a second crystallization from hexane–diethyl ether compound **2c** had m.p. 90 °C; $[\alpha]_D$ +190.6°, $[\alpha]_{546}$ +234.9° (*c* 2.0, $Et_2O$).

N-t-*Butyl*-2-(t-*butylsulphinyl*)*propylamine* **2d**. Oil, m.p. (hydrochloride) 172–176 °C (decomp.) (from THF–$CH_2Cl_2$) [Found: C, 51.4; H, 10.4; N, 5.3. $C_{11}H_{26}ClNOS$ (hydrochloride) requires C, 51.7; H, 10.2; N, 5.5%); $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1030 (S=O).

N-*Benzyl*-2-(p-*tolylsulphinyl*)*propylamine* **2e**. Crystals; the *l*-diastereoisomer had m.p. 58–60 °C (from hexane–$Et_2O$) (Found: C, 70.8; H, 7.4; N, 4.7; S, 10.9. $C_{17}H_{21}NOS$ requires C, 71.1; H, 7.3; N, 4.9; S, 11.15%); $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1030 (S=O).

Crystals of amine *l*-**2e** picrate for X-ray measurements were obtained from acetone (m.p. 173–174 °C).

*Crystal Data for l-***2e** *Picrate*: $C_{17}H_{22}NOS^+ \cdot C_6H_2N_3O_7^-$, M = 516.53, monoclinic unit cell, $a$ = 22.651(3), $b$ = 9.373(2), $c$ = 11.930(2) Å, β = 93.62(2)°, $V$ = 2527.8(8) $Å^3$, space group $P2_1/n$, $Z$ = 4, $D_x$ = 1.308 g $cm^{-1}$. 2898 Observed, unique reflections ($I > 2\sigma_I$) were measured on an automated Siemens AED four-circle diffractometer, with monochromatized Cu-Kα radiation ($\lambda$ = 1.541 78 Å, $\theta_{max}$ = 60°) and 1 standard reflection monitored every 50 measurements. Intensities were corrected for Lorentz, polarization and absorption[20] factors.

*Structure Solution and Refinement*.—The structure was solved by direct methods and refined by full-matrix least-squares procedure using the CRYSRULER package.[21] Hydrogen-atom positions were found from the difference Fourier maps and were refined. Final $R$- and $R_w$-factors with the weighting scheme $w = 1/\sigma_F^2 + 0.012\ F^2$, were 0.0464 and 0.0528, respectively. All calculations were performed on an IBM PS2/30 personal computer.

*Structure Description*.—Tables 5 and 6 present refined, fractional co-ordinates, and selected details of molecular geometry. No particular differences between expected and found geometrical parameters were found in the molecule *l*-**2e**. Interactions between picric acid and the parent molecule are due to both protonation of the N(1) atom by hydrogen from the phenolic-group oxygen O(2) from picric acid, and a hydrogen bond formed between above three atoms [N(1)···O(2) = 2.742(3), H(1)N···O(2) = 1.94(3) Å, angle 161.0(4)°]. A second, fairly strong hydrogen bond is formed *via* the second hydrogen of N(1), and oxygen O(1) from the sulphoxide group

belonging to the molecule transformed by the $\frac{3}{2} - x$, $\frac{1}{2} + y$, $\frac{1}{2} - z$ symmetry [N(1)···O(1) = 2.745(3), H(2)N···O(1) = 1.90(4) Å, angle 178(3)°]. Nitro groups in the *ortho* position are tilted by only 12.6(1) and 15.6(2)° from the phenol ring least-squares plane. Although Fig. 1 suggests the presence of interactions between the phenyl rings from the tolyl group and the picrate anion, the shortest distances found are at least 3.4 Å.

N-*Benzyl*-t-(t-*butylsulphinyl*)*propan*-2-*amine* **4**.—Oil, m.p. (hydrochloride) 175–180 °C (from benzene–chloroform) [Found: C, 58.0; H, 8.3; N, 4.7. $C_{14}H_{24}ClNOS$ (hydrochloride) requires C, 58.0; H, 8.3; N, 4.8%]; $\nu_{max}(CHCl_3)/cm^{-1}$ 1020 (S=O); $\delta_H(C_6D_6$; $Me_4Si)$ 0.93 (9 H, s, $Bu^t$), 1.04 (3 H, d, *J* 6.4, 2-Me), 1.72 (1 H, s, NH), 1.8–2.6 (2 H, m, $SCH_2$), 3.25 (1 H, m, 2-H), 3.70 (2 H, s, $NCH_2$) and 7.1–7.3 (5 H, m, Ph); for the second diastereoisomer: $\delta$ 0.90 (9 H, s, $Bu^t$) and 1.09 (3 H, d, *J* 6.3, 2-Me).

*Complex of Amine* **2e** *with Borane*.—To a solution of amine **2e** hydrochloride [two diastereoisomers (*ca.* 1:1); 0.30 g, 0.9 mmol] in THF (20 $cm^3$) was added sodium borohydride (0.15 g, 3.9 mmol). The reaction mixture was stirred at room temperature for 24 h. After filtration the solution was evaporated to give crystals, which were purified by column chromatography ($CHCl_3$). The resulting complex had identical properties with those of a compound obtained in the reduction of enamine **1e** in entry 5 (Table 1); m.p. 125–130 °C (from $CCl_4$) [Found: $M^+$, 300.1690. $C_{17}H_{24}{}^{10}BNOS$ requires M, 300.1708] [Found: $(M + 1)^+$ 300.1592. $C_{17}H_{24}{}^{11}BNOS$ requires (M − 1), 300.1593]; $\nu_{max}(KBr)/cm^{-1}$ 1040 (S=O) and 2350 (B–H); $\delta_H$(100 MHz; $CDCl_3$; $Me_4Si$) 0.85 (3 H, d, *J* 7.1, 2-Me), 2.40 (3 H, s, Ar*Me*), 2.8 (1 H, m, 2-H), 3.29 (1 H, m, 1-H), 3.60 (1 H, dd, *J* 13.9, *J'* 9.1, C*H*Ph), 3.9 (1 H, m, 1-H), 4.30 (1 H, dd, *J* 13.9, *J'* 3.9, C*H*Ph), 6.3 (1 H, br s, NH) and 7.2–7.7 (9 H, m, ArH); $\delta_C$(25 MHz; $CDCl_3$; $Me_4Si$) 12.5 (2-Me), 21.5 (Ar*Me*), 54.6 (C-2), 57.4 (C-1), 61.0 ($CH_2$Ph) and 125.7, 128.6, 128.9, 129.7, 130.1, 133.6, 139.1 and 143.1 (Ar).

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