



range 60–70%, while in the reduction with sodium borohydride asymmetric induction is always lower and depends to a larger extent on the nature of the substrate.\*

The use of chiral and achiral alkoxy-lithium aluminium hydrides,<sup>10</sup> in the reduction of oxosulphoxides was also investigated. With compounds (1)–(3) it resulted only in lowering of the stereoselectivity. A few representative examples are reported in Table 2. A more

obtained by partial reduction of racemic sulphoxides with chiral hydrides.<sup>12</sup>

Optically active hydroxysulphoxides are useful intermediates for the production, *inter alia*, of optically active alcohols<sup>1,2</sup> and epoxides.<sup>9</sup> Both enantiomers of the sulphoxide (5), and hence of the oxosulphoxides (1)–(4), are easily accessible. Transfer of chirality from sulphur to carbon in the reduction of (1)–(4)

TABLE 2  
Reduction of the  $\beta$ -oxosulphoxides (1)–(3) by complex hydrides at  $-70^\circ\text{C}$  in diethyl ether–tetrahydrofuran

| Oxosulphoxide | Reducing agent <sup>a</sup>           | Hydroxysulphoxides                       |           | Hydroxysulphones                         |                         |                     |
|---------------|---------------------------------------|--|-----------|--|-------------------------|---------------------|
|               |                                       | $[\alpha]_D^{25}(\text{c})$ <sup>b</sup> | Yield (%) | $[\alpha]_D^{25}(\text{c})$ <sup>b</sup> | Enantiomeric excess (%) | M.p. ( $n_D^{20}$ ) |
| (2)           | LiAlH <sub>4</sub> (OBornyl)          | (6), +114.0                              | 80        | (10), -11.7                              | 60                      | 80–82 °C            |
| (2)           | LiAlH <sub>4</sub> (OMenthyl)         | (7), +173.8                              | 83        | (11), -9.6                               | 42                      | (1.5355)            |
| (3)           | LiAlH <sub>4</sub> (OMenthyl)         | (8), +179.2                              | 73        | (12), -6.9                               | 33                      | (1.5307)            |
| (3)           | LiAlH(OBu <sup>t</sup> ) <sub>3</sub> | (8), +189.9                              | 80        | (12), -5.0                               | 20                      | (1.5312)            |

<sup>a</sup> c 2, in chloroform.

interesting situation was encountered with the sulphoxide (4); the diastereoisomeric ratio of the alcohols (9a, b) depends markedly on the nature of the reducing agent, to the point that a large excess of either of the two diastereoisomers (9a) or (9b) can be obtained (Table 3).

TABLE 3

Reduction of the racemic  $\beta$ -oxosulphoxide (4) by lithium aluminium hydrides at  $-70^\circ\text{C}$  in diethyl ether–tetrahydrofuran

| Reducing agent   | Diastereoisomeric ratio (9a) : (9b) | $[\alpha]_D^{25}$ <sup>a</sup> |
|--|-------------------------------------|--------------------------------|
| LiAlH <sub>4</sub>   | 83 : 17                             |                                |
| LiAlH <sub>4</sub> (OXylyl) <sub>2</sub>                             | 76 : 24                             |                                |
| LiAlH <sub>4</sub> (OBornyl)   | 70 : 30                             | -1.5°                          |
| LiAlH <sub>4</sub> (OMenthyl)  | 55 : 45                             | 0                              |
| LiAlH <sub>4</sub> (OMenthyl) <sub>2</sub>                           | 45 : 55                             | 0                              |
| LiAlH(OMe) <sub>3</sub>  | 43 : 57                             |                                |
| LiAlH( <i>N</i> -Methylephedrinyl)(OXylyl) <sub>2</sub> <sup>b</sup> | 29 : 71                             | +13.0°                         |
| LiAlH <sub>4</sub> (Ephedrinyl)                                      | 29 : 71                             | +1.5°                          |
| LiAlH(OBu <sup>t</sup> ) <sub>3</sub>                                | 26 : 74                             |                                |

<sup>a</sup> c 2, in chloroform. <sup>b</sup> Ephedrinyl = 2-( $\beta$ -hydroxy- $\alpha$ -methylphenethylamino)ethyl.

The reduction of racemic oxosulphoxides by chiral hydrides can in principle lead to asymmetric induction and/or kinetic resolution. This possibility can easily be checked since either of the two chiral centres of hydroxysulphoxides can be selectively destroyed by oxidation with peroxy-acids (oxidation of the sulphur) or manganese dioxide (oxidation of the hydroxy function) according to literature methods.<sup>11</sup> Starting from racemic (4), reduction with chiral lithium aluminium hydrides, followed by oxidation to the sulphone (13) and to the oxosulphoxide (4) generally resulted in very low enantioselectivity, if any. This tallies with the low optical purity of optically active simple sulphoxides

\* (+)-(R<sub>8</sub>,R<sub>C</sub>)-(6a) and (+)-(R<sub>8</sub>,S<sub>C</sub>)-(6b) were previously obtained as a 1:1 diastereoisomeric mixture by reaction of benzaldehyde with the  $\alpha$ -sulphinylcarbanion prepared from optically active (+)-(R)-(5), and separated by chromatography and fractional crystallization.<sup>2</sup>

affords hydroxy derivatives of high and known optical purity, whose chirality at carbon can be controlled by the appropriate choice of the chirality at sulphur in the starting sulphoxide (5) and, in some instances, also by the nature of the reducing agent.

#### EXPERIMENTAL

*General.*—Light petroleum had b.p. 40–60 °C. Ether was dried over sodium and tetrahydrofuran was distilled from lithium aluminium hydride. Diethylamine was distilled from potassium hydroxide: n-butyl-lithium was used as *ca.* 2M solutions in hexane. Extractions were performed with dichloromethane and extracts were dried over sodium sulphate. I.r. spectra were recorded on a Perkin-Elmer 377 spectrometer. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. (–)-Menthol,  $[\alpha]_D^{20}$  -49.5° (c 10 in EtOH), (–)-borneol,  $[\alpha]_D^{25}$  -26.6° (c 5.3 in EtOH), and (–)-(1R,2S)-ephedrine,  $[\alpha]_D^{25}$  -35.0° (c 4 in H<sub>2</sub>O-HCl), were commercial products; (–)-*N*-methylephedrine, prepared by literature methods,<sup>13</sup> had  $[\alpha]_D^{20}$  -24° (c 1 in EtOH). Methyl *p*-tolyl sulphoxide, prepared by literature methods,<sup>14</sup> had m.p. 76 °C,  $[\alpha]_D^{25}$  +189.2° (c 1 in CHCl<sub>3</sub>) {lit.,<sup>14</sup>  $[\alpha]_D^{25}$  +189.2° (c 1 in CHCl<sub>3</sub>)}.

*Synthesis of  $\beta$ -Oxosulphoxides.*—n-Butyl lithium (4 mmol) in n-hexane was added dropwise at  $-40^\circ\text{C}$  to a stirred solution of diethylamine (4 mmol) in tetrahydrofuran (10 ml). The mixture was kept for 30 min below 0 °C, cooled to  $-30^\circ\text{C}$ , and methyl *p*-tolyl sulphoxide (2 mmol) in tetrahydrofuran (10 ml) was added dropwise. The mixture was allowed to reach room temperature, cooled again to  $-40^\circ\text{C}$ , and the ester (3 mmol) in tetrahydrofuran (5 ml) added in one portion. The mixture was kept for 30 min at 0 °C, heated at reflux for the appropriate time and quenched with saturated aqueous ammonium chloride. The organic layer was separated off and the aqueous layer was acidified with dilute sulphuric acid to pH 3–4 and extracted with dichloromethane. The combined organic phases were concentrated on a rotary evaporator, and the residue was chromatographed on silica with ether–light petroleum as eluant. Yields, specific rotations, and physical and analytical data are reported in Table 4.

*Reduction of  $\beta$ -Oxosulphoxides to  $\beta$ -Hydroxysulphoxides.*—*Method A.* The  $\beta$ -oxosulphoxide (1 mmol) in absolute

TABLE 4

Data for the  $\beta$ -oxosulphones (+)-*p*-MeC<sub>6</sub>H<sub>4</sub>S(:O)CH<sub>2</sub>C(:O)R

| R               | $[\alpha]_D^{25}$                            | M.p. (°C)<br>( <i>l</i> /°C) | Reaction<br>time/h | Yield<br>(%) | Found (%) |     | Formula  | Requires (%) |     |
|-----------------|--|------------------------------|--------------------|--------------|-----------|-----|--|--------------|-----|
|                 |  |                              |                    |              | C         | H   |  | C            | H   |
| Ph              | +180.9 <sup>a</sup><br>+265.0 <sup>b,c</sup> | 82—83.5                      | 2.5                | 62           |           |     |  |              |     |
| Et              | +210.0 <sup>a</sup><br>+260.3 <sup>b</sup>   | 69—70                        | 2                  | 60           | 62.6      | 6.6 | C <sub>13</sub> H <sub>18</sub> O <sub>2</sub> S | 62.8         | 6.7 |
| Pr <sup>d</sup> | +191.3 <sup>a</sup><br>-255.2 <sup>b</sup>   | 57—59                        | 2.5                | 67           | 64.3      | 7.1 | C <sub>12</sub> H <sub>16</sub> O <sub>2</sub> S | 64.25        | 7.2 |
| Bu <sup>t</sup> | +162.0 <sup>a</sup><br>+241.8 <sup>b</sup>   | 108—108.7                    | 4                  | 82           | 65.8      | 7.6 | C <sub>11</sub> H <sub>14</sub> O <sub>2</sub> S | 65.5         | 7.6 |

<sup>a</sup> *c* 1, in chloroform. <sup>b</sup> *c* 1, in acetone. <sup>c</sup> lit.,<sup>1</sup>  $[\alpha]_D^{25} + 264.2$  (acetone).

ethanol (5 ml) was added at  $-70^\circ\text{C}$  to a stirred solution of sodium borohydride (1 mmol) in absolute ethanol (5 ml). The mixture was kept at  $-70^\circ\text{C}$  for 4 h. Methanol (5 ml) was then added and solvent evaporated off *in vacuo*. Water and dichloromethane were added to the residue; the organic phase was washed with 10% aqueous sodium hydroxide and dried over sodium sulphate. Evaporation gave the product. Yields and specified rotations are reported in Table 1. The diastereoisomeric mixture (6a, b) had m.p. 90—105 °C, (8a, b)  $n_D^{23}$  1.545 5, and (9a, b) m.p. 90—125 °C; the mixture (7a, b) was isolated as waxy solid. Analytical data are reported in Table 5.

TABLE 5

Analytical data for compounds (7)—(13)

| Compound | Found (%) |      | Formula  | Requires (%) |      |
|----------|-----------|------|--|--------------|------|
|          | C         | H    |  | C            | H    |
| (7)      | 62.4      | 7.7  | C <sub>11</sub> H <sub>16</sub> O <sub>2</sub> S | 62.2         | 7.6  |
| (8)      | 63.7      | 8.0  | C <sub>12</sub> H <sub>16</sub> O <sub>2</sub> S | 63.6         | 8.0  |
| (9)      | 65.1      | 8.4  | C <sub>13</sub> H <sub>20</sub> O <sub>2</sub> S | 65.0         | 8.4  |
| (10)     | 65.0      | 5.85 | C <sub>15</sub> H <sub>16</sub> O <sub>3</sub> S | 65.2         | 5.85 |
| (11)     | 57.7      | 7.1  | C <sub>11</sub> H <sub>16</sub> O <sub>3</sub> S | 57.9         | 7.1  |
| (12)     | 59.7      | 7.6  | C <sub>12</sub> H <sub>16</sub> O <sub>3</sub> S | 59.5         | 7.5  |
| (13)     | 60.7      | 7.85 | C <sub>13</sub> H <sub>20</sub> O <sub>3</sub> S | 60.9         | 7.85 |

**Method B.** The  $\beta$ -oxosulphoxide (1 mmol) in tetrahydrofuran (5 ml) was added at  $-70^\circ\text{C}$  under nitrogen to a stirred solution of lithium aluminium hydride (1 mmol) in diethyl ether. The mixture was kept at  $-70^\circ\text{C}$  for 3—5 h. Saturated aqueous ammonium chloride (3 ml) was then added and the mixture allowed to reach room temperature. The organic layer was separated off, the aqueous layer washed twice with diethyl ether, and the combined organic phases were washed with dilute sodium hydroxide solution and dried. Evaporation gave 80—90% yields of product free from unchanged  $\beta$ -oxosulphoxide. Yields and specific rotations are reported in Table 1. The diastereoisomeric mixture (6a, b) had m.p. 95—105 °C, (8a, b)  $n_D^{24}$  1.546 1, and (9a, b) m.p. 78—122 °C; the mixture (7a, b) was isolated as waxy solid.

**Method C.** The alkoxyllithium aluminium hydrides were prepared by literature methods.<sup>10</sup> The reductions were carried out at  $-70^\circ\text{C}$  in diethyl ether–tetrahydrofuran as solvent with a 4 : 1 ratio between the active hydrogen of the reducing agent and the  $\beta$ -oxosulphoxides. After 3—5 h, work-up as just described afforded the crude product which was chromatographed (silica; ether–light petroleum) to give 75—90% yields of product. Optical rotations are reported in Tables 2 and 3.

**Oxidation of  $\beta$ -Hydroxysulphoxides to  $\beta$ -Hydroxysulphones.**—The  $\beta$ -hydroxysulphoxides were oxidized with a stoichiometric quantity of *m*-chloroperoxybenzoic acid

at 20 °C for 24 h and purified by column chromatography (silica; light petroleum–ether 8 : 2). Yields were in the range 80—90%; physical properties and optical rotations are reported in Tables 1 and 2, and analytical data in Table 5. Starting from racemic (4), reduction with chiral lithium aluminium hydrides and subsequent oxidation afforded the  $\beta$ -hydroxysulphone (13) with an optical purity of  $\leq 8\%$ .

**Oxidation of  $\beta$ -Hydroxysulphoxides to  $\beta$ -Oxosulphoxides.**—The oxidations were performed with a large excess (15 mol. equiv.) of active manganese dioxide in dichloromethane solution (25 ml) at room temperature with vigorous stirring, following the methods described in the literature.<sup>11</sup> Starting from (6a, b), compound (1) was obtained in 90% yield after 2 h. Starting from (9a, b),  $[\alpha]_D^{25} + 13.0^\circ$  (*c* 2 in CHCl<sub>3</sub>), compound (4) was obtained in 43% yield after 60 h,  $[\alpha]_D^{25} + 3.0^\circ$  (*c* 3 in CHCl<sub>3</sub>), optical purity 1.8%.

**Determination of the Enantiomeric Purity of Oxosulphoxides and Hydroxysulphones and of the Diastereoisomeric Ratio of Hydroxysulphoxides by <sup>1</sup>H N.m.r. Spectroscopy.**—All spectra were recorded on a Varian HA 100 instrument in deuteriochloroform as solvent. <sup>1</sup>H N.m.r. spectra of the racemic oxosulphoxides (2)—(4) and of the hydroxysulphones (10)—(13) showed for the aromatic protons an AA'BB' system, centred at  $\delta$  ca. 7.4, which revealed doubling of the lower field signals in the presence of the chiral shift reagent Eu(tfc)<sub>3</sub>. For the racemic oxosulphoxide (1) the AB system centred at  $\delta$  4.4 (2 H, CH<sub>2</sub>) showed a doubling in the presence of Eu(tfc)<sub>3</sub>. The ratio of Eu(tfc)<sub>3</sub> to compounds (1)—(4) and (10)—(13) was 1 : 1. The enantiomeric purities of the optically active derivatives were determined under the aforementioned conditions. In the case of the hydroxysulphoxide (9a, b) the diastereoisomeric ratio was determined by the ratio of the intensities of the *t*-butyl proton resonances, singlets at  $\delta$  1.08 and 1.12, respectively.

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