

## Synthesis of Homochiral Amino Alcohols, Aziridines and Diamines *via* Homochiral Cyclic Sulphites†

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Vicinal diols react with thionyl chloride to give 1,2-cyclic sulphites in quantitative yield, which undergo facile ring opening by lithium azide in dimethylformamide to yield azido alcohols and the latter in turn have been stereoselectively transformed into amino alcohols, aziridines and diamines.

Homochiral amino alcohols,<sup>1-3</sup> aziridines<sup>4</sup> and diamines<sup>5,6</sup> have played an important role in asymmetric organic reactions and bioorganic synthesis. Generally, they are synthesized either by the reduction of optically pure amino acids<sup>7</sup> or by resolution processes.<sup>8b,c,9</sup> Recently we have reported an efficient synthesis of substituted aziridines *via* 1,2-cyclic

sulphates.<sup>4</sup> Now we report a simple method for the synthesis of various *N*-unsubstituted amino alcohols, aziridines and diamines *via* stereoselective transformations of cyclic sulphites.

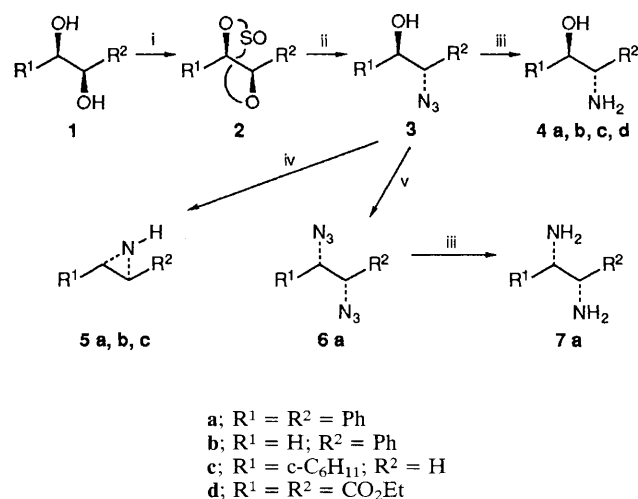
(1*R*,2*S*)- and (1*S*,2*R*)-1,2-Diphenyl-2-aminoethanol **4a**<sup>8</sup> and (*R,R*)- and (*S,S*)-1,2-diphenyl-1,2-diaminoethane **7a**<sup>5,6</sup> have recently been utilized as chiral auxiliaries in the asymmetric synthesis of amino acids,<sup>3</sup> dihydroxylation of alkenes,<sup>5a</sup> aldol<sup>5b,e</sup> and Diels–Alder reactions,<sup>5b</sup> carbonyl allylation,<sup>5c</sup> synthe-

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**Table 1** Cyclic sulphite routes to azido alcohols, amino alcohols, aziridines and diamines<sup>a</sup>

Entry	Compound	Yield (%) <sup>b</sup> (overall)	$[\alpha]_D^{22}$ <sup>c</sup> (c in solv.) <sup>c</sup>	e.e. (%) <sup>d</sup> (config.) <sup>e</sup>
1	<b>3a</b>	81 (1→3)	+111.14 (c, 1.18, CHCl <sub>3</sub> )	≥96 (RS) <sup>f</sup>
2	<b>3b</b>	81 (1→3)	—	≥96 (S)
3	<b>3c</b>	79 (1→3)	-3.51 (c, 0.94, CHCl <sub>3</sub> )	≥96 (R)
4	<b>3d</b>	85 (1→3)	+8.24 (c, 1.88, CHCl <sub>3</sub> )	≥96 (RS) <sup>g</sup>
5	<b>4a</b>	76 (1→4)	-8.80 (c, 0.5, EtOH)	≥96 (RS)
6	<b>4b</b>	58 (1→4)	+28.70 (c, 1.07, EtOH)	≥96 (S) <sup>h</sup>
7	<b>4c</b>	56 (1→4)	-11.20 (c, 0.72, EtOH)	≥96 (R) <sup>i</sup>
8	<b>4d</b>	76 (1→4)	—	≥96 (RS) <sup>j</sup>
9	<b>5a</b>	66 (3→5)	-341.0 (c, 0.83, CHCl <sub>3</sub> )	≥96 (SS)
10	<b>5b</b>	60 (3→5)	-42.50 (c, 10.3, EtOH)	≥96 (S)
11	<b>5c</b>	65 (3→5)	-11.58 (c, 0.90, CHCl <sub>3</sub> )	≥96 (S)
12	<b>7a</b>	80 (3→7)	-85.0 (c, 0.1, ether)	≥96 (SS)

<sup>a</sup> All the new compounds showed satisfactory IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and elemental analysis. <sup>b</sup> The overall yield is reported for the transformation shown in parentheses. <sup>c</sup> The optical rotation is reported in the solvent and concentration indicated in parentheses. <sup>d</sup> The e.e. % was determined by <sup>1</sup>H NMR, <sup>13</sup>C NMR or HPLC using Pirkle A Type column on the corresponding Mosher ester derivatives and by comparison of optical rotation with the known compounds. <sup>e</sup> The absolute configuration is assigned by comparison with the substance of known stereochemistry and is based on the assumption of stereospecific inversion at the stereogenic centre(s) of cyclic sulphites and azido alcohols. <sup>f</sup> M.p. 47 °C. <sup>g</sup> See ref. 11a. <sup>h</sup> M.p. 76–78 °C. <sup>i</sup> M.p. 86–87 °C, reported to be a waxy solid,  $[\alpha]_D^{22}$  -10.22° (c, 1.87, EtOH), ref. 8c. <sup>j</sup> This amino alcohol has been isolated as diethyl *N*-(*t*-butoxycarbonyl)-*L*-erythro-β-hydroxyaspartate, see ref. 11.



**Scheme 1** Reagents and conditions: i, SOCl<sub>2</sub>, CCl<sub>4</sub>; ii, LiN<sub>3</sub>, DMF, 120 °C; iii, H<sub>2</sub>/Pd-C or LiAlH<sub>4</sub>, THF, heat; iv, PPh<sub>3</sub>, THF, heat; v, a, MsCl-Py; b, LiN<sub>3</sub>, DMF, 120 °C

sis of allenyl and propynyl carbinols<sup>5d</sup> and epoxidation of unfunctionalized alkenes.<sup>6</sup> However, both the amino alcohol **4a**<sup>8b</sup> and the diamine **7a**<sup>9</sup> have been synthesized by multistep processes involving resolution. Thus, the stereoselective synthesis of these chiral auxiliaries is highly desirable.

The availability of homochiral diols **1** from the catalytic asymmetric dihydroxylation of alkenes<sup>10</sup> coupled with the facile electrophilic behaviour of derived cyclic sulphites **2** has opened a new possibility of synthesizing 1,2-disubstituted amino alcohols, diamines and *N*-unsubstituted aziridines *via* homochiral azido alcohols (Scheme 1). The cyclic sulphites, prepared in quantitative yield by the reaction of vicinal diols with thionyl chloride in refluxing CCl<sub>4</sub>, undergo facile nucleophilic reaction with lithium azide in dimethylformamide (DMF) at *ca.* 120 °C to afford 79–85% yields of azido alcohols **3**. Reduction of azido alcohols **3** either with LiAlH<sub>4</sub> in tetrahydrofuran (THF) or with H<sub>2</sub>/Pd-C (10%) gave amino alcohols in high yield (Table 1; entries 5–8). In the case of the cyclic sulphite derived from 1-(*R*)-phenylethane-1,2-diol, the nucleophilic attack occurs at the benzylic position giving rise to (*S*)-phenylglycinol (Table 1; entry 6) whereas the cyclic sulphite prepared from 1-(*R*)-cyclohexylethane-1,2-diol furnishes α-aminomethylcyclohexanemethanol (Table 1; entry 7). Amino alcohols containing terminal amino groups are otherwise difficult to prepare. However, treatment of azido alcohols **3** with triphenylphosphine in refluxing THF yielded *N*-unsubstituted aziridines **5** (Table 1; entries 9–11). Azido alcohols have been conveniently transformed to diazides **6** by the reaction of methanesulphonyl chloride (MsCl) in pyridine followed by treatment with lithium azide in DMF at *ca.* 120 °C. The corresponding diazide **6** afforded an almost quantitative yield of diamine **7** when treated with H<sub>2</sub>/Pd-C (10%, 50 atm.) in ethyl acetate or in ethanol (Table 1; entry 12) or with LiAlH<sub>4</sub> in THF.

Thus, we have achieved a very short stereoselective synthesis of several homochiral amino alcohols, aziridines and diamines in good yield and high enantiomeric purity.

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