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

Braj B. Lohray* [a,b] **and Jaimala R. Ahuja** [b]

[a] *Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139, USA*
[b] *Division of Organic Chemistry, National Chemical Laboratory, Pune 411 008, India*

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,[1-3], aziridines[4] and diamines[5,6] 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[7] or by resolution processes.[8b,c,9] Recently we have reported an efficient synthesis of substituted aziridines *via* 1,2-cyclic sulphates.[4] Now we report a simple method for the synthesis of various *N*-unsubstituted amino alcohols, aziridines and diamines *via* stereoselective transformations of cyclic sulphites.

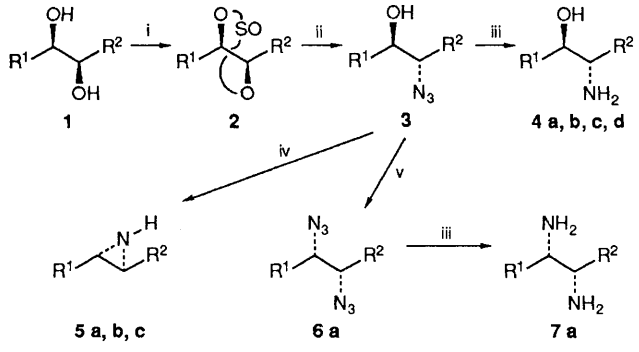
(1*R*,2*S*)- and (1*S*,2*R*)-1,2-Diphenyl-2-aminoethanol **4a**[8] and (*R*,*R*)- and (*S*,*S*)-1,2-diphenyl-1,2-diaminoethane **7a**[5,6] have recently been utilized as chiral auxiliaries in the asymmetric synthesis of amino acids,[3] dihydroxylation of alkenes,[5a] aldol [5b,e] and Diels–Alder reactions,[5b]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

† NCL Communication No. 4377.

Table 1 Cyclic sulphite routes to azido alcohols, amino alcohols, aziridines and diamines[a]

Entry	Compound	Yield (%)[b] (overall)	$[\alpha]_D^{22}$/° (c in solv.)[c]	e.e. (%)[d]	(config.)[e]
1	**3a**	81 (**1** → **3**)	+111.14 (c, 1.18, $CHCl_3$)	≥96	(*RS*)[f]
2	**3b**	81 (**1** → **3**)	—	≥96	(*S*)
3	**3c**	79 (**1** → **3**)	−3.51 (c, 0.94, $CHCl_3$)	≥96	(*R*)
4	**3d**	85 (**1** → **3**)	+8.24 (c, 1.88, $CHCl_3$)	≥96	(*RS*)[g]
5	**4a**	76 (**1** → **4**)	−8.80 (c, 0.5, EtOH)	≥96	(*RS*)
6	**4b**	58 (**1** → **4**)	+28.70 (c, 1.07, EtOH)	≥96	(*S*)[h]
7	**4c**	56 (**1** → **4**)	−11.20 (c, 0.72, EtOH)	≥96	(*R*)[i]
8	**4d**	76 (**1** → **4**)	—	≥96	(*RS*)[j]
9	**5a**	66 (**3** → **5**)	−341.0 (c, 0.83, $CHCl_3$)	≥96	(*SS*)
10	**5b**	60 (**3** → **5**)	−42.50 (c, 10.3, EtOH)	≥96	(*S*)
11	**5c**	65 (**3** → **5**)	−11.58 (c, 0.90, $CHCl_3$)	≥96	(*S*)
12	**7a**	80 (**3** → **7**)	−85.0 (c, 0.1, ether)	≥96	(*SS*)

[a] All the new compounds showed satisfactory IR, ^{1}H NMR, ^{13}C NMR and elemental analysis. [b] The overall yield is reported for the transformation shown in parentheses. [c] The optical rotation is reported in the solvent and concentration indicated in parentheses. [d] The e.e. % was determined by ^{1}H NMR, ^{13}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. [e] 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. [f] M.p. 47 °C. [g] See ref. 11*a*. [h] M.p. 76–78 °C. [i] M.p. 86–87 °C, reported to be a waxy solid, $[\alpha]_D^{22}$ −10.22° (*c*, 1.87, EtOH), ref. 8c. [j] This amino alcohol has been isolated as diethyl *N*-(t-butoxycarbonyl)-L-*erythro*-β-hydroxyaspartate, see ref. 11.



a; $R^1 = R^2$ = Ph
b; R^1 = H; R^2 = Ph
c; R^1 = c-C_6H_{11}; R^2 = H
d; $R^1 = R^2 = CO_2Et$

Scheme 1 *Reagents and conditions*: i, $SOCl_2$, CCl_4; ii, LiN_3, DMF, 120 °C; iii, H_2/Pd·C or $LiAlH_4$, THF, heat ; iv, PPh_3, THF, heat; v, *a*, MsCl–Py; *b*, LiN_3, DMF, 120 °C

sis of allenenyl and propynyl carbinols[5d] and epoxidation of unfunctionalized alkenes.[6] However, both the amino alcohol **4a**[8b] and the diamine **7a**[9] 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 asymmmetric dihydroxylation of alkenes[10] 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_4, 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 $LiAlH_4$ in tetrahydrofuran (THF) or with H_2/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_2/Pd–C (10%, 50 atm.) in ethyl acetate or in ethanol (Table 1; entry 12) or with $LiAlH_4$ 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.

B. B. L. thanks Professor K. B. Sharpless for encouragement. Financial support was provided by NCL, Pune, India and NIH (GM 28384).

Received, 3rd October 1990; Com. 0/04444J

References

1 D. A. Evans; K. A. Lutomski and A. I. Meyers; D. Enders, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, New York, 1984, vol. 3, pp. 1; 213; 217 respectively.
2 Function Regulation of Monoamine Enzymes: *Basic Clin. Aspects Proc. Conf. 2nd.*, eds. E. Usdin, N. Weiner and M. B. H. Youdim, Macmillan, London, 1981.
3 R. M. Williams, *Synthesis of optically active alpha amino acids*, Pergamon Press, Oxford, 1989.
4 B. B. Lohray, Y. Gao and K. B. Sharpless, *Tetrahedron Lett.*, 1989, **30**, 2623 and references cited therein.
5 (*a*) E. J. Corey, P. D. Jardine, S. Virgil, P.-W. Yuen and R. D. Connell, *J. Am. Chem. Soc.*, 1989, **111**, 9243; (*b*) E. J. Corey, R. Imwinkelried, S. Pikul and Y. B. Xiang, *J. Am. Chem. Soc.*, 1989, **111**, 5493; (*c*) E. J. Corey, C. M. Yu and S. S. Kim, *J. Am. Chem. Soc.*, 1989, **111**, 5495; (*d*) E. J. Corey, C. M. Yu and D. H. Lee, *J. Am. Chem. Soc.*, 1990, **112**, 878; (*e*) E. J. Corey and S. S. Kim, *J. Am. Chem. Soc.*, 1990, **112**, 4976.
6 W. Zhang, J. L. Loebach, S. R. Wilson and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1990, **112**, 2801.
7 G. S. Bates and M. A. Varelas, *Can. J. Chem.*, 1980, **58**, 2562; N. Yahiro, *Chem. Lett.*, 1982, 1479; P. R. Pfister, *Synthesis*, 1984, 969; J. W. Kelly, N. L. Eskew and S. A. Evan Jr., *J. Org. Chem.*, 1986, **51**, 95.
8 (*a*) R. M. Williams, P. J. Sinclair, D. Zhai and D. J. Chen, *J. Am. Chem. Soc.*, 1988, **110**, 1547; (*b*) J. Weijland, K. Pfister, E. F. Swanezy, C. A. Robinson and M. Tischler, *J. Am. Chem. Soc.*, 1951, **73**, 1216; (*c*) M. Rafferty, D. S. Wilson, J. A. Monn, P. Krass, R. T. Borchardt and G. L. Grunewald, *J. Med. Chem.*, 1982, **25**, 1198.
9 Resolution: O. F. Williams and J. C. Bailar, *J. Am. Chem. Soc.*, 1959, **81**, 4464; G. G. Hawn, C. A. Chang and B. D. Douglas, *Inorg. Chem.*, 1979, **18**, 1266; K. Saigo, N. Kubota, S. Takebayashi and M. Hasegawa, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 931 (see also ref. 5*b*). The first synthesis of **7a** has since appeared, D. Pini, I. C. Rosini and P. Salvadori, *Synthesis*, 1990, 1023.
10 E. N. Jacobsen, I. Markó, W. S. Mungall, G. Schröder and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 1968; J. S. M. Wai, I. Markó, J. S. Sevendsen, M. G. Finn, E. N. Jacobsen and K. B. Sharpless, *J. Am. Chem. Soc.*, 1989, **111**, 1123; B. B. Lohray, T. H. Kalantar, B. M. Kim, C. Y. Park, T. Shibata, J. S. M. Wai and K. B. Sharpless, *Tetrahedron Lett.*, 1989, **30**, 2041; H.-L. Kwong, C. Sorato, Y. Ogino, H. Chen and K. B. Sharpless, *Tetrahedron Lett.*, 1990, **31**, 3003.
11 (*a*) Y. Gao, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 7538; (*b*) A. Guiller, C. H. Gagnien and H. Pacheco, *Tetrahedron Lett.*, 1985, **26**, 6343; (*c*) S. Saito, N. Bunya, M. Inaba, T. Moriwake and S. Torri, *Tetrahedron Lett.*, 1985, **26**, 5309.