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A Simple Route To Optically Pure 2,3-Diaminobutane

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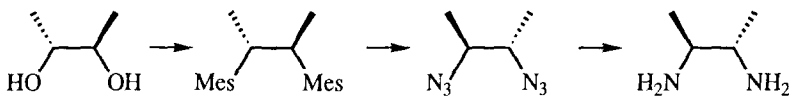
Abstract : Optically pure 2,3-diaminobutane was prepared by a simple and efficient method via the key intermediate 2,3-diazidobutane.

A great deal of attention has been focused on 2,3-diaminobutane because it plays important roles in many aspects of chemistry and medicine. As examples of its applications, we note the anti-cancer properties of its platinum(II) drugs[1], the large number of stereochemical investigations of its metal chelates[2], the high stereoselectivity offered by its transition metal complexes in homogenous asymmetric catalysis[3] and the enhanced activity exhibited by the corresponding cobalt(II) schiff base in the oxygenation of 3-methylindole[4].

2,3-Diaminobutane exists as three stereochemically distinct isomers arising from the two stereogenic carbon centres. The methods used for obtaining the optically pure 2,3-diaminobutane generally involved an initial separation of the racemic and meso diastereomers[5] followed by an optical resolution of the enantiomers[6]. These procedures, however, are not only slow[5], troublesome[7], and difficult[8], they also require experienced researchers with good crystallization skills. A recent report on the asymmetric synthesis of aliphatic 1,2-diamines involved vigorous reaction conditions with moderate yields.[9] The method put forward here provides the optically pure 2,3-diaminobutane in three technically simple steps, using the appropriate enantiomeric forms of 2,3-butanediol as starting materials [via a novel diazido intermediate].



1 **2** **3** **4**

The (*R,R*) form of 2,3-butanediol is commerically available while its enantiomer can be prepared in large scale from the naturally existing (*R,R*)-(+)-tartaric acid[10]. Both forms of the diol can be converted to their dimesylates **2** in practically quantitative yields[11]. Stereospecific conversion of (*R,R*)-**2** to (*S,S*)-**3** can be achieved by treating the former with excess sodium azide in dimethylformamide at 80 °C for 24 hours.[12] The workup involved extraction of the reaction mixture with 10% sodium chloride solution and diethyl-ether (to remove the inorganic salts and DMF) followed by the removal of organic solvent. The optically pure diazide (*S,S*)-**3** was thus obtained as a pale yellow oil with $[\alpha]_D$ +115.20 (c 1.0, CH_2Cl_2)[13]. Reduction of the diazide to

(*S,S*)-**4** can be accomplished by treating the former with lithium aluminum hydride in boiling tetrahydrofuran for 16 hours. After the routine workup[17], optically pure (*S,S*)-**4** was isolated by fractional distillation under nitrogen (bp 126-129 °C); $[\alpha]_D$ +25.11 (neat), +29.40 (c 2.4, benzene), (Lit. values: +25.18 (neat), +29.48 (benzene))[6]. The overall yield of (*S,S*)-**4** from dimesylate was 78%. The enantiomer (*R,R*)-**4** was prepared in similar yield from (*S,S*)-**2**.

The method described is very efficient and large quantities of optically pure 2,3-diaminobutane can be prepared within a few days. No separation of diastereomers is necessary. We are currently preparing a range of functionalized diamines in their enantiomeric pure forms using a similar synthetic scheme.

References and Notes

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12. Reactions were performed under purified nitrogen. The reaction time could be shortened to 6h when DMSO was used as solvent, however, the workup was somewhat more difficult.
13. The diazide was not distilled due to safety considerations[14]. Nevetheless, it was found to be chemically pure by tlc and spectroscopic techniques. The 300 MHz ^{1}H NMR spectrum of the diazide in $CDCl_3$ exhibited the methyl signal as a "doublet" at δ 1.31 (J_{H-H} = 6.5Hz) surrounding by a typical $AX_3A'X'_3$ satellite[15] (J_{H-H} = 3.5Hz). The resonance signals for the non-equivalent methine proton are centred at δ 3.43. The infra red of the neat sample showed a strong azide absorption signal at 2100 cm^{-1}. The absolute configurations and the optical purity of **3** was developed by comparing with those of **1** and **4**[16].
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17. The workup is similar to those described for the isolation of 2,3-butanediol[10].

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