

## A New Synthesis of 1,2,3,4-Tetrahydroisoquinolines

By L. W. DEADY, N. PIRZADA, and R. D. TOPSOM\*

(Department of Chemistry, La Trobe University, Bundoora, Victoria, Australia 3083)

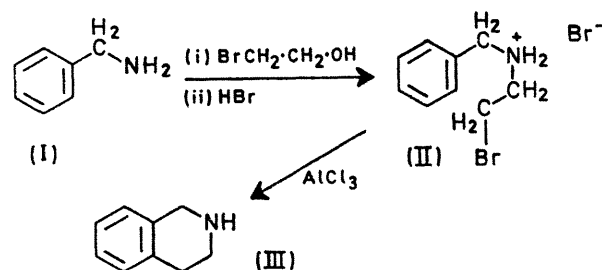
**Summary** Benzylamine and *p*-chlorobenzylamine have been converted into tetrahydroisoquinoline and its previously unreported 6-chloro-derivative by ring closure of the intermediate *N*-(2-bromoethyl)benzylamines.

1,2,3,4-Tetrahydroisoquinoline and its derivatives are usually prepared either by the Pictet–Spengler synthesis,<sup>1</sup> by reduction of the corresponding isoquinolines,<sup>1</sup> or by modifications<sup>2</sup> of the Pomeranz–Fritsch reactions. The range of substituted tetrahydroisoquinolines that can be produced is limited in all three syntheses. We now report a simple synthesis of 1,2,3,4-tetrahydroquinoline and which can be extended to relatively deactivated systems by the synthesis of the previously unreported 6-chloro-1,2,3,4-tetrahydroquinoline. The synthesis may also be valuable for the preparation of related alkaloids.

We first converted benzylamine (I) and *p*-chlorobenzylamine into the respective *N*-(2-bromoethyl)benzylamine hydrobromides by heating under reflux with 2-bromoethanol for 4 h at 50–60° and then treating the intermediate *N*-(2-hydroxyethyl)benzylamines with excess of hydrobromic acid. The unsubstituted compound (II) had m.p. 192–193° (from ethanol), lit.,<sup>3</sup> 190–191°, and the *p*-chloro-derivative had m.p. 210–211° (from methanol).

The hydrobromides were decomposed by reaction with

anhydrous AlCl<sub>3</sub> (3 mol. equiv.) in decalin at 145–155° for 1.5 h. Excess of AlCl<sub>3</sub> was decomposed by addition to ice and normal work-up procedures gave tetrahydroisoquinoline (III) (72%), b.p. 234–236° (picrate, m.p. 194°, lit.,<sup>4</sup> 195°;



hydrochloride, m.p. 195°, lit.<sup>4</sup> 195–197°) and 6-chloro-tetrahydroisoquinoline (60%), b.p. 100° at 5 mmHg (picrate, m.p. 191–192°; hydrochloride, m.p. 236–237°).

Good analytical data were obtained for all previously unreported compounds and i.r. and n.m.r. spectra were as expected.

(Received, April 15th, 1971; Com. 571.)

<sup>1</sup> See, e.g., W. M. Whaley and T. R. Govinclachari, *Org. Reactions*, 1951, **6**, 151; M. H. Palmer, "The Structure and Reactions of Heterocyclic Compounds," Arnold, London, 1967; W. J. Gensler in "Heterocyclic Compounds," ed. R. C. Elderfield, vol. 4, Wiley, New York, 1952.

<sup>2</sup> J. M. Bobbitt and S. Shibuya, *J. Org. Chem.*, 1970, **35**, 1181, and previous papers in the series.

<sup>3</sup> S. Gabriel and R. Stelzner, *Ber.*, 1896, 2383.

<sup>4</sup> Dictionary of Organic Compounds, Eyre and Spottiswoode, London, 4th edn., vol. 5.