

A Novel Synthesis of 4-Phenyl-1,2,3,4-tetrahydroisoquinoline

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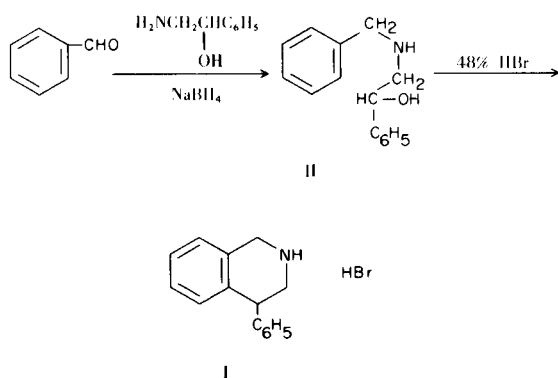
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This note reports a novel synthesis of 4-phenyl-1,2,3,4-tetrahydroisoquinoline hydrobromide (I) by ring closure of 2-benzylamino-1-phenylethanol (II) in refluxing 48% hydrobromic acid in 58% yield.

The structure of I is supported by elemental analysis as well as ir and nmr spectral evidence.

Since the starting carbinol II is easily derivable from β -hydroxyphenethylamine and benzaldehyde, this method offers a two-step method for the desired compound I, the hydrochloride of which has been previously prepared by another method (1).

The scope, limitations and mechanism of this type of ring closure are the subject of further investigation.



EXPERIMENTAL (2)

2-Benzylamino-1-phenylethanol (II).

A mixture of 63.6 g. (0.60 mole) of benzaldehyde, 82.2 g.

(0.60 mole) of β -hydroxyphenethylamine, and 500 ml. of methanol was stirred and refluxed for 1 hour, then cooled to 15-20° while sodium borohydride (17.1 g., 0.45 mole) was added over 45 minutes. The solvents were removed *in vacuo* and the residue was shaken with 400 ml. of water to give 111 g. (82%) of the product.

A portion of the free base upon treatment with methanolic hydrogen chloride gave the hydrochloride, m.p. 229-232°; lit. (3) m.p. 227°; infrared (Nujol) μ : 3.10 (O-H); 9.31 (C-OH).

Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{NO}\cdot\text{HCl}$: C, 68.30; H, 6.88; N, 5.31. Found: C, 68.36; H, 6.65; N, 5.33.

4-Phenyl-1,2,3,4-tetrahydroisoquinoline Hydrobromide (I).

A mixture of 66 g. (0.29 mole) of II and 600 ml. of 48% hydrobromic acid was stirred and refluxed for 3 hours, then cooled and stirred at 0-5° for an additional hour. The solid was filtered, air dried, and washed with ethyl acetate to give 49 g. (58%) of the product. Recrystallization from absolute ethanol gave the analytical sample, m.p. 223-225°; nmr (DMSO- d_6): δ 3.56 (m, 2, CH_2); 4.45 (m, 3, CH_2 , CH); 6.68, 7.25 (m, 9, aromatic C-H); infrared (Nujol) μ : 6.30 (C=C); no O-H absorption at 3.0-3.1.

Anal. Calcd. for $\text{C}_{15}\text{H}_{15}\text{N}\cdot\text{HBr}$: C, 62.06; H, 5.56; N, 4.83. Found: C, 61.72; H, 5.52; N, 4.79.

REFERENCES

- (1) J. Gardent and M. Hamon, *Bull. Soc. Chim. France*, 556 (1966).
- (2) Melting points are uncorrected. The nuclear magnetic resonance spectrum was taken on a Varian A-60A instrument and was compared with TMS as an internal standard.
- (3) A. Dornow and H. Eicholtz, German Patent 942,512; *Chem. Abstr.*, 53, 292f (1959).