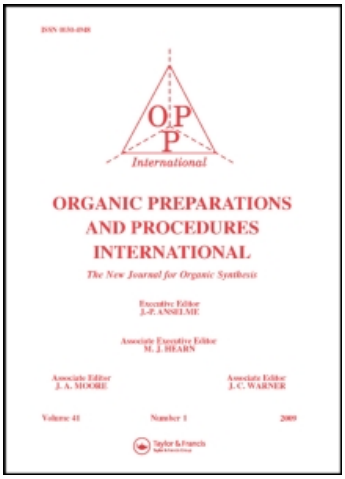

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CORYPALLINE

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CORYPALLINE

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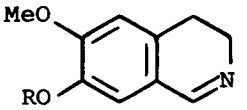
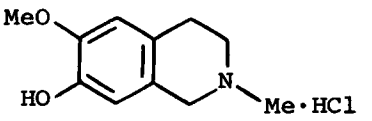


I, R = Me·HBr
II, R = H
III, R = H·MeI



IV

The known alkaloid corypalline (IV)[1,2] can be conveniently prepared from 6,7-dimethoxy-3,4-dihydroisoquinoline (I)[3]. Treatment of I with aqueous 48% HBr gives the monophenol II. Catalytic hydrogenation of its quaternary methiodide III affords directly the alkaloid as its hydrochloride IV in good overall yield.

This procedure is another example of the utilization of the partial O-demethylation of 6,7-dimethoxy-substituted 3,4-dihydroisoquinolines[4] in the synthesis of phenolic tetrahydroisoquinoline alkaloids.[5]

EXPERIMENTAL

A solution of 30 g (0.11 mole) of 6,7-dimethoxy-3,4-dihydroisoquinoline hydrobromide[3] (I) in 160 ml of 48% HBr

is stirred at 95° for 6 hr and evaporated under reduced pressure. The residue is dissolved in 100 ml of H_2O, adjusted to pH 10 with 50 ml of NH_4OH and stored at 4° overnight. The crystals are filtered, dried and recrystallized from 50 ml of MeOH to give 8.9 g (63% based on 20.8 g of I) of 7-hydroxy-6-methoxy-3,4-dihydroisoquinoline (II), mp 189-190° (lit.[4] mp 189-190°). The aqueous and methanolic mother liquors are combined, concentrated to 100 ml, adjusted to pH 13 with NaOH and extracted with CH_2Cl_2 (3 x 100 ml). The extracts are evaporated, the residual oil dissolved in ethanolic HBr, evaporated and crystallized from 50 ml of ethanol to give 9.2 g of I.

A mixture of 8.9 g (0.5 mole) of II and 18 ml of MeI in 500 ml of MeOH is stored at 25° for 17 hr, concentrated to 300 ml, diluted with 240 ml of Et_2O and stored overnight at 4°. The crystals are filtered, washed with Et_2O and dried to give 15.1 g (97%) of 7-hydroxy-6-methoxy-2-methyl-3,4-dihydroisoquinolinium iodide (III), mp 216-218° (lit.[6] mp 218°).

A solution of 15.1 g (0.475 mole) of III in 600 ml of MeOH is hydrogenated in the presence of 2 g of PtO_2 at 50 psi and 25° until the hydrogen uptake ceases. The catalyst is filtered, the filtrate neutralized with $NaHCO_3$, evaporated, the residual solids dried and extracted with Me_2CO. The extract is acidified with ethanolic HCl,

evaporated and crystallized from 100 ml of EtOH to give 9.8 g (90%) of corypalline hydrochloride (IV), mp 203-204°, identical in mmp and spectral properties with a sample prepared by another route.[2]

REFERENCES

1. J. M. Bobbitt, D. N. Roy, A. Marchand, and C. W. Allen, J. Org. Chem., 32, 2225 (1967).

2. M. Tomita and H. Watanabe, J. Pharm. Soc. Japan, 58 783 (1938).

3. E. Späth and N. Polgar, Monatsh. Chem., 51, 190 (1929).

4. H. Bruderer and A. Brossi, Helv. Chim. Acta, 48, 1945 (1965).

5. For its application in the total synthesis of the alkaloid cherylline, see A. Brossi and S. Teitel, Tetrahedron Letters, 417 (1970); idem, J. Org. Chem. 35, 0000 (1970).

6. S. Akabori, Bull. Chem. Soc. Japan, 1, 125 (1926).

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