Studies on the Synthesis of Isocarbostyril Derivatives

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Reduction of homophthalimide derivatives (3a, 3b, 3c, 3d and 3e) with $NaBH_4$ gave 3,4-dihydro-3-hydroxyisocarbostyril derivatives (4a, 4b, 4c, 4d and 4e) which were converted to isocarbostyril derivatives (5a, 5b, 5c, 5d and 5e) by hydrochloric acid in ethanol.

4c and 5c were converted into 2,3-dimethoxy-8-oxoprotoberberine (8) by conc. hydrochloric acid.

Hydrogenation of 5c on 10% Pd-C gave the amide (9). Bischler-Napieralski reaction of 9 followed by reduction with $NaBH_4$ gave the 5,6,8,9-tetrahydro-2,3-dimethoxy-13bH-dibenzo[a,h]quinolizine (10).

Also reduction of 4-substituted homophthalimide (16) with $NaBH_4$ gave 3,4-dihydro-3-hydroxyisocarbostyril derivative, which was converted to 4-substituted isocarbostyril (17) with 10% hydrochloric acid.

17 was reduced with lithium aluminum hydride to give the 1,2-dihydro-4-substituted isoquinoline, which was heated with conc. hydrochloric acid to give cis-4b,5,6,10b,11,12-hexahydro-2,3-dimethoxy-5-methylbenzo[c]phenanthridine (18) and the demethylated benzo[c]phenanthridine (19 or 20).