

Studies on the Synthesis of Isocarbostyryl Derivatives

Hideo Iida and Toyohiko Kikuchi

Tokyo College of Pharmacy

1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan

Reduction of homophthalimide derivatives (3a, 3b, 3c, 3d and 3e) with NaBH_4 gave 3,4-dihydro-3-hydroxyisocarbostyryl derivatives (4a, 4b, 4c, 4d and 4e) which were converted to isocarbostyryl 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-hydroxyisocarbostyryl derivative, which was converted to 4-substituted isocarbostyryl (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).