A PRACTICAL SYNTHESIS OF 4-ARYL-1,2,3,4-TETRAHYDROISOQUINOLINES.

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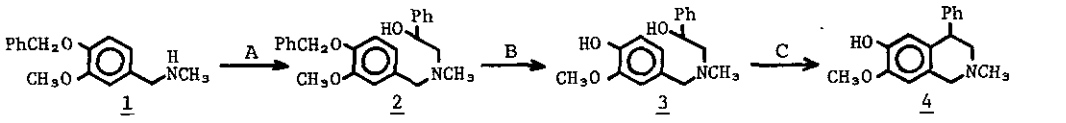
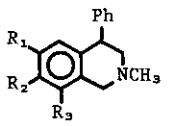
The title compounds were readily synthesized by using a styrene oxide as a synthon. Namely, reaction of benzylamine (1) and styrene oxide at 140° gave β-hydroxyphenethylamine (2) regioselectively. Debenzylation of 2 yielded 3, which was treated with 80% H_2SO_4 to effect cyclization giving 4-phenyl-1,2,3,4-tetrahydroisoquinoline (4) in 87% overall yield from O-benzylvanilline. Similarly, other 4-phenyl isomers (5 and 6) were easily prepared. However, styrene oxides having an electron donating group at the para position reacted with benzylamines to afford non-regioselectively two aminoalcohols. This problem was solved by the following method. Treatment of styrene oxide (7) with $BF_3 \cdot Et_2O$ in methanol gave solely β-methoxyphenethylalcohol (8), which was easily converted into its mesylate (9). Coupling of 9 and benzylamine (10) in the presense of Hünig base at 120° for 24 hour gave β-methoxyphenethylamine (11), acid treatment of which afforded (±)-cherylline (12) in 82% overall yield from *O-benzylisovanillin*.



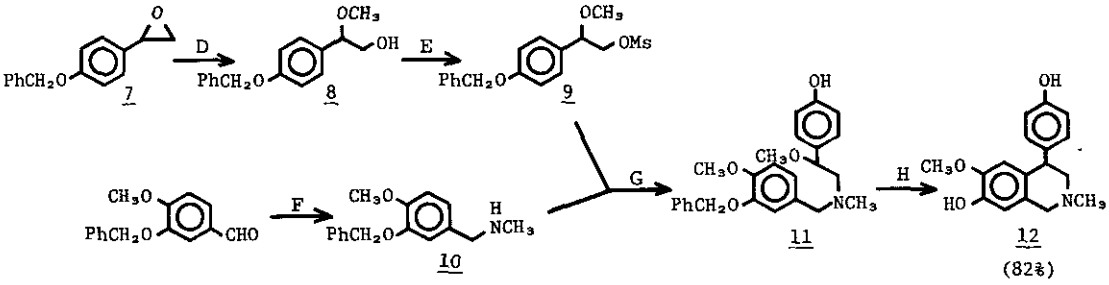
(87%) from O-benzylvanillin



5 R_1=OCH_3, R_2=OH, R_3=H (73%) from isovanillin

6 R_1=H, R_2=OCH_3, R_3=OH (90%) from O-benzylorthovanillin

A: styrene oxide, 140°,
B: c.HCl/benzene, reflux,
C: 80% H_2SO_4, r.t.,



(82%) from O-benzyl-isovanillin

D: $BF_3 \cdot Et_2O$, CH_3OH, 0°, E: CH_3SO_2Cl, pyridine, F: 1) 40% CH_3NH_2 aq., CH_3OH, 2) $NaBH_4$, CH_3OH, G: diisopropylethylamine, 120°, 24 hour, H: c.HCl/benzene, reflux,

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