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THE SYNTHESIS OF 1-(o-NITROBENZYL)-4-HYDROXY-6,7-METHYLENEDIOXY-1,2,3,4-TETRAHYDROISOQUINOLINE. A GENERAL SYNTHESIS OF 1-SUBSTITUTED-4-OXYGENATED-1,2,3,4-TETRAHYDROISOQUINOLINES

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The intense interest in synthetic approaches to 4-oxygenated-1,2,3,4-tetrahydroisoquinolines is evidenced by recent publications which have dealt with their formation.[1] We report here a general synthetic method, carried out on a specific compound, which does not require the use of strong acid (detrimental to the methylenedioxy function[2]) nor initial formation of an imine[3] which, for phenyl ketones, is often difficult.

Methylenedioxybenzene (I)[4], under carefully controlled Friedel-Craft conditions (CH_2Cl_2, $AlCl_3$, -35°) was permitted to react with the acid chloride of o-nitrophenylacetic acid (II) to generate the ketone (III)[5] which, although readily converted to the oxime (IV, R = H) in pyridine with hydroxylamine hydrochloride, failed to form any of the usual derivatives (e.g. imine, ketal, etc.) for which acid catalysis is necessary.

On acylation with acetic anhydride, the oxime yielded the corresponding acetate (IV, R = $COCH_3$) which was reduced to the amine V with diborane.[6]

This primary amine (V) was readily converted to the imine VII when it was permitted to react with diethoxyacetaldehyde (VI)[7] and reduction of VII with sodium borohydride in methanol afforded the base VIII as an oil.

Treatment of VIII with dilute hydrochloric acid[3], followed by removal of the solvent at low temperature yielded the amine hydrochloride IX which crystallized spontaneously.

Additional examples of 1-substituted-4-oxygenated-1,2,3,4-tetrahydroisoquinolines which can be prepared by this method will be reported in the full paper.

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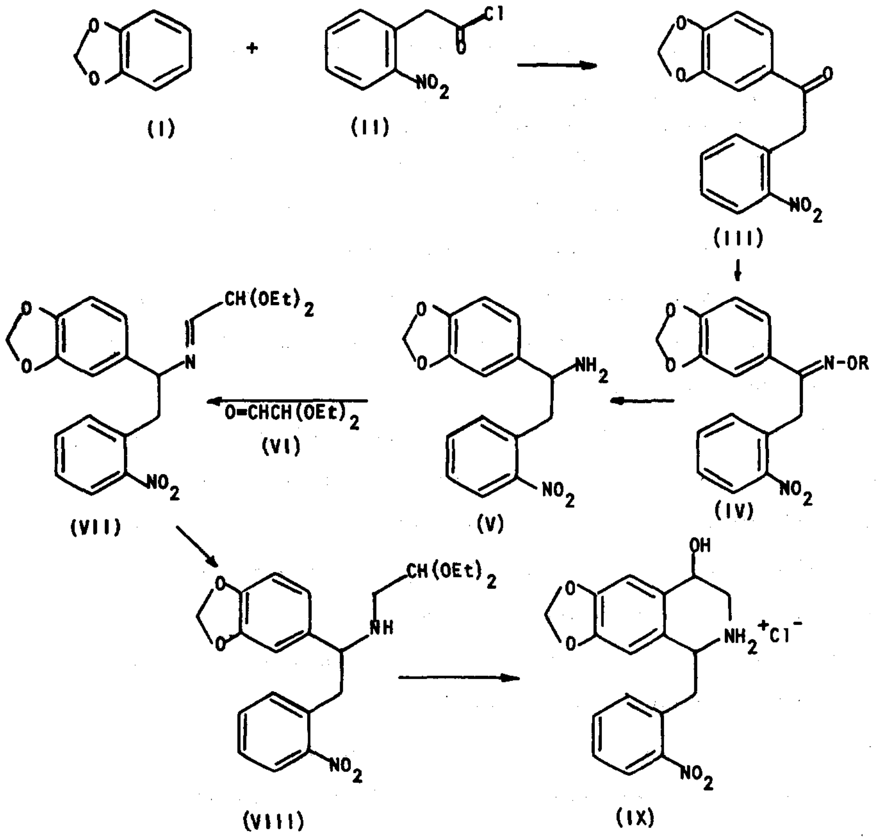

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