CCLXXIX.—*Experiments on the Synthesis of* iso*Quinoline Derivatives. Part I.*

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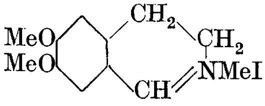
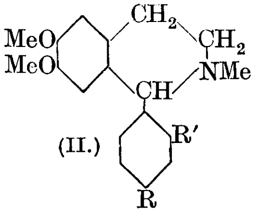
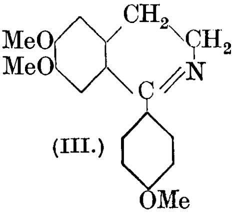
6 : 7-Dimethoxy-3 : 4-dihydro*iso*quinoline methiodide (I) condenses easily with resorcinol in presence of alkali to give a condensation *product* (II; R = R′ = OH), probably analogous to the compound of uncertain constitution obtained by Liebermann (*Ber.*, 1904, **37**, 2744) from cotarnine. Similarly, phloroglucinol and other phenols give related products. Cotarnine and also (I) condense with anisole in boiling toluene in presence of sodium ethoxide to give products such as (II; R = OMe, R′ = H). It seemed of interest to compare the properties of these products with those of 1-aryl-2-methyltetrahydro*iso*quinolines synthesised by unambiguous methods so that their constitutions might be placed beyond doubt.



(I.)



(II.)



(III.)

The benzoyl, cinnamoyl, and dimethoxyphenylacetyl derivatives of β-3 : 4-dimethoxyphenylethylamine have already been converted into the corresponding *iso*quinolines (E.P. 191233), and Späth and Böhm (*Ber.*, 1922, **55**, 2985) have prepared the *iso*quinoline from the trimethoxyphenylacetyl derivative. The *anisoyl* derivative has now been dehydrated in toluene solution with phosphoryl chloride, giving the *dihydro*iso*quinoline* (III). The *methiodide* of this substance when reduced with aluminium amalgam in aqueous-alcoholic solution gives the *tetrahydro-base* (II; R = OMe, R′ = H). This substance is identical with the condensation product isolated in minute amount from (I) and anisole, and should be identical with the methyl ether of dauricine if the structure assigned to the latter by Kondo and Marita (*Ber.*, 1930, **63**, 2420) is correct. We are engaged in synthesising the substance (II; R = R′ = OH) from resorcylic acid by a similar method.

Experimental.

Condensation of 6 : 7-*Dimethoxy*-3 : 4-*dihydro*iso*quinoline Methiodide and Resorcinol.*—A solution of the methiodide (3·3 g.) in absolute alcohol (5 c.c.) containing potassium hydroxide (0·56 g.) was warmed with resorcinol (1·1 g.) on the steam-bath for 15 minutes and left for 48 hours. The *product* (II; R = R′ = OH), which separated slowly, was recrystallised from hot dilute alcohol; m. p. 188° (Found : N, 4·3. $C_{18}H_{21}O_4N$ requires N, 4·4%); more was obtained on dilution of the mother-liquor.

Condensation of Cotarnine with Anisole.—A solution of cotarnine (4·7 g.) and anisole (2·2 g.) in toluene was treated with sodium ethoxide (from 0·5 g. of sodium), heated on the steam-bath for 1 hour, and boiled for ¼ hour. The solvent was distilled off in a vacuum, and the residue triturated with cold alcohol and crystallised from hot 80% alcohol; m. p. 137° (decomp.). The amount was not sufficient for analysis.

Anis-β-3 : 4-*dimethoxyphenylethylamide* was prepared from anisoyl chloride (8·5 g.) in benzene (35 c.c.) and a solution of 3 : 4-dimethoxyphenylethylamine (8·5 g.) in benzene (35 c.c.) and pyridine (3·5 c.c.); after 1 hour, the mixture was warmed on the steam-bath for ¼ hour. The product was washed successively with water, sodium carbonate solution, and dilute hydrochloric acid, freed from benzene, and crystallised from hot benzene (yield, quantitative); m. p. 126° (Found : N, 4·7. $C_{18}H_{21}O_4N$ requires N, 4·4%).

6 : 7 : 4′-*Trimethoxy*-1-*phenyl*-3 : 4-*dihydro*iso*quinoline* (III).—The above amide (3 g.; 1 mol.), dissolved in dry toluene (70 c.c.), was treated with phosphoryl chloride (1·5 mols.) with vigorous shaking, warmed on the steam-bath for ¼ hour, and then gently boiled for ½ hour. The cooled mixture was shaken with ice-cold dilute hydrochloric acid. The acid layer on basification gave the *dihydro*iso*quinoline* (III), which crystallised from very dilute alcohol in colourless needles, m. p. 107° (yield, 65% of the theoretical) (Found : N, 4·8. $C_{18}H_{19}O_3N$ requires N, 4·7%).

The *methiodide* was prepared from the *iso*quinoline and methyl iodide in benzene solution and crystallised in bright yellow prisms, m. p. 194—195° after recrystallisation from methyl alcohol by slow evaporation (yield, quantitative) (Found : I, 28·3. $C_{19}H_{22}O_3NI$ requires I, 28·9%).

6 : 7 : 4′-*Trimethoxy*-1-*phenyl*-2-*methyltetrahydro*iso*quinoline* (II; R = OMe, R′ = H).—The foregoing methiodide (1 g.), dissolved in methyl alcohol (10 c.c.), was diluted with water until a slight turbidity appeared. Amalgam prepared from aluminium (0·5 g.) was then introduced and the solution boiled for ½ hour; after addition of a drop or two of concentrated hydrochloric acid the mixture was heated on the steam-bath for ½ hour. The filtered solution was diluted and basified with sodium hydroxide, and the *product* crystallised twice from dilute methyl alcohol, forming

colourless needles, m. p. 96—97° (yield, quantitative) (Found : N, 4·7. $C_{19}H_{23}O_3N$ requires N, 4·5%). The base is stable to hydrochloric acid and acetic acid.

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