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CONVERSION OF INDONES TO QUINOLINE AND ISOQUINOLINE DERIVATIVES

III.- SCHMIDT REACTION WITH 2,3-DIPHENYLINDONE AND SIMILAR COMPOUNDS

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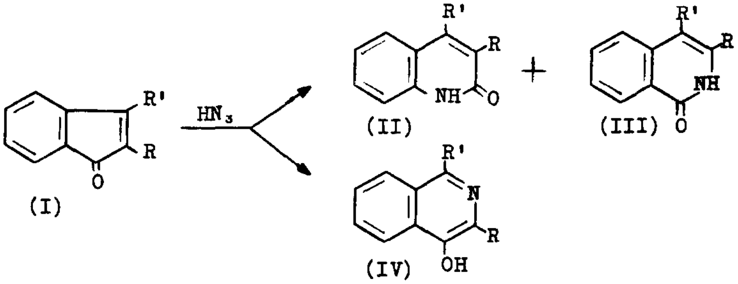
PREVIOUS work [1,2] has shown that indone derivatives (I) behave normally in the Schmidt reaction: when R is an alkyl, CN, CONH$_2$ or CO$_2$C$_2$H$_5$ and R' a phenyl group, carbostyrils (II) and isocarbostyrils (III) are formed, their relative amounts depending upon the bulk of R. When R is CONH$_2$ or CO$_2$C$_2$H$_5$ (R' = phenyl), if the reaction medium is not strongly acidic, an abnormal reaction takes place [2], 1-phenyl-4-hydroxyisoquinoline derivatives (IV) being obtained:



In the present work the reaction of 2,3-diphenylindone, 3-methyl-2-phenylindone and 3-ethyl-2-phenylindone with hydrazoic acid in acetic-sulphuric acid solution was investigated.

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[1] **.- A.Marsili, Ann.Chim.(Rome) 52, 3 (1962).**

[2] **.- A.Marsili and P.Ricci, Ann.Chim.(Rome) 52, 112 (1962).**

From 2,3-diphenylindone two neutral products, 3,4-diphenylcarbostyril (V, m.p.310-311°C) and 3,4-diphenylisocarbostyril (VI, m.p.250-252°C), and two bases (B_1 and B_2) were obtained.

B_1 precipitated as the sulphate, together with the two neutral compounds, when the reaction mixture was diluted with water. Treatment of this sulphate with ammonia generated the free base, $C_{21}H_{14}N_2$ (light yellow prisms from benzene, m.p.235-236°C).

B_2, $C_{21}H_{16}N_2O$ (needles from methanol, m.p.235-237°C), was obtained after neutralisation of the mother liquor from which the three previous products had separated.

The structure of 3,4-diphenylcarbostyril was determined by direct synthesis from 2-(phenylacetamido)benzophenone (IX).

3,4-Diphenylisocarbostyril is a known substance [3].

The I.R. spectrum of B_1 shows a weak NH stretching band (3.3 μ) and a strong band at 6.18 μ (conjugated C=N or C=C); it is very stable to heat, moderately concentrated acids (deep yellow, water-insoluble salts are formed) and bases; it brominates easily (aromatic monosubstitution).

Its structure was determined by direct synthesis: 3-benzamido-2-phenylindole (X) gave with P_2O_5 in boiling nitrobenzene 5-phenyl-11<u>H</u>-indolo[3,2-c]isoquinoline (VIII), identical with B_1. Its nuclear magnetic resonance spectrum was also consistent with this structure.

The I.R. spectrum of B_2 shows strong NH (2.91; 3.00; 3.11 μ) and amide CO (6.08 μ) stretching bands. The compound gave easily a dibenzoate [NH (3.00 μ), ester (5.73 μ) and amide (5.98 μ) CO stretching in its I.R. spectrum], and yielded *o*-benzoylbenzoic acid with $KMnO_4$ in alkaline solution. Very probably, therefore B_2 is

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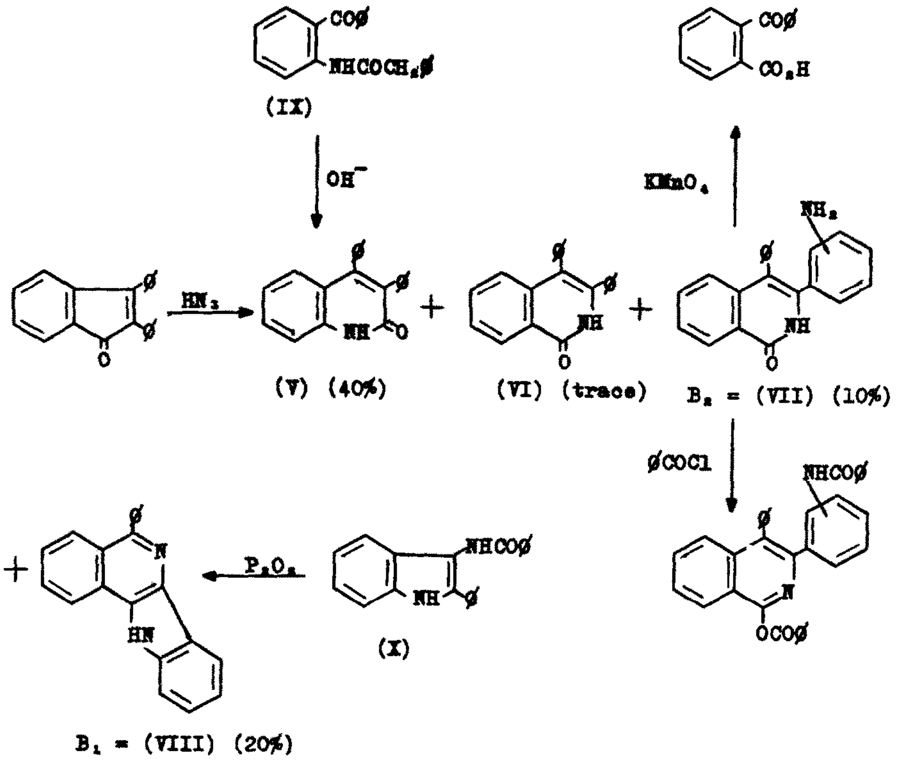
[3] G.Berti and P.Corti, *Gazz.Chim.Ital.* **88**, 704 (1958).

3-[2-(or 4-)aminophenyl]-4-phenylisocarbostyril (VII). The U.V. spectrum of B_2 (λ_{max} 295 mμ, logε 4.09; shoulder at 318 mμ, logε 3.94) is very similar to that of 3,4-diphenylisocarbostyril [4].

The reaction of 2,3-diphenylindone with hydrazoic acid, and the synthesis of some of the reaction products may be so outlined:



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[4] G.Berti and P.Corti, Ann.Chim.(Rome) 49, 2110 (1959).

From the Schmidt reaction with 3-methyl-2-phenylindone and 3-ethyl-2-phenylindone basic products were easily isolated, whose structures were analogous to that of B_1: respectively 5-methyl- and 5-ethyl-11H-indolo[3,2-c]isoquinoline. The I.R. spectra and properties of these substances (for instance, yellow salts and deep violet-blue fluorescence in ethanolic solution) were very similar to those of B_1. The structure of the methyl derivative was also established by comparison with an aunthentic sample, prepared according to Mann [5].

Several points in the reaction described above appear unusual: thus, the formation of relatively large amounts of 3,4-diphenylcarbostyril from 2,3-diphenylindone does not agree with the Smith rule of steric hindrance [6]. The formation of 11H-indolo[3,2-c] isoquinoline derivatives, which involves reaction of a very hindered double bond with hydrazoic acid and aromatic amination, appears quite abnormal. Possibly the same intermediate could be responsible for the formation of B_1 and B_2.

Full experimental details and a discussion on the mechanism of the reactions will be given in a further paper.

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5.- Huang-Hsinmin and F.G.Mann, J.Chem.Soc. 2911 (1949).

6.- P.A.S.Smith, J.Amer.Chem.Soc. 70, 320 (1948); P;A.S.Smith and B.Ashby, Ibid. 72, 2503 (1950); P.A.S.Smith and J.P.Horwitz, Ibid. 72, 3718 (1950).