

SOME NOVEL REARRANGEMENTS
OF 2-BENZYL-3-(α -BROMOBENZYLIDENE)PHthalIMIDINE

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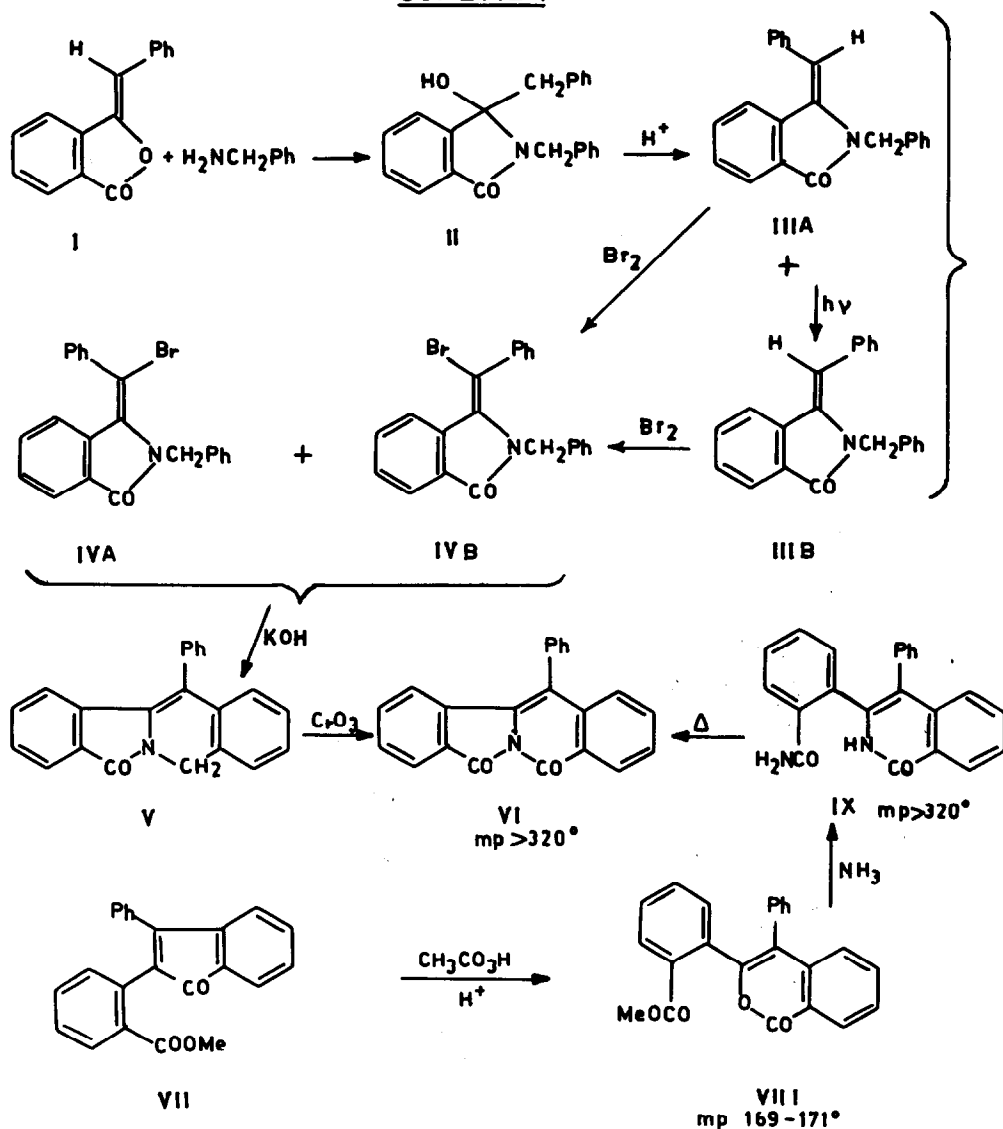
In the course of attempts to devise a new synthetic method of isoquinoline derivatives we reacted trans-3-benzylidenephthalide (I) with various amines, following Gabriel's method¹. We wish to report here the unusual results obtained when the product originating in the reaction between I and benzylamine was submitted to further transformations.

The 3-hydroxyphthalimidine structure II was assigned to the addition product, m.p. 168-170°, on the basis of IR [CDCl₃ solution: λ_{CO} 5.92 μ , λ_{OH} 2.80 (sharp) and 3.01 μ (broad, disappearing on dilution)], UV (λ_{max}^{EtOH} 252 m μ , log ϵ 3.66) and NMR spectrum [C(OH)CH₂Ph, AB quartet at δ 3.05 (ppm, relative to TMS, solvent CDCl₃), Δ_{AB} 35.4 cps, J 14 cps; NCH₂Ph, AB quartet at δ 4.50, Δ_{AB} 8 cps, J 15 cps; OH, δ 3.92].

Product II was dehydrated by treatment with dilute HCl-EtOH to afford a mixture containing 90% IIIA, m.p. 123-125°; λ_{CO} 5.82 μ^2 ; λ_{max} 268, 326 m μ , log ϵ 4.00, 4.13; δ 6.42 (1H, s), 5.08 (2H, s), and 10% IIIB, m.p. 123-125°; λ_{CO} 5.86 μ ; λ_{max} 270, 324 m μ , log ϵ 4.04, 4.18; δ 6.65 (1H, s), 4.90 (2H, s). The second isomer was obtained in almost quantitative yield by sunlight irradiation of IIIA in methanol or benzene solution.

Bromination of IIIA (or IIIB) caused conversion into a mixture of the two isomeric bromo derivatives IVA, m.p. 150-152°; λ_{CO} 5.82 μ ; λ_{max} 268, 320 m μ , log ϵ 4.00, 4.09; δ 5.61 (2H, s), and IVB, m.p. 128-130°; λ_{CO} 5.89 μ ; λ_{max} 268, 330 m μ , log ϵ 4.00, 4.12; δ 4.59 (2H, s). The mixture contained in both

SCHEME I



cases about 55% IVA and 45% IVB³.

When the pure isomers (or their mixture) were refluxed with KOH in ethylene glycol solution, a 70% yield of V, m.p. 262–264°; λ_{CO} 5.92 μ ; δ 5.16 (2H, s) was obtained. The structure of V was determined by oxidation to VI,

also independently prepared from 2-(*o*-carbomethoxyphenyl)-3-phenylindone (VII)⁴ by the route outlined in SCHEME I.

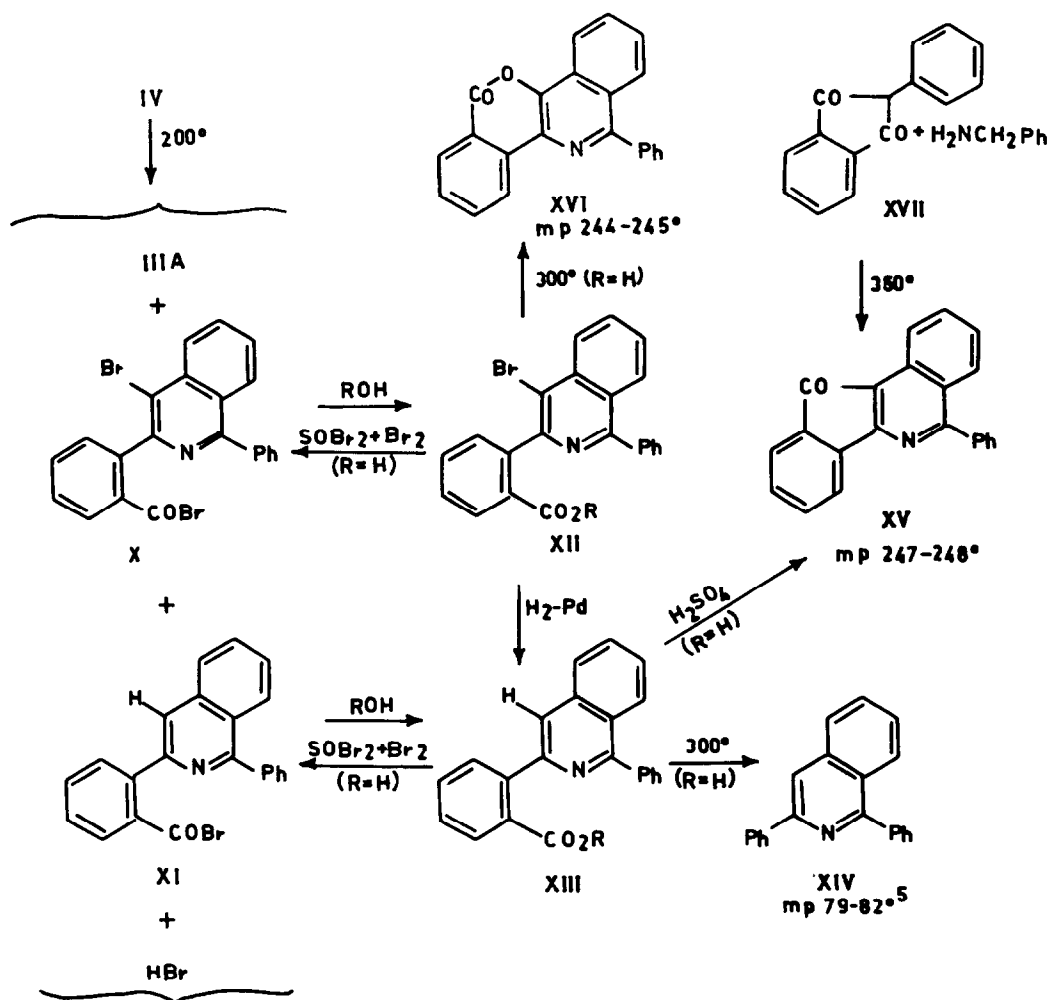
Heating of IVA or IVB (or their mixture) at 180-200°, was accompanied by evolution of some HBr and caused rapid conversion into a mixture containing IIIA (about 2/3 of the total weight) and the yellow acid bromides X and XI (λ_{CO} 5.50 μ); the latter compounds were easily separated from IIIA because of their low solubility in most solvents. It was found that, depending upon the heating time and the solvent used for removing IIIA, the acid bromides contained a variable amount of "active" bromine: indeed, when they were refluxed with acetone or cyclohexene, some bromoacetone or dibromocyclohexane were formed; furthermore, I₂ was liberated by treating these products with KI solution. The methyl esters XII (R = Me), m.p. 169-171°, and XIII (R = Me), m.p. 116-118° were obtained by treatment of the acid bromides with methanol; these derivatives proved to be suitable for the separation of the two components by fractional crystallization. The corresponding pure acids (XII, R = H, m.p. 225-226°, and XIII, R = H, m.p. 187-188°) were recovered from the methyl esters. These acids, on treatment with a mixture of bromine and thionyl bromide, were reconverted into the "active" bromine-containing acid bromides; the "active" bromine content of a sample obtained from XII (R = H) resulted very near to two atoms per molecule of product.

The structures of XII and XIII were determined as outlined in SCHEME II.

An ionic mechanism for the formation of V through extraction of a proton from the methylene group of IV, followed by an intramolecular displacement of bromine can be ruled out on several grounds. Compound V is formed (together with IIIA), even if in low yield, by long reflux of IV with ethylene glycol in the absence of base, and a higher yield is obtained in the presence of a weak base, such as acetate. Moreover, preliminary results have shown that optically active XXI is obtained when optically active XX is refluxed with 10% KOH-EtOH.

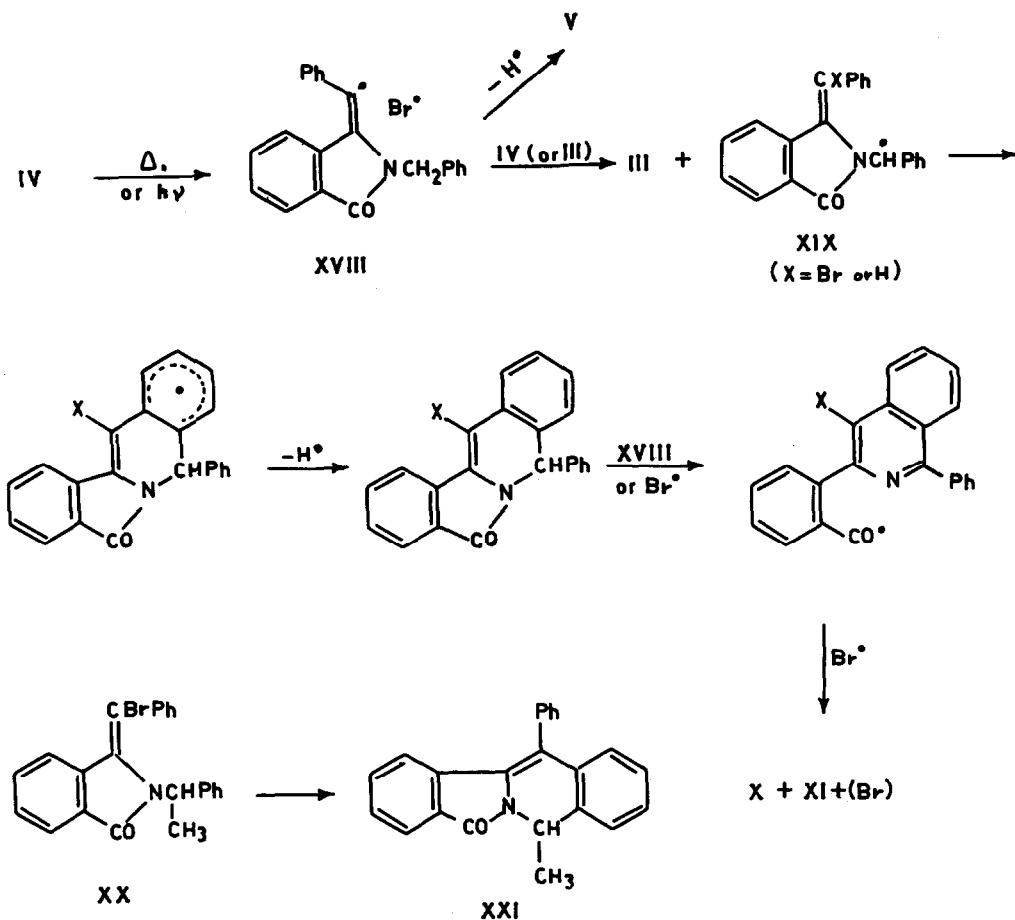
The transformation of IV into IIIA, X and XI (plus bromine) might follow from a primary formation of the radical XVIII (SCHEME III), originated by homolytic fission of the C-Br bond. The radical may then be converted, by a series of reactions (with IV and other successively formed chemical species, e.g. IIIA) into XIX, which reacts with bromine to afford the mixture X + XI (+Br). The radical XVIII could also be responsible for the formation of V, the only

SCHEME II



function of the base being neutralization of HBr as soon as formed. A good yield of V was obtained by sunlight irradiation of IV in methanol solution. Irradiation of IV in benzene solution afforded a low yield of X and XI containing "active" bromine.

SCHEME III



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REFERENCES AND FOOTNOTES

- (¹) S.Gabriel, Ber.dtsch.chem.Ges. 18,1251(1885).
- (²) All following IR spectra were registered on nujol mulls.
- (³) It was not possible to assign the configurations to the cis-trans couples III (A-B) and IV (A-B) on the basis of their UV spectra; this indicates non-coplanarity between the benzylidene phenyl group and the phthalimidine system in both isomers. Therefore, we tentatively based our assignments on the consideration that, very probably, in the B isomers the N-benzyl methylene protons are located in the shielding area of the benzylidene phenyl group, and the corresponding signal is found at higher field in the NMR spectrum. This assumption, while valid enough for IVB, appears somewhat ambiguous for IIIB, and further proofs will be necessary.
- (⁴) H.J.Loewenthal and R.Pappo, J.Chem.Soc. 4799 (1952).
- (⁵) W.Krabbe, K.-H.Schmidt and W.Eisenlohr, Ber.dtsch.chem.Ges. 74,1905(1941).