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REARRANGEMENTS OF PHTHALIMIDINE DERIVATIVES FORMATION OF A PYRROLE AND A BENZAZEPINE FROM 3-(α-BROMOBENZYLIDENE)-2-(β-PHENETHYL)PHTHALIMIDINE

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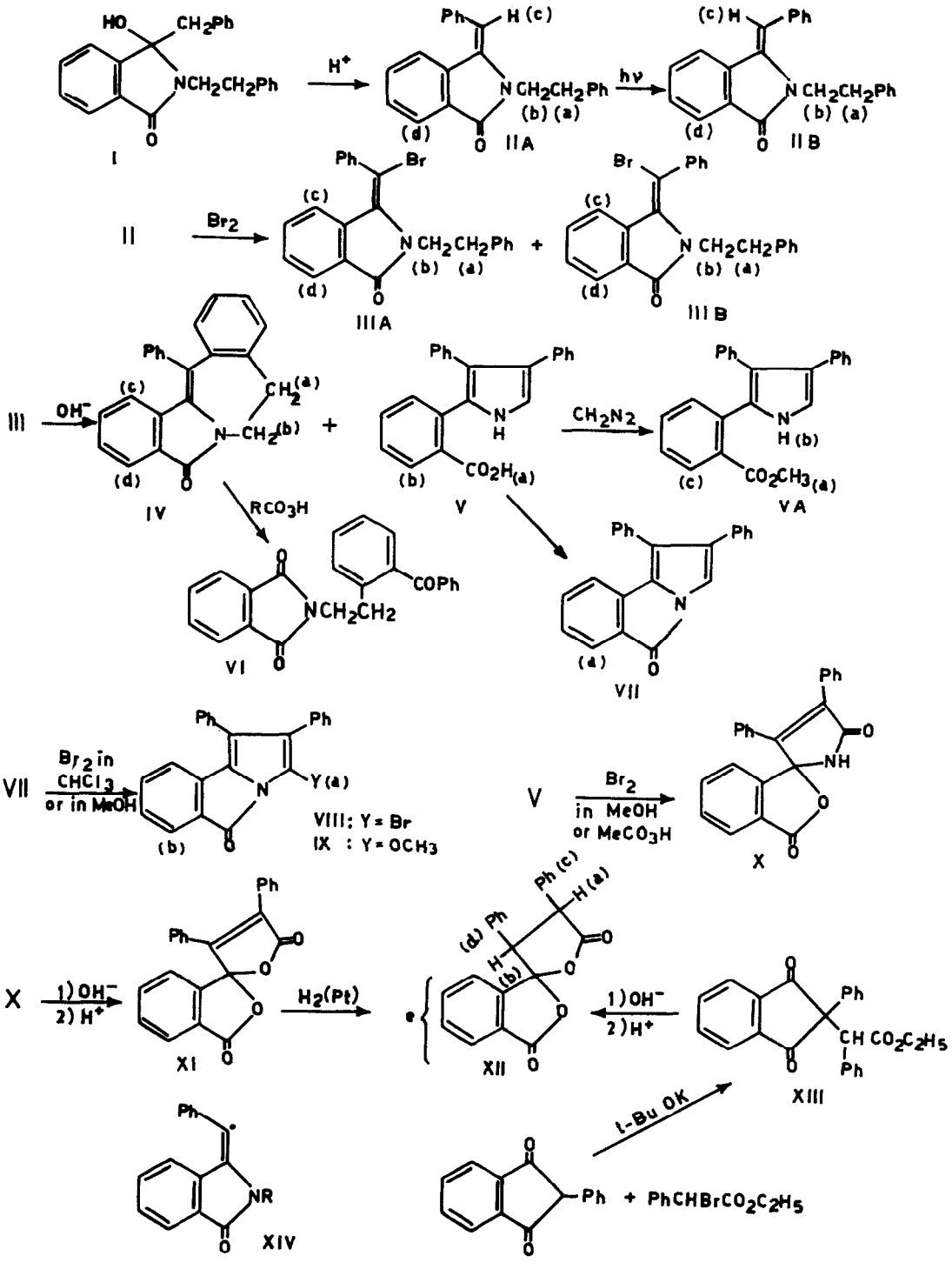
The conversion of 2-benzyl-3-(α-bromobenzylidene)phthalimidine into isoquinoline derivatives has been previously reported.[1,2]

This communication deals with the rearrangement of 3-(α-bromobenzylidene)-2-(β-phenethyl)phthalimidine (IIIA and B) under the action of alkali. The title compound was obtained as follows. Treatment of trans-3-benzylidenephthalide with β-phenethylamine gave 3-benzyl-3-hydroxy-2-(β-phenethyl)phthalimidine (I) which, under the action of strong acids, afforded IIA. This substance could be transformed into the geometrical isomer IIB by irradiation with sunlight. The action of bromine on IIA or IIB resulted in formation of an equilibrium mixture of IIIA and B (67 and 33%); the same mixture was obtained when either isomer was heated with a trace of bromine in chloroform solution. When IIIA and B were treated with KOH in boiling ethylene glycol, the two compounds IV and V were obtained in 10 and 34% yield, respectively. The structure of IV was deduced from its NMR spectrum and from peroxybenzoic acid oxidation to (o-benzoyl-β-phenethyl)phthalimide (VI). The pyrrole derivative V, which gave a positive Ehrlich reaction,[3] was transformed into the corresponding methyl ester by action of diazomethane, and into the pyrroloisoindole derivative VII by pyrolysis or by treatment with acetic anhydride. While compound V exchanged rapidly the carboxyl proton on treatment with D_2O, the rate of exchange of the NH proton in V and its methyl ester was very slow (about 50% after three days at room temperature). In the bromination of VII in chloroform or in methanol solutions were obtained, respectively, the bromo and the methoxy derivatives VIII and IX. Treatment of V with bromine in metha-

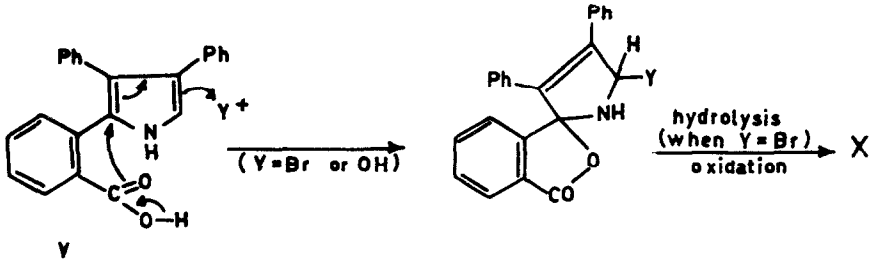

I
IIA
IIB
II
IIIA
IIIB
III
IV
V
VA
VI
VII
VIII: Y = Br
IX : Y = OCH3
X
XI
XII
XIII
XIV
PhCHBrCO2C2H5

PHYSICAL DATA OF COMPOUNDS

Compound	m.p.(°C)[a]	IR (μ, Nujol)	UV [λ (log ε), 95% Ethanol]	NMR (δ, ppm from TMS, $CDCl_3$)[b]
I	155-157	3.10, 5.92, 5.98	———	———
IIA	115-116	5.86	221(4.52), 268(4.00), 326(4.15)	a, 3.00; b, 4.05; c, 6.34(s); d, 7.75
IIB	117-119	5.89	222(4.53), 269(4.05), 324(4.15)	a, 2.41; b, 3.83; c, 6.71(s); d, 7.73
IIIA	135-136	5.86	220(4.54), 268(4.04), 328(4.12)	a, 3.11; b, 4.59; c, 6.01; d, 7.73
IIIB	116-117	5.89	224(4.50), 268(4.00), 332(4.13)	a, 2.50; b, 3.49; c, 8.79; d, 7.80
IV	203-205	5.90	292(3.87), 356(4.38)	a, 3.31; b, 4.20; c, 5.67; d, 7.73
V	238-240	2.97, 5.95	267(4.08)	a, 11.36; b, 8.03[c]
VA	164-166	2.98, 5.90	———	a, 3.63(s); b, 9.05; c, 7.60
VI	117-118	5.63, 5.89, 6.01	———	———
VII	162-163	5.61, 5.71, 5.77	240(4.47), 345(3.86), 271(4.45)	a, 7.56
VIII	229-231	5.72	———	b, 7.66
IX	226-228	5.77	———	a, 3.86(s); b, 7.53
X	251-252	3.10, 3.20, 5.63, 5.86	———	———
XI	162-163	5.59	———	———
XII	206-208	5.58	———	a and b, AB quartet, 4.46(J_{AB} 12.5 Hz, Δ_{AB} 27.2 Hz)
XIII	139-141	5.75, 5.81, 5.89	———	c or d, 7.06(s) and 7.24(s); e, 7.66

a) Satisfactory analyses were obtained for all compounds. b) Letters refer to individual protons (or groups of protons) indicated in the scheme, which appear as multiplets, when no indication in parenthesis is given. For cis-trans isomers, attribution were made by comparison with the 3-benzyl analogues, whose stereochemistry was proven chemically (A.Marsili and V.Scartoni, ref.2 and work to be published). c) DMSO, external TMS.

nol or with hydrogen peroxide in acetic acid, afforded the spirane X. The structure of this compound was confirmed by its transformation into XII, a product independently synthesized by Rădulescu's method,[4] as outlined in the Scheme. Compound X may be considered a derivative of maleimide, and maleimides had been obtained in the oxidative halogenation of pyrrole.[5] A fully concerted mechanism may well operate here for the conversion of V into X, as outlined below.



V

The results reported in this communication, though not excluding at all an ionic mechanism, are in fair agreement with the mechanism previously discussed,[1] in which the intervention of the radical XIV as an intermediate in the rearrangements of 3-(α-bromobenzylidene)phthalimidine derivatives was proposed.

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