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NOVEL SYNTHESIS OF AZAINDOLIZINES BY REACTION OF ISONITROSOFLAVANONE ESTERS WITH PYRIDINE BASES.

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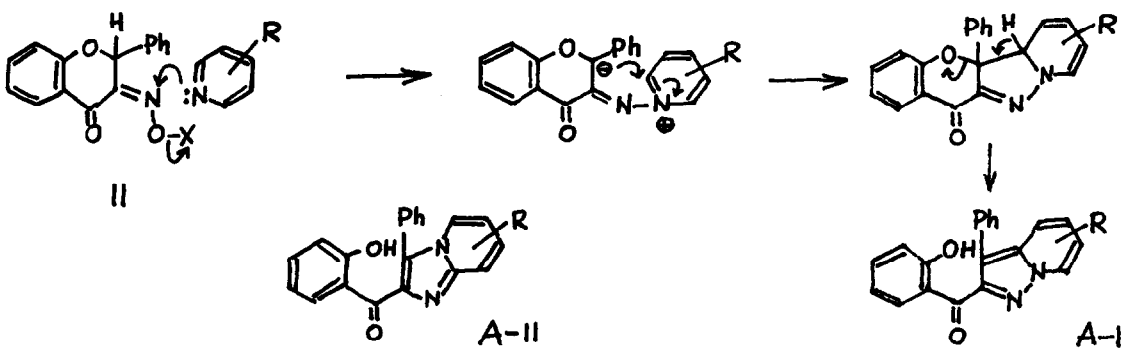
Investigations of the chemical transformations of isonitrosoflavanone[1] have been extended to the rearrangement of its esters in pyridine. The acetate (m.p. 120-3°), the tosylate and the diphenylphosphoryl ester (prepared in situ) (I, X = Ac, Ts, $P(O)(OPh)_2$)when heated with pyridine all gave the same, crystalline, orange-yellow compound (A), m. 150-1°. The yield of (A) varied from 30-85% depending on the ester used. Elemental analysis of compound (A) led to a molecular formula $C_{20}H_{14}O_2N_2$. The molecular weight of 314 was confirmed by mass spectrometry; this figure indicated that a molecule of pyridine had been incorporated into the isonitrosoflavanone at the expense of the esterifying acid anion. The product (A) gives a positive Fe^{III} reaction confirming that it contains a phenolic function. Tosylation of (A) gives the tosyl ester, m.p. 183-5°, identical with the compound obtained in the reaction of isonitroso-flavanone with 2 moles of TsCl and subsequent heating in the presence of pyridine. (A) forms crystalline salts (1:1) with both picric acid (m.p.219-20°) and hydrochloric acid (m.p.224-6°) indicating the presence of a single basic nitrogen atom and gives an oxime, m.p. 274-9°, MW 329.

The reaction most probably proceeds through the following steps :



Similar intramolecular cyclisation reaction leading to 3-azaindolizine and involving 2-(2-Quinolyl)cyclohexanone oxime under conditions of the Beckmann rearrangement has been described by Hamana et al.[2]. Alternative structure A-II containing the 1-azaindolizine ring system seems less probable.

The reaction described above seems to be general since it has been extended to β-picoline (giving B, m.p.138-9°; yield 60% based on isonitrosoflavanone), γ-picoline (giving C, m.p.108-9°; yield 60%), quinoline (giving D, m.p.144-5°; yield 20%) and isoquinoline (giving E, m.p.144-5°; yield 30%). No attempts have been made to maximise the yields. Satisfactory analytical data were obtained for all compounds cited above.

The n.m.r. spectra are more consistent with structure A-I. They show a certain regularity of proton chemical shifts of the free and protonated bases. The lowest-field signal, ascribed to H_α proton in the pyridine ring, is shifted on protonation to a higher field by ca. 0.25 p.p.m. (due to the disappearence of the paramagnetic anisotropy of the N-lone pair attacked by protons), whereas protons or methyl groups at the position β and γ show a distinct downfield shift.

The main peaks in the mass spectra of the series of azaindolizines synthesised in the present investigation correspond to mass fragments M-28, M-29 (characteristic of phenols), M-121 (cleavage at the carbonyl group) and to fragments derived from the usual fragmentation pattern of pyridine, picolines and quinoline, respectively. The spectra are sufficiently characteristic to serve for identification of these compounds.

Furtner investigations are in progress.

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