A New Synthesis of Azabenzoisocoumarins

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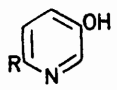
Summary 3-Hydroxypyridine (Ia) and its 6-methyl analogue (Ib) react with the benzyne precursor (IV) to give 1-azabenzoisocoumarins (IIa,b); the latter reaction also yielded 6,7-benzo-5-methyl-8-phenyl-8-azabicyclo[3,2,1]-oct-3-en-2-one (III) as a by-product.

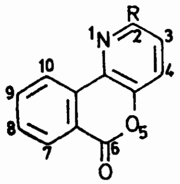
We now describe a synthesis of the novel 1-azabenzoisocoumarin ring system that may be of wide applicability in the preparation of coumarin derivatives (*cf.* ref. 1). 3-Hydroxypyridine (Ia) reacts with the benzyne precursor (IV) to produce 6-oxobenzopyrano[3,2-*b*]pyridine (IIa), m.p. 134—136°.† Similarly, 6-methyl-3-hydroxypyridine (Ib reacts to form the homologous 2-methyl-6-oxobenzopyrano [3,2-*b*]pyridine (IIb), m.p. 138—139°,† together with the cycloadduct (III), m.p. 128—129°, as a by-product expected by analogy with previous results.[2]

The n.m.r. spectra of the 1-azabenzoisocoumarins supported the structural assignments. For instance, 2-methyl-6-oxobenzopyrano[3,2-*b*]pyridine showed δ (CCl_4)‡ 8·76 (dq, 7-H, $J_{7,8}$ 8·00 Hz), 8·41 (dq, 10-H, $J_{7,10}$ 1·00, $J_{9,10}$ 7·75 Hz), 7·86 (td, 9-H, $J_{8,9}$ 7·50, $J_{7,9}$ 1·50 Hz), 7·70 (td, 8-H, $J_{8,10}$ 1·50 Hz), 7·58 (d, 4-H, $J_{3,4}$ 8·50 Hz), 7·30 (d, 3-H, $J_{3,4}$ 8·50 Hz), and 2·71 (s, $C\text{–}CH_3$). These assignments were supported by spin–spin decoupling and lanthanide shift studies.

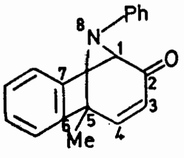
Intermediates of the type (Va) and (Vb) are probably involved and dehydrate under the reaction conditions to give the azabenzoisocoumarins (IIa,b). Benzyne[3] was prepared from anthranilic acid and n-pentyl nitrite. The benzyne precursor (IV) (or its equivalent)[4] has been previously postulated as an intermediate in the formation of benzocoumarin[5] during the pyrolysis of diphenyliodonium-2-carboxylate[5] and from potassium 2-halogenobenzoates.[6] In previously recorded cases,[7] where benzenediazonium-2-carboxylate was decomposed, there was no indication of the presence of (IV).



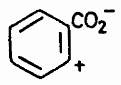
(Ia) R = H
(Ib) R = Me



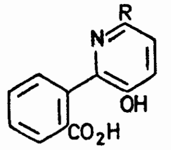
(IIa) R = H
(IIb) R = Me



(III)



(IV)



(Va) R = H
(Vb) R = Me

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† All compounds give satisfactory analyses for C, H. N and structures were elucidated by i.r., u.v., n.m.r., and mass spectroscopy.

‡ Measured at 100 MHz. Chemical shifts relative to Me_4Si.

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[4] R. W. Hoffmann, 'Dehydrobenzene and Cycloalkynes,' a Series of Monographs, ed. A. T. Blomquist, Academic Press, New York, 1967, p. 237.

[5] F. M. Beringer and S. J. Huang, *J. Org. Chem.*, 1964, **29**, 445.

[6] E. McNelis, *J. Org. Chem.*, 1963, **28**, 3188.

[7] Ref. 3, p. 238.