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N-AZIRIN-3-YL AND N-INDOL-3-YL AZAXYLYLENES

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Summary: Flash-vacuum pyrolysis of N-(2,3-diphenylazirin-3-yl)dihydrobenzoxazinones leads to transient N-azirinyl- and N-indolylazaxylylenes which give 2-arylindoles (5) and dihydroindoloquinolines (8) respectively. 5H-1,4-Benzodiazepines are implicated as the precursors to the indoles via the methylene nitrile ylides (9) and an alternative route to the latter by flash pyrolysis of N-(2-methylphenyl)benzimidoyl chlorides (10) provides a new, simple route to 2-arylindoles.

As part of our studies of azaxylylenes[1,2] we were interested in the N-azirinyl derivative (2) as a potential precursor to 5H-1,4- or 5H-1,3-benzodiazepines by $\pi 2 + \pi 2 + \sigma 2$ ring expansion. 5H-1,4-Benzodiazepines (3) are little known[3] and no examples of the 5H-1,3-isomers (4) have yet been reported.

The obvious precursor for azaxylylene (2) is the dihydrobenzoxazinone (1)[4a] which is readily obtained by treatment of the sodium salt of 1,4-dihydro-3,1-benzoxazin-2-one with chlorodiphenylazirine.[5] However, formation of azaxylylenes from dihydrobenzoxazinones requires flash-vacuum pyrolysis (FVP) at ca. 600°C[1] and under these conditions rearrangement of the phenylazirine substituent to an indole[6] might well lead to the N-indolylazaxylylene (7). This would also be of interest since direct routes to N-indolylazaxylylenes and their precursors are not feasible.

In the event FVP of dihydrobenzoxazinone (1; R = H) gives products derived from both azaxylylenes (2) and (7). Thus, at $600°/10^{-2}$ torr the yellow dihydroindoloquinoline (8; R = H) m.p. 194 - 5°C, was formed (25%) together with 2-phenylindole (5; R = H) (30%).[8] The dihydroindoloquinoline structure (8) was supported by spectral data, in particular NH and C=N stretching absorptions at 3145 and 1645 cm^{-1}., an AB pair of doublets, J = 15.5 Hz at δ 3.53 and 3.33 ppm corresponding to the C-12 methylene hydrogens and ^{13}C signals at δ 171.84, 37.69 and 63.58 ppm corresponding to carbons 6, 12 and 13 respectively. The analogous dihydroindoloquinoline[7] (8; R = Me), m.p. 184 - 5°C, and indole (5; R = Me) were obtained in 11% and 30% yields respectively from the dihydrobenzoxazinone (1; R = Me).[4b] Isolation of 5-methyl-2-phenylindole (5; R = Me) from this dihydrobenzoxazinone is especially significant since it shows that the 2-phenylindoles (5) are not simply derived from the azirine moiety in (1).

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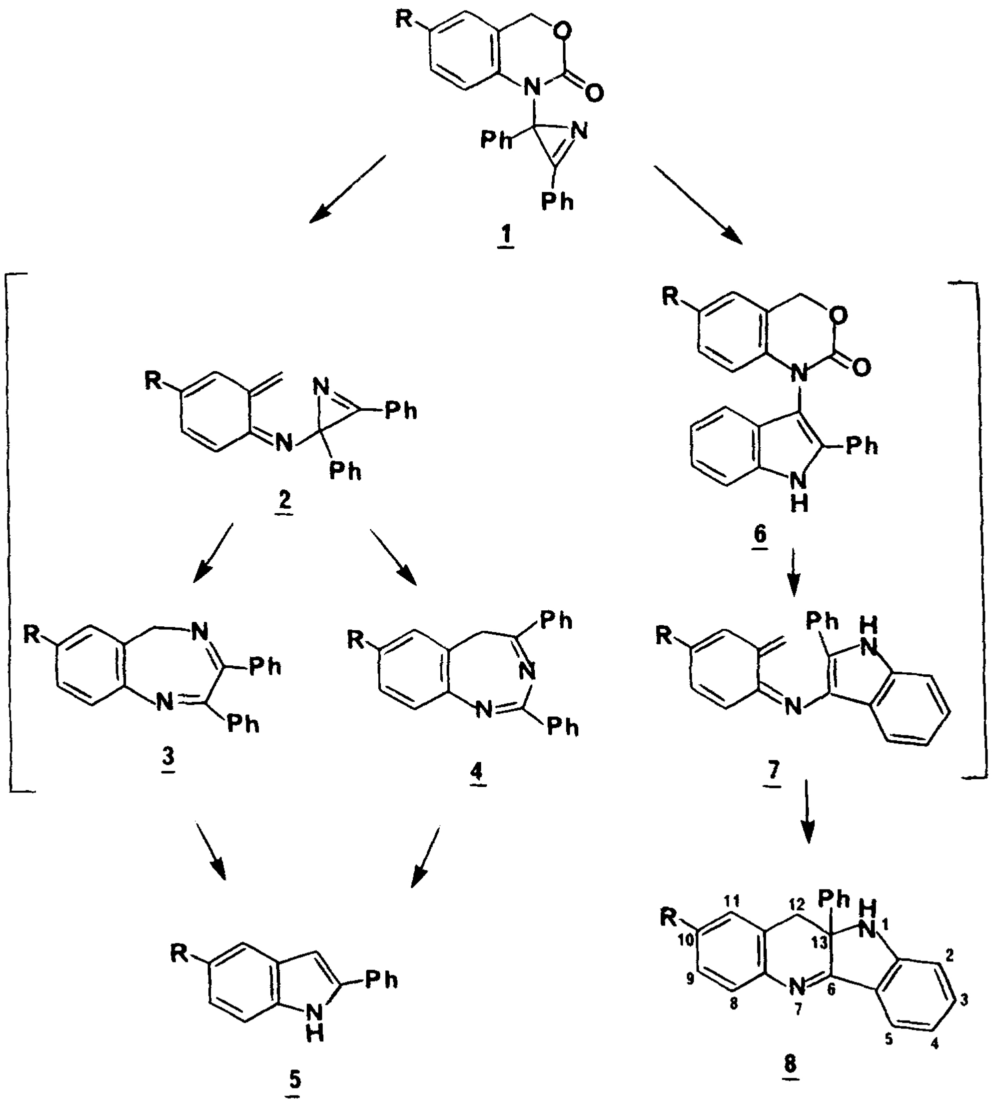
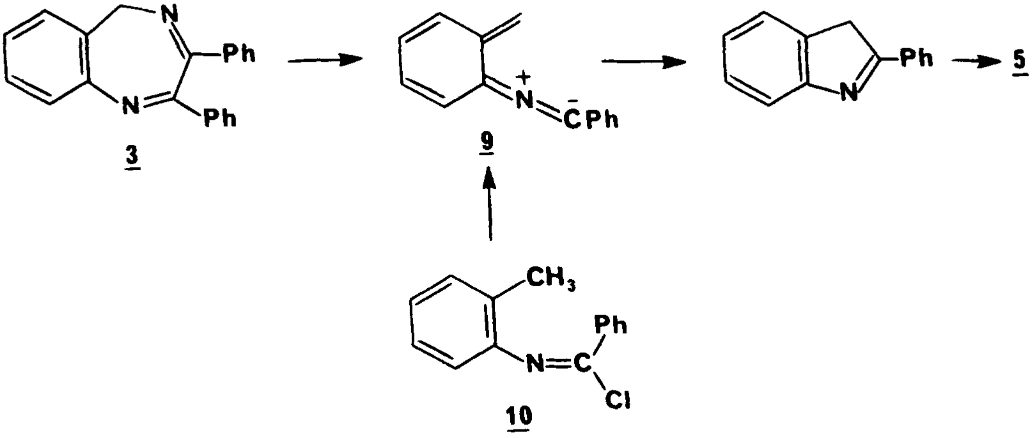


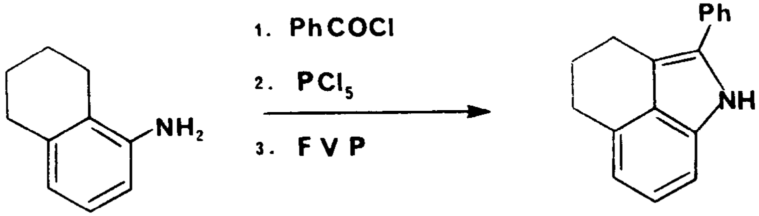
The dihydroindoloquinolines (8) are the result of electrocyclisation of the azaxylylenes (7) and their formation provides a further demonstration of the potential of azaxylylenes in the synthesis of fused heterocycles.[1,2] Attempts to detect the N-indolyldihydrobenzoxazinones (6) at lower pyrolysis temperatures failed; only starting material was recovered.

A reasonable mechanism for formation of indoles (5) involves ring expansion of the azaxylylenes (2) to either the 1,4- or 1,3-benzodiazepines (3) or (4) followed by cycloelimination of a molecule of nitrile and electrocyclisation of the resulting methylene nitrile ylide (9). At present we are unable to comment on the possible role of 1,3-benzodiazepines, but we have recently prepared both 2,3-diphenyl- and 2,3-dimethyl-5H-1,4-benzodiazepines (3) and (3; Me for Ph)[3], and these are indeed converted to 2-phenyl and 2-methylindoles in 63% and 57% yields respectively, under similar pyrolysis conditions. The 5H-1,4-benzodiazepines (3) are, therefore, feasible intermediates, although direct conversion of the azirinylazaxylylene (2) to the methylene nitrile ylide (9) and hence indole (5) is also possible.

Support for the proposed methylene nitrile ylide intermediate (9) in the benzodiazepine decomposition comes from the formation of 2-phenylindole in 76% yield in the FVP of the imidochloride (10). In this case 1,5-elimination of HCl would lead to the same intermediate which can be considered as an azadienyl carbene or a vinyl nitrile ylide.



This last reaction provides a new and very simple route to 2-arylindoles from 2-alkylanilines as illustrated by the conversion, in three steps, of 1-aminotetralin to the fused indole (11),[7] m.p. 118 - 9°C (74%), which has the important ergoline skeleton. Attempts to extend the reaction to give 2-alkylindoles led to complex mixtures possibly because 1,2-elimination in the imidochlorides (10; alkyl for Ph) can now compete.



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1. R.D.Bowen, D.E.Davies, C.W.G.Fishwick, T.O.Glasbey, S.J.Noyce and R.C.Storr, *Tetrahedron Lett.*, 1982, 4501.
2. C.W.G. Fishwick, R.C.Storr and P.W.Manley, *J.C.S.Chem.Commun.*, 1984, 1304.
3. K.R.Randles and R.C.Storr, *J.C.S.Chem.Commun.*, 1984, 1485.
4. (a) M.p. 167 - 8°C, $\nu_{max.}$ 1732 br (C=O, C=N) cm^{-1}., ^{13}C, δ 51.42 p.p.m. (azirine C-3), formed in 74% yield.
   (b) M.p. 138 - 9°C, $\nu_{max.}$ 1725 br (C=O, C=N) cm^{-1}., ^{13}C, δ 51.51 p.p.m. (azirine C-3), formed in 93% yield.
5. T.C.Gallagher and R.C.Storr, *Tetrahedron Lett.*, 1981, 2905.
6. For example, 3-phenylazirines are converted into indoles on pyrolysis : K.Isomura, S.Kobayashi and H.Taniguchi, *Tetrahedron Lett.*, 1968, 3499; J.H.Bowie and B. Nussey, *J.C.S. Perkin Trans 1*, 1973, 1693.
7. Satisfactory spectral, mass spectral and analytical data were obtained for all new compounds.
8. Physical properties of all the indoles were identical with those reported in the literature.

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