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# GENERATION AND REACTIONS OF AZAXYLYLENES

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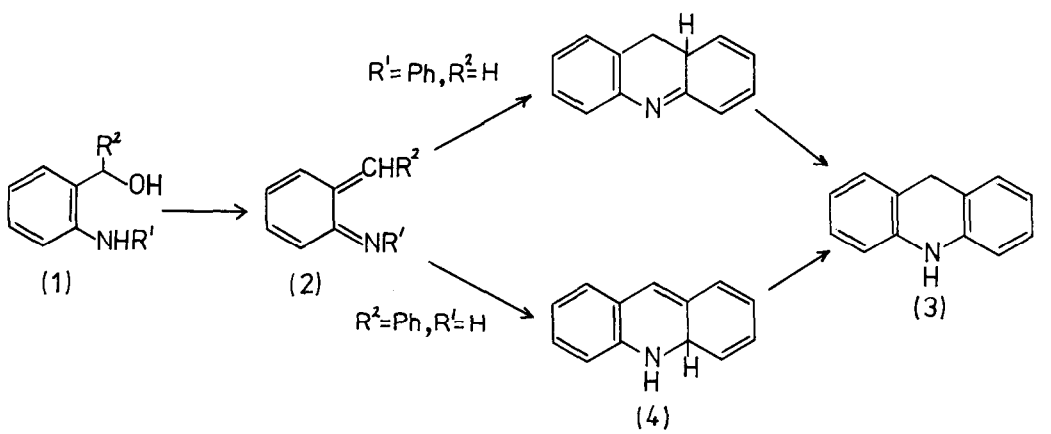
Summary: Azaxylylenes produced by flash vacuum pyrolysis of 2-aminobenzylalcohols, dihydrobenzoxazinones and dihydrobenzoxazines undergo intramolecular cyclisation, H-shifts or Diels-Alder reactions, depending on their substituents.

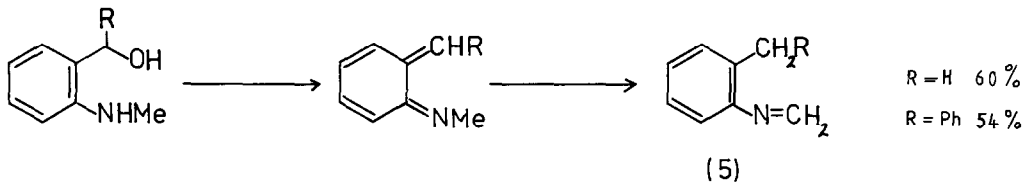
Recently o-xylylenes have found considerable use in organic synthesis.[1] In contrast, their nitrogen analogues, the azaxylylenes, have received little attention despite their obvious potential in heterocyclic chemistry.

In 1980, Boekelheide and Mao[2] reported the formation of acridine in the flash vacuum pyrolysis (FVP) of amino alcohol (1; $R^1$=Ph, $R^2$=H); this was rationalised in terms of formation of the azaxylylene (2; $R^1$=Ph, $R^2$=H) which underwent cyclisation and dehydrogenation. In parallel studies we have observed dihydroacridine (3) from both alcohol (1; $R^1$=Ph, $R^2$=H) and the isomeric benzhydrol (1; $R^1$=H, $R^2$=Ph). In the latter case FVP (650°C/$10^{-2}$ Torr) gave a red pyrolysate which was collected at -80°C. On warming to -20°C, the red colour was rapidly discharged and dihydroacridine and acridine were isolated on work up. Attempts to intercept (2; $R^1$=H, $R^2$=Ph) by nucleophiles or by Diels-Alder reaction with N-phenylmaleimide below -20°C failed; this suggests that the red species was more likely to be the non-aromatic dihydroacridine (4) than azaxylylene.

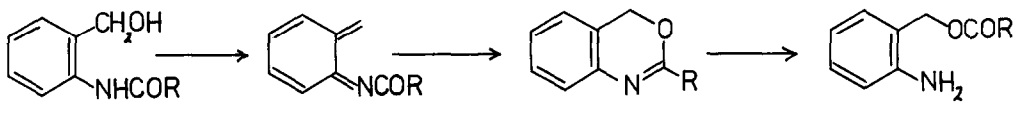



Dehydration of o-aminoalcohols (1) to give transient azaxylylenes on FVP is general, a temperature of 750°C normally being required. When $R^1$ is alkyl, 1,5-H shift in the azaxylylene occurs to give o-alkyl imines (5) which were isolated as their cyclic trimers. When $R^1$ is an unsaturated group, 6π electrocyclic ring closure occurs. Thus the amido-alcohols (6) give dihydrobenzoxazines (7) and the enaminones (9) give the vinylogous amides

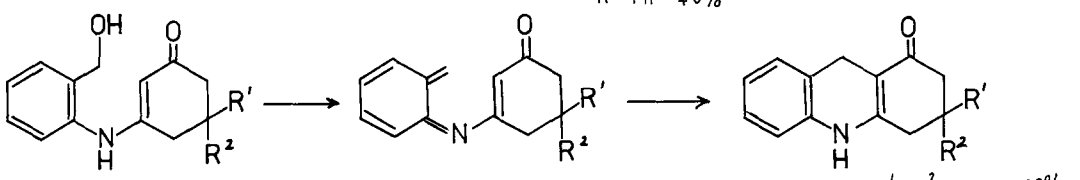
(10). In no case is 4π electrocyclisation to a benzazetidine (13) observed, although these compounds are known to be stable. The product from the amidoalcohol (6; R = Me) was confirmed as dihydrobenzoxazine rather than N-acetylbenzazetidine by hydrolysis. Under mild conditions (standing in chloroform open to the atmosphere) the aminoester (8) is formed as the kinetically controlled product which undergoes subsequent rearrangement to the amidoalcohol (6). Hydrolytic ring cleavage of N-acetylbenzazetidine would lead directly to the amidoalcohol (6).




(5)



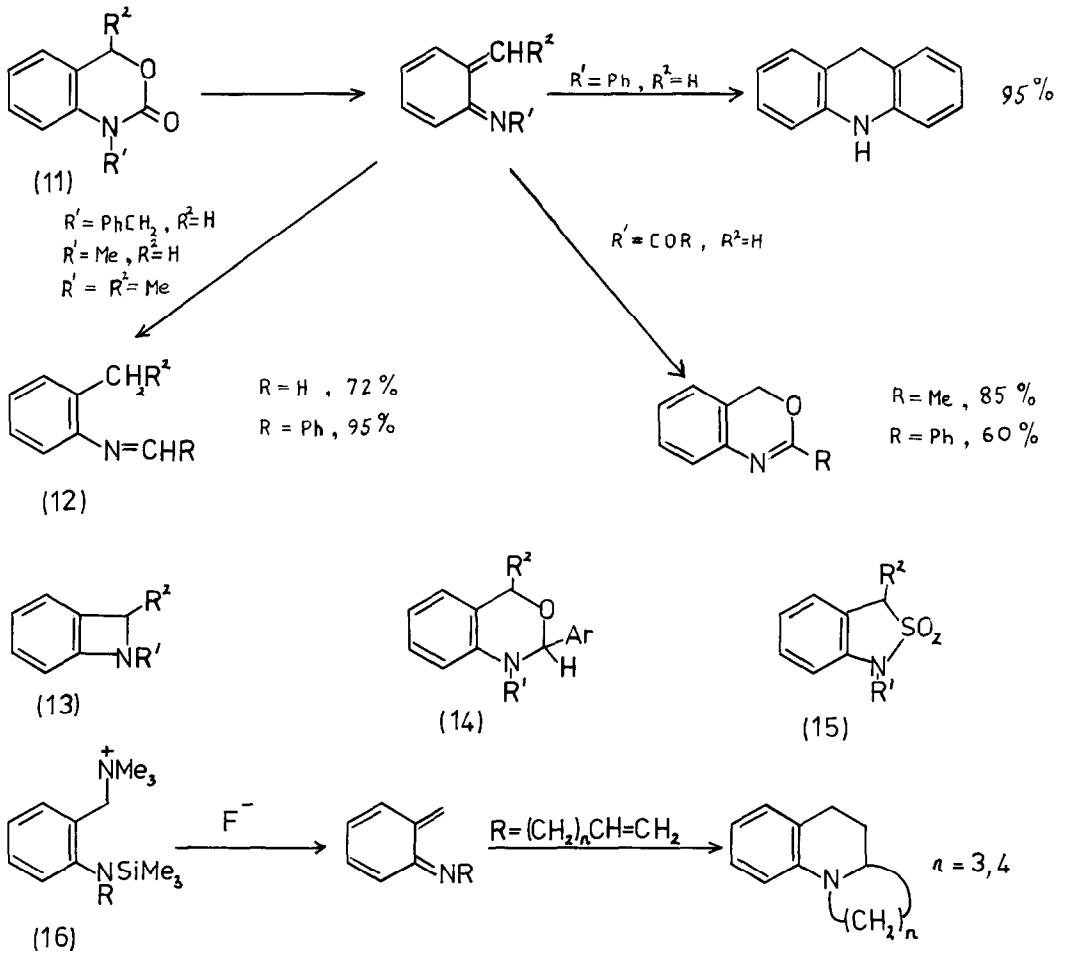

(6) (7) R = Me 43 % R = Ph 40 % (8)




(9) (10) R' = R² = Me 88% R' = R² = H 56%

In an attempt to produce azaxylylenes under milder conditions by retro Diels-Alder reactions the readily available dihydrobenzoxazinones (11)[3] and tetrahydrobenzoxazines (14)[4] were subjected to FVP. Both gave azaxylylenes; the former were more convenient, however, since carbon dioxide is the fragment eliminated. The temperature required (650°C) for cleavage of the benzoxazinones (11) is slightly lower than that for the aminoalcohols (1) and the pyrolysates were generally cleaner. Products were isolated in improved yields, but in all cases were identical to those obtained from the aminoalcohols; in no case was formation of a benzazetidine observed. The exclusive production of imines (12) from pyrolysis of benzoxazinones(11 ; $R^1$=Me, $R^2$=H,Me) contrasts sharply with the reported formation of benzazetidines (13) in the FVP of the related sulphonamides (15).[5] The reason for this difference is not clear, but it would appear that in general azaxylylenes do not ring close to benzazetidines.[6] Indeed, no benzazetidine was reported when the azaxylylene (2; $R^1$=Me, $R^2$=H) was generated in solution at ambient temperature by fluoride ion induced elimination in the silylamine (16).[7]

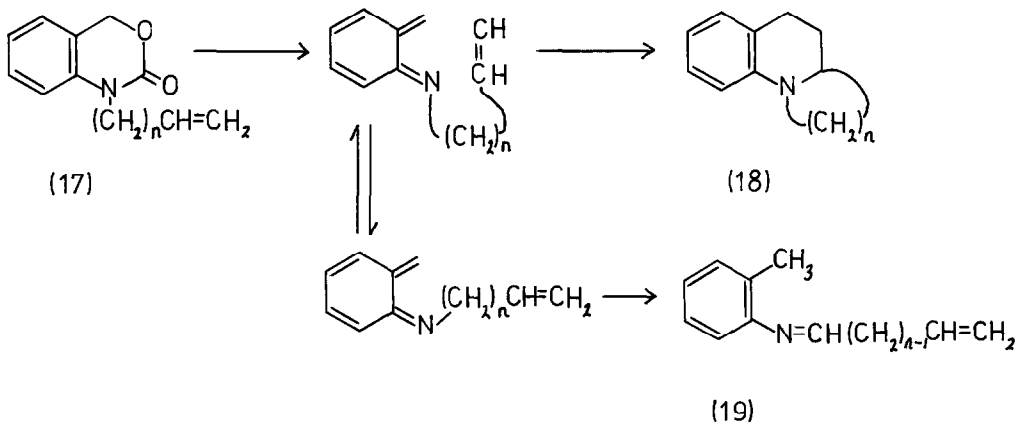
The electrocyclisation and H-shift reactions require that $R^1$ or $R^2$ in the azaxylylene adopts the Z configuration, although this is less stable than the alternative E




configuration for steric reasons. Clearly, when generated by FVP the azaxylylenes have sufficient thermal energy for the necessary configurational changes to occur.[8] This is not the case when azaxylylenes are generated in solution. Thus N-methylazaxylylene (2; $R^1$=Me, $R^2$=H) in solution gives dimer rather than the product of H-shift.[5] Also, no dihydroacridine is formed when N-phenylbenzazetidine is heated to 200°C in a solvent, although the azaxylylene can be trapped by Diels-Alder reaction below this temperature.[9] Significantly, FVP of N-phenylbenzazetidine does give dihydroacridine.

This E-Z configurational mobility in azaxyxlylenes generated by FVP makes pyrolysis of amino alcohols (1) and benzoxazinones (12) the method of choice when intramolecular cyclisation reactions are required. However, in other situations, such ready isomerisation can be a disadvantage. Thus the intramolecular Diels-Alder reactions, which occur in good yield for the alkenyl azaxylylenes generated in solution at room temperature from the silylamines (16),[7] are less efficient when the same species are generated in the gas phase by FVP of the alkenylbenzoxazinones (17). In this case there is competition between H-shifts and intramolecular cycloadditions, which require the N-alkenyl group to have

Z and E configurations, respectively, in the azaxylylenes. The tricyclic amines (18; n = 3 and 4) were isolated in 29% and 10% yields respectively. The imines (19; n = 3 and 4) were not isolated directly but hydrolysis of the crude pyrolysates gave o-toluidine (30% and 60% respectively).



(17) (18) (19)

References and Notes

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8. In the azaxylylenes (2; $R^1$=$R^2$=Ph or Me) where both the nitrogen and the exocyclic carbon bear substituents which can undergo pericyclic transformations, reaction of the N substituent predominates.
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