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A NEW ROUTE TO AZOCINES (1)

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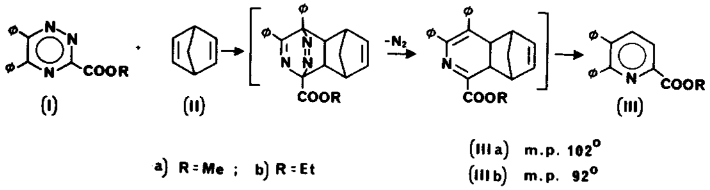
It has recently been reported (2) that 1,2,4-triazines can participate in (4+2)πcycloaddition reactions and two modes of addition were observed depending on the nature of the dienophile (nitrogen elimination to form a pyridine or nitrile elimination to form a pyridazine). The reverse electronic requirement of this diene necessitated the use of electron rich dienophiles to facilitate the reaction. Our own experience with such electron deficient dienes (3) suggested that efficient cycloadditions could also be obtained with dienophiles activated by ring strain. Consistent with this premise was the observation that the triazines (Ia,b) reacted with bicyclo[2.2.1]hepta-2,5-diene (II) (refluxing benzene for 3 days) to form ultimately the pyridines (III a,b)*, presumably via the sequence of cycloaddition/retro Diels-Alder reactions outlined in Scheme 1. This also established that the nitrogen elimination pathway was preferred in the reaction with ring-strained olefins.

SCHEME 1



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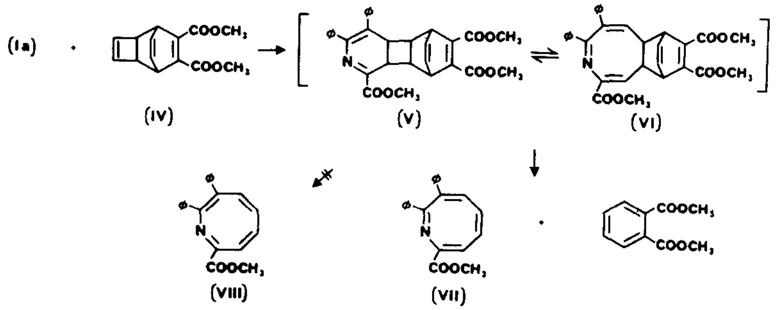
* This result has been fully confirmed recently in an independent study by W. Dittmar, J. Sauer and A. Steigel, *Tetrahedron Letters*, 5171 (1969).

SCHEME 2



Application of a similar sequence of (4+2)π cycloaddition/fragmentation reactions (Scheme 2) utilising dimethyl tricyclo[4.2.2.$0^{2,5}$]deca-3,7,9-triene-7,8-dicarboxylate (IV) and the triazine (Ia) (refluxing toluene for 7 days) formed the azocine (VII), yellow coloured prisms from hexane, m.p. 125° (60% yield. Found *m/e* 315. The i.r. spectrum (ν_{CO}1715 cm^{-1}) indicated the presence of an α,β-unsaturated ester and the ultraviolet spectrum (λ_{max}^{EtOH} 254 nm, ε 2.62 X 10^4, together with tailing up to 360 nm) supported the azocine isomer (VII) rather than the isomer (VIII). This was fully confirmed by the 100 MHz p.m.r. spectrum, the ABMX vinylic proton portion of which is only consistent with structure (VII) and is shown in Figure 1.

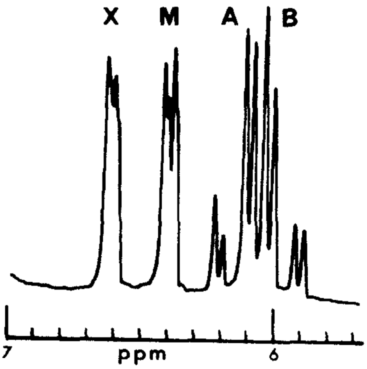
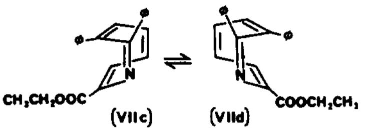
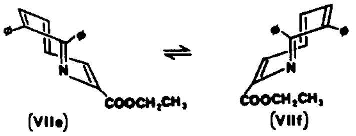


FIGURE 1.
100 MHz p.m.r. spectrum of azocine (VII).
Scale is in ppm, zero at TMS.

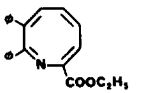
No direct evidence for any of the bicyclic valence isomers could be detected either by p.m.r. spectroscopy (as low as -60°) or by reactions with standard dienophiles like N-phenylmaleimide or tetracyanoethylene. This contrasts with the behaviour of 2-methoxyazocine and related 3,8-disubstituted analogues (4,5) and may reflect the reluctance of the vicinal phenyl groups of (VII) to assume a coplanar or eclipsed configuration. Indirect evidence for the bridgehead nitrogen valence isomer may be reflected in the mass spectrum of the azocine ethyl ester (VII; *m/e* 329.1412, calc. 329.1416) in which the base peak corresponds to tolan (*m/e* 178.0779, calc. 178.0783).



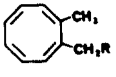
(VIIc) (VIId)



(VIIe) (VIIf)



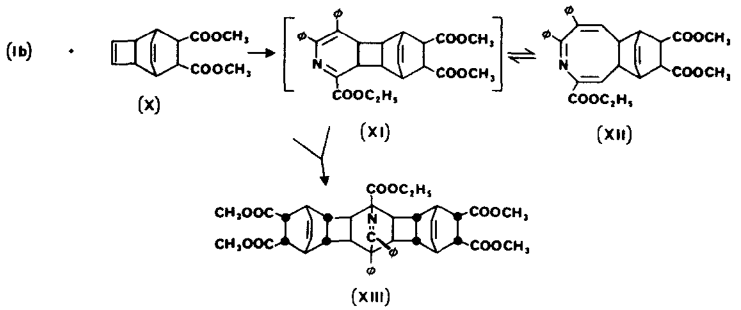
(VIIp)



(IX)

In order to gain some insight into the flexibility of the azocine ring system towards conformational inversion, the related ethyl ester of the azocine (VII) was prepared. In this compound the ester methylene protons are diastereotropic (6,7) and thus their p.m.r. (60 MHz) signal appears as the AB portion of an ABX$_3$ spin system at room temperature due to the chiralty of the azocine ring (either tub or chair). At 150° and above the methylene proton resonances became equivalent (A$_2$X$_3$ system) indicating that ring inversion (VIIc $\rightleftharpoons$ VIId; VIIe $\rightleftharpoons$ VIIf) is occurring and that equal population of each state has been attained (in the ring inversion process the A and B protons of one conformer become the B and A protons of the second conformer). The vinylic proton resonances remain unchanged throughout this temperature range and this is only consistent with a degenerate interchange (ring inversion) and not with bond migration. The higher temperature required to effect rapid ring inversion in this case, in comparison with the related cyclooctatetraenes (8,9) (IX, t = 70-100°) presumably reflects the increased steric interaction of the adjacent phenyl groups in the planar transition state (VIIp) required for ring inversion.

Stable 1:1 adducts of the triazines can be obtained with ring-strain dienophiles if the reverse Diels-Alder reaction is precluded. Thus the cyclobutene (X) reacts with the triazine (Ib) to form two adducts (XII), m.p. 208-209° and (XIII) m.p. 228-230°, separated by preparative t.l.c. on silica/ether. The



p.m.r. spectrum of the 1:1 adduct ($CDCl_3$, δ.p.p.m: 1.21 t, 3H, methyl; 2.80-3.20 m, 6H, bridgehead methine; 3.57 s, 6H, ester methyl; 3.90-4.50, m, 2H, ester methylene; 6.11, t, 2H, olefinic; 645-6.65, m, 2H, olefinic; 7.15-7.50, m, 8H, aromatic; 7.80-8.00, m, 2H aromatic) confirms that the dihydroazocine exists *entirely* in the monocyclic form (XII). This contrasts with the previously described dihydroazocines (10) and with similar cyclooctatriene systems (11). The stereochemistry of adduct (XIII) was assigned after consideration of its separate formation from the 1:1 adduct (XII), (which provides indirect evidence for the valence isomer (XI)), and from its p.m.r. spectrum ($CDCl_3$ δ p.p.m.: 1.40, t, 3H, methyl; 2.20-2.50, m, 8H and 2.75-3.20, m, 8H, bridgehead methine; 3.62, s, 12H, ester methyl; 4.40, q, 2H, ester methylene; 6.55, m, 4H, olefinic; 7.24, m, 10H, aromatic).

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