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PREPARATION AND REACTIONS OF SELECTED 3,4-DIAZABICYCLO[4.2.0]OCTA-2,4-DIENES (1)

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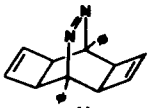
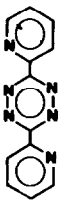
The value of heterocyclic components as dienes in (4+2)π cycloaddition reactions has been amply demonstrated in recent syntheses of azacyclopolyene systems [*inter alia* azocines (2), azepines (3), diazepines (4)]. Attempts to prepare diazocines [or valence isomers thereof] (5) by this route have been less successful (6), although such an intermediate has been invoked (7) in the preparation of the azo-bridged alicycle (1). We now report a convenient entry into the 3,4-diazabicyclo[4.2.0]octa-2,4-diene system and illustrate some of its typical properties.



(1)

i) *Preparation and valence isomerisation*

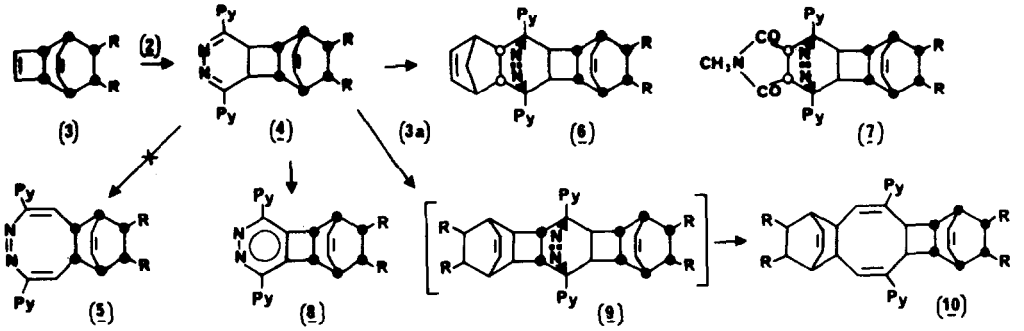
The reaction of ring-strained olefins with s-tetrazines often occurs under mild conditions, and this is true for a range of cyclobutene derivatives (8). This is well demonstrated by reaction of the cyclobutenes (3a,b) with the s-tetrazine (2), (9) [activated in this case by the electron withdrawing α-pyridyl substituents (10)] where reaction occurred at room temperature (2-3 hours). The initially formed adducts rapidly lost nitrogen to yield the 3,4-diazabicyclo[4.2.0]octa-2,4-diene derivatives (4a), m.p. 226-7° and (4b), m.p. 275° resp. (See Scheme 1). The p.m.r. spectrum of compound (4a) was typical of these adducts and the presence of two sets of cyclobutyl protons ruled out the isomeric dihydrodiazocine structure (5). [$CDCl_3$: δ ppm 8.75-7.20 (m, 8H, pyridyl); 6.82 (t, 2H, olefinic); 4.62 (s, 6H, O-CH_3); 3.5 (br d, 2H, allylic cyclobutyl); 3.4 (br m,



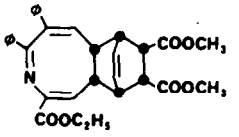
(2)

SCHEME I a) R=COOCH$_3$; b) R⌒R=CO–O–CO ;

● denotes H projecting upwards ; ○ stereochem. unknown ; Py = 2-pyridyl.



2H, allylic); 2.78 (br s, 2H, methine); 2.62 (m, 2H, cyclobutyl)]. The symmetrical nature of the p.m.r. spectrum ($CDCl_3$ or DMSO-d_6) indicated that no prototropic shift had occurred, although such shifts are typical of related 4,5-dihydropyridazines (3,11). Indeed variable temperature studies indicated that compound (4a) remained unchanged in structure up to 130° (higher temperatures were not investigated), a result which also demonstrated that conversion to the dihydrodiazocine (5) was not readily achieved. We defer comment on the generality of this result [see however reference (5)], until a wider range of 3,4-diazabicyclo[4.2.0]octa-2,4-dienes has been studied, since a recent study on the related 3,4-diazanorcaradiene system has revealed a variation in stability depending on the nature and position of the substituents (3d). It is interesting to note that the related dihydroazocine structure is the preferred form of compound (11) (2).



(11)

ii) *Diene Reactivity*

The participation of a 4,5-dihydropyridazine as a diene in (4+2)π cycloadditions has only recently been reported (3c). We have also observed similar cycloaddition reactions between the diene (4a) and N-methylmaleimide, cyclobutene (3a) (both reactions carried out in refluxing toluene) or bicyclo[2.2.1]hepta-2,5-diene (refluxing benzene). Spectral data supported single isomers for the adducts derived from bicyclo[2.2.1]hepta-2,5-diene (6a), m.p. 203-5° and N-methylmaleimide (7a), m.p. 245°, and suggested high stereoselectivity in the cycloadditions, but the exact stereochemistry remains undetermined at this stage.

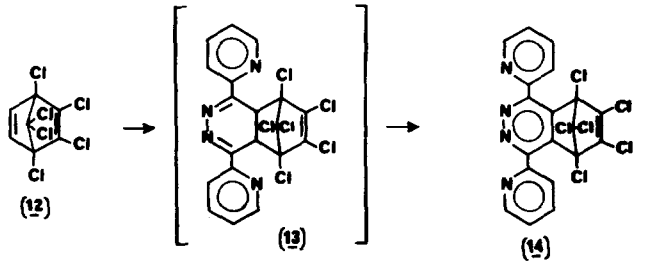
It is significant that both ring-strained and electron deficient dienophiles reacted with (4a) which indicates that a 2,3-diazabuta-1,3-diene moiety is more "normal" in its electronic requirements when part of a dihydropyridazine than when part of a tetrazine (12).

The compound (10a), formed from (4a) and the cyclobutene (3a) under similar conditions, contained no azo-bridge. We interpret this to indicate that stereoselective formation of the *endo*-cyclobutane adduct (9a) had occurred, followed by elimination of nitrogen during the course of the reaction. It is known that σ-bond participation from an *endo*-fused cyclobutane facilitates nitrogen elimination (with concomitant disrotary ring-opening) in such systems (13). The p.m.r. supported structure (10a), the predicted product of such a reaction sequence [vinylic protons δ 6.6-6.8 (m, 4H, unsubstituted etheno-bridges) and δ 6.1-6.3 (m, 2H, α to pyridyl); methyl ester resonances δ 3.5, 3.8 (s, 6H)].

iii) *Oxidation*

The 4,5-dihydropyridazine system is prone to aerial oxidation, and this process can be facilitated by chemical agents such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Thus reaction of the s-tetrazine (2) with 1,2,3,4,7,7-hexachloro-bicyclo[2.2.1]hepta-2,5-diene (13) (7 days reflux in benzene) forms the product (14), m.p. 215°, obviously derived by aerial oxidation of the initially formed dihydro-intermediate (13) (14a) (Scheme II). Similar aerial oxidation occurred with (4b) and the diazabenzocyclobutene derivative (8b), m.p. 329-331° was obtained in high yield. The mass spectrum of (8b) (parent molecular ion $^{m}/e$ 408) together with the increased shielding ($\Delta\nu$ = 49 Hz) of the olefinic protons compared with those in (4b), supports this assignment.

SCHEME II



Photolysis and pyrolysis studies on the compounds described in this communication, and related adducts (14), are under active investigation and will be reported in due course.

ACKNOWLEDGEMENTS: We thank Dr. J.A. Elix for helpful discussions in the latter phases of this work; Mr. R.J. Nicholls for running the variable temperature p.m.r. spectra and Badische Anilin- und Soda-Fabrik, A.G. for a generous gift of cyclooctatetraene.

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14. (a) Evidence for the existence of this ring system has recently been obtained and will be presented separately. (b) Adducts formed from tetrazines and tricyclo [4.2.2.$0^{2,5}$]deca-3,7,9-trienes have been prepared and will be the subject of a separate communication, J.A. Elix, W.S. Wilson and R.N. Warrener, *unpublished results.*