Cycloadditive Coupling Between 3,6-Diphenyl-*s*-tetrazine and Bicyclo[6.1.0]nona-2,4,6-trienes; Pericyclic Synthesis of Pyridazinocyclononene and Pyridazinoazonine Frameworks

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Summary Cycloadditive coupling between 3,6-diphenyl-*s*-tetrazine (**1**) and the bicyclo[6.1.0]nona-2,4,6-trienes (**2a**—**c**) produces the novel [7.4.0] heterobicycles (**3a**—**c**) which undergo ready oxidation to the corresponding annulated pyridazines (**6**); preliminary mechanistic observations suggest that the cycloadduct (**2c**) and, possibly, (**2a**) [and (**2b**)] are formed directly from the bicyclo[6.1.0]nona-2,4,6-triene frame and not from trapping of the corresponding *cis,cis,trans,cis*-monocyclic tetraene.

We recently described the pericyclic synthesis of several cyclic π systems *via* initial cycloadditive trapping of a thermally activated bicyclo[6.1.0]nonatriene with α-pyrone.[1] In an extension to the construction of related molecules incorporating one or more ring heteroatoms in place of sp^2 carbon we studied the use of 3,6-diphenyl-*sym*-tetrazene (**1**)[2] as the 'diene' partner in the cycloaddition process, and now report our preliminary results.

Lengthy (86 h) exposure of the bicyclotriene (**2a**) to the tetrazine (**1**) at ambient temperature in benzene generates a clean mixture consisting of a single 1:1 cycloadduct (**3a**) [yellow needles, m.p. 118—120 °C, ν(KBr) 3160 cm^{-1} (NH); τ (100 MHz; $CDCl_3$) 2·02 (1H, br, s, NH), 2·2—2·8 (10H, m), 3·82 (1H, d, *J* 10·5 Hz), 3·9—4·4 (5H, m), 5·63 (1H, d, *J* 9·5 Hz, H_a), 6·65 [1H, dt, *J* 12·5 (geminal coupling), 9·5, and 9·5 Hz], and 7·27 (1H, ddd, *J ca.* 12·5, 7·0, and 4·5 Hz); λ_{max}(MeCN) 344 (ϵ 5730), 308 (8080), and 248 (18,300) nm; *m/e* 324 (M^+; 100 %)]† as well as unchanged (**1**) and (**2a**) (*ca.* 60 % recovery). The above spectroscopic characteristics establish a basic [7.4.0] frame in (**3a**) while the association of each methylene proton (τ 6·65 and 7·27) with two vicinal coupling constants eliminates structure (**4a**) (or its 'methine' position isomer). However, the olefinic region of the n.m.r. spectrum is not sufficiently well resolved to allow a clear distinction between (**3a**) and (**5a**). The 100 MHz n.m.r. spectrum [$CDCl_3$ and $(CD_3)_2CO$] of the dideuteriated analogue (**3b**) [prepared from (**1**) and (**2b**)] contains two strongly coupled (*J ca.* 11 Hz) 1H doublets centred at τ 3·85 and 4·25, showing the presence of an isolated ethylene function which is consistent with (**3b**) but not (**5b**).

The pyridazinocyclononene (**6a**),† ‡ m.p. 152—153 °C, was prepared in 67% yield on treatment of (**3a**) with *o*-chloranil at ambient temperature.

We also find that the acetamide (**2c**) reacts rapidly (*ca.* 2 h) with (**1**) in benzene at ambient temperature, yielding a single cycloadduct (**3c**) [yellow needles, m.p. 191—192 °C, ν (KBr) 3160 (NH) and 1650 (CO) cm^{-1}; τ [100 MHz; $(CD_3)_2CO$] 0·90 (1H, br, s, NH), 2·1—2·8 (10H m), 3·38 (1H, d, *J* 9·0 Hz), 4·00 (1H, d, *J* 7·5 Hz), 4·28 (1H, d, *J* 7·5 Hz), 4·4—4·6 (3H, m), 4·98 (1H, d, *J* 8·0 Hz, H_a), and 7·82 (3H, s); λ_{max} (MeCN) 396 (ϵ 6080) and 255 (29,600) nm; *m/e* 367 (M^+; 76%)] in 75% yield.§ In turn, (**3c**) under-

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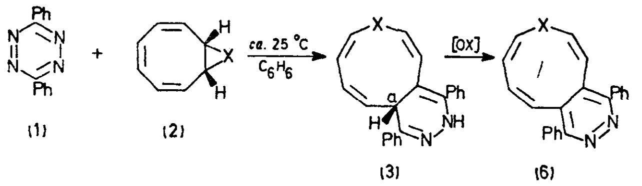
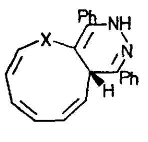
† Elemental composition was established by C,H,N combustion analysis.

‡ This substance was characterized on the basis of fully consistent spectroscopic (i.r., n.m.r., u.v., mass) data.

§ Similar observations have been made in our laboratories by Dr. R. Schaefer with the urethane analogue, *i.e.*, with X = NCO_2Et.

goes high-yield (85%) conversion into the novel pyridazinoazonine (**6c**),†‡ m.p. 173—174 °C, on exposure to *o*-chloranil at ambient temperature.§

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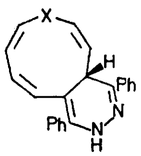
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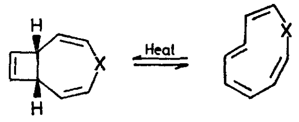

(7) (8)

a; X = CH_2
b; X = CD_2
c; X = NAc

The cycloaddition of (**1**) and (**2**) is reminiscent of the reaction between (**2a**) and tetracyanoethylene[3] or chlorosulphonyl isocyanate[4] and as such its mechanism is not obvious.[5] The cycloadduct (**3**) could be formed *via* direct addition of (**1**) to (**2**), or (**2**) could be first converted into the intermediate *cis,cis,trans,cis*-monocycle (**8**), followed by cycloaddition of (**1**) to the *trans* bond. Since (**8**) could probably be formed from (**2**) only *via* the [5.2.0] isomer[6] (**7**) and since mild heating[7] rapidly effects the conversion of (**2c**) into (**7c**) we examined the reaction between (**7c**) and (**1**). If the *cis,cis,trans,cis*-azonine (**8c**) were the major intermediate in the formation of (**3c**), (**7**) should be at least as reactive as (**2**) and the same cycloadduct (**3**) should be formed starting from (**2**) or from (**7**). In practice, neither expectation was realized. The acetamide (**7c**) reacts slowly with (**1**) [5 days for 50% consumption at ambient temperature in benzene; *cf.* 100% consumption of (**2c**) by (**1**) in 2 h under the same conditions] and does not yield a single product [as in the case of (**2c**)] but instead a 1 : 1 mixture of (**3c**) and a new ($C_{22}H_{16}N_3$)Ac cycloadduct (A),§¶ m.p. 207—208 °C, is formed.

On the basis of these observations and since the [5.2.0] skeleton (**7c**) is the only mechanistically plausible source of *cis,cis,trans,cis*-azonine (**8c**) we conclude that cycloadduct (**3c**) is most likely formed directly from (**2c**) rather than from (**8c**). The unavailability of the hydrocarbon (**7a**) precludes a similar mechanistic test on the origin of (**3a**), although the close structural similarity between (**3a**) and its aza-counterpart (**3c**) suggests that the two systems would be formed in a related fashion.

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¶ This molecule was fully characterized by i.r., n.m.r., u.v., and mass spectra, and its structure will be reported elsewhere.

[1] For a review, see: A. G. Anastassiou, *Pure Appl. Chem.*, in the press.

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[7] A. G. Anastassiou, S. Eachus, R. L. Elliott, and E. Yakali, *J.C.S. Chem. Comm.*, 1972, 531, and references cited therein.