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The Synthesis and Structure of [7](3,6)Pyridazinophane

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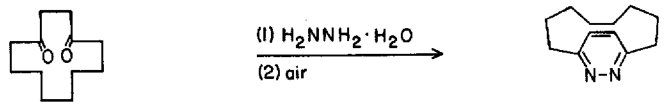
Summary: [7](3,6)Pyridazinophane has been prepared in a five-step synthesis from *cis,trans*-1,3-cycloundecadiene and 4-phenyl-1,2,4-triazoline-3,5-dione. Single crystal X-ray analysis showed the pyridazine ring to be boat shaped with an average bending angle of 17.45°.

The last ten years have witnessed extensive interest in the paracyclophanes. [*n*]Paracyclophanes where n = 7,[1] 6,[2] and 5[3] have been isolated, and the [4]paracyclophane system has been proposed as a transitory intermediate.[4] In contrast to the level of activity devoted to these carbocyclic systems, relatively little attention has been accorded to the related heteroatom containing paracyclophanes. In part, this was due to the lack of suitable synthetic methodology. [8](3,6)Pyridazinophane (**1**) was prepared by the condensation of cyclododecane-1,4-dione (**2**) with hydrazine, followed by air oxidation.[5] We now wish to report a novel synthetic approach to [7](3,6)pyridazinophane (**3**), the next smallest member of this series.



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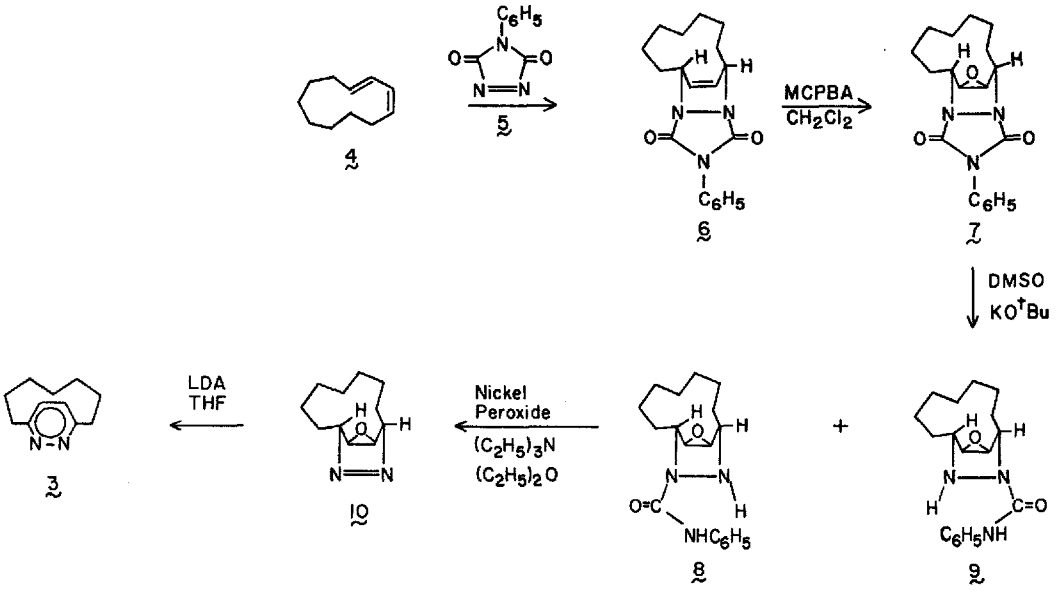
Treatment of *cis,trans*-1,3-cycloundecadiene (**4**) with 4-phenyl-1,2,4-triazoline-3,5-dione (**5**) in chloroform gave a 65% yield of the Diels-Alder adduct **6**.[6] The inside, outside (*i,o*) nature of the skeletal structure of **6** was anticipated on the basis of mechanistic precedence,[7] and was verified experimentally by the observation of ^{13}C NMR resonances ($CDCl_3$) at δ 152.16 (s), 149.63 (s), 133.45 (d), 131.86 (s), 131.43 (d), 128.97 (2C, d), 127.85 (d), 125.76 (2C, d), 55.19 (d), 54.19 (d), 32.34 (t), 28.90 (t), 28.34 (t), 24.06 (t), 23.99 (t), 23.32 (t), and 23.12 (t). The presence of the seventeen carbon resonances precluded the formation of any type of symmetrical [(*i,i*) or (*o,o*)] adduct. Treatment of **6** with 1.6 equivalents of *m*-chloroperbenzoic acid in methylene chloride at ambient temperature gave a 74% yield of **7**, mp 217.5-219.5 °C. When **7** was hydrolyzed through treatment with twenty equivalents of potassium *tert*-butoxide in dimethyl sulfoxide,[8] a 77% yield of a 58:42 mixture of **8** and **9** was obtained. Although these isomers could be separated by fractional recrystallization to give the pure isomers, mp 172-173 °C and mp 165-167 °C, a definitive assignment



of which was **8** and which was **9** has not been made. When the mixture of **8** and **9** was treated with nickel peroxide[9,10] at ambient temperature for 24 h, an 87% yield of **10** was obtained, mp 102-103 °C. Our desire to have **10** was based on our earlier observation that the analogous carbocyclic epoxide could be readily converted to the [7]paracyclophane on treatment with either acid or base.[1b] Surprisingly, the epoxide **10** was inert to treatment with trifluoroacetic acid. It is presumed that this was due to protonation of the more basic nitrogens instead of the epoxide oxygen. Fortunately, treatment of **10** with three equivalents of lithium diisopropylamide (LDA) at 0 °C for 30 min followed by stirring at ambient temperature for 1.5 h gave a 29% yield of **3**, as a white crystalline solid: mp 79-80 °C; ^{1}H NMR ($CDCl_3$) δ 7.19 (2 H, s), 3.08-3.03 (4 H, m), 1.77-1.67 (2 H, m), 1.26-1.11 (2 H, m), 0.88-0.62 (4 H, m), 0.41 (1 H, br m), -1.93 (1 H, br m); ^{13}C NMR ($CDCl_3$) δ 160.66 (s), 124.63 (d), 34.58 (t), 29.33 (t), 28.97 (t), and 24.98 (t). The presence of the two one-proton resonances at δ 0.41 and -1.93, suggested that the central carbon of the 7-carbon bridge was held over the center of the aromatic ring and, as a result, that the attached protons were subjected to the anisotropy effects of the pyridazine moiety. On cooling to -80 °C, the δ -1.93 resonance shifted to δ -2.33, while on heating to 100 °C this same resonance shifted to δ -1.75.[11] The relatively small change in the position of this proton over the 180 °C range studied, indicated that temperature variation had only a relatively small effect on the equilibrium positions of the two hydrogens at C10.

In order to evaluate the effect of the seven-carbon bridge on the structure of the pyridazine ring, a single crystal X-ray structural determination was carried out on **3**.[12,13] Figure 1 shows two different ORTEP drawings of **3**. Of special interest is the degree to which the pyridazine ring is bent into a "boat" like conformation due to the constraint of the seven-carbon bridge. The X-ray analysis showed that the planes formed by N2, C3, C4 and N1, C6, C5 are bent up from the plane formed by N1, N2, C4, C5 by an average of 17.45°. Furthermore, the C3-C13 bond and C6-C7 bonds are distorted out of the planes formed by N2, C3, C4 and N1, C6, C5, respectively, by an average of 8.68°. Thus, it is clear that the seven-carbon bridge distorts the structure of pyridazine to a considerable extent. The seven-carbon chain is also distorted in terms of the C-C-C bond angles. The largest splaying occurred with the C9-C10-C11 bond angle which was expanded to 117.3°.

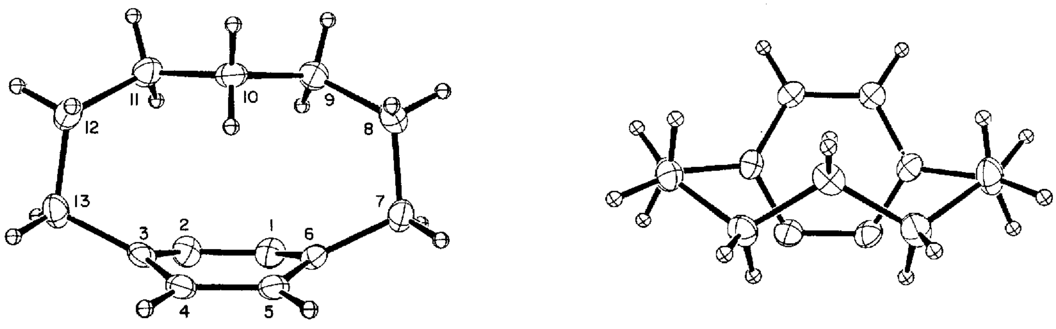


Figure 1. ORTEP drawings of **3** showing the top and side views.

We are continuing to explore the chemistry of **3**, and the synthesis of more strained variants.

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References and Footnotes

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11. In order to achieve the 180 °C temperature range, toluene-d_8 was used as solvent at the higher temperatures, while methylene chloride-d_2 was used at the lower temperatures. The shifts listed at both temperatures are corrected to chloroform-*d*.
12. The white crystals of $C_{11}H_{16}N_2$ belong to the orthorhombic space group Pna2_1. The measured cell constants, a = 23.274(7) Å, b = 7.082(2) Å, c = 5.846(3) Å, V = 963.6 Å^3 for a calculated density of 1.215 g/cc for four molecules in the unit cell at -90 °C. Data were collected on a fully automated Enraf-Nonius CAD4 Diffractometer by using a variable rate ω-2θ scan technique and graphite monochromatized Mo Kα radiation (λ = 0.71069 Å). Reflections (5860) were collected for a hemisphere and then averaged (R_{int} = 0.022) to give 1557 independent reflections of which 1392 (89%) were used with 2θ = 60° and $[F_o^2 \geq 1\ \sigma\ (F_o^2)]$. The structure was solved by direct methods and the final discrepancy factors were R = 0.035 and R_w = 0.033.
13. Full structural details will be presented in a full paper on this subject.

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