

## A Cyclophane Bridged by an Inwardly Pyramidalized Olefin

Robert A. Pascal, Jr.,\* Meredith L. Carter, Mark R. Johnson, and Douglas M. Ho

Department of Chemistry, Princeton University, Princeton, New Jersey 08544 USA

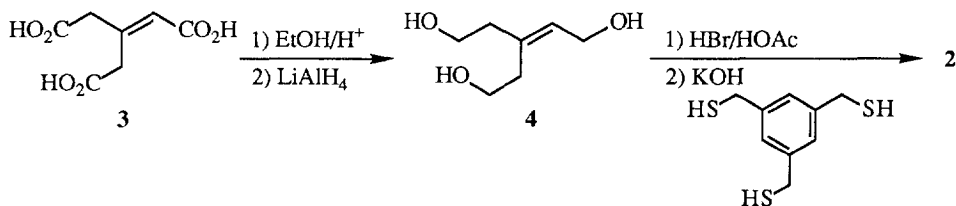
**Abstract:** 2,8,17-Trithia[4<sup>5,12</sup>][9]metacyclophan-4-ene, a cyclophane with a tertiary olefin strapped across the face of a benzene ring, has been prepared and its X-ray structure determined. The olefin is pyramidalized *toward* the benzene ring. The X-ray structure of the corresponding saturated phane (*in*-2,8,17-trithia[4<sup>5,12</sup>][9]metacyclophane, which was synthesized previously) has also been determined. The structure and reactivity of the *in*-olefin are discussed in the context of other structures and the results of computational studies. Copyright © 1996 Elsevier Science Ltd

We have previously described the syntheses and structures of a variety of *in*-cyclophanes in which methine hydrogens<sup>1-3</sup> and silane hydrogens,<sup>4</sup> are projected into the face of a benzene ring. In a similar vein, McMurry has investigated the interactions of *in*-hydrogens with olefins, including the protonation of these compounds to give remarkable  $\mu$ -hydrido cations,<sup>5,6</sup> and all of this chemistry was presaged by Alder's extensive investigations of intrabridgehead interactions in medium-ring, bicyclic amines.<sup>7</sup> Compounds containing inwardly-directed functional groups need not be unstable; indeed, for bicyclic alkanes, *in,out*- or *in,in*-isomers have been calculated to be the preferred geometries in several medium-ring systems.<sup>8</sup>

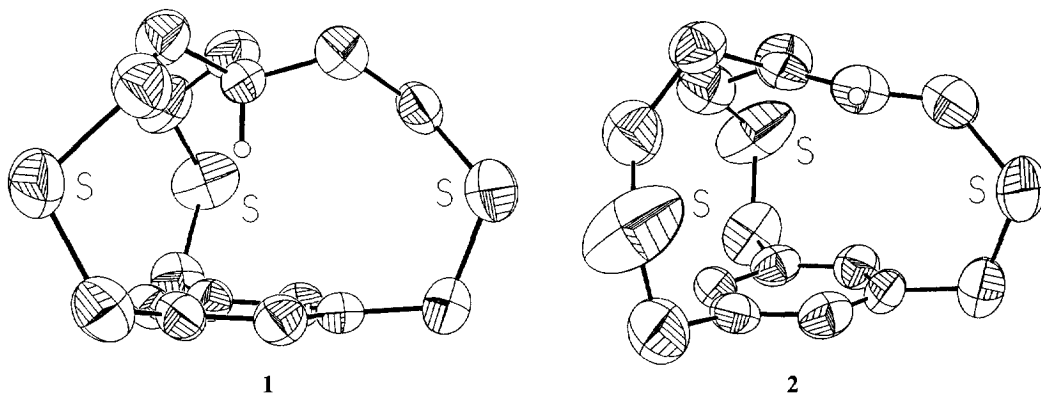
Among our own cyclophanes, 2,8,17-trithia[4<sup>5,12</sup>][9]metacyclophane (**1**) is typical; molecular mechanics calculations indicated that the *in*-isomer is preferred by 7 kcal/mol to the corresponding *out*-cyclophane,<sup>1</sup> primarily for the reason that the *in*-geometry possesses much less angle strain than the *out*-isomer, more than compensating for any steric repulsion between the *in*-hydrogen and the aromatic ring. However, is the *in*-geometry so strongly preferred that a normally planar apical functional group, such as an olefin, would be inwardly pyramidalized, and, if so, how would its reactivity be affected?



In order to address these questions, we prepared 2,8,17-trithia[4<sup>5</sup>,12][9]metacyclophan-4-ene (**2**), an unsaturated analog of **1**. The synthesis paralleled that of similar saturated phanes;<sup>1,3</sup> in this case, isobutylene- $\alpha,\gamma,\gamma'$ -tricarboxylic acid (**3**)<sup>9</sup> was esterified, reduced to the triol (**4**, 87% from **3**),<sup>10</sup> converted to the tribromide, and condensed with 1,3,5-tris(mercaptopomethyl)benzene<sup>11</sup> to give cyclophane **2** (1% from **4**).<sup>12</sup>

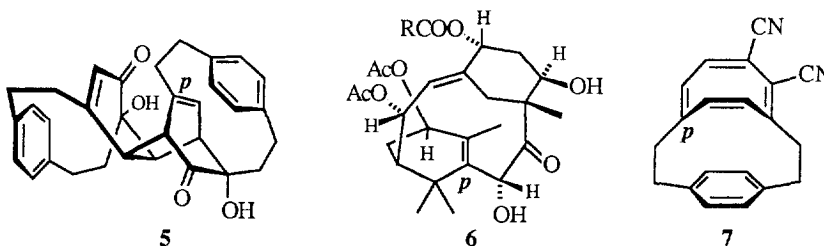


Compound **2** crystallized readily from  $\text{CH}_2\text{Cl}_2\text{-CH}_3\text{OH}$ , and its X-ray structure<sup>13</sup> is shown below along with that of compound **1**,<sup>14</sup> which has not previously been reported. For **1**, the distance from the *in*-hydrogen to the mean plane of the aromatic ring is 2.32 Å,<sup>15,16</sup> and that of the apical carbon 3.29 Å. By contrast, in **2** the olefinic bridgehead carbon rests at a comfortable Van der Waals spacing — 3.44 Å — from the aromatic ring plane. However, this olefin is not planar, it is significantly pyramidalized *toward* the basal aromatic ring, so that the apical carbon is 0.059 Å below the plane defined by its three substituent carbon atoms. The X-ray structure of **2** is complicated by disorder of the molecule across a crystallographic mirror plane, raising some concern that the unusual *in*-geometry might be an artefact. For this reason the structure of **2** was examined by several computational methods, and at every level of theory, inward pyramidalization of the apical carbon was observed. For example, molecular mechanics (MMX<sup>17</sup>) gave an inward deflection of 0.031 Å, a semiempirical molecular orbital calculation (AM1<sup>18</sup>) gave 0.050 Å, and an *ab initio* calculation at the HF/3-21G(\*) level<sup>19</sup> gave 0.058 Å, very close to the experimental value.



Although of modest magnitude, such an *inward* distortion for a bridgehead olefin is very rare, and two recent reviews of bridgehead double bonds<sup>20</sup> and pyramidalized alkenes<sup>21</sup> make no mention of inward pyramidalization. Indeed, a lengthy search of the Cambridge Crystallographic Database<sup>22</sup> (CCD) of a wide variety of unconjugated, cyclic, tri- and tetrasubstituted olefins found only a handful of cage compounds with

inwardly pyramidalized double bonds,<sup>23</sup> and of these only two exhibited distortions comparable to those of **2**; they are illustrated below, with the pyramidalized bridgehead indicated by a “*p*”. The inward displacement in **5** is 0.061 Å,<sup>24</sup> and in **6** 0.070 Å.<sup>25</sup> Gratifyingly, AM1-optimized geometries also showed inward deflections of the bridgeheads (**5**, 0.066 Å; **6**, 0.034 Å). Among conjugated olefins (which were less thoroughly searched), compound **7** is notable,<sup>26</sup> with an inward pyramidalization of 0.051 Å (AM1: 0.046 Å). The reports of **5-7** did not mention pyramidalization of the bridgehead carbons, perhaps because these distortions are much smaller than the outward displacements for the most strained bridgehead olefins, which can exceed 0.25 Å.<sup>27</sup> Nor is this surprising: the greatest degree of pyramidalization, and thus the most attractive synthetic target, is achieved by forcibly strapping back the three or four substituents of a double bond. In **2**, **5**, **6** and **7**, however, the olefin seems to be slightly bent to relieve angle strain in the medium rings.



Several attempts were made to reduce the olefin of **2**, which should yield the less stable *out*-isomer of **1**, but the thioethers preclude normal catalytic hydrogenation. Treatment of **2** with very large excesses of diimide returned only starting material, and hydroboration/protonolysis (with various boranes) returned mostly **2** as well as some unidentified higher molecular weight material. Interestingly, the strain energy (MMX) of **2** is 1.0 kcal/mol greater than **1** but 4.9 kcal/mol less than *out*-**1**, thus **2** is hyperstable<sup>28,29</sup> with respect to *out*-**1** (but not with respect to the *in*-isomer), perhaps explaining its low reactivity to external reagents. Finally, other addition reactions were complicated by the sensitivity of **2** to strong acids and oxidants: hydrobromination gave ring-opened material, and treatment with peracids or hydroboration/oxidation gave no material with the characteristics of the expected epoxides or alcohols, even allowing for oxidation of the sulfides to sulfoxides or sulfones.

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10. For **4**:  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ , DSS ref.)  $\delta$  5.58 (t,  $J = 7$  Hz, 1H, olefinic), 4.15 (d,  $J = 7$  Hz, 2H, allylic  $\text{CH}_2\text{OH}$ ), 3.67 (m, 4H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 2.37 (t,  $J = 7$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 2.31 (t,  $J = 7$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ).
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12. For **2**:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.29 (s, 1H, ArH), 7.09 (s, 1H, ArH), 6.99 (s, 1H, ArH), 4.63 (d,  $J = 9$  Hz, 1H, olefinic), 3.80 (m, 2H,  $\text{SCH}_2\text{Ar}$ ), 3.66 (m, 4H,  $\text{SCH}_2\text{Ar}$ ), 3.08 (dd,  $J = 17$  Hz, 7 Hz, 1H), 2.72 (m, 2H), 2.66 (m, 2H), 2.42 (dt,  $J = 15$  Hz, 5 Hz, 1H), 2.15 (dt,  $J = 15$  Hz, 4 Hz, 1H), 1.99 (m, 2H), 1.82 (m, 1H); MS,  $m/z$  308 ( $\text{M}^+$ , 100), 275 (5, M-SH), 262 (7, M-2SH), 157 (46), 150 (56), 125 (36), 118 (46), 115 (43), 91 (25); exact mass 308.0713, calcd for  $\text{C}_{16}\text{H}_{20}\text{S}_3$  308.0727.
13. A crystal of **2** measuring 0.18 mm x 0.22 mm x 0.45 mm was used for X-ray measurements. Crystal data:  $\text{C}_{16}\text{H}_{20}\text{S}_3$ ; orthorhombic, space group  $Pnma$ ;  $a = 9.711$  (2) Å,  $b = 12.806$  (2) Å, and  $c = 12.304$  (2) Å,  $V = 1530.1$  (3) Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calcd}} = 1.339$  g/cm<sup>3</sup>. Intensity measurements were made with  $4^\circ \leq 2\theta \leq 50^\circ$  by using graphite monochromated Mo K $\alpha$  radiation ( $\lambda = 0.71073$  Å) at 296 K on a Siemens P4 diffractometer. A total of 1425 independent reflections were measured, of which 816 were considered to be observed [ $|F_o| > 3\sigma(F_o)$ ]. The structure was solved by direct methods and refined with the SHELXTL PLUS software. The molecule sits on Wyckoff position 4c, thus it is disordered across a crystallographic mirror. Refinement of 115 parameters converged at  $R(F) = 0.071$ ,  $wR(F) = 0.078$ , with goodness-of-fit = 1.59.
14. A crystal of **1** measuring 0.35 mm x 0.35 mm x 0.42 mm was used for X-ray measurements. Crystal data:  $\text{C}_{16}\text{H}_{22}\text{S}_3$ ; monoclinic, space group  $P2_1/c$ ;  $a = 12.754$  (2) Å,  $b = 13.318$  (2) Å, and  $c = 28.002$  (4) Å,  $\beta = 90.16$  (1) $^\circ$ ,  $V = 4756$  (1) Å<sup>3</sup>,  $Z = 12$ ,  $D_{\text{calcd}} = 1.301$  g/cm<sup>3</sup>. Intensity measurements were made with  $4^\circ \leq 2\theta \leq 50^\circ$  by using Mo K $\alpha$  radiation at 294 K on a Siemens R3m diffractometer. A total of 8325 independent reflections were measured, of which 3598 were considered to be observed [ $|F_o| > 3\sigma(F_o)$ ]. The structure was solved by direct methods and refined with the SHELXTL PLUS software. Refinement of 524 parameters converged at  $R(F) = 0.051$ ,  $wR(F) = 0.049$ , with goodness-of-fit = 1.06.
15. Only one of the three similar but crystallographically independent molecules of **1** is illustrated, but the distances and angles quoted are the averages for the three molecules.
16. X-ray crystallography tends to underestimate the length of C-H bonds (Churchill, M. R. *Inorg. Chem.* **1973**, *12*, 1213-1214). If the *in*-methine is assumed to have a 1.07 Å C-H bond length, then the hydrogen atom is 2.22 Å from the aromatic ring plane.
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