

the temperature. Using relation 1,  $C_{ax}$  is calculated at each temperature from which the equilibrium constant  $K$  and the Gibbs free energy  $\Delta G^\circ$  can be obtained (Table I). The enthalpies  $\Delta H^\circ$  were obtained from the Arrhenius plots, the data points falling very close to a straight line. Aside from experimental uncertainties the accuracy of the calculated thermodynamic data is dependent on the accuracy of the assumed rotational strengths for the conformers involved in the equilibrium. Any uncertainty of the deuterium contribution to  $[R]_{ax}$  and  $[R]_{eq}$  will strongly affect  $C_{ax}$ ,  $K$ , and  $\Delta G^\circ$ , whereas any uncertainty in the methyl contribution will be reflected predominantly in the magnitude of  $\Delta H^\circ$ . Based on the extensive experimental material, the estimates for the methyl groups<sup>10</sup> are probably good within 10%. Estimates for the deuterium contributions<sup>4,5</sup> are based on the rigid adamantane ring system, and whether these are ideal representatives for the more flexible cyclohexanone system must be left open until more data become available. *Irrespective of these uncertainties our results lead to the unambiguous conclusion that axially oriented deuterium is energetically preferred over the corresponding equatorial one.*

A full discussion of the implications of this work together with experimental details will appear in our full paper.

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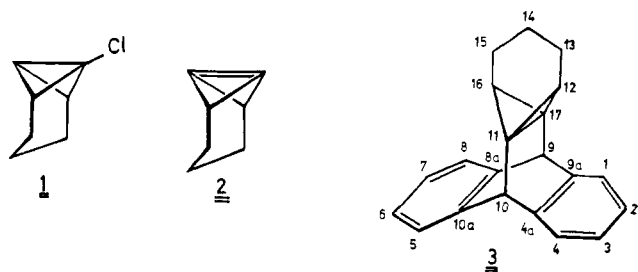
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## A Facile Route to the [4.1.1]Propellane System

Sir:

Recently we presented arguments for the formation of tricyclo[4.1.0.0<sup>2,7</sup>]hept-1(7)-ene (**2**) as a reaction intermediate in the nucleophilic substitution of 1-chlorotri-

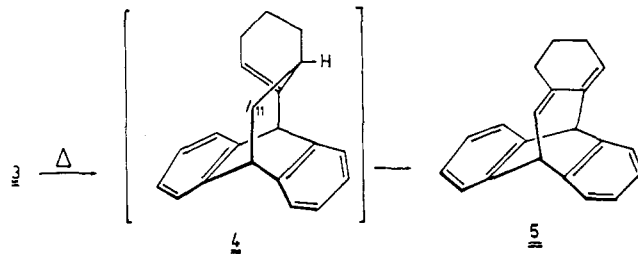


cyclo[4.1.0.0<sup>2,7</sup>]heptane (**1**) with organolithium compounds leading to the corresponding 1-alkyl- or 1-aryltricyclo[4.1.0.0<sup>2,7</sup>]heptanes.<sup>1</sup> These results initiated an attempt to trap the proposed intermediate **2** with a 1,3-diene in a Diels-Alder reaction. The outcome of this experiment is reported in this communication.

When **1**<sup>2</sup> in THF was slowly added to a stirred suspension of anthracene (2 equiv) and lithium 2,2,6,6-tetramethylpiperide (1.5 equiv) in THF at  $-20^\circ\text{C}$ , aqueous workup afforded 9,10-dihydro-9,10-(1,7-tricyclo[4.1.0.0<sup>2,7</sup>]heptano)anthracene (**3**) in an isolated yield of 31% (mp  $160\text{--}162.5^\circ\text{C}$ , from *n*-pentane).<sup>3</sup>

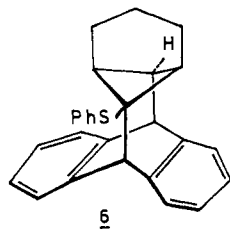
Structure proof for **3** is based on the mass spectrum ( $m/e$  270 ( $M^+$ )), the  $^1\text{H}$  NMR spectrum (( $\text{CDCl}_3$ )  $\delta$  1.26 (narrow m, 6 H, 13-H<sub>2</sub>, 14-H<sub>2</sub>, 15-H<sub>2</sub>), 2.18 (narrow m, 2 H, 12-H, 16-H), 4.60 (s, 2 H, 9-H, 10-H), 7.15 (AA'BB' system, 8 H, aromatic protons)), and the  $^{13}\text{C}$  NMR spectrum (( $\text{CDCl}_3$ )  $\delta$  20.16 (t, C-14), 22.41 (t, C-13, C-15), 22.55 (s, C-11, C-17), 46.68 (d, C-9, C-10), 53.91 (d, C-12, C-16), 124.78, 125.91 (d, C-1, C-4, C-5, C-8, and C-2, C-3, C-6, C-7, or reversed), 141.21 (s, C-4a, C-8a, C-9a, C-10a)).<sup>4</sup>

The chemistry of **3** is in accord with the bicyclo[1.1.0]butane structure. In the temperature range of  $160\text{--}180^\circ\text{C}$  **3** cleanly rearranged to 9,10-dihydro-9,10-[2,7-(3-methylenecyclohex-1-eno)]anthracene (**5**): mp  $211\text{--}213^\circ\text{C}$ , from pentane; mass spectrum  $m/e$  270 ( $M^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.15–1.71 (m, 2 H), 1.82–2.23 (m, 4 H), 4.23 (d,  $J = 8.5$  Hz, 1 H), 4.46 (s, 1 H), 5.82–6.03 (m, 2 H), 6.95–7.37 (m, 8 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  22.29 (t), 26.25 (t), 32.61 (t), 47.52 (d), 57.90 (d), 123.78 (d), 124.38 (d), 124.81 (d), 125.36 (d), 125.57 (d, unresolved superposition of two signals), 131.22 (s), 134.99 (s), 140.61 (s), 144.20 (s). The probable mechanism for this conversion is a retro-carbene ring opening of the bicyclo[1.1.0]butane unit in **3** leading to the intermediate **4** which is then transformed to **5** by hydrogen migration from C-12 to the carbene center.<sup>5</sup>



The diene **5** was also produced in a vigorous reaction when **3** was mixed with  $\text{AgBF}_4$  in  $\text{C}_6\text{D}_6$ .<sup>6,7</sup>

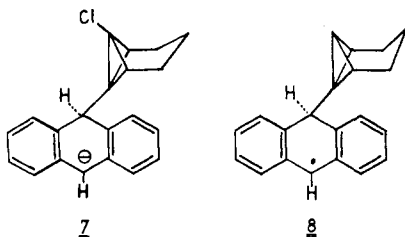
The central bond C-11–C-17 of the bicyclo[1.1.0]butane system in **3** was cleaved selectively when thiophenol was combined with **3** and allowed to add via a radical-chain process.<sup>8</sup> 9,10-Dihydro-9,10-[6-*exo*, 7-*anti*-(6-*endo*-phenylthio)norpinano]anthracene (**6**) was isolated in a practically quantitative yield: mp  $197\text{--}198^\circ\text{C}$ , from ethanol; mass spectrum  $m/e$  380 ( $M^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.43–2.37 (br m, 8 H), 2.63 and 4.17 (AB system,  $J = 9.5$  Hz), 4.44 (s, 1 H), 6.63–7.22 (m, 8 H), 7.27 (br m, 5 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  14.45 (t), 26.92 (t), 37.96 (d), 47.61 (d), 47.85 (d), 57.82 (s), 58.24 (d), 124.16 (d), 125.34 (d), 125.53 (d), 125.68 (d).



126.61 (d), 128.65 (d), 132.33 (d), 134.66 (s), 143.25 (s), 144.70 (s).

It is interesting to note that the adduct **3** contains the structural unit of a [4.1.1]propellane.<sup>9</sup> This system is now easily accessible via the procedure outlined above. Judging from molecular models, the bicyclobutane bridgehead carbon atoms C-11 and C-17 in **3** are positioned outside the tetrahedron formed by the four corresponding substituents, C-10, C-12, C-16, C-17 for C-11, and C-9, C-11, C-12, C-16 for C-17.<sup>10,11</sup>

The formation of the Diels–Alder adduct **3** can be regarded as unequivocal proof for the existence of **2** as an intermediate only, if one were able to exclude alternative routes from **1** to **3** under the experimental conditions employed. This is, however, not the case. The bridgehead bicyclobutyl anion derived from **1** might add to anthracene, the intermediate **7**, after



electron transfer from the carbanionic center to the halogen, might lose the chloride anion, and might form the diradical **8** that could close the ring.

Experiments to differentiate between these mechanistic possibilities are in progress.

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## Metal Ion Binding to Cytidine in Solution. Compelling Raman and Carbon-13 Nuclear Magnetic Resonance Spectral Evidence for Coordination to the Exocyclic Oxygen at Position 2

Sir:

Diverse electrophiles ( $H^+$ ,  $Pt^{II}$ ,  $Hg^{II}$  compounds), which bind to N(3) of cytosine derivatives,<sup>1</sup> cause characteristic Raman difference spectra in the 1100–1400- $cm^{-1}$  region in aqueous<sup>2,3</sup> and dimethyl sulfoxide- $d_6$ <sup>4</sup> solutions. We observe a new type of difference spectrum which can be attributed to the binding of hard metal ions to O(2) of cytidine in  $Me_2SO-d_6$ . Definitive evidence for O(2) binding in solution is lacking but such binding occurs frequently in solids.<sup>5–7</sup> The problem in distinguishing O(2) and N(3) binding sites in solution can be appreciated when it is realized that the sites are strongly coupled electronically and that the expected metal–O(2)–C(2) angle<sup>8</sup> places the metal ion at a position close to that expected for an N(3) bound metal atom.

Except for uridine (thymidine) and N(1) of guanosine, similar complexes are formed between metal ions and nucleosides in water and in  $Me_2SO$ .<sup>1,9</sup> The high solubilities obtainable in  $Me_2SO$  permit weak interactions to be observed. The existence of such interactions for alkaline earth metal ions is the subject of both intense interest and controversy.<sup>1,10–12</sup> For example, the nature of the interaction of  $Mg^{2+}$  with the adenine ring in the  $Mg^{2+}$ –ATP complex is unclear.<sup>13</sup>

We showed that the  $\sim 1$ -ppm shifts observed in the  $^1H$  NMR spectrum of guanosine (in  $Me_2SO$ ) upon addition of alkaline earth chloride salts<sup>11</sup> were largely due to hydrogen-bonding interactions with the chloride counterion.<sup>12</sup> A large chloride ion effect is also observed for cytidine.<sup>10,14,15</sup> The relatively small but reproducible  $^{13}C$  shifts observed for cytidine in  $Me_2SO-d_6$  on addition of alkaline earth chloride salts<sup>10</sup> cannot be attributed to the chloride ion effect.<sup>10,16</sup> In general, the changes in shifts of ligand resonances induced by metal coordination are difficult to interpret. Thus, it was reported<sup>10</sup> that alkaline earth salts caused *downfield* shifts in the C(2) resonance of cytidine in  $Me_2SO-d_6$ , whereas  $HgCl_2$  which binds to N(3) causes large *upfield* shifts and  $ZnCl_2$  (also believed to bind at N(3))<sup>17</sup> causes small upfield shifts of this resonance. Most metal species induce upfield shifts of C(4), but the alkaline earth cations were reported to have a diversity of effects.<sup>10,18</sup> Electrophiles known to bind to N(3) cause upfield shifts in both the C(2) and the C(4) of cytidine in  $Me_2SO$ <sup>16</sup> and aqueous solutions.<sup>2</sup> Results that we have obtained with nitrate salts are given in Table I.

Raman difference spectroscopy is much less subject than NMR spectroscopy to environmental effects.<sup>1–3</sup> The Raman results have been readily interpretable because diverse N(3) bound electrophiles, such as  $HgCl_2$ ,  $H^+$ , and  $Pt^{II}$  complexes, cause similar difference spectra.<sup>1–3</sup> The effects of  $HgCl_2$  and  $H^+$  (not shown) on the Raman spectrum of cytidine are similar

Table I. Metal Ion Induced  $^{13}C$  NMR Shifts in Cytidine<sup>a</sup>

Salt (M)	C-2	C-4	C-5	C-6	C-1'
$HgCl_2$ (0.5)	+2.7	+2.2	–1.7	–0.9	–0.6
$Zn(NO_3)_2$ (0.5)	+0.2	+1.2	–1.3	–0.6	+0.1
$Ba(NO_3)_2$ (0.5)	–0.8	+0.5	–0.6	–0.1	+0.3
$La(NO_3)_3$ (0.47)	–0.8	+0.5	–1.0	–0.1	+0.5
$Pr(NO_3)_3$ (0.46)	+10.1	+2.1	–1.4	+0.7	+1.1
Corrected	+10.9	+1.6	–0.4	+0.8	+0.6

<sup>a</sup> 0.2 M in  $Me_2SO-d_6$ , in parts per million,  $Me_4Si$  reference, upfield shifts from free ligand values positive, Varian CFT-20 instrument. Shifts for the metal free solutions were as follows: C-2 (155.4), C-4 (165.5), C-5 (93.8), C-6 (141.4), and C-1' (89.2). See ref 16 for assignments.