

### Optical Rotatory Dispersion Studies. 123. Experimental Evidence for Preference of Axial Deuterium over Axial Hydrogen<sup>1</sup>

Sir:

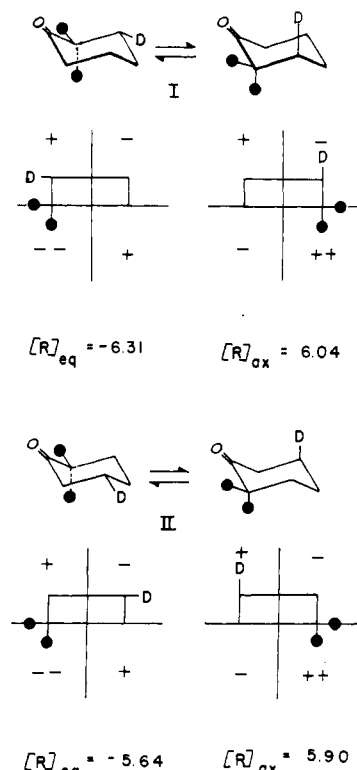
The recent interest in molecules which owe their chirality solely to isotopic substitution<sup>2-8</sup> raises the intriguing question whether circular dichroism (CD) is sufficiently sensitive to determine if in a monodeuterated cyclohexanone deuterium prefers the axial or the equatorial orientation. Lightner<sup>4</sup> and Wynberg<sup>5</sup> have shown that deuterium in the  $\beta$ -axial and  $\beta$ -equatorial positions of adamantanone induce Cotton effects of significant intensity (i.e., one order of magnitude smaller than that exhibited by a methyl group in an equivalent position<sup>9</sup>). The changes of the observed rotational strength  $[R]_{\text{obsd}}$  are directly proportional to the sum of the rotational strengths of the two assumed conformers as summarized below:

$$[R]_{\text{obsd}} = C_{\text{ax}}([R]_{\text{ax}} - [R]_{\text{eq}}) + [R]_{\text{eq}} \quad (1)$$

$$\delta[R]_{\text{obsd}}/\delta C_{\text{ax}} = [R]_{\text{ax}} - [R]_{\text{eq}} \quad (2)$$

where  $C_{\text{ax}}$  is the mole fraction of the conformer with the deuterium in the axial position and  $[R]_{\text{ax}}$  and  $[R]_{\text{eq}}$  are the rotational strengths of the axial and equatorial conformers (see I and II), respectively.

For optically active cyclohexanone-3-*d*,  $[R]_{\text{ax}}$  and  $[R]_{\text{eq}}$  are both small numbers<sup>6</sup> and therefore the temperature dependence of  $[R]_{\text{obsd}}$  will probably be smaller than the accuracy of measurement. However, in a cyclohexanone where one position is substituted with two identical but strongly perturbing groups (e.g., methyl), the situation is quite different as can be seen from the octant diagrams in Figure 1.<sup>10,11</sup> The sign and magnitude of the Cotton effect are now governed by the  $\alpha$ -axial methyl group and  $[R]_{\text{ax}}$  and  $[R]_{\text{eq}}$  will be large numbers of opposite sign. The methyl groups per se do not contribute to the selective stabilization of one conformer over the other but rather act as a chiral probe increasing the sensitivity of the



**Figure 1.** Configurations and their corresponding octant diagrams for 3(*R*)-deuterio-2,2-dimethylcyclohexanone (I) and 5(*S*)-deuterio-2,2-dimethylcyclohexanone (II) (methyl groups are indicated by ●).

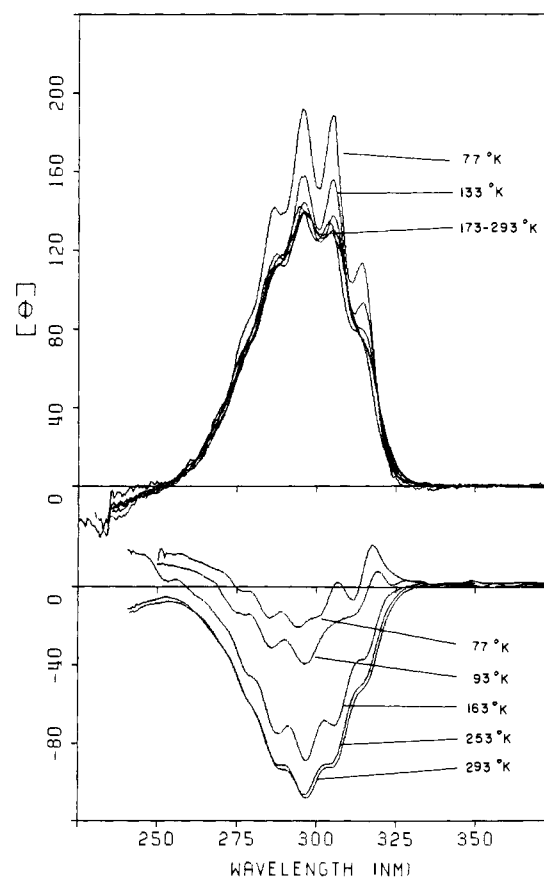
observed rotational strength associated with any shift in the equilibrium position by a factor of  $\sim 40$ .

3(*R*)-2,2-Dimethylcyclohexanone-*d* (I) was synthesized by microbiological reduction<sup>12</sup> of 2,2-dimethylcyclopentane-1,3-dione with *Kloeckera magna* (ATCC 20109) to 3(*S*)-hydroxy-2,2-dimethylcyclopentanone, conversion to the 3(*R*)-deuterated 1-ketone (mesylate,  $\text{LiAlD}_4$ ,  $\text{CrO}_3$ ), ethyl diazoacetate ring expansion,<sup>13</sup> and decarboxylation.<sup>14</sup> 5(*S*)-2,2-Dimethylcyclohexanone-*d* (II) was obtained by methylation (Ireland method<sup>15</sup>) of (+)-*p*-menth-8-en-2-one<sup>16</sup> to 5(*R*)-isopropenyl-2,2-dimethylcyclohexanone, ketalization and successive ozonolysis, Baeyer-Villiger oxidation, saponification, tosylate formation,  $\text{LiAlD}_4$  reduction, and deketalization.

The CD spectra at various temperatures (Figure 2) range from  $[R]_{\text{obsd}} = -0.103$  to  $+0.003$  for I and  $+0.134$  to  $+0.161$  for II. Qualitatively, therefore, the population of the conformer with the positive rotational strength increases with lowering

**Table I.** Percent Axial Conformer, Equilibrium Constant, Enthalpy, and Free Energy at Various Temperatures for I and II

Compd	<i>T</i> , K	$[R]_{\text{obsd}}$	$C_{\text{ax}}$ , %	<i>K</i>	$\Delta G^\circ$ , cal/mol	$\Delta H^\circ$ , cal/mol
I	293	-0.103	50.2	1.009	-5.1	
	253	-0.100	50.2	1.010	-4.8	
	163	-0.072	50.5	1.019	-6.1	-7.3
	93	-0.020	50.9	1.036	-6.6	
	77	0.003	51.1	1.044	-6.6	
II	293	0.134	50.0	1.001	-0.7	
	203	0.133	50.0	1.001	-0.3	
	133	0.141	50.1	1.004	-1.1	-1.3
	77	0.161	50.3	1.007	-1.1	



**Figure 2.** Circular dichroism spectra at various temperatures of 3(*R*)-deuterio-2,2-dimethylcyclohexanone (I) (lower spectra) and 5(*S*)-deuterio-2,2-dimethylcyclohexanone (II) (upper spectra) in isopentane/methylcyclohexane (4:1).

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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## References and Notes

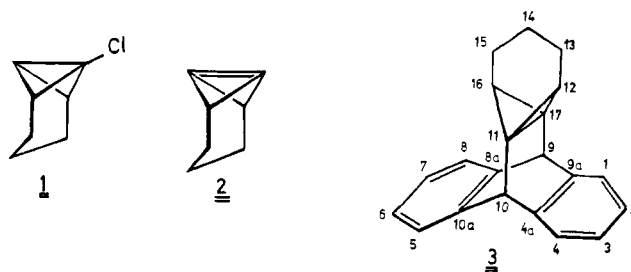
- (1) For part 122 in this series, see ref 6.
- (2) (a) W. C. M. C. Kokke and L. J. Oosterhoff, *J. Am. Chem. Soc.*, **94**, 7583 (1972); (b) W. C. M. C. Kokke and L. J. Oosterhoff, *ibid.*, **95**, 7159 (1973).
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## A Facile Route to the [4.1.1]Propellane 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-

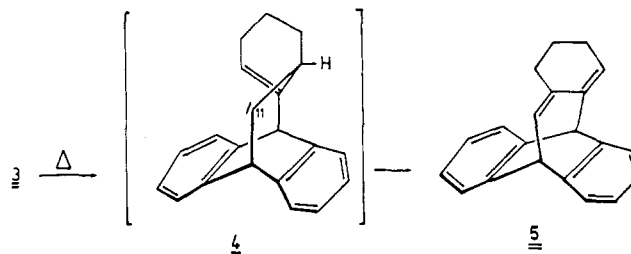


cyclo[4.1.0.0<sup>2,7</sup>]heptane (**1**) with organolithium compounds leading to the corresponding 1-alkyl- or 1-aryltricyclo[4.1.0.0<sup>2,7</sup>]heptanes.<sup>1</sup> These results initiated an attempt to trap the proposed intermediate **2** with a 1,3-diene in a Diels-Alder reaction. The outcome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