

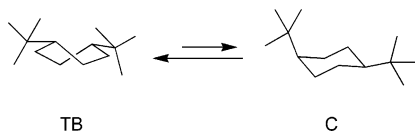
# Conformational Study of *cis*-1,4-Di-*tert*-butylcyclohexane by Dynamic NMR Spectroscopy and Computational Methods. Observation of Chair and Twist-Boat Conformations

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Received August 6, 2005



Low-temperature  $^{13}\text{C}$  NMR spectra of *cis*-1,4-di-*tert*-butylcyclohexane (**1**) showed signals for the twist-boat (**1a**) and chair (**1b**) conformations.  $^{13}\text{C}$  NMR signals were assigned to specific carbons based on the different populations, different symmetries (time-averaged  $C_{2v}$  for **1a** and time-averaged  $C_s$  for **1b**), and calculated chemical shifts (GIAO, HF/6-311+G\*). In addition to slow ring inversion and interconversion of the chair and twist-boat conformations, slow rotation of the *tert*-butyl groups was found. Most of the expected  $^{13}\text{C}$  peaks were observed. Free-energy barriers of 6.83 and 6.35 kcal/mol were found for interconversion of **1a** (major) and **1b** (minor) at  $-148.1^\circ\text{C}$ . Conformational space was searched with Allinger's MM3 and MM4 programs, and free energies were obtained for several low-energy conformations **1a–c**. Calculations were repeated with ab initio methods up to the HF/6-311+G\* level. Molecular symmetries, relative free energies, relative enthalpies and entropies, frequencies, and NMR chemical shifts were obtained. A boat conformation (**1d**;  $C_{2v}$  symmetry) was generated and optimized as a transition state by ab initio, MM3, and MM4 calculations.

## Introduction

The conformations of cyclohexane (**2**) include only two energy minima,<sup>1</sup> in contrast to larger rings.<sup>2</sup> The twist-boat conformation (**2a**), of  $D_2$  symmetry, has been estimated<sup>5</sup> to be 5.5 kcal/mol higher in enthalpy than the chair (**2b**,  $D_{3d}$ ). This value has been obtained as the difference between the barrier for conversion of **2b** to **2a** ( $\Delta H^\ddagger = 10.8$  kcal/mol<sup>6</sup> by dynamic NMR) and the barrier for the reverse process ( $\Delta G^\ddagger \sim \Delta H^\ddagger = 5.3$  kcal/mol).<sup>5</sup> For determination of the latter barrier, cyclohexane heated to  $800^\circ\text{C}$  was cryogenically deposited in a film at 40 K,

and the conversion of **2a** to **2b** was followed at  $72.5\text{--}74^\circ\text{K}$  by IR spectroscopy. The twist-boat conformation of **2** has a higher entropy than the chair by about 3 eu,<sup>7</sup> and the free-energy difference becomes smaller at higher temperatures; a population of about 25% was estimated<sup>5</sup> for **2a** at  $800^\circ\text{C}$ , corresponding to a  $\Delta G^\circ_{800}$  of only 2.3 kcal/mol.<sup>7</sup> The enantiomeric twist-boat conformations interconvert by way of the boat conformation (**2c**,  $C_{2v}$ ) as a transition state which is about 1.1 kcal/mol higher in energy than the twist-boat by MM2 force-field calculations<sup>8a</sup> and ab initio calculations.<sup>8b</sup> The chair can be converted into the twist-boat by a process referred to as K3-kayaking,<sup>8a</sup> and a  $\Delta G^\ddagger$  of 10.3 kcal/mol was determined<sup>6</sup> by NMR for this conversion.

The twist-boat conformation of **2** has not been detected by NMR, due to its low population at low temperatures. Most other flexible six-membered rings also have low populations of the twist-boat, but some exceptions are

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(2) For example, 18 conformers were found<sup>3</sup> for cyclodecane by MM2 and 16 by MM3; the corresponding numbers for cyclododecane were 111 and 90. Two of the conformers of cyclodecane (boat-chair-boat and twist-boat-chair-chair) have been identified by low-temperature NMR,<sup>4</sup> and calculations suggest the possible presence of several percent of the twist-boat-chair at low temperatures.

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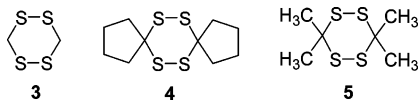
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(7) The increase in free energy and entropy for the chair to twist-boat conversion at  $800^\circ\text{C}$  were reported<sup>5</sup> as 1.3 kcal/mol and 4 eu; the corrected free-energy difference is from ref 1b, p 690, and the corresponding entropy change is 3 eu.

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known. 1,2,4,5-Tetrathiane (**3**)<sup>9</sup> and derivatives 3,3:6,6-bis(tetramethylene)-1,2,4,5-tetrathiane (**4**)<sup>10</sup> and 3,3,6,6-tetramethyl-1,2,4,5-tetrathiane (**5**)<sup>10</sup> were found by NMR to have measurable amounts of the twist-boat conformations. The chair predominates in **3**<sup>9</sup> and **4**,<sup>10</sup> but the twist-boat conformation of **5** has the lower free energy.<sup>10</sup> Cyclohexane-1,4-dione is another example of a compound which adopts a twist-boat conformation.<sup>11</sup> Nonchair conformations were found for the vapor phase,<sup>11a</sup> in solution,<sup>11b</sup> and for the solid state.<sup>11c,d</sup>



*cis*-1,4-Di-*tert*-butylcyclohexane (**1**) and *trans*-1,3-di-*tert*-butylcyclohexane (**6**) have an axial *tert*-butyl group in the chair conformations, and conversion of these conformations of **1** and **6** to twist-boat conformations can place both groups in equatorial positions. A  $\Delta H^\circ$  of  $-5.9 \pm 0.6$  kcal/mol for conversion of **6** to the *cis* isomer, in which both *tert*-butyl groups are equatorial, was obtained in an early experimental study by Allinger,<sup>12</sup> and from the entropy change associated with the conversion, a large population of the twist-boat conformation was predicted for **6**. Later force-field calculations<sup>13</sup> found relative enthalpies of 0.00, 4.86, and 5.41 kcal/mol for *tert*-butylcyclohexane (**7**) with the group in the equatorial chair, equatorial twist-boat, and axial chair conformations, respectively. These results suggested that **6** should exist as a mixture of chair and twist-boat conformations, which was confirmed<sup>13</sup> by IR spectra taken at different temperatures, and  $|\Delta H^\circ|$  for the interconversion was determined to be  $0.37 \pm 0.2$  kcal/mol. The twist-boat conformation was assumed<sup>13</sup> to predominate, based on entropy considerations. Force-field calculations of strain energies have been reported for **1**<sup>14</sup> and **6**,<sup>14c</sup> and ab initio calculations for **1** were obtained at the STO-3G level.<sup>15</sup> The twist-boat conformation of **6** was calculated<sup>14c</sup> by MM3 to have a lower strain energy than the chair by 0.9 kcal/mol, and the corresponding strain-energy difference for **1** was 0.6 kcal/mol. Other cyclohexanes expected to have a lower energy for the twist-boat are described in this paper.<sup>14c</sup> Room temperature <sup>13</sup>C shifts for **1**<sup>16</sup> and **6**<sup>16b,c</sup> also support the presence of twist-boat conformations, as do the coupling constants in partially deuterated derivatives of these compounds.<sup>17</sup> An IR study of many *cis*- and *trans*-1,4-dialkylcyclohexanes showed strong absorption at  $1450 \pm 2$  cm<sup>-1</sup> arising from deformation

vibrations of the methylene groups of the rings; **1**, however, showed only weak absorption at 1451 cm<sup>-1</sup>, which was taken to indicate the presence of a large population of a nonchair conformation.<sup>18</sup> These workers<sup>18</sup> also determined the enthalpy change for conversion of **1** to the *trans* isomer to be  $-4.7$  kcal/mol at 25 °C in the liquid phase from heats of combustion.

For *cis*- and *trans*-1,2-di-*tert*-butylcyclohexane, interactions between adjacent *tert*-butyl groups strongly influence the conformational preferences. The *trans* isomer was predicted<sup>14c</sup> by MM3 strain-energy calculations to exist as a mixture of twist-boat and diaxial chair conformations, with the latter favored by 0.5 kcal/mol. The diequatorial conformation was calculated<sup>14c</sup> to be 6.2 kcal/mol less stable than the diaxial chair. The axial-equatorial chair conformation of *cis*-1,2-di-*tert*-butylcyclohexane was predicted<sup>14c</sup> by MM3 to be favored over the twist-boat conformation by 4.8 kcal/mol, in agreement with earlier <sup>1</sup>H and <sup>13</sup>C NMR studies,<sup>19,20</sup> which showed two chemical shifts for the *tert*-butyl protons by 0 °C and 10 carbon chemical shifts<sup>20</sup> for the compound at  $-20$  °C. A free-energy barrier of 16 kcal/mol was determined<sup>19</sup> for ring inversion. The low-frequency methyl group split<sup>19</sup> by  $-110$  °C into two peaks with an intensity ratio of 2:1, and a free-energy barrier of 10.1 kcal/mol was determined<sup>19</sup> at coalescence ( $-81$  °C). These changes correspond<sup>20,21</sup> to the slowing of the rotation of a *tert*-butyl group. Actually, three peaks of equal intensity are expected under conditions of slow rotation for either *tert*-butyl group, and the finding of two chemical shifts in a 2:1 ratio indicates coincidence for two of the shifts. A free-energy barrier of 6.3 kcal/mol was determined<sup>22</sup> by dynamic <sup>1</sup>H NMR for rotation of the equatorial *tert*-butyl group in *tert*-butylcyclohexane.

The <sup>13</sup>C NMR spectrum of **6** was taken at  $-90$  °C,<sup>16b</sup> but decoalescence was not observed. A study<sup>14a</sup> of **1** combining force-field calculations (two programs) with electron diffraction at 110 °C predicted populations of the chair and two twist-boat conformations as 29%, 48%, and 23% or 43%, 44%, and 13%, depending on the force-field used, but the authors concluded that "these values remain very uncertain at best." In the present work, we have carried out a dynamic <sup>13</sup>C NMR study of **1** to obtain accurate populations and free-energy differences for the chair and twist-boat conformations and free-energy barriers to interconversion of these conformations. Calculations using MM3,<sup>23a</sup> MM4,<sup>23b</sup> and Gaussian 03<sup>24,25</sup> were also done to estimate the relative free energies of several conformations.

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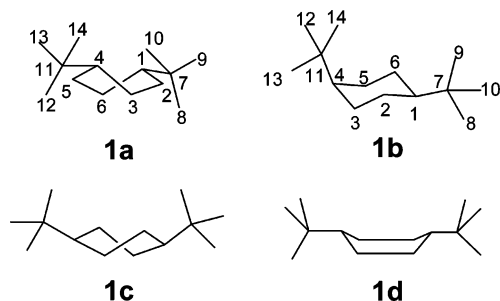
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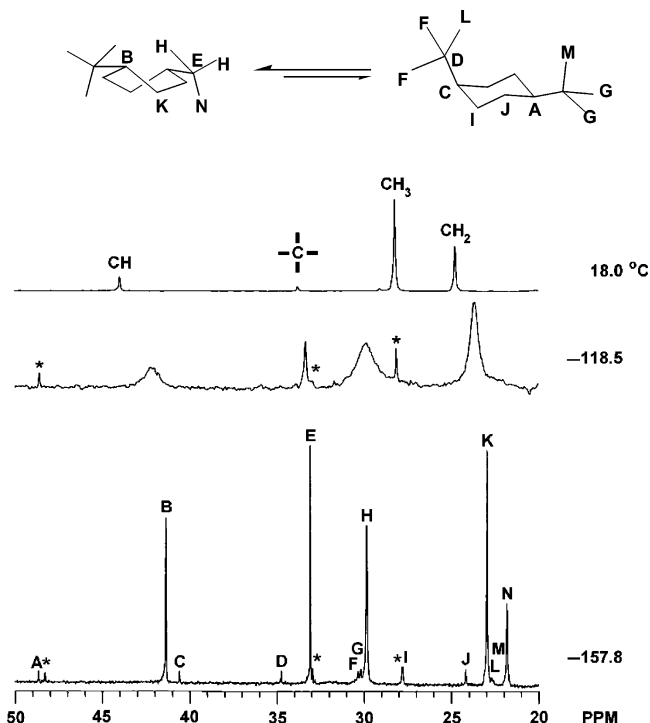
**FIGURE 1.** Conformations of *cis*-1,4-di-*tert*-butylcyclohexane. The carbons in **1a** and **1b** are numbered, and the letter assignments are shown in Figure 2.

## Results and Discussion

Relative energies and lowest frequencies for **1a–d** (Figure 1) from the MM3 and MM4 programs are shown in Table 1, and the results from two levels of ab initio calculations are shown in Table 2. The lowest frequencies are small, which increases the uncertainties in the entropies and relative free energies. The order of free energies in each calculation is **1a** < **1b** < **1c**. Conformations **1a** and **1c** can be derived from the twist-boat conformation of cyclohexane by replacement of equatorial or isoclinal hydrogens, respectively.

The HCCC dihedral angles, where H is the ring CH hydrogen and the last carbon is the methyl carbon which is most nearly trans to the methane hydrogen, were both  $-171^\circ$  for **1a**. The values for **1b** were  $178^\circ$  and  $165^\circ$  for equatorial and axial *tert*-butyl, respectively. These dihedral angles were calculated at the HF/6-311+G\* level.

The chair conformation, **1b**, is calculated to have  $C_1$  symmetry, but time-averaged  $C_s$  symmetry is expected at low temperatures. The diequatorial twist-boat conformation, **1a**, has  $C_2$  symmetry, but rapid equilibration with its enantiomer, as predicted by the low calculated free energies of **1d**, will result in time-averaged  $C_{2v}$  symmetry for **1a**. The barriers to interconversion of **1a** and **1c** are also expected to be low, and the  $^{13}\text{C}$  signals from any small amounts of **1c** will be averaged with those of **1a**. On the basis of the time-averaged symmetries expected for **1a** ( $C_{2v}$ ) and **1b** ( $C_s$ ) at low temperatures under conditions of slow equilibration of these conforma-



**FIGURE 2.**  $^{13}\text{C}$  NMR spectra taken at three temperatures for a 2% solution of *cis*-1,4-di-*tert*-butylcyclohexane in propane.

tions and slow rotation of the *tert*-butyl groups, 5  $^{13}\text{C}$  chemical shifts are expected for **1a** and 10 for **1b**. The difference in symmetry allows unambiguous identification of the two conformations. For example, the ring CH carbons should give rise to three peaks at low temperatures, two of equal intensity for **1b** and a third of different intensity for **1a**, if the barriers to interconversion are sufficiently high and both conformations are appreciably populated.

$^{13}\text{C}$  spectra of **1** at several temperatures are shown in Figure 2. The four peaks observed for  $+18^\circ\text{C}$  at  $\delta$  43.99, 33.81, 28.21, and 24.76 are assigned in agreement with the literature.<sup>16</sup> Each of these peaks broadens by  $-118.5^\circ\text{C}$ , and several impurity peaks, marked by an asterisk, are apparent at  $\delta$  48.40, 32.95, and 27.94. The peak at  $\delta$  48.40 is from the ring CH carbon of the trans isomer of **1**, and the other two may come from the central carbon of the equivalent *tert*-butyl groups and the  $\text{CH}_2$  ring carbons of the trans isomer, respectively.<sup>26</sup> Only the methyl carbons of the trans isomer should show decoalescence, as a consequence of the slow rotation of the *tert*-butyl groups, and the methyl carbon absorption from this compound may be broad at  $-118.5^\circ\text{C}$  for this reason.

Interconversion of **1a** and **1b** and rotation of the *tert*-butyl groups are slow by  $-157.8^\circ\text{C}$  (Figure 2). The two CH ring carbons of **1b** are labeled A and C; the former is close to the corresponding peak from the trans isomer, which has equatorial *tert*-butyl groups, and A is assigned to the ring carbon with equatorial *tert*-butyl. Calculated chemical shifts (Tables 3 and 4) support this assignment. The relatively high intensity of peak B from **1a** shows that the twist-boat conformation predominates. The other

(23) (a) Version MM3 2000 was used. This latest version of the MM3 program is available to academic users from the Quantum Chemistry Program Exchange and to commercial users from Tripos Associates, 1699 South Hanley St., St. Louis, MO 63144. (b) Version MM4 2003.

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(25) Gaussian 03 Revision B.03 was used in calculations for **1a** and **1b** and Revision C.02 used in calculations for **1c** and **1d**.

(26)  $^{13}\text{C}$  chemical shifts for the trans isomer of **1** were reported<sup>16b</sup> to be  $\delta$  48.4 (CH), 28.1 ( $\text{CH}_2$ ), 27.7 ( $\text{CH}_3$ ), and 32.1 (central carbon of *tert*-butyl).

TABLE 1. MM3<sup>a</sup> and MM4<sup>b</sup> Relative Energies and Lowest Frequencies for *cis*-1,4-Di-*tert*-butylcyclohexane

conformer	relative strain energies (kcal/mol)		lowest frequencies (cm <sup>-1</sup> )		relative free energies (kcal/mol)			
					25 °C		-150 °C	
	<i>a</i>	<i>b</i>	<i>a</i>	<i>b</i>	<i>a</i>	<i>b</i>	<i>a</i>	<i>b</i>
<b>1a</b>	0.00	0.00	46.1	46.8	0.00	0.00	0.00	0.00
<b>1b</b>	0.57	-0.47	34.4	31.5	2.62	1.04	1.74	0.59
<b>1c</b>	1.84	1.74	33.9	35.4	3.58	2.93	2.44	2.20
<b>1d</b>	1.56	1.69	-125.4	-130.7	2.00	2.03	1.55	1.57

<sup>a</sup> Calculated with Allinger's MM3 program. <sup>b</sup> Calculated with Allinger's MM4 program.TABLE 2. HF Relative Energies and Lowest Frequencies for *cis*-1,4-Di-*tert*-butylcyclohexane

conformer	25 °C			lowest frequencies <sup>c</sup> (cm <sup>-1</sup> )	−150 °C		
	$\Delta G$ (kcal/mol)	$\Delta H$ (kcal/mol)	$T\Delta S$ (kcal/mol)		$\Delta G$ (kcal/mol)	$\Delta H$ (kcal/mol)	$T\Delta S$ (kcal/mol)
HF/6-31G <sup>*a</sup>							
<b>1a</b>	0.000	0.000	0.000	46.7	0.000	0.000	0.000
<b>1b</b>	1.074	1.253	0.179	27.9	1.207	1.344	0.136
<b>1c</b>	1.817	1.575	−0.242	37.1	1.691	1.627	−0.064
<b>1d</b>	2.882	3.151	0.269	−169.8	3.137	3.387	0.250
HF/6-311+G <sup>*b</sup>							
<b>1a</b>	0.000	0.000	0.000	46.4	0.000	0.000	0.000
<b>1b</b>	1.002	1.204	0.203	27.1	1.129	1.271	0.141
<b>1c</b>	1.838	1.605	−0.233	37.0	1.710	1.647	−0.064
<b>1d</b>	2.843	3.250	0.407	−173.2	3.186	3.468	0.282

<sup>a</sup> Frequencies scaled by 0.8985 were used for thermochemistry. <sup>b</sup> Frequencies scaled by 0.9044 were used for thermochemistry. <sup>c</sup> These frequencies are not scaled.TABLE 3. Calculated and Experimental <sup>13</sup>C Chemical Shifts for Twist-Boat *cis*-1,4-Di-*tert*-butylcyclohexane (**1a**) in ppm ( $\delta$ ), Relative to TMS

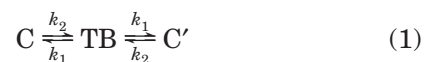
carbon no. <sup>a</sup>	HF/6-31G <sup>*</sup>	HF/6-311+G <sup>*</sup>	assignment <sup>b</sup>	average <sup>c</sup>	experimental $T = -157.8$ °C
12	20.8588	20.8243	N	20.824	21.809
8	20.8588	20.8244	N		
6	19.7126	21.0202	K		
3	19.7126	21.0202	K		
2	22.1428	23.6398	K	22.330	22.965
5	22.1424	23.6399	K		
9	26.4954	27.2091	H		
13	26.4954	27.2091	H		
14	27.9206	28.6759	H	27.943	29.846
10	27.9207	28.6760	H		
7	27.0490	30.3827	E		
11	27.0490	30.3827	E	30.383	33.065
4	34.0463	37.2194	B	37.219	41.387
1	34.0462	37.2194	B		

<sup>a</sup> The carbon number assignments are shown in Figure 1. <sup>b</sup> Letters are assigned to peaks and carbons of **1a** in Figure 2. <sup>c</sup> Chemical shifts calculated at the HF/6-311+G<sup>\*</sup> level are averaged according to the observed time-averaged  $C_{2v}$  symmetry.

four intense peaks at -157.8 °C (E, H, K, and N) are also assigned to **1a**. The finding of one CH<sub>2</sub> peak (K) and two methyl carbon peaks (H and N) in a ratio of 2:1 confirms the rapid pseudorotation of **1a**, which was expected;  $C_2$  symmetry for **1a** would result in three methyl carbon peaks of equal intensity and two CH<sub>2</sub> peaks. The assignments for the seven peaks discussed so far appear secure, but the remaining assignments for **1b** are somewhat speculative. These are based in part on the calculated chemical shifts in Table 4 and the positions of the broad peaks at -118.5 °C and the peaks for **1a** at -157.8 °C, relative to the positions at +18.0 °C for the averaged chemical shifts. No assignment is made at the lowest temperature for the central carbon of the equatorial *tert*-butyl group of **1b**, which could be under peak E, or for the methyl carbons of the trans isomer.

Peaks A, B, and C are well-suited for determining the populations of **1a** and **1b** and for line shape matching to

determine the rate constants and free-energy barriers to interconversion of the two conformations. Calculated line shapes<sup>27</sup> are based on the exchange scheme shown in eq 1



where C and C' represent the chair conformation and the inverted chair and TB is the twist-boat conformation. The experimental and calculated line shapes for three temperatures are shown in Figure 3, and the data used in these calculations and the rate constants and free-energy barriers<sup>28</sup> obtained are shown in Table 5.

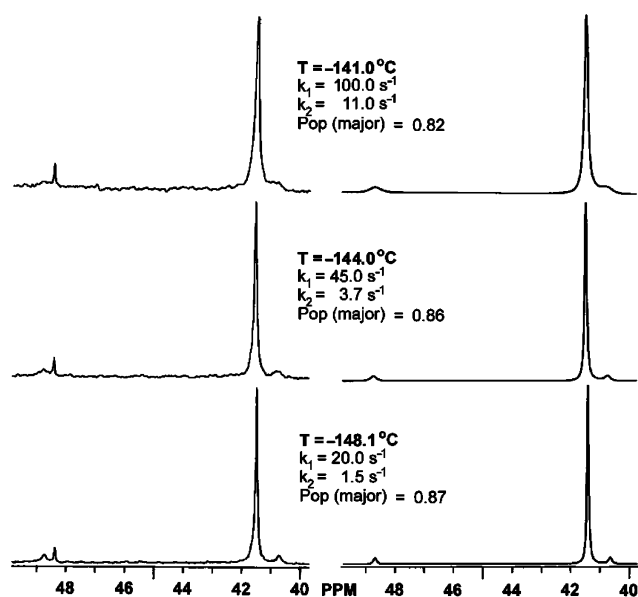
(27) Calculated spectra were obtained using the program DNMR-SIM written by G. Hagele and R. Fuhler, Heinrich-Heine University, Dusseldorf Institute of Inorganic and Structural Chemistry, Dusseldorf, FRG, 1994.



**TABLE 4.** Calculated and Experimental  $^{13}\text{C}$  Chemical Shifts for Chair *cis*-1,4-Di-*tert*-butylcyclohexane (**1b**) in ppm ( $\delta$ ), Relative to TMS

carbon no. <sup>a</sup>	HF/6-31G*	HF/6-311+G*	assignment <sup>b</sup>	average <sup>c</sup>	experimental $T = -157.8\text{ }^\circ\text{C}$
9	21.5282	21.4927	M	21.493	22.606
6	21.2348	22.8140	J		
2	21.5002	23.1443	J	22.979	24.191
3	23.9602	25.9648	I	26.537	27.785
14	26.0241	26.4677	L	26.468	22.717
5	24.8585	27.1089	I		
8	27.8203	28.5380	G	28.598	30.187
10	27.9507	28.6574	G		
12	28.3215	29.1363	F	29.966	30.339
7	27.2106	30.5876			
13	29.7232	30.7951	F		
11	27.9639	31.5344	D	31.534	34.771
4	34.1235	37.8543	C	37.854	40.606
1	40.4350	44.1375	A	44.138	48.622

<sup>a</sup> The carbon number assignments are shown in Figure 1. <sup>b</sup> Letters are assigned to peaks and carbons of **1b** in Figure 2. <sup>c</sup> Chemical shifts calculated at the HF/6-311+G\* level are averaged according to the observed time-averaged  $C_s$  symmetry.

**FIGURE 3.** Line shape analysis at three temperatures.**TABLE 5.** Parameters Used To Calculate Line Shapes for the  $^{13}\text{C}$  Spectra of *cis*-1,4-Di-*tert*-butylcyclohexane and the Free-Energy Barriers Obtained

$T\text{ (}^\circ\text{C)}$	line widths <sup>a</sup> (Hz)	populations		rate constants <sup>b</sup>		$\Delta G^{\ddagger c}$ (kcal/mol)	$\Delta G^{\ddagger d}$ (kcal/mol)
		major	minor	$k_1$ ( $\text{s}^{-1}$ )	$2k_2$ ( $\text{s}^{-1}$ )		
-141.0	3.80	0.82	0.18	100	22.0	6.31	6.71
-144.0	3.94	0.86	0.14	45	7.3	6.36	6.83
-148.1	4.20	0.87	0.13	20	3.0	6.35	6.83

<sup>a</sup> Line widths for the CH ring carbons of *trans*-1,4-di-*tert*-butylcyclohexane. <sup>b</sup>  $k_1$  and  $k_2$  are defined in eq 1. <sup>c</sup> Free-energy barriers for conversion of **1b** to **1a**. <sup>d</sup> Free-energy barriers for conversion of **1a** to **1b**.

The decrease in the chair-to-twist-boat free-energy barriers on going from **2** ( $\Delta G^\ddagger = 10.3\text{ kcal/mol}$ ) to **1** (6.31 kcal/mol at  $-141.0\text{ }^\circ\text{C}$ )<sup>6</sup> is expected as a consequence of the destabilization of the chair conformation of **1** by steric interactions. The chair and twist-boat free-energy dif-

ferences for **1**, calculated from  $-RT\ln K$ , are 0.40, 0.47, and 0.47 kcal/mol at  $-141.0$ ,  $-144.0$ , and  $-148.1\text{ }^\circ\text{C}$ , respectively. The calculations predict 1.74 (MM3), 0.59 (MM4), and 1.13 kcal/mol (HF/6-311+G\*) at  $-150.0\text{ }^\circ\text{C}$  (Tables 1 and 2). The MM4 value comes closest to the experimental number, and the other two calculations overestimate the preference for the twist-boat conformation. As noted above, the small values for the low frequencies contribute to the uncertainties in the free energies.

The finding that **1a** is more stable than **1b** by 0.47 kcal/mol at  $-144.0\text{ }^\circ\text{C}$  indicates that a twist-boat conformation of *tert*-butylcyclohexane (**7**) should also be lower in energy than the axial chair conformation. Recent ab initio calculations<sup>29</sup> for **7** at the MP2/6-311+G\*\*//MP2/6-31G\* level found relative energies of 0.00, 4.98, and 5.11 kcal/mol for the equatorial chair, twist-boat, and axial chair conformations, respectively. The zero point energies, calculated from scaled frequencies determined at the HF/6-31G\* level, were 169.92, 170.18, and 170.00 kcal/mol. Other ab initio calculations<sup>30</sup> for **7**, which did not include the twist-boat, found relative free energies at  $27\text{ }^\circ\text{C}$  of 0.0, 5.45, and 10.52 kcal/mol for the equatorial ( $C_1$ ), axial ( $C_1$ ), and axial ( $C_s$ ) conformations, and an axial-equatorial free-energy difference of 5.74 kcal/mol was found<sup>31</sup> at the QCISD/6-311G\*\*//MP2/6-311G\* level. An indirect experimental study<sup>32</sup> estimated a free-energy difference of 4.9 kcal/mol for axial and equatorial **7**.

The axial conformation of methylcyclohexane is 1.80 kcal/mol higher in free energy than the equatorial conformation.<sup>29</sup> The difference in stability is often explained in terms of steric repulsion between an axial methyl group and the axial hydrogens on carbons 3 and 5 of the ring, but alternative explanations have been proposed. Unfavorable steric interaction between an axial methyl group and the ring carbons, including the gauche torsional interaction, has been suggested<sup>29</sup> to be the major factor in destabilizing the axial conformation. Another explanation in terms of hyperconjugation has

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been proposed.<sup>33,34</sup> The authors concluded<sup>34</sup> that the conformational energies were dominated by hyperconjugation interactions involving the methine hydrogen. Recent calculations predict<sup>31</sup> that hyperconjugation destabilizes the axial conformation of methylcyclohexane by 0.10 kcal/mol but stabilizes the axial conformation of **7** by 1.30 kcal/mol.

## Conclusions

A dynamic NMR study of **1** showed that a twist-boat conformation is favored over the chair conformation, which has an axial *tert*-butyl group, by 0.47 kcal/mol at  $-144.0\text{ }^{\circ}\text{C}$ . Calculations predicted that a twist-boat conformation with diequatorial substitution (**1a**) was favored and that placing the *tert*-butyl groups in isoclinal positions (**1c**) raised the free energy above that of the chair. Calculations also showed that equilibration of the enantiomeric forms of **1a** should be rapid on the NMR time scale at low temperatures, which was confirmed by the observation of one  $\text{CH}_2$  peak instead of two and two methyl signals instead of three at slow exchange. The different symmetries for **1a** and **1b** made possible an unambiguous assignment of peaks. The free-energy barrier (6.31 kcal/mol at  $-141.0\text{ }^{\circ}\text{C}$ ) for conversion of **1b** to **1a** is lower than for cyclohexane, due to destabilization of the ground state of **1b** by steric interactions. The results for **1** suggest that for *tert*-butyl cyclohexane (**7**), a twist-boat conformation should be favored over the axial chair. Other di-*tert*-butyl cyclohexanes may also have measurable amounts of chair and twist-boat conformations, and conformational studies of the 1,1-, *trans*-1,2-, and *trans*-1,3-isomers by dynamic NMR and computational methods are in progress.

## Experimental and Methods Section

1,4-Di-*tert*-butylbenzene (95% pure, 4.0 g) was stirred in a 500 mL flask with 425 mg of platinum(IV) oxide and 100 mL of acetic acid. A condenser equipped with a balloon was attached, and the apparatus was evacuated before filling with hydrogen. The mixture was stirred at an average temperature of  $105 \pm 5\text{ }^{\circ}\text{C}$  for 5 days, replenishing the hydrogen as necessary. The progress of the reaction was followed by  $^{13}\text{C}$  NMR spectroscopy. The resulting solution was filtered, neutralized with a concentrated solution of sodium hydroxide, extracted with ether, and dried over Drierite. The solvent was removed with a rotary evaporator, and the compound was shown by  $^{13}\text{C}$  NMR to have about 5% of the *trans* isomer.<sup>26</sup> Others<sup>18</sup> have reported the synthesis of **1** at  $25\text{ }^{\circ}\text{C}$  and atmospheric pressure with the same solvent and Pt as catalyst and have also found about 5% of the *trans* isomer, which could not be removed by preparative gas chromatography.<sup>18,35</sup> Removal of the *trans* isomer by partial freezing has been described,<sup>18</sup> with the liquid being enriched in **1**, but the yield of **1** was low (2%). Peaks from the *trans* isomer did not interfere with the low-temperature NMR study, which was carried out for the mixture.

A 2% solution in propane of this mixture of **1** and the *trans* isomer was prepared in a 5 mm thin-walled screw-capped NMR tube, and a small amount of TMS was added for an internal reference. *Caution:* high pressure. The sample tube was stored and handled below  $0\text{ }^{\circ}\text{C}$  most of the time. Spectra were recorded on a wide-bore NMR spectrometer operating at 75.57 MHz for carbon. The  $^{13}\text{C}$  spectra for **1** were obtained from  $+18.0$  to  $-165.0\text{ }^{\circ}\text{C}$  with a 5 mm dual probe. A pulse width of  $8.2\text{ }\mu\text{s}$ , corresponding to a tip angle of  $83^{\circ}$ , was used. The pulse repetition period was 1 s at all temperatures. A sweep width of  $\pm 9300\text{ Hz}$ , data size of 64 K, 800 pulses, and 3.0 Hz line broadening were used. Spinning was discontinued below about  $-140\text{ }^{\circ}\text{C}$ . Because ejecting the sample at lower temperatures was difficult, due to ice formation on the inner wall of the stack, the temperature calibrations were performed separately, using a copper–constantan thermocouple immersed in propane solvent contained in a nonspinning dummy sample tube and under conditions as nearly identical as possible. The emf's were measured with a millivolt potentiometer. The uncertainty in the temperatures was estimated to be  $\pm 2\text{ }^{\circ}\text{C}$ .

The initial structure for *cis*-1,4-di-*tert*-butylcyclohexane was generated using Spartan<sup>36</sup> 5.0, and the geometry was exported into Allinger's molecular mechanics (MM3 2000) program. A default stochastic method for searching conformational space was used with a kick size of 2 Å and 1000 pushes. Calculations were repeated with the MM4 force field. Three of the structures (**1a–c**) organized in order of increasing strain energy are shown in Figure 1.

The Cartesian coordinates from MM3 were used to prepare input for ab initio calculations. Full-geometry optimizations were done in each case at the HF/6-31G\* level, and calculations were repeated at the HF/6-311+G\* level. The optimizations were followed by calculations of vibrational frequencies (analytically) for all conformations, and minimum-energy structures were characterized by the absence of imaginary frequencies. A boat conformation (**1d**;  $C_{2v}$  symmetry) was generated and optimized as a transition state by ab initio calculations, and the output from the HF/6-311+G\* level was used as the input for MM3 and MM4 calculations.

Isotropic shielding tensors were calculated for **1a**, **1b**, and TMS at the HF/6-311+G\* level, and NMR chemical shifts were obtained. All calculations were done using the Gaussian 03<sup>24,25</sup> programs, and visualizations were done with either Spartan<sup>36</sup> or Molden.<sup>37</sup>

**Acknowledgment.** We thank the National Science Foundation (CREST Grant No. HRD-9805465) for support of this work and the Mississippi Center for Supercomputing Research for a generous amount of time on the SGI Altrix 3700 and Origin 2800 supercomputers. Some of the calculations were done using the molecular modeling laboratory at Jackson State University, supported by the Army High Performance Computing Research Center.

**Supporting Information Available:** The Cartesian coordinates and calculated energies for all four conformations of *cis*-1,4-di-*tert*-butylcyclohexane at the HF/6-31G\* and HF/6-311+G\* levels. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO051654Z

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