Thermodynamic, Conformational, and Chemical Reactivity Studies of the 2,5-Di-*t*-butylcyclohexyl System. The Reversal of the Thermodynamic Stability with Chemical Reactivity Trends of Cyclohexyl Derivatives[1]

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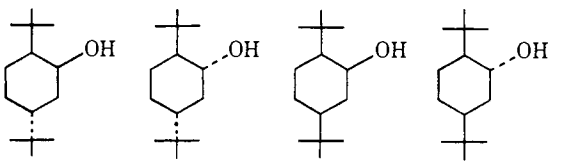
Abstract: The four stereoisomeric 2,5-di-*t*-butylcyclohexanols have been prepared and subjected to detailed thermodynamic and conformational analysis, and chemical reactivity studies. The *cis,trans*-isomer **1**, which exists in a chair conformation with an axial hydroxyl, is more thermodynamically stable than the *trans,cis*-isomer **2** which exists in a chair conformation with an equatorial hydroxyl. The *cis,cis*-isomer **3** exists exclusively in a twist-boat conformation. The *trans,trans*-isomer **4** exists as a mixture of chair (34%) and twist-boat conformations (66%). The detailed conformational analysis of the four alcohols provides the following vicinal *gauche* interaction enthalpies (kcal/mol): for the chair conformation, $t\text{-Bu}_{eq}\text{–OH}_{eq}$, >1.3 and $t\text{-Bu}_{ax}\text{–OH}_{eq}$, >2.0; for the twist-boat conformation, $t\text{-Bu}_{p\text{-}eq}\text{–OH}_{p\text{-}eq}$, ~0.6 and $t\text{-Bu}_{p\text{-}eq}\text{–OH}_{p\text{-}ax}$, >1.5. The ΔG for hydroxyl in the 2,5-di-*t*-butylcyclohexyl system constrained in a twist-boat conformation is ~0.6 kcal/mol. The tosylates of **1**, **2**, and **4** were prepared and subjected to ethanolysis. The axial tosylate of **1** reacts faster than the equatorial tosylate of **2** despite the fact that **1** is more thermodynamically stable! From these studies we conclude that (1) the equatorial tosylates in the 2-mono-*t*-butyl- and 2,5-di-*t*-butylcyclohexyl systems do not solvolyze *via* a boat conformation with an axial tosylate, (2) hydrogen participation is not a dominant factor in determining the rates of solvolysis in these systems, and (3) torsional angle effects play a very important role in determining reactivity in these systems. The solvolysis of the axial tosylates of the *cis*-alcohols **1** and **3** produces only 1,4-di-*t*-butylcyclohexene by a net *anti* elimination, whereas the equatorial tosylates of **2** and **4** give mixtures of *trans*- and *cis*-3,6-di-*t*-butylcyclohexene and 1,4-di-*t*-butylcyclohexene, respectively, the 1,4-di-*t*-butylcyclohexene arising by a net *syn* elimination. The relative reactivities of the four alcohols in chromic acid oxidation parallel the rates of the tosylate solvolysis reactions. Again, the more thermodynamically stable alcohol **1** reacts faster than **2** in contrast to previously observed trends. The rates of acetylation of the four alcohols are consistent with the trends observed for the acetylation of other substituted cyclohexanols. The acetylation rate data do not provide a sensitive probe to evaluate the steric factors leading to the observed thermodynamic trends in these systems.

Since the initial recognition by Barton of the effect of conformation of the thermodynamics and chemical reactivity of cyclohexane derivatives,[3] numerous studies have been carried out in this area. The universal trend has been that (1) equatorially substituted cyclohexanes are more thermodynamically stable than axially substituted systems, (2) reactions at an equatorial substituent are more facile than with axial substituents, and (3) reactions involving the loss of an axial substituent are more facile than with equatorial substituents. A number of rationales have been advanced in the literature which will receive further attention later in this article.

Recently we observed that the hydroxyl in the 2-*t*-butyl- and the *trans*-2,5-di-*t*-butylcyclohexane systems is thermodynamically more stable in the axial position than in the equatorial position.[4] In view of this unusual finding we have studied various chemical reactions of the four stereoisomeric 2,5-di-*t*-butylcyclohexanols (**1**, **2**, **3**, and **4**). These studies have provided some new and interesting insights on the steric interactions of a *t*-butyl group in the cyclohexane system and on the factors which govern the reactivity of substituted cyclohexanes.



1 (*cis,trans*) **2** (*trans,cis*) **3** (*cis,cis*) **4** (*trans,trans*)

Thermodynamic Relationships. The four stereoisomeric 2,5-di-*t*-butylcyclohexanols were equilibrated over Raney nickel (W-2) in cyclohexane (0.2 *M* initial concentration) at temperatures ranging from 78.5 to 179.0°; at higher temperatures extensive decomposition occurred. The rates of attainment of equilibrium were quite slow, requiring 15 days at 78.5°, 10 days at 116°, 3 days at 146°, and 24 hr at 179°. Analysis of the equilibrium mixtures was carried out by glpc using a 45-ft, 5% Carbowax 20 M on Chromosorb G column at 190°. At each temperature the equilibrium was approached from at least two of the alcohols. The equilibrium constants for the various equilibria are given in Table I. The thermodynamic parameters for the various equilibria were calculated and are given in Table II and in Figure 1. Similar data for the 2-*t*-butylcyclohexanol system are also contained in Table I.

In the equilibria involving the *cis,trans*- and *trans,cis*-2,5-di-*t*-butylcyclohexanols and the *cis*- and *trans*-2-*t*-

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(2) Alfred P. Sloan Research Fellow, 1967–1969.

(3) D. H. R. Barton, *Experientia*, **6**, 316 (1950).

(4) D. J. Pasto and R. D. Rao, *J. Amer. Chem. Soc.*, **91**, 2790 (1969).

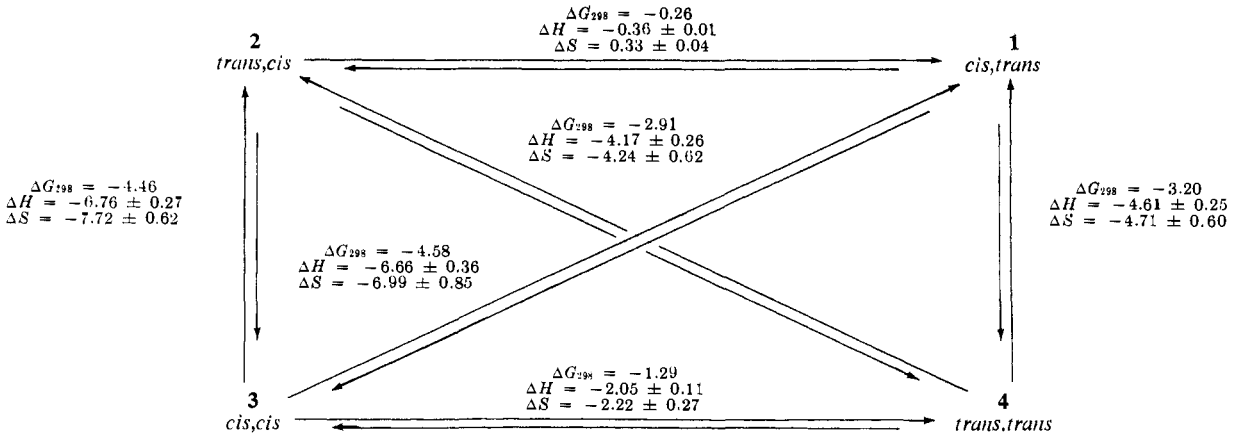


Figure 1. Thermodynamic relationships between the stereoisomeric 2,5-di-*t*-butylcyclohexanols (ΔG and ΔH in kilocalories/mole and ΔS in entropy units).

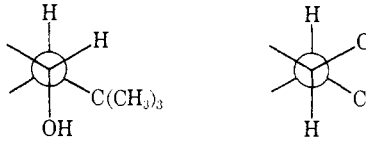
butylcyclohexanols *the isomers with the axial hydroxyl are more thermodynamically stable than the isomers with the equatorial hydroxyl.* To the authors' knowledge these are the first systems reported in which the axial hydroxyl isomers are more stable than their equatorial hydroxyl counterparts. Sicher and Tichy[5] have determined the *gauche* interaction energies between methyl and hydroxyl in the 4-*t*-butyl-2-methylcyclohexanols. In this system the *gauche* interaction energies are: $CH_{3_{eq}}$-OH_{eq}, 0.38; $CH_{3_{eq}}$-OH_{ax}, 0.66; and $CH_{3_{ax}}$-OH_{eq}, 0.83 kcal/mol. Sicher attributes the higher values for the axial-equatorial *gauche* interactions as being due to the known flattening of the cyclohexane ring resulting in a decrease in the axial-equatorial dihedral angle. In the present systems it is obvious that this trend is reversed, *i.e.*, the equatorial-equatorial *gauche* interaction is greater than the axial-equatorial interaction.

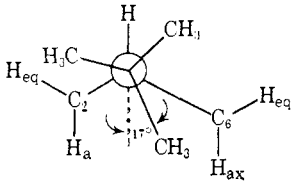
Table I. Equilibrium Constants for the Isomeric Mono-2-*t*-butyl and 2,5-Di-*t*-butylcyclohexanols

	Temp, °C	Equilibrium constant
trans,cis (**2**) ⇄ *cis,trans* (**1**)	78.5	1.41 ± 0.02
	116.0	1.35 ± 0.02
	145.0	1.30 ± 0.02
	179.0	1.26 ± 0.02
trans,trans (**4**) ⇄ *cis,trans* (**1**)	116.0	35.6
	145.0	22.7
	179.0	15.5
cis,cis (**3**) ⇄ *trans,trans* (**4**)	116.0	4.66 ± 0.15
	145.0	3.81 ± 0.22
	179.0	3.22 ± 0.12
cis,cis (**3**) ⇄ *trans,cis* (**2**)	116.0	127.1
	145.0	66.5
	179.0	37.6
cis,cis (**3**) ⇄ *cis-trans* (**1**)	116.0	166.1
	145.0	87.4
	179.0	50.0
trans,trans (**4**) ⇄ *trans,cis* (**2**)	116.0	26.4 ± 2.0
	145.0	17.4 ± 0.2
	179.0	12.5 ± 0.6
trans-2-*t*-Butyl ⇄ *cis*-2-*t*-Butyl	78.5	2.03 ± 0.01
	110.5	1.88 ± 0.02
	142.0	1.70 ± 0.02

(5) J. Sicher and M. Tichy, *Collect. Czech. Chem. Commun.*, **32**, 3687 (1967).

Inspection of undistorted models of the di-*t*-butylcyclohexyl system does not reveal any clue as to what causes the axial isomer to be more stable. The C–OH, C–*t*-Bu dihedral angles in both the axial and equatorial isomers are the same, as are also remote steric interactions between the hydroxyl and the methyl groups of the 2-*t*-butyl group. The *t*-butyl group must cause a distortion of the molecule[6] such that a rather severe interaction is developed between the equatorial hydroxyl and equatorial 2-*t*-butyl group. Calculations by Altona[7] indicate that in the most stable rotational conformation the *t*-butyl group of *t*-butylcyclohexane is rotated by approximately 17°, accompanied by a twisting of the cyclohexane ring, producing a strong repulsive interaction between one of the *t*-butyl methyls and the 2-equatorial hydrogen. The results of these calculations are consistent with the observed greater stability of the axial isomers.





A minimum value for this OH_{eq}–*t*-Bu_{eq} interaction enthalpy is estimated to be 1.3 kcal/mol (ΔH for the *trans,cis* ⇄ *cis,trans* equilibrium + ΔH for an axial hydroxyl in 3-*t*-butylcyclohexanol). The small ΔS for the *trans,cis* ⇄ *cis,trans* equilibrium may be due to the possible loss of a certain degree of flexibility of the distorted *t*-butylcyclohexane system in the *trans,cis*

(6) Chemical evidence has been presented that the *t*-butyl group causes a distortion of the normal geometry about the ring carbon (D. J. Pasto and F. M. Klein, *J. Org. Chem.*, **33**, 1468 (1968), and references cited therein; see also M. Pankova, J. Sicher, M. Tichy, and M. C. Whiting, *J. Chem. Soc., B*, 365 (1968)). This is also evident in the greater *A* values for substituents in the 3-*t*-butylcyclohexyl system relative to the 4-*t*-butylcyclohexyl system (see Pankova, *et al.*).

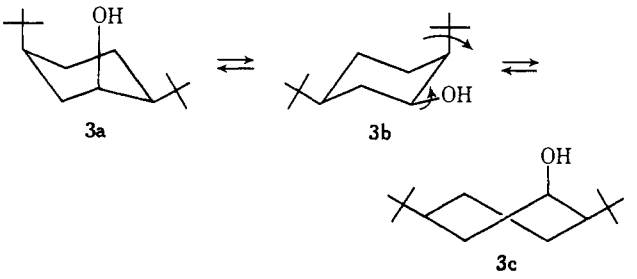
(7) C. Altona and M. Sundaralingam, *Tetrahedron*, **26**, 925 (1970).

Table II. Thermodynamic Parameters for the Equilibria of the Isomeric Mono-2-*t*-butyl and 2,5-Di-*t*-butylcyclohexanols

	ΔG_{298}, kcal/mol	ΔH, kcal/mol	ΔS, eu
trans,cis (2) ⇄ *cis,trans* (1)	−0.26	−0.36 ± 0.01	0.33 ± 0.04
trans,trans (4) ⇄ *cis,trans* (1)	−3.20	−4.61 ± 0.25	−4.71 ± 0.60
cis,cis (3) ⇄ *trans,trans* (4)	−1.29	−2.05 ± 0.11	−2.22 ± 0.27
cis,cis (3) ⇄ *trans,cis* (2)	−4.46	−6.76 ± 0.27	−7.72 ± 0.62
cis,cis (3) ⇄ *cis,trans* (1)	−4.58	−6.66 ± 0.36	−6.99 + 0.85
trans,trans (4) ⇄ *trans,cis* (2)	−2.91	−4.17 ± 0.26	−4.24 ± 0.62
trans-2-*t*-Butyl ⇄ *cis*-2-*t*-butyl	−1.06	−0.80 ± 0.10	−0.87 ± 0.14

isomer and/or the restriction of certain hydroxyl rotational conformations (see discussion on hydrogen bonding effects).

The highly negative ΔH and ΔS values for the *cis,cis* ⇄ *trans,cis* and *cis,cis* ⇄ *cis,trans* equilibria are consistent with twist-boat ⇄ chair interconversions. The possibility that the *cis,cis* isomer may exist in a chair ⇄ twist-boat equilibrium was investigated by variable-temperature infrared techniques. No changes in relative ban intensities were noted (+40 → −90°, 3% in CS_2) indicating that the *cis,cis* isomer must exist almost exclusively (>95%) in a single conformation. However, it is difficult to understand why chair conformations are not present in the *cis,cis* isomer in solution. The chair conformation **3a** is obviously of



3a **3b** **3c**

very high energy, containing an axial *t*-butyl group and an axial hydroxyl, as well as an expectedly severe 1,3-diaxial interaction between the axial *t*-butyl and hydroxyl groups. Conformation **3b**, containing only an axial 2-*t*-butyl, must be deformed (as indicated by the arrows) causing a severe OH_{eq}–*t*-Bu_{ax} interaction. This interaction enthalpy must be $\gtrsim$2.1 ± 0.4 kcal/mol.[8]

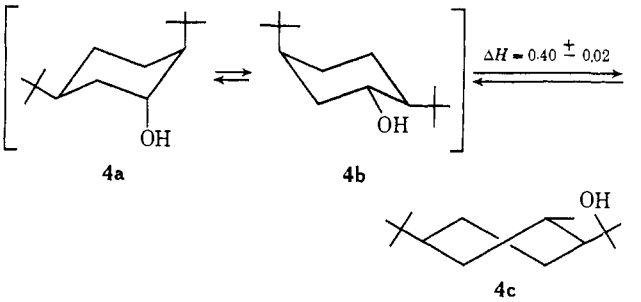
The total interaction enthalpy for the pseudoaxial hydroxyl ($\Delta H_{OH_{p\text{-}ax}} + \Delta H_{OH_{p\text{-}ax}\text{-}t\text{-}Bu_{p\text{-}eq}}$) is calculated to be ≥2.1 ± 0.5 kcal/mol.[9] As $\Delta H_{OH_{p\text{-}ax}}$ should be smaller than $\Delta H_{OH_{ax}}$ in a chair conformation, the majority (an estimated 1.6 kcal/mol) of the 2.1 kcal/mol must arise from the $\Delta H_{OH_{p\text{-}ax}\text{-}t\text{-}Bu_{p\text{-}eq}}$ interaction.

The thermodynamic parameters for the various equilibria involving the *trans,trans* isomer (**4**) indicate that the *trans,trans* isomer is not conformationally homogeneous. The ΔG, ΔH, and ΔS values for the conversion of the *cis,cis* isomer (**3**) to either the *cis,trans* (**1**) or *trans,cis* isomer (**2**) *via* the *trans,trans* isomer (**4**) indicate that ~34% of the *trans,trans* isomer exists in a chair conformation. Variable temperature infrared measurements showed very distinct changes in band intensities with changes in temperature. The intensities of bands at 1032 and 1016 cm^{-1} (apparently belonging to the twist-boat and chair conformations) were measured, and the "equilibrium" constants were calculated (see Table III). A ΔH for the equilibrium

Table III. Variable-Temperature Data for *trans,trans*-2,5-Di-*t*-butylcyclohexanol

Temp, °C	$K(abs_{1016\ cm^{-1}}/abs_{1032\ cm^{-1}})$
−32.0	1.25
−19.0	1.21
−7.0	1.18
34.5	1.03
68.0	0.98
97.0	0.92

was calculated to be 0.40 ± 0.02 kcal/mol.



4a **4b** **4c**

The enthalpies for the three conformations of the *trans,trans* isomer shown can be approximated from previously published conformational enthalpies. **4a** contains an axial *t*-butyl and an axial hydroxyl for a total of 6.3 kcal/mol (5.4 + 0.9); however, this value is probably somewhat high as an expected flattening of the ring due to the axial *t*-butyl would be expected to reduce the ΔH for the axial hydroxyl. **4b** contains an axial *t*-butyl and an OH_{eq}–*t*-Bu_{eq} interaction for a total of ≥6.7 kcal/mol (5.4 + ≥1.3). Thus **4a** is

(8) The OH_{eq}–*t*-Bu_{ax} interaction enthalpy is calculated from eq i

$$\Delta G_{3b\rightleftarrows 3c} = (\Delta H_{3c\ total} - T\Delta S_{3c}) - (\Delta H_{3b\ total} - T\Delta S_{3b}) \quad \text{(i)}$$

where $\Delta H_{3c\ total}$ is the total functional group interaction enthalpy and is equal to ($\Delta H_{3\rightleftarrows 2}$ + $\Delta H_{OH_{eq}\text{-}t\text{-}Bu_{eq}}$) = (6.76 + >1.2) kcal/mol, $T\Delta S_{3c}$ is calculated using $\Delta S_{3\rightleftarrows 2}$ and is −2.3 kcal/mol, $\Delta H_{3b\ total}$ is ($\Delta H_{t\text{-}Bu_{ax}}$ + $\Delta H_{OH_{eq}\text{-}t\text{-}Bu_{ax}}$) and is (5.4 + $\Delta H_{OH_{eq}\text{-}t\text{-}Bu_{ax}}$), and $T\Delta S_{3b}$ is assumed to be 0 for the chair conformation. Assuming that $\Delta G_{OH_{eq}\text{-}t\text{-}Bu_{ax}}$ = $\Delta H_{OH_{eq}\text{-}t\text{-}Bu_{ax}}$ in **3b**, on substitution into eq i $\Delta H_{OH_{eq}\text{-}t\text{-}Bu_{ax}}$ is calculated to have a minimum value of 2.1 ± 0.4 kcal/mol. Similar calculations using the thermodynamic data for the *cis,cis* ⇄ *cis,trans* equilibrium give a calculated value for $\Delta H_{OH_{eq}\text{-}t\text{-}Bu_{ax}}$ of ≥1.8 kcal/mol.

(9) $\Delta H_{OH_{p\text{-}ax}}$ is calculated using eq ii

$$\Delta H_{3\rightleftarrows 2} = \Delta H_{3c\ total} - \Delta H_{2\ total} \quad \text{(ii)}$$

where $\Delta H_{3c\ total}$ is ($\Delta H_{t\text{-}boat}$ + $\Delta H_{OH_{p\text{-}ax}}$ + $\Delta H_{OH_{p\text{-}ax}\text{-}t\text{-}Bu_{p\text{-}eq}}$) and is equal to (5.6[10] + $\Delta H_{OH_{p\text{-}ax}}$ + $\Delta H_{OH_{p\text{-}ax}\text{-}t\text{-}Bu_{p\text{-}eq}}$) and $\Delta H_{2\ total}$ is $\Delta H_{OH_{eq}\text{-}t\text{-}Bu_{eq}}$ and is ≥1.2 kcal/mol from which the total interaction enthalpy involving the pseudoaxial hydroxyl is calculated to be ≥2.1 ± 0.5 kcal/mol. Similar calculations using the thermodynamic data for the *cis,cis* ⇄ *cis,trans* equilibrium give a value of 1.9 ± 0.4 kcal/mol.

(10) N. L. Allinger and L. A. Freiberg, *J. Amer. Chem. Soc.*, **82**, 2393 (1960); W. S. Johnson, V. J. Bauer, J. L. Margrove, M. A. Frish, L. H. Dreger, and W. N. Hubbard, *ibid.*, **83**, 606 (1961).

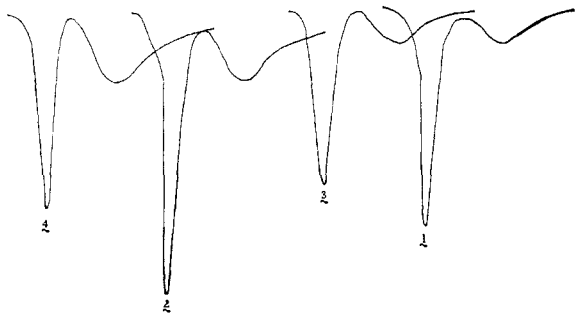


Figure 2. O–H stretching bands of the 2,5-di-*t*-butylcyclohexanols in CCl_4 (0.2 *M*).

expected to be more stable than **4b** by ≥ 0.3 kcal/mol, indicating that both conformations must be present in measurable quantities.

As Allinger[11] has suggested that a twist-boat conformation with an equatorial *t*-butyl is favored over a chair conformation with an axial *t*-butyl by 0.37 kcal/mol, and as the ΔH for the $\mathbf{4}_{chair} = \mathbf{4}_{twist\text{-}boat}$ equilibrium is -0.4 kcal/mol, the $OH_{p\text{-}eq}$–*t*-$Bu_{p\text{-}eq}$ interaction enthalpy in **4c** must be ~ 0.6 kcal/mol. This value is substantially lower than the ΔH for OH_{eq}–*t*-Bu_{eq} in the *trans,cis* isomer of ≥ 1.3 kcal/mol and must be due to a decreased interaction between the OH_{eq} and the methyl groups of the *t*-butyl group.

The conformations assigned to **1**, **2**, and **3**, and for the major conformation of **4**, are nicely supported by ir, nmr, and chemical reactivity trends discussed in the following sections of this paper.

Ir and Nmr Spectral Properties of 1, 2, 3, and 4. The infrared spectra of the four alcohols were recorded in CCl_4 solution. The monomeric O–H stretching bands are given in Table IV along with similar data for the

Table IV. O–H Stretching Frequencies in Dilute CCl_4 Solution

Alcohol	ν_{O-H}, cm^{-1}
1	3620
2	3613
3	3622
4	3616
trans-2-*t*-Butylcyclohexanol	3617[a]
cis-2-*t*-Butylcyclohexanol	3626[a]
trans-4-*t*-Butylcyclohexanol	3624[a]
cis-4-*t*-Butylcyclohexanol	3638.5[a]

[a] See ref 12.

2- and 4-*t*-butylcyclohexanols.[12] In general, the O–H stretching band for axial alcohols occurs at higher frequency than for equatorial alcohols.[12] The O–H stretching band of the *cis,cis* isomer (**3**) occurs at 3622 cm^{-1} consistent with a pseudoaxial hydroxyl, whereas the O–H stretching band for the *trans,trans* isomer (**4**) occurs at 3616 cm^{-1} consistent with a pseudoequatorial hydroxyl in the more dominant conformation **4c**. *All ν_{O-H} bands are consistent with the assigned conformations.*

The trends in hydrogen bonding are also consistent (see Figure 2) with the assigned structures, and surprisingly show little steric inhibition to hydrogen bonding by the 2-*t*-butyl group. All of the alcohols have broad bands centered around 3480–3485 cm^{-1}. In general the equatorial alcohols are more highly hydrogen bonded than their axial counterparts. The extent of hydrogen bonding, as evaluated by dilution studies, decreases in the order **4** > **2** > **3** > **1**.

The nmr data for the carbinol hydrogens for **1**–**4** are given in Table V. The axial carbinol hydrogen of

Table V. Chemical Shifts and Band Widths for the Carbinol Hydrogens in **1**–**4**

Compd	δ (20% in CCl_4)	Band width at half-height, Hz
1	4.25	8.5
2	3.45	19
3	4.18	12.5
4	3.97	7.5

2 appears at higher field than the equatorial carbinol hydrogen in **1**, and also has a wider band width than the equatorial hydrogen in **1**. These data are consistent with the chemical shift and band width trends reported in the literature.[13] The low-field chemical shift of the carbinol hydrogen of **3** is consistent with its pseudoequatorial nature in **3c**; the band width is slightly greater than for an equatorial hydrogen in a chair conformation, but considerably smaller than for an axial hydrogen. The chemical shift of the carbinol hydrogen in **4** is intermediate between purely axial and equatorial hydrogen shifts and is consistent with a nonconformationally homogeneous system.

Solvolysis of the Stereoisomeric 2,5-Di-*t*-butylcyclohexyl Tosylates. The relationship between the structure and the reactivity of substituted cyclohexyl tosylates has received considerable attention. In general, axial tosylates solvolyze faster than their equatorial counterparts, and, in the 2-alkylcyclohexyl tosylates, the *cis* isomer reacts more rapidly than the *trans* isomer. The greater reactivity of the axial tosylates over equatorial tosylates has been attributed to steric acceleration of the axial isomer,[14] due to 1,3-diaxial interactions in the ground state which are relieved in going to the transition state, and hydrogen participation by the 2- and 6-axial hydrogens.[15] Shiner and Jewett[16] and Saunders and Finley[17] have measured hydrogen–deuterium isotope effects (k_H/k_D) in 2- and 6-deuterated 4-*t*-butyl- and cyclohexyl tosylates and have interpreted their results in terms of hydrogen participation. Shiner and Jewett[16] suggested that the much larger k_H/k_D for the axial 2-hydrogen relative to the equatorial 2-hydrogen in **5** is the result of "neighboring hydrogen participation in the solvolytic transition state."[18]

(11) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski, and F. A. Van-Catledge, *J. Amer. Chem. Soc.*, **90**, 1199 (1968).

(12) H. S. Aaron, C. P. Ferguson, and C. P. Rader, *ibid.*, **89**, 1431 (1967).

(13) R. U. Lemieux, R. H. Kulling, H. J. Bernstein, and W. G. Schneider, *ibid.*, **80**, 6098 (1958); E. L. Eliel, M. H. Gianni, Th. H. Williams, and J. B. Stothers, *Tetrahedron Lett.*, 741 (1962).

(14) S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, 77, 5562 (1955).

(15) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan, and H. Marshall, *ibid.*, **74**, 1127 (1952).

(16) V. J. Shiner and J. G. Jewett, *ibid.*, **87**, 1382, 1383 (1965).

(17) W. H. Saunders, Jr., and K. T. Finley, *ibid.*, 87, 1384 (1965).

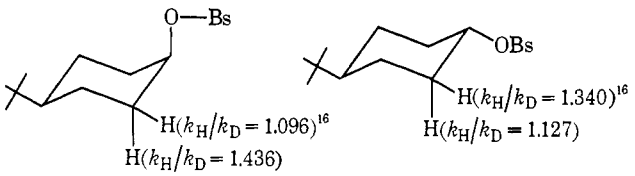
(18) Two modes of participation are available. Shiner and Jewett[16] suggested participation *via* transition state i. An alternate possibility is that shown in transition state ii. The isotope effect in transition state i arises from changes in both bending and stretching modes (and implies

Table VI. Rate Data for the Solvolysis of Cyclohexyl Tosylates

Cyclohexyl tosylate	Temp, °C	$K_1 \times 10^5$, sec^{-1}	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
trans,cis-2,5-Di-*t*-butyl	25.0	0.180	26.3 ± 0.24	3.32 ± 0.14
	44.8	3.00		
	65.1	35.0		
	30.0[a]	0.394		
cis,trans-2,5Di-*t*-butyl	25	2.06	25.23 ± 0.25	4.59 ± 0.09
	44.8	29.2		
	30.0[a]	4.36		
trans,trans-2,5-Di-*t*-butyl	25.0	1.038	24.6 ± 0.24	1.02 ± 0.14
	44.8	14.3		
	65.0	140.4		
	30.0[a]	2.73		
trans-4-*t*-Butyl[b]	30.0[a]	0.0055	26.6	−4
cis-4-*t*-Butyl[b]	30.0[a]	0.015	22.2	−8
trans-2-*t*-Butyl[c]	30.0	0.57		
cis-2-*t*Butyl[c]	30.0	2.84		

[a] Extrapolated from other temperatures. [b] Reference 14. [c] Reference 18.

The larger k_H/k_D for the equatorial hydrogen relative to the axial hydrogen in **6** was interpreted as indicating

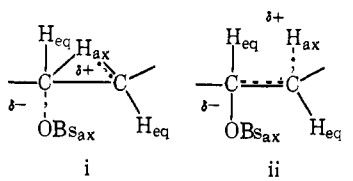


5 **6**

that **6** solvolyzes *via* "a nonchair conformation (twist-boat)"[16] in which the brosylate and the originally equatorial hydrogen become axial. Based on the observation that the *cis/trans* solvolysis rate ratio for the 2-*t*-butylcyclohexyl tosylates was very small (~3) relative to the 2-methyl- and 2-isopropylcyclohexyl tosylates (*cis/trans* rate ratio of ~100), Goering and Reeves[19] suggested that hydrogen participation in the transition state was perhaps not important. However, our earlier observation that the axial–equatorial ground-state stabilities for the 2-*t*-butyl systems are reversed relative to the 2-methyl and 2-isopropyl systems[4] makes Goering's argument tenuous. Sicher and coworkers[20] have recently suggested that *trans*-2-*t*-butylcyclohexyl tosylate is subject to an "unusually large acceleration of the solvolysis" and reacts by way of a boat conformation. Our present *results indicate that with the 2,5-di-t-butylcyclohexyl tosylates ground-state thermodynamic differences and hydrogen participation are not dominant factors controlling solvolytic reactivity, and that equatorial tosylates do not have to assume an axial orientation (either in another chair form or a twist form) for solvolysis.*

The rate data for the solvolysis of the tosylates of **1**, **2**, and **4** in absolute ethanol are given in Table VI.

rearrangement should be possible), whereas in ii essentially only a stretching mode is involved.



i ii

(19) H. L. Goering and R. L. Reeves, *J. Amer. Chem. Soc.*, **78**, 4931 (1956).

(20) M. Tichy, J. Hapala, and J. Sicher, *Tetrahedron Lett.*, 3739 (1969).

The tosylates of **1** and **2** could be prepared in pyridine under normal conditions; however, the reactions were relatively slow, requiring 3 days at room temperature for **1** and **2** and 15 days at 0° for **4**. The tosylate of **4** was very reactive and required storing at 0°. The tosylate of **3** could not be prepared, the rate of reaction with *p*-toluenesulfonyl chloride being very slow and the decomposition of the tosylate of **3** being rapid and giving only 1,4-di-*t*-butylcyclohexene. Attempts to prepare the benzenesulfonate and methanesulfonate of **3** were also unsuccessful.

The only solvolysis products obtained from the tosylates of **1**, **2**, and **4** were the 1,4- and 3,6-di-*t*-butylcyclohexenes (see Table VII); no alcohol or ether

Table VII. Products of Solvolysis of the Stereoisomeric 2,5-Di-*t*-butylcyclohexyl Tosylates

Tosylate	Solvent	Base	Reaction temp, °C	12	13	14
trans,cis	*t*-Butyl alcohol	*t*-Butoxide	82	67.0		33.0
trans,cis	Ethanol		78	68.0		32.0
cis,trans	Ethanol		78	100.0		
cis,trans	Ethanol	Ethoxide	78	100.0		
trans,trans	*t*-Butyl alcohol	*t*-Butoxide	82	82.0	18.0	
trans,trans	Ethanol		25	86.8	13.2	
trans,trans	Ethanol	Ethoxide	25	85.5	14.5	
trans,trans	Ethanol	Hydroxide	25	86.0	14.0	
trans,trans	Ethanol		78	95.5	4.5	
cis,cis	Pyridine[a]		0	100.0		

[a] Isolated as the only product in attempted tosylation of **3**.

products could be detected by glpc. Furthermore, only *trans*-3,6-di-*t*-butylcyclohexene was obtained from **4**, and only *cis*-3,6-di-*t*-butylcyclohexene was obtained from **1** and **2**.

The three isomeric 2,5-di-*t*-butylcyclohexyl tosylates were also solvolyzed in the presence of base (fivefold excess). No increases in the rate of the solvolysis reactions beyond experimental limits were detected. Rate constants calculated using the integrated form of the first-order rate equation were in excellent agreement with the first-order rate constants obtained in the absence of base. Again, only olefinic products were obtained; however, the distribution of the products varied slightly (see Table VII).

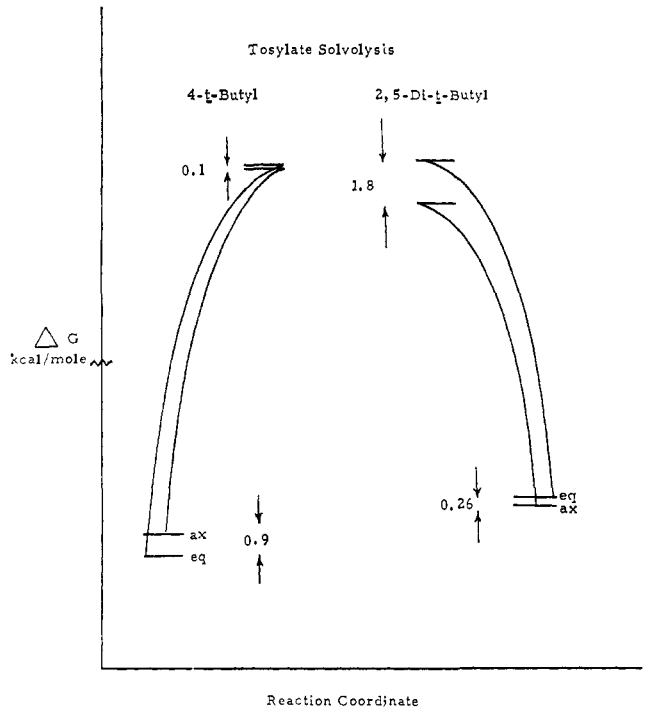
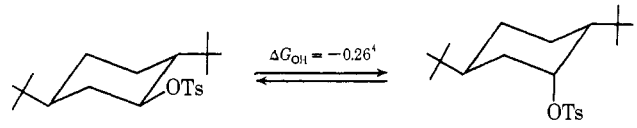


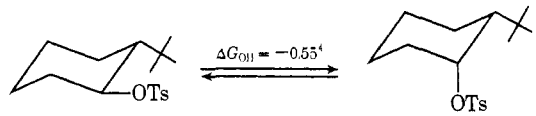
Figure 3. Free-energy diagram for the solvolysis of the *cis*- and *trans*-4-*t*-butylcyclohexyl tosylates and the tosylates of **1** and **2**.

The rates of solvolysis of the *cis,trans*- and *trans,cis*-2,5-di-*t*-butylcyclohexyl tosylates (**7** and **8**) and the *cis*- and *trans*-2-*t*-butylcyclohexyl tosylates (**9** and **10**), and the k_H/k_D for **9**-2-*d* and **10**-2-*d* determined by Sicher[20] are given below their structural formulas.



8 **7**

$k_{solv} \times 10^5$, sec^{-1} 0.39 4.36



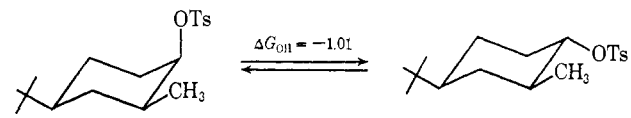
10 **9**

$k_{solv} \times 10^5$, sec^{-1} 0.57[19] 2.84[19]

k_H/k_D 1.24[20] 2.20[20]

The close correspondence of the rates of solvolysis of **7** *and* **9** *and* **8** *and* **10** *strongly indicates that the geometry of the transition states in the axial tosylates and the equatorial tosylates, respectively, are very similar, and that* **10** *does not solvolyze via a nonchair conformation.* The 5-*t*-butyl group of **8** strongly forbids the formation of a conformation in which the tosylate can become axially oriented[21] and thus must solvolyze in the equatorial conformation (structure **8**), and thus we must conclude that **10** does not solvolyze *via* a conformation having an axial tosylate.

It is now instructive to consider a free-energy diagram for the solvolysis of **7** and **8**, and *cis*- and *trans*-4-*t*-butylcyclohexyl tosylate (see Figure 3). In the solvolysis of the *cis*- and *trans*-4-*t*-butylcyclohexyl tosylates the ground states are separated by ~0.9 kcal/mol and the transition states by only ~0.1 kcal/mol. In this system the difference in ground-state energies appears to be predominantly responsible for the greater reactivity of the axial derivative. In contrast, the ground states of **7** and **8** are separated by only 0.26 kcal/mol and the transition states by 1.8 kcal/mol. Thus the greater reactivity of the axial isomer **7** is due to differences in factors arising in the transition states and not in the ground states. Due to the close similarity of the k_H/k_D's of the 2-methyl-4-*t*-butylcyclohexyl tosylates[20] with the 2-*t*-butylcyclohexyl tosylates,[20] but yet distinctly different thermodynamic and kinetic trends compared to the 2-*t*-butyl compounds, we do not believe that the enhanced rate of solvolysis of **7** over **8** can be attributed to a dominant hydrogen participation effect. We believe that torsional angle effects occur in the transition states for the solvolysis of **7** and **8** leading to the observed reactivity relationship.

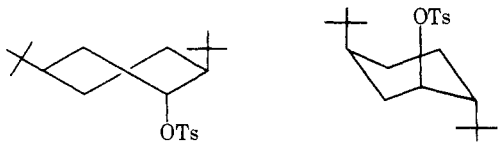


$k_{solv} \times 10^6$, sec^{-1} at 70° 3.67 3.67

k_H/k_D 2.08 1.19

The lack of effect of added ethoxide on the rates of solvolysis of the tosylates of **1**, **2**, and **4** and the lack of solvent-substitution products (see Table VII) are very suggestive that the solvolysis reactions proceed to intimate ion pairs which decompose primarily by abstraction of proton from the carbonium ion by the departing tosylate. Although the tosylate–carbonium ion interaction may have some affect on the free-energy difference in the transition states, we feel that the dominant factor is the effect of torsional angle effects in the transition state for intimate ion-pair formation. In going from the tosylate of **7** to the tight ion pair (illustrated only as the most probable structure of the carbonium ion, **11**) the 1-equatorial hydrogen remains eclipsed with the C–*t*-Bu (or just inside the C–H, C–*t*-Bu angle) and there is little, if any, increase in eclipsing strain energy. In contrast, in going from the tosylate **8** to the carbonium ion, the 1-axial hydrogen must pass by the 2-*t*-Bu group, thus increasing the eclipsing strain energy in the transition state, *e.g.*, the torsional angle energy contribution to the transition state increases.[22,23]

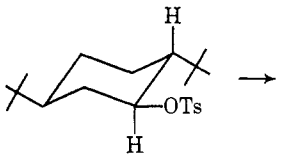
(21) Two conformations are possible in which the tosylate can become axially oriented: the twist-boat conformation iii in which one *t*-butyl and the tosylate become pseudoaxial, the other a chair conformation iv in which both *t*-butyl groups and the tosylate become axial. The conversion of **8** to either iii or iv would be expected to result in the expenditure of well over 10 kcal/mol of energy, a process which we consider unlikely.



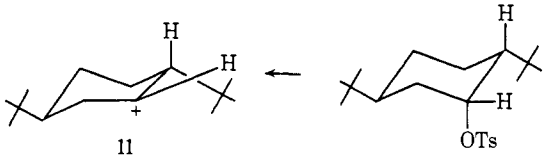
iii iv

(22) Similar torsional angle arguments can be extended to the solvolysis reactions of other 2-alkylcyclohexyl derivatives in which the *cis* isomers react more rapidly than the *trans* isomers.[20] Studies are in progress to evaluate the relative importance of torsional angle effects *vs.* ground-state steric considerations and hydrogen participation in such systems.

(23) The change in the dihedral angles between substituents on the 1- and 2-carbon atoms in going from starting material to the transition states would be expected to give rise to secondary hydrogen–deuterium isotope effects; however, there appears to be no reasonable way to estimate the magnitude of these effects.



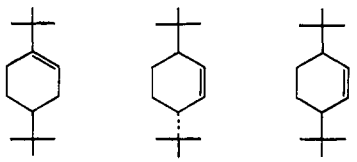
8



11 7

The *trans,trans* isomer solvolyzes at a rate intermediate between the tosylates of **1** and **2**. In view of the fact that **4** exists in a conformational equilibrium involving **4a**, **4b**, and **4c** it is difficult to interpret the factors affecting the rate of solvolysis of the tosylate of **4**. Rate decelerations due to torsional angle effects would be encountered in conformations **4b** and **4c**, and a slight rate deceleration due to loss of hydrogen participation would be expected in **4a**. One fact is obvious, however, that being that a twist-boat cyclohexyl tosylate, *i.e.*, conformation **4c**, does not lead to a large acceleration in the rate of solvolysis of the tosylate.

The products derived from the solvolysis of the tosylates of **1**, **2**, and **4** are given in Table VII. The recovered unreacted tosylates were identical with the starting tosylates. In control experiments it was shown that the olefins, 1,4-di-*t*-butylcyclohexene (**12**), *trans*-3,6-di-*t*-butylcyclohexene (**13**), and *cis*-3,6-di-*t*-butylcyclohexene (**14**), do not isomerize under the reaction conditions.



12 13 14

Several aspects of the data given in Table VII are noteworthy. The two axial *cis*-2-*t*-butyl tosylates derived from **1** and **3** produce only 1,4-di-*t*-butylcyclohexene (**12**) by an apparent *anti* elimination.[24] In contrast, both the 1,4- and 3,6-di-*t*-butylcyclohexenes are formed from the *trans*-2-*t*-butyl tosylates of **2** and **4**; however, only *trans*-3,6-di-*t*-butylcyclohexene (**13**) is formed from the *trans*-di-*t*-butyl isomer **2**, and only *cis*-3,6-di-*t*-butylcyclohexene (**14**) is formed from the *cis*-di-*t*-butyl isomer **4**. *There is no crossover between the cis- and the trans-di-t-butyl systems.*[25] The formation of **12** from the tosylates of **2** and **4** involves a net *syn* elimination, whereas the stereochemistry of the elimination reactions giving **13** and **14**, respectively, cannot be determined from the present data.[26] It would appear that in the *cis*-2-alkyl cases *syn* eliminations are occurring, whereas in the *trans*-2-alkyl cases *anti* eliminations are occurring.[27,28]

Chromic Acid Oxidation of 1–4. The faster rate of chromic acid oxidation of axial alcohols relative to their equatorial counterparts, originally observed by Vavon,[29] has been rationalized on conformational arguments,[3,30] the axial alcohols reacting faster due to relief of ground-state steric strain on going to the transition state. Eliel[31] has recently pointed out that a linear correlation, with a slope of unity, exists between the "relative stability of alcohols (K_{epi}) and their chromic acid oxidation rates (k_a/k_e)." Eliel[31] also noted that the 2-alkylcyclohexanols react faster than the 3- or 4-alkylcyclohexanols because of the additional alkyl–hydroxyl *gauche* interaction energies present in the 2-alkyl systems. It was reported that *cis*-2-*t*-butylcyclohexanol (axial hydroxyl) reacts ~5 times faster than *trans*-2-*t*-butylcyclohexanol (equatorial hydroxyl); however, K_{epi} for this system was not measured and was apparently assumed to be >1 (as did Goering[19] in discussing the rates of tosylate solvolyses), a fact which has been shown not to be true.[4]

The rates of chromic acid oxidation of **1–4** in 75% by volume aqueous acetic acid were measured and are tabulated in Table VIII along with similar data for other systems. The rates of oxidation of **1** and **2** are very similar to those of *cis*- and *trans*-2-*t*-butylcyclohexanol, respectively. In both of these systems *the more reactive epimer is the more thermodynamically stable*, which is not consistent with the previously proposed correlation. The free-energy diagram for the oxidation of **1** and **2** (*trans*-*t*-butyls) and **3** and **4** (*cis*-*t*-butyls) indicate that ground-state energy differences are important in the latter, but that transition-state energy differences are dominant with the former (see Figure 4). Our pres-

Table VIII. Rates of Oxidation of Cyclohexanols

Cyclohexanol	Temp, °C	$k_2 \times 10^3$, l./mol sec	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
cis,trans-2,5-Di-*t*-butyl	25	454, 470	18.7	2.5
	35	1,280		
trans,cis-2,5-Di-*t*-butyl	25	45.0, 50.0	25.4	10.6
	35	191		
cis,cis-2,5-Di-*t*-butyl	25	907, 938	19.1	5.4
	35	2,630		
trans,trans-2,5-Di-*t*-butyl	25	126	22.1	11.3
	35	421.7		
cis-2-*t*-Butyl	25	254.5[a]		
trans-3-*t*-Butyl	25	54.0[a]		
trans-3-*t*-Butyl	25	30.25[a]		
cis,3-*t*-Butyl	25	4.97[a]		
cis-4-*t*-Butyl	25	13.00[a]		
trans-4-*t*-Butyl	25	4.02[a]		

[a] Reference 31.

(24) It is conceivable that if hydrogen participation is important in the ionization of the tosylates of **1** and **3** the C-2 hydrogen could migrate to C-1 giving the 1,4-di-*t*-butylcyclohexyl cation which on loss of hydrogen ion from the original C-1 or C-3 would give **12**. Deuterium labeling studies are being carried out to clarify this point.

(25) Dissolution of the isomeric *cis*- and *trans*-di-*t*-butyl alcohols in magic acid produces two different cations; however, the structures were not fully elucidated (E. Arnett, private communication). We wish to thank Professor Arnett for running these experiments.

(26) The synthesis of stereospecifically 6-deuterium-labeled **3** and **4** is being carried out in order to determine the stereochemistry of the eliminations involved in the formation of **13** and **14** from the tosylates of **2** and **4**.

(27) The very simple product distributions derived from the solvolysis of the tosylates of **1–4** are in distinct contrast with the complex product distributions reported by Sicher (ref 28) for the stereoisomeric 2-methyl-4-*t*-butylcyclohexyl tosylates in which rearrangement products and solvent-containing products were characterized.

(28) See Pankova, *et al.*, ref 6.

(29) G. Vavon and C. Zaremba, *Bull. Soc. Chim. Fr.*, 1931 (1953).

(30) J. Schreiber and A. Eschenmoser, *Helv. Chim. Acta*, **38**, 1529 (1955).

(31) E. L. Eliel, S. H. Schroeter, T. J. Brett, F. J. Biros, and J.-C. Richer, *J. Amer. Chem. Soc.*, **88**, 3327 (1966).

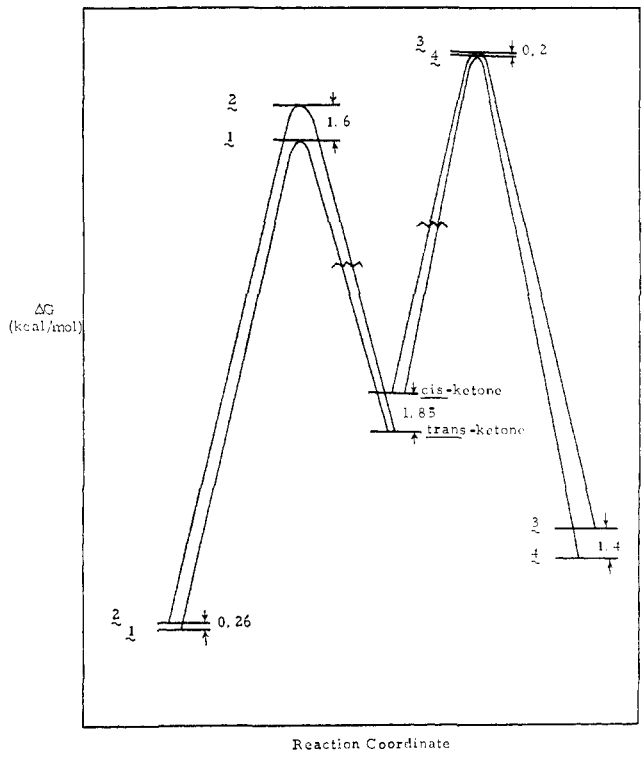


Figure 4. Free-energy diagram for the chromic acid oxidation of **1**, **2**, **3**, and **4** (the free-energy difference between the *cis*- and *trans*-2,5-di-*t*-butylcyclohexanone taken from D. R. Rao, Ph.D. Dissertation, University of Notre Dame, Notre Dame, Ind., 1969.

ent feelings are that torsional angle effects may be operative; however, additional information is required concerning the structure of *trans*-2,5-di-*t*-butylcyclohexanone and other 2-alkylcyclohexanone systems.

The *trans,trans*-isomer **4** reacts at a rate intermediate between **1** and **2**, similar to the rate relationships in the solvolysis of the tosylates of **1**, **2**, and **4**; however, due to the conformational heterogeneity of **4** no definite conclusions can be made concerning the factors affecting the rate of oxidation of **4**.

The *cis,cis*-isomer **3** reacts only slightly faster than **1**, **2**, or **4**. The twist-boat conformation of **3** does not produce an unusually large acceleration in the rate of oxidation of **3** relative to **1**, **2**, or **4**. It would appear that in this case ground-state steric considerations are dominant (see Figure 4), the reaction rate being accelerated by release of the steric strain of the pseudoaxial hydroxyl in **3c**.

Rates of Acetylation of 1–4. Eliel and Biros[32] have measured the rates of acetylation of a number of alkyl-substituted cyclohexanols. In general, equatorial alcohols react faster than their axial counterparts. The observed trends in rates were discussed in terms of steric and polar effects.[32]

The rate constants for the acetylation of **1–4** in pyridine at 25° are given in Table IX along with data for other representative alcohols.[32] The *trans,cis*-isomer **2** reacts ~one-half as fast as *trans*-2-*t*-butylcyclohexanol. In both cases only slight rate decreases are observed in going from the mono-*t*-butyl to the di-*t*-butyl systems.

(32) E. L. Eliel and F. J. Biros, *J. Amer. Chem. Soc.*, **88**, 3334 (1966).

Table IX. Rates of Acetylation of Cyclohexanols

Alcohol	$k \times 10^5$ (l./mol sec)
trans,cis-2,5-Di-*t*-butyl	2.9 ± 0.3
cis,trans-2,5-Di-*t*-butyl	0.12 ± 0.03
trans,trans-2,5-Di-*t*-butyl	2.4 ± 0.2
cis,cis-2,5-Di-*t*-butyl	0.78 ± 0.05
trans-2-*t*-Butyl	5.46[a]
cis-2-*t*-Butyl	0.31[a]
trans-4-*t*-Butyl	10.8[a]
cis-4-*t*-Butyl	2.9[a]

[a] Reference 32.

The *trans,trans*-isomer **4** reacts almost as fast as the *trans,cis*-isomer **2** which possesses an equatorial hydroxyl. This is consistent with the suggestion that **4** exists (and reacts) in the boat conformation **4c** with a pseudoequatorial hydroxyl.

The *cis,cis*-isomer **3** reacts slightly faster than **1** which possesses an axial hydroxyl. Again, this is consistent with the proposed boat conformation **3c** possessing an axial hydroxyl.

Eliel[32] has suggested that the slower rates of acetylation of the 2-*t*-butylcyclohexanols relative to other 2-alkylcyclohexanols are due to the greater steric shielding of the hydroxyl by the 2-*t*-butyl group. Similarly, the use of acetylation as a kinetic tool in conformational analysis[32] implies that the axial alcohols react slower than their equatorial counterparts for steric reasons. It was hoped that a kinetic study of the acetylation of **1–4** might shed some light on the nature of the vicinal OH–*t*-Bu interactions, and reflect some trend in the magnitude of these interactions. However, as was observed in the hydrogen bonding studies of **1–4**, *the rates of acetylation of* **1–4** *do not reflect their relative thermodynamic stabilities.*

Summary. Studies involving the 2-*t*-butyl- and 2,5-di-*t*-butylcyclohexanols have revealed trends which are not consistent with trends in thermodynamic stabilities and chemical reactivity displayed by other alkylcyclohexanols. These differences are (1) the hydroxyl prefers the axial orientation in the chair conformations and (2) despite the fact that the axial isomers are more thermodynamically stable, they undergo chromic acid oxidation more rapidly than the less stable axial isomers and the axial tosylates solvolyze faster than the equatorial tosylates. In contrast, the isomers with equatorial hydroxyl acetylate more rapidly and are more extensively hydrogen bonded than their axial counterparts, consistent with the reactivities of other alkylcyclohexanols. Factors contributing to these thermodynamic stability and chemical reactivity trends are distortions of the *t*-butylcyclohexane system and the incurrence of torsional angle effects in transition states.

Experimental Section

Preparation of the 2,5-Di-*t*-butylcyclohexanols. Hydroboration of 1,4-di-*t*-butylcyclohexene[33] at ice–salt bath temperatures followed by oxidation, hydrolysis, and separation by careful column chromatography on basic Woelm activity II alumina gave mainly *trans,trans*-2,5-di-*t*-butylcyclohexanol (70%, mp 72–73°) with lesser amounts of the *trans,cis* isomer (mp 102–103°).[34]

Hydroboration of 1,4-di-t-butylcyclohexene at room temperature for 24 hr, followed by the general work-up,[34] produced mainly the *trans,cis*- isomer (60%).

(33) R. D. Stolow and J. A. Ward, *J. Org. Chem.*, **31**, 965 (1966).
(34) D. J. Pasto and F. M. Klein, *Tetrahedron Lett.*, 963 (1967).

cis,cis-2,5-Di-*t*-butylcyclohexanol was prepared by hydrogenation of 2,5-di-*t*-butylphenol (25 g) in 100 ml of 80% aqueous ethanol at 73° and 1550 psi over ruthenium oxide. After reduction the catalyst was removed by filtration and the solvent was removed under reduced pressure. The solid product was dissolved in 200 ml of ether. The solution was dried over magnesium sulfate and the solvent was removed under reduced pressure. The residue was chromatographed on basic Woelm activity alumina giving 8 g (32%) of pure (by glpc) *cis,cis*-2,5-di-*t*-butylcyclohexanol (mp 75–76.5°).

The *cis,trans*-2,5-di-*t*-butylcyclohexanol was prepared in the following manner. The crude hydroboration product of 1,4-di-*t*-butylcyclohexene (12 g) was dissolved in 240 ml of reagent acetone and cooled to 0°. A solution of sodium dichromate (10% excess) in 36 ml of 30% sulfuric acid was added dropwise with stirring. After the reaction ceased, the excess oxidizing agent was destroyed by the dropwise addition of methanol. The reaction mixture was poured into 1000 ml of cold water and was extracted with three 200-ml portions of ether. The combined extract was dried over magnesium sulfate and the solvent was removed under reduced pressure giving a mixture of *cis*- and *trans*-2,5-di-*t*-butylcyclohexanone. The ketone mixture was dissolved in 125 ml of absolute ethanol containing 0.12 mol of sodium ethoxide and refluxed for 2 hr. The mixture was poured into water and was extracted with three 100-ml portions of ether. The combined extract was dried over magnesium sulfate and the solvent was removed under reduced pressure. The residue, predominantly *trans*-2,5-di-*t*-butylcyclohexanone, was dissolved in 100 ml of anhydrous ether and was slowly added to a solution of lithium aluminum hydride (15% excess) in 100 ml of ether. The reaction mixture was hydrolyzed with water and the ether layer was removed and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on basic Woelm activity II alumina giving essentially equal amounts (48:52) of the *trans,cis*- and the *cis,trans*-2,5-di-*t*-butylcyclohexanol (mp 118–119°).[34]

Preparation of the 2,5-Di-*t*-butylcyclohexyl *p*-Toluenesulfonates. To solutions of 1 g (5.0 mmol) of the alcohols in 3 ml of pyridine at 0° was added 1.1 g (6.0 mmol) of *p*-toluenesulfonyl chloride dissolved in 2 ml of pyridine. The reaction mixtures were allowed to stand in a refrigerator (4 days for **1** and **2**, 15 days for **4**). The reaction mixtures were poured into 50 ml of ice–water and were extracted with two 75-ml portions of ether. The combined ether extracts were washed successively with three 10-ml portions of cold 4 *N* sulfuric acid, 10 ml of 5% sodium bicarbonate, and saturated sodium chloride, and were dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residues were recrystallized from hexane–ethyl acetate mixtures: *trans,trans*-2,5-di-*t*-butylcyclohexyl tosylate, mp 64° (*Anal.* Calcd for $C_{21}H_{34}O_3S$: C, 68.68; H, 9.33. Found: C, 68.60; H, 9.25); *trans,cis*-2,5-di-*t*-butylcyclohexyl tosylate, mp 76–78° (*Anal.* Calcd for $C_{21}H_{34}O_3S$: C, 68.68; H, 9.33. Found: C, 68.87; H, 9.58); *cis,trans*-2,5-di-*t*-butylcyclohexyl tosylate, mp 65–66° (this compound underwent slow decomposition at room temperature and had to be stored in a refrigerator) (*Anal.* Calcd for $C_{21}H_{34}O_3S$: C, 68.68; H, 9.33. Found: C, 68.31; H, 9.34).

The tosylate of *cis,cis*-di-*t*-butylcyclohexanol could not be prepared, giving instead only 1,4-di-*t*-butylcyclohexene on work-up.

***cis*-3,6-Di-*t*-butylcyclohexene.** To a solution of 1 g (0.005 mol) of *cis,cis*-2,5-di-*t*-butylcyclohexanol in 3 ml of dry pyridine at 0° was added 0.7 ml (0.006 mol) of distilled benzoyl chloride. The reaction mixture was allowed to stand for 24 hr at room temperature. The reaction mixture was poured into 50 ml of ice water and was extracted with three 50-ml portions of ether. The combined ether extract was washed with two 20-ml portions of 4 *N* sulfuric acid, once with 5% sodium bicarbonate solution and saturated sodium chloride solution, and was dried over anhydrous magnesium sulfate. Evaporation of the solvent on a rotary flash evaporator gave 1.4 g (90%) of the benzoate. The benzoate was purified by recrystallization from Skelly Solvent B (mp 45–47°).

cis,cis-2,5-Di-*t*-butylcyclohexyl benzoate (2 g, 0.0065 mol) was pyrolyzed in a large test tube at 330–340° using a Wood's metal bath. The reaction mixture was cooled and was dissolved in 50 ml of ether. The ether solution was washed with 10% sodium bicarbonate solution and saturated sodium chloride solution, and was dried over anhydrous magnesium sulfate. The solution was filtered and the ether was removed under reduced pressure. Nmr analysis of the product indicated the presence of unpyrolyzed benzoate, *cis*-3,6-di-*t*-butylcyclohexene (**14**), and 1,4-di-*t*-butylcyclohexene (**12**). The olefins were separated from the unreacted benzoate by chromatography on neutral alumina using Skelly Solvent B as the eluent.

cis-3,6-Di-*t*-butylcyclohexene (**14**) was separated from **12** by careful chromatography on a 2 × 45 cm silver nitrate coated alumina column using Skelly Solvent B as the eluent (extensive isomerization of **14** to **12** occurred). Pure **14** was distilled at 43° at 0.1 mm. The nmr spectrum of **14** displayed a singlet at δ 0.92 (*t*-Bu), broadened singlet at δ 5.79 (vinyl hydrogens), and complex patterns in the δ 1.2–2.0 region.

Anal. Calcd for $C_{14}H_{26}$: C, 86.52; H, 13.48. Found: C, 86.46; H, 13.34.

***trans*-3,6-Di-*t*-butylcyclohexene.** The product mixture from the solvolysis of *trans,cis*-2,5-di-*t*-butylcyclohexyl *p*-toluenesulfonate (1.0 g) in *t*-butyl alcohol was carefully chromatographed on silver nitrate coated alumina using Skelly Solvent B as eluent giving 20 mg of fairly high purity *trans*-3,6-di-*t*-butylcyclohexene (**13**) along with 1,4-di-*t*-butylcyclohexene as the major product. The nmr spectrum of *trans*-3,6-di-*t*-butylcyclohexene showed a sharp singlet at δ 0.86 (*t*-Bu), a broad singlet at δ 5.67 (vinyl hydrogens), with broad absorption in the δ 2.0–1.0 region.

Kinetics of the Ethanolysis of the 2,5-Di-*t*-butylcyclohexyl *p*-Toluenesulfonates. The *p*-toluenesulfonate was accurately weighed into a 25-ml volumetric flask and the flask was filled to the mark with absolute ethanol at 25°. Aliquots (2 ml) were transferred to 2-ml ampoules with a microburet and the ampoules were sealed. The ampoules were placed in a constant-temperature bath maintained at the desired temperature. "Zero time" was recorded when the ampoules were transferred to the constant temperature bath. The ampoules were taken out at suitable intervals and placed in a Dry Ice–acetone bath. Each ampoule was carefully crushed in a 150-ml beaker, and the contents diluted to 60 ml. The resulting solution was titrated with standard 0.01 *N* sodium hydroxide (standardized by titrating with potassium hydrogen phthalate) using a Beckman research pH meter. Excellent first-order plots were obtained. The individual rate constants are listed in Table X.

Table X. Rate Constants for the Ethanolysis of the Stereoisomeric 3,5-Di-*t*-butylcyclohexyl Tosylates

Cyclohexyl tosylate	Temp, °C	$k_1 \times 10^5$, sec^{-1}
trans,cis-2,5-Di-*t*-butyl	25.0	0.180 ± 0.009
	25.0	0.183 ± 0.006
	44.8	2.899 ± 0.007
	44.8	3.10 ± 0.01
	65.1	34.77 ± 0.02
	65.1	35.23 ± 0.02
cis,trans-2,5-Di-*t*-butyl	25.0	2.06 ± 0.01
	44.8	29.22 ± 0.08
trans,trans-2,5-Di-*t*-butyl	25.0	1.04 ± 0.01
	25.0	1.03 ± 0.02
	44.8	14.02 ± 0.01
	44.8	14.63 ± 0.04
	65.0	147.0 ± 0.6
	65.0	134.0 ± 0.4

Kinetics of the Solvolysis of the 2,5-Di-*t*-butylcyclohexyl *p*-Toluenesulfonates in the Presence of Added Base. The kinetics of the solvolysis of the tosylates in the presence of approximately a fivefold excess of base (sodium ethoxide) were carried out as described above. Analyses were carried out by titration with standard 0.01 *N* potassium hydrogen phthalate. First-order plots were nicely linear; second-order plots displayed considerable curvature. The first-order rate constants derived in the presence of base are given in Table XI.

Table XI. Ethanolysis of the Stereoisomeric 2,5-Di-*t*-butylcyclohexyl Tosylates in the Presence of Sodium Ethoxide

Cyclohexyl tosylate	Temp, °C	$k_1 \times 10^5$, sec^{-1}
cis,trans-2,5-Di-*t*-butyl	25.0	2.11
trans,cis-2,5-Di-*t*-butyl	25.0	0.22
trans,trans-2,5-Di-*t*-butyl	25.0	0.99

Analysis of the Tosylate Solvolysis Reaction Mixtures. The appropriate tosylate (~0.5 g) was dissolved in the desired solvent, with base if desired, and subjected to the reaction conditions specified in Table VII. The reaction mixtures were poured into water and were extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The residues were analyzed by nmr by integrating the olefinic hydrogen signals of **12**, **13**, and **14** appearing at δ 5.42, 5.67, and 5.79, respectively.

Measurement of the Rates of Chromic Acid Oxidation of 1–4. The rates of chromic acid oxidation of **1–4** in 75% by volume aqueous acetic acid were followed spectrophotometrically using the general procedure of Eliel.[31] The rate constants are given in Table VIII.

Measurement of the Rates of Acetylation of 1–4. The rates of acetylation of **1–4** with acetic anhydride in pyridine were measured following the procedure of Eliel and Biros.[32] The rate constants are given in Table IX.

Assignment of Electronic Transitions in the N-Alkyl-N-nitrosoanilines[1a,b]

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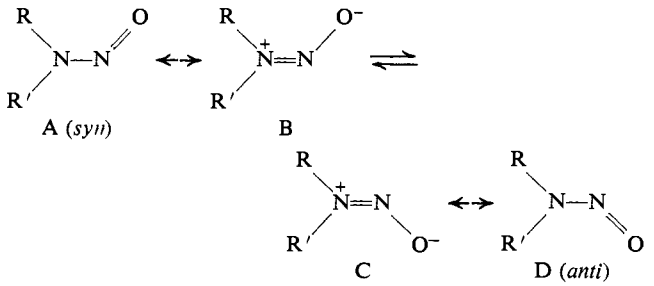
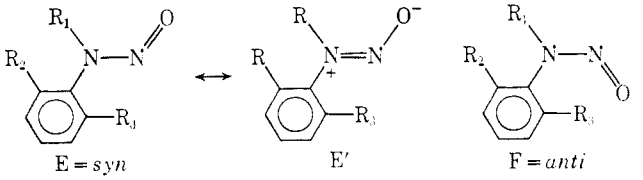
Abstract: The electronic absorption spectra of nine N-alkyl-N-nitrosoanilines have been measured in cyclohexane and ethanol. The spectra fall into two classes: those arising from compounds with planar and near-planar geometries, and those arising from compounds which are highly twisted about the aromatic C–N bond. Band assignments have been made for both classes and are discussed with particular attention to geometric changes within each class. A sequence of average angle of twist was obtained for the entire series; a comparison of the spectra of N-nitrosoindoline and N-methyl-N-nitrosoaniline revealed that the latter compound is not planar. By analysis of the vibrational components of the ^1W band in ethanol, it was possible to obtain a partial sequence of basicity for the series.

N-Nitrosamines were discovered in 1850,[2] yet it is only in recent years that chemists have been concerned with their electronic and molecular structure.[3–7] Haszeldine and Jander[3] were the first to recognize the important contribution of the polar resonance form B in the nitrosamines. This resonance



was later supported by the work of Looney, *et al.*,[4] who derived a barrier to rotation about the N–N bond of about 23 kcal/mol for dimethylnitrosamine; these authors[4] further suggested that this compound was planar. In the nitrosamines derived from unsymmetrical secondary amines, RR'NNO, the proposed planar structure and restricted rotation about the N–N bond suggest that two geometric isomers, A and D, should exist in dynamic equilibrium at room temperature.[4,5] Karabatsos and Taller[5] have made configurational assignments for a series of such nitrosamines, where the relative population of *syn*/*anti* forms (A/D) was determined by integration of their nmr spectra.

In contrast to the aliphatic nitrosamines, the N-alkyl-N-nitrosoanilines have received relatively little attention. In the nmr spectrum of E, with R_1 = methyl (R_2 = R_3 = H), Looney, *et al.*,[4] observed only one methyl signal (in contrast to the two observed for dimethylnitrosamine) and suggested that either rotation about the N–N bond was very rapid or only one isomer was present. The question was settled by Karabatsos and Taller,[5] who established that the single methyl resonance arose only from the *syn* isomer, E.



Of particular interest were the ultraviolet absorption spectra reported by Karabatsos and Taller[5] for three nitrosoanilines. As R was changed from ethyl to isopropyl, the *syn*/*anti* ratio changed from 96/4 to 65/35 and a 25-nm hypsochromic shift was observed for the longest wavelength $\pi \rightarrow \pi^*$ transition; at the same time, a second band appeared at somewhat higher energy. Although the lack of additional information prevented a complete explanation of these observations, these authors[5] did suggest that the isopropyl compound was probably twisted about the aromatic C–N bond in at least one of the isomeric forms, F.

(1) (a) For a preliminary report of this work, see *J. Amer. Chem. Soc.*, 91, 3383 (1969); (b) supported in part by National Science Foundation Grant GP7551; (c) Procter & Gamble Fellow, 1967–1968.
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