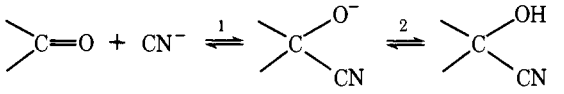

$$(K^D/K^H)_1 \times (K^D/K^H)_2 = (K^D/K^H)_{overall} = 1.28 \quad (7)$$

The limiting value of the isotope effect for the first reaction, which is the kinetically important one since the anionic tetrahedral intermediate is the immediate product of the rate-determining step, is given by:

$$\left(\frac{K^D}{K^H}\right)_1 = \left(\frac{K^D}{K^H}\right)_{overall} \Big/ \left(\frac{K^D}{K^H}\right)_2 \quad (8)$$

The value of $(K^D/K^H)_2$ can be estimated to be near 1.06 on the basis of the influence of single deuterium atoms on the acidity or basicity of formic acid,[20] methylamine,[21] and trimethylamine,[21] as described by Bilkadi et al.[22] It follows that the limiting value of the kinetic secondary isotope effect for addition of cyanide to benzaldehydes should be 1.28/1.06 = 1.21. The fact that the observed effects are near this limit requires that the transition state for benzaldehyde cyanohydrin formation be nearly tetrahedral: the bond order of the incipient carbon-carbon bond must be between 0.7 and unity in the transition state. The observation of a fully formed or nearly fully formed bond between carbonyl carbon and nucleophile in the transition state accords fully with recent data concerning addition of nitrogen nucleophiles to aldehydes.[7,11,23]

As noted above, results obtained in this investigation, together with earlier findings, strongly suggest that rate constants for benzaldehyde cyanohydrin formation are correlated by σ substituent constants although equilibrium constants for the same reactions are correlated by the σ^+ substituent constants. Moreover, the rate constants are much more sensitive to the nature of polar substituents, ρ = 1.8, than are the overall equilibrium constants, ρ^+ = 0.96. This difference may be largely or completely accounted for by the effect of polar substituents on the basicity of the anionic tetrahedral intermediate. For example, values of pK_a for the ionization of the hydrates of substituted trifluoroacetophenones are correlated by the σ substituent constants with a value of ρ of 1.1.[24] In addition, the large value of ρ for the attack reaction may reflect a particularly high sensitivity of the attack of anions to polar substituents.[25]

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π-Electron Steric Effects on Conformational Equilibria

Joseph B. Lambert*[1a] and Richard R. Clikeman[1b]

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60201.

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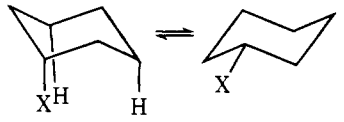
Abstract: Replacement of the geminal protons in a methylene group ($-CH_2-$) of cyclohexane with an exo methylene group [$-C(=CH_2)-$] produces a system suitable for the study of the interaction between the π electrons of the double bond and an axial substituent at the 3 position. The free-energy difference between the 3-axial and 3-equatorial conformers provides a measure of this "steric" interaction by comparison with the values in analogous cyclohexyl systems. The methyl group exhibits a much larger proportion of axial conformer in both nonpolar and polar solvents. In the relatively nonpolar solvent CF_2Cl_2, polar and lone-pair bearing substituents (OH, OCD_3, SCH_3) on the other hand have an even greater equatorial preference in the exo methylene system than in the parent cyclohexane, indicative of a strong repulsive interaction between the π electrons of the double bond and the axial substituent. In the more polar, hydrogen-bonding solvent $CHFCl_2$, all substituents exhibit a smaller equatorial preference in the exo methylene system than in the parent cyclohexane. Thus the "steric effect" of the π electrons can be either attractive or repulsive in comparison to a cyclohexane axial-axial interaction, depending on the nature of the interacting substituent and on the solvent.

In the most general sense, steric effects encompass any interaction that is transmitted through space and depends on the distance and angular relationship between the involved entities. In uncharged systems the organic chemist frequently encounters induced dipole-induced dipole (van der Waals), permanent dipole-induced dipole, and dipole-dipole interactions, all of which should be considered steric effects. The interacting groups may be atoms, lone-pair electrons, or π electrons, although the question of the existence of steric effects due solely to lone pairs or π electrons is still very much open.[2]

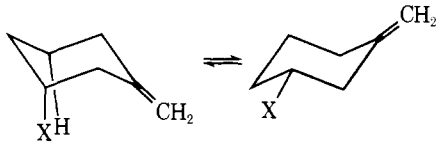
Our present study is concerned with determining the steric role of π electrons in conformational equilibria.

The equilibrium between axial and equatorial forms of monosubstituted cyclohexanes (eq 1) has provided valuable



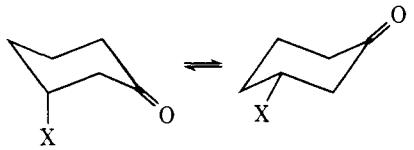
(1)

information on the nature of interactions between atoms. The equilibrium constant is determined by the sum of all atom-atom and bond-bond interactions and at the simplest level is dominated by the highly repulsive 1,3-diaxial interactions in the axial conformation. The system we chose to examine for π interactions is the 3-substituted *exo*-methylenecyclohexane (eq 2), in which a $-CH_2-$ group of cyclohexane has been replaced by a $-C(=CH_2)-$ group. As a result of this transformation, one axial proton is now gone, and in its place is the exo double bond with its π electrons. How then does the equilibrium of eq 2 compare with that of eq 1 for a series of common substituents (X), as measured by the free-energy difference ($\Delta G°$)? If the π electrons of eq 2 are essentially noninteracting,



(2)

one might expect a halving of the free-energy difference from that of eq 1, since one of the two gauche butane interactions has been removed. Such an explanation was invoked for the 3-alkyl ketone effect (eq 3, X = alkyl), in which a greater



(3)

preference of an alkyl group for the axial position was observed.[3] The interactions of polar groups, however, should be more complex.

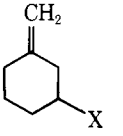
We chose to measure equilibrium constants in the exo methylene system (eq 2) rather than in the ketone system (eq 3) in order to minimize the dipolar interactions within the molecule and to permit equilibrium constant measurement by the direct NMR method.[6] The only previous data pertinent to this problem were obtained by direct equilibration of diastereomeric ketone systems.[3] The method of classical equilibration, however, requires that a chemical process be available that is compatible with a wide variety of substituents X (eq 2, 3) and that an additional substituent be added elsewhere in the ring to provide a handle for determining the stereochemical fate of the X group after equilibration. Because of the nature of the equilibration process, previous studies were limited to alkyl groups, whereas we wanted to look at a wide assortment of groups. Furthermore, the additional substituent can actually alter the final equilibrium constant, whereas we wanted to limit the interactions that must be considered to those between the X group and the exo unsaturation.

These drawbacks are not present in the direct NMR method.[7] The sample is cooled in the NMR probe to a temperature below spectral coalescence associated with slowing of the process of ring reversal on the NMR time scale. Under these conditions separate resonances are observed for the axial and equatorial isomers. The coalescence temperature for ring reversal in cyclohexanones is below -180 °C, even at 251 MHz, and the free energy of activation for the process is about 4.0 kcal/mol.[4] This temperature range is not practical for most polar substituents, so that the ketone system is not feasible for a full study. The coalescence temperature for ring reversal of methylenecyclohexane (eq 2, X = H), however, is only -115 °C at 100 MHz, and the free energy of activation is about 8.4 kcal/mol.[5] This temperature range is quite convenient for examination of a complete series of substituents. The primary drawback we found to the use of the exo methylene system was spectral overlap of resonances, but this problem was resolved by the preparation of suitably deuterated derivatives.

This paper, therefore, reports the preparation and NMR study of a series of 3-substituted *exo*-methylenecyclohexanes (eq 2). From the measured equilibrium constants we have learned that the π electrons of the double bond exhibit "steric" behavior that is a complex function of the nature of the substituent X and the solvent.

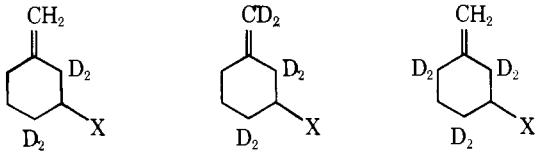
Results

The 3-substituted *exo*-methylenecyclohexane system was prepared with 12 substituents (**1–12**). In order to avoid spectral



X	X
1, OH	**7**, OCD_3
2, OAc	**8**, SCH_3
3, OMs	**9**, SC_6H_5
4, OBs	**10**, CO_2CH_3
5, OTs	**11**, CH_2OH
6, OPNB	**12**, CD_3

overlap and to permit observation of the 3 proton at low temperatures, various ring-deuterated modifications had to be prepared, with the exact pattern of deuteration (a-c) depen-

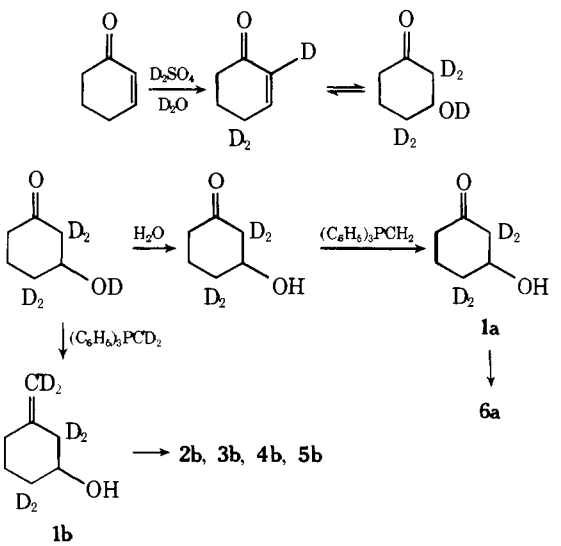


a b c

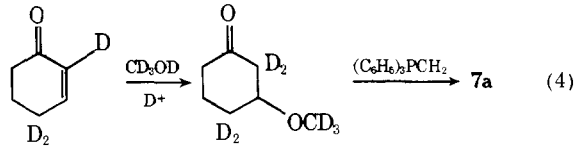
dent on the specific characteristics of the spectrum, as determined from the undeuterated materials. In two cases (**7, 12**), side-chain deuteration on X was also necessary.

All the derivatives of the alcohol were prepared according to the methods shown in Scheme I. Acid-catalyzed deuteration

Scheme I



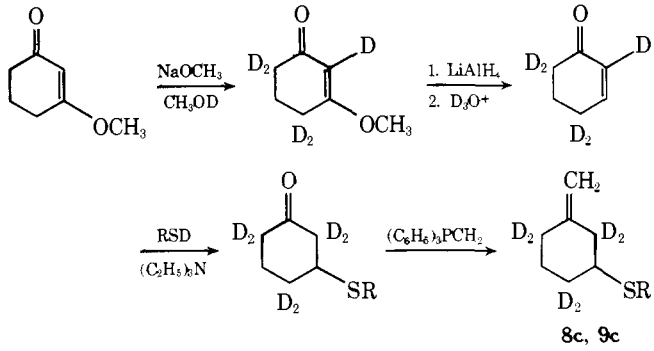
of 2-cyclohexen-1-one, with simultaneous equilibration to the alcohol, yields **1a** or **1b** after the Wittig reaction. Modification of **1a** and **1b** yields the appropriate derivatives of **2–6.** Addition of commercial methanol-d_4 to 2-cyclohexen-1-one-*2,4,4-d*$_3$ (from Scheme I), followed by the Wittig reaction, gives the ether **7a** (eq 4).



(4)

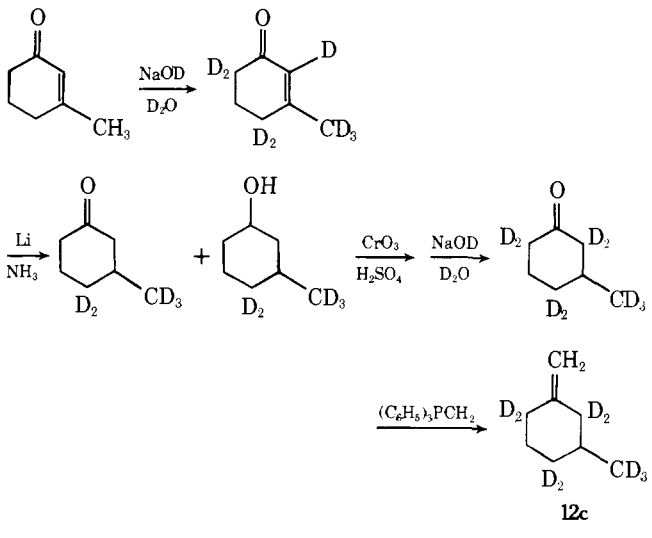
In certain cases, deuterium was also required at the 6 position (c). Base-catalyzed deuterium exchange on 3-methoxy-2-cyclohexen-1-one, followed by lithium aluminum hydride reduction with reversal of the functionalities (Scheme II),

Scheme II



produces 2-cyclohexen-1-one-*2,4,4,6,6-d*$_5$. Addition of deuterated thiol, followed by the Wittig reaction, gives the desired materials 8c and 9c. A special synthesis was required for the alkyl derivative **12** (Scheme III). 3-Methyl-2-cyclohexen-1-one

Scheme III



is treated with deuteroxide and reduced to a mixture of deuterated 3-methylcyclohexanone and 3-methylcyclohexanol, which is oxidized to the ketone and back-exchanged with deuteroxide, followed by the Wittig reaction to give **12c.**

The carbomethoxy compound **10** was obtained via the Wittig reaction from the corresponding ketone, which was obtained by published procedures (see the Experimental Section). Protection of the ketone, reduction of the ester, regeneration of the ketone, and a Wittig reaction produced the hydroxymethyl compound **11** (see the Experimental Section). Deuterated modifications were not used for either of these compounds.

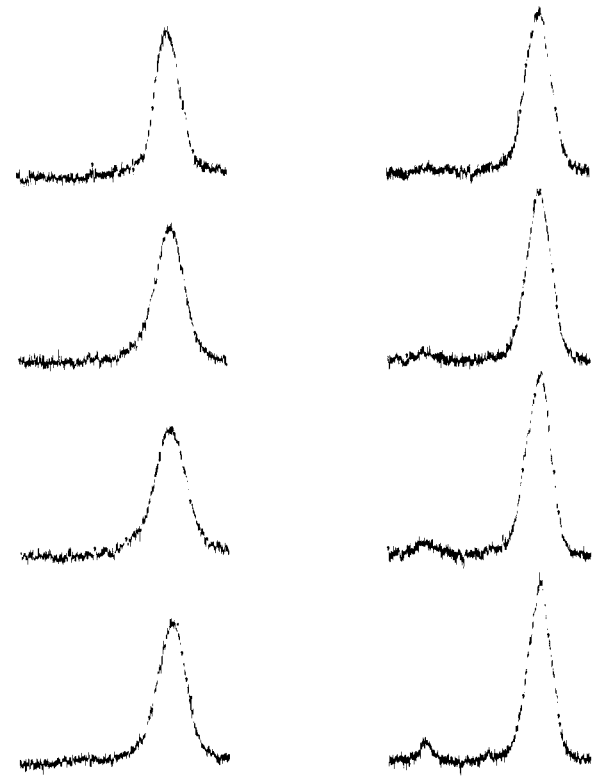


Figure 1. The 90-MHz proton magnetic resonance spectrum of 3-methoxy-1-methylenecyclohexane-*2,2,4,4,8,8,8-d*$_7$ (**7a**) in 2% CF_2Cl_2 as a function of temperature (upper left to lower right, −82, −94, −100, −106, −109, −113, −115, and −121 °C). The scale bar represents 20 Hz.

For all cases but one (**12**), the position of the equilibrium of eq 2 was determined by direct integration of the 3 proton resonances below the temperature of coalescence. At 90 MHz, these measurements could be made at about −120 °C. Deuterium was incorporated at the 2 and 4 positions to sharpen the 3 resonance for a better integration, and also at the 6 or 7 position when dictated by spectral overlap. All compounds were examined as 2% solutions in $CHFCl_2$ and some also in 2% CF_2Cl_2, depending on solubility. The phenylthio compound (**9**) and the sulfonic and benzoic esters (**3–6**) were insoluble in the latter solvent at −120 °C. The spectra are illustrated in Figures 1 ($CHFCl_2$) and 2 (CF_2Cl_2) as a function of temperature for the methoxyl compound (**7**). Illustration of the spectra for the remaining compounds may be found elsewhere.[8] To test for a concentration effect, equilibrium constants were also measured in 6% CF_2Cl_2 for the acetate (**2**). No differences were observed from the 2% solution.

The measured equilibrium constants for **1–9** at −120 °C and the derived free-energy differences are given in Table I. The population ratios are the average of 3–12 runs, observed in both field directions. Care was taken to ensure that there was no saturation at the rf power level used for each measurement. The equilibrium constant was not measured directly for the methyl compound (**12**) since only resonances from the major isomer were observed. The free-energy difference could be obtained, however, by analysis of the temperature dependence of the axial-equatorial chemical shift difference of the 5-proton AB quartet over a 125 °C range, using a computer least-squares fit.[8,9] No changes were observed in the spectra of the carbomethoxy (**10**) and hydroxymethyl (**11**) compounds, and limits were not assigned to the equilibrium constants.

In all cases (**1–9**) the axial protons (equatorial isomers) were observed at higher field, as readily determined in both deuterated and undeuterated systems by the larger bandwidth at half-height. The chemical shifts are recorded in Table II.

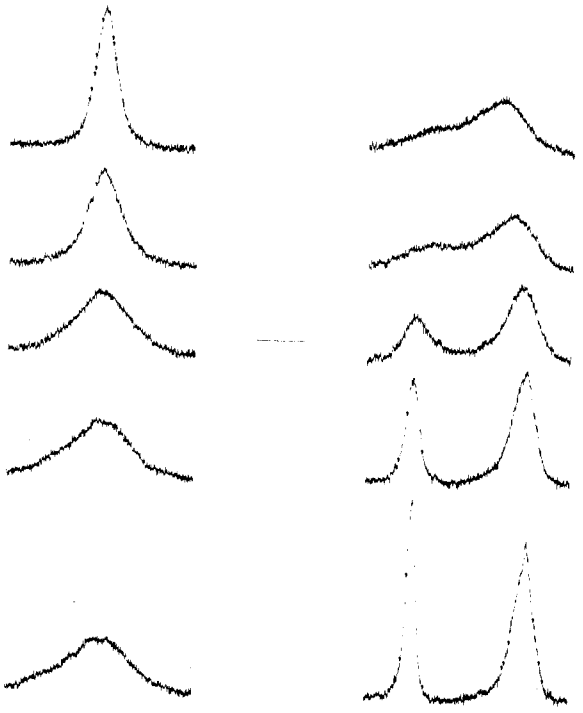


Figure 2. The 90-MHz proton magnetic resonance spectrum of 3-methoxy-1-methylenecyclohexane-*2,2,4,4,8,8,8,8-d*$_7$ (**7a**) in 2% $CHFCl_2$ as a function of temperature (upper left to lower right, −77, −86, −92, −93, −94, −96, −98, −103, −110, and −120 °C). The scale bar represents 20 Hz.

Coalescence temperatures could not be measured with great precision because of the grossly unequal amounts of conformers in some cases. The rate data are collected in Table III. The expression used to calculate k_c is rigorously correct only for an exchange between equally populated sites, so that the accuracy of the results is somewhat limited.

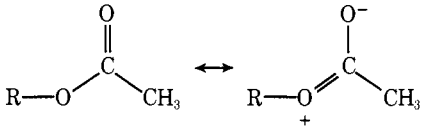
Discussion

It can be reasonably assumed that *exo*-methylenecyclohexanes exist in the chair conformation. Westheimer-type calculations have indicated that the chair is 4.4 kcal/mol stabler than the next best conformation, the twist-boat.[10] The magnitude of the barrier to ring reversal (Table III) is characteristic of chair-chair interconversions, and the chemical shift differences (Table II) are within the range of those observed for cyclohexyl systems.[7] The R value[11] of *exo*-methylenecyclohexane indicates a chair that is slightly flattened from the shape of cyclohexane.[5] This flattening would tend to move the exo methylene group slightly farther from the 3-axial substituent than is the case in cyclohexane, with an apparent reduction in repulsive interactions.

At the most simplistic level, one could ignore the presence of the exo methylene group with its π electrons. Removal of one axial proton (one gauche butane interaction) in cyclohexane (eq 1) would result, at most, in a halving of the free-energy difference between conformers. As a first approximation we find this type of behavior for the methyl compound (**12**). The 3-axial methyl group in the exo methylene system encounters smaller repulsive interactions than in cyclohexane, so the amount of equatorial isomer is reduced and the free-energy difference is approximately halved. The nearly identical results obtained in CF_2Cl_2 and $CHFCl_2$ are similar to those obtained for the ketone systems. The general conclusion from these results is that a nonpolar substituent without lone pair electrons has a less repulsive interaction with a $-C(=X)-$ group than with a $-CH_2-$ group, independent of solvent.

In the relatively nonpolar, non-hydrogen-bonding solvent CF_2Cl_2 (dipole moment, 0.53 D), significant increases with respect to the cyclohexyl system are observed for the free-energy differences of the hydroxyl (**1**), methoxyl (**7**), and thiomethyl (**8**) compounds. The only exception is acetoxyl (**2**), to be discussed below. Although two of the three substituents are highly polar, the only element that is common to all three is the presence of lone pairs. The greater proportion of the equatorial isomer indicates that the interaction between these substituents and the exo methylene unsaturation is even more repulsive than that between the same substituents and the saturated methylene group with its axial proton in cyclohexane. On this purely operational basis, the double bond with its π electrons exhibits a steric interaction, as defined in the first sentence of this paper.

The magnitude of the substituent/double bond repulsive interaction depends on the charge density on oxygen in the series **1, 2, 7.** Hydroxyl and methoxyl have negative charge densities of a similar magnitude, and both have greater equatorial preferences (substituent/double bond repulsions) in the exo methylene series. Because of ester resonance (**13**), there



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is net positive charge on the oxygen atom attached to the ring. In this system there is a greater proportion of the axial conformation than in cyclohexyl, indicative of a reduced substituent/double bond interaction. The acetyl (negative) portion

Table I. Equilibrium Conformational Preferences for 3-Substituted Methylenecyclohexanes[a]

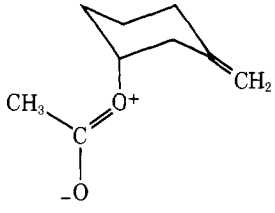
Compd	X	K (CF_2Cl_2)[b]	$-\Delta G°$ (CF_2Cl_2), kcal/mol	K ($CHFCl_2$)[b]	$-\Delta G°$ ($CHFCl_2$), kcal/mol	A[c]
1	OH	40 ± 5	1.12 ± 0.04	9.9 ± 1.1	0.69 ± 0.03	0.97
2	OAc	7.4 ± 0.8	0.61 ± 0.03	3.5 ± 0.2	0.38 ± 0.02	0.71
2	OAc[d]	7.9 ± 0.6	0.63 ± 0.02			0.71
3	OMs			3.6 ± 0.2	0.39 ± 0.02	0.56
4	OBs			3.3 ± 0.5	0.36 ± 0.05	
5	OTs			4.4 ± 0.7	0.44 ± 0.05	0.52
6	OPNB			4.9 ± 0.8	0.48 ± 0.05	
7	OCD_3	14.2 ± 0.9	0.80 ± 0.02	1.45 ± 0.05	0.11 ± 0.01	0.55
8	SCH_3	56 ± 4	1.22 ± 0.02	8.4 ± 1.0	0.65 ± 0.04	1.07
9	SC_6H_5			3.3 ± 0.2	0.36 ± 0.02	
12	CD_3[e]	14± 5	0.80 ± 0.10	10 ± 4	0.70 ± 0.15	1.6[f]

[a] Unless otherwise specified, 2% solutions at −120 °C and 90 MHz. [b] Equatorial/axial ratio. [c] The cyclohexyl A value in CS_2 or CS_2/$CDCl_3$; ref 7; ref 12; R. J. Abraham and T. M. Siverns, *J. Chem. Soc., Perkin Trans. 2*, 1587 (1972); C. H. Bushweller, J. A. Beach, J. W. O'Neil, and G. U. Rao, *J. Org. Chem.*, **35**, 2086 (1970). [d] 6% solution. [e] Measured at 270 MHz and calculated as described in the text. [f] F. A. L. Anet, C. H. Bradley, and G. W. Buchanan, *J. Am. Chem. Soc.*, **93**, 258 (1971).

Table II. Chemical Shifts of the 3-Proton of 3-Substituted Methylenecyclohexanes (−120 °C)

Compd	X	Solvent	ν_{eq},[a] Hz	ν_{ax},[b] Hz	$\Delta\nu_{ae}$, ppm
1	OH	$CFCl_2$	376.5	316.6	0.67
		$CHFCl_2$	380.9	323.8	0.63
2	OAc	CF_2Cl_2	445.6	402.1	0.48
		CF_2Cl_2[c]	445.1	401.9	0.48
		$CHFCl_2$	460.9	414.3	0.52
3	OMs	$CHFCl_2$	456.4	404.4	0.58
4	OBs	$CHFCl_2$	431.1	372.3	0.65
5	OTs	$CHFCl_2$	428.4	371.4	0.63
6	OPNB	$CHFCl_2$	486.5	435.9	0.56
7	OCD_3	CF_2Cl_2	314.9	267.8	0.52
		$CHFCl_3$	333.8	283.4	0.56
8	SCH_3	CF_2Cl_2	271.9	218.0	0.60
		$CHFCl_2$	293.9	232.3	0.68
9	SC_6H_5	$CHFCl_2$	355.6	287.9	0.75

[a] Equatorial chemical shift (90 MHz) from Me_4Si. [b] Axial chemical shift (90 MHz) from Me_4Si. [c] 6% solution; all others are 2%.



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of the acetoxyl group is directly away from the ring (**14**) and hence does not contribute to the repulsive interaction. It is interesting that in cyclohexyl (eq 1), the order of substituent size is methoxyl < acetoxyl < hydroxyl, whereas in the exo methylene system it is acetoxyl < methoxyl < hydroxyl. This inversion of the order of methoxyl and acetoxyl points out the relativity of the concept of steric size. Size depends on the probe used for the measurement. Two saturated CH_2 groups are largely responsible in cyclohexane for the larger apparent size of acetoxyl than methoxyl, but one CH_2 group and one exo methylene group bring about the reverse order.

An increased equatorial preference is also observed with the thiomethyl system (**8**). The polar properties of thiomethyl are not entirely clear. Thus a zero charge density is calculated on sulfur by the Pauling method, because sulfur and carbon have the same electronegativity. Thiomethyl, however, does have a small positive σ_m value, not too different from that of methoxyl, so that it can be considered an electron-withdrawing group. More important may be the fact that the van der Waals radius for sulfur is about 1.85 Å, whereas that for oxygen is 1.40 Å, so that the sulfur atom is much closer to the π electrons of the exo methylene group. The net result is a strong repulsive interaction between the π electrons and either permanent or induced dipoles of the thiomethyl group.

In the more polar, hydrogen-bonding solvent $CHFCl_2$, all substituents, without exception, have a lower equatorial preference than in the cyclohexyl system (Table I). Because of the better solvating power of $CHFCl_2$, we were able to obtain data on three sulfonate esters (**3-5**), one benzoate ester (**6**), and the phenylthio system (**9**), in addition to the four substituents mentioned above (**1, 2, 7, 8**). For these last four substituents, a strong interaction (hydrogen-bonding or dipole-dipole) with the solvent must reduce the electron density on the oxygen or sulfur atom and in essence eliminate the repulsive interaction between the substituent and the unsaturation. The dramatic change in conformational ratios is illustrated for methoxyl in the lowest temperature spectra of Figures 1 and 2. In Figure 1 (CF_2Cl_2), the resonance from the axial conformer is barely visible, whereas in Figure 2 ($CHFCl_2$) the peaks are of almost equal height, corresponding to a change in free-energy difference from 0.80 to 0.11 kcal/mol. Solvent effects of this magnitude are not found in the cyclohexyl series, even for extreme cases such as cyclohexanol,[12,13] for which $\Delta G°$ varies by only 0.3 kcal/mol from cyclohexane to 2-propanol as solvent. Furthermore, in the cyclohexyl system, more polar solvents favor the *equatorial* isomer because of more favorable steric factors for hydrogen-bonding or dipole-dipole interactions in this conformation. In the exo methylene series, the *axial* isomer is favored by the more polar solvent. Thus the full magnitude of the change between solvents is, if anything, underestimated by the measured values of $\Delta G°$.

Table III. Kinetic Data for Ring Reversal in 3-Substituted *exo*-Methylenecyclohexanes

Compd	X	Solvent	T_c,[a] °C	k_c,[b] s^{-1}	$\Delta G_c^{\ddagger}$,[c] kcal/mol
1	OH	CF_2Cl_2	−101	130	9.8
		$CHFCl_2$	−89	127	10.1
2	OAc	CF_2Cl_2	−98	97	10.1
		$CHFCl_2$	−97	104	10.1
3	OMs	$CHFCl_2$	−98	115	10.0
4	OBs	$CHFCl_2$	−96	131	10.1
5	OTs	$CHFCl_2$	−96	127	10.1
6	OPNB	$CHFCl_2$	−90	112	10.5
7	OCD_3	CF_2Cl_2	−100	105	9.9
		$CHFCl_2$	−92	112	10.4
8	SCH_3	CF_2Cl_2	−98	120	10.0
		$CHFCl_2$	−86	137	10.7
9	SC_6H_5	$CHFCl_2$	−89	150	10.4

[a] Temperature of coalescence; the crudeness of this measurement (±5 °C) renders the activation parameters rather inaccurate (±0.5 kcal/mol). [b] Rate constant at the temperature of coalescence, calculated from the chemical shift data of Table II, $k_c = \pi\Delta\nu_{ae}/\sqrt{2}$. [c] Free energy of activation to ring reversal at the coalescence temperature, $\Delta G_c^{\ddagger} = RT_c\,(23.76 + \ln T_c/k_c)$.

Although data could not be obtained for the sulfonate and benzoate esters or for phenylthio in the nonpolar solvents, comparisons can still be made for some of these substituents with the cyclohexyl system. Data are available for only mesylate and tosylate,[7] but in both cases the greater axial preference is found in the exo methylene system. Therefore it appears, in general, that in relatively strongly solvating media the π electrons offer less repulsion with a 3-axial substituent than the CH_2 group of cyclohexanes. It is interesting to note that the relative sizes of tosylate and mesylate are apparently inverted in the two systems (eq 1 and 2). The greater equatorial preference of mesylate in the cyclohexyl series was explained[7] in terms of greater steric demands of the methyl group. The greater equatorial preference of tosylate in the exo methylene series may result from differing inductive effects of the alkyl or aryl group on the interaction of the sulfonyl group with the double bond. In both systems, however, the differences are too small to make a definitive argument.

The much larger equatorial preference of methylthio than phenylthio may reflect the strong electron-withdrawing character of the phenyl ring, which reduces the repulsive interaction with the double bond. In this context data would have been very useful in the nonpolar CF_2Cl_2.

Summary and Conclusions

Replacement of a saturated methylene group of cyclohexane by an exo methylene group, while altering the polar character of the molecule only slightly, has an enormous influence on the

conformational preference of substituents at the 3 position. For an alkyl substituent there is a much larger amount of the axial conformation, indicating reduced repulsion between the axial substituent and the double bond. For polar substituents in a nonpolar solvent, however, an observed increase in the proportion of the equatorial isomer indicates that there is a significantly larger repulsive interaction between the axial substituent and the π electrons. In a more polar and hydrogen-bonding solvent, the opposite is true. Polar substituents in the polar solvent show larger axial preferences than in cyclohexyl, so that a substituent-solvent interaction must serve to reduce the repulsive interaction between the substituent and the unsaturation.

The exact nature of the repulsive interaction between the polar substituents and the double bond in a nonpolar solvent has not yet been specified in this discussion. The simplest mechanism, electron-electron (van der Waals or induced dipolar) repulsion, is unlikely, since the distance from the C—X bond to the C=C bond is over 3 Å. In addition, the effect does not increase when OCD_3 is replaced by SCH_3, which has a larger van der Waals radius; the repulsive effect is absent for the methyl system, which has the closest approach to the double bond π electrons; and the flattening of the ring associated with the sp^2 atom actually moves the 1 carbon further from the 3-axial substituent than in the undistorted cyclohexyl case.

If a van der Waals repulsion can be rejected, then the effect must have an electrostatic origin. For a dipole-dipole interaction, however, the orientations of the substituent (C-X) dipoles in the axial and equatorial conformations are not appreciably different with respect to the exo double bond, although the axial form is slightly more polar. Furthermore, the double bond has a very small dipole (μ = 0.34 D for isobutylene), and a large effect is observed for the relatively nonpolar substituent thiomethyl. The mechanism cannot, however, be entirely rejected.

The next higher order electrostatic term of importance is the dipole-quadrupole interaction. Although this term is ordinarily small, because of the r^{-4} dependence, compared with r^{-3} for the dipole-dipole term, the double bond has a good-sized quadrupole moment (2×10^{-26} esu cm^2),[14] and the orientations between the axial and equatorial dipoles of the C-X bond and the quadrupole of the double bond are distinctly different. We have carried out simple electrostatic calculations based on Dreiding model distances, using the standard dipole-quadrupole interaction equation,[15] and found that the magnitude of the interaction (0.5-0.8 kcal/mol) is sufficient to give rise to the observed changes in free-energy differences. Dipole-dipole calculations with the same geometry gave an approximate interaction of only 0.2 kcal/mol. Thus the large quadrupole moment of the double bond more than compensates for the r^{-4} dependence. Demonstrating feasibility by calculation, however, does not prove the validity of the mechanism. On the basis of the current data, we feel that the repulsive interaction in the axial conformation that is manifested in nonpolar solvents is electrostatic in origin and may be either dipole-dipole or dipole-quadrupole, and at present we favor the latter. Only further experimentation will clarify the situation.

Experimental Section

Infrared spectra were measured on Beckman IR-5 and IR-10 spectrometers. Routine NMR spectra were recorded on Varian Associates T-60 and Hitachi-Perkin Elmer R-20B 60-MHz nuclear magnetic resonance spectrometers. The low-temperature NMR spectra were measured on a Bruker HFX-10 90-MHz spectrometer by Dr. E. S. Magyar, to whom we are very grateful. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Mass spectra were obtained on Consolidated Electrodynamics Corp. 21-104 and Hewlett-Packard 593A spectrometers. Analytical and preparative vapor phase chromatography was performed on a Hewlett-Packard Model 700 Laboratory Chromatograph. Elemental analyses were performed on the undeuterated modifications only, by Micro-Tech Laboratories, Inc., Skokie, Ill. The 270-MHz spectra were taken on the Bruker HX-270 at the University of Chicago, which was purchased in part with funds from the National Science Foundation (Grant GP-33116).

2-Cyclohexen-1-one-*2,4,4-d*$_3$ and 3-Hydroxycyclohexan-1-one-*2,2,4,4,O-d*$_5$. 2-Cyclohexen-1-one (30 g, 0.312 mol, Aldrich) was added to 100 ml of a 0.35 N solution of concentrated sulfuric acid-d_2 (98%, Merck Sharp and Dohme) in D_2O (99.85%, Bio-Rad). The solution was stirred under N_2 at room temperature for 30 days. Separation of a small amount of oil after several days necessitated rapid stirring to ensure contact with the D_2O. Dry ether (100 ml) was then added, and the aqueous phase was neutralized with anhydrous K_2CO_3 and saturated with dry NaCl. The two-phase system was placed in a separatory funnel and the ether removed. The aqueous layer was extracted with dry ether (4 × 200 ml), and the combined ether layers were dried ($MgSO_4$) and filtered, and the ether was removed by rotary evaporation. Distillation of the residue gave 14.2 g (45.8%) of 2-cyclohexen-1-one-*2,4,4-d*$_3$ as a colorless liquid: bp 60–62 °C (13 mm); ir (film) 2950, 2205, 1665, and 1600 cm^{-1}; NMR δ 1.72–2.05 (m, 2 H, ring methylenes at the 5 position), 2.12–2.48 (m, 2 H, ring methylenes at the 6 position), 5.82 (d, 0.09 H, vinyl at the 2 position corresponding to 91% exchange), and 7.00 (broad s, 1 H, vinyl at the 3 position). A second fraction gave 4.86 g (13%) of 3-hydroxycyclohexan-1-one-*2,2,4,4,O-d*$_5$ as a clear, viscous liquid: bp 60–80 °C (0.05 mm); ir (film) 2930, 2520, 2220, and 1706 cm^{-1}; NMR ($CDCl_3$) δ 1.50–2.67 (m, 4.4 H, ring methylene indicating 90% exchange at the 2 and 4 positions).

3-Hydroxy-1-methylenecyclohexane-*2,2,4,4-d*$_4$ (1a). The addition of 62.2 ml (145 mmol) of a 2.33 M solution of phenyllithium in 70/30 benzene/ether (Alfa) to a stirred mixture of 53.9 g (151 mmol) of methyltriphenylphosphonium bromide (Aldrich) in 600 ml of dry ether (distilled from $LiAlH_4$) under N_2 afforded a solution of the corresponding phosphorane. The solution was stirred for 0.5 h, and 4.56 g (38.2 mmol) of 3-hydroxycyclohexan-1-one-*2,2,4,4,O-d*$_5$ in 100 ml of dry ether was added dropwise. The resulting reaction mixture was stirred for 2.0 h, 2 ml of acetone was added, and the mixture was stirred an additional 0.5 h. Water (5 ml) was added, and the stirring was continued for 0.5 h. Magnesium sulfate was then added, and the reaction mixture was filtered. The filtrate was washed with saturated NaCl solution (3 × 50 ml), dried ($MgSO_4$), filtered, and the ether removed by rotary evaporation. The resulting residue was distilled at reduced pressure. A fraction (1.79 g) distilling at 64–66 °C (6 mm) was shown by VPC to be the pure (99%) alcohol (**1a**). A second fraction (1.04 g) distilling at 66–70 °C (6 mm) was shown by VPC and NMR to contain 95% of the alcohol and 5% triphenylphosphine oxide. The first fraction was further purified on an 8 ft × ½ in. column packed with 5% FFAP on Chromosorb W 60/80 at 118 °C and 142 ml/min. The combined yield of alcohol was 2.78 g (23.9 mmol, 62.5%) of a colorless liquid: ir (film) 3360, 2210, 1650, 1453, 1028, and 886 cm^{-1}; NMR ($CDCl_3$) δ 1.11–2.19 (m, 4 H, ring methylene), 1.95 (s, 1 H, hydroxyl, variable), 3.71 (br s, methine), 4.74 (s, 1.6 H, exo methylene), and 4.74 (d, 0.2 H, exo methylene with geminal deuterium resulting from 10% exchange of the vinyl protons); the mass spectrum gave two main parent peaks, with 116 greater than 117, indicating an average of slightly more than four deuterium atoms per molecule. Use of 3-hydroxycyclohexan-1-one-*2,2,4,4-d*$_4$ (no deuterium on the OH) as starting material avoids exchange.

Methyl-*d*$_3$-triphenylphosphonium Bromide was prepared by modifications of the method of Malloy, Hedges, and Fisher.[16] Details are given elsewhere.[8]

3-Hydroxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (1b). A 2.35 M phenyllithium solution (28.5 ml, 70/30 benzene/ether, Alfa) was added via syringe to a mixture of 25.75 g (0.071 mol) of methyl-d_3-triphenylphosphonium bromide in 250 ml of dry ether (from $LiAlH_4$) under N_2. A solution of 3-hydroxycyclohexan-1-one-*2,2,4,4,O-d*$_5$ (distilled just prior to use from a mixture of the alcohol and D_2O) in 50 ml of dry ether was added dropwise to the phosphorane solution. The reaction mixture was stirred 2 h, and the phosphorane was destroyed with acetone. Water (2.5 ml) was added, and the mixture was stirred 0.5 h, followed by addition of $MgSO_4$. The mixture was filtered, and the filtrate was washed with saturated NaCl solution (3 × 40 ml), dried ($MgSO_4$), filtered, and the ether evaporated to yield a residue

containing the desired product, benzene, and triphenylphosphine oxide. Distillation yielded 1.07 g (50.8%) of the product (**1b**) as a colorless liquid, which was further purified on an 8 ft × 0.5 in. column packed with 5% FFAP on Chromosorb W 60/80 at 123 °C and 142 ml/min: bp 62–65 °C (5 mm); ir (film) 3300, 2290, 2190, 2090, 1611, 1055, and 700 cm^{-1}; NMR ($CDCl_3$) δ 1.10–2.20 (m, 4 H, methylene), 2.10 (s, 1 H, hydroxyl), 3.72 (s, deuterium broadened, 1 H, methine), and 4.70 (d, 0.005 H, vinyl); the mass spectrum had a predominant parent peak at 118 mass units. Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 75.10; H, 10.97.

3-Acetoxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (2b). Acetyl chloride (133 mg, 0.12 ml, 1.70 mmol, Baker) was added cautiously via syringe to a stirred solution of 134 mg (1.13 mmol) of 3-hydroxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (**1b**) in 0.27 ml (270 mg, 3.4 mmol) of dry pyridine (from BaO) at 0 °C under N_2 according to the method of Wheeler.[17] Details are given elsewhere.[8] The acetate was isolated by preparative VPC, at 115 °C and 139 ml/min, yielding 99 mg (54.7%) of the desired product as a colorless oil: ir (film) 2295, 2195, 2085, 1730, 1615, 1240, 1030, and 705 cm^{-1}; NMR ($CDCl_3$) δ 1.15–2.20 (m, 4 H, methylene), 2.02 (s, 3 H, methyl), and 4.77 (s, deuterium broadened, 1 H, methine); the mass spectrum had a parent peak at 160 mass units. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.14; H, 9.33.

3-Mesyloxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (3b). A solution of 152 mg (1.29 mmol) of 3-hydroxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (**1b**) in 1.0 ml of dry pyridine (from BaO) under N_2 was allowed to react with methanesulfonyl chloride (295 mg, 0.20 ml, 2.58 mmol) according to the general method of Sneen and Larsen.[18] Details are given elsewhere.[8] The mesylate was obtained as 196 mg (77.8%) of a light yellow oil: ir (film) 2300, 2200, 2090, 1612, 1330, and 1167 cm^{-1}; NMR (50/50 $CFCl_3/CF_2Cl_2$) δ 1.02–2.24 (m, 4 H, methylene), 2.78 (s, 3 H, methyl), and 4.56 (s, deuterium broadened, 1 H, methine); the mass spectrum gave a main parent peak at 196 mass units. Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H, 7.42. Found: C, 50.69; H, 7.43.

3-Brosyloxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (4b). 3-Hydroxy-1-methylenecyclohexane-*2,2,4,4 7,7-d*$_6$ (**1b**, 79 mg, 0.668 mmol) was added cautiously via syringe to a stirred solution of 348 mg (1.36 mmol) of *p*-bromobenzenesulfonyl chloride (Aldrich) in 1 ml of dry pyridine (from BaO) at 0 °C under N_2 according to the general procedure of Brown and Ham.[19] Details are given elsewhere.[8] The brosylate was obtained as 176 mg (78%) of a yellow oil: ir (film) 2300, 2200, 2095, 1611, 1573, 1355, and 1175 cm^{-1}; NMR (CF_2Cl_2) δ 1.10–2.05 (m, 4 H, methylene), 4.54 (s, deuterium broadened, 1 H, methine), and 7.67 (q, 4 H, aromatic). Anal. Calcd for $C_{17}H_{15}BrO_3S$: C, 47.14; H, 4.56. Found: C, 47.38; H, 4.66.

3-Tosyloxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (5b). 3-Hydroxy-1-methylenecyclohexane-*2,2,4,4,7,7-d*$_6$ (**1b**, 74 mg, 0.626 mmol) was added dropwise via syringe to a solution of 255 mg (1.34 mmol) of *p*-toluenesulfonyl chloride (Aldrich) in 1 ml of pyridine (from BaO) at 0 °C under N_2 according to the general procedure of Brown and Ham.[19] Details are given elsewhere.[8] The tosylate was obtained as 129 mg (76%) of a light yellow oil: ir (film) 2300, 2200, 2090, 1615, 1600, 1350, and 1170; NMR (CF_2Cl_2) δ 1.10–2.20 (m, 4 H, methylene), 2.39 (s, 3 H, benzylic methyl), 4.43 (s, deuterium broadened, 1 H, methine), 7.22 (d, 2 H, aromatic), and 7.74 (d, 2 H, aromatic).

3-*p*-Nitrobenzoyloxy-1-methylene-1-cyclohexane-*2,2,4,4-d*$_4$ (6a). Tosyl chloride (1.65 g, 8.62 mmol, Aldrich) and *p*-nitrobenzoic acid (720 mg, 4.31 mmol, Aldrich) were dissolved in 15 ml of pyridine (from BaO) with stirring at room temperature under N_2. The reaction mixture was cooled in an ice/water bath, and 3-hydroxy-1-methylenecyclohexane-*2,2,4,4-d*$_4$ (**1a**) (500 mg, 4.31 mmol) was added dropwise via syringe following the general method Brewster and Ciotti.[20] Details are given elsewhere.[8] The *p*-nitrobenzoate was obtained as 1.00 g (87.6%) of a light yellow oil: ir (film) 2200, 2090, 1725, 1650, 1607, 1525, 1345, 1270, and 1100 cm^{-1}; NMR ($CDCl_3$) δ 1.12–2.20 (m, 4 H, ring methylene), 4.70 (AB quartet, 2 H, exo methylene), 5.03 (s, deuterium broadened, 1 H, methine), and 8.15 (s, AB quartet with very small Δν, 4 H, aromatic).

3-Methoxycyclohexan-1-one-*2,2,4,4,7,7,7-d*$_7$. A solution containing 4.60 g (46.4 mmol) of 2-cyclohexen-1-one-*2,4,4-d*$_3$, 2.0 g (55.6 mmol) of methanol-d_4 (99.5%, Aldrich), and one drop of concentrated sulfuric acid-d_2 (Merck Sharp and Dohme) was stirred for 12 h at room temperature under N_2. The solution was then dissolved in 75 ml of anhydrous ether and washed with a solution of 0.5 g of K_2CO_3 in 5 ml of D_2O. The ether layer was dried ($MgSO_4$) and filtered, and the ether was removed by rotary evaporation. The residue was distilled to yield three fractions containing ratios of unsaturated ketone to saturated ketone of 15.5:1, 7:2, and 1:9, respectively. The third fraction, bp 74–76 °C (7 mm), was utilized in the formation of the corresponding exo methylene compound (**7a**) without further purification. The corrected yield of desired ether obtained in the third fraction was 1.65 g (26%). A portion of the desired product was preparatively separated on an 8 ft × ½ in. column packed with 5% FFAP on Chromosorb W 60/80 at 120 °C and 150 ml/min to yield the pure ether as a colorless liquid ir (film) 2175, 2060, 1705, and 1125 cm^{-1}; NMR ($CDCl_3$) δ 1.46–2.64 (m, 4 H, ring methylene) and 3.69 (br s, 1 H, methine); the mass spectrum gave two main parent peaks at 135 and 136, indicating an average of slightly more than seven deuterium atoms per molecule.

3-Methoxy-1-methylenecyclohexane-*2,2,4,4,8,8,8-d*$_7$ (7a). A 2.33 M solution of phenyllithium (10.0 ml, 23.3 mmol, 70/30 benzene/ether, Alfa) was added via syringe to a stirred mixture of 8.50 g (25.2 mmol) of methyltriphenylphosphonium bromide (Aldrich) in 200 ml of dry ether (from $LiAlH_4$) under N_2. The resulting solution was stirred for 0.5 h, and a solution of 1.53 g (11.3 mmol) of 3-methoxycyclohexan-1-one-*2,2,4,4,7,7,7-d*$_7$ in 50 ml of dry ether was added dropwise. The reaction mixture was stirred a further 2.0 h, and sufficient acetone was added to discharge the orange-yellow phosphorane intermediate. The reaction mixture was filtered, and the filtrate was washed with saturated NaCl solution (3 × 25 ml), dried ($MgSO_4$), filtered, and the ether removed at atmospheric pressure. Pentane (20 ml) was added to the residue to precipitate the triphenylphosphine oxide, and the pentane solution was washed down an alumina column with an additional 200 ml of pentane. The pentane was distilled at atmospheric pressure, and the residue was distilled at reduced pressure. A forerun containing benzene and the desired product was collected, followed by a main fraction containing the pure desired product as 0.51 g (33.8%) of a colorless liquid that was analyzed and preparatively separated from a few small impurities on an 8 ft × ½ in. column packed with 5% FFAP on Chromosorb W 60/80 at 100 °C and 150 ml/min: ir (film) 2200, 2060, 1655, 1450, 1128, and 888 cm^{-1}; NMR ($CDCl_3$) δ 0.96–2.26 (m, 4 H, ring methylene), 3.20 (s, deuterium broadened, 1 H, methine), and 4.70 (s, 2 H, term methylene); the mass spectrum gave two main parent peaks at 133 and 134, indicating an average of slightly more than seven deuterium atoms per molecule. Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.05; H, 11.20.

3-Methoxy-2-cyclohexen-1-one-*2,4,4,6,6-d*$_5$. A solution of 45.80 g (0.363 mol) of 3-methoxy-2-cyclohexen-1-one in 200 ml of 0.525 N sodium methoxide/methanol-*d* (from sodium metal and methanol-*d*)[21] was stirred for 1 day at room temperature under N_2. The solution, protected by a fast stream of N_2, was then neutralized with 6.65 ml of a 15.8 N D^+/D_2O solution (from the cautious addition of about 13 ml of PCl_3 to 43 ml of D_2O). The pH was maintained greater than 7 by the addition of K_2CO_3 when necessary. About two-thirds of the methanol-*d* was removed by rotary evaporation. The remaining mixture was brought to a total volume of 500 ml by the addition of a 50/50 THF/ether solution. The mixture was then filtered. The filtrate was dried ($MgSO_4$), filtered, concentrated, and distilled. The main fraction was subjected to a second cycle using the same quantities of reagents and a third cycle utilizing 285 ml of 0.525 N sodium methoxide/methanol-*d* solution and 9.46 ml of the 15.8 N D^+/D_2O solution. Distilled yields for the first, second, and third cycles were respectively 43.90, 42.46, and 40.60 g. The extent of deuterium incorporation was determined by NMR for each cycle to be respectively 84.3, 93.8, and at least 98.7%. The overall yield of the desired product was 40.60 g (85.3%) of a colorless liquid: bp 69–70 °C (0.08 mm); ir (film) 2290, 2230, 1650, 1575, 1455, and 1330 cm^{-1}; NMR ($CDCl_3$) δ 1.92 (s, deuterium broadened, 2 H, methylene); the mass spectrum gave a main parent peak at 131 mass units.

2-Cyclohexen-1-one-*2,4,4,6,6-d*$_5$. A modification of the procedure of Gannon and House[22] was utilized. A solution of 40.0 g (0.305 mol) of 3-methoxy-2-cyclohexen-1-one-*2,4,4,6,6-d*$_5$ in 100 ml of dry ether (from $LiAlH_4$) was added, at a rate that maintained a gentle reflux, to a stirred suspension of 6.40 g (0.168 mol) of $LiAlH_4$ (Alfa) in 500 ml of dry ether. The ketone addition required 45 min, after which time the mixture was refluxed for 0.5 h. The reaction mixture was then hydrolyzed by the cautious addition of 16 ml of D_2O (Bio-Rad). A 6.7 N D^+/D_2O solution (115 ml, from the addition of about 11 ml of PCl_3 to about 105 ml of D_2O) was added, and the resultant two-phase

system was placed in a separatory funnel. The ether layer was removed, and the aqueous layer was extracted with an additional 4 × 250 ml of anhydrous ether. The combined ethereal layers were dried ($MgSO_4$), filtered, concentrated, and distilled to yield 25.82 g (83.8%) of the desired product as a colorless liquid, which was at least 99% pure by VPC: bp 51–52 °C (9 mm); ir (film) 2205, 2100, 1665, and 1602 cm^{-1}; NMR ($CDCl_3$) δ 2.00 (s, 2 H, methylene) and 7.00 (s, 1 H, vinyl at the 3 position); the mass spectrum had a predominant parent peak at 101 mass units.

3-(Methylthio)cyclohexan-1-one-*2,2,4,4,6,6-d*$_6$. Deuterium oxide (10.7 ml, 11.8 g, 0.592 mol, Bio-Rad), triethylamine (0.40 ml, 0.29 g, 0.00295 mol, Aldrich), and 2-cyclohexen-1-one-*2,4,4,6,6-d*$_5$ (3.0 g, 0.0296 mol) were dissolved in 96.2 ml of dry 1,2-dimethoxyethane (from $LiAlH_4$) under N_2. The reaction flask was cooled in a dry ice/acetone bath and degassed (five cycles). The outlet tube was protected by a $CaSO_4$ drying tube. Methanethiol (3.28 ml, 2.84 g, 0.0592 mol, Matheson) was condensed into a graduated tube at −78 °C and transferred to the reaction flask by bulb-to-bulb distillation in a closed system. The reaction solution, under a slow N_2 flow, was placed in an ice/methanol bath and maintained at −13 °C for 2 days. The bath was removed and a rapid N_2 flow maintained at the surface of the solution overnight to vent any excess mercaptan. The two-phase system was extracted with ether (4 × 100 ml). The combined ethereal layers were dried ($MgSO_4$), filtered, concentrated, and distilled to yield 3.98 g (89.5%) of the desired product as a colorless liquid: bp 68–69 °C (0.03 mm); ir (film) 2210, 2110, 1705 cm^{-1}; NMR ($CDCl_3$) δ 1.86 (AB quartet, 2 H, methylene), 2.08 (s, 3 H, methyl), and 2.90 (s, deuterium broadened, 1 H, methine); the mass spectrum had a predominant parent peak at 150 mass units.

3-(Methylthio)-1-methylenecyclohexane-*2,2,4,4,6,6-d*$_6$ (8c). A phenyllithium solution (16.15 ml, 0.0376 mol, 2.33 M, 70/30 benzene/ether, Aldrich) was added to a stirred mixture of 14.13 g (0.0396 mol) of methyltriphenylphosphonium bromide (Aldrich) in 250 ml of dry ether (from $LiAlH_4$) under N_2. The dropwise addition of 3.00 g (0.0198 mol) of 3-(methylthio)cyclohexan-1-one-*2,2,4,4,6,6-d*$_6$ in 50 ml of dry ether to the phosphorane solution was followed by stirring overnight. The reaction was worked up and the crude product isolated as described for **1a** and **1b** above. The crude residue was purified on an alumina column with pentane as eluent, and the residue was chromatographed on an 8 ft × ½ in. column with 5% FFAP on Chromosorb W 60/80 at 115 °C and 146 ml/min. The product thioether was obtained as 2.31 g (78.7%) of a colorless liquid: bp 55–57 °C (2 mm); ir (film) 2195, 2095, 1645, 1444, and 882 cm^{-1}; NMR ($CDCl_3$) δ 1.60 (AB quartet, 2 H, ring methylene), 2.10 (s, 3 H, methyl), 2.57 (s, deuterium broadened, 1 H, methine), and 4.66 (s, 2 H, exo methylene); the mass spectrum had a main parent peak at 148 mass units. Anal. Calcd for $C_8H_{14}S$: C, 67.54; H, 9.92. Found: C, 67.71; H, 10.13.

Thiophenol-*d*. Thiophenol (7.90 g, 7.38 ml, 0.07 mol, Aldrich) was shaken for 5 min with 14.0 g (12.65 ml, 0.70 ml, Bio-Rad) of D_2O under N_2. The D_2O layer was removed via syringe, and the remaining thiophenol-*d*/deuterium oxide mixture was distilled. A portion of the main fraction, bp 67 °C (20 mm), was immediately utilized in a reaction with 2-cyclohexen-1-one-*2,4,4,6,6-d*$_5$.

3-(Phenylthio)cyclohexan-1-one-*2,2,4,4,6,6-d*$_6$ (9c). Deuterium oxide (7.17 ml, 7.93 g, 0.396 mol, Bio-Rad), triethylamine (0.276 ml, 0.20 g, 0.00198 mol, Aldrich), and 2-cyclohexen-1-one-*2,4,4,6,6-d*$_5$ were dissolved in 64.5 ml of dry 1,2-dimethoxyethane (from $LiAlH_4$) under N_2. The reaction flask was cooled in a dry ice/acetone bath and degassed (five cycles). When the reaction solution returned to room temperature, 4.12 ml (4.41 g, 0.0396 mol) of freshly distilled thiophenol-*d* was added via syringe. The solution was shaken, allowed to stand at room temperature for 2 days, and poured into an addition funnel containing 100 ml of ether and 10 ml of brine. The aqueous phase was extracted with an additional 3 × 10 ml of ether. The organic portions were combined, dried ($MgSO_4$), filtered, concentrated, and distilled to yield 3.94 g (93.5%) of a colorless liquid: bp 140–145 °C (0.05 mm); ir (film) 2200, 2100, 1715, 1585, 1437, 733, and 684 cm^{-1}; NMR ($CDCl_3$) δ 1.88 (AB quartet, 2 H, methylene), 3.40 (s, deuterium broadened, 1 H, methine), and 7.32 (m, 5 H, aromatic); the mass spectrum had a parent peak at 212 mass units. Anal. Calcd for $C_{12}H_{14}OS$: C, 69.86; H, 6.84. Found: C, 69.64; H, 6.93.

3-(Phenylthio)-1-methylenecyclohexane-*2,2,4,4,6,6-d*$_6$ (9c). A phosphorane solution was generated by the addition via syringe of 11.50 ml (0.0268 mol) of 2.33 M phenyllithium solution (70/30 benzene/ether, Alfa) to a stirred mixture of 10.09 g (0.0282 mol) of methyltriphenylphosphonium bromide (Aldrich) in dry ether (from $LiAlH_4$) under N_2. A solution of 3.00 g (0.0141 mol) of 3-(phenylthio)cyclohexan-1-one-*2,2,4,4,6,6-d*$_6$ in 50 ml of dry ether was then added dropwise. The product isolation procedure was analogous to that utilized for **1a** and **1b.** The crude material was eluted with pentane on an alumina column, concentrated, and distilled to give 2.33 g (78.5%) of a colorless liquid: bp 102–105 °C (0.1 mm); ir (film) 2190, 2090, 1643, 1583, 1438, 833, 730, and 683 cm^{-1}; NMR ($CDCl_3$) δ 1.58 (AB quartet, 2 H, ring methylene), 3.12 (s, deuterium broadened, 1 H, methine), 4.65 (s, 2 H, exo methylene), and 7.28 (m, 5 H, aromatic); the mass spectrum had a parent peak at 210 mass units. Anal. Calcd for $C_{13}H_{16}S$: C, 76.41; H, 7.90. Found: C, 76.23; H, 8.03.

3-Carbomethoxy-1-methylenecyclohexane (10). Molecular bromine was added to 3-cyclohexene-1-carboxylic acid (Aldrich) as described by Perkin.[23] The dibromide was converted by the method of Noyce and Dolly[24] to a γ-lactone, which was opened by NaOH to a γ-keto acid.[25] Esterification[26] gave 3-oxo-1-cyclohexane carboxylate, which was converted to the final product (**10**) by the Wittig reaction. These transformations are described in detail elsewhere.[8]

3-(Hydroxymethyl)-1-methylenecyclohexane (11). Protection of the ketone function in 3-oxo-1-cyclohexane carboxylate[26] (see **10**), followed by reduction of the ester to hydroxymethyl, removal of the protecting group, and a Wittig reaction, gave **11.** The details are given elsewhere.[8]

3-Methyl-2-cyclohexen-1-one-*2,4,4,6,6,7,7,7-d*$_8$. The exchange procedure of Thomas, Willhalm, and Bowie[27] was utilized. A small pellet (about 10 mg) of Na was added to a vigorously stirred solution of 10.02 g (0.0907 mol) of 3-methyl-2-cyclohexen-1-one (Aldrich) in 57.5 ml (63.7 g, 3.175 mol) of D_2O and 60 ml of dry 1,4-dioxane under N_2 at 0 °C. The solution was stirred at 25 °C for 50 h, saturated with NaCl, and extracted with 5 × 50 ml of ether. The combined ether layers were dried ($MgSO_4$) and filtered, and the ether was removed. The 1,4-dioxane was removed at reduced pressure (100 mm). This procedure was executed three times, the last work-up being carried out entirely under N_2. The desired product distilled as 6.13 g (57.1%) of a colorless liquid: bp 82 °C (15 mm); NMR δ 1.97 (s, 2 H, ring methylene), 2.27 (m, 0.4 H, methylene α to the carbonyl), and 5.83 (s, 0.01 H, vinyl).

3-Methylcyclohexan-1-one-*4,4,7,7,7-d*$_5$. Lithium metal (0.70 g, 0.101 mol, 3 equiv) and 4.79 ml (3.76 g, 0.0507 mol) of *tert*-butyl alcohol were dissolved in 400 ml of liquid NH_3 (from Na). A solution of 4.0 g (0.0338 mol) of 3-methyl-2-cyclohexen-1-one-*2,4,4,6,6,7,7,7-d*$_8$ in 50 ml of dry THF was added over a period of 15 min with stirring under N_2. The reaction solution was stirred for 2 h, and the blue color was discharged by adding an excess of NH_4Cl. After the NH_3 evaporated, the residue was partitioned between ether and brine. The ether extracts (3 × 200 ml) were dried ($MgSO_4$) and the ether and THF evaporated, yielding 3.85 g of a 2:1 mixture of the desired ketone and the corresponding alcohol. The mixture was oxidized with Jones reagent to give a crude yield of 3.77 g (98%) of ketone.

3-Methylcyclohexan-1-one-*2,2,4,4,6,6,7,7,7-d*$_9$. A small pellet (about 10 mg) of Na was added to a vigorously stirred solution of 3.77 g (0.032 mol) of 3-methylcyclohexan-1-one-*4,4,7,7,7-d*$_5$ in 11.65 ml (12.88 g, 0.644 mol) of D_2O and 11.65 ml of dry 1,4-dioxane under N_2 at 0 °C. The system was stirred at 76 °C for 48 h and extracted with dry ether (5 × 50 ml) after adding NaCl. The combined ether layers were dried ($MgSO_4$) and filtered, and the ether and 1,4-dioxane were evaporated. The residue was distilled, yielding a major fraction (0.97 g, 25%) of ketone: bp 59 °C (16 mm).

3-Methyl-1-methylenecyclohexane-*2,2,4,4,6,6,8,8,8-d*$_9$ (12). The phosphorane solution was generated by the addition via syringe of 6.78 ml (15.8 mmol of a 2.33 M solution of phenyllithium (Alfa) in 70/30 benzene/ether to a stirred mixture of 5.94 g (16.6 mmol) of methyltriphenylphosphonium bromide in 150 ml of ether (from $LiAlH_4$) under N_2. A solution of 0.93 g (7.66 mmol) of 3-methylcyclohexan-1-one-*2,2,4,4,6,6,7,7,7-d*$_9$ in 50 ml of ether was then added dropwise to the phosphorane solution. The reaction mixture was stirred for 2 h and worked up in the usual Wittig manner (see **1a**, **1b**). The crude product was taken up in pentane and washed down an alumina column with 250 ml of pentane. The solvent was removed and the product purified by preparative VPC on an 8 ft × ½ in. column packed with 10% SE-30 on Chromosorb W 60/80 at 100 °C and 107 ml/min. The yield of purified **12** was 0.375 g (41.0%) of a colorless liquid: ir (film) 2200, 2120, 2090, 1640, and 880 cm^{-1}; NMR ($CDCl_3$) δ 1.47 (s, deuterium broadened, 1 H, methine), 1.52 (AB quartet, 2 H, meth-

ylene at 5 position), 2.17 (m, 0.24 H, allylic, corresponding to 94% deuterium incorporation at positions 2 and 6), and 4.58 (s, 2 H, exo methylene); the mass spectrum had a main parent peak at 119 mass units. Anal. Calcd for C_8H_{14}: C, 87.19; H, 12.81. Found: C, 87.15; H, 12.94.

References and Notes

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Effect of Solvents and Counterions on the Equilibrium and Kinetics of Disproportionation of Tetracenide Radical Ions

G. Levin and M. Szwarc*

Contribution from the Department of Chemistry, State University of New York, College of Environmental Science and Forestry, Syracuse, New York 13210.

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Abstract: We studied the disproportionation of the salts of tetracenide radical anions, $2Te^{\cdot-},Cat^+ \rightleftarrows Te + Te^{2-},2Cat^+$, involving Li^+, Na^+, K^+, and Cs^+ cations. The reaction was investigated in the following solvents: tetrahydrofuran, dioxane, and diethyl ether. The disproportionation constant varies within ten orders of magnitude, being as low as 6×10^{-9} for the lithium salt in tetrahydrofuran and as high as 16.4 in diethyl ether. The kinetics of disproportionation was investigated by flash photolysis. The rate constant of disproportionation is very low for the lithium salt in tetrahydrofuran ($\sim 36\ M^{-1}\ s^{-1}$), higher for the other salts in that solvent (10^4–$10^5\ M^{-1}\ s^{-1}$), and very high for the Li^+ and Na^+ salts in dioxane and diethyl ether (10^6–$10^8\ M^{-1}\ s^{-1}$). The rate constants of reapportionation, $Te + Te^{2-},2Cat^+ \rightarrow 2Te^{\cdot-},Cat^+$, are in the range of 10^9–$10^{10}\ M^{-1}\ s^{-1}$ for most of the investigated systems; however, for the Li salt in DOX its value is as low as $1.1 \times 10^8\ M^{-1}\ s^{-1}$ and still lower in diethyl ether, namely $3.6 \times 10^6\ M^{-1}\ s^{-1}$. The significance of these results is discussed.

The thermodynamics of the disproportionation of radical anions

$$2A^{\cdot-} \rightleftarrows A + A^{2-} \qquad K_{dispr}$$

was extensively studied by polarographic[1] and potentiometric[2] techniques. These methods provide us with the first and the second reduction potentials of the parent compounds (ϵ_1 and ϵ_2), and therefore allow us to calculate K_{dispr} from the relation $0.06 \log K_{dispr} = \epsilon_2 - \epsilon_1$. Planar aromatic hydrocarbons were the main objects of these studies. The results showed that K_{dispr}'s are very small, 10^{-5} or less, implying that these disproportionations are highly unfavorable.

Exceptions were known. For example, the disproportionation equilibria of radical anions of tetraphenylethylene,[3] stilbene,[4] or cyclooctatetraene[5] are shifted far to the right, the respective equilibrium constants exceeding 1000 for some of those systems. However, these findings were rationalized by invoking the operation of special factors, e.g., those caused by changes of geometry of the reduced species. Since the reduction of planar aromatic hydrocarbons is not associated with any drastic changes of their geometry, the smallness of the respective K_{dispr}'s remained undisputed.

Subsequent studies, which utilized spectrophotometric and ESR techniques, showed that the disproportionation of radical anions is more complex than has been believed.[6] The radical anions may exist as free ions or be paired with counterions, while three distinct ionic species involve the dianions, namely A^{2-}, A^{2-},Cat^+, and $A^{2-},2Cat^+$. Hence, three elementary equilibria participate in a disproportionation:

$$2A^{\cdot-},Cat^+ \rightleftarrows A + A^{2-},2Cat^+ \qquad K_1$$

$$A^{\cdot-} + A^{\cdot-},Cat^+ \rightleftarrows A + A^{2-},Cat^+ \qquad K_2$$

$$2A^{\cdot-} \rightleftarrows A + A^{2-} \qquad K_3$$

These elementary equilibrium constants, referred to the same system, may greatly differ in their values, e.g., for the system sodium salt of tetraphenylethylene radical anion in THF at 25 °C $K_1 = 400$, $K_2 = 3.6$, and K_3 is probably as low as 10^{-10}.