Electrophilic Bromination of Specifically Deuterated Cyclohexenes: A Combined Experimental and Theoretical Investigation

H. Slebocka-Tilk,[†] A. Neverov,[†] S. Motallebi,[†] R. S. Brown,*,[†] O. Donini,[‡] J. L. Gainsforth,[‡] and M. Klobukowski*,[‡]

Contribution from the Department of Chemistry, Queen's University, Kingston, Ontario, Canada K7L 3N6, and Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

Received April 10, 1997

Abstract: The electrophilic addition of Br_2 to specifically deuterated cyclohexenes (**1**−**5**) was studied methanol (MeOH) by stopped-flow kinetics in order to determine a deuterium kinetic isotope effect (DKIE) for the various isotopomers. The DKIE for bromination of the isotopomers was also determined by a mass spectrometric method where exactly known quantities of two of the cyclohexenes were incompletely brominated in MeOH and where the ratio of the remaining isotopomers was determined. A computational study using density functional theory (DFT) was undertaken to examine the equilibrium isotope effect (EIE) for the equilibrium involving the formation of the cyclohexenyl bromonium ion from cyclohexene plus Br_2. The agreement between experiment and theory is remarkably good and indicates that, for perdeuteriocyclohexene, the inverse DKIE and EIE of ∼1.5 can be partitioned two-thirds to the two vinyl CH's and one-third to the four homoallylic CH's, the four allylic CH's contributing negligibly to the overall effect. The computational study also indicates that there is extensive mixing of the CC and CH vibrational modes and that it is not possible to identify all the individual modes responsible for the large inverse EIE. Analysis of the computational data indicates that the isotopic effects may be divided into two groups; those associated with the deuteriums on the vinyl positions and those associated with the remaining allylic and homoallylic carbons. In the former, the inverse EIE is due to the changes in all bending modes. For the latter, the isotopically sensitive modes are those of all ten C−H stretches with changes in bending frequencies being unimportant. The bending vibrational modes were found to be strongly coupled.

Introduction

Some time ago we reported secondary deuterium kinetic isotope effects (DKIE) for the bromination of H_{10} and D_{10} cyclohexene (**1,** L = H, D) in acetic acid at 25 °C.[1] The inverse value obtained, $k_{D10}/k_{H10} = 1.9 \pm 0.15$, was surprisingly large considering that sparse previous work had indicated that secondary DKIEs for electrophilic brominations were small. For example, Denney and Tunkle[2a] reported that the secondary α-DKIE for bromination of *trans*-stilbene-d_2 was $k_D/k_H = 1.1$, while Wilkins and Regulski[2b] showed that the para-substituted styrenes, when brominated in HOAc at 40 °C, produced small inverse secondary α-DKIE's of $k_D/k_H = 1.01-1.05$. More recently,[3a,b] Bellucci and co-workers have reported inverse DKIEs of about 1.2 for the addition of Br^-/Br_2 (Br_3^-) to each of stilbene, 1,1-diphenylethylene, and α-(3-trifluoromethylphenyl)styrene, the respective values for the addition of Br_2 to these being 1.33, 1.03, and 1.42.[3b] Most of the above results for Br_2 addition were rationalized in terms of the customary model in which changes in the out-of-plane bending frequencies accompanying rehybridization of the α-carbons from sp^2 to sp^3 occurred in the rate-limiting transition state. For 1,1-diphenyl ethylene, rate-limiting bromination proceeds to an α-bromocarbocation so that the nearly unit secondary DKIE comprises two competing effects, an inverse one arising from the rehybridization and a normal one attributable to hyperconjugation of the C−L bonds with the benzylic cationic center.[4b] However, for bromination by tribromide, the DKIE is a complicated mix of rehybridization effects, and those arising from nucleophilic attack of Br^- on the charge-transfer complex.[4a] Note that in any of the above cases, the presence of the phenyl rings introduces the possibility that the bromonium ions and the charge distribution within them may be highly distorted.

In our symmetrical aliphatic cases, although one must be careful about the effect of the remote deuteriums, comparison of the DKIE for bromination of **1**, L = H, D with that for 3,3,6,6-tetradeuteriocyclohexene (**2**) indicated that the allylic deuteriums contributed negligibly to the observed effect. That fact, along with the assumption that the more remote γ-deuteriums could be neglected as contributors to the observed DKIE, led to the conclusion that the two α-deuteriums in cyclohexene contributed equally to the effect, the value per deuterium being roughly $\sqrt{1.9} = 1.4$.

[†] Queen's University.

[‡] University of Alberta.

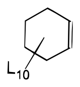
(1) Slebocka-Tilk, H.; Zheng, C. Y.; Brown, R. S. *J. Am. Chem. Soc.* **1993**, *115*, 1347.

(2) (a) Denney, D. B.; Tunkle, N. *Chem. Ind. (London)* **1959**, 1383. Wilkins, C. L.; Regulski, T. W. *J. Am. Chem. Soc.* **1972**, *94*, 6016.

(3) (a) Bellucci, G.; Chiappe, C.; Lo Moro, G. *J. Org. Chem.* **1997**, *62*, 3176. (b) Bellucci, G.; Chiappe, C. *J. Chem. Soc., Perkin Trans. 2* **1997**, 581.

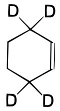
(4) (a) Lowry, T. H.; Richardson, K. S. In *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987; pp 232−244. (b) Maskill, H. In *The Physical Basis of Organic Chemistry*; Oxford University Press: Oxford, 1985; pp 367−404. (c) Westaway, K. C. In *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Vol. 7, pp 275−392.

S0002-7863(97)01145-1 CCC: $15.00



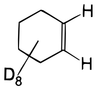
1, L=H, D

D10



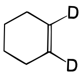
2

D4



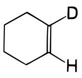
3

D8



4

D2



5

D1

Although the reported DKIE is within the realm of possible values for two olefinic C−L bonds undergoing maximum changes in rehybridization, it is suspiciously large enough that we undertook a more detailed experimental and theoretical study of this process. In particular we were interested in whether neglect of the effect of the γ-deuteriums is warranted. Herein we report our findings for the bromination of specifically deuterated cyclohexenes **1**−**5** in methanol. As well, we report mass spectrometric determination of the DKIE where mixtures of two unreacted alkenes were recovered from the reaction after incomplete competitive bromination in MeOH and analyzed for their isotopic composition. Finally, we report a detailed computational study using density functional theory (DFT) to model the equilibrium deuterium isotope effect (EIE) for the equilibrium involving formation of the cyclohexenyl bromonium ion from cyclohexene and Br_2.

Experimental Section

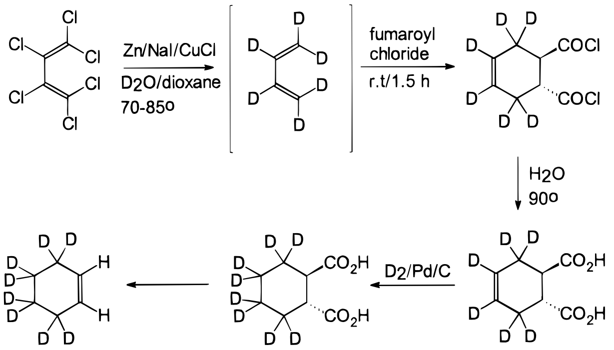
a. Materials. Acetic acid (Fisher, reagent grade, 99.7%) was purified as described.[5] LiBr (General Intermediates) and $LiClO_4$ (Alpha) were dried in a vacuum at 120 °C over P_2O_5 for 48 h. Br_2 (Aldrich) was used as supplied. Methanol (2 L, Sigma-Aldrich, 99.9% ACS HPLC grade) was treated with 2 drops of Br_2 and allowed to stand in the dark for 24 h after which it was distilled through a 70 cm Vigreux column with the middle fraction only being collected.

Cyclohexene-d_{10} (**1,** L = H) was made in ~50% yield by dehydration of cyclohexanol-d_{12} according to a published procedure.[6] Cyclohexene-3,3,6,6-d_4 (**2**) was prepared in 22% yield according to the published procedure of Wolfe and Campbell.[7] Mass analysis indicated a 98% incorporation of deuterium in **2**.

Cyclohexene-1,2-d_2 (**4**) was also prepared by the procedure of Wolfe and Campbell[7] in 33% yield starting from cyclohexane-1,2-dicarboxylic anhydride which was exchanged at the 1,2-positions using D_2SO_4 and D_2O.[8] ^{1}H NMR analysis indicated the product had 93% deuterium at the vinyl positions. Cyclohexene-d_1 (**5**) was prepared by dehydration[9] of d_1-cyclohexanol, this being prepared from the reduction of cyclohexanone with $LiAlD_4$.[10] ^{1}H NMR analysis indicated a 98% incorporation of deuterium at C_1.

Cyclohexene-3,3,4,4,5,5,6,6-d_8 (**3**) was prepared as outlined in the process shown in Scheme 1. Zn dust (98 g, 1.51 mol) and 90 mL of anhydrous dioxane were placed in a 500 mL round-bottom flask equipped with a gas inlet tube, a gas exit tube leading into a thick-walled tube cooled to −78 °C, and a solid addition tube. This was then flushed with Ar and 1.0 g of NaI, 6.0 g of anhydrous CuCl, and 30 mL D_2O were added, and the mixture heated to 80 °C with stirring. To this heated mixture was added, over the course of 3 h, 52 g (0.2 mol) of hexachlorobutadiene. The volatile hexadeuteriobutadiene that was produced was trapped in the thick-walled tube to give a crude yield of 7.25 mL (5.3 g, 44%).[11] To the tube was immediately added 10 mL of $CHCl_3$ and fumaroyl chloride (12.2 g, 0.08 mol) in 45 mL of $CHCl_3$. The tube was sealed and the contents were allowed to reach room temperature after which a mild exothermic reaction takes place (cooling not required). After standing for 15 h, the contents of the tube were transferred to another flask, and 30 mL of D_2O was carefully added. The mixture was then heated to 95 °C for 15 min at which point an exothermic reaction occurred and the dicarboxylic acid precipitated as a white solid. The excess D_2O was removed and the residue washed with a small portion of toluene and then CH_2Cl_2. After drying under vacuum, 13.5 g (95%) of a white solid was obtained: mp 170−172 °C. This was carried on to the next step.

Scheme 1



The above unsaturated dicarboxylic acid (13.0 g, 0.073 mol) was dissolved in 100 mL of dioxane, and 2.0 g of Pd/C was added. This mixture was deuterated under a D_2 atmosphere until no more deuterium was consumed. The suspension was filtered through a pad of Celite, and the solvent removed to give 9.5 g of a white powder: mp 170−172 °C, yield ~72%. The final octadeuteriocyclohexene (**3**) was prepared from the total of the preceding material in 36% yield, (1.6 g), using the procedure of Wolfe and Campbell:[7] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (s); ^{2}H NMR ($CHCl_3$) 1.64 (s), 2.03 (s); GC ir 3031, 2922, 2207 (st), 2112 (st), 1644 cm^{-1}; GC MS, $m/z = 90$. ^{1}H NMR analysis indicated that the above material contained 4.5−5% residual H at $C_{3,6}$ and 8−8.5% at $C_{4,5}$.

b. Kinetics. The rate constants of Br_2 addition to selectively deuterated cyclohexenes were measured at 25 °C under pseudo-first-order conditions of excess olefin in HOAc ($\mu = 0.1$ ($LiClO_4$)), methanol (no salt) using an Applied Photophysics SX-17MX stopped-flow instrument. The olefin concentration was varied $(2-7) \times 10^{-3}$ M (after mixing) and the [Br_2] was varied $(0.5-5) \times 10^{-4}$ M. Solutions were prepared and stored with protection from moisture and light. The pseudo-first-order rate constants were evaluated by nonlinear least-squares fitting of the absorbance vs time traces for the disappearance of Br_2 to an exponential model. The k_{obs} values used were the averages of 10−16 runs. The second-order rate constants were evaluated as $k_2 = k_{obs}/[\text{alkene}]$.

c. Mass Spectrometry. A mass spectrometric method was used wherein mixtures of known quantities of various selectively deuterated cyclohexenes were incompletely brominated in methanol and the unreacted alkenes subjected to GC MS analysis.[12]

In the standard experiment, equimolar amounts (0.04 mmol) of deuturated (d_n) and protonated (H_{10}) cyclohexenes were added to about 6 mL of purified methanol containing 0.01 mmol of benzene as an internal standard. A portion of this mixture was set aside and the exact ratio of its alkene components determined subsequently by GCMS analysis. Approximately 0.04 mmol of Br_2 in methanol was slowly added to the reaction mixture at ambient temperature with vigorous stirring. The remaining amounts of d_n and H_{10}-cyclohexenes in reaction mixture were determined by GCMS analysis using benzene as an internal standard. The analyses were performed on a Fisons Quattro mass spectrometer coupled to a Fisons GC 8000 gas chromatograph; DB-5HS column, 30m, 0.25 mm id, $T = 40$ °C, 4 psi, He carrier. Each sample was subjected to three or four independent analytical runs. Quantitative evaluation was done by determining the ion current corresponding to the molecular ions of the alkenes materials (78 for

---

[5] Brown, R. S.; Gedye, R.; Slebocka-Tilk, H.; Buschek, J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1984**, *106*, 4515.

[6] Waldmann, H.; Petru, F. *Ber. Dtsch. Chem. Ges.* **1950**, *287*, 83.

[7] Wolfe, S.; Campbell, J. R. *Synthesis* **1979**, 117.

[8] Ahlgren, G.; Akermark, B.; Dahlquist, K. I. *Acta Chem. Scand.* **1968**, *22*, 1124.

[9] Monson, R. S. *Tetrahedron Lett.* **1971**, *7*, 567.

[10] (a) Lambert, J. B.; Putz, G. J. *J. Am. Chem. Soc.* **1973**, *95*, 6313. (b) Wolkolf, P.; Holmes, J. L. *Can. J. Chem.* **1979**, *57*, 348.

[11] Charlton, J. L.; Agagnir, R. *Can. J. Chem.* **1973**, *51*, 1852.

[12] Bigeleisen, J.; Wolfsberg, M. *Adv. Chem. Phys.* **1958**, *1*, 15.

benzene, 82 for H_{10} cyclohexene, 83 for **5**, 84 for **4**, 86 for **2**, 90 for **3**, 92 for **1** (d_{10})).

Computational Section

A computational study was undertaken to examine the equilibrium deuterium isotope effect (EDIE) for the equilibrium involving the formation of the cyclohexenyl bromonium ion from cyclohexene plus Br_2. The isotope effects were modeled using results obtained with the DFT. The gradient-corrected (nonlocal) functionals were shown to be very successful in the studies of kinetic isotope effects.[13] Three sets of gradient-corrected functionals were used in the present work. Becke's exchange[14] (B) or Becke's 3-parameter exchange[15] (B3) functionals were combined with two correlation functionals developed by Perdew[16] (P86) and by Lee et al.[17] (LYP). The three combinations were denoted as BP86, BLYP, and B3LYP, respectively. For comparison, the restricted Hartree−Fock (RHF) calculations were also done. To minimize the computational effort, the compact effective core potentials of Stevens et al.[18] were used. The basis sets were used with double-ζ contraction on the carbon atoms and quadruple-ζ contraction on the bromine atom, along with the (31) basis set for the hydrogens obtained from Huzinaga's (4s) expansion.[19] Single-polarization functions were used: d-type on all heavy atoms and p-type on hydrogens. Polarization functions were included in the hydrogen basis sets since it is the effect of the hydrogen atoms on the vibrational structure and the proximity and interactions of hydrogens with the reaction site which are important in this study. Geometry optimization and Hessian evaluation were done using the Gaussian 94 program.[20] All calculations were done in C_1 symmetry allowing for the maximum number of degrees of freedom in the computed structures.

Table 1. Second-Order Rate Constants for the Bromination of Cyclohexenes **1**−**5** in MeOH at 25 °C. No Added Salts

olefin	k_2 ($M^{-1}\,s^{-1}$) ($\times 10^4$)[a]	k_D/k_H[b]
1, L = H	1.14(0.10)	
1, L = D (D_{10})	1.66(0.15)	1.45(0.18)
2	1.11(0.12)	0.97(0.15)
3 (D_8)	1.25(0.14)	1.10(0.15)
4	1.50(0.15)	1.31(0.17)
5	1.35(0.12)	1.18(0.15)

[a] Values are averages of 3 independent runs; bracketed values are errors calculated according to $\delta x = [(\delta a)^2 + (\delta b)^2 + (\delta c)^2]^{1/2}$ where *a*, *b*, and *c* are the standard deviations in the individual numbers. [b] DKIE computed from ratio of k_2 value of deuterated olefin to that of **1**, L = H. Propagated error in ratio where $z = x/y$ given as $\delta z = z[(\delta x/x)^2 + (\delta y/y)^2]^{1/2}$.

The bridged bromonium complex is not a transition state in the reaction, but rather a minimum. Presumably the transition state resembles an ion pair with bromide in solution, perhaps stabilized by counterion(s). However, computation of the true transition state structure for the process Br_2 + alkene bromonium ion + Br^- in the gas phase is not possible due to the prohibitive endothermicity associated with charge separation. Indeed, it is well-known that electrophilic bromination does not occur in the gas phase for the same reason.[21] According to the Hammond principle,[22] it may be assumed that the transition state resembles the bromonium ion more than it does the cyclohexene and bromine reactants. The structure of the bromonium ion can then be used as a qualitative substitute for the genuine transition state. The calculations were done for the equilibrium isotope effect (EIE) in the equilibrium involving the formation of the reaction intermediate $[C_6H_{10}Br]^+$:

$$C_6H_{10} + Br^+ \rightleftharpoons [C_6H_{10}Br]^+$$

For the equilibrium:

$$X \rightleftharpoons Y$$

the EDIE is calculated in the gas phase, rigid rotor, harmonic oscillator approximation according to[22]

$$K_H/K_D = \frac{Q_Y/Q_X}{Q_{Y'}/Q_{X'}} e^{-(\delta_O^Y E - \delta E_O^X)/RT} = F_Q F_{ZPE} \qquad (1)$$

where δE_O^X is the difference between the total molar vibrational zero-point energies for the light and heavy reactant compounds *X* and *X′*, δE_O^X is the difference between the total molar vibrational zero-point energies for the light and heavy product compounds Y and Y′, and *Q* is the total molar partition function.

Results and Discussion

i. Kinetics. Precise stopped-flow kinetic data in HOAc proved difficult to obtain because of slight nonfirst-order behavior of the kinetic plots, so further stopped-flow studies in this solvent were discontinued. Given in Table 1 are the stopped-flow data for the bromination of olefins **1**−**5** in methanol containing no salt at 25 °C. None of the data is corrected for the incomplete deuteration, although such correction would not change the numbers appreciably. The data given in Table 1, while being the result of numerous runs, contain relatively large errors on the order of ±10%. Also, the methanol DKIE of 1.45 ± 0.18 reported in Table 1 for **1**, L = H, D, are lower than those given in our earlier work in acetic acid.[1]

In fact, inspection of the stopped-flow data in Table 1 indicates that many of these experimental numbers are indistinguishable. Since the accumulated errors in the above numbers severely limits mechanistic conclusions, we turned to a competitive technique involving mass spectrometry where exactly known amounts of two of the cyclohexenes were incompletely brominated and the unreacted olefins analyzed by GCMS. The method requires that the ratio of the intensities of the mass ions of the olefins be determined before reaction and at some precisely known time during the reaction. The time-zero ratio incorporates the detector response factors, and importantly, since the mass detector "sees" only the mass ion of the desired isotopomer, the DKIE determined in this manner is corrected

---

(13) Wiest, O.; Black, K. A.; Houk, K. N. *J. Am. Chem. Soc.* **1994**, *116*, 10336.

(14) Becke, A. D. *Phys. Rev. A.* **1988**, *38*, 3098.

(15) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(16) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822.

(17) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(18) Stevens, W. J.; Basch, H.; Krauss, M. *J. Chem. Phys.* **1984**, *81*, 6026. Stevens, W. J.; Krauss, M.; Basch, H.; Jasien, P. G. *Can. J. Chem.* **1992**, *70*, 612.

(19) Huzinaga, S. *J. Chem. Phys.* **1965**, *42*, 1293.

(20) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. GAUSSIAN 94, Revision D.3; Gaussian, Inc.: Pittsburgh, PA, 1995.

(21) Ruasse, M.-F.; Motallebi, S. *J. Phys. Org. Chem.* **1991**, *4*, 527.

(22) Maskill, H. *The Physical Basis of Organic Chemistry*; Oxford University Press: New York, 1985. Also see: van Hook, W. A. In *Isotope Effects in Chemical Reactions*; Collins, C. J., Bowman, N. S., Eds.; Van Nostrand: New York, 1970.

Table 2. DKIEs Determined for Bromination of Specifically Deuterated Cyclohexenes in MeOH Using GC *MS* Analysis[a]

olefin	$k_D/k_H{}^b$ (MeOH)
1, L = D	1.31(0.06)
2	1.07(0.07)
3	1.14(0.07)
4	1.23(0.01)
5	1.06(0.09)

[a] Determined by MS analysis of the intensities of the mass ions of the deuterated and nondeuterated olefins as described in text. [b] KIE errors were computed by using the formula $\delta\text{KIE} = \mathscr{T}\log(\mathrm{R_{af}/R_{ao}})/[\log(1 - f)(1 + \mathrm{R_{ao}})/(1 + R_{af})]\mathscr{T}(((\delta R_{ao}/R_{ao})^2 + (\delta R_{af}/R_{af})^2)/(\ln[R_{af}/R_{ao}])^2 + (((\delta R_{ao}/(1 + R_{ao}))^2 + (\delta R_{af}/(1 + R_{af}))^2)^{0.5} + \delta f/(1 - \mathrm{f}))/\ln[(1 - f)(1 + R_{ao})/(1 + R_{af})])^2)^{0.5}$ where R_{ao} is the experimental ratio of the isotopomers at time zero, R_{af} is the ratio of the isotopomers at final incomplete bromination, and f denotes the fraction of reaction at the time of incomplete bromination.

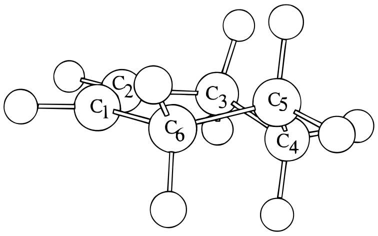


Figure 1. Structure of the cyclohexene twist conformation.

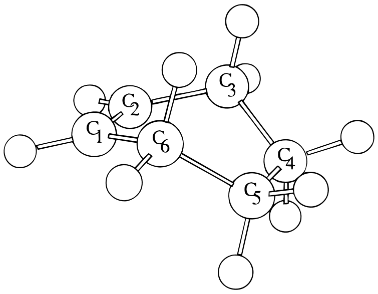


Figure 2. Structure of the cyclohexene boat conformation.

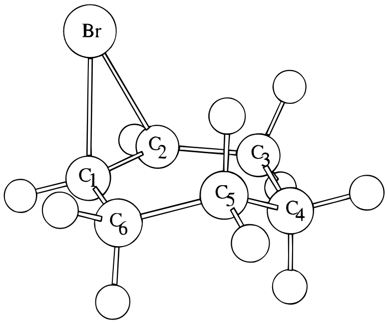


Figure 3. Structure of the cyclohexenyl bromonium ion twist conformation.

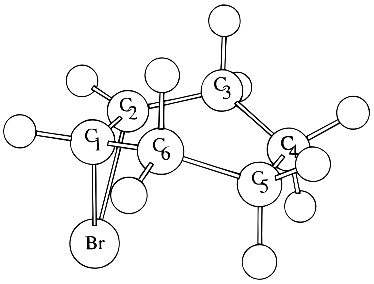


Figure 4. Structure of the cyclohexenyl bromonium ion boat-down conformation.

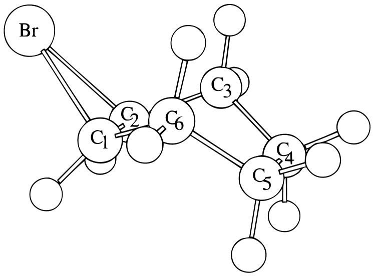


Figure 5. Structure of the cyclohexenyl bromonium ion boat-up conformation.

for incomplete deuteration of the olefin. The data are then analyzed as

$$[(k/k') - 1] = \log(R_{af}/R_{ao})/[\log(1 - \mathrm{f})(1 + R_{ao})/(1 + R_{af})] \tag{2}$$

where R_{ao} and R_{af} are the isotopic ratios of the substrate olefins before reaction, and after a stoichiometrically measured fraction, f, has reacted,[12] and k and k' are the rate constants for the light and heavy cyclohexenes, respectively. Given in Table 2 are the DKIEs determined for bromination of olefins **1**−**5** in MeOH using this technique. Values in HOAc could not be determined this way because direct injections of the solution caused deterioration of the Gc column, and attempted isolation of the products by exhaustive extraction gave irreproducible results. Comparison of the MeOH data in Tables 1 and 2 indicate a consistent trend of k_D/k_H **1** > **4** > **5** ≈ **3** > **2** ≈ **1** (**5** out of order in the two tables), but differing absolute numbers.

Despite the large errors, the kinetic and mass spectrometric data suggest that two-thirds of the DKIE arises from the vinyl hydrogens, one-third from the remote homoallylic hydrogens, and the allylic hydrogens contribute almost nothing. The suggestion that the homoallylic H's contribute so significantly to the DKIE is intriguing, but cannot be verified in our hands by further experimental determinations because of limitations imposed by the cumulative errors in the techniques available to us. Therefore we resorted to high level calculations to provide confirmation of the numbers and insight into the origins of the DKIEs.

ii. Computations. Calculations were carried out with the three density functionals for the two conformers of cyclohexene reactant, twist (TR) and boat (BR), and for the three conformers of the cyclohexenyl bromonium ion product, twist (TP), boat down (BD), and boat up (BU). The five conformers are shown in Figures 1−5. The relative energies for all conformers are shown in Table 3. All methods predict that the twist conformers are most stable. However, the energy differences between the conformers are not large: for cyclohexene, the BR conformer is less stable than TR by about 5 kcal/mol; for the ion, the BU conformer is less stable than TP by about the same amount, while the energy of the BD conformer is higher than that of TP by less than 2 kcal/mol. Furthermore, DFT calculations predict that the $C_6H_{10}Br^+$ ion is thermochemically more stable (by about 130 kcal/mol) than its constituents, Br^+ and C_6H_{10}. It is satisfying to observe that the three DFT methods give essentially identical results, while the RHF method predicts energy spacings that are only about 1 kcal/mol larger than the ones obtained with the DFT methods.

The B3LYP-calculated structural parameters for all systems studied are collected in Table 4. Results obtained with RHF method and with the other functionals are available as Supporting Information. As expected, the RHF bond lengths are

Table 3. Relative Energies and Total Energies[a]

system[b]	RHF		BP86		BLYP		B3LYP	
Br^+		(−12.737 15)		(−12.929 97)		(−12.878 81)		(−12.909 74)
				Cyclohexene				
TR	0.0	(−38.726 02)	0.0	(−40.001 12)	0.0	(−39.671 38)	0.0	(−39.879 77)
BR	6.2		5.1		5.0		5.3	
				Cyclohexenyl bromonium ion				
TP	0.0	(−51.612 59)	0.0	(−53.141 32)	0.0	(−52.748 83)	0.0	(−52.986 06)
Δ_{TP}[c]	−93.8		−131.9		−124.6		−123.3	
BD	2.8		1.4		1.6		1.8	
BU	5.7		4.5		4.5		4.8	

[a] Relative energies in kcal/mol. Total energies in atomic units. Total energies are given in parentheses. [b] See text for the meaning of abbreviations. [c] Calculated exothermicity of the reaction $C_6H_{10} + Br^+ \rightleftharpoons [C_6H_{10}Br]^+$, in kcal/mol.

Table 4. Structural Parameters of Conformers of Cyclohexene and Its Bromonium Ion[a] (distances in Å, Bond Angles in Degrees) as Calculated with B3LYP Functional

parameter[b]	twist (C_6H_{10})	boat (C_6H_{10})	twist ($C_6H_{10}Br^+$)	boat down ($C_6H_{10}Br^+$)	boat up ($C_6H_{10}Br^+$)
C1−C2	1.364	1.363	1.447	1.473	1.475
C2−C3	1.525	1.522	1.523	1.507	1.514
C3−C4	1.548	1.560	1.556	1.552	1.573
C4−C5	1.547	1.568	1.546	1.567	1.569
C5−C6	1.548	1.560	1.545	1.552	1.572
C6−C1	1.525	1.522	1.511	1.507	1.515
C1−H	1.108	1.107	1.104	1.104	1.104
C6−H	1.112	1.115	1.108	1.120	1.105
C2−C1−C6	123.27	118.37	120.73	118.51	116.21
C1−C6−C5	111.93	110.97	113.78	115.61	105.74
C6−C5−C4	110.91	113.44	110.61	115.64	113.30
C6−C1−H	117.54	120.28	118.40	118.86	120.13
C1−C6−H	109.51	109.07	109.99	110.20	110.91
C1−Br			2.127	2.129	2.120
C6−C1−Br			114.55	116.29	117.29
C2−C1−Br			70.18	69.78	69.61

[a] Distances in angstroms, angles in degrees. Results for RHF, BP86, and BLYP are available as Supporting Information. [b] For the definition of structural parameters, see Figures 1−5.

Table 5. Experimental and Calculated Structural Parameters of the Twist Conformer of Cyclohexene (Distances in Å, Bond Angles in Degrees)

parameter[a]	MW[b]	ED[c]	ED[d]	GVB[e]	B3LYP[f]
C1−C2	1.34	1.335	1.334	1.343	1.364
C2−C3	1.51	1.504	1.502	1.526	1.525
C3−C4	1.53	1.515	1.515	1.544	1.548
C4−C5	1.53	1.550	1.537	1.542	1.547
C5−C6	1.53	1.515	1.515	1.544	1.548
C6−C1	1.51	1.504	1.502	1.526	1.525
C1−H	1.09	1.093	1.1		1.108
C6−H	1.1	1.093	1.1		1.112
C2−C1−C6	123.3	123.5	123.4	123.4	123.3
C1−C6−C5	111.6	112.1	111.9	111.8	111.9
C6−C5−C4	110.3	111.0	110.9	110.7	110.9
C6−C1−H		114.0	118.3		117.5
C1−C6−H	109.9	109.5	110.3		109.5
C1−C2−H	119.5	122.5	118.3		119.2

[a] For the definition of structural parameters, see Figure 1. [b] Microwave, ref 23. [c] Electron diffraction, ref 24. [d] Electron diffraction, ref 25. [e] GVB calculations, ref 26. [f] This work, B3LYP results.

shorter that the ones obtained using methods that include electron correlation effects; the three DFT methods give very similar geometrical structures. The B3LYP exchange functional, which contains a contribution from the Hartree−Fock exchange, gives distances shorter than those obtained with the other two functionals. The largest deviation is only about 0.04 Å for the computed bond lengths and less than 0.6° for the angles. Table 4 illustrates the lengthening of the C1−C2 bond upon bromination, from 1.36 Å, characteristic of the double C−C bond to 1.47 Å, shorter than the typical single C−C bond of about 1.55 Å. Compared with their values in the lowest-energy twist conformation, the bond lengths of C−C bonds increase in the distorted boat structures.

While the structure of the ion has not been determined experimentally, there were several studies of the geometry of cyclohexene, using both microwave[23] and electron diffraction[24,25] techniques. The calculated structural parameters for cyclohexene are compared with the experimental values in Table 5. The table also shows the results obtained in GVB calculations that employed the minimal basis set STO-3G.[26] The B3LYP results agree reasonably well with the experimental data. While the bond angles are very close to the ones determined experimentally, the bond lengths are longer by as much as 0.02 Å. The longer computed bonds are probably due to an insufficiently flexible set of polarization functions. Of note is the rather surprising good agreement between both the experimental and DFT values and the ones calculated using the GVB method with very small basis set; this agreement is most likely due to the cancellation of errors, the limited electron correlation effects via GVB leading to distances that are too short and the unpolarized basis set giving ones too long.

The calculated (for the twist conformer) and experimental infrared spectra of cyclohexene are compared in Figure 6. The agreement is remarkable and allows for unambiguous assignment of all the major peaks in the spectrum. In the analysis, the harmonic vibrational modes, as calculated using the Gaussian 94 program, were visualized with the help of programs MOLDEN[27] and MacMolPlt.[28] The assignment of the more prominent peaks is shown in Table 6. It must be stressed here, as it will prove important in the analysis of the isotope effects, that apart from the 10 modes corresponding to the CH stretches, all other vibrations present a complex mixture of CH_2 bends and CC stretches leading to the ring puckering motion.

For the twist conformers, the effects of isotopic substitution on the equilibrium constant in the gas phase, K_D/K_H, computed at 298.15 K and 1 atm pressure, are compared in Table 7 with the experimental values of k_D/k_H as obtained in the bromination of cyclohexene in MeOH at 25 °C (298.15 K). There is considerable agreement between the calculated and experimental magnitudes of the isotope effects. As was the case in the

---

(23) Scharpen, L. H.; Wollrab, J. W.; Ames, D. P. *J. Chem. Phys.* **1968**, *49*, 2368.

(24) Chiang, J. F.; Bauer, S. H. *J. Am. Chem. Soc.* **1969**, *91*, 1898.

(25) Geise, H. J.; Buys, H. R. *Recl. Trav. Chim. Pays-Bas* **1970**, *89*, 1147.

(26) Verbeek, J.; Van Lenthe, J. H.; Timmermans, P. J. J. A.; Mackor, A.; Budzelaar, P. H. M. *J. Org. Chem.* **1987**, *52*, 2955.

(27) Schaftenaar, G. *QCPE Bulletin* **1992**, *12*, 3 (available from http://www.caos.kun.nl/∼schaft/molden).

(28) MacMolPlt is available from http://www.msg.ameslab.gov/GAMESS/Graphics/MacMolPlt.html.

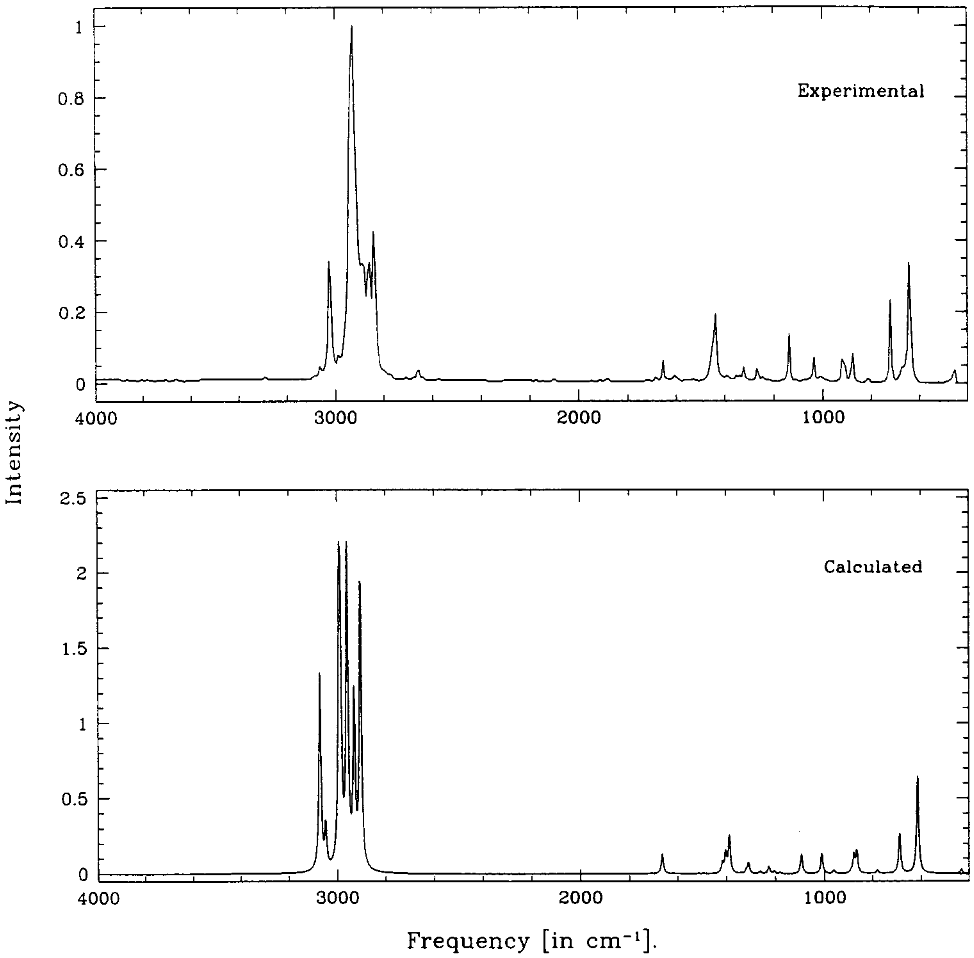


Figure 6. Calculated (unscaled BP86) and experimental (neat film) IR spectra of C_6H_{10}. The intensity units are $D^2Da^{-1}Å^{-2}$ for the calculated spectrum, arbitrary units for the experimental spectrum.

Table 6. Assignment of the IR Spectrum of the Twist Conformer of C_6H_{10}[a]

experimental[b]	calculated[c]	assignment[d]
642	614	out-of-plane CH bending at C_1,C_2
720	689	out-of-plane CH bending at C_1,C_2
875	865	ring deformation: C_1C_6 and C_5C_6 stretch, C_2C_3 and C_3C_4 shorten
918	878	rocking CH_2 at C_3,C_6, twisting CH_2 at C_4,C_5
1036	1012	ring deformation: C_1C_6 and C_3C_4 stretch, C_2C_3 and C_5C_6 shorten
1137	1095	twisting CH_2 at C_3-C_6
1267	1227	twisting CH_2 at C_3-C_6
1322	1310	twisting CH_2 at C_3−C6
1439	1389	out-of-phase scissoring CH_2 at C_3, C_6
	1405	out-of-phase scissoring $_sCH_2$ at C_4, C_5
	1418	in-phase scissoring $_sCH_2$ at C_4, C_5
1654	1664	C=C stretch
2841	2904	out-of-phase stretching $_sCH_2$ at C_3, C_6
2859	2930	in-phase stretching $_sCH_2$ at C_4, C_5
	2931	out-of-phase stretching $_sCH_2$ at C_4, C_5
2889	2959	stretching $_{as}CH_2$ at C_3, C_6
2928	2987	stretching $_{as}CH_2$ at C_4, C_5
	2993	stretching $_{as}CH_2$ at C_4, C_5
3025	3049	out-of-phase stretching CH at C_1, C_2
	3073	in-phase stretching CH at C_1, C_2

[a] Frequencies are in cm^{-1}. [b] The small peaks at 2659, 2986, and 3064 cm^{-1} are not due to the fundamental transitions. [c] Calculated BP86 harmonic vibrational frequencies were not scaled. [d] See Figure 1 for the numbering of atoms. The subscripted "s" and "as" refer to symmetric and antisymmetric modes of vibration.

Table 7. Calculated EDIE (K_D/K_H) for the Process Cyclohexene + $Br^+ \leftrightarrow$ Cyclohexenyl bromonium ion at 298.15 K and 1 atm

	K_D/K_H				
olefin	RHF[a]	BP86	BLYP	B3LYP	k_D/k_H experimental[b]
D_{10} (**1**)	2.78 (3.28)	1.41	1.41	1.48	1.45(0.18)
D_8 (**3**)	1.96 (2.19)	1.14	1.15	1.18	1.10(0.15)
D_4 (**2**)	1.37 (1.47)	1.02	1.01	1.04	0.97(0.15)
D_2 (**4**)	1.37 (1.50)	1.23	1.23	1.25	1.31(0.17)
D_1 (**5**)	1.15 (1.23)	1.11	1.11	1.12	1.18(0.15)
D_2 syn	1.15 (1.21)	1.05	1.05	1.05	
D_2 anti	1.15 (1.22)	1.07	1.07	1.07	

[a] Scaling factor of 0.89 used for calculated harmonic vibrational frequencies. (Unscaled results given in parentheses.) [b] Experimental results, kinetic deuterium isotope effect, k_D/k_H, this work, see Table 3.

molecular geometries, the various functionals predict essentially the same isotope effects. The results of calculations show that, in agreement with the experiment, the largest contribution to the EIE is due to the substitution of the two hydrogens at the vinyl α-carbon atoms (**4**), with $K_D/K_H = 1.28$. The next largest contribution comes from the substitution of eight hydrogens in D_8, $K_D/K_H = 1.19$. Substitution of four hydrogens at positions 3 and 6 (**2**) is calculated to give a modest inverse isotope effect, $K_D/K_H = 1.06$, while experimentally a negligible normal isotope effect is found. However, both the experimental and calculated values are very close to unity. Given that the effect at β-carbons in D4 is so small, we calculated (using the BP86 data) the EIE for only the γ-carbons 4 and 5 (see Figure 1). We found a rather large $K_D/K_H = 1.12$, comparable to that in the D_8 isotopomer, where the isotopic substitution was done at both β- and γ-carbons. Given that the Hessian matrixes were available, it was worthwhile to investigate the nature of this

Table 8. Factorization of the Calculated EDIE into Bending and Stretching Contributions (BP86 Functional)

olefin	F_Q	$\delta E_0^{\mathrm{bend}}$	$\delta E_0^{\mathrm{stretch}}$	$\delta E_0{}^a$	$F_{\mathrm{ZPE}}^{\mathrm{bond}}$	$F_{\mathrm{ZPE}}^{\mathrm{stretch}}$	$F_{\mathrm{ZPE}}{}^b$	$K_H/K_D{}^c$	K_H/K_D
D10 (**1**)	1.13	0.67	0.48	1.15	0.76	0.82	0.63	0.71	1.41
D8 (**3**)	1.03	−0.02	0.43	0.41	1.01	0.84	0.85	0.87	1.14
D4 (**2**)	1.02	−0.10	0.21	0.10	1.04	0.92	0.96	0.98	1.02
D2 (**4**)	1.10	0.70	0.05	0.75	0.75	0.98	0.74	0.81	1.23
D1 (**5**)	1.05	0.35	0.02	0.37	0.87	0.99	0.86	0.90	1.11
D_2 syn	1.00	0.01	0.12	0.12	1.00	0.95	0.95	0.96	1.05
D_2 anti	1.01	0.07	0.11	0.18	0.97	0.96	0.93	0.94	1.07

[a] $\delta E_O \equiv \delta E_O^Y - \delta E_O^X$ see eq 1; note that $\delta E_O = \delta E_O^{\mathrm{bend}} + \delta E_O^{\mathrm{stretch}}$. [b] $\mathrm{FZPE} = e^{-(\delta OY^E - \delta OX^E)/RT}$ see eq 1, note that $\mathrm{FZPE} = F_{\mathrm{ZPE}}^{\mathrm{bend}} F_{\mathrm{ZPE}}^{\mathrm{stretch}}$. [c] $K_H/K_D = F_Q F_{\mathrm{ZPE}}$.

Table 9. Analysis of the Stretching Modes in the D_8 Isotopomer (Calculated Using the BP86 Functional)[a]

reactant			product			
$\nu(C_6H_{10})$	$\nu(D_8{-}C_6H_{10})$	$\Delta_\nu(R)^b$	$\nu(C_6H_{10}Br^+)$	$\nu(D_8{-}C_6H_{10}Br^+)$	$\Delta_\nu(P)^b$	$\Delta(\Delta_\nu)^c$
2903	2117	786	2894	2115	779	−7
2904	2117	787	2948	2150	798	11
2929	2139	790	2960	2162	798	8
2931	2134	797	2968	2164	804	7
2959	2189	770	2995	2216	779	9
2959	2190	769	3011	2224	787	18
2987	2214	773	3033	2248	785	12
2993	2220	773	3039	2253	786	13
3049	3049	0	3066	3066	0	0
3073	3073	0	3077	3077	0	0

[a] All values in cm^{-1}. [b] $\Delta_\nu = \nu - \nu(D_8)$. [c] $\Delta(\Delta_\nu) = \Delta_\nu(P) - \Delta_\nu(R)$.

unusually large isotope effect at the γ-carbons in order to answer the question if the effect could be of steric origin. To this end, the EIEs were calculated for two deuteriums at the syn positions (with respect to bromine), D_2-syn, and for two deuteriums at anti positions, D_2-anti (Table 7). The EIEs arising from both of these arrangements are essentially equal at all levels of theory, ruling out steric origins of the remote γ isotope effect.

It must be added that while different experimental environments produce slightly different values for the KIE (see Tables 1 and 2), both experiment and theory predict very similar ranking of the magnitude of the isotope effects: from experiment, $D_{10} > D_2 > D_1 \approx D_8 > D_4$; according to computations, $D_{10} > D_2 > D_8 > D_1 > D_4$.

The most anticipated benefit of the computational part of the present work was to identify the modes that are responsible for the large inverse EIE. Given that the cyclohexene system gives rise to numerous soft vibrational modes in which the ring puckering vibrations are mixed with the rocking, twisting, and wagging vibrations of the methylene units, this task proved impossible. It was difficult to establish a unique one-to-one correspondence between the reactant and product vibrations. Analysis of the individual contributions to the values of K_H/K_D indicates that the factor due to the partition function, F_Q, deviates only slightly from unity; the bulk of the EIE is carried by the factor F_{ZPE}, which reflects the differential changes in the vibrational zero-point-energy for the reactant and product upon deuteration. To gain some insight into the origin of the isotope effects, we partitioned all vibrations according to their stretching and bending characteristics, and decomposed δE_0 and F_{ZPE} accordingly. Only the C−H stretches could be unambiguously identified. Consequently, two groups of modes were defined; in the first group all ten C−H stretches were included; the second group contained all the remaining modes, predominantly bending modes that were, however, coupled with some stretches of the C−C bonds in the cyclohexane ring. The contributions from the two groups of vibrations, the C−H stretches on one side and all the remaining modes on the other, to the overall EIE were then evaluated separately. The results of the analysis are shown in Table 8. In the Table, the values of $F_{\mathrm{ZPE}} < 1$ lead to inverse isotope effects, while $F_{\mathrm{ZPE}} > 1$ gives normal isotope effects; $F_{\mathrm{ZPE}} \cong 1$ implies no effect in the equilibrium constant upon deuteration. In other words, $F_{\mathrm{ZPE}} < 1$ indicates that in the deuterated product the vibrating atoms experience a steeper potential energy function than in the deuterated reactant. Note that the value of F_{ZPE} is tied to the magnitude of $\delta E_O^Y - \delta E_O^X$, as in eq 1. The results in Table 7 show that there are almost no bending contributions to the EIE for both D_8 and D_4 isotopomers; all EIEs arise from the changes in the vibrational frequencies of the stretching vibrations. The situation is reversed for the bis- and mono-deuterated species, D_2 and D_1, where the stretching vibrations virtually do not affect the computed EIE. With only eight modes to compare, the D_8 system afforded data for a more detailed analysis of the origins of the EIEs in that system. The results are collected in Table 9 in the form of matching stretches in both the product and reactant systems, together with the differences $\Delta_\nu(R)$ and $\Delta_\nu(P)$, showing the reduction of fundamental frequencies upon deuteration in each of them. In addition, the table shows the difference between the reductions of frequencies for products and reactants. Each of the eight CH stretches that dominate the EIE in the D_8 isotopomer is reduced upon deuteration more in $C_6H_{10}Br^+$ than in C_6H_{10}. The average extra reduction of the frequencies in the ion as compared with cyclohexene is small, less than 9 cm^{-1}, leading to the overall contribution to F_{ZPE} of $(^1/_2)(8)(9)\ \mathrm{cm}^{-1} = 36\ \mathrm{cm}^{-1} = 0.43$ kJ/mol (to be compared with the value of 0.41 kJ/mol from the direct calculation, see Table 8). Most importantly, it may be seen from the table that, even though it is the CH stretching vibrations that generate the EIE, no single CH stretching vibration is exclusively responsible for the EIE in the D_8 system. In conclusion, it must be stressed that the isotope effects in the cyclohexene system result from complex interactions between all vibrational modes, in contrast with the simplified picture often presented in textbooks.[22]

Two models were proposed in the past to explain the origin of the secondary α-deuterium isotope effect. The older interpretation suggested by Streitwieser et al.[29] considers the change of some CH vibrational modes due to rehybridization: in a reaction that involves sp^2 to sp^3 rehybridization at the α-carbons an inverse secondary isotope effect should be observed. A more recent, alternative explanation of the secondary isotope effects was offered by Strausz et al.[30] who attributed the effect to the creation of new, isotopically sensitive, vibrations in the transition state. The case of bromination of cyclohexene does not seem to fall into either category. While there is no doubt that the α-carbons in cyclohexene are sp^2 hybridized as the sum of relevant angles around each α-carbon is 360°, the sum of the angles is 356° in the cyclohexenyl bromonium ion, quite far from the value of 330° expected for an ideally sp^3-hybridized carbon atom. The new modes in $C_6H_{10}Br^+$ that may be associated with the three-membered ring BrCC appear in the lowest frequency region, $90-400$ cm^{-1}. They are always inseparable from the motion of the cyclohexene ring, perhaps due to the accidental matching of the atomic mass of bromine (80 Da) and the molecular mass of C_6H_{10} (82 Da). Of the six modes that display large contributions from the bromine displacement, the bending modes (toward the cyclohexene ring) are almost insensitive to isotopic substitution at the carbon atoms C_1 and C_2. Of the BrC stretching modes, the deformation of the BrCC ring remains essentially unchanged while the ring breathing mode is reduced by 7 cm^{-1}. Given the complexity of the cyclohexene bromonium ion, as compared with the systems studied by Strausz et al.,[30] it is perhaps not surprising that no simple picture emerged. A clearer picture could perhaps be obtained in the studies of the bromination of ethylene.[31]

Conclusions

The above study was undertaken to identify more clearly the origins of the DKIE's associated with electrophilic bromination of cyclohexene and its various isotopomers and shows a nice complementarity of experiment and theory. Kinetic measurements based on the rate of disappearance of Br_2 indicated that there is a large inverse DKIE of about $1.4-1.5$ for the bromination of perdeuteriocyclohexene relative to cyclohexene in MeOH. Attempts to sort out the positional substitution effects by looking at the DKIEs for Br_2 addition to various selectively deuterated isotopomers suggested that roughly two-thirds of the effect is associated with the two vinyl hydrogens. One-third of the effect is associated with the four homoallylic hydrogens while the allylic hydrogens contribute almost nothing. An alternative mass spectroscopic method of determining the DKIE provides data consistent with that obtained from the kinetic experiments. Unfortunately, the inherent experimental errors associated with each of the above techniques for measuring the DKIEs limit the certainty of the results and hence the ability to make conclusions concerning the positional origins of the experimental DKIE. Extensive density functional computations of the equilibrium isotope effect (EIE) for the cyclohexene + $Br^+ \rightleftharpoons$ cyclohexenebromonium ion equilibrium confirm the relative magnitude of the DKIE's obtained from the solution studies. From an experimental standpoint the cyclohexene system cannot be considered large or complex. Nevertheless, from a computational standpoint, due to the extensive mixing of ring deformations and CH stretching and bending, it proved impossible to identify all the unique vibrational modes in the reactants and products that are responsible for the EIE. The computations indicate that for the D_8 and D_4 isotopomers the effect is almost entirely associated with the changes in all C$-$H stretching (but not bending) frequencies which are larger upon deuteration in the ion relative to the starting material. Importantly, due to the heavy mixing of these modes, no single C$-$H stretch can be identified as the major contributor. Conversely, the large effects noticed for the vinyl hydrogens, in D_1 and D_2, show almost no isotopic sensitivity to changes in the C$-$H stretching frequencies, but are instead largely associated with the changes in all the remaining vibrations different from the 10 C$-$H stretches.

Acknowledgment. The calculations were done on the RS/6000 workstations and on the SP2 installation at the University of Alberta. This work was financed partly by research grants from NSERC to M.K. and R.S.B., and partly by the University of Alberta and Queen's University. Assistance of Mr. J. Hoyle from the Spectral Services Laboratory at the Department of Chemistry, University of Alberta, is gratefully acknowledged. We are also grateful for the helpful suggestions of the referees.

Supporting Information Available: Structural parameters and atomic coordinates for conformers of cyclohexene and cyclohexenyl bromonium ion (10 pages). See any current masthead page for ordering information and Web access instructions.

JA971145H

---

(29) Streitwieser, A., Jr.; Jagow, R. H.; Fahey, R. C.; Suzuki, S. *J. Am. Chem. Soc.* **1958**, *80*, 2326.

(30) Strausz, O. P.; Safarik, I.; O'Callaghan, W. B.; Gunning, H. E. *J. Am. Chem. Soc.* **1972**, *94*, 1828. Safarik, I.; Strausz, O. P. *J. Phys. Chem.* **1972**, *76*, 3613.

(31) Klobukowski, M.; Gainsforth, J. L.; Koerner, T.; Brown, R. S. To be published.