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Theoretical Calculation of Equilibrium Isotope Effects Using ab Initio Force Constants: Application to NMR Isotopic Perturbation Studies

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Abstract: This article describes the theoretical calculation of equilibrium isotope effects. Cartesian force constants from ab initio molecular quantum mechanics calculations are used to determine reduced isotope partition function ratios for any number of isotopomers, which are then used to calculate theoretical equilibrium isotope effects. The methodology has been implemented in a Fortran program, QUIVER, which employs standard output from the GAUSSIAN 82 or 86 molecular orbital program packages as input. The routine is applied to the cyclopropylcarbinyl–bicyclobutonium and bicyclo[2.1.1]hexyl cationic systems. In the former case, unusual isotope effects observed for the system in the NMR are reproduced and discussed in terms of the pentacoordinated structure. In the latter system, the calculated isotope effects are used in conjunction with calculated IGLO chemical shifts to interpret experimentally observed isotope effects for this carbocation in the NMR.

To obtain maximum benefit from theoretical calculations, it is increasingly desirable to use theoretical techniques to calculate physically observable properties of molecular systems in addition to relative energies and geometries. Characteristics of the structures such as the molecular dipole moment, force constants, and vibrational frequencies are readily available using standard molecular orbital program packages. In many cases, quantities depending on these characteristics may be experimentally measured, and these quantities provide important means of comparing theory and experiment. The use of these and other values to further investigate molecular systems should improve our insight into the nature of chemical bonding.

Carbocations present challenging problems for theoretical techniques. The flat potential energy surfaces responsible for facile rearrangement and the small energy differences between very different structures make confident predictions of the predominant species difficult. Improvement in the basis set used, or the inclusion of electron correlation, may well lead to changes in relative energies,[1] often changing the ordering so as to give a different minimum energy structure.

Isotope effects are important experimental tools for the investigation of molecules and molecular processes.[2] Equilibrium isotope effects have been used by us as sensitive probes of the nature of carbocationic species in stable ion solutions.[3] In systems with low barriers to rearrangement, the observed NMR signals in the nonisotopic molecules are averaged values of the rapidly exchanging positions. The interpretation of these signals is not always straightforward and has been the subject of controversy. Perturbation of a rapid exchange process by isotopic substitution at one of the exchanging sites can be used to investigate these systems. The isotope-induced splittings or shifts can be dramatic,

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† Yale University.
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(1) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley-Interscience: New York, 1986.

(2) For general treatments of isotope effects, see: (a) Bigeleisen, J.; Wolfsberg, M. *Adv. Chem. Phys.* **1958**, *1*, 15. (b) Wiberg, K. B. *Physical Organic Chemistry*; Wiley: New York, 1964. (b) Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley: New York, 1980. (c) Westheimer, F. H. *Chem. Rev.* **1961**, *61*, 265. (e) Collins, C. J.; Bowman, N. S., Eds.; *Isotope Effects in Chemical Reactions*; ACS Monograph No. 167; Van Nostrand Reinhold: New York, 1970. (f) Wolfsberg, M. *Acc. Chem. Res.* **1972**, 7, 225.

(3) (a) Saunders, M.; Telkowski, L.; Kates, M. *J. Am. Chem. Soc.* **1977**, *99*, 8070. (b) Saunders, M.; Kates, M. *J. Am. Chem. Soc.* **1977**, *99*, 8071.

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often distinguishing clearly between various proposed models. The power of this method of isotopic perturbation would be considerably enhanced if one could calculate isotope effects theoretically so that one could quantitatively compare values based upon proposed models with experimental data.

Isotope effects on equilibrium constants can be calculated readily within the framework of the Born–Oppenheimer approximation, using the rigid-rotor harmonic-oscillator approximation and employing only the normal-mode vibration frequencies of a system.[4] While normal-mode vibration frequencies are obtainable from standard molecular orbital packages via a priori calculation of force constants, most published predictions of equilibrium isotope effects to date have been made with other than a priori force constants. Such an approach can be successfully applied to systems for which good force constants are available from analysis of spectral data or where force constants can be expected to be transferable from other molecules where they are known. Unfortunately, force constants for many interesting systems, such as the carbocations studied here, are not known from spectral data and would be very difficult to guess.

Previous work[5] using numerical a priori force constants determined from quantum mechanical calculations has generated results for isotope effects in good agreement with force constants obtained from spectroscopic data. In this previous work, levels of Gaussian calculations from HF/3-21G to MP2/6-31G* were utilized. While it would be an error to use different levels of calculation to obtain the two reduced isotopic partition function ratios (vide infra) which are compared in calculating isotope effects, the consistent use of isotopic partition function ratios obtained at the HF/3-21G level already yielded reasonable results. It is well known[1] that molecular orbital calculations which do not include correlation and which do not properly consider anharmonicity tend to yield high values for the fundamental frequencies and consequently also for reduced isotopic partition function ratios. One might correct for this by appropriately scaling of force constants, but we do not adopt such a procedure. This article describes the calculation of reduced isotopic partition function ratios, $(s_2/s_1)f$, with use of normal-mode vibration frequencies determined from analytical Cartesian second derivatives of the molecular orbital potential energy surface (HF/6-31G*). These $(s_2/s_1)f$ values are subsequently used in the evaluation of isotope effects to compare with the experimentally observed values.

As is often the case, comparison between theory and experiment serves several purposes. On the one hand, agreement of the theoretical analysis with experiment is used as a confirmation for the theoretical model used in the analysis. On the other hand, the agreement of a calculated and an observed isotope effect also serves as a justification of use of the present analysis in future calculations, especially if the theoretical model employed was also obtained from another type of analysis. As one obtains indications of the quality of agreement between theory and experiment, the theoretical calculations can also be used as a guide for indicating whether experimental errors or misinterpretations have been made.

Theory

The present study concerns equilibria between two or more partially deuterated isotopomers of a given conformer or isomer of a molecule. These isotopomers are known to be in rapid equilibrium, based upon measurement of the parent system. For example, consider the equilibrium between two monodeuterated bicyclobutonium ion structures:

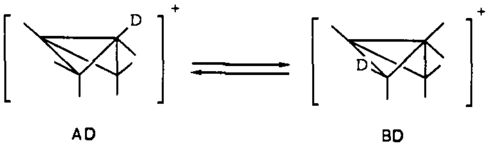

Diagram 1

It follows from standard statistical mechanics arguments[6] that the equilibrium constant in the gas phase for this reaction is given by

$$K_D = Q_{BD}/Q_{AD} \tag{1}$$

where the Q's are the designated molecular partition functions. The corresponding K_H value is obviously unity since AH and BH correspond to the same molecule. Thus, one may write:

$$K_D = \frac{K_D}{K_H} = \frac{Q_{BD}/Q_{BH}}{Q_{AD}/Q_{AH}} \tag{2}$$

It is clear from the formulation of eq 2 that K_D can be considered to be the isotope effect on an equilibrium constant. K_D can be calculated equally well with either eq 1 or eq 2. While eq 2 does involve the calculation of the energy states of the all-H compound not required by eq 1, eq 2 has been employed in this report because it is specifically desired to use isotope ratios (like BD/BH) in future studies.

Bigeleisen and Mayer[4] have demonstrated, in absence of symmetry number effects and within the framework of the Born–Oppenheimer approximation, that the deviation from unity of an isotope effect on an equilibrium constant (eq 2) is a quantum effect, which vanishes in the classical limit, so that eq 2 can be rewritten

$$K_D = \frac{(s_2/s_1)f(\mathrm{BD/BH})}{(s_2/s_1)f(\mathrm{AD/AH})} \tag{3}$$

with the reduced isotopic partition function ratio $(s_2/s_1)f(2/1)$ defined as the quantum mechanical partition function ratio divided by the corresponding classical ratio. By the usual convention,[4] 2 refers to the heavy isotopic molecule, 1 to the light isotopic molecule. A symmetry number effect would have to be considered if the equilibrium structures of BD and AD contained different numbers of rotational symmetry elements in their respective point groups, but this situation does not occur in the present study. For the equilibrium of diagram 1, there are two enantiomers of the monodeuterated species on the right-hand side. Since these two enantiomers are also NMR equivalent, the effective equilibrium constant could be defined by multiplying by a factor of 2, but such factors will be omitted here.

With the rigid-rotor harmonic-oscillator approximation and (as is appropriate in the present application) with the rotational degrees of freedom regarded as classical,[4]

$$(s_2/s_1)f(2/1) = \prod_i^{3N-6} \frac{u_{2i}}{u_{1i}} \frac{1 - e^{-u_{1i}}}{1 - e^{-u_{2i}}} \frac{e^{u_{1i}/2}}{e^{u_{2i}/2}} \tag{4}$$

where

$$u_i = h\nu_i/kT = 1.43\nu_i \text{ (in cm}^{-1}\text{)}/T \tag{5}$$

Here, ν_i refers to normal-mode harmonic frequency,[7] T refers to the absolute temperature, k is Boltzmann's constant, and the product is over the $3N - 6$ normal-mode frequencies of N atomic molecules 1 and 2.

From the correspondence principle of quantum mechanics, for high temperatures and/or for low frequencies ($u_i \ll 1$), quantum mechanics goes over into classical mechanics, and indeed each of the $3N - 6$ multiplicative terms in $(s_2/s_1)f(2/1)$ goes to unity. Consider, for instance, a hydrogen-containing molecule with a "low" frequency $\nu_H = 80$ cm^{-1}, and the corresponding deuterium-containing molecule with corresponding frequency $\nu_D = (80/\sqrt{2})$ cm^{-1}. Already at 198 K, this frequency pair makes a multiplicative contribution of only 1.007 to $(s_2/s_1)f$.

Through eqs 3 and 4, K_D has now been expressed in terms of the normal-mode vibration frequencies of the molecules involved.

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[4] Bigeleisen, J.; Mayer, M. G. *J. Chem. Phys.* **1947**, *15*, 261.

[5] Hout, R. J., Jr.; Hehre, W. J.; Wolfsberg, M. *J. Am. Chem. Soc.* **1980**, *102*, 3296.

[6] MacQuarrie, D. A. *Statistical Mechanics*; Harper and Row: New York, 1976. Mayer, J. E.; Mayer, M. G. *Statistical Mechanics*; Wiley: New York, 1977.

[7] Wilson, E. B., Jr.; Decius, J. C.; Cross, P. C. *Molecular Vibrations: The Theory of Infrared and Raman Spectra*. Dover Publications: New York, 1980.

If standard methods of expressing rotational and vibrational partition functions had been followed, K_D might have been expressed in terms of molecular moments of inertia and masses in addition to normal-mode frequencies. The two ways of expressing K_D can be shown to be equivalent. However, eq 4 is especially appropriate for the present context; as will be pointed out, one of the frequencies of the AD(H) and BD(H) molecules is calculated inaccurately in some calculations here. We believe that the inaccurately calculated frequency would be small when calculated correctly; since it is known that small frequencies ($u_i \ll 1.0$) make little contribution to the reduced isotopic partition function ratio, the unknown frequency is omitted from the frequency product of eq 4.

The Born–Oppenheimer approximation (i.e., the force constants of a molecular are independent of isotopic substitution) is implicitly used here as is the classical rigid-rotor harmonic-oscillator approximation. Correction factors to K_D for these approximations will tend to be small[8] and are not considered here.

The frequencies calculated are those of the isolated ions, and the isotope effect theory discussed here is for the gas-phase reaction, consistent with the frequency calculation. The actual NMR measurements with which comparison is made refer, of course, to a liquid solution. Unless there are specific solute/solvent interactions, or changes of structure on going into solution, one expects that the gas-phase isotope effect is very close to the effect in solution. In principle, one can obtain the value of K_D in solution from that in gas by multiplying the calculated gas-phase value of K_D by a factor which is the ratio of isotopic vapor pressure ratios. This latter factor is expected to deviate very little from unity.

Implementation

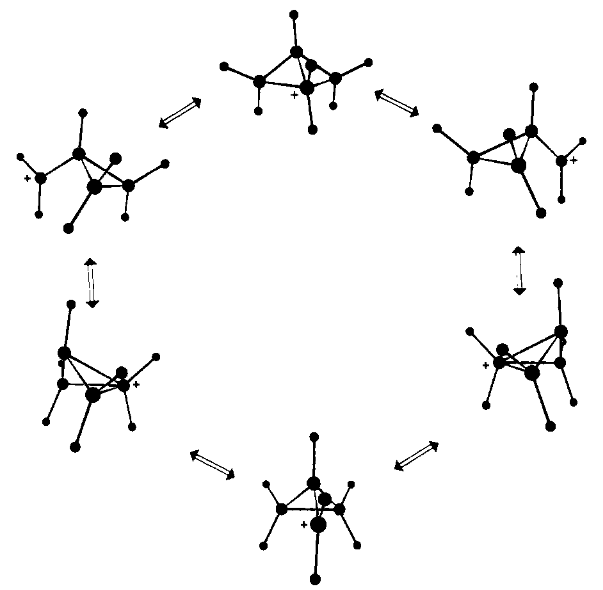
This approach has been implemented in a Fortran program, QUIVER, which has been written so as to use the information as directly as possible from the GAUSSIAN 82 or 86 program packages.[9] For each pair of isotopomers to be compared, QUIVER requires the masses of the atoms, the Cartesian second derivatives (Cartesian force constants), and the temperatures of interest. QUIVER returns the normal-mode vibration frequencies, calculated as in the Gaussian package by diagonalization of the mass-weighted Cartesian force constant matrix, the normal-modes corresponding to the frequencies, and the zero-point energy for each isotopomer. For each pair of isotopomers, the reduced isotope partition function ratio is determined for each temperature input.

Applications

Cyclopropylcarbinyl–Bicyclobutonium Cation. In this section we will first review the ^{13}C NMR data[10] on the isotopically substituted ion, then we will discuss previous electronic structure calculations, and finally we will present calculations concerning the isotope effects and relate them to the experiments.

The carbon NMR spectrum of the stable $C_4H_7^+$ ion,[10a] obtained by ionizing either cyclobutyl or cyclopropylcarbinyl precursors, shows a single peak for the three methylene carbons. Two peaks, each of area three, were observed for the methylene hydrogens in the proton spectrum. Since a 3-fold symmetrical structure (the tricyclobutonium ion) which could account for these results directly is expected from calculation to be relatively high in energy (and may be expected to distort because of the Jahn–Teller effect), the spectrum was interpreted to imply a very rapid equilibrium among degenerate structures of lower symmetry.

Chart I



Isotope effects observed in the NMR spectra of deuterium-substituted ions confirmed this idea.[10b] A mixture of the exo and endo methylene substituted monodeuterated ions, which do not interconvert under the conditions of the experiment, was examined. Deuterium perturbs the system so as to break the energetic degeneracy of the equilibrating ions. Because the equilibrium constant favors deuterium on one of the kinds of interchanging carbon, the frequencies of the deuterated and nondeuterated carbons, averaged over the rapid process described above, are different. In place of the single ^{13}C NMR methylene peak, observed in the ion without deuterium, two isotopically perturbed multiplets were seen (due to the exo and endo isotopomers), with the deuterated carbon (1:1:1 triplet) shifted upfield in one and downfield in the other, the corresponding nondeuterated carbons shifting in the opposite directions (all shifts relative to that in the nondeuterated isotopomer). These shifts were a function of temperature as expected for an isotopically perturbed equilibrium. Similar effects were seen in the proton spectrum.

Two points should be made concerning the spectrum of the deuterated ion. The ^{13}C NMR frequencies of the deuterated carbons are affected by intrinsic isotopic shifts in addition to the shifts resulting from perturbed equilibrium, but these intrinsic shifts are expected, by analogy to other cases, to be temperature independent and small compared with the magnitude of the observed shifts. Also, ^{13}C NMR peaks are only seen in ions containing ^{13}C (present at normal abundance). Therefore, there are carbon isotope effects as well as the deuterium effects mentioned above. As is well known, carbon and deuterium isotope effects interact in an additive fashion. Therefore, while all the ^{13}C NMR methylene peaks are affected by a ^{12}C/^{13}C equilibrium isotope effect, all of them are shifted in the same direction by almost exactly the same amount.

In the prior qualitative interpretations of the experimental results, the structures considered were: three bicyclobutonium structures α which could interconvert via cyclopropylcarbinyl transition states (or intermediates) or three degenerate cyclopropylcarbinyl structures β equilibrating via bicyclobutonium transition states (or intermediates). In either case, these structures are connected in a cycle as shown in Chart I. Each of these species has two kinds of methylene carbon, but a single ^{13}C NMR methylene peak would be expected in the all-protio ion if the barrier for interconversion is low, leading to rapid averaging. The upfield and downfield shifts of the deuterated carbon in the two isotopomers can only be interpreted as indicating that the exo-deuterated and endo- (up and down; see diagram 6) deuterated isotopomers are affected by isotope effects which are opposite in direction. This finding was further interpreted to indicate that the exo and endo C–H bonds on at least one of the methylene carbons probably have significantly stiffer and less stiff stretching and/or bending force constants than corresponding bonds on the other methylene(s).

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(8) Chen, C. L.; Wolfsberg, M. *Isotopenpraxis* **1987**, *23*, 205.

(9) GAUSSIAN 82: Binkley, J. S.; Frisch, M. J.; DeFrees, D. J.; Raghavachari, K.; Whiteside, R. A.; Schlegel, H. B.; Fluder, E. M.; Pople, J. A. Department of Chemistry, Carnegie-Mellon University, Pittsburgh, PA.

(10) (a) Olah, G. A.; Kelly, D. P.; Jeuell, C. J.; Porter, R. D. *J. Am. Chem. Soc.* **1970**, *92*, 2544. (b) Saunders, M.; Siehl, H.-U. *J. Am. Chem. Soc.* **1980**, *102*, 6868. (c) Staral, J. S.; Yavari, I.; Roberts, J. D.; Prakash, G. K. S.; Donovan, D. J.; Olah, G. A. *J. Am. Chem. Soc.* **1978**, *100*, 8016. (d) Brittain, W. J.; Squillacote, M. E.; Roberts, J. D. *J. Am. Chem. Soc.* **1984**, *106*, 7280.

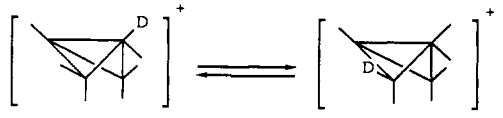
A trideuterated ion of known stereochemistry was used by Roberts et al. to demonstrate that endo deuteration leads to a downfield shift of the ^{13}C NMR peak of the deuterated methylene and exo D produces an upfield shift.[10d] Using this assignment to interpret the ^{13}C NMR spectrum of the monodeuterated ion,[10b] one finds that the deuterium-induced splitting in endo-deuterated ion is about twice as great as that in the exo-deuterated ion. If the exo and endo C–H bonds in one of the types of methylene are of comparable stiffness, then there must be a significant difference in stiffness between the exo and endo bonds in the other kind of methylene. It was considered that the bicyclobutonium ion with its pentacoordinated carbon would be much more likely to show this unusual contrast between hydrogens on the same carbon, and therefore it was suggested that this was the main structure of the ion.[10b]

Recent extensive theoretical investigations of the $C_4H_7^+$ potential energy surface are in close agreement with the above interpretation of the experimental results.[11] High-level ab initio calculations (including correlation) found the bicyclobutonium structure to be 0.25 kcal higher in energy than bisected cyclopropylcarbinyl structure (vide infra) with a low barrier (~1 kcal) pathway between them. Since the uncertainties in the calculation can be estimated to be at least a kilocalorie, these theoretical results agree qualitatively with the experimental results on the ion. However, the extremely small energy differences and the flat nature of the potential energy surface make it impossible to reach unambiguous conclusions concerning the actual structure on the basis of theory alone. One must keep in mind that the calculations possible at this time are for individual ions in the gas phase while the experimental measurements were done in solution. Any small differences in solvation energy between the two structures could easily affect the equilibrium.

The ^{13}C NMR chemical shifts of the various structures have been calculated using the IGLO approach. The values, obtained using a bicyclobutonium structure and averaging the shifts of the nonequivalent methylene carbons (the pentacoordinated carbon predicted to be upfield) because of the rapid process, are in reasonable agreement with the experimental ^{13}C NMR spectra.[11b] Calculations based on a cyclopropylcarbinyl structure do not agree with experiment. While this result favors the proposal that the major isomer is the bicyclobutonium ion, it is desirable to consider as much additional information as possible. For example, a good theoretical model of the major structural isomer should also reproduce the inferred difference in the stiffness of the C–H bonds and permit prediction of the equilibrium isotope effects. We report here the theoretical calculation of reduced isotopic partition function ratios, the use of these in the calculation of experimental observables, and the characteristics of the ion that give rise to the isotope effect on equilibrium.

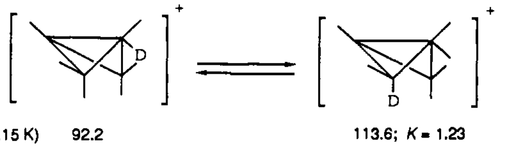
The highest level ab initio molecular orbital calculation at which we have second derivatives with respect to Cartesian displacements is HF/6-31G*, since the force constants for the correlated calculations described in ref 11 are not available. At this level of theory, both the bicyclobutonium and cyclopropylcarbinyl structures are saddle points with one imaginary frequency each. A much less puckered cyclobutyl structure was found as a minimum at this level of theory. The isotope effects on this puckered cyclobutyl structure were also investigated and found not to lead to agreement with the NMR experiment. In fact, both the bicyclobutonium and cyclopropylcarbinyl structures were found to be minima on the electron correlated surface. The imaginary frequency from the HF/6-31G* calculation of the all-hydrogen bicyclobutonium ion is 131i cm^{-1}. Its small magnitude indicates how flat the surface is. We deal with the fact that the bicyclobutonium ion is actually a "stable" molecule by replacing the imaginary frequency in each isotopomer by a zero frequency (which, as already pointed out, makes no contribution to $(s_2/s_1)f(2/1)$ (eq 4)) and by considering the saddle-point geometry as an equilibrium geometry. We are thus assuming that the imaginary frequency is truly small or "zero" and that the other frequencies are unchanged. The procedure for cyclopropylcarbinyl cation is similar.

The equilibrium isotope effects K investigated were the following; for the bicyclobutonium structure,



$(s_2/s_1)f$(198.15 K) 116.4 113.1; $K = 0.97$

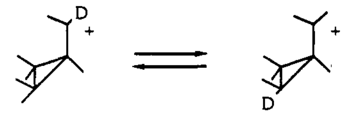
Diagram 2



$(s_2/s_1)f$(198.15 K) 92.2 113.6; $K = 1.23$

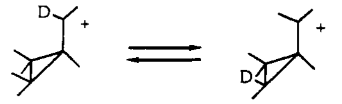
Diagram 3

and for the cyclopropylcarbinyl structure



$(s_2/s_1)f$(198.15 K) 89.3 115.8; $K = 1.30$

Diagram 4



$(s_2/s_1)f$(198.15 K) 84.8 109.9; $K = 1.30$

Diagram 5

For the cyclopropylcarbinyl cation, the deuterium is predicted to prefer to reside on the cyclopropyl ring rather than on the formally cationic carbon for both the endo- and exo-deuterated isomers. For the bicyclobutonium ion structure, the prediction is that exo deuterium prefers to be on the pentacoordinated carbon rather than on the corresponding adjacent (tetracoordinated) methylene positions. In contrast, the endo deuterium is predicted to prefer to be on the adjacent methylene positions rather than on the pentacoordinated carbon

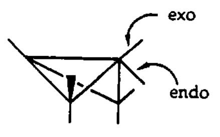


Diagram 6

Thus, the calculated isotope effects for the bicyclobutonium ion structure agree with the striking experimental result that the two different equilibrium isotope effects for the exo and endo (see diagram 6) sets of interchanging methylene hydrogens are opposite in direction. With the assumption that the pentacoordinated carbon is upfield with respect to the tetracoordinated methylenes as predicted by IGLO (and in accord with analogous cases), the theoretical prediction is that the equilibrium of diagram 2 gives rise to an upfield shift for exo-deuterated methylene while the corresponding equilibrium of diagram 3 leads to a downfield shift of the methylene deuterated in the endo position, in accord with experiment already mentioned. The agreement must be judged as qualitative since, while the relative signs and even the trends in the relative magnitudes are correctly predicted, the calculated equilibrium constants are expected to lead to a relative ratio endo/exo larger than two, the observed value. On the other hand,

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(11) (a) McKee, M. L. *J. Phys. Chem.* **1986**, *90*, 4908. (b) Saunders, M.; Laidig, K. E.; Wiberg, K. B.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1988**, *110*, 7652. (c) Koch, W.; Liu, B.; DeFrees, D. J.; *J. Am. Chem. Soc.* **1988**, *110*, 7325.

Table I. Diagonal Valence Force Constants[a] for the Methylene Hydrogens in Bicyclobutonium Cation[b]

s	4–3	6.40	*s*	8–6	6.36
s	5–3	6.20	*s*	10–6	6.29
b	4–3–6	1.18	*b*	8–6–2	1.12
b	4–3–7	1.18	*b*	8–6–3	0.91
b	5–3–6	0.90	*b*	10–6–2	1.08
b	5–3–7	0.90	*b*	10–6–3	1.07

[a] C(3) is the pentacoordinated carbon; C(6) and C(7) are methylene carbons; C(2) is the methine carbon; H(4) and H(5) are exo and endo hydrogens bonded to C(3); H(8) and H(10) are exo and endo hydrogens bonded to C(6). [b] Stretching force constants (s) in mdyn/Å, bending force constants (b) in mdyn·Å).

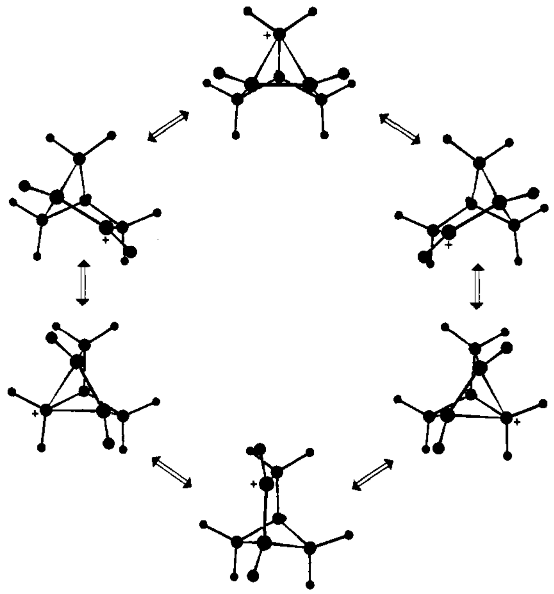
the cyclopropylcarbinyl equilibria of diagrams 3 and 4 would predict exo and endo equilibria of the same sign. It is tempting to account for the observed ratio of isotope effects being smaller than the prediction based on the bicyclobutonium ion by imagining that there is a small amount of the cyclopropylcarbinyl ion present in equilibrium. Inclusion of a small amount of cyclopropylcarbinyl would also improve the agreement between the observed ^{13}C NMR shifts and those calculated using IGLO. We have found no structure other than the bicyclobutonium ion which leads to the prediction that the shifts produced by exo and endo deuteration are opposite in sign.

Since chemists tend to think in terms of valence coordinate force constants (corresponding here to displacements of bond stretches and bond angles from their respective equilibrium values), the force constants for Cartesian coordinate displacements obtained from the quantum mechanics calculations were appropriately transformed into force constants corresponding to a complete set of valence coordinates in order to obtain a better understanding of the isotope effects. A complete set of such coordinates refers to coordinates for the bicyclobutonium ion chosen so that there exists no redundancy conditions among them and so that the force field thus obtained yields the same 27 normal mode vibrational frequencies as those obtained from the Cartesian coordinates.[7] The choices of valence coordinates for ring systems, the complete valence coordinate force field for $C_4H_7^+$, as well as the interpretation of isotope effects, discussed in terms of the force field, by means of statistical mechanical perturbation theory[12] will be presented elsewhere.[13] For the present, only the diagonal force constants corresponding to the stretches and bends involving the exo and endo methylene hydrogens on the pentacoordinated and tetracoordinated carbon atom are shown in Table I. From the listed force constants, the exo hydrogen on the pentacoordinated carbon corresponds to larger force constants than the corresponding endo hydrogen, while on the tetracoordinated carbons these force constants are much more alike. In the same way, the force constants on the endo hydrogen of the tetracoordinated carbon are larger than those on the pentacoordinated carbon so that the equilibrium constant for diagram 3 is expected to be larger than unity.[2] For the exo hydrogens, on the other hand, the force constants are larger on the pentacoordinated carbon so that the equilibrium constants in diagram 2 is expected to be less than unity. In the above-mentioned perturbation theory, the zeroth-order isotope effects depend only on the diagonal force constants, and one can quantitatively evaluate the qualitative arguments just presented. It is quite evident that full elucidation of the isotope effects requires consideration of off-diagonal force constants.

Recently the methylcyclobutyl cation has also been studied experimentally with NMR isotopic perturbation and theoretically using the methods described here.[14]

Bicyclo[2.1.1]hexyl Cation. As in the previous section, we first review the ^{13}C NMR data and electronic structure calculations before presenting calculations on isotope effects and relating the results to the experimental results.

Chart II



Solutions of the bicyclo[2.1.1]hexylcation also show a single peak for the three methylene carbons in the ^{13}C NMR spectrum.[15] Again, there is no reasonable structure with 3-fold symmetry. Once more, there are three equivalent classical structures and three equivalent nonclassically bridged structures, each with a pentacoordinated methylene, which could interconvert rapidly to account for the observed spectrum (see Chart II). Here, there is also a single peak for the two adjacent methine carbons. This result might be due to rapid scrambling if the preferred structure for the ion were the classical one, or it might result from the plane of symmetry in the bridged structure.

Isotopic substitution by deuteration at one of the two methine carbons produced a small splitting in the methine ^{13}C NMR.[3,16] Since, by analogy to the case of dimethylcyclopentyl and other equilibrating classical ions, a large splitting was predicted if bicyclo[2.1.1]hexyl cation were classical, the conclusion was drawn that the major species is the nonclassical bridged structure.

More recently, solvolysis studies by Kirmse with a double tracer labelling scheme indicate that the nonclassical bridged structure is more stable than the open classical ion by about 3 kcal/mol in nucleophilic media.[17] Theoretical investigations into the nature of the ion have also been carried out.[18] A recent ab initio study found the bridged structure to be more stable than the classical with both structures being local minima at HF/6-31G*. At electron correlated levels (MP3(FC)/6-31G*//MP2(FULL)/6-31G*), the bridged structure is found to be more stable by 4.0 kcal/mol.

The ^{13}C NMR isotopic perturbation study[16] strongly indicated that the bicyclo[2.1.1]hexyl ion is nonclassical, but the splitting to be expected for the classical model could not be estimated. It had been assumed that the difference in chemical shift between the two interchanging methine positions would be quite large. This difference between the two positions in the absence of exchange will be defined as Δ, the chemical shift of the cationic carbon minus the chemical shift of the bridgehead methine. The ^{13}C NMR shifts of both the classical and nonclassical structures have been predicted based upon the IGLO formalism,[19] and Δ is predicted to be 253.6 ppm for the classical ion.

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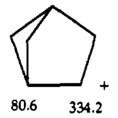

IGLO ^{13}C Chemical Shifts in ppm (vs TMS) for the two methine carbons of the classical ion

Diagram 7

Rapid exchange among the classical structures would yield a single averaged ^{13}C NMR peak midway between the carbocation and noncarbocation methine frequencies in the absence of exchange. Substitution of deuterium at one of these positions would break the degeneracy for this exchange process, and the deuterated and nondeuterated carbons would be expected to be observed at different frequencies. The splitting between these peaks, δ, is the chemical shift of the protiated methine minus that of the deuterated methine, both shifts averaged over the isotopomers by the rapid process.

The most important factor in predicting δ for the classical model is the equilibrium constant K for the interchange of the deuterated and undeuterated methine carbons. We define $K = \text{(II)}/\text{(I)}$, where (I) and (II) represent the concentrations (which are taken to be mole fractions) of the isotopomers with deuterium at the cationic carbon and bridgehead methine, respectively.

Of course, in the nonclassical ion, the two methine positions are equivalent by symmetry. Therefore, there is no isotope effect on equilibrium. A small experimental splitting in the CMR would be expected because of the intrinsic effect of deuterium upon the deuterated carbon's chemical shift. Such intrinsic shifts are commonly seen in ordinary, nonequilibrating deuterated molecules. Typically, a deuterated carbon is shifted upfield by ~0.3 ppm, relative to its protonated counterpart. The observed shift here is somewhat larger (1.3 ppm).

As the sum of the mole fractions of I and II is unity, one can express the mole fractions of the two isotopomers as,

$$\text{(I)} = \frac{1}{1+K} \text{ and } \text{(II)} = \frac{K}{1+K} \tag{6}$$

If we choose the scale for ^{13}C NMR so that the "neutral" bridgehead methine is at zero and the cationic carbon is at Δ, the average chemical shift of the protiated carbon in the monodeuterated ion is the mole fraction of the ion in which the protiated carbon is at the cationic center times Δ, or $\delta_{\text{CH}} = \Delta\text{(II)}$. Similarly, the averaged chemical shift of the deuterated carbon is $\delta_{\text{CD}} = \Delta\text{(I)}$, where (I) and (II) are mole fractions as described in eq 6. Thus the observed splitting can be expressed in terms of the equilibrium constant and the difference in chemical shift between the two static isomers, Δ, both of which are theoretically determinable.

$$\delta = \delta_{\text{CH}} - \delta_{\text{CD}} = \frac{\Delta(1-K)}{(1+K)} \tag{7}$$

With the HF/6-31G* basis set, both the classical and bridged structures are minima. The surface near the classical structure is quite flat, with the lowest normal-mode vibration frequency in the all-protio compound calculated to be 43 cm^{-1}. The normal mode corresponding to this frequency would take the ion toward the nonclassical structure. From the Cartesian coordinate force constants, the reduced isotopic partition function ratios were calculated for the equilibrium shown in diagram 8. The values were calculated at the temperature of the experimental measurements. The calculated reduced partition function ratios are such that the deuterium prefers to be at the bridgehead carbon, away from the positive center, with the equilibrium constant 1.7. Using this equilibrium constant and Δ = 253.6 ppm, we obtain a δ value of +63.0 ppm, which is much larger than the observed value of +1.3 ppm. If we approach the problem in reverse, using the experimental value of δ, 1.3 ppm, and the IGLO value of Δ, 253.6 ppm, the value of K would have to be quite close to unity, 1.01. These results show clearly that the classical model does not fit the ^{13}C NMR isotopic perturbation result.

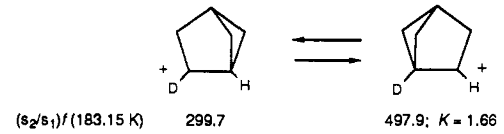

Diagram 8

Conclusions

We have discussed the calculation and use of reduced isotopic partition function ratios evaluated from the normal-mode vibration frequencies which are determined from molecular orbital calculations. We have outlined a general method for these calculations and discussed the Fortran program QUIVER which performs them. We have demonstrated that theoretically determined isotope effects are able to approximate those observed for cationic systems. In addition, we have shown that these approaches can be used, not only to reproduce observed effects, but also to investigate questions concerning which structures are preferred in cases where energies are so similar that comparisons of theoretically predicted relative energies with experimental results leave doubt. The quantitative prediction of equilibrium isotope effects should allow definite conclusions to be drawn when qualitative interpretations are ambiguous. This approach should be useful for researchers who wish to employ theoretical methods in close knit concert with experiment.

Registry No. Cyclopropylcarbinyl cation, 14973-56-9; bicyclo[2.1.1]hexyl cation, 40949-72-2; bicyclobutonium cation, 20671-12-9.