Protium-Deuterium Fractionation Factors for Organic Molecules Calculated From Vibrational Force Fields

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This paper is dedicated to Professor Jacob Bigeleisen on the occasion of his 70th birthday

New valence force fields have been calculated for forty-seven small organic molecules and used to calculate protium-deuterium fractionation factors. Factors for molecules of the type CH_3X and HCOX have been found to correlate with the electronegativities of X and the CX bond lengths. The effects of cumulative substitution on a given C atom on the alpha CH fractionation factors have been examined. Some uses of the factors in mechanistic analysis are discussed.

Key words: Deuterium Isotope Effects, Fractionation Factors

Ever since the development of the fundamental theory of the effects of isotopic substitution on chemical reaction rates and equilibria by Bigeleisen and Mayer [1], isotopic fractionation factors have been of interest to chemists generally and have been extensively exploited in geochemistry [2], biochemistry [3, 4] and the study of organic and inorganic reaction mechanisms [5].

Early applications of the Bigeleisen-Mayer theory involved the calculation of isotopic fractionation factors for small molecules from *observed* vibrational frequencies [6] and provided useful results for sufficiently large primary isotope effects. Following the general availability of computers and the development of programs allowing the application of the Wilson FG matrix method [7] to the solution of the vibrational problem for fairly complex molecules [8, 9] it became possible to improve the accuracy of the calculations through the use of frequencies *calculated* from force fields which had been developed to give the best fit to observed frequencies [10].

Hartshorn [11] reported the first calculation of hydrogen and carbon fractionation factors for a moderate-sized group of small organic molecules; he was able to show that these factors varied in regular and predictable ways with variations in the local structural environment at the site of isotopic substitution. Since that time the number of molecules for which appropriately accurate spectroscopic data are available has expanded markedly, as has the direct measurement and use of fractionation factors.

The purpose of this paper is to report additional fractionation factors calculated from molecular force fields for organic molecules and to re-examine with the larger body of results now available the structural correlations mentioned above.

In particular we wish: a) to examine the variation of H/D fractionation factors with variations in alpha substituent atoms and to correlate these with atomic properties, b) to investigate more closely the effects of cumulative subsitution of one, two and three identical groups at the same carbon atom on the alpha deuterium fractionation factors, c) to investigate with the ethyl halides how successfully one may use 'transferable' force constants to calculate fractionation factors, d) to investigate correlations of fractionation factors for deuterium attached to trigonal carbon and e) to improve the utility of fractionation factors by expanding the catalog of available values.

Theory

The theory of isotope effects on reaction equilibria and rates has been extensively studied and reviewed elsewhere [12–15]. Only a few basic points necessary to understanding the present material will be reviewed here.

Isotope effects on equilibrium constants can be expressed as isotopic exchange equilibrium constants. If R_1 is some chemical reactant that gives a product P_1,

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the equilibrium constant neglecting activity coefficients is

$$K_1 = [P_1]/[R_1].$$

If R_2 represents the same molecule with an isotopic substituent, the equilibrium constant for the conversion to P_2 is

$$K_2 = [P_2]/[R_2].$$

The isotope effect on the equilibrium can then be expressed as

$$K_1/K_2 = ([P_1][R_2])/([P_2][R_1]),$$

K_1/K_2 is the equilibrium constant for the isotope exchange reaction

$$R_1 + P_2 = R_2 + P_1.$$

Isotope effects on reaction rates can also be expressed as isotope exchange equilibrium constants. In transition state theory [16] reactants are said to be in equilibrium with the transition state, and all transition states decompose with the same rate constant. Thus the same expression could be used where R is a reactant and P a transition state.

Bigeleisen and Mayer [1] and Melander [12] developed equations for the evaluation of isotope effects by the application of statistical mechanics. The equations are based on the following assumptions:

1) the Born-Oppenheimer approximation that the potential energy is independent of isotopic substitution, and
2) the partition functions are factorable into rotational, translational and vibrational contributions, and
3) translational and rotational motions are classical, and
4) vibrational motion is harmonic.

When one expresses the equilibrium constant in statistical mechanical terms, the concentrations are replaced by the molecular partition functions of the isotopic molecules and the isotope exchange equilibrium constant can be expressed as

$$K_3 = K_1/K_2 = (Q_{P1}/Q_{P2})/(Q_{R1}/Q_{R2}),$$

where the molecular partition function Q is

$$Q = \sum \exp(-e_i/kT).$$

The sum is taken over all of the energy levels e_i of the molecule. The partition functions Q are assumed to be factorable into rotational, translational and vibrational contributions such that

$$Q = Q_{rot} \cdot Q_{trans} \cdot Q_{vib}.$$

The Bigeleisen equation can be rewritten in two ways which identify the contributions to the overall isotope effect [9]:

$$K_1/K_2 = \text{MMI} \cdot \text{EXC} \cdot \text{ZPE} = \text{VP} \cdot \text{EXC} \cdot \text{ZPE},$$

where MMI is the ratio of ratios of translational and rotational partition functions between initial and final states of two isotopic species in equilibrium and is expressed as ratios of masses and moments of inertia; ZPE is a factor due to zero point energy differences between reactant and product states between the two isotopic molecules; EXC is a factor due to excitation of the vibrational levels above the zeroth level and VP is the ratio of ratios of all vibrational frequencies for reactant and product state between the two isotopic molecules. Through the use of the Teller-Redlich product rule the MMI factor can be replaced by VP.

Isotope effects are generally dominated by the ZPE term, and this contribution is the focus of qualitative discussions explaining isotope effects. ZPE contributions are usually represented in terms of potential energy diagrams with a separate potential well representing each species. The ZPE contribution to the overall effect can be calculated from the formula [17]

$$K_1/K_2 = \exp[0.71929(\nu_{R1} - \nu_{R2} - \nu_{P1} + \nu_{P2})T]$$

for frequencies, ν, in reciprocal centimeters and temperatures, T, in degrees Kelvin and 0.71929 in $hc/2k$. The ν's are the normal mode frequencies for all reactants and products. Since hydrogen is much lighter than other atoms, its vibrations may, to a fair approximation, be considered to be independent of the rest of the molecule. This equation can then be used to obtain a crude estimate of the hydrogen isotope effects on equilibrium constants using only those frequencies which directly involve hydrogen motion.

The *accurate* calculation of isotope effects on equilibria using the complete Bigeleisen equation is straightforward if all the normal mode vibration frequencies are known for all four molecules in the exchange reaction. Computer programs for carrying out these calculations are available.

Determination of Force Fields

In order to calculate the normal mode frequencies for a molecule, a molecular structure and a force field

must be specified. Force fields in the present work were obtained by two approaches. The first was to start with force constants from a published normal coordinate calculation on the molecule of interest. The second, used in the absence of a published normal coordinate analysis, involves using trial values for the force constants estimated from molecules of similar structure. The vibrational program of Schachtschneider and Snyder [8] was then used in both cases to refine the force fields to give the best fit to the observed frequencies.

Starting from an initial set of force constants, the Wilson FG matrix method calculates a set of frequencies. The force constants may then be adjusted to give minimum deviation between observed and calculated frequencies. In cases where the initial force constants were not obtained from a normal coordinate calculation, manual adjustment of the force constants was usually necessary to obtain calculated frequencies close enough to the observed frequencies to allow the program to converge.

To aid in convergence, the *G*-matrix elements were symmetrized using linear combinations of internal valence coordinates. In this way, the *G*-matrix then becomes factored into a number of non-mixing blocks. These blocks can then be fitted individually.

In choosing diagonal force constants and off-diagonal (interaction) force constants, care was taken to keep the force fields consistent throughout a series of molecules of the same symmetry group. For example, the same type of force field was used for CH_3NH_2, CH_3PH_2, and CH_3AsH_2. The same interaction terms were used in each of these molecules resulting in a similar force constant set. The interaction terms that were used were only those obtained from a known convergent normal coordinate analysis. These terms had either atoms or bonds in common. In the methyl-X compounds, the interaction force constants that were used included (CH-str, CH-str), (CH-str, HCH-bend), (CH-str, HCX-bend) and (HCX-bend, HCH-bend). No additional terms were introduced.

A simplex fitting program was written to solve the problem of divergence found with the gradient method of Schachtschneider. The program does converge to a minimum but required many additional cycles and extra computational time. For molecules of eight to ten atoms 50–100 cycles could be run to remove large deviations in the force field which could then be used as input to the Schachtschneider program.

Thus, the criteria adopted for a satisfactory force field were: 1) it should reproduce the observed spectral frequencies as closely as possible and 2) the fitting program converges. Most of the fields gave agreement between calculated and observed frequencies for both hydrogen and fully deuterated compounds with an average error of less than 0.8 pecent.

Calculation of Fractionation Factors

To calculate a fractionation factor (FF) it is necessary to have all of the normal mode frequencies for all of the molecules included in the equilibrium. All FF's reported in this paper were determined using only complete sets of calculated frequencies for each molecule. To determine the best set of calculated frequencies, observed frequencies for a number of isotopic species are necessary. When many deuterated analogs are available, the chance of a frequency misassignment of one of the normal modes is reduced. The more observed frequencies there are to fit, the smaller the effect which one bad assignment would have on the overall fit.

For example, ethene was originally fit by Hartshorn [11] using three isotopic forms; the present calculation uses data from seven isotopic species and the resulting FF is the same as the one calculated by Hartshorn, indicating that the set of frequencies that he obtained was quite satisfactory.

Increasing the number of isotopic species increases the amount of information in the problem and thus allows an increase in the number of force constants that can be determined to fit the observed frequencies[a]. The data necessary for calculation of partition function ratios and fraction factors are: 1) molecular geometry, 2) force constants derived from fitting observed frequencies and 3) the isotopic atomic masses.

Reliability of the Calculated Fractionation Factors

Errors in the calculated fractionation factors can result from three major sources: 1) errors in the molecular geometry, 2) errors in the choice of force field, and 3) errors in the assignment or observation of experimental frequencies.

When available from the literature, the geometries used in the present work were those obtained from

[a] Because of the "sum rules" the information content is, however, not proportional to the number of isotopic species examined [7].

microwave spectral analysis; otherwise tetrahedral geometry around carbon was assumed. If the molecule was known to have a geometry much different from tetrahedral, bond distances and angles would be used from other molecules of similar structure. The greatest uncertainty would appear to occur for the molecules where an assumed structure was used.

Since Hartshorn [11] used tetrahedral geometry for his calculations in the methyl halide series, an estimate of the effect which bond angles have on the FF was obtained by using the geometries calculated for the methyl halides by Allinger [18]. No significant change was found in the fractionation factors of the methyl halides for deviations in the HCX angle of 1.5 degrees from tetrahedral. Where accurate bond distances were not available from the literature they were assumed to be the sum of the covalent radii of the two atoms.

The second source of uncertainty in a FF arises from the choice of the force field used to obtain the calculated frequencies. In most cases, it is impossible to determine all of the elements of the *F*-matrix, thus a choice must be made as to which elements of the matrix will be used to determine the molecular motions. In the ethyl halide series, a diagonal force field with and without off-diagonal elements was fit to the observed frequencies. The differences beetween the calculated FF's were between eight and fourteen percent. Although it is not practical to determine all the off-diagonal elements it is necessary to use a judicously chosen set of them in order to obtain satisfactory results.

By far the most important source of uncertainty depends on the accuracy and assignment of the observed frequencies. Comparisons within a series of molecules having the same symmetry, such as the ethyl halides, can help reduce assignment problems and reduce errors. Additional methods to aid in correct assignments will be discussed below.

As mentioned above, all frequencies are calculated within the harmonic approximation and no corrections for anharmonicity were made. Since harmonic corrections are only available for a limited number of organic molecules it is not practical at this time to try to develop a collection of calculated fractionation factors for which anharmonicity corrections have been made.

A calculation was done to compare the fractionation factors determined from harmonically corrected frequencies and those obtained as described above. The harmonically corrected frequencies for both molecules were used to calculate the fractionation factor for formaldehyde relative to acetylene and the result, 1.114, was very close to the value of 1.1058 obtained from the force field fitted to observed frequencies. This error is within the limits of about 2% which Hartshorn estimated for his results.

Results and Discussion

A number of new H/D fractionation factors have been calculated and are included in three tables in the appendix along with the earlier values of Hartshorn [11]. These are expressed, as in the Hartshorn paper [11], relative to acetylene and represent equilibrium constants at 25 °C for the following type exchange reactions:

$$HCCD + RH = HCCH + RD.$$

On this scale most molecules have FF values greater than unity corresponding to greater net isotopic frequency shifts and stiffer binding. It should be noted that division of the FF for one molecule by that for a second cancels the contribution from the common reference and provides the equilibium constant for isotopic exchange between the two molecules.

Details of the calculations including geometries, masses, internal valence coordinates, symmetry coordinates, valence force constants, symmetry force constants and observed and calculated frequencies for each of the molecules studied are available elsewhere [19] and will not be repeated here because of space limitations.

The calculations of Hartshorn [11] showed that H/D fractionation factors were to a surprising degree only dependent on the *local* structural environment and that they varied with structure in regular and predictable ways. It is something of an irony that fractionation factors can only be calculated accurately by using *all* normal mode frequencies for each molecule but they do not vary appreciably with structural variations away from the local site. Thus fractionation factors are much more localized molecular properties than are molecular vibrations.

The fact that fractionation factors *are* localized properties offers the chemist striking advantages in their use. First, structural reasoning of the kind long practiced by organic chemists allows them to be qualitatively estimated quite readily. Second, since they are not much affected by remote structural variations, in the absence of specific local intermolecular inter-

actions, they are not much different for liquid, gaseous or solution states. Thus, in mechanistic studies the variation of an isotope effect can be interpreted as a variation in transition state structure as, generally, variations in rate or activation parameters or other substituent effects cannot.

The following discussion of the new fractionation factors will be divided into four parts: 1) the variation in alpha CH/CD effects caused by variation in the nature of the substituent atom at carbon; the methyl-X series, 2) the effects of successive substitution of a given atom on carbon on the alpha CH/CD FF's; cumulative effects, 3) ethyl halides and 4) carbonyl compounds. The correlations involved in items 1 and 2 should allow estimation of the FF for almost any H/D attachment to four coordinated carbon.

The Methyl-X Series

Hartshorn found that the fractionation factors for methyl-X compounds generally increased with the electronegativity of X. In order to investigate this and other possible correlations more thoroughly we added to this series additional molecules with the following X substituents: PH_2, SH, OH, SeH, AsH_2, Li, $HgCH_3$, $CdCH_3$, $ZnCH_3$, and $SnCH_3$. The total of calculated factors for twenty molecules in this series covers, for X, a large section of the periodic table and should allow the estimation of FF's for additional members of this series by interpolation and extrapolation. Table 1 shows all of the CH_3-X molecules with their calculated FF's for $^{12}C/^{13}C$ in column 2 and CH/CD in column 3.

In the fitting process careful attention was paid to the type of force field. Since molecules (in this series) with substituents from within a given group in the periodic table share the same symmetry, only one type of force field was needed for each group. When the X substituent atom had other atoms or groups attached to it, for example PH_2, hydrogen was the only atom used except for the group IIB elements Hg, Cd and Zn; in each of these cases a methyl group was attached. No correction was made for the methyl group since the methyl effect from methanol to methyl ether was only 1.446/1.432 or 1% and the effect from methyl mercaptan to dimethyl sulfide was only 1.329/1.350 or 2% (inverse).

The plot of the log of the CH/CD fractionation factors versus the electronegativity of X for the series of methyl-X molecules is nearly linear ($r^2=0.93$).

Table 1. Fractionation factors for methyl-X molecules relative to acetylene at 25 °C.

X	$^{13}CH_3X$ [a]	CH_2DX [a]	CH_2DX [b]	residual
H	1.0050	1.246	–	–
Li	0.9640	0.982	0.975	0.007
CH_3	1.0175	1.361	1.347	0.014
NH_2	–	1.401	1.407	−0.006
OH	–	1.446	1.456	−0.010
F	1.0259	1.465	1.495	−0.030
SiH_3	1.0010	1.243	1.205	0.038
PH_2	1.0099	1.257	1.262	−0.005
SH	1.0044	1.329	1.323	0.006
Cl	1.0058	1.405	1.382	0.023
GeH_3	–	1.275	–	–
AsH_2	1.0094	1.258	1.236	0.022
SeH	1.0076	1.295	1.299	−0.004
Br	1.0027	1.358	1.349	0.009
SnH_3	0.9988	1.196	1.189	0.007
I	0.9955	1.316	1.303	0.013
$ZnCH_3$	0.9901	1.125	1.155	−0.029
$CdCH_3$	0.9879	1.135	1.166	−0.031
$HgCH_3$	0.9936	1.185	1.205	−0.020

[a] Calculated from force field.

[b] Calculated from correlation equation: $\ln(FF)=A\,x^a+B\,d_{CX}^b+C$; where x is electronegativity of X, d_{CX} is CX bond distance in Å, C is intercept, $A=-0.716$, $a=-0.577$, $B=0.170$, $b=-1.535$, $C=0.632$, Std. error = 0.011.

There is still some curvature indicating that more than one effect is necessary to correlate the FF's. Plots of the logs of the FF's versus the C−X bond distances determined from the sum of the covalent radii gave linear relationships for X atoms within a period but different correlation lines for different periods. Similar correlations were found with other atomic properties.

In order to obtain a simple empirical correlation that could be used to estimate FF's in this series for additional X groups it was decided to use the following equation and determine the best fit by varying the parameters therein:

$$\ln(FF)=A\,x^a+B\,d_{CX}^d+C,$$

where x is Pauling's electronegativity and d_{CX} the sum of the covalent radii of C and X. The values of the coefficients A, B, C, a and b were determined using a program written by Nollen [20] which incorporates a simplex minimization routine [21, 22] based on the least squares criterion.

Table 1 also shows in column 3 the FF's calculated from the correlation equation and the differences (residuals) between them and the values calculated from the force fields for each molecule. Note that H and GeH_3 are not fitted. It should also be noted that the values calculated for the coefficients are not

"rugged", that is they change somewhat when a new molecule is used in the fitting; this is probably due to the fact that the surface over which we are trying to minimize is fairly flat. The parameters of the equation indicate, as expected, that as the electronegativity decreases the fractionation factor decreases and as the bond length increases the fractionation decreases.

Cumulative Effects

Identification of trends in fractionation factors is of great importance since it allows extension of the calculated values to other systems where data are not available. Several trends were reported by Hartshorn [11] who noted that in many cases the effect of a given change of a group at the alpha carbon is roughly independent of the other groups attached to that atom. If one compares the ratio of the fractionation factors of CH_2DCl and CH_3D (1.405/1.246 = 1.128) to the ratio for CH_3CHDCl to CH_3CH_2D (1.518/1.361 = 1.115), the factors for the common change of alpha-H to alpha-Cl in methane and ethane are nearly the same and certainly within the error of the calculation of the individual values.

Another trend that was observed earlier was that in some cases the FF's tended to increase by the same factor as each alpha-H was successively replaced by the same substituent atom. For example, replacement of an alpha-H in CH_3D by an alpha methyl group (to give ethane-d) is attended by an increase in the FF of 1.361/1.246 or 1.096 while the addition of another alpha-methyl group (to give CH_3CHDCH_3) causes an increase of 1.501/1.361 or 1.102.

Similar cumulative behavior was also noted where fluorine replaces hydrogen. Because of the utility of being able to predict cumulative behavior, we carried out additional calculations to determine its scope and limitations. For this purpose data for molecules having one, two and three identical groups attached to carbon were required. A total of seventeen molecules including eight not involved in the earlier study and three which were recalculated with new data are represented. The eight new molecules are methyl ether, ethylene ozonide, iodoform, methylene fluoride, methylene chloride, methylene bromide, methylene iodide and malononitrile. All of these except methyl ether and iodoform fit the general formula $CHDX_2$.

Table 2 shows the fractionation factors for all of the molecules of this series. Four of the values are estimated from the trends in the others by a method explained below. For the cases where X = OR, methyl ether and ethylene ozonide were used to represent the mono- and di-substituted derivatives, respectively. Methyl alcohol coud have been used instead of methyl ether (1.446 vs. 1.432) but the hydrogen attached to oxygen gives a local structure with less similarity to ethylene ozonide.

Table 2. Fractionation factors for CH_2X, $CHDX_2$ and CDX_3 relative to acetylene at 25 °C.

X	CH_2DX	$CHDX_2$	CDX_3
F	1.465	1.722	1.993
OR[a]	1.432	1.522[a]	(1.659)[a]
Cl	1.405	1.529	1.656
CN	1.373	1.441	(1.526)[b]
CH_3	1.361	1.501	(1.622)[b]
Br	1.358	1.443	1.516
I	1.316	(1.332)[b]	1.356

[a] For CH_2DX, X = OCH_3; for $CHDX_2$, ethylene ozonide was used.
[b] Numbers in parenthesis are predicted from values in Table 4.

Table 3. Fractionation factors for the addition of each X group.

X	$\frac{CD_2DX}{CH_3D}$[a]	$\frac{CHDX_2}{CH_2DX}$	$\frac{CDX_3}{CHDX_2}$
F	1.175	1.175	1.157
OR	1.149	1.063	(1.09)[b]
Cl	1.128	1.088	1.083
CN	1.102	1.049	(1.059)[b]
CH_3	1.092	1.103	(1.081)[b]
Br	1.090	1.055	1.057
I	1.056	(1.012)[b]	1.018

[a] CH_3D = 1.246 thus: CH_2DF/CH_3D = 1.465/1.246 = 1.175.
[b] Values predicted from Table 4.

Table 3 shows the contribution of each successive additional group to the fractionation factor. It should be noted that there is a large drop-off in the contribution of the second group, relative to the first, but the third group has about the same contribution as the second. The equal contribution of the second and third X group is exhibited by F, Br and Cl.

In Table 4 in column 2 are listed the fractionation factors of methyl fluoride divided by that for each compound in the list; in the third column are shown the square roots, and in the fourth column the cube roots, of the factors for each entry relative in each case to the fluorine analog. Thus these numbers represent the inverse of the average contribution to the fraction-

Table 4. Fractionation factors per X group for CH_2DX, $CHDX_2$ and CDX_3 in each case relative to X = F [a].

X	$(CH_2DX)^1$	$(CHDX_2)^{1/2}$	$(CDX_3)^{1/3}$
F	1.000	1.000	1.000
OR	1.023	1.063	(1.063) [b]
Cl	1.042	1.061	1.063
CN	1.067	1.093	(1.093) [b]
CH_3	1.076	1.071	(1.071) [b]
Br	1.079	1.096	1.095
I	1.113	(1.137) [b]	1.137

[a] For I, $CH_2DF/CH_2DI = 1.465/1.316 = 1.113$.
[b] Predicted values.

ation factor of each group relative to that of fluorine. All of the predicted values in Tables 2 and 3 are projected from the trends in this Table.

These comparisons are used because the bending modes especially are more comparable within the series represented by each vertical column. Since the contributions of Br and Cl are about the same per X for $CHDX_2$ and CDX_3 it was assumed in making the projections that the other molecules would show the same trends. If Table 3 had been used to establish the trends for projection, the predicted values would have come out about the same. The largest difference was about 3% for OR in the CDX_3 molecule (1.620 vs. 1.659). Using the predicted values in Table 4, the fractionation factors become 1.332 for methylene iodide, 1.622 for isobutane, 1.526 for cyanoform, and 1.659 for trimethoxymethane.

Vibrational spectra are available for methylene iodide [23], isobutane [24], trimethoxymethane [25], but not for cyanoform. Replacement of one alpha-H on the methylene carbon in propane with a methyl group gives isobutane. The contribution of the mehyl group as projected adds 1.622/1.501 or 1.081 to the fractionation factor. This is consistent with the contribution of the methyl group in comparing methane with ethane (1.096) and ethane with propane (1.102). Since vibrational frequencies have been reported for four isotopic isobutane species, an attempt was made to fit the observed frequencies using Schachtschneider's force constants for the n-paraffins [8] as a reference force field but we were not able to obtain a reasonable fit. Trimethoxymethane vibrational frequencies are available in the literature but only for the hydrogen compound. Cyanoform was found to be so unstable that no vibrational spectra have been reported.

An attempt was made to calculate the fractionation factor for methylene iodide but the resulting value, 1.307, was even lower than the value for methyl iodide, 1.316; from comparisons with other entries in Table 2 this is not reasonable. The discrepancy would seem to be the result of error in the reported frequency assignments. The CH stretching frequencies and the H/D frequency ratios for methylene iodide seem abnormally low in comparison with those for the chloro and bromo analogs, a trend not shown in the methyl halides [26].

All of the other frequencies of methylene iodide are in the range expected from comparison with the other methylene halide analogs and their isotopic shifts are in the range expected. By comparison among the series one would expect the two CH stretches to have values of about 2995 and 3075 cm^{-1}; the latter band was observed in the infrared of the vapor. Using those two values for the CH stretching frequencies the calculated FF is 1.331, close to that predicted in Table 2. It appears that a correlation of fractionation factors could, in some cases, be of assistance in making frequency assignments.

Of the fractionation factors presented in Table 2 those for the oxygen series are the most interesting from the point of view of mechanistic applications. In the past, fluorine was used as a model for oxygen but now calculated values are available for several new oxygen molecules so that this assumption can be evaluated. It turns out that when only one oxygen is attached to carbon the fluorine analogy is satisfactory but problems arise with further substitution since oxygen does not cause the same cumulative increases in the FF's as does fluorine. The fluorine/oxygen fractionation factor ratio is 1.023 for the monosubstituted methanes and 1.20 for the trisubstituted compounds.

The new oxygen values can be used to help in the analysis of several reaction mechanisms. Hydration of aldehydes such as formaldehyde and acetaldehyde have been found to give equilibium alpha deuterium isotope effects of 1.38 [27–29]. Using the two oxygen model (ethylene ozonide) for the hydrate structure and the calculated value for formaldehyde, the equilibrium effect on hydration is predicted to be 1.522/1.106 or 1.376, in excellent agreement with experiment.

A second example involves acid catalyzed hydrolysis of carboxylic acid esters [30, 31]. The proposed mechanism involves the rate determining formation of a tetrahedral intermediate, the hydrate of the ester. Kirsch [32] determined the alpha-d effect for both

methyl and ethyl formate to be 1.23. Using the fractionation factor for methyl formate (1.338) and our predicted value for three oxygens bound to a central carbon (1.659, Table 1), the isotope effect expected is 1.659/1.338 or 1.24. This indicates that the transition state has essentially complete covalent bonding to all three oxygens.

The cumulative behavior exhibited by successive multiple substitution can also be used to analyze alpha-d effects on carbon atoms bearing two different groups. Wolfenden [28] studied the hydration and thiohemiacetal formation of acetaldehyde. The equilibrium isotope effect observed for hydration of acetaldehyde was 1.37 (D/H). Using 2-mercapto ethanol instead of water he found the equilibrium effect to be 1.25 ± 0.06. To model this reaction one needs to remove the contribution due to sulfur. Using methyl mercaptan and methanol as the sulfur and oxygen models, the equilibrium effect for hydration is multiplied by the ratio of the FF's for methyl mercaptan and methanol: $1.37 \times 1.329/1.446 = 1.26$. The calculated value is, within the limits of error, the same as the observed.

Through the study of the effects of cumulative substitution we have been able to extend the fractionation factor tables and extend modelling of isotope effects to several new reactions.

The Ethyl Halides

With the availability of vibrational spectra for all of the ethyl halides, F, Cl, Br, and I, a study was made to determine the fractionation factors to see if they followed a trend similar to that found in the methyl halides. Also in this series the fractionation factors in the methyl group allow one to assess the effects of beta substitution on the CH/CD FF's. Normal mode frequencies were available for each of the ethyl halides and for the CD_2, CD_3 and C_2D_5 isotopomers. Normal coordinate calculations had been reported for all of the molecules except ethyl fluoride.

As with the methyl halides, the same type of force field was used for all molecules in this series; a valence force field that included the same interaction terms as those used by Dempster and Zerbi in their calculations on ethyl chloride [33]. An attempt was made to find a symmetry force field suitable for all of the ethyl halides, but problems with divergence of the fitting program for ethyl fluoride and chloride led to abandonment of this type of force field.

Table 5. Calculated α-d and β-d fractionation factors for ethyl halides relative to acetylene, 25 °C.

Halide	alpha-d	beta-d
F	1.587	1.371
Cl	1.518	1.312
	(1.501)[a]	(1.341)[a]
Br	1.449	1.340
I	1.401	1.343

[a] Values reported by Hartshorn [11].

One of the problems in using a valence force field is that one does not fit one normal mode in, for example, the undeuterated species to a corresponding normal mode in the di-deuterated isotopomer. A group of normal modes, 21 in the case of the ethyl halides, of one isotopic species is ordered in decreasing magnitude and fit with another isotopic species ordered independently in the same way. There is no correlation between the different isotopic species and the best fit is determined by minimization of the sums of the squares of the residuals. In some cases this led to frequency decreases on deuteration by factors greater than 1.4. This problem is further discussed below.

Table 5 shows the calculated alpha- and beta-d fractionation factors for the ethyl halides. The initial force constants used in the force field for ethyl fluoride were transferred from those of the other ethyl halides and from a normal coordinate calculation of the *n*-propyl fluorides by Tanabe and Saeke [34]. A change in the assignment of two frequencies required a recalculation of the values for ethyl chloride reported earlier [11]. The initial ethyl bromide force field was changed from symmetry to valence and then refit using force constants transferred from ethyl chloride.

A normal coordinate calculation for ethyl iodide was first done using 20 force constants. An additional eight interaction terms were added to create a similar potential function for all of the molecules. The alpha-D fractionation factors show the same trend from fluoride to iodide as found in the methyl halides; as the electronegativity decreases the FF decreases. The beta-d effects are between 1.31 and 1.37 and show no consistent trend. Because the beta-d is so far from the carbon containing the halogen, one expects the values to be about the same.

If the ratio is taken between the alpha-d FF for a given ethyl halide and its methyl analog, the "methyl effect", or the change in FF due to the replacement of an alpha-H by a methyl group, can be calculated.

Table 6. Prediction of the α-D FF and the "methyl effect" for the ethyl halides[a].

Halide	FF (calc)	FF (pred)[b]	Me effect[c]
F	1.587	1.600	1.083
Cl	1.518	1.535	1.080
Br	1.449	1.483	1.067
I	1.401	1.437	1.065

[a] Change in the FF by replacing an α-H of the methyl halide with CH_3.
[b] $CH_3CHDF = CH_2DF \times CH_3CH_2D/CH_3D = 1.465 \times 1.361/1.246 = 1.600$.
[c] $CH_3CHDF/CH_2DF = 1.587/1.465 = 1.083$.

Table 7. FF's for ethyl halides relative to acetylene (25 °C) for various force fields[a].

Ethyl halide		FF 1	FF 2	FF 3	FF 4
F	α-D	1.587	1.584	1.479	1.459
	β-D	1.371	1.346	1.404	1.346
Cl	α-D	1.518	1.494	1.443	1.470
	β-D	1.312	1.349	1.338	1.346
Br	α-D	1.449	1.397	1.346	1.381
	β-D	1.340	1.352	1.322	1.350
I	α-D	1.401	1.344	1.336	1.351
	β-D	1.343	1.344	1.336	1.351

[a] Force fields defined in Table 8.

Table 8. Average errors in frequency fits for various force fields for ethyl halides.

Force field	F	Cl	Br	I
1[a]	8.7 cm^{-1}	8.4 cm^{-1}	7.8 cm^{-1}	6.1 cm^{-1}
	0.74%	0.72%	0.79%	0.55%
2[b]	all	10.2 cm^{-1}	0.98%	
3[c]	3.5 cm^{-1}	28 cm^{-1}	23 cm^{-1}	26 cm^{-1}
	3.7%	2.9%	2.4%	2.7%
4[d]	all	31 cm^{-1}	3.1%	

[a] Full valence force field including interaction terms.
[b] Full valence force field with the same force constants for all mehyl groups.
[c] Diagonal valence force field.
[d] Diagonal force field with the same force constants for all molecules except for those directly involving X.

Table 6 shows the "methyl effects" for each of the halides which vary from 8.3% for the fluorides to 6.5% for the iodides. The smaller methyl effects agree with the results found for the cumulative behavior of substituents, i.e. if two substituents are on the same carbon the effect of each is smaller than when it is the only substituent other than hydrogen.

The fluorides come the closest to showing the 9–10% methyl effects found in the comparisons of methane, ethane and propane. The other ethyl halides show smaller effects for the addition of the second group and smaller methyl effects. The predicted FF was calculated by using the ratios

$$\frac{CH_2DX}{CH_3D} = \frac{CH_3CHDX}{CH_3CH_2D},$$

where X = F, Cl, Br, I and $CH_3D = 1.246$ and $CH_3CH_2D = 1.361$. Although the predicted values are higher than the calculated ones the maximum difference is only 3%.

In order to make the methyl groups as equivalent as possible, a number of force constants for the methyl group were set common to all of the ethyl halides. All sixteen of the molecules (four halides, four isotopic species each) were then fit simultaneously. The force constants with common values were CH stretch, HCH bend, HCC bend and the interaction constants among them. The overall fit of calculated to observed frequencies showed only an average 0.98% deviation. The calculated beta-d effects for the four halides ranged narrowly from 1.346 to 1.352. The alpha-d effects changed slightly with the largest deviation being for the bromide.

A diagonal force field and a transferrable methyl group diagonal force field were also used to calculate fractionation factors. The fractionation factors for the different force fields are found in Table 7. When the off-diagonal terms are removed the errors for the fitted frequencies increase three-fold. For force field 4 the beta-d effects are all about 1.35 which is about the average of the beta-d effects for the best fit force field. The alpha-d effects are all low by as much as 9%. The CH_2 group appears to be much more sensitive to the loss of off-diagonal force constants than does the methyl group. A complete list of observed and calculated frequencies for each of the force fields can be found in [19].

The ethyl halides show fractionation factors similar to those predicted from the methyl halides. They show a small amount of non-cumulative behavior and thus are slightly lower than predicted from application of the ethane/methane methyl effect to the methyl halides, a result expected from our examination of the cumulative effects of multiple substitution.

The variations in the beta-d FF's might suggest that the normal mode frequencies are not as well defined as they are for the methyl halides. When more vibrational analyses of the ethyl halides appear, the reliability of these values can be better assessed.

Frequency Plots

The assignment of frequencies was assisted by two kinds of comparisons. The first involved the use of the H/D frequency ratios and the second involved the use of mass vs. frequency plots. In a series of frequency calculations for ethyl halides, for example, the mass of a given set of "hydrogens" was varied from mass 1 to mass 2 in ten equal steps; the calculated frequencies were plotted versus the total mass of the molecule for each increment. A particular frequency could then be followed from, for example, d_0 to d_2 and the appropriate assignment made.

Four assumptions were made for the use of these two kinds of comparison in assigning frequencies:

1) none of the frequencies should ever go up when the molecule is deuterated, except in the case of Fermi resonance,
2) H/D frequency ratios should not exceed 1.4,
3) if the frequencies appear to cross in the mass vs. frequency plots, they do cross,
4) false indication of non-crossing may occur if Fermi resonance occurs.

The use of frequency plots allows one to check the assignments for the normal modes and predict the frequencies for the deuterated molecules.

Carbonyl Compounds

There have been a number of recent papers reporting studies of deuterium isotope effects on equilibrium constants for enzyme catalyzed reactions [4]. Most of the reactions have involved either formation or reduction of a carbonyl group resulting in a change of the coordination number of carbon between three and four. Fractionation factors have been reported for a few carbonyl compounds by Buddenbaum and Shiner [35]. We have calculated new results for the eight molecules shown in Figure 1.

The formyl-oxygen compounds show a trend that increases steadily as the oxygen function becomes less electron releasing. Formamide and formyl fluoride also fit this trend reasonably well. The low value for acetaldehyde does cause some concern since the methyl effect is only 3% whereas in analogous methyl and ethyl compounds the effect is 6.4 to 10.2%.

Cleland [29] has determined the isotopic exchange equilibrium constant between acetaldehyde and ethanol-1-d using the enzyme alcohol dehydrogenase. He reported an equilibrium isotope effect for the conversion of free aldehyde to ethanol of 1.283. This corresponds to a value of 1.23 for acetaldehyde relative to acetylene; this acetaldehyde FF is 9% larger than the spectroscopically derived value of 1.14 and gives a methyl effect of 1.11 relative to formaldehyde.

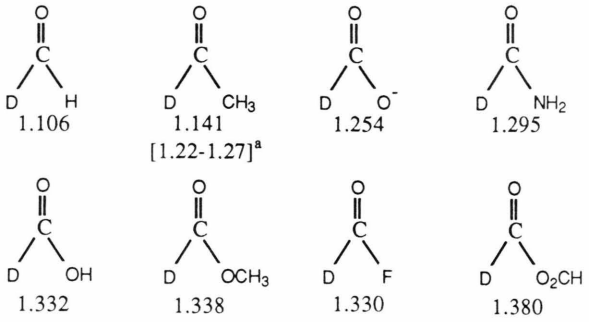

Fig. 1. Fractionation factors for several carbonyl compounds relative to acetylene at 25 °C. [a] Probable value, see text.

The excellent normal coordinate analysis of acetaldehyde reported by Gunthard [36] gives frequencies yielding alpha-d and beta-d fractionation factors lower than expected. The low CH stretching frequencies of aldehydic hydrogens are well known and have been the subject of several studies [37–39]. Acetaldehyde has a much lower CH stretching frequency (2770 $cm\,s^{-1}$) than either formaldehyde (2813), formamide (2852), formic acid (2947) or glyoxal (2844).

These trends have been explained by a model that depends on the availability for donation of a trans-situated oxygen lone pair which can interact through the double bond with an antibonding CH orbital [39]. If a frequency drop is partly the result of a lone pair effect one might expect to see higher frequencies in compounds in which resonance competes for the oxygen lone pair. Such is not the case for CCl_3CHO or CF_3CHO (2851), but inductive effects might also be expected to change the frequency. The lone pair donation idea still does not explain why the calculated fractionation factor for acetaldehyde is so much lower than that predicted from experiments on the hydration equilibrium [29].

Figure 2 shows several series of compounds arranged according to structure. From left to right the group X changes, such as in the methyl-X series; from top down are introduced changes in the environment of the X group. Again one can cross-correlate and generate predicted values. To fit in the trends of this series acetaldehyde should have a FF in the range of

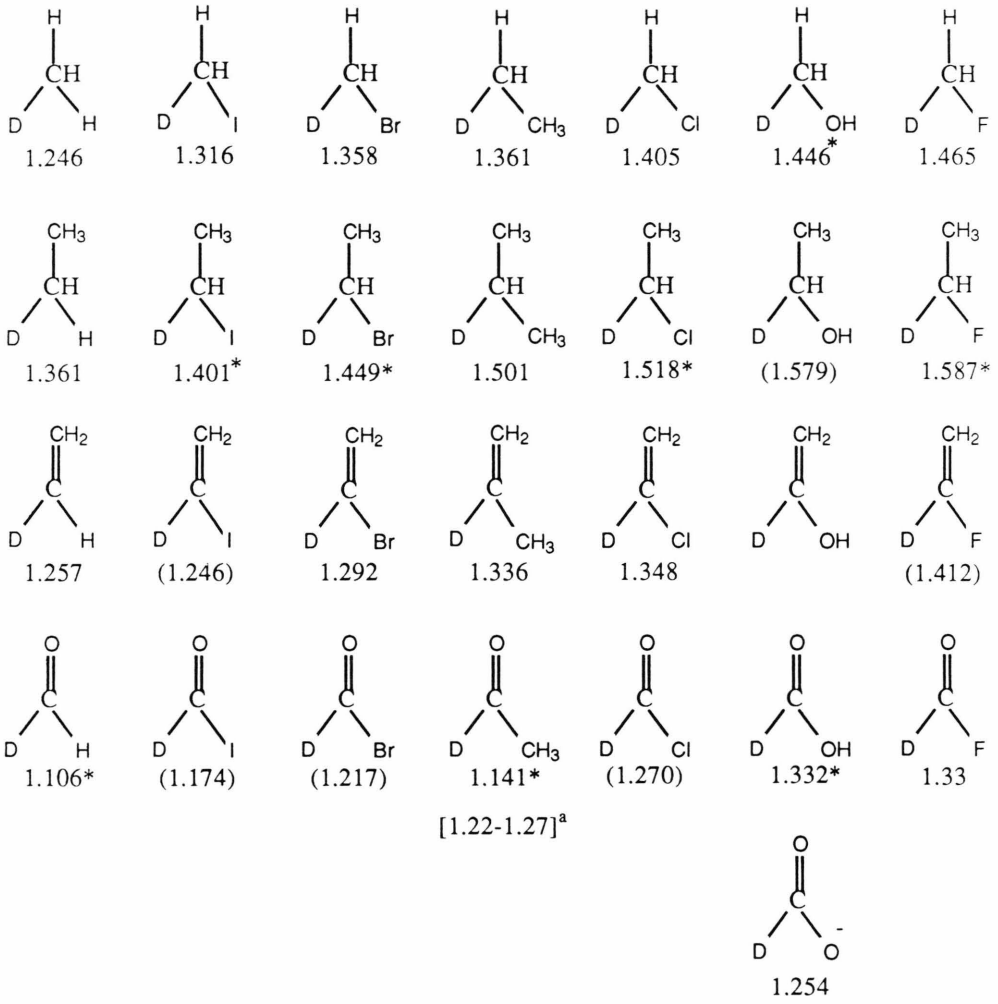

Fig. 2. Fractionation factors relative to acetylene at 25 °C. [a] Probable value, see text. * Present additions to the Table. ( ) Predicted values.

1.22 to 1.27 in agreement with the experimentally derived [29] value of 1.23 but not with the calculated value of 1.141.

Figure 2 can also be used to compare, for example, the effects on the fractionation factor of replacing H by CH_3 in different structures; dividing the FF for a structure on line two by that for the structure on line one immediately above shows that these methyl effects vary from 6.4 to 10% depending on the other substituents present. Similarly, by the values on lines two and three the effect of adding an α-H to an ethylenic carbon varies from 8.2 to 12%. The effect of replacing O of the CO group by CH_2 appears to be about 7%.

The effect of replacing H by various other groups can be assessed by comparing the compounds in different columns with those in column one; these seem to be 3–6%, 6–9%, 11–13%, 16% and 17% for I, Br, Cl, O and F respectively on saturated carbon. The trends for substitution on trigonal carbon are similar but less well defined.

Although these numbers vary a few percent from those used by Clelend [3] the differences are probably within the limits of error. They do suggest that some refinement may be possible through the use of systematic variations that can be correlated with structure; for example, as mentioned above there is a small drop

off in substituent effects as successive H's on carbon are replaced.

A study was carried out of the effect on the calculated fractionation factor for formaldehyde of using different types of force fields: a complete symmetry force field gave a factor of 1.1059, a refit diagonal symmetry force field gave a value of 1.111 and an average error in the frequency fit of 1.28%; a diagonal valence force field gave an FF of 1.112 and an average frequency error of 1.28%. In this example the FF does not vary significantly with the type of force field als long as it is refit.

Some modelling calculations [36, 40] used to interpret kinetic isotope effects involve the use of force constants obtained from normal coordinate calculations; the model is then developed using several force constants hand-picked or systematically varied to predict isotope effects. The above calculations show that force constants from the fitted diagonal force field for acetaldehyde give reasonable results; however a force field using only the diagonal elements of the best valence force field without refitting gave an unrealistic FF of only 0.975. It would seem that one would obtain much more realistic results from model calculations in which fitting to observed frequencies was part of the protocol.

Experimental

The program used for calculation of fraction factors was that of Wolfsberg and Stern [9] which was modified by Buddenbaum [41]. The program consists of three parts, RXCALC, FSRCALC and IECALC. RXCALC calculates the X matrix and sets up the internal coordinates of the molecule. The only required inputs are the bond lengths and angles. FSRCALC sets up the *F* matrix. Force constants are entered for each internal coordinate. Symmetry coordinates can be entered, and transformation between valence and symmetry force fields is also possible. IECALC calculates the *G* matrix, eigenvalues, eigenvectors, vibrational frequencies and the partition function ratios. ISOCAL can also create the input for Schachtschneider's vibrational fitting program [8]. FFIT (SD 3032 VII) [8] requires input of the *G* matrix, observed frequencies, and initial force constants. The program then fits the observed frequencies by a least-squares analysis. The force field from FFIT can then be entered in FSRCALC and the fractionation factor for the molecule can then be calculated.

SMPLX is an optimization program that uses the simplex method. Force fields can be fit to observed frequencies and other vibrational information such as coriolis constants. This method solves the divergence problem of the gradient method but requires more computational time. Tables of data for each molecule are available elsewhere [19].

Ethyl Chloride

The fundamentals of this molecule and the d_2, d_3 and d_5 specifically deuterated analogs have been observed and a number of normal coordinate calculations have been reported [32, 42–44]. The symmetric stretch has been assigned 2932 $cm\,s^{-1}$ instead of 2887 $cm\,s^{-1}$; this agrees with the assignment for the other ethyl halides. The force field used was that of Dempster and Zerbi [33] with geometry of Schwendeman and Jacobs [45]. A valence force field that contained 29 force constants was used (8.3 cm^{-1}, 0.695%).

Ethyl Bromide

Fundamental frequencies have been observed for the d_0, d_2, d_3, and d_5 analogs. A normal coordinate calculation using a symmetry force field has been reported [46, 47]. The force field used for our calculations was the same as that of Flanagan and Pierce [48]. The torsional frequency was calculated from the barrier height [49]. Twenty-nine valence force constants were used in the calculation (Sym: 6.9 cm^{-1}, 0.736%; Val: 8.2 cm^{-1}; 0.840%).

Ethyl Iodide

The four isotopic species d_0, d_2, d_3 and d_5 have been observed and a normal coordinate calculation reported [50, 51]. The torsional frequency was available only for the d_0 molecule. The geometry used was as follows: CC 1,54, CH 1.09, CI 2.135 Å. The angles were the same as those used for ethyl bromide. A valence force field similar to that of ethyl chloride was used. Twenty-nine valence force constants were used in the calculation (6.1 cm^{-1}, 0.545%).

Ethyl Fluoride

Fundamentals for the d_0, d_2, d_3 and d_5 analogs have been observed and tentative assignments made [52]. No normal coordinate analysis that includes the isotopic forms was available. Initial force constants

were obtained from a normal coordinate analysis of n-propyl fluorides [53]. The force field used was the same as that for ethyl chloride. The geometry was assumed to involve tetrahedral angles with CC bond and CF bond lengths of 1.505 and 1.398 Å respectively. Twenty-nine valence force constants were used in the calculation (8.2 cm^{-1}, 0.711%).

Malononitrile

Observed fundamentals are available for d_0, d_1 and d_2 isotopomers [54]. The valence force field used by Yamadera to fit the observed frequencies was used to reproduce the calculated frequencies [55]. The molecule was refit using the geometry of Hirota [56].

Iodoform

The infared spectra of solid iodoform and iodoform-d have been reported [57]. A symmetry force field similar to that used by Hartshorn [11] for chloroform was used to fit the observed frequencies. The geometry was assumed to be tetrahedral (1.7 cm^{-1}, 0.107%).

Ethylene Ozonide

Infrared spectra of three isotope forms, d_0, d_2 and d_4, of the ozonide have been reported [58]. A symmetry force field taken from the normal coordinate analysis was used to fit the frequencies. The geometry was that of Gilles and Kuczkowski [59]. The fractionation factor was determined directly from the reported calculated frequencies.

Methylene Chloride

A number of normal coordinate calculations have been reported for the chloride [60–62]. A set of symmetry coordinates and force constants reported by Shimanouchi [60] were used for initial values. The geometry used was that of Meyers and Gwinn [63]. The fundamental vibrational frequencies were reported for the d_0, d_1 and d_2 isotopomers (2.2 cm^{-1}, 0.276%).

Methylene Fluoride

The fundamentals for the d_0, d_1, and d_2 analogs have been reported and a number of normal coordinate calculations have also been reported [64–66]. Force constants from methylene chloride were used as initial values. The geometry used was that of Hirota [67] (8.3 cm^{-1}, 0.716%).

Methylene Bromide and Methylene Iodide

The vibrational frequencies for CH_2Br_2 and the two deuterated analogs of the bromide have been reported [26]. Only the H and D_2 isotopomers of the iodide have been reported [23]. The force fields and the geometries were the same as those of the chloride (CH_2Br_2, 3.7 cm^{-1}, 0.396%; CH_2I_2, 5.8 cm^{-1}, 0.586%).

Formaldehyde

The fundamental frequencies for the d_0, d_1, and d_2 analogs have been reported [68]. The frequencies used for fitting were both the observed and the harmonically corrected. The two sets were used to determine the effects due to anharmonicity. The force constants for the harmonic frequencies were used as initial values for the anharmonic frequencies (6.4 cm^{-1}, 0.376%).

Formic Acid and Methyl Formate

A normal coordinate calculation for both the acid and the ester have been reported [69]. Transferable force constants were used to fit the H and D species of both molecules. The geometry used was that of Pitzer [70].

Acetaldehyde

A normal coordinate calculation using five isotopic species was reported and the fundamentals were fit using a symmetry force field [36] (8.6 cm^{-1}, 0.532%).

Methanol

Normal coordinate calculations have been reported [71, 72]. Gunthard analyzed seven isotopic species and corrected most of the frequency assignment errors (8.6 cm^{-1}, 0.751%).

Methyl Azide

The fundamental frequencies have been assigned and a normal coordinate calculation reported [73]. Methyl isocyanide was used to help in the assignment of the frequencies of the d_0 and d_3 species. A symmetry force field was used as the potential function and the frequencies reported in the paper were reproduced exactly.

Methyl Lithium

The vibrational frequencies of the monomer in solid argon are reported [74]. Four isotopic species were available; d_0 and d_3 for ^6Li; d_0 and d_3 for ^7Li. A symmetry force field similar to that of the methyl halides was used to fit the frequencies. The geometry was assumed to be tetrahedral (CLi bond length 2.1 Å; 10.8 cm^{-1}, 0.797%).

Methyl Phosphine

The fundamental vibrations for the d_0, d_2, d_3, and d_5 species have been reported [75]. A symmetry force field from a normal coordinate calculation was used. No further refinement was necessary. The torsions were calculated from barrier heights (7.3 cm^{-1}, 0.805%).

Methanethiol

The fundamental frequencies were reported for only the d_0 and d_1 isotopomers [76]. A normal coordinate analysis was reported that used a force field similar to that of methyl selenide. The torsion was determined from the barrier height (5.2 cm^{-1}, 0.464%).

Methyl Arsine

The assignments of the fundamentals for the d_0, d_2, d_3, and d_5 species have been reported along with a normal coordinate analysis [77]. A symmetry force field was used. The interaction terms were the same as those used for methyl phosphine. Only the d_0 torsion was observed (6.6 cm^{-1}, 0.594%).

Methyl Selenol

A normal coordinate analysis for the isotopic species d_0, d_1, d_3, and d_4 has been reported [78]. A symmetry force field was used to fit the frequencies. Only the d_0 torsion was observed (5.9 cm^{-1}, 0.548%).

Methyl Stannane

Vibrational spectra are reported for the d_0, CD_3, SnD_3 and d_6 molecules. A normal coordinate analysis was also carried out using a symmetry force field similar to the one used by Hartshorn [11] for Si and Ge analogs (8.6 cm^{-1}, 1.196%) [79].

Dimethyl Mercury, Cadmium and Zinc

Vibrational spectra are reported for the d_0 and d_6 molecules for each metal [80, 81]. A normal coordinate analysis was carried out on each compound. The same set of symmetry force constants was used for all three molecules. Because of the symmetry of the molecules no torsions were observed. A force constant that would give a frequency at about 10 cm^{-1} was used for the torsion.

t-Dimethyldiazene and t-Methyldiazene

Gas phase and matrix infrared spectra have been reported for the d_0 and d_3 species of t-methyldiazene and d_0, d_3 and d_6 species for t-methyldiazene (azomethane) [82–84].

Benzaldehyde

Vibrational spectra of the d_0, $-CDO$, 4-d_1 and d_6 species have been reported [85, 86]. A complete normal coordinate analysis has also been reported [85]. Calculated frequencies were used to obtain the H/D fractionation factor.

Benzonitrile

Numerous reports have appeared concerning the vibrational assignments for the benzonitrile d_0 and d_5 species [87–91]. Two normal coordinate treatments have been reported [91, 92]. The latest report [92] makes several assignment changes following a normal coordinate analysis of the d_0, 4-d_1 and d_5 species including both in-plane and out-of-plane vibrations. The calculated frequencies were used to determine the fractionation factors.

Nitrobenzene

Vibrational assignments have been made for the d_0, 4-d_1 and d_5 species [93–99]. A normal coordinate analysis using the three deuterated species along with the ^{15}N and ^{18}O species was reported by Kuwae [100]. These calculated frequencies were used to determine the H/D fractionation factor.

Benzene

Vibrational spectra are available for nine isotopic species; d_0, d_1, 1,2-d_2, 1,3-d_2, 1,4-d_2, 1,2,3-d_3, 1,3,4,6-d_4 and d_6. Numerous normal coordinate analyses have been performed [101–105]. The calculated frequencies of Whiffen were used to calculate the H/D fractionation factor [105].

Dimethyl Ether

Vibrational spectra and a normal coordinate analysis have been reported using the d_0, d_3, and d_6 species [106]. The calculated frequencies were used to obtain the H/D fractionation factor.

Bromoform

Bromoform was recalculated using a new structure to determine the effect on the calculation and the fractionation factor [107]. The HCBr angles were compressed giving rise to a greater BrHBr angle. The fractionation factor was unchanged.

Ethylene Glycol

An ab initio calculation and argon matrix infrared analysis of five isotopic species, d_0, d_1, d_2, d_4, and ^{18}O have been reported [108]. The calculated frequencies were used to determine the H/D fractionation factor.

Cyclopentene

Vibrational descriptions for four isotopic species, d_0, 1-d_1, 1, 2, 3, 3-d_4, and d_8 along with a normal coordinate calculation have been reported [109]. The calculated frequencies from this analysis were used for calculation of the H/D FF.

Pyruvic Acid

A detailed examination of pyruvic acid was reported by Gunthard [110] who studied a total of sixteen isotopic species including all d, ^{13}C and ^{18}C species. A normal coordinate calculation fit 200 frequencies with a r.m.s. deviation of 2.5 cm^{-1}. The fractionation factors for pyruvic acid were calculated from the calculated frequencies given in this paper.

Ethyl Cyanide

Vibrational analysis for four isotopic species, d_0, d_2, d_3, and d_5 have been reported in a number of papers [55, 111–113]. The calculated frequencies from the normal coordinate analysis of Durig [113] were used to calculate the H/D fractionation factors.

Ammonia, Phosphine, Arsine and Stibine

A normal coordinate analysis for these XH_3 molecules has been discussed by Duncan and Mills [114]. Ammonia and phosphine were reproduced from this paper and the H/D FF's were determined with the reported frequencies.

Water and Hydrogen Sulfide

The frequencies used to fit force constants were obtained from Herzberg [115]. The frequencies were fit with both FFIT and SMPLX.

Ethylene

Although a fractionation factor had been calculated for ethylene [11], a second calculation was done using the general harmonic force field (GHFF) of Duncan [116]. Using crystal structure analysis, ^{13}C shifts, and other information, he determined with precision all eighteen parameters of the general force field for ethylene. This information was used to determine a force field from anharmonic data. Several isotopic species were used in the calculation. The FF (1.257) was not significantly different from that from Hartshorn's [11] analysis of three isotopic species. The fit was 3.0 cm^{-1} or 0.27% avg.

Dimethyl Sulfide

The calculation of Geiseler and Hanschmann [117] reproduced. Frequency assignments were checked with those of other authors [118, 119]. Dimethyl sulfoxide and dimethylsulfone were also discussed in the paper but were not calculated. The force field was not refit.

Acknowledgements

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Appendix

Table 9. H/D fractionation factors relative to acetylene at 25 °C[a].

SbH_2D	0.425	CI_3D	1.356*
AsH_2D	0.544	tr-$CH_2D-N=N-CH_3$	1.357*[b]
CH_3AsHD	0.549	$BrCH_2D$	1.358
CH_3SD	0.622	p-DC_6H_4-CHO	1.360*[b]
PH_2D	0.649	CH_3CH_2D	1.361
HDS	0.655	$H_2C=CHCH_2D$	1.362
CH_3PHD	0.683	C_6H_5D	1.368*[b]
$LiCH_2D$	0.982	$NCCH_2D$	1.373
FCCD	0.987	$HCO-O-COD$	1.380*
ClCCD	0.994	p-$DC_6H_4-NO_2$	1.385*[b]
BrCCD	0.995	p-DC_6H_4-CN	1.392*[b]
HCCD	1.000	Cl_3CCH_2D	1.397
DCHO	1.106*	t-$CH_2D-N=N-H$	1.397*[b]
CH_3ZnCH_2D	1.125*	cyclopropane-d	1.400
CH_3CDCH_2D	1.135*	cyclobutane-d	1.400
CH_3CDO	1.141*[c]	CH_3CHDI	1.401*
cis-$DCH=CHBr$	1.183	N_3CH_2D	1.401*
CH_3HgCH_2D	1.185*	H_2NCH_2D	1.401
CH_3SnCH_2D	1.196*	$ClCH_2D$	1.405
cis-$DCH=CHCH_3$	1.201	CH_2DCH_2CN	1.419*[b]
cis-$DCH=CHCl$	1.211	CF_3CH_2D	1.427
tr-$DCH=CHCH_3$	1.226	CH_3OCH_2D	1.432*[b]
$BrCH_2D$	1.233	$^+H_3NCH_2D$	1.439*
cyclopentene-1-d	1.239*[b]	$(CN)_2CHD$	1.441*
H_3SiCH_2D	1.243	Br_2CHD	1.443*
CH_3D	1.246	$HOCH_2D$	1.446*
tr-$DHC=CHBr$	1.250	CH_3CHDBr	1.446*
$DCOO^-$	1.254	CH_3CHDCN	1.457*[b]
$H_2C=CHD$	1.257*	FCH_2D	1.465
H_2AsCH_2D	1.258*	O_2NCH_2D	1.471
$F_2C=CHD$	1.259	NH_2D	1.479*
C_6H_5CDO	1.271*[b]	$H-CO-NHD$	1.487*
H_3GeCH_2D	1.275	CH_3CHDCH_3	1.501*
tr-$DCH=CHCl$	1.282	$HO-CH_2-CHD-OH$	1.502*
$H_2C=CDBr$	1.292	$CH_2DO-CHO$	1.511*
$HSeCH_2D$	1.295*	$CDBr_3$	1.516
$D-CO-NH_2$	1.295*	CH_3CHDCl	1.518*
ICH_2D	1.316	ethene ozonide	1.522*
CH_2DCHO	1.321*	Cl_2CHD	1.529*
$CH_3CH_2CH_2D$	1.324	HOD	1.539*
$HSCH_2D$	1.329	CH_3-NHD	1.555*
$CH_2D-CO-COOH$	1.329*[b]	CH_3CHDF	1.587*
DCFO	1.330*	$H-CO-OD$	1.608*
HOCDO	1.332*	CH_3-OD	1.647*
$H_2C=CDCH_3$	1.336	CCl_3D	1.656
CH_3OCDO	1.338*	$H_3C-NH_2D^+$	1.685*
$ClCH_2CH_2D$	1.341	F_2CHD	1.722*
$H_2C=CHDCl$	1.348	$CH_3-CO-COOD$	1.926*[b]
CH_3SCH_2D	1.350*	CF_3D	1.993

[a] These are calculated values at 25 °C for the isotope equilibrium, HCCD + RH = HCCH + RD, where the RD are the structures entered in the table. Values indicated by an asterisk are new; others are from [11] and [35].

[b] Not fit, from calculated frequencies from literature.

[c] Probably should be between 1.23–1.27, see text.

Table 10. Fractionation factors for nitrogen containing compounds[a].

$D-CO-NH_2$	1.295	$(CN)_2CHD$	1.441
t-$CH_2D-N=N-CH_3$	1.357	$CH_3CHD-CN$	1.457
$NC-CH_2D$	1.373	O_2N-CH_2D	1.471
t-$CH_2D-N=N-H$	1.397	NH_2D	1.479
N_3-CH_3D	1.401	$H-CO-NHD$	1.487
H_2N-CH_2D	1.401	CH_3NHD	1.555
$H_3N^+-CH_2D$	1.439	$CH_3-NH_2D^+$	1.685

[a] See footnote in Table 9.

DCHO	1.106	$H-CO-O-CO-D$	1.380
CH_3CDO	1.141 [b]	CH_3OCH_2D	1.432
DCO_2^-	1.254	$HOCH_2D$	1.446
C_6H_5-CDO	1.271	$HO-CH_2CHD-OH$	1.502
$D-CO-NH_2$	1.295	$CH_2D-O-CO-H$	1.511
CH_2D-CHO	1.321	HOD	1.539
$CH_2D-CO-COOH$	1.329	$HCO-OD$	1.608
$D-CO-F$	1.330	CH_3OD	1.647
HOCDO	1.332	$CH_2-CO-COOD$	1.926
$CH_3O-CO-D$	1.338		

Table 11. Fractionation factors for oxygen containing compounds [a].

[a] See footnote [a] in Table 9.
[b] Probably should be in the range 1.22–1.27, see text.

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