

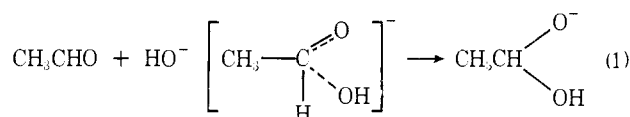
Kinetic Isotope-Effect Probes of Transition-State Structure. Vibrational Analysis of Model Transition States for Carbonyl Addition¹

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Abstract: Model calculations of the ¹H/²H, ¹²C/¹³C, and ¹⁶O/¹⁸O kinetic and equilibrium isotope effects at the starred positions for the carbonyl addition reaction of H₃CC*H*O* with HO*⁻ have been made for two closely related sets of force fields, and for both curved and perpendicular trajectories of nucleophilic approach to carbonyl, for a series of possible transition-state structures at temperatures from 273 to 323 K. In all calculations, the geometrical features and force constants were assumed to change from reactant values toward product values in proportion to the Pauling bond order *B* of the nucleophile-carbonyl bond. The α-deuterium and β-deuterium effects are nearly linear functions of *B* and should be good and consistent probes of transition-state structure. The carbonyl-¹⁸O effect is normal and increases steadily with *B*, as expected. The nucleophile-¹⁸O effect is normal for *B* ≥ 0.5 and inverse for later transition states. The carbonyl-¹³C is about 1.03 for early transition states and falls to an inverse equilibrium effect. No strikingly anomalous temperature dependences were calculated.

Carbonyl-addition reactions, exemplified by the process of eq 1, are of interest in chemistry and biochemistry^{3,4} and the understanding of their dynamics in terms of transition-state structure is the topic of much current research.⁵ A very appealing and effective approach to learning the structure of such transition states lies in the use of kinetic isotope effects.⁵⁻⁷ We have employed vibrational analysis of model structures^{8,9} for the transition state of eq 1 to explore relationships of such



structures to the following isotopic probes: (1) the α-deuterium secondary isotope effect¹⁰ (for the hydrogen attached to the electrophilic carbon); this effect is expected to be inverse ($k_D > k_H$), arising from restrictions to motion of the α hydrogen as the nucleophile binds, and to become more inverse as the transition state more nearly resembles the adduct; (2) the β-deuterium secondary isotope effect¹⁰ (for the hydrogens on the carbon adjacent to the electrophilic center); this effect, assumed to arise from increased binding of the β hydrogens as hyperconjugation of C-H bonding electrons into the carbonyl group is lost upon carbonyl addition,¹¹ should also be inverse and become more so for more adduct-like transition states; (3) the carbonyl-oxygen ¹⁶O/¹⁸O isotope effect; if this effect is regarded as secondary (in a specialized sense, viz., that the oxygen does not participate in reaction-coordinate motion), then it should be normal ($k_{16} > k_{18}$) and larger as the carbonyl group double bond is more nearly converted to the single bond of the adduct,¹² while reaction-coordinate participation should render the effect still larger in the normal sense;¹³ (4) the nucleophile-oxygen ¹⁶O/¹⁸O isotope effect; this effect may be normal for reactant-like ("early") transition states where reaction-coordinate motion of the oxygen dominates the increased binding from formation of the new bond,¹³ but should become inverse for transition-state structures like the adduct; (5) the carbonyl-carbon ¹²C/¹³C isotope effect; the direction and magnitude of this effect are hard to estimate intuitively.

The aim of the calculations is to relate the magnitudes of these isotope effects to the structure of the transition state, but we can do this only approximately at the present time. Even the simplified paradigm of eq 1 has a transition state with nine atoms. Therefore, 21 geometrical coordinates must be specified for a complete structural description, and the force-constant

matrix, even at the harmonic-approximation level, contains 231 distinct elements. Furthermore, kinetic isotope effects of mechanistic significance can arise from force-constant changes between reactants and transition state which are smaller than can be accurately determined by vibrational spectroscopy of analogous stable species. Continuing research by ourselves and others is expected to lead to improved approaches to isotope-effect estimation, but at this time we have made use of the following simplifying protocols.

(1) Diagonal force fields were employed for all species, except that one off-diagonal force constant was added to transition-state force fields to generate the reaction coordinate.

(2) The bond order of the forming carbon-nucleophile bond was chosen as a principal reaction variable and the progress of all other features of transition states was assumed to be equivalent to the progress in formation of this bond.

To increase the generality of the results, calculations were made for different sets of assumptions about transition-state geometries and about the force-constant alterations which generate the isotope effects.

Experimental Section

Method of Calculation. Calculations were carried out with two different computer programs. VIBRANAL was provided us by Dr. Warren Buddenbaum, Department of Chemistry, Indiana University, in a form largely equivalent to the program available from the Quantum Chemistry Program Exchange. Based on the procedures of Schachtneider and Snyder¹⁴ for the vibrational-analysis problem (FG matrix formulation¹⁵) and the Wolfsberg and Stern program⁸ for the calculation of isotope effects, the program was written for a Univac 1108 computer and was modified only slightly to run on the Honeywell 635 and 66/60 computers at the University of Kansas Computation Center. BEBOVIB-IV, now also available from the Quantum Chemistry Program Exchange, was made available by Professor L. B. Sims, Department of Chemistry, University of Arkansas. Professor Sims trained us in the use of this program, which has been employed in several published calculational studies.¹⁶ It solves the vibrational problem directly in Cartesian coordinates¹⁷ and has an easy-to-use polar-coordinate input format for model geometries. Extensive duplication of calculations between the two programs gave exact agreement.

Principal Reaction Variable. The bond distance between the nucleophilic atom and the electrophilic, carbonyl carbon is the structural feature which changes most strikingly in the course of carbonyl addition. We chose the Pauling bond order¹⁸ *B*, related¹⁶ to the bond distance *R_B* (*R₁* for unit *B*) by the equation

$$B = \exp\{(R_1 - R_B)/0.3\} \quad (2)$$

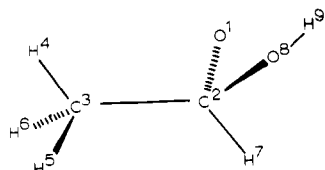


Figure 1. Numbering system used for the designation of internal coordinates for the acetaldehyde-hydroxide system. The structure shown is for the product state. In the reactant state, the C²-O⁸ bond is very long and C³, C², O¹, H⁴, and H⁷ occupy a common plane.

as a principal reaction variable or fundamental descriptor of transition-state structure. Other structural features of transition states were then assumed to have progressed a fraction *B* of the total change experienced in the overall reaction. The models employed in this study are, therefore, *highly coupled*¹⁹ in the sense that all structural features are taken as strongly coupled to the Pauling bond order of the nucleophilic bond.

Reactant and Product Models. The properties chosen for the reactant state, product state, and transition states can be described using the numbering system of Figure 1. The same bond lengths, angles, and force constants were used for all isotopic modifications of each structure and are given in Tables I and II.

For the reactant state, the bond distances and angles of acetaldehyde were taken from the microwave data of Kilb, Lin, and Wilson.²⁰ The free hydroxide ion was assigned the force constant and bond length found in the ab initio quantum-mechanical study of Janoschek, Preuss, and Dierksen.²¹ In the product structure, the geometry around both carbon atoms was assumed to be fully tetrahedral. The C-H bond lengths of the methyl group were kept at 1.086 Å, while the bond lengths and angles about the C² carbon were those used by Timidei and Zerbi²² in their normal coordinate treatment of methanol. The C²-C³ bond length was adjusted to 1.54 Å.

The force constants used for the acetaldehyde part of the reactant state were those determined by Cossee and Schachtschneider²³ (their set VF. 1), with interaction force constants set equal to zero. The diagonal force constants were used directly with the exception of the C²-C³-H⁴ bending force constant, which was made equal to the other two C-C-H bending constants.

Since spectroscopic data are unavailable for the hydroxide adduct of acetaldehyde, force constants were estimated from those for acetaldehyde,²³ methanol,^{22,24,26} propanol,²⁵ and 2,2-difluoropropane.²⁷ Bending force constants for the HC³H and HC³C² angles were made the same as in acetaldehyde, except when their variation was considered as generating the β -deuterium isotope effect (see below). Force constants for the C²O⁸ and O⁸H⁹ stretches were taken from the methanol force field, as were those for the O¹C²H⁷ and H⁷C²O⁸ angle bends, with the former slightly decreased in recognition of the negative charge on O¹. Force constants for 2,2-difluoropropane were used to generate values for O¹C²C³, O⁸C²C³, and O¹C²O⁸, assuming equivalency of fluorine and oxygen. The C²C³ stretching constant was taken from paraffin data, while the C²H⁷ and C³C²H⁷ values are averages of acetaldehyde constants and paraffin methine-group constants. The O¹C² stretching constant was taken as the average of the acetaldehyde and methanol values, to agree with the considerable double-bond character observed theoretically.^{28,29} The 2,2-difluoropropane CH stretching force constant of 4.91 mdyn/Å was used as a guide for the C³H values, which were set either slightly above or below this value, depending on the assumed origin of the β -deuterium isotope effect (see below). Torsional force constants about the C²C³ bond were set to common values²²⁻²⁷ while those about the forming C²O⁸ were set to an arbitrary value near zero. All redundancies were included. All off-diagonal force constants were set equal to zero.

Variation of Reaction Trajectory. Two different geometrical dispositions for reactant-like transition states were assumed (Table I). Then, in each case, a series of intermediate structures was generated by alteration of each geometrical feature from its reactant value toward its product value by a fraction *B* corresponding to the Pauling bond order *B* of the O⁸C² bond. The two series of transition states thus have quite different structures for small *B* ("early" transition states).

One of these models, designated in Table I as the "curved trajectory" model, was constructed to simulate the nonlinear approach of nucleophile suggested by the crystallographic studies of Bürgi, Dunitz,

Table I. Geometrical Parameters for Reactant and Product Models

parameter ^a	reactant, curved trajectory	reactant, perpendicular trajectory	product
O ¹ -C ²	1.22	1.22	1.43
C ² -C ³	1.50	1.50	1.54
C ³ -H ⁴	1.09	1.09	1.09
C ³ -H ⁵	1.09	1.09	1.09
C ³ -H ⁶	1.09	1.09	1.09
C ² -H ⁷	1.11	1.11	1.10
C ² -O ⁸	2.50	2.50	1.43
O ⁸ -H ⁹	0.96	0.96	0.96
O ¹ -C ² -C ³	123.9	123.9	109.5
C ² -C ³ -H ⁴	110.6	110.6	109.5
C ² -C ³ -H ⁵	110.6	110.6	109.5
C ² -C ³ -H ⁶	110.6	110.6	109.5
C ³ -C ² -H ⁷	117.5	117.5	109.5
C ³ -C ² -O ⁸	71.3	90.0	109.5
C ² -O ⁸ -H ⁹	108.9	108.9	108.9
O ¹ -C ² -C ³ -H ⁴	360	0	300
O ¹ -C ² -C ³ -H ⁵	240	120	180
O ¹ -C ² -C ³ -H ⁶	120	120	60
H ⁴ -C ³ -C ² -H ⁷	180	180	180
H ⁴ -C ³ -C ² -O ⁸	120	90	60
C ³ -C ² -O ⁸ -H ⁹	241	25	0

^a Parameters designated by two atoms are bond lengths (Å), by three atoms are bond angles (deg), and by four atoms are dihedral angles (deg).

Table II. Force Constants for Reactant and Product Models^a

internal coordinate	reactant	product, β -stretch varied	product, β -bend varied
O ¹ -C ²	10.77	7.88	7.88
C ² -C ³	4.82	4.30	4.30
C ² -H ⁷	4.24	4.40	4.40
C ² -O ⁸		5.35	5.35
C ³ -H	4.88	5.13	4.88
O ⁸ -H ⁹	7.47	7.62	7.62
O ¹ -C ² -C ³	1.01	1.00	1.00
O ¹ -C ² -H ⁷	0.83	0.80	0.80
O ¹ -C ² -O ⁸		2.00	2.00
C ² -C ³ -H	0.43	0.43	0.47
C ² -O ⁸ -H ⁹		0.77	0.77
C ³ -C ² -H ⁷	0.44	0.50	0.50
C ³ -C ² -O ⁸		1.00	1.00
H-C ³ -H	0.52	0.52	0.60
H ⁷ -C ² -O ⁸	(0.30)	0.85	0.85
O-C ² -C ³ -H	0.027	0.015	0.024
O-C ² -O ⁸ -H ⁹		0.000 09	0.000 09

^a Stretching force constants are in mdyn/Å, bending and torsional force constants in mdyn·Å/rad².

and their collaborators.^{18c} The hydroxide ion thus begins its approach at a point above and behind the carbonyl group, and then develops a more nearly perpendicular line of attack as bond formation becomes more important. The geometrical parameters for a transition state of nucleophilic bond order *B* can be calculated from the initial and final parameters of Table I and the prescription in the last paragraph.

While much is to be said for the physical likelihood of such a trajectory, we felt it necessary to test for the degree to which our results were dependent upon it. A second series of models for a "perpendicular trajectory" was thus constructed. Here, the more familiar view, that even very "loose" transition states involve the alignment of the nucleophilic electron pair along the axis of the bond eventually to be formed, is expressed by the geometrical parameters (Table I).

Force-Field Variations. As explained above, most features of the force fields for reactants and products were generated by analogy with known molecules already studied in detail. Transition-state force fields

Table III. Calculated Isotope Effects ($k_{\text{light}}/k_{\text{heavy}}$) for Carbonyl Addition with the Indicated Structures vs. ($^1\text{H}^{16}\text{O}^-$, $^1\text{H}_3^{12}\text{C}^{12}\text{C}^1\text{H}^{16}\text{O}$) as Functions of Temperature and Transition-State Structure^a

<i>B</i> , Pauling bond order of C ² O ⁸	temp. K	site and character of isotopic substitution				
		² H ₃ CCHO ("β-D ₃ ")	H ₃ CC ² H ("α-D")	H ₃ CCH ¹⁸ O ("carbonyl- ¹⁸ O")	H ₃ C ¹³ CHO ("carbonyl- ¹³ C")	H ¹⁸ O ⁻ ("nucleophile- ¹⁸ O")
0.1	273	0.993	0.980	1.004	1.031	1.031
	298	0.994	0.984	1.004	1.028	1.032
	323	0.995	0.987	1.004	1.026	1.032
0.2	273	0.978	0.943	1.004	1.031	1.021
	298	0.981	0.951	1.004	1.029	1.023
	323	0.983	0.958	1.005	1.027	1.024
0.3	273	0.964	0.906	1.006	1.030	1.011
	298	0.967	0.918	1.006	1.028	1.014
	323	0.970	0.929	1.006	1.026	1.016
0.4	273	0.949	0.870	1.009	1.027	1.002
	298	0.954	0.887	1.009	1.025	1.005
	323	0.958	0.900	1.009	1.024	1.009
0.5	273	0.937	0.836	1.012	1.022	0.993
	298	0.943	0.855	1.012	1.021	0.998
	323	0.948	0.872	1.012	1.020	1.002
0.6	273	0.921	0.805	1.015	1.020	0.983
	298	0.928	0.827	1.015	1.019	0.989
	323	0.934	0.846	1.015	1.018	0.993
0.7	273	0.907	0.776	1.019	1.016	0.974
	298	0.915	0.801	1.018	1.015	0.981
	323	0.922	0.822	1.018	1.015	0.986
0.8	273	0.895	0.749	1.023	1.010	0.966
	298	0.904	0.776	1.022	1.010	0.973
	323	0.912	0.799	1.021	1.010	0.979
0.9	273	0.882	0.725	1.027	1.006	0.958
	298	0.892	0.753	1.026	1.006	0.966
	323	0.901	0.778	1.025	1.007	0.972
1.0 (kinetic)	273	0.870	0.703	1.032	1.001	0.951
	298	0.881	0.733	1.030	1.002	0.959
	323	0.891	0.758	1.029	1.003	0.966
1.0 (equilibrium)	273	0.859	0.690	1.010	0.958	0.920
	298	0.870	0.720	1.009	0.962	0.930
	323	0.880	0.746	1.009	0.967	0.938

^a Values tabulated are those computed on the "curved trajectory with β-stretch varied" model.

were obtained by interpolation, assuming that each force constant had changed by a fraction *B* (Pauling bond order of the forming nucleophile-carbonyl bond in the particular transition state) from its reactant value toward its product value. As will be seen below, this procedure (perhaps in large part by coincidence) produces values of the α-deuterium, carbon, and oxygen isotope effects of interest which are intuitively reasonable and generally in accord with experience. The β-deuterium isotope effects, however, arise from sites more remote from the reaction center, are small, and may well involve smaller force-constant changes. While it seems very probable that they arise from alterations of the force constants for either bending or stretching of the β-CH bonds, or both, their exact origins are unclear. We thus considered two models for this generation and adjusted the values of the appropriate force constants in the product molecule so that the experimental equilibrium isotope effects for carbonyl hydration were roughly reproduced by the calculated equilibrium β-deuterium isotope effects.¹⁰

One of these models relied wholly on variation of the stretching force constants (denoted as "β-stretch varied" in Table II). In this case, the adduct β-CH stretching force constant was taken as 5.13 mdyn/Å (cf. 4.91 mdyn/Å in 2,2-difluoropropane²⁷), and the β-CH bending force constants were left at their initial values.

The second ("β-bend varied") model left the β-CH stretching force constant at its initial value of 4.88 mdyn/Å, while introducing changes in the bending constants for C²C³H, from 0.43 to 0.47 mdynÅ/mdyn², and for HC³H from 0.52 to 0.60 mdynÅ/rad². This model thus simulates a situation in which loss of hyperconjugation of the β-CH electron pairs into the carbonyl group leads mainly to a greater difficulty in bending motions of these bonds, while the model of the previous paragraph posits the effect as being on the difficulty of stretching motions.

Reaction-Coordinate Generation. The transition-state force field must be such that the molecule has one and only one unstable coordinate, corresponding to the reaction coordinate, which carries the

molecule out of the transition state toward reactants or products. In these calculations, this was accomplished by introducing a single, positive off-diagonal element in the **F** matrix, which coupled the carbonyl (O¹C²) stretching motion to the stretching of the nucleophile-carbonyl forming bond (C²O⁸). This makes the reaction coordinate the asymmetric stretching of the O¹C²O⁸ system.³⁰ A value of the off-diagonal element $F_{ij} > (F_{ii}F_{jj})^{1/2}$, with the O¹C² stretch as coordinate *i* and the C²O⁸ stretch as coordinate *j*, then produces an imaginary frequency for the reaction-coordinate motion.^{30,31} The frequencies so generated were usually between about 50*i* and 300*i* cm⁻¹ and are indicated at appropriate points below.

More complex designs for reaction-coordinate motions³⁰ are an important feature for investigation. These are currently under study.

Results

Table III lists the isotope effects at 273, 298, and 323 K for ten different choices of the nucleophile-carbonyl bond order *B*, and equilibrium isotope effects. The calculations listed are for the "curved trajectory" model with "β-stretch varied".

Calculations with the "β-bend varied" showed that no significant difference ever arose for any choice of transition-state structure from this assumption vs. the "β-stretch varied" assumption. Carbon and oxygen isotope effects were absolutely independent of this choice while the hydrogen isotope effects never differed by more than 1–2 parts per thousand. The calculated effects in Table III may, therefore, be assumed, within limits of 1–2 parts per thousand, to apply equally well to models in which β-stretching and β-bending force constants are varied.

Also within limits of 1–2 parts per thousand, the β-D₃ and nucleophile-¹⁸O effects were independent of whether the

Table IV. Contributions to Calculated Kinetic Isotope Effects at 298 K

type of isotope effect ^a	<i>B</i> , Pauling bond order of C ² O ⁸	ν/ν'	MMI	EXC ⁻¹	ZPE	$(k_{\text{light}}/k_{\text{heavy}})^{b,c}$
β -D ₃	0.2	1.008	1.201	1.160	0.947	0.981
	0.5	1.011	1.190	1.143	0.906	0.943
	0.8	1.011	1.186	1.141	0.870	0.904
α -D	0.2	1.011	1.118	1.019	0.866	0.951
	0.5	1.012	1.114	0.992	0.761	0.855
	0.8	1.013	1.113	0.979	0.682	0.776
carbonyl- ¹⁸ O	0.2	1.004	1.021	1.008	0.991	1.004
	0.5	1.007	1.021	1.004	0.995	1.012
	0.8	1.012	1.020	1.003	1.004	1.022
carbonyl- ¹³ C	0.2	1.007	1.017	1.009	1.021	1.029
	0.5	1.007	1.018	1.005	1.008	1.021
	0.8	1.007	1.018	1.003	0.995	1.010
nucleophile- ¹⁸ O	0.2	1.036	1.076	1.020	0.970	1.023
	0.5	1.031	1.078	1.016	0.940	0.998
	0.8	1.026	1.079	1.011	0.912	0.973

^a See Table III for the sites and character of isotopic substitution. ^b Calculations are for the "curved trajectory with β -stretch varied" model. ^c $(k_{\text{light}}/k_{\text{heavy}}) = \text{MMI} \cdot \text{EXC} \cdot \text{ZPE}$.

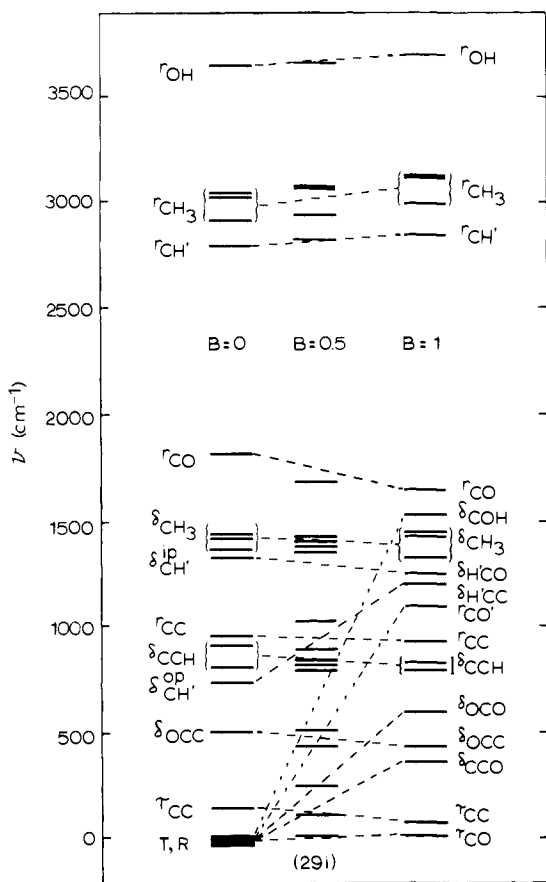


Figure 2. Calculated frequencies at $B = 0$ (reactant state), $B = 0.5$ (a transition state), and $B = 1$ (product state) for the curved-trajectory model (β -stretch varied). Rough assignments deduced from calculated eigenvectors are shown.

"curved trajectory" or "perpendicular trajectory" model was used. The carbonyl-¹⁸O effect was more sensitive, with the perpendicular trajectory generating larger isotope effects by 1–6 parts per thousand than the curved trajectory. The enhancement was most pronounced (as expected) with early transition states (1.009 at 298 K, $B = 0.1$ vs. 1.004; 1.017 vs. 1.012 at $B = 0.5$; 1.027 vs. 1.026 at $B = 0.9$). The α -D effect was, in contrast, more normal with the curved than with the

perpendicular trajectory, a 19 parts per thousand difference at early transition states disappearing at late points (0.984 at 298 K, $B = 0.1$ vs. 0.965; 0.855 vs. 0.845 at $B = 0.5$; 0.753 vs. 0.752 at $B = 0.9$). The carbonyl-¹³C effect was similarly more normal with the curved trajectory and the model dependence was larger relative to the magnitudes of the isotope effects than for the other cases (1.028 at 298 K, $B = 0.1$, vs. 1.015; 1.021 vs. 1.008 at $B = 0.5$; 1.006 vs. 1.004 at $B = 0.9$). Thus neither qualitative nor semiquantitative conclusions from β -D₃, α -D, carbonyl-¹⁸O, or nucleophile-¹⁸O isotope effects are dependent on the curved vs. perpendicular trajectory model. Correspondingly, experiments in which these effects are measured cannot be expected to be useful as probes of features of the transition-state structure related to the curved vs. perpendicular distinction. The carbonyl-¹³C effect is more sensitive to this choice and its determination can thus be expected to convey information about the geometry of nucleophilic attack.

Table IV contains a resolution^{8,9} of the isotope effects into mass/moment of inertia (MMI), excited vibrational states (EXC), and zero-point energy (ZPE) terms for representative transition-state structures at 298 K. Also shown is the ratio of imaginary (reaction-coordinate) frequencies, ν/ν' . The values of EXC are tabulated as EXC⁻¹ to permit quick comparison with MMI. When MMI and EXC⁻¹ are equal, the product MMI·EXC is unity and the isotope effect arises wholly from zero-point energy isotopic differences between reactant state and transition state.

The general behavior of the curved-trajectory, β -stretch-varied model can be inferred from Figure 2. This presents the frequencies calculated for the ¹H₃¹²C¹²C¹H¹⁶O + ¹H¹⁶O⁻ modification at the reactant state ($B = 0$), one transition state ($B = 0.5$), and the product state ($B = 1$). Rough identifications of molecular motions for the frequencies were extracted from the eigenvectors and are shown in the figure. The dashed lines show putative correlations of reactant motions with those in the products. Several features are worthy of note. Five of the zero-frequency translational-rotational (T,R) modes of the reactant state are converted to five internal coordinates of the transition and product states: the C²O⁸H⁹ bend (δ_{COH}), the C²O⁸ stretch (r_{CO}), the O¹C²O⁸ bend (δ_{OCO}), the C³C²O⁸ bend (δ_{CCO}), and the torsion about the C²O⁸ bond (τ_{CO}). In accordance with the model, the CH₃ stretching frequencies (r_{CH_3}) rise, giving the β -D₃ inverse isotope effect. The O¹C² stretch (r_{CO}) falls, as expected for replacement of a double by a single bond. The C²H⁷ out-of-plane frequency ($\delta_{\text{CH}^{\text{OP}}}$) rises

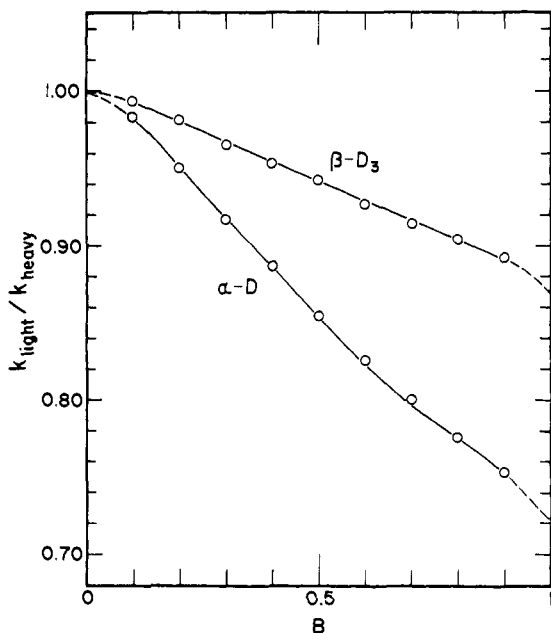


Figure 3. Calculated β -D₃ and α -D secondary isotope effects as a function of B (Table III).

sharply as the motion is converted to the C²C³H⁷ bend (δ_{HCC}), traditionally taken¹⁰ as the origin of the α -D inverse isotope effect. A probably unrealistic feature is the small rise in the O⁸H⁹ stretching frequency (ν_{OH}), but this will have little influence on the calculated isotope effects.

Discussion

Secondary Deuterium Effects. Figure 3 portrays the β -D₃ and α -D isotope effects at 298 K as a function of nucleophile-carbonyl bond order B . The solid lines are drawn smoothly through the calculated points from $B = 0.1$ to $B = 0.9$. The dashed extensions connect to 1.00 at $B = 0.0$ (on the assumption that a truly reactant-like transition state would generate no isotope effect) and to the equilibrium isotope effect at $B = 1.0$.

The calculated equilibrium value for the α -D effect is about 0.72, in excellent agreement with relevant experimental measurements,^{10,32-39} such as Lewis and Wolfenden's value of 0.73 ± 0.02 for the hydration of acetaldehyde.³² Measurements of kinetic effects fall between 1.00 and this value, in consistency with Figure 3. Furthermore, the assumption that the value of B in the transition state can be approximately inferred³⁵ from eq 3 (where k_H/k_D is the kinetic isotope effect and K_H/K_D is the equilibrium isotope effect) is supported by the calculations, since a nearly straight line through the computed kinetic isotope effects connects 1.0 with $K_H/K_D = 0.72$. It was, however, assumed in the model that the force-constant changes for the α -H coordinates were linear in B and this may be the chief reason for the simple relationship found. While such a linear change in force constants is a reasonable expectation (at least for stretching force constants, although bending force constants might present a different picture), whether it is correct must be determined by quantum-mechanical studies now in progress in our group and elsewhere. In the meantime, one can conclude that, if such a linearity is correct, then deductions from eq 3 should be valid.

$$B \approx [(k_H/k_D) - 1]/[(K_H/K_D) - 1] \quad (3)$$

The calculated equilibrium β -D₃ isotope effect of 0.87 agrees with experiment¹⁰ because the β -H force constants were adjusted to cause this and so the agreement is not any test of the model. Here, there is again a roughly linear relation of B and

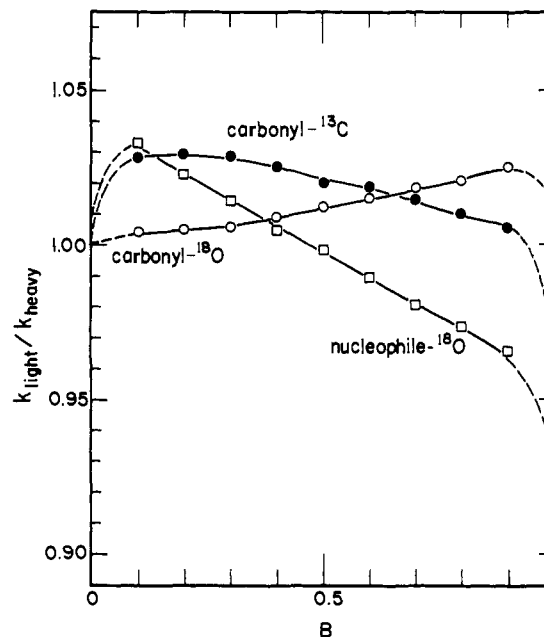


Figure 4. Calculated heavy-atom isotope effects as a function of B (Table III).

k_H/k_D , also probably related to the assumption of the model that force constants at β -H change linearly in B . The computed kinetic isotope effects lie generally closer to unity than the line connecting 1.00 and $K_H/K_D = 0.87$. Thus B calculated from eq 3 will indicate a smaller value of B than the calculations suggest. Thus, even if the assumed linearity of B and force-constant changes should emerge as correct, a simple empirical inference of B from eq 3 (with an experimental value for K_H/K_D) would underestimate B by about 0.05 unit.

Table IV shows the imaginary frequency isotopic ratio, ν/ν' , is never more than 1.5% from unity for both the α and β secondary isotope effects. This indicates minimal participation by these atoms in reaction-coordinate motion, confirming the "secondary" nature of the isotope effects. In both cases the MMI terms exceed EXC⁻¹, by factors of about 1.02-1.04 for the β -D₃ and about 1.09-1.14 for the α -D effects. The observed effects are thus closer to unity by these factors than the ZPE contributions and ought only to this level of approximation to be thought of as ZPE effects.

Heavy-Atom Isotope Effects. Figure 4 shows how the carbonyl-¹³C, carbonyl-¹⁸O, and nucleophile-¹⁸O isotope effects depend on B . The two ¹⁸O effects, as discussed in the Results section, are roughly independent of the geometrical model chosen (curved vs. perpendicular trajectory); the ¹³C effect varies more with this choice, but the qualitative features seen in Figure 4 are likely to be preserved with any reasonable model.

The carbonyl-¹⁸O effect is expected in simple terms to be normal ($k_{16}/k_{18} > 1$) because the carbonyl double bond of the reactant goes over to the C²-O¹ single bond (or nearly single bond) of the adduct. A further contribution to the normal magnitude is expected from the participation of the carbonyl stretching in the reaction-coordinate motion. Thus the behavior seen in Figure 4 is fully expected. The equilibrium effect calculated for our model is 1.009 at 298 K, but this is very much a function of the stretching force constant assumed for the adduct C²-O¹ bond. Our estimate, since we are assuming considerable remaining double-bond character in the adduct, may be a maximum for the force constant and thus our estimated equilibrium isotope effect is a minimum. As the structure of the transition state becomes more adduct-like (i.e., as B increases), k_{16}/k_{18} becomes larger but all calculated values

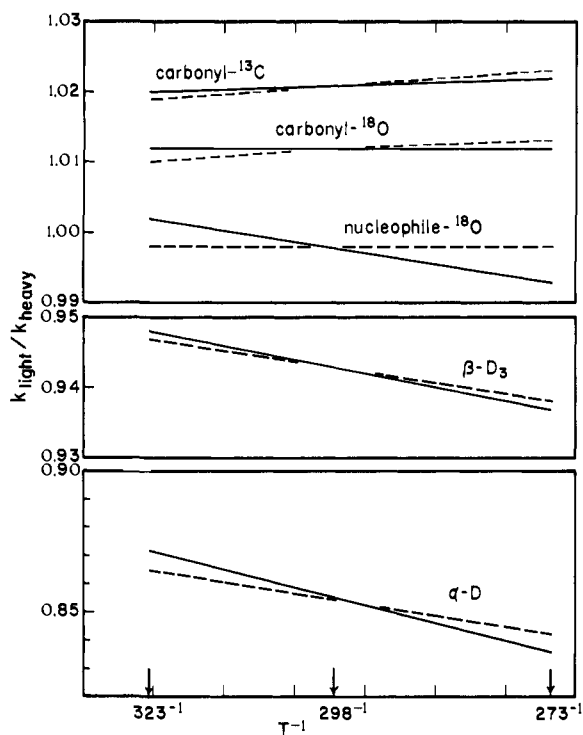


Figure 5. Isotope effects vs. $1/T$ for $B = 0.5$. The solid lines connect computed values from Table III. The dashed lines are from eq 4.

lie above a line connecting $k_{16}/k_{18} = 1.00$ to $k_{16}/k_{18} = K_{16}/K_{18}$. This is because of the reaction-coordinate contribution. As Table IV shows, ν/ν' increases from 1.004 at $B = 0.2$ to 1.012 at $B = 0.8$, as the O^8-C^2 bond becomes stronger and the reaction-coordinate motion becomes the asymmetric stretch of the $O^8-C^2-O^1$ system rather than merely motion of O^8 toward the carbonyl unit. Our earlier measurement¹² of carbonyl- ^{18}O isotope effects of about 1.02 for reaction of methoxide ion with aryl benzoates was interpreted as secondary effects ($\nu/\nu' = 1.0$) and taken to indicate an adduct-like transition state. The same conclusion would be drawn from the present model but only because we have here chosen an adduct force field that gives a smaller ZPE contribution, while coupling the carbonyl stretch into the reaction coordinate to generate a compensating value of ν/ν' .

The carbonyl- ^{13}C effect can be understood very roughly by noting that, in a certain sense, this is a carbon-transfer reaction, inasmuch as one is forming the C^2-O^8 bond while breaking the C^2-O^1 π bond in a manner assumed to be concerted. Such group-transfer reactions tend to give large normal isotope effects at the transferring center for "symmetrical" ($B \sim 0.5$) transition states and smaller effects near $B \sim 0$ and $B \sim 1$, as explained by Westheimer³¹ for the hydrogen-transfer case. In the carbonyl-addition reaction, there will be some transition-state structure for which the symmetric motion of the $O^1-C^2-O^8$ system becomes most nearly independent of the isotopic mass at C^2 . This motion will then not contribute isotopic zero-point energy difference, tending to maximize the ^{13}C -isotope effect. From Table IV, it can be seen that, for $B = 0.2$, the ZPE contribution is indeed normal. As the C^2-O^8 bond tightens, the ZPE contribution becomes inverse. With a constant value of $\nu/\nu' \sim 1.007$, the result is the broad maximum of Figure 4. Finally, an inverse equilibrium effect is calculated, arising essentially from development of the new bond at this center.

The nucleophile- ^{18}O effect has two major contributions. The ZPE effect is inverse, since a new bond is formed to the nucleophilic oxygen. The contribution is small for early transition states and becomes steadily more inverse with larger B .

In the opposite direction, as Fry has explained clearly,¹³ is the reaction-coordinate contribution ν/ν' . This will be largest for early transition states when O^8 moves against the heavy carbonyl group as a unit, and smaller as O^8 begins to participate in an asymmetric stretching motion of the $O^1C^2O^8$ system. Both features can be seen in Table IV. The resultant is then as seen in Figure 4, where a normal value of k_{16}/k_{18} for early transition states crosses over to inverse values at $B \sim 0.5$.

Temperature Dependences. In Figure 5, we compare the computed temperature dependences of the isotope effects from 273 to 323 K with the simplest empirical dependence that might be assumed, namely, that of an exponential with a unit preexponential factor. Basing the exponential argument on the isotope effect at 298 K, we have

$$(k_{\text{light}}/k_{\text{heavy}})_T = \exp\{(298 \ln[(k_{\text{light}}/k_{\text{heavy}})_{298}])/T\} \quad (4)$$

which is plotted as a dashed line for each effect in Figure 5. The calculations were made for a transition state with $B = 0.5$. For the α -D and β -D₃ effects, the computed temperature dependences are slightly stronger than those estimated from eq 2, but data of enormous quality would be required to make the distinction experimentally. The computed dependences for the carbonyl- ^{13}C and carbonyl- ^{18}O effects are weaker than those from eq 4, but again not to a significant degree. The nucleophile- ^{18}O effect is expected to be very nearly temperature independent from eq 4 because the effect is close to unity at 298 K. The computed dependence shows the interesting property of crossing unity, being inverse below about 310 K and normal above this temperature.

Conclusions

These calculations suggest that α -D and β -D₃ secondary isotope effects, if their origins are as simple as current ideas hold¹⁰ and if the models used are sufficiently realistic,^{18c} should be good measures of transition-state structure in carbonyl addition and elimination reactions and should give similar semiquantitative results. Nothing indicates unusual temperature dependences which—when observed^{11b,40}—may arise from mechanistic features such as shifts in pathway or rate-determining step.⁴¹

The carbonyl- ^{18}O isotope effect also appears to exhibit a dependence on structure that would allow it, for example, accurately to probe the relative degree of π -bond fission in a series of transition states. Interpretation of such results must, however, clearly recognize the importance of ν/ν' as well as ZPE in determining the numerical magnitudes. The nucleophile- ^{18}O effect seems to be a particularly promising probe, crossing over the line of unity at roughly central structures ($B \sim 0.5$) for the transition state. It should, however, be borne in mind that both ^{18}O sites of the transition state are undergoing solvation changes. Our failure to include this factor in the model may have produced errors in these effects, since Sims and his group have demonstrated the necessity of considering solvation in other, related cases.¹⁶ Finally, the carbonyl- ^{13}C effect seems worthy of further study from both theoretical and experimental directions. At the current time, its eventual utility is hard to assess.

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Theoretical Search for a New Nonclassical Carbonium Ion: The σ -Allyl Cation^{1,2}

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Abstract: In order to assess the desirability of synthesizing a polycyclic carbonium ion which might exhibit pure pp- σ bonding between the electron-deficient centers, molecular orbital calculations are done on a model system composed of three stacked methyl groups (CH₃)₃⁺ with collinear carbons. Applied are six MO methods spanning a spectrum of complexity, ranging from semiempirical extended Hückel, CNDO/2, and MINDO/3 to ab initio with STO-3G, double- ζ , and 6-31G* basis sets. Whereas CNDO/2, MINDO/3, and STO-3G predict the most stable structure to be symmetrical with a planar central CH₃ unit and pyramidal terminal CH₃ units, the two more lengthy methods predict an asymmetric CH₃CH₃...CH₃ geometry to be preferred. As shown by electron-density maps of the symmetric structure, the σ counterparts of the three familiar π allylic orbitals are present. All MO methods agree that the central carbon of both the symmetric and asymmetric geometries bears more electron density than the terminal carbons and that the peripheral atoms bear most of the cationic charge. MINDO/3 calculations show [C(CH₃)₃]₃⁺ to be unsuitable as a model. Also, MINDO/3 indicates that C₃H₉⁺ isomers with nonlinear backbones are more stable than the (CH₃)₃⁺ model.

A generally accepted definition of the term "nonclassical ion" has been presented by Brown and Schleyer.^{4,5} "A nonclassical carbonium ion is a positively charged species which cannot be represented adequately by a single Lewis structure. Such a cation contains one or more carbon or hydrogen bridges joining the two electron-deficient centers. The bridging atoms have coordination numbers higher than usual, typically five or more for carbon and two or more for hydrogen. Such ions

contain two-electron, three- (or multiple-) center bonds including a carbon or hydrogen bridge."

In order to analyze the nature of bonding in carbonium ions, it will be convenient to focus attention initially on the 2p atomic orbitals. The type of interaction arising from a particular arrangement of p orbitals has been the focal point of several recent studies.^{6,7} A pp- π overlap (A) is, of course, a symmetric combination of parallel p orbitals which are perpendicular to