

than 20 times greater. The solutions were equilibrated to 25.0 °C in the thermostatted cell block of the spectrophotometer and maintained at 25.0 ± 0.1 °C during reactions.

Rate constants were calculated from at least 30 absorbance readings spanning 3 half-lives. An infinity absorbance reading was taken after at least 10 half-lives. Rate constants were calculated as the slope of a plot of $\ln(A_\infty - A_t)$ vs time. It is estimated that the error in any particular measured rate constant is not greater than ca. ±3%.

Deuterium Uptake Experiments. The extent of deuterium uptake and the extent of reaction were measured as described previously.¹⁸ The following is a representative procedure used to evaluate the extent of deuterium exchange at the methyl position and simultaneously the extent of reaction of a methanesulfonate ester.

p-Nitrophenyl methanesulfonate (1) (0.0560 g, 0.260 mmol) was weighed into a flask equipped with a nitrogen inlet and magnetic stirrer and dissolved in magnesium-dried deuterated ethanol (EtOD, 15.0 mL) under a stream of nitrogen. A stock solution of base was prepared by mixing potassium ethoxide (2.00 mL of 1.68 M KOEt in EtOD) and crown ether (6.00 mL of 0.980 M 18-crown-6 in EtOD) solutions in a sealed vial. A portion (6.00 mL, 2.52 mmol KOEt, 4.41 mmol 18-crown-6) of the resulting solution was added to the rapidly stirred ester solution. After stirring briefly under nitrogen, the reaction was stopped by addition of saturated aqueous NaHCO₃ solution (10 mL). Precipitated salts were filtered off, the filtrate was extracted with diethyl ether (6 × 20 mL), and the aqueous solution was saved. The ether extracts were concentrated on a rotary evaporator to 30 mL, then extracted with

5% aqueous Na₂CO₃ solution (6 × 30 mL) and saturated aqueous KCl solution (4 × 30 mL), then dried (anhydrous Na₂SO₄), filtered, and concentrated. (The aqueous carbonate extracts were also saved.)

The extent of deuterium incorporation into the methyl position of the unreacted ester was determined using ¹H NMR by integration of the residual methyl resonance against the aromatic resonances. The methyl signal showed small upfield shifts (ca. 0.015 ppm) and splittings due to H-D coupling ($J_{\text{CH}_2\text{D}} \approx 2.4$ Hz) which are characteristic of partial deuteration of methyl groups.¹³ Overlapping spectra of all three species having protons at the methyl position were observed.

The combined aqueous extracts were adjusted to pH > 10 with aqueous NaOH solution and made up to the mark in a 250-mL volumetric flask, and the absorbance of the resulting solution at 400 nm was measured. This value was used to calculate the extent of reaction (amount of *p*-nitrophenoxide released) using the measured extinction coefficient of *p*-nitrophenoxide under identical conditions.

Acknowledgment. This research was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC). The awards to M.J.P. of a Postgraduate Scholarship by NSERC and a Graduate Award by Queen's University are gratefully acknowledged.

(13) Emsley, J. W.; Feeney, J.; Sutcliffe, L. H. *High Resolution NMR Spectroscopy*; Pergamon Press: Oxford, 1965.

Solvation Changes Accompanying Proton Transfer from a Carbon Acid to Alkoxide Bases As Revealed by Kinetic Isotope Effects

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Abstract: Primary hydrogen isotope effects are reported for the elimination of 4-nitrophenol from 4-(4-nitrophenoxy)-2-butanone in methanolic methoxide at 20 °C and in aqueous hydroxide at 25 °C. The isotope effects do not change significantly when the isotopic composition of the solvents is changed: $(k_{\text{H}}/k_{\text{D}})_{\text{MeOH}} = 6.48 \pm 0.22$, $(k_{\text{H}}/k_{\text{D}})_{\text{MeOD}} = 6.40 \pm 0.24$; and $(k_{\text{H}}/k_{\text{D}})_{\text{HOH}} = 7.54 \pm 0.11$, $(k_{\text{H}}/k_{\text{D}})_{\text{DOD}} = 7.48 \pm 0.21$. Kinetic solvent isotope effects (using the undeuterated substrate) are $k_{\text{MeOD}}/k_{\text{MeOH}} = 2.195 \pm 0.064$ and $k_{\text{DOD}}/k_{\text{HOH}} = 1.526 \pm 0.029$. The experimental results are compared with model vibrational analysis calculations and about 60 literature examples of related solvent isotope effects on proton-transfer rates. The observations of primary hydrogen isotope effects that are unchanged upon isotopic substitution in protonic sites of the solvent were used to conclude that solvent reorganization is not coupled to proton transfer in the reaction coordinate.

The role of solvent reorganization during the course of proton-transfer reactions has been examined from a variety of perspectives.¹ We have investigated the nature of solvation changes that occur in the course of a specific class of proton-transfer reactions, from carbon acid to alkoxide base, in protic solvents.

Our perspective of the problem concerns the solvation changes that occur at the alkoxide base as it becomes a solvent molecule during the course of the reaction. We are interested in learning (1) the extent of solvent reorganization at the rate-limiting step for the proton-transfer process and (2) the degree to which the motion of solvent reorganization is coupled to the proton-transfer event.

Extent of solvent reorganization refers to the progress of solvation changes that has occurred between the reactant state and the transition state for the reaction. A convenient measure of the extent of solvent reorganization can be derived from the kinetic solvent isotope effect and an appropriate equilibrium solvent isotope effect.² If the equilibrium and kinetic solvent isotope

(1) (a) Bell, R. P. *Discuss. Faraday Soc.* 1965, 39, 16-24. (b) Caldin, E. F.; Mateo, S. *J. Chem. Soc., Faraday Trans. 1* 1975, 71, 1876-1904. (c) Barbara, P. F.; Walker, G. C.; Smith, T. P. *Science* 1992, 256, 975-981. (d) Bernasconi, C. F.; *Pure Appl. Chem.* 1982, 54, 2335-2348. (e) Kurz, J. L.; Kurz, L. C. *J. Am. Chem. Soc.* 1972, 94, 4451-4461. (f) German, E. D.; Kuznetsov, A. M.; Dogonadze, R. R. *J. Chem. Soc., Faraday Trans. 2* 1980, 76, 1128-1146. (g) Ritchie, C. D.; McKay, B.; Wright, D. J. In *Reaction Transition States*; DuBois, J. E., Ed.; Gordon and Breach Science Publishers: New York, 1972; pp 55-61. (h) Bednar, R. A.; Jencks, W. P. *J. Am. Chem. Soc.* 1985, 107, 7126-7134. (i) Hynes, J. T. *Annu. Rev. Phys. Chem.* 1985, 36, 573-597. (j) Grunwald, E.; Eustace, D. In *Proton Transfer Reactions*; Caldin, E. F., Gold, V., Eds.; Chapman and Hall: London, 1975; pp 103-120. (k) Hupe, D. J.; Wu, D. *J. Am. Chem. Soc.* 1977, 99, 7653-7659. (l) Murdoch, J. R.; Bryson, J. A.; McMillen, D. F.; Brauman, J. I. *J. Am. Chem. Soc.* 1982, 104, 600-610.

(2) (a) Alvarez, F. J.; Schowen, R. L. In *Isotopes in Organic Chemistry*; Buncl, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Vol. 7, Chapter 1. (b) Kresge, A. J.; More O'Ferrall, R. A.; Powell, M. F. *Ibid.*; Chapter 4. (c) Quinn, D. M.; Sutton, L. D. In *Enzyme Mechanisms from Isotope Effects*; Cook, P. F., Ed.; CRC Press: Boca Raton, FL, 1991; Chapter 3.

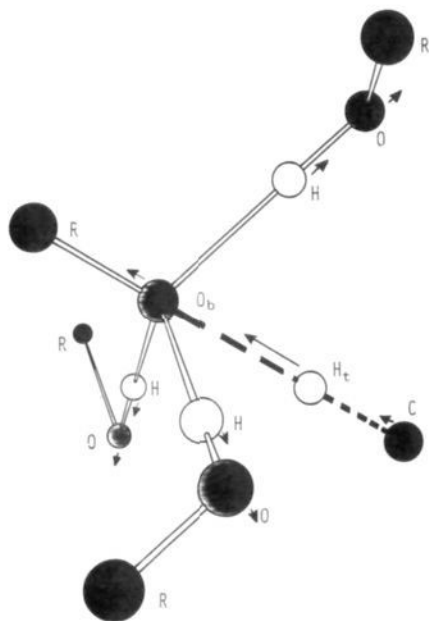


Figure 1. The transition-state model used to estimate the possible influences of isotopic substitution at solvent hydrogens on the primary hydrogen substrate isotope effect for a proton transfer from a carbon acid to a solvated alkoxide ion. The arrows depict relative mass-weighted atomic displacements in one model reaction coordinate (the point in Figure 2 at $C = 1.0$, reaction-coordinate frequency = $982i \text{ cm}^{-1}$). The reaction-coordinate displacements increase the C-H_t and O_b-H bond distances, while the O_b-H_t and H-O bond distances are decreased.

effects match, the simplest analysis yields a 100% extent of solvent reorganization. With a unit kinetic solvent isotope effect, a 0% extent of solvent reorganization is the simplest interpretation. Values intermediate between unity and the equilibrium limit correspond in this analysis to intermediate extents of solvent reorganization.

In this work, the degree of coupling between desolvation and proton transfer refers to the nature of the reaction-coordinate motion for the proton-transfer transition state. A model for coupled desolvation and proton transfer would show concerted desolvation and proton-transfer motions in the reaction coordinate. A model for no coupling of the two types of motions would not show concerted motions in the reaction coordinate. The degree of coupling between types of motions has been probed in recent years³ using isotope effects on isotope effects or, equivalently, tests of the rule of the geometric mean (RGM).⁴ We sought first to establish through vibrational-analysis calculations that RGM violations in models for coupled desolvation and proton transfer can be large enough to be experimentally observed.

An indication that RGM violations might be present in some proton-transfer reactions comes from Gold and Grist,^{5,6} who reported decreases in primary kinetic isotope effects in reactions of methanolic methoxide and aqueous hydroxide when the solvents were changed from MeOH to MeOD or from H₂O to D₂O. For example, the isotope effect ($k_{\text{H}}/k_{\text{D}}$) reportedly drops from 7.4 in MeOH to 6.9 in MeOD.

We chose to study the elimination reaction shown in eq 1. Hupe and Wu^{1k} and Fedor and Glave⁷ have summarized the evidence

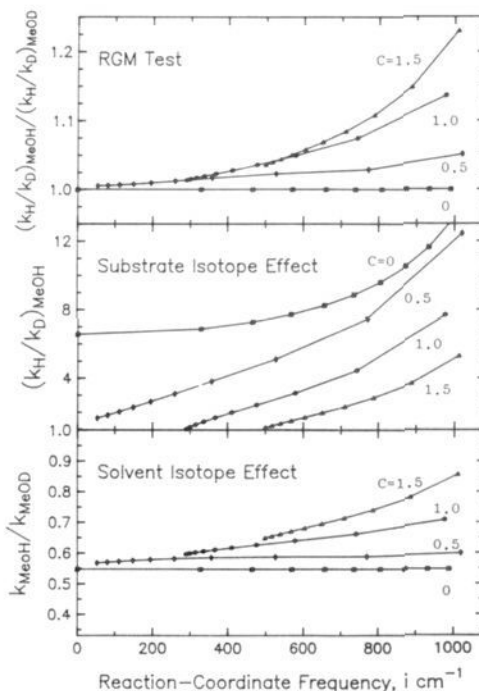
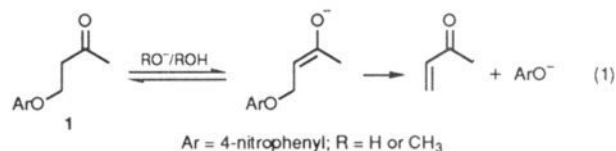


Figure 2. Results from the model calculations described in the text. C is the interaction coefficient used to couple the O_b-H stretch to the O_b-H_t stretch in the model of Figure 1. As C increases, the coupling of desolvation to the reaction-coordinate motion increases. RGM refers to "rule of the geometric mean."

supporting a mechanism that proceeds as shown in eq 1 with rate-limiting proton transfer. This reaction is of special interest



with regard to the role of solvent reorganization during proton transfers, because the nonlinearity of a Brønsted plot for the reaction has been attributed to the effects of desolvation of alkoxide anions.^{1k,8}

Isotope Effects from Model Calculations

Isotope effects were calculated from the Bigeleisen equation⁹ using isotopic frequencies (generated from harmonic valence force fields), moments of inertia, and molecular weights for models of reactant and transition states. The model chosen for the reactant state resembles methanolic methoxide (methoxide ion solvated by three solvent molecules) with a nonbonded carbon acid represented by C-H. The transition-state model, depicted in Figure 1, includes a new partial bond between the oxygen atom of the methoxide ion and the proton being transferred from the carbon acid. Development of the models involved (1) formulation of force fields for methanolic methoxide and methanol that generate an equilibrium solvent isotope effect (H/D) of 1/2.5 for the desolvation of methoxide, (2) specification of a force field for a transition-state complex intermediate between reactant and product force fields, and (3) generation of a reaction-coordinate motion through appropriate force-field coupling. Complete details of the

(7) Fedor, L. R.; Glave, W. R. *J. Am. Chem. Soc.* **1971**, *93*, 985-989.

(8) Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. *J. Am. Chem. Soc.* **1982**, *104*, 7045-7051.

(9) (a) Bigeleisen, J.; Wolfsberg, M. *Adv. Chem. Phys.* **1958**, *1*, 15-76. (b) Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley: New York, 1980. (c) Sims, L. B.; Lewis, D. E. In *Isotopes in Organic Chemistry*; Buncl, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1984; Vol. 6, pp 161-259.

(3) (a) Klinman, J. P. In *Enzyme Mechanisms from Isotope Effects*; Cook, P. F., Ed.; CRC Press: Boca Raton, FL, 1991; Chapter 4. (b) Amin, M.; Price, R. C.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 4085-4086. (c) Huskey, W. P.; Schowen, R. L. *J. Am. Chem. Soc.* **1983**, *105*, 5704-5706. (d) Huskey, W. P. *J. Phys. Org. Chem.* **1991**, *4*, 361-366. (e) Albery, W. J. *J. Phys. Chem.* **1986**, *90*, 3774-3783.

(4) (a) Bigeleisen, J. *J. Chem. Phys.* **1955**, *23*, 2264-2267. (b) Thornton, E. K.; Thornton, E. R. In *Isotope Effects in Chemical Reactions*; Collins, C. J., Bowman, N. S., Eds.; Van Nostrand Reinhold, Co.: New York, 1970; pp 235-237.

(5) Gold, V.; Grist, S. *J. Chem. Soc. B* **1971**, 2282-2285.

(6) Gold, V.; Grist, S. *J. Chem. Soc., Perkin Trans. 2* **1972**, 89-95.

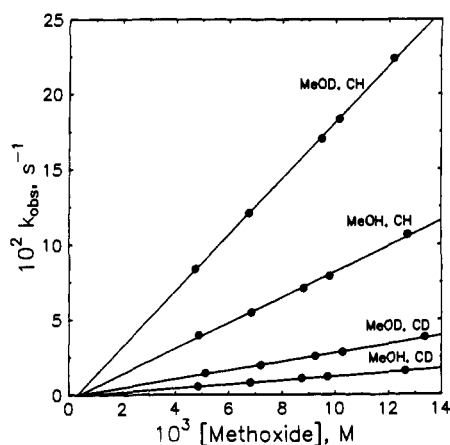


Figure 3. Dependence of pseudo-first-order rate constants on methoxide concentration for the reaction of **1** in MeOH and MeOD at 20 °C and ionic strength = 0.2 M (lithium perchlorate). Standard deviations of the mean rate constants (plotted) are encompassed by the symbols in most cases. Table SI of the supplementary material shows the individual runs at each methoxide concentration. The slopes of the least-squares lines drawn through the points are provided in the Results section.

models used for the calculations are provided in Methods.

The reaction-coordinate motion for one transition-state model is represented by the arrows shown on the structure of Figure 1. The atom marked H_i is seen transferring from atom C to atom O_b , while the three solvent molecules¹⁰ are moving away from the methoxide oxygen (O_b). To generate this sort of reaction-coordinate motion, two types of stretch-stretch coupling force constants were introduced and made sufficiently large to ensure that the motion was unstable. The O_b-H_i and C- H_i stretches were coupled to generate the proton-transfer motion, and the three O_b-H stretches were coupled to the O_b-H_i stretch to tie desolvation to proton transfer. For convenience, the interaction force constants were introduced using eqs 2 and 3. Increasing coefficient C

$$f_{ab} = B(f_{O_b-H_i} f_{C-H_i})^{1/2} \quad (2)$$

$$f_{ac} = C(f_{O_b-H_i} f_{O_b-H})^{1/2} \quad (3)$$

increases the coupling of desolvation to proton transfer. Estimates of the tunneling contributions were made using the truncated Bell tunnel correction¹¹ and are included in each calculated isotope effect.

Computational results are shown in Figure 2 for various degrees of coupling (C) between desolvation and proton transfer. The solvent isotope effect was calculated for replacement of the three "solvent" hydrogens of the model with deuterium. In the absence of desolvation coupling ($C = 0$), the kinetic solvent isotope effect (k_{MeOH}/k_{MeOD}) is 1/1.828 and independent of the magnitude of the reaction-coordinate frequency, the substrate isotope effect is large and increases with increasing reaction-coordinate frequency, and the rule of the geometric mean (RGM) is obeyed (there is no change in the substrate isotope effect when the solvent hydrogens are all replaced with deuterium). As desolvation coupling increases, the solvent isotope effect becomes less inverse as zero-point energy of stable hydrogen-bond coordinates is lost to reaction-coordinate motion and as tunneling contributions to the solvent isotope effect become significant. The substrate isotope effect decreases because increased coupling of desolvation lowers the sensitivity of the reaction coordinate to the mass of H_i , thus increasing the H_i isotopic sensitivity of stable frequencies¹² and decreasing the isotope effect on the tunneling contribution.

(10) Models with fewer than three solvent molecules retained in the transition state are also reasonable.^{3,25}

(11) (a) Bell, R. P. *Trans. Faraday Soc.* 1959, 55, 1-4. (b) Bell, R. P. *The Tunnel Effect in Chemistry*; Chapman and Hall: New York, 1980; pp 60-63.

(12) Burton, G. W.; Sims, L. B.; McLennan, D. J. *J. Chem. Soc., Perkin Trans. 2* 1977, 1847-1853.

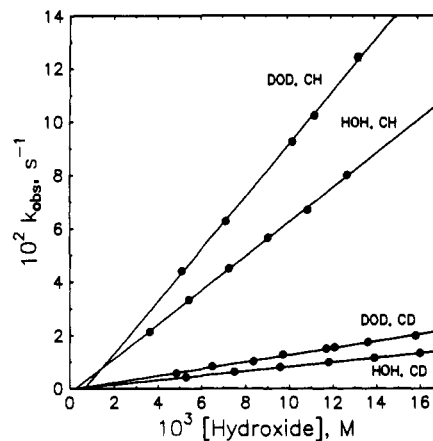


Figure 4. Dependence of pseudo-first-order rate constants on hydroxide concentration for the reaction of **1** in H_2O and D_2O at 25 °C (ionic strength was not controlled). Standard deviations of the mean rate constants (plotted) are encompassed by the symbols in most cases. Table SII of the supplementary material shows the individual runs at each hydroxide concentration. The slopes of the least-squares lines drawn through the points are provided in the Results section.

The top panel of Figure 2 shows that the RGM violation becomes significant as the degree of desolvation coupling with the proton-transfer event is increased. On these models, the substrate isotope effect decreases when the reaction-coordinate frequency (and therefore the tunneling contribution to the isotope effect) becomes sensitive to the mass of the protic sites of the solvent molecules. With these models established as a basis for relating RGM violations to the degree of desolvation participation in reaction-coordinate motion, we conducted experiments to learn about the solvation changes that accompany proton transfer to methanolic methoxide and aqueous hydroxide.

Results

Figure 3 shows first-order rate constants observed for the reaction of **1** with methanolic methoxide (ionic strength = 0.2 M using lithium perchlorate). Reactions in methanol were studied at 20 °C because the reactions (particularly the MeOD reactions) at 25 °C were too fast for our experimental technique. Figure 4 shows rate constants for reactions of **1** with aqueous hydroxide at 25 °C. Ionic strength was not controlled in the hydroxide reactions. The variation in ionic strength over the range of hydroxide concentrations used is small enough that the addition of extra salts is not needed to obtain linear second-order plots. Mean values of observed first-order rate constants are shown in the figures. Individual rate constants (at least four measurements were made for each base concentration) are provided in the supplementary material.

Second-order rate constants were taken as the least-squares estimates of slopes of the second-order plots of Figures 2 and 3. These rate constants (in $M^{-1} s^{-1}$: $k_{H,MeOH} = 8.53 \pm 0.23$; $k_{H,MeOD} = 18.72 \pm 0.20$; $k_{D,MeOH} = 1.316 \pm 0.028$; $k_{D,MeOD} = 2.925 \pm 0.10$; $k_{H,HOH} = 6.397 \pm 0.073$; $k_{H,DOD} = 9.76 \pm 0.15$; $k_{D,HOH} = 0.8488 \pm 0.0077$; $k_{D,DOD} = 1.305 \pm 0.031$) were used to compute isotope effects. In methanolic methoxide (20 °C), the solvent isotope effects were $(k_{MeOD}/k_{MeOH})_{CH} = 2.195 \pm 0.064$ and $(k_{MeOD}/k_{MeOH})_{CD} = 2.223 \pm 0.090$, and the substrate isotope effects were $(k_H/k_D)_{MeOH} = 6.48 \pm 0.22$ and $(k_H/k_D)_{MeOD} = 6.40 \pm 0.24$. Reactions in aqueous hydroxide (25 °C) gave $(k_{DOD}/k_{HOH})_{CH} = 1.526 \pm 0.029$, $(k_{DOD}/k_{HOH})_{CD} = 1.537 \pm 0.039$, $(k_H/k_D)_{HOH} = 7.54 \pm 0.11$, and $(k_H/k_D)_{DOD} = 7.48 \pm 0.21$.

Discussion

Uncoupled Desolvation and Proton Transfer. In both aqueous hydroxide and methanolic methoxide the substrate isotope effects are not significantly different in the light and heavy isotopic solvents. The ratio of the substrate isotope effects (ROH/ROD) is 1.01 in both methanolic methoxide and aqueous hydroxide. Additional reports of kinetic isotope effects that are independent of the isotopic composition of the solvent can be found in the

proton-transfer literature. These include studies of the racemization of mandelate ion,¹³ the enolization of acetone,¹⁴ the racemization of a fluorene derivative,¹⁵ and the racemizations of two nitriles.^{16,17}

Provided that tunneling contributes to the substrate isotope effect (we are presently studying the temperature dependence of the isotope effects), we conclude that desolvation of the base is not strongly coupled to the proton-transfer event. Additional explanations for observations of isotope effects on isotope effects in proton-transfer reactions are also excluded. These include possible models with dominant ground-state tunneling in which the vibrational energies of reactant and product states are sensitive to isotopic substitution of solvent OH groups,¹⁸ changes in transition-state structure arising from variational effects¹⁹ that might be sensitive to solvent isotopes, and effects of nonequilibrium solvation^{1b,e,i,20,21} that could in principle be sensitive to the mass of the solvent. None of these dynamical effects in themselves are excluded; only excluded are the classes of models that show dynamical effects which are sensitive to isotopic substitution in the solvent.

Extent of Solvent Reorganization during Proton Transfer. The constancy of solvent isotope effects for proton transfer to hydroxide and methoxide ions seen over a wide range of carbon acid structures has been noted before.^{2b,22} Recent observations of solvent isotope effects that clearly vary with the reactivity of carbon acids^{23,24} prompted us to examine in some detail the existing literature regarding solvent isotope effects on proton transfers to aqueous hydroxide and methanolic methoxide. We found that most examples of solvent isotope effects on proton transfers from carbon acids to methanolic methoxide are within a narrow range ($k_{\text{MeOD}}/k_{\text{MeOH}} = 2.0\text{--}2.3$), as are most proton transfers to aqueous hydroxide ($k_{\text{DOD}}/k_{\text{HOH}} = 1.3\text{--}1.5$). Cases in which the isotope effects are outside these ranges involve either reactions in which heavy-atom motion (such as leaving-group expulsion) is thought to be coupled to the proton transfer, or reactions in which the proton transfer is thought to have a low intrinsic barrier. We have therefore listed these observations in Table I according to three categories: (1) reactions in which the proton-transfer event appears not to be coupled to substantial heavy-atom rearrangement, (2) reactions in which proton transfer is coupled to heavy-atom motion, and (3) reactions with low intrinsic barriers for proton transfer.

The solvent isotope effects and substrate isotope effects we observed for proton transfer from **1** are similar in magnitude to the isotope effects reported for many proton transfers from carbon acids in the first class of reactions in Table I. The fact that the reactions are faster in methanolic methoxide than in aqueous hydroxide is another characteristic common to many proton transfers from carbon.²⁵ All of the methoxide examples of Table

I seem to fall into the class of reactions with large intrinsic barriers and no coupling of heavy-atom motion to proton transfer. The related class of reactions in aqueous hydroxide also shows a narrow range of kinetic solvent isotope effects, but the effects are smaller (1.3–1.5) than are seen in methanolic methoxide (2.0–2.3). The small ranges of solvent isotope effects in methanolic methoxide and in aqueous hydroxide observed for this collection of carbon acids suggest that isotopic fractionation by the developing carbanions or enolate ions in the transition states is not significant.

The differences in magnitude of the isotope effects in the two solvent systems could be an indication of the differences in extents of base desolvation at the proton-transfer transition state for hydroxide and methoxide reactions. When the extent of base desolvation, x , is represented by eq 4 and a value of 2.5 (for

$$k_{\text{ROD}}/k_{\text{ROH}} = (K_{\text{ROD}}/K_{\text{ROH}})^x \quad (4)$$

complete loss of isotopic fractionation by the solvation shell of methoxide ion)²⁶ is chosen for $K_{\text{ROD}}/K_{\text{ROH}}$, solvent reorganization about the base is estimated to be 75–90% complete at the proton-transfer transition state. For proton transfers to aqueous hydroxide (using $K_{\text{DOD}}/K_{\text{HOH}} = 2.3$ for complete desolvation of hydroxide),^{2,27} extents of base desolvation are estimated to be 30–50% at the rate-limiting transition state. The larger amount of desolvation estimated for proton transfers in methanol could be a consequence of steric differences in the types of solvent molecules.²⁸

The proton transfers from phenylacetylene and chloroform (entries 23 and 25 in Table I) deserve special mention because the reaction rates are limited by a process occurring after the proton-transfer step.²⁹ Larger solvent isotope effects might have been expected in these cases as a consequence of complete loss of the hydroxide ion at the point of the rate-limiting transition state. Isotopic fractionation of solvent hydrogens by the fully developed carbanions has been suggested as an explanation for these results.^{29a}

The reactions thought to have low intrinsic barriers (entries 37 and 38 in Table I) show solvent isotope effects that clearly vary with reactivity, and most of the effects are larger than the kinetic isotope effects of the first class of reactions. The same observation can be made for entries 33–35 of Table I, in which proton transfer is thought to be coupled to heavy-atom motion (leaving-group expulsion in these cases). Coupling to heavy-atom motion seems to increase the sensitivity of the extent of proton transfer and the extent of base desolvation of changes in reactant-state structure, as might be expected according to Bernasconi's principle.³⁰ It would seem that solvent isotope effects on proton-transfer reactions in methanolic methoxide and aqueous hydroxide are useful as a measure of transition-state structure, particularly the region of the structure that concerns desolvation of the base. The apparent constancy of solvent isotope effects on proton transfers from carbon acids without coupled heavy-atom motion or low intrinsic barriers may simply reflect similar transition-state structures for the selection of reactions studied to date.

Conclusions

Our observations for the reaction of **1** with alkoxide bases are representative of the class of proton transfers without coupled heavy-atom motion or a low intrinsic barrier. A transition-state structure consistent with our kinetic isotope effects would have

(13) Pocker, Y. *Chem. Ind. (London)* **1958**, 1117–1118.

(14) Pocker, T. *Chem. Ind. (London)* **1959**, 1383–1384.

(15) Ford, W. T.; Graham, E. W.; Cram, D. J. *J. Am. Chem. Soc.* **1967**, *89*, 4661–4669.

(16) Bergman, N. A.; Källsson, L. *Acta Chem. Scand., Ser. A* **1976**, *30*, 421–424.

(17) Bergman, N. A.; Melander, L. *Acta Chem. Scand., Ser. A* **1974**, *28*, 747–752.

(18) Bosch, E.; Moreno, M.; Lluch, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 2072–2076. In this theoretical study of the intramolecular proton transfer of malonaldehyde, isotopic substitution at a secondary site changes the symmetry of the proton-transfer coordinate.

(19) Truhlar, D. G.; Isaacson, A. D.; Garrett, B. C. In *The Theory of Chemical Reaction Dynamics*; Baer, M., Ed.; CRC Press: Boca Raton, FL, **1985**; pp 65–137.

(20) (a) Tucker, S. C.; Truhlar, D. J. *J. Am. Chem. Soc.* **1990**, *112*, 3347–3361. (b) Zhao, X. G.; Tucker, S. C.; Truhlar, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 826–832.

(21) Kreevoy, M. M.; Kotchevar, A. T. *J. Am. Chem. Soc.* **1990**, *112*, 3579–3583.

(22) Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 3447–3452.

(23) Murray, C. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1990**, *112*, 1880–1889.

(24) Washabaugh, M. W.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 683–692.

(25) Jones, J. R.; Walkin, K. T.; Davey, J. P.; Buncl, E. *J. Phys. Chem.* **1989**, *93*, 1362–1365.

(26) Baltzer, L.; Bergman, N. A. *J. Chem. Soc., Perkin Trans. 2* **1982**, 313–319.

(27) (a) Heinzinger, K.; Weston, R. E., Jr. *J. Phys. Chem.* **1964**, *68*, 2179–2183. (b) Gold, V.; Lowe, B. M. *J. Chem. Soc. A* **1967**, 936–943.

(28) If this is the case, the smaller (less inverse) isotope effects seen in additions of methoxide ion to carbonyl carbon (ref 2; also: Huskey, W. P.; Schowen, R. L. *Gazz. Chim. Ital.* **1987**, *117*, 409–416), where the steric requirements would seem to be more severe, might be an indication of either solvent bridges between the carbonyl carbon and methoxide ion or compensating isotopic fractionation at the developing oxyanion of the carbonyl oxygen.

(29) (a) Kresge, A. J.; Lin, A. C. *J. Am. Chem. Soc.* **1975**, *97*, 6257–6258. (b) Lin, A. C.; Chaing, Y.; Dahlberg, D. B.; Kresge, A. J. *J. Am. Chem. Soc.* **1983**, *105*, 5380–5386.

(30) Bernasconi, G. F. *Acc. Chem. Res.* **1987**, *20*, 301–308.

Table I. Kinetic Solvent Isotope Effects Observed for Reactions Involving Proton Transfers from Carbon Acids to Methanolic Methoxide or Aqueous Hydroxide

	carbon acid	reaction type	$T, ^\circ\text{C}$	$k, \text{M}^{-1} \text{s}^{-1}$	$k_{\text{OD}}/k_{\text{OH}}$	$k_{\text{H}}/k_{\text{D}}$
Methanolic Methoxide						
I. Proton Transfers without Coupled Heavy-Atom Motion						
1	2-nitropropane ⁵	proton transfer ^a	24.8	0.348	2.28	7.40
2	9-methylfluorene ³⁸	exchange	44.7	0.0001 (k_{T})	2.2	2.26 (D/T)
3	pentafluorobenzene ³⁹	exchange	25.0	0.026	2.3	1.0
4	PhCH(CF ₃) ₂ ⁴⁰	exchange	25.0	0.0021 (k_{T})	2.63	1.10
5	CF ₃ (CF ₂) ₆ H ⁴¹	exchange	70.0	0.000 092	1.50 ^b	1.39 (D/T)
6	1-methyl-4-isopropylcyclohexan-3-one ⁴²	racemization	25.0	0.0087	2.04	7.15
7	(CH ₃) ₂ CH ₂ CH(Ph)CO(Ph) ⁵	racemization	24.8	0.001 68	2.04	
8	Ph(CH ₃)CHCN ¹⁶	racemization	25.15	0.217	2.10	2.44
9	(Ph)CH ₂ CH(CH ₃)CN ^{17,43}	racemization	60.0	0.000 007 5	2.11	1.15
			80.0	0.000 13	1.85	
10	CH ₃ CH ₂ CH(Ph)CN ⁴³	racemization	25.0	0.092	2.38	
11	PhCH ₂ CH(CH ₃)COCH ₃ ⁴⁴	racemization	25.0	0.0054	2.03	
12	phenyl 2,2-diphenylcyclopropyl ketone ^{43,44}	racemization	25.0	0.000 037	2.22	3.5 ^f
13	2-[(<i>N,N</i> -dimethylamino)carbonyl]-9-methylfluorene ¹⁵	racemization	24.9	0.0029	2.3	6.7
14	1-methylindene ⁴⁵	racemization	25.0	0.0027	2.04	
15	1,3-dimethylindene ⁴⁵	racemization	25.0	0.000 17	2.03	
16	9-chloro-9,9'-bifluorenyl ⁴⁶	elimination	25.0	0.002	2.30	
17	methyl (X-phenyl)(Y-phenyl)methanesulfinate ⁴⁷	elimination				
	X = H, Y = H		25.0	0.028	2.7 ^c	
	X = 4-methyl, Y = H		25.0	0.012	2.5 ^c	
	X = 4-methoxy, Y = H		25.0	0.0065	2.6 ^c	
	X = 4-methoxy = Y		25.0	0.0027	2.7 ^c	
18	4-(4-nitrophenoxy)-2-butanone ^f	elimination	20.0	8.5	2.20	6.48
Aqueous Hydroxide						
I. Proton Transfers without Coupled Heavy-Atom Motion						
19	2-nitropropane ^{6,48}	proton transfer ^a	25.0	0.35	1.35	7.60
			5.0		1.36	
20	nitroethane ^{48,49}	proton transfer ^a	25.0	5.19		9.3
			5.0		1.39	
			0.0		1.42	
21	X-PhCH(NO ₂)CH ₃ ²²	proton transfer ^a				
	X = <i>m</i> -CH ₃		25.0	5.4	1.37	7.3
	X = H		25.0	6.5	1.42	7.1
	X = <i>m</i> -Cl		25.0	17.5	1.34	7.9
22	1,4-dicyano-2-butene ⁵⁰	exchange	25.0	0.122 (k_{T})	1.39	
23	phenylacetylene ^{29,51}	exchange	25.0	267 (k_{T})	1.34	
			25.0	244 (k_{T})	1.36	
24	<i>t</i> -BuCH(CN) ₂ ⁵²	exchange	25.0	250 000 (k_{T})	1.72	
25	chloroform ²⁹	exchange	25.0	0.163 (k_{T})	1.48	
26	PhCH(OH)COOH ⁵³	racemization	100.0	0.000 021	1.40	4.68
27	acetone ^{14,55}	halogenation	25.0	0.22		7.24
			25.0	0.18	1.46	7.50
28	acetaldehyde ⁵⁴	halogenation	25.0	1.07	1.37	
29	<i>N</i> -[β -(<i>p</i> -nitrophenyl)ethyl]quinuclidinium ion ⁵⁶	elimination	25.0	0.000 86	1.55	8.5
30	2,3-di- <i>O</i> -methyl-D-glyceraldehyde ⁵⁷	elimination	25.0	0.42	1.33	
31	9-(dimethylamino)fluorene ⁵⁸	elimination	25.0	0.017	1.30	
32	4-(4-nitrophenoxy)-2-butanone ^f	elimination	25.0	6.4	1.53	7.54
II. Proton Transfers Coupled to Heavy-Atom Motion						
33	PhCH ₂ CH ₂ S ⁺ (Me) ₂ Br ^{59,60}	elimination	80.45	0.0013	1.57	
			80.0	0.001 22		4.13
			70.0	0.000 42		4.32
			60.0	0.000 14		4.71
34	X-CH ₂ CH ₂ -Y ^{59,60}	elimination				
	X = Ph, Y = N ⁺ (Me) ₃		80.45	0.000 056	1.79	
			50.0 (EtOH)			2.99
	X = <i>p</i> -ClC ₆ H ₄ , Y = N ⁺ (Me) ₃		80.45	0.000 22	1.73	
	X = Ph, Y = N ⁺ (Me) ₂ PhBr		80.45	0.000 29	1.62	
35	<i>p</i> -Me ₂ N ⁺ C ₆ H ₄ CH ₂ CH ₂ -X ⁶¹	elimination				
	X = N(Me) ₃ ⁺		60.0	0.000 51	1.62	
	X = N(Me) ₂ Ph ⁺		60.0	0.001 60	1.68	
	X = S(Me) ₂ ⁺		60.0	0.005 14	1.54	
	X = F		60.0	0.000 037	1.66	
	X = Cl		60.0	0.000 62	1.40	
	X = Br		60.0	0.0126	1.30	
36	PhCH ₂ SO ₂ O-X ⁶²	elimination				
	X = 2,6-dinitrophenyl		25.0	10 000	2.38	
	X = 2,4-dinitrophenyl		25.0	3800		4.0
	X = 3-nitrophenyl		25.0	0.23	1.25	
	X = 4-nitrophenyl		25.0	21	1.56	

Table I (Continued)

	carbon acid	reaction type	T, °C	k, M ⁻¹ s ⁻¹	k _{OD} /k _{OH}	k _H /k _D
III. Proton Transfers with Low Intrinsic Barriers						
37	dimethyl(2-X-9-fluorenyl)sulfonium ion ²³	exchange				
	X = H		28.0	3900 (k _T)	1.9	8.2 (H/T) ^d
	X = Br		28.0	37 000 (k _T)	2.1	4.2 (H/T) ^d
38	3-X-4-methylthiazolium ion ²⁴	exchange				
	X = methyl		30.0	182 000	2.35	2.94 (H/T) ^d
	X = benzyl		30.0	1.14 × 10 ⁶	1.87	6.37 (H/T) ^d
	X = CH ₂ CN		30.0	35.5 × 10 ⁶	1.30	14.7 (H/T) ^d
	thiamin		30.0	4.33 × 10 ⁶	1.92	6.16 (H/T) ^d

^a Direct observation of carbanion production. ^b This solvent isotope effect was calculated from k_H(MeOH), k_D(MeOD), and k_D/k_T(MeOH) using a Swain-Schaad exponent of 2.26. ^c There is considerable uncertainty in these effects. The rate constants in the deuterated solvent (CD₃OD in these cases) were measured at 25.5 °C. The authors estimated the isotope effects by assuming that the CD₃OD rate constants at 25.5 °C were 10% higher than the rate constants would be at 25 °C. ^d These are observed isotope effects, as are all values in this table. ^e This work. ^f We are not certain of the temperature for this primary isotope effect determination.

the transferring proton halfway between the acid and the base (the primary substrate isotope effects are large), with extensive desolvation of methoxide ion (ca. 90% desolvated) and partial desolvation of hydroxide ion (ca. 50% desolvated). The motions of the solvent hydrogens would not be significant in the reaction coordinate for the proton transfer.

Methods

Experimental Procedures. 4-(4-Nitrophenoxy)-2-butanone. This compound was prepared from 4-nitrophenol and methyl vinyl ketone according to the method described by Hupe and Wu.^{1k}

4-(4-Nitrophenoxy)-2-butan-3,3-d₂-one. The deuterated substrate was prepared without significant modification using the procedure of Hupe and Pohl.³¹ Because no C-3 methylene hydrogens could be seen in the 200-MHz ¹H-NMR of the compound, we concluded that the deuterium enrichment at this carbon was at least 95%. Early in our investigation, we used a sample of the deuterated substrate kindly provided by Don Hupe. Deuterated substrate prepared in our lab was used for all results in the present work.

Methoxide and Hydroxide Solutions. MeOH (Fisher, "Spectranalyzed") was allowed to reflux with magnesium turnings³² for 1 h under nitrogen and then allowed to sit overnight at ambient temperature. The MeOH was then distilled and collected. MeOD (Aldrich, 99.5+ atom % D) was purified in the same manner as the MeOH. Concentrated (0.25 M) solutions of sodium methoxide were prepared by adding an appropriate amount of clean sodium to a round-bottom flask containing methanol under nitrogen. Stock methoxide solutions (ca. 0.025 M) were prepared by diluting the concentrated methoxide solution with methanol and bringing the ionic strength to 0.2 M with lithium perchlorate. Stock solutions were then titrated with freshly prepared potassium hydrogen phthalate solution to determine the methoxide concentration. Dilutions of stock methoxide solutions were made volumetrically with 0.2 M lithium perchlorate in methanol solution.

Hydroxide solutions were prepared in a similar fashion, except that the solvent was ice cold before the addition of the sodium and the ionic strength was not adjusted. D₂O (Aldrich, 99.8 atom % D) and doubly distilled water were boiled and collected under nitrogen before use.

Kinetics. The reactions were conducted under pseudo-first-order conditions with the base being in excess by a factor of 50 or greater. Rate constants were obtained by monitoring the appearance of *p*-nitrophenoxide ion at 390 nm using a Varian DMS 300 spectrophotometer. In a typical experiment, the dilute base solution was allowed to equilibrate in the water-jacketed cell holder and compartment of the spectrophotometer at the desired reaction temperature (accurate to ±0.1 °C, reproducible and constant to ±0.05 °C) for at least 10 min before the reaction was initiated by injecting 5 μL of an acetonitrile (distilled from P₂O₅) substrate solution (0.02 M). The reactions were typically followed for at least 3 half-lives.

A microcomputer fitted with an analog-to-digital board was used to digitize the chart-recorder signal of the spectrophotometer. Runs with the undeuterated substrate showed good first-order behavior, and rate constants were obtained from least-squares fits to eq 5, where A_t is

$$A_t = A_\infty - (A_\infty - A_0)e^{-kt} \quad (5)$$

absorbance at time *t*. Reactions with the deuterated substrate showed small deviations from first-order expectations. The residuals showed a systematic trend not accounted for by a single-exponential function. The

deviation is in the wrong direction to be explained by isotopic exchange of substrate deuterium with solvent hydrogen during the course of the reaction.³³ Instead, the behavior can be explained by the presence of small amounts of protiated substrate in the sample of deuterium-labeled substrate. If the substrate is assumed to contain no 1-¹H₂ impurity, eq 6 can be derived to show the time dependence for the production of

$$A_t = A_\infty - (A_\infty - A_0)\{f_{\text{H}}e^{-(k_{\text{HD}}+k_{\text{DH}})t} + (1-f_{\text{H}})e^{-2k_{\text{DD}}t}\} \quad (6)$$

absorbance (A_t) in reactions of a substrate solution containing a fraction f_H of substrate with a single ¹H isotope at C-3. The sum of k_{HD} (for H⁺ transfer from 1-H,D) and k_{DH} (for D⁺ transfer from 1-H,D) was treated as a single parameter in the least-squares fits used to obtain 2k_{DD} as the first-order rate constants appearing in the supplementary material and in Figures 3 and 4 for the deuterated substrate. The statistical factor of 2 was retained for direct comparisons with the rate constants measured for the undeuterated substrate.

Model Calculations

Isotope effects were calculated using the Bigeleisen-Wolfsberg approach.⁹ Models for reactants and transition states were specified in terms of harmonic valence force fields and appropriate geometries and masses. For each model, moments of inertia and vibrational frequencies were calculated using established procedures.³⁴ All calculations were carried out using a program written locally (VIBIE1). All calculations used a temperature value of 25 °C.

Methanolic Methoxide Model. The structure shown in Figure 1 (without H_i and C) was used to represent methoxide ion solvated by three molecules of methanol. Atomic mass units of 15 were assigned to each center identified as "R." The bond distances (in Å) used were R-O_b, 1.50; H-O_b, 1.76; O-H, 1.00; and R-O_b, 1.50. All bond angles were tetrahedral, and the dihedral angles R-O-O_b-R were all 60°.

Force fields employed in a vibrational-analysis study of aqueous hydroxide ion,³⁵ as well as valence force fields for methanol,³⁶ were used as the basis for constructing a force field for methanolic methoxide. The force field was designed to generate an isotope effect close to 2.5 ([MeOH]₃/[MeOD]₃) in a model calculation in which three molecules of methanol form methanolic methoxide. For this calculation, the same geometry was used for the initial and final states (the Figure 1 structure, less H_i and C). Ideally, the initial state might contain three molecules of methanol in some array of hydrogen bonds. Our initial state includes O_b-R, primarily for convenience, but also to eliminate MMI contributions to the isotope effect. By design, the calculated isotope effect derives solely from force-field differences between the initial and final states.

(33) Fishbein, J. C.; Jencks, W. P. *J. Am. Chem. Soc.* **1988**, *110*, 5087-5095.

(34) (a) Wilson, E. B., Jr.; Decius, J. C.; Cross, P. C. *Molecular Vibrations*; Dover: New York, 1980. (b) Gwinn, W. D. *J. Chem. Phys.* **1971**, *55*, 477-481. (c) Harmony, M. D. *Introduction to Molecular Energies and Spectra*; Holt, Rinehart and Winston, Inc.: New York, 1972.

(35) More O'Ferrall, R. A.; Kresge, A. J. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1840-1846.

(36) (a) Timidei, A.; Zerbi, G. Z. *Naturforsch. A: Astrophys., Phys. Phys. Chem.* **1970**, *25*, 1729-1731. (b) Serallach, A.; Meyer, R.; Günthard, H. H. *J. Mol. Spectrosc.* **1974**, *52*, 94-129.

(31) Hupe, D. J.; Pohl, E. R. *J. Am. Chem. Soc.* **1984**, *106*, 5634-5640.

(32) Lund, H.; Bjerrum, J. *Chem. Ber.* **1931**, *64*, 210-213.

For methanolic methoxide, the following bending force constants (mdyn·Å/rad²) were assigned: R–O–H, 0.70; R–O_b–H, 0.02; and H–O_b–H, 0.005. The linear-bend coordinates for each hydrogen bond were assigned values of 0.1. For the methanol model, assignments were 0.70 for R–O–H with the remaining bending constants at half the values specified for the methanolic methoxide model. Torsional force constants were omitted for both models. Stretching force constants (mdyn/Å) for R–O and R–O_b were 5.30 for both models. The O_b–H stretches were assigned values of 0.6 for methanolic methoxide and 0.3 for the methanol model. The remaining stretching force constant, O–H, was adjusted (final value used in both models was 6.00) to generate an O–H stretching frequency³⁷ of 3350 cm⁻¹ for the methanol model. Finally, a

stretch–stretch interaction force constant was introduced in the methanolic methoxide model to couple the O–H and O_b–H bond stretches. This constant was adjusted until the calculation gave a H₃/D₃ isotope effect of 2.493. This coupling constant, as well as others to be specified below, was introduced as an *interaction coefficient*, *a*, defined in eq 7. An interaction coefficient of 0.66 gave the desired isotope effect.

$$f_{ij} = a(f_{ii}f_{jj})^{1/2} \quad (7)$$

Proton-Transfer Model. A proton-transfer model was constructed by adding atoms H_i and C (see Figure 1) to the methoxide model. In the reactant state, the O_b–H_i distance was 1.8 Å and the force constant for this stretch was set equal to 0. The H_i–C distance was 1.1 Å, and the force constant was 4.70 mdyn/Å. For the transition-state model, the O_b–H_i and H_i–C distances were equal at 1.3 Å, and the related stretching force constants were both set to 2.35 mdyn/Å. The force constants and geometry associated with the methanolic methoxide of the reactant state are described above. Force constants for the methanolic methoxide region of the transition-state model were intermediate (halfway) between the force constants for the methanolic methoxide and the methanol force constants described above. A reaction-coordinate motion was generated by introducing a positive interaction coefficient (eq 1) *B* to couple the H_i–O_b and H_i–C stretches and three positive interaction coefficients *C* to couple the H_i–O_b stretch to the three O_b–H stretches. Tunneling contributions were estimated using the truncated Bell correction¹¹ and are included in each isotope effect reported here.

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Supplementary Material Available: Tables SI and SII listing observed first-order rate constants corresponding to the average values plotted in Figures 3 and 4 (4 pages). Ordering information is given on any current masthead page.

(37) Rao, C. N. R.; Agarwal, U. P.; Rao, C. P.; Fernandes, J. R. *J. Phys. Chem.* **1979**, *83*, 722–728.

(38) Streitwieser, A., Jr.; Hollyhead, W. B.; Pudjaatmaka, A. H.; Owens, P. H.; Kruger, T. L.; Rubenstein, P. A.; MacQuarrie, R. A.; Brokaw, M. L.; Chu, W. K. C.; Niemeyer, H. M. *J. Am. Chem. Soc.* **1971**, *93*, 5088–5096.

(39) Streitwieser, A., Jr.; Hudson, J. A.; Mares, F. *J. Am. Chem. Soc.* **1968**, *90*, 648–651.

(40) Koch, H. F.; Dahlberg, D. B.; Lodder, G.; Root, K. S.; Touchette, N. A.; Solsky, R. L.; Zuck, R. M.; Wagner, L. J.; Koch, N. H.; Kuzemko, M. A. *J. Am. Chem. Soc.* **1983**, *105*, 2394–2398.

(41) Andreades, S. *J. Am. Chem. Soc.* **1964**, *86*, 2003–2010.

(42) Anhede, B.; Baltzer, L.; Bergman, N. A. *Acta Chem. Scand., Ser. A* **1982**, *36*, 39–45.

(43) Levin, J. O. *Chem. Scr.* **1973**, *4*, 85–88.

(44) Levin, J. O.; Rappe, C. *Chem. Scr.* **1971**, *1*, 233–235.

(45) Levin, J. O. *Chem. Scr.* **1974**, *6*, 89–91.

(46) Carey, E.; More O'Ferrall, R. A.; Vernon, N. M. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1581–1586.

(47) Kice, J. L.; Rudinski, J. J. *J. Am. Chem. Soc.* **1987**, *109*, 2414–2421.

(48) Maron, S. H.; La Mer, V. K. *J. Am. Chem. Soc.* **1938**, *60*, 2588–2596.

(49) Bell, R. P.; Goodall, D. M. *Proc. R. Soc. London, A* **1966**, *294*, 273–297.

(50) Walters, E. A.; Long, F. A. *J. Phys. Chem.* **1972**, *76*, 362–365.

(51) Halevi, E. A.; Long, F. A. *J. Am. Chem. Soc.* **1961**, *83*, 2809–2814.

(52) Hibbert, F.; Long, F. A. *J. Am. Chem. Soc.* **1971**, *93*, 2836–2840.

(53) Pocker, Y. *Chem. Ind. (London)* **1958**, 1117–1118.

(54) Keefe, J. R.; Kresge, A. J. *Can. J. Chem.* **1988**, *66*, 2440–2442.

(55) Chiang, Y.; Kresge, A. J.; Morimoto, H.; Williams, P. G. *J. Am. Chem. Soc.* **1992**, *114*, 3981–3982.

(56) Alunni, S.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 2052–2059.

(57) Fedoronko, M.; Petrusova, M.; Sticzay, T. *Carbohydr. Res.* **1983**, *115*, 75–83.

(58) Kelly, R. P.; More O'Ferrall, R. A.; O'Brien, M. *J. Chem. Soc., Perkin Trans. 2* **1982**, 211–219.

(59) Steffa, L. J.; Thornton, E. R. *J. Am. Chem. Soc.* **1967**, *89*, 6149–6157.

(60) Saunders, W. H., Jr.; Edison, D. H. *J. Am. Chem. Soc.* **1960**, *82*, 138–142.

(61) Winey, D. A.; Thornton, E. R. *J. Am. Chem. Soc.* **1975**, *97*, 3102–3108.

(62) Davy, M. B.; Douglas, K. T.; Loran, J. S.; Steltner, A.; Williams, A. *J. Am. Chem. Soc.* **1977**, *99*, 1196–1205.