

tion of anthranilamides (II). It accounts for the fact that the rate law for formation of IIc from I and aniline is different from that for formation of IIa from I and *n*-butylamine. It conveniently accommodates the fact that bulkiness in an amine favors formation of type III rather than type II products, in that C-4 of I would be expected to be more sensitive to the steric requirements of an attacking nucleophile than the isocyanate carbon of VIII.

We caution that this agreement of experiment with predictions from the model does not prove that the model is correct. However, we feel that it justifies using the model as a basis for prediction and interpretation unless and until it is shown to be inadequate.

If the model is right in its broader aspects, it may yet be faulty in detail. To be specific, our experiments do not require the isocyanate intermediate VIII. We cannot exclude the possibility that III is formed by direct nucleophilic attack on C-2 of VII, although we find this alternative unattractive on several grounds.²¹

(21) Professor W. P. Jencks has pointed out in private conversation that VIII would be required as a discrete intermediate if it could be demonstrated that the rate of formation of ureidobenzoic acids III from VII was independent of the concentration or identity of the amine nu-

(Also, we note Kopple's infrared evidence that an isocyanate is produced by action of sodium hydride on the N-carboxy anhydride of α -aminoisobutyric acid in dioxane solution.¹⁶)

A point of interest is that our kinetics do not provide any indication that reactions of amines with either C-4 of I or the isocyanate carbon of VIII requires base catalysis. Probably C-N bond formation is rate limiting in the I \rightarrow VI and VIII \rightarrow III transformations.²²

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cleophile. Transformation of VII to VIII would then be indicated as the rate-limiting step. If k_2 and k_{-2} are rate coefficients for the VII \rightarrow VIII transformation and its reverse, one expects $k_U' = k_2 k_4 [\text{RNH}_2] / (k_{-2} + k_4 [\text{RNH}_2])$. In appropriate cases, a plot of k_U' against $[\text{RNH}_2]$ should diminish in slope as amine concentration increases, and a plot of $1/k_U'$ vs. $1/[\text{RNH}_2]$ should be linear with intercept $1/k_2$. Curvature of this sort is evident in Figure 4, and the inversion plot is linear. The reciprocal of its intercept (possibly k_2) is $13.2 \times 10^{-3} \text{ sec}^{-1}$. We caution, however, against accepting the slight curvature in Figure 4 as evidence of a change in rate-limiting step. If the alkaline hydrolysis occurs *via* attack of hydroxide ion on VIII, similar but more pronounced curvature should be evident in a plot of k_H' against $[\text{OH}^-]$, but there is no suggestion of such curvature in the data of Table IV.

(22) Cf. J. F. Bunnett and R. H. Garst, *J. Am. Chem. Soc.*, **87**, 3879 (1965).

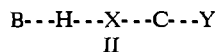
Solvent Isotope Effects in Amide Hydrolysis^{1,2}

Richard L. Schowen, H. Jayaraman,³ Larry Kershner,⁴ and G. W. Zuorick

Contribution from the Department of Chemistry, University of Kansas, Lawrence, Kansas. Received March 24, 1966

Abstract: The rate of hydrolysis of 2,2,2-trifluoro-N-methylacetanilide (I) has been determined as a function of hydroxide ion concentration in protium and deuterium oxide solutions at $25.00 \pm 0.05^\circ$. The kinetic law in both media is shown in eq 2, in agreement with a mechanism involving formation of an adduct of I and hydroxide ion, followed by its general base catalyzed decomposition. The observed kinetic isotope effects are $k_a^{\text{H}_2\text{O}}/k_a^{\text{D}_2\text{O}} = 1.0 \pm 0.2$ (for addition), $k_1^{\text{H}_2\text{O}}/k_1^{\text{D}_2\text{O}} = 3.3 \pm 0.7$ (for solvent-catalyzed elimination), and $k_2^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}} = 2.2 \pm 0.3$ (for hydroxide ion catalyzed elimination). The secondary contributions to the latter two effects are estimated to be $(k_1^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}})_{\text{sec}} = 0.75$ and $(k_2^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}})_{\text{sec}} = 0.48$, leading to estimates for the primary contributions of $(k_1^{\text{H}_2\text{O}}/k_1^{\text{D}_2\text{O}})_{\text{pri}} = 4.4 \pm 1$ and $(k_2^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}})_{\text{pri}} = 4.6 \pm 1$. The rate-determining step appears to involve proton transfer; it is postulated that general base catalyzed reactions are either (a) simple proton-transfer reactions or (b) "solvation rule" reactions, depending on the nature of the leaving group.

Swain, Kuhn, and Schowen⁵ recently examined the magnitudes of solvent isotope effects in a number of general base catalyzed reactions, for which the activated complexes can be represented by structure II, where B is the catalyst, X is an electronegative atom



such as O, N, or S, and Y is a generalized leaving group

(1) This research was supported by the National Science Foundation under Research Grant No. GP-3539 and by the National Institutes of Health under Research Grant No. GM-12477-02 and was carried out in part at the Computation Center of the University of Kansas.

(2) Amide Hydrolysis. III. For part II, see R. L. Schowen, H. Jayaraman, and L. Kershner, *J. Am. Chem. Soc.*, **88**, 3373 (1966).

(3) Madras Christian College, Madras, India; Fellow of the Institute of International Education.

(4) National Defense Education Act Predoctoral Fellow.

(5) C. G. Swain, D. A. Kuhn, and R. L. Schowen, *J. Am. Chem. Soc.*, **87**, 1553 (1965).

(including the π electrons of double bonds). On the assumption that the secondary contributions to the solvent isotope effects are given by eq 1, where β is the slope of the Brønsted catalysis law⁶ plot and

$$(k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}}) = [(k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}})_{\text{max}}]^\beta \quad (1)$$

$(k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}})_{\text{max}}$, the maximum effect, can be estimated according to simple rules,⁵ it was found that no primary isotope effect was produced in these reactions, although all are formulated as "proton-transfer" reactions. The authors⁵ concluded that, in such processes, the transfer of the proton is not concerted with the reorganization of the heavy atoms, which is occurring in the rate-determining activated complex, but instead takes place relatively rapidly either before or after the transition

(6) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, pp 235-242.

state. The role of the general base in accelerating such reactions was suggested to be one of specific "solvation" by hydrogen bonding to the activated complex.⁵

Our discovery that 2,2,2-trifluoro-N-methylacetanilide (I) undergoes hydrolysis in basic media *via* formation of an adduct of I and hydroxide ion,⁷ the decomposition of which is subject to general base catalysis,⁸ provides a field for extension of these ideas to the very important subject of solvent isotope effects and general base catalysis of the hydrolysis of carboxyl derivatives.⁹ We have therefore determined rates of solvolysis of I in basic protium oxide and deuterium oxide solutions and analyzed the results into isotope effects for the various mechanistic steps.

Results

Table I gives values of the observed rate constants for solvolysis of I, as a function of lyoxide concentration,

Table I.^{a, b} Solvolysis of 2,2,2-Trifluoro-N-methylacetanilide in Light and Heavy Water

$10^3[\text{LO}^-],$ M	10^3k_{obsd} $(\text{H}_2\text{O}),$ sec^{-1}	10^3k_{calcd} $(\text{H}_2\text{O}),$ sec^{-1}	10^3k_{obsd} $(\text{D}_2\text{O}),$ sec^{-1}	10^3k_{calcd} $(\text{D}_2\text{O}),$ sec^{-1}
1.5	5.7	5.9	2.4	2.7
3.0	15.3	15.7	8.0	8.2
4.5	27.5	27.8	14.9	15.8
6.0	40.2	41.1	24.5	25.0
8.0	58.3	60.2	38.8	37.8
10.5	92.0	85.0	61.9	58.7
12.0	98.0	101	71.5	71.3
13.5	126.0	117.0	86.7	84.5
15.0	135.0	133.0	106.0	95.9
20.0	176.0	188.0	155.0	143.0
25.0	228.0	224.0	191.0	192.0
30.0	268.0	299.0	243.0	243.0
35.0	345.0	355.0	313.0	299.0

^a Ionic strength 0.01 *M* (added KCl) below 0.008 *M* lyoxide, 0.05 *M* (added KCl) at higher bases. S. S. Biechler and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 4927 (1957), found no salt effects in these reactions. ^b The k_{obsd} values are averages of duplicate determinations, reproducible to $\pm 3\%$; k_{calcd} values are calculated from eq 1 with k_a , k_1 , and k_2 of Table II.

Table II. Rate Constants and Solvent Isotope Effects for Solvolysis of 2,2,2-Trifluoro-N-methylacetanilide in Light and Heavy Water

Rate constant	Solvent	Value	Isotope effect, $k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}}$
k_a	H_2O	$11.0 \pm 0.8 M^{-1} \text{sec}^{-1}$	1.0 ± 0.2
	D_2O	11.3 ± 0.8	
k_1	H_2O	$2.0 \pm 0.2 M^{-1} \text{sec}^{-1}$	3.3 ± 0.7
	D_2O	0.6 ± 0.06	
k_2	H_2O	$2200 \pm 100 M^{-2} \text{sec}^{-1}$	2.2 ± 0.3
	D_2O	1000 ± 100	

at $25.00 \pm 0.05^\circ$ in protium oxide and deuterium oxide and, in each case, corresponding values calculated from eq 2 with the parameters of Table II. The agreement is

$$-d[\text{I}]/dt = k_{\text{obsd}}[\text{I}] = [\text{I}][\text{LO}^-] \frac{k_a(k_1 + k_2[\text{LO}^-])}{k_a + k_1 + k_2[\text{LO}^-]} \quad (2)$$

(7) R. L. Schowen, H. Jayaraman, and L. Kershner, *Tetrahedron Letters*, 497 (1966); see also part II, ref 2.

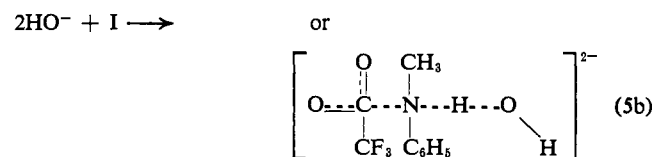
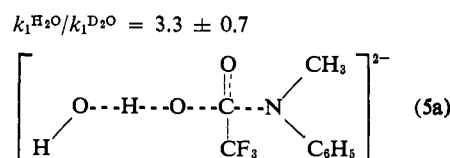
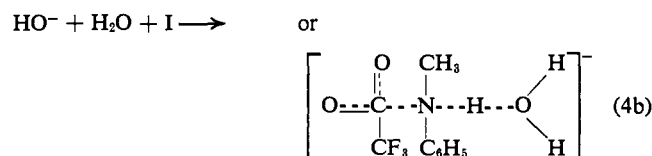
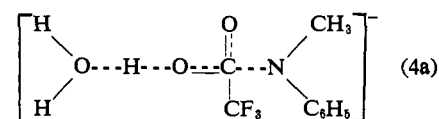
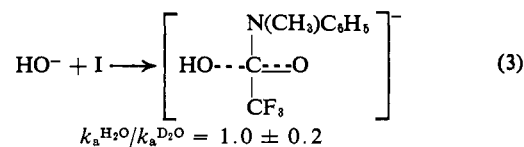
(8) R. L. Schowen and G. W. Zuorick, *J. Am. Chem. Soc.*, **88**, 1223 (1966).

(9) M. L. Bender, E. J. Pollock, and M. C. Neveu, *J. Am. Chem. Soc.*, **84**, 595 (1962); C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 3207, 3214 (1961).

good. Table II also shows the solvent isotope effects derived for each rate constant.

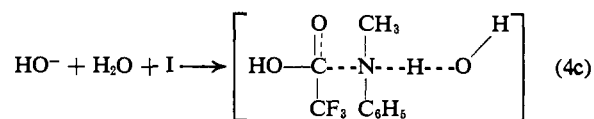
Discussion

The isotope effects of Table II can be associated with the following activation processes²



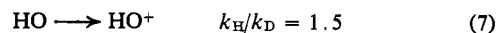
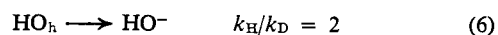
$$k_2^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}} = 2.2 \pm 0.3$$

The dashed lines in these formulas should not be taken as representing formation or cleavage of the associated bonds in the activation process but merely as designating bonds the strengths of which are *possibly* changed on formation of the activated complex. Professor E. R. Thornton has also pointed out the likelihood that the activated complex for the k_1 process could exist in the tautomeric form of eq 4c, corresponding to acid-



catalyzed decomposition of the adduct of hydroxide ion and I.

Estimation of Secondary and Primary Isotope Effects. Swain, Kuhn, and Schowen⁵ suggested that the maximum secondary isotope effects for use in eq 1 be estimated from the following rules



the contributions for individual OH bonds being multiplied together to obtain the resultant effect. The small "h" is appended to the HO of eq 6 to indicate that all cases considered in ref 5 involved the interconversion of hydroxide ion and *hydrogen-bound* hydroxyl, as in an incipient water molecule. We wish to consider here the binding of hydroxide ion to carbon substrates; we obtain a rule for isotope-effect estimation in this circumstance as

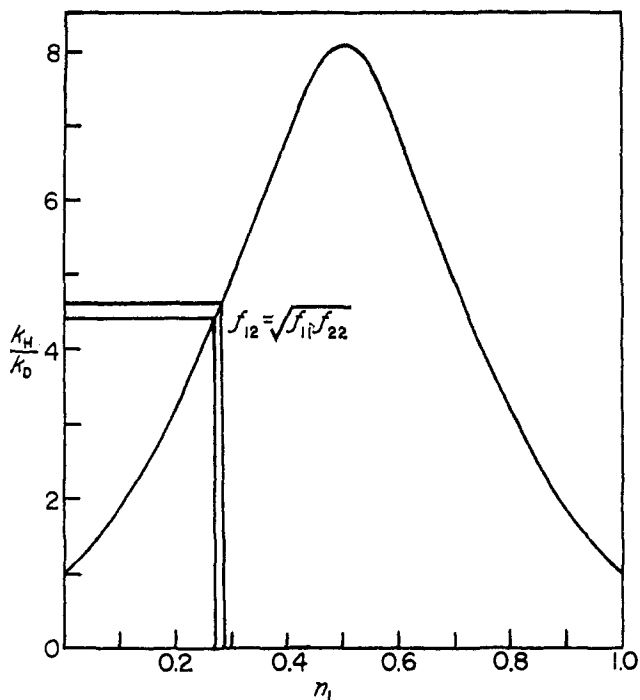
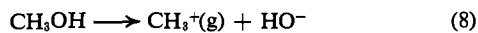


Figure 1. Primary kinetic isotope effect, k_H/k_D , for proton transfer from oxygen to oxygen at 25°, as a function of product-OH bond order, n_1 . Lines show estimated primary effects in the solvolysis of 2,2,2-trifluoro-N-methylacetanilide.

follows. The hypothetical conversion of methanol into hydroxide and a gas phase methyl carbonium ion (eq 8)



will have an isotope effect given by eq 9, where the Q 's

$$K_H/K_D = \frac{Q_{\text{CH}_3\text{OD}}/Q_{\text{CH}_3\text{OH}}}{Q_{\text{DO}^-}/Q_{\text{HO}^-}} = \frac{36.6}{21.4} \approx 1.7 \quad (9)$$

are partition functions. The values of the isotopic partition-function ratios have been calculated from spectroscopic data by Jones^{10a} in Swain's laboratory and by Swain, Ketley, and Bader.^{10b} This should be the appropriate maximum isotope effect for interconversions of hydroxide ion and carbon-bound hydroxyl, as in nucleophilic attack at carbon.

Since we found previously⁸ that $\beta = 0.3$ for this reaction, eq 1 and the rules of eq 6-9 can be used to estimate the secondary contributions to the activation processes of eq 4a,b and 5a,b. The values thus obtained are

$$(k_1^{\text{H}_2\text{O}}/k_1^{\text{D}_2\text{O}})_{\text{sec}} = 0.75 \quad (10)$$

$$(k_2^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}})_{\text{sec}} = 0.48 \quad (11)$$

Because the observed effects must be products of primary and secondary contributions, *i.e.*

$$(k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}})_{\text{obsd}} = (k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}})_{\text{pri}}(k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}})_{\text{sec}} \quad (12)$$

the primary contributions can be estimated

$$(k_1^{\text{H}_2\text{O}}/k_1^{\text{D}_2\text{O}})_{\text{pri}} = 4.4 \pm 1 \quad (13)$$

$$(k_2^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}})_{\text{pri}} = 4.6 \pm 1 \quad (14)$$

The uncertainties given reflect, in part, theoretical

(10) (a) L. B. Jones, Ph.D. Thesis, Massachusetts Institute of Technology, 1964; (b) C. G. Swain, A. D. Ketley, and R. F. W. Bader, *J. Am. Chem. Soc.*, **81**, 2353 (1959).

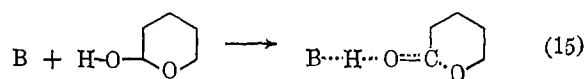
uncertainties in the method of estimation of the secondary isotope effects. The magnitudes of both effects are clearly consistent with rate-determining proton transfer. It remains to compare quantitatively these effects with those predicted from the value of β .

Primary Isotope Effect Calculations. Figure 1 shows a plot of the primary isotope effect, k_H/k_D , for transfer of a proton between two oxygen atoms, as calculated from the Bigeleisen equation¹¹ for various bond orders, n_1 , of the proton-to-product oxygen bond.¹² The transition-state O-H force constants, f_{11} for the product bond and f_{22} for the reactant bond, were assumed to be proportional to the reactant force constant f_0 and the bond orders ($f_{11} = n_1f_0$; $f_{22} = (1 - n_1)f_0$), according to the Johnston-Parr BEBO method.¹³ Bond order to the proton was assumed constant at unity and the critical frequency to be zero ($f_{12} = \sqrt{f_{11}f_{22}}$ is the reactant-bond, product-bond coupling constant). The masses of the oxygen, hydrogen, and deuterium atoms were taken as 16.000, 1.008, and 2.015 amu, respectively, and f_0 as 7.8 mdynes/A, given by Wilson, Decius, and Cross.¹⁴

To the extent that β is a measure of the "degree of protonation" of the catalyzing base in the activated complex,⁶ it should be identifiable with n_1 of Figure 1. The lines drawn on the plot show the estimated primary isotope effects of eq 13 and 14; these effects indicate the product bond order to be about 0.28. The experimental value of $\beta = 0.3$ is in excellent agreement with this prediction from the primary kinetic isotope effect.

Thus the experimental solvent isotope effect can be quantitatively accounted for in terms of primary¹⁵ and secondary contributions, both predictable from the value of the Brønsted law slope β .

Mechanisms of General Base Catalysis.¹⁶ These results show that rate-determining proton transfer is occurring in the over-all process leading to products from the adduct of I and hydroxide ion. They do not indicate what other processes may be occurring simultaneously or "concertedly." The simplest paths consistent with the facts might initially be considered to be those of eq 4a and 5a (base-catalyzed, fully concerted β elimination of N-methylaniline, as proton and anilide ion, from the carbonyl group) or their "inverse" analogs of eq 4b and 5b. It would be necessary, however, to explain the difference between this case and the strongly analogous mutarotation of glucose (eq 15),



where the weight of evidence indicates that transfer of the proton is *not* concerted with the rate-determining

(11) J. Bigeleisen and M. Wolfsberg, *Advan. Chem. Phys.*, **1**, 15 (1958).
(12) The program for this calculation was written when R. L. S. was a research associate in Professor C. G. Swain's laboratory. Further details will be published at a later time. The general method resembles that of A. V. Willi and M. Wolfsberg, *Chem. Ind. (London)*, 2097 (1964).

(13) H. S. Johnston and C. Parr, *J. Am. Chem. Soc.*, **85**, 2544 (1963).
(14) E. B. Wilson, Jr., J. C. Decius, and P. C. Cross, "Molecular Vibrations," McGraw-Hill Book Co., New York, N. Y., 1955, p 175.

(15) Although Figure 1 is calculated for O to O proton transfer, it would be little changed for O to N transfer, as in eq 4b and 5b, since both the reduced mass and associated force constant for the N-H bond are slightly lower than for the O-H bond,¹⁴ leaving the vibration frequencies nearly the same.

(16) We wish to use this term to refer only to "classical" general base catalysis and not to "nucleophilic" catalysis. See ref 8 and M. L. Bender, *Chem. Rev.*, **60**, 53 (1960).

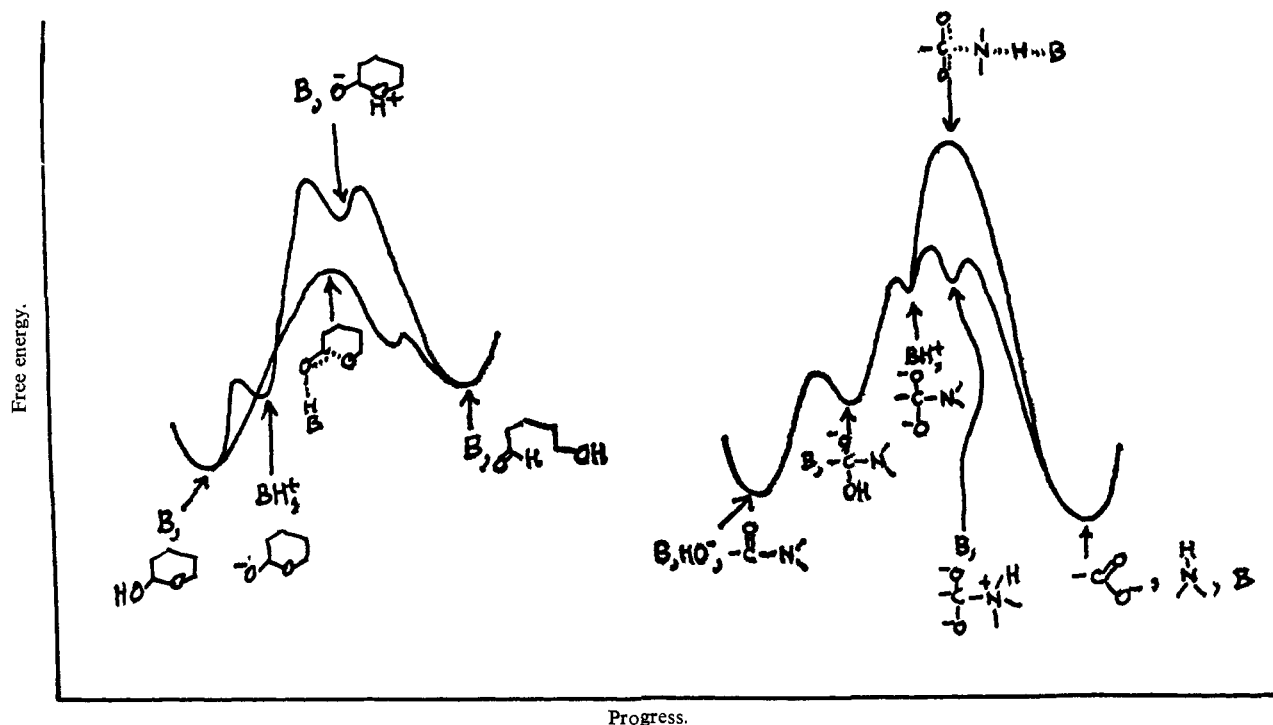
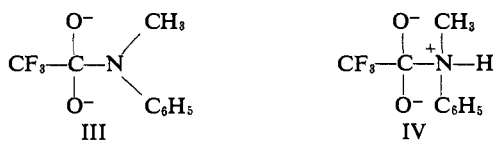


Figure 2. Hypothetical free energy diagrams for the mutarotation of glucose and the hydrolysis of 2,2,2-trifluoro-N-methylacetanilide.

elimination of the alkoxide ion from the carbonyl group.⁵

We suggest, therefore, that the carbon–nitrogen bond in the activated complex for hydrolysis of I is *not* undergoing cleavage. Instead, the rate-determining step is a simple proton-transfer reaction to form either III^{17a} (via eq 4a and 5a) or IV^{17b} (via eq 4b and 5b).



The species thus formed must then decompose toward products more rapidly than it abstracts a proton from solvent (in the case of III) or tautomerizes (in the case of IV), presumably *via* proton donation to solvent. Consultation of the tables of rate constants for proton-transfer reactions given by Eigen and his co-workers¹⁸ reveals no particularly good models for these reactions but suggests that the reaction of such species with solvent will proceed with rate constants of the order 10^6 – 10^{10} sec^{-1} . A simple proton transfer can thus be the sole rate-determining process if decomposition of III or IV toward products occurs with a first-order rate constant in the range 10^7 – 10^{11} sec^{-1} . If $\Delta S^* \sim 0$ for this unimolecular decomposition, activation energies of 3–8 kcal/mole will produce rate constants of these magnitudes. Such values are probably not unreasonable¹⁹ for decomposition of IV, which leads to the stable products trifluoroacetate ion and N-methylaniline, and

(17) (a) This is the mechanism originally suggested by S. S. Biechler and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 4927 (1957), and later rejected by us.⁸ (b) This intermediate was proposed for anilide hydrolysis on the basis of substituent effect data by M. L. Bender and R. J. Thomas, *ibid.*, **83**, 4183 (1961).

(18) M. Eigen, W. Kruse, G. Maass, and L. DeMaeyer, *Progr. Reaction Kinetics*, **2**, 285 (1964).

(19) $\Delta H^* = 6 \pm 1$ kcal/mole for the over-all k_1 process; $\Delta H^* = 7 \pm 1$ kcal for the over-all k_2 process.^{2a}

for decomposition of III, corresponding to conversion of a dialkoxide ion to an amide ion.

The rate-determining formation of IV is favored by other considerations as well. Figure 2 presents our schematic conception of the “free-energy” diagrams for mutarotation of glucose and for hydrolysis of I. The mutarotation proceeds by ordinary classical general base catalysis (or by its “inverse” variant) because the free energy of the zwitterion analogous to IV greatly exceeds that of the activated complex for the classical route, which resembles a specifically solvated alkoxide ion. The corresponding activated complex for the hydrolysis of I, on the other hand resembles a specifically solvated amide (R_2N^-) ion. Because of the high energy of amide ions relative to alkoxide ions, and the low energy of ammonium ions relative to oxonium ions, we postulate that the classical activated complex is of higher energy than the zwitterion IV in the hydrolysis of I. Thus the zwitterionic route, with rate-determining proton transfer, is followed by the system.

The values of the rate constants k_1 and k_2 are not inconsistent with this formulation. The steps leading to the k_1 activated complex are (i) addition to the carbonyl group (equilibrium constant K_{add}); (ii) ionization of the adduct to its conjugate base III and hydronium ion (equilibrium constant K_{ion}); (iii) rate-determining reaction of III and hydronium ion (rate constant k_r). Thus $k_1 = k_r K_{\text{ion}} K_{\text{add}} = 2 \text{ M}^{-1} \text{ sec}^{-1}$. If we assume²⁰ $K_{\text{ion}} \sim 10^{-10} \text{ M}$ and $K_{\text{add}} \sim 2 \text{ M}^{-1}$, then the reasonable value¹⁸ $k_r = 10^{10} \text{ M}^{-1} \text{ sec}$ is obtained. The k_2 activated complex is formed *via* (i) as above, (ii') ionization of the adduct by hydroxide ion to III (equilibrium constant $10^{14} K_{\text{ion}} \sim 10^4$), and (iii') reaction of III with solvent water in a rate-determining step (rate constant k_r').

(20) C. Gustafsson and M. Johanson, *Acta Chem. Scand.*, **2**, 42 (1948), found this value for chloral hydrate. We assume that the electron-releasing effect of O^- (*vs.* OH) is approximately balanced by the electron-withdrawing effects of CF_3 and R_2N (*vs.* CCl_3 and H).

Now $k_2 = k_r'10^{14}K_{\text{ion}}K_{\text{add}} = 2200 M^{-2} \text{ sec}^{-1}$. This yields $k_r' \sim 0.1 \text{ sec}^{-1}$ which seems rather small but not impossible.

If this very speculative analysis is valid, it is to be expected that general base catalyzed reactions which can be formulated according to structure II will fall into two classes, one involving proton transfer as the rate-determining step and the other observing the solvation rule,⁵ the choice depending on the stability of the leaving group. Compounds with good leaving groups should react by a pathway analogous to that of mutarotation, while those with poor leaving groups should follow a route similar to the one deduced here. We hope our studies of heavy-atom isotope effects and structural influences in this system will elucidate these problems.

Isotope Effect on the Addition Step. The absence of an isotope effect on the addition step, in spite of a possible maximum inverse secondary effect of $k_{\text{D}_2\text{O}}/k_{\text{H}_2\text{O}} = 1.7$ (see above), is surprising but explicable in several ways. It is possible that bonding of the hydroxide to the substrate has not proceeded to a great degree at the activated complex for addition and that the resulting small inverse effect is canceled to within experimental error by a regular effect arising from solvent reorganization. However, the similarity of the activation parameters for formation of the addition-activated complex (eq 3) and for formation of the solvent-catalyzed elimination-activated complex (eq 4) indicates similar structures for the two activated complexes,² favoring a strong hydroxide-substrate bond. If this is indeed the case, an inverse isotope effect of nearly 1.7 must be canceled by a regular effect of about the same magni-

tude, presumably from solvent reorganization. We have no data now which permit a choice between these possibilities, but if the latter is the correct explanation, some revision of the estimated isotope effects given above is required. Assuming $K_a^{\text{H}_2\text{O}}/K_a^{\text{D}_2\text{O}} = 1.0$, for the addition equilibrium, we obtain $(k_1^{\text{H}_2\text{O}}/k_1^{\text{D}_2\text{O}})_{\text{sec}} = 1.27$ and $(k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}})_{\text{sec}} = 0.82$ for the secondary contributions, and $(k^{\text{H}_2\text{O}}/k^{\text{D}_2\text{O}})_{\text{pri}} = 2.6 \pm 1$ and $(k_2^{\text{H}_2\text{O}}/k_2^{\text{D}_2\text{O}})_{\text{pri}} = 2.6 \pm 1$ for the primary effects. These results do not support the conclusion that rate-determining proton transfer is occurring, since the primary isotope effects yield $n_1 \sim 0.15$ (Figure 1), no longer in agreement with the value of the Brønsted β . We hope our further work will resolve the dilemma.

Experimental Section

An approximately decinormal solution of sodium deuterioxide in heavy water was prepared by the method of Morgan²¹ and standardized. From this stock solution, the various deuterioxide solutions used for the kinetic runs were prepared by suitable dilutions with heavy water, adding in every case the calculated amount of dry potassium chloride. The 2,2,2-trifluoro-N-methylacetanilide was also dissolved in heavy water inside the drybox. The kinetic methods were identical with those reported previously.⁸

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(21) C. R. Morgan, Ph.D. Thesis, Massachusetts Institute of Technology, 1963, p 19.

Catalysis of a Cycloaddition Reaction by Rhodium on Carbon

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Abstract: The catalysis of a cycloaddition reaction by a noble metal hydrogenation catalyst is described. Refluxing norbornadiene with 5% rhodium on carbon converts the hydrocarbon in nearly quantitative yield to a product of which 70 to 80% is a mixture of dimers and 20 to 30% a trimer. The dimers consist mainly of two products, which the nmr spectra indicate are stereoisomers of structure IV. Small amounts of dimer I are also formed. The nmr spectrum of the trimer indicates that it is VI. The stereochemistry of IV and VI are discussed. The remarkable efficacy of rhodium in catalyzing the oligomerization of norbornadiene is shown by its ability to effect the reaction quickly and quantitatively at reflux (and slowly at room temperature) and to effect formation of the trimer.

The catalysis of reactions that outwardly appear to be simple cycloadditions is unusual because these are not generally subject to catalysis and significant because they are of considerable utility in synthesis.² Such outwardly simple cycloaddition reactions as the cyclooligomerization of acetylenes,³ butadiene,⁴ and

norbornadiene⁵ are catalyzed by a variety of transition metal complexes. In the case of norbornadiene, the

p 380 ff; (c) G. N. Schrauzer, *Chem. Ber.*, **94**, 1403 (1961); (d) E. M. Arnett and J. M. Bollinger, *J. Am. Chem. Soc.*, **86**, 4729 (1964); (e) U. Krüerke and W. Hübel, *Chem. Ber.*, **94**, 2829 (1961); (f) A. T. Blomquist and P. M. Maitlis, *J. Am. Chem. Soc.*, **84**, 2329 (1962); (g) J. L. Boston, D. W. A. Sharp, and G. Wilkinson, *J. Chem. Soc.*, 3488 (1962).

(4) G. Wilke, *Angew. Chem. Intern. Ed. Engl.*, **2**, 105 (1963).

(5) (a) R. Pettit, *J. Am. Chem. Soc.*, **81**, 1266 (1959); (b) C. W. Bird, R. C. Cookson, and J. Hudec, *Chem. Ind. (London)*, 20 (1960); (c) C. W. Bird, D. L. Colinese, R. C. Cookson, J. Hudec, and R. O. Williams, *Tetrahedron Letters*, 373 (1961); (d) G. N. Schrauzer and S. Eichler, *Chem. Ber.*, **95**, 2764 (1962); (e) D. R. Arnold, D. J. Trecker, and E. B. Whipple, *J. Am. Chem. Soc.*, **87**, 2596 (1965); (f) P. W. Jolly, F. G. A. Stone, and K. MacKenzie, *J. Chem. Soc.*, 6416 (1965).

(1) To whom inquiries should be sent.

(2) R. Huisgen, R. Grashey, and J. Sauer, "The Chemistry of the Alkenes," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 739 ff.

(3) (a) G. N. Schrauzer, P. Glockner, and S. Eichler, *Angew. Chem. Intern. Ed. Engl.*, **3**, 185 (1964); (b) H. Zeiss, "Organometallic Chemistry," H. Zeiss, Ed., Reinhold Publishing Corp., New York, N. Y., 1960,