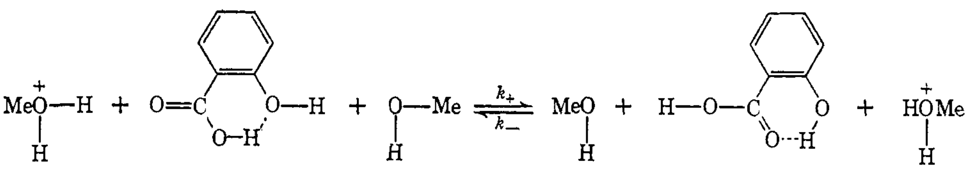
Proton Exchange and Hydrogen Bonding of Salicylic Acid in Methanol[1]

Mohindar S. Puar and Ernest Grunwald

Contribution from the Lecks Chemical Laboratories, Brandeis University, Waltham, Massachusetts 02154. Received March 14, 1967

Abstract: Carboxyl and hydroxyl protons of salicylic acid exchange with hydroxyl protons of methanol in independent, parallel reactions. Kinetic data were obtained at −80 and −95° for uncatalyzed and acid-catalyzed exchange. Uncatalyzed exchange of the carboxyl protons is fast, relative to benzoic acid, suggesting that intramolecular hydrogen bonding is slight. Acid-catalyzed exchange of both carboxyl and hydroxyl protons is relatively very slow, suggesting the formation of a stable bidentate hydrogen-bonded complex with methyloxonium ion. There was no evidence that exchange occurs by proton chain mechanisms involving both carboxyl and hydroxyl protons.

We have measured rates of exchange of carboxyl and hydroxyl protons of salicylic acid and of hydroxyl protons of methanol in the presence of dilute HCl. This system is of interest because of the possibility that proton transfer might occur rapidly along a hydrogen-bonded chain, shown in (1), consisting of $MeOH_2^+$, CO_2H, *o*-OH, and MeOH. A chain mechanism of proton transfer (often called a *Grotthus mechanism* after John Dalton's contemporary who first suggested it[2]) can account for the high conductivity of ice doped with HF.[3] In liquid solution, chain mechanisms of proton transfer are possible in principle, but the longest chain that has been demonstrated to date involves the transfer of three protons.[3-5]



(1)

We found, from nmr measurements of lifetime broadening, that carboxyl and *o*-OH protons of salicylic acid exchange in methanol at widely different rates. We also found, from nmr measurements of exchange broadening of the hydroxyl protons of methanol, that the carboxyl and *o*-OH protons of salicylic acid exchange with protons of methanol rather than with each other (see Figure 1) We infer from these facts that the chain mechanism shown in (1) is insignificant relative to processes in which the carboxyl and *o*-OH groups react separately.[6]

Let $R_{\mathrm{CO_2H}}$, $R_{o\text{-}\mathrm{OH}}$, and R_{MeOH} denote the rate of exchange of the respective protons. Let [S] denote the molar concentration of salicylic acid and $[H^+]$ that of the solvated hydrogen ion. Our nmr data are then consistent with rate laws 2, 3 and 4. Rate constants based on these rate laws are listed in Table I; a typical kinetic plot is shown in Figure 2.

Equations 2 and 3 are exactly analogous to the rate laws for proton exchange between benzoic acid or phenol and acidic methanol.[7] We shall therefore suppose that the reactions that take place are similar, and identify the rate constants as follows.

$$R_{\mathrm{CO_2H}} = k_1[\mathrm{S}] + k[\mathrm{S}][\mathrm{H}^+] \tag{2}$$

$$R_{o\text{-}\mathrm{OH}} = k_3[\mathrm{S}][\mathrm{H}^+] \tag{3}$$

$$R_{\mathrm{MeOH}} = R_{\mathrm{CO_2H}} + R_{o\text{-}\mathrm{OH}} \tag{4}$$

Values of k_1 and k for benzoic acid and of k_3 for phenol are included in Table I. The fact that k_1 for salicylic acid is substantially greater than k_1 for benzoic acid suggests to us that intramolecular hydrogen bonding of salicylic acid is negligible in methanol. If either of structures I or III were dominant, the carboxyl group would be highly unsymmetrical and reaction 5 would be relatively slow. On the other hand, the fact that both k and k_3 are substantially smaller for salicylic acid than for benzoic acid or phenol suggests to us that a hydrogen-bonded complex such as IV, in which $MeOH_2^+$ provides a relatively strain-free bridge between the *o*-CO_2H and OH groups, might be unusually stable.

Previous evidence indicates that the extent of intramolecular hydrogen bonding depends on the solvent. In *nonpolar* solvents it is clear from nmr chemical and infrared frequency shifts that molecules like those of salicylic acid or 2-hydroxybenzaldehyde form intramolecular hydrogen bonds.[8,9] However, these hydrogen bonds are sterically strained, and in hydroxylic solvents the formation of hydrogen bonds to solvent

---

(1) Work supported by the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment is made to the donors of that fund.

(2) C. J. D. von Grotthus, *Ann. Chem.*, **58**, 54 (1806).

(3) M. Eigen and L. De Maeyer, *Proc. Roy. Soc.* (London), **A247**, 505 (1958).

(4) E. Grunwald, C. F. Jumper, and S. Meiboom, *J. Am. Chem. Soc.*, **85**, 522 (1963).

(5) E. Grunwald and M. Cocivera, *Discussions Faraday Soc.*, **39**, 105 (1965).

(6) A detailed discussion is given in the Experimental Section.

(7) (a) E. Grunwald and C. F. Jumper, *J. Am. Chem. Soc.*, **85**, 2051 (1963); (b) E. Grunwald, C. F. Jumper, and M. S. Puar, *J. Phys. Chem.*, **71**, 492 (1967).

(8) C. J. W. Brooks and J. F. Morman, *J. Chem. Soc.*, 3372 (1961).

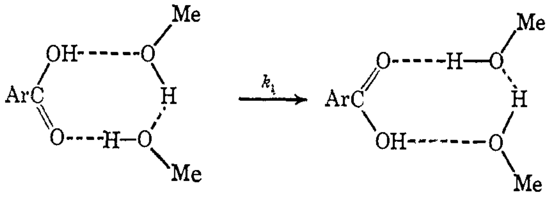
(9) A. L. Porte, H. S. Gutowsky, and I. M. Hunsberger, *J. Am. Chem. Soc.*, **82**, 5057 (1960).

Table I. Rate Constants for Proton Exchange in Methanol[a]

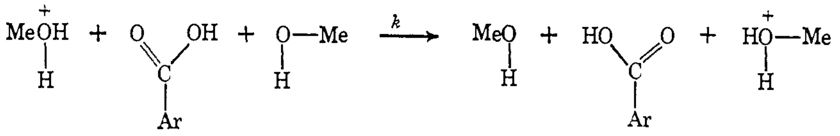
Substrate	Temp, °C	k_1, sec^{-1}	k, sec^{-1} M^{-1}	k_3, sec^{-1} M^{-1}
Salicyclic acid	−79.2	440 ± 30	$(13.5 \pm 0.5) \times 10^4$	$(5.8 \pm 0.5) \times 10^3$
	−94.9	130 ± 30	2.4×10^4	1.5×10^3
Benzoic acid[7]	−81.6	126	5.1×10^6	
Phenol	−82.4			6.2×10^6

[a] Rate constants are defined by the rate laws 2 and 3.

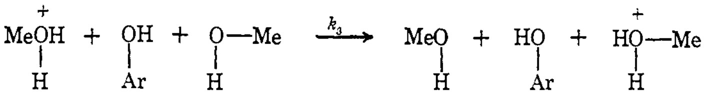
molecules might be favored. Thus the reaction of hydroxide ion with 2-hydroxybenzaldehyde in water is probably diffusion controlled,[10] whereas similar reactions that require the breaking of internal hydrogen bonds are not.[10,11] The high acid strength of salicylic acid in water[12] indicates internal hydrogen bonding in the anion, but not necessarily in the acid.[13]



(5)



(6)



$$\underset{H}{Me\overset{+}{O}H} + \underset{Ar}{OH} + \underset{H}{O{-}Me} \xrightarrow{k_3} \underset{H}{MeO} + \underset{Ar}{HO} + \underset{H}{H\overset{+}{O}{-}Me}$$

(7)

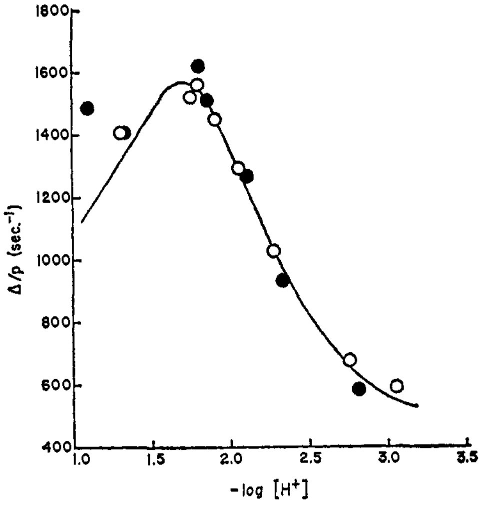


Figure 1. Plot of Δ/p *vs.* $-\log [H^+]$ for the hydroxyl proton resonance of methanol at −79.2°. Δ is the observed exchange broadening; $p = [S]/([MeOH] + [S])$. Open circles, $[S] = 0.55\ M$; closed circles, $[S] = 0.22\ M$; smooth curve, $\Delta/p = R_{CO_2H}[S]\delta_{CO_2H}^2/(R_{CO_2H}^2 + [S]^2\delta_{CO_2H}^2) + R_{o\text{-}OH}[S]\delta^2_{o\text{-}OH}/(R_{o\text{-}OH}^2 + [S]^2\delta_{o\text{-}OH}^2)$. See eq 2 and 3 and rate constants in Table I.

Experimental Section

Materials. Reagent grade salicylic acid was recrystallized from distilled water and dried over magnesium perchlorate before use. Methanol was dried and purified as described previously.[7] Hydrogen chloride was generated from sodium chloride and sulfuric acid in an all-glass apparatus. The dry gas was transferred directly to a flask containing pure methanol and dissolved. Preparation and standardization of solutions were according to standard quantitative procedures.

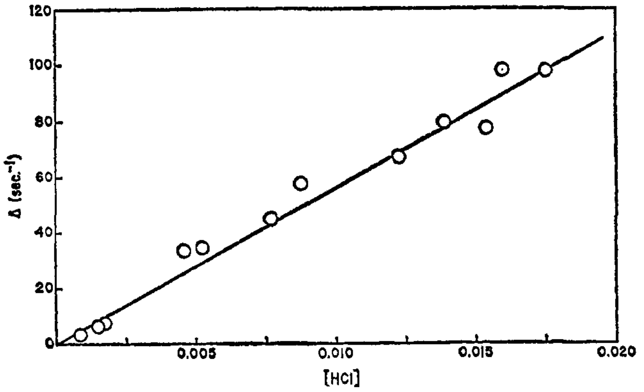


Figure 2. Plot of observed exchange broadening, Δ, of the salicyl hydroxyl proton resonace *vs.* HCl concentration, −79.2°. $\Delta = R_{o\text{-}OH}/[S]$.

Nmr Measurements. All rate measurements of proton exchange were based on slow-passage nmr spectra obtained at 56.4 Mhz under conditions of small or negligible radiofrequency saturation. All solutions were freshly prepared just before the measurements, and there was no evidence that esterification took place at a notable rate. Temperature control was precise to ±0.2° at −80° and ±0.3° at −95°.

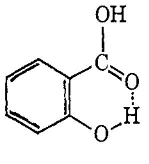
---

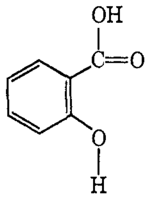
(10) M. Eigen, W. Kruse, G. Maass, and L. De Maeyer, *Progr. Reaction Kinetics*, 2, 285 (1964).

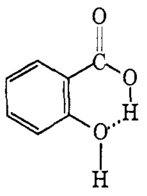
(11) M. H. Miles, E. M. Eyring, W. W. Epstein, and M. T. Anderson, *J. Phys. Chem.*, 70, 3490 (1966).

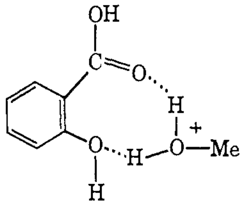
(12) H. C. Brown, D. H. McDaniel, and O. Häfliger in "Determination of Organic Structures by Physical Methods," E. A. Braude and F. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955, p 628.

(13) F. H. Westheimer and O. T. Benfey, *J. Am. Chem. Soc.*, **78**, 5309 (1956).


I


II


III


IV

Calculation of rates from nmr line widths followed established procedures.[7,14,15] The following chemical shifts (in parts per million) were used in the rate calculations: methanol OH, 0.00 (internal standard); salicyl OH, −5.62 (−103°), −5.66 (−80°); salicyl CO_2H, −7.91 (−103), −7.89 (−80°, assumed). At −103°, the areas under the salicyl OH and CO_2H resonances were equal, within the experimental error.

Kinetics of Proton Exchange When Reaction 1 Is Dominant. We shall assume that the rates of interconversion of I $\rightleftarrows$ II $\rightleftarrows$ III (see above) are fast relative to the rate of reaction 1. This is a reasonable assumption because the relaxation time for proton exchange was found to be greater than 5×10^{-4} sec in all experiments. This is considerably longer than known relaxation times for breaking hydrogen bonds in liquid solution[16] and also longer than relaxation times for the rotation of the OH group in most *ortho* hydrogen-bonded phenolic *solids.*[17] Furthermore, the salicyl OH proton resonance in the absence of exchange is a single, sharp line whose width is only slightly greater than that of the hydroxyl resonance of *p*-bromophenol ($1/T_2$ = 10 and 7 sec^{-1}, respectively.)

If the equilibrium I $\rightleftarrows$ II $\rightleftarrows$ III is established rapidly relative to the rate of reaction 1, then we predict that, when reaction 1 is dominant, $R_{CO_2H} = R_{o\text{-}OH} = R_{MeOH} = k_+[III] + k_-[I] = 2k_+[III] = 2k_-[I]$. These equalities are derivable from simple stoichiometric considerations and microscopic reversibility in a system at equilibrium. Since, in fact, $R_{o\text{-}OH} << R_{CO_2H} \approx R_{MeOH}$, reaction 1 cannot be very important.

---

[14] J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chapter 10.

[15] For theory of exchange broadening of the dominant line in a proton system consisting of several lines, see S. Meiboom *J, Chem. Phys.*, **34**, 375 (1961).

[16] See, for example, M. Eigen, *Chem. Eng. News*., **41**, 38 (Dec 2, 1963).

[17] R. J. Meakings, *Trans. Faraday Soc*., **51**, 371 (1966).

Rate Constants for the Dissociation of Amine–Water Hydrogen Bonds and the Effect of Nonpolar Groups in Aqueous Solution[1]

Ernest Grunwald and E. K. Ralph, III

Contribution from the Lecks Chemical Laboratories, Brandeis University, Waltham, Massachusetts 02154. *Received March 14, 1967*

Abstract: It is shown that the rate constant, k_H, for breaking the $R_3N \cdot HOH$ hydrogen bond measures the rate of diffusion of the water molecule into bulk solvent. In sulfuric acid–water mixtures, over a fivefold range of bulk viscosity η, k_H remains proportional to η^{-1}. Substituent effects of nonpolar R groups are large; k_H ranges from 2.2×10^{11} sec^{-1} for H_3N to 2.7×10^9 sec^{-1} for $(PhCH_2)_2NCH_3$. k_H is a monotonic function of the partial molar volume of the amine, but not of its basicity. A simple calculation shows that the substituent effect on k_H is of the same magnitude as the London dispersion interaction between the water molecule and the nonpolar groups. The results are thought to provide a sensitive test as to whether special water structure is induced by the nonpolar groups. No evidence for special ice-like water structure is found.

In experimental studies of solvation one would like to measure the properties of specific solvent molecules at specific sites near the solute molecule, but with few exceptions one is able to measure only those properties that reflect the total solvent–solute interaction. For amines in aqueous solution, one property that might illuminate the solvation mechanism for a specific water molecule at a specific site is the rate constant, k_H, for breaking the hydrogen bond that exists between the amino nitrogen and a water molecule. We shall tentatively formulate this process as in eq 1.

$$R_3N\cdot\mathit{HOH} + \text{HOH(aq)} \longrightarrow R_3N\cdot\text{HOH} + \mathit{HOH}\text{(aq)} \quad (1)$$

Evidence has accumulated in the recent past[2-7] that k_H can be derived with fair accuracy from a kinetic analysis of proton exchange between the ammonium ion, R_3NH^+, and water in aqueous acid.

In this paper we wish to examine the process whose rate constant is k_H. We shall report new k_H values for amines of selected structure and recalculate certain older data for proton exchange in strong acid[3] with the

---

[1] This work was supported by the National Science Foundation under Grant GP 3921, and by the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment is made to the donors of that fund.

[2] C. G. Swain, J. T. McKnight, and V. P. Kreiter, *J. Am. Chem. Soc.*, **79**, 1088 (1957).

[3] M. T. Emerson, E. Grunwald, M. L. Kaplan, and R. A. Kromhout, *ibid.*, **82**, 6307 (1960).

[4] M. Sheinblatt, *J. Chem. Phys.*, **36**, 3103 (1962); **39**, 2005 (1963).

[5] E. Grunwald, *J. Phys. Chem.*, **67**, 2211 (1963).

[6] M. Sheinblatt and H. S. Gutowsky, *J. Am. Chem. Soc.*, **86**, 4814 (1964).

[7] E. K. Ralph and E. Grunwald, *ibid.*, **89**, 2963 (1967).