[CONTRIBUTION FROM THE SANITARY CHEMISTRY BRANCH OF THE U. S. ARMY CHEMICAL WARFARE LABORATORIES]

Kinetics of Some Metal Ion-catalyzed Hydrolyses of Isopropyl Methylphosphonofluoridate (GB) at 25°

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Hydrolysis of isopropyl methylphosphonofluoridate (GB) in water is catalytically accelerated by cerous, cupric and manganous ions. The active forms of these ions are most probably of the type $M(OH)(H_2O)_{x-1}^{z-1}$.

The introduction in recent years of toxic phosphorus-containing chemical warfare agents (nerve gases) has produced a need for rapid and convenient decontaminating methods for removing such substances from water and surfaces. Because of the potency of these compounds even in very dilute aqueous solution,[1] decontaminating reactions possessing high rate constants have been sought. A study of the effect of aquometallic ions on the hydrolysis rate of isopropyl methylphosphonofluoridate (GB) was indicated, both by the abnormally high rates of decomposition of GB in brackish waters[2] (which could be explained by the presence of trace quantities of heavy metal cations) and by extrapolation of the extraordinary enhancing effects of positively charged hydroxometallic ions[3] on the rates of other generally acid–base catalyzed reactions.[4] Furthermore, hydrolysis of this compound is strongly accelerated by certain copper complexes of heterocyclic nitrogen bases.[5] A number of other instances of metal ion-catalyzed hydrolysis of phosphorus esters also have been observed.[6]

The purpose of the present series of experiments was to study the effect of hydrated cupric, cerous and manganous ions on the hydrolysis of GB, and to attempt to correlate the results with known acid–base effects.

It was established that the hydrolysis is catalyzed by metal ions. Although the reaction at constant *p*H is first order with respect to each of the reactants (see data in Table I, cupric ion at *p*H 5.5), first-order kinetics were observed at approximately equal concentrations of reactants (Fig. 1). In bimolecular reactions in which the reactants are present in approximately equal concentrations, first-order kinetics generally are observed only if the concentration of one of the reactants remains constant. In one experiment the rate of decomposition of GB in the presence of an equimolar concentration of cupric ion was determined at constant *p*H. After approximately 80% of the phosphonofluoridate had been hydrolyzed, a quantity of GB, equal to that initially present, was added. The rates of decomposition of the two samples were, within the limits of experimental error, identical.

It was found that the observed first-order rate constants (k_1) varied with both the *p*H and metal ion concentration, but that the function $k_1[H_3O^+]/[M]$ (where [M] is the total concentration of metal ion) was relatively constant (Table I).

TABLE I

DATA FOR HYDROLYSIS OF GB AT VARIOUS CONCENTRATIONS[a] OF METAL AND HYDRONIUM IONS AT 25°

Metal ion (M)	No. of runs	$[M] \times 10^3$ (Molar)	*p*H	$k_1 \times 10^3$, min.$^{-1}$	$k_1[H_3O^+]/[M]$
Cu^{++}	2	1.0	5.0	11.8	1.2×10^{-4}
	1	1.0	5.5	51.3	1.6×10^{-4}
	1[b]	1.0	5.5	51.3	1.6×10^{-4}
	1	2.0	5.5	102.5	1.6×10^{-4}
	2	0.3	6.0	34.7	1.2×10^{-4}
	3	1.0	6.0	110.0	1.1×10^{-4}
				Average	1.4×10^{-4}
Ce^{+++}	1	1.0	4.5	0.40	12.6×10^{-6}
	1	1.0	5.2	1.20	7.5×10^{-6}
	1	1.0	5.6	4.33	10.9×10^{-6}
	2	0.5	6.1	4.33	5.9×10^{-6}
	1[b]	1.0	6.1	9.12	7.2×10^{-6}
	2	1.0	6.1	8.65	6.9×10^{-6}
	1[c]	1.0	6.1	8.15	6.5×10^{-6}
	1[b]	2.0	6.3	19.8	5.0×10^{-6}
	3[b]	1.0	6.4	27.7	11.0×10^{-6}
				Average	8.4×10^{-6}
Mn^{++}	2	10.0	6.0	2.35	2.4×10^{-7}
	1	10.0	6.5	5.33	1.7×10^{-7}
	1	50.0	6.5	23.9	1.5×10^{-7}
	1	10.0	7.0	14.7	1.5×10^{-7}
	1	50.0	7.0	57.8	1.2×10^{-7}
				Average	1.7×10^{-7}

[a] GB concentration 0.001 *M*, except as noted. [b] GB concentration 0.0005 *M*. [c] GB concentration 0.002 *M*.

In the *p*H region studied, the dominant metal ion species are the undissociated ions $Cu(H_2O)_4^{++}$, $Ce(H_2O)_6^{+++}$ and $Mn(H_2O)_6^{++}$ (in general $M(H_2O)_x^z$) with small amounts of the monohydroxo species $Cu(OH)(H_2O)_3^+$, $Ce(OH)(H_2O)_5^{++}$ and $Mn(OH)(H_2O)_5^+$ (in general $M(OH)(H_2O)_{x-1}^{z-1}$), respectively. Their concentrations are related[7] according to the general equation

$$K_A = \frac{[M(OH)(H_2O)_{x-1}^{z-1}][H_3^+O]}{[M(H_2O)_x^z]}$$

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(1) J. Epstein, *Public Health Reports*, **71**, 955 (1956).

(2) J. Epstein and V. E. Bauer, Chemical Corps Medical Division Report No. 147 (1948).

(3) R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941.

(4) M. Kilpatrick and M. L. Kilpatrick, *J. Phys. Colloid Chem.*, **53**, 1371 (1949), showed that diisopropyl phosphorofluoridate (DFP), the behavior of which is qualitatively similar to that of GB, exhibits general acid–base catalyzed hydrolysis.

(5) T. Wagner-Jauregg, B. E. Hackley, Jr., T. A. Lies, O. O. Owens and R. Proper, THIS JOURNAL, **77**, 922 (1955).

(6) E. Bamann, L. F. Sanchez and H. Trapmann, *Chem. Ber.*, **88**, 1846 (1955), and previous work of Bamann cited therein; W. W. Butcher and F. H. Westheimer, THIS JOURNAL, **77**, 2420 (1955); J. A. A. Ketelaar, H. R. Gersmann and M. Beck, *Nature*, **177**, 392 (1956).

(7) The relationship expressed here is most probably a simplification of actual conditions, inasmuch as hydrated metal ions are known to enter into various types of polymerization reactions. It has been assumed that polymerization reactions are negligible in the concentrations and *p*H's used in these experiments (see ref. 14).

where K_A is the acid dissociation constant of the hydrated metal ion.

Thus, the concentration of the monohydroxo species is inversely proportional to the fraction $[H_3O^+]/[M(H_2O)_x^z]$ or $K_w/[OH^-][M(H_2O)_x^z]$ where K_w equals the ion product of water, and, from the kinetic data above, no decision can be made as to whether the decomposition is facilitated by an attack of the monohydroxo species or of both the hydrated metal ion and hydroxyl ion.

On the basis of other reactions of GB and DFP, for which mechanisms have been postulated, we are inclined to favor a mechanism involving the monohydroxo species. The following discussion sets forth the pertinent background.

Where sufficient investigation has been made, series of related reagents have given typical Brönsted relationships.[4,8–10] It has further been observed that although basic catalysis is considerably more effective than acid catalysis,[4] the latter may be considered to play a role of importance in reactions best explained by push–pull (concerted attack) mechanisms.[8–10] Such mechanisms require reagents characterized by centers of both high and low electron density. A dissociated aquometallic ion, of the type $M(OH)(H_2O)_{x-1}^{z-1}$, which has a basic region in the hydroxyl group and an acidic region in the metal might qualify as such a reagent and, indeed, Wagner-Jauregg and co-workers have considered copper chelates of heterocyclic nitrogen bases to act in this fashion.[5] In examining old data[3] on the general base catalysis of the mutarotation of glucose, an inexplicably high activity was noted in the case of two metal complexes. These were the only catalysts in the published series for which centers of high and low electron density can be postulated, and which might, therefore, be expected to function through a push–pull mechanism. The plausibility of such an explanation is increased by other, better substantiated, instances of this type of mechanism in the mutarotation reaction.[11] Finally, the role of metal ions in other examples of catalysis of organic reactions has likewise been recognized and catalysis mechanisms have been postulated.[12]

It is therefore proposed that the metal ion-catalyzed hydrolysis of GB actually takes place through positively charged hydroxometallic bases in a bimolecular mechanism. The second-order rate constant (k_2) equals

$$k_1/[M(OH)(H_2O)_{x-1}^{z-1}] = k_1[H_3O^-]/K_A[M(H_2O)_x^z] \cong k_1[H_3^+O]/K_A[M]$$

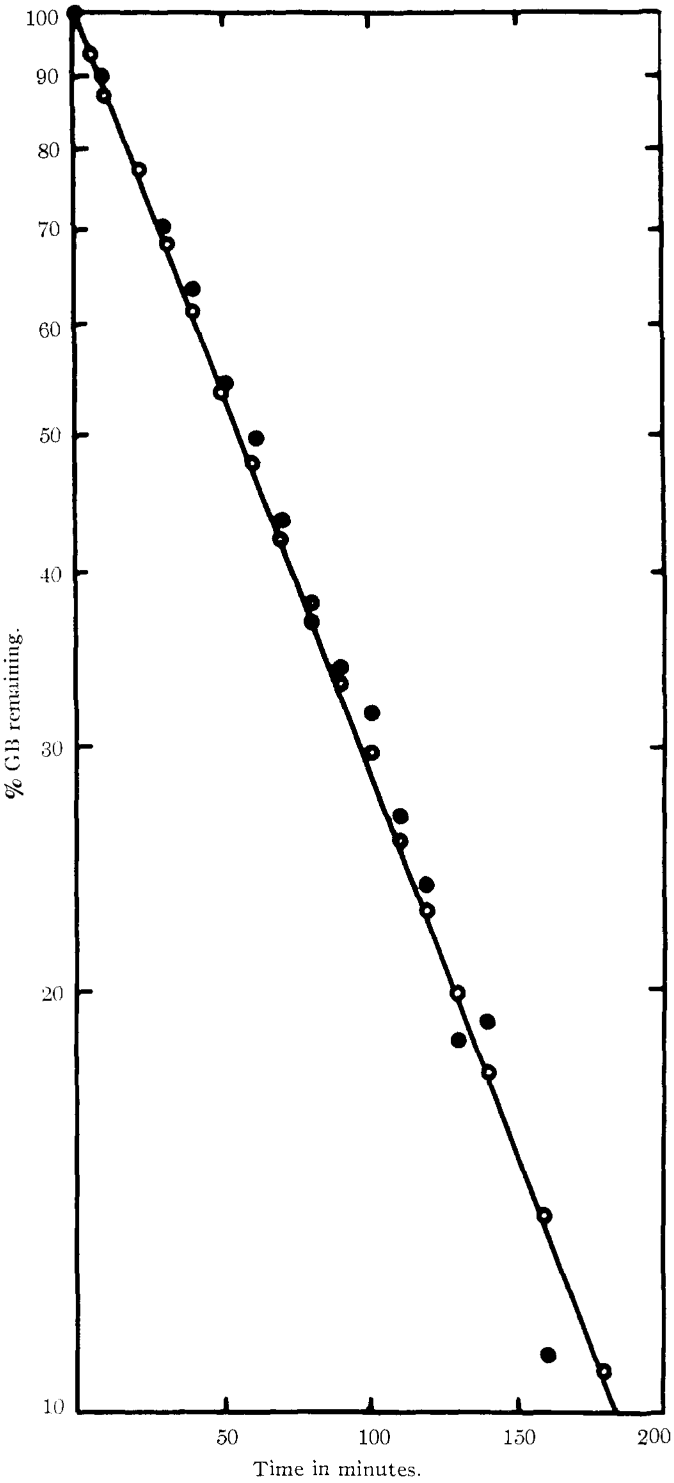

Fig. 1.—First-order plot of GB concentration with time; [GB] $= 1 \times 10^{-3}$ *M*; $[CuCl_2] = 1 \times 10^{-3}$ *M*; *p*H = 5.0; *T* = 25°: ●, H_2O_2–*o*-tolidine method; ○, NaOH titration.

From average values of $k_1[H_3^+O]/[M]$ in Table I and values of K_A from the literature for cupric ion[13]

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(8) J. Epstein, D. H. Rosenblatt and M. M. Demek, THIS JOURNAL, **78**, 341 (1956).

(9) B. E. Hackley, Jr., Ph.D. Dissertation, University of Delaware, 1956.

(10) R. Swidler, R. E. Plapinger and G. M. Steinberg, manuscript in preparation.

(11) C. G. Swain, THIS JOURNAL, **70**, 1119 (1948); **72**, 4578 (1950); C. G. Swain and J. F. Brown, Jr., *ibid.*, **74**, 2534, 2538 (1952).

(12) F. H. Westheimer, *Trans. N. Y. Acad. Sci.*, **18**, 15 (1955).

(13) K. J. Pedersen, *Kgl. Danske Videnskab. Selskab. Math.-Fys. Medd.*, **20**, No. 7 (1943); *C. A.*, **38**, 4854 (1944). In the *p*H range and concentration concerned, the polymerization reactions of hydroxocupric ion are unimportant.

and cerous ion[14] of 1.07×10^{-8} and 5.0×10^{-10}, second-order rate constants of 1.2×10^4 and 1.7×10^4 l. mole.$^{-1}$ min.$^{-1}$, respectively, are obtained for these ions.

Although these hydroxometallic ions are considerably weaker bases than hydroxyl ion (K_A for hydroxyl ion $= 10^{-16}$), they are catalytically more active than the latter (for which $k_2 = 2 \times 10^3$).[15] This would tend to lend support to the view that a push–pull mechanism is involved.

Similar effects have also been observed in these laboratories with magnesium, calcium and uranyl ions. As might be expected, both calcium and magnesium, whose hydrated species have very small dissociation constants, showed this behavior only in alkaline media where the large hydrolytic effect of hydroxyl ions prevented quantitative measurement of the part played by the hydroxometallic ions. Uranyl ion, on the other hand, exhibited a marked effect in extremely dilute solution even at low *p*H levels.

Experimental

Reagents.—C.P. grade chemicals were used as purchased, without further purification. Cupric chloride was obtained as the dihydrate, manganous chloride as the tetrahydrate and cerous nitrate as the hexahydrate. GB of high purity was obtained from the Chemical Research Division of the Chemical Warfare Laboratories.

Apparatus.—In early experiments the Beckman model G *p*H meter was used. Later the *p*H was held constant with a Beckman model K automatic titrator set to deliver the smallest possible increments of titrant, and provided with a 5-ml. base-filled microburet graduated to 0.02 ml. Reaction temperature in a jacketed 250-ml. beaker was maintained at 25.0° by a Precision Scientific Co. constant temperature circulating bath. Reaction mixtures were constantly stirred with a 1-inch Teflon-covered magnetic stirring bar. A Klett–Summerson photoelectric colorimeter provided with a No. 42 filter was used in the analysis for GB.

Kinetic Measurements.—Solutions of GB and the metal salt (on the acid side) were mixed in the reaction vessel to give the required concentration of each, and the *p*H was adjusted with base from the microburet. The amount of base, V_t, required to keep the *p*H constant during the course of reaction (hydrolysis liberates one mole each of isopropylmethylphosphonic acid and hydrofluoric acid) was recorded against time. Basic hydrolysis and back titration of an aliquot of the GB stock gave the volume of base (V_∞) required at infinite time. Suitable corrections were applied to the data to account for initial acidity, withdrawal of samples and volume changes, and the corrected values of $(V_\infty - V_t)/V_\infty$, which represents the fraction of GB remaining, were plotted on semi-logarithmic paper. The plots were virtually linear; thus, the reactions exhibited first-order kinetics. In three experiments these results were confirmed by direct analysis for GB by the peroxide-*o*-tolidine method.[16] Most of the experiments were conducted in the *p*H range 5–6.5, in which the spontaneous hydrolysis rate of GB, due to catalysis by water and by hydroxyl and hydronium ions is negligible. From the slopes of the semi-logarithmic plots, the first-order rate constants, *k*, were calculated in the usual manner.[17] These varied with metal ion concentrations and *p*H. In experiments with manganous and cerous ions, nitrogen had to be bubbled through the reaction mixtures to prevent oxidation, which would have changed the concentration of the desired metal ion and caused an anomalous increase in the uptake of base.

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(16) B. Gehauf, J. Epstein, G. B. Wilson, B. Witten, S. Sass, V. E. Bauer and W. H. C. Rueggeberg, *Anal. Chem.*, **29**, 278 (1957).

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On the *cis-trans* Equilibria in *o*-Halophenols

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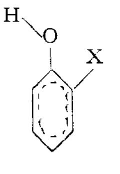
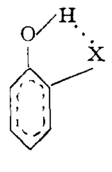
The ν_{OH} stretching frequencies of pure *o*-halophenols show a doubled band having a *trans/cis* ratio considerably smaller than previously observed. Both the $\Delta\nu$ shift and the *trans/cis* ratio increase in the order F < Cl < Br < I. An explanation is offered for this effect based on a destabilization of the *trans* configuration compared to that of the *cis*.

The vibrational spectra of the *o*-halophenols, first investigated in the near infrared region by Wulf, *et al.*,[1] show a doubling of the hydroxyl stretching frequencies at concentrations low enough to prevent intermolecular association. One of the bands occurs at a nearly normal phenolic position while the other, which is always much more intense, is shifted to lower frequencies by an amount dependent on the halogen. Since comparable effects do not occur in the spectra of phenols *o*-substituted with other types of basic atoms such as oxygen, nitrogen or sulfur, the doubling is somewhat anomalous and a complete explanation has not yet been found.

Pauling,[2] and subsequently others,[3,4] ascribed this doubling to an equilibrium involving *cis* and *trans* structures of the type





According to this hypothesis, the O–H bond is partially constrained to the aromatic plane because of resonance interaction between the aro-

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(1) O. R. Wulf, U. Liddel and S. B. Hendricks, THIS JOURNAL, **58**, 2287 (1936).

(2) L. Pauling, *ibid.*, **58**, 94 (1936).

(3) L. R. Zumwalt and R. M. Badger, *ibid.*, **62**, 305 (1940).

(4) M. M. Davies, *Trans. Faraday Soc.*, **36**, 333 (1940).