

zene at 50°, and in tetralin at 92°.²⁸ All polymerization experiments were carried out in sealed and degassed ampoules, the polymer isolated by precipitation with methanol and compared with a control experiment. Polymerization of acrylonitrile is also induced by dianisoyl diimide in ethanol-carbon tetrachloride at 50° and in benzene at 75° and by *p*-methoxy-*p*'-nitrodibenzoyl diimide in ethanol-carbon tetrachloride at 50°, in ethanol-benzene at 50°, and in benzene at 75°. Dibenzoyl diimide failed to initiate polymeri-

(28) L. Horner and W. Naumann, *Ann.*, **587**, 93 (1954), reported no polymerization in refluxing acrylonitrile or in refluxing acrylonitrile-tetralin under carbon dioxide.

zation of acrylonitrile in benzonitrile containing aniline at 75°. However, amines have been reported to inhibit the polymerization of acrylonitrile.²⁹ In none of our qualitative polymerization experiments has there been any noticeable effect of the acrylonitrile on the rate. This was also the case in a kinetic experiment in which *p*-methoxy-*p*'-nitrodibenzoyl diimide was decomposed in 50% ethanol-benzene containing 1% of acrylonitrile. Acrylonitrile does not inhibit the decomposition.

(29) C. J. Stehman, U. S. Patent 2,607,795, August 19, 1952.

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[CONTRIBUTION FROM THE SANITARY CHEMISTRY BRANCH, CHEMICAL CORPS MEDICAL LABORATORIES]

Kinetics of the Reaction of Isopropyl Methylphosphonofluoridate with Catechols at 25°

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The reaction of Sarin (isopropyl methylphosphonofluoridate) with catechol or one of its nuclearly substituted derivatives is of second order; the rate is proportional to the first power of both the Sarin concentration and singly dissociated catechol ion. The second-order rate constant (l. mole⁻¹ min.⁻¹) for the reaction of a particular catechol derivative may be expressed as a function of the basic dissociation constant of the catechol ion, according to the equation $k_2 = 2.57 \times 10^{-6} K_B^{0.89}$. The enhanced reactivity of the catechols toward Sarin as compared to phenols, and the relationship of k_2 to K_B are in agreement with the proposed reaction mechanism.

Sarin (isopropyl methylphosphonofluoridate) is among the more potent of the German nerve gases.¹ It resembles diisopropylphosphorofluoridate in chemical behavior but reacts more rapidly with most reagents. Our purpose, in the present study was to obtain an understanding of the behavior of catechols,² which react more rapidly than phenols,^{3,4} with nerve gases, using Sarin as a model compound, in order to permit prediction of reactive catechol structures. It has been shown³ that the reaction rates of phosphorofluoridate esters with catechols, which, in aqueous solution, increase with rising *p*H, are consistent with the assumption that the rate is dependent upon the concentrations of the dissociated catecholate ions; but the effect of substituents on the aromatic ring has not, up to now, been clarified.

At constant *p*H the rate of disappearance of Sarin when a catechol is present in sufficient excess concentration is of first order. The first-order rate constant thus obtained, corrected for spontaneous hydrolysis, (*i.e.*, $k_1 - k_s$) where k_1 is the observed first-order rate constant, k_s is the rate constant for hydrolysis of Sarin in catechol-free aqueous solution at the *p*H and buffer strength of the experiment, is proportional to the catechol concentration. Thus, an apparent second-order rate constant $k_2' = (k_1 - k_s)/[C]$ may be calculated, where $[C]$ is the molar concentration of catechol plus catecholate ion, and k_1 and k_s are as previously defined.

The apparent second-order rate constant, k_2' , for the reaction of unsubstituted catechol with Sarin over the *p*H range 6–9 varies directly with hy-

droxyl ion concentrations, but the corresponding constants for the more acidic mononitrocatechols approach constancy in the regions of the greatest monodissociation (Fig. 1). While k_2' varies with *p*H,

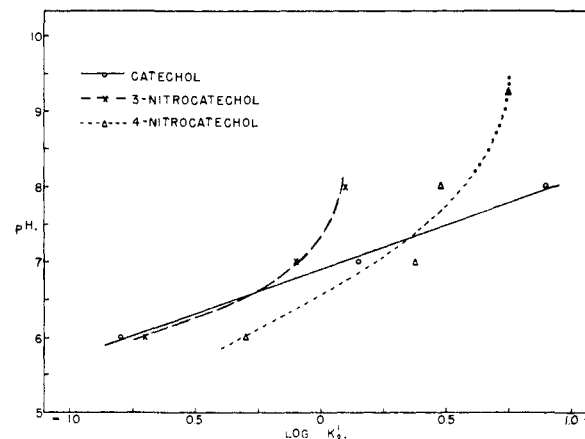


Fig. 1.—Plot of the log k_2' against *p*H for reactions between Sarin and catechol, 3-nitrocatechol and 4-nitrocatechol.

$k_2 = (k_1 - k_s)/[C^-]$ (where $[C^-]$ is the concentration of monocatecholate ion) remains constant over a range of *p*H values (Table I).

TABLE I

EFFECT OF *p*H ON RATE CONSTANTS FOR REACTION OF 3-NITROCATECHOL WITH SARIN

<i>p</i> H	k_1' (l. mole ⁻¹ min. ⁻¹)	k_s (l. mole ⁻¹ min. ⁻¹)	<i>p</i> H	k_1' (l. mole ⁻¹ min. ⁻¹)	k_s (l. mole ⁻¹ min. ⁻¹)
6	0.27	1.48	7	0.80	1.16
6	.24	1.33	8	1.31	1.37
7	.81	1.18	8	1.25	1.31

When $[H^+] =$ hydronium ion concentration, and K_A is known, $[C^-] = K_A[C]/([H^+] + K_A)$.

(1) Anon., *Chem. Eng. News*, **31**, 4676 (1953).

(2) "Catechol" will refer to the class of compounds that includes the parent compound (unsubstituted catechol) and its nuclearly substituted derivatives.

(3) B. J. Jandorf, T. Wagner-Jauregg, J. J. O'Neill and M. Stoberg, *This Journal*, **74**, 1521 (1952).

(4) K. B. Augustinsson, *Acta Chem. Scand.*, **6**, 949 (1952).

TABLE II
BIMOLECULAR RATE CONSTANTS FOR REACTION OF CATECHOLS WITH SARIN

Compound	K_B	k_2 (1. mole ⁻¹ min. ⁻¹)
Unsubstituted catechol	3.03×10^9	589
Protocatechualdoxime	4.76×10^8	158
Protocatechnitrile	5.26×10^7	22.6
2,3,4-Trihydroxyacetophenone	4.17×10^7	17.7
Protocatechualdehyde	2.27×10^7	8.5
4-Nitrocatechol	7.69×10^6	4.6
3-Nitrocatechol	4.54×10^6	1.5

A plot of average values (Table II, showing results of at least four runs per compound) of $\log k_2$ against $\log K_B$ ($K_B = 1/K_A$)⁵ shows a linear relationship (Fig. 2); the line of best fit gives the equation $k_2 = 2.57 \times 10^{-6} K_B^{0.89}$.

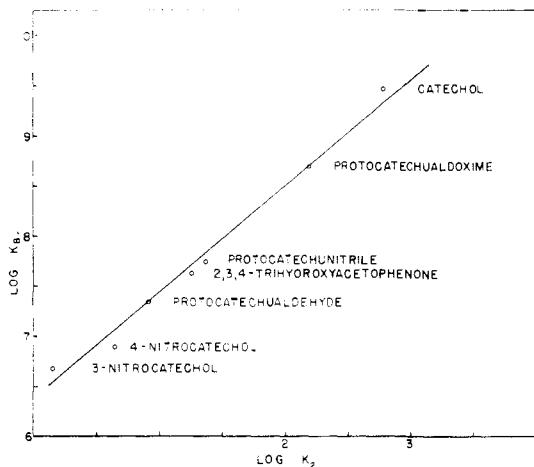


Fig. 2.—Relationship between $\log k_2$ and $\log K_B$ in the reactions between Sarin and a series of catechols.

Experimental

Apparatus.—A Precision Scientific Company constant temperature circulating bath maintained a jacketed cylindrical reaction vessel at $25 \pm 1^\circ$. When buffers were not used, pH was maintained by adding base from a 1-ml. capillary-tipped graduated pipet regulated by a screw-actuated hypodermic syringe. Colorimeter readings were made in a Klett-Summerson photoelectric colorimeter with No. 42 filter and pH was measured with a Beckman Model G pH Meter.

Materials.—Sarin, purified by distillation, was obtained from the Gassing Branch of the Chemical Corps Medical Laboratories. Unsubstituted catechol, m.p. 105° , was recrystallized twice from toluene. With the exception of 2,3,4-trihydroxyacetophenone, which was obtained through the courtesy of Professor William Mosher of the University of Delaware, substituted catechols were prepared in these laboratories.⁵ Other materials were of the best obtainable commercial grade.

o-Tolidine reagent consisted of 1% solution of recrystallized *o*-tolidine hydrochloride in water, kept cold when not in use. Perborate reagent was a 1.25% aqueous solution of sodium perborate, freshly prepared prior to use.

Procedure.—Early experiments with unsubstituted catechol were carried out in 0.01–0.05 *M* phosphate buffers but during all others pH was adjusted manually at short intervals with 0.2 *N* aqueous sodium hydroxide. In each experiment 100 ml. each of freshly prepared Sarin and catechol

(5) D. H. Rosenblatt, J. Epstein and M. Levitch, *THIS JOURNAL*, **75**, 3277 (1953); K_A for catechol from I. M. Heilbron, "Dictionary of Organic Compounds," Vol. 1, Oxford University Press, New York, N. Y., 1934, p. 245; K_A for 2,3,4-trihydroxyacetophenone = 2.4×10^{-4} , reported here for the first time.

solutions, adjusted to the desired pH were added simultaneously to the reaction vessel.

In general, the rate of disappearance of Sarin was followed colorimetrically. Aliquots were withdrawn from time to time for analysis. As checks, the rate constants obtained from the base uptake rates for three experiments with unsubstituted catechol at pH 7 (outside the natural buffer range of the catechol) were compared with the constants from colorimetric measurements; the two methods were in excellent agreement.

In all experiments initial catechol concentrations were at least four times the Sarin concentrations, with $[C]$ varying between 2×10^{-3} and $6 \times 10^{-2} M$ and Sarin concentrations between 5×10^{-4} and $10^{-3} M$.

Colorimetric analyses were performed by two modifications of the *o*-tolidine perborate method.⁵ In experiments with unsubstituted catechol, including all those with buffered media, a suitable aliquot of reaction mixture containing approximately 0.4 mg. of Sarin was added to a mixture of 10 ml. of 0.05 *M* phosphate buffer (pH 8.8), 10 ml. of aldehyde-free⁶ acetone, 2 ml. of *o*-tolidine reagent and 50 ml. water in a 100-ml. volumetric flask; this aliquot was immediately followed by 3 ml. of perborate reagent and the resulting mixture diluted to volume with water; the colorimeter reading was made 20 minutes after addition of the last reagent. In the remaining experiments with unsubstituted catechol, as well as with all other catechols, the procedure was altered, in that the volume of the aliquot was such as to contain approximately 0.04 mg. of Sarin, and 10 ml. of xylene was added before bringing the mixture to the volume. During the 20-minute color development period the flask was inverted a sufficient number of times to effect complete extraction of the yellow dye formed; the xylene volume was then separated and its color measured.

The spontaneous hydrolysis rate constants for Sarin in the absence of catechol for each experimental condition were determined to allow calculations of the k_2 values.

Because the reactions were designed to be of pseudo-first order, the half-lives $t_{1/2}$ could be obtained directly from plots of logarithm of colorimeter reading versus time. First-order constants k_1 or $k_2 = 0.693/t_{1/2}$.

Discussion

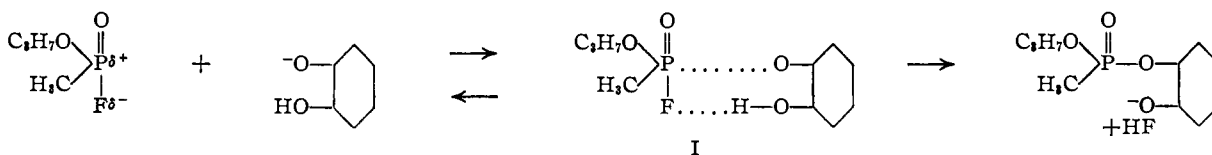
The dependency of reaction rate on Sarin and monocatecholate ion concentrations suggests that the mechanism be formulated with these two species. The disparity between the reactivities of phenols and catechols (of comparable dissociation constants) strongly suggests the participation of the undissociated *o*-hydroxyl group.⁷

In the first case the removal of fluorine is facilitated directly by the hydrogen of the undissociated hydroxyl group; in the second the mediation of a molecule of water in removing the fluorine is postulated.

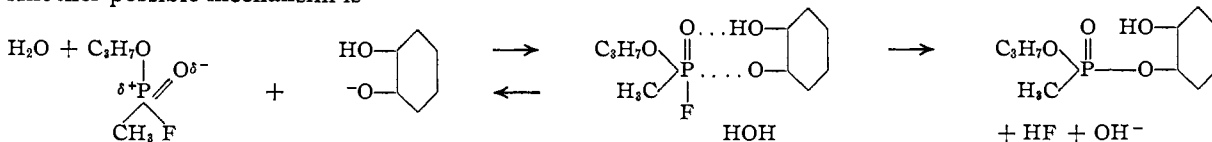
In a series of catechols, the relative values of the equilibrium constants which describe the initial step involving the formation of the Sarin-monocatecholate ion complex (and hence the magnitudes of the k_2 values) will increase with increasing basicity of the monocatecholate ion (Table II). At a given pH , however, outside the regions of greatest dissociation of the catechols, the concen-

(6) J. Epstein, to be published.

(7) That the undissociated *o*-hydroxyl group is involved in the reactivity is further demonstrated by a brief kinetic study on the reaction between Sarin and 3,4-dinitrocatechol at pH of 7.0 and 8.1 at 25° . At pH 7.0, k_2' was found to be 0.1335 l./mole⁻¹ min.⁻¹; at pH 8.1, k_2' was 0.085. Thus at pH 8.1, the reactivity of 3,4-dinitrocatechol is 63.5% that of the reactivity at 7.0. It can be shown from the dissociation constants of 3,4-dinitrocatechol, viz., $K_1 = 4.1 \times 10^{-6}$ and $K_2 = 5.4 \times 10^{-9}$, that the concentration of the monocatecholate ion at pH 8.1 is approximately 63% of that at pH 7.0, indicating the importance of the intact hydroxyl group *ortho* to the phenoxy ion and the relative ineffectiveness of the dicatecholate ion. Also, singly dissociated resorcinol and hydroquinone behave like phenoxides rather than like catecholates.



Another possible mechanism is



trations of the complexes (such as I) formed for two catechols of very different basicities may be close to one another due to the differences in the concentrations of the monocatecholate ions. This is the reason that all shown k_2' values are of the same order of magnitude. This can be shown more clearly from the experimentally derived relationship between the rate constants and the basicity of the catecholate ion. Since $k_2 = 2.57 \times 10^{-6} K_B^{0.89}$ and $k_2 = k_2'(K_B[H^+] + 1)$

$$k_2' = 2.57 \times 10^{-6} K_B^{0.89} / (K_B[H^+] + 1)$$

Thus considering the reactivities of two catechols at pH 6, one having a basic dissociation constant of 10^7 , the other 10^{10} , it is clear that the k_2' values will vary only by 3 to 4 times. By differentiating k_2' with respect to K_B , it can further be shown that, at a given pH, the maximum attainable value of k_2' will be reached at $K_B = 8.1/[H^+]$. Thus, the answer to the question as to which of the nuclearly substituted catechols will have the maximum reactivity with Sarin depends on the pH at which such reactivity is desired.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE SPRAGUE ELECTRIC CO.]

Molecular Compounds. VI. A Reinvestigation of the Picryl Chloride-Hexamethylbenzene Complex; The Effect of Triethylamine on the Equilibrium Constant for Complex Formation

BY SIDNEY D. ROSS, MORTIMER M. LABES AND MEYER SCHWARZ

RECEIVED JUNE 28, 1955

The picryl chloride-hexamethylbenzene complex has been studied in chloroform containing 0.75% ethanol and 93% chloroform-7% ethanol. It is shown that the differences in the equilibrium constants as determined by the spectroscopic method and as measured by the reaction rate method may be attributable to solvation and stabilization of the complex by triethylamine.

In a previous investigation in this Laboratory,¹ the equilibrium constant for complex formation in chloroform between picryl chloride and hexamethylbenzene was determined by a spectroscopic method and a method based on determinations of reaction rates. The latter method gave a value for the equilibrium constant which was more than ten times larger than the spectroscopic value of 0.073 ± 0.009 l. mole⁻¹. The spectroscopic value was taken as a measure of the complexing due to formation of a charge-transfer intermolecular bond, and the larger value, obtained from the reaction rate measurements, was rationalized, by postulating additional interactions capable of affecting the rate of the reaction between picryl chloride and triethylamine.

The reinvestigation of this system was motivated by three major considerations. All of our previous measurements were made in pure chloroform. In the absence of a stabilizer, usually ethanol, chloroform is subject to air oxidation and resultant contamination by traces of phosgene. It seemed, therefore, pertinent to demonstrate that the pre-

viously reported results were not due to solvent instability. More important, Profs. E. Grunwald and J. E. Leffler pointed out to us that for the case of multiple equilibria with only one complex being colored, the spectroscopic method should result in an over-all equilibrium constant which sums all of the complexes.² Finally, our study of solvent effects on molecular complexing³ suggested to us the possibility that the discrepancy between the spectroscopic equilibrium constant and the one derived from the rate studies might be due to solvation and stabilization of the picryl chloride-

(2) Private communication from Profs. E. Grunwald and J. E. Leffler of the Florida State University. For the case of A and B in equilibrium with a series of complexes, AB_i with only one of these complexes being colored

$$[A] = [A_0] - \sum_i [AB_i]$$

$$[B] = [B_0] - \sum_i [AB_i]$$

$$[AB]_{\text{colored}} = f \sum_i [AB_i] = \frac{d}{\epsilon_{AB}}$$

where f is the fraction of the total complexes that is colored.

$$d = f \epsilon_{AB} \sum_i [AB_i] = \epsilon_{\text{apparent}} \sum_i [AB_i]$$

and the equilibrium constant actually determined is given by

$$K = \sum_i [AB_i] / [A][B]$$

(3) S. D. Ross and M. M. Labes, *THIS JOURNAL*, **77**, 4916 (1955).

(1) S. D. Ross, M. Bassin, M. Finkelstein and W. A. Leach, *THIS JOURNAL*, **76**, 69 (1954).