EXPERIMENTAL

Apparatus. A Klett-Summerson photoelectric colorimeter with a No. 42 filter was used for estimation of *p*-nitrophenoxide. Temperature was maintained to within 0.5° of the designated temperature by means of a water-bath. A Beckman Model G *p*H meter was used for all *p*H measurements. Corrections to the *p*H for sodium ion concentration were made by means of a nomograph supplied by Beckman Instruments Inc.

Materials. Paraoxon supplied by the Chemical Division of the Chemical Corps, Chemical and Radiological Laboratories, was *ca.* 95% pure by chemical analysis[8] and contained *ca.* 2% *p*-nitrophenol according to measurements of color immediately developed in aqueous solution of *p*H 10. A 0.3% stock solution of paraoxon in acetone was diluted with water to make up mixtures for kinetic studies; such mixtures never contained more than 0.2% acetone. Buffers consisted of sodium phosphate mixtures (0.025 *M* final concentration) for *p*H 9 to 11 and 0.01 to 0.1 *N* sodium hydroxide for the higher *p*H range. Solutions of C. P. *p*-nitrophenol in the appropriate buffers were used to construct calibration curves for *p*-nitrophenoxide concentration.

Kinetic procedures. Reactant solutions were brought to the desired temperature and mixed rapidly in 100-ml. volumetric flasks, which then were placed in the water-bath. Aliquots were withdrawn from time to time and the color was measured against that of reagent blank.

The actual time of reading was used for the kinetic data, rather than the time of sampling; the interval between sampling and reading was only about 15 seconds. It was thus unnecessary to quench the reaction before reading and even where the reaction half-life was very short, no error of consequence was thereby introduced.

Results. p-Nitrophenoxide concentrations (C_t) at various time intervals were determined by comparison with the calibration curve. Pseudo-first order rate constants (k_1) were calculated[9] from the linear plots obtained (*i.e.*, 2.303 times the slope) when $\log (C_\infty - C_t)$ was plotted against time (where C_∞ is the concentration of *p*-nitrophenol when reaction is complete). That the reaction is first order at a given *p*H, with respect to hydrogen peroxide as well as the paraoxon concentration, is shown by the constancy of k_2' values in Table I where $k_2' = k_1/[H_2O_2]$. True second order rate constants (Tables II and III) were obtained from the equations $k_b = k_1/[OH^-]$ for base-catalyzed hydrolysis[10] or $k_2 = (k_1 - k_b[OH^-])/[HO_2^-]$ for the perhydroxyl reaction[11] where $[HO_2^-]$ was calculated from the *p*H and the acid dissociation constant[12] of hydrogen peroxide (1.98 × 10^{-12} at 25° and 3.46 × 10^{-12} at 37°).

TABLE I

REACTION OF PARAOXON WITH HYDROGEN PEROXIDE AT *p*H 11.3, T = 25°C.

Paraoxon (Mol. liter^{-1})	$[H_2O_2] \times 10^3$ (Mol. liter^{-1})	k_1 (Min.$^{-1}$)	$k_2' \times 10^{-1}$ (Liter mol.$^{-1}$ min.$^{-1}$)
10^{-5}	3.5	4.6×10^{-2}	1.31
	7.0	9.8×10^{-2}	1.40
	14.0	1.69×10^{-1}	1.21
	21.0	3.3×10^{-1}	1.57
2×10^{-5}	3.5	4.7×10^{-2}	1.34
	7.0	1.03×10^{-1}	1.47
	14.0	2.04×10^{-1}	1.46
	17.4	3.08×10^{-1}	1.77

TABLE II

AQUEOUS HYDROLYSIS OF PARAOXON[a] (T = 25°C.)

*p*H	$[OH^-]$ (Mol. liter^{-1})	k_1 (Min.$^{-1}$)	k_b (Liter mol.$^{-1}$ min.$^{-1}$)
10.06	1.14×10^{-4}	6.24×10^{-5}	0.547
11.23	1.68×10^{-3}	8.75×10^{-4}	.521
11.84	6.86×10^{-3}	4.33×10^{-3}	.631
12.23	1.68×10^{-3}	1.06×10^{-2}	.631

[a] Initial concentration of paraoxon = 3 × 10^{-5} M. At 37° k_b was 0.94.

TABLE III

HYDROLYSIS OF 10^{-5} *M* PARAOXON WITH 3.5 × 10^{-5} *M* HYDROGEN PEROXIDE (T = 37°C.)

*p*H	$[OH^-]$ (Mol. liter^{-1})	$[HO_2^-] \times 10^4$ (Mol. liter^{-1})	k_1 (Min.$^{-1}$)	$k_2 \times 10^{-1}$ (L. mol.$^{-1}$ min.$^{-1}$)
9.53	8.09×10^{-5}	0.406	4.7×10^{-3}	11.3
10.07	2.81×10^{-4}	1.37	1.22×10^{-2}	8.7
10.77	1.41×10^{-3}			8.6*
11.3	4.77×10^{-3}	14.3	1.19×10^{-1}	8.0

* Average k_2 value for determinations using concentrations of hydrogen peroxide of 14.7, 34.4, and 44.0 × 10^{-3} *M*.

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(8) Performed by Mr. Samuel Sass, of the Chemical and Radiological Laboratories.

(9) Frost and Pearson, *Kinetics and Mechanism*, John Wiley and Sons, Inc., New York, 1953, p. 8–53.

(10) Values of K_{H_2O} are 2.39 × 10^{-14} at 37° (by interpolation) and 1.008 × 10^{-14} at 25°, according to Glasstone, *Textbook of Physical Chemistry*, 2nd ed., D. van Nostrand Co., New York, 1947, p. 992.

(11) Substitution of the perhydroxyl ion concentration in data shown in Table I gives a k_2 value of 5.06 × 10^1 liter mol.$^{-1}$ min.$^{-1}$ at 25°C.

(12) Calculated from the value of 1.55 × 10^{-12} at 20.1°C, taken from Kargin, *Z. anorg. u. allgem. Chem.*, **183**, 77 (1929), and from the heat of ionization, 8603 calories, according to Joyner, *Z. anorg. Chem.*, **77**, 103 (1912).

Substitution of Halogens by Deuterium in Organic Compounds Without Undesired Exchange of Hydrogen by Deuterium

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The inconvenience associated with the use of the conventional *Grignard* technique for introducing deuterium into organic compounds is well known. A method having wider applicability and, if possible, experimentally simpler would therefore seem to be of rather great interest. It is believed that the method described below has these advantages to a certain extent. Table I summarizes results obtained in successful attempts to prepare deuterated species of a variety of organic compounds.

EXPERIMENTAL

Except for the methyl iodide and methylene iodide the compound to be deuterated was mixed with Zn-dust and

TABLE I

RESULTS FROM PREPARATIONS OF SEVERAL DEUTERATED COMPOUNDS USING A ZN-DUST TECHNIQUE

Compound to be deuterated	Moles taken/ gram-atom of Zn	Reaction medium	Reaction time	Reaction product	Yield, mg. and (%)
2-Bromopyridine[1]	0.0085/0.05	25 ml. of 2 *N* D_2SO_4	100 min.	2D-Pyridine	400 (59)
3-Bromopyridine[1]	0.0085/0.05		100 min.	3D-Pyridine	350 (51)
4-Chloropyridine[1]	0.0085/0.05		100 min.	4D-Pyridine	500 (74)
3-Iodothiophene[2]	0.048/0.107	0.138 mole CH_3COOD + 1.18 moles D_2O	75 min.	3D-Thiophene	2700 (66)
3,4-Diiodothiophene[2]	0.036/0.107		75 min.	3,4 D_2-Thiophene	2000 (64)
2,4,6-Tribromofluorobenzene[3]	0.012/0.246		24 hours	2,4,6 D_3-Fluorobenzene	500 (42)
Tetraiodothiophene[2]	0.034/0.246	0.278 mole CH_3COOD + 1.11 moles D_2O	20 hours	Tetradeuterothiophene	1100 (37)
Methylene iodide	0.039/0.462	0.400 mole CH_3COOD + 1.05 moles D_2O	Instantaneous	Dideuteromethane	300 (43)
Methyl iodide	0.22/1.25	1.10 mole CH_3COOD + 3.20 moles D_2O	Instantaneous	Monodeuteromethane	3540 (93)
1,4-Diiodobenzene	0.076/0.246	0.278 mole CH_3COOD + 2.22 moles D_2O	20 hours	1,4 D_2-benzene	3800 (57)

the solution of CH_2COOD in D_2O [prepared *in situ* from $(CH_3CO)_2O$ and D_2O] at room temperature in a 100-ml. flask fitted with a reflux condenser. The mixture was boiled for the period given in Table I. The deuterated pyridines were isolated *via* complex compounds but the remaining species were distilled-off *in vacuo* with some D_2O and CH_3COOD. Most of the water could then be removed with a syringe. After treating the organic compounds with anhydrous soda they were finally dried over P_2O_5 and distilled. Their identity and the fact that no undesired exchange had taken place was established by investigation of the infrared and microwave spectra of the parent compounds and the deuterated species of Table I.[1,2,3,4]

Because of the vigorous reaction methylene iodide and methyl iodide had to be introduced dropwise. The deuterated methanes obtained were not contaminated by isotopic methanes.

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Preparation and Derivatives of 2-Cyanotetrahydropyran

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This study of 2-cyanotetrahydropyran followed closely to that for cyano-1,4-dioxane.[1] Two differences in experimental procedure were observed: (1) the 2-cyanotetrahydropyran was prepared in better yields using an ether medium rather than toluene, and (2) the reaction between the 2-cyanotetrahydropyran and phenylmagnesium bromide to yield 2-benzoyltetrahydropyran behaved normally. The derivatives of tetrahydropyran were less soluble in the solvents employed than were the corresponding derivatives of 1,4-dioxane and could be worked up more easily.

The hydrolysis of 2-cyanotetrahydropyran produced the corresponding carboxylic acid, which had been prepared previously from acrolein dimer.[2]

N-(2-Tetrahydropyranylmethyl)-4-aminobenzenesulfonamide, produced by the reaction between 2-aminomethyltetrahydropyran and *p*-acetamidobenzenesulfonyl chloride, was tested by Sharp and Dohme, Inc., Philadelphia for physiological activity. It was found to be inactive *in vitro* toward *Proteus vulgaris* and *in vivo* toward a strain of hemolytic streptococcus. Trimethyl(2-tetrahydropyranylmethyl)ammonium iodide, prepared from 2-aminomethyltetrahydropyran and methyl iodide, will be submitted for a physiological activity study.

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EXPERIMENTAL

2-Cyanotetrahydropyran. 2-Chlorotetrahydropyran was prepared at −10° by passing 9.1 g. (0.25 mole) of dry hydrogen chloride into 21.0 g. (0.25 mole) of dihydropyran at a rate to prevent discoloring. Chlorotetrahydropyran was added dropwise to a vigorously stirred suspension of 33.3

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