

Halophenyl Oxalates

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The preparation and properties, including some infrared spectra, of a number of halophenyl oxalates are described. These compounds were prepared by treating an oxalyl chloride with a phenol in the presence of a hydrogen chloride acceptor.

BIOLOGICAL SCREENING of halophenyl carbonates (1, 6) and carboxylates (5) has been reported which indicates significant activity among certain members of these classes. In this investigation a series of halophenyl oxalates were studied similarly, particularly as bacteriostats and fungistats.

The halophenyl oxalates are white solids readily purified by recrystallization and usually melting above 100°. They are moderately soluble in aromatic and polar aliphatic solvents but insoluble in water. Their preparation proceeds quite readily by reacting the appropriate phenol with oxalyl chloride, ethyl oxalyl chloride or an aryl oxalyl chloride in the presence of triethylamine as a hydrogen chloride acceptor, with ether generally serving as the solvent.

Infrared spectra were obtained for the oxalates with the carbonyl absorptions appearing in the 5.6-5.7 micron region. Although there was no direct correlation, doublets were observed when the R and R' groups were different and only one of the groups possessed ortho substitution.

The halophenyl oxalates in general exhibited good in vitro bacteriostatic and fungistatic activity. For example, compound 10, employing a modification of the method of Beaver, Roman, and Stoffel (2), inhibited *Staphylococcus aureus*, *Salmonella typhosa*, and *Aspergillus niger* at a dilution in excess of one part per one hundred thousand.

EXPERIMENTAL

Melting points, taken on a Fisher-Johns Melting Point Apparatus, and boiling points are uncorrected. The infrared spectra (Nujol mull) were obtained using a Beckman IR-5 Spectrophotometer.

Data obtained are listed in Table I.

Oxalyl chloride, ethyl oxalyl chloride and most of the phenols were commercial materials. Tetrachloroguaiacol was prepared by the chlorination of guaiacol (4). Phenyl oxalyl chloride was obtained by reacting phenol with oxalyl chloride (7).

p-Chlorophenyl Oxalyl Chloride. A solution of 63.5 grams (0.5 mole) of oxalyl chloride and 51.4 grams (0.4 mole) of p-chlorophenol in 300 ml. of anhydrous ether was allowed to stand at room temperature for three days. The ether was evaporated and the residue fractionated; b.p. 140-7° (10.5-11.0 mm. of Hg), m.p. 44-6°; 54% yield. *Anal.* Calcd. for C₈H₇Cl₂O₃: Cl, 32.4. Found: Cl, 32.4. Both phenyl and p-chlorophenyl oxalyl chloride are quite unstable in air being readily hydrolyzed to the acid.

Phenyl Oxalates. Triethylamine (0.10 mole) dissolved in about 35 ml. of ether was added dropwise during 15 minutes to a stirred solution of 0.10 mole of the phenol and 0.05 mole of oxalyl chloride in about 300 ml. of ether at 10-15°. The mixture was refluxed for four hours, cooled and the solids separated by filtration. When the product was ether insoluble or partially ether insoluble, it was separated from the by-product amine hydrochloride by treatment of the solids with water. Additional product was obtained by removal of the solvent from the original filtrate with a rotary evaporator. The crude product was purified by recrystallization.

Table I. Halophenyl Oxalates

No.	R	R'	Yield, %	M.P., °C.	Infrared Carbonyl Absorption, Microns	Formula	Carbon, %		Hydrogen, %		Halogen, %	
							Calcd.	Found	Calcd.	Found	Calcd.	Found
1	C ₆ H ₅	C ₆ Cl ₅	68	97-8	5.6; 5.7	C ₁₂ H ₅ Cl ₅ O ₄	32.7	32.9	1.40	1.77	48.4	48.7
2	C ₆ H ₅	C ₆ Br ₅	87	125-6	5.6; 5.7	C ₁₂ H ₅ Br ₅ O ₄	20.4	20.2	0.86	1.12	67.9	67.8
3	C ₆ H ₅	C ₆ H ₄	29	137-8*	5.65	C ₁₂ H ₁₀ O ₄						
4	C ₆ H ₅	C ₆ Cl ₄	93	98-100	5.7	C ₁₂ H ₇ Cl ₄ O ₄	54.1	43.9	2.59	2.80	42.8	43.1
5	C ₆ H ₄	C ₆ H ₃ Cl	71	190-1	5.6; 5.65	C ₁₂ H ₆ ClO ₄	37.5	37.4	0.89	0.90	22.8**	22.7
6	C ₆ H ₃ Cl	C ₆ Cl ₄	76	126-8	5.7	C ₁₂ H ₄ Cl ₅ O ₄	44.2	44.0	1.59	1.60	47.4	47.1
7	C ₆ H ₃ Cl	C ₆ H ₃ Cl	54	144-5	5.7	C ₁₂ H ₃ Cl ₆ O ₄	44.2	44.3	1.59	1.79	37.3	37.0
8	C ₆ H ₃ Cl	C ₆ H ₃ Cl	61	149-50	5.6	C ₁₂ H ₃ Cl ₅ O ₄	37.5	37.5	0.90	1.00	47.4	47.4
9	C ₆ H ₃ Cl	C ₆ H ₃ Cl	73	196-8	5.6	C ₁₂ H ₃ Cl ₄ O ₄	37.5	37.4	0.90	1.10	47.4	47.1
10	C ₆ H ₃ Cl	C ₆ H ₃ Cl	42	193-5	5.6	C ₁₂ H ₃ Cl ₃ O ₄	32.5	32.3	0.39	0.54	54.8	54.6
11	C ₆ H ₃ Cl	C ₆ H ₃ Cl	80	152-3	5.6	C ₁₂ H ₃ Cl ₂ O ₄	28.6	28.6			60.5	60.4
12	C ₆ H ₃ Cl	C ₆ Cl ₄	62	236-8	5.6	C ₁₂ H ₄ Cl ₅ O ₄	16.3	16.1			77.5	77.5
13	C ₆ H ₃ Cl	C ₆ Br ₄	83	294-5	5.6	C ₁₂ H ₄ Br ₅ O ₄	68.4	68.6	4.10	4.08	14.4	14.5
14	C ₆ H ₃ Cl	C ₆ H ₃ Cl	63	129-30	5.65	C ₁₂ H ₃ Br ₄ O ₄	21.3	21.5	0.67	0.84	70.9	70.5
15	C ₆ H ₃ Cl	C ₆ Br ₃	67	259-60	5.65	C ₁₂ H ₃ Br ₄ O ₄	33.2	33.2	1.51	1.22	49.1	48.9
16	C ₆ H ₃ Cl	C ₆ Cl ₂ -2,3,4,5-OCH ₂ -6	62	164-5	5.65	C ₁₂ H ₃ Cl ₄ O ₄	41.9	41.9	1.51	2.33	17.7	18.0
17	C ₆ H ₃ Cl	C ₆ H ₃ Cl-2,NO ₂ -4	58	212-4	5.65	C ₁₂ H ₃ Cl ₄ N ₂ O ₄						

* Lit. (3) m.p. 136°. ** Calcd. N, 6.99. Found: 6.88. Compound 1 was recrystallized from hexane; 2-4, 6-8, and 11 from methylcyclohexane; 5 and 15 from toluene; 9, 10, 14 and 16 from toluene-methylcyclohexane; 12 from benzene; 13 and 17 from chloro-benzene.

When an alkyl or aryl oxalyl chloride was substituted for oxalyl chloride, equimolar quantities of the reactants were used.

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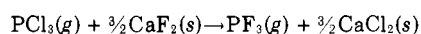
Thermochemistry of Phosphorus Trifluoride

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The heat of reaction between CaF_2 and PCl_3 was obtained at 356.6°C . by a novel technique using a fluidized bed as the reactor. The observed value corrected to 25°C . (298.16°K .) gave $\Delta H = -2.361$ kcal./mole PCl_3 . Reaction was substantially complete and in good agreement with the conversion calculated from the observed enthalpy change and the known entropy change. The enthalpy of formation for PF_3 was calculated to be -226.03 kcal./mole at 298.16°K .

NO THERMOCHEMICAL STUDIES have been made on PF_3 since 1885 when Berthelot (1) obtained a limited supply from the discoverer, Henri Moissan, which he submitted to calorimetric measurement by absorption in KOH . Only three determinations were made giving 109.7, 107.1, and 106.2 kcal./mole PF_3 absorbed, which Berthelot did not regard as very concordant. The reaction was complex and he was unable to establish its course with the analytical methods then available.

Another reaction has now been found which is suitable for thermochemical studies, namely, the metathesis of calcium fluoride with phosphorus trichloride:



The reactants are readily available, and there are no significant by-products, but special techniques must be employed for the measurements. A temperature of 350°C . is needed to get rates rapid enough to follow by simple thermometric equipment. Since one reactant is solid while the other is gaseous, a flow calorimeter using a fluidized bed is also required. To obtain a gas stream adequate for fluidization, the PF_3 must be carried in with an additional volume of inert gas such as nitrogen. A bath of boiling mercury surrounding the apparatus maintains the reaction temperature.

PRINCIPLE OF THE CALORIMETRIC MEASUREMENT

The bed of solid is first brought up to the reaction temperature and then the gaseous reactant is introduced

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preheated to the same temperature. As the reaction proceeds, the gas continues to enter at constant temperature while the solid bed and outlet gas rise in temperature from the heat evolved. Some heat is carried away in the gas while the remainder appears as sensible heat in the solid. When the solid and gas are completely fluidized the two temperatures must be equal, and the heat balance then gives the following differential equation between reaction temperature and amount of PCl_3 converted:

$$q dm = C_s dT + C_g (T - T_0) dm \quad (1)$$

q = heat evolved per unit of PCl_3
 dm = differential amount of PCl_3 reacted
 dT = temperature rise in the solid
 C_s = heat capacity of the solid, including calorimeter walls and thermometer
 C_g = heat capacity of the carrier gas and PCl_3
 T = temperature of the bed
 T_0 = inlet temperature of the gas stream

The first term on the right in Equation 1 represents the sensible heat stored in the solid; the second is the heat carried away by an infinitesimal amount of reactant gas which suffers a finite temperature rise ($T - T_0$).

Integration of Equation 1 gives:

$$m = \frac{-C_s}{C_g} \ln [q - C_g (T - T_0)] + I \quad (2)$$

The initial conditions ($m = 0$, $T = T_0$) determine the integration constant ($I = C_s/C_g \ln q$) and the final equation after rearrangement is:

$$q = C_g (T - T_0) (1 - e^{-m C_g / C_s})^{-1} \quad (3)$$