2-propen-1-ol for comparison with the product obtained in this work, to Dr. D. C. England of the E. I. du Pont de Nemours Co. for a sample of hexafluorocyclopropane, to Dr. D. M. Lemal for several helpful discussions, and to Miss Carol Gross for performing several of the syntheses.

[CONTRIBUTION FROM MONSANTO CHEMICAL CO., RESEARCH DEPARTMENT, INORGANIC CHEMICALS DIVISION, ST. LOUIS, MO.]

Synthesis of Hypophosphite Esters from Orthocarbonyl Compounds

BY STEVEN J. FITCH

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A convenient source of alkyl hypophosphite esters has been found in the reaction of crystalline hypophosphorous acid with orthocarbonates, orthocarboxylates, ketals, or acetals. The only previous preparation of hypophosphite esters was by means of the diazoalkane reaction. Ketals and acetals yield 1-hydroxyphosphinate esters as the final products due to addition of the phosphorus–hydrogen bond of the alkyl hypophosphite to the carbonyl group of the ketone or aldehyde by-product. The reaction between acetone dimethyl ketal and hypophosphorous acid shows an abrupt change in rate, indicating the formation of a weak complex between a reactant and a product, probably the ketal and methyl hypophosphite. P^{31} and H^1 n.m.r. data are presented for the pure esters and some reaction mixtures.

Introduction

Simple esters of the various oxyacids of nonmetals are usually prepared by the reaction of alcohol with the halide, anhydride, or acid of the central element. None of these methods is applicable to the esterification of hypophosphorous acid since the anhydride, $H_2P(O)OP(O)H_2$, and appropriate halide, XH_2PO or HX_2P, are not known. The dihalophosphine would be an appropriate halide by analogy to the alcoholysis of phosphorus trichloride.

$$HX_2P + 2ROH \longrightarrow ROP(O)H_2 + RX + HX \quad (1)$$

The direct esterification of hypophosphorous acid with alcohol has not been reported, and, if it proceeded at all, would probably result in decomposition of the unstable esters.

These conditions have caused hypophosphite esters to be virtually unknown materials, in striking contrast to the thoroughly studied phosphite esters. The only reported preparation of hypophosphite esters is the formation of the methyl and ethyl esters from the acid and the appropriate diazoalkane.[1] The unspecified yields were undoubtedly low since the esters disproportionate rapidly at the reported boiling points.

A new and convenient synthesis of alkyl hypophosphites has been found, based on the reaction of hypophosphorous acid with compounds having an orthocarbonyl function.

$$\underset{\underset{H}{}}{\overset{O}{HOPH}} + R_nC(OR')_{4-n} \longrightarrow \underset{\underset{H}{}}{\overset{O}{R'OPH}} + R'OH + \overset{O}{R_nC(OR')_{2-n}} \quad (2)$$

$n = 0, 1, \text{or } 2$

The scope of the reaction was shown with a series of ortho compounds including orthocarbonates ($n = 0$), orthocarboxylates ($n = 1$), and a ketal and an acetal ($n = 2$).

The esterification is nearly quantitative in most cases, although a severe reduction in yield occurs on distillation due to the disproportionation reaction. However, the fresh reaction product, consisting of the hypophosphite ester dissolved in the by-product alcohol and carbonyl compound, decomposes much more slowly than the pure ester. This medium provides a convenient source of compounds which have two hydrogen atoms bonded to a quadruply connected phosphorus atom and which are therefore difunctional analogs of the dialkyl phosphonates. Only the primary phosphine oxides and hypophosphorous acid, esters, and salts are known to contain this structural unit. Interesting variations on many of the numerous reactions of dialkyl phosphonates should be possible using this reaction mixture as a source of alkyl hypophosphites.

Results and Discussion

The alkyl hypophosphites are prepared simply by mixing crystalline hypophosphorous acid and the ortho compound at room temperature. Two liquid phases are formed, and the system becomes homogeneous as the esterification reaction proceeds. The time required for forming a one-phase system varies from about 1 to 30 min., depending on the ortho compound, the dryness of the acid, and particularly on the rate of agitation. Of the ortho compounds tested, only acetal required heating or long standing to initiate reaction. The course of the esterification in the resulting single-phase system can then be followed by both H^1 and P^{31} n.m.r. to determine when the reaction reaches completion and, in the simpler systems, to determine the stoichiometry by identification of all major components.

The over-all esterification reaction, including the phase change of the crystalline acid, is endothermic, indicating that the entropy increase in forming three molecules from two is an important driving force in the reaction. There is probably an approximate cancellation of the enthalpy effects due to a favorable change in hybridization for carbon and an unfavorable change for phosphorus, in which the π-bond is localized onto only one P–O bond,[2] leaving the entropy increase as a predominant factor.

Methyl and ethyl hypophosphites prepared from the corresponding orthoformates were isolated by distillation. Yellow solids and phosphine were generated in large amounts during distillation, and the yields were variable, depending on the time and temperature of distillation. No attempt was made to distil the butyl ester since it was expected to decompose completely at distillation temperatures. However, most of the butanol and butyl formate by-products were removed by vacuum evaporation to give a concentrated residue having a stronger n.m.r. signal.

It is not necessary to use completely dry hypophosphorous acid in the reaction since any water present in the acid immediately hydrolyzes the hypophosphite ester, which is then regenerated by reaction with additional ortho compound. In fact, a mixture of ethyl hypophosphite and hypophosphorous acid was obtained

(1) M. I. Kabachnik, A. E. Shipov, and T. A. Mastryukova, *Bull. Acad. Sci., USSR*, No. 1, 146 (1960); Engl. trans., p. 138.

(2) J. R. Van Wazer, "Phosphorus and its Compounds," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1958, pp. 437–440.

by treating 50% aqueous hypophosphorous acid with a large excess of ethyl orthoformate and evacuating the mixture to remove ethanol and ethyl formate.

N.m.r. Spectra of Alkyl Hypophosphites.—The P^{31} spectrum of hypophosphorous acid has a 1–2–1 triplet structure due to spin–spin coupling of the phosphorus atom to the two hydrogen atoms bonded directly to it, a chemical shift of about −8 p.p.m. in these mixtures, and a coupling constant of about 535 c.p.s. The hypophosphite esters have similar spectra, shifted about 6–12 p.p.m. to lower field, with the addition of weaker coupling to the more distant protons of the ester group. In methyl hypophosphite, the three methyl protons produce a 1–3–3–1 quartet structure in each of the three hypophosphite resonances with a coupling constant of 13 c.p.s. In ethyl and butyl hypophosphite, only the protons on the carbon nearest to phosphorus give recognizable coupling, superimposing a triplet structure on the hypophosphite peaks.

The primary triplet structure in the P^{31} spectra demonstrates the absence of a detectable amount of the triply connected isomer (RO)(H)POH, as was also shown by the inability of the esters to react further with diazoalkane.[1]

From the spectra of the pure methyl and ethyl hypophosphites, the spectra of the reaction mixtures could be interpreted with considerable confidence. Therefore, most of the remaining experiments were followed by n.m.r. spectra, and the products were not separated. The n.m.r. data are summarized in Table I.

TABLE I

N.M.R. DATA FOR ALKYL HYPOPHOSPHITES

Chemical shift	P^{31} spectra[a]			H^1 spectra PH[b]	J_{P-H}	POCH[c]	J_{POCH}
		$CH_3OP(O)H_2$					
Distilled	−43.1	−18.9	+4.6	428	571	230	13
In reacn. mixt. from							
$C(OCH_3)_4$	−43.1	−19.9	+3.8	428	575	231[d]	13[d]
$HC(OCH_3)_3$	−44.1	−20.4	+3.6	428	575	228	13.0
$CH_3C(OCH_3)_3$	−40.8	−18.5	+4.3	452	579	232	14
$(CH_3)_2C(OCH_3)_2$	−42.1	−18.5	+5.4	431	582	231	12
		$C_2H_5OP(O)H_2$					
Distilled	−38.7	−15.0	+8.4	424	567	244	17.2
In reacn. mixt. from							
$C(OC_2H_5)_4$	−38.2	−14.8	+8.4	429	567	[e]	[e]
$HC(OC_2H_5)_3$	−37.5	−14.1	+9.7	421	570	[e]	[e]
$C_2H_5C(OC_2H_5)_3$	−38.0	−15.2	+7.9				
$CH_3CH(OC_2H_5)_2$	−40	−16	+7	415[d]	547[d]	[e]	[e]
		$C_4H_9OP(O)H_2$					
In reacn. mixt. from							
$HC(OC_4H_9)_3$	−39.2	−15.6	+7.6	429	570	[e]	[e]

[a] Chemical shift in p.p.m. for the three $ROP(O)H_2$ peaks. [b] Midpoint of doublet, c.p.s. [c] Midpoint of doublet or multiplet, c.p.s. [d] Approximate. [e] Obscured by other peaks.

Stoichiometry.—Proton spectra were used to verify eq. 2 with reaction mixtures of hypophosphorous acid and methyl orthocarbonate or methyl orthoformate. Reaction periods of 0.5 and 1 hr., respectively, were chosen to give nearly complete esterification without excessive disproportionation. The P–H and $POCH_3$ resonances were recognized by their doublet structures with coupling constants known from P^{31} spectra, and the remaining peaks were then readily assigned to methanol and methyl carbonate or formate. The assignments were verified and overlapping peaks were accounted for by area measurements and by adding known components to the mixtures. The data are given in Table II, and the agreement is felt to be satisfactory, considering that the products were starting to disproportionate and deposit yellow solids as the spectra were being taken.

The unidentified peak in the methyl orthoformate reaction (Table II) appears from area measurements to "belong to" the overlapping CH_3OH–$HC(OCH_3)_3$ peaks. With a similar reaction at 37-min. reaction time, calculation of the eight separately measureable areas, based on 87% reaction of the methyl orthoformate and 2% hydrolysis of methyl hypophosphite, gave agreement with the measured areas averaging 2.3% (maximum error 6%) when the unidentified peak was included with the CH_3OH–$HC(OCH_3)_3$ peak. When it was not included, the CH_3OH–$HC(OCH_3)_3$ peak was in error by 16%. If the unidentified peak were caused by an unsuspected side reaction, such as methyl ether formation, it is likely that some other peak(s) would be in error by a comparable amount. Therefore, this peak appears to arise from a methoxy group in some intermediate species involved in the removal of methanol from methyl orthoformate. The peak is absent from pure methanol–methyl orthoformate mixtures. Similarly, the unidentified peak at 196 c.p.s. in the methyl orthocarbonate reaction can be explained as a methoxy group in an intermediate species.

TABLE II

H^1 N.M.R. SPECTRA OF REACTION MIXTURES

Shift	Area, H atoms: Found	Expected[a]	Assignment
Methyl orthocarbonate–hypophosphorous acid (equimolar)			
716	1.0[b]	1.0	Half of $CH_3OP(O)H_2$ doublet
299	0.05	0.0	$C(OCH_3)_4$
280[c]	1.2	1.0	$HOCH_3$
254	0.05	0.0	Unidentified
238	1.4	1.5	Half of $CH_3OP(O)H_2$ doublet
226	7.3	1.5	Half of $CH_3OP(O)H_2$ doublet
		6.0	$(CH_3O)_2CO$
208	0.1	0.0	Unidentified
199	2.9	3.0	$HOCH_3$
196	0.9	0.0	Unidentified
140	1.0[b]	1.0	Half of $CH_3OP(O)H_2$ doublet
Methyl orthoformate (5% excess)–hypophosphorus acid			
712	1.0[b]	1.0	Half of $CH_3OP(O)H_2$ doublet
696	0.1	0.0	Half of $HOP(O)H_2$ doublet
488	.9	1.0	HCO_2CH_3
292	.1	0.05	$HC(OCH_3)_3$
278	1.3	1.0	$HOCH_3$
233	1.5	1.5	Half of $CH_3OP(O)H_2$ doublet
220	4.3	1.5	Half of $CH_3OP(O)H_2$ doublet
218		3.0	HCO_2CH_3
208	0.4	0.0	Unidentified
193	4.3	3.0	$HOCH_3$
191		0.45	$HC(OCH_3)_3$
148	0.1	0.0	Half of $HOP(O)H_2$ doublet
134	1.0[b]	1.0	Half of $CH_3OP(O)H_2$ doublet

[a] Expected from eq. 2 for quantitative reaction. [b] Area of one peak of $CH_3OP(O)H_2$ doublet is defined as 1.0 H atom. [c] This peak shifted by 10 c.p.s. between consecutive spectra, owing probably to disproportionation of $CH_3OP(O)H_2$.

Ketal Reaction.—The various orthoesters give by-products which do not react with alkyl hypophosphites, but ketals and acetals give ketones and aldehydes as by-products. These are known to add P–H bonds in a very general reaction. Thus, methyl 1-hydroxy-1,1-dimethylmethylphosphinate is the final product in the reaction with acetone dimethyl ketal.

$$(CH_3)_2C(OCH_3)_2 + HOP(O)H_2 \longrightarrow CH_3OP(O)H_2 + CH_3OH + (CH_3)_2CO$$

$$CH_3OP(O)H_2 + (CH_3)_2CO \longrightarrow CH_3OP(O)(H)C(CH_3)_2OH$$

Hypophosphorous acid itself reacts similarly with acetone at somewhat higher temperatures.[3]

(3) C. Marie, *Compt. rend.*, **133**, 219, 818 (1901).

The kinetic behavior of this reaction is unexpected; with 1 or 2 moles of the ketal per mole of hypophosphorous acid the esterification nearly ceases at roughly one-third or two-thirds of completion, respectively, after about 10 min. Then, over a period of days or weeks the n.m.r. peaks of the phosphinate ester slowly grow, as the peaks for the unreacted hypophosphorous acid and methyl hypophosphite diminish at approximately the same rate. With 3 moles of ketal, the esterification proceeds to completion in about 10 min. at room temperature with negligible phosphinate formation. Then the addition to acetone proceeds to completion in a few hours.

This behavior suggests that a slowly reactive complex is formed between a reactant and a product of the reaction, and that the esterification reaction can proceed only as rapidly as one component of the complex is removed through phosphinate formation, thereby releasing the other component for further esterification.

The abrupt change in reaction rate was not observed in the reaction of 1 mole of ketal with 2 moles of hypophosphorous acid. Rapidly continuing esterification and phosphinate formation were evident from proton spectra taken at 10-, 20-, and 35-min. reaction periods. For the 35-min. spectrum, good agreement was obtained between measured areas and areas calculated for 88% reaction of the ketal, with 41% of the resulting methyl hypophosphite converted to phosphinate ester and 2% hydrolyzed to hypophosphorous acid and methanol. At 16-hr. reaction time, all ketal had reacted and nearly all methyl hypophosphite had been converted to phosphinate ester.

Of the six possible binary combinations of reactant and product, H_3PO_2–CH_3OH and H_3PO_2–$CH_3OP(O)H_2$ are eliminated as possible complex formers owing to their presence in esterifications with other ortho compounds which do not show the abrupt change in reaction rate. CH_3OH–$(CH_3)_2C(OCH_3)_2$ and $(CH_3)_2CO$–$(CH_3)_2C(OCH_3)_2$ are eliminated since equimolar mixtures of these materials reacted in the same manner as ketal alone in 1:1 reactions with hypophosphorous acid. A possible H_3PO_2–$(CH_3)_2CO$ complex is also eliminated by the latter combination. An independent attempt was made to eliminate the H_3PO_2–$(CH_3)_2CO$ combination by treating hypophosphorous acid with equimolar $(CH_3)_2CO$–$HC(OCH_3)_3$. However, the acetone and methyl orthoformate immediately formed ketal in the acidic system,[4] and the ketal reacted as in the normal 1:1 ketal reaction.

Since pure methyl hypophosphite is difficult to prepare and handle, the final possibility, $CH_3OP(O)H_2$–$(CH_3)_2C(OCH_3)_2$, was tested by mixing ketal with equimolar methyl hypophosphite in the form of its reaction product from the methyl orthoformate or methyl orthoacetate reaction. These mixtures were then added to hypophosphorous acid, using both 1 and 2 moles of ketal per mole of hypophosphorous acid in the case of the methyl orthoformate product. In these mixtures, as with ketal alone, a large portion of the hypophosphorous acid was consumed in a few minutes, but the remaining ketal and hypophosphorous acid reacted slowly over a period of days as the phosphinate adduct was formed. This would appear to eliminate a $CH_3OP(O)H_2$–$(CH_3)_2C(OCH_3)_2$ complex as a possibility unless one assumes that the hypothetical complex is weakened by other components of the solution, as appears to occur in the reaction with excess hypophosphorous acid. It may be significant that in the latter reaction, as well as in the mixtures containing added methyl hypophosphite, proton spectra showed the usually sharp methoxy resonance of the ketal to be distinctly broadened.

More precise and extensive kinetic measurements are needed to determine clearly the composition of the complex, but the reactions with 1, 2, and 3 moles of ketal plus the fact that ketal is released for further esterification only as fast as methyl hypophosphite is removed by phosphinate formation favor the formulation of the complex as $2(CH_3)_2C(OCH_3)_2 \cdot CH_3OP(O)H_2$.

Acetal Reaction.—The esterification of hypophosphorous acid with acetal required 5 months at room temperature to approach completion, although the two liquid phases became one in only 4 days. P^{31} n.m.r. showed two doublets growing in the phosphinate region of the spectrum as the ester and acid peaks gradually diminished. This is interpreted as the formation of 1-hydroxyethylphosphinic acid owing to reaction of hypophosphorous acid, as well as its ester, with by-product acetaldehyde.

Experimental

The P^{31} spectra were taken on a Varian high resolution spectrometer with Model V-4311 fixed-frequency radiofrequency unit operating at 24.3 Mc./sec. Chemical shifts were referenced to 85% phosphoric acid (0 p.p.m.) in an internal capillary tube. The proton spectra were taken with a Varian A-60 spectrometer, and chemical shifts are reported in c.p.s. from dissolved tetramethylsilane (0 c.p.s.).

All ortho compounds were checked for purity by proton spectra; impurity peaks, if present, totaled less than about 1% in each case. The methyl orthocarbonate was kindly supplied by Dr. K. Moedritzer of this Laboratory. The ethyl orthocarbonate was obtained from Kay–Fries Chemicals, Inc., the acetone dimethyl ketal from Matheson Coleman and Bell, and the other ortho compounds from Eastman Organic Chemicals.

Crystalline Hypophosphorous Acid.—The commercial 50% solution (Fisher purified grade) was evaporated in a rotary evaporator at 0.02 mm. with Dry Ice–acetone cooling of the condenser. The heating bath was held at about 50° at the start of the evaporation and was allowed to cool to room temperature as the solution of acid became sirupy. Nucleation was effected by cooling a spot on the evaporator flask with Dry Ice. Since the acid is very hygroscopic and melts slightly above room temperature (26.5°), crystallization at room temperature is an indication of a very low water content. The anticipated phosphoric or phosphorous acid impurities could not be detected by n.m.r. in redissolved acid, indicating that purification by partial crystallization[5] is superfluous for preparative purposes with presently available acid. The crystallized acid was refrigerated during storage.

Methyl Hypophosphite.—In a 100-ml. flask equipped with a magnetic stirrer and a simple distillation head, 18.3 g. (0.28 mole) of crystalline hypophosphorous acid was treated with 30.9 g. (0.29 mole) of methyl orthoformate under nitrogen. The temperature dropped to 2° as the solid dissolved and two liquid phases formed. The system became homogeneous as it warmed to room temperature, and periodic n.m.r. spectra showed the esterification to be essentially complete after an additional hour. The flask was evacuated to remove methanol and methyl formate to a Dry-Ice trap, and the product distilled at 22° (0.7 mm.) as simultaneous formation of yellow solids and gases occurred in the distillation flask; yield 10.4 g. (47%), reported b.p.[1] 25–25.5° (2.5 mm.); neut. equiv. after hydrolysis 85, calcd. 80; infrared: P—H at 2420, P→O merged with broad band at 1190–1280 cm.$^{-1}$; n.m.r. showed a few per cent dimethyl phosphonate which was formed by the disproportionation. The distilled ester slowly deposits solids at 0° but is stable at −78°. The phosphine which formed during distillation was collected in a liquid nitrogen trap downstream from the Dry-Ice trap. It was safely disposed of by admitting nitrogen to the trap and allowing the contents to burn off in a hood as they warmed.

Ethyl Hypophosphite. A.—Hypophosphorous acid (27.5 g., 0.417 mole) and ethyl orthoformate (64.8 g., 0.438 mole) were combined as above. The temperature dropped to 5° and n.m.r. showed the reaction to be complete after 30 min. at room temperature. Distillation as above gave 15.3 g. (39%) of ethyl hypophosphite, b.p. 33–35° (1.3 mm.); reported b.p.[1] 31–32° (2 mm.); infrared: P—H at 2424, P→O at 1242 cm.$^{-1}$; n.m.r. showed a few per cent diethyl phosphonate in the distillate.

B.—A mixture of hypophosphorous acid (32.5 g., 0.49 mole) and ethyl orthopropionate (86.9 g., 0.49 mole) became homogeneous after stirring for 2 min. as the temperature dropped to 19°.

(4) H. W. Post, "The Chemistry of the Aliphatic Orthoesters," Reinhold Publishing Corp., New York, N. Y., 1943, pp. 45–48.

(5) W. A. Jenkins and R. T. Jones, *J. Am. Chem. Soc.*, **74**, 1353 (1952).

P^{31} n.m.r. at 15-min. reaction time showed approximately equal amounts of ethyl hypophosphite (−37.1, −14.8, and +8.3 p.p.m.) and hypophosphorous acid (−28.8, −6.9, and +15.2 p.p.m.) with fairly large unidentified peaks at −40.6, −34.9, and −19.4 p.p.m. In 12 hr. the ethyl hypophosphite peaks were seen to be increasing at the expense of the others, and in 4 days the formation of ethyl hypophosphite was nearly complete. The rapid initial reaction rate and unidentified transient peaks suggest the possibility of an orthoester–hypophosphite ester intermediate species, as in the ketal reaction. This reaction mixture appeared to disproportionate more slowly at room temperature than the orthocarbonate or orthoformate reaction mixtures.

Butyl Hypophosphite.—Hypophosphorous acid (16.3 g., 0.25 mole) and butyl orthoformate (60.4 g., 0.26 mole) were combined as above. The temperature dropped to 7° and n.m.r. showed about 90% conversion after 30 min. at room temperature and complete conversion after 3 hr. The reaction mixture was evaporated at 0° and 0.2 mm. in a rotary evaporator for 2 hr. giving 43.8 g. of clear, colorless residue. This weight corresponds to a 69% solution of butyl hypophosphite in its reaction by-products. Identification was by n.m.r. (Table I).

Usual Mixing Procedure.—Most reactions for which separations were not anticipated were carried out in 5-mm. n.m.r. sample tubes. By forcing the open end of the tube into the crystalline acid and tapping the resulting plug of acid to the bottom of the tube, the very hygroscopic acid could be transferred and weighed with very little absorption of atmospheric moisture. The organic reactants were dropped in through a capillary pipet while weighing, and mixing was effectively accomplished with an oscillating vortex mixer. In this manner, reactions could be observed with n.m.r. within about 4 min. of mixing the reactants.

Methyl 1-Hydroxy-1,1-dimethylmethylphosphinate.—In the above manner, 0.444 g. (0.00673 mole) of hypophosphorous acid and 1.400 g. (0.0135 mole) of acetone dimethyl ketal were combined. At 7-min. reaction time, P^{31} n.m.r. showed methyl hypophosphite peaks about twice as large as peaks of unreacted acid. Little change occurred in an additional hour. After 3 days, roughly 75% of the phosphorus was converted to phosphinate, but the remaining methyl hypophosphite peaks were still about twice as large as the acid peaks. After 20 days, conversion to phosphinate was complete. The reaction product was evacuated at room temperature, giving a clear, colorless residue of fairly pure phosphinate. Calcd. for $C_4H_{11}O_3P$: C, 34.8; H, 8.0; P, 22.4. Found: C, 33.9; H, 8.3; P, 22.2. P^{31} n.m.r.: doublet at −33.6 and −56.3 p.p.m.; J_{P-H} = 552 c.p.s. H^1 n.m.r. assignments, measured and theoretical areas (in H atoms), chemical shift in c.p.s., and coupling, respectively, are: *H*OC, 1.1, 1.0, 362,—; CH_3OP, 3.0, 3.0, 227, 11; unidentified, 0.2, 0, 199, —; *H*P(upfield peak only), 0.51, 0.50, —, —; $(CH_3)_2CPH$, 5.9, 6.0, 78, 16 c.p.s. to H*P* and 2.5 c.p.s. to *H*P. The downfield peak of the P–H doublet was observed, but was off-scale on this spectrum. From spectra of reaction mixtures, this doublet is centered at 385 c.p.s. and J_{P-H} = 513 c.p.s.

Ethyl 1-Hydroxyethylphosphinate.—A mixture of 1.43 g. (0.0216 mole) of hypophosphorous acid and 2.56 g. (0.0216 mole) of acetal failed to give a single-phase liquid after violent agitation for 10 min. Addition of a catalytic amount of finely ground ammonium chloride and more mixing produced no visible change. After standing for 4 days, the mixture was homogeneous, and P^{31} n.m.r. showed two approximately equal phosphinate doublets in addition to ethyl hypophosphite and hypophosphorous acid. In 5 months all hypophosphorous acid was consumed and the ethyl 1-hydroxyethylphosphinate doublet (−29.8 and −51.9 p.p.m.) was about three times as large as the 1-hydroxyethylphosphinic acid doublet (−23.4 and −45.3 p.p.m.). Some ethyl hypophosphite remained.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ARIZONA, TUCSON, ARIZ.]

Ionization Constants of 3,5-Dimethyl 4-Substituted Benzoic Acids

BY JOHN P. SCHAEFER AND TERRENCE J. MIRAGLIA[1]

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Ionization constants of a series of 4-substituted 3,5-dimethylbenzoic acids (X = $N(CH_3)_2$, NH_2, $NHCOCH_3$, OH, OC_2H_5, Br, Cl, CN, CO_2CH_3, NO_2) have been measured and the pK_a values are interpreted in terms of steric inhibition of resonance. A comparison of "effective σ-values" with σ_I constants is made and approximate angles of twist for substituents are calculated.

The development and use of linear free-energy relationships represents one of the more significant contributions to organic chemistry since it has provided a critical test for, and facilitated the illucidation of, reaction mechanisms. Hammett,[2] utilizing the extensive data on the ionization constants of benzoic acids, defined parameters (σ-values) for each functional group which reflected its electronic influence at a reaction site either *meta* or *para* to it in a benzene ring; these σ-values were recognized as being compounded of both resonance and inductive effects which could act to reinforce or oppose each other.

Recently Taft[3] and his co-workers have devoted considerable effort to separating the inductive and resonance contributions of a group to the Hammett σ-value and have been able to calculate σ_I constants[4] which denote the portion of σ which is due solely to the inductive influence of a group. These values are certainly qualitatively correct and have at least a semiquantitative significance as demonstrated by the existence of a "linear inductive free-energy relationship" for a diverse series of reactions.[4-6] The resonance contribution to σ can then be obtained by subtracting σ_I from σ. As the resonance interaction of a substituent with the aromatic ring is inhibited, it is to be expected that the apparent σ-value should approach σ_I as a limit.[7] To assess the experimental significance of Taft's parameters we have initiated a study of the variation of electronic influences of substituents with steric environment and now wish to report on the ionization constants of 3,5-dimethyl 4-substituted benzoic acids.

Experimental

Most of the compounds in question were prepared by appropriate modifications of procedures in the literature and were assayed for purity by spectral methods and neutralization equivalents. Melting points are uncorrected.

3,5-Dimethyl-4-nitrobenzoic Acid.—To a 1-l. three-neck flask fitted with a stirrer, dropping funnel, and condenser were added 64 g. (0.38 mole) of nitromesitylene,[8] 300 ml. of glacial acetic acid, and 80 ml. of concentrated sulfuric acid. The mixture was heated to reflux and 120 g. of chromic acid in 400 ml. of water was added at such a rate that a moderate reflux was maintained. After the addition was completed, stirring at reflux was continued for an additional 30 min. and then the reaction mixture was poured onto 750 g. of ice. The crystals were suction filtered from solution, washed well with water, and transferred to a beaker

(1) This work is abstracted from the thesis of Terrence J. Miraglia, presented to the graduate college at the University of Arizona in partial fulfillment of the requirements for the Master of Science degree.

(2) L. P. Hammett, "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

(3) R. W. Taft in "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 13; R. W. Taft, *J. Phys. Chem.*, **64**, 1803 (1960), and papers cited therein.

(4) R. W. Taft and I. C. Lewis, *J. Am. Chem. Soc.*, **80**, 2436 (1958).

(5) J. L. Roberts and H. H. Jaffé, *ibid.*, **81**, 1635 (1959).

(6) Application of the linear inductive free-energy relationship, $\log k_m/k_0 = \alpha \log k_p/k_0 - \sigma_I(\rho_I^m - \alpha\rho_I^p)$, is complicated by the assignment of an appropriate value to α which is a weighting factor indicating the degree to which resonance of a *m*-substituent with the aromatic ring affects the electron density at the reaction site with which it is not necessarily conjugated. In addition it must be assumed that $\rho_I^m = \rho_I^p$ and that inductive effects of groups in the *m* and *p* positions are equal (these are probably good first approximations). The utility of the equation is limited.

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