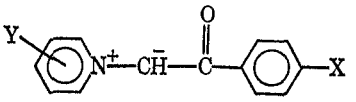
TABLE II

PYRIDINIUM YLIDES



Y	X	Registry no.	Mp, °C, dec	% yield	Nmr (CDCl₃ solvent, τ,[c] multiplicity[d]) Y	α-Pyridine	β- + γ-pyridine	Methine	Aromatic	Neut equiv[e]
H	H	a	89–92[a]	85		m, 0.4	m, 2.2	Not seen	m, 2.7	212 (197)
H	Br	b	133–136[b]	93		m, 0.9	m, 2.2	Not seen	m, 2.2	
CH_3	H	c	110–113		s, 7.3	d, 0.3	m, 2.1	s, 3.2	m, 3.3	214 (211)
CN	H	d	114–118	Quant		d, 0.6[f]	m, 2.0	s, 3.2	m, 2.0	216 (222)
C_2H_5	H	e	103–106	83	q, 7.4 t, 8.8	d, 0.5	m, 2.0	s, 3.2	m, 2.7	
CN	NO_2	f	187–189		[g]					
CN	Cl	g	148–150	32		d, 0.9[f]	m, 2.2	d, 3.3	m, 2.2	265 (257)
H	NO_2	h	Slow dec	Quant		m, 0.3	m, 2.5	s, 3.2	q, 1.9	239 (242)
CH_3	NO_2	i	Slow dec	95	s, 7.5	d, 0.5	m, 2.7	Not seen	q, 1.9	236 (256)
CH_3	Cl	j	86–89	87	s, 7.6	d, 0.6	d, 2.3	s, 3.4	m, 2.8	262 (246)
t-C_4H_9	H	k	155–162		s, 8.7	d, 0.5	m, 2.2	s, 3.2	m, 2.6	
CH_3CO	H	l	93–98		[g]					
H	OCH_3[h]	m	103–107	56		m, 0.4	m, 2.8	Not seen	q, 2.6	233 (227)
CN	OCH_3[i]	n	128–131	Quant		d, 1.0[f]	d, 2.9	s, 3.4	m, 1.8	260 (252)
3-CN	H	o	143–147	82		m, 1.8–2.9[j]	m, 1.8–2.9		m, 1.8–2.0	
3-Br	H	p	118–120	88		s, 0.0 d, 1.0	m, 2.2	Not seen	m, 2.8	274 (276)

[a] Lit.[2] mp 93–96°. [b] Lit.[2] mp 135–136°. [c] Internal TMS. [d] m = unresolved multiplet (the integrations were all consistent with theory), d = doublet, s = singlet, q = quartet, t = triplet. [e] Theoretical values are in parentheses. [f] SO_2 was solvent here. [g] A nmr spectrum was not obtained because of solubility difficulties. [h] The methoxy gives raise to a nmr absorption at τ 6.2 (s). [i] The methoxy gives raise to a nmr absorption at τ 6.1 (s). [j] The phenyl and pyridine protons overlapped here.

TABLE III

RESULTS OF $\sigma\rho$ TREATMENT OF pK_a'S[a]

X varied	Y = H	ρ = +2.3
X varied	Y = CN	ρ = +2.3
X varied	Y = CH_3	ρ = +2.2
X = H	Y varied	ρ = +2.6
X = NO_2	Y varied	ρ = +3.1
X = Br or Cl	Y varied	ρ = +2.9

[a] σ constants are those for substituted benzoic acids except for Y = 4-CN and 4-$COCH_3$, where σ was employed.

Synthesis of Pyridinium Ylides.—The method of Krohnke was followed.[2] An aqueous solution of 10% sodium carbonate was added to an aqueous solution of the pyridinium salt. The ylide was then filtered off and dried. In cases where the ylide was soluble in water, the solution was extracted with chloroform. Table II is a summary of the results. In some cases, the methine proton was not seen in the nmr because of exchange with $CDCl_3$.

Measurement of pK_a Values.—The pK_a values were determined by the method given in ref 14. The ρ's were determined by a least-squares treatment of the data.

N-(4-Nitrophenacyl)pyridazinium Bromide.—To 29.3 g (0.125 mol) of 4-nitrophenacyl bromide in benzene was added 10.0 g (0.125 mol) of pyrazine. After stirring overnight, 30.1 g of a precipitate was filtered off, mp 226–227°.

Anal. Calcd for $C_{12}H_{10}BrN_3O_3$: C, 44.46; H, 3.11; N, 12.96. Found: C, 44.62; H, 3.30; N, 12.75.

N-(4-Nitrophenacyl)pyrimidinium Bromide.—To 6.1 g (0.025 mol) of 4-nitrophenacyl bromide in 300 ml of benzene was added 2.0 g (0.025 mol) of pyrimidine. After heating overnight on a steam bath, 1.5 g of a precipitate which formed was filtered off, mp 187–188°.

Anal. Calcd for $C_{12}H_{10}BrN_3O_3$: C, 44.46; H, 3.11; N, 12.96. Found: C, 44.59; H, 3.18; N, 12.79.

N-(4-Nitrophenacyl)pyrazinium Bromide.—To 30 g of 4-nitrophenacyl bromide in benzene was added 10.0 g (0.125 mol) of pyrazine. After stirring overnight, 4.5 g of a precipitate was filtered off, mp 208–209°.

Anal. Calcd for $C_{12}H_{10}BrN_3O_3$: C, 44.46; H, 3.11; N, 12.96. Found: C, 44.62; H, 3.11; N, 12.99.

(14) A. J. Speziale and K. W. Ratts, *J. Amer. Chem. Soc.*, **85**, 2790 (1963).

Registry No.—Table I—a, 16883-69-5; b, 17282-37-0; c, 7250-28-4; d, 25357-39-5; e, 16844-13-6; f, 25407-29-8; g, 25357-41-9; h, 25407-30-1; i, 25357-42-0; j, 25357-43-1; k, 25357-44-2; l, 25357-45-3; m, 25407-31-2; n, 25407-32-3; o, 25357-46-4; p, 6299-99-6; Table II—a, 17282-43-8; b, 17282-45-0; c, 25357-50-0; d, 25357-51-1; e, 25407-33-4; f, 25357-52-2; g, 25357-53-3; h, 25357-54-4; i, 25357-55-5; j, 25357-56-6; k, 25357-57-7; l, 25357-58-8; m, 25357-59-9; n, 25357-60-2; o, 25357-61-3; p, 25357-62-4; N-(4-nitrophenacyl)pyridazinium bromide, 25357-63-5; N-(4-nitrophenacyl)pyrimidinium bromide, 25357-64-6; N-(4-nitrophenacyl)pyrazinium bromide, 25357-65-7.

Methyl Aryl Ether Cleavage in Benzazole Syntheses in Polyphosphoric Acid

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The polyphosphoric acid method[1] has been extensively employed as a general synthesis of benzazole compounds. As part of some recent studies, a number of substituted 2-phenylbenzazoles have been prepared in PPA, and we now wish to report an interesting ether cleavage reaction accompanying benzazole formation using this method.

The condensation reactions of *o*-methoxybenzoic acid

(1) (a) D. W. Hein, R. J. Alheim, and J. J. Leavitt, *J. Amer. Chem. Soc.*, **79**, 427 (1957). (b) D. W. Hein, R. J. Alheim, and J. J. Leavitt, American Cyanamid Company, U. S. Patent 2,985,611; *Chem. Abstr.*, **57**, 11203c (1962).

(1) with *o*-phenylenediamine, *o*-aminophenol, and *o*-aminothiophenol in PPA at 180–200° proceeded with methyl ether cleavage resulting in the formation of the corresponding 2-(2-hydroxyphenyl)benzazoles (**4**). However, the reaction of **1** with *o*-phenylenediamine in PPA at 135° has been reported to give only the 2-(2-methoxyphenyl)benzimidazole (**3**, X = NH).[2] We have similarly observed the formation of **3** (X = S) as the major product in the condensation of **1** with *o*-aminothiophenol in PPA at 160°. Extended heating of the same reaction mixture at 200° resulted only in the isolation of the ether cleavage product 2-(2-hydroxyphenyl)benzothiazole (**4**, X = S).

Similar demethylations were also observed in the reactions of 3- and 5-methoxysalicylic acids (**5** and **6**) with *o*-aminophenol in PPA at 185 to 195°. The products isolated under these conditions were the corresponding isomeric 2-(dihydroxyphenyl)benzoxazoles (**9** and **10**). In analogy with reactions of *o*-methoxybenzoic acid described above, it is probable that the benzoxazoles (**7** and **8**) were initially formed in the reactions of the isomeric methoxysalicylic acids and were subsequently demethylated under the experimental conditions. Methyl ether cleavage has been observed for the structurally analogous 2-(2-hydroxy-5-methoxyphenyl)benzothiazole in PPA at 170°. In general, demethylation accompanies benzazole formation from methoxy aromatic carboxylic acids in PPA from 170 to 200°, but ether cleavage does not occur below 150°.

Several attempts to extend the ether cleavage in PPA to carbocyclic systems such as β-methoxynaphthalene and 4-methoxybiphenyl were unsuccessful. Numerous examples of chemical reactions in PPA involving methoxy-substituted aromatic compounds have been described.[3] It would appear that the possibility of methyl aryl ether cleavage in these reactions must be given consideration.

(2) M. Dunnenberger, A. E. Siegrist, and E. Maeder, Ciba Ltd., Swiss Patent 350,763; *Chem. Abstr.*, **55**, 19973*a* (1961).

Experimental Section

All melting points were taken on a Thomas–Hoover apparatus and are uncorrected. Infrared and ultraviolet spectra were recorded on the Perkin-Elmer Model 137 and Cary Model 14 spectrophotometers, respectively.

Materials.—Polyphosphoric acid (practical grade) was obtained from Matheson Coleman and Bell, East Rutherford, N. J. 2-(2,5-Dihydroxyphenyl)benzoxazole (mp 207–209°) and 2-(2,5-dihydroxyphenyl)benzothiazole (mp 195–196°) were prepared from the reactions of 5-hydroxysalicylic acid with *o*-aminophenol and *o*-aminothiophenol in PPA, respectively.

3Methoxysalicylic acid (mp 142–144°) was prepared by the oxidation of the corresponding aldehyde according to the procedure described in "Organic Syntheses."[4]

Reaction of *o*-Methoxybenzoic Acid in PPA. A. With *o*-Phenylenediamine.—A mixture of 3.04 g (0.02 mol) of *o*-methoxybenzoic acid, 2.16 g (0.02 mol) of *o*-phenylenediamine, and 60 g of PPA was heated at 130° for 15 hr and for an additional 48 hr at 185–190°. The reaction mixture was cooled, poured into 300 ml of water, and neutralized with 50% aqueous sodium hydroxide solution. The precipitate was removed by filtration, washed with water, and dried under vacuum. Vacuum sublimation of the crude product gave 2-(2-hydroxyphenyl)benzimidazole, 0.6 g (14%), mp 239–240° (lit.[1a] mp 241.6–242.2°). The infrared spectrum of this product was identical with that of 2-(2-hydroxyphenyl)benzimidazole prepared by the literature method.[1a]

B. With *o*-Aminophenol.—A mixture of 2.18 g (0.02 mol) of *o*-methoxybenzoic acid, 2.72 g (0.02 mol) of *o*-aminophenol, and 120 g of PPA was heated at 200° for 24 hr. Work-up as above gave 2-(2-hydroxyphenyl)benzoxazole, 0.3 g (7%), mp 121–123° (lit.[5] mp 123°). The infrared spectrum of this product was identical with that of 2-(2-hydroxy)benzoxazole prepared by the literature method.[5]

C. With *o*-Aminothiophenol.—A mixture of 1.52 g (0.01 mol) of *o*-methoxybenzoic acid, 1.25 g (0.01 mol) of *o*-aminothiophenol, and 75 g of PPA was heated at 200° for 16 hr. Work-up as above in A gave 2-(2-hydroxyphenyl)benzothiazole, 0.5 g (22%), mp 130–132° (lit.[6] mp 131–132°). The infrared spectrum of this product was identical with that of 2-(2-hydroxyphenyl)benzothiazole prepared by the literature method.[6]

The same reaction mixture, when heated at 160° for 16 hr, gave 1 g of a white solid which was established by vpc analysis (4-ft silicone rubber column, 210°) as a 4 to 1 mixture of 2-(2-methoxyphenyl)- and 2-(2-hydroxyphenyl)benzothiazoles, respectively.

Reaction of 3-Methoxysalicylic Acid with *o*-Aminophenol in PPA.—A mixture of 3.4 g (0.02 mol) of 3-methoxysalicylic acid, 2.2 g (0.023 mol) of *o*-aminophenol, and 120 g of PPA was heated at 150° for 2 hr and then at 195° for 14 hr. Work-up as above in A followed by recrystallization from 95% ethanol gave pale pink needles of 2-(2,3-dihydroxyphenyl)benzoxazole, 1.5 g (33%), mp 163–163.5°: ν^{KBr} 3380, 1630, 1245, cm^{-1}; $\lambda_{max}^{95\%\ C_2H_5OH}$ mμ (ε), 330 sh (7880), 304 (25,500), 293 (25,800), and 269 sh (12,500).

Anal. Calcd for $C_{13}H_9NO_3$ (mw 227.21): C, 68.71; H, 3.99; N, 6.17. Found: C, 68.40; H, 4.0; N, 6.24.

Reaction of 5-Methoxysalicylic with *o*-Aminophenol in PPA.—A mixture of 0.6 g (3.6 mmol) of 5-methoxysalicylic acid, 0.39 g (3.6 mmol) of *o*-aminophenol, and 60 g of PPA was heated at 185° for 20 hr. Work-up as above in A was followed by recrystallization from 95% ethanol gave pale yellow needles of 2-(2-hydroxyphenyl)benzoxazole, 0.28 g (33%): mp 206–207°; ν^{KBr} 3400, 3350, 1640, 1245 cm^{-1}; $\lambda_{max}^{95\%\ C_2H_5OH}$ mμ (ε), 350 (11,300), 301 (18,200), 288 (19,200), 280 (19,200), 282 (14,600), and 265 sh (11,400).

Anal. Calcd for $C_{13}H_9NO_2$ (mw 227.21): C, 68.71; H, 3.99; N, 6.17. Found: C, 68.50; H, 4.10; N, 6.10.

(3) (a) F. D. Popp and W. E. McEwen, *Chem. Rev.*, **58**, 321 (1958); (b) F. Uhlig and H. R. Snyder *Advan. Org. Chem.*, **1**, 35 (1960).

(4) "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1963, p 972.

(5) S. Skraup and M. Moser, *Chem. Ber.*, **55B**, 1080 (1922).

(6) M. T. Bogert and H. B. Corbitt, *J. Amer. Chem. Soc.*, **48**, 783 (1926).

Reaction of 2-(2-Hydroxy-5-methoxyphenyl)benzothiazole in PPA.—A mixture of 0.4 g (1.55 mmol) of 2-(2-hydroxy-5-methoxyphenyl)benzothiazole and 60 g of PPA was heated at 170° for 15 hr. Work-up as above in A gave 2-(2,5-dihydroxyphenyl)benzothiazole, 0.12 g (30%), mp 193–196°. An infrared spectrum of the product was identical with that of 2-(2,5-dihydroxyphenyl)benzothiazole prepared from 5-hydroxysalicylic acid and *o*-aminothiophenol in PPA.

Registry No.—**4** (X = O), 835-64-3; **9**, 24978-46-9; 2-(2,5-dihydroxyphenyl)benzothiazole, 24978-47-0.

A Convenient Method of Esterification of Polyphosphonic Acids

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Unlike carboxylic acids, phosphonic acids cannot be esterified by direct reaction with alcohols. Esterification is usually accomplished by converting the phosphonic acid to the corresponding acid chloride which will react with an alcohol in the presence of base to yield the phosphonate ester.[2]

In the course of a recent study it became of interest to synthesize a series of esters from methylenediphosphonic acid (MDP). Siddall and Prohaska[3] have prepared tetra(3-methyl-2-butyl) methylenediphosphonate in 50% yield from methylenediphosphonic tetrachloride and the alcohol in the presence of pyridine. Methylenediphosphonic tetrachloride is also obtained in 50% yield[4] so that the overall conversion from MDP to its tetraalkyl ester proceeds in low yield and involves two rather difficult steps.[3,4]

This note describes a one-step method of esterification of MDP which results in 70–90% yields of the tetraalkyl esters. The method is not limited to MDP but has been shown to be applicable to esterifications of *vic*-tri- and tetraphosphonic acids as well as 1-hydroxy-1,1-diphosphonic acids.

Three literature reports led us to attempt the esterification of polyphosphonic acids with esters of orthoformic acid. Trialkyl orthoformates are known[5] to effect the esterification of carboxylic acids in up to 95% yield. Fitch[6] has prepared alkyl hypophosphites from hypophosphorous acid and trialkyl orthoformates. Finally a 1960 patent[7] describes the esterification of benzenephosphonic acid with triethyl orthoformate.

MDP was found to react at elevated temperatures with trialkyl orthoformates to yield tetraalkyl methylenediphosphonates, along with the corresponding alcohol and alkyl formate (eq 1). It was necessary to continuously remove the lower boiling alcohols and formates (reduced pressure is required when R = $C_{18}H_{37}$) so that higher reaction temperatures could be obtained. Tetramethyl, tetraethyl, tetraallyl, and tetrakis(octadecyl) methylenediphosphonates were successfully prepared *via* this procedure. Their ^{31}P nmr chemical shifts are given in Table I.

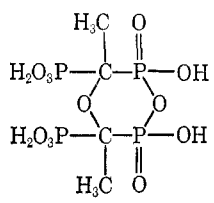
$$H_2O_3PCH_2PO_3H_2 + 4(RO)_3CH \xrightarrow{\Delta} R_2O_3PCH_2PO_3R_2 + 4ROH + 4HC(O)OR \quad (1)$$

To broaden the scope of this esterification method, the recently reported[8] vicinal tri- and tetraphosphonic acids were allowed to react with triethyl orthoformate. Esterification proceeded as described above and hexaethyl propane-1,2,3-triphosphonate and octaethyl butane-1,2,3,4-tetraphosphonate were isolated by distillation. In this case the polyphosphonic acid halides are unknown so that an alternative method of esterification is not available. Phosphorus nmr chemical shifts are given in Table I.

Another class of polyphosphonic acids for which the acid halides are unknown is the alkyl-1-hydroxy-1,1-diphosphonic acids. An attempt was made[9] to esterify ethane-1-hydroxy-1,1-diphosphonic acid with diazomethane. The tetramethyl ester was perhaps prepared initially but completely rearranged to the phosphate-phosphonate.[10a] Under the conditions used,[9] the tetramethyl ester of ethane-1-methoxy-1,1-diphosphonic acid always accompanied the phosphate–phosphonate in the final product.

Reaction of ethane-1-hydroxy-1,1-diphosphonic acid with trimethyl orthoformate was found to produce the corresponding tetramethyl ester which was isolated in about 70% yield by crystallization. This ester proved to be identical with authentic tetramethyl ethane-1-hydroxy-1,1-diphosphonate prepared by a combination of the methods of Fitch and Moedritzer[10a] and Pudovik, *et al.*[10b]

It is known[11] that ethane-1-hydroxy-1,1-diphosphonic acid can dimerize to a very stable cyclic condensate containing C–O–C and P–O–P linkages (compound I). This condensate was easily converted to the hexamethyl ester by reaction with trimethyl orthoformate. As reported elsewhere,[11] the ester was utilized in establishing the structure of I.



I

An attempt to esterify ethane-1-hydroxy-1,1,2-triphosphonic acid with trimethyl orthoformate resulted in partial esterification with concomitant rearrangement to the phosphate–diphosphonate as shown by ^{31}P nmr. To further characterize the course of the re-

(1) (a) To whom correspondence should be addressed. (b) Retired, Nov 1, 1966.

(2) G. M. Kosolapoff, "Organophosphorus Compounds," Wiley, New York, N. Y., 1950, pp 139–140.

(3) T. H. Siddall, III, and C. A. Prohaska, *Inorg. Chem.*, **4**, 783 (1965).

(4) J. J. Richard, K. E. Burke, J. W. O'Laughlin, and C. V. Banks, *J. Amer. Chem. Soc.*, **83**, 1722 (1961).

(5) H. Cohen and J. D. Mier, *Chem. Ind. (London)*, 349 (1965).

(6) S. J. Fitch, *J. Amer. Chem. Soc.*, **86**, 61 (1964).

(7) J. Preston and H. G. Clark, U. S. Patent 2,928,859 (1960).

(8) W. A. Cilley, D. A. Nicholson, and D. Campbell, *J. Amer. Chem. Soc.*, **92**, 1685 (1970).

(9) D. F. Kuemmel, private communication.

(10) (a) S. J. Fitch and K. Moedritzer, *J. Amer. Chem. Soc.*, **84**, 1876 (1962); (b) A. N. Pudovik, I. V. Konovalova, and L. V. Dedova, *Dokl. Akad. Nauk SSSR*, **153**, 616 (1963); *Chem. Abstr.*, **60**, 8060*a* (1964).

(11) J. B. Prentice and O. T. Quimby, manuscript submitted for publication on the preparation of condensates of ethane-1-hydroxy-1,1-diphosphonic acid.