o-PHOSPHORUS-SUBSTITUTED BENZOIC ACIDS

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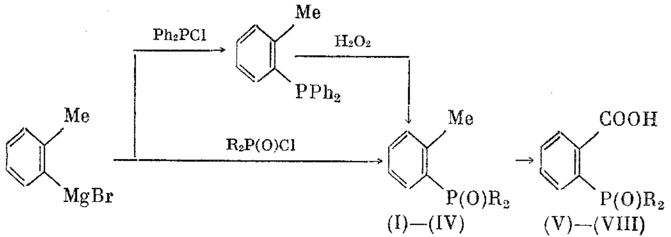
To study the character of H-bonds in oxides of hydroxyl-containing phosphines we synthesized ω-diphenylphosphonyl-substituted aliphatic alcohols [1] and also O-phosphonyl-containing arylaliphatic alcohols [2] and phenols [3].

The synthesis is described in the present work of some o-phosphorus-substituted benzoic acids which has been undertaken with the aim of investigating the influence of the nature of the OH group on the character of the H-bond in the crystalline state and in solution.

o-Phosphorus-substituted toluenes (I-III) served as starting compounds for o-phosphonyl-containing benzoic acids, of which only o-diphenylphosphonylbenzoic acid is known [4]. The starting materials were obtained by the interaction of o-tolylmagnesium bromide with acid chlorides of dialkylphosphinic acids. o-Diphenylphosphonyltoluene (IV) was synthesized from o-tolylmagnesium bromide and Ph_2PCl* with subsequent oxidation of the resulting phosphine with H_2O_2.



R = Me (I), (V); Et (II), (VI); Bu (III), (VII); Ph (IV), (VIII).

o-Phosphonylbenzoic acids (V-VIII) were obtained in high yield with the exception of o-dibutylphosphonylbenzoic acid (VII) by the oxidation of o-phosphonyltoluenes (I-IV) with $KMnO_4$ in aqueous pyridine [5].

Methyl esters (IX-XII) of the synthesized acids (V-VIII) were obtained by esterification in MeOH in the presence of conc. H_2SO_4 or by alkylation of the acids with diazomethane in ether. The constants of the obtained compounds are given in Table 1.

The ionization constants of o-phosphorus-substituted benzoic acids (V-VIII) were measured by us with the aim of comparing them with the analogous para isomers. Ionization constants were measured by potentiometric titration in aqueous alcohol (1:1 and 1:4 by volume) and in water the case of water-soluble acids (Table 2).

EXPERIMENTAL

All operations with P(III) compounds were carried out in an atmosphere of Ar. Melting points were measured with specially short Anschütz thermometers. The $^{31}P-\{H\}$ NMR spectra of solutions of substances in alcohol were taken on a Bruker HX-90 spectrometer (36, 43 MHz) in impulse mode, standard was 85% H_3PO_4. Chemical shifts are given in the new scale [10].

o-Dimethylphosphonyltoluene (I). A solution of $Me_2P(O)Cl$ [11] (26.9 g) in abs. benzene (80 ml) was added dropwise with stirring to the Grignard reagent obtained from Mg (8.3 g) in abs. ether (70 ml) and o-bromotoluene (BT, 58.6 g) in abs. ether (70 ml) (2-и boiling) at 0°C. The mixture was boiled for 3 h and decomposed with dilute HCl (1:1). The aqueous layer was washed three times with petroleum ether, neutralized with dry

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*A simplified synthesis of diphenylchlorophosphine from C_6H_6 and $PCl_3/AlCl_3$ through diphenylphosphinic acid is described in the experimental section.

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TABLE 1. Yields, Constants, and Analytical Data of the Obtained Compounds

Compound	Yield, %	mp °C (solvent) bp °C (mm Hg)	Found, %			Empirical formula	Calculated, %		
			C	H	P		C	H	P
(I)	67	85–86,5 (from hexane–ethyl acetate) 150–152 (2)	64,3	7,8	18,2	$C_9H_{13}OP$	64,3	7,8	18,4
(II)	48	117,5–118 (2) [a]	67,4	8,8	15,6	$C_{11}H_{17}OP$	67,3	8,7	15,8
(III)	44	155–156 (1) [b]	71,2	9,8	12,4	$C_{15}H_{25}OP$	71,4	10,0	12,3
(IV)	83	125–126 [c] (from acetone)							
(V)	70	195,5–196,5 (from water)	54,8	5,7	15,6	$C_9H_{11}O_3P$	54,6	5,6	15,6
(VI)	72	158–158,5 (from methyl ethyl ketone)	58,5	6,8	13,6	$C_{10}H_{15}O_3P$	58,4	6,7	13,7
(VII)	27	113–114 (from MeCN–methyl ethyl ket.)	63,9	8,2	11,1	$C_{15}H_{23}O_3P$	63,8	8,2	11,0
(VIII)	62	252–254 [d] (from MeOH)							
(IX)	93	81,5–83,5 (from cyclohex.–ethyl acetate)	56,5	6,2	14,7	$C_{10}H_{13}O_3P$	56,6	6,2	14,6
(X)	59	166–167 (2) [e]	60,1	7,2	12,8	$C_{12}H_{17}O_3P$	60,0	7,1	12,9
(XI)	90	177–179 (1) [f]	64,8	8,4	10,4	$C_{16}H_{25}O_3P$	64,8	8,5	10,4
(XII)	70	134–135 (from cyclohexane–methyl ethyl ketone)	71,4	5,1	9,3	$C_{20}H_{17}O_3P$	71,4	5,1	9,2

[a] n^{20}_D 1.5435, d_4^{20} 1.0567.
[b] n^{20}_D 1.5216, d_4^{20} 0.9980.
[c] cf. [6].
[d] cf. [4].
[e] n^{20}_D 1.5362, d_4^{20} 1.1285.
[f] n^{20}_D 1.5210, d_4^{20} 1.0785.

$NaHCO_3$, and extracted with $CHCl_3$. The extract was dried over Na_2SO_4, evaporated in vacuum, and the residue distilled. Yield of (I) was 26.0 g.

o-Diethylphosphonyltoluene (II). A solution of $Et_2P(O)Cl$ [12] (21.3 g) in abs. ether (50 ml) was added dropwise with stirring to the Grignard reagent obtained from Mg (4.6 g) in abs. ether (30 ml) and BT (32.3 g) in abs. ether (100 ml) (1-h boiling) at 0°C. The mixture was boiled for 2 h and decomposed with a saturated solution of NH_4Cl. The organic layer was separated, the aqueous extracted with $CHCl_3$, the combined extract dried over Na_2SO_4, evaporated in vacuum, and the residue distilled. From the obtained product (20.8 g) of bp 109-111°C (1 mm) a fraction was distilled off with a fractionating column and had bp 115-120°C (6 mm). The still residue was redistilled twice in vacuum. Yield of (II) was 14.3 g.

o-Dibutylphosphonyltoluene (III). A solution of $Bu_2P(O)Cl$ [13] (38.2 g) in abs. ether (30 ml) was added to the Grignard reagent obtained from Mg (5.9 g) and BT (43.1 g) in abs. ether (125 ml) (2-h boiling) at 0°C. The mixture was boiled for 3 h and decomposed with dilute (1 :3) HCl (120 ml). Three layers formed in the reaction mixture. After washing the middle layer with ether, water (75 ml), $CHCl_3$ (50 ml), and dry $NaHCO_3$ were added to neutral reaction. The organic layer was separated, the aqueous layer was extracted with $CHCl_3$, the combined extract dried over Na_2SO_4, and evaporated in vacuum. From the obtained product* (32.8 g) of bp 163-169°C (2 mm) a fraction was distilled off on a column and had bp 115-125°C (1 mm). The still residue was twice distilled in vacuum. Yield of (III) was 21.2 g. ^{31}P NMR spectrum (δ, ppm): +39.9 s.

Diphenylchlorophosphine.† A mixture of PCl_3 (27.5 g), $AlCl_3$ (26.7 g), and abs. C_6H_6 (62.4 g) was boiled for 15 h. Then C_6H_6 (100 ml) was added to the mixture followed by dilute (1 :4) HCl (200 ml) with cooling and stirring. The upper benzene layer (three layers were formed) was separated, and the aqueous layer was ex-

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* ^{31}P NMR spectrum (δ, ppm): +55.4 s (11%); +39.7 s (83%); +37.0 s (6%).

† In the synthesis a modified procedure for obtaining diphenylphosphinic acid from $PCl_3/AlCl_3$ and C_6H_6 was used [14].

TABLE 2. Ionization Constants of Phosphorus-Substituted Benzoic Acids XC_6H_4COOH in Water and in Aqueous Alcohol (1 :1 and 1 :4 by volume) for o and p Isomers

X	pK_a		
	water	aqueous alcohol	
		1 : 1	1 : 4
p-$Me_2P(O)$ [7]	3,70	4,91	5,91
o-$Me_2P(O)$	3,27	4,54	5,49
p-$Et_2P(O)$ [7]	–	4,92	5,95
o-$Et_2P(O)$	–	4,59	5,54
p-$Bu_2P(O)$ [8]	–	4,98	5,89*
o-$Bu_2P(O)$	–	4,92	5,72
p-$Ph_2P(O)$	–	4,88 [8]	5,82
o-$Ph_2P(O)$	–	5,37	6,21

*Calculated from pK_a in aqueous alcohol (1 :1 by volume) using the equation $pH_{a1:4} = 1.035\, pK_{a1:1} + 0.78$ derived from pK_a values in aqueous alcohol 1 :1 and 1 :4 by volume [9].

tracted with benzene. The combined extract was washed with dilute (1 :4) HCl and combined with the middle layer of oil, previously washed by decantation with dilute (1 :4) HCl. The combined mixture was washed with 20% NaOH solution, and then with dilute (1 :10) HCl and aqueous $NaHCO_3$ to neutral reaction. The benzene solution was dried over Na_2SO_4 and evaporated in vacuum. Benzene (50 ml) and PCl_3 (130 ml) were added to the residue and then petroleum ether (100 ml) 15-20 h later. The solid was filtered off, solvent and PCl_3 were distilled from the filtrate at atmospheric pressure, and the residue was distilled in vacuum. Compound Ph_2PCl (22.8 g, 52%) was obtained having bp 135.5°C (2 mm), n_D^{20} 1.6352, d_4^{20} 1.1905 (cf. [15]).

o-Diphenylphosphonyltoluene (IV). A solution of Ph_2PCl (29.5 g) in abs. ether (10 ml) was added dropwise at 0°C with stirring to the Grignard reagent obtained from Mg (4.3 g) in abs. ether (20 ml) and BT (30.3 g) in abs. ether (70 ml) (1-h boiling). The mixture was boiled for 1 h and decomposed with dilute (1 :5) HCl (75 ml). The organic layer was separated, the aqueous layer extracted with ether, the combined extract washed with saturated $NaHCO_3$ solution, and evaporated in vacuum. The residue was dissolved in acetone (80 ml) and 30% H_2O_2 (15.4 g) in acetone (20 ml) was added dropwise to the solution with stirring. The mixture was evaporated in vacuum. Yield of (IV) was 32.5 g.

o-Dimethylphosphonylbenzoic Acid (V). Powdered $KMnO_4$ (80.9 g) was added with stirring in four portions over 1.5 h to a boiling mixture of (I) (21.6 g), pyridine (100 ml), and water (40 ml), maintaining gentle boiling throughout. After boiling for 2 h, MnO_2 was filtered off and the solid washed with water (70 ml). Pyridine was distilled off from the filtrate as an azeotropic mixture with water (bp 94°C). The residual solution was washed twice with $CHCl_3$ and acidified with dilute (1 :1) HCl until weakly acidic reaction. The precipitated acid was filtered off. Yield of (V) was 22.1 g. ^{31}P NMR spectrum (δ, ppm): +42.5 s.

o-Diethylphosphonylbenzoic Acid (VI). Powdered $KMnO_4$ (31.1 g) was added with stirring in three portions over 1 h to a boiling mixture of (II) (9.7 g), pyridine (40 ml), and water (40 ml), maintaining gentle boiling throughout. After boiling for 2 h, conc. HCl (75 ml) was added to the mixture and then a saturated solution of $NaNO_2$ was added dropwise to decolorize the mixture completely. The precipitated solid was filtered off, dissolved in 20% NaOH (25 ml), the solution filtered, the filtrate acidified with conc. HCl, and the precipitated solid filtered off. Yield of (VI) was 8.0 g. ^{31}P NMR spectrum (δ, ppm): +52.6 s.

o-Dibutylphosphonylbenzoic Acid (VII). Powdered $KMnO_4$ (39.8 g) was added with stirring in five portions over 30 min to a boiling mixture of (III) (15.8 g), pyridine (45 ml), and water (50 ml), maintaining gentle boiling throughout. After boiling for 15 min the mixture was cooled, MnO_2 was filtered off, and the solid was washed with water (30 ml). Pyridine was distilled from the filtrate as the azeotropic mixture with water (bp 94°C). The residual solution was washed twice with $CHCl_3$ and acidified with dilute (1 :1) HCl to weakly acid reaction. The oil which separated was extracted with $CHCl_3$, the extract dried over Na_2SO_4, and evaporated in vacuum. The residue* (12.7 g) was dissolved in abs. MeOH (150 ml) containing conc. H_2SO_4 (2 ml). The solution was boiled for 5 h and evaporated in vacuum. The residue was dissolved in $CHCl_3$, the solution washed three times with 5% NaOH and then with water, dried over Na_2SO_4, and evaporated in vacuum. The residual oil† (8.0 g) was dis-

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*^{31}P NMR spectrum (δ, ppm): +55.8 s (10%), +50.8 s (31%), +42.5 s (59%).

†^{31}P NMR spectrum (δ, ppm): +43.9 s (25.5%), +39.9 s (74.5%).

solved in 50% aqueous alcohol (30 ml) containing KOH (1.5 g). The solution was boiled for 4 h and evaporated in vacuum. The residue was dissolved in water (30 ml), the solution washed twice with $CHCl_3$, and acidified with dilute (1 :1) HCl to weakly acid reaction. The precipitated oil was extracted with $CHCl_3$, the extract dried over Na_2SO_4, and evaporated in vacuum. The residue crystallized on trituration with MeCN. After drying in vacuum* (1-2 mm) at 80°C for 2 d and then at 110°C the yield of (VII) was 4.0 g. ^{31}P NMR spectrum (δ, ppm): +49.7 s.

o-Diphenylphosphonylbenzoic Acid (VIII). Acid (VIII) was obtained from toluene (IV) in a manner similar to (VI). ^{31}P NMR spectrum (DMF, δ, ppm): + 28.9 s.

o-Dimethylphosphonylbenzoic Acid Methyl Ester (IX). A solution of (V) (4.0 g) in abs. MeOH (70 ml) containing conc. H_2SO_4 (1 ml) was boiled for 5 h and evaporated in vacuum. The residue was dissolved in $CHCl_3$ (50 ml), the solution washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and evaporated in vacuum. The yield of (IX) was 3.9 g. ^{31}P NMR spectrum (δ, ppm): + 32.0 s.

o-Diethylphosphonylbenzoic Acid Methyl Ester (X). An ether solution of CH_2N_2 obtained from nitrosomethylurea (2.0 g) [16] was added dropwise with stirring at 20°C to a suspension of (VI) (1.0 g) in abs. C_6H_6 (15 ml). The solution was stirred for 1 h at 20°C, washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, evaporated in vacuum, and the residue distilled. Yield of (X) was 0.6 g.

o-Dibutylphosphonylbenzoic Acid Methyl Ester (XI). Ester (XI) was obtained in a similar manner to (IX) from acid (VII). ^{31}P NMR spectrum (acetone, δ, ppm): + 39.7 s.

o-Diphenylphosphonylbenzoic Acid Methyl Ester (XII). Ester (XII) was obtained in a similar manner to (X) from acid (VIII).

Determination of Ionization Constants. Apparent ionization constants were determined by potentiometric titration [17] with the aid of a pH-340 potentiometer with an ESL-41G-04 glass electrode at 25 ± 0.1°C. A flow-through silver chloride electrode was used as reference electrode. Setting of the instrument was carried out with tartrate (pH 1.68), diphthalate (pH 4.01), phosphate (pH 6.86), and borate (pH 9.18) buffers. The concentrations of solutions being measured were $1 \cdot 10^{-2}$ mole/liter. Mean values obtained from the results of two or more titrations are given. The apparent ionization constant of o-diphenylphosphonylbenzoic acid in aqueous alcohol (1 :1 by volume) and of o-dimethylphosphonylbenzoic acid in water at 25°C were determined by another method [18] (concentration $3 \cdot 10^{-3}$ mole/liter).

Standardization was carried out with benzoic acid. The pK_a obtained were 4.21 (in water), 5.72, and 6.78 (aqueous alcohol 1 :1 and 1 :4 by volume, respectively).

SUMMARY

1. o-Phosphorus-substituted benzoic acids $o\text{-}R_2P(O)C_6H_4COOH$, where R = Me, Et, Bu, and Ph, and their methyl esters have been synthesized.

2. The ionization constants of the synthesized acids have been determined at 25°C in water and in aqueous alcohol (1 :1 and 1 :4 by volume) by potentiometric titration.

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* Before drying the substance melted at 87°C, then solidified, and melted again at 113-114°C.

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REACTION OF 2-PHENYL(ACETYL)-5-METHYLDIAZAPHOSPHOLE WITH PHENYL AZIDE

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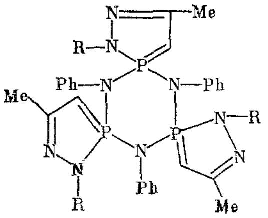
Continuing the study of cycloaddition at the P = C bond of the two-coordinate P atom [1, 2], in the present paper we have investigated the reactions of diazaphospholes with phenyl azide.

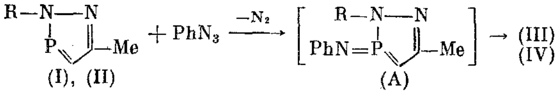
The reaction of 2-phenyl- (I) and 2-acetyl-5-methyldiazaphosphole (II) with phenyl azide was carried out both without a solvent and in ether, pentane, C_6H_6, and CCl_4 and was accompanied by vigorous evolution of nitrogen with the formation of unstable amorphous 1:1 adducts. A comparison of the IR spectra of the obtained adducts with the spectra of the starting diazaphospholes suggests that the diazaphosphole ring was retained in the adducts (presence of a band at 1300 cm^{-1} and pulsational vibrations of the diazaphosphole ring [3]).

The adduct with the phenyl substituent (III) was so unstable in the solvents that it could not be characterized by the ^1H and ^{31}P NMR spectra, although when the reaction was carried out in pentane, a solid product was obtained whose ^{31}P NMR spectrum (in CH_2Cl_2) contained two signals: + 32 and + 20 ppm. Apparently, the latter signal belonged to unchanged (III). Adduct (IV), obtained from (II), was found to be more stable in solvents and was characterized by ^1H and ^{31}P NMR spectra, $\delta^{31}P$ of +17 ppm* ($CHCl_3$). The PMR spectrum (in $CHCl_3$) contained signals with δ 2.3 ($CH_3C = N$) and 2.1 ppm (CH_3CO). However, the nature of the spectrum (broad absorption) indicated that the compound had a high molecular weight. Indeed, the molecular weight determined by cryoscopy in $CHBr_3$ confirmed this assumption, and adduct (IV) was apparently a trimer. The UV spectrum of (IV) contained absorption at 275 nm characteristic of the diazaphosphole ring



R = Ph (III), $\delta^{31}P$ + 20 ppm
R = CH_3CO (IV), $\delta^{31}P$ + 17 ppm

Apparently, the formation of trimers (III) and (IV) was preceded by the appearance of an adduct with diylide structure (A), which underwent trimerization at the P = N bond



With recrystallization of trimeric adduct (III) from alcohol, ethyl acetate, CH_3CN, or nitromethane without protection from moisture of air, crystalline 2-phenyl-3-oxo-3-anilino-5-methyl-1,2,3-diazaphospholine (Va) was obtained, $\delta^{31}P$ +32 ppm (in CH_2Cl_2). The IR spectrum of (Va) contained absorption bands of P = O (1211 cm^{-1}) and NH (3200 cm^{-1}) groups, absent in the spectrum of (III), and the PMR spectrum contained signals of the CH_3 group with δ 2.23 ppm and an H^4 doublet at δ 2.89 ppm, J_{PH} = 14 Hz. Apparently, trimer (III) was so sensitive to moisture that if there were traces of moisture in the solvent, (III) was converted to (Va)

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* The signals in the field which was weak with respect to H_3PO_4 are denoted with a plus sign.

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