EQUILIBRIUM CH ACIDITY OF ORGANOPHOSPHORUS COMPOUNDS

COMMUNICATION 3. ESTERS OF PHOSPHINYLACETIC ACIDS*

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Esters of phosphinylacetic acids are used in synthesis in the form of the corresponding metallic derivatives [3, 4]. And yet, there are no data on the CH acidity of the indicated compounds, possessing an active methylene group, which does not permit an estimation of the influence of structural factors on the reactivity of carbanions of derivatives of phosphinylacetic acids. The ionization constants of phosphinylacetic acids have been used for these purposes [5]; however, as will be shown below, such an indirect method of estimating CH acidity is extremely approximate.

In this work the CH acidity of a number of esters of phosphinylacetic acids in diglyme (DG) and DMSO was studied by the method of transmetallation [1, 2].

The compounds studied were produced by esterification of the corresponding phosphinylacetic acids, by the Michaelis — Becker reaction or the Arbuzov rearrangement of esters of P(III) acids with ethyl bromoacetate.

The values of pK of ethylphosphinyl acetates in DG (Li^+ cation) and in DMSO (K^+ cation),† related to the pK of 9-phenylfluorene, which was assumed equal to 18.5 in both solvents, are cited in Table 1. The

TABLE 1. Equilibrium CH Acidity of Esters of Phosphinylacetic Acids $RR'P(O)CH_2COOC_2H_5$ in Diglyme and Dimethyl Sulfoxide

Compound	R	R'	pK_{DG}	pK_{DMSO}	ΔpK
(I)	CH_3	CH_3	13,6	—	—
(II)	C_2H_5	C_2H_5	13,8	21,3	7,5
(III)	C_3H_7	C_3H_7	13,9	21,1	7,2
(IV)	C_4H_9	C_4H_9	14,1	21,1	7,0
(V)	CH_3	C_2H_5O	13,0	19,9	6,9
(VI)	C_2H_5	C_2H_5O	12,8	19,7	6,9
(VII)	C_2H_5O	C_2H_5O	12,2	19,2	7,0
(VIII)	C_4H_9O	C_4H_9O	12,2	19,2	7,0
(IX)	i-$C_5H_{11}O$	i-$C_5H_{11}O$	12,2	19,1	6,9
(X)	$(CH_3)_2N$	$(CH_3)_2N$	13,3	21,1	7,8
(XI)	$(C_2H_5)_2N$	$(C_2H_5)_2N$	13,4	21,6	8,2
(XII)	C_2H_5	C_6H_5	13,1	20,2	7,1
(XIII)	C_4H_9	C_6H_5	13,2	20,2	7,0
(XIV)	C_2H_5O	C_6H_5	12,2	18,9	6,7
(XV)	C_6H_5	C_6H_5	12,1	18,9	6,8
(XVI)	p-ClC_6H_4	p-ClC_6H_4	11,4	17,8	6,4
(XVII)	m-$O_2NC_6H_4$	m-$O_2NC_6H_4$	10,2	15,9	5,7

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*For the preceding communications of this series, see [1, 2].

†For the causes of the selection of different cations, see [1].

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values of pK, determined by the method of transmetallation, characterize the relative CH acidity of the substances in the given medium according to their ability for conversion to the corresponding organometallic compounds and are only conditionally related to the pK_a scale in water.

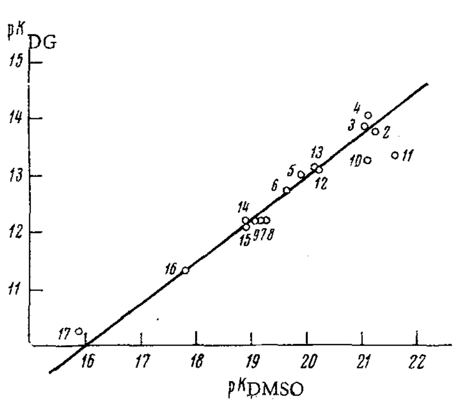

Fig. 1. Relationship between pK of ethylphosphinyl acetates in diglyme and DMSO. Here and in Figs. 2 and 3, the numeration of the points corresponds to the compounds in Table 1.

For the compounds studied, a strong influence of the medium on pK is observed. When DMSO is replaced by DG, and, correspondingly, the K^+ cation is replaced by Li^+, the values of pK of ethylphosphinyl acetates decrease relative to the standard acidity scale, at which the scale of pK of aliphatic-aromatic hydrocarbons is taken [6, 7], by 6-8 units of pK (see ΔpK, Table 1). When the polarity of the solvent and radius of the cation are decreased, probably there is an increase in the strength of the bond of carbanions of the acids studied to the cations in the ion pairs in comparison with the carbanions of the indicator acids. The cause of this is apparently the chelate coordination of the cation with the phosphoryl and carbethoxy groups in the contact ion pair, together with interaction in the carbanion center. If there is only a phosphoryl group in the carbanion, then the differentating effect is decreased to 3-5 units of pK [1, 2].

Between the values of pK measured in DG and DMSO there is a linear relationship, from which the points corresponding to amide derivatives deviate somewhat (Fig. 1)

$$pK_{DG} = -1.6 + 0.73\,pK_{DMSO} \pm 0.2;\quad s_\rho = 0.03;\quad r = 0.989;\quad n = 14$$

$$pK_{DMSO} = 2.6 + 1.34\,pK_{DG} \pm 0.2;\quad s_\rho = 0.06;\quad r = 0.989;\quad n = 14$$

This indicates that the relative CH acidity of the investigated compounds (with the exception of amides) is the same in both solvents.

The effects of the substituents at the P atom in the compounds studied are analogous to those observed previously in the series of α-phosphorus-substituted toluenes [2]. A quite satisfactory linear correlation exists between the values of pK of phosphinyl acetates, classed as phosphine oxides, and the σ^P constants of the substituents at the P atom (Fig. 2)

$$pK_{DG} = 10.5 - 1.49\,\Sigma\sigma^P \pm 0.2;\quad s_\rho = 0.06;\quad r = 0.994;\ n = 9$$

$$pK_{DMSO} = 16.5 - 2.02\,\Sigma\sigma^P \pm 0.3;\quad s_\rho = 0.12;\quad r = 0.988;\quad n = 8$$

Compounds with alkoxyl groups at the P atom in most cases cannot satisfy the correlations cited. Deviations for amides are noted only in the case of pK_{DG}.

A comparison of the values that we found for pK_{DG} of ethylphosphinyl acetates and pK_a of phosphinylacetic acids, measured in aqueous solution (Fig. 3), show that there is no single relationship between these quantities. This hinders the prediction of the reactivity of carbanions of esters of phosphinylacetic acids according to the ionization constants of the corresponding acids. For example, the compounds (I) and (XVI) differ by more than two orders of magnitude in CH acidity in DG, while pK_a of the corresponding carboxylic acids are the same; at the same time, though the CH acidity is close for ethylphosphinyl acetates (V) and (XI), the pK_a values of phosphinylacetic acids differ by almost one unit of pK. In addition, the entire aggregate of points in Fig. 3 can be divided into several groups, in each of which a linear relationship is observed: A represents compounds with other alkyl radicals at the P atom; B represents compounds with one alkyl radical and a group capable of conjugation; C represents compounds with two substituents, capable of conjugation; D represents compounds with two aryl radicals at the P atom. This complex dependence is to some degree analogous to the correlation of pK_a of phosphinylacetic acids with the constants σ^P of the substituents at the P atom. Probably other causes of the construction of the subdependences are also possible; however, in any case the correlation is not unambiguous.

A comparison of the values of pK_{DMSO} of ethylphosphinyl acetates (see Table 1) and diethyl malonate (pK_{DMSO} = 16.7 [7]) permits us to judge the difference in the electronic effects of substituted phosphoryl and carboxyethyl groups. In all cases [with the exception of the nitro derivative (XVII)], substituted phosphinyl groups are inferior to the carbethoxyl group in their acidifying effect. For the diethoxyphosphinyl group (an analog of the carbethoxyl group), this difference is 2.5 units of pK.

TABLE 2. Ethyl Esters of Phosphinylacetic Acids RR'P(O)$CH_2COOC_2H_5$

Compound	Yield, %	bp, °C (p, mm Hg)		mp, °C (our data)	n_D^{20}		d_4^{20}		*MR*	
		our data	literature data		our data	literature data	our data	literature data	our data	literature data
(VI)	89	137—138 (12)	96—96,5 (1) [14]		1,4464	1,4443 [14]	1,0964	1,0935 [14]	50,66	50,59
(VIII)	70	174—175 (12)	176—177 (10) [15]		1,4370	1,4355 [15]	1,0421	1,0382 [15]	70,45	70,14
(IX)	74	148—150 (2)	179—180 (10) [15]		1,4388	1,4371 [15]	1,0158	1,0108 [15]	79,83	79,37
(XII)[a]	91	171—173 (3)		43—44 (ether—pentane)						
(XIII)[b]	95	193—194 (5)		38—39 (ether—pentane)						
(XIV)	66	157—158 (2)	142—148 (0,9) [16]		1,5094	1,5078 [16]	1,1552	1,1529 [16]	66,28	65,46
(XV)[c]	73			75,5—76,5 (benzene—heptane)						
(XVI)[d]	89			126—127 (CCl_4)						
(XVII)[e]	84			109—110 (methyl ethyl ketone—CCl_4)						

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[a] Found: C 59.8; H 7.1; P 12.9%. $C_{12}H_{17}O_3P$. Calculated: C 60.0; H 7.1; P 12.9%.

[b] Found: C 62.6; H 7.8; P 11.5%. $C_{14}H_{21}O_3P$. Calculated: C 62.6; H 7.9; P 11.5%.

[c] Literature data [17], mp 73-75°.

[d] Found: C 53.7; H 4.2; P 8.6%. $C_{16}H_{15}Cl_2O_3P$. Calculated: C 53.8; H 4.2; P 8.7%.

[e] Found: C 50.8; H 4.0; P 8.2%. $C_{16}H_{15}N_2O_7P$. Calculated: C 50.8; H 4.0; P 8.2%.

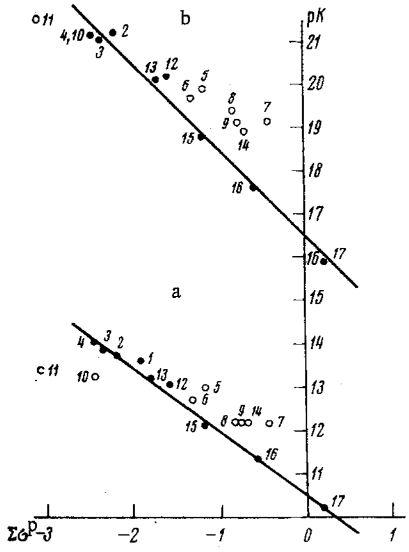

Fig. 2

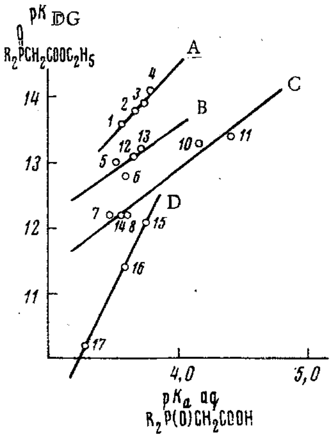

Fig. 3

Fig. 2. Relationship between pK of ethylphosphinyl acetates in diglyme (a) and dimethyl sulfoxide (b) and the σ^P constants of the substituents at the phosphorus atom. The dark points correspond to phosphinyl acetates, belonging to the group of phosphine oxides.

Fig. 3. Relationship between pK of ethylphosphinyl acetates in diglyme and pK_a of phosphinylacetic acids in water.

EXPERIMENTAL METHOD

The determination of the acidity of phosphinylethyl acetates was performed according to [1, 2]. In this case the spectrophotometric determination of the values of the equilibrium constants (K) of the reactions of transmetallation was facilitated by the fact that the carbanions of the investigated compounds do not absorb light in the visible region of the spectrum. The average values of K, average deviations from them, and number of measurements of the value of K(n) are cited in Table 3 (log K is equal to the difference of the values of pK of the indicator and investigated compounds.

The indicators used (with the exception of 9-carbomethoxyfluorine and phenyl-p-biphenylylacetonitrile) and the spectra of their organometallic derivatives were described in [1, 6, 7]. 9-Carbomethoxyfluorene was produced by esterification of fluorinecarboxylic acid, mp 66.0° (compare with [9], mp 64-65°); phenyl-p-biphenylylacetonitrile was synthesized according to [10], recrystallized from a mixture of toluene and petroleum ether, mp 132-133° (cf. [10]). The acidity of 9-carbomethoxyfluorene in DG was determined relative to diethyl-(VII) and diphenylphosphinyl acetate (XV) as indicators (for the values of their pK, see Table 1): $K = 48 \pm 3$, $n = 2$ [according to (VII)] and $K = 52 \pm 5$, $n = 5$ [according to (XV)]; the acidity of phenyl-p-biphenylylacetonitrile in DMSO was established according to diethylmalonate (pK = 16.7): $K = 0.35 \pm 0.04$; $n = 5$.

The values of λ_{max}, nm ($\varepsilon \cdot 10^{-3}$, liters $\cdot$ mole^{-1} $\cdot$ cm^{-1}) of the spectra of the carbanions were: 390 (4.3) — 9-carbomethoxyfluorene in DG; 460 (35) — phenyl-p-biphenylylacetonitrile in DMSO.

The synthesis of the esters (I)-(V), (VII), (X), and (XI) was described in [11-13]. The ethyl ester of ethylethoxyphosphinylacetic acid (VI) was produced by an Arbuzov rearrangement of diethyl ethylphosphonite with ethyl bromoacetate (an exothermic reaction when the reagents are mixed under a vacuum of 70-80 mm). The constants and yields are cited in Table 2. The esters (VIII), (IX), and (XIV) were produced according to [15, 16]. The esters (XII), (XIII), (XV)-(XVII) were synthesized by esterification of the corresponding phosphinylacetic acids [12, 18], according to the following procedure: 0.1 mole of substituted phosphinylacetic acid [12, 18] in 150 ml abs. alcohol and 5 ml conc. H_2SO_4 was boiled for 5 h. The mixture was evaporated under vacuum. A solution of the residue in 100 ml of benzene was washed with water (twice with 20-ml portions) and saturated with $NaHCO_3$ (twice with 15-ml portions), dried with Na_2SO_4, and evaporated under vacuum. The residue was recrystallized. The yields and constants of the esters obtained are cited in Table 2.

TABLE 3. Equilibrium Constants (K) of the Reactions of Transmetallation of Esters of Phosphinylacetic Acids in Diglyme and DMSO

Compound	K_{DG}[a]	n	K_{DMSO}	n	Indicator[b]
(I)	0,038 ±0,015	8	—	—	—
(II)	0,027 ±0,004	8	3,5±0,3	6	BF
(III)	0,020 ±0,003	5	5,8±0,5	6	BF
(IV)	— c	—	3,9±0,3	6	BF
(V)	0,15±0,015	6	0,04±0,005	6	PF
(VI)	0,28±0,045	6	0,07±0,003	6	PF
(VII)	1,07±0,13	8	0,23±0,02	6	PF
(VIII)	1,0±0,1	6	0,20±0,015	6	PF
(IX)	1,05±0,13	6	0,25±0,03	6	PF
(X)	0,085±0,12	6	3,8±0,4	6	BF
(XI)	0,063±0,01	6	1,6±0,15	6	BF
(XII)	0,13±0,02	8	0,020±0,002	4	PF
(XIII)	0,11±0,01	5	0,022±0,002	3	PF
(XIV)	1,05±0,13	6	0,40±0,05	6	PF
(XV)	1,22±0,15	9	0,48±0,04	5	PF
			0,20±0,01	2	DPAN
(XVI)	7,1±20,7	5	3,2±0,2	5	DPAN
(XVII)	1,43±0,14[d]	6	23,5±2	6	PBAN
			175±12	3	DPAN

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[a] In all cases except for (XVII), the indicator was diphenylfluorenyl-9-phosphine oxide, pK 12.2 [1].

[b] Abbreviations (pK) are given in parentheses: BF) 9-benzylfluorene (21.8) [6]; PF) 9-phenylfluorene (18.5) [6]; DPAN) diphenylacetonitrile (18.3) [6]; PBAN) phenylbiphenylylacetonitrile (17.2).

[c] Determined previously according to DPAN [1].

[d] Indicator 9-carbomethoxyfluorene (pK 10.4).

CONCLUSIONS

1. The equilibrium CH acidity of esters of phosphinylacetic acids was determined relative to 9-phenylfluorene in diglyme and in DMSO by the method of transmetallation.

2. The values of pK of ethylphosphinyl acetates in diglyme (Li^+ cation) are 6-8 units of pK lower than in DMSO (K^+ cation). This is explained by the chelate coordination of the metal cation with the phosphoryl and carbethoxyl groups of the carbanion in the contact ion pair, formed in diglyme.

3. A correlation of the values of pK of ethylphosphinyl acetates in both solvents with the σ^p constants of alkyl and aryl substituents at the phosphorus atom was established.

4. There is no single correlation between the values of pK of ethylphosphinyl acetates in diglyme and the ionization constants of phosphinylacetic acids in water.

5. The diethoxyphosphinyl group is inferior to its analog — the carbethoxyl group, with a value of the acidifying effect in dimethyl sulfoxide approximately 2.5 units of pK lower.

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