

THE PREPARATION AND CHARACTERIZATION OF 2-PROPYLPHOSPHINEDIACETIC ACID*

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Received July 23rd, 1987

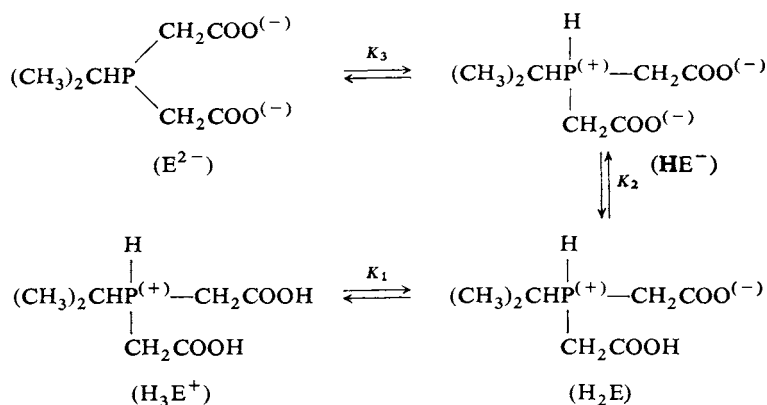
Phosphineacetic acids of the $RP(CH_2COOH)_2$ type, where R is a large substituent with a +I-effect, cannot be prepared by the reaction of chlorophosphine with an organozinc compound because of the lability of the P—CH₂COO bonds. The bis(ethyl ester) of 2-propylphosphine-diacetic acid as the simplest substance of this kind was prepared by the reaction of chlorophosphine with ethylacetate enolate, which is universal for these substituents. 2-Propylphosphine-diacetic acid, obtained from the ester by the usual procedure, was characterized with respect to its use as a hydrophilic phosphine ligand.

The complexing ability of tertiary phosphines and the catalytic properties of their complexes¹ are very dependent on the electronic² and steric³ parameters of the substituents bonded to the phosphorus atom. In a systematic study of phosphine-acetic acids, attention was paid particularly to compounds of the $RP(CH_2COOH)_2$ type, which are suitable models for testing the effect of substituent R on the donor properties of the —P(CH₂COOH)₂ group. Ligands with R = CH₃ (see refs^{4,5}), C₂H₅ (see ref.⁶), and C₆H₅ (see ref.^{7,8}) have been prepared and studied. However, attempts to synthesize substances with more sterically demanding R substituents and with a +I-effect encountered difficulties resulting from hydrolysis of the P—CH₂COO bonds in these substances⁹. Thus methods for the preparation of the simplest ligand with a branched R substituent, 2-propylphosphinediacetic acid (H₂E), were tested. Procedures that do not require hydrolysis of the excess organometallic compound, after transfer of the acetate group to the phosphorus, were studied in detail.

The reaction of chlorophosphine with ethylacetate enolate, prepared in situ by deprotonation of the ethylacetate by sodium bis(trimethylsilyl)amide, was found to be most useful. This method has been used¹⁰ for the preparation of the esters of some related carboxylic acids and orientative experiments with other large R substituents (cyclohexyl, tert-butyl) indicate that it can be generally employed for large substituents with a +I-effect.

* Part XXVII in the series Compounds Structurally Related to Complexones; Part XXVI: Collect. Czech. Chem. Commun. 51, 664 (1986).

The bis(ethyl ester) of 2-propylphosphinediacetic acid obtained was then converted to the hydrochloride of the acid, $H_2E.HCl$, using the standard procedure⁴; the overall yield was 38% of the theoretical amount with respect to the 2-propyldichlorophosphine used. The properties of the product are similar to those of the related methyl⁴ and ethyl⁶ derivatives (the phenyl derivative does not form a crystalline hydrochloride): $H_2E.HCl$ is a crystalline substance that is stable in the air and soluble in strongly polar solvents. Solutions are oxidized by oxygen to form phosphine oxide. It follows from the IR and NMR spectra that the hydrochloride in the solid state and in strongly acid solution ($c > 3 \text{ mol l}^{-1} \text{ HCl}$, CF_3COOH) has the structure of a phosphonium salt with the cation $[(CH_3)_2CHP(H)(CH_2COOH)_2]^+$. Study of protonation of the E^{2-} anion in solution by the methods of potentiometric titration and IR and NMR spectroscopy, carried out as in the previous work⁴, indicated that the equilibria and mechanism of the acid-base processes are described by the Scheme 1



SCHEME 1

where $pK_3 = 6.26 = \log \beta_1$, $pK_2 = 2.69 = \log (\beta_2/\beta_1)$, $pK_1 = 1.3 = \log (\beta_3/\beta_2)$; $\log \beta_1 = 6.26(1)$, $\log \beta_2 = 8.95(1)$ at 25°C , $I = 0.1$ (NaClO_4), potentiometry; $\log \beta_3 = 10.2(1)$ at 25°C , $I = 1.0$ (H, NaCl), IR and NMR. The spectral characteristics of the acid-base forms in solution are listed in Table I.

Thus the H_2E acid has the structure of a zwitterion, similar to the methyl and ethyl derivatives and in contrast to the phenyl derivative; unsuccessful attempts to isolate this ion have indicated that zwitterion structures of phosphineacetic acids are characterized by high solubility, in contrast to classical complexones.

TABLE I
Spectral characteristics of the acid-base forms of ligand in 0.2 mol l⁻¹ solution in [D₂H]₂O, I = 1.0

Species	IR ^a			¹ H NMR ^b			³¹ P{ ¹ H} NMR ^b
	COO ⁽⁻⁾	P ⁽⁺⁾ CH ₂ COO ⁽⁻⁾	COOH	CH ₃	CH	CH ₂	
E ²⁻	1 567 (100)	—	—	0.94	1.91	2.51	-14.6 (10)
HE ⁻	1 568 (52)	1 608 (48)	—	1.17	2.45	3.08	-2.1 (180)
H ₂ E	—	1 612 (53)	1 690 (47)	1.31	2.68	3.50	6.2 (60)
H ₃ E ⁺	—	—	1 703 (100)	1.42	2.83	3.67	10.4 (5)

^a Wavenumber maximum in cm⁻¹ (the values in brackets give the relative intensity in %);

^b limiting value of δ in ppm, calculated from the dependence on the acidity and from the protonation constants (the values in brackets give the half-width in Hz).

EXPERIMENTAL

All operations with phosphines (except for the solid H₂E.HCl) were carried out in an argon or nitrogen atmosphere using solvents freed of dissolved oxygen and dried according to standard procedures. The instruments and methods used are described in the previous work (see ref.⁴ and the references therein). The NMR spectra (δ in ppm, J in Hz) were measured on the Varian XL 200 instrument using frequency standardization formally related to tetramethylsilane (¹H, ¹³C) and 85% H₃PO₄ (³¹P).

The Bis(ethyl ester) of 2-Propylphosphinediacetic Acid

Sodium bis(trimethylsilyl)amide, prepared in the usual manner¹⁰ from 62.8 g (0.39 mol) of hexamethyldisilazane and 22.4 g of a 40% sodium suspension in mineral oil (0.39 mol), was decanted with heptane, dried in vacuo and dissolved in 500 ml of ether. This solution was slowly added dropwise with stirring at -78°C to a mixture of 34.3 g (0.39 mol) ethyl acetate and 300 ml ether, the mixture was stirred for 2 h and then 2-propyldichlorophosphine¹¹ (22.3 g; 0.15 mol) was added all at once. The mixture was allowed to warm to laboratory temperature with stirring and sodium chloride was separated by vacuum filtration through kieselguhr. Fractional distillation through a 30 cm column yielded first hexamethyldisilazane (33°C/4.4 kPa) and then 17.5 g (46% with respect to 2-propyldichlorophosphine) of the bis(ethyl ester) of 2-propylphosphinediacetic acid (104–106°C/0.13 kPa). For C₁₁H₂₁O₄P (248.3) calculated: 53.22% C, 8.53% H, 12.47% P, 58.81% COOC₂H₅; found: 53.18% C, 8.67% H, 12.30% P, 59.0% COOC₂H₅. IR spectrum (neat) $\tilde{\nu}$, cm⁻¹: 1 730 vs (ν (C=O)). NMR spectrum (deuteriochloroform): ¹H: 1.07 dd, 6 H ((CH₃)₂CH, ³J_{P,H} = 15.4, ³J_{H,H} = 7.0); 1.21 t, 6 H (CH₃CH₂, ³J_{H,H} = 7.5); 1.82 doublet of septets, 1 H (CH, ³J_{H,H} = 7.0, ²J_{P,H} = 4.4); 2.63, 2.71 doublet of AB-quartets, 4 H (PCH₂,

$^2J_{P,H} = 2.0$, $^2J_{H,H} = 13.6$; 4.30 q, 4 H (OCH₂, $^3J_{H,H} = 7.5$). $^{13}C\{^1H\}$: 18.74 d ((CH₃)₂CH, $^2J_{P,C} = 16.4$); 19.54 s (CH₂CH₃); 24.82 d (CH, $^1J_{P,C} = 12.3$); 30.01 d, (PCH₂, $^1J_{P,C} = 27.1$); 60.82 s (OCH₂); 171.16 s (C=O). $^{31}P\{^1H\}$: -11.34 s.

The Hydrochloride of 2-Propylphosphinediacetic Acid

A mixture of 12.5 g of the bis(ethyl ester) of 2-propylphosphinediacetic acid (0.05 mol) dissolved in 100 ml of petroleum ether was mixed with the solution formed by the reaction of 2.9 g sodium (0.126 mol) with 100 ml of 96% ethanol. A precipitate of the disodium salt was gradually formed; after standing overnight, it was filtered, washed with ethanol and ether and dried at 25°C/0.3 kPa. An impure salt (11.6 g) was formed which, according to TLC, IR and 1H NMR spectra, contained about 5% phosphine oxide and 3% unhydrolyzed ester groups. Ten grams of the impure salt were dissolved in 20 ml of 15% HCl and the solution was evaporated to dryness at 40°C/0.2 kPa. The residue was extracted with 50 ml of acetic acid and sodium chloride was filtered off. Traces of water were removed from the filtrate by repeated vacuum evaporation with a mixture of acetic acid and benzene until the product began to precipitate in a crystalline form. Double recrystallization from 30 ml of hot acetic acid and drying at 50°C/0.13 kPa yielded a total of 6.5 g of the product (H₂E.HCl) with m.p. 110°C (57% with respect to the bis(ethyl ester)). For C₇H₁₄ClO₄P (228.6) calculated: 36.78% C, 6.17% H, 15.51% Cl, 13.55% P, 1.32% H⁺; found: 36.60% C, 6.28% H, 15.79% Cl, 13.4% P(III), 1.29% H⁺. IR spectrum (hexachlorobutadiene) ν , cm⁻¹: 3 000–3 100 mb ($\nu(OH)$); (Nujol): 1 705 vs ($\nu(C=O)$), 1 360 s (COOH). NMR spectrum (deuterium oxide): 1H : 1.35 dd, 6 H (CH₃, $^3J_{H,H} = 7.0$, $^3J_{P,H} = 19.6$); 2.76 doublet of septets, 1 H (CH, $^3J_{H,H} = 7.0$, $^2J_{P,H} = 11.3$); 3.61 d, 4 H (CH₂, $^2J_{P,H} = 11.0$). $^{13}C\{^1H\}$: 16.98 d (CH₃, $^2J_{P,C} = 2.0$); 21.70 d (CH, $^1J_{P,C} = 36.9$); 169.98 s (C=O). $^{31}P\{^1H\}$: 8.82 s.

The authors wish to thank Dr M. Buděšinský from the Institute of Organic Chemistry and Biochemistry of the Czechoslovak Academy of Sciences for measuring the NMR spectra.

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Translated by M. Štulíková.