ORGANIC PHOSPHORUS COMPOUNDS

LXXI *. PREPARATION, PROPERTIES, AND STRUCTURE OF
BIS(AMINOMETHYL)PHOSPHINIC ACID, $(H_2NCH_2)_2P(O)OH$ **

LUDWIG MAIER

Ciba-Geigy Ltd., Agrochemicals Division, CH-4002 Basel (Switzerland)

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Summary

Bis(aminomethyl)phosphinic acid, $(H_2NCH_2)_2P(O)OH \cdot HCl$, was prepared
by debenzylation of $(C_6H_5CH_2NHCH_2)_2P(O)OH \cdot HCl$ with hydrogen using 5%
Pd on C as catalyst, and from bis(t-butylaminomethyl)phosphinic acid,
$(t\text{-}C_4H_9NHCH_2)_2P(O)OH$, by isobutylene elimination in concentrated aqueous
hydrobromic acid at 175°C in a sealed tube. Interaction of bis(chloromethyl)-
phosphinic acid with ammonia in an autoclave produced methylaminomethyl-
phosphonic acid, $CH_3NHCH_2P(O)(OH)_2$. A mechanism for the formation of this
product is proposed. Several derivatives of $(H_2NCH_2)_2P(O)OH$ such as
$(RNHCH_2)_2P(O)OH$, R = C_6H_5CO, $ClCH_2CO$, $[H_2NHNC(=NH)NHCH_2]_2P(O)OH$
and $[(CH_3)_3SiNHCH_2]_2P(O)OSi(CH_3)_3$ were prepared.

Introduction

While aminomethylphosphonic acid, $H_2NCH_2P(O)(OH)_2$, has been known for
over 25 years [2] and tris(aminomethyl)phosphine oxide for more than ten years
[3], no procedure has yet been developed for the preparation of bis(amino-
methyl)phosphinic acid. Of the several methods which have been used to
prepare aminomethylphosphonic acid (Scheme 1, for a review see [4]) and tris-
(aminomethyl)phosphine oxide, none is directly applicable for the preparation
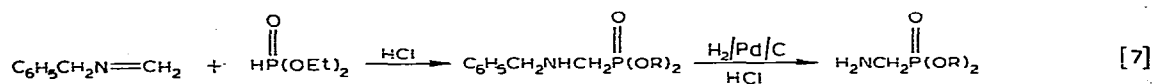of bis(aminomethyl)phosphinic acid. In the following we shall describe the
synthesis, structure, and properties of bis(aminomethyl)phosphinic acid (IX).

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* For part LXX see ref. 1.
** Dedicated to Professor Eugene G. Rochow on the occasion of his 70th birthday on October 4,
   1979.

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SCHEME 1

$$RC(O)NH_2 + CH_2O + PCl_3 \xrightarrow[\text{2.HCl}]{\text{1. AcH}} \left[RC(O)NHCH_2P(O)(OH)_2 \longrightarrow \right] H_2NCH_2P(O)(OH)_2 \qquad [2]$$

$$ClCH_2P(O)(OH)_2 + NH_3 \xrightarrow[\text{1 h / 150°C}]{H_2O} H_2NCH_2P(O)(OH)_2 \qquad [5]$$

Phthalimide-NCH_2Br + $(RO)_3P \longrightarrow$ Phthalimide-$NCH_2P(O)(OR)_2 \xrightarrow{H^+} H_2NCH_2P(O)(OR)_2 \qquad [6]$
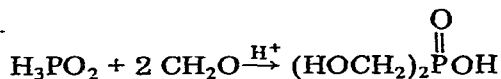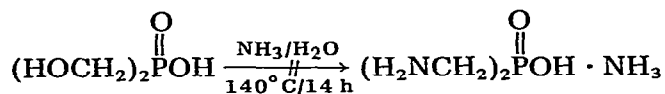
$$C_6H_5CH_2N{=}CH_2 + HP(O)(OEt)_2 \xrightarrow{HCl} C_6H_5CH_2NHCH_2P(O)(OR)_2 \xrightarrow[\text{HCl}]{H_2/Pd/C} H_2NCH_2P(O)(OR)_2 \qquad [7]$$

$$t\text{-BuN}{=}CH_2 + HP(O)(OR)_2 \longrightarrow t\text{-BuNHCH}_2P(O)(OEt)_2 \xrightarrow[\text{175°C}]{HBr} H_2NCH_2P(O)(OR)_2 \qquad [8]$$

$$3 \text{ Phthalimide-NH} + (ClCH_2)_3P{=}O \longrightarrow \left[\text{Phthalimide-NCH}_2 \right]_3 P{=}O \xrightarrow{H_2NNH_2} (H_2NCH_2)_3P{=}O \qquad [3]$$
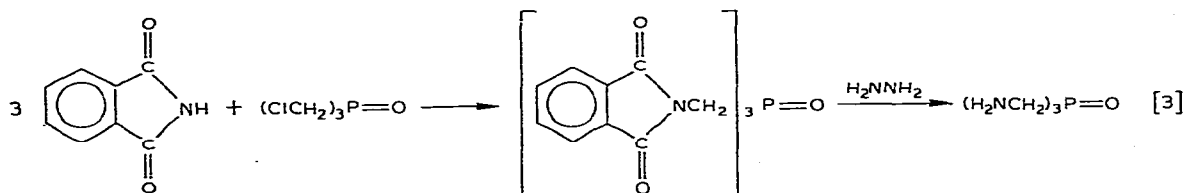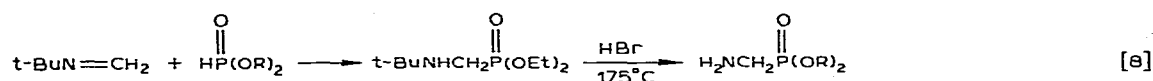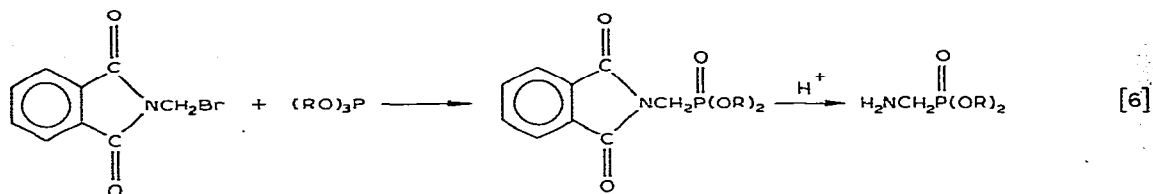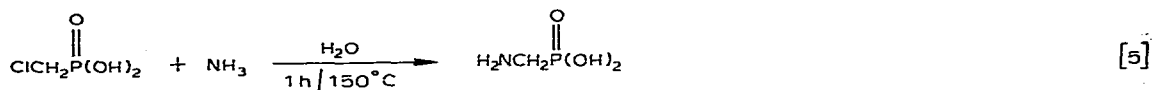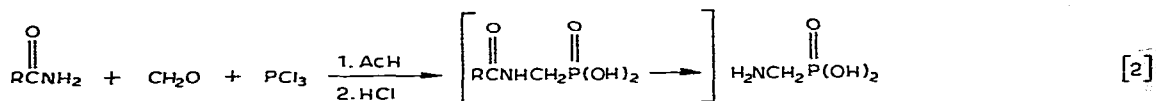
Results and discussion

Bis(hydroxymethyl)phosphinic acid, $(HOCH_2)_2P(O)OH$ (I), is a readily available substance today [9]. We have found that it can be prepared directly in high yield by reaction of hypophosphorous acid (50% aqueous solution) with formaldehyde and hydrochloric acid under reflux. The so far used sodium hypophosphite required an additional purification step [10].

$$H_3PO_2 + 2\ CH_2O \xrightarrow{H^+} (HOCH_2)_2P(O)OH$$

(I)

$$(HOCH_2)_2P(O)OH \xrightarrow[\text{140°C/14 h}]{NH_3/H_2O} (H_2NCH_2)_2P(O)OH \cdot NH_3$$

Attempts to prepare bis(aminomethyl)phosphinic acid directly by heating I

with excess ammonia in an autoclave (40 atmospheres) at 140°C for 14 h were not successful. Only the ammonium salt of I was obtained.

On the other hand it has been reported [11] that in the presence of only one $HOCH_2$ group on phosphorus, the reaction was successful. Thus diphenylamino-methylphosphine oxide was obtained in 40% yield by reaction of ammonia with $Ph_2P(O)CH_2OH$. The same compound was also obtained in the interaction of diphenylchloromethylphosphine oxide with ammonia [11].

$$Ph_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2OH + NH_3 \xrightarrow[140°C]{} Ph_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2NH_2 \ (40\%)$$

$$Ph_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2Cl + NH_3 \rightarrow Ph_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2NH_2$$

However, interaction of bis(chloromethyl)phosphinic acid (III), which was obtained by hydrolysis of bis(chloromethyl)phosphinic chloride (II) in quantitative yield, with excess ammonia (80 atm) at 150°C for 7 h in aqueous solution did not give the expected IX. Instead, methylaminomethylphosphonic acid, $CH_3NHCH_2P(O)(OH)_2$, a white solid of m.p. 270—274° (dec.) which was identified by analysis, NMR spectroscopy (Fig. 1) and comparison with an authentic sample [2,12], was formed. It gave a crystalline t-butylamine salt, m.p. 261—269°C (dec.), ^{31}P chemical shift + 7.4 ppm (in D_2O) *.

$$(HOCH_2)_2\overset{\overset{\displaystyle O}{\|}}{P}OH + 3\ SOCl_2 \rightarrow (ClCH_2)_2\overset{\overset{\displaystyle O}{\|}}{P}Cl \xrightarrow{H_2O} (ClCH_2)_2\overset{\overset{\displaystyle O}{\|}}{P}OH$$

$$\qquad\qquad\qquad\qquad (II)\qquad\qquad\qquad\qquad (III)$$

$$\nrightarrow (H_2NCH_2)_2\overset{\overset{\displaystyle O}{\|}}{P}OH$$

$$(IX)$$

$$(ClCH_2)_2\overset{\overset{\displaystyle O}{\|}}{P}OH + NH_3 \xrightarrow[\text{80 atm } NH_3]{\text{150°C/}H_2O}$$

$$\rightarrow CH_3NHCH_2\overset{\overset{\displaystyle O}{\|}}{P}(OH)_2$$

Apparently ammonia forms with III initially a four-membered ring compound which is not stable to hydrolysis and is cleaved by water to give methylamino-methylphosphonic acid.

Fig. 1. (A) ^{31}P NMR (chem. shift +9.09 ppm, J(PCH) 12.2 Hz) and (B) ^{1}H NMR spectra of CH$_3$NHCH$_2$P-(O)(OH)$_2$ in D$_2$O.

Previously, a similar mechanism was postulated in the interaction of glycine with III in the presence of sodium hydroxide, which resulted in the formation of N-carboxymethyl-N-methylaminomethylphosphonic acid [13].

$$HO_2CCH_2NH_2 + (ClCH_2)_2\overset{\overset{O}{\|}}{P}OH \xrightarrow{NaOH} HO_2CCH_2\overset{\overset{CH_3}{|}}{N}CH_2\overset{\overset{O}{\|}}{P}(OH)_2$$

It should be noted, however, that chloromethylphosphonic acid reacted normally with ammonia to give aminomethylphosphonic acid [5].

$$ClCH_2PO_3H_2 + NH_3 \rightarrow H_2NCH_2PO_3H_2$$
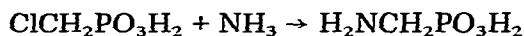
Since it has been reported that heating of N-t-butylaminomethylphosphonic acid with hydrogen bromide at 175°C resulted in the formation of amino-methylphosphonic acid [8], we decided to prepare IX in the same manner. However, in contrast to a literature report [14], which described the straight-forward formation of bis(N-alkyl- and N-aryl-aminomethyl)phosphinic acids by interaction of primary amines with III, we isolated by fractional crystalli-zation two products from the interaction of t-butylamine with III at 110°C in an autoclave. The main product (~30%) was identified as the expected bis(N-t-butylaminomethyl)phosphinic acid (VI), m.p. 260—262° (dec.), ^{31}P chemical shift + 18.5 ppm (D$_2$O), whilst the other product (~3%) was assigned the struc-ture of a phosphonic acid, m.p. 248—252°C (dec.), ^{31}P chemical shift + 7.4 ppm (D$_2$O), based on analytical and spectroscopic data (see Scheme 2 and Fig. 2). The latter compound very likely is formed by hydrolytic cleavage of the intermediately formed four-membered ring compound.

Incidentally, two products are also formed in the interaction of methyl-amine with III, i.e., bis(methylaminomethyl)phosphinic acid and dimethylamino-methylphosphonic acid.

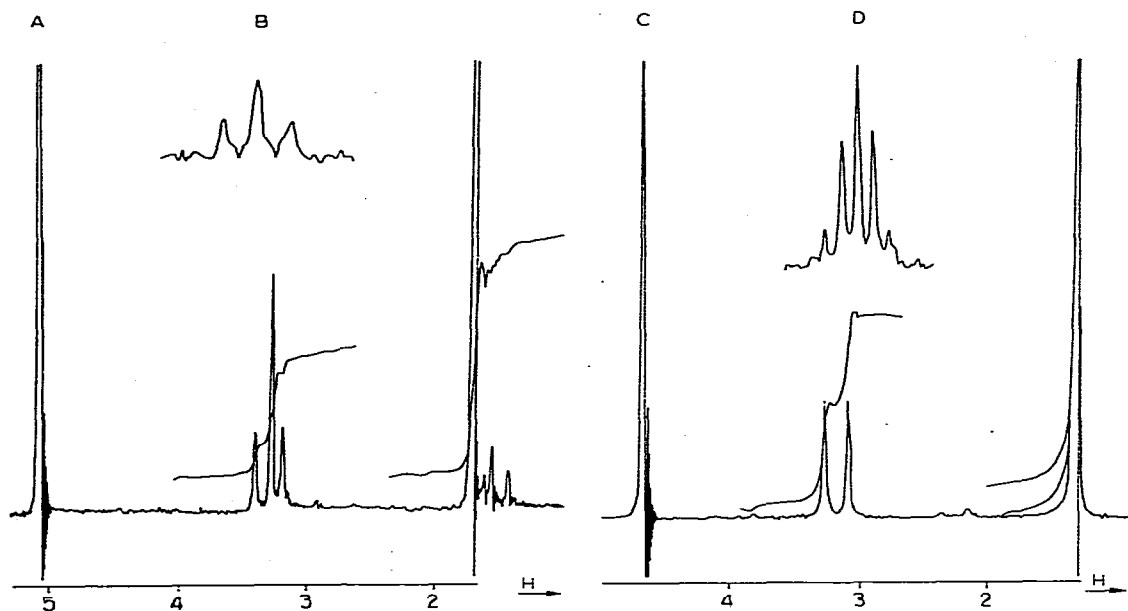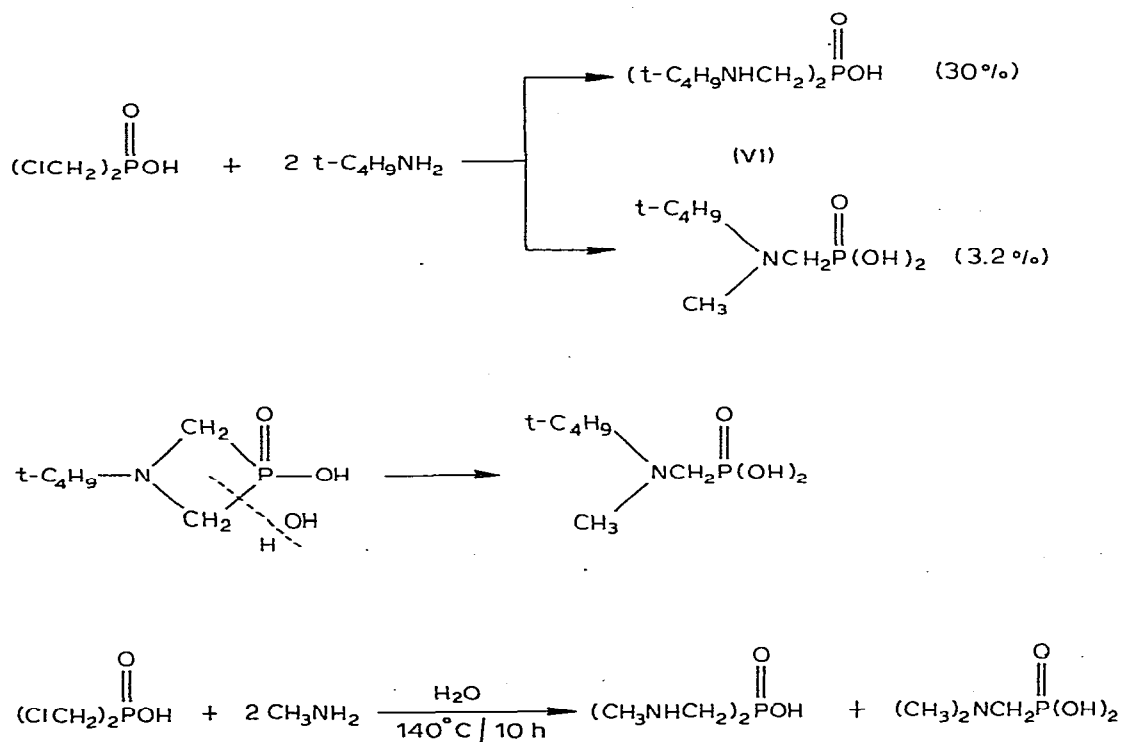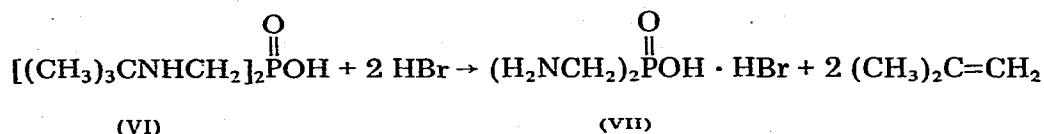Heating VI with concentrated hydrogen bromide in a sealed tube at 175°C for

Fig. 2. (A) ^{1}H NMR and (B) ^{31}P NMR spectra of $(CH_3)_3CN(CH_3)CH_2P(O)(OH)_2$ in D_2O. (C) ^{1}H NMR and (D) ^{31}P NMR spectra of $[(CH_3)_3CNHCH_2]_2P(O)OH$ in D_2O.

SCHEME 2

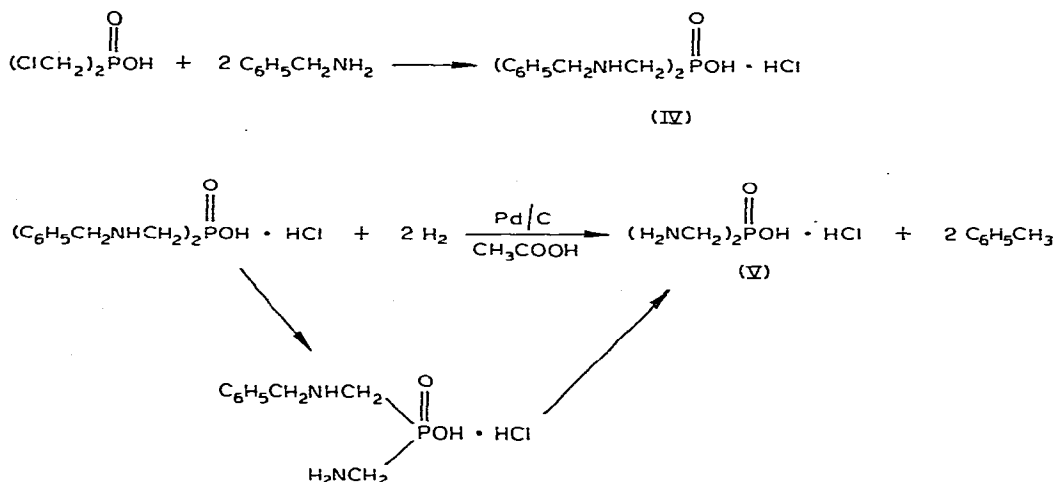24 h gave bis(aminomethyl)phosphinic acid hydrobromide (VII) in 36% yield.

$$[(CH_3)_3CNHCH_2]_2\overset{\overset{\displaystyle O}{\|}}{P}OH + 2\ HBr \rightarrow (H_2NCH_2)_2\overset{\overset{\displaystyle O}{\|}}{P}OH \cdot HBr + 2\ (CH_3)_2C{=}CH_2$$

(VI)   (VII)

Since a literature report indicated [14] that bis(N-benzylaminomethyl)phosphinic acid can be prepared more readily, we also investigated the debenzylation route for preparing bis(aminomethyl)phosphinic acid.

For the preparation of bis(benzylaminomethyl)phosphinic acid (IV) III was heated to 110°C with an excess of benzylamine in order to prevent formation of tarry condensation products. After distilling off excess benzylamine and acidifying the residue with hydrogen chloride, IV was obtained as the hydrochloride. Recrystallization from water gave white crystals, m.p. 257—258°C, equivalent weight found 339, calculated 340.7. The spectral and analytical data confirm the structure (Scheme 3, Fig. 3). The m.p. of 220—222°C reported in the literature [14] seems to be due to an impure product.

Debenzylation of IV with hydrogen in acetic acid was easily achieved in good yield when 5% Pd-on-carbon was used as a catalyst. The debenzylation seems to go stepwise, since small amounts of the monodebenzylated product sometimes also were isolated. The reaction mixture tends to take up more hydrogen than needed for the debenzylation. Apparently, the by-product toluene is hydrogenated after completion of the debenzylation reaction. Thus in one run 120% of the theoretical amount of hydrogen was taken up.

SCHEME 3

The hydrochloride of bis(aminomethyl)phosphinic acid is rather sparingly soluble in acetic acid and precipitated during the debenzylation reaction. It can, however, readily be extracted from the catalyst with boiling water. V is obtained in about 70% yield as a white crystalline solid which turns dark at 290°C and melts at 307°C with decomposition. Titration of V with 0.1 N tetramethylammonium hydroxide solution yields only one inflection point
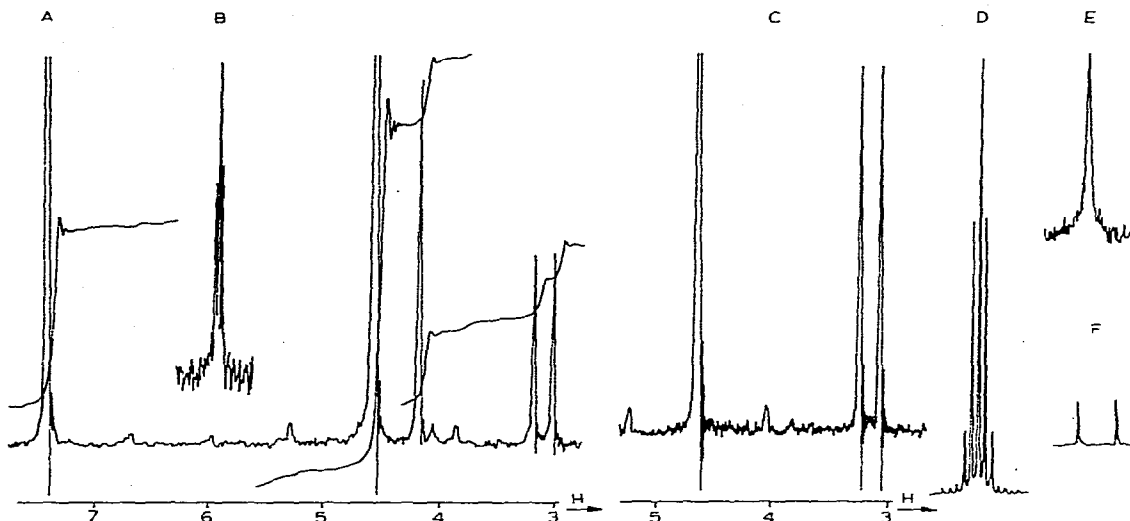
Fig. 3. (A) ^{1}H NMR and (B) ^{31}P NMR spectra of $(C_6H_5CH_2NHCH_2)_2P(O)OH \cdot HCl$ in D_2O. (C) ^{1}H NMR, (D) ^{31}P NMR (at pH 11), (E) ^{31}P NMR (at pH 1) and (F) ^{13}C NMR spectra of $(H_2NCH_2)_2P(O)OH \cdot HCl$ in D_2O.

and gives an equivalent weight of 82 (calcd. 80.2) which indicates that the hydrochloride, as well as the proton of the phosphinic acid, is being titrated at the same pH. Apparently V has the structure of a diammonium salt (Scheme 4).

SCHEME 4
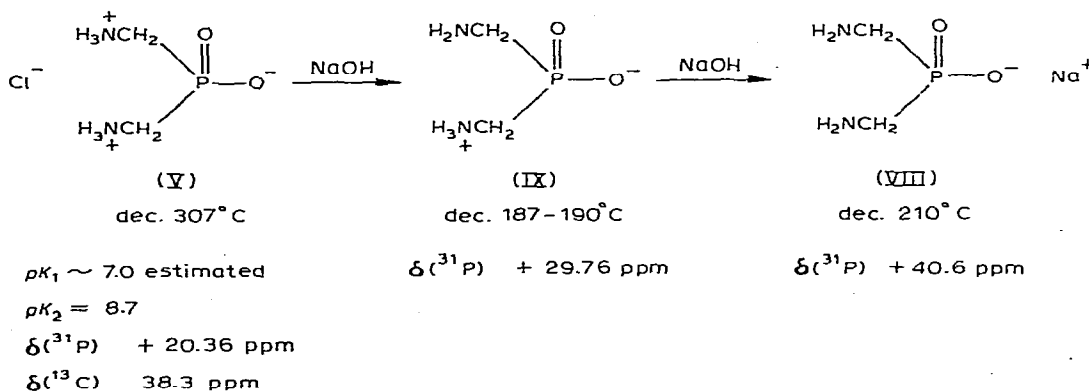
This is supported by the strong dependence of the ^{31}P-chemical shift on the pH (Fig. 4). Pure V, dissolved in water, exhibits a pH of 5 and shows a ^{31}P chemical shift of +20.3 ppm. At pH 8, adjusted with NaOH, the betaine (IX) is formed with a ^{31}P chemical shift of +29.76 ppm and at pH 9 the sodium salt (VIII) with a ^{31}P chemical shift of +40.07 ppm is obtained. The acid V exhibits plant growth regulator properties [15].

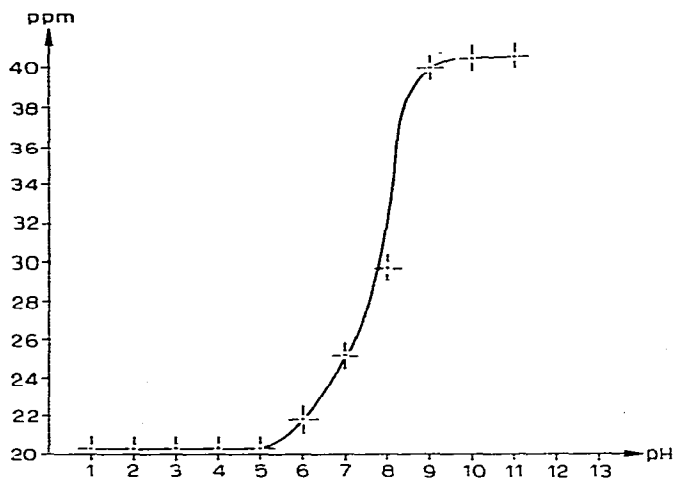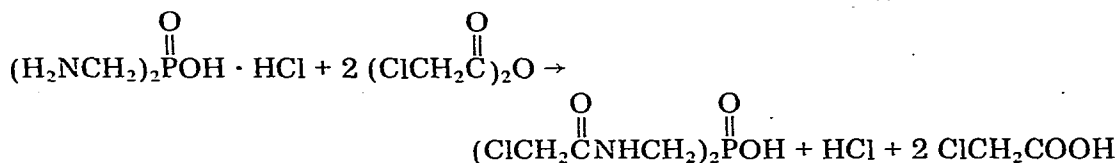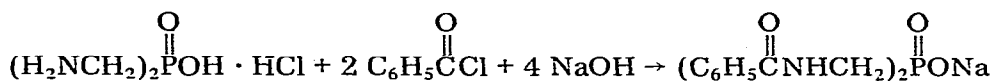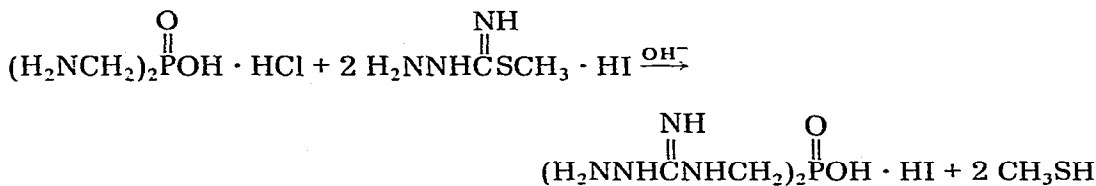Fig. 4. Dependence of the ^{31}P chemical shift of $(H_2NCH_2)_2P(O)OH$ on the pH.

Some derivatives of bis(aminomethyl)phosphinic acid

Benzoylation of V with benzoyl chloride in the presence of sodium hydroxide yielded the sodium salt of bis(*N*-benzoylaminomethyl)phosphinic acid, and chloroacetylation was achieved by heating V with chloroacetic anhydride.

$$(H_2NCH_2)_2\overset{O}{\underset{\|}{P}}OH \cdot HCl + 2\ C_6H_5\overset{O}{\underset{\|}{C}}Cl + 4\ NaOH \rightarrow (C_6H_5\overset{O}{\underset{\|}{C}}NHCH_2)_2\overset{O}{\underset{\|}{P}}ONa$$

$$(H_2NCH_2)_2\overset{O}{\underset{\|}{P}}OH \cdot HCl + 2\ (ClCH_2\overset{O}{\underset{\|}{C}})_2O \rightarrow$$

$$(ClCH_2\overset{O}{\underset{\|}{C}}NHCH_2)_2\overset{O}{\underset{\|}{P}}OH + HCl + 2\ ClCH_2COOH$$
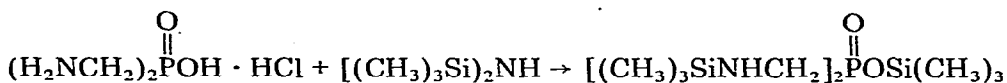
Bis(aminoquanidinomethyl)phosphinic acid (XII) was formed in the interaction of V with *S*-methyl-2-isothiosemicarbazide hydroiodide in aqueous basic solution.

$$(H_2NCH_2)_2\overset{O}{\underset{\|}{P}}OH \cdot HCl + 2\ H_2NNH\overset{NH}{\underset{\|}{C}}SCH_3 \cdot HI \overset{OH^-}{\longrightarrow}$$

$$(H_2NNH\overset{NH}{\underset{\|}{C}}NHCH_2)_2\overset{O}{\underset{\|}{P}}OH \cdot HI + 2\ CH_3SH$$

(XII)

When V was caused to react with excess hexamethyldisilazane at reflux, a water-clear, distillable silyl derivative (XIII) was obtained.

$$(H_2NCH_2)_2\overset{O}{\underset{\|}{P}}OH \cdot HCl + [(CH_3)_3Si)_2NH \rightarrow [(CH_3)_3SiNHCH_2]_2\overset{O}{\underset{\|}{P}}OSi(CH_3)_3$$

(XIII)

Experimental

General comments

Melting points were determined with a Tottoli apparatus in capillary tubes and are uncorrected. Proton NMR spectra were recorded using a Varian EM 360 spectrometer, and proton chemical shifts are reported in units, ppm downfield from internal tetramethylsilane. Phosphorus NMR spectra were recorded using a Bruker Electrospin WP 90 spectrometer at 32.28 MHz, and the chemical shifts are reported in units relative to external 85% phosphoric acid, with negative values being upfield of the standard and positive downfield.

1. Bis(hydroxymethyl)phosphinic acid, (HOCH$_2$)$_2$P(O)OH, (I). A mixture of 610 g (4.6 mol) (50% aqueous solution) of H$_3$PO$_2$, 350 ml concentrated HCl and 290 g of paraformaldehyde was stirred at 40—45°C until a clear solution was obtained and then refluxed for 30 h. Evaporation on a rotavap and finally aceotropic distillation with toluene gave 502 g (86.2%) of I, a highly viscous, slightly yellow colored oil. ^{1}H NMR (D$_2$O): 4.43 (d, $J(^{31}P—CH)$ 5.2 Hz, 4 H, CH$_2$P) and 5.48 (s, 3 H, OH) ppm. ^{31}P NMR (D$_2$O) +45.8 ppm (Lit. [16] +45.8 ppm).

2. Bis(chloromethyl)phosphinic chloride, (ClCH$_2$)$_2$P(O)Cl, (II). To 2745 g of refluxing SOCl$_2$ was slowly added with mechanical stirring 485 g (3.85 mol) of I. Gas evolution (HCl, SO$_2$) was very vigorous and the solution foamed strongly at the beginning. After completion of the addition refluxing was continued for about 5 h until gas evolution ceased. Fractionation yielded, after a small forerun, 606.5 g (87%) II, a colorless liquid, b.p. 80—85°C/0.05—0.1 torr, n_D^{20} 1.5200. ^{1}H NMR (CDCl$_3$) δ 4.07, $J(^{31}P—CH)$ 7.2 Hz; ^{31}P (in CDCl$_3$) +51.2 ppm (Lit. [15] +50.6 ppm).

3. Bis(chloromethyl)phosphinic acid, (ClCH$_2$)$_2$P(O)OH, (III). 606.5 g (3.34 mmol) of II was added slowly with stirring to 500 ml of distilled water and the solution filtered and the filtrate evaporated on a rotavap. As a residue was obtained 515 g (94.5%) of III, a white solid, m.p. 80—81°C (Lit. [17] m.p. 80—81°C). ^{1}H NMR (CD$_3$OD) δ 3.45 (d, $J(^{31}P—CH)$ 8 Hz, CH$_2$P); 5 (s, OH) ppm. ^{31}P (D$_2$O) +32.9 ppm (Lit. [16] +32.0 ppm).

4. Bis(benzylaminomethyl)phosphinic acid · HCl, (C$_6$H$_5$CH$_2$NHCH$_2$)$_2$P(O)-OH · HCl, (IV). To 1000 g of benzylamine was slowly added with stirring 163 g (1 mol) of III. Then the mixture was heated for 15 h to 110°C. On cooling a white precipitate was formed. Excess benzylamine was evaporated at ca. one torr and the white residue dissolved in 2 liters of water, filtered, and to the filtrate 350 ml of concentrated HCl added. After 2 h stirring at room temperature, the precipitate was filtered, washed with water and dried at 80°C under reduced pressure. Yield of IV 289 g (84.8%), white solid, m.p. 253—254°C. An analytically pure sample was obtained by recrystallization from water, m.p. 257—258°C (the m.p. 220—222°C given in the literature [14] is very likely due to an impure product). Titration in water with 0.1 N TMAH solution yielded two breaks, equiv. weight found 339 (calcd. 340.7), second break equiv. weight found 171 (calcd. 170.3). ^{1}H NMR (D$_2$O) δ 3.16 (d, $J(^{31}P—CH)$ 10 Hz, 4 H, PCH$_2$); 4.21 (s, 4 H, CH$_2$Ph); 4.6 (s, 4 H, HCl, OH, NH); 7.4 (m, 10 H, C$_6$H$_5$) ppm. ^{31}P NMR (D$_2$O) +16.08 ppm. IR (in KBr) bands at: 2.9 (NH, OH), 3.36, 3.65 (C—H), 6.3 (OH), 8.3 (P=O) (microns). Analysis: Found: C, 56.2;

H, 6.5; N, 8.0; Cl, 10.6; P, 9.2. $C_{16}H_{21}N_2O_2P \cdot HCl$ calcd.: C, 56.39; H, 6.51; N, 8.22; Cl, 10.4; P, 9.09%.

5. *Bis(aminomethyl)phosphinic acid hydrochloride, ($H_2NCH_2P(O)OH \cdot HCl$, (V)*. 25 g of IV was dissolved in 600 ml of acetic acid; then 2 g of catalyst (5% Pd on C) was added and the mixture hydrogenated at 25°C. After 19% H_2 uptake, another 2 g of catalyst was added. After 54 h, hydrogen uptake stopped (uptake 97% of theory). The catalyst was filtered and the clear, colorless filtrate evaporated on a rotavap. There was obtained as a residue 2.7 g (14.7%) of *N*-benzylaminomethyl-aminomethylphosphinic acid hydrochloride, $(C_6H_5CH_2NHCH_2)(H_2NCH_2)P(O)OH \cdot HCl$, a white solid which sinters at 270°C and melts at 278—281°C (dec.). ^1H NMR (D_2O) δ 3.28 (d, $J(^{31}P-CH)$ 10 Hz, 4 H, PCH_2); 4.2 (s, 2 H, CH_2Ph); 4.75 (s, NH, OH); 7.45 (m, 5 H, C_6H_5) ppm. The filtered catalyst,was heated with water to reflux, filtered, and the filtrate evaporated to give 9 g (76.85%) slightly beige-colored V which on recrystallization from water or H_2O/C_2H_2OH, H_2O/acetone gave white crystalline V which turns dark at 290°C and melts at 307°C (with decomposition).

Titration in water with 0.1 *N* TMAH solution gave one break, equiv. weight found 82, calcd. 80.2. ^1H NMR (D_2O) δ 3.28 (d, $J(^{31}P-CH)$ 10 Hz); 4.73 (s, OH, NH) ppm. ^{31}P NMR (D_2O, pH 5—6, strongly pH dependent) +20.45 ppm. ^{13}C NMR (D_2O) 38.3 ppm (d, $J(^{21}P-^{13}C)$ 98.2 Hz, ref. TMS). Analysis: Found: C, 15.05; H, 6.21; N, 17.04; Cl, 21.26; P, 19.09. $C_2H_9N_2O_2P \cdot HCl$ calcd.: C, 14.96; H, 6.28; N, 17.45; Cl, 22.08; P, 19.3%. In another run 170.4 g (0.5 mol) of IV was dissolved in 3 liters of acetic acid, 17 g of catalyst (5% Pd/C) added and the mixture hydrogenated at 30—35°C. After 108% hydrogen uptake another 8 g catalyst and 500 ml acetic acid were added. After 34 h 120% of theoretical hydrogen uptake was observed. The catalyst was filtered, suspended in one liter of water and refluxed. Filtration and evaporation of the filtrate on a rotavap gave 57 g (71%) of crystalline white V, m.p. 297°C (dec.) which on recrystallization from water/alcohol gave 50.5 g (62.9%) of pure V.

6. *Bis(t-butylaminomethyl)phosphinic acid, ($t-C_4H_3NHCH_2)_2P(O)OH \cdot HCl$, (VI)*. To 366 g (5 mol) of t-butylamine was slowly added with stirring 81.5 g (0.5 mol) of III. After the strongly exothermic reaction had subsided, the mixture was heated in an autoclave with stirring to 120—124°C for 24 h (after 12 h heating reaction was incomplete). Then excess t-butylamine was evaporated, the residue dissolved in hot ethanol and 100 g NaOH, dissolved in ethanol, added. The precipitated NaCl was filtered and the filtrate evaporated. The residue was dissolved in hot ethanol (A) and the insoluble part (B) (16.9 g) filtered off. (B) was dissolved in water and put through a strongly acidic ion exchanger. Eluation with water and evaporation of the eluate gave 6 g (3.2%) $(t-C_4H_9)(CH_3)NCH_2P(O)(OH)_2$ of m.p. 248—252°C (dec.). Titration in H_2O with 0.1 *N* TMAH solution gave one break, equiv. weight found 189: calcd. 188.3. ^1H NMR (D_2O) δ 1.1 (s, 9 H, $t-C_4H_9$); 2.5 (s, 3 H, CH_3); 2.65 (d, $J(^{31}P-CH)$ 10 Hz, 2 H, CH_2P); 4.63 (s, 10 H) ppm. ^{31}P NMR (D_2O) +8.29 ppm. Analysis: Found: C, 37.5; H, 9.2; N, 7.3; P, 16.8; H_2O, 3.8. $C_6H_{16}NO_3P \cdot 0.4 H_2O$ calcd.: 38.5; H, 8.99; N, 7.44; P, 16.44; H_2O, 3.8%.

The ethanol solution (A) was acidified with HCl, the precipitated NaCl filtered and the slightly yellow filtrate evaporated. Extraction of the residue with hot ethanol several times and standing of the solution overnight gave 19.9

g of VI, white crystals, m.p. 260—262°C (dec.). Concentration of the mother liquor gave another 21.6 g VI, yield 41.5 g (30.4%). ^{1}H NMR (D$_2$O) δ 1.3 (s, 18 H, t-C$_4$H$_9$); 3.2 (d, J(^{31}P—CH) 10.8 Hz, 4 H, CH$_2$P); 4.6 (s, OH, NH) ppm. ^{31}P NMR (D$_2$O) +18.5 ppm. Analysis: Found: C, 39.50; H, 8.8; N, 9.4; Cl, 18.2; P, 10.5. C$_{10}$H$_{25}$N$_2$O$_2$P · 1.5 HCl calcd.: C, 41.21; H, 9.1; N, 9.6; Cl, 18.4; P, 10.6%.

7. Bis(aminomethyl)phosphinic acid hydrobromide, (H$_2$NCH$_2$)$_2$P(O)OH · HBr (VII). A mixture of 5.45 g (20 mmol) VI and 20 ml of HBr (48% in H$_2$O) was sealed in a thick-walled tube and heated for 24 h at 175°C. After this period two layers were formed. The upper layer consisted of isomers of C$_4$H$_8$ and was discarded. From the lower aqueous layer crystallized 1.53 g (37.3%) of VII, white crystals, m.p. 260—267°C (dec.). Addition of ethanol to the mother liquor gave another crop of crystals. ^{1}H NMR (D$_2$O) δ 3.1 (d, J(^{31}P—CH) 10 Hz, CH$_2$); 4.53 (s, HN, OH, HBr) ppm; ^{31}P NMR (D$_2$O) +20.11 ppm.

8. Sodium bis(aminomethyl)phosphinate, (H$_2$NCH$_2$)$_2$P(O)ONa, (VIII). To 20.06 g (0.125 mol) of V dissolved in 150 ml H$_2$O was slowly added 10 g (0.25 mol) of NaOH, dissolved in 100 ml H$_2$O. The solution was evaporated and the residue extracted twice with hot ethanol. Evaporation of the ethanol extracts gave 17.1 g (93.7%) of VIII, a white powder which sinters at 160°C, turns waxy at 190°C and decomposes at 210°C with gas evolution. ^{1}H NMR (D$_2$O) δ 2.67 (d, J(^{31}P—CH) 8 Hz, CH$_2$P); 4.6 (s, NH$_2$) ppm. ^{31}P NMR (D$_2$O) +40.3 ppm.

9. Bis(aminomethyl)phosphinic acid, (H$_2$NCH$_2$)$_2$P(O)OH, (IX). To 2 g (12.4 mmol) of V dissolved in H$_2$O was added 0.496 g (12.4 mmol) NaOH dissolved in water. The solution was evaporated and the residue extracted with alcohol. Evaporation of alcohol gave IX, a white powder in quantitative yield. IX is also obtained by hydrolyzing 17 g (0.05 mol) XIII with 50 ml ethanol in 93.5% yield, white powder, m.p. 187—190°C (dec.). Titration in water with 0.1 N TMAH solution gave one break, equiv. weight found 127 (calcd. 124.08) (half neutralization value at pH 8.59). ^{1}H NMR (D$_2$O) δ 2.95 (d, J(^{31}P—CH) 9 Hz, CH$_2$P); 4.7 (s, H$_2$N, OH) ppm. ^{31}P NMR (D$_2$O) +29.21 ppm. Analysis: Found: C, 19.40; H, 6.93; N, 21.39; P, 24.68; H$_2$O, 1.14; C$_2$H$_9$N$_2$O$_2$P calcd.: C, 19.36; H, 7.21; N, 22.58; P, 24.97%.

Derivatives of bis(aminomethyl)phosphinic acid

10. Bis(benzoylaminomethyl)phosphinic acid sodium salt, (C$_6$H$_5$CONHCH$_2$)$_2$-P(O)ONa · 3.5 H$_2$O (X). To 1.6 g (10 mmol) of V and 1.76 g (44 mmol) of NaOH in 30 ml H$_2$O was added with stirring 3.1 g (22 mmol) of benzoyl chloride. An exothermic reaction ensued and on cooling the product crystallized. It was filtered, washed with water and dried, yield 3.45 g (82.7%) X. An analytically pure sample was obtained by recrystallization from ethanol, m.p. 271—272°C (sinters at 130°C with loss of water). ^{1}H NMR (D$_2$O) δ 3.6 (d, J(^{31}P—CH) 10 Hz, 4 H, CH$_2$P); 4.6 (s, OH, NH, H$_2$O); 7.4 (m, 10 H, C$_6$H$_5$) ppm. ^{31}P NMR (D$_2$O) +31.37 ppm. Analysis: Found: C, 46.0; H, 5.6; N, 6.7; P, 7.4. C$_{16}$H$_{16}$N$_2$O$_4$PNa · 3.5 H$_2$O calcd.: C, 46.05; H, 5.56; N, 6.71; P, 7.42%.

11. Bis(N-chloroacetylaminomethyl)phosphinic acid, (ClCH$_2$CONHCH$_2$)$_2$P-(O)OH, (XI). A mixture of 3.2 g (20 mmol) of V and 13.7 g (80 mmol) of chloroacetic acid anhydride was refluxed on a steam bath for 45 min, then

evaporated and the residue recrystallized from 10 ml ethanol. XI was obtained
(2.5 g, 45.1%), white crystals, m.p. 167—171°C. ^{1}H NMR (D$_2$O) δ 3.5 (d,
$J(^{31}$P—CH) 9 Hz, 4 H, CH$_2$P); 4.07 (s, 4 H, ClCH$_2$); 4.63 (s, OH, NH) ppm; ^{31}P
NMR (CD$_3$OD) +38.94 ppm.

*12. Bis(aminoquanidinomethyl)phosphinic acid hydroiodide, [H$_2$NNHC-
(=NH)NHCH$_2$]$_2$P(O)OH · HI, (XII).* To 16.05 g (0.1 mol) of V, dissolved in
75 ml of 4 N NaOH, was added slowly with stirring at 50—60°C 93.2 g (0.4
mol) of s-methyl-2-isothiosemicarbazid hydroiodide dissolved in 100 ml H$_2$O. The
mixture was stirred at 50°C for 1 h and then kept in a refrigerator for 14 days.
Then the crystals were filtered and recrystallized from H$_2$O/C$_2$H$_5$OH. There
was obtained 16.8 g of XII, slightly pink-colored crystals. By concentrating
the filtrate a further 5.3 g XII was isolated, yield 22.1 g (60%), m.p. 247—248°C.
^{1}H NMR (D$_2$O) δ 3.57 (d, $J(^{31}$P—CH) 10 Hz, 4 H, CH$_2$P); 4.77 (s, OH, NH, HI,
12 H) ppm. ^{31}P NMR (D$_2$O) +28.64 ppm. Analysis: Found: C, 13.22; H, 4.48;
N, 30.59; P, 8.51. C$_4$H$_{15}$N$_8$O$_2$P · HI calcd.: C, 13.12; H, 4.41; N, 30.60; P,
8.46%.

*13. Bis(N-trimethylsilylaminomethyl)-O-trimethylsilylphosphinate, [(CH$_3$)$_3$-
SiNHCH$_2$]$_2$P(O)OSi(CH$_3$)$_3$, (XIII).* A mixture of 32.1 g (0.2 mol) of V and 208
ml of hexamethyldisilazane was refluxed for 15 h, during the reaction NH$_4$Cl
sublimed into the condenser. The turbid reaction mixture was filtered and the
filtrate distilled. XIII was obtained (52.8 g, 77.5%) as a water-clear liquid, b.p.
98—105°C/0.05 torr. ^{1}H NMR (CDCl$_3$) δ 0.07 (s, 18 H, (CH$_3$)$_3$SiN); 0.32 (s, 9 H,
(CH$_3$)$_3$SiO); 0.6 (broad, 2 H, NH); 3.1 (d, $J(^{31}$P—CH) 8 Hz, 4 H, CH$_2$P) ppm.
^{31}P NMR (CDCl$_3$) +44.0 ppm. Analysis: Found: C, 38.39; H, 9.68; N, 8.66; P,
9.22. C$_{11}$H$_{33}$N$_2$O$_2$PSi$_3$ calcd.: C, 38.79; H, 9.77; N, 8.23; P, 9.10%.

Acknowledgement

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