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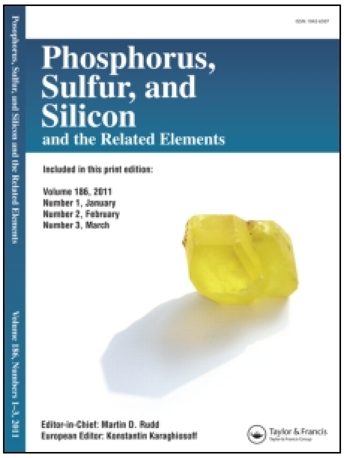

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ORGANIC PHOSPHORUS COMPOUNDS 101.[1] PREPARATION AND PHYSICAL PROPERTIES OF BIS(AMINOALKYL)PHOSPHINIC ACIDS

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ORGANIC PHOSPHORUS COMPOUNDS 101.[1] PREPARATION AND PHYSICAL PROPERTIES OF BIS(AMINOALKYL)PHOSPHINIC ACIDS

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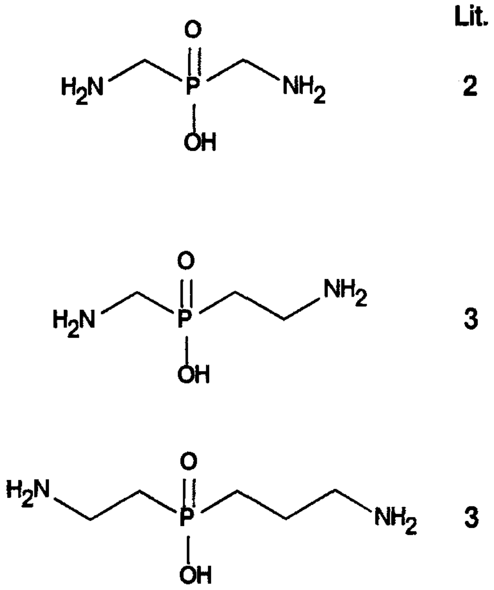
The synthesis, physical and spectroscopic properties of 3-amino-propyl-aminomethylphosphinic acid, **5**, bis(2-aminoethyl)phosphinic acid, **8**, and of bis((3-aminopropyl)phosphinic acid, **10**, are reported.

Key words: 3-Aminopropyl-aminomethylphosphinic acid; bis(2-aminoethyl)phosphinic acid; bis(3-aminopropyl)phosphinic acid; ^{31}P-chemical shifts.

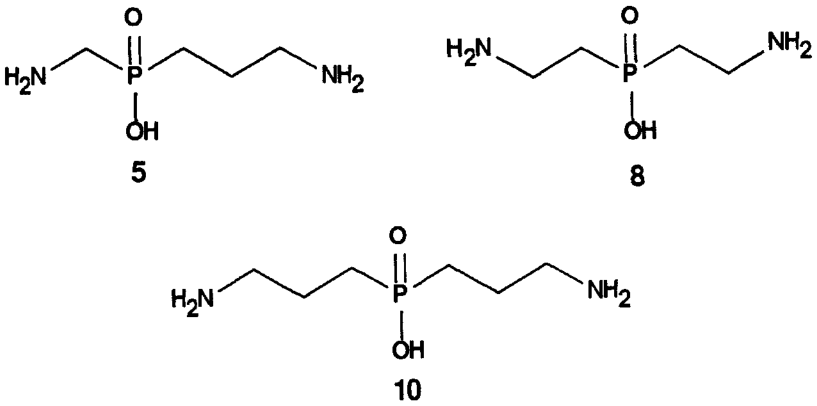
INTRODUCTION

Bis(aminoalkyl)phosphinic acids are interesting starting materials for the preparation of peptides which contain a P=O group in place of a C=O group, and of polymers with a built-in flame retardant. Furthermore, they might show interesting biological activity, e.g., bis(aminomethyl)phosphinic acid is a plant growth regulator.[2]

From the series of bis(aminoalkyl)phosphinic acids with 1–3 carbon atoms the following members are known (Scheme I):



SCHEME I

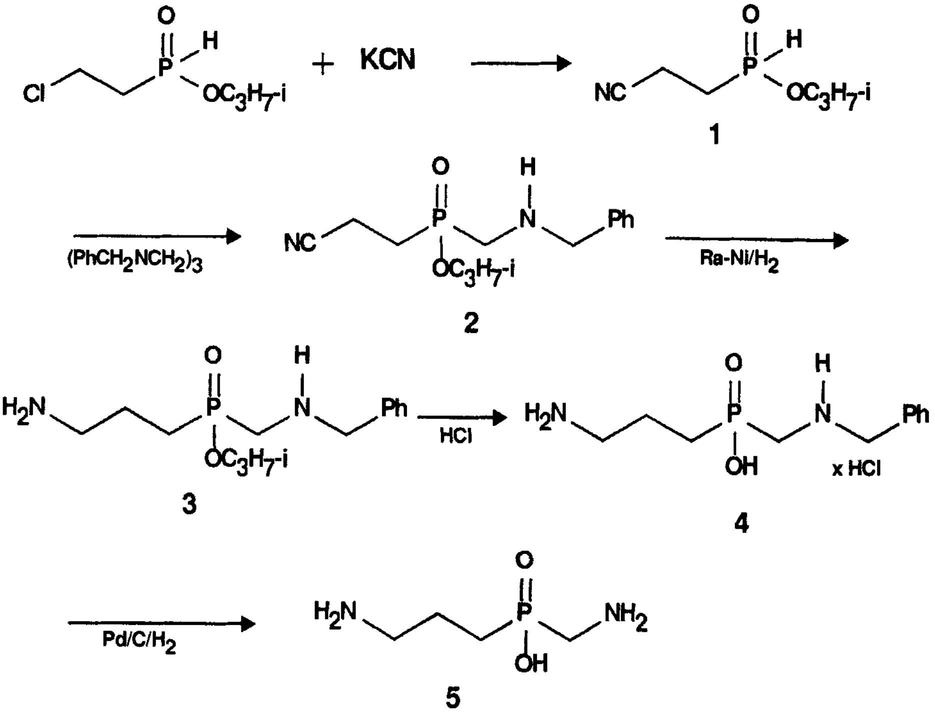


SCHEME II

The missing members (Scheme II) are described in this paper.

RESULTS and DISCUSSION

3-Aminopropyl-aminomethylphosphinic acid, **5**, was prepared as shown in Scheme III:



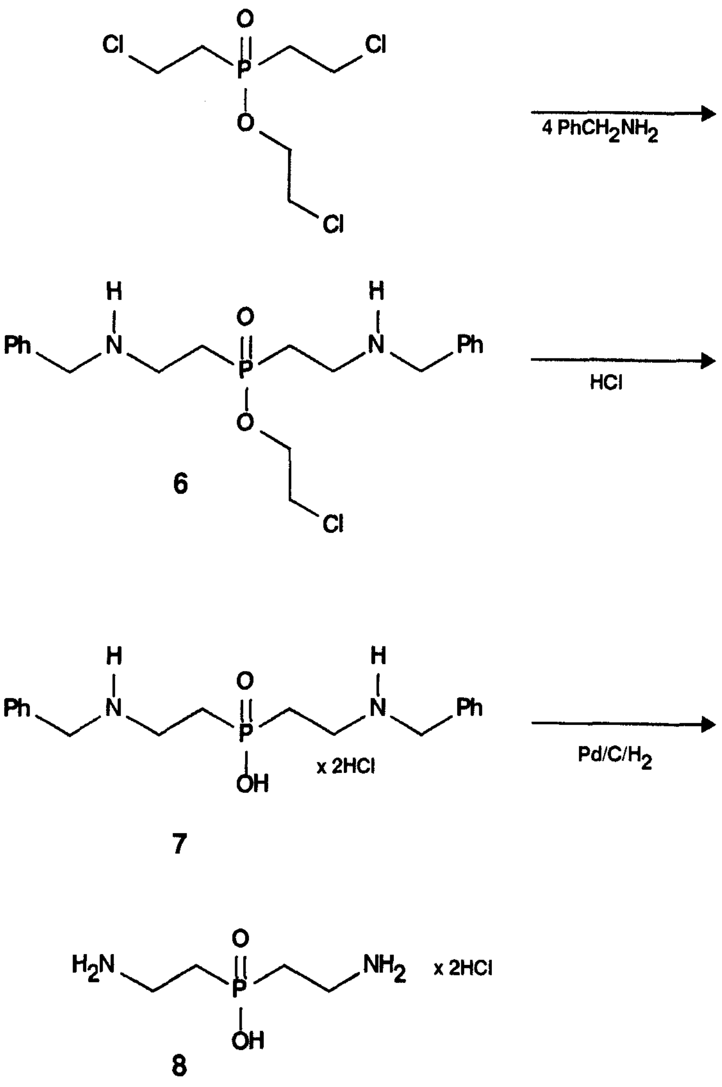
SCHEME III

With the exception of the conversion of O-i-propyl-2-chloroethylphosphonite[4] to O-i-propyl-2-cyanoethylphosphonite, **1**, with KCN in i-propanol, which gave only a 19% yield, all the other steps proceeded with better than 55% yield.

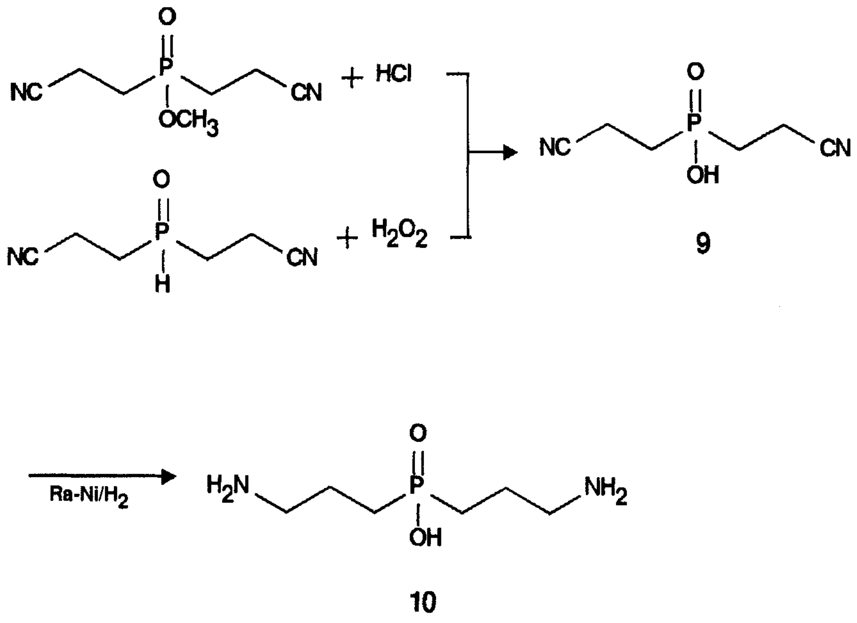
3-Aminopropyl-aminomethylphosphinic acid, **5**, was isolated as its hydrochloride in spite of the fact that propylene oxide was added to the solvents used for recrystallization.

Bis(2-aminoethyl)phosphinic acid, **8**, was readily obtained from O-2-chloroethylbis(2-chloroethyl)phosphinate[5] by treatment with benzylamine followed by hydrolysis and debenzylation with hydrogen over Pd/C as catalyst (Scheme IV).

Compound **8** crystallizes as the dihydrochloride with a decomposition point of 278–279°C.



SCHEME IV



SCHEME V

Bis(3-aminopropyl)phosphinic acid, **10**, was prepared from bis(2-cyanoethyl)phosphinic acid, **9**, by hydrogenation, using Raney Nickel as a catalyst (Scheme V).

The acid **9** was isolated from two different sources, i.e., from bis(2-cyanoethyl)phosphine by oxidation with H_2O_2 or from O-methyl-bis(cyanoethyl)phosphinate[6] by dealkylation with trimethylbromosilane.

BIOLOGICAL ACTIVITY

The compounds described in this paper were tested as herbicides, plant growth regulators, insecticides and fungicides. They showed no biological activity.

EXPERIMENTAL

Phosphorus NMR-spectra were recorded using a Bruker WP 80 spectrometer at 32.28 MHz (ref. 85% H_3PO_4), and ^{1}H-NMR spectra were recorded with a Varian EM 360 spectrometer at 60 MHz or a Bruker WM 250/250 MHz spectrometer (ref. Me_4Si). The chemical shifts are reported in ppm, with negative values being upfield of the standard, and positive downfield. O-Methyl-bis(2-cyanoethyl)phosphinate was prepared as described previously by us.[6] The improvements of its preparation which should result by using triethylamine[7] instead of CH_3ONa as catalyst could not be verified by us.

O-i-Propyl-2-cyanoethylphosphonite, **1**. To 17.06 g (0.1 mol) of O-i-propyl-2-chloroethylphosphonite[4] dissolved in 50 ml of i-propanol is added 8.14 g of KCN and the mixture refluxed for 24 h, then filtered and the solvent evaporated. The crude product is kugelrohr distilled to give 3.1 g (19.2%) of **1**, a clear liquid, b.p. 160–165°C/0.04 torr.

^{1}H-NMR ($CDCl_3$)δ: 1.35 (2d, CH_3); 2.1 (4t, $J_{PCH} = 14$, $J_{HH} = 7$, $J_{HPCH} = 2$, CH_2P); 2.65 (2t, $J_{PCH} = 15$, $J_{HH} = 7$, NCH_2); 4.7 (m, OCH); 7.3 (d, $J_{PH} = 546$, PH).

^{31}P-NMR ($CDCl_3$)δ: 29.0 ppm.

O-i-Propyl-2-cyanoethyl-N-benzylaminomethylphosphinate, **2**. A mixture of 3.1 g (19.4 mmol) of **1** and 2.3 g of N,N′,N″-tribenzylhexahydrotriazine is stirred and heated for 2 h at 110°C. There is obtained 5.4 g (100%) of **2**, an oil.

^{1}H-NMR ($CDCl_3$)δ: 1.3 (2d, CH_3); 1.6 (br., NH); 2.15 (m, CH_2P); 2.65 (m, $NCCH_2$); 2.9 (2d, $J_{PCH} = 13$, $J_{NHCH} = 2$, NCH_2P); 3.8 (d, $PhCH_2$); 4.7 (m, OCH); 7.3 (m, C_6H_5).

O-i-Propyl-3-aminopropyl-N-benzylaminomethylphosphinate, **3**. To 5.4 g (19.4 mmol) of **2** dissolved in 100 ml of i-propanol is added 3.2 g of NH_3, and 1 g of Raney-Ni. Then the mixture is hydrogenated at 70–75°C and 100 bar. After 16 h hydrogen uptake stopped. The catalyst is filtered and the filtrate evaporated to give 5.1 g (92.4%) of crude **3**, a resin.

^{1}H-NMR ($CDCl_3$)δ: 1.3 (2d, CH_3); 1.8 (br. m, $CH_2CH_2P + NH_2$); 2.85 (br., NCH_2P and CCH_2N); 3.8 (s, $PhCH_2$); 4.7 (m, OCH); 7.3 (Ph).

3-Aminopropyl-N-benzylaminomethylphosphinic acid, **4**. A mixture of 5 g (17.6 mmol) of **3** and 35 ml of HCl (20%) is stirred and refluxed for 5 h. Then the solution is evaporated and the residue recrystallized from ethanol/propylene oxide to give 3.3 g (67.2%) of **4** × HCl, a beige solid, m.p. 196–200°C (dec.).

^{1}H-NMR (D_2O, pH = 6)δ: 1.7 (br., CH_2); 1.9 (br., CH_2P); 3.05 (t, CH_2N); 4.35 (s, $PhCH_2$); 4.9 (s, OH, NH_2); 7.5 (s, Ph).

3-Aminopropyl-aminomethylphosphinic acids, **5**. To a solution of 2.79 g (10 mmol) of **4** in 30 ml of water is added 1.4 g of Pd/C (5%) and the mixture hydrogenated at 20–25°C and normal pressure. After 1 h hydrogen uptake stopped. The catalyst is filtered and the filtrate evaporated on a rotavapor. The residue is recrystallized from water/methanol/propylene oxide to give 1.05 g (55.6%) of **5** × HCl, a white solid, m.p. 247–250°C (dec.).

^{1}H-NMR (D_2O) δ: 1.75 (m, CCH_2C); 1.9 (m, CH_2P); 3.08 (d, $J_{PCH} = 9.4$, NCH_2P); 3.09 (t, $J = 7$, CH_2N); 4.9 (s, NH_2, OH).

^{31}P-NMR (D_2O) δ: 32.24 (pH 6).

O-2-Chloroethyl-bis(N-benzyl-2-aminoethyl)phosphinate, **6**. To a solution of 18.9 ml of benzylamine in 40 ml of diethyl ether is added 10.14 g of O-2-chloroethyl-bis(2-chloroethylphosphinate.[5] A slightly exothermic reaction ensues. The mixture is stirred over night at 20°C, the precipitated benzylamine hydrochloride filtered off and the filtrate evaporated to give 15.8 g (100%) of crude **6**, a colorless oil.

^{31}P-NMR ($CHCl_3$) δ: 58.06

Bis(N-benzyl-2-aminoethyl)phosphinic acid, **7**. A mixture of 11.85 g (30 mmol) of crude **6**, and 60 ml of HCl (20%) is refluxed for 5 h. Then the clear solution is evaporated and the residue treated with 50 ml of methanol, filtered and dried to give 2.3 g (20.8%) of **7** × 2 HCl, a white solid, m.p. 281–283°C (dec.).

^{1}H-NMR (D_2O) δ: 2.0 (m, CH_2P); 3.17 (2t, $J_{PCH} = 9$, NCH_2C); 4.1 (s, $PhCH_2$); 4.65 (s, NH, OH); 7.35 (s, C_6H_5).

^{31}P-NMR (D_2O) δ: 37.78 (pH = 1).

$C_{18}H_{25}N_2O_2P$ × 2HCl (405.29) calc.: C 53.34 H 6.72 N 6.91 Cl 17.49 P 7.64%; found: C 52.2 H 6.7 N 6.9 Cl 17.7 P 7.5%

Bis(2-aminoethyl)phosphinic acid, **8**. To a mixture of 2.77 g (7.5 mmol) of **7**, dissolved in 150 ml of acetic acid and 20 ml of water is added 4.5 g of Pd/C (5%) and then hydrogen at normal pressure. After 60 h hydrogen uptake stopped. The catalyst is filtered off and the filtrate evaporated. To the residue is added a few ml of methanol and the mixture is stirred. A white suspension forms. The solid is filtered off and dried to give 0.6 g (42.6%) of **8** × 2 HCl, a white solid, m.p. 278–279°C (dec.).

^{1}H-NMR (D_2O) δ: 2.0 (2t, $J = 8$, CH_2P); 3.1 (2t, $J = 7$, NCH_2); 4.65 (s, NH, OH).

^{31}P-NMR (D_2O) δ: 38.93 (pH = 1).

$C_4H_{13}N_2O_2P$ × 2 HCl × 0.3 H_2O (230.45) calc.: C 20.85 H 6.82 N 12.16 Cl 30.77 P 13.44 H_2O 2.34%; found: C 22.0 H 6.6 N 11.7 Cl 28.1 P 13.3 H_2O 2.39%.

Bis(2-cyanoethyl)phosphinic acid, **9**.

a) From O-methyl-bis(2-cyanoethyl)phosphinate. To a solution of 1.5 g (8 mmol) of O-methyl-bis(2-cyanoethyl)phosphinate[6] in 8 ml of chloroform is added 1.3 ml of bromotrimethylsilane and the solution stirred for 12 h at 20°C. Then it is evaporated on a rotavapor and the residue kugelrohr distilled to give 1.45 g (74.4%) of O-trimethylsilyl-bis(2-cyanoethyl)phosphinate, b.p. 165°C/0.04 torr, a colorless oil which solidifies. This is treated with methanol and the mixture stirred for 30 min. at reflux. On cooling cystals precipitate. These are filtered, washed with ether and dried to give 0.85 g (82.5%) of **9**, a crystalline solid, m.p. 124–126°C (lit.[8] m.p. 124–125°C).

^{1}H-NMR (D_2O) δ: 2.2 (m, CH_2P) and 2.7 (m, CH_2N); 4.73 (s, OH).

$C_6H_9N_2O_2P$ (172.12) calc.: C 41.87 H 5.27 N 16.28 P 18.0%; found: C 41.7 H 5.3 N 16.5 P 18.0%
Equiv. weight found 172; pK = 2.

b) From bis(2-cyanoethyl)phosphine. To a solution of 24.9 g (0.18 mol) of commercially available bis(2-cyanoethyl)phosphine in 100 ml of acetic acid is added with stirring and cooling 35.7 ml of H_2O_2 (30%) in 40 ml of acetic acid. The temperature is kept at 85–90°C. After completion of the addition the mixture is stirred for another half hour and then evaporated on a rotavapor. The residue is recrystallized from methanol to give 21.4 g (69.1%) of **9**, a white solid, m.p. 124–128°C (lit.[8] m.p. 124–125°C).

^{1}H-NMR (D_2O) δ: 2.15 (2t, CH_2P); 2.6 (2t, CCH_2); 4.7 (s, OH).

Bis(3-aminopropyl)phosphinic acid, **10**. A mixture of 17.7 g (0.1 mol) of **9** in 200 ml of methanol is treated with 40 g of liquid NH_3, hydrogen and 1.7 g of Ra-Ni and kept for 6 h at 60–70°C. Then after 10 h each, 3.4 g of Ra-Ni and 20 g of NH_3, 7 g of Ra-Ni and 20 g of NH_3, and again 7 g of Ra-Ni and 20 g of NH_3 is added until hydrogen uptake comes to a stand-still. Then the hydrogenation mixture is filtered and the filtrate evaporated on a rotavapor. An amount of 19.2 g of crude **10** is obtained, 9.6 g of which are treated with 400 ml of HCl (20%) and evaporated. The residue is refluxed with 52 ml of hexamethyldisilazane for 12 h, filtered and the residue kugelrohr distilled to give 8.5 g (40.2%) of $[(CH_3)_3SiNHCH_2CH_2]_2P(O)OSiMe_3$, b.p. 150°C/0.08 torr, a colorless oil.

^{1}H-NMR ($CDCl_3$) δ: 0.2 (s, Me_3Si); 0.27 (s, NH) (20H); 0.47 (s, $OSiMe_3$, 9H); 1.8 (m, CH_2CH_2P, 8H); 2.95 (m, NCH_2, 4H).

The silyl ester is treated with 50 ml of methanol and the mixture refluxed for 1 h. The clear solution is evaporated on a rotavapor and the residue dried at 100°C in the vacuum. There is obtained 3.6 g (40% or 93.3% with respect to silyl ester) of **10**, a slightly yellow, hygroscopic solid.

^{1}H-NMR (D_2O) δ: 1.7 (m, CH_2CH_2P, 8H); 2.9 (m, NCH_2, 4H); 4.9 (s, NH, OH).

^{31}P-NMR (D_2O) δ: 43.82 (pH = 11); 43.82 (pH = 7); 43.82 (pH = 4); 55.58 (pH = 1).

$C_6H_{17}N_2O_2P$ (180.19) calc.: C 40.0 H 9.51 N 15.55%; found: C 40.2 H 9.2 N 15.4%

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