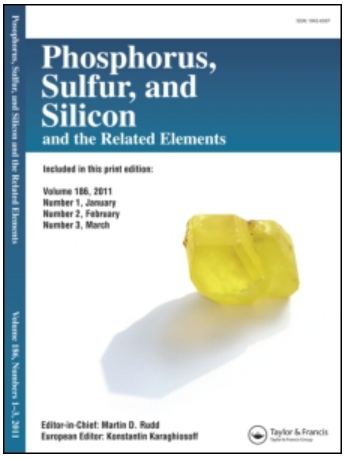

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ORGANIC PHOSPHORUS COMPOUNDS 87[1]: SOME REACTIONS OF 0-ETHYL-2-CHLOROETHYLPHOSPHONITE

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ORGANIC PHOSPHORUS COMPOUNDS 87[1]: SOME REACTIONS OF 0-ETHYL-2-CHLOROETHYLPHOSPHONITE

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Primary and secondary amines react with 0-ethyl-2-chloroethylphosphonite with the formation of 2-substituted aminoethylphosphonites, $RR'NCH_2CH_2P(O)(OC_2H_5)H$, **1**. The reaction very likely proceeds through the intermediate formation of 0-ethyl-vinylphosphonite. Hydrolysis of **1** produces the hydrochlorides of 2-substituted aminoethylphosphonous acids, $RR'NCH_2CH_2PO_2H_2$, **2**. These compounds interact with formaldehyde and benzylglycine to give the phosphinic acid derviatives **3**, $RR'NCH_2CH_2P(O)(OH)CH_2N(CH_2C_6H_5)CH_2CO_2H$, which upon debenzylation produce N-(2-substituted aminoethylphosphinylmethyl)glycines **4**, $RR'NCH_2CH_2P(O)(OH)CH_2NHCH_2CO_2H$. The Mannich type reaction can also be performed with the half-esters **1** and with the acylated compounds **5a** or **5b**. This type of reaction has been used to prepare 2-aminoethyl-aminomethylphosphinic acid, $H_2NCH_2CH_2P(O)(OH)CH_2NH_2$, **8**. Likewise, addition of acrylonitrile to **5b**, followed by hydrogenation, hydrolysis and debenzylation gives 2-aminoethyl-3-aminopropylphosphinic acid, **12**, $H_2NCH_2CH_2P(O)(OH)CH_2CH_2CH_2NH_2$. Interaction of **1f** with a substituted 3,4-dinitrodiphenyl-ether yields a phosphonite half-ester **13** which upon hydrolysis gives the acid **14**. Both these compounds exhibit herbicidal activity.

Key words: 0-Ethyl-2-chloroethylphosphonite; subst. aminoethylphosphonites; subst. aminoethylphosphonous acids; Mannich reaction; 2-aminoethyl-aminomethylphosphinic acid; 2-aminoethyl-3-aminopropylphosphinic acid.

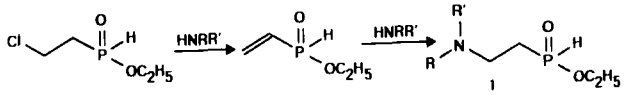
INTRODUCTION

The ready availability of 0-ethyl-2-chloroethylphosphonite[2] made it desirable to investigate the chemical reactivity of this chemical in more detail. Previously we have described the reaction of 0-ethyl-2-chloroethylphosphonite with tris(N-ethoxycarbonylmethyl)hexahydrotriazine which produced 1-ethoxycarbonylmethyl-1,3-azaphospholidine-3-ethoxy-3-oxide[2] and with tertiary amines which gave 0-ethyl-vinylphosphonite.[3] Now we describe the reaction of 0-ethyl-2-chloroethyl-phosphonite with primary and secondary amines and the interaction of the so obtained 0-ethyl-2-aminoethyl-phosphonites with hexahydrotriazine, acrylonitrile, and with dinitrodiphenylether.

RESULTS AND DISCUSSION

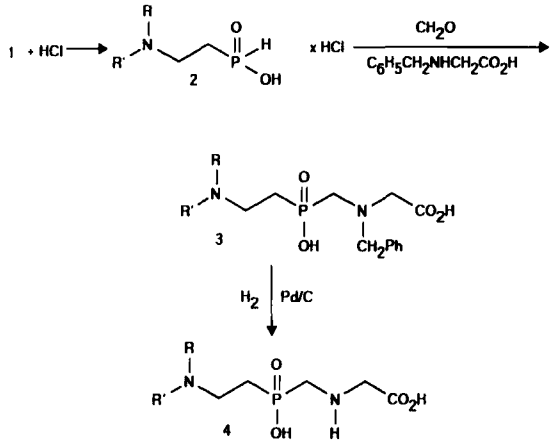
Primary and secondary amines react readily with 0-ethyl-2-chloroethyl-phosphonite and produce 0-ethyl-2-substituted aminoethylphosphonites in good yield. The reaction proceeds very likely through the intermediate formation of 0-ethyl-vinylphosphonite, since this compound has been identified as a by-product

in two cases:

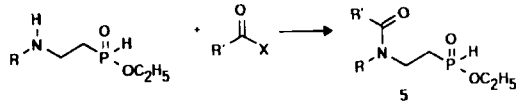


The physical properties of the compounds prepared are listed in Table I. All compounds exhibit a ^{31}P-chem. shift of around 36 ppm with a P—H coupling constant of about 540 Hertz, thus confirming the proposed structure of **1**.

Hydrolysis of **1** with 6N HCl produces the hydrochlorids of 2-substituted aminoethylphosphonous acids **2**, in high yield (Table II). All compounds exhibit a ^{31}P-chem. shift of around 25 ppm with a P—H coupling constant of around 540 Hertz, thus confirming the proposed structure of **2**. These compounds interact in a Mannich type reaction with formaldehyde and benzylglycine to give the phosphinic acid derivatives **3** which upon debenzylation with H_2 in presence of 5% Pd/C produce the 2-aminoethyl-N-hydroxycarbonyl-methyl-aminomethylphosphinic acid derivatives **4**.



In contrast to glyphosate[4] and (N-hydroxycarbonylmethyl-aminomethyl)-alkylphosphinic acids,[5] **4a** and **4f** possess no herbicidal activity. The N—H bond in **1f** and **1g** may be acylated without attacking the P—H bond:

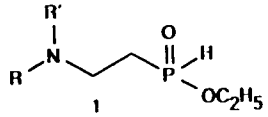


Like the phosphonous acid derivatives **2** the half-esters **1** and **5** also undergo a Mannich type reaction to yield the phosphinate derivatives **6.** These on hydrolysis with HCl yield the phosphinic acids **7**. Debenzylation of **7a** and **7b** with H_2 using Pd/C as a catalyst produces 2-aminoethyl-aminomethyl-phosphinic acid, **8a** and 2-methylaminoethyl-aminomethylphosphinic acid **8b**, respectively.

Likewise, addition of **5b** to acrylonitrile, followed by hydrogenation, hydrolyses

TABLE I

Properties of some 0-ethyl-2-alkylaminoethylphosphonites, **1**



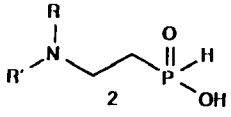
1

R	R'	b.p.°C/torr	Yield %	P-H	^{1}H-NMR ($CDCl_3$) OCH_2	Ch_2N	CH_2P	^{31}P-NMR ppm
$(CH_2)_5$—		115/0.1	78	7.1	4.15	2.3–2.9	2	37.3
$(CH_3)_2CH$—	H	80/0.15	57.5	7.3	4.2	2.6–3.3	2	36.9
n-C_3H_7	H	78–81/0.06	48	7.23	4.2	2.6–3.3	2	36.9
C_2H_5	C_2H_5†	71–74/0.08	15.3	7.2	4.15	2.4–3.1	2	36.7
CH_3	CH_3	57/0.05	59	7.2	4.15	2.2–2.7	1.95	36.4
CH_3	H	73–74/0.04	65	7.2	4.15	2.4–3.2	2	36.75
$C_6H_5CH_2$	H	140/0.15	70	7.1	4.1	2.7–3.2	1.95	36.84
$C_6H_5CH_2$	C_2H_5	140/0.1	69	7.1	4.05	2.3–3.0	2	37.58
$CH_2CH_2OCH_2CH_2$—		110/0.15	48	7.15	4.1	2.3–3.0	1.95	36.29
$CH_2CH_2CH_2CH_2$—		115/0.2	74	7.2	4.15	2.4–3.1	2	36.4
$CH_2CH_2N(CH_3)CH_2CH_2$—		110/0.15	68	7.2	4.1	2.2–2.9	2	36.6
$C_6H_5CH_2$	CH_3	115/0.15	72	7.1	4.1	2.15–2.9	2	36.9
CH=NCH=N—		135/0.15	45.5	7.2	4.1	4.55	2.5	31.4
$(CH_2)_3CH(COOC_2H_5)CH_2$—		120/0.08	75.7		4.1	2.3–3.1	2	

ains CH_2=CH—P(O)(H)(OEt) ^{31}P-NMR 25.68 (J_{PH} 535 Hz).
> H_3PO_4 as ref.)

TABLE II

Properties of some 2-alkylaminoethylphosphonous acid hydrochlorides, **2**

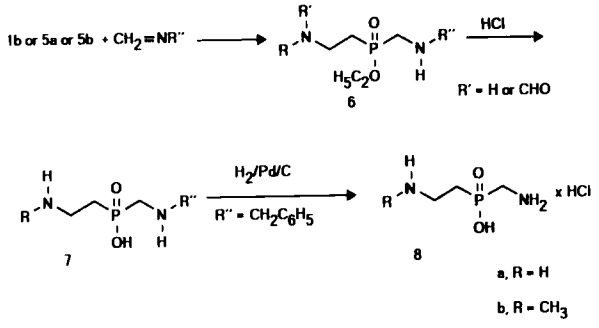


R	R′	m.p.°C(dec.)	Yield %	^{1}H-NMR in D_2O) P-H	OH/HCl	CH_2N	CH_2P	^{31}P-NMR(D_2O) H-P comp. ppm	J_{Ph}
$-(CH_2)_5-$		232–235	98.3	7.5	5.1	3.0–4.1	2.1	25.2	547.8
$(CH_3)_2CH$	H	101–104	100	7	4.55	2.7–3.3	1.9	25.95	548.3
n-C_3H_7	H	127–130	57.3	7.4	5.05	3.0–3.7	2		554
CH_3	CH_3	110–114	99.6	7.2	4.73	2.7–3.6	2.1	25.3	551
CH_3	H†	98–101	59.6	7.1	4.8	2.7(CH_3) 3.2(CH_2)	2.1	26.79	554.2
$C_6H_5CH_2$	H	160–164	76	7.1	4.7	3.2	2	24.19	543
$C_6H_5CH_2$	C_2H_5	resin	100	7.1	4.73	2.9–3.5	2	25.4	551.7
$-CH_2CH_2OCH_2CH_2-$		200–201	64.3	7.5	5.1	3.3–4.0	2.4	23.8	545.4
$-(CH_2)_4-$		162–165	65.9	7.15	5	3.0–4.2	2.4		540
$-CH_2CH_2N(CH_3)CH_2CH_2-$		214–216	69	7.6	5.2	3.3–4.5	2.7	22.3	542.5
$-CH=NCH=N-$		resin	100	7.4	4.9	4.7	2.47	27.35	525.2
$-(CH_2)_3CH(COOH)CH_2-$		resin	97.8	7.3	5.05	2.9–4.0	2.3		550

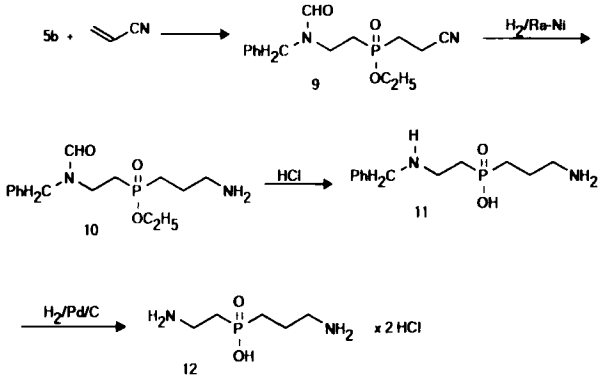
ompound without HCl melts at 179–182°C(dec.).

$_3PO_4$ as ref.

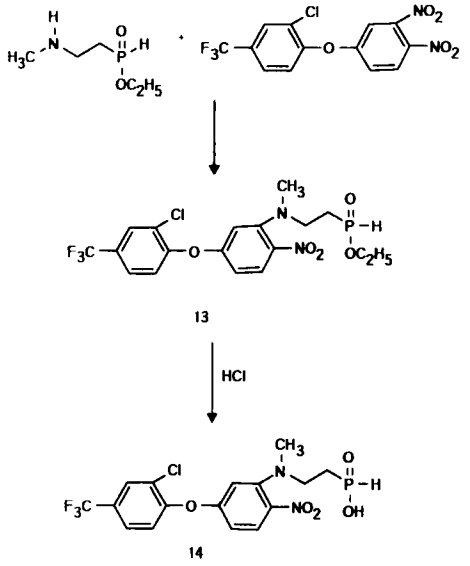
l through exchange of P-H with D_2O to give P-D.



and debenzylation gives 2-aminoethyl-3-aminopropylphosphinic acid, **12**.



Finally interaction of **1f** with 2-chloro-4-trifluoromethyl-3′,4′-dinitro-diphenyl-ether produces the phosphonite ester **13** which on hydrolysis yields the phosphonous acid **14**. **13** and its acid **14** exhibit preemergent and contact herbicidal



activity. Both are selective in rice, whereby the acid exhibits the higher activity and controls at 2 kg/ha echinochloa, scirpus, monochoria and sagittaria to 100 per cent.

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. $(CH_3)_4$)Si). The chemical shifts are reported in ppm with negative values being upfield of the standard, and positive downfield.

1. Preparation of 0-ethyl-2-piperidinylethylphosphonite, **1a**. To a solution of 43.5 ml (0.46 mol) of piperidine in 300 ml of ether is added dropwise 31.3 g (0.2 mol) of 0-ethyl-2-chloroethylphosphonite. An exothermic reaction ensues. The mixture is stirred for 12 hours at 20°C, the precipitate filtered off, and the filtrate evaporated on a rotavapor. The residue is purified by thin layer destillation to give **1a**, b.p. 115°C/0.1 torr, yield 32.0 g (78%).

^{1}H-NMR (in $CDCl_3$) δ = 1.2 (t, CH_3), 1.5 (m, $(CH_2)_3$), 2.0 (m, CH_2P), 2.5 (m, CH_2)(17H); 4.15 (qui, OCH_2, 2H); 7.1 (td, PH, J_{PH} 543.5 Hz; $^3J_{HH}$ 2 Hz, 1H [ppm]

^{31}P-NMR (in $CDCl_3$) δ = 37.3 ppm (J_{PH} 543.5 Hz)

$C_9H_2NO_2P$ (205.24) calc: C 52.67; H 9.83; N 6.83; P 15.09%
found: C 52.74; H 9.71; N 6.85; P 15.02%

The compounds listed in Table I have been prepared similarly.

2. Preparation of 2-piperidinylethylphosphonous acid hydrochloride, **2a**. A mixture of 20.5 g (0.1 mol) of **1a** and 100 ml of 6N HCl is refluxed for 12 hours. Then the clear solution is evaporated on a rotavapor and the crystalline white residue dried at 80°C under reduced pressure. There is obtained 21 g (98.3%) of crystalline **2a**.

^{1}H-NMR (in D_2O) δ = 1.8–2.9 (m, $(CH_2)_3$, PCH_2, 8H); 3–4.1 (m, CH_2N, 6H); 5.15 (s, OH, HCl); 7.5 (td, PH, J_{PH} 547.8 Hz, $^3J_{HH}$ 2 Hz, 1H)[ppm]

^{31}P-NMR (in D_2O)δ = 25.21 ppm (J_{PH} 547.8 Hz)

^{31}P-NMR: Deuterated compound δ = 24.8 ppm (J_{PD} 84.4 Hz)

$C_7H_{17}ClNO_2P$ (213.65) calc: C 39.35; H 8.02; N 6.56; Cl 16.59; P 14.5%
found: C 39.55; H 7.73; N 6.74; Cl 16.68; P 14.29%

Equiv. weight found 219, calc. 213.6; $pK_1 < 2$; pK_2 9.52.
The compounds listed in Table II have been prepared similarly.

3. Preparation of 2-piperidinylethyl-N-benzyl-N-hydroxycarbonylmethyl-aminomethyl-phosphinic acid. **3a**. To a mixture of 10.7 g (0.05 mol) of **2a** and 10.1 g (0.05 mol) of benzylglycinehydrochlorid in 100 ml of HCl (20%) is added at 100–105°C over a period of 30 min 16 ml (0.2 mol) of aquous formaldehyde (35%). The mixture is refluxed with stirring for 4 hrs and then evaporated on a rotavapor. The residue is dissolved in water, ethanol and propylene oxide added and then acetone dropped in until the solution became turbid. A white solid crystallized out. This was filtered off, washed with acetone and dried at 80°C in the vacuum. There is obtained 12.8 g of **3a** (72%), m.p. 210–211°C (dec.).

^{1}H-NMR (in D_2O) δ = 1.4–2.6 (m, $(CH_2)_3$, CH_2P, 8H); 2.7–3.6 (m, CH_2N, 8H); 4.0 (s, $COCH_2$, 2H); 4.7 (s, $PhCH_2$, 2H); 4.8 (s, OH); 7.63 (m, pH, 5H)[ppm].

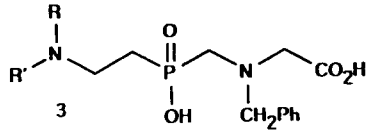
^{31}P-NMR (in D_2O, pH 4) δ = 24.74 ppm

$C_{17}H_{27}N_2O_4P \times H_2O$ (372.4) calc: C 54.83, H 7.85, N 7.52, P 8.32%
found: C 54.97, H 7.88, N 7.62, P 8.81%

Equiv. weight found 365, calc. 372.
The compounds listed in Table III have been prepared similarly.

TABLE III

Properties of some 2-alkylaminoethyl-N-benzyl-N-hydroxycarbonyl-methyl-aminomethylphosphinic acids, **3**



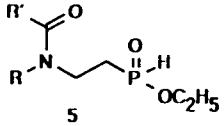
3

No.	R	R′	m.p.°C(dec.)	Yield %	^{1}H-NMR (in D_2O) CCH_2P	NCH_2†	NCH_2P	$COCH_2$	OH	^{31}P-NMR (in I ppm
a	—$(CH_2)_5$—		210–211	72	2.1	3.0–3.8	3.9 (J8)	4.5	5.8	24.74 (pH
b	CH_3	CH_3†	174–176	81.7	1.9 (m)	3.1	3.25 (J9)	3.7	4.57	24.47 (pH
c	$C_8H_5CH_2$	C_2H_5	resin	100	2.35	3.1–3.7	3.5 (J8)	4.4	5.07	
d	—$CH_2CH_2N(CH_3)CH_2CH_2$—		resin	100	2.1	3.2–4.0	3.4 (J8)	4.1	4.8	23.63 (pH

$C_6H_5CH_2N$: 4.4 (s, CH_2); 7.4 (s, C_6H_5).
Silylated compound b.p. 164–168°C/0.04 torr.
85% H_3PO_4 as ref.

TABLE IV

Properties of some 0-ethyl-2-(N-acyl-N-alkyl)aminoethylphosphonites, **5**



5

	R	R′	b.p.°C/torr	Yield %	CH_2P	^{1}H-NMR (in $CDCl_3$) R-N	NCH_3	P-H	^{31}P-NMR (in CDCl ppm	J_P
a	CH_3	H	125/0.1	76.6	2.1	2.9 and 3.0	3.6	7.2	33.96 and 31.91	540 539.
b	$C_6H_5CH_2$	H	160/0.18	51.3	2	4.5 and 4.55 7.31 (Ph)	3.5	7.1	33.96 and 32.0	540 540
c	$C_6H_5CH_2$	$ClCH_2$	oil	80.7	2.1	4.63 7.3 (Ph)	3.7	7.1	32.19 and 34.51	543 542
d	$C_6H_5CH_2$	Cl_2CH	oil	92	2.2	4.7 and 4.6 7.3 (Ph)	3.6	7.1	33.86 and 32.08	543. 544

85% H_3PO_4 as ref.

4. Preparation of 2-piperidinylethyl-n-hydroxycarbonylmethyl-aminomethylphosphinic acid, **4a**. To a solution of 8.86 g (0.025 mol) of **3a** in 90 ml of acetic acid is added 1 g of catalyst (5% Pd/C) and then the mixture hydrogenated at 25°C. After 30 min H_2 uptake ceased. The catalyst is filtered off and the clear, colorless filtrate evaporated on a rotavapor. The residue is recrystallized from a mixture of methanol/acetone. There is obtained 3.31 g (50%) of **4a**, a white solid, m.p. 120–125°C (dec.).

^{1}H-NMR (in D_2O) δ = 1.6–2.7 (m, $(CH_2)_3$, CH_2P, 8H), 2.9–3.9 (m, CH_2N); 3.55 (d, J_{PH} 10 Hz, CH_2P), 4.0 (s, $COCH_2$)(10H); 5.05 (s, OH, NH)[ppm].

^{31}P-NMR (in D_2O, pH 4) δ = 25.3 ppm.

$C_{16}H_{21}N_2O_4P \times H_2O$(282.27) calc: C 42.55, H 8.21, N 9.92, P 10.97%
found: C 43.84, H 7.99, N 10.23, P 10.39%

4f, $(CH_3)_2NCH_2CH_2P(O)(OH)CH_2NHCH_2CO_2H$, was similarly prepared from **3f**, H_2 and Pd/C in acetic acid; yield 84.8%, m.p. 237–238°C (dec.).

^{1}H-NMR (in D_2O) δ = 2.2 (m, CH_2P, 2H); 2.9 (s, $(CH_3)_2N$, 6H); 3.25 (d, J_{PH} 10 Hz, NCH_2P, 2H); 3.4 (m, NCH_2, 2H); 3.7 (s, $COCH_2$, 2H); 4.73 (s, OH, NH)[ppm]

^{31}P-NMR (in D_2O, pH ~ 5) δ = 25.02 ppm.

$C_7H_{17}N_2O_4P \times H_2O$(242.2) calc.; C 34.7, H 7.9, N 11.57, P 12.79%
found: C 34.64, H 7.86, N 11.43, P 12.79%

Equiv. weight found 242, calc. 242; pK_1 = 7.03; pK_2 = 10.04.

5. Preparation of 0-ethyl-2-(N-formyl-N-methyl)aminoethyl-phosphonite, **5a**. A mixture of 16.63 g (0.11 mol) of **1f** and 110 ml of $HCO_2C_2H_5$ is refluxed with stirring for 12 hours. Then the clear solution is evaporated on a rotavapor and the residue purified by thin layer distillation. There is obtained 15.1 g (76.6%) of **5a**, a colorless liquid, b.p. 125°C/0.1 torr.

^{1}H-NMR (in $CDCl_3$) δ = 1.4 (t, CH_3, 3H); 2.1 (m, CH_2P, 2H); 2.9 and 3.0 (s, CH_3N, 3H); 3.6 (m, NCH_2, 2H); 4.15 (qui, OCH_2, 2H); 8.05 and 8.15 (s, CHO, 1H); 7.2 (br, PH, J_{PH} 540 Hz, 1H)[ppm]

^{31}P-NMR (in $CDCl_3$) δ = 33.96 ppm (J_{PH} 540 Hz) and 31.91 ppm (J_{PH} 539.4 Hz)

$C_6H_{14}NO_3P$(179.16) calc: C 40.23; H 7.88; N 7.82; P 17.29%
found: C 40.21; H 8.10; N 7.89; P 17.31%

The compounds listed in Table IV have been prepared similarly.

6. Preparation of 0-ethyl-2-(N-formyl-N-methyl)aminoethyl-N'-benzylaminomethylphosphinate, **6a**. A mixture of 7.17 g (0.04 mol) of **5a** and 4.77 g (0.04 mol) of N,N',N"-tribenzylhexahydrotriazine is stirred and heated at 110°C for 1 hour. A quantitative yield of **6a**, a slightly yellow, viscous oil is obtained.

^{1}H-NMR (in $CDCl_3$) δ = 1.33 (t, CH_3, 3H); 2.1 (m, CH_2P, 2H); 2.8 (m, NCH_3, NCH_2P, 5H); 3.6 (m, NCH_2, 2H); 3.8 (s, $PhCH_2$, 2H); 4.1 (qui, OCH_2, 2H); 7.35 (s, Ph, 5H); 8.0 and 8.1 (s, CHO, 1H)[ppm]

^{31}P-NMR (in $CDCl_3$) δ = 50.52 and 49.96[ppm]
The compounds listed in Table V have been prepared similarly.

7. Preparation of N-benzylaminoethyl-N-benzylaminomethylphosphinic acid hydrochloride, **7a**. A mixture of 11 g (0.0294 mol) of **6b** and 100 ml of HCl (20%) is refluxed for 12 hours, the clear solution evaporated and the residue recrystallized from water-acetone. There is obtained 6.85 g (65.7%) of **7a**, m.p. 273–275°C (dec.).

^{1}H-NMR (in D_2O) δ = 2.0 (m, PCH_2—C, 2H); 3.1 (d, PCH_2N, J_{PH} 9Hz); 3.2 (m, NCH_2—C), (4H), 4.15 and 4.23 (s, $PhCH_2$, 4H); 4.8 (s, OH, NH); 7.43 (s, Ph, 10H)[ppm]

^{31}P-NMR (in D_2O, pH 4) δ = 25.58 ppm.

$C_{16}H_{23}N_2O_2P \times HCl$(342.8) calc: C 56.06, H 7.06, N 8.17, P 9.04, Cl 10.34%
found; C 57.38, H 6.87, N 8.12, P 8.85, Cl 10.13%

2-(N-Methylaminoethyl)-N'-benzylaminomethylphosphinic acid hydrochloride, $CH_3NHCH_2CH_2$-$P(O)(OH)CH_2NHCH_2C_6H_5 \times HCl$, **7b** was similarly obtained from hydrolysis of **6a** with HCl, yield 77.6%, m.p. 217–220°C (dec.).

^{1}H-NMR (in D_2O) $\delta = 2.45$ (m, C—CH_2P, 2H); 3.0 (s, NCH_3, 3H); 3.55 (d, J_{PH} 9Hz, NCH_2P), 3.4 (m, NCH_2)(4H); 4.6 (s, $PhCH_2$, 2H); 5.27 (s, OH, NH); 7.75 (s, Ph, 5H)[ppm]

^{31}P-NMR (in D_2O, pH ~ 1) $\delta = 26.61$ ppm

8. Preparation of 2-aminoethyl-aminomethylphosphinic acid hydrochloride, **8a**. To a solution of 3.43 g (0.01 mol) of **7a** in 35 ml of acetic acid and 3 ml of water is added 1 g of 5% Pd/C and then the mixture hydrogenated at 30–35°C. After 11% H_2 uptake another 1 g of catalyst is added. After 30 hrs H_2 uptake ceased. The catalyst is filtered off and filtrate evaporated on a rotavapor. The solid residue is dissolved in H_2O and the solution again evaporated. This procedure is repeated twice to remove all acetic acid. There is obtained 1.4 g (80%) **8a**, a white solid, m.p. 279–284°C (dec.).

^{1}H-NMR (in D_2O) $\delta = 2.0$ (m, PCH_2C, 2H); 3.0 (d, PCH_2N, J_{PH} 9 Hz); 3.2 (m, NCH_2C)(4H); 4.67 (s, OH, NH)[ppm]

^{31}P-NMR (in D_2O, pH ~ 3) $\delta = 27.72$ ppm.

$CH_3NHCH_2CH_2P(O)(OH)CH_2NH_2xHCl$, **8b** was similarly obtained from **7b** dissolved in acetic acid, catalyst 5% Pd/C and hydrogen. Yield 93.4% **8b**, white hygroscopic solid.

^{1}H-NMR (in D_2O) $\delta =$ (m, PCH_2C, 2H); 2.65 (s, NCH_3, 3H); 3.1 (d, PCH_2N, J_{PH} 10 Hz); 3.2 (m, NCH_2C)(4H)[ppm]

^{31}P-NMR (in D_2O, pH ~ 1) $\delta = 27.91$ ppm.

9. Preparation of 0-ethyl-γ-cyanoethyl-2(N-benzyl-N-formyl)aminoethyl phosphinate, **9**. To 7.5 g (0.0294 mol) of **5b** in 1.94 ml (0.0294 mol) of acrylonitrile are added 25 ml of sodium ethylate (0.25 molar). After an exothermic reaction (the temperature rises up to 47°C) the reaction mixture is stirred for 1 hour at room temperature and then evaporated under reduced pressure. The crude oil is purified by flash chromatography (SiO_2/CH_2Cl_2: MeOH; 95:5) to yield 8.0 g (88.3%) **9**, a yellow oil. $n_D = 1{,}5250$.

^{1}H-NMR (in $CDCl_3$) $\delta = 1{,}27$ (t, CH_3, 3H); 2.1 (m, CH_2PCH_2, 4H); 2.55 (m, CH_2CN, 2H); 3.43 (m, NCH_2, 2H); 4.1 (m, OCH_2, 2H); 4.45 and 4.5 (s, CH_2Ph, 2H); 7.3 (s, Ph, 5H); 8.3 (s, CHO, 1H)[ppm]

^{31}P-NMR (in $CDCl_3$) $\delta = 49.16$ ppm

$C_{15}H_{21}N_2O_3P \times 0.1\ CH_2Cl_2$ (316.8) calc: C 57.2, H 6.7, N 8.8, P 9.8%
found: C 57.8, H 6.9, N 8.8, P 9.5%

10. Preparation of γ-Aminopropyl-2-benzylaminoethylphosphinic acid hydrochloride, **11**. A mixture of 4.7 g (0.0156 mol) of **9**, 5.0 g of liquid ammonia and 0.7 g of Raney-Nickel in 100 ml of ethanol is hydrogenated for 7 hours at 75–80°C. The catalyst is filtered off and the solvent removed by evaporation. The crude oil (4.7 g) of 0-ethyl-γ-aminopropyl-2-N-benzyl-N-formyl)aminoethylphosphinate **10** is hydrolyzed without any further purification by refluxing in 50 ml of HCl 6N for 24 hours. The cooled reaction mixture is evaporated and the residue dried over P_2O_5. The crude crystals are suspended in ether, filtered and dried to afford 3.5 g (70.3%) of **11**, m.p. 253–256°C (dec.).

^{1}H-NMR (in D_2O) $\delta = 2.2$ (m, $CH_2CH_2PCH_2$, 6H); 3.2 (m, NCH_2, 4H), 4.3 (s, $PhCH_2$, 2H); 5.7 (s, NH_2, OH); 7.5 (s, Ph, 5H)[ppm]

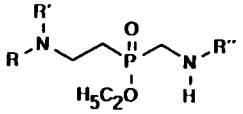
^{31}P-NMR (in D_2O) $\delta = 45.68$ ppm

$C_{12}H_{21}N_2O_2P \times 2.2\ HCl \times 0.3\ H_2O$(342): calc.: C 42.1, H 7.0, N 8.2, Cl 22.8, P 9.0, H_2O 1.6%
found: C 41.5, H 6.8, N 7.7, Cl 22.4, P 8.6, H_2O 1.5%

11. Preparation of γ-Aminopropropyl-β-aminoethylphosphinic acid dihydrochloride, **12**. 2.0 g (0.0061 mol) of **11** and 0.4 g of Pd/C in 20 ml of water are hydrogenated at room temperature for 33 hours. The catalyst is filtered off and the filtrate evaporated. The crude oil (1.7 g) crystallizes spontaneously. The crystals are suspended in ether, filtered and dried yielding 1.2 g (50.2%) of **12**, m.p. 208–210°C (dec.)

TABLE V

Properties of 0-ethyl-2-(N-acyl-N-alkyl)aminoethyl-subst. amino-methylphosphinates, **6**



6

R	R′	R″	b.p.°C/torr	Yield %	^{1}H-NMR($CDCl_3$) CCH_2P	$R + PCH_2N$	NCH_2C	R′	^{31}P-NMR(ppr
CH_3	CHO	$C_6H_5CH_2$	oil	100	2.1	2.8	3.6	8 and 8.1	50.5 a 49.96
$C_6H_5CH_2$	CHO	$C_6H_5CH_2$	oil	60.4	2.2	3.83 and 2.9	3.6	8.3	50.3 a 49.77
CH_3	CHO	$CH_2CO_2C_2H_5$	viscous oil	46.3	2.3	2.9	3.6	8.0 and 8.1	
$(CH_3)_2CH$	H	$C_6H_5CH_2$	160/0.02	29.5	2.1	2.8 and 3.85	2.9	1.7	

85% H_3PO_4 as ref.

^{1}H-NMR (in D_2O) $\delta = 2.2$ (m, $CH_2CH_2PCH_2$, 6H); 3.2 (m, NCH_2, 4H); 5.7 (s, OH, NH_2)[ppm]

^{31}P-NMR (in D_2O) $\delta = 47.11$ ppm.

$C_5H_{15}N_2O_2P \times 2.3\,HCl \times 0.5\,H_2O \times 0.125(C_2H_5)0$ (268.2)

calc.: C 24.6, H 7.2, N 10.4, Cl 30.4, P 11.5, H_2O 3.3%

found: C 24.8, H 6.7, N 10.3, Cl 30.1, P 11.5, H_2O 3.3%

12. Preparation of 2-Nitro-5-(2'chloro-4'-trifluoromethylphenoxy)-phenyl-N-methyl-2-aminoethylphosphonite-0-ethylester, **13**. To 18 g (49.6 mmol) of 1,2-dinitro-4-(2'chloro-4'trifluoromethylphenoxy)-benzene dissolved in 70 ml of toluene is added dropwise at reflux temperature 15.0 g (99.2 mmol) of **1f**. A orange suspension is formed. The mixture is refluxed for 12 hours. The solid is filtered off [2.03 g, m.p. 179–182°C (dec.), 16.6% is $CH_3NHCH_2CH_2PO_2H_2$, comparison with authentic sample], and the filtrate evaporated on a rotavapor. The remaining brown, viscous oil is dissolved in ethyl acetate and chromatographed on Kieselgel. There is obtained 10.85 g (50.2%) of **13**, a viscous, yellow oil.

^{1}H-NMR (in $CDCl_3$) $\delta = 1.33$ (t, CH_3, 3H); 2.2 (m, PCH_2, 2H); 2.87 (s, NCH_3, 3H); 3.5 (m, NCH_2, 2H); 4.1 (qui, OCH_2, 2H); 6.3–8.0 (m, C_6H_3, 6H); 7.3 (d, PH, J_{PH} 548 Hz, 1H)[ppm]

$C_{18}H_{19}ClF_3N_2O_5P$(466.78) calc.: C 46.3, H 4.10, N 6.0, P 6.63%

found: C 44.8, H 4.10, N 6.0, P 6.50%

Dealkylation of **13** with $BrSiMe_3$ followed by hydrolysis of the silyl-ester with C_2H_5OH/H_2O yields the acid **14** in 71.3% yield, m.p. 161–164°C (dec.)

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