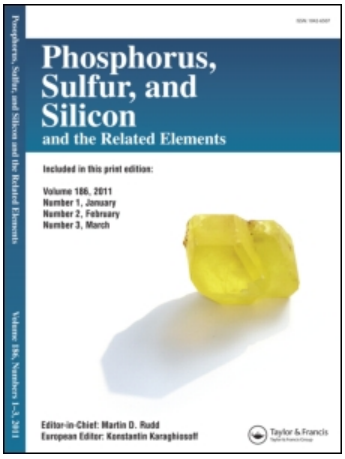

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ORGANIC PHOSPHORUS COMPOUNDS 100[1] SYNTHESIS AND PROPERTIES OF N-HYDROXYCARBONYLMETHYL-AMINOMETHYL-DIALKYLPHOSPHINE OXIDES

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Dedicated to Prof. Dr. Marianne Baudler on the occasion of her 70th birthday

The synthesis, physical and spectroscopic properties of N-hydroxycarbonylmethyl- and N-(1-hydroxycarbonylethyl)-aminomethyl-dimethyl (or diethyl)phosphine oxides and their esters, **1a**, **1b**, **2a**, **2b**, **3**, **4**, and also of N-(2-ethoxycarbonylethyl)-aminomethyl-dimethylphosphine oxide, **5**, and of N-(2-methoxyethyl)-aminoethyl-dimethylphosphine oxide, **6**, are reported. The compounds show only weak biological activity.

Key words: N-hydroxycarbonylmethyl- and N-(1-hydroxycarbonyl-ethyl)-aminomethyl-dimethylphosphine oxides; N-hydroxycarbonyl-methyl-aminomethyl-diethylphosphine oxide; N-(2-ethoxycarbonyl-ethyl)-aminomethyl-dimethylphosphine oxide; N-(2-methoxyethyl)-aminomethyl-dimethylphosphine oxide.

INTRODUCTION

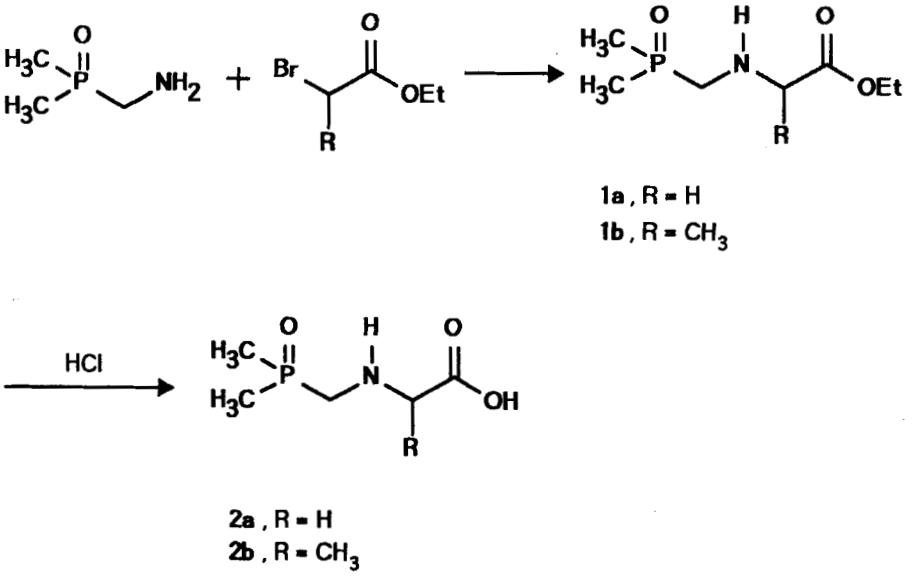
While N-phosphonylmethylglycines (Glyphosphate),[2,3] N-alkylphosphinylmethylglycines[4–6] and some related derivatives[7–9] were investigated intensively because some of these compounds possess herbicidal or plant growth regulating properties, no phosphine oxide substituted glycine has been reported so far in the literature. It seemed of interest to prepare some of these compounds and to determine their biological activity.

RESULTS AND DISCUSSION

The N-ethoxycarbonylmethyl- and N-(1-ethoxycarbonylethyl)-aminomethyl-dimethylphosphine oxides, **1a** and **1b**, were obtained from the interaction of aminomethyl-dimethylphosphine oxide[10] and ethyl bromoacetate or ethyl-1-bromopropionate, respectively. Hydrolysis of the esters with 20% aqueous HCl under reflux produced the corresponding acids **2a** and **2b** (Scheme I).

The Mannich type reaction[11] was used for the synthesis of N-ethoxycarbonylmethyl-aminomethyl-diethylphosphine oxide, **3**, because diethylphosphine oxide is readily available from diethylphosphite and ethyl magnesium bromide.[12] Hydrolysis of the ester **3** with 20% aqueous HCl under reflux afforded the acid **4** in good yield (Scheme II). The structures of the products are confirmed by their ^{1}H-NMR spectra (Fig.)

The uncatalyzed addition of dimethyl-aminomethylphosphine oxide to ethylacrylate in ethanolic solution gave N-(2-ethoxycarbonylethyl)-aminomethyl-dimethylphosphine oxide, **5**, in high yield. And finally the reaction of dimethyl-



SCHEME I

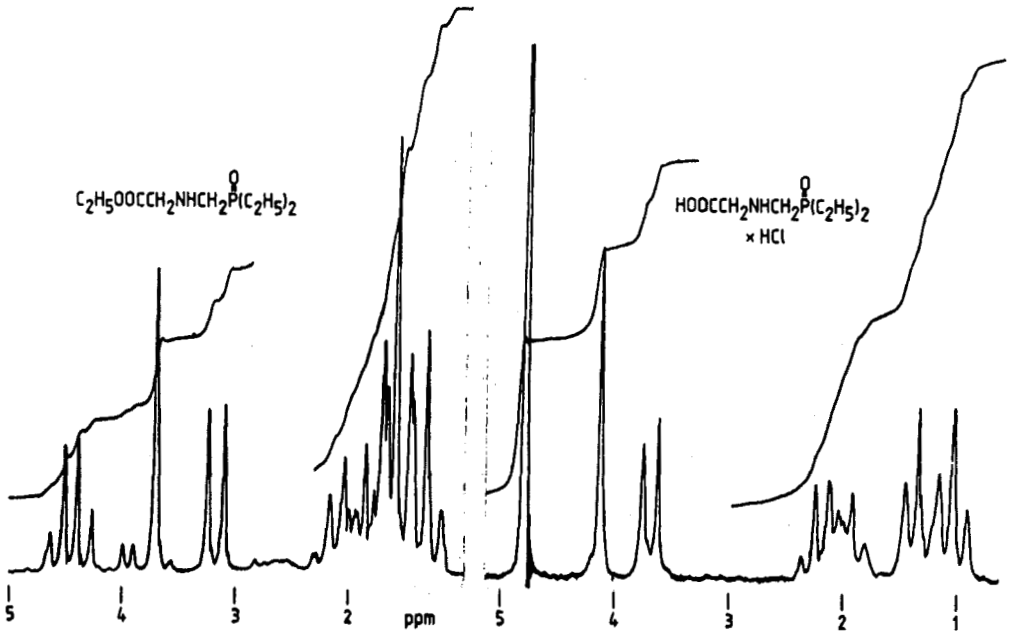
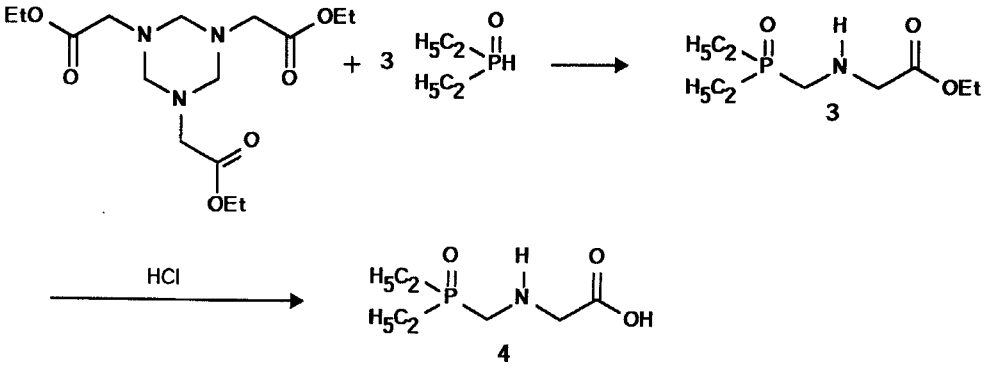
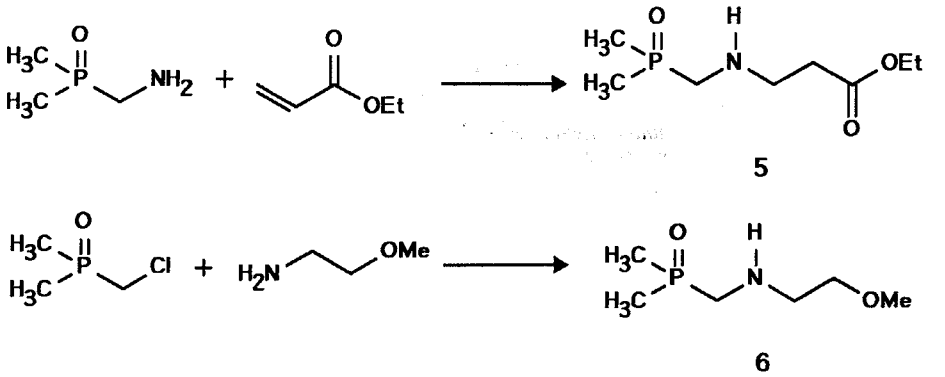


FIGURE ^{1}H-NMR spectra of **3** and **4**.



SCHEME II



SCHEME III

TABLE

Herbicidal activity of **1** to **6** at 4 kg/ha, postemergent

Comp.	Weeds[a)] Avena	Setaria	Lolium	Solanum	Sinapis	Stellaria	Phaseolus
1a	9	9	9	8	7	9	9
1b	9	9	9	9	9	9	9
2axHCl	9	9	9	4	6	9	7
2bxHCl	6	7	9	6	7	7	7
3	8	5	8	6	6	7	8
4	8	6	8	3	6	7	6
5	9	9	9	9	9	9	9
6	9	8	9	4	8	9	5
Glypho-sate	1	1	2	1	1	2	1

a) Percent control: 1=100%; 9=0%.

chloromethylphosphine oxide with 2-methoxyethyl amine in ethanolic solution produced N-(2-methoxyethyl)-aminomethyl-dimethylphosphine oxide, **6** (Scheme III).

BIOLOGICAL ACTIVITY

The herbicidal activity of the compounds **1** to **6** is low as indicated in the Table. Noteworthy is only the activity of **4**, because its symptoms resemble those of Glyphosate. In addition compounds **1b**, **3**, **5**, and **6** exhibit weak insecticidal 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. $(CH_3)_4Si$). The chemical shifts are reported in ppm, with negative values being upfield of the standard, and positive downfield. All reactions were run under an atmosphere of argon.

1. N-Ethoxycarbonylmethyl-aminomethyl-dimethylphosphine oxide, **1a**. To a solution of 22.49 g (0.2 mol) of aminomethyl-dimethylphosphine oxide, $H_2NCH_2P(O)(CH_3)_2$[2], in 25 ml of ethanol is added at room temperature 11.07 ml (0.1 mol) of ethyl bromoacetate. An exothermic reaction ensues and a white suspension forms. After one hour stirring, 100 ml of diethyl ether is added and the suspension filtered (17.46 g of hydrobromide = 92.5%). The filtrate is evaporated and the residue fractionated to give 14.4 g (74.5%) of **1a**, a colorless liquid, b.p. 126–130°C/0.05 torr.
^{1}H-NMR ($CDCl_3$) δ: 1.25 (t, CH_3, 3H); 1.5 (d, J = 14, PCH_3, 6H); 2.03 (s, NH, 1H); 2.97 (d, J = 8, CH_2P, 2H); 3.5 (s, $COCH_2$, 2H); 4.17 (q OCH_2, 2H).
$C_7H_{16}NO_3P$ (193.18) calc.: C 43.52 H 8.35 N 7.25 P 16.03%
found: C 41.6 H 8.4 N 7.3 P 15.9%

1b was obtained similarly from dimethyl-aminomethylphosphine oxide and ethyl-1-bromopropionate in 90.3% yield, b.p. 145°C/0.04 torr.
^{1}H-NMR ($CDCl_3$) δ: 1.27 (t, CH_3); 1.3 (d, J = 7, C—CH_3); 1.5 (d, J = 13, P—CH_3); 1.9 (br. s, NH); 2.9 (2d, J = 8, CH_2P); 3.4 (q, CH); 4.17 (q, OCH_2).
^{31}P-NMR ($CDCl_3$) 41.87 ppm
$C_8H_{18}NO_3P$ (207.21) calc.: C 46.37 H 8.76 N 6.76 P 14.95%
found: C 46.2 H 9.0 N 6.8 P 15.1%

2. N-Hydroxycarbonylmethyl-aminomethyl-dimethylphosphine oxide, **2a**. A mixture of 9.66 g (0.05 mol) of **1a** and 50 ml of 20% HCl-solution is refluxed for 4h. The clear solution is evaporated on a rotavapor and the residue recrystallized from acetone/propylene oxide to give 6.8 g (67.5%) of **2a** × HCl, a white solid, m.p. 185–189°C (dec.)
^{1}H-NMR (D_2O) δ: 1.87 (d, J = 14.4, CH_3P, 6H); 3.57 (d, J = 7.5, CH_2P, 2H); 4.17 (s, $COCH_2$, 2H); 4.9 (s, NH, HCl, 3H).
^{31}P-NMR (D_2O) 46.89 ppm
$C_5H_{12}NO_3P \cdot HCl$ (201.59) calc.: C 29.79 H 6.5 N 6.05 Cl 17.59 P 15.37%
found: C 29.6 H 6.6 N 7.0 Cl 16.3 P 15.5%

2b × HCl was similarly obtained from **1b** and HCl in 95.8% yield, m.p. 221–223°C (dec.)
^{1}H-NMR (D_2O) δ: 1.4 (d, C—CH_3); 1.6 (d, J = 13, CH_3P): 3.47 (d, J = 8, CH_2P); 4.05 (q, CH); 4.65 (s, OH, NH).
^{31}P-NMR (D_2O) 46.98 ppm (pH 1).

3. N-Ethoxycarbonylmethyl-aminomethyl-diethylphosphine oxide, **3**. A mixture of 11.5 g (0.033 mol) of N,N′,N″-tris(ethoxycarbonylmethyl)-hexahydrotriazine and 11.7 g (0.1 mol) of diethylphosphine oxide[12] is heated for 5 h to 100–110°C. Then the product is kugelrohr distilled to give 10.4 g (47%) of **3**, a colorless oil, b.p. 132–134°C/0.03 torr.
^{1}H-NMR ($CDCl_3$) δ: 1–2.2 (m, C_2H_5); 2.5 (s, NH); 3.05 (d, J = 8, CH_2P); 3.5 (s, $COCH_2$); 4.23 (q, OCH_2).

4. N-Hydroxycarbonylmethyl-aminomethyl-diethylphosphine oxide, **4**. From 5.53 g (0.025 mol) of **3** and 25 ml of 20% aqueous HCl, as described for **2**, is obtained 3.6 g (63%) of **4** × HCl, m.p. 204–206°C (dec.) (from water/acetone).
^{1}H-NMR (D_2O) δ: 0.8–2.3 (m, C_2H_5, 10H); 3.63 (d, J = 7, CH_2P, 2H); 4.07 (s, $COCH_2$, 2H); 4.78 (s, OH, NH, HCl, 3H).
^{31}P-NMR (D_2O) 55.08 ppm (pH 1).

$C_7H_{16}NO_3P$ × HCl (229.64) calc.:	C 36.61	H 7.46	N 6.10	Cl 15.44	P 13.49%
found:	C 36.81	H 7.79	N 6.28	Cl 15.50	P 13.63%

Equiv. weight found 234; pK_1 = 2.2; pK_2 = 6.17.

5. N-(2-Ethoxycarbonylethyl)-aminomethyl-dimethylphosphine oxide, **5**. To a solution of 11.78 g (0.1 mol) of aminomethyl-dimethylphosphine oxide in 15 ml of ethanol is dropwise added 10.9 ml of ethylacrylate. A slightly exothermic reaction ensues. The mixture is stirred for 12 h at 20°C and then fractionally distilled to give 19 g (91.7%) of **5**, a colorless liquid, b.p. 150°C/0.04 torr.
^{1}H-NMR ($CDCl_3$) δ: 1.27 (t, CH_3); 1.5 (d, J = 13, CH_3P); 1.7 (s, NH); 2.5 (m, $COCH_2$); 2.93 (d, J = 8, CH_2P); 3.0 (m, NCH_2); 4.15 (q, OCH_2).
^{31}P-NMR ($CDCl_3$) 41.96 ppm.

6. N-(2-methoxyethyl)-aminomethyl-dimethylphosphine oxide, **6**. To a solution of 63.25 g (0.5 mol) of chloromethyl-dimethylphosphine oxide in 100 ml of ethanol is added 86 ml of 2-methoxyethylamine and the mixture stirred and refluxed for 12 h. The orange-red solution is evaporated on a rotavapor, the residue dissolved in 200 ml of water, which is saturated with NaCl and extracted three times with 300 ml of $CHCl_3$ each. The organic phases are dried with Na_2SO_4, filtered and the filtrate fractionally distilled to give 27.8 g (33.7%) of **6**, a colorless liquid, b.p. 86°C/0.06 torr.
^{1}H-NMR ($CDCl_3$) δ: 1.5 (d, J = 13, CH_3P); 1.7 (s, NH); 2.87 (t, NCH_2); 3.0 (d, J = 8, CH_2P); 3.37 (s, OCH_3); 3.5 (t, OCH_2).

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