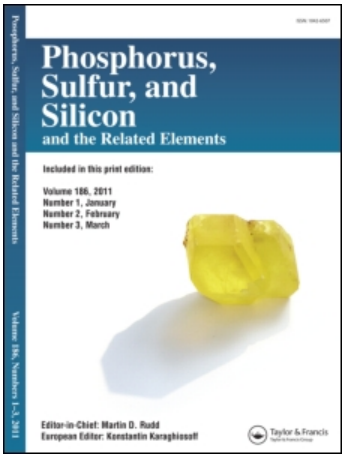

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ORGANIC PHOSPHORUS COMPOUNDS 104.[1] SYNTHESIS AND BIOLOGICAL ACTIVITY OF N-HYDROXYCARBONYLMETHYL-AMINOMETHYL-DI(n-PROPYL)- AND DI(n-BUTYL)PHOSPHINE OXIDES

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The synthesis, physical and spectroscopic properties of N-hydroxycarbonylmethyl-aminomethyl-di(n-propyl)- and di(n-butyl) phosphine oxides, **4a** and **4b**, and their ethyl esters, **3a** and **3b**, and also of aminomethyl-di(n-propyl)- and di(n-butyl)phosphine oxides, **2a** and **2b**, are reported. The compounds showed no biological activity.

Key words: Aminomethyl-di(n-propyl)phosphine oxide; aminomethyl-di(n-butyl)phosphine oxide; N-ethoxycarbonylmethyl-aminomethyl-di(n-propyl)phosphine oxide; N-ethoxycarbonylmethyl-aminomethyl-di(n-butyl)phosphine oxide; N-hydroxycarbonylmethyl-aminomethyl-di(n-propyl)phosphine oxide; N-hydroxycarbonylmethyl-aminomethyl-di(n-butyl)phosphine oxide.

INTRODUCTION

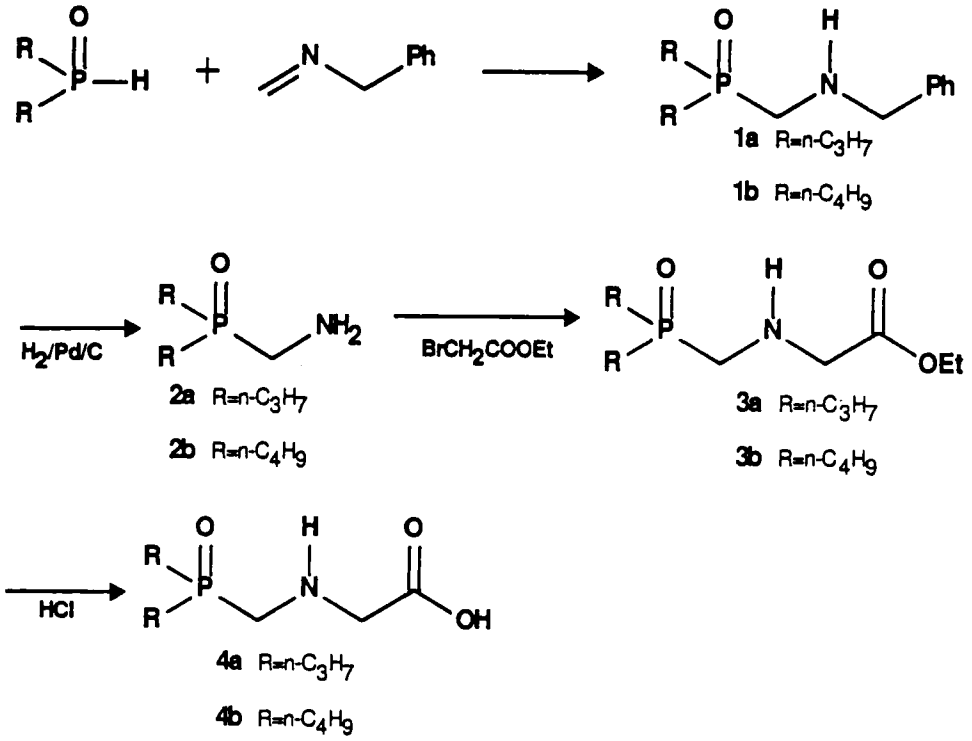
Recently we reported on the preparation and biological activity of N-hydroxycarbonylmethyl-aminomethyl-di(methyl)- and di(ethyl) phosphine oxides.[2] Since the herbicidal activity increased slightly from the dimethyl- to the diethylphosphine oxide derivatives, it seemed of interest to prepare the next higher homologues and screen their activity.

RESULTS AND DISCUSSION

N-Hydroxycarbonylmethyl-aminomethyl-di(n-propyl)- and di(n-butyl) phosphine oxides, **4a** and **4b**, were prepared as shown in the Scheme. On heating the secondary phosphine oxides added readily to N,N′, N″-tribenzylhexahydrotriazine and gave the N-benzyl-aminomethyl-dialkylphosphine oxides, **1a** and **1b**, in high yield. Debenzylation with hydrogen in the presence of Pd/C as catalyst produced the aminomethyl-dialkylphosphine oxides, **2a** and **2b**, again in good yield. It is worth mentioning that the debenzylation proceeded much faster and gave higher yields, when THF was used as solvent instead of n-propanol.

Alkylation of **2** (2 equiv.) with ethyl bromoacetate (1 equiv.) in ethanol yielded the N-ethoxycarbonylmethyl-aminomethyl-dialkyl-phosphine oxides, **3a** and **3b**, in addition to the hydrobromides of **2a** and **2b**.

Hydrolysis of **3** with 20% HCl under reflux gave the N-hydroxycarbonylmethyl-aminomethyl-dialkylphosphine oxides, **4a** and **4b**, which were isolated as hydrochlorides.



SCHEME

BIOLOGICAL ACTIVITY

The compounds described in this report 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 the ^{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. Di(n-propyl)phosphine oxide (^{31}P = 34.11, J_{PH} = 444.5 Hz) and di(n-butyl)phosphine oxide (^{31}P = 35.51, J_{PH} = 444.5 Hz) were prepared as described in the literature.[3]

1. N-Benzyl-aminomethyl-di(n-propyl)phosphine oxide, **1a**. A mixture of 11.92 g (0.1 mol) of N,N′,N″-tribenzylhexahydrotiazine and 13.42 g (0.1 mol) of di(n-propyl)phosphine oxide is stirred and heated to 110–120°C for 2 h. A weak exothermic reaction ensues. The crude product is purified by thin layer distillation. Yield 22.7 g (89.6%) of **1a**, b.p. 145°C/0.08 torr, m.p. 40–43°C.

^{1}H-NMR ($CDCl_3$) δ: 1.05 (t, CH_3); 1.5–1.8 (m, CH_2CH_2); 2.85 (d, J = 7, NCH_2P); 3.85 (s, $PhCH_2$); 7.3 (s, Ph).
^{31}P-NMR ($CDCl_3$) δ: 47.9.

N-Benzyl-aminomethyl-di(n-butyl)phosphine oxide, **1b**, was prepared similarly from di(n-butyl)phosphine oxide, yield 76%, m.p. 58–59°C (from diisopropyl ether).

^{1}H-NMR/$CDCl_3$) δ: 1.0 (t, CH_3); 1.35–1.8 (m, $(CH_2)_3$); 2.85 (d, J = 7, NCH_2P); 3.85 (s, $PhCH_2$); 7.3 (s, Ph).
^{31}P-NMR ($CDCl_3$) δ: 48.5.

2. Di(n-propyl)-aminomethylphosphine oxide, **2a**. To 19 g (0.075 mol) of **1a**, dissolved in 200 ml of n-propanol is added 4 g of Pd/C (5%) and the mixture hydrogenated at 20–25°C and normal pressure. After 76 h hydrogen uptake stopped. The catalyst is filtered and the filtrate evaporated on a rotavapor. The residue is kugelrohr distilled to give 9.3 g (76%) of **2a**, a colorless oil, b.p. 170°C/0.08 torr;

^{1}H-NMR ($CDCl_3$) δ: 1.0 (t, CH_3); 1.25 (s, NH_2); 1.5–1.8 (m, CH_2CH_2); 3.0 (d, J = 7, NCH_2P).
^{31}P-NMR ($CDCl_3$) δ: 48.33
2a · HBr, m.p. 176–181°C; ^{31}P-NMR (D_2O, pH = 6) δ: 53.27.

Di(n-butyl)-aminomethylphosphine oxide, **2b**, was obtained similarly from 18.3 g of **1b**, 200 ml of THF, 4 g of Pd/C (5%) at 20–25°C, normal pressure. In this case debenzylation was already complete after 3 h; yield 11.6 g (93.3%) of **2b**, a colorless oil, b.p. 170°C/0.04 torr.

^{1}H-NMR ($CDCl_3$) δ: 0.95 (t, CH_3); 1.3 (s, NH_2); 1.45 (m, CH_2); 1.6 (m, CH_2); 1.75 (m, CH_2); 3.05 (d, J = 7, NCH_2P.
^{31}P-NMR ($CDCl_3$) δ: 48.87.
2b · HBr, m.p. 93–95°C, ^{31}P-NMR (D_2O, pH = 7) δ: 53.92.

3. N-Ethoxycarbonylmethyl-aminomethyl-di(n-propyl)phosphine oxide, **3a**. To a solution of 9.14 g (56 mmol) of **2a** in 7 ml of ethanol is added with stirring 3.12 ml (28 mmol) of ethyl bromoacetate. An exothermic reaction ensues and the temperature increases to 50°C. The mixture is refluxed for one hour, then cooled to 20°C, 50 ml of diethyl ether added and stirred for another hour. The precipitated hydrobromide of **2a** (m.p. 176–181°C) is filtered and the filtrate evaporated on a rotavapor. Purification of the residue by thin layer distillation gives 5.1 g (73.1%) of **3a**, an oil, b.p. 125°C/0.05 torr.

^{1}H-NMR ($CDCl_3$) δ: 1.1 (t, CH_3); 1.3 (t, $OCCH_3$); 1.6–1.9 (m, CH_2CH_2); 2.25 (br. s, NH); 3.1 (d, J = 8, NCH_2P); 3.55 (s, NCH_2C); 4.25 (q, OCH_2). ^{31}P-NMR ($CDCl_3$) δ: 48.01.

N-Ethoxycarbonylmethyl-aminomethyl-di(n-butyl)phosphine oxide, **3b**, was prepared similarly from **2b** and ethyl bromoacetate. Yield of **3b**, 62.5%, b.p. 130°C/0.01 torr.

^{1}H-NMR ($CDCl_3$) δ: 0.95 (t, CH_3); 1.3 (t, $OCCH_3$); 1.45 (m, CH_2); 1.6 (m, CH_2); 1.75 (m, CH_2); 1.95 (br. s, NH); 3.1 (d, J = 8, NCH_2P); 3.5 (s, NCH_2C); 4.2 (q, OCH_2).
^{31}P-NMR ($CDCl_3$) δ: 48.22.

4. N-Hydroxycarbonylmethyl-aminomethyl-di(n-propyl)phosphine oxide, **4a**. A mixture of 3.37 g (13.5 mmol) of **3a** and 27 ml of HCl (20%) is refluxed for 5 h and then the clear solution evaporated on a rotavapor. The white, solid residue is suspended in acetone, filtered and dried to give 2.9 g (83.3%) of **4a · HCl**, a white solid, m.p. 190–192°C (dec.).

^{1}H-NMR (D_2O) δ: 1.05 (t, CH_3); 1.6 (m, CH_2); 2.05 (m, CCH_2P); 3.5 (d, J = 7, NCH_2P); 4.1 (s, NCH_2CO); 4.8 (s, NH, OH).
^{31}P-NMR (D_2O, pH = 1) δ: 52.34.

N-Hydroxycarbonylmethyl-aminomethyl-di(n-butyl)phosphine oxide, **4b**, was obtained similarly in 76.4% yield from **3b** and HCl. It was also isolated as the hydrochloride, **4b · HCl**, a white solid, m.p. 178–180°C (dec.).

^{1}H-NMR (D_2O) δ: 1.0 (t, CH_3); 1.4–1.7 (m, CH_2CH_2); 2.05 (m, PCH_2); 3.65 (d, J = 7, NCH_2P); 4.05 (s, NCH_2CO); 4.85 (s, NH, OH).
^{31}P-NMR (D_2O, pH = 1) δ: 53.10.

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REFERENCES

1. Part 103: L. Maier, *Phosphorus, Sulfur, and Silicon*, in print.
2. L. Maier, *Phosphorus, Sulfur, and Silicon*, **63**, 237 (1991).
3. L. A. Hamilton and P. S. Landis, in "Organic Phosphorus Compounds," eds. G. M. Kosolapoff and L. Maier, John Wiley & Sons, Inc., New York, N.Y., **4**, 463 (1972).