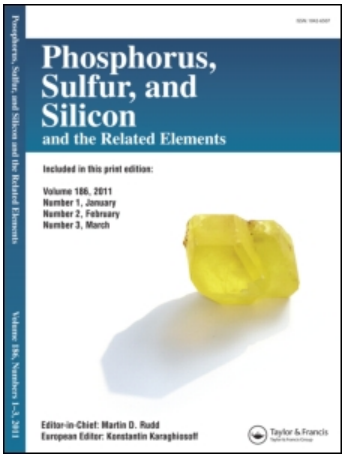

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF METHYL-BIS(AMINOMETHYL)PHOSPHINE OXIDE AND ITS PHTHALIMIDO DERIVATIVES

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To cite this Article Varbanov, S. , Tsvetkov, E. N. and Borisov, G.(1984) 'SYNTHESIS OF METHYL-BIS(AMINOMETHYL)PHOSPHINE OXIDE AND ITS PHTHALIMIDO DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 19: 3, 305 — 309
To link to this Article: DOI: 10.1080/03086648408077594
URL: http://dx.doi.org/10.1080/03086648408077594

Phosphorus and Sulfur, 1984, Vol. 19, pp. 305–309
0308-664X/84/1903–0305/$18.50/0

SYNTHESIS OF METHYL-BIS(AMINOMETHYL)PHOSPHINE OXIDE AND ITS PHTHALIMIDO DERIVATIVES

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(*Received December 15, 1983*)

The synthesis of methyl-bis(aminomethyl)phosphine oxide (Ia) is described starting from methyl-bis(chloromethyl)phosphine oxide (MBCPO) and using as an intermediate methyl-bis(phthalimidomethyl)phosphine oxide (II). The following substituted phthalimido derivatives have also been prepared: methyl-bis(4-nitrophthalimidomethyl)phosphine oxide (III), methyl-bis(4-aminophthalimidomethyl)phosphine oxide (IV), methyl-bis(4-benzamidophthalimidomethyl)phosphine oxide (V), methyl-bis(4-carboxy-phthalimidomethyl)phosphine oxide (VI) and its dicyclohexylammonium salt (VII). Methyl-bis(aminomethyl)-phosphine oxide (Ia) is isolated and characterized as a dihydrochloride (I).

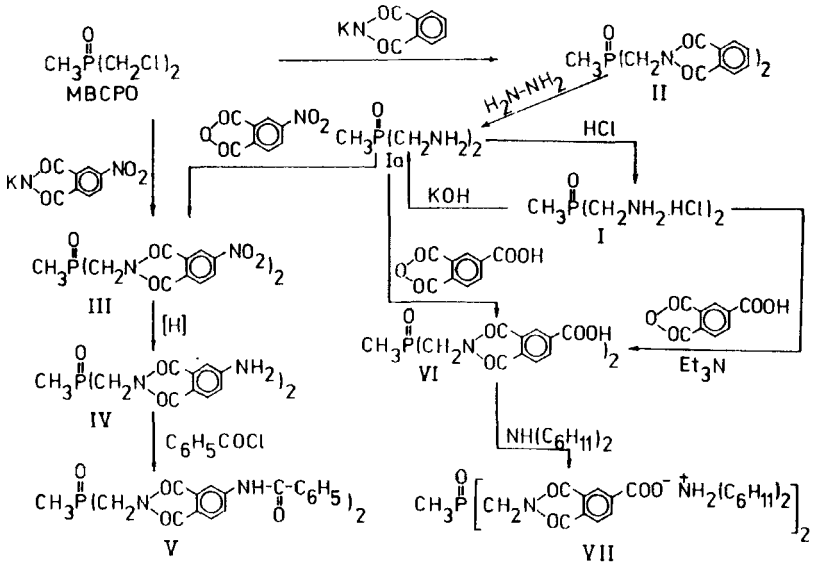
INTRODUCTION

The polyfunctional aminomethyl phosphine oxides and their derivatives, as for example the phthalimide ones, can be of interest as monomers for synthesizing phosphorus-containing polymers. Relatively few such compounds are known from the literature, i.e. tris(aminomethyl)phosphine oxide,[1] phenyl-bis(aminomethyl)phosphine oxide[2] and bis(aminomethyl)phosphinic acid.[3]

The present work, a continuation of our studies on the preparation of phosphorus-containing monomers from methyl-bis(chloromethyl)phosphine oxide,[4] describes the synthesis of methyl-bis(aminomethyl)phosphine oxide (Ia) and some of its substituted bis-phthalimido derivatives (Scheme 1, Table I).

RESULTS AND DISCUSSION

The methyl-bis(aminomethyl)phosphine oxide (Ia) is prepared by the Gabriel procedure from the comparatively accessible methyl-bis(chloromethyl)phosphine oxide (MBCPO). Refluxing this compound in anisol with potassium phthalimide leads almost quantitatively to methyl-bis(phthalimidomethyl)phosphine oxide (II). If dimethylformamide (DMFA) is used as a solvent under the same conditions (refluxing for 9 hrs) the yield of II decreases to about 70%. Introduction of potassium iodide (up to 20% of the stoichiometric requirement) does not lead to significantly higher yields in this case. Treatment of II with hydrazine hydrate affords the phosphine oxide Ia which was isolated as the dihydrochloride I.

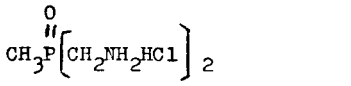
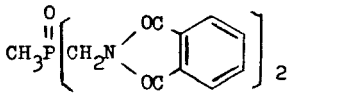
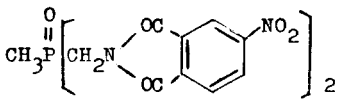
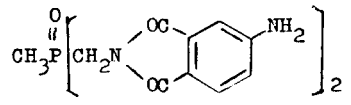
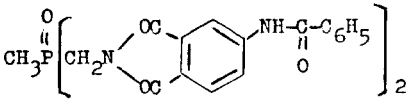
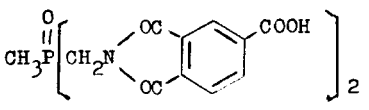
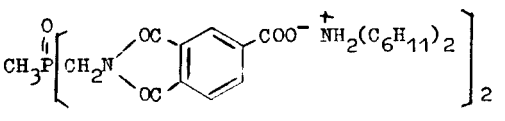


SCHEME 1

Methyl-bis(4-nitrophthalimidomethyl)phosphine oxide (III) was obtained from MBCPO via treatment with potassium 4-nitrophthalimide, but also from Ia and 4-nitrophthalic anhydride. The second approach is better since the yields are higher. Reduction of the nitro group with stannous chloride in hydrochloric acid affords the yellow methyl-bis(4-aminophthalimidomethyl)phosphine oxide (IV). This compound reacts positively with furfural indicating an NH_2 group bonded to an aromatic ring.[5] Benzoylation of IV with benzoyl chloride in dimethylacetamide at -5 to $-10°C$ affords methyl-bis(4-benzamidophthalimidomethyl)phosphine oxide (V). Methyl-bis(4-carboxyphthalimidomethyl)phosphine oxide (VI) was prepared in *m*-cresol at 160–170°C via the interaction between trimellitic anhydride and Ia obtained from I and the respective amount of potassium hydroxide in methanol. Instead of Ia the dihydrochloride I can be used directly adding, however, to the reaction mixture triethylamine. In this case the reaction was conducted in dimethylformamide by gradually increasing the temperature from 120 to 180°C. Compound VI synthesized by the two procedures was recrystallized from DMFA. The products however showed no definite melting point i.e. they melted in the interval between 170 and 230°C. Further increase in temperature brought about a hardening and then the products melted at 308–313°C. Very likely the imide cycles partially cleave forming carboxylic groups. A similar effect has been observed with compounds obtained from ethylenediamine and trimellitic anhydride.[6] The products were heated in diphenyl ether with the view to achieving complete imidization (cyclisation). We therefore carried out a similar treatment which resulted in compound VI melting within a definite temperature interval. Methyl-bis(4-carboxyphthalimidomethyl) phosphine oxide VI was converted into the respective dicyclohexylammonium salt VII.

TABLE I

Methyl-bis(aminomethyl)phosphine oxide and its phthalimido derivatives

No.	Compound	Yield %	M.P. °C	Molecular formula	Analyses			
					% N		% P	
					Calcd.	Found	Calcd.	Found
1	2	3	4	5	6	7	8	9
I		98	195–196.5	$C_3H_{13}Cl_2N_2OP$	14.4	14.3 14.4	15.9	15.5 15.4
II		97	270–271	$C_{13}H_{15}N_2O_5P$	7.3	7.4 7.4	8.1	8.1 8.2
III		92	259–261	$C_{19}H_{13}N_4O_9P$	11.9	11.5 11.6	6.6	6.6 6.6
IV		95	192–193	$C_{45}H_{61}N_4O_9P$	6.7	6.7 6.6	3.7	3.7 3.7
V		98	336–339	$C_{33}H_{25}N_4O_7P$	9.0	9.0 9.1	5.0	4.6 4.7
VI		87	308–313	$C_{21}H_{15}N_2O_9P$	6.0	5.4 5.6	6.6	6.5 6.4
VII		96	192–193	$C_{45}H_{61}N_4O_9P$	6.7	6.7 6.6	3.7	3.7 3.7

Methyl-bis(aminomethyl)phosphine oxide Ia is a colourless oil with an odour of an aliphatic amine. The remaining products are solid and their structures are confirmed by infrared spectra. The following absorption bands are observed: at 1165–1190 cm^{-1} for the phosphoryl group (P=O); at 1305–1315 cm^{-1} for the CH_3–P function; at 720–735 cm^{-1} for the imide ring as well at 1375–1380, 1720–1730 cm^{-1} and 1780 cm^{-1} for compounds II–VII. The infrared spectra of compounds I, III and IV show bands at 2800–3200 cm^{-1} due to a quaternary ammonium salt (CH_2—$\overset{+}{N}H_3$), at 1340–1350 cm^{-1} and 1540–1550 cm^{-1} characteristic for an Ar—NO_2 group and at 3200–3500 cm^{-1} characteristic for an Ar—NH_2. The infrared spectrum of compound V has bands at 1550 cm^{-1} and 1670 cm^{-1} corresponding to amide I and amide II.

EXPERIMENTAL

The melting points were determined on a Kofler apparatus. The infrared spectra were recorded on a UR-20 instrument using potassium bromide pellets. All syntheses were conducted under argon. The 4-nitrophthalic acid, trimellitic acid, potassium phthalimid, hydrazine hydrate (99.5%) and dicyclohexylamine were commercial products; MBCPO, 4-nitrophthalic and trimellitic anhydrides as well as 4-nitrophthalimide were obtained by known methods.[4,7,8] The dimethylformamide was treated subsequently with P_2O_5, K_2CO_3 and molecular sieves type 3A and distilled under vacuum at 100–120°C.

Methyl-bis(phthalimidomethyl)phosphine oxide (II)

Procedure A. The mixture of MBCPO (32.0 g, 0.20 mol) and potassium phthalimide (92.6 g, 0.50 mol) in anisol (200 ml) is refluxed with stirring for 8 hr. The solid product formed is filtered off, washed with acetone, water and again acetone to afford 74.0 g (97%) of material which was recrystallized from DMFA–ethanol (4 : 1).

Procedure B. The mixture of MBCPO (4.80 g, 30 mmol) and potassium phthalimide (14.2 g, 75 mmol) in DMFA (30 ml) is refluxed for 8 hrs. Water (50 ml) is added to the cooled reaction mixture which is then stirred and poured into 200 ml of water. The solid material is filtered off and washed with water and acetone to give 8.10 g (70%) of product which is recrystallized as described above.

Methyl-bis(aminomethyl)phosphine oxide dihydrochloride (I). Hydrazine hydrate (99.5%, 5.25 g, 104 mmol) dissolved in ethanol (50 ml) is added with stirring to the mixture of II (18.90 g, 52 mmol) in absolute ethanol (200 ml) and refluxed for 9 hrs. The reaction mixture is filtered after cooling, the filtrate taken to dryness under reduced pressure at a temperature not exceeding 50°C and the light-yellow oily residue dissolved in 150 ml of dry ethanol to which is added 36% hydrochloric acid (12 ml) diluted with ethanol (30 ml). The white crystalline product formed is filtered off, washed with absolute ethanol and dried to give 10.10 g (98%) of material which is recrystallized from aqueous ethanol.

Methyl-bis(4-nitrophthalimidomethyl)phosphine oxide (III)

Procedure A. Compound I (2.20 g, 11.3 mmol) is added to the solution of potassium hydroxide (1.27 g, 22.6 mmol) in dry methanol (40 ml). After stirring the potassium chloride formed is filtered off and the solvent removed by distillation to give Ia to which is added *m*-cresol (20 ml) and 4-nitrophthalic anhydride (4.36 g, 22.6 mmol). The reaction mixture is then heated at 160–170°C with stirring for 10 hrs the water formed being continuously distilled. After cooling the reaction mixture is poured into diethyl ether. The light brown product is filtered off and washed with diethyl ether to give 4.90 g (92%) of material which is recrystallized from DMFA–water (2 : 1) containing active carbon; the product obtained is a light-yellow powder.

Procedure B: (A) Preparation of potassium 4-nitrophthalimide. To the solution of 4-nitrophthalimide (14.40 g, 75 mmol) in *n*-propanol (600 ml) is added with stirring at a temperature not exceeding 30°C a solution of potassium hydroxide (4.2 g, 75 mmol) in 76% aqueous ethanol (50 ml). The reaction mixture is stirred for 30 min. The solid potassium 4-nitrophthalimide formed is filtered off and washed with a small

amount of *n*-propanol to give after drying at a temperature not higher than 100°C 14.10 g (87%) of substance.

(B) The mixture of MBCPO (3.20 g, 20 mmol) and potassium 4-nitrophthalimide (11.50 g, 50 mmol) in anisol (20 ml) is stirred under reflux for 7 hrs. After cooling the reaction mixture is diluted with acetone to afford a solid product which is filtered off, washed with water, 5% aqueous potassium carbonate and again with water and acetone to give 3.80 g (40%) of material which is recrystallized as described above.

Methyl-bis(4-aminophthalimidomethyl)phosphine oxide (IV). Stannous chloride (5.41 g, 24 mmol) is dissolved in hydrochloric acid, specific gravity 1.16 (16 ml) under heating to 60°C. At room temperature III (1.41 g, 3.0 mmol) is added to this solution and the resulting reaction mixture is stirred and cooled to maintain the temperature at 60°C. The solid phase dissolves under these conditions. The light-brown transparent solution is concentrated to half the initial volume and poured onto 50 ml of water cooled to 5–10°C. After about 30 min. a solid precipitate is formed which is then filtered off and washed with water (until reaction for chloride ions is negative) and then ethanol and dried to afford 1.18 g (95%) of products which is recrystallized from a DMFA–water mixture.

Methyl-bis(4-benzamidophthalimidomethyl)phosphine oxide (V). Benzoyl chloride (0.49 g, 3.5 mmol) is added slowly −5 to −10°C to a solution of IV (0.66 g, 1.6 mmol) in dimethylacetamide (30 ml). The reaction mixture is stirred at −5°C to −10°C for 15 min then at room temperature for another 60 min. The resulting red solution is poured with stirring into water (100 ml) to give a yellow precipitate which after filtration is washed with water and dried to give 0.97 g (98%) of material recrystallized from a DMFA–water mixture.

Methyl-bis(4-carboxyphthalimidomethyl)phosphine oxide (VI)

Procedure A. To a solution of potassium hydroxide (1.00 g, 17.8 mmol) in dry methanol (35 ml) is added I (1.73 g, 8.9 mmol). The formed potassium chloride is filtered off and the methanol distilled. To the residue consisting of Ia is added trimellitic anhydride (3.42 g, 17.8 mmol) and *m*-cresol (20 ml). The reaction mixture is stirred at room temperature for 30 min. and then at 160–170°C for 7 hrs. After cooling the mixture is poured into methanol to give a white precipitate which is filtered off and washed with methanol and then dried to give 3.6 g (87%) of material. This is recrystallized from DMFA, refluxed in diphenyl ether for 1 hr, filtered and washed with benzene and ether.

Procedure B. The mixture of I (3.9 g, 20 mmol), trimellitic anhydride (7.68 g, 40 mmol) and triethylamine (11.10 ml, 80 mmol) in DMFA (28 ml) is stirred for 4 hrs the temperature being gradually brought from 120°C to 180°C. At room temperature the reaction mixture is poured onto 5% hydrochloric acid (150 ml) to give a yellow precipitate. This is filtered, washed with water, methylethyl ketone and dried at 110–120°C to give 8.20 g (88%) of product which is recrystallized and worked up as described in Procedure A.

Dicyclohexylammonium salt of VI (VII). To the solution of VI (0.30 g, 0.64 mmol) in dimethylacetamide (6 ml) is added at room temperature a solution of dicyclohexylamine (0.40 g, 20 mmol) in dry methanol (3.0 ml). The colourless transparent solution is stirred for 30 min. and poured into diethyl ether (20 ml) to give a white precipitate which after filtration is washed with diethyl ether to afford a white precipitate 0.51 g (96%) which is recrystallized from an ethanol–diethyl ether mixture.

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