Synthesis of asymmetric *P,P*-dialkyl-*P',P'*-diphenylethylenediphosphine dioxides

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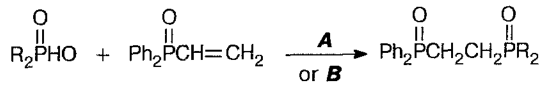
Asymmetric *P,P*-dialkyl-*P',P'*-diphenylethylenediphosphine dioxides were synthesized by the addition of dialkylphosphinous acids to diphenylvinylphosphine oxide in toluene without a catalyst and in DMSO in the presence of concentrated aqueous alkali. The method for isolating dipropyl- and dibutylphosphinous acids obtained by reactions of diethylphosphite with the corresponding alkylmagnesium bromides was improved.

Key words: ethylenediphosphine dioxides; diphenylvinylphosphine oxide; dialkylphosphinous acids; PH-acids; PH-addition.

In order to study the effect of substituents at the P atom on the complexing ability of ethylenediphosphine dioxides, we synthesized ligands of the type $Ph_2P(O)CH_2CH_2P(O)R_2$ by adding dialkylphosphinous acids (**1**) to diphenylvinylphosphine oxide (**2**). The reaction of diethylphosphinous acid (**1b**) with oxide **2** in the presence of Na under drastic conditions (140 °C, 4 h, xylene) has been reported.[1] The low yield (43 %) of the target product may result from disproportionation of acid **1** at the temperature of the synthesis.[2]



$$R_2\overset{O}{\overset{\|}{P}}HO + Ph_2\overset{O}{\overset{\|}{P}}CH{=}CH_2 \xrightarrow[\text{or } B]{A} Ph_2\overset{O}{\overset{\|}{P}}CH_2CH_2\overset{O}{\overset{\|}{P}}R_2$$

1a—d **2** **3a—d**

R = Me (**a**), Et (**b**), Pr (**c**), Bu (**d**)

In fact, our data demonstrate that better results are obtained by heating the above reagents in toluene at 100 °C without a catalyst, by analogy with the addition of diphenylphosphinous acid[3] (method *A*). Since the PH-acidity of dialkylphosphinous acids (p*K* 27—28)[4] is lower than that of diphenylphosphinous acid (p*K* 20.7),[5] in this case the reaction requires somewhat more time (≥ 3 h, ^{31}P NMR spectroscopic monitoring). However, disproportionation of acid **1b** occurs even at 100 °C. Another, more promising method involves the addition of phosphinous acids **1** under relatively mild conditions (55—60 °C) in DMSO in the presence of concentrated aqueous alkali, similarly to the reaction of diaryl- and dialkylphosphinous acids with propen-1-yldiphenylphosphine oxide (method *B*) reported previously.[6,7] Using this method, phosphinous acids **1** are transformed to the corresponding phosphinite anions,[8,9] which readily add at the double bond. Both methods (*A* and *B*) make it possible to synthesize the target dioxides **3a—d** in 60—70 % yields.

The starting phosphinous acids **1** (Table 1) were obtained by various methods. Dimethylphosphinous acid (**1a**) was synthesized by alkaline cleavage of tetramethyldiphosphine disulfide by a reported procedure.[11] Acids **1b—d** were obtained from diethyl phosphite and the corresponding alkylmagnesium bromides, but they were isolated from the reaction mixtures using different methods. To isolate the easily soluble acid **1b**, the reaction mixture was worked-up with saturated K_2CO_3 and the product was extracted with ethanol according to

Table 1. Yields, constants, and parameters of ^{31}P NMR spectra of dialkylphosphinous acids R_2PHO (**1a—d**)

Compound	R	Yield (%)	B.p./°C (*p*/Torr)	^{31}P NMR Solvent	δ	$^1J_{P,H}$/Hz
1a	Me	59	50—52 (1)[2,11]	C_6H_6	17.2	454
1b	Et	52	79—80 (3)[2,14]	H_2O	49.5	456
1c	Pr	60	85—87 (2)[14]	$CDCl_3$	34.3	452
1d*	Bu	71	92—94 (1)[15]	$CHCl_3$	36.2	448

* M.p. 52—54 °C

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† Deceased in 1994.

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Table 2. Yields, constants, and parameters of ^{31}P NMR spectra (in EtOH) of ethylenediphosphine dioxides **3a—d**

Compound	R	Method of synthesis	Yield[a] (%)	B.p./°C (solvent)	^{31}P NMR, δ		
					Ph_2P=O	R_2P=O	$J_{P,H}$/Hz
3a	Me[b]	*A* *B*	72 68	152—153[c] (MeCOOEt)	36.8	50.5	50.0
3b	Et[b]	*A* *B*	62 60	129.5—130.5[d,e] (MeCOOEt)	34.2	55.1	47.2
3c	Pr[b]	*A* *B*	70 72	170—171[f] (MeCOOEt—MeCN)	33.9	51.6	46.7
3d	Bu	*A* *B*	59 70	152—154[g] (MeCOOEt)	36.8	55.1	42.6

[a] The yields are given with respect to analytically pure compounds. [b] The corresponding compounds are hygroscopic. [c] Found (%): C, 62.3; H, 6.6; P, 20.0. $C_{16}H_{20}O_2P_2$. Calculated (%): C, 62.7; H, 6.6; P, 20.0. [d] Forms a solvate with the solvent; the m.p. of the sample dried for 3 h at 110 °C (1 Torr) is given. [e] *Cf.* Ref. 1. [f] Found (%): C, 66.6; H, 8.0; P, 16.6. $C_{20}H_{28}O_2P_2$. Calculated (%): C, 66.3; H, 7.8; P, 17.1. [g] *Cf.* Ref. 10.

Hays' method.[2] Water-insoluble phosphinous acids were usually isolated by acid treatment of the reaction mixture followed by extraction with chloroform. To date, this procedure has only been applied to type **1** crystalline acids with R = C_6H_{13}, C_8H_{17},[12] and $PhCH_2$,[13] whose purification does not require distillation. Low-melting acids **1c,d** could not be obtained using this method, probably due to disproportionation of acids **1** during distillation and because of the presence of acidic admixtures in the reaction mixture that catalyze this process and decrease the temperature at which the process starts.[2] In the present work, after acids **1c,d** were synthesized, the reaction mixture was decomposed with a dilute acid and then with ammonium chloride; during the procedure, the medium was maintained alkaline (pH ≥ 6.5). This approach allowed us to isolate acids **1c,d** thus avoiding their disproportionation during distillation.

Experimental

All operations with P^{III} compounds were performed under dry argon. Melting points were measured using shortened Anschütz thermometers in sealed capillaries. ^{31}P NMR spectra were recorded on a Bruker AC-200 spectrometer relative to 85 % H_3PO_4 as the external standard. The yields, main constants, and parameters of the ^{31}P NMR spectra for dialkylphosphinous acids **1a—d** are presented in Table 1. The yields, main constants, elemental analysis data, and parameters of the ^{31}P NMR spectra for dioxides **3a—d** are shown in Table 2.

Dipropylphosphinous acid (1c). Diethylphosphite (27.6 g, 0.2 mol) was added dropwise with stirring at 20—30 °C over 50 min to a solution of a Grignard reagent obtained from Mg (19.4 g, 0.8 mol) and PrBr (98.4 g, 0.8 mol) by refluxing for 2 h in dry ether (200 mL). The mixture was refluxed for 2 h, dilute H_2SO_4 (1 : 1) (100 mL) was added dropwise at 20—25 °C, then saturated NH_4Cl was added until the precipitate dissolved completely (the pH of the mixture was maintained at ≥ 6.5; if the mixture became acidic, it was neutralized with dry $NaHCO_3$). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2×100 mL). The combined extract was washed with saturated Na_2CO_3, dried with Na_2SO_4, and concentrated *in vacuo* (bath temperature ≤80 °C). The residue was distilled *in vacuo* to give 16.0 g of acid **1c** (see Table 1).

Dibutylphosphinous acid (1d) was synthesized similarly to acid **1c** from Mg (19.4 g, 0.8 mol), BuBr (110.4 g, 0.8 mol), and diethylphosphite (27.6 g, 0.2 mol); yield 23.0 g (see Table 1).

***P,P*-Dialkyl-*P',P'*-diphenylethylenediphosphine dioxides (3a—d).** *A.* A mixture of dialkylphosphinous acid **1** (65 mmol) and oxide **2** (65 mmol) (see Ref. 16) in dry toluene (25 mL) was heated for 3.5 h with stirring at 100 °C. The solution was concentrated *in vacuo* and the precipitate was twice recrystallized (see Table 2).

B. A mixture of dialkylphosphinous acid **1** (6 mmol), oxide **2** (6 mmol), 56 % aqueous KOH (6 mmol), and DMSO (5 mL) was heated at 55—60 °C for 3 h with stirring. Water (10 mL) was added, and the mixture was extracted with $CHCl_3$ (3×15 mL). The extract was washed with 4 % HCl and saturated $NaHCO_3$ and then concentrated *in vacuo*. The residue was kept for 15—20 min at 100—120 °C (1 Torr) and then twice recrystallized (see Table 2).

References

1. M. I. Kabachnik, T. Ya. Medved', I. B. Goryunova, L. I. Tikhonova, and E. I. Matrosov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1974, 2290 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1974, **23**, No. 10 (Engl. Transl.)].
2. H. R. Hays, *J. Org. Chem.*, 1968, **33**, 3690.
3. M. I. Kabachnik, T. Ya. Medved', Yu. M. Polikarpov, and K. S. Yudina, *Izv. Akad. Nauk SSSR, OKhN*, 1962, 1584 (in Russian).
4. E. N. Tsvetkov, M. I. Terekhova, E. S. Petrov, R. A. Malevannaya, S. P. Mesyats, A. I. Shatenshtein, and M. I.

Kabachnik, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1978, 1981 [*Bull. Acad. Sci. USSR, Div. Chem. Sci*, 1978, **27**, 1743 (Engl. Transl.)].

5. E. S. Petrov, M. I. Terekhova, I. G. Malakhova, E. N. Tsvetkov, A. I. Shatenshtein, and M. I. Kabachnik, *Zh. Obshch. Khim.*, 1979, **49**, 2410 [*J. Gen. Chem. USSR*, 1979, **49** (Engl. Transl.)].
6. A. V. Kharitonov, A. E. Antoshin, A. N. Pushin, and E. N. Tsvetkov, *Zh. Obshch. Khim.*, 1988, **58**, 1021 [*J. Gen. Chem. USSR*, 1988, **58** (Engl. Transl.)].
7. A. E. Antoshin, V. I. Evreinov, A. V. Kharitonov, A. N. Pushin, A. N. Yarkevich, Z. V. Safronova, and E. N. Tsvetkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 1860 [*Bull. Acad. Sci. USSR, Div. Chem.*, 1991, **40**, 1647 (Engl. Transl.)].
8. E. N. Tsvetkov, N. A. Bondarenko, I. G. Malakhova, and M. I. Kabachnik, *Zh. Obshch. Khim.*, 1985, **55**, 11 [*J. Gen. Chem. USSR*, 1985, **55** (Engl. Transl.)].
9. E. N. Tsvetkov, N. A. Bondarenko, I. G. Malakhova, and M. I. Kabachnik, *Synthesis*, 1986, 198.
10. J. Gloede, *J. Prakt. Chem.*, 1972, **314**, 281.
11. R. A. Malevannaya, E. N. Tsvetkov, and M. I. Kabachnik, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1976, 952 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1976, **25**, No. 4 (Engl. Transl.)].
12. R. H. Williams and L. A. Hamilton, *J. Am. Chem. Soc.*, 1952, **74**, 5418.
13. R. C. Miller, J. S. Bradley, and L. A. Hamilton, *J. Am. Chem. Soc.*, **78**, 5299.
14. M. I. Kabachnik and E. N. Tsvetkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1963, 1227 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1963, No. 5 (Engl. Transl.)].
15. M. Grayson, C E. Farley, and C. A. Streuli, *Tetrahedron*, **23**, 1965.
16. N. A. Bondarenko and E. N. Tsvetkov, *Zh. Obshch. Khim.*, 1989, **59**, 1533 [*J. Gen. Chem. USSR*, 1989, **59** (Engl. Transl.)].

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