Synthesis of Diisopropyl 1-Nitroalkanephosphonates from Diisopropyl 1-Oxoalkanephosphonates

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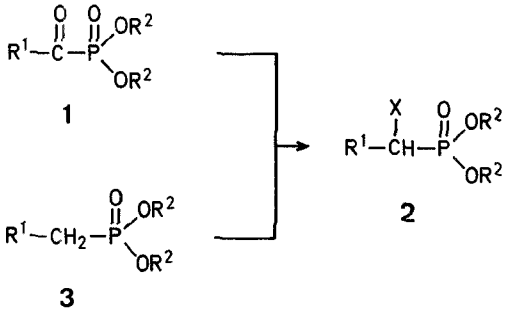
Functional derivatives of alkanephosphonates are used in the PO-activated olefin syntheses[1]. Also some compounds of this type are biologically active[2]. The accessibility of dialkyl 1-oxoalkanephosphonates **1**[3] offers the possibility of the application of these compounds as starting materials for the synthesis of functional derivatives of dialkyl alkanephosphonates **2**. Not many direct examples of functionalization of dialkyl alkanephosphonates **3** are known[4,5].



Continuing the studies on the chemistry of dialkyl 1-oxoalkanephosphonates[6], we were concerned with the oxidation of diisopropyl 1-hydroxyiminoalkanephosphonates **6** to diisopropyl 1-nitroalkanephosphonates **7** and the results obtained are presented in this paper.

Among the dialkyl esters of 1-oxoalkanephosphonic acids **1** we chose the diisopropyl esters **5**, which were prepared by the reaction of acid chlorides **4** with triisopropyl phosphite. Oximation of ketophosphonates **5** afforded crystalline diisopropyl 1-hydroxyiminoalkanephosphonates **6** (Table 1).

There are at least three reagents which oxidize oximes to nitro compounds described in the literature[7–9]. We oxidized the phosphonooximes **6** with *m*-chloroperbenzoic acid in dichloromethane to 1-nitroalkanephosphonates **7** in good yields (Table 2).

Table 1. Diisopropyl 1-Hydroxyiminoalkanephosphonates **6** prepared

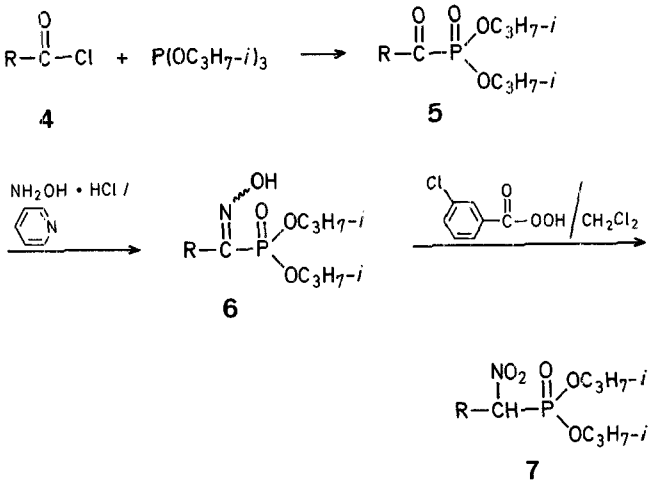
Product No.	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
6a	68	88–89° (cyclohexane)	$C_8H_{18}NO_4P$ (223.2)	3160, 3060, 2995, 1250, 1190, 1000, 775	1.77 [dd, 12H, $J_{H,H}$ = 7 Hz, $(CH_3)_2$—CH]; 2.39 (d, 3H, $J_{P,H}$ = 11 Hz, CH_3); 5.08 [dq, 2H, $J_{H,H}$ = 7 Hz, $J_{P,H}$ = 14 Hz, $(CH_3)_2$—CH]; 11.5 (s, 1H, NOH)
6b	65	50–52° (hexane-cyclohexane)	$C_9H_{20}NO_4P$ (237.2)	3165, 3050, 2995, 1235, 1175, 970, 775	1.45 (t, 3H, $J_{H,H}$ = 7 Hz, CH_3—CH_2); 1.64 [dq, 12H, $J_{H,H}$ = 7 Hz, $J_{P,H}$ = 3 Hz, $(CH_3)_2$—CH]; 2.85 (dq, 2H, $J_{H,H}$ = 7 Hz, $J_{P,H}$ = 13 Hz, CH_3—CH_2); 5.07 [dq, 2H, $J_{H,H}$ = 7 Hz, $J_{P,H}$ = 14 Hz, $(CH_3)_2$—CH]; 11.4 (s, 1H, NOH)
6c	70	95–96° (CCl_4-hexane)	$C_{14}H_{22}NO_4P$ (299.3)	3140, 3010, 2860, 1215, 1025, 970	1.49 [dd, 12H, $J_{H,H}$ = 7 Hz, $J_{P,H}$ = 3 Hz, $(CH_3)_2$—CH]; 4.23 (d, 2H, $J_{P,H}$ = 11 Hz, C_6H_5—CH_2); 4.95 [dq, 2H, $J_{P,H}$ = 14 Hz, $(CH_3)_2$—CH]; 7.3–7.8 (m, 5H_{arom}); 11.6 (s, 1H, NOH)

[a] Satisfactory microanalyses obtained: N ±0.15, P ±0.12.

Table 2. Diisopropyl 1-Nitroalkanephosphonates **7** prepared

Product No	Yield [%]	b.p. [°C]/ torr	n_D^{20}	Molecular formula[a]	I.R. (film) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
7a	50	81–83°/0.9	1.4350	$C_8H_{18}NO_5P$ (239.2)	3000, 1555, 1385, 1350, 1265, 1105, 990	1.62 [dd, 12H, $J_{H,H}$ = 6 Hz, $(CH_3)_2$—CH]; 1.98 (dd, 3H, $J_{H,H}$ = 7 Hz, $J_{P,H}$ = 16 Hz, CH_3—CH); 4.7–5.4 [m, 3H, $(CH_3)_2$—CH + CH—NO_2]
7b	65	98–101°/1	1.4342	$C_9H_{20}HO_5P$ (253.2)	3000, 1555, 1387, 1375, 1265, 1105, 990	1.3 (t, 3H, $J_{H,H}$ = 7 Hz, CH_3—CH_2); 1.6 [dd, 12H, $J_{H,H}$ = 6 Hz, $J_{P,H}$ = 3 Hz, $(CH_3)_2$—CH]; 2.0–2.9 (m, 2H, CH_3—CH_2); 4.6–5.2 [m, $(CH_3)_2$—CH + CH—NO_2]
7c	60	143–147°/1[b]		$C_{14}H_{22}NO_5P$ (315.3)	3000, 1555, 1377, 1355, 1265, 1105, 990	1.56 [d, 12H, $J_{H,H}$ = 6 Hz, $(CH_3)_2$—CH]; 3.3–4.0 (m, 2H, C_6H_5—CH_2); 4.6–5.6 [m, 3H, $(CH_3)_2$—CH + CH—NO_2]; 7.1–7.8 (m, 5H_{arom})

[a] Satisfactory microanalyses obtained: N ±0.16, P ±0.13.
[b] Product solidifies on cooling, m.p. 39–41°C (hexane).



4–7	a	b	c
R	CH_3	C_2H_5	$C_6H_5CH_2$

Attempts to use trifluoroperacetic acid instead of *m*-chloroperbenzoic acid led to nitrophosphonates containing numerous unidentified side products. In this case it was neccessary to use column chromatography to purify the products.

Some examples of dialkyl 1-nitroalkanephosphonates are known. Thus, these compounds were obtained by oxidative nitration of 2-alkoxyalkenephosphonates[10], by oxidation of dialkyl 1-aminoalkanephosphonates[11], by nitration of phosphonocarbanions[4] and by phosphonylation of halonitroalkanes[12]. Our procedure provides a new and convenient route to diisopropyl 1-nitroalkanephosphonates **7**.

I.R. spectra were obtained on a Perkin-Elmer 527 spectrophotometer. ^{1}H-N.M.R. spectra were measured using 100 MHz Tesla BS 497 spectrometer. Column chromatography was performed on silica gel 200–300 mesh, using chloroform/ethyl acetate (9:1, v/v) as eluent.

Diisopropyl 1-Hydroxyiminoalkanephosphonates 6; General Procedure:

Freshly prepared triisopropyl phosphite (37.5 g, 0.18 mol) is added dropwise over 10 min under nitrogen to the hot acyl chloride **4** (0.18 mol; for **4a** and **4b** the reaction is run at reflux temperature, for **4c** at 80°C). The reaction mixture is heated for 10 min more and the volatile components are removed under reduced pressure yielding oily diisopropyl 1-oxoalkanephosphonates **5**. The crude ketophosphonate was added to a suspension of hydroxylamine hydrochloride (15.3 g, 0.22 mol) in dry pyridine (25 ml, 0.3 mol) and absolute ethanol (50 ml) with stirring. The temperature of the reaction mixture is raised to about 45°C. Then the reaction mixture is stirred for 12 h at room temperature. The ethanol is removed under reduced pressure and the residue is dissolved in dichloromethane (150 ml). The solution is extracted with 3 normal aqueous hydrochloric acid (20 ml), water (20 ml), saturated aqueous sodium hydrogen carbo-

nate (20 ml), water 2 × 20 ml, brine (2 × 20 ml) and dried with magnesium sulphate. The solvent is removed and the residue is crystallized (Table 1).

Diisopropyl 1-Nitroalkanephosphonates 7; General Procedure:
To a solution of *m*-chloroperbenzoic acid (80%, 6.45 g, 0.03 mol) in a minimum volume of dichloromethane (~ 90 ml) is added diisopropyl 1-hydroxyimino-alkanephosphonate **6** (0.03 mol) at room temperature. The reaction mixture is stirred and the progress of reaction is monitored by T.L.C. (silica gel, chloroform-ethyl acetate, iodine). After about 72 h the oximinophosphonates have disappeared. The mixture is extracted with saturated aqueous sodium hydrogen carbonate containing sodium sulphite (2 × 50 ml), water (2 × 50 ml), brine (50 ml), and dried with sodium sulphate. The solvent is removed and the residue is distilled under reduced pressure to give pure diisopropyl 1-nitroalkanephosphonates **7** (Table 2).

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