Preparation of Dimethyl (1-Formylalkyl)phosphonates *via* Singlet Oxygen Adducts

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The nitro group of dimethyl (1-nitromethylalkyl)phosphonates is conveniently converted into a formyl group by reaction with singlet oxygen to give dimethyl (1-formylalkyl)phosphonates. (1-Formylbutyl)diphenylphosphine oxide is prepared by the same reaction.

The conversion of nitroalkanes into carbonyl compounds is a synthetically useful functional group interconversion. The reaction is usually carried out under strongly acidic,[1] basic oxidative,[2–8] neutral oxidative,[9] or neutral reductive conditions.[7,10–12] Surprisingly, our numerous attempts to effect the analogous conversion of organophosphorus compounds having a *P*-(2-nitroalkyl) group under various conditions were unsuccessful. However, we then found that oxidation with ozone conveniently converts [1-(nitromethyl)alkyl]diphenylphosphine oxides into (1-formylalkyl)diphenylphosphine oxides;[13] however, overoxidation is problematic and does not allow for efficient scale-up.

Phosphoric esters are widely known to excert a great variety of vital functions. Some phosphonates having a C-P bond, formally being prepared by replacing the O-atom of a P-O-C linkage of phosphoric esters by the isoelectronic CH_2 group, are also naturally occuring, and their metabolism has been investigated.[14] Phosphonic acid derivatives such as (−)-(1*R*, 2*S*)-1,2-epoxypropylphosphonic acid (phosphonomycin) and dimethyl 1-hydroxy-2,2,2-trichloroethylphosphonate (Dipterex) are active substances as antibiotics and pesticides[15,16] and are therefore of practical importance.

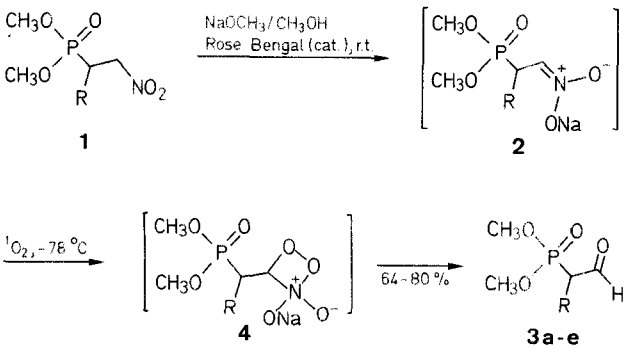
Table. Compounds **3a–e** Prepared

Product	R	Yield[a] (%)	b.p. (°C/torr) or m.p. (°C)	Molecular Formula b.p. (°C/torr) or m.p. (°C) reported[20]	MS *m/e* (M^+)	IR (Film or KBr) $\nu_{C=O}$ (cm^{-1})	^{1}H-NMR ($CDCl_3$) δ, *J* (Hz)
3a	CH_3	80	63/0.2	74/0.1	166	1750, 1670	1.0–1.8 (m, 3H); 2.5–3.4 (m, 1H); 3.69 (d, 6H, J_{HP} = 12); 9.65 (d, 1H, J_{HH} = 3)
3b	C_2H_5	90	70/0.2	75/0.1	180	1740, 1660	0.8–1.4 (m, 3H); 1.6–2.5 (m, 2H); 2.6–3.3 (m, 1H); 3.70 (d, 6H, J_{HP} = 12); 9.60 (d, 1H, J_{HH} = 3)
3c	*n*-C_3H_7	70	76/0.15	$C_7H_{15}O_4P$[b] (194.2)	194	1730, 1650	0.6–1.1 (m, 3H); 1.1–2.2 (m, 4H); 2.6–3.3 (m, 1H); 3.75 (d, 6H, J_{HP} = 12); 9.65 (d, 1H, J_{HH} = 3)
3d	*i*-C_3H_7	73	81/0.1	80/0.1	194	1730, 1660	1.05, 1.10 (2d, 6H, J_{HH} = 6); 2.0–2.6 (m, 1H); 2.8–3.2 (m, 1H); 3.70 (d, 6H, J_{HP} = 12); 9.50 (d, J_{HH} = 3)
3e	C_6H_5	64	106–108	106–108	228	1720, 1670	3.60 (d, 6H, J_{HP} = 12); 3.4–3.8 (m, 1H); 7.1–7.5 (m, 5H); 9.6–9.8 (m, 1H)

[a] Yield of product isolated by distillation or recrystallization.
[b] calc. C 43.30 H 7.79 P 15.95
found 43.02 7.54 15.73

Aldehydes can be converted into various types of useful compounds by reduction, oxidation, and addition or substitution reactions.[17] Therefore, formyl derivatives of alkylphosphonic esters are also valuable intermediates in organophosphorus chemistry. This report describes the synthetic potential of singlet oxygen in effecting the conversion of 1-(nitromethyl)alkylphosphonic esters into 1-formylalkylphosphonic esters.

Dimethyl 1-(nitromethyl)alkylphosphonates **(1)** are prepared by the Michael addition of dimethyl phosphonate to 1-nitro-1-alkenes (1:1 mol ratio) in the presence of triethylamine as catalyst at 40 °C or in the presence of excess dimethyl phosphonate without basic catalyst at 90 °C.[18] Phosphonates **1** are treated with sodium methoxide in methanol to give the nitronate **(2)**. Singlet oxygen is known to act as a 2π component towards olefins or dienes to afford [2 + 2]- or [2 + 4]cycloadducts.[19] The sensitizer, Rose Bengal, was added to a methanolic solution of **1**, followed by introduction of molecular oxygen and then irradiation with a tungsten lamp to effect reaction of $^1O_2$ with the nitronate **2**. Product analysis by MS, IR, and ^{1}H-NMR spectrometry reveals that dimethyl 1-formylalkylphosphonates **(3)** are obtained. The reaction is also applicable to phosphine oxides. Thus, (1-formylbutyl)diphenylphosphine oxide is prepared in 97% yield from 1-(nitromethyl)butyldiphenylphosphine oxide by treatment with singlet oxygen at −78 °C. The reaction seems to proceed as follows:



Temperature dependence of the yield is observed. When the reaction of **1a** with singlet oxygen is carried out in methanol for 30 min at 10 °C, 0 °C, and −78 °C the conversion is 50, 60 or 100%, respectively. The increment of the conversion yield at lower temperature should be attributable to increasing stability of the intermediate dioxazetidines **4** and/or to increasing solubility of oxygen. Any decrease of product yield on scale-up is not observed.

Dimethyl 1-Formylethylphosphonate (3a); Typical Procedure:
A solution of dimethyl 1-(nitromethyl)ethylphosphonate **1a** (1.19 g, 6.0 mmol), sodium methoxide (0.65 g, 12 mmol), and Rose Bengal (0.006 g) in anhydrous MeOH (30 mL) is stirred for 10 min at room temperature. Oxygen is passed through the solution and the mixture is cooled at −78 °C and irradiated with tungsten lamps (2 × 300 W). The reaction is monitored by a gas buret. Then, the solvent is removed *in vacuo* (rotary evaporator) and the residue is taken up into $CHCl_3$ (90 mL). This solution is washed with water (3 × 25 mL), and dried (Na_2SO_4). Evaporation of the solvent followed by distillation affords product **3a**; yield: 0.80 g (80%); b.p. 63 °C/0.2 Torr (Lit.[20] b.p. 74 °C/0.1 Torr).

MS: *m/e* = 166 (M^+).

When a mixture of **1a** (0.21 g), sodium methoxide (0.08 g), and Rose Bengal (0.001 g) in methanol under oxygen atmosphere is irradiated for 30 min at 0 °C product **3a** is obtained in only 60% conversion yield.

(1-Formylbutyl)diphenylphosphine Oxide:
1-(Nitromethyl)butyldiphenylphosphine oxide (0.32 g, 1.0 mmol), sodium methoxide (0.11 g, 2.0 mmol), and Rose Bengal (0.001 g) in MeOH (5 mL). Oxygen is passed through the solution at −78 °C and the mixture is irradiated with tungsten lamps (2 × 300 W). The reaction is monitored by a gas buret until the stoichiometric amount of oxygen has been consumed. The solvent is removed (rotary evaporator), the residue is taken up in $CHCl_3$ (30 mL), the solution is washed with water (5 × 3 mL), dried (Na_2SO_4), and evaporated. The residue is recrystallized from CCl_4/cyclohexane; yield: 0.28 g (97%); m.p. 148–149 °C.

$C_{17}H_{19}O_2P$ (286.3) calc. C 71.32 H 6.69
found 71.09 6.63

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