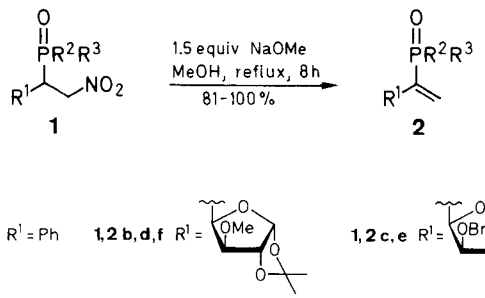
Novel Preparation of Vinylphosphonates, Vinylphosphinates, and Vinylphosphine Oxides via β-Elimination of Nitrous Acid

Mitsuji Yamashita,* Yoshinori Tamada, Akihito Iida, Tatsuo Oshikawa
Department of Applied Chemistry, Faculty of Engineering, Shizuoka University, Hamamatsu 432, Japan

Base treatment of 2-dimethoxyphosphinyl-, 2-methoxyphenylphosphinyl- and 2-diphenylphosphinyl-1-nitroethane derivatives results in β-elimination of nitrous acid to afford the corresponding vinyl derivatives in excellent yield. This is a useful method for the preparation of 5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-, 5,6-dideoxy-5-*C*-(methoxyphenylphosphinyl)-, and 5,6-dideoxy-5-*C*-(diphenylphosphinyl)-*xylo*-hexo-5-enofuranose derivatives as well as 5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-*xylo*-hexofuranose.

The nitro group enhances the activity of C,C double bonds towards the addition of phosphorus derivatives, affording C–P bonded products by polarization of the double bond. The conversion of a nitromethyl group thus prepared into the corresponding formyl group is an important synthetic transformation for the preparation of phosphorus derivatives. There are a number of reported procedures to this reaction, however, many are limited in the substrates that can be employed, and the basic oxidative ozone and the singlet oxygen method are the only successful general methods.[1,2]

Vinyl derivatives of phosphorus compounds such as propenylphosphonates, are important intermediates in the synthesis of antibiotics. For example the preparation of fosfomycin via a stereospecific epoxidation of an unsaturated phosphonate.[3] Vinylphosphonates are prepared by Wittig reaction of acylphosphonates with methylenetriphenylphosphorane, dehydrohalogenation of 2-haloethylphosphonates, and dehydration of α-hydroxyalkylphosphonates.[4-6] Furthermore, unsaturated sugars are important materials, related to biologically active substances such as angustomycin A;[7] therefore, preparation of vinyl derivatives of phosphorus compounds containing a sugar group is of much interest. This communication examines a novel transformation of 2-dimethoxyphosphinyl-, 2-methoxyphenylphosphinyl-, and 2-diphenylphosphinyl-1-nitroethane derivatives containing a sugar moiety into the corresponding vinylphosphonate, vinylphosphinate, and vinyl phosphine oxide derivatives, respectively, via novel β-elimination of nitrous acid.

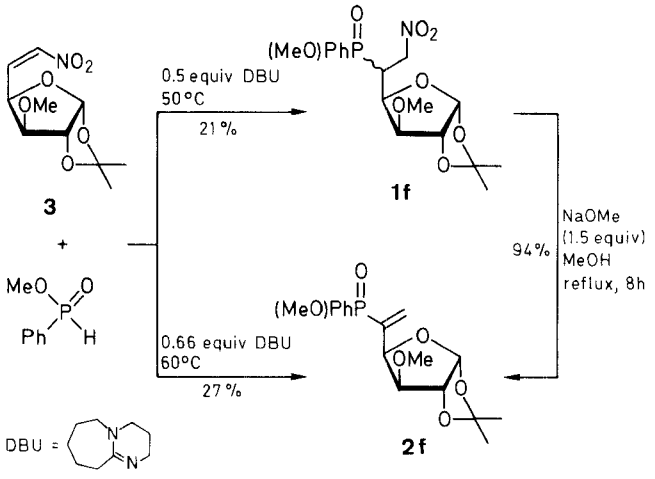


1, 2	R^2	R^3	1, 2	R^2	R^3
a	OMe	OMe	d	Ph	Ph
b	OMe	OMe	e	Ph	Ph
c	OMe	OMe	f	OMe	Ph

2-(Dimethoxyphosphinyl)-1-nitroethanes **1** are prepared by addition of dimethyl phosphite to nitroethenes,[1] prepared from aldehydes and nitromethane, in the presence of triethylamine.[8] Treatment of α-(dimethoxyphosphinyl)-β-nitroethylbenzene **(1a)** with 1.5 equivalents of sodium methoxide in methanol under reflux affords α-(dimethoxyphosphinyl)styrene **(2a)** quantitatively. A large excess of the base (3 equivalents) causes hydrolysis of the phosphonate to produce a water soluble material, whereas if quantities of base not larger than one equivalent are used, then the elimination reaction is incomplete as the liberated nitrous acid neutralizes the basic reaction mixture. The best results are obtained when the reaction mixture is basic, by using 1.5 equivalents of sodium methoxide in methanol under reflux.

Treatment of sugar derivative **1b** with 1.5 equivalents of sodium methoxide in methanol for 8 hours under reflux gives the corresponding 5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexo-5-enofuranose **(2b)** in 97% yield. Ion exchange resin IRA-410 used as the base also affords *xylo*-hexo-5-enofuranoses **2b** in 82% yield (Table).

Reaction of methyl phenylphosphinate with 5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-*C*-nitro-α-D-xylo-*hexo*-5-enofuranose **(3)** in benzene at 50 °C in the presence of 0.5 equivalent of 1,8-diazabicyclo-[5,4,0]-7-undecene (DBU) affords adduct **1f**, while the reaction in the presence of 0.66 equivalent of DBU at 60 °C yields directly the elimination product **2f**. When the reaction is carried out in the presence of 1.5 equivalents of DBU at 60 °C, rapid elimination reaction followed by polymerization occurs. These results show that elimination of nitrous acid from the adduct occurs at elevated temperature (60 °C).

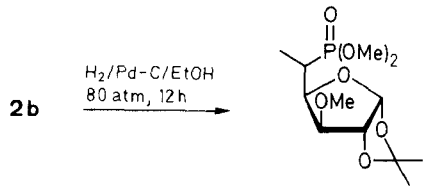


Unsaturated sugar **2b** is hydrogenated with 5% palladium on carbon to afford 5-(*R,S*)-5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranose **(4b)** in 96% yield.

Table. Compounds **2** Prepared[a]

Compound	Base	Yield (%)	Molecular Formula[b]	IR (KBr) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
2a	NaOMe	100	$C_{10}H_{13}O_3P$ (212.2)	1235 (P=O), 1030 (P–O–C), 735, 705 (Ph)	3.62 (d, 6H, J = 11), 6.02 (dm, 1H, J = 24), 6.21 (dm, 1H, J = 44), 7.0–7.7 (m, 5H)
2b	NaOMe	97	$C_{12}H_{21}O_7P$ (308.3)	1260 (P=O), 1030 (P–O–C), 750 (C–P)	1.35, 1.51 (2s, 6H), 3.35 (s, 3H), 3.72 (d, 6H, J = 11), 3.88 (d, 1H, J = 4), 4.59 (d, 1H, J = 4), 4.7–5.0 (m, 1H), 5.92 (d, 1H, J = 4), 6.14 (dm, 1H, J = 24), 6.23 (dm, 1H, J = 46)
2b	IRA-410	82			
2c	NaOMe	88	see experimental		
2d	NaOMe	91	$C_{22}H_{25}O_5P$ (400.4)	1190 (P=O), 1030 (P–O–C), 755, 695 (Ph)	1.22, 1.31 (2s, 6H), 3.08 (s, 3H), 3.82 (d, 1H, J = 3), 4.49 (d, 1H, J = 4), 4.7–5.1 (m, 1H), 5.72 (dm, 1H, J = 37), 5.88 (d, 1H, J = 4), 6.24 (dm, 1H, J = 57), 7.2–8.0 (m, 10H)
2e	NaOMe	81	$C_{28}H_{29}O_5P$ (476.5)	1190 (P=O), 1030 (P–O–C), 755, 695 (Ph)	1.18, 1.24 (2s, 6H), 4.04 (d, 1H, J = 4), 4.42 (s, 2H), 4.51 (d, 1H, J = 4), 4.7–5.0 (m, 1H), 5.57 (dm, 1H, J = 21), 5.83 (d, 1H, J = 4), 6.36 (dm, 1H, J = 42), 6.9–7.9 (m, 15H)
2f	NaOMe	94	$C_{28}H_{29}O_5P$ (354.3)	1225 (P=O), 1030 (P–O–C), 760, 705 (Ph)	1.30, 1.44 (2s, 6H), 3.00, 3.21 (2s, 3H), 3.73 (dd, 3H, J = 11, 11), 3.7–3.9 (m, 1H), 4.53 (d, 1H, J = 4), 4.7–5.0 (m, 1H), 5.84 (d, 1H, J = 4), 6.11 (dm, 1H, J = 22), 6.27 (dm, 1H, J = 41), 7.3–8.0 (m, 5H)

[a] The mass spectra of all compounds are in accordance with their structures.
[b] Satisfactory microanalyses obtained: C ±0.10, H ±0.19.



4

In summary, we have found a novel and excellent method for the preparation of phosphinylethene derivatives, especially 5,6-dideoxy-5-*C*-phosphinyl-*xylo*-hexo-5-enofuranose derivatives as well as 5,6-dideoxy-5-*C*-phosphinyl-*xylo*-hexofuranose derivatives.

Compounds **1a–f** were prepared from the corresponding α,β-unsaturated nitro compounds following the literature procedure.[1]

3-*O*-Benzyl-5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-α-D-xylo-hexo-5-enofuranose (2c); Typical Procedure:
In as flask equipped with a condenser and a drying tube, compound **1c** (2.23 g, 5.18 mmol) is refluxed with NaOMe (1.5 equiv, 0.42 g, 7.8 mmol) in dry MeOH (60 mL) for 8 h. After evaporation of the solvent, the residue is dissolved in $CHCl_3$ (80 mL) and the resulting solution is washed with water (3 × 10 mL) and dried (Na_2SO_4). Removal of the solvent *in vacuo* and recrystallization of the product from hexane/benzene gives **2c**; yield: 1.75 g (88%); mp 117°C; $[\alpha]_D^{27}$ −42.8° (*c* = 2.76, $CHCl_3$).

$C_{18}H_{25}O_7P$ (384.4)	calc.	C 56.25	H 6.56	P 8.06
	found	56.28	6.39	7.81

MS (70 eV): m/z = 384 (M^+).

IR (KBr): ν = 1260 (P=O), 1030 (P–O–C), 750, 700 cm^{-1} (Ph).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.32, 1.51 [2s, 6H, $C(CH_3)_2$], 3.68 [d, 6H, $J_{PO,CH}$ = 10.8 Hz, $P(OCH_3)_2$], 4.14 (d, 1H, $J_{3,4}$ = 3.6 Hz, H-3), 4.56 (s, 2H, OCH_2), 4.60 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-2), 4.7–5.0 (m, 1H, H-4), 5.97 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 6.28 (dm, 1H, $J_{PC,CH}$ = 24.6 Hz, $PC{=}CH_{cis}$), 6.38 (dm, 1H, $J_{PC,CH}$ = 45.0 Hz, $PC{=}CH_{trans}$), 7.2–7.3 (m, 5H_{arom}).

Reaction of Methyl Phenylphosphinate with 3:
Reaction of nitroenose **3** (1.43 g) with methyl phenylphosphinate (1.37 g) in dry benzene (20 mL) in the presence of DBU (0.45 g, 0.5 equiv) for 30 h at 50°C followed by evaporation of the solvent *in vacuo*, which upon separation by column chromatography on silica gel (eluent petroleum ether/EtOAc 1:1) to give **1f**; yield: 0.49 g (21%), gluco/ido ratio 2:1; R_f = 0.19 (petroleum ether/EtOAc, 1:1).

IR (neat): ν = 1565, 1380 (NO_2), 1230 (P=O), 1030 (P–O–C), 755, 700 cm^{-1} (Ph).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.28, 1.42 [2s, 6H, $C(CH_3)_2$], 2.81 (s, 0.66 × 3H, OCH_3, *gluco*), 3.30 (s, 033 × 3H, OCH_3, *ido*), 3.58 [d, 3H, $J_{PO,CH}$ = 10.8 Hz, $P(O)OCH_3$], 3.5–4.0 (m, 2H, H-2,5), 4.2–5.0 (m, 4H, H-3,4,6,6'), 5.74 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 7.3–8.0 (m, 5$_{arom}$).

Reaction of nitroenose **3** (1.97 g) with methyl phenylphosphinate (1.88 g) in dry benzene (20 mL) in the presence of DBU (0.81 g, 0.66 equiv) for 9 h at 60°C affords, after workup and purification as above elimination product **2f**; yield: 0.77 g (27%); R_f = 0.26 (petroleum ether/EtOAc 1:1). The product is identical to that produced by β-elimination from **1f** with NaOMe in MeOH under reflux.

IR (neat): ν = 1445 (P–Ph_5), 1225 (P=O), 1030 (P–O–C), 760, 705 cm^{-1} (Ph).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.30, 1.44 [2s, 6H, $C(CH_3)_2$], 3.11 (d, 3H, $J_{1,2}$ = 12.6 Hz, OCH_3), 3.70, 3.75 [2d, 3H, $J_{PO,CH}$ = 10.8 Hz, $P(O)OCH_3$], 3.7–3.9 (m, 1H, H-3), 4.53 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-2), 4.7–5.0 (m, 1H, H-4), 5.84 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 6.11 (dm, 1H, $J_{PC,CH}$ = 22.2 Hz, $PCH{=}CH_{cis}$), 6.27 (dm, 1H, $J_{PC,CH}$ = 41.4 Hz, $PCH{=}CH_{trans}$), 7.3–8.0 (m, 5H_{arom}).

5-(*R,S*)-5,6-Dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylo-hexofuranose (4)
Compound **2b** (0.207 g, 0.672 mmol) in EtOH (20 mL) is hydrogenated over 5% Pd–C (0.021 g) in an autoclave for 12 h under 80 atmospheric pressure of hydrogen at 40°C. Removal of the catalyst by filtration and evaporation of the solvent *in vacuo* affords the hydrogenated product **4**; yield: 0.202 g (97%); syrup.

MS (70 eV): m/z = 310 (M^+)

IR (neat): ν = 1255 (P=O), 1030 (P–O–C), 725 cm^{-1} (C–P).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.15 (dd, 3 H, J_{HH} = 7.9 Hz, $J_{PC,CH}$ = 14.5 Hz, CH_3), 1.28, 1.44 [s, 6 H, $C(CH_3)_2$], 3.0–4.3 (m, 3 H, H-3,4,5), 3.30 (s, 3 H, OCH_3), 3.64 [d, 6 H, $J_{PO,CH}$ = 10.8 Hz, $P(OCH_3)_2$], 4.43 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-2), 5.77, 5.83 (2d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1).

Received: 23 March 1989; revised: 5 October 1989

(1) Yamashita, M.; Sugiura, M.; Oshikawa, T.; Inokawa, S. *Synthesis* **1987**, 62, and references therein.
(2) Yamashita, M.; Nomoto, H.; Imoto, H. *Synthesis* **1987**, 716, and references therein.
(3) Giordano, C.; Castaldi, G. *J. Org. Chem.* **1989**, *54*, 1470.
(4) Yamashita, M.; Kojima, K.; Yoshida, H.; Ogata, T.; Inokawa, S. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1625.
(5) Worms, K.H.; Schmidt-Dunker, M., in: *Organic Phosphorus Compounds*, Kosolapoff, G.M.; Maier, L. (eds.), Vol. 7, John Wiley & Sons, New York, 1976, Chapt 18.
(6) Yamashita, M.; Morizane, T.; Fujita, K.; Nakatani, K.; Inokawa, S. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 813.
(7) McCarthy, J.R.; Robins, M.J.; Robins, R.K. *J. Chem. Soc., Chem. Commun.* **1967**, 536.
(8) Paulsen, H. *Liebigs. Ann. Chem.* **1963**, *665*, 166.