A Convenient Method for the Synthesis of Substituted 2-Methoxycarbonyl- and 2-Cyanoallylphosphonates. The Allyl Phosphite – Allylphosphonate Rearrangement

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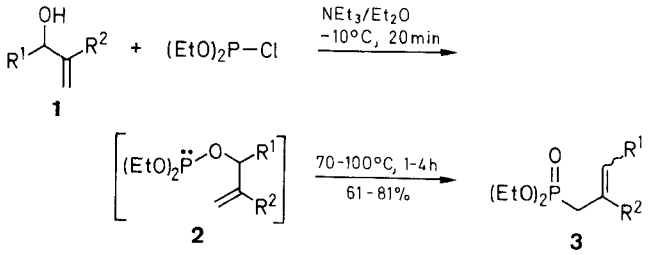
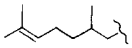
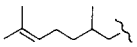
The thermally induced Arbuzov rearrangement of allyl diethyl phosphites gives, under unprecedented mild conditions, a variety of diethyl allylphosphonates with high stereoselectivity and in high yield.

We have recently demonstrated that the Horner–Emmons olefination of diethyl 2-ethoxycarbonylallylphosphonates **3** (R^1 = alkyl or aryl, $R^2 = CO_2Et$) represents a versatile method for the preparation of different synthetically attractive 1,3-butadiene-2-carboxylates.[1] The synthesis of compounds **3** was successfully acomplished by applying the phosphorus version of the Stobbe condensation to diethyl 2-ethoxycarbonylethylphosphonate [ethyl 3-(diethoxyphosphoryl)propanoate] as starting material.

We now report a new approach to diethyl 2-methoxycarbonylallylphosphonates **3a–e** and related 2-cyanoallylphosphonates **3f–i** based on the thermally induced Arbuzov rearrangement[2–7,12] of the diethyl allyl phosphites **2**.



1, 2, 3	R^1	R^2	1, 2, 3	R^1	R^2
a	Me	CO_2Me	**f**	Et	CN
b	*i*-Pr	CO_2Me	**g**	*i*-Pr	CN
c	Ph	CO_2Me	**h**	Ph	CN
d		CO_2Me	**i**		CN
e		CO_2Me			

The procedure involves treatment of the readily and conventionally accessible allyl alcohols **1** with diethyl phosphorchloridite in the presence of triethylamine followed by heating the crude intermediates **2** for several hours at 70–100°C. Under these conditions, the phosphonic esters **3** are formed in good yields and can then be isolated from the reaction mixtures either by distillation or by column chromatography on silica gel. The presence of a methoxycarbonyl or cyano group in **2** facilitates the rearrangement, the optimum temperatures found for the rearrangement **2** → **3** being considerably lower than those reported for the unfunctionalized analogs.

The rearrangement (**2** → **3** is a highly stereoselective process. Products **3a–e**, obtained from **2a–e**, have exclusively the *Z*-configuration whereas products **3f–i**, obtained from **2f–i**, are mixtures of both stereoisomers with the *E*-isomer strongly predominating. It is worthy of note that the observed considerable differences in geometry between compounds **3a–e** and **3f–i** are brought about by relatively small differences in the spatial requirements of the methoxycarbonyl and cyano groups. The structural assigments of all new compounds are consistent with microanalyses, ^{31}P-NMR and ^{1}H-NMR spectra.

In conclusion, the synthesis presented here is advantageous over the previous procedure in terms of short reaction time, simple workup, easily controlled stereoselectivity, and good yield.

^{1}H-HMR spectra were recorded on Bruker HFX-72 or MSL-300 spectrometers at 90 and 300 MHz, respectively. ^{31}P-NMR spectra were recorded on a FT Jeol FX-60 at 24.3 MHz utilizing broadband proton decoupling.

Solvents and commercial reagents were purified by conventional methods before use. Diethyl phosphorchloridite,[8] 3-hydroxy-2-methylenealkanoic esters, i.e., allyl alcohols **1a**,[9] **1c**,[10] and **1e**,[9] and 3-hydroxy-2-methylenealkanenitriles, i.e., allyl alcohols **1f–h**,[11] were prepared as described in the literature.

Table 1. Allyl Alcohols **1b**, **1d**, and **1i** Prepared

Product	Reaction Time (d)	Yield[a] (%)	bp (°C)/Torr	Molecular Formula[b]	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
1b	6	54	72–75/0.8	$C_8H_{14}O_3$ (158.2)	0.87 (d, 3H, J = 6.5), 0.93 (d, 3H, J = 6.5), 1.95 (octet, 1H, J = 6.5), 3.44 (br s, 1H), 3.79 (s, 3H), 4.14 (br d, 1H, J = 6.5), 5.80–5.89 (m, 1H), 6.28–6.37 (m, 1H)
1d	20	77	112–114/0.2	$C_{14}H_{24}O_3$ (240.3)	0.92 (d, 3H, J = 6.0), 1.05–2.20 (m, 13H), 3.13 (br s, 1H), 3.78 (s, 3H), 4.45 (br t, 1H, J = 5.0), 4.83–5.28 (m, 1H), 5.75–5.87 (m, 1H), 6.22 (d, 1H, J = 1.5)
1i	7	85	108–110/0.4	$C_{13}H_{21}NO$ (207.4)	0.95 (d, 3H, J = 5.5), 1.07–2.21 (m, 13H), 2.78 (br s, 1H), 4.27 (br t, 1H, J = 5.0), 4.80–5.25 (m, 1H), 5.83–6.05 (m, 2H)

[a] Yield of isolated product based on the aldehyde used.

[b] Satisfactory microanalyses: C ±0.31, H ±0.23.

Table 2. Diethyl 2-Methoxycarbonyl- and 2-Cyano-2-alkenylphosphonates **3** Prepared

Product	Reaction Conditions: Time (h)/ Temp. (°C)	Yield[a] (%)	bp (°C)/Torr	Molecular Formula[b]	Ratio $E:Z$	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{31}P-NMR ($CHCl_3$/ H_3PO_4) δ
3a	2/70	66	92–96/0.1	$C_{10}H_{19}O_5P$ (250.2)	5 : 95	1.33 (t, 6H, J = 7.0), 1.94 (dd, 3H, J = 6.0, 7.0), 3.08 (d, 2H, J = 22.0), 3.84 (s, 3H), 4.18 (quint, 4H, J = 7.0), 7.17 (quint, 1H, J = 7.0)	25.83
3b	3/80	61	98–100/0.2	$C_{12}H_{23}O_5P$ (278.3)	5 : 95	1.08 (d, 6H, J = 6.5), 1.32 (t, 6H, J = 7.0), 2.40–2.83 (m, 1H), 3.03 (d, 2H, J = 22.0), 3.90 (s, 3H), 4.13 (quint, 4H, J = 7.0), 6.79 (dd, 1H, J = 10.5, 6.0)	25.83
3c	2/80	68	130–131/0.05	$C_{15}H_{21}O_5P$ (312.3)	5 : 95	1.23 (t, 6H, J = 7.0), 3.25 (d, 2H, J = 22.0), 3.83 (s, 3H), 4.08 (quint, 4H, J = 7.0), 7.28–7.70 (m, 5H), 7.85 (d, 1H, J = 5.5)	25.42
3d	2/80	74	145–148/0.4	$C_{18}H_{33}O_5P$ (360.4)	5 : 95	0.92 (t, 3H, J = 6.0), 1.27 (t, 6H, J = 7.0), 1.47–2.41 (m, 13H), 2.96 (d, 2H, J = 22.0), 3.77 (s, 3H), 4.10 (quin, 4H, J = 7.0), 4.91–5.23 (m, 1H), 6.96 (q, 1H, J = 6.5)	26.18
3e	1/70	56	oil[c]	$C_{14}H_{20}NO_5P$ (313.3)	5 : 95	1.22 (t, 6H, J = 7.0), 3.15 (d, 2H, J = 23.0), 3.81 (s, 3H), 4.05 (quint, 4H, J = 7.0), 7.34 (dd, 1H, J = 5.0, 8.0), 7.73 (d, 1H, J = 6.0), 7.95–8.80 (m, 3H)	25.63
3f	4/100	55	128–130/2	$C_{10}H_{18}NO_3P$ (231.2)	70 : 30[d]	[e] 1.07 (t, 3H, J = 8.0), 1.33 (t, 6H, J = 7.0), 2.09–2.62 (m, 2H), 2.67 (d, 2H, J = 20.0), 4.15 (quint, 4H, J = 7.0), 6.37 (q, 1H, J = 7.0)	[e]23.95
						[f]1.07 (t, 3H, J = 8.0), 1.33 (t, 6H, J = 7.0), 1.57–2.12 (m, 2H), 2.70 (d, 2H, J = 20.0), 4.14 (quint, 4H, J = 7.0), 6.48 (q, 1H, J = 7.0)	[f]23.55
3g	3/90	65	110–114/0.4	$C_{11}H_{20}NO_3P$ (245.2)	70 : 30[d]	[e]1.08 (d, 6H, J = 6.0), 1.37 (t, 6H, J = 7.0), 2.67 (d, 2H, J = 21.0), 2.77–2.91 (m, 1H), 4.05–4.22 (m, 4H), 6.18 (dd, 1H, J = 10.5, 5.0)	[e]22.96
						[f]1.05 (d, 6H, J = 6.0), 1.37 (t, 6H, J = 7.0), 2.01–2.17 (m, 1H), 2.74 (d, 2H, J = 21.0), 4.05–4.22 (m, 4H), 6.30 (10.5, 5.5)	[f]22.56
3h	3/90	78	170–173/0.3	$C_{14}H_{18}NO_3P$ (279.3)	60 : 40[d]	[e]1.37 (t, 6H, J = 7.0), 2.82 (d, 2H, J = 21.0), 3.87–4.35 (m, 4H), 7.06 (d, 1H, J = 5.5), 7.26–7.93 (m, 5H)	[e]22.66
						[f]1.37 (t, 6H, J = 7.0), 2.91 (d, 2H, J = 21.0), 3.87–4.35 (m, 4H), 7.26–7.93 (m, 6H)	[f]22.26
3i	3/100	81	146–149/0.2	$C_{17}H_{30}NO_3P$ (327.4)	75 : 25[d]	[e]0.94 (d, 3H, J = 6.0), 1.34 (t, 6H, J = 7.0), 1.52–2.48 (m, 7H), 1.59 (s, 3H), 1.67 (s, 3H), 2.71 (d, 2H, J = 21.0), 4.07–4.25 (m, 4H), 5.02–5.12 (m, 1H), 6.38 (dt, 1H, J = 5.5, 7.5)	[e]23.45
						[f]0.92 (d, 3H, J = 6.0), 1.34 (t, 6H, J = 7.0), 1.52–2.48 (m, 7H), 1.59 (s, 3H), 1.67 (s, 3H), 2.74 (d, 2H, J = 21.0), 4.07–4.25 (m, 4H), 5.02–5.12 (m, 1H), 6.56 (dt, 1H, J = 5.5, 7.5)	[f]23.03

[a] Yield of isolated product, based on **1**.
[b] Satisfactory microanalyses: C ±0.29, H ±0.22, P ±0.35.
[c] Crude **3e** was purified by column chromatography (silica gel, EtOAc/MeOH 9.5 : 0.5).
[d] Estimated from the integrated intensities of the ^{31}P-NMR peaks of the crude products.
[e] Values for E isomer from the spectrum of the E/Z mixture.
[f] Values for Z isomer from the spectrum of the E/Z mixture.

Methyl 3-Hydroxy-4-methyl-2-methylenepentanoate (1b), Methyl 3-Hydroxy-5,9-dimethyl-2-methylene-8-decanoate (1d), and 3-Hydroxy-5,9-dimethyl-2-methylene-8-decenenitrile (1i); General Procedure:

A mixture of the appropriate aldehyde (0.1 mol), methyl acrylate (13.0 g, 0.15 mol; for **1b** and **1d**) or acrylonitrile (7.9 g, 0.15 mol; for **1i**), and 1,4-diazabicyclo[2.2.2]octane (DABCO; 1.6 g, 0.015 mol) is allowed to stand at r.t. for the time given in Table 1. Excess methyl acrylate or acrylonitrile is then removed under reduced pressure. The residue is taken up in Et_2O (100 mL) and washed with 10% aq HCl (50 mL). The ether phase is washed with H_2O (50 mL) and dried ($MgSO_4$). The solvent is removed and the crude product is distilled under reduced pressure to yield pure **1b**, **1d**, or **1i**.

Diethyl 2-Methoxycarbonyl- or 2-Cyano-2-alkenylphosphonates 3a–i; General Procedure:

To a stirred solution of the allyl alcohol **1** (50 mmol) and Et_3N (5.05 g, 50 mmol) in Et_2O (100 mL), diethyl phosphorochloridite (7.82 g, 50 mmol) is added dropwise at −10 °C under argon, and stirring is continued for 20 min at −10 °C. The precipitate is filtered off and washed with Et_2O (2 × 30 mL). The filtrate is evaporated and the residue is heated at 70–100 °C under argon for the time given in Table 2. The resultant product is purified by distillation under reduced pressure or by column chromatography on silica gel.

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(1) Janecki, T.; Bodalski, R. *Synthesis* **1989**, 506.
(2) Pudovik, A.N.; Aladzhyeva, J.M. *Zh. Obshch. Khim.* **1963**, *33*, 3096; C.A. **1963**, *59*, 13798.
(3) Lemper, A.L.; Tickelmann, H. *Tetrahedron Lett.* **1964**, 3053.
(4) Savage, M.P.; Trippett, S. *J. Chem. Soc. (C)* **1966**, 1842.
(5) Herriott, A.W.; Mislow, K. *Tetrahedron Lett.* **1968**, 3013.
(6) Huche, M.; Cresson, P. *Tetrahedron Lett.* **1972**, 4933.
(7) Lu, X.; Zhu, J. *J. Organomet. Chem.* **1986**, *304*, 239.
(8) Michalski, J.; Modro, T.; Zwierzak, A. *J. Chem. Soc.* **1961**, 4904.
(9) Ameer, F.; Drewes, S.E.; Freese, S.; Kaye, P.T. *Synth. Commun.* **1988**, *18*, 495.
(10) Hoffmann, H.M.R.; Rabe, J. *Angew. Chem.* **1983**, *95*, 795; *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 795.
(11) Basavaiah, D.; Gowriswari, V.V.L. *Synth. Commun.* **1987**, *17*, 587.
(12) Mark, V., in: Mechanisms of Molecular Migrations, Thyagarajan, B.S. (ed.), Interscience Publishers, New York, 1969, p. 319.