New Allylphosphonates Derived from $(OCH_2CMe_2CH_2O)PCl$ and Baylis–Hillman Adducts – Stereochemistry and Utility

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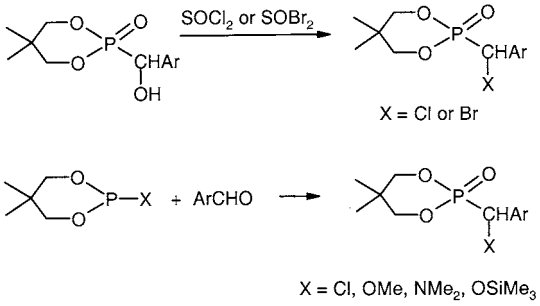
Abstract: New allylphosphonates have been prepared; an X-ray structural proof for the major *Z*-isomer has been given for phosphonate **3**. Horner–Wadsworth–Emmons reaction of **3** or **6** (*Z* isomer) with aromatic aldehydes leads to carbomethoxy/ cyano substituted butadienes. In the reaction using cyanoallylphosphonate **6**, use of either *Z* or *E* isomer leads to the same *E*,*Z* product; stereochemistry of one such cyano product is confirmed by X-ray crystallography. In the reaction of **3** with 4-nitrobenzaldehyde stereochemistry for the (*E*,*E*) isomer is confirmed by X-ray crystallography.

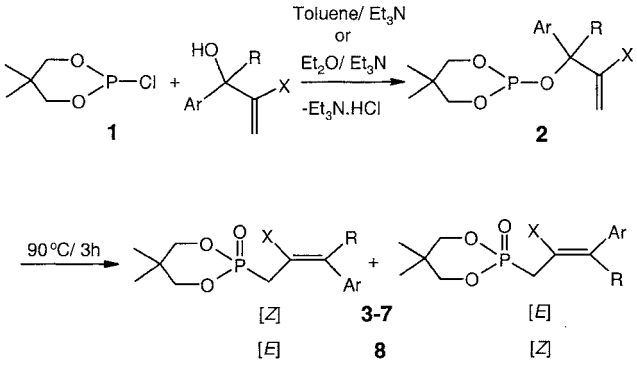
Key words: allylphosphonates, Baylis–Hillman adducts, 2-substituted butadienes, Horner–Wadsworth–Emmons reaction

The enormous synthetic utility of organophosphonates as Horner–Wadsworth–Emmons (HWE) reagents has been abundantly exploited in synthetic organic chemistry and hence there is always scope for developing new phosphonates or improving the existing methodology for their synthesis.[1] In view of the ease of synthesis, cost-effectiveness and stability (towards oxidation) of the cyclic chlorophosphite $(OCH_2CMe_2CH_2O)PCl$ (**1**),[2] we became interested in utilizing this compound to obtain synthetically useful phosphonates. In one approach we utilized the Pudovik product of the phosphite $(OCH_2CMe_2CH_2O)P(O)H$ (readily obtained from the hydrolysis of **1**) with an aldehyde and in the second one, we directly used the reaction of **1** and its substituted products [P-Cl or P(O)H → P-OR or P-NMe_2] with suitable aldehydes (Scheme 1).[2–4] Herein we report (i) the synthesis of phosphonates derived from **1** and the Baylis–Hillman adducts of an aldehyde with acrylonitrile or methylacrylate[5] and (ii) utility of these phosphonates in HWE reactions. We also give the structural proof for the stereochemistry of one of the phosphonates and two of the HWE products, thus facilitating structural assignment in future work. The phosphonates synthesized here can be attractive reagents for further reactions in view of their facile and economic synthesis coupled with the presence of functional groups.



Scheme 1

Synthesis of the phosphonates is accomplished by using allylic type rearrangement of the allylphosphites **2** [Scheme 2; Table 1].[6–8] In the case of 2-carbomethoxy compounds **3**–**5**, the *Z*-isomer is obtained as the most predominant/ exclusive isomer; the stereochemistry has been proven by an X-ray structure determination for the major isomer of **3** (Figure 1). In the case of 2-cyanoallylphosphonates **6**–**8**, both *Z* and *E* isomers are obtained in comparable quantities when the corresponding allylphosphite was heated under neat conditions. In the case of **6** we have isolated both the *E* and *Z* isomers as crystalline solids.



Scheme 2

We have also isolated the intermediate allylphosphites **2** [R = H; X = CO_2Me, Ar = Ph (**a**) or C_6H_4-4-Me (**b**), X = CN, Ar = Ph (**c**) or C_6H_4-4-Me (**d**); δ(P) for these 120.7 ± 0.1)] in a spectroscopically pure state. The rearrangement of **2c** in toluene at 70 °C is essentially complete in 1 h and no intermediate could be detected [^{31}P NMR]. Interestingly, the intensity of the downfield isomer relative to the upfield one increases with time.

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Table 1 Phosphonates **3**–**8** Isolated in the Present Study (cf Scheme 2)[a]

Compd	Ar	X	R	*Z*/*E*	Yield (%)	δ(P)
3	Ph	CO_2Me	H	95:5	90	21.1, 18.2
4	C_6H_4-4-Me	CO_2Me	H	100:0	89	21.3
5	C_6H_4-4-OMe	CO_2Me	H	100:0	87	21.3
6	Ph	CN	H	50:50	80	17.8, 17.6
7	C_6H_4-4-Me	CN	H	60:40	81	18.0, 17.7
8	Ph	CN	CO_2Et	40:60	96	17.0, 15.8

[a] Chemical shifts are referenced to ext. 85% H_3PO_4. We observed a dependence of δ(P) value for the phosphonates on the concentration to an extent of ±1 ppm.

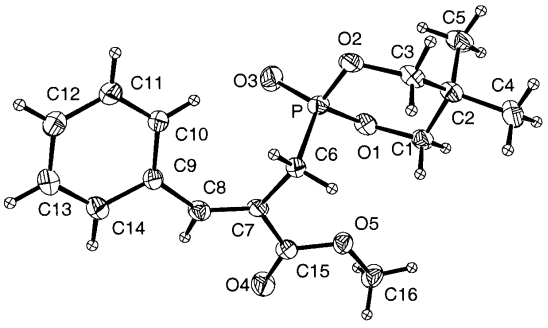
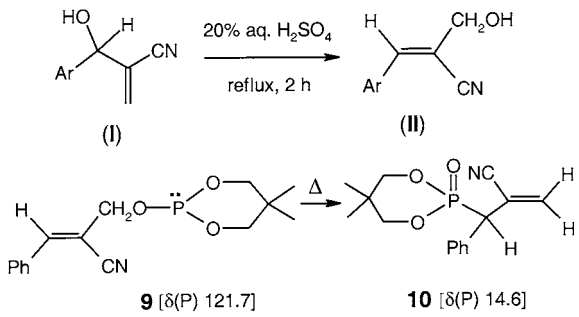


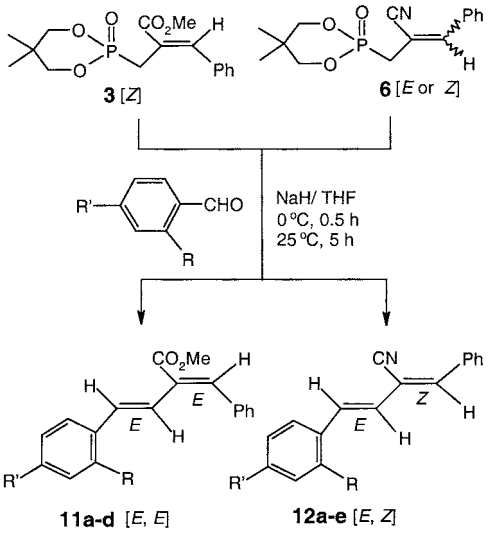
Figure 1 An ORTEP drawing of **3** [*Z* isomer]. Selected bond distances: P-O(1) 1.544(2), P-O(2) 1.554(2), P-O(3) 1.433(3), P-C(6) 1.777(3), C(6)-C(7) 1.488(4), C(7)-C(8) 1.326(4).

In view of a recent report on the facile conversion of allyl alcohols **I** to cinnamyl alcohols **II**,[9] we felt that substituted cinnamyl phosphite **9** derived from **II** (Ar = Ph) also can lead to phosphonates **10** (Scheme 3).[10] However, under the conditions analogous to those used to prepare **3**–**8**, this rearrangement did not take place, probably because of greater steric factors at the terminal CH(Ph) end of the double bond and the non-availability of a convenient transition state. Upon heating **9** at 170 °C, however, formation of a mixture of phosphonates [^{31}P NMR] was noticed and **10** could be isolated in low yields.



Scheme 3

The *Z* isomer of allylphosphonate **3** (X-ray; Figure 1[11,12]) and the *E* isomer of **6** (assignment tentative; see below) were employed to prepare 2-substituted-1,3-butadienes **11a**–**d** and **12a**–**e** by the HWE reaction (Scheme 4; Table 2).[13] The stereochemistry at the newly formed double bond was essentially *E*, with ≤ 5% of a second isomer in the case of **11a**, **11b**, **11d** and **12e**, based on the ^{1}H NMR spectra of the reaction mixtures. The ^3J(H-H) value 16–18 Hz for the protons at the newly formed double bond is also consistent with this. For **11d** the stereochemistry is proven by X-ray structural analysis.[11,12] The *E* stereochemistry at the newly formed double bond and the *Z* configuration at the existing double bond for the cyano system is convincingly proven by an X-ray structure determination of **12b**.[11,12]



Scheme 4

In the case of **6**, from the HWE reaction using the second isomer (assigned *Z* stereochemistry) and 4-chlorobenzaldehyde, we again obtained **12b** as the only isolable product [IR, TLC, mp, ^{1}H and ^{13}C NMR]. This result is different from that reported before by Janecki.[14] There is

Table 2 Details on the Synthesis of 2-Substituted-1,3-butadienes[a]

Entry	R	R′	Product	Yield (%)
1	H	H	**11a**	80
2	H	Cl	**11b**	80
3	Cl	Cl	**11c**	85
4	H	NO_2	**11d**	90
5	H	H	**12a**	92
6	H	Cl	**12b**	94
7	H	OMe	**12c**	90
8	Cl	Cl	**12d**	94
9	H	CH_3	**12e**	90

[a] Isolated yields after column chromatography.

possibly a delocalization of the negative charge in the phosphonate anion [cf. structures **III** and **IV** (Figure 2), which are the extreme resonance canonicals]. Although this feature is possible for carbomethoxy derivatives also, we were not able to verify this because the second isomer is not formed in significant quantities. However, as regards the synthesis of 2-substituted-1,3-butadienes that may be valuable precursors for Diels–Alder reactions, our phosphonates appear to be better than those available previously in view of the ease of preparation.[13]

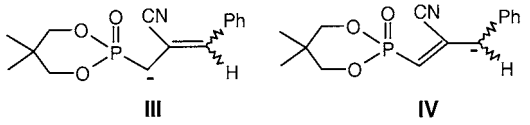


Figure 2

An analogous reaction of phosphonate **8** (*E*/*Z* 1:1) with *p*-chlorobenzaldehyde gave **13** (Figure 3) as a mixture of (*EE*/*EZ*) isomers in 1:1 ratio. This result is in consonance with that described above assuming that the stereochemistry at the newly formed double bond is *E*.

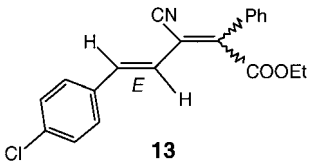


Figure 3

In a previous study, Janecki noted that it was not possible to make unambiguous configurational assignments based on the spectroscopic data for the mixtures of 2-cyanobutadienes. In our case, using a pure isomer of phosphonate, the configurational assignment of the products has been made based on the X-ray structure determination of the carbomethoxy phosphonate (**3**) and the HWE products (**11d** and **12b**). The use of NaH by us, in place of LDA used by Janecki and Bodalski,[14] has probably avoided the formation of other phosphonate side products. In addition (as noted above), since the precursor $(OCH_2CMe_2CH_2O)PCl$ (**1**) is readily prepared and more convenient to handle than $(EtO)_2PCl$, our phosphonates are relatively easier to prepare and are cost effective; the yields are also quite high. Given the synthetic potential of both Baylis–Hillman and HWE reactions, we believe that the results reported here are quite significant and useful.

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(7) The Baylis–Hillman adducts $ArC(R)(OH)\text{-}C(X)=CH_2$ were prepared by literature methods.[5a]

(8) Typical procedure for **6**: To a stirred solution of $(Ph)CH(OH)\text{-}C(CN)=CH_2$ (1.50 g, 9.5 mmol) and Et_3N (0.96 g, 9.5 mmol) in toluene (50 mL), $(OCH_2CMe_2CH_2O)PCl$(**1**) (1.6 g, 9.5 mmol) was added dropwise at 0 °C under nitrogen; stirring was continued for 30 min. The precipitate was filtered off, washed with diethyl ether, and the washings added to the filtrate. The combined filtrate was evaporated to dryness and the residue was heated at 110 °C under nitrogen for 3 h by which time rearrange-

ment had taken place. The isomers of compound **6** (~1:1; total yield 80%) so obtained were separated by column chromato-graphy (hexane–ethyl acetate). Isomer **a** (higher R_f): mp 114–116 °C; IR (cm^{-1}) 2212, 1604; ^{1}H NMR δ 1.05, 1.14 (2 s, 6 H, 2 CH_3), 3.08 [d, ^2J(PH) = 22.2 Hz, 2 H, PCH_2], 3.89–4.30 (m, 4 H, OCH_2), 7.39–7.54 (m, 6 H, olefinic-*H* + Ar-*H*); ^{13}C NMR δ 21.4, 21.5, 27.0 [d, ^1J(PC) = 139.0 Hz], 32.6 [d, ^3J(PC) = 6.2 Hz], 75.7 [d, ^2J(PC) = 6.2 Hz], 104.5, 104.8, 119.5, 128.8, 129.1, 130.0, 132.9, 148.1, 148.3; ^{31}P NMR δ 17.6. Anal. Calcd for $C_{15}H_{18}NO_3P$: C, 61.84; H, 6.24; N, 4.81. Found: C, 61.76; H, 6.18; N, 4.74. Isomer **b** (lower R_f): Mp 128–130 °C; ^{1}H NMR δ 1.03, 1.07 (2 s, 6 H, 2 CH_3), 3.01 [d, ^2J(PH) = 21.3 Hz, 2 H, PCH_2], 3.85–4.22 (m, 4 H, OCH_2), 7.10–7.90 (m, 6 H, olefinic-*H* + Ar-*H*); ^{13}C NMR δ 21.4, 31.6 [d, ^1J(PC) = 138.0 Hz], 32.5 [d, ^3J(PC) = 6.2 Hz], 75.6 [d, ^2J(PC) = 6.2 Hz], 100.1, 100.3, 118.0, 128.8, 130.6, 133.1, 148.0, 148.2; ^{31}P NMR δ 17.8. Anal. Calcd for $C_{15}H_{18}NO_3P$: C, 61.84; H, 6.24; N, 4.81. Found: C, 61.66; H, 6.16; N, 4.70. The HWE reactions of the phosphonates with the aldehydes were conducted in THF using NaH as the base (supplementary material is available from the authors).

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(10) Spectral data for compound **9** (mp 70–72 °C): ^{1}H NMR δ 0.78, 1.28 (2s, 6 H, 2 CH_3), 3.40 (~t, ^2J ~ ^3J ~ 10.2 Hz, 2 H, OCH_2), 4.24 (d, ^3J ~ 10.2 Hz, 2 H, OCH_2), 4.56 [dd, ^3J(PH) ~ 10.2 Hz, ^4J(HH) ~ 1.0 Hz, 2 H, OCH_2], 7.21 [s, 1 H, C*H*=C(CN)], 7.41–7.82 (m, 5 H, Ar-*H*); ^{13}C NMR δ 22.3, 22.7, 32.7 [d, ^2J(PC) = 5.0 Hz], 64.2 [d, ^2J(PC) = 20.5 Hz], 69.2, 108.6, 117.4, 128.2, 128.9, 129.0, 130.8, 132.8, 144.7; ^{31}P NMR δ 121.7. Compound **10** (mp: 168–170 °C). ^{1}H NMR δ 0.95, 1.05 (2 s, 6 H, 2 CH_3), 3.75 (~t, ^2J ~ ^3J ~ 12.0 Hz, 2 H, OCH_2), 4.13 [d, ^3J(PH) ~ 20.0 Hz, 1 H, OCH_2], 4.15–4.30 (~m, 2 H, OCH_2), 6.20 and 6.41 (2 d, ^2J ~ 1.5 Hz, CH_2=C), 7.25–7.55 (m, 5 H, 5 H, Ar-*H*); ^{13}C NMR δ 21.3, 21.5, 32.6 [d, ^{3}J(PC) = 6.0 Hz], 47.7 [d, ^1J(PC) = 137.0 Hz, *C*HPh], 76.2 [d, ^2J(PC) = 20.5 Hz], 117.7 (d, *J* = 10.0 Hz), 118.9, 128.5, 129.0, 129.4, 129.6, 132.9 (*J* = 6.5 Hz), 134.8 (*J* = 8.0 Hz); ^{31}P NMR 14.6.

(11) X-ray data were collected on an Enraf-Nonius-MACH3 at 293 K (**3**, **12b**) or Bruker AXS SMART diffractometer at 296 K(**11d**) using Mo-K_α (λ = 0.71073 Å) radiation and capillary mounting. The structures were solved by direct methods;[12] all non-hydrogen atoms were refined anisotropically. The quality of data of **11d** was only moderate but the stereochemistry is unambiguous. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 190318 – 190320. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk]. ORTEP drawings of **11d** and **12b** are available from the authors.

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