SHORT PAPER

J. Chem. Research (S),
2000, 140–141

A convenient synthesis of (*E*)-α-cyano and (*E*)-α-ethoxycarbonyl vinylphosphonates[†]

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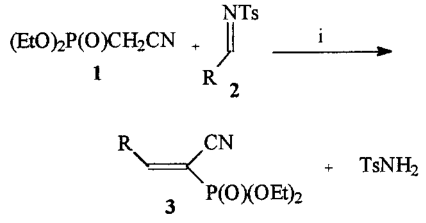
A new olefination catalysed by a base (KOBu^t) and its application to the stereoselective synthesis of substituted (*E*)-α-cyano and (*E*)-α-ethoxycarbonyl vinylphosphonates is described.

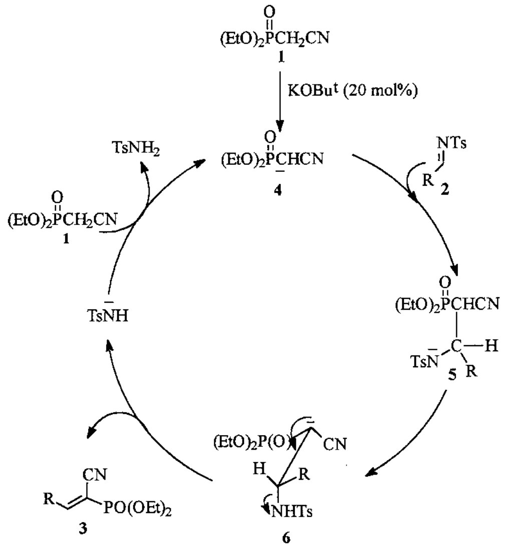
Attention has been devoted to the synthesis of vinylphosphonates bearing electron-withdrawing substituents such as cyano and ethoxycarbonyl groups at the α-position since they are useful intermediates for the construction of heterocyclic or carbocyclic compounds in organic synthesis. The methods for their preparation include the oxidative elimination of α-sulfenyl and α-selenylphosphonates, transition metal catalyzed synthesis, the classic Knoevenagel condensation mediated by titanium compounds and a palladium-catalysed coupling reaction.[1–5] A further convenient method for their preparation would be valuable.

As part of our continuing investigation of new synthetic methodologies for carbon–carbon double bond formation[6] we report a base-catalysed olefination and its application to the stereoselective synthesis of (*E*)-α-cyano and (*E*)-α-ethoxycarbonyl vinylphosphonates. The reaction is shown in Scheme 1.



Scheme 1 Reagents and conditions
i, KOBu^t (20 mol%), THF, 20°C, 2 min.

The catalytic reaction mechanism may be rationalized as shown in Scheme 2.

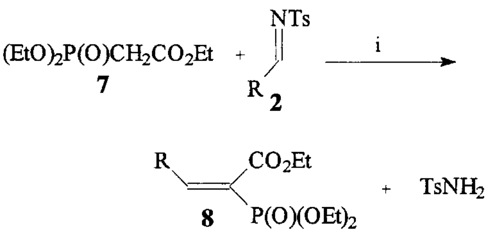


Scheme 2

The phosphoryl-stabilized carbanion **4**, generated from diethyl cyanomethylphosphonate **1** and potassium *tert*-butoxide in tetrahydrofuran (THF) reacts with *N*-tosylsulfonyl imines **2** to afford adduct **5**. An intramolecular hydrogen rearrangement of **5** gave **6**. Elimination of the *p*-toluenesulfonamide anion afforded the product **3**. The *p*-toluenesulfonamide anion abstracted a proton from **1** to give *p*-toluenesulfonamide and regenerate the carbanion **4**. Thus the catalytic cycle was completed. The results are summarized in Table 1.

It has been reported that when the vinyl H is *cis* with respect to the phosphoryl group, the $^3J_{cis,\ H,P}$ equals 21 Hz, but when the vinyl H is *trans* with respect to the phosphoryl group, the $^3J_{trans\ H,P}$ equals 43 Hz.[7] In our cases the $^3J_{H,P}$ is in the range of 20.1 – 21.8 Hz and therefore the configuration is *E*.

This reaction can be extended to the diethyl ethoxycarbonyl-methylphosphonate **7**, but it is necessary to raise the temperature of the reaction to 60 °C.



Scheme 3 Reagents and conditions
i, KOBu^t (20 mol%), THF, 60°C, 2 min.

The results are summarized in Table 2.

This methodology provides a convenient and highly stereoselective synthesis of the title compounds exclusively

Table 1 Preparation of α-cyano-vinylphosphonates **3**

Compound	R	Yield (%)[a]
3a	$2\text{-}CH_3OC_6H_4$	86
3b	C_6H_5	98
3c	$4\text{-}ClC_6H_4$	94
3d	$4\text{-}CH_3OC_6H_4$	81
3e	$4\text{-}CH_3C_6H_4$	83
3f	$4\text{-}(CH_3)_2NC_6H_4$	97
3g[b]	$4\text{-}NO_2C_6H_4$	94
3h	$3\text{-}BrC_6H_4$	89
3i	$2,4\text{-}Cl_2C_6H_3$	92

[a]Isolated yields. [b]The temperature of the reaction was –70 °C.

Table 2 Preparation of α-ethoxycarbonyl-vinylphosphonates **7**

Compound	R	Yield (%)[a]
7a	$4\text{-}ClC_6H_4$	68
7b	$2\text{-}CH_3OC_6H_4$	75
7c	$4\text{-}CH_3OC_6H_4$	80
7d	$4\text{-}CH_3C_6H_4$	86
7e	$3\text{-}BrC_6H_4$	74

[a]Isolated yields.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

containing the E-isomer. They would be expected to be useful intermediates in organic synthesis, particularly in annulation reactions.

Experimental

Melting points are uncorrected. The IR spectra of liquid products were obtained as films on a Digilab FTS-20E spectrometer. ^{1}H NMR spectra were recorded on a Bruker AM-300 (300 MHz) spectrometer (δ values in ppm from tetramethylsilane, in CDC1$_3$, J-values are given in Hz). Mass spectra were measured on a Finnigan GC-MS-4021 mass spectrometer.

Diethyl cyanomethylphosphonate 1 and Diethyl ethoxycarbonylmethyl phosphonate 7 were obtained from Aldrich Company.

General procedure for the preparation of α-Cyano-vinylphosphonates **3**: A mixture of diethyl cyanomethylphosphonate **1** (0.177g, 1 mmol), N-toluene-p-sulfonylarylimine **2** (1 mmol), potassium *tert*-butoxide (0.023g, 0.2 mmol) and tetrahydrofuran (10 cm^3) in a capped vessel under nitrogen at 20 °C was stirred for 2 min. TLC showed that the reaction was completed. The mixture was filtered through a short column of silica gel to remove the precipitate which was identified as p-toluenesulfonamide. The filtrate was concentrated and chromatographed on silica gel, and eluted with petroleum ether (60–90 °C)-ethyl acetate (2:1) to give the product **3**.

(E)-Diethyl 1-cyano-2-(2-methoxyphenyl)-vinylphosphonate (**3a**): Yield: 86%, oil, ν_{max}/cm^{-1}. 2990, 2210, 1590, 1570, 1490, 1260, 1020, 980. δ_H 8.49(d, J = 21.8Hz, 1H), 8.28–8.25(m, 1H), 7.53–7.47(m, 1H), 7.07–6.93(m, 2H), 4.30–4.07(m, 4H), 3.88(s, 3H), 1.40(t, J = 7.1HZ, 6H); m/z 295(M$^+$, 60), 264(45), 208(87), 157(81), 138(62), 111(100), 82(68). (Found: C, 56.81; H, 5.99; N, 4.89. $C_{14}H_{18}NO_4P$ (295.27) requires C, 56.95; H, 6.14; N, 4.74%).

(E)-Diethyl 1-cyano-2-phenyl-vinylphosphonate (**3b**):[8] Yield: 98%, oil, ν_{max}/cm^{-1}. 2990, 2210, 1600, 1570, 1260, 1070, 1020, 980. δ_H 8.02(d, J = 21.8Hz, 1H), 7.98–7.95(m, 2H), 7.58–7.46(m, 3H), 4.30–4.16(m, 4H), 1.41(t, J = 7.0Hz, 6H); m/z 265(M$^+$, 59), 236(100), 219(59), 192(36), 174(41), 156(92), 128(72), 111(81), 82(71).

(E)-Diethyl 1-cyano-2-(4-chlorophenyl)-vinylphosphonate (**3c**):[8] Yield: 94%, oil, ν_{max}/cm^{-1}. 2990, 2210, 1590, 1560, 1490, 1260, 1100, 1020, 980. δ_H 7.94(d, J = 21.3Hz, 1H), 7.89(d, J = 7.0Hz, 2H), 7.46(d, J = 7.0Hz, 2H), 4.28–4.15(m, 4H), 1.39(t, J = 7.1Hz, 6H); m/z 301(M$^+$+2, 28), 299(M$^+$, 100), 270(52), 253(31), 190(57), 163(38), 111(73), 82(62).

(E)-Diethyl 1-cyano-2-(4-methoxyphenyl)-vinylphosphonate (**3d**):[8] Yield: 81%, oil, ν_{max}/cm^{-1}. 2990, 2210, 1610, 1590, 1510, 1260, 1180, 1070, 1020, 980 δ_H 7.96(d, J = 8.8Hz, 2H), 7.91(d, J = 21.2Hz, 1H), 6.97(d, J = 9.0Hz, 2H), 4.24–4.15(m, 4H), 3.87(s, 3H), 1.39(t, J = 7.1Hz, 6H); 295(M$^+$, 100), 280(10), 266(33), 249(32), 186(71), 157(51), 138(41), 111(87), 82(50).

(E)-Diethyl 1-cyano-2-(2-methylphenyl)-vinylphosphonate (**3e**): Yield: 83%, oil, ν_{max}/cm^{-1}. 2990, 2210, 1590, 1560, 1260, 1070, 1020, 980. δ_H 7.95(d, J = 21.4Hz, 1H), 7.86(d, J = 8.2Hz, 2H), 7.28(d, J = 8.1Hz, 2H), 4.27–4.15(m, 4H), 2.43(s,3H), 1.41(t, J = 7.0Hz, 6H); m/z 279(M$^+$,88), 264(30), 250(64), 170(100), 142(58), 111(95), 82(62). (Found: C, 60.14; H, 6.51; N, 5.18. $C_{14}H_{18}NO_3P$ (279.28) requires C, 60.21; H, 6.50; N, 5.02%).

(E)-Diethyl 1-cyano-2-(4-dimethylaminophenyl)-vinylphosphonate (**3f**):[9] Yield: 97%, oil, ν_{max}/cm^{-1}. 2200, 1610, 1570, 1520, 1260, 1020, 970. δ_H 7.90(d, J = 9.0Hz, 2H), 7.80(d, J = 21.0Hz, 1H), 6.68(d, J = 9.0Hz, 2H), 4.23–4.12(m, 4H), 3.09(s,6H), 1.38(t, J = 7.0Hz, 6H); m/z 308(M$^+$,100), 280(17), 234(20), 170(85), 126(7).

(E)-Diethyl 1-cyano-2-(4-nitrophenyl)-vinylphosphonate (**3g**):[9] Yield: 94%, oil, ν_{max}/cm^{-1}. 2990, 2220, 1590, 1520, 1350, 1260, 1010, 980. δ_H 8.34(d, J = 7.0Hz, 2H), 8.09(d, J = 7.0, 2H), 8.06(d, J = 21.2Hz, 1H), 4.30–4.21(m, 4H), 1.42(t, J = 7.0Hz, 6H); m/z 310(M$^+$,24), 293(22), 281(41), 265(84), 235(63), 201(30), 155(67), 111(60), 82(100).

(E)-Diethyl 1-cyano-2-(3-bromophenyl)-vinylphosphonate (**3h**): Yield: 89%, oil, ν_{max}/cm^{-1}. 2990, 2220, 1600, 1560, 1260, 1060, 1020, 980. δ_H 8.01(d, J = 1.5Hz, 1H), 7.92(d, J = 21Hz, 1H), 7.91(d, J = 8.1Hz, 1H), 7.65(dd, J = 8.0, 1.1Hz, 1H), 7.37(,t J = 8.0Hz, 1H), 4.29–4.17(m, 4H), 1.40(t, J = 7.0Hz, 6H); m/z 343(M$^+$-1, 60), 315(51), 296(27), 270(24), 252(23), 236(100), 155(54), 127(75), 111(73), 82(78). (Found: C, 45.31; H, 4.34; N, 5.18. $C_{13}H_{15}BrNO_3P$ (344.14) requires C, 45.37; H, 4.39; N, 4.11%).

(E)-Diethyl 1-cyano-2-(2,4-dichlorophenyl)-vinylphosphonate (**3i**): Yield: 92%, oil, ν_{max}/cm^{-1}. 2990, 2220, 1600, 1580, 1460, 1260, 1050, 1010, 980. δ_H 8.33(d, J = 20.9Hz, 1H), 8.15 (d, J = 8.6Hz, 1H), 7.52(d, J = 2.1Hz, 1H), 7.39(dd, J = 8.6, 2.1Hz, 1H), 4.30–4.22(m, 4H), 1.42(t, J = 7.1Hz,6H); m/z 337(M$^+$+4, 4), 335(M$^+$+2, 22), 333(M$^+$,35), 298(49), 270(19), 242(100), 224(12), 161(9), 111(11). (Found: C, 46.33; H, 4.20; N, 4.15. $C_{13}H_{14}C1_2NO_3P$ (334.14) requires C, 46.73; H, 4.22; N, 4.19%).

General procedure for the preparation of α-ethoxycarbonylvinylphosphonates **7**: The procedure was similar to that for the preparation of **3** but the temperature was raised to 60 °C.

(E)-Diethyl 1-ethoxycarbonyl-2(4-chlorophenyl)-vinylphosphonate (**7a**):[10] Yield: 68%, oil, ν_{max}/cm^{-1}. 2990, 1720, 1620, 1590, 1490, 1260, 1220, 1060, 1020, 970. δ_H 7.58(d, J = 24Hz, 1H), 7.37–7.31(m, 4H), 4.26(q, J = 7Hz, 2H), 4.21–4.12(m, 4H), 1.35(t, J = 7.0Hz, 6H), 1.25(t, J = 7.1Hz, 3H); m/z 348(M$^+$+2,17), 346(M$^+$,68), 300(100), 272(6), 244(4), 163(5), 136(6).

(E)-Diethyl 1-ethoxycarbonyl-2-(2-methoxyphenyl)-vinylphosphonate (**7b**):[10] Yield: 75%, oil, ν_{max}/cm^{-1}. 2990, 1720, 1600, 1260, 1210, 1060, 1020, 970. δ_H 7.90(d, J = 24.2Hz, 1H), 7.33–7.27(m, 2H), 6.88–6.83(m, 2H), 4.20–4.12(m, 6H), 3.78(s, 3H), 1.32(t, J = 7.0Hz, 6H), 1.14(t, J = 7.0Hz, 3H); m/z 343(M$^+$+1,31), 311(54), 297(100), 237(18), 131(32), 209(7).

(E)-Diethyl 1-ethoxycarbonyl-2-(4-methoxyphenyl)-vinylphosphonate (**7c**):[9] Yield: 80%, oil, ν_{max}/cm^{-1}. 2980, 1720, 1600, 1510, 1260, 1060, 1030, 970. δ_H 7.52(d, J = 24.4Hz, 1H), 7.36(d, J = 8.8Hz, 2H), 6.83(d, J = 8.8Hz, 2H), 4.26(q, J = 7.1Hz, 2H), 4.17–4.08(m, 4H), 3.78(s, 3H), 1.31(t, J = 7.0Hz, 6H), 1.24(t, J = 7.1Hz, 3H); m/z 342(M$^+$,21), 297(32), 269(39), 250(38), 213(63), 160(41), 132(30), 81(65), 69(100).

(E)-Diethyl 1-ethoxycarbonyl-2-(4-methylphenyl)-vinylphosphonate (**7d**):[11] Yield: 86%, oil, ν_{max}/cm^{-1}. 2990, 1720, 1610, 1260, 1210, 1060, 1020, 970. δ_H 7.59(d, J = 24.2Hz, 1H), 7.30(d, J = 8.1Hz, 2H), 7.16(d, J = 8.1Hz, 2H), 4.27(q, J = 7.1Hz, 2H), 4.22–4.10(m, 4H), 2.35(s, 3H), 1.34(t, J = 7.0Hz, 6H), 1.25(t, J = 7.1Hz, 3H); m/z 326(M$^+$,21), 281(69), 253(47), 225(48), 197(100), 144(45), 116(48).

(E)-Diethyl 1-ethoxycarbonyl-2-(3-bromophenyl)-vinylphosphonate (**7e**):[9] Yield: 74%, oil, ν_{max}/cm^{-1}. 2990, 1720, 1620, 1560, 1260, 1220, 1060, 1020, 970. δ_H 7.56(d, J = 23.9Hz, 1H), 7.54–7.48(m, 2H), 7.33–7.20(m, 2H), 4.27(q, J = 7.1Hz, 2H), 4.22–4.12(m, 4H), 1.33(t, J = 7.0Hz, 6H), 1.24(t, J = 7.1Hz, 3H); m/z 393(M$^+$+2, 37), 391(M$^+$,40), 344(66), 316(41), 263(100), 210(55), 182(55), 129(65), 101(88).

We thank the National Natural Science Foundation of China, the Laboratory of Organometallic Chemistry, and Academia Sinica for financial support.

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