

Stereoselective Synthesis of Dialkyl 2-(3-Methoxy-1-oxoinden-2-yl)-3-(dimethylphosphonato)-butanedioates†

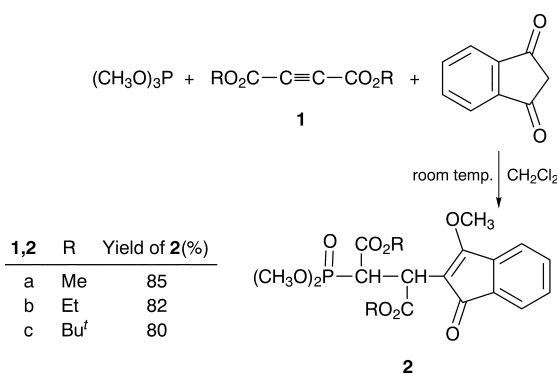
Issa Yavari,^{*a} Mohammad Hossein Mosslemin^b and Ali Reza Montahaei^b

^aChemistry Department, Tarbiat Modarres University, PO Box 14155-4838, Tehran, Iran

^bChemistry Department, Shahid Beheshti University, PO Box 19839, Evin, Tehran, Iran

Protonation of the reactive intermediate produced in the reaction between trimethyl phosphite and dialkyl acetylenedicarboxylates by indane-1,3-dione leads to vinyltrimethoxyphosphonium cation, which undergoes addition reaction with the enolate anion of the CH-acid to produce the title compounds in fairly high yields.

Organophosphorus compounds, *i.e.* those bearing a carbon atom bound directly to a phosphorus atom, are synthetic targets of interest, not least because of their value for a variety of industrial, biological and chemical synthetic uses.^{1–3} As a result a large number of methods have appeared describing novel syntheses of organophosphorus compounds. The attack by nucleophilic trivalent phosphorus on a carbon atom is facilitated when the latter is part of, or conjugated with, a carbonyl group, or when it is part of an unsaturated bond otherwise activated.^{1–9} There are many studies on the reaction between trivalent phosphorus nucleophiles and α,β -unsaturated carbonyl compounds using alcohols or phenols as reaction adjuncts.¹⁰ The work reported here was undertaken in order to determine the possibility of trapping the reactive 1:1 intermediate formed in the initial reaction between trimethyl phosphite and dialkyl acetylenedicarboxylates **1** by a carbon acid such as indane-1,3-dione. Thus, reaction of acetylenic esters **1** with trimethyl phosphite in the presence of indane-1,3-dione leads to dialkyl 2-(3-methoxy-1-oxoinden-2-yl)-3-(dimethylphosphonato)butanedioates **2** in fairly high yields.

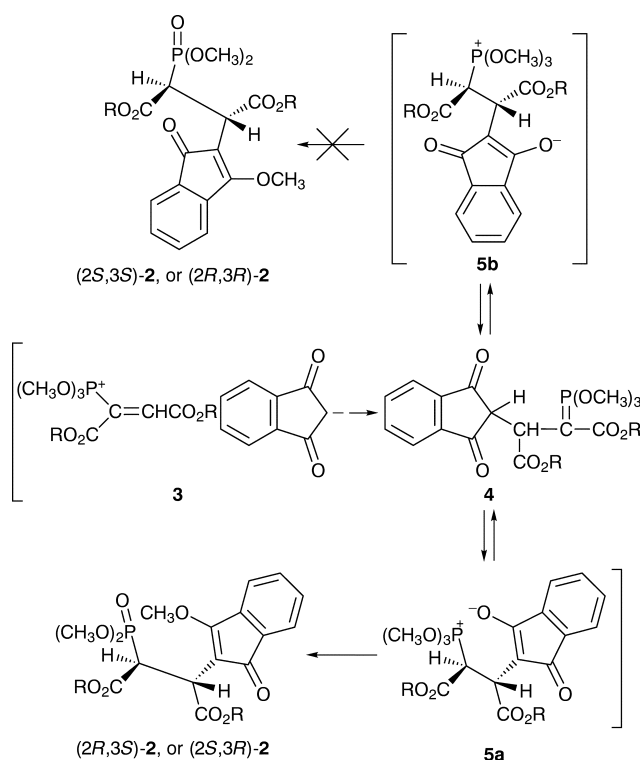


This three-component reaction produces the hitherto unknown butanedioates **2a–c** in 80–85% yields. All the compounds are stable crystalline solids whose structure is fully supported by elemental analyses and IR, ¹H NMR, ¹³C NMR and mass spectral data. The mass spectra of these 1:1:1 adducts displayed molecular ion peaks at *m/z* 412, 440 and 496 for **2a**, **2b** and **2c**, respectively. Any initial fragmentation involved the loss of ester moieties.

On the basis of the well-established chemistry of trivalent phosphorus nucleophiles^{3–10} it is reasonable to assume that compound **2** results from the initial addition of trimethyl phosphite to the acetylenic ester and a concomitant protonation of the 1:1 adduct by indane-1,3-dione (see

Scheme 1). Then, the positively charged ion is attacked by the enolate anion of the CH-acid to form intermediate **4**, which is then converted to the phosphonate ester **2** by nucleophilic attack on the methyl group.

The ¹H NMR spectra of compounds **2a–c** displayed signals for vicinal methine protons at δ 4.22–4.75, which appear as double doublets with ²*J*_{HP} and ³*J*_{HP} values of 20.3–20.7 and 5.6 Hz, respectively. The methyl groups of the phosphonate ester fragment are diastereotopic and show two separate doublets in the ¹H and ¹³C NMR spectra. The methyl group of the enol ether fragment exhibits distinct signals in the ¹H and ¹³C NMR spectra. The presence of the ³¹P nucleus in compounds **2a–c** helps in assignment of the signals by long-range couplings with ¹H and ¹³C nuclei (see Table 1). The vicinal proton–proton coupling constant (³*J*_{HH}) as a function of torsion angle can be obtained from the Karplus equation.¹¹ Typically, *J*_{gauche} varies between 1.5 and 5 Hz and *J*_{anti} between 10 and 14 Hz. Observation of ³*J*_{HH} = 11.5–11.7 Hz for the vicinal protons in compounds **2a–c** (see Table 1) indicates an *anti* arrangement for these protons. Since compound **2** possesses two stereogenic centers, two diastereoisomers with *anti* HCCH arrangements are possible (see Scheme 1).



Scheme 1

*To receive any correspondence

†This is a Short Paper as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 ^1H and ^{13}C NMR data for compounds **2a–c**

Compound	$^1\text{H}/^{13}\text{C}$	δ (ppm) ($\text{CDCl}_3\text{-Me}_4\text{Si}$)
2a	^1H	3.53 (3 H, d $^3J_{\text{PH}}$ 11.2 Hz, P–OCH ₃), 3.67 (3 H, d $^3J_{\text{PH}}$ 11.2 Hz, POCH ₃), 3.68 and 3.84 (6 H, 2 s, 2CO ₂ CH ₃), 4.28 (1 H, dd $^2J_{\text{PH}}$ 20.7 Hz $^3J_{\text{HH}}$ 11.7 Hz, P–CH), 4.50 (3 H, s, OCH ₃), 4.75 (1 H, dd $^3J_{\text{PH}}$ 5.6 Hz, $^3J_{\text{HH}}$ 11.7 Hz, P–C–CH), 7.1–7.5 (4 H, m, Ar)
	^{13}C	39.58 (d $^2J_{\text{PC}}$ 3 Hz, P–C– ^{13}C), 44.39 (d $^1J_{\text{PC}}$ 132.5 Hz, P–C), 52.81 and 52.83 ($^{13}\text{CH}_3\text{O–C=O}$), 53.14 (d $^2J_{\text{PC}}$ 7.3 Hz, POCH ₃), 53.46 (d $^2J_{\text{PC}}$ 7.3 Hz, POCH ₃), 59.53 (CH ₃ –O), 104.63 (d $^3J_{\text{PC}}$ 2.7 Hz, $^{13}\text{C=C–O}$), 119.56, 120.86, 130.06 and 132.79 (CH), 131.77 and 140.16 (2C), 169.03 (d $^3J_{\text{PH}}$ 5.5 Hz, C=O), 171.25 (d $^2J_{\text{PH}}$ 21.2 Hz, C=O), 172.82 (C– $^{13}\text{C=O}$), 194.69 (C=O)
2b	^1H	1.20 (3 H, t $^3J_{\text{HH}}$ 7.2 Hz, CH ₃), 1.34 (3 H, t $^3J_{\text{HH}}$ 7.2 Hz, CH ₃), 3.58 (3 H, d $^3J_{\text{PH}}$ 11.2 Hz, P–OCH ₃), 3.67 (3 H, d $^3J_{\text{PH}}$ 11.2 Hz, P–OCH ₃), 4.15 (2 H, q $^3J_{\text{HH}}$ 7.2 Hz, OCH ₂), 4.23 (2 H, q $^3J_{\text{HH}}$ 7.2 Hz, OCH ₂), 4.30 (1 H, dd $^2J_{\text{PH}}$ 20.6 Hz $^3J_{\text{HH}}$ 11.5 Hz, P–CH), 4.53 (3 H, s, OCH ₃), 4.75 (1 H, dd $^3J_{\text{PH}}$ 5.6 Hz $^3J_{\text{HH}}$ 11.5 Hz, P–C–CH), 7.2–7.6 (4 H, m, Ar)
	^{13}C	14.01 and 14.02 (2CH ₃), 39.78 (d $^2J_{\text{PC}}$ 3 Hz, P–C– ^{13}CH), 44.47 (d $^1J_{\text{PC}}$ 132.5 Hz, P–CH), 53.08 (d $^2J_{\text{PC}}$ 7.4 Hz, P–OCH ₃), 53.38 (d J_{PC} 7.4 Hz, P–OCH ₃), 59.49 (OCH ₃), 61.73 and 61.74 (2OCH ₂), 104.9 (d $^3J_{\text{PC}}$ 2.8 Hz, $^{13}\text{C=C–O}$), 119.43, 120.82, 129.94 and 132.67 (4CH), 131.81 and 140.28 (2C), 168.54 (d $^3J_{\text{PC}}$ 5.5 Hz, C=O), 170.58 (ds $^2J_{\text{PC}}$ 22.1 Hz, C=O), 172.74 (C– $^{13}\text{C=O}$), 194.73 (C=O)
2c	^1H	1.42 and 1.52 (18 H, 2CMe ₃), 3.55 (3 H, d $^3J_{\text{PH}}$ 11.2 Hz, P–OCH ₃), 3.68 (3 H, d $^3J_{\text{PH}}$ 11.2 Hz, P–OCH ₃), 4.22 (1 H, dd $^2J_{\text{PH}}$ 20.3 Hz $^3J_{\text{HH}}$ 11.5 Hz, P–CH), 4.53 (3 H, s, OCH ₃), 4.63 (1 H, dd $^3J_{\text{PH}}$ 5.6 Hz $^3J_{\text{HH}}$ 11.5 Hz, P–C–CH), 7.2–7.6 (4 H, m, Ar)
	^{13}C	27.35 and 27.36 (6CH ₃ of 2CMe ₃), 40.23 (d $^2J_{\text{PC}}$ 3 Hz, P–C– ^{13}C), 44.59 (d $^1J_{\text{PC}}$ 130.7 Hz, P–C), 52.35 (d $^2J_{\text{PC}}$ 7.2 Hz, POCH ₃), 52.65 (d $^2J_{\text{PC}}$ 7.2 Hz, POCH ₃), 58.88 (OCH ₃), 81.32 and 81.48 (2 ^{13}C of 2 $^{13}\text{CMe}_3$), 104.77 (d $^3J_{\text{PC}}$ 2.7 Hz, $^{13}\text{C=C–O}$), 118.70, 120.25, 129.28 and 132.05 (4CH), 131.40 and 139.91 (2C), 166.98 (d $^3J_{\text{PC}}$ 5.5 Hz, C=O), 169.20 (d $^2J_{\text{PC}}$ 22.1 Hz, C=O), 172.04 (C– $^{13}\text{C=O}$), 194.15 (C=O)

The three-bond carbon–phosphorus coupling, $^3J_{\text{CP}}$, depends on configuration, as expected, *transoid* couplings being larger than *cisoid* ones. The Karplus relation can be derived from the data for organophosphorus compounds with tetra- and penta-valent phosphorus.¹² The observation of $^3J_{\text{CP}}$ of 5.5 Hz for the ester C=O group (see Table 1), is in agreement with the (2*R*,3*S*)-**2** and its mirror image (2*S*,3*R*)-**2** geometries.

We have not established a mechanism for the formation (2*S*,3*R*)-**2** and its mirror-image geometry, but a reasonable possibility is indicated in Scheme 1. The enolization step of this mechanism involves two diastereoisomeric enolate anions (**5a** and **5b**). Only one of these diastereoisomers, namely **5a** is well suited for nucleophilic attack on the methyl group to produce the phosphonate ester **2** (see Scheme 1).

Experimental

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses for C and H were performed using a Heraeus CHN-O-Rapid analyser. IR spectra were measured on a Shimadzu IR-470 spectrometer. ^1H and ^{13}C NMR spectra were measured with a JEOL EX-90A spectrometer at 90 and 22.6 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Acetylenic esters, trimethyl phosphite and indane-1,3-dione were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

The typical process for the preparation of dimethyl 2-(3-methoxy-1-oxoinden-2-yl)-3-(dimethylphosphonato)butanedioate **2a** is described as an example. To a magnetically stirred solution of indane-1,3-dione (0.292 g, 2 mmol) and dimethyl acetylenedicarboxylate (0.284 g, 2 mmol) in dichloromethane (4 ml) was added dropwise a mixture of trimethyl phosphite (0.248 g, 2 mmol) in dichloromethane (94 ml) at -5°C over 10 min. The reaction mixture was then allowed to warm to room temperature and stirred for 24 h. The solvent was removed under reduced pressure and the residue was purified by silica gel (Merck silica gel 60, 230–400 mesh) column chromatography using hexane–ethyl acetate as eluent. The solvent was removed under reduced pressure to afford the product (0.70 g, mp $98\text{--}100^\circ\text{C}$, yield 85%) which was recrystallized from ethyl acetate to yield **2a** as yellow crystals (0.64 g), mp $100\text{--}101^\circ\text{C}$. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 1734 (C=O); 1695 and 1617 (C=C–C=O); 1224 (P=O); 1046 and 1033 (C–O and P–O). MS (m/z , %): 412 (M^+ , 6); 380 ($\text{M} - \text{CH}_3\text{OH}$, 56); 348 ($380 - \text{CH}_3\text{OH}$, 27); 321 ($380 - \text{CO}_2\text{CH}_3$, 100); 333 ($348 - \text{CH}_3$, 89); 231 [$\text{M} - \text{CH}(\text{CO}_2\text{CH}_3)\text{PO}(\text{OCH}_3)_2$, 21]; 109 [$(\text{CH}_3\text{O})_2\text{P=O}$, 79].

Anal. calc. for $\text{C}_{18}\text{H}_{21}\text{O}_9\text{P}$ (M^+ 412.32): C, 52.43; H 5.13%. Found: C, 52.3; H, 5.0%. Selected data for **2b**: Yellow crystals, 0.72 g, mp $92\text{--}93^\circ\text{C}$, yield 82%. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 1728 and 1723 (C=O); 1690 and 1615 (C=C–C=O); 1223 (P=O); 1045 and 1031 (C=O and P=O). MS (m/z , %): 440 (M^+ , 4); 394 ($\text{M}^+ - \text{EtOH}$, 30); 379 ($394 - \text{CH}_3$, 31); 333 ($379 - \text{EtOH}$, 58); 321 ($394 - \text{CO}_2\text{Et}$, 100); 109 [$(\text{CH}_3\text{O})_2\text{P=O}$, 62]. Anal. calc. for $\text{C}_{20}\text{H}_{25}\text{O}_9\text{P}$ (M_r 440.37): C, 54.55; H, 5.72%. Found: C, 54.5; H, 5.6%. Selected data for **2c**: Yellow crystals, 0.79 g, mp $101\text{--}102^\circ\text{C}$, yield 80%. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 1729 and 1723 (C=O); 1621 (C=C–C=O); 1049 and 1026 (C–O and P–O). MS (m/z , %): 496 (M^+ , 0.5); 440 [$\text{M}^+ - \text{CH}_2\text{C}(\text{CH}_3)_2$, 1.2]; 109 [$(\text{CH}_3\text{O})_2\text{P=O}$, 7.3]; 57 [$\text{C}(\text{CH}_3)_3$, 100]. Anal. calc. for $\text{C}_{24}\text{H}_{33}\text{O}_9\text{P}$ (M_r 496.47): C, 58.06; H, 6.70%. Found: C, 58.0; H, 6.6%.

Received, 17th February 1998; Accepted, 18th May 1998
Paper E/8/01363B

References cited in this synopsis

- R. Engel, *Synthesis of Carbon-Phosphorus Bonds*, CRC Press, Boca Raton, FL, 1988.
- D. E. C. Corbridge, *Phosphorus, An Outline of Chemistry, Biochemistry and Uses*, 5th edn., Elsevier, Amsterdam, 1995.
- J. I. G. Cadogan, *Organophosphorus Reagents in Organic Synthesis*, Academic Press, New York, 1979.
- H. R. Hudson, in *The Chemistry of Organophosphorus Compounds, Volume 1. Primary, Secondary and Tertiary Phosphines, Polyphosphines and Heterocyclic Organophosphorus (III) Compounds*, ed. F. R. Hartley, Wiley, New York, 1990, pp. 386–472.
- R. A. Cherkasov and M. A. Pudovic, *Russ. Chem. Rev.*, 1994, **63**, 1019.
- A. R. Ardoage III and C. A. Stewart, *Chem. Rev.*, 1994, **94**, 1215.
- K. M. Pietrusiewicz and M. Zablocka, *Chem. Rev.*, 1994, **94**, 1375.
- H. J. Bestmann and O. Vostrowsky, *Top. Curr. Chem.*, 1983, **109**, 86.
- I. Yavari, A. Khorramabadi-Zad, P. Rashidi-Ranjbar and H. Fallah-Bagher-Shaidaii, *J. Mol. Struct. (THEOCHEM)*, 1977, **155**, 389.
- R. Burgada, Y. Leroux and Y. O. El Khoshnieh, *Tetrahedron Lett.*, 1981, **22**, 3533.
- M. Karplus, *J. Am. Chem. Soc.*, 1963, **85**, 2870; C. A. G. Haasnoot, F. A. A. M. de Leeuw and C. Altona, *Tetrahedron*, 1980, **36**, 2783.
- E. Breitmaier and W. Voelter, *Carbon-13 NMR Spectroscopy*, 3rd edn., VCH, New York, 1990, pp. 250–254.