Triphenylphosphine-mediated synthesis of 5-oxo-2,5-dihydrofurans through the reaction of dialkyl acetylenedicarboxylates and butane-2,3-dione

Issa Yavari*, Rahebeh Amiri and Mina Haghdadi

Department of Chemistry, Islamic Azad University, Science and Research Campus, Tehran, Iran and Department of Chemistry, Tarbiat Modarres University, PO Box 14115-175, Tehran, Iran

Dimethyl or diethyl acetylenedicarboxylates undergo smooth reactions with butane-2,3-dione in the presence of triphenylphosphine to yield highly functionalised 5-oxo-2,5-dihydrofurans; using di-*t*-butyl acetylenedicarboxylate affords a cyclopentenone derivative.

Keywords: 1,2-dione, acetylenic esters, triphenylphosphine, 5-oxo-2,5-dihydrofuran, cyclopentenone

The carbonyl group is one of the useful functional groups in organic synthesis due to facile 1,2-addition of nucleophiles across the π-bond. Commercially available compounds containing a C=O unit are abundant, and the products of their addition reactions are valuable synthetic intermediates. 1,2-Diones have been used to produce biologically active compounds.[1–4] The reaction of *ortho*-quinones and dimethyl acetylenedicarboxylate in the presence of triphenylphosphine was reported to produce hetero-spiro compound.[5,6] Previous examples of this reaction seem to include only vicinal diketones that are unable to undergo enolisation.

We now report a simple one-pot preparation of alkyl 2-acetyl-4-alkyloxy-2-methyl-5-oxo-2,5-dihydro-furan-3-carboxylates **2a** and **2b** using butane-2,3-dione, dialkyl acetylenedicarboxylates **1** and triphenylphosphine in fairly good yields (Scheme 1).

Surprisingly, di-*t*-butyl acetylenedicarboxylate **3** reacts with butane-2,3-dione in the presence of triphenylphosphine to afford di-*t*-butyl 3-methyl-4-oxo-cyclopent-2-ene-1,2-dicarboxylate **4** (Scheme 2).

The structures of compounds **2a, 2b,** and **4** were deduced from their elemental analyses and their IR, ^{1}H and ^{13}C NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at appropriate *m*/*z* values.

The ^{1}H NMR spectrum of **2a** exhibited four single sharp lines readily recognized as arising from methoxy (δ = 3.85 and 4.27 ppm) and methyl (δ = 2.18 and 1.75 ppm) protons. The ^{13}C NMR spectrum of **2a** showed 10 distinct resonances in agreement with the proposed structure.

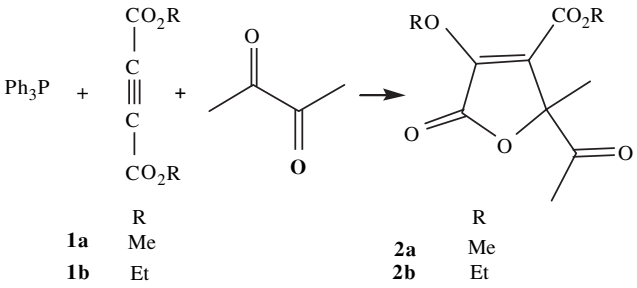
The ^{1}H NMR spectrum of **2b** is similar to that of **2a** except for the alkoxy groups, which give rise to characteristic signals in appropriate regions of the spectrum.

The formation of furanones **2** can be rationalised as shown in Scheme 3. The reaction starts with nucleophilic attack of triphenylphosphine on the electron-deficient acetylenic compound and subsequent addition to one of the carbonyl groups of butane-2,3-dione to give intermediate **5,** which undergoes intramolecular lactonisation and subsequent attack of the alkoxy group on the positively-charged ion **6** to afford **2**.

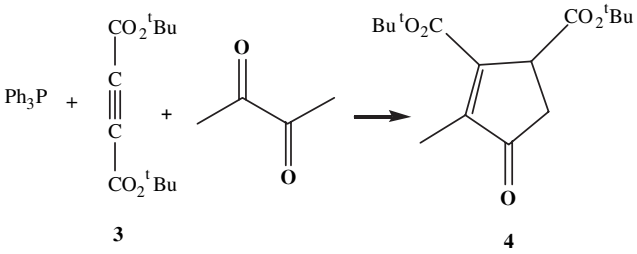
The ^{1}H NMR spectrum of **4** displayed a characteristic ABX system for the CH_2CH moiety of the five-membered ring. The ^{13}C NMR spectrum of **4** showed the carbonyl group at δ = 207.8 ppm.

A plausible mechanism for formation of **4** is proposed in Scheme 4. It is reasonable to assume that ylide **8** results from nucleophilic addition of the enolate anion of butane-2,3-dione to intermediate **7** and subsequent ring closure followed by elimination of triphenylphosphine oxide to produce **4**.

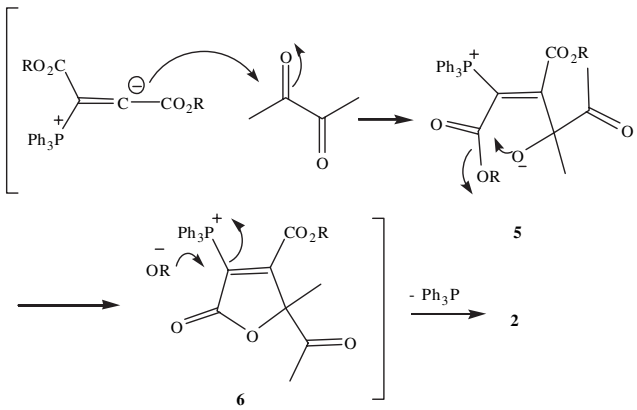
* Correspondence. E-mail: isayavar@yahoo.com



Scheme 1



Scheme 2

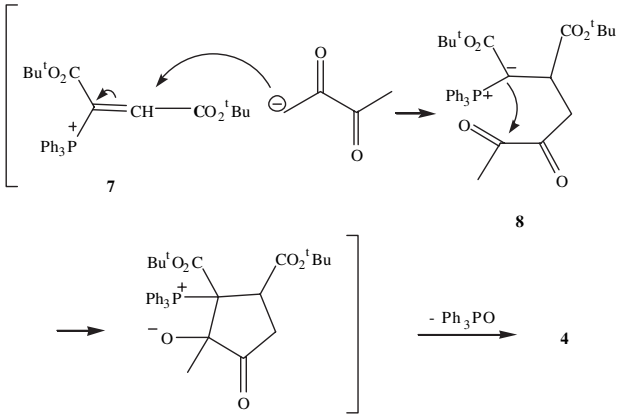


Scheme 3

These reactions provide simple entries to the synthesis of 5-oxo-2,5-dihydrofuran and cyclopantenone derivatives of potential synthetic interest.

Experimental

Melting points were measured on an Electrothermal 9100 apparatus. Elemental analysis for C, H, and N were performed using a Heraeus CHN-O-Rapid analyser. IR spectra were measured on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a Bruker DRX-300 AVANCE instrument with $CDCl_3$ as solvent at



Scheme 4

300.1 and 75.5 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionisation potential of 70 eV. Butane-2,3-dione, dialkyl acetylenedicarboxylates and triphenylphosphine were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

Methyl 2-acetyl-4-methoxy-2-methyl-5-oxo-2,5-dihydro-furan-3-carboxylate (**2a**): To a stirred solution of triphenylphosphine (0.52 g, 2 mmol) and butane-2,3-dione (2 mmol) in CH_2Cl_2 (10 ml) was added drop wise at –5°C over 2 min dimethyl acetylenedicaboxylate (0.28 g, 2 mmol). The reaction mixture was then allowed to warm up to room temperature and stand for 24 h. The residue was separated by thin layer chromatography (Kieselgel 60 $HF_{254+366}$) using 3:1 *n*-hexane-EtOAc. Compound 2a was obtained as yellow oil; yield: 0.19 g (85%). IR (KBr): 1779, 1734, and 1709 (3 C O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.75 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3), 3.85 (s, 3 H, CO_2CH_3), 4.27 (s, 3 H, OCH_3) ppm.

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.0 (CH_3), 32.88 (CH_3), 52.9 (CO_2CH_3), 60.3 (OCH_3), 87.0 (C), 124.0, 148.4 (C=C), 161.8 and 165.9 (2 C=O, ester), 200.6 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 229 (M^++1, 90), 197 (32), 154 (25), 67 (12), 43 (100). Anal. Calcd for $C_{10}H_{12}O_6$ (228.0): C, 52.67; H, 5.26. Found: C, 52.6; H, 5.2.

Ethyl 2-acetyl-4-methoxy-2-methyl-5-oxo-2,5-dihydro-furan-3-carboxylate (**2b**): Yellow oil; yield: 0.20 g (80%). IR (KBr): 1778, 1731, and 1707 (3 C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, 3 H, $^3J_{HH}$ = 7 Hz, CH_3), 1.43 (t, 3 H, $^3J_{HH}$ = 7 Hz, CH_3), 1.73 (s, 3 H, CH_3), 2.16 (s, 3 H, CH_3), 4.29 (q, 2 H, $^3J_{HH}$ = 7 Hz, OCH_2), 4.64 (m, 2 H, ABX_3 System, $^2J_{AB}$ = 15 Hz, $^3J_{AX}$ = 7 Hz, $^3J_{BX}$ = 7 Hz, $\Delta\nu_{AB}$ = 10 Hz, OCH_2) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.3 (CH_3), 15.8 (CH_3), 20.1 (CH_3), 23.8 (CH_3), 62.2 (CO_2CH_2), 69.1 (OCH_2), 87.1 (C), 124.6, 147.9 (C=C), 161.4 and 166.2 (2 C O, ester), 200.7 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 257 (M^++1, 3), 214 (80), 157 (78), 111 (75), 43 (100), 29 (57). Anal. Calcd for $C_{12}H_{16}O_6$ (256.0): C, 56.30; H, 6.25. Found: C, 56.3; H, 6.2.

Di-t-butyl 3-methyl-4-oxo-cyclopent-2-ene-1,2-dicarboxylate (**4**): Yellow oil; yield: 0.22 g (75%). IR (KBr): 1773, 1737, and 1720 (3 C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.46 (s, 9 H, CMe_3), 1.56 (s, 9 H, CMe_3), 2.07 (d, 3H, $^5J_{HH}$ = 2 Hz, CH_3), 2.75, 2.47 (dd, 2 H, $^2J_{HH}$ = 19 Hz, $^3J_{gauche}$ = 3 Hz and $^3J_{anti}$ = 8 Hz, CH_2), 3.83 (dqd, 1 H, $^3J_{anti}$ = 7 Hz, $^3J_{gauche}$ = 3 Hz and $^5J_{HH}$ = 2 Hz, CH), ppm.

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.3 (CMe_3), 28.5 (CMe_3), 30.1 (CH), 38.8 (CH_3), 45.5 (CH_2), 82.1 (CMe_3), 83.0 (CMe_3), 147.7, 154.3 (C=C), 164.1 and 171.7

(2 C=O, ester), 207.8 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 297 (M^++1, 2), 196 (38), 167 (42), 139 (85), 57 (100), 41 (39). Anal. Calcd for $C_{16}H_{24}O_5$ (296.1): C, 64.90; H, 8.10. Found: C, 64.9; H, 8.0.

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