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Regioselective Reaction between 3-Ethoxalyl-5-methylcyclopentane-1,2,4-trione and Vinyltriphenylphosphonium Salts: Convenient Synthetic Route to Functionalized Cyclopenta[*b*]furans†

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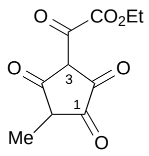
3-Ethoxalyl-5-methylcyclopentane-1,2,4-trione exists, in solution, almost exclusively as the dienol tautomer, which undergoes regioselective intramolecular Wittig reaction with vinyltriphenylphosphonium salts to produce the enol form of dialkyl 4-ethoxalyl-6-methyl-5-oxo-4,5-dihydro-3a*H*-cyclopenta[*b*]furan-2,3-dicarboxylates in moderate yields.

Controlling the regiochemical aspects of reaction selectivity has always been a prime challenge to synthetic organic chemists.[1] These concerns are especially pressing when the preparations of multifunctional substances of specific biological action are involved. Among the various techniques with which a densely functionalized furan ring can be constructed, carbon–carbon bond-forming reactions of readily available precursors by means of various reactive carbon entities are amongst the more widely pursued synthetic strategies.[2] Vinyltriphenylphosphonium salts, used in intramolecular Wittig reactions,[3–5] endowed with variable functionalities would constitute a remarkable premium in terms of synthetic efficiency and flexibility.

3-Ethoxalyl-5-methylcyclopentane-1,2,4-trione (**1**) is a readily available[6] multifunctional system, which is apparently completey enolized in the liquid phase, as indicated by ^{1}H and ^{13}C NMR spectroscopy.



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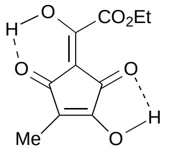


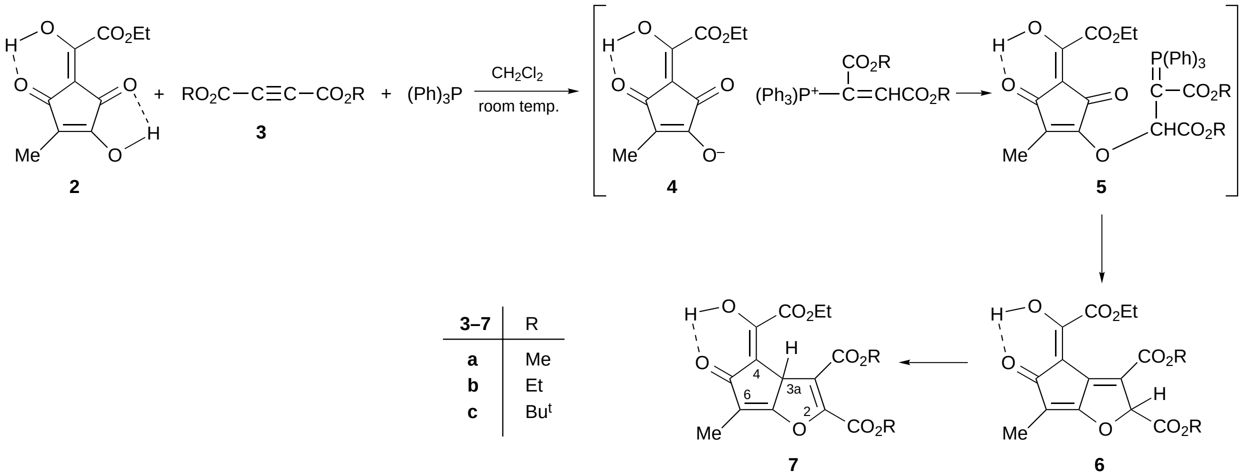
2

The enol tautomer **2** has two acidic protons, of which the proton involved in five-membered-ring hydrogen bonding is the more accessible.[7,8] As part of our current studies on the development of new routes to heterocyclic systems,[9–11] we thought that an easy approach to vinyltriphenylphosphonium salts could represent a practical route to functionalized cyclopentafurans *via* an intramolecular Wittig reaction. We now report a facile one-pot synthesis of dialkyl 4-ethoxalyl-6-methyl-5-oxo-4,5-dihydro-3a*H*-cyclopenta[*b*]furan-2,3-dicarboxylates (**7**) in moderate yields.

Results and Discussion

Several examples are known in which a heterocyclic alkene is produced from a phosphorane connected to a carbonyl group by a chain containing a heteroatom.[3] Thus, the cyclopentafuran derivative **6** may be regarded as a product of an intramolecular Wittig reaction. Such addition–cyclization products apparently result from initial addition of triphenylphosphine to the acetylenic ester and concomitant protonation of the 1:1 adduct, followed by attack of the anion of **2** to vinyltriphenylphosphonium cation to form a phosphorane **5**, which is converted into the furan **6**. Compound **6** apparently isomerizes, under the reaction conditions, to produce the sterically favoured isomer **7** (see Scheme 1).

Structure **7** was assigned to the isolated products on the basis of their elemental analyses and IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. NMR spectroscopy was used to distinguish structure **7** from the primary product, the 2*H*-furan derivative **6**. Thus, the ^{1}H NMR spectrum of each of the isolated products showed a methine proton signal at about δ 4.5. The expected chemical shift for the CH group in structure **6** is *ca.* 5.8 ppm.[10] Further evidence was obtained from the ^{13}C NMR spectra which displayed a methine carbon resonance at δ 44–46. Structure **7** was further confirmed by comparison of the ^{1}H and ^{13}C NMR spectral data for the isolated products with those for the enol tautomers of 3-methylcyclopentane-1,2,4-tione (**8**) and **2**. The methyl carbon resonances of **7a–c**, **8** and **2** all appear at *ca.* δ 6.5, which indicates a fairly similar environment for this group (see Table 1).



3–7	R
a	Me
b	Et
c	Bu^t

Scheme 1

The mass spectra of the isolated products **7a–c** are similar,

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1997, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Proton and carbon-13 NMR data for compounds **8**, **2** and **7a–c**

Compound	$^1H/^{13}C$	δ (ppm) ($CDCl_3$–Me_4Si)
8	^1H	1.96 (3 H, s, CH_3), 2.94 (2 H, s, CH_2), 12.9 (1 H, br s, O—H···O═C)
	^{13}C	6.52 (CH_3), 40.76 (CH_2), 132.46 (^{13}C-CH_3), 167.28 (C═C—O), 196.31 and 197.70 (2 C═O)
2	^1H	1.41 (3 H, t, *J* 7.3 Hz, CH_3), 1.95 (3 H, s, CH_3), 4.43 (2 H, q, *J* 7.3 Hz), 7.9 (2 H, br s, 2 O—H···O═C)
	^{13}C	6.35 (CH_3), 14.05 (CH_3), 62.30 (CH_2O), 103.55 (C-3), 124.73 (C-5), 154.90, 163.01 and 165.16 (2 C═C—O and C═O ester), 187.44 and 191.96 (2 C═O)
7a	^1H	1.42 (3 H, t, *J* 7.3 Hz, CH_3), 1.87 (3 H, s, CH_3), 3.80 and 3.86 (6 H, 2 s, 2 OCH_3), 4.57 (1 H, s, OCH), 4.64 (2 H, q, *J* 7.3 Hz, OCH_2), 12.4 (1 H, br s, O—H···O═C)
	^{13}C	6.52 (CH_3), 15.56 (CH_3), 44.34 (CH), 52.53 and 53.18 (2 OCH_3), 69.02 (OCH_2), 104.49 (C-4), 112.63 (C-3), 127.66 (C-6), 154.21 and 158.81 (C-2 and C-6a), 161.74 and 162.96 (C—-OH and $^{13}CO_2Et$), 167.48 and 169.72 (2 $^{13}CO_2Me$), 194.20 (C═O)
7b	^1H	1.0–1.5 (9 H, m, 3 CH_3 ester), 1.85 (3 H, s, CH_3), 4.56 (1 H, s, OCH), 4.0–4.7 (6 H, m, 3 OCH_2 ester), 12.5 (1 H, br s, O—H···O═C)
	^{13}C	6.52 (CH_3), 13.90, 14.05 and 15.56 (3 CH ester), 44.75 (CH), 61.69, 62.26 and 69.10 (3 OCH_2 ester), 104.33 (C-4), 112.84 (C-3), 128.27 (C-6), 154.13 and 158.85 (C-2 and C-6a), 161.82 and 162.44 (C—OH and $^{13}CO_2Et$), 167.48 and 169.32 (2 $^{13}CO_2Et$), 194.40 (C═O)
7c	^1H	1.40 (3 H, t, *J* 7.3 Hz, CH_3), 1.47 and 1.54 (18 H, 2 s, 2 CMe_3), 4.40 (1 H, s, CH), 4.57 (2 H, q, *J* 7.3 Hz, OCH_2), 12.5 (1 H, br s, O—H···O═C)
	^{13}C	6.52 (CH_3), 15.56 (CH_3 ester), 27.81 and 28.10 (6 CH_3 of 2 CMe_3), 44.06 (CH), 68.70 (OCH_2), 82.95 and 83.11 (2 C of CMe_3), 103.96 (C-4), 113.37 (C-3), 130.88 (C-6), 153.52 and 158.08 (C-2 and C-4a), 161.66 and 161.90 (C—OH and $^{13}CO_2Et$), 167.73 and 168.09 (2 $^{13}CO_2CMe_3$), 194.77 (C═O)

as expected, and confirm their molecular weights. Initial fragmentations involve loss of the ester side chains (ROH, CO_2R, CH_2═CH_2, CO_2Et).

The ^1H NMR spectrum of **7a** displayed four single sharp lines, readily recognizeable as arising from methyl (δ 1.87), methoxy (δ 3.80 and 3.86) and methine (δ 4.57) protons, along with characteristic resonances for the ethoxy group (δ 1.42 and 4.61). A fairly broad band was observed for the OH group at δ 12.4, indicating extensive intramolecular hydrogen-bond formation with the carbonyl group.[12]

The ^{13}C NMR spectrum of **7a** showed sixteen distinct resonances in agreement with the 3a*H*-cyclopentafuran structure. Partial assignments of these resonances are given in Table 1.

The ^1H and ^{13}C NMR spectra of **7b** and **7c** are similar to those of **7a**, except for the ester groups, which display characteristic resonances with appropriate chemical shifts (see Table 1).

Experimental

Mps were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyser. IR spectra were recorded on a Shimadzu IR-460 spectrometer. UV spectra were measured for solutions in ethanol (95%) on a Shimadzu UV-2100 spectrometer. ^1H and ^{13}C NMR spectra were measured with a JEOL EX-90A spectrometer at 90 and 22.65 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Dialkyl acetylenedicarboxylates (**3a–c**), butan-2-one and diethyl oxalate were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

3-Ethoxalyl-5-methylcyclopentane-1,2,4-trione (**2**) and 3-methylcyclopentane-1,2,4-tioine (**8**) were prepared by known methods[6] and identified as shown in Table 1.

A typical process, for the preparation of dimethyl 4-ethoxalyl-6-methyl-5-oxo-4,5-dihydro-3a*H*-cyclopenta[*b*]furan-2,3-dicarboxylate (**7a**), is described below.

Preparation of **7a**.—To a magnetically stirred solution of triphenylphosphine (0.524 g, 2 mmol) and 3-ethoxalyl-5-methylcyclopentane-1,2,4-trione (**2**) (0.452 g, 2 mmol) in CH_2Cl_2 (10 ml) was added, dropwise, a mixture of dimethyl acetylenedicarboxylate (2 mmol) in CH_2Cl_2 (2 ml) at −10 °C over 10 min. The reaction mixture was then allowed to warm up to room temperature and stirred for 24 h. The solvent was removed under reduced pressure and the viscous residue was purified by silica gel (Merck silica gel 60, 230–400 mesh) column chromatography using ethyl acetate–hexane (1:3) as eluent. The solvent was removed under reduced pressure and the product (0.18 g, yellow oil, 52%) was obtained. Recrystallization from absolute ethanol yielded **7a** as a yellow *solid* (0.16 g, 46%), mp 98 °C; ν_{max}/cm^{-1} (KBr) 3400 (OH); 1681, 1701, 1752 and 1782 (C═O), 1222 and 1245 (C—O); *m*/*z* (%) 352 (M^+, 5), 293 ($M^+ - CO_2Me$, 13), 233 ($M^+ - CO_2Me - OMe - C_2H_5$, 79), 205 ($M^+ - 2CO_2Me - C_2H_5$, 86), 149 ($M^+ - 2CO_2Me - CCO_2Et$, 100) (Found: C, 54.6; H, 4.5. $C_{16}H_{16}O_9$ requires C, 54.55; H, 4.58%).

Selected data for **7b**: yellow *oil*, yield 0.31 g (41%); ν_{max}/cm^{-1} (KBr) 3440 (OH), 1690, 1727 and 1795 (C═O), 1175 and 1212 (C—O); *m*/*z* (%) 382 ($M^+ + 2$, 1), 307 ($M^+ - CO_2Et$, 10), 279 ($M^+ - CO_2Et - CH_2{=}CH_2$, 14), 233 ($M^+ - CO_2Et - OEt - C_2H_5$, 94), 205 ($M^+ - 2CO_2Et - C_2H_5$, 100), 149 ($M^+ - 3CH_2{=}CH_2 - 2CO_2 - CH_3$, 65) (Found: C, 56.3; H, 5.4. $C_{18}H_{20}O_9$ requires C, 56.84; H, 5.30%).

Selected data for **7c**: *crystals* mp 86–88 °C, yield 0.33 g (38%); ν_{max}/cm^{-1} (KBr) 3420 (OH), 1690, 1721 and 1794 (C═O), 1199 and 1233 (C—O); *m*/*z* (%) 336 ($M^+ - CH_2{=}CMe_2 - CO_2$, 28), 307 ($M^+ - CO_2Bu^t - CH_2{=}CH_2$, 14), 280 ($M^+ - 2CH_2{=}CMe_2 - CO_2$, 100), 234 ($M^+ - 2CO_2Bu^t$, 80), 205 ($M^+ - 2CO_2Bu^t - C_2H_5$, 87) (Found: C, 61.0; H, 6.6. $C_{22}H_{28}O_9$ requires C, 60.55; H, 6.47%).

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