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Stereoselective Synthesis of Tetraalkyl Cyclobutene-1,2,3,4-tetracarboxylates. Synthesis of Tetraalkyl (*Z,Z*)-Buta-1,3-diene-1,2,3,4-tetracarboxylates†

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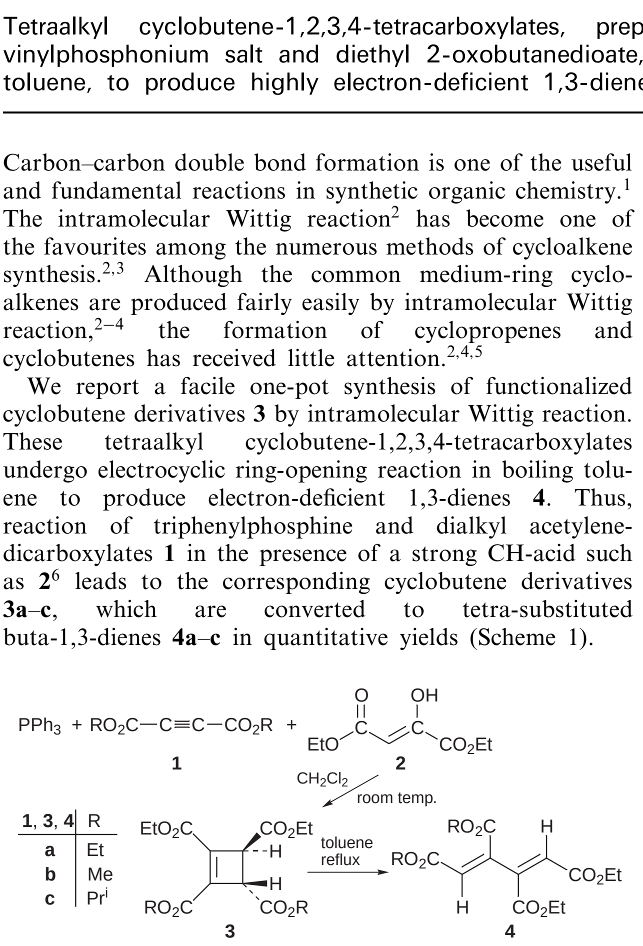
Tetraalkyl cyclobutene-1,2,3,4-tetracarboxylates, prepared by intramolecular Wittig reaction between a vinylphosphonium salt and diethyl 2-oxobutanedioate, undergo electrocyclic ring-opening reactions, in boiling toluene, to produce highly electron-deficient 1,3-dienes.

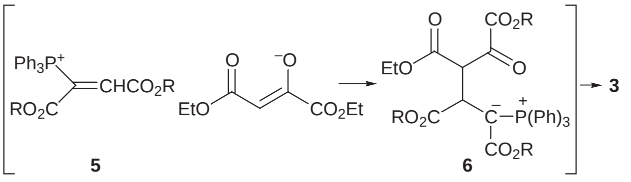
Carbon–carbon double bond formation is one of the useful and fundamental reactions in synthetic organic chemistry.[1] The intramolecular Wittig reaction[2] has become one of the favourites among the numerous methods of cycloalkene synthesis.[2,3] Although the common medium-ring cycloalkenes are produced fairly easily by intramolecular Wittig reaction,[2–4] the formation of cyclopropenes and cyclobutenes has received little attention.[2,4,5]

We report a facile one-pot synthesis of functionalized cyclobutene derivatives **3** by intramolecular Wittig reaction. These tetraalkyl cyclobutene-1,2,3,4-tetracarboxylates undergo electrocyclic ring-opening reaction in boiling toluene to produce electron-deficient 1,3-dienes **4**. Thus, reaction of triphenylphosphine and dialkyl acetylenedicarboxylates **1** in the presence of a strong CH-acid such as **2**[6] leads to the corresponding cyclobutene derivatives **3a**–**c**, which are converted to tetra-substituted buta-1,3-dienes **4a**–**c** in quantitative yields (Scheme 1).



Scheme 1

On the basis of the chemistry of trivalent phosphorus nucleophiles[7] it is reasonable to assume that cyclobutene derivative **3** result from initial addition of triphenylphosphine to the acetylenic ester and subsequent protonation of the reactive 1 : 1 adduct by **2**, followed by attack of the carbon atom of the anion of **2** to vinyltriphenylphosphonium cation **5** to generate ylide **6**, which is converted into strained carbocyclic ring system **3** (Scheme 2).



Scheme 2

Structure **3** was assigned to the isolated products on the basis of their elemental analyses and IR, ^{1}H, ^{13}C NMR and mass spectral data. The methine protons of **3a** show a signal at δ 3.8 which is identical within experimental error with that reported[8] for the *trans*-isomer of tetramethyl cyclobutene-1,2,3,4-tetracarboxylate. The ^{1}H NMR spectra of compounds **3b** and **3c** displayed signals for vicinal methine protons at δ 3.8–3.9 which appear as doublets with $^3J_{HH} = 1.5$ Hz. The torsional angles in cyclobutene derivatives are known. Typically, J_{cis} varies between 3 to 6 Hz and J_{trans} 0.5–2 Hz.[9] Observation of $J_{HH} = 1.5$ Hz for the vicinal protons in **3b** and **3c** indicates a *trans* arrangement for these protons. The ^{13}C NMR spectrum of **3a** exhibited eight distinct resonances in agreement with the cyclobutene structure. Partial assignments of these resonances are given in the Experimental section.

The ^{1}H and ^{13}C NMR spectra of **4a** are similar to those of **3a**, except for the methine groups, which display characteristic resonances with appropriate chemical shifts in the olefinic region. The vinyl protons of **4a**–**c** occur at δ *ca.* 6 which corresponds to the signal at δ 6.0 reported[10] for the vinyl protons of tetraethyl (*Z,Z*) buta-1,3-diene-1,2,3,4-tetracarboxylate. The structures of **3b**, **3c**, **4b** and **4c** are fully supported by NMR and other spectral data (see Experimental section).

The structural assignments made on the basis of the NMR spectra of compounds **3** and **4** were supported by measurement of their IR spectra. Of special interest is the carbonyl absorption (1717–1745 cm^{-1}) for these compounds. Conjugation with the carbon–carbon double bond appears to be a plausible factor in the reduction of the wavenumber of the carbonyl absorption bands.[11]

In summary, the reaction of diethyl 2-oxobutane-1,3-dioate with dialkyl acetylenedicarboxylates in the presence of triphenylphosphine provides a simple one-pot entry into the synthesis of polyfunctional cyclobutene derivatives of potential synthetic interest. Further investigation of the present method will be required to establish its utility and scope.

Experimental

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were recorded on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a Bruker DRX-500 AVANCE instrument with CDCl$_3$ as solvent and Me$_4$Si as an internal standard at 500 and 125.7 MHz, respectively. Mass spectra were recorded on a Finningan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Dialkyl acetylenedicarboxylates **1a**–**c**, triphenylphosphine and diethyl oxalate were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

A typical process for the preparation of *tetraethyl cyclobutene*-1,2,3,4-*tetra carboxylate* **3a** is described as an example: to a magnetically stirred solution of triphenylphosphine (0.52 g,

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2 mmol) and diethyl 2-oxobutane-1,3-dioate (0.38 g, 2 mmol) in CH_2Cl_2 (4 ml) was added dropwise, a solution of diethyl acetylenedicarboxylate (0.34 ml, 2 mmol) in CH_2Cl_2 (2 ml) at −10 °C over 3 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 viscous residue was purified by silica gel (Merck silica gel 60, 230–400 mesh) column chromatography using ethyl acetate–hexane (1 : 5) as eluent. The solvent was removed under reduced pressure and the product (colorless oil, 0.54 g, yield 80%) was obtained. ν_{max}/cm^{-1} (KBr) 1730–1740 (C=O). *m/z* (%): 343 ($M^+ + 1$, 100), 342 (M^+, 18), 297 (55), 296 (68), 251 (45), 224 (63). δ_H 1.28 (6 H, t, $^3J_{HH}$ 7.2 Hz, 2 CH_3) 1.32 (6 H, t, $^3J_{HH}$7.2 Hz, 2 CH_3), 3.8 (2 H, s, CHCH), 4.21 (4 H, q, $^3J_{HH}$ 7.2 Hz, 2 CH_2), 4.30 (4H, q, $^3J_{HH}$ 7.2 Hz, 2 CH_2). δ_C 13.63 (2 CH_3) 13.68 (2 CH_3) 45.44 (2 CH), 61.00 (2 CH_2), 61.11 (2 CH_2), 140.93 (2 C), 159.17 (2 C=O), 168.42 (2 C=O) (Found: C, 56.3; H, 6.8. $C_{16}H_{22}O_8$ requires C, 56.13; H, 6.48%).

3b: colorless oil, 0.50 g, yield 85%, ν_{max}/cm^{-1} (KBr) 1722–1740 (C=O). *m/z*(%): 314 (M^+, 2), 212 (4), 153 (8), 109 (17), 59 (100), 53 (20). δ_H 1.28 (3 H, t, $^3J_{HH}$ 7.2 Hz, CH_3), 1.33 (3 H, t, $^3J_{HH}$ 7.2 Hz, CH_3), 3.74 (3 H, s, OCH_3), 3.81 (H, d, $^3J_{HH}$ 1.5 Hz, CH), 3.82 (3 H, s, OCH_3) 3.83 (H, d, $^3J_{HH}$ 1.5 Hz, CH), 4.22 (2 H, q, $^3J_{HH}$ 7.2 Hz, CH_2), 4.29 (2 H, q, $^3J_{HH}$ 7.2 Hz, CH_2). δ_C 13.88 and 13.92 (2 CH_3), 45.44 and 45.89 (2 CH), 52.16 and 52.49 (2 OCH_3), 61.36 and 61.53 (2 OCH_2), 140.61 and 141.71 (C=C), 159.38, 159.91, 168.58 and 169.19 (4 C=O) (Found: C, 53.3; H, 5.9. $C_{14}H_{18}O_8$ requires C, 53.50; H, 5.77%).

3c: colorless oil, 0.60 g, yield 80%, ν_{max}/cm^{-1} (KBr) 1730–1745 (C=O). *m/z*(%): 371 ($M^+ + 1$, 55), 370 (M^+, 4), 286 (100), 268 (90), 224 (20), 196 (5). δ_H 1.25–1.33 (18 H, m, 6CH_3), 3.83 (1H, d, $^3J_{HH}$ 1.5 Hz, CH), 3.85 (1 H, d, $^3J_{HH}$ 1.5 Hz, CH), 4.21 (2 H, q, $^3J_{HH}$ 7.2 Hz, CH_2), 4.27 (2 H, q, $^3J_{HH}$ 7.2 Hz, CH_2), 5.05 (H, sept, $^3J_{HH}$ 7.2 Hz, CH), 5.11 (1 H, sept, $^3J_{HH}$ 7.2 Hz, CH). δ_C 14.33 (2 CH_3), 21.91 (4CH_3), 45.97 and 46.34 (2 CH), 61.62 and 61.75 (2 CH_2), 69.45 and 69.53 (2 OCH), 141.14 and 142.20 (C=C), 159.42, 159.92, 169.58 and 169.21 (4 C=O) (Found: C, 58.9; H, 7.2. $C_{18}H_{26}O_8$ requires C, 58.37; H, 7.08%).

Tetraethyl(Z,Z)-buta-1,3-*diene*-1,2,3,4-*tetracarboxylate* **4a**: compound **3a** (0.68 g, 2 mmol) in toluene (8 ml) was refluxed for 48 h. The solvent was removed under reduced pressure and the product **4a**, was obtained as a white solid, 0.48 g, 70% yield, mp 66–68 °C (lit.,[10] 67 °C), ν_{max}/cm^{-1} H (KBr) 1721–1740 (C=O). *m/z*(%): 342 (M^+, 7), 297 (55), 269 (60), 241 (30), 195 (100), 167 (62). δ_H 1.28 (6 H, $^3J_{HH}$ 7.2 Hz, 2 CH_3), 1.36 (6 H, t, $^3J_{HH}$ 7.2 Hz, 2 CH_3), 4.22 (4 H, q, $^3J_{HH}$ 7.2 Hz, 2 CH_2), 4.4 (4 H, q, $^3J_{HH}$ 7.2 Hz, 2 CH_2), 6.10 (2 H, s, 2 CH). δ_C 13.93 (2 CH_3), 14.05 (2 CH_3), 61.53 (2 CH_2), 62.43 (2 CH_2), 124.24 (2 CH), 142.73 (2 C), 163.90 and 165.29 (4 C=O) (Found: C, 56.9; H, 6.5. $C_{16}H_{22}O_8$ requires C, 56.13; H, 6.48%).

4b: colorless oil, 0.48 g, yield 70%, ν_{max}/cm^{-1} (KBr) 1733–1743 (C=O). *m/z* (%): 314 (M^+, 5), 283 (14), 269 (30), 255 (38), 241 (58), 181 (100), 59 (7). δ_H 1.29 (3 H, t, $^3J_{HH}$ 7.2 Hz, CH_3), 1.36 (3 H, t, $^3J_{HH}$ 7.2 Hz, CH_3), 4.22 (2 H, q, $^3J_{HH}$ 7.2 Hz, CH_2), 4.4 (2 H, q, $^3J_{HH}$ 7.2 Hz), 6.07 (1 H, d, $^5J_{HH}$ 0.5 Hz, CH), 6.11 (1 H, d, $^5J_{HH}$ 0.5 Hz, CH). δ_C 13.89 and 14.05 (2 CH_3), 52.45 and 53.10 (2 CH_3), 61.57 and 62.43 (2 CH_2), 123.83 and 124.57 (2 CH), 142.40 and 142.89 (2C), 163.82, 164.39, 165.12 and 165.97 (4 C=O) (Found: C, 53.5; H, 5.9. $C_{14}H_{18}O_8$ requires C, 53.50; H, 5.77%).

4c: white solid, mp 77–79 °C, 0.52 g, yield 70%, ν_{max}/cm^{-1} (KBr) 1717–1737 (C=O). *m/z* (%): 371 ($M^+ + 1$, 25), 370 (M^+, 6), 286 (30) 268 (24), 195 (100), 167 (73), 124 (10). δ_H 1.20–1.52 (18 H, m, 6 CH_3), 4.25 (2 H, q, $^3J_{HH}$ 7.2 Hz, CH_2), 4.4 (2 H, q, $^3J_{HH}$ 7.2 Hz, CH_2), 5.15 (1 H, sept, $^3J_{HH}$ 6.3 Hz, OCH), 5.20 (1 H, sept, $^3J_{HH}$ 6.3 Hz, OCH), 6.02 (1 H, d, $^3J_{HH}$ 0.3 Hz, CH), 6.06 (1 H, d, $^5J_{HH}$ 0.3 Hz, CH). δ_C 13.88 and 14.05 (2 CH_3), 21.62 (2 CH_3), 21.70 (2 CH_3), 61.45 and 62.34 (2 CH_2), 69.18 and 70.24 (2 OCH), 123.83 and 124.52 (2 CH), 142.60 and 143.01 (2 C), 163.33, 163.94, 164.76 and 165.33 (4 C=O) (Found: C, 58.8, H, 7.01. $C_{18}H_{26}O_8$ requires C, 58.37; H, 7.08%).

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