Efficient Synthesis of Trialkyl 3-Phenylbuta-1,3-diene-1,2,4-tricarboxylates by a Novel One-Pot Multicomponent Reaction

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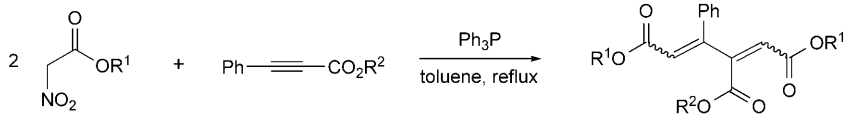
Alkyl 2-nitroacetates **2** react with alkyl phenylpropiolates **1** in the presence of Ph_3P in a mechanistically novel reaction to afford trialkyl 3-phenylbuta-1,3-diene-1,2,4-tricarboxylates in yields of 60–80% under neutral conditions.

Introduction. – Buta-1,3-dienes are versatile building blocks for the construction of a multitude of functionalized ring systems *via Diels–Alder* reaction [1]. Bioactive systems, such as analogues of rebeccamycin [2] or the alkaloid arcyriaflavin-A [3], are readily prepared from buta-1,3-dienes. Recently, an efficient synthetic pathway for the preparation of buta-1,3-dienes by elimination of hydrogen halides from homoallylic halides has been developed [4]. Conjugate addition of nitroalkanes to electron-poor alkenes is of importance among the large body of synthetic processes devoted to carbon–carbon bond formation [5]. The NO_2 group in nitroalkanes can be eliminated under basic conditions as nitrous acid under formation of a C=C bond [6].

In continuation of our work on the chemistry of alkyl 2-nitroacetates **1** [7–9], we herein report on the reaction of these compounds with alkyl phenylpropiolates **2** in the presence of Ph_3P to access a series of functionalized buta-1,3-dienes of type **3** (*Scheme 1*).

Scheme 1



1 R^1 = Me, Et **2** R^2 = Me, Et

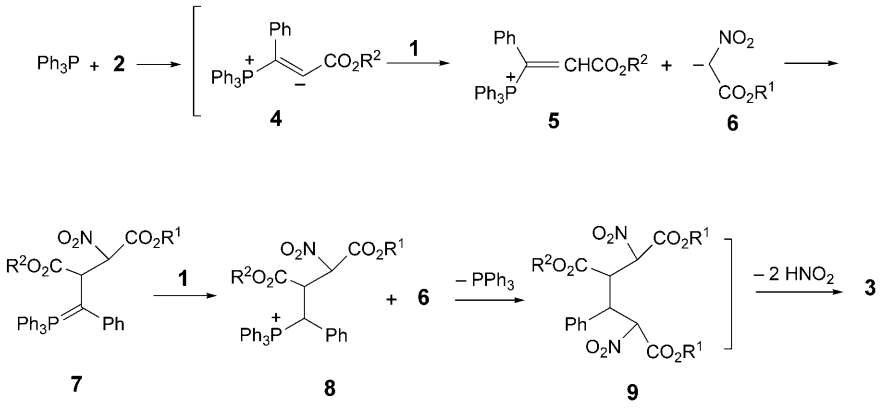
	R^1	R^2	Yield
3a	Me	Me	80%
3b	Et	Me	75%
3c	Me	Et	65%
3d	Et	Et	60%

Results and Discussion. – The reaction of the activated acetylenes **2** with the acetates **1** in the presence of Ph_3P under reflux in toluene was complete within a few hours. The ^{1}H- and ^{13}C-NMR spectra of the crude reaction mixtures clearly indicated the formation of the butadienes **3a**–**3d** (*Scheme 1*). No other products were detected

by NMR spectroscopy. The structures of the products were corroborated by IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis. For example, the ^{1}H-NMR spectrum of **3a** exhibited five sharp *singlet*s, readily assigned to three MeO groups (δ(H) 3.62, 3.66, 3.80) and two olefinic H-atoms (δ(H) 7.05, 7.85), as well as characteristic *multiplet*s for the Ph group (δ(H) 7.32–7.35). The ^{1}H-decoupled ^{13}C-NMR spectrum of **3a** showed 14 distinct resonances (see *Exper. Part*), in agreement with the proposed structure. The ^{1}H- and ^{13}C-NMR spectra of **3b**–**3d** were similar to those of **3a**, except for the alkoxy moieties, which exhibited characteristic signals with appropriate chemical shifts.

Although the mechanistic details of the above reaction are unknown, a plausible pathway may be advanced to rationalize product formation (*Scheme 2*). Presumably, a zwitterionic intermediate [10] such as **4**, formed from Ph_3P and **2**, is protonated by **1** to furnish the intermediate **5**, which is attacked by anionic **6** to produce ylide **7**. The latter would then react with a second molecule of **1** to the intermediate **8**, which again reacts with anionic **6** to form the dinitro derivative **9**. Finally, **9** is converted to **3** by elimination of 2 equiv. of HNO_2 [5].

Scheme 2



In conclusion, we have revealed a novel transformation involving alkyl phenylpropiolates, alkyl 2-nitroacetates, and Ph_3P. The one-pot reaction proceeds through a complex process, affording trialkyl 3-phenyl-buta-1,3-diene-1,2,4-tricarboxylates in medium-to-good yield. The present procedure has the advantage that the reaction can be performed under neutral conditions and that the reagents can be simply mixed without any activation or modification.

Experimental Part

General. Compounds **1**, **2**, and Ph_3P were obtained from *Fluka* and used without further purification. IR Spectra: *Shimadzu IR-460* spectrometer; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker DRX-500-Avance* instrument; in $CDCl_3$ at 500.1 and 125.7 MHz, resp; δ in ppm, J in Hz. EI-MS (70 eV): *Finnigan MAT-8430* mass spectrometer; in m/z. Elemental analyses (C, H, N): *Heraeus CHN-O-Rapid* analyzer.

General Procedure for the Preparation of Compounds **3**. To a stirred soln. of Ph_3P (0.57 g, 2.2 mmol) and **1** (4 mmol) in anh. toluene (10 ml) was added dropwise a mixture of **2** (2 mmol) in toluene (4 ml).

The mixture was heated at reflux for 24 h. The solvent was removed under reduced pressure, and the residue was separated by column chromatography (SiO_2; hexane/AcOEt 5:1) to afford the pure title compounds.

Trimethyl 3-Phenylbuta-1,3-diene-1,2,4-tricarboxylate (**3a**). Yield: 0.24 g (80%). Yellow oil. IR (KBr): 2925; 1707, 1715, 1721 (C=O); 1254; 1174; 1023; 759. ^{1}H-NMR: 3.62, 3.66, 3.80 (3*s*, 3 MeO); 7.05 (*s*, CH); 7.32–7.35 (*m*, 5 CH); 7.85 (*s*, CH). ^{13}C-NMR: 52.1, 52.4, 52.8 (3 MeO); 126.1 (C); 128.6 (2 CH); 129.5 (CH); 129.6 (2 CH); 131.3 (CH); 134.5 (C); 140.8 (C); 142.0 (CH); 164.4, 165.5, 166.3 (3 C=O). EI-MS: 332 (10, M^+), 251 (60), 231 (28), 213 (100), 199 (24), 171 (32), 155 (43), 105 (51), 77 (22), 55 (31). Anal. calc. for $C_{16}H_{16}O_6$ (304.30): C 63.15, H 5.30; found: C 63.15, H 5.30.

1,4-Diethyl 2-Methyl 3-Phenylbuta-1,3-diene-1,2,4-tricarboxylate (**3b**). Yield: 0.25 g (75%). Yellow oil. IR (KBr): 2950; 1711, 1718, 1720 (C=O); 1253; 1096; 781. ^{1}H-NMR: 1.04, 1.21 (2*t*, ^3J=7.2 each, 2 Me); 3.79 (*s*, MeO); 4.07, 4.12 (2*q*, ^3J=7.2 each, 2 OCH_2); 7.06 (*s*, CH); 7.30–7.33 (*m*, 5 CH); 7.85 (*s*, CH). ^{13}C-NMR: 13.8, 14.0 (2 Me); 52.3 (MeO); 61.1, 61.9 (2 OCH_2); 126.3 (C); 128.6 (2 CH); 129.5 (CH); 129.7 (2 CH); 131.7 (CH); 134.7 (C); 140.8 (C); 141.8 (CH); 164.7, 165.0, 166.4 (3 C=O). EI-MS: 332 (11, M^+), 279 (62), 259 (20), 213 (100), 199 (44), 171 (48), 155 (52), 127 (50), 105 (52), 77 (31), 55 (18). Anal. calc. for $C_{18}H_{20}O_8$ (332.36): C 65.05, H 6.07; found: C 65.15, H 6.20.

2-Ethyl 1,4-Dimethyl 3-Phenylbuta-1,3-diene-1,2,4-tricarboxylate (**3c**). Yield: 0.20 g (65%). Yellow oil. IR (KBr): 2946; 1705, 1718, 1719 (C=O), 1247; 1094; 1020; 763. ^{1}H-NMR: 1.28 (*t*, ^3J=7.2, Me); 3.61, 3.65 (2*s*, 2 MeO); 4.26 (*q*, ^3J=7.2, OCH_2); 7.05 (*s*, CH); 7.31–7.34 (*m*, 5 CH); 7.86 (*s*, CH). ^{13}C-NMR: 14.2 (Me); 51.9, 52.8 (2 MeO); 61.3 (OCH_2); 126.4 (C); 128.6 (2 CH); 129.5 (CH); 129.6 (2 CH); 131.2 (CH); 134.6 (C); 140.8 (C); 141.8 (CH); 165.0, 165.6, 165.7 (3 C=O). EI-MS: 318 (12, M^+), 258 (20), 245 (38), 213 (100), 199 (82), 185 (50), 155 (41), 129 (48), 127 (65), 115 (85), 105 (40). Anal. calc. for $C_{17}H_{18}O_6$ (318.33): C 64.14, H 5.70; found: C 64.29, H 5.59.

Triethyl 3-Phenylbuta-1,3-diene-1,2,4-tricarboxylate (**3d**). Yield: 0.20 g (60%). Yellow oil. IR (KBr): 1716, 1719, 1724 (C=O); 1454; 1244. ^{1}H-NMR: 1.03, 1.19, 1.28 (3*t*, ^3J=7.5 each, 3 Me); 4.01, 4.11, 4.24 (3*q*, ^3J=7.2 each, 3 OCH_2); 7.04 (*s*, CH); 7.29–7.32 (*m*, 5 CH); 7.83 (*s*, CH). ^{13}C-NMR: 13.7, 13.9, 14.2 (3 Me); 61.1, 61.2, 61.8 (3 OCH_2); 126.6 (C); 128.6 (2 CH); 129.4 (CH); 129.6 (2 CH); 131.6 (CH); 134.8 (C); 140.8 (C); 141.5 (CH); 164.7, 165.1, 165.8 (3 C=O). EI-MS: 346 (12, M^+), 293 (47), 273 (20), 213 (100), 171 (41), 155 (53), 105 (81), 77 (28), 55 (22). Anal. calc. for $C_{19}H_{22}O_6$ (346.38): C 65.88, H 6.40; found: C 65.66, H 6.32.

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