# A Novel Synthesis of Highly Substituted But-2-enoic Acid Esters by the Reaction of DMAP–Methyl Phenylpropiolate Zwitterion and Diaryl 1,2-Diones

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Abstract: This work describes a novel reaction involving 4-(*N*,*N*-

dimethylamino)pyridine (DMAP)-methyl phenylpropiolate zwitterion and diaryl 1,2-diones, leading to the facile synthesis of substituted butenoic acid esters.

**Key words:** zwitterions, DMAP, methyl phenylpropiolate, benzil, diaryl 1,2-diones

Although zwitterions have been known for a long time,<sup>1</sup> their utility in organic synthesis has remained largely unexplored. In recent years, we have developed a general strategy for the generation of zwitterionic species by the addition of a wide range of nucleophiles to acetylenic esters, followed by their trapping with a variety of electrophiles such as, for example, aldehydes, N-tosylimines, chalcones and activated styrenes.<sup>2</sup> The overall process mainly constituted multicomponent reactions and, in most of the reactions reported so far, doubly activated acetylenes were used for zwitterion generation.<sup>3</sup> Subsequently, we undertook some investigations into the zwitterion formed by the addition of pyridine as well as 4-dimethylaminopyridine (DMAP) to the monoactivated acetylene, methyl phenylpropiolate. The results obtained from trapping this zwitterion with diaryl 1,2-diones are presented in this paper.

In an initial experiment, a solution of benzil (1a), methyl phenylpropiolate (2) and pyridine (20 mol%) in anhydrous dimethoxyethane (DME) was heated under reflux for 48 hours. The solvent was removed under reduced pressure and the product was purified by column chromatography on silica gel to afford the product in 23% yield. Since the product was obtained in low yield, we repeated the reaction with DMAP as the catalyst under identical reaction conditions. Interestingly, in this experiment, the reaction reached completion in 36 hours and the product was obtained in 61% yield (Scheme 1).

The product **3a** was characterized using standard spectroscopic techniques. In the IR spectrum, a signal corresponding to the ester carbonyl was observed at  $1722 \text{ cm}^{-1}$ . The signal corresponding to the carbomethoxy group was

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visible at  $\delta = 3.61$  ppm in the <sup>1</sup>H NMR spectrum and the resonance signals for the benzoyl carbonyls ( $\delta = 194.3$  and 193.1 ppm) and the ester carbonyl ( $\delta = 164.1$  ppm) were observed in the <sup>13</sup>C NMR spectrum. The compound also gave satisfactory elemental analysis. Finally, the structure and stereochemistry of **3a** was unequivocally established by single-crystal X-ray analysis (Figure 1).<sup>4</sup>



Figure 1 ORTEP diagram of compound 3a

The reaction was found to be general with analogues of benzil and the products were obtained in moderate yields. The results are summarized in Table 1.

A plausible mechanism for the reaction is outlined in Scheme 2. In the initial step, the zwitterion formed by the addition of the nucleophile (DMAP) adds to one of the carbonyl groups of the 1,2-dione to form the species  $\mathbf{A}$ , which can conceivably add to the second carbonyl to form the epoxy derivative  $\mathbf{B}$ . On ring fragmentation, the latter Table 1

Reaction of Benzil Analogues with Methyl Phenylpropiolate (2)CO<sub>2</sub>Me o ∬ CO<sub>2</sub>Me DMAP (20 mol%) ılı.

R	DME, reflux, 36	h Ph	→ R
1b–f	2	3b-f	
Entry	R	Product	Yield (%)
1	4-bromophenyl (1b)	3b	58
2	4-trifluoromethylphenyl (1c)	3c	60
3	3-chlorophenyl (1d)	3d	55
4	4-methoxyphenyl (1e)	3e	44
5	2-thienyl (1f)	3f	49

yields the ylide C which rearranges to D, and the latter, presumably for steric reasons, undergoes  $\sigma$ -bond rotation to assume the conformation shown in E, thus allowing the elimination of the nucleophile to occur and delivering the product in the E-stereochemistry. It is noteworthy that this mechanistic postulate precludes the formation of the Zproduct since this would require elimination of the nucleophile from a species with a sterically unfavorable disposition.

In conclusion, we have uncovered a facile reaction for the preparation of highly substituted butenoic acid esters. The experimental simplicity as well as the stereoselectivity of the reaction is especially noteworthy.

All reactions were carried out in oven-dried glassware under argon atmosphere. Progress of reactions were monitored by TLC on glass plates coated with silica gel containing CaSO<sub>4</sub> as the binder; visualization was effected by exposure to UV light or I2. Purification was effected by silica gel column chromatography (100-200 mesh silica gel) using mixtures of hexane-EtOAc as eluent. NMR data were collected at r.t. in CDCl<sub>3</sub> at an operating frequency of 300 MHz (<sup>1</sup>H) and 75 MHz (13C) on a Bruker Avance DPX-300 MHz NMR spectrometer. Chemical shifts ( $\delta$ ) are reported relative to TMS (<sup>1</sup>H) or CDCl<sub>3</sub> (<sup>13</sup>C). IR spectra were recorded on a Bomem MB Series FT-IR spectrophotometer. Melting points were recorded on a Büchi melting point apparatus and are uncorrected. Elemental analyses were performed using a Perkin-Elmer 2400 CHNS analyzer. Highresolution mass spectra were recorded under EI/HRMS (at 5000 resolution) using a Jeol JMS 600H mass spectrometer. Commercial grade solvents were distilled prior to use. Methyl phenylpropiolate and DMAP were purchased from Merck and used directly.

#### Preparation of Butenoic Acid Esters; General Procedure

Benzil (1 equiv), methyl phenylpropiolate (1.2 equiv) and DMAP (0.2 equiv) were taken in anhydrous DME (10 mL) and the reaction mixture (monitored by TLC), was refluxed for 36 h. The solvent was distilled off in vacuo using a rotary evaporator and the residue was subjected to column chromatography (EtOAc-hexane, 5% then 20%) to afford the product, which was recrystallized from  $CH_2Cl_2$ hexane solvent mixtures.

#### 3a

Colorless solid; mp 131-133 °C.

IR (KBr): 2933, 1722, 1692, 1581, 1452, 1425, 1292, 1119 cm<sup>-1</sup>. <sup>1</sup>H NMR:  $\delta$  = 7.84 (d, J = 7.50 Hz, 2 H), 7.71 (d, J = 7.59 Hz, 2 H), 7.44-7.32 (m, 8 H), 7.23-7.15 (m, 3 H), 3.61 (s, 3 H).



#### Scheme 2

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<sup>13</sup>C NMR: δ = 194.3, 193.1, 164.1, 135.8, 135.2, 133.7, 133.4, 132.5, 129.9, 129.4, 129.1, 128.7, 128.6, 128.2, 52.6.

Anal. Calcd for  $C_{24}H_{18}O_4$ : C, 77.82; H, 4.90. Found: C, 77.66; H, 4.71.

#### 3b

Colorless solid; mp 148–150 °C.

IR (KBr): 2941, 1720, 1688, 1587, 1463, 1411, 1229, 1144 cm<sup>-1</sup>.

<sup>1</sup>H NMR: δ = 7.91 (d, J = 8.01 Hz, 4 H), 8.06 (d, J = 8.20 Hz, 4 H), 7.58–7.51 (m, 5 H), 3.81 (s, 3 H).

<sup>13</sup>C NMR:  $\delta$  = 191.7, 190.6, 163.9, 137.1, 135.5, 134.4, 133.1, 132.8, 130.6, 129.7, 129.3, 128.8, 126.7, 53.6.

HRMS (EI): m/z calcd for  $C_{24}H_{16}Br_2O_4$ : 528.1894; found: 528.1881.

# 3c

Colorless solid; mp 143-145 °C.

IR (KBr): 2957, 1718, 1674, 1569, 1443, 1404, 1221, 1152 cm<sup>-1</sup>.

<sup>1</sup>H NMR:  $\delta$  = 8.32 (d, *J* = 7.13 Hz, 4 H), 8.08 (d, *J* = 7.26 Hz, 4 H), 7.56–7.46 (m, 5 H), 3.82 (s, 3 H).

<sup>13</sup>C NMR:  $\delta$  = 190.1, 189.8, 164.5, 138.1, 137.6, 136.1, 135.4, 134.3, 133.7, 132.4, 129.4, 128.5, 126.6, 52.1.

HRMS (EI): *m/z* calcd for C<sub>26</sub>H<sub>16</sub>F<sub>6</sub>O<sub>4</sub>: 506.3933; found: 506.3912.

### 3d

Colorless solid; mp 145–147 °C.

IR (KBr): 2941, 1726, 1670, 1515, 1478, 1409, 1356, 1238, 1144 cm<sup>-1</sup>.

<sup>1</sup>H NMR:  $\delta$  = 8.01 (s, 2 H), 7.73 (d, *J* = 7.40 Hz, 4 H), 7.60–7.51 (m, 5 H), 7.45 (t, *J* = 7.60 Hz, 2 H), 3.76 (s, 3 H).

<sup>13</sup>C NMR:  $\delta$  = 191.3, 190.8, 162.6, 138.9, 135.7, 134.8, 134.3, 132.4, 132.1, 129.5, 128.1, 127.7, 53.9.

HRMS (EI): m/z calcd for  $C_{24}H_{16}Cl_2O_4$ : 439.2868; found: 439.2860.

### 3e

Colorless solid; mp 153-155 °C.

IR (KBr): 2939, 1723, 1676, 1517, 1501, 1463, 1262, 1175 cm<sup>-1</sup>.

<sup>1</sup>H NMR:  $\delta$  = 8.13 (d, *J* = 8.36 Hz, 4 H), 7.46 (d, *J* = 8.29 Hz, 4 H), 7.59–7.54 (m, 5 H), 3.84 (s, 3 H), 3.71 (s, 6 H).

 $^{13}\text{C}$  NMR:  $\delta$  = 190.8, 190.1, 163.1, 159.2, 136.4, 135.2, 134.8, 134.3, 133.1, 132.7, 128.5, 126.8, 121.4, 53.5.

HRMS (EI): *m/z* calcd for C<sub>26</sub>H<sub>22</sub>O<sub>6</sub>: 430.4493; found: 430.4491.

#### 3f

Colorless solid; mp 102–104 °C.

IR (KBr): 3091, 2941, 1718, 1646, 1518, 1461, 1231, 1145, 1063 cm<sup>-1</sup>.

<sup>1</sup>H NMR:  $\delta$  = 7.69 (d, *J* = 5.0 Hz, 2 H), 7.64–7.56 (m, 7 H), 7.19–7.15 (m, 2 H), 3.83 (s, 3 H).

<sup>13</sup>C NMR: δ = 197.2, 196.6, 163.9, 138.7, 136.8, 136.7, 136.5, 134.3, 133.9, 133.1, 128.6, 127.6, 53.2.

HRMS (EI): *m/z* calcd for C<sub>20</sub>H<sub>14</sub>S<sub>2</sub>O<sub>4</sub>: 382.4548; found: 382.4556.

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- (4) Crystal data for **3a**: Empirical formula:  $C_{24}H_{18}O_4$ ; Unit cell parameters: a = 8.332(9) Å, b = 8.609(10) Å, c = 14.263(16) Å,  $a = 76.913(18)^\circ$ ,  $\beta = 86.448(17)^\circ$ ,  $\gamma = 72.752(17)^\circ$ ; Space group *P*–1. CCDC 653243 contains the supplementary crystallographic data for compound **3a**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data\_request/ cif.