

Article

## A Facile One-Pot Synthesis of $\alpha$ -Bromo- $\alpha,\beta$ -unsaturated Esters from Alcohols

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**Abstract:** Treatment of *N*-bromosuccinimide (NBS) with (carboethoxymethylene) triphenylphosphorane (**1**) in CH<sub>2</sub>Cl<sub>2</sub> followed by the addition of an alcohol in the presence of manganese dioxide under ultrasonic irradiation constitutes a stereoselective one-pot procedure for the preparation of *Z*-configured  $\alpha$ -bromo- $\alpha,\beta$ -unsaturated esters in good to excellent yield.

**Keywords:** one-pot synthesis; bromoylides; oxidation;  $\alpha$ -bromo- $\alpha,\beta$ -unsaturated esters

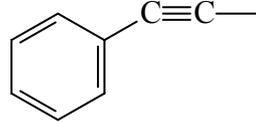
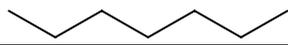
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### 1. Introduction

The Wittig reaction is one of the most powerful and attractive methods for the construction of various alkenes [1]. Nicolaou and his coworkers [2] have highlighted the utility of the Wittig olefination and related reactions in natural products synthesis both in the research laboratory and industrial settings.  $\alpha$ -Halo- $\alpha,\beta$ -unsaturated esters are useful intermediates in organic synthesis [3]. For example, the synthesis of  $\alpha$ -trifluoromethyl- $\alpha,\beta$ -unsaturated esters was based on trifluoromethylation of  $\alpha$ -iodo- $\alpha,\beta$ -unsaturated esters [4] as well  $\alpha$ -bromo- $\alpha,\beta$ -unsaturated esters [5]. They are usually prepared by the Wittig reaction of aldehydes with haloylides [6,7] and condensation of aldehydes with halo-phosphonates in the presence of a base [8]. Only aldehydes have been used as substrates in this typical method. Taylor [9] described the development of an *in situ* alcohol oxidation-Wittig reaction using (carboethoxymethylene)triphenylphosphorane and manganese dioxide to produce  $\alpha,\beta$ -unsaturated esters. This method avoids the most common problems associated with the handling of



Table 1. Cont.

Entry <sup>a</sup>	R	Product	Yield (%) <sup>b</sup>	Z:E <sup>c</sup>
4		3d	90	100:0
5		3e	86	92:8
6	CH <sub>3</sub> CH <sub>2</sub> —C≡C—	3f	87	76:24
7		3g	21	90:10

<sup>a</sup> One equiv. of alcohol, 1.3 equiv. of (1), 1.4 equiv. of NBS and 10 equiv. of MnO<sub>2</sub> were used and reaction mixture was sonicated for 10 h; <sup>b</sup> Yields were based on alcohols; <sup>c</sup> This ratio was determined by <sup>1</sup>H-NMR spectroscopy.

### 3. Experimental

#### 3.1. General

IR spectra were recorded on a Perkin-Elmer 883 spectrophotometer and are expressed as  $\nu$  in cm<sup>-1</sup>. NMR spectra were recorded on JEOL ECP 400 (400 MHz) in CDCl<sub>3</sub> and chemical shifts are expressed as  $\delta$  in ppm, and coupling constants (J) were given in Hertz. MS spectra were obtained using EI at 70 eV. The ultrasonic reactions were carried out using a Sonerex 200 operating at 50 W power and a frequency of 35 kHz.

#### 3.2. General procedure for the synthesis of (Z)- $\alpha$ -bromo- $\alpha,\beta$ -unsaturated esters

Activated manganese dioxide (purchased from Aldrich, 10 mmol) was added to a solution of (carboethoxymethylene)triphenylphosphorane (1.3 mmol), *N*-bromosuccinimide (1.4 mmol) and alcohol (1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (12 mL) and the mixture was sonicated for 10 hours. The manganese dioxide was removed by filtration through Celite, which was washed well with CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic portions were concentrated under vacuum to ca. 1-2 mL, the residue was purified by column chromatography on silica gel (petroleum ether-ethyl acetate 15:1).

(*Z*)-Ethyl 2-bromo-3-phenylpropenoate (**3a**) [12]: Yellow oil, <sup>1</sup>H-NMR:  $\delta$  = 1.38 (t, *J* = 7.3 Hz, 3H); 4.33 (q, *J* = 7.3 Hz, 2H); 7.41-7.45 (m, 3H, arom-H); 7.83-7.85 (m, 2H, arom-H); 8.21 (s, 1H); IR ( $\nu_{\max}$ , thin film) 2980, 1724, 1610, 1259, 1037, 765; MS (EI), *m/z* (%) = 256 (54), 254 [M<sup>+</sup>] (54), 175 (91), 174 (100), 102 (97).

(*ZZ*, *4E*)-Ethyl 2-bromo-5-phenylpenta-2,4-dienoate (**3b**) [12]: Yellow oil, <sup>1</sup>H-NMR:  $\delta$  = 1.37 (t, *J* = 7.3 Hz, 3H); 4.29 (q, *J* = 7.3 Hz, 2H); 7.04 (d, *J* = 16.1 Hz), 7.13-7.19 (dd, *J* = 10.3 Hz, *J* = 16.1 Hz), 7.32-7.39 (m, 3H, arom-H); 7.51-7.53 (m, 2H, arom-H); 7.81 (d, *J* = 10.3 Hz); IR ( $\nu_{\max}$ , thin film) 2980, 1714, 1614, 1583, 1261, 1041, 744; MS (EI), *m/z* (%) = 282 (26), 282 [M<sup>+</sup>] (27), 155 (47), 129 (100), 102 (25).

(*Z*)-Ethyl 3-(furan-2-yl)-2-bromo-3-propenoate (**3c**) [12]: Yellow oil,  $^1\text{H-NMR}$ :  $\delta = 1.33$  (t,  $J = 7.3$  Hz, 3H); 4.30 (q,  $J = 7.3$  Hz, 2H); 6.54 (m, 1H), 7.42 (d,  $J = 3$  Hz, 1H), 7.57 (d,  $J = 2$  Hz, 1H); 8.13 (s, 1H); IR ( $\nu_{\text{max}}$ , thin film) 2981, 1716, 1249, 1039, 748; MS (EI),  $m/z$  (%) = 246 (39), 244 [ $\text{M}^+$ ] (38), 165 (58), 137 (100), 92 (30).

(*2Z, 4E*)-Ethyl 2-bromohepta-2,4-dienoate (**3d**): Yellow oil.  $^1\text{H-NMR}$ :  $\delta = 1.04$  (t,  $J = 7.3$  Hz, 3H); 1.31 (t,  $J = 6.6$  Hz, 3H); 2.22 (quint,  $J = 7.3$  Hz, 2H); 4.25 (q,  $J = 7.3$  Hz, 2H); 6.32-6.44 (m, 2H); 7.63 (d,  $J = 10$  Hz, 1H); IR ( $\nu_{\text{max}}$ , thin film) 3055, 1726, 1265, 705; MS (EI),  $m/z$  (%) = [ $\text{M}^+$  cannot be detected], 208 (41), 206 (36), 106 (39), 104 (39).

(*2Z*)-Ethyl 2-bromo-5-phenylpent-2-en-4-ynoate (**3e**): Yellow oil.  $^1\text{H-NMR}$ :  $\delta = 1.34$  (t,  $J = 7.3$  Hz, 3H); 4.33 (q,  $J = 7.3$  Hz, 2H); 7.29-7.58 (m, 4H, arom-H); 7.50 (s, 1H); IR ( $\nu_{\text{max}}$ , thin film) 2980, 1718, 1265, 738; MS (EI),  $m/z$  (%) = 280 (42), 278 [ $\text{M}^+$ ] (42), 199 (73), 171 (100), 106 (39), 126 (97).

(*Z*)-Ethyl 2-bromohept-2-en-4-ynoate (**3f**): Yellow oil.  $^1\text{H-NMR}$ :  $\delta = 1.21$  (t,  $J = 8$  Hz, 3H); 1.30 (t,  $J = 7.3$  Hz, 3H); 2.44 (dq,  $J = 7.3$  Hz,  $J = 2.2$  Hz, 2H), 4.27 (q,  $J = 7.3$  Hz, 2H), 7.26 (t,  $J = 2.2$  Hz, 1H); IR ( $\nu_{\text{max}}$ , thin film) 2998, 1718, 1265, 740; MS (EI),  $m/z$  (%) = 232 (49), 230 [ $\text{M}^+$ ] (51), 186 (40), 151 (96), 77 (100).

(*Z*)-Ethyl 2-bromonon-2-enoate (**3g**) [13]: Yellow oil,  $^1\text{H-NMR}$ :  $\delta = 1.24$  (t,  $J = 7.3$  Hz, 3H); 1.27-1.32 (m, 11H), 2.33 (q,  $J = 7.3$  Hz, 2H), 4.27 (q,  $J = 7.3$  Hz, 2H); 7.27 (t,  $J = 7.30$  Hz, 1H); IR ( $\nu_{\text{max}}$ , thin film) 2926, 1732, 1259, 1041, 802.

#### 4. Conclusions

In summary, we have developed an efficient ultrasonic-assisted one-pot general procedure for a domino primary alcohol oxidation-Wittig reaction for the highly stereoselective synthesis of *Z*- $\alpha$ -bromo- $\alpha,\beta$ -unsaturated esters **3**. These results demonstrate the value of ultrasonic-assisted chemistry.

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*Sample Availability:* Samples of the compounds **3a-3g** are available from the authors.

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