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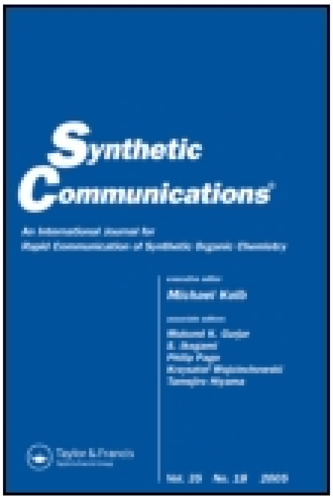

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A Facile One-Pot Synthesis of α-Iodo-α,β-unsaturated Esters

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A Facile One-Pot Synthesis of α-Iodo-α,β-unsaturated Esters

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ABSTRACT

Aldehydes reacted with (ethoxycarbonyliodomethyl)triphenylphosphonium iodide, tetrabutylammonium bromide, and potassium carbonate in methanol at 40°C to give α-iodo-α,β-unsaturated esters in good to excellent yield.

Key Words: One-pot synthesis; α-Iodo-α,β-unsaturated esters; ^{1}H NMR; Iodoylides.

INTRODUCTION

α-Halo-α,β-unsaturated esters are useful intermediates in organic synthesis. They are usually prepared by the Wittig reaction of aldehydes with

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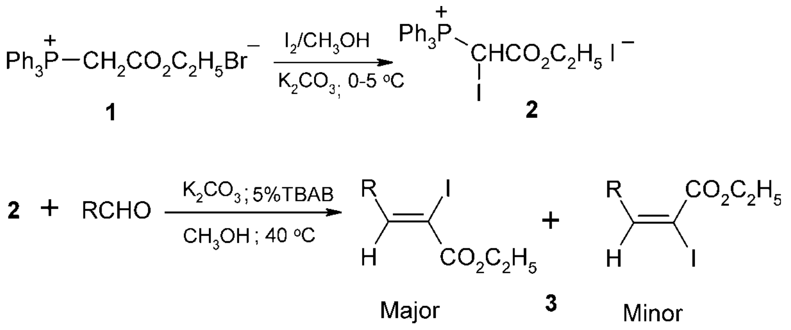
haloylides[1,2] and the condensation of aldehydes with halophosphonates in presence of base.[3] It is well-known that α-iodo-α,β-unsaturated esters are easily deprived of hydrogen iodide under basic or high temperature conditions to turn into the corresponding propiolates. In addition, it is difficult to obtain iodoylides. So, the above methods are not suitable for preparation of α-iodo-α,β-unsaturated esters. Recently, Huang[4] reported a method to prepare α-iodo-α,β-unsaturated esters via arsonium salts, but the reaction time was too long: 14–33 hr. Kayser[5] also reported a procedure to prepare them through the reaction of carboethoxymethylenetriphenylphosphorane, potassium carbonate, *N*-iodosuccinimide, and aldehyde, but this reaction was also carried out in low temperature for a long time. Herein, we report our method to prepare α-iodo-α,β-unsaturated esters by modified Chenault's procedure[6] (Sch. 1).

A suspension of (ethoxycabonyliodomethyl)triphenylphosphonium iodide **2**, tetrabutylammonium bromide, and aldehyde in methanol was stirred at 40°C, 1.0 equiv. of potassium carbonate was added in three portions (a portion per 2 hr) to the mixture 4 hr, and the reaction was stirred for 2 hr. We were delighted to found that (*Z*)-α-iodo-α,β-unsaturated esters were the predominant product in high yields. The results were summarized in Table 1.

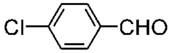
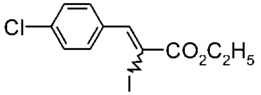
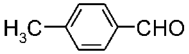
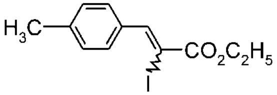
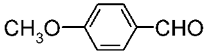
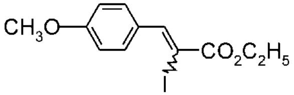
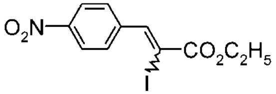
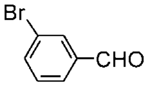
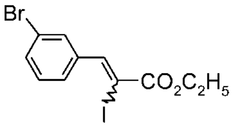
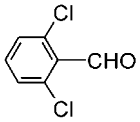
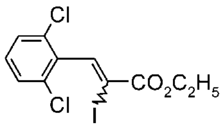
It is noteworthy that propiolic ester could be found in the product if addition of potassium carbonate was too fast and if the quantity of potassium carbonate was more than 1.0 equiv. The presence of tetrabutylammonium bromide was essential to this reaction. If tetrabutylammonium bromide was not added, the yield would had a obvious decline, especially when R was not aryl groups. Therefore, α-iodo-α,β-unsaturated esters could be easily prepared in good yields by our facile one-pot reaction.

α-Iodo-α,β-unsaturated esters **3** have recently emerged as valuable reagents for organic synthesis. For example, the synthesis of α-trifluoromethyl-α,β-unsaturated ester **4** was based on the trifluoromethylation of



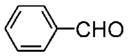
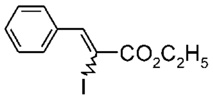
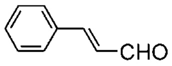
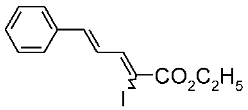
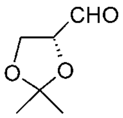
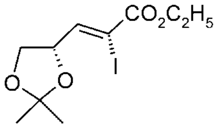
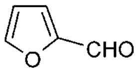
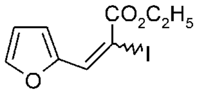
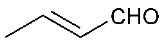
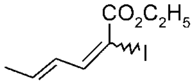
Scheme 1.

Table 1. Synthesis of compounds **3a–k**.

Entry	Aldehyde	Product 3[a]	Yield (%)[b]	Ratio (*Z*/*E*)[c]
1		 **3a**	93	85 : 15
2		 **3b**	83	90 : 10
3		 **3c**	85	88 : 12
4		 **3d**	82	84 : 16
5		 **3e**	86	83 : 17
6		 **3f**	83	96 : 4

(*continued*)

Table 1. Continued.

Entry	Aldehyde	Product **3**[a]	Yield (%)[b]	Ratio (*Z*/*E*)[c]
7		 **3g**	87	81 : 19
8		 **3h**	81	90 : 10
9		 **3i**	78	89 : 11
10		 **3j**	84	86 : 14
11		 **3k**	85	84 : 16

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[a] All compounds were confirmed by ^{1}H NMR, IR, and MS.

[b] Yields were based on aldehyde.

[c] This ratio was determined by HPLC.

α-iodo-α,β-unsaturated esters **3c**. Treatment of a 88 : 12 mixture of *Z*- and *E*-**3c** with $FSO_2CF_2CO_2Me$ and CuI in DMF/HMPA at 70°C gave a 88 : 12 mixture of *Z*- and *E*-**4** in 89 %[7] (Sch. 2).

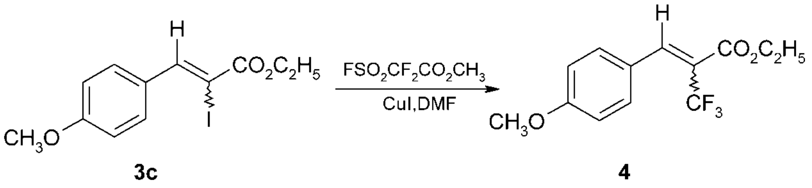
EXPERIMENTAL

^1H NMR was determined with a Bruker Avance 300 MHz spectrometer using tetramethylsilane as the internal standard. ^{19}F NMR spectra was obtained on a 300 MHz spectrometer using trifluoroacetic acid as external standard, downfield shifts being designated as negative. All chemical shift (δ) were expressed in parts per million, and coupling constants (J) were given in Hertz. Mass spectra were obtained using EI at 70 eV. IR spectra were recorded on a Bruker Equinox 55 spectrometer.

General Procedure for the Synthesis of 3a–k

A suspension of (ethoxycarbonyliodomethyl)triphenylphosphonium iodide **2** (6.02 g, 10 mmol), 5% equivalent of tetrabutylammonium bromide (161 mg, 0.5 mmol), and aldehyde (10 mmol) in methanol (40 mL) was stirred at 40°C, 1.0 equiv. of potassium carbonate (690 mg, 5 mmol) was added in three portions (230 mg per 2 hr) to the mixture in 4 hr. The color of the mixture turned to dark brown and the suspension dissolved completely during the addition. After the finish of addition, the reaction was stirred for 2 hr. After removal of methanol, the residue was purified by column chromatography on silica gel with 20 : 1 petroleum ether (60–90°C) and ethyl acetate to give α-iodo-α,β-unsaturated esters **3**.

(*Z*)-**3a**. Oil. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.20$ (s, 1H), 7.72 (d, $J = 8.4$ Hz, 2H), 7.38 (d, $J = 8.4$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.40 (t, $J = 7.1$ Hz, 3H); m/z (EI): 337 ($M^+ + 1$, 21), 336 (M^+, 52), 209 (43), 181 (100), 136 (89); IR (ν_{max}, thin film): 2982, 1712, 1595, 1490, 1249 cm^{-1}.



Scheme 2.

(Z)-**3b**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.25$ (s, 1H), 7.74 (d, $J = 7.9$ Hz, 2H), 7.23 (d, $J = 7.9$ Hz, 2H), 4.35(q, $J = 7.1$ Hz, 2H), 2.38 (s, 3H), 1.35(t, $J = 7.1$ Hz, 3H); m/z (EI): 316 (M^+, 71), 189 (48), 161 (100), 115 (96); IR (ν_{max}, thin film): 2981, 1716, 1599, 1511, 1445, 1180 cm^{-1}.

(Z)-**3c**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.25$ (s, 1H), 7.88 (d, $J = 8.1$ Hz, 2H), 6.95 (d, $J = 8.1$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 3.88 (s, 3H), 1.40 (t, $J = 7.1$ Hz, 3H); m/z (EI): 333 ($M^+ + 1$, 47), 332 (M^+, 100), 287 (46), 205 (41), 127 (2); IR (ν_{max}, thin film): 2981, 1712, 1606, 1511, 1254, 1176 cm^{-1}.

(Z)-**3d**. Solid: m.p. 98–100°C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.30$–8.28 (m, 3H), 7.85 (m, 2H), 4.38 (q, $J = 7.1$ Hz, 2H), 1.42 (t, $J = 7.1$ Hz, 3H); m/z (EI): 348 ($M^+ + 1$, 56), 347 (M^+, 64), 302 (20), 220 (71), 192 (100); IR (ν_{max}, KBr): 2987, 1716, 1640, 1520, 1347, 1251 cm^{-1}.

(Z)-**3e**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.70$ (s, 1H), 7.60–7.45 (m, 2H), 7.25 (m, 1H), 6.48 (d, $J = 15.7$ Hz, 1H), 4.28 (q, $J = 7.1$ Hz, 2H), 1.35 (t, $J = 7.1$ Hz, 3H); m/z (EI): 382/380 (M^+, 24), 337/335 (9), 211 (92), 209 (100), 127 (4); IR (ν_{max}, thin film): 2979, 1711, 1640, 1312, 1179, 1035 cm^{-1}.

(Z)-**3f**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.78$ (d, $J = 16.4$ Hz, 1H), 7.26 (m, 1H), 7.15 (m, 1H), 6.58 (d, $J = 16.4$ Hz, 1H), 4.32 (q, $J = 7.1$ Hz, 2H), 1.38 (t, $J = 7.1$ Hz, 3H); m/z (EI): 373 ($M^+ + 2$, 2), 371 (M^+, 3), 244 (6), 181 (100), 127 (14); IR (ν_{max}, thin film): 2984, 1722, 1429, 1305, 1189, 1035 cm^{-1}.

(Z)-**3g**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.28$ (s, 1H), 7.80 (m, 2H), 7.42 (m, 2H), 7.32 (m, 1H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.40 (t, $J = 7.1$ Hz, 3H); m/z (EI): 303 ($M^+ + 1$, 71), 302 (M^+, 100), 257 (45), 175 (91), 127 (4); IR (ν_{max}, thin film): 2982, 1717, 1599, 1233, 1035 cm^{-1}.

(Z)-**3h**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.80$ (d, $J = 9.2$ Hz, 1H), 7.68 (m, 2H), 7.40 (m, 3H), 7.15 (d, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.38 (t, $J = 7.1$ Hz, 3H); m/z (EI): 329 ($M^+ + 1$, 13), 328 (M^+, 40), 202 (14), 173 (10), 129 (100), 127 (60); IR (ν_{max}, thin film): 2982, 1708, 1613, 1258, 1226, 1149 cm^{-1}.

(Z)-**3i**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.38$ (d, $J = 8.1$ Hz, 1H), 4.85 (m, 1H), 4.28 (m, 3H), 3.68 (m, 1H), 1.45–1.25 (m, 9H); m/z (EI): 327 ($M^+ + 1$, 21), 311 (67), 269 (100), 127 (5); IR (ν_{max}, thin film): 2987, 1720, 1372, 1241, 1062, 1031 cm^{-1}.

(Z)-**3j**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.30$ (s, 1H), 7.63 (d, 2H), 6.62 (m, 1H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.38 (t, $J = 7.1$ Hz, 3H); m/z (EI): 392 (M^+, 78), 165 (69), 137 (100), 92 (63); IR (ν_{max}, thin film): 2982, 1712, 1605, 1472, 1235, 1038 cm^{-1}.

(Z)-**3k**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.55$ (m, 1H), 6.62 (m, 1H), 6.40 (m, 1H), 4.28 (q, $J = 7.1$ Hz, 2H), 1.90 (d, $J = 5.1$ Hz, 3H), 1.30 (t, $J = 7.1\,\text{Hz}$, 3H); m/z (EI): 266 (M^+, 100), 238 (35), 223 (81), 111 (69), 66 (88); IR ($\nu_{\max}$, thin film): 2981, 1711, 1633, 1577, 1443, 1224 cm^{-1}.

The Synthesis of α-Trifluoromethyl-α,β-unsaturated Ester 4

A solution of $FSO_2CF_2CO_2CH_3$ (0.5 mL, 4 mmol) in DMF(10 mmol) was added dropwise over a period of 3 hr to a mixture of ester **3c** (2 mmol), CuI (96 mg, 0.5 mmol), and HMPA (1 mL) in DMF (15 mL) at 65°C. The reaction was stirred at 65°C for 10 hr before being cooled to room temperature. Saturated aqueous NH_4Cl (30 mL) was added and the mixture was extracted with ether. The extracts were washed with brine, and dried over Na_2SO_4. The solvent was removed in vacuo. Purification of the residue by column chromatography on silica gel and elution with 25 : 1 hexane and ethyl acetate gave compounds **4**.

(*Z*)-**4**. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.99$ (s, 1H), 7.41 (d, $J = 9.5\,\text{Hz}$, 2H), 6.91 (m, 2H), 4.34 (m, 2H), 3.83 (s, 3H), 1.37 (t, $J = 7.1\,\text{Hz}$, 3H), ^{19}F NMR (300 MHz, $CDCl_3$): $\delta = -20.6$ (s); m/z (EI): 275 ($M^+ + 1$, 18), 274 (M^+, 100), 205 (8), 69 (12); IR ($\nu_{\max}$, thin film): 2982, 1726, 1606, 1514, 1265, 1178 cm^{-1}.

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