

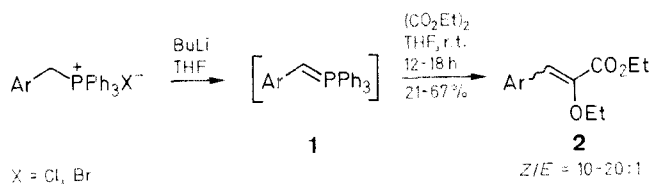
### Stereoselective Synthesis of Ethyl (*Z*)-3-Aryl-2-ethoxyacrylates: Wittig Reaction of Diethyl Oxalate

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The Wittig olefination of diethyl oxalate with a variety of arylmethylenetriphenylphosphoranes **1** proceeds readily in tetrahydrofuran at room temperature to give ethyl 3-aryl-2-ethoxyacrylates **2** with a *Z/E* selectivity of  $\geq 10:1$ .

Although most esters react with non-stabilized phosphorus ylides by acylation to produce  $\beta$ -oxo ylides,<sup>1</sup> a few types such as formates, trifluoroacetates and oxalates instead undergo Wittig olefination. A recent comprehensive review on this area<sup>2</sup> prompts us to report our results on the olefination of diethyl oxalate. Previous studies on this reaction using both non-stabilized<sup>3</sup> and stabilized<sup>4</sup> ylides have been carried out by boiling in solvents such as dioxane, toluene, and xylene, and under these conditions the products were obtained as a mixture of the *Z*- and *E*-isomers of **2**. The alternative approach to **2** by reaction of aromatic aldehydes with ethyl  $\alpha$ -ethoxy-(diethylphosphono)acetate also proceeds with low stereoselectivity.<sup>5</sup> We now report a convenient synthesis of **2**, which uses milder reaction conditions to produce good *Z/E* selectivity. The products, ethyl-3-aryl-2-ethoxyacrylates ( $\alpha$ -ethoxycinnamates),



<b>1, 2</b>	<b>Ar</b>	<b>1, 2</b>	<b>Ar</b>
<b>a</b>	Ph	<b>f</b>	3,4-(methylenedioxy) $\text{C}_6\text{H}_3$
<b>b</b>	4- $\text{CH}_3\text{C}_6\text{H}_4$	<b>g</b>	1-naphthyl
<b>c</b>	4-MeOC $_6\text{H}_4$	<b>h</b>	2-naphthyl
<b>d</b>	4-ClC $_6\text{H}_4$	<b>i</b>	2-thiophenyl
<b>e</b>	2-MeOC $_6\text{H}_4$		

Table. Compounds 2a-i Prepared

Prod- uct	Reaction Time (h)	Yield (%)	Z/E Ratio	bp (°C)/ mbar	Molecular Formula <sup>a</sup> or Lit. bp(°C)/ mbar	IR (film) ν(cm <sup>-1</sup> )	<sup>1</sup> H-NMR (CDCl <sub>3</sub> /TMS) <sup>b</sup> δ, J(Hz)	MS (70 eV) m/z (%)
<b>2a</b>	18	63	15:1	135–137/ 0.07	114–115/ 1.3 <sup>c,3</sup> C <sub>13</sub> H <sub>16</sub> O <sub>3</sub> (220.3)	1715	1.36 (t, 6H); 4.01 (q, 2H); 4.29 (q, 2H); 6.97 (s, 1H); 7.1–7.4 (m, 3H); 7.65– 7.85 (m, 2H)	220 (M <sup>+</sup> , 25); 193 (23); 175 (13); 119 (58); 118 (100)
<b>2b</b>	18	55	15:1	152–155/ 0.03	C <sub>14</sub> H <sub>18</sub> O <sub>3</sub> (234.3)	1715, 1632, 1610	1.37 (t, 6H); 2.36 (s, 3H); 4.01 (q, 2H); 4.29 (q, 2H); 6.98 (s, 1H); 7.18, 7.70 (AB, 4H, J = 8)	234 (M <sup>+</sup> , 70); 149 (10); 133 (32); 132 (100); 121 (18); 105 (66); 104 (70)
<b>2c</b>	12	51	20:1	167–170/ 0.07	C <sub>14</sub> H <sub>18</sub> O <sub>4</sub> (250.3)	1712, 1630, 1604	1.35 (t, 3H); 1.36 (t, 3H); 3.80 (s, 3H); 3.97 (q, 2H); 4.27 (q, 2H); 6.86, 7.72 (AB, 4H, J = 9); 6.94 (s, 1H)	250 (M <sup>+</sup> , 65); 234 (30); 193 (22); 148 (66); 136 (57); 135 (100); 132 (60)
<b>2d</b>	18	66	16:1	157–159/ 0.013	C <sub>13</sub> H <sub>15</sub> ClO <sub>3</sub> (254.7)	1720, 1632, 1590	1.35 (t, 3H); 1.37 (t, 3H); 4.02 (q, 2H); 4.29 (q, 2H); 6.89 (s, 1H); 7.30, 7.70 (AB, 4H, J = 8)	256, 254 (M <sup>+</sup> , 26, 80); 154 (70); 152 (100); 141 (21); 139 (22); 125 (60); 124 (62)
<b>2e</b>	12	47	12:1	178–181/ 0.07	C <sub>14</sub> H <sub>18</sub> O <sub>4</sub> (250.3)	1713, 1630, 1598	1.32 (t, 3H); 1.36 (t, 3H); 3.87 (s, 3H); 3.96 (q, 2H); 4.31 (q, 2H); 6.8–7.4 (m, 3H); 7.45 (s, 1H); 8.19 (m, 1H)	250 (M <sup>+</sup> , 50); 193 (7); 165 (11); 148 (100); 133 (27); 121 (37)
<b>2f</b>	18	21	16:1	190–193/ 0.13	C <sub>14</sub> H <sub>16</sub> O <sub>5</sub> (264.3)	1712, 1630	1.36 (t, 3H); 1.37 (t, 3H); 3.99 (q, 2H); 4.28 (q, 2H); 5.98 (s, 2H); 6.78 (half AB, 1H, J = 8); 6.90 (s, 1H); 7.13 (half AB of d, 1H, J = 8, 2); 7.50 (d, 1H, J = 2)	264 (M <sup>+</sup> , 58); 207 (21); 153 (14); 152 (100); 125 (33); 124 (35)
<b>2g</b>	72	65	6:1	186–188/ 0.07	C <sub>17</sub> H <sub>18</sub> O <sub>3</sub> (270.3)	1712, 1638	1.22 (t, 3H); 1.41 (t, 3H); 3.90 (q, 2H); 4.36 (q, 2H); 7.25–8.25 (m, 8H)	270 (M <sup>+</sup> , 10); 168 (100); 167 (67); 165 (62); 153 (95); 152 (58); 142 (98); 141 (97)
<b>2h</b>	18	64	10:1	196–200/ 0.13 (mp. 33–35)	C <sub>17</sub> H <sub>18</sub> O <sub>3</sub> (270.3)	1713, 1631, 1592	1.38 (t, 3H); 1.40 (t, 3H); 4.06 (q, 2H); 4.33 (q, 2H); 7.15 (s, 1H); 7.35–7.55 (m, 2H); 7.70–8.05 (m, 4H); 8.21 (m, 1H)	270 (M <sup>+</sup> , 70); 185 (7); 168 (100); 157 (7); 139 (100); 129 (7)
<b>2i</b>	18	67	19:1	148–150/ 0.03	C <sub>11</sub> H <sub>14</sub> O <sub>3</sub> S (226.3)	1710, 1625	1.35 (t, 3H); 1.44 (t, 3H); 4.09 (q, 2H); 4.28 (q, 2H); 7.01 (dd, 1H, J = 6, 4); 7.20–7.45 (m, 3H)	226 (M <sup>+</sup> , 36); 169 (12); 125 (23); 124 (100); 113 (14); 97 (50); 96 (85)

<sup>a</sup> Satisfactory microanalyses obtained: C ± 0.32, H ± 0.33.<sup>b</sup> Spectra are reported for the major Z-isomer only, the small singlet for (E)-2 generally appeared at δ = ~6.0. For all triplets and quartets J = 7 Hz.<sup>c</sup> Mixture of E- and Z-isomers (ref. 3).

would seem to have considerable synthetic potential, since they can be regarded either as α-ethoxy-α,β-unsaturated esters or as the enol-ethers of 3-arylpurvic esters.

The reactions were carried out by adding diethyl oxalate (1.04 equiv) to a solution of ylides 1 formed by treatment of the appropriate phosphonium salts with butyllithium in tetrahydrofuran, at room temperature. After the appropriate reaction time a simple extractive workup followed by direct distillation of the organic products afforded the desired esters 2 in moderate to good yield (Table). Of the nine different aryl groups examined, only 1-naphthyl was particularly slow to react requiring 72 h to achieve a reasonable yield (this example also gave the poorest Z/E selectivity).

The Z/E ratio was determined in each case both by <sup>1</sup>H-NMR using the integrals of the singlets of the olefinic proton at C-3 (δ<sub>Z</sub> ≈ 7, δ<sub>E</sub> ≈ 6) and by GC (3% OV 101, 220°C). In all cases the Z isomer of 2 predominated and the Z/E ratio was generally between 10:1 and 20:1. The literature report<sup>3</sup> of the preparation of 2a in boiling toluene does not mention the Z/E ratio obtained, but in our hands the reaction of diethyl oxalate with 1a, generated using either butyllithium or sodium *tert*-amyloxide, in boiling toluene for 1 h gave 2a with a Z/E ratio of 6–7:1.

IR spectra were recorded on a Perkin Elmer 1420 spectrophotometer. <sup>1</sup>H-NMR were measured using a Jeol FX-90 spectrometer and mass spectra were recorded on an AEI MS-902 instrument.

#### Ethyl (Z)-3-Aryl-2-ethoxyacrylates 2; General Procedure:

A suspension of the (arylmethyl)triphenylphosphonium halide (25 mmol) in dry THF (100 mL) is stirred at r.t. under N<sub>2</sub> while a 2.5 M solution of BuLi in hexane (10 mL, 25 mmol) is added by a syringe. After 30 min redistilled diethyl oxalate (3.5 mL, 3.8 g, 26 mmol) is added and the mixture stirred at r.t. under N<sub>2</sub> for 18–72 h. The mixture is then added to water (250 mL) and the product extracted with Et<sub>2</sub>O (3 × 100 mL). The extract is dried (MgSO<sub>4</sub>) and evaporated. Kugelrohr distillation of the residue at 0.133 mbar gives the desired esters 2 (Table) as colourless liquids boiling between 150 and 200°C (oven temperature). Triphenylphosphine oxide remains in the distillation flask.

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