Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
ELSEVIER
Tetrahedron 62 (2006) 476–482

A Practical, efficient, and atom economic alternative to the Wittig and Horner–Wadsworth–Emmons reactions for the synthesis of (*E*)-α,β-unsaturated esters from aldehydes

Benjamin List,[a,*] Arno Doehring,[a] Maria T. Hechavarria Fonseca,[a] Andreas Job[b] and Ramon Rios Torres[a]

[a]*Max-Planck-Institut für Kohlenforschung, 45470 Mülheim an der Ruhr, Germany*
[b]*Lanxess Deutschland GmbH, Building Q-18, 51369 Leverkusen Germany*

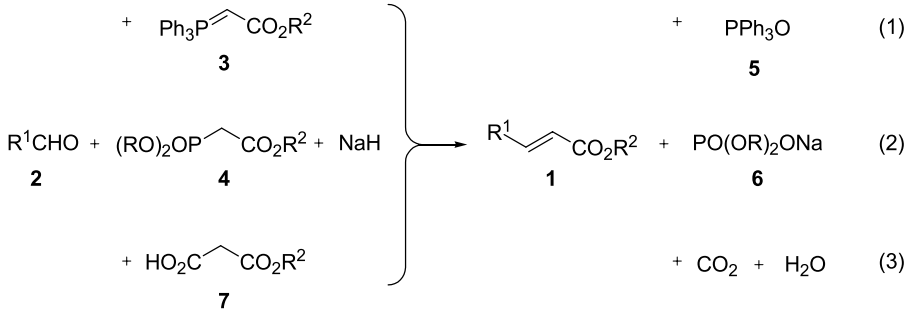
Received 7 July 2005; revised 8 September 2005; accepted 16 September 2005

Available online 20 October 2005

Abstract—We describe a highly efficient new methodology for the synthesis of (*E*)-α,β-unsaturated esters from aldehydes. In our DMAP-catalyzed reaction, both aromatic as well as aliphatic aldehydes furnish the desired products highly regio- and stereoselectively if treated with commercially available or synthetically easily accessible malonic acid half ester. A large scale application in the synthesis of *p*-methoxycinnamates, which are of use as sunscreen ingredients, is described.

1. Introduction

The synthesis of α,β-unsaturated esters **1** from aldehydes **2** is regularly required and a variety of methods have been developed for this transformation.[1,2,3] Because the classical Claisen-type aldol condensation of esters with aldehydes is limited to non-enolizable aldehydes, Wittig- (Eq. 1) or Horner–Wadsworth–Emmons-reactions (Eq. 2) using carbalkoxymethylene triphenylphosphoranes **3** or trialkylphosphonoacetates **4**, respectively, are commonly used alternatives and both high yields and (*E*)-stereoselectivities are typically obtained. A significant limitation, however, in particular concerning large scale applications, is the modest atom economy of these reactions. In the Wittig reaction, triphenylphosphine oxide **5** is a stoichiometric by-product and has to be removed chromatographically only to be disposed.[4] The Horner–Wadsworth–Emmons variant has the advantage of producing a water-soluble phosphate salt **6** as the by-product, which can be removed via aqueous extraction. This variant, however, typically requires the use of a strong base such as sodium hydride and, as in the Wittig reaction stoichiometric by-product formation can challenge waste-management. The decarboxylative Knoevenagel-type reaction of malonic acid half esters **7** with aldehydes to give α,β-unsaturated esters (Eq. 3) is another alternative yet rarely used process.[5] Because only water and carbon dioxide are produced as by-products, this reaction has a significantly improved atom economy. In addition, half-esters of



malonates **7** are as inexpensive as the corresponding phosphorous-based reagents (e.g., **3** and **4**) and can also be obtained easily from even less expensive dialkyl malonates.[6]

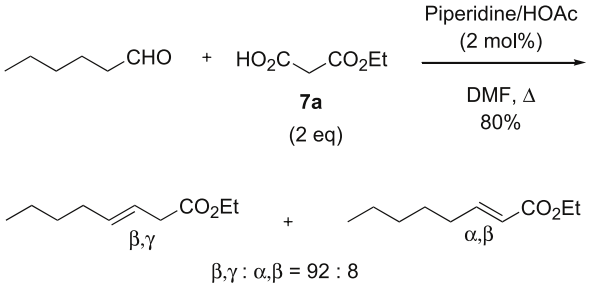
Keywords: (*E*)-Stereoselectivity; α,β-Unsaturated esters; Doebner–Knoevenagel reaction; DMAP-catalysis.
* Corresponding authors.

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.09.081

While advantageous in principle, the Knoevenagel (or Doebner–Knoevenagel) reaction variant is much less frequently used. Among the main reasons are the generally required reaction conditions, which include using a larger excess of the malonic half ester, catalysis with piperidine in pyridine as the solvent, and elevated temperatures (typically pyridine/reflux). In addition, (*E*)- versus (*Z*)-selectivity varies. The most important drawback, however, results form the fact that in the reaction with enolizable aldehydes, not α,β- but rather β,γ-unsaturated esters (or their mixtures) are commonly obtained.[7]

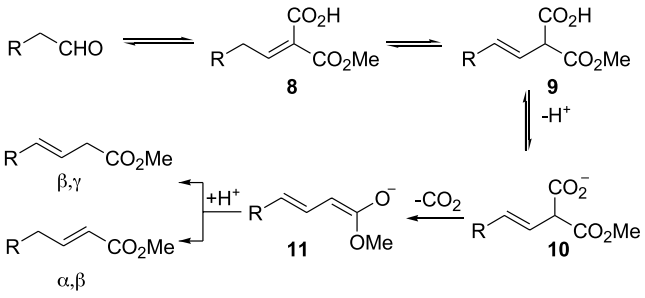
In the context of several other projects we realized the need for a clean, by-product-free, and reliably selective methodology for the production of α,β-unsaturated esters from aldehydes. A desirable feature of such a process would be applicability to large scale production and no requirement for heating or strong bases. We set up a study aimed at overcoming the disadvantages of the traditional Claisen-aldol, Wittig, Horner–Wadsworth–Emmons, and Knoevenagel reactions. Here, we report the full details of our investigation, which resulted in the development of a practical and highly efficient synthesis of α,β-unsaturated esters from aldehydes.[8]

At the onset, we identified the low α,β- versus β,γ-selectivity in the reaction of aliphatic and unbranched aldehydes with malonic acid half esters as the primary issue to be addressed in our studies. Surprisingly, it has been found that under standard Knoevenagel conditions the thermodynamically less stable β,γ-isomer usually dominates. For example, treating *n*-hexanal with ethyl hydrogen malonate **7a** in the presence of piperidinium acetate results in the selective formation of the β,γ-unsaturated ester (Eq. 4).[7b]



(4)

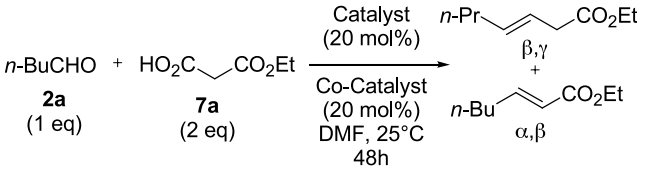
Mechanistic studies by Corey led to the proposal that the reaction in pyridine proceeds via decarboxylation of intermediate **10** to give the dienolate **11**. Its protonation occurs irreversibly at the more reactive α-position resulting in the predominant generation of the β,γ-unsaturated ester (Eq. 5).[9]



(5)

We reasoned that if a catalyst was used that in contrast to pyridine would be able to establish an equilibrium between the β,γ- and the α,β-isomer, the latter should be favoured thermodynamically. In addition, we envisioned alternative mechanistic modes of the decarboxylation, such as conjugate addition of a Lewis basic catalyst to Knoevenagel product **8**, followed by a decarboxylative elimination. Thus, screening alternative catalysts seemed attractive to us.

We decided to initiate our study with a screen of several different amine catalysts in the presence of various base co-catalysts for the reaction of *n*-pentanal **2a** with half ester **7a** (for selected examples see Eq. 6, Table 1). Most combinations led to mixtures of α,β- and β,γ-isomer in various ratios, the β,γ-isomer typically dominating. Remarkably, however, in reactions where we used DMAP as the co-catalyst, the selectivity shifted towards the desired α,β-isomer, independent of the amine catalyst. Moreover, when DMAP was used alone, only the α,β-isomer was formed and gratifyingly with high diastereoselectivity (*E*:*Z*=95:5).



(6)

After further optimization studies, we established reaction conditions that could be used with a large variety of aliphatic aldehydes (Eq. 7, Table 2). Thus, upon treating

Table 1. Screening of catalyst combinations

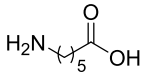
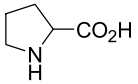
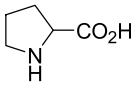
Entry	Catalyst	Co-catalyst	Yield	α,β:β,γ (GC)
1		$NaHCO_3$	60	1:5
2		Na_2CO_3	50	1:3
3		DMAP	80	10:1
4	DMAP	—	91	>20:1

Table 2. Synthesis of α,β-unsaturated esters from aliphatic aldehydes

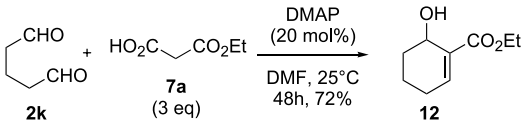
Entry	R	Yield	*E*:*Z* (GC)
1[a]	**a**	91	95:5
2[a]	**b**	95	96:4
3[a]	**c**	92	95:5
4[a]	**d**	91	95:5
5[a]	**e**	91	98:2
6	**f**	96	>99:1
7	**g**	92	98:2
8[b]	**h**	91	>99:1
9	**i**	92	>99:1
10	**j**	92	94:6

[a] Reaction at 10 °C.
[b] Piperidine as co-catalyst (10 mol%).

aliphatic aldehydes **2** with ethyl hydrogen malonate (**7a**, 1.5 equiv) in the presence of DMAP (10 mol%) at rt or below, in DMF, the corresponding α,β-unsaturated esters **1** were obtained with high yields, essentially complete α,β-selectivities, and also highly (*E*)-stereoselective.[10] An aqueous extraction was sufficient to obtain the products in excellent purities and chromatographic purification of the products was generally not required. The reaction proceeds efficiently with both simple unbranched aliphatic aldehydes (entries 1–4), branched aldehydes (entries 6–8), and also with an α-trisubstituted aldehyde (entry 9). Ketones are tolerated in the reaction at least as long as an aldehyde is also present such as in keto aldehyde **2e** (entry 5). This substrate readily undergoes an intramolecular base-catalyzed aldolization but under our reaction conditions this intramolecular process is completely suppressed and only the desired olefination occurs.[11] Despite the initially mildly acidic reaction conditions, aliphatic acetals are preserved in the process (entry 10).[12]

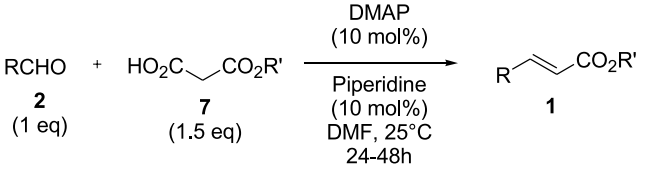
(7)

Not unexpectedly, a tandem olefination, Morita–Baylis–Hilmann reaction to hydroxyl ester **12** was observed with dialdehyde **2k** even when an excess of malonate **7a** was used (Eq. 8).[13]



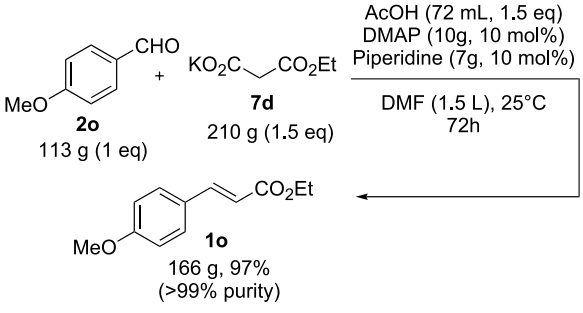
(8)

Aromatic aldehydes can also be used under our reaction conditions. However, the reaction times are generally somewhat longer. Gratifyingly, we found that the reaction rate could be significantly increased when we added piperidine (10 mol%) as co-catalyst. These conditions could be applied to a number of different aromatic and heteroaromatic aldehydes (Eq. 9, Table 3). In general, (*E*)/(*Z*)-selectivities are excellent exceeding 99:1 (by GC and NMR). In addition to ethyl esters (R^2=Et), both *tert*-butyl (R^2=*t*-Bu, entry 2) and benzyl esters (R^2=Bn, entry 3) can be obtained with comparable efficiency. As expected, rates are generally faster with electron poor aldehydes (entries 8, 11–13) and can be relatively slow with electron rich aromatic aldehydes such as *p*-hydroxybenzaldehyde (entry 9). *p*-Terephtalaldehyde **2v** and isophthalaldehyde **2w** in the presence of 3 equiv of malonate **7** gave the expected bis-enoates **1v** and **1w** in good yield (entries 13 and 4).



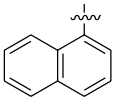
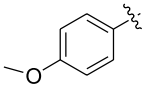
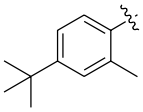
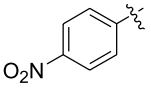
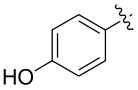
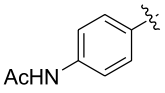
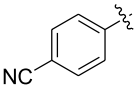
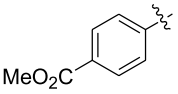
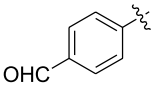
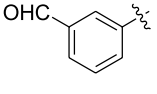
(9)

The synthesis of *p*-methoxyethylcinnamate (**1o**, entry 6) has been scaled up to illustrate the practicability of our process (Eq. 10).[14] In this reaction, we generated malonate **7a** in situ from the even less expensive potassium salt **7d** with acetic acid. Transesterification of cinnamate **1o** with 2-ethyl hexanol or isoamyl alcohol gave industrially relevant cinnamates **13** and **14**, UV-light absorbing ingredients of commercially available sunscreens (Eq. 11).

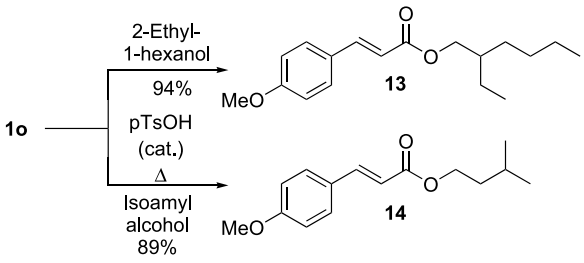


(10)

Table 3. Synthesis of α,β-unsaturated esters from aromatic aldehydes

Entry	R	R′	Yield	*E*:*Z* (GC)
1		Et (**a**)	92	>99:1
2		*t*-Bu (**b**)	87	>99:1
3		Bn (**c**)	96	>99:1
	l			
4		Et	92	>99:1
	m			
5		Et	91	>99:1
	n			
6		Et	99	>99:1
	o			
7		Et	89	>99:1
	p			
8		Et	86	>99:1
	q			
9[a]		Et	90	>99:1
	r			
10[a]		Et	92	>99:1
	s			
11		Et	94	>99:1
	t			
12		Et	92	>99:1
	u			
13[b]		Et	93	>99:1
	v			
14[b]		Et	93	>99:1
	w			

[a] Reaction time (168 h).
[b] bis-Enoate was obtained using 3 equiv of halfester.



(11)

In summary, we have developed a new synthesis of α,β-unsaturated esters from aldehydes. Our reaction is mild, efficient, catalytic, practical, (atom-)economic, and highly α,β-regio-, and (*E*)-stereoselective. The reaction tolerates various functional groups and can be used with both aliphatic and aromatic aldehydes. Future studies in our laboratory will focus on exploring the full scope of this reaction and of related decarboxylative carbon–carbon bond forming reactions.[15]

2. Experimental

2.1. General procedure for the reaction with the malonic acid monoethyl ester (7a)

4-Dimethylaminopyridine (24.4 mg, 0.20 mmol) was dissolved in 5 mL of DMF. The malonic acid half ester (3.00 mmol) followed by the aldehyde (2.00 mmol) were added, and the reaction was stirred at 10 °C or rt until the aldehyde was consumed.[16] The mixture was extracted with Et_2O and the organic layer was washed successively with NH_4Cl, water, $NaHCO_3$, and once again with water. After drying (Na_2SO_4) and filtering, all volatiles were evaporated in vacuo yielding, without any further purification, the pure α,β-unsaturated ester in the reported yields.

2.2. Scale up for *p*-methoxyethylcinnamate (1o)

4-Dimethylaminopyridine (10 g, 81.9 mmol) was dissolved in DMF (1.5 L). The potassium salt of the malonic acid half ester (**7d**, 210.1 g, 1234.4 mmol) followed by *p*-anisaldehyde (**2o**, 113.0 g, 829.0 mmol) were added. This suspension was stirred at 10 °C and acetic acid (72.2 mL, 1262.4 mmol) and piperidine (7 g, 82.2 mmol) were added dropwise consecutively. The mixture was stirred at rt until the aldehyde was consumed (72 h). After the standard aqueous work (see above) and recrystallization from ethanol, 165.8 g (803.9 mmol, 97%) of ester **1o** was obtained as white needles.

2.2.1. Transesterification of *p*-methoxyethylcinnamate (1o) with 2-ethyl-1-hexanol. *p*-Methoxyethylcinnamate **1o** (24.8 g, 120.3 mmol) and *p*-TsOH (2.3 g, 12.1 mmol) were dissolved in 2-ethyl-1-hexanol (223.0 g, 1712.3 mmol). The resulting solution was heated overnight to reflux. The reaction was quenched with saturated $NaHCO_3$ solution and extracted with Et_2O. The organics were dried (Na_2SO_4) and concentrated in vacuo to give ester **13** (32.8 g, 113 mmol, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, 6H, J=7.3 Hz), 1.30–1.44 (m, 8H); 1.64–1.67 (m, 1H), 3.84 (s, 3H), 4.11 (d, 2H, J=5.8 Hz), 6.31 (d, 1H, J=15.9 Hz), 6.91 (d, 2H, J=6.8 Hz), 7.48 (d, 2H, J=6.8 Hz), 7.63 (d, 1H, J=15.9 Hz). ^{13}C NMR δ11.0, 14.1, 23.0, 23.9, 29.0, 30.5, 38.9, 55.4, 66.8, 114.3, 115.9, 127.3, 129.7, 144.2, 161.3, 167.6.

2.2.2. Transesterification of *p*-methoxyethylcinnamate (1o) with isoamyl alcohol. *p*-Methoxyethylcinnamate **1o** (101 g, 489.7 mmol) and *p*-TsOH (5.3 g, 27.9 mmol) were dissolved in isoamyl alcohol (432.1 g, 4901.9 mmol). The resulting solution was heated overnight to reflux. The reaction was quenched with saturated $NaHCO_3$ solution and extracted with Et_2O. The organics were dried (Na_2SO_4) and concentrated in vacuo to give isoamylester **14** (108.4 g, 436.5 mmol, 89%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (d, 6H, J=6.7 Hz), 1.58–1.63 (m, 4H), 1.71–1.77 (m, 1H), 3.80 (s, 3H), 4.23 (t, 2H, J=6.7 Hz), 6.30 (d, 1H, J=15.9 Hz), 6.91 (d, 2H, J=8.6 Hz), 7.49 (d, 2H, J=8.6 Hz), 7.63 (d, 1H, J=15.9 Hz). ^{13}C NMR δ 22.5, 25.1, 37.5, 55.4, 63.1, 114.3, 115.8, 129.7, 144.2, 161.3, 167.4.

2.2.3. Ethyl-(*E*)-3-phenyl-2-propenoate (1l–a). Colourless oil (325.3 mg, 1.85 mmol, 92%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[17]

2.2.4. *tert*-Butyl-(*E*)-3-phenyl-2-propenoate (1l–b). Colourless oil (354.6 mg, 1.74 mmol, 87%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[18]

2.2.5. Benzyl-(*E*)-3-phenyl-2-propenoate (1l–c). Colourless oil (456.8 mg, 1.92 mmol, 96%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[19]

2.2.6. Ethyl-(*E*)-3-(1-naphthalenyl)-2-propenoate (1m). Colourless oil (417.1 mg, 1.84 mmol, 92%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[20]

2.2.7. Ethyl-(*E*)-3-(2-furanyl)-2-propenoate (1n). Colourless oil (302.1 mg, 1.82 mmol, 91%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[21]

2.2.8. Ethyl-(*E*)-3-(4-methoxyphenyl)-2-propenoate (1o). Colourless needles (408.1 mg, 1.98 mmol, 99%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[17]

2.2.9. Ethyl-(*E*)-3-(2-methyl-4-*tert*-butylphenyl)-2-propenoate (1p). Colourless oil (437.1 mg, 1.77 mmol, 89%, *E*:*Z*>99:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 9H), 1.28 (t, 3H, J=7.1 Hz), 2.33 (s, 3H); 4.21 (q, 2H, J=7.1 Hz), 6.30 (d, 1H, J=15.9 Hz), 7.07 (d, 1H, J=8.0 Hz), 7.24 (dd, 1H, J=8.0, 2 Hz), 7.49 (d, 1H, J=2 Hz), 7.91 (d, 1H, J=15.9 Hz). ^{13}C NMR δ 13.9, 18.8, 30.9, 34.1, 60.1, 118.6, 122.9, 124.0, 126.9, 130.2, 132.0, 142.6, 148.8, 166.0.

2.2.10. Ethyl-(*E*)-3-(4-nitrophenyl)-2-propenoate (1q). Pale-yellow needles (378.8 mg, 1.71 mmol, 86%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[22]

2.2.11. Ethyl-(*E*)-3-(4-hydroxyphenyl)-2-propenoate (1r). Colourless oil (346.0 mg, 1.8 mmol, 90%, *E*:*Z*>99:1). The NMR data is in accordance with the lit.[23]

2.2.12. Ethyl-(*E*)-3-(4-acetamidophenyl)-2-propenoate (1s). Pale-yellow needles (427.6 mg, 1.83 mmol, 92%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[24]

2.2.13. Ethyl-(*E*)-3-(4-cyanophenyl)-2-propenoate (1t). Colourless oil (379.5 mg, 1.89 mmol, 94%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[25]

2.2.14. Ethyl-(*E*)-3-(4-acetoxyphenyl)-2-propenoate (1u). White needles (429.2 mg, 1.83 mmol, 92%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[22]

2.2.15. Bis-ethyl-(*E*)-3,3′-(1,4-phenylene)-2-propenoate (1v). White needles (510.8 mg, 1.86 mmol, 93%, *E*:*Z*>99:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, 6H, J=7.1 Hz), 4.21 (q, 4H, J=7.1 Hz), 6.39 (d, 2H, J=15.9 Hz), 7.47 (s, 4H), 7.59 (d, 2H, J=15.9 Hz). ^{13}C NMR δ 14.7, 61.0, 119.8, 128.9, 136.5, 143.8, 167.1.

2.2.16. Bis-ethyl-(*E*)-3,3′-(1,3-phenylene)-2-propenoate (1w). White needles (511.4 mg, 1.86 mmol, 93%, *E*:*Z*>99:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (t, 6H, J=7.1 Hz), 4.27 (q, 4H, J=7.1 Hz), 6.47 (d, 2H, J=16.0 Hz), 7.41 (dd, 1H, J=7.5 Hz), 7.54 (d, 2H, J=7.5 Hz), 7.65 (t, 1H, J=7.5 Hz), 7.68 (d, 2H, J=16.0 Hz). ^{13}C NMR δ 14.3, 60.6, 119.3, 127.6, 129.4, 129.5, 135.2, 143.6, 166.7.

2.2.17. Ethyl-(*E*)-2-heptenoate (1a). Colourless oil (284.0 mg, 1.82 mmol, 91%, *E*:*Z*=95:5). NMR data is in accordance with the lit.[26]

2.2.18. Ethyl-(*E*)-2-nonenoate (1b). Colourless oil (350.9 mg, 1.90 mmol, 95%, *E*:*Z*=96:4). NMR data is in accordance with the lit.[27]

2.2.19. Ethyl-(*E*)-5-methyl-2-hexenoate (1c). Colourless oil (287.3 mg, 1.84 mmol, 92%, *E*:*Z*=95:5). NMR data is in accordance with the lit.[28]

2.2.20. Ethyl-(*E*)-5-phenyl-2-pentenoate (1d). Colourless oil (370.1 mg, 1.81 mmol, 91%, *E*:*Z*=95:5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (t, 3H, J=7.1 Hz), 2.43–2.48 (m, 2H), 2.67–2.72 (m, 2H), 4.10 (q, 2H, J=7.1 Hz), 5.78 (d, 1H, J=15.6 Hz), 6.90 (dt, 1H, J=15.6 Hz), 7.10–7.14 (m, 3H), 7.17–7.23 (m, 2H). ^{13}C NMR δ 15.3, 35.0, 35.5, 61.3, 123.0, 127.2, 129.4, 129.6, 141.9, 149.1, 167.7.

2.2.21. Ethyl-(*E*)-8-oxo-2-nonenoate (1e). Colourless oil (360.6 mg, 1.82 mmol, 91%, *E*:*Z*=98:2). NMR data is in accordance with the lit.[29]

2.2.22. Ethyl-(*E*)-4-methyl-2-pentenoate (1f). Colourless oil (273.2 mg, 1.92 mmol, 96%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[28]

2.2.23. Ethyl-(*E*)-3-cyclohexyl-2-propenoate (1g). Colourless oil (335.4 mg, 1.84 mmol, 92%, *E*:*Z*=98:2). NMR data is in accordance with the lit.[22]

2.2.24. Ethyl-(*E*)-4,4-diphenyl-2-butenoate (1h). Colourless oil (483.1 mg, 1.81 mmol, 91%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[22]

2.2.25. Ethyl-(*E*)-4,4-dimethyl-2-pentenoate (1i). Colourless oil (286.5 mg, 1.83 mmol, 92%, *E*:*Z*>99:1). NMR data is in accordance with the lit.[28]

2.2.26. Ethyl-(*E*)-6,6-dimethoxy-2-hexenoate (1j). Colourless oil (373.1 mg, 1.85 mmol, 92%, *E*:*Z*=94:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, 3H, J=7.1 Hz), 1.66–1.71 (m, 2H), 2.17–2.22 (m, 2H), 3.25 (s, 6H), 4.12 (q, 2H, J=7.1 Hz), 4.30 (t, 1H, J=5.6 Hz), 5.78 (d, 1H, J=15.6 Hz), 6.89 (dt, 1H, J=15.6 Hz). ^{13}C NMR δ 13.9, 26.9, 30.5, 52.5, 59.8, 103.3, 121.3, 147.7, 166.2.

Acknowledgements

Generous gifts of chemicals by Degussa and general support of our work by Lanxess is most gratefully acknowledged. We thank Kathrin Wobser, Hendrik van Thienen, and Pedro Llamas Galilea for technical assistance.

References and notes

1. Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863–927.
2. For selected alternative processes, see: (a) Claisen–Schmidt-type condensation of aromatic aldehydes: Hatsuda, M.; Kuroda, T.; Seki, M. *Synth. Commun.* **2003**, *33*, 427–432. Kisanga, P.; 'Sa, B. D.; Verkade, J. *Tetrahedron* **2001**, *57*, 8047–8052. (b) From ethyl diazoacetate and stoichiometric phosphine via transition metal catalysis: Hermann, W. A.; Wang, M. *Angew. Chem.* **1991**, *103*, 1709–1711. Hermann, W. A.; Wang, M. *Angew. Chem.* **1991**, *30*, 1641–1643. Ledford, B. E.; Carreira, E. M. *Tetrahedron Lett.* **1997**, *38*, 8125–8128. Lee, M.-Y.; Chen, Y.; Zhang, X. P. *Organometallics* **2003**, *22*, 4905–4909. (c) From methyl dichloroacetate and stoichiometric $CrCl_2$: Barma, D. K.; Kundu, A.; Bandyopadhyay, A.; Sangras, B.; Briot, A.; Mioskowski, R.; Falck, J. R. *Tetrahedron Lett.* **2004**, *45*, 5917–5920. (d) Via Peterson-type olefination with ethyl(trimethlysilyl)acetate: Taguchi, H.; Shimoji, K.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2529–2531. (e) From mercapto acetates: Matui, S.; Tanaka, K.; Kaji, A. *Synthesis* **1983**, *2*, 127–128. (f) From ethyl bromoacetate and *n*-Bu_3Sb: Huang, Y.; Shen, Y.; Chen, C. *Tetrahedron Lett.* **1986**, *27*, 2903–2904. (g) From ethyl bromoacetate and *n*-Bu_2Te: Huang, X.; Xie, L.; Wu, H. *Tetrahedron Lett.* **1987**, *28*, 801–802. (h) From ethyl bromoacetate in the presence of a Te-catalyst, potassium carbonate, sodium bisulfite, and triphenyl phosphite: Huang, Z.-Z.; Ye, S.; Sia, W.; Tang, Y. *Chem. Commun.* **2001**, *15*, 1384–1385. (i) From α-chloroacetaldehyde dialkylacetal via alkoxyacetylide anions: Olah, G. A.; Wu, A. H.; Farooq, O.; Prakash, G. K. *Synthesis* **1988**, *7*, 537–538. (j) From orthoacetates: Sapath Kumar, H. M.; Shesha Rao, M.; Joyasawal, S.; Yadav, J. S. *Tetrahedron Lett.* **2003**, *44*, 4287–4289. (k) From ethoxycarbonylmethanesulfonyl fluoride: Kagabu, S.; Shimizu, C.; Takahashi, J.; Hara, K.; Koketsu, M.; Ishida, M. *Bull. Soc. Chim. Fr.* **1992**, *129*, 435–439. (l) From ethyl(benzothiazol-2-ylsulfonyl)acetate: Blakemore, P. R.; Ho, D. K. H.; Nap, W. M. *Org. Biomol. Chem.* **2005**, *3*, 1365–1368.
3. For comparably efficient atom economic approaches to α,β-unsaturated esters that do not rely on aldehydes, see for example: (a) Heck-reaction,Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066. (b) Cross metathesis, Chatterjee, A. K.; Toste, F. D.; Choi, T.-L.; Grubbs, R. H. *Adv. Synth. Catal.* **2002**, *6–7*, 634–637.
4. For a two step methodology for the recycling of triphenylphosphine oxide (via Ph_3PCl_2), see: Process for the manufacture of triphenyl phosphine. Hermeling, D.; Bassler, P.; Hammes, P.; Hugo, R.; Lechtken, P.; Siegel, H., (BASF AG, Germany). Eur. Pat. Appl. EP 6385807, 1995, p 7, CAN 123:9689.
5. (a) For aromatic aldehydes, see: Galat, A. *J. Am. Chem. Soc.* **1946**, *68*, 376–377. (b) For linear aldehydes, see: Martin, C. J.; Schepartz, A. I.; Daubert, B. F. *J. Am. Chem. Soc.* **1948**, *70*, 2601–2602. (c) Klein, J.; Bergmann, E. D. *J. Am. Chem. Soc.* **1957**, *79*, 3452–3454. (d) Shabtai, J.; Ney-Igner, E.; Pines, H. *J. Org. Chem.* **1981**, *46*, 3795–3802.
6. Aldrich cataloge: (carbethoxymethylene)triphenylphosphorane (3, R^2=Et), 10 mmol ca. 17 €; triethylphosphono acetate (4, R^2=Et), 10 mmol ca. 2 €; mono-ethyl malonate (**7a**, R^2=Et) 10 mmol ca. 5 €; mono-ethyl malonate, potassium salt (**7d**), 10 mmol ca. 2 €.
7. (a) Carmona, A. T.; Fuentes, J.; Robina, I.; Rodriguez Garcia, E.; Demange, R.; Vogel, P.; Winters, A. L. *J. Org. Chem.* **2003**, *68*, 3874–3883. (b) Ragoussis, N.; Ragoussis, V. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3529–3533. (c) Influence of heteroaromatic amines on Knoevenagel condensation: Yamanaka, H.; Yokoyama, M.; Sakamoto, T.; Shiraishi, T.; Sagi, M.; Mizugaki, M. *Heterocycles* **1983**, *20*, 1541–1544.
8. For a preliminray communication of our results, see: List, B.; Doehring, A.; Hechavarria Fonseca, M. T.; Wobser, K.; van Thienen, H.; Rios Torres, R.; Llamas Galilea, P., *Adv. Synth. Catal.* **2005**, in press.
9. For mechanistic discussions of this observation, see: Corey, E. J. *J. Am. Chem. Soc.* **1952**, *74*, 5897–5905. Corey, E. J. *J. Am. Chem. Soc.* **1953**, *75*, 1163–1167.
10. In one report DMAP has been used as a catalyst for the reaction of malonic acid half esters with α,β-unsaturated aldehydes at elevated temperature in pyridine to give the corresponding α,β,γ,δ-unsaturated esters. See: Rodriguez, J.; Waegell, B. *Synthesis* **1988**, 534–535.
11. See for example: Lalande, R.; Moulines, J.; Duboudin, J. *Bull. Soc. Chim. Fr.* **1962**, 1087–1089. Also see: List, B. In Mahrwald, R., Ed.; Modern Aldol Reactions; Wiley-VCH: Weinhein, Germany, 2004; Vol. 1, pp 161–200.
12. In our experience, acetals of aromatic aldehydes can be transformed into the α,β-unsaturated ester under the slightly acidic reaction conditions. Also see: Klein, J.; Bergmann, E. D. *J. Am. Chem. Soc.* **1957**, *79*, 3452–3454.
13. Dinon, F.; Richards, E.; Murphy, P. J. *Tetrahedron Lett.* **1999**, *40*, 3279–3282.
14. 'Process for the production of olefins from carbonyl compounds' (Studiengesellschaft Kohle mbH), Patent pending.
15. For recent studies on the use of malonic acid half thioesters in asymmetric catalysis, see: Magdziak, D.; Lalic, G.; Lee, H. M.; Fortner, K. C.; Aloise, A. D.; Shair, M. D. *J. Am. Chem. Soc.* **2005**, *127*, 7284–7285.
16. In selected cases (see Tables), piperidine (10 mol%) was added as co-catalyst (at 10 °C) to reduce the reaction times.

17. Aggarwal, V. K.; Fulton, J. R.; Sheldon, C. G.; de Vicente, J. *J. Am. Chem. Soc.* **2003**, *125*, 6034–6035.
18. Sato, Y.; Takeuchi, S. *Synthesis* **1983**, *9*, 734–735.
19. Hon, Y. S.; Chang, R. C.; Chau, T. Y. *Heterocycles* **1990**, *31*, 1745–1750.
20. Dickinson, J. M.; Murphy, J. A.; Patterson, C. W.; Wooster, N. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1179–1184.
21. Kasahara, A.; Izumi, T.; Ogihara, T. *J. Heterocycl. Chem.* **1989**, *26*, 597–599.
22. Chen, Y.; Huang, L.; Ranade, M. A.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 3714–3717.
23. Patel, C. K.; Owen, C. P.; Aidoo-Gyamfi, K.; Ahmed, S. *Lett. Drug Des. Discovery* **2004**, *1*, 35–44.
24. Abe, Y.; Kayakiri, H.; Satoh, S.; Inoue, T.; Sawada, Y.; Inamura, N.; Asano, M.; Hatori, C.; Sawai, H.; Oku, T.; Tanaka, H. *J. Med. Chem.* **1998**, *41*, 4053–4061.
25. Cheng, G.; Mirafzal, G. A.; Woo, L. K. *Organometallics* **2003**, *22*, 1468–1474.
26. Matsui, S. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 426–434.
27. Cativiela, C.; Diaz De Villegas, M. D.; Galvez, J. A.; Ronco, E. *Chirality* **2004**, *16*, 106–111.
28. Tay, M. K.; About-Jaudet, E.; Collignon, N.; Teulade, M. P.; Savignac, P. *Synth. Commun.* **1988**, *18*, 1349–1362.
29. Fukuzawa, S.; Nakanishi, A.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1669–1675.