Facile Synthesis of 5-Arylpent-4-enoates from the Baylis-Hillman Acetates

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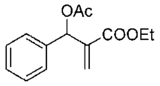
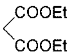
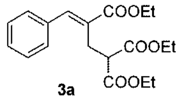
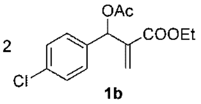
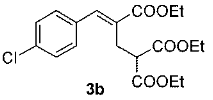
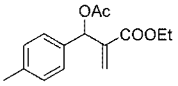
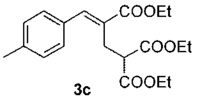
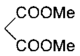
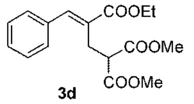
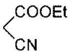
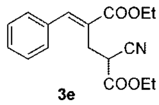
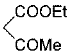
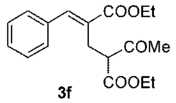
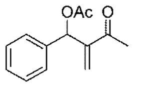
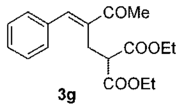
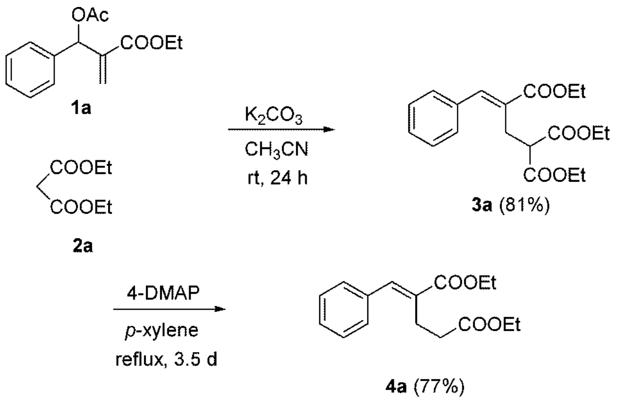
Recently, Basavaiah *et al.* have published some papers dealing with the Johnson-Claisen rearrangement of the Baylis-Hillman adducts.[1] 5-Arylpent-4-enoates or 4-cyanoalk-4-enoates can be obtained from the above reaction in moderate yields. Shen *et al.* have also reported the synthesis of the latter compounds by using the sequential Michael reaction and Horner-Wadworth-Emmons (HWE) reaction of phosphonates.[2]

During our studies on the Baylis-Hillman chemistry[3] we found another efficient method for the synthesis of the abovementioned compounds. As shown in Scheme 1 the reaction of the Baylis-Hillman acetate **1a** and diethyl malonate (**2a**) in CH_3CN in the presence of K_2CO_3 gave the allylic rearrangement product **3a** in good yield. The structure of **3a** was exclusively *E*-form as in our previous papers.[3] Trace amount (*ca.* 5%) of the corresponding *Z*-form was observed in ^{1}H NMR spectrum. The separation of *E* and *Z*-form was difficult at this stage. Thus, we used the mixture directly in the next reaction without further purification. Following decarbethoxylation was conducted in *p*-xylene in the presence of 4-dimethylaminopyridine (4-DMAP).[4a,4b] We could isolate the desired compound **4a** in 77% yield. At this stage, pure **4a**-*E* could be separated easily from the minor component, **4a**-*Z*. In the reaction, DABCO (1,4-diazabicyclo[2.2.2]octane) and DBN (1,5-diazabicyclo[4.3.0]non-5-ene) could also be used as reported in similar systems.[4c,4d] However, the use of DMAP in refluxing xylene gave the best results.[5]

Table 1. Synthesis of allylic rearrangement products **3**

Entry	B-H acetate **1**	**2**	Conditions	Product	Yield (%)
1	 1a	 2a	K_2CO_3 CH_3CN rt, 24 h		81[a]
2	 1b	2a	K_2CO_3 CH_3CN rt, 24 h		87[a]
3	 1c	2a	K_2CO_3 CH_3CN rt, 20h		78[a]
4	1a	 2b	K_2CO_3 CH_3CN rt, 20 h		73[a]
5	1a	 2c	K_2CO_3 CH_3CN rt, 16h		40
6	1a	 2d	K_2CO_3 CH_3CN rt, 32 h		55
7	 1d	2a	K_2CO_3 CH_3CN rt, 24 h		72

[a] Trace amounts (*ca.* 5%) of the corresponding *Z*-isomer were observed in their ^{1}H NMR spectra.

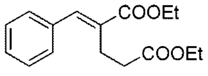
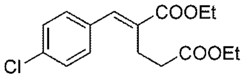
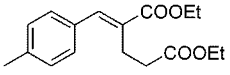
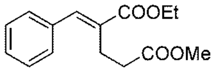
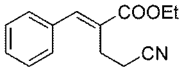
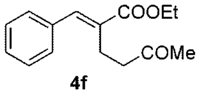
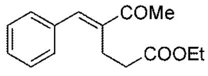


Scheme 1

The representative results for the synthesis of the allylic rearrangement products **3a-g** are summarized in Table 1. Besides of diethyl malonate (**2a**, entries 1-3) and dimethyl malonate (**2b**, entry 4), some other activated methylene compounds such as ethyl cyanoacetate (**2c**, entry 5) and ethyl acetoacetate (**2d**, entry 6) gave similar results. The Baylis-Hillman acetate **1d**, derived from benzaldehyde and methyl vinyl ketone, gave **3g** similarly (entry 7). The results of selective decarbethoxylation of **3a-g** with 4-DMAP (5 equiv.) are summarized in Table 2.

A typical procedure for the synthesis of **3a** and **4a** is as follows: To a stirred solution of **1a** (496 mg, 2.0 mmol) and diethyl malonate (360 mg, 2.2 mmol) in CH_3CN (5 mL) was added K_2CO_3 (305 mg, 2.2 mmol) and the mixture was stirred at room temperature for 24 h. After usual workup and column chromatographic purification (hexane/ether, 8 : 1)

Table 2. Synthesis of 5-arylpent-4-enoate derivatives **4**

Entry	3	Conditions	Product[a]	Yield (%)[b]
1	**3a**	4-DMAP (5.0 equiv.) *p*-xylene reflux, 3.5 days	 **4a**	77
2	**3b**	4-DMAP (5.0 equiv.) *p*-xylene reflux, 3 days	 **4b**	67
3	**3c**	4-DMAP (5.0 equiv.) *p*-xylene reflux, 6 days	 **4c**	40
4	**3d**	4-DMAP (5.0 equiv.) *p*-xylene reflux, 2 days	 **4d**	50
5	**3e**	4-DMAP (5.0 equiv.) *p*-xylene reflux, 2 days	 **4e**	57
6	**3f**	4-DMAP (5.0 equiv.) *p*-xylene 120 °C, 4 days	 **4f**	64
7	**3g**	4-DMAP (5.0 equiv.) *p*-xylene reflux, 6 days	 **4g**	45

[a]Pure *E*-form. [b]Products were obtained as clear oil except for **4f** (mp 44-46 °C).

3a was obtained as a clear oil, 565 mg (81%).[6] A stirred solution of **3a** (348 mg, 1.0 mmol) and 4-DMAP (610 mg, 5 mmol) in dry xylene (3 mL) was heated to reflux under nitrogen atmosphere for 3.5 days. After removal of the solvent and column chromatographic purification (hexane/ether, 8 : 1) **4a** was obtained as an oil, 213 mg (77%).[6]

In conclusion we disclosed a facile synthetic method of synthetically useful 5-arylpent-4-enoate derivatives.[1,2]

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References and Notes

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5. Decarbethoxylation of **3a** with DABCO (10 equiv) in refluxing xylene gave **4a** in 45% yield after 2 days. The use of DBN (5 equiv.) in similar reaction conditions gave intractable mixtures.
6. Selected data for **3a** and **4a**. **3a**: oil; IR (KBr) 1746, 1733, 1707 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.15 (t, J = 7.2 Hz, 6H), 1.34 (t, J = 7.2 Hz, 3H), 3.20 (d, J = 7.8 Hz, 2H), 3.79 (t, J = 7.8 Hz, 1H), 3.98-4.15 (m, 4H), 4.27 (q, J = 7.2 Hz, 2H), 7.25-7.38 (m, 5H), 7.77 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 13.79, 14.13, 26.15, 50.42, 60.87, 61.18, 127.83, 128.14, 128.46, 129.01, 134.92, 141.44, 167.32, 168.72. **4a**: oil; IR (KBr) 1734, 1707 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.15 (t, J = 7.2 Hz, 3H), 1.27 (t, J = 7.2 Hz, 3H), 2.45-2.51 (m, 2H), 2.77-2.83 (m, 2H), 4.03 (q, J = 7.2 Hz, 2H), 4.20 (q, J = 7.2 Hz, 2H), 7.27-7.32 (m, 5H), 7.65 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 14.07, 14.19, 22.99, 33.44, 60.32, 60.81, 128.47, 128.49, 129.05, 131.38, 135.21, 140.01, 167.69, 172.61.