Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 47 (2006) 7619–7623

Treatment of Baylis–Hillman adducts with triethyl orthoacetate in the presence of heterogeneous catalysts: a method for the stereoselective synthesis of two different types of trisubstituted alkenes☆

Biswanath Das,* Anjoy Majhi and Joydeep Banerjee

Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Received 14 July 2006; revised 7 August 2006; accepted 17 August 2006
Available online 8 September 2006

Abstract—Baylis–Hillman adducts on treatment with triethyl orthoacetate in the presence of $HClO_4$–SiO_2 afford the corresponding allyl ethyl ethers while in the presence of $NaHSO_4$–SiO_2 undergo the Johnson–Claisen rearrangement to form ethyl alk-4-enoates. Thus two different types of trisubstituted alkenes are produced in a stereoselective manner using two different hetereogeneous catalysts.

Baylis–Hillman adducts,[1] 3-hydroxy-2-methylene-alkanoates **1** and 3-hydroxy-2-methylene-alkanenitriles **2**, are important precursors for the stereoselective synthesis of different multifunctional molecules.[2] These adducts have been utilized by us for the synthesis of (*E*) and (*Z*) trisubstituted alkenes.[3] Trisubstituted alkene moieties occur widely in various naturally occurring bioactive molecules including various important pheromones and antibiotics.[4] The biological activity of these alkenes is highly dependent on their isomeric purity. Thus the stereoselective synthesis of trisubstituted alkenes is an important task in organic chemistry.

In continuation of our work,[5] on the applications of heterogeneous catalysts for the development of useful synthetic methodologies we have examined the effects of these catalysts on the reaction of Baylis–Hillman adducts **1** and **2** with triethyl orthoacetate.

Allyl alcohols, including Baylis–Hillman adducts, on the treatment with triethyl orthoacetate in the presence of propionic acid are known to undergo the Johnson–Claisen rearrangement.[6] However, an interesting observation here is that silica-supported perchloric acid ($HClO_4$–SiO_2) catalyzed the formation of the corresponding allyl ethyl ethers **3** and **4** while silica-supported sodium hydrogen sulfate ($NaHSO_4$–SiO_2) catalyzed the production of the Johnson–Claisen rearrangement products **5** and **6** (Scheme 1).

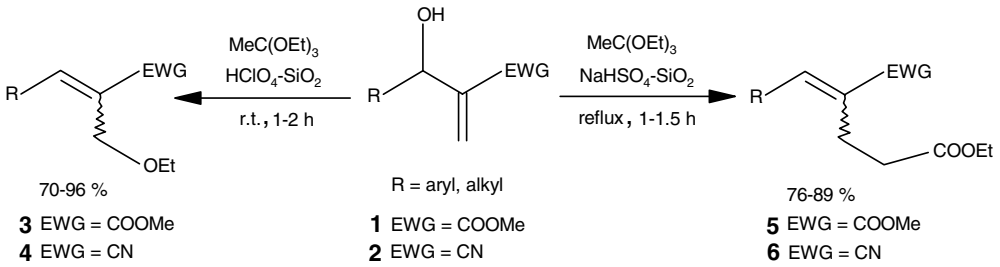
Various Baylis–Hillman adducts **1** and **2** containing both the ester and nitrile moieties were converted into the corresponding allyl ethyl ethers (Table 1) and the Johnson–Claisen rearrangement products (Table 2) with the proper choice of the catalyst ($HClO_4$–SiO_2/$NaHSO_4$–SiO_2) on reaction with triethyl orthoacetate. The catalysts, $HClO_4$–SiO_2[7] ($HClO_4$: 1.25 g; SiO_2: 23.75 g) and $NaHSO_4$–SiO_2[8] ($NaHSO_4$: 4.14 g; SiO_2: 10 g), were prepared from their readily available ingredients. The first catalyst catalyzed the conversion at room temperature to form the allyl ethyl ethers in very high yields. The Johnson–Claisen rearrangement products were not detected at all. The conversion was complete within 1–2 h. The treatment of the adducts with MeOH or EtOH (instead of triethyl orthoacetate) afforded no product in the presence of this catalyst.[9] The other catalyst, $NaHSO_4$–SiO_2 catalyzed the reaction of the Baylis–Hillman adducts with triethyl orthoacetate under reflux to produce only the Johnson–Claisen

Keywords: Baylis–Hillman adduct; $HClO_4$–SiO_2; $NaHSO_4$–SiO_2; Heterogeneous catalyst; Trisubstituted alkene.

☆ Part 107 in the series, 'Studies on novel synthetic methodologies'; IICT Communication No. 060808.

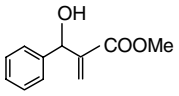
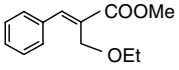
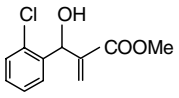
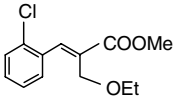
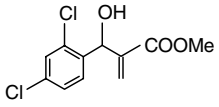
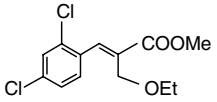
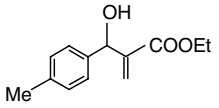
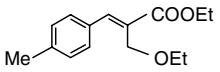
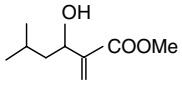
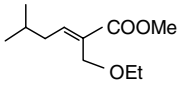
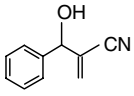
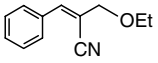
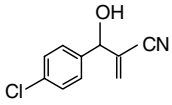
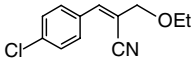
* Corresponding author. Tel./fax: +91 40 27160512; e-mail: biswanathdas@yahoo.com

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.08.060



Scheme 1.

Table 1. Synthesis of allyl ethyl ethers using $HClO_4$–SiO_2[a]

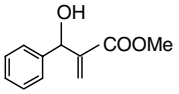
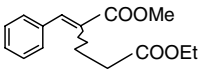
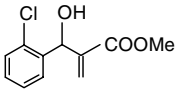
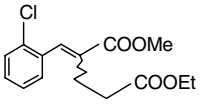
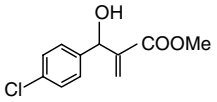
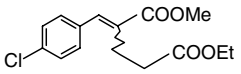
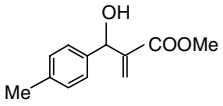
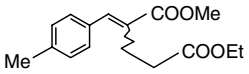
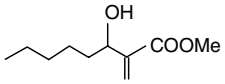
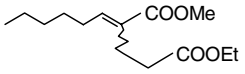
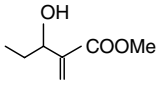
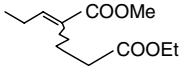
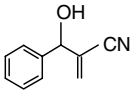
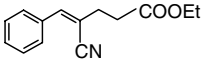
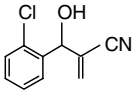
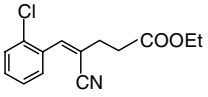
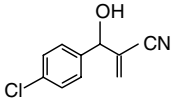
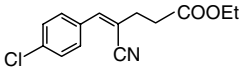
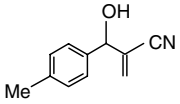
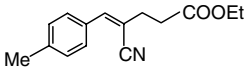
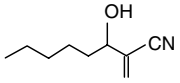
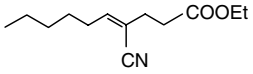
Entry	Substrate	Product	Time (h)	Isolated yield (%)
3a			1	89
3b			1	93
3c			1	96
3d			1	88
3e			1.5	70
4a			2	78
4b			1.5	86

[a] The structures of the allyl ethers were determined from their spectral (IR, ^{1}H NMR and MS) and analytical data.

rearrangement product in impressive yields, and the allyl ethers were not formed at all. The catalyst, $HClO_4$–SiO_2 or $NaHSO_4$–SiO_2, can easily be removed from the reaction mixture by filtration, making the experimental procedure very simple. Silica alone induced no reaction under the present experimental conditions.

In the present conversion both the allyl ethyl ethers and Johnson–Claisen rearrangement products (ethyl alk-4-enoates) were formed in a stereoselective manner. The allyl ethyl ethers containing an ester moiety were produced with the (*E*) configuration while those containing a nitrile had the (*Z*) configuration. On the other hand, the ethyl alk-4-enoates having an ester group at C-4 were obtained with a high (*E*) selectivity when C-5 carried an aryl group and with high (*Z*) selectivity when C-5 carried an alkyl group. However, the alkenes with a nitrile group at C-4 were formed with (*Z*) selectivity. The ^{1}H NMR spectra of the products were used to settle their structures and stereochemistry by comparison with reported data of known compounds.[6b,c,9] In the ^{1}H NMR spectrum of a trisubstituted alkene the β-vinylic protons, cis and trans to the ester group are reported to appear at ca. δ 7.5 and 6.5, respectively, when R is aryl.[10a,b] The same protons cis and trans to an ester group resonate at ca. δ 6.5 and 5.7, respectively, when R is alkyl.[10c,d] Similarly, the β-vinylic protons cis and trans to a nitrile group resonate at ca. δ 7.6 and 7.2, respectively, when R is aryl[3b,10e,f] while the same protons cis and trans to the nitrile group resonate at ca. δ 6.8 and 6.3, respectively, when R is alkyl.[3b,10g,h] These known ^{1}H NMR values were useful in determining the stereochemistry of the trisubstituted alkenes prepared in this work.

Table 2. Synthesis of ethyl alk-4-enoates using $NaHSO_4$–SiO_2[a]

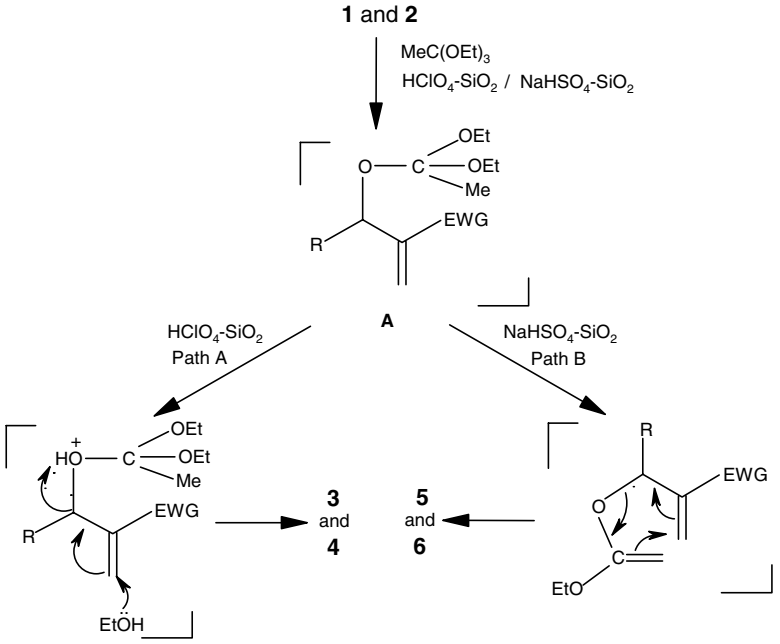
Entry	Substrate	Product	Time (h)	Isolated yield (%)	*E*:*Z*[b]
5a			1	89	81:19
5b			1	88	85:15
5c			1	86	79:21
5d			1	83	80:20
5e			1.5	80	22:78
5f			1.5	79	25:75
6a			1	84	0:100
6b			1.5	81	0:100
6c			1	87	0:100
6d			1.5	82	0:100
6e			1.5	76	0:100

[a] The structures of the alk-4-enoates were determined from their spectral (IR, ^1H NMR and MS) and analytical data.
[b] *E*:*Z* was determined from ^1H NMR spectral analysis.

The conversion of the Baylis–Hillman adducts into allyl ethers and alk-4-enoates possibly takes place through a common intermediate **A** (Scheme 2). With the stronger acidic catalyst ($HClO_4$–SiO_2) the reaction follows path A to form the allyl ethers **3** and **4** while with a catalyst of a weaker acidity ($NaHSO_4$–SiO_2) the reaction follows path B to yield the rearranged products **5** and **6**. Thus the product formation is dependent on the nature of the catalyst. The involvement of an intermediate **A** is supported by the fact that the Baylis–Hillman adducts did not afford any product on treatment with MeOH or EtOH in the presence of $HClO_4$–SiO_2 but the bulky leaving group present in **A** facilitated the formation of **3** and **4**.

In conclusion, we have developed an efficient and convenient method for stereoselective conversions of the Baylis–Hillman adducts by the treatment with triethyl orthoacetate into two different types of trisubstituted alkenes (allyl ethers and alk-4-enoates) by applying two different heterogeneous catalysts, $HClO_4$–SiO_2 and $NaHSO_4$–SiO_2.

General experimental procedure: To a mixture of Baylis–Hillman adduct (1 mmol) and triethyl orthoacetate (5 mmol) $HClO_4$–SiO_2 or $NaHSO_4$–SiO_2 (100 mg) was added. The mixture was stirred at room temperature using the first catalyst or heated under reflux with the second catalyst. The reaction was monitored by TLC.



Scheme 2.

After completion the mixture was filtered and the filtrate was concentrated. The residue was subjected to column chromatography (silica gel, 2% (for **3** and **4**) and 3% (for **5** and **6**) EtOAc in hexane) to obtain pure trisubstituted alkene.

The spectral (IR, ^{1}H NMR and MS) and analytical data of some representative allyl ethyl ethers and the unknown alk-4-enoates[6b] are given below.

Compound **3c**: IR (KBr): υ_{max} 1720, 1637, 1468, 1236 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.92 (1H, s), 7.69 (1H, d, $J = 8.0$ Hz), 7.48 (1H, d, $J = 2.0$ Hz), 7.32 (1H, dd, $J = 8.0$, 2.0 Hz), 4.16 (2H, s), 3.89 (3H, s), 3.55 (2H, q, $J = 7.0$ Hz), 1.22 (3H, t, $J = 7.0$ Hz); FABMS: m/z 315, 313, 311 $[M+Na]^+$. Anal. Calcd for $C_{13}H_{14}Cl_2O_3$: C, 53.98; H, 4.84. Found: C, 53.91; H, 4.89.

Compound **3e**: IR (KBr): υ_{max} 1674, 1638, 1353, 1219 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.20 (1H, t, $J = 7.0$ Hz), 4.08 (2H, s), 3.75 (3H, s), 3.48 (2H, q, $J = 7.0$ Hz), 2.42 (2H, t, $J = 7.0$ Hz), 1.75 (1H, m), 1.21 (3H, t, $J = 7.0$ Hz), 0.94 (6H, d, $J = 7.0$ Hz); FABMS: m/z 223 $[M+Na]^+$. Anal. Calcd for $C_{11}H_{20}O_3$: C, 66.00; H, 10.00. Found: C, 66.13; H, 10.17.

Compound **4b**: IR (KBr): υ_{max} 2214, 1625, 1592, 1481 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.70 (2H, d, $J = 8.0$ Hz), 7.39 (2H, d, $J = 8.0$ Hz), 7.08 (1H, s), 4.16 (2H, s), 3.59 (2H, q, $J = 7.0$ Hz), 1.25 (3H, t, $J = 7.0$ Hz); FABMS: m/z 246, 244 $[M+Na]^+$. Anal. Calcd for $C_{12}H_{12}ClNO$: C, 65.01; H, 5.42; N, 6.32. Found: C, 65.17; H, 5.36; N, 6.38.

Compound **5b**: IR (KBr): υ_{max}1729, 1637, 1437 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.73, 6.88 (1H, 2s), 7.48–7.13 (4H, m), 4.12, 4.08 (2H, 2q, $J = 7.0$ Hz), 3.84, 3.55 (3H, 2s), 2.74, 2.71 (2H, 2t, $J = 7.0$ Hz), 2.55, 2.46 (2H, 2t, $J = 7.0$ Hz), 1.25, 1.10 (3H, 2t, $J = 7.0$ Hz); FABMS: m/z 321, 319 $[M+Na]^+$. Anal. Calcd for $C_{15}H_{17}ClO_4$: C, 60.71; H, 5.73. Found: C, 60.78; H, 5.68.

Compound **6b**: IR (KBr): υ_{max} 2361, 1734, 1622, 1438 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.93 (1H, d, $J = 8.0$ Hz), 7.45–7.23 (4H, m), 4.12 (2H, q, $J = 7.0$ Hz), 2.76 (2H, t, $J = 7.0$ Hz), 2.66 (2H, t, $J = 7.0$ Hz), 1.28 (3H, t, $J = 7.0$ Hz); FABMS: m/z 288, 286 $[M+Na]^+$. Anal. Calcd for $C_{14}H_{14}ClNO_2$: C, 63.76; H, 5.31; N, 5.31. Found: C, 63.71; H, 5.28; N, 5.39.

Acknowledgement

The authors thank UGC and CSIR, New Delhi for their financial assistance.

References and notes

1. Baylis, A. B.; Hillman, M. E. D. German Patent 2155113, 1972; *Chem. Abstr.* **1972**, *77*, 34174q.
2. (a) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811–891; (b) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94–110; (c) Buchholz, R.; Hoffmann, H. M. R. *Helv. Chim. Acta* **1991**, *74*, 1213–1220.
3. (a) Das, B.; Banerjee, J.; Ravindranath, N.; Venkataiah, B. *Tetrahedron Lett.* **2004**, *45*, 2425–2426; (b) Das, B.; Banerjee, J.; Ravindranath, N. *Tetrahedron* **2004**, *60*, 8357–8361; (c) Das, B.; Banerjee, J.; Mahender, G.; Majhi, A. *Org. Lett.* **2004**, *6*, 3349–3352; (d) Das, B.; Majhi, A.; Banerjee, J.; Chowdhury, N.; Venkateswarlu, K. *Tetrahedron Lett.* **2005**, *46*, 7913–7915; (e) Das, B.; Chowdhury,

N.; Banerjee, J.; Majhi, A.; Mahender, G. *Chem. Lett.* **2006**, *35*, 358–359.
4. (a) Bradshaw, J. W. S.; Baker, R.; Howse, P. E. *Nature* **1975**, *258*, 230–231; (b) Rossi, R.; Carpita, A.; Messeri, T. *Synth. Commun.* **1992**, *22*, 603–616; (c) Garson, M. J. *Chem. Rev.* **1993**, *93*, 1699–1733.
5. (a) Das, B.; Mahender, G.; Kumar, V. S.; Chowdhury, N. *Tetrahedron Lett.* **2004**, *45*, 6709–6711; (b) Srinivas, K. V. N. S.; Das, B. *Synlett* **2004**, 1715–1718; (c) Das, B.; Venkateswarlu, K.; Mahender, G.; Mahender, I. *Tetrahedron Lett.* **2005**, *46*, 3041–3044; (d) Das, B.; Ravikanth, B.; Ramu, R.; Rao, B. V. *Chem. Pharm. Bull.* **2006**, *54*, 1044–1045.
6. (a) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741–743; (b) Basavaiah, D.; Pandiaraju, S. *Tetrahedron Lett.* **1995**, *36*, 757–758; (c) Basavaiah, D.; Pandiaraju, S.; Krishnamacharyulu, M. *Synlett* **1996**, 747–748.
7. Chakraborti, A. K.; Gulhane, R. *Chem. Commun.* **2003**, 1896–1897.
8. Breton, G. W. *J. Org. Chem.* **1997**, *62*, 8952–8954.
9. Basavaiah, D.; Hyma, R. S.; Muthukumaran, K.; Kumaragurubaran, N. *Synthesis* **2000**, 217–219.
10. (a) Larson, G. L.; de Kaifer, C. F.; Seda, R.; Torres, L. E.; Ramirez, J. R. *J. Org. Chem.* **1984**, *49*, 3385–3388; (b) Basavaiah, D.; Sarma, P. K. S.; Bhavani, A. K. D. *J. Chem. Soc., Chem. Commun.* **1994**, 1091–1092; (c) Baraldi, P. G.; Guarneri, M.; Pollini, G. P.; Simoni, D.; Barco, A.; Benetti, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2501–2505; (d) Tanaka, K.; Yamagishi, N.; Tanikaga, R.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3619–3625; (e) Tanaka, K.; Yamagishi, N.; Tanikaga, R.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 528–532; (f) Boche, G.; Buckl, K.; Martens, D.; Schneider, D. R. *Tetrahedron Lett.* **1979**, 4967–4970; (g) Minami, I.; Yahara, M.; Shimizu, I.; Tsuji, J. *J. Chem. Soc., Chem. Commun.* **1986**, 118; (h) Oda, M.; Yamamuro, A.; Watabe, T. *Chem. Lett.* **1979**, 1427–1430.