Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 47 (2006) 3475–3478
Tetrahedron Letters

Synthesis of trisubstituted alkenes by reductive dehydroxylation of Baylis–Hillman adducts using polymethylhydrosiloxane (PMHS) and catalytic $B(C_6F_5)_3$☆

S. Chandrasekhar,* G. Chandrashekar, K. Vijeender and M. Srinivasa Reddy

Indian Institute of Chemical Technology, Hyderabad 500 007, India

Received 7 January 2006; revised 20 February 2006; accepted 2 March 2006

Abstract—$B(C_6F_5)_3$ as a catalyst and polymethylhydrosiloxane as a hydride source have been employed for the reductive dehydroxylation of Baylis–Hillman adducts wherein the hydride adds in an S_N2' manner onto the unactivated allyl alcohol moiety with concomitant elimination of the hydroxy group along with double bond migration. The products formed were found to be *E* in the case of ester adducts and *Z* in the case of nitrile adducts.

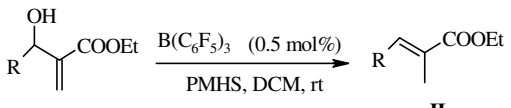
1. Introduction

The Baylis–Hillman coupling is a versatile and 'atom economic' reaction.[1] In addition, this protocol provides a well functionalized synthon, which allows one to perform diverse functional transformations. It generates an allyl alcohol, which can be advantageous in certain circumstances whilst it can be a hindrance in other cases.

The stereodefined trisubstituted alkene moiety manifests a significant role in many biologically active compounds,[2,3] various terpenoids and insect pheromones.[4] The biological properties of these alkenes are highly dependent on their isomeric purity.[5] Deoxygenation of this hydroxy group and halogenation via S_N2' displacement have been studied by the groups of Basavaiah,[6] Das[7] and others.[8] Also, carbon nucleophiles[9] efficiently add to allylic acetate adducts when mediated by Zn. The $TiCl_3$–$LiAlH_4$[10] combination was also efficient in hydride transfer onto Baylis–Hillman adducts whilst their reduction with $NaBH_4$[11] and $LiAlH_4$[12] furnished the methyl cinnamate derivatives. Palladium catalysis[13] was also efficient in the stereoselective reduction to produce methyl cinnamates. However, in all the cases of reduction to methyl cinnamate, the hydroxy group has been protected as the acetate. We have observed previously that $B(C_6F_5)_3$[14] activates polymethylhydrosiloxane (PMHS)[15] to produce a hydride source, which can even deoxygenate a carbonyl group to a methylene.[16]

We were interested in exploring the possibility of displacing the 2^0 allylic alcohol group in Baylis–Hillman adducts using this hydride source. We discovered that the hydroxy group did not require prior acetylation and smooth S_N2' hydride transfer was observed and resulted in trisubstituted alkenes with exclusive *E* geometry[11a] for ester adducts (Scheme 1) and *Z* geometry[12] for nitrile adducts (Scheme 2) as evidenced from NMR spectal data.[17,18] The details of this study are presented herein.

We initially treated Baylis–Hillman adduct **1a** (Table 1, entry 1) with PMHS (2 equiv) and $B(C_6F_5)_3$ (0.5 mol %) in CH_2Cl_2 as solvent at room temperature. Rapid dehydroxylation and hydride addition to the double bond occurred yielding ethyl (4-nitrophenyl)-2-methyl-(2*E*)-propionate **1b** in 85% yield in 20 min. It was interesting



I R = aryl, alkyl

II *E* - alkenes

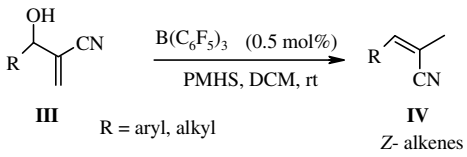
Scheme 1.

Keywords: Baylis–Hillman adducts; *E* and *Z*-trisubstituted alkenes; PMHS-$B(C_6F_5)_3$; Dehydroxylation.

☆ IICT Communication No. 060103.

* Corresponding author. Tel.: +91 40 27193434; fax: +91 40 27160512; e-mail addresses: srivaric@iict.res.in; srivaric@gmail.com

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.03.014



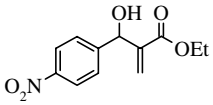
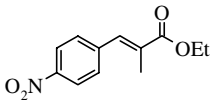
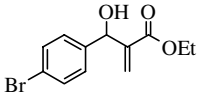
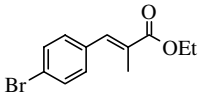
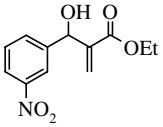
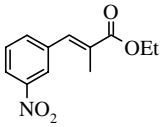
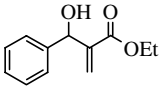
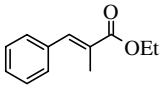
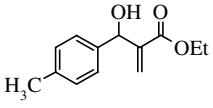
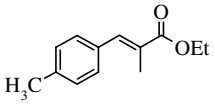
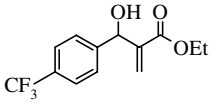
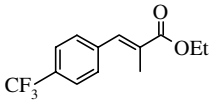
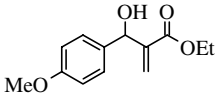
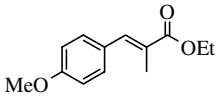
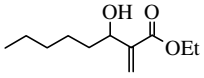
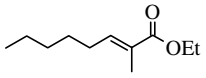
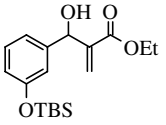
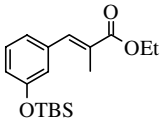
Scheme 2.

to note that under the present reduction protocol, nitro and ester groups were unaffected. In the case of entry 2 smooth reduction of the hydroxy group with double bond migration occurred to yield **2b**, without affecting the bromo group. Entries 3–7 demonstrate further the generality of this reaction. The aliphatic example (entry 8) was also a reasonable substrate, however, the reaction time was longer with moderate yield. Entry 9 demonstrates the stability of a silyl group to these reaction conditions.

The Baylis–Hillman acrylonitrile adducts were also efficiently dehydroxylated under similar conditions. The resulting *Z*-trisubstituted alkenes[12] were obtained in excellent yields (Table 2, entries 1–6). Interestingly, the cyano group was resistant to reduction.[19]

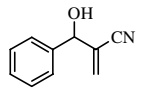
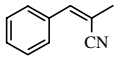
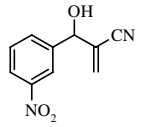
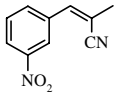
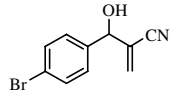
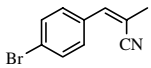
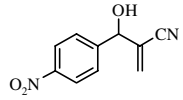
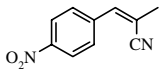
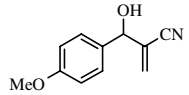
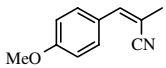
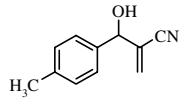
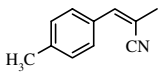
A classical 'Lewis acid assistance' mechanism holds good for this operation. We propose that complex **A** (Scheme 3), which is formed from $B(C_6F_5)_3$ and PMHS is responsible for elimination of the hydroxy group and hydride addition to the double bond of the Baylis–Hillman adducts. The reaction of **I** with complex **A** forms intermediate **B** which undergoes elimination of the hydroxy group from the sterically preferred conformation **C** resulting in trisubstituted alkenes with *E* geometry. In contrast the cyano adduct III results in trisubstituted alkenes with exclusive *Z* geometry via preferred conformation **E** due to the smaller size of the

Table 1. Synthesis of trisubstituted *E*-alkenes using PMHS and catalytic $B(C_6F_5)_3$

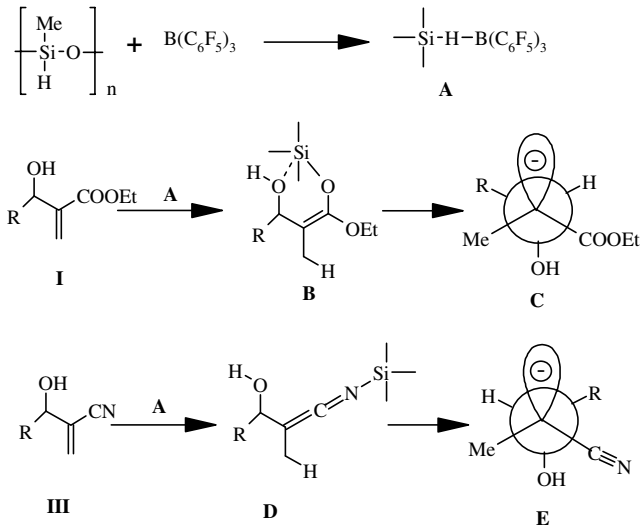
Entry	Compound **a**	Product[a] **b**	Time	Yield (%)[b]
1			20 min	85
2			30 min	78
3			30 min	81
4			30 min	75
5			1 h	80
6			40 min	73
7			1 h	68
8			4 h	65
9			2 h	60

[a] All products were characterized by ^1H NMR, IR and mass spectroscopy.
[b] Isolated yields after column chromatography.

Table 2. Synthesis of trisubstituted *Z*-alkenes using PMHS and catalytic $B(C_6F_5)_3$

Entry	Compound **c**	Product[a] **d**	Time	Yield (%)[b]
1			40 min	72
2			40 min	78
3			1.5 h	75
4			30 min	82
5			3 h	80
6			4 h	83

[a] All products were characterized by ^1H NMR, IR and mass spectroscopy.
[b] Isolated yields after column chromatography.



Scheme 3.

cyano group when compared to methyl functionality and a bulky ethoxy carbonyl group.

In conclusion, this protocol describes for the first time, PMHS-$B(C_6F_5)_3$ as a source of hydride for S_N2' displacement of –OH groups in Baylis–Hillman adducts without the need for prior acylation. This methodology is versatile and allows one to reduce hydroxy groups in the presence of other sensitive functional groups. The application of this procedure in the synthesis of complex bioactive compounds is currently being pursued.

2. General experimental procedure

To a solution of the Baylis–Hillman adduct (2 mmol) in anhydrous methylene chloride (5 mL) was added $B(C_6F_5)_3$ (0.01 mmol) and PMHS (4 mmol) and the solution was stirred at room temperature for the appropriate period of time (monitored by TLC). Water was added to the reaction mixture, which was extracted with methylene chloride (3×5 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, concentrated under in vacuo and the crude product was purified by flash chromatography.

Acknowledgements

G.C., K.V. and M.S.R. thank CSIR, New Delhi, for the financial support in the form of fellowships.

References and notes

1. (a) Baylis, A. B; Hillman, M. E. D. German Patent 2155-113, 1972; *Chem. Abstr.* **1972**, *77*, 34174q; (b) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001–8062.
2. Senokuchi, K.; Nakai, H.; Nakayama, Y.; Odagaki, Y.; Sakaki, K.; Kato, M.; Maruyama, T.; Miyazaki, T.; Ito, H.; Kamiyasu, K.; Kim, S.; Kawamaura, M.; Hamanaka, N. *J. Med. Chem.* **1995**, *38*, 2521–2523.
3. Watanabe, T.; Hayashi, K.; Yoshimatsu, S.; Sakai, K.; Takeyama, S.; Takashima, K. *J. Med. Chem.* **1980**, *23*, 50–59.
4. (a) Anderson, R. J.; Coleman, J. E.; Piers, E.; Wallace, D. J. *Tetrahedron Lett.* **1997**, *38*, 317–320; (b) Tanaka, H.; Kuroda, A.; Marusawa, H.; Hatanaka, H.; Kino, T.; Goto, T.; Hashimoto, M. *J. Am. Chem. Soc.* **1987**, *109*, 5031–5033; (c) Ishibashi, Y.; Ohba, S.; Nishiyama, S.; Yamamura, S. *Tetrahedron Lett.* **1996**, *37*, 2997–3000.
5. Marfat, A.; McGuirk, P. R.; Helquist, P. *J. Org. Chem.* **1979**, *44*, 3888–3901.
6. Basavaiah, D.; Rao, S. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811–891, and references cited therein.
7. (a) Das, B.; Banerjee, J.; Ravindranath, N. *Tetrahedron* **2004**, *60*, 8357–8361; (b) Das, B.; Banerjee, J.; Ravindranath, N.; Venkataiah, B. *Tetrahedron Lett.* **2004**, *45*, 2425–2426; (c) Das, B.; Majhi, A.; Banerjee, J.; Chowdhury, N.; Venkateswarlu, K. *Tetrahedron Lett.* **2005**, *46*, 7913–7915.
8. (a) Guriece, A.; Goucaud, A. *New J. Chem.* **1991**, *15*, 943; (b) Rabe, J.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 795; (c) Hoffmann, H. M. R.; Rabe, J. *J. Org. Chem.* **1985**, *50*, 3849–3859.
9. Das, B.; Banerjee, J.; Mahender, G.; Majhi, A. *Org. Lett.* **2004**, *6*, 3349–3352.
10. Shadakshari, U.; Nayak, S. K. *Tetrahedron Lett.* **2001**, *57*, 4599–4602.
11. (a) Basavaiah, D.; Krishnamacharyulu, M.; Hyma, R. S.; Sarma, P. K. S.; Kumaragurubaran, N. *J. Org. Chem.* **1999**, *64*, 1197–1200; (b) Das, B.; Banerjee, J.; Majhi, A.; Mahender, G. *Tetrahedron Lett.* **2004**, *45*, 9225–9227.

12. Basavaiah, D.; Sarma, P. K. S. *J. Chem. Soc., Chem. Commun.* **1992**, 955–995, and references cited therein.
13. Pachamuthu, K.; Vankar, Y. D. *Tetrahedron Lett.* **1998**, *39*, 5439–5442.
14. Chandrasekhar, S.; Babu B. N.; Chandrashekar, G. Review on tris(pentafluorophenyl)borane. *Contribution for Electronic Encyclopedia of Organic Reagents for Organic Synthesis. eEROS*, 2005 and references cited therein.
15. Our contributions with PMHS: (a) Chandrasekhar, S.; Chandrashekar, G.; Babu, B. N.; Vijeender, K.; Venkatram Reddy, K. *Tetrahedron Lett.* **2004**, *45*, 5497–5499; (b) Chandrasekhar, S.; Babu, B. N.; Ahmed, Md.; Reddy, M. V.; Srihari, P.; Jagadeesh, B.; Prabhakar, A. *Synlett* **2004**, 1303–1305; (c) Chandrasekhar, S.; Reddy, Ch. R.; Babu, B. N. *Tetrahedron Lett.* **2003**, *44*, 2057–2059; (d) Chandrasekhar, S.; Reddy, Ch. R.; Rao, R. J. *Synlett* **2001**, 1561–1562; (e) Chandrasekhar, S.; Reddy, Ch. R.; Rao, R. J. *Tetrahedron* **2001**, *57*, 3435–3438; (f) Chandrasekhar, S.; Chandraiah, L.; Reddy, M. V. *Synlett* **2000**, 1351–1353; (g) Chandrasekhar, S.; Reddy, Ch. R.; Ahmed, Md. *Synlett* **2000**, 1655–1657; (h) Chandrasekhar, S.; Chandraiah, L.; Reddy, Ch. R.; Reddy, M. V. *Chem. Lett.* **2000**, 780–781; (i) Chandrasekhar, S.; Ahmed, Md. *Tetrahedron Lett.* **1999**, *40*, 9325–9327; (j) Chandrasekhar, S.; Reddy, M. V.; Chandraiah, L. *Synth. Commun.* **1999**, *29*, 3981–3987; (k) Chandrasekhar, S.; Reddy, Y. R.; Reddy, Ch. R. *Chem. Lett.* **1998**, *29*, 1273–1274; (l) Chandrasekhar, S.; Reddy, Y. R.; Ramarao, C. *Synth. Commun.* **1997**, *27*, 2251–2254.
16. Chandrasekhar, S.; Reddy, C. R.; Babu, B. N. *J. Org. Chem.* **2002**, *67*, 9080.
17. In the ^{1}H NMR spectrum of the product **3b**, a resonance at δ 7.69 was assigned to the olefine proton of the *E* trisubstituted alkene.[11a] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.25 (s, 1H), 8.19–8.03 (m, 1H), 7.69–7.41 (m, 3H), 4.29 (q, $J = 7.2$ Hz, 2H), 2.10 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.8, 137.5, 135.7, 135.2, 129.3, 129.1, 124.0, 122.8, 61.2, 14.2, 13.9; IR (KBr): 2983, 1711, 1637, 1531, 1352, 1254 cm^{-1}; ESI-MS: *m*/*z* 236 $(M+1)^+$.
18. The *Z*-stereochemistry of **1d** was assigned on the basis of ^{1}H and ^{13}C chemical shifts in comparison with literature values.[12] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.72–7.23 (m, 5H), 6.89 (br s, 1H), 2.17 (d, $J = 1.5$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.3, 133.3, 129.1, 128.1, 127.7, 118.5, 105.3, 21.1; IR (KBr): 2362, 1618 cm^{-1}: ESI-MS: *m*/*z* 144 $(M+1)^+$.
19. Spectral data for selected products: Compound **2b**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.56 (s, 1H), 7.49 (d, $J = 8.7$ Hz, 2H), 7.23 (d, $J = 8.7$ Hz, 2H), 4.24 (q, $J = 7.2$ Hz, 2H), 2.08 (s, 3H), 1.35 (t, $J = 7.2$Hz, 3H); IR (KBr): 2927, 1707, 1618, 1252 cm^{-1}; ESI-MS: *m*/*z* 269 (M^+), 271 $(M+2)^+$.
Compound **6b**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.65–7.45 (m, 5H), 4.25 (q, $J = 7.0$ Hz, 2H), 2.10 (s, 3H), 1.36 (t, $J = 7.0$ Hz, 3H); IR (KBr): 1721, 1630, 620 cm^{-1}; ESI-MS: *m*/*z* 281 $(M+Na)^+$.
Compound **8b**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.76–6.68 (m, 1H) 4.15 (q, $J = 7.2$ Hz, 2H), 2.14 (q, $J = 7.2$ Hz, 2H), 1.18 (s, 3H), 1.15–1.22 (m, 9H), 0.90 (t, $J = 6.8$ Hz, 3H); IR (KBr): 2930, 1719, 1620 cm^{-1}; ESI-MS: *m*/*z* 184 $(M)^+$.
Compound **9b**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.57 (s, 1H), 7.25–6.92 (m, 2H), 6.82–6.50 (m, 2H), 4.23 (q, $J = 7.0$ Hz, 2H), 2.10 (s, 3H), 1.25 (t, $J = 7.0$ Hz, 3H), 0.98 (s, 9H), 0.20 (s, 6H); IR (KBr): 2985, 1721, 1628 cm^{-1}; ESI-MS: *m*/*z* 320 $(M)^+$.
Compound **4d**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.27 (d, $J = 9.1$ Hz, 2H), 7.82 (d, $J = 9.1$ Hz, 2H), 6.98 (s, 1H), 2.24 (s, 3H); IR (KBr): 2211, 1617, 1519, 1345 cm^{-1}: ESI-MS: *m*/*z* 187 $(M-1)^+$.