Montmorillonite clay-catalyzed stereoselective syntheses of aryl-substituted (*E*)- and (*Z*)-allyl iodides and bromides

Jhillu S. Yadav,* Basi V. Subba Reddy and Chinnala Madan

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad-500 007 India. E-mail: yadav@iict.ap.nic.in; Fax: +91-40-7170512

Received (in Montpellier, France) 30th April 2001, Accepted 4th July 2001
First published as an Advance Article on the web 16th August 2001

An efficient and rapid procedure for the synthesis of allyl iodides and bromides from Baylis–Hillman adducts using clay-supported sodium iodide and sodium bromide is described. Improved yields and enhanced rates have been achieved by employing microwave irradiation.

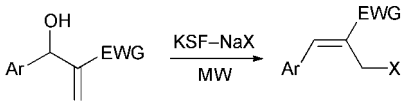
The coupling of activated vinyl moieties with aldehydes in the presence of 1,4-diazabicyclo[2,2,2]octane (DABCO), known as the Baylis–Hillman reaction, is widely used for the direct synthesis of α-hydroxy alkyl- or arylvinyl systems.[1] The Baylis–Hillman adducts are very useful precursors for the synthesis of a variety of biologically active natural products.[2] In particular, 2-(halomethyl)alk-2-enolates are an important class of compounds for the stereoselective synthesis of many natural products[3] such as α-alkylidene-β-lactams, α-methylene-γ-butyrolactones and necic acids. As a result, several methods have been developed for the direct conversion of 3-hydroxy-2-methylene alkanoates to 2-(halomethyl)alk-2-enoates, including those using $HBr–H_2SO_4$,[3b] NBS–Me_2S,[2c] PBr_3,[4] MsCl–Et_3N[5] and $CuBr_2$–silica gel.[6] Recently, the synthesis of 2-(halomethyl)alk-2-enoates has been reported from the acetyl derivative of Baylis–Hillman adducts[7] using $MgBr_2$–THF and $AlCl_3$–CH_2Cl_2. However, there is no report of the synthesis of allyl iodides from Baylis–Hillman adducts.

The use of corrosive and/or hazardous reagents and harmful organic solvents is undesirable in view of today's environmental consciousness. There is much to be gained in developing simple and convenient procedures using inexpensive solid acids[8] such as clays, zeolites and ion-exchange resins. In particular, clays are most attractive[9] because of their reusability, environmental compatibility, low cost, non-toxicity, and operational/experimental simplicity. In continuation of our interest in the applications of clays[10] for various transformations, we report here the remarkable catalytic activity of a montmorillonite clay for the synthesis of 2-(iodo or bromomethyl)aryl-2-enoates from 3-hydroxy-2-methylene alkanoates (Scheme 1). In addition, microwave irradiation, which has become a powerful tool[11] for the rapid synthesis of a variety of organic compounds, is used to enhance the rates of reaction.

The treatment of Baylis–Hillman adducts derived from acrylate esters such as 3-hydroxy-2-methylene alkanoates with clay-supported NaI and NaBr under microwave irradiation leads to the formation of the corresponding (*Z*)-allyl iodides and bromides in high yields (Table 1). However, the reaction did not proceed in the absence of clay, even under microwave irradiation. This clearly indicates the role of the catalyst for the success of the reaction. These allyl bromides and iodides are important precursors for the stereoselective synthesis of allyl amines and azetidines.[12] Furthermore, the reactions of 4-hydroxy-3-methylene alkan-2-ones with NaI and NaBr in the presence of KSF clay gave the corresponding (*Z*)-allyl iodides and bromides in high yields under microwave irradiation. The *Z* stereochemistry of the products was assigned on the basis of the chemical shift values of the vinyl and allylic protons in the ^{1}H NMR spectra of the products and also by a comparison of the spectral data with authentic compounds. In the ^{13}C NMR spectra of trisubstituted olefins, an allylic carbon *cis* to the aryl group appears upfield while the same carbon *trans* to the aryl group appears downfield.[13]

The reactions proceeded smoothly under microwave irradiation and produced high yields of products. The reactions are very clean and highly stereoselective. The reaction rates and yields are dramatically enhanced by microwave irradiation. The rate enhancement under microwave irradiation may be attributed to the absorption of more microwave energy by the polar media, which generates heat energy as required to promote the reaction. The irradiation was carried out at 450 W using a BPL, BMO-700T domestic microwave oven. The reaction temperature reached 110 °C after 3 min pulsed irradiation (1 min on with 20 s off interval) at constant power. The same reaction, under thermal conditions, at 110 °C took 5–8 h to afford yields comparable with those that are obtained by microwave irradiation.

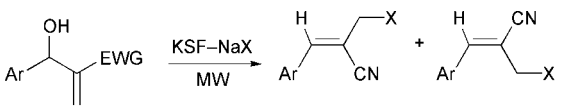
The reactions of Baylis–Hillman adducts derived from acrylonitrile, that is 3-hydroxy-2-methylene alkanenitriles with NaI and NaBr in the presence of KSF clay, produced the corresponding (*E*)- and (*Z*)-allyl iodides and bromides in high yields (Scheme 2). Under these conditions, the products were obtained as a mixture of *E* and *Z* isomers. The ratio of the isomers was determined from the integration ratios of the isomeric olefinic and allylic methylene protons in the ^{1}H NMR spectra of the products. The *E* stereochemistry of the major isomer was assigned by comparing the chemical shift values of allylic methylene and vinyl protons with those of authentic compounds.[13] Several examples illustrating this



1 **2**

A = aryl; EWG = COOMe, COMe, X = I, Br

Scheme 1

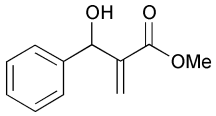
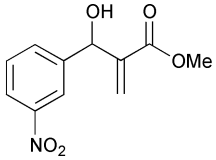
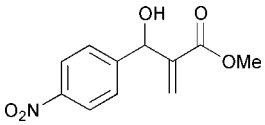
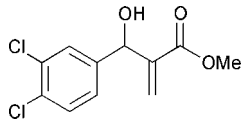
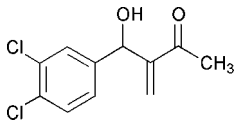
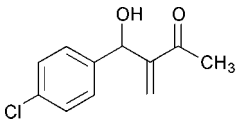
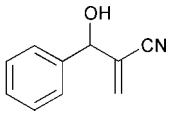
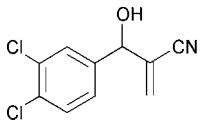
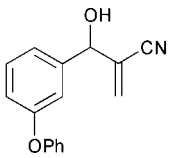


1 **3** (*E*) **4** (*Z*)

Scheme 2

 DOI: 10.1039/b103850h

Table 1 Microwave-assisted synthesis of allyl iodides and bromides

Entry	Substrate	Nucleophile	Reaction time (yield (%))		$E : Z^c$
			Irradiation[a]/min	Conventional[b]/h	
a		NaBr	4 (87)	6 (73)	0 : 100
b		NaI	3 (89)	5 (81)	0 : 100
c		NaI	3 (80)	7 (74)	0 : 100
d		NaBr	5 (78)	8 (65)	0 : 100
e		NaI	4 (85)	7 (70)	0 : 100
f		NaBr	5 (81)	8 (63)	0 : 100
g		NaI	4 (90)	6 (77)	0 : 100
h		NaBr	5 (84)	8 (75)	0 : 100
i		NaI	4 (87)	6 (80)	0 : 100
j		NaI	3 (85)	5 (78)	87 : 13
k		NaBr	4 (78)	6 (65)	89 : 11
l		NaI	3 (83)	5 (71)	91 : 09
m		NaBr	4 (80)	7 (68)	93 : 07
n		NaI	3 (88)	5 (70)	95 : 05

[a] Pulsed irradiation (1 min with 20 s interval). [b] Conventional heating at 110 °C. [c] $E : Z$ ratio was based on integration ratios of isomeric allylic and vinylic protons in ^{1}H NMR spectra.

novel and rapid procedure for the synthesis of (*Z*)- and (*E*)-allyl iodides and bromides are listed in Table 1.

After completion of the reaction, the clay was recovered by filtration, washed with methanol and reused in subsequent reactions (after activation at 120 °C for 4–5 h) with a gradual decrease in activity; for example, the reaction of methyl 2-hydroxy(phenyl)methyl acrylate (entry **b**) and NaI under microwave radiation gave 89, 77 and 75% yields over three cycles. These results clearly show the advantage of our method over protic and Lewis acid-catalyzed procedures. The recovered clay could also be activated by microwave irradiation at 450 W for 10–15 min.

In summary we have demonstrated a rapid and highly efficient procedure for the synthesis of (*Z*)- and (*E*)-allyl iodides and bromides using clay-supported NaI and NaBr. The method offers several advantages including mild reaction conditions, enhanced rates, improved yields, greater selectivity, experimental simplicity and reusability of the catalyst, which

makes it a convenient, more economical and environmentally benign process.

Experimental

Conventional method

A mixture of the Baylis–Hillman adduct (5 mmol), NaI or NaBr (6 mmol) and KSF clay (1 g, Aldrich Co.) was heated at 110 °C for the time specified in the table. After complete conversion, as indicated by TLC, the reaction mixture was filtered and washed with dichloromethane (2 × 15 mL). The solvent was removed *in vacuo* and the residue purified by column chromatography (Merck, 100–200 mesh, ethyl acetate–hexane 5 : 95) to afford pure product.

Under microwave irradiation

The Baylis–Hillman adduct (5 mmol), NaI or NaBr (6 mmol) and KSF clay (1 g, Aldrich Co.) were admixed in a Pyrex test tube and subjected to microwave irradiation at 450 W using a BPL, BMO-700T microwave oven for 3–5 min. After complete conversion, as indicated by TLC, the reaction mixture was filtered and washed with dichloromethane (2 × 15 mL). The solvent was removed *in vacuo* and the residue purified by column chromatography (Merck, 100–200 mesh, ethyl acetate–hexane 5 : 95) to afford pure product.

2a. Liquid: ^{1}H NMR ($CDCl_3$) δ: 3.90 (s, 3H), 4.35 (s, 2H), 7.45 (m, 3H), 7.55 (m, 2H), 7.85 (s, 1H). ^{13}C NMR ($CDCl_3$, proton decoupled) δ: 26.7, 52.35, 128.70, 128.85, 129.60, 134.27, 142.78, 166.38. IR (KBr) ν/cm^{-1}: 1714.2, 1632.8, 1587.9, 1469.9, 1135.6, 1068.2, 765.

2b. Solid, m.p. 50–52 °C: ^{1}H NMR ($CDCl_3$) δ: 3.90 (s, 3H), 4.30 (s, 2H), 7.45–7.65 (m, 6H). ^{13}C NMR ($CDCl_3$, proton decoupled) δ: 25.18, 25.90, 129.6, 129.7, 129.8, 134.35, 137.45, 142.70, 197.05. EI-MS m/z: 238 M$^+$, 158, 143, 115, 77, 57. IR (KBr) ν/cm^{-1}: 2950, 1617, 1625.

2c. Liquid: ^{1}H NMR ($CDCl_3$) δ: 3.90 (s, 3H), 4.28 (s, 2H), 7.70 (t, 1H, J = 7.8 Hz), 7.75 (s, 1H, Z isomer), 7.90 (d, 1H, J = 8 Hz), 8.28 (d, 1H, J = 8 Hz), 8.40 (s, 1H). EI-MS m/z: 347 M$^+$, 316, 220, 174, 150, 128,115, 89, 59. IR (KBr) ν/cm^{-1}: 1742.5, 1667, 1624, 1465, 1026.8, 816.5, 668.7.

2d. Solid, m.p. 125 °C: ^{1}H NMR ($CDCl_3$) δ: 3.90 (s, 3H), 4.30 (s, 2H), 7.65 (d, 2H, J = 8.4 Hz), 7.80 (s, 1H), 8.20 (d, 2H, J = 8.4 Hz). IR (KBr) ν/cm^{-1}: 2960, 1725, 1630, 1520.

2e. Viscous liquid: ^{1}H NMR ($CDCl_3$) δ: 3.90 (s, 3H), 4.28 (s, 2H), 7.40 (dd, 1H, J = 7.8 and 2.0 Hz), 7.60 (s, 1H, Z isomer), 7.65 (d, 1H, J = 7.8 Hz), 7.68 (d, 1H, J = 2.0 Hz). EI-MS m/z: 370 M$^+$, 243, 213, 183, 150, 128, 113, 74, 59. IR (KBr) ν/cm^{-1}: 1713.2, 1631.9, 1550.5, 1469.9, 1283.5, 1068.2, 822.7.

2f. Semi-solid: ^{1}H NMR ($CDCl_3$) δ: 3.90 (s, 3H), 4.30 (s, 2H), 7.45 (dd, 1H, J = 7.8 and 2.0 Hz), 7.65 (s, 1H, Z isomer), 7.70 (d, 1H, J = 2.0 Hz). EI-MS m/z: 324 M$^+$, 243, 212, 184, 148, 113, 74, 63. IR (KBr) ν/cm^{-1}: 1742.5, 1696.8, 1433.1, 1215.4.

2g. Liquid: ^{1}H NMR ($CDCl_3$) δ: 2.50 (s, 3H), 4.25 (s, 2H), 7.40 (s, 1H, Z isomer), 7.50 (dd, 1H, J = 8.0 and 2.1 Hz), 7.65 (d, 1H, J = 8 Hz), 7.70 (d, 1H, J = 2.1 Hz). EI-MS m/z: 354 M$^+$, 227, 212, 192, 184, 148, 129, 115, 75, 63.

2h. Liquid: ^{1}H NMR ($CDCl_3$) δ: 2.50 (s, 3H), 4.28 (s, 2H), 7.30 (s, 1H, Z isomer), 7.45 (dd, 1H, J = 8.0 and 2 Hz), 7.60 (d, 1H, J = 8 Hz), 7.70 (d, 1H, J = 2 Hz). EI-MS m/z: 308 M$^+$, 226, 184, 149, 113, 74, 63.

2i. Viscous liquid: ^{1}H NMR ($CDCl_3$) δ: 2.45 (s, 3H), 4.20 (s, 2H), 7.20 (s, 1H, Z isomer), 7.30 (d, 2H, J = 7.8. Hz), 7.70 (d, 2H, J = 7.8 Hz). EI-MS m/z: 320 M$^+$, 193, 178, 150, 115, 75, 63.

3j. Semi-solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.19 (s, 2H, Z isomer, –CH_2–), 4.21 (s, 2H, E isomer –CH_2–), 7.19 (s, 1H, E isomer –CH=C), 7.22 (s, 1H, Z isomer –CH=C), 7.45–7.55 (m, 3H), 7.75–7.85 (m, 2H). ^{13}C NMR ($CDCl_3$, proton decoupled) δ: 28.81, 38.69, 109.62, 116.9, 128.35, 128.86, 129.0, 129.7, 129.93, 130.64, 130.92, 132.54, 144.38, 144.71.

3k. Liquid: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.18 (s, 2H, Z isomer –CH_2–), 4.20 (s, 2H, E isomer –CH_2–), 7.18 (s, 1H, E isomer –CH=C), 7.28 (s, 2H, Z isomer –CH=C), 7.40–7.55 (m, 3H), 7.75–7.85 (m, 2H). ^{13}C NMR ($CDCl_3$, proton decoupled) δ: 26.67, 32.75, 108.06, 117.07, 129.10, 129.23, 130.45, 131.38, 132.40, 146.50, 147.18. IR (KBr) ν/cm^{-1}: 2960, 2125, 1620, 1580.

3l. Liquid: ^{1}H NMR ($CDCl_3$) δ: 4.09 (s, 2H, Z isomer –CH_2–), 4.15 (s, 2H, E isomer –CH_2–), 7.05 (s, 1H, E isomer –CH=C), 7.20 (s, 1H, Z isomer –CH=C), 7.50 (d, 1H, J = 8.0 Hz), 7.70 (dd, 1H, J = 8.0 and 2.0 Hz), 7.80 (d, 1H, J = 2.0 Hz). EI-MS m/z: 337 M$^+$, 210, 177, 140, 127, 113, 87, 75, 63, 50.

3m. Liquid: ^{1}H NMR ($CDCl_3$) δ: 4.15 (s, 2H, Z isomer –CH_2–), 4.18 (s, 2H, E isomer –CH_2–), 7.10 (s, 1H, E isomer –CH=C), 7.20 (s, 1H, Z isomer –CH=C), 7.55 (d, 1H, J = 8.0 Hz), 7.75 (dd, 1H, J = 8.0 and 2.0 Hz), 7.80 (d, 1H, J = 2.0 Hz). EI-MS m/z: 289 M$^+$, 210, 175, 140, 88. IR (KBr) ν/cm^{-1}: 3060, 2360.7, 1623.4, 1449, 1215.3, 1078.9, 755.7, 690.8.

3n. Semi-solid: ^{1}H NMR ($CDCl_3$) δ: 4.15 (s, 2H, Z isomer –CH_2–), 4.20 (s, 2H, E isomer –CH_2–), 7.10–7.25 (m, 5H), 7.35–7.50 (m, 4H), 7.60 (d, 1H, J = 7.8 Hz). ^{13}C NMR ($CDCl_3$, proton decoupled) δ: 27.60, 35.80, 110.5, 118.1, 118.7, 119.2, 119.5, 119.8, 121.0, 123.25, 123.87, 124.19, 129.87, 130.02, 130.46, 134.22, 143.74, 144.09, 157.89. FAB-MS m/z: 354 M$^+$, 329, 307, 244, 212, 186, 172, 156, 129, 115, 105, 81, 69, 57. IR (KBr) ν/cm^{-1}: 2354.4, 1695.8, 1541.8.

Acknowledgement

B. V. S. R. thanks CSIR (New Delhi) for the award of a fellowship.

References

1 (*a*) A. D. Baylis and M. E. D. Hillman, *Ger. Pat.* 2155113, 1972; (*b*) S. E. Drewes and G. H. P. Roos, *Tetrahedron*, 1988, **44**, 4653; (*c*) K. Mortia, Z. Suzuki and H. Hirose, *Bull. Chem. Soc. Jpn.*, 1968, **41**, 2815.
2 (*a*) S. E. Drewes and N. D. Emslie, *J. Chem. Soc., Perkin Trans. 1*, 1982, 2079; (*b*) H. M. R. Hoffmann and J. Rabe, *Helv. Chim. Acta*, 1984, **67**, 413; (*c*) H. M. R. Hoffmann and J. Rabe, *J. Org. Chem.*, 1985, **50**, 3849.
3 (*a*) H. M. R. Hoffmann and J. Rabe, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 94; (*b*) R. Buchholz and H. M. R. Hoffmann, *Helv. Chim. Acta*, 1991, **74**, 1213; (*c*) F. Ameer, S. E. Drewes, R. F. A. Hoole, P. T. Kaye and A. T. Pitchford, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2713.
4 M. F. Semmelhack and E. S. C. Wu, *J. Am. Chem. Soc.*, 1976, **98**, 3384.
5 S. P. Chavan, K. S. Ethiraj and S. K. Kamat, *Tetrahedron Lett.*, 1997, **38**, 7415.
6 A. Gruiec and A. Foucaud, *New J. Chem.*, 1991, **15**, 943.
7 (*a*) D. Basaviah, A. K. D. Bhavani, S. Pandiaraju and P. K. S. Sarma, *Synlett.*, 1995, 243; (*b*) D. Basaviah, S. Pandiaraju and K. Padmaja, *Synlett.*, 1996, 393.

8 (*a*) A. Cornelis and P. Laszlo, *Synlett*., 1994, 155; (*b*) S. E. Sen, S. M. Smith and K. A. Sullivan, *Tetrahedron*, 1999, **55**, 12657.
9 M. Balogh and P. Laszlo, *Organic Chemistry using Clay*, Springer–Verlag, New York, 1993; (*b*) P. Laszlo, *Science*, 1987, **235**, 1473.
10 (*a*) J. S. Yadav, B. V. S. Reddy, G. M. Kumar and C. V. S. R. Murthy, *Tetrahedron Lett*., 2001, **42**, 89; (*b*) J. S. Yadav, B. V. S. Reddy, M. Rasheed and H. M. S. Kumar, *Synlett*., 2000, 487; (*c*) H. M. S. Kumar, B. V. S. Reddy, P. K. Mohanty and J. S. Yadav, *Tetrahedron Lett*., 1997, **38**, 3619.
11 (*a*) S. Caddick, *Tetrahedron*, 1995, **51**, 10403; (*b*) A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacquault and D. Mathe, *Synthesis*, 1998, 1213; (*c*) A. Loupy, *Pure Appl. Chem*., 2001, **73**, 193; (*d*) R. S. Varma, *Green Chem*., 1999, 43; (*e*) S. Deshayes, M. Liagre, A. Loupy, J.-L. Luche and A. Petit, *Tetrahedron*, 1999, **55**, 10851; (*f*) R. S. Varma, *J. Heterocycl. Chem*., 1999, **36**, 1565.
12 M. C. Eagen and N. H. Cromwell, *J. Org. Chem*., 1974, **39**, 911.
13 (*a*) R. Rossi, A. Carpita, M. G. Quirici and C. A. Veracini, *Tetrahedron*, 1982, **38**, 639; (*b*) T. Funabiki, H. Hosomi, S. Yoshida and K. Tarama, *J. Am. Chem. Soc*., 1982, **104**, 1560; (*c*) J. J. Gajewski, R. Weber, R. Braun, M. L. Manion and B. Hymen, *J. Am. Chem. Soc*., 1977, **99**, 816.