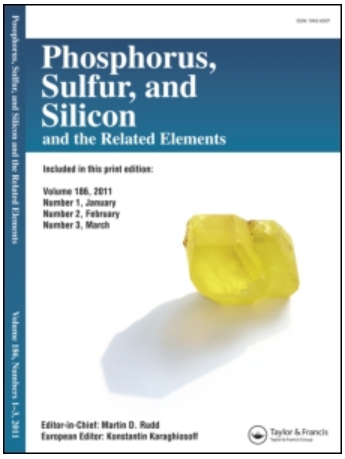


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

A FACILE CONVERSION OF THE BAYLIS-HILLMAN ADDUCTS INTO TRIMETHYLSILYL ETHERS WITH HEXAMETHYLDISILAZANE CATALYSED BY IODINE

Manouchehr Mamaghani[a]; Abed Badrian[a]
[a] University of Guilan, Rasht, Iran

Online publication date: 16 August 2010

Phosphorus, Sulfur, and Silicon, 179:1181–1186, 2004

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500490459803

Taylor & Francis
Taylor & Francis Group

A FACILE CONVERSION OF THE BAYLIS-HILLMAN ADDUCTS INTO TRIMETHYLSILYL ETHERS WITH HEXAMETHYLDISILAZANE CATALYSED BY IODINE

Manouchehr Mamaghani and Abed Badrian
University of Guilan, Rasht, Iran

(Received October 14, 2003; accepted October 16, 2003)

*The hydroxy group of the Baylis-Hillman adducts was protected with trimethylsilyl (TMS) group using the reaction of adducts **1a–h** with hexamethyldisilazane (HMDS) catalyzed by iodine under nearly neutral reaction conditions.*

Keywords: Baylis-Hillman adducts; HMDS; protecting group; trimethylsilyl ethers

The Baylis-Hillman reaction,[1] has attracted the attention of many synthetic organic chemists because the resulting adducts can be transformed into a variety of natural and unnatural compounds.[2] Several biologically natural and unnatural products such as (+)-mikanecic acid,[3] sarcomycin ester,[4] sitophilate,[5] epopromycin B,[6a] and (−)-mycestericin E,[6b] have been synthesized using this reaction as a key step.

The β-hydroxy-α-methylene esters **1a–h** were important acceptor reactants in many types of transformations. The alkene and ester moieties could be used in alkylation, conjugate addition, cyclization, and cycloaddition reactions. However the hydroxy group containing an active hydrogen may be protected in some of the reactions.[7]

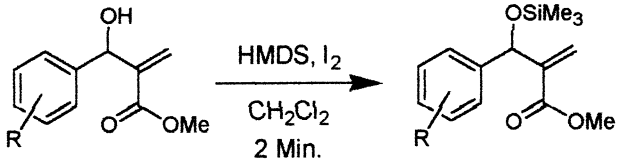
The role of silyl group has already been recognized of late, as an important part of organic chemistry from both analytical and synthetic point of view, especially as protecting group in many syntheses of reasonable complexity.[8] Generally, the formation of silylethers is carried out by treatment of alcohols with silyl chlorides or silyl triflates in the

We are grateful to the University of Guilan Research Council for financial support of our research program.

Address correspondence to Manouchehr Mamaghani, Department of Chemistry, Faculty of Sciences, University of Guilan, PO Box 41335-1914, Rasht, Iran. E-mail: m-chem41@guilan.ac.ir

presence of a base[9] (e.g., imidazole and DMAP), Li_2S,[10] and sometimes a nonionic super base catalyst.[11] However, some of these methods frequently suffered from drawbacks such as lack of reactivity, the long reaction times (e.g., 6 h–48 h), or the difficulty in removal of amine salts derived from the reaction of by-produced acid and cobases during the silylation reaction.

Recently Karimi et al.[12] reported a mild and highly efficient method for the silylation of alcohols using HMDS catalyzed by iodine under nearly neutral reaction conditions.



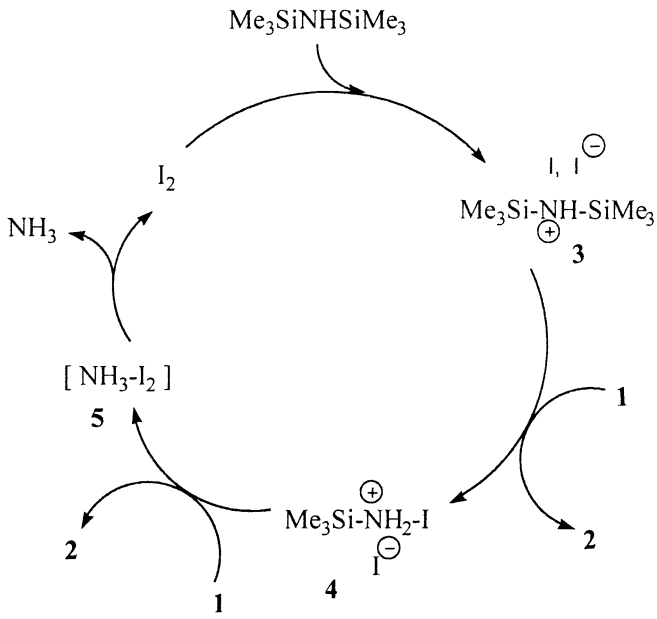
1(a-h) **2**(a-h)

SCHEME 1

In continuation of our interest for the Baylis-Hillman adducts and transformation of them into a variety of natural and unnatural compounds, herein we wish to report our results for the protecting of the hydroxy group of these adducts with TMS group using the reaction of adducts **1a–h** with HMDS catalyzed by iodine (Scheme 1). The HMDS is stable, commercially available, and a cheap reagent for trimethyl silylation of hydrogen-labile substrates, giving ammonia as the only by-product.[13] On the other hand, silylation using this silazane-type reagent is nearly neutral and does not need special precautions. In the cases of Baylis-Hillman type allylic alcohols used in this study, after addition of the reagent, the reactions were completed within less than 2 min in CH_2Cl_2 at room temperature accompanied by a fast evolution of NH_3 gas from the reaction mixture.

In this transformations, the reactivity of the hydroxy group decreases and reduces polar and hydrogen interactions. The main purpose of silylation is as follows: 1) protection of reactive hydroxy group during chemical reactions; 2) improvement of reaction selectivity; 3) improvement of stability during distillation; 4) improvement of solubility in polar and/or nonpolar solvents; and 5) elimination of hydrogen bonds results in increased volatility.

A proposed mechanism of this transformation is depicted in Scheme 2.[12] The reaction is initiated through polarizing the Si—N bond in HMDS by I_2 to produce the reactive silylating agent **3**. A rapid



SCHEME 2 A proposed mechanism of the trimethylsilylation with HMDS and I_2.

reaction with alcohol then ensues, leading to the iodoammonium silylating species **4** and concomitant release of the corresponding silyl ether then results in the formation of the unstable ammonia-iodine complex **5**. Irreversible cleavage of **5**, leading to the fast evolution of NH_3 and release of I_2. The prepared trimethylsilyl ethers are summarized in Table I.

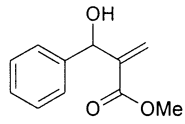
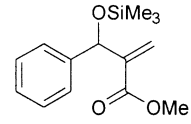
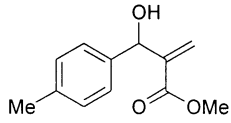
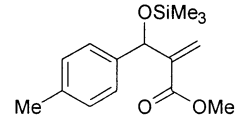
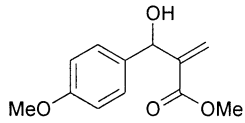
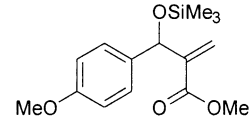
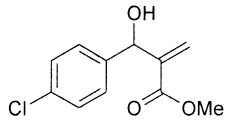
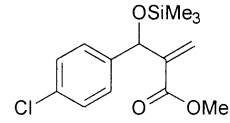
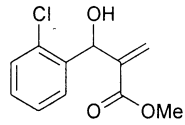
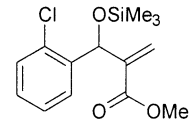
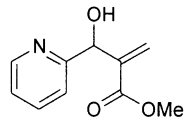
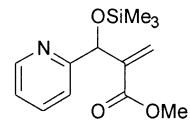
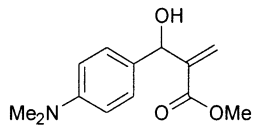
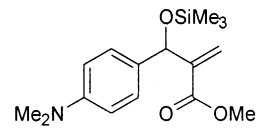
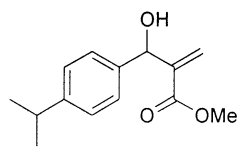
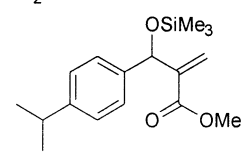
In conclusion a practical, highly efficient, and convenient protocol with mild conditions (25°C) has been developed for trimethylsilylation of the Baylis-Hillman adducts. This reaction can be applied to the protection of hydroxy groups and the synthesis of multiplepoint pharmacophores of natural and unnatural compounds.

EXPERIMENTAL

General

Chemical were purchased from Merck and Fluka. Baylis-Hillman adducts were prepared according to the literature.[1] IR spectra were determined on a Shimadzo IR-470 spectrometer. ^{1}H NMR spectra were recorded on a Bruker AC, FT-NMR (80 MHz) in $CDCl_3$ with

TABLE I Product Distribution Data and the Yield of the Products

Entry	Alcohols (**1**)	Products (**2**)	Time (min)	% Yield[a]
a			2	98
b			2	97
c			2	97
d			2	99
e			2	99
f			2	99
g			2	98
h			2	98

[a]Isolated yields.

tetramethylsilane (TMS). Preparative thin layer chromatography was prepared from Merck Kieselgel 60 H, F_{254}, Art No 7730. GC was carried out using Buck Scientific 910 (capillary column, MXT-5, 15 m). All solvents used were dried and distilled according to standard procedures.

General Procedure for Trimethylsilylation of Baylis-Hillman Adducts

To a stirred solution of alcohol **1** (5 mmol) and I_2 (0.05 mmol) in CH_2Cl_2 (20 mL) was added HMDS (4 mmol in 6 mL of CH_2Cl_2) dropwise within 4 min. After completion of the reaction (TLC or GC), finely powdered $Na_2S_2O_4$ (1.5 g. portion wise) was added, the mixture was stirred for additional 30 min and the resulting mixture was filtered through a short pad of silica gel. The filter cake was washed twice with CH_2Cl_2 (20–30 mL). Evaporation of the solvent under reduced pressure gave almost pure products. Further purification was achieved by vacuum distillation or recrystalization to afford pure silyl ether **2**. The isolated yield for each product is given in parentheses and the IR, ^{1}HNMR data for the compounds **2a–h** are given below.

2a: Colorless oil (98%); (Found: C, 63.40; H, 7.70; Si, 10.60 $C_{14}H_{20}O_3Si$ requires C, 63.60; H, 7.62; Si, 10.62%); IR (film, cm^{-1}); 1725, 1254, 845, ^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 3.7 (s, 3H), 5.2 (s, 1H), 6.1 (s, 2H), 7.2 (s, 5H).

2b: Colorless oil (97%); (Found: C, 64.50; H, 8.0; Si, 10.10 $C_{15}H_{22}O_3Si$ requires C, 64.71; H, 7.96; Si, 10.09%); IR (film, cm^{-1}); 1722, 1254, 845, ^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 2.3 (s, 3H), 3.7 (s, 3H), 5.2 (s, 1H), 6.1 (s, 2H), 6.9–7.1 (m, 4H).

2c: Colorless oil (97%); (Found: C, 61.20; H, 7.50; Si, 9.60 $C_{15}H_{22}O_4Si$ requires C, 61.19; H, 7.53; Si, 9.54%); IR (film, cm^{-1}); 1725, 1250, 844, ^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 3.7 (s, 3H), 3.8 (s, 3H), 5.2 (s, 1H), 6.1 (s, 2H), 6.7–7.1 (s, 4H).

2d: Colorless oil (99%); (Found: C, 56.20; H, 6.45; Cl, 11.78; Si, 9.46 $C_{14}H_{19}ClO_3Si$ requires C, 56.27; H, 6.40; Cl, 11.86; Si, 9.40%); IR (film, cm^{-1}); 1725, 1259, 846, ^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 3.7 (s, 3H), 5.2 (s, 1H), 6.1 (s, 2H), 7.0–7.2 (m, 4H).

2e: Colorless oil (99%); (Found: C, 56.22; H, 6.43; Cl, 11.80; Si, 9.36 $C_{14}H_{19}ClO_3Si$ requires C, 56.27; H, 6.40; Cl, 11.86; Si, 9.40%); IR (film, cm^{-1}); 1725, 1259, 846, ^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 3.7 (s, 3H), 5.2 (s, 1H), 6.1 (s, 2H), 7.0–7.2 (m, 4H).

2f: Yellow oil (99%); (Found: C, 58.62; H, 7.25; N, 5.30; Si, 10.45 $C_{13}H_{19}NIO_3$ Si requires C, 58.84; H, 7.22; N, 5.28, Si, 10.58%); IR (film, cm^{-1}); 1730, 1260, 848, ^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 3.7 (s, 3H), 5.2 (s, 1H), 5.8 (s, 1H), 6.4 (s, 1H) 7.4–8.6 (m, 4H).

2g: Solid (m.p. 65–67°C, 98%); (Found: C, 62.42; H, 8.25; N, 4.47; Si, 9.16 $C_{16}H_{25}NO_3Si$ requires C, 62.50; H, 8.20; N, 4.56; Si, 9.13%); IR (film, cm^{-1}); 1720, 1251, 843, ^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 2.8 (s, 6H), 3.7 (s, 3H), 5.2 (s, 1H), 5.5 (s, 1H), 6.1 (s, 1H), 6.5–7.1 (m, 4H).

2h: Yellow oil (98%); (Found: C, 66.55; H, 8.50; Si, 9.20 $C_{17}H_{26}O_3Si$ requires C, 66.62; H, 8.55; Si, 9.16%); IR (film, cm^{-1}); 1723, 1253, 845,

^{1}H NMR ($CDCl_3$, δ); 0.1 (s, 9H), 1.3 (d, 6H), 3.1 (m, 2H), 3.7 (s, 3H), 5.2 (s, 1H), 5.5 (s, 1H), 6.1 (s, 1H), 6.9–7.2 (m, 4H).

REFERENCES

[1] a) D. Basavaiah, P. D. Rao, and R. S. Hyma, *Tetrahedron*, **52,** 8001 (1996); b) E. Ciganek, *Org. React*., **51,** 201 (1997); c) Y. Iwabuchi, M. Nakatani, N. Yokoyama, and S. Hatakeyama, *J. Am. Chem. Soc*., **121,** 10219 (1999).

[2] a) R. Buchholz and H. M. R. Hoffmann, *Helv. Chim. Acta*, **74,** 1213 (1991); b) H. M. R. Hoffmann, A. Weichert, A. M. Z. Slawin, and D. J. Williams, *Tetrahedron*, **46,** 5591 (1990); c) P. Bauchat and A. Foucaud, *Tetrahedron Lett*., **30,** 6337 (1989); d) L. A. Paquette and J. M. Andino, *Tetrahedron Lett.*, **49,** 4301 (1999); e) D. Basavaiah, N. Kumaragurubaran, and D. S. Sharada, *Tetrahedron Lett*., **42,** 85 (2001); f) D. Basavaiah, N. Kumaragurubaran, D. S. Sharda, and R. M. Reddy, *Tetrahedron*, **57,** 8167 (2001); g) A. Weichert and H. M. R. Hoffmann, *J. Chem. Soc. Perkin Trans*., **1,** 2154 (1990).

[3] D. Basavaiah, S. Pandiaraju, and P. K. S. Sarma, *Tetrahedron Lett*., **35,** 4227 (1994).

[4] H. Amri, M. Rambaud, and J. Villieras, *Tetrahedron Lett.*, **30,** 7381 (1989).

[5] C. R. Mateus, M. P. Feltrin, A. M. Costa, F. Coelho, and N.-P. Almeida, *Tetrahedron*, **57,** 6901 (2001).

[6] a) Y. Iwabuchi, T. Sugihara, T. Esumi, and S. Hatakeyama, *Tetrahedron Lett.*, **42,** 7867 (2001); b) Y. Iwabuchi, M. Furukawa, T. Esumi, and S. Hatakeyama, *Chem. Commun.*, 2030 (2001).

[7] R. Annunziata, M. Benaglia, M. Cinquini, F. Cozzi, and L. Raimondi, *J. Org. Chem.*, **60,** 4697 (1995).

[8] a) T. W. Greene and P. G. M. Wuts, *Protective Gropus in Organic Synthesis* (Wiley; New York, 1991) 2nd ed.; b) P. J. Kocienski, *Protective Groups*, edited by R. Enders, R. Noyori, and B. M. Trost (Thieme; Stuttgart, 1994).

[9] a) S. K. Chaudhary and O. Hernandez, *Tetrahedron Lett.*, 99 (1979); b) P. Wipf, W. Xu, *Org. Synth*., **74,** 205 (1997).

[10] G. A. Olah, B. G. B. Gupta, S. C. Narang, and R. Malhotra, *J. Org. Chem*., **44,** 4272 (1979).

[11] a) B. A. D. Sa, D. McLeod, and J. G. Verkade, *J. Org. Chem.*, **62,** 5057 (1997); b) B. A. D. Sa and J. G. Verkade, *J. Am. Chem. Soc*., **118,** 12832 (1996).

[12] B. Karimi and B. Golshani, *J. Org. Chem*., **65,** 7228 (2000).

[13] M. Lalonde and T. H. Chan, *Synthesis*, 817 (1985).