DOI: 10.1002/ejoc.200700817

Bismuth Triflate Catalyzed Allylation of Aldehydes with Allylstannane under Microwave Assistance

Thierry Ollevier*[a] and Zhiya Li[a]

Dedicated to Barry M. Trost on the occasion of his 65th birthday

Keywords: Allylation / Bismuth / Lewis acids / Microwaves / Allyltin

In the presence of a catalytic amount of bismuth triflate and under microwave irradiation, mixtures of aldehyde and allylstannane afforded smoothly the corresponding homoallylic alcohol. A wide variety of aldehydes were treated under these conditions. The reactions proceeded rapidly and afforded smoothly the corresponding homoallylic alcohol in good to very good yields using catalytic amounts of $Bi(OTf)_3·4H_2O$ (0.5 mol-%) and under microwave irradiation for a short time.

Introduction

The development of new methods for the preparation of homoallylic alcohols is an important area of synthetic efforts.[1] Homoallylic alcohols are extremely important as precursors of biologically active molecules.[2] Among the variety of synthetic methods so far reported, the reaction of carbonyl compounds with allylsilanes and -stannanes provides an efficient route for the synthesis of homoallylic alcohols.[3] Catalytic allylation reactions have been reported by several groups as an efficient method to prepare homoallylic alcohols.[4]

Recently, several laboratories have disclosed significant advances regarding rare-earth and lanthanide triflates as catalysts for allylation reactions.[5] High catalytic activity, low toxicity, moisture and air tolerance make lanthanide triflates valuable catalysts. However, the high cost of these catalysts restricts their use. Bismuth compounds provide a good alternative as they have recently attracted attention due to their low toxicity, low cost, and good stability.[6] Bismuth salts have been reported as catalysts for the Sakurai reaction,[7] opening of epoxides,[8] Mukaiyama aldol reaction,[9] Mannich-type reactions,[10] formation or deprotection of acetals,[11] Friedel–Crafts reactions,[12] and Fries and Claisen rearrangements.[13] $Bi(OTf)_3$ is particularly attractive because it is commercially available or can be easily prepared from commercially available compounds.[14]

As a part of our ongoing interest in bismuth(III)-catalyzed Sakurai reactions,[15] we report herein our results in the bismuth(III)-catalyzed allylation of carbonyl compounds by allyltributylstannane. This is the first disclosed microwave-enhanced bismuth-catalyzed Sakurai reaction. Homoallylic alcohols are obtained efficiently in the presence of 0.5 mol-% of $Bi(OTf)_3·4H_2O$. To the best of our knowledge, a truly catalytic version of this bismuth(III)-mediated reaction has never been reported. The bismuth(III)-catalyzed allylation reaction of aldehydes has only been reported in two very specific cases. A first report disclosed the allylation using allyltributylstannane involving a carboxylic acid, like benzoic acid, used in a stoichiometric quantity as a co-catalyst.[7f] More recent work by Mohan reported the efficient preparation of homoallylic ethers and acetates using allylsilanes in a $Bi(OTf)_3$-catalyzed process.[7b,7c] However, the direct bismuth(III)-catalyzed allylation of aldehydes with allylsilanes leading to homoallylic alcohols has never been achieved because it is a slow reaction and diallylation occurs as a major side reaction.[7b] We have indeed shown that the $Bi(OTf)_3$-catalyzed allylation of benzaldehyde led to a poor yield of the corresponding homoallylic alcohol [with 1.5 equiv. allyltrimethylsilane, 5 mol-% of $Bi(OTf)_3·4H_2O$, 22 °C, 4 h, yield of homoallylic alcohol 25%, homoallylic alcohol/diallylation product = 10:1; with 1.0 equiv. allyltributylstannane, 5 mol-% of $Bi(OTf)_3·4H_2O$, 22 °C, 24 h, yield of homoallylic alcohol 30%].

Microwave-assisted organic synthesis is currently gaining importance in synthetic chemistry largely due to the advancement in the technology that provides precision-controlled microwave equipments.[16] Previous studies showed that various bismuth-catalyzed reactions can be conducted

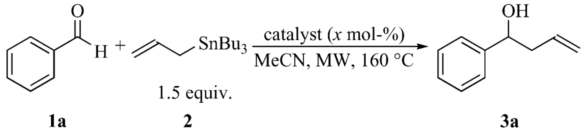
---

[a] Département de Chimie, Université Laval, Québec
Québec, Canada G1K 7P4, Canada
Fax: +1-418-656-7916
E-mail: thierry.ollevier@chm.ulaval.ca

under microwave irradiation.[17] We wish to disclose our results in this area, i.e, the development of an efficient and mild, microwave-assisted bismuth-catalyzed Sakurai reaction using allyltributylstannane.

Results and Discussion

Initial investigations in the allylation of aldehydes with allyltributylstannane involved benzaldehyde as the model substrate (Scheme 1, Table 1). Reaction times as short as 3–5 min allowed a full conversion, and the corresponding homoallylic alcohol was obtained in a good yield (Table 1, Entries 3 and 4). While $BiCl_3$ gave almost no conversion (Table 1, Entry 2), the corresponding homoallylic alcohol **3a** could be obtained in good yield with 1 mol-% of $Bi(OTf)_3 \cdot 4H_2O$ as the catalyst (Table 1, Entry 3). A lower loading of $Bi(OTf)_3 \cdot 4H_2O$ (0.5 mol-%) led to an increased yield (85% of **3a**) (Table 1, Entry 5). Other metal triflate catalysts, e.g., $Sc(OTf)_3$ and $Zn(OTf)_2$, appeared to be as efficient as $Bi(OTf)_3 \cdot 4H_2O$ but at higher loading (Table 1, compare Entries 6–7 with Entry 5). As an increase of the quantity of allyltributylstannane used led only to a slightly increased yield (2.0 equiv. of allyltributylstannane, 82% of **3a**; 1.5 equiv. of allyltributylstannane, 77% of **3a**), 1.5 equiv. of allyltributylstannane was systematically used for our optimization studies (Tables 1 and 2).



Scheme 1. Metal salt catalyzed microwave-assisted allylation of benzaldehyde.

Table 1. Metal salt catalyzed allylation of benzaldehyde under microwave assistance.

Entry	Catalyst	x mol-%	Time [min]	Yield **3a** [%][a]
1	–	–	5	4[b]
2	$BiCl_3$	1	5	7
3	$Bi(OTf)_3 \cdot 4H_2O$	1	5	77
4	$Bi(OTf)_3 \cdot 4H_2O$	1	3	80
5	$Bi(OTf)_3 \cdot 4H_2O$	0.5	5	85
6	$Sc(OTf)_3$	1	5	86
7	$Zn(OTf)_2$	1	5	85

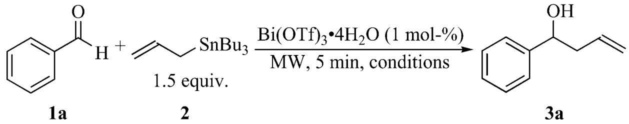
[a] Isolated yield. [b] Yield determined by ^1H NMR spectroscopy.

Table 2. $Bi(OTf)_3$-catalyzed allylation of benzaldehyde under microwave assistance: effect of solvent and temperature.

Entry	Solvent	Temp [°C]	Yield **3a** [%][a]
1	CH_2Cl_2	160	16
2	PhMe	160	23
3	THF	160	16
4	Et_2O	120	7
5	MeCN	160	77
6	MeCN	80	11

[a] Isolated yield.

At first, we screened various solvents for the Sakurai reaction of benzaldehyde with allyltributylstannane in the presence of 1 mol-% of $Bi(OTf)_3 \cdot 4H_2O$ (Scheme 2). Interestingly, when **1a** was treated with 1 mol-% of $Bi(OTf)_3 \cdot 4H_2O$ in CH_2Cl_2 (1.5 equiv. allyltributylstannane, microwaves, 5 min), the corresponding homoallylic alcohol **3a** was isolated in low yield (16%) (Table 2, Entry 1). A less polar solvent like toluene or ethereal solvents (THF, ether) did not give good yields of the expected product (Table 2, Entries 2–4). Among various solvents tested, acetonitrile furnished the expected product in the highest yield using a temperature of 160 °C (Table 2, Entry 5), a lower temperature leading to a decrease in yield (Table 2, Entry 6). Thus, acetonitrile was selected as the solvent of choice.

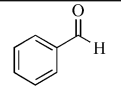
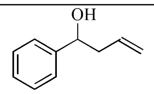
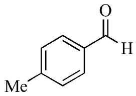
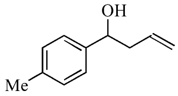
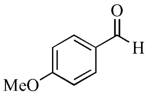
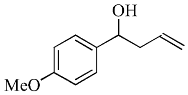
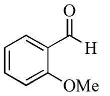
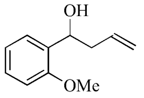
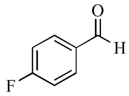
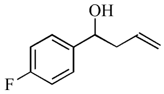
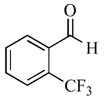
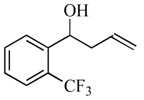
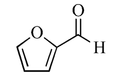
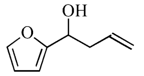
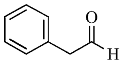
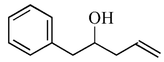
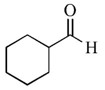
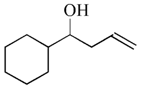
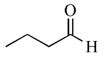
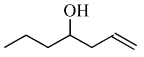


Scheme 2. $Bi(OTf)_3$-catalyzed microwave-assisted allylation of benzaldehyde: effect of solvent and temperature.

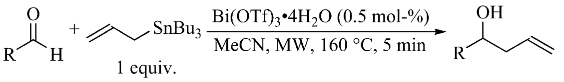
Several examples of $Bi(OTf)_3 \cdot 4H_2O$-catalyzed Sakurai reactions of various aldehydes **1** with allyltributylstannane are summarized in Table 3 (Scheme 3). A variety of differently substituted benzaldehydes were treated in acetonitrile under our optimized conditions, except regarding the quantity of the allyltributylstannane used (only 1.0 equiv.). With both electron-poor, electron-rich and *o*-substituted benzaldehydes, the corresponding homoallylic alcohols **3** were obtained in moderate to excellent yields (Table 3, Entries 1–6). In addition, heteroaromatic aldehyde **1g** could also serve as a substrate in this reaction, albeit giving the corresponding homoallylic alcohol in a moderate yield (Table 3, Entry 7). Our conditions proved to be mild enough to prevent furane from side reactions such as polymerization frequently encountered with furane compounds.[18] Aliphatic aldehydes led to a moderate to good yield of **3** (Table, Entries 8–10).

Given that the allylation reaction with **1a** still proceeds in the presence of a proton scavenger [1 equiv. of **1a**, 1 equiv. of allyltributylstannane **2**, 0.5 mol-% of $Bi(OTf)_3 \cdot 4H_2O$, 1.5 mol-% of N^1,N^1,N^8,N^8-tetramethylnaphthalene-1,8-diamine proton sponge®, 160 °C, microwaves, 5 min, 69% of **3a**; or 1 equiv. of **1a**, 1 equiv. of allyltributylstannane **2**, 0.5 mol-% of $Bi(OTf)_3 \cdot 4H_2O$, 1.5 mol-% K_2CO_3, 160 °C, microwaves, 5 min, 66% of **3a**], a Lewis acid is clearly involved in the mechanism. However, when HOTf is used as the catalyst, the reaction proceeds to afford the expected product **3a**, indicating that HOTf could also be a catalyst for the transformation (1 equiv. of **1a**, 1 equiv. of allyltributylstannane **2**, 1.5 mol-% of HOTf, 160 °C, microwaves, 5 min, 81% of **3a**). This observation suggests that HOTf is likely to be involved to some extent as a Brønsted acid as well. More detailed investigations on the mechanism of this transformation are in progress.

Table 3. $Bi(OTf)_3$-catalyzed allylation of various aldehydes under microwave assistance.

Entry	Reactant **1**	Product **3**[a]	**3**	Yield **3** [%][b]
1			**3a**	85
2			**3b**	81
3			**3c**	64
4			**3d**	93
5			**3e**	82
6			**3f**	86
7			**3g**	64
8			**3h**	83
9			**3i**	68
10			**3j**	74

[a] All compounds were characterized by ^1H NMR and ^{13}C NMR spectroscopy. [b] Isolated yield.



1 **2** **3**

Scheme 3. $Bi(OTf)_3$-catalyzed microwave-assisted allylation of various aldehydes.

Conclusions

As an improvement over other catalytic systems, $Bi(OTf)_3 \cdot 4H_2O$ is a versatile catalyst for the microwave-assisted allylation of aldehydes.[19] The reaction affords moderate to good yields in homoallylic alcohols in a very short reaction time (5 min), and using as low as 0.5 mol-% of catalyst under microwave assistance. This method offers several advantages including mild reaction conditions, only 1 equiv. of allylstannane used as nucleophile, highly catalytic process, no formation of by-products, and no workup. The conditions are suitable for a variety of aldehydes. Also, the practical use of $Bi(OTf)_3 \cdot 4H_2O$ is highly valuable as an attractive alternative to other Lewis acids and as a valuable surrogate for HOTf since the latter is very corrosive and difficult to handle. Because of its numerous benefits, this method for the straightforward synthesis of homoallylic alcohols using $Bi(OTf)_3 \cdot 4H_2O$ catalysis should find utility in the synthesis of biologically active compounds. Research is on its way to demonstrate other significant applications of this $Bi(OTf)_3 \cdot 4H_2O$-catalyzed Sakurai reaction.

Experimental Section

General Procedure for the Microwave-Enhanced Bismuth Triflate-Catalyzed Allylation of Aldehydes: All reactions were performed using a 400 W Biotage Initiator™ microwave synthesis instrument. In the capped microwave reactor, the aldehyde (0.5 mmol), the allyltributylstannane (0.5 mmol), and $Bi(OTf)_3 \cdot 4H_2O$ (0.0025 mmol) were mixed together in dry MeCN (1 mL) under nitrogen. The solution was then brought up to 160 °C for 5 min under microwave irradiation. The resulting mixture was concentrated directly in a rotary evaporator to afford the crude product which was purified by column chromatography [eluent: hexane/EtOAc (95:5) or toluene]. Spectral data agree with those previously reported in the literature.[19]

Acknowledgments

This work was financially supported by the Natural Sciences and Engineering Research Council of Canada (NSERC), the Fonds Québécois de la Recherche sur la Nature et les Technologies (FQRNT, Québec, Canada), the Canada Foundation for Innovation, and the Université Laval. We thank Rhodia (Lyon, France) and Sidech s. a. (Tilly, Belgium) for a generous gift of chemicals. We appreciate the help and support provided by R. Kadri (Biotage AB).

---

[1] a) O. Piechaczyk, T. Cantat, N. Mezailles, P. LeFloch, *J. Org. Chem.* **2007**, *72*, 4228–4237; b) I. Marek, G. Sklute, *Chem. Commun.* **2007**, 1683–1691; c) K. J. Szabó, *Synlett* **2006**, 811–824; d) H.-S. Cheng, T.-P. Loh, *Pure Appl. Chem.* **2005**, *77*, 1199–1206; e) S. E. Denmark, J.-P. Fu, *Chem. Rev.* **2003**, *103*, 2763–2793; f) C. E. Masse, J. S. Panek, *Chem. Rev.* **1995**, *95*, 1293–1316; g) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207–2293; h) N. Aoyama, T. Hamada, K. Manabe, S. Kobayashi, *Chem. Commun.* **2003**, 676–677; i) S. Kobayashi, S. Nagayama, T. Busujima, *Chem. Lett.* **1997**, *26*, 959–960.

[2] a) N. Makita, Y. Hoshino, H. Yamamoto, *Angew. Chem. Int. Ed.* **2003**, *42*, 941–943; b) T. W. Lee, E. J. Corey, *J. Am. Chem. Soc.* **2001**, *123*, 1872–1877.

[3] a) K. Takeuchi, T. Takeda, T. Fujimoto, I. Yamamoto, *Tetrahedron* **2007**, *63*, 5319–5322; b) Q.-B. Su, L. A. Dakin, J. S. Panek, *J. Org. Chem.* **2007**, *72*, 2–24; c) M. Georgy, P. Lesot, J.-M. Campagne, *J. Org. Chem.* **2007**, *72*, 3543–3549; d) L. V. Heumann, G. E. Keck, *Org. Lett.* **2007**, *9*, 1951–1954.

[4] a) D. R. Williams, A. I. Morales-Ramos, C. M. Williams, *Org. Lett.* **2006**, *8*, 4393–4396; b) K. Kimura, A. Ezoe, M. Mori, K. Iwata, Y. Tamaru, *J. Am. Chem. Soc.* **2006**, *128*, 8559–8568; c) K.-H. Shen, C.-F. Yao, *J. Org. Chem.* **2006**, *71*, 3980–3983; d) Q.-W. Yao, M. Sheets, *J. Org. Chem.* **2006**, *71*, 5384–5387; e) C. Ogawa, M. Sugiura, S. Kobayashi, *Chem. Commun.* **2003**, 192–193; f) S. Kobayashi, N. Aoyama, K. Manabe, *Synlett* **2002**, 483–485.

[5] a) S. Kobayashi, M. Sugiura, H. Kitagawa, W. W.-L. Lam, *Chem. Rev.* **2002**, *102*, 2227–2302; b) H. C. Aspinall, A. F. Browning, N. Greeves, P. Ravenscroft, *Tetrahedron Lett.* **1994**,

35, 4639–4640; c) H. C. Aspinall, N. Greeves, E. G. McIver, *Tetrahedron Lett.* **1998**, *39*, 9283–9286; d) V. K. Aggarwal, G. P. Vennall, *Tetrahedron Lett.* **1996**, *37*, 3745–3746; e) T. Akiyama, J. Iwai, M. Sugano, *Tetrahedron* **1999**, *55*, 7499–7508.

[6] a) H. Suzuki, Y. Matano, Y. *Organobismuth Chemistry*, Elsevier, Amsterdam, **2001**; b) H. Gaspard-Iloughmane, C. Le Roux, *Eur. J. Org. Chem.* **2004**, 2517–2532; c) N. M. Leonard, L. C. Wieland, R. S. Mohan, *Tetrahedron* **2002**, *58*, 8373–8397.

[7] BiX_3-mediated allylations: a) N. Komatsu, M. Uda, H. Suzuki, T. Takahashi, T. Domae, M. Wada, *Tetrahedron Lett.* **1997**, *38*, 7215–7218; b) P. W. Anzalone, A. R. Baru, E. M. Danielson, P. D. Hayes, M. P. Nguyen, A. F. Panico, R. C. Smith, R. S. Mohan, *J. Org. Chem.* **2005**, *70*, 2091–2096; c) L. C. Wieland, H. M. Zerth, R. S. Mohan, *Tetrahedron Lett.* **2002**, *43*, 4597–4600; d) B. Leroy, I. E. Markó, *Org. Lett.* **2002**, *4*, 47–50; e) P. Sreekanth, J. K. Park, J. W. Kim, T. Hyeon, B. M. Kim, *Catal. Lett.* **2004**, *96*, 201–204; f) B. M. Choudary, S. Chidara, C. V. Raja Sekhar, *Synlett* **2002**, 1694–1696; g) Y. Nagano, A. Orita, J. Otera, *Adv. Synth. Catal.* **2003**, *345*, 643–646; h) B. M. Choudary, C. Sridhar, M. Sateesh, B. Sreedhar, *J. Mol. Catal. A* **2004**, *212*, 237–243; Bi^0-mediated allylations: i) M. Minato, J. Tsuji, *Chem. Lett.* **1988**, *17*, 2049–2052; j) M. Wada, H. Ohki, K.-y. Akiba, *J. Chem. Soc. Chem. Commun.* **1987**, 708–709; k) P. C. Andrews, A. C. Peatt, C. L. Raston, *Green Chem.* **2001**, *3*, 313–315.

[8] a) C. Ogawa, S. Azoulay, S. Kobayashi, *Heterocycles* **2005**, *66*, 201–206; b) T. Ollevier, G. Lavie-Compin, *Tetrahedron Lett.* **2004**, *45*, 49–52; c) T. Ollevier, G. Lavie-Compin, *Tetrahedron Lett.* **2002**, *43*, 7891–7893.

[9] a) C. Le Roux, L. Ciliberti, H. Laurent-Robert, A. Laporterie, J. Dubac, *Synlett* **1998**, 1249–1251; b) S. Kobayashi, T. Ogino, H. Shimizu, S. Ishikawa, T. Hamada, K. Manabe, *Org. Lett.* **2005**, *7*, 4729–4731; c) T. Ollevier, V. Desyroy, C. Catrinescu, R. Wischert, *Tetrahedron Lett.* **2006**, *47*, 9089–9092; d) T. Ollevier, V. Desyroy, E. Nadeau, *ARKIVOC* **2007**, *X*, 10–20.

[10] a) T. Ollevier, E. Nadeau, *J. Org. Chem.* **2004**, *69*, 9292–9295; b) T. Ollevier, E. Nadeau, J.-C. Eguillon, *Adv. Synth. Catal.* **2006**, *348*, 2080–2084; c) T. Ollevier, E. Nadeau, *Synlett* **2006**, 219–222; d) T. Ollevier, E. Nadeau, A.-A. Guay-Bégin, *Tetrahedron Lett.* **2006**, *47*, 8351–8354; e) T. Ollevier, E. Nadeau, *Org. Biomol. Chem.* **2007**, *5*, 3126–3134.

[11] a) N. M. Leonard, M. C. Oswald, D. A. Freiberg, B. A. Nattier, R. C. Smith, R. S. Mohan, *J. Org. Chem.* **2002**, *67*, 5202–5207; b) M. D. Carrigan, D. Sarapa, R. C. Smith, L. C. Wieland, R. S. Mohan, *J. Org. Chem.* **2002**, *67*, 1027–1030.

[12] a) C. Le Roux, J. Dubac, *Synlett* **2002**, 181–200; b) J. R. Desmurs, M. Labrouillère, C. Le Roux, H. Gaspard, A. Laporterie, J. Dubac, *Tetrahedron Lett.* **1997**, *38*, 8871–8874; c) S. Répichet, C. Le Roux, J. Dubac, J. R. Desmurs, *Eur. J. Org. Chem.* **1998**, 2743–2746.

[13] a) T. Ollevier, V. Desyroy, M. Asim, M.-C. Brochu, *Synlett* **2004**, 2794–2796; b) T. Ollevier, T. M. Mwene-Mbeja, *Synthesis* **2006**, 3963–3966; c) T. Ollevier, T. M. Mwene-Mbeja, *Tetrahedron Lett.* **2006**, *47*, 4051–4055.

[14] a) S. Répichet, A. Zwick, L. Vendier, C. Le Roux, J. Dubac, *Tetrahedron Lett.* **2002**, *43*, 993–995; b) M. Labrouillère, C. Le Roux, H. Gaspard, A. Laporterie, J. Dubac, J. R. Desmurs, *Tetrahedron Lett.* **1999**, *40*, 285–286; c) M. Peyronneau, C. Arrondo, L. Vendier, N. Roques, C. Le Roux, *J. Mol. Catal. A* **2004**, *211*, 89–91. $Bi(OTf)_3 \cdot 4H_2O$ has been prepared from Bi_2O_3 according to ref.[14a]

[15] a) T. Ollevier, Z. Li, *Org. Biomol. Chem.* **2006**, *4*, 4440–4443; b) T. Ollevier, T. Ba, *Tetrahedron Lett.* **2003**, *44*, 9003–9005.

[16] a) C. R. Strauss, R. S. Varma, *Top. Curr. Chem.* **2006**, *266*, 199–231; b) A. Loupy, *Microwaves in organic synthesis*, Wiley-VCH, Weinheim, **2002**; c) P. Lidström, J. Tierney, B. Wathey, J. Westman, *Tetrahedron* **2001**, *57*, 9225–9283.

[17] a) D. D. Laskar, M. Gohain, D. Prajapati, J. S. Sandhu, *New J. Chem.* **2002**, *26*, 193–195; b) A. Boruah, B. Baruah, D. Prajapati, J. S. Sandhu, *Tetrahedron Lett.* **1997**, *38*, 4267–4268; c) B. Baruah, A. Boruah, D. Prajapati, J. S. Sandhu, *Tetrahedron Lett.* **1997**, *38*, 1449–1450; d) J. Marquié, A. Laporterie, J. Dubac, N. Roques, J.-R. Desmurs, *J. Org. Chem.* **2001**, *66*, 421–425.

[18] C. Le Roux, H. Gaspard-Iloughmane, J. Dubac, *Bull. Soc. Chim. Fr.* **1993**, *130*, 832–842.

[19] **3a**, **3c**, **3e**, **3g**, **3i**: a) G. L. Li, G. Zhao, *J. Org. Chem.* **2005**, *70*, 4272–4278; **3b**: b) K.-H. Shen, C.-F. Yao, *J. Org. Chem.* **2006**, *71*, 3980–3983; **3h**: c) J.-X. Wang, X.-F. Jia, T.-J. Meng, L. Xin, *Synthesis* **2005**, 2838–2844; **3d**: d) M. Yasuda, T. Fujibayashi, A. Baba, *J. Org. Chem.* **1998**, *63*, 6401–6404; **3f**: e) Q.-S. Zhang, Z.-Y. Luo, D. P. Curran, *J. Org. Chem.* **2000**, *65*, 8866–8873; **3j**: f) A. Hosomi, S. Kohra, K. Ogata, T. Yanagi, Y. Tominaga, *J. Org. Chem.* **1990**, *55*, 2415–2420.

Received: September 4, 2007