Lewis Acid-Induced Chemo- and Stereoselective Allylation of α-Iodo Mixed Acetal with Allylsilane

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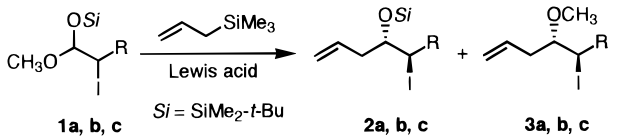
Received April 28, 1997

The Lewis acid-catalyzed reaction of acetals with allylsilanes has been widely studied for the formation of new carbon−carbon bonds under mild conditions.[1] However, only a few reports[2] have been published on the reaction of α-hetero-substituted acetal. Here we wish to report the highly chemo- and stereoselective reaction of α-iodo mixed acetals ($RCHICH(OMe)(OSiR_3)$)[3−5] with allylsilanes in the presence of various Lewis acids.

Mixed iodo acetals **1** were easily prepared stereoselectively by an addition of a solution of silyl enol ether in dichloromethane to a stirred heterogeneous mixture of *N*-iodosuccinimide (NIS) and methanol in dichloromethane at −78 °C.[6]

The stereo- and chemoselectivities in the reaction of α-iodo mixed acetals with allylsilane heavily depended on the nature of the Lewis acid employed. Regardless of whether titanium tetrachloride[7] or trimethylsilyl trifluoromethanesulfonate[8,9] (TMSOTf) is employed, α-iodo acetals **1** react with allylsilane to give *anti*-iodohydrin derivatives selectively; on the other hand, titanium tetrachloride induces attack at the methoxy group to afford iodohydrin silyl ethers **2**, whereas TMSOTf eliminates the siloxy moiety exclusively to give iodohydrin methyl ethers **3** (Table 1). The *anti* selectivity decreased with increase of the bulkiness of the R group (entries 5 and 6 in Table 1). The stereochemistry of the starting iodo acetals did not affect the stereochemical outcome of the products. For instance, *erythro*-**1a** and *threo*-**1a**[10] gave the same allylated iodohydrin silyl ether **2a** in 86% and 96% yield, respectively, upon treatment with $TiCl_4$. In addition, *erythro*-**1a** and *threo*-**1a** afforded the same methyl ether **3a** upon treatment with TMSOTf.

Table 1. Allylation of Iodoacetal with Allylsilane[a]



1a, b, c **2a, b, c** **3a, b, c**

				% yield (*anti*/*syn*)	
entry	no.	R	Lewis acid	**2**	**3**
1	**1a**	*n*-C_8H_{17}	$TiCl_4$	85 (>99/1)	
2	**1a**	*n*-C_8H_{17}	TMSOTf		89 (96/4)
3	**1b**	CH_3	$TiCl_4$	92 (>99/1)	
4	**1b**	CH_3	TMSOTf		68 (94/6)
5	**1c**	*i*-C_3H_7	$TiCl_4$	50 (82/18)	
6	**1c**	*i*-C_3H_7	TMSOTf		74 (61/39)

[a] Starting acetals **1a**, **1b**, and **1c** were mixtures of diastereomers (*erythro*/*threo* = 2/1).

Scheme 1

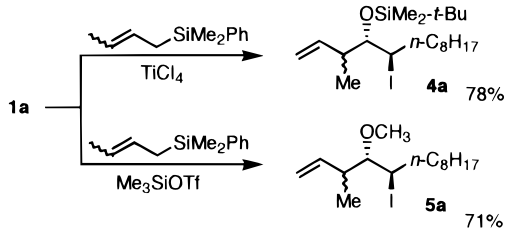
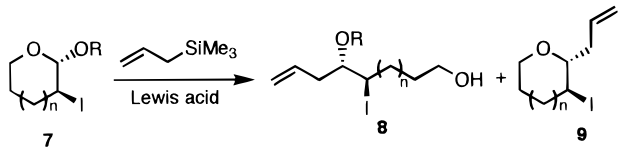


Table 2. Allylation of Cyclic Acetals with Allylsilane



7 **8** **9**

					% yield	
					8	**9**
entry	no.	*n*	R	Lewis acid	(*anti*/*syn*)	(*trans*/*cis*)
1	**7a**	0	$SiMe_2$-*t*-Bu	$TiCl_4$	58 (>99/1)	—
2	**7a**	0	$SiMe_2$-*t*-Bu	TMSOTf	—	90 (>99/1)
3	**7b**	1	$SiMe_2$-*t*-Bu	$TiCl_4$	72 (>99/1)	—
4	**7b**	1	$SiMe_2$-*t*-Bu	TMSOTf	—	91 (>99/1)
5	**7c**	0	CH_3	$TiCl_4$	44 (89/11)	
6	**7d**	1	CH_3	$TiCl_4$	70 (82/18)	

The use of crotylsilane instead of allylsilane gave the corresponding adducts **4a** and **5a**. The reaction proceeded regioselectively at the γ-carbon atom of the allylic silane (Scheme 1). Dienylsilane (CH_2=CHCH=$CHCH_2$-$SiMe_2Ph$) also produced an expected *anti*-iodohydrin methyl ether **6a** (CH_2=CHCH=$CHCH_2C(OCH_3)CHI$(*n*-C_8H_{17})) in good yield (83%) upon treatment of **1a** in the presence of TMSOTf. In contrast, prenylsilane provided complex mixtures in the reaction under $TiCl_4$ or TMSOTf catalysis.

The cyclic acetals **7a** and **7b** gave similar results as the acyclic iodo mixed acetal **1a** and **1b** (Table 2). Thus, $TiCl_4$ attacked at the oxygen which existed in a five-membered or six-membered ring to afford open-chain product **8a** or **8b** in the reaction of **7a** or **7b**, whereas TMSOTf replaced the siloxy group by the allyl moiety to give allylated tetrahydrofuran derivative **9a** or tetrahy-

(1) Colvin, E. W. *Silicon in Organic Synthesis*, Butterworth and Co. Ltd.: London, 1981; Chapter 9, pp 97−124. Fleming, I. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 2, Chapter 2.2, p 563; Yamaguchi, M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 1, Chapter 1.11, p 325.

(2) (a) α-Sulfenyl acetal: Kudo, K.; Hashimoto, Y.; Sukegawa, M.; Hasegawa, M.; Saigo, K. *J. Org. Chem.* **1993**, *58*, 579. (b) α-Amino acetal: Polt, R.; Peterson, M. A.; Young, L. D. *J. Org. Chem.* **1992**, *57*, 5469. (c) α-Bromo acetal: Mukaiyama, T.; Ishihara, H.; Inomata, K. *Chem. Lett.* **1975**, 527, 531.

(3) Recently we have reported the stereoselective synthesis of allyl vinyl ethers from α-iodoacetals: Maeda, K.; Shinokubo, H.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1996**, *61*, 2262.

(4) The preparation and synthetic use of monosilyl acetal ($RCHOR'(OSiMe_3)$) have been reported: Mukaiyama, T.; Ohshima, M.; Miyoshi, N. *Chem. Lett.* **1987**, 1121. Kiyooka, S.; Kaneko, Y.; Komura, M.; Matsuo, H.; Nakano, M. *J. Org. Chem.* **1991**, *56*, 2276. Kiyooka, S.; Shirouchi, M.; Kaneko, Y. *Tetrahedron Lett.* **1993**, *34*, 1491.

(5) The selective formation of ethers or thioethers from monothioacetals by the appropriate choice of Lewis acid has been reported: Sato, T.; Okura, S.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1987**, *28*, 6299. Sato, T.; Otera, J.; Nozaki, H. *J. Org. Chem.* **1990**, *55*, 6116.

(6) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303.

(7) Mukaiyama, T.; Murakami, M. *Synthesis* **1987**, 1043.

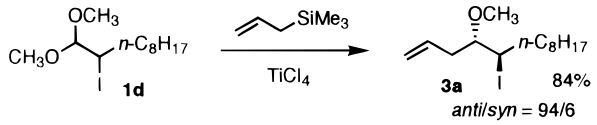
(8) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 71; Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 3248.

(9) Treatment of **1a** with $SnCl_4$ afforded **2a** (*anti*/*syn* = >99/1) in 54% yield. The use of BF_3·OEt_2 resulted in formation of a small amount of **3a** (<15%).

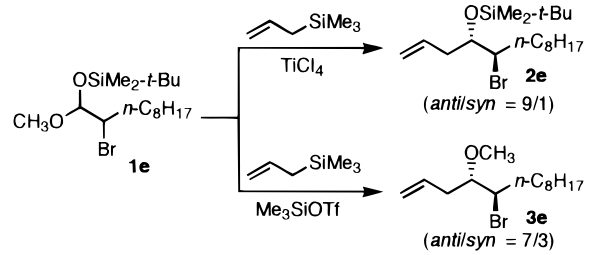
(10) For the nomenclature of *erythro* and *threo*, see: Noyori, R; Nishida, H. *J. Am. Chem. Soc.* **1981**, *103*, 2106.

S0022-3263(97)00753-6 CCC: $14.00

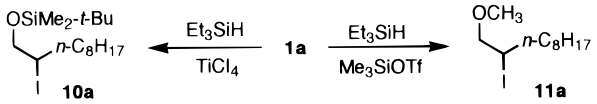
Scheme 2



Scheme 3



Scheme 4

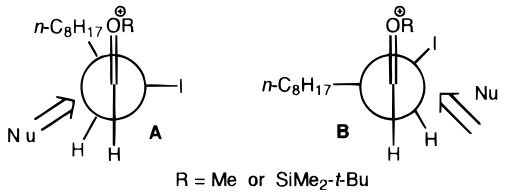


dropyran derivative **9b**. Treatment of cyclic dialkyl acetals **7c** and **7d** with $TiCl_4$ in the presence of allylsilane provided an open-chain allylated product **8c** and **8d**, respectively, as in the case of the reaction of **7a** and **7b**. However, the stereoselectivities for the reaction of **7c** and **7d** were lower than those for **7a** and **7b**. Trimethylsilyl trifluoromethanesulfonate-induced reaction of **7c** and **7d** resulted in recovery of the starting materials.

In order to elucidate the reaction mechanism, the following two experiments were performed using dimethyl acetal **1d** and bromo acetal **1e** as substrates (Schemes 2 and 3). Titanium tetrachloride-induced allylation of **1d** with allyltrimethylsilane provided *anti* iodohydrin derivative **3a** (*anti*/*syn* = 94/6) in 84% yield. In contrast, TMSOTf-mediated allylation gave **3a** in only 15% yield. The bromo acetal **1e** provided allylated bromohydrin silyl ether **2e** (98%) in the reaction with allylsilane in the presence of $TiCl_4$ and gave methyl ether **3e** (41%) in the TMSOTf-mediated reaction with allyltrimethylsilane. The allylation of bromo acetal **1e** proceeded in somewhat lower selectivity compared to that of iodoacetal **1a**, and *anti*- and *syn*-isomers were obtained in 9:1 or 7:3 ratio, respectively. The stereochemistry of **1e** did not affect the stereochemical results of the product **2e**. Thus, both an isomeric mixture **1e** (*erythro*/*threo* = 34/66) and *erythro* rich **1e** (*erythro*/*threo* = 90/10) gave the same isomeric mixture of **2e** (*anti*/*syn* = 9/1) upon treatment with $TiCl_4$.

Dichloromethane and toluene were equally effective as a solvent. For instance, treatment of a mixture of **1a** and allyltrimethylsilane with $TiCl_4$ in CH_2Cl_2 or toluene gave **2a** in 89% or 84% yield, respectively, and the reaction with TMSOTf in CH_2Cl_2 or toluene afforded **3a** in 87% or 92% yield, respectively. Several other nucleophiles were examined. Among them, triethylsilane gave the corresponding hydrogenated iodohydrin silyl ether **10a** (63%) or methyl ether **11a** (89%), respectively, upon treatment of **1a** in the presence of $TiCl_4$ or TMSOTf (Scheme 4).[11] The use of vinyltrimethylsilane or silyl enol ether such as $CH_2{=}CH(Ph)OSiMe_3$ instead of allyltrimethylsilane in the presence of $TiCl_4$ or TMSOTf resulted in formation of complex mixtures or recovery of the starting iodo acetal **1a**.

We are tempted to assume the following reaction mechanism[12] for the chemoselective formation of allylated product **2a** or **3a** from **1a** by changing Lewis acids. As described above, the chemoselectivity of the reaction was not affected by the stereochemistry of iodoacetals **1**. This fact indicates that the unique switching effect would be ascribed to the difference in reactivity of the Lewis acids, $TiCl_4$ and TMSOTf (acidity, chelation ability).[13] The strong Lewis acid $TiCl_4$ coordinates the methoxy group in preference to the bulky *tert*-butyldimethylsiloxy moiety. On the other hand, a weaker Lewis acid, TMSOTf, prefers a stronger leaving group, the siloxy group.[14] Meanwhile, the stereoselective formation of the *anti* allylated product could be explained as follows. An oxocarbenium ion can possibly be formed by the elimination of either the methoxy or siloxy group of the acetal moiety. The stereochemistry is determined by the Felkin−Anh model[15,16] of two possible conformers, **A** and **B**,



which give the *anti* and *syn* allylation products, respectively. Due to the electronic effect of the iodide group, conformer **A** is considered to be preferable for **1a** and **1b**; the *anti* isomer is formed selectively. The decrease in stereoselectivity for **1c** can be attributed to a severe steric repulsion between isopropyl and the oxonium group in **A**; the reaction through conformer **B** would compete with the reaction through **A**. On the other hand, the loss of stereoselectivity for **1e** can be consistently explained by a smaller steric repulsion between bromide and the oxonium group compared to that between iodide and the oxonium group.

One-pot synthesis of **3a** from silyl enol ether **12** has been examined. Treatment of a dichloromethane solution of **12** with *N*-iodosuccinimide in the presence of methanol at −78 °C followed by an addition of allyltrimethylsilane and TMSOTf provided **3a** in 91% overall yield (Scheme 5).

(11) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1979**, 4679.

(12) Many mechanistic studies of acetal reactions have been reported: Yamamoto, Y.; Nishii, S.; Yamada, J.-I. *J. Am. Chem. Soc.* **1986**, *108*, 7116. Yamamoto, Y.; Yamada, J.-I. *J. Chem. Soc. Chem. Commun.* **1987**, 1218. Murata, S.; Suzuki, M.; Noyori, R. *Tetrahedron* **1988**, *44*, 4259. Denmark, S. E.; Wilson, T. M. *J. Am. Chem. Soc.* **1993**, *115*, 10695. For a review, see: (a) Alexakis, A.; Mangeney, P. *Tetrahedron*: *Asymmetry* **1990**, *1*, 477. (b) Mash, A. E. In *Studies in Natural Product Synthesis*; Atta-Ur Rahman, Ed.; Elsevier: Amsterdam, 1988; Vol. 1, p 577. (c) Seebach, D.; Imwinkelried, R.; Weber, T. In *Modern Synthetic Methods*; Sheffold, R., Ed.; Springer-Verlag; Berlin, 1986; Vol. 4, p 125.

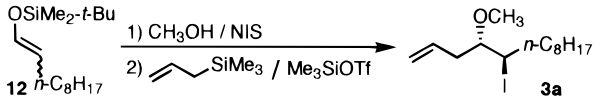
(13) The iodide did not play a critical role in the chemoselective ionization of the mixed acetal. This was confirmed by the following experiments. Treatment of n-$C_9H_{19}CH(OMe)(OSiMe_2$-t-Bu), generated from **1a** by n-Bu_3SnH reduction, with $TiCl_4$ and allylsilane provided silyl ether (n-$C_9H_{19}CH(OSiMe_2$-t-Bu)$CH_2CH{=}CH_2$) in 92% yield. In contrast, the use of TMSOTf eliminated the siloxy group to give methyl ether (n-$C_9H_{19}CH(OMe)CH_2CH{=}CH_2$) in 89% yield.

(14) Silanol is more acidic than the corresponding alcohol. Bassindale, A. R.; Taylor, P. G. In *The Chemistry of Organic Silicon Compounds Part 1*; Patai, S.; Rappoport, Z., Eds.; John Wiley & Sons: Chichester, 1989; Chapter 12, pp 809−838.

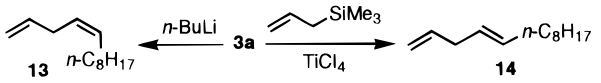
(15) Cherest, M.: Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. Anh, N. T. *Topics Curr. Chem.* **1980**, *88*, 145.

(16) *anti*-Selective reaction of α-sulfenyl acetals with allylsilane has been reported. See ref 2a.

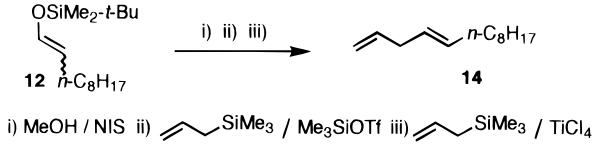
Scheme 5



Scheme 6



Scheme 7



anti-Iodohydrin methyl ether **3a** was converted into (*Z*)-alkene **13** (*E*/*Z* = 7/93) in 61% yield upon treatment with *n*-BuLi in hexane−ether (1:1) at −78 °C.[17] In addition, the reaction of **3a** with $TiCl_4$ in the presence of allyltrimethylsilane provided (*E*)-alkene **14** (*E*/*Z* > 99/1) in 83% yield. Therefore, by changing the reagents, both (*Z*)- and (*E*)-1,4-tridecadiene (**13** and **14**) could be prepared selectively from the same iodohydrin methyl ether **3a** (Scheme 6).

Finally, the conversion of **12** into *E*-alkene **14** was performed in one pot. Allyltrimethylsilane and $TiCl_4$ were added to a dichloromethane solution of **3a**, generated from **12** as described above, to afford (*E*)-alkene **14** in 76% overall yield (Scheme 7).

Experimental Section

General Procedure for Allylation. A dichloromethane solution (6 mL) of iodoacetal **1a** (0.43 g, 1.0 mmol) was cooled to −78 °C under an argon atmosphere. Allyltrimethylsilane (0.32 mL, 2.0 mmol) was added at −78 °C. Then, a dichloromethane solution of $TiCl_4$ (1.0 M, 1.0 mL, 1.0 mmol) or TMSOTf (1.0 M, 0.2 mL, 0.2 mmol) was added and the resulting solution was stirred for another 30 min ($TiCl_4$) or 1 h (TMSOTf) at −78 °C. Extractive workup (hexane−aqueous NH_4Cl or hexane−aqueous $NaHCO_3$) followed by silica gel column chromatography (hexane or hexane−ethyl acetate = 40/1) provided allylated product **2a** or **3a** in 89% or 87% yield, respectively.

(17) Maeda, K.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **1996**, *61*, 6770.

***anti*-4-(*tert*-Butyldimethylsiloxy)-5-iodo-1-tridecene (2a)**: bp 131 °C (0.5 Torr); IR (neat) 1643, 1074 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05 (s, 3H), 0.08 (s, 3H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 1.20−1.40 (m, 12H), 1.48−1.81 (m, 2H), 2.24 (ddd, *J* = 13.8, 7.3, 5.0 Hz, 1H), 2.45 (ddd, *J* = 13.8, 7.3, 6.3 Hz, 1H), 3.47 (ddd, *J* = 6.3, 5.0, 4.8 Hz, 1H), 4.07 (ddd, *J* = 9.3, 4.8, 4.7 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 5.09 (d, *J* = 17.3 Hz, 1H), 5.78 (ddt, *J* = 17.3, 10.2, 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −4.62, −4.35, 13.99, 18.03, 22.55, 25.78, 28.74, 29.14, 29.30, 29.73, 31.76, 35.24, 40.25, 44.99, 75.34, 117.79, 134.25. Anal. Calcd for $C_{19}H_{39}IOSi$: C, 52.04; H, 8.96. Found: C, 52.06; H, 8.86.

***anti*-5-Iodo-4-methoxy-1-tridecene (3a)**: bp 115 °C (0.5 Torr); IR (neat) 1642, 1459, 1093 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (t, *J* = 6.8 Hz, 3H), 1.17−1.41 (m, 12H), 1.51−1.87 (m, 2H), 2.35 (ddd, J = 14.6, 7.2, 4.7 Hz, 1H), 2.43 (ddd, J = 14.6, 7.2, 7.2 Hz, 1H), 2.95 (ddd, *J* = 7.2, 4.7, 4.5 Hz, 1H), 3.39 (s, 3H), 4.21 (ddd, *J* = 9.9, 4.5, 3.6 Hz, 1H), 5.07 (d, *J* = 10.2 Hz, 1H), 5.12 (d, *J* = 17.0 Hz, 1H), 5.83 (ddt, *J* = 17.0, 10.2, 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.97, 22.54, 28.73, 29.12, 29.29, 29.74, 31.74, 35.18, 37.28, 40.77, 57.80, 84.00, 117.55, 134.30. Anal. Calcd for $C_{14}H_{27}IO$: C, 49.71; H, 8.04. Found: C, 49.49; H, 7.91.

***anti*-4-(*tert*-Butyldimethylsiloxy)-3-iodo-6-hepten-1-ol (8a)**: bp 121 °C (0.5 Torr); IR (neat) 3326, 1643, 1068 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 3H), 0.13 (s, 3H), 0.90 (s, 9H), 1.87−1.96 (br, 1H), 1.91−1.99 (m, 2H), 2.34 (ddd, *J* = 14.1, 7.2, 6.3 Hz, 1H), 2.42 (ddd, *J* = 14.1, 7.2, 6.3 Hz, 1H), 3.64−3.77 (m, 1H), 3.69 (dt, *J* = 3.8, 6.3 Hz, 1H), 3.80−3.90 (m, 1H), 4.36 (ddd, *J* = 7.4, 5.7, 3.8 Hz, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 5.11 (d, *J* = 17.2 Hz, 1H), 5.76 (ddt, *J* = 17.2, 10.1, 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −4.51, −4.41, 18.05, 25.80, 36.92, 39.36, 40.24, 62.18, 76.17, 118.14, 133.82. Anal. Calcd for $C_{13}H_{27}IO_2Si$: C, 42.16; H, 7.35. Found: C, 42.43; H, 7.61.

***trans*-3-Iodo-2-(2-propenyl)-1-oxacyclopentane (9a)**: bp 123 °C (10 Torr); IR (neat) 1642, 1075, 1057 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.17−2.32 (m, 2H), 2.42−2.55 (m, 2H), 3.79 (ddd, *J* = 7.8, 7.2, 6.9 Hz, 1H), 3.84−3.93 (m, 2H), 4.09 (ddd, *J* = 7.0, 6.9, 4.7 Hz, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 5.11 (d, *J* = 17.1 Hz, 1H), 5.81 (dddd, *J* = 17.1, 10.2, 7.2, 6.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.42, 36.72, 38.17, 67.09, 87.18, 117.89, 133.69. Anal. Calcd for $C_7H_{11}IO$: C, 35.32; H, 4.66. Found: C, 35.34; H, 4.64.

Acknowledgment. Financial support by Grant-in Aid for Encouragement of Young Scientists from the Ministry of Education, Science, Sports, and Culture, Japan is acknowledged.

Supporting Information Available: Compound characterization data for **1a**−**e**, **2b**−**e**, **3b**−**e**, **6a**, **7a**−**d**, **8b**−**d**, **9b**, and **10a** (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.

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