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Strong Counteranion Effects on the Catalytic Activity of Cationic Silicon Lewis Acids in Mukaiyama Aldol and Diels–Alder Reactions

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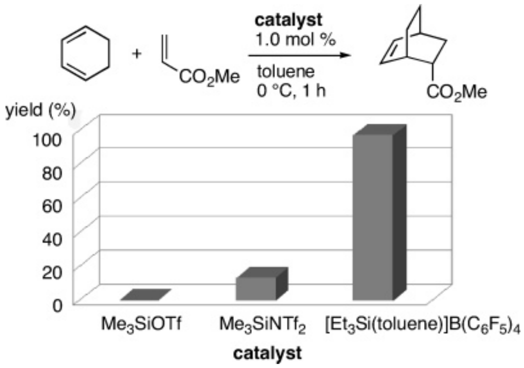
ABSTRACT



A toluene-coordinated silyl borate, $[Et_3Si(toluene)]B(C_6F_5)_4$, demonstrated catalytic activities significantly higher than those of Me_3SiOTf and Me_3SiNTf_2 in Mukaiyama aldol and Diels–Alder reactions.

Various Lewis acids have been employed as catalysts for synthetic organic reactions. Although silicon Lewis acids are typically silyl chlorides or silyl triflates (R_3SiOTf),[1] several other new types of silicon Lewis acids have been utilized. For example, silyl bis(trifluoromethansulfonyl)imides **1** (R_3SiNTf_2) can act as stronger Lewis acids than Me_3SiOTf and, consequently, have been used as an efficient catalyst for Friedel−Crafts alkylation,[2a] allylation of ketal,[2a] Diels−Alder reaction,[2b−d] Mukaiyama aldol reaction,[2e] and Sakurai−Hosomi allylation.[2e] Another new type of the silicon Lewis acid is the cationic silicon species such as silyl borates $[R_3Si(L)]BAr_4$ (**2**), where Ar is a flourine-containing aromatic substituent and L is a donor group that can coordinate to the silicon center.[3,4]

R_3SiNTf_2 **1** $[R_3Si(L)]BAr_4$ **2**   (Ar = $3,5\text{-}(CF_3)_2C_6H_3$, C_6F_5)

Although several previous studies have focused on the catalytic activity of silyl borates **2**, their cationic characters were far from those of a “true silyl cation”. One of these catalysts was used in a strong donor solvent (CH_3CN),[5] while others were coordinated with an intramolecular donor group.[6] In both cases, the coordination would decrease the inherent

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(1) Dilman, A. D.; Loffe, S. L. *Chem. Rev.* **2003**, *103*, 733.

(2) (a) Ishii, A.; Kotera, O.; Saeki, T.; Mikami, K. *Synlett* **1997**, 1145. (b) Mathieu, B.; Ghosez, L. *Tetrahedron Lett.* **1997**, *38*, 5497. (c) Mathieu, B.; de Fays, L.; Ghosez, L. *Tetrahedron Lett.* **2000**, *41*, 9561. (d) Mathieu, B.; Ghosez, L. *Tetrahedron* **2002**, *58*, 8219. (e) Ishihara, K.; Hiraiwa, Y.; Yamamoto, H. *Synlett* **2001**, 1851.

(3) For reviews, see: (a) Lambert, J. B.; Kania, L.; Zhang, S. *Chem. Rev.* **1995**, *95*, 1191. (b) Reed, C. A. *Acc. Chem. Res.* **1998**, *31*, 325.

(4) Lambert, J. B.; Zhang, S. *J. Chem. Soc., Chem. Commun.* **1993**, 383.

(5) Johannsen, M.; Jørgensen, K. A.; Helmchen, G. *J. Am. Chem. Soc.* **1998**, *120*, 7637.

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Lewis acidities of the silicon center. In contrast, a silyl borate that possesses a strong cationic character is $[Et_3Si(toluene)]B(C_6F_5)_4$ (**2a**), a silyl cation coordinated by toluene[7] that was first reported by Lambert et al. (eq 1).[4]

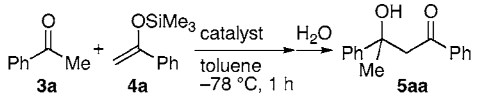
$$Et_3Si\text{-}H + Ph_3CB(C_6F_5)_4 \xrightarrow[\text{toluene}]{} \underset{\mathbf{2a}}{[Et_3Si(toluene)]B(C_6F_5)_4} + Ph_3CH \quad (1)$$

Despite their use as catalysts for the hydrosilylation of 1,1-diphenylethene[8] and for the hydrodefluorination of benzylic C−F bonds,[9] the application of such silyl borates for the formation of C−C bonds remains uncommon. Mukaiyama et al. have used silyl borate Me_3SiBAr_4 ($Ar = C_6F_5$), generated in situ from Me_3SiCl and $AgBAr_4$, as a catalyst for the aldol-type reaction between an enol ester and an aldehyde; unfortunately, the improved catalytic activity, in comparison to that of Me_3SiOTf, was not clearly demonstrated.[10] Herein, we report on the improved catalytic activity of $[Et_3Si(toluene)]B(C_6F_5)_4$ (**2a**), in comparison to Me_3SiOTf and Me_3SiNTf_2, as a precatalyst in Mukaiyama aldol and Diels−Alder reactions.

The catalytic performance of toluene-coordinated silyl borate **2a** was first examined in the Mukaiyama aldol reaction of ketone, for which only a limited number of effective catalysts has been reported to date.[2b,6,11] In the presence of **2a** (1.0 mol %), the reaction of acetophenone (**3a**) with enol silyl ether **4a** was carried out at −78 °C and was complete within 1 h to afford, after hydrolytic workup, aldol product **5aa** in a quantitative yield (Table 1, entry 1). In contrast, conversion was not observed using Me_3SiOTf catalyst (1 mol %) at −78 °C (entry 9). The catalytic activities of Me_3SiNTf_2 (**1a**) and Et_3SiNTf_2 (**1b**) were higher than that of Me_3SiOTf, in accordance with previously reported results, but afforded only 12% and 8% yields, respectively, under the same reaction conditions (entries 10 and 11).

To determine the possibility of a proton-promoted reaction, the experiment was repeated, but with a proton scavenger, 2,6-di-*tert*-butylpyridine. As shown in entry 2, the presence of such a scavenger did not affect the yield, thus excluding such proton-promoted reactions. At lower catalyst loading (0.5 mol %), the catalyst remained effective (97% yield) (entry 3); however, 0.1 mol % resulted in an incomplete conversion (34% yield) (entry 4).

Table 1. Mukaiyama Aldol Reaction with Acetophenone Catalyzed by Silicon Lewis Acids[a]



entry	catalyst	amount of catalyst (mol %)	solvent	yield (%)[b]
1	**2a**	1.0	toluene	96
2[c]	**2a**	1.0	toluene	97
3[d]	**2a**	0.5	toluene	97
4[e]	**2a**	0.1	toluene	34
5	**2a**	1.0	CH_2Cl_2	12
6	**2a**	1.0	Et_2O	0
7[f]	**2a**	1.0	CH_3CN	6
8[g]	**2a**	1.0	no solvent	98
9	Me_3SiOTf	1.0	toluene	0
10	Me_3SiNTf_2 (**1a**)	1.0	toluene	12
11	Et_3SiNTf_2 (**1b**)	1.0	toluene	8

[a] Reaction conditions: **3a** (0.50 mmol), **4a** (1.1 equiv), **2a** (1.0 mol %), toluene (1.5 mL), −78 °C, 1 h. [b] Determined by NMR analysis of the crude product using CH_2Br_2 as an internal standard. [c] 2,6-Di-*tert*-butylpyridine (2.0 mol %) was added. [d] Reaction at 1.0 mmol scale. [e] Reaction at 5.0 mmol scale. [f] Reaction at −40 °C. [g] Reaction at 25 °C.

In terms of the solvent, switching from toluene to CH_2Cl_2, Et_2O, or CH_3CN caused a drastic decrease in the yields (entries 5−7). The negative effect of Et_2O or CH_3CN is attributable to the coordination of the solvent molecules. In the case of CH_2Cl_2, the low catalytic activity is most likely due to the abstraction of a chloride by the cationic silicon center.[12] As a note, the solvent-free reaction attained complete conversion (98% yield) at 25 °C in 1 h (entry 8).

To explore the range of the reaction, the Mukaiyama aldol reaction in the presence of **2a** was carried out using other substrates (Table 2). Enol silyl ether **4a** reacted with both acyclic (**3b**) and cyclic (**3c**) aliphatic ketones at −78 °C to afford the corresponding products quantitatively (entries 1 and 2). Benzaldehyde (**3d**) afforded aldol product **5da** in 96% yield without any trace of byproducts (entry 3). α-Monosubstituted enol silyl ether **4b** was converted to addition product **5ab** in 94% yield in 8 h with 72% *threo*-selectivity (entry 4). The reaction of ketene silyl acetal **4c** afforded hydroxy ester **5ac** with consecutive, quarternary carbons in 95% yield (entry 5).

Next, the catalytic performance of **2a** for Diels−Alder reactions was evaluated. Results for the reaction of 1,3-cyclohexadiene and methyl acrylate in the presence of various silicon-based catalysts (toluene, 0 °C, 1 h) are summarized in Table 3. As shown in entry 1, Me_3SiOTf (10 mol %) did not exhibit any catalytic activity. The presence of **1a** (1 mol %) or **1b** (1 mol %) did afford cycloadduct **6a**, but in yields of merely 13% (entry 2) and 6% (entry 3), respectively. Using **2a** (1 mol %) as a precatalyst, however, almost complete conversion of 97% (entry 4) was observed. Similarly as above, the presence of a proton scavenger did not affect the yield (entry 5).

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(6) Hatanaka, Y.; Tanaka, M. *Abstracts of Papers, 81st Spring Meeting of the Chemical Society of Japan, Tokyo*; Chemical Society of Japan: Tokyo, 2001; 2G608.

(7) Olah and other researchers have pointed out that **2a** is not a coordinated "silyl cation" but silylated toluenium. See: Olah, G. A.; Rasul, G.; Purkash, G. K. S. *J. Am. Chem. Soc.* **1999**, *121*, 9615 and references therein.

(8) Lambert, J. B.; Zhao, Y.; Wu, H. *J. Org. Chem.* **1999**, *64*, 2729.

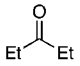
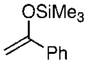
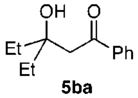
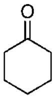
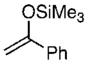
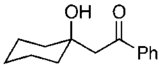
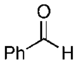
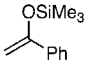
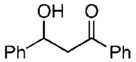
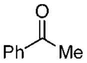
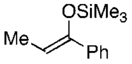
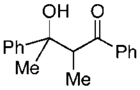
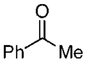
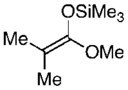
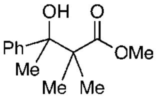
(9) Scott, V. J.; Çelenligil-Çetin, R.; Ozerov, O. V. *J. Am. Chem. Soc.* **2005**, *127*, 2852.

(10) Yanagisawa, M.; Shimamura, T.; Iida, D.; Matsuo, J.; Mukaiyama, T. *Chem. Pharm. Bull.* **2000**, *48*, 1838.

(11) For selected papers on catalytic Mukaiyama aldol reactions with ketones, see: (a) Hollis, T. K.; Robinson, N. P.; Bosnich, B. *Tetrahedron Lett.* **1992**, *33*, 6423. (b) Ohki, H.; Wada, M.; Akiba, K. *Tetrahedron Lett.* **1988**, *29*, 4719. (c) Marx, A.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 178. (d) Oishi, M.; Aratake, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1998**, *120*, 8271.

(12) Kira, M.; Hino, T.; Sakurai, H. *J. Am. Chem. Soc.* **1992**, *114*, 6697.

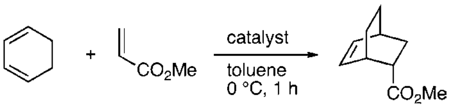
Table 2. Mukaiyama Aldol Reaction Catalyzed by $[Et_3Si(toluene)]B(C_6F_5)_4$ (**2a**)[a]

entry	ketone or aldehyde	enol silyl ether	product	yield (%)[b]
1	 **3b**	 **4a**	 **5ba**	97
2	 **3c**	 **4a**	 **5ca**	99
3	 **3d**	 **4a**	 **5da**	96
4[c]	 **3a**	 (E/Z = 96/4) **4b**	 **5ab**	94[d]
5	 **3a**	 **4c**	 **5ac**	95

[a] Reaction conditions: **3** (0.50 mmol), **4** (1.1 equiv), **2a** (1.0 mol %), toluene (1.5 mL), −78 °C, 1 h. [b] Isolated yield. [c] Reaction for 8 h. [d] Diastereoselectivity of the product **5ab** was 72:28 (*threo*:*erythro*).

Results of Diels−Alder reaction catalyzed by **2a** using combinations of other substrates are summarized in Table 4. Methyl crotonate reacted with 1,3-cyclohexadiene at 25 °C to afford adduct **6b** in 93% yield in 13 h with 98% *endo*-selectivity (entry 1). It should be noted that the methyl crotonate is a dienophile of poor reactivity and that the catalytic reaction of this particular substrate with simple diene is rare.[13] Both methyl vinyl ketone and crotonaldehyde reacted with 1,3-cyclohexadiene to afford cycloadducts **6c** and **6d** almost quantitatively without any trace of byproducts (entries 2 and 3, respectively). The reaction of 2,3-dimethyl-1,3-butadiene with methyl acrylate gave addition product **6e** in a high yield (entry 4).

Table 3. Diels−Alder Reaction Catalyzed by Silicon Lewis Acids[a]

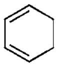
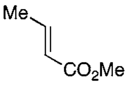
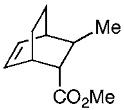
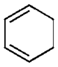
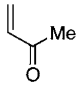
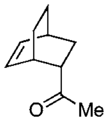
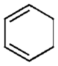
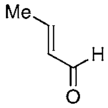
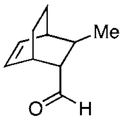
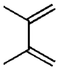
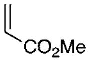
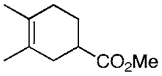


6a

entry	catalyst	mol %	yield (%)[b]
1	Me_3SiOTf	10	0
2	Me_3SiNTf_2 (**1a**)	1.0	6
3	Et_3SiNTf_2 (**1b**)	1.0	13
4	$[Et_3Si(toluene)]B(C_6F_5)_4$(**2a**)	1.0	97
5[c]	$[Et_3Si(toluene)]B(C_6F_5)_4$(**2a**)	1.0	97

[a] Reaction conditions: methyl acrylate (0.50 mmol), 1,3-cyclohexadiene (2.0 equiv), silicon catalyst (10 or 1.0 mol %), toluene (1.5 mL), 0 °C, 1 h. [b] Yields were determined by NMR analysis of the crude product using CH_2Br_2 as an internal standard. [c] 2,6-Di-*tert*-butylpyridine (2.0 mol %) was added.

Table 4. Diels−Alder Reaction Catalyzed by Silyl Borate **2a**[a]

entry	diene	dienophile	temp time	product	yield (%)[b]
1			25 °C 13 h	 **6b**	93[c]
2			0 °C 1 h	 **6c**	98[c]
3			0 °C 1 h	 **6d**	95[d]
4[e]			25 °C 13 h	 **6e**	91

[a] Reaction conditions: dienophile (0.50 mmol), diene (2.0 equiv), **2a** (1.0 mol %), toluene (1.5 mL), 0 °C, 1 h. [b] Isolated yield. [c] *endo*:*exo* = 98:2. [d] *endo*:*exo* = 99:1. [e] The diene containing 100 ppm (w/w) of 2,6-di-*tert*-butyl-4-methylphenol was used to inhibit the polymerization of the dienes.

In summary, the high catalytic activity of $[Et_3Si(toluene)]B(C_6F_5)_4$ (**2a**), in comparison to those of Me_3SiOTf and Et_3SiNTf_2 (**1b**), was clearly demonstrated in Mukaiyama aldol and Diels−Alder reactions. Studies to explore the scope of the strongly cationic silyl borate catalyst are currently underway in our laboratory.

Supporting Information Available: Experimaental procedures and characterization data for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) Reported catalytic Diels−Alder reactions of methyl crotonate with simple diene were conducted with higher catalyst loading (10 mol %). For details, see ref 2c,d and Ishihara, K.; Kobayashi, J.; Inagawa, K.; Yamamoto, H. *Synlett* **2001**, 394.