(2,7-Dimethyl-1,8-biphenylenedioxy)bis(dimethylaluminum) as a Bidentate Lewis Acid: Its Reactivity and Selectivity in Organic Synthesis

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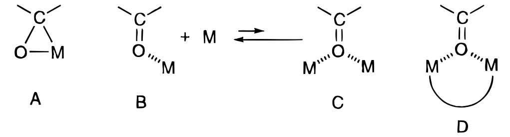
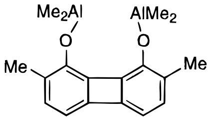
Electrophilic activation of carbonyl groups with certain Lewis acids is a well-established method for enhancing their reactivity and selectivity toward nucleophilic addition.[1] The two principal modes of coordination of carbonyls to metals are the π-bonding (**A**) and σ-bonding (**B**).[2] The latter mode is generally preferred with main group Lewis acids. In addition, simultaneous coordination to carbonyl groups with two metals of type **C** would alter the reactivity and selectivity of the carbonyl substrates.[3,4] Examples of such double coordination with two main group metals are rare despite its potential importance,[5,6] simply because of the high preference for a single-coordination mode (**B**) even in the presence of excess Lewis acids, and hence the nature of such di-σ-bonding (**C**) remains an elusive phenomenon.[7,8] In this context, we have been interested in the possibility of designing a bidentate Lewis acid that is capable of preferable di-σ-bonding (**D**) with two main group metals. Among various main group elements, organoaluminums seem to be the reagent of choice in view of their high affinity toward an oxygen atom.[9] Here we wish to disclose our initial results on this study using the modified bis(organoaluminum) reagent **1** for the efficient simultaneous coordination toward carbonyls, thereby elucidating the characteristics of the double electrophilic activation of carbonyl substrates.





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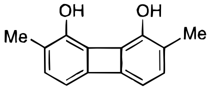

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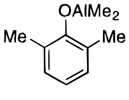

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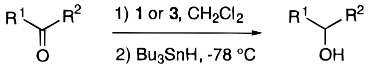
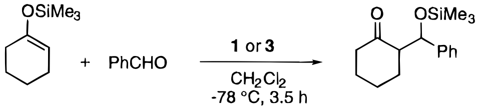
The requisite bidentate ligand 2,7-dimethyl-1,8-biphenylenediol (**2**) was synthesized according to the literature procedure,[10] and the bidentate organoaluminum reagent (2,7-dimethyl-1,8-biphenylenedioxy)bis(dimethylaluminum) (**1**) was prepared by treatment of the biphenylenediol **2** with Me$_3$Al (2 equiv) in CH$_2$Cl$_2$ at room temperature for 30 min. Initial complexation of 5-nonanone with the *in situ*-generated **1** (1.1 equiv) in CH$_2$Cl$_2$ and subsequent reaction of Bu$_3$SnH (1.2 equiv) at −78 °C for 20 min gave rise to the corresponding 5-nonanol in 86% yield. In marked contrast, however, reduction of 5-nonanone with Bu$_3$SnH in the presence of monodentate organoaluminum reagent **3** (prepared from 2,6-xylenol and Me$_3$Al (1:1 molar ratio)) under similar reaction conditions afforded 5-nonanol in only 6% yield. These results clearly demonstrate that the bidentate Lewis acid **1** strongly enhances the reactivity of ketone carbonyl toward hydride transfer via the double electrophilic activation of carbonyl moiety. It should be noted that reduction of excess 5-nonanone (2 equiv) with bidentate **1** (1.1 equiv)/Bu$_3$SnH (2.4 equiv) in CH$_2$Cl$_2$ at −78 °C for 20 min lowered the yield of 5-nonanol (47%), suggesting the intervention of the 1:1 ketone/Lewis acid complex even in the presence of excess ketone. Furthermore, use of excess **3** (2 equiv) resulted in formation of 5-nonanol in 10% yield, implying the favorable monocoordination complex **B** with excess Lewis acids.



$R^1 = R^2 = Bu$: 86% with **1** (6% with **3**)
$R^1 = Ph, R^2 = Me$: 91% with **1** (9% with **3**)

A similar tendency is observed in the acetophenone carbonyl reduction. Furthermore, the Mukaiyama aldol reaction of 1-trimethylsiloxy-1-cyclohexene and benzaldehyde was effected by the bidentate **1**, giving the aldol products (*erythro/threo* = 1:3) in 87% yield, although its monodentate counterpart **3** showed no evidence of reaction under similar conditions.



87% with **1**
~0% with **3**

Although double-coordination behavior of the bidentate **1**/carbonyl complex is consistent with the above experimental findings, more direct evidence was obtained by low-temperature ^{13}C NMR spectroscopy using DMF as a carbonyl substrate. Thus, the 75 MHz ^{13}C NMR measurement of the 1:1 monodentate **3**/DMF complex **E** in CDCl$_3$ at −50 °C showed that the original signals of the DMF carbonyl at δ 162.66 shifted downfield to δ 164.05. In contrast, 1:1 bidentate **1**/DMF chelation complex under similar conditions undergoes a further downfield shift for the DMF carbonyl (δ 165.62), implying the strong electrophilic activation of the DMF carbonyl by the intervention of a double-coordination complex (**F**). Addition of 1 equiv more of DMF to the 1:1 bidentate **1**/DMF complex results in two signals at δ 163.71 and δ 165.63 in a ratio of about 1:1, suggesting an equilibrium between the coordination complex **G** and the double coordination complex **F**.

Another interesting feature of the bidentate Lewis acid **1** in organic synthesis is the regio- and stereocontrolled Michael addition of silyl ketene acetals to α,β-unsaturated ketones as

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(1) For review, see: Shambayati, S.; Schreiber, S. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: New York, 1991; Vol. 1, Chapter 1.10, p 283.

(2) (a) Harman, W. D.; Fairlie, D. P.; Taube, H. *J. Am. Chem. Soc.* **1986**, *108*, 8223. (b) Huang, Y.-H.; Gladysz, J. *J. Chem. Educ.* **1988**, *65*, 298. (c) Klein, D. P.; Dalton, D. M.; Mendez, N. Q.; Arif, A. M.; Gladysz, J. *J. Organomet. Chem.* **1991**, *412*, C7.

(3) (a) Viet, M. T. P.; Shrama, V.; Wuest, J. D. *Inorg. Chem.* **1991**, *30*, 3026. (b) Bachand, B.; Wuest, J. D. *Organometallics* **1991**, *10*, 2015. (c) Beauchamp, A. L.; Olivier, M. J.; Wuest, J. D.; Zacharie, B. *J. Am. Chem. Soc.* **1986**, *108*, 73.

(4) For a theoretical study of formaldehyde/borane (1:2) complex, see: Lepage, T. J.; Wiberg, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 6642.

(5) For the bidentate boron/2,6-dimethylpyranone complex, see: (a) Reilly, M.; Oh, T. *Tetrahedron Lett.* **1995**, *36*, 217. (b) Reilly, M.; Oh, T. *Ibid.* **1995**, *36*, 221. See also: Reilly, M.; Oh, T. *Tetrahedron Lett.* **1994**, *35*, 7209.

(6) For an intramolecular version of a bidentate aluminum Lewis acid, see: Sharma, V.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1992**, *114*, 7931.

(7) For bidentate transition metal/carbonyl complexes, see: (a) Adams, H.; Bailey, N. A.; Gauntlett, J. T.; Winter, M. J. *J. Chem. Soc., Chem. Commun.* **1984**, 1360. (b) Erker, G.; Dorf, U.; Czisch, P.; Petersen, J. L. *Organometallics* **1986**, *5*, 668. (c) Waymouth, R. W.; Potter, K. S.; Schaefer, W. P.; Grubbs, R. H. *Ibid.* **1990**, *9*, 2843. (d) Adams, R. D.; Chen, G.; Chen, L.; Wu, W.; Yin, J. *J. Am. Chem. Soc.* **1991**, *113*, 9406. (e) Simard, M.; Vaugeois, J.; Wuest, J. D. *Ibid.* **1993**, *115*, 370.

(8) Bidentate Brönsted acids: (a) Hine, J.; Linden, S.-M.; Kanagasabapathy, V. M. *J. Org. Chem.* **1985**, *50*, 5096. (b) Hine, J.; Ahn, K. *Ibid.* **1987**, *52*, 2083. (c) Kelly, T. R.; Meghani, P.; Ekkundi, V. S. *Tetrahedron Lett.* **1990**, *31*, 3381.

(9) (a) Mole, T.; Jeffery, E. A.*Organoaluminum Compounds*; Elsevier: Amsterdam, 1972. (b) Maruoka, K.; Yamamoto, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 668.

(10) (a) Hine, J.; Hahn, S.; Miles, D. E.; Ahn, K. *J. Org. Chem.* **1985**, *50*, 5092. (b) Hine, J.; Ahn, K. *Ibid.* **1987**, *52*, 2089.

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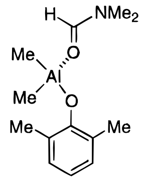

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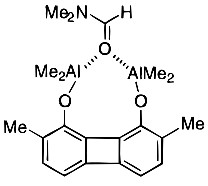

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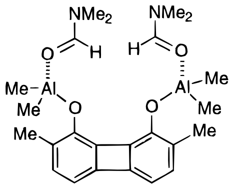
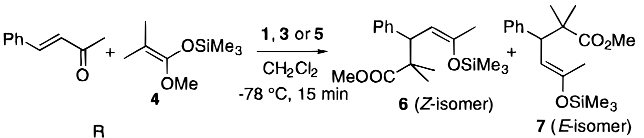
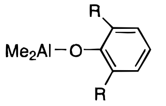


G

acceptors.[11] Reaction of benzalacetone and silyl ketene acetal **4** with dimethylaluminum aryloxides of type **5** gave rise to a mixture of Michael adducts **6** and **7** almost exclusively, where the *Z* selectivity decreased with increase in the steric size of a phenoxy ligand in **5**. Indeed, switching the phenoxy group to 2,6-xylenoxy, 2,6-diisopropylphenoxy, and 2,6-di-*tert*-butylphenoxy groups, the *Z* selectivity decreased from 80:20 to 70:30, 67:33, and 33:67, respectively. Based on the experimental findings, the stereochemical outcome of the *Z*-isomeric Michael adduct **6** is interpreted for by the preferrable complex (**H**) formation of benzalacetone with sterically less hindered **5a** or **3**. With more hindered **5b** or **5c**, the coordination complex (**J**) is then favored rather than the sterically congested complex (**I**), thereby increasing the formation of *E*-isomeric Michael adduct **7.** In the ultimate case, bidentate **1** can be utilized to obtain *E*-isomeric **7** as a major product via the complex (**K**) formation with *s-trans* conformation.[12]

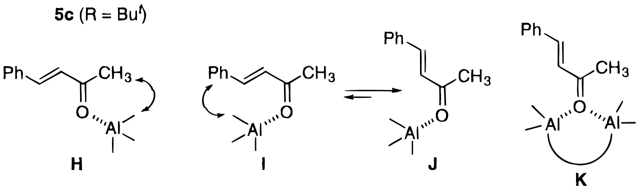


4 **6** (*Z*-isomer) **7** (*E*-isomer)



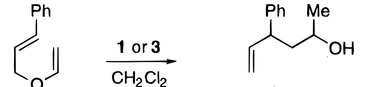
5a (R = H)
5b (R = Pr^i)
5c (R = Bu^t)

Lewis acid	**5a**	**3**	**5b**	**5c**	**1**
Z/*E* ratio	80:20	70:30	67:33	33:67	28:72
% yield	74	80	75	53	73



H **I** **J** **K**

The high double-coordination ability of bidentate Lewis acid **1** is, in principle, applicable to the activation of the ethereal substrates as exemplified by the Lewis acid-promoted Claisen rearrangement of allyl vinyl ethers. Indeed, treatment of *trans*-cinnamyl vinyl ether (**8**) with bidentate **1** in CH_2Cl_2 at 0 °C for 1 h produced the rearrangement−methylation product **9** in 96% yield.[13] With monodentate Lewis acid **3**, however, the reaction is very sluggish, resulting in almost total recovery of the starting material under the comparable reaction conditions.



8 **9**

96% with **1**
~0% with **3**

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[11] (a) Heathcock, C. H.; Norman, M. H.; Uehling, D. E. *J. Am. Chem. Soc.* **1985**, *107*, 2797. (b) Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1986**, 221. (c) Mukaiyama, T.; Tamura, M.; Kobayashi, S. *Ibid.* **1986**, 1017. (d) Kobayashi, S.; Mukaiyama, T. *Ibid.* **1985**, 1805. (e) Heathcock, C. H.; Uehling, D. E. *J. Org. Chem.* **1986**, *51*, 280. (f) Mukaiyama, T.; Hara, R. *Chem. Lett.* **1989**, 1171. (g) Oare, D. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 157. (h) Sato, T.; Wakahara, Y.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1990**, *31*, 1581. (i) Lohray, B. B.; Zimbiniski, R. *Ibid.* **1990**, *31*, 7273. (j) Grieco, P. A.; Cooke, R. J.; Henry, K. J.; VanderRoest, J. M. *Ibid.* **1991**, *32*, 4665. (k) Fukuzumi, S.; Fujita, M.; Otera, J.; Fujita, Y. *J. Am. Chem. Soc.* **1992**, *114*, 10271. (l) Ranu, B. C.; Saha, M.; Bhar, S. *Tetrahedron Lett.* **1993**, *34*, 1989.

[12] The *E*-isomer **7** is a thermodynamically less stable product, and standing of **7** resulted in gradual conversion to a thermodynamically more stable *Z*-isomer **6**.

[13] (a) Takai, K.; Mori, I.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 3985. (b) Takai, K.; Mori, I.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 446. See also: Maruoka, K.; Nonoshita, K.; Banno, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 7922. Maruoka, K.; Saito, S.; Yamamoto, H. *Ibid.* **1995**, *117*, 1165.