Enhancement of Lewis Acidity by Ligand-Defined Metal Geometry: A Catalytic Allylation of Aldehydes with Allyltrimethylsilane

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Dedicated to Professor Dieter Seebach on the occasion of his retirement.

Abstract: A highly Lewis acidic aluminum complex was produced using a tridentate ligand 1. The enhanced Lewis acidity of 1–Al was attributed to the combination of a stereoelectronic effect and an electrostatic effect. Comparison with an unstrained complex 4–Al indicated that the ligand-defined sp³ geometry of the aluminum in 1–Al led to the lower LUMO level and the larger LUMO coefficient on the aluminum. 1–Al promotes a catalytic allylation of aromatic aldehydes using allyltrimethylsilane. A catalytic amount of excess ligand added to the aluminum was important for high chemical yield. The excess ligand might act as a proton source to facilitate ligand exchange on the highly Lewis acidic aluminum.

Key words: Lewis acid, metal, ligand, allylation, aluminum

Lewis acid catalysis is one of the most important and powerful concepts in synthetic organic chemistry.1 Lewis acids catalyze a broad range of important reactions such as the Mukaiyama aldol reaction, Diels–Alder reactions, and the Sakurai reaction. The current focus in this field is to further broaden the scope of Lewis acid-catalyzed reactions to less reactive (thus, more stable) substrates with the aim of further broadening the scope of Lewis acid-catalyzed reactions to less reactive (thus, more stable) substrates with the aim of Lewis acidity enhancement.4 We are interested in this approach because a rational ligand design could produce a highly active Lewis acid complex that might be extended to an enantioselective catalyst. Herein we describe our preliminary results of enhanced Lewis acidity of an aluminum complex by controlling the geometry using a tridentate ligand 1 (Figure 1).

The basic ideas behind the design of ligand 1 were as follows. (1) Upon complex formation with a trivalent metal (elements from group 3 or 13), the ligand would geometrically induce an sp³ hybridization (i.e., tetrahedral geometry) of the metal, thus preorganizing vacant orbital orientation (a stereoelectronic effect). (2) The strongly electron-withdrawing trifluoromethanesulfonyl group would increase the positive charge on the metal (an electrostatic effect). Ligand 1 was easily synthesized from commercially available triol 3 through trifluoromethanesulfonylation of the known triamine 5 (Tf₂O, Et₃N, CH₂Cl₂, −40–0 °C, 50% yield). Similarly, tosyl amide ligand 2 was synthesized through tosylation (TsCl, Et₃N, CH₂Cl₂, 4 °C, 92% yield).6 We targeted a catalytic allylation of aldehydes with allyltrimethylsilane (the Sakurai reaction) because a catalytic amount of conventional Lewis acids cannot promote this reaction. Using 1 as a ligand, Lewis acid metals were first screened for allylation of benzaldehyde 5a. The aluminum complex prepared from Me₃Al and 1 in a 1:1 ratio (1–Al: 10 mol%) promoted the reaction smoothly at room temperature in dichloromethane and the desired product 6a was obtained in 59% yield, together with byproduct 7a in 5% yield (Scheme 1). Complexes with other metals [B(OMe)₃, Ga(i-PrO)₃, In(i-PrO)₃, La(i-PrO)₃, Ti(i-PrO)₃, and Zr(i-BuO)₃] did not give any product even after a prolonged reaction time. Aluminum complexes containing less electron-withdrawing ligands (2 and 3) than 1 did not promote the reaction at all. More importantly, no reaction proceeded with a catalyst prepared from Me₃Al and 4 in a 1:3 ratio (4–Al). This sharp contrast in catalyst activity between 1–Al and 4–Al must be due to the ligand-defined geometry of the aluminum, as these complexes should contain a similar positive charge on the aluminum. Molecular modeling studies support this as they show that the aluminum geometry is completely different in these two complexes (Figure 2). The most stable conformation of 1–Al contains a pyramidal sp³ hybridized aluminum with a large LUMO, predominantly on the aluminum.
However, 4–Al contains a planar sp$^2$ hybridized aluminum. In this case, although the largest LUMO coefficient exists in the p-orbital of the aluminum, the LUMO coefficient was reduced due to a partial orbital diffusion to another part of the molecule. Therefore, in the case of 1–Al, the ligand-defined geometry of the aluminum should produce a lower LUMO level (sp$^3$ vs. p-orbital) and a larger LUMO coefficient than 4–Al (Figure 2). This stereoelectronic effect is the key for enhancement of the Lewis acidity and the catalyst activity in the case of 1–Al.

Scheme 1

![Scheme 1](image1)

Figure 2  LUMO of Al-complexes in the most stable conformations.

Once preliminary experimental support for the concept was obtained, we began optimization of the reaction conditions using 1–Al as catalyst. The major byproduct 7a was produced through a benzylic cation formation from the initial product, by the Lewis acid, and subsequent allylation. To prevent this over-reaction, we performed the reaction at a lower temperature. Thus, the yield of 6a was improved to 73% at 4 °C with very little formation of 7a. The yield was further improved to 81% when the amount of catalyst was reduced to 5 mol%. Solvents other than dichloromethane gave less satisfactory results. During the optimization, the reaction was sometimes unpredictable and in some cases the chemical yield decreased to ca. 50%. Careful investigation revealed that the ligand/Al ratio was very important for a clean conversion (Figure 3). When the ligand/Al ratio was less than 1, many byproducts were produced and the desired 6a was obtained in only ca. 50% yield. The yield increased as the ligand/Al ratio increased and up to an 84% yield was obtained when ligand/Al = 1:1.1.

Table 1  Catalytic Allylation of aldehydes Using Allyltrimethylsilane

<table>
<thead>
<tr>
<th>Entry</th>
<th>R (aldehyde)</th>
<th>Cat. (X mol%)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C$_7$H$_5$</td>
<td>5a</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>4-O$_2$NCC$_6$H$_4$</td>
<td>5b</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>4-BrC$_6$H$_4$</td>
<td>5c</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>5d</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>5e</td>
<td>10</td>
<td>4</td>
</tr>
</tbody>
</table>

In summary, we developed aluminum complex 1–Al with an enhanced Lewis acidity. The higher activity of 1–Al was due to the combination of a stereoelectronic effect and an electrostatic effect enhanced by the ligand-defined geometry of the aluminum. 1–Al can promote catalytic alkylation of aromatic aldehydes using allyltrimethylsilane. Further efforts to extend the scope of this type of catalyst.
and to develop an asymmetric catalyst based on this concept are currently ongoing.

Typical Procedure (Table 1, Entry 1)
A hexane solution of Me₃Al (49 µL, 0.055 mmol) was added to a suspension of I (28 mg, 0.055 mmol) in CH₂Cl₂ at r.t. and the resulting solution was stirred for 1 h. After the solution was cooled to –20 °C, 5a (102 µL, 1 mmol) and allyltrimethylsilane (238 µL, 1.5 mmol) were added and the reaction temperature was maintained at –20 °C for 30 min. The reaction temperature was gradually raised to 4 °C and after 4 h, 2 M HCl aq in MeOH (1:1) was added for desilylation.

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References


Selected spectral data of ligand 1

1H NMR (CDCl₃, 500 MHz): δ = 1.05 (s, 3 H), 3.17 (d, J = 7.0 Hz, 6 H), 5.61 (t, J = 7.0 Hz, 3 H)

13C NMR (DMSO-d₆, 126 MHz): δ = 15.89, 38.4, 46.32, 118.5 (q, J = 33 Hz)

19F NMR [CDCl₃, 470 MHz, CF₃CO₂H used as the external standard (± 0 ppm)]; δ = −76.9.


(6) (a) pKa values in DMSO–CF₃SO₂NH₂ (9.7), PhSO₂NH₂ (16.1), CH₂OH (29.0) (b) Bordwell, F. G. Acc. Chem. Res. 1988, 21, 456.

(7) These calculations were performed using the UNIVERSAL forcefield (v. 1.02) performed on Cerius 2 4.0 (Molecular Simulations Inc.): (a) Rappé, A. K.; Casewit, C. J.; Colwell, K. S.; Goddard, W. A. III; Skiff, W. M. J. Am. Chem. Soc. 1992, 114, 10024. (b) Casewit, C. J.; Colwell, K. S.; Rappé, A. K. J. Am. Chem. Soc. 1992, 114, 10035. (c) Casewit, C. J.; Colwell, K. S.; Rappé, A. K. J. Am. Chem. Soc. 1992, 114, 10046; An N-methyl analog, instead of 4, was used in these calculations for simplification.

(8) The chemical yield decreased when catalyst loading of less than 5 mol% was used, <50% with 2 mol% and no reaction with 1 mol%.

(9) Trifluorotoluene (CF₃C₆H₅), toluene, and acetonitrile gave the product in 10%, 50%, and 0% yield, respectively.

(10) Unfortunately, the desired allylation did not proceed from pivalaldehyde and secondary alkyl substituted aldehydes. No reaction occurred from aliphatic aldehydes or α, β-unsaturated aldehydes. Cyclic trioxanes were the major products from primary and secondary alkyl substituted aldehydes. No reaction occurred from pivalaldehyde and α, β-unsaturated aldehydes.


(12) Side-reaction pathways mediated by a reagent-derived Lewis acid silicon are problematic, especially in the case of catalytic enantioselective reactions: Carreira, E. M. In Comprehensive Asymmetric Catalysis, Vol. 3; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Heidelberg, 1999, Chap. 29; the possibility that the Lewis acidic silicon of 8 is the actual catalyst in the present case is unlikely due to the fact that the control catalyst 4–Al did not promote the reaction.