A Novel Classification of Lewis Acids on the Basis of Activity and Selectivity

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Abstract: Group 3–15 metal chlorides (Lewis acids) were classified on the basis of activity and aldehyde- and aldimine-selectivity in an addition reaction of a silyl enol ether. Based on the experimental results, metal chlorides (Lewis acids) were classified as follows: A, active; B, weak; C, inactive for the activation of the aldehyde and/or aldimines. Groups A and B were further divided into A-1 or B-1 (aldehyde-selective), A-2 or B-2 (aldimine-selective), and A-3 or B-3 (neutral). The final classification is as follows: A-1, BCl_3, $AlCl_3$, $TiCl_4$, $GaCl_3$, $ZrCl_4$, $SnCl_4$, $SbCl_5$, $SbCl_3$, $HfCl_4$, $ReCl_5$; A-2, $ScCl_3$, $FeCl_3$, $InCl_3$, $BiCl_3$; A-3, $NbCl_5$, $MoCl_3$, $MoCl_5$, $SnCl_2$, $TaCl_5$, WCl_5, WCl_6, $ReCl_3$, $TlCl_3$; B-1, none; B-2, $SiCl_4$, $FeCl_2$, $CoCl_2$, CuCl, $CuCl_2$, $GeCl_4$, YCl_3, $OsCl_3$, $PtCl_2$; B-3, $ZnCl_2$, $RuCl_3$; C, VCl_3, $CrCl_3$, $MnCl_2$, $NiCl_2$, $RhCl_3$, $PdCl_2$, AgCl, $CdCl_2$, $IrCl_3$, AuCl, $HgCl_2$, HgCl, $PbCl_2$. This classification has revealed several new fundamental aspects of elements (metal chlorides) as Lewis acids.

Keywords: acidity · Lewis acids · periodic table

Introduction

Lewis acid catalyzed reactions are now of great interest because of their unique reactivity and selectivity, and the mild conditions used.[1] While various types of Lewis acids have been employed in many reactions, they have been chosen after experimental trial and error. This is because the character of Lewis acids is just roughly understood on the basis of the periodic table, etc. Evidently, fundamental understanding and classifications of Lewis acids derived not only from organic chemistry but also from inorganic and general chemistry are expected to give a solution to this problem; however, only limited examples have been reported in the literature. For example, Pearson classified a number of Lewis acids into two classes, "hard" and "soft."[2] It was also reported that Lewis acidic activities followed the order $BCl_3 > AlCl_3 > TiCl_4 > BF_3 > SnCl_4 > ZnCl_2$ in the acylation of olefins.[3] On the other hand, Olah et al. classified Lewis acids in the Friedel–Crafts alkylation reaction into four categories: very active; moderately active; weak; very weak or inactive.[4] Furthermore, several attempts to scale the strength of Lewis acidity based on nuclear magnetic resonance (NMR) data[5] or theoretical background[6] were reported. However, these efforts did not go far enough because various types of Lewis acids including rare earth and late transition elements are now used in modern chemistry,[1, 7] while only traditional Lewis acids were investigated previously except for the Olah's study. In addition, recent research efforts have revealed that use of strong Lewis acids does not necessarily promote reactions smoothly,[8] and that selectivities, one of the most important issues in modern organic synthesis, are strongly dependent on the Lewis acids used.[9] We now report here a novel classification of Lewis acids based on the activity and selectivity in an addition reaction of a silyl enolate to an aldehyde and an aldimine.

Results and Discussion

As the model for our studies we chose the reaction of benzaldehyde, *N*-benzylideneaniline, and the silyl enol ether derived from propiophenone.[10, 11] The precise experimental conditions are as follows:[12] In the presence of one equivalent of a metal chloride, benzaldehyde (1 equiv) and *N*-benzylideneaniline (1 equiv) were combined in dichloromethane at $-23\,^{\circ}C$. After the mixture had been stirred for 10 min at the same temperature, the silyl enol ether derived from propiophenone (1 equiv) was added. The mixture was stirred for 12 h, and saturated aqueous sodium hydrogen carbonate was added to quench the reaction. After usual workup, the crude products were separated by using preparative TLC to determine the yield and the ratio of the aldehyde adduct and the aldimine–adduct. We screened Group 3–15 metal chlorides, and the results are summarized in Table 1.[13]

Based on the results in Table 1, metal chlorides (Lewis acids) were classified as follows: A, active; B or C, weak or

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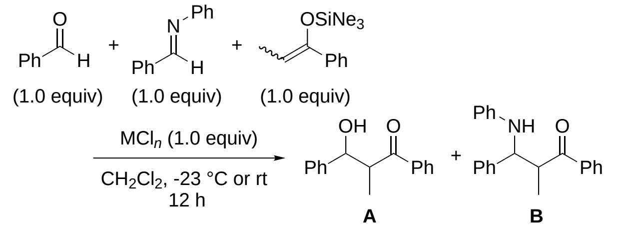
Table 1. Effect of Lewis acids.[a]



Entry	MCl_n	Group	T [°C]	Yield [%]	**A/B**
1	$\mathrm{ScCl_3}$	3	−23	68	3/97
2	$\mathrm{YCl_3}$	3	−23	12	> 1/> 99
3[b,c]	$\mathrm{YbCl_3}$	3	rt	28	> 1/> 99
4	$\mathrm{TiCl_4}$	4	−23	96	96/4
5	$\mathrm{ZrCl_4}$	4	−23	75	95/5
6	$\mathrm{HfCl_4}$	4	−23	47	79/21
7	$\mathrm{NbCl_5}$	5	−23	85	72/28
8	$\mathrm{TaCl_5}$	5	−23	75	64/36
9	$\mathrm{MoCl_3}$	6	−23	70	43/57
10	$\mathrm{MoCl_5}$	6	−23	64	59/41
11	$\mathrm{WCl_5}$	6	−23	72	50/50
12	$\mathrm{WCl_6}$	6	−23	69	43/57
13	$\mathrm{ReCl_3}$	7	−23	60	42/58
14	$\mathrm{ReCl_5}$	7	−23	63	79/21
15	$\mathrm{FeCl_3}$	8	−23	quant	30/70
16	$\mathrm{FeCl_2}$	8	−23	22	16/84
17[b]	$\mathrm{RuCl_3}$	8	rt	36	44/56
18[b]	$\mathrm{OsCl_3}$	8	rt	34	28/72
19[b]	$\mathrm{CoCl_2}$	9	rt	36	9/91
20[b]	$\mathrm{PtCl_2}$	10	rt	64	11/89
21[b]	CuCl	11	rt	37	5/95
22[b]	$\mathrm{CuCl_2}$	11	rt	60	9/91
23	$\mathrm{ZnCl_2}$	11	−23	23	49/51
24	$\mathrm{BCl_3}$	13	−23	67	93/7
25	$\mathrm{AlCl_3}$	13	−23	92	88/12
26	$\mathrm{GaCl_3}$	13	−23	91	93/7
27	$\mathrm{InCl_3}$	13	−23	92	17/83
28	$\mathrm{TlCl_3}$	13	−23	84	39/61
29	$\mathrm{SiCl_4}$	14	−23	8	25/75
30	$\mathrm{GeCl_4}$	14	−23	27	17/83
31	$\mathrm{SnCl_4}$	14	−23	77	89/11
32	$\mathrm{SnCl_2}$	14	−23	66	52/48
33	$\mathrm{SbCl_5}$	15	−23	53	76/24
34	$\mathrm{SbCl_3}$	15	−23	47	77/23
35	$\mathrm{BiCl_3}$	15	−23	53	24/76

[a] The reaction proceeded sluggishly even at room temperature (rt) when $\mathrm{VCl_3}$, $\mathrm{CrCl_3}$, $\mathrm{MnCl_2}$, $\mathrm{RhCl_3}$ $\mathrm{IrCl_3}$, $\mathrm{NiCl_2}$, AgCl, AuCl, $\mathrm{CdCl_2}$, HgCl, $\mathrm{PbCl_2}$, or $\mathrm{PCl_5}$ was used. [b] The reaction proceeded sluggishly at −23 °C. [c] $\mathrm{YbCl_3}$ was used as a representative of $\mathrm{LnCl_3}$.

inactive for the activation of the aldehyde and/or aldimines. Group A was further divided into A-1 (aldehyde-selective), A-2 (aldimine-selective), and A-3 (neutral). For some metal chlorides classified into Group B or C, the model reactions were performed again at room temperature (the results are also summarized in Table 1). Based on these results, group B (weak) and group C (inactive) were separated. Group B was divided into B-1 (aldehyde-selective, actually none), B-2 (aldimine-selective), and B-3 (neutral). The final classification is shown in Table 2 and Table 3 (the criteria are shown in legend a of Table 2).

Interestingly, all the Group 4 metal (Ti, Zr, Hf) chlorides are active and give the aldehyde – adduct selectively, while the Group 3 metal, rare-earth chlorides ($\mathrm{ScCl_3}$, $\mathrm{YCl_3}$, $\mathrm{YbCl_3}$) show different activities and selectivities. For the Groups 5 – 7 a similar tendency is observed; that is the first transition series (V, Cr, Mn) are classified into Group C (inactive), and the second and third transition series are active and display no selectivity, except for $\mathrm{NbCl_5}$ and $\mathrm{ReCl_5}$ which are active and give the aldehyde – adduct selectively.[14] As for the late transition metal chlorides, most are weak or inactive, but $\mathrm{FeCl_3}$ is active and gives the aldimine – adduct selectively. On the other hand, in the Group 13 metal chlorides, all are active. For selectivities, the first three (B, Al, Ga) give the aldehyde – selective adducts, while In gives the aldimine – adduct selectively and Tl is neutral. A similar switch is observed between Sb and Bi. In the case of Group 14, $\mathrm{SiCl_4}$ and $\mathrm{GeCl_4}$ give the aldimine – adduct selectively, while $\mathrm{SnCl_4}$ gives the aldehyde – adduct selectively. As for the late transition metal chlorides, most are weak or inactive, but $\mathrm{FeCl_3}$ is active and gives the aldimine – adduct selectively. Notably, most metal chlorides divided into Group B give the aldimine – adduct selectively. In the cases of $\mathrm{NbCl_5}$, $\mathrm{MoCl_3}$, $\mathrm{MoCl_5}$, $\mathrm{SnCl_2}$, $\mathrm{TaCl_5}$, $\mathrm{WCl_5}$, $\mathrm{WCl_6}$, $\mathrm{ReCl_3}$, and $\mathrm{TlCl_3}$, the yields were greater than 40 % and the aldehyde/aldimine selectivities were less than 2/1, and they were classified into A-3 (active, neutral). Similarly, $\mathrm{ZnCl_2}$ and $\mathrm{RuCl_3}$ were classified into B-3 (weak, neutral). For low/high-valent elements, the same activities and selectivities are observed in cases of Fe, Cu, Mo, Sb, and W, while different selectivities are observed in the cases of Sn and Re. Notably, in the latter two cases, high-valent metal chlorides which have higher Lewis acidity give the aldehyde – adduct selectively.

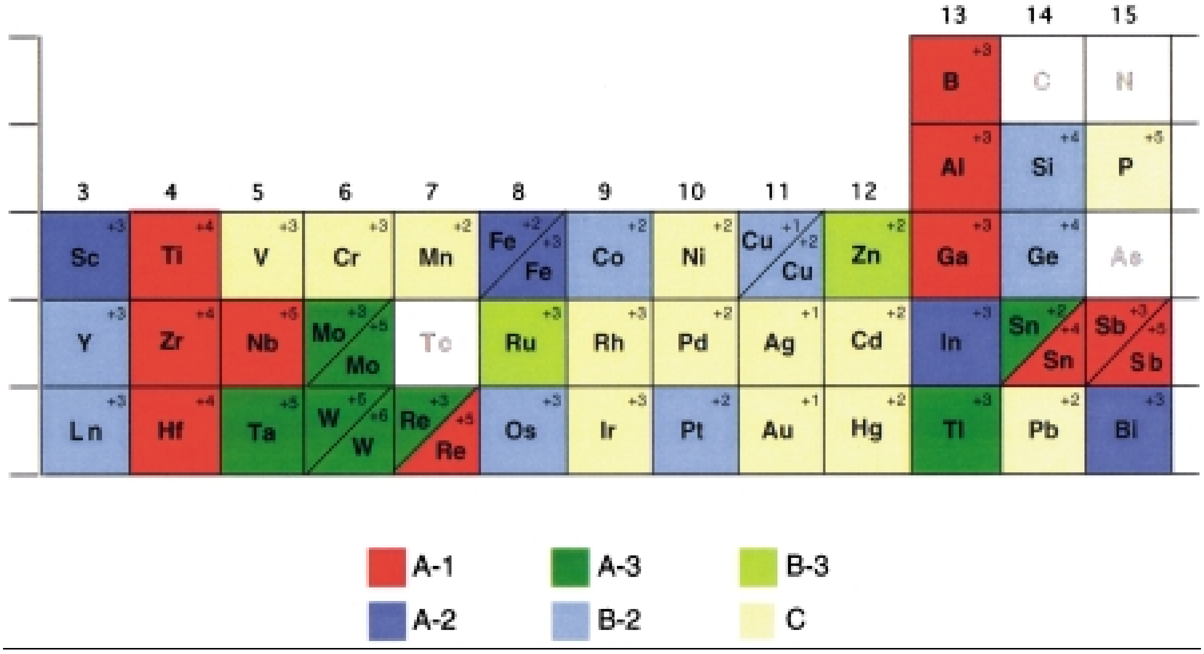
The reaction courses of the aldehyde-selective or aldimine-selective reactions are explained on the basis of Scheme 1.[15] Metal chlorides (Lewis acids) coordinate an aldehyde and/or aldimine under equilibrium conditions. Neither the aldehyde nor the aldimine reacts with a silyl enol ether at all without the coordination of the metal chlorides. On the other hand, if the aldehyde and/or the aldimine are coordinated by metal

Table 2. Classification of Lewis acids.[a]

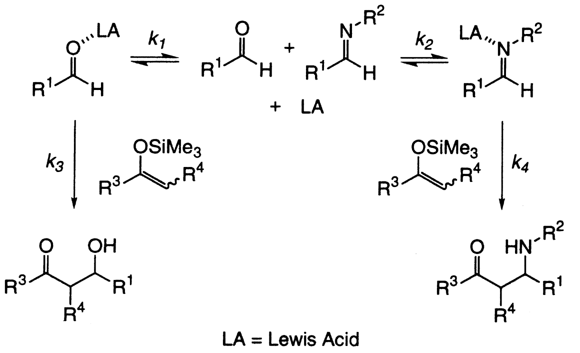
Group A (active)	
A-1 (aldehyde-selective	$\mathbf{BCl_3}$, $\mathrm{ACl_3}$, $\mathbf{TiCl_4}$, $\mathbf{GaCl_3}$, $\mathbf{ZrCl_4}$, $\mathrm{NbCl_5}$, $\mathrm{SnCl_4}$, $\mathrm{SbCl_5}$, $\mathrm{SbCl_3}$, $\mathrm{HfCl_4}$, $\mathrm{ReCl_5}$
A-2 (aldimine-selective)	$\mathbf{ScCl_3}$, $\mathrm{FeCl_3}$, $\mathrm{InCl_3}$, $\mathrm{BiCl_3}$
A-3 (neutral)	$\mathrm{MoCl_5}$, $\mathrm{MoCl_3}$, $\mathrm{SnCl_3}$, $\mathrm{TaCl_5}$, $\mathrm{WCl_6}$, $\mathrm{WCl_5}$, $\mathrm{ReCl_3}$, $\mathrm{TiCl_3}$
Group B (weak)	
B-1 (aldehyde-selective)	none
B-2 (aldimine-selective)	$\mathrm{SiCl_4}$, $\mathrm{FeCl_2}$,[b] $\mathbf{CoCl_2}$, $\mathbf{CuCl_2}$, **CuCl**, $\mathrm{GeCl_4}$, $\mathbf{YCl_3}$, $\mathbf{YbCl_3}$, $\mathrm{OsCl_3}$, $\mathrm{PtCl_2}$
B-3 (neutral)	$\mathrm{ZnCl_2}$, $\mathrm{RuCl_3}$
Group C (inactive)	
$\mathrm{PCl_5}$, $\mathrm{VCl_3}$,[b] $\mathrm{CrCl_3}$, $\mathrm{MnCl_2}$, $\mathrm{NiCl_2}$, $\mathrm{RhCl_3}$, $\mathrm{PdCl_2}$, AgCl, $\mathrm{CdCl_2}$, $\mathrm{IrCl_3}$, AuCl, $\mathrm{HgCl_2}$, HgCl, $\mathrm{PbCl_2}$	

[a] Active: Yield = > 40 % (−23 °C, 12 h). Weak or inactive: Yield = < 40 % (−23 °C, 12 h). Aldehyde-selective: **A/B** = > 2/1. Aldimine-selective: **B/A** = > 2/1. Bold: **A/B** = > 9/1 or **B/A** = > 9/1. [b] See ref. [13].

Table 3. Classification of Lewis acids.



3	4	5	6	7	8	9	10	11	12	13	14	15
										B +3	C	N
										Al +3	Si +4	P +5
Sc +3	Ti +4	V +3	Cr +3	Mn +2	Fe +2 / Fe +3	Co +2	Ni +2	Cu +1 / Cu +2	Zn +2	Ga +3	Ge +4	As
Y +3	Zr +4	Nb +5	Mo +3 / Mo +5	Tc	Ru +3	Rh +3	Pd +2	Ag +1	Cd +2	In +3	Sn +2 / Sn +4	Sb +3 / Sb +5
Ln +3	Hf +4	Ta +5	W +5 / W +6	Re +3 / Re +5	Os +3	Ir +3	Pt +2	Au +1	Hg +2	Tl +3	Pb +2	Bi +3



Scheme 1. The reaction courses in the presence of a Lewis acid.

chlorides and sufficiently activated, the silyl enol ether attacks the aldehyde and/or the aldimine to afford the aldehyde–adduct and/or the aldimine–adduct. The yields and the selectivities are dependent on the metal chloride (Lewis acids) used. The selectivities also depend on the counter-anions of Lewis acids and the amounts of Lewis acid. While the aldimine selectivity increases when weakly basic counter-anions (OTf^-, ClO_4^-, etc.) are used,[16] the aldehyde–selectivity increases when using large quantities of Lewis acids (> 1.0 equiv).[15b, 17] While the methods used in this paper to classify metal chlorides (Lewis acids) may seem to be simple, the reaction conditions shown here were selected after several trials.[12] In addition, the classification shown in Tables 2 and 3 will be applied to many other nucleophilic addition reactions of aldehydes and aldimines.[15]

Conclusion

Metal chlorides (Lewis acids) were classified on the basis of activity and aldehyde- and aldimine-selectivity in the addition reaction of a silyl enol ether. As regards the activities, while some results obtained are comparable with other empirical results shown in the literature, some other results, especially on transition metals and the Group 14 and 15 elements, are unexpected. On the other hand, many new findings have been obtained in the aldehyde/aldimine selectivities. It is noted that a classification of Lewis acids has been efficiently performed from two dimensions (activity and selectivity). Moreover, although the method for the classification shown here is based on organic chemistry, it has contributed to general chemistry to reveal basic characteristics of elements (metal chlorides). These results will lead to a better understanding of metal chlorides (Lewis acids) in inorganic chemistry and organometallic chemistry as well as to providing a guide to the choice of the appropriate Lewis acids in many synthetic organic reactions.

Experimental Section

General: NMR spectra were recorded on a JEOL JNM-LA-300 FT-NMR system. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for ^1H NMR, and $CDCl_3$ was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. Preparative thin-layer chromatography was carried out using Wakogel B-5F. Dichloromethane was distilled twice from P_2O_5 and CaH_2, respectively. Benzaldehyde and *N*-benzylideneaniline were purified before use. All metal chlorides (anhydrous, > 98% purity (mostly > 99%)) are comercially available. $ReCl_3$, $OsCl_3$, $RhCl_3$, $PdCl_2$, $PtCl_2$, AuCl, and BCl_3 were purchased from Aldrich. All other metal chlorides were purchased from Soekawa Chemical. All glasswares were dried at 100 °C under reduced pressure to remove water.

Methods: To classify metal chlorides efficiently, we examined several reaction conditions (temperature, solvent, concentration, quantities of aldehyde, aldimine, and metal chloride, etc.), and finally selected the following reaction conditions.

In the first screening, all metal chlorides were tested at −23 °C. Under argon atmosphere, a metal chloride (0.50 mmol), benzaldehyde

(0.50 mmol), and *N*-benzylideneaniline (0.50 mmol) were combined in dichloromethane (1.5 mL) at −23 °C. After the mixture had been stirred for 10 min at the same temperature, the silyl enol ether derived from propiophenone (0.50 mmol) in dichlorometahne (1.5 mL) was added. The mixture was stirred for 12 h, and saturated aqueous sodium hydrogen carbonate (10 mL) was added to quench the reaction. After the organic layer was separated, the aqueous layer was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated. The crude products were separated by using preparative TLC to determine the yield and the ratio of the aldehyde–adduct and the aldimine–adduct. (Both adducts are known,[15] and ^{1}H and ^{13}C NMR spectra were consistent with those reported.)

Decomposition of the silyl enol ether was not observed under strict anhydrous conditions except for the experiments using $SiCl_4$ and PCl_5. In the reactions using $SiCl_4$ and PCl_5, decomposition of the silyl enol ether was observed in TLC before quenching the reactions.

Based on the results obtained in the above experiments, metal chlorides were classified into Group A (active) and Group B or C. For some metal chlorides classified into Group B or C, the same reaction (the reaction of benzaldehyde with *N*-benzylideneaniline) was performed at room temperature. On the basis of all these experiments, metal chlorides were classified into several groups shown in Tables 2 and 3 (see also text).

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[12] Details are shown in Experimental Section.

[13] Decomposition of the silyl enol ether was not observed except for the experiments using $SiCl_4$ and PCl_5. In the cases using $SiCl_4$ and PCl_5, the decomposition was observed in TLC before quenching the reactions.

[14] These elements have several oxidation states and direct comparison of the metal chlorides in the same group could not be performed, because commercial sources of these metal chlorides are limited.

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[16] For example, aldimine-selective reactions with high yields and high selectivities were performed by using $Yb(OTf)_3$ as a catalyst, while $YbCl_3$ was classified into Group B-2 (weak, aldimine-selective).

[17] These selectivities are expected based on Scheme 1. Since weakly basic counteranions stabilize aldimine/Lewis acid complexes, aldimine-selectivities are increased. Similarly, strongly basic counteranions (OAc^-, OPh^-, etc.) increase aldehyde-selectivities. In the presence of large quantities of Lewis acids, both aldehydes and aldimines are activated and aldehyde-selectivities are increased. Similarly, small quantities of Lewis acids increase aldimine-selectivities. These expectations were actually confirmed by experiments.

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