Air- and Water-Tolerant Rare Earth Guanidinium BINOLate Complexes as Practical Precatalysts in Multifunctional Asymmetric Catalysis

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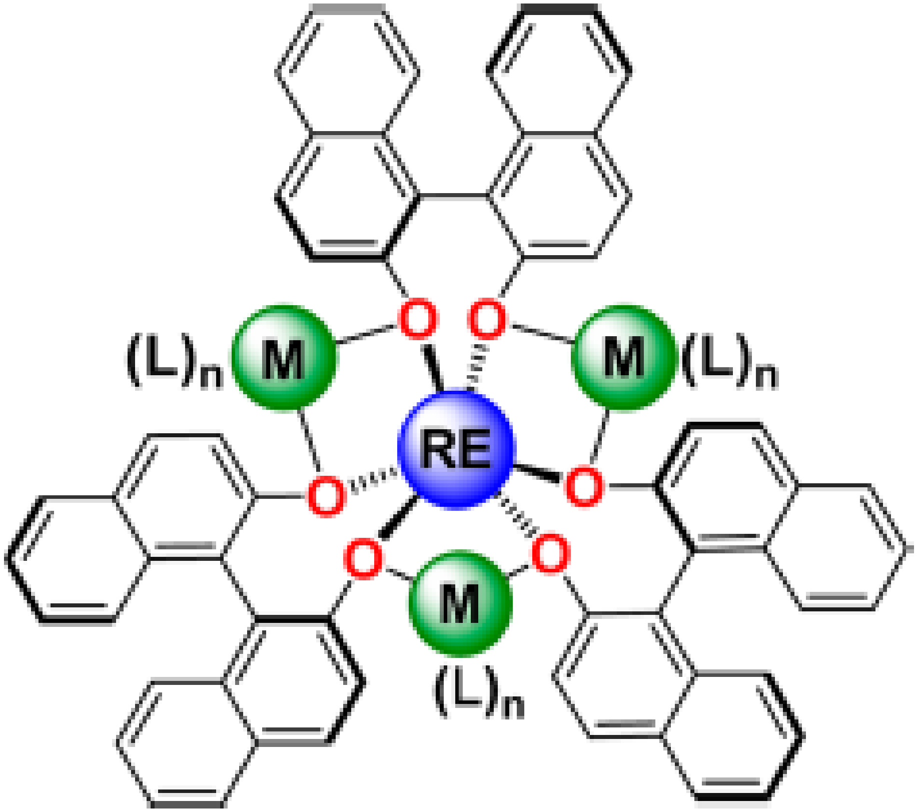
Wipf group current literature
Zhizhou Yue 07052014



Shibasaki’ s REMB.

RE = Sc, Y, La−Lu;
M = Li, Na, K;
B = (S)-BINOLate;
RE/M/B = 1/3/3.

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- **Most successful heterobimetallic enantioselective asymmetric catalysts;**

- **Tune the reactivity and selectivity by simply changing RE and M;**

- **Catalyze the formation of C−C and C−E (E = N, O, P, S) bonds with high stereoselectivity; atom economy;**

- **Act as both a Brønsted base by virtue of the metal alkoxide and a Lewis acid via the RE ion.**

Two Challenges

- It is sensitive to trace amounts water.
- Each RE/M combination must be prepared independently. It is not attractive to high-throughpout experimentation strategies.

Need

- Air- and water-tolerant REMB precatalysts.

Important Observations Before

- **Noncovalent interactions** in the secondary coordination sphere can tune the reactivity and properties of REMB catalyst.
- The **alkali metal cations** modulate the electronics at the RE cation.
- **BINOLate oxygen atoms** are the primary determinant for the ability of the RE cation to act as a Lewis acid.

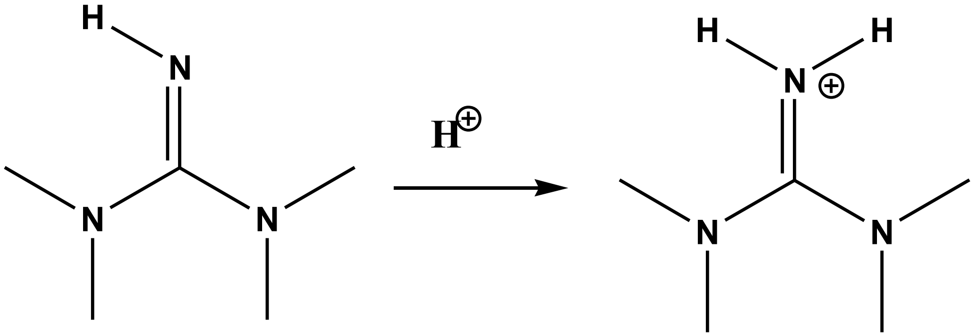
Angew. Chem., Int. Ed. 2012, 51, 10159−10163
J. Am. Chem. Soc. 2013, 135, 19016−19024.

Hypothesis

- The isoelectronic replacement of alkali metal cations with the appropriate ammonium cations would result in the formation of complexes with intramolecular ionic hydrogen-bonding networks.
- Relatively weak interactions should allow for facile exchange of H-bonded ammonium cations for alkali metal cations, which would provide a rapid and unified entry to various REMB catalyst.

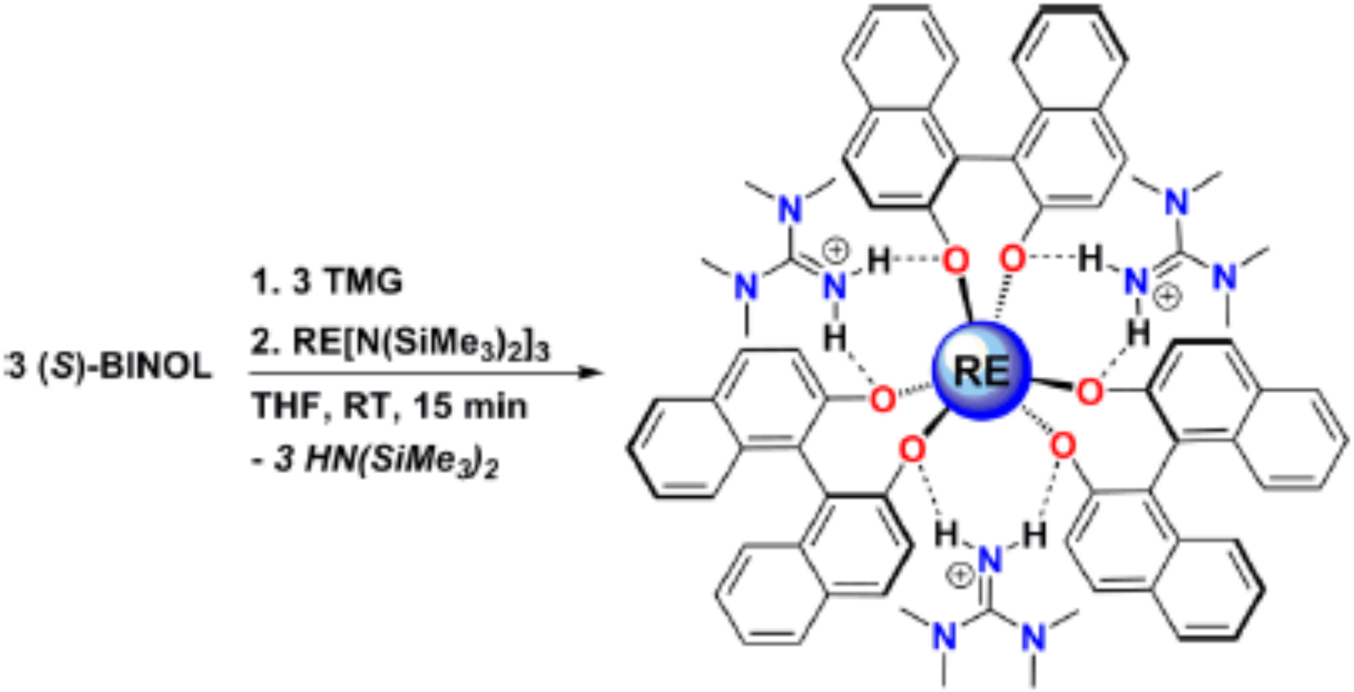
Chem. Soc. Rev. 1993, 22, 397-407
Angew. Chem., Int. Ed. 2002, 41, 48−76.
Chem. Rev. 2012, 112, PR22−PR103.

1,1,3,3-Tetramethylguanidine (TMG)



- **When protonated, it is a dual H-bond donor (can replace the interactions of the main group metal with two BINOLate ligands)**
- **Sufficiently basic, pKa (TMG−H+) = 13.6 in H2O [pKa (ArOH) = 10.0 in H2O]**
- **H-bond donors for a variety of anionic hosts.**

1:3:3 Complex [TMG−H+]3[RE (BINOLate)3]



RE: La (*91% yield*) **1-La**
Eu (*92% yield*) **1-Eu**
Yb (*93% yield*) **1-Yb**
Y (*91 % yield*) **1-Y**

Synthesis of 1−RE from rigorously anhydrous conditions

Water Tolerance

- **In previous REMB catalyst, the acidity of H2O coordinated to RE cations is increased by ~5−6 orders of magnitude, resulting in enhanced rates of ligand hydrolysis. (sensitive to trace amounts water)**

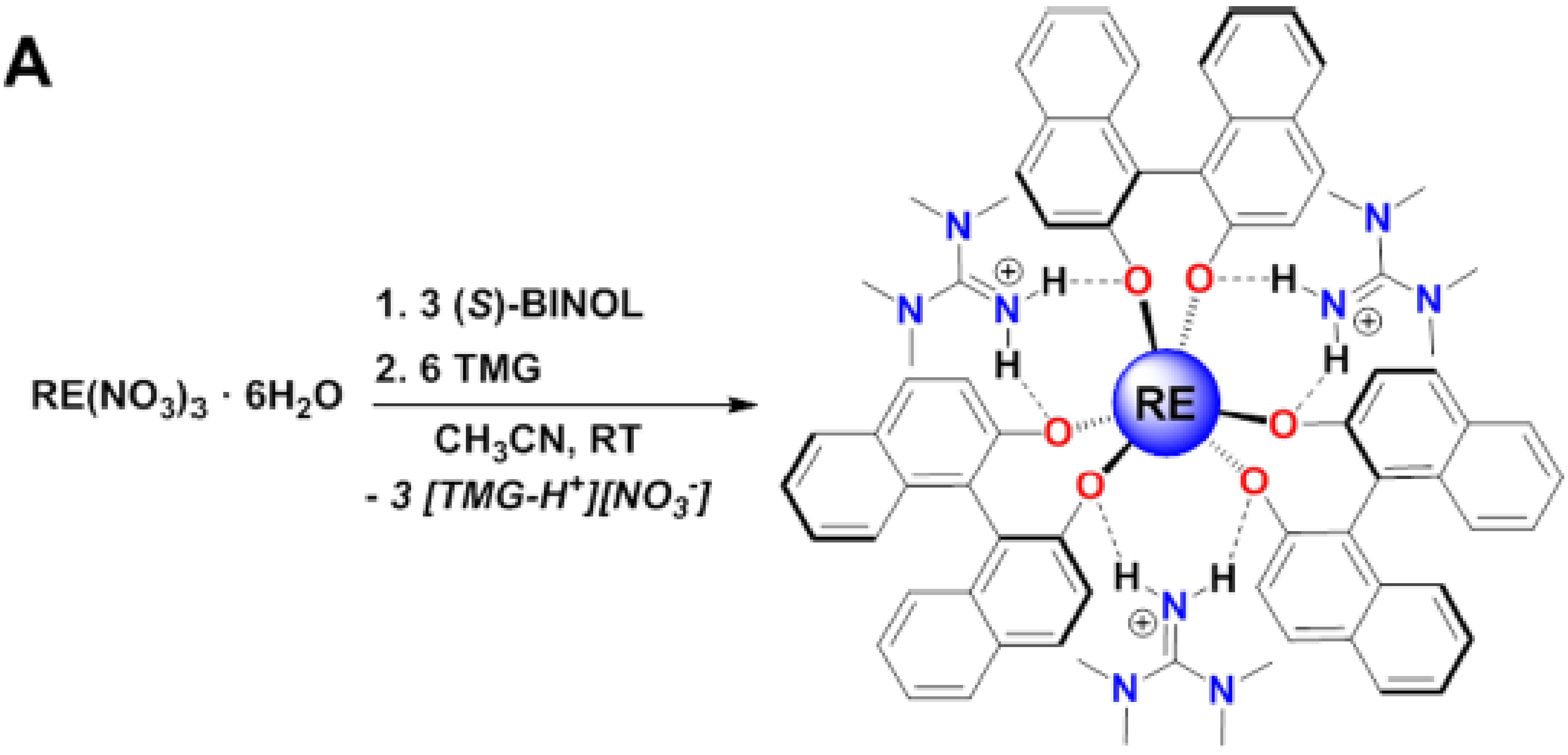
- **In 1-RE cation, there is strong preference for a six-coordinate geometry. It is due to the unique intramolecular, ionic H-bonding interactions and the H-bond donors, H−TMG+, that maximize the strength of the directional H-bonding interactions.**

Water Tolerance

- Both RE−BINOLAM and REMB complexes will coordinate H2O to adopt seven-coordinate geometries, would increase the energy of the system (by weakening those intramolecular H-bonding interactions). The seven-coordinate geometries is disfavored.

- The hydrophobic methyl substiutents of TMG−H + contribute to the nonhygroscopic properties.

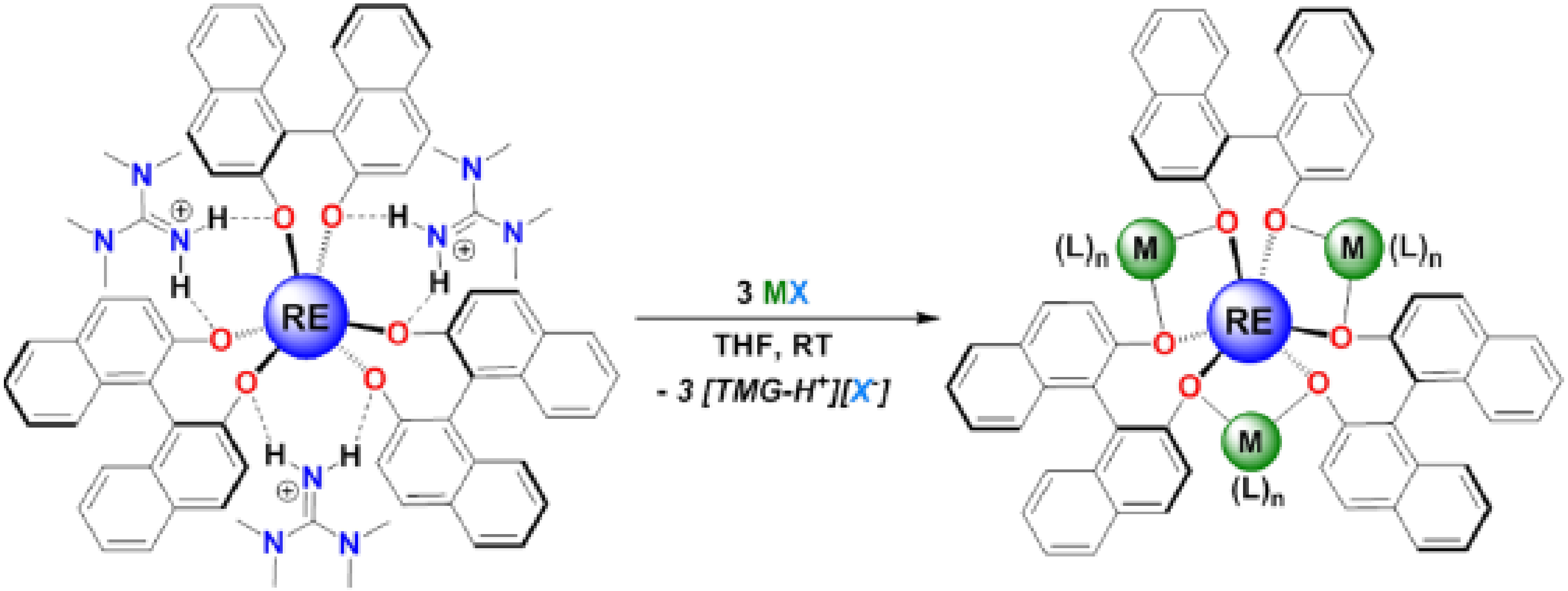
Modified, Open-air, Benchtop Synthesis(1-RE)



1-RE

- **Addition of 6 equiv of TMG to concentrated stirring solutions of RE(NO3)3·6H2O/(S)-BINOL (1:3 ratio) resulted in the immediate precipitation of 1−RE;**
- **Could be crystallized from CH2Cl2/pentane in 70−85% yield;**
- **Was easily prepared on a 25 g scale.**
- **Inexpensive hydrated RE starting materials;**
- **Convenient and expedient synthetic procedure;**

Generation of REMB from Rare Earth BINOLate Ammonium Complexes



1-RE **REMB**

Cation-exchange

- **Cation-exchange: Addition of excess LiI to ammonium precursor immediately generated RELB as the single observable RE-containing product.**
- **The generation from ionic H-bonding interactions (in 1−RE) to new M−OBINOLate bonds (more stable) provides a strong thermodynamic driving force for the formation of the REMB complexes from 1−RE (either acid −base or cation-exchange methods)**
- **No presence of coordinated water to the REMB**

Asymmetric Michael Addition

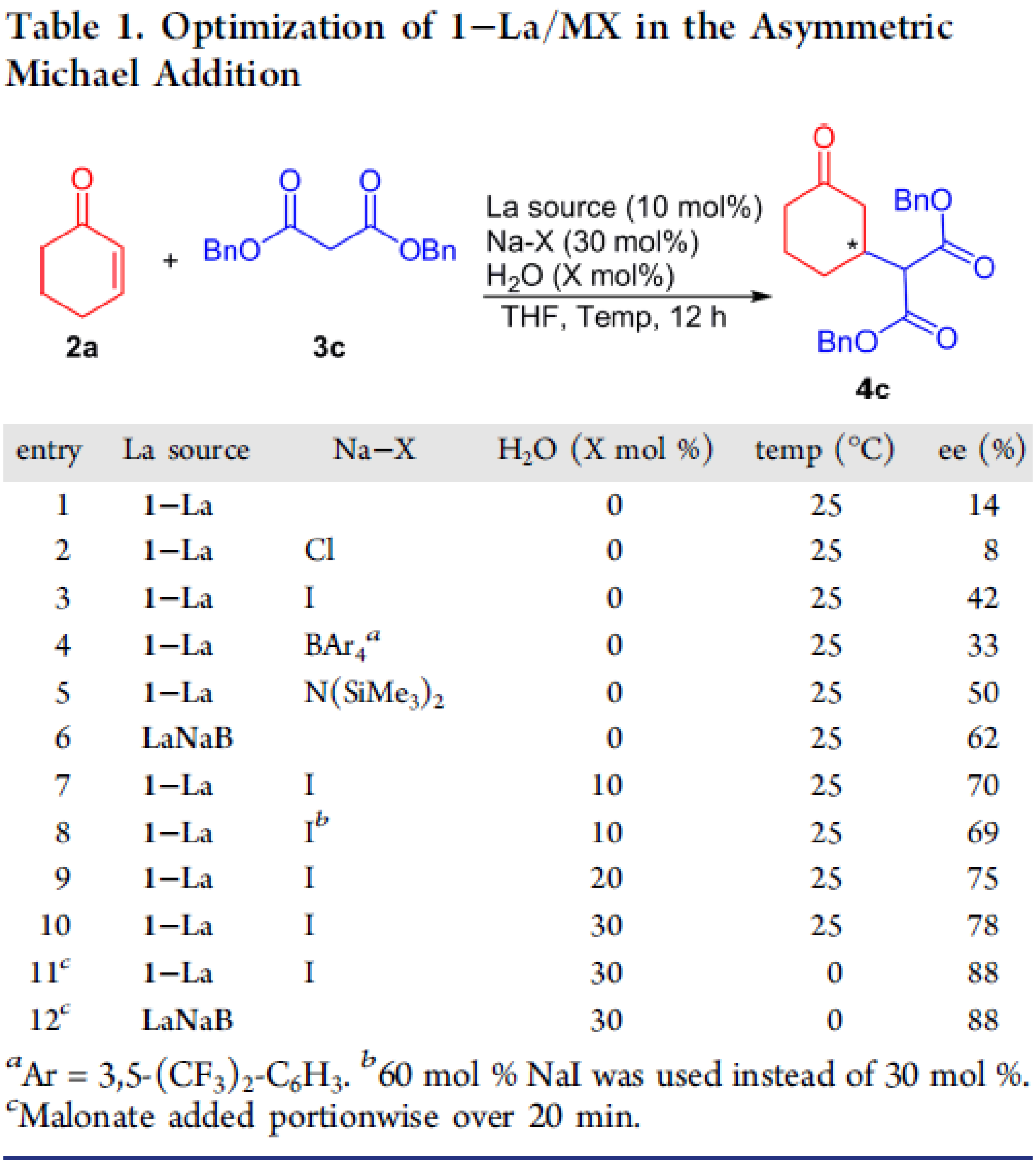
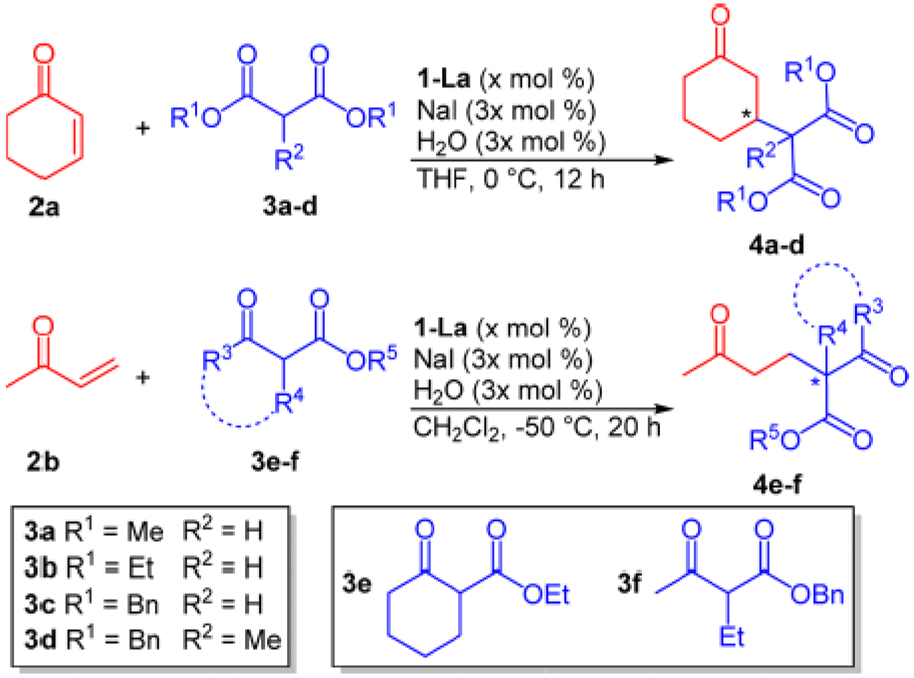


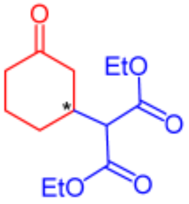
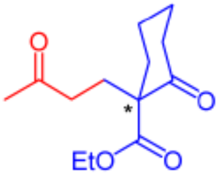
Table 1. Optimization of 1−La/MX in the Asymmetric Michael Addition

entry	La source	Na−X	H_2O (X mol %)	temp (°C)	ee (%)
1	1−La		0	25	14
2	1−La	Cl	0	25	8
3	1−La	I	0	25	42
4	1−La	BAr_4[a]	0	25	33
5	1−La	$N(SiMe_3)_2$	0	25	50
6	LaNaB		0	25	62
7	1−La	I	10	25	70
8	1−La	I[b]	10	25	69
9	1−La	I	20	25	75
10	1−La	I	30	25	78
11[c]	1−La	I	30	0	88
12[c]	LaNaB		30	0	88

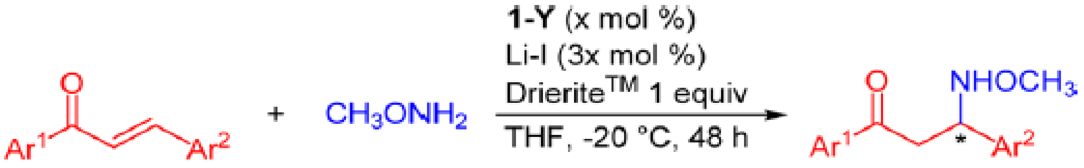
[a] Ar = 3,5-$(CF_3)_2$-C_6H_3. [b] 60 mol % NaI was used instead of 30 mol %. [c] Malonate added portionwise over 20 min.



3a R^1 = Me R^2 = H
3b R^1 = Et R^2 = H
3c R^1 = Bn R^2 = H
3d R^1 = Bn R^2 = Me

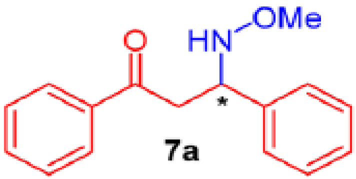
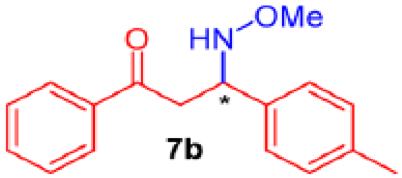
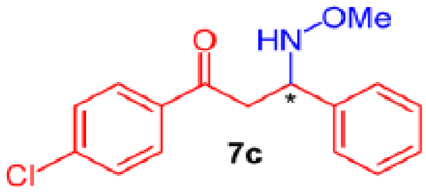
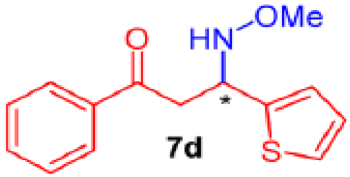
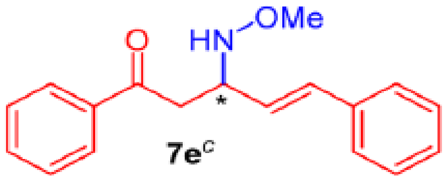
Entry	Michael Donor	Product		x	Yield %[a]	ee %[a]
1	**3a**		**4a**	10[b]	87 (98)[c]	94 (83)[c]
2				5[d]	93	90
3				2.5[d]	91[e]	89[e]
4	**3b**		**4b**	10[b]	90 (97)[c]	96 (81)[c]
5	**3c**		**4c**	10[b]	94 (97)	88 (88)
6	**3d**		**4d**	10[b]	89 (91)	96 (92)
7	**3e**		**4e**	5[d]	87 (89)	98 (91)
8	**3f**		**4f**	5[d]	84 (98)	>99 (89)

Asymmetric aza-Michael Addition of Chalcone Derivatives

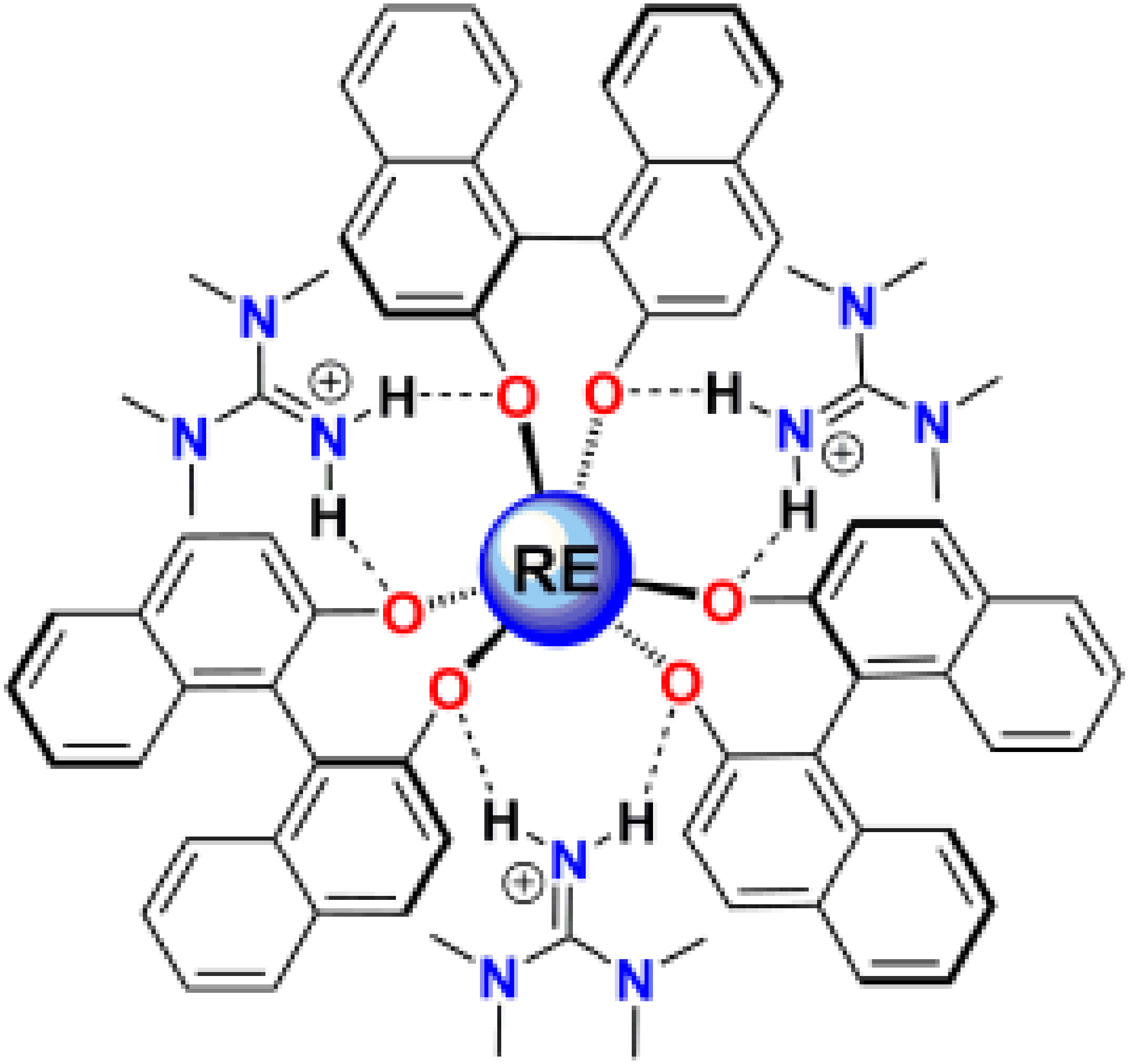


1-Y (x mol %)
Li-I (3x mol %)
Drierite™ 1 equiv
THF, -20 °C, 48 h

5a-e **6** **7a-e**

Entry	Product	x	Yield %[a]	ee %[a]
1	 **7a**	3	88 (97)	91 (95)
2		3	93[b]	93[b]
3		0.5	90[b,c] (96)	88[b,c] (96)
4	 **7b**	3	91 (96)	94 (96)
5	 **7c**	3	96 (96)	94 (96)
6	 **7d**	3	93 (96)	93 (95)
7	 **7e**[c]	3	97[d] (91)	91[d] (94)

Conclusion



- Incorporation of hydrogen-bonded guanidinium cations in the secondary coordination sphere to prepare the Bench-stable precatalysts for Shibasaki’ s REMB catalysts.
- 1−RE/MI could be applied as a general precatalyst system to generate quantitatively Shibasaki’s REMB catalyst through either acid−base or cation exchange methods in both traditional bench-scale and HTE techniques.

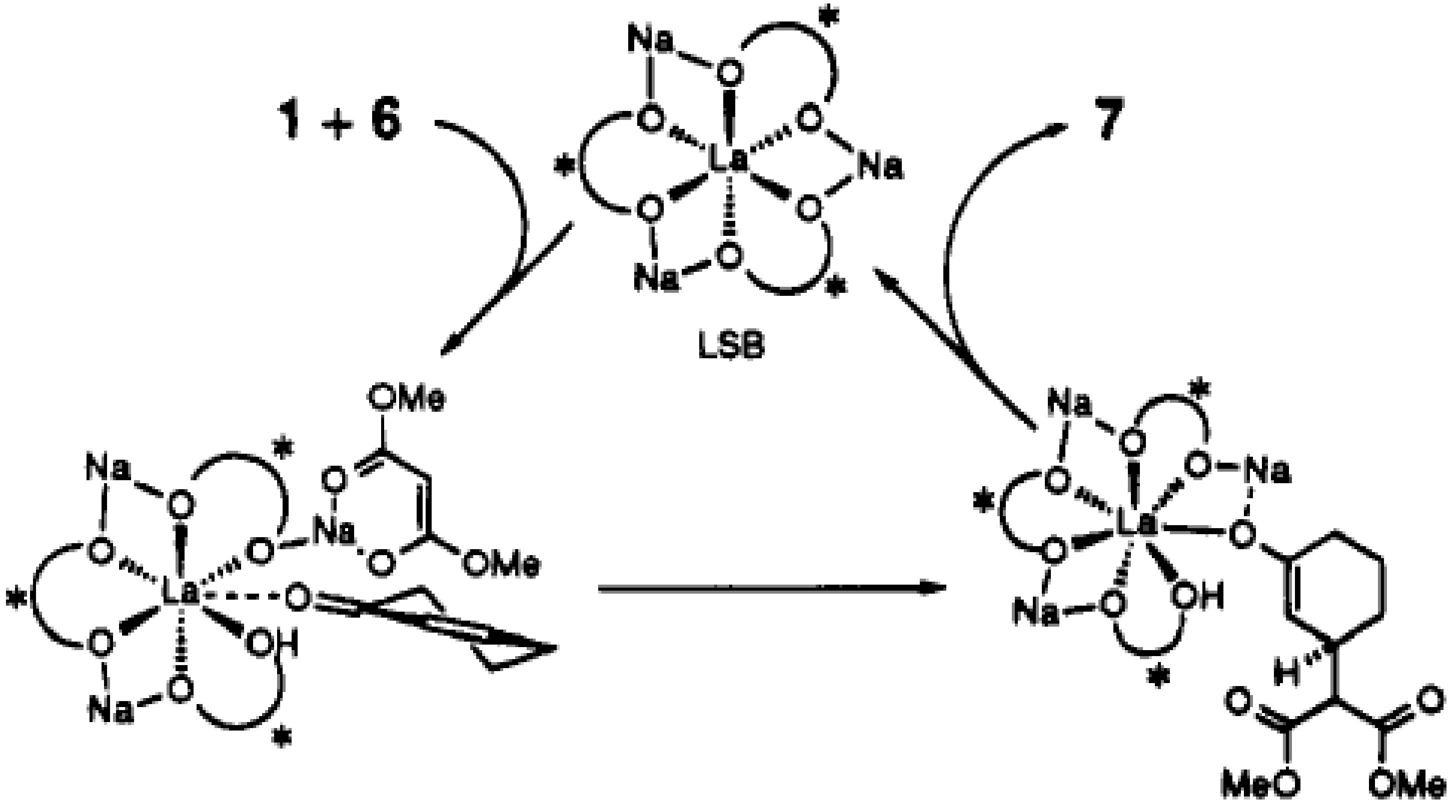
- Markedly improved stability toward moisture in solution and in the solid state.
- Avoiding the use of strong bases that are typically moisture sensitive.
- Low cost; easy to handle.

- Cation-exchange Method

  Via this method, large variety of inexpensive MX salts and amine bases of varying pKa should help the identification of new heterobimetallic catalyst.

Thank You

Scheme 2. Proposed Catalytic Cycle of the Asymmetric Michael Reaction Promoted by LSB



J. Am. Chem. SOC. ***1995,117,*** 6194-6198

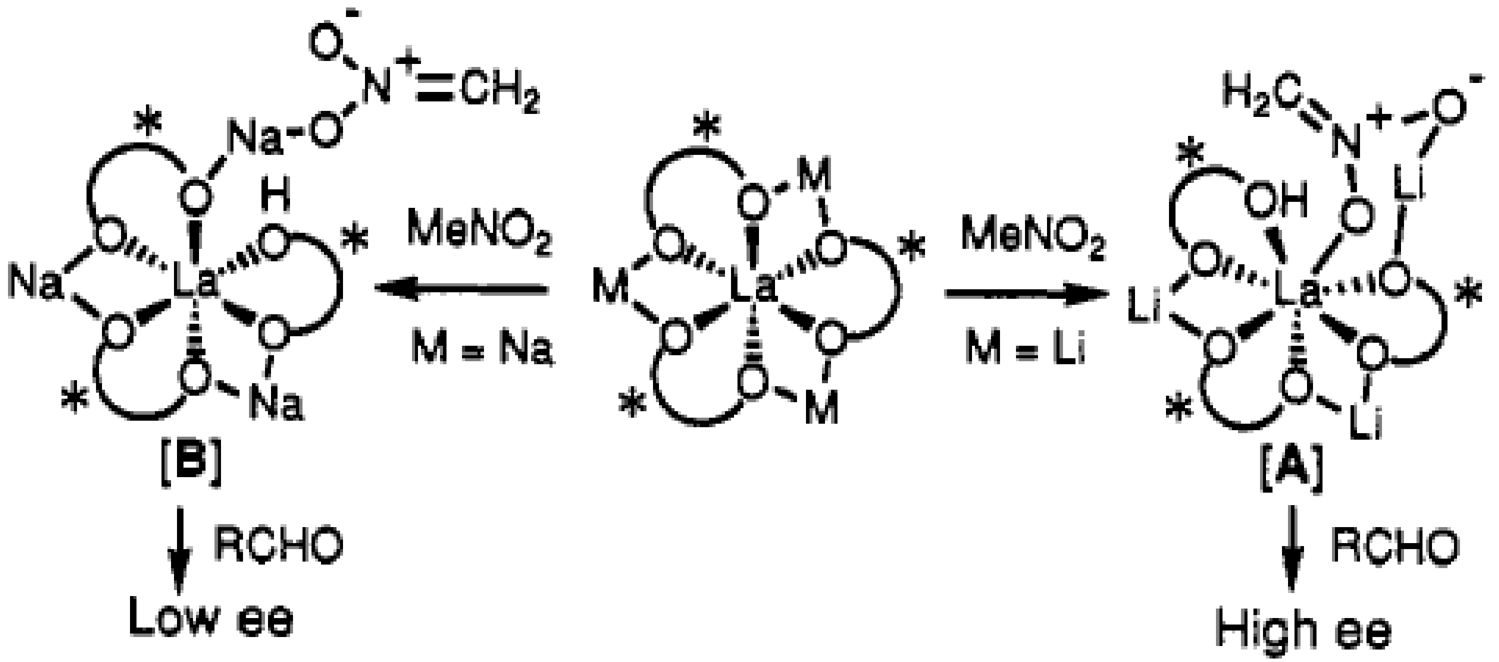


Figure 3. Proposed mechanisms for the rare earth BINOL complex catalyzed asymmetric nitroaldol reactions.

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