A New Multicomponent Reaction Catalyzed by [Lewis acid]$^+$[Co(CO)$_4$]$^-$ Catalyst

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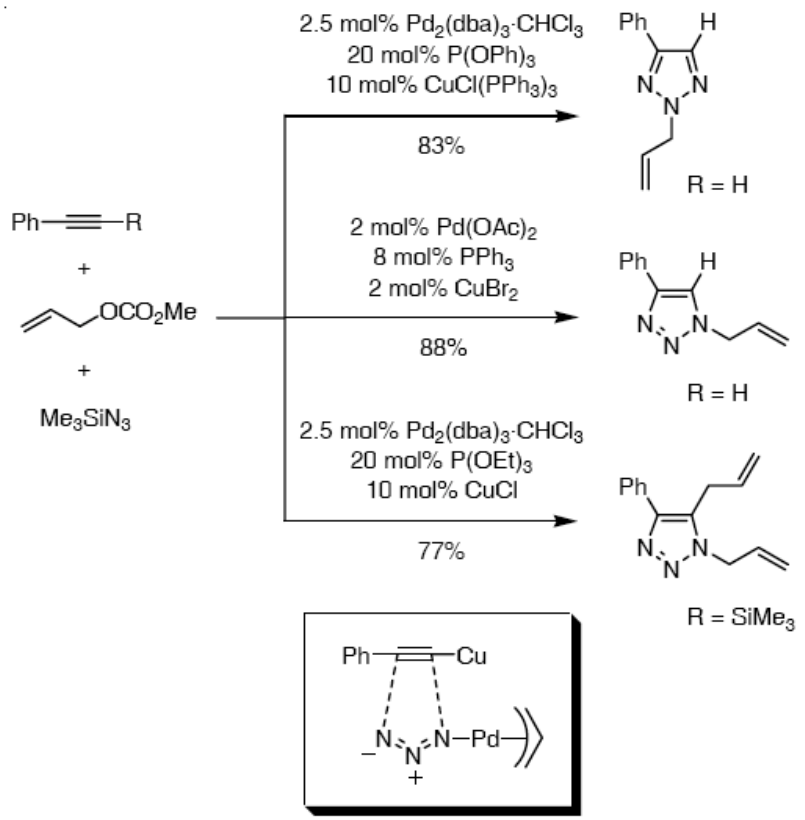
Multimetallic Catalysis

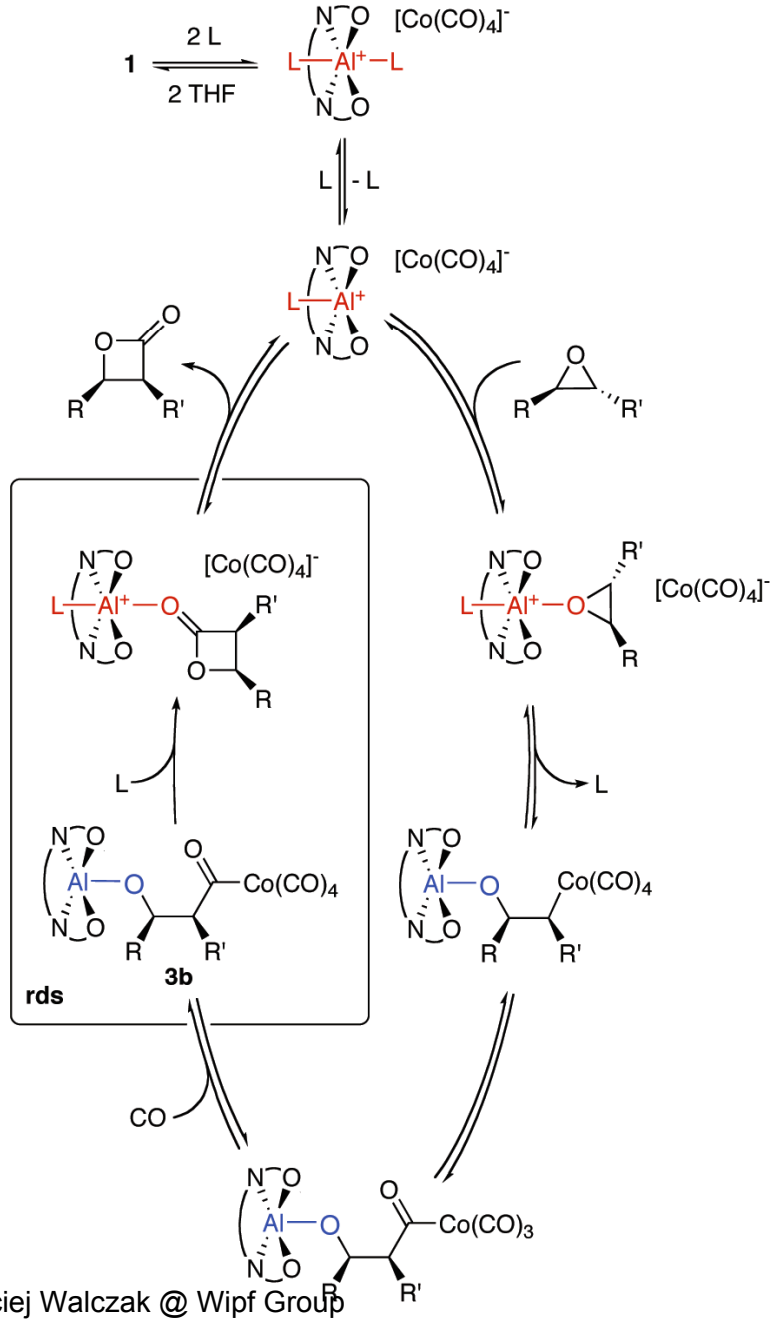
- Majority of the catalytic systems are based on catalytic-stoichiometric systems (NHK coupling).

- Although sequential addition of metal catalyst has been successfully applied, there are only few well-defined, multimetallic (multifuntional) catalytic systems (Sonogashira coupling, Wacker oxidation).

- Ideally, multimetallic catalyst (heteronuclear) would be superior to a mixture of salts.

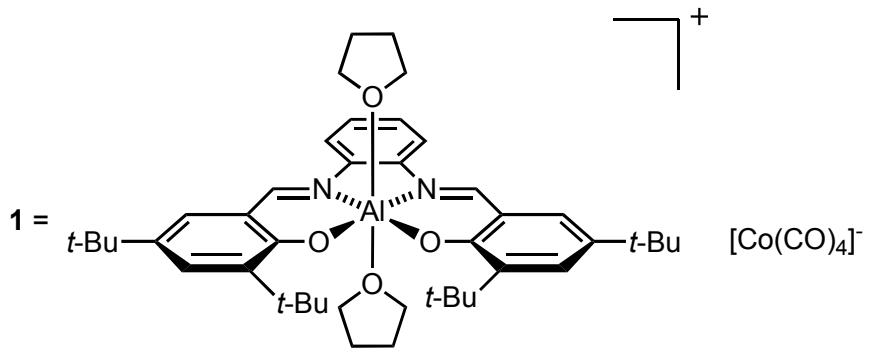


Epoxide Carbonylation

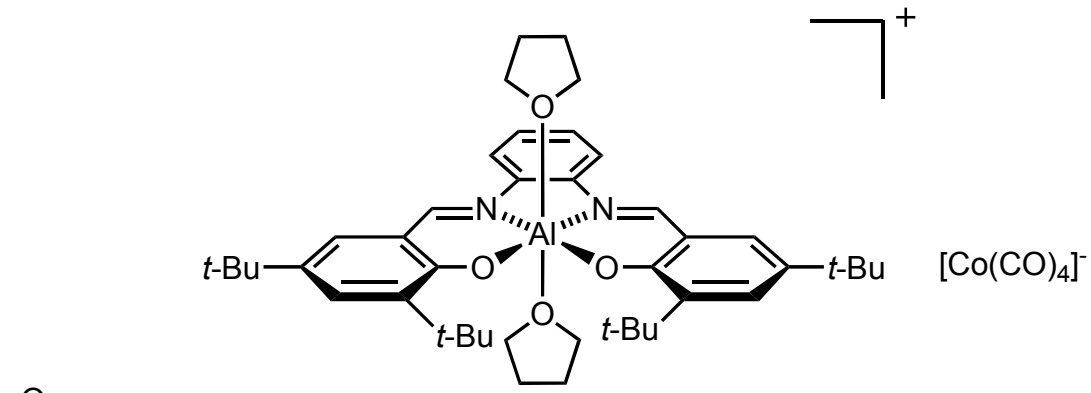


- Detailed mechanistic studies showed that reaction rate is independent on epoxide and CO, but 1st order in catalyst.
- The rate is strongly dependent on the polarity of the solvent.
- Rate determining step is lactone formation.
- Solvents with a strong donating capabilities help to stabilize aluminum cation formed after lactone formation.

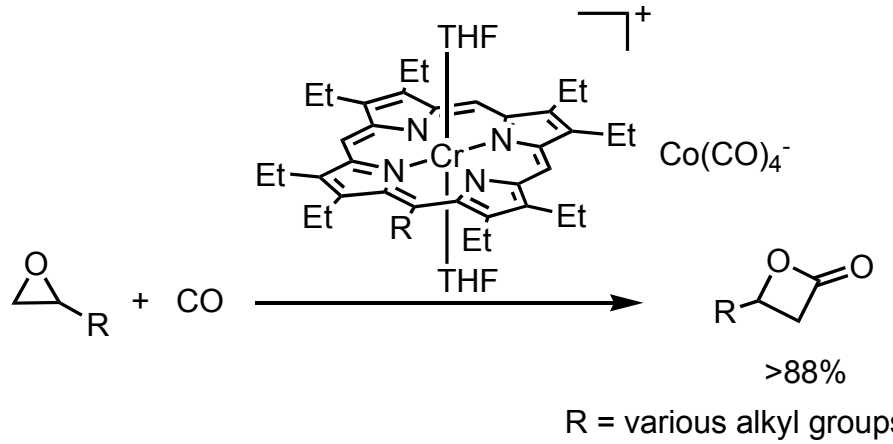
Coates
J. Am. Chem. Soc. **2006**,, *128*, 10125



Epoxide Carbonylation



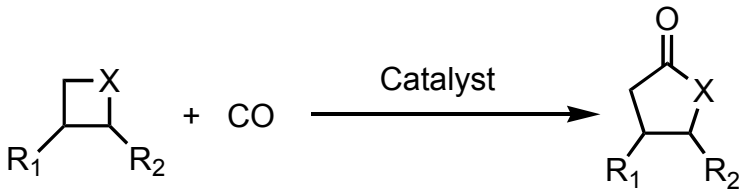
Coates *J. Am. Chem. Soc.* **2002**, *124*, 1174
Coates *Angew. Chem. Int. Ed.* **2002**, *41*, 2781
Coates *J. Am. Chem. Soc.* **2005**, *127*, 11426



- A practical procedure for carbonylation of epoxides has been also developed (1 atm CO, yields >98%).

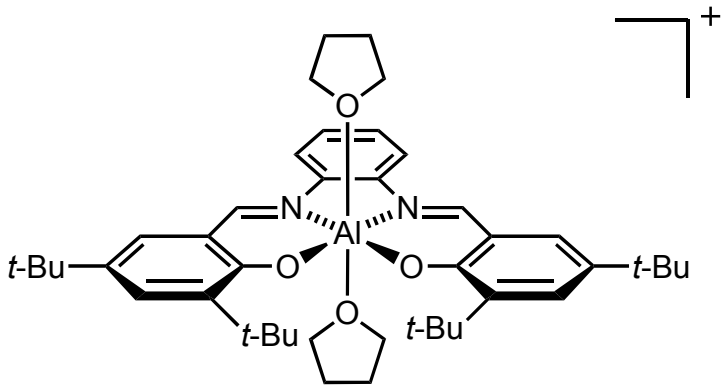
Coates *Org. Lett.* **2006**, *8*, 3709

Carbonylation of 4-membered Heterocycles



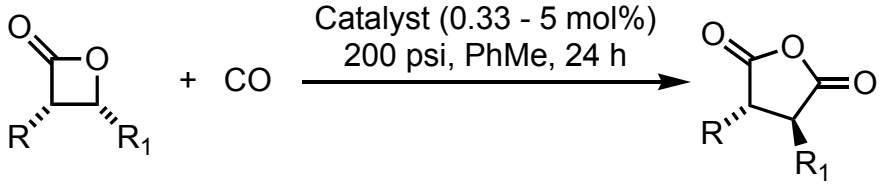
Entry	Catalyst	mol%	E	R^1	R^2	*P*/ atm	*T*/ °C	Yield (%)
1	$Co_2(CO)_8/Ru_3(CO)_{12}$[a]	10–20	O	H	H	60	190	70
2	**1**[b]	0.5	O	H	H	14	80	>99
3	$Co_2(CO)_8/Ru_3(CO)_{12}$[a]	10–20	S	H	H	60	125	100
4	(dppe)(Me)Pt–$Co(CO)_4$[c]	2	S	H	H	10	100	99
5	(dppe)(Me)Pt–$Mn(CO)_5$[c]	5	S	H	H	10	100	0
6	$Co_2(CO)_8/Ru_3(CO)_{12}$[a]	10–20	S	Me	H	60	120	95
7	(dppe)(Me)Pt–$Co(CO)_4$[c]	2	S	Me	H	10	100	89
8	$Co_2(CO)_8/Ru_3(CO)_{12}$[a]	10–20	S	H	OMe	60	145	87

1 =



$[Co(CO)_4]^-$

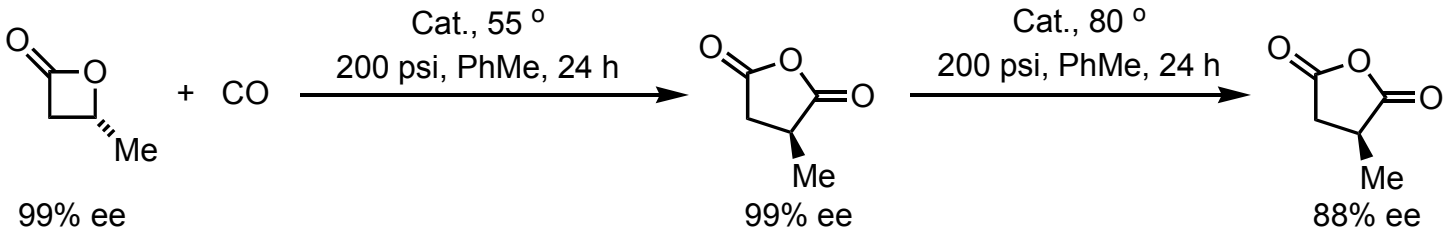
Synthesis of Anhydrides



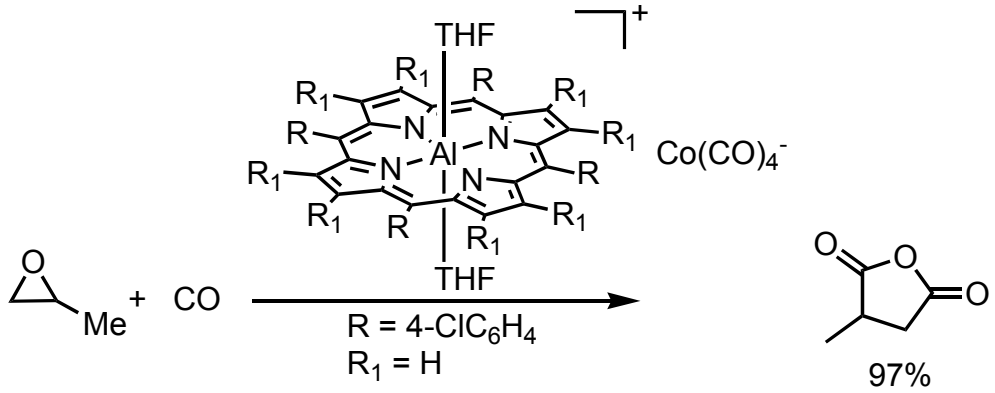
Inversion of configuration is consistent with mechanism involving nucleophilic displacement by CO.

yields: 90-99%
R = H, Me
R_1 = only alkyl

Coates *J. Am. Chem. Soc.* **2004**, *126*, 6842

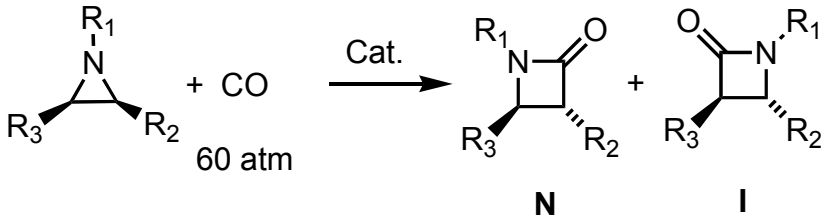


However, partial racemization was observed when the reaction was carried out at elevated temperatures (80 °).



Direct insertion into epoxides:
Coates *Chem. Comm.* **2006**, 657

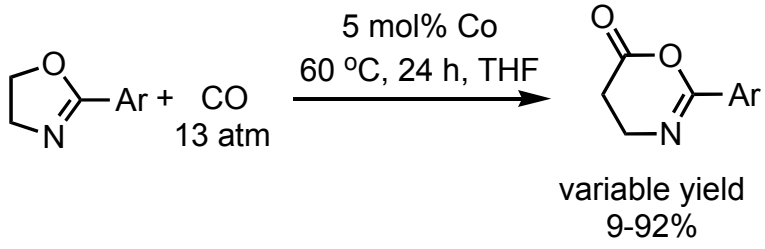
Insertion into Nitrogen Heterocycles



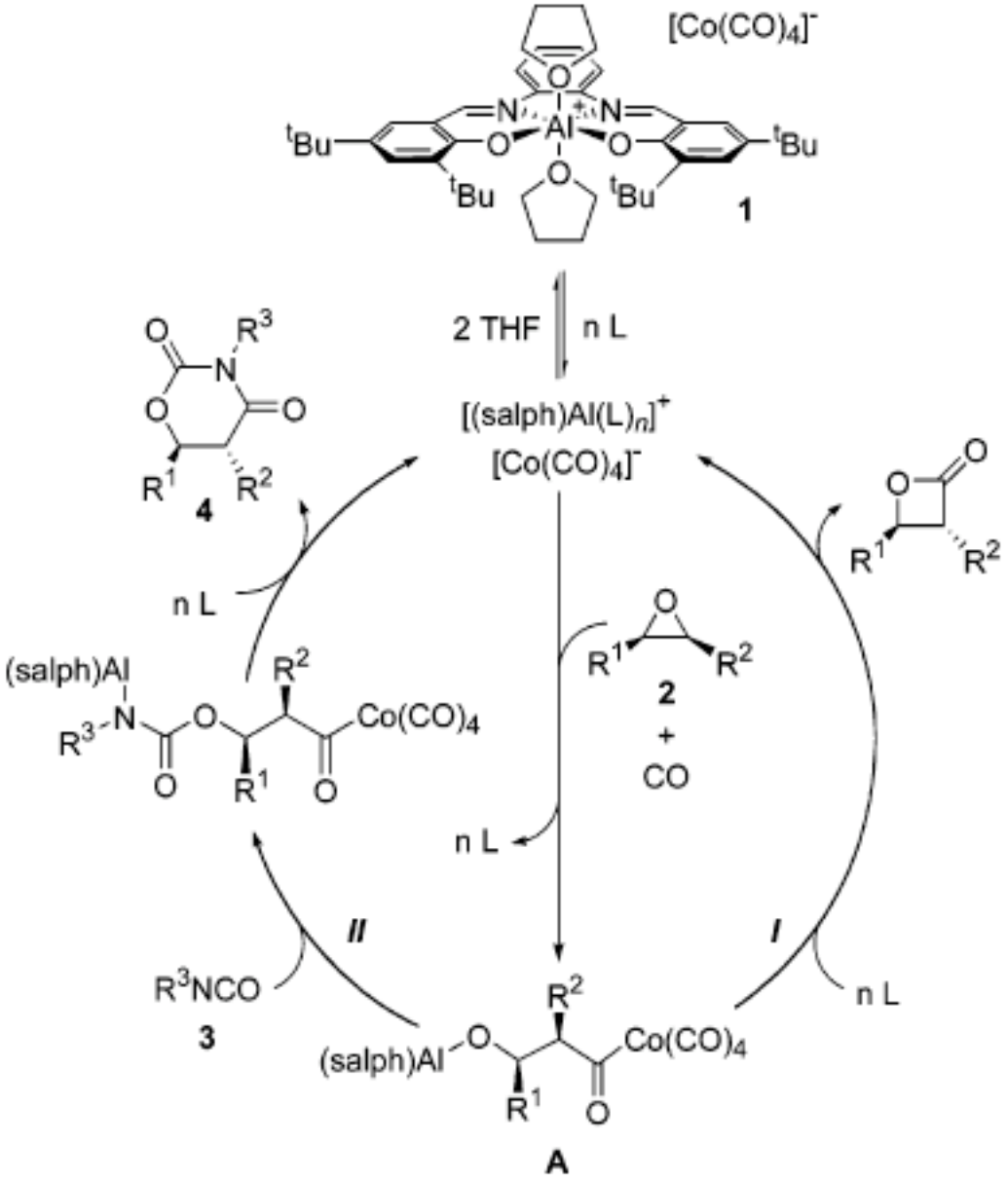
Coates *Angew. Chem. Int. Ed.* **2002**, *41*, 2781

Entry	R_1	R_2	R_3	Cat.	Mol%	N	I
1	Bn	H	Me	A	5	90	ND
2	Bn	H	Me	B	5	50	ND
3	Bn		$-(CH_2)_4-$	A	5	80	ND
4	Bn		$-(CH_2)_4-$	B	5	<5	ND
5	Bn		$-(CH_2)_4-$	$Co_2(CO)_8$	8	28	ND
6	Tos	H	Me	A	5	35	ND
7	Tos	H	Me	B	5	99	ND
8	Bn	Me	CH_2OTBS	A	5	90	5
9	Bn	Me	CH_2OTBS	$Co_2(CO)_8$	8	92	8

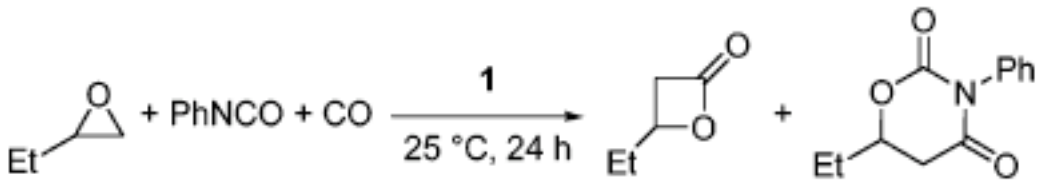
Other heterocycles, such as azirines, α-lactams, diaziridines, azetidines and oxazilines have been described.



Title Paper - Experiment Design



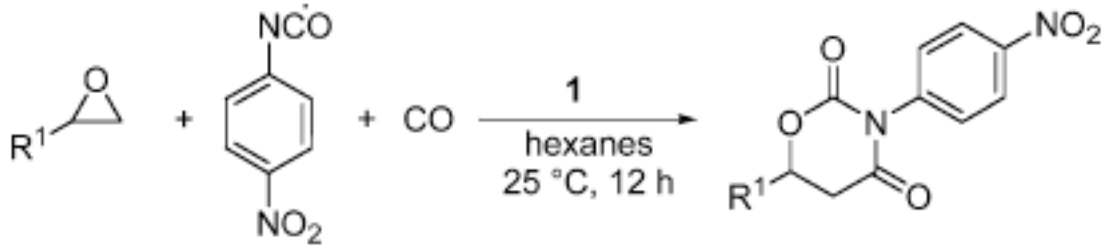
Title Paper - Optimization Studies



2a **3a´** **4aa´**

entry	solvent	lactone[b] [%]	OD[b] [%]	selectivity[c] [%]
1	hexanes	8	40	83
2	pentane	5	24	82
3	toluene	20	10	33
4	diethyl ether	36	17	32
5	1,2-difluorobenzene	36	14	28
6	*tert*-butyl methyl ether	34	13	28
7	tetrahydropyran	74	4	5
8	acetonitrile	77	3	4
9	1,4-dioxane	>97	nd[d]	0
10	2,5-dimethyltetrahydrofuran	>97	nd[d]	0
11	1,2-dimethoxyethane	91	nd[d]	0
12	2-methyltetrahydrofuran	91	nd[d]	0
13	tetrahydrofuran	83	nd[d]	0

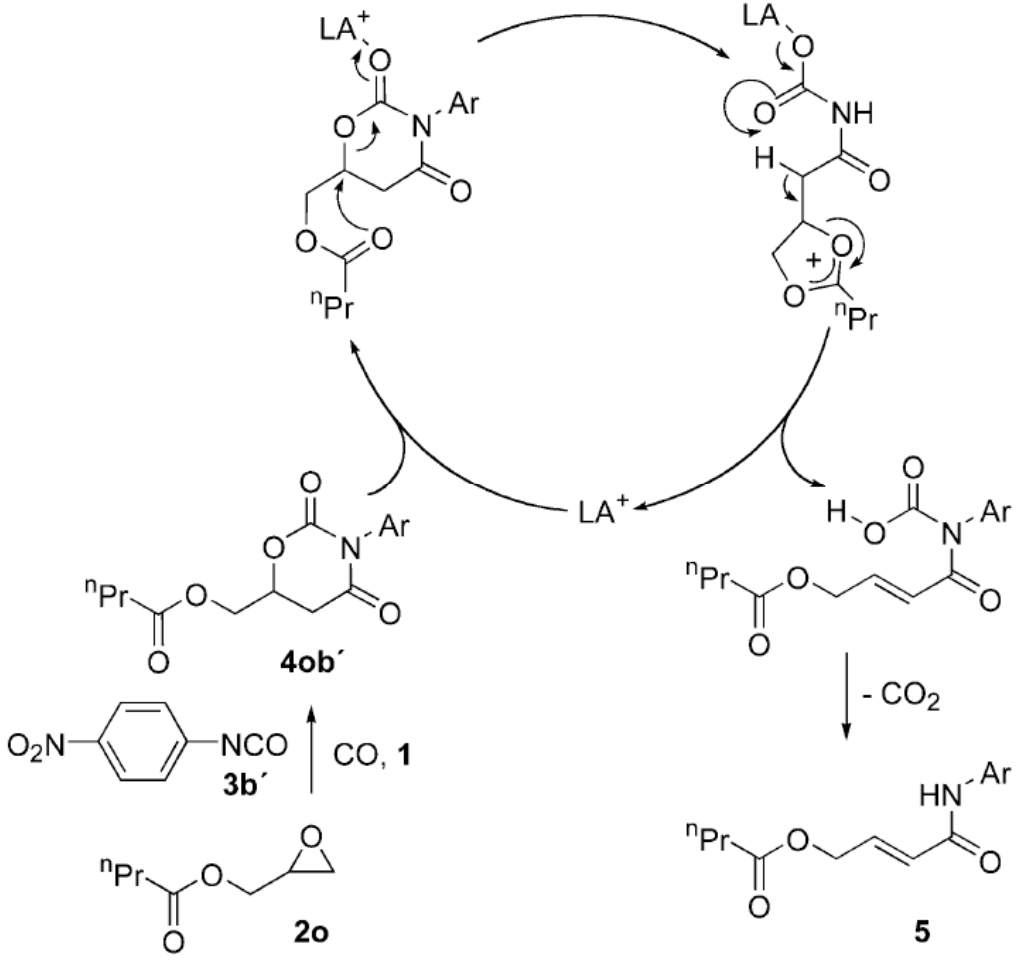
Title Paper - Reaction Scope



2a - 2n **3b´** **4ab´ - 4nb´**

entry	R^1	OD	lactone[b] [%]	OD[b] [%]	selectivity[c] [%]
1	Et	**4ab´**	nd[d]	>97	>97
2	Me	**4bb´**	nd[d]	>97	>97
3	^{n}Bu	**4cb´**	nd[d]	>97	>97
4	*c*-C_6H_{11}	**4db´**	3	94	97
5	^{t}Bu	**4eb´**	9	10	53
6	$(CH_2)_2CH{=}CH_2$	**4fb´**	nd[d]	>97	>97
7	$CH_2OCH_2CH{=}CH_2$	**4gb´**	6	94	94
8	CH_2O^nBu	**4hb´**	2	>97	>97
9	CH_2OBn	**4ib´**	8	80	88
10	$CH_2OSiMe_2{}^tBu$	**4jb´**	3	97	97
11[e]	CH_2Cl	**4kb´**	nd[d]	70	>97
12	$(CH_2)_2CO_2{}^nPr$	**4lb´**	nd[d]	>97	>97
13	$(CH_2)_3OC(O)^nPr$	**4mb´**	nd[d]	>97	>97
14	Ph	**4nb´**	nd[d]	nd[d]	na[f]

Lewis Acids Promote Acyl Migration



Summary and Outlook

- Lewis acids combined with nucleophilic metal carbonyls are powerful catalyst for carbonylations of epoxides and aziridines.

- Detailed mechanistic studies allowed for development of efficient multicomponent reactions using epoxides, CO, and isocyanates.

Future Directions:

Reaction scope needs to be improved - since CO is an invariable component, other electrophilic acceptors may be used.

Although some efforts were directed towards development of enantioselective version of the epoxide carbonylation, more research is needed to develop optimal conditions for kinetic resolution.

A concept of Lewis acid activation followed by trapping by nucleophilic metal centers could be potentially extended towards other substrates.