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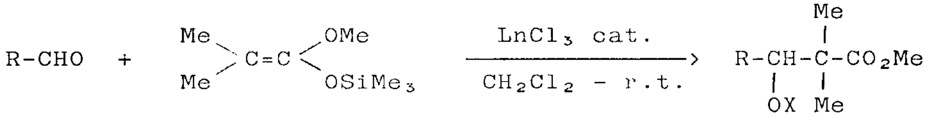
LANTHANIDES AS LEWIS-ACID CATALYSTS IN ALDOL ADDITION, CYANOHYDRIN-FORMING AND OXIRANE RING OPENING REACTIONS

Angelos E.VOUGIOUKAS and Henri B.KAGAN*

Laboratoire de Synthèse Asymétrique, associé au CNRS, Bât. 420
Centre d'Orsay, Université Paris-Sud, 91405 Orsay Cedex France

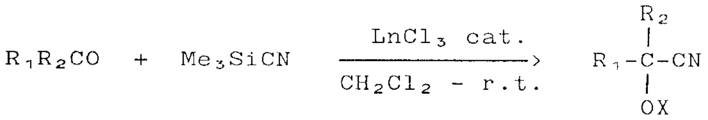
Summary: Lanthanide trichlorides (Ln = La,Ce,Sm) and Eu(fod)$_3$ catalyze the aldol addition of silyl enol ethers to aldehydes, the addition of trimethylsilyl cyanide to aldehydes and ketones as well as the synthesis of β-cyanosilyl ethers.

The formation of C-C bonds promoted by Lewis acids is of prime importance in organic synthesis, especially when it proceeds smoothly under mild conditions[1]. Typical processes mediated by Lewis acids (such as BF_3,$SnCl_4$,$TiCl_4$, etc., either in stoichiometric or, less commonly, in catalytic amounts) are the cross-aldol addition[2] of aldehydes to silyl enol ethers[3] (eq [1]), the cyanohydrin formation[4] (eq [2]) and the oxirane ring opening[5] (eq [3]). Lanthanide complexes have been used as Lewis-acid catalysts in some organic transformations[6], such as the Diels-Alder[7] and the Friedel-Crafts[8] reactions. Anhydrous lanthanide trichlorides, which are considered as hard acids[6], are now reported to be efficient, low-cost catalysts for the processes mentioned above under mild conditions.

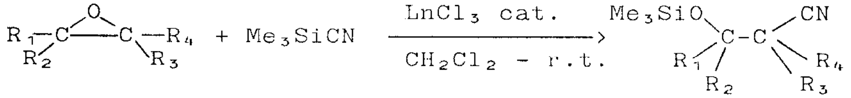


$$\text{R-CHO} + \text{Me}_2\text{C=C}\langle^{\text{OMe}}_{\text{OSiMe}_3} \xrightarrow[\text{CH}_2\text{Cl}_2\text{ - r.t.}]{\text{LnCl}_3\text{ cat.}} \text{R-}\underset{\text{OX}}{\text{CH}}\text{-}\overset{\text{Me}}{\underset{\text{Me}}{\text{C}}}\text{-CO}_2\text{Me} \qquad [1]$$

R = C_6H_5 or n-C_5H_{11} ; Ln = La,Ce,Sm ; X = Me_3Si or H



$$R_1R_2CO + Me_3SiCN \xrightarrow[CH_2Cl_2\ -\ r.t.]{LnCl_3\ cat.} R_1-\overset{\overset{\displaystyle R_2}{|}}{\underset{\underset{\displaystyle OX}{|}}{C}}-CN \qquad [2]$$



[3]

R_{1-4} = H,alkyl or aryl ; Ln = La,Ce,Sm ; X = Me_3Si or H

Table (I) : Ln(III) - Catalyzed Aldol Addition of Trimethylsilyl Ketene Acetal to Aldehydes (eq. [1])

Entry	R	Catalyst (mol equiv.)		Reaction Conditions	Isolated yield (%) O-Silylated Aldol	Aldol
1	C_6H_5	$SmCl_3$	(0.1)	r.t./ 12 h	66	28
2	C_6H_5	$CeCl_3$	(0.1)	r.t./ 24 h	61	27
3	C_6H_5	$LaCl_3$	(0.1)	r.t./ 4 days	21	42
4	C_6H_5	$LaCl_3$	(0.05)	r.t./ 4 days	23	41
5	C_6H_5	$LaCl_3$	(0.1)	Δ / 18 h	17	51
6	C_6H_5	Eu(fod)$_3$[a]	(0.05)	r.t./ 8 h	48	19
7	n-C_5H_{11}	$SmCl_3$	(0.1)	r.t./ 36 h	47	16
8	n-C_5H_{11}	$CeCl_3$	(0.1)	r.t./ 1 week	11	12
9	n-C_5H_{11}	$LaCl_3$	(0.1)	r.t./ 1 week	No reaction[b]	
10	n-C_5H_{11}	Eu(fod)$_3$[a]	(0.1)	r.t./ 36 h	16	45

(a) : Homogeneous solution ; Eu(fod)$_3$ = tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium (III). (b) : Product traces on TLC plate not observed.

A typical preparative procedure (equations [1] and [2]) involves the addition of equimolar amounts of reagents (eg : benzaldehyde and silyl-enol ether, 8 mmol each) to a suspension of $LnCl_3$ catalyst (0.05 or 0.10 mol equiv.) in CH_2Cl_2 (2 ml) under argon at ambient temperature. After the given time[9] (Table (I)) the solvent was evaporated in vacuo and the non-hydrolyzed residue was extracted with hexane/ethyl acetate (4:1) and then chromatographed (flash/SiO_2, hex./EtOAc = 4:1). The isolated

Table (II) : Ln(III)-Catalyzed Addition of Trimethylsilyl Cyanide to Aldehydes and Ketones (eq.[2])

Entry	R_1R_2CO	Catalyst (mol equiv.)		Rxn. Time (h)	Isolated yield (%)	
					O-Si prod.	O-H prod.
1	PhCHO	$SmCl_3$	(0.05)	6	> 98	a
2	PhCHO	$CeCl_3$	(0.05)	10	> 98	a
3	PhCHO	$LaCl_3$	(0.05)	18	92	a
4	PhCHO	$Eu(fod)_3$[b]	(0.05)	4	26	62
5	$n-C_5H_{11}$	$SmCl_3$	(0.1)	18	14	61
6	$n-C_5H_{11}$	$LaCl_3$	(0.1)	18	34	39
7	$n-C_5H_{11}$	$Eu(fod)_3$[b]	(0.1)	8	31	47
8	$(CH_3)_2CHCH_2CHO$	$SmCl_3$	(0.1)	18	33	38
9	$(CH_3)_2CHCH_2CHO$	$LaCl_3$	(0.1)	48	11	37
10	$(CH_3)_2CHCHO$	$SmCl_3$	(0.1)	12	83	a
11	$(CH_3)_2CHCHO$	$LaCl_3$	(0.1)	72	15	17
12	$PhCOCH_3$	$SmCl_3$	(0.1)	18	50	a
13	$PhCOCH_3$	$LaCl_3$	(0.1)	48	35	a
14	$PhCOCH_3$	$Eu(fod)_3$[b]	(0.1)	18	25	29
15	$CH_3CO(n-C_4H_9)$	$SmCl_3$	(0.1)	18	14	31
16	$CH_3CO(n-C_4H_9)$	$LaCl_3$	(0.1)	48	35	a

(a) : Only traces on TLC plate observed ; (b) : Homogeneous solution.

yields of both the O-silylated and desilylated products are summarized in Tables (I) and (II). The identity of the products was confirmed by spectral data comparison[1,2,10]. Complete desilylation using $HF/H_2O/THF$ is possible[1,2]. Although kinetic studies were not undertaken yet, it is evident that the comparative catalyst efficiency is in the order Sm > Ce > La when the reaction mixture is in the form of a suspension in CH_2Cl_2. Lower amounts of catalyst (eg : 0.01-0.03 mol equiv.) afford products (eqs. [1] and [2]) with considerably lower yields and after extended reaction times. $Eu(fod)_3$ plays the role of a soluble, efficient but more expensive catalyst.

Preliminary studies show that lanthanide chlorides are also efficient catalysts in oxirane ring-opening[5]. For example, propylene oxide reacts with Me_3SiCN (8 mmol each - eq. [3]) to yield 3-methyl-3-[(trimethylsilyl)oxy]propionitrile[11] in the presence of 0.1 mol equiv. $LnCl_3$ in CH_2Cl_2 (2 ml) at room temperature (Ln = Sm : 5 h, 88% ; Ln = Ce : 8 h, 85% ; Ln = La : 18 h, 77%).

Our research efforts continue in the field of the application of lanthanides as catalysts in organic synthesis including enantioselective C-C bond formation.

Acknowledgements

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