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OXIRANE RING OPENING REACTIONS WITH THIOLS CATALYZED BY LANTHANIDE COMPLEXES

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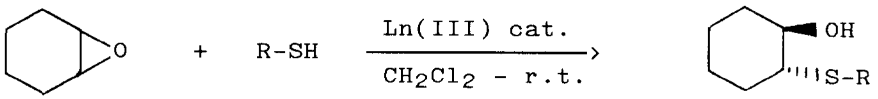
Summary : $LnCl_3$ (Ln = Ce,Sm) and $Eu(fod)_3$ act as Lewis-acid catalysts in stereo- and regioselective epoxide ring opening reactions with thiols under mild conditions in CH_2Cl_2.

The application of lanthanide chemistry to organic synthesis has been growing considerably since the late seventies[1]. Lanthanide complexes have been used as Lewis-acid catalysts in some organic transformations such as the Diels-Alder[2] and the Friedel-Crafts[3] reactions. Recently, their applications to the cross-aldol addition reaction of aldehydes to silyl enol ethers and the cyanohydrin formation have been reported[4]. Another type of reaction, the oxirane ring opening with various nucleophiles (eg : Me_3SiCN, Me_3SiN_3, RSH, etc.) has been reported previously to be promoted by certain Lewis acids such as $AlCl_3$[5], $AlEt_3$[6], $ZnCl_2$[7], ZnI_2[8], $Ti(O\text{-}iPr)_4$[9], $VO(O\text{-}iPr)_4$[10], etc., usually necessitating long reaction times (5-7 days) at ambient temperature. Anhydrous lanthanide trichlorides, which are considered as hard acids[1], are now reported to catalyze the oxirane ring opening reaction with thiols stereo- or regio-selectively under mild conditions.

Two types of Ln-catalyzed processes were considered : (i) the stereoselective reaction of cyclohexene oxide with certain thiols (eqn.(1)) and (ii) the regioselective alkyl-monosubstituted epoxide ring opening



(1)

TABLE (I) : Cyclohexene oxide ring opening with thiols catalyzed by Ln(III) complexes.

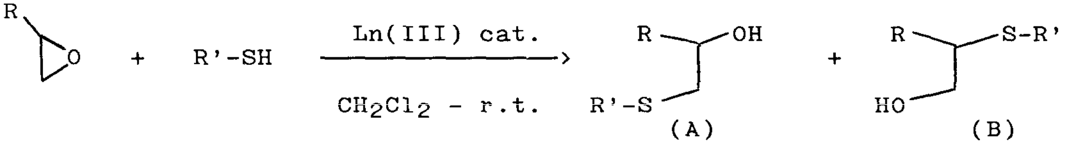
Entry N°	R	Catalyst (mol equiv.)	Rxn. Time (h)	Isolated yield (%)
1	Phenyl	$SmCl_3$ (0.1)	48	84
2	Phenyl	$CeCl_3$ (0.1)	72	77
3	Phenyl	Eu(fod)$_3^a$ (0.05)	120	41
4	p-Tolyl	$SmCl_3$ (0.1)	72	84
5	p-Tolyl	Eu(fod)$_3^a$ (0.05)	120	49
6	p-Anisyl	$SmCl_3$ (0.1)	48	81
7	p-Anisyl	$CeCl_3$ (0.1)	48	74
8	Benzyl	$SmCl_3$ (0.1)	120	78
9	Benzyl	$CeCl_3$ (0.1)	120	75

a : Homogeneous solution. Eu(fod)$_3$ = tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium (III).

with them (eqn.(2)). The results are summarized in Tables (I) and (II) respectively.

A typical preparative procedure (equations (1) and (2)) involves the addition of equimolar amounts of reagents (eg : cyclohexene oxide and phenyl thiol, 8 mmol each-Table (I), entries (1) and (2)) to a suspension of $LnCl_3$ (0.1 mol equiv.) in CH_2Cl_2 (2 ml) under argon at ambient temperature. After the given time[11] (Tables (I) and (II)) the solvent was evaporated in vacuo and the residue was extracted with hexane/ethyl acetate (4:1) and then chromatographed (flash/SiO_2,hex./EtOAc = 4:1). The isolated yields of the products are summarized in Tables (I) and (II). Their identity was confirmed by ^1H and ^{13}C NMR spectroscopy[12-14]. When $SmCl_3$ or $CeCl_3$ are used as catalysts, traces of cis-2-thioethercyclohexan-1-ol (ca.5%) can be detected by NMR[15].

It is worth mentioning that when Eu(fod)$_3$ is used as catalyst in the reaction of cyclohexene oxide with a thiol (eqn.(1)), the trans-2-thioethercyclohexan-1-ol appears to be the only product as shown by ^1H and ^{13}C



(2)

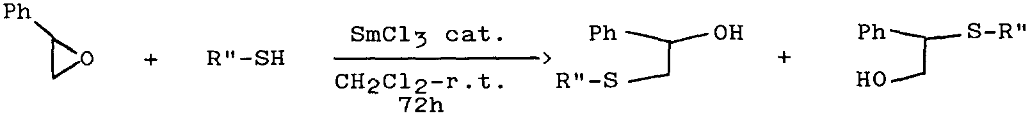
TABLE (II) : Regioselective oxirane ring opening with thiols catalyzed by Ln(III) complexes.

Entry N°	R	R'	Catalyst (mol equiv.)	Rxn.Time (h)	Isolated yield (A)(%)	(B)(%)
1	Me	p-Anisyl	$SmCl_3$ (0.1)	72	84	a
2	Me	Benzyl	$SmCl_3$ (0.1)	72	81	a
3	Et	p-Anisyl	$SmCl_3$ (0.1)	72	83	a
4	Et	Benzyl	$SmCl_3$ (0.1)	72	77	a
5	Me	p-Tolyl	$CeCl_3$ (0.1)	72	82	a
6	Me	p-Tolyl	$Eu(fod)_3^b$ (0.05)	120	51	a

a : Traces of (B) were not observed by TLC. b : Homogeneous solution.

NMR spectroscopy (Table (I), entries (3) and (5)). The enantioselective version of this reaction using chiral lanthanide reagents has not been developed yet[16].

Preliminary experiments suggest that the reaction of aryl-substituted epoxides with thiols catalyzed by $LnCl_3$ in CH_2Cl_2 is less selective than in the cases reported in Table (II). For example, styrene oxide reacts with benzyl thiol in the presence of $SmCl_3$ (0.1 mol equiv.) yielding a mixture of products[17] (eqn. (3) ; A'/B' = 3:1 ; 75% total isolated yield). Low selectivity for this reaction when using other catalysts has also been reported[18].



(3)

R" = $PhCH_2$ (A') (B')

We are currently investigating further applications of lanthanide complexes to organic synthesis.

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(11) The reaction progress was followed by TLC (SiO_2,hex./EtOAc = 4:1).

(12) Typical spectral data, eg. Table (I), entry (4) : ^{1}H-NMR ($CDCl_3$, 250MHz,δ) : 7.4(m,2H, phenyl), 7.1(m,2H,phenyl), 3.7(m,1H, $>$C$\underline{H}$-OH, cis), 3.2(m,1H, $>$C$\underline{H}$-OH,trans), 2.6(m,1H, CH-S-),2.3(s,3H,Me),2.0(m,2H,-CH_2-),1.6(m,2H, -CH_2-),1.2(m,4H,-CH_2-). ^{13}C-NMR ($CDCl_3$, 62.9MHz,ppm) : trans : 138,134,130,128,71.5,56.0,33.5,32.5,26.5,24.5,21.0 (all s); cis : 138,134,130,128,73.0,66.5,35.0,33.5,25.5,23.5,21.0(all s).

(13) Typical spectral data, eg. Table (II), entry (4), product (A) : ^{1}H-NMR($CDCl_3$,250MHz, δ) : 7.3(m,5H,phenyl), 3.7(s,2H,-S-C$\underline{H_2}$-Ph), 3.5(m,1H, $>$C$\underline{H}$-OH),2.6(dd,1H,J=3.5, 14.3Hz, -S-C$\underline{H_A}H_B$-C-OH),2.35(dd,1H,J=18.8,32.6Hz,-S-C$H_A\underline{H_B}$-C-OH), 1.5(m,2H,MeC$\underline{H_2}$-),0.85(t,3H,Me). ^{13}C-NMR ($CDCl_3$,62.9MHz,ppm) : 139.0,129.5,128.5,127.0,71.5,38.5,36.5,29.0,10.5(all s).

(14) Authentic cis- and trans-2-thioethercyclohexan-1-ols : R.L.Crumbie, B.S.Deal,J.E.Nemorin and D.D.Ridley, Aust.J.Chem., 31,1965 (1978) ; G.H.Posner, D.Z.Rogers, C.M.Kinzig and G.M.Gurria, Tetrahedron Lett., 16, 3597 (1975).

(15) The trans- and cis- products (Table (I)) appeared to be inseparable by TLC as well as by flash chromatography.

(16) For an enantioselective ring opening reaction of cyclohexene oxide with thiols catalyzed by chiral zinc complexes, see : H.Yamashita and T.Mukaiyama,Chem.Lett., 1643 (1985).

(17) Products (A') and (B') were separated by each other (flash/SiO_2, hex./EtOAc =4:1) and dully characterized.

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