Communications to the Editor *Chem. Pharm. Bull.* **42**(2) 402—404 (1994) Vol. 42, No. 2

NOVEL REDUCTION OF CARBOXYLIC ACID, ESTER, AMIDE AND NITRILE WITH SAMARIUM OR YTTERIBIUM METAL—HYDROCHLORIC ACID SYSTEM

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The reduction of organic functionalities with a samarium or ytteribium metal—hydrochloric acid system was investigated. Carboxylic acid, ester, amide and nitrile were rapidly reduced to the corresponding alcohol or primary amine with samarium or ytteribium metal in the presence of hydrochloric acid at room temperature under an argon atmosphere in good yields. Carboxylic acid was similarly reduced to alcohol with a magnesium or yttrium—hydrochloric acid system.

KEYWORDS reduction; samarium—hydrochloric acid system; ytteribium—hydrochloric acid system; carboxylic acid; ester; nitrile

Lanthanoid reagents are useful for synthetic organic chemistry, with their unique characteristics such as strong reducing potential, oxophilicity and Lewis acidity.[1)] Especially, because of high reduction potential values as well as Mg and some other metals, it is assumed that lanthanoid metals have powerful reducing property in acidic medium, so an application of lanthanoid metals for reduction of organic functionalities is an interesting subject. Recently, Fujiwara et al.[2a)] and Imamoto[2b)] achieved the reduction of some functional groups by the use of Yb, Sm or Ce metal. However, we know of no previous report on reduction of organic functionalities using the combination of lanthanoid metal and mineral acid. Taking into account the decreasing of reduction potential values of the many organic functional groups, it is assumed that a lanthanoid metal—acid system is able to use as the strong reducing agent for the organic functional groups. It has been reported that a variety of organic functionalities was rapidly reduced with the SmI_2—base, acid and H_2O systems at room temperature.[3)] As a continuation of these works, the present paper deals with the reduction of carboxylic acids, esters, amides and nitriles with Sm or Yb—hydrochloric acid system (Chart 1).

$$\text{R-COOH, R-COOR'} \xrightarrow{\text{lanthanoid metal, 10-20\% HCl, RT, Ar}} \text{R-CH}_2\text{OH}$$

$$\text{R-CN, R-CONH}_2 \longrightarrow \text{R-CH}_2\text{NH}_2\ (+\ \text{R-CH}_2\text{OH})$$

Chart 1

The results are summarized in Tables I and II. In general, carboxylic acid is hardly reduced into alcohol with the ordinary reducing reagents except for diborane, $LiAlH_4$ and a few of the metal complex hydrides. And little work has been reported on the direct reduction of carboxylic acid into alcohol with the combination of lanthanoid metal and acid. However, as is shown in Table I, aromatic carboxylic acids (**1**—**7**) were rapidly reduced to the corresponding alcohols (**11**—**19**) with 8 mol eq of Sm or Yb metal (powder, 40 mesh) in the presence of 10% hydrochloric acid at room temperature under an argon atmosphere, with good yield. However, the reduction of aliphatic carboxylic acids (**8**—**10**) with these systems was generally unsatisfactory in yield. In these reactions, chloro, nitro and carbamoyl functionalities were also reduced to give the corresponding products. Interestingly, acid **1** was similarly reduced with Y, La, Pr, Nd or Gd metal (powder, 40 mesh)—10% hydrochloric acid system to afford alcohol **11** in 48, 82, 79, 66 and 69% yields, respectively. However, similar reductions using the other lanthanoid metals gave more moderate yields.

On the other hand, the oxidation-reduction potential value (E^0, V) of $Mg(Mg^{2+})$ (−2.37) or $Y(Y^{3+})$ (−2.37) metal is comparable to that of lanthanoid metals, such as $Sm[(Sm^{3+})$ −2.41], and $Yb[(Yb^{3+})$ −2.27].[4)] Taking into account these facts and the above results, our next trial was conducted with the reaction of acid (**1**) with Mg or Y metal—hydrochloric acid system. Acid **1** (0.5 mmol, in 2 ml of MeOH) was unexpectedly reduced with 20 mmol of Mg metal (powder, 50 mesh)–20% hydrochloric acid (8 ml) within 5 minutes at room temperature under an argon atmosphere to give alcohol **11** in 82% yield. Moreover, acid **1** was reduced with Y metal (4 mmol, powder, 40 mesh)–10% hydrochloric acid (4 ml) under similar conditions to afford alcohol **11** in 89% yield. We know of no previous report on reduction of carboxylic acid into alcohol using Mg or Y metal—hydrochloric acid system, so it can be presumed that this method also provides a useful and convenient route for the direct reduction of carboxylic acid.

Table I. Reduction of Carboxylic Acids with Sm or Yb–HCl System[a)]

R-COOH[b)] R (No.)	Metal (mmol)	HCl (%)	HCl (ml)	Time (min)	Product (No.)	Yield (%)[c)] (Sm)	Yield (%)[c)] (Yb)
Ph (**1**)	4	10	4	5	$PhCH_2OH$ (**11**)	99	
Ph (**1**)	4	10	3	10	$PhCH_2OH$ (**11**)		99
$2\text{-}MeC_6H_4$ (**2**)	4	10	4	10	$2\text{-}MeC_6H_4CH_2OH$ (**12**)	94	73
$4\text{-}MeC_6H_4$ (**3**)	4	10	4	10	$4\text{-}MeC_6H_4CH_2OH$ (**13**)	97	67
$2\text{-}ClC_6H_4$ (**4**)	4	10	4	10	$2\text{-}ClC_6H_4CH_2OH$ (**14**)	75	52
					$PhCH_2OH$ (**11**)	22	43
					$PhCOOH$ (**1**)	1	1
$2\text{-}O_2NC_6H_4$ (**5**)	4	10	4	10	$2\text{-}H_2NC_6H_4CH_2OH$ (**15**)	59	27
					$2\text{-}H_2NC_6H_4COOH$ (**6**)	20	48
$2\text{-}H_2NC_6H_4$ (**6**)	4	10	4	10	$2\text{-}H_2NC_6H_4CH_2OH$ (**15**)	88	73
$2\text{-}AcNHC_6H_4$ (**7**)	4	10	4	10	$2\text{-}H_2NC_6H_4CH_2OH$ (**15**)	87	92
					$2\text{-}AcNHC_6H_4CH_2OH$ (**16**)	8	3
$PhCH_2$ (**8**)	4	10	4	30	$PHCH_2CH_2OH$ (**17**)	41	12
$PhCH_2CH_2$ (**9**)	4	10	4	30	$Ph(CH_2)_3OH$ (**18**)	34	6
$Me(CH_2)_6$ (**10**)	4	10	4	30	$Me(CH_2)_7OH$ (**19**)	39	9

a) To a suspension of acid and lanthanoid metal in MeOH was added 10–20% hydrochloric acid with stirring for 5 min at room temperature under Ar. b) Substrate (0.5 mmol) was dissolved in 2 ml of MeOH (anthranilic acid **6** was dissolved in 1 ml of 10% hydrochloric acid). c) Isolated yield.

Furthermore, as shown in Table II, ester, amide and nitrile were similarly reduced with Sm or Yb—hydrochloric acid system. Esters (**20**–**22**) were rapidly reduced with these systems under similar conditions to give the corresponding alcohols in good yield. On the similar reductions of amides (**23**–**25**), the corresponding amines (**30**–**32**) and alcohols were obtained. Hydrazide and hydroxamic acid were also reduced under similar conditions. However, aliphatic amide gave only small amounts of amine under similar conditions. Interestingly, nitriles (**26**–**28**) were rapidly reduced with these systems to afford only the corresponding primary amines in quantitative yields. However, similar reductions of aliphatic nitriles afforded primary amines in low yield.

As a general procedure, 6–8 mol eq of lanthanoid metal was added to MeOH (1-2 ml) solution of substrate (0.5 mmol) at room temperature under an argon atmosphere, then 2–4 ml of 10–20% hydrochloric acid was added to the mixture dropwise with stirring within 5–30 s. After the exothermic reaction subsided, the mixture was stirred for 5–30 min at room temperature. After the usual work-up, the reduction products were obtained as shown in Tables I and II.

Though the actual reductant and detailed mechanism of these systems remains obscure at the present stage, it is assumed that the present reduction by lanthanoid metal—hydrochloric acid system proceeds also by single electron transfer of active low valence lanthanoid species ($LnCl^{5)}$ or $LnCl_2$) generated from lanthanoid metal with hydrochloric acid, in addition to electron transfer from lanthanoid metal in acidic medium.

It is noteworthy that the new lanthanoid metal—hydrochloric acid system can be used for the direct conversion of carboxylic acid, ester, amide and nitrile into the corresponding alcohols or primary amines under mild conditions in good yield, so this system provides a useful and facile synthetic route in synthetic chemistry.

Further studies on the reduction of other functionalities with this system are in progress.

Table II. Reduction of the Other Functionalities with Sm or Yb—HCl System[a)]

Substrate (No.)[b)]	Metal (eq mol)	HCl (%)	HCl (ml)	Time (min)	Product (No.)	Yield (%)[c)] (Sm)	Yield (%)[c)] (Yb)
PhCOOMe (**20**)	8	10	4	10	$PhCH_2OH$ (**11**)	87	
PhCOOMe (**20**)	8	10	3	10	$PhCH_2OH$ (**11**)		69
$2\text{-}MeC_6H_4COOMe$ (**21**)	8	10	4	5	$2\text{-}MeC_6H_4CH_2OH$ (**12**)	72	
$4\text{-}H_2NC_6H_4COOMe$ (**22**)	8	10	4	5	$4\text{-}H_2NC_6H_4CH_2OH$ (**29**)	70	
$PhCONH_2$ (**23**)	6	20	3	10	$PhCH_2NH_2$ (**30**)	64	61
					$PhCH_2OH$ (**11**)	29	23
$2\text{-}MeC_6H_4CONH_2$ (**24**)	6	10	3	5	$2\text{-}MeC_6H_4CH_2NH_2$ (**31**)	50	
					$2\text{-}MeC_6H_4CH_2OH$ (**12**)	34	
$4\text{-}ClC_6H_4CONH_2$ (**25**)	6	10	3	5	$4\text{-}ClC_6H_4CH_2NH_2$ (**32**)	47[d)]	
					$4\text{-}ClC_6H_4CH_2OH$ (**33**)	50	
PhCN (**26**)	8	10	3	5	$PhCH_2NH_2$ (**30**)	99	
PhCN (**26**)	8	10	3	10	$PhCH_2NH_2$ (**30**)		88
$2\text{-}MeC_6H_4CN$ (**27**)	8	10	3	5	$2\text{-}MeC_6H_4CH_2NH_2$ (**31**)	98	
$4\text{-}MeC_6H_4CN$ (**28**)	8	10	3	5	$4\text{-}MeC_6H_4CH_2NH_2$ (**34**)	92	

a) To a suspension of substrate and Sm or Yb metal (powder) was added hydrochloric acid with stirring at room temperature under Ar. b) 0.5 mmol. c) Yield was determined by gas chromatography. d) By-product; trace of benzylamine (**30**).

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(Received October 5, 1993; accepted December 14, 1993)