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REDUCTION USING SAMARIUM DIIODIDE-BASE SYSTEM

Yasuko Kamochi and Tadahiro Kudo*
Daiichi College of Pharmaceutical Sciences, 22-1 Tamagawa-cho,
Minami-ku, Fukuoka 815, Japan

Summary: Ester, anhydride, amide, oxime and carbonyl compound were reduced to the corresponding alcohols as the major products with samarium diiodide under basic medium at room temperature.

Recently, the chemistry of samarium diiodide (SmI_2) has become a useful reagent in organic synthesis.[1)] However, the reduction of carboxylic acid, ester, anhydride and amide to alcohol with SmI_2 has not been previously reported. We reported in the preceding paper that carboxylic acids were immediately reduced to the corresponding alcohols with SmI_2 in the presence of sodium hydroxide.[2)] Based on our previous observation that the electron transfer from SmI_2 was highly promoted by coexisting base, such as sodium hydroxide, lithium amide and ammonia,[2)] we report herein the reduction of ester, anhydride, amide, oxime and carbonyl compound with SmI_2 in the presence of base ($LiNH_2$, $LiOCH_3$ and KOH), as is indicated in the following schemes:

$$PhCO\text{-}R^1 \xrightarrow[\text{THF-R'OH, RT}]{SmI_2\text{, Base}} PhCH_2OH\ (+\ (PhCH(OH))_2 + PhCH_2CH(OH)Ph + PhCH_2COPh)$$

Ph: Phenyl R^1: CH_3O, PhCOO, PhCH(OH), PhCO Base. $LiNH_2$, $LiOCH_3$ or KOH
R': CH_3, H

$$PhCONH\text{-}R^2 \xrightarrow{SmI_2\text{, Base, THF-R'OH, RT}} PhCH_2OH + PhCH_2NH\text{-}R^2$$

$$PhCH{=}NOH \xrightarrow{SmI_2\text{, Base, THF-R'OH, RT}} PhCH_2NH_2$$

R^2: H, Ph

In the general procedure, a methanol (2-4 ml) solution of compounds as shown in Table 1 and 2 were added dropwise to $LiNH_2$ ($LiOCH_3$ or KOH) (6-8 mol eq) suspended in a SmI_2-THF (4 mol eq, 0.1 M) solution at room temperature under an atmosphere of argon. After the typical blue colour of SmI_2 was decoloured, the reaction mixture was poured into an aqueous sodium hydroxide (50%, 5-7 ml) and stirred at room temperature for 10 minutes. The THF layer was separated and the aqueous layer was extracted with ether. After the usual work-up, followed by column chromatographic purification (SiO_2) gave the reduction products as shown in Table 1 and 2.

Kagan et al.[3)] reported that ester could not be reduced by SmI_2. However, as shown in

Table 1, reduction of methyl benzoate (**1**) proceeded with 4 equivalent moles of SmI$_2$ in THF containing methanol (hydrogen source) under basic medium (base: LiNH$_2$, LiOCH$_3$ and KOH) to afford benzyl alcohol (**5**). Similarly, benzoic anhydride (**2**) was reduced to give alcohol **5** as major product (Entry 4 and 6) accompanied with benzaldehyde (**6**).4) On the other hand, benzoin (**3**) was rapidly reduced under the similar conditions to afford 1,2-diphenyl-1,2-ethanediol (**7**) and 1,2-diphenylethanol (**8**), and the similar reaction of benzil (**4**) gave deoxybenzoin (**9**) as major product.5)

Table 1. Reduction of a Variety of Carbonyl Compounds with SmI$_2$ under Basic Medium at Room Temperature a)

Entry (No.)	Compound (No.) b)	SmI$_2$ c) (mmol)	Base(mmol)	Time (min)	Product (No.)	Yield d) (%)
1	PhCOOCH$_3$ e) (**1**)	1	LiNH$_2$ (3)	14	PhCH$_2$OH (**5**)	64
2	PhCOOCH$_3$ (**1**)	2	LiOCH$_3$ (4)	27	PHCH$_2$OH (**5**)	59
3	PhCOOCH$_3$ (**1**)	2	KOH (4)	8	PHCH$_2$OH (**5**)	68
4	(PhCO)$_2$O e) (**2**)	1	LiNH$_2$ (3)	3	PhCH$_2$OH (**5**)	62
					PhCHO (**6**)	4
					PhCOOCH$_3$ (**1**)	4 f)
5	(PhCO)$_2$O (**2**)	2	LiOCH$_3$ (4)	46	PhCH$_2$OH (**5**)	12
					PhCHO (**6**)	38
					PhCOOCH$_3$ (**1**)	52 f)
6	(PhCO)$_2$O (**2**)	2	KOH (4)	7.6	PhCH$_2$OH (**5**)	50
					PhCHO (**6**)	14
					PhCOOCH$_3$ (**1**)	16 f)
7	PhCOCH(OH)Ph e) (**3**)	1	LiNH$_2$ (3)	3(sec)	PhCH(OH)CH(OH)Ph(**7**)	36
					PhCH$_2$CH(OH)Ph (**8**)	40
					PhCH$_2$COPh (**9**)	trace
					PhCH$_2$OH (**5**)	trace
8	PhCOCOPh e) (**4**)	1	LiNH$_2$ (3)	25	PhCH(OH)CH(OH)Ph(**7**)	10
					PhCH$_2$CH(OH)Ph (**8**)	5
					PhCH$_2$COPh (**9**)	45
					PhCH$_2$OH (**5**)	13

a) Reactions were carried out under argon. b) Compounds (0.5 mmol) were dissolved in methanol (2 ml). c) SmI$_2$ in THF (0.1M). d) Isolated yields. e) Compounds (0.25 mmol) were dissolved in methanol (1 ml). f) Side reaction proceeded.

Little work has been reported on the reduction of amide into alcohol, except for the reduction with sodium bis(2-methoxyethoxy)aluminum hydride,6) sodium-ethanol system7) and catalytic hydrogenation with copper chromite.8) Our next trial was conducted with the reaction of amide and oxime with SmI$_2$ under the similar conditions.

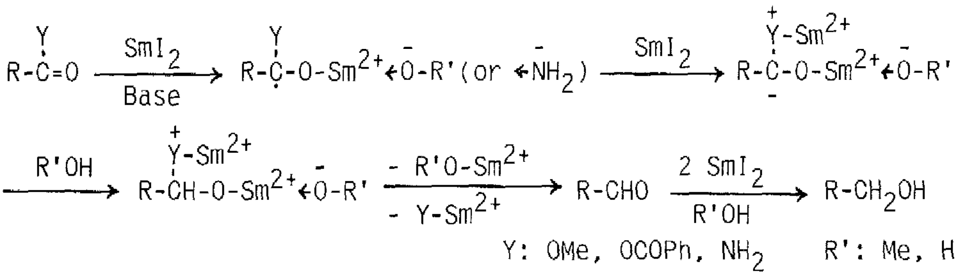
Interestingly, as shown in Table 2, benzamide (**10**), N-phenylbenzamide (**11**), α-phenylacetamide (**12**) and 3-phenylpropionamide (**13**) were reduced with SmI_2 in the similar conditions to give the corresponding alcohols **5**, (**18**) and (**20**) as the major products accompanied by the corresponding amines (**15**), (**16**), (**17**), (**19**) and (**21**). Benzaldehyde oxime (**14**) afforded benzylamine **15** under the similar conditions in a moderate yield.[9]

Table 2. Reduction of Amides and Oxime with SmI_2 under Basic Medium at Room Temperature[a]

Entry (No.)	Compound (No.)[b]	SmI_2[c] (mmol)	Base(mmol)	Time (sec)	Product (No.)	Yield[d] (%)
1	$PhCONH_2$[e] (**10**)	1	$LiNH_2$ (3)	180	$PhCH_2OH$ (**5**)	81
					$PhCH_2NH_2$ (**15**)	8
2	$PhCONH_2$ (**10**)	1	$LiNH_2$ (3)	32	$PhCH_2OH$ (**5**)	28
					$PhCH_2NH_2$ (**15**)	trace
3	$PhCONH_2$ (**10**)	2	$LiNH_2$[f] (3)	3	$PhCH_2OH$ (**5**)	72
					$PhCH_2NH_2$ (**15**)	5
4	$PhCONH_2$ (**10**)	2	$LiOCH_3$ (4)	510	$PhCH_2OH$ (**5**)	72
					$PhCH_2NH_2$ (**15**)	4
5	$PhCONH_2$ (**10**)	2	KOH (4)	123	$PhCH_2OH$ (**5**)	82
					$PhCH_2NH_2$ (**15**)	8
6	PhCONHPh[e] (**11**)	1	$LiNH_2$ (3)	60	$PhCH_2OH$ (**5**)	31
					$PhCH_2NHPh$ (**16**)	20
					$PhNH_2$ (**17**)	28
7	$PhCH_2CONH_2$ (**12**)	2	$LiNH_2$ (3)	77 min	$PhCH_2CH_2OH$ (**18**)	30
					$PhCH_2CH_2NH_2$ (**19**)	2
8	$PhCH_2CONH_2$ (**12**)	2	$LiNH_2$[f] (3)	68	$PHCH_2CH_2OH$ (**18**)	56
					$PhCH_2CH_2NH_2$ (**19**)	2
9	$PhCH_2CH_2CONH_2$ (**13**)	2	$LiNH_2$ (3)	83 min	$PhCH_2CH_2CH_2OH$ (**20**)	24
					$PhCH_2CH_2CH_2NH_2$ (**21**)	2
10	$PhCH_2CH_2CONH_2$ (**13**)	2	$LiNH_2$[f] (3)	111	$PhCH_2CH_2CH_2OH$ (**20**)	69
					$PhCH_2CH_2CH_2NH_2$ (**21**)	trace
11	PhCH=NOH (**14**)	2	$LiNH_2$ (4)	3	$PhCH_2NH_2$ (**15**)	45
					$PhCH_2OH$ (**5**)	3

a) Reactions were carried out under argon. b) Compounds (0.5 mmol) were dissolved in methanol (2 ml). c) SmI_2 in THF (0.1 M). d) Isolated yields. e) Compounds (0.25 mmol) were dissolved in methanol (1 ml). f) After 1 ml of H_2O was added to a suspension of SmI_2 and $LiNH_2$ in THF, a methanol (0.5 ml) solution of substrate was added.

As mentioned above, it was revealed that addition of base accelerated the electron transfer process and protic solvent improved the yield. Particularly, it seems that base possessed the important role in these reductions since these reductions did not proceed in the absence of base. Compared with the relative reactivity of the tested SmI_2-base systems, SmI_2-$LiOCH_3$ system was inferior to the other systems for reaction time-consuming. Though detailed mechanism has remained obscure, it is presumed that reductant may also be R_1-Sm-R_2 (R_1, R_2: I, NH_2, OH or OCH_3) in addition to SmI_2. A possible mechanism is proposed in Scheme 1.



Y: OMe, OCOPh, NH_2 R': Me, H

Scheme 1

It is noteworthy that the present method can be used for the conversion of ester, anhydride and amide to alcohol by the direct and facile reduction, so the SmI_2-base system provides a useful and simple synthetic route in synthetic chemistry.

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