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NOVEL AND FACILE REDUCTION OF PHENOL DERIVATIVES WITH SAMARIUM DIIODIDE–BASE SYSTEM

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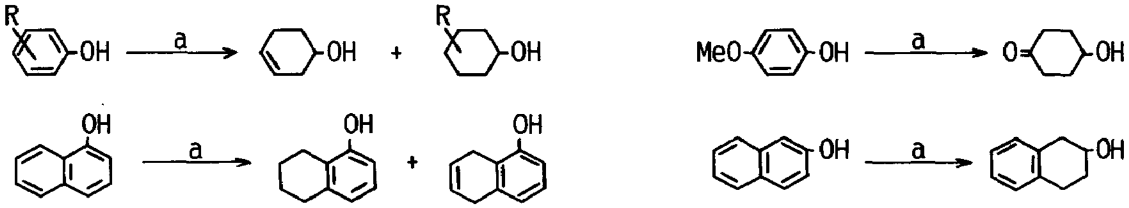
Summary: Phenol was rapidly reduced with samarium diiodide–base system in the presence of protic solvent at room temperature to afford 3-cyclohexen-1-ol accompanied by cyclohexanol. The similar reduction of 4-methoxyphenol and 2-naphthol gave 4-hydroxycyclohexanone and 1,2,3,4-tetrahydro-2-naphthol in excellent yield, respectively.

Recently, samarium diiodide (SmI_2) has been attracting much attention as useful reagent for organic synthesis utilizing unique characteristics such as strong reducing power, a high coordination number and oxophilicity.[1) However, the reduction of aromatic compounds with SmI_2 has not been previously reported. We reported in the preceding papers that a variety of organic functionalities were immediately reduced to the corresponding products with SmI_2 in good yield in the presence of base,[2) acid[3) or H_2O.[4) Base on our previous observation that the electron transfer from SmI_2 was highly promoted by coexisting additive, such as base, acid and H_2O, the present paper deals with the reduction of phenol and its derivatives with SmI_2–base system in the presence of protic solvent, as is indicated in the following scheme.

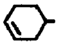


a: 6 SmI_2/Base/THF/R'OH/Ar/RT   R: H, Cl, OH   R'OH: H_2O, MeOH   Base: KOH, LiOMe

In general, the hydrogenation of phenols in vapor or liquid phase over Pt or Ni catalyst yields cyclohexanones, cyclohexanols or cyclohexanes,[5) Birch reduction of phenol gives cyclohexanone[6) and Benkeser reduction of phenol also affords the mixture of cyclohexane and cyclohexanol.[7) Taking into account of the utility of direct reduction of phenol derivatives to alcohols, the development of a facile method has been desirable from a synthetic viewpoint.

The reduction of phenol (**1**) did not proceed with SmI_2 alone or SmI_2-protic solvent (H_2O or MeOH) even after 5 hours. Similarly, phenol (**1**) was unaffected with SmI_2–acid system (such as H_3PO_4 or 20% HCl aq.) under similar conditions. However, as shown in Table 1, phenol (**1**) was rapidly reduced with 6 equivalent moles of SmI_2 in THF containing protic solvent in the presence of base to give 3-cyclohexen-1-ol (**2**)[8) as a major product accompanied by cyclohexanol (**3**). Among the bases tested for reduction of phenol (**1**) in these SmI_2–base systems, the SmI_2—KOH or LiOMe system yielded the better results (Entries 5 and 9-11) than the other tested SmI_2—base systems. The reductions of phenol (**1**) with this system in H_2O exhibited the shorter reaction time (Entry 8 and 9) compared with those in MeOH.

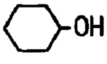
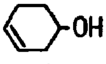
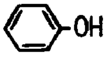
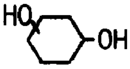
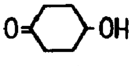
Table 1. Reduction of Phenol (**1**) with SmI_2—Base System[a)]

Entry (No.)	SmI_2[b)] (eq mol)	Base (eq mol)	ROH (ml)	Time	Product (No.)/Yield (%)	
					-OH (3)	-OH (2)
1	2	KOH (4)	MeOH (2)	20 min	3	38
2	4	KOH (8)	MeOH (3)	30 min	10	73
3	6	KOH (12)	MeOH (4)	45 min	13	78
4	10	KOH (20)	MeOH (4)	100 min	36	63
5	6	LiOMe (12)	MeOH (2)	6 h	5	87
6	6	KOH (12)	H_2O (2)	31 min	19	62
7	6	KOH (24)	H_2O (4)	13 min	14	76
8	6	KOH (48)	H_2O (6)	5 min	11	78
9	8	KOH (16)	H_2O (6)	1 min	16	83
10	10	KOH (20)	H_2O (6)	2 min	33	64
11[c)]	4	KOH (8)	10%KOH (3)	18 min	15	83
12[c)]	6	KOH (12)	10%KOH (3)	30 min	16	82
13[d)]	6	KOH (1)	50%KOH (1)	100 min	21	76
14[d)]	6	KOH (1)	50%KOH (4)	6 min	33	65
15[e)]	6	KOH (1)	50%KOH (4)	30 s	15	81

a) ROH was added to a THF solution of substrate (1 mmol), base and SmI_2 with stirring at room temperature under an argon atmosphere. b) 0.1 M in THF. c) A solution of substrate in 3 ml of 10% KOH aq. was added to a THF solution of SmI_2 and KOH. d) A aqueous solution of KOH (50%, 1 ml) was added to a THF solution of phenol and SmI_2. e) Reflux in THF.

On the reduction of substituted phenols by SmI_2—50% KOH, both the reductive elimination of functional groups and the reduction of aromatic nucleus proceeded. As shown in Table 2, chlorophenols (**4-6**) and 1,2-benzenediol (**7**) were reduced with this system to give 3-cyclohexen-1-ol (**2**) as major product (Entries 1-4). Contrary to these results, 1,4-benzenediol (**11**) was reduced to 1,4-cyclohexanediol (**12**) alone under the similar conditions in excellent yield (Entry 6). However, 1,3-benzenediol (**8**) gave 1,3-cyclohexanediol (**10**) in low yield (Entry 5). As described above, taking into account of the formation of 3-cyclohexen-1-ol (**2**) from phenol derivatives, it was presumed that the similar reduction of 3- or 4-alkoxyphenol afford 3- or 4-hydroxycyclohexanone since the intermediate of 3- or 4-alkoxy-3-cyclohexen-1-ol was hydrolyzed to these hydroxy ketones in the course of post-treatment by H_3O^+. In fact, 4-methoxyphenol (**13**) was reduced with SmI_2—50% KOH system under similar conditions followed by the usual treatment to give 4-hydroxycyclohexanone (**14**) in excellent yield (Entry 7).[9)] However, the similar reduction of 3-methoxyphenol gave 3-hydroxycyclohexanone in 26% yield accompanied by the other reduced products.

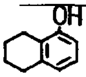
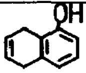
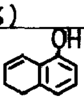
Table 2. Reduction of Phenols with SmI_2–50% KOH System[a]

Entry (No.)	R (No.)	SmI_2 (eq mol)	50%KOH (ml)	Time (min)	Product (No.)/Yield (%)				
					 (**3**)	 (**2**)	 (**1**)		 (**14**)
1	2-Cl (**4**)	6	2	3	13	75	9		
2	3-Cl (**5**)	6	2	2	11	70	13		
3[b]	4-Cl (**6**)	6	2	3.5	8	52	35		
4	2-OH (**7**)	6	2	5	9	49		(**9**) 3	
5	3-OH (**8**)	6	2	3	4	1		(**10**) 39	
6	4-OH (**11**)	6	2	3				(**12**) 98	
7	4-OMe (**13**)	6	2	7					97

a) After a THF solution of substrate (0.5 mmol), KOH (0.5–1 mmol) and SmI_2 (0.1 M in THF) was stirred for a few minutes at room temperature under an argon atmosphere, a aqueous solution of KOH (50%) was added. b) By-product; 4-chlorotetrahydrophenol 3% (from mass data, unidentified).

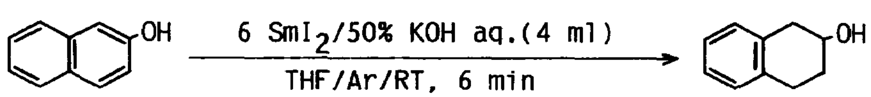
On the similar reaction of naphthols (Table 3), 1-naphthol (**15**) was rapidly reduced with SmI_2–50% KOH system to give 5,6,7,8-tetrahydro-1-naphthol (**17**) and 5,8-dihydro-1-naphthol (**18**) in 49% and 50% yields, respectively (Entry 3). 5,6-Dihydro-1-naphthol (**19**) was also obtained decreasing amounts of SmI_2 (Entries 1 and 2), so it appears that tetrahydro product **17** was reduced via dihydro product **18** increasing amounts of SmI_2.

Table 3. Reduction of 1-Naphthol (**15**) with SmI_2–50% KOH System[a]

Entry (No.)	SmI_2 (eq mol)	50%KOH (ml)	Time (min)	Product /Yield (%)		
				 (**17**)	 (**18**)	 (**19**)
1	2	1	0.5	2	44	29
2	3	1	1	8	48	25
3	6	4	5	49	50	

a) A THF solution of SmI_2 (0.1 M in THF) was added to a THF solution (1 ml) of substrate (1 mmol) and KOH (1 mmol) with stirring under an argon atmosphere at room temperature, then a aqueous solution of KOH (50%) was added.

In contrast to these results, 2-naphthol (**16**) was reduced under similar conditions to afford 1,2,3,4-tetrahydro-2-naphthol (**20**) alone in excellent yield (95%).



(**16**) 1 mmol (**20**) 95%

As a typical procedure, a THF solution of substrate (1 mmol), SmI_2 (6 eq. mol, 0.1 M in THF) and KOH (1-2 mmol) was stirred for a few minutes at room temperature under an argon atmosphere, then 50% KOH aq. (4 ml) was immediately added by a syringe pump to a THF solution. After the typical blue color of SmI_2 was disappeared, the reaction mixture was acidified by the addition of 10% HCl aq. 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 (silica gel), the reduction products listed in Tables 1 and 2 were obtained. Products were characterized with the authentic samples on the basis of comparisons of their UV, IR, NMR, GC/FT-IR and GC/MS spectral data.

Little work has been reported on the reduction of aromatic nucleus with SmI_2. As mentioned above, phenol and its derivatives were unexpectedly reduced into alcohols and the reductive elimination of phenolic hydroxy functionality of dihydric phenols was partly recognized with SmI_2—KOH system in the presence of protic solvent at room temperature. However, these reductions have never proceeded with SmI_2—acid or H_2O systems and the similar reduction of anisole did not proceed. Moreover, adding alternately a THF solution of phenols and base to SmI_2, the yield of products decreased generally. Therefore, though the detailed mechanism of these reductions have remained obscure, it is assumed that phenolate ion forms firstly the coordination bond with SmI_2 followed by the coordination of base (ligand) toward Sm in this complex. Thus, the one electron donor ability of SmI_2 is strongly affected by ligands around Sm^{2+}, and it would be expected to facilitate relatively the release of electron from SmI_2 when a sufficient electron is supplied from ligands around Sm^{2+}. Accordingly, it is assumed that the highly promoted electron transfer from SmI_2 would be enhanced by the coordination of base to SmI_2.

Present reduction with SmI_2—base system can be used for the direct conversion of phenol derivatives to the corresponding alcohols, such as 3-cyclohexen-1-ol (Table 1, Entries 5 and 9), 1,4-cyclohexanediol (Table 2, Entry 6), 4-hydroxycyclohexanone (Table 2, Entry 7) and 1,2,3,4-tetrahydro-2-naphthol, by one pot reaction under mild conditions, so it can be presumed that this system provides a useful and convenient synthetic method in synthetic chemistry.

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