

Novel Reduction of Carboxylic Acids, Esters, Amides and Nitriles  
Using Samarium Diiodide in the Presence of Water

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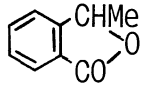
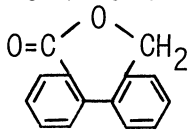
Aromatic carboxylic acids, esters, amides, nitriles, chlorides, ketones and nitro compounds were rapidly reduced by the samarium diiodide-H<sub>2</sub>O system to the corresponding products at room temperature in good yields.

Kagan et al. reported that carboxylic acid, ester and nitrile could not be reduced by samarium diiodide (SmI<sub>2</sub>).<sup>1)</sup> However, in the investigation of the effect on the reducing power of SmI<sub>2</sub> with the additive, it has been reported that the addition of acid or base to SmI<sub>2</sub> proved to have a stronger reducing ability than the use of SmI<sub>2</sub> alone and a variety of functionalities containing carboxyl group were reduced by these systems.<sup>2)</sup> Generally, it could be expected to facilitate relatively the release of electron from metal ion when a sufficient electron is supplied from ligands around metal ion. Therefore, it has been summarized that the reducing ability can be greatly enhanced by the coordination of additive to SmI<sub>2</sub>. From this viewpoint, it can be presumed that H<sub>2</sub>O also functions as a ligand to SmI<sub>2</sub> and the reducing ability of this complex is enhanced as compared with SmI<sub>2</sub> alone. As a continuation of the investigation of the effect on the reducing ability of SmI<sub>2</sub> with the additive, we report here the rapid and convenient reduction of carboxylic acid<sup>3)</sup> and the other functionalities by the new SmI<sub>2</sub>-H<sub>2</sub>O system under extremely mild conditions.

As shown in Table 1, benzoic acid (**1**) was rapidly reduced to benzyl alcohol (**2**) by the SmI<sub>2</sub> (4 mol eq)-H<sub>2</sub>O (56 mol eq, H<sub>2</sub>O was used 14 mol eq against SmI<sub>2</sub>) system at room temperature in an excellent yield (Entry 1). In this reduction, an additional amount of H<sub>2</sub>O was correlated with the rate of reaction and reduction yield. Thus, with decreasing amounts of H<sub>2</sub>O (14 or 28 mol eq), yield of **2** was decreased and the longer reaction time was required (Entries 2 and 3). Similarly, aromatic carboxylic acids (**3-16**) were reduced to the corresponding alcohols in good yield. In these reactions, a few of characteristic results were also recognized as follows; 1) chloro moiety of 2- and 4-chlorobenzoic acids (**6** and **8**) (Entries 7 and 9), carbamoyl (Entry 11) and carbonyl (Entry 12) functionalities were also reduced by this system, 2) carboxy moiety of dicarboxylic acids (**14-16**) was partially reduced into methyl group (Entries 14-16), 3) olefinic moiety of cinnamic acid (**17**) was reduced faster compared with carboxy group and aliphatic carboxy group was unaffected by this system (Entry 17).

Furthermore, as shown in Table 2, esters (**37-40**), amides (**42-47**) and nitriles (**49-53**) were

Table 1. Reduction of Aromatic Carboxylic Acids with SmI<sub>2</sub>-H<sub>2</sub>O System<sup>a)</sup>

Entry	R-COOH <sup>b)</sup>	SmI <sub>2</sub> <sup>c)</sup>	H <sub>2</sub> O	Time	Product (No.)	Yield <sup>d)</sup>
No.	R (No.)	mol eq	ml(mol eq)	min		%
1	Ph (1)	4	1 (56)	1	PhCH <sub>2</sub> OH (2)	89
2	Ph (1)	4	0.5 (28)	3	PhCH <sub>2</sub> OH (2)	80
3	Ph (1)	4	0.25 (14)	40	PhCH <sub>2</sub> OH (2)	64
4	2-MeC <sub>6</sub> H <sub>4</sub> (3)	4	1 (56)	10	2-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (18)	88
5	3-MeC <sub>6</sub> H <sub>4</sub> (4)	4	1 (56)	3	3-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (19)	90
6	4-MeC <sub>6</sub> H <sub>4</sub> (5)	4	1 (56)	8	4-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (20)	90
7	2-ClC <sub>6</sub> H <sub>4</sub> (6)	6	1.5 (83)	3	PhCH <sub>2</sub> OH (2)	60
					2-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (21)	29
					PhCOOH (1)	8
8	3-ClC <sub>6</sub> H <sub>4</sub> (7)	6	1.5 (83)	3	3-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (22)	96
9	4-ClC <sub>6</sub> H <sub>4</sub> (8)	4	1 (56)	1	4-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (23)	83
					PhCH <sub>2</sub> OH (2)	15
10	2-H <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> (10)	4	1 (56)	2	2-H <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (24)	88
11	2-AcNHC <sub>6</sub> H <sub>4</sub> (11)	4	1 (56)	2	2-H <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COOH (10)	37
					2-H <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (24)	9
					2-AcNHC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (25)	28
12	2-AcC <sub>6</sub> H <sub>4</sub> (12)	4	1 (56)	2	2-EtC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (26)	11
					2-MeCH(OH)C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (27)	36
					 (28)	41
13	4-AcC <sub>6</sub> H <sub>4</sub> (13)	4	1 (56)	35	4-MeCH(OH)C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (29)	74
					4-EtC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (30)	9
14	2-HOOC <sub>6</sub> H <sub>4</sub> (14)	8	2 (112)	60	2-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (18)	27
					1,2-C <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> OH) <sub>2</sub> (31)	42
15	4-HOOC <sub>6</sub> H <sub>4</sub> (15)	8	2 (112)	165	4-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (20)	18
					1,4-C <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> OH) <sub>2</sub> (32)	52
16	2-(2'-C <sub>6</sub> H <sub>4</sub> COOH)C <sub>6</sub> H <sub>4</sub> (16)	8	2 (112)	75	2-(2'-MeC <sub>6</sub> H <sub>4</sub> )C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (33)	9
					 (34)	52
					2,2'-(C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH) <sub>2</sub> (35)	29
17	PhCH=CH (17)	6	1 (56)	80	PhCH <sub>2</sub> CH <sub>2</sub> COOH (36)	>99

a) H<sub>2</sub>O was added to a THF solution of carboxylic acid and SmI<sub>2</sub> and reactions were carried out at room temperature under argon. b) R-COOH; 0.5 mmol. c) 0.1 M in THF. d) Isolated yield.

similarly reduced by the  $\text{SmI}_2\text{-H}_2\text{O}$  system in good yield. Particularly, yields of esters using this system were improved compared with the previous results using  $\text{SmI}_2$ -base system.<sup>2)</sup> In these reactions, yields of ester and nitrile were generally decreased decreasing amounts of  $\text{H}_2\text{O}$  and benzylamine (**58**) was obtained only in low yield (6%) from the reaction of benzonitrile (**49**) using 0.25 ml (14 mol eq) of  $\text{H}_2\text{O}$ . Interestingly, differing from the results by the  $\text{SmI}_2$ -base or acid system,<sup>2c)</sup> nitriles were reduced by this system to the corresponding primary amines alone and the reductive elimination and the reduction into methyl group of cyano group of dinitrile (**52**) were observed under the similar conditions (Entry 16). In the similar reductions of cinnamamide (**48**) and cinnamitrile (**54**), olefinic moiety was partially reduced to give amide

Table 2. Reduction of the Other Functionalities with  $\text{SmI}_2\text{-H}_2\text{O}$  System<sup>a)</sup>

Entry No.	Substrate (No.) <sup>b)</sup>	$\text{SmI}_2$ <sup>c)</sup> mol eq	$\text{H}_2\text{O}$ ml	Time min	Product (No.)	Yield <sup>d)</sup> %
1	PhCOOMe ( <b>37</b> )	4	1	3 s	PhCH <sub>2</sub> OH ( <b>2</b> )	93
2	2-MeC <sub>6</sub> H <sub>4</sub> COOMe ( <b>38</b> )	4	1	1	2-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH ( <b>18</b> )	94
3	2-ClC <sub>6</sub> H <sub>4</sub> COOMe ( <b>39</b> )	6	1.5	0.5	PhCH <sub>2</sub> OH ( <b>2</b> ) 2-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH ( <b>21</b> )	53 <sup>e)</sup> 23
4	4-ClC <sub>6</sub> H <sub>4</sub> COOMe ( <b>40</b> )	6	1.5	8	4-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH ( <b>23</b> )	89 <sup>f)</sup>
5	4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COOMe ( <b>41</b> )	8	2	2	4-H <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COOMe ( <b>55</b> )	89
6	PhCONH <sub>2</sub> ( <b>42</b> )	4	1	3 s	PhCH <sub>2</sub> OH ( <b>2</b> )	94
7	2-MeC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> ( <b>43</b> )	4	1	10 s	2-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH ( <b>18</b> )	96
8	3-ClC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> ( <b>44</b> )	6	1	10 s	3-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH ( <b>22</b> )	>99
9	4-ClC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> ( <b>45</b> )	6	1	10 s	4-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH ( <b>23</b> )	>99
10	1,2-C <sub>6</sub> H <sub>4</sub> (CONH <sub>2</sub> ) <sub>2</sub> ( <b>46</b> )	8	1	1	1,2-C <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> OH) <sub>2</sub> ( <b>31</b> )	98
11	PhCONHPh ( <b>47</b> )	4	1	10 s	PhCH <sub>2</sub> OH ( <b>2</b> ) PhCH <sub>2</sub> NHPh ( <b>56</b> )	45 54
12	PhCH=CHCONH <sub>2</sub> ( <b>48</b> )	4	1	0.5	PhCH <sub>2</sub> CH <sub>2</sub> CONH <sub>2</sub> ( <b>57</b> )	99
13	PhCN ( <b>49</b> )	4	1	5	PhCH <sub>2</sub> NH <sub>2</sub> ( <b>58</b> )	88
14	2-MeC <sub>6</sub> H <sub>4</sub> CN ( <b>50</b> )	4	1	13	2-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> NH <sub>2</sub> ( <b>59</b> )	94
15	2-ClC <sub>6</sub> H <sub>4</sub> CN ( <b>51</b> )	6	1.5	1	PhCH <sub>2</sub> NH <sub>2</sub> ( <b>58</b> ) 2-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> NH <sub>2</sub> ( <b>60</b> )	37 62
16	2-NCC <sub>6</sub> H <sub>4</sub> CN ( <b>52</b> )	8	2	1.5	2-MeC <sub>6</sub> H <sub>4</sub> CN ( <b>50</b> ) PhCN ( <b>49</b> )	33 66
17	1-Naphthonitrile ( <b>53</b> )	4	1	1	(1-Naphthyl)methylamine( <b>61</b> )	95
18	PhCH=CHCN ( <b>54</b> )	6	1.5	3	PhCH <sub>2</sub> CH <sub>2</sub> CN ( <b>62</b> )	99

a)  $\text{H}_2\text{O}$  was added to a solution of substrate and  $\text{SmI}_2$  in THF and reactions were carried out at room temperature under argon. b) Substrate; 0.5 mmol. c) 0.1 M in THF. d) Isolated yield. e) By-product: PhCOOMe **37**, 13%. f) By-product: PhCH<sub>2</sub>OH **2** 5%.

(57) and nitrile (62) (Entries 12 and 18), respectively. These results exhibited that aliphatic amide and nitrile were also unaffected by this system similar to the result of cinnamic acid **17** (Entry 17 in Table 1). Throughout these reductions, the yield of products was decreased when a THF solution of substrate and H<sub>2</sub>O was added alternately to a THF solution of SmI<sub>2</sub>.

In the general procedure, H<sub>2</sub>O was immediately added by the use of a syringe pump to a THF solution of substrate and SmI<sub>2</sub> with stirring at room temperature under argon. After the typical blue color of SmI<sub>2</sub> was disappeared, the reaction mixture was poured into an aqueous sodium hydroxide (50%, 10 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 (alumina) gave the reduction products as shown in Tables 1 and 2. Products were characterized with the authentic samples on the basis of comparisons of their GC/FT-IR and GC/MS and yields were calculated by GC/FT-IR data.

As described above, compared with the proceeding reduction by the SmI<sub>2</sub>-base or acid system,<sup>2)</sup> the present reductions of a variety of functionalities by the SmI<sub>2</sub>-H<sub>2</sub>O system could be performed under the extremely mild conditions in good yield. Though the actual reductant and detailed mechanism of these reductions have remained obscure at the present stage, taking into account of the poor reducing ability of SmI<sub>2</sub> alone toward carboxylic acid, ester and nitrile and the decrease of product yield adding alternately a THF solution of substrate and H<sub>2</sub>O to SmI<sub>2</sub>, it can be assumed that the release of one electron from Sm<sup>2+</sup> on this system is enhanced by the coordination of H<sub>2</sub>O toward Sm<sup>2+</sup> similar to the interactions of base and acid in SmI<sub>2</sub>-base and acid systems.<sup>2)</sup>

The striking characteristic of the present reduction is the neutral condition, the short reaction time and the high yield of products, so it can be presumed that the present SmI<sub>2</sub>-H<sub>2</sub>O system provides an useful and convenient method for the direct reduction of tested functionalities in synthetic chemistry.

## References

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- 2) a) Y. Kamochi and T. Kudo, *Chem. Lett.*, **1991**, 893; b) Y. Kamochi, T. Kudo, *Tetrahedron Lett.*, **32**, 3511 (1991); c) Y. Kamochi and T. Kudo, *Tetrahedron*, **48**, 4301 (1992); d) Y. Kamochi and T. Kudo, *Bull. Chem. Soc. Jpn.*, **65**, 3049 (1992); e) Y. Kamochi and T. Kudo, *Nippon Kagaku Kaishi*, **1993**, 500.
- 3) It has been reported that carboxylic acids were reduced with diborane, lithium aluminum hydride, sodium bis(2-methoxyethoxy)aluminum hydride and diisobutylaluminum hydride. However, these reducing agents cannot be used in the presence of water.

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