# NOVEL AND FACILE REDUCTION OF HETEROCYCLIC COMPOUNDS WITH LANTHANOID METAL-HYDROCHLORIC ACID SYSTEM

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

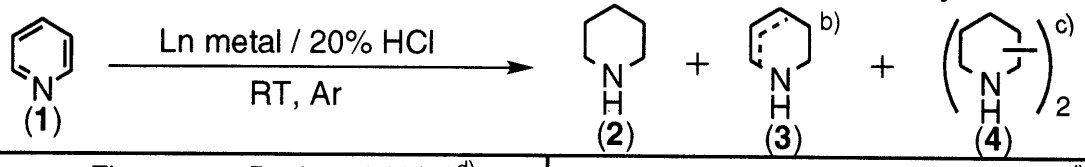
Pyridines were rapidly reduced to piperidines with Sm or Yb-HCl system at room temperature in quantitative yields. Quinolines and isoquinolines were similarly reduced to the corresponding 1,2,3,4-tetrahydro-derivatives with Sm-HCl system in good yields.

**KEY WORDS** reduction; samarium-hydrochloric acid system; pyridine; quinoline; isoquinoline; piperidine

Recently, numerous researchers[1] achieved the reduction of some organic functional groups by Yb, Sm or Ce metal. Since lanthanoid metals have high reduction potential, similarly to Mg and some other metals, it is assumed that lanthanoid metals exhibit a powerful reducing property in acidic medium for organic functionalities. However, to date, little has been reported on the reduction of organic functionalities with the combination of lanthanoid metal and acid. The reduction potentials of many organic functionalities generally decrease in an acidic medium. In the previous paper,[2] we reported that carboxylic acid, ester, amide and nitrile were rapidly reduced to the corresponding alcohols or primary amines with Sm or Yb metal, respectively, in the presence of hydrochloric acid at room temperature in good yield. Also it was reported that pyridines were similarly reduced to piperidine with $SmI_2$-$H_2O$ system in good yields.[3] As a continuation of these works, the present paper deals with the reduction of heterocyclic compounds with lanthanoid metal-HCl system.

In order to compare the reducing abilities of lanthanoid metals and the other some metals toward heterocyclic compounds in an acidic medium, our first attempt was at the reduction of pyridine (**1**) with these metals-HCl systems. As can be seen in Table 1, pyridine **1** was rapidly reduced with a Y-20% HCl system at room temperature to give piperidine (**2**) in moderate yield (57%) accompanied

**Table 1. Reduction of Pyridine with Ln Metal-20% HCl Systems**[a]




| Metal | Time (min) | Product yield (%)[d] (2) | (3) | (4) | Metal | Time (min) | Product yield (%)[d] (2) | (3) | (4) |
|---|---|---|---|---|---|---|---|---|---|
| Sc | 10 | | 8 | | Eu | 10 | | | |
| Y | 10 | 57 | 20 | | Gd | 10 | | 29 | |
| Mg | 10 | 16 | 34 | | Td | 10 | 13 | 15 | |
| | | | | | Dy | 10 | 14 | 18 | |
| La | 10 | 6 | 20 | | Ho | 10 | | | |
| Ce | 10 | | 16 | | Er | 10 | | 28 | |
| Pr | 10 | | 11 | | Tm | 10 | | | |
| Nd | 10 | | 7 | | Yb | 10 | 89 | 9 | |
| Sm | 10 | 94 | 2 | Trace | Lu | 10 | | 12 | Trace |

a) Reactions were carried out at room temperature under argon and 1 mmol of substrate (**1**) was used. b) Tetrahydropyridine (from mass data, unidentified). c) Piperidine dimer (from mass data, unidentified). d) Isolated yield.

* To whom correspondence should be addressed.

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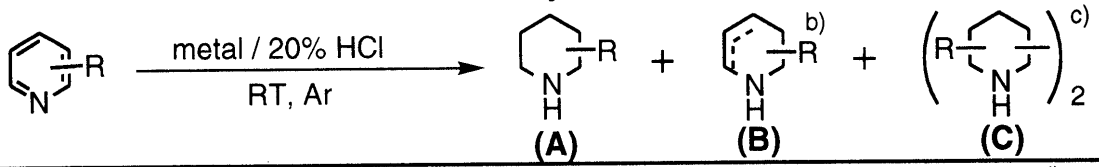
by tetrahydropyridine (**3**). Interestingly, among the tested lanthanoid metals, pyridine **1** was reduced to piperidine **2** with Sm and Yb-HCl systems in quantitative yields. However, the results of the other lanthanoid metal-HCl systems under similar conditions were unsatisfactory.

Similarly, as shown in Table 2, pyridine derivatives (**4**-**8**) were rapidly reduced to the corresponding piperidine derivatives with Sm-20% HCl system in good yields. In particular, 2-phenylpyridine (**4**) was reduced to 2-phenylpiperidine (**9**) in a quantitative yield. Also, pyridine **1** was reduced with Mg-20% HCl system to give 2-phenylpiperidine **9** in 33% yield.

**Table 2. Reduction of Substituted Pyridines with Sm or Mg-HCl System[a)]**




| Substrate R (No.) | mmol | Metal (mmol) | 20% HCl (mol eq) | Time (min) | Product yield (%)[d)] (A) | (B) | (C) |
|---|---|---|---|---|---|---|---|
| 2-Ph (**4**) | 1 | Sm (12) | 57 | 10 | 96 | | |
| 2-Me (**5**) | 1 | Sm (12) | 57 | 10 | 67 | 24 | 3 |
| 3-Me (**6**) | 1 | Sm (12) | 57 | 10 | 85 | 11 | Trace |
| 4-Me (**7**) | 1 | Sm (12) | 57 | 10 | 56 | 39 | 4 |
| 2-Ph (**8**) | 8 | Mg (60) | 120 | 10 | 33 | | |

a) Reactions were carried out at room temperature under argon. b) Tetrahydro-pyridine derivatives (from mass data, unidentified). c) Piperidine dimers (from mass data, unidentified). d) Isolated yield.

In similar reactions of 2- and 4-aminopyridines (**10** and **11**), the amino group was unexpectedly eliminated with Sm-20% HCl system at room temperature to afford piperidine **2** as a major product. Similarly, 2-, 3- and 4-chloropyridines (**12**, **13** and **14**) were reduced with this system to give piperidine **2** as a major product along with their respective by-products. Also, 2- and 4-pyridine-

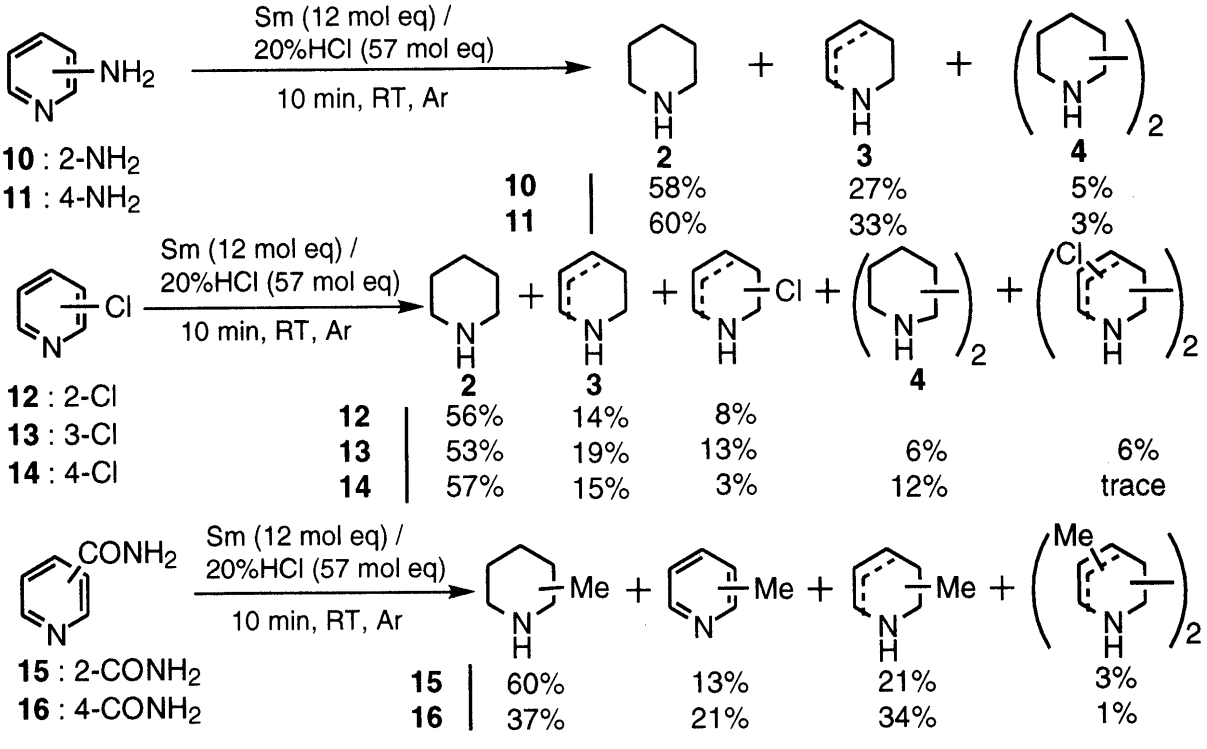



**Chart 1**

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carboxamides (**15**-**16**) were reduced with this system to afford the corresponding methylpyridines as the major products.

As shown in Chart 2, quinoline and its derivatives (**17**-**20**) were rapidly reduced with Sm-HCl system to give 1,2,3,4-tetrahydroquinoline derivatives as major products in good yields. In the reaction of 2-aminoquinoline **20**, the amino group was eliminated to afford 1,2,3,4-tetrahydroquinoline (**21**) in excellent yield. This system also reduced isoquinoline (**22**) and 3-methylisoquinoline (**23**) into 1,2,3,4-tetrahydroisoquinolines (**24**-**25**) in a quantitative yield.

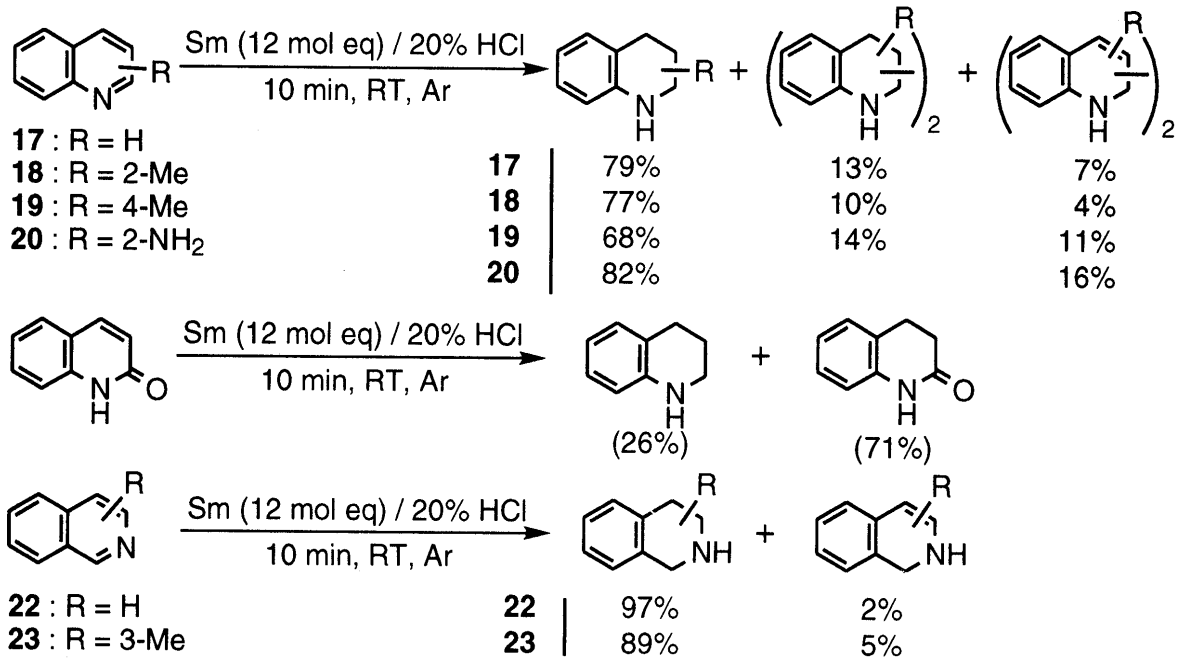


**Chart 2**

Although the actual reductant and the detailed mechanisms remain obscure at the present stage, it is assumed that these reductions also proceed by electron transfer from active low-valence lanthanoid species generated from the lanthanoid metal with HCl, in addition to the Béchamp-type reduction.

It is noteworthy that the lanthanoid metal-HCl system can be use for the reduction of aromatic nuclei of heterocyclic compounds. The striking characteristic of the present reduction is the short reaction time at room temperature and the high yield of product, and hence the present method provides a useful and facile route in synthetic chemistry.

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