

Catalytic HgCl_2 -Samarium System Induced Reductive Coupling of Nitriles with Nitro Compounds

Ji Ming ZHANG¹, Yong Min ZHANG^{1,2*}

¹Department of Chemistry, Zhejiang University (Campus Xixi), Hangzhou 310028

²State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032

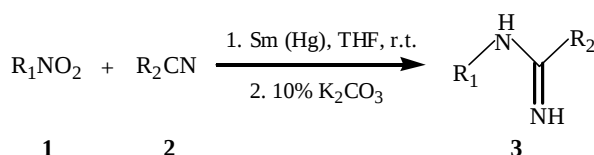
Abstract: The intermolecular coupling of a nitro group with a cyano group mediated by a $\text{Sm}(\text{Hg})$ amalgam prepared from metal samarium powder and catalytic mercury dichloride was studied.

Keywords: Mercury dichloride, samarium, reductive coupling, nitro group, cyano group, amidine.

Compared to the extensive applications of samarium diiodide in organic synthesis^{1a-1d}, little attention was paid to the use of samarium metal in organic synthesis. Metallic samarium is stable in air and its strong reducing power ($\text{Sm}^{3+}/\text{Sm} = -2.41 \text{ V}$) is similar to that of magnesium ($\text{Mg}^{2+}/\text{Mg} = -2.37 \text{ V}$), and superior to that of zinc ($\text{Zn}^{2+}/\text{Zn} = -0.71 \text{ V}$). As early as 1971, Evans and his co-workers² found that metal samarium is not active as metal ytterbium. In order to improve the activity of samarium metal, some additives were added, such as HgCl_2 ³, $\text{NH}_4\text{Cl}(\text{aq.})$ ⁴, or TMSCl ⁵, etc.. Our group has applied Sm/HgCl_2 system to the reduction of ArSeSeAr ⁶, ArSO_2Cl ⁷, pinacolic coupling of aromatic aldehydes and ketones⁸. Amidines are the nitrogen analogues of carboxylic acids and this unit is a moiety of several biologically interested compounds⁹. They can be prepared by reacting aromatic amines with nitriles under intensive reaction conditions¹⁰, such as high temperatures and long reaction time, using sodium or lithium. Recently, L. Zhou and Y. Zhang have reported a facile synthesis of amidines *via* the intermolecular reductive coupling of nitriles with nitro compounds mediated by samarium (II) iodide¹¹. Sm/HgCl_2 as a good reductive system, if it could take the place of samarium (II) iodide to induce the coupling reaction of nitriles with nitro compounds? The answer is positive. Here we wish to report our results on the intermolecular reductive coupling of nitriles with nitro compounds mediated by $\text{Sm}(\text{Hg})$ amalgam prepared from metal samarium powder and catalytic amount of mercury dichloride to give the corresponding amidines (as shown in **Scheme 1**).

When aromatic nitro compounds **1** and nitriles **2** were treated with Sm/HgCl_2 system in dry THF, the intermolecular reductive cross coupling products, amidines **3** were found. The results on the reaction of nitro compounds and nitriles are summarized in **Table 1**. From **Table 1**, we found that aromatic nitro compounds reacted with the aromatic or aliphatic nitriles to give the corresponding amidines in moderate to good

yields. However, aliphatic nitro compounds failed to react with the aromatic or aliphatic nitriles to give the similar amidines as products under the same conditions, at low temperature or under refluxing conditions. Amidines **3** are not derived from the reaction of the nitriles with amines produced by the reduction of nitro compounds, since treatment of nitriles with amines under the same reaction conditions did not lead to the formation of amidines.

Scheme 1

Although the detailed mechanism of the intermolecular reductive coupling of nitriles with nitro compounds mediated by Sm/HgCl₂ system has not been clarified yet, amidine formation can be explained by the possible mechanism presented in **Scheme 2**.

Table 1 Intermolecular reductive coupling of nitriles with nitro compounds mediated by Sm/HgCl₂ system

Entry	R ₁	R ₂	Time/hr	Yields (%) ^a
a	C ₆ H ₅	C ₆ H ₅	4	63
b	4-CH ₃ C ₆ H ₄	C ₆ H ₅	8	60
c	2-CH ₃ C ₆ H ₄	C ₆ H ₅	4	59
d	C ₆ H ₅	C ₆ H ₅ CH ₂	4	55
e	4-CH ₃ C ₆ H ₄	C ₆ H ₅ CH ₂	8	67
f	4-ClC ₆ H ₄	C ₆ H ₅ CH ₂	8	57
g	4-ClC ₆ H ₄	4-ClC ₆ H ₄	4	70
h	4-CH ₃ C ₆ H ₄	4-ClC ₆ H ₄	5	77
i	C ₆ H ₅	4-ClC ₆ H ₄	4	81
j	4-ClC ₆ H ₄	C ₆ H ₅	4	75
k	4-ClC ₆ H ₄	3-CH ₃ C ₆ H ₄	6	70
l	4-CH ₃ C ₆ H ₄	3-CH ₃ C ₆ H ₄	6	69
m	C ₆ H ₅	3-CH ₃ C ₆ H ₄	5	66
n	CH ₃	C ₆ H ₅	10	0 ^b
o	CH ₃	C ₆ H ₅ CH ₂	10	0 ^b

^aIsolated yields.

^bThe reaction proceeded under 0°C, at 25°C and under refluxing conditions.

In summary, a catalytic amount of HgCl₂-Sm reductive system has been applied to the synthesis of amidines *via* the intermolecular reductive coupling of nitriles with nitro compounds in mild and neutral conditions with good yields. The operation is easy.

Experimental

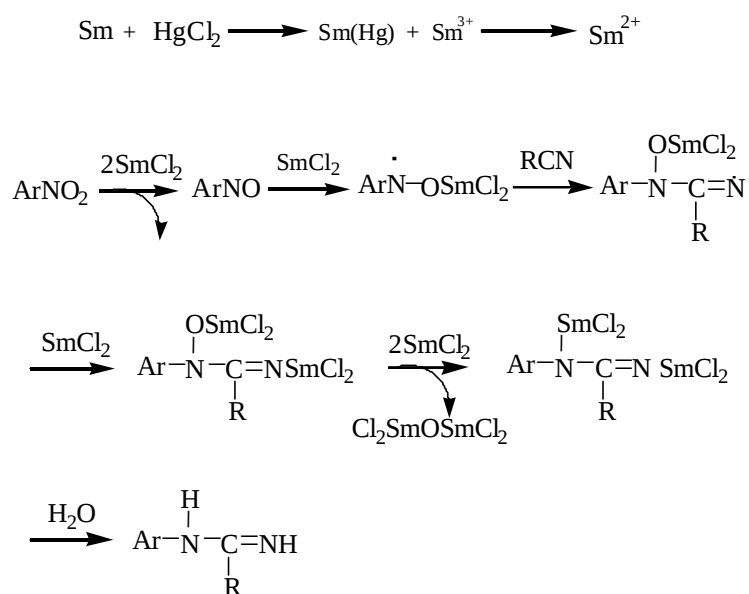
Tetrahydrofuran (THF) was distilled from sodium-benzophenone immediately *prior* to use. All reactions were performed under a nitrogen atmosphere. Thermometer was

uncorrected. Infrared spectra were recorded on an IR-408 spectrometer in KBr with absorptions in cm⁻¹. ¹H NMR spectra were recorded on a Bruker AC-80 spectrometer using CDCl₃ as the solution. J values are in Hz. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane.

General procedure

To a mixture of Sm powder (1 mmol) and HgCl₂ (0.1 mmol) was added THF (20 mL), then a solution of nitro compound **1** (1 mmol) and nitrile **2** (1.2 mmol) in anhydrous THF (3 mL) was added dropwise under a nitrogen atmosphere at room temperature. Then the mixture was heated to reflux. After completion of the reaction, the reaction mixture was poured into 10% K₂CO₃ solution (50 mL) and extracted with diethyl ether (3×20 mL). The combined extracts were washed with saturated solution of Na₂S₂O₃ (15 mL), saturated brine (15 mL), and dried over anhydrous Na₂SO₄. After evaporating the solvent under reduced pressure, the crude product was purified by preparative thin layer chromatography using ethyl acetate and cyclohexane (1:4) as eluant.

Scheme 2



Acknowledgment

We thank the National Natural Science Foundation of China (Project No. 20072033) and Natural Science Foundation of Zhejiang province for financial support.

References

1. (a) H. B. Kagan, J. L. Namy, *Tetrahedron*, **1986**, 42, 6573.
(b) G. A. Molander, *Chem. Rev.*, **1992**, 92, 29.
(c) G. A. Molander, *Organic Reaction*, **1994**, 46, 211.
(d) G. A. Molander, C. R. Harris, *Chem. Rev.*, **1996**, 96, 307.
2. D. F. Evans, G. V. Fszakerley, R. F. Philips, *J. Chem. Soc. A*, **1971**, 1931.
3. (a) G. A. Molander, L. S. Harring, *J. Org. Chem.*, **1989**, 54, 3525.
(b) D. L. J. Clive, S. Daigneault, *J. Org. Chem.*, **1991**, 56, 3801.
4. L. Wang, Y. Zhang, *Tetrahedon Lett.*, **1998**, 39, 5257.
5. (a) L. Wang, Y. Zhang, *Tetrahedron*, **1998**, 54, 11129.
(b) M. Lautens, Y. Ren, *J. Org. Chem.*, **1996**, 61, 2210.
6. L. Wang, Y. Zhang, *Heteroatom Chem.*, **1999**, 10, 203.
7. M. Yu, Y. Zhang, *Youjihuaaxue*, **2001**, 5, 395.
8. L. Wang, Y. Zhang, *Syn. Commun.*, **1998**, 28, 3991.
9. (a) S. Patai, Z. Rappoport, *The Chemistry of Amidines and Imidates*, Wiley, New York, **1991**, 27, p.226.
(b) A. Kreutzberger, *Progress in Drug Reseach*, ed. by E. Jucker, BirklauserVerlag, Basel, **1968**, p.356-445.
10. (a) Lottermoser, *J. Prakt. Chem.*, **1896**, 54, 116.
(b) F. C. Cooper, M. W. Partridge, *J. Chem. Soc.*, **1953**, 255.
(c) N. A. Kalashnikova, G. N. Kul'bitskii, B. V. Passet, B. Z. Askinazi, *Zh. Org. Khim.*, **1974**, 10 (7), 1529.
11. L. H. Zhou, Y. M. Zhang, *J. Chem. Res (s)*, **1998**, 596.

Received 12 June, 2001