SHORT PAPER

J. Chem. Research (S),
2000, 250–251

Samarium (ii) iodide promoted reductive coupling of ketones and imines†

Yongmin Ma[a], Yongmin Zhang*[a] and Longhu Zhou[a,b]

[a]*Department of Chemistry, Zhejiang University, Xixi Campus, Hangzhou, 310028, P.R. China*
[b]*Department of Chemistry, Xuzhou Normal University, Xuzhou, 221009, P.R. China*

The cross-coupling reactions of imines with aromatic ketones induced by SmI_2/THF system were studied; 2-amino alcohols are prepared in good yields under refluxing conditions.

Applications of samarium diiodide to organic synthesis have significantly grown in the last decade.[1] Pioneering work performed by Kagan[2] with SmI_2 has served to outline the uses of this reagent in synthetic organic chemistry. Investigations revealed that SmI_2 is exceedingly reliable, mild, neutral, selective and versatile single electron transfer reagent in synthetic chemistry. For example, Barbier reactions, Reformatsky reactions, pinacol couplings and ketone-olefin reductive couplings have been reported using SmI_2 as the reagent.

However, the cross-coupling of ketones with imines has received little attention. Imamoto has described a procedure to couple benzophenone or fluorenone anil with cyclohexanone using SmI_2 in refluxing THF, but the method is not efficient for other imines.[3] Kise has promoted electroreductive coupling of aromatic imines with electrophiles in the presence of chlorotrimethylsilane.[4] Recently, Namy has reported that Samarium diiodide/nickel diiodide induced coupling reactions of imines and aliphatic ketones.[5] Here we wish to describe our preliminary results on reductive couplings of aromatic ketones and aromatic aldimines promoted by samarium diiodide in tetrahydrofuran.

When the mixture of aromatic aldimine **1** and aromatic ketone **2** was treated with SmI_2 in dry THF at 65°C under a nitrogen atmosphere, the reductive product 2-amino alcohol **3** was obtained.

Table 1 summarizes our results on the ketone-imine reductive couplings, aromatic ketones reacted with aromatic aldimines to produce 2-amino alcohols in good yields. However, cross-coupling between acetophenone and aromatic imines failed because of the fast homocoupling reaction of the ketone.[6]

In the cross-coupling reaction, when we add the mixture of aldimine and ketone quickly, the self-coupling product of the imine was not be found. Hence we believe that the imine's radical anion intermediate can be ruled out. Therefore, according to our previous work,[7] we assume that the formation of 2-amino alcohol can be explained by the mechanism presented in Scheme 2.

In conclusion, SmI_2 promotes a novel reductive reaction of aromatic aldimines and aromatic ketones, which has not been achieved previously by other reductants. Further studies to develop other new reactions using SmI_2 are now in progress.

Table 1 Cross-coupling reactions of ketones and imines induced by SmI_2

Entry	Ar¹	AR²	Ar³	t(h)	Yield(%)[a]
a	C_6H_5	C_6H_5	C_6H_5	5	84
b	*p*-$CH_3C_6H_4$	C_6H_5	C_6H_5	4	81
c	*p*-ClC_6H_4	C_6H_5	C_6H_5	6	85
d	3,4-$(OCH_2O)C_6H_3$	C_6H_5	C_6H_5	4	80
e	*p*-ClC_6H_4	*p*-$CH_3C_6H_4$	C_6H_5	6	77
f	3,4-$(OCH_2O)C_6H_3$	*p*-$CH_3C_6H_4$	C_6H_5	4	83
g	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	C_6H_5	4	86
h	*p*-$CH_3C_6H_4$	3,4-$Cl_2C_6H_3$	C_6H_5	5	79
i	3,4-$(OCH_2O)C_6H_3$	3,4-$Cl_2C_6H_3$	C_6H_5	5	72
j	*p*-CH_3-C_6H_4	C_6H_5	*p*-CH_3O-C_6H_4	5	88

[a]Isolated yield.

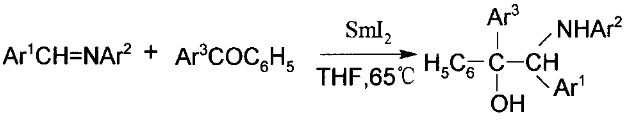
Experimental

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 683 spectrometer in KBr with absorptions in cm^{-1}. ^{1}H-NMR spectra were determined on a Bruker AC 80 spectrometer as $CDC1_3$ solutions. Chemical shifts were expressed in ppm downfield from internal tetramethylsilane. Mass spectra were recorded on HP5989B Mass spectrometer. Elemental analyses were carried out on an EA 1110 instrument.

General procedure for the synthesis of 2-amino alcohols **3**: A solution of imine **1** (1 mmol) and ketone **2** (1 mmol) in anhydrous THF (3 ml) was added to a solution of SmI_2 (2.2 mmol) in THF (20 ml) at 65°C under a dry nitrogen atmosphere and the reaction mixture was stirred under N_2. At completion, the reaction mixture was poured into 1N HCl (5 ml) and extracted with diethyl ether (3 × 15 ml). The combined extracts were washed with a saturated solution of $Na_2S_2O_3$ (15 ml) and a saturated solution of NaCl (15 ml) and dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate-cyclohexane (1:8) as eluent.

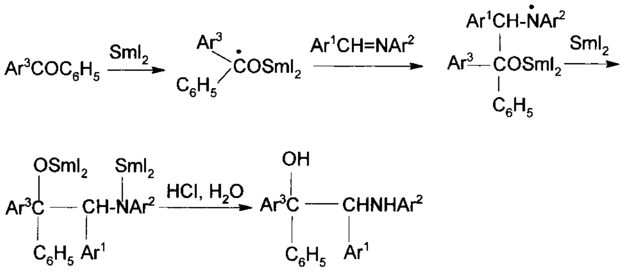
Compound **3a**: mp 169–171 °C (*lit.,[8] 171–173 °C), ν_{max} (cm^{-1}): 3600, 3445, 1615, 1175. δ_H (ppm) 2.60 (1 H, s, NH), 4.50 (1 H, br s, OH), 5.20 (1 H, s, CH), 6.70–7.70 (20 H, m, ArH).

Compound **3b**: mp 171–173 °C. ν_{max} (cm^{-1}): 3580, 3405, 1610, 1185. δ_H (ppm) 2.30 (3 H, s, CH_3), 2.70 (1 H, s, NH), 4.67 (1 H, br s, OH), 5.33 (1 H, s, CH), 6.60–7.70 (19 H, m, ArH). *m/z*: 380 (M+1,



1 **2** **3**

Scheme 1



Scheme 2

---

* To receive any correspondence.

† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

1.2), 287 (2.0), 197 (16.9), 196 (100), 105 (7.8), 104 (20.1), 77 (18.3). Anal. Calcd. For $C_{27}H_{25}NO$: C, 85.45; H, 6.64; N, 3.69. Found: C, 85.47; H, 6.69; N, 3.60.

Compound **3c**: mp 140–142°C. ν_{max} (cm^{-1}): 3580, 3445, 1620, 1175. δ_H (ppm) 2.77 (1H, s, NH), 4.60 (1 H, br s, OH), 5.12 (1 H, s, CH), 6.63–7.60 (19 H, m, ArH). *m/z*: 400 (M+1, 0.2), 218 (33.4), 217 (17.2), 216 (100), 105 (24.3), 104 (28.1), 77 (39.9). Anal. Calcd. For $C_{26}H_{22}ClNO$: C, 78.09; H, 5.55; N, 3.50. Found: C, 77.64; H, 5.58; N, 3.49.

Compound **3d**: mp 166–168 °C. ν_{max} (cm^{-1}): 3540, 3410, 1615, 1170. δ_H (ppm) 2.60 (1 H, s, NH), 4.40 (1 H, br s, OH), 5.10 (1 H, s, CH), 6.00 (2 H, s, CH_2), 6.50–7.60 (18 H, m, ArH). *m/z*: 410 (M+1, 0.40), 317 (1.7), 227 (16.3), 226 (100), 105 (7.0), 104 (26.8), 77 (15.8). Anal. Calcd. For $C_{27}H_{23}NO_3$; C, 79.20; H, 5.66; N, 3.42. Found: C, 79.22; H, 5.61; N, 3.43.

Compound **3e**: mp 190–192 °C. ν_{max} (cm^{-1}): 3580, 3440, 1640, 1165. δ_H (ppm) 2.12 (3 H, s, CH_3), 2.45 (1 H, s, NH), 4.30 (1 H, br s, OH), 5.12 (1 H, s, CH), 6.63–7.50 (18 H, m, ArH), *m/z*: 414 (M+1, 0.4), 232 (34.9), 231 (17.7), 230 (100), 118 (11.4), 105 (7.7), 91 (14.5), 77 (8.4). Anal. Calcd. For $C_{27}H_{24}ClNO$; C, 78.34; H, 5.84; N, 3.38. Found: C, 77.51; H, 5.87; N, 3.31.

Compound **3f**: mp 176–178 °C. ν_{max} (cm^{-1}): 3585, 3440, 1630, 1195. δ_H (ppm) 2.12 (3 H, s, CH_3), 2.55 (1 H, s, NH), 4.25 (1 H, br s, OH), 5.05 (1 H, s, CH), 5.85 (2 H, s, CH_2), 6.56–7.50 (17 H, m, ArH). *m/z*: 424 (M+1, 0.2), 317 (0.8), 241 (17.4), 240 (100), 118 (21.0), 105 (4.7), 91 (12.7), 77 (5.1). Anal. Calcd. For $C_{28}H_{25}NO_3$: C, 79.41; H, 5.95; N, 3.31. Found: C, 78.88; H, 5.89, N, 3.34.

Compound **3g**: mp 166–168 °C. ν_{max} (cm^{-1}): 3580, 3420, 1630, 1175. δ_H (ppm) 2.27 (3 H, s, CH_3), 2.37 (3 H, s, CH_3), 2.84 (1 H, s, NH), 4.50 (1 H, br s, OH), 5.50 (1 H, s, CH), 6.53–7.47 (18 H, m, ArH). *m/z*: 394 (M+1, 10.9), 287 (8.7), 211 (17.2), 210 (100), 118 (12.3), 105 (7.6), 91 (12.5), 77 (6.5). Anal. Calcd. For $C_{28}H_{27}NO$: C, 85.46; H, 6.92; N, 3.56. Found: C, 85.33; H, 6.93, N, 3.52.

Compound **3h**: mp 149–151 °C. ν_{max} (cm^{-1}): 3560, 3410, 1615, 1140. δ_H (ppm) 2.19 (3 H, s, CH_3), 2.70 (1 H, s, NH), 4.80 (1 H, br s, OH), 5.20 (1 H, s, CH), 6.50–7.60 (17 H, m, ArH). *m/z*: 448 (M+1, 0.6), 287 (6.2), 268 (10.7), 266 (64.6), 265 (17.9), 264 (100), 174 (9.6), 172 (14.6), 105 (10.9), 77 (8.3). Anal. Calcd. For $C_{27}H_{23}Cl_1NO$: C, 72.32; H, 5.17; N, 3.12. Found: C, 72.05, H, 5.23; N, 3.08.

Compound **3i**: mp 159–161 °C. ν_{max} (cm^{-1}): 3560, 3425, 1610, 1140. δ_H (ppm) 2.50 (1 H, s, NH), 4.50 (1 H, br s, OH), 4.97 (1 H, s, CH), 5.80 (2 H, s, CH_2), 6.70–7.70 (16 H, m, ArH). *m/z*: 478 (M+1, 0.3), 317 (14.3), 298 (11.3), 296 (65.5), 295 (17.8), 294 (100), 174 (10.5), 172 (16.3), 105 (10.8), 77 (8.8). Anal. Calcd. For $C_{27}H_{21}Cl_2NO_3$: C, 67.79; H, 4.42; N, 2.92. Found: C, 67.89; H, 4.51; N, 2.87.

Compound **3j**: mp 122–124 °C. ν_{max} (cm^{-1}): 3480, 3420, 1610, 1180. δ_H (ppm) 2.23 (3 H, s, CH_3), 2.53 (1 H, s, NH), 3.77 (3 H, s, CH_3), 4.53 (1 H, br s, OH), 5.23 (1 H, s, CH), 6.40–7.40 (18 H, m, ArH). *m/z*: (M+1, 2.8), 317 (4.9), 197 (18.0), 196 (100), 105 (7.0), 104 (15.9), 77 (13.2). Anal. Calcd. For $C_{28}H_{27}NO_2$: C, 82.12; H, 6.65; N, 3.42. Found: C, 82.45; H, 6.71; N, 3.40.

We are grateful to the National Natural Science Foundation of China (Project No. 29872010), the NSF of Zhejiang Province, China, and the Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences for financial support.

Received 27 December 1999; accepted 27 March 2000
Paper 99/100

References

1 For reviews see: (a) Molander, G.A., Harris, C.R. *Chem. Rev*. 1996, **96**, 307; (b) Matsuda F, *Synth. Org. Chem. Jpn*. 1995, **53**, 987; (c) Imamota T, Lanthanides in Organic Synthesis; Academic Press: London, 1994; Chapter 4; (d) Shibasaki, M; Sasai, H., *Synth. Org. Chem. Jpn*., 1993, **51**, 972; (e) Curran D.P, Fevig T.L., Jasperse C.P., Totleben, M.J., *Synlett*. 1992, 943; (f) Soderquist J.A., *Aldrichim. Acta*, 1991, **24**, 15.

2 (a) P. Girard, J.L. Namy and H.B. Kagan, *J. Am. Chem Soc*., 1980, **102**, 2693; (b) J. L. Namy, P. Girard and H.B. Kagan, *Nauv. J. Chim*., 1977, **1**, 5; (c) H.B. Kagan, *New. J. Chem*., 1990, **14**, 453.

3 Imamoto T, Nishimura S., *Chem. Lett*., 1990, 1141–1142.

4 Tjatsuya Shono, Naoki Kise, *Chem. Lett*., 1991, 2191–2194.

5 Namy J.L. Machrouhi F., *Tetrahedron Lett*., 1999, **40**, 1315.

6 Namy J.L., Souppe J., Kagan H.B., *Tetrahedron Lett*., 1983, **24**, 765–766.

7 Zhou L.H., Zhang Y.M., Shi D.Q., *Tetrahedron Lett*., 1998, **39**(46), 8491.

8 Katritzky, A.R., Akutagawa, K., Fan wei-Qiang, *Acta. Chim. Sin*., 1989, **5**, 471.