SHORT PAPER

J. Chem. Research (S),
2001, 32–33

Samarium diiodide induced reductive coupling of nitriles with azides[†]

Weike Su,[a,b] Yongshu Li[a] and Yongmin Zhang[b,c]

[a]*College of Chemical Engineering, Zhejiang University Of Technology, Hangzhou, 310014, P.R. China*
[b]*Department of Chemistry, Zhejiang University at Xixi Campus, Hangzhou, 310028, P.R. China*
[c]*Shanghai Institute of Organic Chemistry, Chinese Academy of Science, Shanghai, Shanghai, 200032, P. R. China*

A series of amidine derivatives were synthesized *via* the intermolecular reductive coupling of nitriles with azides induced by samarium diiodide in good yields under mild and neutral conditions.

Keywords: samarium diiodide, reductive coupling, nitriles, azides

Since Kagan and co-workers[1] demonstrated a simple preparation of samarium diiodide from samarium metal and 1,2-diiodoethane, SmI_2 has been extensively developed as a mild, neutral and versatile single electron transfer reductant in synthetic chemistry.[2] Barbier reactions, Reformatsky reactions, pinacol coupling and ketone–olefin reduction have all been reported using SmI_2 as the reagent. The reactivity of various nitrogen functional groups (imine,[3b] oxime,[3b] nitro,[3] azo,[4] hydrazones,[3b,5] azides[6] and hydroxylamines[7]) towards SmI_2 have been examined.

Amidines are the nitrogen analogues of carboxylic acids and from part of several compounds of biological interest[8]. They can be prepared by reacting aromatic amines with nitriles under intensive reaction conditions[9], such as high temperature and long reaction times, using sodium or lithium. Our group has studied synthesis of amidines *via* reductive coupling of nitriles with nitro compounds[10] and azobenenes promoted by samarium diiodide in mild and neutral condition under nitrogen.

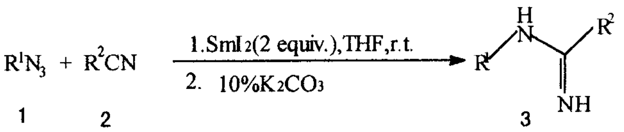
Table 1 Intermolecular reactions of azides with nitriles induced by SmI_2[a]

Entry	R_1	R_2	Reaction time/min	Yield/%[b]
a	C_6H_5	C_6H_5	2	72
b	C_6H_5	$C_6H_5CH_2$	5	60
c	C_6H_5	*m*-$CH_3C_6H_4$	2	75
d	*m*-$CH_3C_6H_4$	C_6H_5	2	76
e	*m*-$CH_3C_6H_4$	$C_6H_5CH_2$	5	62
f	*m*-$CH_3C_6H_4$	*m*-$CH_3C_6H_4$	2	72
g	*o*-ClC_6H_4	C_6H_5	2	74
h	*o*-ClC_6H_4	$C_6H_5CH_2$	5	63
i	*o*-ClC_6H_4	*m*-$CH_3C_6H_4$	2	73
j	*o*-$CH_3C_6H_4$	$C_6H_5CH_2$	5	60
k	*o*-$CH_3C_6H_4$	*m*-$CH_3C_6H_4$	2	68

[a]1 equiv. azides, 1.1 equiv. nitriles and 2 equiv. SmI_2 were used.
[b]Isolated yield based on azides.

Results and discussion

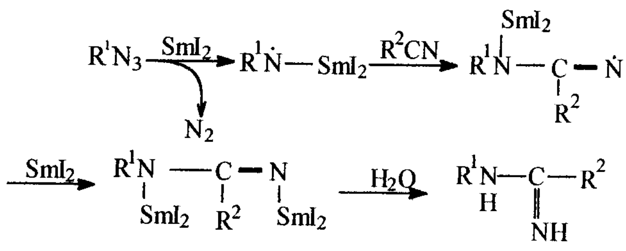
Here, we report a facile synthesis of amidines from aromatic azides and nitriles promoted by SmI_2 in THF. When aromatic azides **1** and nitriles **2** were treated with SmI_2, the intermolecular reductive cross coupling product amidines **3** were obtained (Scheme 1). The results are summarized in Table 1.



Scheme 1

In our experimental work, it was found that aromatic azides reacted with aromatic or aliphatic nitriles to produce amidines in good yields, but no reaction took place when corresponding amines were treated with nitriles under the same reaction condition. It was also found that 2 equiv. of SmI_2 were enough to accomplish the reaction, but 6 equiv. and 4 equiv. of SmI_2 were consumed respectively for the reaction of nitro compounds[10]and azobenzenes with nitriles under similar conditions. The reductive coupling of nitriles with azides completed within 2 to 5 minutes, while with nitro compounds it was 4 hours and with azobenzenes it was 18 to 24 hours.

Though the detailed mechanism of the above reaction has not been clarified yet, the possible mechanism may be postulated as shown in Scheme 2.



Scheme 2

In conclusion, with good yields, mild and neutral conditions as well as a straightforward procedure, we think that the work described herein provides a useful method for the preparation of aromatic amidines.

Experimental

Tetrahydrofuran was distilled from sodium/benzophenone ketyl immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are unconnected. Infrared spectra were recorded on a PE-683 spectrometer in KBr with absorptions in

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

cm^{-1}. ^{1}H-NMR spectra were determined on a Bruker 80MHz instrument with CCl_4 used as the solvent. Chemical shifts are expressed in p.p.m. downfield from internal tetramethylsilane. Mass spectra were recorded on ZAB-HS or Finnigan MAT GC–MS spectrometers. Microanalysis were carried out on Perkin–Elmer 24°C or Carlo-Erba 1106 instruments.

General procedure: A solution of azides **1** (1 mmol) and nitrites **2** **(**1.1 mmol) in anhydrous THF (1ml) was added dropwise to a solution of SmI_2 (2 mmol) in THF (20 ml) at room temperature under a nitrogen atmosphere. After the completion of addition, the mixture was stirred for 2–5 min under a N_2 atomosphere. After the reaction was completed, the reaction mixture was treated with 10% K_2CO_3 (30 ml) and extracted with diethyl ether (3 × 30 ml). The combined extracts were washed with saturated aqueous $Na_2S_2O_3$ (10 ml), brine (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(1:3)as eluent.

3a: m.p. 113–114 °C (Lit[11]., 112 °C); ν_{max}/cm^{-1} 3500, 3380, 1630, 1600, 1580, 1490, 1450, 1380, 1240, 1170, 1080, 1020, 835, 770, 750, 700; δ_H 5.30 (2H, brs, NH, C=NH), 6.87–7.83 (10H, m, ArH)

3b: m.p. 128–129 °C (Lit[12]., 127–130 °C); ν_{max}/cm^{-1} 3470, 3320, 1650, 1610, 1490, 1400, 1070, 860, 790; δ_H 3.63 (2H, S, CH_2), 4.8 (2H, brs, C=NH), 6.80–7.3 (10H, m, ArH)

3c: m.p. 105–106 °C (Lit[12]., 104–106 °C); ν_{max}/cm^{-1} 3460, 3320, 1640, 1590, 1490, 1390, 1240, 1170, 1020, 840, 800, 770, 720, 695; δ_H 2.37 (3H, s, CH_3), 5.2 (2H, brs, NH, C=NH), 6.907.80 (9H, m, ArH).

3d: oil; ν_{max}/cm^{-1} 3440, 3280, 2375, 1640, 1610, 1575, 1475, 1450, 1390, 1260, 1175, 1020, 920, 820, 780, 700; δ_H 2.23 (3H, s, CH_3), 4.65 (2H, br s, NH, C=NH), 6.57–7.70 (9H, m, ArH); *m/z* 212 (M^{+2}, 5), 211 (M^{+1}, 38), 210 (M^+, 100), 194(22), 107(62), 107(62), 106(28), 104(32), 91(35), 77(24); Anal. Calcd for $C_{14}H_{14}N_2$: C, 80.00; H, 6.67; N, 13.33. Found: C,79.84; H, 6.73; N, 13.43

3e: m.p. 98–99 °C; ν_{max}/cm^{-1} 3425, 3300, 2920, 2360, 1640, 1610, 1575, 1500, 1425, 1390, 1290, 1270, 1175, 1075, 1025, 910, 800, 740, 700; δ_H 2.15 (3H, s, CH_3), 3.45 (2H, s, CH_2), 4.15 (2H, brs NH, C=NH), 6.5–7.3 (9H, m, ArH); *m/z* 225 (M^{+1}, 11), 224 (M^{+1}, 11), 224 (M^+, 34), 133(100), 107(12), 91(48); Anal. Calcd for $C_{15}H_{16}N_2$: C, 80.35; H, 7.14; N, 12.51; Found:C, 80.19; H, 7.23; N, 12.58

3f: m.p. 98–99 °C; ν_{max}/cm^{-1} 3450, 3300, 2950, 1630, 1580, 1485, 1365, 1290, 1265, 1160, 920, 790, 690; δ_H 2.1 (3H, s, CH_3), 2.25 (3H, s, CH_3), 4.1–4.4 (2H, brs, NH, C=NH), 6.2–7.5 (8H, m, ARH); *m/z* 225 (M^{+1}, 25), 224 (M^+, 100), 208(21), 107(94), 91(45), 106(38), 77(7). Anal.$C_{15}H_{16}N_2$. Calcd: C, 80.35; H, 7.14; N, 12.51. Found: C, 80.19; H, 7.18; N, 12.63

3g: m.p. 115–116 °C (Lit[13]., 116 °C); ν_{max}/cm^{-1} 3440, 3250, 1640, 1610, 1570, 1500, 1465, 1385, 1320, 1260, 1235, 1125, 1050, 1030, 940, 870, 840, 780, 750, 690; δ_H 4.3–4.7 (2H, br s, NH, C=NH), 6.8–7.8(9H, m, ArH); *m/z* 231 (M^{+1}, 27), 230 (M^+, 100), 214(36), 175(52), 127(68), 104(50), 77(65). Anal. Calcd for $C_{13}H_{11}N_2Cl$: C, 67.68; H, 4.77; N, 12.18. Found: C, 67.59; H, 4.83; N, 12.09.

3h: m.p. 88–89 °C; ν_{max}/cm^{-1} 3440, 3300, 1640, 1580, 1490, 1460, 1420, 1400, 1300, 1260, 1230, 1125, 1050, 1030, 980, 820, 760, 720, 690; δ_H 3.5 (2H, s, CH_2), 3.7, 4.2 (2H, brs, NH,C=NH), 6.8–7.5 (9H, m, ArH) *m/z* 246 (M^{+2}, 11), 245 (M^{+1}, 11), 244 (M^+, 33), 209(20), 153(100), 127(12), 118(13), 111(9), 91(26)Anal. Calcd for $C_{14}H_{13}N_2Cl$: C, 68.71; H, 5.32; N, 11.45. Found: C, 68.58; H, 5.24; N, 11.76.

3i: m.p. 117–118 °C; ν_{max}/cm^{-1}3450, 3300, 1630, 1600, 1570, 1460, 1440, 1380, 1290, 1260, 1235, 1120, 1050, 1030, 940, 920, 865, 840, 790, 780, 740, 690; δ_H 2.3(3H, S, CH_3), 4.4–4.7 (2H,br, s, NH, C=NH), 6.8–7.6 (8H, m, ArH); *m/z* 246 (M^{+2}, 33), 245 (M^+, 100), 244 (M^+, 100), 228(32), 209(63), 127(61), 118(41), 111(15), 91(49); Anal. Calcd for $C_{14}H_{13}N_2Cl$: C, 68.71; H, 5.32N, 11.45. Found: C, 68.66; H, 5.40; N, 11.38

3j: m.p. 95–96 °C; ν_{max}/cm^{-1} 3475, 3300, 2340,1640, 1590, 1480, 1390, 1280, 1230, 1040, 820, 790, 740, 720, 690; δ_H 1.95 (3H, s, CH_3), 3.4 (2H, s, CH_2), 4.15–4.8 (2H, brs, NH, C=NH), 6.6–7.3 (9H, m, ArH); *m/z* 225 (M^{+1}, 10), 224 (M^+, 42), 133(100), 107(10), 106(29), 91(40), 77(5)

3k: m.p. 107–108 °C; ν_{max}/cm^{-1} 3430, 3290, 2375, 1640, 1600, 1580, 1480, 1375, 1240, 1110, 1020, 910, 840, 790, 740, 700; δ_H 2.0 (3H, s, CH_3), 2.35 (3H, s, CH_3), 4.25–4.35 (2H, brs, NHC=NH), 6.4–7.4 (8H, m, ArH); *m/z* 225 (M^{+1}, 3) 224 (M^+, 100), 209(33),118(34), 107(65, 106(38), 91(29), 77(6); Anal, Calcd for $C_{15}H_{16}N_2$: C, 80.35; H, 7.14; N, 12.51. Found: C, 80.21; H, 7.21; N, 12.58

We are grateful to the National Natural Science Foundation of China (project No.29872010) for financial support.

Received 1 September 2000; accepted 7 November 2000
Paper 00/498

References

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

2 For reviews see (a) G.A. Molander and C.R.Harris, *Chem. Rev*, 1996, **96**, 307; (b) F. Matsuda, *Synth. Org. Chem. Jpn*., 1995, **53**, 987; (c) G.A. Molander, *Org. React*., 1994, **46**, 221; (d) T. Imamota, *Lanthanides in Organic Synthesis*, Acedemic Press, London, 1994, ch. 4; (e) M. Shibasaki and H. Sasai, *Synth. Org. Chem. Jpn*., 1993, **51**, 972; (f) Molnder, G. A., *Chem. Rev.*, 1992, **92**, 29; (g) D.P. Curran, T.L. Feving, C.P. Jasperse, and M.J. Totleben, *Synlett*, 1992, 943; (h) J.A. Soderquist, *Aldrichim Acta*, 1991, **24**, 15; (i) G.A. Monlander, *Comprehensive Organic Synthesis*, ed. B.M. Trost.; I. Fleming, Pergamon, Oxford, Vol. 1, 1991, 25; (j) G.A. Molander, *The Chemistry of the Metal-Carbon Bond* ed. F.R. Hartly, Wiley, Chichester, *Vol. 5. Ch*. 1989, 8; (k) H.B. Kagan, M. Sasaki and J. Collin, *Pure Appl. Chem*., 1988, **60**, 1725; (l) H.B. Kagan, and J.L. Namy, *Tetrahedron*, 1986, **42**, 6573.

3 (a) Y. Zhang and R. Lin, *Synth. Common*., 1987, **17**, 329; (b) J. Souppe, L. Danon, L. Dannon, J.L. Namy and H.B. Kagan, *J. Organomet Chem*., 1983, **250**, 227; (c) T. Mukaigama, K. Yoyozu, K. Kato and T. Yamada, *Chem. Lett*., 1992, 181.

4 A.S. Kende and J.S. Mendoza, *Tetrahedron Lett*., 1991, **32**, 1699.

5 M.J. Burk and J.E. Feaster, *J. Am Chem. Soc*., 1992, **114**, 6266

6 (a) N.R.Natale, *Tetrahadron Lett*., 1982, **23**, 5009; (b) L. Benati, P.C. Monevecohi, D. Nanni, P. Spagnolo and M. Volta, *Tetrahedron Lett*., 1995, **36**, 7313; (c) Goulaouic – C. Dunois and M. Hesse, *Tetrahedron Lett.*, 1995, **36**, 7472.

7 G.E. Keck, S.F. Mchardy and T.T. Wager, *Tetrahedron Lett*., 1995, **36**, 7419.

8 (a) S. Patai and Z. Rappoport, *The Chemistry of Amidines and Imidates*, Wiley, New York, 1991, **27**, 226; (b) A. Kreutzverger, *Progress in Drug Research*, ed. E. Jucker, Birklauser Verlag, Basel, 1968, pp. 356-445.

9 (a) F.C. Cooper and M.W. Partridge, *J. Chem. Soc.*, 1953, 255; (b) N.A. Kalashnikova, G.N. Kullbitskii, B.V. Passet and B. Askinazi, Z. *Zh. Org. Khim*., 1974, **10**, 1529.

10 L. Zhou and Y. Zhang, *J. Chem. Soc*. *Perkin Trans I*, 1998, **28**, 2899.

11 P. Oxley, M.W. Partridge and W.F. Short, *J. Chem. Soc.*, 1947, 1110.

12 P. Oxley and W.F. Short, *J. Chem. Soc*., 1946, 147.

13 P. Oxley and W.F. Short, *J. Chem. Soc*., 1949, 449–456.