Facile Synthesis of Amidines *via* Intermolecular Reductive Coupling of Nitriles with Azobenzene Promoted by Samarium Diiodide

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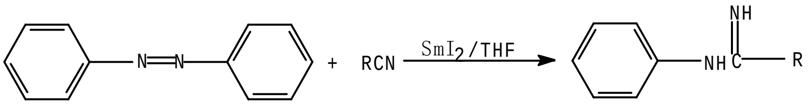
Abstract: The intermolecular reductive coupling of nitriles with azobenzene induced by SmI_2 was studied. Amidine derivatives were prepared in good yields under neutral and mild conditions.

Keywords: Synthesis, samarium, amidines, nitriles, azobenzene.

Since introduced by Kagan and his groups[1], SmI_2 has been extensively investigated as a mild, neutral, selective and versatile single electron transfer reductant in synthetic chemistry[2]. Such as, Barbier reactions, Reformatsky reactions, pinacol coupling and ketone – olefin reductive have been reported using SmI_2 as reagent. The reactivities of various nitrogen functional groups (imine, oxime, nitro, azo, cyano) towards SmI_2 have also been examined. Recently, our group has reported the intermolecular reductive coupling of nitro groups with cyano groups induced by SmI_2[3].

Scheme 1



Amidines are the nitrogen analogues of carboxylic acids and this unit consists in several compounds of biological interest[4]. They can be prepared by reaction of aromatic amines with nitriles under drastic reaction condition[5]. For example, high temperatures and long reaction times are necessary. Kagan has reported that azobenzene can be reduced by SmI_2 to give moderate yields of amines if methanol is present[6]. Here, we wish to report a new method for the synthesis of amidines promoted by SmI_2 (**Scheme 1**) in THF. When azobenzene and nitriles were treated with SmI_2, the intermolecular reductive coupling products were founded (**Table 1**). Study on the reaction shows that the nitriles with the withdrawing groups are prone to the reaction.

Table 1 Intermolecular reaction of azobenzene with nitriles induced by SmI_2 in THF

Products	R	T(℃)/t(h)	Yield(%)
a	C_6H_5	55/24	70
b	$C_6H_5CH_2$	55/24	71
c	*m*-$CH_3C_6H_4$	55/24	65
d	*p*-$CH_3OC_6H_4$	60/24	60
e	4,5-$(OCH_2O)C_6H_3$	60/24	60
f	*p*-ClC_6H_4	50/18	75
g	2,4-$Cl_2C_6H_3$	50/18	80
h	2,6-$Cl_2C_6H_3$	50/18	70

Isolated yields based on azobenzene. All products were confirmed by ^1H NMR and IR.

In conclusion, we think that the present work provides a useful method for the preparation of amidines with high yields, mild and neutral conditions as well as a straightforward procedure. Further studies to develop other new uses for SmI_2 are now in progress in our laboratory.

Experimental

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points were uncorrected. Infrared spectra were recorded on Perkin-Elmer 683 spectrometers in KBr with absorptions in cm^{-1}. ^1H NMR spectra were determined in Bruker AC 80 instrument as $CDCl_3$ solutions. Mass spectra were obtained on a HP 5989A mass spectrometer using electron impact mode (70 ev).

General procedure

Under the nitrogen atmosphere, A solution of azobenzene (0.05mmol) and nitriles (1.1mmol) in anhydrous THF (2ml) was added to a solution of SmI_2 (4.5mmol) in THF (35ml). Then the solution was stirred at the temperature for the time indicated in **Table 1**. At completion, 10% K_2CO_3 (2mmol) was added and the mixture was extracted with ether (2 x 15), The extracts were washed with brine. After being dried over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure. The crude product was purified by preparative TLC on silica gel, using ethyl acetate – cyclohexane (1: 10) as eluent.

The spectral data and physical chemical constants of compounds **a-h** are as follows.

a: mp 114-116℃ (lit.,[6] 112-115℃).ν/cm^{-1} 3500, 3410, 1620 , 1596, 1570, 1480 , 1240, 1170 , 1080, 1020, 835, 770, 750, 700. δ_H 5.40 (2 H, br s, NH, C=NH), 6.50-7.69(10

H, m, ArH).

b: mp 127-129℃ (lit.,[7]127-130℃). ν /cm^{-1} 3480, 3330, 1660, 1620, 1490, 1410, 1080, 870, 790. δ_H 3.53 (2 H, s, CH_2), 5.20 (2 H, br s, NH, C=NH), 6.80-7.65 (10 H, m, ArH).

c: mp 103-105℃ (lit.,[3]104-106℃). ν/m^{-1} 3450, 3310, 1632, 1570, 1480, 1380, 1240, 1170, 1030, 840, 800, 770, 720, 680. δ_H 2.32 (3 H, s, CH_3), 5.20 (2 H, br s, NH, C=NH), 6.80-7.90 (9 H, m, ArH).

d: mp 110-111℃ (lit.[3], 110-112℃) ν. /cm^{-1} 3460, 3320, 1640, 1580, 1479, 1370, 1240, 1080, 1020, 830, 810, 760, 710, 690. δ_H 3.70 (3 H, s, CH_3) 5.30 (2 H, br s, NH,C=NH), 6.80-7.80 (9 H, m, ArH).

e: mp 115-117℃ (lit.,[3] 116-118℃). ν/cm^{-1} 3500, 3370, 1650, 1620, 1580, 1480, 1450, 1380, 1230

f: mp 112-116℃ (lit.,[3] 8 112-115℃). ν/cm^{-1} 3480, 3380, 1630, 1610, 1575, 1490, 1450, 1380, 1240, 1110, 1010, 860, 750, 700. δ_H 5.20 (2 H, br s, NH, C=NH), 6.70-8.00 (9 H, m, ArH).

g: mp 118-120℃. ν (KBr)/cm $^{-1}$ 3410, 3200, 1640, 1530, 1490, 800, 710. δ_H 5.20 (2 H, br s, NH, C=NH), 6.70-8.00 (8 H, m, ArH). *m/z*: 264(M+), 266 , 77.

h: mp 115-117℃. ν (KBr)/cm $^{-1}$ 3470, 3330, 1650, 1520, 1480, 820, 700. δ_H 5.40 (2 H, br s, NH, C=NH), 6.75-8.10 (8 H, m, ArH). *m/z*: 264(M+), 266 , 77.

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