Catalytic Cyclotrimerization of Arylnitriles Using the Novel Samarium(II) Complexes as Catalysts[†]

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Samarium(II) complexes or Samarium(II) complexes/*n*-hexylamine systems were found to be efficient catalysts for cyclotrimerization of arylnitriles. A variety of nitriles can be converted into the corresponding substituted-s-triazines under mild conditions in good to high yields by using samarium(II) complexes/*n*-hexylamine as catalysts. The same reaction catalyzed by samarium(II) complexes alone gives s-triazines in moderate yields.

Keywords synthesis, catalysis, arylnitrile, 2,4,6-trisubstituted-s-triazine, samarium(II) complex

Introduction

Triazines are useful precursors of many biologically active compounds,[1-3] and several s-triazines[4,5] are also recognized to be the powerful chelating agents. The common methods leading to s-triazines include oxidation of aromatic aldehydes and cyclotrimerization of nitriles. The former needs long reaction time and achieves low yields,[6-8] while the latter needs rather harsh conditions of pressure[9-12] and temperature.[13,14] Acids such as CF_3SO_3H[15] or bases such as NaH[16] and $EtONa$[17] were usually used to promote the cyclotrimerization, but the highly acidic or basic conditions would likely destroy the other functional groups present in the system. Lewis acids such as $SnCl_4$[17] or Lewis acid-metal system such as Cu_2Cl_2-Zn[18] were also found to be effective, but high temperature

could not be dispensed. Forsberg et al.[19] reported that $Y(OTf)_3$ or $La(OTf)_3$ (OTf = trifluoromethanesulfonate) can catalyze the cyclotrimerization of various nitriles with ammonia as cocatalyst to give s-triazines in good yields at the temperature as high as 200 ℃.

In recent years the application of Sm(II) complexes, especially SmI_2, in organic synthesis has received great attention.[20,21] Sm(II) complexes have been found to be the mild and versatile single electron transfer agents for a variety of reactions.[22] More recently, it was reported that SmI_2 could be used as a precatalyst in several organic reactions such as aldol reaction, Michael addition, Diels-Alder reaction and ring opening reaction.[21] Recently, we reported[23] that SmI_2 could effectively catalyze the cyclotrimerization of nitriles, such as benzonitrile, acetonitrile and benzyl nitrile, to give the corresponding 2,4,6-trisubstituted-s-triazines under mild reaction conditions with *n*-hexylamine as cocatalyst. After this report, it can be found that various substituted aromatic and heteroaromatic nitriles can be effectively converted to the corresponding trisubstituted-s-triazines in the presence of catalytic amount of some other divalent complexes of samarium, such as $(CH_3C_5H_4)_2Sm$, $(Ar'O)_2Sm$, with *n*-hexylamine as cocatalyst under mild conditions.

SmI_2, $(CH_3C_5H_4)_2Sm$, or $(Ar'O)_2Sm$ alone was surprisingly found to be able to catalyze the cyclotrimerization reaction of arylnitriles although nitriles had been

found to be inert towards SmI_2 alone at room temperature.[24] Herein, we would like to present the results.

Results and discussion

Cyclotrimerization of nitriles by SmI_2/ n-hexylamine

SmI_2 can effectively catalyze the cyclotrimerization of both unsubstituted and substituted aromatic nitriles as well as heteroaromatic nitriles to give the corresponding trisubstituted-s-triazines in good yields (Scheme 1). It is somewhat surprising that SmI_2 can tolerate the polar group like Cl on the aromatic ring in these reactions. The results obtained under different reaction conditions are summarized in Table 1. As indicated in Table 1, the yields depend greatly on the structure of nitriles. The nitrile with the more electron-withdrawing group shows the greater activity. For example, the reaction with 4-pyridylnitrile, the most electron-deficient one among these nitriles, goes so fast that the yield reaches as high as 93% in the first 10 min (Entry 2). However, the two nitriles, 2-pyridylnitrile and 3-methoxybenzonitrile, give the lowest yields under the same reaction condition. The reason is not yet clear. The solid nitriles give relatively lower yields when the reactions are carried out in the absence of solvent. The reason for it may lie in their poor mixing with SmI_2 in solid phase. In fact, considerably increasing yields are observed when certain amount of toluene is added into the reaction systems (Entries 1 and 3—5). n-Propyl- or n-hexyl-amine is used in the cyclotrimerization of benzonitrile respectively and the yields obtained are almost the same (Entry 1). However, the amount of the amine is a main factor for improving the rate of cyclotrimerization. For example, the reaction of benzonitrile with n-hexylamine at 80 ℃ for 1 h gives 2,4,6-triphenyl-s-triazine in 86% yield in the case of a 4:1 (nitrile: amine) molar ratio, while only 23% yield in 20:1 molar ratio. Both increasing temperature and prolonging reaction time can raise the yields (Entries 5—7). It is interesting to find that the reaction system remains active after the

Scheme 1

$$3 \text{ ArCN} \xrightarrow[n\text{-C}_6\text{H}_{13}\text{NH}_2]{2.5 \text{ mol}\% \text{ SmI}_2}$$
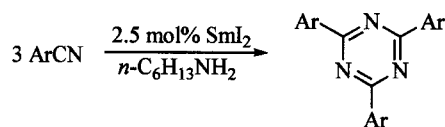
first part of 4-pyridylnitrile has been completely converted to s-triazines, and the second part of 4-pyridylnitrile added to the reaction system gives s-triazine in an 86% yield.

Table 1 Cyclotrimerization of nitriles catalyzed by $SmI_2/n\text{-}C_6H_{13}$-NH_2[a]

Entry	Ar	Temp. (℃)	Time (h)	Isolated yield (%)[b]	
1	Ph	80	3	92 (89[c])	99
2	4-Py	80	10 min	—	93
3	4-Py	80	5	83	99
4	4-ClPh	80	5	59	81
5	2-Py	80	5	38	49
6	2-Py	120	5	67	—
7	2-Py	120	24	98	—
8	3-CH₃Ph	80	5	82	—
9	4-CH₃Ph	80	5	83	—
10	4-CH₃Ph	120	48	99	—
11	3-CH₃OPh	120	48	45	—
12	4-CH₃OPh	120	48	73	—

[a] Reaction conditions: 4:1 nitrile: $n\text{-}C_6H_{13}NH_2$, 2.5 mol% SmI_2 relative to the nitrile. [b] The first column is for the reactions without solvent. The second one is for the reactions in toluene in which the concentration of SmI_2 is about 0.3 mol/L. [c] n-Propylamine is used instead of n-hexylamine.

Cyclotrimerization of nitriles by Ln(II) complexes/ n-hexylamine

It is interesting to know whether the reaction can also be catalyzed by other divalent complexes of lanthanides. Therefore we synthesized the complexes $(Ar'O)_2Sm$ ($Ar' = 2,6\text{-di-}t\text{-butyl-4-methylphenyl}$), $(Ar'O)_2Yb$, $(Ar'O)_2Eu$, $(CH_3C_5H_4)_2Sm$, $(CH_3C_5H_4)_2\cdot Yb$ and $(Ph_2N)_2Sm$, and tested their catalytic activity in the cyclotrimerization reaction of benzonitrile with n-hexylamine as cocatalyst. The results are listed in Table 2.

As shown in Table 2, the catalytic activity of these Ln(II)/amine systems is affected by the anions bonded to central metals. $(Ar'O)_2Sm$ and $(CH_3C_5H_4)_2Sm$ are both effective and the reactions with $(Ar'O)_2Sm$ or $(CH_3C_5H_4)_2Sm$ give 2,4,6-triphenyl-s-triazine almost quantitatively by heating the mixture at 80 ℃ for 24 h. Central metal also has a great effect on the activity. The active order is Sm > Yb > Eu, which is in consistency with the order of the reduction potential of lanthanide metals.

Table 2 Cyclotrimerization of PhCN catalyzed by Ln(II) complexes/ n-C$_6$H$_{13}$NH$_2$

| Entry	Catalyst	Isolated yield (%)[a]
1	(Ar'O)$_2$Sm[b]	99 (74[c])
2	(Ar'O)$_2$Yb[b]	8
3	(Ar'O)$_2$Eu[b]	0
4	(CH$_3$C$_5$H$_4$)$_2$Sm	99 (33[c])
5	(CH$_3$C$_5$H$_4$)$_2$Yb	21
6	(Ph$_2$N)$_2$Sm	10

[a] Reaction conditions: 4:1 nitrile: n-C$_6$H$_{13}$NH$_2$, 2.5 mol% catalyst relative to the nitrile, 80 ℃, 24 h. [b] Ar' = 2,6-di-t-butyl-4-methylphenyl. [c] The reaction time is 5 h.

The results of the reaction of several nitriles catalyzed by (Ar'O)$_2$Sm/n-hexylamine are summarized in Table 3. (Ar'-O)$_2$Sm can also tolerate the existence of polar groups on aromatic rings and all the nitriles tested are cyclotrimerized in moderate to good yields by use of 2.5 mol% (Ar'O)$_2$Sm with n-hexylamine. However, the activity of (Ar'O)$_2$Sm is somewhat lower than that of SmI$_2$. The reaction of benzonitrile in toluene gives much lower yield in comparison with that without toluene (Entry 1). The reason may be that the addition of toluene results in the decrease of the reactant concentration.

Table 3 Cyclotrimerization of nitriles catalyzed by (Ar'O)$_2$Sm/n-C$_6$H$_{13}$NH$_2$

Entry	Ar	Temp. (℃)	Time (h)	Isolated yield (%)[a]
1	Ph	80	5	27 (74[b])
2	4-Py	80	5	97
3	4-ClPh	80	24	33
4	2-Py	80	24	28

[a] Reaction conditions: 4 : 1 nitrile : n-C$_6$H$_{13}$NH$_2$, 2.5 mol% (Ar'O)$_2$Sm relative to the nitrile, solvent toluene. [b] Without toluene.
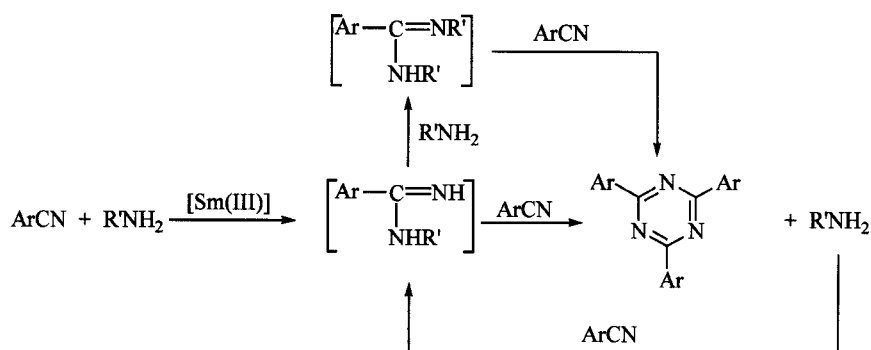
The color change of the reaction mixture from dark blue or dark brown to light brown is observed immediately after the addition of the nitrile to Sm(II) complex/amine system. This color change indicates the transformation of Sm(II) ions into Sm(III) ions.[25] So the active species for this reaction can be supposed to be a Sm(III) intermediate, which is formed by the reaction of Sm(II) complex with the nitrile and amine. It is probable that Sm(III) ions function as Lewis acid in these reactions to activate nitrile molecules and then the addition of the amine to the activated nitrile forms N-substituted amidine, which can be detected by GC-MS. Forsberg et al.[19] supposed that N-substituted amidine is directly converted to s-triazine. We found that the monosubstituted amidine already formed can be sequentially transformed into N, N'-disubstituted amidine. This amidine reacts with excess nitrile in the presence of catalytic amount of SmI$_2$ leading to the formation of the corresponding s-triazine and amine as shown in Scheme 2. In order to confirm the inference, the reactions of N, N'-di-n-butyl-benzamidine with benzonitrile at a 1 : 2 molar ratio at 80 ℃ for 24 h in the presence and absence of SmI$_2$ (7.5 mol% relative to the amidine) were studied respectively and 2,4,6-triphenyl-s-triazine in 27% yield was isolated for the former reaction, while no s-triazine in the latter case.

Cyclotrimerization of nitriles by Ln(II) *complexes*

The cyclotrimerization reaction of benzonitrile in the presence of catalytic amount of divalent complexes of samarium without n-hexylamine successfully proceeds at 120 ℃ and gives 2,4,6-triphenyl-s-triazine in moderate yields (Scheme 3).

Scheme 2

Scheme 3

$$3 \text{ PhCN} \xrightarrow{\text{SmI}_2} \text{2,4,6-triphenyl-s-triazine}$$
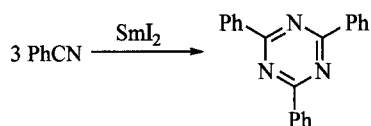
Increasing temperature and prolonging reaction time are favorable to the reaction, as multiplying the amount of catalyst. For example, when SmI_2 is 2.5 mol% relative to benzonitrile, only minor amount of the product can be isolated, while the amount of SmI_2 is raised to 20 mol%, a 35% yield is gained (Table 4, Entries 1 and 3). Similarly, when the reaction time is prolonged from 1 d to 3 d, the yield goes up to 44% (Entry 4). As in the above mentioned reaction in the presence of n-hexylamine, catalytic activity of SmI_2 is higher than $(CH_3C_5H_4)_2Sm$ and $(Ar'O)_2Sm$ (Table 5). The trivalent complexes $(CF_3SO_3)_3Sm$ and $(CH_3C_5H_4)_3Sm$, however, are catalytically inactive under the same condition.

Table 4 Formation of 2,4,6-triphenyl-s-triazine

Entry	Substrate	Amount of catalyst (mol%)	Temp. (°C)	Time (h)	Isolated yield (%)
1	—	2.5	120	24	3
2	—	10	120	24	28
3	PhCN	20	120	24	35
4	—	20	120	72	44
5	—	20	150	68	54

Table 5 Cyclotrimerization of nitriles[a]

Catalyst	Yield of different substrates (%)[b]		
	PhCN	4-ClPhCN	2-PyCN
SmI_2	35 (36^c)	39	70^c
$(CH_3C_5H_4)_2Sm$	13 (17^c)	36	71^c
$(Ar'O)_2Sm^d$	13 (15^c)	30	32^c

[a] Reaction conditions: 20 mol% catalyst relative to the nitrile, 120 °C, 24 h. [b] Isolated yields. [c] Yields measured on the crude reaction mixture by UV. [d] $Ar' = 2,6$-di-t-butyl-4-methylphenyl.

In all the cases with divalent complexes of samarium, the color change of the reaction mixture from dark blue to deep yellow or brown is observed. The fact shows that the real active species for this reaction should be $Sm(III)$ ion rather than $Sm(II)$ ion.[25] The reaction pre-

sumably involves an initial electron transfer from SmI_2 with formation of a $Sm(III)$ intermediate, though the detailed mechanism is not yet clear.

In summary, the combined $Sm(II)$ complexes/n-hexylamine catalytic systems or $Sm(II)$ complexes alone have proved to be highly efficient for the catalytic cyclotrimerization of arylnitriles to the corresponding s-triazines under mild conditions. Further applications of $Sm(II)$ complexes to other catalytic reactions are under investigations in our laboratory.

Experimental

SmI_2 was synthesized by stirring a mixture of metal Sm and I_2 in a THF solution at room temperature for several hours.[26] The other $Ln(II)$ complexes, $(Ar'O)_2Sm$ $(Ar' = 2,6$-di-t-butyl-4-methylphenyl),[27] $(Ar'O)_2Yb$,[28] $(Ar'O)_2Eu$,[29] $(CH_3C_5H_4)_2Sm$, $(CH_3C_5H_4)_2Yb$[30] and $(Ph_2N)_2Sm$[31], were prepared according to the reported method. The liquid nitriles and n-hexylamine were distilled over CaH_2 prior to use. Toluene was dried by refluxing for several hours over sodium/benzophenone and then distilled. All the manipulations were conducted under dry Ar atmosphere with flame-dried glassware. The structure of s-triazines were determined by conventional ^1H NMR, IR, MS and elemental analyses.

General procedure of cyclotrimerization of nitriles to 2,4, 6-trisubstituted-s-triazines

Catalyzed by $Ln(II)$ complexes/ n-hexylamine

A mixture of nitrile (6 mmol), n-hexylamine (0.75 mmol) and $Ln(II)$ catalyst (0.15 mmol) was heated in a sealed tube at the desired temperature for the given time. Then the reaction mixture was allowed to cool to room temperature and the solvent was removed in vacuo from the mixture. The product was scraped from the container and washed with ethyl ether or methylene chloride to remove unreacted nitrile. Recrystallization gave the pure triazines as high melting white solids.

Catalyzed by $Ln(II)$ complexes

A mixture of nitrile (6 mmol) and $Ln(II)$ catalyst (1.2 mmol) was heated in a sealed tube at the desired

temperature for the given time. The product was obtained and purified by the same procedure described above.

Triphenyl-s-triazine ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 7.59—8.80 (m); IR (KBr) ν: 3050, 1620, 1524, 745 cm^{-1}; MS m/z (%): 309 (M$^+$, 2), 105 (65), 103 (100), 77 (64). Anal. calcd for C$_{21}$H$_{15}$N$_3$: C 81.53, H 4.89, N 13.58; found C 81.49, H 4.73, N 13.66.

Tri-4-pyridyl-s-triazine ^{1}H NMR (d_6-DMSO, 400 MHz) δ: 8.65 (d, $J = 5.6$ Hz, 6H), 8.96 (d, $J = 5.6$ Hz, 6H); IR (KBr) ν: 3036, 1578, 992, 795 cm^{-1}; MS m/z (%): 312 (M$^+$, 95), 105 (33), 104 (100), 77 (28). Anal. calcd for C$_{18}$H$_{12}$N$_6$: C 69.21, H 3.87, N 26.91; found C 69.00, H 3.87, N 26.71.

Tri-p-chlorophenyl-s-triazine ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 7.55 (d, $J = 8.8$ Hz, 6H), 8.69 (d, $J = 8.8$ Hz, 6H); IR (KBr) ν: 3075, 1520, 1404, 1092, 806 cm^{-1}; MS m/z (%): 415 (27), 413 (M$^+$, 87), 411 (88), 139 (53), 137 (100). Anal. calcd for C$_{21}$H$_{12}$N$_3$Cl$_3$: C 61.11, H 2.93, N 10.18; found C 61.02, H 2.96, N 10.10.

Tri-2-pyridyl-s-triazine ^{1}H NMR (d_6-DMSO, 400 MHz) δ: 7.73 (t, $J = 5.8$ Hz, 3H), 8.14 (t, $J = 7.6$ Hz, 3H), 8.76 (d, $J = 8$ Hz, 3H), 8.92 (d, $J = 4$ Hz, 3H); IR (KBr) ν: 3056, 1524, 992, 768, 741 cm^{-1}; MS m/z (%): 312 (M$^+$, 100), 105 (31). Anal. calcd for C$_{18}$H$_{12}$N$_6$: C 69.21, H 3.87, N 26.91; found C 68.88, H 3.88, N 26.71.

Tri-m-tolyl-s-triazine ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 2.54 (s, 9H), 7.42—7.50 (m, 6H), 8.58—8.60 (m, 6H); IR (KBr) ν: 3052, 1590, 1536, 775 cm^{-1}; MS m/z (%): 352 (31), 351 (M$^+$, 100), 118 (37), 117 (79), 116 (17). Anal. calcd for C$_{24}$H$_{21}$N$_3$: C 82.05, H 5.98, N 11.96; found C 82.06, H 5.99, N 12.02.

Tri-p-tolyl-s-triazine ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 2.48 (s, 9H), 7.37 (d, $J = 8$ Hz, 6H), 8.66 (d, $J = 8$ Hz, 6H); IR (KBr) ν: 3036, 1609, 1512, 1404, 799, 772 cm^{-1}; MS m/z (%): 352 (72), 351 (M$^+$, 97), 118 (67), 117 (100), 116 (48). Anal. calcd for C$_{24}$H$_{21}$N$_3$: C 82.05, H 5.98, N 11.96; found C 82.17, H 6.00, N 12.03.

Tri-m-methoxyphenyl-s-triazine ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 3.98 (s, 9H), 7.16—7.19 (m, 3H), 7.48—7.52 (m, 3H), 8.31—8.39 (m, 6H); IR (KBr) ν: 3083, 1601, 1528, 1227, 1084, 1042, 787 cm^{-1}; MS m/z (%): 400 (23), 399 (M$^+$,

100), 398 (98), 369 (36), 134 (78). Anal. calcd for C$_{24}$H$_{21}$N$_3$O$_3$: C 72.15, H 5.31, N 10.53; found C 72.40, H 5.18, N 10.52.

Tri-p-methoxyphenyl-s-triazine ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 3.93 (s, 9H), 7.06 (d, $J = 8$ Hz, 6H), 8.71 (d, $J = 8$ Hz, 6H); IR (KBr) ν: 3067, 1605, 1520, 1420, 1250, 1146, 772 cm^{-1}; MS m/z (%): 400 (40), 399 (M$^+$, 100), 134 (17), 133 (91). Anal. calcd for C$_{24}$H$_{21}$N$_3$O$_3$: C 72.15, H 5.31, N 10.53; found C 72.16, H 5.24, N 10.50.

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