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Received October 21, 1987

Lanthanum and yttrium trifluoromethanesulfonates at 1 mole % concentration, have been found to catalyze a reaction between ammonia and aromatic nitriles to yield symmetrically substituted 2,4,6-triaryl-*s*-triazines. The generally high yields and relatively mild reaction conditions of this procedure suggest it as an alternative to other aromatic nitrile cyclotrimerization reactions. Of the aliphatic nitriles studied, acetonitrile and cyclopropanecarbonitrile gave good yields of triazine, propionitrile and butyronitrile gave significantly reduced yields of triazines **3b** and **3c** respectively. Rearrangement of **3a** and **3b** to alkylated-4-aminopyrimidines was observed.

J. Heterocyclic Chem., **25**, 767 (1988).

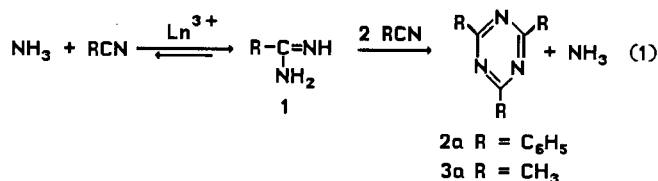
Recently we have reported on the lanthanide(III) ion catalyzed reactions of primary or secondary amines with nitriles [1]. The products of these reactions depended upon the nature of the amine or nitrile and included *N,N'*-disubstituted amidines, 1,3-diazacycloalkenes, or pyrimidines. In each instance, evolution of ammonia accompanied formation of the organic product. In addition, we observed that several of the reactions involving benzonitrile or acetonitrile produced a by-product, in variable yield, which was identified as the respective 2,4,6-trisubstituted-*s*-triazine **2a** or **3a**.

To account for the formation of triazines in these reactions we proposed that initially, the lanthanide ion catalyzed a reaction between ammonia and the nitrile to produce the mono-substituted amidine intermediate **1**. Subsequent reaction of **1** with two additional molecules of nitrile followed by cyclization and loss of ammonia would lead to **2a** or **3a** (eq 1). It is also apparent from eq 1 that the reaction is autocatalytic in ammonia.

The role of the Ln³⁺ ion in these systems is to polarize the cyano group of the nitrile through an ion-dipole interaction thus promoting the addition of ammonia. It is also likely that the Ln³⁺ ion is involved in the subsequent steps leading to triazine. The advantages of lanthanide ions compared to other typical Lewis acids in the reactions of amines with nitriles has been discussed previously [1].

Heretofore, trisubstituted-*s*-triazines have been prepared directly from nitriles only under conditions of extreme pressure (35-50 kbar) and high temperatures [2a-b] or by treatment with strong acids or bases [3]. Although ammonia and low molecular weight alcohols have been shown to promote the cyclotrimerization of nitriles, pressures in the range of 7-10 kbar are still required. Furthermore, synthesis of *s*-triazines *via* the cyclotrimerization of amidines has been shown to be useful only with formamidine or amidines prepared from aliphatic nitriles containing strongly electronegative groups on the alpha carbon atom [5]. However, the analogous alkyl imidates,

produced from nitriles and alcohols, can be converted to trisubstituted-*s*-triazines by acid catalysis [6].



The procedures described herein deal with the cyclotrimerization of nitriles using lanthanide trifluoromethanesulfonates (lanthanide triflates) and ammonia as co-catalysts. This represents, especially for aromatic nitriles, an improved procedure for the preparation of symmetrically substituted triazines, both in terms of increased yields and relatively mild reaction conditions.

The reaction of various aromatic and heteroaromatic nitriles (Table 1) with ammonia is catalyzed by anhydrous lanthanum or yttrium triflate [7]. The latter salt appears to have slightly greater catalytic activity in these systems [8]. The triazines were obtained by heating a mixture containing 1 mole % yttrium triflate and a 1:1 nitrile:ammonia mole ratio for 24 hours at 200° in a stainless steel vessel. The percent yields obtained in these reactions are shown in Table 1. It is apparent from these data that the reaction appears subject to a pronounced steric effect as evidenced by the fact that *o*-methylbenzonitrile failed to react even after prolonged heating.

The formation of trialkyl-*s*-triazines by the direct cyclotrimerization of aliphatic nitriles at temperatures greater than 150° and high pressures is fraught with generally low yields and the formation of pyrimidines as temperature dependent by-products [4]. We have found that lanthanum and yttrium triflate will catalyze a reaction between ammonia and aliphatic nitriles yielding 2,4,6-trialkyl-*s*-triazines. Of the aliphatic nitriles used in this study, however,

Table I
Formation of 2,4,6-Triaryl-*s*-triazines [a]

| Compound | R | % Isolated yield | Compound | R | % Isolated yield |
|-----------|------------------------|------------------|-----------|-------------------------|------------------|
| 2a | Phenyl | 100 | 2f | <i>o</i> -Tolyl | 0 [b] |
| 2b | <i>p</i> -Nitrophenyl | 95 | 2g | <i>p</i> -Methoxyphenyl | 63 |
| 2c | <i>p</i> -Chlorophenyl | 99 | 2h | 4-Pyridyl | 91 |
| 2d | <i>p</i> -Tolyl | 80 | 2i | 2-Pyridyl | 100 |
| 2e | <i>m</i> -Tolyl | 75 | 2j | 2-thienyl | 69 |

[a] Typical reaction conditions: 1:1 ammonia:nitrile molar ratio, 1 mole% yttrium triflate, 200° for 24 hours. [b] The reaction mixture was heated for 7 days at 200°.

only acetonitrile [9] and cyclopropanecarbonitrile gave good yields of triazine. Alkylated-4-aminopyrimidines have also been observed as persistent by-products in some of the trimerization reactions described herein, most notably with propionitrile. The yields of *s*-triazines obtained from the cyclotrimerization reactions of the aliphatic nitriles with ammonia are listed in Table II.

Table II
Formation of 2,4,6-Trialkyl-*s*-triazines

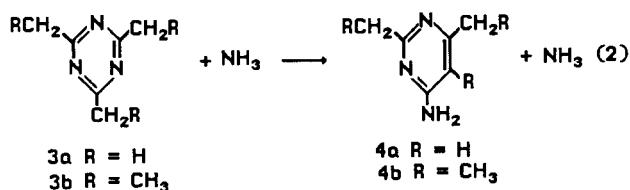
| Compound | R | % Isolated yield |
|-----------|------------------|------------------|
| 3a | methyl | 62 [a,b] |
| 3b | ethyl | 20-30 [c] |
| 3c | <i>n</i> -propyl | 4 |
| 3d | cyclopropyl | 88 [d] |

[a] Reaction conditions: 1:1 ammonia:nitrile molar ratio, 1 mole% yttrium triflate, 200° for 24 hours. [b] A 73% yield was obtained when a similar ammonia:nitrile mole ratio was heated at 110° with 2 mole% of lanthanum triflate for 5 days. [c] Variable yields were obtained when mixtures consisting of a 1:1 ammonia:nitrile molar ratio, 5 mmoles (1 mole%) of yttrium triflate, and 20 mmoles of TMED were heated at 80° for 6 days. Heating a similar reaction mixture, without TMED for 6 days at 120° produced 24% of **3b**. [d] Lanthanum triflate (1 mmole), cyclopropanecarbonitrile (150 mmoles), and ammonia (200 mmoles), heated at 100° for 6 days.

To be certain that the low yields obtained in the reactions using propionitrile and butyronitrile were not due to the insolubility of the catalyst, TMED (*N, N, N', N'*-tetramethylethylenediamine) was added to help ensure a homogeneous reaction mixture. Lanthanide-TMED complexes are expected to be labile as observed for the analogous ethylenediamine chelates [1], and therefore are not expected to interfere with the catalytic ability of the lanthanide(III) ion. However, the presence of TMED only marginally increased the yields of triazine.

Yanagiya, *et al.* have studied the mechanism of the rearrangement of trialkyl-*s*-triazines to 4-amino-2,5,6-trialkyl-

pyrimidines, which occurs in the high pressure trimerization of aliphatic nitriles in mixtures containing amines and methanol [10]. They concluded that pyrimidine formation was initiated by attack of an amine at the carbon atom of the triazine. It is likely that formation of **4a** and **4b** in the lanthanide catalyzed reaction similarly results from an attack of the triazines **3a** or **3b** by ammonia or possibly **1** (eq 2). Although **1** was generally not observed in reaction mixtures having a nitrile:ammonia mole ratio of 1:1, when



a reaction mixture containing a 1:3 propionitrile:ammonia mole ratio was kept at 80° for 6 days, 30-50% of **1** (R = Et) was observed with only a trace of **3b**. Evidently, increasing the pressure of ammonia causes a shift in the equilibrium shown in eq 1. Since ammonia is both a reactant and product, the direction of the shift favors formation of **1**. Cairns, *et al.* [5] report that when acetonitrile saturated with ammonia is heated at 150° and 7.3-6.0 kbar for 17 hours a 67% yield of **4a** is obtained. Interestingly, we have observed that heating a 1:1 acetonitrile:ammonia mixture in the presence of 1 mole % yttrium triflate at 200° in a stainless steel pressure vessel for 24 hours resulted in a 62% yield of **3a** with only a trace of **4a**. In contrast, we found that, heating a reaction mixture containing propionitrile at 110° for 6 days produced about 1% of **4b** whereas increasing the temperature to 150° resulted in a 17% yield of **4b**.

EXPERIMENTAL

Materials and Methods.

Acetonitrile, propionitrile, butyronitrile, and benzonitrile were distill-

ed from phosphorus pentoxide prior to use. All other nitriles were used as received. The nmr spectra were obtained on Varian XL-100 or EM-360 spectrometers using TMS as the internal standard. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Syntheses.

All manipulations were carried out in a glovebox under a nitrogen atmosphere [11]. The lanthanum or yttrium trifluoromethanesulfonates [1] and the desired amount of nitrile were placed inside a stainless steel pressure vessel. The vessel was sealed, removed from the glovebox and attached to a vacuum line for addition of ammonia. The desired amount of anhydrous ammonia was collected under vacuum in a calibrated tube cooled by an acetone-dry ice bath and then transferred under vacuum to the cooled reaction vessel. The vessel was removed from the vacuum line, placed in a furnace or sand bath and heated to the desired temperature.

General Procedures for 2,4,6-Triaryl-s-triazines 2a-j.

Triazines **2a-j** were obtained by heating a mixture of the nitrile and ammonia (1:1 molar ratio) and lanthanum or yttrium triflate (1 mole % relative to the nitrile or ammonia) at 200° for 24 hours. The reaction mixture was allowed to cool to room temperature and then the ammonia was allowed to bleed from the mixture. The product was scraped from the container and washed with ether or methylene chloride to remove unreacted nitrile. Recrystallization gave the triazines as high melting solids.

2,4,6-Triphenyl-s-triazine (2a).

This compound was obtained from toluene, mp 237-238° (lit [6] 235-237°).

Anal. Calcd. for $C_{21}H_{15}N_3$: C, 81.55; H, 4.85; N, 13.59. Found: C, 81.44; H, 4.96; N, 13.39.

2,4,6-Tri-*p*-nitrophenyl-s-triazine (2b).

The product did not melt below 410° (lit [6] mp > 360°).

Anal. Calcd. for $C_{21}H_{12}N_6O_6$: C, 56.75; H, 2.70; N, 18.92. Found: C, 56.59; H, 2.61; N, 18.90.

2,4,6-Tri-*p*-chlorophenyl-s-triazine (2c).

This compound was obtained from toluene, mp 338-340° (lit [14] 337-340°).

Anal. Calcd. for $C_{21}H_{12}Cl_3N_3$: C, 58.40; H, 3.50; N, 9.73. Found: C, 58.32; H, 3.04; N, 9.86.

2,4,6-Tri-*p*-tolyl-s-triazine (2d).

This compound was obtained from toluene, mp 284-286° (lit [14] 283-285°).

Anal. Calcd. for $C_{21}H_{21}N_3$: C, 82.05; H, 5.98; N, 11.96. Found: C, 82.04; H, 6.02; N, 11.94.

2,4,6-Tri-*m*-tolyl-s-triazine (2e).

This compound was obtained from hexane, mp 146-147° (lit [14] 142-147°).

Anal. Calcd. for $C_{21}H_{21}N_3$: C, 82.05; H, 5.98; N, 11.96. Found: C, 81.83; H, 6.19; N, 11.81.

2,4,6-Tri-*p*-methoxyphenyl-s-triazine (2g).

This compound was obtained from dimethylformamide, mp 219-220° (lit [14] 216.5-219°).

Anal. Calcd. for $C_{24}H_{21}N_3$: C, 72.15; H, 5.31; N, 10.53. Found: C, 72.29; H, 5.46; N, 10.53.

2,4,6-Tri-(4-pyridyl)-s-triazine (2h).

This compound was obtained from pyridine, mp > 360° (lit [12] mp > 360°).

Anal. Calcd. for $C_{18}H_{12}N_6$: C, 69.23; H, 3.85; N, 26.92. Found: C, 69.09; H, 4.00; N, 26.82.

2,4,6-Tri-(2-pyridyl)-s-triazine (2i).

This compound was obtained from water:ethanol (1:1), mp 249-251° (lit [15] 249-250°).

Anal. Calcd. for $C_{18}H_{12}N_6 \cdot 2.5H_2O$: C, 60.81; H, 4.73; N, 23.65. Found: C, 60.65; H, 4.81; N, 23.76.

2,4,6-Tri-(2-thienyl)-s-triazine (2j).

This compound was obtained from methanol, mp 193-195° (lit [16] 192-194°).

Anal. Calcd. for $C_{18}H_8N_3S_3$: C, 55.05; H, 2.75; N, 12.84. Found: C, 54.74; H, 2.97; N, 12.66.

2,4,6-Trimethyl-s-triazine (3a).

A mixture of acetonitrile (10.4 ml, 200 mmoles), anhydrous ammonia (5 ml, 200 mmoles), and yttrium trifluoromethanesulfonate (1.07 g, 2 mmoles) was allowed to react in a stainless steel pressure vessel for 24 hours at 200°. The vessel was cooled and then the ammonia was allowed bleed off. About 250 ml of ether was added to the reaction mixture and the insoluble triflate salt removed by filtration. Rotary evaporation of the ether left 5.1 g (62%) of **3a**. Purification of **3a** was accomplished by vacuum sublimation (mp 55-56°, lit. [5] 59-60°). The ¹H nmr (100 MHz, perdeuterioacetonitrile) spectrum revealed only a singlet at δ 2.41.

Anal. Calcd. for $C_6H_6N_3$: C, 58.54; H, 7.32; N, 34.15. Found: C, 58.47; H, 7.26; N, 33.97.

In a separate experiment, the reaction mixture was heated at 200° for 48 hours. Washing the cooled reaction mixture with ether gave 1.58 g of insoluble material. Recrystallization from methanol gave 0.05 g of 4-amino-2,6-dimethylpyrimidine **4a** as a white crystalline solid, mp 182-184° (lit [12] mp 182-184°): ¹H nmr (100 MHz, perdeuterioacetonitrile): δ 2.20 (s, 3H), 2.28 (s, 3H), 6.10 (s, 1H).

Anal. Calcd. for $C_6H_6N_3$: C, 58.54; H, 7.31; N, 34.15. Found: C, 58.24; H, 7.31; N, 34.22.

Evaporation of the ether solution from the above experiment yielded 3.6 g (44%) of **3a**.

2,4,6-Triethyl-s-triazine (3b).

A mixture of propionitrile (14.1 ml, 200 mmoles), anhydrous ammonia (5 ml, 200 mmoles) and yttrium trifluoromethanesulfonate (1.07 g, 2 mmoles) contained in a pressure vessel was heated at 120°. After 6 days, the vessel was allowed to cool to room temperature and the ammonia removed. The reaction mixture was filtered to remove 0.27 g of 4-amino-2,6-diethyl-5-methylpyrimidine (**4b**), mp 193.5-195° (lit [13] mp 189-190°): ¹H nmr (60 MHz, perdeuterioacetonitrile): δ 1.3 (t, 3H), 2.8 (q, 2H).

Anal. Calcd. for $C_9H_{15}N_3$: C, 65.45; H, 9.09; N, 25.45. Found: C, 65.16; H, 9.04; N, 25.60.

The filtrate from the above experiment was vacuum distilled to yield 2.6 g (24%) of **3b**, bp 120° (10 mm Hg). A sample of **3b** crystallized and melted at 24-25° (lit [12] mp 23°): ¹H nmr (100 MHz, perdeuterioacetonitrile): δ 1.25 (t, 3H), 2.25 (q, 2H).

Anal. Calcd. for $C_9H_{15}N_3$: C, 65.45; H, 9.09; N, 25.45. Found: C, 65.06; H, 9.32; N, 25.40.

In a separate reaction, propionitrile (7.0 ml, 100 mmoles), ammonia (2.5 ml, 100 mmoles), yttrium trifluoromethanesulfonate (2.68 g, 5 mmoles) and TMED (3.0 ml, 20 mmoles) were combined in a pressure vessel and heated at 80° for 6 days. The reaction vessel was then allowed to cool to room temperature and ammonia removed. Analysis (nmr) of several runs indicated about 20-30% of **3b**.

2,4,6-Tri-*n*-propyl-s-triazine (3c).

Butyronitrile (8.7 ml, 100 mmoles), ammonia (2.5 ml, 100 mmoles), yttrium trifluoromethanesulfonate (2.14 g, 4 mmoles), and TMED (2.4 ml, 16 mmoles) were added to a pressure vessel and allowed to react at 200° for 7 days. The reaction container was cooled and the ammonia allowed to bleed from the mixture. A ¹H nmr spectrum (perdeuterioacetonitrile) of the reaction mixture indicated a 10% conversion of nitrile to **3c**. Distillation under reduced pressure yielded 0.26 g (4%) of **3c**; ¹H nmr (60 MHz, deuteriochloroform): δ .86 (t, 3H), 1.56 (m, 2H), 2.66 (t, 2H).

Anal. Calcd. for $C_{12}H_{21}N_3$: C, 69.56; H, 10.14; N, 20.29. Found: C, 69.45; H, 10.44; N, 20.43.

2,4,6-Tricyclopropyl-s-triazine (**3d**).

Cyclopropanecarbonitrile (9.11 g, 150 mmoles), ammonia (5 ml, 200 mmoles), and lanthanum trifluoromethanesulfonate (0.59 g, 1 mmole) were allowed to react for 6 days at 100°. After removal of ammonia from the cooled reaction mixture the solid residue was washed out of the vessel using methylene chloride. Rotary evaporation of the solvent following removal of the triflate salt yielded 7.90 g (88%) of a pale yellow solid. Recrystallization from from methanol gave **3d** as a white crystalline solid, mp 83-85° (lit [13] mp 84-85°).

Anal. Calcd. for $C_{13}H_{15}N_3$: C, 71.64; H, 7.46; N, 20.89. Found: C, 71.41; H, 7.55; N, 20.80.

Acknowledgement.

We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

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