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Tricarbamate of 1,3,5-Triaminobenzene via Curtius Rearrangement of Trimesic Acid and Subsequent Nitration

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Abstract: The triethyl tricarbamate of 1,3,5-triaminobenzene was prepared from trimesic acid in five steps with 70% overall yield. The tricarbamate underwent nitration to give the mono-, di-, or trinitro analogs in excellent yield.

Keywords: Curtius rearrangement, nitration, 1,3,5-triaminobenzene, trimesic acid

The conventional synthesis of 1,3,5-triaminobenzene is by oxidizing TNT (2,4,6-trinitrotoluene) to 2,4,6-trinitrobenzoic acid followed by decarboxylation to TNB (1,3,5-trinitrobenzene) and finally reduction.[1–3] A method that avoids the use of compounds that are explosive would be advantageous. In 1915, Curtius described the transformation of trimesic acid (1,3,5-benzenetricarboxylic acid, **1**) into the triethyl tricarbamate of 1,3,5-triaminobenzene (**6**).[4] Because trimesic acid is relatively cheap, the oxidation product of mesitylene (1,3,5-trimethylbenzene),[5] it appeared worthwhile to determine whether this was a viable entry to 1,3,5-triaminobenzene derivatives.

The route as reported by Curtius includes five steps from **1** to **6** (Scheme 1). Trimesic acid was first converted into trimesoyl chloride (**2**) by refluxing in thionyl chloride.[6] Trimesoyl chloride was then transformed into the triethyl triester (**3**) simply by heating in ethanol, the product precipitated from the reaction mixture. Next, **3** was converted into the tricarboxylic trihydrazide (**4**)

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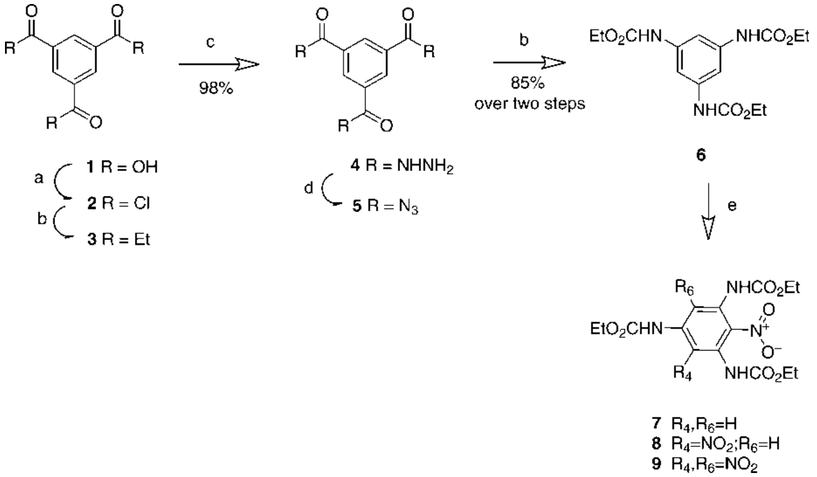

Scheme 1. Reagents and conditions: a) $SOCl_2$, quant: b) EtOH, reflux, 84%: c) N_2H_4, reflux: d) H_2O, HCl, $NaNO_2$: e) H_2SO_4, 1 equiv, 2 equiv or excess HNO_3, 0° –rt.

by heating in ethanol in the presence of excess hydrazine. Attempts to prepare **4** directly from **2,** as reported, failed.[6] The tricarboxylic trihydrazide (**4**) was then converted into the triacyl triazide (**5**) by reaction with nitrous acid at low temperature.[7] Care was taken during the isolation of **5**. By keeping the temperature low during evaporation of the ether extracts and immediate use, no problems occurred. Then **5** underwent tris-Curtius rearrangement in boiling ethanol trap the *in situ* triisocyanate and gave the tricarbamate (**6**).[8] All of the products of the route were solids.

A previous report described the decomposition of 1,3,5-triacetamidobenzene under nitration conditions.[9,10] In contrast, nitration of **6** in mixed acid at 0 °C gave the unreported mono-, di-, or trinitro products **7**–**9** with excellent yields. The overall yield of the five-step route from trimesic acid to tricarbamate (**1** → **6**) was 70%. Future studies will explore hydrolysis of **9** to 1,3,5-triamino-2,4,6-trinitrobenzene[11] and reduction of **9** to an orthogonally protected hexaaminobenzene.

EXPERIMENTAL

Melting points were collected on an electrothermal capillary melting-point apparatus and are not corrected. All NMR spectra were obtained on a Bruker AC-200 spectrometer (^1H at 200 MHz, ^{13}C at 50 MHz), except spectra for **7** and **8**, which were collected on a Bruker Avance II spectrometer (^1H at 300 MHz, ^{13}C at 75.5 MHz) and are referenced to solvent or tetramethylsilane. All reagents were purchased from Aldrich Chemical Co.

(Milwaukee) and used as received. Elemental analysis was performed by Atlantic Microlab, Inc. (Norcross, GA).

1,3,5-Benzenetricarbonyl Trichloride (2)

A 500-mL round-bottomed flask equipped with magnetic stirbar was charged with 20 g of 1,3,5-benzenetricarboxylic acid (0.095 mol), 50 mL of $SOCl_2$, and 1 drop of DMF. The mixture was refluxed for 8 h, resulting in a pale yellow solution. The $SOCl_2$ was distilled at atmospheric pressure before the product was distilled (3 mm Hg) to obtain 25 g of title compound as a colorless liquid that slowly crystallized (100%). δ_H ($CDCl_3$): 9.11 (s, 3H); δ_C ($CDCl_3$): 166.31, 138.36, 135.77.

Triethyl 1,3,5-Benzenetricarboxylate (3)

A 250-mL Erlenmeyer flask equipped with magnetic stirbar was charged with 50 mL of EtOH. The mixture was stirred while 15.78 g **2** (0.059 mol) was added in one portion. The mixture warmed to 80°C, and a white solid precipitated. The mixture was heated at reflux for 30 min and then allowed to cool to rt (~1 h) before filtering on a medium-porosity glass frit. The solid were washed with 25 mL of cold EtOH and air dried on the frit overnight (16.47 g). The crude was recrystallized from 75 mL of EtOAc to yield the title compound as colorless needles (14.56 g, 84%). Mp 128–131°C (lit.[12] 134–139°C). δ_H ($CDCl_3$): 8.85 (s, 3H), 4.45 (q, $J = 7.1$ Hz, 6H), 1.44 (t, $J = 7.1$ Hz, 9H); δ_C ($CDCl_3$): 165.20, 134.57, 131.63, 61.84, 14.38.

1,3,5-Benzenetricarboxylic Acid Trihydrazide (4)

A 500-mL round-bottomed flask equipped with magnetic stirbar was charged with 14.56 g of **3** (0.049 mol), 200 mL of EtOH, and 9.5 g of anhydrous N_2H_4 (0.297 mol, 6 equiv). The mixture was refluxed for 18 h. The white solid that precipitated was filtered on a medium-porosity glass frit and dried under vacuum (60°C). The yield of the title compound was 12.32 g (98%). No attempts were made to recrystallize the product. Mp 300°C (dec.; lit. >265°C,[13] 300°C[4,6]). δ_H (DMSO): 9.86 (s, 3H), 8.35 (s, 3H), 4.58 (s, 6H); δ_C (DMSO): 165.05, 133.85, 128.09.

Triethyl *N*,*N*′,*N*″-1,3,5-Triaminobenzenetricarbamate (6)

[*Warning*! The 1,3,5-benzenetricarbonyl triazide (**5**) intermediate during this preparation is potentially explosive. Its ether extract should be evaporated at room temperature (22°C). The 1,3,5-benzenetricarbonyl triazide (**5**) should not be stored but immediately dissolved in alcohol and reacted.] A 1-L, two-neck, round-bottomed flask equipped with magnetic stirbar was charged with 200 mL of H_2O, and 20 mL of conc. HCl (0.238 mol, 6 equiv) was added over 5 min. In one portion, 10 g of **4** (0.039 mol) was added, and the mixture was allowed to stir for 15 min, becoming a pale yellow solution. The mixture was placed in an ice bath, and a thermometer was equipped to monitor internal temperature. An addition funnel containing a solution of 17 g of $NaNO_2$ (0.199 mol, 5 equiv) in 50 mL of H_2O was equipped to the second neck. The nitrite solution was added over 1 h, making sure to keep the temperature at $\sim$ 10°C. The 1,3,5-benzenetricarbonyl triazide (**5**) [δ_H ($CDCl_3$): 8.86 (s, 3H); δ_C ($CDCl_3$): 170.77, 135.14, 132.51] intermediate precipitated during the addition as copious white solids. The mixture was stirred 20 min further in the ice bath. Ether (200 mL) was added, and the cooling bath was removed. The organic phase was separated, and the aqueous phase was extracted twice more with 200-mL portions of Et_2O. The organic extracts were collected and washed with 200 mL of H_2O, 100 mL of saturated aqueous Na_2CO_3, and finally 200 mL of brine. The organic phase was dried over anhydrous $MgSO_4$, transferred to a 2-L, round-bottomed flask and rotary evaporated (10 mm Hg, 22°C). Absolute EtOH (1 L) followed by a magnetic stirbar were immediately added to the flask containing **5**, and the mixture was refluxed for 18 h. The pale yellow solution was rotary evaporated, leaving an off-white foamy residue (11.45 g, 85%). The residue was recrystallized from $MeCN/H_2O$ to give the title compound as a white crystalline powder. Mp 101–105°C (lit.[4] 110–111°C). δ_H (DMSO): 9.49 (s, 3H), 7.28 (s, 3H), 4.09 (q, $J = 7.2$ Hz, 6H), 1.23 (t, $J = 7.2$ Hz, 9H); δ_C (DMSO): 153.45, 139.59, 103.79, 59.96, 14.54.

Triethyl *N,N′,N″*-1,3,5-Triamino-2-nitrobenzenetricarbamate (7)

A 25-mL, round-bottomed flask equipped with magnetic stirbar was charged with 10 mL of conc. H_2SO_4. The flask was cooled in an ice bath before adding 1 g of **6** (2.9 mmol) in a single portion. The cooling bath was removed, and the mixture was stirred at rt. After all the solids dissolved, the flask was cooled in the ice bath, and 130 μL of 100% HNO_3 (3.2 mmol, 1.1 equiv) was added dropwise in 10 min. Immediately the mixture becomes a dark brown color. The cooling bath was removed, and the mixture slowly becomes light brown in color. After 30 min, the mixture was poured onto 100 mL of crushed ice and H_2O, and a light yellow solid precipitated. The product was collected on a coarse-porosity glass frit and washed with H_2O several times. Recrystallized from $HOAc/H_2O$ to give bright yellow needles. Mp 134–136°C. δ_H (DMSO, 300 MHz): 10.15 (s, 1H), 9.44 (s, 2H), 7.48 (s, 2H), 4.13 (q, $J = 7.9$ Hz, 2H), 4.05 (q, $J = 7.9$ Hz, 4H), 1.24 (t, $J = 7.9$ Hz, 3H), 1.19 (t, $J = 7.9$ Hz, 6H); δ_C (DMSO, 300 MHz): 153.73, 153.23, 142.12, 133.43, 132.77, 110.57, 60.89, 60.79, 14.36.

Triethyl *N*,*N*′,*N*″-1,3,5-Triamino-2,4-dinitrobenzenetricarbamate (8)

A procedure similar to that for the preparation of **7** was used with 1 g of **6**, 10 mL of conc. H_2SO_4, and 260 μL of 100% HNO_3 (2 equiv). Recrystallized from hexanes/EtOAc to give pale yellow needles. Mp 179–181°C. δ_H (DMSO, 300 MHz): 10.11 (s, 2H), 9.66 (s, 1H), 7.79 (s, 1H), 4.13 (q, $J = 7.0$ Hz, 4H), 4.03 (m, 2H), 1.23 (t, $J = 7.2$ Hz, 6H), 1.17 (m, 3H); δ_C (DMSO, 300 MHz): 153.45, 137.36, 134.04, 127.45, 117.87, 61.59, 61.35, 14.27.

Triethyl *N*,*N*′,*N*″-1,3,5-Triamino-2,4,6-trinitrobenzene-tricarbamate (9)

A procedure similar to that for the preparation of **7** was used with 1 g of **6**, 10 mL of conc. H_2SO_4, and 1 mL of 100% HNO_3 (23.8 mmol, 8.2 equiv). The solid was air dried on the frit overnight (1.4 g, 100%). The crude product was quite pure by NMR. A sample was recrystallized from HOAc to give the title compound as very fine, pale yellow needles. Mp 248–250°C (dec.). δ_H ($CDCl_3$): 7.86 (bs, 3H), 4.27 (q, $J = 7.2$ Hz, 6H), 1.34 (t, $J = 7.1$ Hz, 9H); δ_H (DMSO): 10.43 (bs, 3H), 4.09 (q, $J = 7.4$ Hz, 6H), 1.18 (t, $J = 7.4$ Hz, 9H); δ_C (DMSO): 153.48, 143.21, 127.77, 62.08, 14.13. Elemental analysis calculated for $C_{15}H_{18}N_6O_{12}$: C, 37.98; H, 3.82; N, 17.72. Found: C, 37.84; H, 3.79; N, 17.62.

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