Synthesis and Some Reactions of Hexaazatriphenylenehexacarbonitrile, a Hydrogen-Free Polyfunctional Heterocycle with D_{3h} Symmetry

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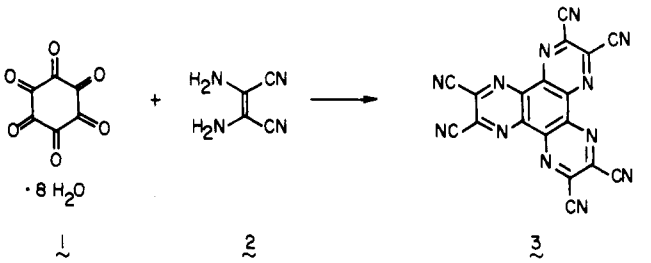
In this paper, we report for the first time the synthesis of hexaazatriphenylenehexacarbonitrile, abbreviated HAT-hexacarbonitrile. This hydrogenless, symmetrically branched compound can be prepared in analytically pure form on a large scale by using commercially available starting materials. The conversions of HAT-hexacarbonitrile to the corresponding hexaamide, hexaacid, hexaester, and trianhydride derivatives were also accomplished.

In this paper we report the first synthesis of hexaazatriphenylenehexacarbonitrile (HAT-hexacarbonitrile) (**3**) by a simple method from readily available precursors. Derivatives of this compound, containing no hydrogen, are potentially useful in the preparation of thermally stable, oxidation-resistant polymers.[1] Hexaazatriphenylene (HAT-H_6) itself has been made previously, but the first reported sequence[2] is rather long and does not suggest an easy way to incorporate the kind of multiple functionality present in hexacarbonitrile **3**. Recent methods using hexaaminobenzene[3] as the starting material are shorter, but have been utilized preparatively only in the syntheses of hexaalkyl-HAT's[3a] and, more recently, HAT-H_6 itself.[3b] Therefore, we now describe the one-step synthesis of hexacarbonitrile **3** and its conversion to hexaamide **4**, hexaacid **5**, hexaester, and trianhydride **6** derivatives.

Our starting material, hexaketocyclohexane octahydrate (**1**), is available commercially but is rather expensive. We have therefore prepared it in a two-step reaction from glyoxal; self-condensation to afford tetrahydroxyquinone proceeds as described previously,[4] and then oxidation to compound **1** was accomplished by using a modified literature[5] method. Reaction of hexaketone **1** with an excess of diaminomaleonitrile (**2**) in refluxing glacial acetic acid affords hexacarbonitrile **3** in 81% yield as shown in Scheme I. Our procedure is in close analogy to that used by Skujins and Webb in their condensation of hexaketone **1** with *o*-phenylenediamine.[6] Hexacarbonitrile **3** is isolated by simple filtration from the hot reaction mixture and is analytically pure after drying. Its ^{13}C NMR spectrum reveals the simple pattern expected for a compound with D_{3h} symmetry, and we observe three singlets: one for nitrile carbons, one for peripheral aromatic carbons, and one for internal aromatic carbons. As anticipated, the compound is quite insoluble in nonpolar organic solvents, but solutions in DMF or Me_2SO can be made. A DMF solution with tetrabutylammonium perchlorate as the supporting electrolyte was used to establish a chemically reversible couple centered at −0.105 V (ΔE_p 100 mV) vs.

Scheme I



aqueous SCE (−0.595 V vs. ferrocene) for compound **3** leading to its radical anion; a second, irreversible couple leading to the dianion was observed at −0.495 V.

Hydration of hexacarbonitrile **3** to hexaamide **4** is accomplished readily using concentrated sulfuric acid at room temperature for 3 days (Scheme II). As in every reaction involving derivatives of **3**, it is particularly important that *all* of the functional groups be converted to the next in very high yield; a procedure that afforded the pentacarboxamide mononitrile as a contaminant, for example, would be useless. ^{13}C NMR of hexaamide **4** again reveals the simple pattern expected, except that the peripheral carbons are coupled to one of the amide NH's.[7] Coupling to only *one* of the two amide NH's can be rationalized by recalling that $J_{C,H}$ experiences the same kind of angular dependence that $J_{H,H}$ does.[8] The approximately 7-Hz coupling constant we measure is consistent with long-range C–H coupling, and only the amide NH syn to the carbonyl oxygen exists in a "w conformation" with respect to the peripheral carbon; we propose, therefore, that it is the only proton coupling to that carbon. Of special interest is the ability of laser desorption Fourier transform ion cyclotron resonance mass spectrometry[9] to yield a molecular ion for this highly polar, nonvolatile molecule (K^+ complex ion observed). No other mass spectrometric technique we have tried gave us any interpretable data on this compound.

Attempted basic hydrolyses ($NaOH/H_2O$/heat or Na_2O_2/H_2O) of hexaamide **4** to hexaacid **5** consistently yielded mixtures of partially hydrolyzed polyacids, determined by ion-exchange chromatography and by paper electrophoresis; this result is not too surprising, as hydroxide attack is expected to become progressively slower on the progressively greater charged polyacid. Acidic hydrolysis methods also gave mixtures of insoluble products that were not readily characterized. We were suc-

(1) For introductory reading, see: (a) Labana, S. S., Ed. *Chemistry and Properties of Crosslinked Polymers*; Academic: New York, 1977; pp 85–137. (b) Frazier, A. H., *High Temperature Resistant Polymers*; Wiley: New York, 1698; pp 285–318.

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(3) (a) Kohne, B.; Praefcke, K. *Liebigs Ann. Chem.* **1985**, 522. (b) Rogers, D. Z. *J. Org. Chem.* **1986**, *51*, 3904 (this paper describes both a convenient synthesis of hexaaminobenzene and its conversion to hexaazatriphenylene with glyoxal in 83% crude yield).

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(5) (a) Nietzki, R.; Benckiser, T. *Ber.* **1885**, *18*, 506. (b) Ochiai, E.; Kobayashi, Y.; Haginiwa, T.; Takeuchi, S.; Fujimoto, M. *Chem. Abstr.* **1967**, *66*, 104832.

(6) Skujins, S.; Webb, G. A. *Tetrahedron* **1969**, *25*, 3935.

(7) It is not surprising that the carbonyl carbon does not couple to the adjacent amide proton; the almost complete lack of carbonyl coupling to adjacent (but not directly bonded) protons allowed early ^{13}C NMR investigators to observe signals before the advent of decoupling methods.

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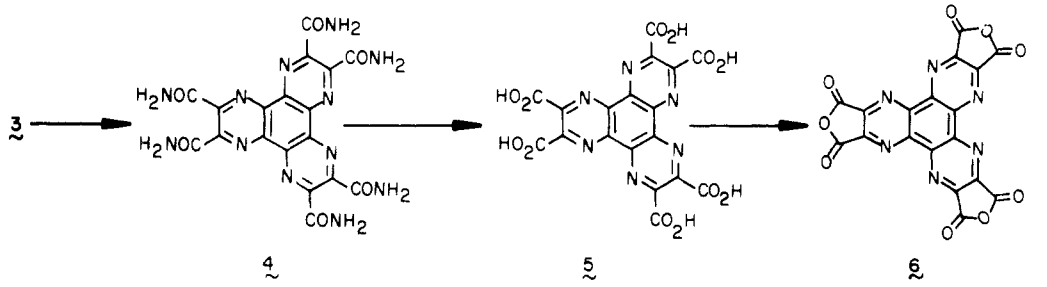
Scheme II



cessful in converting hexaamide to hexaacid under diazotizing conditions[10] by using sodium nitrite in trifluoroacetic acid, and precipitation of the sodium salt afforded the hexacarboxylate as confirmed by its microanalysis and simple ^{13}C NMR spectrum taken in D_2O/H_2O. As compared to the highly water-insoluble hexacarbonitrile or hexaamide, hexaacid **5** is very water soluble as its polycarboxylate. Vigorous treatment with HCl results in ion exchange and precipitation of the less soluble carboxylic acid form with no observable decarboxylation; acid-catalyzed esterification with methanol yields the hexamethyl ester in 84% yield. In addition, the hexaacid forms water-insoluble metal ion complexes; this work is still in progress and will be reported at a later date.

Trianhydride formation was accomplished by using hot acetic anhydride by analogy to the known[11] conversion of pyrazine-2,3,5,6-tetracarboxylic acid to the corresponding dianhydride. Temperature control seems particularly important in our conversion, as does starting with a sample of the hexaacid that has been completely converted to the H^+ form. We find that heating a suspension of hexaacid **5** in freshly distilled acetic anhydride at 114–116 °C for 10 min yields a homogeneous solution that, upon evaporation, gives the trianhydride **6** as a moisture-sensitive solid. Crystallization from acetonitrile/benzene/trifluoroacetic anhydride affords a crystalline, moisture-sensitive solid whose ^{13}C NMR spectrum consists of three lines. Treatment of the ^{13}C NMR sample with 1 equiv of H_2O led to a significantly complicated spectrum that, upon further addition of excess H_2O, again demonstrated a three-line spectrum identical with that of the hexaacid in the same solvent. The trianhydride is much more soluble in organic solvents (e.g., acetonitrile) than the other HAT derivatives we have prepared.

In summary, we have reported a one-step tricondensation reaction that leads to the hexaazatriphenylene nucleus in excellent yield. Manipulation of the functionality available on HAT-hexacarbonitrile will lead to derivatives heretofore unavailable, such as the three we have described in this paper. We expect to report on the synthetic methods required, as well as studies on the physical properties of these compounds, as our work in this area continues.

Experimental Section

General. Melting points were taken on an Electrothermal melting point apparatus and are uncorrected. Microanalyses were carried out at Canadian Microanalytical Service, New Westminster, B.C. Mass spectra were obtained by use of a Kratos-30 mass spectrometer. FT-NMR spectra at 11.75 (500 MHz) or 7.0 T (300 MHz) were obtained with equipment funded in part by NIH Grant 1 S10 RR01458-01A1. We thank Richard Weisenberger and Dr. C. E. Cottrell for their assistance in obtaining mass and high-field ^1H NMR spectra, respectively, at The Ohio State University Chemical Instrumentation Center, and Carl Engelman for other NMR assistance.

Hexaketocyclohexane Octahydrate (1). We have modified the original procedure reported by Nietzki et al.[5a] as follows: Powdered sodium tetrahydroxyquinone[4] (10.8 g, 50 mmol) was added in portions to a stirred, ambient temperature solution of 25% HNO_3 (150 mL) over a period of 10 min. The temperature of the vigorous reaction was controlled at 45 ± 5 °C by using an ice bath, and the resulting clear, light yellow solution was cooled at 5 °C. Colorless crystals formed and were collected by filtration, washed with cold water (3 × 30 mL), and dried to give **1** (11.7 g, 80%): mp 95–96 °C dec (lit.[5b] mp 95–96 °C dec).

Hexaazatriphenylenehexacarbonitrile (3). A mixture of hexaketocyclohexane octahydrate (10.0 g, 32 mmol) and diaminomaleonitrile (26.0 g, 240 mmol) in glacial acetic acid (1200 mL) was heated to reflux with stirring for 2 h. The black reaction was filtered hot, and the solid was washed with hot glacial acetic acid (3 × 150 mL). Drying over KOH pellets at 150 °C and 0.01 torr for 2 h afforded a brown-black[13] solid (10.1 g, 81%): mp >350 °C; ^{13}C NMR ($(CD_3)_2SO$) δ 114.2 (br s, CN's), 135.4 (s, internal Ar carbons), 141.6 (s, peripheral Ar carbons); IR (KBr pellet) 2250 cm^{-1} (weak, CN); UV (Me_2SO) 288 nm, 310; desorption chemical ionization mass spectrum (CH_4), *m/e* (relative intensity) 385 (100, $[M + 1]^+$).

Anal. Calcd for $C_{18}N_{12}$: C, 56.25; H, O; N, 43.75. Found: C, 56.09; H, 0.14; N, 43.60.

Hexaazatriphenylenehexacarboxamide (4). A solution of HAT-hexacarbonitrile (4.80 g, 12.5 mmol) in concentrated H_2SO_4 (100 mL) was stirred at room temperature for 72 h and then was added dropwise to rapidly stirred ice–water (3 L). The solid was collected by filtration, washed with water (3 × 100 mL) and acetone (3 × 100 mL), and dried at 100 °C and 0.01 torr for 14 h to provide a gray-black solid (5.38 g, 87%): mp >350 °C; ^{13}C NMR ($(CD_3)_2SO$) δ 140.5 (s, internal Ar carbons), 148.3 (d, J = 7.3 Hz, coalesces to s with broad-band ^1H decoupling, peripheral Ar carbons), 166.2 (s, $CONH_2$'s); IR (KBr pellet) 1680 cm^{-1} (strong, C=O); UV (Me_2SO) 280 nm, 322; laser desorption FT ICR mass spectrum; *m/e* (relative intensity) 531 (100, $[M + K]^+$).

Anal. Calcd for $C_{18}H_{12}N_{12}O_6 \cdot H_2O$: C, 42.35; H, 2.77; N, 32.94. Found: C, 42.62; H, 2.74; N, 33.00.

Hexaazatriphenylenehexacarboxylic Acid (5). A solution of HAT-hexacarboxamide (4.92 g, 10 mmol; **4**) in trifluoroacetic acid (150 mL) was stirred at room temperature. Solid sodium nitrite (7.0 g, 90 mmol) was added to this solution portionwise over a period of 15 min, with the temperature kept under 25 °C by cooling with an ice bath. An initial brisk evolution of gas was noted, and the black solution changed to an orange brown suspension. Acetic acid (150 mL) was added, the mixture was stirred

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(11) Hirsch, S. S. *J. Polym. Sci.* **1969**, *7*, 15.
(12) While the ^{13}C NMR spectrum of this compound clearly demonstrates its structure as the trianhydride, its high reactivity with water has frustrated our efforts at microanalysis. Even with desiccated shipping methods, this compound analyzed correctly for $C_{18}N_6O_9$ plus 0.6 molecules of H_2O, indicating partial hydrolysis.
(13) One reviewer has suggested that this color is due to an impurity of the phthalocyanine self-condensation product of nitrile **3**, which could form during the initial acetic acid reaction. In our experience, the only way to check the purity of this compound is to take its ^{13}C NMR spectrum. The Me_2SO-d_6 solution used must be stirred for several hours at room temperature to ensure complete dissolution. Samples that are either (a) impure because of defective starting materials or improper reaction conditions or (b) incompletely dissolved will demonstrate very broad singlets even for the aromatic carbons. We now routinely test every batch of HAT-hexacarbonitrile in this way before its further conversion.

for 12 h and poured into ice-water (300 mL), and the crude product was collected by filtration. The solid was dissolved in sodium bicarbonate solution (20 g in 150 mL water) and filtered to remove any insoluble solid. The filtrate was treated with activated charcoal, heated to boiling, and filtered to give a clear yellow solution that was treated with a cold sodium hydroxide solution (20.0 g in 100 mL water). An immediate precipitation of sodium HAT-hexacarboxylate as a yellow solid occurred, and complete precipitation of the salt was effected by the addition of ethanol (30 mL). The product was filtered, washed with 50% aqueous alcohol (3 × 50 mL), and dried under vacuum [100 °C (0.1 torr)] to afford 4.53 g of the polysodium salt of **5**: IR (KBr pellet) μ 1618 cm^{-1} (>C=O); ^{13}C NMR (D_2O/H_2O) δ 140.00 (s, internal carbons), 151.08 (s, peripheral carbons), 171.70 (s, carboxylate carbons).

The **free acid** was obtained as follows: Polysodium HAT-hexacarboxylate (2.52 g, 40 mmol) was suspended in water (100 mL), heated to 50 °C, and acidified by adding concentrated HCl (100 mL). The mixture that formed was heated at 90 °C for 1 h, then was filtered, washed with 10% HCl (3 × 25 mL), and finally washed with deionized water 2 × 25 mL). The product was dried at 120 °C (0.1 torr) to give **5** (1.88 g, 89.5%) as its sesquihydrate: mp >350 °C; ^{13}C NMR (D_2O/dilute NH_4OH) δ 140.1 (s, internal Ar carbons), 151.2 (s, peripheral Ar carbons), 171.7 (s, carboxyl carbons); IR (KBr pellet) μ 1730 cm^{-1} (>C=O); UV (Me_2SO) 278 nm, 316.

Anal. Calcd for $C_{18}H_6N_6O_{12}\cdot1.5H_2O$: C, 41.16; H, 1.73; N, 15.99. Found: C, 41.07; H, 1.91; N, 15.82.

The **hexamethyl ester** was prepared as follows: A solution of hexaacid acid **5** (525 mg of the sesquihydrate, 1 mmol) in absolute methanol (200 mL) and concentrated sulfuric acid (1 mL) was heated to reflux with stirring for 10 h. The solid was collected by filtration, washed with aqueous methanol (50 mL), and dried at 100 °C and 0.01 torr for 6 h to provide a cream colored solid (490 mg, 84%) that could be recrystallized from acetonitrile: mp >350 °C; ^{13}C NMR (Me_2SO-d_6) δ 164.02 (s, ester carbonyl carbons), 145.08 (s, internal or peripheral Ar carbons), 142.23 (s, internal or peripheral Ar carbons), 53.63 (s, methyl carbons); ^{1}H NMR ($CDCl_3/CF_3COOH$) δ 4.17 (s, CH_3); IR (KBr pellet) μ 1750 cm^{-1} (strong, C=O); UV (Me_2SO) 274 nm, 312; FAB mass spectrum, m/e 583 ($M^+ + 1$).

Anal. Calcd for $C_{24}H_{18}N_6O_{12}$: C, 49.48; H, 3.09; N, 14.43. Found: C, 49.12; H, 3.14; N, 14.50.

Hexaazatriphenylenehexacarboxylic Acid Trianhydride (6). HAT-hexacarboxylic acid (1.25 g, 23.8 mmol; **5**) was added to freshly distilled acetic anhydride (60 mL) and heated to 115 ± 2 °C under a nitrogen atmosphere. The vigorously stirred mixture turned to a clear brown solution within 10 min, then heating was discontinued, and the solution was allowed to cool over a period of 20 min. The solvent was removed by rotary evaporation under reduced pressure, and the residue was recrystallized from acetonitrile and benzene (by using a few drops of trifluoroacetic anhydride as desiccant) to give **6** (963 mg, 95%) as moisture-sensitive needles: mp >350 °C; ^{13}C NMR (CD_3CN) δ 159.58 (s, carbonyl carbons), 148.62 (s, internal or peripheral Ar carbons), 148.15 (s, internal or peripheral Ar carbons); IR (KBr) μ 1820 (strong), 1880 cm^{-1} (>C=O).

Anal.[12] Calcd for $C_{18}N_6O_9\cdot0.6\,H_2O$: C, 47.51; H, 0.27; N; 18.47. Found: C, 47.88; H, 0.30; N, 18.11.

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Allylic Selenides in Organic Synthesis: New Methods for the Synthesis of Allylic Amines

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Oxidative rearrangement of allylic selenides in the presence of various amine nucleophiles provides synthetic access to a variety of allylic amine derivatives. The stereochemical outcome of these reactions has been investigated, and is consistent with a [2,3]-sigmatropic rearrangement mechanism. Several D-α-amino acids and racemic β,γ-unsaturated α-amino acids were prepared in this manner. A variant of this process employing an achiral allylic selenide and chiral amide afforded protected allylic amines in low diastereoisomeric excess.

The amine function is nearly ubiquitous in the molecules of nature. For this reason, methods which provide synthetic access to amines are of some significance. Allylic amines, for example, are both useful synthetic intermediates[1] and are a common structural element in naturally occurring substances.[2] Unfortunately, unlike the closely related allylic alcohol function, for which many synthetic methods exist, allylic amines are available by a relatively limited number of procedures.[3] We describe in this paper a complete account of our own synthetic studies of allylic amine synthesis using organoselenium intermediates.[4]

We became concerned with the preparation of optically active allylic amines, due to an interest in peptide isosteres

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