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Synthetic methods and product characterizations for the conversions of 1,4,5,8,9,12-hexaazatriphenylene-hexacarboxylic acid to the corresponding triester triacid, triamic acid, triimide, triester triacid chloride, trimethyl triethyl hexaester, trimethyl ester tri(*N,N*-dimethyl)amide, hexaamide, tri(*N,N*-dimethyl)amide triacid, tri(*N,N*-dimethyl)amide triacid chloride, and trisphthalhydrazide derivatives are described.

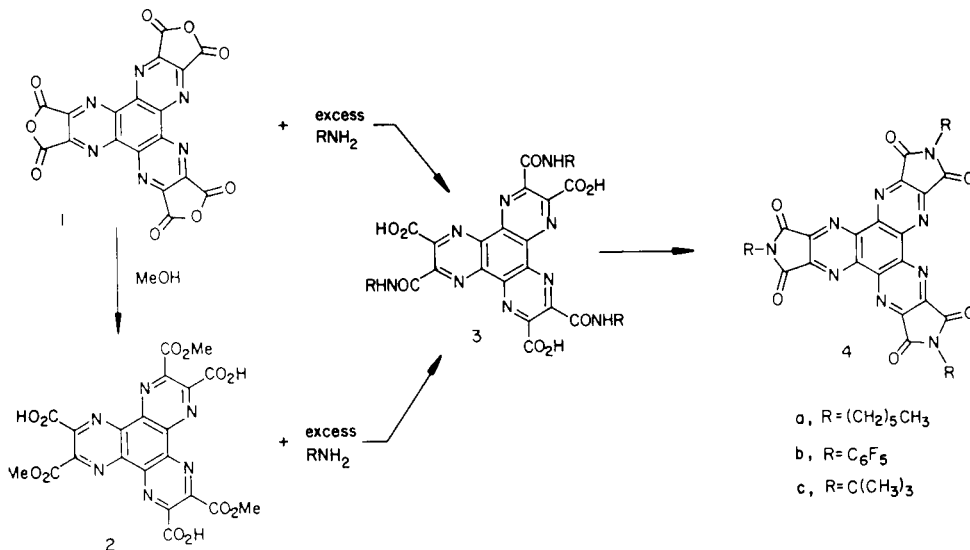
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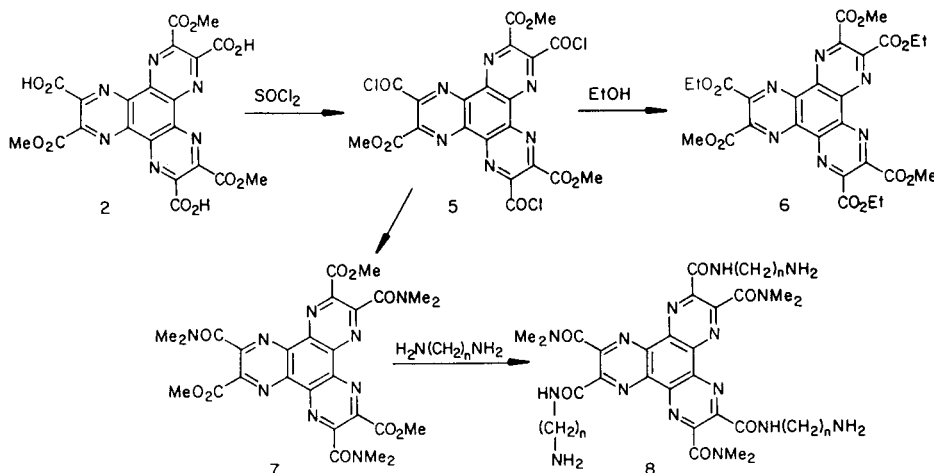
As part of our interest in the use of hexaazatriphenylene (HAT) derivatives for the synthesis of thermooxidatively-stable polymers [1], we have been studying the chemistry of hexaazatriphenylene trianhydride (**1**). In this report, we focus on the synthesis of hexasubstituted derivatives of HAT useful for the preparation of polyimides [2], *i.e.*, all substituents at the carboxylic acid oxidation level.

Hexaazatriphenylene trianhydride (**1**) proved to be an unusually reactive aromatic anhydride. While it can be obtained in crystalline form [3], reaction with atmospheric moisture is extremely facile; for this reason, it is not convenient to store the anhydride. As one solution, we reacted anhydride **1** immediately with anhydrous methanol to afford the triester triacid **2**, which is a solid and infinitely stable when stored in a desiccator. Two isomeric triester triacids are possible in this reaction: compound **2**, which possesses D_{3h} symmetry, and the unsymmetrical derivative in which one set of ester and acid groups has been interchanged. To the limits of our analytical detection (*ca.* 5% by ^1H nmr), only the symmetrical isomer **2** is obtained in this reaction, based on the simplicity of the ^1H and ^{13}C nmr spectra obtained. Of course, this conclusion is based on an imperfect assumption that the two isomers would not have superimposable spectra.

Both trianhydride **1** and triester triacid **2** can be reacted with primary amines to provide symmetrical amic acids **3**, although the trianhydride route is preferable with relatively unreactive amines (*e.g.*, *t*-butylamine). The amic acids can be conveniently isolated by acid-precipitation from aqueous solution. Chemical imidization (*i.e.*, **3** \rightarrow **4**) was accomplished using a variety of dehydrating agents, including acetic anhydride, trifluoroacetic anhydride, and thionyl chloride. The resulting triimides **4a-c** were high-melting solids, whose ^{13}C nmr spectra revealed the simple patterns expected for symmetrical compounds [4].

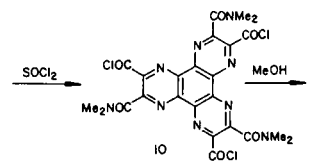
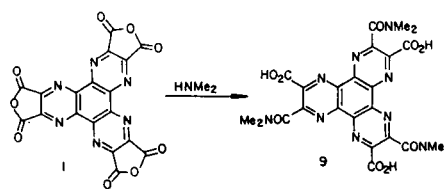
The preparation of triamic acids derived from α,ω -diamines led to zwitterionic products with unacceptable solubility properties. For example, the reaction of trianhydride **1** with 1,6-hexanediamine provides compound **3**, $\text{R} = (\text{CH}_2)_6\text{NH}_2$, that is soluble in water but highly insoluble in methanol, chloroform, THF, DMF, dimethylacetamide, and DMSO. Chemical imidization with acetic anhydride affords triimide **4**, $\text{R} = (\text{CH}_2)_6\text{NHAc}$, which is highly soluble to organic solvents; however, we have (not surprisingly) been unable to remove the acetyl groups without hydrolyzing the imide group. Inasmuch as the polymerization reaction cannot be conducted in water, a suitably protected, organic soluble derivative of the



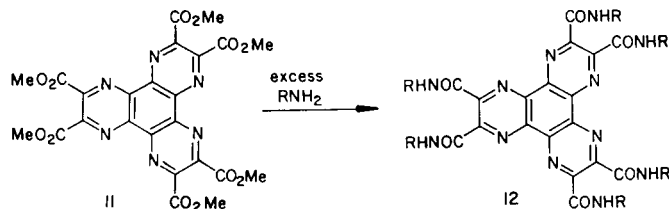


triamic acids was sought. We found that conversion of triester triacid **2** to the corresponding triacid chloride **5** could be accomplished using standard conditions. While the acid chloride was not characterized, conversion to the trimethyl triethyl ester **6** by treatment with ethanol provided both a structure proof for **5** and additional evidence that compound **2** is, in fact, a single isomer.

Reaction of acid chloride **5** with excess dimethylamine provides triester triamide **7** with no apparent further reaction to higher amide derivatives. Compound **7** is a very useful protected version of triester **2**, and therefore of trianhydride **1**. The nmr spectra of **7** are complex, we feel owing to the various conformational isomers that the functional groups of **7** can adopt (e.g., the amide and ester groups can be "above" or "below" the heterocycle plane, etc.). Indeed, heating a solution of **7** in DMSO- d_6 results in a coalescence of the amide methyl peaks from a multiplet at 2.95-3.25 ppm (30°) to two broad singlets at 3.07 and 3.18 ppm (130°). Compound **7** affords mixed hexaamides in the reaction with primary diamines; for example, treatment of **7** with 1,6-hexanediamine affords hexaamide **8**, which is soluble in both water and polar organic solvents like acetonitrile and chloroform. We have observed on a small scale that reaction of hexaamide **8** with trifluoroacetic anhydride and heat provides the *N*-trifluoroacetylated triamide as product. Interestingly, **7** is quite unreactive towards substitution by a secondary amine; attempted reaction of **7** with excess dimethylamine returns starting material as the only product. Additionally, reaction of **7** with 1-hexylamine under the same conditions gives only starting material back. Intermediate **7** may also be obtained *via* the *N,N*-dimethylamic acid **9**. Conversion to the *N,N*-dimethylamic acid chloride **10** with thionyl chloride and methanolysis gave triester triamide **7** that was identical to that prepared using the other route. In practice, we find that the sequence **2** → **5** → **7** is the simplest to perform, and is therefore preferable.

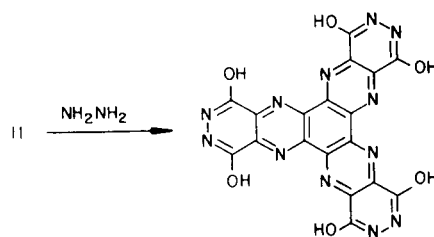


As reported previously, the hexamethyl ester of HAT **11** may be prepared straightforwardly from the hexaacid [3]. Predictably, these ester groups are highly reactive towards acyl substitution reactions. Reaction of **11** with either



a, R = (CH₂)₅ CH₃

b, R = (CH₂)₉ CH₃



1-hexyl- or 1-decylamine provides the corresponding hexamides **12a** and **12b**. Both compounds are highly insoluble in neutral media (e.g., chloroform, DMF, DMSO), perhaps because of the very favorable amide-amide hydrogen-bonding interaction made possible in a stacked HAT assembly; this hypothesis is being checked by X-ray crystallography.

Finally, reaction of hexaester **11** with hydrazine hydrate affords the corresponding trisphthalhydrazide **13** as a black solid. This compound is soluble in basic aqueous solution, and its ^{13}C nmr spectrum reveals the simple three-line pattern expected for the symmetrical product. Conversion to the trisodium salt with sodium hydroxide again afforded a black solid, which gave appropriate microanalytical data.

EXPERIMENTAL

Mass spectra were obtained by use of a Kratos-30 mass spectrometer. The Ft-nmr spectra at 11.75 tesla (500 MHz) or 7.0 tesla (300 MHz) were obtained using equipment funded in part by NIH Grant #1 S10 RR01458-01A1. We thank Mr. Richard Weisenberger and Mr. Carl Engelman for their assistance in obtaining mass and high-field ^1H nmr spectra, respectively. 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. Many of the compounds in this series are hygroscopic; satisfactory microanalyses were calculated based on hydrated samples. Perhaps for the same reason, the melting points of some compounds in this series were found to be variable.

2,6,10-Tricarbomethoxy-1,4,5,8,9,12-hexaazatriphenylene-3,7,11-tricarboxylic Acid (**2**).

A mixture of hexaazatriphenylenehexacarboxylic acid [**3**] (1.5 g, 3 mmoles) in acetic anhydride (40 ml) was heated to 115° briefly to obtain a homogeneous solution. After cooling and evaporation, trianhydride **1** [**3**] was obtained as an oil that was used without purification. Anhydrous methanol (25 ml) was added, then the solution was concentrated and poured into ice water (25 ml). The solid was filtered, washed with water, and dried *in vacuo* to give triester triacid **2** as a light yellow solid (1.49 g, 92%), mp $205\text{--}207^\circ$ dec; uv (DMSO): 276, 314 nm; ^1H nmr (DMSO- d_6): 4.1 (s, 3H, OCH_3) ppm; ^{13}C nmr (DMSO- d_6): 53.6 (CH_3), 141.9 and 142.3 (internal aromatic carbons), 145.6 and 146.4 (peripheral aromatic carbons), 164.7 and 165.4 (ester and acid carbonyl carbons) ppm; Fab ms: m/e 542 ($\text{M}^+ + 2$), 541 ($\text{M}^+ + 1$).

Anal. Calcd. for $\text{C}_{21}\text{H}_{12}\text{N}_6\text{O}_{12} \cdot 1.5\text{H}_2\text{O}$: C, 44.55; H, 2.66; N, 14.81. Found: C, 44.27; H, 2.87; N, 14.52.

Tri(*N*-*n*-hexyl)-1,4,5,8,9,12-hexaazatriphenylene-2,3,6,7,10,11-hexacarboxylic Acid Trisimide (**4a**).

Trianhydride **1**, prepared as described above from the hexaacid (996 mg, 2 mmoles), was dissolved in dry acetonitrile (50 ml) and *n*-hexylamine (2.1 g, 20 mmoles) was added. The yellow precipitate that formed was filtered and washed with acetonitrile. The solid was suspended in water (400 ml), acidified with concentrated hydrochloric acid (10 ml), stirred vigorously for one hour, filtered, washed with water, and dried *in vacuo* to afford triamic acid **3a** (1.4 g, 88%), which decomposes above 180° . The crude amic acid (1.11 g, 1.5 mmoles) was mixed with acetic anhydride (50 ml) and trifluoroacetic acid (0.5 ml), refluxed for 2 hours, and the resulting clear solution was evaporated to dryness. The residue was dissolved in hot toluene, treated with charcoal, filtered, and recrystallized with addition of hexane to give trisimide **4a** (884 mg, 85%), mp $246\text{--}248^\circ$; uv (DMSO): 288, 338 nm; ^1H nmr (deuteriochloroform): 0.9 (t,

3H, CH_3), 1.35 (m, 6H, 3 x CH_2), 1.85 (quintet, 2H, CH_2), 4.0 (t, 2H, NCH_2) ppm; ^{13}C nmr (deuteriochloroform): 14.0, 22.5, 26.6, 28.4, 31.3, 39.8 (aliphatic carbons), 144.6 (internal aromatic carbons), 148.8 (peripheral aromatic carbons), 162.0 (carbonyl carbons) ppm; Fab ms: m/e 696 ($\text{M}^+ + 3$).

Anal. Calcd. for $\text{C}_{36}\text{H}_{39}\text{N}_9\text{O}_6$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.05; H, 5.62; N, 18.14.

Tri(*N*-pentafluorophenyl)-1,4,5,8,9,12-hexaazatriphenylene-2,3,6,7,10,11-hexacarboxylic Acid Trisimide (**4b**).

Trianhydride **1**, prepared as described above from the hexaacid (350 mg, 0.79 mmole) was dissolved in dry dimethylacetamide (15 ml) and treated with pentafluoroaniline (1.43 g, 7.5 mmoles). The mixture was heated on a steam bath for 15 minutes, cooled, poured onto ice (35 g), and acidified with concentrated hydrochloric acid (15 ml). The resulting solid was filtered, washed with water, and dried *in vacuo* at room temperature. The crude triamic acid was mixed with trifluoroacetic anhydride (5 ml) and trifluoroacetic acid (0.3 ml) and heated in a sealed tube on a steam bath for 48 hours. The reaction was evaporated to dryness and the residue was recrystallized/precipitated from ethyl acetate/toluene to afford trisimide **4b** (485 mg, 65%), mp $>360^\circ$; uv (DMSO): 292, 328 nm; ^{13}C nmr (DMSO- d_6): 135.9, 139.9, 141.1, 145.0 (phenyl carbons; all signals are broad "singlets" or multiplets due to C-F coupling), 144.5 (internal aromatic carbons), 148.6 (peripheral aromatic carbons), 160.6 (carbonyl carbons) ppm; Fab ms: m/e 942 ($\text{M}^+ + 3$).

Anal. Calcd. for $\text{C}_{36}\text{F}_{13}\text{N}_9\text{O}_6$: C, 46.03; F, 30.34; N, 13.42. Found: C, 46.00; F, 30.22; N, 13.04.

Tri(*N*-*t*-butyl)-1,4,5,8,9,12-hexaazatriphenylene-2,3,6,7,10,11-hexacarboxylic Acid Trisimide (**4c**).

The trianhydride (320 mg, 0.72 mmole), prepared as described above, was treated with a solution of *t*-butylamine (5 ml) in dry acetonitrile (20 ml). After stirring for 1 hour, the reaction was evaporated to dryness. The residue was suspended in acetonitrile, filtered, and washed with acetonitrile to give trisamic acid **3c** (500 mg) as a colorless solid. The crude product was dissolved in thionyl chloride (10 ml) and heated on a steam bath for 30 minutes. Excess thionyl chloride was removed by evaporation, then the residue was dissolved in chloroform and precipitated by addition of hexane. The resulting solid was filtered, washed with hexane and water, then recrystallized from chloroform/hexane with the use of decolorizing carbon to give the trisimide **4c** as a light yellow solid (350 mg, 76%), mp $>320^\circ$; uv (DMSO): 284, 338; ^1H nmr (deuteriochloroform): 1.85 (s, CH_3); ^{13}C nmr (deuteriochloroform/DMSO- d_6): 28.6 (CH_3), 59.0 ($\text{N}-\text{C}(\text{CH}_3)_2$), 144.4 (internal aromatic carbons), 147.8 (peripheral aromatic carbons), 164.8 (carbonyl carbons); Fab ms: m/e 612 ($\text{M}^+ + 3$).

Anal. Calcd. for $\text{C}_{30}\text{H}_{27}\text{N}_9\text{O}_6 \cdot 1.5\text{H}_2\text{O}$: C, 56.60; H, 4.75; N, 19.80. Found: C, 56.39; H, 4.78; N, 19.48.

2,6,10-Tri(carbomethoxy)-3,7,11-tri(carbomethoxy)-1,4,5,8,9,12-hexaazatriphenylene (**6**).

Triester triacid **2** (540 mg, 1 mmoles) in a solution of thionyl chloride (10 ml) and dry benzene (20 ml) was heated on a steam bath for 4 hours and the reaction was evaporated to dryness. The crude triester/triacid chloride **5** was mixed with 15 ml of dry ethanol, upon which a yellow solid immediately separated. The excess alcohol was removed *in vacuo* and the residue was recrystallized from chloroform/hexane to provide hexaester **6** (500 mg, 80%), mp $217\text{--}218^\circ$; uv (DMSO): 274, 312; ^1H nmr (perdeuterioacetonitrile): 1.46 (t, 3H, CH_2CH_3), 4.11 (s, 3H, OCH_3), 4.57 (q, 2H, CH_2CH_3) ppm; ^{13}C nmr (perdeuterioacetonitrile): 14.4 ($\text{C}-\text{CH}_3$), 54.6 (OCH_3), 64.4 (CH_2CH_3), 143.1, 143.2 (internal aromatic carbons), 147.15, 147.21, 147.64, 147.72 (peripheral aromatic carbons), 165.0, 165.5 (carbonyl carbons) ppm; Fab ms: m/e 626 ($\text{M}^+ + 2$).

Anal. Calcd. for $\text{C}_{27}\text{H}_{24}\text{N}_6\text{O}_{12}$: C, 51.93; H, 3.87; N, 13.46. Found: C, 51.45; H, 3.84; N, 13.38.

2,6,10-Tri(carbomethoxy)-3,7,11-tri(*N,N*-dimethylcarboxamido)-1,4,5,8,9,12-hexaazatriphenylene (**7**).

To a solution of triester triacid chloride **5**, prepared from the hexaacid (500 mg, 1 mmole) as described above, in dry acetonitrile was added a solution dimethylamine (3 ml) in dry acetonitrile. The resulting solution was stirred for 15 minutes and evaporated to dryness. The crude product was dissolved in acetonitrile, a little decolorizing carbon was added and the mixture was passed through a short column of silica gel, eluting with acetonitrile. Evaporation of the eluant gave a light yellow solid (410 mg, 66%), mp 211-212°; uv (DMSO): 286, 322; ¹H nmr (deuteriochloroform): 2.99, 3.02, 3.05, 3.10 (rotameric and conformational isomers of one of the amide methyl groups, coalesce on heating to 130°), 3.21, 3.22 (rotameric and conformational isomers of the other amide methyl group; also coalesce at 130°), 4.06, 4.08 (conformational isomers of the ester methyl group) ppm; ¹³C nmr (deuteriochloroform): 34.99, 35.05 (one of the amide methyl carbons), 38.18, 38.26, 38.32, 38.42 (the other amide methyl carbon), 53.7 (s, ester methyl), 140-167 (complex multiplet for the aromatic and carbonyl carbons) ppm; Fab ms: m/e 623 (M⁺ + 2).

Anal. Calcd. for C₂₇H₂₇N₃O₆·0.5H₂O: C, 51.43; H, 4.47; N, 19.99. Found: C, 51.26; H, 4.36; N, 19.71.

Compound **7** could also be made from the anhydride as follows. Trianhydride **1** (444 mg, 1 mmole) was dissolved in freshly distilled dry acetonitrile (100 ml) and dry dimethylamine gas was carefully bubbled into the solution. A yellow solid quickly started separating and addition of the dimethylamine gas was discontinued immediately before the solid started to dissolve. The solid was filtered, washed with acetonitrile, and dried to afford triamic acid **9** that was directly mixed with thionyl chloride (10 ml) and heated on a steam bath for 30 minutes. Excess thionyl chloride was removed *in vacuo* and anhydrous methanol (20 ml) was added. After 15 minutes methanol was removed *in vacuo*. Contaminating dimethylammonium chloride was removed by passage of the reaction mixture through a short column of silica gel using chloroform as eluent to give, after evaporation, triester/triamide **7** with spectral properties identical to those obtained by using the other method.

3,7,11-Tri[*N*-(6-amino)hexyl]carboxamido-2,6,10-tris(*N,N'*-dimethyl)carboxamido-1,4,5,8,9,12-hexaazatriphenylene (**8**).

To a solution of 1,6-hexanediamine (2.48 g, 21 mmole) in dry acetonitrile (100 ml) was added dropwise a solution of triester/triamide **9** (207 mg, 0.33 mmole) in dry acetonitrile (25 ml). The resulting mixture was heated for 10 minutes over a steam bath then the solvent was removed *in vacuo*, the residue was dissolved in chloroform, and the product was precipitated by adding hexane. This process was repeated several times to remove excess hexanediamine, then the solid was triturated with hexane, filtered, and dried to afford hexaamide **8** (174 mg, 60%), mp > 320°, darkens above 290°; uv (DMSO): 286, 326; ¹H nmr (deuteriochloroform): 1.3-3.7 (m) ppm; ¹³C nmr (deuteriochloroform): complicated multiplets in aliphatic and aromatic regions; Fab ms: m/e 875 (M⁺ + 2).

Anal. Calcd. for C₄₂H₃₃N₁₅O₆·3H₂O: C, 54.35; H, 7.49; N, 22.63. Found: C, 54.64; H, 7.07; N, 22.40.

2,3,6,7,10,11-Hexa(*N*-(*n*-hexyl))carboxamido-1,4,5,8,9,12-hexaazatriphenylene (**12a**).

To a solution of ester **11** [3] (582 mg, 1 mmole) in 2:1 chloroform/THF (150 ml; solubilized with warming) was added *n*-hexylamine (1.55 g, 15 mmole) and the mixture was refluxed for 24 hours. The colorless solid that precipitated was filtered, washed with chloroform, and recrystallized from trifluoroacetic acid/water to afford hexaamide **12a** (851 mg, 86%), mp > 350°; uv (DMSO): 282, 324 nm; ¹H nmr (deuteriochloroform): 0.95 (t, 3H, CH₃), 1.5 (m, 6H, 3 x CH₂), 1.8 (quintet, 2H, CH₂), 3.7 (q, 2H, N-CH₂), 9.2 (br s, NH) ppm; ¹³C nmr (deuteriochloroform/trifluoroacetic acid): 13.8, 22.4, 26.5, 28.4, 31.3, 42.0 (all single lines, hexyl carbons), 141.6 (s, internal aromatic carbons), 145.4 (s, peripheral aromatic carbons), 164.7 (s, carbonyl carbons) ppm. No identifiable signals were seen by Fab mass spectrometry.

Anal. Calcd. for C₅₄H₇₈N₁₂O₆·0.5H₂O: C, 64.84; H, 7.96; N, 16.80. Found: C, 64.81; H, 8.33; N, 16.89.

2,3,6,7,10,11-Hexa(*N*-(*n*-decyl))carboxamido-1,4,5,8,9,12-hexaazatriphenylene (**12b**).

To a solution of ester **11** [3] (500 mg, 0.86 mmole) in 1:1 chloroform/dry THF (300 ml) was added *n*-decylamine (3.0 g, 19 mmole) and the solution was refluxed for 20 hours. The solid that precipitated was filtered, washed with acetonitrile, and dried to afford hexaamide **12b** (600 mg, 56%). Recrystallization from acetonitrile/trifluoroacetic acid/water and again from trifluoroacetic acid/acetic acid gave the hexaamide as a light brown solid, mp 331-332°; ¹H nmr (deuteriochloroform/trifluoroacetic acid): 0.9 (t, 3H, CH₃), 1.2-1.6 (m, 14H, 7 x CH₂), 1.9 (quintet, 2H, CH₂), 3.7 (q, 2H, CH₂), 9.6 (t, 1H, amide NH) ppm.

Anal. Calcd. for C₅₄H₇₈N₁₂O₆·0.5H₂O: C, 64.84; H, 7.96; N, 16.80. Found: C, 64.81; H, 8.33; N, 16.89.

Hexaazatriphenylene trisphthalhydrazide (**13**).

To a solution of hexaester **11** (582 mg, 1 mmole) in 1:1 chloroform/methanol (100 ml) was added hydrazine hydrate (3 ml), and a black solid quickly formed. The suspension was refluxed for 3 hours, filtered, washed with methanol and chloroform, and dried to afford the trisphthalhydrazide (428 mg, 88%) as a black solid, mp > 350°; ¹³C nmr (triethylamine/deuterium oxide): 160.6 (oxygen bearing carbon), 146.4 ("peripheral" HAT carbons), 142.7 (internal aromatic carbons) ppm.

A sample for microanalysis was prepared by dissolving **11** in triethylamine/water and adding an excess of aqueous sodium hydroxide. The precipitate was filtered, washed with methanol, aqueous ethanol, and a small amount of distilled water. The resulting black solid was dried at 110°/1 torr; uv (sodium salt/water): 282, 334, 430 (br) nm.

Anal. Calcd. for the trisodium salt (C₁₈H₃N₁₂Na₃O₆·6H₂O): C, 32.74; H, 2.29; N, 25.45; Na, 10.44. Found: C, 32.91; H, 2.08; N, 25.22; Na, 10.6.

Acknowledgment.

We thank Ms. Bonnie Grotjohn for technical assistance in obtaining spectral data on some of these compounds. Mass spectra were obtained by use of a Kratos-30 mass spectrometer. The ft-nmr spectra at 11.75 tesla (500 MHz) or 7.0 tesla (300 MHz) were obtained using equipment funded in part by NIH Grand #1 S10 RR01458-01A1. We thank Mr. 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 Mr. Carl Engelman for other nmr assistance. Funding from the Army Research Office is acknowledged with gratitude.

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- [4] Using the same procedure for the preparation of **4b**, we also prepared triphenyl trisimide using aniline. The product afforded ¹³C nmr and mass spectra supportive of the structure assignment; however, because a microanalysis agreeing to within 0.4% on all elements could not be obtained, we are unable to report this compound.