the racemic material, except that the intermediate aldehyde in the sequence (exogonal) was oxidized to the acid by a different procedure.[27] Methylation (CH_2N_2) then provided methyl exogonate as the 2*R*,5*R*,7*S* *E*,*E* and 2*R*,5*S*,7*S* *Z*,*Z* stereoisomers, $[\alpha]^{20}_D$ −4.3° (*c* 5.05, $CHCl_3$). The methyl ester of purified natural exogonic acid exhibited $[\alpha]^{20}_D$ +7.6°. The ^1H and ^{13}C NMR spectra and GC-MS data of this synthesized methyl exogonate were identical with those previously reported.[5] ^{13}C NMR ($CDCl_3$): 2*R*,5*R*,7*S* *E*,*E* δ 21.01, 30.10, 32.04, 35.39, 35.07, 40.47, 51.52, 74.01, 74.19, 114.97, 171.46; 2*R*,5*S*,7*S* *Z*,*Z* 22.91, 30.58, 32.48, 35.68, 36.05, 42.56, 51.44, 75.43, 76.10, 114.74, 171.97.

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Supplementary Material Available: ^{13}C and ^1H NMR spectra of the synthetic (2*R*,5*R*,7*S*)-(*E*,*E*)- and (2*R*,5*S*,7*S*)-(*Z*,*Z*)-methyl exogonates (i.e., mirror images of **3** and **4**) and the ^{13}C NMR spectrum of natural **2** (4 pages). Ordering information is given on any current masthead page.

Cascade Polymers:[1] Synthesis and Characterization of Four-Directional Spherical Dendritic Macromolecules Based on Adamantane

George R. Newkome,* Ashutosh Nayak,[2] Rajani K. Behera,[3] Charles N. Moorefield, and Gregory R. Baker

Center for Molecular Design and Recognition, Department of Chemistry, University of South Florida, Tampa, Florida 33620-5250

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The syntheses and spectral characteristics of four-directional spherical dendritic macromolecules utilizing an adamantane core have been described. The dendrimer syntheses utilized 4-amino-4-(3-acetoxypropyl)-1,7-diacetoxyheptane or di-*tert*-butyl 4-amino-2-[(*tert*-butoxycarbonyl)ethyl]heptanedioate as the key building block. An improved synthetic procedure to 1,3,5,7-adamantanetetracarboxylic acid is reported.

Introduction

The design and construction of polyfunctionalized dendritic macromolecules based on a four-directional *C*-core[4-7] have afforded a microenvironment which affords entrance to the field of unimolecular micelles.[8] Work on related dendritic macromolecules has been reviewed[9] and recently reported.[10] Cascade molecules, particularly silvanols[11] and arborols,[12] possessing other orders of directionality, have unique molecular shapes and have been shown to aggregate in a specific manner dependent directly on complementary interactions. For example, two-directional cascade molecules possessing a dumbbell shape organize in an orthogonal array to form aqueous gels,[13,14] or when possessing an unsaturated core organize in a nonorthogonal manner giving rise to supramolecular helical ropes.[15] Combined with our continued interest in dendritic polymers and micellar mimics, convenient preparation of a bridgehead-functionalized adamantane to provide a core topology approximating a tetrahedral nucleus facilitates the synthesis of a spherical, four-directional cascade infrastructure. We herein describe the divergent syntheses and characterization of four-directional spherical dendritic macromolecules, which utilize the bridgehead positions of adamantane as the molecular core.

Results and Discussion

The directionality inherent in the admantane nucleus provides the desired tetrahedral motif; however, functionalization of the unactivated bridgehead CH bonds has been limited.[16] Direct, selective oxyfunctionalization of adamantane with methyl(trifluoromethyl)dioxirane has recently been shown[17] to afford the adamantane-1,3,5,7-tetrol in good yields. Treatment of this tetrol with chloroacetic acid or an acrylic ester would afford the homolo-

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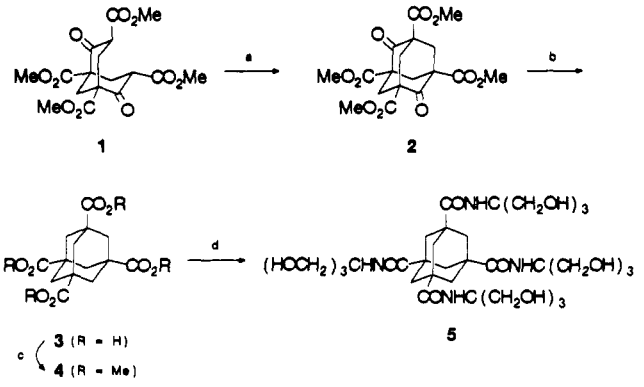
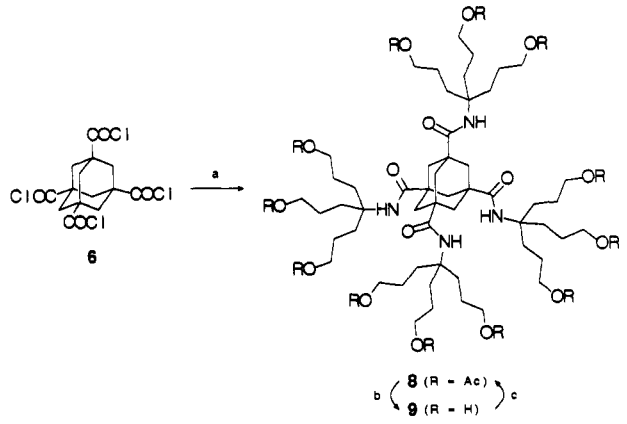
Scheme I[a]



[a] (a) CH_2Br_2, NaOMe, MeOH, reflux; (b) $H_2NNH_2{\cdot}H_2O$, NaOMe, reflux; (c) (1) $SOCl_2$, reflux, (2) MeOH, reflux; (d) $H_2NC(CH_2OH)_3$, K_2CO_3, Me_2SO, 25 °C, 12 h.

Scheme II[a]



[a] (a) Amine 7, NEt_3, C_6H_6, 25 °C, 20 h; (b) K_2CO_3, EtOH, 25 °C, 15 h; (c) Ac_2O, py.

gated tetraacids and provide a series of core building blocks possessing increasing porosity. Prior to attempting these procedures, a simple route to adamantanetetracarboxylic acid was devised.

A. Improved Synthesis of Adamantanetetracarboxylic Acid. Recently, 1,3,5,7-adamantanetetracarboxylic acid (**3**) was used to generate the first optically active organic molecule with *T* symmetry of known configuration[18] and to describe its 5-fold diamond structure.[19] The latter researcher obtained his sample from the original source,[20] whereas the former prepared their sample by a lengthy, modified procedure[21] of Stetter et al.[20] We devised an improved three-step procedure to this tetracarboxylic acid, which circumvents the cumbersome procedures associated with these routes.

Initially, Meerwein ester[22] **1** was prepared (80%) from dimethyl malonate and aqueous formaldehyde in the presence of Et_2NH *instead* of piperidine. The yield was improved by lengthening the initial reaction time at 25 °C and removal of unreacted malonate prior to the addition of sodium methoxide. The ^1H NMR spectrum of **1** showed two sharp singlets at 3.78 and 3.76 ppm, corresponding to methyl protons of ester functions in different environments, and two singlets at 2.32 and 2.87 ppm, corresponding to two and four methylene protons, respectively. The peaks at 96.9 and 168.2 ppm and the absence of peaks beyond 200 ppm in ^{13}C NMR spectrum of **1** are consistent with the structural assignment. During the workup of **1**, the crystalline 1,1,3,3,5,5-pentanehexacarboxylic ester was also isolated and characterized by NMR spectral data.

Treatment of Meerwein's ester **1** with CH_2Br_2 and sodium methoxide in a sealed tube, according to Böttger's procedure,[23] afforded (31%) the dione tetraester **2** as colorless crystals. The cyclized product **2** showed (^{13}C NMR) two peaks at 203.4 and 168.5 ppm, corresponding to keto and ester carbonyl groups, respectively. Although Landa and Kamycek[21] reported that the reduction of dione **2** using alkaline hydrazine hydrate generated (80–90%) the tetraacid **3**, in our hands their procedure gave a mixture of products from which the desired tetraacid could not be isolated in pure form. Modification of their procedure by using a steel bomb at 200 °C and venting the gaseous products prior to continued heating at 240–250 °C for 8 h gave excellent, reproducible (90%) yields of the colorless crystalline tetraacid **3**. The symmetrical tetraacid **3** showed only three peaks (^{13}C NMR) at 177.7, 42.1, and 38.6 ppm, corresponding to the carbonyl, bridgehead, and methylene carbon atoms, respectively. The tetraacid was treated with $SOCl_2$ to generate tetraacyl chloride **6**, which was not isolated but with absolute MeOH was directly converted (86% overall) to the crystalline tetramethyl ester **4**. The two singlets (^1H NMR) at 1.98 and 3.82 ppm for the ring methylenes and ester methyls, respectively, are in accord with the assignment.

B. Four-Directional Cascade Construction. The tetramethyl ester **4** upon treatment with "Tris" in the presence of anhydrous K_2CO_3 in dry Me_2SO furnished the desired dodecol **5** as a very hygroscopic, white crystalline solid. The absence (^{13}C NMR) of the peak at 52.2 ppm (CH_3) and appearance of new peaks at 62.4 and 60.9 ppm assigned to the quaternary carbon and hydroxymethyl carbon in the side chains confirm the arborol structure.

The neighboring bridgehead position[24] of the interent neopentyl moiety[25] of the "tris" terminal groups, causing chemical retardation, must be circumvented prior to further tier construction. Homologation by introduction of a separate spacer is possible[12] but adds further synthetic steps in the process. Therefore, 4-amino-4-(3-acetoxypropyl)-1,7-diacetoxyheptane (**7**) was previously created[26] to incorporate the needed three-atom spacer.

1,3,5,7-Tetrakis(chlorocarbonyl)adamantane (**6**) was treated with amine **7** to afford (68%) the dodecaacetate **8** as a thick oil. The ^{13}C NMR spectrum of **8** confirmed the transformation by the presence of the peaks at 170.7 (COOMe) and 174.4 ppm (CONH) in a near 3:1 ratio and at 57.9 ppm for the side-chain quaternary carbon. The ester **8** was quantitatively converted to alcohol **9** by transesterification with anhydrous K_2CO_3 in absolute ethanol. The absence of the peaks (^{13}C NMR) at 20.8 (CH_3) and 170.7 ppm (COMe) confirmed the transformation. The spectral data support the structure of the dodecaalcohol **9**, but the analytical datum was outside acceptable limits

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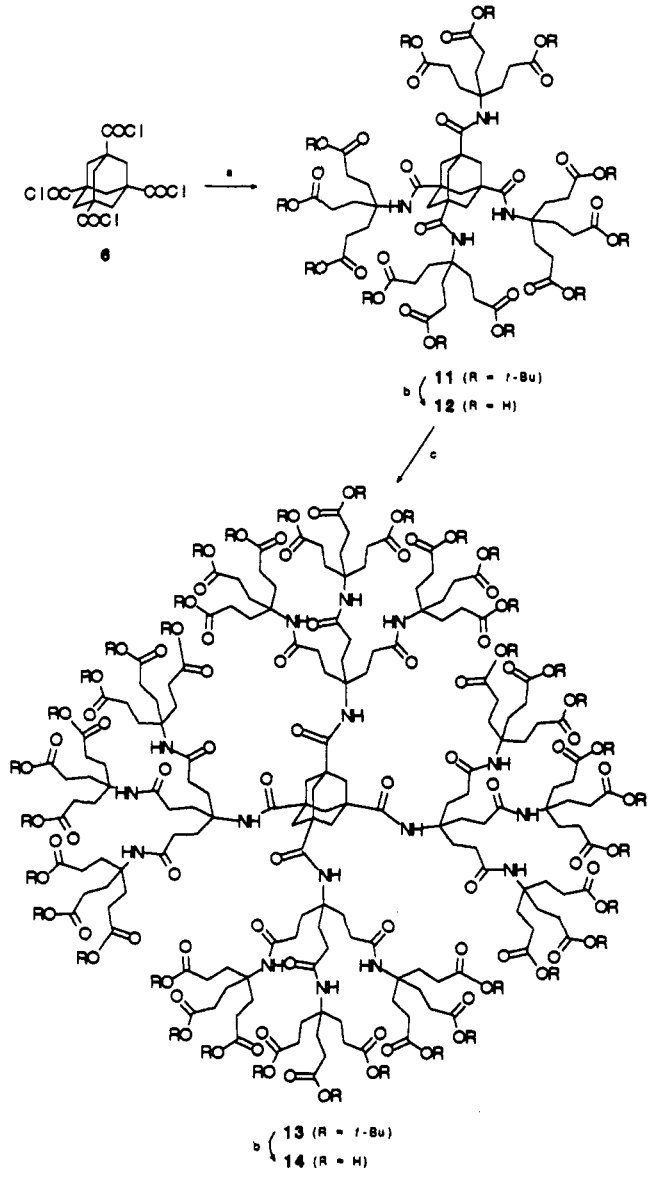
due to its hygroscopic nature. Thus, reaction of **9** with Ac_2O in pyridine regenerated the initial dodecaacetate **8**, which was confirmed from the comparison of spectral data.

Attempts to make the dodecaacid **12**, needed to build the second tier, via oxidation of dodecaalcohol **9** by different procedures[27] were unsuccessful because of incomplete oxidation or difficulties in isolation and purification of the water-soluble product. Use of di-*tert*-butyl 4-amino-2-[(*tert*-butoxycarbonyl)ethyl]heptanedioate (**10**)[24] circumvented the above problem and offered additional advantages: (a) the *tert*-butyl esters are easily purifiable solids and (b) fewer reactions are required to obtain the desired acids.

Treatment of acid chloride **6** with amine **10** afforded (61%) the dodecaester **11** as a white solid (Scheme III). The presence of peaks at 173.1 (ester CO) and 177.6 ppm (CONH) in a near 3:1 intensity ratio and at 58.6 ppm for the side-chain quaternary carbon in the ^{13}C NMR for **11** confirmed the transformation. Hydrolysis of the ester **11** with formic acid (96%) gave the dodecaacid **12** in good yield which was supported (^{13}C NMR) by the loss of peaks at 80.2 and 28.1 ppm for the *tert*-butyl groups and appearance of a peak at 177.8 (CO_2H) ppm. The coupling of acid **12** with amine **10** in the presence of dicyclohexylcarbodiimide (DCC) and 1-hydroxybenzotriazole[28] in dry DMF afforded (58%) of the ester **13**. The presence (^{13}C NMR) of two carbonyl peaks at 172.8 (ester CO) and 177.8 (CONH) ppm and peaks at 57.6 and 57.0 ppm for the two side-chain quaternary carbons support the structural assignment. The specific assignments of internal and external methylene carbons were based on intensity ratios and peak shape (the internal methylene carbon peaks were smaller and broader). The ^1H NMR of **13** showed only one large singlet at 1.40 [$C(CH_3)_3$] ppm, which overwhelmed the other proton signals.

Acid **14** was obtained (95%) by the treatment of ester**13** with anhydrous formic acid. The obvious absence of peaks due to *tert*-butyl groups in the NMR spectra and the shift of the carbonyl 172.8 (ester) to 178.0 (acid) ppm support the hydrolysis. The analytical datum for the acid **14** was outside of acceptable limits due to its inherent hygroscopic character; however, its ^1H NMR, ^{13}C NMR, and IR spectra support the assigned structure.

Scheme III[a]



[a] (a) Amine **10**, NEt_3, C_6H_6, 25 °C, 20 h; (b) 96% formic acid, 25 °C, 20 h; (c) amine **10**, DCC, 1-hydroxybenzotriazole, DMF, 25 °C, 48 h.

Conclusions

Spherical cascade polymers derived from an adamantane core can be easily prepared and offer a readily available alternative to tetrakis(substituted ethyl or propyl)methane derivatives. The utilization of adamantane homologated tetracarboxylic acids to probe questions associated with porosity and molecular inclusion within these simple dendritic macromolecules is currently in progress.

Experimental Section

General Comments. Melting point data were obtained in capillary tubes and are uncorrected. ^1H and ^{13}C NMR spectra were obtained in $CHCl_3$, except where noted, with Me_4Si as the internal standard (δ 0 ppm) and recorded at either 80 or 360 MHz. IR spectral data were obtained on an IBM IR-38 spectrometer. Elemental analyses were preformed by MicAnal Laboratories in Tucson, AZ.

An Improved Synthesis of 1,3,5,7-Adamantanetetracarboxylic Acid. A. Tetramethyl 2,6-Dioxobicyclo[1.3.3]nonane-1,3,5,7-tetracarboxylate (1). A mixture of dimethyl malonate (65 g, 0.5 mol) and aqueous formaldehyde (40%, 30 g) at 0 °C was treated with Et_2NH (2.5 g), followed by sufficient MeOH (10 mL) to give a clear solution. After 12 h at 0 °C, 24 h at 25 °C, 48 h at 40 °C, and then cooling to 0 °C, the aqueous layer was removed and the organic residue was washed successively with 2 N H_2SO_4 and water. The residual viscous liquid was heated under vacuum [100 °C (1 mm)] for 12 h to remove unreacted malonate. The resulting thick oil (62 g) was treated with NaOMe, prepared from sodium (8.5 g) in MeOH (120 mL), and then refluxed for 4 h at 100 °C, during which a pale yellow solid separated. MeOH was removed in vacuo to afford a residue, which was treated with ice-cold water (100 mL). The insoluble turbid materials were removed by ether extraction. A stream of CO_2 gas was passed through the aqueous solution to give a pale yellow solid, which was filtered, washed thoroughly with excess water, and finally recrystallized from boiling MeOH to afford (80%) dione **1** as light rose-colored prismatic crystals: 30 g; mp 163 °C (lit.[22] mp 163–164 °C); ^1H NMR δ 2.32 (s, CCH_2C, 2 H), 2.87 (s, $CH_2C{=}$, 4 H), 3.76–3.78 (br s, CH_3O, OH, 14 H); ^{13}C NMR δ 29.7 (CCH_2C), 35.4 (CCH_2), 47.7 ($CH_2C{=}$), 51.9, 52.7 (2 CH_3O), 96.90 (C), 168.21 (=COH), 171.9, 172.5 (2 ester C=O); IR (KBr) 3400, 3000, 1740, 1622 cm^{-1}.

B. Tetramethyl 2,6-Dioxoadamantane-1,3,5,7-tetracarboxylate (2). A mixture of dione **1** (10 g), CH_2Br_2 (16 mL), and a NaOMe, prepared from sodium (1.4 g) with dry MeOH (18

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mL), was heated at 130 °C in a sealed tube for 10 h. After cooling overnight at 25 °C, the resultant solid was filtered and washed with MeOH and then a copious amount of water. After drying, the solid was recrystallized [dioxane–MeOH (1:2)] to give (31%) tetraester **2**, as transparent globules: 3.2 g; mp 286 °C (lit.[23] mp 283.5–284.5 °C); ^{1}H NMR (Me_2SO-d_6) δ 2.89 (s, CCH_2, 8 H), 3.79 (s, CH_3O, 12 H); ^{13}C NMR δ 41.7 (β-CH_2), 52.3 (α-C), 55.3 (CH_3O), 168.5 (C=O, ester), 203.4 (C=O, ketone); IR (KBr) 1734, 1710, 3000, 2850 cm^{-1}.

C. 1,3,5,7-Adamantanetetracarboxylic Acid (3). A mixture of dione **2** (2 g), hydrazine hydrate (85%; 12 mL), and a solution of NaOMe, prepared from sodium (1.2 g) and absolute MeOH (20 mL), was heated slowly in a steel bomb. When the temperature rose to 200 °C, *the gaseous products were slowly and carefully removed.* Heating was continued until the temperature reached 240–250 °C, and then the temperature was maintained for 8 h. After cooling, the dry reaction product was dissolved in water (50 mL), treated with charcoal, warmed, and filtered. The pale yellow filtrate was concentrated (20 mL) in vacuo and acidified with concentrated HCl (pH 1–2) to give (90%) tetraacid **3** as colorless crystals: 600 mg; mp 390 °C dec (lit.[21] mp 395 °C dec); 1H NMR (Me_2SO-d_6) δ 2.6 (bs, CH_2, 12 H), 3.6 (bs, OH, 4 H, exchanged with D_2O); ^{13}C NMR δ 38.6 (β-CH_2), 42.1 (α-C), 177.7 (C=O); IR (KBr) 3105 (broad), 1709, 1450, 1398, 1194 cm^{-1}.

Tetramethyl 1,3,5,7-Adamantanetetracarboxylate (4). A mixture of tetraacid **3** (175 mg, 560 μmol) and redistilled[29] $SOCl_2$ (1.5 mL) was refluxed for 4 h. Excess $SOCl_2$ was removed in vacuo to give a dry mass, which was treated carefully with absolute MeOH (10 mL), and then the stirred solution was refluxed for 12 h. After cooling, the tetramethyl ester **4** separated (86%) as colorless needles: mp 168 °C (lit.[21] mp 168–169 °C); 180 mg; ^{1}H NMR δ 1.98 (s, CH_2, 12 H), 3.82 (s, CH_3O, 12 H); ^{13}C NMR δ 38.7 (β-CH_2), 42.0 (α-C), 52.2 (CH_3O), 175.6 (C=O).

Hexaethyl 1,1,3,3,5,5-Pentanehexacarboxylate. Diethylamine (750 mg) was added slowly to a stirred mixture of diethyl malonate (48 g) and aqueous formaldehyde (40%, 15 g) at 0 °C and maintained for 8 h. After the mixture was heated (100 °C) for 8 h and then left to stand at 25 °C for 24 h, the water/MeOH were removed in vacuo and the resulting thick oil was kept at −15 °C for 48 h. The solids (~3 g) were filtered, and the syrupy filtrate was refluxed in EtOH (50 mL) and concentrated H_2SO_4 (0.5 mL) for 10 h. The excess alcohol was distilled, water (50 mL) was added, and the organic material was extracted with CCl_4. The extract was washed sequentially with 10% aqueous Na_2CO_3, water, and finally with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to afford a viscous residue, which was distilled in vacuo to give (40%) the ester, as a colorless oil, which crystallized on standing: 25 g; mp 62 °C (lit.[22] mp 62–63 °C); ^{1}H NMR δ 1.25, 1.30 (2 t, CH_3, J = 7 Hz, 18 H), 2.55 (d, CH_2, J = 6 Hz, 4 H), 3.54 (t, CH, J = 6 Hz, 2 H), 4.13, 4.31 (2 q, OCH_2, J = 7 Hz, 12 H); ^{13}C NMR δ 13.9 (CH_3), 32.1 (CCH_2CH), 48.2 (CH), 57.7 (CC=O), 61.6 (CH_2O), 168.9, 170.0 (C=O); IR (KBr) 2948, 2872, 1740, 1035 cm^{-1}.

1,3,5,7-Tetrakis{[*N*-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]carbonyl}adamantane (5). A mixture of ester **4** (100 mg), Tris (130 mg), and anhydrous K_2CO_3 (700 mg) in Me_2SO (10 mL) was stirred at 25 °C for 12 h. After workup, according to the above method, the very hygroscopic tetraamide **5** was isolated as a white solid: mp 210 °C dec; ^{1}H NMR (D_2O) δ 1.82 (s, CH_2, 12 H), 3.52 (s, CH_2OH, 24 H); ^{13}C NMR δ 38.8 (β-CH_2), 42.7 (α-C), 60.9 (CH_2O), 62.4 (CCH_2O), 177.9 (CO); IR (KBr) 3500–3330, 2936, 1666, 1248, 1036 cm^{-1}.

1,3,5,7-Tetrakis{[*N*-[4-acetoxy-1,1-bis(3-acetoxypropyl)butyl]amino]carbonyl}adamantane (8). A mixture of **3** (156 mg, 500 μmol) and freshly distilled $SOCl_2$ (2 mL) was refluxed for 4 h. Excess $SOCl_2$ was removed in vacuo. Benzene (5 mL) was added to the mixture, and then the solution was concentrated in vacuo to yield **6** as a white solid. Crude **6**, 4-amino-4-(3-acetoxypropyl)-1,7-diacetoxyheptane[26] (**7**; 830 mg, 2.5 mmol), and Et_3N (200 mg, 2 mmol) in dry benzene (10 mL) were stirred at 25 °C for 20 h. The mixture was sequentially washed with aqueous $NaHCO_3$ (10%), water, cold aqueous HCl (10%), and brine. The organic phase was dried over anhydrous Na_2SO_4. Removal of the solvent furnished a thick viscous residue, which was flash chromatographed (SiO_2) eluting with 25% MeOH in EtOAc to yield (68%) the dodecaacetate **8** as a thick oil: 500 mg; bp >300 °C (2 mm); ^{1}H NMR δ 1.39–1.65 (m, CH_2, 60 H), 185 (s, CH_3, 36 H), 3.84 (t, CH_2O, J = 6.1 Hz, 24 H), 5.25 (bs, NH, 4 H); ^{13}C NMR δ 20.8 (CH_3), 22.3 (CH_2CH_2O), 30.2 (CCH_2), 39.2 (β-CH_2), 42.9 (α-C), 57.9 (NHC), 64.1 (CH_2O), 170.7 ($COCH_3$), 174.4 (CONH); IR (neat) 3352, 2930, 1740, 1651, 1262, 1038 cm^{-1}. Anal. Calcd for $C_{78}H_{124}N_4O_{28}$: C, 59.83; H, 7.98; N, 3.58. Found: C, 59.85; H, 7.97; N, 3.52.

1,3,5,7-Tetrakis{[*N*-[4-hydroxy-1,1-bis(3-hydroxypropyl)butyl]amino]carbonyl}adamantane (9). A mixture of dodecaacetate **8** (400 mg, 260 μmol) and K_2CO_3 (100 mg) in absolute EtOH (10 mL) was stirred at 25 °C for 15 h. The mixture was filtered through Celite, and the solvent was removed in vacuo to give (97%) dodecol **9** as a very hygroscopic white solid: 260 mg; ^{1}H NMR (CD_3OD) δ 1.6 (m, CH_2, 60 H), 3.43 (t, CH_2OH, J = 6.4 Hz, 24 H); ^{13}C NMR δ 27.4 (CH_2CH_2O), 32.2 (CCH_2), 40.3 (β-CH_2), 44.7 (α-C), 59.7 (HNC), 63.2 (CH_2OH), 177.6 (CONH); IR (KBr) 3304–3409, 2936, 1648, 1550, 1059 cm^{-1}.

1,3,5,7-Tetrakis{[*N*-[3-(*tert*-butoxycarbonyl)-1,1-bis[2-(*tert*-butoxycarbonyl)ethyl]propyl]amino]carbonyl}adamantane (11). A mixture of **3** (78 mg, 250 μmol) and freshly distilled $SOCl_2$ (2 mL) was refluxed for 4 h. Excess of $SOCl_2$ was removed in vacuo, benzene (5 mL) was added, and the solution was concentrated in vacuo to yield **6**, as a white solid.

Crude **6**, amine **10**[24] (450 mg, 1.1 mmol), and Et_3N (110 mg, 1.1 mmol) in dry benzene (10 mL) were stirred at 25 °C for 20 h. Additional benzene (40 mL) was added, and the mixture was sequentially washed with aqueous $NaHCO_3$ (10%), water, cold aqueous HCl (10%), and brine. The organic phase was dried (Na_2SO_4) and then concentrated in vacuo to furnish a viscous oil, which was chromatographed (SiO_2), eluting with 5% MeOH in EtOAc to yield (61%) the dodecaester **11** as a white solid: 290 mg; mp 105–107 °C; ^{1}H NMR δ 1.40 (s, CH_3, 108 H), 1.72 (s, CH_2, 12 H), 2.24 (m, CH_2, 48 H), 5.88 (bs, NH, 4 H); ^{13}C NMR δ 28.1 (CH_3), 30.0, 30.4 (CCH_2CH_2COO), 39.0 (β-CH_2), 42.8 (α-C), 57.1 (HNC), 80.2 (CCH_3), 173.1 (COO), 177.6 (CONH); IR (KBr) 3348, 2930, 2845, 1740, 1645, 1260, 1038 cm^{-1}. Anal. Calcd for $C_{102}H_{172}O_{28}N_4$: C, 64.38; H, 9.12; N, 2.95. Found: C, 64.52; H, 8.91; N, 2.86.

1,3,5,7-Tetrakis{[*N*-[3-carboxy-1,1-bis(2-carboxyethyl)propyl]amino]carbonyl}adamantane (12). A solution of dodecaester **11** (190 mg, 100 μmol) in formic acid (96%, 2 mL) was stirred at 25 °C for 20 h. Excess solvent was removed in vacuo, and toluene (3 × 2 mL) was added. The solvents were removed in vacuo to give (94%) the dodecaacid **12** as a white solid: 115 mg; mp 282–284 °C dec; ^{1}H NMR (D_2O) δ 1.84 (s, CH_2, 12 H), 2.34 (m, CH_2, 48 H); ^{13}C NMR (D_2O) δ 30.1 (CCH_2CH_2COOH), 38.8 (β-CH_2), 42.7 (α-C), 58.6 (HNC), 177.8 (COOH), 180.4 (CONH); IR (KBr) 3360, 3330–2600, 2903, 1745, 1690, 1245, 1090 cm^{-1}. Anal. Calcd for $C_{54}H_{76}O_{28}N_4$: C, 52.75; H, 6.23; N, 4.56. Found: C, 52.59; H, 6.22; N, 4.51.

1,3,5,7-Tetrakis{[*N*-[3-[[*N*-[3-(*tert*-butoxycarbonyl)-1,1-bis[2-(*tert*-butoxycarbonyl)ethyl]propyl]amino]carbonyl]-1,1-bis[2-[[*N*-[3-(*tert*-butoxycarbonyl)-1,1-bis[2-(*tert*-butoxycarbonyl)ethyl]propyl]amino]carbonyl]ethyl]propyl]amino]carbonyl}adamantane (13). A mixture of dodecaacid **12** (74 mg, 60 μmol), amine **10**[24] (330 mg, 790 μmol), dicyclohexylcarbodiimide (DCC; 150 mg, 720 μmol), and 1-hydroxybenzotriazole (100 mg, 740 μmol) in dry DMF[30] (3 mL) was stirred at 25 °C for 48 h. After filtration of dicyclohexylurea, the solvent was removed in vacuo to give a residue, which was dissolved in EtOAc (25 mL) and was sequentially washed with cold aqueous HCl (10%), water, aqueous $NaHCO_3$ (10%), and brine. The organic phase was dried (Na_2SO_4) and concentrated in vacuo, and the residue was chromatographed (SiO_2), eluting first with EtOAc/CH_2Cl_2 (1:1) to remove some impurities and then with 5% MeOH in EtOAc to furnish (58%) ester **13** as a white solid: 200 mg; mp 138 °C; ^{1}H NMR δ 1.40 (s, CH_3); ^{13}C NMR δ 28.1 (CH_3), 30.0 (CCH_2CH_2CONH), 29.8, 30.2 (CCH_2CH_2COO), 38.9 (β-CH_2), 42.4 (α-C), 57.2 (CCH_2CH_2COO), 57.6 (CCH_2CH_2CONH), 80.0 (CCH_3), 172.8 (COO), 177.8 (CONH); IR

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(KBr) 3350, 2938, 2846, 1740, 1680, 1260, 1045 cm^{-1}. Anal. Calcd for $C_{318}H_{544}O_{88}N_{16}$: C, 63.64; H, 9.14; N, 3.74. Found: C, 63.28; H, 8.96; N, 3.77.

1,3,5,7-Tetrakis{[*N*-[3-[[*N*-[3-carboxy-1,1-bis(2-carboxyethyl)propyl]amino]carbonyl]-1,1-bis[2-[[*N*-[3-carboxy-1,1-bis(2-carboxyethyl)propyl]amino]carbonyl]ethyl]propyl]amino]carbonyl}adamantane (14). A solution of ester **13** (150 mg, 25 μmol) in formic acid (96%, 2 mL) was stirred at 25 °C for 20 h. Workup and purification, similar to that of acid **12**, gave (95%) acid **14**, as a very hygroscopic solid:[31] mp 350–354 °C dec; ^{1}H NMR (D_2O) δ 1.80 (s, CH_2, 12 H), 2.18–2.41 (m, CH_2, 192 H); ^{13}C NMR (D_2O) δ 30.2 (CCH_2CH_2COOH), 30.8, 31.6 (CCH_2C-H_2CONH), 39.1 (β-CH_2), 42.8 (α-C), 58.1 (CCH_2CH_2CONH), 58.5 (CCH_2CH_2COOH), 178.0 (COOH), 180.2 (CONH); IR (KBr) 3360, 3340–2600, 2920, 1745, 1685, 1240, 1060 cm^{-1}.

(31) Purity was judged to be >95% based on ^{13}C NMR spectral data.

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Relatively Stable *N*-Benzhydryl- and *N*-Benzyldiarylketene Imines and Their Conversion to Cyanodiarylmethanes via an Isolable Radical

Leo F. Clarke, Anthony F. Hegarty,* and Pat O'Neill

Chemistry Department, University College Dublin, Dublin 4, Ireland

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An efficient synthetic route to the sterically hindered ketene imines *N*-benzyl- and *N*-benzylhydrylbis(pentamethylphenyl)ketene imines **8** from dipentamethylphenyl ketene **6** is described. The thermal stability of these ketene imines is in marked contrast to the diphenylketene imine analogues which rearrange rapidly to C-trisubstituted nitriles. On heating **8b** is converted to the relatively stable free radical **13** which can be reduced to the nitrile **10** in a variety of solvents. These radicals are proposed intermediates in the ketene imine–nitrile rearrangement, and the mechanism of this reaction is considered in terms of these results.

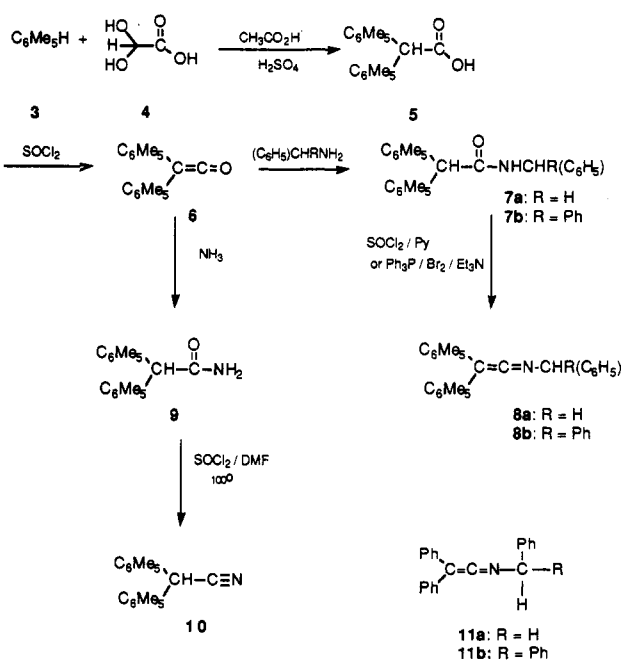
The conversion of ketene imines **1** to nitriles **2** is known to occur with varying degrees of ease and through competing reaction pathways depending on the nature of substituents R^1, R^2, and R^3.

1 **2**

N-Stannylketene imines, for example, are known to react with a variety of reagents which cleave the nitrogen–tin bond to generate nitriles in high yield.[1] The photochemical conversion of *N*-methylarylketene imine to a trisubstituted acetonitrile has also been reported.[2,3] *N*-*tert*-Butyldiphenylketene imine, on the other hand, undergoes a disproportionation reaction at 125 °C to yield diphenylacetonitrile, *tert*-butyl chloride, and isobutylene.[4] The *N*-(arylmethyl)diphenylketene imine system has also been noted for its ease of ketene imine to nitrile conversion. The modest temperatures (25–65 °C) required to induce thermal rearrangement and the good yield of nitrile has made this system a prime candidate for mechanistic investigations.[5]

Singer et al. have shown[5,6] through kinetic, stereochemical, and trapping experiments involving *N*-benzyl- and other *N*-(arylmethyl)diphenylketene imines that this thermal [1,3] nitrogen to carbon rearrangement proceeds via a free-radical mechanism. On the basis of their accumulated results they concluded that the rate-determining step was the homolytic cleavage of the ketenimine's N–R_3 bond to form a cage radical pair which subsequently recombines to nitriles.

Scheme I



Because of our continued interest in understanding the effects of bulky aromatic groups on unstable reaction intermediates[7,8] we have now investigated the influence of

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