Synthesis and Chemistry of Novel Dendritic Macromolecules Possessing Internal Electroactive Anthraquinonoid Moieties

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Currently, there is a growing interest in the syntheses and supramolecular chemistry of dendritic or "cascade" macromolecules[1] as evidenced by the growth in papers and reviews published in this field. These discrete macromolecular assemblies are constructed by repetitive monomer addition sequences using either a convergent method, a divergent method, or a combination of the two methodologies. A logical progression in molecular building block design is to incorporate internal utilitarian loci to ensure the proper number, location, and desired functionality within the macromolecular superstructure. Introduction of photo-, electro-, and ionoactive compounds into supramolecular architectures is important from a variety of perspectives. These include a propensity for them to participate in ordered supramolecular assemblies[2] when appropriately substituted, serving as photosensitizers and electron sinks in organized assemblies, such as micelles,[3] and acting as localized geometrical control elements.[4] Such assemblies may also be able to perform highly selective tasks of molecular recognition,[5] transfer, and structure generation for signal and information processing at the (supra)molecular levels.[6] Dendritic molecules, which incorporate in their building units functionalities capable of absorbing and emitting light and reversibly exchanging electrons, are of particular interest, for example, for use as a solvatochromic probe,[7] a directional molecular antenna[8] or molecular light harvesters.[9] Such molecules could find applications as components in molecular electronics, solar energy conversion, and storage and photochemical molecular devices.[10] Transition metal complexes have been used to construct such dendrimers.[11] Several redox-active organic and organometallic groups have been incorporated in dendrimers and related systems with several aims in mind, such as, new electron transfer catalysts, organic semiconductors, and mimics of biological redox processes among others.[12]

Encapsulated electroactive dendrimers have been reported aimed at mimicking biological systems and considered for their potential usefulness in molecular electronic devices.[13] Miller et al. reported the synthesis of electrically conducting macromolecules by modifying the periphery of higher generation ($G \geq 2$) PAMAM dendrimers with redox-active naphthalene diimide anion radicals.[14] Thus, dendrimers with electroactive units at either the focal point or the periphery of the molecule as well as those randomly encapsulated have been reported, but limited examples exist where such moieties are specifically pinned within the infrastructure.

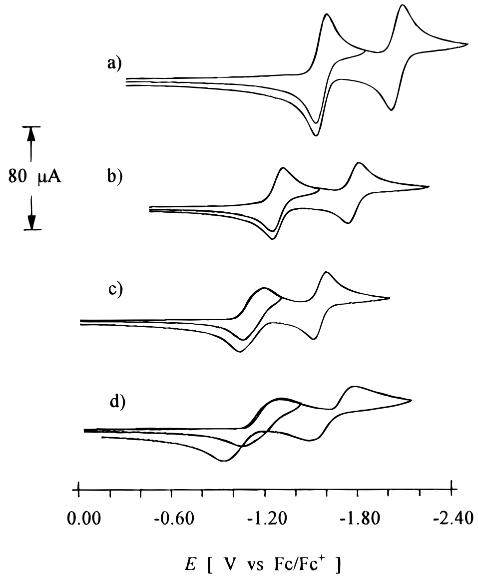

Figure 1. Cyclic voltammograms of (a) **1**, (b) **3**, (c) **5**, and (d) **7**. All voltammograms were obtained from MeCN/100 mM (TBA)PF$_6$ at a scan rate of 100 mVs^{-1}, with a glassy-carbon working electrode, a Pt counterelectrode, and a Ag wire pseudo-reference electrode. The potential is referred to the internally added ferrocene/ferrocenium (Fc/Fc$^+$) couple.

Table 1. Reduction Potentials, $E_{1/2}$ Values [mV] for the Compounds Studied in 0.1 M nBu$_4$PF$_6$/CH$_3$CN^a

compound^b	$E_{1/2}(1)$	$E_{1/2}(2)$
1 (a)	−1577 (74)	−2063 (74)
3 (b)	−1293 (71)	−1785 (75)
5 (c)	−1123 (145)	−1564 (88)
7 (d)	−1122 (157)	−1620 (272)

^{a} Fc/Fc+ as internal standard. ^{b} a−d refer to Figure 1. Numbers in parentheses refer to the peak-to-peak separations.

Anthraquinone derivatives, in particular, have long been used in the dye industry and recently in medicinal applications with cancer chemotherapy, as exemplified by mitoxanthrone, and in anthracycline antitumor agents, such as adriamycin and daunomycin.[15] Introduction of anthraquinone chromophoric units into "higher order assemblies" such as dendrimers should serve as electron accepting units in biomimetic systems and photoinduced electron transfer reactions.[16] Further, electrochemical reduction of these quinonoid assemblies in the presence of metal ions have implications in research related to metal ion transport across bulk liquid membranes.[17]

We herein report the synthesis of a novel series of structured dendritic macromolecules incorporating covalently linked diaminoanthraquinones. The connection of several components in a single reaction can be achieved by proper consideration of reagent stoichiometry and concentration. Thus, the controlled stepwise acylation utilizing a bis(acid chloride) affords, in good yield, the desired "extended building block" (Scheme 1). Using a high dilution technique, commercially available 1,4-DAAQ (1,4-diaminoanthraquinone), **1**, was reacted with glutaryl chloride and amine **2** to give (ca. 35−40%) the amino triester **3**.[18]

The monoamine monomer **3** possesses a deep red coloration compared to the deep purple color of diamine **1**. Evidence for the formation of amine **3** includes ^{13}C

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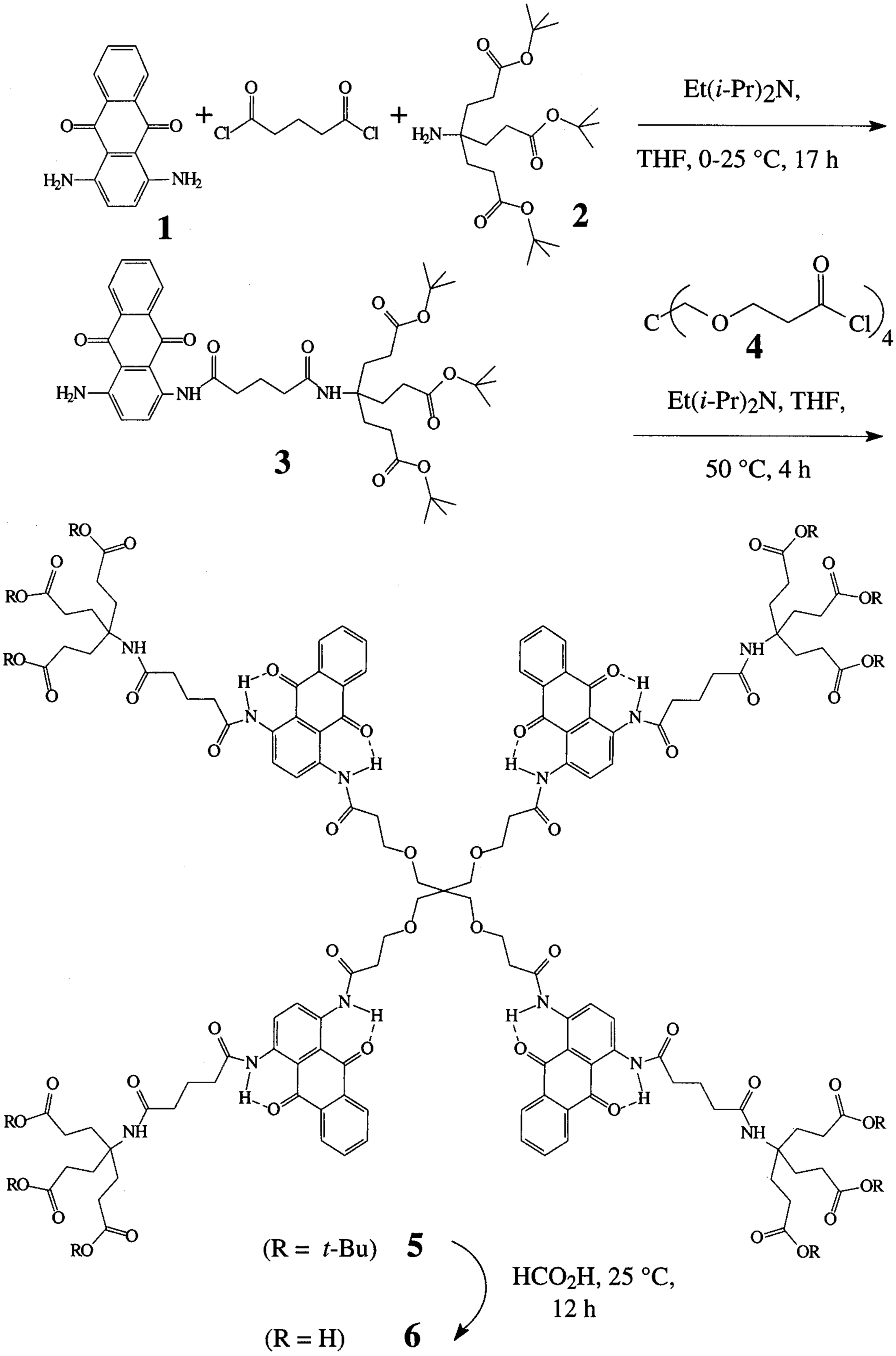
Scheme 1. Synthesis of Diaminoanthraquinone Monomer 3 and First Tier Cascade Molecules 5 and 6



NMR absorptions at 21.6, 36.3, 37.7 ($CH_2CH_2CH_2$), 57.4 ($NHC_4°$), 27.9 (CH_3), and 80.5 [CMe_3] ppm; the aromatic region displayed 12 signals reflecting the unsymmetrical anthraquinone unit, while the five downfield signals were indicative of the respective carbonyl moieties. The UV spectrum of **3** exhibited an observed blue shift (Δ 20 nm), when compared to the starting quinone, for the absorption maxima at the longest wavelength shifts.

Subsequently, treatment of the tetravalent tetrakis(acyl halide) core[19] **4** with amine **3** generated (60%) the first tier, dodecaester dendrimer **5** (Scheme 1). The tetrakisquinonoid dendrimer **5**[20] exhibits (^{13}C NMR) the previously described building block alkyl resonances and a simplified set of six aromatic absorptions indicating core to building block attachment. Expansion of the aromatic region revealed slight differences in the chemi-

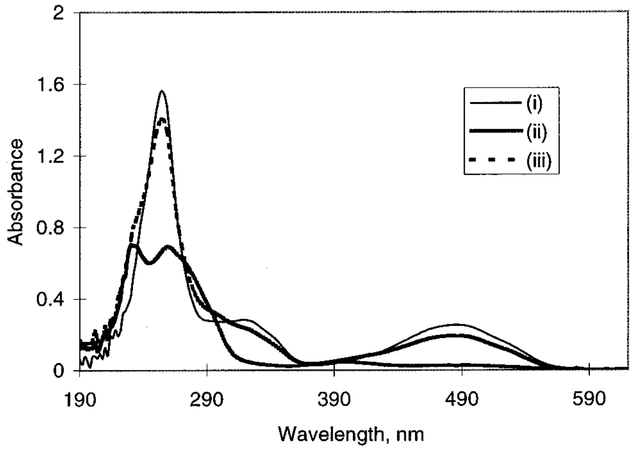


Figure 2. Reversible reduction of **5** using $NaBH_4$ and air: (i) 10 μM solution of **5** in THF; (ii) 1 mg of $NaBH_4$ in 2 mL of solution i; (iii) 30 min of air oxidation of solution ii.

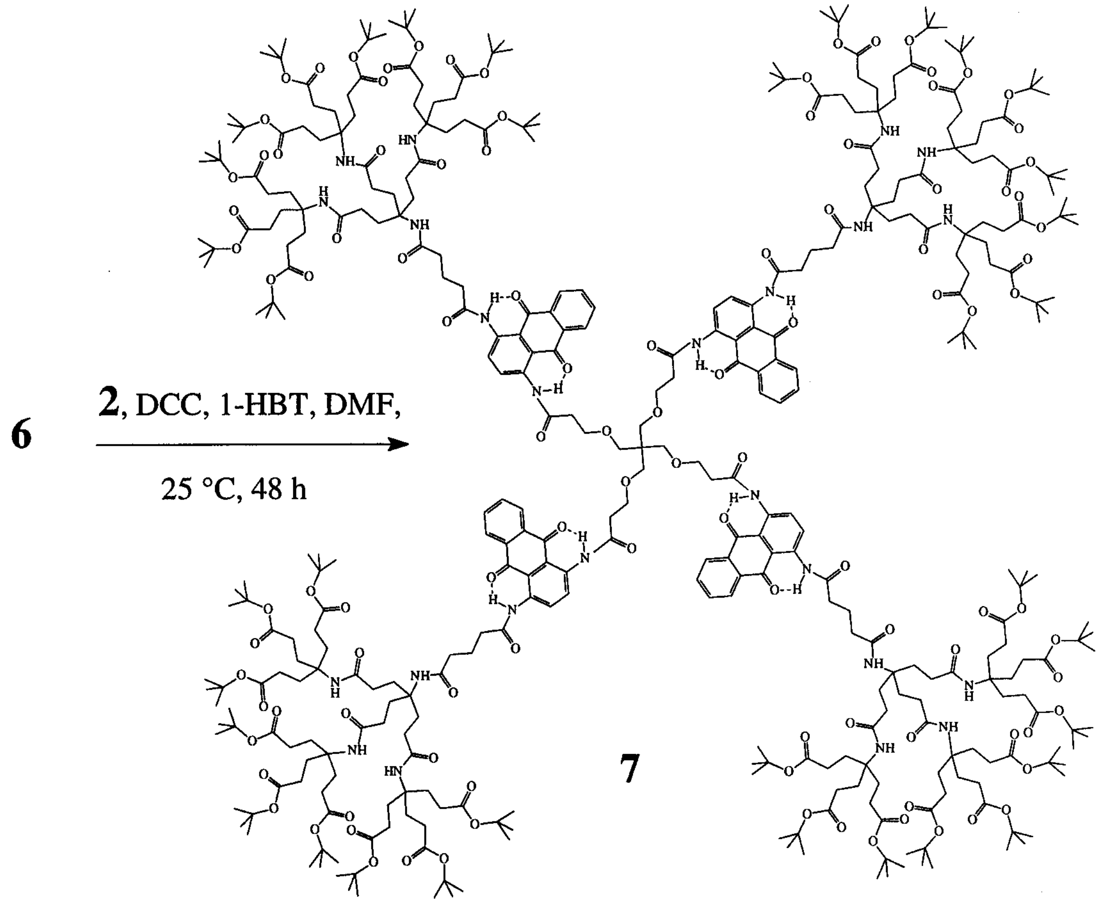
cal shift of similarly juxtaposed carbons. The ^{13}C NMR spectrum ($CDCl_3$) further displayed[20] the expected six different C=O signals. ^{1}H NMR spectra of the monomer **3** and the first tier dodecaester **5** displayed the expected first-order analyses; as well, far downfield absorptions (12.1 and 12.2 ppm) attributed to the amide N*H* moieties adjacent to the quinones suggest *H*-bonded, cyclic conformations. Additional data, including elemental analysis and MALDI-TOF mass spectra[21] of the above compounds support the desired structures. Results from UV measurement[22] indicated an expected blue shift (Δ 40 nm) for the absorption maxima at the longest (524−484 nm) wavelength, in the conversion of **3** to **5**.

The first tier dendrimer **5** is deep orange when compared to the bright red of the extended building block **3**. Reaction of the dodecaester **5** with formic acid yielded (80%) dodecaacid **6**,[23] which when coupled[24] with amine **2** afforded (50%) the second tier dendrimer **7** (Scheme 2).[25] The signals in the ^{13}C NMR spectrum of **7** are similar to that in **5**, but for a few distinguishing peaks. Two new peaks at 57.8 and 173.0 ppm support the desired structure, and the signals in the aromatic region are decreased in intensity. Repetition of the above reaction sequences on **7** led to the third generation dendrimer **8**.[26]

A sequence of experimental cyclic voltammograms[27] is shown (Figure 1) for the diamine **1**, the monoamide **3**, and diamides **5** and **7** (dendrimers). Modification of the amine into the amide functionality results in a positive shift of the reduction potentials of the anthraquinonoid moieties. This was anticipated and is a direct consequence of the lower electron releasing nature of the amide substituents compared with that of the related amines. In addition to the electronic effect that results in an amidic shift, progressive steric congestion around the electroactive center results in slower electron transfer kinetics and thus in irreversible electrochemistry. It is to be noted that the potential values reported (Table 1) are averages between cathodic and anodic peak potentials. Since the processes observed for **5** and **7**, especially the latter, are electrochemically irreversible, the $E_{1/2}$ values lack thermodynamic validity. This electrochemical behavior is consistent with the previous results reported by us as well as others.[13b,28]

Not surprisingly, when the second amine group is transformed to an amide group (**5** vs **3**), a further positive shift of the reduction potentials is observed as

Scheme 2. Synthesis of Second Generation Dendrimer 7



well as increased irreversibility of the voltammetric waves. Interestingly, careful inspection of the first wave by using Osteryoung square wave voltammetry shows an apparent splitting into two waves. Whether this reflects the presence of nonequivalent anthraquinone units or arises as a consequence of other factors as well as ion pairing effects due to the presence of countercations is currently under investigation. This could have broad implications in the possible role of these redox active dendrimers as potential cation transporting switches. Dendrimers based on isomers of 1,4-DAAQ were also synthesized[29] to examine the effect of changing the position of the amino groups of the anthraquinone on the redox properties of the dendrimers.

Chemically, these dendrimers have been reduced[30] with $NaBH_4$ in THF, as solvent (Figure 2) and shown to undergo facile, redox processes. Investigation of the chemistry *within* dendritic superstructures is in progress.

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(18) **3**: 30−35%, purple-red solid, mp 78−79 °C; ^{13}C NMR ($CDCl_3$) δ 21.6 ($CH_2CH_2CH_2$), 27.9 [$C(CH_3)$], 29.9, 30.2 ($CH_2CH_2CO_2$), 36.3, 37.7 ($CH_2CH_2CH_2$), 57.4 ($NHC_4°$), 80.5 [CMe_3], 110.4, 116.1, 126.3, 126.6, 126.7, 126.8, 132.8, 133.2,133.8, 133.9, 134.6, 148.3, (C_{Ar}), 171.8, 172.2, 172.8 ($CONH$), 183.6, 187.1 (CO_{quin}); MALDI-TOF-MS *m/z* 749 (M − H). Anal. Calcd for $C_{41}H_{55}N_3O_{10}$: C, 65.70; H, 7.40; N, 5.60. Found: C, 65.55; H, 7.19; N, 5.44.

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(20) Dendrimer **5**: 60%, deep-orange microcrystals, mp 96−98 °C; ^{13}C NMR ($CDCl_3$) δ 21.4 ($CH_2CH_2CH_2$), 28.0 CH_3, 29.8, 29.9, ($CH_2CH_2CO_2$), 36.3, 37.7 ($CH_2CH_2CH_2$), 39.5 (OCH_2-CH_2), 46.0 (4°C core), 57.4 ($NHC_4°$), 67.2, 69.9, (CH_2OCH_2), 80.6 [$C(CH_3)_3$], 116.3, 126.9, 128.8, 132.8, 134.4, 138.1, (C_{Ar}), 170.9, 171.6, 172.2 ($CONH$), 172.8 (COO), 186.3, 186.4 (CO_{quin}); MALDI-TOF-MS *m/z* 3373 (M + Na). Anal. Calcd for $C_{181}H_{240}N_{12}O_{48}$: C, 64.86; H, 7.22; N, 5.01. Found: C, 64.69; H, 7.18; N, 4.89.

(21) MALDI-TOF experiments were conducted with a 337 nm N_2 laser (one-stage acceleration, 1 m path length, 200−600 FWHM resolution, and accuracy of mass determination ±0.1%); DHB was used as the matrix.

(22) Micromolar solutions of **1**, **3**, and **5**−**8** were made in THF and UV spectra obtained on a HP 8452 diode-array spectrophotometer.

(23) **6**: 80%, mp 140−142 °C; IR (KBr) 3400 (O−H, broad), 1700 (C═O) cm^{-1}; ^{13}C NMR (DMSO-d_6) δ 21.2 ($CH_2CH_2CH_2$), 29.2, 30.7 ($CH_2CH_2CO_2$), 35.1, 37.2 ($CH_2CH_2CH_2$), 45.5 (4°C_{core}), 56.4 ($NHC_4°$), 68.0, 69.9 (CH_2OCH_2), 116.0, 127.7, 132.1, 134.5, 137.1, 137.3 (C_{Ar}), 170.3, 171.5, 171.7 ($CONH$), 174.7 (CO_2H), 185.5 (CO_{quin}); MALDI-TOF-MS *m/z* 2704 (M + Na). Anal. Calcd for $C_{133}H_{144}N_{12}O_{48}$: C, 59.64; H, 5.42; N, 6.27. Found: C, 59.42; H, 5.28; N, 6.09.

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(25) **7**: 49.5%, bright orange solid, mp 92−94 °C; 360 mg (48 μmol); *m/z* 7740, calculated mass 7449 amu. Anal. Calcd for $C_{397}H_{624}N_{24}O_{108}$: C, 63.99; H, 8.28; N, 4.52. Found: C, 63.81; H, 8.13; N, 4.40.

(26) **8**: 50%, bright orange solid, mp 65−69 °C; Anal. Calcd for $C_{1045}H_{1728}N_{60}O_{288}$: C, 63.58; H, 8.82; N, 4.26. Found: C, 63.33; H, 8.62; N, 4.33. It was also noted that **8**, unlike **5** or **7**, was soluble even in petroleum ether.

(27) Cyclic voltammograms at 20 °C were recorded on a BAS-100-W electrochemical apparatus from Bioanalytical systems, Inc. A conventional three-electrode configuration was used with a 3 mm diameter glassy-carbon disk as the working electrode, a platinum working electrode, and a silver wire pseudo-reference electrode. Electrochemical grade $(TBA)PF_6$ was recrystallized (EtOH, 2×) and pulverized. HPLC grade MeCN was dried (P_4O_{10}) and vapor transferred directly into the electrochemical cell after three freeze−pump−thaw degassing cycles at 10^{-5}−10^{-6} mm Hg. In general, a 0.5 mL sample solution containing 1 mM metal complex and 100 mM $(TBA)PF_6$ was prepared by drying the solid reagents directly in the electrochemical cell at 10^{-5}−10^{-6} mm Hg and then transferring the solvent directly into it through the vacuum line. Micromolar solutions of **1**, **3**, and **5**−**8** were made in THF and UV spectra obtained on a HP 8452 diode-array spectrophotometer.

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(29) Due to the low solubility of 2,6-DAAQ in most solvents, the extended building block was obtained in low yields; hence their dendritic construction was not pursued. Whereas, the related building block obtained from 1,5-DAAQ was subsequently dendrimerized up to the second tier; similar properties to those of 1,4-DAAQ were experienced. The cyclic voltammograms for the 1,5-DAAQ series were conducted in DMF due to their poor solubility in MeCN in the presence of (TBA)PF_6.

(30) THF solutions of all the dendrimers are reduced instantaneously with addition of stoichiometric amounts of $NaBH_4$. The reduced form was readily reoxidized on exposure to air (see Figure 2).

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