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Surface-Confined Monomers on Electrode Surfaces. 7. Synthesis of Pyrrole-Terminated Poly(propylene imine) Dendrimers

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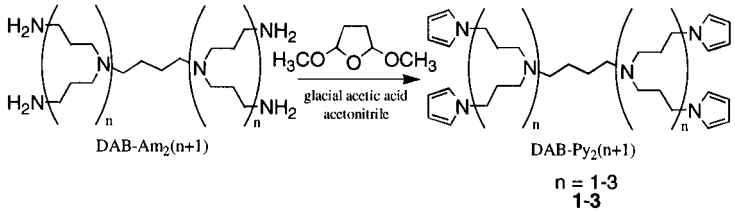
ABSTRACT



Poly(propylene imine) dendrimers containing a diaminobutane core with pyrrole groups at the dendrimer periphery have been synthesized for the first time. The fully functionalized (as determined by mass spectrometry and NMR), pyrrole-terminated dendrimers (DAB-Py$_X$ (X = 4, 8, 16)) were synthesized from 2,5-dimethoxytetrahydrofuran and commercially available poly(propylene imine) dendrimers containing a diaminobutane core (DAB-Am$_X$). Adsorption of the pyrrole-terminated dendrimers on Au surfaces is evidenced by the reflection–absorption infrared (RAIR) spectra of Au surfaces exposed to micromolar solutions of the dendrimers.

Recent studies have demonstrated that poly(propylene imine) dendrimers with a diaminobutane core, DAB dendrimers, and poly(amido amine) dendrimers can be adsorbed onto gold and silica surfaces to form monolayers of a given dendrimer.[1] These previous studies have focused on either the native amine-terminated dendrimers or dendrimers functionalized (<100% functionalization) with a select few moieties. For gold surfaces this route to chemical modification offers a variety of applications including catalysis,[2] small molecule delivery, synthesis of nanostructures, sensing, and adhesion promotion. Functionalization of the dendrimers (either before[3] or after[4] adsorption) with a variety of chemical moieties, in high derivatization yields, is key to the successful development of these applications.

Another approach for the creation of complex nanostructures utilizing dendrimers is the oligomerization of monomer groups at the periphery of the dendrimers; this includes dendrimers that are free in solution[5a,b] or adsorbed on surfaces.[5c] The resulting ring or shell structures from these

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coupling reactions may be used in the construction of functional nanostructures, particularly those capable of specifically recognizing a class of analytes or trapping and releasing small molecules.[5,6]

We have used the commercially available DAB-Am$_X$ (X = 4, 8, 16) (Aldrich) as molecular substrates onto which pyrrole groups are placed. The DAB-Py$_X$ (X = 4, 8, 16) were constructed via a modified Clauson-Kaas[7] ring closure reaction of 2,5-dimethoxytetrahydrofuran (Aldrich) with the primary amines of the DAB-Am$_X$ periphery. DAB-Py$_4$, **1**, was prepared by sequential addition of DAB-Am$_4$ (0.200 g, 0.632 mmol, 2.53 mmol of NH_2 terminal groups), 2,5-dimethoxytetrahydrofuran (0.341 g, 2.58 mmol, 1.02 equiv per terminal NH_2 group), degassed glacial acetic acid (2.00 g, 9 equiv per NH_2 terminal group), and degassed acetonitrile (2.08 g, 20 equiv per NH_2 end group) to a 100-mL round-bottom flask under argon. The reaction mixture was stirred at 45 °C (flask interior) for 24 h. MALDI-MS (matrix-assisted laser desorption/ionization mass spectrometry) was used to monitor the reaction. Upon completion, the pH of the amber solution was adjusted to 9 using degassed aqueous 1 M KOH, and the resulting solution was then extracted with degassed dichloromethane (DCM). After centrifugation, the organic portion was dried (Na_2SO_4) and filtered, and the solvent was removed under vacuum to yield an amber, glassy material. The DAB-Py$_8$, **2**, and the DAB-Py$_{16}$, **3**, were synthesized by the same method as the DAB-Py$_4$.[8]

Although simple in principle, successful synthesis of DAB-Py$_X$ using the ring closure reaction requires careful control of the ratio of 2,5-dimethoxytetrahydrofuran to DAB-Am$_X$. For production of the fully functionalized pyrrole-terminated dendrimers without side products, the scale of the reagents is determined by the terminal primary amines, not the dendrimer molecules themselves, paying special attention to the 1.02 equiv (2% excess) of 2,5-dimethoxytetrahydrofuran per equivalent of NH_2 terminal group, Figure 1A. Deviations

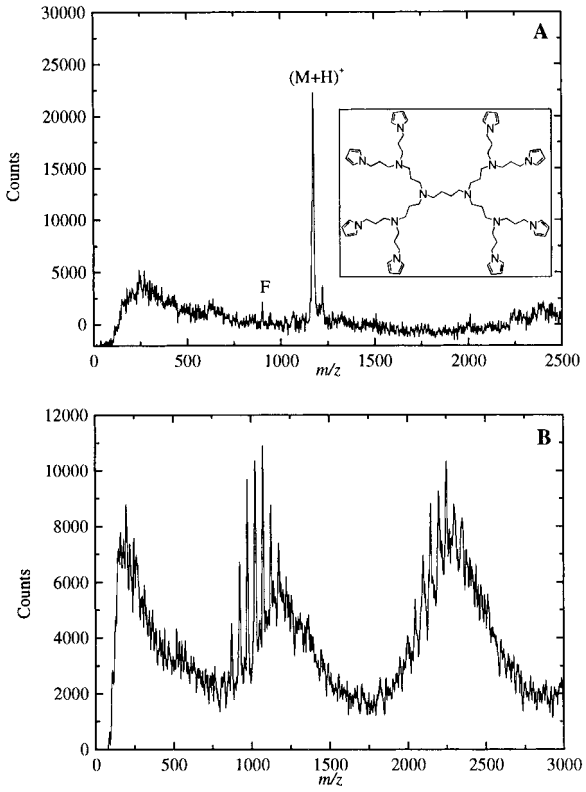

Figure 1. MALDI-TOF mass spectra of product from reaction of DAB-Am$_8$ with (A) 1.02 and (B) 1.1 equiv of 2,5-dimethoxytetrahydrofuran per terminal NH_2. F denotes fragment ion in A.

in the amount of 2,5-dimethoxytetrahydrofuran used can lead to multiple intradendrimer and interdendrimer side reactions, resulting in a wide distribution of products.[9] Some of the side products are those containing indoles and unclosed rings (dangling aldehydes). In addition, it has been found that side products can be formed by reactions involving a dangling aldehyde and a second terminal amine from the same or separate dendrimers, resulting in products with incomplete pyrrole ring derivatization (intradendrimer) or those which are composed of dendrimers connected together by four carbon units (interdendrimer).

The latter case of interconnected dendrimers is noted when >1.02 equiv of 2,5-dimethoxytetrahydrofuran is used and

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(8) Spectroscopic and analytical data. **DAB−Py$_4$:** 92% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.65 (d, 8H, Py-2,5-*H*), 6.16 (d, 8H, Py-3,4-*H*), 3.91 (t, 8H, -C*H*$_2$-Py), 2.40 (t, 12H, N(C*H*$_2$)$_3$), 1.85 (m, 8H, CH$_2$C*H*$_2$CH$_2$), 1.35 (br, 4H, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$N). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 120.3 (-Py-2,5-*C*), 108.1 (-Py-3,4-*C*), 53.6 (N*C*H$_2$CH$_2$CH$_2$*C*H$_2$N), 50.6 (*C*H$_2$CH$_2$CH$_2$-Py), 47.3 (*C*H$_2$-Py), 28.6 (CH$_2$*C*H$_2$CH$_2$-Py), 24.5 (NCH$_2$CH$_2$*C*H$_2$CH$_2$N). FTIR (NaCl): ν(C−H)$_{ring}$ 3099, ν_a(CH$_2$) 2942, ν_s(CH$_2$) 2865, ν(CH$_2$)$_{Py-CH_2}$ 2808, ν(C═C)$_{ip-ring}$ 1659, ν(C═C)$_{ip-ring}$ 1501, δ(CH$_2$) 1448, ν(C−N)$_{aliphatic}$ 1282, δ(C−H)$_{ip-ring}$ 1089, δ(C−H)$_{ip-ring}$ 1063, ω(C−H)$_{oop-ring}$ 970, ω(C−H)$_{oop-ring}$ 724 cm^{-1}. MALDI-MS [M + H$^+$] 516.2 *m*/*z* (516.8). **DAB−Py$_8$:** 95% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.62 (d, 16H, Py-2,5-*H*), 6.13 (d, 16H, Py-3,4-*H*), 3.88 (t, 16H, -C*H*$_2$-Py), 2.37 (t, 36 H, N(C*H*$_2$)$_3$), 1.85 (t, 24H, CH$_2$C*H*$_2$CH$_2$), 1.53 (br, 4H, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$N).^{13}C NMR ($CDCl_3$, 75 MHz): δ 120.3 (-Py-2,5-*C*), 107.9 (-Py-3,4-*C*), 53.6 (N*C*H$_2$-CH$_2$CH$_2$*C*H$_2$N), 51.8 (CH$_2$*C*H$_2$CH$_2$), 50.6 (N(*C*H$_2$)$_3$), 47.3 (*C*H$_2$-Py), 28.6 (CH$_2$*C*H$_2$CH$_2$-Py), 23.8 (NCH$_2$*C*H$_2$*C*H$_2$CH$_2$N). FTIR (NaCl): ν(C−H)$_{ring}$ 3095, ν_a(CH$_2$) 2947, ν_s(CH$_2$) 2865, ν(CH$_2$)$_{Py-CH_2}$ 2803, ν(C═C)$_{ip-ring}$ 1668, ν(C═C)$_{ip-ring}$ 1501, δ(CH$_2$) 1457, ν(C−N)$_{aliphatic}$ 1282, δ(C−H)$_{ip-ring}$ 1089, δ(C−H)$_{ip-ring}$ 1063, ω(C−H)$_{oop-ring}$ 960, ω(C−H)$_{oop-ring}$ 723 cm^{-1}. MALDI-MS [M + H$^+$] 1174.3 (1173.7), fragment 904.0 *m*/*z*. **DAB−Py$_{16}$:** 86% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.67 (d, 32H, Py-2,5-*H*), 6.18 (d, 32H, Py-3,4-*H*), 3.92 (t, 32H, -C*H*$_2$-Py), 2.41 (br, 84 H, N(C*H*$_2$)$_3$), 1.87 (t, 56 H, CH$_2$C*H*$_2$CH$_2$), 1.58 (br, 4H, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$N). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 120.3 (-Py-2,5-*C*), 107.9 (-Py-3,4-*C*), 52.3 (N*C*H$_2$-CH$_2$CH$_2$*C*H$_2$N), 51.1 (CH$_2$*C*H$_2$CH$_2$), 49.9 (*C*H$_2$CH$_2$CH$_2$-Py), 46.6 (*C*H$_2$-Py), 27.9 (CH$_2$*C*H$_2$CH$_2$-Py), 22.8 (NCH$_2$*C*H$_2$*C*H$_2$CH$_2$N). FTIR (NaCl): ν(C−H)$_{ring}$ 3095, ν_a(CH$_2$) 2942, ν_s(CH$_2$) 2866, ν(CH$_2$)$_{Py-CH_2}$ 2800, ν(C═C)$_{ip-ring}$ 1668, ν(C═C)$_{ip-ring}$ 1499, δ(CH$_2$) 1462, ν(C−N)$_{aliphatic}$ 1280, δ(C−H)$_{ip-ring}$ 1087, δ(C−H)$_{ip-ring}$ 1063, ω(C−H)$_{oop-ring}$ 962, ω(C−H)$_{oop-ring}$ 721 cm^{-1}. MALDI-MS [M + H$^+$] 2488.4 (2487.8), fragments: 2215.6, 1216.7, and 714.3 *m*/*z*.

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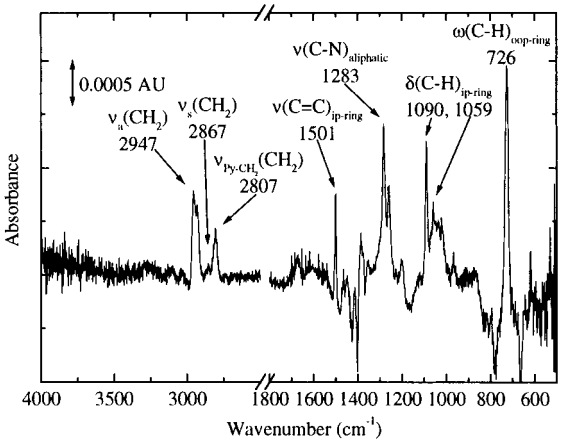

Figure 2. RAIR spectra of **2**/Au prepared by immersion of evaporated Au film[10b] in 500 μM **2**/dichloromethane for 5 h followed by sonication in dichloromethane. A total of 1024 scans averaged at 2 cm^{-1} resolution with a bare Au background.

is exemplified in Figure 1B, where the dimer of two partially pyrrole-functionalized dendrimers is evident at roughly *m*/*z* 2200. Larger connected dendrimer products (trimers, tetramers, pentamers, etc.) are also evident (data not shown). Undesired side products and incompletely functionalized dendrimers are easily detected by MALDI-MS and ^{1}H and ^{13}C NMR.

The formation of DAB-Py$_X$ (X = 4, 8, 16) monolayers on gold surfaces has been observed using RAIRS. A typical RAIR spectrum of DAB-Py$_8$ on Au is displayed in Figure 2.

The majority of the bands of the pyrrole-terminated dendrimer bulk transmission spectrum[8] are observed in the RAIR spectrum. Similar results have been obtained for **1** and **3**. There seems to be no preferred orientation of the pyrrole groups with respect to the Au surface as noted by comparisons of band intensity ratios for the transmission and RAIR spectra.[8,10]

Preliminary studies have confirmed that upon electrochemical oxidation of **3**/Au the pyrrole moieties undergo *intra*molecular oligomerization.[5c,10b] However, **1**/Au surfaces treated similarly do not undergo intramolecular coupling reactions. These preliminary studies indicate that adsorption of **3** onto Au results in a forcing of the pyrrole groups into close proximity so that they may couple together to form oligomers. The binding sites, structural characteristics, and oligomerization reactions of the adsorbed dendrimers on Au are currently under investigation and will be reported soon.[5c]

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