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Positive Dendritic Effects on the Electron-Donating Potencies of Poly(propylene imine) Dendrimers

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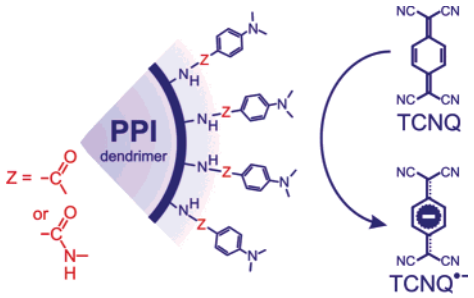
ABSTRACT



Two series of poly(propylene imine), PPI, dendrimers terminated with a redox-active donor, 4-dimethylaminobenzyl (4-DMAB), including their respective nondendronized model compounds, are reported. In these two series, a positive dendritic effect was observed for the formation of charge-transfer (CT) complexes between the dendrimers and 7,7,8,8-tetracyanoquinodimethane (TCNQ). However, the nondendronized compounds did not form CT complexes with TCNQ, even though their redox potentials are similar to those of the 4-DMAB units attached to the dendrimers.

Despite the large sizes and complexities of functionalized dendrimers,[1] interest in these macromolecules continues to increase because their well-defined structures allow chemists to precisely tailor them with different property-responsive groups. For example, unsymmetric-type dendrimers (like those pioneered by the groups of Frechét and Newkome[2]) provide motifs for core functionalization, while the symmetric types such as the commercially available poly(amido amine) (PAMAM), cyclotriphosphazene (PMMH), and poly(propylene imine) (PPI) dendrimers are generally the most widely used in studies of periphery modification.[3]

The current literature contains no report that straightforwardly correlates the voltammetric potentials of redox-responsive dendrimers with the strengths of their charge-transfer (CT) complexes in bulk solutions. A comprehensive understanding of this phenomena involving dendrimers needs to be addressed, because its fundamental and noncovalent nature will, for example, benefit the development of dendritic materials that contain platforms based on supramolecular interactions.[4]

We commence our research efforts in the area of supramolecular dendrimers by focusing our initial studies on PPI dendrimers functionalized with multiple redox-responsive groups at their peripheries. Though any substituent can be covalently attached to these dendrimers, whose native structures feature multiple tiers of electron-rich tertiary amines, the desired CT activities of the resulting dendrimers can be further enhanced if the proper groups are selected. Specifically, if the oxidation potentials of the added groups are less anodic than those of the interior tertiary amines of the PPI dendrimers, the electron-donating potencies of the resulting dendrimers are expected to be improved. We show that this is the case when 7,7,8,8-tetracyanoquinodimethane (TCNQ) is utilized as the acceptor and the end groups of the PPI dendrimers are modified with the redox-responsive 4-dimethylamino (4-DMAB) moieties.

(1) Fischer, M.; Vögtle, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 885.
(2) (a) Hawker, C.; Frechét, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638. (b) Newkome, G. R.; Weis, C. D.; Childs, B. J. *Des. Monomers Polym.* **1998**, *1*, 3.
(3) For reviews, see: (a) Grayson, S. M.; Frechét, J. M. J. *Chem. Rev.* **2001**, *101*, 3819. (b) Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *38*, 885.
(4) For recent examples, see: (a) Ornatska, M.; Bergman, K. N.; Rybak, B.; Peleshanko, S.; Tsukruk, V. V. *Angew. Chem., Int. Ed.* **2004**, *43*, 5246. (b) Ooe, M.; Murata, M.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2004**, *126*, 1604.

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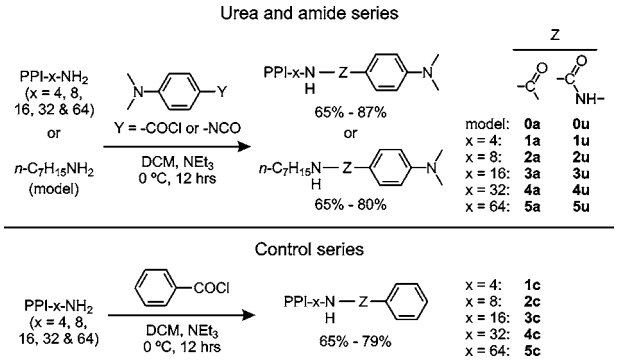
Scheme 1. Synthesis of the (4-DMAB)- and Phenyl-Terminated PPI Dendrimers and Their Model Compounds[6]



Scheme 1 shows the synthetic route for the five PPI dendrimer generations having either urea (**1u**−**5u**) or amide[5] (**1a**−**5a**) connectivities between the native dendrimer structures and the 4-DMAB units and for the corresponding model compounds (**0u** and **0a**, respectively) containing only an *n*-heptyl group in place of the dendrimers (representative structures shown in Figure 1). We also prepared a control

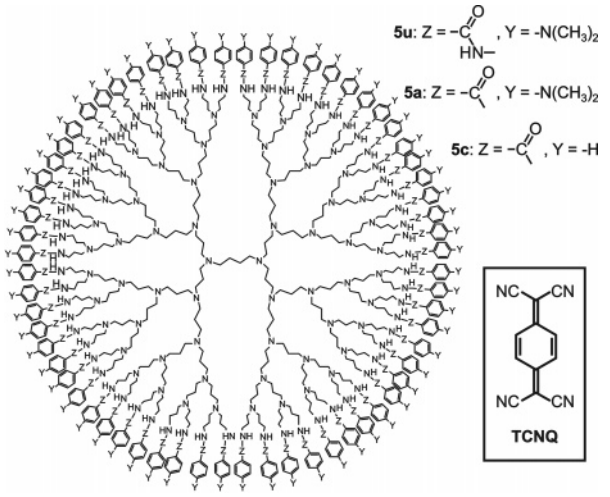


Figure 1. Structures of **5** and TCNQ.

series (**1c**−**5c**), composed of dendrimers terminated with redox-inactive phenyl units, to provide baseline activity profiles for the two (4-DMAB)-terminated dendrimer series. Briefly, these molecules were prepared in one step by condensing the toluene-stripped parent PPI dendrimers with either 4-(dimethylamino)benzoyl chloride, 4-(dimethylamino)-phenyl isocyanate, or benzoyl chloride in dry CH_2Cl_2 overnight to yield the corresponding amide, urea, or control series, respectively, in satisfactory yields (65−87%).[6] The crude reaction solutions were purified with minimal exposure to ambient light because the title dendrimers and model compounds are photolabile. In addition to the high symmetry expected for the ^{1}H and ^{13}C NMR resonances (Figures S1 and S2, Supporting Information) of these compounds, MALDI-TOF MS analyses confirmed that the dendrimers were completely terminated with 4-DMAB or benzyl units. Surprisingly, dendrimers **1u** and **2u** are sparingly soluble in CH_2Cl_2 and $CHCl_3$ ($<1 \times 10^{-4}$ M in end group [4-DMAB]) considering that their higher generation homologues **3u**−**5u** are soluble at similar end group concentration levels in the same solvents.

Cyclic voltammetry (CV) experiments in CH_2Cl_2 reveal that the dendrimers in the urea and amide series, as well as model compounds **0a** and **0u**, can be oxidized at accessible potentials (Figure S3, Supporting Information).[6] The model compound **0a** displays a quasi-reversible behavior with an oxidation peak potential (E_{pa}) of +1.17 V vs $Me_{10}Fc^{0/+}$, while the dendritic analogues **1a**−**5a** show an irreversible voltammetric behavior, i.e., no voltammetric responses are observed in the cathodic scans. On the other hand, while the CV of **0u** is reversible (E_{pa} = +0.65 V vs $Me_{10}Fc^{0/+}$), those of its dendritic analogues **1u**−**5u** are severely distorted by precipitation effects upon oxidation. For both (4-DMAB)-terminated series, the E_{pa} values for the 4-DMAB units remain constant within a series ($E_{pa(amide)}$ = +1.09 V and $E_{pa(urea)}$ = +0.56 V vs $Me_{10}Fc^{0/+}$), which means that the thermodynamic demand for heterogeneous electron transfer (ET) in these dendrimers is unaffected by dendritic growth.[7] For the control series **1c**−**5c**, only weak voltammetric responses between +0.7 and +1.0 V (vs $Me_{10}Fc^{0/+}$), arising from the interior branching tertiary amines, are observed. This is a clear indication that the heterogeneous ET events emanating from the inner tertiary amines of the PPI dendrimers are kinetically too slow relative to both the time scale of the voltammetric experiments (scan rate = 0.1 V/s) and the ET rates observed for the 4-DMAB urea and amide series (representative CVs in Figure S4, Supporting Information).[6]

The E_{pa} values for the urea and amide series are noticeably distinct from each other. The difference of these values, ΔE_{ox}, arbitrarily defined here as $E_{pa(amide)} - E_{pa(urea)}$, is approximately +0.53 V in CH_2Cl_2 (corresponding $\Delta(\Delta G_{ox})$ of +12 kcal mol^{-1}), indicating that the urea series is thermodynamically much easier to oxidize than the amide series. The rationale behind this observation is that the lone electron pair of the additional N atom in the urea series (the atom between the urea carbonyl and 4-DMAB) facilitates oxidation by providing further stability to the oxidized 4-DMAB$^+$ units through resonance interactions.

The aforementioned electrochemical data suggest that, in purely voltammetric terms, the urea series should be a better electron donor than the amide series. To gain further insight to this dissimilarity, or lack thereof, we probed the electron-donating abilities of **1u**−**5u** and **1a**−**5a** by investigating their efficiencies in reducing the well-known electron acceptor

(5) Amide dendrimer series has been reported previously (for details, see: Put, R. J. H.; Clays, K.; Persoons, A.; Biemans, H. A. M.; Luijkx, C. P. M.; Meijer, E. W. *Chem. Phys. Lett.* **1996**, *260*, 136). However, in the reported approach, the unreacted 4-(dimethylamino)benzoyl residues could not be removed from **5a**. In our protocol,[6] we did not encounter this situation.

(6) See Supporting Information for details.

(7) This is commonly observed with other symmetric-type dendrimers terminated with multiple redox sites. For example, see: Casado, C. M.; Cuadrado, I.; Morán, M.; Alonso, B.; García, B.; González, B.; Losada, J. *Coord. Chem. Rev.* **1999**, *185*−*186*, 53.

TCNQ. This acceptor, which has a reduction potential of approximately +0.30 V vs $Me_{10}Fc^{0/+}$ (CH_2Cl_2/0.20 M Bu_4NPF_6) for the formation of its radical anion, is known to undergo a one-electron reduction process in the presence of PPI dendrimers to produce the corresponding $TCNQ^{\cdot-}$ ammonium noncovalent CT pairs.[8]

Figure 2 shows that the absorption spectrum of TCNQ in

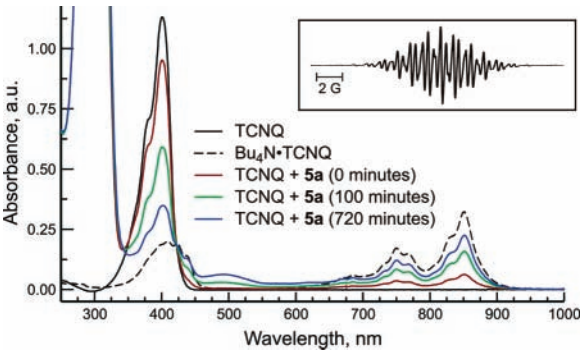


Figure 2. Absorption spectra of TCNQ (1.66×10^{-5} M) before and after the addition of **5a** (end group [4-DMAB] = 1.91×10^{-4} M) and of Bu_4N·TCNQ in degassed CH_2Cl_2. Inset shows the ESR spectrum of a TCNQ solution obtained 720 min after the addition of **5a**.

degassed CH_2Cl_2 displays an absorption band centered at 401 nm. Upon addition of **5a**, this band decreases in magnitude as new bands progressively emerge from 650 to 900 nm, indicating the formation of the TCNQ radical anion. The ESR spectrum of this solution, taken 720 min after the addition of **5a**, is consistent with the signature resonances of $TCNQ^-$ (a_N = 1.01 G, a_H = 1.42 G).[9] The absorption spectrum of the radical anion $TCNQ^{\cdot-}$, obtained from its tetrabutylammonium form (Bu_4N·TCNQ), is also shown for comparison. The rest of the TCNQ·dendrimer solutions also exhibit similar spectral features (ESR and absorption) as that of the **5a**·TCNQ complex.

Table 1 and Figure 3 describe the loss of TCNQ as it is being reduced by the dendrimers. The complex nature of the CT interactions[10] may have prevented us from extracting any kinetic parameters.[11] Nonetheless, it is very clear that the urea series is more efficient than the amide and control series in reducing TCNQ. For example, among third-generation dendrimers, **3u** quantitatively reduced TCNQ, while **3a** and **3c** converted it by only 73 and 36%, respectively, after 250 min.

Perhaps, the most dramatic observation in Figure 3 and Table 1 is the amplification of the reduction of TCNQ by

Table 1. Conversion of TCNQ to Its Radical Anion Form at Different Times After the Addition of the Dendritic (**1**−**5**) and Model (**0**) Donors

	% conversion			% conversion	
donor	250 min	600 min	donor	250 min	600 min
0a	0	0	**3c**	36	45
0c	0	0	**4a**	66	77
1a	17	23	**4u**	96	>99
1c	4.1	6.8	**4c**	55	66
2a	63	76	**5a**	66	77
2c	31	40	**5u**	92	99
3a	73	87	**5c**	61	72
3u	>99	>99			

the dendrimers, especially by the higher-generations belonging to the (4-DMAB)-terminated series. *Both model molecules **0u** and **0a**, which have individual E_{pa} values only slightly more anodic than their respective dendrimer homologues ($\leq$+0.09 V, $\Delta(\Delta G_{ox}) \leq 2$ kcal mol^{-1}), did not reduce TCNQ at all after 600 min!* This is unexpected considering that, for example, **3u**, utilized at the same effective [4-DMAB] as **0u**, completely (>99% conversion) reduced TCNQ in less than 250 min. Even **1c**, a donor that is not as thermodynamically potent as **0u** (on the basis of the respective E_{pa} values), reduced TCNQ to some extent after 600 min (6.8%). Additional experiments utilizing a 10-fold excess of **0u** or **0a** (relative to the concentrations described in Figure 3) only led to reduction of TCNQ by 1% after 1500 min (data not shown). In all of the experiments in Figure 3, the analytical concentrations of the dendrimers were adjusted in order to normalize the effective concentrations of the 4-DMAB units.[12] Thus, any enhancement in the reduction efficiency of TCNQ by using dendrimers is the result of a *positive dendritic effect*.[13] This effect is surprising from a thermodynamic standpoint, especially for the (4-DMAB)-terminated

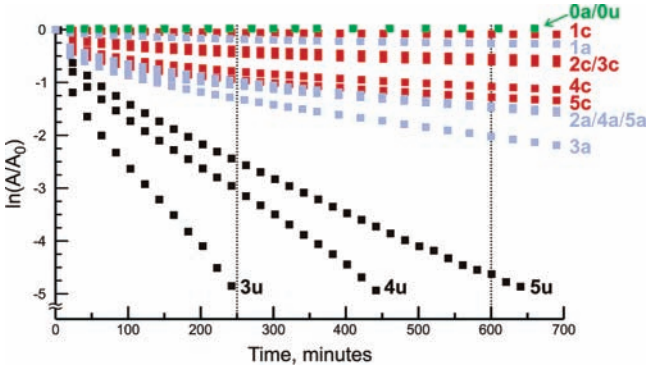


Figure 3. Kinetic profile for the decay of the corrected Abs_{401nm} value of TCNQ in the presence of the urea, amide, and control dendrimer series in CH_2Cl_2. In all cases, the [TCNQ] and end-group [4-DMAB] (**0u**, **0a**, and urea and amide series) or [phenyl] (control series) were fixed at 1.66×10^{-5} and 1.90×10^{-4} M, respectively. The dotted lines at 250 and 600 min represent the times of the conversion profiles depicted in Table 1. Measurements for **1u** and **2u** were omitted due to the limited solubilities of these dendrimers in CH_2Cl_2.

(8) Jansen, J. F. G. A.; de Brabander-van den Berg, E. M. M.; Meijer, E. W. *Science* **1994**, *265*, 1226.

(9) Simulation of the $TCNQ^{\cdot-}$ spin system using these a_N and a_H values, g = 2.003, and line broadening = 0.19 yielded the best fits to the experimental spectrum. For the literature a_N and a_H values of $TCNQ^-$, see: Jones, M. T.; Hertler, W. R. *J. Am. Chem. Soc.* **1964**, *86*, 1881.

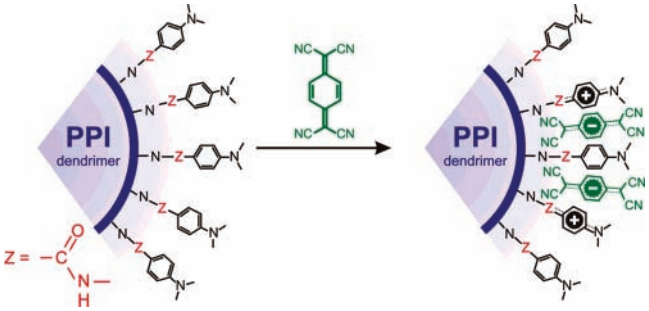
(10) Dendrimers in the amide and urea series contain two thermodynamically distinct types of donors (interior PPI amines and 4-DMAB units) that can compete for CT interactions with TCNQ.

(11) We could not fit the corrected absorption changes into the standard decay forms. Thus, the profiles in Figure 3 are arbitrarily plotted in the first-order form for ease of comparison.

series, because even though the oxidation potential of the 4-DMAB units in a given series is unaffected by dendritic growth, their reduction potencies toward TCNQ *are* affected (Table 1 and Figure 3). Most likely, the increased local concentrations of the 4-DMAB residues in dendrimers, relative to the model compounds, allow the dendronized 4-DMAB units to intramolecularly cooperate in "chelating" the TCNQ guests. At the concentration levels used in this work, the most effective CT partners for TCNQ in the urea and amide series are the third generations **3u** and **3a**, respectively. Perhaps, the size of a third-generation PPI dendrimer offers a geometric dimension such that the stability of the predominant TCNQ·4-DMAB CT pairs is maximized.

Dendrimers belonging to the (4-DMAB)-terminated series contain two electron-donating sites: interior branching amines and peripheral 4-DMAB units. Thus, the incoming TCNQ molecules can distribute themselves at these two competing sites, the degree of which will be governed by the physical accessibilities and thermodynamic requirements of the hosting sites. For the urea dendrimers **3u**−**5u**, CT formation dominates at the peripheral 4-DMAB units of the dendrimers because of their assumed exterior location (Scheme 2), less anodic oxidation potentials (thermodynamic), and more efficient ET rates (kinetic), as suggested by the CV data, relative to those of the interior amines. On the other hand, with all other parameters being similar to the urea series except for the +12 kcal mol^{-1} gap of the individual 4-DMAB units, the reducing efficiencies of **1a**−**5a** are retarded relative to **3u**−**5u**. In this case, the lack of ET activity from the 4-DMAB units of the amide series allows the interior amines of the dendrimers to substantially compete as electron donors in the overall CT formation process. Thus, it is not too surprising to realize from Figure 3 and Table 1 that the presence of the relatively dormant 4-DMAB groups in **1a**−**5a** only makes the amide series a slightly better donor than the control series.[14]

Scheme 2. Reduction of TCNQ by the (4-DMAB)-Terminated Urea Dendrimers



The residence site of most of the CT pairs in the urea series is most likely at the periphery of the dendrimers (Scheme 2). In going from the urea to the amide series, the E_{pa} values of the 4-DMAB units uniformly shift to more anodic values by approximately +0.53 V. In accompanying this thermodynamic transition, the CT sites subsequently and partially migrate from the peripheries to the interior branching amines of the dendrimers. Taken together, this transition will effectively result in the formation of CT pairs wherein the TCNQ anions are partially encapsulated by the dendrimers in the amide series.[15] Thus, in the case of the amide, and hence the control series as well, this internal location can pose as a kinetic barrier in the reduction process because the diffusing TCNQ molecules must penetrate the outer layers of the dendrimers before docking at the internal hosting sites.

The role of the PPI interior amines toward the reduction of TCNQ is very apparent in the case of the control dendrimers **1c**−**5c**. This series, which does not contain any other competing sites for CT pair formation with TCNQ other than the interior amines of the dendrimers, convincingly shows that the reduction efficiencies of the PPI dendrimers steadily increase with increasing generation (from 6.8% for **1c** up to 72% for **5c** after 600 min).

To the best of our knowledge, the study presented here is the first report to straightforwardly correlate the reducing efficiencies of dendrimers with the oxidation potentials of their substituents. We are also currently expanding this work to other solvent systems because the structures of the title dendrimers contain critical solvent-dependent sites (e.g., ureas for mutual H-bonding) that can potentially alter the course and rate of reduction of TCNQ and other acceptors.

In conclusion, judging from the data in Figure 3 and Table 1, we have shown that the absence of the PPI backbone muted the reducing activity of 4-DMAB. On the other hand, the *positive dendritic effect* is reflected in the two series of (4-DMAB)-terminated dendrimers: the dendrimers in these two series, which have structurally similar reducing units yet markedly different E_{pa} values, showed improved reducing activities toward TCNQ at rates corresponding to the E_{pa} values of the 4-DMAB units.

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Supporting Information Available: Synthesis of dendrimers **1**−**5** and model compounds **0**, including their ^{1}H and ^{13}C NMR spectra, and CV data of **1a**−**5a**, **1u**−**5u**, and **1c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Even though the effective [4-DMAB] has been constrained, the total number of donor groups (4-DMAB and interior tertiary amines) still slightly varies between generations but not to a significant extent. See ref 14 for details.

(13) For recent examples of *positive dendritic effects*, see: (a) Delort, E.; Darbre, T.; Reymond, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 15642. (b) Dahan, A.; Portnoy, M. *Org. Lett.* **2003**, *5*, 1197.

(14) One must realize that the total number of donor sites for the dendrimers in the (4-DMAB)-terminated series is almost doubled relative to those in the control series. As an example, the theoretical number of donor sites in the amide series **1a**−**5a**, ordered as 4-DMAB and interior tertiary amine units, respectively, is as follows: **1a**, 4 and 2; **2a**, 8 and 6; **3a**, 16 and 14; **4a**, 32 and 30; **5a**, 64 and 62.

(15) The "dendritic box",[8] a *t*-Boc-L-Phe-terminated, fifth-generation PPI dendrimer, encapsulates $TCNQ^{\cdot-}$ in its dimeric form (see: Bosman, A. W.; Jansen, J. F. G. A.; Janssen, R. A. J.; Meijer, E. W. *Polym. Mater. Sci. Eng.* **1995**, *73*, 340). In all of our absorption measurements, we did not observe any spectral features associated with $(TCNQ)_2^{2-}$ formation.