

Redox Modulation of Benzene Triimides and Diimides via Noncovalent Interactions

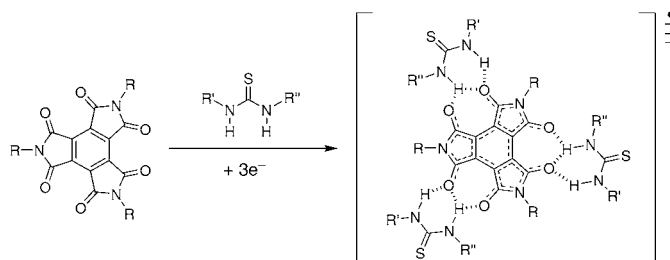
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ABSTRACT



Mellitic triimides undergo three sequential one-electron reduction processes whose potentials are significantly lowered in the presence of alkyl thioureas. The two sequential reductions of benzene diimides are similarly stabilized. Calculation of the relative free energy change between the different electronic states of the imide acceptors and their corresponding alkyl thiourea complexes indicates dramatic increases in hydrogen bond strength with increasing acceptor charge density.

Supramolecular building blocks that possess both useful electronic behaviors, i.e., the capacity to readily accept or donate one or more electrons, and molecular recognition elements have emerged as useful components of functional molecular ensembles and aggregates.¹ Units whose molecular recognition capacity can be modulated via an electrochemical input offer a pathway to control supramolecular conformation: for example, shuttling of 4,4'-bipyridinium (Paraquat)-based catenanes and rotaxanes has been demonstrated by Stoddart and co-workers.²

Previously, we have shown that electron-deficient unsubstituted imide systems such as flavins and naphthalimides provide a platform for specific, three-point hydrogen bonding interactions, the strength of which may be controlled through

electrochemical conversion to and from the radical anionic state. This feature has been exploited to incorporate aromatic imides in systems exhibiting redox- or photocontrolled switching and recognition capabilities.³ Additional studies have shown that two-point hydrogen bonding to quinones is also an effective tool for redox-modulated recognition.⁴

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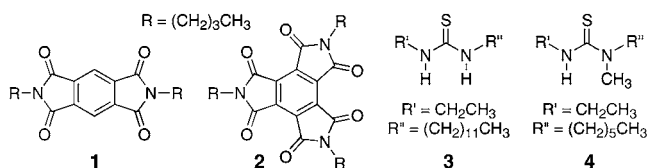
(4) Methods for supramolecular coordination of quinone-type electron acceptors include: (a) Aoyama, Y.; Endo, K.; Anzai, T.; Yamaguchi, Y.; Sawaki, T.; Kobayashi, K.; Kanehisa, N.; Hashimoto, H.; Kai, Y.; Masuda, H. *J. Am. Chem. Soc.* **1996**, *118*, 5562–5571. (b) Hayashi, T.; Miyahara, T.; Koide, N.; Kato, Y.; Masuda, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1997**, *119*, 7281–7290.

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(1) (a) Kaifer, A. E.; Gómez-Kaifer, M. *Supramolecular Electrochemistry*; Wiley-VCH: Weinheim, **1999**. (b) Boulas, P. L.; Gómez-Kaifer, M.; Echegoyen, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 216–247.

Benzene diimides (**1**) are readily prepared organic electron acceptors that, together with their naphthalene analogues, have found favor in a variety of contexts: from components of molecular electronic materials⁵ to DNA intercalators and building blocks for catenanes and rotaxanes.⁶ Both of these planar electron-accepting frameworks share the bipyridinium dication's ability to accept two electrons at distinct potentials. Mellitic triimides (**2**) are *three*-electron-accepting hexasubstituted benzene derivatives that remained unexplored until recently⁷ but are now emerging as useful supramolecular building blocks that provide an alternative symmetry to more familiar C_2 -symmetric organic electron acceptors. In this letter, we report the modulation of diimide and triimide reduction processes via noncovalent interactions with thiourea derivatives.



The acceptors used in this study were prepared using published procedures.⁸ Cyclic voltammetric (CV) traces of **1** and **2** were recorded in dichloromethane solution with $n\text{-Bu}_4\text{N}^+\text{ClO}_4^-$ as a supporting electrolyte⁹ (Figure 1).

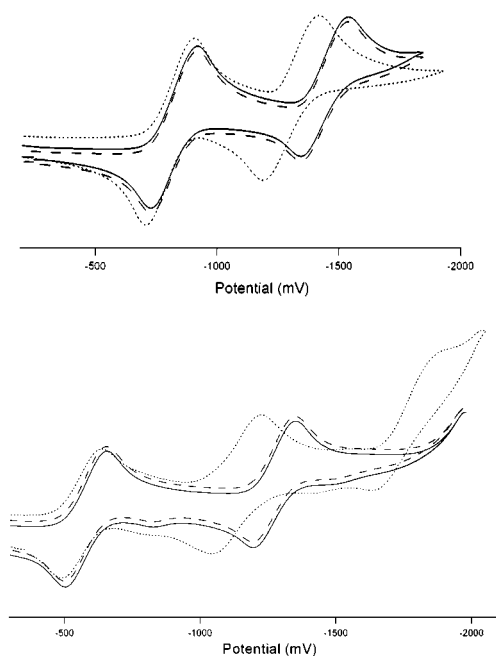


Figure 1. CV traces for diimide **1** (top) and triimide **2** (bottom): pure acceptor (—), acceptor plus excess **3** (····), acceptor plus excess **4** (— —).

Additional traces for both materials were recorded in the presence of di-*N*-alkyl thiourea **3** (30 equiv) and, as a control for multiple-point hydrogen bond formation, tri-*N*-alkyl thiourea **4** (50 equiv).¹⁰

Diimide **1** exhibits two reversible one-electron reductions at well-established potentials (Table 1).¹¹ Significant shifts

Table 1. Potentials (mV) for the Reduction Processes Associated with Diimide **1** and Triimide **2**

material	¹ $E_{1/2}$	² $E_{1/2}$	³ $E_{1/2}$
1	-843	-1440	
1 + excess 3	-815	-1305	
ΔE	+28	+139	
1 + excess 4	-843	-1440	
2	-577	-1250	< -2000 ^a
2 + excess 3	-557	-1135	-1724
ΔE	+20	+115	> +276
2 + excess 4	-577	-1250	< -2000 ^a

^a Lower limit from experiments in THF⁵ and CH₂Cl₂.

of both features are observed upon titration with increasing amounts of dialkyl thiourea **3**. No detectable shift in reduction potential was occasioned by the presence of up to 50 equiv of trialkyl thiourea **4**, highlighting the necessity of bifurcated hydrogen bonding interactions for effective stabilization at the examined concentrations (Figure 2). The electrochemical

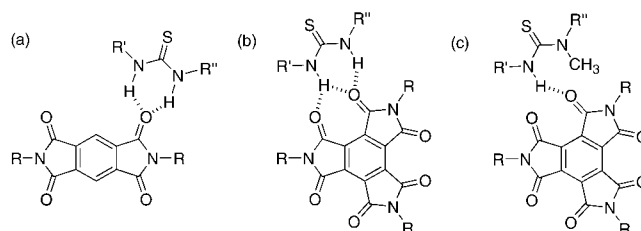


Figure 2. Examples of stabilizing hydrogen bond complexes between (a) diimide **1** and a single dialkyl thiourea **3** and (b) the corresponding complex for triimide **2** with **3**. In panel c, the presence of an additional *N*-methyl group removes the possibility of multiple-point association between **2** and **4**.

behavior of triimide **2** mirrors that of the diimide: in the dichloromethane solvent window, two reversible one-electron reductions are revealed, though the more strongly electron-accepting nature of this system ensures that both the first and second electrons are more readily introduced than for

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(6) (a) Guelev, V.; Sorey, S.; Hoffman, D. W.; Iverson, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 2864–2865. (b) Raehm, L.; Hamilton, D. G.; Sanders, J. K. M. *Synlett* **2002**, 1743–1761.

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(8) Hamilton, D. G.; Prodi, L.; Feeder, N.; Sanders, J. K. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1057–1065. See also ref 5.

(9) Since perchlorates are powerful oxidizers, they are potentially hazardous, especially when in contact with reducing materials. Extreme caution was exercised in preparation of electrolyte solutions for CV studies: Sax, N. I.; Lewis, R. J. *Dangerous Properties of Industrial Materials*, 7th ed.; Van Nostrand Reinhold: New York, 1989; Vol. 3.

the diimide. In the presence of excess **3**, both reductions shift toward more positive potentials: the magnitudes of each shift are very similar to those recorded for the diimide. More dramatically, the third reduction of the triimide, formerly outside of the useful solvent window, is shifted by a *minimum* of +276 mV into the observable range for dichloromethane. As with diimide **1**, no shifts in reduction potential were observed in the presence of excess trialkyl thiourea **4**.

Computational analysis was used to determine the minimum energy binding modes of some simplified imide acceptor–thiourea complexes in each of the experimentally accessible electronic states possessed by the acceptor systems (Figures 3 and 4).¹² The chosen hybrid level of theory has

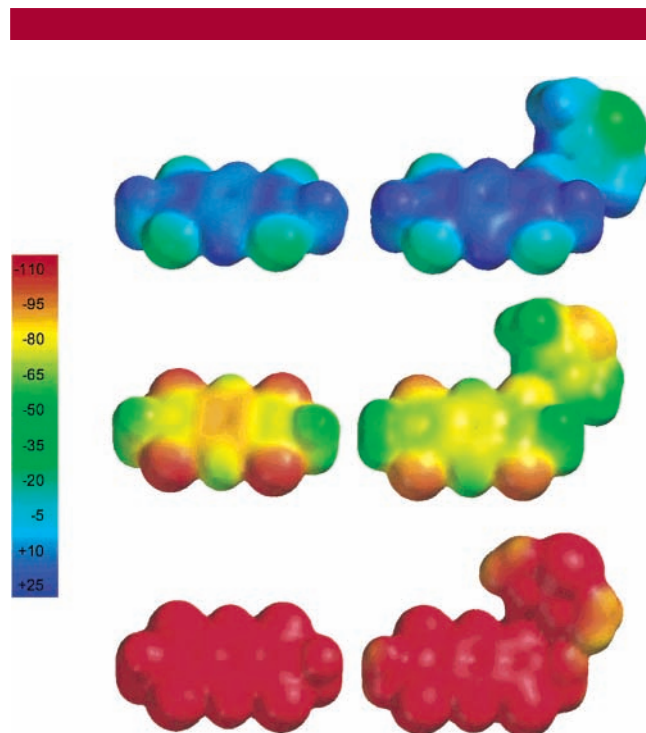


Figure 3. Electrostatic potential maps for *N,N'*-dimethyl diimide *alone* (left) and *bound* to a single *N,N'*-dimethyl thiourea (right) in its neutral (top), radical anionic (middle), and dianionic (bottom) states. Energies are relative to the neutral form (kcal/mol).

been shown to be particularly successful for calculations on systems involving radical anionic species. For both the

(10) **Typical Procedure.** CV traces were recorded for a CH_2Cl_2 blank, then for a solution of the diimide or triimide and decamethylferrocene (as a reference), and finally for the same sample containing excess alkyl thiourea. All solutions were purged with Ar for several minutes prior to data collection. Differences in half-wave potentials were determined using square-wave voltammetry. All scans were recorded at a sweep rate of 200 mV/s, without iR compensation.

(11) (a) Viehbeck, A.; Goldberg, M. J.; Kovac, C. A. *J. Electrochem. Soc.* **1990**, *137*, 1460–1466. (b) Hamilton, D. G.; Montalti, M.; Prodi, L.; Fontani, M.; Zanello, P.; Sanders, J. K. M. *Chem. Eur. J.* **2000**, *6*, 608–617.

(12) All geometries were optimized at the HF/3-21G* level. DFT-B3LYP/6-31G* single-point energy calculations were used to obtain the electrostatic potential surfaces using Spartan '02 (Wavefunction, Inc.). See: (a) Niemz, A.; Rotello, V. M. *J. Am. Chem. Soc.* **1997**, *119*, 6833–6836. (b) Cuello, A. O.; McIntosh, C. M.; Rotello, V. M. *J. Am. Chem. Soc.* **1998**, *120*, 8606–8609.

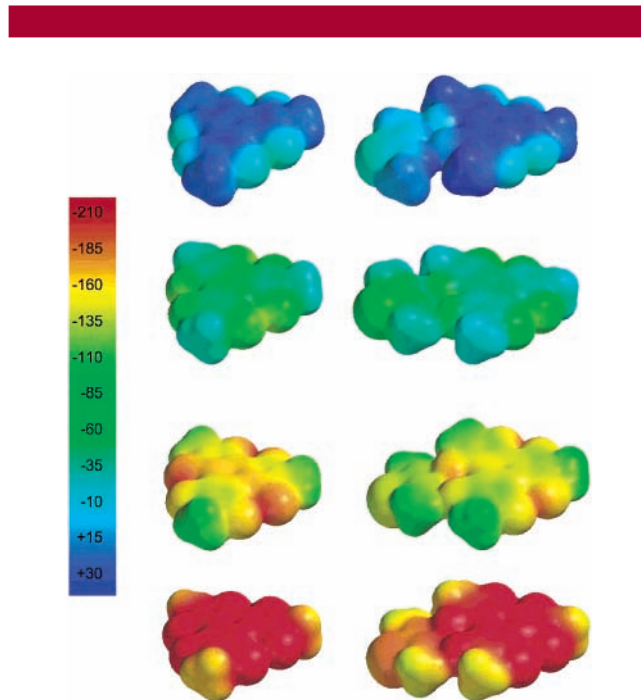


Figure 4. Electrostatic potential maps for *N,N',N''*-trimethyl triimide *alone* (left) and *bound* to a single *N,N'*-dimethyl thiourea (right) in its (from top to bottom) neutral, radical anionic, dianionic, and radical trianionic states. Energies are relative to the neutral form (kcal/mol).

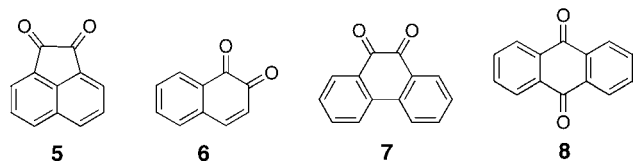
diimide and triimide complexes, the predicted energy minimum conformation involves bifurcated contacts, as schematically depicted in Figures 2a and 2b.

For purposes of comparison with the current systems, the effect of urea on the reduction potential for a series of aromatic quinones may be considered.

Acenaphthenequinone **5**, 1,2-naphthoquinone **6**, and phenanthrenequinone **7** all act as selective redox-dependent receptors for diphenyloxyureas, their first reduction potentials shifting to more positive values by +120–140 mV in the presence of this hydrogen bond donor.¹³ The readily soluble dialkyl thioureas **3** used in our systems are more acidic than previously investigated oxyurea systems, providing a stronger hydrogen bonding interaction without any evidence of proton transfer as was observed with diphenylthioureas.¹³ Quinone shifts of this magnitude with diphenyloxyureas were not observed with hydrogen bond donors that lacked the capacity to form multiple contacts or with anthraquinone **8** and diphenylurea. On the basis of these and other observations, it was concluded that both proximal carbonyl groups *and* a multiple hydrogen bond donor were required for significant stabilization of the quinone radical anions. However, the fact that the shifts we observe for both the diimide and triimide are close in value argues against the necessity of proximal carbonyl groups for achieving significant stabilization in the current systems. In fact, the shifts of the first and second reduction potentials of the diimide exceed those of the

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triimide, yet the diimide clearly cannot involve two carbonyl groups in noncovalent interaction with thiourea.



It is clear from our studies that the gross supramolecular action of thiourea **3** on these systems significantly stabilizes their reduced forms. An understanding of this process involves recognition of the fact that although the reduced forms of the acceptors are delocalized, the bulk of the negative charge in these systems will reside on the electronegative imide carbonyl oxygen atoms. Accordingly, the hydrogen bonds established between the acceptors and thiourea **3** will increase markedly in strength as charge is introduced to the acceptor core: increased charge density on the oxygens leading to stronger interactions with partially positively charged hydrogen donor atoms.¹⁴

Thermodynamic cycles for the imide acceptor/thiourea systems were constructed to determine the relative change ($\Delta\Delta G$) in free energy arising from the observed decreases of reduction potential in the bound states.⁴ Association of thiourea **3** with the acceptors in their neutral forms is expected to be weak; this fact, coupled with the possibility for multiple binding equilibria, conspired to prevent measurement of the ΔG of association. Two- and three-state cycles, for the diimide and triimide, respectively, are shown in Figure 5. On each level of the cycles, left to right transitions represent the *relative* binding equilibria between the appropriate form of the acceptor and thiourea **3** (one-to-one complex), and top to bottom transitions represent the stepwise introduction of electrons to each acceptor.

The thermodynamic cycles reveal modest increases in the ΔG of association of thiourea with the radical anionic forms of both acceptors. More substantial increases are recorded upon generation of the dianionic forms of each system, indicating a substantial strengthening of the noncovalent bonds within the corresponding complex. The substantial shift of the third reduction potential of the triimide in the

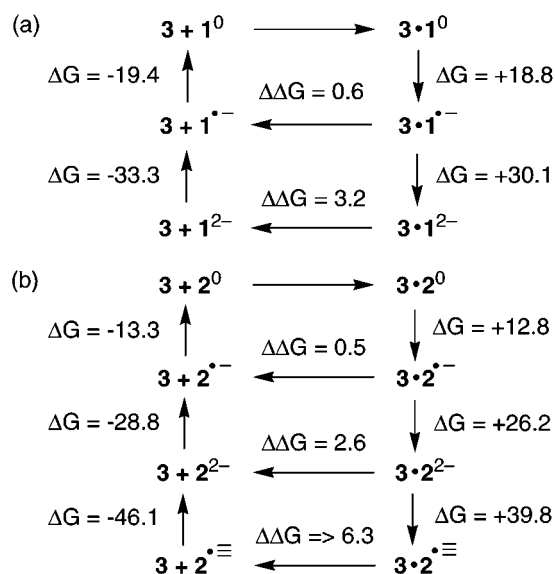


Figure 5. Thermodynamic cycles quantifying redox-modulated binding in (a) the diimide **1**/thiourea **3** system and (b) the triimide **2**/thiourea **3** system. All energies are in kcal/mol.

presence of thiourea **3** translates into a 6.3 kcal/mol stabilization of the trianion.

In summary, these results demonstrate that diimide and triimide species act as redox-triggered switches for hydrogen bond-mediated aggregation processes. For example, the conversion from a weakly associated complex with the neutral form of the acceptor to a strongly bound complex with a reduced form could be used to facilitate an aggregation process controlled by competing kinetic and thermodynamic factors. Extending this methodology to multidirectional systems that associate stronger than simple alkyl thioureas in neutral forms, e.g., guanadinium derivatives, offers the ability of engineering well-defined, extended structures with tunable, redox-controlled interactions. The possibility also exists to examine the perturbation of hydrogen bonded aggregates via addition of a diimide or a triimide, subsequent reduction of the acceptors leading to competitive hydrogen bonding and aggregate disruption.

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(14) For additional examples of hydrogen bonding of oxyanions to urea- and thiourea-based receptors, see: (a) Wilcox, C.; Kim, E.; Romano, D.; Kuo, L.; Burt, A.; Curran, D. *Tetrahedron* **1995**, *51*, 621–634. (b) Haushalter, K.; Lau, J.; Roberts, J. *J. Am. Chem. Soc.* **1996**, *118*, 8891–8896. (c) Smith, P.; Reddington, M.; Wilcox, C. *Tetrahedron Lett.* **1992**, *33*, 6085–6088. (d) Albert, J.; Hamilton, A. *Tetrahedron Lett.* **1993**, *34*, 7363–7366. (e) Hughes, M.; Smith, B. *J. Org. Chem.* **1997**, *62*, 4492–4499.