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“*ortho*-Wurster’s Crowns”: Synthesis and Properties of a Novel Phenylenediamine-Based Redox-Active Macrocyclic Ligand

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A hybrid, macrocyclic structure based on *o*-phenylenediamine and a crown ether promotes an intimate mutual interaction with a bound potassium ion in the form of chelation by the redox-active moiety. A general synthetic method and properties are described for the first member of a new class of redox-active, lariat-type macrocycles called the “*o*-Wurster’s crowns”.

The development of electrochemically responsive ligand systems in which a redox-active component interacts with a bound guest has attracted considerable attention for over two decades.[1,2] Of the variety of reported hosts, a predominance incorporate ferrocene[3] or tetrathiafulvalene[4] as the electrochemically active moiety owing to their well-studied reversible oxidation processes. More recently, we and others have investigated general synthetic methods and properties of *p*-phenylenediamine/crown hybrids.[5−7] The choice of *p*-phenylenediamine is based on its comparative ease of introduction into a macrocyclic framework, the potential of the amine functionality to participate in guest binding, and the established reversible electrochemistry of the famed Wurster’s reagent[8] (*N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine, *p*-TMPD). Inspired by the structural relationship, the trivial name “Wurster’s crowns”[5] has been used to distinguish *p*-phenylenediamine-containing macrocycles as a distinct class (see Figure 1). While Wurster’s crowns provide a macrocyclic N atom that is integral to both complex stability and redox activity, an even greater interaction between the redox and binding components of the host system would enhance the desired mutual interaction. Further, the low oxidation potential of the *p*-phenylenediamine unit precludes its use in the capture of guests with even modest oxidizing ability. We, therefore, became interested in a more robust host motif that maintains the desirable features associated with N,N′-peralkylated *p*-phenylenediamines while promoting stronger communication between the redox center and a guest.

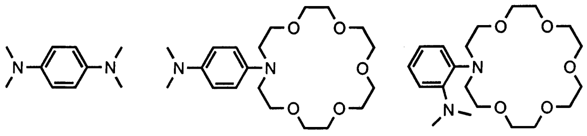

Figure 1. Wurster’s reagent and the Wurster’s crown analogues of 18-crown-6.

We describe here synthetic procedures, properties, and coordination chemistry for the first member of a new class of redox-active ligands, the *ortho*-Wurster’s crowns, based on *o*-phenylenediamine. Similar to their para predecessors, these macrocycles provide for an intimate interaction between the redox center and bound cationic guest via direct coordination through the endocyclic N atom. However, the “*o*-Wurster’s crowns” are lariat ethers wherein both the endo- and exocyclic N atoms can participate in stabilizing a complex through chelation. It is anticipated that both increased complex stability and a stronger link to the guest species will result. Additionally, the first oxidation of *N*,*N*,*N*′,*N*′-tetramethyl-*o*-phenylenediamine (*o*-TMPD) is 430 mV higher than that of *p*-TMPD due to pronounced steric effects in the ortho isomer.[9] The oxidation of the *o*-Wurster’s crowns should then occur at a substantially higher potential than their para counterparts with the concomitant ability to form complexes with a wider variety of metal cations.

To develop a general synthetic method and probe the impact of the *o*-phenylenediamine moiety on the coordination chemistry of the host, we chose an analogue of 18-crown-6 as the initial target, the rationale being that, for comparative purposes, there is an established coordination chemistry for

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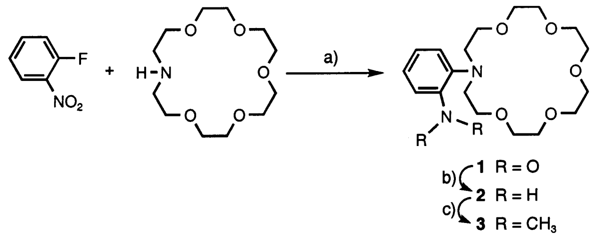
Scheme 1 [a]



[a] (a) Cs_2CO_3, 60 °C, 24 h, 98%; (b) H_2, 10% Pd/C, EtOAc, 25 °C, 24 h, 100%; (c) CH_3I, Cs_2CO_3, CH_3OH, 35 °C, 24 h, 90%.

18-crown-6[10] and several reported redox-active macrocycles with comparable binding cores.[3,4] As shown in Scheme 1, reaction of 1-aza-18-crown-6 with 2-fluoronitrobenzene in the presence of Cs_2CO_3 formed **1** in 98% yield. Reduction of the nitro functionality was achieved quantitatively by catalytic hydrogenation to form **2**. Subsequent methylation with iodomethane in the presence of Cs_2CO_3 produced the new *o*-Wurster's crown **3** in an overall yield of 88% after purification by column chromatography. Importantly, this short synthetic sequence can easily accommodate the introduction of any number of azacrown macrocycles.

The electrochemical properties of compound **3** and its alkali metal complexes were studied by cyclic voltammetry. As shown in Figure 2a, *o*-TMPD displays two reversible oxidations that correspond to the generation of a delocalized radical cation and a quinoid dication,[9] respectively. At a scan rate of 200 mV s^{-1}, **3** is oxidized at a potential similar to that for oxidation of *o*-TMPD (590 mV for *o*-TMPD; 577 mV for **3** vs Ag/AgCl), however, surprisingly, not reversibly (see Figure 2b). Such behavior stands in stark contrast to that observed for *p*-phenylenediamine-containing crowns.[6] Preliminary computational studies suggest the crown ether undergoes a conformational change upon oxidation to facilitate intramolecular stabilization of the radical species.[11] At a faster scan rate (3 V s^{-1}, Figure 2c), **3** shows the expected two reversible oxidations characteristic of *o*-TMPD, indicating that the rate of electron transfer is now faster than the putative conformational change.

The capture of cationic guests by redox-active hosts is known to cause anodic shifts in the oxidation potential of the free ligands.[1,2] The addition of 1.5 equiv of $LiBF_4$, $NaClO_4$, KPF_6, $RbClO_4$, or $CsClO_4$ to acetonitrile solutions of **3** (3−4 mM) resulted in significant anodic shifts of the first oxidation wave of the *o*-phenylenediamine moiety. For all of the cations studied the anodic shift was accompanied by a complete loss of reversibility independent of scan rate. The size of the anodic shift tracks the known selectivity of the parent macrocycle, 18-crown-6,[10] with the largest caused by the potassium cation (ΔE = 297 mV, Figure 2d). Thus, complex stability plays a more prominent role than charge density in the electrochemical response of these ligands to alkali metal cations. Upon the return sweep, two smaller reduction waves appear at potentials similar to that of the free crown, which indicates that the metal cation may be lost upon oxidation. Due to the strong contribution of the redox center in stabilizing the complex, the magnitude of the anodic shift in the K^+ complex of **3** is considerably higher than that typically seen for K^+ complexes of other "neutral-to-cationic" redox-active hosts based on 18-crown-6.[3,4] Perhaps most interesting is the comparison to a *p*-phenylenediamine-containing analogue of 18-crown-6 with a reported shift of 200 mV upon treatment with 15 equiv of added K^+.[6]

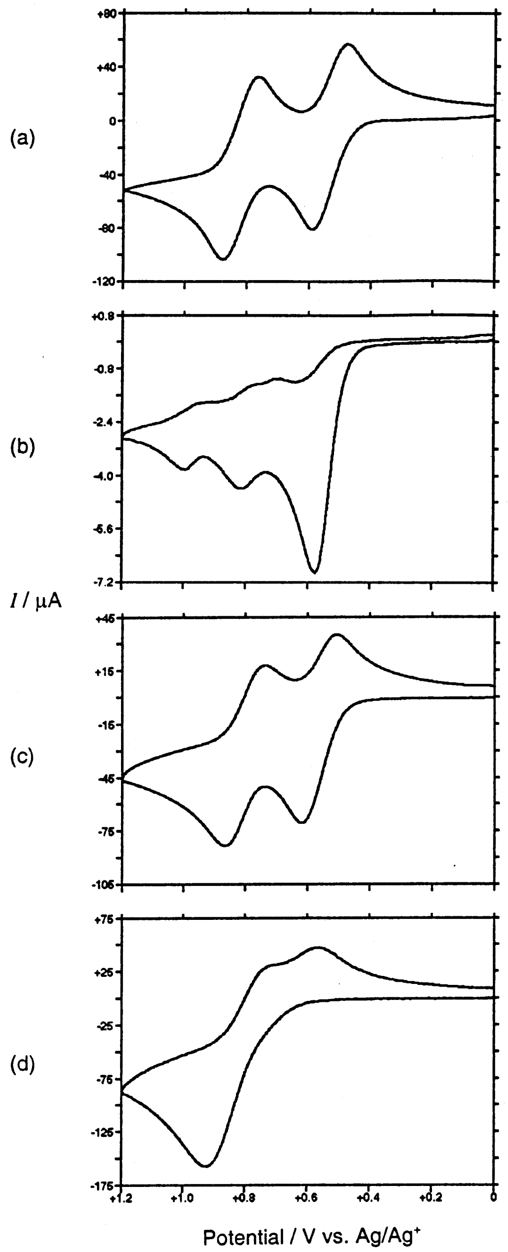


Figure 2. Cyclic voltammograms (CH_3CN, 0.1 M Et_4NClO_4) of (a) *o*-TMPD, 200 mV s^{-1}; (b) **3**, 200 mV s^{-1}; (c) **3**, 3 V s^{-1}; (d) **3**·KPF_6, 3 V s^{-1}.

The potassium complex of **3** has been characterized by X-ray crystallography (Figure 3).[12] Two distinct complexes are present, although, in terms of the complex cation, the geometric parameters are nearly identical, with each unequivocally showing direct participation of the dimethylamino group in complex formation. The macrocyclic ring adopts a chair conformation of D_{3d} symmetry with K^+

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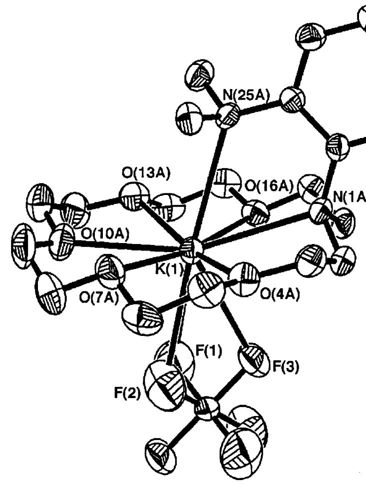

Figure 3. X-ray structure of **3**·KPF_6 (H atoms omitted for clarity). Selected distances (Å): K−N(25A) = 2.959; K−N(1A) = 2.949; $K-O_{av}$ = 2.822.

disposed slightly below the plane of the six macroring donor atoms. This arrangement is similar to that for potassium complexes of 18-crown-6[13] and 1-aza-18-crown-6.[14] The average K−O distances in **3** (2.822 Å) are consistent with those reported for 1-aza-18-crown-6 (2.816 Å) and 18-crown-6 (2.805 Å). The pendant arm nitrogen atom from the dimethylamino group is positioned above the macrocycle in an apical coordination position. A hexafluorophosphate counterion occupies the opposite face. As has been shown in lariat ether complexes,[15] the pendant arm in **3** is not holding the metal ion between it and the macrocycle core but, instead, seemingly pushing it through the ring. Bond length analysis reveals essentially equivalent interactions between the potassium ion and both the dimethylamino and the macroring nitrogen atoms, 2.959 and 2.949 Å, respectively. Though slightly longer than those reported for a K^+ complex of 1-aza-18-crown-6,[14] they are in agreement with N-alkylated azacrown ether complexes.[15] Further, C−N−C bond angles in the dimethylamino group (109.2°) and the macrocycle (110.5°) are consistent with complete pyramidalization of each nitrogen atom.

To examine the K^+ coordination in solution, a ^{13}C NMR study in deuterated acetonitrile was undertaken. Chemical shifts for **3** are as expected for a hybrid structure of *o*-TMPD and a crown ether. Upon complexation,[16] the ^{13}C methylene resonances next to the O atoms shift upfield (average δ, CH_2O: **3**, 70.92; **3**·KPF_6, 70.43). This behavior is typical for crown ethers and is attributed to conformational changes in the crown upon complex formation.[17] The resonances for both the methylene groups next to the N atom (δ, CH_2N: **3**, 51.84; **3**·KPF_6, 58.71) and the methyl groups (δ, CH_3N: **3**, 42.32; **3**·KPF_6, 47.16), however, shift downfield upon complexation, indicating their contribution to stabilizing the complex and highlighting the strong interaction of the redox center with the bound guest in solution.

In summary, *o*-Wurster's 18-crown-6, **3**, represents the first member of a novel class of redox-active macrocycles based on *o*-TMPD. A general, scalable, and high-yielding synthetic scheme has been devised such that nearly any macrocycle containing a secondary amine can be readily converted into an *o*-Wurster's crown. Like 18-crown-6, compound **3** displayed selectivity for the potassium cation, resulting in a large anodic shift upon coordination. Intriguingly, these results suggest that the addition of this redox-active moiety to a crown will have minimal effect on the crown's inherent binding characteristics, thus allowing future investigations to take advantage of the rich history of crown chemistry for the development of new sensors and use in redox-switchable applications.

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Supporting Information Available: Experimental section, computational results, and X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Crystal structure of **3**·KPF_6: $C_{20}H_{34}F_6KN_2O_5P$, $M_r = 566.56$ g mol^{-1}, orthorhombic, space group *Pbca*, $a = 18.912(4)$ Å, $b = 18.447(4)$ Å, $c = 30.856(6)$ Å, $V = 10765$ Å^3, $Z = 16$, $\rho_{calcd} = 1.398$ g cm^{-3}, $T = 293$ K. 6930 unique reflections were collected on a Bruker CCD SMART system equipped with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) and corrected for Lorentz and polarization effects. Data collection and unit cell and space group determination were all carried out in the usual manner.[18] The structure was solved by direct methods (SHELXTL),[19] and the model was refined using full-matrix least squares techniques.[20] The non-hydrogen atoms were refined with anisotropic thermal parameters. All hydrogen atoms were placed in calculated positions [$U_{iso} = 1.3U(C)$; $d_{C-H} = 0.95$ Å] for refinement. Refinement of positional and anisotropic thermal parameters led to convergence. The structure was refined on F^2 to R1 = 0.0633 and wR2 = 0.1947 for 4222 reflections with $I > 2\sigma(I)$.

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