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Tetraazacyclophanes by Palladium-Catalyzed Aromatic Amination. Geometrically Defined, Stable, High-Spin Diradicals

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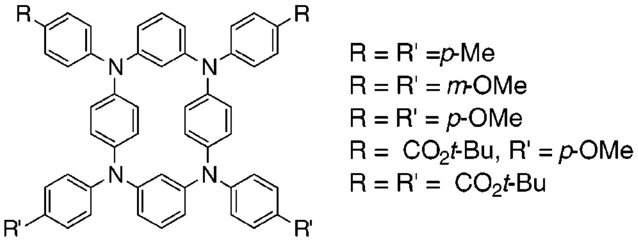
ABSTRACT



Neutral tetraazacyclophanes were prepared in a one-step palladium-catalyzed amination reaction. Simple oxidation of these materials creates dication diradicals that are stable at room temperature and that are geometrically well defined. The electronic and magnetic properties of the dications were investigated by CV, UV–vis, and EPR spectroscopy. These spectral data and solution phase magnetic susceptibility measurements indicate high spin ground states in certain media. EPR zero field splitting parameters for the diradical suggest that the distance between the two radical sites can be approximated simply by the distance between alternating nitrogens in the macrocycle.

The unusual stability of triarylamine radical cations allows the design and preparation of organic materials with interesting and important electronic properties. For example, high spin triarylamine polyradicals have been generated for studies on magnetic materials, and triarylamines are standard hole transport materials.[1−5] However, the modest yields of copper-mediated reactions that are conventionally used to prepare triarylamines have limited the size and topology of this class of material. Our recent synthesis of triarylamine polymers by palladium-catalyzed amination of aryl halides suggested that conditions to generate macrocyclic triarylamine materials conveniently with alternating *m*- and *p*-regiochemistry could be found.[6,7] We report a one-step cyclization to form symmetrical tetraazacyclophanes that contain two *p*-phenylenediamine units connected by a *m*-phenylene unit, a multistep cyclization to form unsymmetrical analogues, and physical measurements that indicate triplet spin states for the dication diradicals generated by oxidation in certain media. The two *p*-phenylenediamine units of these materials produce diradicals that are stable at room temperature,[8−10] the *m*-phenylene connection provides high spin structures,[11,12]

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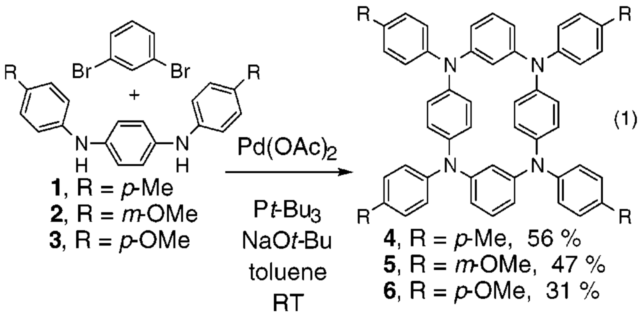
and the cyclophane structure ensures a defined geometry. Electrochemical and spectroscopic properties of the neutral and dicationic materials support these claims, including the generation of triplet spin states.

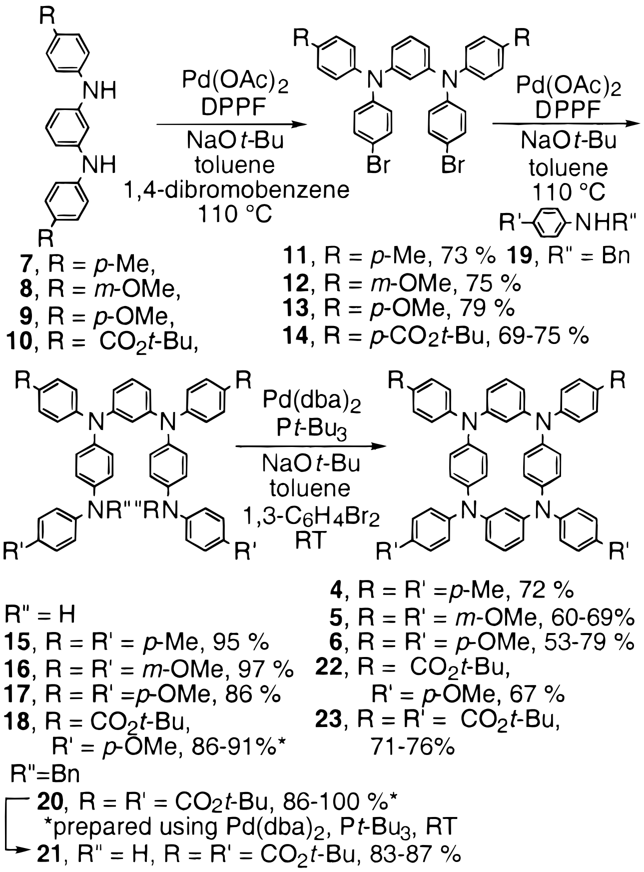
Our synthetic efforts focused on two routes using palladium-catalyzed amination of aryl halides.[13−15] For use in the one-step cyclization procedure, *N*,*N′*-diarylphenylenediamine units **1** and **2** were prepared in 74% and 65% yields by reacting 1,4-dibromobenzene with a substituted aniline using Pd(OAc)$_2$ and DPPF as catalyst in toluene at 110 °C. Diamine **3** was obtained in only 44% yield with this catalyst, but our recent protocol involving a 1:0.8 ratio of Pd and P(*t*-Bu)$_3$[16] gave diamine **3** in 83% yield at room temperature. Reactions of **1**−**3** with 1,3-dibromobenzene using 5% Pd(dba)$_2$ and 4% P(*t*-Bu)$_3$ at room temperature gave tetraazacyclophanes **4**−**6** (eq 1) in remarkable yields for a process that forms four new aromatic C−N bonds and a cyclic structure. Reactions were run at a concentration of 1 mM at room temperature in toluene to favor formation of the cyclic material instead of the polymer. The low reaction temperatures favor cyclization. In all cases, the tetraazacyclophane was the fastest running material by silica gel chromatography, simplifying the isolation of pure material.



To prepare macrocycles with more than one type of substituent, the stepwise approach in Scheme 1 was also investigated. Reaction of substituted anilines with 1,3-dibromobenzene produced 1,3-phenylenediamines **7**−**9** in yields ranging from 60% to quantitative, depending on the substituent. Reactions involving the most electron-rich *p*-methoxyaniline gave products in lower yield, but this reduced yield resulted from partial oxidation of the electron-rich product. Reaction of 4-*tert*-butylbromobenzoate with 1,3-phenylenediamine, rather than reaction of the substituted aniline with dibromobenzene, was used to prepare phenylenediamine **10**, which contains electron-poor *N*-aryl groups. Palladium-catalyzed amination reactions provide higher yields when electron rich arylamines are reacted with electron-poor aryl halides.[14]

These diamines were reacted with an excess of *p*-dibromobenzene as the second stage of the stepwise synthesis to produce compounds **11**−**14** in yields ranging from 69 to 79%. These materials were then reacted with a second type of aniline to provide tetraamines **15**−**18** in high yield, except when the electron-poor 4-*tert*-butylcarboxyaniline was used. To overcome the lower yields with this aniline, *N*-benzyl-4-*tert*-butylcarboxy aniline **19** was reacted with dibromide **14** to provide **20** and then **21** after hydrogenolysis. Reaction of these tetraamines with 1,3-dibromobenzene using a 1:1 ratio of substrates at a 0.01 M concentration gave cyclophanes **4**−**6**, **22**, and **23** in yields ranging from 53 to 79%.

Scheme 1



A single crystal of *p*-tolyl compound **4** was obtained from a toluene/hexane solution, and the structure of this material was determined by X-ray crystallography (Figure 1, inset). The molecule possesses a crystallographic mirror plane. Each nitrogen is planar, with the sum of the three C−N−C angles being 360.0(2)° and 359.7(2)° for the two crystallographically distinct nitrogens. The aromatic groups provide the conventional propeller arrangement of simple triarylamines, causing the 1,3-phenylenediamine units to be canted out of the plane of the four nitrogens. The two 1,4 phenylenediamine units form a concave surface, rather than adopting a parallel arrangement. The distances between the nitrogens are 4.86 and 5.65 Å on the sides of the rectangle formed by the four nitrogens and 7.45 Å along the diagonal. The distances from the center of one external aromatic ring to the other are 8.78 and 9.36 Å along the sides of the rectangle and 12.83 Å along the diagonal.

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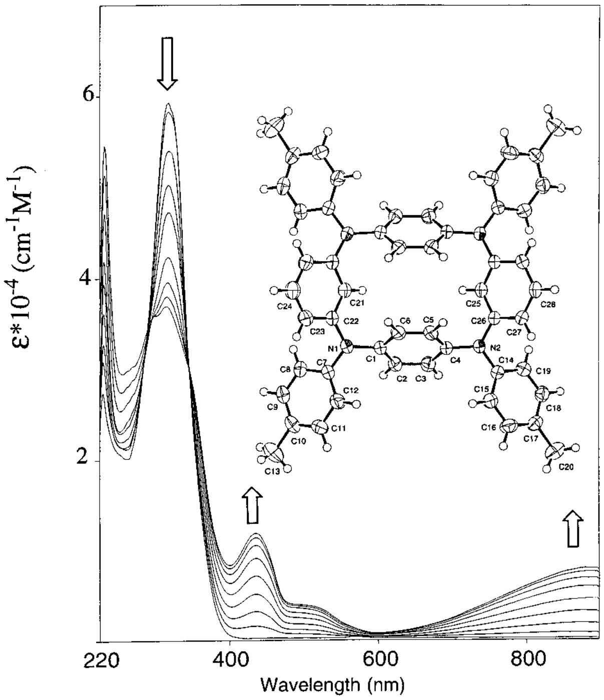

Figure 1. UV−vis spectra for oxidation of **4**. Inset: ORTEP drawing of **4**.

The electronic properties of these unusual structures were examined by cyclic voltammetry as well as UV−vis and EPR spectroscopy. The redox potentials were measured in a 0.1 M solution of tetrabutylammonium hexafluorophosphate (TBAH) in dichloromethane using a Ag/AgNO$_3$ reference electrode and a carbon working electrode. The voltammograms exhibited four reversible waves (Table 1) corresponding to oxidation of each of the nitrogens. *p*-Anisyl structure **6** showed the lowest oxidation potentials, and carboxy-substituted **23** showed the highest, confirming the ability to use *N*-aryl groups to tune the potentials. The electrochemical potentials were also evaluated in acidic media (1% trifluoroacetic acid, 0.1 M TBAH in CH$_2$Cl$_2$). The electrochemistry of **23** in acidic medium was essentially identical to that in the neutral medium, but the potential and peak-to-peak separation for the first oxidation of **4** and **6** increased in the presence of TFA. The redox process was chemically reversible; an identical trace was observed for a second scan, but the large peak to peak separation indicates electrochemical irreversibility. Anodic potentials in CH$_2$Cl$_2$/TFA are, therefore, provided in Table 1. The smaller difference in the first and second potentials indicates that some disproportionation will be observed.

Table 1. Redox Potentials of **6**, **4**, and **23** (in volts) vs Ag/AgNO$_3$ in CH$_2$Cl$_2$ and in CH$_2$Cl$_2$ with 1 vol % of Trifluoroacetic Acid Added

	no TFA added			
	E^0_1	E^0_2	E^0_3	E^0_4
6	0.107	0.386	0.736	0.876
4	0.134	0.416	0.836	1.045
23	0.427	0.623	1.054	1.236

	1 vol % of TFA added[a]			
	E_{a1}	E_{a2}	E_{a3}	E_{a4}
6	0.490	0.592	0.840	0.989
4	0.542	0.660	0.922	1.134
23	0.544	0.748	1.140	1.332

[a] Because of large peak to peak separations for the first oxidation in this medium, the anodic potentials (E_a) are reported (see text).

Chemical oxidation of the macrocycles with bis(trifluoroacetoxy)iodobenzene (PIFA)[17] was monitored by UV−vis spectroscopy in CH$_2$Cl$_2$ in the presence and absence of added TFA. A 0.05 mM solution of macrocycle in dichloromethane was sequentially treated with portions of a 0.01 M solution of PIFA under nitrogen, and a representative set of spectra are provided for *p*-tolyl **4** in Figure 1. Solutions of the neutral materials displayed a single absorption band at 319 nm in dichloromethane. The addition of an oxidant produced overlapping absorptions for the mono- and dications of **4** and **6** at 435 and 900 nm, which are similar to those of related oxidized open chain oligomeric triarylamines with alternating *m*- and *p*-regiochemistry.[3] *p*-Anisyl **6** showed an additional band at 570 nm due to the presence of the conjugated but less symmetrical *p*-aminoanisole unit. Addition of excess PIFA to either **4** or **6** did not produce new absorptions for the tri- and tetracations; thus, an excess of PIFA will cleanly generate the dication. The oxidation of **4** in the presence of 1% TFA resulted in a similar set of spectra, with a slight shift in absorption maxima to 409 and 875 nm. As determined by ^{1}H NMR spectrometry, the intact, neutral macrocycle was regenerated by addition of hydrazine after oxidation of the macrocycles by PIFA in the presence of TFA. No change in the UV−vis spectrum of the 4-*tert*-butoxycarbonyl macrocycle **23** was observed upon addition of 1 equiv of PIFA.

Strong doublet EPR signals were observed at $g = 1.98$ at 20 K after addition of 1 equiv of PIFA to cyclophanes **4** and **6** in CH$_2$Cl$_2$/1% TFA. Analogous experiments with **23** were not conducted because a clear oxidation of **23** was not observed by UV−vis spectroscopy. Studies with macrocycle **5**, which has a potentially reactive *p*-position, may be complex and will be pursued in the future. When EPR spectra for the monocation radical of **4** were obtained after addition of 0.1 equiv of oxidant to a 0.2 mM solution of **4**, this dilute solution of $\mathbf{4}^{+\bullet}$ displayed nitrogen hyperfine splittings. Addition of 2 equiv of PIFA and then 1 vol % trifluoroacetic acid to **4** and **6** in dichloromethane produced samples that displayed a triplet resonance at $g = 1.98$ with peak separations of $2D' = 111 \pm 10$ G for **4** and 103 ± 10 G for **6**. A $\Delta M_S = 2$ half-field transition at $g = 4.02$ was also observed for each dication. The triplet signals were not observed in the absence of TFA. Nearly quantitative replacement of the doublet signal by that for a triplet dication was

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observed for macrocycle **6**. Lower conversion to the triplet dication was observed upon addition of a second equivalent of PIFA to macrocycle **4**, although the stability of the dication was high. After 2 h at room temperature, the same signal for $\mathbf{4}^{2+}$ with similar intensity was observed, indicating that the diradicals are stable at room temperature. Integration of the EPR signal ascribed to the triplet state of $\mathbf{6}^{2+}$ versus a standard sample of Fremy's salt[18] showed that roughly 90% of triplet $\mathbf{6}^{2+}$ was produced upon oxidation of **6** by 2 and 4 equiv of PIFA, followed by addition of TFA (Figure 2).

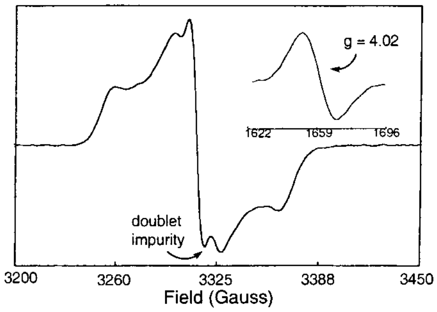

Figure 2. EPR spectrum of **6** at 20 K in CH_2Cl_2/1% TFA after addition of 2 equiv of PIFA.

Temperature-dependent EPR studies and magnetic susceptibility measurements were conducted on $\mathbf{6}^{2+}$ to evaluate further the multiplicity of the ground state. The intensity of the $g = 4$ signal displayed simple Curie behavior between 10 and 45 K, indicating a ground state triplet or nearly degenerate singlet and triplet states. Magnetic susceptibility was measured at 25 °C using the Evans method.[19,20] In methylene chloride without added TFA, the dication displayed a magnetic moment of 1.12 μ_B, suggesting that the singlet is the major species under these conditions, as was determined by EPR spectroscopy. However, the magnetic susceptibility was dependent on the amount of TFA added. The different concentrations of $\mathbf{6}^{2+}$ in the magnetic susceptibility and EPR experiments, the dependence of the triplet population on medium, and the potential dependence of solvent magnetic susceptibility upon addition of TFA make it difficult to correlate the two experiments. However, the μ_{eff} of a solution of **6** and 2 equiv of oxidant in a methylene chloride solution containing 10% TFA was 1.9 ± 0.2 μ_B, indicating that roughly 45% of **6** was converted to triplet $\mathbf{6}^{2+}$ and that the singlet and triplet states lie close to each other in energy. The ground state of dication diradicals is well known to depend on medium,[21,22] and previous observations of triplet triarylamine diradicals in the presence, but not absence, of TFA[3,23] led us to use these conditions in our EPR study.

The role of the acid in creating a triplet ground state remains unclear. However, we have shown that the TFA does not react irreversibly with the neutral macrocycles. ^{1}H NMR signals of neutral **4** are broad and then shifted in the presence of incrementally increasing amounts of added TFA, but the original spectrum for **4** is regenerated after addition of bicarbonate base.

Previous reports of diradicals generated from open chain analogues of **4**−**6** have included a distance between diradicals derived from EPR zero field splitting parameters.[3,24] This distance is difficult to interpret because a variety of conformations of the open chain materials are possible. In contrast, the cores of structures **4**−**6** are well defined. The dominant resonance contributors to the dication diradical of these materials are structures with the radical cations located at alternating nitrogens to maximize the distance between charges. Thus, the diagonal N−N distance of 7.45 Å found in the X-ray structure of **4** might correspond to the distance between the two radical sites in $\mathbf{4}^{2+}$. Indeed, a zero field splitting of 103 G for **4** provides a distance of 8.1 ± 0.3 Å between the two spins that create the triplet state. A splitting of 111 ± 10 G provides a distance of 7.9 ± 0.3 Å for that of **6**. The splitting was determined for **6** at different temperatures, and the value was temperature independent. The core structure is unlikely to be altered substantially upon oxidation, but the *N*-aryl groups are likely to carry some spin density, creating an effective distance between spins that is larger than simply the diagonal N−N distance. A more detailed analysis of the role of these groups on the electronic and magnetic properties of tetraazacyclophanes will be the subject of future studies, along with the use of our facile synthesis to prepare variants of these materials that adopt organized solution or solid phase structures.

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Supporting Information Available: Experimental procedures and spectroscopic and analytical data for **1**−**23**. X-ray diffraction data for **4**. Cyclic voltammetry and EPR data. This material is available free of charge via the Internet at http://pubs.acs.org.

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