Pergamon

*Tetrahedron Letters*, Vol. 38, No. 29, pp. 5123-5126, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01091-5

# Manipulation of the Reduction Potentials of Wurster's Blue Derivatives via Steric and Conformational Effects

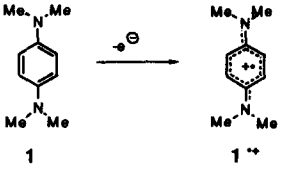
by Anthony J. Pearson* and Ann M. Gelormini

Department of Chemistry, Case Western Reserve University,

Cleveland, OH 44106-7078

***Abstract***: Using [$\eta^6$-cyclopentadienyliron]$^+$-mediated $S_NAr$ chemistry, a series of symmetrical and 2-alkyl tetra-alkyl-*p*-phenylenediamines have been prepared. The amine/amine$^{\bullet+}$ first redox couple has been determined for each member of the series and is influenced by remote steric, electronic, and conformational effects. © 1997 Elsevier Science Ltd.

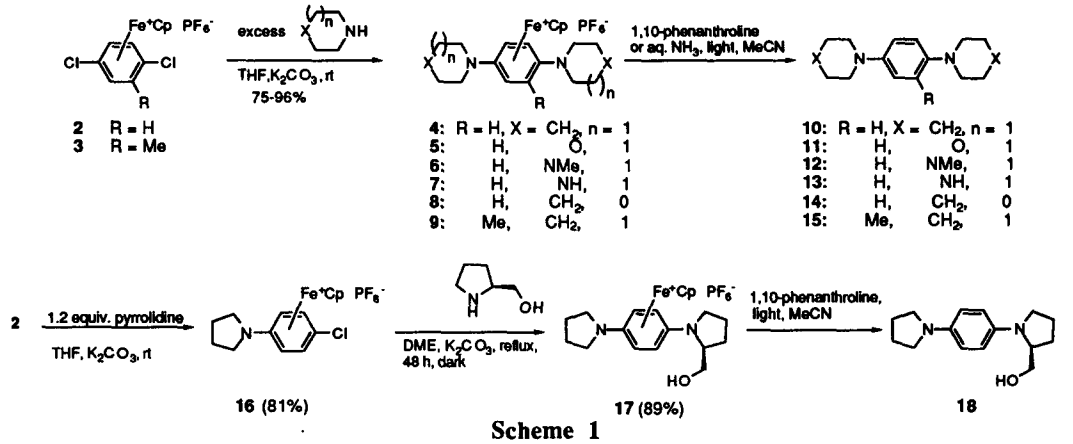
Since the late 19th century,[1-3] tetramethyl-p-phenylenediamine (TMPD, **1**) and its radical cation, Wurster's Blue, have been the subjects of many reports detailing various aspects of the chemistry of this redox couple. The ease of this oxidation was first noted by Wurster. Michaelis[4] later noted a qualitative increase in the reduction potential of 2-methyl-TMPD relative to the parent compound, however this difference was not then quantifiable. Contemporary investigations of this system include the preparation of derivatives which give a Wurster's Blue radical anion,[5,6] and the preparation of a dihydrazine derivative which gives evidence for localization of charge in the radical cation.[7]



**1** **1**$^{\bullet+}$

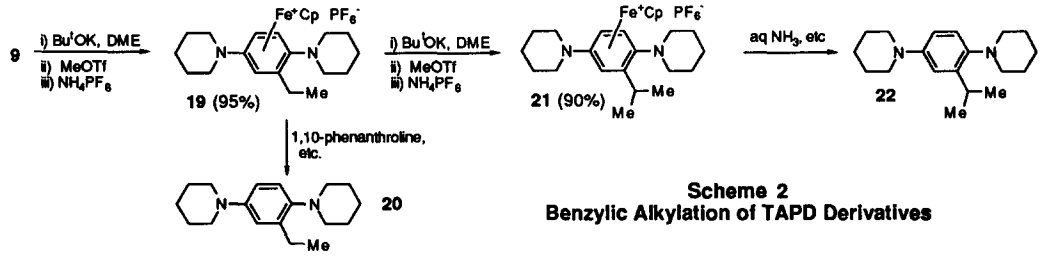
We have recently reported on the synthesis[8] and physical studies[9] of a series of covalently-linked donor-acceptor dyads and acceptor-donor-acceptor triads based on tetra-alkyl-p-phenylenediamines (TAPD) as the donor units. In the course of this work, we noted an attenuation of the first reduction potential of the phenylenediamines as a function of the remote substitution on the amine nucleophile.[8] The use of transition metal-mediated nucleophilic aromatic substitution in the construction of the donor and in subsequent manipulation of the device offers several advantages over conventional methods for the preparation of these derivatives, specifically: 1) The ease of performing sequential nucleophilic substitutions on *p*-dichlorobenzene-$Fe^+Cp$ $PF_6^-$, **2**, facilitates the preparation of unsymmetrical derivatives. 2) The acidity of benzylic protons of alkyl-substituted arene-metal complexes (e.g. **3**) provides another handle for functionalizing these complexes. 3) The $Fe^+Cp$ moiety is an effective protecting group for the reactive and oxidation-prone phenylenediamine. We now report that this methodology may be used to prepare tetra-alkyl-*p*-phenylenediamine (TAPD) derivatives where the first reduction potentials of these molecules are controlled as functions of both arene ring substitution and nucleophile ring size, thus providing a convenient route to the first examples of TAPD derivatives which are *more easily* oxidized than the parent TMPD (**Scheme 1**). The symmetrical derivatives **10**, **11**, **13**, and **14** have been previously reported,[10-14] however these earlier syntheses generally suffer from very low yields, and side reactions,[11,13,14] the need for very high temperatures and exotic equipment,[11] or the formation of isomer mixtures resulting from the presence of a benzyne intermediate.[12] Our study complements earlier work by the Nelsen group on manipulation of the reduction potentials and other physical properties of hydrazines, tetrazines,[15,16] and *o*-phenylenediamines[17] by remote steric and stereoelectronic effects.

We earlier reported that the bis-piperidine derivative **10** exhibited a reversible first oxidation at 192 mV vs NHE.[8] The difference between this and the known tetramethyl derivative **1** (121 mV)[18] was attributed to the more demanding steric environment in **10**, presumably resulting in a corresponding difficulty in attaining the requisite planarity of the diamine-radical cation. Similarly, steric inhibition of resonance can be invoked to explain the increased reduction potential of the ortho-methyl derivative **15**, and the corresponding ethyl and isopropyl derivatives **20** and **22**, as is summarized in the **Table**.




**Scheme 1**
**Preparation of TAPD Derivatives**

Compound **20** was prepared via benzylic alkylation of **9**, which may be performed by benzylic deprotonation with potassium tert-butoxide, followed by addition of 2 equiv. of methyl triflate. Although methyl iodide is the usual reagent in this reaction,[19] it is a very inefficient electrophile with these complexes, often requiring 10-fold (or larger) excesses. Compound **21** was prepared in an analogous sequence, from **19**.




**Scheme 2**
**Benzylic Alkylation of TAPD Derivatives**

The pyrrolidine and pyrrolidine/prolinol derivatives **14** and **18** exhibit first oxidations at 58 mV and 90 mV, respectively. This may be attributed to the greater availability of the nitrogen lone pairs in the 5 vs. 6-membered rings, a property which is reflected in the relative pKa's of the various amine substituents.[20-22] Also, the pyrrolidine derivatives suffer fewer eclipsing interactions on planarization and need to undergo much less conformational reorganization in order to attain planarity at the $R_2N$-$\phi$ dihederal than do the 6-membered ring derivatives. These contributions are, in some cases, predicted by Taft $\sigma^*$ parameters.[23] The inductive electron withdrawal by remote heteroatoms may also be used to manipulate the reduction potential of these derivatives, as is seen by comparing the bis-morpholine adduct **11**, with the bis-piperidine, N-methylpiperaz-

ine, and piperazine derivatives **10**, **12**, and **13**.[8] This effect again correlates with the pKa's of the amine substituents[20-22] and also manifests itself in the preparation of these derivatives: the bis-morpholine adduct requires much more vigorous conditions (excess morpholine and $K_2CO_3$, refluxing THF, darkened flask, 48 h) than the other derivatives (room temperature, overnight).

**Table**
**Summary of the Reduction Potentials of TAPD Derivatives as Functions of Steric and Conformational Influences**

| Compound | Yield | E1/2 (mV) vs NHE | pKa of Corresponding amine at 25 °C[21] |
|---|---|---|---|
| **14** | 17%* | 58 | pyrrolidine, 11.35 |
| **18** | 41% | 90 | pyrrolidine, 11.35<br>prolinol, 10.09[a] |
| **1** | N.App | 121[15] | dimethylamine, 10.7[b] |
| **10** | 51% | 192 | piperidine, 11.12 |
| **13** | 73% | 246 | piperazine, 10.20 |
| **12** | 67% | 299 | 1-Methylpiperazine, 9.85 |
| **15** | 53% | 351 | morpholine, 8.45 |
| **11** | 61% | 343 | piperidine |
| **20** | 50% | 365 | piperidine |
| **22** | 30%# | 377 | piperidine |

*This low yield is probably a consequence of the extreme oxidative instability of the product.
#Compound **22** is often obtained contaminated with traces of compound **20**,which is difficult to separate. Before separation, the yield, by NMR is *ca.* 60% . [a]From Ref. 22. [b]From Ref.20.

## Conclusions

We have illustrated that the position of the first redox couple of TMPD derivatives may be controlled over a range of 320 mV, as consequences of steric, remote electronic, and substituent conformational effects. Investigations employing this new latitude in the design of new electroactive systems are currently under investigation.

## Acknowledgements

We are grateful to the National Science Foundation (DMR91-22227) for financial support, and to Professor Fred L. Urbach and Shawn Swavey for invaluable help with the cyclic voltammetry experiments.

## Experimental

General considerations and procedures for $S_NAr$ reactions, demetalations, and electrochemical measurements may be found in reference 9.

**[[($\eta^5$-Cyclopentadienyl)($\eta^6$-(2,5-dipiperidino)-1-(2-propyl)benzene)]iron]$^+$ $PF_6^-$ (21).** A 0.05 mmol sample of complex **9** was stirred in 2 mL DME under Ar. To this was added 0.075 mmol of KO*t*-Bu (75 μL of a 1.0 M solution in THF), whereupon the mixture turned dark red. To this was added 0.15

mmol (25 mg, 17 μL) MeOTf. The mixture was stirred for 1 h and quenched by addition of 100 μL of saturated aqueous $NH_4PF_6$. The mixture was diluted to 10 mL with dichloromethane and washed with water (2 x 2 mL) and dried over $MgSO_4$. The solvent was removed and the residue was redissolved in a minimum of dichloromethane and added dropwise to 15 mL ether. The resulting precipitate was allowed to settle and the solvent was decanted. The precipitate was rinsed with ether and dried under high vacuum, giving **19** in 95% yield. $^1$H NMR δ 6.02 (1H, d, $J$ = 2.3 Hz), 5.92 (1H, d, $J$ = 2.3 Hz), 5.90 (1H, s), 5.02 (5H, s), 3.56 (4H, t, $J$ = 6.0 Hz), 3.10 (6H, m), 1.94-1.66 (12H, m), 1.46 (3H, t, $J$ = 7.5 Hz). $^{13}$C NMR δ 125.4, 120.8, 103.0, 75.9, 72.7, 67.8, 64.8, 54.4, 48.2, 26.9, 26.0, 24.9, 24.7, 24.1, 15.0. Compound **21** was obtained from **19** by an analogous procedure, using 2 equiv. KOt-Bu and 5 equiv. MeOTf. Yield: 90%. $^1$H NMR δ 6.20 (1H, d, $J$ = 7.2 Hz), 6.04 (1H, dd, $J$ = 6.2, 2.5 Hz), 5.91(1H, d, $J$ = 2.5 Hz), 5.15 (5H, s), 4-3 (9H, unresolved), 1.8-1.9 (12H, m), 1.62 (3H, d, $J$ = 7.0 Hz), 1.27 (3H, d, $J$ = 7.0 Hz). $^{13}$C NMR δ 124.9, 119.5, 105.0, 79.8, 75.1, 65.6, 63.6, 55.9, 48.1, 27.7, 27.1, 26.1, 25.3, 24.5, 24.0, 21.7.

## References and Notes


(1) Wurster, C.; Sendtner, R. *Ber. Dtsch. Chem. Ges.* **1879,** *12*, 1803-1807.

(2) Wurster, C.; Schobig, E. *Ber. Dtsch. Chem. Ges.* **1879,** *12*, 1807-1813.

(3) Wurster, C.; Morley, H. F. *Ber. Dtsch. Chem. Ges.* **1979,** *12*, 1814-1815.

(4) Michaelis, L.; Schubert, M. P.; Granick, S. *J. Am. Chem. Soc.* **1939,** *61*, 1981-1992.

(5) Bock, H.; Göbel, I.; Näther, C.; Havlas, Z.; Gacezzotti, A.; Filipini, G. *Angew. Chem. Int. Ed. Engl.* **1993,** *32*, 1755-1758.

(6) Bock, H.; Meuret, J.; C., N.; Krynitz, U. *Tetrahedron Lett.* **1993,** *47*, 7553-7556.

(7) Nelsen, S. F.; Ismagilov, R. F.; Powell, D. R. *J. Am. Chem. Soc.* **1996,** *118*, 6313-6314.

(8) Pearson, A. J.; Gelormini, A. M.; Fox, M. A.; Watkins, D. *J. Org. Chem.* **1996,** *61*, 1297-1305.

(9) Fossum, D.; Fox, M. A.; Gelormini, A. M.; Pearson, A. J. *J. Phys. Chem., A.* **1997,** *101*, in press.

(10) Axe, W. N.; Freeman, C. *J. Am. Chem. Soc.* **1934,** *56*, 478-479.

(11) Hargis, D. C.; Shubkin, R. L. *Tetrahedron Lett.* **1990,** *31*, 2991-2994.

(12) Moreau-Hochu, M. F.; Caubere, P. *Tetrahedron* **1977,** *33*, 955-959.

(13) Leonard, N. J.; Sauers, R. R. *J. Org. Chem.* **1956,** *21*, 1187-1188.

(14) Prelog, V.; Blazek, Z. *Collect. Czech. Chem. Commun.* **1934,** *6*, 211-224.

(15) Nelsen, S. F.; Peacock, V.; Weisman, G. R. *J. Am. Chem. Soc.* **1976,** *98*, 5269-5277.

(16) Nelsen, S. F. *Isr. J. Chem.* **1979,** *18*, 45-55.

(17) Nelsen, S. F.; Clennan, E. L.; Echegoyan, L.; Grezzo, L. A. *J. Org. Chem.* **1978,** *43*, 2621-2628.

(18) Nelsen, S. F.; Yunta, M. J. R. *J. Phys. Org. Chem.* **1994,** *7*, 55-62.

(19) Astruc, D.; Hamon, J.-R.; Althoff, G.; Román, E.; Batail, P.; Michaud, P.; Mariot, J.-P.; Varret, F.; Cazak, D. *J. Am. Chem. Soc.* **1979,** *101*, 5445-5447.

(20) *The CRC Handbook of Chemistry and Physics*; 50th ed.; Weast, R. C., Ed.; Chemical Rubber Company: Cleveland, 1969.

(21) Frenna, V.; Vivona, N.; Consiglio, G.; Spinelli, D. *J. Chem. Soc. Perkin Trans. II* **1985,** 1865-1868.

(22) Searles, S. J.; Rolelofs, G. E.; Tamres, M.; McDonald, R. N. *J. Org. Chem.* **1965,** *30*, 3443-3446.

(23) Taft, R. W. In *Steric Effects in Organic Chemistry*; M. S. Newman, Ed.; Wiley: New York, 1956; pp Chapter 13.


(*Received in USA* 1 *April* 1997; *revised* 23 *May* 1997; *accepted* 26 *May* 1997)