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Super-Electron Donors: Bis-pyridinylidene Formation by Base Treatment of Pyridinium Salts

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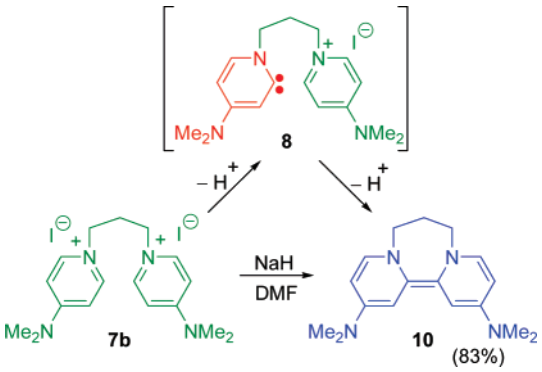
ABSTRACT



Deprotonation of bispyridinium salt 7b affords bispyridinylidene 10, a very powerful neutral organic two-electron donor [$E_{1/2}$ (DMF) = –1.13 V vs Ag/AgCl/KCl (sat)], presumably via the pyridinylidene 8. Donor 10 reduces aryl iodides and bromides to aryl anions in excellent yield and also reductively cleaves selected phenylalkylsulfones very efficiently.

Metal-based reducing agents dominate the field of electron-transfer reactions, particularly for thermodynamically difficult reductions such as Birch reductions,[1] acyloin condensations,[2,3] and reductions of aryl halides.[4] We recently questioned whether difficult reductions could alternatively be achieved by simple but powerful *neutral organic* electron donors, working under mild conditions in the ground state. If such reducing agents could be prepared, they could have significant attractions for use in synthetic chemistry in terms of selectivity, tolerance of other functional groups, tunability, ease of attachment to solid supports, and ease of regeneration.

With this in mind, we recently showed that compound **1** is the first neutral ground-state organic donor (super-electron donor, S.E.D.) to succeed in converting iodoarenes to aryl radicals by electron transfer.[4] More recently, we showed[5] that the more powerful donor **3**[6] is the first S.E.D. to convert haloarenes to aryl *anions*, following transfer of two electrons. Donor **3** undergoes reversible oxidation to **4** and then **5** at

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(2) Finley, K. T. *Chem. Rev.* **1964**, *64*, 573−589.
(3) Rühlmann, K. *Synthesis* **1971**, 236−253.
(4) Murphy, J. A.; Khan, T. A.; Zhou, S.-Z.; Thomson, D. W.; Mohan, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1356−1360.
(5) Murphy, J. A.; Zhou, S.-Z.; Thomson, D. W.; Schoenebeck, F.; Mohan, M.; Park, S. R.; Tuttle, T.; Berlouis, L. E. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5178−5183.

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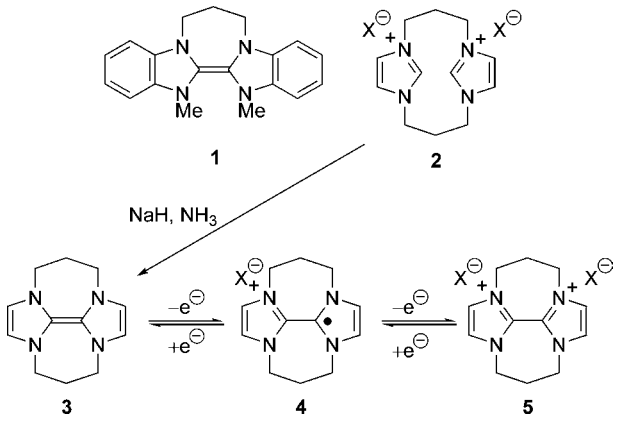
much more negative potentials than **1** [For **3**, $E_{1/2}$ (DMF) = −1.11 V vs Ag/AgCl/KCl (sat)] (Scheme 1).[7]

Scheme 1. Strong Donors **1** and **3**, Their Formation, and Their Reactivity



Although **3** is an excellent electron donor, development of more powerful bisimidazolylidene electron donors related to **3** would be nontrivial. To avoid isomeric mixtures of imidazole-derived donors, and thereby develop donors that can be precisely characterized, symmetrical 4,5-disubstituted imidazoles would be needed as synthetic precursors. However, the available range of such imidazoles is limited, and so the attractions of developing the bisimidazolylidene nucleus recede.

Accordingly, we set out to find alternatives to imidazoles as the basis of S.E.D. reagents that would be capable of reducing aryl halides and other difficult substrates; this paper announces our success in developing a new structural motif for that purpose through the same convenient deprotonation route routinely used for the preparation of bisimidazolylidenes and used above in the preparation of donor **3** from **2**.[5]

Our primary focus was on pyridine-based structures. In principle, bispyridinylidene **6**[8] might be formed through deprotonation of a bridged bispyridinium salt **7a**. However, the 2-position of pyridinium salts will be less acidic than the 2-position of imidazolium salts, and it was very possible that deprotonation would occur from the trimethylene bridge, to afford a benzylic anion, rather than from the 2-position of the ring. Such exocyclic deprotonations have literature precedent.[9] However, selective base-induced proton exchange in the 2-position of pyridinium salts has been shown under some conditions.[10] To make the proposed electron donor as electron-rich as possible, dimethylamino analogue **10** was selected for synthesis. This molecule has the advantage of four nitrogen atoms, each of which adds electron density to the π-system.

Diiodide **7b** was easily prepared from reaction of the easily available and economical 4-dimethylaminopyridine[11] with 1,3-diiodopropane. The crucial questions were (i) whether **7b** could be selectively deprotonated to afford a carbene **8** and (ii) whether such a carbene would undergo nucleophilic attack on the adjacent pyridinium ring, ultimately leading to **10**. (In this regard, our attempts to prepare **13** by deprotonation of bisimidazolium salt **12** had failed,[12,13] whereas deprotonation of **2** to form **3** had proceeded in high yield.[5] Clearly, in that case, the presence of *two* trimethylene bridges had been necessary to create the reactive alkene.)

To test our case, **7b** was now treated with NaH in liquid ammonia. Evaporation of the ammonia, followed by extraction with diethyl ether and solvent removal,[5] afforded air-sensitive bispyridinylidene **10** (83%) as a purple solid. ^{13}C NMR and ^{1}H NMR spectra supported its structural assignment with the central alkene carbons resonating at δ 116 ppm. It was further characterized by reaction with iodine to afford the diiodide **11**. Here, the NCH_2 protons show nonequivalence, and their diastereotopic nature must reflect the nonplanarity of the positively charged ring systems as the two rings twist to avoid interaction. This is analogous to the dication derived from **1**[4] but entirely different to the essentially planar dication **5** derived from **3**.[5]

Electrochemical characterization of **10** showed a single reversible two-electron peak at $E_{1/2}$ (DMF) = −1.13 V vs Ag/AgCl/KCl (sat), and hence this molecule is as strong a donor as compound **3**. However, whereas cyclic voltammetry of compound **3** showed two electron-transfer steps at almost identical potentials (a shoulder appears on the peak in both oxidative and reductive mode, implying that the loss of its second electron is only slightly more difficult than its first), compound **10** showed a clean, single two-electron peak, indicating that the loss of the second electron occurs at essentially the same potential as the first, under the conditions of the experiment (see Figure 1).[14]

(6) Literature measurements of the redox potentials of the bromide salt analogous to **3**, $E_{1/2}$ (MeCN)[7a] = −1.18 V and −1.37 V (ir) vs. S.C.E., where "ir" represents an irreversible step; $E_{1/2}$ (DMF)[7a] = −1.20 V vs. S.C.E.; and $E_{1/2}$ (MeCN)[7b] = −1.12 V and −1.28 V (ir) vs S.C.E.].

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(8) Alternative routes to bis-2-pyridinylidenes are known through reduction of pyridine-borane complexes and of 2,2-bipy salts: (a) Koester, R.; Bellut, H.; Ziegler, E. *Angew. Chem.* **1967**, *79*, 241−242. (b) Kuck, M. A.; Urry, G. *J. Am. Chem. Soc.* **1966**, *88*, 426−431. (c) Maeda, K.; Matsuyama, Y.; Isozaki, K.; Yamada, S.; Mori, Y. *J. Chem. Soc., Perkin Trans. 2* **1996**, 121−126. (d) Hünig, S.; Gross, J. *Tetrahedron Lett.* **1968**, *9*, 2599−2604.

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(13) The delicate balance between tetrazaalkenes and imidazolylidene precursors is seen in ref 7c. (See also Hahn, F. E.; Wittenbecher, L.; Le Van, D.; Fröhlich, R. *Angew. Chem., Int. Ed.* **2000**, *39*, 541−544).

(14) For a discussion of 2-electron transfer, see: Evans, D. H.; Hu, K. *J. Chem. Soc., Fraraday Trans.* **1996**, *92*, 3983−3990.

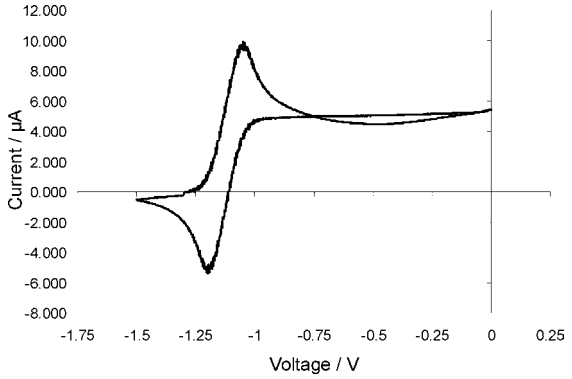
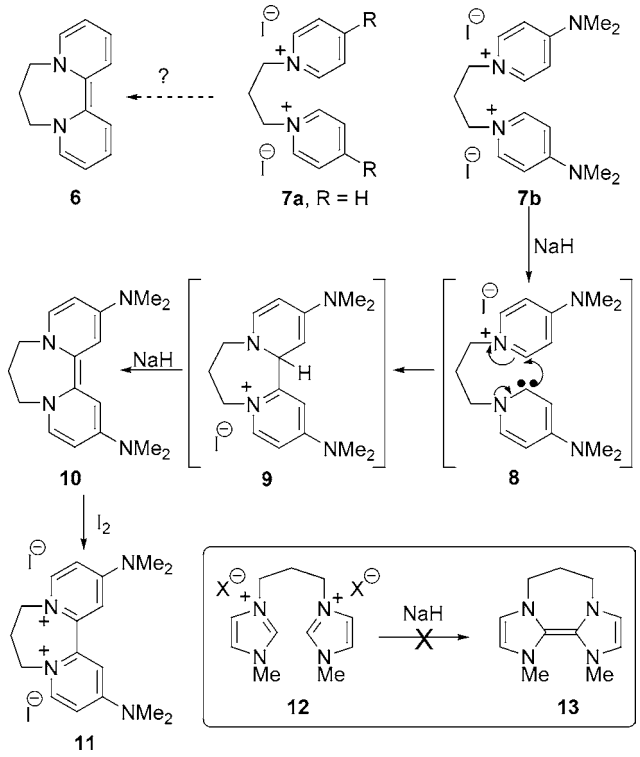


Figure 1. Cyclic voltammogram of donor **10**.

Bispyridinylidene **10** is the first bis-2-pyridinylidene to be reported by this deprotonation route.[8] The formation of **10** must feature initial deprotonation in the 2-position of pyridinium salt **7b** to form pyridinylidene **8** (Scheme 2).

Scheme 2. Formation and Reaction of Bispyridinylidene **10**

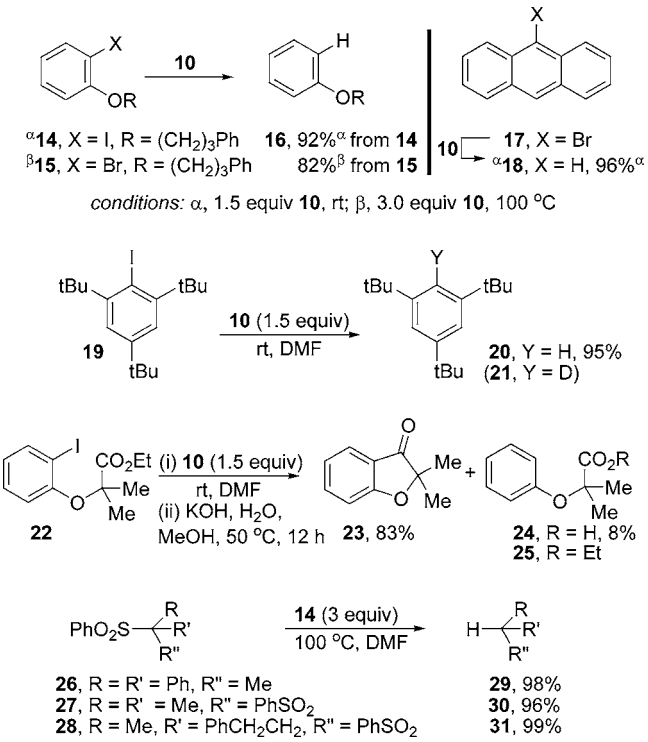


Assuming that the pathway to bispyridinylidene **10** is analogous to that seen in the formation of bisimidazolylidenes,[15] then subsequent nucleophilic attack on the remaining pyridinium salt would afford **9**, and this would be followed by deprotonation to give **10**.

Since the formation of **10** proceeded efficiently, it follows that carbene formation in this system is facile under these conditions. The ease of formation of carbenes from deprotonation of "unactivated" pyridinium salts has rarely been previously recognized; however, metal-bound pyridinylidines featuring a strategically placed extra functional group to activate the precursor pyridinium salt for proton removal have been formed in this way.[16−18]

We then explored the reactivity of donor **10** in dehalogenation reactions (Scheme 3). Aryl iodide **14** and 9-bromoanthracene **17** were reduced at room temperature (92% and 96% yields of **16** and **18**, respectively), whereas reduction of bromide **15** at 100 °C afforded **16** in 82% yield. These outcomes compare very favorably with the best current results with a neutral organic electron donor, namely **3**.[5]

Scheme 3. Reduction of Organic Substrates by Donor **10**



It is likely that these reductions proceed via aryl anion intermediates. Some evidence for this was found when donor **10** was reacted with the hindered iodide **19**. Clean reduction to **20** (95%) was effected at room temperature. When the reaction was repeated, this time with D_2O present in the reaction from the start, a mixture of **20** and the deuterated analogue **21** (1:4) was produced (94%). This regiospecific formation of the C−D bond is consistent with an aryl anion

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intermediate, but the experiment is also important in demonstrating the mildness of the reaction conditions, with aryl anion formation occurring in the presence of D_2O. To look for further evidence of aryl anion intermediates, donor **10** was then reacted with iodoester **22**. We have recently shown[5] that conversion of **22** and related substrates to cyclic ketones (here **23**) identifies the presence of aryl anions (as opposed to aryl radicals) as reaction intermediates. Here, the ketone **23** was formed together with the ester **25** as an inseparable mixture. Hydrolysis of the ester in the mixture afforded ketone **23** in an excellent 83% yield as well as acid **24** (8%). This shows that at least 83% yield of aryl anions was produced during the reaction that formed the indanone, and this is higher than any previous generation of aryl anions by donor **3**.

Finally, to give the donor **10** a very severe test, three sulfones **26**−**28** were reacted with **10**. Reductive cleavage in excellent yield (96−99%) was seen in each case. Reduction of sulfones is among the most difficult of organic reductions, and substrates such as **26**−**28** are routinely reduced with sodium metal.[19]

The bipyridinylidene, **10**, therefore proves to be a very strong electron donor. The preparation of **10** features the deprotonation of an "unactivated" pyridinium salt to form an *N*-heterocyclic carbene as an intermediate. The efficient preparation of donor **10** from 4-DMAP in two steps makes this the most conveniently prepared S.E.D. to date. The ease of deprotonation of the unactivated pyridinium salt **7b** opens the door not only to widespread studies on new S.E.D.s derived from deprotonation of pyridinium salts but also to the wider use of pyridinium-derived carbenes in chemistry.

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Supporting Information Available: Experimental details and spectral data for compounds. This material is available free of charge via the Internet at http://pubs.acs.org

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