
This version is available at https://strathprints.strath.ac.uk/46029/

Strathprints is designed to allow users to access the research output of the University of Strathclyde. Unless otherwise explicitly stated on the manuscript, Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Please check the manuscript for details of any other licences that may have been applied. You may not engage in further distribution of the material for any profitmaking activities or any commercial gain. You may freely distribute both the url (https://strathprints.strath.ac.uk/) and the content of this paper for research or private study, educational, or not-for-profit purposes without prior permission or charge.

Any correspondence concerning this service should be sent to the Strathprints administrator: strathprints@strath.ac.uk
A Novel Neutral Organic Electron Donor with Record Half-Wave Potential

Hardeep S. Farwaha\textsuperscript{a}, Goetz Bucher\textsuperscript{b} and John A. Murphy\textsuperscript{a}\textsuperscript{*}

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Tricyclic donor 26 has been prepared and is the most reducing neutral ground-state organic molecule known, with an oxidation potential 260 mV more negative than the previous record. Cyclic voltammetry shows that a 2-electron reversible redox process occurs in DMF as solvent at $-1.46 \text{ V vs. Ag/AgCl.}$

Introduction

The most challenging electron transfer reductions, such as Birch reductions,\textsuperscript{1} acyloin couplings\textsuperscript{2,3} and reduction of dinitrogen in nitrogenase enzymes,\textsuperscript{4} are achieved by reactive metals and their complexes.\textsuperscript{5} Recently, a number of organic electron donors have been synthesized that are very strong reducing agents (1-8). All of these compounds critically contain nitrogen atoms that are capable of stabilizing both positive charge and radical character, as the donors undergo oxidation. The aromaticity of their oxidation products (radical cations and dications) following loss of one and two electrons respectively, also plays an important role in determining the strength of these electron donors. Table 1 compares the oxidation potentials of these compounds with the widely used sulfur-containing electron donor, tetraethylnvalene (TTF).\textsuperscript{6}

Among the nitrogen-containing electron-donors, TDAE (1) is the parent compound in the series and the standard by which the others can be judged.\textsuperscript{7} Neither 1 nor its oxidized products is aromatic. Compound 2 could be considered anti-aromatic\textsuperscript{8} if planar and so its oxidation through loss of two electrons might expect to be strongly driven; however it is quite deformed from planarity and it contains two aromatic pyrrole rings -- as a result it is not a strong reducing agent. Compound 3\textsuperscript{9} is already aromatic and hence its oxidation does not benefit from aromatization as a driving force, and so it also is not a strong donor of electrons. In contrast, donors 4-8 are all converted into aromatic products upon oxidation\textsuperscript{10-19} and this adds to their strength as reducing agents. To illustrate the aromaticity that arises, the oxidation products of compound 8 are also shown in Figure 1. Loss of one electron leads to radical cation 13 featuring one pyridinium ring, while loss of a second electron affords the aromatic disalt 14. In terms of the applications of these stronger electron donors, benzimidazole-derived 6 converts iodoarenes into aryl radicals,\textsuperscript{15} while the stronger donors 7 and 8 reduce the same substrates to aryl anions.\textsuperscript{12,14} Donors 7 and 8 are also able to reduce arenesulfonamides,\textsuperscript{16} Weinreb amides\textsuperscript{17} and acyloin derivatives.\textsuperscript{18}

![Figure 1](link) Known neutral organic electron donors 1-8 and related compounds.
Table 1 Oxidation potentials of neutral organic electron donors.

<table>
<thead>
<tr>
<th>Compound</th>
<th>$E^1_{1/2}$</th>
<th>$E^2_{1/2}$</th>
<th>solvent</th>
<th>$E^1_{1/2}$ vs SCE (converted)</th>
<th>$E^2_{1/2}$ vs SCE (converted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTF$^a$</td>
<td>+0.37 V (SCE)</td>
<td>+0.67 V (SCE)</td>
<td>DCM</td>
<td>+0.37 V</td>
<td>+ 0.67 V</td>
</tr>
<tr>
<td>1$^b$</td>
<td>$-0.78$ V (SCE)</td>
<td>$-0.61$ V (SCE)</td>
<td>MeCN</td>
<td>$-0.78$ V</td>
<td>$-0.61$ V</td>
</tr>
<tr>
<td>2$^b$</td>
<td>$-0.59$ V (Fc/Fc')</td>
<td>$-0.26$ V (Fc/Fc')</td>
<td>THF</td>
<td>$-0.14$ V</td>
<td>+0.19 V</td>
</tr>
<tr>
<td>3$^b$</td>
<td>$-0.32$ V (SCE)</td>
<td>---</td>
<td>MeCN</td>
<td>$-0.32$ V</td>
<td>---</td>
</tr>
<tr>
<td>4$^{13}$</td>
<td>$-1.33$V (Fc/Fc')</td>
<td>$-1.14$V (Fc/Fc')</td>
<td>DMF</td>
<td>$-0.88$ V</td>
<td>$-0.69$ V</td>
</tr>
<tr>
<td>5$^{11}$</td>
<td>$-1.48$ V (Fc/Fc')</td>
<td>$-1.48$V (Fc/Fc')</td>
<td>THF</td>
<td>$-1.03$ V</td>
<td>$-1.03$ V</td>
</tr>
<tr>
<td>6$^{10}$</td>
<td>$-0.82$ V (SCE)</td>
<td>$-0.76$ V (SCE)</td>
<td>DMF</td>
<td>$-0.82$ V</td>
<td>$-0.76$ V</td>
</tr>
<tr>
<td>7$^{10}$</td>
<td>$-1.20$ V (SCE)</td>
<td>$-1.20$ V (SCE)</td>
<td>DMF</td>
<td>$-1.20$ V</td>
<td>$-1.20$ V</td>
</tr>
<tr>
<td>8$^{14, 19}$</td>
<td>$-1.69$ V (Fc/Fc')</td>
<td>$-1.69$ V (Fc/Fc')</td>
<td>DMF</td>
<td>$-1.24$ V</td>
<td>$-1.24$ V</td>
</tr>
</tbody>
</table>

5 Although these are highly reactive organic compounds, their reducing power is significantly less than that of the strongest metals (e.g. the oxidation potential of Li, $E^2 = -3.02$ V)\textsuperscript{20} and questions arise about whether a limit is being approached in the design of organic neutral donors.

10 Molecule 5a features a number of rings, all of which could become aromatic (5b) on loss of two electrons.\textsuperscript{11} However, if such a donor has a sufficient number of linked rings, the aromatic stabilization energy might ensure that the ground-state of 5a will instead be diradical 5c and then the oxidation to 5b by loss of two electrons would only convert the two terminal rings to aromatic rings. Whether 5 exists as 5a or 5c is not entirely settled. The compound did not afford a well-defined NMR spectrum that would characterize a closed-shell structure,\textsuperscript{11} indicating that it might be a diradical, although no EPR evidence for radical character was seen. The second indication of a reactivity limit related to the imidazole-derived compounds 7, 9-12. Although the doubly trimethylene-tethered compound 7 has been fully characterized, efforts to make simpler analogues of this compound, for example 9-11, had proved impossible.\textsuperscript{21, 22} Attempted preparations of compound 11 had instead led to dicarbone 12, possibly through spontaneous rupture of the central alkene to the dicarbone, but more likely through activation by a proton source or by a metal cation\textsuperscript{23} - the dicarbone 12 is not an electron donor. The instability of the tetraazafulvalene central double-bond was evident also from calculations that showed bond strength for molecule 10 of only 4 kJ mol\textsuperscript{-1}.\textsuperscript{23} In fact, compound 9 and 10 have recently been prepared in our laboratories,\textsuperscript{24} but have been shown to be very short-lived.

35 Results and Discussion

To probe whether more powerful donors could be prepared, it was therefore important to avoid compounds like 7 and 9-12. Compound 8 offered the best design lead. This compound was a purple solid and was stable in the absence of air and moisture.

8 Unlike imidazole-derived 7, which required both trimethylene bridges, it had been possible to synthesise some analogues of the pyridine-derived 8, including the compound 15 that features no trimethylene bridges. These compounds were, together with 7, the strongest neutral organic ground-state donors known. To enhance the donor strength, two possibilities were considered: (i) introduction of appropriately placed electron-releasing substituents on the pyridine-derived rings or (ii) extension of the polycyclic system by inclusion of more rings. We recently reported that our initial efforts to prepare analogues derived from 2-(dialkylamino)pyridines had led in an unexpected direction\textsuperscript{25, 26} but we now address both points in extending the polycyclic system.

The strategy for development of extended donors and more powerful donors involved using pyrrole-derived units. Interpolation of a pyrroldiylidene between the two pyridine-derived rings of donor 15 would result in 16.\textsuperscript{27-30} Here, five nitrogen atoms would stabilize the transition states and products of oxidation, and three rings would develop aromaticity in the

![Scheme 1 Proposed new electron donors 16.](image-url)
two-electron conversion to pyrrole-dipyridinium salt 18 (Scheme 1).

The synthesis of 16 was achieved as shown in scheme 2. Initially, the synthesis of diketone 22 directly from Weinreb amide 19 and 4-DMAP 20 was attempted using Fort’s direct deprotonation protocol, however this was unsuccessful. Kessar used N-trifluoroboration of pyridine to acidify the 2-position of the ring, and the resulting pyridinium ylid was used for C-C bond-formation. The same BF₃ adduct has also been utilized by Sammakia and Vedejs. The trifluoroborate salt was easily prepared (76% yield) from reaction of 20 with BF₃·Et₂O followed by filtration of the hygroscopic white solid. Formation of diketone 22 from lithiation of the BF₃ adduct was unsuccessful using LDA, n-BuLi or t-BuLi and so a lithium-halogen exchange using 2-bromo-4-DMAP 21 followed by addition of Weinreb amide 19 was attempted. The synthesis of 21 was successful and optimized by forming the trifluoroborate adduct in situ and using tetrabromomethane as the halogenation source, as opposed to bromine. A minor side-product 23 arose from nucleophilic attack by t-BuLi. From 22, formation of the central pyrrole ring to give compound 24 was efficient, as was the methylation of the pyridine rings to give dication 25 (79% and 96% yields respectively, scheme 2).

Scheme 2 Synthesis of new electron donor 26.

Cyclic voltammetry of compound 25 (figure 2 shows the voltammogram together with that of 14) revealed a reversible two-electron wave at $E_{1/2} = -1.46$ V vs. Ag/AgCl in DMF (equating to $-1.50$ V vs. SCE). This is 260 mV more negative than the half-wave potential for 8, and so compound 26 is now by far the most powerful neutral ground-state organic electron donor yet synthesized. Donor 26 was prepared by reduction of disalt 25 with sodium amalgam in DMF. The compound was then removed from the amalgam for analysis and to explore its reactivity.

**Figure 2** Comparison of cyclic voltammograms of 25 (purple) and 14 (green) vs. Ag/AgCl in DMF at 50 mV s⁻¹ scan rate.

Characterisation of 26 proved interesting. As previously seen for compound 5, this compound did not give a well resolved 'H NMR spectrum in DMF-d$_2$. Attempts to achieve a sharper spectrum by cooling, or by heating to 90 °C, were not successful, and so we sought further information at room temperature. To do this, ESR spectra were recorded and a weak signal detected that was consistent with an organic radical, but not with a triplet diradical. This species may be the radical cation 27 or may be another radical derived from 26. Quantitative ESR measurements undertaken using diphenylpicrylhydrazyl (DPPH) as a calibrant indicated that the radical concentration accounted for only 0.012% of the concentration of 26, and so this cannot be the cause of the broadness in the NMR spectrum. The alternative possibility of rotation about the inter-ring C=C bonds through a suitable low-energy triplet was also explored. A low energy triplet (M05-2X/cc-pVTZ: $\Delta U_{T,calc} = 11.0$ (12.9) kcal mol⁻¹, gas phase (DMF)) exists (see SI file); however since this is not observed in ESR, it could only be a conduit between configurational isomers about the inter-ring C=C bonds. However, the energies
of the configurational isomers are very high relative to 26, (density functional calculations using the B3LYP 6-31G* functional in a DMF continuum show that changing one of the inter-ring alkenes from E to Z affords the next most favourable isomer, but that is 23 kcal/mole higher in energy than 26) and accordingly, populations of minor isomers arising in this way are unlikely as the cause of the broad signals in the NMR spectrum.

The product of the oxidation of 26 by molecular iodine was characterized as the diiodide salt 25. Further characterization of donor 26 was achieved through performing the experiment quantitatively by using titration. The compound 26 was treated with excess iodine to afford 25; following this reaction, the unreacted residual iodine was then back-titrated with sodium thiosulfate. This titration showed that the donor had reacted with exactly one equivalent of iodine, in line with expectation for two-electron donor 26.

![Scheme 3](image)


The reactivity of 26 towards organic substrates was now tested. Donor 26 reduced Weinreb amide 28 (96% yield) using just 1.5 eq. of donor at room temperature (Scheme 3). Reduction of tosylamides 30, 32 and 34 was then carried out. Substrate 30 was of interest as 4-DMAP-based donor 8 had reduced substrate 30 with difficulty in 22% yield at 100 °C, and six equivalents of imidazole-based donor 7 had been required to reduce 32 in 96% yield at 110 °C. However, donor 26 now reduced 30 and 32 in 68% and 87% yield respectively, both times requiring only 3 equivalents of donor at 100 °C indicating that it is more efficient at performing difficult reductions. It has been previously established that the deprotection of these sulfonamides affords nitrogen anions and sulfinate anions. In this way, reaction of substrate 34 affords dianion 36, leading to isolated sulfonamide 35, on workup. Overall, pyrroldiyldiene donor 26 represents a new generation of highly electron-rich and purely organic reducing agents with a half-wave potential of ~1.5 V vs. SCE and the ability to carry out ever more challenging reductions.

Conclusions

A new powerful neutral organic electron donor 26 has been synthesized and is able to reduce appropriate tosylamides with greater efficiency than any previously synthesized neutral organic donor. With a half-wave potential of ~1.46 V vs. Ag/AgCl in DMF (equating to of ~1.5 V vs. SCE), it is the most reducing neutral organic species known.

Experimental Section

General: Proton NMR (1H) spectra were recorded at 500 MHz (on a Bruker® AV500™ spectrometer) or at 400.13 MHz (on a Bruker® DPX 400™ or Bruker® AV400™ spectrometer). Carbon NMR (13C) spectra were recorded at 125 MHz or 100 MHz using a J-mod pulse program to determine carbon assignments. Experiments were carried out using deuterated chloroform (CDCl3) unless otherwise stated and chemical shifts are reported in parts per million (ppm), calibrated on the solvent residual peak and referenced to tetramethylsilane. Coupling constants J are reported in Hertz (Hz). The following abbreviations are used for the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet.

High resolution mass spectra were recorded at the EPSRC National Mass Spectrometry Service Centre, Swansea on a JLZX 102™, VGZAB-™ or a VG™ micromass instrument.

Low resolution mass spectra were recorded at the University of Strathclyde Mass Spectrometry Service on a ThermoFinnigan™ PolarisQ Ion Trap Spectrometer and trace GC instrument using a ZB-5 column (30 metres).

Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR™ spectrometer as films applied on sodium chloride plates or mixed and pressed into potassium bromide disks. Melting points were recorded using either a Griffin or a Gallenkamp melting point apparatus.

Column chromatographies on silica gel were performed using Prolabo 35-75 µm particle sized silica gel 60 (200-400 mesh). Crude mixtures were studied using thin layer chromatography (TLC) carried out on Merck silica gel 60 F254 precoated aluminium plates. Visualization was achieved under UVP mineralight UVG-11 lamp or by developing plates with methanolic vanillin or potassium permanganate. Concentration of solutions under reduced pressure (1-10 mbar) was achieved using a diaphragm pump vacuum. Drying of solids under reduced pressure was performed at room conditions.
temperature firstly under 1-10 mbar using a diaphragm pump vacuum then under 0.001-0.01 mbar using a rotary oil pump. All reagents were obtained from commercial suppliers and used without further purification unless stated otherwise. Tetrahydrofuran, dichloromethane, hexane, diethyl ether and toluene were dried and deoxygenated with a Pure-Solv 400 solvent purification system (by Innovative Technology Inc., USA). n-BuLi was obtained as a 2.5 M solution in hexane and t-BuLi as a 1.7 solution in hexane. Titration of both reagents, prior to use, was achieved by dropwise addition of either reagent solution _via_ syringe to a solution of diphenylacetic acid (1 mmol) in THF (10 mL) under argon. Addition was stopped with the first appearance of a yellow colour (diphenylacetate dianion) and the volume of lihatiating reagent was measured. The procedure was carried out _in triplicate_ so that an average concentration could be calculated for each reagent. _N,N_-Dimethylformamide was obtained from commercial suppliers as anhydrous (99.98%) and used directly. Sodium hydride was dried and deoxygenated with a Pure-Solv 400 solvent purification system (by Innovative Technology Inc., 2002). This was further verified by inspecting the flask for traces of organic phase was washed with water (2 x 50 mL) to remove traces of toluene were dried and deoxygenated with a Pure-Solv 400 solvent purification system (by Innovative Technology Inc., 2002). Sodium amalgam was prepared by addition of freshly cut sodium (50 mg) to a flame-dried 25 mL round bottom flask containing anhydrous DMF (15 mL) followed by pyrrole-based diiodide salt mercury (5 g) under a strong flow of argon. To this was added 2-bromo-4-dimethylaminopyridine 21

45 Preparation of _N,N’_-dimethoxy- _N,N’_-dimethylsucinamide 19:

Potassium hydroxide (50.95 g, 908 mmol, 6 eq.) was added to a solution of _N,O_-dimethyldihydroxylamine hydrochloride (59.05 g, 605 mmol, 4 eq.) in water (150 mL) slowly at 0 °C with vigorous stirring. The free amine was distilled from the solution at 42 °C and added _via_ dropping funnel to a solution of succinyl chloride (16.6 mL, 151 mmol, 1 eq.) in dry DCM (300 mL) under argon at -10 °C with vigorous stirring. The reaction mixture was brought to room temperature and left stirring under argon atmosphere for 16 h. The reaction mixture was concentrated under reduced pressure to 100 mL, washed with 0.5M hydrochloric acid (5 x 50 mL), NaHCO₃ (3 x 50 mL), brine (50 mL) and dried over Na₂SO₄. The crude solution was concentrated under reduced pressure and purified by column chromatography (firstly with neat EtOAc to remove less polar impurities then 20% MeOH/EtOAc) to afford _N,N’_-dimethoxy- _N,N’_-dimethylsuccinamide 19 (20.1 g, 65%) as a clear oil, which crystallised on standing to give white crystals; m.p. 73-75 °C (lit. 73-75 °C); [Found: (ESI⁺) (M+H)+] 205.1183, C₂H₁₂N₂O₂ (MH) requires 205.1183); νmax (film/cm⁻¹) 3493, 2963, 2942, 2830, 1731, 1660, 1460, 1422, 1390, 1194, 1097, 994, 934, 795, 745; 1H-NMR (500 MHz, CDCl₃) δ 2.78 (4H, s, CH₂), 3.12 (6H, s, OCH₃), 3.74 (6H, s, OCH₃); 13C-NMR (125 MHz, CDCl₃) δ 25.9 (CH₃), 31.1 (NCH₂), 60.7 (OCH₃), 172.9 (C); m/z (ESI⁺) 205 ([M⁺H]+, 100%), 239 (21), 357 (51), 515 (2).

46 Preparation of 2-bromo-4-dimethylaminopyridine 21 (a) preparation of 4-dimethylaminopyridinium trifluoroborate:

To a solution of 4-dimethylaminopyridine (4.89g, 40 mmol, 1 eq.) in a 1:1 mixture of dry THF (50 mL) and Et₂O (50 mL) was added boron trifluoride diethyl etherate (6.01 mL, 48.9 mmol, 1.22 eq.) in dry THF (100 mL) was added dropwise. The white suspension was stirred at room temperature for 3 h and the precipitate was filtered via a sinter funnel. The white solid was dissolved in DCM (100 mL), washed with water (2 x 50 mL), brine (50 mL), dried over Na₂SO₄ and concentrated under reduced pressure to afford 4-dimethylaminopyridinium trifluoro borate (5.80 g, 76%) as a white solid; m.p: 128-130 °C (lit. 129.8-130.9 °C); [Found: (ESI⁺) (M+Na)+] 208.1227, [M+NH₄]+ 213.0086; [M+Na]⁺ 208.12277; νmax (KBr)/cm⁻¹ 2939, 1646, 1568, 1404, 1113, 914; 1H-NMR (400 MHz, CDCl₃) δ 3.18 (6H, s, NCH₃), 6.64 (2H, s, J = 7.3 Hz, ArH), 8.03 (2H, d, J = 7.3 Hz, ArH); 13C-NMR (125 MHz, CDCl₃) δ 40.0 (CH₂), 106.3 (CH), 142.2 (CH), 156.9 (C); 19F-NMR (125 MHz, CDCl₃) δ 152.07-152.18 (BF₂); m/z (ESI⁺) 207 ([M+NH₄]+, 24 %), 213 ([M+Na]⁺, 68), 231 (13).

(b) preparation of 2-bromo-4-dimethylaminopyridine 21:

To a solution of 4-dimethylaminopyridine (25.45 g, 208 mmol, 1 eq.) in dry THF (300 mL) at room temperature was added freshly purchased boron trifluoro diethyl etherate (30.9 mL, 250 mmol, 1.2 eq.) and solution was stirred for 30 min before cooling to -78 °C under vigorous flow of argon. n-BuLi in hexane (100 mL, 250 mmol, 1.2 eq.) was added dropwise under argon to the cream coloured suspension, keeping the temperature below -70 °C. After 30 min, a solution of carbon tetrabromide (82.91 g, 250 mmol, 1.2 eq.) in dry THF (100 mL) was added dropwise _via_ cannula.
under argon (again keeping temperature below -70 °C) and the dark brown reaction mixture was left to warm to room temperature overnight. THF was removed under reduced pressure and the residue was partitioned between DCM (250 mL) and sat. NaHCO₃aq (100 mL). The organic layer was washed with sat. NaHCO₃aq (2 x 100 mL), brine (100 mL) and dried over Na₂SO₄. The crude solution was concentrated under reduced pressure and purified by column chromatography (10-30% EtOAc/Hexane) to afford 2-bromo-4-dimethylaminopyridine 21 (30.59 g, 75%) as an orange semi-solid; [Found: (ESI⁺) (M⁺) 32.0 (CH), 109.2 (CH), 149.1 (CH), 153.7 (C), 155.1 (C), 201.6 (C); 1H-NMR (500 MHz, CDCl₃) δ 2.99 (6H, s, NCH₃) 6.43 (1H, dd, J = 2.5 Hz, 6 Hz, ArH); 6.63 (1H, d, J = 2.5Hz, ArH); 7.93 (1H, d, J = 6 Hz, ArH); 11-C-NMR (125 MHz, CDCl₃) δ 39.5 (NCH₃), 106.4 (CH), 109.4 (CH), 143.2 (C), 149.5 (CH), 156.0 (C); m/z (CT) 202 ([M⁺]+), 73%); 263 ([M+H]⁺, 63%), 204 ([M+H]+, 81%); 123 (100%). Data were consistent with precedent. 42

Preparation of 1,4-bis-(4-dimethylamino-2-pyridyl)butane-1,4-dione 22, with 1-(4-dimethylamino-2-pyridyl)-5,5-dimethylhexane-1,4-dione 23 as by-product.

To a solution of 2-bromo-4-dimethylaminopyridine 21 (300 mg, 1.49 mmol, 2.05 eq.) in dry THF (20 mL) at -78 °C under argon was added t-BuLi (2.01 mL, 3.02 mmol, 4.15 eq.) dropwise using argon pressure. The reaction was stirred for 60 min and a solution of N,N-dimethoxy-N,N-dimethylsucinimide (149 mg, 0.73 mmol, 1 eq.) in THF (10 mL) was added dropwise using argon pressure. The reaction was then left to warm to room temperature overnight. After quenching the reaction by dropwise addition of water (5 mL), THF was removed under reduced pressure. The red residue was dissolved in DCM (40 mL) and washed with water (2 x 20 mL), sat. NaHCO₃aq (1 x 20 mL), brine (1 x 20 mL) and dried over Na₂SO₄. The crude solution was concentrated under reduced pressure and purified by column chromatography (1% Et₂N/EtOAc). Since the product is insoluble in EtOAc, the crude material was washed with EtOAc in a sinter funnel to remove unreacted 4-dimethylaminopyridine. The yellow solid was then dried under reduced pressure to afford 1,4-bis-(4-dimethylamino-2-pyridyl)-butane-1,4-dione 22 (5.3 g, 49%) as a yellow powder; m.p. 165-167 °C; [Found: (EI⁺) (M⁺) 19,24,302,1692,1600,1509,1432,1377,1226,985,810,1H-NMR (400 MHz, CDCl₃) δ 3.04 (12H, s, NCH₃), 3.64 (4H, s, CH₂), 6.63 (2H, dd, J = 2.5 Hz, 6 Hz, ArH), 7.31 (2H, d, J = 2.5 Hz, ArH), 8.31 (2H, d, J = 6 Hz, ArH); 11-C-NMR (125 MHz, CDCl₃) δ 32.5 (CH₂), 39.2 (NCH₃), 104.9 (CH), 109.2 (CH), 149.1 (CH), 153.7 (C), 155.1 (C), 201.6 (C); m/z (EI⁺) 326 (M⁺), 100%, 327 (21), 328 (5).

1-(4-Dimethylamino-2-pyridyl)-5,5-dimethylhexane-1,4-dione 23 (623 mg, 6.5%) was also separately isolated as a yellow oil [Found: (ESI⁺) (M⁺) 263.1754; C₁₅H₁₇N₂O₂ requires MH, 263.1754]; [Found: (ESI⁻) (M⁻) 246 (16), 265 (5).

Preparation of N-ethyl-2,5-bis-(4-dimethylamino-2-pyridyl)-pyrrole 24:

To a solution of 1,4-bis-(4-dimethylamino-2-pyridyl)butane-1,4-dione 22 (1.56 g, 4.79 mmol, 1 eq.) in methanol (10 mL) was added freshly distilled ethylamine (aq) 20 mL). The reaction was stirred at room temperature overnight and concentrated under reduced pressure. The residue was purified by column chromatography (EtOAc to 2% Et₂N/EtOAc) and washed in a sinter funnel with diethyl ether to remove further impurities to afford N-ethyl-2,5-bis-(4-dimethylamino-2-pyridyl)pyrrole 24 (1.26 g, 79%) as a light brown semi-solid; [Found: (ESI⁺) (M⁺) 336.2183; C₁₅H₁₉N₃ requires MH, 336.2183]; [Found: (ESI⁻) (M⁻) 263.1754; C₁₅H₁₉N₃ requires MH, 263.1754].

EPR measurements:

Deoxygenated dry DMF (15 mL) was added under a flow of argon to an oven-dried 25 mL round-bottom flask containing sodium amalgam (prepared from 50 mg of sodium in 5 g of mercury) and the donor precursor diiodide salt (69.7 mg, 0.113 mmol, 1 eq). The deep purple reaction mixture was stirred at room temperature under fast argon flow for 3 h. Three test aliquots of this 0.0075 M solution were transferred into an oven dried syringe needle and the centre of a freshly created stream of this air-sensitive solution was immediately drawn from inside the tip of the syringe needle into a 1 mm diameter glass capillary (with a sample height of around 5 cm) before being sealed at the open end by flame-gun. This was repeated a fourth time until there was great confidence that no oxygen was present in the sample solution (which maintained a deep purple colour). ESR data were then obtained for this sample, which showed a signal with g-factor 2.0035.

To an oven-dried 25 mL round bottom flask containing diphenylpicrylhydrazyl (DPPH, 44.5 mg, 0.113 mmol, 1 eq.) was added deoxygenated dry DMF (15 mL) and a sample of this 0.0075 M solution was transferred into a 1 mm capillary in an identical manner to that mentioned above so that a reference ESR signal could be obtained (g-factor 2.0035). Comparison of the signal intensities indicated a concentration of 9 x 10⁻⁷ M, corresponding to 0.012 M conversion of the donor to the radical cation within that solution.

Preparation of N-ethyl-2,5-bis-(N'-methyl-4-dimethylamino-2-pyridinium iodide)pyrrole 25:

Methyl iodide (12 mL, 192 mmol, 15 eq.) was added dropwise to a solution of N-ethyl-2,5-bis-(4-dimethylamino-2-pyridyl)pyrrole 24 (4.30 g, 12.8 mmol, 1 eq.) in acetonitrile (80 mL) under argon. The solution was refluxed and the suspension formed was left stirring overnight. The suspension was cooled to room temperature, diethyl ether (100 mL) was added and the solid was filtered via suction and washed with diethyl ether several times to afford N-ethyl-2,5-bis-(N'-methyl-4-dimethylamino-2-pyridinium iodide)pyrrole 25.
Preparation of N-methyl-1-naphthamide 29:

The general procedure for electron transfer reactions was applied to N-methoxy-N-methyl-1-naphthamide (116 mg, 0.54 mmol, 1 eq.) using pyrrole salt (500 mg, 0.81 mmol, 1.5 eq.). The reaction was stirred at room temperature and the crude material was purified by column chromatography (5% EtOAc/DCM) to give N-methyl-1-naphthamide 29 (102 mg, 96%) as a white crystalline solid. m. p. 159 – 161 °C (lit.15: 159 – 160 °C). 1H-NMR (500 MHz, CDCl₃) δ 3.08 (3H, d, J = 4.9 Hz, CH₃), 6.05 (1H, bs, NH), 7.42-7.47 (1H, m, ArH), 7.51-7.60 (3H, m, ArH), 7.85-7.92 (2H, m, ArH), 8.29-8.31 (1H, m, ArH); 13C-NMR (125 MHz, CDCl₃) δ 26.8 (CH₃), 124.7 (CH), 124.9 (CH), 125.5 (CH), 126.4 (CH), 127.1 (CH), 128.3 (CH), 130.1 (C), 130.5 (CH), 133.7 (C), 134.7 (C), 170.3 (C).

Preparation of N-phenyl-N-benzyl-4-methylbenzenesulfonamide 30:

An oven-dried flask containing N-phenylalanine (2.01 g, 11.0 mmol, 1 eq.) and NaH (60 % dispersed in mineral oil, 526 mg, 13.2 mmol, 1.2 eq.) under flow of argon, was washed with dry hexane (3 x 20 mL) prior to addition of dry THF (100 mL). To this was added a solution of tosyl chloride (2.10 g, 11.0 mmol, 1 eq.) in THF (30 mL). Solution was stirred at room temperature overnight. THF was removed under reduced pressure and partitioned between EtOAc and 1M HClaq. The organic phase was washed with NaHCO₃aq (1 x 100 mL), brine (1 x 100 mL) and dried over Na₂SO₄. The crude solution was concentrated under reduced pressure and recrystallised in DCM/Hexane to afford N-phenyl-N-benzyl-4-methylbenzenesulfonamide 30 (3.38 g, 91%) as a white solid; m.p. 138-140 °C (lit.15; 139-140 °C); 1H-NMR (500 MHz, CDCl₃) δ 2.45 (3H, s, CH₃), 4.73 (2H, s, CH₂), 4.98-7.00 (2H, m, ArH), 7.20-7.23 (8H, m, ArH), 7.27-7.29 (2H, m, ArH), 7.55-7.56 (2H, m, ArH); 13C-NMR (125 MHz, CDCl₃) δ 21.2 (CH₂), 54.7 (CH₂), 127.6 (CH), 127.8 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 129.0 (CH), 129.5 (CH), 135.7 (C), 136.0 (C), 139.0 (C), 143.5 (C). Data were consistent with those previously published.16

Preparation of N-benzylalanine 31:

The general procedure for electron transfer reactions was applied to N-benzylalanine (90.8 mg, 0.27 mmol, 1 eq.) using pyrrole salt 25 (500 mg, 0.81 mmol, 3 eq.). The reaction was heated to 100 °C and the crude material was purified by column chromatography (20% EtOAc/Pet. Ether) to give N-benzylalanine 31 (33 mg, 68%) as a white solid; m. p. 35-37 °C (lit.35; 35-38 °C); 1H-NMR (500 MHz, CDCl₃) δ 4.08 (1H, t, J = 7 Hz, ArH), 7.12-7.21 (2H, m, ArH), 6.74 (1H, ArH), 7.30-7.36 (1H, m, ArH). This journal is © The Royal Society of Chemistry [year].
Preparation of 3-(2-(p-toluenesulfonylamo)ethyl)indole 35:

The general procedure for electron transfer reactions was applied to N,N,N-tris(toluenesulfonyl)tryptamine 34 (200 mg, 0.30 mmol, 1 eq.) using pyrrole salt 25 (748 mg, 1.20 mmol, 4 eq.). The reaction was heated to 100 °C and the crude material was purified by column chromatography (30 % EtOAc/hexane) to give 3-(2-(p-toluenesulfonylamo)ethyl)indole 35 (89 mg, 94%) as a clear oil. 1H-NMR (500 MHz, CDCl3) δ 2.41 (3H, s, CH3), 2.94 (2H, t, J = 6.4 Hz, CH2), 3.28 (2H, q, J = 6.4 Hz, CH2), 4.50 (1H, t, J = 6.4 Hz, NH), 6.97 (1H, ArH), 7.06 (1H, J = 7.8 Hz, ArH), 7.18-7.23 (3H, m, ArH), 7.38 (1H, d, J = 8 Hz, ArH), 7.43 (1H, d, J = 8 Hz, ArH), 7.64 (2H, d, J = 8 Hz, ArH), 8.09 (1H, brs, ArNH); 13C-NMR (125 MHz, CDCl3) δ 21.5 (CH3), 25.5 (CH2), 43.1 (NCH3), 111.3 (CH), 111.6 (C), 118.5 (CH), 119.5 (CH), 122.3 (CH), 122.4 (CH), 126.9 (C), 127.0 (CH), 129.6 (CH), 136.4 (C), 136.8 (C), 143.3 (C). Data were consistent with those published in literature.13

Acknowledgements. We thank Professor John C. Walton and Dr. Michael J. Corr for EPR measurements (St. Andrews University), and we thank University of Strathclyde, Scottish Funding Council and BAE Systems for a SPIRIT studentship to HSF. Mass spectrometry data were acquired at the EPSRC UK National Mass Spectrometry Facility at Swansea University.

Notes and references

† Electronic Supplementary Information (ESI) available: computational coordinates and NMR spectra are provided. See DOI: 10.1039/b000000x/