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Controlling electron delocalisation in constrained *N*,*N*′-dimethyl-4,4′-bipyridinium dications

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Abstract—The synthesis is described of two *N*,*N*′-dimethyl-4,4′-bipyridinium salts for which the two pyridinium rings are connected via varying length alkoxy chains attached at the 3,3′-locations.

In the field of electron transfer, one of the most ubiquitous electron acceptors is *N*,*N*′-dimethyl-4,4′-bipyridinium cation (Fig. 1), commonly referred to as methyl viologen (MV^{2+}) or paraquat.[1] There occurs, upon one-electron reduction of this electron acceptor, a significant alteration in dihedral angle between the two pyridinium rings. This structural change can be attributed to increased double-bond character in the connecting C–C bond after one-electron reduction, since in the dicationic form the two pyridinium rings are almost orthogonal.[2] Electronic coupling between the two rings is readily evident in the cyclic voltammetry of MV^{2+}, which displays two well-separated fully reversible one-electron reduction waves.[3] To what extent the dihedral angle change plays on this intra-ring communication is not clear, but it is probably complicated by quantum mechanical tunnelling and thermal fluctuations around the C–C connector bond. In an attempt to unravel the effect of these processes, we envisaged a strategy of controlling the dihedral angle by synthetic means, and in the first instance looking to see what effect this had on the electrochemical behaviour. The first of our synthetic targets, in which the two pyridinium rings are connected via alkoxy constraining straps, are reported herein (Fig. 1).

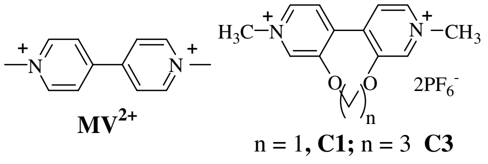

Figure 1. Illustrations of methyl viologen dication and alkoxy constrained analogues.

Despite the widespread use of MV^{2+}, examples of 3,3′-difunctionalised derivatives are quite rare. Some years ago, Sleegers and Dehmlow[4] prepared 3,3′-dimethoxy-4,4′-bipyridine by the self-coupling of 3-methoxypyridine. This compound was used to synthesise the hydroxy version by demethylation using relatively harsh conditions. To the best of our knowledge, no linked systems have been made from this precursor. Also, the methylated versions of these two compounds were not reported. Our initial plan was to follow the outlined literature procedure, but to connect the two oxygens together using standard coupling procedures. It soon became apparant, however that an improved strategy was required for producing the required 4,4′-bipyridinyl-3,3′-diol. In recent years, Suzuki coupling[5] has found wide application in C–C coupling of aromatics, and so we considered taking advantage of this attractive chemistry. Outlined in Scheme 1 is the synthetic approach we developed to prepare 4,4′-bipyridinyl-3,3′-diol and its strapped derivatives.

In order to avoid harsh deprotection procedures, the commercially available pyridin-3-ol was used as starting material, and carbamoyl was identified as a suitable protecting group. Thus, compounds **2** and **3** were prepared by literature methods.[6,7] Selective lithiation of the

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Keywords: Methyl viologen; Electrochemistry; Dihedral angle; Electron delocalisation.

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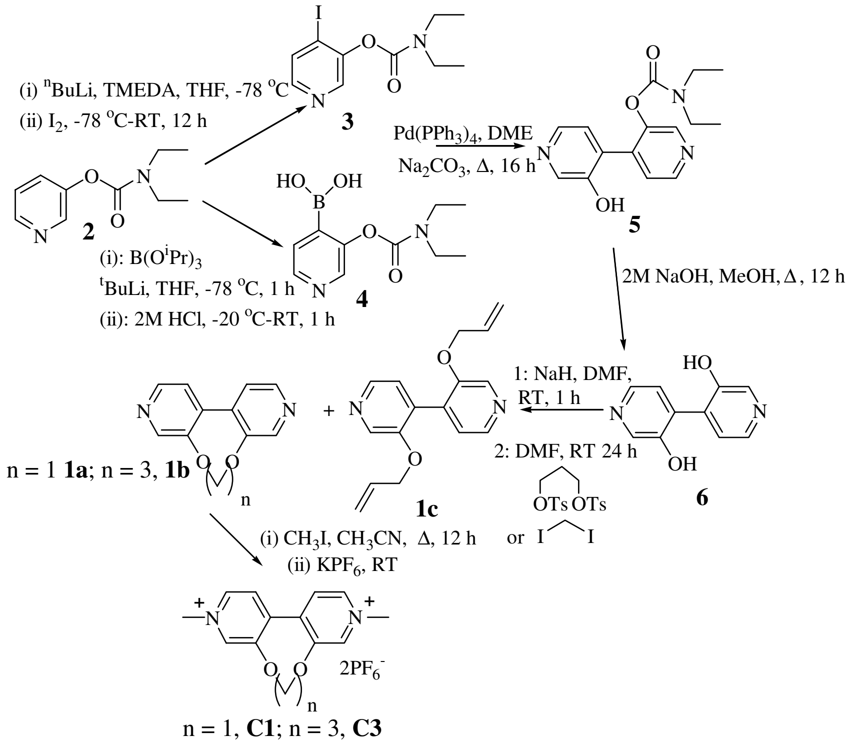

Scheme 1. Methods used in the preparation of the strapped methyl viologen derivatives.

4-position in **2** and subsequent reaction with $B(O^iPr)_3$ followed by hydrolysis gave **4** in 65% yield. Interestingly, cross-coupling of **3** and **4** using standard Suzuki coupling[5] conditions and workup afforded the monoprotected derivative **5**, instead of the expected diprotected product. It would seem that the basic reaction conditions selectively remove one of the carbamoyl protecting groups. The final carbamoyl group was readily removed from **5** using NaOH to afford **6** in 75% yield. Cyclisation reactions using **6** were performed by mild deprotonation of the hydroxy groups using NaH in DMF, followed by slow addition, carried out over several hours, of either diiodomethane or 1,3-propandiol di-tosylate. The non-optimised yields of **1a** and **1b** were rather low (9–13%). The low yield of **1b** can be attributed to generation of the isolated diallyl derivative side-product **1c**; this latter material originates from HOTs elimination of doubly alkylated material. A further complication of the cyclisation reaction that probably makes an important contribution to poor yields, is N-alkylation of the pyridine units. Simple methylation of **1a** and **1b** with methyl iodide followed by anion exchange with hexafluorophosphate afforded the desired MV^{2+} analogues **C1**[8] and **C3**[9] as white solids. All compounds afforded analytical data consistent with the structures.

The electrochemical behaviour of **C1** and **C3** was investigated by cyclic voltammetry in acetonitrile (0.1 M *n*-tetrabutylammonium tetrafluoroborate background electrolyte) at a glassy carbon working electrode. As shown in Figure 2, the reductive electrochemistry of the two compounds is dominated by two well-separated one-electron[10] electrochemically reversible waves, and a general appearance similar to that found for MV^{2+}. The first real noticeable difference between **C3** and MV^{2+}

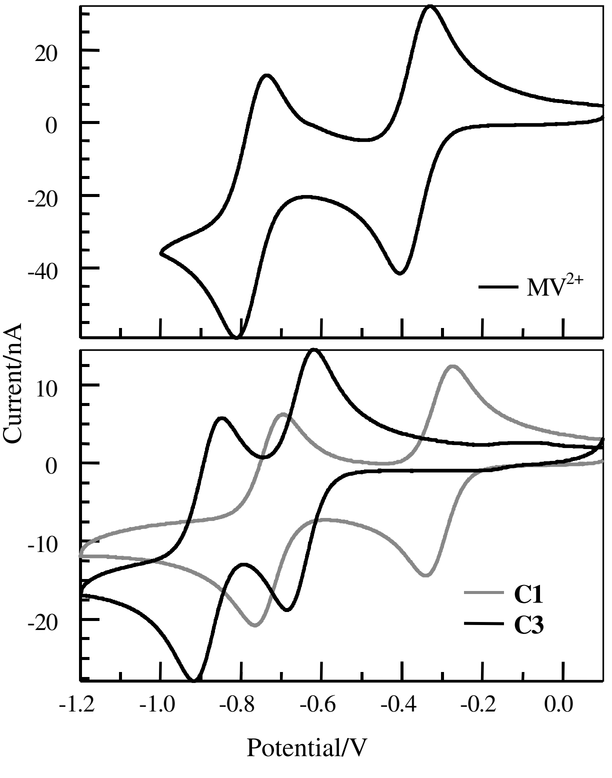

Figure 2. Cyclic voltammograms of MV^{2+} (top) and constrained derivatives **C1** (concd 0.67 mM) and **C3** (concd 0.97 mM) in acetonitrile containing 0.1 M TBATFB at 25 °C versus Fc/Fc^+. Note: concentrations used in the three experiments are not identical.

concerns the values of the reduction potentials. For **C3**, the first ($E_1 = -0.64$ V (57 mV) vs Fc/Fc$^+$) and second ($E_2 = -0.87$ V (60 mV) vs Fc/Fc$^+$) reduction potentials are located at more negative potentials than those observed for **MV**$^{2+}$ ($E_1 = -0.35$ V (70 mV); $E_2 = -0.76$ V (70 mV) vs Fc/Fc$^+$) under identical experimental conditions. This observation can be attributed to the alkoxy substituents at the 3,3′-positions donating electron density into the pyridinium rings. However, it is worth noting that the values of E_1 and E_2 are very similar for **C1** ($E_1 = -0.31$ V (51 mV) $E_2 = -0.73$ V (61 mV) vs Fc/Fc$^+$) and **MV**$^{2+}$. The peak difference ($E_2 - E_1$, ΔE) for **C3** ($\Delta E_{C3} = 0.23$ V) is considerably smaller than those found for either **C1** ($\Delta E_{C1} = 0.42$ V) or **MV**$^{2+}$ ($\Delta E^{2+}_{MV} = 0.41$ V). In comparing the two strapped derivatives it is clear that ΔE_{C1} is considerably larger than ΔE_{C3}. That the length of the constraining strap can significantly alter the reduction potential is consistent with reports by Thummel et al. on analogues. They showed that the first reduction potential of diquat (2,2′-dipyridinium) derivatives, where the two nitrogen atoms were linked via alkyl spacers, gradually shifted to more negative potentials as the length of the spacer increased.[11] No detailed theoretical description to account for the observations was given.

Molecular modelling calculations[12] were carried out on **C1**/**C3** and MV^{2+} to calculate dihedral angles for the dicationic (fully oxidised) and mono-cationic (one-electron reduced) species (Table 1). Evidently, the short methylene constraining strap of **C1** severely restricts the connector C–C bond rotation and hence dihedral angle, whereas for both **C3** and MV^{2+} there is more flexibility (Fig. 3). Mono-reduction of both **C1** and **C3** does not lead to a fully planar structure, as in the case for MV$^{+\bullet}$, suggesting that the alkoxy chain severely curtails C–C bond rotation.

Table 1. Calculated torsion angles for constrained derivatives and methylviologen

Compound	Dihedral angle +2 (°)[a]	Dihedral angle +1 (°)[b]	Angle change (°)
C1	35.0	22.3	12.7
C3	57.6	42.7	14.9
MV^{2+}	89.7	0.0	89.7

[a] Fully oxidised dicationic compound.

[b] One-electron reduced mono-cationic compound.

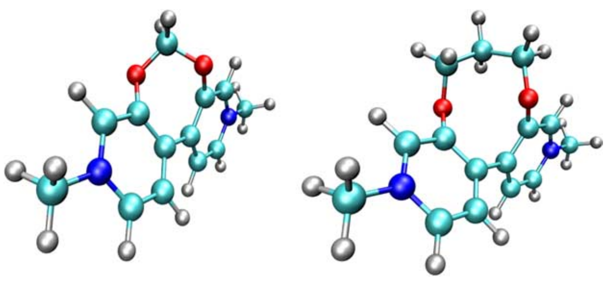

Figure 3. Ball and stick molecular modelling representations of **C1** (left) and **C3** (right).

Tentatively, there seems to be a correlation between ΔE and the dihedral angle for the one-electron reduced form,[13] but the true relationship will only become more clear when a sizable series of strapped derivatives are available. These are currently under preparation and will be reported at a later date when a full theoretical model to explain the angle effect will also be presented.

Acknowledgements

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9. Analytical data: ^{1}H NMR (δ, 300 MHz, CD_3CN): 2.25 (q, $J = 5.1$Hz, 2H, –CH_2–), 4.39 (s, 6H, CH_3), 4.66 (t, $J = 5.1$Hz, 4H, H of –OCH_2–), 8.04 (d, $J = 6.1$Hz, 2H, Py–H^6), 8.57 (d, $J = 6.1$Hz, 2H, Py–H^5), 8.77 (s, 2H, Py–H^3). ^{13}C NMR (δ, 75 MHz, CD_3CN): 28.9, 48.5, 74.3, 127.6, 137.4, 140.5, 141.6, 155.6. ES-MS (*m*/*z*): 403.2 (calcd $M_r = 403.1$ for $[M-PF_6]^+$), 257.1 (calcd $M_r = 257.1$ for $[M-2PF_6-H]^+$), 128.9 (calcd $M_r = 129.1$ for $[M-2PF_6]^{2+}$). Anal. Calcd for $C_{15}H_{18}N_2O_2{\cdot}P_2F_{12}$: C, 32.86; H, 3.31; N, 5.11. Found: C, 33.15; H, 3.49; N, 5.10.
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