Electrochemical synthesis of cyclo[8]pyrrole

Christophe Bucher,*[a] Charles H. Devillers,[a] Jean-Claude Moutet,[a] Jacques Pécaut[c] and Jonathan L. Sessler*[b]

The utility of an electrochemical oxidative strategy in the synthesis of expanded porphyrins is demonstrated by the preparation of cyclo[8]pyrrole in high yield *via* a bipyrrole C(2)–C(2)′ coupling process.

The number of strategies available to prepare porphyrin analogues is currently quite limited.[1,2] Among the more promising new methods to be introduced in recent years are those based on direct oxidative couplings.[1,3,4] Such approaches have allowed for the synthesis *inter alia* of expanded porphyrins containing six, seven, and eight pyrroles, as well as various heteroatom analogues. To date, however, only a very few chemical oxidants, namely high potential quinones and the high-valent cations Cr(VI) and Fe(III), have been used successfully in the context of this strategy. Expanding the scope of available oxidants could lead to important advances in synthesis, including the preparation of known targets with greater ease or efficiency. Here we report a new oxidative coupling strategy based on electrochemical oxidation, demonstrating it by the synthesis of cyclo[8]pyrrole, a flat, aromatic expanded porphyrin macrocycle previously obtained by chemical-based oxidative coupling.[4]

Electrochemical oxidations have previously been used to generate pyrrole-based radical cations, which are known to undergo spontaneous C(2)–C(2)′ coupling reactions leading to conducting or amorphous polymeric structures.[5,6] Interestingly, however, there have been only a few reports describing the electrochemically driven formation of non-linear polypyrrolic stuctures from highly pre-organized synthons.[7–10] None of these involved an N-unsubstituted expanded porphyrin.

To test the potential utility of the electrochemical strategy in producing expanded porphyrins, cyclo[8]pyrrole was selected as the synthetic target. This choice reflects the fact that this particular species is well characterized, can be prepared in good yield *via* a chemical-based oxidative coupling,[4] and the requisite precursor, 3,3′,4,4′-tetraethylbipyrrole **1**, is readily available. It was thus thought that electrochemically induced cyclization of this latter building block would produce the desired cyclo[8]pyrrole target.

Prior to commencing studies of the putative cyclization process, the electrochemical activity of the starting 3,3′,4,4′-tetraethylbipyrrole **1**[11–13] was investigated in dichloromethane (with 0.1 M tetra-*n*-butylammonium perchlorate as supporting electrolyte) using cyclic voltammetry† (Fig. 1, A).

The irreversible oxidation of the pyrrole fragments was observed at a rather low potential (E_a = 150 mV *vs.* Ag/Ag⁺), in accord with what would be expected given the electron-donating effect of the β-substituents and the reduction in the HOMO–LUMO gap resulting from conjugation between the aromatic pyrrole fragments (Fig. 1, A).[14–17] The irreversible nature of this process, observed at all studied scan rates (100 to 10 V s⁻¹), clearly highlights the limited stability of the cation radical [**1**]⁺•, and serves to confirm its known tendancy to evolve towards oligomeric materials as the result of fast coupling reactions.

This preliminary investigation also revealed that repetitive cycling does not lead to the expected polymer-based enhancement in current intensity, typically observed when a progressive increase in the surface concentration of an electroactive species is seen. This
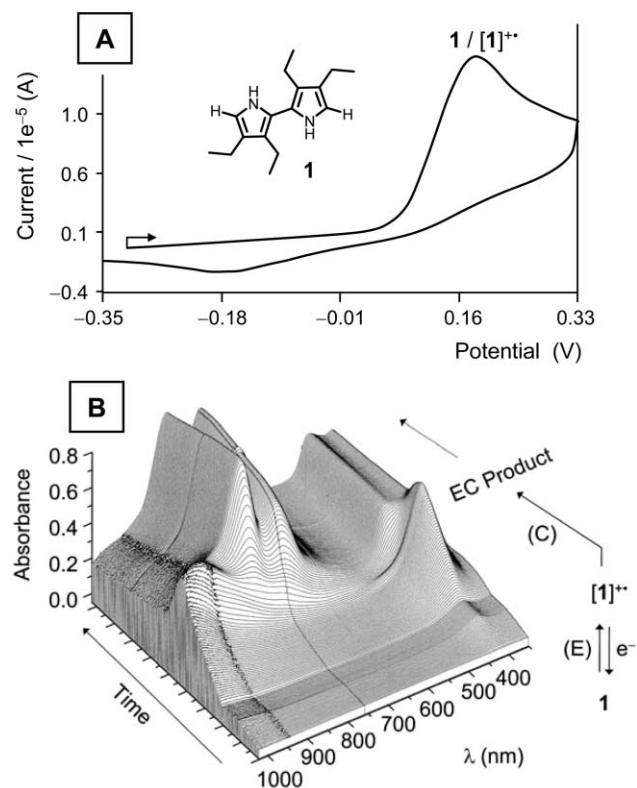

Fig. 1 A) Cyclic voltammogram of **1** (5×10^{-4} M) recorded in CH₂Cl₂ containing 0.1 M TBAP (vitreous carbon working electrode, 100 mV s⁻¹). B) Electrolysis of a 5×10^{-4} M solution of **1** followed by UV-Vis spectroscopy (l = 1 mm; 0.25 M TBAHSO₄ in CH₂Cl₂, E_{app} = 0.3 V *vs.* Ag/Ag⁺, platinum plate working electrode).

[a]Laboratoire d'Electrochimie Organique et de Photochimie Rédox, UMR CNRS 5630, Institut de Chimie Moléculaire de Grenoble, FR CNRS 2607, Université Joseph Fourier, BP 53, 38041, Grenoble Cédex 9, France. E-mail: christophe.bucher@ujf-grenoble.fr
[b]Department of Chemistry and Biochemistry, University of Texas, 1 University Station A5300 Austin, Texas, 78712-0165, USA. E-mail: sessler@mail.utexas.edu
[c]CEA/DRMFC/SCIB, Laboratoire de Coordination et Nanochimie, 17 rue des Martyrs, 38054, Grenoble Cédex 9, France

observation led to the consideration that the oxidized species generated *in situ* were remaining in solution and thus could possibly lead, *via* electrochemical/chemical (EC) coupled processes, to expanded porhyrin-like architectures,[2] such as cyclo[*n*]pyrrole,[4,18,19] which are known to be stable under most laboratory conditions. Our objectives were thus to investigate the presumed electrochemical/chemical (EC) mechanism and to isolate and identify putative polypyrrole cyclic species.

To address the question of whether a non-oligomeric, macrocyclic product could be obtained under conditions of electrochemical oxidation, an initial bulk electrolysis of bipyrrole **1** in dichloromethane (5×10^{-4} M) was conducted under argon atmosphere using tetra-*n*-butylammonium hydrogenosulfate as the supporting electrolyte (0.25 M) and a conventional three-electrode cell with a platinum plate as working electrode. Upon setting the working electrode potential at 300 mV (*vs.* Ag/Ag$^+$), way above the oxidation potential of the bipyrrole synthon, the solution turned progressively from colourless to highly coloured. This bulk electrolysis was followed *in situ* by UV-Vis absorption spectroscopy, leading to the growth of a sharp peak at 427 nm and a broad absorption above 900 nm in the resulting spectrum (Fig. 1, B). As the total coulombic charge consumed reached *ca.* 2 molar equivalents of electrons per monomer **1**, the spectrum changed drastically, with the broad band in the near-infrared region disappearing, while two sharp and intense absorptions between 750 and 850 nm were seen to grow. Concomitant changes were observed at lower wavelengths, with the initial signal at 427 nm splitting to produce two less intense bands located at 427 and 481 nm. After these new spectroscopic signatures were fully developed, further oxidation up to a net deficit of 3 molar equivalents of electrons per monomer **1** failed to produce any significant additional changes in the UV-Vis absorption spectrum. At this juncture the reaction was thus considered complete.

Work-up involved evaporating the highly coloured reaction mixture to dryness under reduced pressure. The resulting oily residue was then dissolved in aqueous H$_2$SO$_4$ (0.1 M) and filtered to afford a deeply coloured solid. TLC analysis of the latter material revealed one major component whose absorption spectrum was in agreement with that for cyclo[8]pyrrole.[4] The bulk electrochemical synthesis was thus scaled up, both to assess its efficiency and to generate sufficient material to permit detailed characterization. In this way, starting from a 5×10^{-3} M solution of **1**, a crude solid material was obtained after filtration that was then further purified by column chromatography (silica gel; eluent 1 to 5% MeOH in DCM). This afforded one major fraction, the mass spectrum of which corresponded to that expected for cyclo[8]pyrrole **2**.[4] An X-ray diffraction analysis conducted on single crystals obtained by evaporation of a DCM–hexane solution provided a definitive proof of the structure (Fig. 2).‡ As expected from the literature, cyclo[8]pyrrole **2** was isolated in the form of its diprotonated sulfate salt, with the counter-anion being tightly bound within the macrocyclic cavity.[4] The overall yield of expanded porphyrin product **2** obtained in this way was 68%, which is competitive with the best yields obtained using chemical oxidants.

The electrochemical synthesis of **2** from four bipyrrole building blocks under appropriate anodic voltage requires the net loss of 2.5 electrons per bipyrrole unit (Fig. 3). The mechanism is yet not fully understood, but the reaction presumably proceeds in a
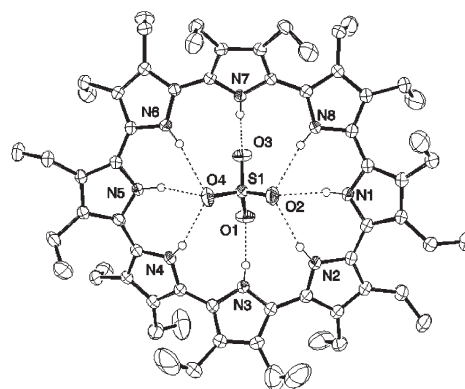

Fig. 2 Top view of an ORTEP[20] image of **2**. Thermal ellipsoids are scaled to the 50% probability level.
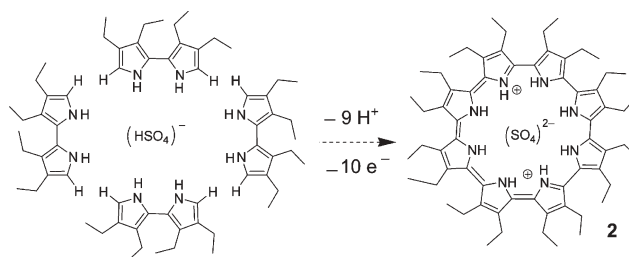

Fig. 3 Schematic representation of the coupled electrochemical/chemical (EC) coupled processes leading to the cyclo[8]pyrrole **2** from four molar equivalents of bipyrrole **1**.

stepwise fashion and involves the C(2)–C(2)′ coupling of electrogenerated radical cations or a similar coupling between radical cations and non-oxidized pyrrole fragments[6,21] (Fig. 3). From the solid-state structure, it can, however, be assumed that sulfate anions play a significant part in the topological control of this coupling process through what may involve an anion–oligopyrrole hydrogen-bonding templating effect.

The cyclic voltammogram† of **2**, recorded in dichloromethane containing 0.1 M TBAP, is consistent with previous findings,[15,19] with two monoelectronic successive oxidation waves at 80 and 495 mV and a two-electron reduction wave at −530 mV (Fig. 4, A). As previously reported in the case of the bis-chloride analogue,[19] a third oxidation process could also be clearly observed at higher potential ($E_{peak} = 1100$ mV). The ease with which **2** undergoes electrochemical oxidation is consistent with the *in situ* generation of a cation radical [**2**]$^{+\bullet}$ in the course of the bulk electrolysis of **1** that then plays a key role in a follow-up EC reaction process, presumably by functioning as an electron transfer mediator. A UV-Vis spectroelectrochemistry experiment was thus carried out to characterize [**2**]$^{+\bullet}$ and confirm its part in the EC process. The initial absorption spectra of a DCM solution of **2** (with 0.25 M TBAHSO$_4$) was seen to evolve quickly upon setting the platinum plate working electrode potential to 0.2 V. As already observed upon subjecting **1** to electrolysis, the broad absorption above 900 nm progressively vanishes. This reduction in intensity was accompanied by the growth of two sharp signals at 744 and 832 nm, while the band at 427 nm gradually underwent splitting into two less intense absorption bands at 481 and 427 nm (Fig. 4, B). A metastable situation could be obtained when one molar
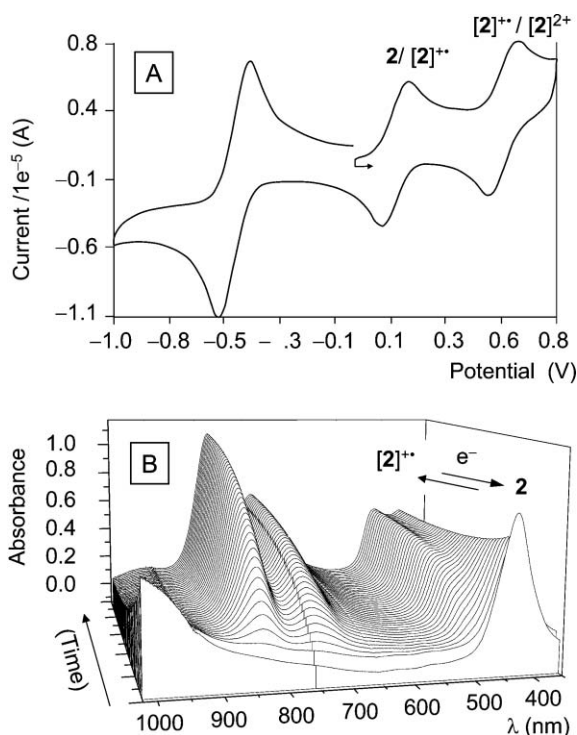
Fig. 4 A) Cyclic voltammogram of **2** (5×10^{-4} M) recorded in CH_2Cl_2 containing 0.1 M TBAP (vitreous carbon working electrode, 100 mV s^{-1}). B) Electrolysis of a 1.25×10^{-4} M solution of **2** followed by UV-Vis spectroscopy ($l = 1$ mm; 0.25 M TBAHSO$_4$ in CH_2Cl_2, $E_{app} = 0.2$ V *vs.* Ag/Ag$^+$, platinum plate working electrode).

electron equivalent of **2** was converted to **[2]$^{+•}$**, whose stabilty on the electrolysis time scale could be evaluated through a bulk reduction at 0 V, a process that yielded back the initial solution of **2**.

On the basis of these findings, the consecutive steps observed in the course of the UV-Vis spectroelectrochemical experiment depicted in Fig. 1 are thought to involve the formation of the cyclo[8]pyrrole product **2**, produced through a C(2)–C(2)′ coupling process of an α-free bipyrrolic precursor, followed by a conversion at the applied potential into the radical cation **[2]$^{+•}$**, a species that may be easily identified from its UV-Vis absorption signature (Fig. 4, B).

In summary, we have shown how cyclo[8]pyrrole **2** may be prepared in very good yield using an unprecedented electrochemical oxidation strategy. The success of this approach leads us to propose that analogous electrochemical oxidation processes could be used to generate a range of new and existing expanded porphyrin products. Unlike chemical oxidants, which must generally be tested emperically for a given expanded porphyrin-generating transformation, the electrochemically based oxidative strategy offers the advantage that one has the opportunity, at least in principle, to tune the reactivity of the "reagent" by the choice of anodic voltage. It is thus possible that electrochemical oxidation procedures could evolve to complement those based on more classical chemical oxidants. Studies designed to test this hypothesis are currently in progress in our laboratories.

Notes and references

1 J. L. Sessler and D. Seidel, *Angew. Chem., Int. Ed.*, 2003, **42**, 5134.
2 J. L. Sessler, A. Gebauer and S. J. Weghorn, *Expanded Porphyrins*, Academic, San Diego, 2000, vol. 2, p. 55.
3 S. K. Pushpan and T. K. Chandrashekar, *Pure Appl. Chem.*, 2002, **74**(11), 2045.
4 D. Seidel, V. Lynch and J. L. Sessler, *Angew. Chem., Int. Ed.*, 2002, **41**(8), 1422.
5 A. Deronzier and J.-C. Moutet, *Acc. Chem. Res.*, 1989, **22**, 249.
6 G. Sabouraud, S. Sadki and N. Brodie, *Chem. Soc. Rev.*, 2000, **29**(5), 283.
7 D. Jeyakumar, K. M. Snow and K. M. Smith, *J. Am. Chem. Soc.*, 1988, **110**, 8562.
8 T. P. Wijesekera and D. Dolphin, *Chemtracts: Org. Chem.*, 1990, **3**(5), 375.
9 K. I. Chane-Ching, J.-C. Lacroix, R. Baudry, M. Jouini, S. Aeyach, C. Lion and P.-C. Lacaze, *J. Electroanal. Chem.*, 1998, 139.
10 M. Lazerges, M. Jouini, P. Hapiot, P. Guiriec and P.-C. Lacaze, *J. Phys. Chem. A*, 2003, **107**, 5042.
11 E. Vogel, P. Koch, X.-L. Hou, J. Lex, M. Lausmann, M. Kisters, M. A. Aukauloo, P. Richard and R. Guilard, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1600.
12 J. L. Sessler and M. C. Hoehner, *Synlett*, 1994, **3**, 211.
13 M. R. Johnson, C. Slebodnick and J. A. Ibers, *J. Porphyrins Phthalocyanines*, 1997, **1**(1), 87.
14 G. Zotti, S. Martina, G. Wegner and A.-D. Schlüter, *Adv. Mater.*, 1992, **4**, 12.
15 L. Guyard, P. Hapiot and P. Neta, *J. Phys. Chem. B*, 1997, **101**, 5698.
16 C. P. Andrieux, P. Hapiot, P. Audebert, L. Guyard, M. Nguyen Dinh An, L. Groenendaal and E. W. Meijer, *Chem. Mater.*, 1997, **9**, 723.
17 T. Benincori, E. Brenna, F. Sannicolò, G. Zotti, S. Zecchin, G. Schiavon, C. Gatti and G. Frigerio, *Chem. Mater.*, 2000, **12**, 1480.
18 T. Köhler, D. Seidel, V. Lynch, F. O. Arp, Z. Ou, K. M. Kadish and J. L. Sessler, *J. Am. Chem. Soc.*, 2003, **125**(23), 6872.
19 A. Gorski, T. Köhler, D. Seidel, L. J. T. G. Orzanowka, J. L. Sessler and J. Waluk, *Chem. Eur. J.*, 2005, **11**, 4179.
20 L. J. Farrugia, *J. Appl. Crystallogr.*, 1997, **30**, 565.
21 C. P. Andrieux, P. Audebert, P. Hapiot and J. M. Savéant, *J. Phys. Chem.*, 1991, **95**, 10158.