

Electrochemically Driven Intramolecular Ring Closure of a Linear Hexapyrrole

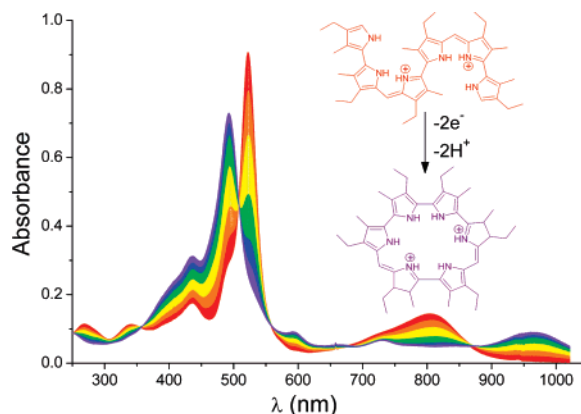
Adriana Iordache,[†] Patricia Melfi,[§] Christophe Bucher,^{*,†} Mihai Buda,^{†,‡}
Jean-Claude Moutet,[†] and Jonathan L. Sessler^{*,§}

Département de chimie moléculaire, laboratoire de chimie inorganique rédox,
UMR-5250, ICMG FR-2607, Institut de Chimie Moléculaire de Grenoble, FR CNRS
2607, Université Joseph Fourier, BP 53, 38041 Grenoble Cédex 9, France, and
Department of Chemistry and Biochemistry, University of Texas, 1 University
Station-A5300, Austin, Texas 78712-0165

christophe.bucher@ujf-grenoble.fr; sessler@mail.utexas.edu

Received November 19, 2007

ABSTRACT



[24]Hexaphyrin(1.0.1.0.0.0) was electrochemically synthesized in good yield starting from a linear hexapyrrolic precursor. This straightforward approach provides an efficient “green” alternative to the reported chemical synthesis, which requires the use of trifluoroacetic acid as the solvent and toxic chromium(VI) salts as the oxidant.

We have recently become interested in pursuing the use of electrochemical synthesis as a possible “green” alternative to classic, chemical reagent-based processes. While the generality of this approach is still far from established, we have recently succeeded in effecting the electrochemically driven, template-mediated synthesis of cyclo[8]pyrrole from four bipyrrole precursors.¹ This unprecedented result led us to consider that analogous electrochemical oxidation processes could be used to generate a range of expanded

porphyrin products and that such procedures could evolve to complement those based on more classical chemical oxidants. We especially considered that such an approach, were it rendered efficient, could be used to avoid the use of the hazardous reagents often required in the multistep syntheses of expanded porphyrin.² One expanded porphyrin of particular current interest is [24]hexaphyrin(1.0.1.0.0.0) (“isoamethyrin”, **1**) since it shows promise as a colorimetric sensor for high-valent actinide cations.³ Unfortunately, the final step in the “chemical” synthesis of isoamethyrin involves treating an hexapyrrolic linear precursor, **2**, with

[†] Université Joseph Fourier.

[‡] Permanent address: Department of Applied Physical Chemistry and Electrochemistry, “POLITEHNICA” University of Bucharest, Calea Grivitei 132, 010737, Bucharest, Romania.

[§] University of Texas.

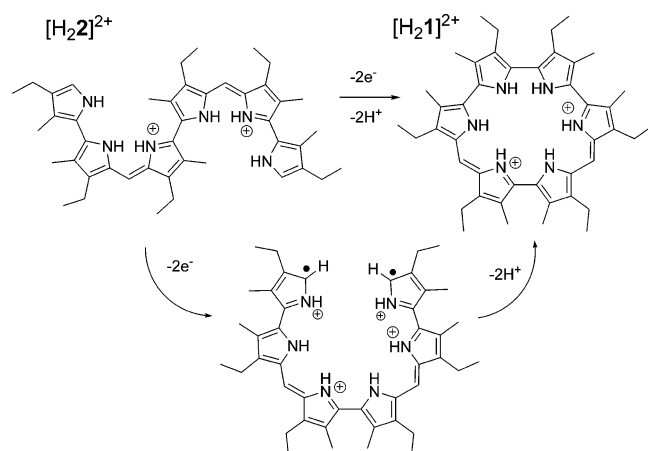
(1) Bucher, C.; Devillers, C. H.; Moutet, J.-C.; Pécaut, J.; Sessler, J. L. *ChemComm.* **2006**, 3891.

(2) Sessler, J. L.; Gebauer, A.; Weghorn, S. J. *Expanded Porphyrins*; Academic: San Diego, 2000; Vol. 2, p 55.

(3) Sessler, J. L.; Melfi, P. J.; Seidel, D.; Gordon, A. V.; Ford, D. K.; Palmer, P. D.; Tait, C. D. *Tetrahedron* **2004**, 60, 11089.

the strong oxidizing agent $\text{Na}_2\text{Cr}_2\text{O}_7$ in pure trifluoroacetic acid.^{4,7} Although the preparation of the hexapyrrolic precursor **2** is straightforward, all efforts to develop alternative methods for effecting the final ring-closure step (Scheme 1) have so

Scheme 1. Schematic Representation of the Coupled Electrochemical/Chemical (EC) Coupled Processes Leading to the Formation of $[\text{H}_2\text{1}]^{2+}$ from the Linear Hexapyrrolic Precursor $[\text{H}_2\text{2}]^{2+}$



far failed, even though theoretical calculations show that charged long-chain oligopyrroles have a tendency to wrap around an anion, thus likely to facilitate ring closure.⁵ We now show that this “hard to effect” transformation can be accomplished through a simple and straightforward intramolecular electrochemically driven ring closure.

Prior to attempting the ring closure of the linear hexapyrrolic linear precursor,^{6,7} the electrochemical activity of its diprotonated salt, $[\text{H}_2\text{2}]^{2+} \cdot 2\text{Cl}^-$, was investigated. This was done by cyclic voltammetry in a mixture of $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ (90/10 v/v) containing 0.1 M *n*-tetraethylammonium perchlorate (TEAP). The resulting voltammogram, shown in Figure 1, revealed a broad oxidation wave at $E_{\text{pa}} = 0.55$ V, which proved to be fully irreversible at all accessible scan rates (0.1–10 $\text{V} \cdot \text{s}^{-1}$).

This irreversibility is a common feature of most pyrrole oligomers, although higher order oligopyrroles (≥ 4 units) show usually a more reversible behavior,^{8,9} which is generally attributed to a coupled electrochemical–chemical (EC) mechanism, wherein electrochemically generated unstable pyrrole-based radical cations evolve quickly, through successive α – α coupling processes, leading to the formation of higher order oligomers, polymers,¹⁰ or, as in the present case, macrocyclic species.

(4) Sessler, J. L.; Seidel, D.; Lynch, V. *J. Am. Chem. Soc.* **1999**, *121*, 11257.

(5) Tamm, T.; Tamm, J.; Karelson, M. *Int. J. Quantum Chem.* **2002**, *88*, 296.

(6) Sessler, J. L.; Weghorn, S. J.; Lynch, V.; Fransson, K. *J. Chem. Soc., Chem. Commun.* **1994**, 1289.

(7) Sessler, J. L.; Seidel, D.; Vivian, A. E.; Lynch, V.; Scott, B. L.; Keogh, D. W. *Angew. Chem., Int. Ed.* **2001**, *40*, 591.

(8) Audebert, P.; Catel, J.-M.; Duchenet, V.; Guyard, L.; Hapiot, P.; Le Coustumer, G. *Synth. Met.* **1999**, *101*, 642.

(9) Andrieux, C. P.; Hapiot, P.; Audebert, P.; Guyard, L.; Nguyen Dinh An, M.; Groenendaal, L.; Meijer, E. W. *Chem. Mater.* **1997**, *9*, 723.

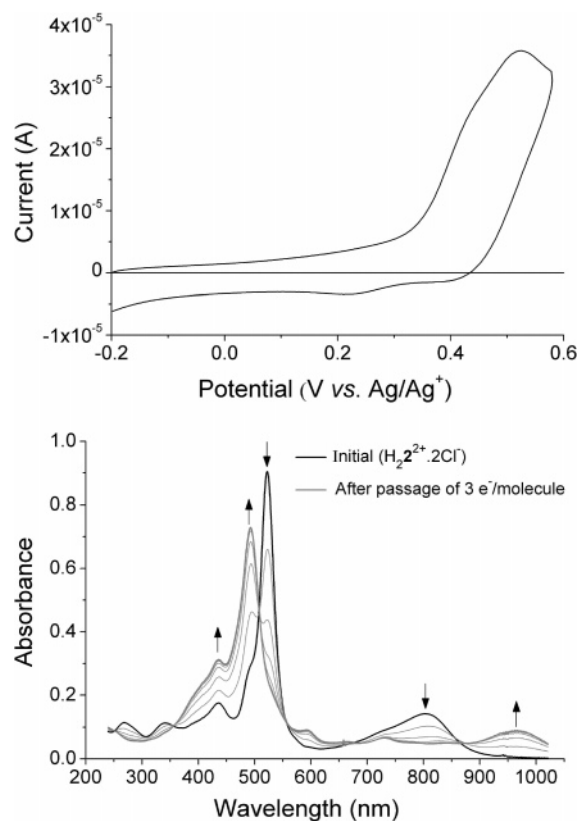


Figure 1. (Top) Cyclic voltammetry of $[\text{H}_2\text{2}]^{2+} \cdot 2\text{Cl}^-$ (10^{-4} M) in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ (90/10 v/v) + 0.1 M TEAP mixture (Pt, $d = 5$ mm, 0.1 V/s). (Bottom) Evolution of the UV–vis spectrum ($l = 1$ mm) seen during the electrochemical oxidation of $[\text{H}_2\text{2}]^{2+} \cdot 2\text{Cl}^-$ on a Pt grid at 0.55 V.

In spite of its extended conjugation and the significant electron-donating contribution of the β -pyrrole alkyl substituents, the diprotonated hexapyrrole $[\text{H}_2\text{2}]^{2+} \cdot 2\text{Cl}^-$ is oxidized at a rather high potential compared to shorter oligomers as bipyrrrole or terpyrrrole.^{11,12} Such a disparity likely reflects in part the protonation of both imine-like pyrrolic nitrogen atoms within the linear backbone. However, independent of the rationale, the oxidation potential is not so high as to lead one to assume a priori a need for the very strong oxidants (such as $\text{Na}_2\text{Cr}_2\text{O}_7$), that have so far been required to effect the conversion of **2** into **1**. In other words, less obvious chemical effects could be involved. We therefore felt it was worth exploring electrochemical ring-closure strategies. We were motivated to do so since, as noted above, previous studies using similar compounds have proved that in certain instances electrosynthesis can provide a viable alternative to chemical-based transformations.^{1,13–14}

To test whether macrocycle **1** could be obtained under conditions of mild electrochemical oxidation, an initial bulk

(10) Sabouraud, G.; Sadki, S.; Brodie, N. *Chem. Soc. Rev.* **2000**, *29*, 283.

(11) Guyard, L.; Hapiot, P.; Neta, P. *J. Phys. Chem.* **1997**, *101*, 5698.

(12) Wenbo, E.; Ohkubo, K.; Sanchez-Garcia, D.; Zhang, M.; Sessler, J. L.; Fukuzumi, S.; Kadish, K. M. *J. Phys. Chem. B* **2007**, *111*, 4320.

electrolysis of $[\text{H}_2\text{2}]^{2+}\cdot 2\text{Cl}^-$ was carried out under inert atmosphere, using a conventional, three-electrode cell, with a Pt grid ($\sim 1\text{ cm}^2$) as the working electrode. We considered it important to choose a supporting electrolyte that was soluble in both water and dichloromethane, for easy removal at the end of the electrolysis. Among the salts tested in this regard, TEAP gave the best results.

In order to monitor changes in the visible absorption signature of the electrolytic solution throughout the oxidation process, a UV–vis probe (1 mm optical path) was introduced in the electrochemical cell, and spectra were recorded every 10 s. The UV–vis spectrum of the starting material $[\text{H}_2\text{2}]^{2+}\cdot 2\text{Cl}^-$ shows a Soret-like band at 525 nm and a broad, less intense, absorption around 800 nm (Figure 1). After commencing electrolysis, with the potential of the working electrode set at 0.55 V, the intensity of these signals progressively decreased, while a new band started developing at 493 nm. The oxidation was then continued until the charge consumed reached a value corresponding to the removal of two electrons from each molecule of $[\text{H}_2\text{2}]^{2+}\cdot 2\text{Cl}^-$. The supporting electrolyte was then removed by first evaporating off the solvent, then adding aqueous HCl (0.1 M)¹⁵ (to dissolve the electrolyte), and finally filtering off the crude product, $[\text{H}_2\text{1}^{2+}]\cdot 2\text{Cl}^-$. This was found to be the dominant product as inferred from TLC analysis ($R_f = 0.65$ in 0.6% MeOH/ CH_2Cl_2 , a retention factor identical to that recorded for a bona fide sample of $[\text{H}_2\text{1}^{2+}]\cdot 2\text{Cl}^-$ obtained using the previously reported “chemical” procedure⁷).

Given the success of this preliminary procedure, the electrochemical synthesis was scaled up using a larger quantity of the starting material. Although, theoretically, a net loss of 2.0 electron per molecule of $[\text{H}_2\text{2}]^{2+}$ is required to effect ring closure to $[\text{H}_2\text{1}]^{2+}$ (Scheme 1), we noticed that the starting material was only being completely consumed after an oxidation involving 2.5 electrons/molecules. Using a workup analogous to that described above, followed by chromatographic purification over silica gel (0–1% gradient of MeOH in CH_2Cl_2 as the eluent). The peak at $m/z = 667.45$ observed in the mass spectrum of the major yellow-brown fraction was fully consistent with the expected cyclic protonated $[\text{H1}]^+$ species, while both the ^1H NMR and UV–vis spectra were in full agreement with the published data.⁷

The overall yield of this electrochemically driven intramolecular cyclization compares with that of the chemical strategy, using chromium as oxidizing agent, and varies between 64% and 56% (for an electrolysis corresponding to a net removal of 2.5 and 3 electrons/molecule, respectively).¹⁶ To complete the present study, the electrochemical signature of the targeted [24]hexaphyrin(1.0.1.0.0.0) was then analyzed

(13) Jeyakumar, D.; Snow, K. M.; Smith, K. M. *J. Am. Chem. Soc.* **1988**, *110*, 8562.

(14) Swanson, K. L.; Snow, K. M.; Jeyakumar, D.; Smith, K. M. *Tetrahedron* **1991**, *47*, 685.

(15) The electrolyte can also be removed by exposure to water, although such a “green chemistry” washing procedure does not guarantee the protonation status of the final macrocyclic derivative.

(16) The limited yield can be easily understood in light of the high reactivity and poor stability of the oxidized starting material. The dark residue retained on the silica gel support during the purification step is explicitly attributed to polymeric materials formed through competing intermolecular coupling pathways.

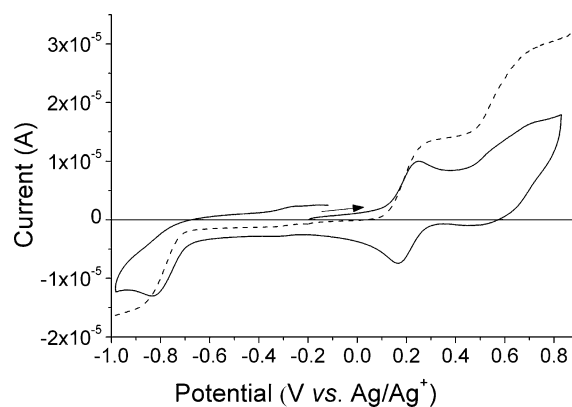


Figure 2. Cyclic voltammetry of $[\text{H}_2\text{1}]^{2+}\cdot 2\text{Cl}^-$ ($5 \times 10^{-4}\text{ M}$) in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ (90/10 v/v) + 0.1 M TEAP mixture (vitreous carbene, $d = 3\text{ mm}$, 0.1 V/s). The dotted line shows the corresponding RDE voltammogram curve (0.01 V/s).

in a $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ mixture (90:10 v/v) using TEAP (0.1 M) as the supporting electrolyte.

Both cyclic and RDE voltammetric analyses revealed two one-electron oxidation peaks at 0.28 and 0.75 V vs Ag/Ag^+ ,

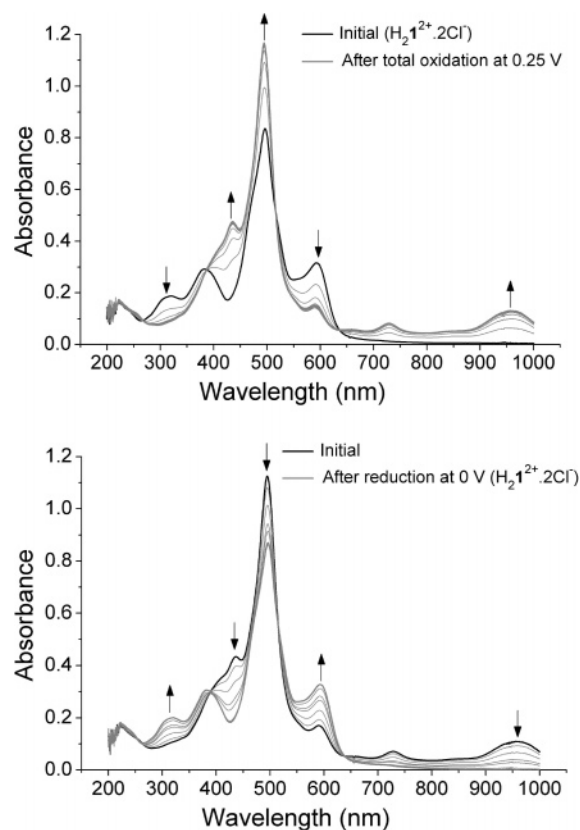


Figure 3. (Top right) Evolution of the UV–vis spectrum ($l = 1\text{ mm}$) seen during the course of the electrochemical oxidation of $[\text{H}_2\text{1}^{2+}]\cdot 2\text{Cl}^-$ at 0.25 V (total oxidation corresponds to passage of $2\text{ e}^-/\text{molecule}$). (Bottom right) Evolution of the UV–vis spectrum ($l = 1\text{ mm}$) during re-reduction to $[\text{H}_2\text{1}^{2+}]\cdot 2\text{Cl}^-$ at 0 V (reduction stopped after passing $2\text{ e}^-/\text{molecule}$).

as well as a one-electron reduction peak (-0.835 V). However, only the first oxidation process displayed reversible behavior on the time scale of the experiment (Figure 2). The reversibility and stability of the electro-generated species were further checked by spectroelectrochemistry; this was done by monitoring the changes in the UV–vis spectrum of a solution of $[\text{H}_2\mathbf{1}^{2+}]\cdot 2\text{Cl}^-$ seen over the course of a bulk oxidation carried out at $E_{\text{ap}} = 0.25$ V (Figure 3). During this latter oxidation, the UV–vis spectrum gradually evolved. Particularly notable was the slow decrease in the main Soret-like signal and the concomitant development of a new band centered at 950 nm, similar to that observed when the open-chain precursor $[\text{H}_2\mathbf{2}^{2+}]\cdot 2\text{Cl}^-$ was subjected to electrochemical oxidation. These changes could be reversed by subjecting the resulting solution to subsequent reduction at $E_{\text{ap}} = 0$ V; using this procedure, the initial spectrum of $[\text{H}_2\mathbf{1}^{2+}]\cdot 2\text{Cl}^-$ could be regenerated. On this basis, we conclude that the radical cation of the hexaphyrin $[\text{H}_2\mathbf{1}^{2+}]\cdot 2\text{Cl}^-$ is reasonably stable on the time scale of the electrochemical synthesis.

In summary, we have shown that [24]hexaphyrin-(1.0.1.0.0.0) can be synthesized easily and in good yield from

a hexapyrrolic linear precursor under mild conditions via electrochemical oxidation. The electrochemistry of [24]-hexaphyrin(1.0.1.0.0.0) shows a reversible oxidation at 0.25 V, an irreversible oxidation at 0.75 V and a reduction wave at -0.835 V. Further research is being carried out with the goal of extending this electrochemical approach to the oxidative synthesis of other conjugated macrocycles, including those containing heterocycles other than pyrrole.

Acknowledgment. The work in Austin was supported by the National Science Foundation (Grant No. CHE-0515670 to J.L.S.). M.B. and A.I. gratefully acknowledge the support from the CNRS and from the French Ministry of Research.

Supporting Information Available: General experimental procedures and characterization data for key compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL702798E