ORGANIC LETTERS

2009
Vol. 11, No. 11
2261−2264

Isolable Zwitterionic Pyridinio-semiquinone π-Radicals. Mild and Efficient Single-Step Access to Stable Radicals

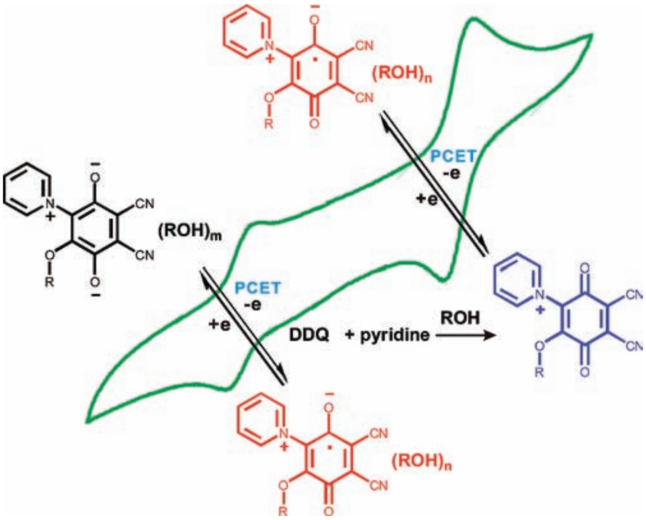
Chenyi Yi,[†] Carmen Blum,[†] Shi-Xia Liu,*[,†] Tony D. Keene,[†] Gabriela Frei,[†] Antonia Neels,[‡] and Silvio Decurtins[†]

Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland, and XRD Application LAB, CSEM Centre Suisse d'Electronique et de Microtechnique SA, Jaquet-Droz 1, Case postale, CH-2002 Neuchâtel, Switzerland

liu@iac.unibe.ch

Received March 17, 2009

ABSTRACT



A rational design based on the proton-coupled electron transfer (PCET) concept allows us to structurally characterize for the first time isolable, air- and moisture-stable semiquinone radicals in a zwitterionic neutral form. The presence of an alkoxy and the bulky pyridinio substituents causes only a minor perturbation of either the redox potentials or the spectral UV−vis characteristics of the semiquinone core but significantly stabilizes the new radicals.

Quinones and their reduced forms, semiquinones and dihydroquinones, represent prototypical examples of organic redox systems. Besides a profound chemical interest, it is widely accepted that quinone-based redox couples play key biological functions as electron−proton transfer agents in bioenergetic processes such as respiration and photosynthesis, which are essential for life.[1] Since hydrogen bonding and protonation are decisive factors controlling potentials and

---

[†] Universität Bern.

[‡] CSEM Centre Suisse d'Electronique et de Microtechnique SA.

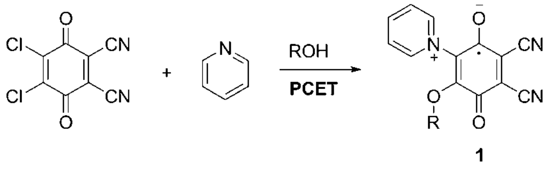
[1] (a) *The Photosynthetic Reaction Center*; Deisenhofer, J., Norris, J. R., Eds.; Academic Press: San Diego, CA, 1993. (b) Kaim, W.; Schwederski, B. *Bioinorganic Chemistry: Inorganic Elements in the Chemistry of Life*; John Wiley & Sons: Chichester, U.K., 1994. (c) Ferguson-Miller, S.; Babcock, G. T. *Chem. Rev.* **1996**, *96*, 2889. (d) *The Chemistry of the Quinonoid Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1988.

10.1021/ol900559p CCC: $40.75

mechanisms in the reduction of quinones, the proton-coupled electron-transfer (PCET) concept is far-reaching. In particular, the promotion effects of the proton on ET are often modulated by Brønsted bases (:B).[2] As a case in point, consider the protonated amino acid promoted ET reduction of a quinone by hydrogen-bond formation with the resulting semiquinone radical anion.[3] Such semiquinone intermediates have sufficiently long lifetimes to be observed during mechanistic studies by conventional spectroscopic methods.[3,4] However, they have not been isolated as pure compounds: they are transient organic radicals. Ideally, one would like to study discrete and reversible one-proton/one-electron PCET processes which, however, generally lead to the formation of highly reactive radicals.

The present study reports the preparation and characterization of isolable semiquinone radicals, namely zwitterionic pyridinio-semiquinone π-radicals of the type 2,3-dicyano-1-hydroxy-5-alkoxy-4-oxo-6-pyridiniocyclohexa-2,5-dien-1-yl ion[5] (Scheme 1). Their stability arises not only from π-conjugation which offers the possibility of the free spin to be delocalized over any part of the conjugated π-system and from the zwitterionic structure (thermodynamic stabilization) but also from the steric protection of the substituents (kinetic stabilization). A more detailed discussion on the above-mentioned criteria for the stabilization of radicals is given in a recent review by Hicks.[6]

Scheme 1. Synthetic Route to **1** (**1a** R = Methyl; **1b** R = Propyl; **1c** R = 2-Methoxyethyl)



The reaction used to prepare the stable radical compounds is intriguing because of its simplicity and robustness. Thus, 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) was dissolved in an alcohol ROH and treated with an excess of pyridine to generate a deep red solution (Scheme 1). By slow evaporation, air- and moisture-stable zwitterionic pyridinio-semiquinone π-radicals **1** were obtained as dark-colored single crystals suitable for X-ray crystal-structure analysis.

Although the work presented here does not address a detailed reaction mechanism directly, a plausible PCET process is involved as depicted in Scheme 1. Thereby, DDQ initially undergoes two nucleophilic substitution reactions giving rise to a weakly basic quinone intermediate. The following step may be discussed in terms of the demonstration that positive shifts in the reduction potentials of different quinones in the presence of an alcohol are ascribed to quite specific hydrogen-bonding equilibria involving mono- and dianions.[7] Consequently, this PCET-related effect will facilitate the reduction of the quinone derivative while stabilizing the reduced species.

For a representative structural characterization of the radical compounds **1a-c**, the 5-propoxy-substituted derivative **1b** will be chosen. This radical crystallizes in the monoclinic crystal system, space group $P2_1/c$. The ORTEP drawing along with selected geometrical parameters is shown in Figure 1.

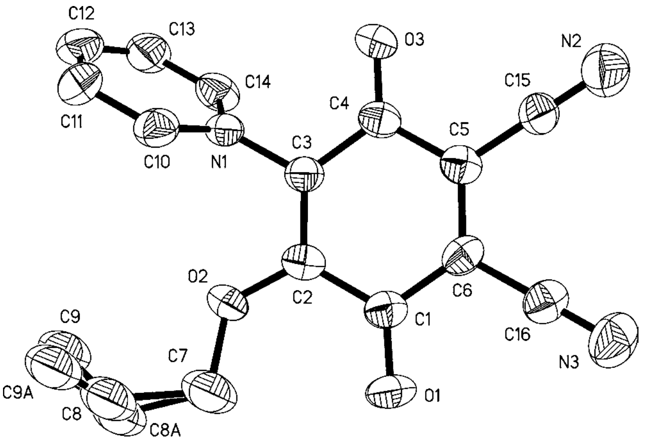


Figure 1. X-ray crystal structure of **1b** (ORTEP; thermal ellipsoids set at the 50% probability level). Selected bond lengths (Å): O1−C1 1.256(4), C1−C2 1.470(5), C2−C3 1.363(4), C3−C4 1.447(5), C4−O3 1.238(4), C4−C5 1.453(5), C5−C6 1.387(4), and C6−C1 1.444(5). Hydrogen atoms are omitted for clarity.

The neutral molecule consists of a negatively charged semiquinone moiety which is tetrasubstituted with two cyano, one propoxy, and one pyridinio group. The molecule, disregarding the pyridinio and the propyl groups, exhibits a planar geometry (rms deviation from a least-squares plane amounts to only 0.06 Å; maximum deviation for O1: 0.177(2) Å). The bond lengths within the semiquinoid moiety are in the range observed for semiquinones in charge-transfer (CT) salts;[8] however, the actual asymmetric substitution pattern and the zwitterionic electronic structure is reflected, to some extent, in bond-length distortions of the benzenoid ring. The

---

(2) (a) Stowell, M. H. B.; McPhillips, T.; Rees, D. C.; Soltis, S. M.; Abresch, E.; Feher, G. *Science* **1997**, *276*, 812. (b) Jordan, B. J.; Pollier, M. A.; Miller, L. A.; Tiernan, C.; Clavier, G.; Audebert, P.; Rotello, V. M. *Org. Lett.* **2007**, *9*, 2835. (c) Kirby, J. P.; Roberts, J. A.; Nocera, D. G. *J. Am. Chem. Soc.* **1997**, *119*, 9230.

(3) (a) Yuasa, J.; Yamada, S.; Fukuzumi, S. *J. Am. Chem. Soc.* **2008**, *130*, 5808. (b) Eisenberg, A. S.; Schelvis, J. P. M. *J. Phys. Chem A* **2008**, *112*, 6179.

(4) (a) Lonnon, D. G.; Lee, S. T.; Colbran, S. B. *J. Am. Chem. Soc.* **2007**, *129*, 5800. (b) Valgimigli, L.; Amorati, R.; Fumo, M. G.; DiLabio, G. A.; Pedulli, G. F.; Ingold, K. U.; Pratt, D. A. *J. Org. Chem.* **2008**, *73*, 1830. (c) Song, Y.; Buettner, G. R.; Parkin, S.; Wagner, B. A.; Robertson, L. W.; Lehmler, H.-J. *J. Org. Chem.* **2008**, *73*, 8296. (d) Fukuzumi, S.; Okamoto, K.; Yoshida, Y.; Imahori, H.; Araki, Y.; Ito, O. *J. Am. Chem. Soc.* **2003**, *125*, 1007.

(5) Bünzli-Trepp, U. *Systematic Nomenclature of Organic, Organometallic and Coordination Chemistry*; EPFL: Lausanne, 2007.

(6) Hicks, R. G. *Org. Biomol. Chem.* **2007**, *5*, 1321.

(7) (a) Costentin, C. *Chem. Rev.* **2008**, *108*, 2145. (b) Gupta, N.; Linschitz, H. *J. Am. Chem. Soc.* **1997**, *119*, 6384.

(8) Yan, Y. K.; Mingos, D. M. P.; Müller, T. E.; Williams, D. J.; Kurmoo, M. *J. Chem. Soc., Dalton Trans.* **1995**, 2509.

pyridinium and benzenoid planes exhibit a dihedral angle of 65.63(9)°.

The characteristic feature of the crystal packing is the columnar stacking of the semiquinoid rings along the *a*-axis (Figure S3, Supporting Information). Thereby, within these one-dimensional chains, two adjacent molecules form centrosymmetrically related π-stacked dimers with a *trans*-cofacial mode of association; hence their electric dipoles are pointing in opposite directions, and their semiquinoid rings are partially slipped. Within these closely packed dimers, the short interplanar separation amounts to only 2.931(4) Å which is substantially less than the van der Waals separation (3.70 Å). The interplanar separation between the dimers is 3.702(4) Å.

As the single-crystal X-ray analysis reveals, the radicals associate as spin-paired dimers in the solid state, thus the short intradimer contacts render the crystalline material diamagnetic, which was confirmed by magnetic susceptibility (SQUID) measurements.

The electrochemical properties of **1a**−**c** in CH_3CN were investigated by cyclic voltammetry (Figure 2 and Figures S6 and S7, Supporting Information). They show almost the same redox behavior. As shown in Figure 2, **1a** exhibits two well-separated and reversible one-electron redox waves for the oxidation and reduction of the semiquinone radical at 0.73 and −0.05 V vs Ag/AgCl, respectively. Under the same conditions, DDQ shows two reversible one-electron reduction waves at 0.66 and −0.16 V. Consequently, the neutral radical **1a** exhibits a fairly wide electrochemical stability range of 0.78 V and, moreover, the reversibility of the two redox processes still remains.

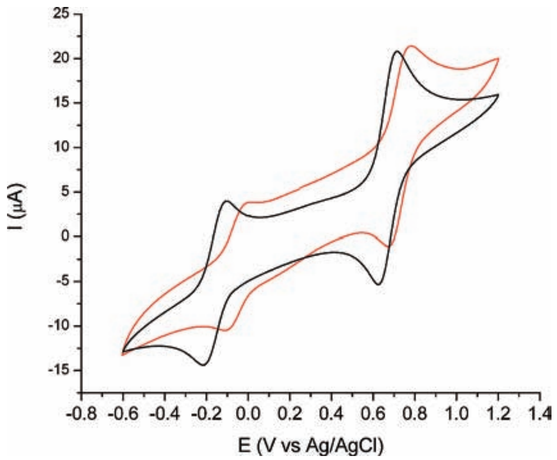


Figure 2. Cyclic voltammograms of **1a** (red line, 5×10^{-4} M) and DDQ (black line, 5×10^{-4} M) in CH_3CN, supporting electrolyte 0.1 M $(Bu_4N)PF_6$, scan rate 100 mV s^{-1}.

Compounds **1a**−**c** strongly absorb in the UV−vis spectral region as evidenced by their dark color (Figure S8, Supporting Information). The intense absorption bands in the UV and blue part of the spectrum are characteristic for $\pi-\pi^*$ transitions, specifically of the pyridinium and semiquinone subunits. More importantly, the π-radical is characterized by diagnostic absorption bands at 340 nm (29410 cm^{-1}), 420 nm (23810 cm^{-1}), 445 nm (22470 cm^{-1}), 550 nm (18180 cm^{-1}), and 590 nm (16950 cm^{-1}), as illustrated in Figure 3 for **1a**, which are well comparable to those of the anion radical $DDQ^{\bullet-}$ in CT salts.[9] The presence of π-stacked radical dimers **1a·1a** within the crystalline solid is corroborated by an absorption band at 755 nm (13250 cm^{-1}) (Figure S9, Supporting Information). However, this π-stacking association process[10] is not noticeable in solution at room temperature, since no long-wavelength electronic transition was observed, even at high concentrations and in polar solvents.

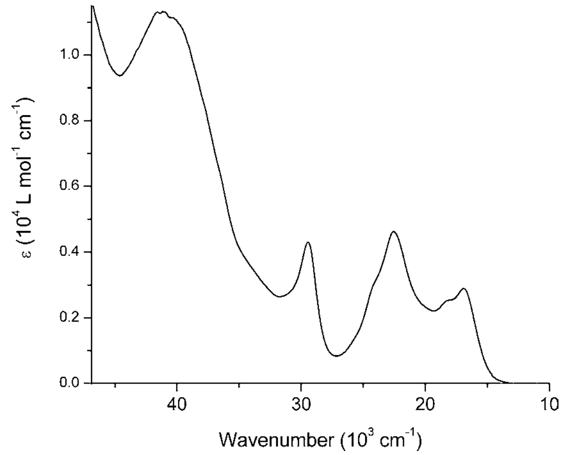


Figure 3. Electronic absorption spectrum of **1a** in CH_3CN solution at room temperature.

The resulting paramagnetic characteristic in solution causes compounds **1a**−**c** to be ^{1}H NMR silent. This observation is also manifested in an isotropic EPR signal ($g_{iso} = 2.002$) in DMF solution (Figures S10−S12, Supporting Information). The main IR stretching frequencies ν(C≡N) and ν(C=O) of **1a** at 2208 and 1627 cm^{-1}, respectively, represent a low energy shift in comparison to DDQ (2232 and 1674 cm^{-1}). These data point consistently to the presence of the semiquinone unit.

From an unrestricted DFT calculation,[11,12] the SOMO of the π-radical **1a** is found to be as illustrated in Figure 4 and the spin-density distribution as in Figure S13, Supporting Information.

It should be noted that about 80% of the odd-electron density lies on the semiquinoid unit, and some lower densities are found on the oxygen atom of the methoxy group and on

---

[9] Salman, H. M. A.; Mahmoud, M. R.; Abou-El-Wafa, M. H. M.; Rabie, U. M.; Crabtree, R. H. *Inorg. Chem. Commun.* **2004**, *7*, 1209.

[10] (a) Yamagishi, A. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2440. (b) Lü, J.-M.; Rosokha, S. V.; Kochi, J. K. *J. Am. Chem. Soc.* **2003**, *125*, 12161.

[11] The DFT method was employed with the B3LYP functional and the TZVP (valence triple-ζ plus polarization) basis set. All calculations were done with the TURBOMOLE V5.10 program package.

[12] (a) Treutler, O.; Ahlrichs, R. *J. Chem. Phys.* **1995**, *102*, 346. (b) Eichkorn, K.; Weigend, F.; Treutler, O.; Ahlrichs, R. *Theor. Chem. Acc.* **1997**, *97*, 119.

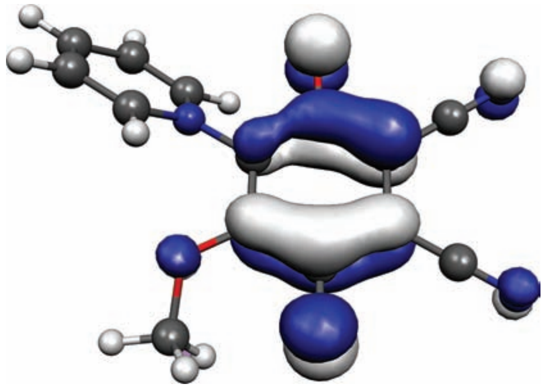


Figure 4. SOMO of **1a**. The isosurface is shown at a cutoff value of 0.05 e Å^{-3}.

the nitrogen atoms of the two cyano groups. This π-type SOMO bears a nodal plane passing through the two shortest carbon−carbon bonds of the benzenoid ring. Not unexpectedly for this "inner-salt"-type molecule, the calculated electric-dipole (ED) moment in the ground state (D_0) amounts to a considerably high value of 17.8 D. The ED vector points, as one may expect, in the direction of the pyridinio group (δ^+ pole).

In summary, we have directed attention toward the preparation of isolable, air- and moisture-stable semiquinone radicals in a zwitterionic neutral form, which adds a valuable molecule family to the class of radical compounds.[6,13] The presence of an alkoxy and the bulky pyridinio substituents causes only a minor perturbation of either the redox potentials or the spectral UV−vis characteristics of the semiquinone core. However, most significantly, these substituents render the new radicals quite stable, in anology to the recently reported imino-semiquione radicals.[13] In light of these results, further investigations on this PCET reaction of DDQ in the presence of a variety of nucleophiles using a broader range of alcohols as solvents are underway. On the one hand, it is intended to explore how the basicity of nucleophiles affects the occurrence of the PCET pathway. On the other hand, the properties and functionalities of the resulting radicals can be largely modified, thus it opens the possibility of exploring their potential application in the field of single-component conductors and multifunctional materials.[14] As predicted, these molecules also bear the potential for the study of interesting photochemical reactions based on their radical nature.

Acknowledgment. This work was supported by the Swiss National Science Foundation (Grant No. 200020-116003).

Supporting Information Available: General experimental details and characterization data for compounds **1a**−**c**; CIF files for **1a**−**c** and other additional figures. This material is available free of charge via the Internet at http://pubs.acs.org.

OL900559P

---

[13] Carter, S. M.; Sia, A.; Shaw, M. J.; Heyduk, A. F. *J. Am. Chem. Soc.* **2008**, *130*, 5838.

[14] (a) Miller, J. S.; Epstein, A. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 385. (b) Miyasaka, H.; Izawa, T.; Takahashi, N.; Yamashita, M.; Dunbar, K. R. *J. Am. Chem. Soc.* **2006**, *128*, 11358.