Communication

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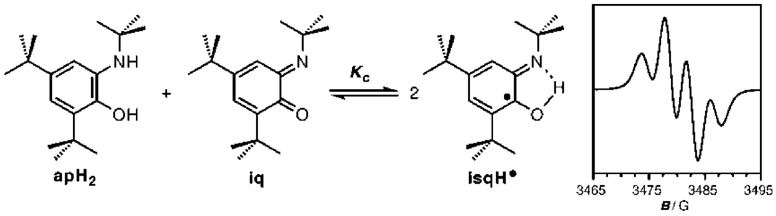

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Isolation and Characterization of a Neutral Imino-semiquinone Radical

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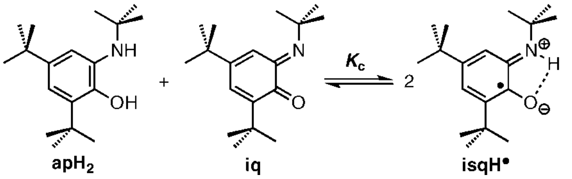
Quinone and semiquinone molecules play an important role in organic synthesis, metal coordination chemistry, and biological chemistry.[1] For example, copper amine oxidases (CAOs) use quinone-derived cofactors in the aerobic oxidative deamination catalysis of amines. Recent studies of CAOs have shown that *o*-aminophenols and *o*-iminoquinones are formed during the copper-catalyzed conversions of primary amines to aldehydes,[2] and short-lived imino-semiquinone intermediates have been observed during mechanistic studies. It has been speculated that imino-semiquinone formation occurs by the conproportionation of iminoquinone and aminophenol, yet this reaction has not been observed in a synthetic system.[3] Herein, we report the preparation and characterization of the first stable imino-semiquinone radical (isqH$^{\bullet}$, 4,6-di-*tert*-butyl-2-*tert*-butylimino-semiquinone), along with an evaluation of the thermodynamic parameters leading to the stabilization of the imino-semiquinone relative to the iminoquinone (iq, 4,6-di-*tert*-butyl-2-*tert*-butyliminoquinone) and aminophenol (apH$_2$, 4,6-di-*tert*-butyl-2-*tert*-butylaminophenol) congeners.

The aminophenol, apH$_2$, was used to prepare iq and isqH$^{\bullet}$. Condensation of ^{t}BuNH$_2$ with 3,5-di-*tert*-butylcatechol yields apH$_2$.[4] The iminoquinone, iq, was prepared by deprotonation of apH$_2$ with *n*-BuLi, followed by oxidation with PhICl$_2$. The neutral imino-semiquinone, isqH$^{\bullet}$, was generated by the reaction of apH$_2$ with iq according to eq 1. A dark-blue reaction solution in DMSO yielded the four-line EPR spectrum shown in Figure 1 (inset) and is consistent with the formation of the isqH$^{\bullet}$ radical. The isqH$^{\bullet}$ radical cocrystallized with apH$_2$ from cold MeCN,[5] and iq crystallized from cold pentane.[6] Figure 1 shows the structure of the isqH$^{\bullet}$ fragment along with select metrical parameters; structural details for apH$_2$ and iq can be found in the Supporting Information.



(1)

Bond lengths within isqH$^{\bullet}$ are consistent with the assigned oxidation state. Specifically, C−N and C−O bond lengths of 1.34 and 1.26 Å, respectively, are shorter than the corresponding bonds in apH$_2$ (1.44 and 1.37 Å, respectively) but longer than those in iq (1.28 and 1.22 Å, respectively). While average C−C bond distances of 1.39 Å are consistent with fully delocalized π bonding in the aromatic ring of apH$_2$, localization of double bond character is pronounced in the C−C bond distances of isqH$^{\bullet}$ (see Figure 1). Iq is best described as a cyclohexadiene ring with fully localized C−C double bonds, as denoted by bond lengths of 1.34 Å.

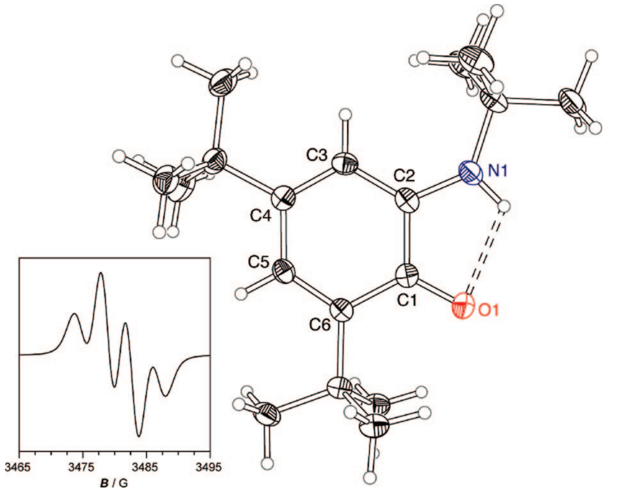


Figure 1. Solid-state molecular structure of isqH$^{\bullet}$ and its X-band EPR spectrum (DMSO, 298 K; $g = 2.0061$). The neutral radical cocrystallizes with apH$_2$, which has been omitted for clarity. Selected bond lengths in Å: O1−C1 1.2577(14); N1−C2 1.3455(16); C1−C2 1.4716(17); C2−C3 1.4047(17); C3−C4 1.3747(18); C4−C5 1.4294(17); C5−C6 1.3644(17); C1−C6 1.4502(17).

The reaction used to prepare isqH$^{\bullet}$ is intriguing because mixtures of catechols and quinones usually are stable toward conproportionation. For example, 1:1 mixtures of colorless 3,5-di-*tert*-butylcatechol and red 3,5-di-*tert*-butyl-*ortho*-quinone are stable, showing no evidence for conproportionation to the semiquinone radical. Solutions of these mixtures are orange, consistent with the color of the *ortho*-quinone, and the ^{1}H NMR spectrum of the mixture is a composite of the separate catechol and quinone spectra. Conversely, 1:1 mixtures of apH$_2$ and iq afford blue solutions with a strong absorbance in the visible region. NMR spectra of these solutions are essentially featureless, consistent with paramagnetic line broadening.

To elucidate the stability of the isqH$^{\bullet}$ radical in different solvents, spectrophotometric titrations were conducted. Figure 2 displays the absorption data for the titration of iq with apH$_2$ in DMSO at room temperature. Addition of apH$_2$ gave an increase in absorbance at 734 nm, which eventually reached a plateau. Similar results were obtained for titrations of apH$_2$ with iq. A plot of absorbance at 734 nm versus [apH$_2$] added, shown as an inset to Figure 2, was used to extract the equilibrium or conproportionation constant of eq 1. Table 1 gives K_c values for eq 1 along with the extrapolated extinction coefficient for isqH$^{\bullet}$ at 734 nm in several solvents. Similar equilibrium constants were obtained when the titrations were carried out in 1 M HCl solutions of DMSO or MeCN.

Electrochemical and acid−base studies were used to examine the thermodynamic parameters leading to the formation of isqH$^{\bullet}$.

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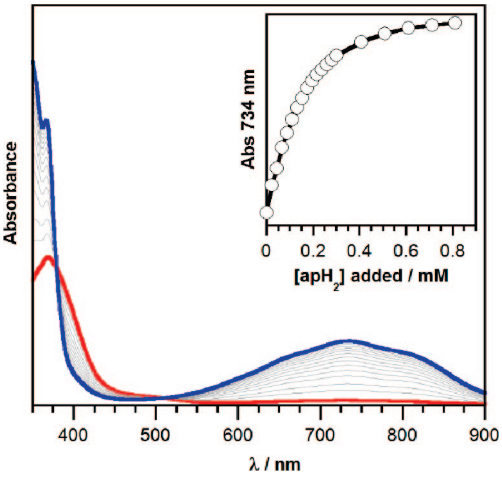


Figure 2. Changes in the electronic absorption spectrum during titration of a DMSO solution of iq (0.186 mM) with 1.59 mM apH_2 (inset: absorbance at 734 nm as a function of added apH_2).

Table 1. Spectral Data and Conproportionation Constants for $isqH^•$ in Various Solvents

solvent	$\epsilon_{734\ nm}$/M^{-1} cm^{-1}	K_c
C_6H_5Me	929	20
MeCN	859	9
CH_2Cl_2	901	10
DMSO	710	5.75

Previous studies by Bordwell and co-workers[7] have shown that the homolytic bond dissociation energies (BDEs) can be calculated from the energy of electron ($E°'$) and proton (pK_a) transfer processes according to eq 2.[8,9] Although it is actually the free energy (ΔG) of the bond dissociation that is being calculated, this energy approximates the bond dissociation energy (ΔU) assuming negligible entropic or work contributions.

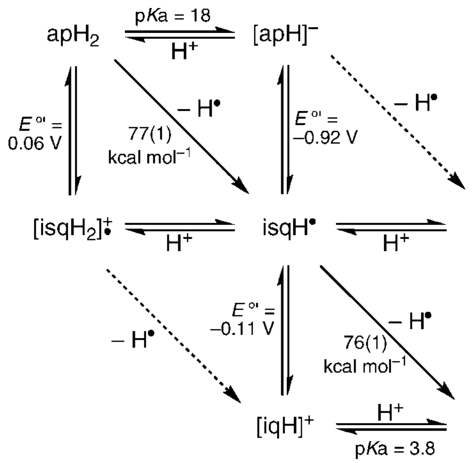
$$E_{HAT} = 23.06E°' + 1.37pK_a + C \qquad (2)$$

The one-electron redox potentials of the blue semiquinone radical were readily obtained.[6] DMSO solutions of $isqH^•$ yielded reversible, one-electron redox features by cyclic voltammetry that were absent in solutions of pure apH_2 or pure iq. A one-electron oxidation was observed for $isqH^•$ at $E°'(ox) = -0.112$ V vs $Cp_2Fe^{0/+}$, while a one-electron reduction was observed at $E°'(red) = -0.924$ V vs $Cp_2Fe^{0/+}$. Under similar conditions, apH_2 showed a partially reversible one-electron oxidation at $+0.06$ V vs $Cp_2Fe^{0/+}$ and iq showed a partially reversible one-electron reduction at -1.368 V vs $Cp_2Fe^{0/+}$.

The pK_a values for apH_2 and iqH^+ in DMSO were estimated from spectrophotometric titrations. Saccharin (pK_a ≅ 4.0 in DMSO)[10] proved to be a suitable acid for the protonation of iq and afforded a pK_a of 3.8 for iqH^+.[11] Titration of apH_2 with $[Bu_4N][NHCOCF_3]$ (pK_a of NH_2COCF_3 ≅ 17.2 in DMSO)[10,12] gave a pK_a of 18.0, which is similar to the pK_a of phenol in DMSO.[13]

The thermodynamic data summarized in Scheme 1 suggest that the *tert*-butylimino group is responsible for the stability of $isqH^•$. The calculated energy for the removal of a hydrogen atom from apH_2 (76.7 kcal mol^{-1}) is similar to the literature value for 3,5-di-*tert*-butylcatechol (78.2 kcal mol^{-1}),[14] suggesting that a weak BDE in apH_2 is not responsible for the ready formation of $isqH^•$. Instead, the key feature stabilizing $isqH^•$ appears to be the basicity of the *tert*-butylimino group. According to the solid-state X-ray diffraction data, the active proton of $isqH^•$ is bound to the nitrogen and forms a hydrogen bond to the oxygen, giving the *ortho*-iminium phenoxide zwitterionic structure drawn in eq 1. Accordingly, $isqH^•$ is both a poor Brönsted acid and a poor Brönsted base.[15] The lack of a basic site in $isqH^•$ is reflected in the pK_a of $(isqH_2^•)^+$, which is estimated to be 1.5 according to the HAT energy in Scheme 1. Furthermore, the hydrogen-bonded imminium proton has a high estimated pK_a of 25, which is significantly less acidic than the corresponding 3,5-di-*tert*-butyl-*ortho*-semiquinone radical (pK_a ≅ 6.0 in aqueous solution).[16]

Scheme 1. Electrochemical (vs $Cp_2Fe^{0/+}$) and pK_a Measurements Relating apH_2, $isqH^•$, and iq in DMSO



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Supporting Information Available: Detailed experimental procedures, titration calculations, and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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