Supporting information for
Structural Effects on the pH-Dependent Redox Properties of Organic Nitroxyls: Pourbaix Diagrams for TEMPO, ABNO and Three TEMPO Analogs
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1. NMR and UV-visible pH titrations of TEMPOH, TEMMOH, ACTH, ABNOH, AMTH and AMT:

**Figure S1.** NMR spectra showing the methyl peaks of TEMPOH in D₂O vs. pH. In the spectra shown in red, the signals corresponding to methyl groups *cis-* and *trans-* to the hydroxylammonium OH have become slowly exchanging.

**Figure S2.** TEMPOH methyl group chemical shift vs. pH. The points shown for pH 6.42 and pH 2.45 are an average of the two peaks (see Figure S1). The line is a fit indicating a pKₐ of 7.34.
Figure S3. TEMMOH methyl and methylene group chemical shifts vs. pH. The points shown for the methyl groups at pH 4.33 and pH 1.35 are an average of the two peaks. The lines are fits indicating a \( pK_a \) of 5.25.
Figure S4. ACTH methine (a); methylene (•, x), acetyl (+), and methyl (*) (b) group $^1$H chemical shifts vs. pH. The points shown for the methyl groups are an average of the two peaks. ACTH $^{13}$C NMR peaks vs. pH (c). The lines are fits indicating a $pK_a$ of 6.4.
Figure S5. ABNOH $^1$H (a, b) and $^{13}$C (c - e) chemical shifts vs. pH. The lines are fits indicating a $pK_a$ of 6.90.
Figure S6. 4-amino-TEMPOH $^1$H chemical shifts vs. pH. The lines are fits indicating a $pK_{a1}$ of 5.58 and a $pK_{a2}$ of 10.08.

Figure S7. UV-vis pH titration of 4-amino-TEMPO. 4-amino-TEMPO absorption vs. pH at 400 nm (+) and 450 nm (x). The lines are fits indicating a $pK_a$ of 8.87.
2. Decomposition of 4-oxo-TEMPO on oxidation:

Cyclic voltammetry of 4-oxo-TEMPO at low pH showed an oxidation that became irreversible at higher pH. The irreversibility was greater at slower scan rates, indicating that a base-dependent decomposition of the oxoammonium was taking place (eq S1). The decomposition reaction kinetics were estimated by numerical simulation (Figure S8). At lower pH, the oxoammonium is stable enough to produce CV scans that appear reversible. However, the voltammetry of this compound was not investigated in detail.

\[
\text{products} \quad \text{via} \quad \text{N} \quad \text{O}
\]

\[
\text{N} \quad \text{O} - e^- \rightsquigarrow \text{N} \quad \text{O}
\]

Figure S8. a) Voltammograms of 4-oxoTEMPO in pH 4.63 aqueous 0.1 M acetate buffer at scan rates of 10, 25, 50, and 100 mV/s. As the scan rate increases, the oxidation becomes more reversible. b) Fit to a CV at 10 mV/s, experimental data are in red; the fitted model is in black. Fitting parameters are: \( E^o = 944 \text{ mV} \), \( D_O = D_R = 5 \times 10^{-6} \text{ cm}^2/\text{s} \), \( k_f = 0.075 \text{ s}^{-1} \).
3. CV of nitroxyls in alkaline media:

When electron-poor or sterically unencumbered nitroxyls are oxidized in alkaline media, hydroxide can reversibly add to the oxoammonium ion to form a hydroxylamine N-oxide. This has been observed with TEMMO at pH 12.4 and 13, ACT at pH 13, ABNO and pH 10.3 and 12.4, and TEMPO at pH 14 (Figures S9, 4 in the main text, S10, S11, S12, S13, respectively). Kinetic parameters for this coupled equilibrium were estimated by numerical modeling with good agreement between trends in calculated rates vs. pH and a reaction that is first-order in hydroxide. See Appendix for a description of the modeling method.

![CV of TEMMO in pH 12.4 phosphate buffer at 10, 50, and 400 mV/s.](image1)

**Figure S9.** CV of TEMMO in pH 12.4 phosphate buffer at 10, 50, and 400 mV/s. As the scan rate increases, the oxidation becomes less reversible. Experimental data are in red; the fitted model is in black. Fitting parameters are: $E^\circ = 900$ mV, $D_O = D_R = 3 \times 10^{-6}$ cm$^2$/s, $k_f[OH^-] = 1000$ s$^{-1}$, $k_b = 40$ s$^{-1}$.

![Voltammograms of ACT in pH 13 aqueous 0.1 M NaOH at 10, 100, and 800 mV/s.](image2)

**Figure S10.** Voltammograms of ACT in pH 13 aqueous 0.1 M NaOH at 10, 100, and 800 mV/s. As the scan rate increases, the oxidation becomes less reversible. Experimental data are in red; the fitted model is in black. Fitting parameters are: $E^\circ = 858$ mV, $D_O = D_R = 6 \times 10^{-6}$ cm$^2$/s, $k_f[OH^-] = 4000$ s$^{-1}$, $k_b = 500$ s$^{-1}$.
**Figure S11.** Voltammograms of ABNO in pH 10.3 carbonate buffer at 10, 100, and 800 mV/s. As the scan rate increases, the oxidation becomes less reversible. Experimental data are in red; the fitted model is in black. Fitting parameters are: $E^\circ = 742$ mV, $D_O = D_R = 6 \times 10^{-6}$ cm$^2$/s, $k_f[OH^-] = 100$ s$^{-1}$, $k_b = 10$ s$^{-1}$.

**Figure S12.** Voltammograms of ABNO in pH 12.4 carbonate buffer at 10, 100, and 800 mV/s. As the scan rate increases, the oxidation becomes less reversible. Experimental data are in red; the fitted model is in black. Fitting parameters are: $E^\circ = 742$ mV, $D_O = D_R = 6 \times 10^{-6}$ cm$^2$/s, $k_f[OH^-] = 10000$ s$^{-1}$, $k_b = 1$ s$^{-1}$.

**Figure S13.** Voltammograms of TEMPO in pH 14 1 M NaOH at 10, 100, and 800 mV/s. As the scan rate increases, the oxidation becomes less reversible, although the main observable effect is a shift of $E_{1/2}$ to be lower than $E^\circ$ by ~ 50 mV. Experimental data are in red; the fitted model is in black. Fitting parameters are: $E^\circ = 745$ mV, $D_O = D_R = 6 \times 10^{-6}$ cm$^2$/s, $k_f[OH^-] = 3000$ s$^{-1}$, $k_b = 1000$ s$^{-1}$.
4. EPR spectrum of TEMMO:

![EPR Spectrum](image)

**Figure S14.** EPR spectrum at 9.297382 GHz of TEMMO in toluene solution at 212 K. The experimental data are in black; the simulation is in red. Fitting parameters were $g_{\text{iso}} = 2.0061$, $A_{\text{iso}} = 43.537 \text{ MHz}$, linear A-strain of -0.0002, and a linewidth of 1.0 G.
5. GC-MS data of nitroxyls:

a) GC-MS trace of TEMPO and b) mass spectrum of the peak eluting at 6.377 minutes.

Figure S15. a) GC-MS trace of TEMPO and b) mass spectrum of the peak eluting at 6.377 minutes.
Figure S16. a) GC-MS trace of ACT and b) mass spectrum of the peak eluting at 10.193 minutes.
Figure S17. a) GC-MS trace of TEMMO and b) mass spectrum of the peak eluting at 6.093 minutes.

Figure S18. a) GC-MS trace of AMT and b) mass spectrum of the peak eluting at 7.777 minutes.
Figure S19. a) GC-MS trace of ABNO and b) mass spectrum of the peak eluting at 8.077 minutes.
Appendix: Portable, Spreadsheet-Based Numerical Modeling of Cyclic Voltammetry Experiments Including Coupled Chemical Reactions

In the course of these experiments, it became useful to us to model cyclic voltammetry data. Based on the resulting fit of the model to the data and knowing parameters such as initial concentrations, temperature, and so on, it is possible to extract $E^\circ$, diffusion constants, and rates of coupled stoichiometric or catalytic chemical reactions. Although CV modeling and simulation are not new, we are not aware of a readily available cross-platform implementation with similarly available source code. Herein, we fully describe our implementation of one method of cyclic voltammetry modeling.

It is possible to simulate CV experiments by a finite element approach where the relevant diffusion equations are solved over an array of small solution volumes that extend from the electrode surface.\(^1\) This process must be repeated at many close time intervals to simulate the evolution of concentration gradients in response to the changing electrode potential and any coupled chemical processes. It is also possible to model the same experiment by numerical integration of the same equations with boundary conditions that are dependent on the reaction mechanism being modeled. This latter approach was developed by Nicholson and Shain in the 1960s, with implementation on a then-state-of-the-art IBM 704 computer.\(^2,3\) The resulting models were described by tabulated values and equations describing trends of points on the experimental voltammogram such as $E_{1/2}$ potentials, peak potentials and peak currents. Although useful, the tabulated data do not easily lend themselves to direct comparison with, or extraction of parameters by curve-fitting to experimental data.

Software is available to perform simulation-based fitting of CV data, however it is either expensive, tied to obsolescent operating systems, or does not have freely available source code that can be inspected to verify the implementation of the underlying algorithm.\(^4\) Thus, we decided to implement Nicholson and Shain's methods in a highly portable, user modifiable form: spreadsheets. The factor of $\sim 10^5$ increase in speed from the IBM 704 used by Nicholson and Shain to currently available personal computers allows for a correspondingly less efficient implementation to be equally usable.\(^5\) The notation employed here, especially abbreviated constants, is the same as in Nicholson and Shain's paper except where noted.

A recurrent motif in these modeling algorithms is an integral of the form
\[
\int_0^n \frac{\chi(\delta v)}{\sqrt{n-v}} \, dv
\]
which is a Riemann integral and can be approximated by the following sum
\[
2 \left[ \chi(1)\sqrt{n} + \sum_{i=1}^{n-1} \sqrt{n-i}[\chi(i+1) - \chi(i)] \right].
\]
This sum can be implemented as the spreadsheet function `SUMPRODUCT()` applied to the previous terms in the sum. In the spreadsheet, each time interval of the integration is of the form of one or more `SUMPRODUCT()` functions that depend on the previous time steps. As more efficient implementations of this function become available, the usability of the spreadsheet will rise dramatically.

Different mechanisms, such as reversible electrochemical processes, EC or CE coupled equilibria, and so on correspond to different boundary conditions that produce different integrals. We have implemented each of the cases discussed by Nicholson and Shain in a separate
spreadsheet, with input fields for experimental parameters such as concentrations and temperature. Additional fields contain fitting parameters such as $E^\circ$ and $k_f$. Depending on the specific mechanism being modeled, different fitting parameters are available (e.g., in pre- or post-equilibria, $k_f$ and $k_b$ are included, but $k_b$ is meaningless in mechanisms with irreversible reactions). In several cases, the spreadsheet also contains columns for experimental data that the model can be compared to. These cases are discussed below in the context of worked examples involving data generated by our experiments. It is straightforward to add experimental data columns to the other spreadsheets; this is left as an exercise to readers whose experiments produce appropriate data.

**Worked examples with comparison to experiment**

The simplest CV experiment features a solute with fast electrode kinetics that is in reversible Nernstian equilibrium at the electrode. This case is modeled by the integral:

$$\sqrt{\delta} \int_{0}^{p} \frac{\chi(\delta v) dv}{\sqrt{p - v}} = \frac{1}{1 + \gamma \theta S_{\delta \lambda}(\delta p)}$$

(Note that we diverge from Nicholson and Shain's notation by the use $p$ instead of $n$ for the number of steps in the numerical integration. This avoids confusion with the use of $n$ for the number of electrons transferred in the reaction.), or the sum:

$$2\sqrt{\delta} \left[ \chi(1)\sqrt{p} + \sum_{i=1}^{p-1} \sqrt{p-i}[\chi(i+1) - \chi(i)] \right] = \frac{1}{1 + \gamma \theta S_{\delta \lambda}(\delta p)}$$

which can be solved for $\chi(at)$ where $at = nFvt/RT = (nF/RT)(E_i - E)$, by reduction to:

$$\frac{1}{2\sqrt{\delta}(1 + \gamma \theta S_{\delta \lambda}(\delta p))} \left[ \chi(1)\sqrt{p} + \sum_{i=1}^{p-2} \sqrt{p-i}\chi(i+1) - \sum_{i=1}^{p-1} \sqrt{p-i}\chi(i) \right] = \chi(\delta p)$$

In spreadsheet form, this corresponds to:

$$\chi(\delta p) = (1/((1+\Gamma*\Theta*S(\delta p))*2*SQRT(\delta)) - (\chi(\delta 1)*SQRT(\delta)) - SUMPRODUCT(\chi(\delta 1),\chi(\delta(p-1)),SQRT(p - (1:p-1))) - SUMPRODUCT(\chi(\delta 2),\chi(\delta(p-1)),SQRT(p - (1:p-2))))$$

where $\Gamma = SQRT(D_0/D_R)$, $\Theta = EXP((E_i - E^\circ)*n*F/(R*T))$, and $S(\delta p) = IF(p < \lambda , EXP(-\delta*p) , EXP(\delta*p - 2*\delta*p))$.

An archetypal reversible redox couple is the ferrocene/ferrocenium couple, which can be well fit by this model (Figure A1). The fitting parameters are the same at widely different scan rates, indicating that the correct model has been selected. The fit across multiple scan rates also indicates that the correct combination of parameters has been selected whereas a good fit at a single scan rate may not be unique or physically correct. This model also assumes that iR drop is not significant.
The reduction of TEMPO to TEMPOH (Scheme A1) involves a fast, irreversible chemical step (protonation) subsequent or coupled to electron transfer. This process can be modeled as an irreversible electrochemical reaction (Scheme A1b). The integral that is at the heart of this model

\[ 1 - \int_{0}^{bt} \frac{\chi(z)dz}{\sqrt{bt - z}} = (e^{u-bt})\chi(bt) \]

is

\[ e^u = \left( \frac{\sqrt{\pi D_0 b / k_s}}{k_s} \right) e^{[(\alpha n F / RT)(E_i - E_c)]} \]

and

\[ bt = (\alpha n F / RT)(E_i - E_c) \]

The corresponding sum is reduced as above, and in spreadsheet instructions is:

\[
\chi(\delta p) = (1 - 2\text{SQRT}(\delta) \ast (\text{SQRT}(p) \ast \chi(\delta 1) - \\
\text{SUMPRODUCT}(\chi(\delta 1) \ast \chi(\delta(p-1)) \ast \text{SQRT}(p - (1:p-1))) + \\
\text{SUMPRODUCT}(\chi(\delta 2) \ast \chi(\delta(p-1)) \ast \text{SQRT}(p - (1:p-2)))))/K(bt) \\
\]

where

\[ K(bt) = 2\text{SQRT}(\delta) + (\text{SQRT}(3.1415 * D_0 * b)/k_s) \ast \text{EXP}(\alpha n F (E - E_c)/(R T)) \]

As can be seen, \( E_c \) and \( k_s \) cannot be independently solved for without other information. Nonetheless, it is possible to fit this model to experimental data and extract a composite parameter that can constrain other experimental data (Figure A2). Other parameters such as \( D \) and \( \alpha \) can be determined unambiguously. Again, a good fit must be obtained at multiple scan rates with the only parameter that is adjusted being the scan rate itself.

**Scheme A1:** Proton-coupled reduction of TEMPO to TEMPOH can take place by either a) stepwise, or b) concerted processes.

a)

\[ \begin{align*}
O^+ & \overset{\text{e}^-}{\rightleftharpoons} N^+ \\
\text{E}_c & \overset{k_i}{\rightarrow} OH \\
\end{align*} \]

b)

\[ \begin{align*}
O^- & \text{e}^- \rightarrow N^- \\
\text{E}_c, k_i & \rightarrow OH \\
\end{align*} \]
An interesting phenomenon appears when a reversible electrochemical process is coupled to a chemical equilibrium. If the forward rate of the equilibrium is very slow or the reverse rate is very fast, there is no observable effect on the CV data regardless of the equilibrium constant. If the equilibrium strongly favors the reaction product, then it more resembles an irreversible reaction and should be modeled as such. However, if the equilibrium is composed of forward and reverse rates that are in a range compatible with CV study, the voltammogram will exhibit scan-rate dependent features. The integral and spreadsheet code to model this process are

\[
1 - \int_{0}^{at} \frac{\chi(z)dz}{\sqrt{at-z}} = \frac{1}{1 + K} \theta S_{a\lambda}(at) \int_{0}^{at} \frac{\chi(z)dz}{\sqrt{at-z}} + \frac{K}{1 + K} \theta S_{a\lambda}(at) \int_{0}^{at} \frac{e^{-(l/\alpha)(at-z)} \chi(z)dz}{\sqrt{at-z}}
\]

and:

\[
\chi(\delta p) = \chi(\delta(p-1)) + ((1 - (K*\text{SQRT}(3.1415))/((1 + K)*\text{SQRT}(k_f + k_b)))\Theta*\text{S}(\delta p)\chi(\delta(p-1))*\text{ERF}(\text{SQRT}(\delta p)*\text{SQRT}(p) + \text{SUMPRODUCT}(\text{ERF}(\text{SQRT}(\delta p)*\text{SQRT}(p - 1:(p-2)))))) - ((2*\text{SQRT}(\delta) + (2*\text{SQRT}(\delta)/(1 + K)))\Theta*\text{S}(\delta p))\chi(\delta(p-1)))/(2*\text{SQRT}(\delta) + ((2*\text{SQRT}(\delta)/(1 + K))\Theta*\text{S}(\delta p) + (K*\text{SQRT}(3.1415))/((1 + K)*\text{SQRT}(\delta))))
\]

where \( K \) is the equilibrium constant of the coupled chemical reaction and \( l \) is the sum of the forward and reverse rate constants \((k_f + k_b)\). In alkaline media, the compound TEMMO will reversibly react with hydroxide following oxidation in this fashion (Scheme A2). At very slow scan rates, the voltammogram will appear reversible but its \( E_{1/2} \) will be displaced from the \( E^\circ \) of the electrochemical step. At faster scan rates, the chemical equilibrium cannot keep pace with the changing electrochemical equilibrium and the CV trace is distorted. Concurrently, the \( E_{1/2} \) of the wave is shifted towards the \( E^\circ \) value. From fitting at multiple scan rates, it is possible to extract \( E^\circ, k_f, \) and \( k_b \) for the process (Figure A3).
Scheme A2: Electrochemical oxidation of TEMMO coupled to reversible nucleophilic addition of hydroxide.

Scheme A2: Electrochemical oxidation of TEMMO coupled to reversible nucleophilic addition of hydroxide.

\[ \begin{align*}
N^+ & \xrightleftharpoons[k_f]{E^0} N^+ + OH^- & k_b \\
& & k_{[OH^-]}
\end{align*} \]

Figure A3: CV of TEMMO in pH 12.4 phosphate buffer at 10, 50, and 400 mV/s. As the scan rate increases, the oxidation becomes less reversible. Experimental data are in red; the fitted model is in black. Fitting parameters are: \( E^0 = 835 \text{ mV}, D_O = D_R = 3 \times 10^{-6} \text{ cm}^2/\text{s}, k_{[OH^-]} = 1000 \text{ s}^{-1}, k_b = 40 \text{ s}^{-1}. \)

A reversible electrochemical reaction can be followed by an irreversible reaction whose rate is competitive with the time-scale of the CV experiment. The degradation of 4-oxoTEMPO following oxidation in aqueous media at moderate pH is such a process, where the voltammogram changes from appearing reversible at fast scan rates to clearly irreversible at slow scan rates (Scheme A3, Figure A4). This process can be modeled by the integral

\[ 1 - \int_0^{at} \frac{\chi(z)dz}{\sqrt{at-z}} = y\theta S_{ax}(at) \int_0^{at} e^{-(k_f/a)(at-z)} \frac{\chi(z)dz}{\sqrt{at-z}}, \]

which can be reduced to the spreadsheet code:

\[
\chi(\delta p) = \chi(\delta(p-1)) + ((1 - (\Gamma^*\text{SQRT}(3.1415)/(\text{SQRT}(k_f/a))))*\Theta*p*(\chi(\delta1)\text{ERF}(\text{SQRT}(\delta\psi)\text{SQRT}(p)) + \text{SUMPRODUCT}(\text{ERF}(\text{SQRT}(\delta\psi)\text{SQRT}(p - 1:(p-2))), (\chi(\delta2)-\chi(\delta1)))(\chi(\delta(p-2)) - \chi(\delta(p-1))))) - 2*\text{SQRT}(\delta1)*\text{SQRT}(p) + \text{SUMPRODUCT}(\text{SQRT}(p - 1:(p-2)), (\chi(\delta2)-\chi(\delta1)))(\chi(\delta(p-2)) - \chi(\delta(p-1))))/(2*\text{SQRT}(\delta) + (\Gamma^*\text{SQRT}(3.1415)/(\text{SQRT}(k_f/a))))*\Theta*p(\delta p)*\text{ERF}(\text{SQRT}(\delta\psi)))
\]

From fitting of experimental data, one can obtain \( E^0 \) and \( k_f \) for the process.

Scheme A3: Reversible oxidation of 4-oxoTEMPO in pH 4.63 acetate buffer coupled to the irreversible degradation of the oxoammonium cation.

\[ \begin{align*}
N^+ & \xrightleftharpoons[E^0]{H^+, k_f} N^+ + OH^- & \text{Degradation products}
\end{align*} \]
Figure A4: Fit to a CV of 4-oxoTEMPO in pH 4.63 aqueous 0.1 M acetate buffer at 10 mV/s, experimental data are in red; the fitted model is in black. Fitting parameters are: $E^\circ = 884$ mV, $D_O = D_R = 5 \times 10^{-6}$ cm$^2$/s, $k_f = 0.075$ s$^{-1}$.

At the present, it is possible to iteratively solve for fitting parameters by minimizing the RMS difference between the model and the data. However, due to the slow pace of each iteration step, this remains impractical in our implementation using the non-linear solvers implemented in spreadsheet programs that we have used for testing. Instead, manual fitting and parameter adjustment can give reasonably well-minimized data by exploiting the knowledge of the program operator. These performance limitations are justified by the portability of spreadsheets and the ease with which they can be inspected and extended by scientists who do not consider themselves computer programmers. All of the spreadsheets are implemented for reductive processes using polarographic sign conventions. The most direct way to use the spreadsheets to model oxidative processes and/or to fit data recorded with IUPAC sign conventions is to adjust the signs of data values and parameters as necessary when importing and exporting.

With these spreadsheets, as it always is in electrochemical modeling, it is up to the user to choose a model that is appropriate to the underlying chemistry. Otherwise, one moves from simulation into the realm of simulacrums, which can be described as accurate models of a hallucinatory reality. Therein, one can fit diverse models to the same data by using sufficiently absurd parameters. To guard against this blunder, the model that one chooses must be consistent with all the data, voltammetric and otherwise. If this is done, the parameters extracted from modeling are real and can be used to predict other reactivity, e.g. steady-state catalysis.

Appendix acknowledgement:
J.B.G. thanks Prof. Andrew Bocarsly for helpful discussions concerning CV simulation during a visit to his lab. These discussions included a highly motivating suggestion that it couldn't be done in a spreadsheet, which we took as a challenge.
References.


5. Although this may seem to be exactly what Joslin & Pletcher would have referred to as an "extravagant use of a computer" (cf. ref. 1a), circumstances have shifted to make the programmer's time more precious than the computer's.

6. The spreadsheets have been tested and used primarily in OpenOffice and LibreOffice, but were also exported to the appropriate file formats and found to work in Microsoft Excel and gnuplot.