

# Electrocatalytic Alcohol Oxidation with TEMPO and Bicyclic Nitroxyl Derivatives: Driving Force Trumps Steric Effects

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## 1. Experimental procedures

### General Considerations.

**Solvents and Reagents.** Deionized water and acetonitrile were used without purification. Keto-ABNO was synthesized and purified according to literature protocols,<sup>1</sup> while the other nitroxyl catalysts and five alcohol substrates (1-butanol, 2-butanol, benzyl alcohol, 1-phenyl ethanol, and neopentyl alcohol) were purchased from Sigma-Aldrich and used without further purification. The nitroxyl radicals that have been considered for this study includes: 1-Methyl-2-azaadamantane-N-oxyl (1-Me-AZADO), 2-Azaadamantane-N-oxyl (AZADO), 9-Azabicyclo[3.3.1]nonane N-oxyl (ABNO), Keto-ABNO (9-azabicyclo[3.3.1]nonan-3-one-N-oxyl), 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO), 4-methoxy-TEMPO (4-MeO-TEMPO), 4-acetamido-TEMPO (ACT), 4-Hydroxy-TEMPO benzoate (4-PhCO<sub>2</sub>-TEMPO) and 4-oxo-TEMPO.

**Cyclic voltammetry studies.** All cyclic voltammetric and chronoamperometric measurements were performed at room temperature using a Pine WaveNow PGstat. The experiments were carried out in a three-electrode cell configuration with a glassy carbon (GC) working electrode (3 mm diameter), a platinum wire counter electrode. The potentials were measured versus an Ag/AgCl reference electrode (all electrodes from BASi). The GC working electrode was polished with alumina before each experiment.

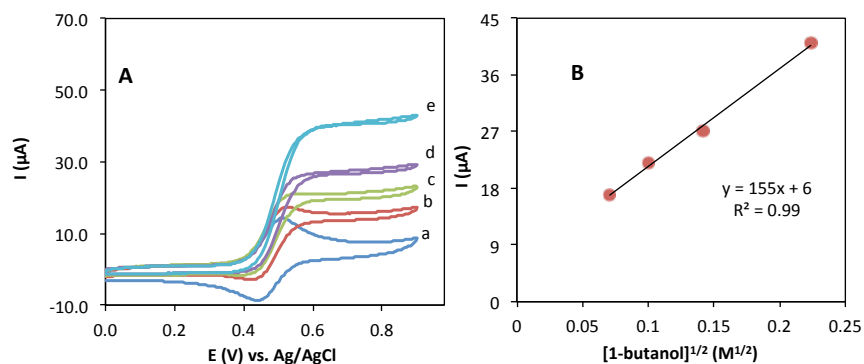
**Electrolysis reactions.** Bulk electrolysis experiments were performed in a 10 mL undivided cell, with two blocks of reticulated vitreous carbon (RVC) as the working electrode and a platinum wire counter electrode. The immersed area of the RVC electrode (48 cm<sup>2</sup>) was determined by capacitance measurement and comparison of the current relative to a glassy carbon disk electrode. Products were quantified by <sup>1</sup>H NMR using a Bruker 400 MHz *Avance III* spectrometer.

**Spectroelectrochemical experiments.** Spectroelectrochemical studies were performed in a thin-layer spectroelectrochemical cell from BASi, consisting of a thin-layer quartz cuvette (1mm path length), a platinum mini-grid working electrode, a platinum wire as counter electrode and an Ag/AgCl reference electrode. UV-visible spectra were obtained with a Varian Cary 50 Scan spectrophotometer.

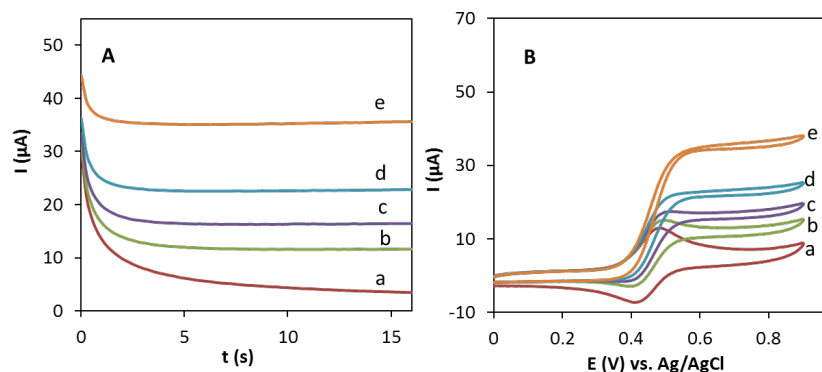
**Rotating disc voltammetry and cyclic chronoamperometry.** All electrochemical studies using a rotating disc electrode (RDE) (Pine, 5 mm diameter) attached to an electrode rotor (Pine) were performed in a 200 mL electrochemical cell vial (BASi).

## 2. Voltammetric and chronoamperometric data.

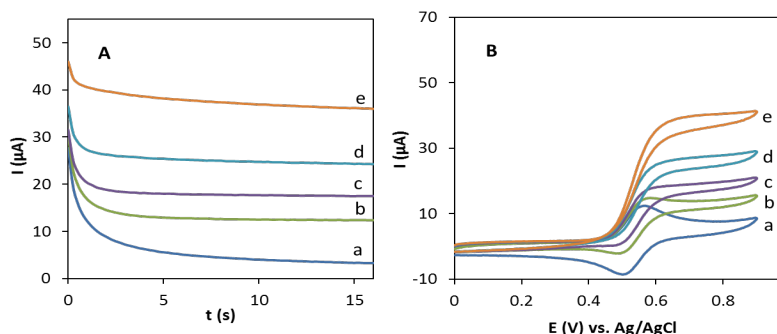
Cyclic voltammograms (CVs) and chronoamperograms (CAs) were obtained for each of the four nitroxyls (AZADO, ABNO, TEMPO and ACT) in the absence and presence of each of the five alcohol substrates at pH values of 8, 9, 10, 11, 12 and 13. Figure S1A shows CV data for ABNO complementing the CA data presented in Figure 2A of the manuscript, and Figure S1B shows that the catalytic current obtained from the CVs exhibits a linear dependence on the square root of the 1-butanol concentration, complementing the same trend derived from the CA data (cf. Figure 2B in the manuscript). Representative CV and CA data for each of the other three nitroxyls (AZADO, TEMPO and ACT) with 1-butanol at pH 10 are shown in Figures S2-S4.



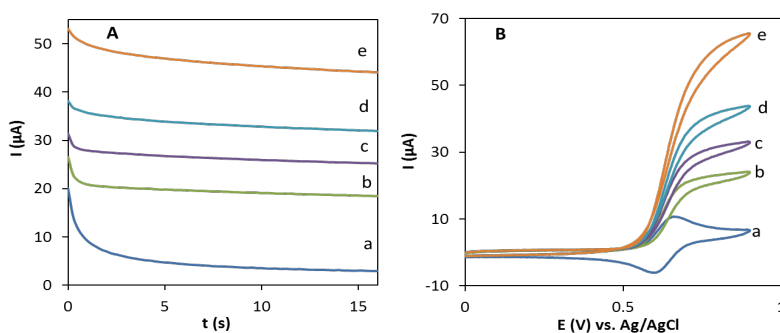
**Figure S1.** A) CVs of ABNO (1 mM) in the absence (a) and presence of 1-butanol at 5 mM (b), 10 mM (c), 20 mM (d) and 50 mM (e) concentrations in  $\text{HCO}_3^-/\text{CO}_3^{2-}$  electrolyte (pH=10). B) Plot of the anodic peak current vs  $[1\text{-butanol}]^{1/2}$ .



**Figure S2.** CAs (A) and CVs (B) of AZADO (1 mM) in the absence (a) and presence of 1-butanol at 5 mM (b), 10 mM (c), 20 mM (d) and 50 mM (e) concentrations in  $\text{HCO}_3^-/\text{CO}_3^{2-}$  electrolyte (pH=10).



**Figure S3.** CAs (A) and CVs (B) of TEMPO (1 mM) in the absence (a) and presence of 1-butanol at 5 mM (b), 10 mM (c), 20 mM (d) and 50 mM (e) concentrations in  $\text{HCO}_3^-/\text{CO}_3^{2-}$  electrolyte (pH=10).

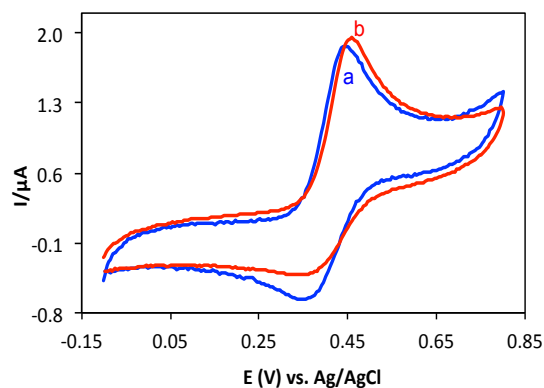


**Figure S4.** CAs (A) and CVs (B) of ACT (1 mM) in the absence (a) and presence of 1-butanol at 5 mM (b), 10 mM (c), 20 mM (d) and 50 mM (e) concentrations in  $\text{HCO}_3^-/\text{CO}_3^{2-}$  electrolyte (pH=10).

### 3. Bulk Electrolysis reactions (cf. Table 2).

Suitable amounts of catalyst and alcohols were added to  $\text{HCO}_3^-/\text{CO}_3^{2-}$  electrolyte (pH=10) in the electrolysis cell, and the mixture was electrolyzed at a potential of 100 mV higher than the oxidation peak potential of the nitroxyl radical. The electrolysis was terminated when the current decayed by 98% relative to the initial current. After acidification of the solution with 6.0 M HCl, the reaction mixture was extracted with  $\text{CHCl}_3$ .

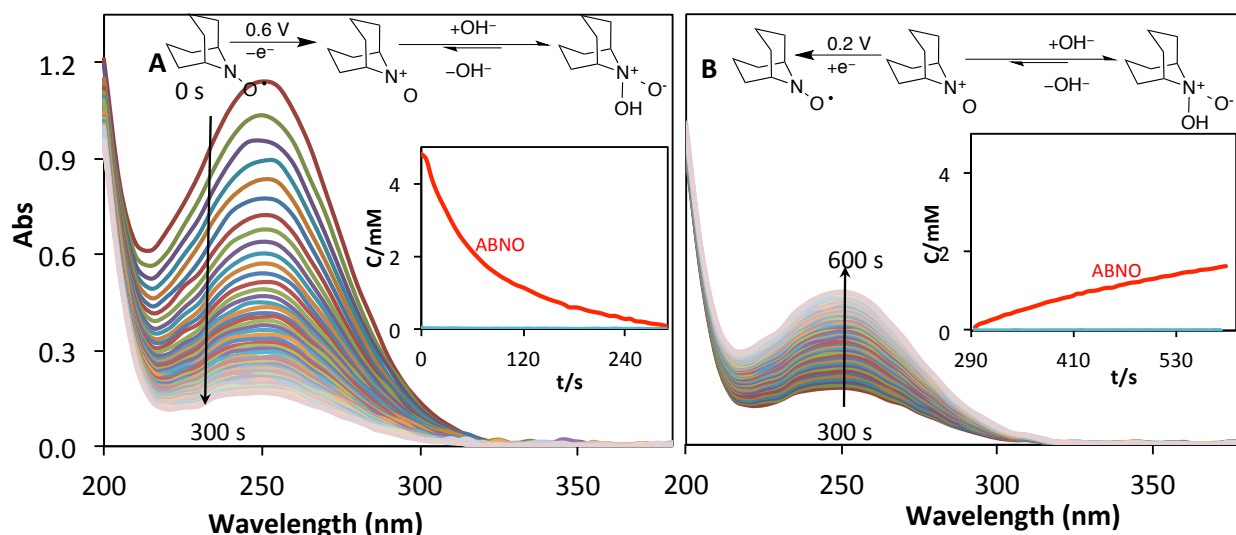
### 4. Scan-rate effects on the reversibility of ABNO/ABNO<sup>+</sup> at pH 11.



**Figure S5.** Normalized-current CVs (i.e., current divided by the square root of scan rate) of 1.0 mM ABNO in  $\text{HCO}_3^-/\text{CO}_3^{2-}$  electrolyte (pH=11) at two scan rates (a)  $10 \text{ mVs}^{-1}$  and (b)  $100 \text{ mVs}^{-1}$ , showing that by increasing the scan rate, thereby decreasing the experiment time scale, the height of the reduction peak decreases.

## 5. Spectroelectrochemical studies.

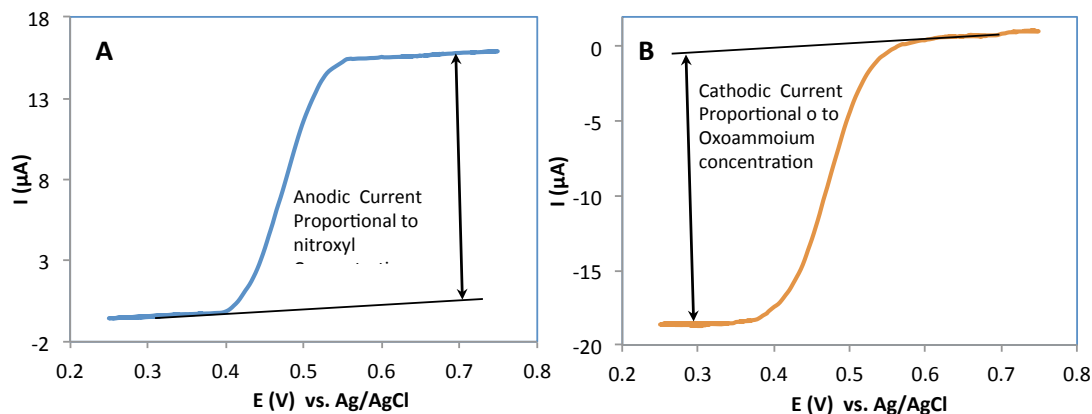
Spectroelectrochemical studies (see Figures 5, 6, and S6) were performed in a thin-layer quartz electrochemical cell by applying a potential step of 150-180 mV higher than the oxidation peak potential of the nitroxyl and recording UV-visible spectra for 5 min during the electrolysis. The electrochemical oxidation was followed by electrochemical reduction by applying a potential 150-180 mV lower than the reduction peak potential of the oxoammonium and recording UV-visible spectra for 5 min during the reductive electrolysis. The 6 s time interval was used between each spectrum. The concentration profile of ABNO and ABNO<sup>+</sup> concentrations were derived from fitting of time-course spectra using spectra from independently prepared samples of ABNO and ABNO<sup>+</sup>. The concentration profiles of ABNOOH were derived by subtraction of ABNO and ABNO<sup>+</sup> concentrations from initial analytical concentration of ABNO.



**Figure S6.** Spectra collected during oxidation of ABNO (A) in  $\text{HCO}_3^-/\text{CO}_3^{2-}$  electrolyte (pH 12.1) at 0.6 V vs. Ag/AgCl for 300 s (time interval 6 s), immediately followed by reduction of the in situ generated ABNO<sup>+</sup> (B) at 0.2 V vs. Ag/AgCl for 300 s (time interval 6 s). Insets: Concentration profiles of ABNO during electrochemical oxidation (A) and reduction (B).

## 6. Chronoamperometric analysis of solution of nitroxyls in the presence of bleach.

Nitroxyl speciation in reactions with bleach were analyzed in the absence and presence of 1-butanol by cyclic chronoamperometry. Linear sweep voltammograms or cyclic chronoamperograms were recorded using a RDE. For cyclic chronoamperometric experiments, multiple potential steps were applied to the RDE immersed in aqueous solutions containing nitroxyl/bleach/ $\text{NaHCO}_3$  or nitroxyl/bleach/ $\text{NaHCO}_3$ /1-butanol (see figure captions below for detailed conditions). The potential at the RDE was alternated between approximately 180 mV above and 180 mV below the midpoint potential of the nitroxyls, the potentials correspond to the plateau current of RDE. The current was monitored for 3 s at each potential step to ensure a steady-state faradaic current value was reached, and this steady-state value was used to determine the [nitroxyl] and [oxoammonium] relative to stock solutions of known concentrations of these species.

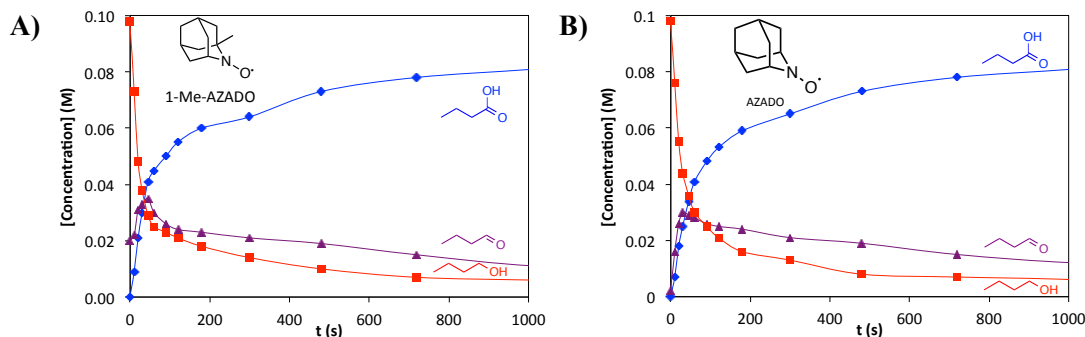


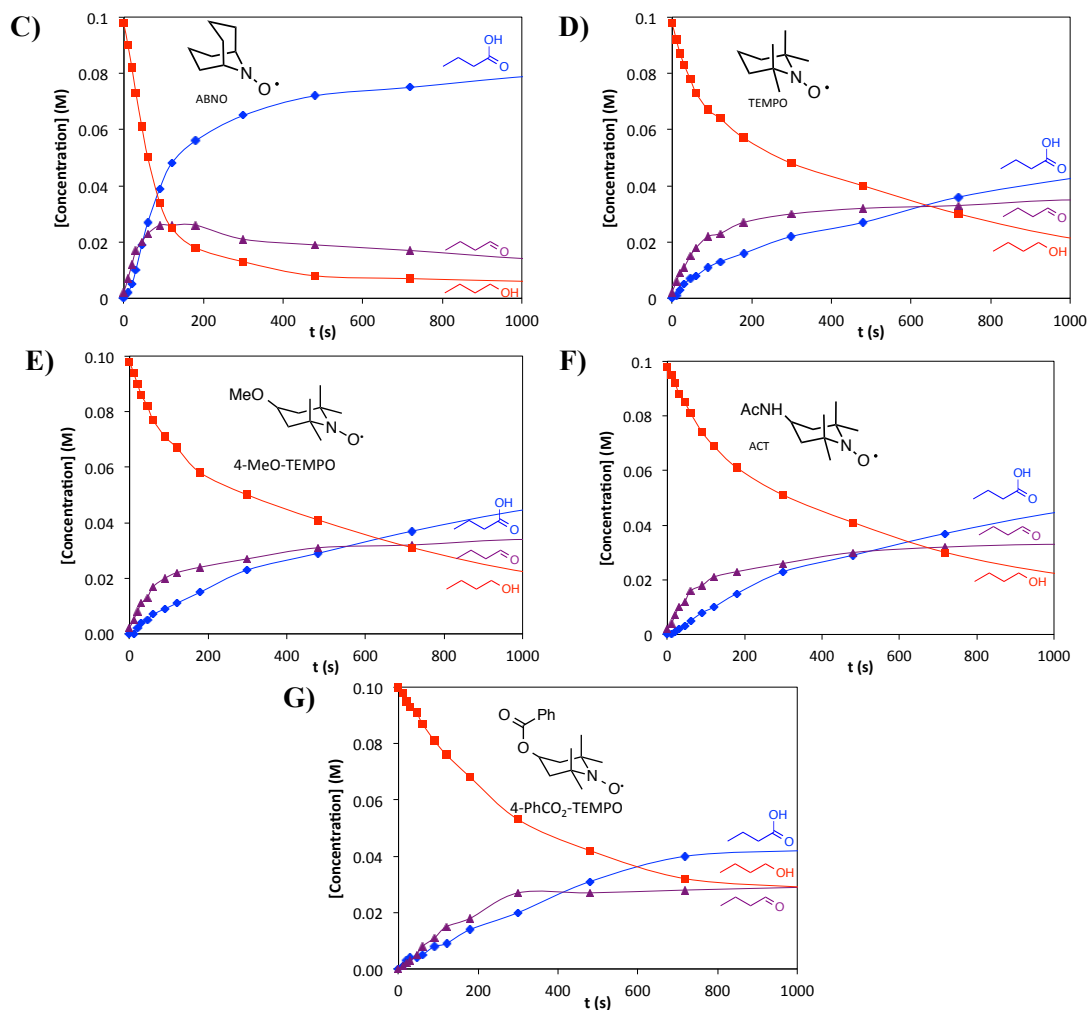
**Figure S7.** (A) Linear sweep voltammogram of a 160 mL solution of 1.0 mM TEMPO, NaHCO<sub>3</sub> 0.15 M (pH 8), recorded using a rotating disc electrode (scan rate 10 mV s<sup>-1</sup>, rotation rate 1000 rpm). (B) Linear sweep voltammogram of a 160 mL solution of 1.0 mM TEMPO<sup>+</sup>, obtained as the product of oxidation of TEMPO (1.0 mM) by bleach (0.1 M) in aqueous NaHCO<sub>3</sub> 0.15 M (pH 8), using a rotating disc electrode (scan rate 10 mV s<sup>-1</sup>, rotation rate 1000 rpm).

### 7. Time-course analysis oxidation of nitroxyl-catalyzed oxidation of 1-butanol by bleach

Time-course data for nitroxyl-catalyzed 1-butanol oxidation by bleach were acquired under the same conditions used to obtain chronoamperometric data. Aliquots of the reaction mixture were removed, and analyzed by <sup>1</sup>H NMR spectroscopy. In a typical experiment, 1-butanol (16 mmol) was added to a solution of bleach (32 mmol), and NaHCO<sub>3</sub> (32 mmol) in deionized water (160 mL), and the reaction was initiated by addition of the nitroxyl (0.8 mmol dissolved in 1 mL acetonitrile). The solution was mixed by using the RDE (2000 rpm; without applied potential) to simulate the condition of the CA experiments, for 4-PhCO<sub>2</sub>-TEMPO mediated oxidation mixture of acetonitrile/water (25/75) has been used instead of water because 4-PhCO<sub>2</sub>-TEMPO is not water soluble. Aliquots of the reaction mixture (1 mL) were withdrawn at the desired time points, and the sample was quenched by addition of acidic brine (1 mL; 1 M HCl/sat'd NaCl) and extracted with CDCl<sub>3</sub> (0.5 mL). The CDCl<sub>3</sub> solution was analyzed by <sup>1</sup>H NMR spectroscopy. The time courses obtained in this manner from reactions with each of the seven nitroxyls are shown in Figure S8.

**Relative Rates:** Me-AZADO > AZADO > ABNO > TEMPO > 4-MeO-TEMPO > ACT > 4-PhCO<sub>2</sub>-TEMPO  
 $k_{\text{obs}} \text{ (s}^{-1}\text{)} = 0.0251 \quad 0.0232 \quad 0.0112 \quad 0.0051 \quad 0.0033 \quad 0.003 \quad 0.0027$





**Figure S8.** Concentration profile of 1-butanol and its resulted oxidation products, butanal and butanoic acid, (initial concentration of 1-butanol 0.1 M) during oxidation by bleach (0.2 M) mediated by 1-Me-AZADO (A), AZADO (B), ABNO (C), TEMPO (D), 4-MeO-TEMPO (E), ACT (F) and 4-PhCO<sub>2</sub>-TEMPO (G), nitroxyl radical concentrations 5 mM, 160 mL NaHCO<sub>3</sub> 0.2 M (pH 8.3).

Data for the linear free-energy correlation shown in Figure 10 of the manuscript were obtained in the manner described here, with the rate constants based on initial rate determination for the reaction at pH 8.3.

## 8. Reference

1. Sonobe, T.; Oisaki, K.; Kanai, M. *Chem. Sci.* **2012**, *3*, 3249.