Communication

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J. Am. Chem. Soc., **Just Accepted Manuscript** • Publication Date (Web): 12 Jun 2014

Proton-Coupled Electron Transfer in Azobenzene-Hydrazobenzene Couples with Pendant Acid-Base Functions. Hydrogen-Bonding and Structural Effects

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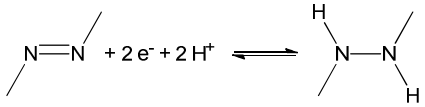
ABSTRACT. Electron transfer in azobenzene derivatives bearing two carboxylic acid groups is coupled with intramolecular proton transfer in a stepwise manner in the title $2e^- + 2H^+$ redox couple. The presence of the pendant acid-base functions pushes the redox chemistry of the azo/ hydrazo couple toward positive potentials by as much as 0.75 V. This is essentially the result of H-bonding of one of the nitrogen atoms by the neighboring carboxylic group and H-bonding of one carboxylate by the neighboring protonated nitrogen atom. The two electron transfer reactions, particularly, the second one, are accompanied by strong structural changes, which results in the occurrence of a square scheme mechanism in which electron transfer and structural change are not concerted. These are typical phenomena that are likely to be encountered when attempting to boost proton-coupled electron transfer stoichiometric or catalytic processes by installing pendant acid/ base functionalities in the close vicinity of the reacting center.

There are several reasons for the longstanding interest aroused by azo/ hydrazo couples:



One resorts to the general scheme of N-N multiple bonds activation. A seminal example is the electrochemical reduction of the nitrogen molecule (N_2) into ammonia (NH_3) as one of the most arduous challenges for contemporary chemistry.[1] This $6e^- + 6H^+$ reaction has attracted much attention over the past decades, particularly due to the fact that biological N_2 fixation can be performed at ambient pressure and temperature by nitrogenase enzymes, with a heterometallic iron/molybdenum/sulfur/carbon cluster active.[2] The need for mechanistic studies for the strong N-N triple bond activation is thus imperative to unravel general trends towards the design of new types of electrocatalysts.[3]

Another series of motives deal with the microbial degradation of azo dyes. In biology, azoreductases are enzymes that catalyze the $4e^- + 4H^+$ anaerobic reduction of azobenzene derivatives by the conversion of azo bonds to aniline moieties. This enzymatic reaction is important considering detoxification of azo dyes produced by the textile industry [4] and activation of anti-inflammatory azo pro-drugs.[5] In these systems, the bond cleavage requires two reductive cycles with the reduction of FMN to $FMNH_2$ by NADPH to give the hydrazo intermediate in the first step and release aniline in a second reductive step.[6] Research activities are thus focusing on the design of novel dyes/ pro-drugs where the biodegradability (i.e. the cleavage of the azo bond by azoreductases) is adjusted by the chemical structure of the molecule.[4c]

The electrochemistry of azo/ hydrazo couples, and specifically the azobenzene/ hydrazobenzene couple has been investigated since a long time,[7,8,9,10,11,12,13] mostly by means of cyclic voltammetry in aprotic media (acetonitrile and N,N' dimethylformamide (DMF)), with the aim of assessing the number of electron transfer reactions, their degree of reversibility and the role of added Brönsted acids. The latter aspect is at the origin of our interest in the electron transfer chemistry of azobenzene/ hydrazobenzene couples in the framework of proton coupled electron transfer (PCET) reactions.[14] More specifically, the present work concerns the role of proximal acid/ base couples attached to the same structure as the PCET substrate: do they act as H-bonds promoters and/ or proton donors? This question is currently attracting active attention in the framework of stoichiometric [15,16,17,18] and catalytic reactions connected with the resolution of modern energy challenges.[19,20]

The structures of the azobenzene and hydrazobenzene that we investigated are shown in Chart 1. They correspond to the compounds noted **A1** and **C3** in the mechanistic Scheme 1.

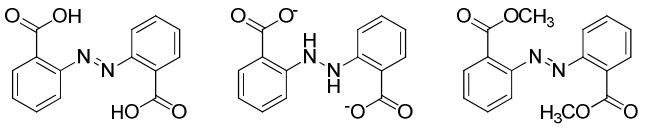
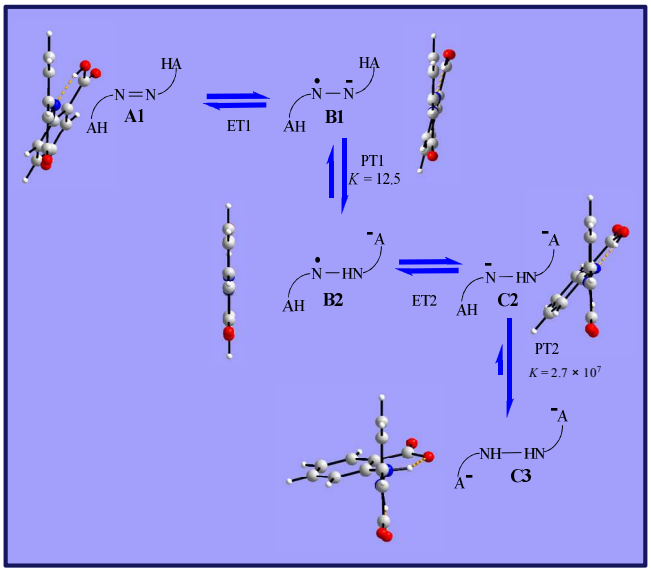


Chart 1. Structure of the azobenzene (**A1**) and hydrazobenzene (**C3**) molecules bearing with the attached carboxylic and carboxylate groups, respectively and of the methyl ester of **A1** (**A-Me**).

The cyclic voltammetric responses (see the Supporting Information (SI) for experimental details) observed at low scan rate (figure 1) confirm that the azo and hydrazo compounds are redox partners: the reverse CV trace of the azo compound is similar to the forward trace of the hydrazo compound and *vice versa*. Each of the two compounds exhibits two waves, with the first close to be reversible, as do the simple azo and hydrazo benzenes in similar conditions.[7,9,10,11] This is also the case for the methyl ester of the azo compound (figure 1). The reduction potentials of **A1** and oxidation potentials of **C3** are however considerably shifted toward positive values, by *ca* 800 mV, as compared to **A-Me** or to the simple azo- and hydrazo- benzenes. Since inductive effects are expected to be of the same order of magnitude in **A1** and **A-Me**, it appears that the presence of the two carboxylic groups in **A1** and carboxylate groups in **C3** is responsible for this huge change of the redox chemistry of the azo/ hydrazo couple, therefore likely to be due to intramolecular proton transfer and/ or intramolecular hydrogen bonding.

Among the nine possible intermediates (see SI) of the two-



Scheme 1. Mechanistic reaction scheme including the electron and proton transfer steps together with views of each molecule showing their degree of torsion around the N-N bond.

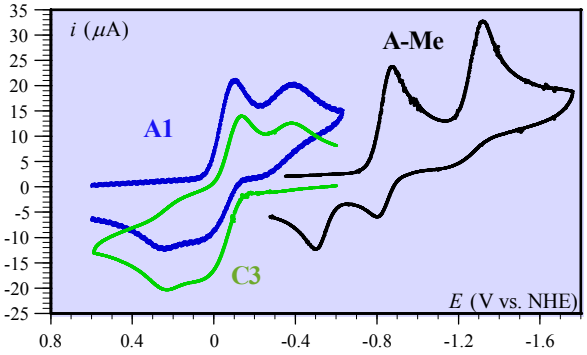
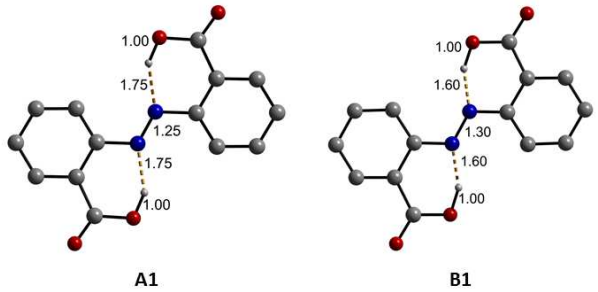


Fig. 1. Cyclic voltammetry of 1 mM **A1**, **C3** and **A-Me** (see Chart 1) in in DMF + 0.1 M *n*-NBu_4BF_4 at 0.2 V/s.

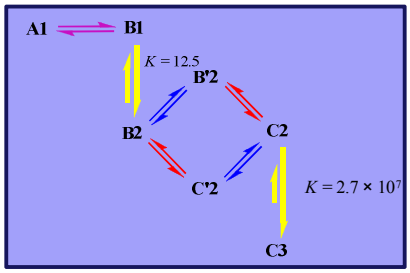
proton and two-electron transfers, Density Functional (DFT) calculations (see SI) revealed that only the intermediates shown in Scheme 1 are not too unreasonably high in energy to partake in the reaction, leading to a classical "ECEC" mechanism,[21] or even a classical "ECE mechanism" since the last step is likely to be slow enough to be neglected within the time scale of cyclic voltammetry as discussed below. We may thus assign (see figures 1 and 2) the first group of waves to the reduction of **A1** to **B2** (and reverse oxidation) and the second group of waves to the reduction of **B2** to **C3** (and reverse oxidation). The DFT calculations also indicate that the anion radical **B2**, which derives from **B1** by the transfer of the proton of one carboxylic group to the neighboring nitrogen atom, is only slightly more stable than its parent (equilibrium constant 12.5). This proton transfer is likely to be rapid in both directions because the structure does not change much from **B1** to **B2**. It follows that the protonation reaction counts for *ca* 60 mV in the shift of the reduction potential over a total value of 800 mV. The total stabilization of the anion radicals by H-bonding thus reaches the very large value of 740 mV. It involves H-bonding of one of the nitrogen atom by the neighboring carboxylic group in **B1** and H-bonding of one carboxylate by the neighboring protonated nitrogen atom in **B2**. It is interesting to note that the large increase of the strength of H-bonding from the starting azo compound, **A1**, to the anion radical **B1** is the result of the change of molecular structure accompanying electron transfer that makes the distance between the each nitrogen atom and the hydrogen atom of the proximal carboxylic acid pass from 1.75 to 1.60 Å while the O-H distance in the carboxylic groups remains almost constant (Scheme 2).



Scheme 2. Variation of the H-bonding distances (in Å) upon electron transfer from **A1** to **B1** (gray: carbon; red: oxygen; blue: nitrogen).

Another important remark derives from the quasi-absence of H/D isotope effects. The CV responses are indeed almost the same in the presence of 1 % CH_3OH and 1 % CD_3OD (see SI). The small changes may be attributed to marginal thermodynamic effects. It may thus be concluded from this absence of kinetic H/D isotope effect that the coupling between proton and electron transfer follows stepwise pathways rather than concerted pathways [14] as sketched in Scheme 1 (concerted pathways would imply going directly from **A1** to **B2** and from **B2** to **C3**).

The DFT calculations also showed (see inserts in Scheme 1) that the radical anions (compounds **B** in Scheme1) are almost planar, whereas the starting azo compound exhibits torsion around the N=N bond. This is much more pronounced in the dianions (compounds **C** in Scheme 1). It follows that we must envisage that electron transfer ET2 may not be a single step process in which the accompanying strong structural change would not be concerted with electron transfer but would involve discrete intermediates [22] as shown in Scheme 3. **B'2**



Scheme 3. Stepwise and concerted mechanisms in the reactions where electron transfer is accompanied by a strong structural change. Blue: electron transfers with little structural changes, red: structural changes, magenta: electron transfer concerted with a modest structural change, yellow: proton transfer. The values of the equilibrium constants shown in the diagram were obtained from DFT calculation (see SI).

The **C2** to **C3** reaction albeit thermodynamically favorable may be neglected within the cyclic voltammetric time scale since it is likely to be very slow in view of the considerable change of structure it involves.

We may finally attempt to simulate the CV responses obtained as various scan rates that are reported in left figure 2. The main trends of the CV responses as a function of the scan rates are reproduced by simulation of Scheme 1, completed by Scheme 2 for the values of the thermodynamic and kinetic constants listed in Table 1. [23]

Table 1. Constants for simulation according to Schemes 1 and 2.

Reaction	Thermodynamic and kinetic constants [a]
ET1 **A1** ⇌ **B1**	E^o = 0.002, α = 0.5, k_S = 0.006
PT1 **B1** ⇌ **B2**	K = 13, $k_f = 10^{10}$, $k_b = 8\times10^8$
ET2	
B2 ⇌ **B'2**	E^o = -0.42, α = 0.5, k_S = 0.001
B'2 ⇌ **C2**	$K = 10^3$, $k_f = 10^6$, $k_b = 10^3$
C'2 ⇌ **C2**	E^o = -0.13, α = 0.5, k_S = 0.002
B2 ⇌ **C'2**	$K = 3\times10^{-2}$, $k_f = 10^3$, $k_b = 3.6\times10^6$

a: standard potentials in V vs. NHE, standard rate constant in cm s^{-1}, first order homogeneous rate constants in s^{-1}.

In summary, three main conclusions emerge from the present study. (i) The mutual $2e^-$ + $2H^+$ of the azo/ hydrazo couple involves the intramolecular displacement of the protons born by the pendant carboxylic/ carboxylate functionalities placed in the vicinity of the azo/ hydrazo group. These intramolecular electron and proton transfers occur in a stepwise manner, rather than concertedly. (ii) The presence of the pendant carboxylic/ carboxylate functionalities in the vicinity of the azo/ hydrazo N-N group produces a considerable positive shift in the characteristics standard potentials, as large as *ca* 0.75 V. Rather that being caused by intramolecular proton transfer, this is essentially the result of H-bonding of one of the nitrogen atoms by the neighboring carboxylic group and H-bonding of one carboxylate by the neighboring protonated nitrogen atom. (iii) Intramolecular proton-coupled electron transfer in these molecules is accompanied by considerable structural changes. Injection of one electron into the initially distorted azo compound flattens out the molecule. The resulting anion radical keeps the same geometry after intramolecular migration of one proton to one of the nitrogen of the azo group. The most dramatic distortion however occurs upon injection of a second electron and intramolecular displacement of one proton. Migration of the second proton produces an even more distorted di-anion. (iv) These strong structural changes have important mechanistic and kinetic consequences. While during the first electron uptake, the change in structure seems to occur concertedly with electron transfer, this is not the case during the second electron transfer, which involves a much larger distortion of the molecular frame. In this case, the reaction occurs according to a square-scheme mechanism, which involves as intermediates a di-anion that has the same flat structure as the initial anion radical and an anion radical that has the same distorted structure as the final di-anion.

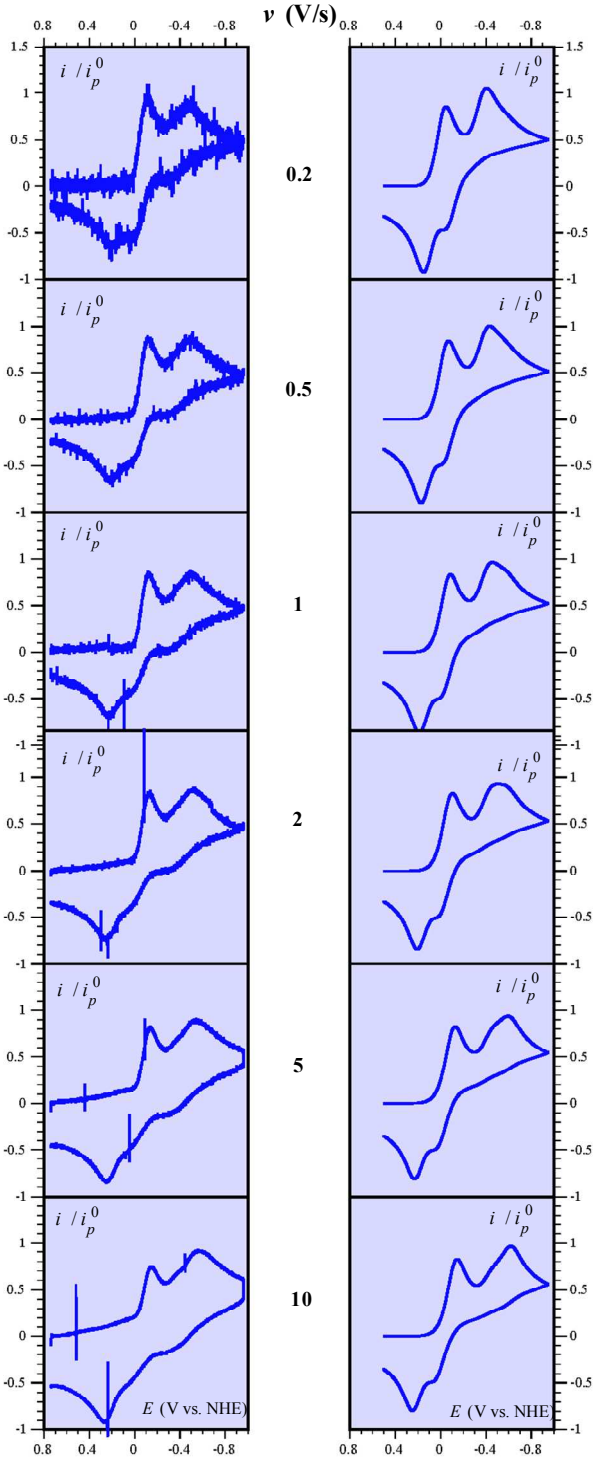


Fig. 2. Cyclic voltammetry of 1 mM **A1** in DMF + 0.1 M *n*-NBu_4BF_4 as a function of the scan rate. Left: experimental, right: simulated (see text and Table 1). The current is normalized toward the peak current of a one-electron reversible Nernstian wave $i_p^0 = 0.446\, FSC^0\sqrt{D}\,\sqrt{Fv/RT}$ (v: scan rate in V/s, S: electrode surface area, 0.07 cm^2, C^o: azobenzene concentration, 1 mM)

We hope that these findings will help understanding the numerous existing attempts to boost PCET stoichiometric or catalytic processes by installing pendant acid/ base function-

alities in the close vicinity of the reacting center and devising new such systems.

ACKNOWLEDGMENT. Aurélie Perrier-Pineau and Arnaud Fihey are gratefully thanked for helpful advice and suggestions on the DFT calculations.

SUPPORTING INFORMATION. Experimental details, DFT calculations procedures.

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23. The simulations do not reproduce exactly the experiments in terms of vertical location of the second waves. This often happens, probably as the result of the diffusion regime at a glassy carbon electrode is not exactly a linear diffusion regime as assumed in the simulations. It is reassuring reassured that the shape (splitting-overlapping) and location of the second wave system are well reproduced by the simulations.

SYNOPSIS TOC