Theoretical exploration of 2,2’-bipyridines as electro-active compounds in flow batteries

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Abstract

Compounds from the 2,2’-bipyridine molecular family were investigated for use as redox-active materials in organic flow batteries. For 156 2,2’-bipyridine derivatives reported in the academic literature, we calculated the redox potential, the pK a for the first protonation reaction, and the solubility in aqueous solutions. Using experimental data on a small subset of derivatives, we were able to calibrate our calculations. We find that functionalization with electron-withdrawing groups leads to an increase of the redox potential and to an increase of the molecular acidity (as expressed in a reduction of the pK a value for the first protonation step). Furthermore, calculations of solubility in water indicate that some of the studied derivatives have adequate solubility for flow battery applications. Based on an analysis of the physiso-chemical properties of the 156 studied compounds, we down-select five molecules with carbonyl- and nitro-based functional groups, whose parameters are especially promising for potential application as negative redox-active material in organic flow batteries.

Keywords:

Flow batteries have received significant attention in recent years due to the promise of delivering low-cost energy storage solutions for large-scale applications such as the integration of intermittent renewable generation sources and the deferral of transmission and distribution infrastructure investments.[1] As opposed to sealed batteries (e. g. lithium-ion batteries), the active materials in flow batteries are liquid electrolytes that are stored in separate storage tanks for the positive and negative electrolytes. These electrolytes are flown to an electrochemical reactor (the ”stack”), in which the electrolytes can be charged or discharged. The power capacity (unit: kW or MW) of the flow battery is determined by the available electrochemical surface area in the battery stack, whereas the energy capacity (unit: kWh or MWh) is defined by the characteristics of the liquid electrolytes (electrolyte volume, concentration of the redox-active compounds, cell voltage). State-of-the-art flow battery electrolytes are aqueous due to the low cost of water as a solvent and due to the compatibility of aqueous electrolytes with stack components. In particular, the ion-exchange membranes in the stack —that separate the positive and negative compartments in the electrochemical cell repeat unit preventing the positive and negative electrolytes from mixing— are typically less selective when in contact with non-aqueous solvents. A review on the progress on flow battery stack and system configurations as well as flow battery electrolytes can be found in references.[2, 3, 4]

In spite of the significant progress in flow battery development over the past two decades, the two most mature flow battery technologies —based on the all-vanadium and zinc-bromine chemistries— are facing intense competition from increasingly cheaper lithium-ion batteries.[5] The main reasons for flow batteries not yet having fulfilled their promise are the high cost of (electro-active) materials and/or the high cost to engineer systems that deploy corrosive electrolytes.[5] As a consequence, a quest for low-cost and non-corrosive electrolytes has directed many researchers

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to investigate organic molecules for use as low-cost flow battery redox couples. The advantages of this molecular flow battery approach over traditional electrolytes are multi-fold. First and foremost, molecular redox-active compounds have the potential to be produced from low-cost and earth-abundant resources, allowing for massive-scale deployment of energy storage systems at low cost. Furthermore, the flexibility in varying the molecular composition allows for tailoring of the physicochemical properties. For instance, by adding electron-donating or electron-withdrawing functional side groups, it has been shown that the standard redox potential \( (E^0) \) of the molecular compounds can be shifted.\([6]\) A tunable redox potential allows one to maximize the cell voltage (within the window of electrochemical stability of the aqueous solvent) resulting in the optimization of the electrolyte energy density. Additionally, functionalization of organic molecules with polar side groups can increase the solubility in water, potentially resulting in higher electrolyte energy densities as well. Also, the tailoring of the molecular size can impact the net charge of the redox-active compounds. Such molecular modifications can result in more selective operation of the ion-exchange membranes within the flow battery stacks due to enhanced steric or electrostatic exclusion.\([7, 8]\) Finally, using organic redox-active compounds potentially enables non-corrosive electrolytes. As opposed to metallic redox-active ions (such as vanadium ions), organic molecules are often soluble over a wide pH range, potentially allowing for flow battery operation in neutral pH conditions.

An important aspect of the above-mentioned exploration of novel molecular flow battery redox couples is the deployment of computational techniques to expedite the down-selection of promising new redox compounds. Synthesis, electrochemical evaluation, and cell testing are all costly activities and as such, theoretical screening can be helpful in targeting only the most promising new compounds. In particular, it has been shown that the addition of electron-donating or electron-withdrawing moieties can have a profound effect on the electrochemical and chemical properties of molecules. Specifically, calculations are performed to evaluate the redox potential, the solubility and the electrochemical and chemical stability as a function of molecular configuration. These parameters have been explored in high-throughput calculations in which ”molecular sieve” techniques are used to identify especially promising compounds within large molecular spaces.\([9, 10]\) Alternatively, computational techniques (\( e.g. \) Density Functional Theory, DFT, calculations) are performed on a relatively small number of predefined molecular derivatives (10 -100) to calculate the parameters of interest.\([6, 11, 12, 13, 14, 15]\) To date, computational approaches have been utilized to guide research efforts in identifying benzoquinone,\([14]\) anthraquinone,\([6, 9, 11]\) thiophenoquinone,\([10]\) alloxazine,\([12]\) and 4,4’-bipyridinium\([9, 13]\) derivatives with enhanced properties for use in flow batteries.

The above-mentioned advantages of organic redox couples and recent advances in computational techniques have resulted in an extensive exploration of organic molecules for use in flow battery applications. As negative redox-active compounds, several molecular families has been studied including quinones (\( e.g. \) benzoquinones, naphtoquinones, and anthraquinones),\([6, 9, 11, 10, 16, 14, 15, 17]\) alloxazines,\([12]\) and bipyridiniums.\([9, 7, 18, 19, 20, 21, 13, 22, 3, 8, 23, 24]\) As for the positive electro-active compounds, academic studies have focused on TEMPO-derivatives,\([7, 19, \)
Proton-Coupled Electron Transfer (PCET)  

Electron Transfer (ET)

\[
\begin{align*}
\text{Bpy} & \quad + e^- & \quad \text{Bpy}^- & \quad + e^- & \quad \text{Bpy}^{2-} \\
+ \text{H}^+ & \quad \rightarrow & \quad 1 & \quad + 1/2 \text{H}_2 & \quad \rightarrow & \quad \text{C} & \quad 2C & \quad \rightarrow & \quad \text{E} \\
\text{H}\text{Bpy}^+ & \quad \rightarrow & \quad \text{3} & \quad \rightarrow & \quad \text{HBpy} & \quad \rightarrow & \quad \text{4} & \quad \rightarrow & \quad \text{HBpy}^- \\
+ \text{H}^+ & \quad \rightarrow & \quad \text{B} & \quad \rightarrow & \quad \text{3B} & \quad \rightarrow & \quad \text{D} & \quad + 1/2 \text{H}_2 & \quad \rightarrow & \quad \text{F} \\
\text{H}_2\text{Bpy}^{2+} & \quad \rightarrow & \quad \text{5} & \quad \rightarrow & \quad \text{H}_2\text{Bpy}^+ & \quad \rightarrow & \quad \text{6} & \quad \rightarrow & \quad \text{H}_2\text{Bpy} \\
\end{align*}
\]

Figure 2: All possible reactions for the various pH-independent electron transfer (reactions 1-6), and pH-dependent proton (reactions A-F) and proton-coupled electron transfer (reactions 1A, 2C, 3B, and 4D) processes that occur in 2,2'-bipyridines.

20, 3, 23] with TEMPO being (2,2,6,6-tetramethylpiperidin-1-yl)oxyl.

Bipyridines are considered an especially attractive class of redox compounds for the negative electrolyte in flow batteries. In the flow battery literature, all theoretical and experimental work has focused on 4,4'-bipyridine derivatives. The baseline molecule in flow battery studies is methyl viologen (MV, dimethyl 4,4'-bipyridine),[7, 18, 22] a molecule that has been used as redox indicator and in opto-electronic applications.[25] As can be seen in Figure 1a, the oxidized form of the molecule (MV$^{2+}$) has a net charge of 2$^+$ and a first reduction step (at $-0.45$ V vs. the normal hydrogen electrode, NHE) results in the formation of MV$^+$, which can subsequently be reduced to the neutral MV$^0$ species at $-0.76$ V vs. NHE.[13] MV exhibits outstanding solubility (3.0 mol L$^{-1}$ in water) and excellent electrochemical reversibility for the first electron-reducing step. The electrochemical reversibility for the second electron-reducing step, however, is poor due to the limited solubility of the neutral MV$^0$ species.[13] As such, the full theoretical energy density of MV-based electrolyte cannot be accessed. Another limitation of MV is the fact that the molecule is positively charged or neutral in all its oxidation states (Figure 1a). In order to prevent cross-over of positively-charged MV species, anion-exchange membranes (AEMs) are typically used to separate the negative and positive compartments in flow battery cells, which are not optimal from a resistance and durability point of view compared to more mature cation-exchange membranes (CEMs). Lastly, MV molecules are prone to chemical degradation due to a second-order decomposition mechanism.[21]

To overcome the known limitations of MV for use in flow batteries, MV-based molecular derivatives have been explored. Firstly, molecular modification has been aimed at enhancing the electrochemical reversibility and solubility of the doubly-reduced compound.[13, 23] Furthermore—in order to avoid the use of AEMs—MV have been immobilized on soluble polymer chains allowing for the use of porous membranes instead of AEMs.[7] As an alternate approach, 4,4'-bipyridines have been functionalized with negatively-charged sulfonate side groups,[8] resulting in overall negatively charged molecules that enabled the use of CEMs instead of AEMs.[8] Lastly, 4,4'-bipyridines have been functionalized with side groups in order to suppress chemical degradation mechanisms.[21]

To date, all research on bipyridinium-based redox compounds for flow batteries has focused on MV and MV-derivatives in which the functional groups are attached to the nitrogen atoms at the 4,4'-position. Until now, no attention has been directed to 2,2'-bipyridine (Bpy) compounds for flow battery applications, in spite of the excellent electrochemical reversibility reported for some compounds [26, 27] and an exhaustive body of literature on synthetic
approaches that yield functionalized 2,2’-bipyridines.[28] Interestingly, the addition of functional groups to 2,2’-bipyridine typically takes place on any position of the aromatic rings in contrast to 4,4’-bipyridine that is typically functionalized on the N-position, opening up a much larger molecular space that could be beneficial for selecting an optimal molecule for flow battery applications. In contrast with 4,4’-bipyridine derivatives such as methyl viologen, 2,2’-bipyridines, shown in Figure 1b, are organic compounds that have the potential to exhibit two reduction and two protonation processes. Figure 2 depicts all possible reactions for the various pH-independent electron transfer (reactions 1-6), and pH-dependent proton (reactions A-F) and proton-coupled electron transfer (reactions 1A, 2C, 3B, and 4D) processes. In the present report we have analyzed computationally all possible electron, proton and proton coupled electron transfers. However, the experimental evidence guided us to focus on the first reduction steps of 2,2’-bipyridine and its derivatives, which are described by reactions 1, 3 and 5 of Figure 2. The solution pH will determine which of the reactions occurs and whether the reaction entails just an electron transfer (reactions 1, 3 or 5) step or a proton-coupled —pH dependent— electron transfer step (reaction 1A or 3B). For flow battery application of 2,2’-bipyridines, it is important to identify the acidity conditions (i.e. the pH region) under which the redox reactions are independent of pH. The solution pH will have an effect on solubility as it is known for unsubstituted 2,2’-bipyridine (Bpy) that the protonated species (HBpy) is independent of pH. The solution pH will determine the soluble species, even in pH windows in which both N-positions are deprotonated.

The exploration presented in this article aims at predicting several physicochemical properties for 156 known 2,2’-bipyridine derivatives reported in the academic literature.[28] The properties calculated are the redox potential, the acid dissociation constant in terms of pK_a and the solubility (log S). Selected experimental measurements were carried out to support all the calculations performed. In the first part of this paper, we present an experimental study of unsubstituted 2,2’-bipyridine, in which the redox potential was determined as a function of pH. This allowed us to establish the pH region in which the pH-independent reaction 3 occurs (see Figure 2). The study of E as a function of pH in aqueous solution was also used to —for the first time to our knowledge— infer the pK_a of the 2,2’-bipyridine reduced species (HBpy) in Figure 2). Using this information, we next calculated the redox potential associated to reaction 3 for a selection of five specific 2,2’-bipyridine derivatives, and also determined the redox potential experimentally for these five compounds. This experimental data set was used to calibrate the calculated E^0 values for the set of five redox compounds, the parameters of the calibration were subsequently used to predict new calculated E^0 values of all 156 2,2’-bipyridine derivatives for all electron transfer reactions depicted in Figure 2 (taking into account all possible protonation states). Further, our predicted E^0 and pK_a values for the set of 156 bipyridines was used to visualize the effect of the Hammett substituent constant (describing the extent to which a side group is electron-withdrawing or electron-donating) on both these parameters. These results —in combination with solubility calculations— served as a guide to down-select several concrete 2,2’-bipyridine derivatives to be further explored in experimental flow battery studies.

1. Experimental and computational methods

Cyclic voltammetry (CV) electrochemical studies were performed using a CH Instruments potentiostat (model CHI760E). The three-electrode setup comprised a glassy carbon working electrode (active area: 3 mm diameter), a Ag/AgCl/KCl 0.1 mol L^-1 pseudo-reference electrode and a platinum wire as counter electrode. The acquisition of all voltammograms was initiated at open circuit potential (OCP) and collected in positive and negative directions. The ferricinium/ferrocene redox couple was used as reference and the potential values were corrected in all voltammograms. For CV measurements of 2,2’-bipyridine and its derivatives, the electrodes were immersed into a solution containing 1 mmol L^-1 of these compounds in an H_2SO_4 solution (except for compound 4 in Table S8, were a saturated solution at lower concentration was used). Experiments to study the dependence of the redox properties as a function of pH were carried out using a 1 mmol L^-1 solution of 2,2’-bipyridine in different media (H_2SO_4 for pH 1.04 and 1.62, a chloroacetic acid / chloroacetate buffer for pH 2.58, 2.79, 3.00, 3.25, 3.40 and 3.56 and acetic acid / acetate buffer for pH 3.68). All experiments were performed at room temperature, under a nitrogen gas atmosphere, and using a scan rate of 100 mV s^-1.

The molecular structures of the 156 derivatives investigated are summarized in Tables S1 to S6 of the Supporting Information. All these compounds are n,n’-disubstituted-2,2’-bipyridines, where n = n’ = 3, 4, 5 and 6 (Figure 1c). First, molecular information in SMILES code was used as input in Open Babel 2.4.0 [29] to find the minimum
energy conformer using the MMFF94[30, 31, 32, 33, 34] force field. The generated geometries provided the cartesian coordinates that were used to generate a Gaussian input file. In some cases, it was necessary to apply a preliminary minimization using pseudopotentials (PM7[35]) before performing the actual DFT calculation. Molecular energies of the 156 2,2'-bipirydines were obtained using the Gaussian 16 suite [36] at DFT, with B3LYP [37] hybrid functional and 6-31G(d) basis. Analysis of vibrational frequencies was performed to verify the existence of an energy minimum. All geometries were optimized using both the polarizable continuum model (PCM) [38, 39] and the solvation model based on density (SMD) [40] with water as solvent; the results presented below correspond to SMD as it is better correlated with experimental values (see S2 section in the SI).

Next, redox potentials for the first and second electron transfers and the acid dissociation constants expressed in logarithmic form (pK$_a$) were calculated for the set of 156 n,n'-disubstituted-2,2'-bipyridines. In order to obtain the best values, a benchmark study was performed to determine the best approximations. Redox potential was calculated through the Born-Haber cycle shown in Figure 3, which has been widely used to estimate redox potentials with accurate results.[9, 10, 41]

Equations involved in these calculations are:

\[
\Delta G_{s,redox}^0 = -nFE_{calc}
\]

\[
G = H - TS = E_{elec} + E_{vib}
\]

\[
\Delta G_{s,redox}^0 = \Delta G_{s,redox}^0 + \Delta G_{solv}^0(\text{Red}) - \Delta G_{solv}^0(\text{Ox})
\]

\[
\Delta G_{s,redox}^0 = G(\text{Red}_{(s)}) - G(\text{Ox}_{(s)})
\]

All calculated redox potentials were referenced to the standard hydrogen electrode (SHE) in water with an absolute redox potential of 4.44 V.[42]

Protonation reactions involve different species at different pH values. To estimate each species present, we performed, in a similar way to redox potentials, pK$_a$ calculations based on the thermodynamic cycle shown in Figure 4. For the 156 n,n'-disubstituted-2,2'-bipyridines, only the first protonation was considered.

On the other hand, we also considered electronic and Gibbs free energies as well as PCM and SMD solvation models, where $\Delta G^0$ is obtained through Equations 6 and 7 respectively. The equations involved in these calculations are:

\[
pK_a^{HBpy} = \frac{\Delta G^0}{RT\ln 10} + pK_a^{HRef}
\]
\[
\Delta G^o = \Delta G^o_g + \Delta G^o_{\text{solv}}(\text{Bpy}) + \Delta G^o_{\text{solv}}(\text{HRef}^+) + \Delta G^o_{\text{solv}}(\text{Ref}) - \Delta G^o_{\text{solv}}(\text{HBpy}^+) - \Delta G^o_{\text{solv}}(\text{Bpy})
\]

Finally, we need to consider aqueous solubility for the species present at the selected pH operating conditions. Solubility, calculated as the logarithm of intrinsic solubility (log S), was obtained using ChemAxon suite [43] which implements the structure-property relations described by Xu et al. [44, 45]. Calculations were performed at pH values one unit below the first pK_a for each molecule, in order to guarantee that the redox reaction studied corresponds to the mono-protonated species (see reaction 3 in Figure 2). A calibration of this methodology was performed using Xu [45] and Yalkowsky [46] training sets in order to verify to what extent this approach is able to predict solubility (for details, see section S3 in the SI).

2. Results and Discussion

The starting point of our exploration of the 2,2'-bipyridine molecular family is the unsubstituted 2,2'-bipyridine molecule itself. Our initial focus is on the first reduction step of HBpy^+ into HBpy, although the H_2Bpy^2+ and Bpy species are in principle promising species for flow battery applications as well. To be able to calibrate our theoretical calculations of \( E^o \) with experimental data, it is important to accurately measure the redox potential for a well-defined equilibrium reaction. As shown in Figure 2, the reduction process of HBpy^+ can occur via reaction 3 (pH-independent electron transfer) and/or reaction 3B (proton-coupled electron transfer). For reaction 3B to take place, the operational pH needs to be in the range \( pK_{a2}^1 \leq pH \leq pK_{a2}^2 \), where \( pK_{a2}^1 \) and \( pK_{a2}^2 \) are the negative logarithms to second acidity constants for the oxidized and first reduced species respectively. Under these pH conditions, HBpy^+ would be protonated into H_2Bpy^+ species during the reduction step. As such, it is important to understand how the pH affects the different reactions in Figure 2 when experimentally determining the redox potential. For this reason, the redox potential of 2,2'-bipyridine (\( pK_{a1} = 4.3 \) and \( pK_{a2} = -0.2 \) [47]), as a function of pH was experimentally determined from pH = 1 to 4 where we expected to observe the change from the pH-dependent electron transfer equilibrium (reaction 3B) into the pH-independent equilibrium (reaction 3). Figure 5 shows a Pourbaix diagram for the first reduction step of the HBPy^+ system in which two separate regimes are observed: a pH-dependent region for values lower than 2.99 (\( pK_{a2}^1 \)) and a pH-independent region for values between 2.99 and 4.3. In the first region, the predominant reaction is 3B, whereas reaction 3 dominates in the pH-independent regime. These results allow us to conclude that HBpy^+ is a weaker base than its reduced species HBpy, since the pK_{a2} increases from -0.2 to 2.99 upon reduction. The trends observed in Figure 5 allow us to assume a pH interval in which the first reduction step of the HBPy^+ species is dominated by reaction 3 (Figure 2). Specifically, we assumed that for all derivatives investigated, the experimental redox potential is exclusively associated with reaction 3 (Figure 2) at a pH value one unit lower than the pK_{a1} value of each derivative.
Figure 5: Experimental diagram of $E$ vs. pH for unsubstituted Bpy in different electrolytic solutions for the first reduction process. At pH $\leq 3$, the redox reaction was observed to be pH-dependent, whereas $E$ was observed to be independent of pH at pH values $\geq 3$.

2.1. $pK_a$ calculations

In the thermodynamic cycle shown in Figure 4, the introduction of a reference species allow us to get a $pK_a$ value without the need to calculate the proton directly. In order to get accurate $pK_a$ values, this reference must be structurally similar to the systems under investigation.$^{[48, 49]}$ For this reason, we chose 2,2'-bipyridine as the reference system. Using this approach, the $pK_a$ values are related to $\Delta G^0_s$ by Equation 5, $pK_{HBpy}$ corresponds to the experimental value of the reference system (a value of 4.30 for the first protonation step of unsubstituted 2,2'-bipyridine).

Figure 6 shows the predicted $pK_a$ values (associated to reaction A in Figure 2, $pK_{a1}$) for a variety of 2,2'-bipyridine derivatives in the oxidized form. In the case of substitutions with electron-donating functional groups (Hammett substituent factor $\sigma > 0$), a slight decrease of the acidity of the nitrogen atoms on the ring resulted on average into somewhat higher values for $pK_{a1}$ (maximum change of 2 pH units), although this trend does not seem very pronounced. When adding both electron-attracting and electron-withdrawing substituents, the values for $pK_{a1}$ are trending below 4.3 (the $pK_{a1}$ value for 2,2'-bipyridine). Finally, substitutions with only electron-withdrawing functional groups (Hammett substituent factor $\sigma < 0$), resulted in a marked change towards lower $pK_{a1}$ values (maximum change of 8 pH units). This last observation can be rationalized as follows. When side groups are strongly electron-withdrawing, the electronic density on the nitrogen atoms on the rings is reduced, making it easier for protons to dissociate, which is expressed in a lower value for $pK_{a1}$. Conversely, we had expected that the addition of electron-donating side groups would inhibit the dissociation of protons, resulting in higher values for $pK_{a1}$. This expected trend was only clearly observed for two derivatives with strongly electron-donating side groups on the 6,6-position (two purple dots in the upper right-hand side of Figure 6) but in general, functionalization with more moderately electron-donating group (Hammett constants between $-0.2$ and 0) only lead to a small change of the $pK_{a1}$ value.
2.2. Calculated standard redox potentials for 2,2'-bipyridine derivatives

The calculation of standard redox potentials for organic redox-active molecules has been widely described in the academic literature.\[9, 10\] In the Born-Haber cycle, $\Delta G^{\text{redox}}_0$ is directly related to the redox potential (Equation 1), and can be obtained from energy differences of the oxidized (Ox) and reduced (Red) species involved in the cycle. For each derivative, we consider both electronic ($E_{\text{elec}}$) and Gibbs free energies ($G$), with the latter concept comprising the vibrational and thermal corrections (as can be seen in Equation 2), which should in principle result in a better approximation. In addition, to include solvent effects, two different implicit solvation models were used: PCM and SMD, along with Equation 3.

Theoretical calculations allow for the estimation of standard redox potentials referenced to the standard hydrogen electrode (SHE), but the absolute values of such results are often unreliable due to offsets, the magnitude of which depend on the exact computational methodology that is employed. Usually, these offsets can be corrected for using a calibration curve, which is an empirical relation between experimental and theoretical values. We obtained such calibration curve by calculating the redox potential for five specific 2,2'-bipyridine derivatives (for the pH-independent reaction 3) and by measuring the experimental redox potential for the same derivatives at a pH value one unit lower than its $pK_a$ value (see Figure S1). Here, we assumed that the value for $pK_{a2}$ of the reduced species is at least one pH unit lower than the $pK_{a1}$ value for its corresponding species in the oxidized form, as in 2,2 bipyridine. Under this assumption, the selected pH values in the experimental studies resulted in the exclusive occurrence of the pH-independent reaction 3 (Figure 2). Correcting the calculated values for the standard redox potential with the calibration curve of Figure S2 allowed us to estimate the reduction potential for all reactions of Figure 2 for the 156 2,2'-bipyridine derivatives of interest. For each reaction in Figure 2, Figure 7 shows the statistical variations of the...
predicted standard reduction potentials, presented in four blocks according to the position on the aromatic ring of the side-group functionalization for the SMD solvation model. Redox potential values obtained for first reduction step of the protonated species $\text{H}_2\text{Bpy}^{2+}$ to $\text{H}_2\text{Bpy}^+$ and $\text{HBpy}^+$ to $\text{HBpy}$ (described by reactions 5 and 3, respectively) exhibit less negative redox potential values compared to the reduction of the deprotonated species $\text{Bpy}$ to $\text{Bpy}^-$ (reaction 1), which can be explained by the stability added to the reduced species in the presence of a proton. Relative to the first reduction step, the calculated redox potential for the second reduction step occurs at more negative potential values for all protonation states. Comparing the values of $E^\circ$ obtained for reactions 1, 3 and 5 it can be concluded that on average the redox potentials associated with reaction 5, and especially reaction 3, are optimal for use in aqueous flow batteries. For reaction 1, the predicted redox potentials are very negative ($\ll -1.0 \text{ V vs. SHE}$), which will result in significant hydrogen evolution (i.e. water reduction) on carbon based electrodes that are typically used in aqueous flow batteries.[50] In contrast, the redox potentials associated with reaction 5 are rather positive ($>-0.5 \text{ V vs. SHE}$) which will avoid the hydrogen evolution reaction but may result in a sub-optimal cell voltage and electrolyte energy density. In addition, reaction 5 is associated with extremely acidic electrolyte conditions which may be undesirable from an engineering perspective. The values of $E^\circ$ for reaction 3, on the other hand, lie on average between $-0.5$ and $-1.0 \text{ V vs. SHE}$, with values around $-0.5 \text{ V}$ being optimal in the context of optimizing electrolyte energy density while avoiding excessive parasitic reaction such as hydrogen evolution. Also, reaction 3 is accessible at moderately...
acidic electrolyte conditions (see Figure 6), which is desirable from an engineering point of view. All the calculated redox potentials as well as the pKa values are summarized in Tables S1-S6 of the Supplementary Information (SI). It must be noted that the above discussion does not exclude the use of reactions 1 or 5 for flow battery applications. The above-mentioned observations are high-level trends, but deviations to these trends can be observed in Figure 7 and as such, the above-mentioned trends should be used as a guideline but not as definitive information to exclude the use of reactions 1 and 5 for 2,2'-bipyridines for flow battery applications. During the analysis process to produce Figure 7, molecules considered outliers were removed from the data set. In-depth analysis of these outliers made us conclude that the extreme values observed for $E^0$ for these outliers were due to optimizations in the calculations that lead to the breakage of a chemical bond in the reduced species. Such phenomena would be indicative of possible decomposition reactions associated with the electron transfer. Some examples of these decomposition reactions are described in more detail in Figure S3.

2.3. Functional group effect in 2,2’-bipyridines

According to Schrier, the addition of different functional groups on thiophenoquinone aromatic rings results in shifts of redox potential value of up to 0.8 V.[10] Figure 8 displays the estimated reduction potential of 2,2’-bipyridine derivatives for reaction 3 (Figure 2), where each value is identified by the Hammett substituent constant ($\sigma$) associated to each functional group and to discriminate between electron donating or withdrawing groups ($\sigma \leq 0$ and $\sigma > 0$, respectively). It can be observed that electron withdrawing groups increase the reduction potential ($E^0$) respect to the bare 2,2’-bipyridine. This response can be attributed to the stabilizing effect conferred by these groups to the aromatic ring. Contrarily, electron donating groups hinder entry of electrons due to conferred charge density on the aromatic
ring, therefore $E^0$ is shifted to more negative values. The latter are significant observations, since electron withdrawing groups could increase reversibility of 2,2'-bipyridine derivatives by stabilizing the electron in the reduction process. Figure 8 also shows that in molecules with different substituents on each ring ($\sigma_1 \neq \sigma_2$), the electron withdrawing effect is predominant, that is, the reduction potential values are mostly shifted in the positive direction above $-0.826 \text{ V}$. Finally, it is noteworthy that the electron withdrawing effect is more significant than the electron donating one: for electron-donating groups with $\sigma = -0.6$, the maximum decrease of the downward shift of the reduction potential is only $0.25 \text{ V}$ with respect to bare 2,2'-bipyridine, whereas electron-withdrawing groups with $\sigma = 0.7$ can lead to an upward shift of up to $0.78 \text{ V}$.

![Figure 9: Theoretical molar solubility (S) of molecular species, represented as log S versus Gibbs free energies for the mono protonated species of the first redox couple involved in reaction 3 (HBpy+/HBpy).](image)

### 2.4. Solubility

Theoretical solubility ($S$, intrinsic solubility in moles per liter) of molecular species can be obtained as,[51]

$$\Delta G_{\text{dissolution}} = \Delta G_{\text{sub}} + \Delta G_{\text{solv}} = -RT \ln S V_m$$

(8)

where ($\Delta G_{\text{sub}}$) is the sublimation free energy, ($\Delta G_{\text{solv}}$) the solvation free energy and $V_m$ is the molar volume of the crystal. For novel compounds, however, limited data exists on $\Delta G_{\text{sub}}$ and $V_m$ which can complicate the prediction of compound solubility. However, the solvation free energy of a molecule can be used to approximate trends in solubility when screening large databases of molecules.[9, 10] On the other hand, as mentioned above, methods which implement structure-property relations have been used to estimate solubility of novel compounds.[10] Solubility values (log
S), were obtained with ChemAxon suite and compared with $\Delta G_{\text{solv}}$—calculated via DFT—in order to correlate tendencies between both thermodynamic properties. Results for reacting species, HBpy$^+$ and HBpy, presented in Figure 9, show that oxidized species have larger absolute values for $\Delta G_{\text{solv}}$ than neutral species, while maintaining a similar scattering for all molecules (see section S3, Figure S8 in the SI, for more information).

In Figure 9, three different regions can be resolved along y-axis for both species. The first region (log S < −5.0) corresponds to molecules with small absolute values for $\Delta G_{\text{solv}}$, indicating a correspondence between poor solubility and weak $\Delta G_{\text{solv}}$ values; confirming the undesirable low solubility of these molecules. A second region can be defined for the interval log S = [−5.0, −1.0] where most candidates are concentrated. Molecules belonging to this region should be studied in more detail in order to establish more accurate values of solubility (perhaps experimentally). The last region (log S > −1.0) contains the derivatives with highest solubilities; better candidates should be those which also have larger absolute values for $\Delta G_{\text{solv}}$ (dots in the top-left corner of each data set). These results allow us to apply the present methodology for estimating the solubility as a rapid preliminary screening of candidate molecules.

![Graph showing standard reduction potential values of 2,2'-bipyridines as function of logarithmic solubility values (log S) calculated with ChemAxon software and their corresponding Hammett substituent factor.](image)

2.5. Selection of molecules as possible negolytes in flow batteries.

Selecting suitable redox couples for use in flow batteries usually results in a trade-off between various physicochemical properties. On the one hand, an ideal molecule for aqueous flow batteries must exhibit a redox potential within the electrochemical window of stability of the solvent (i.e., water) on graphitic electrodes that are typically used in flow batteries. In other words, parasitic solvent dissociation reactions such as water reduction or oxidation must be avoided to prevent challenges from a battery operation point of view. On the other hand, the difference between the redox potential for the negative and positive electro-active compounds (the cell voltage) should be sufficiently high
to ensure high electrolyte energy density. Furthermore, the molecule must exhibit high solubility in water, again to ensure high energy density.

We attempted to visualize this trade-off between redox potential and energy density in Figure 10, in which each dot represents one 2,2'-bipyridine derivative (its color represents the Hammett substituent factor). The blue horizontal line intersects the y-axis at a value of −0.5 V vs. SHE, below which we assume the parasitic reaction of water reduction (i.e. hydrogen evolution) to be problematic. Similarly, the red vertical line intersects the x-axis at a value of log \( S = -1 \), below which the compound solubility is deemed to be unattractive from an electrolyte density point of view (log \( S = -1 \) corresponds to a solubility of 0.1 mol L\(^{-1} \)). As such, the dots located in the upper right quadrant of Figure 10 represent the most interesting compounds from an operational stability (no hydrogen evolution) and electrolyte energy density point of view.

As can be observed in Figure 10, molecular derivatives with electron-withdrawing groups exhibit on average more positive redox potentials, reducing the impact of parasitic hydrogen evolution. In contrast, no clear trends can be observed with respect to the effect of the addition of electron-withdrawing or electron-donating side groups on the solubility (log \( S \)). As such, the nine candidate compounds in the upper right quadrant are all functionalized with electron-withdrawing groups. Figure 11 shows that, within this group of nine, three subsets of molecules with different functional groups can be identified:

1. Carbonyl-functionalized derivatives B4446, B4452, B4454, B4461, B5519 and B6635
2. Sulfonate-functionalized derivatives B4455 and B5522
3. Nitro-functionalized derivatives B5543

For compounds B4455 (\( E^0 = -0.31 \) V, pK\(_{a1} = -1.23 \)) and B5522 (\( E^0 = -0.29 \) V, pK\(_{a1} = -1.89 \)), the low values of pK\(_{a1}\) would require operation in extremely acidic electrolyte (> 17 mol L\(^{-1} \)) for reaction 3 to be the predominant redox reaction. A similar behavior is observed for compound B6635 (\( E^0 = -0.45 \) V, pK\(_{a1} = -3.94 \)) and B4454 (\( E^0 = -0.30 \) V, pK\(_{a1} = 0.18 \)), as result of which these compounds would also require operation in highly concentrated acidic media. On the other hand, the compounds functionalized with carbonyl groups (B4446, B4452, B4461, and B5519) and nitro substituents (B5543) have acidity constants greater than 1, which would ease the requirement of the electrolyte acidity (< 1 mol L\(^{-1} \)). Reduction potential values for these compounds fluctuate within −0.34 and −0.45 V which makes them promising candidates with respect to the methylviologen benchmark, which has a reduction potential of −0.45 V. In addition, this last set of molecules should be the one with the best reversibility due to stability conferred by the electron withdrawing group. As a consequence, the carbonyl- and nitro-functionalized 2,2'-bipyridine derivatives presented in Figure 11 constitute the most promising candidates for further evaluation in flow battery testing.
3. Conclusions

Redox properties, acidity and solubility of 156 substituted 2,2’-bipyridine derivatives were studied for their possible application as active materials in organic flow battery electrolytes. The study of the acidity constants showed that functionalization with electron-withdrawing groups increase the acidity with respect to unsubstituted 2,2’-bipyridine, as evidenced by a decrease in predicted values for pK_a constants of such compounds. In contrast, functionalization with electron-donating groups increase the basicity of the substituted molecules increasing the values of the first acidity constant. At the same time, we found that the reduction potential of the monoprotonated 2,2’-bipyridine derivatives shift to more positive values (relative to bare 2,2’-bipyridine) when the molecular backbone is functionalized with electron-withdrawing groups. Compounds functionalized with electron-donating groups, however, exhibit a slight negative shift decrease in the reduction potential, the magnitude of which was less significant relative to the positive shift observed for functionalization with electron-withdrawing groups. These results can be rationalized by analyzing the molecular structure of the investigated molecules, in particular with respect to the value of the Hammett substituent factor of the functional groups of each 2,2’-bipyridine derivative. The analysis of the estimated redox potential and solubility values for the 156 investigated compounds indicates that compounds with carbonyl- and nitro-based functional groups (B4446, B4452, B4461, B5519, and B5543) are the most promising candidates within the set of investigated molecules for successful application as negative electrolytes in organic flow batteries.

Conflicts of interest

There are no conflicts to declare.

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