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

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S1 Tables

Table S1: 3,3'-disubstituted-2,2'-bipyridines.

#	R	R'	E^0	pK_a
B3301	CH_3	CH_3	-0.99	3.12
B3302	OH	OH	-0.85	4.47
B3303	OCH_3	OCH_3	-0.91	3.33
B3304	CO_2H	CO_2H	-0.54	-0.73
B3305	CO_2CH_3	CO_2CH_3	-0.67	2.00
B3306	CO_2H	CO_2CH_3	-0.62	-0.87

Table S2: 4,4'-disubstituted-2,2'-bipyridines.

#	R	R'	E^0	pK_a
B4401	CH_3	CH_3	-0.91	5.03
B4402	C_9H_{19}	C_9H_{19}	-1.02	3.93
B4403	$(CH_2)_{10}CH_3$	$(CH_2)_{10}CH_3$	-0.90	1.16
B4404	$(CH_2)_{11}CH_3$	$(CH_2)_{11}CH_3$	-0.89	4.94
B4405	$(CH_2)_{12}CH_3$	$(CH_2)_{12}CH_3$	-0.87	-0.94
B4406	$(CH_2)_{14}CH_3$	$(CH_2)_{14}CH_3$	-0.89	4.18
B4407	$(CH_2)_{18}CH_3$	$(CH_2)_{18}CH_3$	-0.91	7.13
B4408	CH_3	$CH_2CH_2OCH_3$	-0.90	4.28
B4409	CH_3	$CH=CH_2$	-0.88	4.02
B4410	$CH=CH_2$	$CH=CH_2$	-0.71	3.02
B4411	$C\equiv CH$	H	-0.77	4.22
B4412	$C\equiv CH$	$C\equiv CH$	-0.60	3.62
B4413	CH_2CH_2Ph	CH_2CH_2Ph	-0.90	4.75
B4414	$PhCH_3$	$PhCH_3$	-0.81	3.88
B4415	PhOH	PhOH	-0.81	3.94
B4416	PhOMe	PhOMe	-0.81	3.95
B4417	PhCl	PhCl	-0.72	3.15
B4418	Br	H	-0.72	2.31
B4419	Br	Br	-0.62	2.14
B4420	CH_3	CH_2Br	-0.64	3.40
B4421	CH_3	CH_2CH_2Br	-0.87	3.99
B4422	CH_3	$(CH_2)_3Br$	-0.91	4.63
B4423	CH_3	$(CH_2)_4Br$	-0.91	3.97
B4424	CH_3	$(CH_2)_5Br$	-0.91	4.47
B4425	CH_3	$(CH_2)_6Br$	-0.93	4.90
B4426	CH_3	$(CH_2)_7Br$	-0.89	3.98
B4427	$PhCH_2Br$	$PhCH_2Br$	-0.73	3.32
B4428	CH_2Br	CH_2Br	-0.62	2.49
B4429	C_4H_8Br	C_4H_8Br	-0.90	4.08
B4430	CH_3	CH_2CH_2Cl	-0.89	4.27
B4431	CH_2Cl	CH_2Cl	-0.51	2.36
B4432	CH_2TMS	CH_2TMS	-0.89	4.02
B4433	CF_3	CF_3	-0.52	0.34
B4434	CH_2I	CH_2I	-0.30	3.90
B4435	CH_3	$(CH_2)_3OH$	-0.92	4.24
B4436	CH_3	CH_2OH	-0.90	4.13
B4437	CH_3	$(CH_2)_4OH$	-0.89	4.66
B4438	CH_2OH	CH_2OH	-0.85	3.94
B4439	C_4H_8OH	C_4H_8OH	-0.92	4.57
B4440	OH	OH	-0.95	4.16

Table S3: 4,4'-disubstituted-2,2'-bipyridines (cont...).

#	R	R'	E^0	pK_a
B4441	OCH$_3$	OCH$_3$	-0.95	4.43
B4442	SCH$_3$	SCH$_3$	-0.85	3.19
B4443	SCH$_2$CH$_3$	SCH$_2$CH$_3$	-0.85	3.65
B4444	CH$_3$	CHO	-0.70	3.58
B4445	CH$_3$	(CH$_2$)$_3$CHO	-0.90	4.35
B4446	CHO	CHO	-0.34	1.29
B4447	CH$_3$	CN	-0.74	4.59
B4448	CH$_3$	CH$_2$CH$_2$CN	-0.89	4.05
B4449	CN	CN	-0.36	0.97
B4450	CH$_3$	CH$_2$CO$_2$H	-0.86	3.94
B4451	CH$_3$	(CH$_2$)$_3$CO$_2$H	-0.91	4.48
B4452	CO$_2$H	CO$_2$H	-0.40	1.02
B4453	COCl	COCl	-0.18	-0.46
B4454	CONHS	CONHS	-0.30	0.18
B4455	SO$_3$H	SO$_3$H	-0.31	-1.23
B4456	CH$_3$	COCl	-0.55	2.54
B4457	COCl	CO$_2$CH$_2$CH$_3$	-0.41	0.69
B4458	H	CO$_2$CH$_3$	-0.74	3.21
B4459	CH$_3$	CH$_2$CO$_2$CH$_3$	-0.88	3.73
B4460	CO$_2$H	CO$_2$CH$_3$	-0.45	1.27
B4461	CO$_2$CH$_3$	CO$_2$CH$_3$	-0.44	1.14
B4462	CH$_3$	(CH$_2$)$_4$NH$_2$	-0.91	4.70
B4463	CH$_3$	CH=NOH	-0.81	3.77
B4464	CH$_3$	CH$_2$NH$_2$	-0.91	4.57
B4465	CH$_2$CHOHPh	CH$_2$CHOHPh	-0.86	4.31

Table S4: 5,5'-disubstituted-2,2'-bipyridines.

#	R	R'	E^0	pK_a
B5501	CH_3	H	-0.86	3.81
B5502	CH_3	CH_3	-0.90	4.03
B5503	$C\equiv CH$	H	-0.72	2.97
B5504	$C\equiv CH$	$C\equiv CH$	-0.60	1.45
B5505	$C\equiv CSi(CH_3)_3$	$C\equiv CSi(CH_3)_3$	-0.59	1.48
B5506	$SiMe_3$	$SiMe_3$	-0.77	3.93
B5507	Si_2Me_5	Si_2Me_5	-0.80	4.33
B5508	CH_3	CH_2Br	-0.79	3.53
B5509	CH_2Br	H	-0.75	3.16
B5510	CH_2Br	CH_2Br	-0.65	2.03
B5511	CF_3	CF_3	-0.51	0.39
B5512	Br	H	-0.76	2.85
B5513	Br	Br	-0.62	0.41
B5514	Cl	H	-0.76	2.81
B5515	$CH(CH_3)OH$	$COCH_3$	-0.64	3.00
B5516	$CH(CH_3)OTBDMS$	$COCH_3$	-0.66	3.46
B5517	SH	SH	-0.76	2.18
B5518	CHO	H	-0.55	2.40
B5519	$COCH_3$	$COCH_3$	-0.43	1.23
B5520	CN	CN	-0.34	-0.99
B5521	H	SO_3H	-0.57	1.92
B5522	SO_3H	SO_3H	-0.29	-1.89
B5523	H	CO_2CH_3	-0.65	2.78
B5524	CO_2Et	CO_2Et	-0.47	1.10
B5525	$SCOCH_3$	H	-0.74	3.22
B5526	$SCOCH_3$	$SCOCH_3$	-0.63	1.20
B5527	SC(S)OEt	H	-0.70	2.74
B5528	SC(S)OEt	SC(S)OEt	-0.53	0.95
B5529	NH_2	CO_2H	-0.75	3.29
B5530	NH_2	CO_2Me	-0.79	3.56
B5531	NH_2	CO_2Et	-0.79	3.37
B5532	NO_2	CO_2Me	-0.27	0.57
B5533	$NHCO_2Et$	CO_2Et	-0.70	2.83
B5534	CON_3	CO_2Et	-0.40	0.91
B5535	$CONHNH_2$	CO_2Et	-0.51	1.26
B5536	$CONHNH_2$	$CONHNH_2$	-0.56	1.58
B5537	NH_2	H	-0.96	4.76
B5538	NH_3Cl	NH_3Cl	0.26	1.85
B5539	CH_2NEt_2	CH_2NEt_2	-0.83	3.82
B5540	CH_2NMePh	CH_2NMePh	-0.82	3.58

Table S5: 5,5'-disubstituted-2,2'-bipyridines (cont...).

#	R	R'	E^0	pK_a
B5541	CH$_2$N(CH$_2$CH$_2$OH)$_2$	CH$_2$N(CH$_2$CH$_2$OH)$_2$	-0.82	3.42
B5542	N=CHPh	N=CHPh	-0.76	3.30
B5543	NO$_2$	H	-0.32	1.73
B5544	NO$_2$	NO$_2$	-0.06	-2.16
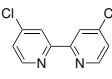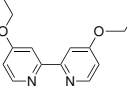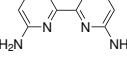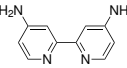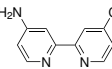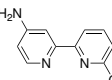
Table S6: 6,6'-disubstituted-2,2'-bipyridines.

#	R	R'	E^0	pK_a
B6601	CH_3	CH_3	-0.88	4.28
B6602	CH_3	H	-0.87	4.59
B6603	CH_2CH_3	H	-0.87	4.46
B6604	$CH=CH_2$	$CH=CH_2$	-0.73	3.71
B6605	$C\equiv CH$	$C\equiv CH$	-0.64	1.39
B6606	$C\equiv CSi(CH_3)_3$	$C\equiv CSi(CH_3)_3$	-0.63	1.06
B6607	CH_2Br	CH_3	-0.84	4.17
B6608	CH_2Br	CH_2Br	-0.61	2.00
B6609	CH_2Cl	H	-0.80	3.20
B6610	CH_2Cl	CH_2Cl	-0.71	2.36
B6611	CF_3	CF_3	-0.54	-1.14
B6612	Br	CH_3	-0.79	3.69
B6613	Cl	CH_3	-0.80	3.71
B6614	Br	H	-0.74	2.81
B6615	Br	Br	-0.57	-2.01
B6616	Br	OC_6H_{13}	-0.79	1.05
B6617	CH_2OTBS	H	-0.86	4.94
B6618	CH_2Cl	CH_2OH	-0.84	3.13
B6619	CH_2OH	CH_2OH	-0.83	3.41
B6620	CH_2OAc	CH_2OAc	-0.75	2.67
B6621	OCH_3	OCH_3	-0.86	1.76
B6622	OC_6H_{13}	OC_6H_{13}	-0.87	1.47
B6623	OMe	OMe	-0.86	1.76
B6624	OEt	OEt	-0.88	2.09
B6625	OPr	OPr	-0.86	2.11
B6626	OBu	OBu	-0.87	2.26
B6627	OHex	OHex	-0.87	1.47
B6628	manisyl	manisyl	-0.82	3.64
B6629	$CH(OH)CH_3$	$CH(OH)CH_3$	-0.85	3.68
B6630	$CH(OAc)CH_3$	$CH(OAc)CH_3$	-0.85	3.37
B6631	$CHOCH_3$	$CHOCH_3$	-0.85	4.01
B6632	SEt	H	-0.81	3.37
B6633	CHO	CHO	-0.38	0.59
B6634	$COCH_3$	$COCH_3$	-0.49	0.19
B6635	CO_2H	CO_2H	-0.45	-3.94
B6636	H	CO_2CH_3	-0.76	2.82
B6637	CN	CN	-0.41	-2.28
B6638	CH_2NH_2	CH_2NH_2	-0.92	5.63
B6639	NH_2	NH_2	-1.02	5.60
B6640	NH_2	$NHC_{12}H_{25}$	-1.07	6.22
B6641	$NHC_{12}H_{25}$	$NHC_{12}H_{25}$	-1.04	5.42

S2 *E* and p*K*a calibrations

Calculations for E and pK_a values were calibrated with a set of molecules whose experimental value was reported or measured experimentally. For the pK_a a set of 14 n,n-disubstituted-2,2-bipyridines (shown in Table S7) was calculated for the first protonation (reaction A in Figure 2) with the methodology described in the main article. The correlation between calculated and experimental values are shown in Figure S1 for PCM and SMD solvation models.

Table S7: Molecules used in the calibration of pK_a and their experimental values.

Number	Structure	pK_a(exp)	Ref
1		4.30	[1]
2		5.42	[1]
3		2.80	[1]
4		5.70	[1]
5		6.72	[2, 3]
6		5.80	[3]
7		5.70	[3]
8		5.60	[3]
9		8.10	[3]
10		8.80	[3]
11		7.40	[3]
12		7.70	[3]
13		3.80	[3]
14		3.70	[3]

From the calibration we selected SMD solvation model as a better approach to estimate pK_a values, with correlations of 0.9667 and 0.9763 for pK_a values calculated with E_{elec} and G respectively. With this fitting we calibrate the calculated values (p$K_{a(calc)}$) for the set of 156 n,n-disubstituted-2,2-bipyridines to get the best predicted values (p$K_{a(pred)}$).
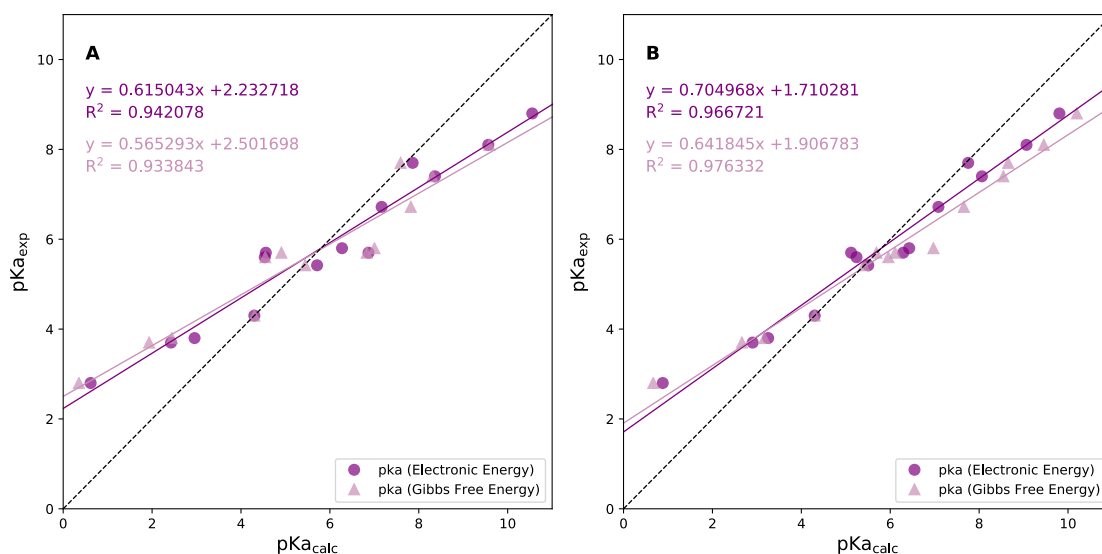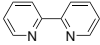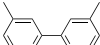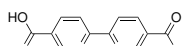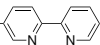
Figure S1: Correlation between calculated and experimental pK_a values for a set of 14 molecules. Calculations performed for the first protonation (reaction A), with A) PCM solvation model and B) SMD solvation model.

For the redox potentials we prepared a set of molecules whose E^0 values were measured experimentally under the conditions reported in the experimental methodology. First we calculate and calibrate the pK_a for the set of molecules. These pK_a's were used to estimate the pH of measurement for the redox potentials. To ensure all molecules were protonated we consider a pH of measurement one unit below the predicted pK_a value. Results are shown in Table S8 and the respective correlation between the calculated and experimental redox potentials are shown in Figure S2.

Table S8: Molecules used in the calibration of redox potentials (E). $pK_{(a2)}^o$ and $pK_{(a1)}^r$ predicted values, experimental pH values and redox potentials (E) measured.

Number	Structure	pK_{a2}^o	pK_{a1}^r	pH_{exp}	E_{exp}
1		4.66	2.98	3.6	-0.826
2		5.38	3.63	4.3	-0.879
3		5.76	3.72	4.7	-0.942
4		1.69	-1.49	0.6	-0.385
5		5.26	3.49	4.2	-0.904

The calibration shows that the calculated redox potentials are in agreement with the experimental ones with a correlation greater that 0.99 for both solvation models and energies used in the calculations.
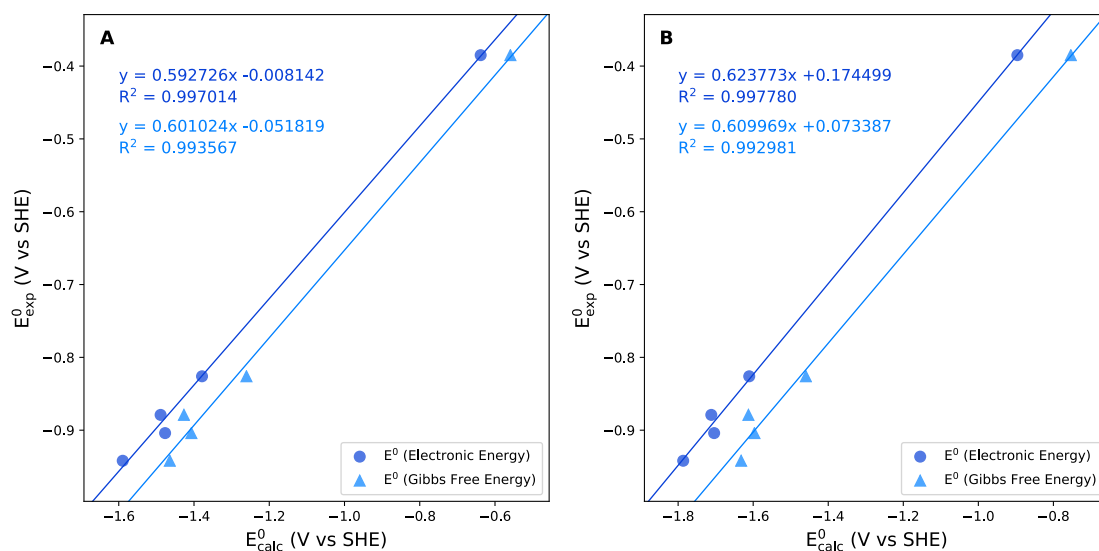
Figure S2: Correlation between calculated and experimental redox potentials for a set of five molecules. Calculations performed for reaction 3 with A) PCM solvation model and B) SMD solvation model.

Redox potentials for the 156 n,n'-disubstituted-2,2-bipyridines were calculated and calibrated for all reactions present in the PCET scheme (Figure 2 in the main article). The distribution of the predicted values is observed in Figure S2 for the SMD solvation model. On the screening procedure molecules with deviated values considered as outliers were taken off the distribution. These deviated outliers values were analyzed and are associated to optimizations that lead to a bond breaking of the reduced species. This indicates possible decomposition reactions associated to the electron transfer in reactions 14, 14, 11 and 4 molecules for reactions 2, 4, 5 and 6 respectively. Some examples of these decomposition reactions are shown in Figure S3.
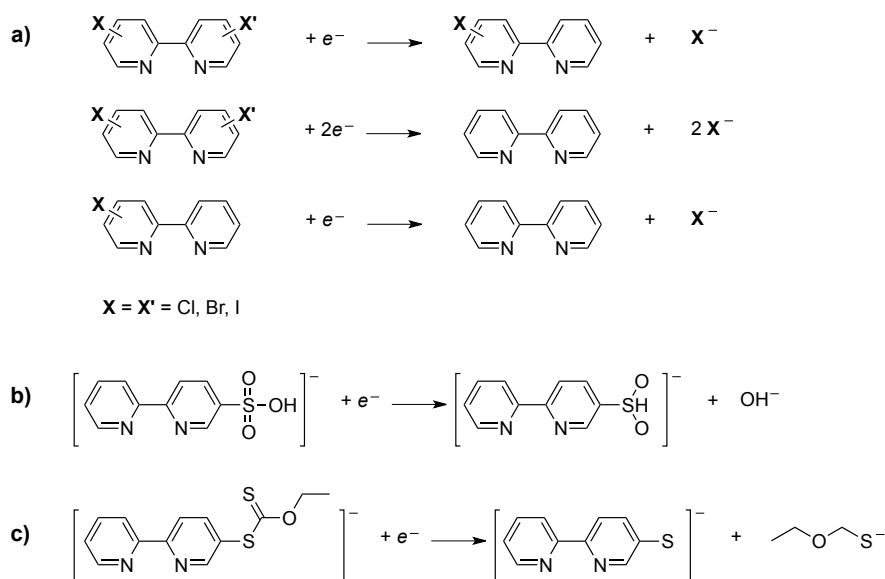
Figure S3: Decomposition reactions found in the screening of redox potentials. a) Halogen decomposition found for one and two electron transfers (reactions 1 and 1-2 respectively). b) Sulfonate decomposition and c) dithio decomposition found for the second electron transfer (reaction 2).

S3 Estimation of aqueous solubility

Xu's model use Equation S3 to describe the contribution to log S (the logarithm of the intrinsic solubility) of each atomic subunit that constitutes the molecule, namely

$$\log S = C_D + \sum_i a_i n_i + \sum_j b_i B_j$$

where a_i is the contribution of the i-eth subunit, b_i are correction factors, n_i and B_j are the corresponding occurrences for coefficients a_i and b_i, and C_D the solvent constant (for group types, contributions and correction factors see references [4, 5]).

Models based on Equation S3 can be easily extended incorporating different descriptors and correction factors (a comprehensive review can be found in reference [5]). In Xu's model Solvent Accessible Surface Area (SASA) descriptor is included, which considers the relative interactions between solute-solute, solute-water and water-water, and that more exposed atoms have bigger contributions that inner ones [6]. However, we use Xu's model with out SASA descriptor [4] because our results show that no significant improvements are observed and yet we can gain computer time with a more simplified model.

Calibration consisted in comparing our results (log S) against the experimental and theoretical values of Xu's [4] and Yalkowsky's [7] data sets in order to validate our methodology (see Figs. 4-7). In the case of Yalkowsky's set (18 molecules), theoretical predictions were calculated by Xu et al. and are labeled as log S_{YH} , while experimental values are identified as log S_{YE}; in the case of Xu's data (50 molecules), experimental values are labeled as log S_{HE} and theoretical values as log S_{HH}.
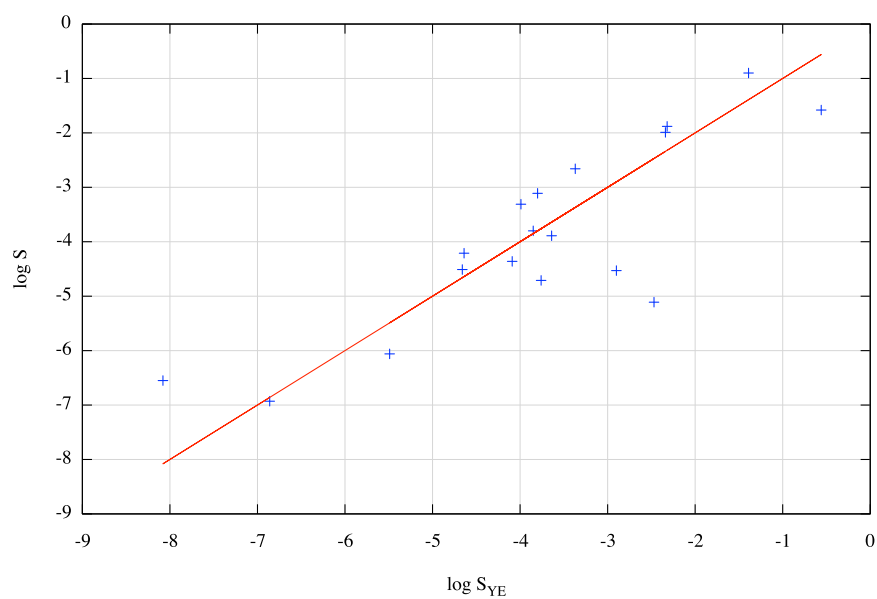
Figure S4: Calibration using Yalkowsky's experimental data set (log S_{YE}). Correlation coefficient r = 0.8446 with log S = 0.7909 log S_{YE} - 0.8966.
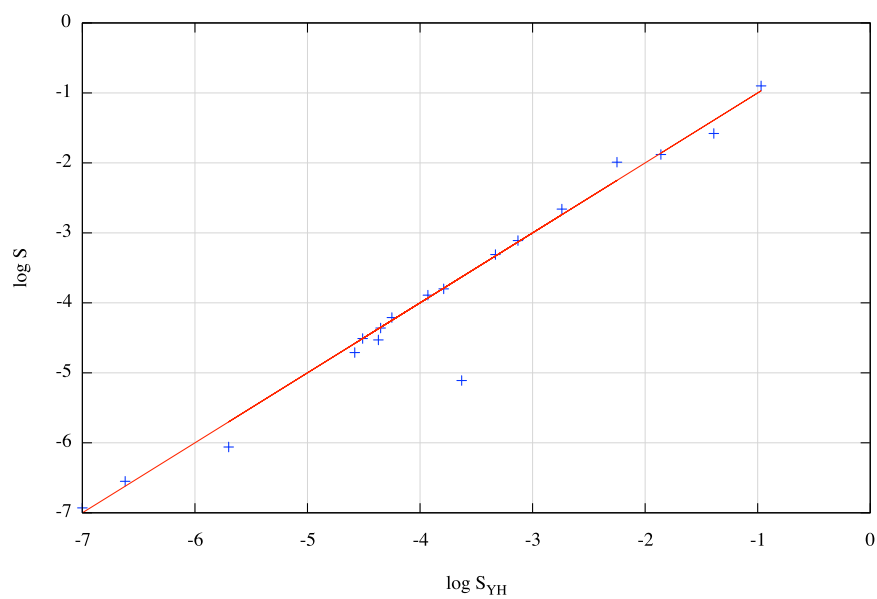

Figure S5: Calibration using Yalkowsky's theoretical data set (log S_{YH}). Correlation coefficient r = 0.9578 with log S = 1.0090 log S_{YH} - 0.0607.
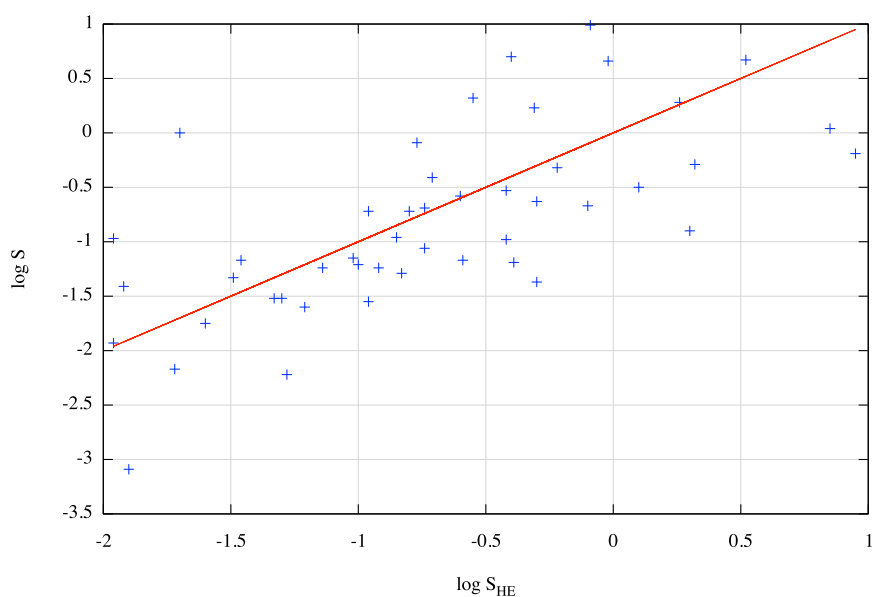
Figure S6: Calibration using Xu's experimental data set (log S_{HE}). Correlation coefficient r = 0.6746 with log S = 0.7739 log S_{HE} - 0.2633.
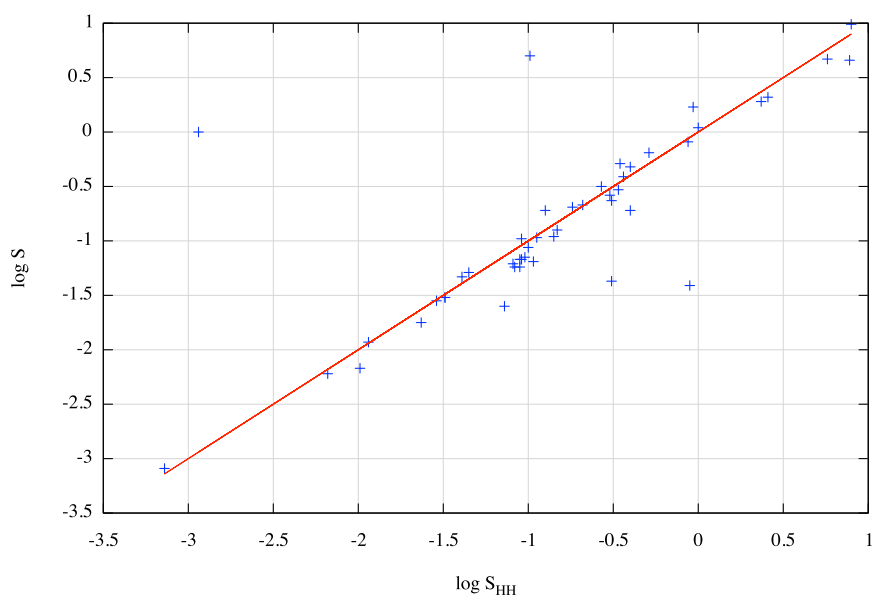

Figure S7: Calibration using Xu's theoretical data set (log S_{HH}). Correlation coefficient r = 0.7712 with log S = 0.7605 log S_{HH} - 0.1838.

Figures S5 and S7 show that our theoretical results do not differ significantly from the corresponding Xu's and Yalkowsky's sets, proving that our errs are similar to those of the theoretical framework proposed by Xu et al. Comparison between calculated log S and experimental data for both sets (Figs. S4 and S6), exhibit a sufficiently good correlation that allow us to validate our methodology.

It has been mentioned in the manuscript that oxidized species have bigger absolute values for ΔG_{solv},

however, for log S values and the general behaviour between both properties, not considerably differences can be observed. To prove the above, ΔG_{solv} and log S values between species $HBpy^+$ and HBpy were compared and results depicted in Figures S8 and S9.
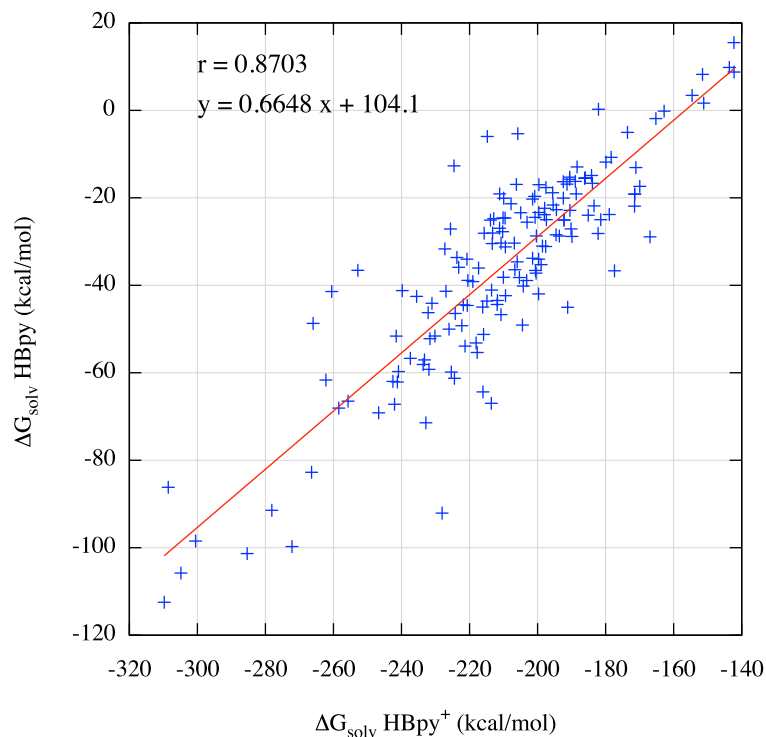

Figure S8: Comparison of Δ G_{solv} energies between species HBpy+ and HBpy.

Figure S8 shows that ΔG_{solv} energies of both species are fair enough correlated, which can be explained because charged molecules, in general, need greater absolute values for ΔG_{solv}. Therefore, the shift towards these values for charged molecules is linear as it was supposed. In Figure 9 it is observed that in the case of log S this correlation is even stronger, and so solubility it is not considerably affected by the presence of charge molecules.
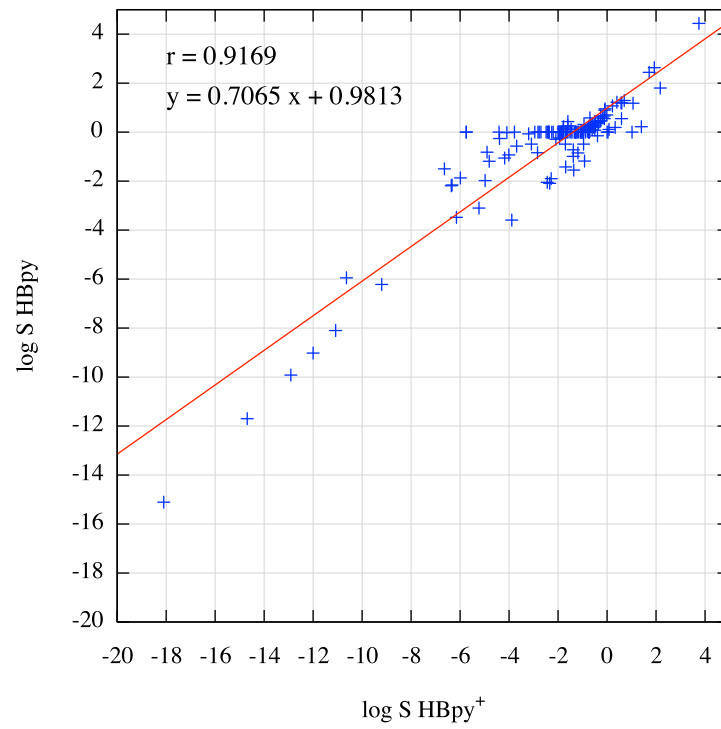
Figure S9: Comparison of $\log S$ values between species HBpy$^+$ and HBpy.
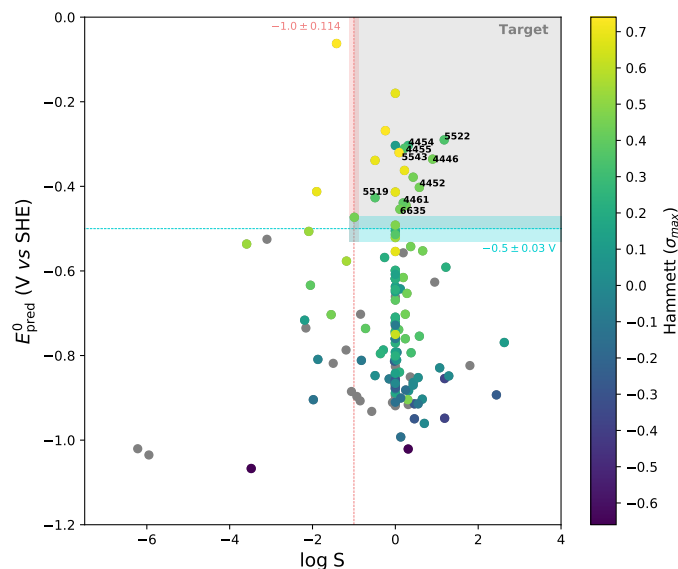
S4 Reduced 2,2'-bipyridines

Figure S10: Standard reduction potential values of 2,2'-bipyridines as function of logarithmic solubility values (log S) for HBpy calculated with ChemAxon software and their corresponding Hammett substituent factor.

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