Gutmann´s Donor and Acceptor Numbers for ionic liquids and deep eutectic solvents

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Abstract

An experimental and computational methodology for the analysis of the Lewis acid/base responses of ionic liquids (IL) and deep eutectic solvents (DES) is proposed. It is based on the donor and acceptor of electronic charge ability of Lewis acid and bases concepts (donicity and acceptor numbers, DN and AN, respectively) proposed by Viktor Gutmann. The enthalpy of interaction between the IL/DES with the probe antimony pentachloride ($SbCl_5$) in dichloroethane displays good correlations with experimental data. This approach could serve as a first approximation to predict the responses to H-Bonding abilities of new IL or DES. Although useful, the problems encountered to model the electron AN of these solvents limit the usefulness of the approach to completely describe their polarity properties. The experimental data were recorded using UV-Vis spectroscopy for a wide range of IL and a couple of DES. Two reactions were used as benchmarks to test the reliability of the DN model to discuss the reactivity of real systems in these neoteric solvents.
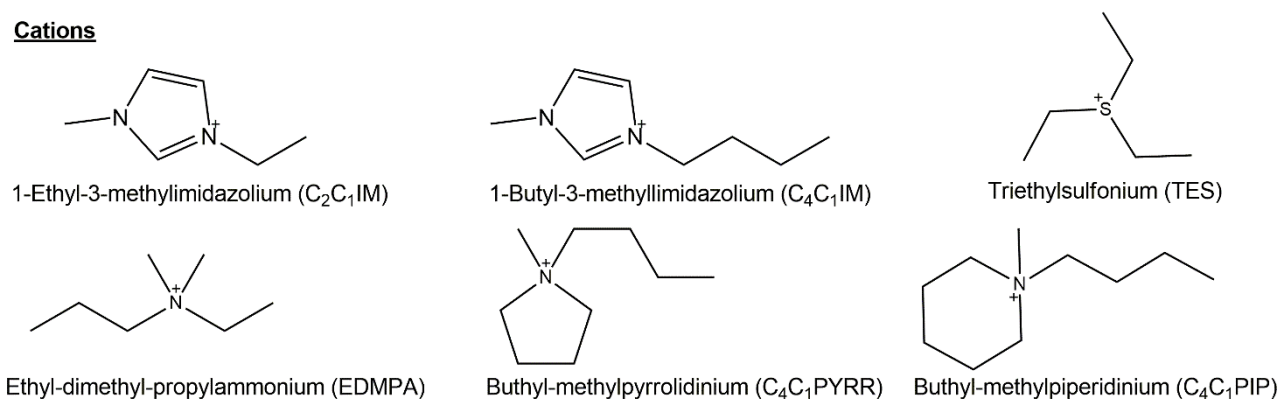
1 Introduction

Ionic liquids (ILs) are defined as molten salts (composed entirely of cations and anions) that melt below 100°C (Hallett and Welton 2011). ILs have been a focus of study in the past decades due to their interesting physical properties like low vapor pressure (Earle et al. 2006; Zaitsau et al. 2006), large electrochemical window (Buzzeo, Evans, and Compton 2004) and catalytic effect over a varied set of chemical reactions. However, the principal property that makes them an interesting alternative to conventional solvents is their huge combinatorial flexibility ranging about 10^{12} possible combinations that prompted several authors to propose them as *designer solvents* or *task specific*
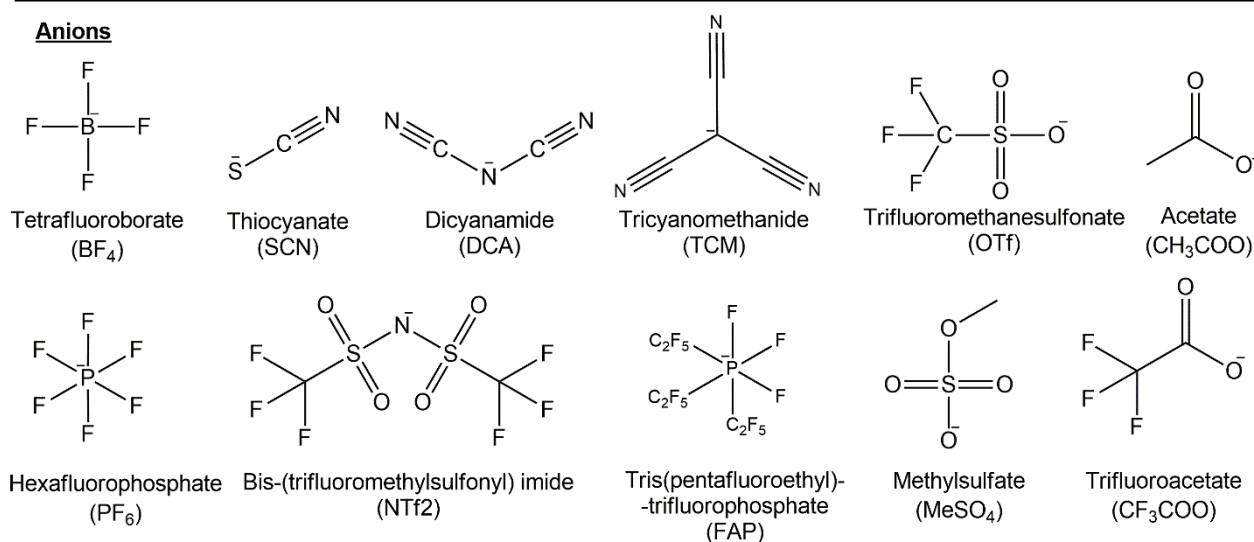
solvents (Giernoth 2010). Scheme 1 shows the acronyms for the different ionic liquids used in this work.

Cations

1-Ethyl-3-methylimidazolium (C_2C_1IM)

1-Butyl-3-methyllimidazolium (C_4C_1IM)

Triethylsulfonium (TES)

Ethyl-dimethyl-propylammonium (EDMPA)

Buthyl-methylpyrrolidinium (C_4C_1PYRR)

Buthyl-methylpiperidinium (C_4C_1PIP)

Anions

Tetrafluoroborate (BF_4)

Thiocyanate (SCN)

Dicyanamide (DCA)

Tricyanomethanide (TCM)

Trifluoromethanesulfonate (OTf)

Acetate (CH_3COO)

Hexafluorophosphate (PF_6)

Bis-(trifluoromethylsulfonyl) imide (NTf2)

Tris(pentafluoroethyl)--trifluorophosphate (FAP)

Methylsulfate ($MeSO_4$)

Trifluoroacetate (CF_3COO)

Scheme 1. Structures of anions and cations of ionic liquids and the acronyms used in this study.

On the other hand, Deep Eutectic Solvents (DES) has been perceived as a new class of IL analogues because they share many characteristics and properties with ILs (Zhang et al. 2012). However, it has been recently pointed out that ILs and DESs are two different types of materials. DESs are systems formed from a eutectic mixture of Lewis or Brønsted acids and bases which can contain a variety of anionic and/or cationic species. The classification of DES considers four types of groups based on the nature of the complexion agent. The most common DES (type III) studied are formed from the hydrogen bond acceptor (HBA) choline chloride and hydrogen bond donors (HBDs) (Hansen et al. 2021). A DES is a solvent that has a lower melting point than the melting point of each of the components. In terms of properties, the depression in the melting point is attributed to the hydrogen bond interaction in a similar vein to the interaction between the HBD and the HBA and the asymmetry shared with ILs. DES are able to solve the following aspects associated with the first generation of ILs: i) high cost, ii) presence of impurities, iii) antibacterial activity and toxicity and iv) decomposition towards hydrofluoric or phosphoric acids in water induced by the anions (Płotka-
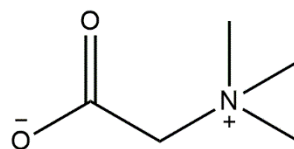
Wasylka et al. 2020). DES share some properties with ionic liquids in the sense that they have low vapor pressures, low flammability, and a high combinatorial flexibility due to the high number of donors and acceptors that allows for the tuning of chemical properties, with the added benefit of being generally cheaper to prepare (using low-cost materials and simpler synthesis and purification methods), biocompatibility and biodegradability. Scheme 2 shows the reagents used to prepare the DES used in this study.
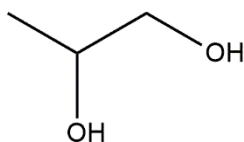
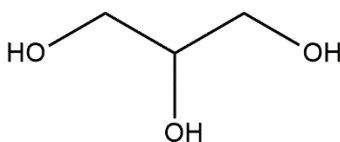**Hydrogen Bond Acceptor (HBA)**
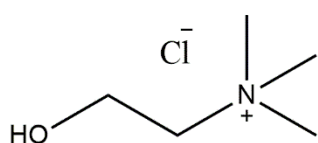
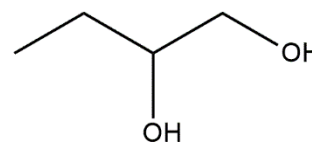Choline Chloride (ChCl)   Betaine (Bet)

Hydrogen Bond Donor (HBD)

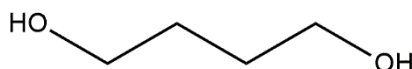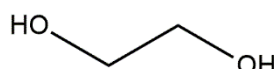1,2 propanediol   Glycerol   1,2 butanediol
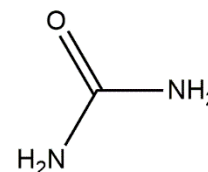
1,4 Butanediol   Ethanediol   Urea

Scheme 2. Structures of HBA and HBD of DES and the acronyms used in this study.

The selection of an appropriate solvent for a given reaction can drastically affect the course of a chemical transformation, so a proper understanding of the solvent properties is needed to predict and rationalize the mechanism involved in the reaction. In this regard, solvent polarity is an important parameter to understand the solute-solvent interactions. However, its loose definition as *"the overall solvation power of a solvent which depends on the sum of all interactions, specific and nonspecific between solute and solvent"* (McNaught and Wilkinson 1997) implies that there is not a unique probe or method capable of measuring all aspect of polarity. As a result, several empirical scales of polarity (for both conventional solvents and ionic liquids) have been proposed (Weingärtner 2006; Reichardt 2005; Schmeisser et al. 2012a), each one with their strengths and drawbacks.

The polarity scale involved in this study are based on the Acceptor and Donor numbers (AN and DN respectively), proposed by Viktor Gutmann, (Viktor Gutmann 1978) as the negative of the molar enthalpy for the reaction between the donor $SbCl_5$ on a dilute solution of dichloromethane for the DN

(V Gutmann 1976); and the chemical ^{31}P NMR shift of the triethyl phosphine oxide in the respective pure solvent for the AN. (Mayer, Gutmann, and Gerger 1975) An alternative to the calorimetric determination of the DN is the chemical shift of ^{23}Na NMR of the $NaClO_4$ probe which gives a good correlation with the thermodynamic measures; (Schmeisser et al. 2012a) and allows the determination of the DN for a wider range of solvents, including the ILs considered in study. The work of Schmeisser et al. (Schmeisser et al. 2012b) on the series of $[C_2C_1im]^+$ ionic liquids it's the most comprehensive source on ILs´s polarity with this technique.

In this context, the evaluation of the Lewis acid/base responses for a series of ILs and DES was carried out in this work to determine the DN and AN descriptors proposed by Gutmann. Two model reactions were used as benchmarks to test the reliability of the DN model to discuss the reactivity of real systems in these neoteric solvents.

2   Materials and Methods

2.1   Materials

All the reagents used such as choline chloride, betaine, 1,2-propanediol, glycerol, urea, ethylene glycol, 1,2 butanediol, 1,4 butanediol and ILs were commercially available by Sigma-Aldrich, Merck and IoLITech. The certificate of analysis guarantees purity $\geq$ 99%. DESs were prepared by mixing the corresponding components at the desired mole ratio and heating them for 3 hours at 70-80°C until a clear liquid appeared. Previously, the reagents choline chloride, urea and IL were put under vacuum at 70°C for 3 hours to ensure the removal of traces of water before being used. HBD like 1,2-propanediol, glycerol and 1,2-butanediol were dried with molecular sieves. After prepared, they were stored in a desiccant prior to be used.

The probe ferrocyphen was purchased on BOC Science and used without further purifying. The probe $Cu(acac)(tmen)^+ClO_4^-$ was synthetized using the procedure indicated in literature (Kuzmina et al. 2017) and purified through hot filtration and recrystallization.

2.2   Experimental Measurements

Kinetic measurements: The studied reactions correspond to: 2,4,6-trinitrophenyl phenyl ether (TNPPE) with piperazine and 2-chloro-5-nitro pyrimidine (CNP) and morpholine in ILs and DES as reaction media. The kinetics were carried out spectrophotometrically by means of a diode array spectrophotometer HP 8453 with a recirculating bath, keeping the temperature at 25±0.1°C (40±0.1°C for some DES). All the reactions were studied under excess amine over the substrate to ensure the pseudo-first order condition, in which the amine concentrations were at least 10 times greater than the substrate concentration. The reactions were started by injection of a substrate (20 μL) stock solution in acetonitrile (0.0015 M) into the amine solution (1 mL in the spectroscopy cell). The pseudo first order constant) (k_{obs}) values were spectrophotometrically determined at the wavelengths corresponding to their kinetic products (415 nm and 380 nm, respectively).

Solvatochromic shift measurements: A small amount of the probes (ferrocyphen or $Cu(acac)(tmen)^+ClO_4^-$) was dissolved in each IL and DES studied. Previously, the probe was

homogenized and stabilized for 24 hours. The measurements were performed in a diode array spectrophotometer HP 8453 at 25±0.1°C using the spectral software.

Product analysis: In the studied reactions, the increase of the bands centered in the range of 415 - 380 nm were observed. It was attributed to the corresponding kinetic reaction products for the studied reactions. (Ormazabal-Toledo et al. 2013; Campodónico, Olivares, and Tapia 2020)

2.3   Computational Method.

All calculations were performed using the Gaussian 09 package visualized by the Gaussview 5.0 program. Initially, the calculations were made at the M06/6-31+g(d,p) level of theory. Antimony atom was represented by the pseudopotential core LanL2DZ, and all the calculation were performed using the SMD model of implicit solvation to represent the solvent dichloroethane. An optimization of geometries at the length of interaction followed by a frequency analysis was performed to characterize the thermodynamic parameters of the system. These energies were compared to the energy of the probe and anion/IL at non-interacting distance to get the enthalpy of interaction. This was done in order to account for the error of superposition of bases by using the same Hamiltonian to represent the complete system in both cases. Later, the calculations were redone in different levels of theory, changing the DFT functional (to B3LYP and ωB-97XD) and the basis size (to 6-311+g(2df,2p) for elements of the first three rows and cc-pVTZ-PP for antimony), to ensure the independence of the results on basis set and functional used.

3   Results and Discussion

Solvatochromic determination of Gutmann Numbers

Table 1 shows the experimental values of DN and AN determined by the solvatochromic shift of the probes of copper and iron (Cu(acac)(tmen)$^+$ClO$_4$$^-$, ferrocyphen) dissolved in ILs. As expected, most of the AN fall in a narrow range of variations, or slightly lower when compared to the C_4C_1IM cation with the $C_2C_1IM^+$ analogous. Consider for instance the slight reduction when C_4C_1IMSCN (AN=25,6) and C_2C_1IMSCN (AN=27,1) are compared, or the null effect observed after comparing $C_4C_1IMCF_3COO$ (AN=27,0) with $C_2C_1IMCF_3COO$ (AN=27,1). Therefore, the increase in the chain length has a little impact on the capacity of the cation to accept electric charge density from a donor. A more significant effect can be observed when the nature of the cation is changed. For example, going from an imidazolium cation such as C_2C_1IMDCA (AN=28,4) to a pyrrolidinium cation $C_4C_1PYRRDCA$ (AN=23,1) with the same counter anion, shows a greater decrease in the capacity to accept charge. This fact may be traced to the enhanced ability of imidazolium cation to delocalize electronic charge by the presence of nitrogen atoms and double bonds in comparison to pyrrolidinium cation. (See Scheme 1).

Table 1. Solvatochromic shifts of the Fe^{+2} and Cu^{+2} dyes and their respective Gutmann Numbers for a series of ionic liquids.

Ionic Liquid	λ Fe^{+2} (nm)	AN	λ Cu^{+2} (nm)	DN
C_2C_1IM DCA	580,2	28,4	-	-
C_2C_1IM SCN	583,5	27,1	764,5	76,2
C_2C_1IM NTf_2	574,8	30,1	-	-
C_2C_1IM $MeSO_4$	-	-	793,9	71,9
C_2C_1IM Ac	591,0	24,2	651,4	45,1
C_2C_1IM CF_3COO	583,5	27,1	685,1	52,5
C_2C_1IM TCM	579,8	28,5	617,1	36,8
C_2C_1IM $MeSO_3$	586,0	26,1	683,0	52,0
C_2C_1IM $ETSO_4$	587,0	25,7	653,7	45,7
C_2C_1IM FAP	575,1	30,4	-	-
C_4C_1PYRR DCA	594,0	23,1	646,4	44,0
C_4C_1IM BF_4	584,6	26,7	544,0	15,7
C_4C_1IM PF_6	577,0	29,6	523,8	8,8
C_4C_1IM DCA	-	-	646,1	43,9
C_4C_1IM SCN	587,4	25,6	730,4	61,3
C_4C_1IM OTf	582,4	27,5	594,0	30,7
C_4C_1IM NTf_2	574,3	30,7	550,4	17,8
C_4C_1IM $MeSO_4$	-	-	798,2	72,5
C_4C_1IM Ac	591,4	24,1	678,0	51,0
C_4C_1IM CF_3COO	583,7	27,0	679,0	51,2
C_4C_1IM TCM	583,7	27,0	607,8	34,4
C_4C_1PYRR NTf_2	587	25,9	556	19,6
C_4C_1PIP NTf_2	548	25,8	548	17,0
EDMPA NTf_2	579	28,8	553	18,6
TES NTf_2	580	28,6	550	17,7

In ILs, the AN is in general associated to the cationic component of the IL. To assess the influence of the type of cation on the AN´s responses, the anion NTf_2^-, was kept fixed. The cations considered include aromatic heterocyclic ring (imidazolium, AN close to 30, for both chain length); piperidinium and pyrrolidinium cations, both with AN close to 26; quaternary amine (ethyl dimethyl propyl ammonium EDMPA, AN=28,8) and a sulfonium cation (triethylsulfonium TES, AN=28,6). The values of AN fall within the range between 25,6 to 30 as shown in Table 1. These values could be either evidence for the low response of the capacity to accept charges in IL or it may be attributable to the probe which could be unsuitable to resolve finer differences of the solvent responses. This fact presents an additional problem when a computational method is used to model the system (IL-probe), because a low variance in the experimental data gives flat curves in the correlation between calculated parameters and experimental data. Then, a careful approach is needed to analyze these data.

On the other hand, the DN is associated with the anion of the ILs. Table 1 shows a significant difference in the values of DN. In this case, the probe chosen has enough sensitivity to give a wide range of values which facilitates the comparison with calculated data. As expected, presence of an

oxygen-containing group or cyanate group increases the value of the DN, while the increase in the side chain length of the imidazolium only has a small decreasing effect on the DN in most of the IL tested. It is worth noting that several ILs reacted with the probes in such a way that spectrophotometric measures can no longer be used reliably.

3.1   Theoretical Gutmann numbers for ILs

To set up a reliable model for the donicity number for ILs, the original definition proposed by Gutmann was slightly adapted to consider the variation in the interaction enthalpy of solvent- probe systems, including the presence of the solvent. The calculated results display a qualitative agreement with experimental data. A good linear relationship between them is obtained, as shown in Figure 1.

As it was explained in the methodology section, the geometries of probe-anion and probe-IL pairs were optimized, adding one molecule of dichloroethane as an explicit solvent in the simulation. The stabilization of charges of the anions given better results which resulted closely correlated to the experimental data as compared to the same calculation in the gas phase. The choice of solvent was the same as the original work, the focus was to simulate the original experimental conditions in the calculations. However, the computational model treats the IL as a solute which differs from experimental values, because in the UV-Vis experiments, the ILs act as solvents. In this case bulk properties do not appear to influence the donicity of the system, so we conclude that this is good approximation.
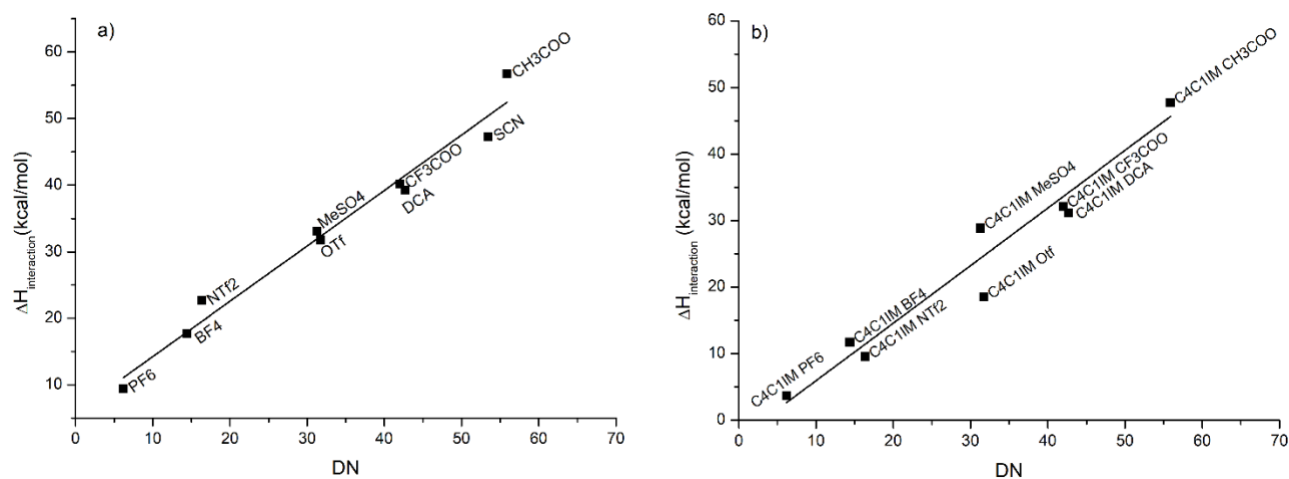

Figure 1. Correlation between the experimental DN values and the calculated enthalpies of interaction between antimony pentachloride and a) the corresponding anion, where the equation that fit this correlation is $y = 0,83\,DN + 5,89$ with a correlation coefficient $R^2 = 0,968$ and **b)** ionic liquid. The equation that fit this correlation is $y = 0,86\,DN - 2,70$ with an adjusted R-square value of $R^2 = 0,937$. The IL C$_4$C$_1$IMSCN was excluded due to problems of convergence.

All the calculations made supported the original predictions of the change in geometry and coordination number of the antimony atom, going from a trigonal bipyramidal geometry to a more octahedral one. As noted by Gutmann, stronger donors have a smaller antimony-donor distance and longer Sb-Cl distance, as it is shown on Table 2 for the series of anions: $MeSO_4^-$, CF_3COO^-, CH_3COO^-. As noted by Gutmann, there is a bigger influence on the Sb-O distance than the Sb-Cl.

Table 2. Average distance between antimony and chlorine; distance of antimony and oxygen for a series of similar anions of ILs for the calculated geometries at the M06/6-31+g(d,p) (LanL2DZ for antimony) level of theory.

Anion	Sb-Cl distance (Å)	Sb-O distance (Å)
CH_3COO^-	2,390	2,0276
CF_3COO^-	2,377	2,0745
$MeSO_4^-$	2,374	2,0948

Table 2 emphasizes a qualitative agreement with Gutmann´s proposal, in the sense that shorter Sb-O distances are in line with a more favorable probe-anion interaction. The results for the calculated DN are contrasted against the experimental values for the cases of single anions of the IL and the pair cation-anion in Figure 1. As expected, the major contribution to the DN is given by the anion which gives good correlation with the experimental values. When the cation is added, less dispersion of the data can be observed, thereby suggesting that even at a very low level of approximation (first order approximation) the pair probe-anion is qualitatively assessed at lower computational cost. It is worth noting that this methodology treats the ILs as an ion pair which is not necessarily true for this kind of solvents, but we believe that in this specific case the addition of extra pairs of IL will not change the results drastically.

An additional problem arises when an anion has multiple possible interaction centers that give different local minima configurations. For example, the anion SCN^- could interact with the probe through the sulfur atom or through the nitrogen atom, and both configurations seem to be stable enough to generate a minimum in energy. The configuration that gets closer agreement with the experimental values for the DN and more importantly, that is consistent with the correlation found for the remaining elements of the series is when the molecule interacts through the nitrogen as it has a bigger interaction enthalpy than the other configuration and thus gets closer to the trend. The choice of the configuration to be used to model the interaction depends on the nature of molecules that surround the anion, since the different polarizabilities of each interaction site is determinant to decide which side the anion is going to be preferred to interact with. In this case, both the antimony probe for the calculation and the experimental probe based on copper seem to prefer to interact with the nitrogen side of the anion, but that is not necessarily the case for all solutes.

Figure 2 shows the behavior of the pair anion-probe when the functional, and the basis set is changed. As observed, although there is a small difference in the absolute values and slopes for each method, the placement of each IL doesn´t change and the same order is predicted for all of them. The increase in base size gives a small improvement in accuracy thereby lowering the dispersion of the data, yet it's not enough to justify the increase in calculation time that this change originates: a smaller base set with the appropriate functional can give similar results at a lower computational cost.
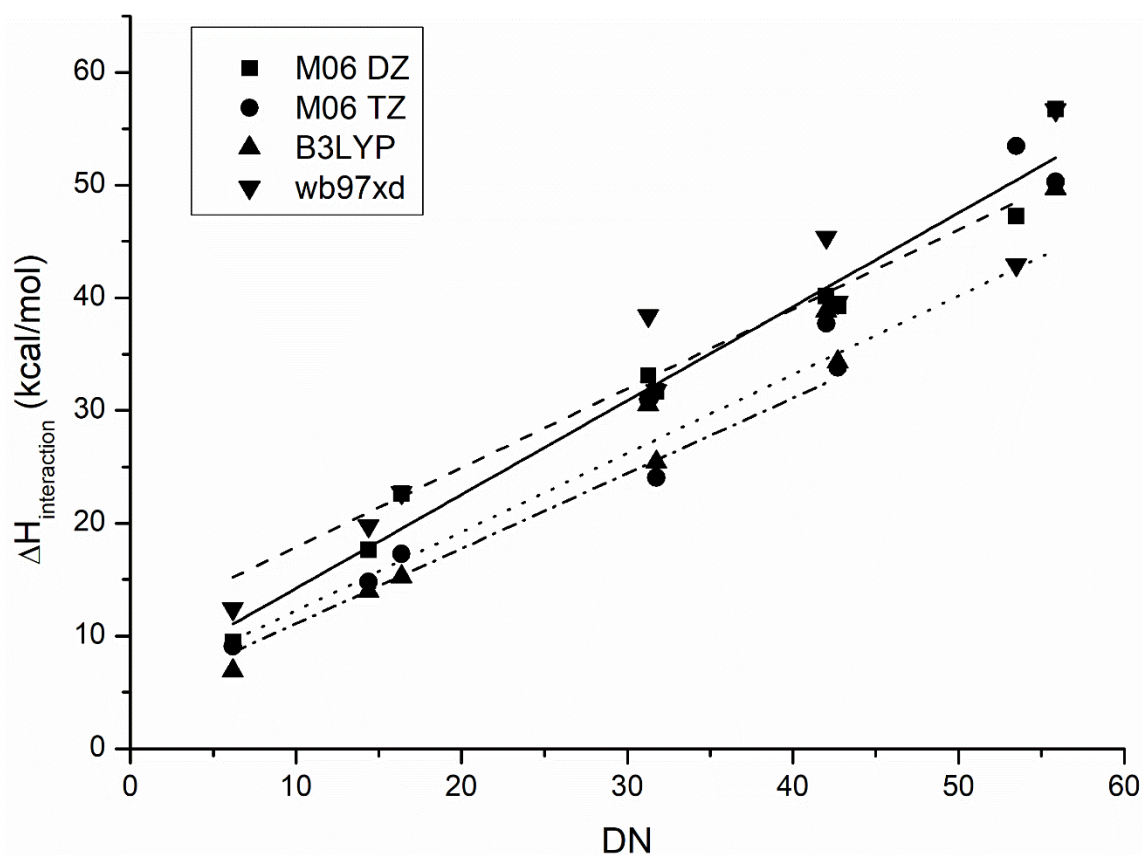
Figure 2. Correlation between the experimental values of the donor numbers and the calculated enthalpies of interaction between antimony pentachloride and the corresponding ionic liquid when the functional and basis set is changed.

When a similar approach was attempted to model the AN of ILs, no correlation could be found between the calculated data and the experimental data. Since the acceptor scale proposed by Gutmann was established based on the NMR shift of the phosphorus atom of the probe triethylphosphine oxide, this probe was used in the optimization with each IL. Neither enthalpies of interaction between probe and solvent, nor RMN shifts of the phosphorous atom displayed good correlations with the experimental data, as shown in Figure 3. This could be traced to the fact that in contrast to the DN scale, in the AN scale the IL acts as a solvent in which the probe is dissolved. Since the addition of an implicit solvent in the calculation of the DN parameter improved the correlation with the experimental data, we expected a similar response. This result suggest that Donor and Acceptor molecules behaves hardly different. We think that a more universal quantum chemical model incorporating second order effects, including polarizability effects. Work along this line is under development in our group.
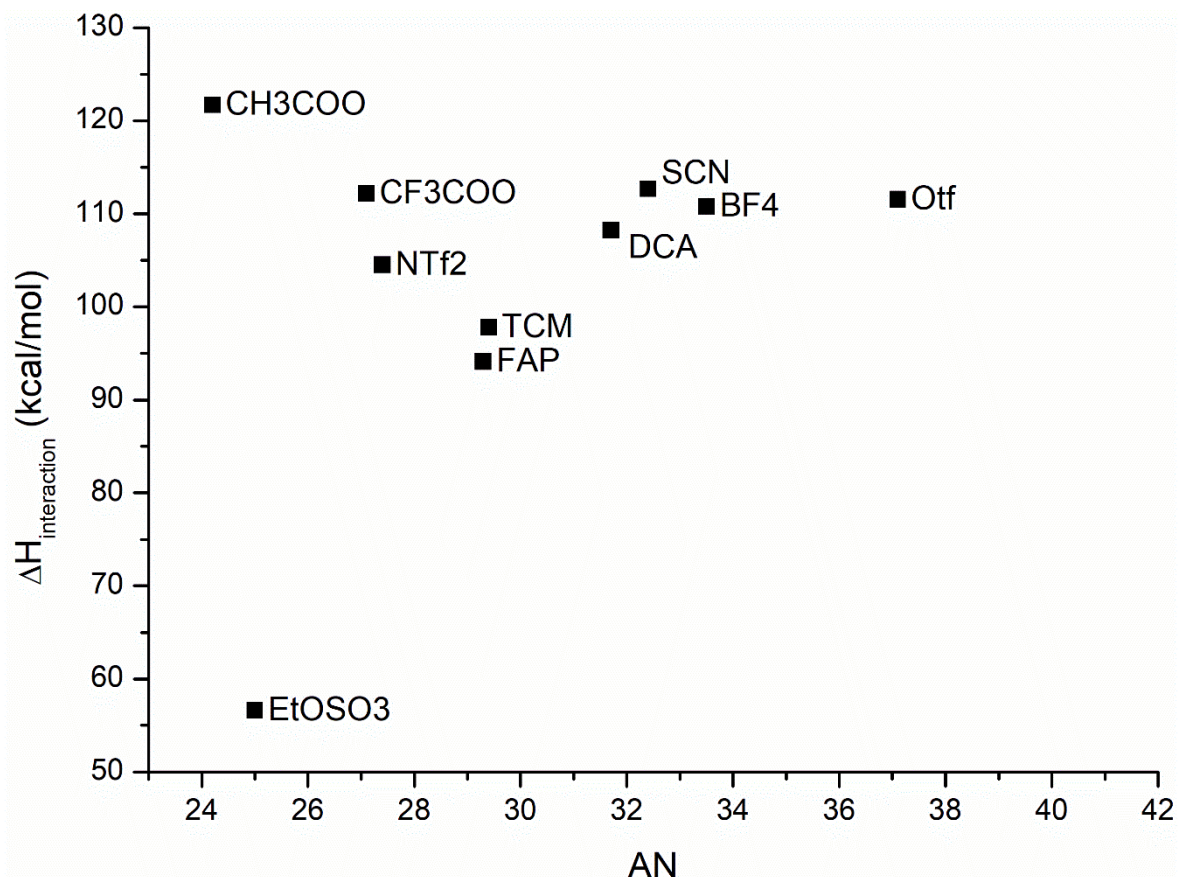
Figure 3. Acceptor number and enthalpies of interaction between the probe and the IL. The lack of a discernible trend prevents us from considering successful this methodology of calculation.

3.2 Gutmann Numbers for DES

Following a similar approach to determine AN and DN numbers for ionic liquid, the donicity of DES was determined by UV-Vis spectroscopy. The results are summarized in Table 3. When compared to ILs, DES studied show in general higher AN; falling within the range of 30-40, compared to ILs series which show variations within the range 20-30. Note also that the variability within the series is in general low. The DN values for DES also have less variability than the IL examined having a range from 35-45 while ILs have a much higher range with values ranging from 8-70. This result can be traced to the short series used because it contains only three HBD examined; two of them bearing alcohol groups as the main site of interaction, in contrast to IL where the anion changed within a larger series, varying much more in size and nature of the interacting groups.

Table 3. Absorption maxima of solvatochromic dyes and the corresponding AN and DN associated with DES at their eutectic ratio.

DES	Molar Ratio	λ Cu^{+2} (nm)	DN	λ Fe^{+2} (nm)	AN
ChCl-ethylene glycol	1:2	630	40,1	554	39,1
ChCl-propanediol	1:2	655	45,9	558	37,4
ChCl-glycerol	1:2	615	36,3	546	42,6
ChCl-1,2-butanediol*	1:2	646	43,9	563	35,3
ChCl-1,4-butanediol*	1:2	-	-	558	37,4
ChCl-urea	1:2	644	43,4	549	41,2
Betaine-ethylene glycol	1:2	618	37,1	558	37,4
Betaine-propanediol	1:2	625	38,8	562	35,7
Betaine-glycerol	1:2	618	37,1	553	39,5
Betaine-1,2butanediol*	1:2	633	40,8	566	34,1
Betaine-urea	1:2	652	45,3	557	37,8

*Measures of the absorption maxima were taken at higher temperatures than 25°C due to the difficulty to maintain the liquid phase stable at lower temperatures.

From Table 3, the following observations are pertinent: the change in HBA from choline chloride to betaine has the effect of lower AN for the betaine-based DES as compared to the corresponding choline-based DES. This result may be traced to the presence of the carboxylic group of betaine, because choline has an alcohol group further away in the side chain and a completely detached chlorine ion that can move to accommodate the extra electron density with much more ease than the betaine group can accommodate.

On the other hand, the changes in HBD shows that an increase in alcohol groups does not necessarily leads to a higher DN as one could expect, but a decrease as is shown in Table 3 after comparing propanediol and glycerol. This could arise because a higher amount of alcohol groups creates a network of hydrogen bonds stronger that the probe must break to interact with one of the donor groups.

For the DES choline chloride 1,2 propanediol the effect of the proportion between the components and the donicity number of the resulting solvent was also analyzed. The ratio 1:1 couldn't be measured at room temperature because it took the form of a solution of propylene glycol with undissolved crystals of choline. For the remaining proportions, the results are shown in Table 4. The eutectic ratio 1:2 has the higher donicity of the series; and beyond this point, the donicity remains relatively constant, probably due to the saturation of the probe chosen. This result is consistent with the previous experiment where increasing the number of alcohol groups when changing the HBD from propanediol to glycerol did not increase the donicity of the system, but it decreased. In a similar way, increasing the amount of alcohol groups available to hydrogen bonds when increasing the ratio of propanediol does not increase the donicity of the system but it lowers it because the intermolecular network of hydrogen bonds works against the interaction of another molecule with the system.

Table 4. Absorption maxima of solvatochromic dyes and the corresponding AN & DN associated for a series of choline chloride -1,2propanediol at different molar ratios.

Molar Ratio	λ Cu^{+2} (nm)	DN	λ Fe^{+2} (nm)	AN
1:1	650	44,8	565	34,5
1:2	655	45,9	558	37,4
1:3	633	40,8	554	39,1
1:4	633	40,8	554	39,1
1:5	633	40,8	554	39,1
1,2-Propanediol	582	27,4	550	40,8

A major difference in the approach taken when analyzing the polarity of DES when compared to ionic liquids is the effect that water may have as an impurity in the solvent. Therefore, it is required to evaluate the role that water may have in the polarity of the solvent after increasing water composition. The results are summarized in Figure 4. As it can be seen, when the mole fraction of water is small, the absorption maxima of the probe remain relatively stable being very close to the value of the pure DES, as the mole fraction of water is increased, both values of the absorption maxima of the probes shifted to lower values, getting away from the normal value of the water-free DES. This result gives a little flexibility in the handling of the DES since even if a little amount of water may be present the properties of the solvent shouldn't change to a significant extent. Also, since choline is highly hygroscopic one could reasonably expect to find a small amount of water in this solvent. The variation of light absorption with increasing water content is depicted in Figure 4.

Finally, experimental DN values were compared with theoretical ones, using the interaction enthalpy model already applied to ILs series. Since DES are usually in a molar ratio of 1:2 this relationship was maintained in the simulation, although a water molecule was not considered in the case of betaine even when the reactive used was a monohydrate. In the IL case we had a three-component system (cation, anion, and probe) with a clear separation of charges and therefore a clear zone of interaction between the probe and the solvent. In the DES case we have four or five bodies interacting (2 HBD molecules, the HBA and the detached chlorine contra anion in the case of choline, and the probe) with the added complexity of a partial charge separation, after all both choline chloride and betaine have their own electron donor groups that could interact with the probe.

This increase in complexity in the possible configurations that the system could adopt made the previously successful method of calculating enthalpies of interaction ineffective as it often gave negatives energies and no correlation at all. Since not all possible configurations were explored it could be the case that a further exploration of the system could show correlation between the donor number and the enthalpy of interaction of the system, but it would be more sensible to approach the problem from a different perspective, as is currently being worked by the research team.
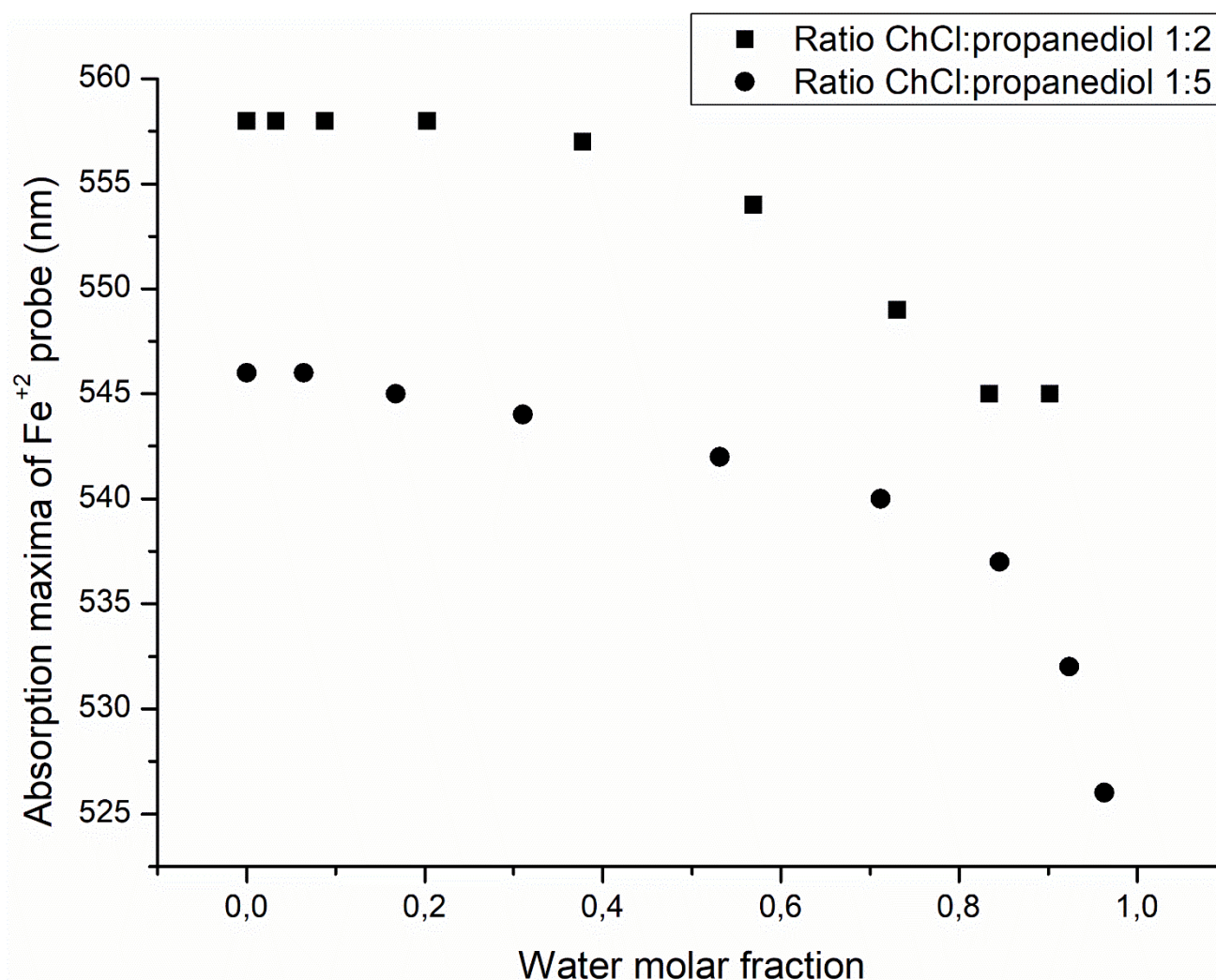
Figure 4. Changes in the absorption maxima of the Fe probe as the molar fraction of water is increased

3.3 Reaction Kinetics

The DN scales obtained for ILs, and DES were used to study solvent effects in a model the reaction between 2,4,6-trinitro phenyl phenyl ether (TNPPE) and a secondary alicyclic amine (piperazine) (Ormazabal-Toledo et al. 2013). Scheme 3 shows the accepted mechanism for this S_NAr reaction. It occurs in activated aromatic substrates bearing strong electron withdrawing groups (-NO_2 groups in this case) and a good leaving group (2,4,6-trinitro phenol for this reaction) through an addition-elimination process (Crampton et al. 2004; Terrier 2013). The first step for a stepwise mechanism is the nucleophilic attack to the substrate (k_1 channel in Scheme 3a) leading an anionic σ-adduct named Meisenheimer complex (MC in Scheme 3a). Then, two processes for its decomposition have been postulated: i) expulsion of the leaving group (LG) followed a fast proton loss to give the reaction product (k_2 in Scheme 3a) and ii) the base-catalyzed deprotonation of the MC that loss the LG to give

the reaction product (k_3 channel in Scheme 3a). The pseudo first order rate constant (k_{obs}) can be expressed as shown in Equation 1, in which [Nu] represents the concentration of nucleophile.

$$k_{obs} = \frac{k_2 k_1 [Nu] + k_1 k_3 [Nu]^2}{k_{-1} + k_2 + k_3 [Nu]} \tag{1}$$

If pathway k_2 is faster than k_3[Nu], then $k_2 \gg k_3$[Nu] therefore, the expression simplifies to:

$$k_{obs} = \frac{k_2 k_1 [Nu]}{k_{-1} + k_2} \tag{2}$$

Note that, the values of k_{obs} are in accordance with Eq. 2 were the rate of solvolysis (k_0) and the nucleophilic rate of the reaction (k_N) are obtained as the intercept (k_0) and slope (k_N) of linear plots of Eq. 3.

$$k_{obs} = k_N [Nu] + k_0 \tag{3}$$

The straight lines of these plots in all the solvents tested suggest that k_3 channel can be discarded as rate determining step (RDS) in the reaction mechanism.

The studied reaction in ILs showed a low donicity for C_2C_1IM PF$_6$ and C_2C_1IM BF$_4$. In these solvents under the same experimental conditions, no significant amount of product was detected after 3 hours. On the other hand, ILs with high donicity like C_2C_1IM DCA, the solvent established a competitive reaction with the nucleophile for the same reaction site. This fact was evidenced with a change on the reaction product spectra and the kinetic profile. In this case, changing λ_{max} from 416 nm to 441 nm and changing the color associated to the reaction product. This behavior was not observed in DES in comparison to the ILs studied. In this context, the behavior of the reaction in DES was found to be consistent with the general mechanism for S$_N$Ar reaction.

Note that, this kind of specific interactions between the solvent and reagents cannot be described only by a simple polarity model so it is important to keep in mind that even when the Gutmann numbers scale can be used to predict reactivity of a system, it only describes one aspect of the interaction between solvent and solute and no scale and due to the complexity of the possible interactions between the pair, no single scale can describe all the interactions.

a)

b)

c)
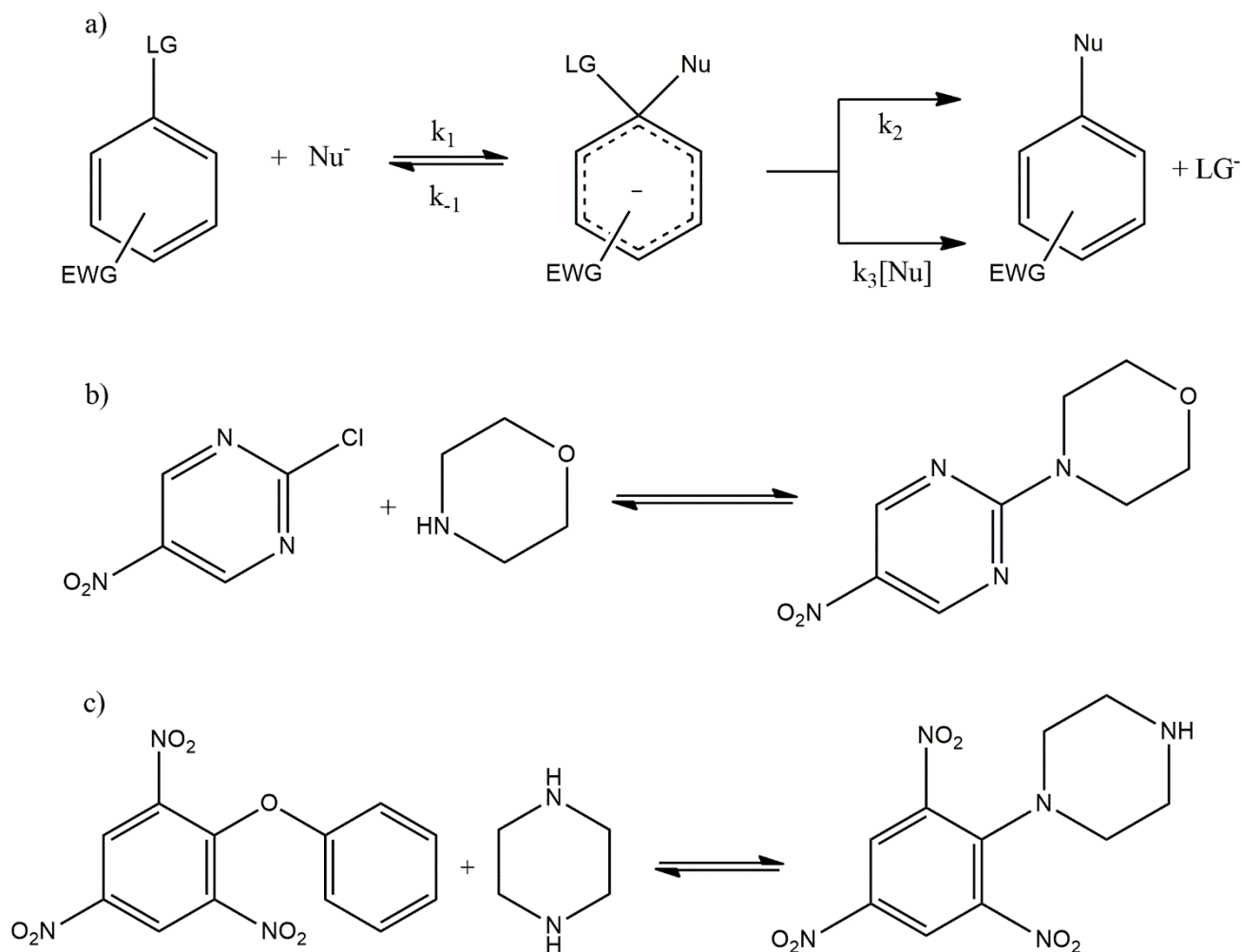
Scheme 3. a) General mechanism for a nucleophilic aromatic substitution. The substrate has a leaving group (LG) and some electron withdrawing group (EWG) to favor the substitution. The nucleophile (Nu) attaches to the ring to form the Meisenheimer complex that can generate the desired product through a first order decomposition (k_2) or a second order decomposition with the help of a second molecule of nucleophile (k_3). **b)** Scheme for the product reaction between CNP and morpholine. **c)** Scheme for the product reaction between TNPPE and piperazine.

Table 5 shows the k_N values and the molar ratio of the reagents used to prepare the studied DES. Note that, the donicity trend and the nucleophilic rate coefficients decreases with the increase of the propanediol ratio, however the constant decrease in the reaction rate even when the DN remained constant, thereby indicating that the donor capabilities of the solvents are not the only factor that affects the reaction. Since in DES we have neutral components that have lower nucleophilicity, the problems encountered with IL were not found, yet it is important to indicate that the others DES that were attempted (like choline-urea and choline-glycerol) were not suitable to the kinetic measurements since the high viscosity of the liquid prevented the mixing of the reactants in the cuvette. In the case of choline glycerol an increase in temperature decreased enough the viscosity of the solvent to enable the measurement of the reaction rates. However, for choline urea even this increase was not enough to overcome the difficulties encountered. Since temperature affects the reaction rate of the system, to compare the rates between propanediol and glycerol, the test with propanediol was repeated at higher temperature in which case we can see that the DES with

propanediol has a higher reaction rate than the DES with glycerol. Unfortunately, difficulties in dissolving the solvatochromic dyes in the choline-glycerol mixture prevented us from measuring the Gutmann numbers of this solvent. The viscosity problem of DES is an important barrier for the use of these solvents in most cases.

Table 5. Nucleophilic reaction rates for the reaction between 2,4,5-trinitro phenyl phenyl ether and piperazine in DES.

DES	Molar ratio	Temperature (°C)	k_N (M^{-1}s^{-1})
ChCl-propanediol	1:2	25	9,42 ± 0,80
ChCl-propanediol	1:3	25	8,14 ± 0,59
ChCl-propanediol	1:4	25	7,31 ± 0,51
ChCl-propanediol	1:5	25	6,48 ± 0,57
ChCl-propanediol	1:2	40	23,24 ± 1,47
ChCl-glycerol	1:2	40	15,21 ± 0,95
ChCl-ethylene glycol	1:2	25	9,70 ± 0,69
Betaine-ethylene glycol	1:2	25	12,28 ± 0,71

Since the previous reaction was not a suitable model for ionic liquids, another reaction was chosen to prove the prediction capabilities of the donicity model. The reaction between 2-chloro-5-nitro-pyrimidine (CNP) and morpholine was tested in 11 ILs as shown in Table 6. All solvents showed a linear relationship between the nucleophile concentration and the apparent reaction rate that indicates that the mechanism goes through a k_2 path with no catalysis of a second nucleophile molecule. Since all the solvent had the same reaction mechanism it is possible to compare them with the donicity of each solvent to see if a trend appears. When plotting the k_N of each system against the DN in Figure 5, a general upward trend can be seen where a higher donor number gives a faster reaction rate. The IL C_2C_1IM SCN has a lower than expected reaction rate when compared to the remaining elements of the series.

Table 6. Donor number and nucleophilic rate constant for the reaction between 2-chloro-5-nitropirimidine and morpholine in different ILs.

LI	DN	k_N (M^{-1}s^{-1})
C$_4$C$_1$IM BF4	15,7	12,69 ± 0,29
C$_4$C$_1$IM PF6	8,8	7,34 ± 0,50
C$_2$C$_1$IM DCA	41,5	12,36 ± 1,10
C$_2$C$_1$IM SCN	76,2	26,19 ± 1,69
C$_4$C$_1$PYRR DCA	44	26,49 ± 1,10
C$_2$C$_1$IM Ntf2	17,8	5,68 ± 0,41
Et3S Ntf2	17,7	5,17 ± 0,33
C$_4$C$_1$PIP Ntf2	17	7,33 ± 0,25
C$_4$C$_1$IM MeSO4	52	37,37 ± 1,36
C$_2$C$_1$IM MeSO4	72,5	55,78 ± 3,01
C$_2$C$_1$IM EtSO4	45,7	45,80 ± 1,53
C$_2$C$_1$IM CF3COO	52,5	43,54 ± 1,80

Note that in plot 6b) a loose linear relationship could be established, after dropping C$_2$C$_1$M SCN and C$_2$C$_1$M DCA points; that coincides with the most polarizable (softer) anions present in the corresponding IL. This result emphasizes the necessity of including second order effects embodying dipole polarizability contributions within the model.

When the reaction was run in DES (choline chloride with propanediol, glycerol and urea), the presence of the nucleophile destabilized the solvent, thereby forcing it to precipitate, so no kinetic data could be recorded. This result is a reminder that specific interactions between the solute and solvents are to be incorporated via a super molecule-like approach, and therefore the implicit third body effects are important. As a result, a simple model based only on solvent polarity is not suitable enough when dealing with the kinetics of these model reactions.
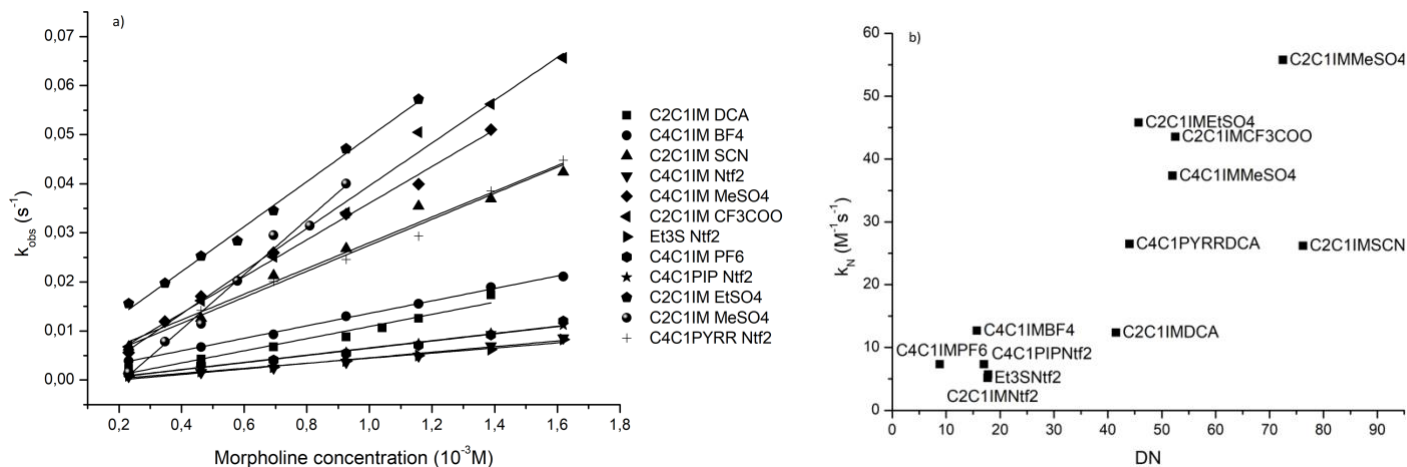
Figure 5. Plots of nucleophile concentration *vs* observed pseudo first order rate (a) and donor number vs nucleophilic reaction rate (b).

4   Conclusions

An integrated experimental and theoretical study was performed in a series of neoteric solvents, including ionic liquids and deep eutectic solvents. The main message we would send is that a first order theoretical model, based on the interaction energy (enthalpy) between probes and solvents is insufficient to embody solvent effects within a unified solvation effects model on chemical reactivity in these systems. Second order effect, incorporating polarizability contributions should give better responses, because the presence of sizable anions in both, ILs and DES. This second order model is at present under development in our group. The best predictive capabilities of the donor number scale on a real system using the reaction rates of a S_NAr reaction reveals that a high DN solvent leads to higher reaction rates. It was found that the acceptor and donor capabilities of a DES varies when the molar ratio of the HBD/HBA is modified away from the eutectic ratio but then remains constant for higher ratios. It was also shown that there is a small window of water content in which the polarity properties of the DES remain constant but at higher concentration of water there is a rapid decrease of the donor/acceptor properties of these new generation of solvents.

5   Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

6   Author Contributions

BS: Performed both experimental studies and quantum chemical calculations and wrote the paper.

PRC: Proposed the experimental determination of AN and DN numbers, the application to the kinetics of a model S_NAr reaction as benchmark and wrote the paper.

RC: Proposed the Gutmann´s AN and DN concepts to model hydrogen bond basicity and acidity in both, ILs and DES and wrote the paper.

7   Acknowledgments

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