We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

Open access books available
177,000
International authors and editors
195M
Downloads

154
Countries delivered to
TOP 1%
Our authors are among the most cited scientists
12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Chapter

Solvent Effect on a Model of S_NAr Reaction in Conventional and Non-Conventional Solvents

Paola R. Campodónico

Abstract

In this chapter some theoretical and experimental reports in order to elucidate solvent effects (preferential solvation and iso-solvation effects, respectively) over nucleophilic aromatic substitution reactions as reaction model were examined. Solvent effects phenomena are introduced to predict their mechanism highlighting the hydrogen bond role mainly in ionic liquids, a new generation of solvents that can be designed in order to improve the reactivities of the reacting pair and intermediate species through of the potential energy surface (PES). Then, the preferential solvent effect may be defined as the difference between local and bulk compositions of the solute with respect to the various components of the solvent; usually mixtures of solvents and iso-solvation effect indicate the composition of a mixture in which the probe under consideration is solvated by approximately an equal number of cosolvent molecules in the solvent mixture.

Keywords: solvent effects, preferential solvation, S_NAr reaction, ionic liquids, iso-solvation effect

1. Introduction

Studies suggest that nucleophilic aromatic substitution (S_NAr) reactions are significantly affected by the reaction media, because it involves the stabilization of species associated to the potential energy surface (PES) determining selectivity, reaction rates, and mechanisms [1–3]. In this chapter an integrative analysis based on experimental and theoretical results as an input to perform a deeper analysis based on preferential solvation and iso-solvation effects, respectively, is described. This chapter is organized by summarizing the main achievements on solvent effects based on S_NAr reactions considering that these reactions have widely been studied in water, conventional organic solvents (COS), and more recently in ionic liquids (IL) and mixtures of them [1–11]. Note that the most discussed articles are based on kinetic responses in order to evaluate the solvent effect over this reaction which has been used as model.

2. Nucleophilic aromatic substitution reactions

Nucleophilic substitution is an addition-elimination (A_N_D_N) process that depending on the nature of the substrate, the attacking nucleophile, and the solvent
effect may lead to a nucleophilic substitution (NS) product or an SNAr product or both [12–16]. An SNAr reaction occurs in activated aromatic compounds bearing good leaving groups (LG). In general, it is widely accepted that the mechanism of the SNAr reactions involves the formation of a σ-complex (also called Meisenheimer complex (MC)) that occurs after the nucleophilic attack step at the ipso atom of the aromatic moiety. Next, the departure of LG with re-aromatization of the aromatic ring closes the set of steps to give the desired product. Commonly, the LG departure step is faster than the nucleophilic attack; therefore, the addition of the nucleophile to the ring moiety appears as the rate-limiting step in these processes [13, 17–24]. In the last time, a concerted reaction mechanism could be prevailing [25–27]. A lot of work has been carried out to clarify whether the concerted mechanism is an exception or the dominant pathway in these processes [28, 29].

2.1 Hydrogen Bond in SNAr Reactions

Bernasconi et al. [23, 30] postulated the existence of an intramolecular hydrogen bond between a hydrogen atom of the nucleophilic center in the nucleophile and the ortho-NO₂ group of the substrate in order to explain the reactivity trends in ortho-halonitrobenzenes to respect para-halonitrobenzenes toward amines. Ormazábal-Toledo et al. [31] carried out computational studies about the role of HB effects along the intrinsic reaction coordinate profile, demonstrating that it promotes the activation of both the substrate and nucleophile, respectively. Note that the analysis was performed in transition state (TS) structures, because the reactant states hide most of the information about specific interactions that characterize the SNAr reactions. Recently, Gallardo-Fuentes and Calfumán et al., respectively, showed that the HB not only determines the reactivities, but also it could be involved in concerted routes in SNAr reactions [1, 26, 32].

3. Room temperature ionic liquids

Ionic liquids or room temperature ionic liquids (RTILs) are defined as molten salts (composed entirely of cations and anions) that melt below 100°C [33] with remarkable physicochemical properties: non-flammable, non-corrosive, nonvolatile, and bulk physical constant, which can be tuned by the combination of different cations and anions [34–38]. RTILs are composed by bulky organic cations usually imidazolium or pyridinium derivatives substituted with alkyl chains and an inorganic or organic anion (usually a halide, tetrafluoroborate, hexafluorophosphate, and others). The high combinatorial flexibility has converted these materials into “designer solvents” or “task-specific” solvents [33, 35, 38] whose properties can be specified to suit the requirements of a particular reaction [2, 4, 12, 39]. For these reasons, RTILs have gained importance in the solvent effects field being recognized as very promising reaction media with green features.

3.1 SNAr reactions in ionic liquids

A series of reaction have been studied in RTILs and mixtures of them with water or COS. The criteria to select the RTILs were based on the following: (i) the solubility of substrates and nucleophiles; (ii) to have a reasonable number of anions and cations to assess anion and cation effects; and (iii) to ensure that these RTILs do not interfere with the reaction [12]. Solvent effects in RTILs are a complex problem, because the solute-solvent interactions will be masked by the leading solvent-solvent interactions that are coulombic in nature. Some strategies to study
Solvent Effect on a Model of S\textsubscript{N}Ar Reaction in Conventional and Non-Conventional Solvents

DOI: http://dx.doi.org/10.5772/intechopen.89838

Solvent effects in RTILs consider a reasonable large number of these and to evaluate their performance by fixing the anion and varying the cation and vice versa. For instance, a complete study based on the reaction of DNBSCl with piperidine was performed in 17 RTILs considering water as a solvent reference. This study identified three groups of RTILs showing 1-ethyl-3-methylimidazolium dicyanamide (EMIMDCN) as the best solvent considering all the studied RTILs and 21 COS [12, 40]. EMIMDCN shows a catalytic behavior attributed to its high polarizability given by the dicyanamide anion (DCN\textsuperscript{−}), which presents a highly rich π electron density, and its size could be in relationship with steric hindrance effects. Note that ethylammonium nitrate (EAN) was the only protic RTIL that decreased the reaction time in comparison to water and EMIMDCN, respectively. Then, a comparative study of the reaction of DNBSCl and propylamine in COS and RTILs, respectively, was performed in order to analyze the nature of the nucleophile. Piperidine showed to be more active than propylamine in polar solvents with the ability to donate and accept HB, while the reaction of propylamine was favored only with solvent that can accept HB, being the best COS solvent: N,N-dimethylformamide (DMF). Note that, in all the studied RTILs for propylamine, the reactivities of the reactions were lower than piperidine. This response was attributed to the capacity of the RTILs to donate/accept HB in agreement with the COS behavior [12]. On the other hand, propylammonium nitrate (PAN) was able to emulate the HB behavior of water toward the reaction between 4-chloroquinazoline and aniline [39]. PAN could be donating an HB by the ammonium moiety of PAN toward the substrate emulating an electrophilic solvation suggested in aqueous media improving its reactivity toward the nucleophile. These results are in agreement with the report of Welton et al. [2] based on the task-specific design of RTILs in order to optimize those properties that enhanced the reaction reactivities. Harper et al. reported the main role of the RTIL structure on the reaction rates of S\textsubscript{N}Ar reactions [41, 42].

3.2 Binary mixtures based on ionic liquids

The use of RTILs or ionic liquid binary mixtures could give variations in the structure of the ionic lattice of neat ILs after mixing [43–45]. This fact may have significant repercussions on the nature and strength of the interactions that contribute mainly to coulomb interactions that determine the 3D structure of ILs [46, 47]. Studies of binary mixtures with common anions, for instance, the same cation but different anions, have shown how the presence of random co-networks or block co-networks depends on the size of the anions [4, 47, 48]. Seddon suggests the use of IL mixtures to expand the range of room temperatures in ILs [49]. Initially, the hygroscopic nature of the ILs was a problem; however the high capacity of the ILs to solubilize water opens a wide spectrum of reaction media, mainly based on the role of the hydrogen bond (HB) and electrostatic interactions between molecules in the mixture. Reports have shown that the addition of COS to ILs may affect significantly the density, viscosity, and conductivity with respect to pure ILs. For instance, the direct relationships between the viscosity of the IL/COS mixtures with the solvent dielectric constant (\(\varepsilon\)) of the COS pure [50, 51]. It may be attributed to the difference in the ion-dipole interactions between the ions and solvents. The addition of water to ILs may change the molecular structure of pure ILs probably due to HB between the water molecules and the anions of the ILs [52, 53]. Sanchez et al. studied solvent mixtures between 1-butyl-3-methyl imidazolium tetrafluoroborate (BMIMBF4)/water at different molar fractions, observing on the studied range of compositions, a border line located close to \(\chi = 0.2\). Before this value indicates that the added RTIL promotes the reactivity of the substrate by preferential solvation. After this value, the rate coefficients remain approximately constant. At low concentrations the water begins to break down the 3D
structure of the ILs, which then goes on to form ionic clusters as the concentration of water increases until eventually ion pairs form, which are the dominant species in the aqueous solution [10, 46, 48].

4. Interactions and solvent effects

It is well known that the chemical reactivity is determined by the ability of the solvent to interact with solute, intermediates, and transition state (TS) structures along the reaction pathway [1–3]. The main difference between COS and RTILs are the electrostatic solvent-solvent interactions between cation-anion and cation-cation interactions [33]. These interactions in the COS are moderate dipole-dipole interactions; in the RTILs they become the leading term (ion-ion interactions) that are expected to outweigh the target solute-solvent interactions. Solute-solvent interactions contain the relevant information about catalysis, stabilizing/destabilizing effects affecting the electrophile/nucleophile pair (solute), TS structures, and the intermediate in a polar process [1]. Solvent effects can be split into two types: non-specific interactions and specific interactions, including all the possible interactions that can occur between solvent and the electrophile/nucleophile pair [5, 52].

4.1 Preferential solvation

Solvent effects can be split into two types: non-specific and specific interactions, including all the possible interactions that can occur between the solvent and solute [5, 39, 54]. Then, preferential solvent may be defined as the difference between local and bulk composition of the solute with respect to the various components of the solvent, usually mixtures of solvents [5, 55–57]. The “bulk of the solvent” is treated as the external shell, and it can be described using the classic theories of Kirkwood-Onsager, models of solvation based on reaction field theory or molecular dynamic [55, 58, 59]. Then, in a binary mixture of protic solvents, the “preferential solvation” may be cast into the form of specific solute-solvent interactions described as local solvation, which may be defined as a “first solvation shell.” The local solvation may be classified as electrophilic or nucleophilic, respectively [17, 60–63]. Electrophilicity and nucleophilicity concepts are related to electron-deficient (electrophile) and electron-rich (nucleophile) species [39, 64, 65]. These concepts are based on the valence electron theory of Lewis [66] and the general acid–base theory of Brønsted and Lowry [67, 68] and introduced by Ingold in 1934. Then, for a mixture of polar solvents, the “electrophilic solvation” represents the specific interaction through a HB with the hydrogen atom of the solvent, whereas “nucleophilic solvation” describes a specific interaction through a HB between an acidic hydrogen atom of the solute and the heteroatom of the solvent [5, 60–63]. Mancini et al. have reported preferential solvation of 1-halo-2,4-dinitrobenzenes with amines in mixtures of dichloromethane with polar protic/polar aprotic solvents [7, 44, 45, 69, 70]. Ormazabal-Toledo et al. [5] reported an integrated experimental and theoretical study of 2,4,6-trinitrophenyl ether with a series of secondary alicyclic (SA) amines in ethanol/water mixtures at different compositions. In it only piperidine was sensitive to preferential solvation at high proportion of water. Piperidine increases its rate coefficient values suggesting a stabilization of the MC by HB displayed by the presence of more water molecules in the first shell at these proportions of water in the studied mixtures. This result shows that the environment of the MC changes for different solvent compositions. Then, for the remaining amines the environment showed to be similar being it attributed to polar nature of the substituent at position 4, suggesting that their kinetic responses are independent of the bulk properties of the reaction media. On
the other hand, Alarcón-Espósito et al. [1] studied the reaction between 1-chloro and 1-fluoro-2,4-dinitrobenzenes, respectively (ClDNB and FDNB, respectively) with morpholine (a SA amine) in acetonitrile (MeCN)/water mixtures at different compositions. Experimental results were complemented with a theoretical analysis in order to study the bulk and specific interactions of solute-solvent in mixtures of a COS (MeCN) and water. Note that both solvents display significant HB abilities. Then, in 90% vol. MeCN substrates both displayed the maximum value of the rate coefficient constants. On the other hand, the exploration of the PES using the “super-molecule method” revealed that the solvation of the TS structure associated to the rate determining step (RDS) of the reaction mechanism expressed in the mode water/MeCN outweighs over MeCN/water, suggesting a preferential solvation in favor of the aqueous phase. The super-molecule model introduces solvent molecules explicitly around the solute. This model provides a detailed synopsis of the field of solvation sufficient to describe the interactions between the solute and solvent [71].

4.2 Iso-solvation

The concept of iso-solvation has been introduced to indicate the composition of a mixture in which the probe under consideration is solvated by an approximately an equal number of cosolvent molecules in the solvent mixture [48]. This effect has been extensively observed in COS mixtures [72–74]. Alarcón-Espósito et al. [48] studied the reaction between ClDNB with morpholine in a series of mixtures of ILs involving imidazolium cations. Iso-solvation effects were observed in the following mixtures: 1-ethyl-3-methyl imidazolium thiocyanate/1-ethyl-3-methyl imidazolium dicyanamide (EMIMSCN/EMIMDCN), 1-butyl-3-methyl imidazolium dicyanamide/1-butyl-3-methyl imidazolium tetrafluoroborate (BMIMDCN/BMIMBF$_4$), BMIMBF$_4$/1-butyl-3-methyl imidazolium hexafluorophosphate (BMIMPF$_6$), and BMIMPF$_6$/1-butyl-3-methyl imidazolium tris(pentafluoroethyl)trifluorophosphate (BMIMFAP), respectively. Iso-solvation regimes correspond to a solvent composition regime where the solute is being solvated by approximately the same number of different solvent molecules in the mixture. These results showed that for significant changes in composition, the rate coefficients remain approximately constant. On the other hand, for the solvent mixture BMIMBF$_4$/BMIMPF$_6$ at 0.9 molar fraction of BMIMBF$_4$, a slightly better kinetic response is observed than the pure BMIMBF$_4$ and BMIMPF$_6$. Another interesting result was observed in the mixture of EMIMSCN/EMIMDCN; an increasing proportion of EMIMSCN with respect to EMINDCN results in a decrease of the rate coefficient within the range 0.1–0.75 in molar fraction of EMIMSCN. This result could be expressed as a competition between the anions toward the reaction center driven by the basicity of the reaction media.

4.3 Polarity and solvent effects

Experimentally, the most common way to measure the polarity of a solvent is through its (bulk) dielectric constant ($\varepsilon$). The concept of polarity has been defined as the sum of all possible intermolecular interactions between the solvent and the solute, including specific interactions, for instance, HB effects, dipole-dipole, dipole-induced dipole, electron pair acceptor-electron pair donor, and acid-base interactions [1, 33]. Gazitúa et al. [12, 40] studied the solvation patterns of 21 COS and water over the reaction between 2,4-dinitrophenylsulfonyl chloride (DNBSCl) with SA amines in order to determine the solvent polarity effect on the reaction mechanism. Note that solvent polarity became relevant only in the reactions that proceeded by the non-catalyzed route. On this way, water and tetrahydrofuran
(THF) have a key role due to its ambiphilic character as an HB donor/acceptor that promotes a nucleophilic activation at the nitrogen center of the piperidine (nucleophile).

5. Solvent models

5.1 Kamlet-Taft model

Solvent effect studies have been focused mainly on the polarity of the reaction medium as a determinant of chemical reactivity properties. Experimentally, the most common way to measure the polarity of a solvent is through the $\varepsilon$. However, the measure requires that the reaction medium will be non-conductive, which does not happen in the RTILs. The concept of polarity has been defined as the sum of all possible intermolecular interactions between the solvent and a solute, excluding those interactions that lead toward chemical reactions of the solute and including Coulombic interactions, HB interactions, dipole-dipole, dipole-induced dipole, electron pair acceptor-electron pair donor, and acid-base interactions [1, 33]. There are many empirical solvent polarity scales [75–83] that attempt to give quantitative estimates of solvent polarity, some of those were applied to RTILs [84]. However, the high number of interactions in non-conventional reaction media cannot be incorporated in a measurement or polarity scale. The most used solvent polarity scale is the one developed by Kamlet and Taft [78] based on solvatochromism properties that show specific and non-specific interactions. Solvatochromism is solvent dependence of the electronic spectrum of chromophore. Intensity, position, and shape of absorption bands of dissolved chromophores are influenced by the change in solvents or mixture of solvents, according to their electronic and molecular structure, due to the different stabilization of their electronic ground and excited states. Therefore, any solvent-dependent property (SDP) in solution is normally expressed as a linear solvation free energy relationship (LSER) as follows:

$$SDP = SDP_0 + a \alpha + b \beta + s \pi^*$$  \hspace{1cm} (1)  

where $SDP$ corresponds to any kinetic property, namely, selectivity or reaction rate coefficients, which is modeled as a linear combination of two H-bond terms, one for hydrogen bond donor ($a \alpha$) and hydrogen-bond acceptor ($b \beta$), and a dipolarity/polarizability term ($s \pi^*$), with SDP$_0$ a constant describing intrinsic properties of the solute [84]. In this approach, empirical solvatochromic parameters are introduced to describe specific HB interaction, ion-dipole, dipole-dipole, dipole-induced dipole, solvophobic, dispersion London, and possible $\pi-\pi$ and $p-\pi$ stacking effects. The reason is that while empirical solvatochromic parameters in COS work reasonably well, for RTILs they consistently fail. The main reason seems to be the transferability of the response of a particular probe chromophore from some known SOC to RTILs. This transferability would warrant that the polarities of the RTILs and the SOC are the same and that the appropriate value of the parameter can then safely be assigned to the RTIL. The second implicit assumption is that the effect of transferring from a SOC to an RTIL is the same for all probes. They conclude that it is important to consider the nature of the chromophore as well as the solvent when establishing reliable solvent polarity parameters, mainly when this chromophore is transferred from a neutral molecular solvent to an RTIL. The main message, however, is that it cannot be a priori established if one solvent polarity scale with respect to another one is right or wrong: “each scale will turn useful in a given set of circumstances and in other ones they will not” [1, 12].
5.2 Theoretical models of solvation

In pure conventional solvents, the determination of properties and type of interactions has been reasonably achieved with the use of non-specific solute-solvent interactions, based on continuum dielectric models [85, 86]. In RTILs, the results are both scarce and not yet systematized [87, 88]. The super-molecule model provides a detailed synopsis of the field of solvation [71].

5.3 Gutmann's donor and acceptor numbers

Donor (DN) and acceptor (AN) numbers proposed by Gutmann [89–91] are used to describe acid-base solvent properties in RTILs based on a reformulation by Schmeisser et al. [92, 93]. On the original definition of Gutmann, DN and AN are a quantitative measure of Lewis basicity and acidity of a solvent, generally a nonaqueous media [4, 91]. These numbers can be measured by calorimetric technique and by using the chemical shift in $^{31}$P NMR spectra [92, 94]. In COS these parameters are used in order to describe the ability of solvents to donate or accept electron pairs or at least electron density to the substrate. Then, DN represents a measure for the donor properties of a solvents, and AN is a measure of the electrophilic properties of a solvent. DN parameter in RTILs shows a strong dependence on the anionic component of the RTIL; however, AN is dependent on both anionic and cationic moieties of the RTIL [92].

Alarcón-Espósito et al. [4] studied three families of RTILs, based on 1-ethyl-3-methyl imidazolium (EMIM$^+$), 1-butyl-3-methyl imidazolium (BMIM$^+$), and 1-butyl-1-methyl-pyrrolidinium (BMPyr$^+$) cations, respectively, with a wide series of anions in order to evaluate both models of solvent effects toward the reaction between 1-chloro-2,4-dinitrobenzene with morpholine by kinetic experiments. The first approximation of solvent effects was attributed to an "anion effect." This effect appears to be related to the anion size, polarizability, and its HB ability toward the substrate. The comparison between rate constants and Kamlet-Taft solvatochromic model systematically failed. However, the anion effect was confirmed by performing a comparison of the rate constants and DN emphasizing the main role of the charge transfer from the anion to the substrate.

6. Conclusions

In this chapter some theoretical and experimental reports in order to elucidate solvent effects over nucleophilic aromatic substitution reactions were examined. Solvent effects are introduced over mechanistic behaviors highlighting the HB role mainly in RTILs, a new generation of solvents that can be designed in order to improve the reactivities of the reacting pair and intermediate species through the PES. For instance, (i) solvent polarity could be modulating the reaction pathways differently; (ii) the ability of the solvent to establish HB could drive the reaction mechanism opening the possibility of preferential solvation; (iii) in mixtures of solvents and depending on the constituents of them could be affecting the reaction rate by solvent structural organization, viscosity, and HB interactions; and (iv) in ionic liquids the solvent effect could be attributed to an anion effect being it related to the size and HB abilities of the anions.

Acknowledgements

This work was supported by Fondecyt Grant 1150759 (PC), Proyecto de Mejoramiento Institucional postdoctoral fellowship PMI-UDD from Instituto...
Author details

Paola R. Campodónico
Facultad de Medicina, Centro de Química Médica, Clínica Alemana Universidad del Desarrollo, Santiago, Chile

*Address all correspondence to: pcampodonico@udd.cl
Solvent Effect on a Model of SN Ar Reaction in Conventional and Non-Conventional Solvents
DOI: http://dx.doi.org/10.5772/intechopen.89838

References

[1] Alarcón-Espósito J, Tapia RA, Contreras R, Campodónico PR. Changes in the SNAr reaction mechanism brought about by preferential solvation [Internet]. RSC Advances. 2015;5:99322-99328. DOI: 10.1039/c5ra20779g

[2] Newington I, Perez-Arlandis JM, Welton T. Ionic li-quids as designer solvents for nucleophilic aromatic substitutions. Organic Letters. 2007;9:5247-5250

[3] D’Anna F, Marullo S, Noto R. Aryl azides formation under mild conditions: A kinetic study in some ionic liquid solutions. The Journal of Organic Chemistry. 2010;75:767-771

[4] Alarcón-Espósito J, Contreras R, Tapia RA, Campodónico PR. Gutmann’s donor numbers correctly assess the effect of the solvent on the kinetics of SN Ar reactions in ionic liquids. Chemistry. 2016;22:13347-13351

[5] Ormañabal-Toledo R, Santos JG, Ríos P, Castro EA, Campodónico PR, Contreras R. Hydrogen bond contribution to preferential solvation in SNAr reactions. The Journal of Physical Chemistry. B. 2013;117:5908-5915

[6] Um I-H, Min S-W, Dust JM. Choice of solvent (MeCN vs H2O) decides rate-limiting step in SNAr aminolysis of 1-fluoro-2,4-dinitrobenzene with secondary amines: Importance of Brönsted-type analysis in acetonitrile [Internet]. The Journal of Organic Chemistry. 2007;72:8797-8803. DOI: 10.1021/jo0701549h

[7] Nudelman NS, Mancini PME, Martinez RD, Vottero LR. Solvents effects on aromatic nucleophilic substitutions. Part 5. Kinetics of the reactions of 1-fluoro-2,4-dinitrobenzene with piperidine in aprotic solvents [Internet]. Journal of the Chemical Society, Perkin Transactions. 1987;2:951. DOI: 10.1039/p29870000951

[8] Swager TM, Wang P. A negotiation between different nucleophiles in SNAr reactions. Synfacts. 2017;13:0148-0148

[9] Park S, Lee S. Effects of ion and protic solvent on nucleophilic aromatic substitution (SNAr) reactions. Bulletin of the Korean Chemical Society. 2010;31:2571-2573

[10] Marullo S, D’Anna F, Campodonico PR, Noto R. Ionic liquid binary mixtures: How different factors contribute to determine their effect on the reactivity. RSC Advances. 2016;6:90165-90171

[11] D’Anna F, Frenna V, Noto R, Pace V, Spinelli D. Study of aromatic nucleophilic substitution with amines on nitrothiophenes in room-temperature ionic liquids: Are the different effects on the behavior of para-like and ortho-like isomers going from conventional solvents to room-temperature ionic liquids related to solvation effects? [Internet]. The Journal of Organic Chemistry. 2006;71:5144-5150. DOI: 10.1021/jo060435q

[12] Gazitúa M, Tapia RA, Contreras R, Campodónico PR. Mechanistic pathways of aromatic nucleophilic substitution in conventional solvents and ionic liquids. New Journal of Chemistry. 2014;38:2611-2618

[13] Bunnett JF, Zahler RE. Aromatic nucleophilic substitution reactions [Internet]. Chemical Reviews. 1951;49:273-412. DOI: 10.1021/cr60153a002

[14] Choi JH, Lee BC, Lee HW, Lee I. Competitive reaction pathways in the nucleophilic substitution reactions of aryl benzenesulfonates.
with benzylamines in acetonitrile. The Journal of Organic Chemistry. 2002;67:1277-1281

[15] Um I-H, Hong J-Y, Kim J-J, Chae O-M, Bae S-K. Regioselectivity and the nature of the reaction mechanism in nucleophilic substitution reactions of 2, 4-dinitrophenyl X-substituted benzenesulfonates with primary amines. The Journal of Organic Chemistry. 2003;68:5180-5185

[16] Um I-H, Chun S-M, Chae O-M, Fujio M, Tsuno Y. Effect of amine nature on reaction rate and mechanism in nucleophilic substitution reactions of 2, 4-dinitrophenyl X-substituted benzenesulfonates with alicyclic secondary amines. The Journal of Organic Chemistry. 2004;69:3166-3172

[17] Mortier J. Arene Chemistry: Reaction Mechanisms and Methods for Aromatic Compounds. Chapter 7. New Jersey, USA: John Wiley & Sons; 2015. p. 175-193

[18] Buncel E, Norris AR, Russell KE. The interaction of aromatic nitro-compounds with bases. Quarterly Reviews, Chemical Society. 1968;22:123-146

[19] Bunnett JF. Some novel concepts in aromatic reactivity. Tetrahedron. 1993;49:4477-4484

[20] Miller J. 1918. Aromatic Nucleophilic Substitution. 1968. Available from: http://agris.fao.org/agris-search/search.do?recordID=US201300456768

[21] Bernasconi CF. Kinetic behavior of short-lived anionic .sigma. complexes. Accounts of Chemical Research. 1978;11:147-152

[22] Bunnett JF, Creary X. Nucleophilic replacement of two halogens in dihalobenzenes without the intermediacy of monosubstitution products. The Journal of Organic Chemistry. 1974;39:3611-3612

[23] Bernasconi CF, De Rossi RH. Influence of the o-nitro group on base catalysis in nucleophilic aromatic substitution. Reactions in benzene solution [internet]. The Journal of Organic Chemistry. 1976;41:44-49. DOI: 10.1021/jo00863a010

[24] Crampton MR, Emokpae TA, Howard JAK, Isanbor C, Mondal R. Leaving group effects on the mechanism of aromatic nucleophilic substitution (SNAr) reactions of some phenyl 2,4,6-trinitrophenyl ethers with aniline in acetonitrile [Internet]. Journal of Physical Organic Chemistry. 2004:65-70. DOI: 10.1002/poc.690

[25] Terrier F. Modern Nucleophilic Aromatic Substitution [Internet]. Chapter 1. Weinheim, Germany: Wiley-VCH; 2013.6. DOI: 10.1002/9783527656141

[26] Calfumán K, Gallardo-Fuentes S, Contreras R, Tapia RA, Campodónico PR. Mechanism for the SNAr reaction of atrazine with endogenous thiols: Experimental and theoretical study [Internet]. New Journal of Chemistry. 2017;41:12671-12677. DOI: 10.1039/c7nj02708g

[27] Kwan EE, Zeng Y, Besser HA, Jacobsen EN. Concerted nucleophilic aromatic substitutions. Nature Chemistry. 2018;10:917-923

[28] Neumann CN, Hooker JM, Ritter T. Concerted nucleophilic aromatic substitution with (19)F(−) and (18)F(−). Nature. 2016;534:369-373

[29] Neumann CN, Ritter T. Facile C–F bond formation through a concerted nucleophilic aromatic substitution mediated by the phenofluor reagent. Accounts of Chemical Research. 2017;50:2822-2833
[30] Bunnett JF, Morath RJ. The rates of condensation of piperidine with 1-chloro-2,4-dinitrobenzene in various solvents [Internet]. Journal of the American Chemical Society. 1955;5:5165-5165. DOI: 10.1021/ja01624a063

[31] Ormazábal-Toledo R, Contreras R, Tapia RA, Campodónico PR. Specific nucleophile-electrophile interactions in nucleophilic aromatic substitutions. Organic & Biomolecular Chemistry. 2013;11:2302-2309

[32] Gallardo-Fuentes S, Tapia RA, Contreras R, Campodónico PR. Site activation effects promoted by intramolecular hydrogen bond interactions in SNAr reactions. RSC Advances. 2014;4:30638-30643

[33] Hallett JP, Welton T. Room-temperature ionic liquids: Solvents for synthesis and catalysis. 2. Chemical Reviews. 2011;111:3508-3576

[34] Welton T. Room-temperature ionic liquids. Solvents for synthesis and catalysis. Chemical Reviews. 1999;99:2071-2084

[35] Earle MJ, Seddon KR. Ionic liquids. Green solvents for the future. Journal of Macromolecular Science Part A Pure and Applied Chemistry. 2000;72:1391-1398. Available from: https://www.degruyter.com/view/j/pac.2000.72.issue-7/pac200072071391/pac200072071391.xml

[36] Sheldon RA. Green solvents for sustainable organic synthesis: State of the art. Green Chemistry. 2005;7:267-278

[37] Rogers RD, Seddon KR. Chemistry. Ionic liquids—Solvents of the future? Science. 2003;302:792-793

[38] Seddon KR. Ionic liquids for clean technology. Journal of Chemical Technology & Biotechnology: International Research in Process, Environmental and Clean Technology. 1997;68:351-356

[39] Sánchez B, Calderón C, Tapia RA, Contreras R, Campodónico PR. Activation of electrophile/nucleophile pair by a nucleophilic and electrophilic solvation in a SNAr reaction [Internet]. Frontiers in Chemistry. 2018;6:509-517. DOI: 10.3389/fchem.2018.00509

[40] Gazitúa M, Tapia RA, Contreras R, Campodónico PR. Effect of the nature of the nucleophile and solvent on an SNAr reaction [Internet]. New Journal of Chemistry. 2018;42:260-264. DOI: 10.1039/c7nj03212a

[41] Tanner EEL, Hawker RR, Yau HM, Croft AK, Harper JB. Probing the importance of ionic liquid structure: A general ionic liquid effect on an S(N)Ar process. Organic & Biomolecular Chemistry. 2013;11:7516-7521

[42] Tanner EEL, Hawker RR, Yau HM, Croft AK, Harper JB. Probing the importance of ionic liquid structure: A general ionic liquid effect on an SNAr process. Organic & Biomolecular Chemistry. 2013;11:7516-7521

[43] Dawber JG, Ward J, Williams RA. A study in preferential solvation using a solvatochromic pyridinium betaine and its relationship with reaction rates in mixed solvents. Journal of the Chemical Society, Faraday Transactions 1: Physical Chemistry in Condensed Phases. 1988;84:713-727

[44] Mancini PM, Terenzani A, Adam C, Vottero LR. Solvent effects on aromatic nucleophilic substitution reactions. Part 9. Special kinetic synergistic behavior in binary solvent mixtures [Internet]. Journal of Physical Organic Chemistry. 1999;12:430-440. DOI: 10.1002/(SICI)1099-1395(199906)12:6<430::AID-POC142>3.0.CO;2-W

[45] Mancini PM, Terenzani A, Adam C, Pérez A d C, Vottero LR.
Characterization of solvent mixtures: Preferential solvation of chemical probes in binary solvent mixtures of polar hydrogen-bond acceptor solvents with polychlorinated co-solvents [Internet]. Journal of Physical Organic Chemistry. 1999;12:713-724. DOI: 10.1002/(SICI)1099-1395(199909)12:9<713::AID-POC182>3.0.CO;2-O

[D’Anna F, Marullo S, Vitale P, Noto R. Binary mixtures of ionic liquids: A joint approach to investigate their properties and catalytic ability. ChemPhysChem. 2012;13:1877-1884

[Xiao D, Rajian JR, Hines LG, Li S, Bartsch RA, Quitevis EL. Nanostructural organization and anion effects in the optical Kerr effect spectra of binary ionic liquid mixtures [Internet]. The Journal of Physical Chemistry B. 2008;112:13316-13325. DOI: 10.1021/jp0804417

[Alarcón-Espósito J, Contreras R, Campodónico PR. Iso-solvation effects in mixtures of ionic liquids on the kinetics of a model SNAr reaction [Internet]. New Journal of Chemistry. 2017;41:13435-13441. DOI: 10.1039/c7nj03246c

[Holbrey JD, Seddon KR. Ionic liquids. Clean Products and Processes. 1999;1:223-236

[Mele A, Tran CD, De Paoli Lacerda SH. The structure of a room-temperature ionic liquid with and without trace amounts of water: The role of C-H⋯O and C-H⋯F interactions in 1-n-butyl-3-methylimidazolium tetrafluoroborate [Internet]. Angewandte Chemie International Edition. 2003;115:4364-4366. DOI: 10.1002/anie.200351783

[Saha S, Hamaguchi H-O. Effect of water on the molecular structure and arrangement of nitrile-functionalized ionic liquids. The Journal of Physical Chemistry. B. 2006;110:2777-2781

[Sánchez B, Calderón C, Garrido C, Contreras R, Campodónico PR. Solvent effect on a model SNAr reaction in ionic liquid/water mixtures at different compositions [Internet]. New Journal of Chemistry. 2018;42:9645-9650. DOI: 10.1039/c7nj04820c

[Crowhurst L, Mawdsley PR, Perez-Arlandis JM, Salter PA, Welton T. Solvent–solute interactions in ionic liquids [Internet]. Physical Chemistry Chemical Physics. 2003;5:2790-2794. DOI: 10.1039/b303095d

[Chiappe C, Pomelli CS, Rajamani S. Influence of structural variations in cationic and anionic moieties on the polarity of ionic liquids. The Journal of Physical Chemistry. B. 2011;115:9653-9661

[Ben-Naim A. Preferential solvation in two-and in three-component systems. Journal of Macromolecular Science, Part A Pure and Applied Chemistry. 1990;62:2041-2058

[Covington AK, Newman KE. Approaches to the problems of solvation in pure solvents and preferential solvation in mixed solvents. Journal of Macromolecular Science, Part A Pure and Applied Chemistry. 1979;51:2041-2058

[Langford CH, Tong JPK. Preferential solvation and the role of solvent in kinetics. Examples from ligand substitution reactions. Accounts of Chemical Research. 1977;10:258-264

[Sengwa RJ, Khatri V, Sankhla S. Dielectric behaviour and hydrogen bond molecular interaction study of formamide-dipolar solvents binary mixtures. Journal of Molecular Liquids. 2009;144:89-96

[Kirkwood JG. Theory of solutions of molecules containing widely separated
Solvent Effect on a Model of S_N2Ar Reaction in Conventional and Non-Conventional Solvents

DOI: http://dx.doi.org/10.5772/intechopen.89838

charges with special application to zwitterions. The Journal of Chemical Physics. 1934;2:351-361

[60] Olah GA, Klumpp DA. Superelectrophilic solvation. Accounts of Chemical Research. 2004;37:211-220

[61] Bentley TW, William Bentley T, Llewellyn G, Ryu ZH. Solvolytic reactions in fluorinated alcohols. Role of nucleophilic and other solvation effects [Internet]. The Journal of Organic Chemistry. 1998;63:4654-4659. DOI: 10.1021/jo980109d

[62] Schadt FL, Bentley TW, Schleyer PR. The SN2-SN1 spectrum. 2. Quantitative treatments of nucleophilic solvent assistance. A scale of solvent nucleophilicities. Journal of the American Chemical Society. 1976;98:7667-7675

[63] Weinstein S, Grunwald E, Jones HW. The correlation of solvolysis rates and the classification of solvolysis reactions into mechanistic categories. Journal of the American Chemical Society. 1951;73:2700-2707

[64] Ingold CK. The principles of aromatic substitution, from the standpoint of the electronic theory of valency. Recueil des Travaux Chimiques des Pays-Bas. 1929;48:797-812. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/recl.19290480808

[65] Ingold CK. Principles of an electronic theory of organic reactions. Chemical Reviews. 1934;15:225-274

[66] Lewis GN. Valence and the Structure of Atoms and Molecules. T.M. Lowry, New York. USA: Chemical Catalog Company, Incorporated; 1923

[67] Brønsted JN. Some remarks on the concept of acids and bases. Recueil des Travaux Chimiques des Pays-Bas. 1923;42:718-728

[68] Lowry TM. The uniqueness of hydrogen. Journal of Chemical Technology and Biotechnology. 1923;42:43-47

[69] Mancini PME, Terenzani A, Adam C, Vottero LR. Solvent effects on aromatic nucleophilic substitution reactions. Part 7. Determination of the empirical polarity parameter ET (30) for dipolar hydrogen bond acceptor-co-solvent (chloroform or dichloromethane) mixtures. Kinetics of the reactions of halonitrobenzenes with aliphatic amines. Journal of Physical Organic Chemistry. 1997;10:849-860

[70] Martinez RD, Mancini PME, Vottero LR, Nudelman NS. Solvent effects on aromatic nucleophilic substitutions. Part 4. Kinetics of the reaction of 1-chloro-2,4-dinitrobenzene with piperidine in protic solvents. Journal of the Chemical Society, Perkin Transactions. 1986;2:1427-1431

[71] Beveridge DL, Schnuelle GW. Statistical thermodynamic consideration of solvent effects on conformational stability. Supermolecule-continuum model. The Journal of Physical Chemistry. 1974;78:2064-2069

[72] Baltzer L, Bergman N-Å, Drakenberg T, Raldow W, Nielsen PH. Solvation of the sodium ion in mixtures of methanol and dimethyl sulfoxide [Internet]. Acta Chemica Scandinavica. 1981;35:759-762. DOI: 10.3891/acta.chem.scand.35a-0759

[73] Frankel LS, Stengle TR, Langford CH. A study of preferential solvation utilizing nuclear magnetic resonance [Internet]. Chemical Communications (London). 1965;17:393. DOI: 10.1039/c19650000393

[74] Taha A, Ramadan AAT, El-Behairy MA, Ismail AI, Mahmoud MM. Preferential solvation
studies using the solvatochromic dicyanobis(1,10-phenanthroline) iron(II) complex [Internet]. New Journal of Chemistry. 2001;25:1306-1312. DOI: 10.1039/b104093f

[75] Buncel E, Rajagopal S. Solvatochromism and solvent polarity scales. Accounts of Chemical Research. 1990;23:226-231

[76] Kamlet MJ, Taft RW. The solvatochromic comparison method. I. The .beta.-scale of solvent hydrogen-bond acceptor (HBA) basicities. Journal of the American Chemical Society. 1976;98:377-383

[77] Kamlet MJ, Abboud JLM, Taft RW. The solvatochromic comparison method. 6. The .pi.* scale of solvent polarities. Journal of the American Chemical Society. 1977;99:6027-6038

[78] Kamlet MJ, Abboud JLM, Abraham MH, Taft RW. Linear solvation energy relationships. 23. A comprehensive collection of the solvatochromic parameters, .pi.*, .alpha., and .beta., and some methods for simplifying the generalized solvatochromatic equation. The Journal of Organic Chemistry. 1983;48:2877-2887

[79] Catalan J. Solvent effects based on pure solvent scales [Internet]. ChemInform. 2003;34:583-616. DOI: 10.1002/ chin.200320297

[80] Cerón-Carrasco JP, Jacquemin D, Laurence C, Planchat A, Reichardt C, Sraidi K. Solvent polarity scales: Determination of newET(30) values for 84 organic solvents [Internet]. Journal of Physical Organic Chemistry. 2014;27:512-518. DOI: 10.1002/poc.3293

[81] Barton AFM. Solvent scales [Internet]. In: CRC Handbook of Solubility Parameters and Other Cohesion Parameters. Chapter 8. 2017:178. DOI: 10.1201/9781315140575-8

[82] Reichardt C, Welton T. Solvents and Solvent Effects in Organic Chemistry. Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA; 2011

[83] Reichardt C. Polarity of ionic liquids determined empirically by means of solvatochromic pyridinium N-phenolate betaine dyes [Internet]. Green Chemistry. 2005;7:339. DOI: 10.1039/b500106b

[84] Cerda-Monje A, Aizman A, Tapia RA, Chiappe C, Contreras R. Solvent effects in ionic liquids: Empirical linear energy-density relationships [Internet]. Physical Chemistry Chemical Physics. 2012;14:10041. DOI: 10.1039/c2cp40619e

[85] Rostov IV, Basilevsky MV, Newton MD. Advanced dielectric continuum models of solvation, their connection to microscopic solvent models, and application to electron transfer reactions [Internet]. Simulation and Theory of Electrostatic Interactions in Solution. AIP Conference Proceeding. 1999;492:331-351. DOI: 10.1063/1.1301535

[86] Contreras R, Aizman A. On the SCF theory of continuum solvent effects representation: Introduction of local dielectric effects [Internet]. International Journal of Quantum Chemistry. 1985;27:293-301. DOI: 10.1002/qua.560270307

[87] Kobrak MN, Li H. Electrostatic interactions in ionic liquids: The dangers of dipole and dielectric descriptions. Physical Chemistry Chemical Physics. 2010;12:1922-1932

[88] Gölllei A. Dielectric characteristics of ionic liquids and usage in advanced energy storage cells [Internet]. Progress and Developments in Ionic Liquids. IntechOpen; 2017:451-473. Chapter 17. DOI: 10.5772/66948

[89] Baker SN, Baker GA, Bright FV. Temperature-dependent microscopic
solvent properties of “dry” and “wet” 1-butyl-3-methylimidazolium hexafluorophosphate: Correlation with ET(30) and Kamlet–Taft polarity scales [Internet]. Green Chemistry. 2002;4:165-169. DOI: 10.1039/b111285f

[90] Gutmann V, Wychera E. Coordination reactions in non aqueous solutions—The role of the donor strength [Internet]. Inorganic and Nuclear Chemistry Letters. 1966;2:257-260. DOI: 10.1016/0020-1650(66)80056-9

[91] Mayer U, Gutmann V, Gerger W. The acceptor number? A quantitative empirical parameter for the electrophilic properties of solvents [Internet]. Monatshefte für Chemie. 1975;106:1235-1257. DOI: 10.1007/bf00913599

[92] Schmeisser M, Illner P, Puchta R, Zahl A, van Eldik R. Gutmann donor and acceptor numbers for ionic liquids. Chemistry. 2012;18:10969-10982

[93] Schmeisser M, Illner P, Puchta R, Zahl A, van Eldik R. Cover picture: Gutmann donor and acceptor numbers for ionic liquids (Chem. Eur. J. 35/2012) [Internet]. Chemistry—A European Journal. 2012;18:10765-10765. DOI: 10.1002/chem.201290149

[94] Coleman S, Byrne R, Minkovska S, Diamond D. Investigating nanostructuring within imidazolium ionic liquids: A thermodynamic study using photochromic molecular probes. Journal of Physical Chemistry B. 2009;113:15589-15596