

Decoding The Effect of Anion Identity on the Solubility of *N*-(2-(2-methoxyethoxy)ethyl)phenothiazine (MEEPT)

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Abstract

Variations in the solubility of redox-active organic molecules (ROM) of interest for non-aqueous redox flow batteries (RFB), especially as the ROM state-of-charge changes during charge-discharge cycling, present significant molecular design challenges. The situation is further complicated as ROM solubility can be regulated by the choice of electrolyte salt and solvent that together with the ROM comprise the catholyte or anolyte (redox electrolyte) formulation, presenting materials design challenges. The ROM *N*-(2-(2-methoxyethoxy)ethyl)phenothiazine (MEEPT) is a viscous liquid at room temperature and is miscible in several organic solvents, including acetonitrile and propylene carbonate. The MEEPT radical cation (MEEPT^{•+}) paired with tetrafluoroborate (BF₄⁻) in acetonitrile presents a 0.5 M solubility, a dramatic decrease when compared to the viscous liquid of neutral MEEPT. Here we present a joint experimental, regression modeling, and molecular dynamics (MD) simulations investigation to explore MEEPT-X (where X represents the counter-anion) salt solubility variability as a function of concentration and counter-anion chemistry in acetonitrile. We find a strong dependence of the salt solubility on the counter-anion and relate these findings to explicit intermolecular interactions between MEEPT^{•+} and the counter-anion in the electrolyte solution.

Introduction

Solubility plays a critical role in the function of redox-active organic molecules (ROM) in non-aqueous redox flow batteries (RFB), with large ROM solubilities being needed for large RFB energy densities.^{1, 2} From the molecular design perspective, for a ROM core of a given oxidation or reduction potential, ROM solubility is generally tuned through chemical substitution on the core periphery – for example, with solubilizing (e.g., polyethylene glycol) or charged (e.g., ammonium) groups – or imbuing structural asymmetry to the ROM.³⁻⁵ Notably, such substitutions are typically considered in the design process to increase ROM solubility in the neutral state of charge.

In RFB design, the positive and negative compartments contain complex redox electrolyte solutions comprised of the ROM, salt, and solvent; the solution in the positive compartment is often referred to as the catholyte or posolyte, while the solution in the negative compartment is the anolyte or negolyte. During RFB charge-discharge cycling, ROM solubility generally decreases on going from the neutral to the charged state(s),⁶⁻⁸ a result of a complex interplay of noncovalent intermolecular interactions among the ROM, salt, and solvent. While solvent-dependent solubilities of ROM-based salts – where the ROM in a given state-of-charge is paired with a counter-ion – can provide important information on the complex physicochemical features that govern catholyte and anolyte properties,⁹⁻¹³ such systems themselves are not well understood. Hence, there remain considerable molecular and solution (material) design challenges that need to be overcome to affect widespread RFB adoption.

Here, we investigate the non-aqueous solubilities of ROM-based charged salts through a combination of experimental solubility measurements, quantitative structure-property-relationship (QSPR) models, and molecular dynamics (MD) simulations. As a model ROM, we choose *N*-(2-(2-methoxyethoxy)ethyl)phenothiazine (MEEPT),^{6, 9, 10, 14-23} a widely studied ROM for RFB that is a viscous liquid and is miscible with several organic solvents when in the neutral state. The phenothiazine (PT) core

is widely used as a drug to treat psychiatric conditions, though it has been demonstrated to have application in energy storage due to its stable redox properties.^{6, 24-32} Ten MEEPT-counter-anion (MEEPT-X) salt combinations (Figure 1) were synthesized and their solubilities in acetonitrile evaluated. The investigation builds upon previous efforts to understand and predict the solubilities of 30 PT,³³ wherein the oxidizable PT core was chemically modified with different side groups, through a combination of nuclear magnetic resonance (NMR)-based solubility measurements and QSPR models.³⁴⁻³⁶ Of the various methods for solubility determination, we chose quantitative-NMR (Q-NMR) as it allows solubility determination without additional analysis (e.g., density measurements to account for volume expansion in shake flask method, NMR to ensure complete evaporation in the weighing method, or sample dilution for spectrophotometric method) and in the presence of supporting salts.³³ Q-NMR is also gaining attention as a high-throughput method to determine ROM solubility.³⁷ MD simulations, which have been previously demonstrated to provide insights into ROM solubility,^{17, 38-45} are used to derive atomic-scale insights into MEEPT-X solubility variations. The combined experimental, regression modeling, and MD simulation approach presents several key insights that can be used to design ROM-electrolyte systems for RFB.

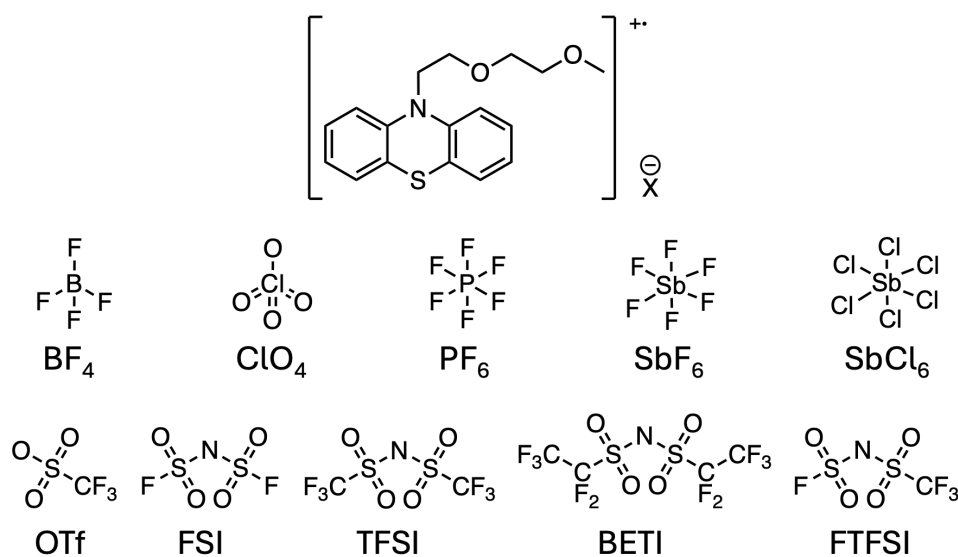


Figure 1. Structural representations of MEEPT^{+•} and ten counter-anions (X⁻) under consideration.

Methods

MEEPT–X synthesis

MEEPT–X salts were synthesized by chemical oxidation (Scheme S1, Supporting Information [SI]) using nitrosonium, antimony, and silver salts.^{9, 14, 46} The general experimental details for each oxidant are provided in this section. See SI for further details on general experimental, yields, and characterization of MEEPT–X.

General procedure for synthesis of MEEPT–X using NO–X as the chemical oxidant

An oven-dried 50-mL round-bottomed flask containing a stir bar was cooled to RT with a stream of nitrogen. MEEPT (1.00 g, 3.32 mmol) was added, and the flask was capped with a rubber septum. The subsequent steps were carried out under nitrogen atmosphere. Anhydrous dichloromethane (DCM, 10 mL) was added to the flask, and the resultant pale-yellow solution was stirred. The reaction flask was then placed in an ice bath. NO–X (3.49 mmol) was added to the solution, and the solution immediately turned dark orange. The reaction mixture was stirred for an additional 1 h, after which diethyl ether (20 mL) was added gradually with continued stirring, resulting in the formation of a dark precipitate. The precipitate was collected by filtration, dissolved in DCM (10 mL), and re-precipitated by the addition of diethyl ether (20 mL). This purification process was repeated once. The final precipitate was collected by filtration and dried under vacuum. The product was crystallized by dissolving the powder in DCM. The solution was then transferred to small (~ 15 mL) scintillation vials. These vials were placed in a glass jar containing diethyl ether, ensuring that the volume of diethyl ether was lower than that of the solution in the vials. The jar was then capped and stored in a freezer, allowing crystals to form via vapor diffusion. The resulting crystals were collected by filtration and dried under vacuum.

General procedure for synthesis of MEEPT–X using Ag–X as the chemical oxidant

An oven-dried 50-mL round-bottomed flask containing a stir bar was cooled to RT with a stream of nitrogen. MEEPT (1.00 g, 3.32 mmol) was added, and the flask was capped with a rubber septum. The subsequent steps were carried out under nitrogen atmosphere. Anhydrous acetonitrile (ACN, 15 mL) was added to the flask, and the resultant pale-yellow solution was stirred. Iodine (0.421 g, 1.66 mmol) and Ag–X (3.38 mmol) were then added to the solution, and the solution immediately became dark orange. The reaction mixture was stirred for an additional 1 h, after which the reaction mixture was passed through a short pad of celite. Additional ACN was added to wash the celite pad, and the resultant filtrate was concentrated to a viscous liquid (~ 2 mL). Diethyl ether (20 mL) was added gradually, resulting in the formation of a dark precipitate. The precipitate was collected by filtration and washed with diethyl ether (20 mL) and hexanes (20 mL). The final precipitate was dried under vacuum. The product was crystallized by dissolving the powder in DCM. The solution was then transferred to small (~ 15 mL) scintillation vials. These vials were placed in a glass jar containing diethyl ether, ensuring that the volume of diethyl ether was lower than that of the solution in the vials. The jar was then capped and stored in a freezer, allowing crystals to form via vapor diffusion. The resulting crystals were collected by filtration and dried under vacuum.

Synthesis of MEEPT–SbCl₆ using SbCl₅ as the chemical oxidant

An oven-dried 50-mL round-bottomed flask containing a stir bar was cooled to RT with a stream of nitrogen. MEEPT (1.00 g, 3.32 mmol) was added, and the flask was capped with a rubber septum. The subsequent steps were carried out under nitrogen atmosphere. Anhydrous ACN (15 mL) was added to the flask, and the resultant pale-yellow solution was stirred. The reaction flask was then placed in an ice bath. Antimony pentachloride (0.59 mL, 4.65 mmol) was added to the solution, and the solution became dark

orange. The reaction mixture was stirred for an additional 30 min, after which diethyl ether (20 mL) was added gradually with continued stirring, resulting in the formation of a dark precipitate. The precipitate was collected by filtration under nitrogen and was washed with more diethyl ether (20 mL). The precipitate was dissolved in anhydrous ACN and re-precipitated by the addition of diethyl ether. The precipitate was then collected by filtration and dried under vacuum (brown powder, 72.6%). The product was crystallized by dissolving the powder in DCM. The solution was then transferred to small (~ 15 mL) scintillation vials. These vials were placed in a glass jar containing diethyl ether, ensuring that the volume of diethyl ether was lower than that of the solution in the vials. The jar was then capped and stored in a freezer, allowing crystals to form via vapor diffusion. The resulting crystals were collected by filtration and dried under vacuum.

NMR solubility determination

Saturated solutions (dark orange) of MEEPT–X were prepared by dissolving excesses of the salt in ACN. The solution was stirred overnight to equilibrate, after which the remaining solids were removed by filtration through a syringe filter (0.22 μm pore size, PTFE membrane). The solution (100 μL) was added to an NMR tube containing excess sodium thiosulfate ($\text{Na}_2\text{S}_2\text{O}_3$) to convert the radical-cation MEEPT^{•+} back to MEEPT. This step was repeated in triplicate. Chemical reduction is needed due to paramagnetic broadening of NMR resonances in charged solutions. After quenching (solution color turns pale yellow), 50 μL of 1.0 M (in $\text{DMSO}-d_6$) solution of the internal standard (1,4-bis(trifluoromethyl)benzene) was added to NMR tube. The NMR tube is then filled with 0.4 mL of $\text{DMSO}-d_6$. ^1H NMR spectra were acquired on a 400 MHz Bruker Avance NEO (equipped with a Smart Probe) and recorded using a 25 s delay. MEEPT–X solubility for each salt was estimated by comparing integration ratios of MEEPT and the standard resonance lines in the ^1H NMR spectra.

QSPR models

QSPR has been used to determine solubility correlations for a variety of ROM.³⁴⁻³⁶ To develop the QSPR models for the MEEPT-X salts, a limited number of molecular descriptors were used. Experimental parameters included molecular weight, crystal packing density, and molar density of MEEPT-counter-anion complexes. Computational descriptors, where parameters are only considered for the counter-anions as they are each paired with MEEPT⁺, were determined by density functional theory (DFT) calculations at the M06-2X/def2TZVP level of theory.^{47, 48} DFT calculations were undertaken in the gas phase and with the CPCM (conductor-like polarizable continuum model) solvent model for an implicit representation of ACN.^{49, 50} The Gaussian16 (Revision A.03) software suite was used to perform all DFT calculations.⁵¹ Descriptors for the free energy of solvation, solvent accessible surface area (SASA), entropy estimated using partition functions, dipole moment, and polarizability were determined from the DFT calculations. The procedure and algorithms for the QSPR approach used herein were adapted from work by Guo *et al.*⁵² A forward, stepwise, linear regression was performed, and the selection of training and validation sets were automated following preset rules as described in the same publication to obtain the QSPR models.⁵² The models were tested using multiple cross-validation techniques. Built-in functions in the Statistics and Machine Learning Toolbox™ and Bioinformatics Toolbox™ in MATLAB® were used for the evaluations.⁵³

MD Simulations

MD simulations were carried out for eight MEEPT-X systems in three concentrations: 0.1, 0.4, and 1 M. MD simulations for MEEPT-SbF₆ and MEEPT-SbCl₆ were not undertaken due to the need for additional force-field development for the counter-anions, which is beyond the scope of this work. The 0.1 M simulations were used as the basis for comparison for all systems as each of the eight systems is experimentally soluble at this concentration. The larger 0.4 and 1 M concentrations were used to

investigate intermolecular interactions that may drive insolubility, as the 0.1 M MD simulations were too dilute to adequately observe such interactions during the simulation times.

The OPLS-AA (optimized potential for liquid simulations-all atomic) force field was used for the MD simulations. Topology files were created with the LigParGen server⁵⁴ with geometric and partial charge parameters derived from DFT calculations at the M06-2X/def2TZVP level of theory.^{47, 48} Partial charges were derived using the molecular electrostatic potential (ESP) method to be consistent with the parameters obtained by Doherty *et al.* for the counter-anions. The OPLS-based parameters were used with ESP-derived partial charges, and we evaluated non-scaled charges and charges scaled by 80% to assess the best approach;⁵⁵ charge scaling was applied to compensate for charge screening effects that a non-polarizable forcefield such as OPLS does not capture.⁵⁶ From the evaluations, we selected the 80% charge-scaling approach, which is consistent with our previous studies of solutions of redox-active active molecules,⁴⁴ where we observed the best agreement of simulated viscosity and conductivity with experiment, and with other previous literature^{43, 55} (and specifically with MEEPT).^{17, 19} Using the charge-scaling approach, the MD simulations resulted in solution densities (within 1%) and viscosities (within 5%) that agreed well with experimental measurements for the systems reported here.

The GROMACS 2019 software package was used to perform the MD simulations.⁵⁷ Initial configurations for the simulations were created with Packmol, which uses a geometric optimization to place molecules in a defined area to avoid close contacts and overlaps.⁵⁸ Cubic simulation boxes were constructed with dimensions of 100 x 100 x 100 Å and were populated with DFT-optimized molecules corresponding to the number of molecules for each concentration. The MD systems were then subject to energy minimization (maximum of 100,000 steps) with the steepest descent algorithm as implemented in GROMACS, followed by NVT (constant number of molecules, volume, and temperature) ensemble equilibration for 5 ns with the leap-frog algorithm with a time step of 2 fs.⁵⁹ Two subsequent simulations were then conducted under the NPT (constant number of molecules, pressure, and temperature) ensemble – initially stabilizing the

volume by applying the Berendsen⁶⁰ barostat for 30 ns, followed by 120 ns with the Parrinello–Rahman⁶¹ barostat to allow further dynamic changes. Three-dimensional periodic boundary conditions (PBC) were applied with a coupling time of 1.0 ps and compressibility of $4.5 \times 10^{-5} \text{ bar}^{-1}$. A van der Waals (vdW) cut-off of 1.4 nm and a particle-mesh Ewald (PME)⁶² cut-off of 1.4 nm for long-range Coulomb interactions were utilized in all simulations.

Results and Discussion

Ten MEEPT–X salts were synthesized by chemical oxidation (Scheme S1) using nitrosonium, antimony, and silver salts (experimental details in Methods section and SI). The syntheses used mild conditions and are scalable. After the oxidation reactions, the salts were isolated as solids that were crystallized by liquid-liquid diffusion of diethyl ether into solutions in DCM (at low temperature). The isolated crystalline salts (Figure S1, thermal ellipsoid plots) were also analyzed using CHN elemental analysis.

A notable feature of MEEPT in the MEEPT–X salts is a planar PT core⁶³ that allows for stacking of the π backbones (Figure 2); such interactions can facilitate crystallization / self-assembly and influence the salt solid-state properties. The MEEPT–X salts crystallize in structures with different space groups – $P2_1/n$ (and $P2_1/c$), $P\bar{1}$ and $P2_12_12_1$ (Table S1) – and pack either as columnar stacks or as isolated dimers. The salts with smaller counter-anions, MEEPT–BF₄, –ClO₄, –PF₆, –SbF₆ and –FSI, have columnar stacks running along one axis (Figure 2, top). Within these stacks, the PT cores are arranged in an anti-parallel arrangement related to each other by inversion. The PT moieties of the MEEPT–BF₄ salt show two nearly equivalent interplanar distances (Table S1) of 3.35 and 3.33 Å; the interplanar separations between adjacent PT moieties is calculated as the average distances from the core atoms of one molecule to the plane of the other. The interplanar distances between adjacent PT moieties in MEEPT–ClO₄ (3.37 and 3.54 Å), MEEPT–PF₆ (3.26 and 3.39 Å), MEEPT–SbF₆ (3.35 and 3.57 Å), and MEEPT–FSI (3.37, 3.43 Å) on the other hand, are different.

MEEPT-OTf, -FTFSI, -SbCl₆, -TFSI, and -BETI present as isolated stacks of dimers (Figure 2, bottom) where the overlap with the next pair depends on the counter-anion.

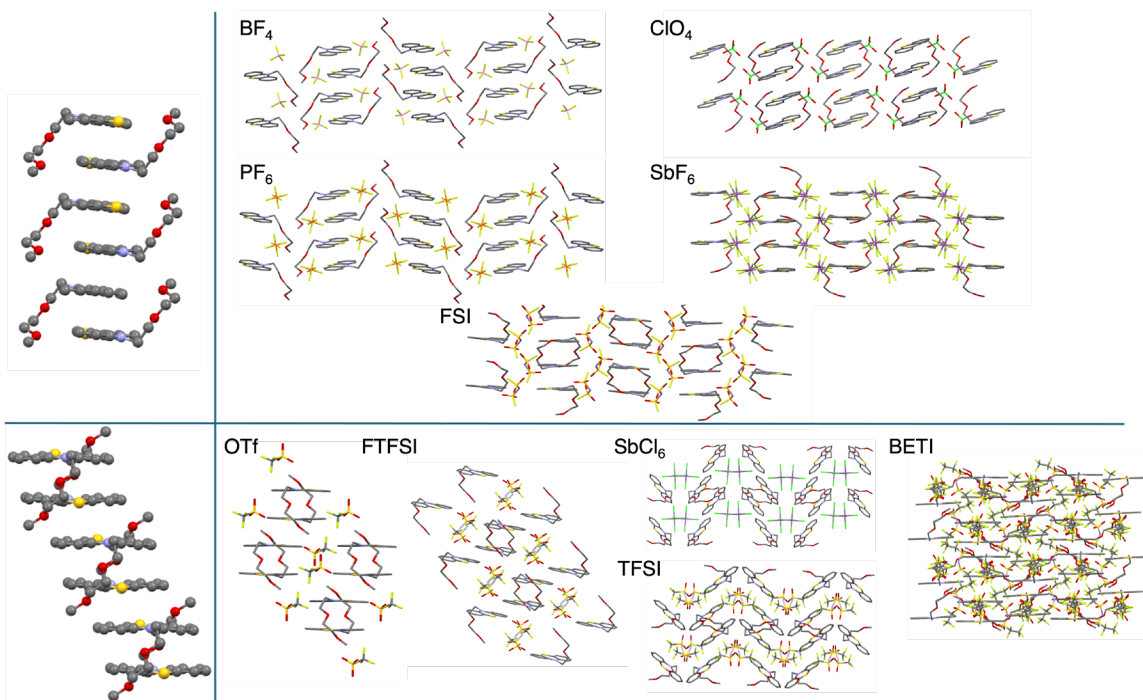


Figure 2. Crystal structure packing for MEEPT-X: Columnar stacks (top) and isolated dimers (bottom).

Molar densities (in the solid state) (Table 1) were determined based on the crystal structure densities (Table S2). The molar densities range from 2.51 M for MEEPT-BETI to 3.93 M for MEEPT-BF₄, and vary directly with the size of the counter-anion: The smaller the counter-anion, the larger the molar density. MEEPT-X melting temperatures (Table 1, Figure S2) were determined by differential scanning calorimetry (DSC). For salts with inorganic anions, melting transitions were only observed for MEEPT-SbCl₆, -BF₄, -ClO₄ in the temperature range evaluated (~-80 to 140-145 °C). No correlation with either the counter-anion size or molar density could be identified. We note that the MEEPT-X series begins to decompose by 150 °C (as determined by thermogravimetric analysis⁹) and thus 145 °C was the maximum temperature used.

MEEPT–X solubility in ACN was determined using the Q-NMR method (Table 1). MEEPT–ClO₄ and MEEPT–SbCl₆ have the lowest solubilities, 0.13 and 0.16 M, respectively. MEEPT with –BF₄, –PF₆, –SbF₆, –OTf, or –FSI have moderate solubilities of ~0.5 M. MEEPT with –BETI, –TFSI and –FTFSI, on the other hand, have much higher solubilities (> 1 M), with MEEPT–FTFSI soluble to 1.98 M in ACN. Salts with inorganic anions have low to moderate solubilities, whereas salts with the more flexible organic anions have moderate to high solubilities; here, we use the term flexible broadly for systems that have several rotatable bonds that lead to different conformations. Asymmetry in the counter-anion, such as in FTFSI, further increases the solubility. While no correlation between the molar density and solubility could be identified, general trends could be identified by the packing type: MEEPT–X salts with columnar stacks have low to moderate solubilities, while salts with isolated dimers have moderate to high solubilities (with the exception of MEEPT–SbCl₆). A clear correlation was found between MEEPT–X solubility in ACN and the melting temperature for salts containing organic ions (Figure S2c): The higher the melting temperature, the lower the solubility, as one may expect. Notably, the more soluble salts have melting points below 100 °C.

Table 1. MEEPT–X molar density (M), melting temperature (°C), and solubility (M) in acetonitrile (ACN).

MEEPT–X X =	Molar Density (M)	Melting Temperature (°C)	ACN Solubility (M)*
BF ₄	3.93	137.0	0.553 ± 0.015
ClO ₄	3.90	144.1	0.125 ± 0.002
PF ₆	3.65	>145.0 or decomp	0.523 ± 0.009
OTf	3.49	118.8	0.530 ± 0.006
SbF ₆	3.47	>145.0 or decomp	0.504 ± 0.007
FSI	3.39	127.0	0.468 ± 0.002
FTFSI	3.04	69.1	1.983 ± 0.032
SbCl ₆	2.83	117.9	0.163 ± 0.001
TFSI	2.81	85.0, 88.5 [†]	1.537 ± 0.007
BETI	2.51	98.1, 130.4 [‡]	1.352 ± 0.031

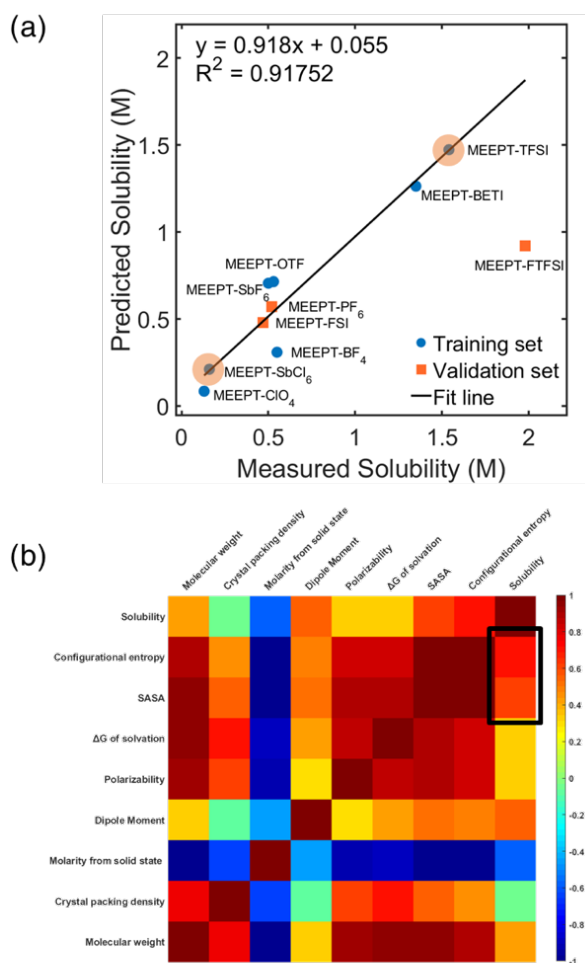
*Standard deviations are calculated from triplicate runs.

[†]Bifurcated peak; [‡]Two melting points, possibly due to multiple polymorphs

MEEPT-X viscosity and conductivity in ACN were measured (Figure S4) as a function of salt concentration. MEEPT-X salts have conductivities that range from $\sim 8\text{--}10\text{ mS/cm}$ and viscosities from $\sim 0.35\text{--}0.41\text{ mPa}\cdot\text{s}$ at 0.1 M (Figure S4a–b). Both conductivity and viscosity increase as concentration increases from 0.1 to 0.4 M for moderately soluble MEEPT-X. For the highly soluble MEEPT-TFSI and MEEPT-FTFSI (Figure S4c), the viscosity and conductivity measurements were carried out up to 1.5 M. The viscosities initially increase linearly with concentration, with a significant increase in slope visible at 0.75 M for MEEPT-TFSI and 1.25 M for MEEPT-FTFSI. MEEPT-TFSI has almost twice the viscosity at 1.5 M ($3.7\text{ mPa}\cdot\text{s}$ for –TFSI and $1.6\text{ mPa}\cdot\text{s}$ for –FTFSI) when compared with MEEPT-FTFSI. Notably, both MEEPT-TFSI (28 mS/cm) and MEEPT-FTFSI (30 mS/cm) show a maximum in their conductivity at 0.75 M. Increased ionic association in this regime is a known explanation for the decrease in conductivity as observed in our previous work with extensive X-ray and computational analysis.¹⁷ MEEPT-FTFSI shows higher conductivity at higher concentrations but follows an analogous trend to MEEPT-TFSI.

QSPR models using a combination of experimental and calculated parameters were developed to identify MEEPT-X property correlations with solubility in ACN. Since the number of data points available for training and validation are limited, the modeling was limited to the use of two to three variables (descriptors) used per model to avoid chance correlations.^{64, 65} Generally, the QSPR models (Figure 3) show reasonable statistical performance, with the counter-anion size in the solvent (represented by SASA, Table S5) and counter-anion configurational entropy (a function of the number of rotatable bonds) being essential factors that govern MEEPT-X solubility. Notably, the correlation of configurational entropy to solubility is stronger than that for SASA with solubility. Small counter-anions (BF_4^- , ClO_4^- , PF_6^- , SbF_6^- , OTf^- , and FSI^-) have small SASA, correlating with low to moderate MEEPT-X solubilities. TFSI[−], BETI[−], and FTFSI[−] each have large SASA and large configurational entropy, correlating with high MEEPT-X solubilities. The heatmap in Figure 3 (with corresponding numerical values in Table S6) represents the normalized univariate correlation coefficients of each molecular descriptor with respect to the solubility of all

considered MEEPT–X systems. SbCl_6^- presents an interesting counterexample to these trends as it has a large SASA but low configurational entropy, with MEEPT– SbCl_6 having a low solubility. These results demonstrate that while a large-sized counter-anion can assist with solubility, larger configurational entropy is more important.



SASA | TFSI = 456.9 Å² ; SbCl₆ = 440.4 Å²
 Solubility | TFSI = 1.53 M ; SbCl₆ = 0.16 M

Figure 3. (a) Best performing QSPR solubility model for MEEPT–X in ACN. (b) Heat map representing linear correlations of the solubility descriptors.

MD simulations were employed to further explore the structure-property relationships of MEEPT-X solubility in ACN. The force-field parameters and the charge scaling method were validated against multiple concentrations using macroscopic viscosity (η) values determined using the transverse current autocorrelation function (TCAF) method.⁶⁶ We note that we did not undertake simulations for MEEPT-SbF₆ and MEEPT-SbCl₆ due to the need for additional force-field development. The MD simulations reproduce experimental viscosity values (where available) within 5% for each of the 0.1, 0.4, and 1 M concentrations (Table 2). Based on the viscosity (η) versus k -vector plots (Figure S5–6), the solutions follow the expected physical trends used to model viscosity using TCAF. The macroscopic viscosity was obtained by extrapolating the curve to $k = 0$ (using curve fitting), where k is the wave vector of the fluctuation. The slight deviation for 1 M concentrations can be associated to time averaging when calculating the transverse current autocorrelation functions and curve fitting regions.

Table 2. MD-simulated and experimental MEEPT–X viscosities in ACN as a function of MEEPT–X concentration. Standard deviations are reported from three replicate runs.

MEEPT–X X =	0.1 M		0.4 M		1 M	
	MD Viscosity (mPa·s)	Experimental Viscosity (mPa·s)	MD Viscosity (mPa·s)	Experimental Viscosity (mPa·s)	MD Viscosity (mPa·s)	Experimental Viscosity (mPa·s)
BF ₄	0.37	0.35 ± 0.028	0.52	0.50 ± 0.034	–	–
ClO ₄	0.35	0.37 ± 0.019	–	–	–	–
PF ₆	0.37	0.36 ± 0.038	0.46	0.48 ± 0.025	–	–
OTf	0.37	0.40 ± 0.050	0.50	0.58 ± 0.064	–	–
FSI	0.34	0.41 ± 0.049	0.44	0.53 ± 0.070	–	–
FTFSI	0.36	0.40 ± 0.031	0.45	0.51 ± 0.058	0.73	*
TFSI	0.37	0.38 ± 0.023	0.48	*	0.92	*
BETI	0.38	0.40 ± 0.047	0.50	0.60 ± 0.048	0.92	1.78 ± 0.084

Note: Hyphens (–) represent situations where the systems are no longer solutions at these concentrations. Stars (*) represent systems where the experimental viscosity has not been determined.

MEEPT–X solubility in ACN covers a wide range, though small numerical differences among select pairs of salts make it difficult to capture explicit differences from the MD simulations. We therefore derived a categorization based on solubility ranges – low (< 0.3 M), moderate (0.3 – 1.0 M), and high (>1.0 M) – and used these classifications for further analyses. Radial distribution functions (RDF) were evaluated with the centers-of-mass (COM) of MEEPT⁺• and the counter-anions (X[–]) as reference points, and coordination numbers (the average number of molecules forming the first solvation shell around MEEPT⁺•) between a MEEPT⁺• and other MEEPT⁺•, counter-anions, and ACN were determined (representative examples are provided Figure 4). Given simulation size and time constraints, the 0.1 and 0.4 M MD simulations did not present data that was sufficient to analyze parameters related to the intermolecular interactions that

govern solubility. While data for these simulations are presented in the SI (Figures S5, S7, S8, S10 and Tables S3–S4), we focus our attention here on comparing select simulations for 1 M MD simulations.

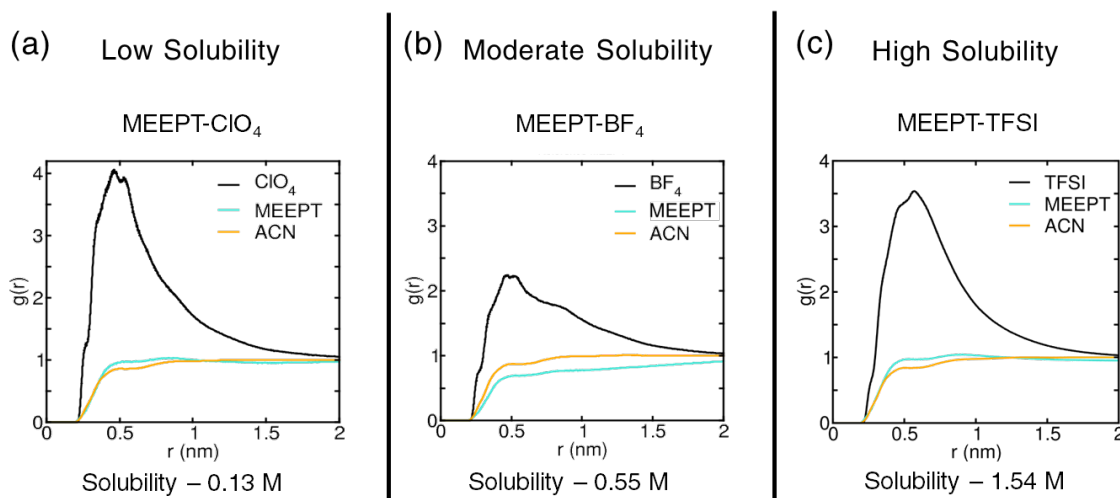


Figure 4. RDF plots of MEEPT–X systems – (a) MEEPT–ClO₄, (b) MEEPT–BF₄, (c) MEEPT–TFSI – at 0.1 M concentration to represent the solubility categorizations. The RDF are plotted with respect to the centers-of-mass (COM) of MEEPT to the counter-anions, the solvent (ACN), and other MEEPT molecules.

Results for 1 M MEEPT–BF₄ and MEEPT–TFSI in ACN are shown in Figures 5 and S8; these two systems are chosen for comparison as the experimentally determined solubilities are 0.55 M for MEEPT–BF₄ and 1.54 M for MEEPT–TFSI. The 1 M MD simulations reveal a lower coordination between MEEPT⁺• and BF₄[−] (CN ≈ 1.6) when compared to MEEPT⁺• and TFSI[−] (CN ≈ 6.4). In addition to having a higher estimated entropy, larger and flexible counter-anions (here, represented by TFSI[−], but also consistent for BETI[−] and FTFSI[−]) also appear to hinder MEEPT⁺•–MEEPT⁺• contacts, leading to a more homogeneous solution. We also observe that the interactions of MEEPT⁺• with the counter-anions occur mainly through the PT core and N and S atoms, as derived by atom-specific RDF analyses (Figure S10). We previously reported a related observation for PT where we identified, through QSPR descriptors with strong correlation, that PT solubility can be linked to the susceptibility of the N atom and partial charges on the S atom.³³ The atom-centered RDF (Figure S10) also suggests that MEEPT⁺• interacts primarily with the N and O/C of the sulfonic

acid anion systems (TFSI⁻, BETI⁻, FTFSI⁻, FSI⁻, and OTf⁻), rather than the CF₃ end of the fluoro-sulfonic anion, which has also been previously reported for triflates with cations;⁶⁷ these results are consistent with our previous findings concerning intermolecular interactions and the solubilities of PT.³³

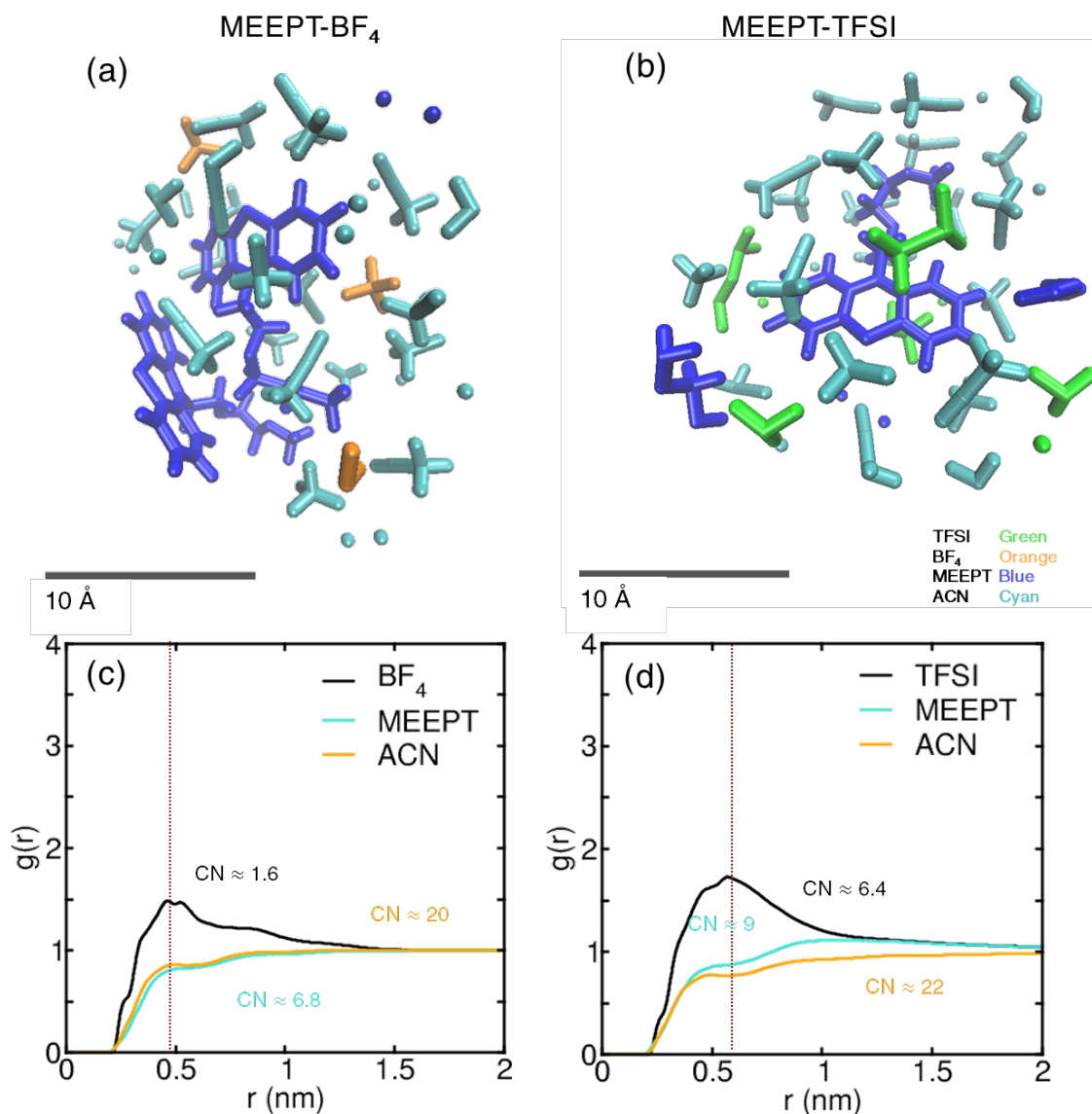


Figure 5. RDF plots and local environment of MEEPT-TFSI and MEEPT-BF₄ at 1 M showing stacking/clustering of MEEPT⁺ where MEEPT⁺-MEEPT⁺ interactions are hindered in the TFSI⁻ case but not the BF₄⁻ case. The red dotted lines represent the highest probability density corresponding to the first solvation shell for each system.

The experimental, regression modeling, and MD simulation results provide a more detailed understanding of MEEPT-X solubility in ACN. Intermolecular interactions amongst MEEPT⁺• molecules are a key feature that limits solubility. Generally, counter-anions that lead to high solubility systems are flexible and large in size (Table S3/S5). These properties hinder inter-MEEPT⁺• contacts. The highly soluble BETI⁻, TFSI⁻, and FTFSI⁻ systems are surprisingly similar in their number of MEEPT⁺•–MEEPT⁺• contacts (≈ 5) and minimum distances (≈ 4.46 Å), implying that this behavior is very likely a function of the anion size and flexibility (Table S4).

In contrast, MEEPT–BF₄, which is moderately soluble in ACN, shows the shortest MEEPT⁺•–MEEPT⁺• contact distance, resulting in the largest number of contacts in the systems studied. We also note that MEEPT–BF₄ shows one of the longest distances between MEEPT⁺• and the counter-anion, resulting in the smallest number for this contact type (Table S4). The large number of MEEPT⁺•–MEEPT⁺• contacts and small number of MEEPT–BF₄ contacts can be attributed to the small size of BF₄⁻ and its compact, and tetrahedral shape. The remaining moderately soluble systems (OTf⁻, PF₆⁻, and FSI⁻) generally show large numbers of contacts and short minimum distances when compared to the high solubility systems. PF₆⁻ is large, compact, octahedral, and shows some similar trends to BF₄⁻ (which is small and tetrahedral), with the largest distances between MEEPT⁺• and the counter-anion for an overall lower number of contacts compared to other moderate and high solubility systems (Table S4).

Although our results suggest that MEEPT⁺•–MEEPT⁺• aggregation is a leading cause of limited solubility, we cannot rule out the possibility of strong ion association (contact-ion pair formation) leading to poor solubility. MEEPT–ClO₄, which is the only salt in the low solubility category, presents different trends when compared to the other systems. Here we use the 0.4 M simulation results for MEEPT–ClO₄ as 0.4 M is above the solubility limit. It is notable that the number of MEEPT⁺•–MEEPT⁺• contacts in MEEPT–ClO₄ is not very high. In fact, the number of MEEPT⁺•–MEEPT⁺• contacts is less than half those observed in MEEPT–BF₄, which has an approximately five times higher solubility than MEEPT–ClO₄. MEEPT–ClO₄ has an

exceptionally large number of MEEPT-ClO₄ contacts, and the minimum contact distance is extremely small, strongly suggesting the formation of contact ion pairs (Table S4). These results suggest that the solubility of MEEPT-X systems can be determined by both solute-solute and solute-counter-anion interactions, and that the individual chemistries of the systems will determine those interactions that are most important. We also note that solvent pocket and solvent shell-like formations were observed for many systems irrespective of the solubility limit, which has also been previously reported for similar redox-active systems.⁴⁵

Conclusions

Through a combined experimental, regression modeling, and MD simulation investigation, we identified key features that govern the solubility of MEEPT-X salts in acetonitrile. Ten MEEPT-X were isolated, and robust physicochemical experimental analyses, regression modeling and MD simulations were undertaken. Non-compact and flexible counter-anions tend to lead to higher MEEPT-X solubility when compared to compact and rigid counter-anions. These larger counter-anions tend to have more configurational entropy and hinder inter-MEEPT⁺• contacts, which combine to maintain a more homogeneous solution. MEEPT-ClO₄, which generally falls outside of the trends of the systems investigated here, shows signs of strong ion association, possibly contact ion pair formation, contributing to its overall poor solubility. This work presents a molecular strategy for enhancing the solubility of charged ROM, combined with a physicochemical understanding of the factors contributing to improved solubility, which opens possibilities for creating ROM-electrolyte systems for more energy dense RFB.

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Supporting Information

The Supporting Information is available free of charge at:

- Additional information and results pertaining to the synthesis of N-(2-(2-methoxyethoxy)ethyl)-phenothiazinium radical cation salts, X-ray crystallography (the deposition numbers of crystal structures reported in this paper are CCDC: 2418993 (MEEPT-SbCl₆), CCDC: 2418994 (MEEPT-

OTf), CCDC: 2418995 (MEEPT–FSI), CCDC: 2418996 (MEEPT–BETI), CCDC: 2418997 (MEEPT–FTFSI) and CCDC: 2418998 (MEEPT–SbF₆)), differential scanning calorimetry (DSC), UV-vis spectroscopy, ionic conductivity, and viscosity measurements, and MD simulations.

Notes

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