Ionic liquids and solids: open-access data, modeling and design

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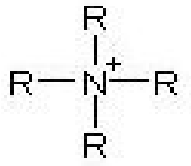
Outline

- **Introduction: Ionic liquids and sustainable chemistry (green chemistry)**
- **Information on ionic compounds: ILThermo and Chemical Property Viewer (CPV)**
- **Property estimation methods: comparing approaches for undissociated and ionic compounds**
- **Selected properties, applications and design of ionic liquids**

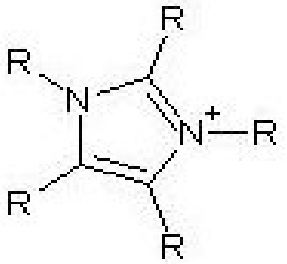
What are Ionic Liquids (ILs)?

- **ILs are defined as salts (ionic compounds) with a melting point below the boiling point of water (100 °C);**
- **Synonyms: low-melting salts, molten salts, liquid organic salts (!);**
- **Main characteristics: composition of (organic) cation and organic or inorganic anion, ionic conductivity;**
- **ILs also can be mixtures of salts (eutectic compostions).**

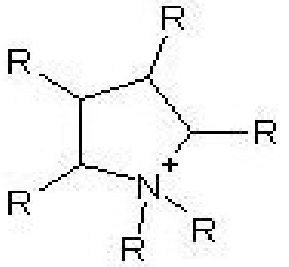
Common cations in ILs



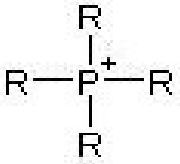
ammonium



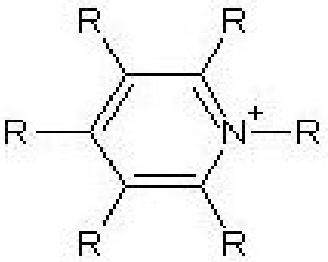
imidazolium



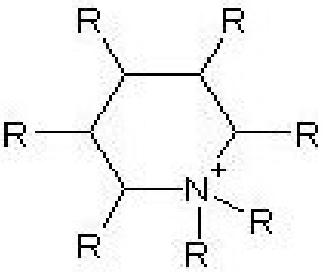
pyrrolidinium



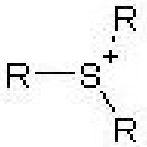
phosphonium



pyridinium



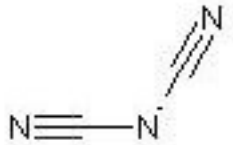
piperidinium



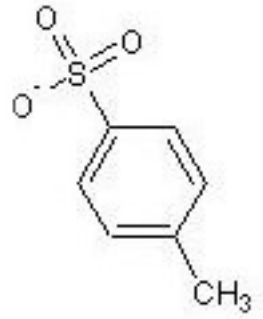
sulfonium

Common anions in ILs

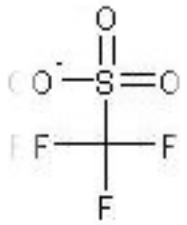
Cl^- Br^- I^- $(HF)nF^-$



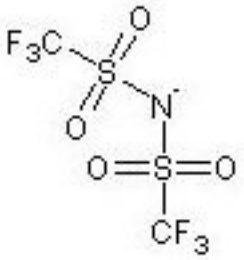
dicyanamide (DCA)



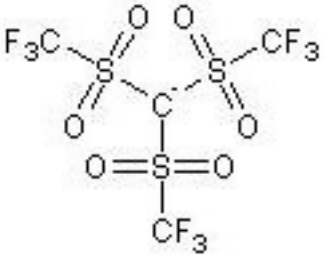
p-toluenesulfonate (tosylate)



triflate (TfO)



TFSA or NTf2



methide

The “green solvents” buzz

Ionic liquids have **low vapor pressures** and **low flammabilities** in comparison to often used organic solvents such as volatile organic compounds (VOCs). **HOWEVER: ILs may**

- **hydrolyze, see [1Bu-3Me-IM][PF6]** (*Green. Chem.*, **2003**, 5, 361-363; DOI: 10.1039/b304400a)
- **decompose into hazardous products**
- **bioaccumulate and show (eco)toxicity**

Sustainable chemistry perspective of ILs

- **Replacement of VOCs as medium in synthesis**
- **Replacement of (organic solvent + solid salt) systems in electrochemistry)**
- **Catalysts in organic synthesis**
- **Extraction of metal cations**
- **Novel devices for a sustainable economy: fuel cells, batteries, dye-sensitized photovoltaic cells**
- **Speciality applications: new, safer thermometer liquids, high-refraction liquids in mineralogy,...**

Task-Specific Ionic Liquids (TSILs)

Cation-anion combinatorics, selection of charged heterocycles, and variation of functionalized side chains affords application-specific design of Ils.

Cheminformatics should support :

- **search and estimation of properties for candidate Ils**
- **design of novel Ils by structural modification and optimized composition of IL mixtures**

http://ilthermo.boulder.nist.gov/ILThermo/mainmenu.uix

Ionic Liquids Database- (ILThermo)
NIST Standard Reference Database #147

- IUPAC Ionic Liquids Database Project
- Thermodynamics Research Center
- National Institute of Standards and Technology

IUPAC Ionic Liquids Database, ILThermo, is a free web research tool that allows users worldwide to access an up-to-date data collection from the publications on experimental investigations of thermodynamic, and transport properties of ionic liquids as well as binary and ternary mixtures containing ionic liquids.

Pure Ionic Liquids Data

SEARCH BY **Ions** **Ionic Liquids** **Property** **Literature**

Binary Mixtures Data Containing Ionic Liquids

SEARCH BY **Ions** **Compounds** **Property** **Literature**

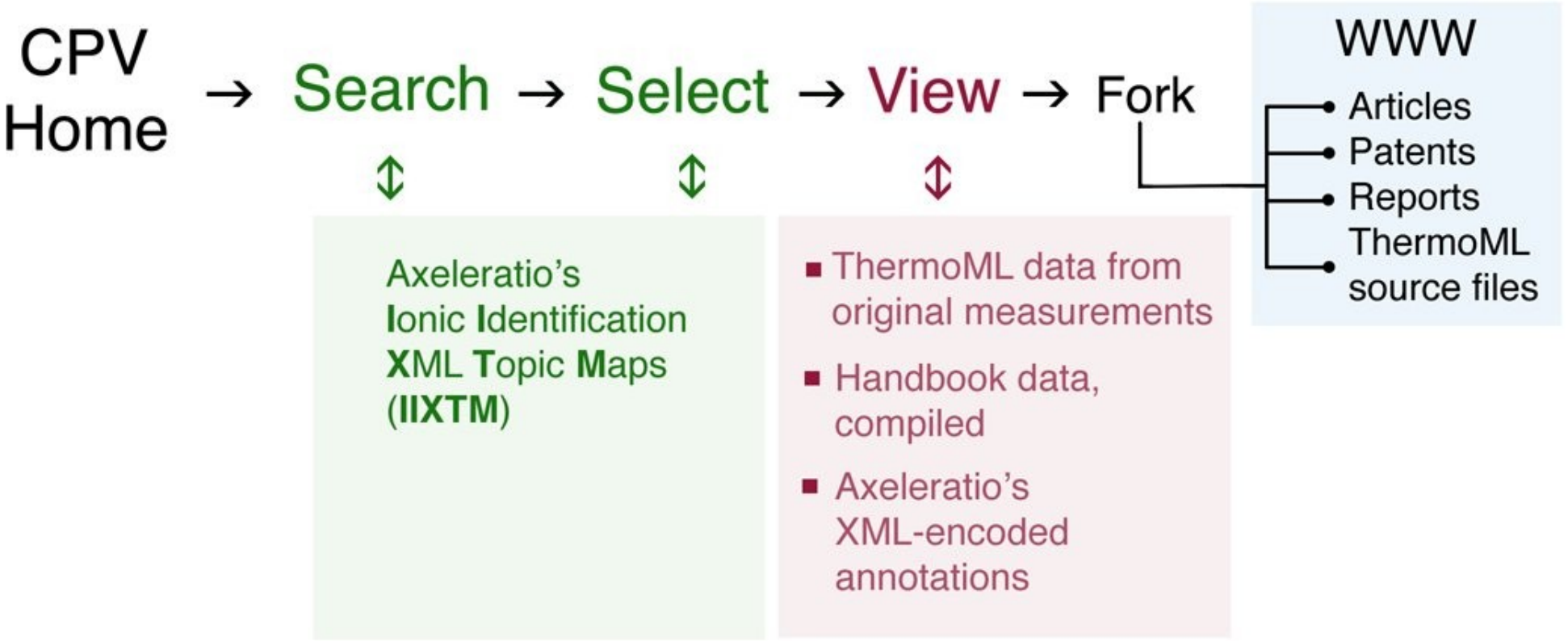
Ternary Mixtures Data Containing Ionic Liquids

SEARCH BY **Ions** **Compounds** **Property** **Literature**

Chemical Information ONLY (no path to data)

SEARCH BY **Ions** **Ionic Liquids**

Chemical Property Viewer (CPV) Search Flow



http://www.axeleratio.com/cpv

Chemical Property Viewer

The Chemical Property Viewer (CPV) is designed to find, browse, view and compare property data of chemical substances, mixtures, and materials. Goal of the CPV Project is to provide free, quick-by-click, and informed access to chemical information that supports advanced material science and sustainable chemistry.

Info & News
:: About CPV
:: Data scope

ThermoML
:: Archive
:: Properties

Ionic Liquids
:: Getting Started
:: ILThermo
:: ThermoML Organic Salts

Literature
:: EnviroInfo2007 Paper

Liability
:: Statement
:: Disclaimer

Contact
:: Axel at axeleratio@yahoo.com

Customize: Temperature Pressure

Select ThermoML-Archive substance by

- Inorganic compound name
- Organic compound name
- CAS registry number
- Molecular formula

Special substances and materials

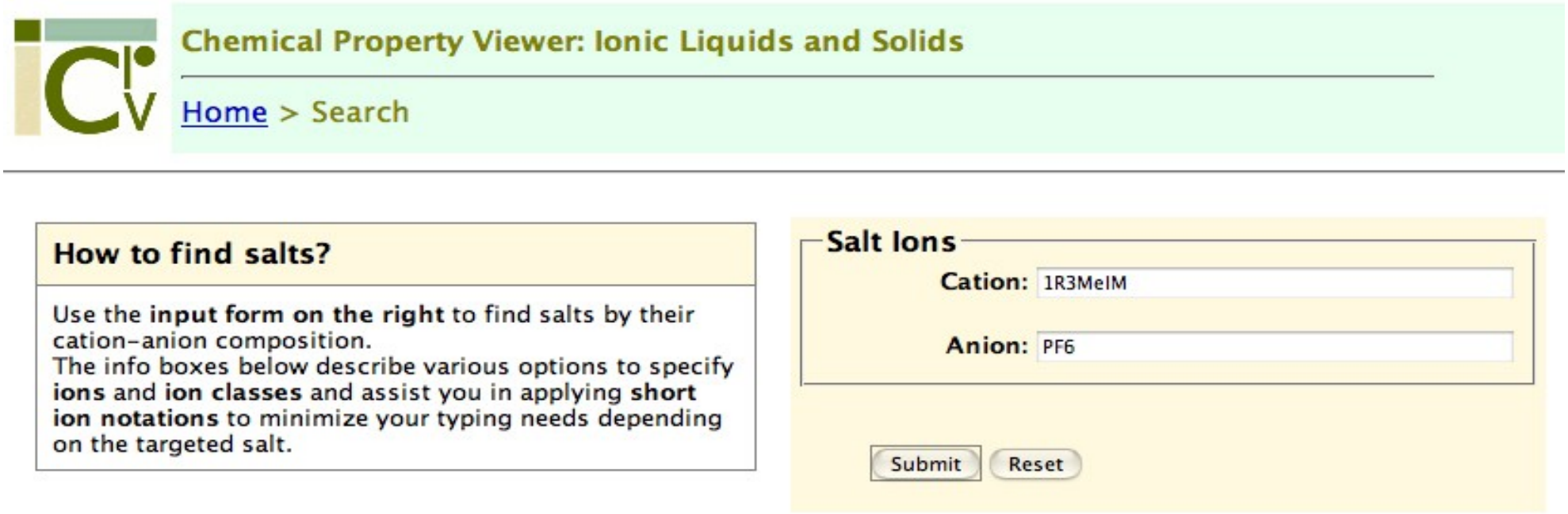
- Ionic liquids and solids

Chemical Species

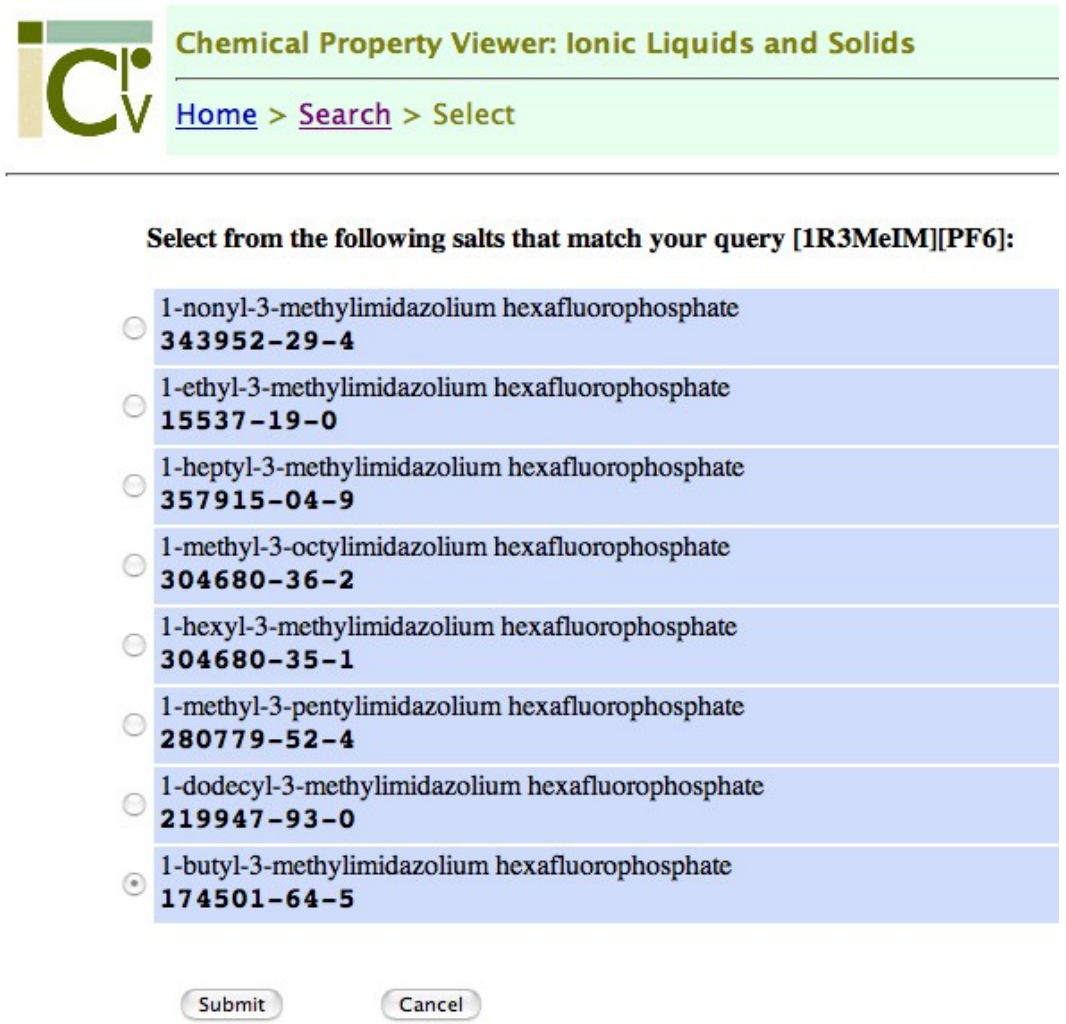
- Cation
- Anion

Search example: 1-alkyl-3-methyl-imidazolium hexafluorophosphates

- **Cation** query using short, semi-structural notation: **1R3MeIM**
- **Anion** query using formula: **PF6**

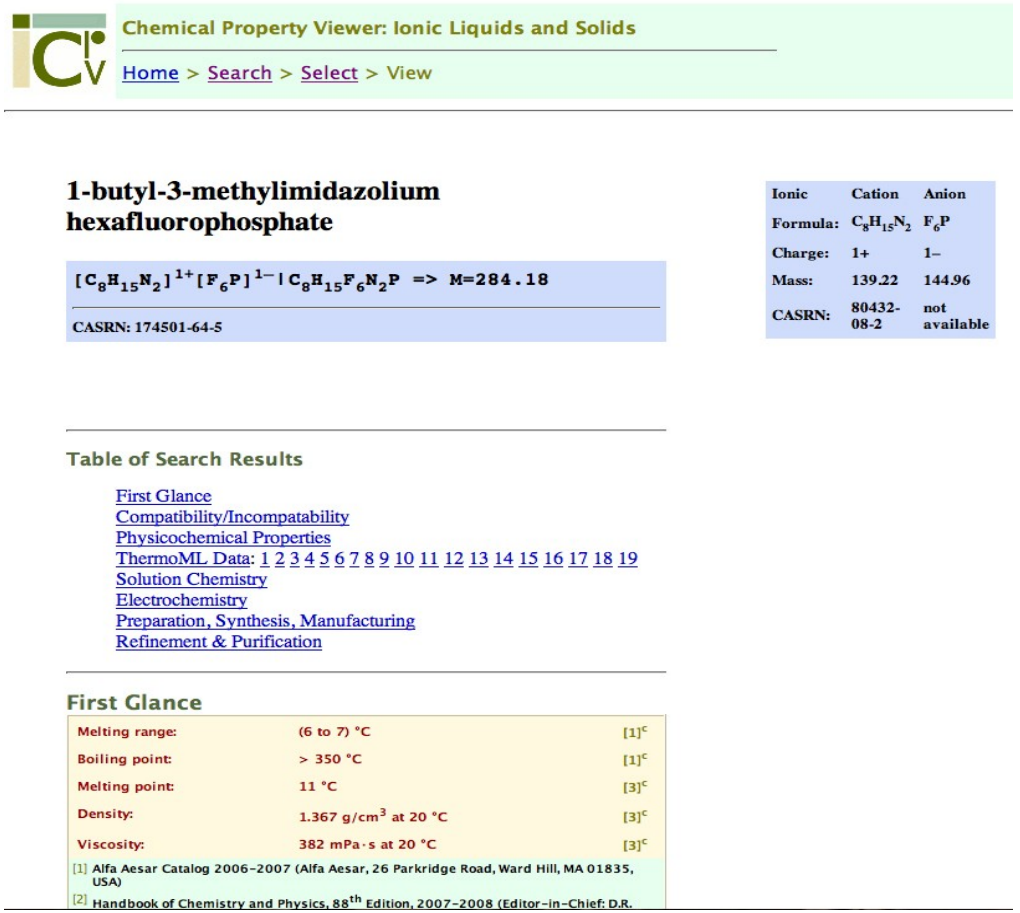


Select



- **Selection menu lists members of the cation class “1-alkyl-3-methylimdazolium”**
- **Specication of ion classes is made possible by Axeleratio’s IIXTM base**
- **Ion classes may be entered as name or (as in this example) short notations**

View results for selected compound



- **Results are displayed by topics**
- **Results include property data from ThermoML and Axeleratio's annotation database**
- **References are given in “traditional form” and *via* links such as the Document Object Identifier (DOI)**

Sections of CPV's result page for 1-butyl-3-methylimidazolium hexafluorophosphate

Compatibility/Incompatability

Attacking gold:	[BMIM][PF6] has been reported to attack gold surfaces. The aggressiveness increases with increasing water content due to the formation of HF from [BMIM][PF6] decomposition.	[2]°

[1] Frank Endres and Sherif Zein El Abedin: Air and water stable ionic liquids in physical chemistry, *Phys. Chem. Chem. Phys.* 2006, *8*, 2101–2116. | DOI: 10.1039/b600519p

[2] text on page(s) 2101 in [1]

Physicochemical Properties

Density:	1.363 g/mL at room temperature (weighing of sample in volumetric flask by removing air bubbles with a heat gun)	[2]°

[1] S. Chun, S. V. Dzyuba and R. A. Bartsch: Influence of Structural Variation in Room-Temperature Ionic Liquids on the Selectivity and Efficiency of Competitive Alkali Metal Salt Extraction by a Crown Ether, *Anal. Chem.* 2002, *73*, 3737–3741. | DOI: 10.1021/ac010061v

[2] Table 1 on page(s) 3739 in [1]

Ionic Liquids (ILs) and XML

- **Axeleratio's Ionic Identification XML Topic Maps (IIXTM)**
  http://www.axeleratio.com/axel/posters.htm
- **Axeleratio's XML-encoded annontations for ILs and other compounds (of interest in electro-chemistry and semiconductor research)**
- **XML-encoded thermodynamic property data in ThermoML archive**

ThermoML is an XML application

XML = eXtensible Markup Language

ThermoML = Thermodynamic Markup Language to capture and exchange thermodynamic data

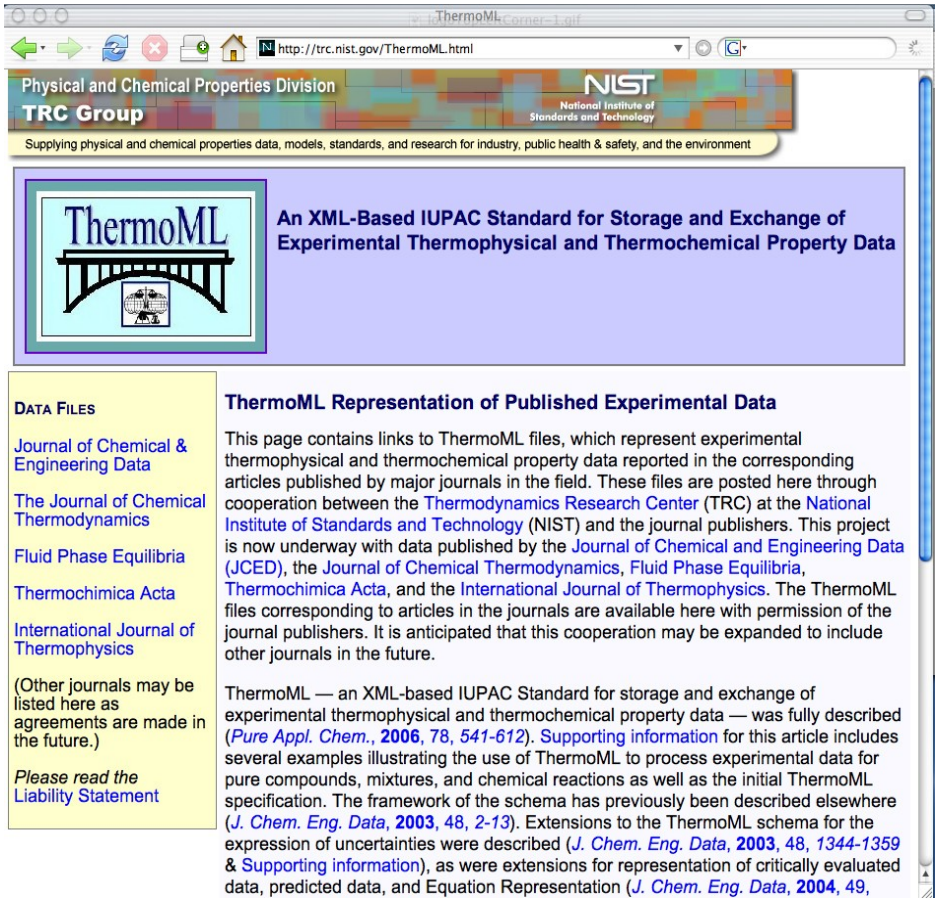
Other XML applications of interest in science and environmental chemistry:

- **MathML to represent and apply equations, functions, etc.**
- **CML to encode molecular structure**
- **CDX for Central Data Exchange of environmental information at US-EPA**

To explore XML applications and initiatives go to:
http://xml.coverpages.org/xmlApplications.html

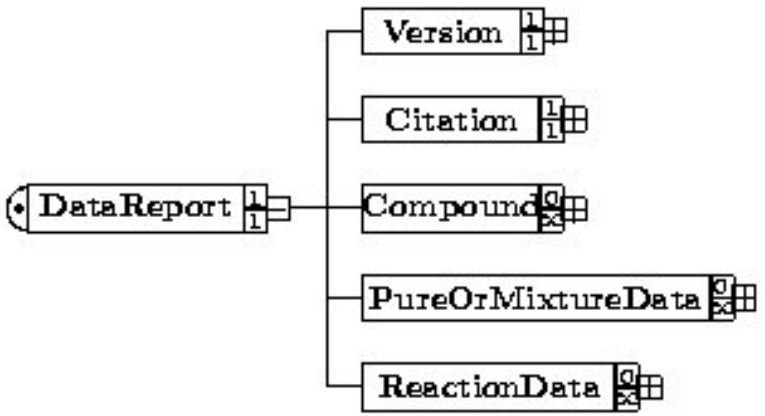
ThermoML Archive Portal

http://trc.nist.gov/ThermoML.html



- General Information
- Links to publications about ThermoML
- Links to ThermoML files with chemical property data of articles from five journals
- Schema: trc.nist.gov/ThermoML.xsd

ThermoML root and first layer nodes



- Exactly one **<Version>** and one **<Citation>** subtree
- None to many **<Compound>**, **<PureOrMixtureData>** and **<ReactionData>** subtrees

Programming approaches
using the Document Object Model (DOM)

Off-line scripting

Python, XML access via `xml.dom.minidom` module

Python scripts implemented for

- **Inspection of ThermoML files**
- **Extraction of data**
- **XML-to-XML conversions**

(chemical dictionary generation)

Web design

JavaScript for browser-side tasks, DOM functions slow for huge XML files

PHP for server-side tasks including dictionary browsing and generation of result pages

(`XMLReader` extension for parsing huge XML documents)

Molecular/Ionic property estimation and modeling

Theoretical approaches:

Main goal: to gain insight, understanding
Examples: HF, DFT, force field methods
Work flow: off-line studies -> publications

(Semi-)empirical approaches:

Main goal: to rationalize, data fitting
Examples: QPPRs, QSPRs, GCMs, ANNs
Work flow: off-line design -> on-line methods

Networking approaches:

Main goal: to compare, relate to known facts
Examples: structural similarity/difference
Work flow: on-line, highly interactive, supportive of chemical reasoning

Intermolecular and interionic interaction energy w

depends inversely on inter-distance r:

Ionic-ionic
Coulomb energy: $w(r) \sim r^{-1}$

Hydrogen bonding: $w(r) \sim r^{-2}$

Dipole-based: $w(r) \sim r^{-2}$ to r^{-6}

Nonpolar-nonpolar
London dispersion energy: $w(r) \sim r^{-6}$

Quantitative Property/Property Relationships (QPPRs) and Quantitative Structure/Property Relationships (QSPRs)

QPPRs and QSPRs are relations representing a property *P* as function of descriptors:

$$P = f(D_1, D_2, \ldots),$$

where the *D*'s are (molecular) descriptors that are experimentally or structurally derived.

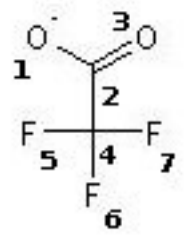
Reviewed for molecular compounds, for example, in "**Handbook for Estimating Physicochemical Properties of Organic Compounds**," by M. Reinhard and A. Drefahl, Wiley & Sons, N.Y. 1999.

Molecular structure input for derivation of descriptors

- **Molecular graph** (drawing converted into connection table), user-friendly
- **CML**, database- and exchange-friendly
- **InChI** (IUPAC International Chemical Identifier), database-, exchange-friendly
- **SMILES** (**S**implified **M**olecular **I**nput **L**ine **E**ntry **S**ystem, *J. Chem. Inf. Comput. Sci.* **1988**, *28*, 31-36), user-, database-, exchange-friendly, unique key *via* canonicalization (**CANGEN**-algorithm, (*J. Chem. Inf. Comput. Sci.* **1989**, *29*, 97-101)

SMILES-to-topological-matrix example

trifluoroethanoate:



SMILES:

[O-]C(=O)C(F)(F)F

	1	2	3	4	5	6	7
1	0	1	0	0	0	0	0
2	1	0	1	1	0	0	0
3	0	1	0	0	0	0	0
4	0	1	0	0	1	1	1
5	0	0	0	1	0	0	0
6	0	0	0	1	0	0	0
7	0	0	0	1	0	0	0

adjacency matrix

=>

	1	2	3	4	5	6	7
1	0	1	2	2	3	3	3
2	1	0	1	1	2	2	2
3	2	1	0	2	3	3	3
4	2	1	2	0	1	1	1
5	3	2	3	1	0	2	2
6	3	2	3	1	2	0	2
7	3	2	3	1	2	2	0

distance matrix

From topological matrix to topological indices and substructure partitions

Molecular descriptors such as topological indices and **substructure partitions** are key parameters in **advanced chemical search** (similarity search) and **modeling** (clustering, property prediction).

Applications illustrated in:

A. Drefahl “Modellentwicklung zur Vorhersage des Umweltverhaltens organischer Verbundungen auf der Basis computergestützter Struktur/Eigenschafts-Transformationen”, Dissertation, TU Munich, 1988.

M. Reinhard and A. Drefahl “Handbook for Estimating Physicochemical Properties of Organic Compounds,” Wiley & Sons, N.Y. 1999.

Molar *vs*. molecular: the volume descriptor

Molar volume: $\mathbf{V_M = M/D}$

is defined by molar mass **M** and density **D**.

Molecular volume is derived from atom radii (crystallographic data).

Approach for **binary ionic liquids**:

$$\mathbf{V_{IL} = V_{ion}(A^+) + V_{ion}(X^-)}$$

with ionic volumes $\mathbf{V_{ion}}$ for cation and anion.

QPPRs based on ionic volumes

Density $= M \cdot p \cdot V_{IL}^{-q}$

Viscosity $= r \cdot e^{sV_{IL}}$

Conductivity $= t \cdot e^{-uV_{IL}}$

---

p, q, r, s, t, u are adjustable parameters

Reference:

“How to Predict Physical Properties of Ionic Liquids: A Volume Based Approach,” *Angew. Chem. Int. Ed.* 2007, 46, 5384-5388; DOI: 10.1002/anie.200700941

Note: Data from highly purified ILs with low halide and water content

Measuring structural similarity

- **Isomerism (atomic composition, tautomerism, chirality)**
- **Molecule fragmentation and comparison of fragment frequencies**
- **Alignment of sequences in linear or uniquely enumerated structures**
- **Conformational analysis and mapping**
- **Space groups (crystalline compounds)**

Head group/side-chain approach for cations

Head group: heterocyclic ring system
Side chains: ring substituents
Limitations: ring-containing substituents

Approach for **property estimation and design of strategies for (eco)toxicological hazards** : **Classification by head group** (supported by short structural notations in IIXTM base)

Certain properties (**lipophilicity, cytotoxicity**) are mainly influenced by side chain functionalization (-> **structural difference** and discovery of toxicophore substructures)

For example: *Green Chem*. **2007**, *9*, 760-767; DOI: 10.1039/b615326g

Structural similarity vs. structural difference

Similarity: **measurement** depending on **definition** (procedure easy on computer, difficult for humans, “intuition is great, but lacks quantification”)

Difference: **recognition** task (procedure easy for humans, difficult to implement on computer)

Automatic difference recognition desirable for **IL design**:
the goal is to relate **novel (virtual) ILs** to known, **synthesized** ones and optimize properties by structural modification.

Approaches to automatic structural difference recognition

- **Maximum common subgraph (MCS)** recognition

- **Group interchange method (GIM)** based on generation of unique SMILES notations and **linear notations for group interchange (LNGI)**: *J. Chem. Inf. Comput. Sci*. **1993**, *33*, 886-895.

Quantitative Source/Target Relationships (QSTDs)

QSTDs represent correlations between properties of compounds (**targets**) and **source** compounds that differ from the target by a defined structural difference.

Example (estimation of **flash point** for substuted **germane** from **silane** analog):

$$T_f\{R_4Ge\} = 19.0 + 0.91 T_f\{R_4Si\}$$

(m=13, r=0.9832)

see Axel Drefahl's paper in session 7 at iEMSs 2006:
http://www.iemss.org/summit/session/s7.html

Structural difference: insertion of -CF_2- group(s)

Example: **perfluoroalkyltrifluoroborate** anion, **$[CF_3(CF_2)_nBF_3]^-$** (better water-stability than **$[BF_4]^-$**, hydrophobic, explored for electronic devices)

T_m $[CF_3(CF_2)_nBF_3]^-$< T_m $[BF_4]^-$, if same cation; lowest T_m typically for n=1.

Thermal stability increases with n, but **$[BF_4]^-$** most stable.

Density increases with n.

Viscosity is in range of $[NTf_2]^-$ for all n.

Conductivity decreases with n.

Electrochemical window exceeds -2.4 to 2.1 V range, independent of n.

Reference:
Chemistry-A European Journal **2004**, *10*, 6581-91;
DOI: 10.1002/chem.200400533)

Physicochemical properties of Ils depend strongly on impurities

Small amounts of **impurities** (halides, water) can have a **drastic effect on IL properties**.

Typical **purification procedures**:

- storing at elevated temperature and reduced pressure;
- gas bubbling

Alternate synthetic routes to purer Ils are explored.

Melting Points of ILs

Warning! The **melting temperature T_m** is sometimes confused with the **glass transition temperature T_g**.

T_m: thermodynamic property

T_g: kinetic property

Of primary interest is the **liquidus range** from T_m or T_g up to the **temperature of degradation onset**.

Cation effect on melting temperature of ILs

Some general trends:

- $\boldsymbol{T}_{\mathbf{m}}$ is lowered by by disruption of Coulombic packing

- D ifferent sizes of alkyl substituents (asymmetry) lower $\boldsymbol{T}_{\mathbf{m}}$ (in dialkylimidazolium salts)

- Replacement of -CH_2- by -O- in imidazolium side chain in perfluorotrifluoroborates increase $\boldsymbol{T}_{\mathbf{m}}$ by more than 20 degrees (*Chemistry-A European Journal* **2004**, *10*, 6581-91; DOI: 10.1002/chem.200400533).

Anion effect on melting temperature of ILs

$\boldsymbol{T_m}$ decreases with increase of size of anion (addition of weakly interacting substituents to charge center).

$[N(SO_3CF_3)_2]^-$ (NTf2), $[N(CN)_2]^-$, $[CF_3SO_3]^-$, and $[CF_3CO_2]^-$ salts typically exhibit low $\boldsymbol{T_m}$.

References: Table 3.1-2 in “Ionic Liquids in Synthesis” by P. Wasserscheid and T. Welton (Eds.), Wiley-VCH, Weinheim,2003; and A. Drefahl’s note at: http://www.axeleratio.com/ip/QSPRs/order_ion/mpTf2N.htm

Involatile or not?

Involatility is a property that is often mentioned as common to all non-decomposing ILs (supported by long-term tests without significant loss: 3 month, 175° C, 50 millibar; *Chem. Ing. Tech*. **2005**, *77*, 1800-1808).

However, **some ILs can be distilled**:

[1C$_6$3MeIM][NTf$_2$], for example, at 170 °C and 0.07 millibar (*Nature* **2006**, *439*, 831-4; DOI: 10.1038/nature04451);

[1C$_{10}$3MeIM][NTf$_2$] and **[1C$_{12}$3MeIM][NTf$_2$**] at 177 °C and reduced pressure (*J. Phys. Chem. B* **2005**, 1099, 6040-3; DOI: 10.1021/jp050430h).

Equation of State (EoS) for ILs?

EoS models rationalize ***p,V,T*-data** for pure compounds and mixtures.

ThermoML data provide an excellent base to (semi-)automatically validate, extend and develop new EoSs.

Currently, the database of **density** and **surface tension** data for **ILs** is small. Measurement of **IL vapor pressures** has been proposed (*J. Phys. Chem. B* **2005**, 1099, 6040-3; DOI: 10.1021/jp050430h).

Selected reviews on IL applications in synthesis and catalysis

- T. Welton: "**Room-Temperature Ionic Liquids. Solvents for Synthesis and Catalysis**" *Chem. Rev.* **1999**, *99*, 2071-2083.
- P. Wasserscheid and W. Keim : "**Ionic Liquids – New 'Solutions' for Transition Metal Catalysis**" *Angew. Chem. Int. Ed.* **2000**, *39*, 3772-3789.
- Also see links in left column at http://www.axeleratio.com/cpv

Electrochemical deposition (ECD) using ILs

Many Ils exhibit an excellent **electro-chemical window** (roughly from -3 to 3 V) at and above room temperature.

Metal and semiconductor deposition is currently actively studied, including elements (**Si, Ge, Ga-As, Cu-In-Se**) that are of interest in **phtovoltaic devices**.

A **literature overview** is given at:
http://www.axeleratio.com/ip/salts/-IonicLiquids/ElectrodeposMeILsOverview.htm

Fluorohydrogenates, $[F(HF_{2.3})]^-$

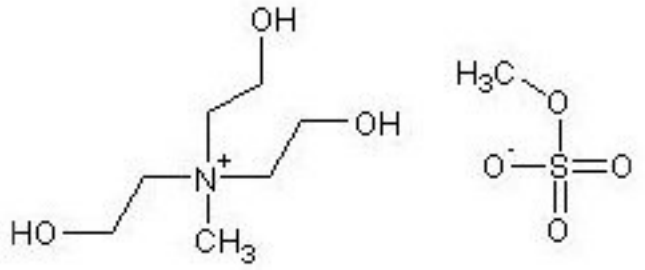
ILs with 1,3-dialkylimidazolium cations, **[1R3MeIM]**$^-$, and oligimeric anion, **$[(HF)_nF]^-$**, have relatively low viscosities and are air-stable and Pyrex-compatible.

Property variation from R = **Me** to **Hx**;

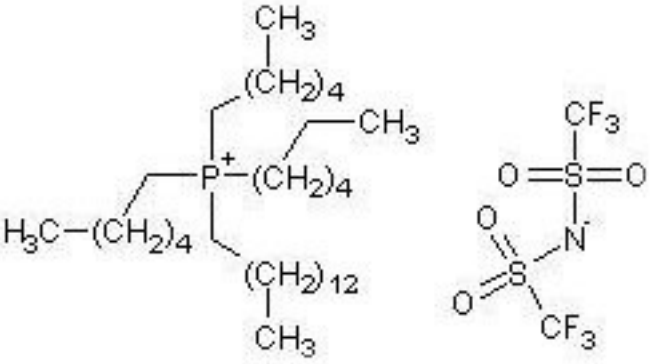
Density/(g/cm^3):	1.17 to 1.09
Viscosity/cP:	5.1 to 25.8
Specific conductivity/(mS/cm):	110 to 16

J. Electrochem. Soc. **2003**, *150*, D195-D199; DOI: 10.1149/1.1621414

Thermometer liquids with low toxicicity (I) and large liquidus range from -76 to 400 °C (II)



(I) tris(2-hydroxyethyl)methyl-ammonium methylsulfate



(II) trihexyl(tetradecyl)phosphonium bis[(trifluoromethyl)sulfonyl]amide

Green Chem. *2008*, 10, 501-507; DOI: 10.1039/b800366a

Hazard potential of ILs

MSDSs of commercial ILs: blanks for most properties.

Hazard assessment: testing (chemical legislation, OECD guidelines) and life-cycle analysis (LCA).

T-SAR (**t**hinking in terms of **s**tructure-**a**ctivity **r**elationships) **concept** is applied to ILs (see, for example: *Green Chem*. **2006**, *8*, 621-629; DOI: 10.1039/b602161a).

Use knowledge of **bioaccumulation, bio-degradability** and **(eco)toxiphores** in design of more sustainable ILs.

Anion effect on IL toxicity

The following toxicity classification is taken from a systematic study of IL cytotoxicity using a reproducible cell test (university-industry partnership, Germany) following toxicity classification:

low: Cl^-, Br^-, I^-, $MeOSO_3^-$

moderate: $N(SO_2CF_3)_2^-$ (NTf2)

high: $C(SO_2CF_3)_2^-$ (methide), SbF_6^-,

based on alkali and imidazolium salt,
for a complete anion list and details see: *Green Chem*. **2006**, *8*, 621-629; DOI: 10.1039/b602161a

Cation effect on IL toxicity

Some **general trends** by comparing cytotoxicity of salts with constant anion:

Head group (constant side chain):
alkali metal salt < organic cation salt,
otherwiseno significant differences

Side chain (constant head group):
- increase with length of alkyl chain
- decrease with introduction of -O-, -OH, and -CN

Déjà vu:structural difference recognition assists toxicity evaluation
Note: these are rough generalizations and need to be cross-evaluated with other bioassay results

Ecotoxicology: Freshwater algae growth inhibition by ILs

Case study: **1,3-dialkylimidazolium bromides, [1R3MeIM][Br]; algae: *Selenastrum capricornutum***

R:	**Oc**	**>**	**Hx**	**>**	**Bu**	**≈**	**Pr**
48h-EC_{50}/μM:	**44.7**		**371**		**2884**		**2884**
72h-EC_{50}/μM:	**47.9**		**347**		**2290**		**1949**
96h-EC_{50}/μM:	**38.2**		**288**		**1047**		**1380**

Reference: *Chemosphere* **2007**, *69*, 1003-1007; DOI:10.1016/j.chemosphere.2007.06.023

Summary

- **Information on ionic liquids (ILs) is (selectively) published in defined formats (ThermoML, IIXTM)**
- **IL data is accessible via ILThermo and CPV**
- **Future design and modeling of Ils will be advanced by current platform-independent, XML-based data abstraction.**

These slides can be revisited at

www.axeleratio.com/UNR2008/slides.pdf

Thank You!