Ionic Liquids in the Biorefinery

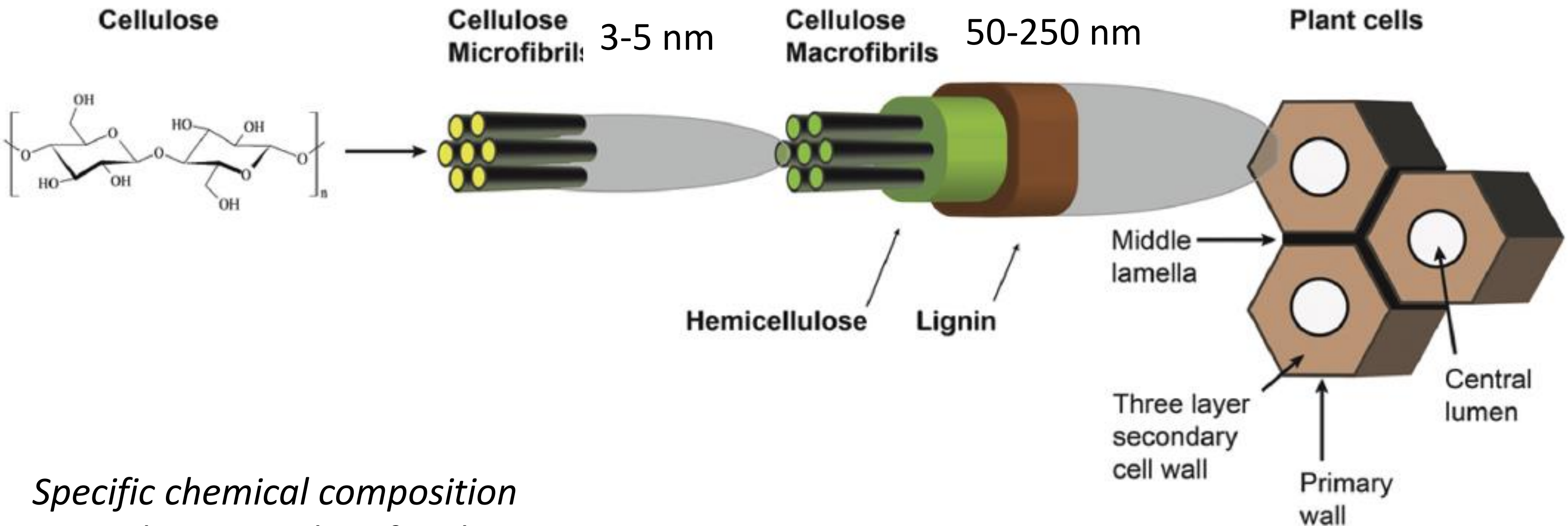
Lecture 11
Biofuels and Bioproducts

Bronx Community College - 2017
Chemistry and BioEnergy Technology for Sustainability NSF ATE 1601636

Outline

- Lignocellulose Recalcitrance, Pretreatment Strategies and “Bio-manufacturing”
- Introduction to Ionic Liquids
  - Structures, pH, as biomass solvents
- Ionic Liquids in the Biorefinery
  - Significance and Challenges
  - Protic IL Distillation (thin film, PV)
  - Biochemicals/Bioproducts (chitin, lignin)
- Costs, Environmental Aspects and Critical Evaluation

The Lignocellulosic Substrate



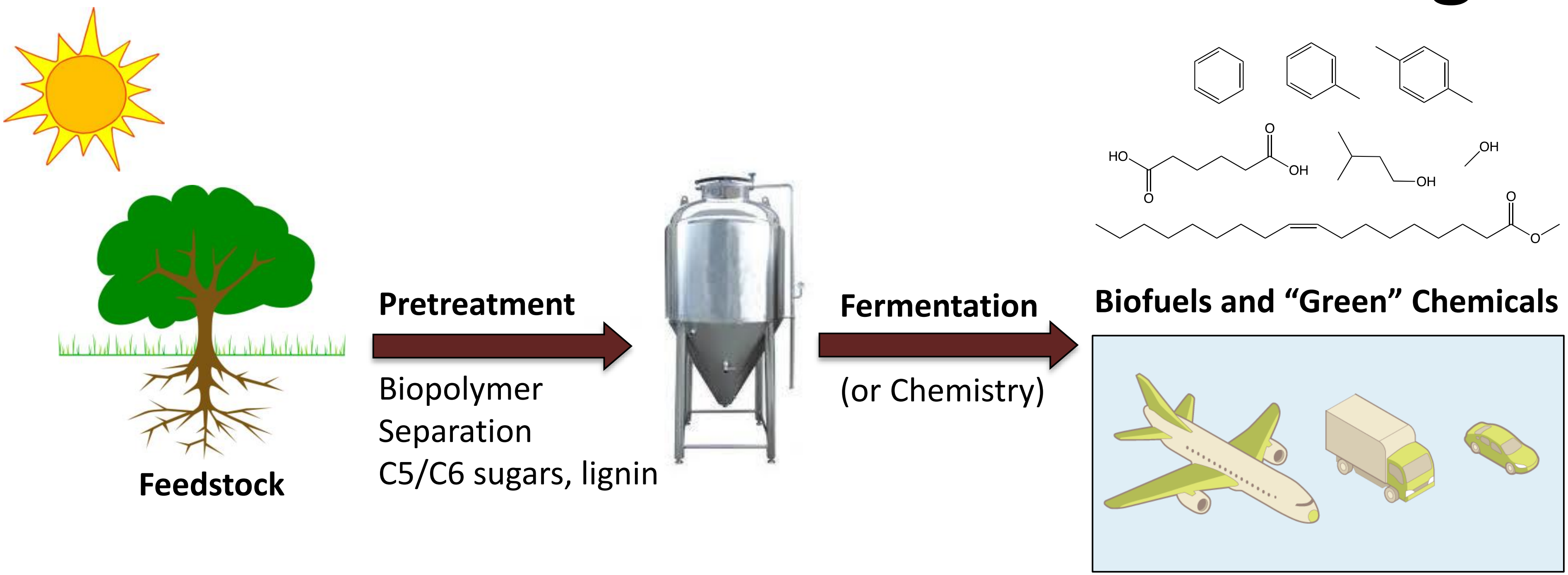
Specific chemical composition varies between plant families (hardwood, softwood, grasses)

Generic Composition:
45% Cellulose
25% Hemicellulose
25% Lignin
5% Protein, Ash, Extractables

- Cellulose (hexose = glucose)
- Hemicellulose (pentose/hexose)
- Lignin (phenylpropanoid)

Image: Zhang. *Green Chem* **2016** (18) 360

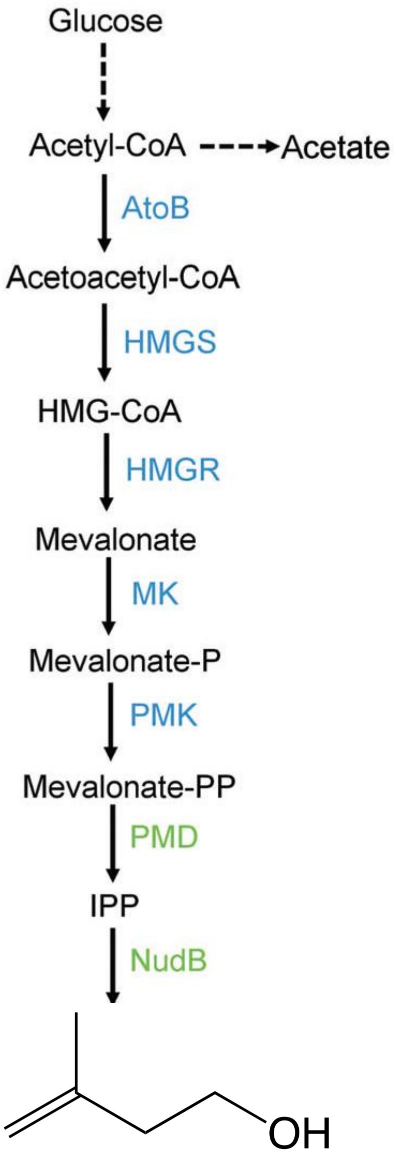
From Biomass to Biomanufacturing



- United States has 700M tons of non-food biomass/year[1]
- 50% conversion of this material could replace 50 billion gallons of oil/year[2]
- Global market for petroleum-replacement chemicals estimated at $500B[3]
- United States has committed to 36 billion gallons renewable fuel by 2020[4]

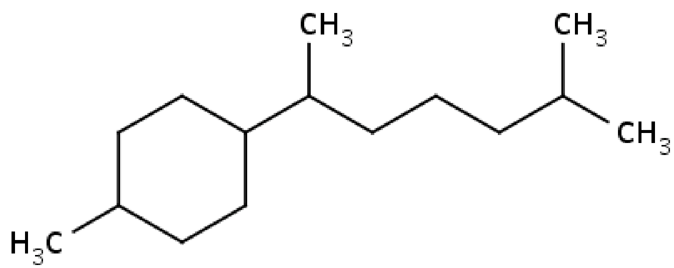
[1]Klein-Marcuschamer et al. *Biofuels Bioproducts and Biorefining*, 2011. **5** (5): p. 562-569.
[2]BIO, Current uses of synthetic biology for renewable chemicals and biofuels (2013)
[3]Frank and Solomon
[4]U.S. Energy Independence and Security Act of 2007

Heterologous Expression of Terpene Biofuels (and Medicines)

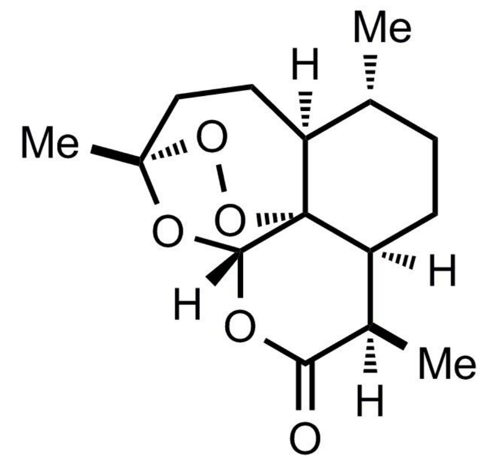


Isopentenol

a "drop-in" gasoline replacement



Bisabolane:
Produced heterologously in
S. cerevisiae and E. coli
- 125,000 BTU/Gal
- JP5 Fuel replacement
- model biofuel



Artemisinin:
- Antimalarial drug
- Modular production in Asia, Africa, South America (50+ tons 100 million treatments)

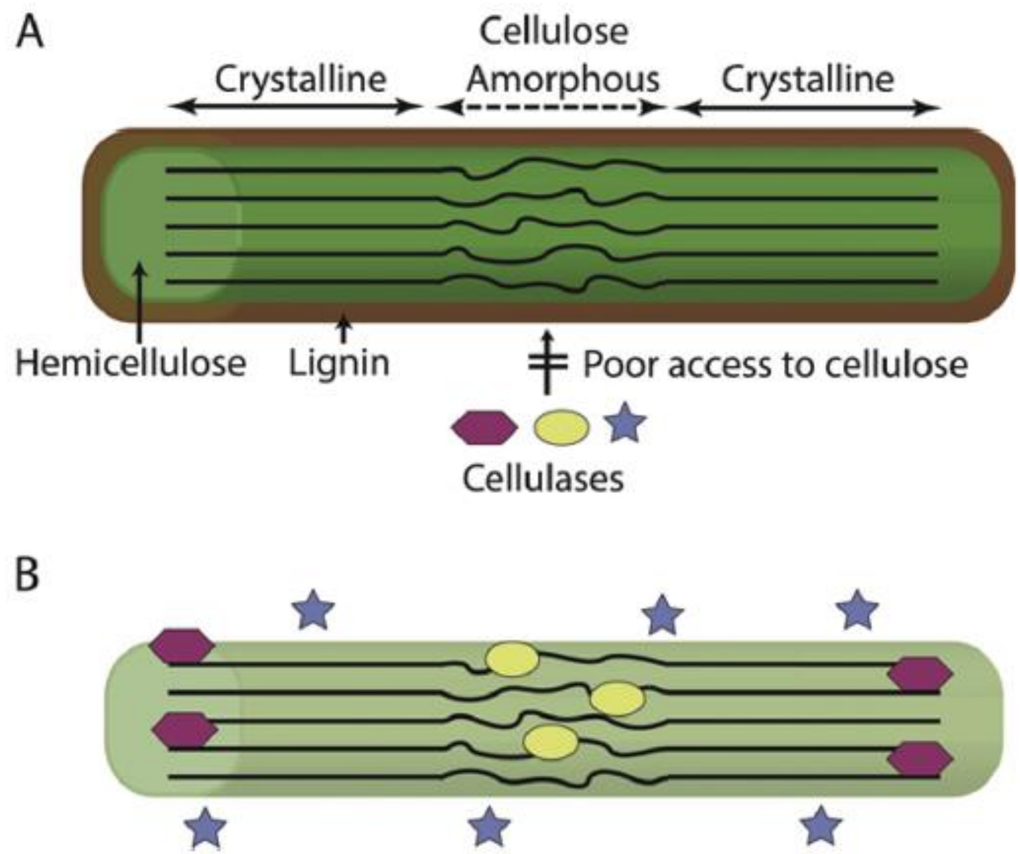
George et al Biotech Bioeng 2014 111
Ro et al *Nature* 440, 940, 2016
Keasling J. *Nature Communications* 2011, 483

Biomass Pretreatment

- Can be chemical, physical and/or biological
- Enhances extent and rate of enzymatic saccharification
- Impacts feedstock selection, handling and processing
- Pretreatment vessel composition and size
- Fermentation efficiency
- Enzyme loading and composition
- Waste disposal/water Use
- Opportunities to generate co-products

‘Organosolv’ Pretreatment

- Short-chain aliphatic alcohols, polyols, organic acids, acetone, dioxane, phenol, NMMO, 2Me-THF, Me-iBu-ketone, Ionic Liquids (ILs)
- Can produce “high quality lignin” e.g. low sulfur, less condensed
- Higher dielectric constant of solvent = higher ‘acid potential’ for catalyst
- Other considerations = cost, ease of recovery, toxicology, safety, environmental impact
- Solvent viscosity and ‘penetration’ into substrate
- H-Bonding and Polarizability



Reviewed: Zhang et al Green Chem 2016, 18, 360

Solvent Parameters

Substrate Solubilty:

- When δ is similar to the substrate, good dissolution is expected
- δ is not known for cellulose/lignocellulose
- δ is estimated at 22.5 for lignin
- Many of aforementioned organic solvents δ range is 17-27.

Solvent Reactivity (e.g. cellulose swelling):

- Measured empirically
- Calculated by multiple linear regression analysis
- Kamlet-Taft Parameters used for ILs

Hildebrand Solubility (δ)

$$\delta = \sqrt{c} = \left[\frac{\Delta H - Rt}{V_m}\right]^{1/2}$$

c = cohesive energy density ($MPa^{1/2}$)
ΔH = heat of vaporization ($J\ mol^{-1}$)
R = gas constant (8.324 $J\ K^{-1}\ mol^{-1}$)
t = temperature (^oC)
V_m = molar volume of solvent ($cm^3\ mol^{-1}$)

Kamlet-Taft Polarity (γ)

Well correlated with Cellulose Swelling

Measurement:

- ILs and IL water mixtures are tested
- Reichardt's Dye and TMS references
- H-bond acceptor and donor solvents (below)

$$\gamma = \gamma_0 + s\pi^* + A\alpha + B\beta$$

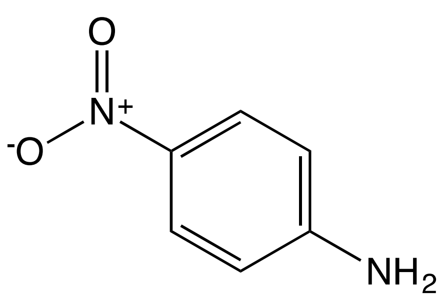
γ_o = regression value based on a reference solvent

π^* = index of solvent dipolarity/polarizability

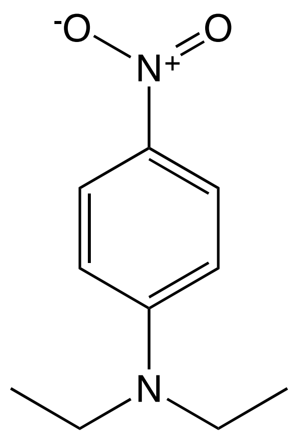
α = solvent hydrogen bond donor acidity

β = solvent hydrogen bond acceptor basicity

s, A, B = regression coefficients



4-nitroaniline



N,N-diethyl-4-nitroaniline

Ionic Liquids vs. Molecular Solvents

- Billions of structures (compared to 10s)
- Virtually no vapour pressure, no boiling point
- Virtually non flammable
- Excellent thermal stability up to 300°C and more
- Catalytic and unusual solvation properties
- Extreme low compressibility
- No cavitation even at up to -1000 bar tension
- Corrosion: Analogy to inorganic salts falls short
- Nanostructural segregation, Magnetic properties
- Very small friction coefficients = good lubricants
- Electrical conductivity 50 mS/cm down to nearly zero
- Can have bacteriocidal and bacteriostatic properties
- Can have low toxicity

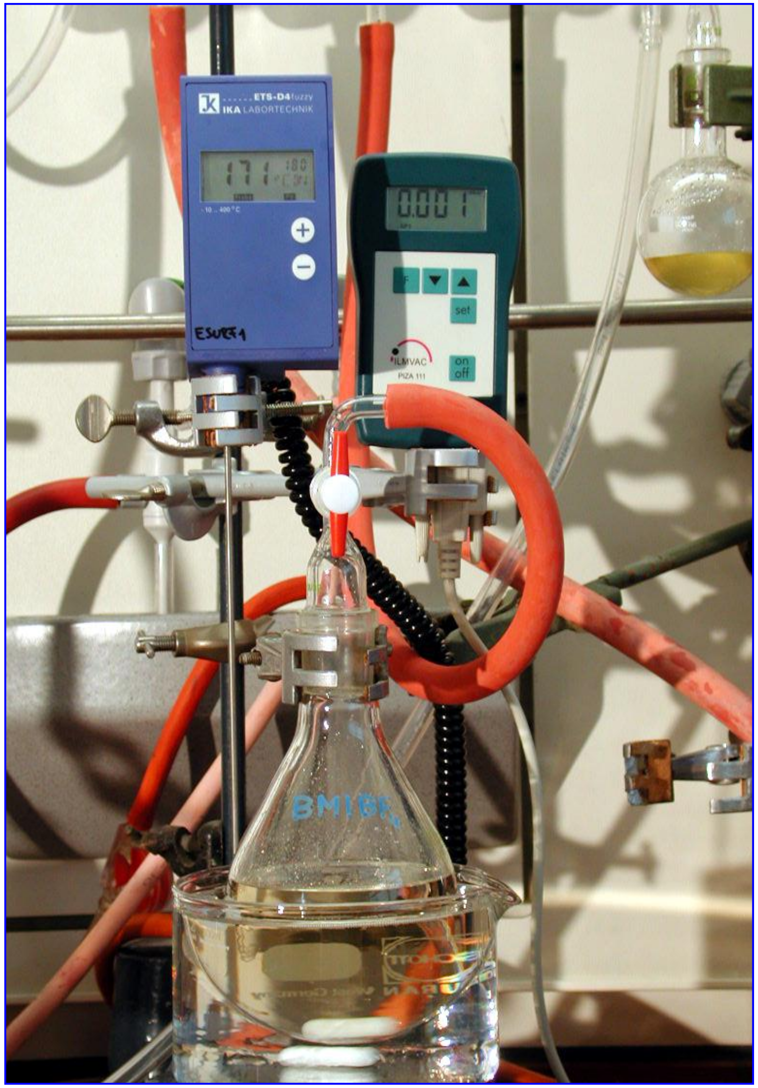
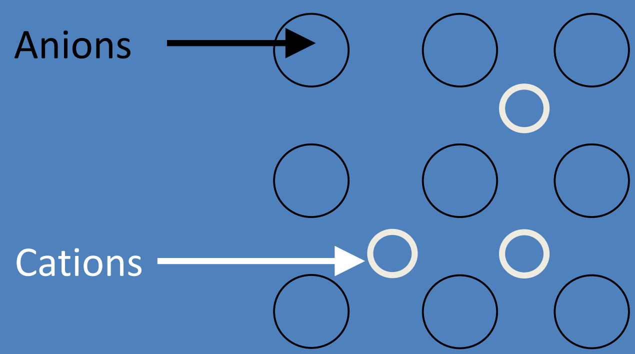


Photo: Proionic, GmbH

Ionic Liquids vs. Salts: Asymmetry Leads to Lower Melting Points (T_m)

“Fixed“ lattice structure

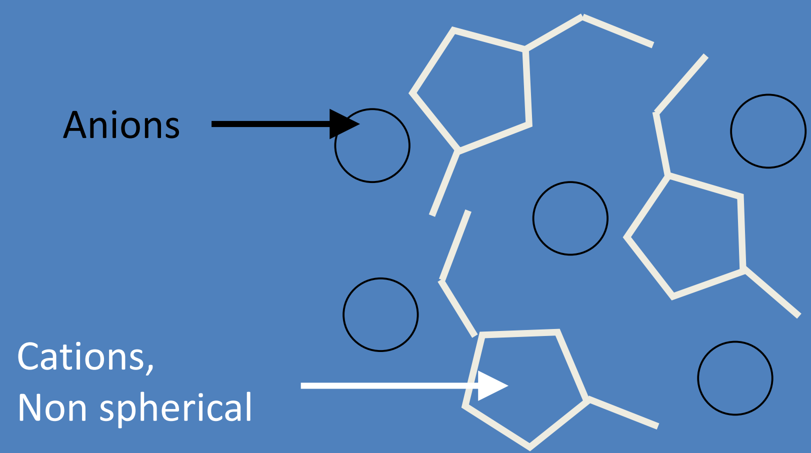
→ Solid



NaCl T_m = 801°C

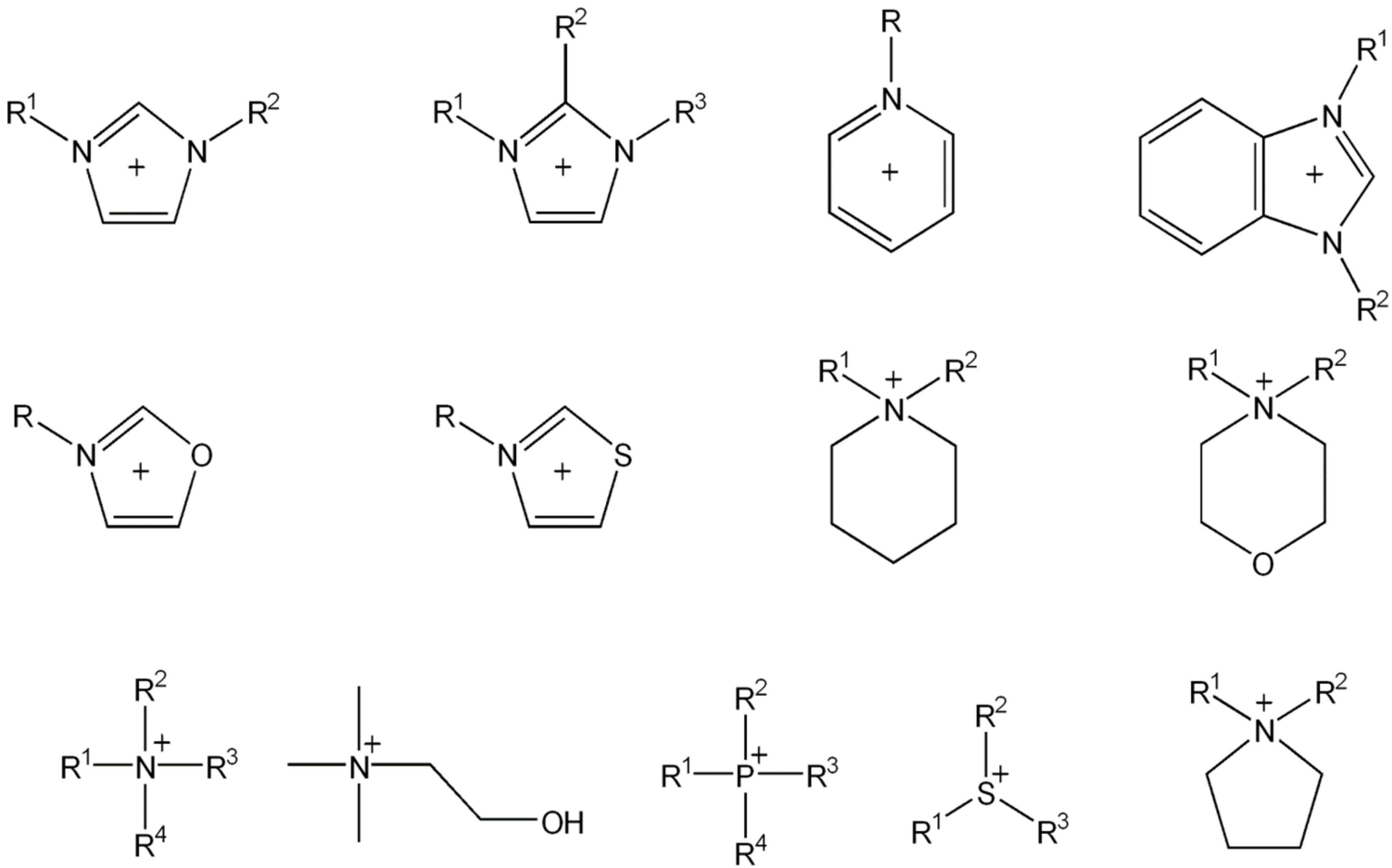
“Mismatched“ ion pairing

→ Liquid



ILs T_m < 100°C

Ionic Liquid Cations



Ionic Liquid Anions

F^-

Cl^-

Br^-

I^-

NO_3^-

PO_4^{3-}

SO_4^{2-}

SCN^-

CN^-

ClO_4^-

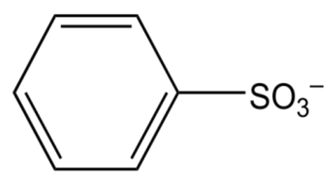
$B(CN)_4^-$

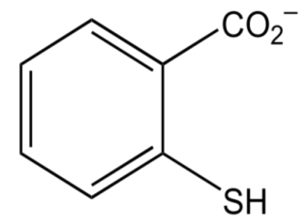
PF_6^-

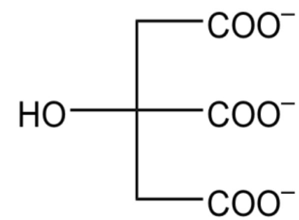
BF_4^-

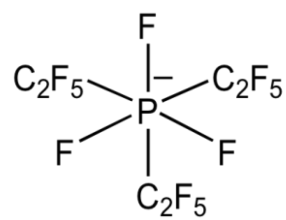
$AlCl_4^-$

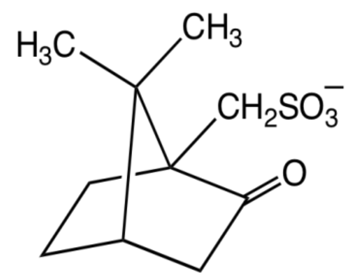
$FeCl_4^-$

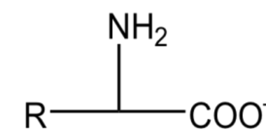










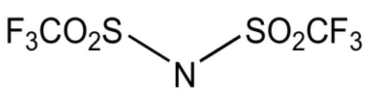


$CH_3CO_2^-$

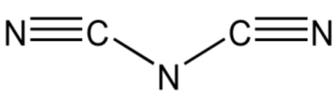
$(C_4H_9)_2PO_4^-$

$CH_3SO_3^-$

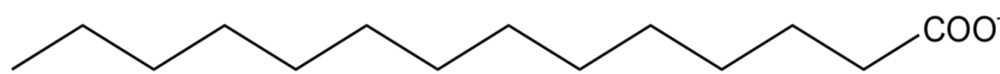
$CH_3SO_4^-$

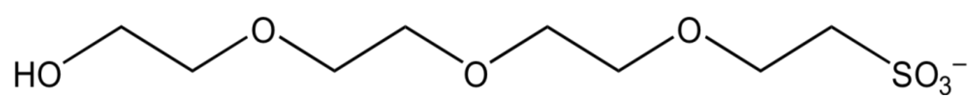


$CF_3CO_2^-$

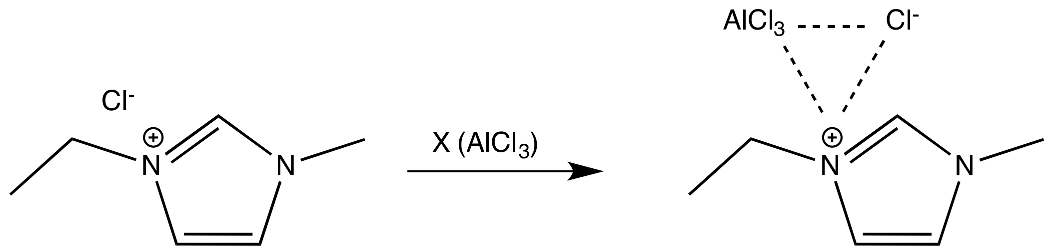


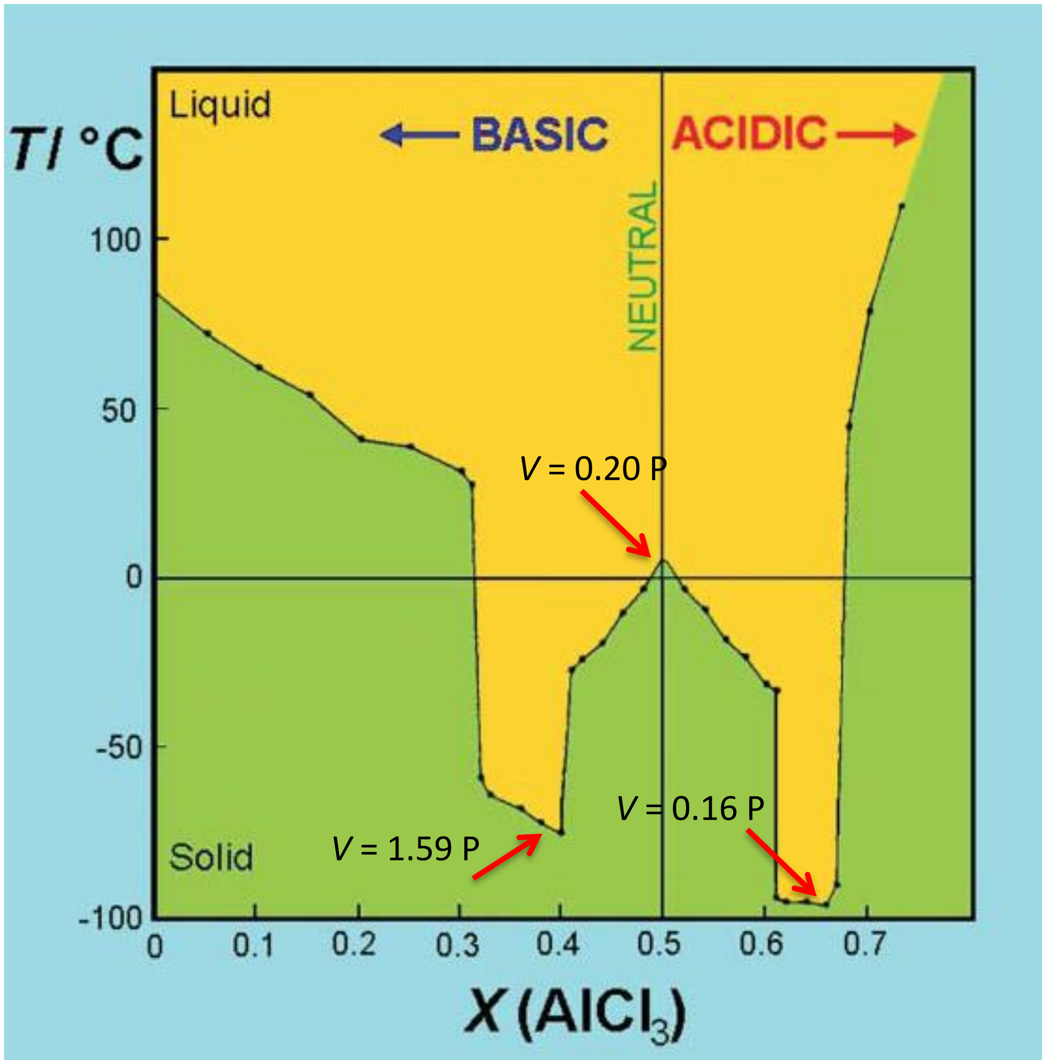
$CF_3SO_3^-$





Organoaluminate Molten Salts Demonstrate the "Tunable" Relationship between IL Structure, pH and Viscosity





- Viscosity (V) and Melting Point (T) vary with mole fraction (X) of anion ($AlCl_3$)

- The same principals are used to prepare "task-specific" ionic liquids

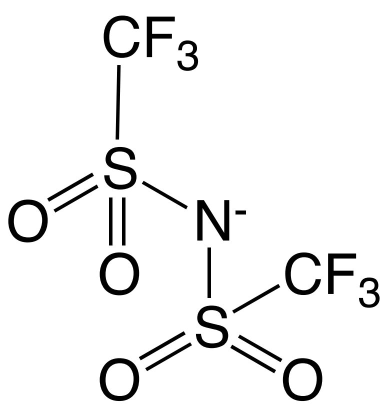
- Important considerations for biomass pretreatment = pH, water miscibility, (ease of IL separation and purification)

Fannin et *al J. Phys. Chem.*, 1984, 88, 2614–2621.

Anion Selection

water-immiscible → water-miscible

$[PF_6]^-$



$[BR_4]^-$

$[BF_4]^-$

[OTf]-

$[N(CN)_2]^-$

$[CH_3CO_2]^-$

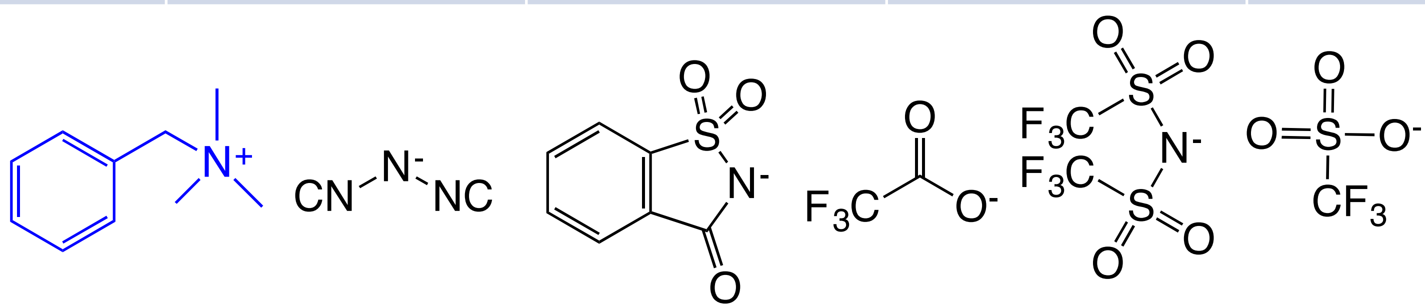
$[CF_3CO_2]^-$, $[NO_3]^-$

[Br]- , [Cl]- , [I]-

$[Al_2Cl_7]^-$, $[AlCl_4]^-$

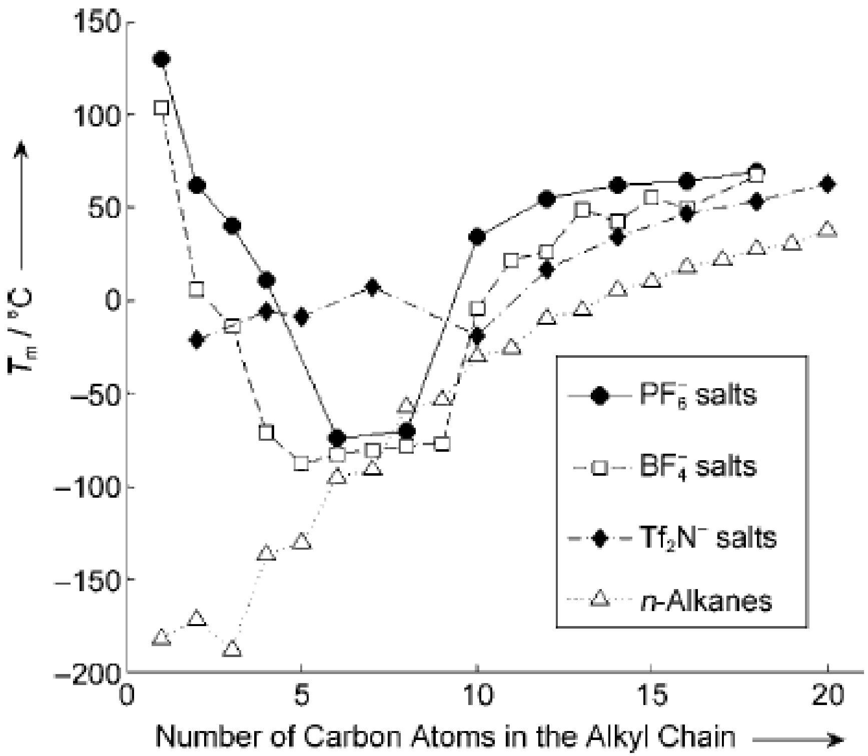
Effect of Anion Pairings on Physical Properties of BzTEA ILs

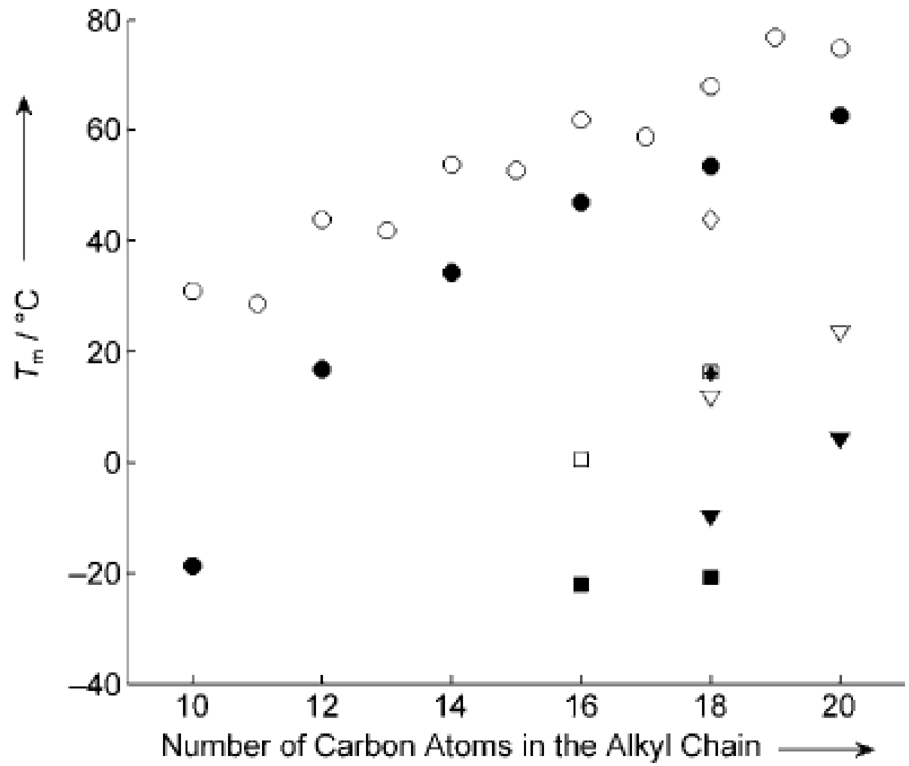
Anion	Melting Point (°C)	Thermal Decomposition Temp (°C)	Miscible	Immiscible
DCA	83	236	water	EtOAc, hexanes, ether
SAC	151	209	water	EtOAc, hexanes, ether
TFA	-49	199	water, EtOAc	hexanes, ether
Tf_2N	-52	>300	EtOAc	water, hexanes, ether,
TfO	109	>300	water	EtOAc, hexanes, ether



$BzTEA^+$ DCA^- SAC^- TFA^- Tf_2N^- TfO^-

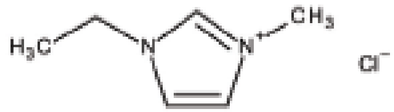
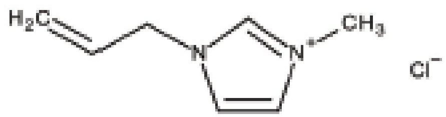
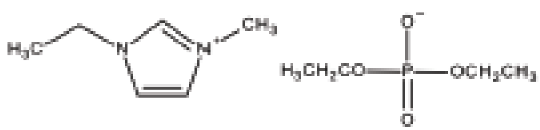
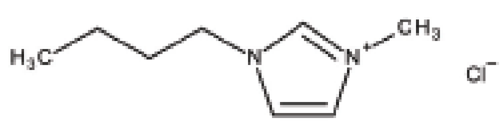
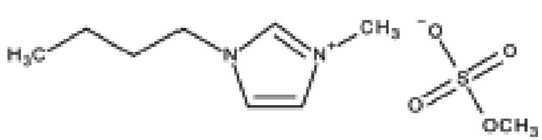
Bio-based ILs: Lipid-Like Cations
Chain Length and Degrees of Unsaturation Effect T_m





- ○ Saturated fatty acids
- ● Saturated alkyl MIM+ Tf_2N- ILs
- □ 9-cis fatty acids
- ■ 9-cis alkyl MIM+ Tf_2N- ILs
- ◇ 9-trans fatty acids
- ◆ 9-trans alkyl MIM+ Tf_2N- ILs

Murray et al *Angew Chem* **2010** 49 1-5

Name / abbreviation	Structure
1-ethyl-3-methylimidazolium chloride [EMIM][Cl]	
1-ethyl-3-methylimidazolium acetate [EMIM][CH_3COO]	
1-allyl-3-methylimidazolium chloride [AMIM][Cl]	
1-ethyl-3-methylimidazolium diethylphosphate [EMIM][DEP]	
1-butyl-3-methylimidazolium chloride [BMIM][Cl]	
1-butyl-3-methylimidazolium acetate [BMIM][CH_3COO]	
1-butyl-3-methylimidazolium methylsulfate [BMIM][$MeSO_4$]	

IONIC LIQUIDS for Cellulose Dissolution:

- Commonly imidazolium cations with 'coordinating' anions (H-bond acceptors, high β value)
- 5-25% cellulose dissolution obtained at 100°C
- Cellulose dissolution rate increased by MW heating
- Wood dissolves 2-10% at 130°C
- The presence of water in IL (even 1% w/w) decreases cellulose dissolution
- *Dissolution offers potential for chemistry (e.g. acetylation, cellulose/lignin depolymerization)*
- The science is not new…

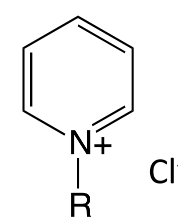
Patented Jan. 9, 1934 **1,943,176**

UNITED STATES PATENT OFFICE

1,943,176

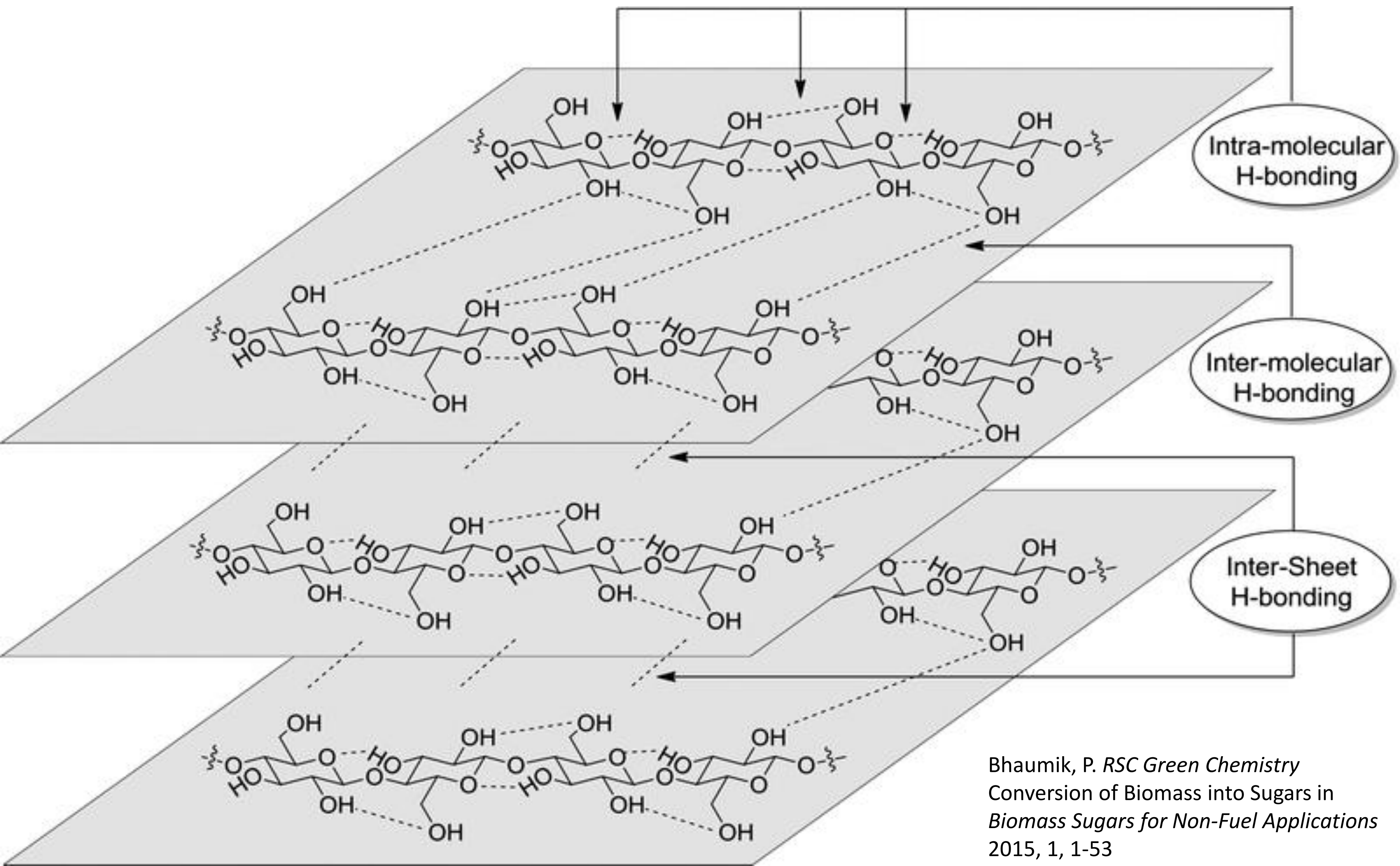
CELLULOSE SOLUTION

Charles Graenacher, Basel, Switzerland, assignor to Society of Chemical Industry in Basle, Basel, Switzerland



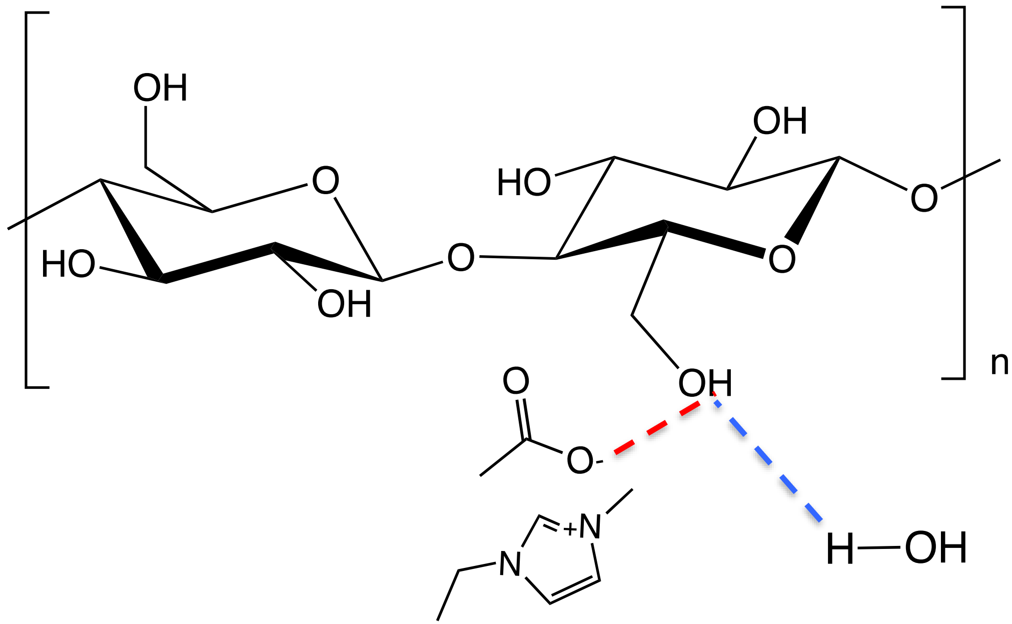
Swatlowski JACS Comm. 2002
Reddy S. African J Sci 2015
Plechkova and Seddon *Chem Soc Rev*, 2008

Cellulose Crosslinking *via* H-Bonding



Bhaumik, P. *RSC Green Chemistry*
Conversion of Biomass into Sugars in
Biomass Sugars for Non-Fuel Applications
2015, 1, 1-53

Anion – Cellulose Interaction & Anti-Solvent Effects



- Following Pretreatment, water (or EtOH) are used as 'anti-solvent' to precipitate cellulose
- Cellulose has lost its crystallinity -> therefore more "accessible" to enzyme hydrolysis
- Depending on IL, Lignin and Hemicellulose can remained dissolved in IL
- Kosmotropic anions (e.g. phosphate, carbonate, sulfate) are "water structuring" and form aqueous bi-phasic (and tri-phasic) systems -> allows for less water consumption

Reddy, 2015
Brandt et al. Green Chem 12(4):672–679
Hauru et al. Biomacromolecules 13(9): 2896–2905.
Parviainen A, et al. ChemSusChem 6(11):2161–2169.

A Typical IL Pretreatment Mass Balance

Forest Residues and Douglas Fir Woodchips (3 hr, 160°C, 10% solid loading)

Douglass Fir
un-milled
100 g dry weight

(1)

40.0 g glucan
14.3 g mannan
2.2 g xylan
3.2 g galactan
2.2 g arabinan
24.6 g lignin

Cellulose in

Pretreatment
10% Solids loading
Atmospheric pressure
(160°C, 3h)

Ionic liquid Pretreatment

(2)

Ionic Liquid

4.8 g glucose
9.6 g mannose
1.6 g xylose
1.5 g galactose
2.2 g arabinose
4.6 g lignin

70.0 g
Pretreated
Biomass
Solid
Precipitate

(3)

35.6 g glucan
5.6 g mannan
0.8 g xylan
1.8 g galactan
0.2 g arabinan
20.0 g lignin

Saccharification (50°C, 72 h)
10% solids loading
20 mg protein/ g glucan (Ctec 2)
4.5 mg protein/ g mannan (Htec 2)

Enzymatic Saccharification

(4)

35.0 g glucose
4.3 g mannose

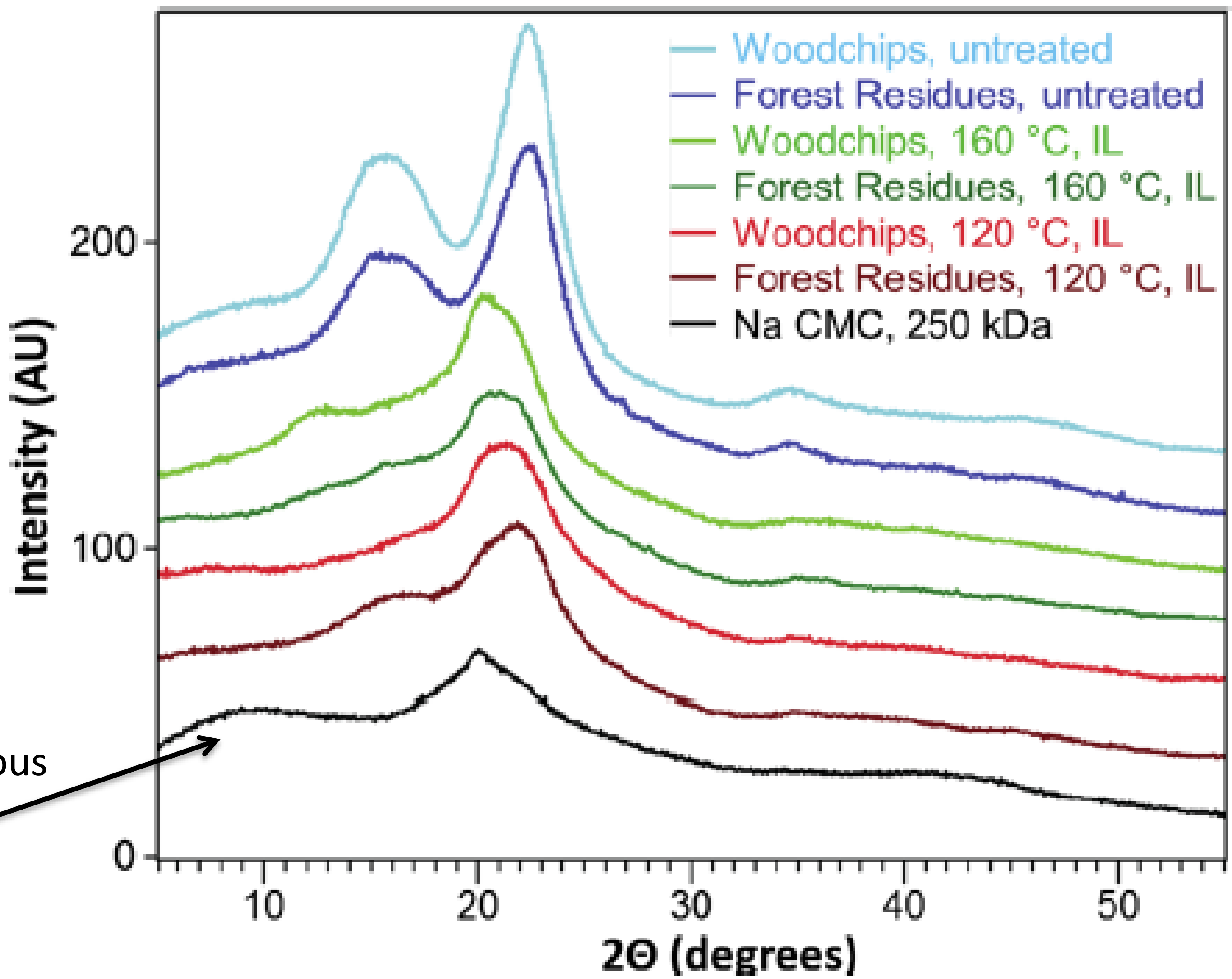
Glucose out
(~80% yield)

28.6 g
Residue

(5)

4.0 g glucan
1.7 g mannan
0.5 g xylan
1.1 g galactan
20.1 g lignin

XRD shows loss of cellulose crystallinity



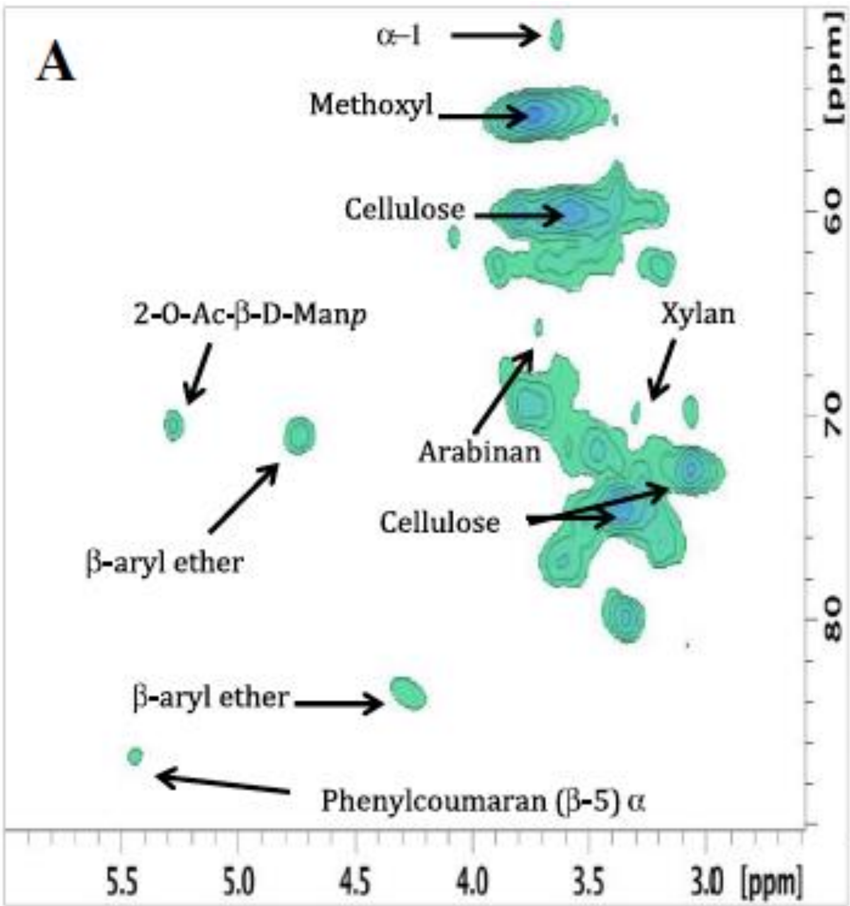
Amorphous control

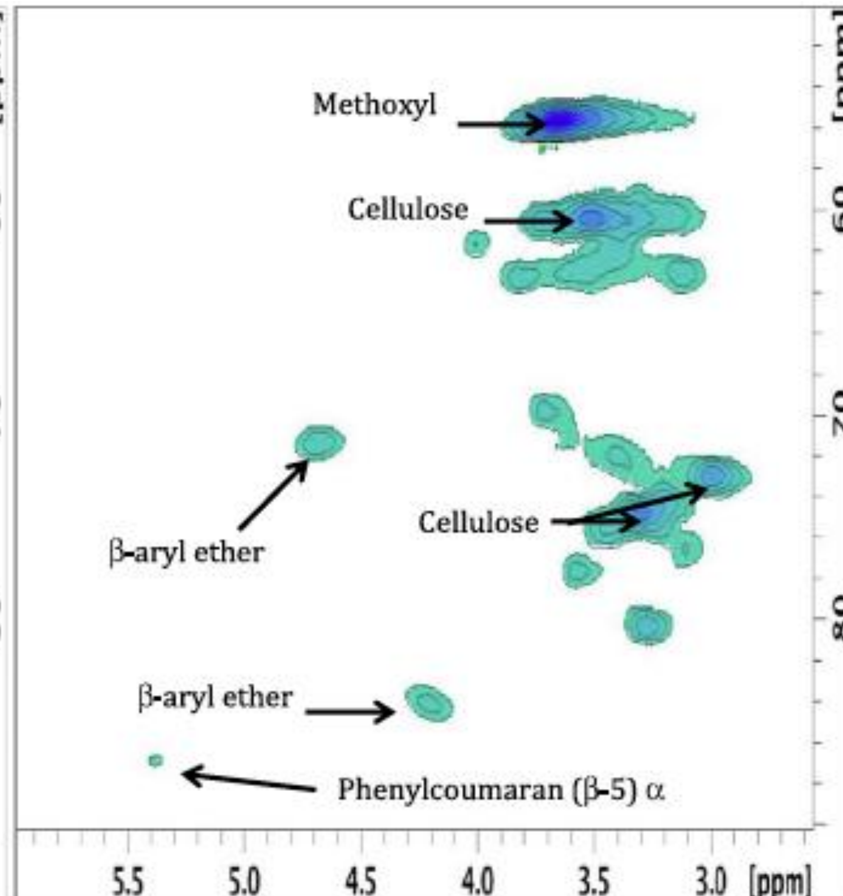
Figure 3 XRD patterns of samples used in this study and relative comparison with amorphous cellulose (Na CMC).

HSQC NMR shows bond-specific hemi-cellulose and lignin scission and stability

Woodchips Untreated

Woodchips + IL 160°C

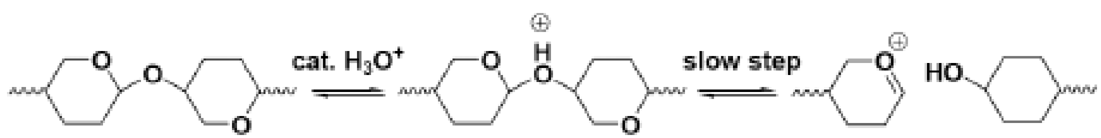


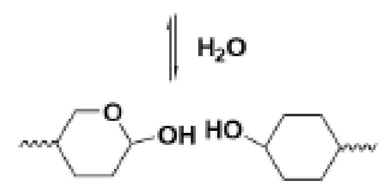


Socha. et al, *Biotech for Biofuels* (2013) 6, 61.

Cellulose Hydrolysis in IL

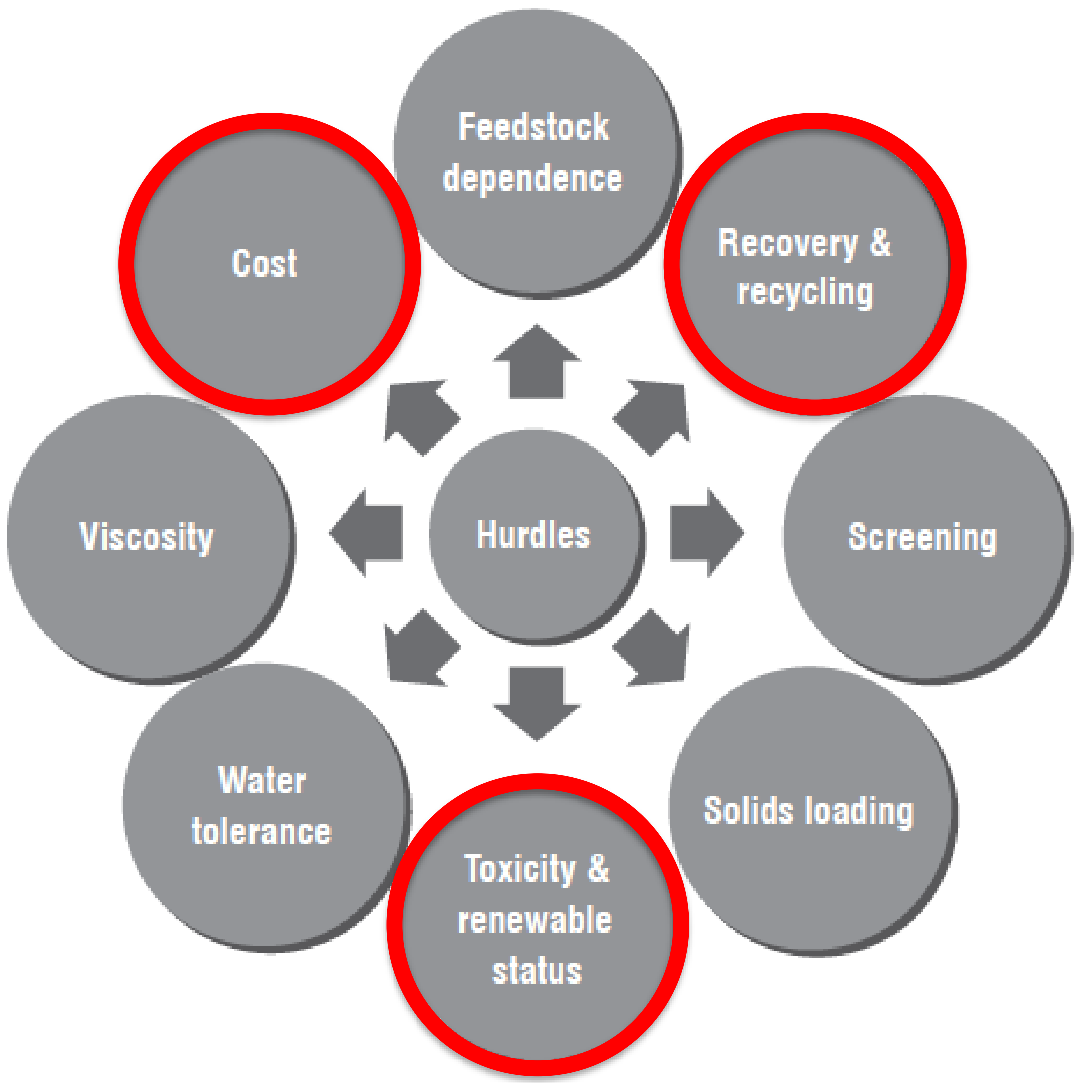
- H_2SO_4 = HCl = HNO_3 > maleic > H_3PO_4 in [BMIM] [Cl]
- Acid : Cellulose mass ratio as low as 0.1 : 1
- Reducing sugar yields ~ 66-81%
- 100^{o}C, 60 min
- Grasses and softwoods (pine)
- Monomeric sugar removal/separation from oligomers is challenging/costly



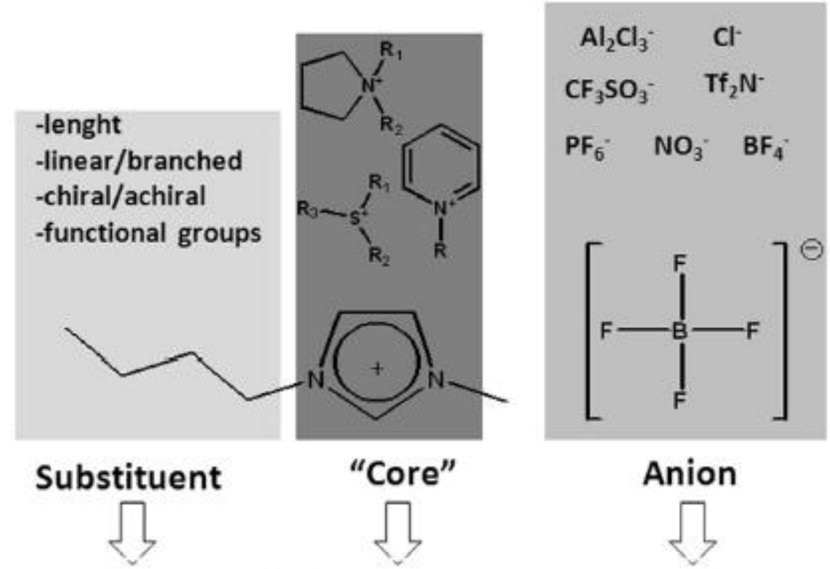


Problem is that strong acids will easily protonate strong bases of high β value ILs - so you can't have a "good cellulose dissolving IL" without it scavenging protons in your IL : acid mixture.

So why not use ILs all the time???



Ionic Liquid Toxicity & Biodegradibility



Guidelines for designing greener ionic liquids

	Substituent	"Core"	Anion
TOXICITY	***Recommended*** - introduction of short polar side-chains ***Not recommended*** - introduction of long hydrophobic alkyl chains	***Recommended*** - use of morpholinium and pyridinium ILs ***Not recommended*** -use of imidazolium ILs	***Recommended*** -use of anions like alkyl sulphates, alkyl sulphonatesalkyl benzene sulphonates, and salts of organic acids ***Not recommended*** - fluorine-containing ionic liquid anions
BIODEGRADIBILITY	***Recommended*** - introduction of long hydrophobic alkyl chains ***Not recommended*** - intorduction of polar functional groups (e.g. ether, hydroxyl or nitrile functions) into side-chain	***Recommended*** - use of pyridinium ILs ***Not recommended*** -use of imidazolium ILs	***Recommended*** -use of anions like alkyl sulphates, alkyl sulphonatesalkyl benzene sulphonates, and salts of organic acids ***Not recommended*** - fluorine-containing ionic liquid anions

Bubalo, et al. Ecotoxicology and Environ Safety 2014, 99, 1-12

Cholinium-Amino Acid based Ionic Liquids: Toxicity & Biodegradibility

[Ch][AA] + [BMIM] [BF_4] ILs
Toxicity vs. Acetylcholineesterase

Entry	ILs	$EC_{50}\pm SD$ / μM
1	[Ch][Gly]	3830±170
2	[Ch][Ala]	3330±100
3	[Ch][Val]	3060±120
4	[Ch][Leu]	3360±50
5	[Ch][Ile]	3570±70
6	[Ch][Ser]	3560±150
7	[Ch][Thr]	3450±150
8	[Ch][Met]	3130±140
9	[Ch][Asp]	3810±90
10	[Ch][Glu]	3720±70
11	[Ch][Asn]	3940±50
12	[Ch][Gln]	3510±160
13	[Ch][Lys]	3480±130
14	[Ch][His]	3630±40
15	[Ch][Arg]	3670±70
16	[Ch][Pro]	3370±160
17	[Ch][Phe]	2740±100
18	[Ch][Trp]	2450±20
19	[Ch][Cl]	3160±90
20	[Bmim][BF_4]	330±10

Biodegradibility (%)

ILs	7 days	14 days	21 days	28 days
[Ch][Gly]	58.3±2.3	72.3±0.1	75.0±1.2	82.6±1.1
[Ch][Ala]	61.9±0.8	66.8±0.1	77.6±1.2	80.0±0.4
[Ch][Val]	49.6±0.1	61.3±0.8	65.6±0.5	69.4±0.6
[Ch][Leu]	46.3±0.8	68.5±1.6	70.7±0.9	72.4±0.1
[Ch][Ile]	57.3±2.4	68.4±0.1	70.5±0.3	71.6±0.8
[Ch][Ser]	53.8±2.2	72.0±0.7	73.5±1.7	80.6±1.5
[Ch][Thr]	44.6±2.3	64.9±1.7	70.0±1.1	74.3±1.5
[Ch][Met]	54.3±0.3	63.7±0.1	64.7±0.3	66.1±0.9
[Ch][Asp]	68.9±1.2	79.5±0.6	86.5±0.5	87.1±0.6
[Ch][Glu]	70.0±0.1	71.3±1.1	83.1±1.4	86.3±0.2
[Ch][Asn]	53.9±0.5	71.8±1.1	85.7±0.7	87.1±1.2
[Ch][Gln]	58.5±2.3	80.5±0.7	83.8±1.5	86.6±1.4
[Ch][Lys]	54.4±3.7	62.4±0.4	65.9±1.0	67.7±1.0
[Ch][His]	46.5±3.5	60.1±1.2	63.4±0.0	65.3±1.3
[Ch][Arg]	59.6±2.3	62.3±0.9	65.3±0.1	67.6±0.2
[Ch][Pro]	58.0±0.9	66.4±0.1	68.5±0.9	71.3±0.1
[Ch][Phe]	44.0±0.2	68.8±0.2	71.0±1.1	70.8±0.1
[Ch][Trp]	55.1±1.1	60.2±0.6	62.7±1.1	65.9±0.2
[Ch][AcO]	46.7±0.4	63.6±0.8	66.5±0.5	68.1±1.9
Sodium benzoate	60.1±0.2	75.0±1.0	78.5±0.6	81.1±0.8

Xue-Dan Hou, PLOS one 2013, 8, 3, e59145

IL Toxicity and *in situ* Enzyme Hydrolysis

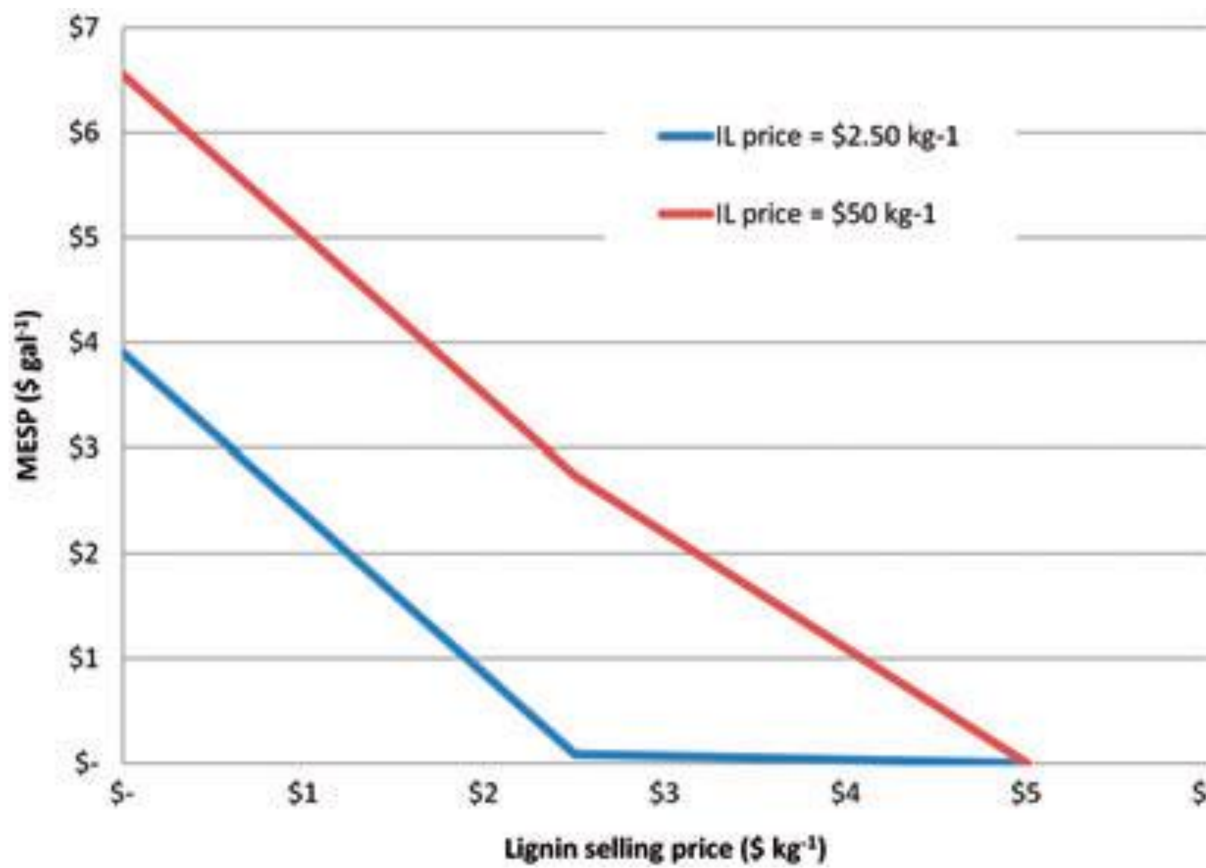
- IL Requirements = good cellulose dissolution, enzyme compatibility + low viscosity

  - e.g. chloride, dicyanamide, formate, acetate (viscous and strong H bond acceptors) = incompatible with enzymes

- IL : water (1:4) has shown compatibility using [EMIM][DEP]
- Additives such as tris-(2-hydroxyethyl)methylammonium methylsulfate have been shown to stabilize IL/enzyme mixtures to 120^{o}C

The Bottom Line for Biofuels: IL Pretreatment and Lignin Prices

- 99.6% IL Recycling
- 10% solid loading



Klein-Marcuschamer, *Biofuels, Bioprod. Bioref*. **2011**

Different Types of Lignin have Different Values

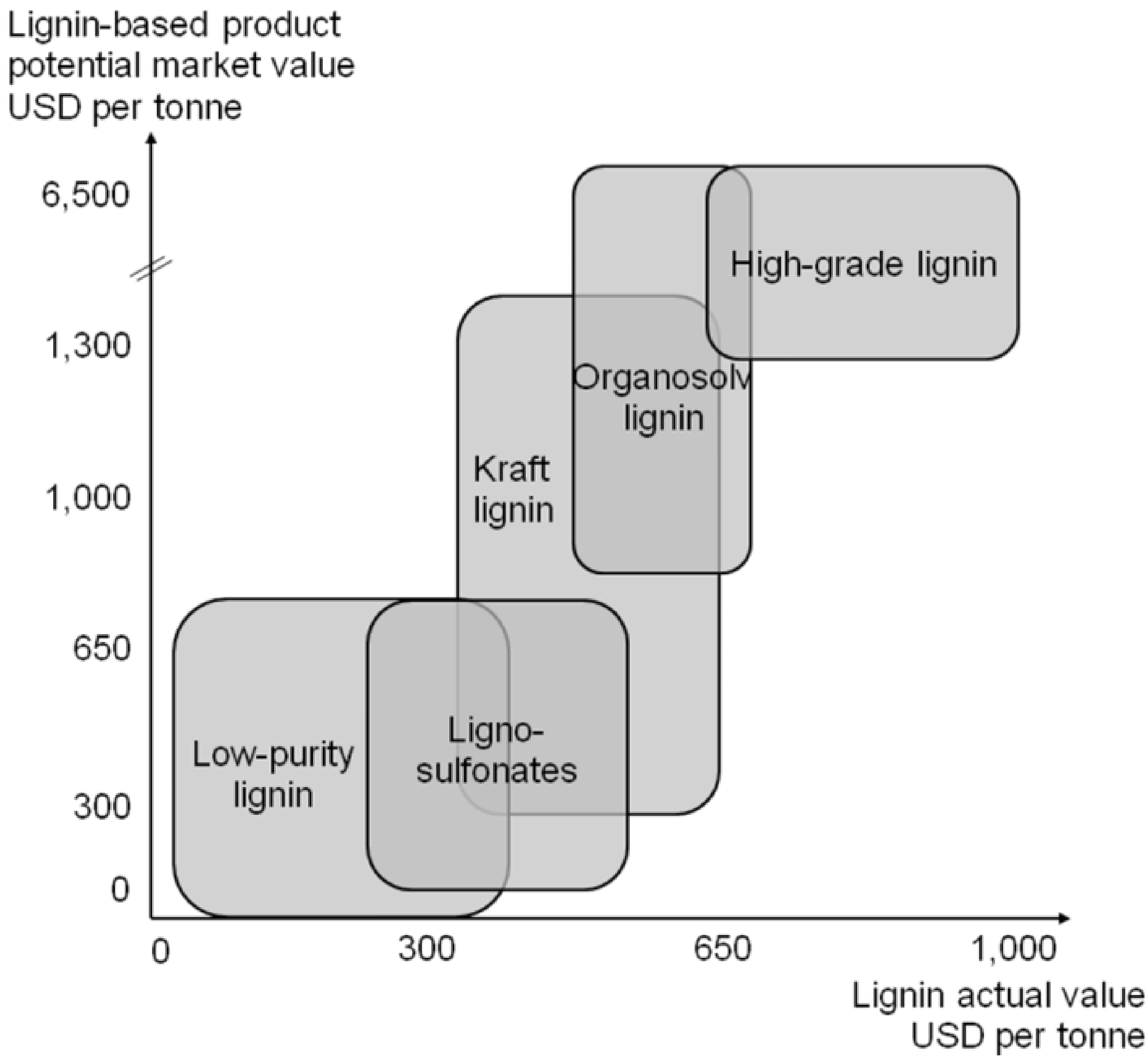
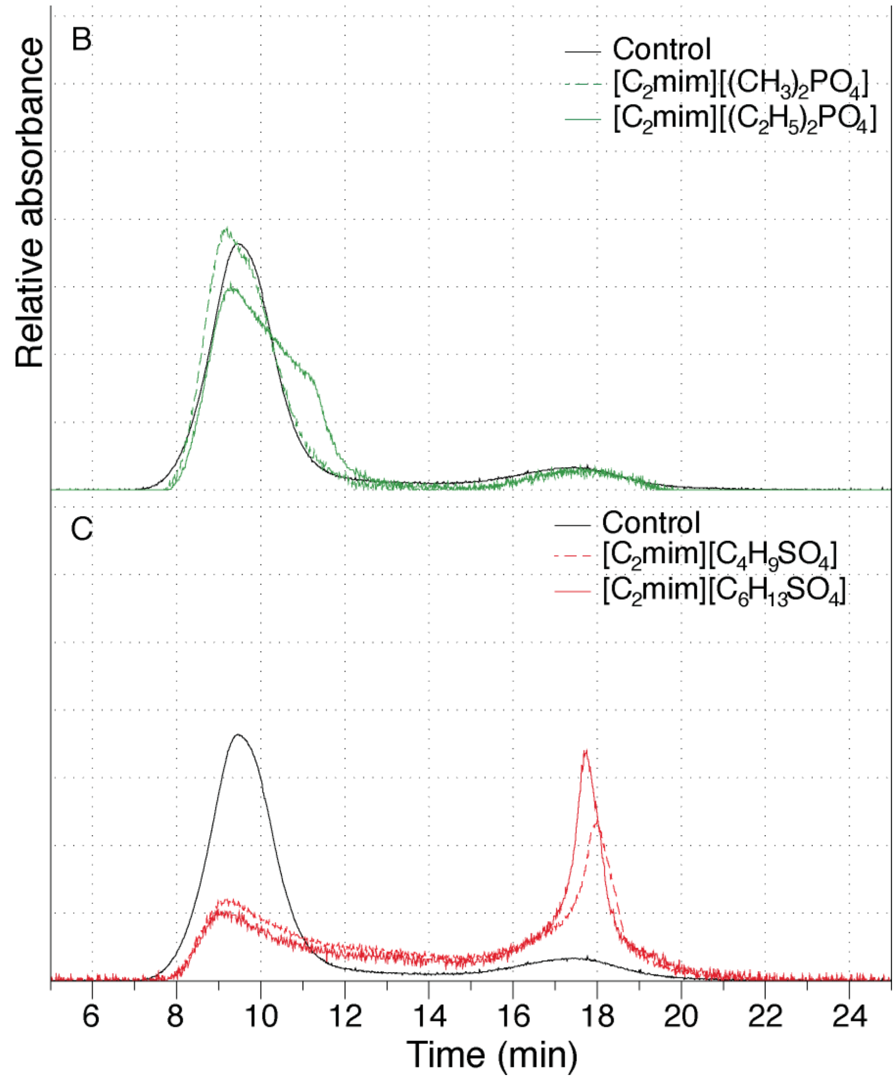


Figure: Gosselink, 2011

Effect of IL Anion on Lignin

- ILs were used to treat technical lignins (organosolv, alkali, alkali low-sulfonate)
- Size reduction of lignin measured by SEC
- Size reduction hierarchy: Sulfates > lactate > acetate > chlorides > phosphates
- Different anions cleave different lignin linkages, e.g. β-O-4
- Organosolv > ALS > alkali for cleavage efficiency
- Organosolv lignin became more conjugated after IL treatment -> indicating strong nucleophilic destruction mechanism
- Much like the Kraft pulping process, the S anion is a strong nucleophile in sulfate ILs
- Cation has little effect on lignin cleavage



It is possible to use IL mixtures to control degree of lignin depolymerization

George et al Green Chem 2011, 13, 2275

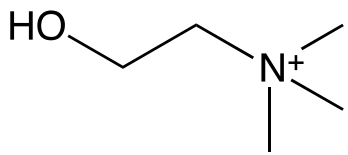
IL Recycling

- Bi-phasic systems are never completely biphasic
- IL recycling of 99.9% required for cost-effective IL use in a biorefinery
- Soluble Lignin other Solute Removal From ILs
  - 30kD polysulfone membrane filter
  - 1 MPa N_2, 20^{o}C, overnight
- Pervaporation with fluoropolymer membrane (Compact Membrane Systems)
- Wiped Film Evaporation (Molecular Distillation)

Sun et al Efficient dehydration and recovery of ionic liquid after lignocellulosic processing using pervaporation *Biotech for Biofuels* ***2017 Accepted***

Inspiration for Bio-Based ILs

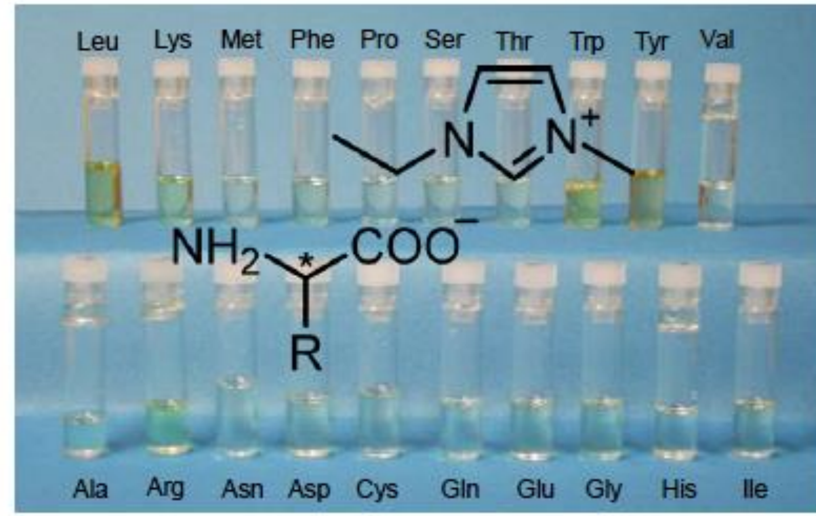
Cholinium – Based ILs



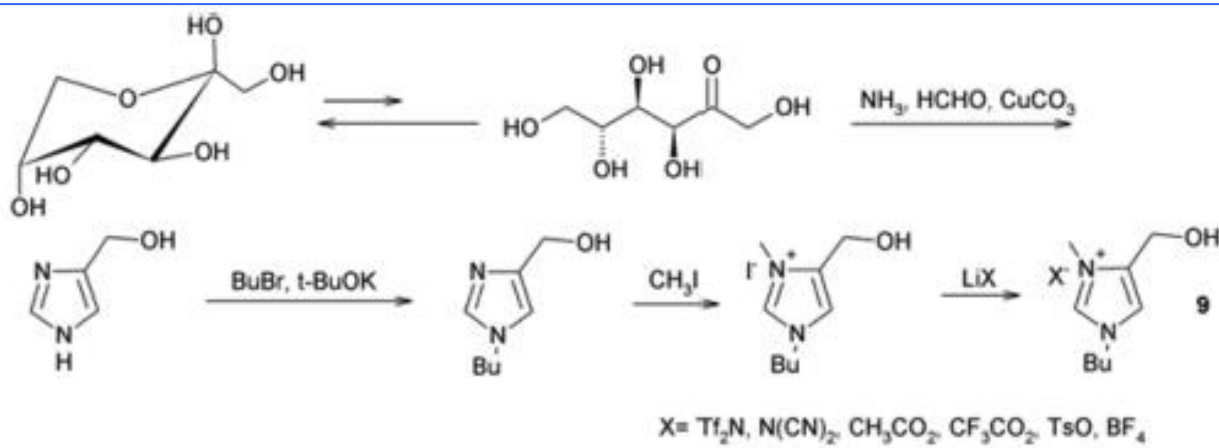
63 ILs

Rodgers, R. *Chemistry* 2007 13, 24, 6817

Amino acid ionic liquids



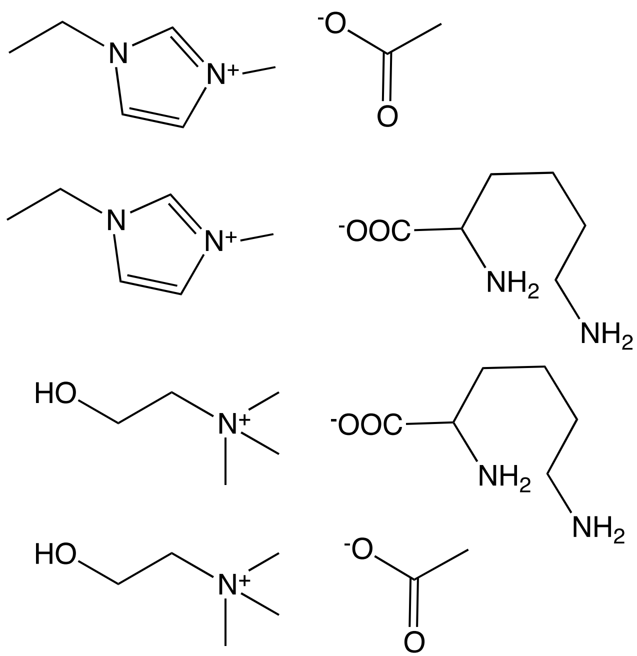
K. Fukumoto, M. Yoshizawa, H. Ohno
J. Am. Chem. Soc., **2005**, *127*, 2398-2399

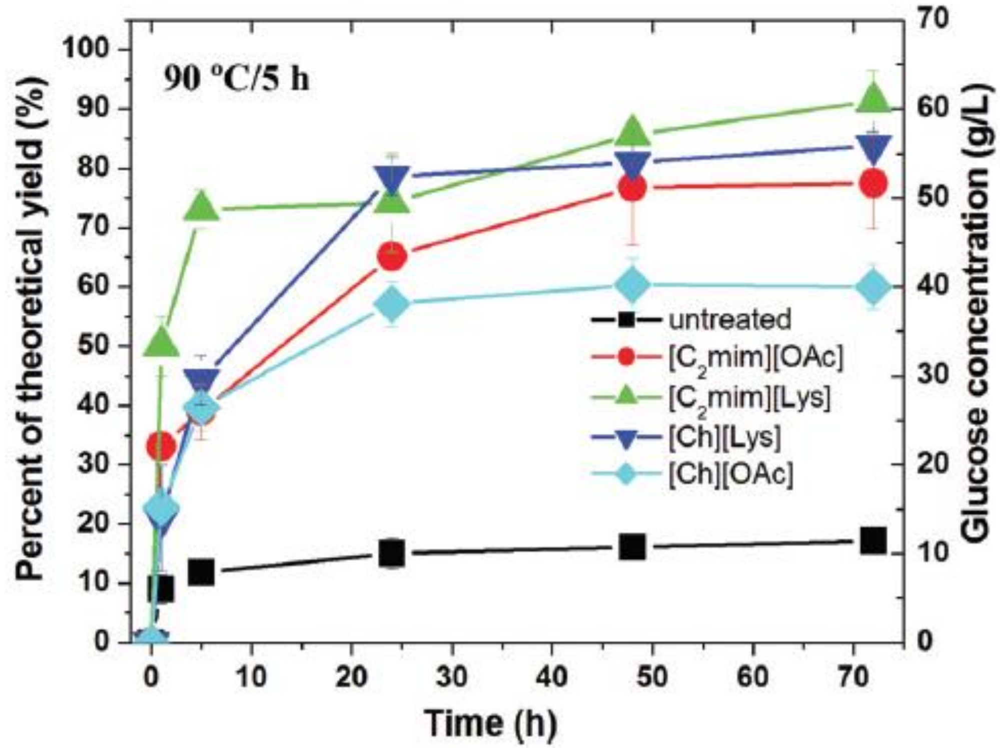


A: Fructose-based IL synthesis.

Reviewed: Hulsbosch et al *ACS Sust. Chem Eng* **2016**, 4, 2917-2931

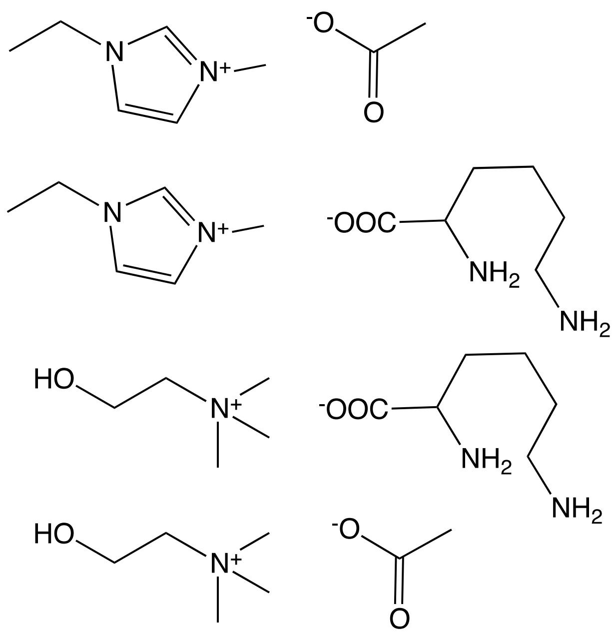
Low Temperature Pretreatment Comparison (EMIM vs. Cholinium)

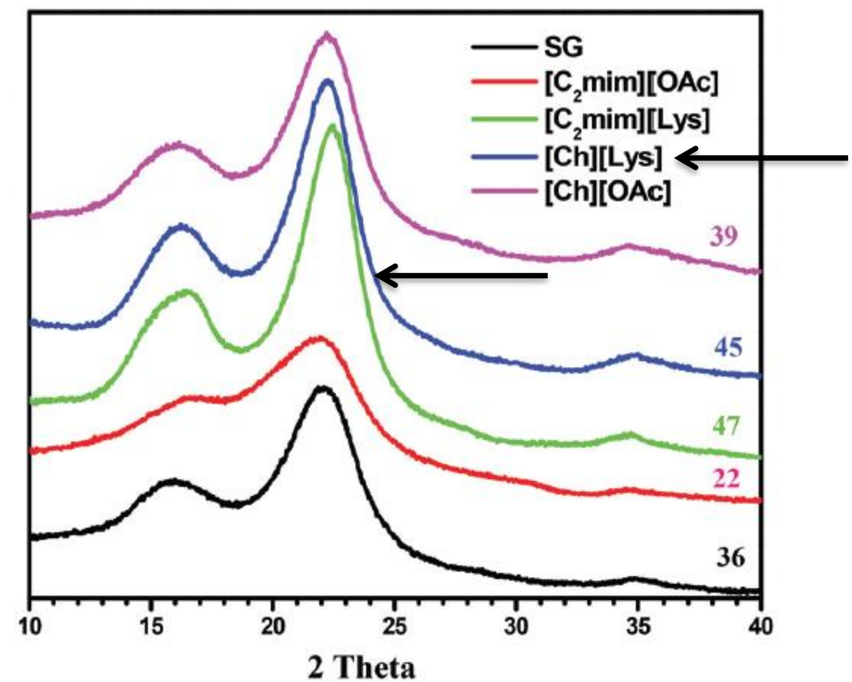




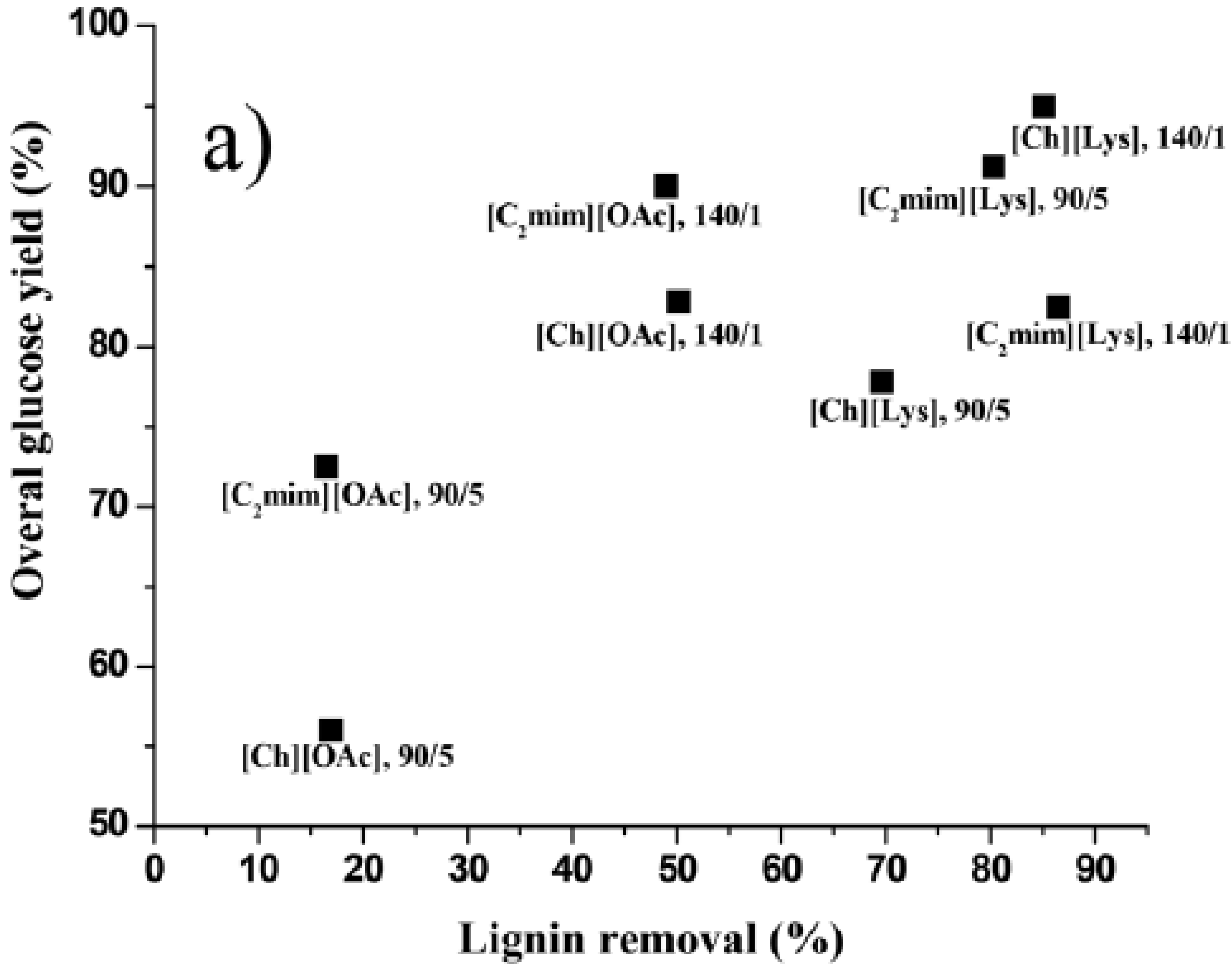
High β values, but no loss of cellulose crystallinity…

ILs	π		α		β	
	30 °C	90 °C	30 °C	90 °C	30 °C	90 °C
$[C_2mim][OAc]$	1.04	0.91	0.47	0.51	1.14	1.23
$[C_2mim][Lys]$	0.64	0.60	N/D[a]	N/D	1.28	1.29
[Ch][Lys]	0.67	0.64	N/D[a]	N/D[a]	1.30	1.31 ←
[Ch][OAc]	N/A[b]	0.76	N/A[b]	0.68	N/A	1.22





Lignin Removal as a Driver for Pretreatment Efficacy



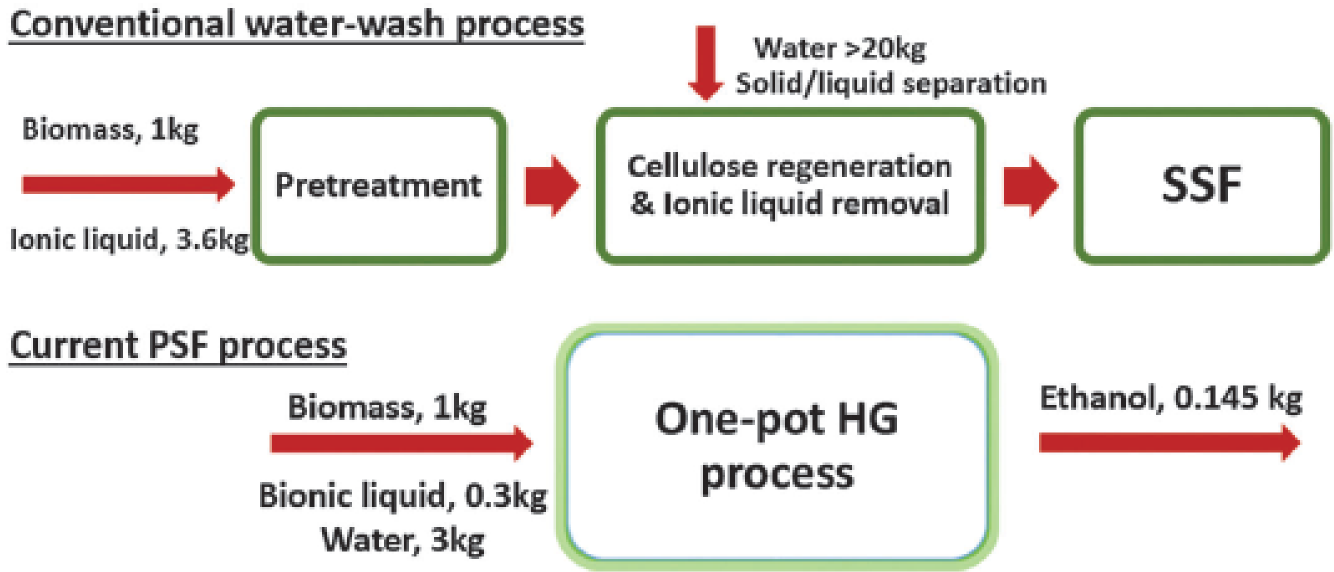
Lysinate Anion is a very good "Lignin Remover" when paired with Cholinium or EMIM

Table 1 Compositional analysis after IL pretreatment

Pretreatment			Composition of pretreated biomass (%)		
ILs	*T*/*t*	Solid recovery (%)	Glucan	Xylan	Lignin
—			37.5 ± 1.5	21.9 ± 2.0	18.9 ± 1.3
[C_2mim][OAc]	90/5	92.3 ± 5.7	38.0 ± 3.2	23.5 ± 3.3	17.1 ± 1.2
[C_2mim][Lys]	90/5	58.2 ± 0.2	65.2 ± 1.3	18.9 ± 0.6	6.4 ± 0.4
[Ch][Lys]	90/5	70.7 ± 4.9	49.2 ± 0.9	21.7 ± 0.2	8.2 ± 0.6
[Ch][OAc]	90/5	87.2 ± 4.4	40.2 ± 2.4	24.7 ± 2.8	18.0 ± 1.3
[C_2mim][OAc]	140/1	70.5 ± 0.3	50.0 ± 1.0	21.2 ± 1.1	13.7 ± 0.2
[C_2mim][Lys]	140/1	50.8 ± 0.3	63.2 ± 0.1	17.2 ± 1.0	5.0 ± 0.9
[Ch][Lys]	140/1	56.6 ± 0.7	65.6 ± 3.6	23.9 ± 0.1	5.0 ± 0.1
[Ch][OAc]	140/1	66.7 ± 0.3	49.8 ± 1.8	20.8 ± 2.8	14.1 ± 1.0

Sun, Socha, et al. *Green Chem* (2014) 16, 2546

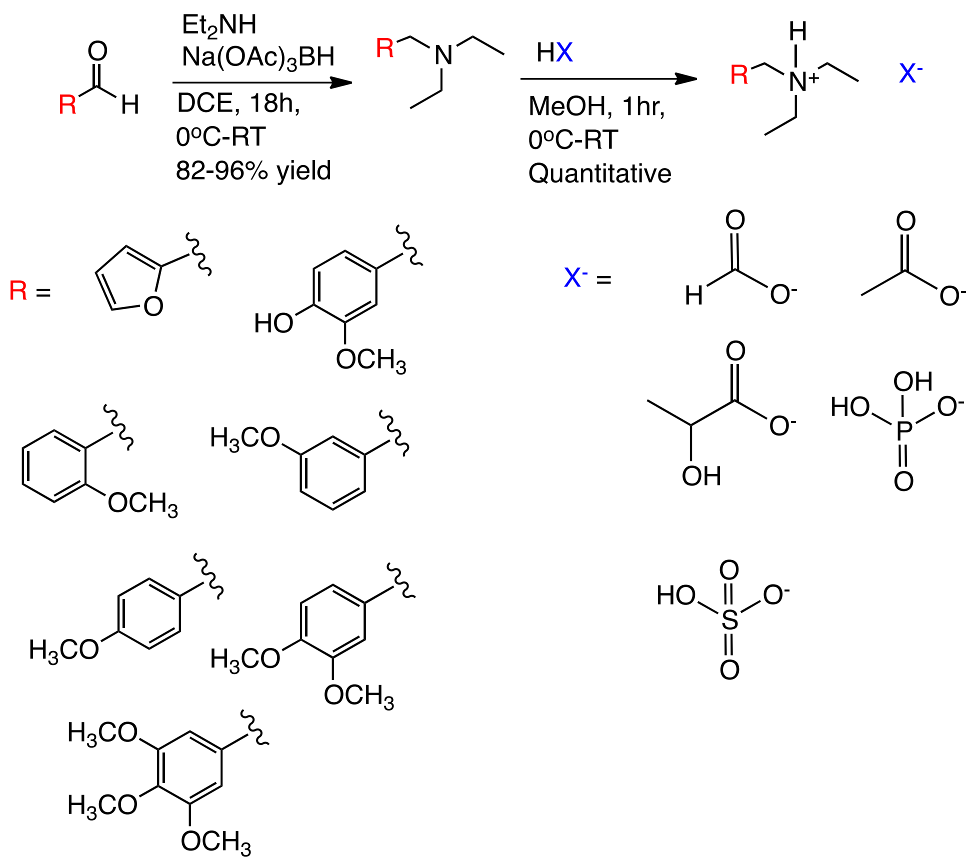
The "One Pot + High Gravity" Process

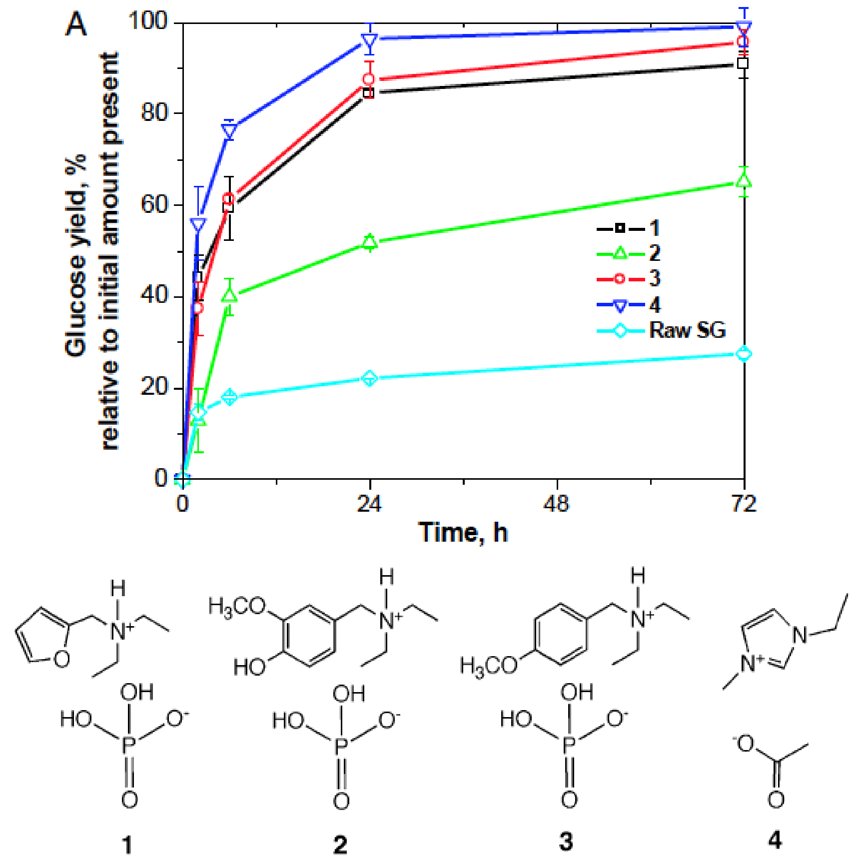


- [Ch][Lys] and [Ch][Asp] used as 10% aq solutions
- Pretreatment, Saccharification and Fermentation in One Pot
- IL is not removed or recycled (because it's inexpensive!)
- 30% biomass loading (corn stover)
- 75% yield of ethanol (on a glucose basis)
- 85% reduction in water input/wastewater
- 40% reduction in cost

Xu et al *Energy & Environ Sci* **2016**

Pretreatment of Switchgrass with Vanillin and Furfural Derived ILs





10% water + 90% ILs
10% solids loading, 160ºC, 3 hr
15mg CTec2 enzyme per gram of raw biomass 1.5mg HTec2 enzyme per gram of raw biomass.

Socha et al *Proc Nat Acad Sci* **2014** 11, 35

Homework Questions

1) What are some <u>chemical considerations</u> when selecting an ionic liquid for pretreatment? How would you design a test?
2) What are key <u>engineering considerations</u> when selecting an ionic liquid for pretreatment?
3) What are key <u>cost considerations</u> when selecting an ionic liquid for pretreatment?