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Directed discovery of greener cosolvents: new cosolvents for use in ionic liquid based organic electrolyte solutions for cellulose dissolution

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KEYWORDS

1-Ethyl-3-methylimidazolium acetate, ionic liquid, cellulose, dissolution, organic electrolyte solutions (OESs), reference interaction site model (RISM), γ -butyrolactone, γ -valerolactone

ABSTRACT

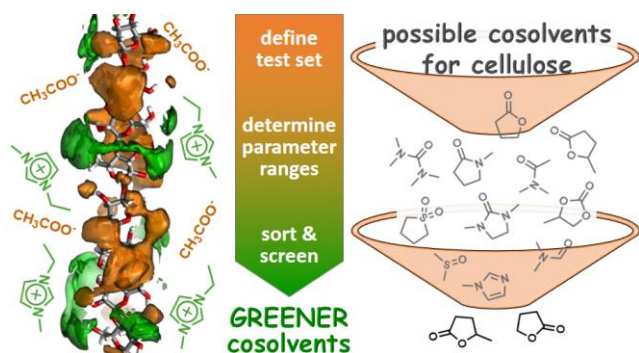
Cellulose is an abundant, cheap, renewable, yet recalcitrant, material, which, if dissolved, may be formed into a wide range of materials, composites and mixtures. Much attention has recently been focused on the use of mixtures of ionic liquids and some solvents (so-called organic electrolyte solutions, OESs) as efficient cellulose dissolution solvents, but many of the cosolvents used lack green credentials – a perennial problem where dipolar aprotic solvents are the solvents of choice. We present a rational approach, based on definition of ranges of solvent parameters gathered together in recently published databases, to find ‘greener’ cosolvents for OES formation. Thus, γ -butyrolactone is identified as a suitable OES former for dissolution of microcrystalline cellulose and biobased γ -valerolactone as a marginally less efficient, but significantly safer, alternative. Comparison of cosolvent efficiency reveals that previous use of measures of mass, or concentration, of cellulose dissolved may have masked the similarities between 1-methylimidazole, dimethylsulfoxide (DMSO), *N,N*-dimethylformamide, *N,N'*-dimethylimidazolidinone, *N,N*-dimethylacetamide, *N*-methylpyrrolidinone and sulfolane (seldom considered), while comparison on a molar basis reveals that the molar volume of the solvent is an important factor. Reference-interaction site model (RISM) calculations for the DMSO/1-ethyl-3-methylimidazolium acetate OES suggest competition between DMSO and the acetate anion and preferential solvation of cellulose by the ionic liquid.

TOC ENTRY

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Solvent selection, using parameters ranges matched to experimentally determined “good” cosolvents, allows identification of renewably derived, non-hazardous γ -valerolactone as a viable alternative to dipolar aprotic solvents in ionic liquid mediated dissolution of cellulose.



INTRODUCTION

Cellulose is an abundant and renewable biopolymer produced in large quantities in the plant kingdom. Estimates vary, but of the 56×10^9 tonnes of biomass produced annually, approximately 40-60 % is cellulose.¹ It is a critical structural biopolymer, providing rigidity to plants cell walls and, while highly hydrophilic, it is also very difficult to solubilize, and thus to reform into new structures, forms or composites. As it is not a thermoplastic polymer, processing of cellulose often relies on functionalization to yield a soluble polymer (which means sacrificing its exquisite structural characteristics resulting from hydrogen bonding) or dissolution, either using solvent mixtures, or via reversible reaction, e.g. the xanthate process for producing viscose.² Alternative direct dissolution methods do exist, such as the Lenzing process, using *N*-methylmorpholine-*N*-oxide hydrate (NMMO) to dissolve cellulose, but, for various reasons, including mitigation of use of hazardous materials (e.g. CS₂ in the xanthate process), excessive cost, difficulties in recovery and recycling of solvent systems, and ease of application, alternatives are still sought.

A seminal paper by Swatloski and Rogers, describing the dissolution of cellulose in ionic liquids (ILs) followed by anti-solvent phase inversion to yield regenerated cellulose in a different form,³ precipitated an avalanche of reports of both similar solvent systems and production of cellulose based materials using this method of processing.^{4,5,6,7,8,9,10} A recent review provides an excellent overview of regenerated cellulose materials, including from ILs, or containing IL mixtures.¹¹ Positive aspects of ionic liquid based dissolution/regeneration of cellulose include the lack of vapor pressure of the ionic liquid (mitigating fugative emissions, such as those always attendant on, for example, the xanthate process, or dissolution in NMMO) and the apparent ease of recycling of the solvent salt by recovery of the anti-solvent using distillation. The latter is

facilitated by the vast difference in vapor pressure between anti-solvents, such as lower alcohols or water, and the ionic liquid. It should be noted that such separation is seldom as facile as reported, can be costly with respect to energy use and that final removal of traces of water can be challenging,¹² although rigorously dried ILs are not required for cellulose dissolution¹³ and, recently, ILs containing 40 wt % water (effectively aqueous solutions of ILs) have even been reported for cellulose dissolution.¹⁴

A range of ILs has been demonstrated to dissolve cellulose and combinations of 1,3-dialkylimidazolium cations with chloride, acetate, or alkylphosphate ester anions have proven particularly effective – data pertaining to solubility of cellulose in these, and a plethora of other ILs, are comprehensively summarized in a review by Wang, Gurau and Rogers.¹⁵ In 2011 Rinaldi reported the use of combinations of ILs and dipolar aprotic solvents, mixtures which he termed “organic electrolyte solutions (OESs)” (these are analogues of well-known cellulose solvent systems, such as LiCl/dimethylacetamide), to dissolve cellulose¹⁶ and this methodology has also been enthusiastically adopted by many, as the use of a cosolvent may mitigate the cost of the IL and facilitates processing by reduction of viscosity of cellulose solutions. The utility of “OESs” was presaged by an earlier report of the use of an amino acid derived IL, *N,N*-diethyl-*N*-(2-methoxyethyl)-*N*-methylammonium alanine, in combination with DMSO to dissolve up to 23 wt % of cellulose.¹⁷

While many computational^{18,19,20,21,22} and experimental²³ studies dedicated to understanding the source of the enhanced dissolution^{24,25,26} (at least with respect to *rate* of dissolution, e.g. Rinaldi’s “instantaneous dissolution”¹⁶), or tailoring OESs²⁷ have appeared, there has not, to our knowledge, been a systematic study geared towards maximising the efficiency of dissolution while minimising the quantity of IL required. As many of the objections to the use of ILs at

scale are based on cost, minimising the quantity of IL required could be key to the production at scale of any of the interesting materials and composites reported.

Although there is no doubt that the discovery of OES solvent systems for cellulose dissolution has vastly expanded the range of solvents useful in cellulose processing, the dipolar aprotic solvent components of OESs present some health and safety challenges. For example, dimethylformamide carries the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) phrase H360 “*may damage fertility or the unborn child*” and is included in the candidate list of Substances of Very High Concern under REACH regulation (Article 57c), and dimethylsulfoxide (the most effective cosolvent in Rinaldi’s list), which may be an attractive replacement on toxicological grounds, has a propensity to undergo highly energetic decomposition when subjected to strong bases, electrophiles and heat.²⁸

Hydrogen bond basicity has long been held to be an important factor in cellulose dissolution by ILs²⁹ and Rinaldi considered the effect of addition of IL to dipolar aprotics on Kamlett-Taft solvent parameters and suggested that the molecular solvent (and the IL) should have high hydrogen-bond basicity (β) and no hydrogen-bond acidity (α).¹⁶ While this is a useful guide, many potential solvents that fulfill these requirements are not good cosolvents for cellulose and it is often the absolute amount of cellulose that can be dissolved rather than “instantaneous dissolution” that is the required quantity. Herein, we report the relative efficacy of a range of cosolvents for the dissolution of microcrystalline cellulose using the ionic liquid 1-ethyl-3-methyl imidazolium acetate ([EMIm][OAc]) (one of the most widely used ILs for cellulose dissolution) to form OESs and use comparisons of solvent parameters to reveal new candidates for OES formation. The focus is on using a rational approach to selecting the greenest possible cosolvent for preparation of cellulose solutions.

EXPERIMENTAL

Materials

1-Ethyl-3-methylimidazolium acetate (>95 % purity, Sigma Aldrich) and microcrystalline cellulose (Sigma Aldrich, 20 μm particle size) were dried at 80 $^{\circ}\text{C}$ under reduced pressure to constant mass. Dipolar aprotic solvents (all >99 % purity, Sigma Aldrich) were used as received, bar sulfolane, which was dried over activated 3 \AA molecular sieves. The water content of the ionic liquid and solvents was measured by Karl Fisher titration and found to be: [EMIm][OAc] 1.1 %; 1-methylimidazole 0.2 %; dimethylsulfoxide 1.1 %; *N,N*-dimethylformamide 0.3 %; *N,N'*-dimethylimidazolidinone 0.7 %; *N,N*-dimethylacetamide 0.4 %; sulfolane 0.1 %; propylene carbonate 0.1 %; γ -valerolactone 0.8 %; *N,N,N',N'*-tetramethylurea 0.3 %; *N*-methylpyrrolidinone 0.8 %; γ -butyrolactone 0.3 %.

Solubility tests

Solubility tests were conducted at 70 $^{\circ}\text{C}$. As the cellulose solutions formed are viscous and not amenable to filtration, solubility was determined by addition of small aliquots of dried microcrystalline cellulose (MC) to mixtures of [EMIm][OAc]/cosolvent of appropriate composition. The maximum amount of MC that dissolved, *a*, and minimum amount that did not dissolve, *b*, were recorded giving an under- and over-estimate for the maximum amount of MC dissolvable, *v*. Repeated determinations, using smaller incremental added weights of MC then led to a narrow range between “soluble” and “insoluble”. (As MC tended to form aggregates when added directly to OESs, a slightly modified procedure was followed once approximate solubility values were known at any given OES composition: to a weighed quantity of dried MC was added a measured quantity of the selected cosolvent; after stirring for 1 min to wet and disperse the MC powder, calculated quantities of IL were added and then small, weighed aliquots

added until no further MC would dissolve.) Apparently “insoluble” samples were maintained for a minimum of 16 h at 70 °C to confirm the lack of further dissolution.

Each pair of points (a_i, b_i) was given a weight, w_i :

$$w_i = \sqrt{\frac{1}{v_i^2}} \quad \text{Eq. 1}$$

based on, v_i , the errors on a_i and b_i , as given by: $v_i = (b_i - a_i)/2$, such that the uncertainties on points a_i and b_i are: $a_i + v_i$ and $b_i - v_i$ respectively. Other sources of error are much smaller in comparison.

Data analysis and fitting

Weighted fits were computed using NonLinearModelFit in Mathematica, with weights w_i as given in Equation 1, and the equation

$$c = 1 + \text{Max}[c] - e^{(m \chi_{IL} + d)^2} \quad \text{Eq. 2}$$

which arises from modelling dissolution as a 1-dimensional process, where $\sqrt{\ln[\Delta c]}$ varies linearly with χ_{IL} ($\Delta c = 1 + \text{Max}[c] - c$), c is the weight percent of cellulose, and $\text{Max}[c]$ is the maximum measured weight percent of dissolved MC. For comparison, the data were normalized using the maximum value of c from the fit. The maximum value of a fit over a range was computed using the Mathematica ‘Maximize’ function within the range of measured data (e.g. $\text{Min}[\chi_{IL}] < \chi_{IL} \leq 1$). Weighted averages, \bar{x} , of a set of n points $\{x_i\}$ were computed from:

$$\bar{x} = \frac{\sum_{i=1}^n w_i x_i}{\sum_{i=1}^n w_i} \quad \text{Eq. 3}$$

using the WeightedData function in Mathematica. The ‘efficiency measure’ was calculated as the mass of MC dissolved over the mass of ionic liquid, divided by the maximum mass of MC dissolvable.

Cosolvent search

To search for cosolvents expected to yield OESs capable of dissolving MC on the basis of similarities in key solvent parameters, Excel spreadsheets of solvent parameters from Catalán³⁰ and Laurence *et al.*³¹ were loaded into Mathematica. Minimum and maximum values for each solvent parameter were input to define a search range, which could then be padded by a percentage of the selected range. A simple search over the datasets provided a count of the number of times each solvent (in the superset) appeared within the search range and solvent list was sorted according the number of ‘hits’. As not all the solvent entries were complete, the percentage data matched was also determined. Annotated sample Mathematica code is given in the Supporting Information. The solvent parameters were not normalized.

Reference Interaction Site Model (RISM) - 3D-RISM theory

The 3D-RISM theory is a fully atomistic molecular theory of solvation based on first principle statistical mechanics that provides a computational framework to obtain solvation properties for a variety of molecular systems in solution. Starting from the molecular coordinates and interaction potentials, the ensemble-averaged solvation structure and thermodynamics can be effectively computed within the 3D-RISM approach. Details of the theory and the computational methods involved are provided elsewhere.^{32,33,34}

RISM - Computational modeling and system setup

The radial pair distribution functions for a mixture of molar fraction composition of 0.95 DMSO and 0.05 IL were obtained by the dielectrically consistent RISM theory (DRISM) complemented by the one-dimensional Kovalenko-Hirata (KH) closure.^{32,33,35} The pair distribution functions were later used as input for the 3D-RISM calculations. The DRISM equations were iteratively solved in a radial grid of 0.1 Å resolution containing $2^{13} = 8192$ points, considering the temperature of 298 K, the DMSO density of 1.091 g.cm⁻³ and dielectric

constant of 46.4.³⁶ To solve the DRISM equations for the mixture, calculations were performed for increasing values of IL concentration, from 0 to 0.05. Solvent distribution around a glucan chain of DP=12 previously equilibrated in DMSO was obtained using the 3D-RISM theory with the 3D Kovalenko-Hirata closure.^{32,33,34} The 3D-RISM equations were iteratively solved in grid of size 128 Å × 128 Å × 128 Å containing 256 × 256 × 256 points. For both DRISM and 3D-RISM calculations, the modified direct inversion in the iterative subspace (MDIIS) solver³² was employed to reach a relative mean square accuracy of 10⁻¹⁰ for DRISM and 10⁻⁴ for 3D-RISM. Partial atomic charges and Lennard-Jones parameters for acetate and cellulose were taken from the CHARMM force field.^{37,38} The parameters for DMSO and EMIM were taken from Strader and Feller³⁹ and Kelkar *et al.*,⁴⁰ respectively. The solvent distribution was represented in terms of the specific solvation free energy density (SFED) function. The SFED indicates spatial regions around the solute that concentrate solute-solvent stabilizing interactions.^{34,41,42} The specific SFED, defined as SFED per unit of solvent molecules, provides the intrinsic solvation capacity of each component of the solvent.

The glucan chain used in the 3D-RISM calculations was equilibrated in DMSO using molecular dynamics (MD) simulations. Using Packmol,⁴³ the glucan chain was immersed in a cubic box of side 90 Å containing 6000 DMSO molecules. The MD simulation was performed employing periodic boundary conditions. Electrostatics were evaluated with particle mesh Ewald⁴⁴ and the short-range interactions were truncated at 12 Å. A timestep of 2 fs was used to solve the equations of motion. The bonds involving hydrogen atoms were constrained at their equilibrium lengths. The simulation was propagated for 2 ns at 300 K and 1 atm using NAMD.⁴⁵ Three different glucan conformations were randomly taken from the simulation for post-processing with 3D-RISM.

RESULTS AND DISCUSSION

The goals of this study were twofold: (i) to compare the relative efficiency of IL use in cellulose dissolution in OESs comprised of different solvents with [EMIm][OAc] with a view to mitigating use of costly IL and (ii) to use a rational approach to discover new greener solvents for the formation of OESs to be used in cellulose dissolution.

Microcrystalline cellulose (MC) was selected as the test substrate as its relatively low average degree of polymerization of 150-300⁴⁶ provides solutions of reasonable viscosity. The elevated temperature used was selected as readily accessible using a wide range of cosolvents of variable boiling points, while remaining below the temperatures at which cellulose degradation has been shown to be significant.⁴⁷ (While it is acknowledged that an increase in temperature does not thermodynamically favor the dissolution of cellulose,⁴⁸ it does enhance the rate of dissolution.) The structures of all solvents tested as OES components with [EMIm][OAc] are presented in Chart 1 and included: 1-methylimidazole (1-MI); dimethylsulfoxide (DMSO); *N,N*-dimethylformamide (DMF); *N,N'*-dimethylimidazolidin-2-one (DMI); *N,N*-dimethylacetamide (DMAc); sulfolane; γ -butyrolactone (γ -but); γ -valerolactone (γ -val); propylene carbonate (PC); *N,N,N',N'*-tetramethylurea (TMU); and *N*-methylpyrrolidinone (NMP).

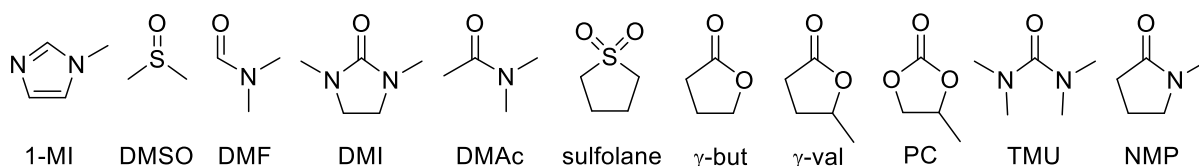


Chart 1. Cosolvents tested in organic electrolyte solutions (OESs) with the ionic liquid [EMIm][OAc].

As expected from Rinaldi's earlier results,¹⁶ addition of modest quantities of an IL to a range of dipolar aprotic solvents led to enhanced dissolution of MC and, as the mole fraction of IL, χ_{IL} ,

increased, the quantity of MC dissolved tended to the value soluble in pure [EMIm][OAc], Figure 1a.

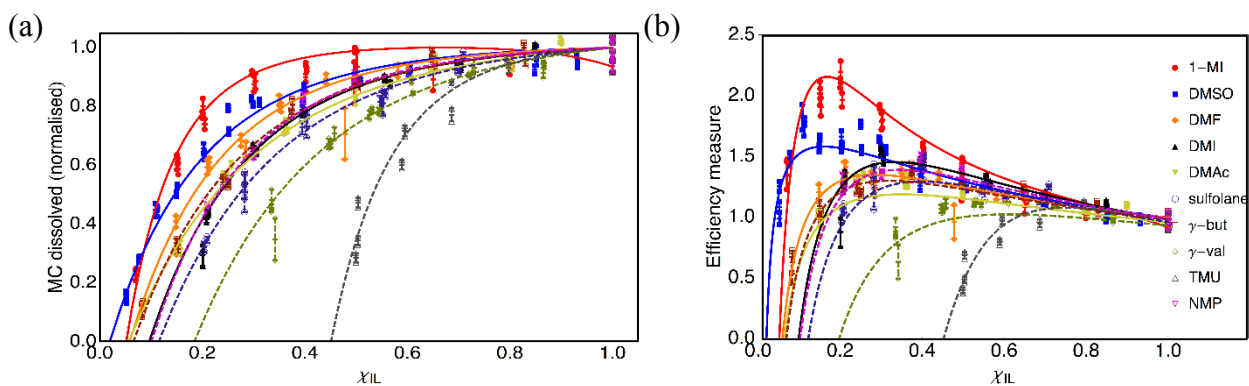


Figure 1. (a) Normalized wt % of MC dissolved in OESs *versus* mole fraction of ionic liquid, χ_{IL} (dissolved MC reaches a maximum of 22-23 wt % and curves of wt % MC dissolved *versus* χ_{IL} appear in the Supporting Information). Points are pairs of over- and underestimates on the maximum amount of MC soluble in each OES at that composition, the uncertainties on these measurements are presented as error bars and used to determine their weighting in the fit (Equation 1). Lines are the fits calculated using Equation 2, yielding $R^2 > 0.99$ in all cases. (b) Dissolution efficiency expressed as grams of MC dissolved per gram of IL *versus* χ_{IL} , relative to the efficiency at Max[c]. Lines are transformed fitted curves. The best OESs can dissolve >70 % of the maximum amount of MC soluble in pure IL at χ_{IL} as low as 0.3, with up to twice the efficiency per unit mass of IL.

Clearly, comparison of the OESs on the basis of mole fraction IL required to effect dissolution of a given quantity of MC suggests that some solvents, notably 1-MI, DMSO, DMF etc. are “good” cosolvents, while others, such as TMU, are significantly less effective. This reflects the conclusion reached by Olsson *et al.* with respect to 1-MI⁴⁹ and expands on Rinaldi’s findings (of instant dissolution),¹⁶ completing the data across a range of IL concentrations for a number of

solvents. In general, the IL will be the most costly (and sometimes the least green) component of the OES, so we consider a measure of the efficiency of IL use in MC dissolution, Figure 1b. Differences between the relative efficacies of the solvents are starkly highlighted, with 1-MI yielding the greatest mass of MC dissolved per unit mass of IL. DMSO follows a close second, while DMF, DMAc, NMP, sulfolane and DMI are similar, Table 1. TMU, in spite of its significant structural similarity to DMI, is the poorest solvent tested using the efficiency measure. Interestingly, the most efficient IL cosolvent, 1-MI, is not the solvent with the lowest limiting χ_{IL} required to effect dissolution of MC. Indeed, there are clues that 1-MI might be distinct from the other solvents as the shape of the curve reflecting quantity of cellulose dissolved *versus* IL concentration does not match that of all other solvents tested, possibly pointing to some mechanistic peculiarity. It is notable that this is the only cosolvent in the group with a nitrogen atom hydrogen (H)-bond acceptor (all others are oxygen atom acceptors), nonetheless, as our focus was on efficient and green cosolvents, this was not explored further.

Table 1. Limiting quantities of [EMIm][OAc] required to produce an OES for dissolution of cellulose for all solvents tested and measures of the efficiency of the OESs formed.

	Minimum χ_{IL} required to initiate dissolution	χ_{IL} required for maximum efficiency	Maximum efficiency measure
1-MI	0.052	0.168	2.16
DMSO	0.019	0.160	1.58
DMF	0.058	0.284	1.35
γ-but	0.065	0.318	1.30
DMI	0.096	0.333	1.45
DMAc	0.056	0.349	1.19

NMP	0.100	0.344	1.39
sulfolane	0.115	0.399	1.29
γ-val	0.184	0.609	1.20
TMU	0.451	0.752	1.08

The inclusion of some solvents, such as γ -but and γ -val, is not obvious and does not follow from the previous reports of instantaneous dissolution, or any of the plethora of publications that have drawn on that work for inspiration. In addition, the alert reader will note that PC has not yet been considered - we return to discussion of these greener solvents later.

While the wt % MC dissolved in an OES of given composition is a useful comparative value, this treatment does not provide for direct comparison of the efficiency of the dissolution of MC in a given OES on a molar basis. Considering the mole fraction of the cellobiose unit *versus* the mole fraction of IL in the OES provides solubility curves that more accurately reflect the molecular composition of the solutions, Figure 2.

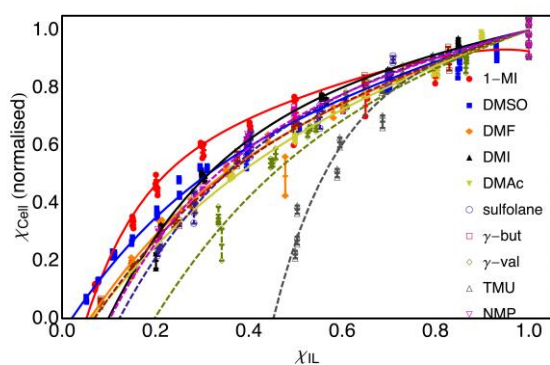


Figure 2. Mole fraction of the MC cellobiose repeat unit, χ_{Cell} (calculated from the previously normalized values), *versus* mole fraction of IL in the OES. As before, lines are transformed fits of Equation 2. Presenting the data in this way removes the effect of cosolvent molar volume.

All effective cosolvents now exhibit similar curves with only TMU and, to a lesser extent, γ -val appearing to be significantly different from the others.

Represented thus, on a comparative molar basis, the differences between the solvents are significantly reduced and it becomes clear that the apparently significant differences noted by Rinaldi and highlighted in Figure 1, are due to the variable molar volume of the individual solvents. Thus, sulfolane, with $V_m = 95.27 \text{ cm}^3 \cdot \text{mol}^{-1}$ is a less effective cosolvent than DMSO, with $V_m = 71.30 \text{ cm}^3 \cdot \text{mol}^{-1}$, but by a far smaller margin than previously implied.

With efficiency considered, we turn to the discussion of solvent selection and greenness. Rinaldi and others used Kamlett-Taft parameters as the basis for comparison of solvents, but here we use the recently compiled databases of Catalán³⁰ and Laurence and coworkers³¹ providing solvent parameters for 160 and >300 solvents respectively. Catalán defines four empirically derived parameters: solvent polarizability (SP); solvent dipolarity (SdP); solvent acidity (SA); and solvent basicity (SB). Notably, in this scale, the so-called non-specific solvent/solute interactions are described by two parameters (polarizability and dipolarity), thus avoiding confounding these two different effects.³⁰ Laurence *et al.* define solvent parameters describing solute/solvent interactions: dispersion induction (DI); electrostatic (ES); solute Lewis base/solvent Lewis acid (α_1); and solute hydrogen bond donor/solvent hydrogen bond acceptor (β_1) interactions.³¹ Clearly these scales and parameters are not dissimilar and it may be possible to select a single set of parameters to describe solvent/solute interactions. However, the goal here is to use such solvent parameter scales as tools for solvent selection. Specifically, we seek “greener” solvents for use in OESs for dissolution of cellulose to facilitate large scale production of novel materials, such as cellulose composites.

While the terms solute and solvent may be a little confusing, here both [EMIm][OAc] and cellulose are common to all systems, thus the only variable to be considered is the cosolvent used to form the OES. Using the six solvents confirmed to form effective OESs for dissolution of cellulose when combined with [EMIm][OAc] that appear in both databases (DMSO, DMF, 1-MI, sulfolane, NMP, DMAc) we define ranges for each of the four parameters described by Catalán and Laurence, Table 2. These are represented graphically in Figure 3 and it is clear that the parameters describing these solvents fall into narrow bands.

Table 2. Solvent parameters from Catalán³⁰ and Laurence³¹ for the six solvents selected as effective cosolvents in OESs with [EMIm][OAc], γ -but and two solvents with some structural similarities with these: TMU and PC.

	Catalán				Laurence			
	SP	SdP	SA	SB	DI	ES	α_1	β_1
DMSO	0.830	1.000	0.072	0.647	0.84	1.00	0.00	0.71
DMF	0.759	0.977	0.031	0.613	0.78	0.87	0.00	0.69
1-MI	0.834	0.959	0.069	0.658	0.86	0.97	0.00	0.70
Sulfolane	0.830	0.896	0.052	0.365	0.85	0.93	0.00	0.34
NMP	0.812	0.959	0.024	0.613	0.83	0.80	0.00	0.76
DMAc	0.763	0.987	0.028	0.650	0.79	0.85	0.00	0.75
Max^a	<i>0.834</i>	<i>1.000</i>	<i>0.072</i>	<i>0.658</i>	<i>0.86</i>	<i>1.00</i>	<i>0.00</i>	<i>0.76</i>
Min^a	<i>0.759</i>	<i>0.896</i>	<i>0.024</i>	<i>0.365</i>	<i>0.78</i>	<i>0.80</i>	<i>0.00</i>	<i>0.34</i>
Range^a	<i>0.075</i>	<i>0.104</i>	<i>0.048</i>	<i>0.293</i>	<i>0.08</i>	<i>0.20</i>	<i>0.00</i>	<i>0.42</i>
% of total range^a	<i>7.5</i>	<i>9.5</i>	<i>4.5</i>	<i>29.3</i>	<i>7.0</i>	<i>17.5</i>	<i>0.0</i>	<i>33.5</i>
γ-but^b	0.775	0.945	0.057	0.399	0.79	0.94	0.00	0.45

TMU^c	0.778	0.878	0.000	0.624	0.81	0.71	0.00	0.75
PC^d	0.746	0.942	0.106	0.341	0.77	1.07	0.00	0.40

^a The minimum and maximum values of the six selected solvents were used to search the databases, and the percentage range over the parameter is included as a measure of specificity; ^b new greener cellulose dissolving OES former identified in this analysis; ^c a poor cosolvent not included in the range analysis – tested due to superficial structural similarity with DMI; ^d bears a superficial structural similarity to γ -but and γ -val.

We hypothesized that interrogation of the Catalán³⁰ and Laurence³¹ databases (conveniently provided as supporting information for their publications) for solvents falling in, or close to, these ranges might offer up some candidates for new OES production. Remarkably, interrogation of both databases for solvents falling within the ranges defined by the parameters for the six selected solvents $\pm 5\%$ of the range, yields only one further solvent expected to form an OES capable of efficiently dissolving MC: γ -but (full sorted lists are contained in the supporting information). Testing of this solvent showed that it does, indeed, form an efficient cellulose dissolving OES, with a solubility curve falling well within the group comprised of the six solvents selected plus DMI (Figure 1) and with efficiency closely matching that of DMF and other dipolar aprotic solvents (Table 1 and Figure 2).

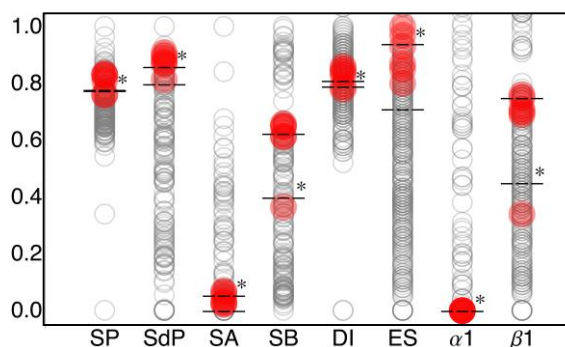


Figure 3. Catalán and Laurence parameters presented as ranges for each of the four parameters defined in each database. The values for the six representative solvents selected are represented in red and it is clear that these fall into narrow bands (as expected for solvents with similar characteristics). Parameters describing the newly identified greener solvent, γ -but, are indicated as ---* and those for TMU (a rather poor solvent) as ---. (Note: solvent parameters have not been normalized and some ranges have a small number of solvents with values >1, off-scale in the figure.)

This encouraging result led to consideration of other solvents that might provide greener options for OES based processing of cellulose. While γ -but is not associated with any of the known or potential reproductive hazards identified for DMF, NMP and others in the group, it nonetheless remains *harmful if swallowed* (H302), *causes serious eye damage* (H318), and *may cause drowsiness or dizziness* (H336). It is produced in large quantities as an industrial solvent and intermediate in the production of, for example, pyrrolidinones, but there are significant concerns about the ease with which it may be converted into γ -hydroxybutyrate (GHB), a compound listed in Schedule II of the 1971 UN Convention on Psychotropic Substances,⁵⁰ or simply ingested directly as an intoxicant (γ -but is metabolized to GHB).⁵¹ As the dose-effect curve is steep, the difference between doses yielding only “*euphoria, relaxation, reduced inhibition and sedation*” and those progressing to “*vomiting, urinary and fecal incontinence, agitation, convulsions, bradycardia, respiratory depression, coma and death*” can be slight.⁵¹ Thus, γ -butyrolactone is a controlled substance in some countries. In the hope of retaining solvent efficacy, but mitigating the potential for unwitting (or intentional) narcotic doses, the structurally similar compound, γ -val, was tested.

γ -Val proved to form a reasonably effective OES for cellulose dissolution when combined with [EMIm][OAc] (Figure 1 and 2) and would be an effective alternative to γ -but for generation of MC solutions significantly below the saturation concentration of MC in most of the OESs (~22-23 wt %). γ -Val can be produced from biomass⁵² and has appropriate physical properties for use as a solvent (including modest vapor pressure, limiting fugative emissions); its credentials as a “green” solvent have been described.⁵³ Finally, as it can be readily separated from water, γ -val may be more amenable to recovery post phase inversion in water – the process frequently used to generate cellulose composites, or formed, materials from OES solution.

Following the success of OES formation with two cyclic lactones (γ -but and γ -val), PC, a solvent which bears some structural similarities to these was (optimistically) tested. PC combined with [EMIm][OAc] was shown to form an OES capable of dissolving some cellulose, but required $>0.5 \chi_{IL}$ and the solubility plateau noted for all other OESs was only approached in solutions of almost pure IL. Indeed, PC could perhaps be better described as a “diluent or contaminant that is not quite an anti-solvent for MC”. The solvent parameters for PC do not, at first glance, appear to be very far removed from the ranges indicated (Table 2), but inspection of the sorted lists (Supporting Information) suggests that PC is indeed, not predicted to be a good OES former for cellulose dissolution. The values for SA and ES fall well outside the ranges defined.

The significant effect of small changes in molecular structure of OES cosolvent on cellulose solubility is reflected in another pair of good/modest solvents with very small structural differences: the cyclic urea DMI ($C_5H_{10}N_2O$) combined with [EMIm][OAc] yields an OES with good dissolving power for MC, while the open chain urea TMU ($C_5H_{12}N_2O$) combined with the same IL requires a high IL concentration to effect dissolution.

Designation of the most discriminatory parameters may be based on the tightness of the range within which ‘good’ cosolvents fall. A critical parameter would be expected to yield a tight range, while for a parameter less important in defining MC dissolution in the OES a wider spread of values might be noted. Thus, the value “% of total range” (Table 2) may be used: the smaller the value, the more similar the parameter for the selected solvents and, on a qualitative basis, the more dissimilar the selected solvents from other solvents in the database (this would only be quantitative if all solvents were uniformly distributed over the parameter space). In both databases, the parameters describing the basic nature of the cosolvents (SB and β_1) spread over ranges of 30 % or more, suggesting that this is not a key characteristic of a good cosolvent. Conversely, α_1 is limited to zero for all solvents found to form MC dissolving OESs and the similar solvent acidity measure, SA, in the Catalán database is restricted to a narrow range of low values. Given the plethora of studies that have suggested strong interactions between cellulose and acetate ions^{54,55,56} this is not surprising, but does perhaps provide an indication of why PC, while appearing to fall well within most ranges, is a poor cosolvent in this context: SA for PC = 0.106 places this solvent 70 % above than the upper bound of the range defined for SA using the six selected cosolvents. Finally, polarity (SdP) and polarizability (SP), show intermediate spread for acceptable OES formers, and this is reflected in the DI values in the Laurence database, while ES values appear to be less useful in selecting cosolvents.

To gain a molecular level view of the distribution of IL components relative to dissolved cellulose chains in MC solutions in OESs, RISM calculations were conducted. DMSO was selected as the solvent of choice for this study since it required the least quantity of added IL (χ_{IL} = 0.019) to generate an OES capable of initiating MC dissolution.

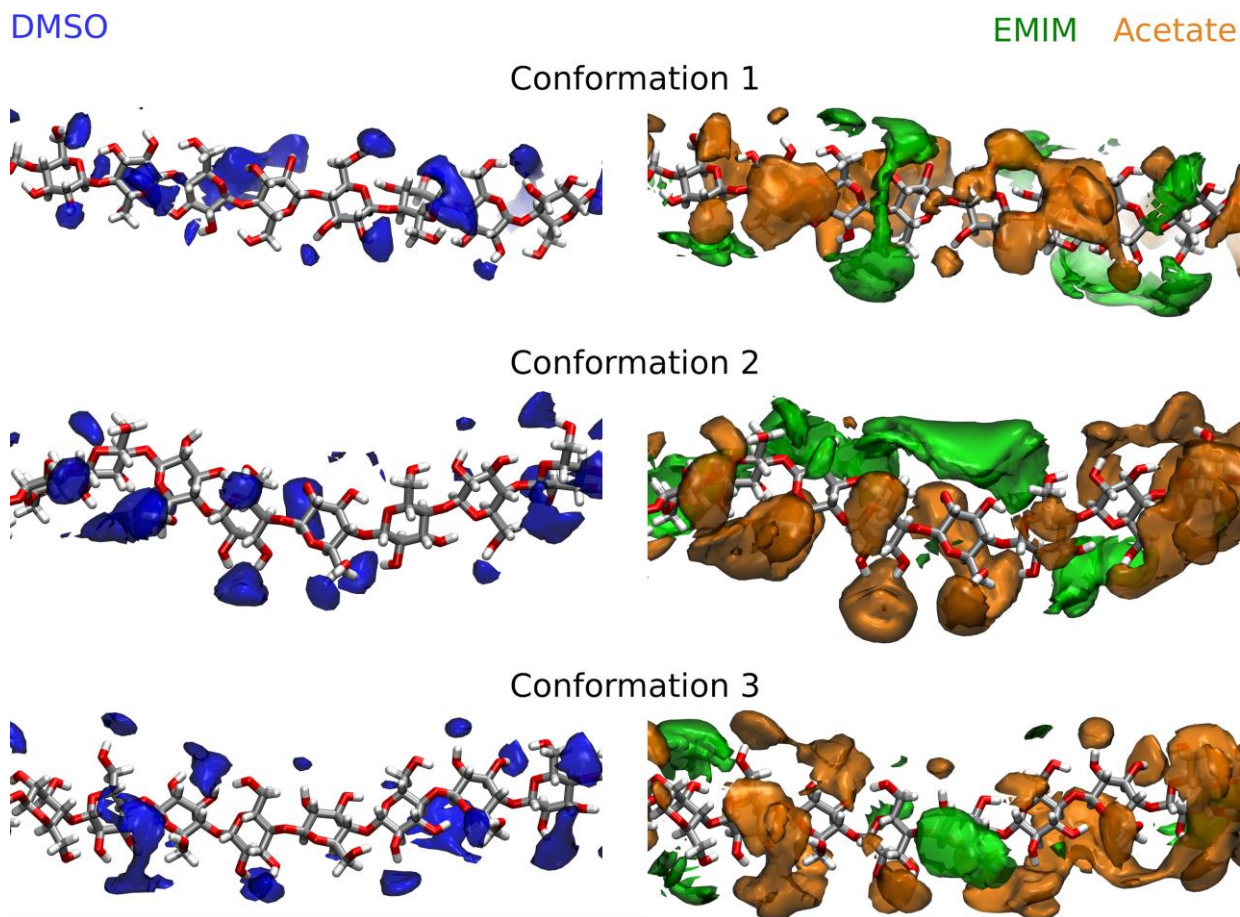


Figure 4. Specific solvation free energy density for DMSO (blue), $[\text{EMIm}]^+$ (green) and acetate (orange) around a glucan chain in three different conformations. The surfaces indicate spatial regions around the solute that concentrate stabilizing solute-solvent interactions (negative solvation free energy values). The isosurfaces were built considering the isovalue of $-18 \text{ kcal}\cdot\text{mol}^{-1}\cdot\text{\AA}^{-3}$ (chosen for best visualization).

Figure 4 shows a map of specific solvation free energy density (SFED) to represent interactions of DMSO, $[\text{EMIm}]^+$ and acetate with a glucan chain in three different conformations. Solvent-solvent and solute-solvent interactions are fully taken into account in these computations. The results show that DMSO is able to solvate the glucan chain by acting as an H-bond acceptor, concentrating around the hydrogen atoms of the exposed hydroxyl groups.

The acetate anions also concentrate around the hydroxyl hydrogen atoms and exhibit a stronger H-bond acceptor character than DMSO. Therefore, acetate and DMSO seem to compete for the same sites on cellulose, with a preferential solvation by acetate. Alternatively, this could be viewed as DMSO fulfilling a similar H-bond accepting role to acetate, albeit more weakly. We also observe that acetate can concentrate over the glucose pyranose rings and interact with their (weakly positive) hydrogen atoms. In contrast, [EMIm]⁺ is distributed around the oxygen atoms of the exposed hydroxyl groups and glycosidic bonds, with a smaller intensity compared to acetate. Therefore, whereas DMSO, as a dipolar aprotic solvent, is capable of acting only as H-bond acceptor, the ionic liquid can act as both H-bond acceptor and donor, establishing stronger interactions with the glucan chain than does the DMSO cosolvent. The fact that IL-glucan interactions are stronger suggests that small amounts of IL would be able to create the first solvation shell around the cellulose glucan chains, while DMSO would be predominant in the outer solvation shells, thereby interacting less directly with cellulose. In the dynamical equilibrium underlying the solvation phenomenon, with rapid exchange between solvation shell and free species, the ability of DMSO to fulfill some of the H-bond accepting role of acetate, might also explain why the DMSO/[EMIm][OAc] OES is effective even at very low χ_{IL} . This propensity of the IL to solvate cellulose fits well with the shape of the dissolution curves, that is: as long as the cellulose glucan chains are largely solvated by IL, further increase of the IL concentration would not lead to substantial increase in cellulose-IL interactions.

CONCLUSIONS

A range of OESs comprising mixtures of [EMIm][OAc] and various solvents (selected from common low to medium molecular weight dipolar aprotic solvents) have been shown to have

very similar efficacy for dissolution of cellulose when compared using appropriate measures of mole fractions of solutes and solvents. Thus, 1-MI, DMSO, DMF, DMAc, NMP, DMI and sulfolane all provide OESs that are effective cellulose solvents at low mole fraction of added ionic liquid. Definition of ranges of solvent parameters derived from the databases of Catalán and Laurence and coworkers and comparison of the relative degree of restriction of the ranges for each confirms others' assertions that cosolvents must not compete with cellulose with respect to H-bond donation to the IL anion, but the wide range of "allowed" basicity (H-bond acceptor) values, and RISM studies on one system, suggest that hydrogen bond accepting capability may not be deleterious to efficient dissolution of cellulose at low χ_{IL} . Most importantly, given the hazards associated with many of the widely used OES cosolvent components (particularly the reproductive hazards associated with many dipolar aprotic solvents), we have identified an alternative, biobased solvent, γ -valerolactone, as a suitable cosolvent for formation of cellulose dissolving OESs with [EMIm][OAc]. (While γ -butyrolactone also proved to be an excellent cosolvent, significant concerns associated with its use in the preparation of a dangerous drug of abuse, militate against its use.) This offers significant improvements, with regards to safety profiles and sourcing of solvents from renewable sources, for large scale processing of cellulose to form more sustainable materials.

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ASSOCIATED CONTENT

Supporting Information. Original wt % solubility data, annotated Mathematica Code for database sorting, fitting coefficients and sorted tables of solvents from the Catalán and Laurence databases. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

ABBREVIATIONS

IL: ionic liquid; 1-ethyl-3-methylimidazolium acetate: [EMIm][OAc]; OES: organic electrolyte solution; RISM: reference interaction site model; H-bond: hydrogen bond

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