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Amino Acid Ionic Liquid as an Efficient Cosolvent of Dimethyl Sulfoxide to Realize Cellulose Dissolution at Room Temperature

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A mixture of dimethyl sulfoxide (DMSO) and *N*,*N*-diethyl-*N*-(2-methoxyethyl)-*N*-methylammonium alanine ($[N_{221ME}]$[Ala]) dissolved cellulose at rt; the solubility of cellulose depended on the content of the ionic liquid in DMSO and reached 23 wt % (vs. solvent) in a 1:1 mixture. The solution coagulated in water or ethanol to obtain a transparent regenerated cellulose in quantitative yield.

Various types of cellulose fibers are used as essential materials for our modern life. The first step in manufacturing cellulose fiber is the dissolution of cellulose in an appropriate solvent,[1,2] and numerous solvent systems for such dissolution have been developed: *N*-methylmorpholine oxide,[3] *N*,*N*-dimethylacetamide/lithium chloride (DMAc/LiCl),[4] 1,3-dimethyl-2-imidazolidinone/lithium chloride (DMI/LiCl),[5] dimethyl sulfoxide/tetrabutylammonium fluoride (DMSO/Bu_4NF),[6] carbon disulfide/sodium hydroxide (CS_2/NaOH),[7] molten salt of lithium perchlorate trihydrate ($LiClO_4 \cdot 3H_2O$),[8] and several aqueous solutions of metal complexes.[9] However, there is a serious environmental drawback to such traditional solvent systems: they generally require large quantities of hazardous chemicals and high temperature. From the standpoint of Green Chemistry, therefore, development of a safer and more efficient cellulose dissolution process has been strongly desired.

Ionic liquids (ILs) have been of growing interest in various fields of chemistry because of their unique physicochemical properties, such as low vapor pressure, high thermal stability, wide electrochemical window, broad liquid range, and excellent ability to dissolve many organic and inorganic compounds.[10] Since they are easily recyclable, ILs are viewed as one of the key materials to realize Green Chemistry.[10] In 2002, Rogers and coworkers opened the door of a new cellulose chemistry using ionic liquids: they demonstrated that cellulose dissolved in an ionic liquid, 1-butyl-3-methylimidazolium chloride ($[C_4mim]$Cl), and that the cellulose regenerated from the IL solution was less crystalline than the original cellulose.[11] Since then, extensive investigations have been carried out to develop ILs that possess the capability to dissolve cellulose.[12,13] Although this research has been carried out to develop a pretreatment method of cellulose for bioethanol production, ILs are now also seen as attractive solvents for cellulose fiber production.[1,2,12,13] Recently we developed a novel amino acid ionic liquid,[14] *N*,*N*-diethyl-*N*-(2-methoxyethyl)-*N*-methylammonium alanine ($[N_{221ME}]$[Ala]) and demonstrated that it dissolved cellulose very well.[15] Furthermore, we succeeded in demonstrating its recyclable uses while maintaining its original dissolving properties.

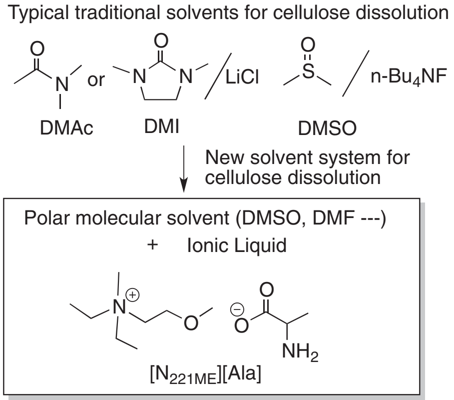

Figure 1. Working hypothesis of the design of novel cellulose dissolution solvent consisting of polar organic solvent with a salt.

During our investigation of the applicability of this IL for use in cellulose fiber production, we recognized some traditional solvents composed of a highly polar molecular solvent and an appropriate salt material, such as DMSO/Bu_4NF, DMAc/LiCl, or DMI/LiCl as noted earlier. Furthermore, recently, Rinaldi reported that addition of $[C_4mim]$Cl or $[C_4mim]$[OAc] to DMI, DMF, sulfolane, or DMSO caused effective dissolution of cellulose.[16] Inspired by these results, we decided to investigate an appropriate combination of polar solvent, such as DMSO or DMF, with an ionic liquid as a cellulose dissolution solvent (Figure 1). We initially tested the dissolving property of a mixed solvent of DMSO and $[C_4mim]$Cl (1:1 (w/w)) against cellulose using microcrystalline cellulose (Avicel®)[17] as a model compound. However, no dissolution of cellulose took place in the solvent (Table 1, Entry 1). We next prepared various types of mixed solvent of DMSO with hydrophobic ILs (1:1 (w/w)) such as $[C_4mim][NTf_2]$, $[C_4mim][PF_6]$, $[C_4mim]$[C5F8],[18] $[N_{221ME}][NTf_2]$, $[N_{221ME}][PF_6]$, $[N_{221ME}]$[C5F8], $[P_{444ME}][NTf_2]$, $[P_{444ME}][PF_6]$, $[P_{444ME}]$[C5F8], $[C_4Py][NTf_2]$, $[C_4Py][PF_6]$, and $[C_4Py]$[C5F8]. These mixed solvents did not dissolve cellulose at all even at 100 °C.

On the other hand, we found that by switching the IL to a hydrophilic liquid like $[C_4mim]$[OAc] or $[N_{221ME}]$[OAc], the corresponding mixed solvent (DMSO:IL = 1:1 (w/w)) dissolved cellulose slightly (5 and 7 wt % vs. solvent, respectively) at 100 °C (Table 1, Entries 2 and 3). Encouraged by the results, we attempted to evaluate amino acid ILs as cosolvent for DMSO. Since $[N_{221ME}]$[Ala] dissolved the best among amino acid ILs,[15] we prepared a 1:1 mixed solvent of DMSO and $[N_{221ME}]$[Ala] and found that the resulting solution dissolved cellulose very well (11 wt %) after just 10 min of stirring at rt (25 °C), and a total of 22 wt % of cellulose was dissolved in this solvent at 100 °C (Table 1, Entry 4). Furthermore, 23 wt % of

Table 1. Cellulose solubility in various types of mixed solvent of DMSO, DMF, and acetonitrile with ILs[22]

Entry	Mixed solvent system[a]		Solubility wt % vs. solvent[b]		
	Molecular solvent	IL[c]	25 °C	100 °C	Total
1	DMSO	$[C_4mim]Cl$	0	0	0
2	DMSO	$[C_4mim][OAc]$	0	5.0	5.0
3	DMSO	$[N_{221ME}][OAc]$	0	7.0	7.0
4	DMSO	$[N_{221ME}][Ala]$	11	11	22
5	DMSO	$[N_{221ME}][Ala]$	23[d]	—	23
6	DMSO	$[N_{221ME}][Lys]$	5.0	6.0	11
7	CH_3CN	$[N_{221ME}][Ala]$	1.0	13	14
8	DMF	$[N_{221ME}][Ala]$	9.0	2.0	11

[a]The solvent was mixed with the organic solvent and IL at a ratio of 1:1 (w/w). [b]Complete dissolution was observed with less than 2 h stirring. [c]Water content was less than 800 ppm (0.08 wt %). [d]Complete dissolution required 6 h stirring.

cellulose dissolved even at rt with long stirring (ca. 6 h) (Entry 5). Although more cellulose seemed to dissolve in the solvent, the solution became a highly viscous gel and was difficult to stir with a magnetic stirrer. Interestingly, poor solubility was recorded in a mixed solvent of DMSO and $[N_{221ME}][Lys]$ (Entry 6), though pure $[N_{221ME}][Lys]$ showed a similar ability to dissolve cellulose as that of $[N_{221ME}][Ala]$.[15] Mixed solvents of acetonitrile or DMF with $[N_{221ME}][Ala]$ also caused dissolution of cellulose (Entries 7 and 8), although the solubilities were inferior to that of DMSO-based solvent.

On the contrary, no dissolution was observed for solvent of a 1:1 mixture of $[N_{221ME}][Ala]$ with the molecular solvents, water, methanol, acetone, ethanol, $CHCl_3$, THF, dioxane, toluene, dichloromethane, or ethyl acetate. It was thus established that $[N_{221ME}][Ala]$ was an excellent cosolvent especially for DMSO, acetonitrile, or DMF for cellulose dissolution, but it was essential to use dry DMSO and $[N_{221ME}][Ala]$ to achieve good dissolution of cellulose; addition of more than 35% (v/v) of water to the mixed solvent caused complete inhibition of its dissolution ability.

We next attempted to optimize the ratio of $[N_{221ME}][Ala]$ to DMSO for the cellulose dissolution. The solubility significantly depended on the ratio of the IL as shown in Figure 2: cellulose did not dissolve in pure DMSO at all, and the highest solubility was recorded for ca. a 1:1 mixture of DMSO and $[N_{221ME}][Ala]$ which coincidentally was the same ratio as our initial testing solvent. The resulting solution coagulated in water or methanol to obtain a transparent regenerated cellulose in quantitative yield, and XRD analysis confirmed that the cellulose regenerated from this solution was only Type II form.[19] The recovery of the IL was accomplished by removing DMSO under vacuum (266 Pa) at 50 °C for 2 h, and we succeeded in demonstrating five recyclable uses of the IL while maintaining the same dissolving properties.

Ohno and co-workers proposed a hypothesis[20] that cellulose could be dissolved in ionic liquids which have large hydrogen bond basicity β values on the Kamlet–Taft parameter.[21] $[N_{221ME}][Ala]$ has a high β value (1.041), which is almost the same as that reported for $[C_2mim][Ala]$ (1.036).[20b] Rinaldi reported that β value of the mixed solvent of DMI–$[C_2mim][OAc]$ increased when the ratio of the IL was increased and reached the highest value at the χ_{IL} = ca. 0.1 for the DMI–$[C_2mim][OAc]$ solvent system, where χ_{IL} means the molar ratio of the IL in the solvent system.[16] From around χ_{IL} 0.10, the values are identical to those of the neat IL.[16] Since we used a 1:1 (w/w) mixture of DMSO–$[N_{221ME}][Ala]$ and χ_{IL} is calculated as 0.25, the β value of the solvent might be the same as $[N_{221ME}][Ala]$. High hydrogen bond basicity of the mixed solvent of DMSO–$[N_{221ME}][Ala]$ might contribute to breaking the inter or intramolecular hydrogen bonds of cellulose and causing its dissolution in the solvent as proposed by Ohno et al.[20]

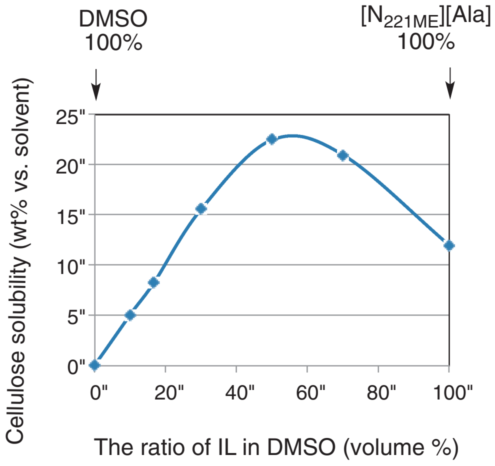

Figure 2. Cellulose solubility change in solvent composed of a ratio of $[N_{221ME}][Ala]$ and DMSO. Cellulose solubility was determined after 2 h stirring at 25 °C.

Renaldi also reported that instantaneous dissolution of the cellulose (10 wt %) took place when $[C_2mim][OAc]$ was added to DMI in a ratio of over χ_{IL} 0.4 at 100 °C.[16] We confirmed that a 1:1 mixture of DMSO and $[C_4mim][OAc]$ (χ_{IL} 0.31) caused 5.0 wt % dissolution of cellulose at 100 °C, while no dissolution of cellulose took place at rt in the solvent (Entry 2, Table 1). A similar solubility was obtained in the mixed solvents of DMSO and $[N_{221ME}][OAc]$ (χ_{IL} 0.28) (Entry 3). On the other hand, the mixture of DMSO–$[N_{221ME}][Ala]$ (χ_{IL} 0.25) dissolved cellulose even at rt (Entries 4 and 5). There was a clear contrast in the dissolution property between $[N_{221ME}][OAc]$ and $[N_{221ME}][Ala]$. Amino acid-based IL is obviously so effective as a cosolvent or salt that it dissolves more cellulose in DMSO than conventional acetate-based ILs. We anticipate that the hydrogen bond acceptor property of [Ala] and [OAc] might be different in the mixed solvent and reflect a different solubility. We previously established that free amino group of alanine was essential to realize high cellulose dissolution.[15] Therefore, we anticipate that the amino group of [Ala] may interact with a certain part of cellulose and contribute to breaking the hydrogen bond network of cellulose. However, since the cellulose solubility is also modified by the cationic part of the IL, cation might play an important cooperative role in the mechanism for cellulose dissolution, although its origin is still unclear.

Development of an efficient means to dissolve cellulose in a simple solvent at rt has been a long-standing goal in the cellulose industry. We have established that a mixed solvent of DMSO and $[N_{221ME}][Ala]$ dissolved cellulose at rt. It should be emphasized that our ionic liquid, $[\mathrm{N_{221ME}}]$[Ala], is a halogen-free and safe solvent, composed of a nontoxic ammonium cation and a natural amino acid. Further investigation of the scope and limitation of our ionic liquid technology will make it even more beneficial in cellulose science.

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