

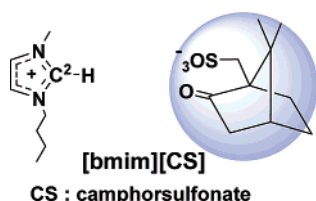
Camphor Ionic Liquid: Correlation between Stereoselectivity and Cation–Anion Interaction

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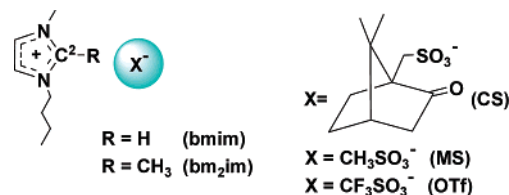
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As a halogen-free anion for an imidazolium room temperature ionic liquid, the use of a camphorsulfonate causes an increase in the number of free (naked) imidazolium cations, which produces an effective *endo/exo* stereoselective Diels–Alder reaction.

Room temperature ionic liquids (ILs) have been widely used as solvents for various reactions due partly to their unique and the environmentally benign properties.¹ Since a Diels–Alder addition can sensitively reflect the microscopic environment of solutes surrounded by medium,² the reaction has often been applied for IL.^{2b,3} The reaction in imidazolium ILs showed that the hydrogen bond between dienophile and the imidazolium cation via the C₂–H affected the *endo/exo* stereoselectivity of the product.^{3d} In particular, the counterion of the imidazolium cation is known to have an influence on the hydrogen bond.^{3d,4} That is, an anion acting as a poor hydrogen bond acceptor is supposed to show high ste-

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reoselectivity. However, the question still remains as to what anionic structures of imidazolium IL are most appropriate for effective stereoselectivity.

For the purpose of nonfluorous imidazolium ILs such as sugar type salts,⁵ in this research we use a camphor-sulfonate (CS) as one of the halogen-free anions with 1-butyl-3-methylimidazolium (bmim) cation in favor of its bulky shape. This attempt allows us to confirm first, despite its bulkiness and high molecular weight, that the camphor salt ([bmim][CS]) becomes a viscous liquid even on a salted ice bath, while the bmim methanesulfonate ([bmim][MS]) is solid at room temperature.⁶ In this study, we describe the preparation and physicochemical properties of the camphor ILs with a focus on the *endo/exo* stereoselectivity of a Diels–Alder reaction in ILs. The reactivity and the liquescency are to be viewed from the microscopic environment of ions, i.e., ion states such as contact ion pair and free ions.

Adopting the anion-exchange resin method for [bmim]-[Br] and [bm₂im][Cl] with chiral camphor-10-sulfonic acid produced a pale yellow liquid [bmim][CS] and a solid [bm₂im][CS], respectively, with quantitative yields regardless of its chirality. The ion exchanged ratios for both salts were ascertained to be above 98.5% by ¹H NMR spectra. The aqueous solutions of (*S*)-(+)-[bmim][CS] and (*R*)-(–)-[bmim][CS] showed symmetrical circular dichroism spectra and specific rotations.⁷ The [bmim][CS] was miscible with acetone and protic solvents such as water and alcohols, and immiscible with hexane, ether, and ethyl acetate. The [bmim][CS] (1.9 × 10⁴ cP at 25 °C) showed 229 times the viscosity of the ordinary IL, [bmim][BF₄] (83 cP at 25 °C). The liquid of (*S*)-(+)-[bmim][CS] containing water by 0.04 wt % and the solid of (*S*)-(+)-[bm₂im][CS] were used for the following experiments.

Since the undiluted [bmim][CS] is too viscous to use as a reaction solvent, we mixed it with a fluid IL for a Diels–Alder reaction. The reaction between cyclopentadiene and ethylacrylate was conducted without any catalyst in the [Im][CS] (Im = bmim, bm₂im) diluted with [bmim][BF₄] by 15/100 molar ratio. As the control experiments, the reactions were also carried out in the mixture of [bmim][X] (X = MS, OTf) and [bmim][BF₄] by the same molar ratio as the [bmim][CS]. Even after addition of diene and dienophile, all the reaction mixtures retained a single homogeneous phase. The *endo/exo* ratios of the isolated products were calculated by the ¹H NMR spectra.

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(7) (*S*)-(+)-[bmim][CS]: +1700 ΔE at 290 nm, [α]_D²⁵₅₈₉ +7.9; (*R*)-(–)-[bmim][CS]: –1700 ΔE at 290 nm, [α]_D²⁵₅₈₉ –7.6.

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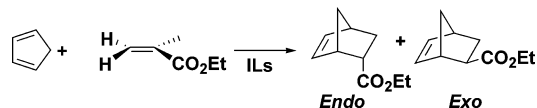
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TABLE 1. Effect of Anion of IL on the Stereoselectivity of Diels–Alder Reaction in ILs

added sulfonate in [bmim][BF ₄]	T/°C	[endo]/[exo] ^a	isolated yield/%
none	20	3.4	36
[bmim][MS] ^b		4.1	42
[bmim][OTf] ^b		4.0	16
[bmim][CS] ^b		6.1	29
none	-10	6.1	60
[bmim][CS] ^b		10.3	66
[bm ₂ im][CS] ^b	20	3.0	28

^a Calculated from ¹H NMR spectra, [diene] = 2.0 M, [dienophile] = 1.3 M, reaction time 20 h. ^b The molar ratio of [bmim][X]/[bmim][BF₄] is 15/100 (X = MS, OTf, CS).

Table 1 shows the *endo/exo* ratio of the isolated product in the ILs. For the bmim ILs, the pure [bmim][BF₄] at 20 °C allowed the reaction to show the lowest *endo/exo* value to be 3.4, which is comparable to that of a diethyl ether.⁸ On the other hand, adding the sulfonates heightened the value by 0.7, 0.6, and 2.7 for [bmim][MS], [bmim][OTf], and [bmim][CS], respectively. The added [bmim][CS] nearly doubled the stereoselectivity of the pure [bmim][BF₄] solvent. The *endo* form is more favorable in the IL with bulky [CS] than with small [MS] or [OTf]. Reducing the reaction temperature down to -10 °C for the [bmim][BF₄] with and without [bmim][CS] improved both the isolate yields and the *endo* selectivity to be around 60% and above 6.1, respectively. The addition of [bmim][CS] at -10 °C resulted in an increase in the *endo/exo* stereoselectivity to 10.3 similar to the reaction done at 20 °C. These findings provide evidence that the *endo* selectivity is attributed to the presence of the [bmim][CS] regardless of the reaction temperature. Such high stereoselectivity shows the *endo/exo* value to be 10 or over, which was reported only in the cases where catalysts were used.^{3g} As far as we know, however, no such excellent stereoselectivity to achieve the value to be as much as 10.3 in ILs, without using catalyst, has been reported heretofore.

As aforementioned, the use of the CS anion facilitates the *endo* selective reaction when the cationic module is bmim. On the contrary, when [bm₂im][CS] is applied in place of [bmim][CS], the *endo/exo* ratio is as little as 3.0. This value is 0.4 less than that of the pure [bmim][BF₄]. Unlike bmim, the bm₂im ring lacks the C₂-H by which the hydrogen bond between dienophile and the imidazolium ring can be formed. These findings, therefore, indicate that the presence of C₂-H accompanied by a CS anion is instrumental for the effective *endo/exo* selectivity.

Changing the anion of a salt affects the microenvironment of ions. In this study we evaluated the cation–anion association in the ILs by means of the specially designed ES mass spectrometer with positively charged mode. In this mass spectrometry, fragmentation of emerged liquid

droplets via adiabatic expansion in a vacuum chamber generates molecular clusters of the ILs. Unless the interaction between cation(s) and anion(s) is strong enough to be detected as clusters, the emerged clusters eventually become vaporized as monomeric ions. Therefore, a comparison of the cluster peaks of the ion pair with the monomeric peaks allows us to estimate the cation–anion interaction.

Figure S5 (see the Supporting Information) shows the mass spectra measured for the methanol solutions of the sulfonate ILs. To obtain efficiently liquid droplets by the electrospray, the ILs were dissolved in methanol. The detected clusters from the CS and other sulfonate salts were found to be very different. The [bmim][MS] and [bmim][OTf] both provide the nonsolvated imidazolium free cation, [bmim]⁺, and the nonsolvated clusters composed of the ion pairs ranging from monomer (*n* = 0) to heptamer (*n* = 7), [bmim]⁺([bmim]⁺[X]⁻), X = MS, OTf._{*n*}. On the contrary, the [bmim][CS] shows predominantly the nonsolvated imidazolium free cations which never produce such clusters of ion pairs except in the case of the monomeric ion pairs, [bmim]⁺([bmim]⁺[CS]⁻)₁. Even the monomeric ion pair of CS salt was outnumbered by that of MS or OTf salts. The same phenomenon as the [bmim][CS] can be observed for the methanolic [bm₂im][CS]. The difference in the clustering indicates that the bulky [CS] anion binds more loosely with the imidazolium cation than the small [MS] or [OTf] anions. As a result, [bmim][CS] and [bm₂im][CS] both provide free (naked) imidazolium cation more efficiently than [bmim][MS] or [bmim][OTf].

Unlike inorganic salts such as LiCl,⁹ the organic ILs show almost no solvated peaks.¹⁰ Hence, the observed difference in the ion states of the methanolic ILs could be adopted for the corresponding undiluted ILs. In fact, ¹H NMR spectra of the undiluted ILs revealed a weak interaction between imidazolium and the bulky [CS] as well as the ES-MS analysis of the methanolic solutions. The undiluted [bmim][CS] exhibits the lowest chemical shift of the C₂ proton at 8.68 ppm among a series of undiluted [bmim][X], namely, the chemical shifts in ppm at 30 °C for [BF₄]⁻, [TFSI]⁻,^{3d} [CF₃SO₃]⁻,^{3d} and [CF₃CO₂]⁻^{3d} are 8.84, 8.70, 9.00, and 9.80, respectively. The lower value than [bmim][BF₄], whose anion acts as a poor hydrogen bond acceptor, means that the bulky [CS] anion is better suited for forcing the cation to be free from hydrogen bonds than the other anions.

The calculated molecular volume for CS (196 Å³) is 3.4 and 2.9 times larger than that for MS (57 Å³) and OTf (68 Å³), respectively.¹¹ Among three sulfonates, the largest CS anion could place the cationic bmim as far away as possible from itself, increasing naked bmins. It is reasonable for us to conclude that the large CS anion impairs the molecular packing of the salt to the point of becoming liquid and causes an increase in the number

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(11) Molecular volumes estimated with the CSPropPro calculation for MS, OTf, CS, bmim, the used diene, and dienophile are 57, 68, 196, 144, 63, and 142 Å³, respectively.

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