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Toward Understanding the Origin of Positive Effects of Ionic Liquids on Catalysis: Formation of More Reactive Catalysts and Stabilization of Reactive Intermediates and Transition States in Ionic Liquids

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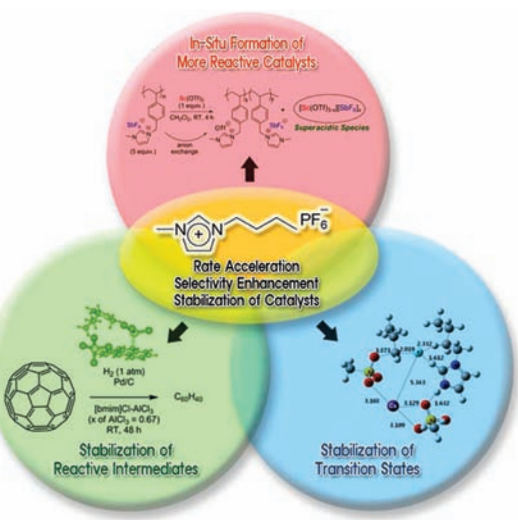

Over the past decade, ionic liquids have received a great deal of attention as a new means for catalyst immobilization. Large numbers of catalysts having polar or ionic character have been successfully immobilized in ionic liquids, thus allowing their recovery and recycling. However, catalyst immobilization is not the only benefit of ionic liquids in catalysis, of greater importance are the positive effects of ionic liquids on catalytic rates. In this Account, we highlight our work in elucidating the origin of the accelerating effects of ionic liquids in a range of catalytic reactions.

Lewis acidic metal triflates often become much more reactive in ionic liquids containing noncoordinating anions as a result of “anion exchange.” Consequently, the more electrophilic Lewis acidic species generated *in situ* accelerate the catalytic reactions dramatically. In some cases, highly reactive intermediates, such as vinyl cations, arenium cations, oxygen radical anions, and so forth, can be stabilized in the presence of ionic liquids, thus increasing the reactivity and selectivity of the reactions.

Concerted processes such as S$_N$2 and Diels−Alder reactions can also be accelerated through the cooperative activation of both the nucleophile and the electrophile by ionic liquids. In transition metal-catalyzed reactions, certain catalytically active oxidation states can be stabilized in ionic liquids against deactivation to catalytically inactive species. Thus it is clear that gaining an understanding of the origin of these “positive ionic liquid effects” is highly important, not only for predicting the effects of ionic liquids on other organic reactions but also for designing new catalytic reactions.

Ionic liquids, by virtue of (typically) having a synthetically accessible carbon backbone, are amenable to tailoring by the organic chemist. Accordingly, their molecular structures can be subtly varied to give “tunable” properties, which can then be used to rationally examine the fundamental reasons that they accelerate catalyzed reactions. Although the origins of enhanced catalytic rates by ionic liquids have been elucidated in many areas, other undiscovered ionic liquid phenomena remain to be unearthed. Developing a better understanding of these modularly tunable liquid salts will foster new discoveries of catalytic reactions that are accelerated by ionic liquids as solvents or additives.

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Introduction

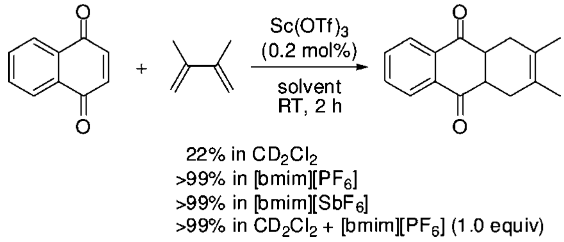
Ionic liquids (ILs) are organic salts with melting points near room temperature. They have a negligible vapor pressure, high thermal stability, and a nonflammable nature. Moreover, the physicochemical properties of ionic liquids, such as their melting temperature and hydrophilicity/hydrophobicity, can be fine-tuned by changing the structure of the cations and anions.[1] In this way, they can be tailored to be immiscible with water or with certain organic solvents. These tunable properties can also be transferred onto solid surfaces through the formation of self-assembled monolayers with task-specific functionalized ionic liquids.[2,3] Ionic liquids are capable of virtually all possible types of interactions with solutes and can solubilize a variety of organic and inorganic compounds. Hence, many neutral and ionic metal species are easily dissolved in ionic liquids, making them useful for facilitating the recovery of the catalyst from the reaction mixture. In recent years, the use of ionic liquids in catalysis has become very common, and many different kinds of homogeneous catalytic reactions have been transposed into ionic liquids. In most cases, the focus is put on the possibility of recycling the catalyst, and many excellent accounts and reviews have already published on this topic.[4−9] However, catalyst immobilization is not the only benefit of ionic liquids in catalysis. Of greater importance are the positive effects of ionic liquids on catalysis: the catalysts often become more reactive in the presence of ionic liquids, and in some cases, the reactive catalytic species or reaction intermediates can be stabilized in ionic liquids, which often results in a significant improvement in the catalytic performance or even makes it possible to achieve catalytic reactions that are not possible to conduct in common organic solvents. Therefore, understanding of the origin of these positive ionic liquid effects will give a significant impact for predicting the effect of ionic liquids on the other organic reactions and, moreover, for designing new catalytic reactions that are not working efficiently in conventional organic solvents.

In this Account, we present our most exciting findings on catalysis in the presence of ionic liquids, demonstrating such positive ionic liquid effects. Studies on the elucidation of origin of the positive ionic liquid effects will also be described.

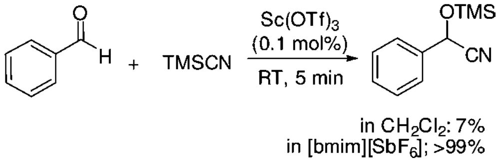
Formation of More Reactive Catalytic Species in Ionic Liquids

Rare Earth Triflate Catalyzed Reactions in Ionic Liquids. Metal triflates are ubiquitous in different types of Lewis acid catalyzed C−C bond forming reactions.[10] However, their low turnover numbers (their TONs are usually <10−20) became a major driving force for the development of different kinds of supported catalysts.[11] Our investigations on metal triflate catalyzed C−C bond forming reactions in ionic liquids were also initiated with the rather simple goal of exploring the possible repetitive use of the catalyst. Fortuitously, during these studies, the significant rate accelerations have also been observed in a range of metal triflate catalyzed reactions in ionic liquids.[12−15] For example, the Diels−Alder reaction of 1,4-naphthoquinone with 1,3-dimethylbutadiene proceeded effectively in [bmim][PF_6] or [bmim][SbF_6] with only 0.2 mol % $Sc(OTf)_3$ to afford the corresponding Diels−Alder product.[12] In contrast, the same reaction in CH_2Cl_2 is extremely sluggish. The catalytic efficiency was increased even in the presence of 1.0 equiv of [bmim][PF_6] (Scheme 1). Similarly, the cyanosilylation of benzaldehyde was also completed within 5 min in the presence of 0.1 mol % $Sc(OTf)_3$ in the ionic liquid [bmim][SbF_6]. Even in the presence of 0.01 mol % $Sc(OTf)_3$, the reaction was completed in 30 min. However, in CH_2Cl_2, conversions of less than 10% were observed (Scheme 2).[13] These results suggested that the Lewis acidity of the $Sc(OTf)_3$ catalyst may be increased in ionic liquids. Obviously, the $Sc(OTf)_3$ catalyst immobilized in ionic liquid can be successfully recovered and reused several times.

SCHEME 1. $Sc(OTf)_3$-Catalyzed Diels-Alder Reaction in Ionic Liquids

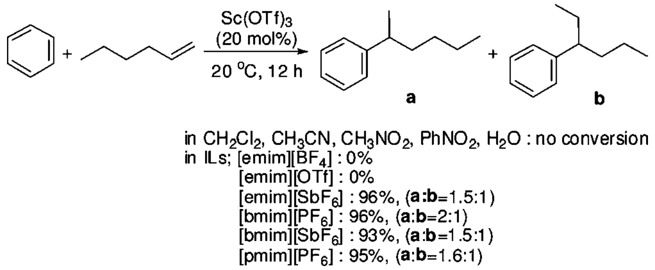


SCHEME 2. $Sc(OTf)_3$-Catalyzed Cyanosilylation of Benzaldehyde

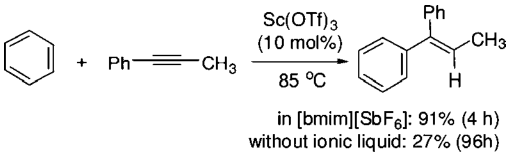


More profound positive ionic liquid effects have been observed in $Sc(OTf)_3$-catalyzed Friedel−Crafts alkylations, which were not possible to conduct in conventional organic solvents.[14] As shown in Scheme 3, the $Sc(OTf)_3$-catalyzed Friedel−Crafts alkylation of benzene with 1-hexene does not occur in common organic solvents or H_2O at all. However, surprisingly, in ionic liquids bearing noncoordinating anions such as [bmim][PF_6] and [bmim][SbF_6], it proceeded smoothly at room temperature, and quantitative conversion was obtained after 12 h. The observation of no catalytic activity of $Sc(OTf)_3$

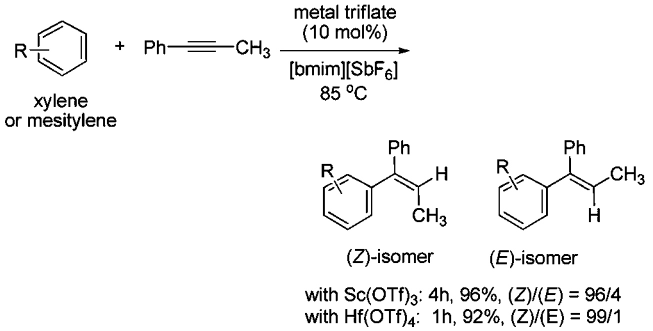
SCHEME 3. $Sc(OTf)_3$-Catalyzed Friedel–Crafts Alkylation of Benzene with 1-Hexene in Various Solvents



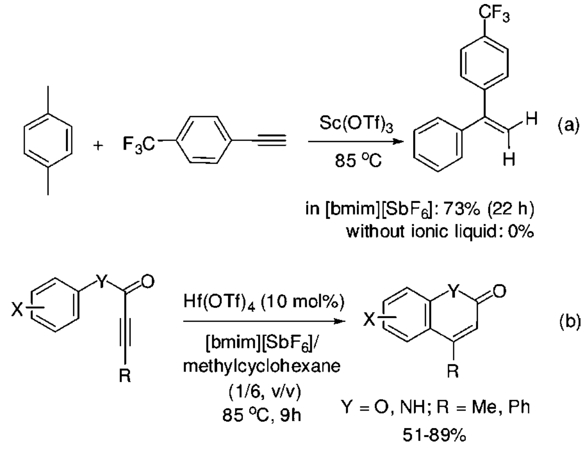
SCHEME 4. Friedel–Crafts Alkenylation of Benzene with 1-Phenyl-1-propyne



SCHEME 5. Regio- and Stereoselctive Metal Triflate Catalyzed Friedel–Crafts Alkenylation



SCHEME 6. Inter- and Intramolecular Friedel–Crafts Alkenylation of Arenes with Electron-Deficient Alkynes



SCHEME 7. Proposed Anion Exchange between Metal Triflate and $[bmim][SbF_6]$

in ionic liquids containing the [OTf] and $[BF_4]$ anions, whose coordinating ability is stronger than that of PF_6^- and SbF_6^-, suggested that the increased catalytic activity may be largely related to the counteranion of ionic liquids. Formation of the isomerized alkylated product, such as **b** (Scheme 3), clearly indicates that the reaction proceeds via a carbocation. Dramatic rate accelerations have also been observed in the metal triflate catalyzed Friedel–Crafts alkenylation of aromatic compounds with alkynes.[15] The alkenylation of benzene with 1-phenyl-1-propyne in the presence of 10 mol % $Sc(OTf)_3$ without an ionic liquid proceeded very slowly with a yield of only 27% after 96 h (Scheme 4). In contrast, the catalytic activity of metal triflates such as $Sc(OTf)_3$ and $Hf(OTf)_4$ was dramatically enhanced in $[bmim][PF_6]$ or $[bmim][SbF_6]$ resulting in the thermodynamically favorable (*Z*)-alkenylation product in excellent yields within 4 h (Scheme 5; see the original paper for the stability of (*E*)- and (*Z*)-alkenylation products).[16] Notably, electron-deficient terminal alkynes such as *p*-trifluoromethylphenylacetylene and *p*-chlorophenylacetylene could also be alkenylated efficiently using $Sc(OTf)_3$ in $[bmim][SbF_6]$, whereas without $[bmim][SbF_6]$, no conversion was observed (Scheme 6a). Moreover, the intramolecular alkenylations also efficiently proceeded in $[bmim][SbF_6]$ (Scheme 6b). Here again, the alkenylations were not effective in $[bmim][BF_4]$ and [bmim][OTf].

The Question Is How the Metal Triflate-Catalysts Are Activated in an Ionic Liquid Bearing Noncoordinating Anions. To elucidate the origin of these increased catalytic activities observed in the metal triflate-catalyzed reactions in ionic liquids, detailed studies were performed with the hypothesis that the anion exchange of the metal triflate with a noncoordinating anion[17] such as SbF_6 or PF_6 generates more electrophilic Lewis acidic catalysts such as **1** (Scheme 7).[18]

To facilitate the isolation of the anion-exchanged species, the Merrifield's resin-bound imidazolium hexafluoroantimonate **2** was treated with $Sc(OTf)_3$. The solid-state ^{19}F NMR spectra of the separated Merrifield's resin **3** clearly indicated the presence of both hexafluoroantimonate and triflate anions implying that the OTf anion of $Sc(OTf)_3$ was exchanged with the SbF_6 anion. The singlet peak at −82.5 ppm corresponds to the OTf anion (compare with the solid-state ^{19}F NMR spectrum of the resin-bound imidazolium triflate, which was prepared independently, Figure 1). The formation of the superacidic species **1** was also detected from the FAB-MS analysis of the filtrate. Based on these results, it can be concluded that formation of the more electrophilic Lewis acidic catalyst

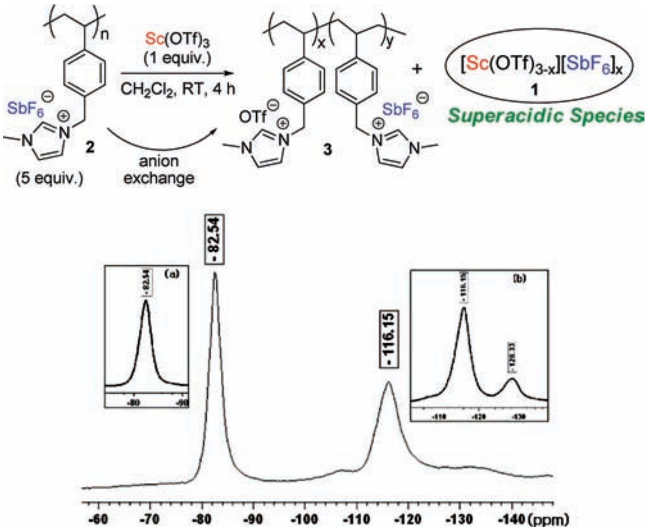
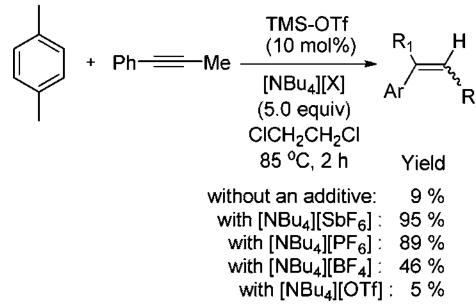


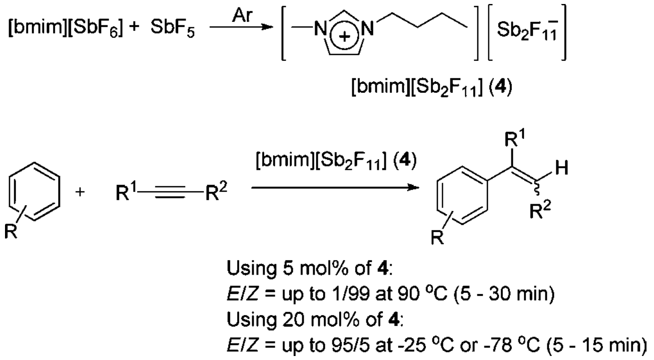
FIGURE 1. The anion exchange with the Merrifield's resin-bound imidazolium hexafluoroantimonate **2**, and the solid-state ^{19}F NMR spectra of polymer **3**. The inset shows (a) the solid-state ^{19}F NMR spectrum of the resin-bound imidazolium triflate and (b) the ^{19}F NMR spectrum of **2**.

1, generated *in situ* via anion exchange in [bmim][SbF_6], could be the key factor responsible for the rate acceleration and enhanced selectivity observed in various kinds of metal triflate-catalyzed reactions.

SCHEME 8. TMS-OTf-Catalyzed Friedel–Crafts Alkenylation



SCHEME 9. Synthesis of Superacidic Ionic Liquid **4** and Thermodynamically and Kinetically Controlled Friedel–Crafts Alkenylation



Tunable Lewis Acidity in Ionic Liquids. On the basis of the anion-exchange mechanism for the activation of the metal triflate catalysts, it would be expected that the Lewis acidity of a metallic or nonmetallic Lewis acid can be simply tuned by the proper selection of the counteranions of the salts.[18] In order to clarify the *"anion effect"* on the activation of Lewis acid, the alkenylation of *p*-xylene with 1-phenyl-1-propyne using TMS-OTf as catalyst was carried out in the presence of several quaternary ammonium salts bearing different anions such as SbF_6^-, PF_6^-, BF_4^-, and OTf^-. As expected, the Lewis acidity of the TMS-cation increased with decreasing nucleophilicity (coordinating ability) of the counteranion of the salts in the order of $SbF_6^- > PF_6^- > BF_4^- > OTf^-$, and thus, in the presence of [NBu_4][SbF_6], the reaction was completed within 2 h, affording the corresponding adduct in 95% yield (Scheme 8). According to the *ab initio* calculations, as would be expected, the atomic charge (2.007 e^+ in the gas phase) at the Si of [TMS][SbF_6] was found to be much more positive than that (1.991 e^+) of TMS-OTf and quite close to the charge (2.102 e^+) of the naked TMS-cation.[18] Similar catalyst activation by an anion-exchange mechanism has also been observed in a series of C–C bond-forming reactions catalyzed by metal halide Lewis acid catalysts such as $InCl_3$.[18] All of these experimental and theoretical results strongly indicate that the anionic nature of the organic salts plays a crucial role in the activation of the Lewis acids, and thus, the acidity of a metallic or nonmetallic Lewis acid can be very simply tuned by the proper selection of the counteranions of the salts.

The conformation of anion-directed tunable Lewis acidity of ionic liquids prompted us to use a novel ionic liquid, **4**, having a superacidic fluoroantimonate(V) anion, for Friedel–Crafts alkenylation. Although, as described above, the substrate scope of metal triflate catalyzed alkenylation was markedly broadened by employing an ionic liquid, the Lewis activity of this catalyst system is still not high enough to conduct the reaction at a low temperature, which would be desirable to obtain the kinetically controlled products. However, by employing the superacidic fluoroantimonate(V) IL **4** as a catalyst, one could obtain both the thermodynamically controlled (*Z*)- and kinetically controlled (*E*)-isomers selectively from the Friedel–Crafts alkenylations.[19] When the reaction was conducted in the presence of 5 mol % superacidic ionic liquid **4** at high temperature, the (*Z*)-isomer was formed selectively, whereas the (*E*)-isomer was formed selectively at a lower reaction temperature (Scheme 9).

Although the positive ionic liquid effects on the formation of more reactive catalytic species are mainly observed in metal triflate-catalyzed reactions, there may obviously be numbers of other catalytic reactions exhibiting higher catalytic activity via formation of more reactive catalytic species in

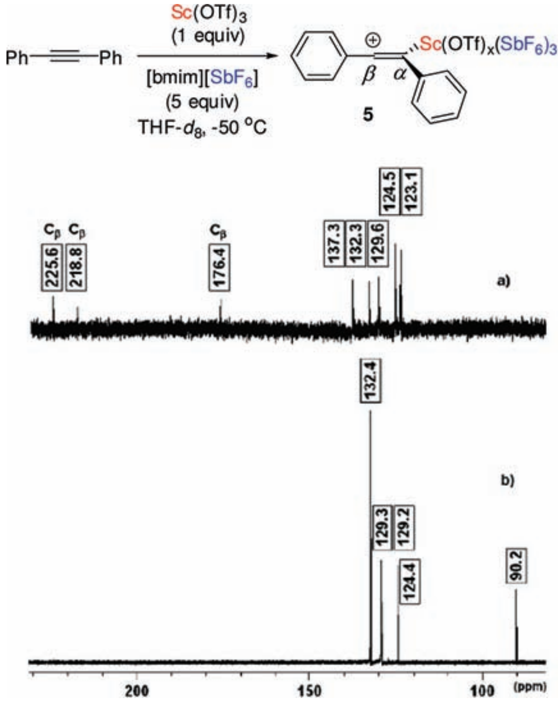


FIGURE 2. (a) Part of ^{13}C NMR spectrum of cation **5** at −50 °C in THF-d_8 and (b) ^{13}C NMR spectrum of diphenylacetylene.

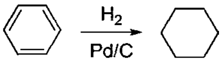
ionic liquids. Therefore, the origin of these positive ionic liquid effects described here would provide new opportunity to design more reactive catalytic systems.

Stabilization of Reactive Intermediates in Ionic Liquids

Due to the polar nature of ionic liquids, it is also generally accepted that the activation barrier of the reactions can be reduced by the stabilization of the polar transition states or reaction intermediates in polar ionic liquids. The following examples demonstrate the significant "positive effect" of an ionic liquid caused by the stabilization of the reactive intermediates such as vinyl and arenium cations or oxygen radical anion intermediates.

Stabilization of Vinyl Cationic Intermediates. Another significant observation from the metal triflate catalyzed Friedel−Crafts alkenylations of arenes with alkynes described above is that the reactive vinyl cation intermediates can be stabilized in ionic liquids.[16] In the presence of the ionic liquid [bmim][SbF$_6$], the vinyl cationic species **5** are stabilized to the point that they can be even be detected by ^{13}C NMR. As shown in Figure 2a, from an equivalent mixture of diphenylacetylene and Sc(OTf)$_3$ in the presence of 5 equiv of [bmim][SbF$_6$] in THF-d_8 at −50 °C, three characteristic signals for vinyl cations initially appeared at 225.6, 218.8, and 176.4 ppm, which can be ascribed to the formation of several Sc species by the anion exchange between Sc(OTf)$_3$ and [bmim][SbF$_6$] as shown in Scheme 7.[16] Thus, in addition to the formation of more Lewis acidic species by anion exchange, the significant rate acceleration can also be ascribed to the stabilization of the unstable vinyl cationic intermediate in an ionic liquid, in which the reactive vinyl cationic intermediates gain a longer lifetime.

TABLE 1. Pd-Catalyzed Hydrogenation of Benzene in the Presence of the [bmim]Cl-AlCl$_3$ (*x* of AlCl$_3$ = 0.67; **6**)

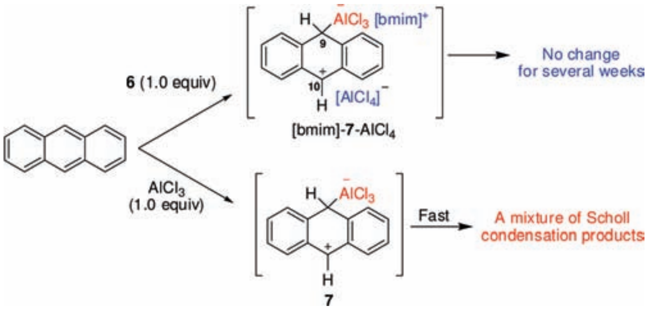


Pd/C (equiv.)	Lewis acid (equiv.)	P_{H_2} (bar)	time (h)	conv. (%)
0.02		3	6	*a*
	6 (0.5)	3	6	*a*
0.02	**6** (0.5)	3	6	>99
0.1	**6** (1.0)	1	24	>99
0.02	AlCl$_3$ (0.5)	3	6	*a*

[a] No reaction.

Stabilization of Arenium Intermediates: Tackling Aromaticity. The hydrogenation of an aromatic compound generally requires harsh reaction conditions, and thus development of a catalytic system allowing the hydrogenations under mild reaction conditions has become a longstanding goal. Recently, we discovered that the cooperative catalytic system, composed of Pd/C and a Lewis acidic ionic liquid, [bmim]Cl-(AlCl$_3$)$_x$ (x = 0.67, where x = mole fraction of AlCl$_3$) (**6**), is highly efficient for the hydrogenation of arenes and C$_{60}$ fullerene under ambient conditions.[20] As shown in Table 1, benzene can be completely hydrogenated to cyclohexane by using 2 mol % Pd/C catalyst in the presence of 0.5 equiv of **6** at room temperature under H$_2$ at a pressure of 3 atm. When the amounts of **6** and Pd/C were increased to 1.0 equiv and 10 mol %, respectively, the hydrogenation was accomplished even under H$_2$ at a pressure of 1 atm. However, without the Lewis acidic ionic liquid **6** or with the common Lewis acid AlCl$_3$, the reaction did not proceed at all. The hydrogenation of bicyclic and polycyclic aromatic compounds, which are more reactive to hydrogenation than benzene, was also ineffective in the absence of the Lewis acidic ionic liquid **6**, even under higher pressures of H$_2$. When [bmim]Cl-(AlCl$_3$)$_x$ (x = 0.67) (**6**) was replaced with AlCl$_3$, various inseparable condensation products (>99%) were formed by the Scholl reaction. The ^{1}H and ^{13}C NMR spectra obtained from a stoichiometric mixture of anthracene and **6** in ClCD$_2$CD$_2$Cl clearly indicated the formation of the anthracenium ionic intermediate, bmim-**7**-AlCl$_4$, which is so stable that the NMR signals did not change appreciably for several weeks at 25 °C. In sharp contrast, mixing anthracene and a stoichiometric amount of AlCl$_3$ resulted in the rapid oligomerization of the arene, affording a mixture

SCHEME 10. Two Different Anthracenium Intermediates Generated by Mixing Anthracene with [bmim]Cl-$AlCl_3$ (*x* of $AlCl_3$ = 0.67) (**6**) and $AlCl_3$



of Scholl condensation products, without showing the characteristic NMR signals for the anthracenium intermediate (Scheme 10). Hence, it could be concluded that the activation of the arene and the stabilization of the resulting arenium intermediate by the Lewis acidic ionic liquid is the key factor responsible for these hydrogenations (Figure 3). Computational calculations also indicated that the role of the ionic liquid is to provide both kinetic and thermodynamic stabilization for the arenium intermediate (Figure 4). Interestingly, in this catalytic system, C_{60} fullerene, which usually requires extremely harsh conditions (120 bar of H_2 at 400 °C),[21] can also be hydrogenated under ambient conditions (1 bar of H_2 and RT, Figure 5). Quite recently, our dual activation concept was successfully applied to the selective phenol hydrogenation to cyclohexanone.[22] This novel concept will also be extrapolated to many other metal-catalyzed reactions in near future.

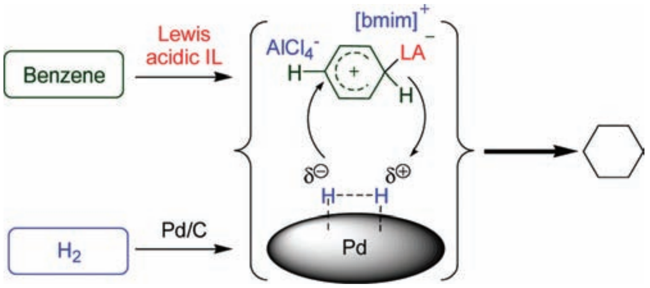


FIGURE 3. Concept of a cooperative catalytic system for the double activation of an arene and molecular hydrogen.

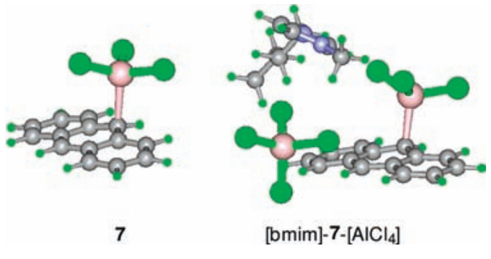


FIGURE 4. Computed structures of the complexes of **7** and [bmim]-**7**-[$AlCl_4$].

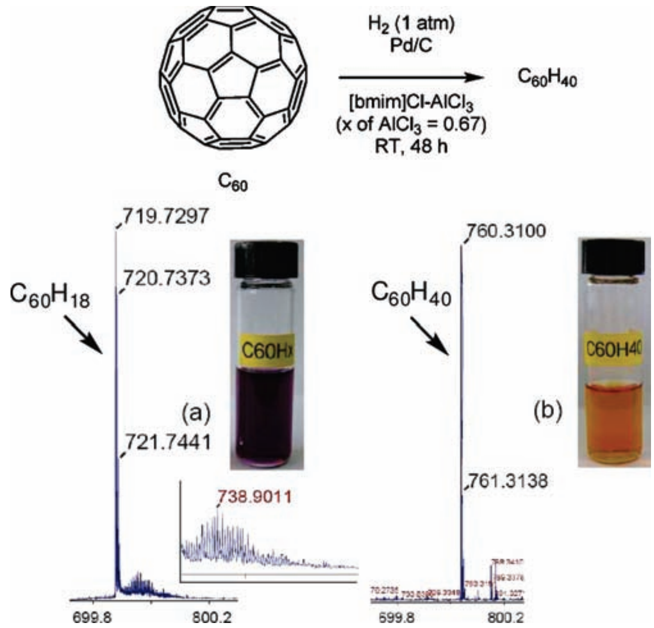
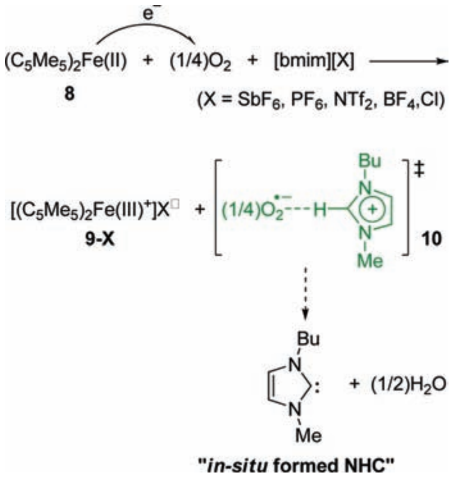


FIGURE 5. Pd-catalyzed hydrogenation of C_{60} in the presence of the [bmim]Cl-$(AlCl_3)_x$ (*x* = 0.67, **6**).

Stabilization of Anionic Oxygen Radical Intermediate: Accelerated Electron Transfer Reactions in Ionic Liquids. In nature, electron transfer plays a fundamental role in most important processes such as photosynthesis, respiration, and nitrogen fixation. Transition metals such as copper and iron are known to play a crucial role in electron transport by acting as one-electron redox-active centers within proteins.[23] Mimicking these biological systems enables the aerobic oxidation of metal complexes, which is promoted by Brønsted and Lewis acids. Mechanistically, these aerobic oxidations proceed through electron transfer from metal complexes to an oxygen molecule, thereby affording an oxygen radical anion intermediate, which can be stabilized by coordinating it with an acid, consequently lowering the activation energy.[24,25] On the process of our research into ionic liquids, we recognized that the acidic C2−H of imidazolium could also be used for the stabilization of the oxygen radical anion (**10** in Scheme 11).[26]

The positive ionic liquid effects on electron transfer can be supported by the fact that the aerobic oxidation of metal complexes such as $(C_5Me_5)_2Fe(II)$ (**8**) proceeded rapidly in the presence of the ionic liquid [bmim][X] (X = SbF_6, PF_6, NTf_2, BF_4, and Cl) in CH_2Cl_2. As shown in the UV−vis spectra in Figure 6 (curves a−e), in the presence of [bmim][X], a strong red shift was observed in the specific absorption of the Fe(II) complex **8** from 423 to 779 nm of the Fe(III)-X (**9-X**) complex. In contrast to these results, no oxidation was detected in the absence of [bmim][X] (curve f), indicating that the presence of the ionic liquid is crucial for the aerobic oxidation of the metal com-

SCHEME 11. Proposed Mechanism for Aerobic Oxidation of **8** to **9-X** Promoted by [bmim][X]



plex **8**. Moreover, the oxidation rate was highly dependent on the anion's structure and thus decreased in the order of SbF_6^- > PF_6^- > NTf_2^- > BF_4^- ≫ Cl^- which reflects the relative acidity of the C2−H caused by the coordinating ability of the counteranion. We also observed that [*N*-butylthiazolium][SbF_6], possessing a more acidic proton than [bmim][SbF_6], accelerated the oxidation rate more dramatically than [bmim][SbF_6] did. All these observations strongly support our assumption that the *in situ* generated oxygen radical anion is stabilized by its coordination with the acidic C2-proton of the imidazolium ring and, thus, the oxidation rate is dependent on the acidity of C2−H. It was also reported that [bmim][PF_6] is capable of stabilizing electrochemically generated superoxide ion ($O_2^{\bullet-}$).[27] Moreover, the effect of ionic liquids on the stabilization of highly reactive 9-chloroanthracene radical anion has also been investigated.[28]

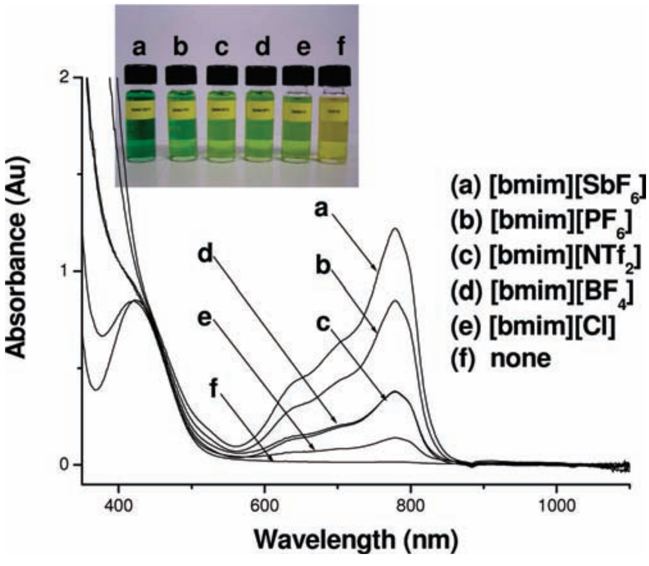
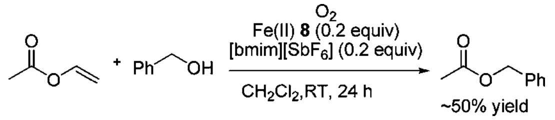


FIGURE 6. UV−vis spectra of a mixture of **8** with or without [bmim][X] in CH_2Cl_2 (10 mL) after 1 h.

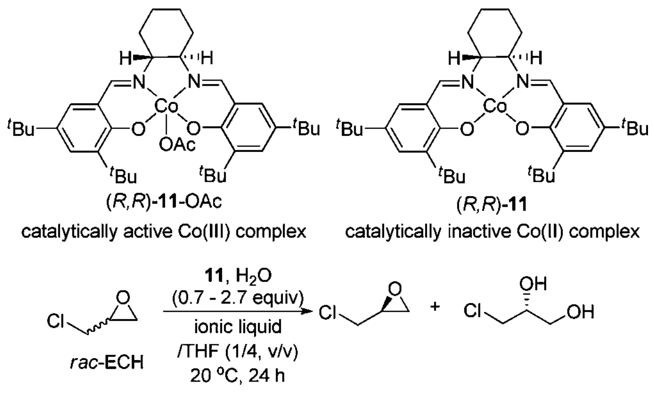
SCHEME 12. Transesterification Catalyzed by Base-Free Generated NHC



The *in situ* formation of *N*-heterocyclic carbenes (NHCs) during the aerobic oxidation of metal complexes promoted by imidazolium IL was proven by carrying the transesterification reaction under the aerobic oxidation condition of metal complexes,[26] since nucleophilic NHCs are known to be efficient catalysts for this reaction.[29,30] As shown in Scheme 12, the reaction proceeded smoothly, and the resulting acylated product (benzyl acetate) was able to be isolated in about 50% yield, although sterically nonhindered NHCs such as **10** may be highly unstable. Thus, the aerobic oxidation of metal complexes promoted by imidazolium IL can also be utilized as a base-free method of generating *N*-heterocyclic carbenes, which are able to catalyze many organic reactions.

Stabilization of Anionic Oxygen Radical Intermediate: Stabilization of the Catalytically Active Oxidation State in the Chiral Co(III)(salen)-Catalyzed Hydrolytic Kinetic Resolution of *rac*-Epoxides. Generally, it is well-known that when organic solvents are used as reaction media during the hydrolytic kinetic resolution (HKR) of racemic epoxides catalyzed by the chiral Co(III)(salen)-OAc catalyst (*R*,*R*)-**11a**-OAc, the catalytically active Co(III) oxidation state of (*R*,*R*)-**11a**-OAc is reduced to the catalytically inactive Co(II)(salen) complex (*R*,*R*)-**11**,[31] and thus, when it is recovered, it needs to be reoxidized to the Co(III) complex with acetic acid under air before reuse. In contrast, the catalytically active Co(III) oxidation state can be

TABLE 2. Co(salen)-Catalyzed HKR of *rac*-ECH in Ionic Liquids



catalyst (mol %)	ionic liquid	conv. (%)	% ee of epoxide	% ee of diol
(*R*,*R*)-**11**-OAc (0.5)	[bmim][PF_6]	52	>99	91.9
(*R*,*R*)-**11a**-OAc (0.1)	[bmim][PF_6]	52	>99	91.2
(*R*,*R*)-**11** (0.5)	[bmim][NTf_2]	53	>99	86.0
(*R*,*R*)-**11** (0.025)	[bmim][NTf_2]	53	>99	87.1

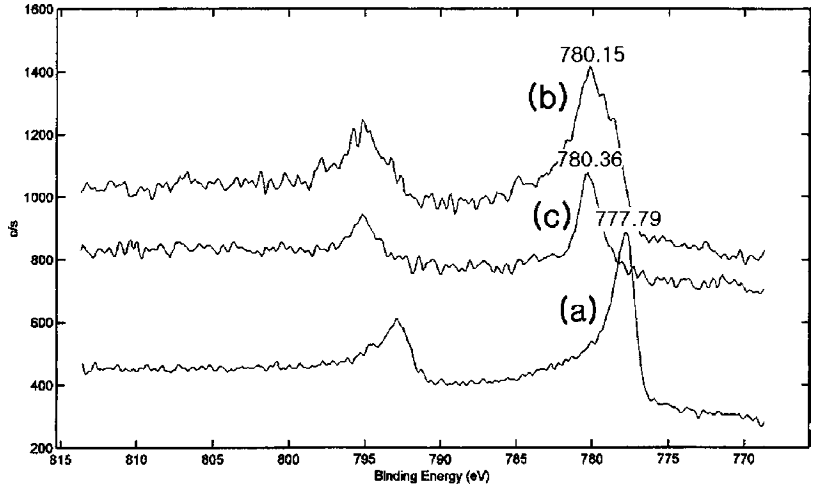
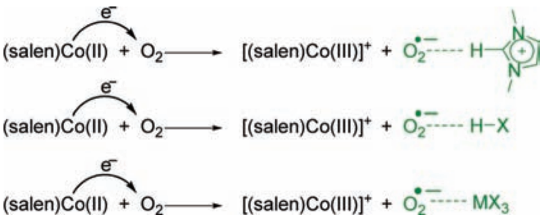


FIGURE 7. XPS spectra of (a) Co(II)(salen) complex, (b) Co(III)(salen) complex, and (c) the recovered Co(salen) complex after HKR of ECH in THF-[bmim][PF_6] with (*R*,*R*)-**11**.

stabilized in ionic liquids.[31] For example, when the HKR of *rac*-epichlorohydrin (ECH) with 0.1 mol % of (*R*,*R*)-**11a**-OAc was conducted in a mixture of THF and [bmim][PF_6] (4/1, v/v), the yield and enantiomeric excess were quite comparable with those obtained in an organic solvent, and thus, the enantioenriched (*S*)-ECH (>99% ee) and (*R*)-diol (92% ee) could be obtained (Table 2). Interestingly, in the X-ray photoelectron spectroscopy (XPS) spectra of both the recovered Co(salen) complex and Co(III)(salen)(PF_6) complex **11**-PF_6, the Co $2p_{3/2}$ line appeared at ~780 eV, whereas the XPS line of the Co(II)(salen) complex **11** appeared at ~777 eV indicating that the oxidation state of the recovered Co complex was not +II but +III (Figure 7). More interestingly, it was also found that in the presence of the ionic liquid, the catalytically inactive Co(II) complex (*R*,*R*)-**11** can be directly used as a catalyst precursor instead of the Co(III) complex (*R*,*R*)-**11**-OAc. The catalytically inactive Co(II) complex (*R*,*R*)-**11** is oxidized, in the absence of acetic acid, to the catalytically active Co(III)-complex (*R*,*R*)-**11**-OAc during the HKR reactions, which is not possible in conventional organic solvents. Thus, all of the HKRs of *rac*-ECH using catalytic amounts of Co(II)(salen) complex ((*R*,*R*)-**11**) in [bmim][PF_6] or [bmim][NTf_2] proceeded smoothly, even when only 0.025 mol % of (*R*,*R*)-**11** was used. The stabilization of the Co(III) complex against reduction to the Co(II) complex can be ascribed to the ionic liquid-promoted aerobic oxidation of Co(II) to Co(III).[32] Similar to the cases with Brønsted and Lewis acids,[33] the acidic C2−H of imidazolium ionic liquids stabilizes the oxygen radical anionic intermediates (Scheme 13). Accordingly, here again, the profile of the electron transfer promoting effect of the ionic liquids is consistent with the relative acidity scale of the C2-proton.

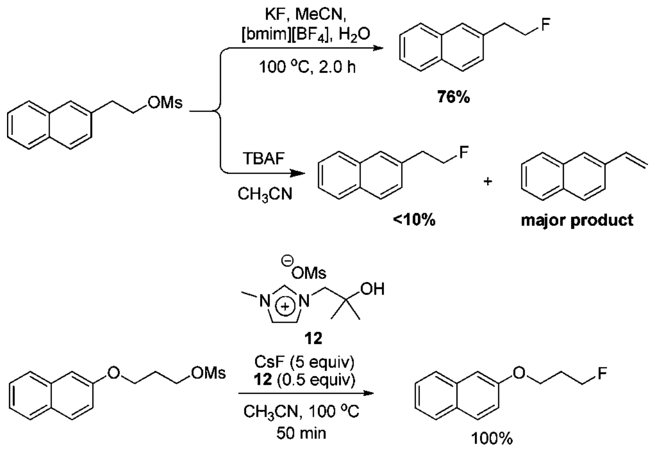
SCHEME 13. Aerobic Oxidation of Co(II)(Salen) to $[Co(III)(Salen)]^+$ Promoted by an Acid



Stabilization of Transition State: Nucleophilic Fluorination in Ionic Liquids

As discussed previously, the reactions that proceeded via reactive intermediates (alkyl, vinyl, arenium carbocations, and oxygen radical anion) showed pronounced positive ionic liquid effects such as rate acceleration and increased regio- and stereoselectivity, which originated from the stabilization of the reactive intermediates. In addition to these multistep reactions, significantly enhanced reactivity and selectivity have also been observed in nucleophilic substitution reactions in ionic liquids.[34−36] For instance, the use of an ionic liquid for the nucleophilic fluorination reaction of primary, secondary, and benzylic halides or mesylates with KF afforded the corresponding fluoroalkanes with high chemoselectivity and remarkable rate acceleration, in contrast to the corresponding reactions in common organic solvents (Scheme 14).[34] More interestingly, the use of an ionic liquid suppresses the elimination reaction in the fluorination of haloethyl- or alkanesulfonylethyl aromatic compounds, which tend to undergo such an elimination reaction to produce the styrene derivative. Quite recently, the efficiency of nucleophilic fluorination was further improved by employing the modified ionic liquid **12**, where the polar protic OH group may offer balanced propensity to reduce the basicity of the fluoride anion.[37] These

SCHEME 14. Nucleophilic Fluorination in the Presence of an Ionic Liquid



fluorination protocols using ionic liquids will open up new perspectives for ^{18}F labeling chemistry for positron emission tomography (PET),[38] because of their use of readily available alkali metal fluorides as nucleophilic sources, as well as their unprecedentedly fast reaction rates and excellent product selectivity.[36] In the nucleophilic substitution reactions, the ionic liquid might play an ambiphilic "electrophile–nucleophile" dual activation role (i.e., the counteranion of the ionic liquid acts as a Lewis base toward K^+, drastically reducing its electrostatic effects and thereby "freeing" the F^- nucleophile and the acidic C2-proton interacts with the mesylate leaving group, helping it to detach from the reactant). A similar amphiphilic "electrophile–nucleophile" dual activation role of an ionic liquid in the rate acceleration of the 1,2-addition reaction of an indole to an aldehyde was reported quite recently.[39]

Conclusions and Outlook

The results discussed in this Account demonstrated the "positive effects of ionic liquids" in catalysis. Obviously, these positive ionic liquid effects on catalysis are mainly due to the unique environment imposed by the ionic liquid, causing positive changes to the active catalytic species, as well as the reaction profile. Lewis acidic catalysts become more reactive in ionic liquids containing noncoordinating anions via "anion exchange". Consequently, the more electrophilic Lewis acidic species generated *in situ* accelerate the catalytic reactions dramatically. In some cases, highly reactive intermediates, such as vinyl cations, arenium cations, and oxygen radical anions, can be stabilized in ionic liquids, which increases the reactivity and selectivity or makes it possible to achieve catalytic reactions that are not possible to conduct in organic solvents. In certain cases, a catalytically active oxidation state can be stabilized in an ionic liquid, thereby preventing it from being deactivated to a catalytically inactive species. Although the origins of many of these "positive ionic liquid effects" have been elucidated, other unexplored and undiscovered ionic liquid phenomena are still waiting to be unearthed. Our attempts to understand these modularly tunable liquid salts will continue to foster new "positive ionic liquid effects" in catalytic reactions.

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FOOTNOTES

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