

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/224038738>

ChemInform Abstract: Strong Lewis Acids of Air-Stable Metallocene Bis(perfluorooctanesulfonate)s as High-Efficiency Catalysts for Carbonyl-Group Transformation Reactions.

ARTICLE *in* CHEMISTRY - A EUROPEAN JOURNAL · OCTOBER 2012

Impact Factor: 5.73 · DOI: 10.1002/chem.201103874 · Source: PubMed

CITATIONS

17

READS

51

6 AUTHORS, INCLUDING:



Renhua Qiu

Hunan University

67 PUBLICATIONS 529 CITATIONS

SEE PROFILE



Xinhua Xu

Hunan University

44 PUBLICATIONS 305 CITATIONS

SEE PROFILE



Yalei Zhao

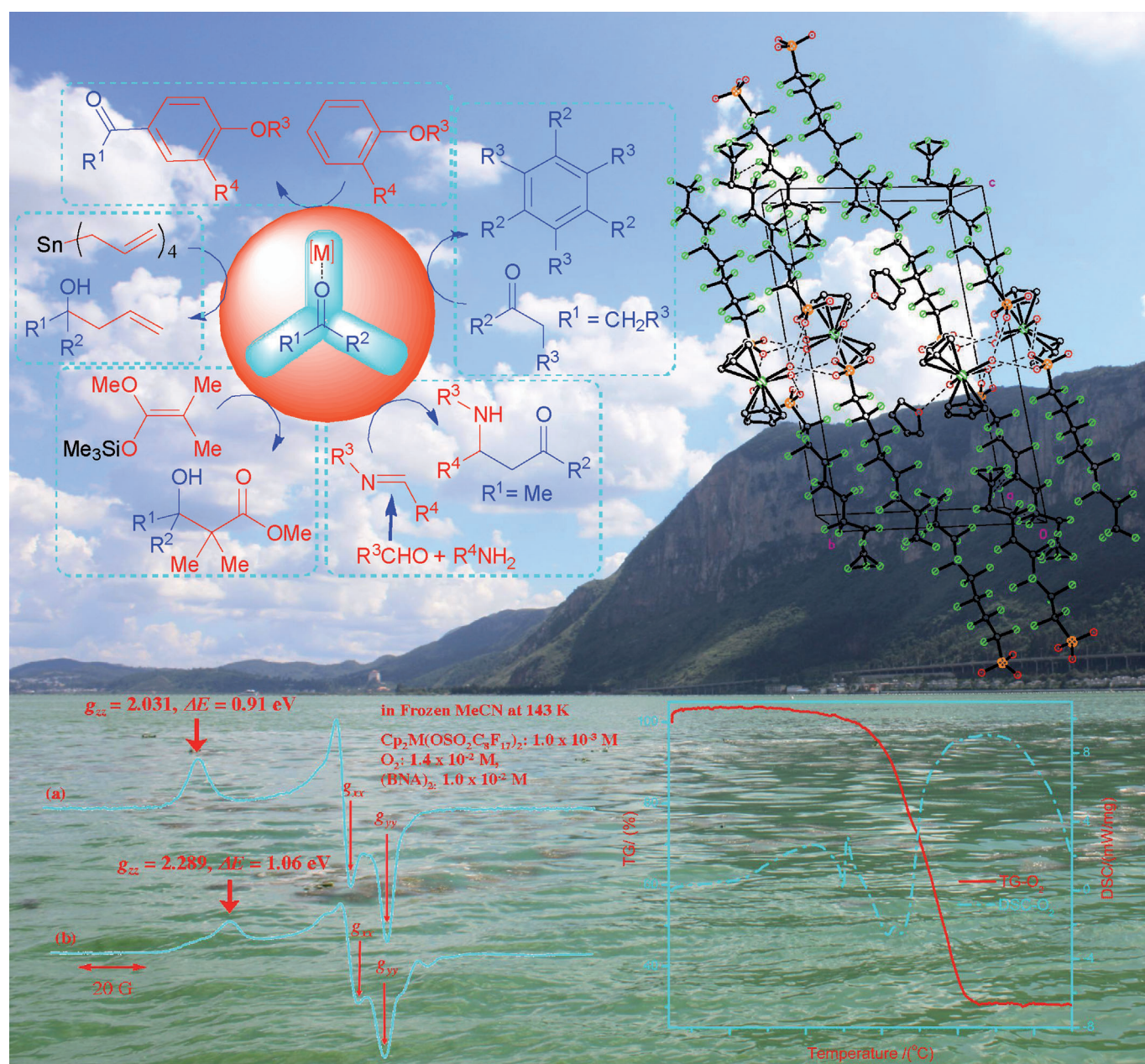
Hunan University

11 PUBLICATIONS 75 CITATIONS

SEE PROFILE

Strong Lewis Acids of Air-Stable Metallocene Bis(perfluorooctanesulfonate)s as High-Efficiency Catalysts for Carbonyl-Group Transformation Reactions

Renhua Qiu,^[a] Xinhua Xu,^{*,[a, b]} Lifeng Peng,^[a] Yalei Zhao,^[a] Ningbo Li,^[a] and Shuangfeng Yin^{*,[a]}



Abstract: Strong Lewis acids of air-stable metallocene bis(perfluorooctanesulfonate)s $[M(Cp)_2][OSO_2C_8F_{17}]_2 \cdot nH_2O \cdot THF$ ($M = Zr$ (**2a**·3 $H_2O \cdot THF$), $M = Ti$ (**2b**·2 $H_2O \cdot THF$)) were synthesized by the reaction of $[M(Cp)_2]Cl_2$ ($M = Zr$ (**1a**), $M = Ti$ (**1b**)) with $nBuLi$ and $C_8F_{17}SO_3H$ (2 equiv) or with $C_8F_{17}SO_3Ag$ (2 equiv). The hydrate numbers (n) of these complexes were variable, changing from 0 to 4 depending on conditions. In contrast to well-known metallocene triflates, these complexes suffered no change in open air for a year. thermogravimetry–differential scanning calorimetry (TG-DSC) analysis showed that **2a** and **2b** were thermally stable at 300 and 180 °C, respectively. These complexes exhibited

unusually high solubility in polar organic solvents. Conductivity measurement showed that the complexes (**2a** and **2b**) were ionic dissociation in CH_3CN solution. X-ray analysis result confirmed **2a**·3 $H_2O \cdot THF$ was a cationic organometallic Lewis acid. UV/Vis spectra showed a significant red shift due to the strong complex formation between 10-methylacridone and **2a**. Fluorescence spectra showed that the Lewis acidity of **2a** fell between those of Sc^{3+} ($\lambda_{em} = 474$ nm) and Fe^{3+} ($\lambda_{em} =$

478 nm). ESR spectra showed the Lewis acidity of **2a** (0.91 eV) was at the same level as that of Sc^{3+} (1.00 eV) and Y^{3+} (0.85 eV), while the Lewis acidity of **2b** (1.06 eV) was larger than that of Sc^{3+} (1.00 eV) and Y^{3+} (0.85 eV). They showed high catalytic ability in carbonyl-compound transformation reactions, such as the Mannich reaction, the Mukaiyama aldol reaction, allylation of aldehydes, the Friedel–Crafts acylation of alkyl aromatic ethers, and cyclotrimerization of ketones. Moreover, the complexes possessed good reusability. On account of their excellent catalytic efficiency, stability, and reusability, the complexes will find broad catalytic applications in organic synthesis.

Keywords: carbonyl-group transformations • homogeneous catalysis • Lewis acids • metallocenes • sustainable chemistry

Introduction

Reactions of carbonyl groups that are activated by Lewis acids are involved in several important organic transformations, such as in the synthesis of β -amino carbonyl compounds, β -hydroxyl ketones, β -hydroxyl esters, allyl alcohols, aryl ketones, multiaromatic compounds, and so forth.^[1] The Mannich reaction,^[2] allylation,^[3] the Mukaiyama aldol reaction,^[4] the Friedel–Crafts acylation,^[5] and cyclotrimerization of ketones^[6] are typical carbonyl-group transformation reactions for the synthesis of the above compounds. Coordination of the carbonyl oxygen to a Lewis acid site induces polarization in the molecule, effectively enhancing its reactivity by augmenting its electrophilicity. Recently, many kinds of Lewis acid catalysts have been used in these reactions. Unfortunately, most of these catalysts have one or more disadvantages, such as: 1) air or moisture sensitive, 2) poor selectivity or functional intolerance, and 3) unrecoverable. In addition, although some catalysts show high catalytic efficiency in one of these reactions, they are poor in

other reactions due to requirement of different Lewis acidity. With the emphasis on the “green” and “sustainable” chemistry,^[7] the design and synthesis of highly catalytic efficient, cheap, stable, versatile, and green Lewis acids for carbonyl-group transformation is a key issue in Lewis acid chemistry.

Cationic Group 4 metallocene compounds as Lewis acid catalysts have attracted increasing attention in modern organic synthesis recently.^[8] Such Lewis acids should be as strongly acidic as possible to acquire higher activity; however, they become more susceptible to hydrolysis upon increasing the acidity. For example, metallocene triflates $[M(Cp)_2][OSO_2CF_3]_2$ ($M = Zr$ and Ti) were successfully employed as catalysts for Diels–Alder reaction,^[9] Mukaiyama aldol reaction,^[10] glycosylation,^[11] and so forth. Unfortunately, these complexes are not stable in air, suffering from facile hydrolysis.^[12] Thus, they must be handled under strictly anhydrous conditions. Another notable species are putative metallocene perchlorates $[M(Cp)_2][ClO_4]_2$ ($M = Hf$ and Zr), which have found extremely versatile application in glycosylation technology.^[13] These species cannot be isolated due to their hydrolytic instability, and thus they are usually generated in situ prior to reaction by treating $[M(Cp)_2]Cl_2$ with potentially explosive $AgClO_4$. Therefore, improvement of the hygroscopic character of the cationic metallocene derivatives is highly demanding from the standpoint of practical utilization as catalysts.

Recently, the use of longer perfluoroalkylsulfonate groups as effective counter anions was found to provide air-stable and water-tolerant organometallic species, which are in sharp contrast to the corresponding hygroscopic organometallic triflates.^[6b,14] This finding has led us to postulate that longer perfluoroalkanesulfonate groups serve to overcome

[a] Dr. R. Qiu, Prof. Dr. X. Xu, Dr. L. Peng, Dr. Y. Zhao, Dr. N. Li, Prof. Dr. S. Yin
State Key Laboratory of Chemo/Biosensing and Chemometrics
College of Chemistry and Chemical Engineering
Hunan University, Changsha, 410082 (P.R. China)
Fax: (+86) 731-88821310
E-mail: xhx1581@hnu.edu.cn
sf_yin@hnu.edu.cn

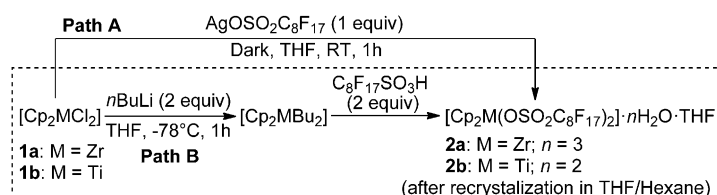
[b] Prof. Dr. X. Xu
State Key Laboratory of Elemento-Organic Chemistry
Nankai University, Tianjing, 300071 (P.R. China)

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/chem.201103874>.

the hydrolytic instability of the cationic organometallic species in a general sense.^[14a] With this in mind, we herein successfully isolated two air-stable mononuclear metallocene bis(perfluorooctanesulfonate) complexes $[M(Cp)_2][OSO_2C_8F_{17}]_2$ ($M = Zr, Ti$),^[15] which enabled facile assessment of Lewis acidity and catalytic activity in carbonyl-group transformation reactions; for example, the Mannich reaction, allylation of aldehydes, the Mukaiyama aldol reaction, the Friedel–Crafts acylation, and cyclotrimerization of ketones.

Results and Discussion

There are two paths for synthesis of zirconocene and titanocene bis(perfluoroalkanesulfonate) $[M(Cp)_2][OSO_2C_8F_{17}]_2$ ($M = Zr$ (**2a**), Ti (**2b**)) (Scheme 1). Path A is treatment of $[M(Cp)_2]Cl_2$ ($M = Zr$ (**1a**), Ti (**1b**)) with $AgOSO_2C_8F_{17}$



Scheme 1. Synthesis of zirconocene and titanocene bis(perfluoroalkanesulfonate)s.

(2 equiv) in THF,^[15] while path B is treatment of $[M(Cp)_2] \cdot [nBu]_2$ {prepared from $[M(Cp)_2]Cl_2$ ($M = Zr$ (**1a**), Ti (**1b**)) with $nBuLi$ (2 equiv) in THF} with $C_8F_{17}SO_3H$ (2 equiv) in THF; both of the two paths allowed us to isolate **2a**·3H₂O·THF and **2b**·2H₂O·THF (after recrystallization from THF/hexane) as stable hydrated species. The hydration number (n) of **2** was variable upon standing. ¹H NMR spectroscopy (in anhydrous CH₃CN) and elemental analysis showed that freshly prepared samples after recrystallization contained 2 or 3 water molecules along with solvating THF for **2a** and **2b**. Pumping these complexes in vacuum for a week at room temperature caused complete dehydration giving $n = 0$. Standing the freshly prepared compounds **2a** and **2b** in open air for two days induced desolvation of the THF and the water content increased to $n = 4$. Such durability, though being hydrated, presents a sharp contrast to the corresponding triflate $[Zr(Cp)_2][OSO_2CF_3]_2$ (**3**), which undergoes facile hydrolysis to binuclear $[Zr_2(Cp)_2(H_2O)_6(\mu^2-OH)_2][OSO_2CF_3]_4 \cdot 4THF$.^[16] Notably, **2** exhibited no sign of structural change after being kept in open air for a year. The solid samples remained as dry crystals or powder and suffered no color change. Therefore, the metallocene perfluorooctanesulfonates are storable in open air, showing a great advantage over the metallocene triflates or perchlorates from an operational point of view.

As depicted in Figure 1 (top), the thermogravimetric (TG) curve of **2a**·3H₂O·THF shows three stages of weight

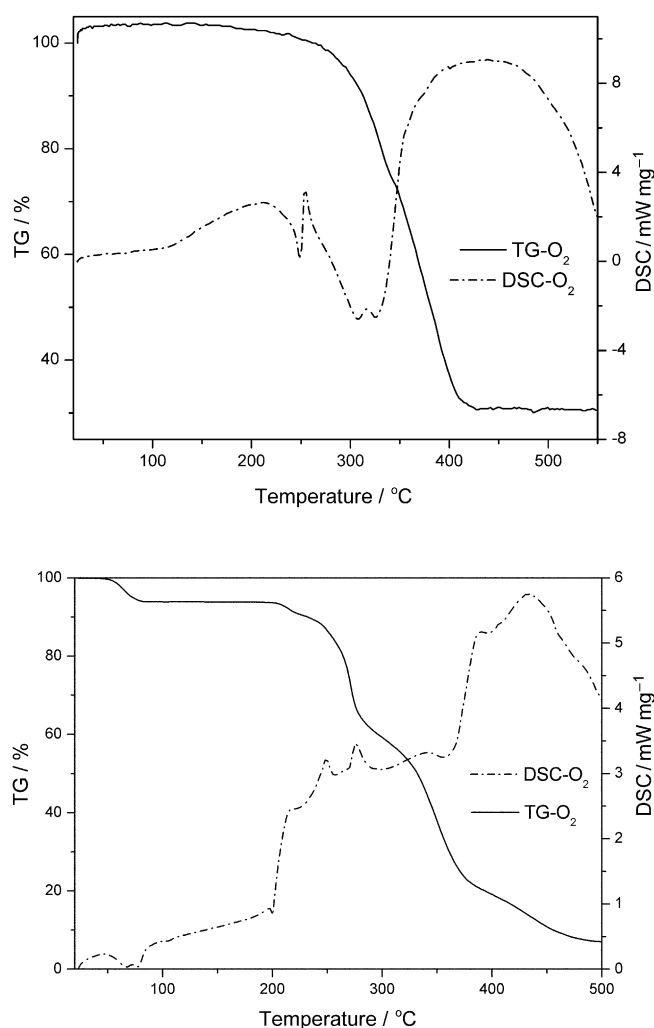


Figure 1. The TG-DSC curves of complex **2a**·3H₂O·THF (top) and **2b**·2H₂O·THF (bottom).

loss. The endothermic step below 220°C can be assigned to the removal of water molecules. The material is stable up to about 300°C. Over 300°C two weight losses of exothermic nature appear, plausibly due to the oxidation of organic entities. We observed the removal of perfluorooctanesulfonyl ligands at 400°C, leaving zirconium fluoride behind. As shown in Figure 1 (bottom), the TG curve of **2b**·2H₂O·THF shows three stages of weight loss. The endothermic step below 100°C can be assigned to the removal of water molecules. The material is stable up to about 200°C, and then two weight losses of exothermic nature appear, plausibly due to the oxidation of organic entities. We observed the removal of perfluorooctanesulfonyl ligands at 250°C, leaving titanium fluoride behind. We hence deduce that **2a** and **2b** are thermally stable at 300 and 180°C, respectively. We also employed ¹H and ¹⁹F NMR techniques to analyze the **2b**·2H₂O·THF sample that had undergone thermal treatment at 180°C for two days, and observed no change.

Other notable features of complexes **2a**·3H₂O·THF and **2b**·2H₂O·THF were their unusual high solubility in MeOH,

Table 1. The solubility of the mononuclear metallocene perfluorooctane-sulfonates in organic solvents at 25 °C.^[a]

Solvent	Solubility [g L ⁻¹]	
	2a ·3H ₂ O·THF	2b ·2H ₂ O·THF
acetone	957	275
THF	244	121
EtOAc	729	19
MeOH	186	128
CH ₃ CN	143	530
Et ₂ O	21	11
CH ₂ Cl ₂	0	0
toluene	0	0
hexane	0	0

[a] All samples were freshly prepared and recrystallized.

acetone, THF, EtOAc, and CH₃CN (Table 1). In acetone, the solubility of **2a**·3H₂O·THF was extraordinarily high and amount up to 957 g L⁻¹; it is better to say that they were miscible with each other to form a slightly viscous liquid. Both complexes exhibited normal solubility in less polar Et₂O, but were poorly soluble in CH₂Cl₂. This is quite surprising behavior because CH₂Cl₂ was usually the best solvent for similar metallocene bis(triflate) derivatives. Consistently, they were not soluble in much less polar toluene and apolar *n*-hexane. Furthermore, as they were apparently insoluble in water, these complexes were hydrophobic, which

could be attributed to the long fluoroalkyl chain in the sulfonate ligand. The unusual solubility reflects the amphiphilic nature of the long fluoroalkyl chain.^[14a] Upon dissolving the metallocene complex in polar solvents, the solvent molecules can approach the coordination sphere of the metal atom to replace the hydrated water on account of their compatibility, and the resulting solvated species are highly soluble in the same polar solvents. By contrast, CH₂Cl₂ as well as hydrocarbons cannot reach the metal atoms because of the interference of water with these hydrophobic solvents. It can be concluded that the metallocene perfluorooctanesulfonates were neither hydrophilic nor lipophilic in their hydrated form, and accordingly they were not soluble in both strongly hydrophobic organic solvents and water, while the water was readily replaced by the polar organic solvents to generate the highly soluble solvated species.

The high solubility of the complexes **2a** and **2b** in polar organic solution encouraged us to investigate their structure in a solid state. We take **2a** as an example. The structure of **2a**·3H₂O·THF in the solid state was confirmed by X-ray analysis.^[8c] The crystals suitable for the X-ray diffraction were obtained by diffusion of hexane into saturated solution of **2a**·3H₂O·THF in THF. The crystal structure and packing together with selected bond lengths and angles are shown in Figure 2. The zirconium atom in the cationic ion is coordi-

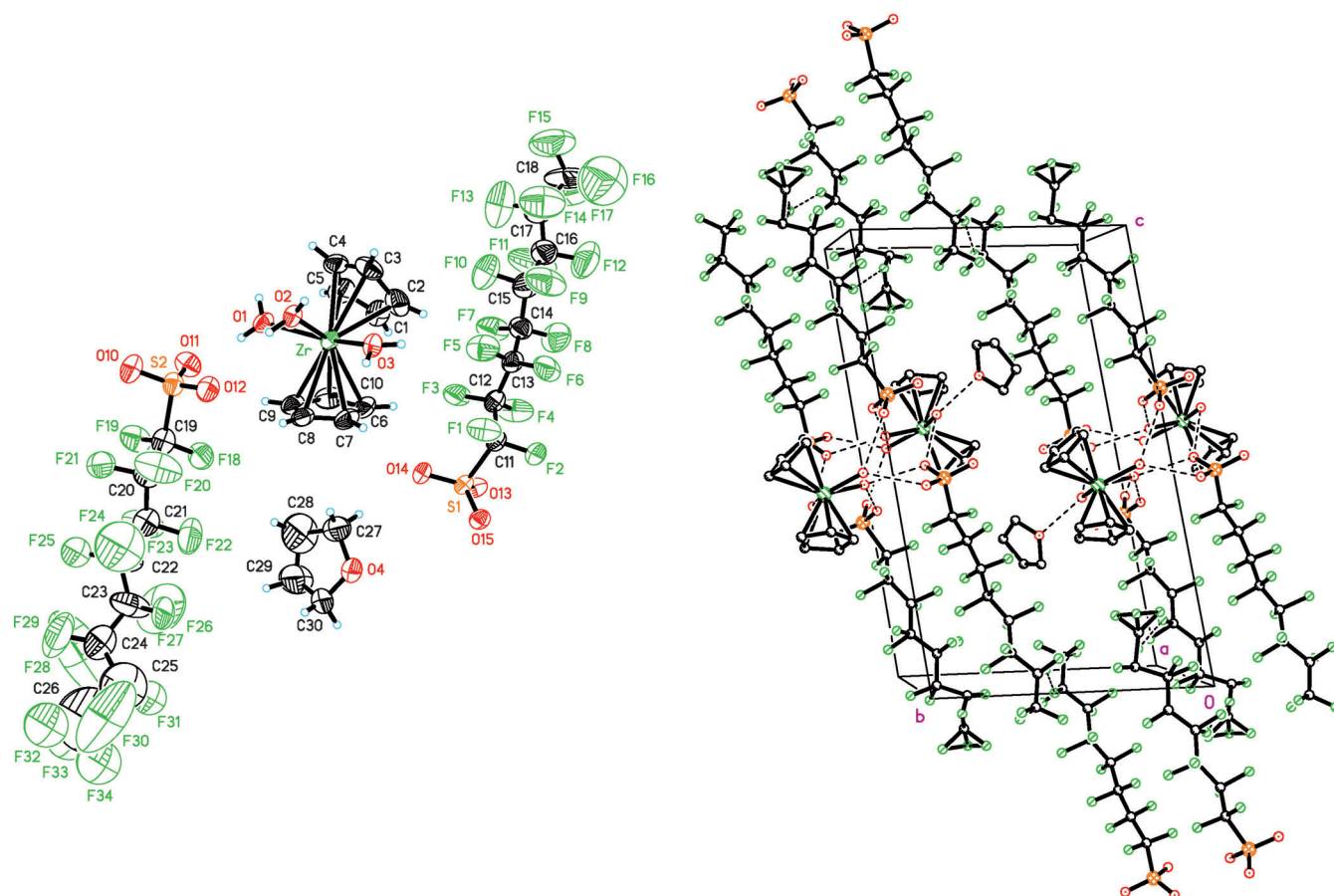


Figure 2. An ORTEP view showing 50% probability ellipsoids and packing of [Zr(Cp)₂(H₂O)₃][OSO₂C₈F₁₇]₂·THF (**2a**·3H₂O·THF).

nated by three water molecules and not by THF. Hence, the geometry of the $[\text{Zr}(\text{Cp})_2(\text{H}_2\text{O})_3]^{2+}$ ion is similar to that of $[\text{Zr}(\text{Cp})_2(\text{H}_2\text{O})_3]^{2+}[\text{OSO}_2\text{C}_8\text{F}_{17}]_2^{2-}$.^[17] The three H_2O molecules lie on the plane that bisects the angle between the Cp ring planes. The $\text{OSO}_2\text{C}_8\text{F}_{17}^-$ ions and the THF molecule are packed around the zirconium cation in such a way that their oxygen atoms point towards the H_2O ligands. The C_8F_{17} chains of the anion, on the other hand, are clustered together so as to produce hydrophobic domains in the crystal structure. Unfortunately, in spite of many attempts we were unable to obtain suitable crystals of **2b** for X-ray analysis. However, due to the similar chemical structure, we deduced that the complex **2b** could be also cationic organometallic species which was confirmed by conductivity measurements.

We applied conductivity measurements to investigate their ionic dissociation behavior in solution. The molar conductivities (Λ) of **2a**·3 H_2O ·THF ($\Lambda = 136.1 \mu\text{S cm}^{-1}$ in CH_3CN (1.0 mmol L^{-1}) at 15 °C) and **2b**·3 H_2O ·THF ($\Lambda = 114.5 \mu\text{S cm}^{-1}$ in CH_3CN (1.0 mmol L^{-1}) at 15 °C) were nearly in the same level as that of complex $[\text{Zr}(\text{Cp})_2][\text{OSO}_2\text{C}_8\text{F}_{17}]_2 \cdot 3\text{H}_2\text{O} \cdot \text{THF}$ ($\Lambda = 158.1 \mu\text{S cm}^{-1}$ in CH_3CN (1.0 mmol L^{-1}) at 15 °C). The large molar conductivity values are consistent with complete ionization into a 1:2 electrolyte in CH_3CN , implying that these complexes are cationic in the solid state and in solution.

Since the metallocene Lewis acid is desired to be as strongly acidic as possible to acquire higher activity, we decided to estimate the Lewis acidity of **2a** and **2b**. We first applied UV/Vis spectra (Figure 3, top) to qualitatively determine the Lewis acidity of **2a**, and observed a significant red shift due to the strong complex formation between 10-methylacridone and **2a**, illustrating a large Lewis acidity ability of **2a**. Previously, Fukuzumi et al. reported that the Lewis acidity of the metal complexes can be quantitatively estimated by the red shift (λ_{em}) of Lewis acid metal ions with 10-methylacridone on the basis of fluorescence spectra.^[18] Thus, we measured the fluorescence spectra of 10-methylacridone and **2a** to determine the λ_{em} values, which are shown in Figure 3 (middle). The significant red shift of fluorescence spectrum maximum due to the complex formation between 10-methylacridone and **2a** ($\lambda_{\text{em}} = 476 \text{ nm}$) indicates that the Lewis acidity of **2a** falls between those of Sc^{3+} ($\lambda_{\text{em}} = 474 \text{ nm}$) and Fe^{3+} ($\lambda_{\text{em}} = 478 \text{ nm}$). The Lewis acidity of the metal complexes can be also quantitatively estimated by the binding energies (ΔE values) of Lewis acid metal ions with $\text{O}_2^{\cdot-}$ on the basis of ESR spectra.^[19] To estimate the Lewis acidity of **2a** and **2b** exactly, we measured the ESR spectra of the $\text{O}_2^{\cdot-}$ -**2a** and $\text{O}_2^{\cdot-}$ -**2b** complexes to determine their ΔE values. As shown in Figure 3 (bottom), the ΔE value of the titanium complex ($\text{O}_2^{\cdot-}$ -**2b**) is significantly larger (Ti^{4+} : $g_{\text{zz}} = 2.0289$, $\Delta E = 1.06 \text{ eV}$) than that of $\text{Sc}(\text{OTf})_3$ ($g_{\text{zz}} = 2.0304$, $\Delta E = 1.00 \text{ eV}$) and is the largest among the ΔE values ever reported by Fukuzumi group.^[19b] The ΔE of the zirconium complex ($\text{O}_2^{\cdot-}$ -**2a**) exhibits a relatively large value (Zr^{4+} : $g_{\text{zz}} = 2.0331$, $\Delta E = 0.91 \text{ eV}$), which falls between those of $\text{Sc}(\text{OTf})_3$ and $\text{Y}(\text{OTf})_3$ ($g_{\text{zz}} = 2.0349$, $\Delta E = 0.85 \text{ eV}$). Since Lewis acids with a ΔE value larger than 0.88 were presumed

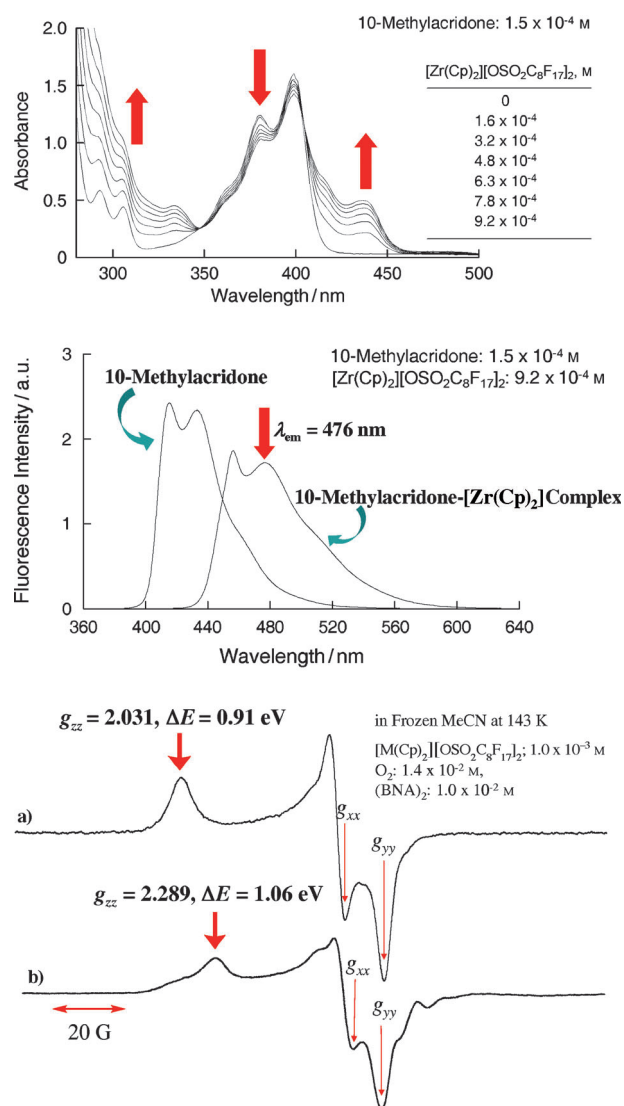


Figure 3. Top: UV/Vis spectral changes of complex formation between 10-methylacridone and **2a**. Middle: Fluorescence spectral changes of complex formation between 10-methylacridone and **2a**. Bottom: ESR spectra of a) $\text{O}_2^{\cdot-}$ -**2a** (**2a**) and b) $\text{O}_2^{\cdot-}$ -**2b** (**2b**).

to be capable for inducing carbon-carbon bond-forming reactions,^[14a] it is reasonable to expect that the Lewis acidity of **2a** and **2b** is high enough to trigger synthetically useful reactions. We also employed Hammett indicator method to determine the acidity of the complex **2a** and **2b**, and found both of them have relatively strong acidity with acid strength of $0.8 < H_0 \leq 3.3$ (H_0 being the Hammett acidity function). The characteristics of **2a** and **2b** stimulated us to evaluate its performance as a Lewis acid catalyst for carbonyl-group transformation reactions, such as the solvent-free Mannich reaction, the Mukaiyama aldol reaction, allylation of aldehydes, the Friedel-Crafts acylation of alkylaromatic ethers, and cyclootrimerization of ketones.

The Mannich reaction is one of the most useful carbonyl transformation reactions for the synthesis of nitrogen-containing compounds as well as an effective method for the

construction of C–C, C–N bonds.^[20] A proper control of the three components (unmodified ketones donor, amine, and aldehyde acceptor) of the Mannich reaction is challenging, because side reactions such as aldol reaction could lower the product yield. Impressive achievements have been made in Mannich reaction over various Lewis acid or Lewis base catalysts.^[21] However, aldol addition and condensation products were also observed, longer reaction times were needed, and the use of imine is “environmentally unfriendly” and not “atom economic”. Furthermore, the methods have disadvantage(s) such as low yield, poor selectivity, and use of organic solvent and/or need of strictly anhydrous reaction conditions.

It is highly desirable to develop catalytic systems that can affect organic reactions in solvent-free conditions with excellent efficiency and stereoselectivity. Despite the recent emphasis on solvent-free synthesis, reports on the Mannich reaction conducted in solvent-free conditions are few.^[22] Due to the fact that the Mannich reaction only needs a weak Lewis acidic catalyst, and with the unique characters of **2a** in mind, we performed the direct Mannich reaction in solvent-free conditions. As expected, high efficiency and chemoselectivity were obtained (Table 2).

Table 2. Product yields in Mannich reactions of aldehyde (**4a–e**) with amine (**5a–c**) and acetophenone (**6a**) catalyzed by **2a**.^[a]

$\text{R}^1\text{CHO} + \text{R}^2\text{NH}_2 + \text{Ph}-\text{C}(=\text{O})\text{Me} \xrightarrow[\text{RT, Solvent-Free, 5 min}]{\text{2a, 5.0 mol\%}} \text{Ph}-\text{C}(=\text{O})\text{CH}(\text{R}^1)\text{CH}_2\text{NH}(\text{R}^2)$				
Entry	R ¹	R ²	Product (7)	Yield [%]
1 ^[b]	Ph (4a)	Ph (5a)	7a	8
2	Ph (4a)	Ph (5a)	7a	97
3	<i>p</i> -MeC ₆ H ₄ (4b)	Ph (5a)	7b	95
4	<i>p</i> -ClC ₆ H ₄ (4c)	Ph (5a)	7c	99
5	<i>p</i> -CF ₃ C ₆ H ₄ (4d)	Ph (5a)	7d	99
6	<i>p</i> -O ₂ NC ₆ H ₄ (4e)	Ph (5a)	7e	99
7	Ph (4a)	<i>p</i> -MeC ₆ H ₄ (5b)	7f	99
8	Ph (4a)	<i>p</i> -O ₂ NC ₆ H ₄ (5c)	7g	96

[a] Catalyst **2a** (0.05 mmol); R¹CHO (**4**; 1.0 mmol); R²NH₂ (**5**; 1.0 mmol); acetophenone (**6a**; 1.0 mmol); solvent-free conditions; RT; 5 min, isolated yield. [b] No Catalyst, 120 min.

In order to demonstrate the excellent catalytic efficiency of **2a**, we examined direct Mannich reaction of different aldehydes with one equivalent of aniline and acetophenone in the presence of 5.0 mol% catalyst **2a**. Aromatic aldehydes with electron-donating and electron-withdrawing groups were employed (Table 2, entries 2–6). Despite variation of reaction rate, the yields are high. The aldehydes with electron-withdrawing groups (such as chloride and trifluoromethyl) in the phenyl plane exhibit higher reaction activity than the aldehydes with electron-donating groups (for example, methyl) (Table 2, entries 2–6). Two other amines were also examined with benzaldehyde and acetophenone in the presence of 5.0 mol% **2a** under solvent-free conditions (Table 2, entries 7 and 8). As expected, an -NO₂ group in

the *para*-position exhibits higher activity, owing to the large electron-withdrawing ability of -NO₂, which enhanced the nucleophilic ability of the amine in Mannich reaction, whereas that with a methyl group in the *para*-position shows lower activity, since the electron-donating ability of *p*-CH₃ reduced the nucleophilic ability of the amine in Mannich reaction. Without the catalyst, the reaction basically does not take place; only 8% yield of the desired product is obtained.

The allylation of aldehydes and the Mukaiyama aldol reaction mediated by a Lewis acid are among the most convenient processes for carbonyl-compound transformation in organic synthesis. The addition reactions are intrinsically efficient in the production of useful building blocks such as homoallylic alcohols^[23] and β-hydroxyl ketone or ester derivatives,^[24] because new stereogenic centers and new carbon–carbon bonds can be formed in a single operation. Several efficient Lewis acid catalysts that are based on boron, titanium, zirconium, copper, and so forth, have been reported. In most cases, temperatures of –20 to –78 °C and strictly anhydrous conditions are required.^[25] In the present investigation, we address these problems by fabricating the extremely air-stable metallocene perfluorooctanesulfonate catalysts **2a** and **2b**, and report the highly efficient catalytic activity over the catalyst in allylation and Mukaiyama aldol reactions of aldehydes.

The reactions of aldehydes (**4a–d, f–h**) with nucleophiles, such as tetraallyltin (**8**), ketene silyl acetals (**9**) were examined over **2a** and **2b** (Table 3). As expected, the reactions resulted in good yields of homoallyl alcohols (**10a–h**) and β-hydroxy ester (**11a–h**) derivatives in CH₃CN or Et₂O. A similar catalytic activity of complexes **2a** and **2b** was observed when aliphatic aldehydes and aromatic aldehydes with electron-donating or electron-withdrawing groups were investi-

Table 3. Product yields in reactions of aldehyde (**4**) with nucleophiles (**7**, **8**) catalyzed by **2a** and **2b**.^[a]

Reaction 1: $\text{R}-\text{CHO}$ (**4**) + $(\text{CH}_3)_2\text{C}=\text{CH}-\text{CH}_2\text{SnMe}_3$ (**8**) $\xrightarrow[\text{RT, CH}_3\text{CN, 1 h}]{\text{2a/2b, 5.0 mol\%}}$ $\text{R}-\text{CH}(\text{OH})-\text{CH}_2-\text{CH}(\text{CH}_3)_2$ (**10**)

Reaction 2: $\text{R}-\text{CHO}$ (**4**) + $(\text{CH}_3)_2\text{C}(\text{OSiMe}_3)=\text{CHOMe}$ (**9**) $\xrightarrow[0^\circ\text{C to RT, Et}_2\text{O, 6 h}]{\text{2a/2b, 5.0 mol\%}}$ $\text{R}-\text{CH}(\text{OH})-\text{C}(\text{CH}_3)_2\text{C}(=\text{O})\text{OMe}$ (**11**)

Entry	R (4)	Yield [%]					
		10 ^[a]	2a	2b	11 ^[b]	2a	2b
1	Ph (4a)	10a	94	82	11a	92	80
2	<i>p</i> -MeC ₆ H ₄ (4b)	10b	91	79	11b	92	81
3	<i>p</i> -MeOC ₆ H ₄ (4f)	10c	90	80	11c	93	80
4	<i>p</i> -ClC ₆ H ₄ (4c)	10d	93	82	11d	94	84
5	<i>p</i> -CF ₃ C ₆ H ₄ (4d)	10e	94	83	11e	96	85
6	PhCH=CH (4f)	10f	90	82	11f	90	80
7	PhCH ₂ CH ₂ (4g)	10g	93	82	11g	87	76
8	C ₇ H ₁₅ (4h)	10h	87	75	11h	83	70

[a] RCHO (**4**; 1.0 mmol); tetraallyltin (**8**; 0.3 mmol); **2a** or **2b** (0.05 mmol); CH₃CN (3.0 mL); 1 h, isolated yield. [b] RCHO (**4**; 1.0 mmol); ketene silyl acetals (**9**; 1.2 mmol); **2a** or **2b** (0.05 mmol); Et₂O (3.0 mL); RT, 6 h, isolated yield.

gated. It is worth noting that **2a** with a more appropriate Lewis acidity is better than **2b** for these two carbon–carbon forming reactions, since the nucleophiles **8** and **9** are sensitive to high Lewis acidic catalysts and easily decompose rather than react with the aldehyde (**4a–d, f–i**).

Because of the high tolerance of **2a** and **2b** towards hydrolysis, the solvents adopted in these reactions were used as received and were not subject to any kind of drying procedure. Usually a highly reactive reagent would cause poor chemoselectivity. For example, Grignard, lithium, and titanium reagents often fail to make discrimination between aldehydes and ketones. With **2a** and **2b**, however, we observed good chemoselectivity. Ketones were less reactive: the addition reaction of acetophenone (**6a**) with nucleophiles **8** and **9** did not occur at room temperature, but the corresponding homoallyl alcohol (**12**) was obtained in 87 or 70% yields at 65 °C for 24 h in the presence of **2a** or **2b**, respectively.

The Friedel–Crafts acylation of aromatic compounds is one of the most important reactions in organic chemistry.^[5a] Traditionally, AlCl₃ is used as a Lewis acid promoter, and stoichiometric amounts of AlCl₃ are needed due to the formation of stable adduct compound resulting from the interaction between the catalyst and the carbonyl oxygen of the ketone product. The compound Sc(OTf)₃ was applied in this reaction and a good result was obtained; however, the high price of Sc(OTf)₃ limits its further utilization.^[26] Hf(OTf)₄/LiClO₄ and NbCl₅/AgClO₄ were also reported as Friedel–Crafts acylation catalysts.^[27] However, larger equivalents of potentially explosive perchlorate salts have to be used as co-catalyst. Furthermore, most of these Lewis acids are air or moisture sensitive.

We assessed the **2b** (5.0 mol %) catalyst for the Friedel–Crafts acylation of structurally diverse alkyl aromatic ether with 2.0 equivalents of acetic chloride at room temperature in CH₃CN, and good-to-excellent product yields were obtained (Table 4). The electron-donating groups attached to the aromatic ring enhanced the reaction activity. As expected, this reaction showed high regioselectivity (*para*-isomer > 99%). In addition, the activity of AlCl₃ was markedly low under the present mild reaction conditions. No product was obtained in the absence of the catalyst. Thus, complex **2b**

Table 4. Product yields in reactions of Friedel–Crafts acylation of alkyl aromatic ether (**13**) catalyzed by **2b**.^[a]

Entry	Substrate (13)	Product (14)	Yield [%]
1	PhOMe (13a)	14a	70
2	PhOBu (13b)	14b	65
3 ^[b]	PhOBz (13c)	14c	63
4	<i>o</i> -MeC ₆ H ₄ OMe (13d)	14d	62
5	<i>o</i> -MeC ₆ H ₄ OBu (13e)	14e	60

[a] Substrate (**13**; 1.0 mmol); acetyl chloride (2.0 mmol); **2b** (0.05 mmol); CH₃CN (5 mL); RT, 4 h; isolated yield of *para*-substituted product. [b] 80 °C, 10 h.

can be considered to be an excellent catalyst in terms of good yields and *para*-regioselectivity in Friedel–Crafts acylation.

The cyclotrimerization reaction of ketones has provided a powerful strategy for the construction of polyaromatic compounds, such as 1,3,5-trisubstituted benzene moieties or hexasubstituted (trisannulated) benzenes.^[28] The common approach for preparation of polyaromatic compounds is the cyclotrimerization of ketones. The reported methods to induce cyclotrimerization of ketones involve using strong proton acids and metallic halides as Lewis acids as promoters. Other approaches include cyclotrimerization of alkynes in the presence of organometallic reagents, for example, the Pd-, Ir- and Ru-catalyzed multifold sequential Suzuki–Miyaura reaction between oligohalarenes with organometallic partners.^[29] However, most of these procedures are often complicated by inefficient, harsh reaction conditions, lack of regioselectivity, formation of undesirable 1,2,4-trisubstituted by-products, and requirement of expensive or specialized organometallic catalysts. Moreover, most of these Lewis acids are highly sensitive to air, and cannot be reused. Thus, there is a need to develop an air-stable, highly efficient and recyclable catalyst for the cyclotrimerization of ketones.

We assessed complex **2a** (5.0 mol %) as a catalyst for the cyclotrimerization of structurally diverse ketones in refluxing toluene, and good-to-excellent yields were obtained (Table 5). All the results showed that the reaction proceeded well for a variety of acetophenones (Table 5, entries 1–6).

Table 5. Yields of 1,3,5-trisubstituted benzenes synthesized from acetophenones catalyzed by **2a** in refluxing toluene.^[a]

Entry	RCOR'	<i>t</i> [h]	Product (15)	Yield [%] ^[b]
1	PhC(O)CH ₃ (6a)	3	15a	98
2	<i>p</i> -Cl-C ₆ H ₄ C(O)CH ₃ (6b)	6	15b	89
3	<i>p</i> -Br-C ₆ H ₄ C(O)CH ₃ (6c)	6	15c	85
4	<i>p</i> -Me-C ₆ H ₄ C(O)CH ₃ (6d)	3.5	15d	95
5	<i>p</i> -MeO-C ₆ H ₄ C(O)CH ₃ (6e)	3	15e	93
6	<i>p</i> -NO ₂ -C ₆ H ₄ C(O)CH ₃ (6f)	24	15f	78
7	cyclohexanone (6g)	3	15g	85

[a] Ketone (1.0 mmol); **2a** (0.05 mmol); toluene (3.0 mL); reflux. [b] Isolated yield.

The acetophenones with electron-donating groups in the *para*-position of the phenyl plane (e.g., methyl and methoxyl) exhibited higher reactivity in the cyclotrimerization reaction than that with electron-withdrawing groups (e.g., Cl, Br, and NO₂). It can be deduced that the electron-donating groups enhanced the density of super-conjugated π electrons in the phenyl plane and carbonyl group, leading to a stronger interaction of carbonyl group of the acetophenones with the zirconium atom of complex **2a**. We then examined the cyclotrimerization reaction of cyclohexanone (Table 5,

entry 7). In this case, it gave the desired triannulated benzene (**15g**) in yields of 85% for 3 h in refluxing toluene. This fact illustrates that this method can be also applied in cyclotrimerization of aliphatic ketones.

To show the advantage of metallocene perfluorooctanesulfonates (**2a**, **2b**) over $[\text{Zr}(\text{Cp})_2]\text{Cl}_2$ (**1a**), and $[\text{Zr}(\text{Cp})_2][\text{OSO}_2\text{CF}_3]_2$ (**3**), the catalytic activities of **2a/2b**, **1a** and a control cationic species were assessed for the Mannich reaction (**4a**+**5a**+**6a**→**7a**), allylation (**4a**+**8**→**10a**), the Mukaiyama aldol reactions (**3a**+**8**→**10a**), and for the Friedel–Crafts acylation (**13a**+**AcCl**→**14a**). The yields of the respective reactions are compiled in Table 6. High yields were constantly attained over **2a/2b**, while the other cata-

Table 6. Yields in reactions of carbonyl compounds (En) with nucleophiles (Nu) catalyzed by **2a/2b**, **1a**, and **3**.^[a]

Entry	En	Nu	Product	Yield [%]		
				2a/2b	1a	3 ^[a]
1 ^[a]	4a + 5a	6a	7a	97	15	95
2 ^[b]	4a	8	10a	94	14	89
3 ^[c]	4a	9	11a	92	30	93
4 ^[d]	AcCl	13a	14a	70	12	51 ^[e]
5 ^[f]	6a		15a	98	–	–

[a] **4a** (1.0 mmol); **5a** (1.0 mmol); **6a** (1.0 mmol); **2a/2b/1a/3** (0.05 mmol); RT, 5 min; isolated yield. [b] **4a** (1.0 mmol); **8** (0.3 mmol); **2a/2b/1a/3** (0.05 mmol); CH_3CN (3.0 mL); RT, 1 h; isolated yield. [c] **4a** (1.0 mmol); **9** (1.2 mmol); **2a/2b/1a/3** (0.05 mmol); Et_2O (3.0 mL); 0°C to RT, 6 h; isolated yield. [d] **4a** (1.0 mmol); **AcCl** (2.0 mmol); **2a/2b/1a/3** (0.05 mmol); CH_3CN (5.0 mL); RT, 4 h; isolated yield of *para*-isomer. [e] Mixture of *o*- and *p*-isomers. [f] **6a** (1.0 mmol); **2a/2b** (0.05 mmol); toluene (3.0 mL); reflux, isolated yield.

lysts showed much lower yields, plausibly due to their lower Lewis acidity and/or more air- and moisture-sensitive features. However, $\text{CF}_3\text{SO}_3\text{H}$, which is considered as a powerful catalyst by Hollis and Bosnich, can be formed through facile hydrolysis of $[\text{Zr}(\text{Cp})_2][\text{OSO}_2\text{CF}_3]_2$ (**3**).^[10] and there is enhancement of catalytic activity as a result. It is worth pointing out that only a 35% yield of homoallyl alcohol (**10a**) and no desired aldolate products (**11a**) were obtained in the absence of catalyst under similar conditions, an explicit indication of the effectiveness of the catalysts. With regards to metal sulfonate catalysis, it must be taken into account that a sulfonic acid arising in situ during the reaction may possibly work as an active species.^[30] Thus, the reaction of **4a** with **8** or **9** was conducted in the presence of $\text{C}_8\text{F}_{17}\text{SO}_3\text{H}$ (5.0 mol %). The reaction was rather complex because many spots were detected in TLC analysis, and only 17–19% yield of desired products were reported.

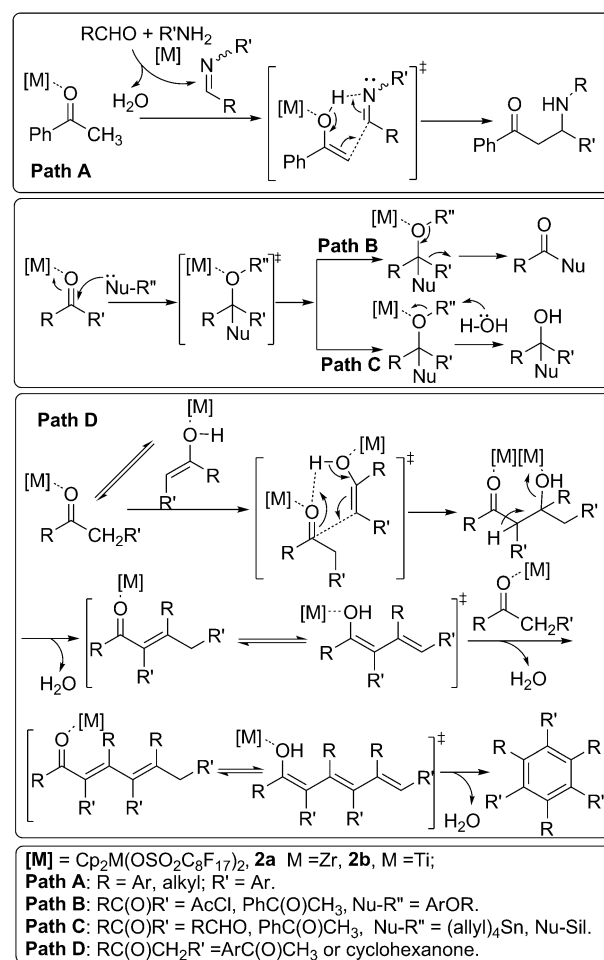
To test the reusability of the catalyst and reproducibility of catalytic performance, **2a** was subjected to several cycles of the Mannich reaction (**4a**+**5a**+**6a**→**7a**), allylation (**4a**+**8**→**10a**) and the Mukaiyama aldol reactions (**4a**+**9**→**11a**) (Table 7). The detected change in product yield was minimal in a trial of five cycles, indicating that the catalyst is stable and suitable for reuse. Therefore, complex **2a** has the advantages of being high in activity, selectivity, stability, and reusability.

Table 7. Yields of Mannich reaction (**4a**+**5a**+**6a**→**7a**), allylation (**4a**+**8**→**10a**) and Mukaiyama-aldol reactions (**4a**+**9**→**11a**) catalyzed by recovered catalyst **2a**.^[a]

Cycle	Yield [%] ^[b]		Cat. [%] ^[c]		Yield [%] ^[b]		Cat. [%] ^[c]	
	4a + 5a + 6a → 7a		4a + 8 → 10a		4a + 9 → 11a		4a + 9 → 11a	
1	97	99	94	99	92	99		
2	96	97	94	98	90	98		
3	97	99	95	97	91	96		
4	98	98	94	98	91	97		
5	96	96	93	97	90	96		

[a] **4a** (10 mmol); **5a** (10 mmol) and **6a** (10 mmol) or **7** (0.3 mmol) or **8** (1.2 mmol); **2a** (0.5 mmol); RT. [b] Isolated yield of desired product. [c] Isolated yield of recovered catalyst.

According to the findings reported so far,^[15] the mechanism of the nucleophilic reaction of carbonyl compounds, such as acetic chloride, aldehydes, or acetophenone in the presence of solid **2a/2b** is postulated (Scheme 2). When solid **2a/2b** is added to the reaction solution, the zirconium or titanium cationic groups dissociate occur immediately. At this stage, there is frequent intra- and intermolecular exchange of substrate and organic solvent/other substrate. The



Scheme 2. A proposed mechanism of reaction of carbonyl compounds transformation catalyzed by **2a** or **2b**.

carbonyl compound coordinates with the metal cations and is activated. **Path A:** The Mannich reaction of the amine (**5**) component with the activated non-enolizable carbonyl compound (**4**) to give a hemiaminal, which after losing a molecule of water to give the electrophilic intermediate ($\text{ArCH}=\text{NAr}$, confirmed by NMR spectroscopy), then reacts with the enolized carbonyl compound (**6**, nucleophile) at its α -carbon atom in an aldol-type reaction to give rise to the Mannich base (**7**). Due to the solvent-free condition, the reaction is much faster than that of the other three reactions. **Path B:** The nucleophilicities of alkyl aromatic ether (**13**) attack the activated carbonyl compounds (acetic chloride) to produce the desired *para*-alkoxyaromatic ketone (**14**), while in **Path C** nucleophilicities such as tetrallytin (**8**) and ketene silyl acetals (**9**) attack the activated carbonyl compounds [aldehydes (**4**) or ketones (**6**)] to produce the corresponding homoallyl alcohols (**10**) and β -hydroxyl ester (**11**) derivatives. **Path D:** This pathway involves the in situ formation of the central benzene moiety (**15**) by a triple aldolization and dehydration of three equivalents of adolizable ketones (**6**). The catalysts **2a/2b** are renewed with the intake of solvating ligand or substrate. At the present stage of investigation, we are still not sure of the transient intermediates that are possibly formed during the reaction. Current work is still being conducted for the understanding of this aspect.

Conclusion

In summary, we have successfully synthesized and characterized the cationic mononuclear zirconocene and titanocene perfluorooctanesulfonate complexes. They are strongly acidic and air-stable, and show highly catalytic activity in the Mannich reaction under solvent-free conditions, allylation of aldehydes, Mukaiyama aldol reaction, and Friedel–Crafts acylation of alkyl aryl ethers, and could be reused. On account of their excellent catalytic efficiency as well as reusability, the complexes will find broad catalytic applications in organic synthesis.

Experimental Section

General: The chemicals were purchased from Aldrich. Co. as well as from other chemical companies, such as TCI (Shanghai), Alfa Aesar (Tianjing), and Sinopharm Chemical Reagent, and were used as received unless otherwise specified. The preparation of catalyst was carried out under nitrogen atmosphere with freshly distilled solvents unless otherwise noted. THF was distilled from sodium/benzophenone, while CH_3CN was distilled from CaH_2 . Acetone was refluxed with KMnO_4 for 4 h and distilled, and then dried with K_2CO_3 ; after that, it was distilled and kept inside a dry box. The catalytic reactions were carried out in air, and the solvents were used as received. NMR spectra were recorded at 25°C on an INOVA-400M spectrometer (USA) calibrated with tetramethylsilane (TMS) as an internal reference. Elemental analyses were performed on a VARIO EL III instrument (Germany). Conductivity was measured on a REX conductivity meter DDS-307 (China). TG-DSC analysis was performed on a NETZSCH-STA-449C instrument. X-ray single crystal dif-

fraction analysis was performed on a SMART-APEX diffractometer in Shanghai Institute Organic Chemistry, China Academy of Science. The Lewis acidity estimation was performed by means of ESR, UV/Vis and fluorescence spectroscopy in Okayama University of Science and Osaka University (Japan). The acidity was measured by Hammett indicator method as described previously.^[15a] Acid strength was expressed in terms of Hammett acidity function (H_0) as scaled by $\text{p}K_a$ value of the indicators.

Preparation of $[\text{M}(\text{Cp})_2][\text{OSO}_2\text{C}_8\text{F}_{17}]_2$ ($\text{M}=\text{Zr}$, **2a**; $\text{M}=\text{Ti}$, **2b**)

Path A: A solution of $\text{AgOSO}_2\text{C}_8\text{F}_{17}$ ^[14a] (1.21 g, 2.0 mmol) in THF (10 mL) was added to a solution of $[\text{M}(\text{Cp})_2]\text{Cl}_2$ (1.0 mmol) in THF (20 mL). After the mixture was stirred at room temperature for an hour, it was filtered. Dry *n*-hexane (40 mL) was laid over the colorless filtrate, and after keeping in the refrigerator for 24 h, the colorless crystal was collected. ($\text{M}=\text{Zr}$, **2a**·3H₂O·THF, 0.794 g, 65%; $\text{M}=\text{Ti}$, **2b**·2H₂O·THF, 693 mg, 54%).

Path B: A solution of $\text{C}_8\text{F}_{17}\text{SO}_3\text{H}$ (1.0 g, 2.0 mmol) in THF (10 mL) was added to a solution of $[\text{M}(\text{Cp})_2][\text{Bu}]_2$ in THF (20 mL) prepared from $[\text{M}(\text{Cp})_2]\text{Cl}_2$ (1 mmol) with *n*BuLi (1 mL, 1 M) at -78°C for 1 h. After the mixture was stirred at -78°C to room temperature for an hour, it was evaporated. The residue was dissolved with Et_2O , filtrated, evaporated, then the resulted residue was dissolved with THF (20 mL). Dry *n*-hexane (40 mL) was laid over the colorless filtrate, and after keeping in the refrigerator for 24 h, the colorless crystal was collected ($\text{M}=\text{Zr}$, **2a**·3H₂O·THF, 1.18 g, 97%; $\text{M}=\text{Ti}$, **2b**·2H₂O·THF, 1.11 g, 87%).

Data for 2a·3H₂O·THF: M.p. 133–136°C; ¹H NMR (400 MHz, TMS, 25°C, CD₃CN): δ =6.65 (s, 10H; Cp), 3.78 (s, 4H; THF), 2.37 (s, *n*H; H₂O), 1.93 ppm (t, J =6.4 Hz, 4H; THF); ¹⁹F NMR (376 MHz, CD₃CN): δ =−79.96 to −79.00 (t, J =9.0 Hz, 3F; CF₃−), −112.79 (s, 2F; −CF₂−), −118.66 (s, 2F; −CF₂−), −119.62 to −119.81 (d, J =71.4 Hz, 6F; −(CF₂)₃−), −120.65 (s, 2F; −CF₂−), −124.03 to −124.13 ppm (m, 2F; −CF₂−); elemental analysis calcd (%) for **2a** (C₂₆H₁₀F₃₄O₆S₂Zr) after pumping for a week: C 25.60, H 0.83; found: C 25.67, H 0.82; elemental analysis calcd (%) for **2a**·4H₂O (C₂₆H₁₈F₃₄O₁₀S₂Zr) after standing in open air for 2 days: C 24.18, H 1.40; found: C 24.34, H 1.33; X-ray data: formula: C₃₀H₂₄F₃₄O₁₀S₂Zr; prismatic, colorless, M_r =1345.83, ρ_{calcd} =1.905 Mg m^{−3}, triclinic, $P\bar{1}$, a =9.9295(13), b =11.9551(16), c =20.269(3) Å, α =82.833(3), β =79.491(3), γ =87.397(3)°, V =2346.7(5) Å³, Z =2, θ =1.7–25.5°, 0.50×0.24×0.21 mm, T =293(2) K, measured reflections/independent reflections 12436/8583, R_{int} =0.104, h =−12–11, k =−14–11, l =−24–22, R_1 =0.095, wR_2 =0.277, S =0.95.

Data for 2b·2H₂O·THF: M.p. 206–210°C; ¹H NMR (400 MHz, CD₃CN, TMS): δ =6.95 (s, 10H; Cp), 3.62–3.67 (m, 4H; THF), 3.56 (s, *n*H; H₂O), 1.78–1.83 ppm (m, 4H; THF). ¹⁹F NMR (376 MHz, 25°C, CD₃CN): δ =−79.66 to −79.75 (m, 3F; CF₃−), −113.28 to −113.38 (t, J =16.5 Hz, 2F; −CF₂−), −119.36 to −119.43 (t, J =3.8 Hz, 2F; −CF₂−), −120.34 to −120.54 (m, 6F; −(CF₂)₃−), −121.36 to −121.41 (t, J =8.6 Hz, 2F; −CF₂−), −124.72 to −124.87 (m, 2F; −CF₂−); elemental analysis calcd (%) for **2b** (C₂₆H₁₀F₃₄O₆S₂Ti) after pumping for a week: C 26.55, H 0.86; found: C 26.76, H 0.86; elemental analysis calcd (%) for **2b**·4H₂O (C₂₆H₁₈F₃₄O₁₀S₂Ti) after standing in open air for 2 days: C 25.02, H 1.45; found: C 25.28, H 1.42.

Determination of hydration number: Molecular sieves (4 Å, 11.0 g, dried at 355°C in a muffle furnace for 5 h) were added to CD₃CN (25.0 g), and the mixture was kept under nitrogen atmosphere overnight. In this CD₃CN, water was not detected by ¹H NMR spectroscopy. The dehydrated CD₃CN was added to a freshly prepared (**2a**·3H₂O·THF) (10.0 mg, recrystallized from THF/hexane (3:4) followed by drying under reduced pressure for a week), and the solution was analyzed by ¹H NMR spectroscopy. Then the sample was subjected to elemental analysis.

UV/Vis spectra detection of the 10-methylacridone/2a complex: The formation of metal ion complexes with 10-methylacridone was examined from the change in the UV/Vis spectra in the presence of various concentrations of metal ions (M^{n+}) by using a Hewlett–Packard 8452 A diode array spectrophotometer. The formation constants were determined from linear plots of $(A-A_0)^{-1}$ versus $[\text{M}^{n+}]^{-1}$, in which A and A_0 are the absorbance at λ_{max} in the presence of the metal ion and the absorbance at the same wavelength in the absence of the metal ion, respectively.

Fluorescence spectra detection of the 10-methylacridone/2a complex:

The fluorescence measurement of 10-methylacridone/2a complex was performed on a spectrofluorophotometer. The excitation wavelength of 10-methylacridone/2a or 2b complexes was 413 nm in MeCN. The MeCN solutions were deaerated by argon purging for 7 min prior to the measurements.

ESR detection of $O_2^-/2a$ or 2b complex: A quartz ESR tube (4.5 mm i.d.) containing an oxygen-saturated solution of dimeric 1-benzyl-1,4-dihydropyridine (BNA)₂ (1.0×10^{-2} M) and 2a·3H₂O·THF or 2b·2H₂O·THF (1.0×10^{-3} M) in MeCN was irradiated in the cavity of the ESR spectrometer with the focused light of a 1000 W high-pressure Hg lamp through an aqueous filter. Dimeric (BNA)₂, which was used as an electron donor to reduce oxygen, was prepared according to the literature. The ESR spectra of $O_2^-/2a$ or 2b complex in frozen MeCN were measured at 143 K with a JEOL X-band apparatus under nonsaturating microwave power conditions. The *g* values were calibrated precisely with a Mn²⁺ marker, which was used as a reference.

Crystal data refinements details: Refinement of F^2 was against all reflections. The weighted *R* factor (*wR*) and goodness of fit (*S*) were based on F^2 , conventional *R* factors (*R*) were based on *F*, with *F* set to zero for negative F^2 . The threshold expression of $F^2 > 2\sigma(F^2)$ was used only for calculating *R* factors(gt) and so forth and was not relevant to the choice of reflections for refinement. *R* factors based on F^2 were statistically about twice as large as those based on *F*, and *R* factors based on all data were even larger. Data collection: Bruker SMART; cell refinement: Bruker SMART; data reduction: Bruker SHELXTL; program used to solve structure: SHELXS97;^[31] program used to refine structure: SHELXL97;^[31] molecular graphics: Bruker SHELXTL;^[31] software used to prepare material for publication: Bruker SHELXTL.^[31] CCDC-631296 (2a·3H₂O·THF) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Typical procedure for Mannich reaction of benzaldehyde (4a) with aniline (5a) and acetophenone (6a) catalyzed by 2a: Catalyst 2a (61 mg, 0.05 mmol), PhCHO (106 mg, 1.0 mmol), PhNH₂ (93 mg, 1.0 mmol), and acetophenone (120 mg, 1.0 mmol) were placed in a 50 mL round-bottomed flask. Then the mixture was stirred for 1 h under the TLC analysis until the PhCHO and PhNH₂, as well as the intermediate *N*-benzylideneaniline obtained from PhCHO and PhNH₂, were consumed completely. Then the solvents of the resulting mixture were removed by evaporation in vacuum, and the residue was dissolved in CH₂Cl₂ and filtered. The filtrate was subject to volatilization at room temperature and the colorless crystals were obtained that were suitable for ¹H NMR measurements. An alternative workup procedure is as follows: the mixture was extracted with CH₂Cl₂ (10 mL×3), and the resulting residue was subject to column chromatograph (petroleum ether/ethyl acetate=5:1). Yield, 291 mg, 97%. Aldehydes and amines such as 4a–g, 5a–c and nucleophiles acetophenone 6a are commercially available.

Typical procedure for allylation of benzaldehyde (4a) with tetrallyltin (8) catalyzed by 2a: Complex 2a (61 mg, 0.05 mmol) was added to a solution of benzaldehyde (4a; 1.0 mmol) in CH₃CN (3.0 mL). Tetrallyltin (8; 0.3 mmol) was then added to the mixture at room temperature. After the mixture was stirred at room temperature for an hour and monitored by TLC, it was evaporated in vacuum at room temperature. *n*-Hexane (10 mL×3) was added to the residue; the catalyst precipitated and was recovered by filtration for the next reaction cycle. The combined *n*-hexane solution was concentrated, and then MeOH and HCl (aq) was added and stirred for 15 min. NaHCO₃ (aq) was added for neutralization. After the mixture was subject to evaporation, the as-obtained solids were dissolved in AcOEt and water. After extraction with AcOEt (three times), the organic layer was washed with NaCl (aq) and dried over MgSO₄. After evaporation, GLC yield was measured. Alternatively, the residue was subject to silica gel column chromatography (petroleum ether/ethyl acetate=8:1) and 10a was obtained as a colorless oil (139 mg, isolated yield 94%). Aldehydes such as 4a–d and 4f–h and nucleophiles tetraallyltin (8) are commercially available.

Typical procedure for Mukaiyama-aldol reaction of benzaldehyde (4a) with ketene silyl acetals (9) catalyzed by 2a: Complex 2a (61 mg, 0.05 mmol) and (1-methoxy-2-methylprop-1-enyloxy)trimethylsilane (9; 208 mg, 1.2 mmol) were added to a solution of benzaldehyde (4a; 1.0 mmol) in diethyl ether (3.0 mL) at 0°C. Then the temperature was raised to room temperature slowly. After the mixture was stirred at room temperature for 6 h and monitored by TLC, it was subject to evaporation in vacuum at room temperature, the residue was dissolved in *n*-hexane (10 mL×3) and the catalyst was collected by means of filtration for the next cycle of reaction. To the combined hexane solution, MeOH and HCl (aq) were added and the mixture was stirred for 15 min. NaHCO₃ (aq) was added for neutralization. The mixture was subject to evaporation, and the solids thus obtained were dissolved in AcOEt and water. After extraction with AcOEt (three times), the organic layer was washed with NaCl (aq) and dried over MgSO₄. After evaporation, the GLC yield was measured. Alternatively, the residue was subject to silica gel column chromatography (petroleum ether/ethyl acetate=10:1), colorless crystals of 11a were obtained (191 mg, isolated yield 92%). Aldehydes such as 4a–d, and 4f–h and nucleophiles silica enol ether 9 are commercially available.

Typical procedure for Friedel–Crafts acylation of anisole (13a) with acetic chloride catalyzed by 2a: Anisole (13a) (108 mg, 1.0 mmol) was placed in a 50 mL round-bottomed flask and a solution of catalyst (61 mg, 0.05 mmol) in CH₃CN (5.0 mL) and acetic chloride (157 mg, 2.0 mmol) was added through a syringe. Then the mixture was stirred at room temperature for 4 h. After that, the mixture was subject to silica gel column chromatograph; the Friedel–Crafts acylation product (14a) was obtained: 105 mg, isolated yield 70%. Alkyl aryl ethers 13a–e and nucleophile acetic chloride are commercially available.

All products have been reported, and the experimental details and ¹H NMR spectra data of the products can be found in the Supporting Information.

Acknowledgements

This work was partially supported by the National Natural Science Foundation of China (21172061, 21003040, and 20973056). We thank the helpful discussion of Profs. J. Otera, A. Orita (Okayama University of Science), C.-T. Au, and W.-Y. Wong (Hong Kong Baptist University). We also thank Prof. S. Fukuzumi for the Lewis acidity estimation of 2a and 2b.

- [1] a) A. Corma, H. Garcia, *Chem. Rev.* **2002**, *102*, 3837–3892; b) A. Corma, H. Garcia, *Chem. Rev.* **2003**, *103*, 4307–4365.
- [2] a) K. Juhl, N. Gathergood, K. A. Jorgensen, *Angew. Chem.* **2001**, *113*, 3083–3085; *Angew. Chem. Int. Ed.* **2001**, *40*, 2995–2997; b) S. Kobayashi, R. Matsubara, Y. Nakamura, H. Kitagawa, M. Sugiura, *J. Am. Chem. Soc.* **2003**, *125*, 2507–2515.
- [3] a) K. Shibatomi, *Synthesis* **2010**, 2679–2702; b) C. Pan, Z. Wang, *Coord. Chem. Rev.* **2008**, *252*, 736–750; c) R. B. Kargbo, G. R. Cook, *Curr. Org. Chem.* **2007**, *11*, 1287–1309.
- [4] T. D. Machajewski, C. H. Wong, *Angew. Chem.* **2000**, *112*, 1406–1430; *Angew. Chem. Int. Ed.* **2000**, *39*, 1352–1374.
- [5] a) K. Binnemans, *Chem. Rev.* **2007**, *107*, 2592–2614; b) A. Corma, H. Garcia, *Adv. Synth. Catal.* **2006**, *348*, 1391–1412; c) H. Gaspard-Illoughmane, C. Le Roux, *Eur. J. Org. Chem.* **2004**, 2517–2532.
- [6] a) Y. Zhao, J. Li, C. Li, K. Yin, D. Ye, X. Jia, *Green Chem.* **2010**, *12*, 1370–1372; b) W.-B. Yi, C. Cai, X. Wang, *J. Fluorine Chem.* **2007**, *128*, 919–924; c) X. B. Jing, F. Xu, Q. H. Zhu, X. F. Ren, C. G. Yan, L. Wang, J. R. Wang, *Synth. Commun.* **2005**, *35*, 3167–3171; d) I. Amer, H. Schumann, V. Ravindar, W. Baidossi, N. Goren, J. Blum, *J. Mol. Catal.* **1993**, *85*, 163–171.
- [7] a) M. North, F. Pizzato, P. Villuendas, *ChemSusChem* **2009**, *2*, 862–865; b) A. A. Kiss, A. C. Dimian, G. Rothenberg, *Adv. Synth. Catal.* **2006**, *348*, 75–81; c) R. A. Sheldon, *Green Chem.* **2005**, *7*, 267–278.

- [8] a) Y. X. Chen, C. L. Stern, S. T. Yang, T. J. Marks, *J. Am. Chem. Soc.* **1996**, *118*, 12451–12452; b) L. Jia, X. M. Yang, C. Stern, T. J. Marks, *Organometallics* **1994**, *13*, 3755–3757; c) A. Decken, E. G. Ilyin, H. D. B. Jenkins, G. B. Nikiforov, J. Passmore, *Dalton Trans.* **2005**, 3039–3050; d) R. Qiu, G. Zhang, X. Xu, K. Zou, L. Shao, D. Fang, Y. Li, A. Orita, R. Saijo, H. Mineyama, T. Suenobu, S. Fukuzumi, D. An, J. Otera, *J. Organomet. Chem.* **2009**, *694*, 1524–1528.
- [9] a) W. Odenkirk, B. Bosnich, *J. Chem. Soc. Chem. Commun.* **1995**, 1181–1182; b) T. K. Hollis, N. P. Robinson, B. Bosnich, *Organometallics* **1992**, *11*, 2745–2748; c) W. Odenkirk, A. L. Rheingold, B. Bosnich, *J. Am. Chem. Soc.* **1992**, *114*, 6392–6398; d) T. K. Hollis, N. P. Robinson, B. Bosnich, *J. Am. Chem. Soc.* **1992**, *114*, 5464–5466.
- [10] T. K. Hollis, B. Bosnich, *J. Am. Chem. Soc.* **1995**, *117*, 4570–4581.
- [11] a) K. Ohmori, K. Hatakeyama, H. Ohrai, K. Suzuki, *Tetrahedron* **2004**, *60*, 1365–1373; b) M. I. Barrera, R. Echarri, S. Castillon, *Synlett* **1996**, 675–676; c) M. I. Matheu, R. Echarri, S. Castillon, *Tetrahedron Lett.* **1993**, *34*, 2361–2364; d) M. I. Matheu, R. Echarri, S. Castillon, *Tetrahedron Lett.* **1992**, *33*, 1093–1096.
- [12] T. K. Hollis, N. P. Robinson, B. Bosnich, *Tetrahedron Lett.* **1992**, *33*, 6423–6426.
- [13] a) H. Kuyama, T. Nukada, Y. Ito, Y. Nakahara, T. Ogawa, *Carbohydr. Res.* **1995**, *268*, C1; b) T. Matsumoto, T. Hosoya, K. Suzuki, *Synlett* **1991**, 709; c) P. Wipf, J. T. Reeves, *J. Org. Chem.* **2001**, *66*, 7910–7914.
- [14] a) D. L. An, Z. Peng, A. Orita, A. Kurita, S. Man-e, K. Ohkubo, X. Li, S. Fukuzumi, J. Otera, *Chem. Eur. J.* **2006**, *12*, 1642–1647; b) C. Cai, W.-B. Yi, W. Zhang, M.-G. Shen, M. Hong, L.-Y. Zeng, *Mol. Diversity* **2009**, *13*, 209–239; c) T. Hanamoto, Y. Sugimoto, T. Z. Jin, J. Inanaga, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 1421–1426; d) W.-B. Yi, C. Cai, *J. Fluorine Chem.* **2008**, *129*, 524–528.
- [15] a) R. Qiu, G. Zhang, Y. Zhu, X. Xu, L. Shao, Y. Li, D. An, S. Yin, *Chem. Eur. J.* **2009**, *15*, 6488–6494; b) R. Qiu, X. Xu, Y. Li, G. Zhang, L. Shao, D. An, S. Yin, *Chem. Commun.* **2009**, 1679–1681; c) R. Qiu, Y. Zhu, X. Xu, Y. Li, L. Shao, X. Ren, X. Cai, D. An, S. Yin, *Catal. Commun.* **2009**, *10*, 1889–1892; d) R. Qiu, Y. Qiu, S. Yin, X. Xu, S. Luo, C.-T. Au, W.-Y. Wong, S. Shimada, *Adv. Synth. Catal.* **2010**, *352*, 153–162; e) R. Qiu, S. Yin, X. Zhang, J. Xia, X. Xu and S. Luo, *Chem. Commun.* **2009**, 4759–4761; f) R. Qiu, Y. Qiu, S. Yin, X. Song, Z. Meng, X. Xu, X. Zhang, S. Luo, C.-T. Au, W.-Y. Wong, *Green Chem.* **2010**, *12*, 1767–1771; g) R. Qiu, G. Zhang, X. Ren, X. Xu, R. Yang, S. Luo, S. Yin, *J. Organomet. Chem.* **2010**, *695*, 1182–1188; h) J. Xia, R. Qiu, S. Yin, X. Zhang, S. Luo, C.-T. Au, K. Xia, W.-Y. Wong, *J. Organomet. Chem.* **2010**, *695*, 1487–1492; i) R. Qiu, S. Yin, X. Song, Z. Meng, Y. Qiu, N. Tan, X. Xu, S. Luo, F.-R. Dai, C.-T. Au, W.-Y. Wong, *Dalton Trans.* **2011**, *40*, 9482–9489; j) R. Qiu, Z. Meng, S. Yin, X. Song, N. Tan, Y. Zhou, K. Yu, X. Xu, S. Luo, C.-T. Au, W.-Y. Wong, *ChemPlusChem*, **2012**, DOI: 10.1002/cplu.201200030.
- [16] W. Lasser, U. Thewalt, *J. Organomet. Chem.* **1986**, *311*, 69–75.
- [17] U. Thewalt, L. Wiltrand, *J. Organomet. Chem.* **1984**, *276*, 341–348.
- [18] S. Fukuzumi, K. Ohkubo, *J. Am. Chem. Soc.* **2002**, *124*, 10270–10271.
- [19] a) S. Fukuzumi, K. Ohkubo, *Chem. Eur. J.* **2000**, *6*, 4532–4535; b) K. Ohkubo, S. C. Menon, A. Orita, J. Otera, S. Fukuzumi, *J. Org. Chem.* **2003**, *68*, 4720–4726.
- [20] a) K. Mikami, S. Fustero, M. Sanchez-Rosello, J. Luis Acena, V. Soloshonok, A. Sorochinsky, *Synthesis* **2011**, 3045–3079; b) G. Della Sala, A. Russo, A. Lattanzi, *Curr. Org. Chem.* **2011**, *15*, 2147–2183; c) A. Bartoli, F. Rodier, L. Commeiras, J.-L. Parrain, G. Chouraiqui, *Nat. Prod. Rep.* **2011**, *28*, 763–782; d) B. Weiner, W. Szymanski, D. B. Janssen, A. J. Minnaard, B. L. Feringa, *Chem. Soc. Rev.* **2010**, *39*, 1656–1691.
- [21] a) B. M. Trost, J. Jaratjaroonpong, V. Reutrakul, *J. Am. Chem. Soc.* **2006**, *128*, 2778–2779; b) B. M. Trost, L. R. Terrell, *J. Am. Chem. Soc.* **2003**, *125*, 338–339; c) J. W. Yang, C. Chandler, M. Stadler, D. Kampen, B. List, *Nature* **2008**, *452*, 453–455; d) J. W. Yang, M. Stadler, B. List, *Nat. Protoc.* **2007**, *2*, 1937–1942; f) B. List, *Acc. Chem. Res.* **2004**, *37*, 548–557; e) T. B. Poulsen, C. Alemparte, S. Saaby, M. Bella, K. A. Jørgensen, *Angew. Chem.* **2005**, *117*, 2956–2959; *Angew. Chem. Int. Ed.* **2005**, *44*, 2896–2899.
- [22] M. A. P. Martins, C. P. Frizzo, D. N. Moreira, L. Buriol, P. Machado, *Chem. Rev.* **2009**, *109*, 4140–4182.
- [23] a) Y. Nagano, A. Orita, J. Otera, *Adv. Synth. Catal.* **2003**, *345*, 643–646; b) P. Sreekanth, S.-W. Kim, T. Hyeon, B. M. Kim, *Adv. Synth. Catal.* **2003**, *345*, 936–938; c) A. Yanagisawa, H. Inoue, M. Morodome, H. Yamamoto, *J. Am. Chem. Soc.* **1993**, *115*, 10356–10357; d) X. Zhang, D. H. Chen, X. H. Liu, X. M. Feng, *J. Org. Chem.* **2007**, *72*, 5227–5233.
- [24] a) H. Ishitani, Y. Yamashita, H. Shimizu, S. Kobayashi, *J. Am. Chem. Soc.* **2000**, *122*, 5403–5404; b) S. Kobayashi, M. Ueno, S. Saito, Y. Mizuki, H. Ishitani, Y. Yamashita, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5476–5481; c) J. J. Song, Z. Tan, J. T. Reeves, N. K. Yee, C. H. Senanayake, *Org. Lett.* **2007**, *9*, 1013–1016; d) M. Takeuchi, R. Akiyama, S. Kobayashi, *J. Am. Chem. Soc.* **2005**, *127*, 13096–13097.
- [25] R. Mahrwald, *Chem. Rev.* **1999**, *99*, 1095–1120.
- [26] A. Kawada, *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2325–2333.
- [27] a) S. Arai, Y. Sudo, A. Nishida, *Tetrahedron* **2005**, *61*, 4639–4642; b) I. Hachiya, M. Moriwaki, S. Kobayashi, *Tetrahedron Lett.* **1995**, *36*, 409–412.
- [28] A. W. Amick, L. T. Scott, *J. Org. Chem.* **2007**, *72*, 3412–3418.
- [29] a) A. W. Fatland, B. E. Eaton, *Org. Lett.* **2000**, *2*, 3131–3133; b) F. C. Pigge, F. Ghasedi, *Tetrahedron Lett.* **2000**, *41*, 6545–6549.
- [30] R. Dumeunier, I. E. Marko, *Tetrahedron Lett.* **2004**, *45*, 825–829.
- [31] a) G. M. Sheldrick, SADABS, *An Empirical Absorption Correction Program for Area Detector Data*, University of Göttingen, Göttingen, **1996**; b) G. M. Sheldrick, SHELXS-97, University of Göttingen, Göttingen, **1997**; c) SMART, Version 5.628; Bruker AXS Inc.; d) SAINTB, Version 6.22a; Bruker AXS Inc.; e) SHELXTL NT/2000, Version 6.1.1; f) G. M. Sheldrick, *Acta Cryst., Sect. A*, **2008**, *64*, 112–122.

Received: December 10, 2011
Published online: April 13, 2012