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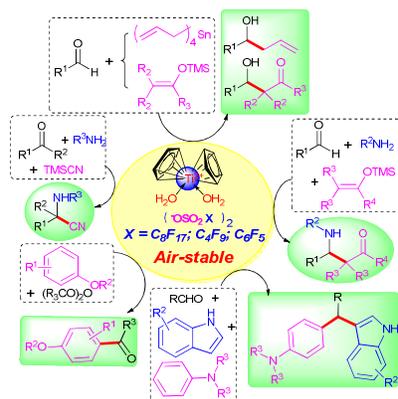
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Graphical Abstract

Strong Lewis acid of air-stable cationic titanocene perfluoroalkyl(aryl)sulfonate complexes as **highly** efficient and recyclable catalysts for C-C bond forming reactions

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A series of titanocene perfluoroalkyl(aryl)sulfonate complexes were successfully synthesized and found to show high catalytic efficiency in the the Strecker reaction, Mannich-type reaction, allylation of aldehydes, Mukaiyama aldol reaction, Friedel-Crafts acylation and aza-Friedel-Crafts reactions. Moreover, these complexes possessed good reusability. On account of their high catalytic efficiency as well as reusability, the complexes will find broad catalytic application in organic synthesis.

ARTICLE

Strong Lewis acid of air-stable cationic titanocene perfluoroalkyl(aryl)sulfonate complexes as highly efficient and recyclable catalysts for C-C bond forming reactions

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A series of strong Lewis acid of air-stable titanocene perfluoroalkyl(aryl)sulfonate complexes $\text{Cp}_2\text{Ti}(\text{OH}_2)_2(\text{OSO}_2\text{X})_2\cdot\text{THF}$ ($\text{X} = \text{C}_8\text{F}_{17}$, **1**·THF; $\text{X} = \text{C}_4\text{F}_9$, **2**·H₂O·THF; $\text{X} = \text{C}_6\text{F}_5$, **3**) were successfully synthesized by the treatment of Cp_2TiCl_2 with $\text{C}_8\text{F}_{17}\text{SO}_3\text{Ag}$, $\text{C}_4\text{F}_9\text{SO}_3\text{Ag}$ and $\text{C}_6\text{F}_5\text{SO}_3\text{Ag}$, respectively. In contrast to well-known titanocene bis(triflate), these complexes suffered from no change in open air over three months. TG-DSC analysis showed that **1**·THF, **2**·H₂O·THF and **3** were thermally stable at 230 °C, 220 °C and 280 °C, respectively. Conductivity measurements showed that these complexes underwent ionic dissociation in CH_3CN solution. X-ray analysis results confirmed that **2**·H₂O·THF and **3** were cationic. ESR spectra showed the Lewis acid of **1**·THF (1.06 eV) was larger than that of Sc^{3+} (1.00 eV) and Y^{3+} (0.85 eV). UV/Vis spectra showed a significant red shift due to the strong complex formation between 10-methylacridone and **2**·H₂O·THF. Fluorescence spectra showed that the Lewis acidity of **2** ($\lambda_{em} = 477$ nm) was larger than that of Sc^{3+} ($\lambda_{em} = 474$ nm). These complexes showed highly catalytic ability in various carbon-carbon bond forming reactions. Moreover, they possessed good reusability. Compared with **1**·THF, **2**·H₂O·THF and **3** exhibit higher solubility and better catalytic activity, and will find broad application in organic synthesis.

Introduction

Since the discovery of Zeigler-Natta catalyst, titanium(IV) compounds, derived from halide, alkoxide, phenolate, or triflate ligands, have aroused much interest in the past decades due to their extensive application in organic synthesis.¹ Among them, the titanocene complexes have attracted much attention because of their high potential in catalysis.² Recently, many research groups have made great contributions to the development of highly efficient catalytic systems based on titanocene complexes.³ For example, Ashfeld developed a bifunctional titanocene-catalyzed ($\text{Cp}_2\text{TiCl}_2/\text{Zn}/\text{Ac}_2\text{O}/\text{R}_3\text{P}$; $\text{R} = t\text{-Bu}$, 4-OMeC₆H₄) multicomponent coupling based on the premise that redox- and Lewis acid-relay catalysis, resulting in a convergent assembly of 1,4-diyne, 1,5-enynes, unsymmetrical diaryethynyl methanes, β -alkynyl ketones.⁴ Kambe *et al* found $\text{Cp}_2\text{TiCl}_2/n\text{-BuMgCl}$ catalytic system shows high efficiency and regioselectivity in C-Si⁵ and C-C bond-forming reaction.⁶ Huang *et al* reported titanocene-catalyzed dehydroxylative radical coupling of hemiaminal with active alkenes.⁷ Roy *et al* demonstrated a titanocene(III) chloride (Cp_2TiCl) mediated

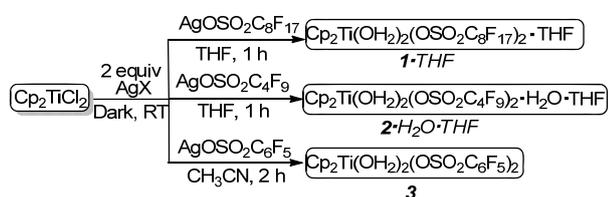
radical induced Wagner-Meerwein-type rearrangement, for the preparation of homoallyl amines and substituted alkenes stereoselectively.⁸ Among these catalytic systems, most of them⁴⁻⁸ focus on the Ti^{IV}-Ti^{III} multi valent ability. However, their potential as air-stable Lewis acid catalysts for organic synthesis has been rarely referred, which may be owing to the lower Lewis acidity of Cp_2TiCl_2 and its derivatives.⁹

To increase the Lewis acidity of the titanocene complexes, one method is to attach electron-withdrawing group(s) on titanium. For example, titanocene bis(triflate) $\text{Cp}_2\text{Ti}(\text{OSO}_2\text{CF}_3)_2$ was successfully synthesized by Thewalt and Klein¹⁰, and was employed by the groups of Bosnich and Collins for the formation of C-C bonds.¹¹ However, the anhydrous titanocene bis(triflate) was hydroscopic^{11a} and easily formed aquo complex $\text{Cp}_2\text{Ti}(\text{OH}_2)_2(\text{OSO}_2\text{CF}_3)_2\cdot\text{THF}$ (**4**·THF),^{11d} which were also active as Brønsted and/or Lewis acid catalysts.^{11a-11c} Brønsted acidity was disadvantageous for applications involving asymmetric catalysis.^{11f} Recently, Otera and co-worker found that the longer perfluorooctanesulfonate groups could be used as effective counter anions to provide air-stable and water-tolerant organometallic species in sharp

contrast to the corresponding hygroscopic organometallic triflates.¹² Based on this idea and as part of our ongoing efforts devoted to metallocene complexes, herein we put forth a full account of synthesis and characterization of a series of air-stable titanocene perfluoroalkyl(aryl)sulfonate complexes $\text{Cp}_2\text{Ti}(\text{OH})_2(\text{OSO}_2\text{X})\cdot\text{THF}$ ($\text{X} = \text{C}_8\text{F}_{17}$, **1**·THF; $\text{X} = \text{C}_4\text{F}_9$, **2**· $2\text{H}_2\text{O}\cdot\text{THF}$; $\text{X} = \text{C}_6\text{F}_5$, **3**). Furthermore, their catalytic activities are assessed in various C-C bond-forming reactions, including the Strecker reaction, Mannich-type reaction, allylation of aldehydes, Mukaiyama aldol reaction, Friedel-Crafts acylation and aza-Friedel-Crafts reactions.

Results and discussion

Shown in Scheme 1 is the synthetic route for the titanocene perfluoroalkyl(aryl)sulfonate complexes **1-3** by treatment of Cp_2TiCl_2 with silver perfluoroalkyl(aryl)sulfonate (AgX , for **1**, $\text{X} = \text{OSO}_2\text{C}_8\text{F}_{17}$; for **2**, $\text{X} = \text{OSO}_2\text{C}_4\text{F}_9$; for **3**, $\text{X} = \text{OSO}_2\text{C}_6\text{F}_5$) (2 equiv) in THF or CH_3CN , respectively.



Scheme 1 Synthesis of **1**·THF, **2**· $\text{H}_2\text{O}\cdot\text{THF}$ and **3**

^1H NMR and elemental analysis results show that the freshly prepared samples after recrystallization from THF/hexane contained 2 or 3 water molecules along with solvating THF for **1** and **2**, and contain only two H_2O molecules for **3**. Much attempt to prepare the complexes without hydrates failed. Since the preparation was not done in the glove box, the solvent transformation may cause some air moisture come into the reaction mixture. Keeping the fresh prepared complexes **1** and **2** in open air for 2 days, the desolvation of the THF was observed and the water molecule number increased to 4. Noting that, after keeping in open air over three months, the solid samples still remain as dry crystals or powder and exhibits no sign of skeleton change by ^1H NMR spectroscopy analysis. Therefore, the titanocene perfluoroalkyl(aryl)sulfonate complexes are storable in open air, showing a great advantage over titanocene bis(triflate) from an operational point of view.^{11a}

The cationic structures of **2**· $\text{H}_2\text{O}\cdot\text{THF}$ and **3** in the solid state were confirmed by X-ray analysis. The crystals suitable for the X-ray diffraction analysis were obtained by diffusion of hexane into saturated solution of complexes in THF. An ORTEP representation of **2**· $\text{H}_2\text{O}\cdot\text{THF}$ and **3** and selected bonds and angles were shown in Fig. 1 and Fig. 2. It is clear that the titanocene component in **2**· $\text{H}_2\text{O}\cdot\text{THF}$ and **3** are cationic, while the $\text{Cp}_2\text{Ti}(\text{OSO}_2\text{CF}_3)_2$ possesses a covalent structure.¹⁰ The anhydrous titanocene bis(triflate) [$\text{Cp}_2\text{Ti}(\text{OSO}_2\text{CF}_3)_2$] readily

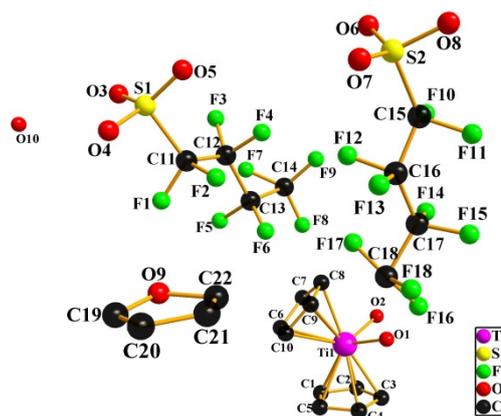


Fig. 1. ORTEP view of crystal structure of **2**· $\text{H}_2\text{O}\cdot\text{THF}$. Selected Bond (Å) and angles (deg): Ti1-O1, 2.026(3); Ti1-O2, 2.006(2); Ti1-C1, 2.343(4); Ti1-C2, 2.337(4); Ti1-C3, 2.336(3); Ti1-C4, 2.356(3); Ti1-C5, 2.355(3); Ti1-C6, 2.358(3); Ti1-C7, 2.363(3); Ti1-C8, 2.341(3); Ti1-C9, 2.353(3); Ti1-C10, 2.327(4); O2-Ti1-O1, 90.75(10). The torsion angle between the two Cp ring planes is 46.9 deg. The proton is omitted for clarity.

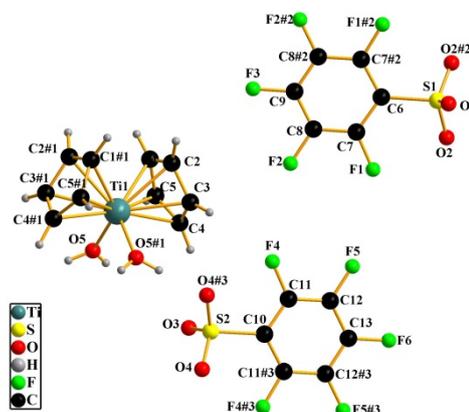


Fig. 2. ORTEP view of crystal structure of **3**. Selected Bond (Å) and angles (deg): Ti1-O5, 2.0226(17); Ti1-O5#, 2.0226(17); Ti1-C1, 2.351(2); Ti1-C2, 2.354(2); Ti1-C3, 2.374(2); Ti1-C4, 2.357(2); Ti1-C5, 2.364(2); Ti1-C1#, 2.351(2); Ti1-C2#, 2.354(2); Ti1-C3#, 2.374(2); Ti1-C4#, 2.357(2); Ti1-C5#, 2.364(2); O5-Ti1-O5A, 92.75(11). The torsion angle between the two Cp ring planes is 47.00 deg.

formed aquo complexes [$\text{Cp}_2\text{Ti}(\text{OH})_2(\text{OSO}_2\text{CF}_3)_2$], which is an cationic complex.^{11d} The titanium atom in the cationic ion is coordinated by two water molecules, which lie on the plane that bisects the angle between the Cp ring planes. The $\text{C}_4\text{F}_9\text{SO}_3^-/\text{C}_6\text{F}_5\text{SO}_3^-$ ions, the dissociated H_2O molecules, and solvating ligand THF are packed around the complex cationic ion in such a way that their oxygen atoms point towards the H_2O ligands. The $\text{C}_4\text{F}_9/\text{C}_6\text{F}_5$ side chains of the anions, on the other hand, are clustered together to produce hydrophobic domains. Unfortunately, in spite of many attempts, we were unable to obtain the suitable crystals of **1**·THF for X-ray analysis. However, due to the similar chemical structure, we deduced that **1**·THF could be also cationic organometallic species, which was confirmed by conductivity measurements.

Conductivity measurement was applied to investigate their ionic dissociation behaviour in CH₃CN. The large molar conductivity value (**1**·THF: $\Lambda = 117 \mu\text{S}\cdot\text{cm}^{-1}$; **2**·H₂O·THF: $\Lambda = 165 \mu\text{S}\cdot\text{cm}^{-1}$; **3**: $\Lambda = 143 \mu\text{S}\cdot\text{cm}^{-1}$ in CH₃CN (1.0 mmolL⁻¹) at 15 °C) are consistent with the complete ionization into a 1:2 electrolyte,¹⁴ implying that these complexes are cationic in the solid state and in solution.

The thermal behaviour of three complexes **1**·THF, **2**·H₂O·THF and **3** were investigated by TG-DSC in an N₂ atmosphere (Fig. 3). The TG-DSC curves showed three stages of weight loss. The endothermic step below 100 °C can be assigned to the removal of water molecules that corresponded obvious endothermic peaks. Complexes **1**, **2** and **3** are thermally stable and could be up to about 230 °C, 220 °C and 280 °C, respectively. Obviously, complex **3** shows better thermal stability, which may be owing to the perfluorophenyl anions. Then two weight losses of exothermic nature appear, plausibly due to the oxidation of organic entities with a large quantity of heat to release. We observed the removal of perfluoro(alkyl)phenylsulfuryl ligands at 300 °C, leaving titanium fluoride behind. We also employed ¹H and ¹⁹F NMR techniques to analyze the **2**·H₂O·THF samples, which underwent thermal treatment at 180 °C for two days, and no change was observed.

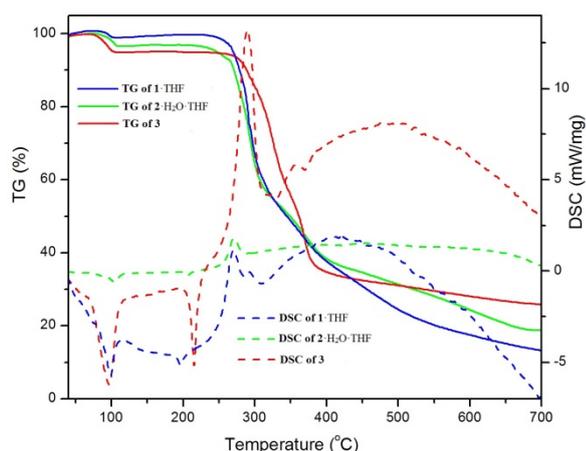


Fig. 3. TG-DSC curves of complexes **1**·THF, **2**·H₂O·THF and **3**.

Table 1. The solubility of titanocene perfluoro(octane, butane, phenyl)sulfonates in organic solvents at 25 °C^a

Solvent	1 ·THF ^b	2 ·H ₂ O·THF ^b	3 ^b
Acetone	284	1541	968
MeOH	136	746	534
THF	130	827	638
EtOAc	26	395	278
CH ₃ CN	510	1027	742
Et ₂ O	13	116	87
CH ₂ Cl ₂	0	0	0
Toluene	0	0	0
<i>n</i> -Hexane	0	0	0

^aAll samples are freshly prepared and recrystallized, ^b Solubility gL⁻¹.

Another notable feature is the unusual solubility of **1**·THF, **2**·H₂O·THF and **3** in Acetone, THF, CH₃CN, EtOAc and

MeOH (Table 1). One can see that **2**·H₂O·THF and **3** show higher solubility in common polar organic solvents compared with the solubility of **1**·THF. It is deduced that such difference may be owing to the strongly lipophobic property of perfluorooctyl group.¹³ Another quite surprising behaviour is that these complexes is insoluble in CH₂Cl₂, because CH₂Cl₂ is usually the best solvent for similar titanocene bis(triflate).^{11d} Consistently, they are not soluble in much less polar toluene and nonpolar *n*-hexane. Furthermore, as it is apparently insoluble in water, these complexes are hydrophobic, which could be attributed to the fluoroalkyl(aryl) chain in the sulfonate ligand.

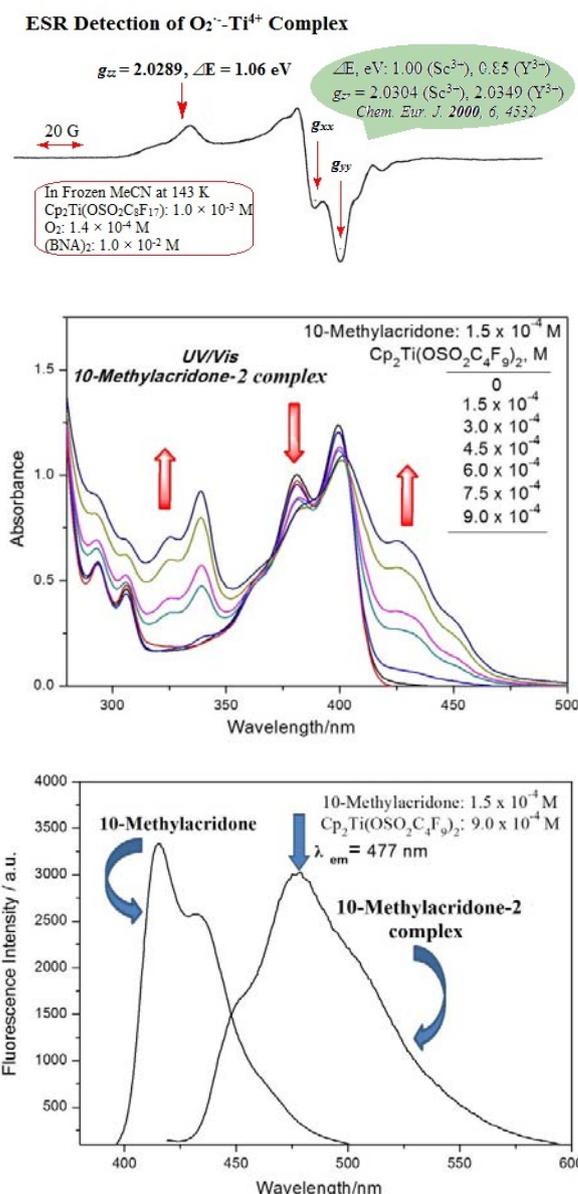


Fig. 4. Top: ESR spectra of O₂⁻·Ti⁴⁺ (**1**); Middle: UV/Vis spectra changes of complex formation between 10-methylacridone and **2**; Bottom: fluorescence spectra changes of complex formation between 10-methylacridone and **2**.

Then, we decided to estimate their Lewis acidity by different ways, since the titanocene Lewis acid is desired to be as strongly acidic as possible to acquire higher catalytic activity. First, to estimate the Lewis acidity of **1** exactly, we measured the ESR spectra of the $O_2^{\cdot-}\cdot\mathbf{1}$ complex to determine its ΔE value,¹⁵ which is the binding energies of Lewis acid metal ions with $O_2^{\cdot-}$.

As shown in Fig. 3 (top), the ΔE value of the titanium complex ($O_2^{\cdot-}\cdot\mathbf{1}$) is significantly larger (Ti^{4+} : $g_{zz} = 2.0289$, $\Delta E = 1.06$ eV) than that of $Sc(OTf)_3$ ($g_{zz} = 2.0304$, $\Delta E = 1.00$ eV) and it is the largest among the ΔE values ever reported by Fukuzumi group.^{15b} Since the Lewis acids with a ΔE value larger than 0.88 eV were presumed to be capable for inducing C-C bond-forming reactions,^{12a} thus, it is reasonable to expect that the Lewis acidity of **1** is higher enough to trigger synthetically useful reactions. We also applied UV/Vis spectra (Fig. 4, middle) to qualitatively determine the Lewis acidity of **2**, and observed a significant red shift due to the strong complex formation between 10-methylacridone and **2**, illustrating a larger Lewis acidity ability of **2**. Meanwhile, we estimated the Lewis acidity of **2** by the red shift (λ_{em}) of Lewis acid metal ions (Ti^{4+}) with 10-methylacridone on the basis of fluorescence spectra. The fluorescence maximum (λ_{em}) of **2** is 477 nm (Fig. 4, bottom), which is slightly larger than Sc^{3+} (474 nm).¹⁶ In addition, we also employed Hammett indicator method to determine the acidity of $\mathbf{1}\cdot\text{THF}$, $\mathbf{2}\cdot\text{H}_2\text{O}\cdot\text{THF}$ and **3**, and found all of them have relatively strong acidity showing acid strength $0.8 < H_o \leq 3.3$ (H_o being the Hammett acidity function).¹⁷ The characteristics of these complexes encouraged us to evaluate its performance as a Lewis acid catalyst for carbon-carbon bond-forming reactions, such as the Strecker reaction, Mannich-type reaction, Mukaiyama aldol reaction, allylation of aldehydes, Friedel-Crafts acylation and aza-Friedel-Crafts reactions.

The Strecker reaction is one of the most efficient and straightforward methods for the synthesis of α -aminonitriles,¹⁸ which are very important intermediates for the synthesis of α -amino acids and various nitrogen-containing heterocycles.¹⁹ In recent years, in the research for novel and efficient protocols for the synthesis of α -aminonitriles, a broad spectrum of metal complexes, Lewis acids, solid acids and organic catalysts have been developed to promote this reaction.²⁰ However, some of these methods have one or more disadvantage(s) such as low reactivity, poor selectivity, use of organic solvent and/or need of strictly anhydrous reaction conditions. It is highly desirable to develop catalytic systems that can affect the Strecker reaction in solvent-free conditions with excellent efficiency and stereoselectivity. We hence assessed the catalytic efficiency with $\mathbf{1}\cdot\text{THF}$ in one-pot Strecker reaction under solvent-free conditions, and the high efficiency and chemoselectivity was obtained (Table 2).

In order to demonstrate the excellent catalytic efficiency of $\mathbf{1}\cdot\text{THF}$, we examined the Strecker reaction of different aldehydes/ketones with aniline and trimethylsilyl cyanide in the presence of 1.0 mol% of catalyst $\mathbf{1}\cdot\text{THF}$. Aromatic aldehydes with electron-donating and electron-withdrawing groups were employed. Despite variation of reaction rate, the yields are

high. However, the yield of **9a** is only 37% in the presence of Cp_2TiCl_2 . The aromatic aldehydes with electron-withdrawing groups (e.g., F, Cl, Br) exhibit higher reactivity in Strecker reaction than that with electron-donating groups in the *para*-position of the phenyl plane (e.g., methyl and methoxyl) (Table 2, **8a-8f**, 91-96%). Gratifyingly, cinnamaldehyde and furfural are also tolerated in this process, and show high reactivity with 90% and 89% yields, respectively (**8g**, **8h**). In addition, the alkyl aldehydes also show good reactivity with 82% yield (**8i**) in the presence of $\mathbf{1}\cdot\text{THF}$. Substituted phenylamine and 8-aminoquinoline also exhibit high reactivity in this catalytic system with benzaldehyde and trimethylsilylcyanide and the yields are 95%, 92% and 85%, respectively (**8j**, **8k**, **8l**). 2-bromobenzaldehyde reacts with trifluoromethoxyaniline yielded compounds **8m** in the yield of 91%. Acetophenone, cyclohexanone and 4-methylcyclohexanone react with aniline and trimethylsilylcyanide, giving **8n**, **8o**, **8p** in 80%, 89% and 83%, respectively. Thus, an efficient protocols for the synthesis of α -aminonitriles have been developed.

Table 2 The Strecker reaction of aldehydes/ketones with amines and trimethylsilylcyanide catalyzed by $\mathbf{1}\cdot\text{THF}$ ^a

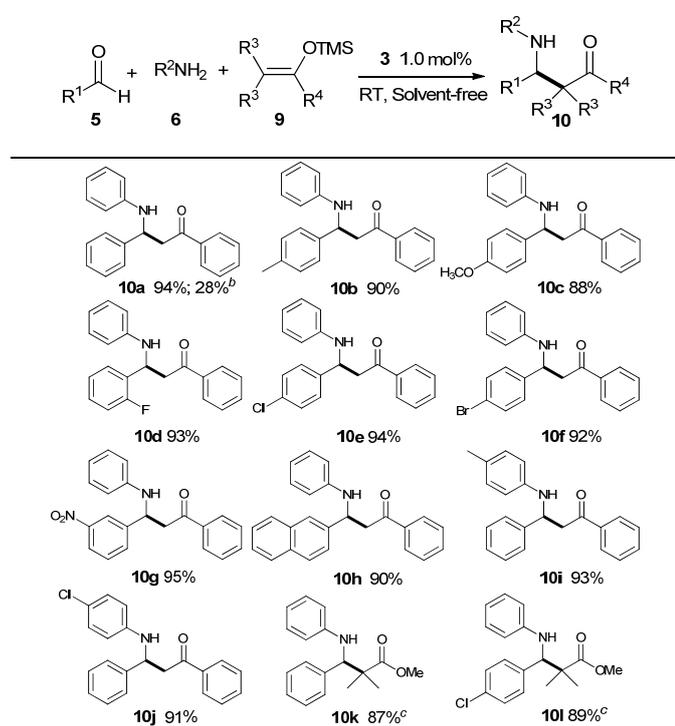
$R^1-C(=O)-R^2 + R^3NH_2 + TMSCN \xrightarrow[RT, \text{Solvent-free}]{\mathbf{1}\cdot\text{THF } 1.0 \text{ mol}\%} R^1-CH(NHR^3)-C(=O)-R^2$			
5	6	7a	8
8a 95%; 37% ^b			8b 92%
			8c 91%
			8d 94%
			8e 96%
			8f 95%
			8g 90%
			8h 89%
			8i 82% ^c
			8j 95%
			8k 92%
			8l 85%
			8m 91%
			8n 80% ^c
			8o 89% ^d
			8p 83% ^d

^a Catalyst $\mathbf{1}\cdot\text{THF}$ (0.01 mmol); $R^1C(O)R^2$ (**5**: 1.0 mmol); R^2NH_2 (**6**: 1.0 mmol); TMSCN (**7a**: 1.2 mmol); Solvent-free conditions; temp: RT; **8a-8h**, **8j-8m**: 30 min; isolated yield. ^b Cp_2TiCl_2 (0.01 mmol). ^c**8i**: 1 h, isolated yield. ^d**8n-8p**: 2 h, isolated yield.

The Mannich-type reaction is a powerful tool for the preparation of synthetically useful β -amino carbonyl compounds, which are extremely important compounds as biologically active molecules.²¹ A proper control of the three components (enol silyl ethers donor, amine, aldehyde acceptor)

of the Mannich-type reaction is challenging, since the side reactions such as aldol reaction may lower the product yield. Impressive achievements have been made in Mannich-type over various Lewis acid catalysts.²² However, the methods involving the aldol addition side products, longer reaction time, and the use of imine is “environmentally unfriendly” and not “atom economic”. Recently, synthetic methods involving the rare-earth and lanthanide triflates as catalysts for Mannich-type reactions have been reported.²³ The lanthanide triflates as attractive catalyst has highly catalytic activity, low toxicity, air-stability, but it is not recyclable. Another disadvantage is that most of these catalysts need organic solvents as media. Thus, we assessed **3** as a catalyst (1.0 mol%) in one-pot Mannich-type reaction at room temperature under solvent-free conditions, and good-to-excellent yields were obtained (Table 3).

Table 3 The Mannich-type reaction of aldehydes, amines and enol silyl ethers/ ketene silyl acetals catalyzed by **3**^a



^a Catalyst **3** (0.01 mmol); R¹CHO (**5**; 1.0 mmol); R²NH₂ (**6**; 1.0 mmol); enol silyl ethers (**9**; 1.2 mmol); Solvent-free conditions; temp: RT., **10a-10j**: 20 min, isolated yield. ^b Cp₂TiCl₂ (0.01 mmol). ^c **10k, 10l**: 1.5 h, isolated yield.

As shown in Table 3, the reaction with variety of aromatic aldehydes with aniline and trimethyl(1-phenyl-vinyloxy)silane (Table 3) were assessed, the yields of **10a-10g** are 88-95%. However, the yield of **10a** was only 28% using Cp₂TiCl₂ as catalyst. The aromatic aldehydes with electron-withdrawing groups (e.g., F, Cl, Br, and NO₂) exhibited higher reactivity in Mannich-type reaction than that with electron-donating groups (e.g., methyl and methoxyl) (Table 3, **10b-10g**). 2-Naphthaldehyde was also tolerated in this process, providing the compound **10h** in 90% yield (Table 3, **10h**). Substituted anilines were also examined with benzaldehyde and

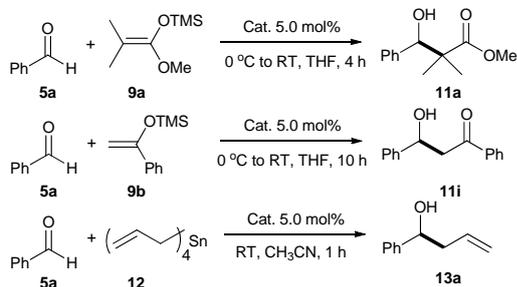
trimethyl(1-phenyl-vinyloxy)silane, while the electron-donating groups (CH₃) and electron-withdrawing groups (Cl) can proceed smoothly to afford their corresponding products in high yields (Table 3, **10i, 10j**). In addition, ketene silyl acetals also have good reactivity in current catalytic system with benzaldehyde (4-chlorobenzaldehyde) and aniline in the yield of 87% and 89%, respectively (Table 3, **10k, 10l**).

Due to the fact that the above two kinds of reactions only need a weak Lewis acidic catalyst, then we investigated other C-C bond-forming reactions requiring higher acidic Lewis acid catalyst. The allylation of aldehydes and Mukaiyama-aldol reaction mediated by a Lewis acid are the most convenient processes for the construction of carbon-carbon bonds in organic synthesis. This route provides a rapid access to synthesis of β -hydroxy ester/ketones and homoallylic alcohols derivatives, these motifs often exist in natural products and bioactive molecules.²⁴ Several efficient Lewis acid catalysts based on titanium, zirconium, copper and Brønsted acids have been developed.²⁵ But in most cases, the temperature of -20 °C to -80 °C and strictly anhydrous conditions are required. Recently, the highly efficient system of silica-Sc-IL/[DBIm]SbF₆ developed by Kobayashi should be the most promising method, which required ionic liquids as co-catalyst.²⁶ therefore, higher efficient method for the these reaction is still desired.

The catalytic activities of Cp₂TiCl₂, **1**·THF, **2**·H₂O·THF, **3** together with **4**·THF were assessed for various carbon-carbon bond-forming reactions. First, reaction of benzaldehyde with nucleophiles, such as ketene silyl acetals, enol silyl ethers and tetraallyltin were scrutinized (Scheme in Table 4). All reactions were carried out in the presence of above catalysts, and the yields of the respective are compiled in Table 4. High yields were attained over **2**·H₂O·THF/**3**, while the other catalysts showed much lower yields, plausibly due to their lower Lewis acidity or moisture-sensitive features. Notably, the solvents in these reactions, such as THF and CH₃CN, were used as received owing to the water-tolerance ability of the titanocene perfluoroalkyl(aryl)sulfonate complexes, in sharp contrast to titanocene of **4**·THF. To our surprise, titanocene perfluorooctanesulfonate (**1**·THF) only shows moderate catalytic efficiency in above carbon-carbon bond-forming reactions compared with **2**·H₂O·THF/**3**. We speculated that the relatively lower catalytic efficiency of **1**·THF may be owing to the strongly lipophobic property of perfluorooctyl group. Because the perfluoro anions well wrapping the cationic metal center make the lipophilic substrates hard to approach the center metal atom for activating. Besides, due to the strongly lipophobic property of perfluorooctyl group, the complex usually exhibited moderate solubility in common organic solvents, which may be another reason for the decline of catalytic efficiency. Thus, **2**·H₂O·THF and **3** as Lewis acid catalysts are better than **1**·THF for carbon-carbon bond-forming reactions. In addition, perfluorooctanesulfonate compounds (PFOS) have been found to be potentially toxic to animals and human beings^{27a} and will result in environmental pollution.^{27b} However, pefluorobutanesulfonate and pefluorophenylsulfonate

compounds exhibited lower toxicity to humans and animals than PFOS,²⁸ which fulfill the requirement of the green chemistry.

Table 4 Yield [%] in reactions of benzaldehyde with silyl and stannyl nucleophiles catalyzed by Cp₂TiCl₂, titanocene perfluoroalkyl(aryl)sulfonate complexes and titanocene bis(triflate)s (**4**·THF).



Entry	Nu Product		Catalyst				
	9a	11a	Cp ₂ TiCl ₂	1·THF	2·H ₂ O·THF	3	4·THF
1 ^a	9a	11a	26	79	94	89	81
2 ^b	9b	11i	19	72	90	85	76
3 ^c	12	13a	12	80	95	90	84

^a Catalyst (0.05 mol); **5a** (1.0 mmol); **9a** (1.2 mmol); THF (3 ml); temp: 0 °C to RT; 4 h; isolated yield. ^b Catalyst (0.05 mol); **5a** (1.0 mmol); **9b** (1.2 mmol); THF (3 ml); temp: 0 °C to RT; 10 h; isolated yield. ^c Catalyst (0.05 mol); **5a** (1.0 mmol); **12** (0.3 mmol); CH₃CN (3 ml); temp: RT; 1 h; isolated yield.

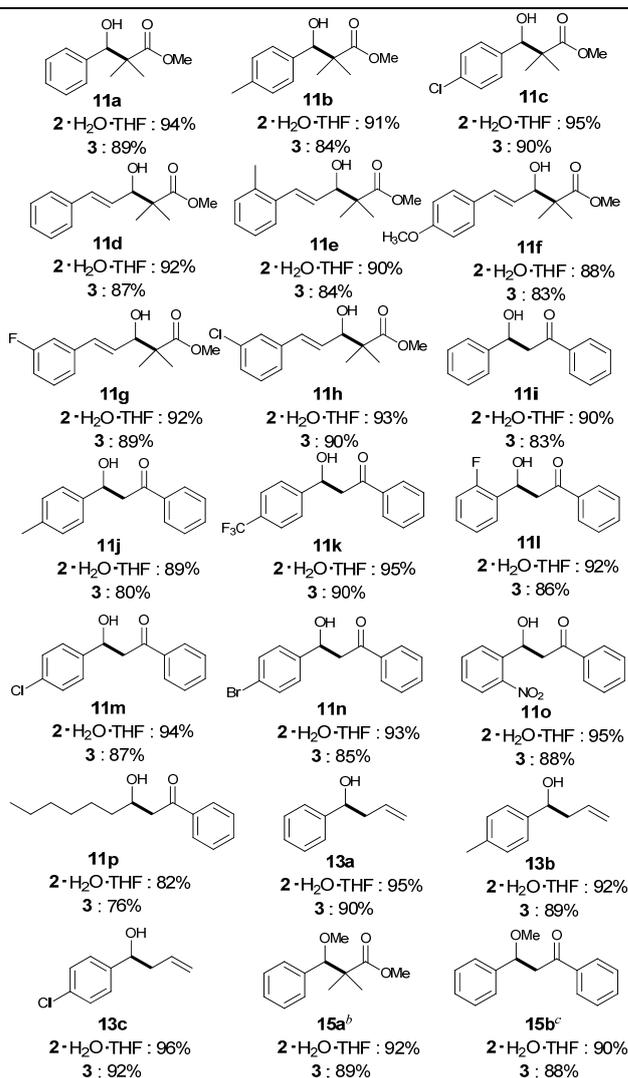
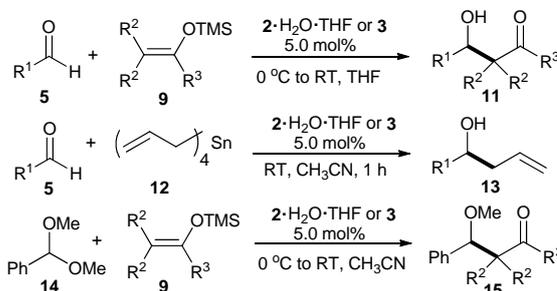
Next, we mainly accessed the catalytic activities of 2·H₂O·THF and **3**. The reaction of different aldehydes and benzaldehyde dimethyl acetal with nucleophiles, such as ketene silyl acetals, enol silyl ethers and tetraallyl tin were examined over 2·H₂O·THF/**3** (Table 5).

As expected, the β-hydroxy ester/ketones derivatives and homoallylic alcohols can be obtained in high yields in THF or CH₃CN (Table 5). For Mukaiyama-aldol reaction, aldehydes with electron-withdrawing groups (e.g., CF₃, Cl, Br, NO₂) in the phenyl plane exhibit higher reaction activity than the aldehydes with electron-donating groups (e.g., methyl) (Table 5, **11b**, **11c**, **11j**–**11o**). The cinnamaldehyde derivatives with a double bond are also tolerated in this catalytic system, and successfully react with ketene silyl acetals to form 1,2-addition adducts in high yields (Table 5, **11d**–**11h**). The alkyl aldehyde also shows good reactivity with 82% yield (Table 5, **11p**), while the yield of **11p** with complex 1·THF in current conditions is only 58% yield. For the allylation of aldehydes, different aromatic aldehydes also display high reactivity with tetraallyl tin (Table 5, **13**–**13c**). In addition, benzaldehyde dimethyl acetal, as a substitution of benzaldehyde, can react with different enol silyl ethers to give the desired products in high yields (Table 5, **15a**, **15b**). It is worth noting that **3** also showed relatively high catalytic efficiency towards Mukaiyama-aldol reaction and allylation of aldehydes (Table 5).

Later we moved to the Lewis acids-catalyzed Friedel-Crafts acylation of aromatic compounds, which is another important C-C bond forming reaction in organic chemistry.²⁹ Some traditional Lewis acids (such as ZnCl₂, AlCl₃, FeCl₃, SnCl₄, and TiCl₄) or strong protic acids (like HF, CF₃SO₃H or H₂SO₄) were utilized to catalyze the electrophilic acylation reaction.³⁰ However, more than stoichiometric amount of

catalysts are needed owing to the formation of strong complex from the interaction between the catalyst itself and the ketone product.³¹ Whereas the compound Sc(OTf)₃ was applied in this

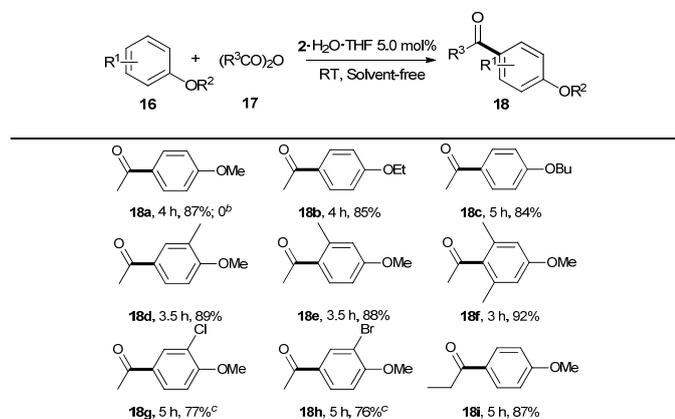
Table 5 The Mukaiyama-aldol reaction of aldehydes with ketene silyl acetals/enol silyl ethers and allylation of aldehydes catalyzed by 2·H₂O·THF or **3**.^a



^a Catalyst 2·H₂O·THF or **3** (0.05 mmol); R¹CHO (**5**; 1.0 mmol) or Ph(OMe)₂ (**14**; 1.0 mmol); ketene silyl acetals/Enol silyl ethers (**9**; 1.2 mmol) or tetraallyl tin (**12**; 0.3 mmol); THF/CH₃CN (3 ml); temp: RT; **11a**–**11h**: 4 h; **11i**–**11o**: 10 h; **11p**: 12 h; **13a**–**13c**: 1 h, isolated yield. ^b **15a**: 5 h, isolated yield. ^c **15b**: 12 h, isolated yield.

reaction and a good result can be achieved,³² the high price of $\text{Sc}(\text{OTf})_3$ limits its application. Furthermore, many catalysts, such as $\text{NbCl}_5/\text{AgClO}_4$ and $\text{Hf}(\text{OTf})_4/\text{AgClO}_4$ were reported as Friedel-Crafts acylation catalysts, while larger equivalents of potentially explosive perchlorate salts have to be used as co-catalyst.³³

Table 6 Friedel-Crafts acylation of alkyl aryl ethers with anhydrides catalyzed by $2 \cdot \text{H}_2\text{O} \cdot \text{THF}$ ^a



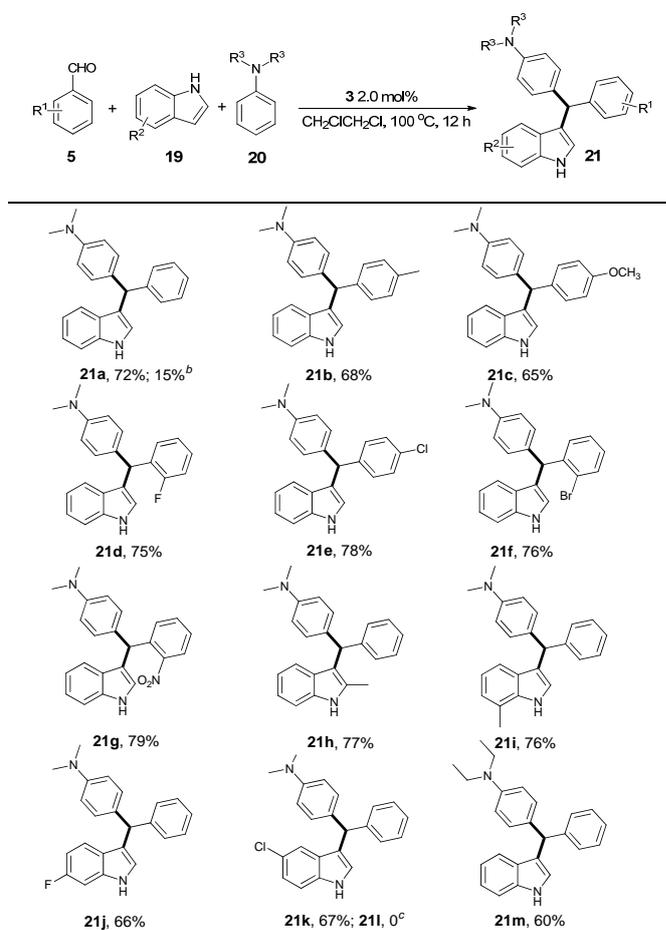
^a Catalyst $2 \cdot \text{H}_2\text{O} \cdot \text{THF}$ (0.05 mmol); **16** (1.0 mmol); **17** (2.0 mmol); Solvent-free conditions; temp: rt., 4 h, isolated yield. ^b No catalyst or the catalyst was Cp_2TiCl_2 (0.05 mmol), 12 h. ^c at 50°C.

Thus, we assessed $2 \cdot \text{H}_2\text{O} \cdot \text{THF}$ as a catalyst for the Friedel-Crafts acylation of structurally diverse anisoles with 2.0 equiv of acetic(propionic) anhydride at room temperature under solvent-free conditions and good yields were obtained (Table 6, **18a-18i**, 76-92%). Different substituted benzene (e.g. methoxy, ethoxy, butoxy) has high reactivity in current catalytic system with acetic anhydride and the yield is high from 84% to 87% (Table 6, **18a-18c**). The electron-donating groups attached to the aromatic ring enhance the reaction activity (Table 6, **18d-18f**), but the anisole with 2-Cl and 3-Br groups keeps intact at room temperature, giving their corresponding products in lower yields even at 50°C (Table 6, **18g, 18h**). Meanwhile, propionic anhydride also exhibits good reactivity with 80% yield (Table 6, **18i**). Furthermore, the reaction shows high regioselectivity (*para*-regioisomer > 99%). Controlled experiments were performed in the absence of $2 \cdot \text{H}_2\text{O} \cdot \text{THF}$ or in the presence of Cp_2TiCl_2 , no product are obtained. Therefore, in contrast to Cp_2TiCl_2 , complex $2 \cdot \text{H}_2\text{O} \cdot \text{THF}$ can be considered to be an excellent catalyst in view of catalytic efficiency and *para*-regioselectivity in the Friedel-Crafts acylation.

Indoles are an important class of heterocycles that exist in many natural products.³⁴ Many natural and synthetic indoles exhibit a broad range of biological activities, including anticancer,^{35a} antiangiogenic,^{35b} antiparasitic^{35c} and antitumor activities.^{35d} Among indole derivatives, bis-indolyl alkanes, 3-alkyl indoles, and 3-diarylmethyl indoles are important class of bioactive metabolite, which can be synthesized by Lewis acid (e.g. InCl_3 ($\text{In}(\text{OTf})_3$),^{36a} $\text{Sc}(\text{OTf})_3$,^{36b} FeCl_3 ,^{36c} CeCl_3 ^{36d} or $\text{Al}(\text{OTf})_3$ ^{36e}) or protic acid (e.g. HCl , HClO_4 , H_2SO_4). Although the synthesis of 3-alkyl indoles has been extensively studied, the synthesis of other unsymmetrical

indole derivatives is still highly desirable in synthetic community since it needs more practical procedures and mild reaction conditions.³⁷

Table 7 The aza-Friedel-Crafts reactions of indoles, aldehydes and *N,N*-dialkylaniline catalyzed by **3**^a



^a Catalyst **3** (0.02 mmol); R^1CHO (**5**; 1.0 mmol); indoles (**19**; 1.0 mmol); *N,N*-dialkylaniline (**20**; 1.1 mmol); Solvent: $\text{CH}_2\text{ClCH}_2\text{Cl}$ (3 ml); temp: 100 °C; isolated yield. ^b Cp_2TiCl_2 (0.02 mmol). ^c PhCHO (1.0 mmol); 5-nitroindole (1.0 mmol); *N,N*-dimethylaniline (**20a**; 1.1 mmol).

Herein we report the complex **3**-catalyzed one-pot three-component aza-Friedel-Crafts reactions of indoles, aldehydes, and tertiary aromatic amines. The reactions generated the corresponding 3-diarylmethyl indole derivatives in good yields under mild reaction conditions (Table 7). In order to demonstrate the good catalytic efficiency of **3**, the scope of indoles and benzaldehydes for the three-component aza-Friedel-Crafts reactions using **3** as catalyst was evaluated. One can see that benzaldehydes bearing electron-withdrawing groups (F, Cl, Br, NO_2) give the corresponding products in higher yields than those with electron-donating groups (CH_3 , OCH_3) (Table 7, **21b-21g**). On the contrary, indoles bearing electron-donating groups (methyl), show slightly higher reactivity than those with electron-withdrawing groups, like F, Cl (Table 7, **21h-21k**). However, the yield of **21a** was only 15% using Cp_2TiCl_2 as catalyst. Meanwhile, *N,N*-diethylaniline

can also react with benzaldehyde and indole with 60% yield (Table 7, **21m**). It is worth noting that no reaction was observed when 5-nitroindole (bearing the strong electron-withdrawing group) was employed as the substrate (Table 7, **21l**).

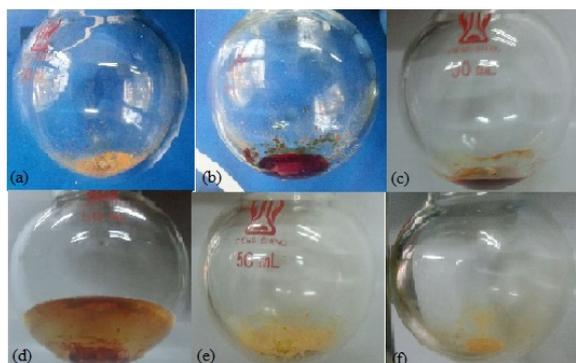


Fig. 5 (a) Catalyst **2**·H₂O·THF (0.05 mmol, 45 mg); (b) Adding starting materials [PhOMe (1.0 mmol, 108 mg) + Ac₂O (2.0 mmol, 204mg)]; (c) The reaction was complete as indicated by TLC; (d) Adding 10 ml *n*-hexane; (e) Removing the liquid reaction mixture by syringe (or filtration) and washing the residue with hexane (three times); (f) Scraping the catalyst in flask wall (43 mg).

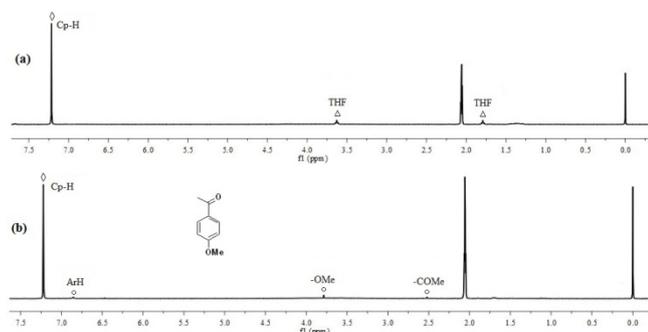


Fig. 6 The ¹H NMR spectra comparison of the recovered catalyst **1** in Friedel-Crafts acylation as shown in the scheme in Table 1, (◇ = catalyst peak (Cp-H); △ = THF peak; ○ = recycled catalyst contains some impurities which are products and starting materials).

To test the reusability of the catalyst and the reproducibility of catalytic performance, the **1**·THF or **2**·H₂O·THF/**3** was subject to recycling experiments of above reactions (eq **1**: **5a** + **6a** + **7a** → **8a**; eq **2**: **5a**+**6a** + **9b** → **10a**; eq **3**: **5a** + **9a** → **11a**; eq **4**: **16a** + **17a** → **18a**). We took Friedel-Crafts acylation (**16a** + **17a** → **18a**) as an example for the catalyst recovery process. As shown in Fig. 5, the catalyst can be easily recycled by adding solvent *n*-hexane (three times). Moreover, the final recovered catalyst was analyzed by ¹H NMR. It is clear that ¹H NMR spectra of the recovered catalyst is same as that of catalyst **2**·H₂O·THF (Fig. 6), implying the catalyst is stable and suitable for reuse. According to this procedure, the above reactions were carried out and the results were shown in Table 8. The change in product yield was negligible in a trial of five recycling experiments.

Table 8 Yields of the Strecker reaction (eq **1**); Mannich-type reaction (eq **2**); Mukaiyama aldol reaction (eq **3**) and Friedel-Crafts acylation (eq **4**) by recover catalyst.^a

Cycle	Yield (%) ^e	Cat (%) ^f						
	Eq 1 ^a		Eq 2 ^b		Eq 3 ^c		Eq 4 ^d	
1	95	96	94	96	94	96	87	89
2	96	97	95	97	95	97	88	90
3	95	97	94	96	96	98	86	88
4	95	96	94	96	94	96	87	88
5	96	97	93	95	94	97	88	91

^a **5a** (1.0 mmol); **6a** (1.0 mmol); **7a** (1.2 mmol); **1**·THF (0.01 mmol); rt. [b] **5a** (1.0 mmol); **6a** (1.0 mmol); **9b** (1.2 mmol); **3** (0.01 mmol); RT. [c] **5a** (1.0 mmol); **9a** (1.2 mmol); cat. **2**·H₂O·THF/**3** (0.05 mmol); RT. [d] **16a** (1.0 mmol); **17a** (2.0 mmol); **2**·H₂O·THF (0.05 mmol); RT. [e] Isolated yield of desired product. [f] Isolated yield of recovered catalyst.

Conclusion

We have synthesized and characterized a series of mononuclear titanocene perfluoroalkyl(aryl)sulfonate complexes. These complexes are strongly acidic and air-stable, and show highly catalytic activity in the Strecker reaction, Mannich-type reaction, allylation of aldehydes, Mukaiyama aldol reaction, Friedel-Crafts acylation and aza-Friedel-Crafts reactions. Moreover, these complexes possess good reusability. Compared with **1**·THF, **2**·H₂O·THF and **3** exhibit higher solubility and better catalytic activity. Due to their highly catalytic efficiency, stability, storability, low toxicity and reusability, they will find broad application in organic synthesis.

Experimental section

General: All chemicals were purchased from Aldrich. Co. Ltd as well as other chemicals provider and used as received unless otherwise indicated. The preparation of catalyst was carried out under nitrogen atmosphere with freshly distilled solvents. THF and hexane were distilled from sodium/benzophenone. Acetonitrile was distilled from CaH₂. The NMR spectra were recorded at 25 °C on INOVA-400M (USA) calibrated with tetramethylsilane (TMS) as an internal reference. Elemental analyses were performed by VARIO EL III. TG-DSC analysis was performed on a HCT-1 (HENVEN, Beijing, China) instrument. Conductivity was measured on REX conductivity meter DDS-307. IR spectra were recorded on NICOLET 6700 FTR spectrophotometer (Thermo Electron Corporation). X-ray single crystal diffraction analysis was performed with SMART-APEX and RASA-7A by Shanghai Institute Organic Chemistry,

China Academy of Science. The Lewis acidity estimation was performed by means of ESR in Osaka University. UV/Vis (SHIMADZU UV-1601) and Fluorescence spectroscopy (HITACHI F-4600) were measured in State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University (China). The acidity was measured by Hammett indicator method as described previously. Acid strength was expressed in terms of Hammett acidity function (H_0) as scaled by pK_a value of the indicators

Preparation of 1·THF:

To a solution of Cp_2TiCl_2 (0.249 g, 1.0 mmol) in 20 mL THF was added a solution of $AgOSO_2C_8F_{17}$ (1.24 g, 2.05 mmol) in 10 mL THF. After the mixture was stirred at 25 °C for 1 hour in the absence of light, it was filtrated. The filtrate was placed in a small jar and then put into a larger jar which was added 40 mL dry hexane and then the larger jar was obdurate. After keeping in the refrigerator for 24 hours, the yellow crystal was obtained (744 mg, 58 %). 1H NMR (400 MHz, acetone- d_6) δ 7.22 (s, 10H, Cp), 3.64 to 3.61 (m, THF), 1.82 to 1.76 (m, THF); ^{19}F NMR (376 MHz, acetone- d_6) δ -81.67 (t, $J = 19.9$ Hz, 3F, CF_3^-), -115.03 (s, 2F, $-CF_2^-$), -121.06 to 121.12 (m, 2F, $-CF_2^-$), -122.14 to -122.51 (m, 6F, $-CF_2^-$), -123.26 to -123.33 (m, 2F, $-CF_2^-$), -126.73 to -126.80 (m, 2F, $-CF_2^-$); IR(KBr): $\nu = 3411, 1632, 1518, 1313, 1253, 1124, 1031, 965, 823, 725$ cm^{-1} ; Elemental analysis calculate (%) for $C_{22}H_{14}F_{10}O_8S_2Ti$ (as two hydrates): C, 37.30; H, 1.99; found: C 37.28; H, 2.01.

Preparation of 2·H₂O·THF:

To a solution of Cp_2TiCl_2 (0.249 g, 1.0 mmol) in 20 mL THF was added a solution of $AgOSO_2C_4F_9$ (0.832 g, 2.05 mmol) in 10 mL THF. After the mixture was stirred at 25 °C for 1 hour in the absence of light, it was filtrated. The filtrate was placed in a small jar and then put into a larger jar which was added 40 mL dry hexane and then the larger jar was obdurate. After keeping in the refrigerator for 24 hours, the yellow crystal was obtained (631 mg, 70%). 1H NMR (400 MHz, acetone- d_6) δ 7.22 (s, 10H, Cp), 3.64 to 3.61 (m, THF), 1.82 to 1.76 (m, THF); ^{19}F NMR (376 MHz, acetone- d_6) δ -81.81 (t, $J = 20.3$ Hz, 3F, CF_3^-), -115.03 (s, 2F, $-CF_2^-$), -122.04 to 122.10 (m, 2F, $-CF_2^-$), -126.57 to -126.68 (m, 2F, $-CF_2^-$); IR(KBr): $\nu = 3439, 3104, 2874, 1635, 1441, 1358, 1262, 1217, 1134, 1063, 1022, 815, 744, 703, 661$ cm^{-1} ; Elemental analysis calculate (%) for $Cp_2Ti(OSO_2C_4F_9)_2$ after pumping for a week: $C_{18}H_{10}F_{18}O_6S_2Ti$: C, 27.85; H, 1.30; found: C, 27.82; H, 1.35.

Crystal data for 2·H₂O·THF: $C_{22}H_{24}F_{18}O_{10}S_2Ti$; $Mr = 898.40$, Monoclinic, space group $P21/c$, $a = 16.1896(17)$ Å, $b = 12.8505(13)$ Å, $c = 19.6306(15)$ Å; $V = 3538.8(6)$ Å³; $T = 293$ (2) K; $Z = 4$; Reflections collected/unique, 23243/6888, $R_{int} = 0.0175$, Final R indices [$I > 2\sigma(I)$] $R_1 = 0.0536$, $wR_2 = 0.1465$; R indices (all data), $R_1 = 0.0597$, $wR_2 = 0.1484$. $GOF = 1.089$; CCDC No. 894849.

Preparation of 3:

To a solution of Cp_2TiCl_2 (0.249g, 1.0 mmol) in 20 mL CH_3CN was added a solution of $AgOSO_2C_6F_5$ (0.791g, 2.05 mmol) in 10 mL CH_3CN . After the mixture was stirred in the absence of light at room temperature for 2 hours, it was filtrated and evaporated in the vacuum and the resulted residue was diluted with 10 mL THF and followed by five drops of dry hexane and then was maintained in the refrigerator for 24 hours, the yellow crystal was obtained (517 mg, 73%). Recrystallization of this complex in THF/hexane produced good crystals suitable for X-ray analysis. Mp: 214-216 °C; 1H NMR (400 MHz, acetone- d_6) δ 7.13 (s, 10H, Cp), ^{19}F NMR (376 MHz, acetone- d_6): δ -139.33 (s, 2F, $C_6F_5^-$), -152.20 (s, 1F, $C_6F_5^-$), -163.00 (s, 2F, $C_6F_5^-$); IR(KBr): $\nu = 3411, 1632, 1518, 1313, 1253, 1124, 1031, 965, 823, 725$ cm^{-1} ; Elemental analysis calculate (%) for $C_{22}H_{14}F_{10}O_8S_2Ti$ (as two hydrates): C, 37.30; H, 1.99; found: C 37.28; H, 2.01.

Crystal data for 3: $C_{22}H_{14}F_{10}O_8S_2Ti$; $Mr = 708.35$, Monoclinic, space group $C2/m$, $a = 14.3586(13)$ Å, $b = 15.8694(16)$ Å, $c = 12.0211(11)$ Å; $V = 2593.8(4)$ Å³; $T = 100(2)$ K; $Z = 4$; Reflections collected/unique, 9551/2501, $R_{int} = 0.0257$, Final R indices [$I > 2\sigma(I)$] $R_1 = 0.0294$, $wR_2 = 0.0771$; R indices (all data), $R_1 = 0.0337$, $wR_2 = 0.0795$. $GOF = 1.146$; CCDC No. 938518.

Typical procedure for solubility of 1·THF, 2·H₂O·THF and 3:

Acetone (0.5 mL) was placed in a test tube; the complex 1·THF was added gradually at room temperature. When the amount of added 1·THF exceeds 142 mg, insoluble 1·THF appeared. Based on this data, solubility of 1·THF was determined to be 284 gL⁻¹. According to the same procedure, the solubilities of complexes 2·H₂O·THF and 3 were determined.

Typical procedure for Conductivity measurement:

Acetonitrile (10 mL) was placed in a beaker; the complex 2·H₂O·THF (4.5 mg, 0.005 mmol) was added at room temperature. The probe was placed in the solution for the measurement of correlative conductivity. According to the same procedure, the conductivities of 1·THF and 3 were measured.

ESR detection of O₂⁻¹ complex:

A quartz ESR tube (4.5 mm i.d.) containing an oxygen-saturated solution of dimeric 1-benzyl-1,4 dihydronicotinamide (BNA)₂ (1.0×10^{-2} M) and 1·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 O₂⁻¹ 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 Mn^{2+} marker, which was used as a reference.

UV/Vis spectra detection of the 10-methylacridone/2·H₂O·THF:

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 $[M^{n+}]^{-1}$, 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.

Typical procedure for fluorescence spectra detection of $2 \cdot H_2O \cdot THF$:

The fluorescence measurement of 10-methylacridone/ $2 \cdot H_2O \cdot THF$ was performed on a spectrofluorophotometer. The excitation wavelength of 10-methylacridone/ $2 \cdot H_2O \cdot THF$ was 413 nm in MeCN. The MeCN solutions were desalted by argon purging for 7 min prior to the measurements.

Crystal data refinements details

Refinement of F^2 against All reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > 2 \sigma(F^2)$ is used only for calculating R -factors (gt) etc. and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger. Data collection: Bruker SMART; cell refinement: Bruker SAINT; data reduction: Bruker SHELXTL; program(s) used to solve structure: SHELXS97 (Sheldrick, 1990); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: Bruker SHELXTL; software used to prepare material for publication: Bruker SHELXTL. CCDC-894849 and CCDC-938518 contain 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 the Strecker reaction of benzaldehyde (5a) with aniline (6a) and trimethylsilyl cyanide (7a) catalyzed by $1 \cdot THF$:

A mixture of PhCHO (106 mg, 1 mmol), PhNH₂ (93 mg, 1 mmol), trimethylsilylcyanide (119 mg, 1.2 mmol) and Catalyst $1 \cdot THF$ (9 mg, 0.01 mol) was stirred at room temperature until the reaction was complete. It was subject to evaporation in vacuum at room temperature, the residue was dissolved in CH₂Cl₂ (10 mL \times 3) and the catalyst was collected by means of filtration for the next cycle of reaction. To the filtrate, after evaporation of the solvent a pale yellow solid mixture was obtained. The products **8a** were isolated by silica gel column chromatography on silica gel (petroleum ether:EtOAc = 8:1) in yield 95% (198 mg) as pale yellow solid. Aldehydes/Ketones (**5**) and amines (**6**) and nucleophiles trimethylsilyl cyanide (**7a**) are commercially available.

Typical procedure for the Mannich-type reaction of benzaldehyde (5a) with aniline (6a) and trimethyl(1-phenyl-vinyloxy)silane (9b) catalyzed by **3**:

Complex **3** (7 mg, 0.01 mmol), PhCHO (106 mg 1.0 mmol), PhNH₂ (93 mg, 1.0 mmol) and trimethyl(1-phenyl-vinyloxy)silane (230 mg, 1.2 mmol) were placed in a 50 mL round-bottomed flask. Then the mixture was stirred at room temperature until the reaction was complete as indicated by TLC. Then the solvents of the resulting mixture were removed by evaporation in vacuum, the residue was dissolved CH₂Cl₂ (10 mL \times 3) and the catalyst was collected by means of filtration for the next cycle of reaction. The filtrate was subject to volatilization and the pale yellow solids were obtained, the products **10a** were isolated by silica gel column chromatography on silica gel (petroleum ether : EtOAc = 5:1) in yield 94% (283mg) as white solid. Aldehydes (**5**) and amines (**6**) and nucleophiles ketene silyl acetals (**9a**) and enol silyl ethers (**9b**) are commercially available.

Typical procedure for the Mukaiyama-aldol reaction of benzaldehyde (5a) with ketene silyl acetals (9a) catalyzed by $2 \cdot H_2O \cdot THF$:

Complex $2 \cdot H_2O \cdot THF$ (45 mg, 0.05 mmol), and ketene silyl acetal (**9a**) (209 mg, 1.2 mmol) were added to a solution of PhCHO (**5a**) (106 mg, 1.0 mmol) in THF (3.0 mL) at 0 °C. Then the temperature was raised to room temperature slowly. After the mixture was stirred at room temperature for 5 h and monitored by TLC, it was subject to evaporation in vacuum at room temperature, the residue was dissolved in *n*-hexane (10 mL \times 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 minutes. 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 residue was subject to silica gel column chromatography (petroleum ether : ethyl acetate = 10:1), colourless crystals of (**11a**) were obtained, (196 mg, isolated yield 95%). Aldehydes (**5**) and nucleophiles ketene silyl acetals (**9a**) and enol silyl ethers (**9b**) are commercially available.

Typical procedure for allylation of benzaldehyde (5a) with tetrallyltin (12) catalyzed by $2 \cdot H_2O \cdot THF$:

Complex $2 \cdot H_2O \cdot THF$ (45 mg, 0.05 mmol) was added to a solution of benzaldehyde (106 mg, 1.0 mmol) in CH₃CN (3.0 mL). Tetrallyltin (**12**; 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 \times 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 **13a** was obtained as a colorless oil (139 mg, isolated yield 95%). Aldehydes (**5**) and tetraallylalin (**12**) are commercially available.

Typical procedure for the Mukaiyama-aldol reaction of Benzaldehyde dimethyl acetal (14**) with ketene silyl acetals or enol silyl ethers (**9**) catalyzed by 2·H₂O·THF:**

[The operation method is similar to Mukaiyama-aldol reaction of benzaldehyde(**5a**) with ketene silyl acetals (**9a**). The solvent was replaced with CH₃CN. Benzaldehyde dimethyl acetal (**14**) and nucleophiles ketene silyl acetals (**9a**) and enol silyl ethers (**9b**) are commercially available].

Typical procedure for Friedel-Crafts acylation of anisole (16a**) with acetic anhydride (**17a**) catalyzed by 2·H₂O·THF:**

To a 50 mL round-bottom flask was added anisole (**16a**) (108 mg, 1.0 mmol), acetic anhydride (**17a**) (204 mg, 2.0 mmol) and catalyst 2·H₂O·THF (45 mg, 0.05mmol). Then the mixture was stirred at room temperature until complete consumption of starting material as monitored by TLC or GC-MS analysis. After that, 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. The solvent was removed by evaporation in vacuum and was then subject subject to silica gel column chromatograph; the Friedel-Crafts acylation product (**18a**) was obtained: 131 mg, isolated yield 87%. Alkyl aryl ethers (**16**) and anhydrides (**17**) are commercially available.

Typical procedure for the aza-Friedel-Crafts of benzaldehyde (5a**) with indole (**19a**) and *N,N*-dimethylaniline (**20a**) catalyzed by complex **3**:**

To a 50 mL round-bottom flask was added benzaldehyde (106 mg, 1.0 mmol), indole (117 mg, 1.0 mmol) and *N,N*-dimethylaniline (133 mg, 1.1 mmol), CH₂ClCH₂Cl (3 mL) and catalyst **3** (14 mg, 2 mol%). Then the mixture was stirred at 100 °C until complete consumption of starting material as monitored by TLC. Then the reaction mixture was evaporated in vacuum, CH₂Cl₂ (10 mL × 3) was added to the reaction mixture and the catalyst was filtered for the next cycle of reaction. The combined CH₂Cl₂ solution was removed by evaporation in vacuum and was then subject to silica gel column chromatograph; the one-pot three-component aza-Friedel-Crafts product (**21a**) was obtained, white solid, 235 mg, isolated yield 72%. Aldehydes (**5**) and indoles (**19**) and nucleophiles *N,N*-dialkylaniline (**20**) are commercially available.

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† Electronic Supplementary Information (ESI) available: [Cif files of 2·H₂O·THF and **3**, ¹H and ¹³C NMR spectra, MS spectra characterization data for compounds of application reaction; The copies of all compounds' spectra including the ¹H NMR, ¹³C NMR spectra and the ¹H NMR and ¹⁹F NMR spectra of complexes **1**·THF, **2**·H₂O·THF and **3**]. See DOI: 10.1039/b000000x/

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