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Development of unique dianionic Ir(III) CCC pincer complexes with a favourable spirocyclic NHC framework

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A new type of dianionic Ir(III) CCC pincer complexes (SNHC-Ir, **1a**–**1c**) is successfully designed and synthesized by developing a one-step methodology, which involves an initial coordination of Ir(I) with the NHC and subsequent metallation of double sp^{2}C–H bonds. This method is considerably useful over those reported by using strong coordination ligand or carbonic anion exchange, and would provide an alternative efficient template of organometallics synthesis. Experimental and density functional theory (DFT) calculation results indicate that the spirocyclic framework is a favourable factor for the facile formation and stabilization of these complexes. Primary investigation shows that chloride **1b** can well catalyze homo and hetero addition of styrene derivatives and remote olefin isomerization, which represents the first catalytic application of the dianionic CCC pincer complexes.

spirocyclic NHC framework, dianionic CCC pincer complexes, iridium-catalyzed, C–H activation

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Over the past decades, a number of pincer complexes have been explored due to their novel reactivities and potential applications in catalytic chemistry [1]. For a certain central metal atom (M) of a pincer complex, its chemical reactivity largely relies on the chelation mode, the nature of three coordination atoms (W and 2×Z) around M and ligand backbone [1a,2a]. Among the pincer complexes developed so far, most members fall into the category of type A (Figure 1), which have two or three heteroatomic (N, O, P) coordination sites [2]. Hitherto, however, only sporadic examples have been reported to possess all three carbon centers as coordination atoms (‘CCC’ pincer complexes), and even fewer contained two or more carbon-M covalent bonds (di- or multi-anionic complexes) [3]. An earlier example of dianionic CCC pincer complexes was reported by Cavell and co-workers in 2005 [4], which requires the strong electron donating ligands and the remove of the cod ligand to facilitate C–H bond metallation (type B). To our best knowledge, the catalytic activities of these dianionic CCC pincer complexes have not been investigated.

The potential versatile reactivities of CCC pincer complexes, especially those with two or more carbon-M covalent bonds have spurred our research interests. Initially, we synthesized the BF_4^- salt with the typical *N,N*-diphenyl 1,3-hexahydro-pyrimidine and 1,3-imidazole carbene, but failed to obtain the expected pincer complexes after treatment with several metal species $[Ir(cod)Cl]_2$, $[Rh(cod)Cl]_2$, $Pd(cod)Cl_2$

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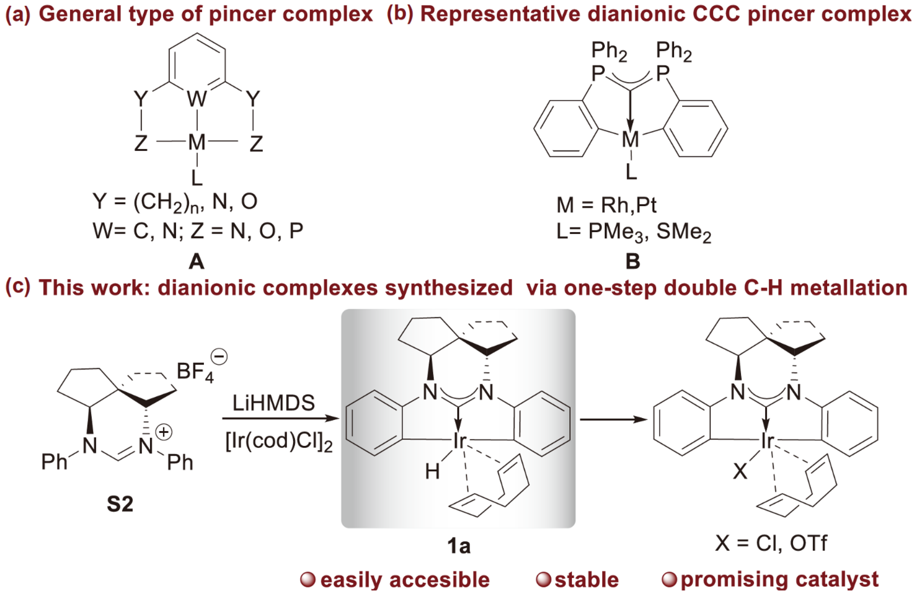
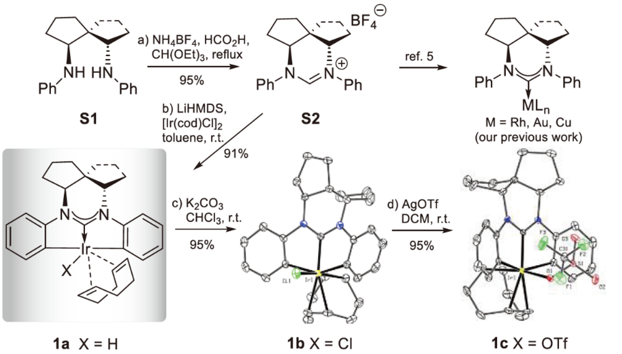


Figure 1 Representative cyclometalated pincer complexes (color online).

or Ni(cod)$_2$ using a general procedure [5]. In most cases, only the mono NHC-ligated products were obtained.

In connection with our long-standing interest in spirocyclic frameworks [6], we envisioned that the presence of such a structural moiety with a rigid quaternary carbon center in NHC ligand would probably exert spatial constraints to facilitate the formation of a stabilized dianionic CCC pincer complex [7]. Consequently, a six- membered cyclic carbene BF_4^- salt **S2** with a spirocyclic skeleton was prepared (Figure 1(c)). While **S2** was alkalized with lithium hexamethyldisilazide (LiHMDS) followed by treatment with transition-metal salts [Rh(cod)Cl]$_2$, Au(Me$_2$-S)Cl, or CuCl, the reaction still gave the simple NHC-ligated complex [5]. Pleasingly, when [Ir(cod)Cl]$_2$ was used, an expected dianionic CCC pincer complex **1a** was isolated in about 20% yield. This complex was possibly formed through a tandem NHC→M coordination and subsequent double consecutive sp^{2}C–H metallation. Thereafter, we have made a great effort to optimize and extend this preparation process. Herein, we present our synthetic procedures of dianionic Ir(III) CCC pincer complexes **1a**–**1c** and investigation of their primary properties.

The racemic *cis*,*cis*-spirodiamine **S1** was treated with NH_4BF_4 in CH(OEt)$_3$ in the presence of formic acid (0.1 equiv.) over 4 h at 120 °C, affording the carbene BF_4^- salt **S2** in 95% yield. Subsequently, **S2** was alkalized and treated with [Ir(cod)Cl]$_2$ at room temperature would afford the expected pincer complex **1a** in 91% yield after purification by flash column chromatography. The other two derivatives **1b** and **1c** were easily obtained by treatment of a solution of **1a** with K_2CO_3 in $CHCl_3$ or **1b** with AgOTf in CH_2Cl_2, respectively (Scheme 1). It was notable that complex **1a** was bench stable for at least two weeks. In comparison, **1b** and **1c** were much more stable than **1a** and did not decompose even at their melting points in air. The structures of **1a**–**1c** were confirmed by X-ray diffraction analysis (Section 3 in Supporting Information online).



Scheme 1 Synthesis of pincer complexes **1a**–**1c** (color online).

As shown in the crystal structure of **1a** (Figure 2), the bond length (1.967(8) Å) of Ir(1)–C(1) was within the normal range of NHC–Ir coordination bonds [8]. And the bond lengths (2.118(8) and 2.123(9) Å) of Ir(1)–C(12) and Ir(1)–C(22), respectively, indicated the formation of two sp^{2}C–Ir covalent bonds [9]. These evidences confirmed the presence of the central CCC pincer chelation mode. Furthermore, the hydrogen nuclear magnetic resonance (^{1}H NMR, singlet at −10.58 ppm), high-resolution mass spectra (HRMS, *m*/*z*: 639.2327, calcd. for $[C_{30}H_{35}N_2Ir+Na]^+$), and infrared spectra (IR, *ν* 2,085 cm^{-1}) also suggested the existence of Ir–H in **1a**. Of note, instead of a typical chair conformation, the hexahydro-pyrimidine NHC moiety showed an unusual envel-

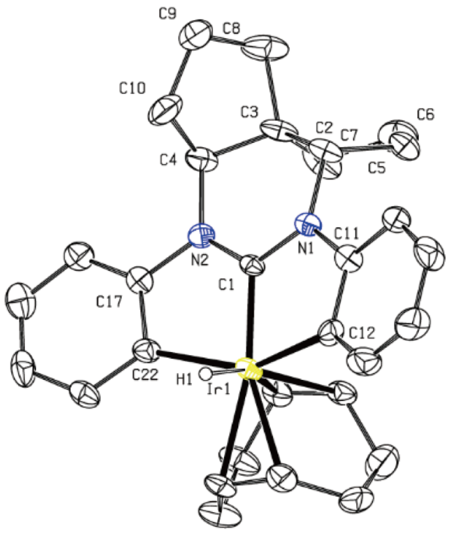


Figure 2 X-ray crystal structure of **1a**. Selected bond lengths (Å) and angles (°): Ir(1)–C(1) 1.967(8), Ir(1)–C(12) 2.118(8), Ir(1)–C(22) 2.123(9), Ir(1)–H(1) 1.80(7), C(2)–C(3)–C(4) 112.7°(8) (color online).

ope conformation with five atoms (C2, N1, C1, N2, C4) in a plane and the quaternary C(3) out of it. In addition, the X-ray structure of spiro[4.4]nonane-1,6-diamine moiety in **1a** showed that the angle (112.7°) of ∠C(2)–C(3)–C(4) was comparable to that (117.5°) of a free spirocyclic diol molecule [10].

Computational studies were next carried out to insight into the possible formation mechanism of **1a** (Figure 3). The calculation using density functional theory (DFT) suggested that the reaction was initiated by generation of a spirocyclic NHC from **S2** under basic condition, which was coordinated with $[Ir(cod)Cl]_2$ to give the Ir(I) intermediate **A4**. Subsequently, the common transition states [11] such as oxidative addition (**TS2-1** and **TS2-2**) and base-promoted C–H metallation (**TS2-3**) (energy barriers of 31.8, 33.7 and 85.2 kcal/mol, respectively) of the key C–H activation were calculated, but these high energy barriers did not match with our mild experimental condition. A more rational intermediate **A5** with one Ir(I)-cod coordinate bond dissociated was then proposed, after which an oxidative addition of Ir(I) to sp^2C–H would occur with a reasonable energy barrier (23.0 kcal/mol) through **TS2**, affording the Ir(III) intermediate **A6**. Elimination of HCl from **A6** and spontaneous recombination of the cod ligand would give intermediate **A8**. Finally, the second sp^2C–H metallation took place through **TS3** to afford the product **1a**. During the process (**A4-1a**), the overall energy barrier was 24.0 kcal/mol, which agreed well with our experimental facts. And the HCl produced above would irreversibly react with HMDS to drive the equilibrium forwards [12]. Of note, M06-2X functional was chose to explain the abnormal results (energy of **A8** was similar to **1a**) caused by the use of low accuracy B3LYP functional, and finding the energy of **1a** was 3.9 kcal/mol below than **A8**. As comparison, higher energy barriers of the simple six-membered-ring (**TS2′**, 25.4 kcal/mol) and five-membered-ring (**TS2″**, 32.2 kcal/mol) NHC precursors without spirocyclic moiety were calculated by the same method, which also supported the unsuccessful preparation of their Ir(III) complexes (for computational details, see section 5 in Supporting Information online).

To develop the chemical reactivity of above complexes, we have hopefully tested their catalytic activity toward inert C–H activation and subsequent transformations, though many conversions mediated by Ir catalysts have been reported [13], they generally involved the Ir(III)/Ir(I) processes. We hoped to achieve the unusual Ir(III)/Ir(V) mechanism, which would be further verified in our later period work. The first was toward the selective sp^2C–H ac-

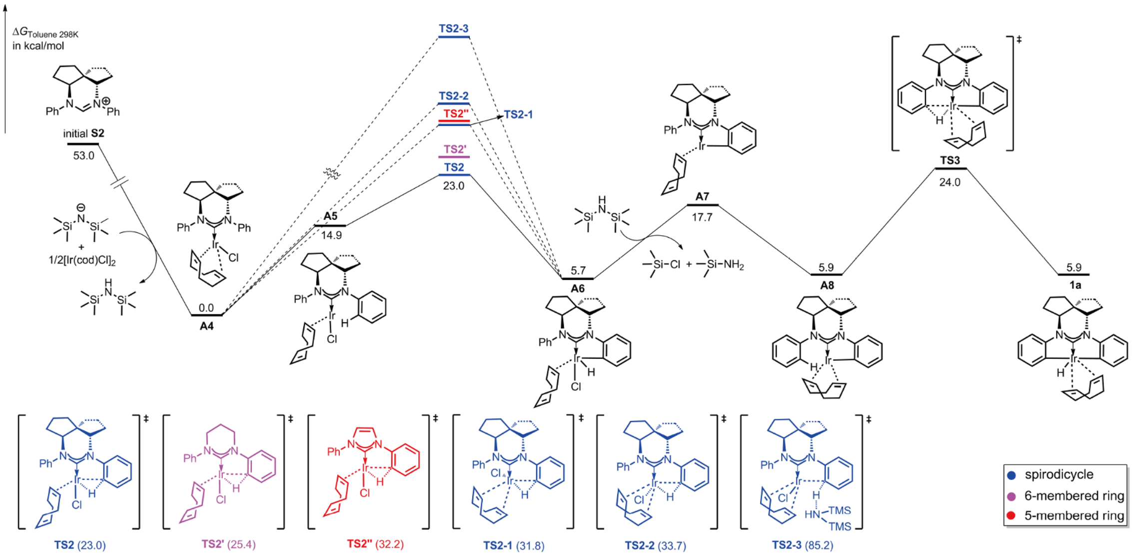


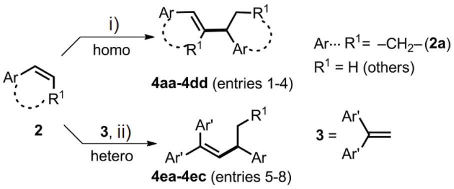
Figure 3 Energy profiles for the formation of complex **1a** from **S2**. Bond distances were given in Å (color online).

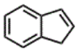
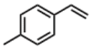
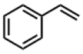
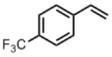
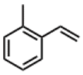
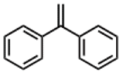
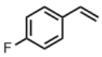
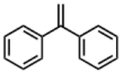
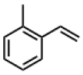
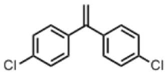
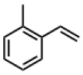
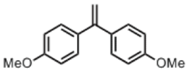
tivation/addition of styrene derivatives. Such a direct conversion did not require hetero-atomic induction, thus is of step- and atom-economy and environment benign [14]. Importantly, some precursors of anti-cancer pharmaceuticals, such as toremifene and tamoxifen [15], could be prepared by means of this straightforward transformation. Though several catalytic systems based on Ni, Pd and Ru complexes have been employed [16], more effective catalysts are still in high demand.

Hence, after screening of reaction conditions under the catalysis of complexes **1a**–**1c** (Table S21, Supporting Information online), a low catalyst loading of **1b** (0.5 mol%–1.0 mol%) combined with AgOTf (5.0 mol%) in ether solvents (except entry 4) was found to enable the homo or hetero addition in moderate to high yields (64%–92%) and excellent regioselectivities. It should be noted that **1c** was also highly effective in catalyzing the reaction, and the precipitation of AgCl did not influence the experimental results according to our tests.

As summarized in Table 1, homo addition of styrene derivatives **2a**–**2d** were successfully conducted, providing the desired products **4aa**–**4dd** in high yields (entries 1–4) re-

Table 1 **1b**-catalyzed head-to-tail addition of styrenes a)



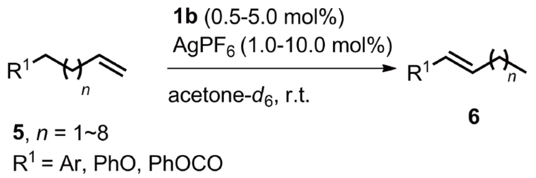
Entry	2	3	Time (h)	4	Conversion (%) b)	Yield (%) c)
1	 **2a**	–	16	**4aa**	>99	92
2	 **2b**	–	16	**4bb**	>99	83
3	 **2c**	–	16	**4cc**	95	89
4 d)	 **2d**	–	24	**4dd**	95	85
5	 **2e**	 **3a**	8	**4ea**	>99	83
6	 **2f**	 **3a**	8	**4fa**	>99	75
7	 **2e**	 **3b**	8	**4eb**	>99	88
8	 **2e**	 **3c**	8	**4ec**	>99	64

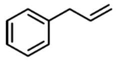
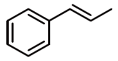
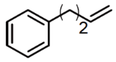
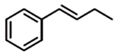
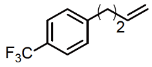
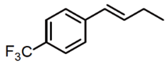
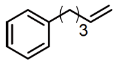
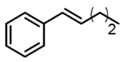
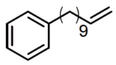
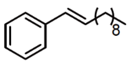
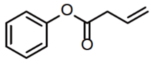
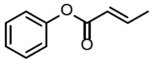
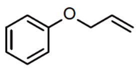
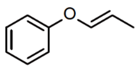
a) Conditions: i) for entries 1–4, **2** (1.0 mmol), **1b** (0.5 mol%) and AgOTf (5.0 mol%) in tetrahydrofuran (THF, 0.5 mL) at 80 °C for 16–24 h; ii) for entries 5–8, **2**(0.5 mmol), **3** (1.25 mmol), **1b** (1.0 mol%) and AgOTf (5.0 mol%) in dioxane (0.5 mL) at 100 °C for 8 h. b) Crude products were analyzed by LC-MS. c) Isolated yields. d) 0.5 mL 1,2-dichloroethane (DCE) was used for **2d** only.

gardless of the electronic properties of the aryl substrates. Specifically, when an inert EWG (*p*-CF_3) **2d** was used, the reaction still proceeded in DCE (85% yield, entry 4). Next, the more challenging hetero addition with different styrenes **2** and **3** also proved feasible. To achieve a highly regioselective hetero head-to-tail addition and avoid undesired self-addition, sterically hindered 1,1-substituted styrene diarylethenes **3** should be used in excess equivalents. In these cases, hetero addition products were generally obtained in moderate to good yields and high regioselectivities (entries 5–8). Of note, when a highly reactive EDG-(MeO) substituted substrate **3c** was used, the reaction still gave **4ec** as a dominant product, albeit in moderate 64% yield along with minor homo addition product of **3c** (entry 8).

The second investigation was performed toward the controlled isomerization of olefins (Table 2). This transformation can provide access to some hard-to-obtain olefin derivatives. Several metal (Rh, Ru, Pd and Co) catalysts have been reported [17], but most required external hydrogen sources and are often confronted with selective issues, such as regio- and *E/Z* selectivity. As expected, combination of a low loading of **1b** (0.5 mol%–5.0 mol%) with $AgPF_6$ (1.0 mol%–10.0 mol%) was demonstrated to enable the isomerization of a diverse range of olefins (Table S22), generating single regioselective products in high yields (except entry 5) and high *E/Z* ratios of 97:3–99:1 (except entry 7). The remarkable features of this protocol included: (1) Broad substrate scope, including not only a series of terminal olefins with a distal phenyl group (entries 1–5), but also the phenyl allylcarbonate ester (entry 6) and the phenyl

Table 2 **1b**-Catalyzed isomerization of various 1-olefins [a)]



Entry	5	1b (mol%)	Time (h)	6	Yield (%) [b)]	*E/Z* [c)]
1	 **5a**	0.5	6	 **6a**	92	98:2
2	 **5b**	2.5	20	 **6b**	94	98:2
3	 **5c**	2.5	20	 **6c**	92	98:2
4	 **5d**	2.5	20	 **6d**	82	99:1
5 [d)]	 **5e**	5.0	48	 **6e**	65	97:3
6	 **5f**	2.5	24	 **6f**	96	98:2
7	 **5g**	0.5	2	 **6g**	95	85:15

a) Unless otherwise specified, reactions were conducted with **5** (0.5 mmol), **1b** (0.5 mol%–5.0 mol%), $AgPF_6$ (1.0 mol%–10.0 mol%) in acetone-d_6 (1.0 mL) at r.t.; b) isolated yields; c) determined by ^1H NMR; d) yield determined by ^1H NMR using CH_2Br_2 as internal standard.

allyl ether (entry 7); (2) notably, a remote C=C bond migration crossing nine methylenes intervals still gave high *E*/*Z* ratio of 97:3 and 65% yield (entry 5). Moreover, due to the high performance of this reaction, acetone-d_6 could be directly used as the solvent to obtain NMR spectra without purification of the reaction system.

In conclusion, we have designed and successfully synthesized a new class of unique dianionic Ir(III) CCC pincer complexes (SNHC-Ir) by developing a concise template method under mild conditions. The experimental and DFT calculation results proved that the spirocyclic skeleton was a favourable structure element for the formation and stabilization of this type of complex. The catalytic effect of chloride **1b** toward the styrene addition and remote olefin isomerization was just a preliminary testing result, and a further verification of unusual Ir(III)/Ir(V) mechanism during these processes is ongoing. In addition, more spirocyclic complexes with other frameworks, and more significant properties would be developed with our further research.

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Conflict of interest The authors declare no conflict of interest.

Supporting information The supporting information is available online at http://chem.scichina.com and http://link.springer.com/journal/11426. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.

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