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N-Methylation of *ortho*-Substituted Aromatic Amines with Methanol Catalyzed by 2-Arylbenzo[*d*]oxazole NHC-Ir(III) Complexes

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Seven new chelated cyclometalated Ir complexes $^{ABO}N,P$, $^{ABO}N,O$, $^{ABO}N,C_{(carbene)}$ based on a rigid and tunable 2-arylbenzo[*d*]oxazole backbone have been prepared for *N*-methylation of amines. Among these three coordinated mode, $^{ABO}N,C_{(carbene)}$ chelate iridium-based catalysts exhibited well performance in monomethylation of aromatic amines with methanol (MeOH) as green methylation reagent. The steric modified synthesis of $^{ABO}N,C_{(carbene)}$ complexes was described. The most active $^{ABO}N,C_{(carbene)}$ complex with the small steric hindrance as catalyst, was obtained from benzoxazole ring without substituent and methyl group benzoimidazole ring on the N-heterocyclic carbenes (NHC) ligand. A variety of amines including *para*- and *meta*- substituted aromatic amines as well as heterocyclic amines were suitable substrates. Importantly, this catalyst greatly promoted yield of *N*-methylation of *ortho*-substituted aromatic amines. Controlled kinetic experiments and deuterium-labeling reaction of *ortho*- substituted amines were conducted under the optimized conditions. On the basis of experimental results, a plausible mechanism was proposed.

Introduction

The *N* - monomethyl group is an important component in many synthetic structures, including pharmaceuticals, agrochemicals, natural products and materials. [1-4] Traditional synthetic process involves toxic methyl halides. Using methanol to introduce methyl group can offer an alternative "green" approach for monomethylation of amines, as water is the only byproduct. [5, 6] However, methylation with methanol need to go through a dehydrogenation process, and the value of dehydrogenation enthalpy (ΔH_{MeOH} = 84 kJ mol^{-1}) is large, which is a great challenge. [7-9]

Since the pioneering work of Grigg and co-workers in 1981 initiated with $RhH(PPh_3)_4$, applied in *N*-methylation of $PhNH_2$ (Ph=phenyl) using MeOH, [10] a variety of catalysts supported by different ligands, covering with mutidentate nitrogen [11-14] or phosphine [15,16] ligands, *N^P* or *N^P^N* pincer ligands, [17-22] N-heterocyclic carbene (NHC) [23,24] and others, [25,26] have been developed.

For instance, Li and coworkers described in the presence of a weak base (Cs_2CO_3), *N*-methylation of aromatic and aliphatic amines catalyzed by Cp*Ir complex with 2,2'-bibenzoimidazole ligand. [12] The group of Seayad reported $[RuCp^*Cl_2]_2$ (Cp* = η^5-C_5Me_5) and bidentate phosphine ligand dpePhos as a catalyst under mild conditions (40-100 °C), for *N*-methylation of primary anilines, aliphatic amines and sulfonamides with MeOH. [15] Ogata and Kayaki et al reported *N*-monomethylation of aromatic amines with low catalyst loading (0.02-0.1mol %) of PN^HP pincer Ru complex (PN^HP = bis(2-diphenylphosphinoethyl) amine)). [21] Crabtree and co-workers described the first bis-N-heterocyclic carbene Ir compound for methylation of aromatic anilines under MW irradiation. [23] Despite much progress mentioned above, most of them suffer from unavailability of particular substrates, especially *ortho*-substituted aromatic amines. Chen' group developed a new complex bearing a 2-hydroxy-6-((6-hydroxypridin-2-yl)methyl)pyridine ligand as catalyst applied in methylation of anilines with methanol, which revealed *ortho*-bromoaniline (62%) from large steric hindrance was less active than *meta*- and *para*- bromoanilines (75% and 90%). [14]

Taking the aforementioned points into account, to expand the scope and explore the steric effect of *ortho*-substituted aromatic amines were significantly crucial. Hence, to design appropriate catalysts to explore the relationship between catalytic system and steric hindrance of substrates, in order to improve catalytic reactivity for *N*-methylation of *ortho*-substituted aromatic amines with methanol, is highly needed.

Steric hindrance and electronic effect of different substituents from ligands or catalysts can be greatly influenced

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† Electronic Supplementary Information (ESI) available: Details of crystallographic, collection and refinement data for **1**, **2**·H_2O, **4**, **7** and selected bond lengths (Å) and angles (°) in the complexes **1**, **2**·H_2O, **4**, **7**. CCDC 1887419–1887422. [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

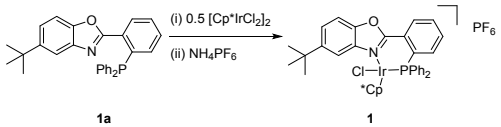
on the catalytic activity of reactions. [27-29] 2-Arylbenzoxazole is a tunable framework with controllable steric congestion and electronic characteristics. [30] By introducing with different coordinated atoms such as P, O, it can be effectively prepared cyclometalated complexes with steric hindrance and electronic effect. NHC ligands are also switchable and tunable. The NHC part of ligand with a weakly functionality, such as N from 2-arylbenzoxazole can coordinate with metal to form *N,C*$_{(carbene)}$ chelate complexes with modifed steric and electronic properties. [31] And the configuration of 2-arylbenzo[*d*]oxazole skeleton is the planar geometry, which coordinate with metal center to form a distorted-octahedral configuration. [32] Inspired by mentioned above, based on our laboratory exploring synthesis and application of 2-arylbenzo[*d*]oxazoles [33,34] and N-heterocyclic carbenes, [35-38] combining them to design and synthesize suitable catalysts with tunable steric hindrance and electronic effect to enhance catalytic performance, could be realized.

Herein, we reported a series of new chelated 2-arylbenzo[*d*]oxazolelyl functionalized ^{ABO} *N,P*, ^{ABO}*N,O* and ^{ABO}*N,C*$_{(carbene)}$ Ir(III) complexes. We took advantage of 2-arylbenzoxazole as the skeleton and the planar geometry of ligands to form complexes with steric effect and a certain steric configuration. After such modifications, the catalysts well matched with substrates, to achieve greatly promote the catalytic reactivity toward *N*-methylation of *ortho*-substituted aromatic amines.

Results and Discussion

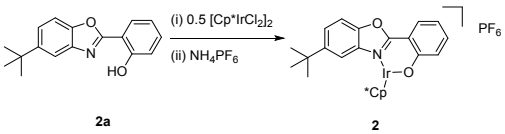
Synthesis of ^{ABO}*N,P*- and ^{ABO}*N,O*- chelated Ir(III) complexes

The brominated product, 2-(2-bromophenyl)-5-(*tert*-butyl)benzo[*d*]oxazole, was synthesized according to our group's previous reported procedures. [39,40] Then by lithiation with *n*-butyl lithium and phosphorization, the ^{ABO}*N,P* lignd **1a** were afforded. The ^{ABO}*N,O* ligand **2a**, 2-(5-(*tert*-butyl)benzo[*d*]oxazol-2-yl)phenol, was followed by the similar method of above brominated product. ^{ABO}*N,P*- and ^{ABO}*N,O*-chelated Ir(III) complexes **1** and **2** were prepared with $[Cp^*IrCl_2]_2$ in the presence of ammonium hexafluorophosphate (NH_4PF_6) (Scheme 1 and 2). The ^{1}H NMR spectra of **1** and **2** reveals a singlet *tert*-butyl resonance at δ 1.35 and 1.40. The Cp* group resonates at δ 1.53 and 1.35 (15H), respectively. Crystals of complexes **1** and **2** suitable for X-ray crystallography were grown from dichloromethane layered with *n*-pentane. Observed from Fig. 2, the complex **2** has converted to **2**·H_2O, which had one molecular H_2O coordinated with Ir metal center. [41] The bound H_2O molecule in the X-ray structure came from the diffusion solvent in the process of crystal growth..The geometry at the metal of **1** and **2**·H_2O are classic three-legged piano stool (Fig. 1 and 2).



1a **1**

Scheme 1 Synthesis of ^{ABO}*N,P*-chelated Ir(III) complex **1**.



2a **2**

Scheme 2 Synthesis of ^{ABO}*N,O*-chelated Ir(III) complex **2**.

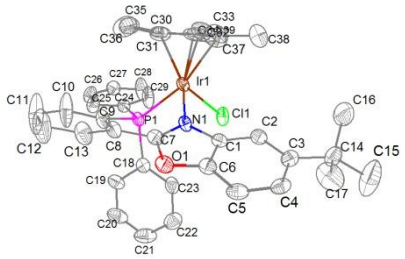


Fig. 1 Molecular structure of **1**. Ellipsoids are drawn at the 50 % probability level. Hydrogen atoms and noncoordinated PF_6^- anions omitted for clarity. Selected bond lengths (Å) and angles (deg) for molecule **1**: Ir(1)-N(1) 2.094(4); Ir(1)-P(1) 2.2933(12); Ir(1)-Cl(1) 2.4036(14); N(1)-Ir(1)-P(1) 82.26(11); N(1)-Ir(1)-Cl(1) 92.57(12).

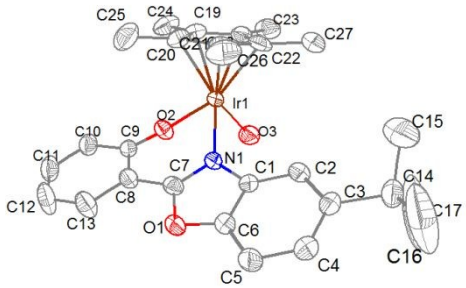


Fig. 2 Molecular structure of **2**·H_2O. Ellipsoids are drawn at the 50 % probability level. Hydrogen atoms and noncoordinated PF_6^- anions omitted for clarity. Selected bond lengths (Å) and angles (deg) for molecule **2**·H_2O: Ir(1)-N(1) 2.092(5); Ir(1)-O(2) 2.103(4); Ir(1)-O(3) 2.137(5); O(2)-C(9) 1.311(8) N(1)-Ir(1)-O(2) 83.15(19); N(1)-Ir(1)-O(3) 88.1(2); O(2)-Ir(1)-O(3) 78.9(2); C(9)-O(2)-Ir(1) 122.4(4)

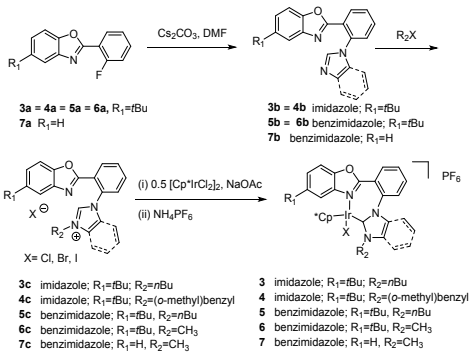
Synthesis of ^{ABO}*N, C*$_{(Carbene)}$-chelated Ir(III) complexes

2-(2-Fluorophenyl)benzo[*d*]oxazole or 5-(*tert*-butyl)-2-(2-fluorophenyl)benzo[*d*]oxazole, were afforded as similar method of **2a**. Then by nucleophilic aromatic substitution (S_NAr) under treatment with Cs_2CO_3, according to our previous literature, [34] fluorine-substituted 2-arylbenzoxazoles were converted into the products with imidazole. After adding alkyl halide reagent, ^{ABO}*N, C*$_{(Carbene)}$ ligands namely imidazole salts **3c-7c**, were afforded. They contained different substituents, including *ter*-butyl from benzo[*d*]oxazole ring, and *n*-butyl, (*o*-methyl)benzyl, methyl groups on the imidazole ring from the NHC ligands. Different substituents on 2-arylbenzo[*d*]oxazole skeleton or NHC ligands would affect electronic and steric

hindrance of ^{ABO}N, $C_{(Carbene)}$ ligands, even complexes forming with metals. [42]

The corresponding Ir complexes **3-7** were obtained by the reactions of **3c**-**7c** with $[Cp^*IrCl_2]_2$ in the presence of sodium acetate (NaOAc) [43] (Scheme 3). All of them have been characterized by ^1H and ^{13}C NMR spectra, high-resolution mass spectrometry (HRMS) and infrared spectra (IR).

In the ^1H NMR spectra of **3-7**, the corresponding NHC precursors C-H signal observed in ligands at δ =9.75- 10.59 ppm was absent. The $^{13}C\{^1H\}$ NMR spectra of **3-7** showed the characteristic resonance for the C atoms from NHC ligands at δ = 163.3-171.9 ppm, downfield shifted from the C resonance of the parent salt (δ = 157.7-158.7 ppm). [44] The representative complexes **4** and **7** were crystallized from dichloromethane / *n*-pentane and were further confirmed by single-crystal X-ray diffraction analysis (Fig. 3 and 4). The X-ray crystallographic data for **4** indicated the presence of small amounts of bromido instead of chlorido ligands, which indicated that the coordination ability of bromide is a little stronger than that of chloride in this system. [45,46] The ^{ABO}N, $C_{(Carbene)}$- chelated Ir(III) complexes featured a seven-membered ring consisting of two bonds between N atom of benzo[*d*]oxazolely and C of N-heterocyclic carbene. The Ir-N bonds and Ir-C bonds distance in **4** and **7**, were within the range of reported values in similar iridium complexes. [32] The torsion angles of N1-C7-C8-C13 in **4** and N1-C7-C8-C9 in **7** were 39.4 ° and 41.9 °, respectively, which showed a large twist compared with almost coplanar 2-arylbenzo[*d*]oxazole.



Scheme 3 Synthesis of $^{ABO}N,C_{(Carbene)}$- chelated Ir(III) complexes **3-7**.

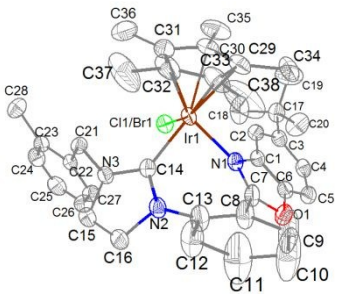


Fig. 3 Molecular structure of **4**. Ellipsoids are drawn at the 50 % probability level. Hydrogen atoms and noncoordinated PF_6^- anions omitted for clarity. Selected bond lengths (Å) and angles (deg) for molecule **4**: Ir(1)-C(14) 2.049(3); Ir(1)-N(1) 2.110(3); C(14)-Ir(1)-N(1) 88.28(11).

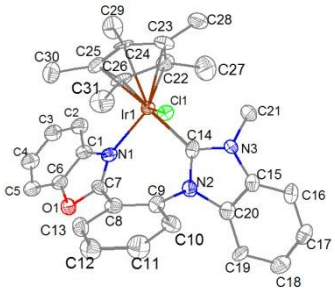


Fig. 4 Molecular structure of **7**. Ellipsoids are drawn at the 50 % probability level. Hydrogen atoms and noncoordinated PF_6^- anions omitted for clarity. Selected bond lengths (Å) and angles (deg) for molecule **7**: Ir(1)-C(14) 2.021(8); Ir(1)-N(1) 2.115(7); C(14)-Ir(1)-N(1) 89.5(3).

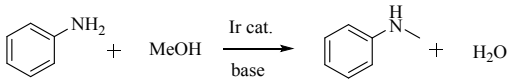
Catalytic activity

The $^{ABO}N,P$ chelated iridium complex **1** has been successfully applied in *α*-, *β*- and *N*-alkylation with primary alcohol. [40] Here, we used it for the *N*-methylation with MeOH as comparison. Initially, **1** and **2** as catalysts, were tested. Aniline was chosen as model substrate using MeOH as solvent. Reaction of aniline (0.5 mmol), KO^{t}Bu (1.0 eqv.), **1** (0.5 mol %) in 2 mL of MeOH at 130 °C for 12 h, in a sealed tube resulted in moderate (58 %) yield (Table 1, entry 1), as revealed by NMR with 1,3,5-trimethoxybenzene as the internal standard. While using **2** as catalyst resulted in 59 % yield, (Table 1, entry 2). Subsequently, the $^{ABO}N,C_{(Carbene)}$ -coordinated iridium complexes **3-5** were probed. In contrast with $^{ABO}N,P$- or $^{ABO}N,O$-chelated Ir(III)-complexes, $^{ABO}N,C_{(Carbene)}$ -coordinated iridium complexes showed a higher catalytic activity (62-96 %) in the methylation process (Table 1, entry 3-5). Among them, the catalytic activity of **5** from benzo[*d*]oxazole ring with *ter*-butyl substituent and *n*-butyl group benzoimidazole ring on the NHC ligand was more active than that of **3** with *ter*-butyl or **4** with (*o*-methyl)benzyl group imidazole ring on the NHC ligand.

With the most active compound **5** in hand, other reaction factors were screened. After reaction for 8 h, the target product was also obtained, albeit in lower yield (78%, entry 6 in Table 1). KO^{t}Bu was found to be the best base, whereas inorganic bases such as K_3PO_4 and KOH were inefficient (Table 1, entries 7-11). Interestingly, the amount of MeOH further increased (3 mL) or reduced (0.5 mL) with a significant decrease in the yield (Table 1, entry 12-14). Less the catalyst loading and the amount of base under this condition decreased the yield to 40 % and 31 %, respectively (entry 15-16), whereas the presence of 1.5 equiv of KO^{t}Bu was also inferior (Table 1, entry 17 *vs* 5). Another crucial factor was the temperature. No product was detected at 100 °C (entry 18). Only a trace amount of product was observed at 120 °C (entry 19). However, the yield was improved to 98 % with lengthened reaction time (entry 13 *vs* entry 20). Finally, the reaction with 0.5 mol% of **5** as catalyst, 1 equiv of KO^{t}Bu as base, using

MeOH (1 mL) as methylation reagent at 130 °C was found to be complete in 12 h.

Table 1 Optimization of the reaction conditions for *N*-methylation of aniline with MeOH [a]



Entry	Cat. (mol%)	Base (equiv)	Volume (mL)	Time (h)	Temp. (°C)	Yield (%)[b]
1	**1** (0.5)	KO^{t}Bu (1.0)	2	12	130	58
2	**2** (0.5)	KO^{t}Bu (1.0)	2	12	130	59
3	**3** (0.5)	KO^{t}Bu (1.0)	2	12	130	62
4	**4** (0.5)	KO^{t}Bu (1.0)	2	12	130	73
5	**5** (0.5)	KO^{t}Bu (1.0)	2	12	130	96
6	**5** (0.5)	KO^{t}Bu (1.0)	2	8	130	78
7	**5** (0.5)	NaO^{t}Bu (1.0)	2	8	130	64
8	**5** (0.5)	K_3PO_4 (1.0)	2	8	130	trace
9	**5** (0.5)	KOH (1.0)	2	8	130	22
10	**5** (0.5)	K_2CO_3(1.0)	2	8	130	36
11	**5** (0.5)	Cs_2CO_3 (1.0)	2	8	130	73
12	**5** (0.5)	KO^{t}Bu (1.0)	3	8	130	27
13	**5** (0.5)	KO^{t}Bu (1.0)	1	8	130	89
14	**5** (0.5)	KO^{t}Bu (1.0)	0.5	8	130	32
15	**5** (0.2)	KO^{t}Bu (1.0)	1	8	130	40
16	**5** (0.5)	KO^{t}Bu (0.5)	1	8	130	31
17	**5** (0.5)	KO^{t}Bu (1.5)	1	8	130	77
18	**5** (0.5)	KO^{t}Bu (1.0)	1	8	100	trace
19	**5** (0.5)	KO^{t}Bu (1.0)	1	8	120	5
20	**5** (0.5)	KO^{t}Bu (1.0)	1	12	130	98

[a] Reaction conditions: aniline (0.5 mmol).
[b] With 1,3,5-trimethoxybenzene as the internal standard.

Next, having established optimal conditions in hand, a variety of substrates were examined (Table 2). It can be observed that *meta*- or *para*- substituted anilines such as 4-methoxyaniline, 4-aminobenzonitrile, 3-methoxyaniline and 3-bromoaniline could obtained desired products from good to excellent yields (80%-93%, entry 2 to 5) using **5** as catalyst. Unfortunately, attempts to *ortho*-substituted electron-deficient or electron-richness anilines (*-OMe*, *-Me*, *-Cl*, *-Br*, *-I*) resulted in 15-21% yield (entry 6 to 10). This phenomenon also generally appeared in previous reports, [15, 23] presumably due to steric hindrance effect.

Table 2 *N*-methylation of aromatic amines using MeOH catalyzed by **5-7** [a]

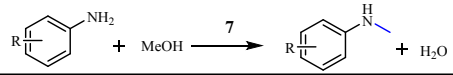
Entry	substrates	yield $_5$ (%)[b]	yield $_6$ (%)[b]	yield $_7$ (%)[b]
1	aniline	95	96	99
2	4-methoxyaniline	80	85	89
3	4-aminobenzonitrile	88	89	98
4	3-methoxyaniline	89	91	92
5	3-bromoaniline	93	94	96
6	2-methoxyaniline	21	42	68 (86) [c]
7	*o*-toluidine	17	34	55 (73) [c]
8	2-bromoaniline	18	30	65 (83) [c]
9	2-iodoaniline	15	27	60 (78) [c]
10	2-chloroaniline	20	48	75

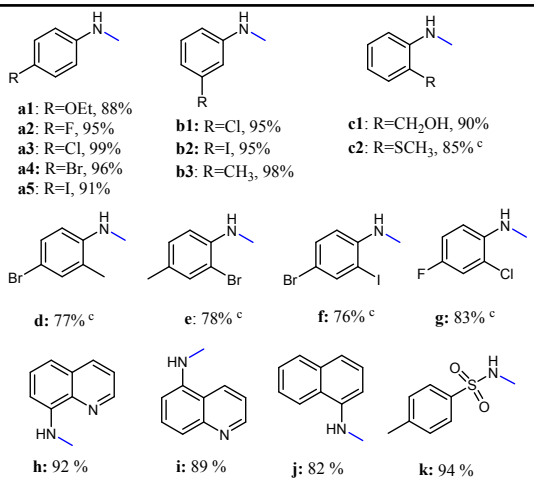
[a] Reaction conditions: anilines (0.5 mmol), **5-7** (0.5 mol%), KO^{t}Bu (1.0 equiv), MeOH (1 mL), 130 °C, 12 h. [b] Isolated yield. [c] 24 h.

To solve this problem, based on 2-arylbenzo[*d*]oxazole backbone and benzoimidazole ring on the NHC ligand, the complexes **6** from benzo[*d*]oxazole ring with *ter*-butyl substituent and methyl group benzoimidazole ring, and **7** from benzo[*d*]oxazole ring without substituent and methyl group benzoimidazole ring on the NHC ligand, were synthesized. No significant effect on *meta*- and *para*- position substrates catalyzed by **5**, **6** or **7**, was observed when either electron-withdrawing or electron-donating group. (entry 1 to 5). Surprisingly, we found that **6** were able to obtain the 2-methoxy-*N*-methylaniline (entry 6) in 42% yield while the **7** was even more promising (68 % yield). *o*-Toluidine (entry 7) was obtained 34 % catalyzed by the **6**, and 55 % yield by the **7**, which was higher than that of reported literature (45% using 5 equiv of base *vs* substrate). [23]

The *ortho*-substituted halogenated anilines (*-Cl, -Br, -I*) were remarkably improved by the **7** compared to **5** and **6**. (entry 8 to 10) After prolonging the reaction time to 24 h, the *ortho*-substituted anilines were obtained good yields (73-86 %).To expand the scope of substrates, other *para-, meta-* and *ortho*-substituted substrates using **7** with smaller steric bulk than that of **5** and **6**, were shown in Table 3. Both electron-rich and electron-deficient, *para-* (**a1**-**a5**), *meta-* (**b1**-**b3**) and *ortho*-(**c1**-**c2**) substituted substrates were produced in excellent yields (88-98%). The halogen groups were also fully compatible, and the corresponding *N*-methylated products (**d-g**) without dehalogenation were isolated in 76-83% yields. A wide range of heterocycles such as aminoquinoline (**h-i**), 1-naphthalamine (**j**), and sulfonamide (**k**) were also tolerated with 82-94% yields. However, 2,6-diisopropylaniline from highly steric hindrance was failed. Benzamide or benzylamine weren't also succeeded. Maybe they weren't suitable for this kind of catalysts. These results complied with previous findings regarding the importance of steric bulkiness of catalysts for *ortho*-substituted substrates. We attribute the superior performance of **7** over **5** and **6** to the weaker steric congestion attributed to tunable electronic properties and steric profile by the 2-arylbenzo[*d*]oxazole and NHC scaffold.

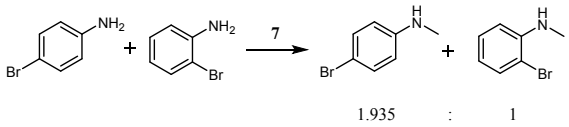
Table 3 *N*-methylation of aromatic amines using MeOH catalyzed by **7** [a]





[a] Reaction conditions: aniline (0.5 mmol), **7** (0.5 mol%), KO^{t}Bu (1.0 equiv), MeOH (1 mL), 130 °C, 12 h. [b] Isolated yield. [c] 24 h.

To further assess the difference of catalytic activity between *ortho*- and *para*- substituted substrates, a control experiment using 2-bromoaniline and 4-bromoaniline into the corresponding bromo-*N*-methylaniline carried out under the optimized reaction conditions with catalyst **7** (Scheme 4). The results showed that their products were obtained in a 1.9 :1 ratio. The yield from 4-bromoaniline was nearly twice from 2-bromoaniline, indicating *para*- substituted amines were more reactive in the methylation when both *ortho*- and *para*-substituted substrates were present in the reaction mixture, which was consistent with the reports. [14, 21]



Scheme 4 Control experiment under optimized conditions.

To explore influence on catalytic activity of *ortho*- substituted amines, 2-bromoanilin as example, the kinetic profiles of sequential reaction were investigated. NMR monitoring of the reactions progress for 2-bromoaniline with MeOH catalyzed by **5-7** confirmed yield of amines substrate in 12 h (Fig. 5). The results showed that the yield of 2-bromoaniline by **7** was much higher than that of **5** and **6**. And catalytic activity of **6** was more active than that of **5**, in agreement with the observation (Table 2) that *N*-methylation of *ortho*- substituted amines proceeded with a comparatively slow conversion by **5**.

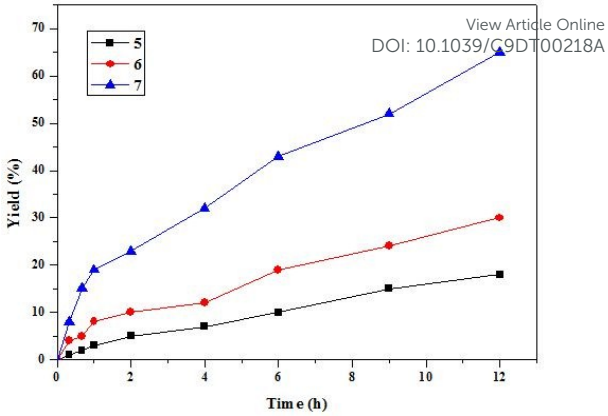
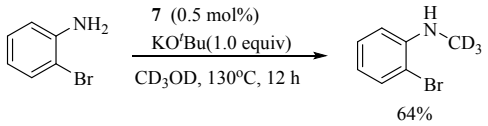


Fig. 5 Reaction profiles of 2-bromoaniline catalyzed by **5**-**7**.

Plausible mechanism

To elucidate the relationship between the steric bulkiness of catalysts and reactivity of substrates, deuteration experiments were performed (Scheme 5). The reaction of 2-bromoaniline carried out with 0.5 mol % of **7** in methanol-d_4 at 130 °C. 2-Bromo-*N*-methylaniline-d_3 was obtained in 64% yield after 12 h. Deuterium atoms were selectively located at the *N*-methyl group with no incorporation into the phenyl group. Based on previous reports, [12, 15] a proposed mechanism consistent with our experimental results was depicted in Scheme 6.



Scheme 5 Selective *N*-methylation in CD_3OD.

We took $^{ABO}N,C_{(Carbene)}$ -chelated iridium complexes **5**-**7** as catalysts. In the presence of KO^{t}Bu at 130 °C, MeOK was obtained. It attacked the metal center of **5-7** to form active Ir-methoxy complexes (III) **A**, respectively. By β-hydride elimination, **A** converted to Ir-H species (III) **B**, releasing formaldehyde. Then, the condensation between the resulting formaldehyde and *para*-, *meta*- or *ortho*- substituted amines gave corresponding unsaturated imines. The *ortho*-substituted unsaturated imines had larger steric hindrance than the corresponding ones with *para*- and *meta*-substitution. It was more difficulty in inserting into the iridium-hydride **B**. Due to the different steric bulk of catalysts (**5** > **6** > **7**), obviously, *ortho*- substituted unsaturated imines more easily touched Ir(III) metal center from **C** by **7** compared with **5** and **6**, due to **7** with smallest steric hindrance. Herein, the higher conversions were afforded by **7**. Subsequently, **D** occurred by simultaneous delivery of the hydride between **C** and unsaturated imines. The products of *N*-methylamines were released and the catalytic species **A** were regenerated. From the above mechanism, the steric hindrance of catalyst had great influence on the catalytic activity of *ortho*-substituted substrates.

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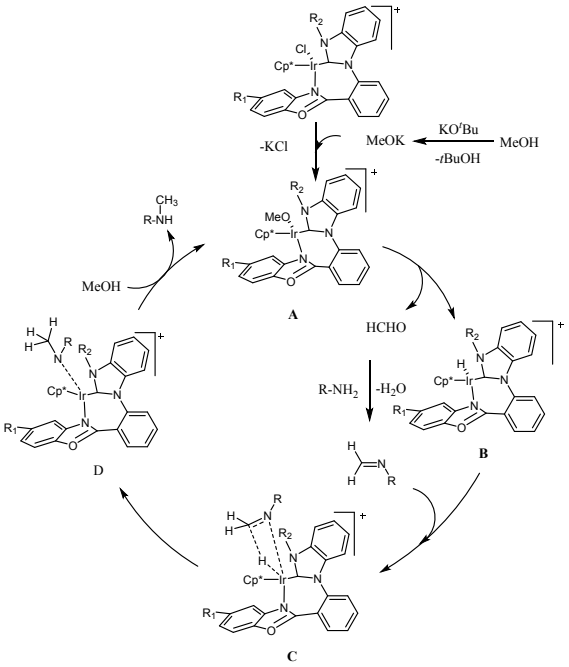

Scheme 6 Proposed mechanism by **5-7**.

Conclusions

We have demonstrated, seven chelated cyclometalated Ir complexes, including three kinds of different coordinated modes, $^{ABO}N,P$, $^{ABO}N,O$, $^{ABO}N,C_{(carbene)}$, bearing 2-arylbenzo[*d*]oxazole framework have been described. By modification on catalysts with electronic effect and steric hindrance based on 2-arylbenzo[*d*]oxazole backbone and NHC ligands, the yields of *ortho*- substituted aromatic amines for *N*-methylation using methanol has greatly remarkably improved. The scope of substrates has been broadened, covering electron-rich/deficient aromatic amines at *para*-, *meta*- and *orth*-position, heterocyclic amines, and many functional groups could be also tolerance. The mechanism of $^{ABO}N,C_{(carbene)}$Ir-catalyzed *N*-methylation of amines with MeOH has been elucidated according to our experimental observation and previous studies. Further research on transition-metal catalysis is ongoing in our lab.

Experimental section

General procedures

All commercially available compounds (Acros, Aldrich, Fluka, Merck, etc.) were used without purification. Dry solvents (such as dichloromethane) were collected from solvent dispenser system. All reaction vials were purchased from Beijing Synthware Glass. Analytical thin layer chromatography was performed on GF 254 plates. Flash Chromatography was performed on silica gel (200 ~300 mesh) by standard technical eluting with solvents as indicated. Reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. All starting material for substrates synthesis were purchased from Energy Chemical, Macklin, Aladdin and used as received unless otherwise stated. The starting material [{Cp*IrCl$_2$}$_2$] was synthesized according to the literature procedure. [47]

^{1}H, and ^{13}C NMR: Recorded on Bruker Avance III 400 MHz NMR Spectrometer, spectra were recorded at 295 K in $CDCl_3$ or DMSO-d_6. HRMS(ESI) analyses were performed at the EPSRC UK National Mass Spectrometry Facility (NMSF), Swansea. GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). Compounds described in the literature were characterized by comparison of their ^{1}H, and/or ^{13}C NMR spectra to the previously reported data. Fourier transform infrared (FT-IR) spectra were performed on a Nicolet AVATAR-360 IR using KBr discs in the range of 4000-400 cm^{-1}.

Synthesis of 1a-7a

1a was synthesized according to our published procedure.[39, 40] The 2-(2-bromophenyl)-5-(*tert*-butyl)benzo[*d*]oxazole (5 mmol) was dissolved in dry THF (30 mL) under N_2. After the solution was cooled to -78 °C, *n*-butyl lithium (*n*-BuLi) 2.3 mL (5.5 mmol, 2.4 M, 1.1 equiv) was added dropwisely *via* syringe during 15 min. The reaction mixture was stirred at -78 °C for 0.5 h. Then diphenylphosphine chloride (5.5 mmol) was added. The reaction mixture was allowed to warm to room temperature and stirred overnight. Added water and ethyl acetate to the mixture. The organic phase was extracted and concentrated. Then dried over anhydrous Na_2SO_4. Finally, it was purified by silica gel column chromatography to obtain the corresponding product **1a**.

1a: 75 % Isolated yield (light green solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (m, 1H, Ph), 7.71 (s, 1H, Ph), 7.49 (t, *J* = 7.5 Hz, 1H, Ph), 7.41 - 7.29 (m, 14H, Ph), 7.06 (m, 1H, Ph), 1.37 (s, 9H, Ph-C(C*H*$_3$)$_3$) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.56 (*C,* benzoxazole), 148.41(Ph), 147.70 (Ph), 141.67 (Ph), 139.06 (Ph), 138.80 (Ph), 137.57 (d, *J* = 10.5 Hz) (Ph), 134.55 (Ph), 134.07 (d, *J* = 20.5 Hz) (Ph), 131.55 (Ph), 131.34 (Ph), 130.74 (Ph), 130.47 (Ph), 130.03 (d, *J* = 3.0 Hz) (Ph), 128.48(d, *J* = 23.3.0 Hz) (Ph), 128.43 (Ph), 122.75 (Ph), 116.86 (Ph), 109.50 (Ph), 34.85 (*C*(CH$_3$)$_3$), 31.73 (C(*C*H$_3$)$_3$) ppm; ^{31}P NMR (162 MHz, $CDCl_3$) δ -6.14 (s) ppm; HRMS (ESI) calcd for $C_{29}H_{27}NOP$ [M+H$^+$] 436.1830, found: 436.1813.

General procedure for the synthesis of **2a-7a** was according to our previous report. [39]

2a: 81 % Isolated yield (white solid):^{1}H NMR (400 MHz, $CDCl_3$) δ 11.56 (s, 1H, Ph-O*H*), 8.02 (dd, *J* = 7.8, 1.5 Hz, 1H, Ph), 7.76 (d, *J* = 1.7 Hz, 1H, Ph), 7.51 (d, *J* = 8.6 Hz, 1H, Ph), 7.48 – 7.39 (m, 2H, Ph), 7.14 (d, *J* = 8.3 Hz, 1H, Ph), 7.01 (t, *J* = 7.6 Hz, 1H, Ph), 1.43 (s, 9H, Ph-C(C*H*$_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.82 (*C,* benzoxazole), 157.56 (Ph), 147.40 (Ph), 145.96 (Ph), 138.80 (Ph), 132.23 (Ph), 125.90 (Ph), 121.94 (Ph), 118.33 (Ph), 116.23 (Ph), 114.65 (Ph), 109.59 (Ph), 108.64 (Ph), 33.86 (*C*(CH$_3$)$_3$), 30.67 (C(*C*H$_3$)$_3$); HRMS (ESI) calcd for $C_{17}H_{18}NO_2$ [M + H$^+$] 268.1388, found 268.1397.

3a: 89 % Isolated yield (white solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (t, *J* = 7.5 Hz, 1H, Ph), 7.89 (s, 1H, Ph), 7.50 (m, *J* = 19.1, 8.7 Hz, 3H, Ph), 7.34 - 7.22 (m, 2H, Ph), 1.42 (s, 9H, Ph-

C(CH_3)$_3$);^{13}C NMR (101 MHz, $CDCl_3$) δ 162.07 (s) (*C,* benzoxazole), 159.49 (Ph), 148.51 (Ph), 148.26 (Ph), 141.73 (Ph), 132.90 (d, *J* = 8.6 Hz) (Ph), 130.43 (Ph), 124.45 (d, *J* = 3.4 Hz) (Ph), 123.28 (Ph), 117.19 (Ph), 117.19 - 116.62 (m) (Ph), 115.70 (d, *J* = 10.4 Hz) (Ph), 109.82 (Ph), 34.97 (*C*(CH_3)$_3$), 31.78 (C(*C*H_3)$_3$); ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.11 (s); HRMS (ESI) calcd for $C_{17}H_{17}FNO$ [M + H^+] 270.1289, found 270.1298.

7a: 72 % Isolated yield (white solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H, Ph), 7.84 (d, *J* = 3.1 Hz, 1H, Ph), 7.61 (d, *J* = 5.7 Hz, 1H, Ph), 7.50 (s, 1H, Ph), 7.39 (s, 2H, Ph), 7.29 (d, *J* = 4.5 Hz, 2H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.96 (*C,* benzoxazole), 159.39 (Ph), 150.34 (Ph), 141.65 (Ph), 132.96 (d, *J* = 8.6 Hz) (Ph), 130.39 (Ph), 125.35 (Ph), 124.55 (Ph), 124.35 (d, *J* = 3.3 Hz) (Ph), 120.23 (Ph), 117.05 (Ph), 116.94 (d, *J* = 21.5 Hz) (Ph), 115.38 (d, *J* = 10.3 Hz) (Ph), 110.56 (Ph); HRMS (ESI) calcd for $C_{13}H_9FNO$ [M + H^+] 214.0668, found 214.0679.

Synthesis of 3b-7b

General procedure for the synthesis of **3b-7b** was according the previous report. [34] Into a glass tube, **3a-7a** (1 mmol,), Cs_2CO_3 (652 mg, 2 mmol, 2.0 equiv), imidazole or benzoimidazole (2 mmol), DMF (2 mL), were sealed by rubber stopper. The glass tube was stirred under preheated 120 °C oil bath for 12 h. After being finished, the reaction solution was diluted by NH_4Cl solution (20 mL), extracted by ethyl acetate (EA) (3 × 10 mL), combined the organic phase, washed by brine (2 × 10 mL), dried by anhydrous sodium sulfate, and concentrated under reduced pressure, and the residue was applied on silica gel chromatography.

3b: 93 % Isolated yield (yellow solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H, C*H*, imidazole), 8.82 (d, *J* = 1.9 Hz, 1H, C*H*, imidazole), 8.77 (d, *J* = 2.5 Hz, 1H, Ph), 8.66 (d, *J* = 2.9 Hz, 2H, Ph), 8.55 – 8.44 (m, 2H, Ph), 8.41 (d, *J* = 3.5 Hz, 1H, Ph), 8.30 (d, *J* = 2.2 Hz, 1H, Ph), 8.15 (d, *J* = 2.7 Hz, 1H, C*H*, imidazole), 2.46 (s, 9H, Ph-C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.09 (s) (*C,* benzoxazole), 148.54 (*C*H, imidazole), 148.07 (Ph), 141.37 (Ph), 137.89 (*C*H, imidazole), 135.89 (Ph), 131.85 (Ph), 131.11 (Ph), 129.42 (Ph), 129.012 (Ph), 127.91 (*C*H, imidazole), 123.95 (Ph), 123.47 (Ph), 120.81 (Ph), 116.65 (Ph), 109.85 (Ph), 34.86 (*C*(CH_3)$_3$), 31.72 (C(*C*H_3)$_3$); HRMS (ESI) calcd for $C_{20}H_{20}N_3O$ [M + H^+] 318.1606, found 318.1646.

5b: 89 % Isolated yield (white solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 7.2, 2.2 Hz, 1H, C*H*, benzoimidazole), 8.08 (s, 1H, Ph), 7.91 (d, *J* = 8.1 Hz, 1H, Ph), 7.70 (s, 2H, Ph), 7.64 (d, *J* = 1.5 Hz, 1H, Ph), 7.61 - 7.53 (m, 1H, Ph), 7.35 -7.26 (m, 2H, Ph), 7.25 - 7.11 (m, 3H, Ph), 1.33 (s, 9H, Ph-C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.82 (s) (*C,* benzoxazole), 148.38 (*C*H, benzoimidazole), 148.11 (Ph), 143.62 (Ph), 143.31 (Ph), 141.13 (Ph), 135.04 (Ph), 134.31 (Ph), 131.99 (Ph), 131.37 (Ph), 129.35 (Ph), 128.97 (Ph), 125.02 (Ph), 123.46 (Ph), 123.38 (Ph), 122.33 (Ph), 120.17 (Ph), 116.70 (Ph), 109.81 (Ph), 109.61 (Ph), 34.77 (*C*(CH_3)$_3$), 31.56 (s) (C(*C*H_3)$_3$); HRMS (ESI) calcd for $C_{24}H_{22}N_3O$ [M + H^+] 368.1763, found 368.1788.

7b: 85 % Isolated yield (white solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46-8.40 (m, 1H, C*H*, benzoimidazole)), 8.07 (s, 1H, Ph), 7.90 (d, *J* = 8.1 Hz, 1H, Ph), 7.69 (s, 2H, Ph), 7.60 (d, *J* = 5.8 Hz, 1H, Ph), 7.57 -7.53 (m, 1H, Ph), 7.30- 7.11 (m, 6H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.91 (s) (*C,* benzoxazole), 150.45 (*C*H, benzoimidazole), 143.63 (Ph), 143.46 (Ph), 141.27 (Ph), 137.52 (Ph), 135.16 (Ph), 134.53 (Ph), 132.34 (Ph), 131.60 (Ph), 129.51 (Ph), 129.09 (Ph), 125.63 (Ph), 124.92 (Ph), 124.66 (Ph), 123.60 (Ph), 122.49 (Ph), 120.35 (Ph), 120.32 (Ph), 110.60 (Ph), 109.90 (Ph); HRMS (ESI) calcd for $C_{20}H_{14}N_3O$ [M + H^+] 312.1137, found 312.1116.

Synthesis of 3c-7c

Synthesis of **3c-7c**: Into a 15*150 mm tube,**3b-7b** (1 mmol), the corresponding alkyl halide reagent (2 mmol), acetonitrile (2 ml), were sealed by rubber stopper. The mixture was stirred under 82 °C oil-bath for 12 h. After being finished, the reaction solution was concentrated under vacuum, and the residue was washed three times by ethyl acetate (EA) (3 × 10 mL), which afforded the corresponding products.

3c: Using **3b** (1 mmol), 1-iodobutane (C_4H_9I) (2 mmol), 95 % Isolated yield (yellow solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H, C*H*, imidazole), 8.34 (d, *J* = 7.6 Hz, 1H, C*H*, imidazole), 7.92-7.80 (m, 2H, Ph), 7.72 (dd, *J* = 14.3, 7.6 Hz, 2H, Ph), 7.43 (d, *J* = 9.6 Hz, 3H, Ph), 7.30 (s, 1H, C*H*, imidazole), 4.63 (t, *J* = 7.0 Hz, 2H, CH_2), 2.11-1.96 (m, 2H, CH_2), 1.52 (dd, *J* = 15.1, 7.5 Hz, 2H, CH_2), 1.32 (s, 9H, Ph-C(CH_3)$_3$), 0.99 (t, *J* = 7.3 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.78 (*C,* benzoxazole), 148.71 (*C*, imidazole), 147.86 (Ph), 141.31 (Ph), 137.43 (*C*, imidazole), 132.51 (Ph), 131.86 (Ph), 130.31 (Ph), 129.11 (*C*, imidazole), 124.36 (Ph), 123.72 (Ph), 122.71 (Ph), 116.56 (Ph), 109.92 (Ph), 50.31 (*C*H_2), 34.88 (*C*(CH_3)$_3$), 32.38 (*C*H_2), 31.60 (C(*C*H_3)$_3$), 19.24 (*C*H_2), 13.70 (*C*H_3); HRMS (ESI) calcd for $C_{24}H_{28}N_3O$ [M - I^-] 374.2232, found 374.2242.

4c: Using **4b** (1 mmol), 2-methylbenzyl bromide (C_8H_9Br) (2 mmol), 91 % Isolated yield (gray solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H, C*H*, imidazole), 8.36 (dd, *J* = 7.7, 1.5 Hz, 1H, C*H*, imidazole), 7.93 (d, *J* = 7.3 Hz, 1H, Ph), 7.80 - 7.67 (m, 2H, Ph), 7.55 (d, *J* = 7.1 Hz, 1H, Ph), 7.49 (s, 1H, Ph), 7.47 - 7.39 (m, 3H, Ph), 7.34 (d, *J* = 6.9 Hz, 1H, Ph), 7.27 (dd, *J* = 10.9, 5.7 Hz, 3H, C*H*, imidazole and Ph), 5.94 (s, 2H, CH_2), 2.48 (s, 3H, Ph-CH_3), 1.37 (s, 9H, Ph-C(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.82 (*C,* benzoxazole), 148.68 (*C*, imidazole), 147.96 (Ph), 141.33 (Ph), 138.18 (Ph), 137.58 (*C*, imidazole), 132.46 (d, *J* = 17.3 Hz, Ph), 131.83 (Ph), 131.14 (Ph), 130.29 (d, *J* = 5.0 Hz, Ph), 129.74 (Ph), 129.37 (*C*, imidazole), 126.89 (Ph), 124.32 (Ph), 123.73 (Ph), 121.89 (Ph), 116.67 (Ph), 109.89 (Ph), 52.36 (s, *C*H_2), 34.95 (s, *C*(CH_3)$_3$), 31.67 (s, C(*C*H_3)$_3$), 19.45 (s, Ph-*C*H_3); HRMS (ESI) calcd for $C_{28}H_{28}N_3O$ [M – Br^-] 422.2232, found 422.2214.

5c: Using **5b** (1 mmol), 1-iodobutane (C_4H_9I) (2 mmol), 94 % Isolated yield (pale yellow solid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.59 (s, 1H, C*H*, benzoimidazole), 8.52 (s, 1H, Ph), 8.04 (s, 1H, Ph), 7.95 (s, 1H, Ph), 7.89 (s, 2H, Ph), 7.71 (s, 1H, Ph), 7.56 (s, 1H, Ph), 7.43 (s, 2H, Ph), 7.29 (s, 2H, Ph), 5.24 (d, *J* = 6.3 Hz, 1H, CH_2), 4.89-4.56 (m, 1H, CH_2), 2.24 (s, 2H, CH_2), 1.68 (d, *J* = 6.5 Hz, 2H, CH_2), 1.32 (s, 9H, Ph-C(CH_3)$_3$), 1.11 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.10 (*C,* benzoxazole), 148.78 (*C*, benzoimidazole), 148.04 (Ph), 143.28 (Ph), 141.41 (Ph), 133.10

(Ph), 133.94 (Ph), 132.45 (Ph), 131.25 (Ph), 130.87 (Ph), 130.16 (Ph), 127.96 (Ph), 127.61 (Ph), 124.63 (d, *J* = 12.3 Hz, Ph), 116.51 (Ph), 113.63 (Ph), 113.02 (Ph), 110.12 (Ph), 48.13 (*C*H_2), 35.06 (*C*(CH_3)$_3$), 31.84 (C(*C*H_3)$_3$), 31.79 (*C*H_2), 19.88 (*C*H_2), 14.11 (*C*H_3); HRMS (ESI) calcd for $C_{28}H_{30}N_3O$ [M – I^-] 424.2389, found 424.2373.

6c: Using **6b** (1 mmol), iodomethane (CH_3I) (2 mmol), 92 % Isolated yield (pale yellow solid): ^{1}H NMR (400 MHz, DMSO) δ 10.15 (s, 1H, C*H*, benzoimidazole), 8.57 - 8.49 (m, 1H, Ph), 8.22 (d, *J* = 8.4 Hz, 1H, Ph), 8.00 (s, 3H, Ph), 7.76 (t, *J* = 7.8 Hz, 1H, Ph), 7.62 (t, *J* = 7.8 Hz, 1H, Ph), 7.56 (d, *J* = 9.1 Hz, 1H, Ph), 7.49 (d, *J* = 8.3 Hz, 1H, Ph), 7.46 (dt, *J* = 4.1, 2.0 Hz, 2H, Ph), 4.30 (s, 3H, C*H*$_3$), 1.26 (s, 9H, Ph-C(C*H*$_3$)$_3$);^{13}C NMR (101 MHz, DMSO) δ 158.80 (*C,* benzoxazole), 148.74 (*C*, benzoimidazole), 148.00 (Ph), 145.10 (Ph), 141.16 (Ph), 133.72 (Ph), 132.67 (Ph), 132.02 (Ph), 131.14 (Ph), 130.86 (Ph), 130.29 (Ph), 128.03 (Ph), 127.25 (Ph), 124.65 (Ph), 124.10 (Ph), 116.83 (Ph), 114.44 (Ph), 113.36 (Ph), 110.61 (Ph), 35.15 (*C*H_3), 34.22 (*C*(CH_3)$_3$), 31.88 (C(*C*H_3)$_3$); HRMS (ESI) calcd for $C_{25}H_{24}N_3O$ [M – I^-] 382.1919, found 382.1935.

7c: 7b (1 mmol), iodomethane (CH_3I) (2 mmol), 96 % Isolated yield (yellow solid): ^{1}H NMR (400 MHz, DMSO) δ 10.18 (s, 1H, C*H*, benzoimidazole), 8.58 (d, *J* = 2.6 Hz, 1H, Ph), 8.23 (d, *J* = 8.3 Hz, 1H, Ph), 8.04 (s, 3H, Ph), 7.77 (t, *J* = 7.7 Hz, 1H, Ph), 7.69 (d, *J* = 8.0 Hz, 1H, Ph), 7.62 (t, *J* = 7.7 Hz, 1H, Ph), 7.52 (dd, *J* = 13.9, 8.1 Hz, 2H, Ph), 7.42 (t, *J* = 7.5 Hz, 1H, Ph), 7.34 (t, *J* = 7.5 Hz, 1H, Ph), 4.30 (s, 3H, C*H*$_3$);^{13}C NMR (101 MHz, DMSO) δ 158.72 (*C,* benzoxazole), 149.93 (*C*, benzoimidazole), 145.10 (Ph), 141.11 (Ph), 133.88 (Ph), 132.70 (Ph), 132.01 (Ph), 131.23 (Ph), 131.11 (Ph), 130.29 (Ph), 128.01 (Ph), 127.26 (Ph), 126.95 (Ph), 125.66 (Ph), 124.02 (Ph), 120.67 (Ph), 114.36 (Ph), 113.37 (Ph), 111.44 (Ph), 34.19 (*C*H_3); HRMS (ESI) calcd for $C_{21}H_{16}N_3O$ [M – I^-] 326.1293, found 326.1268.

Synthesis of 1-7

General procedure for the synthesis of complexes **1**-**2** was according the previous report. [48]

Ligands **1a** (or **2a**) (0.1 mmol) with $[Cp^*IrCl_2]_2$ (40 mg, 0.05 mmol) were added to a 25 mL Schlenk flask. Added into 2 mL of anhydrous dichloromethane. The reaction mixture was warmed to 82 °C for 14 h. Then ammonium hexafluorophosphate (NH_4PF_6) (48.9 mg, 0.3 mmol) was added. By centrifugal separation, the corresponding products **1** (or **2**) was obtained.

1: 89 % Isolated yield (yellow solid): FT-IR (KBr)： 2975 (w), 1635 (m), 1485 (w), 1434 (m), 1353 (m), 1278 (w), 1111 (w), 836 (s), 778 (w), 738 (w), 692 (w), 565 (m), 536 (w); ^{1}H NMR (400 MHz, DMSO) δ 8.50 (dd, *J* = 7.4, 3.6 Hz, 1H, Ph), 8.10 (dt, *J* = 14.8, 7.7 Hz, 2H, Ph), 7.99 (t, *J* = 7.6 Hz, 1H, Ph), 7.95- 7.82 (m, 4H, Ph), 7.80 - 7.69 (m, 4H, Ph), 7.24- 7.03 (m, 5H, Ph), 1.35 (s, 25H, Cp*, Ph-C(C*H*$_3$)$_3$); ^{13}C NMR (101 MHz, DMSO) δ 161.12 (d, *J* = 6.7 Hz, *C,* benzoxazole), 149.97 (Ph), 148.70 (Ph), 135.57 (d, *J* = 12.7 Hz, Ph), 134.46 (d, *J* = 7.0 Hz, Ph), 133.68 (Ph), 133.27 (d, *J* = 6.8 Hz, Ph), 132.67 (Ph), 131.11 (Ph), 130.15 (d, *J* = 11.7 Hz, Ph), 129.37 (Ph), 128.61 (Ph), 128.56 -127.73 (m), 126.64 (Ph), 124.44 (Ph), 116.67 (Ph), 112.42 (Ph), 35.43 (*C*(CH_3)$_3$), 31.68 (C(*C*H_3)$_3$), 8.55 (*C*, Cp*); ^{31}P NMR (162 MHz, DMSO) δ -3.00 (s), -144.19 (hept); ^{19}F NMR (376 MHz, DMSO) δ -70.16 (d); HRMS (ESI) calcd for $C_{39}H_{41}ClIrNOP$ [M - PF_6^-] 798.2244, found 798.2210.

2: 75 % Isolated yield (yellow solid): FT-IR (KBr)： 2970 (w), 1593 (m), 1529 (w), 1457 (m), 1425 (w), 1314 (w), 1258 (m), 1155 (w), 1075 (w), 1035 (w), 836 (s), 764 (w), 549 (m); ^{1}H NMR (400 MHz, DMSO) δ 7.80 (t, *J* = 8.9 Hz, 2H, Ph), 7.59 (d, *J* = 9.3 Hz, 1H, Ph), 7.35 (d, *J* = 10.2 Hz, 2H, Ph), 6.85 (d, *J* = 8.0 Hz, 1H, Ph), 6.72- 6.59 (m, 2H, Ph), 1.54 (s, 15H, *H*, Cp*), 1.40 (s, 9H, Ph-C(C*H*$_3$)$_3$); ^{13}C NMR (101 MHz, DMSO) δ 168.40 (*C,* benzoxazole), 159.26 (Ph), 149.37 (Ph), 147.88 (Ph), 138.67 (Ph), 134.72 (Ph), 128.25 (Ph), 124.46 (Ph), 123.56 (Ph), 116.54 (Ph), 114.92 (Ph), 112.14 (Ph), 111.19 (Ph), 35.65 (*C*(CH_3)$_3$), 31.96 (C(*C*H_3)$_3$), 9.14 (*C*, Cp*); ^{31}P NMR (162 MHz, DMSO) δ -144.20 (hept);^{19}F NMR (376 MHz, DMSO) δ -70.55 (d); HRMS (ESI) calcd for $C_{27}H_{31}IrNO_2$ [M –PF_6^-]594.1984, found594.1970.

General procedure for the synthesis of complexes **3-7** was according the previous report. [43]

3: 63 % Isolated yield (yellow solid): FT-IR (KBr)： 2954 (s), 1616 (m), 1489 (s), 1473 (w), 1417 (w), 1346 (m), 1266 (w), 1091 (w), 1067 (w), 1019 (m), 844 (s), 773 (m), 549 (s); ^{1}H NMR (400 MHz, DMSO) δ 8.30 (d, *J* = 1.6 Hz, 1H, C*H*, imidazole), 8.20 (d, *J* = 7.8 Hz, 1H, Ph), 7.99- 7.95 (m, 1H, Ph), 7.93 (dd, *J* = 6.6, 2.0 Hz, 2H, Ph), 7.88 (d, *J* = 8.8 Hz, 1H, Ph), 7.81 (t, *J* = 7.6 Hz, 1H, Ph), 7.74 (d, *J* = 8.0 Hz, 1H, Ph), 7.68 (dd, *J* = 8.8, 1.8 Hz, 1H, C*H*, imidazole), 4.41 (td, *J* = 12.2, 4.9 Hz, 1H, C*H*$_2$), 4.13 -3.95 (m, 1H, C*H*$_2$), 1.44 -1.39 (m, 4H, C*H*$_2$), 1.35 (s, 9H, Ph-C(C*H*$_3$)$_3$), 1.32 (s, 15H, *H*, Cp*), 0.95 (t, *J* = 7.4 Hz, 3H, C*H*$_3$); ^{13}C NMR (101 MHz, DMSO) δ 163.07 (*C,* benzoxazole), 157.41 (*C*, imidazole), 148.80 (Ph), 148.42 (Ph), 139.01 (Ph), 137.75 (*C*, imidazole), 134.84 (Ph), 134.66 (Ph), 133.76 (Ph), 129.31 (*C*, imidazole), 126.02 (Ph), 125.72 (d, *J* = 27.3 Hz, Ph), 124.59 (Ph), 120.35 (Ph), 118.86 (Ph), 111.62 (Ph), 50.83 (*C*H_2), 35.30 (*C*(CH_3)$_3$), 32.89 (*C*H_2), 31.64 (C(*C*H_3)$_3$), 19.89 (*C*H_2), 14.04 (*C*H_3), 8.58 (*C*, Cp*); ^{31}P NMR (162 MHz, DMSO) δ-144.21 (hept); ^{19}F NMR (377 MHz, DMSO) δ -70.11 (d); HRMS (ESI) calcd for $C_{35}H_{42}ClF_6IrN_3OP$ [M - PF_6^-] 736.2646, found 736.2643.

4: 70 % Isolated yield (yellow solid): FT-IR (KBr)： 2970 (s), 1609 (m), 1497 (s), 1481 (w), 1402 (w), 1346 (m), 1234 (m), 1099 (w), 1067 (w), 1019 (w), 828 (s), 749 (m), 549 (s); ^{1}H NMR (400 MHz, DMSO) δ 8.31 (d, *J* = 15.3 Hz, 1H, C*H*, imidazole), 8.25 (d, *J* = 7.8 Hz, 1H, Ph), 8.07-7.97 (m, 2H, Ph), 7.94 - 7.89 (m, 2H, , Ph), 7.86 (t, *J* = 7.7 Hz, 1H, Ph), 7.70 (dd, *J* = 8.8, 1.9 Hz, 1H, Ph), 7.62 (dd, *J* = 12.7, 2.0 Hz, 1H, Ph), 7.28 (d, *J* = 7.3 Hz, 1H, Ph), 7.23 (t, *J* = 7.3 Hz, 1H, Ph), 7.17 (t, *J* = 7.3 Hz, 1H, Ph), 6.79 (d, *J* = 7.6 Hz, 1H, C*H*, imidazole), 5.84 (d, *J* = 16.4 Hz, 1H, C*H*$_2$), 5.63 (d, *J* = 16.4 Hz, 1H, C*H*$_2$), 2.36 (s, 3H, C*H*$_3$), 1.36 (s, 9H, Ph-C(C*H*$_3$)$_3$), 1.31 (s, 3H, *H*, Cp*), 1.27 (s, 12H, *H*, Cp*); ^{13}C NMR (101 MHz, DMSO) δ 163.43 (*C,* benzoxazole), 158.31 (*C*, imidazole), 149.04 (Ph), 148.53 (Ph), 139.02 (Ph), 137.87 (*C*, imidazole), 136.18 (Ph), 135.36 (Ph), 134.94 (Ph), 134.03 (Ph), 130.54 (Ph), 129.58 (d, *J* = 5.8 Hz, *C*, imidazole), 127.76 (Ph), 127.31 -126.01 (Ph), 125.99 (Ph), 125.68 (Ph), 120.81 (Ph), 119.06 (Ph), 111.82 (Ph), 91.56 (d, *J* = 10.9 Hz, Ph), 55.33 (Ph), 52.37 (Ph), 35.43 (*C*(CH_3)$_3$), 31.76 (C(*C*H_3)$_3$), 19.27 (*C*H_2), 8.93 (*C*H_3), 8.71 (*C*, Cp*); ^{31}P NMR (162 MHz, DMSO) δ-144.19

(hept); ^{19}F NMR (376 MHz, DMSO) δ -70.15 (d); HRMS (ESI) calcd for $C_{38}H_{42}ClIrN_3O$ [M- PF_6^-] 784.2646, found 784.2685.

5: 75 % Isolated yield (yellow solid): FT-IR (KBr) : 2961 (w), 1640 (w), 1505 (w), 1473 (m), 1393 (w), 1346 (w), 1282 (w), 1202 (w), 1075 (w), 1027 (w), 828 (s), 757 (m), 549 (s); ^{1}H NMR (400 MHz, DMSO) δ 8.36 (dd, *J* = 3.2, 1.9 Hz, 1H, Ph), 8.34 - 8.28 (m, 1H, Ph), 8.01 (s, 1H, Ph), 7.96 - 7.84 (m, 4H, Ph), 7.68 (dt, *J* = 8.8, 1.7 Hz, 1H, Ph), 7.47 (s, 1H, Ph), 7.38 (dd, *J* = 15.1, 7.6 Hz, 2H, Ph), 4.80 -4.61 (m, 1H, C*H*$_2$), 4.60 - 4.32 (m, 1H, C*H*$_2$), 2.32 - 1.72 (m, 2H, C*H*$_2$), 1.70 - 1.53 (m, 2H, C*H*$_2$), 1.51 (s, 9H, C(C*H*$_3$)$_3$), 1.38 (d, *J* = 6.1 Hz, 15H, *H*, Cp*), 1.03 (t, *J* = 7.3 Hz, 3H, C*H*$_3$); ^{13}C NMR (101 MHz, DMSO) δ 171.06 (s, *C,* benzoxazole), 169.51 (s, *C*, benzoimidazole), 163.66 (d, *J* = 37.7 Hz, Ph), 148.79 (d, *J* = 6.5 Hz, Ph), 148.33 (s, Ph), 147.20 (s, Ph), 140.10 (s, Ph), 136.81 (s, Ph), 135.48 (s, Ph), 134.83 (d, *J* = 26.8 Hz, Ph), 134.57 (s, Ph), 134.29 (s, Ph), 130.65 - 128.88 (m, Ph), 125.57 (d, *J* = 19.4 Hz, Ph), 124.96 (s, Ph), 122.24 (s, Ph), 118.74 (s, Ph), 113.48 (d, *J* = 24.8 Hz, Ph), 111.60 (s, Ph), 92.75 (s, Ph), 91.95 (s, Ph), 49.94 (s, *C*H$_2$), 35.32 (s, *C*(CH$_3$)$_3$), 31.61 (s, C(*C*H$_3$)$_3$), 20.18 (s, *C*H$_2$), 14.10 (s, *C*H$_2$), 9.41 (s, *C*H$_3$), 8.65 (s, *C*, Cp*); ^{31}P NMR (162 MHz, DMSO) δ-144.20 (hept); ^{19}F NMR (376 MHz, DMSO) δ -70.13 (d); HRMS (ESI) calcd for $C_{38}H_{45}ClIrN_3O$ [M+ - PF_6^-] 786.2802, found 786.2807.

6: 73 % Isolated yield (yellow solid): FT-IR (KBr) : 2961 (w), 1609 (w), 1473 (w), 1369 (w), 1258 (w), 1091 (m), 1035 (w), 836 (s), 749 (w), 557 (s); ^{1}H NMR (400 MHz, DMSO) δ 8.34 (d, *J* = 12.2 Hz, 2H, Ph), 8.03 (d, *J* = 7.9 Hz, 1H, Ph), 7.91 (dd, *J* = 13.0, 5.9 Hz, 3H, Ph), 7.84 (d, *J* = 7.9 Hz, 1H, Ph), 7.68 (d, *J* = 8.3 Hz, 1H, Ph), 7.50 (d, *J* = 3.7 Hz, 1H, Ph), 7.42 (d, *J* = 3.5 Hz, 2H, Ph), 4.21 (s, 3H, C*H*$_3$), 1.42 (s, 15H, *H*, Cp*), 1.37 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (101 MHz, DMSO) δ 171.91 (s, *C,* benzoxazole), 163.53 (*C*, benzoimidazole), 148.93 (Ph), 148.52 (Ph), 139.18 (Ph), 136.29 (Ph), 135.67 (d, *J* = 8.8 Hz, Ph), 134.70 (Ph), 134.29 (Ph), 129.93 (d, *J* = 5.5 Hz, Ph), 125.86 - 125.19 (Ph), 125.19 - 124.76 (Ph), 122.15 (Ph), 118.99 (Ph), 113.19 (Ph), 112.36 (Ph), 111.69 (Ph), 92.87 (Ph), 92.05 (Ph), 55.34 (Ph), 36.72 (*C*H$_3$), 35.45 (*C*(CH$_3$)$_3$), 31.79 (C(*C*H$_3$)$_3$), 8.87 (*C*, Cp*); ^{31}P NMR (162 MHz, DMSO) δ -144.16 (hept); ^{19}F NMR (376 MHz, DMSO) δ -70.17 (d); HRMS (ESI) calcd for $C_{35}H_{38}ClIrN_3O$ [M - PF_6^-] 744.2333, found 744.2337.

7: 78 % Isolated yield (yellow solid): FT-IR (KBr) : 2945 (w), 1624 (w), 1505 (w), 1465 (w), 1378 (w), 1234 (w), 1099 (w), 1059 (w), 836 (s), 749 (w), 542 (m); ^{1}H NMR (400 MHz, DMSO) δ 8.35 (d, *J* = 6.9 Hz, 1H, Ph), 8.28 (d, *J* = 8.1 Hz, 1H, Ph), 8.09 - 7.96 (m, 2H, Ph), 7.92 (dd, *J* = 7.4, 4.0 Hz, 2H, Ph), 7.84 (d, *J* = 8.0 Hz, 1H, Ph), 7.62 (t, *J* = 7.4 Hz, 1H, Ph), 7.58 - 7.45 (m, 2H, Ph), 7.42 (d, *J* = 3.9 Hz, 2H, Ph), 4.21 (s, 3H, C*H*$_3$), 1.41 (s, 15H, *H*, Cp*); ^{13}C NMR (101 MHz, DMSO) δ 171.75 (*C,* benzoxazole), 163.36 (*C*, benzoimidazole), 150.69 (Ph), 139.09 (Ph), 136.15 (Ph), 135.55 (Ph), 134.61 (Ph), 134.36 (Ph), 129.74 (Ph), 127.81 (Ph), 125.50 (Ph), 125.09 (d, *J* = 11.1 Hz, Ph), 122.23 (Ph), 122.00 (Ph), 113.13 (Ph), 112.31 (d, *J* = 14.6 Hz, Ph), 91.97 (Ph), 36.59 (*C*H$_3$), 8.76 (*C*, Cp*); ^{31}P NMR (162 MHz, DMSO) δ-144.18 (hept); ^{19}F NMR (376 MHz, DMSO) δ-70.44 (d); HRMS (ESI) calcd for $C_{31}H_{30}ClIrN_3O$ [M - PF_6^-] 688.1707, found 688.1714.

Table 4. X-ray crystallographic data for complexes **1**, **2**·H_2O, **4**, and **7**.

	1	**2**·H_2O	**4**	**7**
Formula	$C_{39}H_{41}ClF_6IrNOP_2$	$C_{27.50}$ H_{34} ClF_6IrNO_3P	C_{38} $H_{42}Br_{0.13}Cl_{0.87}F_6Ir$ N_3OP	$C_{31}H_{30}Cl$ F_6IrN_3OP
Formula weight	943.32	799.17	935.15	833.20
Crystal system	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
Space group	$P2_1/n$	$P2_1/n$	$P2_1/c$	$Pca2_1$
***a* [Å]**	15.7381(6)	17.1859(9)	10.9323(4)	12.7553(6)
***b* [Å]**	24.1696(10)	12.0306(5)	20.3254(7)	16.3267(8)
***c* [Å]**	20.8139(7)	29.5949(16)	17.5400(6)	14.7234(7)
***α* [°]**	90°	90°	90°.	90°
***β* [°]**	101.870(2)	95.508(2)°	106.6660(10)	90°
***γ* [°]**	90°	90°	90°	90°
***V* [Å^3]**	7748.0(5)	6090.7(5)	3733.7(2)	3066.2(3)
Z	8	8	4	4
ρ $_{calcd}$ [mg mm^{-3}]	1.617	1.743	1.673	1.805
***μ* [mm^{-1}]**	5.699	6.878	5.755	6.835
***F* (000)**	3744	3144	1866	1632
ϑ range [°]	2.468 to 58.266	2.488 to 59.419	3.784 to 57.030	4.634 to 58.242
Reflns collected / Indep reflns	57341/16496	48562/13412	33567/7625	20617/5195
***R* $_{(int)}$**	0.0576	0.0559	0.0414	0.0570
data / restraints / parameters	16496 / 246 / 1045	13412 / 54 / 746	7625 / 114 / 524	5195 / 74 / 449
GOF	1.050	1.070	1.103	1.058
***R*$_1$ (*I*>2σ(*I*))**	0.0590	0.0834	0.0301	0.0341
***wR*$_2$**	0.1747	0.2208	0.0710	0.0889

General procedure for the *N*-methylation of amines using methanol

A mixture of aromatic amine (0.5 mmol), **1**-**7** (0.5 mol%) KO^{t}Bu (56 mg, 1.0 equiv), methanol (1 mL), in a 15 mL pressure tube with magnetic bar was stirred at desired temperature for

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desired reaction time. After cooling to the room temperature, the solvents were removed under vacuum, and the residue was purified by column chromatography (PE/EtOAc 50:1~1:1). the product was annualized by NMR spectroscopy.

X-ray crystallography

Intensity data for the compounds were collected on Bruke Smart APEX (at 293 K) and Bruker APEX DUO diffract meters (at 173 K). Both are equipped with 2.4 kW sealed tube X-ray source (Mo-Kα radiation, λ = 0.71073 Å) operating at 50 kV and 30 mA. A hemisphere of intensity data was collected at room temperature with a scan width of 0.60° in ω. Empirical absorption corrections were based on SADABS program. [49] The structures were solved by direct methods and refined by full-matrix least squares refinement using the SHELXTL-97 program. [50] The positions of all non-hydrogen atoms were refined with anisotropic displacement factors. The hydrogen atoms were generated theoretically onto the specific atoms and refined.

CCDC-1887419 (**1**), 1887420 (**2**·H_2O), 1887421 (**4**), 1887422 (**7**), 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.

Conflicts of interest

There are no conflicts to declare.

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ARTICLE

N-Methylation of *ortho*-Substituted Aromatic Amines with Methanol Catalyzed by 2-Arylbenzo[*d*]oxazole NHC-Ir(III) Complexes

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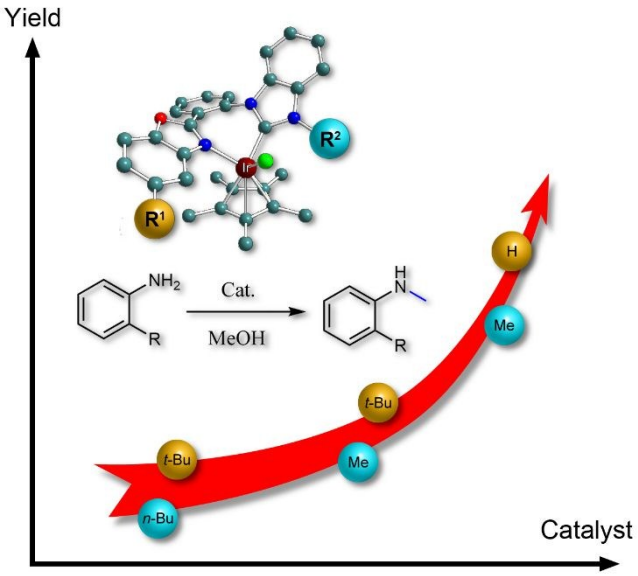

By modification on benzo[*d*]oxazolyl-NHC ligated cyclometalated Ir complexes, *N*-methylation of *ortho*-substituted aromatic amines with methanol has remarkably improved.