Received: 17 February 2019 | Accepted: 26 March 2019

DOI: 10.1002/jccs.201900057

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

SPECIAL ISSUE PAPER

Naphthyridine-based iridium complexes: Structures and catalytic activity on alkylation of aryl ketones

Po-Hao Chen | **Yi-Hung Liu** | **Shiuh-Tzung Liu**

Department of Chemistry, National Taiwan University, Taipei, Taiwan

Correspondence
Shiuh-Tzung Liu, Department of Chemistry, National Taiwan University, Taipei 10617, Taiwan.
Email: stliu@ntu.edu.tw

Funding information
Ministry of Science and Technology, Taiwan, Grant/Award Number: MOST-106-2113-M-002-018 Dedicated to Professor Shie-Ming Peng on the occasion of his 70th birthday and retirement from NTU.

Abstract

Iridium(III) complexes containing a designed ligand, 2-amino-7-(2-pyridinyl)-1,-8-naphthyridine derivative, were prepared and all complexes were characterized using spectroscopic and crystallographic methods. These new Ir(III) complexes are able to act as catalysts for the *C*-alkylation of aryl alkyl ketones with the use of alcohols as the alkylating agent. Typically, acetophenone undergoes alkylation with methanol and ethanol to yield isobutyrophenone and butyrophenone, respectively.

KEYWORDS

alkylation, catalysis, iridium, naphthyridine ligand

1 | INTRODUCTION

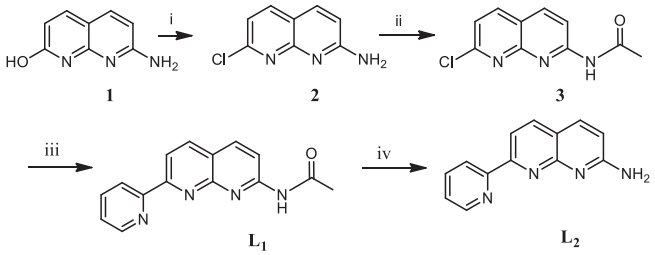
Since 1970s, the use of 1,8-naphthyridine and its derivatives as ligands has received much interest due to the diverse coordination modes.[1] Among 1,8-naphthyridine derivatives, compounds with extra coordinative donors at position 2 and/or 7 are of particular interest because of the increasing stability through the chelation effect and easy preparation of these compounds. Indeed, quite a number of 2 and/or 7-substituted 1,8-naphthyridine-based ligands have been investigated for their coordination and catalytic activity.[2–10]

Besides acting as a donor in coordination, the nitrogen atom in naphthyridine is also able to act as a pendant group to serve as a base for promotion of the catalytic reactions. In a recent report, Bera et al found that complex [RuH(CO)(py-NP)(PPh3)2]Cl [py-NP = 2-pyridinyl-1,8-naphthyridine] is able to catalyze the oxidation of primary alcohols into the corresponding carboxylic acid via the dehydrogenation of alcohol followed by a hydroxide/water attack on the metal-bound aldehyde.[9c] Through kinetic and isotope studies, authors proposed that the nitrogen donor at the 8 position assists the attack of hydroxide/water on the coordinated aldehyde leading to the final product. Such pendant groups in a splitting of water and subsequent hydroxide attack for promoting chemical reactions have been investigated widely.[11] In this regard, we thought that a compound of 2-amino-7-(2-pyridinyl)-1,8-naphthyridine with a pendant amino group in the ring should have a similar effect or even enhanced. Here, we reported the preparation of iridium complexes containing 2-amino-7-(2-pyridinyl)-1,8-naphthyridine derivatives and their catalytic activity on alkylation of ketones with alcohols.

2 | RESULTS AND DISCUSSION

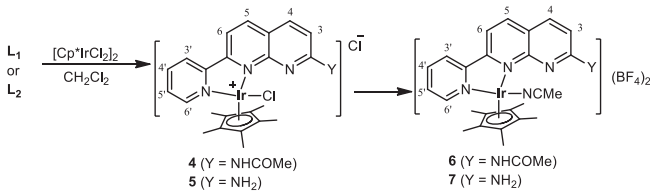
2.1 | Preparation and characterization

The desired ligand, 2-amino-7-(2-pyridinyl)-1,8-naphthyridine ($\mathbf{L_2}$), was prepared according to Scheme 1. Treatment of **1** with phosphoryl chloride gave the chloro compound **2**, which reacted with acetic anhydride to give the corresponding amide **3**. The Stille coupling of compound **3** with (2-pyridinyl)tributyltin provided the desired ligand $\mathbf{L_1}$, which was then hydrolyzed to yield $\mathbf{L_2}$. It should be mentioned that a direct coupling reaction of **2** with tin reagent could not yield



i. $POCl_3$; ii. Ac_2O; iii. (2-pyridinyl)$SnBu_3$, $Pd(PPh_3)_2Cl_2$; iv. $NaOH/H_2O$

SCHEME 1 Preparation of naphthyridine-based ligands



SCHEME 2 Preparation of iridium complexes

the desired compound $\mathbf{L_2}$. Thus, the protection of the amino functionality is necessary for the subsequent coupling reaction. Both $\mathbf{L_1}$ and $\mathbf{L_2}$ are potential chelating ligands for complexation because they all have a bipyridine fragment in the molecules.

Substitution reaction of $[Cp^*IrCl_2]_2$ with $\mathbf{L_1}$ and $\mathbf{L_2}$ in a dichloromethane solution at ambient temperature readily gave the corresponding complexes **4** and **5**, respectively (Scheme 2). Treating the complexes **4** and **5** with $AgBF_4$ in acetonitrile affords the nitrile-substituted iridium complexes **6** and **7**, respectively. All structures of these new iridium complexes were fully characterized using nuclear magnetic resonance (NMR) and Mass spectroscopy. The ^1H NMR resonances of pyridinyl-naphthyridinyl protons in ligands and complexes are summarized in Table 1, for comparison. Upon complexation, all resonances of aromatic protons in ligands exhibit coordination chemical shifts ($\Delta_{(ppm)}$) (the change in the NMR signal when a ligand binds to a metal, $\Delta_{(ppm)} = \delta_{(complex\ ligand)} - \delta_{(free\ ligand)}$). Typically, there are about 0.3 ppm shifts of $H^{6'}$ protons in all complexes, which is a characteristic downfield coordination chemical shift for bipyridine metal complexes. In addition to the spectroscopic characterization, detailed structural formulations of complexes **4**, **5**, and **6** were confirmed using a single-crystal X-ray study.

The coordination structures of complexes **4**–**6** and their numbering schemes are depicted in Figures 1–3, respectively. Selected bond lengths and angles are listed in Table 2. Each complex has the expected pseudo-octahedral half-sandwich piano stool geometry. The distance between the iridium center and the centroid of η^5-cyclopentadienyl ring is 2.17 Å. Both complexes **4** and **5** have similar Ir-Cl distances, whereas the distance of metal to the coordinating acetonitrile Ir(1)-N(5) is 2.038(6) Å, slightly shorter than that of Ir-Cl. Ligands behave as bidentate donors using a bipyridine moiety chelating with the metal ion, whereas both N(3) and N(4) nitrogen remain as free donors. The Ir-N bond lengths in all three complexes are quite similar. However,

TABLE 1 Chemical shifts (ppm) of the protons in ligands and complexes

Compound	H^3	H^4	H^5	H^6	$H^{3'}$	$H^{4'}$	$H^{5'}$	$H^{6'}$
$\mathbf{L_1}$	8.21	8.24	8.54	8.61	8.70	7.85	7.36	8.72
$\mathbf{L_2}$	6.78	7.90	8.08	8.43	8.70	7.84	7.34	8.78
4	8.46	8.69	8.81	8.89	8.94	8.37	7.94	9.05
5	7.11	8.16	8.40	8.50	8.77	8.28	7.82	8.99
6	8.48	8.72	8.87	9.00	9.04	8.53	8.04	9.18
7	7.13	8.20	8.49	8.65	8.91	7.98	8.47	9.04

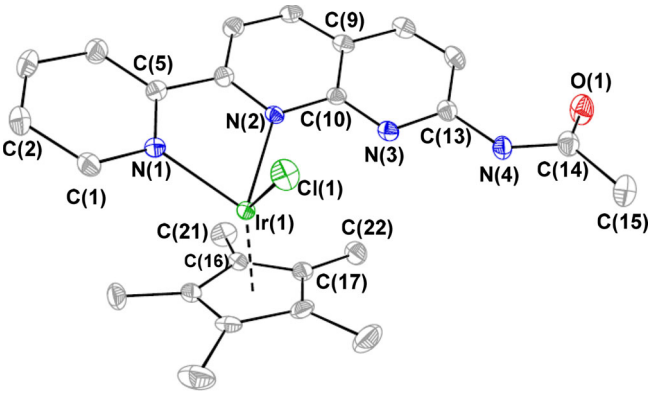


FIGURE 1 ORTEP plot of cationic part of **4** (30% probability ellipsoids)

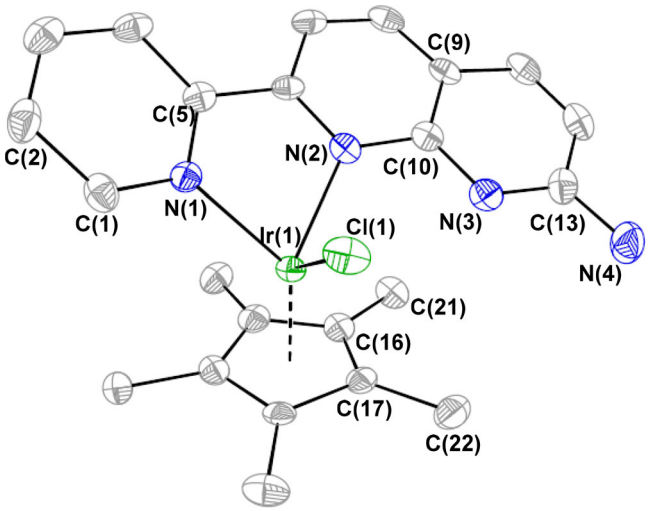


FIGURE 2 ORTEP plot of cationic part of **5** (30% probability ellipsoids)

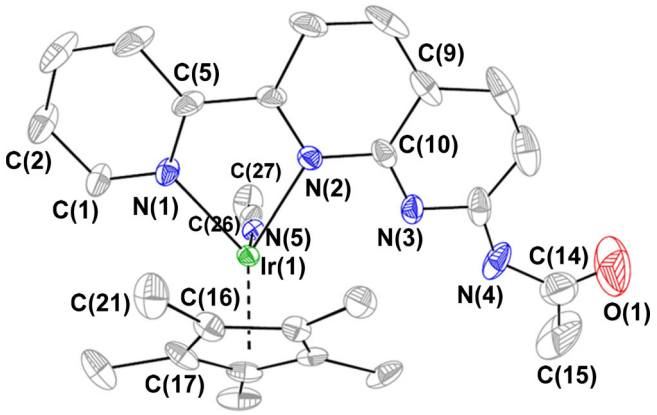


FIGURE 3 ORTEP plot of cationic part of **6** (30% probability ellipsoids)

TABLE 2 Selected bond distances (Å) and bond angles (deg)

Complex	4, X = Cl(1)	5, X = Cl(1)	6, X = N(5)
Ir(1)-X	2.3951(9)	2.3839(14)	2.038(6)
Ir(1)-N(1)	2.077(3)	2.088(5)	2.099(5)
Ir(1)-N(2)	2.112(3)	2.099(4)	2.118(5)
Ir(1)-C(x)	2.171	2.168	2.168
N(1)-Ir(1)-N(2)	75.54(11)	75.88(17)	75.5(2)
X-Ir(1)-N(1)	86.08(9)	86.56(13)	85.8(2)
X-Ir(1)-N(2)	89.60(8)	89.06(14)	88.4(2)
Ir(1)-N(5)-C(26)	—	—	175.1(6)

slight differences between the distance of Ir-N(1) and Ir-N (2) were observed in all complexes, presumably due to the crystal packing. The bite angles N(1)-Ir(1)-N(2) in three complexes are in the range of 75.5–75.9°, much deviated from 90°, which are typical in the bipyridine complexes. Some distances involving N-H to metal center and chloride are collected below for references: complex **4**, H(4)-Ir (1) 4.753 Å, H(4)-Cl(1) 4.290 Å; complex **5**, H(4A)-Ir (1) 4.932 Å, H(4A)-Cl(1) 4.587 Å; complex **6**, H(4)-Ir (1) 4.796 Å, H(4)-N(5) 4.456 Å. These distances are far away for direct interaction, but suitable for hydrogen-bonding interaction of a water molecule between these atoms.

The iridium complex containing ligand $\mathbf{L_3}$, without the amino group in the naphthyridine ring, was also prepared for comparison (Scheme 3). Recrystallization in a chloroform solution gave **8**.$CHCl_3$ as single crystals suitable for X-ray crystallography. Figure 4 shows the ORTEP plot of cationic portion of **8**. Similar to the above complexes, complex **8** adopts piano-stool configuration, with Cp* acting as the seat and bipyridine moiety of $\mathbf{L_3}$ and chloride groups as the legs. The average distance of Ir(1) to carbons of Cp* is 2.18

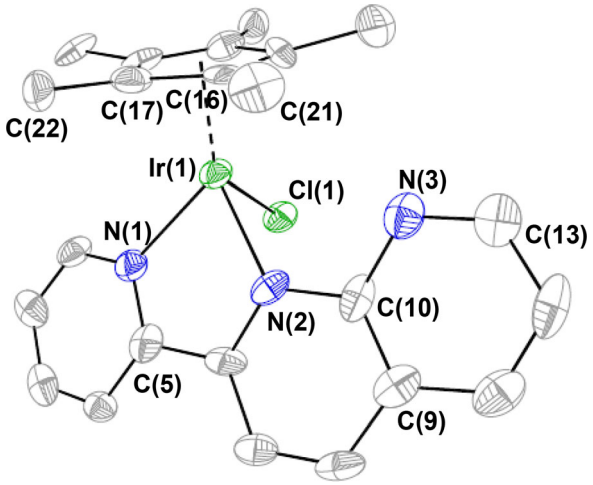


FIGURE 4 ORTEP plot of cationic part of **8** (30% probability ellipsoids)

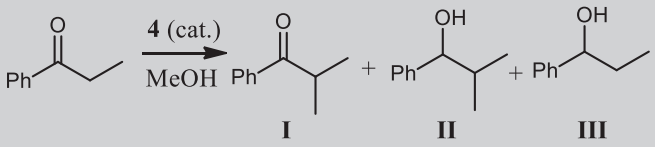
(1) Å, whereas both bond lengths of Ir(1)-N(1) and Ir(1)-N (2) are the same in 2.11(1) Å. The angle of N(2)-Ir(1)-N(1) is 76.1(4)°. No significant discrepancies in other bond lengths and angles are noticed in complex **8**, as compared to complexes **4**–**6**.

2.2 | Catalysis-methylation of aryl ketones

C-Alkylation of ketones with alcohols as alkylating agents via a borrowing hydrogen manner is of great interest to chemists due to the atom economy and environmental benignity of this reaction.[12] Thus, complex **4** was first tested as a precatalyst in this regard. To search the optimal conditions, methylation of propiophenone in methanol was selected as the model study (Table 3). At an oil bath temperature of 120°C, in the presence of 1.0 equiv. base, 1 mol% of 4 and methanol in a sealed tube, reactions proceeded well with 100% conversion (Table 3, entries 1–6). However, these reactions provided not only the α-methylation product I also the further reduction product II in different ratios. With the use of Li_2CO_3, the direct reduction of substrates to yield 1-phenylpropanol III was accompanied by the alkylation product (Table 3, entry 8). By increasing the amount of KOH, the production of 1-phenylpropanol III is also increased. However, running the reaction under a diluted medium would slow down the reduction, that is, the amount of II is diminished. The best condition for this methylation is running the reaction using propiophenone (0.5 mmol), 1.0 equiv. of KOH, and 1 mol% of 4 in methanol (3 mL) at 120°C (entry 13). In the absence of 4, the catalytic reaction did not proceed at all (entry 14), indicating the necessity of metal complex in this reaction.

To understand more about the pathway of this catalytic reaction, experiments of the kinetics of the resultant reaction profile for the alkylation of propiophenone catalyzed by 4 were performed under the optimal conditions (Figure 5).

TABLE 3 Optimization of conditions with **4** as the catalyst[a]



I II III

Entry	Base (equiv.)	Time (hr)	Conv. (%)	Yield (%)[b]		
				I	II	III
1	—	24	11	0	0	Trace
2	KOH (1.0)	24	100	17	56	Trace
3	NaOH (1.0)	24	100	29	51	Trace
4	K_2CO_3 (1.0)	24	100	56	32	Trace
5	K_3PO_4 (1.0)	24	100	65	26	Trace
6	Cs_2CO_3 (1.0)	24	100	43	46	Trace
7	Na_2CO_3 (1.0)	24	78	49	20	Trace
8	Li_2CO_3 (1.0)	24	62	19	2	24
9	KOH (2.0)	24	100	3	83	Trace
10	KOH (3.0)	24	100	0	71	Trace
11[c]	KOH (1.0)	24	100	61	24	Trace
12[d]	KOH (1.0)	24	100	72	24	Trace
13[d]	KOH (1.0)	4	97	74	5	4
14[e]	KOH (1.0)	24	9	0	0	0

[a]Reaction conditions: a mixture of propiophenone (0.5 mmol) and **4** (5×10^{-3} mmol) in methanol (1 mL) was heated at 120°C.
[b]Yields were determined by NMR.
[c]In methanol (2 mL).
[d]In methanol (3 mL).
[e]No catalyst.

This catalytic system shows the immediate conversion of the substrate into product as the reaction starts, that is, a very short induction period. The production of the desired product proceeded very rapidly, almost within the first couple hours.

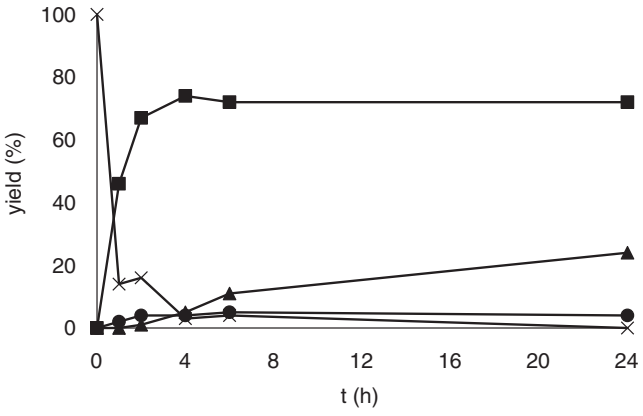
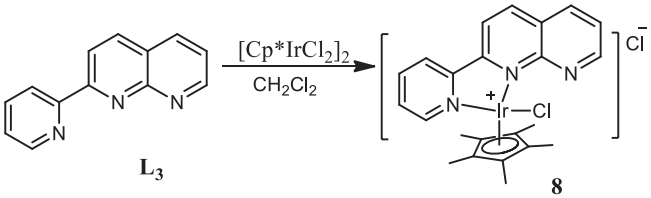


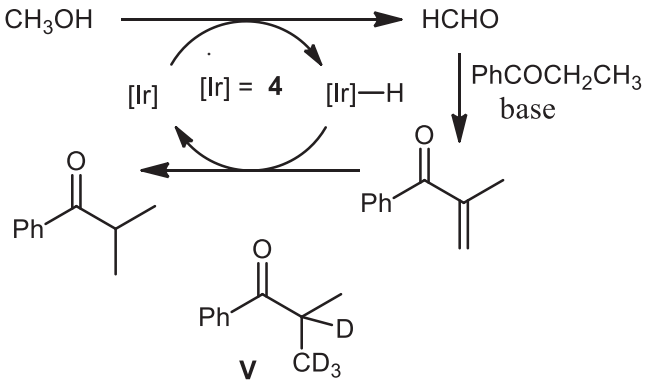
FIGURE 5 Reaction profile of alkylation of propiophenone (0.5 mmol) catalyzed by **4** (1 mol%) in MeOH at 120°C. Propiophenone (✻); $PhC(O)CH(CH_3)_2$ (▣); $PhCH(OH)CH(CH_3)_2$ (▲); $PhCH(OH)CHCH_3$ (●)

It is noticed that the direct reduction of propiophenone leading to 1-phenylpropanol (III) occurred at the beginning of the reaction with a small portion, indicating the inevitable competition. After 2 hr, 1-phenyl-2-methyl-1-propanol (II), the reduction of alkylation product I, is generated. As the reaction proceeds, the amount of II increases slowly, suggesting that the catalyst is active on the reduction of carbonyl functionality. In fact, compound II could be obtained in 58% yield after a period of 24 hr.

The pathway of this methylation of propiophenone with MeOH may proceed according to the previously reported manner.[12] Presumably, the first step is the dehydrogenation of methanol catalyzed by the metal complex resulting in the



SCHEME 3 Preparation of iridium complex **8**



SCHEME 4 Reaction pathway of alkylation catalyzed by **4**

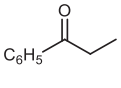
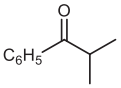
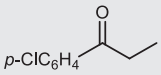
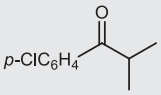
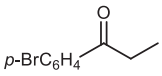
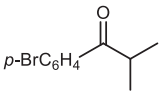
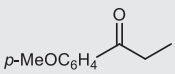
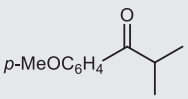
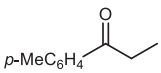
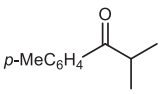
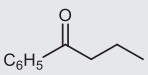
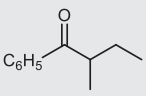
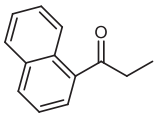
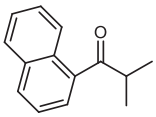
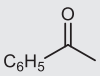
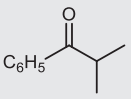
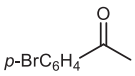
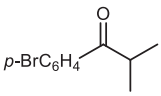
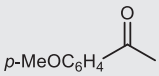
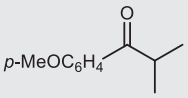
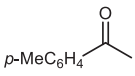
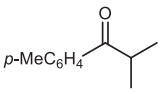
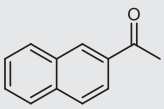
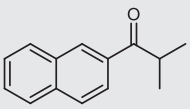
formation of formaldehyde and a metal-hydride species (denoted as [Ir]-H). Subsequently, cross-aldol condensation of formaldehyde and propiophenone promoted by the base takes place to yield 2-methyl-1-phenylprop-2-en-1-one, which is further reduced by [Ir]-H to render the product (Scheme 4). Running the reaction in the medium of CD_3OD gave the deuterated species V, clearly supporting the proposed pathway.

The methylation of various alkyl aryl ketones with methanol was then examined by using **4** as the catalyst. Some representative results are shown in Table 4. Propiophenones having either electron-donating (such as OMe and Me) or halo groups on the phenyl ring were suitable for this reaction and afforded the methylation product in good yields (entries 1–6). In some substrates, the reactions required a longer period to reach a reasonable yield. Methylation of 1-propionylnaphthalene under the standard conditions gave the desired product in a high yield (90%). For the acetophenone substrates, double methylation products were obtained predominantly (entries 8–11).

2.3 | Catalysis-alkylation of aryl ketones

Instead of methanol, one would expect to have the corresponding ethylation product via carrying out the catalysis in ethanol. Indeed, the reaction of acetophenone with ethanol catalyzed by **4** did proceed, but with a complicated product distribution (Table 5). Apparently, the reduction product increases in a significant amount as compared to those in methanol even by varying the conditions with various parameters such amount of KOH, concentration, and using toluene as solvents (Table 5, entries 7–9). In addition, unlike methanol, double ethylation did not take place in these reactions. Presumably, these are attributed to the slower reaction rate in condensation of acetaldehyde with acetophenone as compared to that of formaldehyde with acetophenone. This is supported by the observation of a full reduction of acetophenone in isopropanol under the optimal catalytic conditions (Table 5, entry 10).

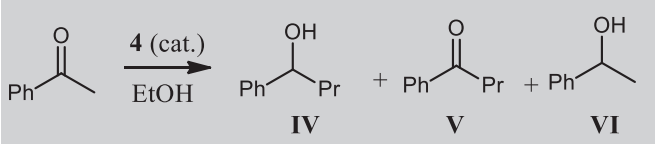
TABLE 4 Substrate scope for the catalytic alkylation[a]

Entry	Substrate	Time (hr)	Product (yield)[b]
1		4	
2		4	
3		4	
4[c]		6	
5[c]		4	
6[c]		4	
7		4	
8		4	
9		1	
10		12	
11		7	
12		4	

[a]Reaction conditions: a mixture of ketone (0.5 mmol), KOH (0.5 mmol), and **4** (5×10^{-3} mmol) in methanol (3 mL) was heated at 120°C for a period of time.
[b]Isolated yields.
[c]In methanol (1 mL).

Besides *C*-alkylation, the *N*-alkylation reaction of amines with alcohols catalyzed by **4** was examined. In a typical example, a mixture of aniline, benzyl alcohol (2 equiv.), and Cs_2CO_3 in the presence of 4 (1 mol%) was heated at 120°C for 20 hr, which provided the secondary amine *N*-benzylaniline in a quantitative yield, without any complication of imine product formation (Scheme 5). It is noteworthy that this *N*-alkylation is not required running the reaction in a solvent medium.

TABLE 5 Ethylation of acetophenone catalyzed by **4**[a]



Entry	KOH (equiv.)	EtOH (mL)	Time (hr)	Conv. (%)	Yield (%)[b] IV	V	VI
1	1	3	4	100	20	34	45
2	1	1	4	100	50	10	25
3	0.5	1	1	93	12	34	26
4	0.3	0.5	1	93	11	39	23
5	0.5	1	1	74	0	24	25
6[c]	1	1	1	100	0	33	13
7	0.3	[d]	1	62	0	37	16
8	0.3	[e]	1	76	0	36	17
9	1	[d]	1	95	19	61	14
10	0.3	[f]	1	97	0	0	92

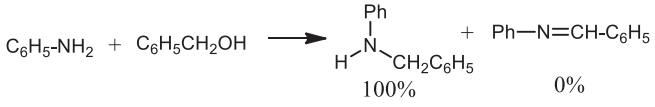
[a]Reaction conditions: a mixture of acetophenone (0.5 mmol), base, and **4** (5×10^{-3} mmol) in ethanol was heated at 120°C.
[b]Yields were determined by NMR.
[c]At 100°C.
[d]5 equiv. EtOH in toluene (0.5 mL).
[e]10 equiv. EtOH in toluene (0.5 mL).
[f]In isopropanol.

2.4 | Comparison of activity of metal complexes

Because various Ir(III) complexes were prepared in this work, we also evaluated the efficacy of these species in *C*-methylation under the best optimal conditions (Table 6). Complexes **4**, **5**, **6**, and **8** do exhibit good activity for the catalysis, whereas $[Cp^*IrCl_2]_2$ and [Cp*Ir(bpy)Cl]Cl show poor activity in this alkylation, clearly indicating the necessity of the naphthyridine-pyridine ligand. To our disappointment, the reactivity of **8** appears to be superior to other naphthyridine-pyridine complexes **4**, **5**, and **6**, indicating that the extra pendant functionality does not have the directing effect in the reactions.[13]

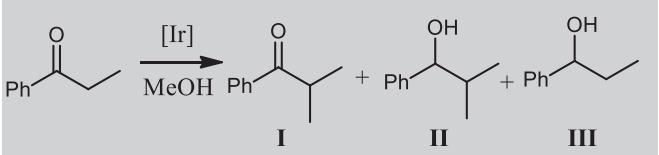
3 | CONCLUSIONS

A series of iridium(III) complexes **4–7** were synthesized by a reaction of $[Cp^*IrCl_2]_2$ with the designed ligands



SCHEME 5 *N*-alkylation of amines with alcohols

TABLE 6 Comparison of activity of various Ir complexes[a]



Entry	Ir complex	Conv. (%)	Yield (%)[b] I	II	III
1	**4**	97	74	5	<5
2	**5**	77	46	5	9
3	**6**	80	71	<5	<5
4	**8**	100	77	<5	0
5	$[Cp^*IrCl_2]_2$	24	0	0	0
6	[Cp*Ir(bpy)Cl]Cl	54	32	0	0

[a]Reaction conditions: a mixture of acetophenone (0.5 mmol), KOH (0.5 mmol), and Ir complex (5×10^{-3} mmol) in methanol (1 mL) was heated at 120°C.
[b]Yields were determined by NMR.

L_1–L_2. Complexes **4**, **5**, and **6** were further characterized using X-ray crystallography. All new Ir(III) complexes appear to be good catalysts for the alkylation of ketones with alcohols as the alkylating agent presumably due to the influence of nitrogen sites of naphthyridine assisting the dehydration of alcohols, not the pendant amino groups. Studies on the catalytic reactivity and ligand effects on these complexes toward other reactions are ongoing in our laboratory.

4 | EXPERIMENTAL

4.1 | General information

Chemicals including iridium complexes and solvents were of analytical grade and were used without further purification. Nmr spectra were recorded on a 400 MHz spectrometer. Chemical shifts are given in parts per million relative to Me_4Si for ^1H and ^{13}C NMR. Compounds **1** and **L_3** were prepared according to the reported method.[14]

4.2 | 2-Chloro-7-amino-1,8-naphthyridine (2)

Phosphoryl chloride (60 mL) was slowly added to a flask loaded with **1** (11.03 g, 68.4 mmol) and the resulting mixture was heated to reflux for 24 hr. After cooling, the reaction mixture was adjusted to basic condition by adding NaOH at ice-cooled temperature and the crude product was precipitated from the solution. Upon filtration, the residue was extracted with methanol by a Soxhlet setup. After concentrating, the desired compound was obtained as a yellow solid (7.14 g, 58%): ^1H NMR (400 MHz, DMSO-d_6): δ 8.22 (d,

$J = 8.4$, 1H), 8.12 (d, $J = 8.8$ Hz, 1H), 7.35 (d, $J = 8$ Hz, 1H), and 6.97 (d, $J = 9.2$, 1H); ^{13}C NMR (100 MHz): δ 159.6, 152.5, 151.6, 140.1, 139.2, 118.9, 115.5, and 114.3. These spectral data were consistent to those reported.[15]

4.3 | 2-Acetylamino-7-chloro-1,8-naphthyridine (3)

A mixture of **2** (1.0 g, 5.6 mmol) and acetic anhydride (863.4 mg, 8.45 mmol) and triethylamine (685.1 mg, 6.8 mmol) in dimethylforamide (5 mL) was stirred and heated at 60–70°C overnight. Water (10 mL) and CH_2Cl_2 (20 mL) were added to extract the product. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL) again. The combined organic extracts were dried and concentrated to give 3 as a bright yellow solid (1.0 g, 80%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (s, 1H), 8.57 (d, $J = 8.8$ Hz, 1H), 8.19 (d, $J = 8.8$ Hz, 1H), 8.07 (d, $J = 8.4$ Hz, 1H), 7.39 (d, $J = 8.4$ Hz, 1H), and 2.32 (s, 3H); ^{13}C NMR (100 MHz): δ 170.2, 154.9, 154.2, 154.1, 139.1, 138.8, 122.0, 119.1, 115.9, and 25.0. These spectral data were consistent to those reported.[15]

4.4 | 2-Acetylamino-7-(2-pyridinyl)-1,8-naphthyridine (L_1)

A mixture of **3** (377.5 mg, 1.7 mmol), 2-(tri-butylstannyl) pyridine (1.250 g, 3.4 mmol), and $Pd(PPh_3)_2Cl_2$ (64 mg, 0.085 mmol) in toluene (7 mL) was heated to reflux under a nitrogen atmosphere overnight. After cooling, the mixture was filtrated through Celite and the filtrate was concentrated. The residue was chromatographed on silica gel with elution of acetone/dichloromethane (1:1) to yield $\mathbf{L_1}$ as a light yellow solid (247 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.29 (br, 1H), 8.73–8.70 (m, 2H), 8.61 (d, $J = 8.4$ Hz, 1H), 8.54 (d, $J = 8.8$ Hz, 1H), 8.25–8.20 (m, 2H), 7.85 (t, $J = 7.6$ Hz, 1H), and 7.36 (t, $J = 6$ Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz): δ 169.9, 159.6, 155.6, 154.7, 154.3, 149.4, 139.6, 137.6, 137.2, 124.9, 122.5, 120.9, 118.9, 115.6, and 25.2. HRMS electrospray ionisation time-of-flight mass spectrometry (ESI-TOF) calcd. for $C_{15}H_{13}N_4O$ $(M + H)^+$ $m/z = 265.1084$, found 265.1089.

4.5 | 2-Amino-7-(2-pyridinyl)-1,8-naphthyridine (L_2)

A mixture of $\mathbf{L_1}$ (101.8 mg, 0.385 mmol) and NaOH (64 mg) in a mixed solvent of methanol/dioxane (1:9) (4 mL) was stirred at 80°C for 24 hr. After cooling, the mixture was extracted with dichloromethane/water. The organic extracts were dried and concentrated under vacuum to give $\mathbf{L_2}$ as a yellow solid (76 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, $J = 8$ Hz 1H), 8.70 (d, $J = 4$ Hz, 1H), 8.43 (d, $J = 8.2$ Hz, 1H), 8.08 (d, $J = 8.2$ Hz, 1H), 7.90 (d, $J = 8.7$ Hz, 1H), 7.84 (td, $J = 7.7$ Hz, 1.6 Hz, 1H), 7.35–7.32 (m, 1H), 6.78 (d, $J = 8.6$ Hz, 1H), and 5.09 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 158.5, 156.2, 155.9, 148.9, 138.2, 137.1, 136.9, 124.2, 122.3, 117.8, 116.2, and 112.5. HRMS (ESI-TOF) calcd. for $C_{13}H_{11}N_4$ $(M + H)^+$ $m/z = 223.0978$, found 223.0970.

4.6 | Complex 4

A reaction tube was loaded with $\mathbf{L_1}$ and $[Cp^*IrCl_2]_2$ (160.2 mg, 0.2 mmol) was flashed with nitrogen gas. Dichloromethane (2 mL) was syringed into the vessel and the resulting solution was stirred at ambient temperature for 24 hr. Filtration gave **4** as an orange solid (226 mg, 86%): ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.54 (s, 1H), 9.05 (d, $J = 5.6$ Hz, 1H), 8.94 (d, $J = 8$ Hz, 1H), 8.89 (d, $J = 8.4$ Hz, 1H), 8.81 (d, $J = 8.4$ Hz, 1H), 8.69 (d, $J = 8.8$ Hz, 1H), 8.46 (d, $J = 8.8$ Hz, 1H), 8.37 (t, $J = 8.0$ Hz, 1H), 7.94 (t, $J = 6.8$ Hz, 1H), 2.30 (s, 3H), and 1.48 (s, 15H); ^{13}C NMR (100 MHz): δ 171.2, 158.4, 156.2, 155.9, 153.3, 142.3, 140.9, 140.7, 129.9, 126.2, 122.8, 119.6, 89.4, 24.7, and 9.0. HRMS (ESI-TOF) calcd. for $C_{25}H_{27}ClIrN_4O$ $[M\text{-}Cl]^+$ $m/z = 627.1497$, found 627.1503.

4.7 | Complex 5

A reaction flask was loaded with $\mathbf{L_2}$ and $[Cp^*IrCl_2]_2$ (104.5 mg, 0.131 mmol) was flashed with nitrogen gas. Dichloromethane (1.5 mL) was syringed into the flask and the resulting solution was stirred at ambient temperature for 24 hr. Filtration gave **5** as orange solid (92.5 mg, 57%): ^{1}H NMR (400 MHz, (DMSO-d_6): δ 8.99 (d, $J = 4.4$ Hz, 1H), 8.77 (d, $J = 7.6$ Hz, 1H), 8.50 (d, $J = 8.0$ Hz, 1H), 8.40 (d, $J = 8.0$ Hz, 1H), 8.28 (t, $J = 7.6$ Hz, 1H), 8.16 (d, $J = 9.2$ Hz, 1H), 7.82 (t, $J = 6.0$ Hz, 1H), 7.11 (d, $J = 8.8$ Hz, 1H), and 1.52 (s, 15H); ^{13}C NMR (100 MHz): δ 161.7, 156.4, 155.6, 155.2, 152.8, 140.3, 140.1, 138.0, 128.6, 124.5, 119.9, 116.8, 115.5, 88.7, and 8.9. HRMS (ESI-TOF) calcd. for $C_{23}H_{25}ClIrN_4$ $[M\text{-}Cl]^+$ $m/z = 585.1391$, found 585.1338.

4.8 | Complex 6

A mixture of **4** (50 mg, 0.062 mmol) and $AgBF_4$ (27 mg, 0.136 mmol) in acetonitrile (1 mL) was stirred at room temperature under dark conditions for 20 hr. After filtration through Celite, complex **6** was obtained as a bright yellow solid (45.2 mg, 90%): ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.54 (s, 1H), 9.18 (d, $J = 5.6$ Hz, 1H), 9.04 (d, $J = 8.4$ Hz, 1H), 9.00 (d, $J = 8.4$ Hz, 1H), 8.87

(d, $J = 8.4$ Hz, 1H), 8.72(d, $J = 8.8$ Hz, 1H), 8.53 (t, $J = 8.0$ Hz, 1H), 8.48 (d, $J = 9.2$ Hz, 1H), 8.04 (t, $J = 6.4$ Hz, 1H), 2.31 (s, 3H), 2.04 (s, 3H), and 1.45 (s, 15H); ^{13}C NMR (100 MHz): δ 175.2, 170.6, 159.6, 157.4, 156.7, 154.2, 153.0, 143.6, 142.4, 141.1, 130.5, 127.6, 123.3, 120.4, 119.6, 97.5, 24.6, 8.3, and 1.1. HRMS (ESI-TOF) calcd. for $C_{27}H_{30}B_3F_{12}IrN_5O$ $[M+(BF_4)]^-$ $m/z = 894.2167$, found 894.1893.

4.9 | Complex 7

The procedure is similar to that for **6**. Complex **7** was obtained as a bright yellow solid (46.5 mg, 94%): ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.04 (d, $J = 5.6$ Hz, 1H), 8.65 (d, $J = 8.0$ Hz, 1H), 8.49 (d, $J = 8$ Hz, 1H), 8.47 (d, $J = 7$ Hz, 1H), 8.20 (d, $J = 8.8$ Hz, 1H), 7.98 (t, $J = 6.4$ Hz, 1H), 7.59 (br, 1H), 7.13 (d, $J = 9.2$ Hz, 1H), 2.05 (s, 3H), and 1.48 (s, 15H); ^{13}C NMR (100 MHz): δ 162.4, 157.9, 156.2155.6, 153.6, 142.2,141.8, 138.5, 129.8, 126.5, 120.9, 118.2, 117.7, 117.0, 96.8, 8.3, and 1.2. HRMS (ESI-TOF) calcd. for $C_{23}H_{25}IrN_4$ $[M\text{-}CH_3CN\text{-}2(BF_4)]^{2+}$ $m/z = 275.0851$, found 275.0877.

4.10 | Complex 8

The procedure is similar to that for **4**. Complex **8** was obtained as a dark red solid (161 mg, 99%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.46 (d, $J = 7.6$ Hz, 1H), 9.39 (d, $J = 8.4$ Hz, 1H), 9.17 (d, $J = 2.4$ Hz, 1H), 8.95 (d, $J = 4.4$ Hz, 1H), 8.90 (d, $J = 8.0$ Hz, 1H), 8.57 (d, $J = 7.6$ Hz, 1H), 8.29 (t, $J = 6.8$ Hz, 1H), 7.86 (t, $J = 6.0$ Hz, 1H), 7.78 (dd, $J = 8$, 4 Hz, 1H), and 1.61 (s, 15H); ^{13}C NMR (100 MHz): δ 159.3, 156.5, 155.5, 152.6, 151.7, 143.7, 141.3, 139.1, 129.8, 128.6, 125.5, 125.4, 123.0, 90.2, and 9.9. HRMS (ESI-TOF) calcd. for $C_{23}H_{24}ClIrN_3$ $[M\text{-}Cl]^+$ $m/z = 570.1281$, found 570.1304.

4.11 | Crystallography

Crystals suitable for X-ray determination were obtained for **4**, **5**, and **6** by recrystallization. Cell parameters were determined using a Siemens SMART CCD diffractometer. The structure was solved using the SHELXS-97 program[16a] and refined using the SHELXL-97 program[16b] by full-matrix least-squares on $F2$ values.

Crystal data for **4**·$(CH_3OH)_2$: $C_{27}H_{34}Cl_2IrN_4O_3$, $F_w = 725.69$, Triclinic, P-1, $a = 8.9429(3)$ Å, $b = 10.5905$ (3) Å, $c = 15.5026(5)$ Å, $\alpha = 109.119(3)°$, $\beta = 93.143(3)°$, $\gamma = 93.133(3)°$, $V = 1{,}381.06(8)$ Å^3, $Z = 2$, $D_{calcd} = 1.747$ Mg/m^3, $F(000) = 720$, crystal size: $0.20 \times 0.15 \times 0.10$ mm^3, 2.86 to 27.50°, 12,868 reflections collected, 6,125 reflections [R(int) = 0.0303], Final R indices [I > 2sigma(I)]: R1 = 0.0285, wR2 = 0.0673, for all data R1 = 0.0333, wR2 = 0.0699, and Goodness-of-fit on $F^2 = 1.070$.

4.11.1 | Crystal data for 5·0.5(CH_3OH)

$C_{23.5}H_{25}Cl_2IrN_4O_{0.50}$, $F_w = 634.58$, Orthorhombic, P2(1)2(1)2 (1), $a = 8.2689$ (2) Å, $b = 14.3470(4)$ Å, $c = 21.1985$ (4) Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 2{,}514.86(10)$ Å^3, $Z = 4$, $D_{calcd} = 1.676$ Mg/m^3, $F(000) = 1{,}236$, crystal size: $0.20 \times 0.15 \times 0.10$ mm^3, 2.84 to 27.50°, 12,662 reflections collected, 5,339 reflections [R(int) = 0.0283], Final R indices [I > 2sigma(I)]: R1 = 0.0265, wR2 = 0.0711, for all data R1 = 0.0277, wR2 = 0.0718, and Goodness-of-fit on $F^2 = 1.055$.

4.11.2 | Crystal data for 6·CH_3CN

$C_{29}H_{32}B_2F_8IrN_6O$, $F_w = 847.43$, Triclinic, P-1, $a = 9.6684$ (4)Å, $b = 10.9459(3)$ Å, $c = 16.9247(6)$ Å, $\alpha = 98.702(3)°$, $\beta = 106.336(4)°$, $\gamma = 104.037(3)°$, $V = 1{,}620.48(10)$ Å^3, $Z = 2$, $D_{calcd} = 1.737$ Mg/m^3, $F(000) = 832$, crystal size: $0.25 \times 0.20 \times 0.15$ mm^3, 2.83 to 27.50°, 15,310 reflections collected, 7,169 reflections [R(int) = 0.0476], Final R indices [I > 2sigma(I)]: R1 = 0.0466, wR2 = 0.1087, for all data R1 = 0.0567, wR2 = 0.1183, and Goodness-of-fit on $F^2 = 1.034$.

4.11.3 | Crystal data for 8·$CHCl_3$

$C_{24}H_{25}Cl_5IrN_3$, $F_w = 724.92$, Triclinic, P-1, $a = 8.8701$ (3) Å, $b = 15.7083(7)$ Å, $c = 18.9653(6)$ Å, $\alpha = 96.332(3)°$, $\beta = 99.809(3)°$, $\gamma = 97.682(3)°$, $V = 2{,}556.45(17)$ Å^3, $Z = 4$, $D_{calcd} = 1.883$ Mg/m^3, $F(000) = 1{,}408$, crystal size: $0.20 \times 0.15 \times 0.10$ mm^3, 3.3650–26.6680°, 15,857 reflections collected, 8,973 reflections [R(int) = 0.0695], Final R indices [I > 2sigma(I)]: R1 = 0.0641, wR2 = 0.1317, for all data R1 = 0.1090, wR2 = 0.1628, and Goodness-of-fit on $F^2 = 1.032$.

CCDC 1892203–1892206 for **4**, **5**, **6** and **8** contain the supplementary crystallographic data for this article. These data can be obtained free of charge from The Cambridge Crystallographic Data Center.

4.12 | Catalysis

A mixture of ketone compound (0.5 mmol) and complex (5×10^{-3} mmol) in methanol (0.5 mL) was loaded in a sealed reaction vessel with a stirring bar. The mixture was stirred at 120°C for a period of time (see Tables). After the reaction, methanol was removed under reduced pressure. The residue was extracted with ether (3 mL × 3) and the

combined organic extracts were dried and concentrated. The residue was analyzed using NMR spectroscopy. After purification, chromatography on silica gels provided the desired compound in the pure form. The spectral data of the organic products are essentially identical to those reported ones. ^{1}H and ^{13}C NMR spectral data for all compounds are deposited in the Supporting information.

ACKNOWLEDGMENTS

We thank the Ministry of Science and Technology for financial support (MOST-106-2113-M-002-018). "National Taiwan University Mass Spectrometry-based Proteomics Core Facility" is acknowledged for the measurement of ESI mass data.

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AUTHOR BIOGRAPHIES

Po-Hao Chen was born in 1991 in Kaohsiung, received his BS degree in Public Health from National Taiwan University in 2013, and worked at Taiwan Environmental Protection Administration (EPA) from 2013 to 2016. After his career with EPA, he pursued his MS program in Chemistry in 2016 at NTU under the guidance of Prof. Shiuh-Tzung Liu and received the degree in 2018. Po-Hao is currently a Process Engineer in the Department of Etching Engineer in Taiwan Semiconductor Manufacturing Company.

Yi-Hung Liu was born in 1968 in Keelung. He obtained his BS degree in Earth Science from National Cheng Kung University in 1992. He served as an assistant in National Taiwan University (NTU) in 1995. After receiving the qualification of level-two technician in 1996, he became the technical staff of X-ray diffractometer of Instrumentation Center, NTU. In the year of 2011, he was promoted as a level-three technician.

Shiuh-Tzung Liu was born in 1954, and is a full professor of Chemistry Department and currently serves as the dean of College of Science, National Taiwan University. He studied chemistry at the National Taiwan University (BS in 1977), and then pursued his graduate program in the University of Texas at Austin (PhD in 1985). After spending 1 year as a postdoctoral fellow at Texas, he took the faculty position at NTU. His research interests include the study of ligand design, fundamental processes in organometallic chemistry, synthetic

methodology, and homogeneous catalysis. He published more than 160 articles in the international journals.

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How to cite this article: Chen P-H, Liu Y-H, Liu S-T. Naphthyridine-based iridium complexes: Structures and catalytic activity on alkylation of aryl ketones. *J Chin Chem Soc*. 2019;1–10. https://doi.org/10.1002/jccs.201900057