# **ORGANOMETALLICS**

# Synthesis and Reactivity of Cationic Iridium Aminocarbenes Derived from Terminal Alkynes and 2-Aminopyridines

Elumalai Kumaran, Kai Tong Sonia How, Rakesh Ganguly, Yongxin Li, and Weng Kee Leong\*

Division of Chemistry and Biological Chemistry, Nanyang Technological University, 21 Nanyang Link, Singapore 637371

### **Supporting Information**

**ABSTRACT:** The reaction of a terminal alkyne (RCCH) and 2aminopyridine  $(R'C_5NH_3NH_2)$  with the dinuclear species  $[Cp*IrCl_2]_2$ afforded the cationic aminocarbene derivatives  $Cp*Ir(Cl)[=C-(CH_2R)NHC_5NH_3R']$  via a hydroamination and a ligand substitution. The reaction pathway has been examined through computational studies.



# INTRODUCTION

Even though several methodologies have been developed,<sup>1</sup> nucleophilic attack at the  $\alpha$ -carbon of a vinylidene intermediate is one of the best and most attractive synthetic routes to transition-metal carbenes. Transition-metal vinylidenes are susceptible to a wide number of nucleophiles, including amines,<sup>2,3</sup> water,<sup>4</sup> alcohols,<sup>5</sup> thiols,<sup>6</sup> phosphines,<sup>7</sup> and even fluoride.<sup>8</sup> A large variety of Fischer-type transition-metal carbenes have been made available using this methodology, including, alkoxy-,<sup>5</sup> thio-,<sup>6</sup> and aminocarbenes.<sup>3</sup> We have also recently utilized this method toward the synthesis of a variety of ortho-metalated iridium aminocarbene derivatives, with the reaction of  $[Cp*IrCl_2]_2$  (1) with a terminal alkyne (2) and an aniline as the nucleophile.

In this report, we wish to report our attempt at extending this methodology to the use of a 2-aminopyridine (3) as the nucleophile. Two possible products, of structure I or II, may be expected a priori (Figure 1), and the outcome should be



Figure 1. Possible products from the reaction of  $[Cp*IrCl_2]_2$  (1) with a terminal alkyne (2) and a 2-aminopyridine (3).

dictated by the feasibility of C–H activation versus ligand substitution. Literature on transition-metal aminocarbenes having the aminopyridine moiety is extensive for ruthenium.<sup>3</sup> However, there has been much less work carried out with iridium and that mainly involved double C–H activation of the corresponding *N*-alkyl-2-aminopyridines.<sup>1a,9</sup>

# RESULTS AND DISCUSSION

The reaction of 1 with the terminal alkyne 2 and the 2aminopyridine 3 afforded an iridium aminocarbene complex of the type  $[Cp*Ir(=C(NHC_5NH_3R')(CH_2R))Cl]Cl$  (4·Cl) in 59–82% yields (Scheme 1). A wide variety of aminopyridines



and terminal alkynes can be employed; the reaction proceeded smoothly with both aliphatic and aromatic terminal alkynes but failed to afford aminocarbenes with internal alkynes (diphenylacetylene and prop-1-ynylbenzene), and both electron-withdrawing and -donating substituents on the 2-aminopyridine can be tolerated.

The products have all been characterized completely by spectroscopy, elemental analysis, and, in the case of **4c·Cl**, by a single-crystal X-ray crystallographic study as well; an ORTEP plot of the cation **4c** is shown in Figure 2. Similar iridacycles which have been structurally characterized include  $Tp^{Ph}Ir(H)$ -(=CHNMePy),<sup>9a</sup> [Ir(H)<sub>2</sub>{=C(Me)NEtPy}(PPh\_3)<sub>2</sub>]<sup>+,9c</sup> and [Ir(H)<sub>2</sub>{=C(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Ph)NMePy}(PPh\_3)<sub>2</sub>]<sup>+,9c</sup> The <sup>1</sup>H NMR spectra of the aminocarbene complexes were characterized by two doublet resonances arising from the diastereotopic CH<sub>2</sub> protons and a resonance at ~242 ppm in the  $^{13}C{^{1}H}$  NMR spectra which is typical for a transition-metal carbene.

Received: April 17, 2013



Figure 2. ORTEP plot (50% probability thermal ellipsoids) showing the molecular structure of the cation 4c. H atoms are omitted for clarity.

The proposed reaction pathway to 4 (Scheme 2) is similar to that which we have proposed earlier for the ortho-metalated



aminocarbene complexes and differs only in the final step;<sup>3j</sup> the Gibbs free energies (in kJ mol<sup>-1</sup>) for each step have also been evaluated computationally with DFT and are shown.

Deuterium labeling experiments involving phenylactylene-d with 1 and 2-amino-6-bromopyridine and phenylacetylene with 1 and 2-amino-6-bromopyridine in the presence of D<sub>2</sub>O afforded 4e with no deuterium and two deuteriums, respectively, incorporated at the diastereotopic CH<sub>2</sub> protons. This is consistent with the alkyne-vinylidene rearrangement from A to B via intermolecular proton transfer with adventitious water. Nucleophilic attack by the aniline functionality at the vinylidene  $\alpha$ -carbon followed by proton transfer would afford the aminocarbene intermediate C. From there, ligand displacement of a chloride by the pyridyl N would result in 4; the alternative ortho metalation to afford the neutral aminocarbene 4' that was observed with aniline<sup>3j</sup> is energetically less favorable (Scheme 3). An alternative pathway which we have also examined computationally involved the formation of a cationic intermediate early in the pathway, in which



binding of the alkyne followed displacement of a chloride. The energetics for this pathway were comparable to that outlined above and hence could not be confidently excluded, but such a pathway may not be favored in a relatively nonpolar environment such as that employed here.

It was also found that 4, which contains a benzylic group  $\alpha$  to the carbene moiety, was susceptible to aerial oxidation to form complexes 5; those with aliphatic substituents, such as 4c, were resistant to oxidation under similar conditions (Scheme 4). These oxidation products have also been characterized completely; **Se**•Cl has been characterized by a single-crystal X-ray structural study as well.



In both 4 and 5, the NH proton is expected to be acidic. Indeed, treatment with triethylamine afforded the neutral cyclometalated species 6 and 7, respectively (Scheme 3). The reaction is reversible, as treatment of 6 with HBF<sub>4</sub> afforded  $[Cp^*(Cl)Ir=C(CH_2^{t}Bu)NHPy]BF_4$  (4c·BF<sub>4</sub>); the chloride salt, 4c·Cl, could be obtained by treatment with concentrated HCl.

In addition to  $4c \cdot Cl$  and  $5e \cdot Cl$ , the complexes  $4c \cdot BF_4$ ,  $5g \cdot Cl$ , 6b, and 7e have also been characterized crystallographically. Selected bond parameters for the six structures are given in Table 1.

The Ir-C(4) bond lengths in the cationic species are comparable to or shorter than the corresponding bond lengths in the ortho-metalated aminocarbenes<sup>3j</sup> and hence are clearly indicative of Ir=C double-bond character. The corresponding bond in the neutral species (6b and 7e) is longer but not appreciably so, suggesting some double-bond character as well. Indeed, the C-N bond lengths for all six crystals show similar variations, suggesting similar delocalization of electrons about the metallacycles. This is corroborated by the <sup>13</sup>C NMR spectra, which show a distinct downfield peak at ~225-245 ppm for all of the complexes in this study, both cationic and neutral. The structures of 5e,g and 7e suggest that the ketone functionality in these complexes is not conjugated to the metallacycle; the dihedral angle between the Ir-C(4)-N(3)and C(4)-C=O planes ranges from about 68 to 79°. However, the infrared spectroscopic data ( $\nu_{C=0}$  bands are 1659, 1654, 1653, and 1651 cm<sup>-1</sup> for **5e**,**5g** and **7e**,**g**, respectively, in comparison to 1686 cm<sup>-1</sup> in acetophenone) suggests that in solution there is conjugation.

Scheme 5





	4c.Cl	4c.BF <sub>4</sub>	6b	7e	5e	5g
Bond parameters	$X = Cl(c), BF_4(c^3)$		$R=CH_{2}^{1}Bu: R'=5-Br (6b)$		$R = Ph(\mathbf{e}), p-tolyl(\mathbf{g})$	
			$\mathbf{K} = \mathbf{COPn}: \mathbf{K} = 0 - \mathbf{Br}(\mathbf{R})$			
Bond lengths / Å						
Ir Cl	2 370(2)	2 385(2)	2 388(2)	2 3008(13)	2 302(2)	2 3023(18)
11-01	2.379(2)	2.383(2)	2.388(2)	2.3336(13)	2.392(2) 2 403(2)	2.3923(18) 2 3951(19)
Ir-N(1)	2.118(8)	2.120(7)	2.060(6)	2.113(5)	2.103(2) 2.121(7)	2.142(6)
					2.130(7)	2.124(6)
Ir-C(4)	1.990(10)	1.967(9)	2.002(8)	2.015(6)	1.971(8)	1.978(8)
					1.969(9)	1.981(8)
N(1)-C(2)	1.359(12)	1.340(10)	1.361(10)	1.369(7)	1.353(11)	1.347(9)
					1.345(11)	1.370(9)
N(3)-C(2)	1.382(13)	1.391(12)	1.382(11)	1.388(7)	1.397(11)	1.380(10)
					1.384(11)	1.383(10)
N(3)-C(4)	1.332(12)	1.338(11)	1.320(10)	1.284(7)	1.324(11)	1.323(9)
					1.309(11)	1.315(9)
Bond angles / degree						
N(1) - Ir - C(4)	77.9(3)	78.3(3)	76.2(3)	75.0(2)	76.7(3)	77.0(3)
					76.3(3)	76.8(3)
C(2) - N(3) - C(4)	120.9(8)	118.9(7)	112.7(7)	112.6(5)	118.6(7)	119.5(6)
					117.3(8)	118.5(7)
N(1) - C(2) - N(3)	112.2(8)	114.0(7)	116.9(7)	117.4(5)	112.1(7)	113.3(7)
					114.0(7)	113.2(6)
N(3) - C(4) - Ir	114.6(7)	114.8(6)	120.1(6)	122.2(4)	117.4(6)	116.3(6)
	1	1	1	1	1118 5(6)	$\pm 117.7(6)$

<sup>a</sup>The two sets of values given for 5e,g are for the two crystallographically independent molecules found in the crystals.

# CONCLUSION

In this report, we have described a synthetic route to cationic aminocarbene complexes of iridium(III) by the reaction of 1 with aminopyridines and terminal alkynes. They can undergo reversible deprotonation at the NH moiety, and those containing a benzylic group at the metallacycle can readily undergo aerial oxidation. These are characteristic of electron delocalization within, and hence aromaticity in, the metallacycle and is also corroborated by the structural and NMR parameters for these complexes.

## EXPERIMENTAL SECTION

**General Considerations.** All reactions and manipulations, except for TLC separations, were performed under argon by using standard Schlenk techniques. All other reagents were from commercial sources and used without further purification. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a JEOL ECA400 or ECA400-SL NMR spectrometer as CDCl<sub>3</sub> solutions; chemical shifts reported were referenced against the residual proton signals of the solvent at 7.26 and 77.24 ppm for <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR, respectively. ESI/MS were recorded in EI mode on a MATLCQ spectrometer. High-resolution mass spectra (HRMS) were recorded in ESI mode on a Waters UPLC-Q-TOF mass spectrometer.  $[Cp*IrCl_2]_2$  (1) was prepared according to the published method.<sup>10</sup> Elemental analyses were performed by the microanalytical laboratory at NTU.

**Reaction of 1 with Alkyne and 2-Aminopyridine.** In a 50 mL Carius tube, a dichloroethane solution (5 mL) of  $[Cp*IrCl_2]_2$  (40 mg, 50  $\mu$ mol), 3,3-dimethyl-1-butyne (125  $\mu$ L, 1 mmol), and 2-aminopyridine (10 mg, 100  $\mu$ mol) was stirred at 40 °C for 24 h. The reaction solvent was then removed under reduced pressure, followed by recrystallization from dichloromethane/diethyl ether to give pure 4a·Cl (45 mg, 80%).

Aerial Oxidation of 4e-Cl and 4g-Cl. In a 50 mL roundbottomed flask, 4e-Cl (20 mg, 29.7  $\mu$ mol) was dissolved in dichloromethane (5 mL) and hexane (15 mL) and the reaction mixture was refluxed in the open at 50 °C overnight. The solvent was then removed under reduced pressure, followed by recrystallization from dichloromethane/diethyl ether to give pure Se-Cl (15 mg, 74%).

**Reversible Deprotonation of 4.** To a solution of 4a·Cl (20 mg, 34.8  $\mu$ mol) in dichloromethane (5 mL) was added triethylamine (6  $\mu$ L, 42  $\mu$ mol), the mixture was stirred at RT room temperature for 15 min and filtered through silica gel, and the solvent was evaporated under reduced pressure to afford pure 6a. A similar procedure was used for 6b,c. The reversible protonation of 6c (20 mg, 32.5  $\mu$ mol) in dichloromethane (5 mL) with HBF<sub>4</sub>·OEt<sub>2</sub> (5  $\mu$ L, 39  $\mu$ mol) afforded 4c·BF<sub>4</sub> (22 mg, 96%).

**X-ray Crystallographic Studies.** Crystals were grown from dichloromethane/hexane solutions and mounted on quartz fibers. X-ray data were collected on a Bruker AXS APEX system, using Mo K $\alpha$  radiation, with the SMART suite of programs.<sup>11</sup> Data were processed and corrected for Lorentz and polarization effects with SAINT<sup>12</sup> and for adsorption effects using SADABS.<sup>13</sup>

The structures were solved by direct methods to locate the heavy atoms, followed by difference maps for the light, non-hydrogen atoms. Hydrogen atoms were placed in calculated positions and refined with a riding model. There were two formula units per asymmetric unit for Se·Cl and Sg·Cl. Dichloromethane solvates were found in the crystals of 4c·Cl, 5e·Cl, and 5g·Cl. For the last two crystals, four sites were found for the solvates, which were modeled with various occupancies, and with 5e·Cl, one of the solvates was modeled as disordered with two alternative positions for one of the Cl atoms. The crystal of 4c·BF<sub>4</sub> showed disorder of the anion, which was modeled with two alternative sites for each of the F atoms, with occupancies of 0.7 and 0.3, respectively. The crystal of **6b** exhibited disorder of the CH<sub>2</sub><sup>t</sup>Bu group, which was modeled with two alternative sites with their occupancies summed to unity. Appropriate restraints on the bond and thermal parameters were placed on all the disordered parts. All non-hydrogen atoms were given anisotropic displacement parameters in the final model.

**Computational Studies.** The reaction energetics was studied using DFT theory utilizing Becke's three-parameter hybrid function<sup>14</sup> and Lee–Yang–Parr's gradient-corrected correlation function (B3LYP).<sup>15</sup> The LanL2DZ (Los Alamos effective core potential double- $\zeta$ ) basis set together with an f polarization function was employed for the Ir atom, and the 6-311+G(2d,p) basis set was used for all other atoms. Spin-restricted calculations were used for geometry optimization, and harmonic frequencies were then calculated to characterize the stationary points as equilibrium structures with all real frequencies and to evaluate zero-point energy (ZPE) corrections. All calculations were performed using the Gaussian 09 suite of programs.<sup>16</sup>

#### ASSOCIATED CONTENT

#### **S** Supporting Information

Tables, figures, and CIF files giving crystallographic data, experimental details and characterization data for the complexes, and optimized geometries of all computed structures. This material is available free of charge via the Internet at http://pubs.acs.org.

#### AUTHOR INFORMATION

#### Notes

The authors declare no competing financial interest.

#### ACKNOWLEDGMENTS

This work was supported by Nanyang Technological University and the Ministry of Education (Research Grant No. M4011017). E.K. thanks the university for a Research Scholarship.

#### REFERENCES

(1) (a) Clot, E.; Chen, J.; Lee, D. H.; Sung, S. Y.; Appelhans, L. N.;
 Faller, J. W.; Crabtree, R. H.; Eisennstein, O. J. Am. Chem. Soc. 2004, 126, 8795–8804.
 (b) Vignolle, J.; Gornitzka, H.; Donnadieu, B.;
 Bourissou, D.; Bertrand, G. Angew. Chem., Int. Ed. 2008, 47, 2271–2274.
 (c) Standfest-Hauser, C. M.; Mereiter, K.; Schimid, R.; Kirchner, K. Organometallics 2002, 21, 4891–4893.
 (d) Hou, H.; Gantzel, P. K.;
 Kubiak, C. P. J. Am. Chem. Soc. 2003, 125, 9564–9565.
 (e) Vyklicky, L.; Dvorakova, H.; Dvorak, D. Organometallics 2001, 20, 5419–5424.
 (a) Bianchini, C.; Peruzzini, M.; Romerosa, A.; Zanobini, F.

*Organometallics* **1995**, *14*, 3152–3153. (b) Bianchini, C.; Masi, D.; Romerosa, A.; Zanobini, F.; Peruzzini, M. Organometallics **1999**, *18*,

2376–2386. (c) Kumaran, E.; Leong, W. K. Organometallics 2012, 31, 4849–4853.

(3) (a) Yam, V. W. W.; Chu, B. W. K.; Cheung, K. K. Chem. Commun. 1998, 2261–2262. (b) Bianchini, C.; Masi, D.; Romerosa, A.; Zanobini, F.; Peruzzini, M. Organometallics 1999, 18, 2376–2386. (c) Yam, V. W. W.; Chu, B. W. K.; Ko, C. C.; Cheung, K. K. J. Chem. Soc., Dalton Trans. 2001, 1911–1919. (d) Rüba, E.; Hummel, A.; Mereiter, K.; Schmid, R.; Kirchner, K. Organometallics 2002, 21, 4955–4959. (e) Sonja, P.; Mereiter, K.; Puchberger, M.; Kirchner, K. Organometallics 2005, 24, 3561–3575. (f) Sun, Y.; Chan, H. S.; Xie, Z. Organometallics 2006, 25, 3447–3453. (g) Kopf, H.; Holzberger, B.; Pietraszuk, C.; Hübner, E.; Burzlaff, N. Organometallics 2008, 27, 5894–5905. (h) Cross, R. J.; Davidson, M. F. J. Chem. Soc., Dalton Trans. 1988, 1147–1152. (i) Ipaktschi, J.; Uhlig, S.; Dülmer, A. Organometallics 2001, 20, 4840–4846. (j) Kumaran, E.; Sridevi, V. S.; Leong, W. K. Organometallics 2010, 29, 6417–6421.

(4) (a) Bianchini, C.; Casares, J. A.; Peruzzini, M.; Romerosa, A.; Zanobini, F. J. Am. Chem. Soc. 1996, 118, 4585-4594. (b) Sridevi, V. S.; Fan, W. Y.; Leong, W. K. Organometallics 2007, 26, 1173-1177.
(c) Sullivan, B. P.; Smythe, R. S.; Kober, E. M.; Meyer, T. J. J. Am. Chem. Soc. 1982, 104, 4701. (d) O'Connor, J. M.; Pu, L. J. Am. Chem. Soc. 1990, 112, 9013. (e) Jimenez, M. V.; Sola, E.; Martinez, A. P.; Lahoz, F. J.; Oro, L. A. Organometallics 1999, 18, 1125. (f) Chin, C. S.; Chong, D.; Maeng, B.; Ryu, J.; Kim, H.; Kim, M.; Lee, H. Organometallics 2002, 21, 1739.

(5) (a) Barthel-Rosa, L. P.; Maitra, K.; Fischer, J.; Nelson, J. H. Organometallics 1997, 16, 1714–1723. (b) O'Connor, J. M.; Pu, L. J. Am. Chem. Soc. 1987, 109, 7579–7581. (c) O'Connor, J. M.; Pu, L. J. Am. Chem. Soc. 1989, 111, 4130–4131. (d) O'Connor, J. M.; Pu, L.; Rheingold, A. L. J. Am. Chem. Soc. 1990, 112, 6232–6247. (e) Barrett, A. G. M.; Carpenter, N. E. Organometallics 1987, 6, 2249–2250.

(6) Mantovani, N.; Marvelli, L.; Rossi, R.; Bertolsi, V.; Bianchini, C.; Rios, I. L.; Peruzzini, M. *Organometallics* **2002**, *21*, 2382–2394.

(7) Senn, D. R.; Wong, A.; Patton, A. T.; Marsi, M.; Strouse, C. E.; Gladysz, J. A. J. Am. Chem. Soc. **1988**, 110, 6096–6109.

(8) Ting, P. C.; Lin, Y. C.; Lee, G. H.; Cheng, M. C.; Wang, Y. J. Am. Chem. Soc. 1996, 118, 6433-6444.

(9) (a) Werner, H. Angew. Chem., Int. Ed. 2010, 49, 4714–4728.
(b) Lee, D. H.; Chen, J.; Faller, J. W.; Crabtree, R. H. Chem. Commun. 2001, 213–214. (c) Li, X.; Appelhans, L. N.; Faller, J. W.; Crabtree, R. H. Organometallics 2004, 23, 3378–3387.

(10) Ball, R. G.; Graham, A. G.; Heinekey, D. M.; Hoyano, , J. K.; McMaster, A. D.; Mattson, B. M.; Michel, S. T. *Inorg. Chem.* **1990**, *29*, 2023.

(11) SMART version 5.628; Bruker AXS Inc., Madison, WI, 2001.

(12) SAINT+ version 6.22a; Bruker AXS Inc., Madison, WI, 2001.

(13) Sheldrick, G. M. *SADABS*; University of Göttingen, Göttingen, Germany, 1996.

(14) Becke, A. D. J. Chem. Phys. 1993, 98, 568-5652.

(15) Lee, C.; Yang, W.; Parr, R. G. Phys. Rev. B 1998, 37, 785-789. (16) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian 03; Gaussian Inc., Wallingford, CT, 2004.