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Expedient Synthesis of Highly Functionalized Abnormal Carbenegold(I) Complexes

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S Supporting Information

ABSTRACT: The reaction of 4-substituted imidazol-2ylidenes with various electrophiles produces a series of 2,4functionalized imidazolium salts. Subsequent metalation of these precursors using AuCl(SMe₂) provides the first examples of highly functionalized abnormal carbenegold(I) complexes. The present protocol introduces a new strategy for the synthesis of metallic abnormal carbenes featuring diverse functional groups

The use of N-heterocyclic carbenes (NHCs) in transitionmetal chemistry has experienced an exponential growth over the last 2 decades.¹ Because of the accessible modification of their structural features, a vast amount of metal complexes with NHCs have been reported and numerous applications found in catalysis and other related areas.² Although many examples show that NHCs coordinate the metal centers through the C2 position (I), in 2001 Crabtree and co-workers discovered the first example of a metallic carbene featuring coordination at the C5 position (II).³ Ligands of the latter type, named abnormal carbenes (aNHCs, or mesoionic carbenes, MICs), have demonstrated enhanced σ -donor and weaker π -accepting properties compared to classical NHCs, unveiling new opportunities in carbon-based coordination chemistry (Figure 1).⁴



Figure 1. Imidazole-based NHCs (I and II), Crabtree's first aNHC-Ir complex (III), and Bertrand's free aNHC (IV).

Since Crabtree's finding (III), a number of aNHC-metal complexes have been reported to date; however, most of them are the result of serendipitous discoveries.^{4b,e} Besides Bertrand's report of the first crystalline aNHC in 2009 (IV),⁵ only a few rational synthetic methods to aNHC complexes are present in the literature.⁶

Because of the commonly practiced routes, most of the aNHC complexes based on the imidazole framework feature alkyl or aryl groups at the C2 and C4 positions.^{5,7} The rare exceptions include

the palladium $(\mathbf{V})^8$ and ruthenium $(\mathbf{VI})^9$ complexes featuring C2 metalation, the gold complex $(\mathbf{VII})^{10}$ containing fluoroarenes at the C2 and C4 positions, and the gallium complex $(\mathbf{VIII})^{11}$ C2-protected by a trimethylsilyl group (Figure 2).



Figure 2. Metallic complexes featuring functionalized NHCs.

With the premise that functionalization of NHCs at the C4 and C5 positions has significant consequences on the electronic properties of the carbene center, ^{1,12} the development of new synthetic routes for functionalized metallic aNHCs is highly attractive. Herein, we report the expedient synthesis of a series of 2,4-functionalized imidazolium salts and their subsequent one-pot metalation to generate abnormal gold(I) complexes featuring various functional groups. The present methodology could open a new door for the synthesis of abnormal metallic carbenes with tailored substitution patterns.

Normally, the preparation of metallic NHCs relies on deprotonation of the C2 position, which is usually the most acidic in an imidazolium precursor. Hence, a simple way to block deprotonation at the C2 position and to favor formation of an aNHC is to introduce a C2 substituent in the imidazolium salt.¹³ However, this logical strategy is not always reliable and, in several cases, fails.¹⁴ Among the most striking cases, in 2010 Bertrand discovered that deprotonation of various C2-functionalized imidazolium salts leads to the formation of C4-functionalized NHCs instead the expected aNHC carbenes.¹⁵ This rearrangement presumably takes place via a fleeting aNHC intermediate, which abstracts the E⁺ at the C2 position of a neighboring imidazolium salt, displacing the less nucleophilic NHC as the leaving group (Scheme 1).

The latter results suggest that the aNHC intermediate attack is facilitated by the lability of the imidazolium C2 electrophile and the absence of substitution at the C4 position, which favors the nucleophile approach. With this in mind, we envisaged the

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Scheme 1. Deprotonation of C2-Functionalized Imidazolium Salts



preparation of 2,4-functionalized imidazolium salts as suitable precursors for metallic aNHC complexes. Advantages of the latter precursors include a single acidic C5-H(+) moiety for deprotonation and the overall increased steric bulk in the imidazolium ring. Thus, following a slightly modified synthetic route,¹⁵ we treated the C4-benzoyl (1) and C4-diphenylphosphine (2) imidazolylidenes with equimolar amounts of benzoyl chloride in order to generate the C2,C4-functionalized imidazolium salts 3 and 4 [Scheme 2 and Data 1571459 is

Scheme 2. Synthesis of C2,C4-Functionalized Salts 3 and 4



actually for complex **5**]. After workup, the products were easily isolated after a simple washing with diethyl ether and characterized by NMR spectroscopy and elemental analysis. Formation of the expected salts was corroborated by the presence of a single imidazolium CH(+) peak located at 8.70 and 8.62 ppm for 3 and 4, respectively. Additionally, in ¹³C NMR, the presence of new aromatic peaks and the CO group located above 180 ppm was consistent with the addition at the C2 position.

With imidazoliums 3 and 4 in hand, we then proceeded to investigate a suitable route for metalation at the C5 position. We decided to initially investigate coordination of the gold(I) center because a new series of carbene ligands with the structurally abnormal metal bonding at the position C5 have recently been reported and investigated in gold catalysis.¹⁶ Experimentally, our first attempt involved the reaction of cationic precursors with 0.5 equiv of silver oxide in dichloromethane, followed by the addition of stoichiometric amounts of AuCl(SMe₂) (Scheme 3).





After workup, the reaction mixture showed a new metallic carbene species in a mixture with a large amount of unreacted cationic precursor (ca. 35%). After separation by a chromatographic column, the metallic carbenes were properly characterized by ¹³C NMR spectroscopy, displaying new peaks at 155 and 161 ppm. The high-field signals for the Au=C bond are similar to the previously reported data for imidazole-based aNHC-Au complexes (143–164 ppm),^{5,10,17} suggesting the formation of complexes 5 and 6, respectively (Scheme 3). Because the isolated yields using this methodology were rather low, we then carried out the one-pot reaction of 3 or 4 with potassium bis(trimethylsilyl)amide (KHMDS) in the presence of AuCl(SMe₂) at -78 °C. After purification, the desired aNHC-Au^I complexes **5** and **6** were isolated in 87 and 93% yield, respectively. Interestingly, in the case of complex **6**, coordination of the gold center is selective to the carbene moiety, as denoted by the negligible shift of its phosphine signal in ³¹P NMR (-37.4 ppm) compared to the starting imidazolium salt (-36.8 ppm).

The composition and coordination features of complex 5 were unequivocally established by an X-ray diffraction study. Single crystals of 5 were obtained by hexanes vapor diffusion into a concentrated dichloromethane solution at room temperature. The molecular structure confirms coordination of the gold center to the C5 position, as previously assumed by the high field C= Au signal in ¹³C NMR (Figure 3). The coordination geometry



Figure 3. Molecular structure of complex **5**. Ellipsoids are shown at 50% of probability. Hydrogen atoms are omitted for clarity.

around the gold center is slightly distorted linearly with a bond angle C5–Au1–Cl1 of 177.30(13)°. The C5–Au bond length of 1.990(4) Å falls in the range observed previously for conventional aNHC-Au^I complexes.^{5,10,17,18}

Motivated by these interesting results, we sought to explore the reaction scope for the preparation of C2,C4-functionalized imidazolium salts. We chose the 4-benzoyl-substituted NHC (1) as the starting material and carried out its treatment with equimolar amounts of various electrophiles in tetrahydrofuran. According to Scheme 4, the formation of imidazolium salts 7a-7e proceeds smoothly, delivering moderate-to-good yields (57–83%). Of special interest is the fact that imidazolium salts featuring mixed electron-withdrawing and -donating groups can be achieved.

Scheme 4. Stepwise synthesis of imidazolium salts 7a–e, aNHC-Au complexes 8a–e, and relevant NMR spectroscopy data



With the series of functionalized aNHC precursors 7a-7e, we then proceeded to the one-pot metalation route using KHMDS in the presence of AuCl(SMe₂), observing the exclusive production of the aNHC-Au^I complexes 8a-8e in good yields. All complexes display excellent solubility in chlorinated solvents and are both air- and moisture-stable. According to the data depicted in Scheme 4, all complexes display a high-field ¹³C NMR shift for the carbenic gold peak, consistent with the abnormal coordination fashion. Special is the case of the triflate-functionalized complex **8e**, where the metallic carbenegold moiety shifts up to 161.8 ppm, suggesting an increased π -acceptor capacity of the aNHC ligand.

In summary, we have reported the expedient synthesis of a series of 2,4-functionalized imidazolium salts and their one-pot metalation to generate abnormal gold(I) complexes containing various functional groups. The overall two-step methodology expands the range of substrates available for the functionalization of free NHCs and could open a new door for the synthesis of abnormal metallic carbenes with designed substitution patterns. The successful metalation of salts 7a-7e, leading to the aNHC-Au complexes 8a-8e, highlights the stability conferred by the high level of substitution at the C2 and C4 positions of the imidazole ring. Further studies on the catalytic applications¹⁹ of the highly functionalized aNHCs are underway in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorg-chem.7b02774.

General experimental methods, synthetic procedures for catalytic experiments, and sample ¹H and ¹³C NMR spectra for new compounds (PDF)

Accession Codes

CCDC 1571459 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For recent reviews, see: (a) Würtemberger-Pietsch, S.; Radius, U.; Marder, T. B. 25 Years of N-Heterocyclic Carbenes: activation of both main-group element-element bonds and NHCs themselves. *Dalton Trans.* **2016**, *45*, 5880. (b) Diez-Gonzalez, S., Ed. *N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools*, 2nd ed.; Royal Society of Chemistry: Cambridge, U.K., 2016. (c) Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F. An overview of N-heterocyclic Carbenes. Nature 2014, 510, 485. (d) Janke, M. C.; Hann, F. E. Chemistry of N-Heterocyclic Carbene Ligands. *Top. Organomet. Chem.* 2010, 30, 95.

(2) For example, see: (a) Nolan, S. P., Ed. N-Heterocyclic Carbenes: Effective Tools for Organometallic Synthesis; Wiley-VHC: Weinheim, Germany, 2014. (b) Liu, W.; Gust, R. Metal N-Heterocyclic carbene complexes as potential antitumor metallodrugs. *Chem. Soc. Rev.* 2013, 42, 755. (c) Fevre, M.; Pinaud, J.; Gnanou, Y.; Vignolle, J.; Taton, D. N-Heterocyclic carbenes (NHCs) as organocatalysts and structural components in metal free polymer synthesis. *Chem. Soc. Rev.* 2013, 42, 2142. (d) Cazin, C. S. J., Ed. N-Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis; Springer: Berlin, 2011. (e) Díez-González, S.; Marion, N.; Nolan, S. P. N-Heterocyclic carbenes in late transition metal catalysis. *Chem. Rev.* 2009, 109, 3612. (f) Arnold, P. L.; Casely, I. J. F-block N-Heterocyclic carbene complexes. *Chem. Rev.* 2009, 109, 3599. (g) Hahn, F. E.; Jahnke, M. C. Heterocyclic carbenes: Synthesis and coordination chemistry. *Angew. Chem., Int. Ed.* 2008, 47, 3122.

(3) Grundemann, S.; Kovacevic, A.; Albrecht, M.; Faller Robert, J. W.; Crabtree, R. H. Abnormal binding in a carbine complex formed from an imidazolium salt and a metal hydride complex. *Chem. Commun.* **2001**, 2274.

(4) For example, see: (a) Ghadwal, R. S. Carbon-based two electron σ donor ligands beyond classical N-Heterocyclic carbenes. *Dalton Trans.* **2016**, 45, 16081. (b) Crabtree, R. H. Abnormal, mesoionic and remote N-heterocyclic carbine complexes. *Coord. Chem. Rev.* **2013**, 257, 755. (c) Krüger, A.; Albrecht, M. Abnormal N-heterocyclic carbine complexes: More than just exceptionally strong donor ligands. *Aust. J. Chem.* **2011**, 64, 1113. (d) Melaimi, M.; Soleilhavoup, M.; Bertrand, G. Stable Cyclic Carbenes and related species beyond diaminocarbenes. *Angew. Chem., Int. Ed.* **2010**, 49, 8810. (e) Schuster, O.; Yang, L.; Raubenheimer, H. G.; Albrecht, M. Beyond conventional Nheterocyclic carbenes: Abnormal, remote, and other classes of NHC ligands with reduced heteroatom stabilization. *Chem. Rev.* **2009**, 109, 3445–3478.

(5) Aldeco-Perez, E.; Rosenthal, A. J.; Donnadieu, B.; Parameswaran, P.; Frenking, G.; Bertrand, G. Isolation of a C5-deprotonated imidazolioum, a crystalline "abnormal" N-heterocyclic carbene. *Science* **2009**, *326*, 556.

(6) For example, see: (a) Ghadwal, R. S.; Reichmann, S. O.; Herbst-Irmer, R. Palladium-catalysed direct C2-arylation of an N-heterocyclic carbene: an atomo-economic route to mesoionic carbene ligands. Chem. - Eur. J. 2015, 21, 4247. (b) Uzelac, M.; Hernan-Gomez, A.; Armstrong, D. R.; Kennedy, A. R.; Hevia, E. Rational synthesis of normal, abnormal and anionic NHC-gallium alkyl complexes: structural, stability and isomerization insights. Chem. Sci. 2015, 6, 5719. (c) Day, B. M.; Pugh, T.; Hendriks, D.; Guerra, C. F.; Evans, D. J.; Bickelhaupt, F. M.; Layfield, R. A. Normal to Abnormal rearrangement and NHC activation in threecoordinate iron(II) carbene complexes. J. Am. Chem. Soc. 2013, 135, 13338. (d) Bhunia, M.; Hota, P. K.; Vijaykumar, G.; Adhikari, D.; Mandal, S. K. A highly efficient based-metal catalyst: Chemoselective reduction of imines to amines using and abnormal- NHC-Fe(0) complex. Organometallics 2016, 35, 2930. (e) Vijaykumar, G.; Mandal, S. K. An abnormal NHC carbene based nickel complex for catalytic reduction of nitroarenes. Dalton Trans. 2016, 45, 7421. (f) Hota, P. K.; Vijaykumar, G.; Pariyar, A.; Sau, S. C.; Sen, T. K.; Mandal, S. K. An abnormal NHC carbene-based palladium dimer: Aqueous oxidative Heck coupling under ambient temperature. Adv. Synth. Catal. 2015, 357, 3162. (g) Sau, S. C.; Roy, S. R.; Sen, T. K.; Mullangi, D.; Mandal, S. K. An abnormal N-heterocyclic-Copper(I) complex in click chemistry. Adv. Synth. Catal. 2013, 355, 2982. (h) Sau, S. C.; Santra, S.; Sen, T. K.; Mandal, S. K.; Koley, D. Abnormal N-heterocyclic carbene palldium complex: living catalyst for activation of aryl chlorides in Suzuki-Miyaura cross coupling. Chem. Commun. 2012, 48, 555.

(7) (a) Ung, G.; Bertrand, G. Stability and electronic properties of imidazole-based mesoionic carbenes. *Chem. - Eur. J.* 2011, *17*, 8269.
(b) Viciano, M.; Feliz, M.; Corberan, R.; Mata, J. A.; Clot, E.; Peris, E. Aliphatic versus aromatic C-H activation in the formation of abnormal carbenes with iridium: A combined experimental and theoretical study.

Organometallics 2007, 26, 5304. (c) Albrecht, M. C4-bound imidazolylidenes: from curiosities to high-impact carbene ligands. *Chem. Commun.* 2008, 3601. (d) Arnold, P. L.; Pearson, S. Abnormal N-heterocyclic carbenes. *Coord. Chem. Rev.* 2007, 251, 596.

(8) Krüger, A.; Kluser, E.; Müller-Bunz, H.; Neels, A.; Albrecht, M. Chelating C4-bound imidazolylidene complexes through oxidative addition of imidazolium salts to palladium(0). *Eur. J. Inorg. Chem.* **2012**, 2012, 1394.

(9) Bitzer, M. J.; Pöthig, A.; Jandl, C.; Kühn, F. E.; Baratta, W. Ru-Ag and Ru-Ag dicarbene complexes form an abnormal carbene ruthenium system. *Dalton Trans.* **2015**, *44*, 11686.

(10) Kim, Y.; Lee, E. Activation of C-F bonds in fluoroarenes by Nheterocyclic carbenes as an effective route to synthesize abnormal NHC complexes. *Chem. Commun.* **2016**, *52*, 10922.

(11) Uzelac, M.; Kennedy, A. R.; Hernan-Gomez, A.; Fuentes, M. A.; Hevia, E. Heavier alkali-metal gallates as platforms for accessing functionalized abnormal NHC carbene gallium complexes. *Z. Anorg. Allg. Chem.* **2016**, *642*, 1241.

(12) Arduengo, A. J., III; Davidson, F.; Dias, H. V. R.; Goerlich, J. R.; Khasnis, D.; Marshall, W. J.; Prakasha, T. K. An air stable carbene and mixed carbene dimers. *J. Am. Chem. Soc.* **1997**, *119*, 12742.

(13) (a) Iglesias, M.; Albrecht, M. Expanding the family of mexoionic complexes: donor properties and catalytic impact of palladated isoxazolylidenes. *Dalton Trans.* **2010**, *39*, 5213. (b) Yang, L.; Kruger, A.; Neels, A.; Albrecht, M. Rhodium(III) complexes containing c4-bound N-heterocyclic carbenes: Synthesis, coordination chemistry, and catalytic activity in transfer hydrogenation. *Organometallics* **2008**, *27*, 3161. (c) Chianese, A. R.; Kovacevic, A.; Zeglis, B. M.; Faller, J. W.; Crabtree, R. H. Abnormal C5-bound N-heterocyclic carbenes: extremely strong electron donor ligands and their iridium(I) and iridium(III) complexes. *Organometallics* **2004**, *23*, 2461.

(14) For example, see: (a) Petronilho, A.; Müller-Bunz, H.; Albrecht, M. Mesoionic oxides: facile access from triazolium salts or triazolylidene copper precursors, and catalytic relevance. *Chem. Commun.* **2012**, *48*, 6499. (b) Kascatan-Nebioglu, A.; Panzner, M.; Tessier, C. A.; Cannon, C. L.; Youngs, W. J. N-heterocyclic-silver complexes: A new class of antibiotics. *Coord. Chem. Rev.* **2007**, *251*, 884. (c) Lin, I. J. B.; Vasam, C. S. Preparation and applications of N-heterocyclic carbene complexes of Ag(I). *Coord. Chem. Rev.* **2007**, *251*, 642. (d) Chianese, A. R.; Zeglis, B. M.; Crabtree, R. H. Unexpected oxidative C-C cleavage in the metalation of 2-substitued imidazolium salts to give N-heterocyclic carbene complexes. *Chem. Commun.* **2004**, *19*, 2176.

(15) Mendoza-Espinosa, D.; Donnadieu, B.; Bertrand, G. Synthesis of 4- and 4,5-functionalized imidazol-2-ylidenes from a single 4,5unsubstituted imidazol-2-ylidene. *J. Am. Chem. Soc.* **2010**, *132*, 7264.

(16) (a) Hashmi, A.S. K.; Riedel, D.; Rudolph, M.; Rominger, F.; Oeser, T. Regioselective formation of saturated abnormal NHC-gold(I) complexes by [3 + 2] cycloaddition of azomethine ylides and isonitrile gold(I) complexes. *Chem. - Eur. J.* **2012**, *18*, 3827. (b) Manzano, R.; Rominger, F.; Hashmi, A. S. K. Saturated abnormal NHC-Au(I) complexes: Synthesis and catalytic activity. *Organometallics* **2013**, *32*, 2199. (c) Manzano, R.; Wurm, T.; Rominger, F.; Hashmi, A. S. K. Roo, temperature hydrohydrazination of terminal alkynes by saturated abnormal N-heterocyclic carbene-gold(I) complexes. *Chem. - Eur. J.* **2014**, *20*, 6844.

(17) Xu, X.; Kim, S. H.; Zhang, X.; Das, A. K.; Hirao, H.; Hong, S. H. Abnormal N-heterocyclic carbene gold(I) complexes: Synthesis, structure, and catalysis in hydration of alkynes. *Organometallics* **2013**, 32, 164.

(18) (a) Mendoza-Espinosa, D.; González-Olvera, R.; Negrón-Silva, G. E.; Angeles-Beltrán, D.; Suárez-Castillo, O. R.; Álvarez-Hernández, A.; Santillan, R. Phenoxy-linked mesoionic triazol-5-ylidenes as platforms for multinuclear transition metal complexes. *Organometallics* **2015**, *34*, 4529. (b) Ung, G.; Mendoza-Espinosa, D.; Bertrand, G. Ynamides: stable ligand equivalents of unstable oxazol-4-ylidenes (novel mesoionic carbenes). *Chem. Commun.* **2012**, *48*, 7088. (c) Ung, G.; Mendoza-Espinosa, D.; Bouffard, J.; Bertrand, G. A stable acyclic ligand equivalent of an unstable 1,3-dithiol-5-ylidene. *Angew. Chem., Int. Ed.* **2011**, *50*, 4215. (d) Mendoza-Espinosa, D.; Ung, G.; Donnadieu, B.; Bertrand, G. Mesoionic thiazol-5-ylidenes as ligands for transition metal complexes. *Chem. Commun.* **2011**, *47*, 10614.

(19) Hashmi, A. S. K. Gold-catalyzed organic reactions. Chem. Rev. 2007, 107, 3180.