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## Syntheses of tetrahydroquinoline-based chiral carbene precursors and the related chiral NHC–Au(I) complex†

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Four tetrahydroquinoline-based chiral carbene precursors were synthesized using unsymmetrical *N,N'*- diarylformamidines and chiral 2-allyloxiranes as starting materials. A representative NHC–gold complex has been prepared and fully characterized, the crystal structure of which reveals an intramolecular Au…H–C(sp<sup>3</sup>) interaction between Au(I) and the hydrogen atom of the isopropyl moiety in the *N*-aryl group.

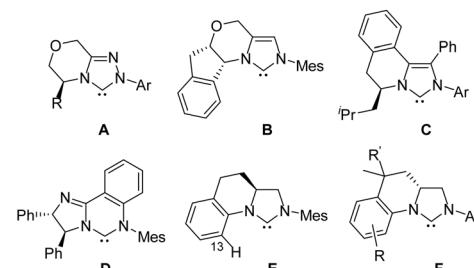
Imidazolidin-2-ylidene carbenes are among the most important N-heterocyclic carbenes (NHCs) due to their widespread and spectacular applications as organocatalysts and as ligands for organometallic catalysis.<sup>1</sup> Over the past twenty years, a great deal of effort has been made to employ chiral NHCs as organocatalysts and as ligands in asymmetric catalysis.<sup>2</sup> Despite the successful applications of a variety of chiral NHCs in asymmetric catalysis, the development of facile methodologies for structurally-specific chiral NHCs with structural diversity is highly desirable and a challenging issue in asymmetric catalysis. Several types of chiral backbone-unsaturated NHCs having a fused ring in their scaffolds, such as **A**,<sup>3</sup> **B**,<sup>4</sup> **C**,<sup>5</sup> and **D**,<sup>6</sup> have been successfully developed for organocatalysts and/or as ligands for organometallic catalysis (Scheme 1a). In their scaffolds, chiral moiety is directly linked to the N-atom and embedded in a fused ring. Due to the rigidity of the fused ring, the rotation of chiral moiety about the N–C bond is restricted, thereby enhancing the asymmetric induction of the NHCs in controlling the stereochemistry of the asymmetric catalytic reaction.

With different design strategy, Blechert *et al.* have developed chiral imidazolidin-2-ylidene **E** having a fused ring in the scaffold, which exhibited high efficiency in Ru-catalyzed asymmetric ring-opening cross-metathesis.<sup>7</sup> The fused ring in **E** twists the framework, hampers rotation of the *N*-aryl substituent, and thus reaches the optimal transfer of chirality, while at the same time second *N*-mesityl substituent adopts a planar orientation. However, the approach for the synthesis of the

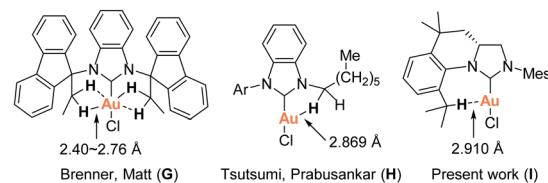
carbene precursors, imidazolinium salts requires uncommon starting material and a kinetic enzymatic resolution, which limit modification of NHC ligands. Additionally, only the imidazolinium salt of type **E** having no C13 substituent was prepared by the method.<sup>8</sup> Varying the *N*-aryl substituents with different steric bulkiness in **E** might create a tunable chiral environment closer to the reactive site. Until very recently, a consecutive intermolecular reductive amination/asymmetric hydrogenation has been developed for the synthesis of the precursors of **E**.<sup>8</sup>

As part of our studies on the design and synthesis of various novel NHC ligands for carbene chemistry and catalysis,<sup>9</sup> we herein wish to report a new synthetic strategy for the facile

a) Selected chiral NHCs having a fused ring in their scaffolds



b) Au(I)-NHC complexes with intramolecular Au…H–C(sp<sup>3</sup>) interactions

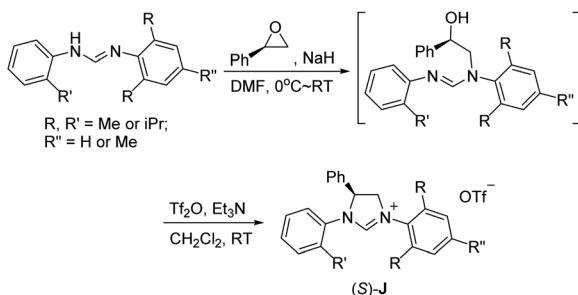


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Scheme 1 Chiral NHCs having a fused ring in their scaffolds and related NHC–Au(I) complexes with intramolecular Au…H–C(sp<sup>3</sup>) interaction.





Scheme 2 Synthesis of chiral backbone-monosubstituted imidazolinium salts from the reaction of formamidines with alkene oxide.<sup>9a</sup>

preparation of various tetrahydroquinoline-based chiral carbene precursors of NHCs **F** using unsymmetrical *N,N'*-diarylformamidines and chiral 2-allyloxiranes as starting materials. A representative NHC–gold complex **I** has been prepared and structurally characterized. The crystal structure of the NHC–gold reveals an intramolecular  $\text{Au}(\text{i})\cdots\text{H}-\text{C}(\text{sp}^3)$  interaction between  $\text{Au}(\text{i})$  and the hydrogen atom of isopropyl moiety

Table 1 Synthesis of chiral backbone-allyl-substituted imidazolinium salts from the reaction of formamidines with chiral 2-allyloxiranes<sup>a</sup>

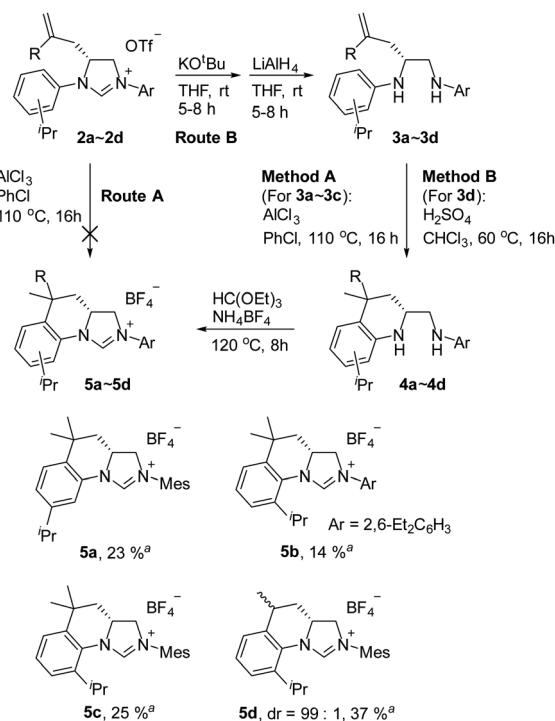
| Entry | <i>N,N'</i> -Diarylformamide | R  | Imidazolinium salt <sup>b</sup> |
|-------|------------------------------|----|---------------------------------|
| 1     |                              | Me |                                 |
| 2     |                              | Me |                                 |
| 3     |                              | Me |                                 |
| 4     |                              | H  |                                 |

<sup>a</sup> Reaction conditions. Step 1: **1** (1.0 equiv.), 2-allyloxirane (1.2 equiv.),  $\text{NaH}$  (1.5 mmol), DMF (10 mL), 0–70 °C, 6 h. Step 2:  $\text{Tf}_2\text{O}$  (1.1 equiv.),  $\text{Et}_3\text{N}$  (1.1 equiv.),  $\text{DCM}$  (5 mL), 25 °C, 5–8 h. <sup>b</sup> Isolated yield over two steps.

(Scheme 1b). Recently, the  $\text{Au}(\text{i})\cdots\text{H}-\text{C}(\text{sp}^3)$  hydrogen-bonding interaction have been observed in NHC– $\text{Au}(\text{i})$  complexes **G** and **H**, which are believed to either stabilise the out-of-plane conformation (**G**)<sup>10a</sup> or make partial contributions to the luminescence properties of the NHC– $\text{Au}(\text{i})$  complex (**H**)<sup>10b</sup> (Scheme 1b). Additionally,  $\text{Au}\cdots\text{H}-\text{C}$  hydrogen-bonding interactions in NHC–Au complexes have been proposed as key intermediates in the mechanistic studies of NHC–Au catalyzed C–H activation.<sup>11</sup>

We have previously developed a versatile and modular method for the preparation of various backbone-substituted imidazolinium salts from the reaction of formamidines with alkene oxides.<sup>9a</sup> The methodology exhibits high regiochemistry. When reacting styrene oxide with the unsymmetrical *N,N'*-diarylformamidines bearing a mono-*o*-substituted aryl group and a di-*o*-substituted aryl group, only one regioisomer in which the backbone-substituted phenyl group is on the carbon atom close to the mono-substituted aryl ring was formed. More importantly, chiral monosubstituted imidazolinium salts, (*S*)-**J** could be obtained when using (*R*)-styrene oxide, indicating that inversion of the configuration of (*R*)-styrene oxide occurred in the two-step synthesis (Scheme 2).<sup>9a</sup> Therefore, we decide to use (*S*)-2-allyloxirane and the unsymmetrical *N,N'*-diarylformamidines to synthesize chiral backbone-allyl-substituted imidazolinium salts, which is supposed to undergo intramolecular Friedel–Crafts alkylation<sup>12</sup> to afford chiral imidazolinium salts as the precursors of the chiral NHCs of type **F**.

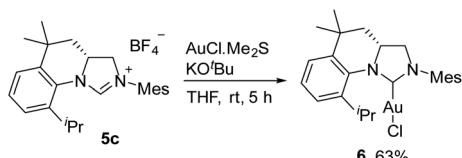
As expected, the ring opening reaction of unsymmetrical *N,N'*-diarylformamidines **1a–1d** with (*S*)-2-allyloxiranes followed by cyclization afforded four backbone-allyl-substituted



<sup>a</sup> Isolated yield over four steps

Scheme 3 Synthesis of the desired chiral tetrahydroquinoline-based imidazolinium salts **5a–5d**.





Scheme 4 Synthesis of a representative chiral NHC–gold complex 6.

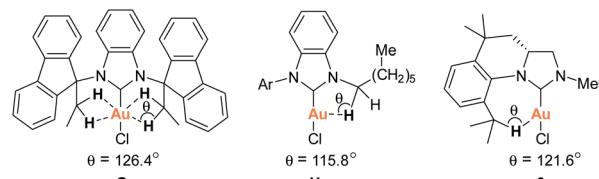


Fig. 2 Comparison of  $\text{Au}\cdots\text{H}-\text{C}(\text{sp}^3)$  angles in G, H and 6.

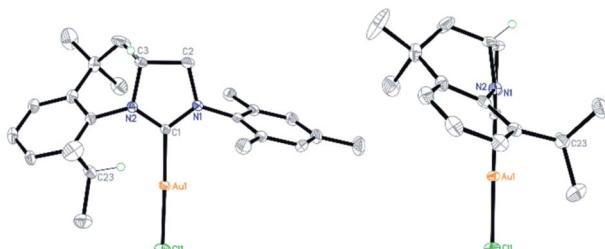


Fig. 1 Left: molecular structure of 6. Right: side-view of 6 (mesityl group omitted for clarity). Selected bond distances ( $\text{\AA}$ ) and angles (deg):  $\text{Au}(1)-\text{C}(1)$  1.972(6),  $\text{Au}(1)-\text{Cl}(1)$  2.278(2),  $\text{N}(1)-\text{C}(1)$  1.327(7),  $\text{N}(1)-\text{C}(2)$  1.482(8),  $\text{N}(2)-\text{C}(1)$  1.352(8),  $\text{N}(2)-\text{C}(3)$  1.484(8),  $\text{C}(2)-\text{C}(3)$  1.519(10),  $\text{N}(1)-\text{C}(1)-\text{Au}(1)$  126.2(5),  $\text{N}(2)-\text{C}(1)-\text{Au}(1)$  125.3(4).

imidazolinium salts **2a–2d**, respectively (Table 1). However, attempts to direct Friedel–Crafts alkylation of **2a–2d** failed (Route A, Scheme 3). Therefore, an alternative route was investigated. In the presence of  $\text{KO}^+\text{Bu}$  as base, the ring opening of **2a–2d** followed by reduction using  $\text{LiAlH}_4$  afforded diamines **3a–3d** (Route b, Scheme 3).<sup>13</sup> Delightfully, in the presence of either  $\text{AlCl}_3$  (for **3a–3c**) or  $\text{H}_2\text{SO}_4$  (**3d**), the resulting amines could smoothly undergo intramolecular Friedel–Crafts alkylation to give diamines **4a–4d**. Finally, cyclization of the diamines **4a–4d** with  $\text{HC}(\text{OEt})_3$  in the presence of  $\text{NH}_4\text{BF}_4$  generated the desired chiral imidazolidinium salts **5a–5d**. During the transformations, a partial racemization was detected. The ee value of **4a** was determined as 88% on the basis of chiral HPLC analysis (p. S8, see ESI†).

The ability of the novel tetrahydroquinoline-based chiral imidazolidin-2-ylidene carbene to ligate a transition metal fragment was also examined. Treatment of the *in situ* generated free carbene with  $\text{AuCl}\cdot\text{Me}_2\text{S}$  gave the chiral NHC–gold complex **6** in 63% yield (Scheme 4). The structure of **6** was determined by single-crystal X-ray diffraction, which exhibits the expected linear coordination geometry, and also shows that the chiral NHC in **6** has the R configuration (Fig. 1). In **6**, the  $\text{Au}-\text{C}$  bond length at the normal  $\text{C}2$  position ( $1.972(6)$   $\text{\AA}$ ) is typical of NHC–Au complexes.<sup>14</sup> The crystal structure also reveals that the  $\text{C}2$  bridge at the chirality center leads to a dihedral angle of  $58^\circ$  between the *N*-aryl group and the imidazoline plane and enforces a close approach of isopropyl group to the coordination sphere of the gold center. The  $\text{Au}\cdots\text{H}-\text{C}$  distance found in **6** ( $2.910$   $\text{\AA}$ ) is comparable with that of a NHC–Au(i) complex ligated by *N*-(9-anthracenyl)-*N'*-(heptyl) benzimidazol-2-ylidene ( $2.869$   $\text{\AA}$ ), and van der Waals radii ( $2.86$   $\text{\AA}$ ),<sup>10</sup> suggesting the presence of a rare  $\text{Au}\cdots\text{H}-\text{C}(\text{sp}^3)$  interaction in gold complex **6** (Scheme 1b). The  $\text{Au}\cdots\text{H}-\text{C}(\text{sp}^3)$  angle in **6** ( $121.6^\circ$ ) is similar to those observed in **G** ( $126.4^\circ$ ) and **H** ( $115.8^\circ$ ) (Fig. 2). The  $^1\text{H}$  NMR resonance for the hydrogen atom  $\text{H}23$  in **6** appears

at  $4.10$  ppm downfield relative to that for its precursor, imidazolidinium salt **5c**.

In conclusion, we present a method for the synthesis of tetrahydroquinoline-based chiral carbene precursors using unsymmetrical *N,N'*-diarylformamidines and 2-allyloxiranes as starting materials. Treatment of unsymmetrical *N,N'*-diarylformamidines with 2-allyloxirane followed by cyclization gave backbone-allyl-substituted imidazolidinium salts, which could be transformed into the desired tetrahydroquinoline-based chiral carbene precursors through a key intramolecular Friedel–Crafts alkylation. A representative chiral NHC–gold complex has been prepared by the reaction of the *in situ* generated free carbene with  $\text{AuCl}\cdot\text{Me}_2\text{S}$ . The crystal structure of the NHC–gold complex reveals a rare intramolecular  $\text{Au}\cdots\text{H}-\text{C}(\text{sp}^3)$  interaction between Au(i) and the hydrogen atom of isopropyl moiety. We are currently exploring the application of the resulting chiral carbene metal complexes in transition metal-catalyzed asymmetric synthetic transformations.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

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