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A Novel Fluorinated Gold(I) N-Heterocyclic Carbene Complex: Exploiting Fluorine Stereoelectronic Effects To Control Molecular Topology

Susann Paul, W. Bernd Schweizer, Marc-Olivier Ebert, and Ryan Gilmour*

Laboratory for Organic Chemistry, ETH Zurich, Hönggerberg, Wolfgang-Pauli-Strasse 10,
8093 Zurich, Switzerland

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Summary: The synthesis of a novel fluorinated Au(I) N-heterocyclic carbene is disclosed together with solid-state and solution-phase conformational analysis. The potential of the fluorine gauche effect [$\sigma_{C-H} \rightarrow \sigma^*_{C-F}$] for controlling the topology of catalytically relevant architectures is showcased by a representative NHC in which the C−F bond is β to the triazolium moiety.

The highly polarized nature of the C−F bond, attributable to the electronegativity of fluorine ($\chi_F \approx 4$), often elicits intriguing physical and electronic properties.[1] Importantly, the low-lying σ^*_{C-F} antibonding orbital can readily interact with adjacent, vicinal σ-bonds and nonbonding electron pairs, resulting in the rich diversity of stereoelectronic effects that are associated with organofluorine compounds.[2−4] These stereoelectronic effects are necessarily accompanied by conformational changes which, if used appropriately, provide the foundations for effective preorganization strategies. Moreover, the small van der Waals radius of fluorine coupled with its high bond strength to carbon (105.4 kcal mol^{-1}) render it an excellent, chemically inert steering group for controlling molecular topology. However, of the numerous fluorine conformational effects that are known, relatively few have been consciously employed in the design of catalytically relevant scaffolds with a view to modulating reactivity (Figure 1).[3−5] Early examples from this laboratory include a dynamic gauche effect that is induced when chiral secondary β-fluoroamines are condensed with α,β-unsaturated aldehydes to form iminium ions, a concept that has been successfully applied in enantioselective epoxidation reactions,[3] and the development of novel, conformationally restricted surface modifiers for the asymmetric heterogeneous platinum-catalyzed hydrogenation of α-keto esters.[4]

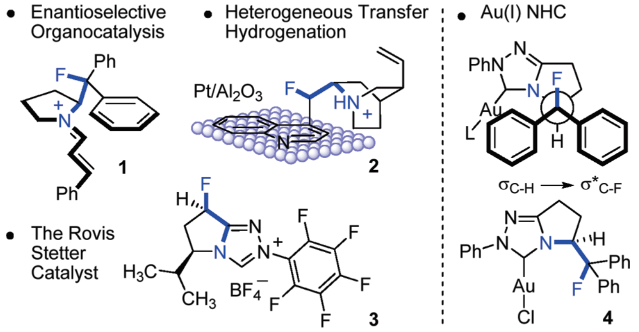
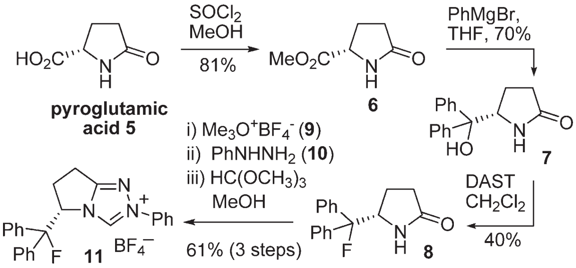


Figure 1. Examples of the C−F bond being used in catalyst design.[3,4,5b]

Scheme 1. Synthesis of 11 from Pyroglutamic Acid (5)



In order to expand the repertoire of this design approach, a study of other catalyst architectures that might benefit from having a β-fluoroamine-derived conformational restraint embedded in the structure was initiated. N-heterocyclic carbenes (NHCs) are excellent candidates, owing to their synthetic versatility as both nucleophilic organocatalysts[6] and ancillary ligands for an array of metals.[7] In particular, recent advances in gold catalysis have challenged our preconceptions of the synthetic potential of this noble metal.[8] The Lewis acidity of cationic Au(I) complexes, the associated relativistic effects (expanded 5d and contracted 6s orbitals), and its resistance to oxidation endow gold complexes with unique reactivity. Furthermore, gold chemistry can often be performed in the presence of oxygen without detrimental effects, and concerns pertaining to oxidation state shuttling [Au(I) ↔ Au(III)] can be largely dismissed. Recently, Rovis

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*To whom correspondence should be addressed. E-mail: ryan.gilmour@org.chem.ethz.ch. Tel: +41 44 632 79 34.

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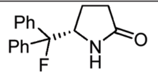
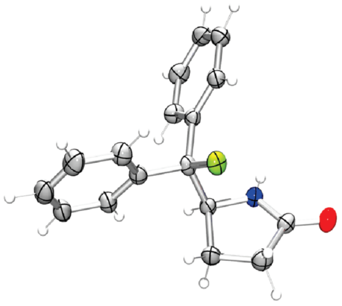
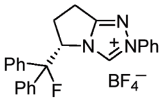
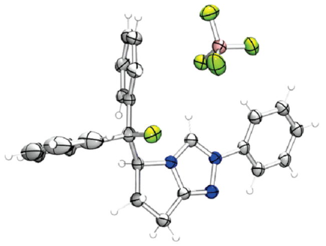
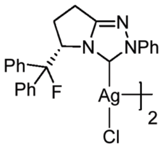
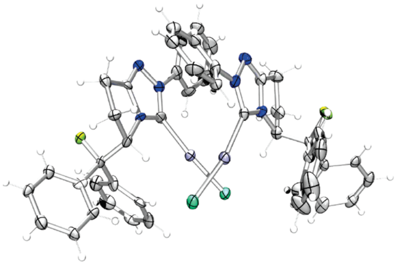
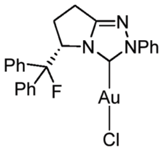
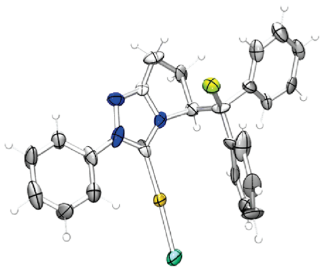
Table 1. Selected X-ray Data for Compounds 8, 11, 16, and 13

Compound	X-ray Structure	Selected Data
 **8**		Orthorhombic $P2_12_12_1$ a = 7.5353 Å b = 7.8131 Å c = 23.4370 Å $\varphi_{[NCCF]}$ = **–60.4°** CCDC 782695
 **11**		Monoclinic C2 a = 16.8056 Å b = 6.9654 Å c = 18.7706 Å $\varphi_{[NCCF]}$ = **–54.0°** CCDC 782696
 **16**		Orthorhombic $P2_12_12_1$ a = 9.6676 Å b = 20.1778 Å c = 27.1375 Å $d_{[Ag–Ag]}$ = 3.12 Å $\varphi_{[NCCF]}$ = **–64.4°** / **–52.4°**[a] CCDC 782697
 **13**		Orthorhombic $P2_12_12_1$ a = 9.8352 Å b = 9.8352 Å c = 27.0406 Å $d_{[Au–Au]}$ = 3.31 Å $\varphi_{[NCCF]}$ = **–61.9°** / **–48.6°**[b] CCDC 782698

[a] Dimeric species. Pentane was omitted for clarity. [b] Only one of the two symmetry-independent molecules in the unit cell is shown for clarity.

reported on the enhanced performance of NHC-based Stetter organocatalysts upon fluorination of the bicyclic core (Figure 1, lower).[5b] In contrast, we sought to probe the utility of the C–F bond in restricting the relative conformational freedom of a model Au(I) NHC bearing a pendant (diphenylfluoro)methyl moiety (Figure 1, right). Key to our design was the installment of a C–F bond in a vicinal relationship to the azolium nitrogen atom at the ring junction. We envisaged that the fluorine would adopt an antiperiplanar alignment to the vicinal C–H bond such that hyperconjugative electron donation of the type [$\sigma_{C-H} \rightarrow \sigma^*_{C-F}$] would be operational, thus rigidifying the ancilliary ligand sphere and efficiently shielding one face of the Au center. To test this hypothesis, the NHC precursor **11** was prepared in a concise six-step sequence from pyroglutamic acid (**5**) (Scheme 1).

The synthetic sequence began with esterification of the starting acid **5** to form the methyl ester **6** (81% yield), followed by the chemoselective double addition of phenylmagnesium bromide to generate carbinol **7**.[9] Deoxyfluorination of the tertiary alcohol using (diethylamino)sulfur trifluoride (DAST) in CH_2Cl_2 at 0 °C furnished the expected β-fluoroamide derivative **8** as a solid. Gratifyingly, it was possible to grow crystals of the fluoride that were suitable for X-ray analysis, ultimately allowing the torsion angle $\varphi_{NCCF} = -60.4°$ to be measured (Table 1).[2a]

Subsequent alkylation with the Meerwein salt followed by successive treatment with phenylhydrazine and then methyl orthoformate furnished the desired NHC precursor **11** in excellent overall yield (47% over three steps). X-ray analysis of this salt revealed a clear gauche orientation between the C−F bond and the vicinal C−N bond ($\varphi_{NCCF} = -54.0°$, Table 1), indicating that the delocalized positive charge of the triazolium ring system is sufficient to induce structural rigidification. Conversion of the tetrafluoroborate salt **11** to the desired Au(I) NHC began with formation of the intermediate silver complex **12** by treatment with Ag_2O in CH_2Cl_2. It should be noted that the formation of the bis-NHC structure **12** is consistent with the findings of Wang and Lin on related Ag(I)−carbene transfer agents.[10] Finally, transmetalation using $AuCl(SMe_2)$[11] furnished the desired Au(I) species as a mixture of the mono- and bis-NHC species **13** and **14** (1.33:1). Interestingly, by simple counterion exchange from the tetrafluoroborate (**11**) to the chloride (**15**), it was possible to suppress formation of the bis-NHC Ag(I) species **12** with the mono-NHC compound **16** being isolated exclusively. This material was then smoothly processed to give the Au(I)−NHC species **13** in 71% overall yield (Scheme 2). Gratifyingly, it was possible to unambiguously establish the molecular connectivities of both the Ag and Au complexes (**16** and **13**, respectively) by single-crystal diffraction analysis. The Ag(I) complex **16** crystallizes in the orthorhombic space group $P2_12_12_1$ with two symmetry-independent molecules in the asymmetric unit cell. An interatomic Ag−Ag distance of 3.12 Å was measured, which is indicative of a metallotropic interaction. Furthermore, the NCCF dihedral angles in the solid state are $\varphi_{NCCF} = -64.4$ and −52.4°, as was predicted at the outset of this study. Similarly, the Au(I) species **13** crystallizes in the same orthorhombic space group as complex **16** ($P2_12_12_1$) with two symmetry-independent molecules in the asymmetric unit cell. As in the case of the Ag(I) precursor, the X-ray analysis revealed a relatively short Au−Au contact of 3.31 Å and a clear gauche orientation of the fluorine with respect to the triazolium ring system ($\varphi_{NCCF} = -61.9$ and −48.6°). The C_α−Au−Cl angles in the dimeric solid-state structure were found to be 175.8 and 177.0°, confirming the expected linear, binuclear coordination geometry of the gold center. Comparison of the C_α−M bond lengths in the Ag and Au complexes revealed only a slight difference ($\Delta_{Ag-Au} \approx 0.1$ Å). It is noteworthy that the aurophilic

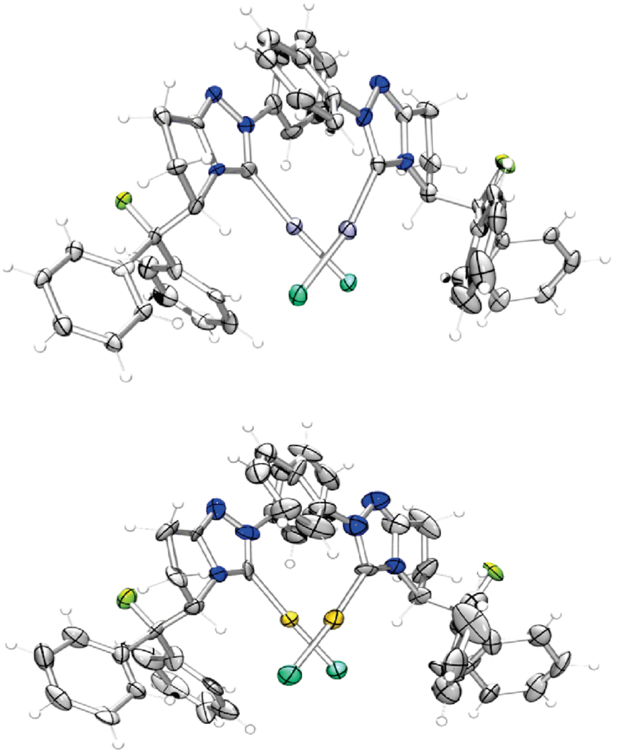
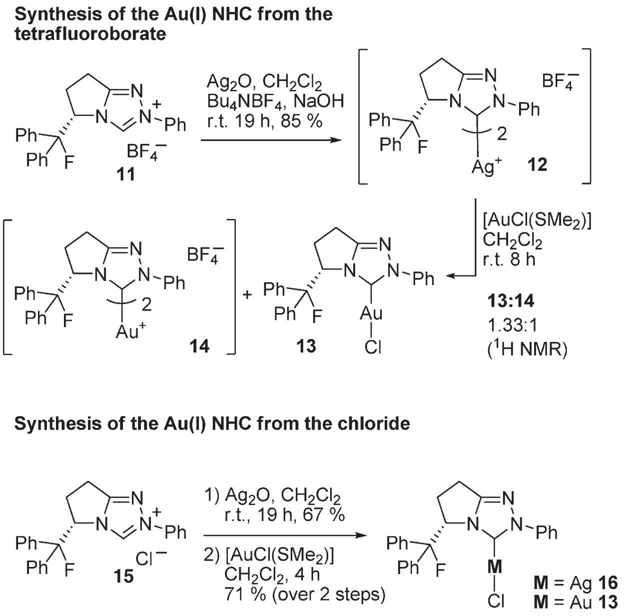


Figure 2. X-ray structures of complexes **16** (top) and **13** (bottom), showing the metallophilic interactions (d_{Ag-Ag} = 3.12 Å; d_{Au-Au} = 3.31 Å).

Scheme 2. Synthesis of Complex 13



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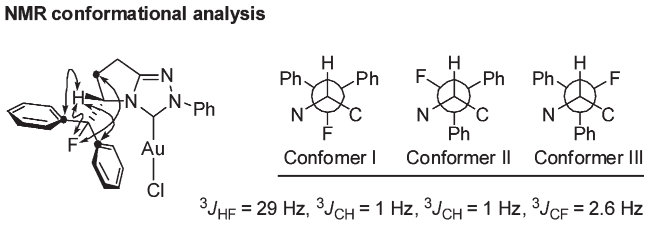

Figure 3. Conformational analysis of **13** in the solution phase.

interaction that is observed in the solid-state analysis of complex **13** (d_{Au-Au} = 3.31 Å) is frequently observed in closed-shell Au(I) systems ($5d^{10}$) and other transition-metal complexes.[12] Intriguingly, the interatomic distance is marginally longer than that of the Ag(I) precursor (d_{Ag-Ag} = 3.12 Å), which also displays a clear interaction between the metal centers (Figure 2). This shorter argentophilic interaction as compared to the aurophilic interaction is consistent with a recent report from Ghosh and coworkers, who observed similar differences in metallophilicity when comparing dimeric Au and Ag N-heterocyclic carbenes.[13]

To complement the crystallographic investigation, we then performed a solution-phase conformational analysis of **13** by NMR spectroscopy. Initial studies revealed a low-field ^{13}C-{^{1}H} NMR shift of the carbenic carbon at 171.3 ppm (100 MHz, $CDCl_3$) and a ^{19}F NMR signal at −168.2 ppm (376 MHz, $CDCl_3$). Assuming that only staggered conformations are significantly populated in solution, the observed vicinal coupling constant $\langle J \rangle$ between two nuclei sitting at tetrahedral carbons flanking a rotatable bond can be described by

$$\langle J \rangle = x_1 J_1 + x_2 J_2 + x_3 J_3 \tag{1}$$

where J_i values are the individual couplings of the three rotamers and x_i values are their molar fractions. If the J_i values are known independently and at least two vicinal coupling constants can be measured, then the rotamer populations can be determined. Very often, however, the function relating the dihedral angle between two nuclei to the corresponding coupling constant is approximately symmetric around zero.[14] Assuming that the three rotamers can be described by dihedral angles of 60° (+gauche), −60° (−gauche), and 180° (anti) then the following expression holds, $J_{+g} = J_{-g} = J_g$. In this case the molar fraction x_a of the conformer in which these two nuclei are in an anti relationship can be calculated with[15]

$$x_t = (\langle J \rangle - J_g)/(J_a - J_g) \tag{2}$$

For $^3J_{CF}$ consensus values of 1.2 Hz (J_g) and 11.2 Hz (J_a) are reported in the literature.[16] For $^3J_{HF}$ the corresponding coupling constants were calculated to be 7.6 and 36 Hz, respectively, using a modified Karplus relation.[17] Independently inserting the experimentally determined coupling constants of 29 Hz ($^3J_{HF}$) and 2.6 Hz ($^3J_{CF}$) in eq 2 yields populations of conformation I and II (Figure 3) of 75% and 14%, respectively. Recently a modified Karplus relation based on DFT calculations was reported for vicinal coupling constants between ^{1}H and ^{13}C.[18] In the case of the substitution pattern present in **13** this equation predicts significant deviation of $^3J_{CH}$ from symmetry around $\varphi_{HCCC} = 0°$ (J_{+g} = 0.3 Hz, J_{-g} = 2.7 Hz, J_a = 4.2 Hz). Resorting to eq 1 and inserting $^3J_{C1H}$ and $^3J_{C2H}$, which are equal within the assumed error limits and thus render stereoselective assignment dispensible, in a system of two equations yields populations of 80% (I), 10% (II), and 10% (III). These values are in good agreement with the populations derived from $^3J_{HF}$ and $^3J_{CF}$. The coupling constants for the individual rotamers derived from Karplus equations are a known source of systematic error.[19] We therefore treat these results as a qualitative finding, nevertheless clearly identifying rotamer I as the dominant conformation in solution ($\varphi_{NCCF} = 60°$).

In summary, we have disclosed the synthesis and conformational analysis of a novel fluorinated Au(I) NHC. By inserting a C−F bond in a vicinal relationship to the triazolium nitrogen atom at the ring junction, it has been possible to control the relative molecular topology of the flanking diphenylfluoromethyl group and the core scaffold by means of a stabilizing hyperconjugative interaction.

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Supporting Information Available: Text, figures, tables and CIF files giving synthetic and spectroscopic data for compounds **6**, **7**, **8**, **11**, **12**, **13**, **15**, and **16**, crystallographic data for **8**, **11**, **13**, and **16** and a detailed solution-phase NMR analysis of **13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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