Organofluorine compounds have found widespread and growing use in the pharmaceutical, materials, and other industries. Transition metals offer great potential improvements in the scope, selectivity, and convenience of fluorination chemistry. Their use in C–F bond formation, however, has only begun to be explored. Examples to date include electrophilic fluorinations of arenes and enols, the reductive elimination of allyl or acyl C–F bonds, and nucleophilic halide displacement reactions.

Recent years have seen a resurgence in gold catalysis, notably in the formation of C–C, C–N, and C–O bonds from alkynes. We now report the reversible addition of a gold(I) fluoride across an unactivated alkyne. This addition is a likely key step in a new hydrofluorination of alkynes under mild conditions, using gold(I) precatalysts and a relatively benign HF source.

The gold(I) fluoride complex (SIPr)AuF (1; SIPr = 1,3-bis(2,6-diisopropynyl)imidazolin-2-ylidene) reacts with excess 3-hexyne (150 equiv) in CH₂Cl₂ solution at 20 °C. After 10 min, the reaction mixture displays a new triplet resonance (δ = −95.5 ppm, J = 21 Hz), representing >95% of the original peak area of 1 (relative to C₂H₂F internal standard), in its ¹⁹F NMR spectrum. This resonance is assigned to the β-(fluorovinyl)gold complex 2a, formed by addition of fluoride and gold(I) across the alkyne (Scheme 1). Removal of solvent and excess alkyne from 2a, over a period of 30 min, results in quantitative regeneration of 1. Rapid (≤5 min) concentration affords mixtures of 1 and 2a, which regain equilibrium within 2 h after redissolution in CH₂Cl₂.

Analysis of mixtures formed from different concentrations of 1 and 3-hexyne at 20 °C gives an equilibrium constant of 2.7 ± 0.2 M⁻¹ for the addition process, corresponding to ΔG° = −0.58 ± 0.04 kcal/mol (Table S1, Supporting Information). Certain [Cu⁰]X complexes react with acetylene reversibly, forming trans-β-haloacetylene products, but fluoride addition was not observed. The addition of AgF across an alkyne is known but requires a highly electronegative substrate. Reversible metal-mediated C–F bond rupture has been demonstrated intramolecularly in α-fluoride elimination from Ru and Os trifluoromethyl complexes.

Addition product 2b, formed from 1 and 1-phenyl-1-propyne, proved more amenable than 2a to isolation and crystallization. Dissolution of 2b in a 1:1 mixture of 1-phenyl-1-propyne and CH₂Cl₂, followed by vapor diffusion of n-pentane at −40 °C, afforded crystals of 2b suitable for X-ray diffraction. The resulting structure (Figure 1) displays a 1,1-arrangement of the phenyl group and gold and confirms the trans-arrangement of gold and fluoride about the vinylic C≡C bond.

The trans-addition of fluoride and gold(I) across the triple bond could proceed via displacement of fluoride from 1 by alkyne, followed by nucleophilic addition of fluoride to the resulting cationic gold(I)–alkyne complex. Abstraction of chlorine from (SIPr)AuCl by AgBF₄ in the presence of 3-hexyne affords an independent route to the cationic complex 3, [{(SIPr)Au[p²-(3-hexyne)]}⁺][BF₄]⁻. This complex decomposes in CH₂Cl₂ solution over a period of several days but is stable in the solid state for roughly 2 weeks at ambient temperature.

Treatment of 3 with an organic-soluble fluoride source, [(Me₂N₂)P]₃N⁺F⁻, results in predominant displacement of alkyl fluoride by fluoride, re-establishing the equilibrium between 1 and 2a. In contrast, the reaction of 3 with Et₃NF·3HF (1 equiv, Scheme 1), a fluoride source that is both nucleophilic and mildly acidic, results in hydrofluorination of the coordinated alkyne to form (Z)-3-fluoro-3-hexene (64%, relative to BF₄⁻, by ¹⁹F NMR). The same fluoroalkene is observed in >95% yield (¹⁹F NMR, relative to internal standard) when 2a is treated with CF₃CO₂H.

This observation of tandem C–F and C–H bond formation led us to seek conditions for a catalytic transformation of alkynes to fluoroalkenes using Et₃N·3HF. Alkynes react directly with the more harshly acidic reagent pyridine/HF (70% HF), and although fluoroalkenes may be observed as byproducts in some cases, only gem-difluoroalkanes are isolated in useful yields. Alkynes activated by highly electron-withdrawing groups undergo trans-hydrofluorination on reaction with [H₂F₃]⁻ salts[16,17] or by heating with CsF in wet DMF. Generally, however, fluoroalkenes are obtained indirectly,[18] and control over the stereochemistry often requires careful strategy.[19] Given the interest in fluoroalkenes for medicinal chemistry,[21] stereoselective addition of HF to alkynes under mild conditions could be important synthetically.

Initial catalytic screening reactions between 3-hexyne and Et₃N·3HF, using 3 as precatalyst, afforded fluoroalkene in yields up to 53% as judged by ¹⁹F NMR relative to internal standard. Product yields were not significantly improved by an increase in catalyst loading from 1 to 5 mol %. Reasoning that decreasing acidity, as HF was consumed, caused the reactions to stall before complete conversion was attained, we examined the effects of acidic additives on the reaction efficiencies. The presence of powdered KHSO₄ in conjunction with the CH₃Cl₂-soluble acid cocatalyst PhNMMe+HOTf (10 mol %), resulted in greatly increased yields of fluoroalkene.

Both SIPr and its imidazolylidene analogue IPr are moderately effective supporting ligands for the catalytic hydrofluorination of 6-dodecyne. Very similar results were obtained using (SIPr)AuOtr-Bu or (SIPr)AuCl/AgBF₄ as precatalysts. The use of less sterically demanding NHCS, or triphenylphosphine, led to poor catalytic conversions (see Table S2, Supporting Information), with rapid precipitation of gold metal. Complete consumption of...
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Supporting Information Available: Experimental details and characterization data for new compounds; comparison of different precatalysts. Crystallographic data for 2b are provided as a CIF. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(22) Selected references: (a) Liu, B.; de Brabander, J. K. Org. Lett. 2006, 8, 4907–4910.
(27) Teles, J. H.; Brode, S.; Cabanas, M. Angew. Chem., Int. Ed. 1998, 37, 1415–1418. See also ref 4a, 4b.

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