Supporting Information

Designer HF-Based Fluorination Reagent: Highly Regioselective Synthesis of Fluoroalkenes and $gem$-Difluoromethylene Compounds from Alkynes

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1. General

$^1$H and $^{13}$C NMR spectra were recorded at 500 and 126 (or 400 and 101) MHz respectively, using CDCl$_3$ as a solvent. The chemical shifts are reported in $\delta$ (ppm) values ($^1$H and $^{13}$C NMR relative to CHCl$_3$, $\delta$ 7.26 ppm for $^1$H NMR and $\delta$ 77.0 ppm for $^{13}$C NMR, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants, $J$, are reported in Hertz (Hz). All air and/or moisture sensitive reactions were carried out under argon atmosphere. Solvents (1,2-dichloroethane and dichloromethane) were chemically dried using a commercial solvent purification system. All other reagents and solvents were employed without further purification. The products were purified using a commercial flash chromatography system or a regular glass column. TLC was developed on Merck silica gel 60 F254 aluminum sheets. Gold pre-catalyst (Au-1) was prepared using our published procedure.$^1$

2. Preparation of DMPU/HF complex (HF 65% w/w)

DMPU (5 g) was added into a long Teflon tube, the Teflon tube was cooled to 0°C, and 9.3 g of HF gas was condensed into the Teflon tube under stirring. The obtained liquid was stored in a 25 mL Teflon vial with a screw cap at room temperature.

The boiling point of DMPU/HF complex (HF 65% w/w) is around 50-120 °C. The boiling point is not well defined (HF evaporates continuously in the range of 50-120 °C).

We also conducted HF loss experiment in open air at 55°C (the reaction temperature we used in our synthetic applications). In a well-vented fume hood, 1 gram of DMPU/HF complex (HF 65% w/w) was added to 5 mL polypropylene vial, the vial was heated to 55°C in open air (without
cap), and we measured the weight of polypropylene vial periodically. We calculated the percent of HF left over time (we assumed evaporation of DMPU was negligible).

3. General Procedures for preparation of 2 and 3

Reactions were performed in 5 mL polypropylene vials with cone-lined caps. GC-MS and $^{19}$F NMR analysis were used to monitor the progress of reactions.

General procedure for synthesis of fluoroalkene 2

Using synthesis of 2a as an example:

\[
\text{Au-1} = \text{L-Au-N} \quad L = \text{JohnPhos}
\]

To a solution of 5-phenyl-1-pentyne 1a (14.4 mg, 0.10 mmol) in DCE (0.5 mL) in a polypropylene vial, imidogold precatalyst Au-1 (2 mol%, 0.01 M stock solution in DCE) was added at room temperature. The reaction mixture was stirred for 3 h at 55°C. Upon completion, the reaction was quenched with saturated sodium bicarbonate. The mixture was extracted with hexane and washed with brine; the organic layer was collected, dried over anhydrous MgSO$_4$ and filtered. The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography purification (eluent: hexane) to give fluoroalkene 2a as a colorless oil.

General procedure for synthesis of gem-difluoromethylene compounds 3

Using synthesis of 3a as an example:

To a solution of 5-phenyl-1-pentyne (14.4 mg, 0.10 mmol) in DCE (0.5 mL), imidogold precatalyst Au-1 (2 mol% from a 0.01 M solution in DCE), KHSO$_4$ (1.5 equiv) were added at room temperature. The mixture was stirred for 24 h at 55°C. Upon completion, the reaction was
quenched with saturated sodium bicarbonate. The mixture was separated with hexane and washed with brine; the organic layer was collected, dried over anhydrous MgSO₄ and filtered. The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography purification (eluent: hexane) to give 3a as a colorless oil.

4. Spectroscopic data of 2 and 3

(4-fluoropent-4-en-1-yl) benzene (2a)

\[
\text{\textit{2a}} \quad \text{\textit{F}}
\]

$^1$H NMR (400 MHz, CDCl₃) $\delta$ 7.27 – 7.18 (m, 5H), 4.52 (dd, $J$ = 17.6, 2.6 Hz, 1H), 4.31 – 4.12 (m, 1H), 2.66 (t, $J$ = 7.7 Hz, 2H), 2.27 – 2.13 (m, 2H), 1.92 – 1.78 (m, 2H). $^{19}$F NMR (376 MHz, CDCl₃) $\delta$ -94.91 (ddd, $J$ = 50.0, 33.4, 16.4 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl₃) $\delta$ 141.62, 128.41, 128.34, 125.89, 89.80, 89.60, 34.89, 31.56, 31.38, 31.11, 27.60, 22.63. HRMS (EI +) for C₁₁H₁₃F Cald = 164.1001, found 164.1001.

2-fluorooc-t-1-ene (2b)

\[
\text{\textit{2b}} \quad \text{\textit{F}}
\]

$^{19}$F NMR (CCl₄) 93.5 ppm (CFCl₃) (m). Its spectroscopic data is consistent with a literature report.$^2$

(3-fluorobut-3-en-1-yl) benzene (2c)

\[
\text{\textit{2c}} \quad \text{\textit{F}}
\]

$^1$H NMR (400 MHz, CDCl₃): $\delta$ = 2.46-2.62 (m, 2H), 2.48-2.92 (m, 2H), 4.45 (dd, $^2J_{H-F}$ = 50.0 Hz, $J$ = 2.5 Hz, 1H), 4.61 (dd, $^2J_{H-F}$ = 18.0 Hz, $J$ = 2.5 Hz, 1H), 7.22-7.33 (m, 3H), 7.47-7.55 ppm (m, 2H); $^{19}$F NMR (470 MHz, CDCl₃): $\delta$ = -95.5 ppm (dq, $^3J_{F-(olefin)=49.8$ Hz, $^3J_{F-H} = ^3J_{F-Hcis(olefin)=17.4$ Hz, 1F}). Its spectroscopic data is consistent with a literature report.$^3$

5-fluorohe-x-5-enenitrile (2d)
$^1$H NMR (400 MHz, CDCl$_3$) δ 4.59 (dd, $J = 17.2$, 3.0 Hz, 1H), 4.31 (dd, $J = 49.7$, 2.9 Hz, 1H), 2.48 – 2.28 (m, 4H), 1.87 (m, 2H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -97.09 (m, 1F). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 165.25, 162.69, 118.95, 91.68, 91.48, 30.71, 30.43, 21.83, 16.16. HRMS (ESI +) Calcd. for C$_6$H$_9$FN 114. 0719, found 114.0720.

(1-fluorovinyl) benzene (2e)

Following general procedure for synthesis of 2 except ratio of phenylacetylene and DMPU/HF is 2:1. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.57-7.55 (m, 2H), 7.38-7.37 (m, 3H), 5.04 (dd, 1H, $J = 49.7$; 3.4 Hz), 4.85 (dd, 1H, $J = 17.7$, 3.4 Hz). $^{19}$F NMR (282 MHz, CDCl$_3$): δ –108.47 (dd, $^3$J$_{HF}$ = 51.9; 18.3 Hz). Its spectroscopic data is consistent with a literature report.

1-(1-fluorovinyl)-4-(trifluoromethyl)benzene (2f)

$^1$H NMR (CDCl$_3$, 300 MHz): δ 4.98 (dd, 1 H, $J = 17.5$, 3.7 Hz), 5.14 (dd, 1H, $J = 48.9$, 3.7 Hz, H$_B$), 7.58–7.70 (m, 4H). $^{19}$F NMR (CDCl$_3$, 282 MHz): δ 63.42 (s, 3F, CF$_3$), 108.72 (dd, 1F, $J = 50.8$, 17.7 Hz, 1-CF). Its spectroscopic data is consistent with a literature report.

1-(1-fluorovinyl)-4-methoxybenzene (2g)

Following general procedure for synthesis of 2 except ratio of phenylacetylene and DMPU/HF is 2:1. $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.50 (d, $J = 8.8$ Hz, 2 H), 6.90 (d, $J = 8.7$ Hz, 2 H), 4.89 (dd,
$J = 3.4, 50.2 \text{ Hz, 1 H)}, 4.74 (\text{dd, } J = 3.4, 18.1 \text{ Hz, 1 H}), 3.84 (\text{s, 3 H}) \text{ ppm.}^{19}\text{F NMR (CDCl}_3, 376 \text{ MHz)} \delta -107.2 (\text{dd, } ^3J_{F-H} = 18.1, 50.0 \text{ Hz, 1 F}). \text{ Its spectroscopic data is consistent with a literature report.}^5$

2-(4-fluoropent-4-en-1-yl)isoindoline-1,3-dione (2h)

![Chemical structure of 2h](image)

$^{1}\text{H NMR (400 MHz, CDCl}_3) \delta 7.89 - 7.80 (\text{m, 2H}), 7.72 (\text{dt, } J = 4.5, 3.6 \text{ Hz, 2H}), 4.52 (\text{dd, } J = 17.5, 2.2 \text{ Hz, 1H}), 4.28 (\text{dd, } J = 50.2, 2.1 \text{ Hz, 1H}), 3.73 (\text{t, } J = 7.1 \text{ Hz, 2H}), 2.25 (\text{dt, } J = 15.3, 7.6 \text{ Hz, 2H}), 1.99 - 1.83 (\text{m, 2H}).^{19}\text{F NMR (376 MHz, CDCl}_3) \delta \text{-95.15 (m, 1F).}^{13}\text{C NMR (101 MHz, CDCl}_3) \delta 168.31, 166.63, 164.08, 133.96, 132.02, 123.23, 90.28, 90.08, 77.32, 77.00, 76.68, 37.16, 29.45, 29.17, 25.04. \text{HRMS (CI +) calcd. for C}_{13}\text{H}_{13}\text{FNO}_2 234.0930, \text{ found 234.0930.}$

(Z)-ethyl 3-fluoro-3-phenylacrylate (2i)

![Chemical structure of 2i](image)

$^{1}\text{H NMR (400 MHz, CDCl}_3) \delta 7.62 (\text{d, } J = 7.6 \text{ Hz, 2H}), 7.38-7.47 (\text{m, 3H}), 5.88 (\text{d, } J = 33.4 \text{ Hz, 1H}), 4.23 (\text{q, } J = 7.2 \text{ Hz, 2H}), 1.30 (\text{t, } J = 7.2 \text{ Hz, 3H});^{13}\text{C NMR (100 MHz, CDCl}_3) \delta 166.1 (\text{d, } J = 275.9 \text{ Hz}), 163.90 (\text{d, } J = 2.3 \text{ Hz}), 125.5 (\text{d, } J = 8.0 \text{ Hz}), 97.1 (\text{d, } J = 6.8 \text{ Hz}), 60.3, 14.1.^{19}\text{F NMR (376 MHz, CDCl}_3) \delta 96.16 (\text{d, } J = 33 \text{ Hz, 1F}). \text{ Its spectroscopic data is consistent with a literature report.}^6$

(Z)-(1-fluoroethene-1,2-diyl)dibenzene (2j)

![Chemical structure of 2j](image)

$^{1}\text{H NMR (CDCl}_3, 400 \text{ MHz)} \delta 7.67-7.69 (\text{m, 4 H}), 7.37-7.46 (\text{m, 5 H}), 7.27-7.31 (\text{m, 1 H}), 6.34 (\text{d, } J = 39.5 \text{ Hz, 1 H}) \text{ ppm.}^{19}\text{F NMR (CDCl}_3, 376 \text{ MHz)} \delta -114.2 (\text{d, } ^3J_{F-H} = 39.9 \text{ Hz).}$

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spectroscopic data is consistent with literature report.\(^7\)

(Z)-5-fluorodec-5-ene (2k)

\[
\begin{align*}
\text{n-C}_4\text{H}_9 & \quad \text{n-C}_4\text{H}_9 \\
\text{2k} & \\
\end{align*}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 4.46 \text{ (dt, } J = 38.4, 7.2 \text{ Hz, 1H), 2.14 \text{ (dt, } J = 17.2, 7.2 \text{ Hz, 2H), 2.08-2.03 \text{ (m, 2 H), 1.51-1.43 \text{ (m, 2H), 1.39-1.28 \text{ (m, 6H)}, 0.95-0.88 \text{ (m, 6H); } {^{19}}\text{F NMR (376 MHz, CDCl}_3\text{)} \delta = -110.7 \text{ (dt, } J = 38.4, 16.9 \text{ Hz). Its spectroscopic data is consistent with a literature report.}\(^8\)

Dimethyl 2-(2-fluoroallyl)malonate (2l)

\[
\begin{align*}
\text{CO}_2\text{Me} & \quad \text{CO}_2\text{Me} \\
\text{2l} & \\
\end{align*}
\]

\(^1\)H NMR (700 MHz, CDCl\(_3\)) \(\delta = 4.59 \text{ (dd, } J = 17.0, 2.6 \text{ Hz, 1H), 4.33 \text{ (dd, } J = 49.4, 2.8 \text{ Hz, 1H), 3.73 \text{ (s, 3H), 3.65 \text{ (s, 3H), 2.81 \text{ (dd, } J = 17.0, 7.6 \text{ Hz, 2H); } {^{19}}\text{F NMR (470 MHz, CDCl}_3\text{)} \delta = 97.34 \text{ (m, 1F). } {^{13}}\text{C NMR (176 MHz, CDCl}_3\text{)} \delta = 168.58, 166.89, 92.34, 92.23, 52.78, 52.53, 48.80, 41.10, 31.47, 31.31. }\text{EI-} \text{HR MS (ESI +) Calcd for C}_8\text{H}_11\text{FO}_4\text{ 190.0641, found: 190.0639.}

Ethyl 2-fluoroacrylate (2m)

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{2m} & \\
\end{align*}
\]

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 5.67 \text{ (dd, 1H, } J = 43.5, 3.4 \text{ Hz), 5.31 \text{ (dd, 1H, } J = 13.2, 3.4 \text{ Hz), 4.30 \text{ (q, 2H, } J = 7.2 \text{ Hz), 1.34 (t, 3H, } J = 7.1 \text{ Hz). } {^{19}}\text{F NMR (282 MHz, CDCl}_3\text{)}: \delta = -117.72 \text{ (d, } \text{ } \text{ } J_{HF} = 42.7 \text{ Hz). Its spectroscopic data is consistent with literature report.}\(^9\) Pure 2m was not isolated due to its volatility.

(4, 4-Difluoropentyl)benzene (3a)

\[
\begin{align*}
\text{3a} & \\
\end{align*}
\]

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta = -90.529 \text{ (m, 1F). HRMS (EI +) calcd. for C}_{11}\text{H}_{14}\text{F}_2 \text{ 184.1064;}

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found 184.1064. Note: The product 3a is very volatile and usually cyclizes on silica gel chromatography, so analytically pure 3a couldn’t be obtained.

(1,1-Difluoroethyl)benzene (3b)

\[ \text{F} \quad \text{F} \]

\[ \text{3b} \]

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -87.16 (q, $J$ =18.6 Hz). Its spectroscopic data is consistent with a literature report.$^{10}$

1-(1,1-Difluoroethyl)-4-methoxybenzene (3c)

\[ \text{MeO} \quad \text{F} \quad \text{F} \]

\[ \text{3c} \]

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -86.4 (q, $J$ =18.6 Hz). Its spectroscopic data is consistent with a literature report.$^{11}$

1-(1,1-difluoroethyl)-4-fluorobenzene (3d)

\[ \text{F} \quad \text{F} \]

\[ \text{3d} \]

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -86.08 (q, $J$ = 19.0 Hz, 2F), -113.17 (m, 1F). Its spectroscopic data is consistent with a literature report.$^{12}$

2-(4,4-difluoropentyl)isoindoline-1,3-dione (3e)

\[ \text{O} \quad \text{N} \]

\[ \text{3e} \]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.88-7.83 (m, 2H), 7.76-7.70 (m, 2H), 3.74 (t, $J$ = 6.6 Hz, 2H),
1.93-1.87 (m, 4H), 1.59 (t, $J_{HF} = 18.4$ Hz, 3H). $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ - 91.4 (m). Its spectroscopic data is consistent with a literature report.$^{13}$

(1,1-difluoroethane-1,2-diyl)dibenzene (3f)

$^{1}$H NMR $\delta$: 3.46 (t, 2H, $J = 15.8$ Hz), 7.13-7.16 (m, 2H), 7.28-7.30 (m, 3H), 7.37-7.42 (m, 5H), $^{19}$F NMR $\delta$: -94.7 (t, 2F, $J = 15.8$ Hz). Its spectroscopic data is consistent with a literature report.$^{14}$

5. Copies of NMR spectra for compounds 2 and 3
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