Electronic Supplementary Information

Ir-Catalysed Formation of C–F Bonds. From Allylic Alcohols to α-Fluoroketones.

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General

Air and moisture sensitive reactions were carried out under an atmosphere of dry nitrogen. Reagents were used as obtained from commercial suppliers without further purification. THF was used as obtained from supplier (puriss. p. a., stabilized with 2,6-di-tert-butyl-4-methylphenol ~250 mg/l). The undistilled THF used in the reactions tested negative for peroxides (0% by Quantofix peroxide). A potassium dihydrogen phosphate/disodium hydrogen phosphate buffer (pH 7; per litre: 3.54 g KH2PO4/14.7g Na2HPO4) was used as obtained from supplier. Flash chromatography was carried out on 60 Å (35-70 µm) silica gel. Spectra were recorded at 400 or 500 MHz for 1H NMR, at 100 or 125 MHz for 13C NMR, and at 376 MHz for 19F NMR on a Bruker Advance spectrometer. 1H and 13C NMR chemical shifts (δ) are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard, (CDCl3: δH 7.26 and δC 77.16). 19F NMR chemical shifts (δ) (1H-decoupled) are reported in ppm from CFCl3 with C6H5F (δ -113.15) as internal standard. Coupling constants (J) are given in Hz. High resolution mass spectra (HRMS) were recorded on Bruker microTOF ESI-TOF mass spectrometer.
Preparation of allylic alcohols

Alcohols 1a and 1e were used as obtained from supplier. Allylic alcohols 1c, 1f, and 1h were prepared as described in the literature.

Allylic alcohols 1b-d were prepared in a similar manner to 1h:

The corresponding aldehyde (1 equiv) was added to a solution of vinylmagnesium bromide (1M in THF, 1.1 equiv) at 0 °C, and then the reaction mixture was slowly warmed to room temperature. On consumption of the aldehyde (as monitored by TLC: EtOAc/Pentane 1:20), the reaction was quenched with NH₄Cl (aq), extracted with EtOAc (x 3) and washed with brine. The combined organic phases were dried over MgSO₄ and the solvent was removed under reduced pressure. Purification by column chromatography (EtOAc/Pentane 1:20 – 1:5) afforded the pure allylic alcohols.

Synthesis of 2-Methylnon-1-en-3-ol (1g):

A solution of hexylmagnesium bromide (2M, in diethylether, 20 mmol) was added to a suspension of methacrolein (20 mmol) and CeCl₃ (20 mmol) in dry THF (100 mL) at -78 °C. The reaction was left to slowly warm to room temperature overnight (15 h). The mixture was quenched with NH₄Cl (aq), extracted with Et₂O (x 3) and washed with brine. Purification by column chromatography (EtOAc/Pentane 1:30 – 1:10) afforded 1g as a colourless oil.

Synthesis of (E)-4-Phenyl-3-buten-2-deuterium-2-ol (1f-d₁):

NaBD₄ (172 mg, 4.1 mmol) was added in portions to a solution of benzylideneacetone (585 mg, 4 mmol) and CeCl₃·7H₂O (372 mg, 4.5 mmol) in MeOH (25 mL) at 0 °C. The reaction
mixture was stirred at room temperature for 2 h before the addition of HCl (aq, 1M). The methanol was removed under reduced pressure, and the product extracted repeatedly with Et$_2$O. The combined organic phases were dried over MgSO$_4$, and solvents were evaporated. Purification by column chromatography (Pentane/EtOAc 10:1) afforded 1f-d$_1$ as a white solid (540 mg, 92 %, 96 %[D] (D content determined by $^1$H NMR and HRMS-ESI).

**Characterization data of allylic alcohols (1b, 1d, 1g and 1f-d$_1$):**

4-Ethyloct-1-en-3-ol (1b)

Yellow oil, 73 % isolated yield as a mixture of 2 diastereomers (dr = 1:1): $^1$H NMR (CDCl$_3$, 400 MHz, mixture of diastereomers): $\delta$ 4.87 (ddd, $J_{HH} = 17.0$ Hz, $J_{HH} = 10.5$ Hz, $J_{HH} = 6.1$ Hz, 2H), 5.25-5.20 (m, 2H), 5.16-5.13 (m, 2H), 4.14-4.10 (m, 2H), 1.65-1.16 (m, 16H), 0.92-0.87 (m, 12H); $^{13}$C NMR (CDCl$_3$, 125 MHz, mixture of diastereomers): $\delta$ 139.9, 139.8, 115.2, 115.1, 74.8, 74.7, 45.1, 45.0, 29.6, 29.5, 23.0 (2C), 22.3, 21.8, 14.1 (2C), 11.7, 11.5.

1-(Benzylxoy)but-3-en-2-ol (1d)

Colourless oil, 76 % isolated yield: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.38-7.28 (m, 5H), 5.84 (ddd, $J_{HH} = 17.2$ Hz, $J_{HH} = 10.5$ Hz, $J_{HH} = 5.5$ Hz, 1H), 5.37 (dt, $J_{HH} = 17.2$ Hz, $J_{HH} = 1.5$ Hz,1H), 5.20 (dt, $J_{HH} = 10.5$ Hz, $J_{HH} = 1.5$ Hz,1H), 4.58 (s, 2H), 4.36 (m, 1H), 3.55 (dd, $J_{HH} = 9.6$ Hz, $J_{HH} = 3.4$ Hz,1H), 3.39 (dd, $J_{HH} = 9.6$ Hz, $J_{HH} = 7.9$ Hz,1H), 2.51 (br s, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 137.9, 136.7, 128.6 (2C), 128.0, 127.9 (2C), 116.6, 74.1, 73.5, 71.6; HRMS-ESI: m/z 201.0884 ([M+Na]$^+$, calcd. for C$_{11}$H$_{16}$O$_2$Na$_1$: 201.0886)

The NMR data were identical to those previously reported for this compound.

2-Methylnon-1-en-3-ol (1g)

Colourless oil, 53 % isolated yield: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 4.93 (m, 1H), 4.83 (m, 1H), 4.04 (t, $J_{HH} = 6.5$ Hz, 1H), 1.72 (m, 3H), 1.58-1.51 (m, 2H), 1.40-1.22 (m, 8H), 0.88 (t,
$J_{HH} = 7.0 \text{ Hz, 3H}$; $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 147.8, 111.1, 76.2, 35.1, 31.9, 29.4, 25.7, 22.7, 17.6, 14.2.

The NMR data were identical to those previously reported for this compound.$^5$

**(E)-4-Phenyl-3-buten-2-deuterium-2-ol (1f-d$_1$):**

\[
\begin{align*}
\text{Ph} & \quad \text{D} & \quad \text{OH} \\
1f-d_1
\end{align*}
\]

White solid, 92% isolated yield: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.40-7.36 (m, 2H), 7.34-7.29 (m, 2H), 7.26-7.22 (m, 1H), 6.56 (d, $J_{HH} = 15.9$ Hz, 1H), 6.26 (d, $J_{HH} = 15.9$ Hz, 1H), 1.97 (s, 1H), 1.37 (s, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 136.8, 133.6, 129.4, 128.7 (2C), 127.7, 126.5 (2C), 66.6 (t, $J_{CD} = 22$ Hz), 23.4; HRMS-ESI: m/z 172.0840 ([M+Na]$^+$, calcd. for C$_{10}$H$_{11}$D$_1$O$_1$Na$_1$: 172.0843).

**General procedure for the isomerization/fluorination of allylic alcohols**

[IrCp*Cl$_2$]$_2$ (4 mg, 5·10$^{-3}$ mmol, 1 mol%) was dissolved in a mixture of THF (2.5 mL) and H$_2$O (0.5 mL) at 30 °C. Selectfluor® (0.63 mmol, 1.25 eq) and the corresponding allylic alcohol (0.5 mmol) were added to the reaction mixture. The reaction was stirred at 30 °C for the time indicated in Table 3. On completion (as monitored by TLC) water (1 mL) was added and the reaction mixture was extracted with Et$_2$O (3x2 mL), and dried over MgSO$_4$. Evaporation of the solvent afforded a mixture of $\alpha$-fluorinated ketone (2a-h) and non-fluorinated ketone (3a-h). The yield and F/H ratios were determined by $^1$H NMR using 1,4-dimethoxybenzene (0.25 mmol) as an internal standard. Isolated products were purified by column chromatography (EtOAC/Pentane or Et$_2$O/Pentane 1:40 – 1:20). TLC plates were developed with KMnO$_4$ or Cerium Molybdate (Hanessian’s stain).

**Characterization data of isolated $\alpha$-fluoroketones 2c, 2d, 2f and 2h:**

**4-Fluoro-1-phenylpentan-3-one (2c)**

Pale yellow oil, 77% isolated yield: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.31-7.26 (m, 2H), 7.22-7.20 (m, 3H), 4.87 (dq, $J_{HH} = 6.9$ Hz $J_{HF} = 49.6$ Hz, 1H), 2.99-2.89 (m, 4H), 1.44 (dd, $J_{HH} = 6.9$ Hz $J_{HF} = 23.9$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 209.4 (d, $J_{CF} = 24$ Hz), 140.9,
128.7 (2C), 128.5 (2C), 126.4, 92.7 (d, $J_{CF} = 181$ Hz), 39.2, 28.9 (d, $J_{CF} = 2$ Hz), 17.6 (d, $J_{CF} = 22$ Hz); $^{19}$F NMR (CDCl$_3$, 376.4 MHz): $\delta$ -184.5; HRMS-ESI: m/z 203.0837 ([M+Na]$^+$, calcd. for C$_{11}$H$_{13}$O$_1$F$_1$Na$_1$: 203.0843).

1-(Benzyloxy)-3-fluorobutan-2-one (2d)

Pale yellow oil, 74 % isolated yield: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.37-7.28 (m, 5H), 5.05 (dq, $J_{HH} = 6.9$ Hz, $J_{HF} = 48.8$ Hz, 1H), 4.63 (s, 2H), 4.49-3.97 (m, 2H), 1.52 (dd, $J_{HH} = 6.9$ Hz, $J_{HF} = 24.3$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 206.2 (d, $J_{CF} = 23$ Hz), 137.1, 128.7 (2C), 128.3, 128.2 (2C), 92.2 (d, $J_{CF} = 179$ Hz), 73.6, 71.9 (d, $J_{CF} = 4$ Hz), 17.7 (d, $J_{CF} = 21$ Hz); $^{19}$F NMR (CDCl$_3$, 376.4 MHz): $\delta$ 191.3; HRMS-ESI: m/z 219.0782 ([M+Na]$^+$, calcd. for C$_{11}$H$_{13}$O$_2$F$_1$Na$_1$: 219.0792).

3-Fluoro-4-phenylbutan-2-one (2f)

Pale yellow oil, 67 % isolated yield: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.34-7.22 (m, 5H), 4.94 (ddd, $J_{HH} = 3.8$ Hz, $J_{HH} = 7.5$ Hz, $J_{HF} = 49.9$ Hz, 1H), 3.19 (ddd, $J_{HH} = 3.8$ Hz, $J_{HH} = 14.7$ Hz, $J_{HF} = 28.9$ Hz, 1H), 3.05 (ddd, $J_{HH} = 7.5$ Hz, $J_{HH} = 14.7$ Hz, $J_{HF} = 26.2$ Hz, 1H), 2.14 (d, $J_{HF} = 4.9$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 208.1 (d, $J_{CF} = 26$ Hz), 135.4, 129.6 (2C), 128.7 (2C), 127.2 (2C), 96.0 (d, $J_{CF} = 185$ Hz), 38.2 (d, $J_{CF} = 21$ Hz), 26.5; $^{19}$F NMR (CDCl$_3$, 376.4 MHz): $\delta$ 188.2; HRMS-ESI: m/z 189.0694 ([M+Na]$^+$, calcd. for C$_{10}$H$_{11}$O$_1$F$_1$Na$_1$: 189.0686).

The NMR data were identical to those previously reported for this compound.6

2-Fluoro-1-phenylpropan-1-one (2h)
Colourless oil, 68 % (contaminated with ~4 % propiophenone): $^1$H NMR (CDCl$_3$, 400 MHz): δ 8.01-7.99 (m, 2H), 7.65-7.61 (m, 1H), 7.53-7.49 (m, 2H), 5.73 (dq, $J_{HH} = 6.8$ Hz, $J_{HF} = 48.6$ Hz, 1H), 1.69 (dd, $J_{HH} = 6.8$ Hz, $J_{HF} = 24$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): δ 197.1 (d, $J_{CF} = 19.3$ Hz), 134.2, 133.9, 129.1 ($J_{CF} = 3.7$ Hz, 2C), 128.9 (2C), 90.4 (d, $J_{CF} = 180$ Hz), 18.4 (d, $J_{CF} = 23$ Hz); $^{19}$F NMR (CDCl$_3$, 376.4 MHz): δ -181.4; HRMS-ESI: $m/z$ 175.0537([M+Na]$^+$, calcd. for C$_9$H$_9$O$_1$F$_1$Na$: 175.0530$)

The $^1$H NMR data were identical to those previously reported for this compound. $^7$

Litt $^{19}$F NMR: -180.6 to -181.9 to -182.3 and -183.5

**Selected NMR data of α-fluoroketones 2a, 2b, 2g and 2f-d**:

α-Fluoroketones 2c-d, 2f and 2h were not isolated due to difficulty of separation, volatility and difficulty of detection by TLC. Yields were calculated using 1,4-dimethoxybenzene or fluorobenzene as internal standard and are shown in Table 3. Selected $^1$H and $^{19}$F NMR peaks are presented here:

**2-Fluoro-octan-3-one (2a)**

\[ \text{2a} \]

$^1$H NMR (CDCl$_3$, 400 MHz): δ 4.85 (dq, $J_{HH} = 6.9$ Hz, $J_{HF} = 49.6$ Hz, 1H), 2.59 (dt, $J_{HH} = 3.7$ Hz, $J_{HF} = 2.9$ Hz, 2H), 1.63-1.53 (m, 2H), 1.46 (dd, $J_{HF} = 24$ Hz, $J_{HH} = 6.9$ Hz, 3H), 1.37-1.20 (m, 4H), 0.89 (t, $J_{HH} = 6.8$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): δ 210.7 (d, $J_{CF} = 24$ Hz), 92.7 (d, $J_{CF} = 181$ Hz), 37.5, 31.5, 22.54, 22.53, 17.8 (d, $J_{CF} = 23$ Hz), 14.0; $^{19}$F NMR (CDCl$_3$, 376.4 MHz): δ -184.2

**4-Ethyl-2-fluoro-octan-3-one (2b)**

\[ \text{2b} \]

Mixture of 2 diastereomers (dr = 1:1): $^1$H NMR (CDCl$_3$, 400 MHz, two diastereomers): δ 4.88 (dq, $J_{HH} = 6.9$ Hz $J_{HF} = 49.5$ Hz, 1H), 4.87 (dq, $J_{HH} = 6.9$ Hz $J_{HF} = 49.5$ Hz, 1H), 2.93-2.87 (m, 2H), 1.72-1.53 (m, 4H), 1.55-1.34 (m, 4H), 1.46 (dd, $J_{HH} = 6.9$ Hz $J_{HF} = 23.8$ Hz, 6H), 1.33-1.14 (m, 8H), 0.89-0.81 (m, 12H); $^{13}$C NMR (CDCl$_3$, 125 MHz, two diastereomers): δ 213.70 (d, $J_{CF} = 22$ Hz), 213.67 (d, $J_{CF} = 23$ Hz), 92.58 (d, $J_{CF} = 182$ Hz), 92.56 (d, $J_{CF} = 182$ Hz),
(Hz), 48.0, 47.9, 30.6, 30.2, 29.8, 29.7, 24.3, 23.9, 22.9 (2C), 17.6 (d, \( J_{CF} = 22 \) Hz), 17.5 (d, \( J_{CF} = 22 \) Hz), 14.0 (2C), 12.0, 11.8; \(^{19}\)F NMR (CDCl\(_3\), 376.4 MHz, 2 diastereomers): \( \delta = -184.56, -158.57 \)

3-fluoropentan-2-one (2e)

\[
\begin{align*}
\text{O} & \\
\text{F} & \\
\end{align*}
\]

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta = 4.67 \) (ddd, \( J_{HH} = 4.5 \) Hz, \( J_{HH} = 7.5 \) Hz, \( J_{HF} = 50.2 \) Hz, 1H), 2.25 (d, \( J_{HF} = 4.8 \) Hz, 3H), 1.93-1.74 (m, 2H), 1.01 (t, \( J_{HH} = 7.5 \) Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta = 208.5 \) (d, \( J_{CF} = 26 \) Hz), 97.0 (d, \( J_{CF} = 184 \) Hz), 26.2, 25.3 (d, \( J_{CF} = 21 \) Hz), 8.9 (d, \( J_{CF} = 4.3 \) Hz); \(^{19}\)F NMR (CDCl\(_3\), 376.4 MHz): \( \delta = -191.1 \)

2-Fluoro-2-methylnonan-3-one (2g)

\[
\begin{align*}
\text{O} & \\
\text{F} & \\
\end{align*}
\]

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta = 2.64 \) (dt, \( J_{HH} = 7.4 \) Hz, \( J_{HF} = 3.2 \) Hz, 2H), 1.64-1.18 (m, 8H), 1.43 (d, \( J_{HF} = 23 \) Hz, 6H), 0.92-0.82 (m, 3H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta = 212.8 \) (d, \( J_{CF} = 28 \) Hz), 99.1 (d, \( J_{CF} = 179 \) Hz), 36.6, 31.7, 29.0, 24.3 (d, \( J_{CF} = 24 \) Hz, 2C), 23.0 (d, \( J_{CF} = 2 \) Hz), 22.6, 14.2; \(^{19}\)F NMR (CDCl\(_3\), 376.4 MHz): \( \delta = -149.0 \)

3-Fluoro-4-deuterium-4-phenylbutan-2-one (2f-\(d_1\))

\[
\begin{align*}
\text{D} & \\
\text{F} & \\
\end{align*}
\]

Mixture of 2 diastereomers. Deuterium content was 95% as determined by \(^1\)H NMR and \(^{19}\)F NMR. \(^1\)H NMR (CDCl\(_3\), 400 MHz, two diastereomers): \( \delta = 7.34-7.22 \) (m, 10H), 5.01-4.85 (m, 2H), 3.25-2.98 (m, 2H), 2.138 (d, \( J_{HF} = 4.9 \) Hz, 3H), 2.136 (d, \( J_{HF} = 4.9 \) Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta = 208.1 \) (d, \( J_{CF} = 26 \) Hz), 135.4, 129.6 (2C), 128.7 (2C), 127.3, 90.0 (d, \( J_{CF} = 187 \) Hz), 37.9 (dt, \( J_{CF} = 20 \) Hz, \( J_{CD} = 20 \) Hz), 26.5; \(^{19}\)F NMR (CDCl\(_3\), 376.4 MHz, two diastereomers): \( \delta = -188.44 \) (t, \( J_{DF} = 4.4 \) Hz), -188, 47 (t, \( J_{DF} = 4.0 \) Hz). Minor peak (5%) from non deuterated 2f at -188.2; HRMS-ESI: \( m/z \) 190.0749 ([M+Na]\(^+\), calcd. for C\(_{10}\)H\(_{10}\)D\(_1\)O\(_1\)F\(_1\)Na\(_1\): 190.0749)
Crude NMR of 2a:
Crude NMR of 2b
Crude NMR of 2g
Crude NMR of 2e in THF-\(d_8\)
Control experiment: fluorination of allylic alcohol 1c (1 equiv) in the presence of ketone 3a
95 % [D] [Two diastereomers: two 1:1 triples @ 188.42 and 188.47]
5 % non-deuterated D [signal at 188.2]
Crossover experiment of 1f-d₁ and 1i:

Analysis of the reaction mixture by $^1$H, $^{19}$F and $^{13}$C NMR showed 2f-d₁ and 2i as only products. However, due to the difficulty of detecting minor amounts of deuterated 2i by NMR (overlapping signals), the ketones were reduced to the corresponding alcohols (4f, 4i) with NaBH₄ in THF/H₂O, and analysed by HRMS-ESI (unreduced 2i and 2f-d₁ did not give sufficient intensities accurate detection of small amounts of deuterium).

The height of m/z peaks were corrected for the natural $^{13}$C content.

HRMS-ESI: m/z 205.1009 ([M+Na]⁺, calcd. for C₁₁H₁₅F₁O₁Na₁: 205.0999) 100 %

HRMS-ESI: m/z calcd. for C₁₁D₁H₁₄F₁O₁Na₁: 206.1062 0 %

HRMS-ESI: m/z 192.0913 ([M+Na]⁺, calcd. for C₁₀H₁₂D₁F₁O₁Na₁: 192.0905) 95 %

HRMS-ESI: m/z 191.0851 ([M+Na]⁺, calcd. for C₁₀H₁₃F₁O₁Na₁: 191.0843) 5 %