Electronic Supplementary Information

Accessing novel fluorinated heterocycles with the hypervalent fluoroiodane reagent by solution and mechanochemical synthesis

William Riley,[a] Andrew C. Jones,[b] Kuldip Singh,[a] Duncan L. Browne,*[c] and Alison M. Stuart*[a]

[a] School of Chemistry, University of Leicester, Leicester, LE1 7RH, UK. Alison.Stuart@le.ac.uk

[b] Cardiff Catalysis Institute, School of Chemistry, Cardiff University, Cardiff, CF10 3AT.

[c] School of Pharmacy, UCL, London, WC1X 1AX, UK. Duncan.Browne@ucl.ac.uk

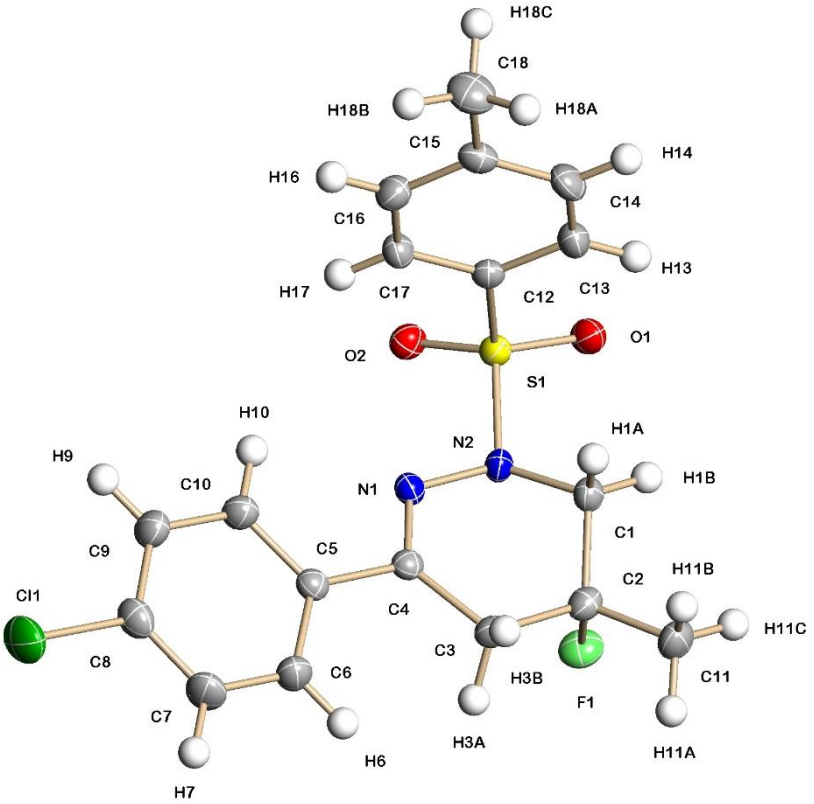


Figure S1 Molecular structure of 3-(4-chlorophenyl)-5-fluoro-5-methyl-1-tosyl-1,4,5,6-tetrahydro-pyridazine **3a** showing 50% displacement ellipsoids.

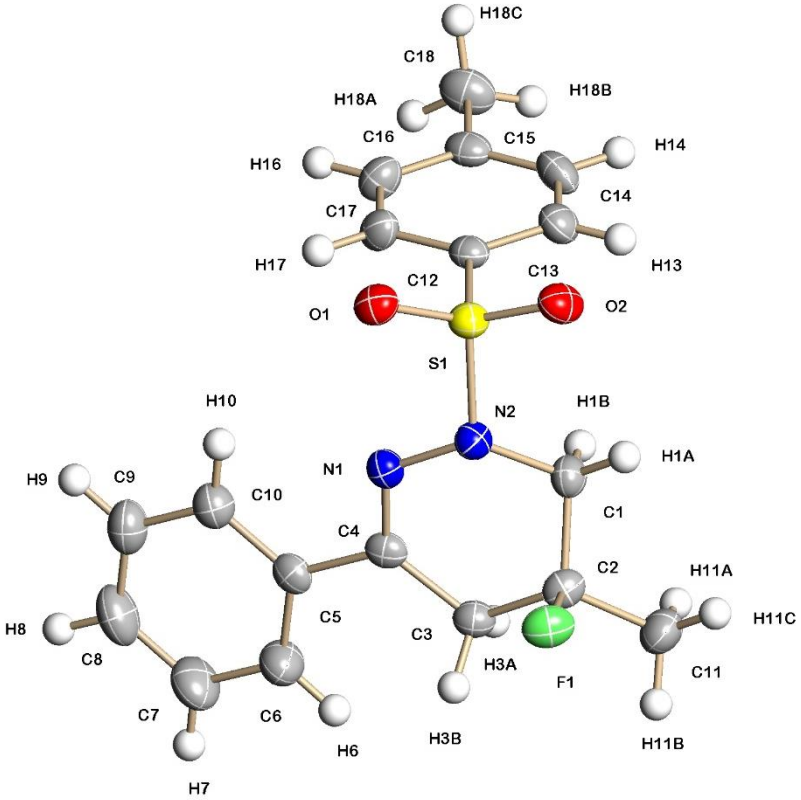


Figure S2 Molecular structure of 5-fluoro-5-methyl-3-phenyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3c** showing 50% displacement ellipsoids.

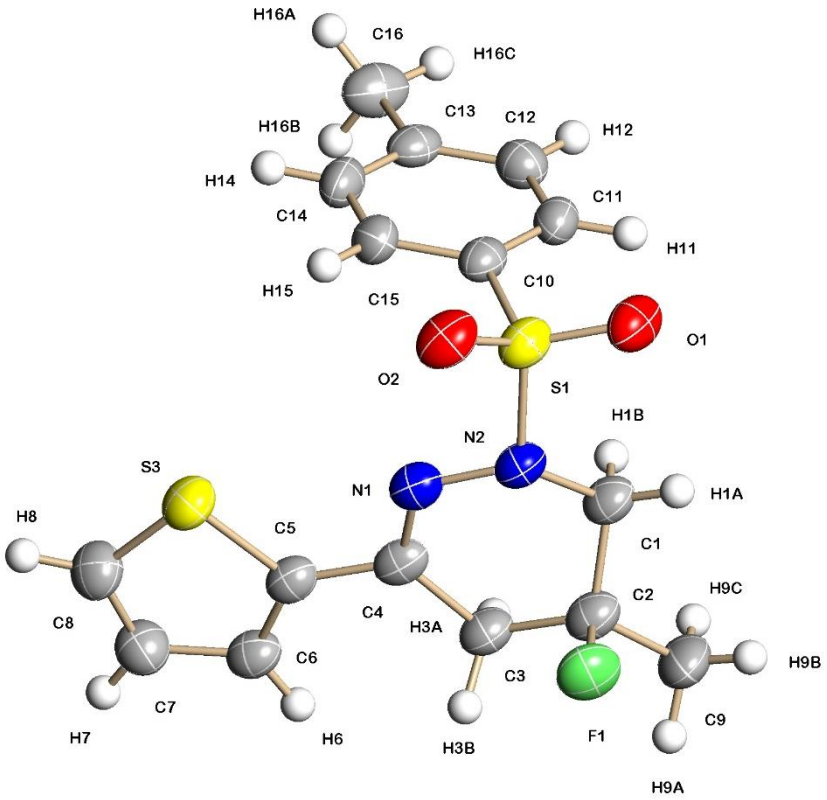


Figure S3 Molecular structure of 5-fluoro-5-methyl-3-(thiophen-2-yl)-1-tosyl-1,4,5,6-tetrahydro-pyridazine **3h** showing 50% displacement ellipsoids.

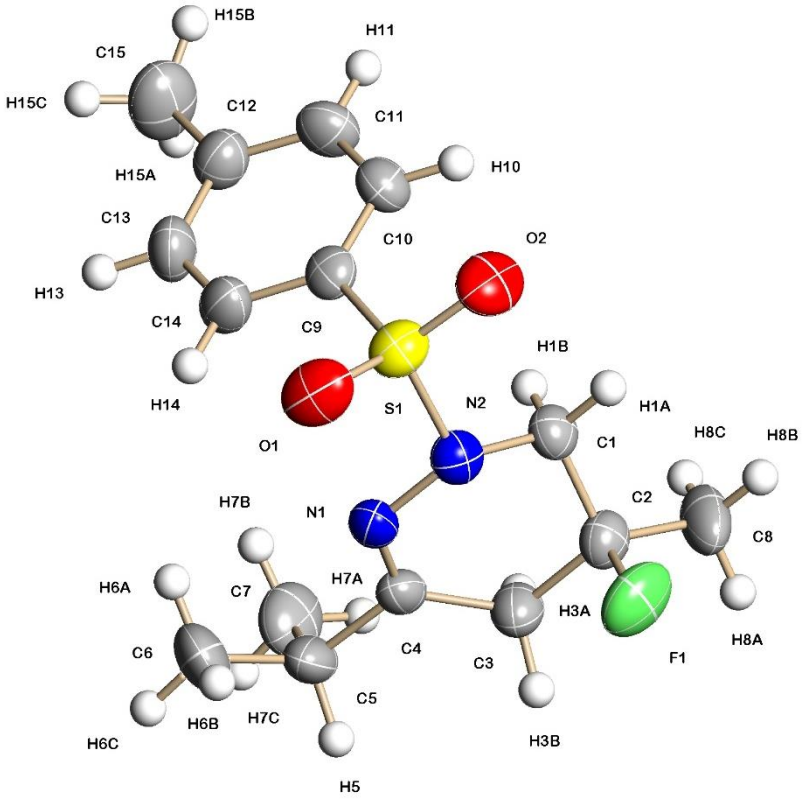


Figure S4 Molecular structure of 5-fluoro-3-isopropyl-5-methyl-1-tosyl-1,4,5,6-tetrahydro-pyridazine **3j** showing 50% displacement ellipsoids.

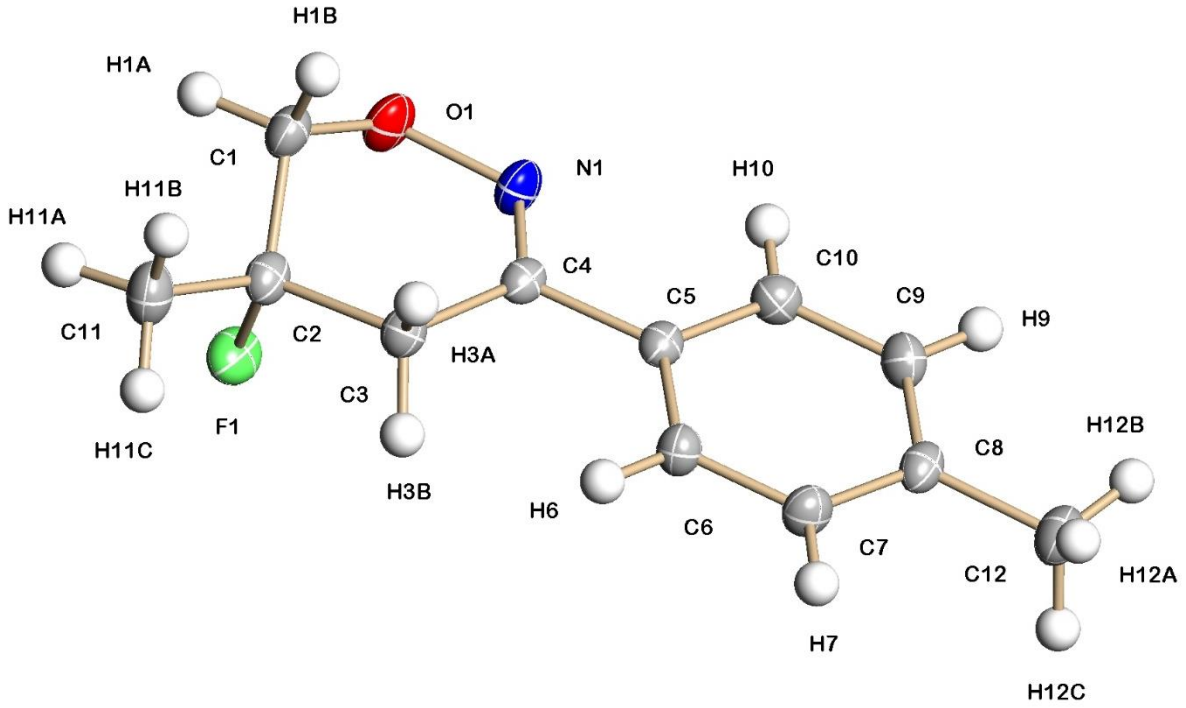


Figure S5 Molecular structure of 5-fluoro-5-methyl-3-(*p*-tolyl)-5,6-dihydro-4*H*-1,2-oxazine **7c** showing 50% displacement ellipsoids.

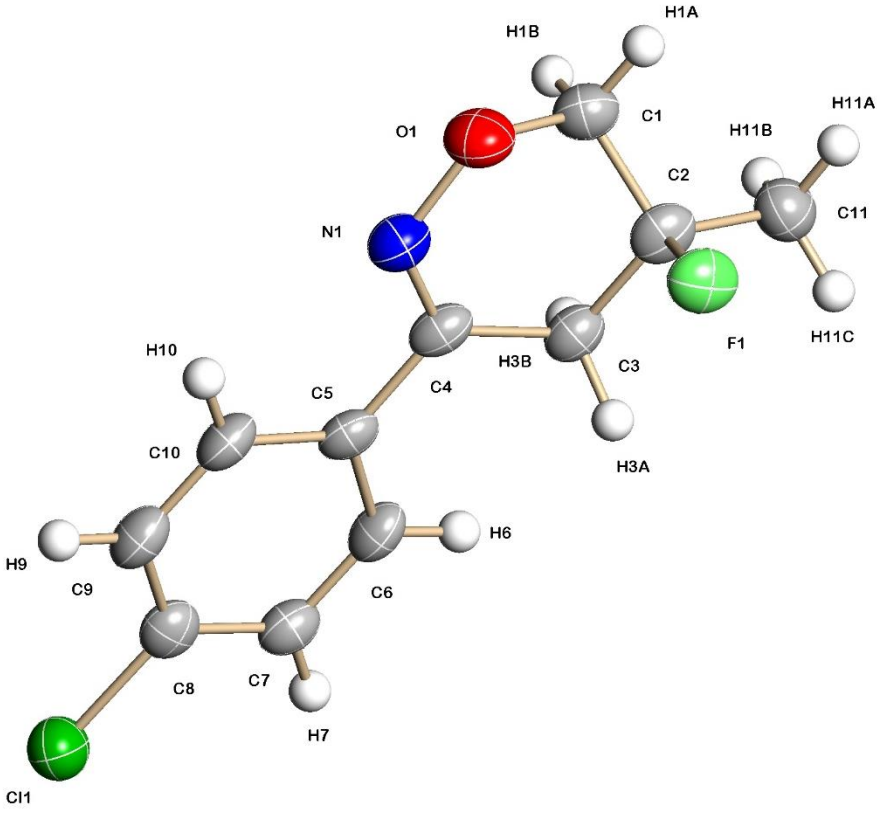


Figure S6 Molecular structure of 3-(4-chlorophenyl)-5-fluoro-5-methyl-5,6-dihydro-4*H*-1,2-oxazine **7d** showing 50% displacement ellipsoids.

Table S1 Selected bond lengths (Å) and bond angles (°) with estimated standard deviations (e.s.d.s.) in parenthesis for fluorinated tetrahydropyridazines **3a**, **3c**, **3h** and **3j**

Bond lengths (Å) and bond angles (°)	**3a** R = 4-C_6H_4Cl	**3c** R = Ph	**3h** R = 2-thienyl	**3j** R = $CH(CH_3)_2$
C(2)-F(1)	1.420(2)	1.418(3)	1.417(3)	1.417(3)
C(4)-N(1)	1.281(2)	1.286(3)	1.293(3)	1.273(3)
N(1)-N(2)	1.405(2)	1.408(3)	1.397(43)	1.400(3)
N(2)-C(1)	1.472(2)	1.475(3)	1.464(3)	1.465(3)
C(1)-C(2)-C(3)	110.58(15)	110.2(2)	110.4(2)	109.4(2)
F(1)-C(2)-C(11/9/8)	107.86(16)	107.66(19)	107.3(3)	108.4(2)
C(4)-N(1)-N(2)	117.61(15)	118.2(2)	118.7(2)	118.0(2)
N(1)-N(2)-C(1)	116.80(15)	117.33(18)	118.4(2)	116.52(19)

Table S2 Selected bond lengths (Å) and bond angles (°) with estimated standard deviations (e.s.d.s.) in parenthesis for fluorinated dihydrooxazines **7c** and **7d**

Bond lengths (Å) and bond angles (°)	**7c** R = 4-$C_6H_4CH_3$	**7d** R = 4-C_6H_4Cl
C(2)-F(1)	1.422(2)	1.435(5)
C(4)-N(1)	1.283(2)	1.287(6)
N(1)-O(1)	1.425(2)	1.400(5)
O(1)-C(1)	1.422(2)	1.435(6)
C(1)-C(2)-C(3)	108.19(15)	109.0(4)
F(1)-C(2)-C(11)	107.46(16)	106.6(4)
C(4)-N(1)-O(1)	118.27(16)	119.2(4)
N(1)-O(1)-C(1)	116.51(13)	117.2(4)

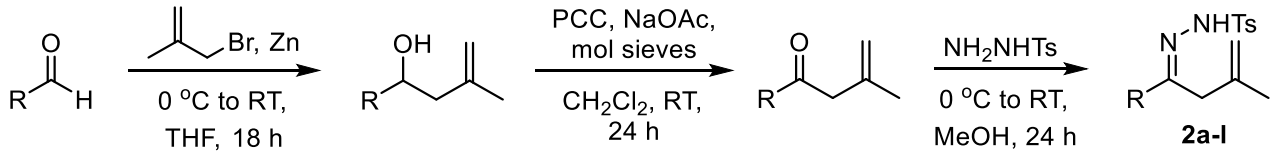
Experimental

Proton, ^{19}F and ^{13}C NMR spectra were recorded on either a Bruker AV400 or a DRX 400 spectrometer at 400.13, 376.46 and 100.62 MHz respectively, or ^{1}H and ^{13}C NMR spectra were recorded on an AV500 spectrometer at 500.13 and 125.76 MHz. The ^{1}H and ^{13}C NMR spectra were referenced to external $SiMe_4$ using the high frequency positive convention. Atmospheric Solids Analysis Probe (ASAP) mass spectra were recorded on a Xevo QTof mass spectrometer (Waters) and Electrospray (ESI) mass spectra were obtained by LC-MS using a Xevo QTof mass spectrometer (Waters) coupled to an Acquity LC system (Waters) with an Acquity UPLC BEH C18 column (2.1 x 50 mm). X-ray crystallography data were collected on a Bruker Apex SMART 2000 diffractometer using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å).

Dichloromethane and tetrahydrofuran were obtained dry from a Puresolve^{TM} solvent purification system and were stored in sealed ampoules over 4Å molecular sieves under an atmosphere of dry nitrogen. Hexafluoroisopropanol (HFIP) was purchased from Fluorochem and stored in sealed ampoules over 4Å molecular sieves under an atmosphere of dry nitrogen. The hypervalent fluoroiodane reagent **1**,[4c] and the unsaturated carboxylic acids **12a-f**,[6a] were prepared following the literature procedures.

The ball mill used was a Retsch MM 400 mixer mill. Milling balls were purchased from Bearingboys. Unless otherwise stated, mechanochemical reactions were performed in 10 mL Retsch stainless steel jars with one stainless steel ball of mass 2.5 g. It is worth noting that "under an air atmosphere" means that no precaution was taken to exclude air and moisture, much like running reactions that are not considered to be air or moisture sensitive.

Procedure for preparation of unsaturated hydrazones 2



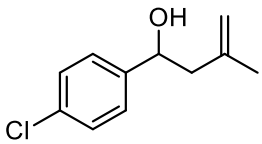
General Procedure for the activation of zinc[12]

Activated zinc was prepared by stirring powdered zinc (10 g, 153 mmol) in deionised water (100 mL) that was acidified using concentrated 38 % HCl (2 mL). The suspension was stirred for 20 minutes during which time the activated zinc would undergo sedimentation. The acidified aqueous layer was decanted after the period of stirring and the zinc was washed with water (2 x 50 mL) followed by decanting. The zinc was then washed with organic solvents; reagent grade acetone (2 x 40 mL) and diethyl ether (2 x 30 mL). After decanting the final wash solvent the zinc was stirred slowly whilst under reduced pressure for up to 2 hours with flame drying before use. Activated zinc (9.7 g, 97 % recovery) was typically obtained and could be stored under an inert atmosphere, however to ensure reproducibility of the Barbier-type reaction the zinc was prepared fresh for each use.

General Procedure for the synthesis of unsaturated alcohols[12]

The flask was charged with activated zinc dust (15 mmol), whilst the equilibrating dropping funnel was charged with aldehyde (10 mmol), 3-bromo-2-methylpropene (15 mmol) and dry THF (10 mL) under an inert atmosphere. The solution was added dropwise over half an hour to the suspension of zinc dust whilst maintaining the temperature at 0 °C with external cooling for 2 hours. The reaction was warmed to room temperature and stirred overnight. After quenching with ammonium chloride solution (40 mL), the reaction mixture was stirred for a further 5 minutes. The reaction mixture was diluted with diethyl ether (50 mL) and was filtered, and the reaction flask was washed with diethyl ether (3 x 50 mL). The organic layers were combined, and washed with water (2 x 40 mL) and brine (3 x 40 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to obtain the unsaturated alcohol.

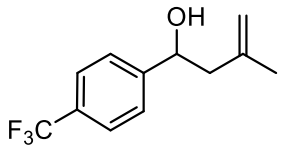
1-(4-Chlorophenyl)-3-methylbut-3-en-1-ol



The general procedure was followed using 4-chlorobenzaldehyde (3.0 g, 21.3 mmol), activated zinc dust (2.1 g, 32.0 mmol), 3-bromo-2-methylpropene (3.3 mL, 32.0 mmol) and dry THF (20 mL). The pure product was obtained as a colourless oil (3.84 g, 92 %) and the characterisation was in agreement with the literature.[13] δ_H ($CDCl_3$, 500 MHz) 1.79 (3H, s, CH_3), 2.20 (1H, br s, OH), 2.32 - 2.45 (2H, m, CH_2), 4.78 (1H, dd,

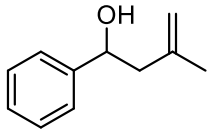
$^3J_{HH}$ = 7.5 Hz, $^3J_{HH}$ = 5.8 Hz, C*H*OH), 4.84 (1H, s, =CH_2), 4.93 (1H, s, =CH_2), 7.31 (4H, s, ArH). δ_C ($CDCl_3$, 126 MHz) 22.3 (CH_3), 48.4 (CH_2), 70.7 (CH), 114.4 (CH_2), 127.2 (CH), 128.5 (CH), 133.1 (C), 142.0 (C), 142.5 (C). m/z (ASAP) 179.0637 (M-OH^+, $C_{11}H_{12}{}^{35}Cl$ requires 179.0628, 100 %), 181.0600 (M-OH^+, $C_{11}H_{12}{}^{37}Cl$ requires 181.0598, 33 %).

3-Methyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol



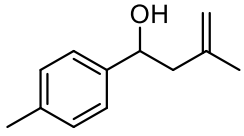
The general procedure was followed using activated zinc dust (0.85 g, 22.0 mmol), 3-bromo-2-methylpropene (1.3 mL, 12.9 mmol) and 4-trifluoromethylbenzaldehyde (1.50 g, 8.6 mmol) in dry THF (20 mL). The pure product was obtained as a colourless oil (1.90 g, 96 %) and the characterisation data was in agreement with the literature.[14] δ_H ($CDCl_3$, 400 MHz) 1.80 (3H, s, CH_3), 2.31 - 2.46 (3H, m, CH_2 and OH), 4.78 - 4.90 (2H, C*H*OH and =CH_2), 4.95 (1H, s, =CH_2), 7.48 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 7.60 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.3 (CH_3), 48.5 (CH_2), 70.8 (CH), 114.7 (CH_2), 124.3 (q, $^1J_{CF}$ = 272.8 Hz, C) 125.4 (q, $^3J_{CF}$ = 4.2 Hz, CH), 126.1 (CH), 129.7 (q, $^2J_{CF}$ = 31.8 Hz, C), 141.8 (C), 148.1 (C). δ_F ($CDCl_3$, 376 MHz) -62.4 (s). m/z (ESI) 213.0888 (M-OH^+, $C_{12}H_{12}F_3$ requires 213.0891, 100 %).

3-Methyl-1-phenylbut-3-en-1-ol



The general procedure was followed using benzaldehyde (4.8 mL, 47.1 mmol), activated zinc dust (6.2 g, 94.2 mmol), 3-bromo-2-methylpropene (9.5 mL, 94.2 mmol) and dry THF (40 mL). The reaction yielded the product as a colourless oil (6.38 g, 84 %) and the characterisation data was in agreement with the literature.[15] δ_H ($CDCl_3$, 400 MHz) 1.79 (3H, s, CH_3), 2.15 (1H, d, $^3J_{HH}$ = 2.5 Hz, OH), 2.40 - 2.45 (2H, d, $^3J_{HH}$ = 6.7 Hz, CH_2), 4.80 (1H, td, $^3J_{HH}$ = 6.7 Hz, $^3J_{HH}$ = 2.5 Hz, C*H*OH), 4.85 (1H, s, =CH_2), 4.92 (1H, s, =CH_2), 7.24 - 7.29 (1H, m, ArH), 7.30 - 7.40 (4H, m, ArH). δ_C ($CDCl_3$, 126 MHz) 22.4 (CH_3), 48.4 (CH_2), 71.4 (CH), 114.1 (CH_2), 125.8 (CH), 127.5 (CH), 128.4 (CH), 142.4 (C), 144.1 (C). m/z (ASAP) 145.1015 ((M-OH)$^+$, $C_{11}H_{13}$, requires 145.1017, 100 %).

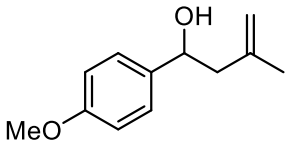
3-Methyl-1-(*p*-tolyl)but-3-en-1-ol



The general procedure was followed using 4-methylbenzaldehyde (3.0 g, 25.0 mmol), activated zinc dust (2.5 g, 37.5 mmol), 3-bromo-2-methylpropene (3.8 mL, 37.5 mmol) and dry THF (25 mL). The pure product was obtained as a colourless oil (3.52 g, 80 %) and the characterisation was in agreement with the literature.[16] δ_H ($CDCl_3$, 400 MHz) 1.79 (3H, s, CH_3), 2.06 (1H, br s, OH), 2.34 (3H, s, ArCH_3), 2.40 - 2.44 (2H, m, CH_2), 4.76 – 4.80 (1H, m, C*H*OH), 4.85 (1H, s, =CH_2), 4.91 (1H, s, =CH_2), 7.16 (2H, d, $^3J_{HH}$ = 7.8

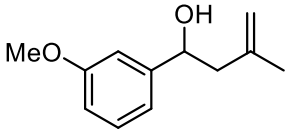
Hz, ArH), 7.27 (2H, d, $^3J_{HH}$ = 7.8 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.1 (CH_3), 22.4 (CH_3), 48.3 (CH_2), 71.3 (CH), 114.0 (CH_2), 125.7 (CH), 129.1 (CH), 137.1 (C), 141.1 (C), 142.5 (C). m/z (ASAP) 159.1172 (M-OH^+, $C_{12}H_{15}$ requires 159.1174, 100 %).

1-(4-Methoxyphenyl)-3-methylbut-3-en-1-ol



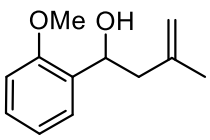
The general procedure was followed using 4-methoxybenzaldehyde (2.5 g, 18.4 mmol), activated zinc dust (1.8 g, 37.5 mmol), 3-bromo-2-methylpropene (2.8 mL, 27.5 mmol) and dry THF (20 mL). The pure product was obtained as a colourless oil (3.00 g, 85 %) and the characterisation was in agreement with the literature.[17] δ_H ($CDCl_3$, 400 MHz) 1.79 (3H, s, CH_3), 2.08 (1H, d, $^3J_{HH}$ = 2.3 Hz, OH), 2.28 - 2.51 (2H, m, CH_2), 3.81 (3H, s, OCH_3), 4.77 (1H, m, C*H*OH), 4.85 (1H, s, =CH_2), 4.92 (1H, s, =CH_2), 6.89 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.31 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.4 (CH_3), 48.3 (CH_2), 55.3 (CH_3), 71.1 (CH), 113.8 (CH), 114.0 (CH_2), 127.0 (CH), 136.2 (C), 142.5 (C), 159.0 (C). m/z (ASAP) 175.1123 (M-OH^+, $C_{12}H_{15}O$ requires 175.1123, 60 %).

1-(3-Methoxyphenyl)-3-methylbut-3-en-1-ol



The general procedure was followed using activated zinc dust (1.44 g, 22.0 mmol), 3-bromo-2-methylpropene (2.2 mL, 22.0 mmol) and 3-methoxybenzaldehyde (2.00 g, 14.7 mmol) in dry THF (20 mL). The pure product was obtained as a colourless oil (2.76 g, 98 %) and the characterisation data was in agreement with the literature.[18] δ_H ($CDCl_3$, 400 MHz) 1.80 (3H, s, CH_3), 2.12 (1H, br s, OH), 2.42 (2H, d, $^3J_{HH}$ = 6.7 Hz, CH_2), 3.82 (3H, s, OCH_3), 4.79 (1H, t, $^3J_{HH}$ = 6.7 Hz, C*H*OH), 4.86 (1H, s, =CH_2), 4.93 (1H, s, =CH_2), 6.81 (1H, ddd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 2.4 Hz, $^4J_{HH}$ = 1.1 Hz, ArH), 6.92 - 6.97 (2H, m, ArH), 7.23 - 7.29 (1H, m, ArH). δ_C ($CDCl_3$, 126 MHz) 22.3 (CH_3), 48.4 (CH_2), 55.2 (CH_3), 71.3 (CH), 111.2 (CH), 113.0 (CH), 114.1 (CH_2), 118.1 (CH), 129.4 (CH), 142.4 (C), 145.8 (C), 159.8 (C). m/z (ESI) 175.1124 (M-OH^+, $C_{12}H_{15}O$ requires 175.1123, 100 %).

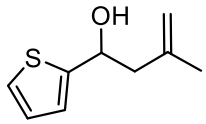
1-(2-Methoxyphenyl)-3-methylbut-3-en-1-ol



The general procedure was followed using activated zinc dust (1.10 g, 16.5 mmol), 3-bromo-2-methylpropene (1.7 mL, 16.5 mmol) and 2-methoxybenzaldehyde (1.50 g, 11.0 mmol) in dry THF (20 mL). The pure product was obtained as a white solid (2.00 g, 95 %) and the characterisation data was in agreement with the literature.[19] Mp 35-37 ^oC (lit,[20] 35-36 ^oC). δ_H ($CDCl_3$, 400 MHz) 1.81 (3H, s, CH_3), 2.39 (1H, ddd, $^2J_{HH}$ = 14.0 Hz, $^3J_{HH}$ = 9.0 Hz, $^4J_{HH}$ = 0.8 Hz, C$H_A$$H_B$), 2.48 (1H, d, $^3J_{HH}$ = 4.7 Hz, OH), 2.51 (1H, br dd, $^2J_{HH}$ = 14.0 Hz, $^3J_{HH}$ = 4.5 Hz, C$H_A$$H_B$), 3.85 (3H, s, OCH_3), 4.82 (1H, s, =CH_2), 4.87 (1H, s, =CH_2), 5.08 (1H, td,

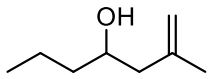
$^3J_{HH}$ = 7.8 Hz, $^3J_{HH}$ = 4.7 Hz, C*H*OH), 6.87 (1H, dd, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 6.96 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.24 (1H, td, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 1.7 Hz, ArH), 7.39 (1H, dd, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.7 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.4 (CH_3), 46.3 (CH_2), 55.3 (CH_3), 67.7 (CH), 110.4 (CH), 113.3 (CH_2), 120.7 (CH), 126.5 (CH), 128.2 (CH), 132.2 (C), 143.1 (C), 156.3 (C). m/z (ASAP) 175.1122 (M-OH^+, $C_{12}H_{15}O$ requires 175.1123, 100 %).

3-Methyl-1-(thiophen-2-yl)but-3-en-1-ol



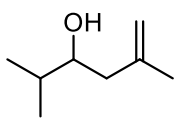
The general procedure was followed using activated zinc dust (1.75 g, 26.8 mmol), 3-bromo-2-methylpropene (2.6 mL, 26.8 mmol) and 4-thiophene-2-carboxaldehyde (2.00 g, 17.8 mmol) in dry THF (20 mL). The pure product was obtained as a colourless oil (2.65 g, 88 %) and the characterisation data was in agreement with the literature.[21] δ_H ($CDCl_3$, 400 MHz) 1.82 (3H, s, CH_3), 2.27 (1H, d, $^3J_{HH}$ = 3.1 Hz, OH), 2.58 (2H, d, $^3J_{HH}$ = 6.7 Hz, CH_2), 4.90 (1H, s, =CH_2), 4.96 (1H, s, =CH_2), 5.11 (1H, td, $^3J_{HH}$ = 6.5 Hz, $^3J_{HH}$ = 3.0 Hz, C*H*OH), 6.99 (1H, dd, $^3J_{HH}$ = 4.9 Hz, $^3J_{HH}$ = 3.5 Hz, ArH), 7.01 - 7.03 (1H, m, ArH), 7.28 (1H, dd, $^3J_{HH}$ = 5.0 Hz, $^4J_{HH}$ = 1.0 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.3 (CH_3), 48.2 (CH_2), 67.6 (CH), 114.4 (CH_2), 123.6 (CH), 124.5 (CH), 126.6 (CH), 141.8 (C), 147.9 (C). m/z (ESI) 151.0586 (M-OH^+, $C_9H_{11}S$ requires 151.0581, 100 %).

2-Methylhept-1-en-4-ol



The general procedure was followed using butanal (3.0 g, 41.6 mmol), activated zinc dust (4.1 g, 62.4 mmol), 3-bromo-2-methylpropene (6.3 mL, 62.4 mmol) and dry THF (40 mL). The pure product was obtained as a colourless oil (4.55 g, 85 %) and the characterisation data was in agreement with the literature.[22] δ_H ($CDCl_3$, 400 MHz) 0.94 (3H, t, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.32 - 1.56 (4H, m, CH_2), 1.76 (3H, s, CH_3), 1.82 - 1.89 (1H, m, OH), 2.09 (1H, dd, $^2J_{HH}$ = 13.7 Hz, $^3J_{HH}$ = 9.4 Hz, C*H*$_A$H$_B$), 2.20 (1H, dd, $^2J_{HH}$ = 13.7 Hz, $^3J_{HH}$ = 3.6 Hz, CH$_A$*H*$_B$), 3.72 - 3.77 (1H, m, C*H*OH), 4.80 (1H, s, =CH_2), 4.88 (1H, s, =CH_2). δ_C ($CDCl_3$, 126 MHz) 14.1 (CH_3), 18.9 (CH_2), 22.4 (CH_3), 39.3 (CH_2), 46.2 (CH_2), 68.4 (CH), 113.4 (CH_2), 142.9 (C). m/z (ESI, ASAP, ACPI, GC) No ionisation achieved.

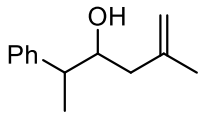
2,5-Dimethylhex-5-en-3-ol



The general procedure was followed using activated zinc dust (4.10 g, 62.4 mmol), 3-bromo-2-methylpropene (6.29 mL, 62.4 mmol) and isobutyraldehyde (3.00 g, 41.6 mmol) in dry THF (40 mL). The pure product was obtained as a colourless oil (3.50 g, 66 %) and the characterisation data was in agreement with the literature.[23] bp ~65 ^{o}C at 1 atm. δ_H ($CDCl_3$, 400 MHz) 0.87 (3H, d, $^3J_{HH}$ = 6.6 Hz, CH_3), 0.88 (3H, d, $^3J_{HH}$ = 6.6 Hz, CH_3), 1.57 (1H, d,

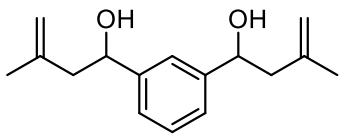
$^3J_{HH}$ = 2.9 Hz, OH), 1.63 (1H, septet of doublets, $^3J_{HH}$ = 6.6 Hz, $^3J_{HH}$ = 5.5 Hz, C*H*(CH_3)$_2$), 1.70 (3H, s, CH_3), 1.99 (1H, dd, $^2J_{HH}$ = 13.7 Hz, $^3J_{HH}$ = 10.7 Hz, CH_AH$_B$), 2.16 (1H, dd, $^2J_{HH}$ = 13.7 Hz, $^3J_{HH}$ = 2.9 Hz, CH$_A$$H_B$), 3.42 (1H, ddt, $^3J_{HH}$ = 10.2 Hz, $^3J_{HH}$ = 5.5 Hz, $^3J_{HH}$ = 2.9 Hz, CH), 4.74 (1H, s, =CH_2), 4.82 (1H, s, =CH_2). δ_C ($CDCl_3$, 101 MHz) 17.6 (CH_3), 18.6 (CH_3), 22.3 (CH_3), 33.4 (CH), 42.9 (CH_2), 73.1 (CH), 113.5 (CH_2), 145.8 (C). m/z (ESI/GCMS/ASAP) No ionisation achieved.

5-Methyl-2-phenylhex-5-en-3-ol



The general procedure was followed using activated zinc dust (1.1 g, 16.8 mmol), 3-bromo-2-methylpropene (1.7 mL, 16.8 mmol) and 2-phenylpropionaldehyde (1.5 g, 11.2 mmol) in dry THF (20 mL). The pure product was obtained as a mixture of diastereomers (anti:syn = 3:1) as a colourless oil (2.04 g, 96 %) and the characterisation data was in agreement with the literature.[24] δ_H ($CDCl_3$, 400 MHz) 1.32 (3H, d, $^3J_{HH}$ = 7.2 Hz, CH_{3syn}) 1.37 (3H, d, $^3J_{HH}$ = 7.1 Hz, CH_{3anti}), 1.59 (1H, br s, OH_{syn}), 1.69 (3H, s, CH_{3anti}), 1.76 (4H, br s, CH_{3syn} and OH_{anti}), 1.94 - 2.32 (2H, m, C$H_A$$H_{B}$$_{mix}$), 2.70 - 2.86 (1H, m, C*H*(CH_3)$_{mix}$), 3.75 - 3.91 (1H, m, C*H*(OH)$_{mix}$), 4.77 (1H, s, =CH_2), 4.86 (1H, s, =CH_2), 7.14 - 7.40 (5H, m, ArH). δ_C ($CDCl_3$, 101 MHz) 16.6 (CH_{3anti}), 17.7 (CH_{3syn}), 22.2 (CH_{3anti}), 22.4 (CH_{3syn}), 43.3 (CH_{2syn}), 44.0 (CH_{2anti}), 45.7 (CH_{syn}), 45.8 (CH_{anti}), 72.9 (CH_{anti}), 73.0 (CH_{syn}), 113.4 (CH_{2syn}), 113.5 (CH_{2anti}), 126.4 (CH_{anti}), 126.6 (CH_{syn}), 127.8 (CH_{anti}), 128.2 (CH_{syn}), 128.4 (CH_{syn}), 128.5 (CH_{anti}), 142.98 (C_{syn}), 143.03 (C_{anti}), 143.4 (C_{syn}), 144.6 (C_{anti}). m/z (ESI) 173.1326 ((M-OH)$^+$, $C_{13}H_{17}$ requires 173.1330, 100 %).

1,1'-(1,3-Phenylene)bis(3-methylbut-3-en-1-ol)

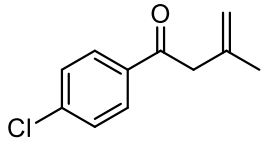


The general procedure was followed but using twice the typical equivalents of activated zinc and 3-bromo-2methylpropene (3 equiv): activated zinc dust (2.2 g, 33.5 mmol), 3-bromo-2-methylpropene (3.4 mL, 33.5 mmol) and isophthalaldehyde (1.5 g, 11.2 mmol) in dry THF (40 mL). The pure product was obtained as a colourless oil (2.71 g, 98 %) and the characterisation data was in agreement with the literature.[25] δ_H ($CDCl_3$, 500 MHz) 1.81 (6H, s, CH_3), 2.17 (2H, d, $^3J_{HH}$ = 1.8 Hz, OH), 2.43 (4H, d, $^3J_{HH}$ = 6.9 Hz, CH_2), 4.82 (2H, td, $^3J_{HH}$ = 6.8 Hz, $^3J_{HH}$ = 1.9 Hz, C*H*(OH)), 4.87 (2H, s, =CH_2), 4.94 (2H, s, =CH_2), 7.27 - 7.31 (2H, m, ArH), 7.31 - 7.36 (1H, m, ArH), 7.38 - 7.45 (1H, m, ArH). δ_C ($CDCl_3$, 101 MHz) 22.3 (CH_3), 48.5 (CH_2), 71.4 (CH), 114.2 (CH_2), 123.1 (CH), 124.9 (CH), 128.5 (CH), 142.4 (C), 144.3 (C). m/z (ESI/ASAP/GC) No ionisation obtained.

General Procedure for synthesis of unsaturated ketones[26]

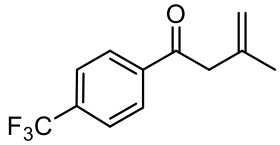
A dry 3 necked round bottom flask was charged with anhydrous sodium acetate (5.0 mmol), 4 Å molecular sieves (5.00 g), unsaturated alcohol (10 mmol) and dry DCM (60 mL). PCC (15 mmol) was then added portion wise. The reaction was stirred at room temperature for 24 hours under an inert atmosphere. The reaction mixture was diluted with diethyl ether (50 mL) and was filtered through a silica plug. The reaction flask was washed with diethyl ether (3 x 50 mL) which was also passed through the silica plug. The organic layers were combined and concentrated *in vacuo* to obtain the corresponding unsaturated ketone.

1-(4-Chlorophenyl)-3-methylbut-3-en-1-one



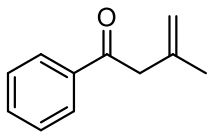
The general procedure was followed using anhydrous sodium acetate (0.63 g, 7.6 mmol), 4 Å molecular sieves (5.00 g), 1-(4-chlorophenyl)-3-methylbut-3-en-1-ol (3.00 g, 15.3 mmol) and PCC (5.00 g, 22.8 mmol) in dry DCM (60 mL). The pure product was obtained as a yellow oil (2.42 g, 81 %). δ_H ($CDCl_3$, 400 MHz) 1.81 (3H, s, CH_3), 3.65 (2H, s, CH_2), 4.85 (1H, s, $=CH_2$), 4.99 (1H, s, $=CH_2$), 7.43 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.92 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.8 (CH_3), 47.8 (CH_2), 115.2 (CH_2), 128.9 (CH), 129.8 (CH), 135.1 (C), 139.5 (C), 139.6 (C), 196.9 (CO). m/z (ASAP) 195.0576 (MH^+, $C_{11}H_{12}O^{35}Cl$ requires 195.0576, 100 %), 197.0560 (MH^+, $C_{11}H_{12}O^{37}Cl$ requires 195.0547, 33 %).

3-Methyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-one



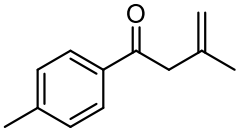
The general procedure was followed using anhydrous sodium acetate (0.45 g, 5.5 mmol), molecular sieves (4.00 g), 1-(4-trifluoromethylphenyl)-3-methylbut-3-en-1-ol (2.00 g, 10.9 mmol) and PCC (3.53 g, 16.4 mmol) in dry DCM (60 mL). The pure product was obtained as a white solid (1.45 g, 81 %). The characterisation data was in agreement with the literature.[27] Mp 36-38 °C. δ_H ($CDCl_3$, 400 MHz) 1.83 (3H, s, CH_3), 3.71 (2H, s, CH_2), 4.87 (1H, s, $=CH_2$), 5.01 (1H, s, $=CH_2$), 7.73 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 8.08 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.8 (CH_3), 48.0 (CH_2), 115.5 (CH_2), 123.6 (q, $^1J_{CF}$ = 273.4 Hz, C), 125.7 (q, $^3J_{CF}$ = 3.6 Hz, CH), 128.8 (CH), 134.4 (q, $^2J_{CF}$ = 32.7 Hz, C), 139.2 (C), 139.4 (C), 197.1 (CO). δ_F ($CDCl_3$, 376 MHz) -63.1 (s). m/z (ESI) 229.0845 (MH^+, $C_{12}H_{12}F_3O$ requires 229.0840, 100 %).

3-Methyl-1-phenylbut-3-en-1-one



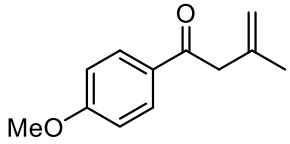
The general procedure was followed using anhydrous sodium acetate (0.51 g, 6.2 mmol), 3-methyl-1-phenylbut-3-en-1-ol (2.04 g, 12.4 mmol), PCC (4.00 g, 18.5 mmol) and dry DCM (60 mL). The reaction yielded the desired product as a yellow oil (1.61 g, 80 %) and the characterisation data was in agreement with the literature.[28] δ_H ($CDCl_3$, 400 MHz) 1.82 (3H, s, CH_3), 3.69 (2H, s, CH_2), 4.85 (1H, s, $=CH_2$), 4.98 (1H, s, $=CH_2$), 7.45 (2H, t, $^3J_{HH}$ = 7.6 Hz, ArH), 7.55 (1H, t, $^3J_{HH}$ = 7.4 Hz, ArH), 7.98 (2H, d, $^3J_{HH}$ = 7.7 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.8 (CH_3), 47.7 (CH_2), 115.0 (CH_2), 128.4 (CH), 128.6 (CH), 133.11 (CH), 136.8 (C), 139.76 (C), 198.1 (CO). m/z (ASAP) 161.0960 (MH^+, $C_{11}H_{13}O$ requires 161.0966, 5 %).

3-Methyl-1-(*p*-tolyl)but-3-en-1-one



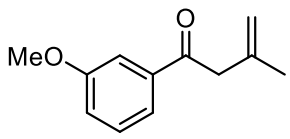
The general procedure was followed using anhydrous sodium acetate (0.70 g, 8.50 mmol), 4 Å molecular sieves (6.00 g), 3-methyl-1-(*p*-tolyl)but-3-en-1-ol (3.00 g, 17.0 mmol) and PCC (5.50 g, 25.5 mmol) in dry DCM (60 mL). The pure product was obtained as a colourless crystal/ white solid (2.00 g, 68 %). Mp 55-56 ^oC. δ_H ($CDCl_3$, 400 MHz) 1.81 (3H, s, CH_3), 2.40 (3H, s, $ArCH_3$), 3.65 (2H, s, CH_2), 4.84 (1H, s, $=CH_2$), 4.97 (1H, s, $=CH_2$), 7.25 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.88 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 22.8 (CH_3), 47.7 (CH_2), 114.8 (CH_2), 128.6 (CH), 129.2 (CH), 134.4 (C), 140.0 (C), 143.9 (C), 197.8 (CO). m/z (ASAP) 175.1126 (MH^+, $C_{12}H_{15}O$ requires 175.1123, 100 %).

1-(4-Methoxyphenyl)-3-methylbut-3-en-1-one



The general procedure was followed using anhydrous sodium acetate (0.70 g, 8.59 mmol), 4 Å molecular sieves (6.00 g), 1-(4-methoxyphenyl)-3-methylbut-3-en-1-ol (3.30 g, 17.2 mmol) and PCC (5.55 g, 25.8 mmol) in dry DCM (60 mL). The pure product was obtained as a colourless oil (2.24 g, 69 %). δ_H ($CDCl_3$, 400 MHz) 1.81 (3H, s, CH_3), 3.64 (2H, s, CH_2), 3.87 (3H, s, OCH_3), 4.85 (1H, s, $=CH_2$), 4.97 (1H, s, $=CH_2$), 6.93 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.97 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.9 (CH_3), 47.6 (CH_2), 55.5 (CH_3), 113.7 (CH), 114.7 (CH_2), 129.9 (C), 130.7 (CH), 140.2 (C), 163.5 (C), 196.7 (CO). m/z (ASAP) 191.1068 (MH^+, $C_{12}H_{15}O_2$ requires 191.1072, 10 %).

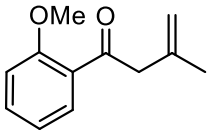
1-(3-Methoxyphenyl)-3-methylbut-3-en-1-one



The general procedure was followed using anhydrous sodium acetate (0.45 g, 5.5 mmol), molecular sieves (4.00 g), 1-(3-methoxyphenyl)-3-methylbut-3-en-1-ol (2.00 g, 10.9 mmol) and PCC (3.53 g, 16.4 mmol) in dry DCM (60 mL). The pure product was obtained as a colourless oil (1.63 g, 83 %). The

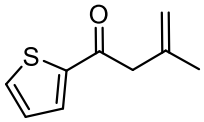
characterisation data was in agreement with the literature.[29] δ_H ($CDCl_3$, 400 MHz) 1.82 (3H, s, CH_3), 3.67 (2H, s, CH_2), 3.85 (3H, s, OCH_3), 4.85 (1H, s, =CH_2), 4.98 (1H, s, =CH_2), 7.11 (1H, ddd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 2.6 Hz, $^4J_{HH}$ = 0.9 Hz, ArH), 7.36 (1H, t, $^3J_{HH}$ = 7.9 Hz, ArH), 7.51 (1H, dd, $^4J_{HH}$ = 2.5 Hz, $^4J_{HH}$ = 1.6 Hz, ArH), 7.56 (1H, dt, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.3 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.8 (CH_3), 47.9 (CH_2), 55.4 (CH_3), 112.6 (CH), 114.9 (CH_2), 119.6 (CH), 121.1 (CH), 129.5 (CH), 138.2 (C), 139.8 (C), 159.8 (C), 197.9 (CO). m/z (ESI) 191.1076 (MH^+, $C_{12}H_{15}O_2$ requires 191.1072, 100 %).

1-(2-Methoxyphenyl)-3-methylbut-3-en-1-one



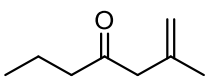
The general procedure was followed using anhydrous sodium acetate (0.45 g, 5.5 mmol), molecular sieves (4.00 g), 1-(2-methoxyphenyl)-3-methylbut-3-en-1-ol (2.00 g, 10.9 mmol) and PCC (3.53 g, 16.4 mmol) in dry DCM (60 mL). The pure product was obtained as a colourless oil (1.50 g, 75 %). The characterisation data was in agreement with the literature.[30] δ_H ($CDCl_3$, 400 MHz) 1.79 (3H, s, CH_3), 3.71 (2H, s, CH_2), 3.90 (3H, s, OCH_3), 4.78 (1H, s, =CH_2), 4.91 (1H, s, =CH_2), 6.96 (1H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 6.99 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.45 (1H, td, $^3J_{HH}$ = 7.4 Hz, $^4J_{HH}$ = 1.9 Hz, ArH), 7.67 (1H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.8 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.9 (CH_3), 52.3 (CH_2), 55.5 (CH_3), 111.5 (CH), 114.3 (CH_2), 120.7 (CH), 128.4 (C), 130.4 (CH), 133.4 (CH), 140.1 (C), 158.4 (C), 200.5 (CO). m/z (ESI) 191.1068 (MH^+, $C_{12}H_{15}O_2$ requires 191.1072, 100 %).

3-Methyl-1-(thiophen-2-yl)but-3-en-1-one



The general procedure was followed using anhydrous sodium acetate (0.66 g, 8.0 mmol), 4 Å molecular sieves (6.00 g), 3-methyl-1-(thiophen-2-yl)but-3-en-1-ol (2.70 g, 16.1 mmol) and PCC (5.20 g, 24.1 mmol) in dry DCM (60 mL). The pure product was obtained as a colourless oil (2.15 g, 81 %). δ_H ($CDCl_3$, 400 MHz) 1.83 (3H, s, CH_3), 3.62 (2H, s, CH_2), 4.91 (1H, s, =CH_2), 4.99 (1H, s, =CH_2), 7.13 (1H, dd, $^3J_{HH}$ = 5.0 Hz, $^3J_{HH}$ = 3.8 Hz, ArH), 7.64 (1H, dd, $^3J_{HH}$ = 4.9 Hz, $^4J_{HH}$ = 1.2 Hz, ArH), 7.77 (1H, dd, $^3J_{HH}$ = 3.8 Hz, $^4J_{HH}$ = 1.1 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.7 (CH_3), 48.7 (CH_2), 115.1 (CH_2), 128.1 (CH), 132.4 (CH), 133.8 (CH), 139.5 (C), 144.1 (C), 190.8 (CO). m/z (ESI) 167.0533 (MH^+, $C_9H_{11}OS$ requires 167.0531, 100 %).

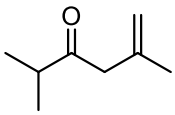
2-Methylhept-1-en-4-one



The general procedure was followed using anhydrous sodium acetate (0.4 g, 5.03 mmol), 4 Å molecular sieves (4.00 g), 2-methylhept-1-en-4-ol (1.29 g, 10.1 mmol) and PCC (3.25 g, 15.1 mmol) in dry DCM (30 mL). The pure product was obtained as a colourless

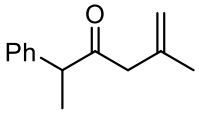
oil (0.87 g, 68 %). δ_H ($CDCl_3$, 400 MHz) 0.91 (3H, t, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.60 (2H, sxt, $^3J_{HH}$ = 7.3 Hz, CH_2), 1.75 (3H, s, CH_3), 2.43 (2H, t, $^3J_{HH}$ = 7.3 Hz, CH_2), 3.10 (2H, s, CH_2), 4.81 (1H, s, =CH_2), 4.94 (1H, s, =CH_2). δ_C ($CDCl_3$, 126 MHz) 13.7 (CH_3), 17.2 (CH_2), 22.6 (CH_3), 43.8 (CH_2), 52.2 (CH_2), 114.8 (CH_2), 139.3 (C), 208.9 (CO). m/z (ASAP) 127.1124 (MH^+, $C_8H_{15}O$ requires 127.1123, 100 %).

2,5-Dimethylhex-5-en-3-one



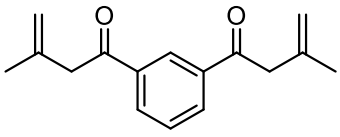
The general procedure was followed using anhydrous sodium acetate (1.12 g, 13.7 mmol), molecular sieves (9.00 g), 2,5-dimethylhex-5-en-3-ol (3.50 g, 27.3 mmol) and PCC (8.83 g, 41.0 mmol) in dry DCM (100 mL). The pure product was obtained as a colourless oil (2.84 g, 83 %). The characterisation data was in agreement with the literature.[31] δ_H ($CDCl_3$, 400 MHz) 1.03 (6H, d, $^3J_{HH}$ = 6.9 Hz, CH_3), 1.68 (3H, s, CH_3), 2.65 (1H, sept, $^3J_{HH}$ = 6.9 Hz, C*H*(CH_3)$_2$), 3.10 (2H, s, CH_2), 4.72 (1H, s, =CH_2), 4.87 (1H, s, =CH_2). δ_C ($CDCl_3$, 101 MHz) 18.3 (CH_3), 22.7 (CH_3), 40.2 (CH_2), 49.8 (CH), 114.8 (CH_2), 139.4 (C), 212.5 (CO). m/z (ASAP) 127.1120 (MH^+, $C_8H_{15}O$ requires 127.1123, 100 %).

5-Methyl-2-phenylhex-5-en-3-one



The general procedure was followed using anhydrous sodium acetate (0.43 g, 5.25 mmol), 4 Å molecular sieves (4.50 g), 5-methyl-2-phenylhex-5-en-3-ol (2.00 g, 10.5 mmol) and PCC (3.40 g, 15.8 mmol) in dry DCM (60 mL). The pure product was obtained as a colourless oil (1.85 g, 94 %). δ_H ($CDCl_3$, 400 MHz) 1.39 (3H, d, $^3J_{HH}$ = 6.9 Hz, CH(C*H*$_3$)$_2$), 1.64 (3H, s, CH_3), 3.00 (1H, d, $^2J_{HH}$ = 15.2 Hz, C*H*$_A$H$_B$), 3.10 (1H, d, $^2J_{HH}$ = 15.1 Hz, CH$_A$*H*$_B$), 3.88 (1H, q, $^3J_{HH}$ = 6.9 Hz, C*H*(CH_3)$_2$), 4.70 (1H, s, =CH_2), 4.89 (1H, s, =CH_2), 7.19 - 7.24 (2H, m, ArH), 7.25 - 7.29 (1H, m, ArH), 7.29 - 7.36 (2H, m, ArH). δ_C ($CDCl_3$, 101 MHz) 17.6 (CH_3), 22.5 (CH_3), 50.2 (CH_2), 52.0 (CH), 114.9 (CH_2), 127.2 (CH), 128.0 (CH), 128.9 (CH), 139.3 (C), 140.4 (C), 208.5 (CO). m/z (ESI) 189.1278 (MH^+, $C_{13}H_{17}O$ requires 189.1279, 100 %).

1,1'-(1,3-Phenylene)bis(3-methylbut-3-en-1-one)

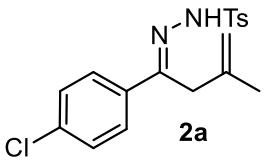


The general procedure was followed but using twice the typical equivalents of anhydrous sodium acetate anhydrous, PCC and 4 Å molecular sieves: anhydrous sodium acetate (0.87 g, 5.35 mmol), 4 Å molecular sieves (8.00 g), 1,1'-(1,3-Phenylene)bis(3-methylbut-3-en-1-ol) (2.62 g, 10.7 mmol) and PCC (6.89 g, 32.0 mmol) in dry DCM (60 mL). The pure product was obtained as a colourless oil (1.93 g, 75 %). δ_H ($CDCl_3$, 400 MHz) 1.83 (6H, s, CH_3), 3.73 (4H, s, CH_2), 4.88 (2H, s, =CH_2), 5.01 (2H, s, =CH_2), 7.57 (1H, t, $^3J_{HH}$ = 7.7 Hz, ArH), 8.17 (2H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.7 Hz, ArH),

8.58 (1H, t, $^4J_{HH}$ = 1.6 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 22.8 (CH_3), 47.9 (CH_2), 115.3 (CH_2), 128.3 (CH), 129.1 (CH), 132.6 (CH), 137.0 (C), 139.4 (C), 197.3 (CO). m/z (ESI) 243.1378 (MH^+, $C_{16}H_{19}O_2$ requires 243.1385, 100 %).

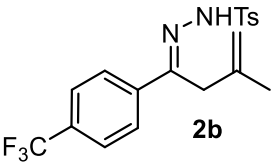
General Procedure for preparation of unsaturated tosyl hydrazones 2[32]

A flask was charged with unsaturated ketone (10 mmol) in absolute methanol (50 mL) and cooled to 0 ºC for 30 minutes. After adding tosyl hydrazide (15 mmol) at 0 ºC, the reaction mixture was stirred at 0 ºC for 30 minutes before warming to room temperature and stirring for 24 hours under an inert atmosphere. The reaction mixture was concentrated *in vacuo* and purified by column chromatography using petroleum ether : ethyl acetate (4 :1). Compounds **2a-l** were prepared using this procedure.



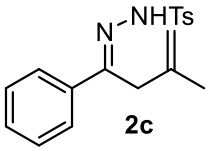
2a

The general procedure was followed using 3-methyl-1-(4-chlorophenyl)-but-3-en-1-one (300 mg, 1.5 mmol) and tosyl hydrazide (431 mg, 10.4 mmol) in absolute methanol (10 mL). (*E*)-*N*'-(1-(4-Chlorophenyl)-3-methylbut-3-en-1-ylidene)-4-methylbenzenesulfonohydrazide **2a** was obtained as a white solid (473 mg, 85 %). Mp 145-149 ºC. δ_H ($CDCl_3$, 400 MHz) 1.78 (3H, s, CH_3), 2.41 (3H, s, $ArCH_3$), 3.26 (2H, s, CH_2), 4.30 (1H, s, =CH_2), 4.76 (1H, s, =CH_2), 7.29 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.30 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 7.55 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.65 (1H, s, NH), 7.83 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 23.0 (CH_3), 36.1 (CH_2), 112.6 (CH_2), 127.6 (CH), 128.0 (CH), 128.7 (CH), 129.6 (CH), 135.2 (C), 135.3 (C), 135.8 (C), 137.8 (C), 144.3 (C), 152.2 (C). m/z (ESI) 363.0934 (MH^+, $C_{18}H_{20}{}^{35}ClN_2O_2S$ requires 363.0934, 100 %), 365.0909 (MH^+, $C_{18}H_{20}{}^{37}ClN_2O_2S$ requires 365.0905, 45 %).



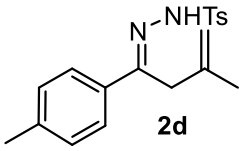
2b

The general procedure was followed using 3-methyl-1-(4-(trifluoromethyl)phenyl)-but-3-en-1-one (1.40 g, 6.1 mmol) and tosyl hydrazide (1.72 g, 9.2 mmol) in absolute methanol (25 mL). (*E*)-4-Methyl-*N*'-(3-methyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1- ylidene) benzene-sulfonohydrazide **2b** was obtained as a white solid (2.38 g, 98 %). Mp 90-93 ºC. δ_H ($CDCl_3$, 400 MHz) 1.80 (3H, s, CH_3), 2.41 (3H, s, $ArCH_3$), 3.30 (2H, s, CH_2), 4.28 (1H, s, =CH_2), 4.77 (1H, s, =CH_2), 7.30 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.59 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.72 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 7.79 (1H, s, NH), 7.84 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 23.0 (CH_3), 36.1 (CH_2), 112.8 (CH_2), 123.9 (q, $^1J_{CF}$ = 272.5 Hz, C), 125.4 (q, $^3J_{CF}$ = 3.6 Hz, CH), 126.6 (CH), 128.0 (CH), 129.6 (CH), 131.3 (q, $^2J_{CF}$ = 32.4 Hz, C), 135.1 (C), 137.6 (C), 140.2 (C), 144.4 (C), 151.7 (C). δ_F ($CDCl_3$, 376 MHz) -62.8 (s). m/z (ESI) 397.1199 (MH^+, $C_{19}H_{20}F_3N_2O_2S$ requires 397.1198, 100 %).



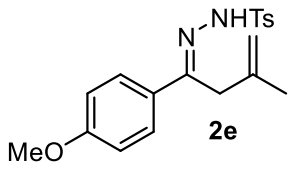
2c

The general procedure was followed using 3-methyl-1-phenylbut-3-en-1-one (2.10 g, 13.1 mmol) and tosyl hydrazide (3.66 g, 19.7 mmol) in absolute methanol (70 mL). (*E*)-4-Methyl-*N*'-(3-methyl-1-phenylbut-3-en-1-ylidene)benzenesulfonohydrazide **2c** was obtained as a white solid/colourless crystal (3.31 g, 77 %). The characterisation data was in agreement with the literature.[33] Mp 141-145 °C (lit,[33] 145-146 °C). δ_H ($CDCl_3$, 400 MHz) 1.78 (3H, s, CH_3), 2.40 (3H, s, $ArCH_3$), 3.30 (2H, s, CH_2), 4.34 (1H, s, $=CH_2$), 4.76 (1H, s, $=CH_2$), 7.29 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 7.32 - 7.37 (3H, m, ArH), 7.58 - 7.66 (3H, m, ArH and NH) 7.85 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 23.0 (CH_3), 36.3 (CH_2), 112.6 (CH_2), 126.3 (CH), 128.1 (CH), 128.4 (CH), 129.5 (CH), 129.7 (CH), 135.3 (C), 136.9 (C), 138.0 (C), 144.1 (C), 153.5 (C). m/z (ASAP) 329.1331 (MH^+, $C_{18}H_{21}N_2O_2S$ requires 329.1324, 100 %).



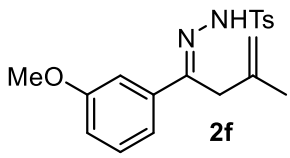
2d

The general procedure was followed using 3-methyl-1-(4-methylphenyl)-but-3-en-1-one (1.76 g, 10.1 mmol) and tosyl hydrazide (2.82 g, 15.2 mmol) in absolute methanol (50 mL). (*E*)-4-Methyl-*N*'-(3-methyl-1-(*p*-tolyl)but-3-en-1-ylidene)benzenesulfonohydrazide **2d** was obtained as a white solid (2.00 g, 58 %) after recrystallisation from DCM post chromatography. Mp 127-128 °C. δ_H ($CDCl_3$, 400 MHz) 1.76 (3H, s, CH_3), 2.34 (3H, s, $ArCH_3$), 2.39 (3H, s, $ArCH_3$), 3.27 (2H, s, CH_2), 4.31 (1H, s, $=CH_2$), 4.73 (1H, s, $=CH_2$), 7.14 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.28 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.52 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 7.64 (1H, s, NH), 7.84 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.3 (CH_3), 21.6 (CH_3), 23.0 (CH_3), 36.2 (CH_2), 112.5 (CH_2), 126.3 (CH), 128.1 (CH), 129.1 (CH), 129.5 (CH), 134.1 (C), 135.3 (C), 138.2 (C), 139.9 (C), 144.0 (C), 153.5 (C). m/z (ASAP) 343.1485 (MH^+, $C_{19}H_{23}N_2O_2S$ requires 343.1480, 100 %).



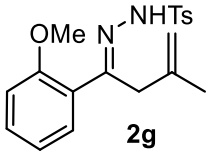
2e

The general procedure was followed using 3-methyl-1-(4-methoxyphenyl)-but-3-en-1-one (2.68 g, 14.1 mmol) and tosyl hydrazide (3.94 g, 21.1 mmol) in absolute methanol (75 mL). (*E*)-*N*'-(1-(4-Methoxyphenyl)-3-methylbut-3-en-1-ylidene)-4-methylbenzenesulfonohydrazide **2e** was obtained as a white solid (3.68 g, 86 %). Mp 136-138 °C. δ_H ($CDCl_3$, 500 MHz) 1.77 (3H, s, CH_3), 2.40 (3H, s, $ArCH_3$), 3.27 (2H, s, CH_2), 3.81 (3H, s, OCH_3), 4.30 (1H, s, $=CH_2$), 4.73 (1H, s, $=CH_2$), 6.85 (2H, d, $^3J_{HH}$ = 8.9 Hz, ArH), 7.29 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.53 (1H, s, NH), 7.58 (2H, d, $^3J_{HH}$ = 8.9 Hz, ArH), 7.85 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 23.0 (CH_3), 36.1 (CH_2), 55.3 (CH_3), 112.4 (CH_2), 113.8 (CH), 127.8 (CH), 128.1 (CH), 129.4 (C), 129.5 (CH), 135.3 (C), 138.2 (C), 144.0 (C), 153.4 (C), 160.9 (C). m/z (ESI) 359.1435 (MH^+, $C_{19}H_{23}N_2O_3S$ requires 359.1429, 100 %).



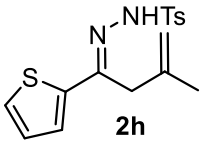
2f

The general procedure was followed using 3-methyl-1-(3-methoxyphenyl)-but-3-en-1-one (1.80 g, 9.5 mmol) and tosyl hydrazide (2.65 g, 14.2 mmol) in absolute methanol (50 mL). (*E*)-*N*'-(1-(3-Methoxyphenyl)-3-methylbut-3-en-1-ylidene)-4-methylbenzenesulfonohydrazide **2f** was obtained as a white solid (2.17 g, 64 %). Mp 126-128 ºC. δ_H ($CDCl_3$, 400 MHz) 1.77 (3H, s, CH_3), 2.40 (3H, s, $ArCH_3$), 3.28 (2H, s, CH_2), 3.81 (3H, s, OCH_3), 4.33 (1H, s, $=CH_2$), 4.75 (1H, s, $=CH_2$), 6.91 (1H, dd, $^4J_{HH}$ = 2.5 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.14 - 7.21 (2H, m, ArH), 7.22 - 7.27 (1H, m, ArH), 7.29 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.66 (1H, s, NH), 7.85 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 100 MHz) 21.6 (CH_3), 23.0 (CH_3), 36.4 (CH_2), 55.3 (CH_3), 111.7 (CH), 112.6 (CH_2), 115.4 (CH), 118.9 (CH), 128.1 (CH), 129.4 (CH), 129.5 (CH), 135.2 (C), 138.0 (C), 138.3 (C), 144.2 (C), 153.3 (C), 159.6 (C). m/z (ESI) 359.1432 (MH^+, $C_{19}H_{23}N_2O_3S$ requires 359.1429, 100 %).



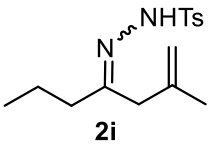
2g

The general procedure was followed using 3-methyl-1-(2-methoxyphenyl)-but-3-en-1-one (1.60 g, 8.4 mmol) and tosyl hydrazide (2.40 g, 12.6 mmol) in absolute methanol (50 mL). (*E*)-*N*'-(1-(2-Methoxyphenyl)-3-methylbut-3-en-1-ylidene)-4-methylbenzenesulfonohydrazide **2g** was obtained as a white solid (2.18 g, 79 %). Mp 135-37 ºC. δ_H ($CDCl_3$, 400 MHz) 1.63 (3H, s, CH_3), 2.44 (3H, s, $ArCH_3$), 3.35 (2H, s, CH_2), 3.76 (3H, s, OCH_3), 4.46 (1H, s, $=CH_2$), 4.76 (1H, s, $=CH_2$), 6.84 (1H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 6.89 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.11 (1H, dd, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.8 Hz, ArH), 7.28 - 7.36 (3H, m, ArH), 7.85 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.94 (1H, s, NH). δ_C ($CDCl_3$, 126 MHz) 21.7 (CH_3), 22.7 (CH_3), 39.5 (CH_2), 55.3 (CH_3), 111.0 (CH), 112.5 (CH_2), 120.6 (CH), 128.0 (C), 128.1 (CH), 129.4 (CH), 130.2 (CH), 130.6 (CH), 135.5 (C), 138.9 (C), 144.0 (C), 155.3 (C), 157.4 (C). m/z (ESI) 359.1429 (MH^+, $C_{19}H_{23}N_2O_3S$ requires 359.1429, 100 %).



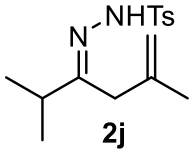
2h

The general procedure was followed using 3-methyl-1-(thiophen-2-yl)but-3-en-1-one (2.34 g, 14.1 mmol) and tosyl hydrazide (3.93 g, 21.1 mmol) in absolute methanol (60 mL) for 96 hours. (*E*)-4-Methyl-*N*'-(3-methyl-1-(thiophen-2-yl)but-3-en-1-ylidene)benzenesulfonohydrazide **2h** was obtained as a pale yellow solid (3.45 g, 73 %). Mp 156-157 ºC. δ_H ($CDCl_3$, 400 MHz) 1.71 (3H, s, CH_3), 2.41 (3H, s, $ArCH_3$), 3.31 (2H, s, CH_2), 4.41 (1H, s, $=CH_2$), 4.77 (1H, s, $=CH_2$), 6.96 (1H, dd, $^3J_{HH}$ = 5.0 Hz, $^3J_{HH}$ = 3.8 Hz, ArH), 7.17 (1H, dd, $^3J_{HH}$ = 3.6 Hz, $^4J_{HH}$ = 0.9 Hz, ArH), 7.27 - 7.33 (3H, m, ArH), 7.57 (1H, s, NH), 7.87 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 22.7 (CH_3), 36.8 (CH_2), 113.1 (CH_2), 126.9 (CH), 127.2 (CH), 128.2 (CH), 128.7 (CH), 129.5 (CH), 135.1 (C), 138.0 (C), 142.4 (C), 144.2 (C), 149.4 (C). m/z (ESI) 335.0889 (MH^+, $C_{16}H_{19}N_2O_2S_2$ requires 335.0888, 100 %).



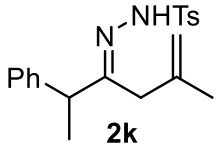
2i

The general procedure was followed using 2-methylhept-1-en-4-one (0.87 g, 6.9 mmol) and tosyl hydrazide (1.92 g, 10.3 mmol) in absolute methanol (25 mL). The inseparable 60:40 mixture of (*Z*)- and (*E*)-4-Methyl-*N*'-(2-methylhept-1-en-4-ylidene)benzenesulfonohydrazide **2i** was obtained as a white solid (1.63 g, 81 %). Mp 67-70 ^{o}C (of mixture 60:40). δ_H ($CDCl_3$, 400 MHz) 0.83 (3H, t, $^3J_{HH}$ = 7.3 Hz, Major CH_3), 0.88 (3H, t, $^3J_{HH}$ = 7.3 Hz, Minor CH_3), 1.36 - 1.53 (7H, m, Major CH_2, Minor CH_2 and Minor CH_3), 1.66 (3H, s, Major CH_3), 2.00 - 2.10 (2H, m, Minor CH_2), 2.11 - 2.20 (2H, m, Major CH_2), 2.42 (3H, s, Minor $ArCH_3$), 2.43(3H, s, Major $ArCH_3$), 2.84 (2H, s, Major CH_2), 2.87 (2H, s, Minor CH_2), 4.30 (1H, s, Major $=CH_2$), 4.64 (1H, s, Minor $=CH_2$), 4.72 (1H, s, Major $=CH_2$), 4.77 (1H, s, Minor $=CH_2$), 7.29 (4H, d, $^3J_{HH}$ = 8.0 Hz, Major and Minor ArH), 7.50 (1H, s, Major NH), 7.56 (1H, s, Minor NH), 7.80 (2H, d, $^3J_{HH}$ = 8.4 Hz, Major ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.4 Hz, Minor ArH). δ_C ($CDCl_3$, 126 MHz) 13.7 (CH_3), 14.1 (CH_3), 18.5 (CH_2), 19.1 (CH_2), 21.57 (CH_3), 21.60 (CH_3), 22.9 (CH_3), 30.2 (CH_2), 38.6 (CH_2), 40.2 (CH_2), 45.8 (CH_2), 112.4 (CH_2), 113.7 (CH_2), 127.9 (C), 128.0 (C), 128.1 (CH), 129.3 (CH), 129.41 (C), 129.45 (C), 135.3 (C), 138.2 (C), 143.9 (C), 158.3 (C). m/z (ASAP) 295.1468 (MH^+, $C_{15}H_{23}N_2O_2S$ requires 295.1480, 100 %).



2j

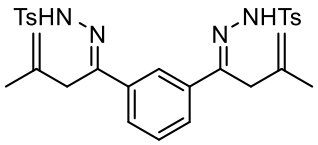
The general procedure was followed using 2,5-dimethylhex-5-en-3-one (2.92 g, 23.2 mmol) and tosyl hydrazide (6.46 g, 34.7 mmol) in absolute methanol (100 mL). (*E*)-*N*'-(2,5-Dimethylhex-5-en-3-ylidene)-4-methylbenzenesulfonohydrazide **2j** was obtained as a white solid (1.79 g, 26 %). Mp 78-80 ^{o}C. δ_H ($CDCl_3$, 400 MHz) 0.94 (6H, d, $^3J_{HH}$ = 6.9 Hz, CH_3), 1.60 (3H, s, CH_3), 2.35 (1H, sept, $^3J_{HH}$ = 6.9 Hz, C*H*$(CH_3)_2$), 2.36 (3H, s, $ArCH_3$), 2.77 (2H, s, CH_2), 4.07 - 4.13 (1H, s, $=CH_2$), 4.63 (1H, s, $=CH_2$), 7.22 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 7.32 (1H, s, NH), 7.73 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). δ_C ($CDCl_3$, 101 MHz) 19.5 (CH_3), 21.6 (CH_3), 23.0 (CH_3), 36.7 (CH), 36.9 (CH_2), 112.3 (CH_2), 128.1 (CH), 129.3 (CH), 135.3 (C), 138.2 (C), 143.9 (C), 161.8 (C). m/z (ESI) 295.1481 (MH^+, $C_{15}H_{23}N_2O_2S$ requires 295.1480, 100 %).



2k

The general procedure was followed using 5-methyl-2-phenylhex-5-en-3-one (0.88 g, 4.7 mmol) and tosyl hydrazide (1.30 g, 10.3 mmol) in absolute methanol (25 mL). (*E*)-4-methyl-*N*'-(5-methyl-2-phenylhex-5-en-3-ylidene)benzene-sulfonohydrazide **2k** was obtained as a white solid (1.12 g, 67 %). Mp 117-119 ^{o}C. δ_H ($CDCl_3$, 500 MHz) 1.35 (3H, d, $^3J_{HH}$ = 7.0 Hz, CH_3), 1.50 (3H, s, CH_3), 2.47 (3H, s, $ArCH_3$), 2.63 (1H, d, $^2J_{HH}$ = 16.8 Hz, C*H*$_A$H$_B$), 2.71 (1H, d, $^2J_{HH}$ = 16.8 Hz, CH$_A$*H*$_B$), 3.52 (1H, q, $^3J_{HH}$ = 6.9 Hz, C*H*(CH_3)), 4.20 (1H, s, $=CH_2$), 4.67 (1H, s, $=CH_2$), 7.06 (2H, d, $^3J_{HH}$ = 6.5 Hz, ArH), 7.18 - 7.24 (3H, m, ArH), 7.32 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.53 (1H, s, NH), 7.83 (2H, d, $^3J_{HH}$ = 8.2 Hz). δ_C ($CDCl_3$, 126 MHz) 18.7 (CH_3), 21.7 (CH_3), 22.7 (CH_3), 37.8 (CH_2), 47.9 (CH), 112.7 (CH_2), 126.9

(CH), 127.8 (CH), 128.2 (CH), 128.6 (CH), 129.3 (CH), 135.3 (C), 138.3 (C), 141.7 (C), 144.0 (C), 158.9 (C). m/z (ESI) 357.1642 (MH^+, $C_{20}H_{25}N_2O_2S$ requires 357.1637, 100 %).

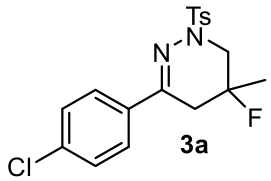


2l

The general procedure was followed but using twice the typical equivalents of tosyl hydrazide: 1,1'-(1,3-Phenylene)bis(3-methylbut-3-en-1-one) (1.00 g, 4.1 mmol) and tosyl hydrazide (2.31 g, 12.4 mmol) in absolute methanol (25 mL). *N*',*N*'''-((1*E*,1'*E*)-1,3-Phenylenebis(3-methylbut-3-en-1-yl-1-ylidene))bis(4-methylbenzenesulfono-hydrazide) **2l** was obtained as a white solid (1.48 g, 62 %). Mp 168-170 °C. δ_H ($CDCl_3$, 400 MHz) 1.79 (6H, s, CH_3), 2.40 (6H, s, $ArCH_3$), 3.29 (4H, s, CH_2), 4.34 (2H, s, $=CH_2$), 4.78 (2H, s, $=CH_2$), 7.27 - 7.34 (5H, m, ArH), 7.58 (2H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.8 Hz, ArH), 7.68 (2H, s, NH), 7.84 (4H, d, $^2J_{HH}$ = 8.3 Hz, ArH), 7.96 (1H, t, $^4J_{HH}$ = 1.7 Hz, ArH). δ_C ($CDCl_3$, 101 MHz) 21.6 (CH_3), 23.0 (CH_3), 36.2 (CH_2), 112.8 (CH_2), 124.1 (CH), 127.4 (CH), 128.0 (CH), 128.6 (CH), 129.6 (CH), 135.2 (C), 137.1 (C), 138.0 (C), 144.3 (C), 152.7 (C). m/z (ESI) 579.2100 (MH^+, $C_{30}H_{35}N_4O_4S_2$ requires 579.2100, 100 %).

General Procedure A for fluorocyclisations of unsaturated tosyl hydrazones 2 using fluoroiodane and $AgBF_4$ (Scheme 2)

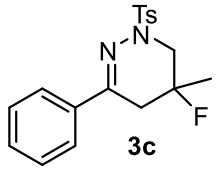
A Schlenk flask was charged with unsaturated tosyl hydrazone (0.71 mmol), $AgBF_4$ (140 mg, 0.71 mmol), fluoroiodane (300 mg, 1.07 mmol), 4 Å powdered molecular sieves (180 mg) in dry DCM (2.5 mL) under an inert atmosphere. The reaction mixture was stirred for 15 minutes at room temperature before being concentrated *in vacuo* and the crude product was purified by column chromatography using petroleum ether : ethyl acetate (4:1). Fluorinated tetrahydropyridazines **3a**, **3c**, **3d**, **3e** and **3i** were prepared using this procedure.



3a

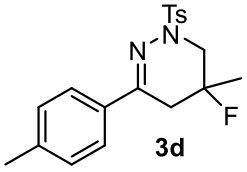
3-(4-Chlorophenyl)-5-fluoro-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3a** was obtained as a white solid (246 mg, 91 %). Crystals suitable for X-ray crystallography were grown by slow evaporation from a DCM and hexane (1:2) solution. Mp 186-189 °C. δ_H ($CDCl_3$, 400 MHz) 1.56 (3H, d, $^3J_{HF}$ = 20.7 Hz, CH_3), 2.40 (3H, s, $ArCH_3$), 2.55 (1H, ddd, $^3J_{HF}$ = 26.2 Hz, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH_D), 2.81 (1H, t, $^2J_{HH}$ = $^3J_{HF}$ = 18.2 Hz, CH_CH_D), 3.21 (1H, dd, $^3J_{HF}$ = 23.3 Hz, $^2J_{HH}$ = 11.8 Hz, NCH_AH_B), 3.77 (1H, ddd, $^2J_{HH}$ = 11.8 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 2.0 Hz, NCH_AH_B), 7.30 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH) 7.33 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.61 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.82 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.56 (3H, s, CH_3), 2.40 (3H, s, $ArCH_3$), 2.55 (1H, dd, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH_D), 2.81 (1H, d, $^2J_{HH}$ = 18.4 Hz, CH_CH_D), 3.21 (1H, d, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B),

3.77 (1H, dd, $^2J_{HH}$ = 11.8 Hz, $^4J_{HH}$ = 2.1 Hz, NCH$_A$*H*$_B$), 7.30 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH) 7.33 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.61 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.82 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 24.8 (d, $^2J_{CF}$ = 24.1 Hz, CH_3), 35.0 (d, $^2J_{CF}$ = 26.1 Hz, CH_2), 50.3 (d, $^2J_{CF}$ = 25.1 Hz, CH_2), 87.6 (d, $^1J_{CF}$ = 175.7 Hz, C), 126.7 (CH), 128.4 (CH), 128.7 (CH), 129.6 (CH), 133.2 (C), 134.4 (C), 135.8 (C), 144.4 (C), 145.9 (C). δ_F ($CDCl_3$, 376 MHz) -142.1 (s). m/z (ESI) 381.0841 (MH^+, $C_{18}H_{19}{}^{35}ClFN_2O_2S$ requires 381.0840, 100 %), 383.0816 (MH^+, $C_{18}H_{19}{}^{37}ClFN_2O_2S$ requires 383.0810, 40 %).



3c

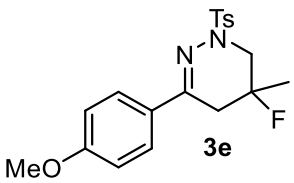
5-Fluoro-5-methyl-3-phenyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3c** was obtained as a white solid (229 mg, 93 %). Crystals suitable for X-ray crystallography were grown by slow evaporation from a DCM and hexane (1:2) solution. Mp 157-158 ºC. δ_H ($CDCl_3$, 400 MHz) 1.56 (3H, d, $^3J_{HF}$ = 20.5 Hz, CH_3), 2.40 (3H, s, ArCH_3), 2.59 (1H, ddd, $^3J_{HF}$ = 25.3 Hz, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.6 Hz, C*H*$_C$H$_D$), 2.86 (1H, t, $^2J_{HH}$ = $^3J_{HF}$ = 18.4 Hz, CH$_C$*H*$_D$), 3.21 (1H, dd, $^3J_{HF}$ = 22.5 Hz, $^2J_{HH}$ = 11.7 Hz, NC*H*$_A$H$_B$), 3.72 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 2.0 Hz, NCH$_A$*H*$_B$), 7.30 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.33 - 7.43 (3H, m, ArH), 7.59 - 7.74 (2H, m, ArH), 7.85 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.56 (3H, s, CH_3), 2.40 (3H, s, ArCH_3), 2.59 (1H, br d, $^2J_{HH}$ = 18.2 Hz, C*H*$_C$H$_D$), 2.86 (1H, br d, $^2J_{HH}$ = 18.4 Hz, CH$_C$*H*$_D$), 3.24 (1H, br d, $^2J_{HH}$ = 11.7 Hz, NC*H*$_A$H$_B$), 3.72 (1H, dd, $^2J_{HH}$ = 11.7 Hz, $^4J_{HH}$ = 1.8 Hz, NC*H*$_A$H$_B$), 7.30 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.34 - 7.40 (3H, m ArH), 7.63 - 7.71 (2H, m, ArH), 7.85 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) [overlapping CH signals at 128.4] 21.6 (CH_3), 24.9 (d, $^2J_{CF}$ = 24.1 Hz, CH_3), 35.2 (d, $^2J_{CF}$ = 25.1 Hz, CH_2), 50.5 (d, $^2J_{CF}$ = 26.1 Hz, CH_2), 87.9 (d, $^1J_{CF}$ =175.7 Hz, C), 125.5 (CH), 128.4 (CH), 129.6 (CH), 129.8 (CH), 133.3 (C), 135.9 (C), 144.2 (C), 147.2 (C). δ_F ($CDCl_3$, 376 MHz) -141.9 (s). m/z (ESI) 347.1231 (MH^+, $C_{18}H_{20}FN_2O_2S$ requires 347.1230, 100 %).



3d

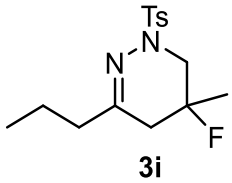
5-Fluoro-5-methyl-3-(*p*-tolyl)-1-tosyl-1,4,5,6-tetrahydropyridazine **3d** was obtained as a white solid (241 mg, 94 %). Mp 161-163 ºC. δ_H ($CDCl_3$, 400 MHz) 1.55 (3H, d, $^3J_{HF}$ = 20.7 Hz, CH_3), 2.36 (3H, s, ArCH_3), 2.39 (3H, s, ArCH_3), 2.57 (1H, ddd, $^3J_{HF}$ = 25.0 Hz, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.9 Hz C*H*$_C$H$_D$), 2.83 (1H, t, $^2J_{HH}$ = $^3J_{HF}$ = 18.4 Hz, CH$_C$*H*$_D$), 3.23 (1H, br dd, $^3J_{HF}$ = 22.3 Hz, $^2J_{HH}$ = 11.7 Hz, NC*H*$_A$H$_B$), 3.68 (1H, ddd, $^2J_{HH}$ = 11.6 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 1.9 Hz, NCH$_A$*H*$_B$), 7.17 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.29 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.58 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 7.84 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.55 (3H, s, CH_3), 2.36 (3H, s, ArCH_3), 2.39 (3H, s, ArCH_3), 2.57 (1H, br d, $^2J_{HH}$ = 18.4 Hz, C*H*$_C$H$_D$), 2.83 (1H, br d, $^2J_{HH}$ = 18.4 Hz, CH$_C$*H*$_D$), 3.23 (1H, br d, $^2J_{HH}$ = 11.7 Hz, NC*H*$_A$H$_B$), 3.68 (1H, dd, $^2J_{HH}$ = 11.7 Hz, $^4J_{HH}$ = 1.9 Hz, NCH$_A$*H*$_B$), 7.17 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH),

7.29 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.58 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 7.84 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) [overlapping C signals at 133.2] 21.3 (CH_3), 21.6 (CH_3), 24.9 (d, $^2J_{CF}$ = 24.1 Hz, CH_3), 35.2 (d, $^2J_{CF}$ = 25.1 Hz, CH_2), 50.5 (d, $^2J_{CF}$ = 26.1 Hz, CH_2), 88.0 (d, $^1J_{CF}$ = 175.7 Hz, C), 125.4 (CH), 128.4 (CH), 129.1 (CH), 129.5 (CH), 133.2 (C), 139.9 (C), 144.2 (C), 147.4 (C). δ_F ($CDCl_3$, 376 MHz) -141.7 (s). m/z (ESI) 361.1382 (MH^+, $C_{19}H_{22}FN_2O_2S$ requires 361.1386, 100 %).



3e

5-Fluoro-3-(4-methoxyphenyl)-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3e** was obtained as a white solid (243 mg, 91 %). Mp 163-165 °C. δ_H ($CDCl_3$, 400 MHz) 1.55 (3H, d, $^3J_{HF}$ = 20.7 Hz, CH_3), 2.40 (3H, s, $ArCH_3$), 2.57 (1H, ddd, $^3J_{HF}$ = 26.4 Hz, $^2J_{HH}$ = 18.5 Hz, $^4J_{HH}$ = 1.5 Hz, CH_CH_D), 2.82 (1H, t, $^2J_{HH}$ = $^3J_{HF}$ = 18.5 Hz, CH_CH_D), 3.21 (1H, dd, $^3J_{HF}$ = 22.0 Hz, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B), 3.66 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 1.8 Hz, NCH_AH_B), 3.83 (3H, s, OCH_3), 6.88 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.30 (2H, d, $^3J_{HH}$ = 8.1 Hz, ArH), 7.63 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.84 (2H, d, $^3J_{HH}$ = 8.1 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.55 (3H, s, CH_3), 2.39 (3H, s, $ArCH_3$), 2.57 (1H, dd, $^2J_{HH}$ = 18.5 Hz, $^4J_{HH}$ = 1.5 Hz, CH_CH_D), 2.82 (1H, br. d, $^2J_{HH}$ = 18.5 Hz, CH_CH_D), 3.21 (1H, br. d, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B), 3.67 (1H, dd, $^2J_{HH}$ = 11.7 Hz, $^4J_{HH}$ = 1.9 Hz, NCH_AH_B), 3.82 (3H, s, OCH_3), 6.87 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.30 (2H, d, $^3J_{HH}$ = 8.1 Hz, ArH), 7.63 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.84 (2H, d, $^3J_{HH}$ = 8.1 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 24.9 (d, $^2J_{CF}$ = 24.1 Hz, CH_3), 35.2 (d, $^2J_{CF}$ = 25.1 Hz, CH_2), 50.5 (br d, $^2J_{CF}$ = 27.1 Hz, CH_2), 55.4 (CH_3), 88.1 (d, $^1J_{CF}$ = 175.7 Hz, C), 113.8 (CH), 127.0 (CH), 128.5 (CH), 128.6 (C), 129.5 (CH), 133.2 (C), 144.2 (C), 147.2 (C), 160.9 (C). δ_F ($CDCl_3$, 376 MHz) -141.6 (s). m/z (ESI) 377.1344 (MH^+, $C_{19}H_{22}FN_2O_3S$ requires 377.1335, 100 %).



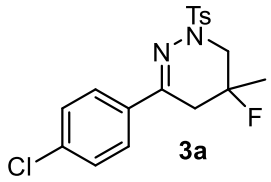
3i

5-Fluoro-5-methyl-3-propyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3i** was obtained as a white solid (180 mg, 81 %). Mp 75-77 °C. δ_H ($CDCl_3$, 400 MHz) 0.82 (3H, t, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.45 (3H, d, $^3J_{HF}$ = 20.8 Hz, CH_3), 1.50 (2H, sxt, $^3J_{HH}$ = 7.4 Hz, CH_2), 2.07 - 2.19 (3H, m, CH_2 and CH_CH_D), 2.33 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.5 Hz, CH_CH_D), 2.42 (3H, s, $ArCH_3$), 3.09 (1H, dd, $^3J_{HF}$ = 21.9 Hz, $^2J_{HH}$ = 11.5 Hz, NCH_AH_B), 3.49 (1H, ddd, $^2J_{HH}$ = 11.5 Hz, $^3J_{HF}$ = 8.2 Hz, $^4J_{HH}$ = 1.9 Hz, NCH_AH_B), 7.29 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.78 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 0.82 (3H, t, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.45 (3H, s, CH_3), 1.50 (2H, sxt, $^3J_{HH}$ = 7.4 Hz, CH_2), 2.09 - 2.20 (3H, m, CH_2 and CH_CH_D), 2.31 (1H, d, $^2J_{HH}$ = 18.8 Hz, CH_CH_D), 2.42 (3H, s, $ArCH_3$), 3.09 (1H, br d, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B), 3.49 (1H, dd, $^2J_{HH}$ = 11.7 Hz, $^4J_{HH}$ = 1.8 Hz, NCH_AH_B), 7.29 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.78 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 13.4 (CH_3), 19.4 (CH_2), 21.6 (CH_3), 24.7 (d, $^2J_{CF}$ = 24.1 Hz, CH_3), 37.5 (d, $^2J_{CF}$ = 25.1 Hz, CH_2), 39.0 (CH_2), 50.7 (d, $^2J_{CF}$ = 27.1 Hz, CH_2), 88.1 (d, $^1J_{CF}$ =

175.7 Hz, C), 128.5 (CH), 129.3 (CH), 132.9 (C), 144.0 (C), 153.3 (C). δ_F ($CDCl_3$, 376 MHz) -141.7 (s). m/z (ESI) 313.1381 (MH^+, $C_{15}H_{22}FN_2O_2S$ requires 313.1386, 100 %).

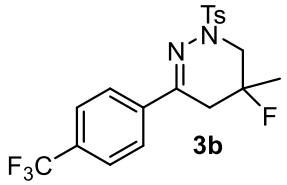
General Procedure B for fluorocyclisations of unsaturated tosyl hydrazones 2 using fluoroiodane in HFIP (Scheme 2)

A Schlenk flask was charged with unsaturated tosyl hydrazone (0.71 mmol), fluoroiodane **1** (300 mg, 1.07 mmol), 4 Å powdered molecular sieves (180 mg) and dry HFIP (1.2 mL) under an inert atmosphere. The reaction mixture was stirred for 15 minutes at room temperature before being concentrated *in vacuo* and the crude product was purified by column chromatography using petroleum ether : ethyl acetate (4:1). Fluorinated tetrahydropyridazines **3a-l** were prepared using this procedure.



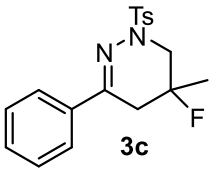
3a

3-(4-Chlorophenyl)-5-fluoro-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3a** was obtained as a white solid (250 mg, 93 %).



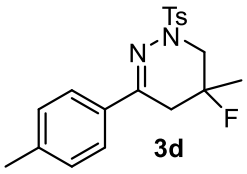
3b

5-Fluoro-5-methyl-1-tosyl-3-(4-(trifluoromethyl)phenyl)-1,4,5,6-tetra-hydropyridazine **3b** was obtained as a white solid (265 mg, 90 %). Mp 197-198 ºC. δ_H ($CDCl_3$, 400 MHz) 1.58 (3H, d, $^3J_{HF}$ = 20.2 Hz, CH_3), 2.41 (3H, s, $ArCH_3$), 2.58 (1H, ddd, $^3J_{HF}$ = 27.0 Hz, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.6 Hz, CH_CH$_D$), 2.85 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.4 Hz, CH$_C$$H_D$), 3.24 (1H, dd, $^3J_{HF}$ = 24.5 Hz, $^2J_{HH}$ = 11.9 Hz, NCH_AH$_B$), 3.84 (1H, ddd, $^2J_{HH}$ = 12.0 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 2.1 Hz, NCH$_A$$H_B$), 7.31 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.62 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 7.78 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.58 (3H, s, CH_3), 2.41 (3H, s, $ArCH_3$), 2.58 (1H, dd, $^2J_{HH}$ =18.4 Hz, $^4J_{HH}$ = 1.6 Hz, CH_CH$_D$), 2.85 (1H, d, $^2J_{HH}$ =18.4 Hz, CH$_C$$H_D$), 3.24 (1H, d, $^2J_{HH}$ = 11.9 Hz, NCH_AH$_B$), 3.84 (1H, dd, $^2J_{HH}$ = 12.0 Hz, $^4J_{HH}$ = 2.1 Hz, NCH$_A$$H_B$), 7.31 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.62 (2H, d, $^3J_{HH}$ = 8.6 Hz, ArH), 7.78 (2H, d, $^3J_{HH}$ = 8.6 Hz, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 100 MHz) 21.6 (CH_3), 24.8 (d, $^2J_{CF}$ = 24.0 Hz, CH_3), 35.0 (d, $^2J_{CF}$ = 25.6 Hz, CH_2), 50.3 (d, $^2J_{CF}$ = 25.6 Hz, CH_2), 87.4 (d, $^1J_{CF}$ = 176.2 Hz, C), 123.9 (q, $^1J_{CF}$ = 272.2 Hz, C), 125.4 (q, $^3J_{CF}$ = 3.8 Hz, CH), 125.7 (CH), 128.3 (CH), 129.7 (CH), 131.4 (q, $^2J_{CF}$ = 32.3 Hz, C), 133.3 (C), 139.2 (C), 144.5 (C), 145.3 (C). δ_F ($CDCl_3$, 376 MHz) -62.8 (3F, s, CF_3), -142.3 (1F, s, $CF(CH_3)$). m/z (ESI) 415.1102 (MH^+, $C_{19}H_{19}F_4N_2O_2S$ requires 415.1103, 100 %).



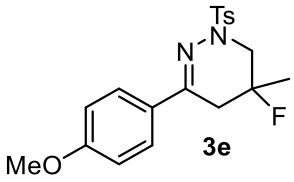
3c

5-Fluoro-5-methyl-3-phenyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3c** was obtained as a white solid (243 mg, 99 %).



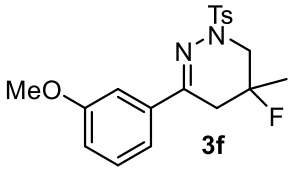
3d

5-Fluoro-5-methyl-3-(*p*-tolyl)-1-tosyl-1,4,5,6-tetrahydropyridazine **3d** was obtained as a white solid (233 mg, 92 %).



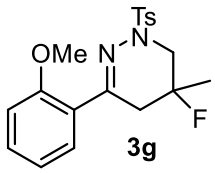
3e

5-Fluoro-3-(4-methoxyphenyl)-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3e** was obtained as a white solid (240 mg, 90 %).



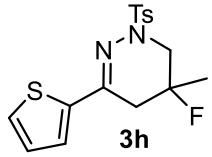
3f

5-Fluoro-3-(3-methoxyphenyl)-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3f** was obtained as an off-white solid (253 mg, 95 %). Mp 114-116 ºC. δ_H ($CDCl_3$, 400 MHz) 1.55 (3H, d, $^3J_{HF}$ = 20.5 Hz, CH_3), 2.40 (3H, s, $ArCH_3$), 2.57 (1H, ddd, $^3J_{HF}$ = 26.1 Hz, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.8 Hz, CH_CH_D), 2.83 (1H, td, $^2J_{HH} = {}^3J_{HF}$ = 18.2 Hz, $^4J_{HH}$ = 1.0 Hz, CH_CH_D), 3.21 (1H, ddd, $^3J_{HF}$ = 23.1 Hz, $^2J_{HH}$ = 11.8 Hz, $^4J_{HH}$ = 1.8 Hz, NCH_AH_B), 3.74 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 7.6 Hz, $^4J_{HH}$ = 2.0 Hz, NCH_AH_B), 3.84 (3H, s, OCH_3), 6.91 (1H, ddd, $^3J_{HH}$ = 8.1 Hz, $^4J_{HH}$ = 2.4 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.21 (1H, dt, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.5 Hz, ArH), 7.24 - 7.27 (2H, m, ArH), 7.30 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.84 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.55 (3H, s, CH_3), 2.39 (3H, s, $ArCH_3$), 2.57 (1H, dd, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.8 Hz, CH_CH_D), 2.84 (1H, d, $^2J_{HH}$ = 18.4 Hz, CH_CH_D), 3.21 (1H, d, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B), 3.75 (1H, d, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B), 3.83 (3H, s, OCH_3), 6.91 (1H, ddd, $^3J_{HH}$ = 8.1, $^4J_{HH}$ = 2.5 Hz, $^4J_{HH}$ = 1.1 Hz, ArH), 7.18 - 7.23 (1H, m, ArH), 7.24 - 7.27 (2H, m, ArH), 7.29 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.84 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 24.9 (d, $^2J_{CF}$ = 24.0 Hz, CH_3), 35.3 (d, $^2J_{CF}$ = 25.6 Hz, CH_2), 50.4 (d, $^2J_{CF}$ = 25.7 Hz, CH_2), 55.3 (CH_3), 87.9 (d, $^1J_{CF}$ = 175.9 Hz, C), 110.8 (CH), 115.6 (CH), 118.0 (CH), 128.5 (CH), 129.4 (CH), 129.6 (CH), 133.3 (C), 137.4 (C), 144.3 (C), 147.0 (d, $^3J_{CF}$ = 1.9 Hz, C), 159.6 (C). δ_F ($CDCl_3$, 376 MHz) -141.9 (s). m/z (ESI) 377.1336 (MH^+, $C_{19}H_{22}FN_2O_3S$ requires 377.1335, 100 %).



3g

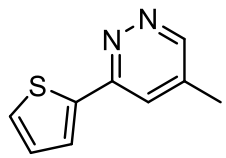
5-Fluoro-3-(2-methoxyphenyl)-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3g** pure product was obtained as a white solid (232 mg, 87 %). Mp 133-135 ºC. δ_H ($CDCl_3$, 400 MHz) 1.51 (3H, d, $^3J_{HF}$ = 20.5, CH_3), 2.43 (3H, s, $ArCH_3$), 2.72 (1H, ddd, $^3J_{HF}$ = 24.4 Hz, $^2J_{HH}$ = 18.6 Hz, $^4J_{HH}$ = 1.0 Hz, CH_CH_D), 2.83 (1H, td, $^3J_{HF}$ = $^2J_{HH}$ = 18.6 Hz, $^4J_{HH}$ = 1.0 Hz, CH_CH_D), 3.27 (1H, ddd, $^3J_{HF}$ = 24.4 Hz, $^2J_{HH}$ = 12.0 Hz, $^4J_{HH}$ = 1.0 Hz, NCH_AH_B), 3.74 (1H, ddd, $^2J_{HH}$ = 12.0 Hz, $^3J_{HF}$ = 10.5 Hz, $^4J_{HH}$ = 2.1 Hz, NCH_AH_B), 3.78 (3H, s, OCH_3), 6.86 (1H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 0.8 Hz, ArH), 6.93 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.28 - 7.35 (4H, m, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.50 (3H, s, CH_3), 2.43 (3H, s, $ArCH_3$), 2.72 (1H, dd, $^2J_{HH}$ = 18.6 Hz, $^4J_{HH}$ = 1.0 Hz, CH_CH_D), 2.83 (1H, dd, $^2J_{HH}$ = 18.6 Hz, $^4J_{HH}$ = 1.5 Hz, CH_CH_D), 3.27 (1H, d, $^2J_{HH}$ = 12.0 Hz, NCH_AH_B), 3.74 (1H, dd, $^2J_{HH}$ = 12.0 Hz, $^4J_{HH}$ = 2.1 Hz, NCH_AH_B), 3.78 (3H, s, OCH_3), 6.87 (1H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 0.8 Hz, ArH), 6.93 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.29 - 7.35 (4H, m, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.4 Hz, ArH). δ_C ($CDCl_3$, 100 MHz) 21.6 (CH_3), 24.7 (d, $^2J_{CF}$ = 24.2 Hz, CH_3), 38.3 (d, $^2J_{CF}$ = 24.8 Hz, CH_2), 51.0 (d, $^2J_{CF}$ = 25.7 Hz, CH_2), 55.4 (CH_3), 88.0 (d, $^1J_{CF}$ = 175.1 Hz, C), 111.1 (CH), 120.8 (CH), 126.6 (C), 128.5 (CH), 129.4 (CH), 129.9 (CH), 130.6 (CH), 133.5 (C), 144.0 (C), 150.4 (d, $^3J_{CF}$ = 2.3 Hz, C), 157.5 (C). δ_F ($CDCl_3$, 376 MHz) -142.3 (s). m/z (ESI) 377.1340 (MH^+, $C_{19}H_{22}FN_2O_3S$ requires 377.1335, 100 %).



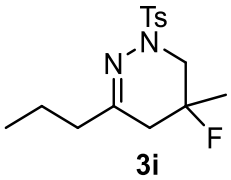
3h

5-Fluoro-5-methyl-3-(thiophen-2-yl)-1-tosyl-1,4,5,6-tetrahydropyridazine **3h** was obtained as an off-white solid (178 mg, 71 %) along with the by-product, 5-methyl-3-(thiophen-2-yl)-pyridazine (20 mg, 16 %). Crystals suitable for X-ray crystallography were grown by slow evaporation from a DCM and hexane (1:2) solution. Mp 150-154 ºC. δ_H ($CDCl_3$, 400 MHz) 1.55 (3H, d, $^3J_{HF}$ = 20.3 Hz, CH_3), 2.40 (3H, s, $ArCH_3$), 2.59 (1H, ddd, $^3J_{HF}$ = 25.0 Hz, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH_D), 2.84 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.3 Hz, CH_CH_D), 3.18 (1H, dd, $^3J_{HF}$ = 22.7 Hz, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B), 3.69 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 7.5 Hz, $^4J_{HH}$ = 2.1 Hz, NCH_AH_B), 6.98 (1H, dd, $^3J_{HH}$ = 4.9 Hz, $^3J_{HH}$ = 3.7 Hz, ArH), 7.13 (1H, dd, $^3J_{HH}$ = 3.7 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.27 – 7.35 (3H, m, ArH), 7.85 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.55 (3H, s, CH_3), 2.40 (3H, s, $ArCH_3$), 2.59 (1H, dd, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH_D), 2.84 (1H, dd, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 0.9 Hz, CH_CH_D), 3.18 (1H, d, $^2J_{HH}$ = 11.7 Hz, NCH_AH_B), 3.69 (1H, dd, $^2J_{HH}$ = 11.9 Hz, $^4J_{HH}$ = 2.0 Hz, NCH_AH_B), 6.98 (1H, dd, $^3J_{HH}$ = 5.1 Hz, $^3J_{HH}$ = 3.7 Hz), 7.13 (1H, dd, $^3J_{HH}$ = 3.7 Hz, $^4J_{HH}$ = 1.0 Hz, ArH), 7.27 – 7.35 (3H, m, ArH), 7.85 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 24.8 (d, $^2J_{CF}$ = 24.0 Hz, CH_3), 35.6 (d, $^2J_{CF}$ = 25.6 Hz, CH_2), 50.7 (d, $^2J_{CF}$ = 25.9 Hz, CH_2), 87.8 (d, $^1J_{CF}$ = 176.6 Hz, C), 125.7 (CH), 127.1 (CH), 128.0 (CH), 128.6 (CH), 129.5 (CH), 132.9 (C), 141.4 (C), 144.0 (d, $^3J_{CF}$ = 2.3

Hz, C), 144.3 (C). δ_F ($CDCl_3$, 376 MHz) -142.3 (s). m/z (ESI) 353.0799 (MH^+, $C_{16}H_{18}FN_2O_2S_2$ requires 353.0794, 100 %).

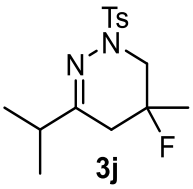


5-Methyl-3-(thiophen-2-yl)-pyridazine was obtained as an orange solid (20 mg, 16 %). The characterisation data was in agreement with the literature.[34] Mp 119-120 °C (lit: 118-120 °C).[34] δ_H ($CDCl_3$, 400 MHz) 2.40 (3H, s, CH_3), 7.16 (1H, dd, $^3J_{HH}$ = 5.1 Hz, $^3J_{HH}$ = 3.7 Hz, ArH), 7.49 (1H, dd, $^3J_{HH}$ = 5.1 Hz, $^4J_{HH}$ = 1.2 Hz, ArH), 7.58 (1H, d, $^4J_{HH}$ = 1.0 Hz, ArH), 7.68 (1H, dd, $^3J_{HH}$ = 3.7 Hz, $^4J_{HH}$ = 1.2 Hz, ArH), 8.91 (1H, br s, ArH). δ_C ($CDCl_3$, 126 MHz) 18.5 (CH_3), 122.5 (CH), 126.1 (CH), 128.0 (CH), 129.1 (CH), 137.9 (C), 140.7 (C), 151.5 (CH), 154.5 (C). m/z (ESI) 177.0491 (MH^+, $C_9H_9N_2S$ requires 177.0486, 100 %).



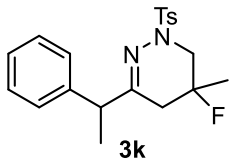
3i

5-Fluoro-5-methyl-3-propyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3i** was obtained as a white solid (180 mg, 81 %).



3j

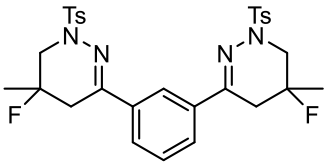
The general procedure was followed on a reduced scale; using **2j** (209 mg, 0.5 mmol), fluoroiodane (210 mg, 0.75 mmol), 4 Å powdered molecular sieves (130 mg) and dry HFIP (0.9 mL). 5-Fluoro-3-isopropyl-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3j** was obtained as a white solid (122 mg, 78 %). Crystals suitable for X-ray crystallography were grown by slow evaporation from a DCM and hexane (1:2) solution. Mp 110-112 °C. δ_H ($CDCl_3$, 400 MHz) 1.05 (3H, d, $^3J_{HH}$ = 6.9 Hz, CH_3), 1.05 (3H, d, $^3J_{HH}$ = 6.9 Hz, CH_3), 1.46 (3H, d, $^3J_{HF}$ = 20.7 Hz, CH_3), 2.13 (1H, ddd, $^3J_{HF}$ = 24.5 Hz, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.5 Hz, CH_CH$_D$), 2.34 (1H, td, $^3J_{HF}$ = $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.0 Hz, CH$_C$$H_D$), 2.42 (3H, s, ArH), 2.43(1H, sept, $^3J_{HH}$ = 6.9 Hz, CH), 3.11 (1H, ddd, $^3J_{HF}$ = 22.0 Hz, $^2J_{HH}$ = 11.7 Hz, $^4J_{HH}$ = 0.6 Hz, CH_AH$_B$), 3.46 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 8.7 Hz, $^4J_{HH}$ = 1.8 Hz, CH$_A$$H_B$), 7.29 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.78 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.05 (3H, d, $^3J_{HH}$ = 6.9 Hz, CH_3), 1.05 (3H, d, $^3J_{HH}$ = 6.9 Hz, CH_3), 1.46 (3H, s, CH_3), 2.13 (1H, dd, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.5 Hz, CH_CH$_D$), 2.34 (1H, dd, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.0 Hz, CH$_C$$H_D$), 2.42 (3H, s, ArH), 2.43(1H, sept, $^3J_{HH}$ = 6.9 Hz, CH), 3.11 (1H, dd, $^2J_{HH}$ = 11.7, $^4J_{HH}$ = 0.6 Hz, CH_AH$_B$), 3.46 (1H, dd, $^2J_{HH}$ = 11.7, $^4J_{HH}$ = 1.8 Hz, CH$_A$$H_B$), 7.29 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.78 (2 H, d, $^3J_{HH}$ = 8.3 Hz, ArH). δ_C ($CDCl_3$, 101 MHz) 19.8 (CH_3), 19.9 (CH_3), 21.6 (CH_3), 24.7 (d, $^2J_{CF}$ = 24.4 Hz, CH_3), 35.3 (d, $^2J_{CF}$ = 25.2 Hz, CH_2), 35.5 (CH), 50.9 (d, $^2J_{CF}$ = 26.3 Hz, CH_2), 88.2 (d, $^1J_{CF}$ = 175.5 Hz, C), 128.6 (CH), 129.2 (CH), 132.8 (C), 144.0 (C), 157.5 (d, $^3J_{CF}$ = 1.7 Hz, C). δ_F ($CDCl_3$, 376 MHz) -141.8 (s). m/z (ESI) 313.1387 (MH^+, $C_{15}H_{22}FN_2O_2S$ requires 313.1386, 100 %).



3k

The general procedure was followed using (*E*)-4-methyl-*N*'-(5-methyl-2-phenylhex-5-en-3-ylidene)benzenesulfonohydrazide **2k** (178 mg, 0.5 mmol) and 5-fluoro-5-methyl-3-(1-phenylethyl)-1-tosyl-1,4,5,6-tetrahydropyridazine **3k** (149 mg, 80 %) was formed as a mixture of two diastereomers (dr: 1:1) which were separated by purification by column chromatography. *Data for diastereomer 1*: Mp 107-110 °C. δ_H ($CDCl_3$, 400 MHz) 1.32 (3H, d, $^3J_{HF}$ = 20.7 Hz, CH_3), 1.41 (3H, d, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.93 (1H, dd, $^3J_{HF}$ = 25.2 Hz, $^2J_{HH}$ = 17.5 Hz, NCH_AH$_B$), 2.14 (1H, br t, $^3J_{HF}$ = $^2J_{HH}$ = 17.7 Hz, NCH$_A$$H_B$), 2.47 (3H, s, Ar$CH_3$), 3.01 (1H, dd, $^3J_{HF}$ = 23.5 Hz, $^2J_{HH}$ = 11.6 Hz, CH_CH$_D$), 3.50 (1H, q, $^3J_{HH}$ = 7.1 Hz, CH(CH_3)), 3.58 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 8.0 Hz, $^4J_{HH}$ = 2.0 Hz, CH$_C$$H_D$), 6.99 (2H, dd, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.3 Hz, ArH), 7.18 - 7.25 (3H, m, ArH), 7.34 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.32 (3H, s, CH_3), 1.41 (3H, d, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.93 (1H, d, $^2J_{HH}$ = 18.5 Hz, NCH_AH$_B$), 2.14 (1H, d, $^2J_{HH}$ = 18.2 Hz, NCH$_A$$H_B$), 2.47 (3H, s, Ar$CH_3$), 3.01 (1H, dd, $^2J_{HH}$ = 11.9 Hz, CH_CH$_D$), 3.50 (1H, q, $^3J_{HH}$ = 7.1 Hz, CH(CH_3)), 3.58 (1H, dd, $^2J_{HH}$ = 11.8 Hz, $^4J_{HH}$ = 2.0 Hz, CH$_C$$H_D$), 6.99 (2H, dd, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.3 Hz, ArH), 7.18 - 7.25 (3H, m, ArH), 7.34 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.3 Hz, ArH). δ_C ($CDCl_3$, 101 MHz) 18.6 (CH_3), 21.6 (CH_3), 24.4 (d, $^2J_{CF}$ = 24.4 Hz, CH_3), 36.2 (d, $^2J_{CF}$ = 25.0 Hz, CH_2), 47.0 (CH), 50.8 (d, $^2J_{CF}$ = 25.7 Hz, CH_2), 87.9 (d, $^1J_{CF}$ = 175.7 Hz, C), 127.0 (CH), 127.4 (CH), 128.7 (CH), 128.7 (CH), 129.4 (CH), 132.9 (C), 142.3 (C), 144.1 (C), 154.8 (d, $^3J_{CF}$ = 1.7 Hz, C). δ_F ($CDCl_3$, 376 MHz) -142.60 (s). m/z (ESI) 375.1541 (MH^+, $C_{20}H_{24}FN_2O_2S$ requires 375.1543, 100 %).

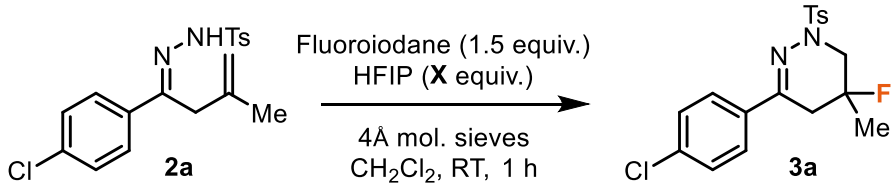
Data for diastereomer 2: Mp 144-145 °C. δ_H ($CDCl_3$, 400 MHz) 1.36 (3H, d, $^3J_{HF}$ = 20.6 Hz, CH_3), 1.41 (3H, d, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.91 (1H, dd, $^3J_{HF}$ = 25.5 Hz, $^2J_{HH}$ = 18.3 Hz, NCH_AH$_B$), 2.18 (1H, br t, $^3J_{HF}$ = $^2J_{HH}$ = 18.1 Hz, NCH$_A$$H_B$), 2.47 (3H, s, Ar$CH_3$), 3.05 (1H, dd, $^3J_{HF}$ = 23.5 Hz, $^2J_{HH}$ = 11.6 Hz, CH_CH$_D$), 3.47 - 3.61 (2H, m, CH(CH_3) and CH$_C$$H_D$), 6.99 (2H, dd, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.3 Hz, ArH), 7.16 - 7.23 (3H, m, ArH), 7.34 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.36 (3H, s, CH_3), 1.41 (3H, d, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.91 (1H, d, $^2J_{HH}$ = 18.3 Hz, NCH_AH$_B$), 2.18 (1H, d, $^2J_{HH}$ = 18.3 Hz, NCH$_A$$H_B$), 2.47 (3H, s, Ar$CH_3$), 3.05 (1H, d, $^2J_{HH}$ = 11.8 Hz, CH_CH$_D$), 3.47 - 3.61 (2H, m, CH(CH_3) and CH$_C$$H_D$), 6.99 (2H, dd, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.3 Hz, ArH), 7.16 - 7.23 (3H, m, ArH), 7.34 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.83 (2H, d, $^3J_{HH}$ = 8.2 Hz, ArH). δ_C ($CDCl_3$, 101 MHz) 18.6 (CH_3), 21.6 (CH_3), 24.5 (d, $^2J_{CF}$ = 24.2 Hz, CH_3), 35.8 (d, $^2J_{CF}$ = 25.6 Hz, CH_2), 46.7 (CH), 50.8 (d, $^2J_{CF}$ = 25.9 Hz, CH_2), 87.8 (d, $^1J_{CF}$ = 175.9 Hz, C), 126.9 (CH), 127.4 (CH), 128.65 (CH), 128.67 (CH), 129.3 (CH), 132.9 (C), 142.1 (C), 144.1 (C), 154.9 (C, d, $^3J_{CF}$ = 1.7 Hz). δ_F ($CDCl_3$, 376 MHz) -142.7 (s). m/z (ESI) 375.1542 (MH^+, $C_{20}H_{24}FN_2O_2S$ requires 375.1543, 100 %).



3l

The general procedure was followed using *N*',*N*'''-((1*E*,1'*E*)-1,3-phenylenebis(3-methylbut-3-en-1-yl-1-ylidene))bis(4-methylbenzene-sulfonohydrazide) **2l** (145 mg, 0.25 mmol) and 1,3-bis(5-fluoro-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazin-3-yl)benzene **3l** (71 mg, 46 %) was formed as a mixture of two diastereomers (dr: 1:1) which were inseparable by purification by column chromatography. Mp 177-178 ^{o}C. δ_H ($CDCl_3$, 400 MHz) 1.59 (6H, d, $^3J_{HF}$ = 20.5 Hz, CH_3), 2.39 (6H, s, $ArCH_3$), 2.57 (2H, dd, $^3J_{HF}$ = 26.5 Hz, $^2J_{HH}$ = 18.4 Hz, CH_CH$_D$), 2.86 (2H, br t, $^3J_{HF}$ = $^2J_{HH}$ = 18.2 Hz, CH$_C$$H_D$), 3.22 (2H, dd, $^3J_{HF}$ = 23.5 Hz, $^2J_{HH}$ = 11.0 Hz, NCH_AH$_B$ diastereomer1), 3.25 (2H, dd, $^3J_{HF}$ = 23.5 Hz, $^2J_{HH}$ = 11.0 Hz, NCH_AH$_B$ diastereomer2), 3.79 (2H, dd, $^2J_{HH}$ = 12.0 Hz, $^3J_{HF}$ = 7.9 Hz, NCH$_A$$H_B$ diastereomer1), 3.80 (2H, dd, $^2J_{HH}$ = 12.0 Hz, $^3J_{HF}$ = 7.9 Hz, NCH$_A$$H_B$ diastereomer2), 7.29 - 7.39 (5H, m, ArH), 7.62 (2H, dt, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 2.0 Hz, ArH), 7.87 (4H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 2.0 Hz, ArH), 8.05 (1H, d, $^3J_{HH}$ = 5.4 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.59 (6H, s, CH_3), 2.39 (6H, s, $ArCH_3$), 2.59 (2H, br d, $^2J_{HH}$ = 18.4 Hz, CH_CH$_D$), 2.86 (2H, br d, $^2J_{HH}$ = 18.4 Hz, CH$_C$$H_D$), 3.22 (2H, d, $^2J_{HH}$ = 11.0 Hz, NCH_AH$_B$ diastereomer1), 3.25 (2H, d, $^2J_{HH}$ = 11.0 Hz, NCH_AH$_B$ diastereomer2), 3.79 (2H, dd, $^2J_{HH}$ = 11.8 Hz, $^4J_{HH}$ = 1.7 Hz, NCH$_A$$H_B$ diastereomer1), 3.80 (2H, dd, $^2J_{HH}$ = 11.8 Hz, $^4J_{HH}$ = 1.7 Hz, NCH$_A$$H_B$ diastereomer2), 7.33 (5H, m, ArH), 7.62 (2H, d, $^3J_{HH}$ = 7.8 Hz, ArH), 7.87 (4H, dd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 1.9 Hz,), 8.04 (1H, d, $^4J_{HH}$ = 1.7 Hz). δ_C ($CDCl_3$, 101 MHz) 21.6 (CH_3), 24.9 (d, $^2J_{CF}$ = 24.0 Hz, CH_3), 35.1 (d, $^2J_{CF}$ = 24.2 Hz, CH_2), 50.4 (d, $^2J_{CF}$ = 25.6 Hz, CH_2), 87.8 (d, $^1J_{CF}$ = 175.9 Hz, C), 122.6 (CH), 126.6 (CH), 128.4 (CH), 128.6 (CH), 129.7 (d, $^5J_{CF}$ = 1.1 Hz, CH), 133.2 (C), 136.2 (C), 144.4 (C), 146.4 (C). δ_F ($CDCl_3$, 376 MHz) -141.86 (s), -141.90 (s). m/z (ESI) 615.1910 (MH^+, $C_{30}H_{33}F_2N_4O_4S_2$ requires 615.1911, 100 %).

Exploring substoichiometric activator in solution

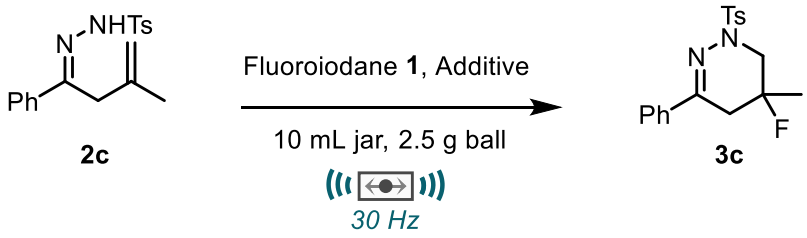


X	Yield
1	93
0.25	93
0.1	90

Reaction conditions: unsaturated hydrazone **2a** (0.71 mmol), fluoroiodane **1** (1.07 mmol), 4 Å molecular sieves (180 mg), HFIP (X equiv.) CH_2Cl_2 (2.5 mL), RT, 1 hour. Isolated yields reported.

Scheme S1. Substoichimetric HFIP studies.

Table S3: Mechanochemical optimisation for fluorocyclisation of unsaturated hydrazone **2c** with fluoroiodane **1**



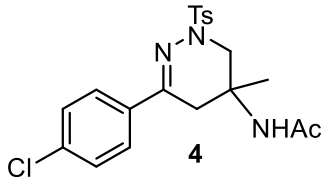
Entry	F-iodane equiv.	Time (min)	Additive	Yield 3c[a]
1	1.5	15	No additive	52
2	1.5	15	HFIP (1 equiv.)	72
3	1.5	15	HFIP (2 equiv.)	92 (91)[b]
4	1.5	15	HFIP (3 equiv.)	90
5	1.5	15	HFIP (4 equiv.)	90
6	1.5	15	HFIP (5 equiv.)	91
7	1.5	5	HFIP (2 equiv.)	73
8	1.5	10	HFIP (2 equiv.)	87
9	1.25	15	HFIP (1 equiv.)	72
10	1.75	15	HFIP (3 equiv.)	91

[a] Yield determined by ^{19}F NMR spectroscopy using benzotrifluoride (10 µL, 0.083 mmol) as an internal standard. [b] Isolated yield

General Procedure C for fluorocyclisations of unsaturated tosyl hydrazones 2 using fluoroiodane in a ball-mill (Scheme 2)

To a 10 mL stainless steel jar (Retsch) was added a 2.5 g stainless steel milling ball. Unsaturated hydrazone (0.25 mmol), fluoroiodane **1** (0.1050 g, 0.375 mmol) and 1,1,1,3,3,3-hexafluoro-2-propanol (52 µL, 0.5 mmol) were added under an air atmosphere. The milling jar was then screwed closed and milled at 30 Hz for 15 minutes. After the desired reaction, the mixture was transferred to a flask with $CHCl_3$ (~2-5 mL). The crude NMR yield was determined by adding benzotrifluoride (10 µL, 0.083 mmol) as an internal standard. The crude product was concentrated under reduced pressure and purified by flash column chromatography using petroleum ether : ethyl acetate (4:1). Fluorinated tetrahydropyridazines **3b**, **3c**, **3d**, **3e**, **3k** and **3l** were prepared using this procedure.

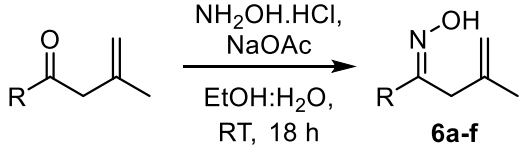
***N*-(6-(4-Chlorophenyl)-4-methyl-2-tosyl-2,3,4,5-tetrahydropyridazin-4-yl)acetamide 4**



4

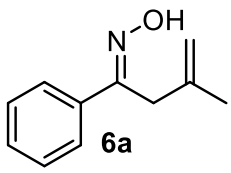
During optimisation (Table 1: entry 6), a Schlenk flask was charged with **2a** (258 mg, 0.71 mmol), fluoroiodane (300 mg, 1.07 mmol), 4 Å powdered molecular sieves (180 mg) in dry MeCN (2.5 mL) under an inert atmosphere. The reaction mixture was stirred for 1 hour at 40 °C before being concentrated *in vacuo* and the crude product was purified by column chromatography using petroleum ether : ethyl acetate (4:1). 3-(4-Chlorophenyl)-5-fluoro-5-methyl-1-tosyl-1,4,5,6-tetrahydropyridazine **3a** was obtained as a white solid (89 mg, 31 %). The Ritter product *N*-(6-(4-chlorophenyl)-4-methyl-2-tosyl-2,3,4,5-tetrahydropyridazin-4-yl)acetamide **4** was obtained as a white solid (62 mg, 23 %). Mp 225-227 °C. δ_H ($CDCl_3$, 400 MHz) 1.55 (3H, s, CH_3), 1.92 (3H, s, CH_3), 2.23 (1H, d, $^2J_{HH}$ = 18.8 Hz, CH_CH$_D$), 2.41 (3H, s, ArCH_3), 2.64 (1H, d, $^2J_{HH}$ = 11.3 Hz, NCH_AH$_B$), 3.58 (1H, dd, $^2J_{HH}$ =18.8 Hz, $^4J_{HH}$ = 0.8 Hz, CH$_C$$H_D$), 3.94 (1H, dd, $^2J_{HH}$ = 11.3 Hz, $^4J_{HH}$ = 2.0 Hz, NCH$_A$$H_B$), 5.79 (1H, s, NH), 7.29 - 7.35 (4H, m, ArH), 7.64 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.81 (2H, $^3J_{HH}$ = 8.4 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.6 (CH_3), 24.3 (CH_3), 24.7 (CH_3), 33.2 (CH_2), 48.7 (C), 51.7 (CH_2), 126.9 (CH), 128.4 (CH), 128.6 (CH), 129.8 (CH), 132.4 (C), 134.6 (C), 135.9 (C), 144.7 (C), 149.2 (C), 170.4 (CO). m/z (ESI) 420.1144 (MH^+, $C_{20}H_{23}{}^{35}ClN_3O_3S$ requires 420.1149, 100 %), 422.1124 (MH^+, $C_{20}H_{23}{}^{37}ClN_3O_3S$ requires 422.1119, 40 %).

General Procedure for preparation of unsaturated oximes 6[35]



6a-f

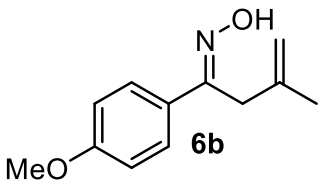
A flask was charged with unsaturated ketone (10 mmol), hydroxylamine hydrochloride (50 mmol) and sodium acetate (70 mmol) in a water: ethanol mixture (1:1, 100 mL) at room temperature. The reaction mixture was stirred overnight for 18-24 hours under an inert atmosphere. The reaction mixture was concentrated *in vacuo* and was then extracted into DCM (3 x 30 mL). The combined organic layer was washed with water (2 x 50 mL) and brine (3 x 50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography using petroleum ether : ethyl acetate (5:1) to yield the pure unsaturated oxime.



6a

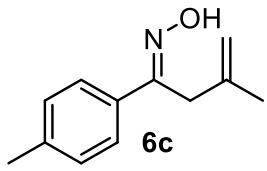
The general procedure was followed using 3-methyl-1-phenylbut-3-en-1-one (1.40 g, 8.72 mmol), hydroxylamine hydrochloride (3.00 g, 43.6 mmol) and sodium acetate (5.00 g, 61.2 mmol) in an ethanol : water mixture (1:1, 100 mL). (*E*)-3-methyl-1-phenylbut-3-en-1-one oxime **6a** was obtained as an off-white

solid (0.94 g, 62 %). Additionally, the minor regioisomer, (*Z*)-3-methyl-1-phenylbut-3-en-1-one oxime, was isolated as a yellow oil (0.09 g, 6 %). The characterisation data was in agreement with the literature.[36] Mp 48-52 °C (lit.,[36] 41-43 °C). δ_H ($CDCl_3$, 400 MHz) 1.84 (3H, s, CH_3), 3.58 (2H, s, CH_2), 4.78 (1H, s, $=CH_2$), 4.86 (1H, s, $=CH_2$), 7.35 - 7.45 (3H, m, ArH), 7.61 - 7.71 (2H, m, ArH), 8.86 (1H, br s, OH). δ_C ($CDCl_3$, 101 MHz) 23.1 (CH_3), 34.3 (CH_2), 112.2 (CH_2), 126.4 (CH), 128.5 (CH), 129.3 (CH), 135.8 (C), 140.3 (C), 157.0 (C). m/z (ASAP) 176.1077 (MH^+, $C_{11}H_{14}NO$ requires 176.1075, 95 %), 158.0979 ($(M\text{-}OH)^+$, 100 %).



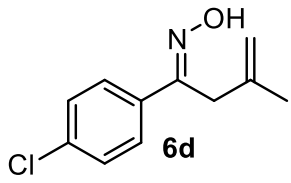
6b

The general procedure was followed using 3-methyl-1-(4-methoxyphenyl)-but-3-en-1-one (2.52 g, 13.2 mmol), hydroxylamine hydrochloride (4.60 g, 66.2 mmol) and sodium acetate (7.60 g, 92.7 mmol) in an ethanol : water mixture (1:1, 150 mL). (*E*)-1-(4-Methoxyphenyl)-3-methylbut-3-en-1-one oxime **6b** was obtained as a white solid (1.58 g, 73 %) and the characterisation data was in agreement with the literature.[36] Mp 81-84 °C (lit.,[36] 84-85 °C). δ_H ($CDCl_3$, 400 MHz) 1.81 (3H, s, CH_3), 3.52 (2H, s, CH_2), 3.82 (3H, s, OCH_3), 4.73 (1H, s, $=CH_2$), 4.83 (1H, s, $=CH_2$), 6.89 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.59 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.84 (1H, s, OH). δ_C ($CDCl_3$, 126 MHz) 23.1 (CH_3), 34.1 (CH_2), 55.3 (CH_3), 112.1 (CH_2), 113.8 (CH), 127.7 (CH), 128.3 (C), 140.6 (C), 156.6 (C), 160.5 (C). m/z (ESI) 206.1179 (MH^+, $C_{12}H_{16}NO_2$ requires 206.1181, 100 %).



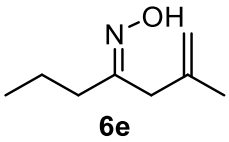
6c

The general procedure was followed using 3-methyl-1-(4-methylphenyl)-but-3-en-1-one (2.05 g, 11.5 mmol), hydroxylamine hydrochloride (3.99 g, 57.4 mmol) and sodium acetate (6.60 g, 80.0 mmol) in an ethanol : water mixture (1:1, 120 mL). (*E*)-3-methyl-1-(*p*-tolyl)but-3-en-1-one oxime **6c** was obtained as colourless crystals/ white solid (1.45 g, 63 %). Additionally, the minor regioisomer, (*Z*)-3-methyl-1-(*p*-tolyl)but-3-en-1-one oxime, was isolated as a white solid (0.09 g, 4 %). Mp 60-62 °C. δ_H ($CDCl_3$, 400 MHz) 1.80 (3H, s, CH_3), 2.35 (3H, s, $ArCH_3$), 3.54 (2H, s, CH_2), 4.74 (1H, s, $=CH_2$), 4.82 (1H, s, $=CH_2$), 7.16 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.52 (2H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 9.23 (1H, br s, OH). δ_C ($CDCl_3$, 126 MHz) 21.3 (CH_3), 23.1 (CH_3), 34.3 (CH_2), 112.2 (CH_2), 126.2 (CH), 129.2 (CH), 133.0 (C), 139.3 (C), 140.5 (C), 156.8 (C). m/z (ASAP) 190.1239 (MH^+, $C_{12}H_{16}NO$ requires 190.1232, 100 %).



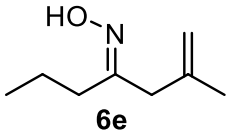
6d

The general procedure was followed using 3-methyl-1-(4-chlorophenyl)-but-3-en-1-one (2.65 g, 13.6 mmol), hydroxylamine hydrochloride (4.73 g, 68.1 mmol) and sodium acetate (7.82 g, 95.3 mmol) in an ethanol : water mixture (1:1, 150 mL). (*E*)-1-(4-Chlorophenyl)-3-methylbut-3-en-1-one oxime **6d** was obtained as colourless crystals/ white solid (1.71 g, 60 %). Additionally, the minor regioisomer, (*Z*)-1-(4-chlorophenyl)-3-methylbut-3-en-1-one oxime, was isolated as a white solid (0.42 g, 15 %). Mp 79-81 ^{o}C. δ_H ($CDCl_3$, 400 MHz) 1.80 (3H, s, CH_3), 3.52 (2H, s, CH_2), 4.71 (1H, s, =CH_2), 4.83 (1H, s, =CH_2), 7.33 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.57 (2H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 8.54 (1H, br s, OH). δ_C ($CDCl_3$, 126 MHz) 23.0 (CH_3), 34.1 (CH_2), 112.4 (CH_2), 127.6 (CH), 128.7 (CH), 134.2 (C), 135.3 (C), 140.1 (C), 156.1 (C). m/z (ASAP) 210.0681 (MH^+, $C_{11}H_{13}NO^{35}Cl$ requires 210.0686, 100 %), 212.0657 (MH^+, $C_{11}H_{13}NO^{37}Cl$ requires 212.0656, 33 %).



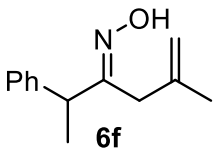
6e

The general procedure was followed using 2-methylhept-1-en-4-one (1.25 g, 9.9 mmol), hydroxylamine hydrochloride (3.44 g, 49.5 mmol) and sodium acetate (5.69 g, 69.3 mmol) in an ethanol : water mixture (1:1, 100 mL). (*Z*)-2-methylhept-1-en-4-one oxime **6e** was obtained as a mixture of isomers as a colourless oil (0.99 g, 71 % (47:53 mixture of (*Z*)- & *(E)*-isomers). Minor (*Z*)-isomer: δ_H ($CDCl_3$, 400 MHz) 0.92 (3H, t, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.48 - 1.60 (2H, m, CH_2), 1.75 (3H, s, CH_3), 2.15 (2H, t, $^3J_{HH}$ = 7.4 Hz, CH_2), 3.11 (2H, s, CH_2), 4.74 (1H, s, =CH_2), 4.83 (1H, s, =CH_2), 8.46 (1H, br s, OH). δ_C ($CDCl_3$, 126 MHz) 13.8 (CH_3), 19.6 (CH_2), 22.8 (CH_3), 35.5 (CH_2), 35.7 (CH_2), 112.6 (CH_2), 141.4 (C), 160.1 (C). m/z (ASAP) 142.1232 (MH^+, $C_8H_{16}NO$ requires 142.1232, 100 %).



6e

Major (*E*)-isomer: δ_H ($CDCl_3$, 400 MHz) 0.95 (3H, t, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.48 - 1.60 (2H, m, CH_2), 1.71 (3H, s, CH_3), 2.31 (2H, t, $^3J_{HH}$ = 7.8 Hz, CH_2), 2.87 (2H, s, CH_2), 4.81 (1H, s, =CH_2), 4.87 (1H, s, =CH_2), 8.46 (1H, br s, OH). δ_C ($CDCl_3$, 126 MHz) 14.3 (CH_3), 19.0 (CH_2), 22.1 (CH_3), 28.9 (CH_2), 42.7 (CH_2), 113.6 (CH_2), 140.5 (C), 159.0 (C). m/z (ASAP) 142.1232 (MH^+, $C_8H_{16}NO$ requires 142.1232, 100 %).

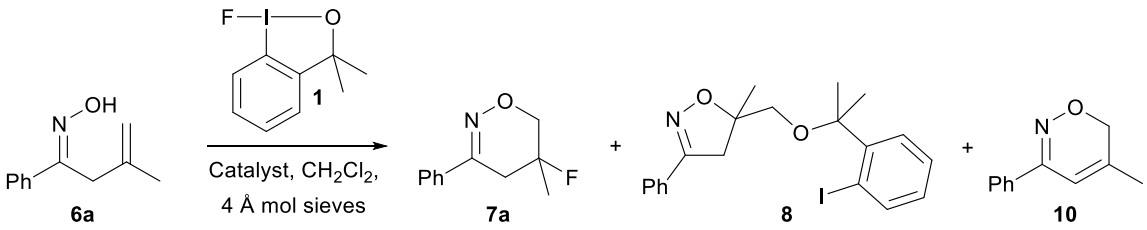


6f

The general procedure was followed using 5-methyl-2-phenylhex-5-en-3-one (0.88 g, 4.7 mmol), hydroxylamine hydrochloride (1.62 g, 23.2 mmol) and sodium acetate (2.67 g, 32.5 mmol) in an ethanol : water mixture (1:1, 50 mL). (*E*)-5-Methyl-2-phenylhex-5-en-3-one oxime **6f** was obtained as a white solid (774 mg, 82 %). Mp 67-68 ^{o}C. δ_H ($CDCl_3$, 400 MHz) 1.43 (3H, d, $^3J_{HH}$ = 7.2 Hz, CH(CH_3)), 1.71 (3H, s, CH_3), 2.54 (1H, d, $^2J_{HH}$ = 14.5 Hz, CH_AH$_B$), 3.39 (1H, d, $^2J_{HH}$ = 14.5 Hz, CH$_A$$H_B$), 3.66 (1H, q, $^3J_{HH}$ = 7.2 Hz, CH(CH_3)), 4.68 (1H, s, =CH_2), 4.82 (1H, s, =CH_2), 7.21 - 7.27 (3H, m, ArH), 7.27 -

7.34 (2H, m, ArH), 8.57 (1H, br s, OH). δ_C ($CDCl_3$, 101 MHz) 19.2 (CH_3), 22.8 (CH_3), 35.1 (CH_2), 44.1 (CH), 112.5 (CH_2), 126.8 (CH), 127.8 (CH), 128.6 (CH), 140.6 (C), 142.9 (C), 160.9 (C). m/z (ESI) 204.1388 (MH^+, $C_{13}H_{18}NO$ requires 204.1388, 100 %).

Table S4 Optimisation of intramolecular fluorocyclisation of unsaturated oxime **6a**[a]

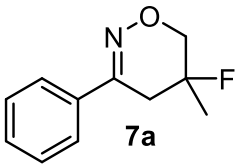


Entry	Catalyst (Equiv)		Temp (°C)	Time (h)	Convn[b] (%)	7a[c] (%)	8[c] (%)	10[c] (%)
1	$AgBF_4$	1	40	20	>95	trace	15	20
2	$AgBF_4$	0.2	40	20	>95	trace	10	20
3	$AgBF_4$	0.2	40	4	>95	28	10	15
4	$AgBF_4$	0.2	40	1	>95	45	10	<5
5	No catalyst	0	40	1	>95	trace	0	-
6	$AgBF_4$	0.2	RT	1	>95	46	10	<5
7[d]	$AgBF_4$	0.2	RT	1	>95	29	10	<5
8	$[Cu(MeCN)_4]BF_4$	0.2	RT	1	>95	23	10	<5
9	$ZnBF_4.H_2O$	0.2	RT	1	>95	0	10	23
10	**$AgBF_4$**	**1**	**RT**	**0.25**	**>95**	**46**	**15**	**<5**
11	$AgBF_4$	0.2	RT	0.25	86	21	10	<5

[a] Reaction conditions: unsaturated oxime **6a** (0.71 mmol), fluoroiodane **1** (1.07 mmol), 4 Å molecular sieves (180 mg), CH_2Cl_2 (0.4 mL); [b] Conversion denoted by consumption of starting material; [c] Isolated yield; [d] Without 4Å molecular sieves; - not quantified.

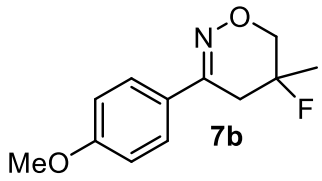
General Procedure A for intramolecular fluorocyclisations of unsaturated oximes 6 (Scheme 4)

A Schlenk flask was charged with unsaturated oxime **6** (0.71 mmol), fluoroiodane **1** (1.07 mmol), $AgBF_4$ (0.71 mmol) and 4 Å powdered molecular sieves (180 mg) in dry dichloromethane (0.4 mL) under an inert atmosphere. The reaction mixture was stirred for 15 minutes at room temperature before being concentrated *in vacuo* and the crude product was purified by column chromatography using petroleum ether : ethyl acetate (4 : 1).



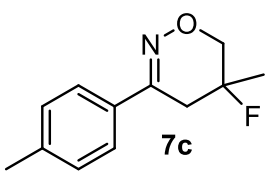
7a

5-Fluoro-5-methyl-3-phenyl-5,6-dihydro-4*H*-1,2-oxazine **7a** was obtained as a white solid (62 mg, 46 %). Mp 62-65 ºC. δ_H ($CDCl_3$, 400 MHz) 1.55 (3H, d, $^3J_{HF}$ = 20.5 Hz, CH_3), 2.68 (1H, ddd, $^3J_{HF}$ = 25.9 Hz, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH$_D$), 2.91 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.3 Hz, CH$_C$$H_D$), 3.75 (1H, br dd, $^3J_{HF}$ = 23.4 Hz, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 4.09 (1H, ddd, $^2J_{HH}$ = 11.6 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 2.1 Hz, OCH$_A$$H_B$), 7.40 - 7.42 (3H, m, ArH), 7.67 - 7.75 (2H, m, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.53 (3H, s, CH_3), 2.68 (1H, dd, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH$_D$), 2.91 (1H, br d, $^2J_{HH}$ = 18.3 Hz, CH$_C$$H_D$), 3.75 (1H, br d, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 4.09 (1H, dd, $^2J_{HH}$ = 11.7 Hz, $^4J_{HH}$ = 2.0 Hz, OCH$_A$$H_B$), 7.40 - 7.42 (3H, m, ArH), 7.67 - 7.75 (2H, m, ArH). δ_C ($CDCl_3$, 126 MHz) 23.5 (d, $^2J_{CF}$ = 25.2 Hz, CH_3), 33.5 (d, $^2J_{CF}$ = 26.4 Hz, CH_2), 70.0 (d, $^2J_{CF}$ = 23.9 Hz, CH_2), 87.2 (d, $^1J_{CF}$ = 173.5 Hz, C), 125.5 (CH), 128.6 (CH), 130.0 (CH), 134.8 (C), 153.6 (C). δ_F ($CDCl_3$, 376 MHz) -147.0 (s). m/z (ASAP) 194.0981 (MH^+, $C_{11}H_{13}NOF$ requires 194.0981, 100 %).



7b

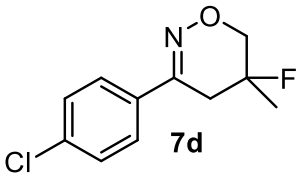
5-Fluoro-3-(4-methoxyphenyl)-5-methyl-5,6-dihydro-4*H*-1,2-oxazine product **7b** was obtained as colourless crystals/ white solid (80 mg, 53 %). Mp 105-107 ºC. δ_H ($CDCl_3$, 400 MHz) 1.54 (3H, d, $^3J_{HF}$ = 20.7 Hz, CH_3), 2.66 (1H, ddd, $^3J_{HF}$ = 25.9 Hz, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH$_D$), 2.88 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.3 Hz, CH$_C$$H_D$), 3.72 (1H, dd, $^3J_{HF}$ = 23.4 Hz, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 3.83 (3H, s, OCH_3), 4.06 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 2.0 Hz, OCH$_A$$H_B$), 6.91 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.64 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.53 (3H, s, CH_3), 2.66 (1H, dd, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH$_D$), 2.88 (1H, br d, $^2J_{HH}$ = 18.3 Hz, CH$_C$$H_D$), 3.72 (1H, br. d, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 3.83 (3H, s, OCH_3), 4.06 (1H, dd, $^2J_{HH}$ = 11.6, $^4J_{HH}$ = 2.1 Hz, OCH$_A$$H_B$), 6.91 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH), 7.63 (2H, d, $^3J_{HH}$ = 9.0 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 23.6 (d, $^2J_{CF}$ = 25.1 Hz, CH_3), 33.4 (d, $^2J_{CF}$ = 26.1 Hz, CH_2), 55.4 (CH_3), 70.9 (d, $^2J_{CF}$ = 24.1 Hz, CH_2), 87.4 (d, $^1J_{CF}$ = 173.7 Hz, C), 113.9 (CH), 126.9 (CH), 127.3 (C), 153.3 (C), 161.0 (C). δ_F ($CDCl_3$, 376 MHz) -146.8 (s). m/z (ESI) 224.1089 (MH^+, $C_{12}H_{15}FNO_2$ requires 224.1087, 100 %).



7c

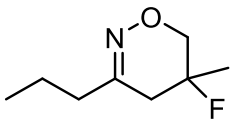
5-Fluoro-5-methyl-3-(*p*-tolyl)-5,6-dihydro-4*H*-1,2-oxazine **7c** was obtained as colourless crystals/ white solid (62 mg, 42 %). Crystals suitable for X-ray crystallography were grown by slow evaporation from a DCM and hexane (1:2) solution. Mp 103-104 ºC. δ_H ($CDCl_3$, 400 MHz) 1.53 (3H, d, $^3J_{HF}$ = 20.5 Hz, CH_3), 2.37 (3H, s, ArCH_3), 2.66 (1H, ddd, $^3J_{HF}$ = 25.9 Hz, $^2J_{HH}$ = 18.3 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH$_D$), 2.89 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.3 Hz, CH$_C$$H_D$), 3.73 (1H, dd, $^3J_{HF}$ = 23.4 Hz, $^2J_{HH}$ = 11.5 Hz, OCH_AH$_B$), 4.07 (1H, ddd, $^2J_{HH}$ = 11.5 Hz, $^3J_{HF}$ = 7.7 Hz, $^4J_{HH}$ = 2.0 Hz, OCH$_A$$H_B$), 7.20 (2H, d, $^3J_{HH}$ = 8.1 Hz, ArH), 7.58 (2H, d, $^3J_{HH}$ = 8.1 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.53 (3H, s, CH_3), 2.37 (3H, s,

$ArCH_3$), 2.66 (1H, dd, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.6 Hz, CH_CH$_D$), 2.89 (1H, br d, $^2J_{HH}$ = 18.4 Hz, CH$_C$$H_D$), 3.73 (1H, br d, $^2J_{HH}$ = 11.6 Hz, OCH_AH$_B$), 4.06 (1H, dd, $^2J_{HH}$ = 11.5 Hz, $^4J_{HH}$ = 2.0 Hz, OCH$_A$$H_B$), 7.20 (2H, d, $^3J_{HH}$ = 8.6 Hz, ArH), 7.58 (2H, d, $^3J_{HH}$ = 8.6 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 21.3 (CH_3), 23.6 (d, $^2J_{CF}$ = 24.6 Hz, CH_3), 33.5 (d, $^2J_{CF}$ = 26.0 Hz, CH_2), 70.9 (d, $^2J_{CF}$ = 24.6 Hz, CH_2), 87.4 (d, $^1J_{CF}$ = 173.5 Hz, C) 125.4 (CH), 129.29 (CH), 132.0 (C), 140.2 (C), 153.7 (C). δ_F ($CDCl_3$, 376 MHz) -146.8 (s). m/z (ASAP) 208.1138 (MH^+, $C_{12}H_{15}FNO$ requires 208.1138, 100 %).



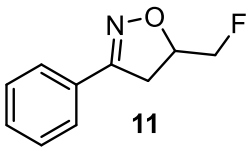
7d

3-(4-Chlorophenyl)-5-fluoro-5-methyl-5,6-dihydro-4*H*-1,2-oxazine **7d** was obtained as a colourless crystals/ white solid (61 mg, 42 %). Crystals suitable for X-ray crystallography were grown by slow evaporation from a DCM and hexane (1:2) solution. Mp 98-99 ºC. δ_H ($CDCl_3$, 400 MHz) 1.55 (3H, d, $^3J_{HF}$ = 20.5 Hz, CH_3), 2.64 (1H, ddd, $^3J_{HF}$ = 26.5 Hz, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH$_D$), 2.87 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.4 Hz, CH$_C$$H_D$), 3.74 (1H, dd, $^3J_{HF}$ = 24.1 Hz, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 4.10 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 7.6 Hz, $^4J_{HH}$ = 2.2 Hz, OCH$_A$$H_B$), 7.37 (2H, d, $^3J_{HH}$ = 8.7 Hz, ArH), 7.63 (2H, d, $^3J_{HH}$ = 8.7 Hz, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.55 (3H, s, CH_3), 2.64 (1H, dd, $^2J_{HH}$ = 18.4 Hz, $^4J_{HH}$ = 1.7 Hz, CH_CH$_D$), 2.87 (1H, br d, $^2J_{HH}$ = 18.4 Hz, CH$_C$$H_D$), 3.74 (1H, br d, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 4.10 (1H, dd, $^2J_{HH}$ = 11.6, $^4J_{HH}$ = 2.2 Hz, OCH$_A$$H_B$), 7.37 (2H, d, $^3J_{HH}$ = 8.7 Hz, ArH), 7.63 (2H, d, $^3J_{HH}$ = 8.7 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 23.5 (d, $^2J_{CF}$ = 24.2 Hz, CH_3), 33.3 (d, $^2J_{CF}$ = 26.2 Hz, CH_2), 71.0 (d, $^2J_{CF}$ = 25.2 Hz, OCH_2), 86.9 (d, $^1J_{CF}$ = 174.1 Hz, C), 126.7 (CH), 128.8 (CH), 133.3 (C), 136.1 (C), 152.5 (C). δ_F ($CDCl_3$, 376 MHz) -147.4 (s). m/z (ASAP) 228.0591 (MH^+, $C_{11}H_{12}NO^{35}ClF$ requires 228.0591, 100 %), 230.0575 (MH^+, $C_{11}H_{12}NO^{37}ClF$ requires 230.0562, 33 %).



7e

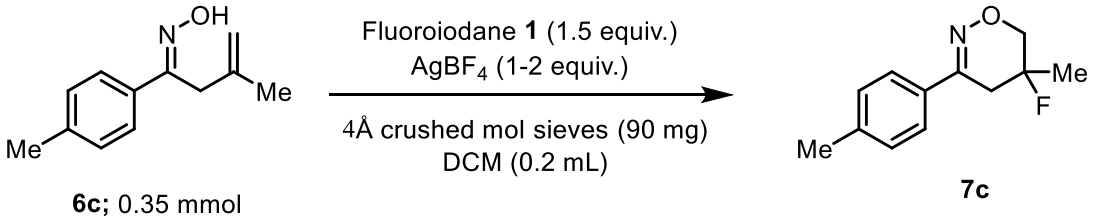
5-Fluoro-5-methyl-3-propyl-5,6-dihydro-4H-1,2-oxazine **7e** was obtained as a colourless oil (25 mg, 22 %). δ_H ($CDCl_3$, 400 MHz) 0.95 (3H, t, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.44 (3H, d, $^3J_{HF}$ = 20.5 Hz, CH_3), 1.52 - 1.63 (2H, m, CH_2), 2.20 - 2.25 (3H, m, CH_2 and CH_CH$_D$), 2.41 (1H, t, $^3J_{HF}$ = $^2J_{HH}$ = 18.0 Hz, CH$_C$$H_D$), 3.61 (1H, dd, $^3J_{HF}$ = 23.0 Hz, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 3.91 (1H, ddd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HF}$ = 8.0 Hz, $^4J_{HH}$ = 2.0 Hz, OCH$_A$$H_B$). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 0.95 (3H, t, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.44 (3H, s, CH_3), 1.52 - 1.63 (2H, m, CH_2), 2.20 - 2.25 (3H, m, CH_2 and CH_CH$_D$), 2.41 (1H, d, $^2J_{HH}$ = 18.0 Hz, CH$_C$$H_D$), 3.61 (1H, d, $^2J_{HH}$ = 11.7 Hz, OCH_AH$_B$), 3.91 (1H, dd, $^2J_{HH}$ = 11.7 Hz, $^4J_{HH}$ = 2.0 Hz, OCH$_A$$H_B$). δ_C ($CDCl_3$, 126 MHz) 13.5 (CH_3), 19.5 (CH_2), 23.4 (d, $^2J_{CF}$ = 25.1 Hz, CH_3), 34.8 (d, $^2J_{CF}$ = 26.1 Hz, CH_2), 37.2 (CH_2), 70.7 (d, $^2J_{CF}$ = 25.1 Hz, CH_2), 87.5 (d, $^1J_{CF}$ = 173.7 Hz, C), 157.4 (C). δ_F ($CDCl_3$, 376 MHz) -146.8 (s). m/z (ASAP) 160.1136 (MH^+, $C_8H_{15}FNO$ requires 160.1136, 100 %).



11

5-(Fluoromethyl)-3-phenyl-4,5-dihydro-1,2-oxazole **11** was obtained as a white solid (29 mg, 23 %). The characterisation data was in agreement with the literature.[3a] δ_H ($CDCl_3$, 400 MHz) 3.32 (1H, dd, $^2J_{HH}$ = 17.0 Hz, $^3J_{HH}$ = 7.2 Hz, C*H*$_A$H$_B$), 3.48 (1H, dd, $^2J_{HH}$ = 17.0 Hz, $^3J_{HH}$ = 11.2 Hz, CH$_A$*H*$_B$), 4.57 (2H, ddd, $^2J_{HF}$ = 48.0 Hz, $^3J_{HH}$ = 4.4 Hz, $^4J_{HH}$ = 1.6 Hz, CH_2F), 4.99 (1H, dddt, $^3J_{HF}$ = 19.3 Hz, $^3J_{HH}$ = 11.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 4.4 Hz, CH), 7.37 - 7.50 (3H, m, ArH), 7.65 - 7.74 (2H, m, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 3.31 (1H, dd, $^2J_{HH}$ = 16.7 Hz, $^3J_{HH}$ = 7.8 Hz, C*H*$_A$H$_B$), 3.48 (1H, dd, $^2J_{HH}$ = 16.7 Hz, $^3J_{HH}$ = 11.2 Hz, CH$_A$*H*$_B$), 4.55 (2H, d, $^3J_{HH}$ = 4.4 Hz, CH_2F), 4.98 (1H, ddt, $^3J_{HH}$ = 11.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 4.4 Hz, CH), 7.39 - 7.48 (3H, m, ArH), 7.65 - 7.73 (2 H, m, ArH). δ_C ($CDCl_3$, 100 MHz) 36.2 (d, $^3J_{CF}$ = 6.4 Hz, CH_2), 78.7 (d, $^2J_{CF}$ = 20.7 Hz, CH), 82.8 (d, $^1J_{CF}$ = 174.8 Hz, CH_2), 126.8 (CH), 128.8 (CH), 129.1 (C), 130.3 (CH), 156.2 (C). δ_F ($CDCl_3$, 376 MHz) -230.5 (s). m/z (ESI) 180.0825 (MH^+, $C_{10}H_{11}FNO$ requires 180.0824, 100 %).

Table S5: Comparison of intramolecular fluorocyclisation of unsaturated oxime **6c** with 1 and 2 equivalents of $AgBF_4$ in solution



6c; 0.35 mmol

7c

Time (min.)	Yield **7c** (1 equiv. $AgBF_4$)[a]	Yield **7c** (2 equiv. $AgBF_4$)[a]
15	44	38
60	46	48
180	47	49

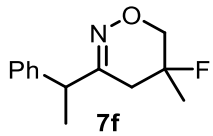
[a]Yield determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard

General Procedure for Table S5

A flame-dried flask was charged with unsaturated oxime **6c** (66 mg, 0.35 mmol), fluoroiodane **1** (146 mg, 0.525 mmol), $AgBF_4$ (1 or 2 equiv.) and 4 Å powdered molecular sieves (90 mg) in dry dichloromethane (0.2 mL) under an inert atmosphere. Finally, benzotrifluoride (14 µL, 0.116 mmol) was added as an internal standard. After the desired reaction periods, aliquots (20 µL) were taken from the reaction mixture and diluted with dichloromethane (~1 mL). The yield was then determined by ^{19}F NMR spectroscopy within 3-5 minutes of the aliquot being taken.

General Procedure B for intramolecular fluorocyclisations of unsaturated oximes 6 with fluoroiodane in a ball-mill (Scheme 4)

To a 10 mL stainless steel jar (Retsch) was added a 2.5 g stainless steel milling ball. Unsaturated oxime (0.25 mmol), fluoroiodane **1** (0.1050 g, 0.375 mmol) and silver tetrafluoroborate (0.0974, 0.5 mmol) were added under an air atmosphere. The milling jar was then screwed closed and milled at 30 Hz for 1 hour. After the desired reaction, the mixture was transferred to a flask with $CHCl_3$ (~2-5 mL). The crude NMR yield was determined by adding benzotrifluoride (10 µL, 0.083 mmol) as an internal standard. The crude product was concentrated under reduced pressure and purified by flash column chromatography using petroleum ether: ethyl acetate (4:1). In some cases the product could then be further purified by triturating with hexane to remove any iodoalcohol (by-product from fluoroiodane reagent). Fluorinated dihydrooxazines **7a-d** and **7f** were prepared using this procedure.



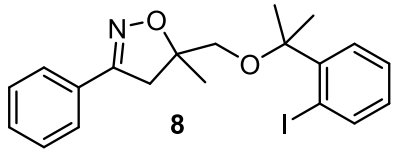
7f

The crude product was purified initially by flash column chromatography (5-20% EtOAc in hexane) and then further purified by vacuum Kugelröhr distillation (80-85° C) to give 5-fluoro-5-methyl-3-(1-phenylethyl)-5,6-dihydro-4H-1,2-oxazine (21 mg, 47%) as a colourless oil with an approximate d.r. of 3:2.

Data for major diastereomer: δ_H (500 MHz, $CDCl_3$) 1.33 (3H, d, $^3J_{HF}$ = 20.7 Hz, $CFCH_3$), 1.50 (3H, d, $^3J_{HH}$ = 7.1 Hz, $CHCH_3Ph$), 1.89-2.35 (2H, m, CH_2), 3.51-3.73 (2H, m, OCH_2), 3.86-3.99 (1H, m, C*H*Ph), 7.24-7.28 (3H, m, ArH), 7.32-7.36 (2H, m, ArH). δ_C (126 MHz, $CDCl_3$) 18.0 (CH_3), 23.4 (d, $^2J_{CF}$ = 24.8 Hz, CH_3), 33.1 (d, $^2J_{CF}$ = 25.9 Hz, CH_2), 45.4 (CH), 71.1 (d, $^2J_{CF}$ = 24.7 Hz, CH_2), 87.6 (d, $^1J_{CF}$ = 174.0 Hz, C), 127.3 (CH), 127.6 (CH), 129.0 (CH), 141.7 (C), 159.8 (C). δ_F (376 MHz, $CDCl_3$) -147.3 (s). m/z (ESI) 229.1298 (MH^+, $C_{13}H_{17}FNO$ requires 222.1924).

Data for minor diastereomer: δ_H (500 MHz, $CDCl_3$) (*selected*) 1.31 (3H, d, $^3J_{HF}$ = 20.7 Hz, $CFCH_3$). δ_C (126 MHz, $CDCl_3$) 18.3 (CH_3), 23.3 (d, $^2J_{CF}$ = 24.8 Hz, CH_3), 33.7 (d, $^2J_{CF}$ = 25.9 Hz, CH_2), 46.0 (CH), 71.1 (d, $^2J_{CF}$ = 24.4 Hz, CH_2), 87.6 (d, $^1J_{CF}$ = 173.7 Hz, C), 127.3 (CH), 127.6 (CH), 129.0 (CH), 142.0 (C), 159.5 (C). δ_F (376 MHz, $CDCl_3$) -147.5. m/z (ESI) 229.1298 (MH^+, $C_{13}H_{17}FNO$ requires 222.1924).

5-(((2-(2-Iodophenyl)propan-2-yl)oxy)methyl)-5-methyl-3-phenyl-4,5-dihydroisoxazole 8

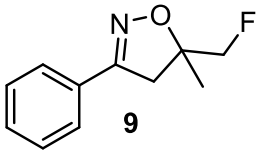


8

δ_H ($CDCl_3$, 400 MHz) 1.52 (3H, s, CH_3), 1.69 (3H, s, CH_3), 1.71 (3H, s, CH_3), 2.97 (1H, d, $^2J_{HH}$ = 16.6 Hz, CH_AH_B), 3.19 (1H, d, $^2J_{HH}$ = 9.5 Hz, OCH_CH_D), 3.23 (1H, d, $^2J_{HH}$ = 9.5 Hz, OCH_CH_D), 3.70 (1H, d, $^2J_{HH}$ = 16.6 Hz, CH_AH_B), 6.89 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.6 Hz, ArH), 7.29 (1H, td, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.4 Hz, ArH), 7.37-7.41 (4H, m, ArH), 7.65 - 7.68 (2H, m, ArH), 7.98 (1H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.4 Hz, ArH). δ_C ($CDCl_3$, 126 MHz) 23.8 (CH_3), 26.8 (CH_3), 43.0 (CH_2), 66.7 (CH_2), 77.5

(C), 86.4 (C), 93.8 (CI), 126.6 (CH), 128.0 (CH), 128.1 (CH), 128.6 (CH), 128.9 (CH), 129.8 (CH), 130.2 (C), 143.2 (CH), 145.1 (C), 156.7 (C). m/z (ASAP) 436.0775 (MH^+, $C_{20}H_{23}INO_2$ requires 436.0773, 100 %).

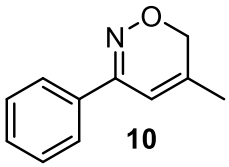
5-(Fluoromethyl)-5-methyl-3-phenyl-4,5-dihydroisoxazole 9



9

The pure product **9** was obtained as a colourless oil and the characterisation data was in agreement with the literature.[3a] δ_H ($CDCl_3$, 400 MHz) 1.52 (3H, d, $^4J_{HF}$ = 2.0 Hz, CH_3), 3.09 (1H, dd, $^2J_{HH}$ = 16.7 Hz, $^4J_{HF}$ = 1.7 Hz, CH_AH$_B$), 3.44 (1H, dd, $^2J_{HH}$ = 16.7 Hz, $^4J_{HF}$ = 1.0 Hz, CH$_A$$H_B$), 4.36 (1H, dd, $^2J_{HF}$ = 47.0 Hz, $^2J_{HH}$ = 9.4 Hz, CH_AH$_B$F), 4.42 (1H, dd, $^2J_{HF}$ = 47.0 Hz, $^2J_{HH}$ = 9.4 Hz, CH$_A$$H_B$F), 7.35 - 7.46 (3H, m, ArH), 7.59 - 7.73 (2H, m, ArH). $\delta_{H\{F\}}$ ($CDCl_3$, 400 MHz) 1.52 (3H, s, CH_3), 3.09 (1H, d, $^2J_{HH}$ = 16.7 Hz, CH_AH$_B$), 3.44 (1H, d, $^2J_{HH}$ = 16.7 Hz, CH$_A$$H_B$), 4.36 (1H, d, $^2J_{HH}$ = 9.4 Hz, CH_AH$_B$F), 4.42 (1H, d, $^2J_{HH}$ = 9.4 Hz, CH$_A$$H_B$F), 7.36 - 7.44 (3H, m, ArH), 7.59 - 7.73 (2H, m, ArH). δ_C ($CDCl_3$, 126 MHz) 22.0 (d, $^3J_{CF}$ = 3.2 Hz, CH_3), 42.2 (d, $^3J_{CF}$ = 4.0 Hz, CH_2), 85.2 (d, $^2J_{CF}$ = 18.3 Hz, C), 85.5 (d, $^1J_{CF}$ = 178.0 Hz, CH_2), 126.6 (CH), 128.7 (CH), 129.6 (C), 130.2 (CH), 156.2 (C). δ_F ($CDCl_3$, 376 MHz) -225.3 (s). m/z (ASAP) 194.0981 (MH^+, $C_{11}H_{13}NOF$ requires 194.0981, 100 %).

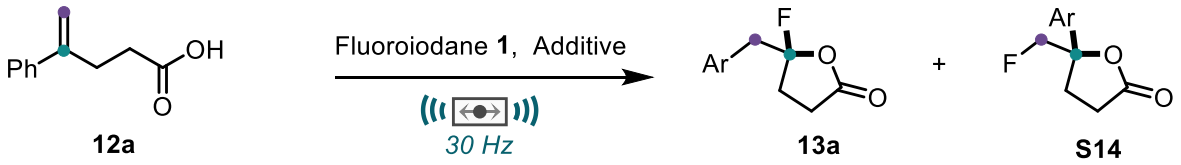
5-Methyl-3-phenyl-6*H*-1,2-oxazine 10



10

The characterisation data was in agreement with the literature.[37] Mp 34-36 ºC (lit.,[37] 32-33 ºC). δ_H ($CDCl_3$, 400 MHz) 1.99 (3H, s, CH_3), 4.38 (2H, s, OCH_2), 6.20 (1H, s, CH), 7.34 - 7.46 (3H, m, ArH), 7.60 - 7.76 (2H, m, ArH). δ_C ($CDCl_3$, 126 MHz) 19.7 (CH_3), 66.5 (CH_2), 110.9 (CH), 126.0 (CH), 128.6 (CH), 129.9 (CH), 134.0 (C), 141.5 (C), 156.9 (C). m/z (ASAP) 174.0916 (MH^+, $C_{11}H_{12}NO$ requires 174.0919, 100 %).

Table S6: Mechanochemical optimisation of intramolecular fluorocyclisation of unsaturated carboxylic acid **12a**

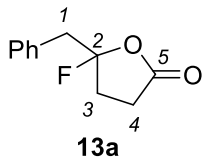


Entry	Scale (mmol)	Jar	Ball	F-iodane equiv.	Time (h)	Additive	Yield 13a[a]	Yield S14[a]
1	0.5	10 mL	2.5 g	1.5	2	X	23	0
2	0.5	10 mL	2.5 g	1.5	2	HFIP (2 equiv.)	44	0
3	0.25	5 mL	1 x 1.5	1.5	2	HFIP (2 equiv.)	25	0
4	0.25	5 mL	3 x 0.5	1.5	2	HFIP (2 equiv.)	40	0
5	0.25	10 mL	1 x 2.5	1.5	2	HFIP (2 equiv.)	55	0
6	0.125	5 mL	3 x 1.5	1.5	2	HFIP (2 equiv.)	34	0
7	0.25	10	2.5	1.5	0.5	HFIP (2 equiv.)	36	0
8	0.25	10	2.5	1.5	1	HFIP (2 equiv.)	57	0
9	0.25	10	2.5	1.5	1	HFIP (1 equiv.)	22	0
10	0.25	10	2.5	1.5	1	HFIP (3 equiv.)	70	0
11	0.25	10	2.5	1.5	1	HFIP (4 equiv.)	83	0
12	0.25	10	2.5	1.5	1	HFIP (5 equiv.)	96 (96)[b]	0
13	0.25	10	2.5	1	1	HFIP (5 equiv.)	84	0

[a] Yield determined by ^{19}F NMR spectroscopy using benzotrifluoride (10 µL, 0.083 mmol) as an internal standard. [b] Isolated yield

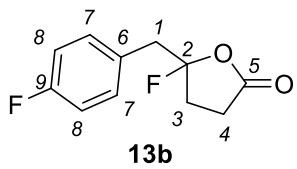
General procedure for the intramolecular fluorocyclisations of unsaturated carboxylic acids 12 in a ball-mill (Scheme 5)

To a 10 mL stainless steel jar (Retsch) was added a 2.5 g stainless steel milling ball. Unsaturated carboxylic acid (0.25 mmol), fluoroiodane **1** (0.1050 g, 0.375 mmol) and 1,1,1,3,3,3-hexafluoro-2-propanol (130 µL, 1.25 mmol) were added under an air atmosphere. The milling jar was then screwed closed and milled at 30 Hz for 1 hour. After the desired reaction, the mixture was transferred to a flask with $CHCl_3$ (~2-5 mL). The crude NMR yield was determined by adding benzotrifluoride (10 µL, 0.083 mmol) as an internal standard. The crude product was concentrated under reduced pressure and purified by flash column chromatography using the noted solvent systems.



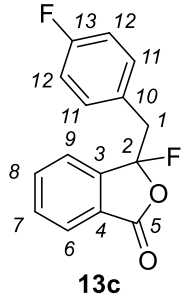
13a

The crude product was purified by column chromatography (dichloromethane) to give 5-benzyl-5-fluorodihydrofuran-2(3*H*)-one **13a** as a colourless oil (47 mg, 96%). The characterisation data was in agreement with the literature.[6a] δ_H ($CDCl_3$, 400 MHz) 2.15-2.30 (2H, m, H_3 and $H_{3'}$), 2.42 (1H, dm, on fluorine decoupling simplifies to ddd, $^2J_{HH}$ = 17.8 Hz, $^3J_{HH}$ = 8.7 Hz, $^3J_{HH}$ = 3.1 Hz, H_4), 2.74 (1H, ddd, $^2J_{HH}$ = 17.8 Hz, $^3J_{HH}$ = 10.5 Hz, $^3J_{HH}$ = 9.3 Hz, $H_{4'}$), 3.29 (2H, d, $^3J_{HF}$ = 14.7 Hz, H_1 and $H_{1'}$), 7.28 – 7.36 (5H, m, ArH); δ_F ($CDCl_3$, 376 MHz) -97.0 (s); δ_C ($CDCl_3$, 100 MHz) 27.0 (CH_2), 30.9 (d, $^2J_{CF}$ = 27.7 Hz, CH_2), 42.7 (d, $^2J_{CF}$ = 28.0 Hz, CH_2), 119.2 (d, $^1J_{CF}$ = 230.7 Hz, C), 127.6 (CH), 128.6 (CH), 130.4 (CH), 133.0 (d, $^3J_{CF}$ = 5.1 Hz, C), 174.7 (CO); *m/z* (ASAP) 195.0822 (MH^+. $C_{11}H_{12}FO_2$ requires 195.0821, 20 %), 175.0722 ($(M-F)^+$, 100%).



13b

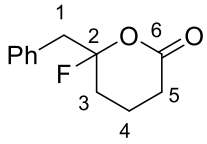
The crude product was purified by column chromatography (dichloromethane) to give 5-fluoro-5-(4-fluorobenzyl)-dihydrofuran-2(3*H*)-one **13b** as a colourless oil (48 mg, 90%). The characterisation data was in agreement with the literature.[6a] δ_H ($CDCl_3$, 400 MHz) 2.14-2.34 (2H, m, H_3 and $H_{3'}$), 2.42 – 2.49 (1H, m, on fluorine decoupling simplifies to ddd, $^2J_{HH}$ = 18.1 Hz, $^3J_{HH}$ = 9.3 Hz, $^3J_{HH}$ = 2.3 Hz, H_4), 2.75 (1H, ddd, $^2J_{HH}$ = 18.1 Hz, $^3J_{HH}$ = 10.7 Hz, $^3J_{HH}$ = 9.4 Hz, $H_{4'}$), 3.26 (2H, d, $^3J_{HF}$ = 14.8 Hz, H_1 and $H_{1'}$), 7.02 (2H, t, $^3J_{HF}$ = $^3J_{HH}$ = 8.7 Hz, ArH), 7.26 (2H, dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HF}$ = 5.5 Hz, ArH); δ_F ($CDCl_3$, 376 MHz) -97.8 (1F, s, CF), -114.8 (1F, s, ArF); δ_C ($CDCl_3$, 100 MHz) 26.9 (CH_2), 30.9 (d, $^2J_{CF}$ = 28.8 Hz, CH_2), 41.8 (d, $^2J_{CF}$ = 28.1 Hz, CH_2), 115.5 (d, $^2J_{CF}$ = 22.2 Hz, CH), 118.9 (d, $^1J_{CF}$ = 231.4 Hz, C), 128.7 (C), 131.9 (d, $^3J_{CF}$ = 8.0 Hz, CH), 162.3 (d, $^1J_{CF}$ = 245.9 Hz, C), 174.7 (CO); *m/z* (ASAP) 193.0664 ($(M-F)^+$. $C_{11}H_{10}FO_2$ requires 193.0665, 100 %).



13c

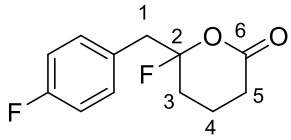
The crude product was purified by column chromatography (dichloromethane) to give 3-fluoro-3-(4-fluorobenzyl)isobenzofuran-1(3*H*)-one **13c** as a white solid (57 mg, 88%). The characterisation data was in agreement with the literature.[6a] mp 69 – 71 °C. δ_H ($CDCl_3$, 400 MHz) 3.51 (1H, dd, $^2J_{HH}$ = 14.5 Hz, $^3J_{HF}$ = 14.3 Hz, H_1), 3.57 (1H, dd, $^2J_{HH}$ = 14.5 Hz, $^3J_{HF}$ = 12.7 Hz, $H_{1'}$), 6.93 (2H, t, $^3J_{HH}$ = $^3J_{HF}$ = 8.6 Hz, ArH), 7.17 (2H, dd, $^3J_{HH}$ = 8.6 Hz, $^4J_{HF}$ = 5.5 Hz, ArH), 7.37 (1H, d, $^3J_{HH}$ = 7.5 Hz, ArH), 7.60 (1H, t, $^3J_{HH}$ = 7.6 Hz, ArH), 7.69 (1H, t, $^3J_{HH}$ = 7.5 Hz, ArH), 7.81 (1H, d, $^3J_{HH}$ = 7.5 Hz, ArH); δ_F ($CDCl_3$, 376 MHz) -101.0 (1F, s, CF), -114.6 (1F, s, ArF); δ_C ($CDCl_3$, 125 MHz) 41.6 (d, $^2J_{CF}$ = 31.3 Hz, CH_2), 115.0 (d, $^1J_{CF}$ = 233.2 Hz, CF), 115.4 (d, $^2J_{CF}$ = 21.7 Hz, CH), 123.0 (CH), 125.8 (CH), 126.3 (d, $^3J_{CF}$ = 1.4 Hz, C), 127.8 (dd, $^3J_{CF}$ = 5.6 Hz, $^4J_{CF}$ = 3.2 Hz, C), 131.7 (d, $^3J_{CF}$ = 2.3 Hz, CH), 132.2 (d, $^3J_{CF}$ = 8.3 Hz, CH), 134.8 (CH), 144.5 (d, $^2J_{CF}$ = 21.2 Hz, C), 162.3 (d, $^1J_{CF}$ = 246.9

Hz, C), 166.4 (d, $^{3}J_{CF}$ = 2.1 Hz, CO); *m/z* (ASAP) 241.0656 ((M-F)$^{+}$. $C_{15}H_{10}O_2F$ requires 241.0665, 100%), 213.0694 ((M-COF)$^{+}$, 95%).



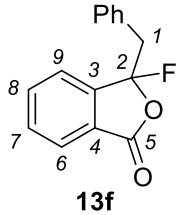
13d

The crude product was purified by column chromatography (dichloromethane) to give 6-benzyl-6-fluorotetrahydro-2*H*-pyran-2-one **13d** as a colourless oil (38 mg, 73%). The characterisation data was in agreement with the literature.[6a] δ_H ($CDCl_3$, 400 MHz) 1.63 – 1.82 (2H, m, H_3 and H_4), 1.96 – 2.11 (2H, m, $H_{3'}$ and $H_{4'}$), 2.35 – 2.45 (1H, m, H_5), 2.69 (1H, dm, $H_{5'}$), 3.20 (2H, d, $^{3}J_{HF}$ = 14.8 Hz, H_1 and $H_{1'}$), 7.26 – 7.34 (5H, m, ArH); δ_F ($CDCl_3$, 376 MHz) -96.8 (s); δ_C ($CDCl_3$, 100 MHz) 14.8 (d, $^{3}J_{CF}$ = 3.2 Hz, CH_2), 28.8 (d, $^{2}J_{CF}$ = 26.9 Hz, CH_2), 29.1 (CH_2), 45.2 (d, $^{2}J_{CF}$ = 26.7 Hz, CH_2), 115.5 (d, $^{1}J_{CF}$ = 228.0 Hz, C), 127.4 (CH), 128.5 (CH), 130.5 (CH), 133.5 (d, $^{3}J_{CF}$ = 5.5 Hz, C), 168.8 (CO); *m/z* (ASAP) 189.0923 ((M-F)$^{+}$. $C_{12}H_{13}O_2$ requires 189.0916, 5%), 161.0948 ((PhCH$_2$COCH$_2$CH$_2$CH$_2$)$^{+}$, 100%).



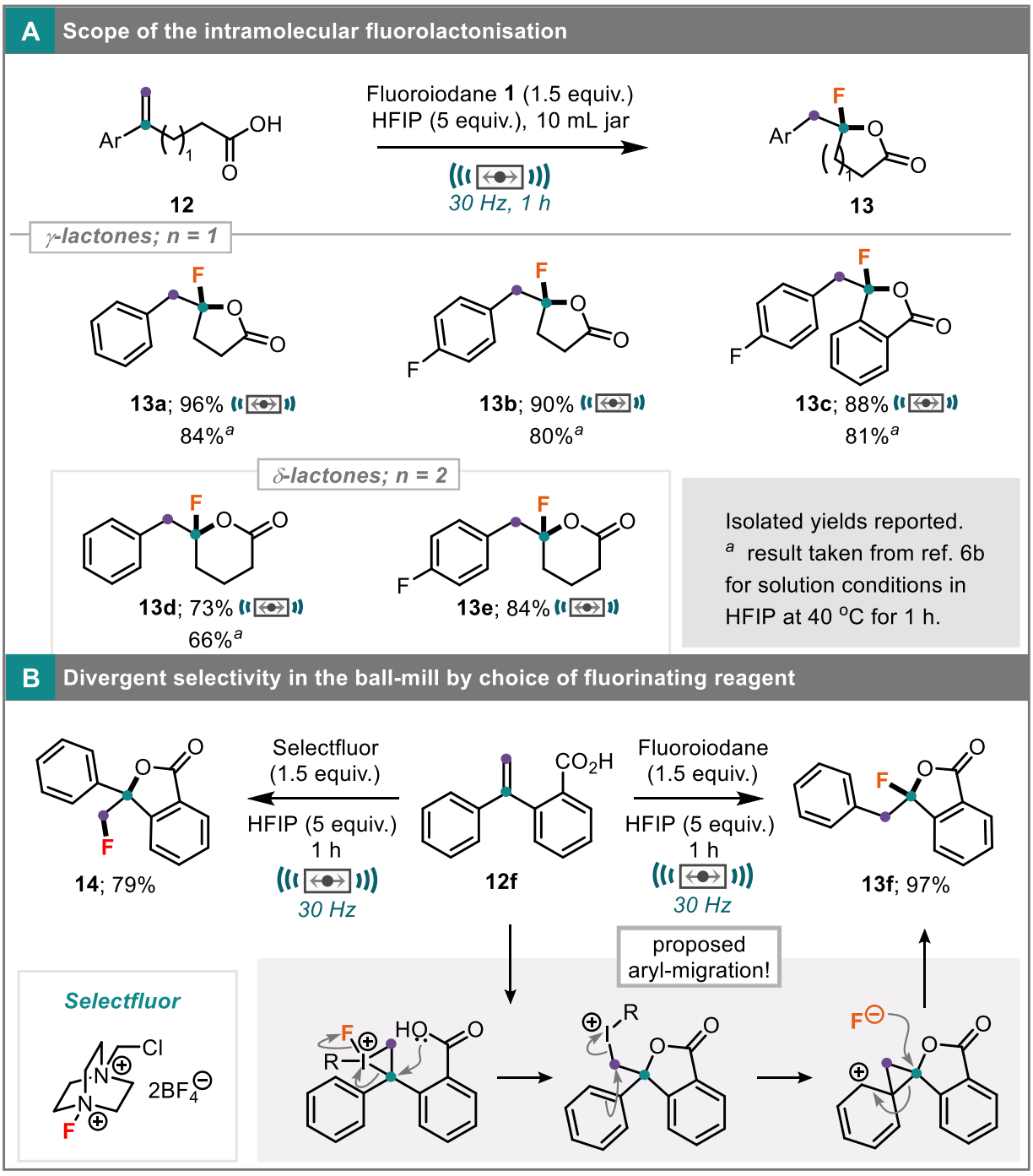
13e

The crude product was purified by column chromatography (5% then 20% EtOAc in hexane) to give 6-fluoro-6-(4-fluorobenzyl)tetrahydro-2*H*-pyran-2-one **13e** as a colourless oil (48 mg, 84%). δ_H ($CDCl_3$, 500 MHz) 1.63 – 1.84 (2H, m, H_3 and H_4), 1.95 – 2.12 (2H, m, $H_{3'}$ and $H_{4'}$), 2.36 – 2.46 (1H, m, H_5), 2.69 (1H, dddd, $^{2}J_{HH}$ = 17.9 Hz, $^{3}J_{HH}$ = 6.7 & 3.6 Hz, $^{4}J_{HH}$ = 1.3 Hz, $H_{5'}$), 3.17 (2H, d, $^{3}J_{HF}$ = 14.9 Hz, H_1 and $H_{1'}$), 6.97 – 7.04 (2H, m, ArH), 7.21 – 7.29 (2H, m, ArH); δ_F ($CDCl_3$, 376 MHz) -97.4 (1F, s, CF), -115 2 (1F, s, ArF); δ_C ($CDCl_3$, 100 MHz) 14.9 (d, $^{3}J_{CF}$ = 2.9 Hz, CH_2), 29.0 (d, $^{2}J_{CF}$ = 26.3 Hz, CH_2), 29.2 (CH_2), 44.5 (d, $^{2}J_{CF}$ = 26.7 Hz, CH_2), 115.4 (dd, $^{1}J_{CF}$ = 227.2 Hz, $^{6}J_{CF}$ = 1.4 Hz, C), 115.5 (d, $^{2}J_{CF}$ = 21.3 Hz, CH), 129.3 (dd, $^{3}J_{CF}$ = 5.5 Hz, $^{4}J_{CF}$ = 3.4 Hz, C), 132.1 (d, $^{3}J_{CF}$ = 8.1 Hz, CH), 162.4 (d, $^{1}J_{CF}$ = 246.1 Hz, C), 168.8 (d, $^{3}J_{CF}$ = 1.4 Hz, CO); *m/z* (ASAP) 207.0820 ((M-F)$^{+}$. $C_{12}H_{12}FO_2$ requires 207.0821, 37%), 179.0876 ((4-FC$_6$H$_4$CH$_2$COCH$_2$CH$_2$CH$_2$)$^{+}$, 100%).



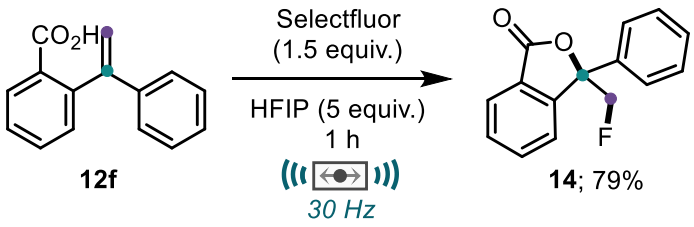
13f

The crude product was purified by column chromatography (dichoromethane) to give 3-benzyl-3-fluoroisobenzofuran-1(3*H*)-one **13f** as a colourless oil (59 mg, 97%). The characterisation data was in agreement with the literature.[6a] δ_H ($CDCl_3$, 400 MHz) 3.52 (1H, dd, $^{2}J_{HH}$ = 14.4 Hz, $^{3}J_{HF}$ = 14.3 Hz, H_1), 3.63 (1H, dd, $^{2}J_{HH}$ = 14.4 Hz, $^{3}J_{HF}$ = 12.3 Hz, $H_{1'}$), 7.19-7.26 (5H, m, ArH), 7.34 (1H, d, $^{3}J_{HH}$ = 7.5 Hz, ArH), 7.59 (1H, t, $^{3}J_{HH}$ = 7.5 Hz, ArH), 7.69 (1H, t, $^{3}J_{HH}$ = 7.5 Hz, ArH), 7.80 (1H, d, $^{3}J_{HH}$ = 7.5 Hz, ArH); δ_F ($CDCl_3$, 376 MHz) -100.6 (s); δ_C ($CDCl_3$, 100 MHz) 40.6 (d, $^{2}J_{CF}$ = 28.2 Hz, CH_2), 113.4 (d, $^{1}J_{CF}$ = 232.2 Hz, C), 121.4 (CH), 124.0 (CH), 124.5 (C), 125.9 (CH), 126.7 (CH), 128.8 (CH), 129.8 (CH), 130.2 (d, $^{3}J_{CF}$ = 4.5 Hz, C), 132.9 (CH), 142.8 (d, $^{2}J_{CF}$ = 21.2 Hz, C), 164.8 (CO); *m/z* (ASAP) 223.0758 ((M-F)$^{+}$. $C_{15}H_{11}O_2$ requires 223.0759, 100%), 195.0813 ((M-COF)$^{+}$, 70%).



Scheme S2 Intramolecular fluorolactonisations and switching of cyclisation selectivity

Mechanochemical intramolecular fluorolactonisation of unsaturated carboxylic acid 12f to 14 with Selectfluor



To a 10 mL stainless steel jar (Retsch) was added a 2.5 g stainless steel milling ball. Unsaturated carboxylic acid **12f** (0.056 g, 0.25 mmol), Selectfluor (0.1329 g, 0.375 mmol) and 1,1,1,3,3,3-hexafluoro-2-propanol (130 µL, 1.25 mmol) were added under an air atmosphere. The milling jar was then screwed closed and milled at 30 Hz for 1 hour. After the desired reaction time, the mixture was transferred to a flask with $CHCl_3$ (~2-5 mL). The reaction mixture was filtered to remove insoluble salts. The crude product was concentrated under reduced pressure and purified by flash column chromatography (5% EtOAc / hexane) to give 3-(fluoromethyl)-3-phenylisobenzofuran-1(3*H*)-one **14** as a white solid (48 mg, 79%). The characterisation data was in agreement with the literature.[38] mp 100-102 °C (lit.,[39] 103-105 ºC). δ_H (500 MHz, $CDCl_3$) 4.92 (1H, dd, $^2J_{HF}$ = 47.0, $^2J_{HH}$ = 10.0 Hz, CH_AH$_B$Ph), 4.95 (1H, dd, $^2J_{HF}$ = 47.0, $^2J_{HH}$ =10.0 Hz, CH$_A$$H_B$Ph), 7.36 – 7.43 (3H, m, ArH), 7.54 – 7.62 (3H, m, ArH), 7.68 (1H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.71 – 7.77 (1H, m, ArH), 7.95 (1H, d, $^3J_{HH}$ = 7.7 Hz, ArH). δ_C (126 MHz, $CDCl_3$) 84.9 (d, $^1J_{CF}$ = 185.1 Hz, CH_2), 87.7 (d, $^2J_{CF}$ = 19.6 Hz, C), 123.1 (CH), 125.8 (CH), 126.3 (CH), 126.4 (C), 129.1 (CH), 129.3 (CH), 130.1 (CH), 134.5 (CH), 135.8 (d, $^3J_{CF}$ = 3.0 Hz, C), 148.6 (d, $^3J_{CF}$ = 2.0 Hz, C), 169.3 (CO). δ_F (471 MHz, $CDCl_3$) -222.0 (t, $^2J_{HF}$ = 47.0 Hz, CH_2F). m/z (ESI) 243.0833 (MH^+, $C_{15}H_{12}FO_2$ requires 243.0821).

Structure solution and refinement

Tables S6 and S7 summarise the crystallographic data for fluorinated tetrahydropyridazines **3a, 3c, 3h** and **3j**, and fluorinated dihydrooxazines **7c** and **7d**. The data for the compounds were collected on a Bruker APEX 2000 CCD diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). The data were corrected for Lorentz and polarization effects, and empirical absorption corrections were applied. The structures were solved by direct methods and refined by full-matrix least squares cycles on F^2 for all data, using SHELXTL version 6.10.[40] All hydrogen atoms were included in calculated positions (C-H = 0.95-0.99 Å) riding on the bonded atom with isotropic displacement parameters set to 1.5 Ueq(C) for methyl H atoms and 1.2 Ueq(C) for all other H atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with

the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC: 2083051-2083056. Copies of the data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

References

12. J. Wang, X. Jia, T. Meng, L. Xin, *Synthesis*, 2005, **17**, 2838-2844.
13. M. Cai, Y. Huang, H. Zhao, R. Zhang, *J. Organomet. Chem.*, 2004, **689**, 2436-2440.
14. W. V. Kandur, K. J. Richert, C. J. Rieder, A. M. Thomas, C. Hu, J. W. Ziller, K. A. Woerpel, *Org. Lett.*, 2014, **16**, 2650‑2653.
15. T. Imai, S. Nishida, *Synthesis*, 1993, **4**, 395-399.
16. H. Zhao, J. Peng, R. Xiao, W. Hao, M. Cai, *J. Organomet. Chem.*, 2011, **696**, 2030-2034.
17. M. Nakajima, S. Kotani, T. Ishizuka, S. Hashimoto, *Tetrahedron Lett.*, 2005, **46**, 157-159.
18. S. Samanta, H. Mohapatra, R. Jana, J. K. Ray, *Tetrahedron Lett.*, 2008, **49**, 7153-7156.
19. R. Dran, T. Prange, *C. R. Hebd. Seances Acad. Sci. Ser. C*, 1966, **262**, 492.
20. Y. Ueki, H. Ito, I. Usui, B. Breit, *Chem. Eur. J.*, 2011, **17**, 8555‑8558.
21. M. Sai, H.Yorimitsu, K. Oshima, *Angew. Chem. Int. Ed.*, 2011, **50**, 3294‑3298.
22. M. Cai, Y. Huang, H. Zhao, R. Zhang, *J. Organomet. Chem.*, 2004, **689**, 2436-2440.
23. K. Miura, D. Wang, A. Hosomi, *J. Am. Chem. Soc.*, 2005, **127**, 9366-9367.
24. C. H. Heathcock, S. Kiyooka, T. A. Blumenkopf, *J. Org. Chem.*, 1984, **49**, 4215-4223.
25. M. Mahlau, P. Garcia-Garcia, B. List, *Chem. Eur. J.*, 2012, **18**, 16283-16287.
26. L. A. Paquette, M. J. Earle, G. F. Smith, *Org. Synth.* 1996, **73**, 132-135.
27. Y. Chen, M. Zhu, T. Loh, *Org. Lett.*, 2015, **17**, 2712‑2715.
28. R. D. Rieke, W. R. Klein, T. C. Wu, *J. Org. Chem.*, 1993, **58**, 2492-2500.
29. M. Moss, X. Han, J. M. Ready, *Angew Chem. Int. Ed.*, **2016**, 55, 10017-10021.
30. S. Inaba, R. D. Rieke, *J. Org. Chem.*, 1985, **50**, 1373-1381.
31. L. Pascal, *Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques*, 1969, **268**, 1177.
32. X. Hu, J. Chen, Q. Wei, F. Liu, Q. Deng, Y. Zou, W. Xiao, *Eur. J. Org. Chem.*, 2014, **15**, 3082-3086.
33. X. Hu, X. Q, J. Chen, Q. Wei, Q. Zhao, Y. Lan, W. Xiao, *Nat. Commun.*, 2016, **7**, 11188.
34. G. A. Marriner, S. A. Garner, H. Jang, M. J. Krische, J. *Org. Chem.*, 2004, **69**, 1380-1382.
35. D. Jiang, J. Peng, Y. Chen, *Org. Lett.*, 2008, **10**, 1695‑1698.
36. M. Zhu, J. Zhao, T. Loh, *J. Am. Chem. Soc*, 2010, **132**, 6284-6285.

37. R. Zimmer, H. Reissig, *Angew. Chem. Int. Ed.*, 1988, **27**, 1518-1519.
38. H. Egami, J. Asada, K. Sato, D. Hashizume, Y. Kawato and Y. Hamashima, *J. Am. Chem. Soc.*, 2015, **137**, 10132-10135.
39. J.-F. Zhao, X.-H. Duan, H. Yang and L.-N. Guo, *J. Org. Chem.*, 2015, **80**, 11149-11155.
40. G. M. Sheldrick, SHELXTL Version 6.10, Bruker AXS, Inc., Maddison, Wisconsin, USA, 2000.

Table S7. Crystallographic data for tetrahydropyridazines **3a** (R = 4-C_6H_4Cl), **3c** (R = Ph), **3h** (R = 2-thienyl) and **3j** (R = $CH(CH_3)_2$).

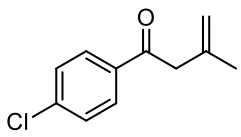
	3a (R = 4-C_6H_4Cl)	**3c** (R = Ph)	**3h** (R = 2-thienyl)	**3j** (R = $CH(CH_3)_2$)
Formula	$C_{18}H_{18}ClFN_2O_2S$	$C_{18}H_{19}FN_2O_2S$	$C_{16}H_{17}FN_2O_2S_2$	$C_{15}H_{21}FN_2O_2S$
Formula weight	380.85	346.41	352.44	312.40
Crystal system	Monoclinic	Orthorhombic	Trigonal	Orthorhombic
Space group	P2(1)/n	Pbca	R-3	P2(1)2(1)2(1)
Unit cell dimensions				
a (Å)	11.028(3)	18.644(4)	20.185(3)	8.315(3)
b (Å)	9.215(3)	9.1535(18)	20.185(3)	11.835(5)
c (Å)	17.393 (5)	20.027(4)	21.625(5)	16.239(6)
α (°)	90	90	90	90
β (°)	98.322(5)	90	90	90
γ (°)	90	90	120	90
U (Å^3)	1748.9(9)	3417.7(11)	7630(2)	1598.0(11)
Temperature (K)	150(2)	150(2)	150(2)	150(2)
Z	4	8	18	4
D_c (Mg m^{-3})	1.446	1.346	1.381	1.298
μ(Mo-Kα) (mm^{-1})	0.362	0.212	0.334	0.219
F (000)	792	1456	3312	664
Dimensions (mm^3)	0.48 x 0.37 x 0.25	0.38 x 0.15 x 0.11	0.35 x 0.18 x 0.14	0.43 x 0.31 x 0.20
Data collection range (°)	2.06 – 26.00	2.03 – 26.00	2.02 – 26.00	2.13 – 26.00

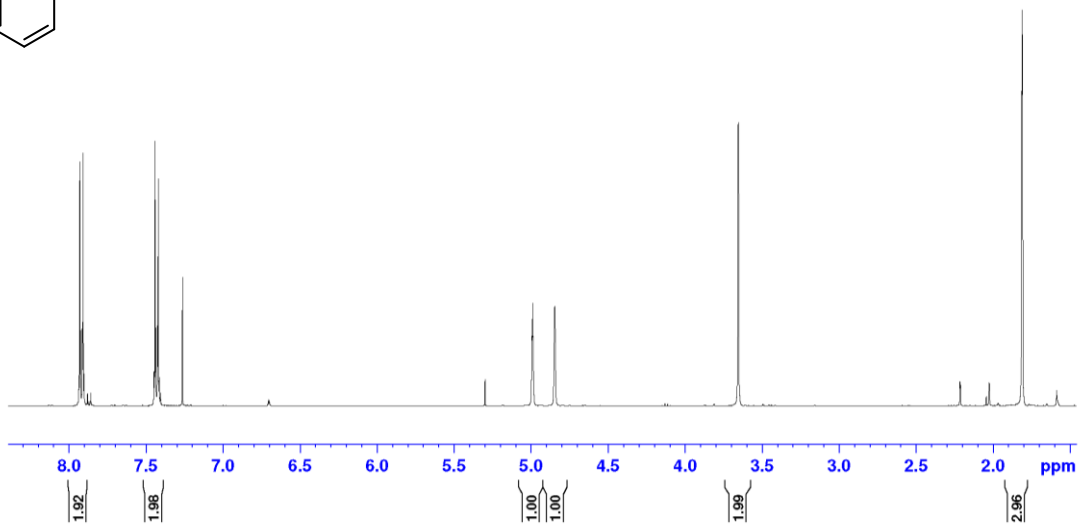
Index ranges	-13 ≤ h ≤ 13	-22 ≤ h ≤ 22	-24 ≤ h ≤ 24	-10 ≤ h ≤ 10
	-11 ≤ k ≤ 11	-11 ≤ k ≤ 11	-24 ≤ k ≤ 24	-14 ≤ k ≤ 14
	-21 ≤ l ≤ 21	-24 ≤ l ≤ 24	-26 ≤ l ≤ 26	-20 ≤ l ≤ 20
Reflections	13028	24963	19944	12402
Unique reflections (R_{int})	3445 (0.0471)	3361 (0.1007)	3323 (0.0973)	3140 (0.0625)
θ_{max} (% complete)	26.00 (99.8)	26.00 (100.0)	26.00 (99.9)	26.00 (100.0)
Absorption correction	Empirical	Empirical	Empirical	Empirical
Max/min transmission	0.914 / 0.717	0.914 / 0.726	0.901 / 0.580	0.875 / 0.572
Data/restraints/parameters	3445 / 0 / 228	3361 / 0 / 219	3323 / 0 / 210	3140 / 0 / 195
Goodness of fit on F^2	1.039	0.958	0.974	1.072
Final R indices [$I > 2\sigma(I)$]				
R_1	0.0433	0.0511	0.0546	0.0497
wR_2	0.1041	0.1004	0.1106	0.1054
R indices (all data)				
R_1	0.0515	0.0859	0.0934	0.0607
wR_2	0.1081	0.1105	0.1225	0.1100
Largest diff. peak, hole (eÅ^{-3})	0.706, -0.259	0.288, -0.312	0.338, -0.273	0.258, -0.182

Table S8 Crystallographic data for dihydrooxazines **7c** (R = 4-$C_6H_4CH_3$) and **7d** (R = 4-C_6H_4Cl).

	7c	**7d**
	R = 4-$C_6H_4CH_3$	R = 4-C_6H_4Cl
Formula	$C_{12}H_{14}FNO$	$C_{11}H_{11}ClFNO$
Formula weight	207.24	227.66
Crystal system	Orthorhombic	Orthorhombic
Space group	Pbca	Pbca
Unit cell dimensions		
a (Å)	9.348(5)	9.503(6)
b (Å)	8.856(5)	9.161(6)
c (Å)	25.174(13)	24.001(15)
α (°)	90	90
β (°)	90	90
γ (°)	90	90
U (Å^3)	2084.1(18)	2090(2)
Temperature (K)	150(2)	150(2)
Z	8	8
D_c (Mg m^{-3})	1.321	1.447
μ(Mo-Kα) (mm^{-1})	0.096	0.350
F (000)	880	944
Dimensions (mm^3)	0.48 x 0.43 x 0.05	0.45 x 0.28 x 0.04
Data collection range (°)	1.62 – 25.99	1.70 – 25.97
Index ranges	-11 ≤ h ≤ 11	-11 ≤ h ≤ 11
	-10 ≤ k ≤ 10	-11 ≤ k ≤ 11
	-30 ≤ l ≤ 31	-29 ≤ l ≤ 29
Reflections	14961	15005
Unique reflections (R_{int})	2047 (0.1179)	2049 (0.1739)
θ_{max} (% complete)	25.99 (100.0)	25.97 (100.0)
Absorption correction	Empirical	Empirical
Max/min transmission	0.983 / 0.301	0.942 / 0.163
Data/restraints/parameters	2047 / 0 / 138	2049 / 0 / 137
Goodness of fit on F^2	0.990	1.037
Final *R* indices [$I > 2\sigma(I)$]		
R_1	0.0594	0.0865
wR_2	0.1462	0.1974
R indices (all data)		
R_1	0.0783	0.1401
wR_2	0.1565	0.2267
Largest diff. peak, hole (eÅ^{-3})	0.341, -0.376	0.768, -0.421

^{1}H NMR Spectrum





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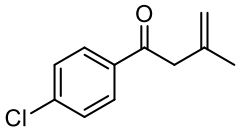

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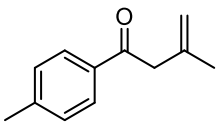

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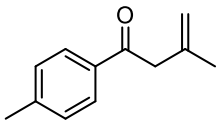

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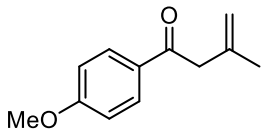

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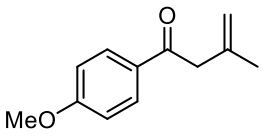

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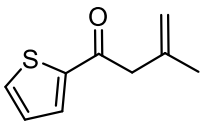

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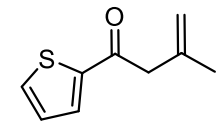

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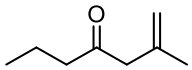

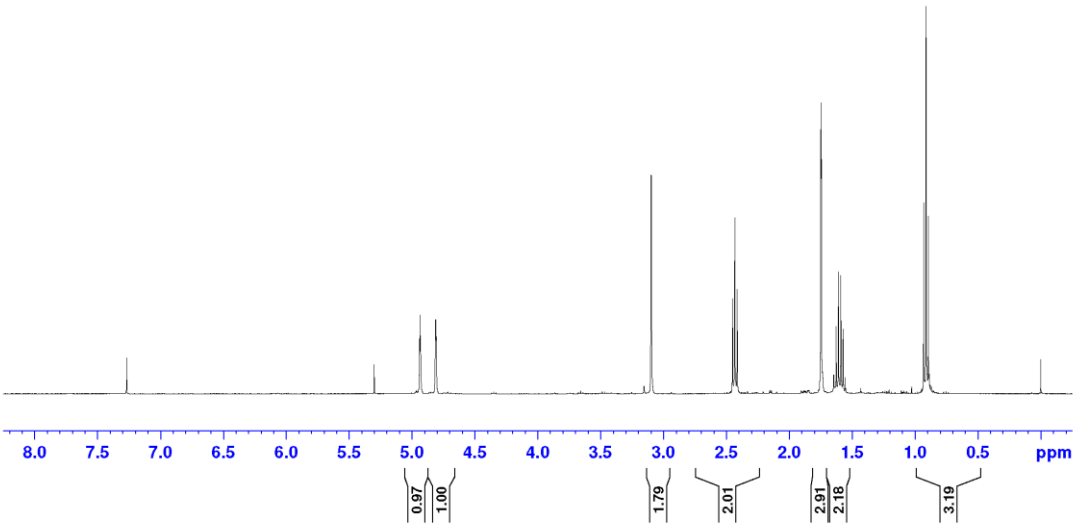

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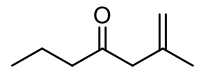

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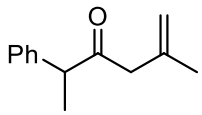

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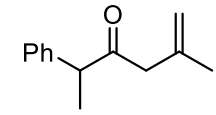

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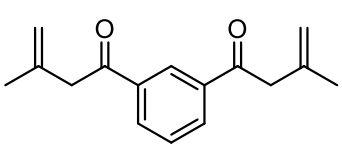

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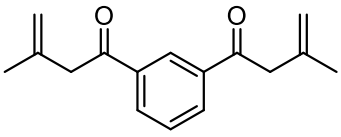

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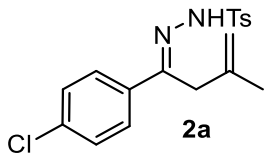

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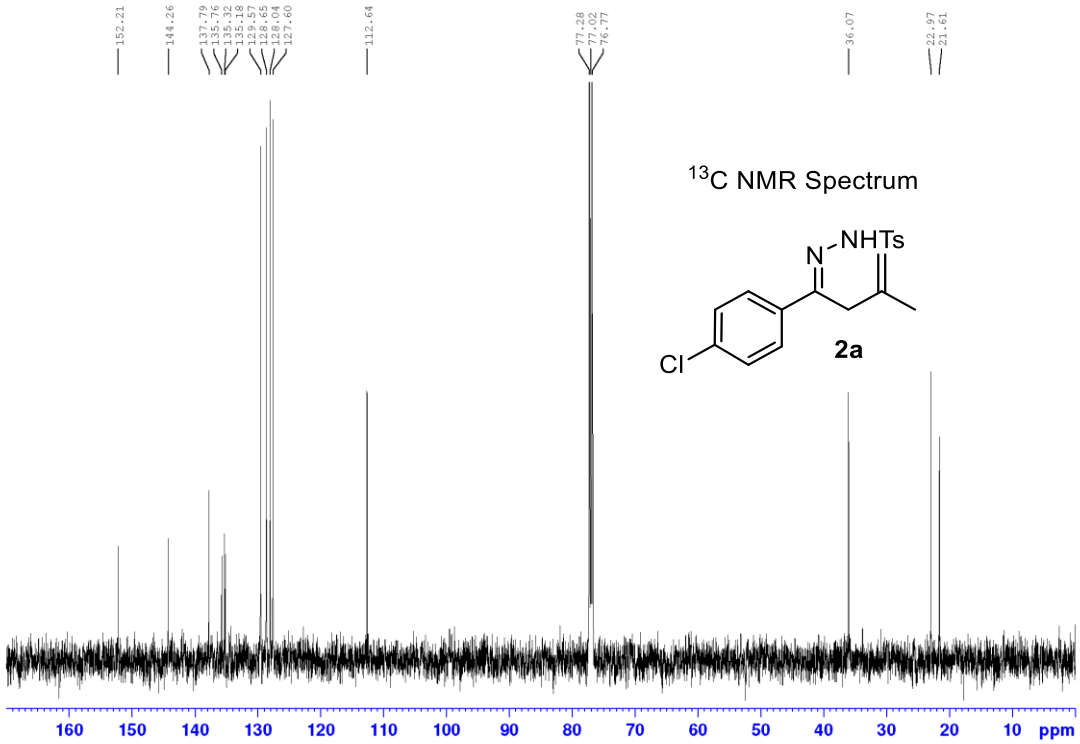
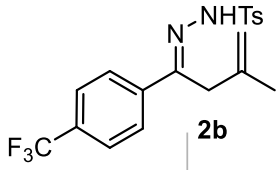


^{13}C NMR Spectrum

2a

^{1}H NMR Spectrum



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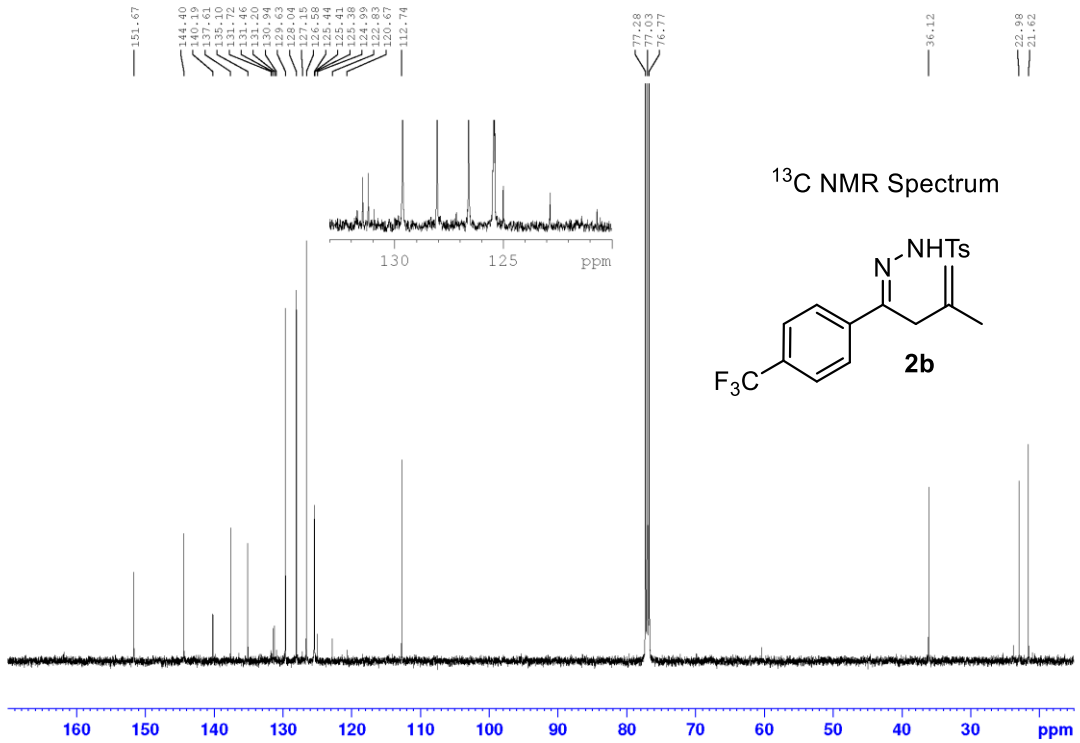

^{13}C NMR Spectrum

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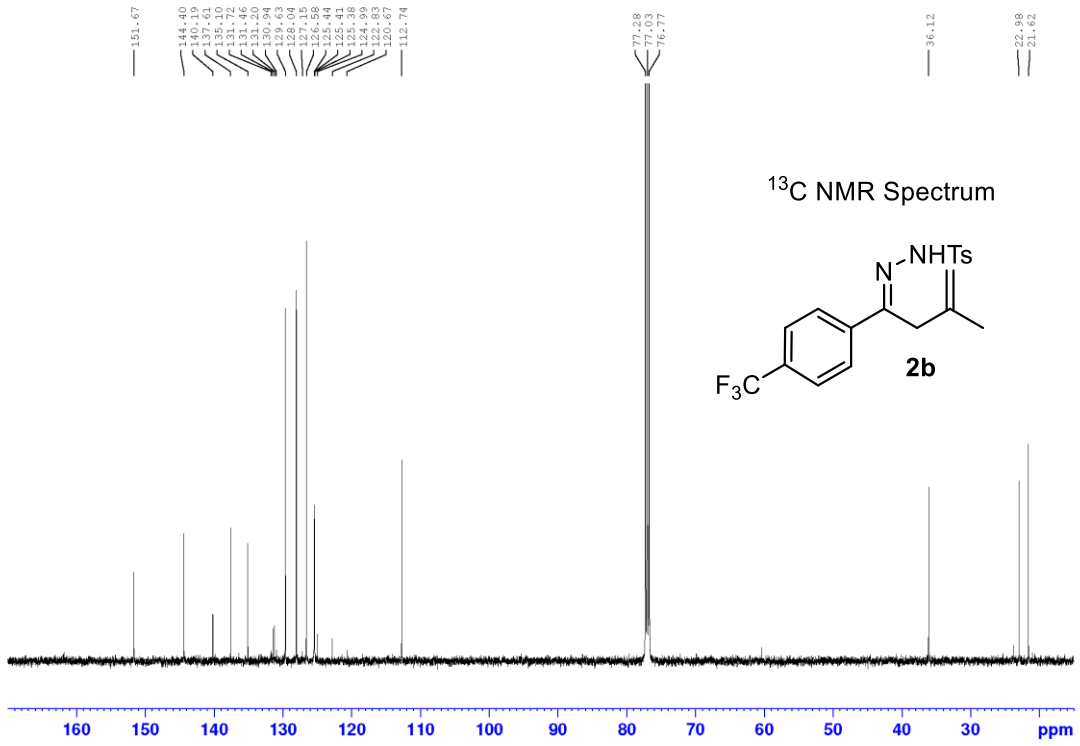
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125.38
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122.83
120.67
112.74
77.28
77.03
76.77
36.12
22.98
21.92
13C NMR Spectrum
NHTs
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F3C
2b
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150
140
130
120
110
100
90
80
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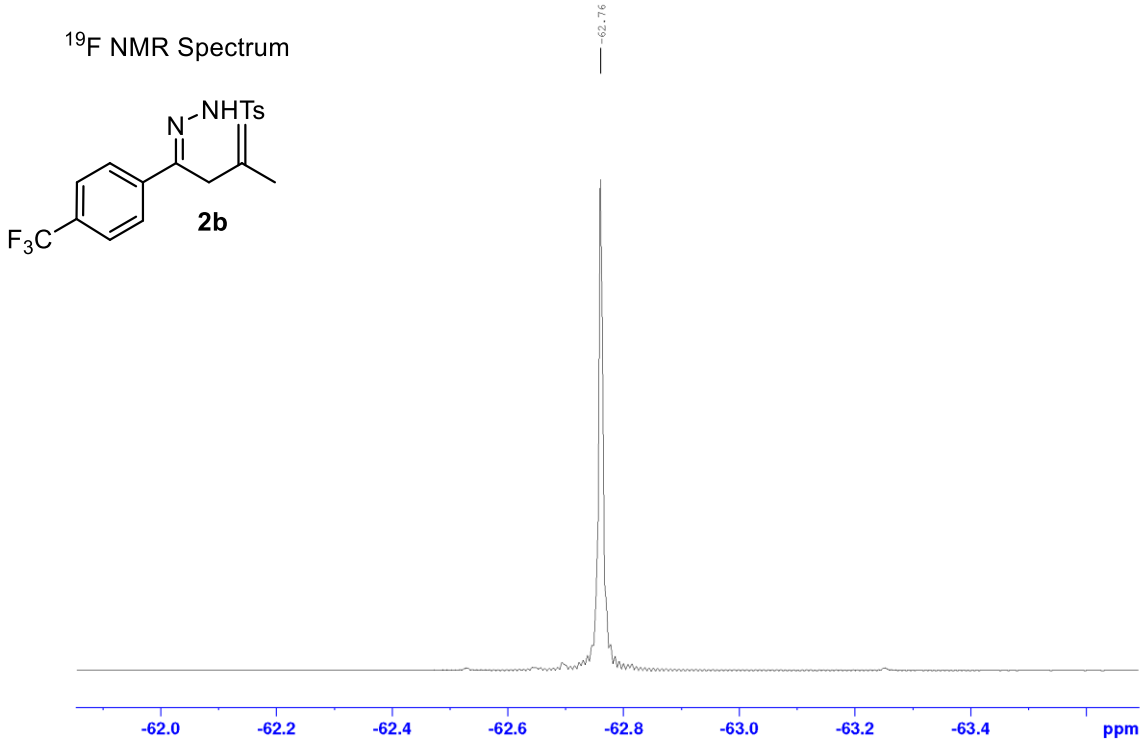
60
50
40
30
ppm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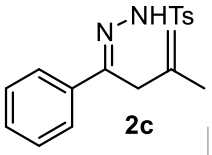
^{1}H NMR Spectrum



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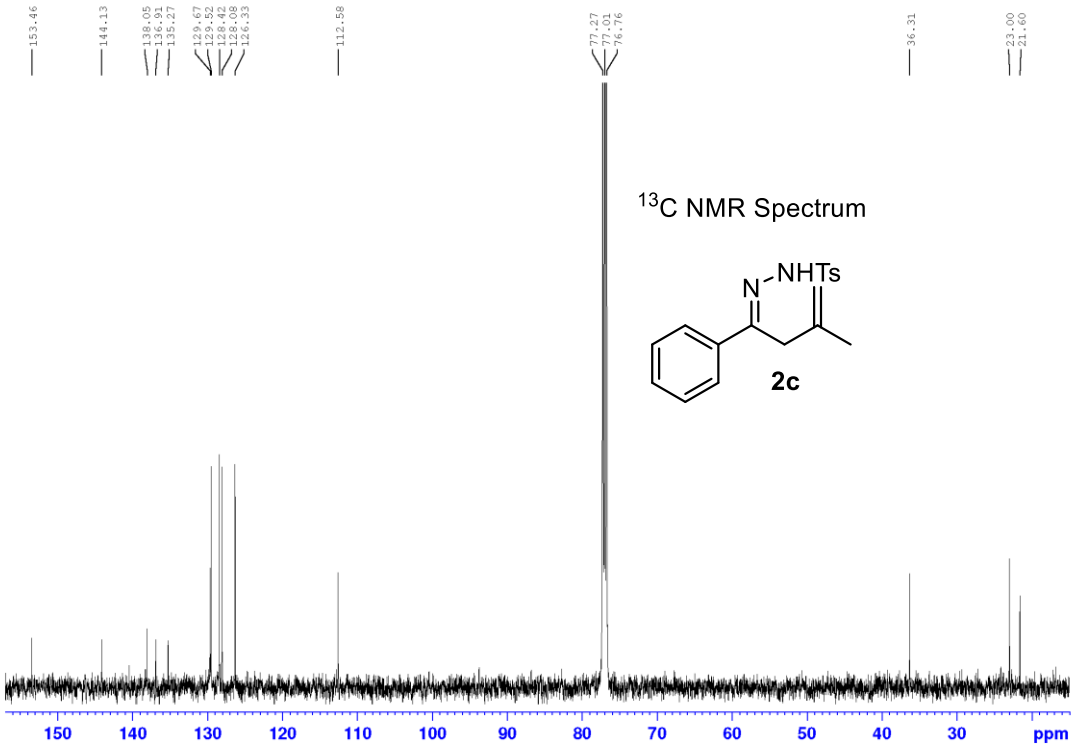
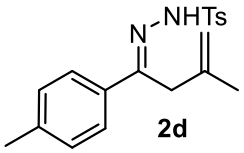


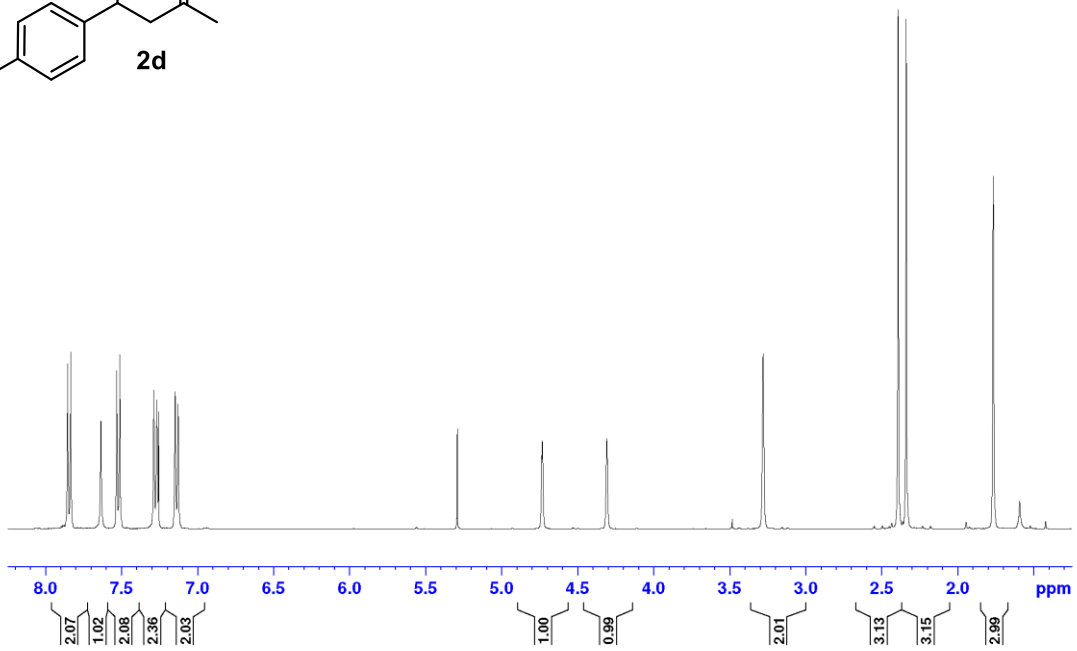
^{13}C NMR Spectrum

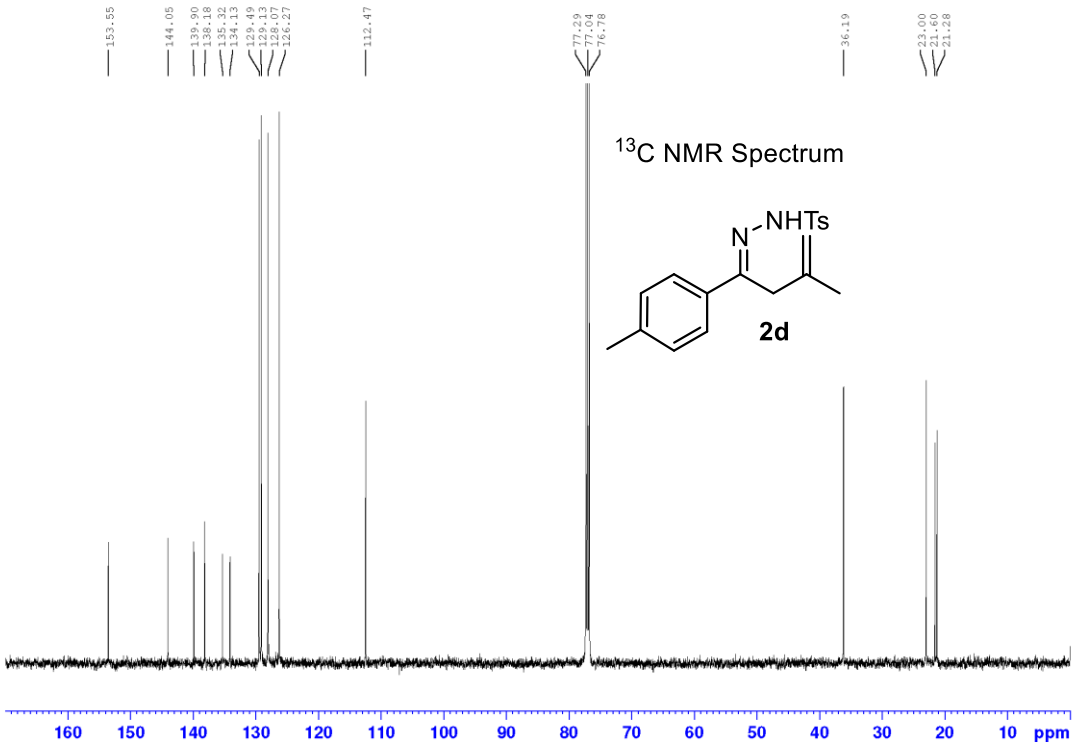
2c

^{1}H NMR Spectrum



2d

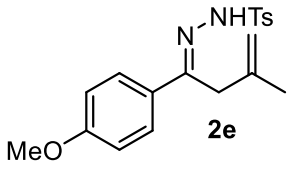




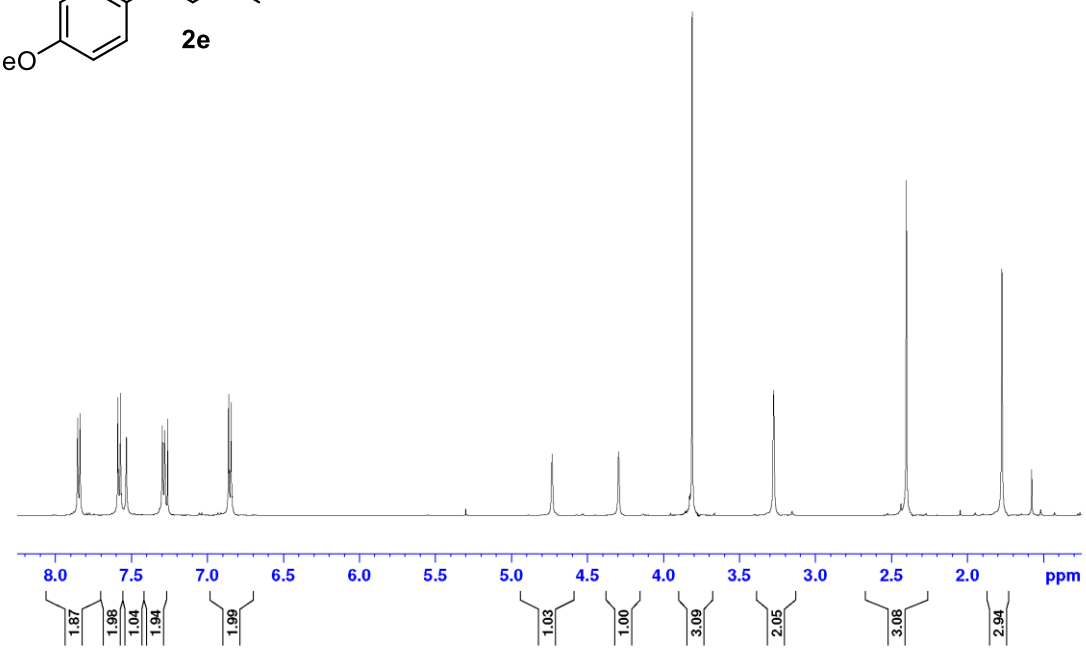
^{13}C NMR Spectrum

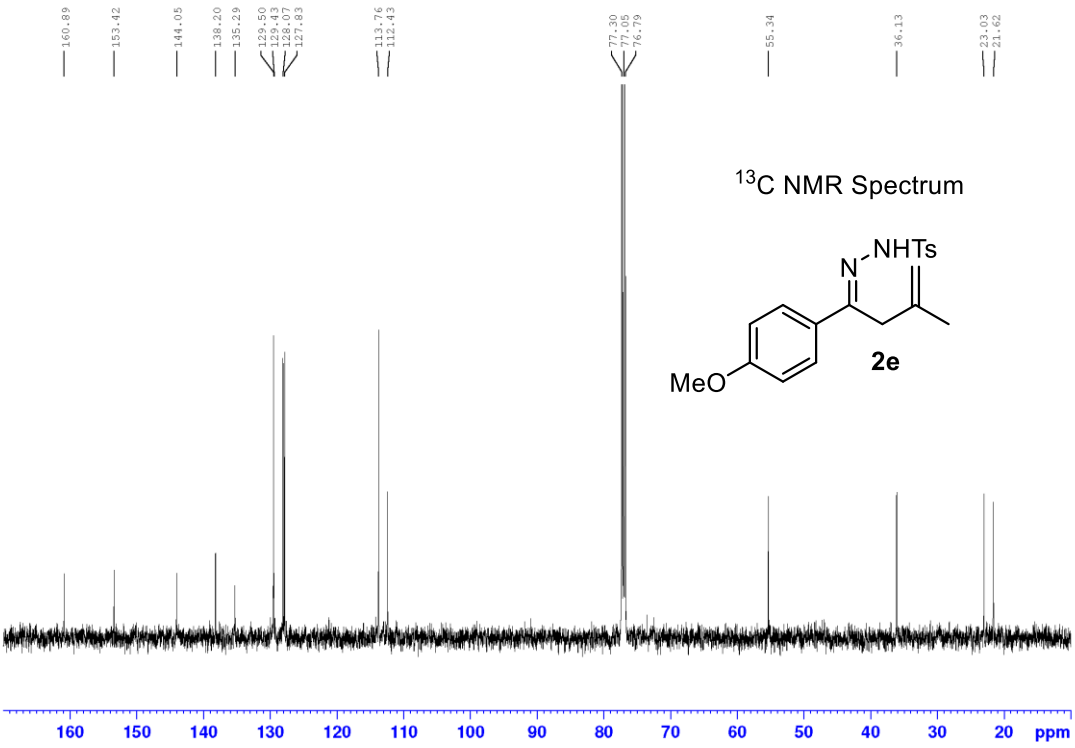
2d

^{1}H NMR Spectrum



2e

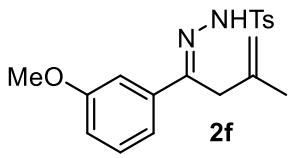




^{13}C NMR Spectrum

2e

^{1}H NMR Spectrum



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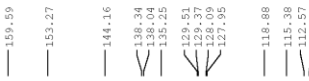
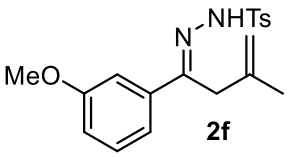
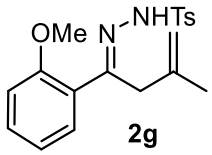


^{13}C NMR Spectrum

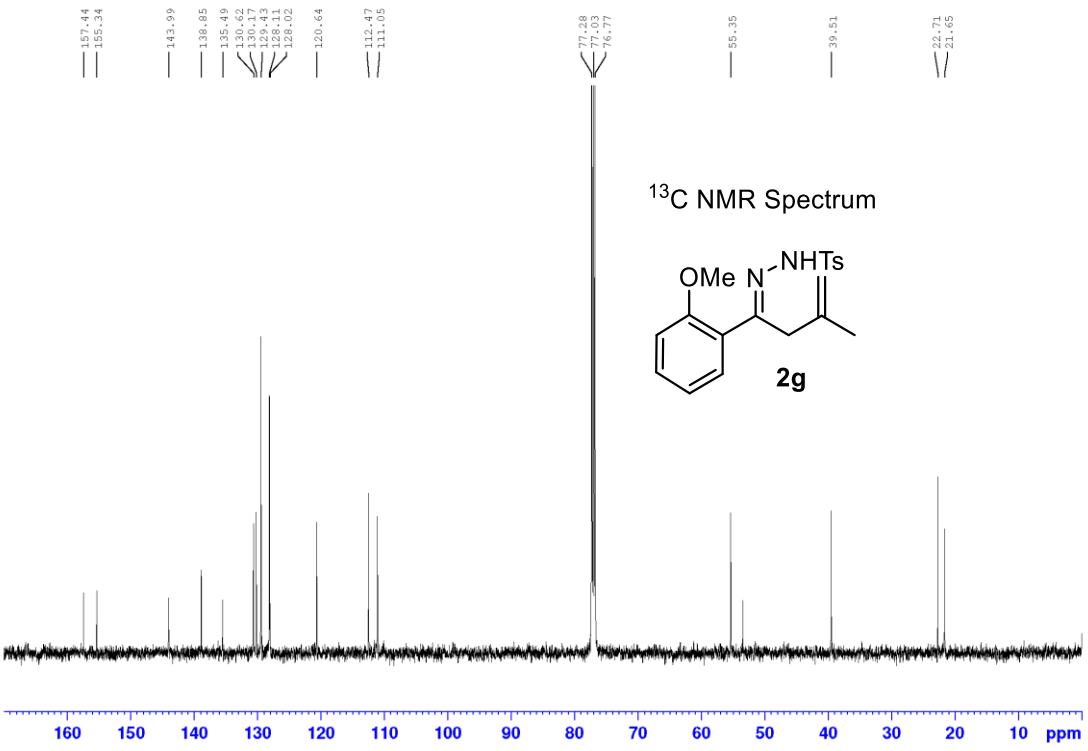


2f

^{1}H NMR Spectrum



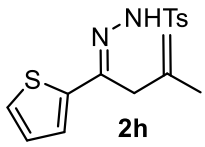
2g



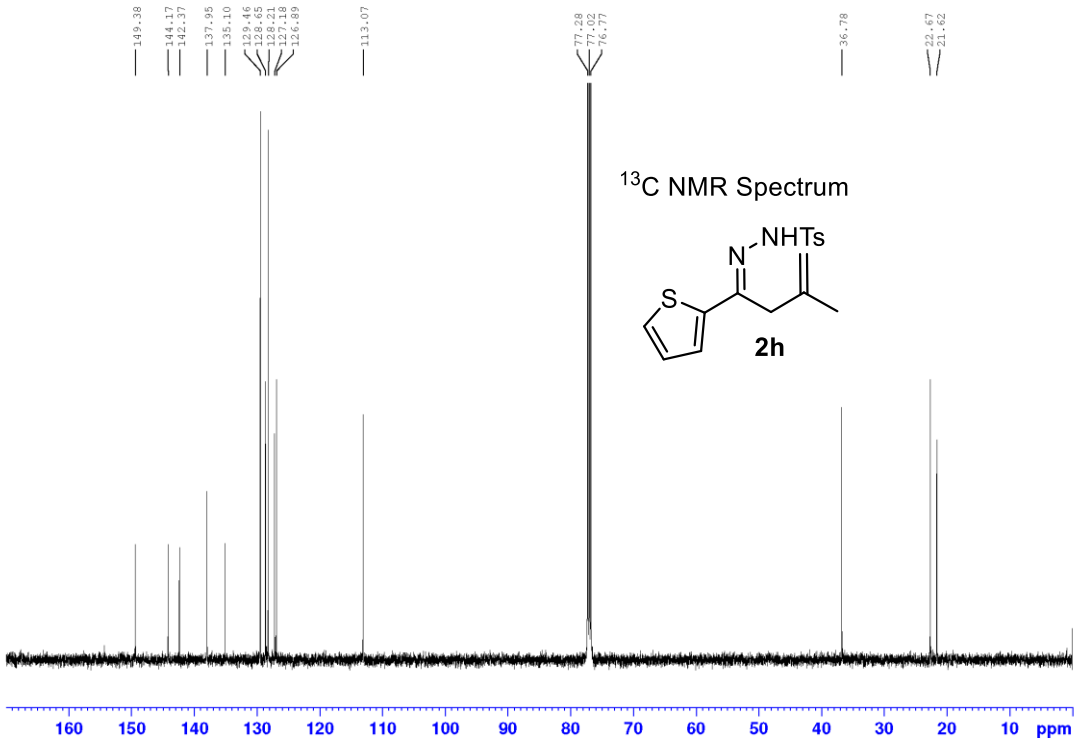
^{13}C NMR Spectrum

2g

^{1}H NMR Spectrum



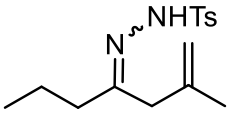
2h



^{13}C NMR Spectrum

2h

^{1}H NMR Spectrum



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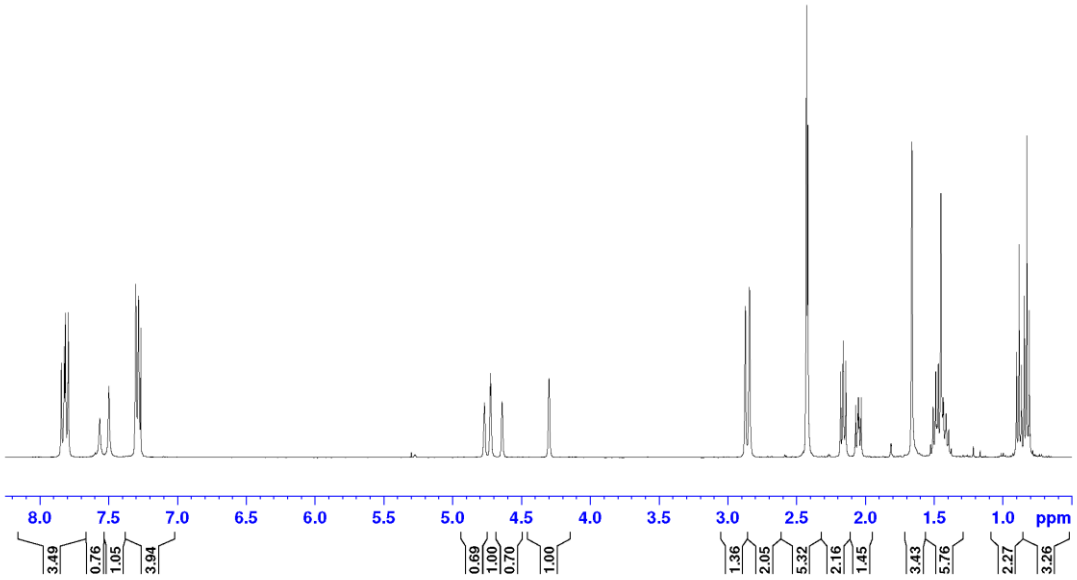
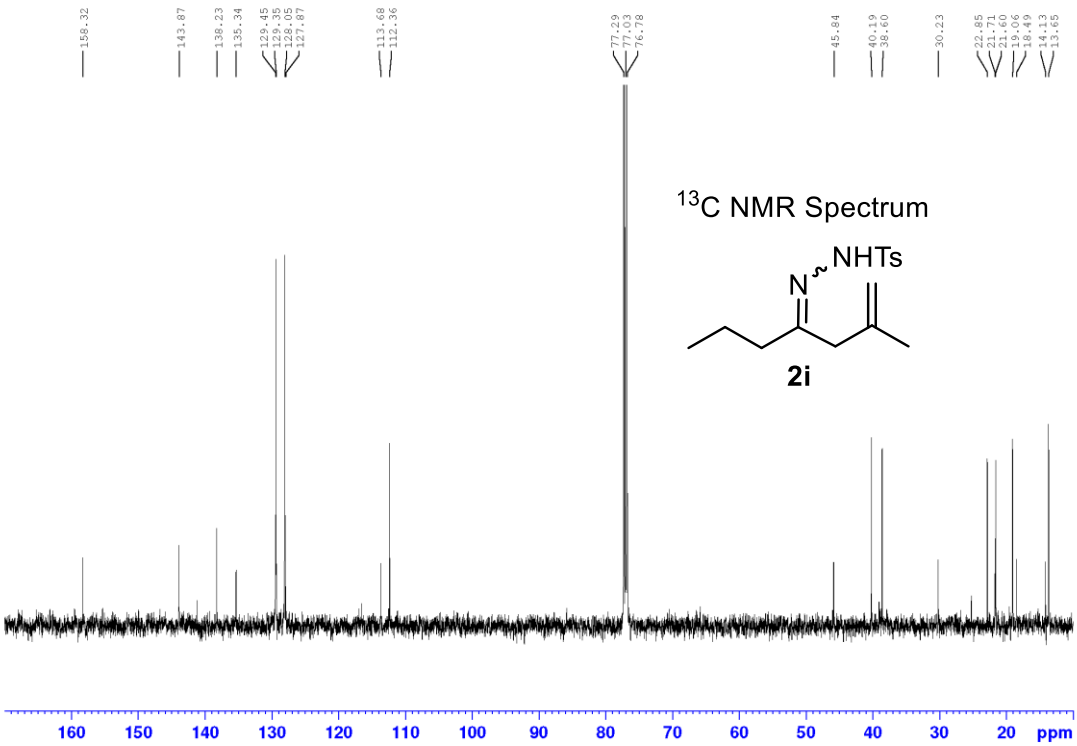
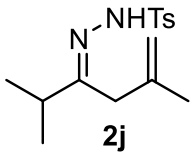




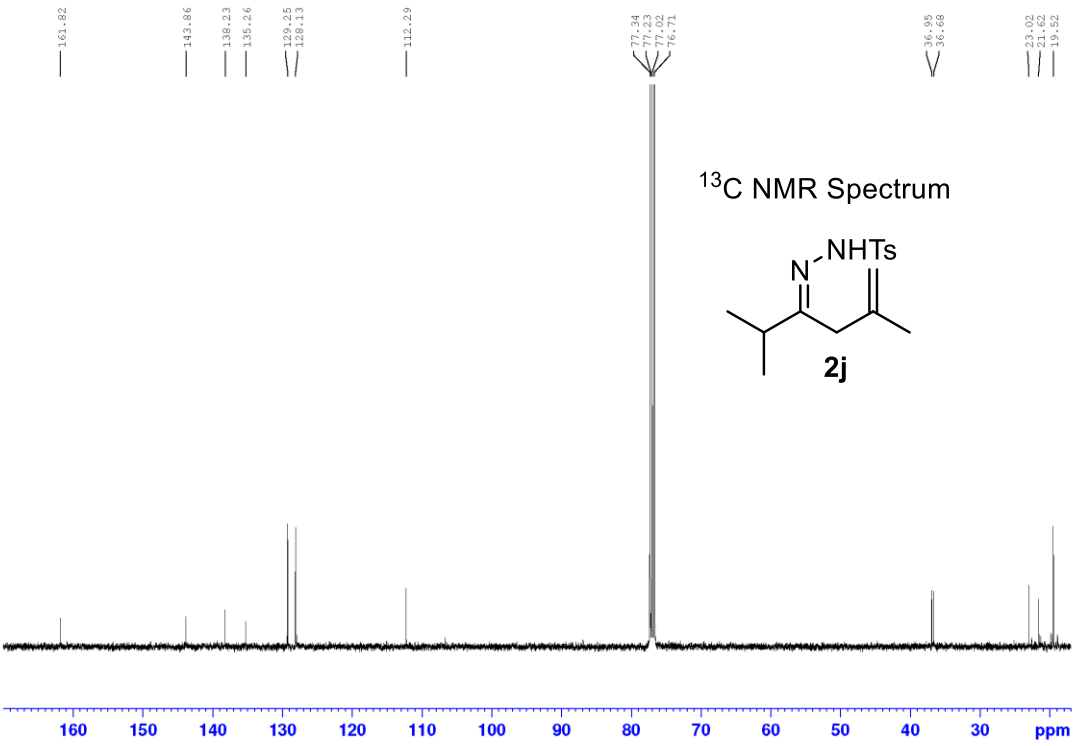
^{13}C NMR Spectrum

2i

^{1}H NMR Spectrum



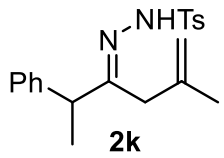
2j



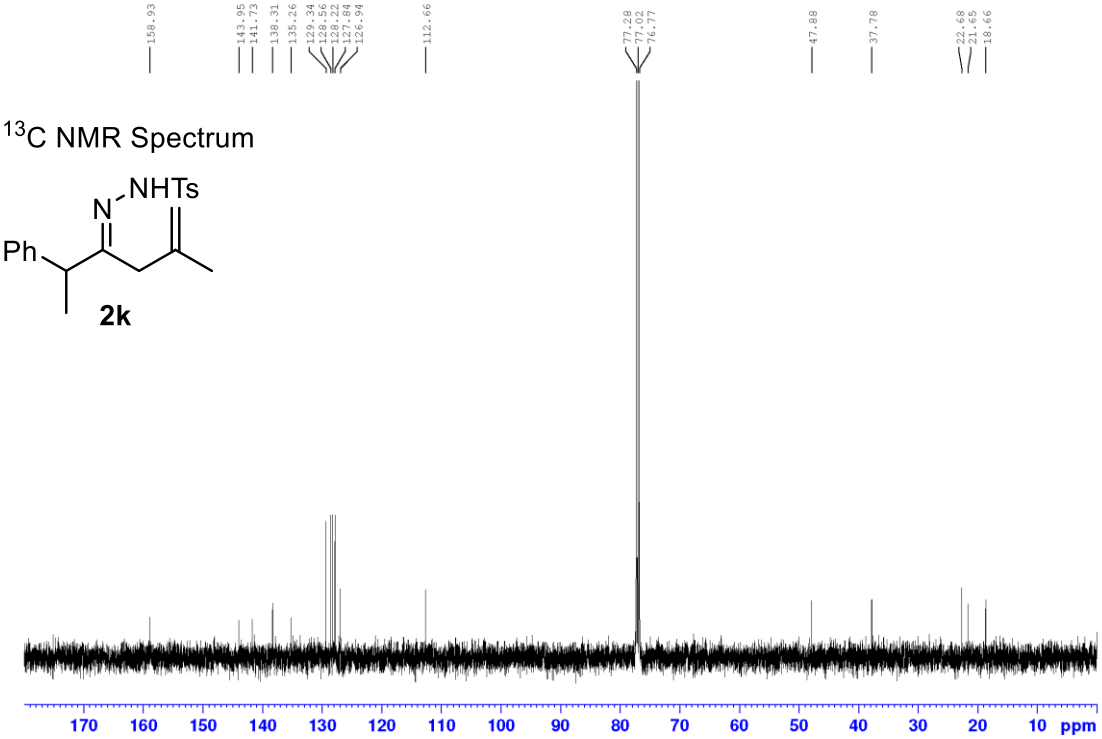
^{13}C NMR Spectrum

2j

^{1}H NMR Spectrum



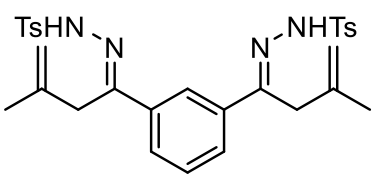
2k



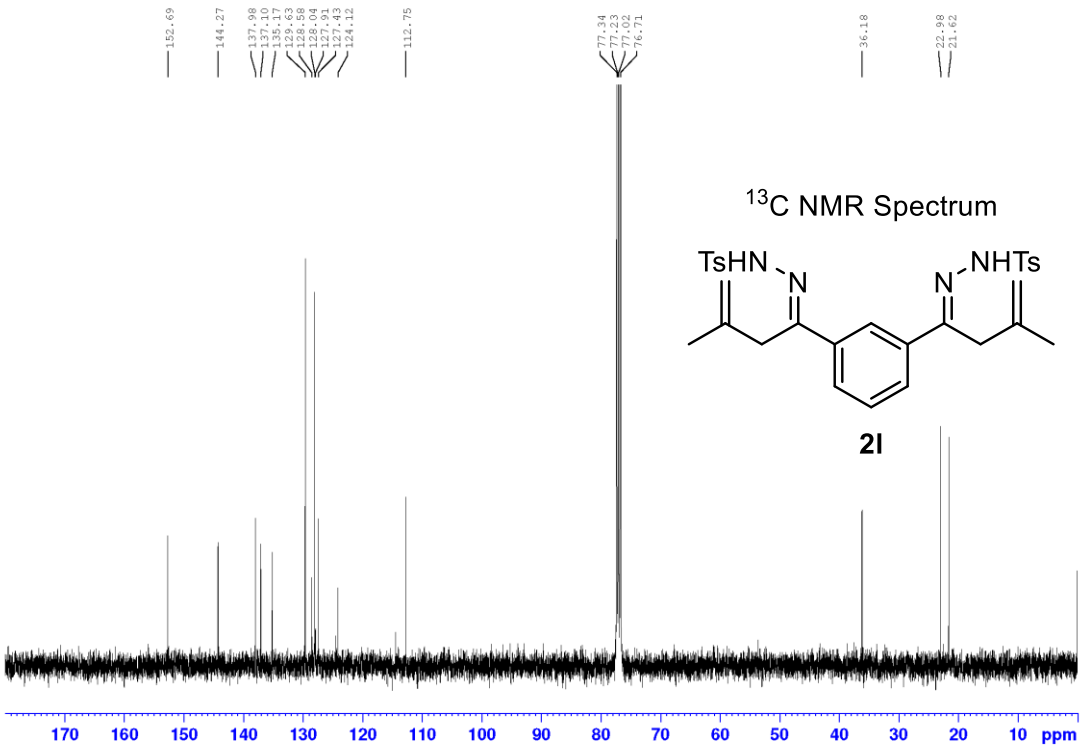
^{13}C NMR Spectrum

2k

^{1}H NMR Spectrum



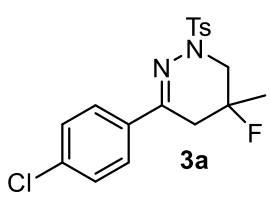
2l

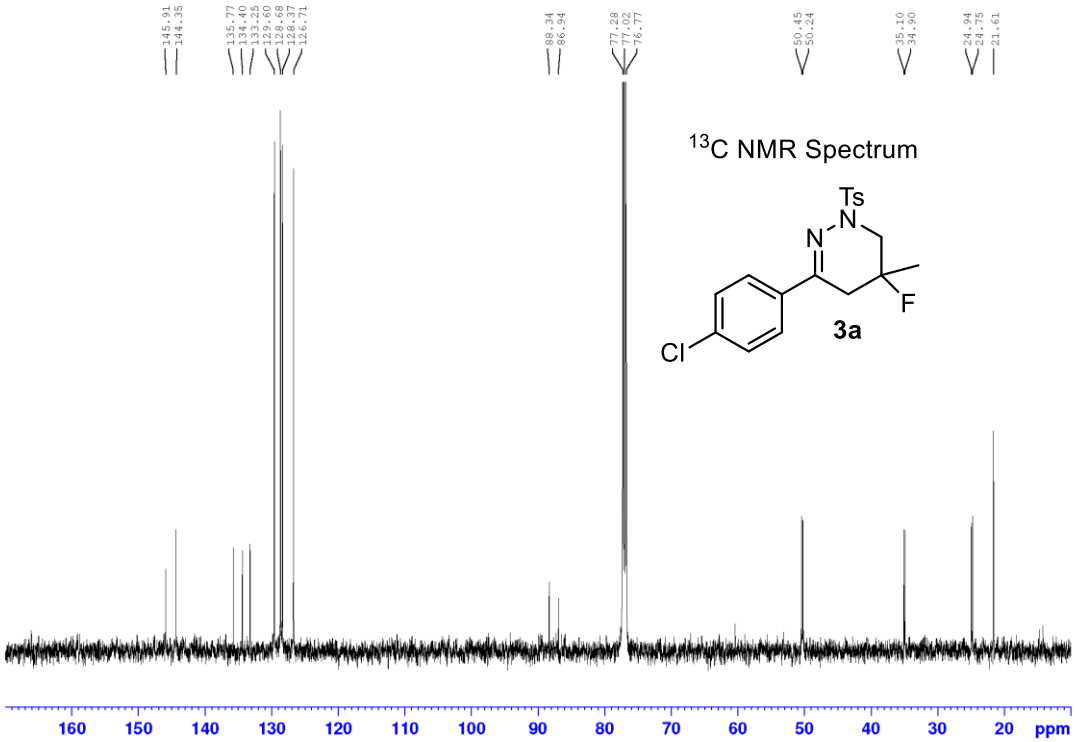


^{13}C NMR Spectrum

2l

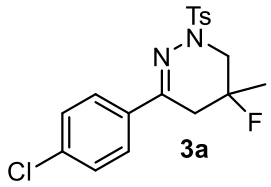
^{1}H NMR Spectrum





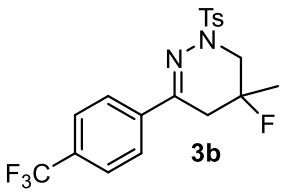
^{13}C NMR Spectrum

^{19}F NMR Spectrum

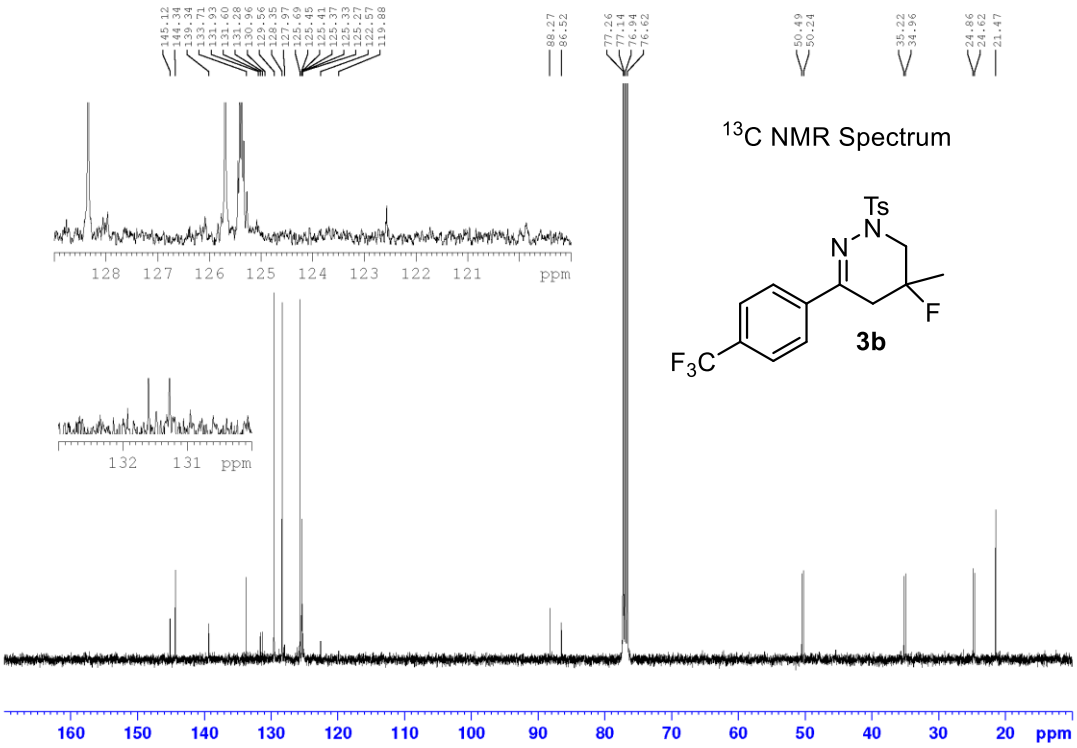


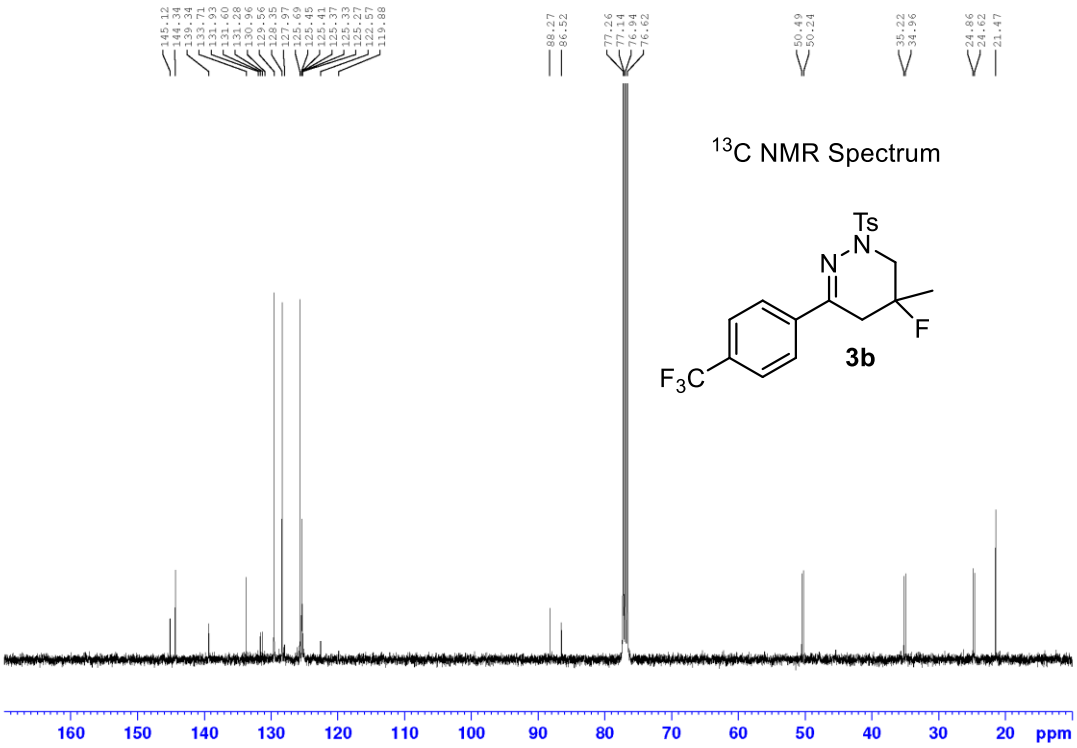
3a

^{1}H NMR Spectrum



3b


145.12
144.34
139.34
133.71
131.93
131.60
131.28
130.96
129.56
128.35
127.97
125.69
125.45
125.41
125.37
125.33
125.27
122.57
119.88
88.27
86.52
77.26
77.14
76.94
76.62
50.49
50.24
35.22
34.96
24.86
24.62
21.47
128 127 126 125 124 123 122 121 ppm
132 131 ppm
13C NMR Spectrum
Ts
N
N
F
F3C
3b
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


145.12
144.34
139.34
133.71
131.93
131.60
131.28
130.96
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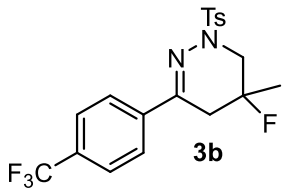
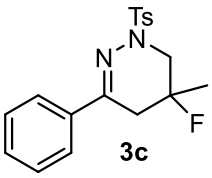
128.35
127.97
125.69
125.45
125.41
125.37
125.33
125.27
122.57
119.88
88.27
86.52
77.26
77.14
76.94
76.62
50.49
50.24
35.22
34.96
24.86
24.62
21.47
13C NMR Spectrum
Ts
N
N
F
F3C
3b
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

^{19}F NMR Spectrum



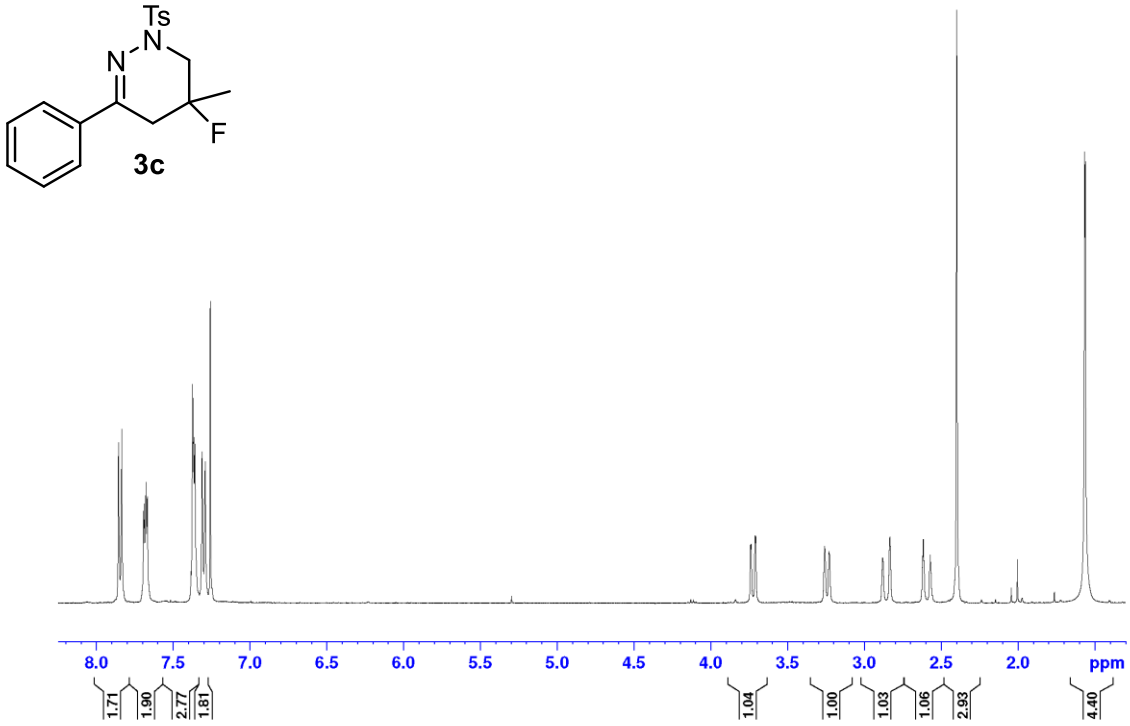
3b

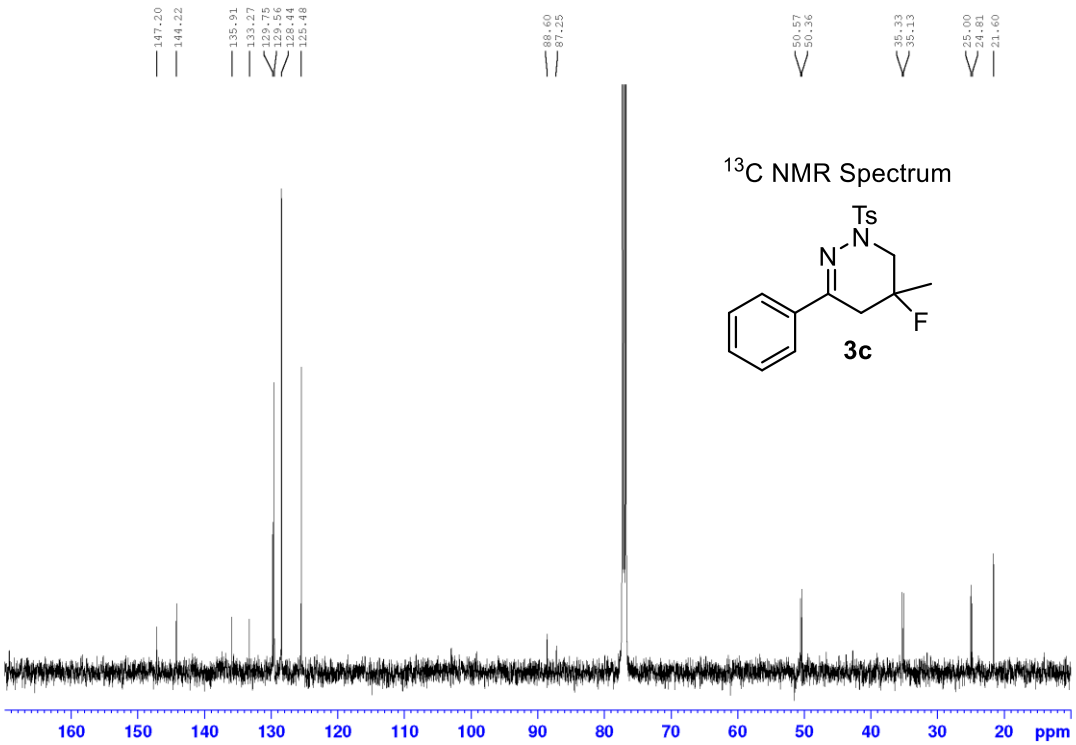
^{1}H NMR Spectrum



3c

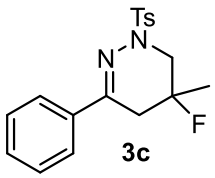
$^{1}H\{^{19}F\}$ NMR Spectrum





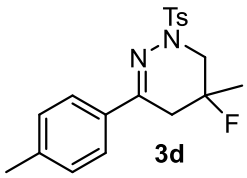
^{13}C NMR Spectrum

^{19}F NMR Spectrum

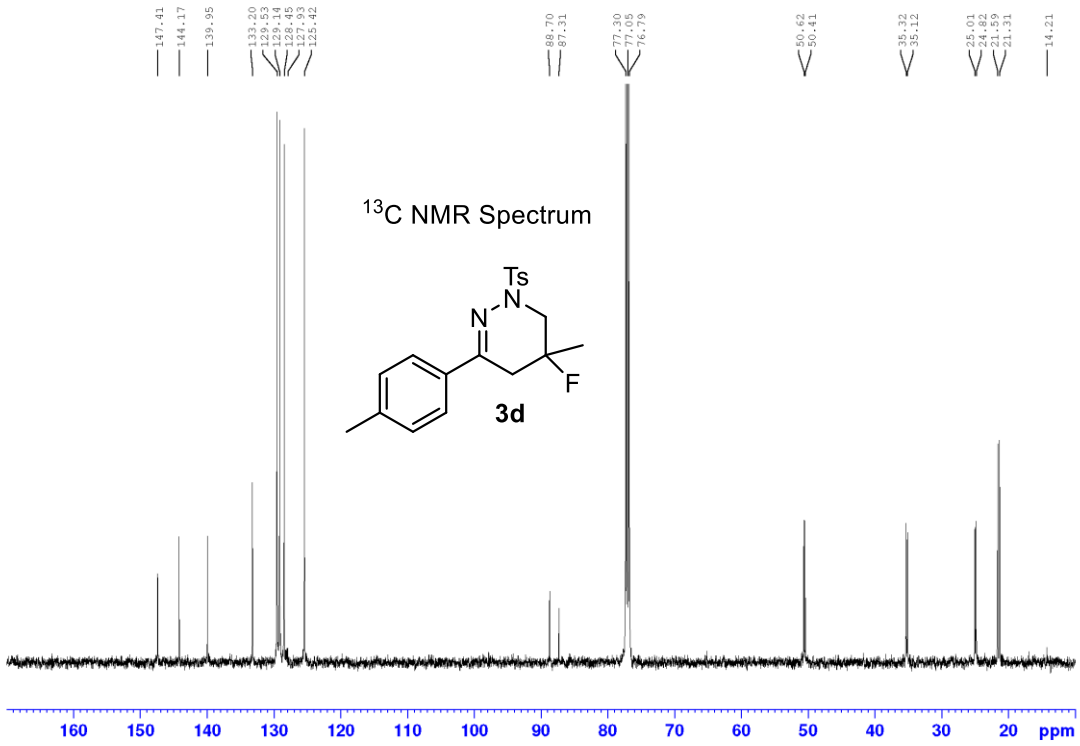


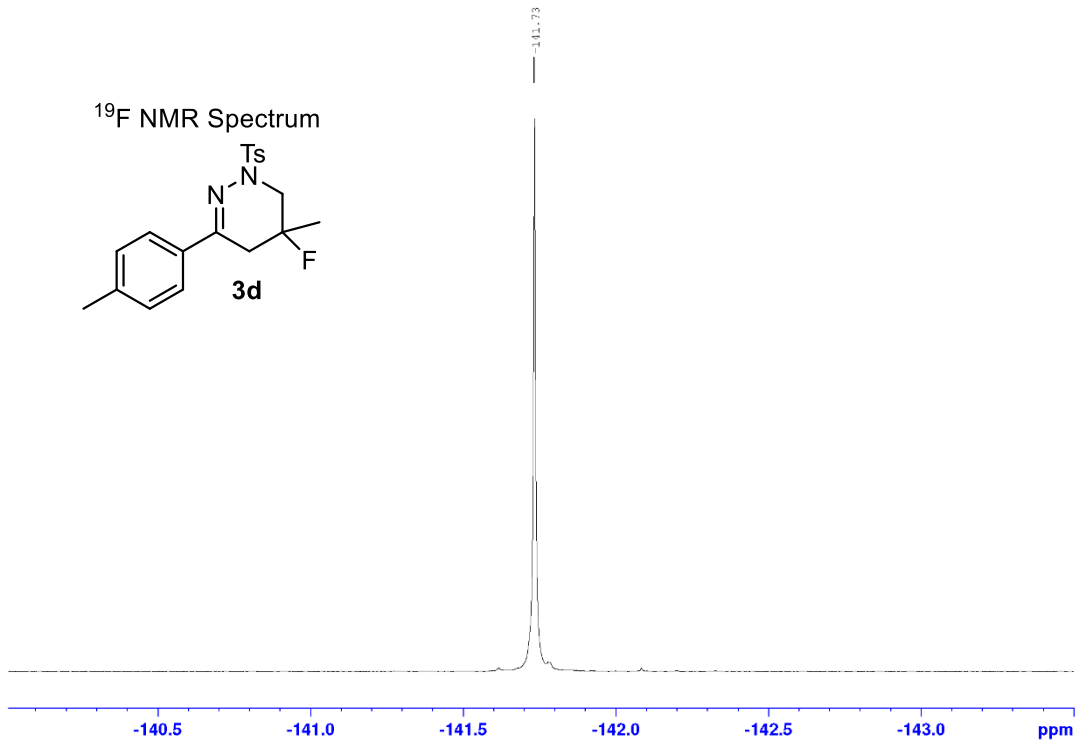
3c

^{1}H NMR Spectrum

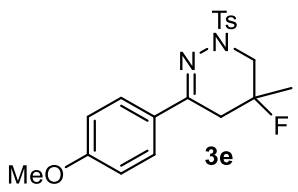


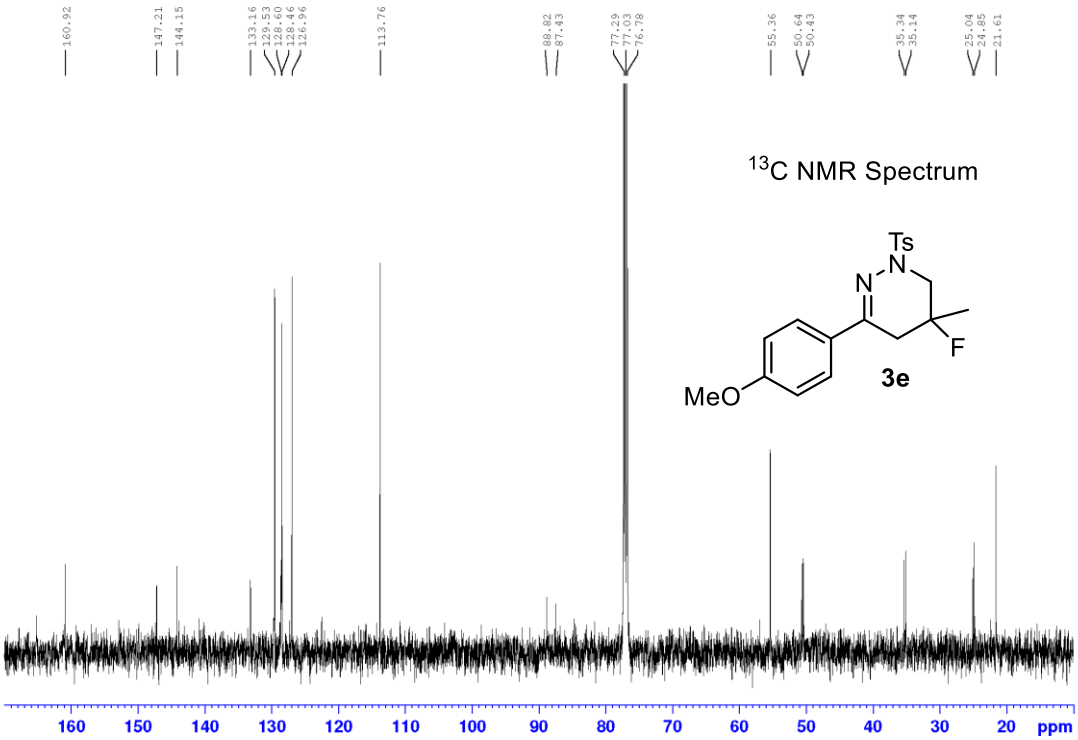
3d


147.41
144.17
139.95
133.20
129.53
129.14
128.45
127.93
125.42
88.70
87.31
77.30
77.05
76.79
50.62
50.41
35.32
35.12
25.01
24.82
21.59
21.31
14.21
13C NMR Spectrum
Ts
N
N
F
3d
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-141.73
19F NMR Spectrum
Ts
N
N
F
3d
-140.5
-141.0
-141.5
-142.0
-142.5
-143.0
ppm

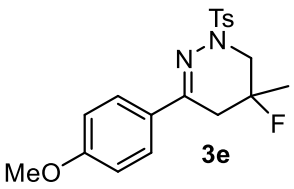
^{1}H NMR Spectrum





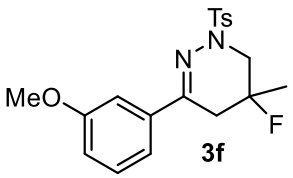
^{13}C NMR Spectrum

^{19}F NMR Spectrum



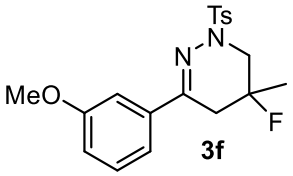
3e

^{1}H NMR Spectrum

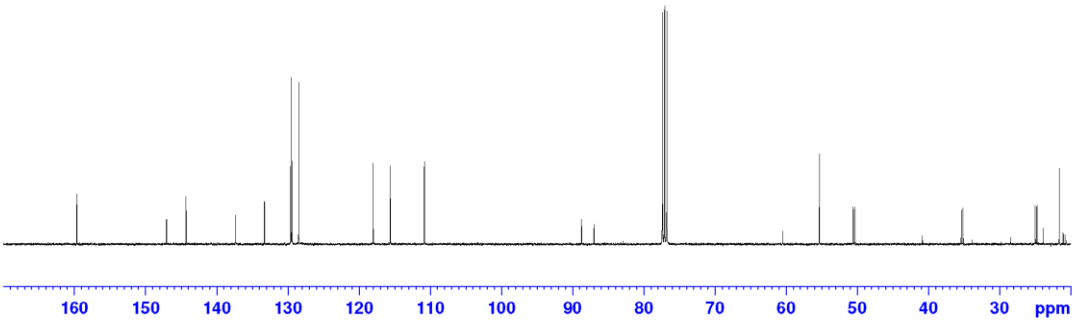


3f

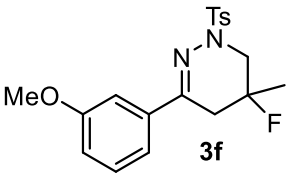
^{13}C NMR Spectrum



3f

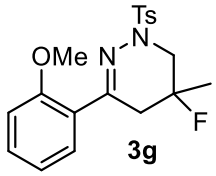


^{19}F NMR Spectrum



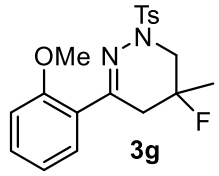
3f

^{1}H NMR Spectrum



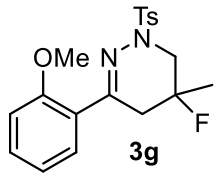
3g

^{13}C NMR Spectrum



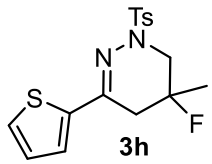
3g

^{19}F NMR Spectrum

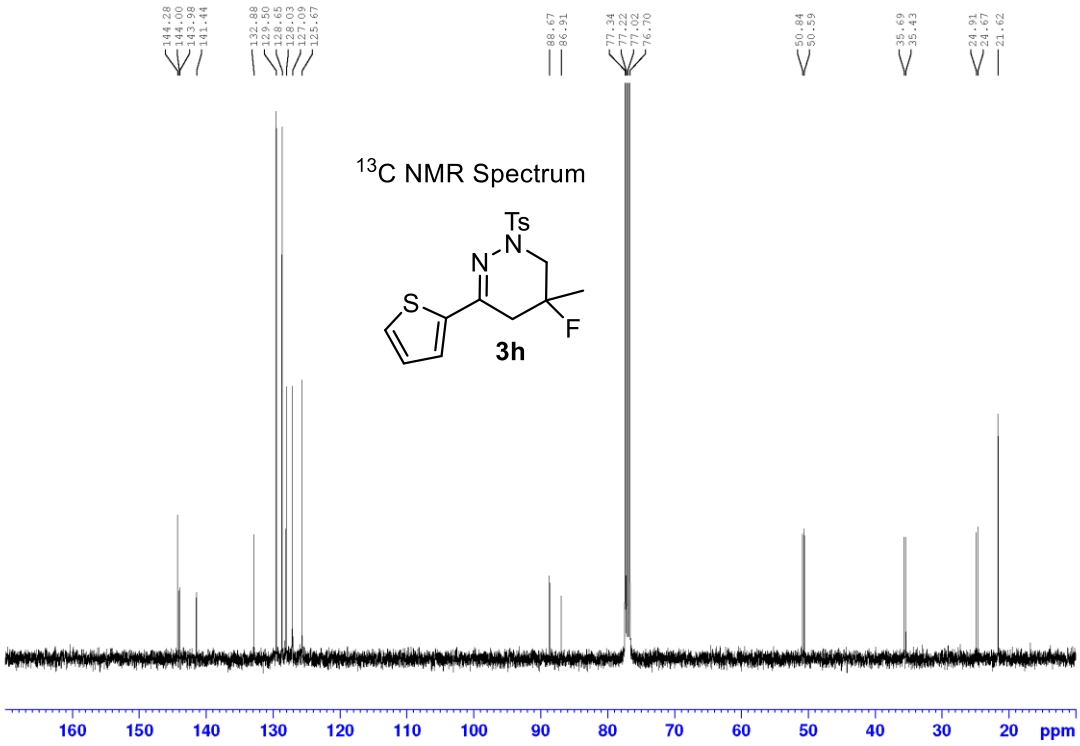


3g

^{1}H NMR Spectrum



3h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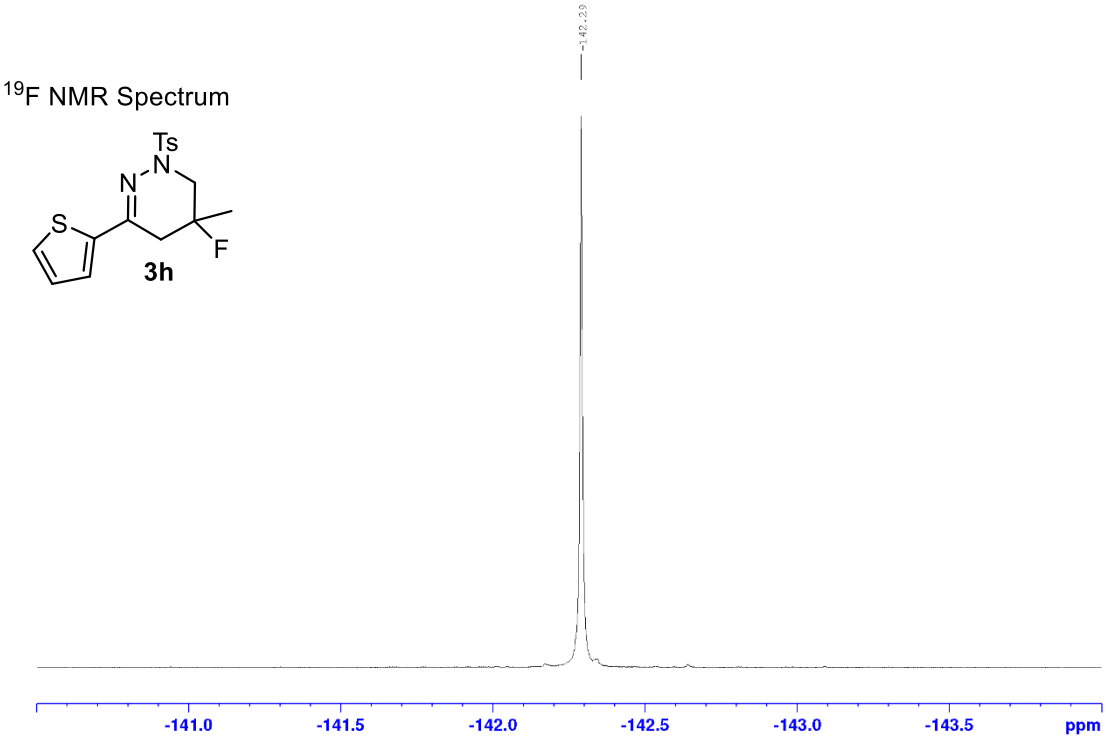
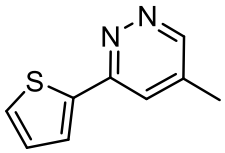
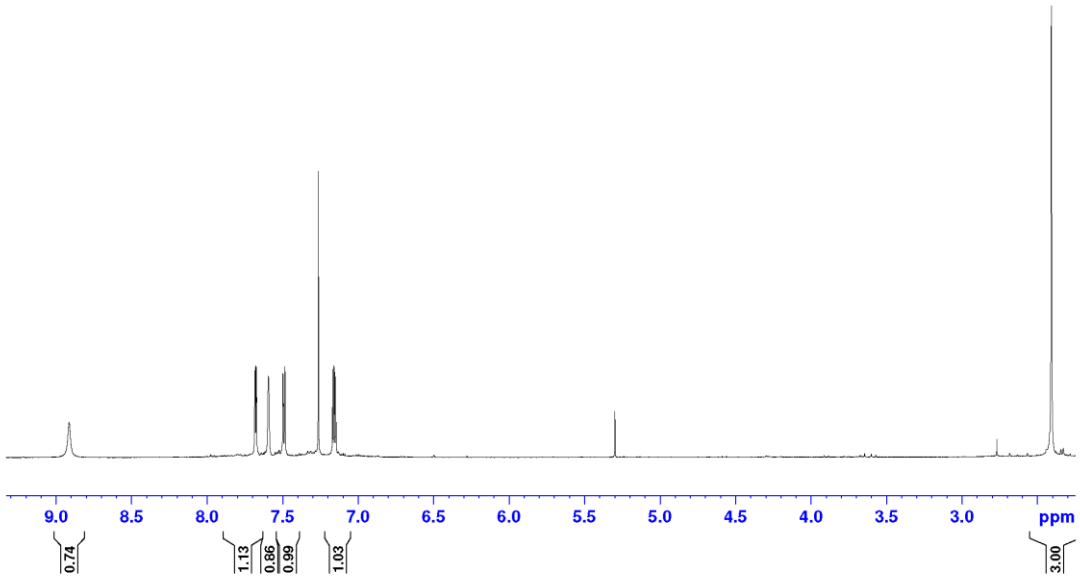
143.98
141.44
132.88
129.50
128.65
128.03
127.09
125.67
88.67
86.91
77.34
77.22
77.02
76.70
50.84
50.59
35.69
35.43
24.91
24.67
21.62
13C NMR Spectrum
Ts
N
N
S
F
3h
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

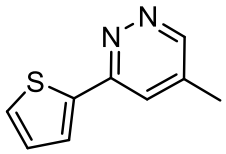

-142.09
19F NMR Spectrum
Ts
N
N
S
F
3h
-141.0
-141.5
-142.0
-142.5
-143.0
-143.5
ppm

^{1}H NMR Spectrum

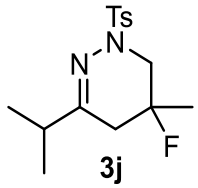




^{13}C NMR Spectrum

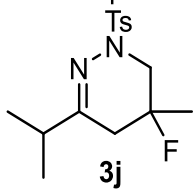


^{1}H NMR Spectrum



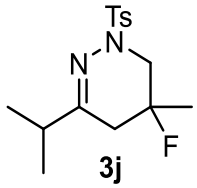
3j

^{13}C NMR Spectrum



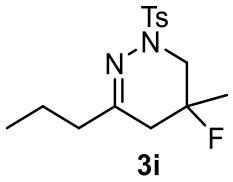
3j

^{19}F NMR Spectrum

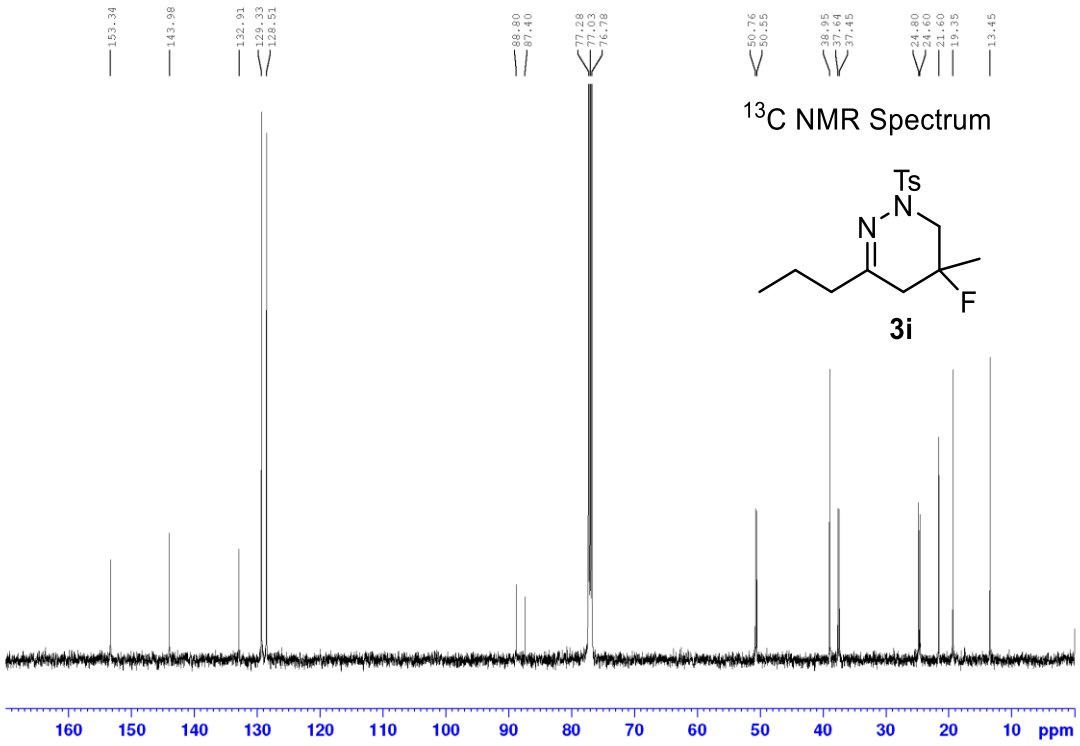


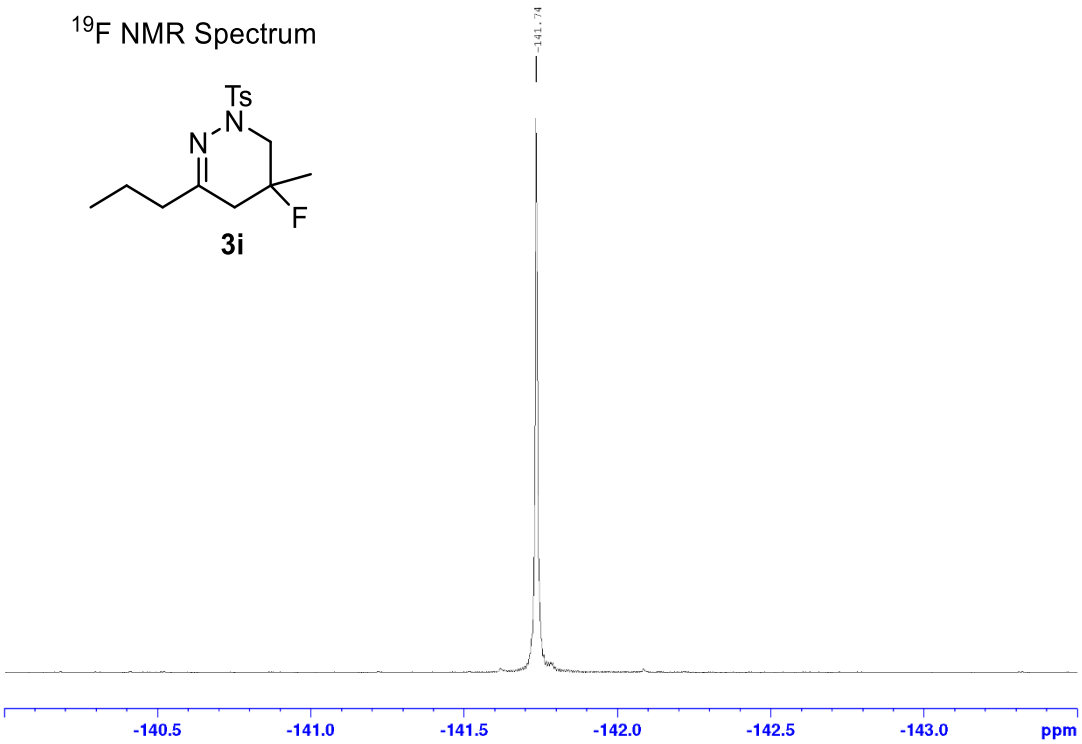
3j

^{1}H NMR Spectrum

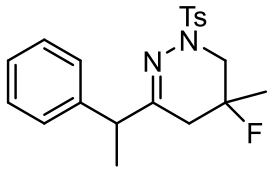


3i

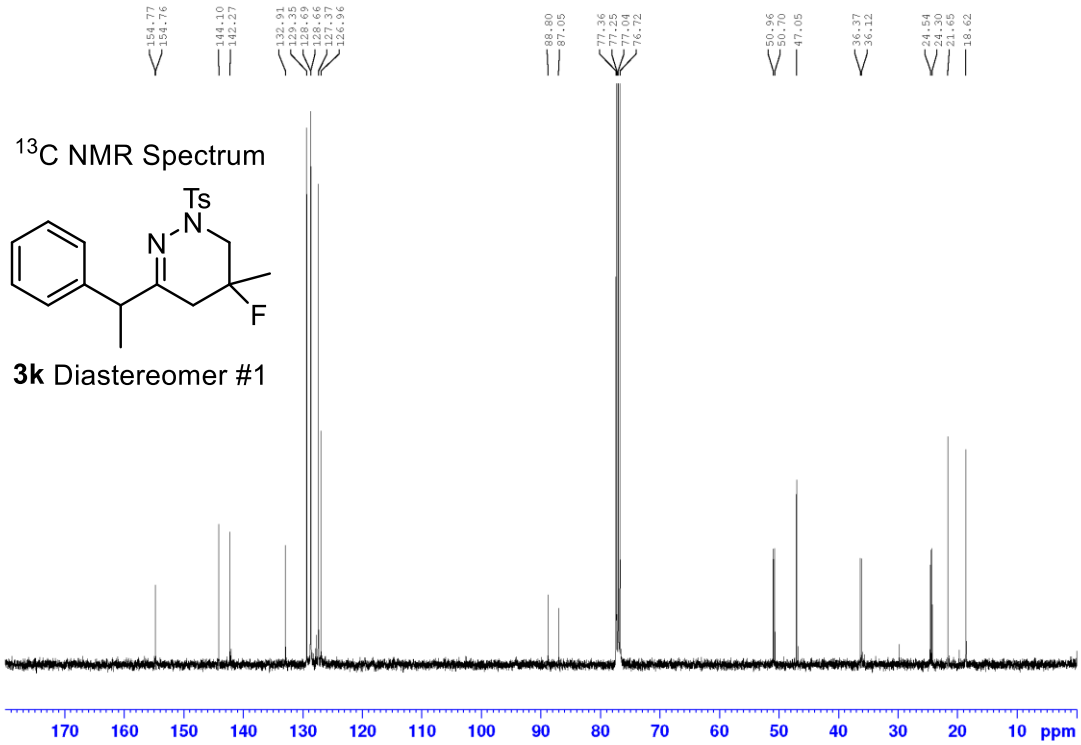

153.34
143.98
132.91
129.33
128.51
88.80
87.40
77.28
77.03
76.78
50.76
50.55
38.95
37.64
37.45
24.80
24.60
21.60
19.35
13.45
13C NMR Spectrum
Ts
N
N
F
3i
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


19F NMR Spectrum
Ts
N
N
F
3i
-141.74
-140.5
-141.0
-141.5
-142.0
-142.5
-143.0
ppm

^{1}H NMR Spectrum



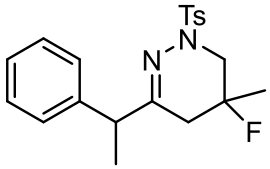
3k Diastereomer #1



^{13}C NMR Spectrum

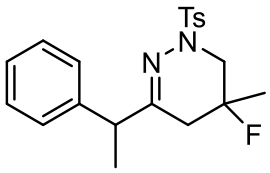
3k Diastereomer #1

^{19}F NMR Spectrum

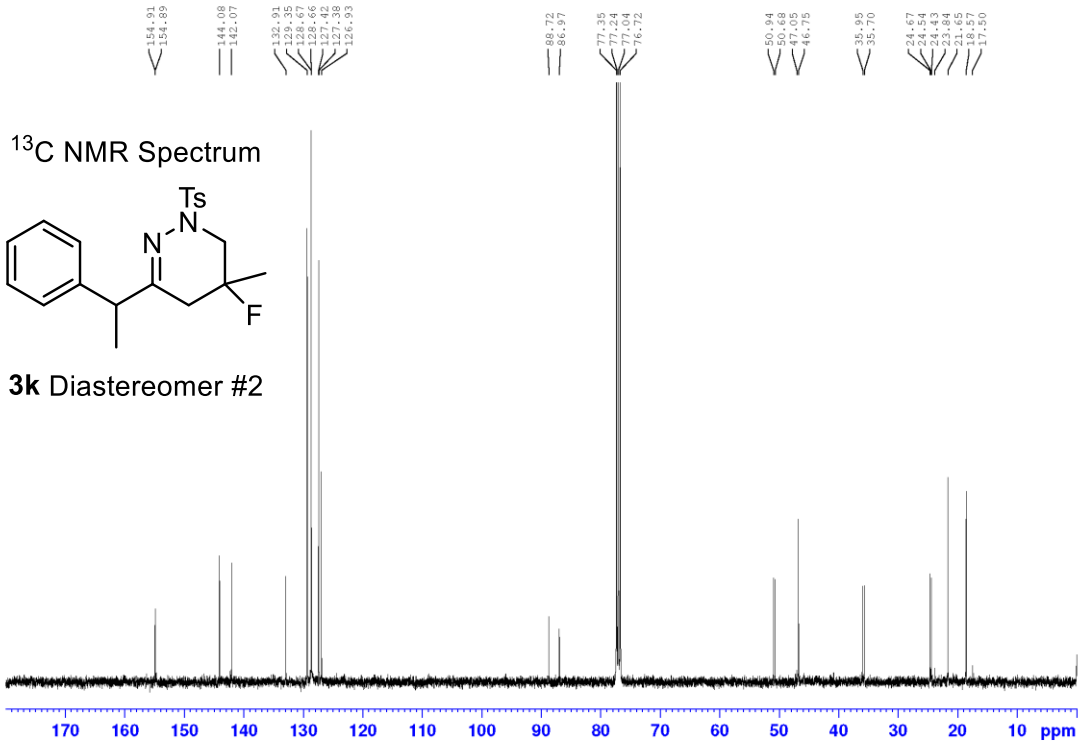


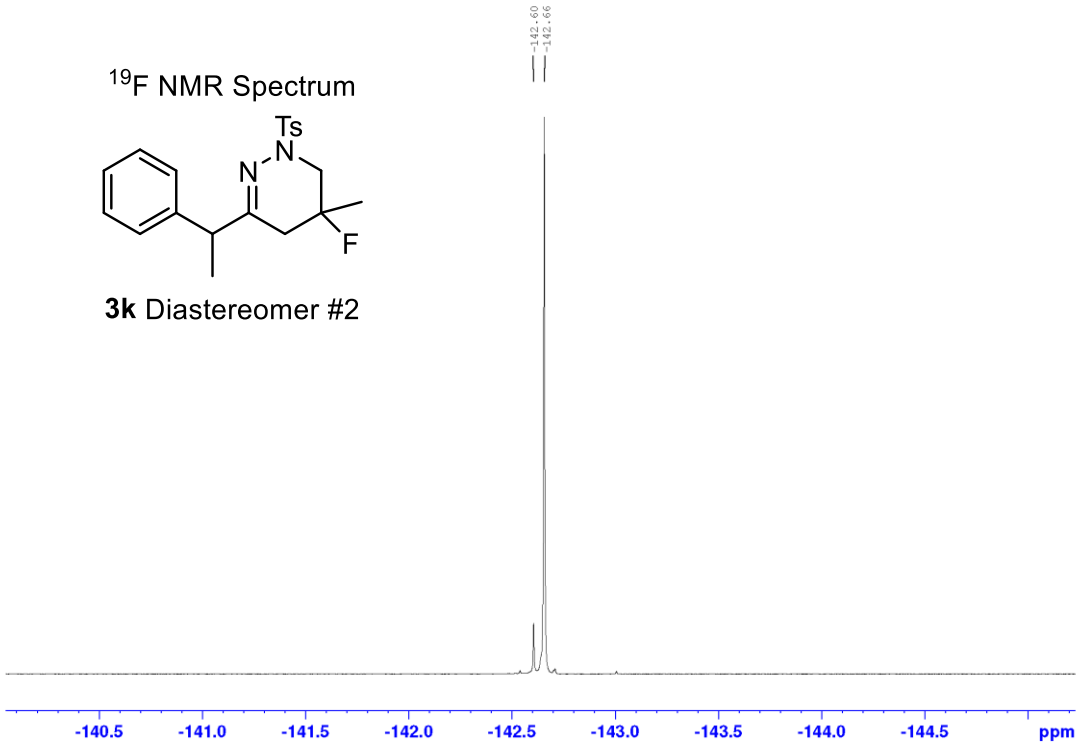
3k Diastereomer #1

^{1}H NMR Spectrum

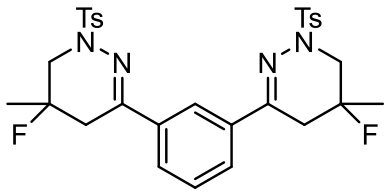


3k Diastereomer #2

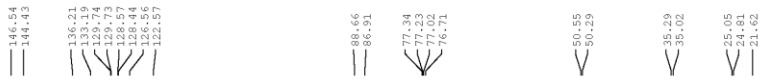

154.91
154.89
144.08
142.07
132.91
129.35
128.67
128.66
127.42
127.38
126.93
88.72
86.97
77.35
77.24
77.04
76.72
50.94
50.68
47.65
46.75
35.95
35.70
24.67
24.54
24.43
23.48
21.65
18.57
17.50
13C NMR Spectrum
Ts
N
N
F
3k Diastereomer #2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


-142.60
-142.66
19F NMR Spectrum
Ts
N
N
F
3k Diastereomer #2
-140.5
-141.0
-141.5
-142.0
-142.5
-143.0
-143.5
-144.0
-144.5
ppm

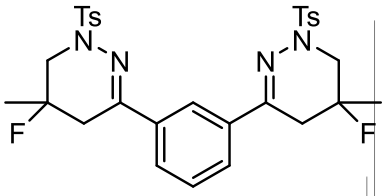
^{1}H NMR Spectrum



3l

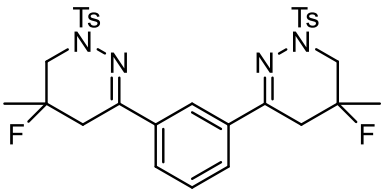


^{13}C NMR Spectrum



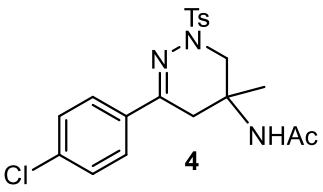
3l

^{19}F NMR Spectrum

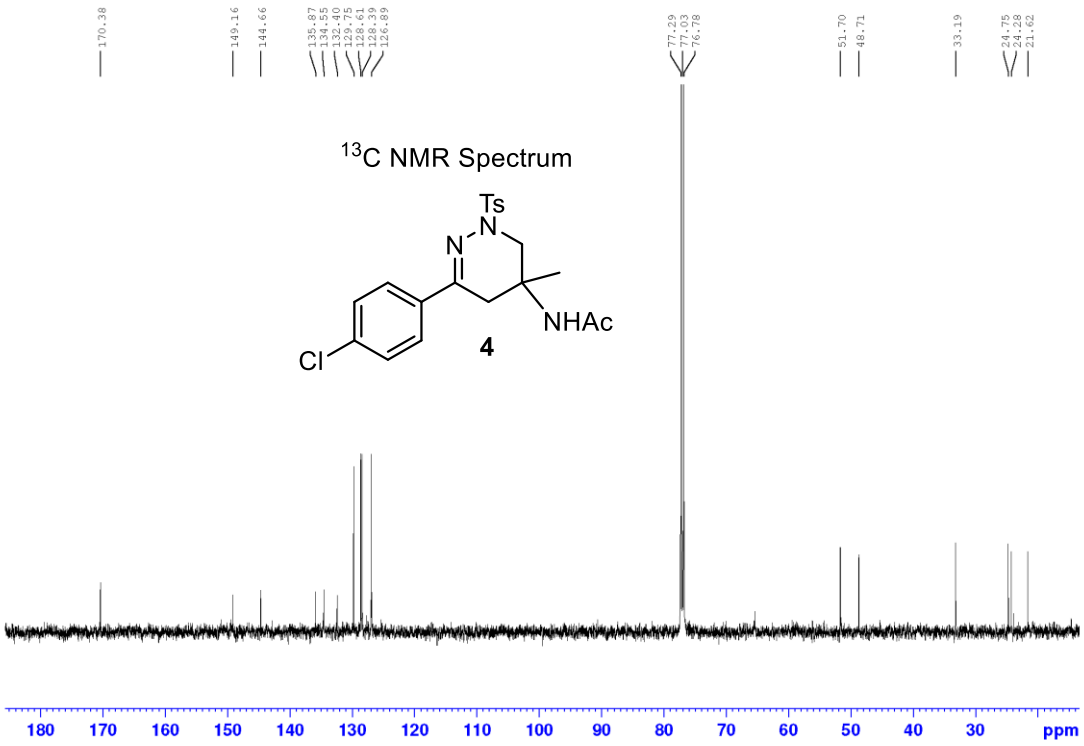


3l

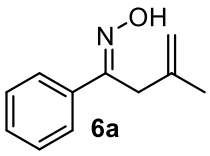
^{1}H NMR Spectrum



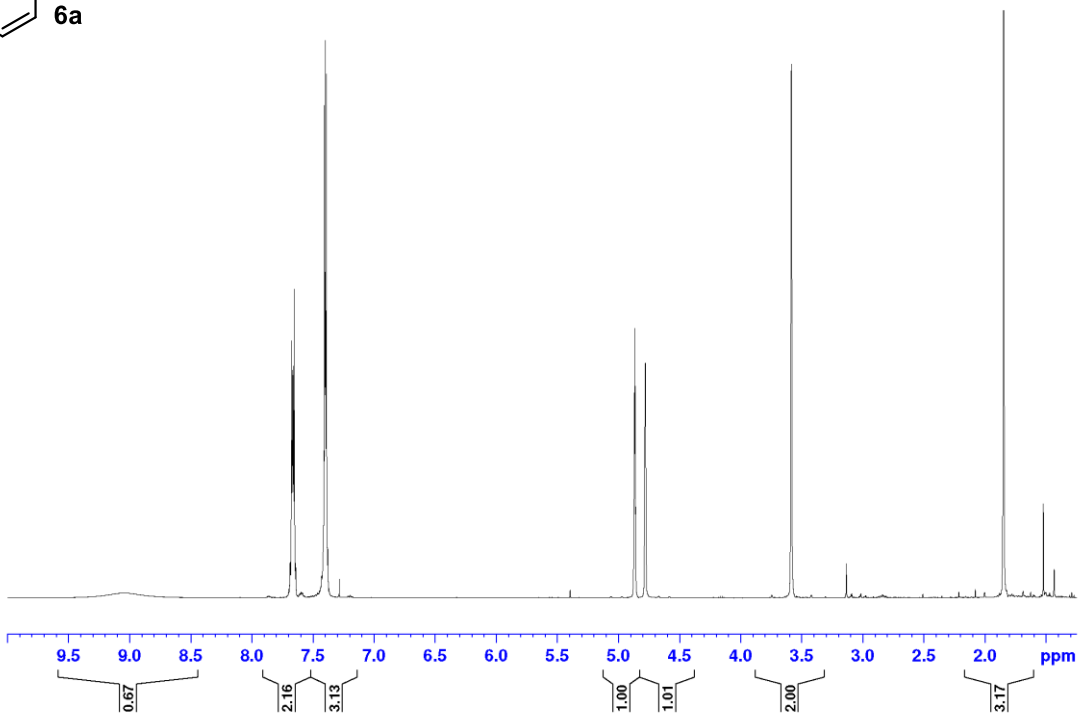
4

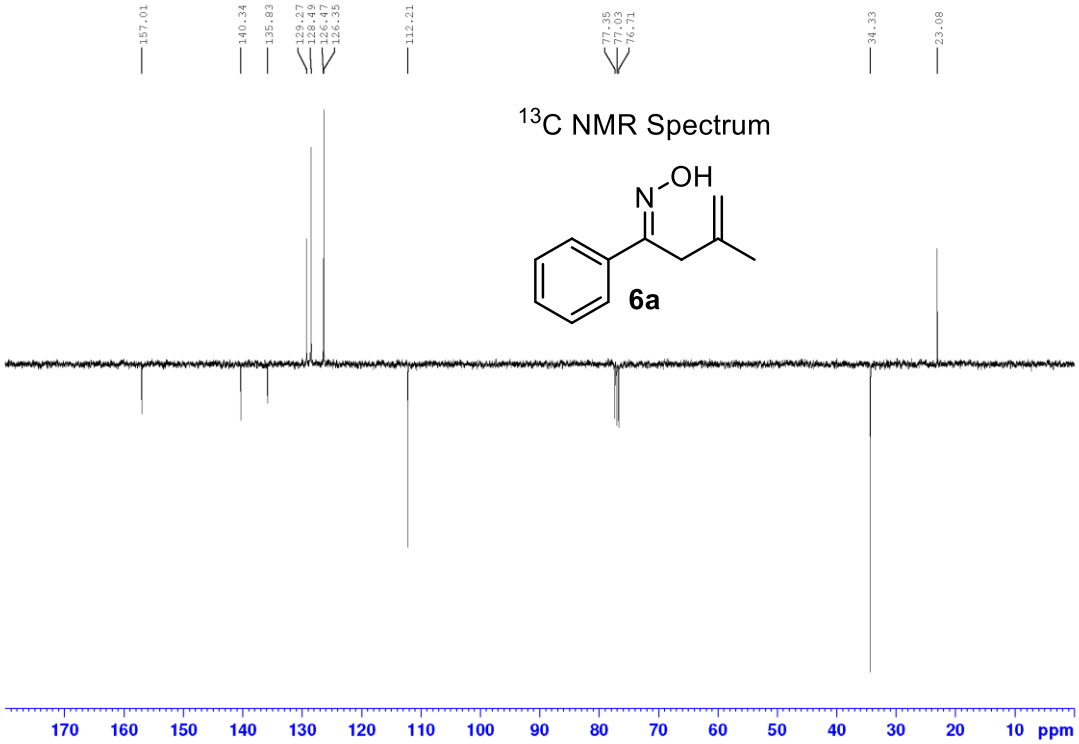

170.38
149.16
144.66
135.87
134.55
132.40
130.75
128.61
128.39
126.89
77.29
77.03
76.78
51.70
48.71
33.19
24.75
24.28
21.62
13C NMR Spectrum
Ts
N
N
NHAc
Cl
4
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

^{1}H NMR Spectrum



6a

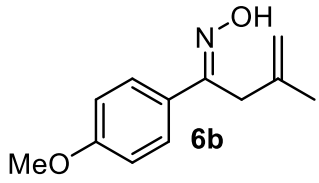




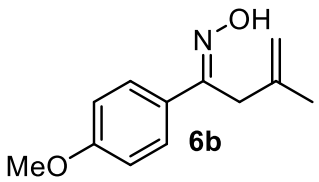
^{13}C NMR Spectrum

6a

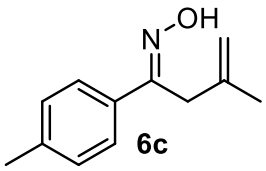
^{1}H NMR Spectrum



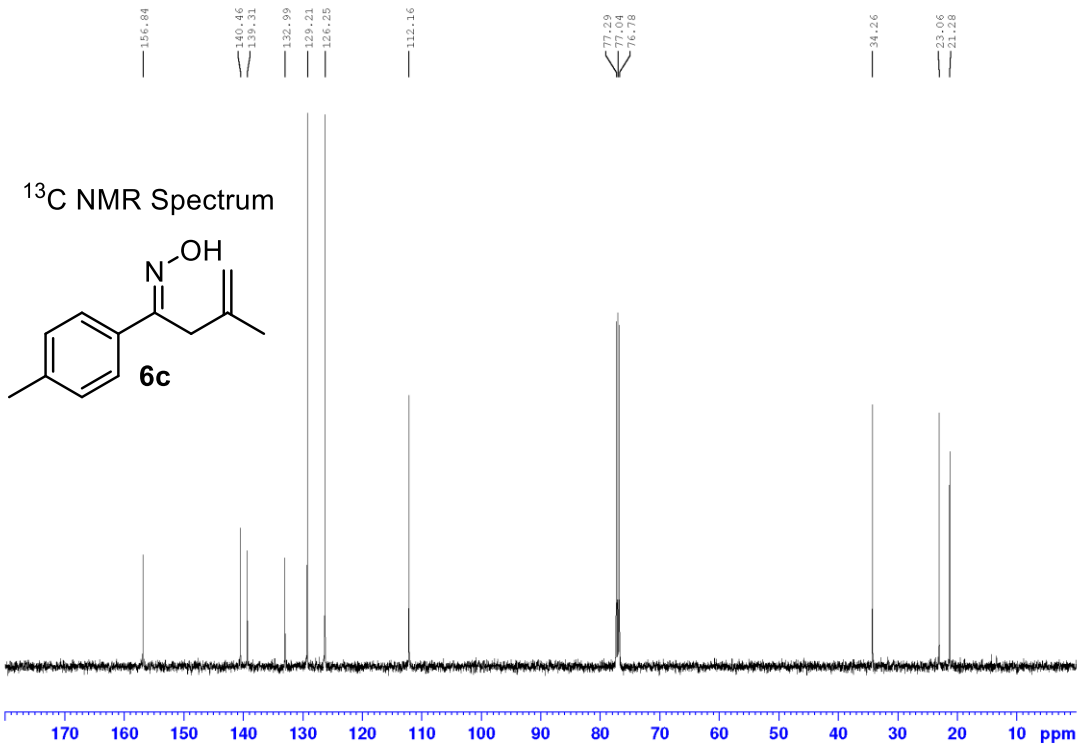
^{13}C NMR Spectrum



^{1}H NMR Spectrum



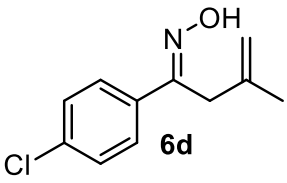
6c

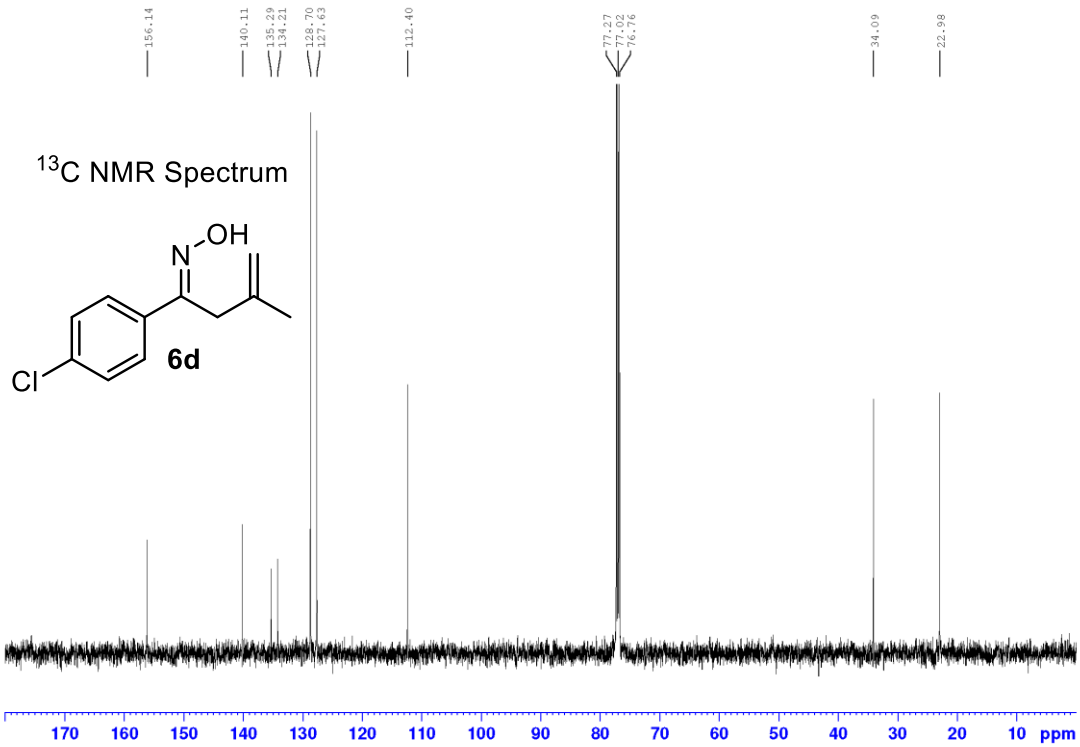


^{13}C NMR Spectrum

6c

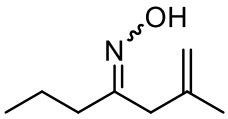
^{1}H NMR Spectrum





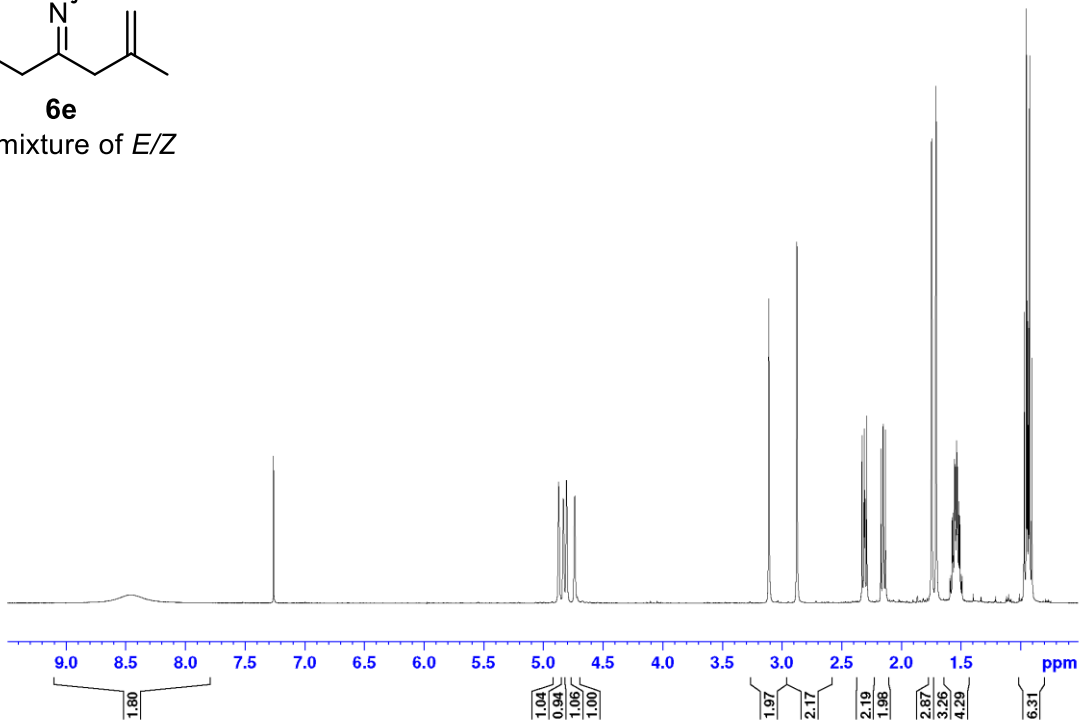
^{13}C NMR Spectrum

^{1}H NMR Spectrum

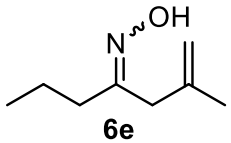


6e

1:1 mixture of *E/Z*



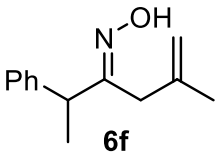
^{13}C NMR Spectrum



6e

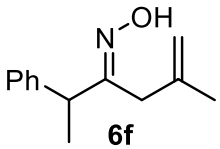
1:1 mixture of *E/Z*

^{1}H NMR Spectrum



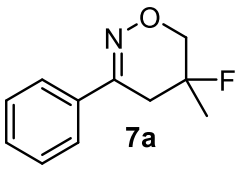
6f

^{13}C NMR Spectrum



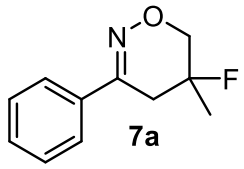
6f

^{1}H NMR Spectrum



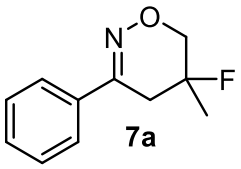
7a

^{13}C NMR Spectrum



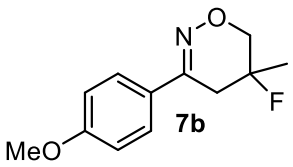
7a

^{19}F NMR Spectrum

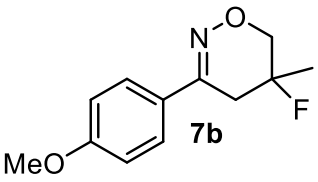


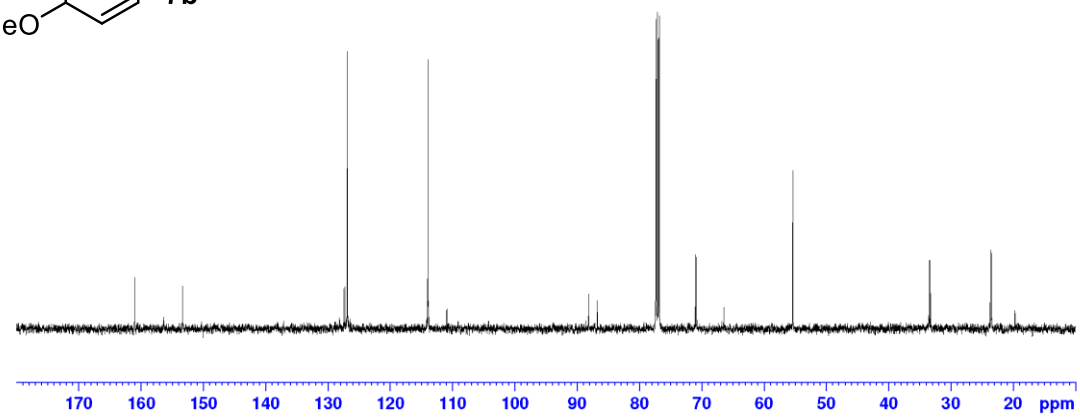
7a

^{1}H NMR Spectrum

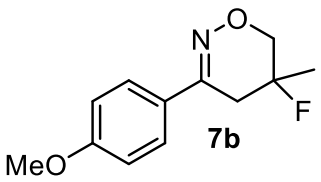


^{13}C NMR Spectrum



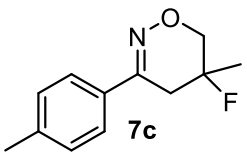


^{19}F NMR Spectrum

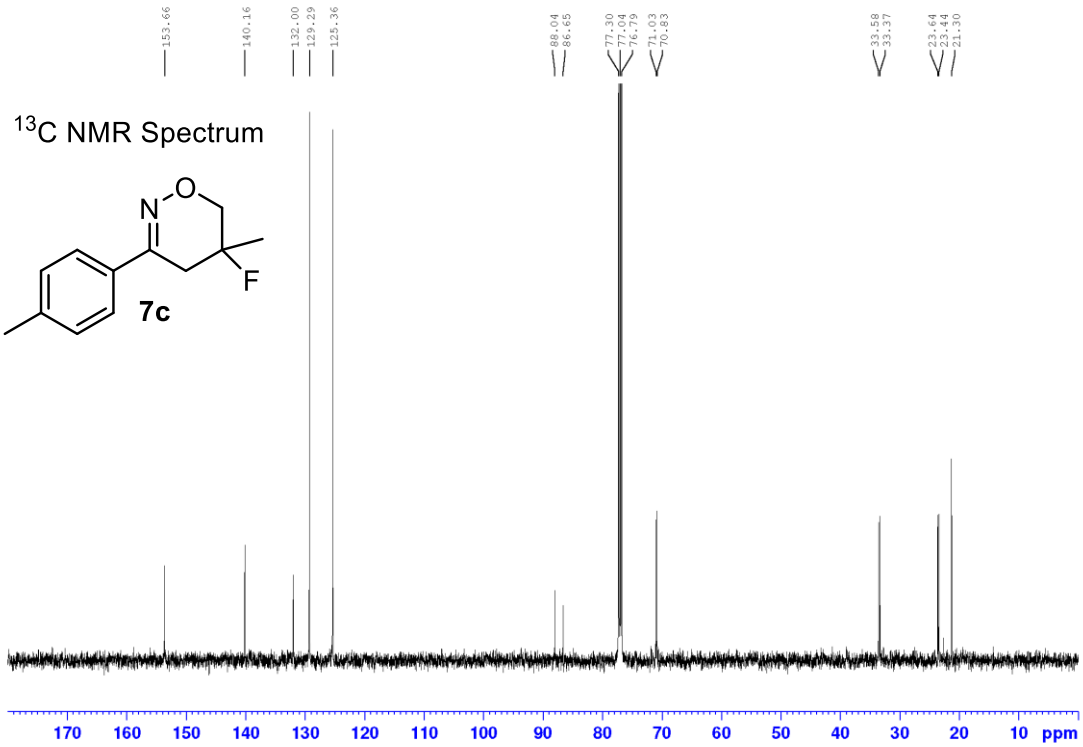


7b

^{1}H NMR Spectrum



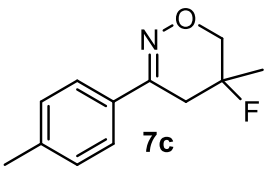
7c



^{13}C NMR Spectrum

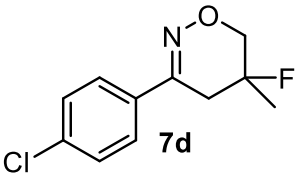
7c

^{19}F NMR Spectrum

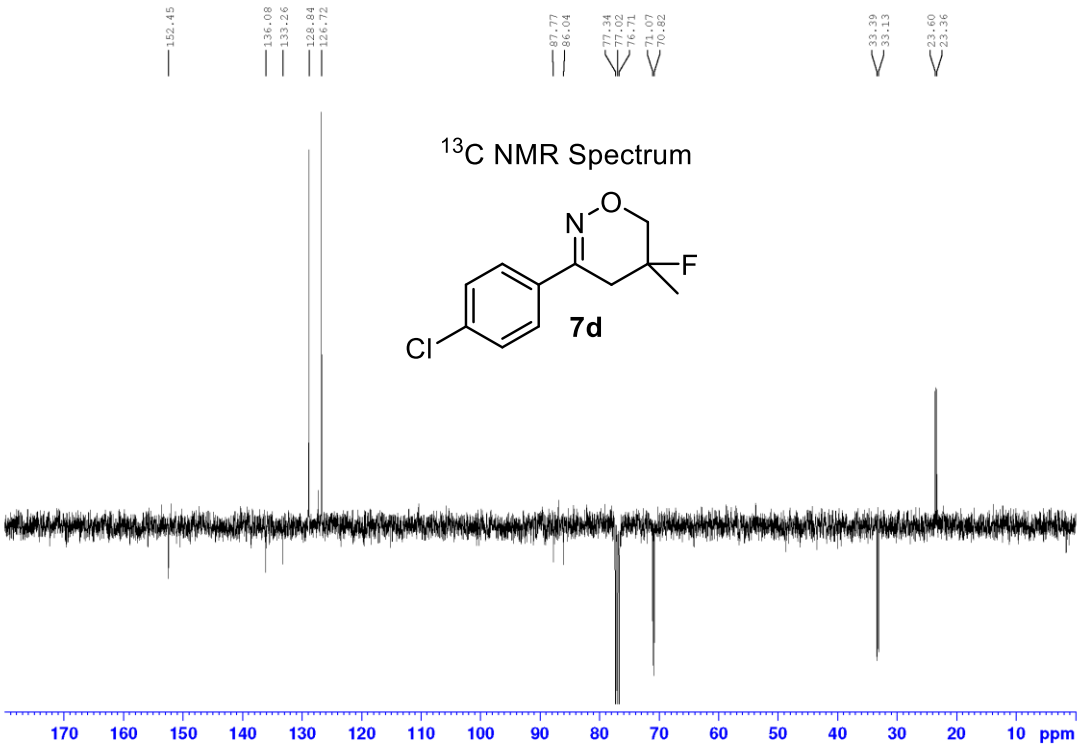


7c

^{1}H NMR Spectrum



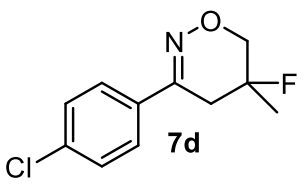
7d



^{13}C NMR Spectrum

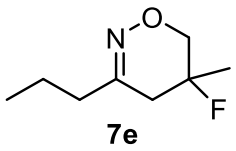
7d

^{19}F NMR Spectrum



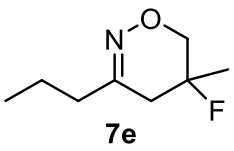
7d

^{1}H NMR Spectrum



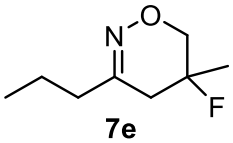
7e

^{13}C NMR Spectrum

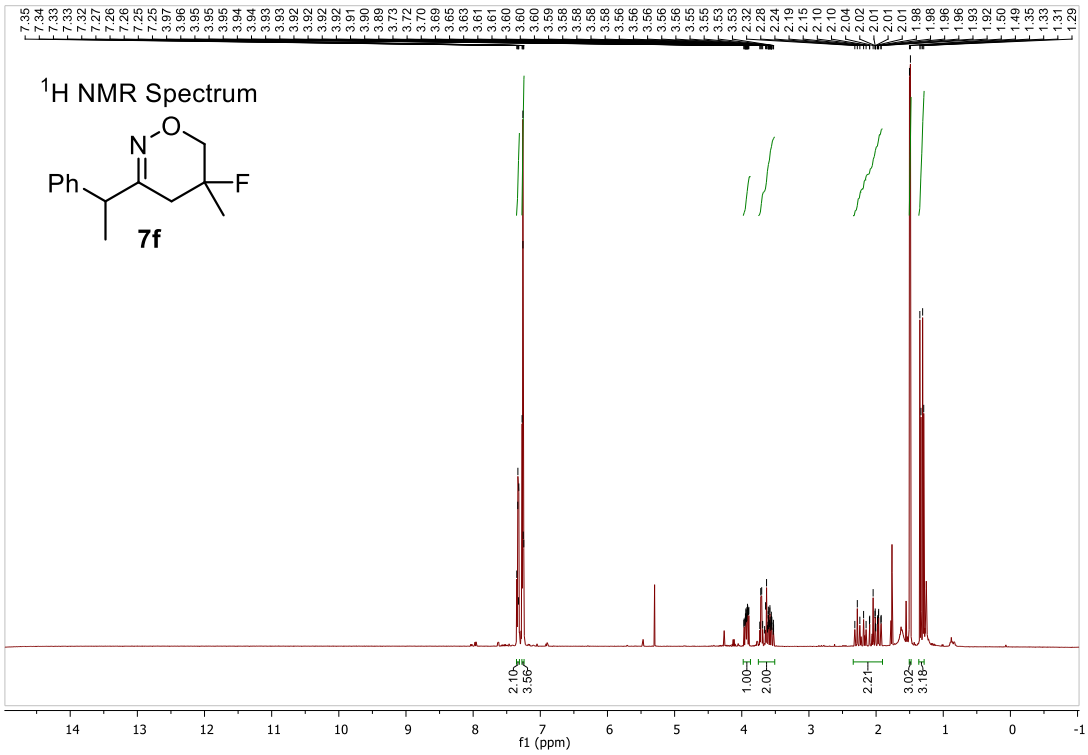


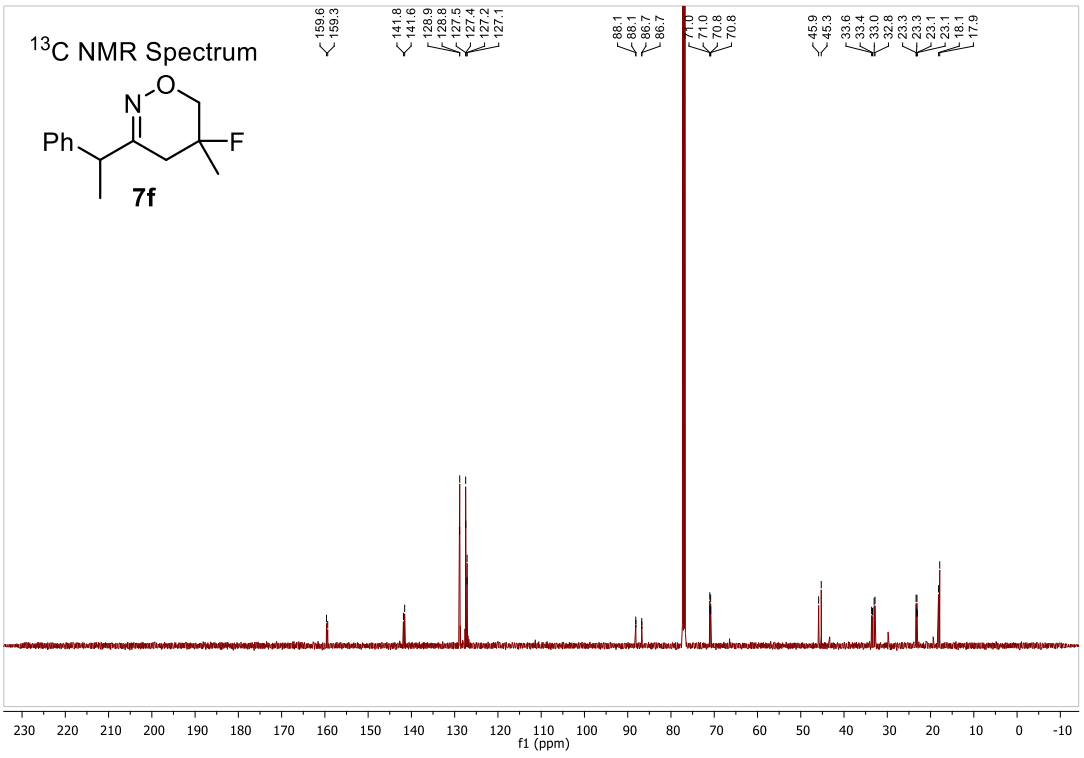
7e

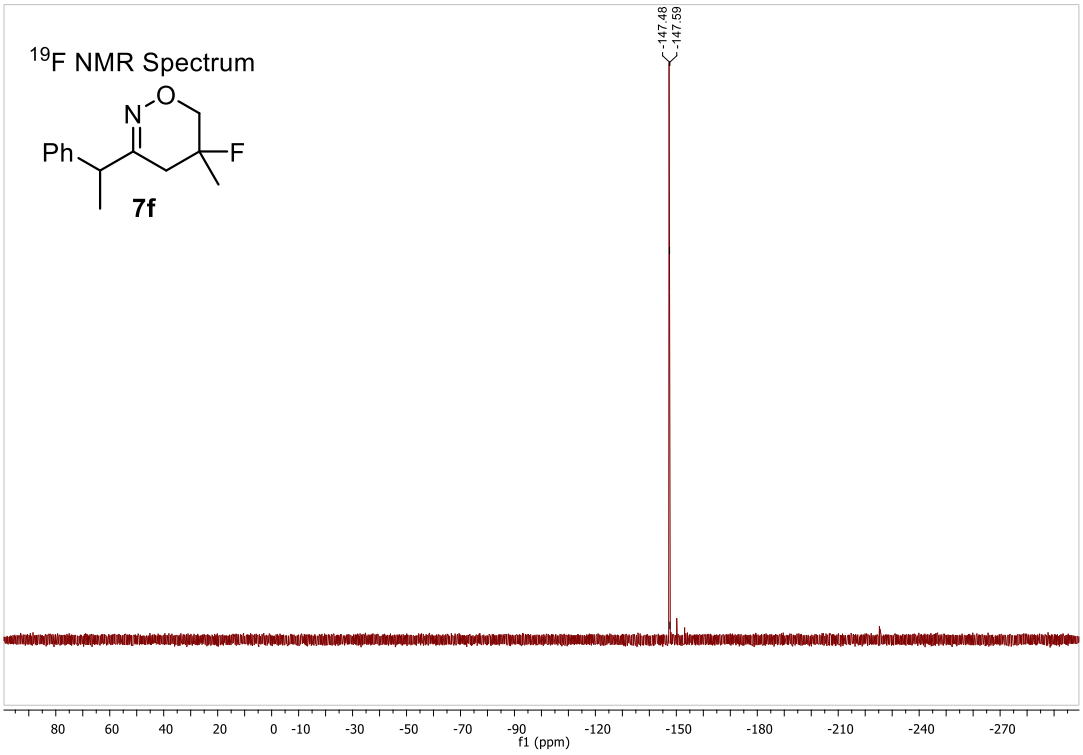
^{19}F NMR Spectrum



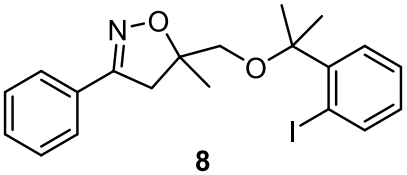
7e


^{1}H NMR Spectrum
Ph
F
7f
f1 (ppm)


^{13}C NMR Spectrum
Ph
F
7f
f1 (ppm)

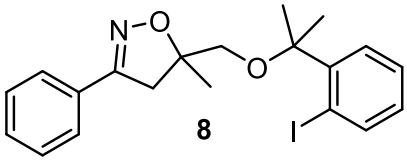

19F NMR Spectrum
N
O
Ph
F
7f
-147.48
-147.59
80
60
40
20
0
-10
-30
-50
-70
-90
-120
-150
-180
-210
-240
-270
f1 (ppm)

^{1}H NMR Spectrum



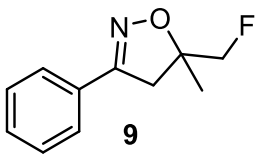
8

^{13}C NMR Spectrum



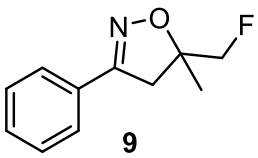
8

^{1}H NMR Spectrum



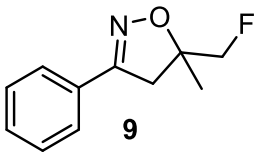
9

^{13}C NMR Spectrum



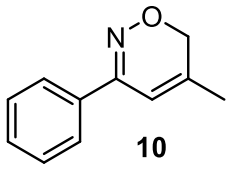
9

^{19}F NMR Spectrum

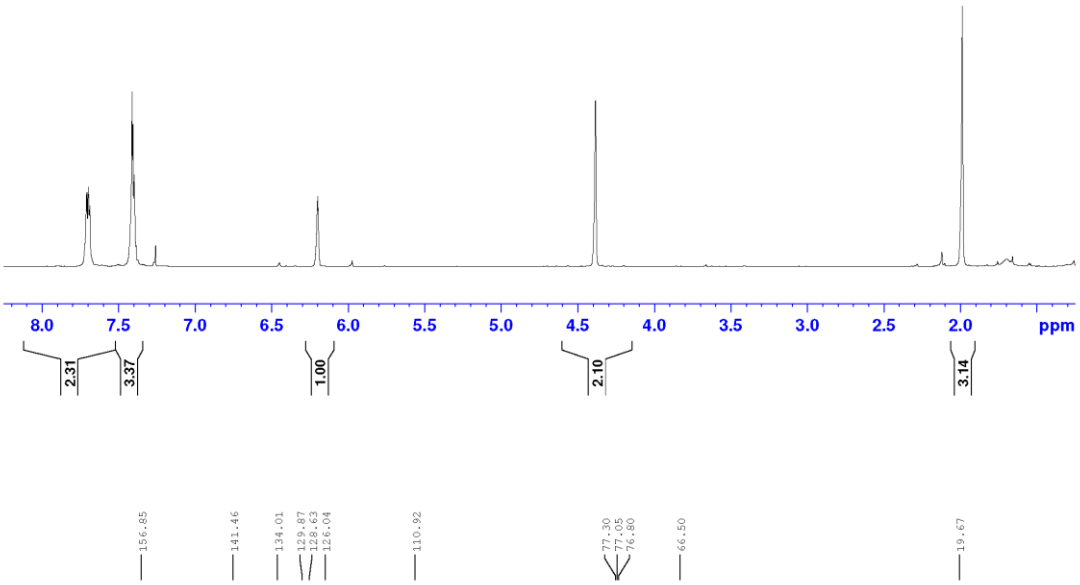


9

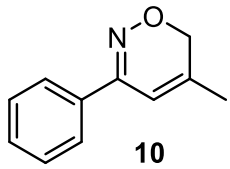
^{1}H NMR Spectrum



10

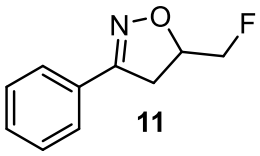


^{13}C NMR Spectrum

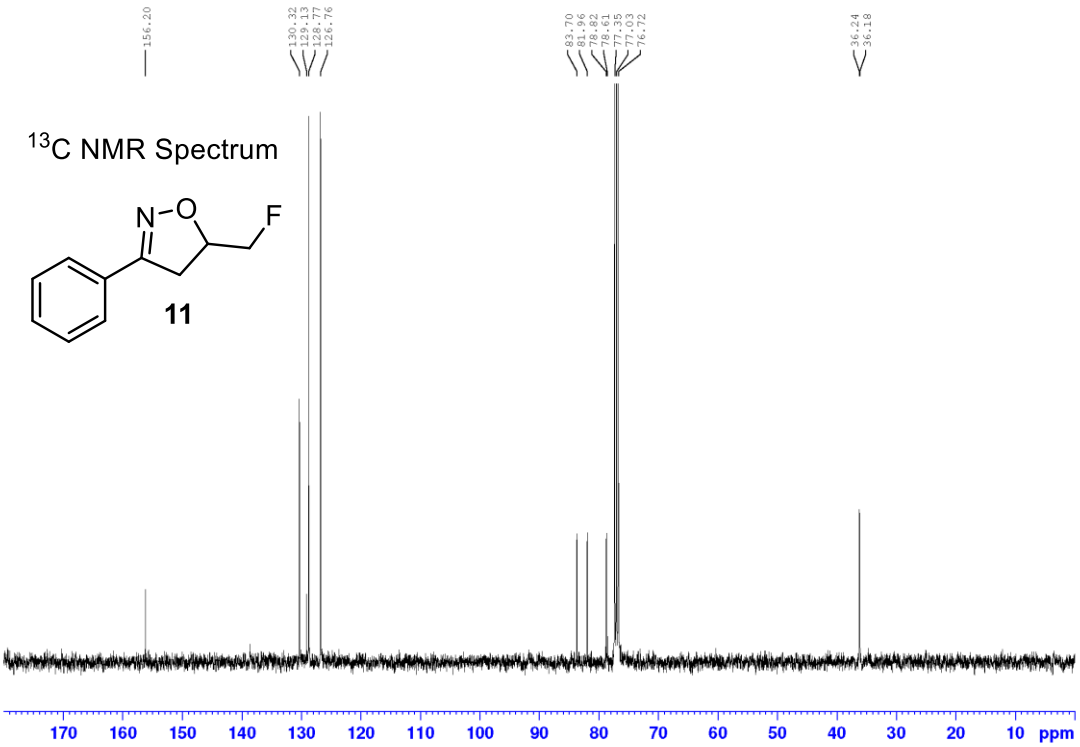


10

^{1}H NMR Spectrum



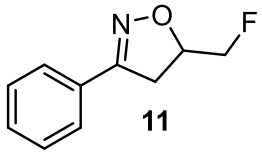
11



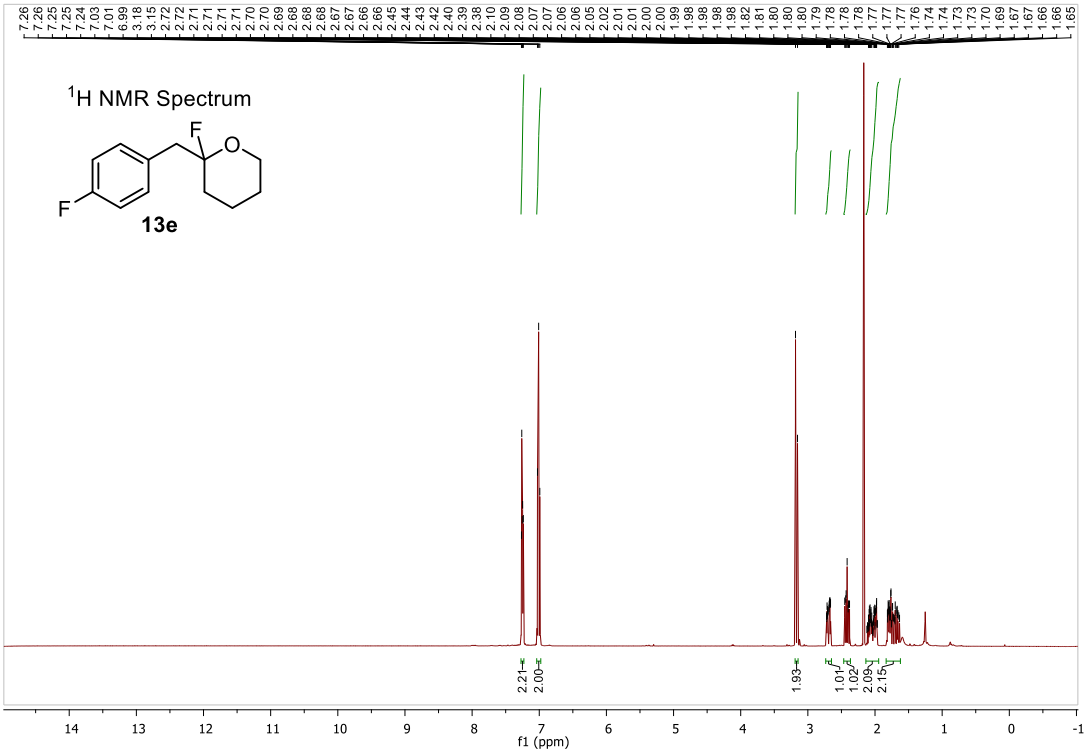
^{13}C NMR Spectrum

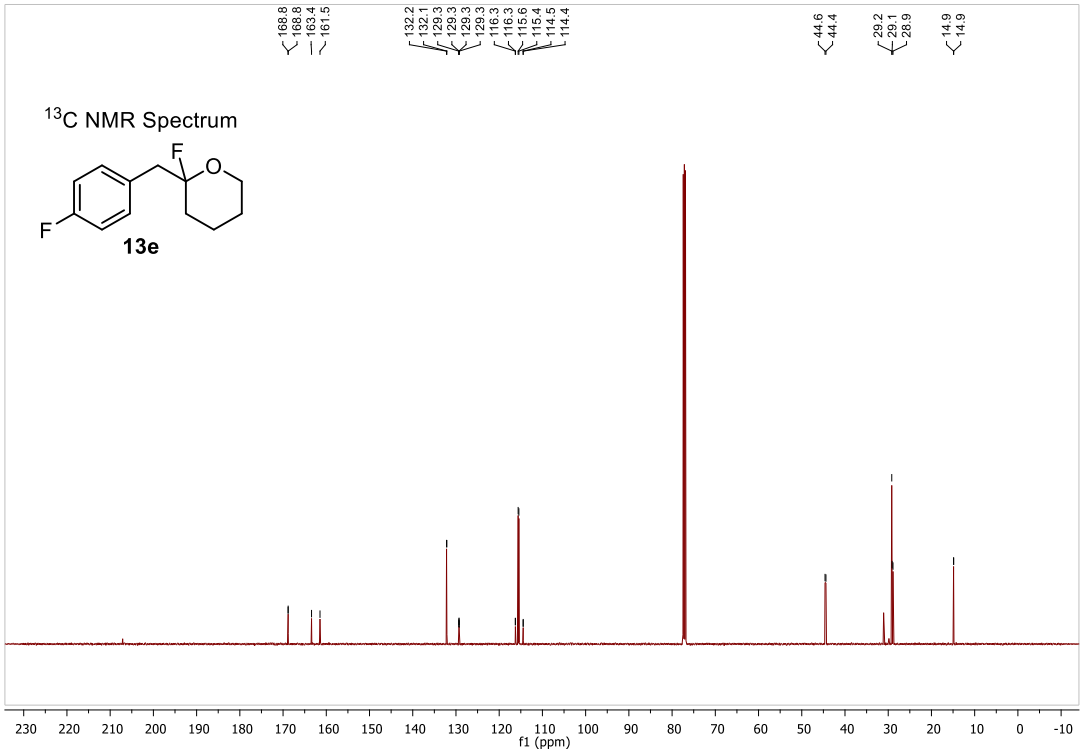
11

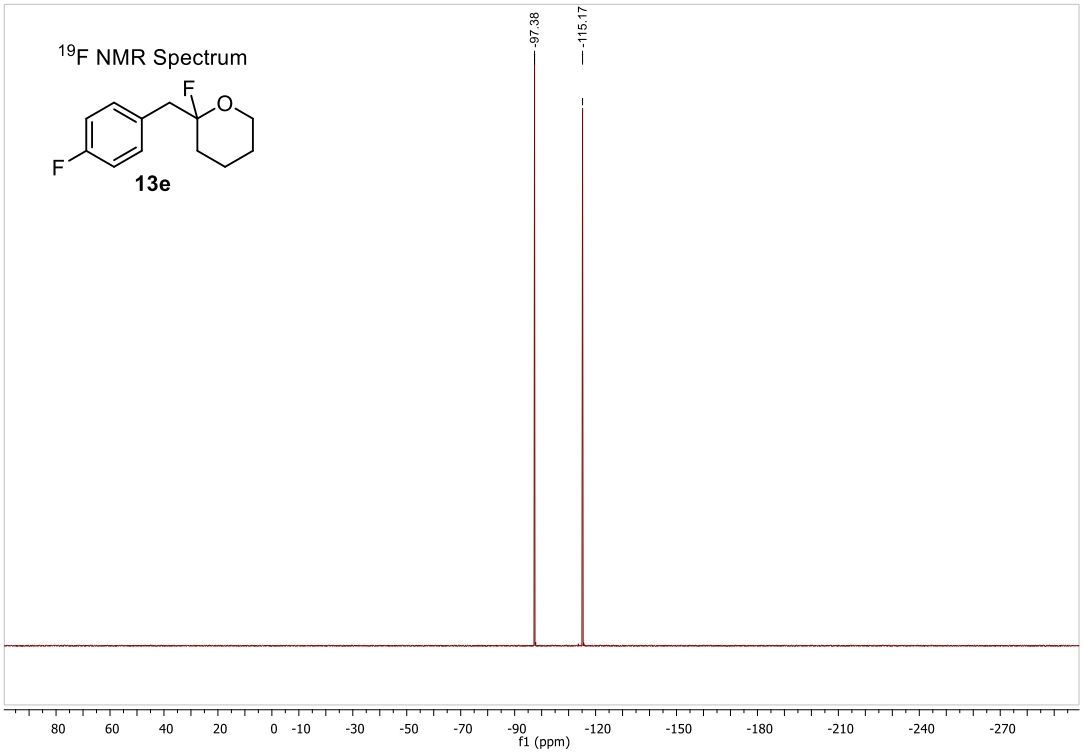
^{19}F NMR Spectrum



11




168.8
168.8
163.4
161.5
132.2
132.1
129.3
129.3
129.3
129.3
116.3
116.3
115.6
115.4
114.5
114.4
44.6
44.4
29.2
29.1
28.9
14.9
14.9
13C NMR Spectrum
F
O
F
13e
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


19F NMR Spectrum
-97.38
-115.17
F
O
F
13e
80 60 40 20 0 -10 -30 -50 -70 -90 -120 -150 -180 -210 -240 -270
f1 (ppm)