# SUPPORTING INFORMATION

Synthesis and Reactivity of [<sup>18</sup>F] N-Fluorobenzenesulfonimide

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#### **General Information**

<sup>1</sup>H NMR spectra were recorded in deuterated solvents using Bruker DPX200, DPX400, AV400 and AVC500 spectrometers, calibrated using residual undeuterated solvent as an internal reference. <sup>13</sup>C NMR spectra were recorded in deuterated solvents using Bruker DPX200, DPX400, AV400 and AVC500 spectrometers. <sup>19</sup>F spectra were recorded on a Bruker AV400. Chemical shifts ( $\delta$ ) are quoted in parts per million (ppm) and coupling constants (J) are measured in hertz (Hz). The following abbreviations are used to describe multiplicities s=singlet, d=doublet, t=triplet, q=quartet, b=broad, m=multiplet. NMR were processed in either MestRe-C or ACD/SpecManager. IUPAC names were obtained using the ACD/I-lab service. Mass spectra (m/z) were recorded on Micromass GCT in Chemical Ionisation (NH<sub>3</sub>,  $CI^+$ ) or Electron Impact (EI). IR spectra were recorded as thin films on NaCl plates in solution in CHCl<sub>3</sub> on a Paragon 1000 FT-IR spectrometer. Absorptions are measured in wavenumbers and only peaks of interest are reported. Analytical thin layer chromatography (TLC) was performed on Merck Silica gel 60 F<sub>254</sub> plates. All reactions requiring anhydrous conditions were conducted in dried apparatus under an inert atmosphere of argon or nitrogen. Solvents were dried and purified before use according to standard procedures. High performance column chromatography (HPLC) was performed on a Spectra SYSTEM P2000 with a Spectra SYSTEM UV2000 detector and a Bioscan flow-count radioactivity detector using a reverse phase analytical column (Waters Nova-Pak C-18 Column, 150mm x 3.9mm).  $[^{18}F]$ Fluorine was produced on a Scandatronix MC40 cyclotron via the  $^{18}O(p,n)^{18}F$ nuclear reaction in an aluminium-body target using a two-step proton irradiation method. The first irradiation produced nucleogenic fluorine-18 by the  ${}^{18}O(p,n){}^{18}F$  nuclear reaction on enriched [<sup>18</sup>O]oxygen gas using 19MeV protons (40 µA beam current) for 5 minutes. After irradiation, the [<sup>18</sup>O]oxygen gas was recovered cryogenically for re-use and the target refilled with an argon/neon/fluorine (92.10:7.75/0.15 v/v) gas mixture (200psi). The target was then irradiated a second time using 19 MeV protons (30 µA beam current) for 20 minutes.

[<sup>18</sup>F]N-fluorobenzenesulfonimide. Sodium dibenzenesulfonimide (15 mg, 0.05 mmol) was solubilized in CH<sub>3</sub>CN:H<sub>2</sub>O (9:1) (2 mL). [<sup>18</sup>F]F<sub>2</sub> gas from the cyclotron target was passed through the reaction mixture to prepare [18F]NFSi. Typically, 1-2GBq fluorine-18 was trapped in the reaction solution. A small portion (corresponding to ca. 370MBq) of the resulting solution was taken and subjected to azeotropic drying. Drying was achieved by removal of the MeCN/H<sub>2</sub>O azeotrope by distillation at 110°C for 20 minutes. Upon cooling to room temperature, the residue was solubilized in 1 mL anhydrous CH<sub>3</sub>CN

affording a solution of [<sup>18</sup>F]NFSi (ca. 150MBq). The identity of the [<sup>18</sup>F]NFSi (t<sub>r</sub> = 32.29 mins.) was confirmed by isocratic radio-HPLC analysis. (1 mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 7:3 mobile phase). MS(CI)<sup>+</sup> m/z: for: C<sub>12</sub>H<sub>10</sub>FNaNO<sub>4</sub>S<sub>2</sub> 337.01 found 337.8 [M+Na];

**2-Methyl-1-trimethylsilyloxytetral-1-ene (1).** 2-Methyl tetralone (0.2 g, 1.3 mmol) was slowly added to a stirred solution of freshly prepared LDA (1.26 mmol) in anhydrous THF (4 mL) at -78°C and stirred for 20 minutes. Trimethylsilyl chloride was then added to this solution and the reaction mixture was stirred at this temperature for 3 hours, before allowing it to warm to room temperature, and stirring

for a further 20 hours. Saturated aqueous NH<sub>4</sub>Cl (6 mL) was added and the mixture was extracted with diethyl ether. The combined organic layers were dried over MgSO<sub>4</sub> and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography (petroleum ether 40-60: diethyl ether, 19:1) afforded the desired compound (0.221 g, 76% yield). The spectroscopic data for which were fully consistent with those reported;<sup>1</sup> HPLC analysis (1mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 7:3 mobile phase), t<sub>r</sub> = 11.42 mins.

(2-benzyl-3*H*-inden-1-ylmethyl)trimethylsilane (2). To a solution of 2-benzyl-1*H*indene (0.171 g, 0.8 mmol) in THF (1 mL) at 0°C was added dropwise *n*BuLi (2M in hexanes, 0.33 mL). The reaction mixture was allowed to warm to room temperature and stirred for 3 hours. The anion solution was then added dropwise to a solution of chloromethyl trimethyl silane (0.12 mL, 0.8 mmol) in anhydrous THF (0.5 mL) at -78°C. After addition was

complete, the reaction mixture was allowed to warm to room temperature and stirred for 20 hours. The red/brown mixture was then evaporated to dryness, and the residue was redissolved in DCM. After filtration through celite, removal of the solvent under reduced pressure afforded the crude allylsilane. Purification by column chromatography (hexane: diethyl ether, 19:1) afforded the desired product (0.094 g, 39%). The spectroscopic data for which were fully consistent with those reported;<sup>2</sup> HPLC analysis (1 mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 6:4 mobile phase), t<sub>r</sub> = 25.09 mins.

(2-Phenylallyl)trimethylsilane (3). A mixture of phenyl triflate (0.49 mL, 3 mmol), acetate 0.09 palladium (0.020)mmol). 1.1'g, bis(diphenylphosphino)ferrocene (0.219 g, 0.4 mmol), allyltrimethyl silane (1.2 mL, 15 mmol), triethylamine (0.84 mL, 6.0 mmol), and dry acetonitrile (12 mL) was placed in a pressure tube. The tube was sealed and the reaction mixture was heated, with stirring, to 60°C for 20 hours. After allowing the resulting black solution to cool to room temperature, the reaction mixture was quenched with water (24 mL) and extracted with Et<sub>2</sub>O (3 x 25 mL). The combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Purification by column chromatography (petroleum ether, 40-60%, Rf = 0.45) afforded the desired product as a colourless oil (0.413 g, 72%). The spectroscopic data for which were fully consistent with those reported;<sup>3</sup> HPLC analysis (1 mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 1:1

**2-Fluoro-2-methyl tetralone (4).** To a solution of 2-Methyl-1-trimethylsilyloxytetral-1ene (0.060 g, 0.26 mmol) in acetonitrile (3.0 mL) was added NFSi (1.1 eq., 0.098 g). The reaction mixture was heated to 80°C and stirred at this temperature, under an atmosphere of nitrogen, for 30 minutes, before quenching with water and extracting with ethyl acetate (3 x 10 mL). The

mobile phase),  $t_r = 10.25$  mins.

combined organic phases were then washed with 5% aq. HCl, sat. NaHCO<sub>3</sub> and brine, before drying over MgSO<sub>4</sub> and concentrating under reduced pressure. Purification by flash chromatography (hexane: diethyl ether, 19:1) afforded the pure ketone in 76% yield (0.035 g, 0.2 mmol). MS(CI)<sup>+</sup> m/z: for C<sub>11</sub>H<sub>11</sub>FO 178.2, found 178.9 [M<sup>+</sup>]; <sup>1</sup>H NMR (400MHz, Acetone-D<sub>6</sub>),  $\delta$  1.56 (d, 3H, J<sub>H-F</sub> = 22.3, CH<sub>3</sub>), 2.39 (m, 2H, CH<sub>2</sub>,

C(F)(Me)C<u>H</u><sub>2</sub>), 3.07 (ddd, 1H, J = 17.4, 8.4 and 5.2 Hz, C(F)CH<sub>2</sub>C<u>H</u><sub>2</sub>Ar), 3.18 (ddd, 1H, J = 17.4, 11.7 and 5.8 Hz, C(F)CH<sub>2</sub>C<u>H</u><sub>2</sub>Ar), 7.39 (m, 2H, ArH), 7.60 (ddd, 1H, J = 8.9, 7.5 and 1.4 Hz, ArH), 7.98 (dd, 1H, J = 7.8 and 1.0 Hz, ArH) ); <sup>13</sup>C NMR (100.6 MHz, Acetone D<sub>6</sub>),  $\delta$  20.5 (CH<sub>3</sub>, Me), 26.0 (CH<sub>2</sub>, C(F)CH<sub>2</sub>CH<sub>2</sub>Ar), 35.2 (CH<sub>2</sub>, C(F)(Me)CH<sub>2</sub>), 93.1 and 94.8 (CF, <u>C</u>(F)(Me)CH<sub>2</sub>), 127.3 (CH, Ar), 127.9 (Ar), 129.4 (Ar), 131.0 (4° C, Ar), 134.3 (CH, Ar), 143.8 (4° C, Ar), 205.7 (C=O); <sup>19</sup>F {<sup>1</sup>H} NMR (376.56 MHz, Acetone-D<sub>6</sub>):  $\delta = -153.1$ ; IR (film)  $v_{max}$  (cm<sup>-1</sup>): 1703, 738; HPLC analysis (1 mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 7:3 mobile phase), t<sub>r</sub> = 8.24 mins.

#### General Procedure for the fluorination of allylsilanes 2, 3, 4

A solution of the allylsilane (1 mmol) in anhydrous acetonitrile (8 mL) was treated with NFSi (0.315 g, 1 eq.). The reaction mixture was stirred at 80°C for 30 minutes. After 30 minutes the reaction was allowed to cool to room temperature and poured into a separating funnel charged with saturated aqueous NaHCO<sub>3</sub>. After extracting with ether, the combined organic layers were washed with brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure.

**2-Benzyl-2-fluoro-1-methylene-indan (5).** Following the general procedure for the fluorination of allylsilanes, starting with 0.089 g (2-benzyl-3*H*-inden-1-ylmethyl)trimethylsilane (0.3 mmol), and 0.101 g of NFSi in 1 mL acetonitrile. Purification by column chromatography (hexane : diethyl ether, 4:1, Rf = 0.58) afforded 0.055 g (76%) of the desired product.

HRMS calculated for C<sub>17</sub>H<sub>15</sub>F 238.1158, found 238.1148; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 2.95 - 3.38 (m, 4H, ArCH<sub>2</sub>CF(CH<sub>2</sub>Ph) and ArCH<sub>2</sub>CF(CH<sub>2</sub>Ph)), 5.29 (dd, *J*=3.9, 0.9 Hz, 1H, C=CH<sub>A</sub>H<sub>B</sub>), 5.72 (dd, *J*=4.3, 1.0 Hz, 1 H, C=CH<sub>A</sub>H<sub>B</sub>), 7.22 - 7.34 (m, 8H, ArH), 7.49 - 7.54 (m, 1H, ArH); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>-*d*) δ 41.9 (d, <sup>2</sup>*J*<sub>C-F</sub> =24.3 Hz, CFCH<sub>2</sub>Ph), 44.3 (d, <sup>2</sup>*J*<sub>C-F</sub> =26.7 Hz, ArCH<sub>2</sub>CF), 101.0 - 102.7 (d, <sup>1</sup>*J*<sub>C-F</sub> = 184.1 Hz, CCF(CH<sub>2</sub>Ph)(CH<sub>2</sub>)), 107.1 (d, <sup>3</sup>*J*<sub>C-F</sub> =5.7 Hz, C=CH<sub>2</sub>) 121.1 (ArC), 125.2 (d, <sup>3</sup>*J*<sub>C-F</sub> =1.9 Hz, ArC), 126.8 (ArC), 127.2 (ArC), 128.1 (ArC), 129.3 (ArC), 130.6 (d, <sup>4</sup>*J*<sub>C-F</sub> =1.4 Hz, ArC), 136.0 (d, <sup>4</sup>*J*<sub>C-F</sub> =0.95 Hz, ArC), 138.3 (d, <sup>3</sup>*J*<sub>C-F</sub> =2.9 Hz, ArC), 140.9 (d, <sup>3</sup>*J*<sub>C-F</sub> =3.3 Hz, ArC), 151.1 (d, <sup>2</sup>*J*<sub>C-F</sub> =17.17 Hz, (Ar)C(=CH<sub>2</sub>)(CF)); <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ = -137.9; IR (film) v<sub>max</sub> (cm<sup>-1</sup>): 733; HPLC analysis (1 mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 6:4 mobile phase),NFSi: t<sub>r</sub> = 2.19 mins, compound **5**: t<sub>r</sub> = 5.09 mins.

(1-Fluoromethylvinyl)benzene (6). Following the general procedure for the fluorination of allylsilanes, starting with 0.190 g (2-phenylallyl)trimethylsilane (1 mmol). Purification by column chromatography (Petroleum ether 30-40%) afforded the desired product (0.069 g, 57%).

HRMS calculated for C<sub>9</sub>H<sub>9</sub>F 136.0688, found 136.0683; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.25 (dm, 2H,  $J_{\text{H-F}}$ =47.2 Hz, PhC(CH<sub>2</sub>)(CH<sub>2</sub>F)), 5.44 (m, 1H, PhC=CH<sub>2</sub>), 5.62 (m, 1H, PhC=CH<sub>2</sub>), 7.36 (m, 3H, ArH), 7.46 (m, 2H, ArH); <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>)  $\delta$  84.3 (d,  $J_{C-F}$ =169 Hz, PhC(CH<sub>2</sub>)(CH<sub>2</sub>F)), 115.3 (d,  $J_{C-F}$ =10.4Hz, PhC=CH<sub>2</sub>), 125.9 (ArC), 128.2 (ArC), 128.6 (ArC), 137.3 (ArC), 143.1 (PhC(CH<sub>2</sub>)(CH<sub>2</sub>F)); <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>)  $\delta$  -212.8 (dt,  $J_{F-H}$ =47.0 Hz,  $J_{F-H}$ =2.9 Hz); IR (film) v<sub>max</sub> (cm<sup>-1</sup>): 742; HPLC analysis (1 mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 1:1 mobile phase), NFSi: t<sub>r</sub> = 6.00 mins, compound **6**: t<sub>r</sub> = 4.49 mins.

#### *tert*-Butyl{[(2*E*)-2-((3*S*,5*R*)-5-{[*tert*-butyldimethylsilyl]oxy}-3-fluoro-2-methylene



cyclohexylidene)ethyl]oxydiphenylsilane ((3S,5R)-8), and tert-Butyl{[(2E)-2-((3R,5R)-5-{[tertbutyldimethylsilyl]oxy}-3-fluoro-2-methylene cyclohexylidene)ethyl]oxy}diphenylsilane ((3R,5R)-8). Following the general procedure for the fluorination of allylsilanes, starting with 20 mg of dienyl silane (S)-7

(0.03 mmol), and 10 mg of NFSi in 0.5 mL acetonitrile. <sup>19</sup>F NMR analysis of the crude reaction mixture indicated the formation of two diastereomers in a 3:1 ratio. Purification by column chromatography (hexane : diethyl ether, 45:1) afforded 0.007 g (44%) of the desired product. HRMS (EI)<sup>+</sup> calculated for  $C_{31}H_{49}FNO_2Si_2$  [M+NH<sub>4</sub><sup>+</sup>] m/z 542.3278, found ([MH]<sup>+</sup>) m/z 542.3280; Analysis corresponded with that known in the literature.<sup>4</sup> HPLC analysis (1 mL/min, CH<sub>3</sub>CN:H<sub>2</sub>O, 1:19 t=0 mins, 19:1 t=25 mins mobile phase), starting material:  $t_r = 30.07$  mins, NFSi:  $t_r = 16.46$  mins, (3S, 5R)-8:  $t_r = 34.35$  mins, (3R, 5R)-8: t<sub>r</sub> = 36.04.

### General procedure for the [<sup>18</sup>F]-labelling of test substrates with [<sup>18</sup>F]NFSi.

The test substrate (5 mg) was weighed into a Wheaten vial. To this was added freshly prepared [<sup>18</sup>F]NFSi, predissolved in anhydrous acetonitrile (0.9 mL). The reaction mixture was then stirred at 80°C for up to 30 minutes, before analytical radio-HPLC analysis was carried out. Yields for the reactions were determined by integration of analytical radio-HPLC traces.

2-[<sup>18</sup>F]Fluoro-2-methyl tetralone ([<sup>18</sup>F]4). Following the general procedure described



above, 2-[<sup>18</sup>F]fluoro-2-methyl tetralone was prepared from 2-methyl-1trimethylsilyloxytetral-1-ene (5 mg, 0.02 mmol). HPLC analysis showed considerable consumption of the  $[^{18}F]NFSi$  after 5 minutes, with quantitative formation of [<sup>18</sup>F]4 after 15 minutes. HPLC retention times for the radioactive product corresponded directly with the reference sample prepared from commercial NFSi.

### 2-Benzyl-2-[<sup>18</sup>F]fluoro-1-methylene-indan ([<sup>18</sup>F]5).



Following the general procedure described above, 2-Benzyl-2-[<sup>18</sup>F]fluoro-1-methylene-indan from (2-benzyl-3H-inden-1was prepared ylmethyl)trimethylsilane (5 mg, 0.02 mmol). HPLC analysis showed formation of [<sup>18</sup>F]5 in 51% yield after 5 mins, in 89% yield after 15 mins,

and in 95% yield after 30 mins. HPLC retention times for the radioactive product corresponded directly with the reference sample prepared from commercial NFSi.

## (1-[<sup>18</sup>F]Fluoromethylvinyl)benzene ([<sup>18</sup>F]6).



Following the general procedure described above, (1-<sup>18</sup>F]Fluoromethylvinyl)benzene prepared from (2 was phenylallyl)trimethylsilane (3) (5 mg, 0.03 mmol). HPLC analysis showed formation of [<sup>18</sup>F]6 in 30% yield after 30 mins. HPLC retention times for the radioactive product corresponded directly with the reference sample prepared from commercial NFSi.

tert-Butyl{[(2E)-2-((3S,5R)-5-{[tert-butyldimethylsilyl]oxy}-3-[<sup>18</sup>F]fluoro-2-



methylene cyclohexylidene)ethyl]oxy}diphenylsilane ([<sup>18</sup>F](3S,5R)-8) and *tert*-Butyl{[(2E)-2-((3R,5R)-5-{[*tert*-butyldimethylsilyl]oxy}-3-[<sup>18</sup>F]fluoro-2methylene cyclohexylidene)ethyl]oxy}diphenylsilane ([<sup>18</sup>F](3R,5R)-8). Following the general procedure

described above, tert-Butyl{[(2E)-2-((3S,5R)-5-{[tert-butyldimethylsilyl]oxy}-3-[<sup>18</sup>F]fluoro-2-methylene cyclohexylidene)ethyl]oxy}diphenylsilane was prepared from tert-butyl[((2E)-2-(5S)-5-{[tert-butyl(dimethyl)silyl]oxy}-2-

{[(trimethylsilyl)methyl]cyclohex-2-en-1-ylidene}ethyl)oxy]diphenyl silane (5 mg, 0.009 mmol). HPLC analysis showed formation of [<sup>18</sup>F]8 in 87% yield after 30 mins, dr = 4:1 *anti:syn*. HPLC retention times for the radioactive product corresponded directly with the reference sample prepared from commercial NFSi.

# HPLC traces and NMR spectra.









(2-Phenylallyl)trimethylsilane (3)













# (1-Fluoromethylvinyl)benzene (6)





 $tert-Butyl\{[(2E)-2-((3S,5R)-5-\{[tert-butyldimethylsilyl]oxy\}-3-fluoro-2-methylene cyclohexylidene)ethyl]oxy\}diphenylsilane ((3S,5R)-8) and tert-Butyl\{[(2E)-2-((3R,5R)-5-\{[tert-butyldimethylsilyl]oxy\}-3-fluoro-2-methylene cyclohexylidene)ethyl]oxy}diphenylsilane ((3R,5R)-8)$ 



*tert*-Butyl{[(2*E*)-2-((3*S*,5*R*)-5-{[*tert*-butyldimethylsilyl]oxy}-3-[<sup>18</sup>F]fluoro-2methylene cyclohexylidene)ethyl]oxy}diphenylsilane ([<sup>18</sup>F](3*S*,5*R*)-8) and *tert*-Butyl{[(2*E*)-2-((3*R*,5*R*)-5-{[*tert*-butyldimethylsilyl]oxy}-3-[<sup>18</sup>F]fluoro-2-methylene cyclohexylidene)ethyl]oxy}diphenylsilane ([<sup>18</sup>F](3*R*,5*R*)-8)



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