Catalytic Hydrotrifluoromethylation of Unactivated Alkenes

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1. General Information

All NMR spectra were recorded on BrukerDPX200, DPX250, AV400, AVC500, AVB500 and DRX500 spectrometers. ^{1}H and ^{13}C NMR spectral data are reported as chemical shifts (δ) in parts per million (ppm) relative to the solvent peak using the Bruker internal referencing procedure (edlock). ^{19}F NMR spectra are referenced relative to $CFCl_3$ in $CDCl_3$. Chemical shifts (δ) 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, pent=pentet, br=broad, m=multiplet. NMR spectra were processed in ACD/Spec Manager. High resolution mass spectra (HRMS, *m*/*z*) were recorded on a Bruker MicroTOF spectrometer using positive electrospray ionization (ESI) or on a Micromass GCT spectrometer using field ionization (EI/FI) or chemical ionization (CI). IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer. Absorptions are measured in wavenumbers and only peaks of interest are reported. Optical rotations were measured on a PerkinElmer Polarimeter model 341 and are reported as $[\alpha]_D^{20}$ value; the corresponding concentration (c) is given in g/100 mL. Melting points of solids were measured on a Griffin apparatus and are uncorrected. IUPAC names were obtained using the ACD/ILab service. Weighing was perfomed with a 4 decimal place balance. All reactions for hydrotrifluoromethylation of alkenes were conducted in non-dried glassware with magnetic stirring under an inert atmosphere, unless otherwise noted. All solvents were dried on a column of alumina prior to use. Flash column chromatography was performed over Merck silica gel C60 (40−60 μm) using the eluent system described for each experiment. $Ru(bpy)_3Cl_2 \cdot 6H_2O$, CuCl, Hantzch ester **VI** and Umemoto reagent **V** were purchased from Sigma-Aldrich. Unless otherwise specified, other reagents were obtained from commercial suppliers. In a general experiment, a 14 W fluorescent light bulb (OSRAM DULUXSTAR®), were used as a visible light source. The light source was placed at a distance of approximately 5.0 cm from the reaction vial. It noted that identical chloro- and oxy-trifluoromethylated side-products were provided in very low yield in some reactions of hydrotrifluoromethylation. The yields were determined by the isolation on SiO_2 gel column chromatografy, and the purity for the desired products was determined by ^{19}F NMR spectra.

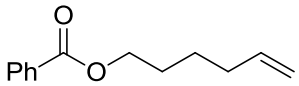
14 W Fluorescent Light Bulb

Reaction Setup

2 Experimental Procedures and Characterization Data

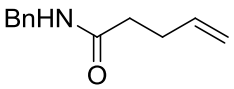
2-1. Synthesis of Alkenes Starting Materials

Hex-5-en-1-yl benzoate (1a) [1]



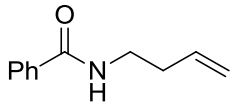
To a flame-dried 250 mL two-neck flask containing a magnetic stir bar, were added hex-5-en-1-ol (2.51 g, 25 mmol) and anhydrous DCM (50 mL). The solution was cooled to 0 °C in an ice bath. DMAP (306 mg, 2.5 mmol) and pyridine (6.1 mL, 75 mmol) were added successively, followed by dropwise addition of benzoyl chloride (5.8 mL, 50 mmol). The solution was allowed to warm to room temperature and stir for 2 hrs. The reaction was quenched with H_2O (20 mL), and the phases were separated. The aqueous phase was extracted with DCM (2 × 20 mL). The organic layers were combined, washed with H_2O (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting residue was purified by silica gel column chromatography (hexanes → 16:1 hexanes:EtOAc) gave **1a** as a colorless oil (4.50 g, 88% yield). Analytical data matched previously reported data.[1] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.60–1.54 (m, 2H), 1.79 (quint, J = 6.8 Hz, 2H), 2.13 (q, J = 7.2 Hz, 2H), 4.33 (t, J = 6.4 Hz, 2H), 5.07–4.96 (m, 2H), 5.83 (ddt, J_1 = 10.2 Hz, J_2 = 16.8 Hz, J_3 = 6.8 Hz, 1H), 7.46–7.42 (m, 2H), 7.58–7.53 (m, 1H), 8.06–8.03 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 25.29, 28.15, 33.31, 64.88, 114.87, 128.31, 129.52, 130.43, 132.82, 138.35, 166.67; **IR** (neat) ν 2938, 1719, 1452, 1272, 1113, 711 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{13}H_{16}NaO_2$ $[M+Na]^+$ 227.1037, found 226.9513.

***N*-Benzylpent-4-enamide (1f)** [2]



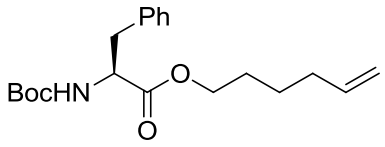
To a flame-dried 100 mL two-neck flask containing a magnetic stir bar, were added 4-pentenoic acid (1.00 g, 10.0 mmol), benzylamine (1.07 g, 10.0 mmol), DMAP (122 mg, 1.0 mmol), and anhydrous DCM (20 mL). The solution was cooled to 0 °C in an ice bath. DCC (2.27 g, 11.0 mmol) in anhydrous DCM (20 mL) was added dropwise. The solution was allowed to warm to room temperature and stir for 12 hrs, during which time a cloudy white precipitate was observed. The crude reaction mixture was then loaded directly onto a bed of silica gel for purification *via* column chromatography (4:1 hexanes:EtOAc → 1:1 hexanes:EtOAc), which gave **1f** as an off-white solid (1.78 g, 94% yield). Analytical data matched previously reported data.[2] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.31–2.27 (m, 2H), 2.42–2.37 (m, 2H), 4.40 (d, J = 5.6 Hz, 1H), 5.08–4.98 (m, 2H), 5.81 (ddt, J_1 = 10.4 Hz, J_2 = 17.2 Hz, J_3 = 6.4 Hz, 1H), 6.20 (bs, 1H), 7.28–7.24 (m, 3H), 7.34–7.30 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 29.53, 35.65, 43.41, 115.49, 127.33, 127.65, 128.54, 136.93, 138.25, 172.19; **IR** (neat) ν 3283, 3078, 2927, 1640, 1546, 1453,1267, 913, 697 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{12}H_{15}NNaO$ $[M+Na]^+$ 212.1046, found 212.1037.

***N*-(but-3-en-1-yl)benzamide (1h)**[3]



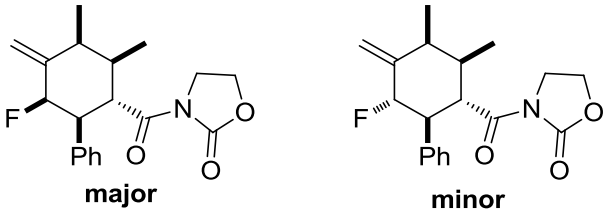
To a flame-dried 100 mL two-neck flask, were added anhydrous DCM, freshly distilled Et_3N (4.2 mL, 12 mmol), and 3-buten-1-amine (711 mg, 10 mmol). The solution was cooled to 0 °C in an ice bath. Benzoyl chloride (1.4 mL, 12 mmol) was added dropwise over 5 min. The reaction mixture was allowed to warm to room temperature and stir for 24 hrs. The solution was diluted with Et_2O (20 mL) and filtered. The filtrate was concentrated *in vacuo*, diluted with Et_2O (20 mL), and filtered again. The filtrate was concentrated *in vacuo*, and the resulting yellow residue was purified by silica gel column chromatography (4:1 hexanes:EtOAc → 1:1 hexanes:EtOAc) to give **1h** as a yellow oil (1.37 g, 85% yield). Analytical data matched previously reported data.[3] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.37 (q, J = 6.8 Hz, 2H), 3.52 (q, J = 6.8 Hz, 2H), 5.17–5.10 (m, 2H), 5.80 (ddt, J_1 = 10.4 Hz, J_2 = 17.2 Hz, J_3 = 6.8 Hz, 1H), 6.32 (br. s, 1H), 7.43–7.39 (m, 2H), 7.50–7.46 (m, 1H), 7.76–7.73 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 33.71, 38.76, 117.37, 126.78, 128.50, 131.32, 134.66, 135.29, 167.47; **IR** (neat) ν 3307, 1636, 1538, 1490, 1309, 916 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{11}H_{13}NNaO$ $[M+Na]^+$ 198.0889, found 198.0887.

(*S*)-Hex-5-en-1-yl 2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanoate (1l)



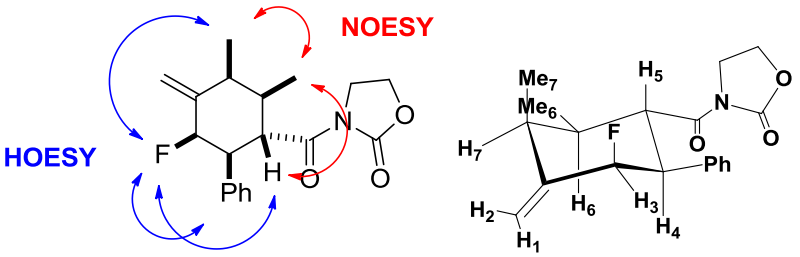
To a flame-dried 250 mL two-neck flask containing a magnetic stir bar, were added Boc-Phe-OH (2.65 g, 10 mmol), hex-5-en-1-ol (1.10 g, 11 mmol), triphenylphosphine (2.89 g, 11 mmol), and anhydrous DCM (80 mL). DEAD (1.7 mL, 11 mmol) was added dropwise, and the reaction was allowed to stir at room temperature for 18 hrs. The solvent was removed *in vacuo*, and the residue was dissolved in a minimal amount of Et_2O (approximately 70 mL). The flask was transferred to a –20 °C freezer for several hours, at which point a large quantity of colorless crystals of PPh_3 were observed. The mixture was filtered through a plug of cotton, and the filtrate was concentrated *in vacuo*. The resulting residue was purified by silica gel column chromatography (10:1 hexanes:EtOAc) to give **1l** as a colorless oil (3.44 g, 99% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.42 (s, 1H), 1.60 (quint, J = 6.4 Hz, 2H), 2.05 (q, J = 6.0 Hz, 2H), 3.13–3.03 (m, 2H), 4.14–4.04 (m, 2H), 4.59–4.54 (m, 1H), 5.03–4.96 (m, 2H), 5.77 (ddt, J_1 = 10.2 Hz, J_2 = 16.8 Hz, J_3 = 6.8 Hz, 1H), 7.13 (d, J = 6.8 Hz, 2H), 7.30–7.21 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 25.03, 27.86, 28.29, 33.20, 38.44, 54.45, 65.25, 79.83, 114.93, 126.97, 128.50, 129.31, 136.06, 138.18, 155.06, 171.96; **IR** (neat) ν 3367, 2977, 1714, 1497, 1366, 1249, 1166 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{20}H_{29}NO_4$ $[M]^+$ 347.2097, found 347.2094.

3-{[(1S,2S,3R,5S,6R)-3-Fluoro-5,6-dimethyl-4-methylene-2-phenylcyclohexyl]carbonyl}-1,3-oxazolidin-2-one, *anti,syn,syn,syn* (1o)[4]



3-({(1*S*,2*S*,5*S*,6*R*)-5,6-Dimethyl-2-phenyl-4-[(trimethylsilyl)methyl]cyclohex-3-en-1-yl}carbonyl)-1,3-oxazolidin-2-one[4] (386 mg, 1 mmol), Selectfluor (531 mg, 1.5 mmol) in MeCN (10 mL). The reaction was stirred for 2 hrs. The solvent was evaporated under reduced pressure. The residue was diluted with sat. aq. $NaHCO_3$. and then extracted with Et_2O (2 × 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting residue was purified by SiO_2 gel Column chromatography (*n*-hexane/EtOAc = 5:1) to give the allylic fluoride (**1o**) as a colorless gum (262 mg, 79% yield), of which the epimeric ratio was found to be 8:1 in favor of the Ph/F *syn* isomer by ^{19}F-NMR analysis.

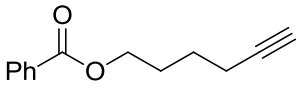
Characterization data for the *major* isomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.01 (q, J = 6.9 Hz, 3H), 1.26 (dd, J_1 = 2.5 Hz , J_2 = 6.0Hz, 3H), 2.15–2.23 (m, 1H), 2.59–2.64 (m, 1H), 3.11 (ddd, J_1 = 2.5 Hz, J_2 = 12.0 Hz, J_3 = 37.5 Hz, 1H), 3.47 (ddd, J_1 = 6.0 Hz, J_2 = 9.2 Hz, J_3 = 11.0 Hz, 1H), 3.79–3.85 (m, 1H), 3.98 (dd, J_1 = 7.6 Hz, J_2 = 8.8 Hz, 1H), 4.23 (dt, J_1 = 5.7 Hz, J_2 = 8.8 Hz, 1H), 4.94 (dd, J_1 = 2.2 Hz, J_2 = 49.9 Hz, 1H), 4.97 (t, J = 11.0 Hz, 1H), 5.06 (dd, J_1 = 1.6 Hz, J_2 = 5.4 Hz, 1H), 5.09–5.11 (m, 1H), 7.22–7.35 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 15.07, 16.11, 39.50, 40.82, 41.32, 42.23, 52.90 (d, J = 19.7 Hz), 61.40, 95.30 (d, J= 173.7 Hz), 115.25 (d, J = 7.3 Hz), 127.06, 128.11, 128.86, 139.01, 148.61 (d, J = 14.2 Hz), 153.08, 175.60; **IR** (neat) ν 2968, 1772. 1693, 1384, 1360, 1291, 1217, 1100, 1041, 916, 760, 701 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{19}H_{22}FNO_3$ $[M+Na]^+$ 354.1466, found 354.1476. **^{19}F {H}NMR** (471 MHz, $CDCl_3$) δ –174.81 (s, 3F).



^{1}H NMR δ (H_3)	^{1}H NMR δ (H_4)	^{1}H NMR δ (H_5)	$^2J_{H3-F}$	$^3J_{H4-F}$	$^3J_{H4-H5}$
4.94	3.11	4.97	49.9 Hz	37.5 Hz	12.0 Hz

The characteristic NMR data (key coupling constants: $^3J_{H-F}$ axial/axial = ~ 40 Hz,[5] $^3J_{H-H}$ axial/axial = ~ 10 Hz) allowed assignment of the orientation of F atom, H_4 and H_5 which are axially positioned. NOEand HOESY experiments on the major product indicated that the structure featured a *syn* relationship between the fluorine and phenyl substituents.

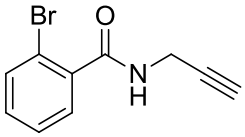
6-Benzoyloxy-1-hexyne[6]



To a solution of 5-hexyn-1-ol (0.55 mL, 5 mmol, 1.0 eq), in anhydrous DCM (0.5 M, 10 mL) at 0°C was added successively DMAP (61.1 mg, 0.5 mmol, 10 mol%), pyridine (1.2 mL, 15 mmol, 3.0 eq) and benzoyl chloride (1.2 mL, 10 mmol, 2.0 eq). The solution was allowed to warm to room temperature and stirred for 1hr, after which the crude reaction mixture was purified by SiO_2 gel column chromatography (1:3 EtOAc/Hexane) which afforded benzoyloxy-1-hexyne as a pale yellow oil (1.0 g, quantitative yield). Analytical data are consistent with the literature. [6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71 (tt, J = 8.0 Hz, 2H), 1.92 (tt, J = 7.0 Hz, 2H), 2.0 (t, J = 3.0 Hz, 1H), 2.30 (dt, J = 7.0 Hz, 3.0 Hz, 2H), 4.36 (t, 6.5 Hz, 2H), 7.45 (tt, J = 7.5 Hz, 1.5 Hz, 2H), 7.57 (tt, J = 7.5 Hz, 1.5 Hz, 1H), 8.06 (dt, J = 7.5 Hz, 1.5 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 18.1, 25.1, 27.8, 64.4, 68.8, 83.9, 128.4, 129.5, 130.3, 132.9, 166.6.

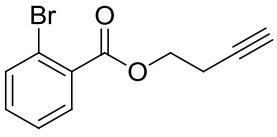
2-Bromo-*N*-(prop-2-yn-1-yl)benzamide[7]



To a solution of propargylamine (0.32 mL, 5.0 mmol, 1.0 eq) and NEt_3 (1.4 mL, 10.0 mmol, 2.0 eq) in DCM (35 mL, 0.14 M) at 0°C was added 4-bromobenzoyl chloride (0.72 mL, 5.5 mmol, 1.1 eq). The reaction was stirred for 3h, before quenching with water. The mixture was extracted with DCM (x3), washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (2:3 EtOAc/Hexane) gave 2-bromo-*N*-(prop-2-yn-1-yl)benzamide as an off-white solid (1.2 g, quantitative yield). Analytical data are consistent with the literature.[7]

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (t, J = 2.5 Hz, 1H), 4.15 (d, J = 2.5 Hz, 1H), 4.17 (d, J = 2.5 Hz, 1H), 6.31 (brs,1H, N*H*), 7.20 (dt, J = 8.0 Hz, 2.0 Hz), 7.27 (dt, J = 7.5 Hz, 1.0 Hz), 7.44 (dd, J = 7.5 Hz, 2.0 Hz), 7.50 (dd, J = 8.0 Hz, 1.0 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 29.8, 72.1, 78.9, 119.4, 127.6, 129.7, 131.6, 133.5, 136.9, 167.2.

But-3-yn-1-yl 2-bromobenzoate



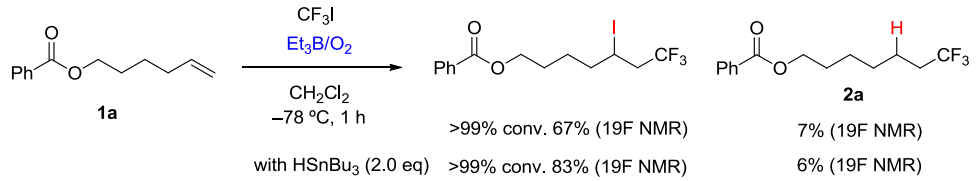
To a solution of 3-butyn-1-ol (0.38 mL, 5.0 mmol, 1.0 eq) and NEt_3 (1.4 mL, 10.0 mmol, 2.0 eq) in DCM (35 mL, 0.14 M) at 0°C was added 4-bromobenzoyl chloride (0.72 mL, 5.5 mmol, 1.1 eq). The reaction was stirred for 1h, before quenching with water. The mixture was extracted with DCM (x3), washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (1:9 EtOAc/Hexane) afforded but-3-yn-1-yl 2-bromobenzoate as a yellow oil (1.26 g, quantitative yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97 (t, J = 2.5 Hz, 1H), 2.61 (dt, J = 7.0 Hz, 2.5 Hz, 2H), 4.38 (t, J = 7.0 Hz, 2H), 7.24-7.32 (m, 2H), 7.59 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.76 (dd, J = 7.5 Hz, 2.0 Hz, 1H); **^{13}C NMR** (100 MHz,

$CDCl_3$) δ 19.0, 63.2, 70.2, 79.9, 121.8, 127.2, 131.5, 131.8, 132.7, 134.4, 165.8; **IR** (neat) ν 3297, 1729, 1290, 1247, 1133, 1108, 1028, 743, 642; **HRMS** (CI) *m/z* Calcd for $C_{12}H_{10}BrO_2$ $[M+H]^+$ 252.9864, found 252.9871.

2-2. Control Experiments

Hydromethylation carried out applying reaction condition described in *Org. Biomol. Chem* **2012**, *10*, 8583-8586.

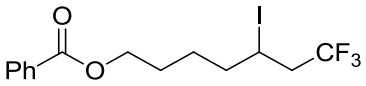


In a 10 mL round bottom flask, hex-5-en-1-yl benzoate **1a** (40.8 mg, 0.20 mmol) was dissolved in dichloromethane (1.0 mL). The flask was sealed, and the air was substituted with O_2 using two vacuum/O_2 balloon cycles. The solution was cooled to -78 °C and then trifluoroiodomethane (10 equiv.) and triethylborane (5.0 equiv., 1.0 M in hexane) were added. After stirring at -78 °C for 1 hr, the mixture was quenched by addition of 0.1 M HCl solution at room temperature. The aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude mixture was analyzed by ^{19}F NMR using benzotrifluoride as an internal standard, it found that ATRA product (trifluoromethyl-iodo adduct) and **2a** in 67% and 7% yield were afforded.

The reaction in the presence of $HSnBu_3$ (2.0 equiv.) under same condition gave ATRA product and **2a** in 83% and 6% yield, respectively.

2-3. General Procedure: Trifluoromethylation of Alkenes

7,7,7-Trifluoro-5-iodoheptyl benzoate

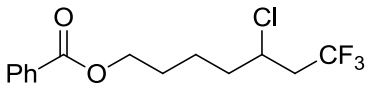


Hex-5-en-1-yl benzoate (30.6 mg, 0.15 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (5.6 mg, 0.0075 mmol), Umemoto reagent (72.4 mg, 0.18 mmol) and MeOH (0.3 mL) were placed in a vial which was equipped with a magnetic stir bar. The vial was cooled to −78 ˚C and trifluoroiodomethane (352.0 mg, 1.8 mmol) was then added. The reaction mixture was warm to room temperature, then exposed to a 14 W fluorescent light bulb at ambient temperature while stirring for 24 hrs. The reaction mixture was quenched with sat. aq. $NaHCO_3$, and the aqueous phase was extracted with Et_2O (× 2). The combined organic phases were washed with water and brine, then dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography on SiO_2 gel (EtOAc/*n*-hexane = 1:20) gave the desired CF_3 product (35.7 mg, 53%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46–1.57 (m, 1H), 1.63–1.83 (m, 5H), 2.71 (ddq, J_3 = 15.6 Hz, 1H), 2.86 (ddq, J_1 = 5.8 Hz , J_2 = 10.5 Hz, J_3 = 15.6 Hz, 1H), 4.11–4.18 (m, 1H), 4.27 (dt, J_1 = 1.7 Hz , J_2 = 6.1 Hz, 2H), 7.38 (t, J = 7.3 Hz, 2H), 7.49 (tt, J_1 = .5 Hz , J_2 = 7.3 Hz, 1H), 7.98 (dd, J_1 = 1.4 Hz , J_2 = 8.6 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 14.10, 21.12 (q, J = 2.9 Hz), 22.63, 26.19, 27.69, 31.57, 39.13, 44.92 (q, J = 28.4 Hz), 64.43, 125.53 (q, J = 276.7 Hz), 128.35, 129.54, 130.26, 132.92, 166.57; **^{19}F NMR** (377 MHz, $CDCl_3$) δ –63.89 (t, J = 10.4 Hz, 3F), **IR** (neat) ν 1716, 1315, 1271, 1142, 1111, 1070, 1026, 710 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{14}H_{16}F_3IO_2$ $[M]^+$

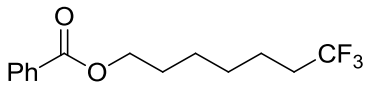
400.0152, found 400.0147.

5-Chloro-7,7,7-trifluoroheptyl benzoate



Hex-5-en-1-yl benzoate (30.6 mg, 0.15 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (5.6 mg, 0.0075 mmol), CF_3SO_2Cl (19.2 μL, 0.18 mmol) and MeOH (0.3 mL) were placed in a vial which was equipped with a magnetic stir bar. The vial was exposed to a 14 W fluorescent light bulb at room temperature while stirring for 24 hrs. The reaction mixture was quenched with sat. aq. $NaHCO_3$, and the aqueous phase was extracted with Et_2O (× 2). The combined organic phases were washed with water and brine, then dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography on SiO_2 gel (Et_2O /*n*-hexane = 1:20) gave the title compound (12.0 mg, 26%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.52–1.60 (m, 1H), 1.67–1.89 (m, 5H), 2.48 (ddq, J_1 = 5.7 Hz , J_2 = 10.1 Hz, J_3 = 15.5 Hz, 1H), 2.58 (ddq, J_1 = 7.5 Hz , J_2 = 10.4 Hz, J_3 = 15.5 Hz, 1H), 4.04–4.09 (m, 1H), 4.27 (dt, J_1 = 1.9 Hz , J_2 = 6.3 Hz, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.50 (tt, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H), 7.97 (dd, J_1 = 1.6 Hz, J_2 = 8.2 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 22.63, 28.02, 37.56, 42.45 (q, J = 28.4 Hz), 53.88 (q, J = 2.9 Hz), 64.45, 125.19 (q, J = 275.8 Hz), 128.37, 129.53, 130.26, 132.95, 166.59;**^{19}F NMR** (377 MHz, $CDCl_3$) δ –63.77 (t, J = 10.4Hz, 3F); **IR** (neat) ν 1717, 1270, 1113, 711 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{14}H_{16}F_3ClO_2$ $[M]^+$ 308.0789, found 308.0791.

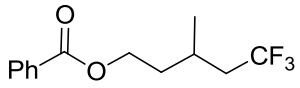
7,7,7-trifluoroheptyl benzoate (2a)



General procedure for trifluoromethylation of terminal olefin with Umemoto trifluoromethylating reagent under photocatalysis:

Hex-5-en-1-yl benzoate (30.6 mg, 0.15 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (5.6 mg, 0.0075 mmol), Umemoto reagent (72.4 mg, 0.18 mmol) and MeOH (0.3 mL) were placed in a vial which was equipped with a magnetic stir bar. The vial was exposed to a 14 W fluorescent light bulb at room temperature while stirring for 24 hrs. The reaction mixture was quenched with sat. aq. $NaHCO_3$, and the aqueous phase was extracted with Et_2O (× 2). The combined organic phases were washed with water and brine, then dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography on SiO_2 gel (Et_2O /*n*-hexane = 1:20) gave the desired CF_3 product **2a** (19.2 mg, 78%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.44–1.50 (m, 4H), 1.57–1.62 (m, 2H), 1.80 (pent, J = 6.6 Hz, 2H), 2.04–2.14 (m, 2H), 4.34 (t, J = 6.3 Hz, 2H), 7.45 (t, J = 7.9 Hz, 2H), 7.51 (tt, J_1 = 1.5 Hz, J_2 = 7.6 Hz, 1H), 8.05 (dd, J_1 = 1.5 Hz, J_2 = 8.6 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.80 (q, J = 2.9 Hz), 25.72, 28.35, 28.48, 33.64 (q, J = 28.4 Hz), 64.78, 127.17 (q, J = 274.8 Hz), 128.34, 129.51, 130.38, 132.87, 166.64; **^{19}F NMR** (377 MHz, $CDCl_3$) δ –66.34 (t, J = 11.5 Hz, 3F); **IR** (neat) ν 2945, 1718, 1272, 1254, 1138, 1134, 711 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{14}H_{17}F_3O_2$ $[M+Na]^+$ 297.1072, found 297.1073.

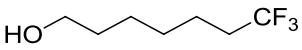
5,5,5-Trifluoro-3-methylpentyl benzoate (2b)



Prepared following general procedure using 3-methylbut-3-en-1-yl benzoate (47.6 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.7 mg, 0.30 mmol) and MeOH (0.5 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:20) provided **2b** (35.3 mg, 53% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (d, *J* = 7.0 Hz, 3H), 1.68–1.75 (m, 1H), 1.91–1.98 (m, 1H), 2.00–2.26 (m, 3H), 4.38–4.41 (m, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.58 (dt, J_1 = 1.3 Hz, J_2 = 7.6 Hz, 1H), 8.04 (dd, J_1 = 1.3 Hz, J_2 = 8.5 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 19.61, 25.07 (d, *J* = 1.9 Hz), 35.26, 40.19 (q, *J* = 26.5 Hz), 62.44, 126.96 (q, *J* = 275.8 Hz), 128.40, 129.52, 130.13, 132.99, 166.53; **^{19}F NMR** (236 MHz, $CDCl_3$) *δ* –63.72 (t, *J* = 10.8 Hz, 3F), **IR** (neat) ν 1718, 1271, 1140, 1111, 1070, 1050, 1027, 709 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{13}H_{15}F_3O_2$ $[M]^+$ 260.1024 found 260.1023.

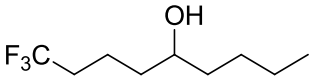
7,7,7-trifluoroheptan-1-ol (2c)



Prepared following general procedure using 5-hexen-1-ol (40.1 mg, 0.40 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (14.9 mg, 0.020 mmol), Umemoto reagent (193.1 mg, 0.48 mmol) and MeOH (0.8 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:4) provided **2c** (31.7 mg, 47% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39–1.42 (m, 4H), 1.51 (br. s, OH), 1.54–1.61 (m, 5H), 2.07 (tq, J_1 = 7.9 Hz, J_2 = 11.1 Hz, 2H), 3.65 (t, *J* = 6.6 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.81(q, *J* = 2.8 Hz), 25.34, 28.44, 32.39, 33.62 (q, *J* = 27.5 Hz), 62.73, 127.21 (q, *J* = 274.8 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) *δ* –66.42 (t, *J* = 12.2 Hz, 3F), **IR** (neat) ν 3338, 2940, 1252, 1134, 1046 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_7H_{13}F_3O$ $[M+H]^+$ 170.0918 found 170.0915.

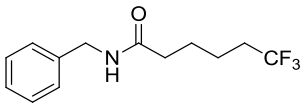
1,1,1-Trifluorononan-5-ol (2d)



Prepared following general procedure using oct-1-en-4-ol (50.0 mg, 0.39 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (14.6 mg, 0.0195 mmol), Umemoto reagent (189.1 mg, 0.47 mmol) and MeOH (0.8 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:30 to 1:20) provided **2d** (46.4 mg, 60% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.1 Hz, 3H), 1.18–1.74 (m, 10H), 1.97–2.01 (m, 2H), 3.54 (sept, *J* = 4.0 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 14.03, 18.29 (q, *J* = 2.8 Hz), 22.67, 33.73 (q, *J* = 28.4 Hz), 36.17, 37.28, 71.45, 127.16 (q, *J* = 274.8 Hz); **^{19}F NMR** (236 MHz, $CDCl_3$) *δ* –66.80 (t, *J* = 11.0 Hz, 3F), **IR** (neat) ν 3356, 233, 1252, 1140 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_9H_{17}F_3O_2$ $[M–H_2O]^+$ 180.1126, found 180.1327.

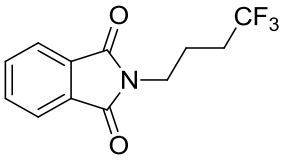
N-Benzyl-6,6,6-trifluorohexanamide (2e)



Prepared following general procedure using *N*-benzylpent-4-enamide (47.3 mg, 0.25 mmol), Umemoto reagent (120.7 mg, 0.30 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol) and MeOH (0.5 mL). Purification by SiO_2 gel column chromatography (*n*-hexane/EtOAc = 3/1) provided **2e** (28.4 mg, 44% yield) as a white crystalline.

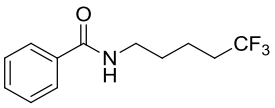
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.57–1.63 (m, 2H), 1.72–1.78 (m, 2H), 2.05–2.15 (m, 2H), 2.24 (t, *J* = 7.4 Hz, 2H), 4.44 (d, *J* = 5.7 Hz, 2H), 5.84 (s, 1H), 7.26–7.30 (m, 3H), 7.34 (t, *J* = 7.1 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.59 (q, *J* = 2.9 Hz), 24.59, 33.50 (q, *J* = 28.6 Hz), 36.04, 43.62, 127.57, 127.00 (q, *J* = 276.2 Hz), 127.79, 128.73, 138.17, 171.96; **^{19}F NMR** (377 MHz, $CDCl_3$) *δ* –66.35 (t, *J* = 10.9 Hz); **IR** (neat) ν 2941, 1644, 1551, 1455, 1390, 1255, 1135, 1028 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{13}H_{16}F_3NO$ $[M+Na]^+$ 282.1073, found 282.1068; **M.p.** 54–59 ˚C (recrystallization from dichloromethane/*n*-hexane).

***N*-(4,4,4-trifluorobutyl)phthalimide (2f)**



Prepared following general procedure using *N*-allylphthalimide (46.8 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.9 mg, 0.30 mmol) and MeOH (0.5 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:20) provided the title compound (36.5 mg, 57% yield) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.86–1.92 (m, 2H), 2.04–2.15 (m, 2H), 3.69 (t, *J* = 7.0 Hz, 2H), 7.66 (dd, J_1 = 3.2 Hz, J_2 = 5.4 Hz, 2H), 7.79 (dd, J_1 = 3.2 Hz, J_2 = 5.4 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.47 (q, *J* = 2.9 Hz), 31.52 (q, *J* = 28.4 Hz), 36.72, 123.36, 126.69 (q, *J* = 274.8 Hz), 131.89, 134.12, 168.20; **^{19}F NMR** (236 MHz, $CDCl_3$) *δ* –66.80 (t, *J* = 10.5 Hz, 3F), **IR** (neat) ν 1694, 1340, 1350, 1241,1173, 1087, 998, 912, 856, 716 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{12}H_{10}F_3NO_2$ $[M]^+$ 257.0664, found 257.0666; **M.p.** 54–55 °C (recrystallized from $CHCl_3$)

***N*-(5,5,5-trifluoropentyl) benzamide (2g)**

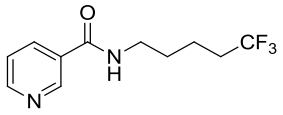


Prepared following general procedure using *N*-(but-3-en-1-yl)benzamide (43.8 mg, 0.25 mmol), Umemoto reagent (120.7 mg, 0.30 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol) and MeOH (0.5 mL). Purification by SiO2 gel column chromatography (*n*-hexane/EtOAc = 4/1) provided **2g** (30.8 mg, 50% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.61–1.73 (m, 4H), 2.08-2.17 (m, 2H), 3.47 (q, *J* = 6.5 Hz 2H), 6.40 (s, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.77 (d, *J* = 7.3 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 18.40 (q, *J* = 2.8 Hz), 27.80, 32.34 (q, *J* = 28.7 Hz), 38.46, 125.83, 126.02 (q, *J* = 276.2 Hz), 127.57, 130.47, 133.52, 166.70; **^{19}F**

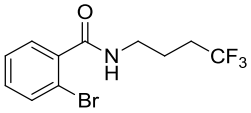
NMR (377 MHz, $CDCl_3$) δ –66.27 (t, J = 10.8 Hz, 3F); **IR** (neat) ν 3295,2950, 1633, 1544, 1489, 1391, 1307, 1246, 1136, 1086, 1035, 915, 806 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{12}H_{14}F_3NO$ $[M+Na]^+$ 268.0920, found 268.0917. mp 52–59 ˚C (recrystallization from dichloromethane/*n*-hexane).

_N_-(5,5,5-trifluoropentyl)nicotinamide (2h)



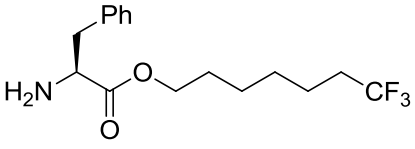
Prepared following general procedure using *N*-(but-3-en-1-yl)nicotinamide (44.1 mg, 0.25 mmol), Umemoto reagent (120.7 mg, 0.30 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (9.4 mg, 0.0125 mmol) and MeOH (0.5 mL). Purification by SiO_2 gel column chromatography (*n*-hexane/EtOAc = 1/2) provided **2h** (29.3 mg, 48% yield) as a white solid.
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.62–1.75 (m, 4H), 2.09-2.19 (m, 2H), 3.50 (q, J = 6.6 Hz, 2H), 6.55 (s, 1H), 7.39 (s, 1H), 8.11 (d, J = 7.9 Hz, 1H), 8.71 (s, 1H), 8.97 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 19.42 (q, J = 2.9 Hz), 28.70, 33.30 (q, J = 28.6 Hz), 39.58, 123.58, 126.95 (q, J = 274.8 Hz), 130.24, 135.14, 147.68, 152.17, 165.75; **^{19}F NMR** (377 MHz, $CDCl_3$) δ –66.28 (t, J = 10.9 Hz); **IR** (neat) ν 2947, 1637, 1590, 1555, 1460, 1419, 1388, 1332, 1250, 1214, 1133, 1085, 1034, 916, 833 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{11}H_{14}F_3N_2O$ $[M]^+$ 247.1053, found 247.1053; **M.p.** 91–98 ˚C (recrystallization from dichloromethane/*n*-hexane).

2-bromo-_N_-(4,4,4-trifluorobutyl)benzamide (2i)



Prepared following general procedure using *N*-allyl-2-bromobenzamide (60.0 mg, 0.25 mmol), Umemoto reagent (120.7 mg, 0.30 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (9.4 mg, 0.0125 mmol) and MeOH (0.5 mL). Purification by SiO_2 gel column chromatography (*n*-hexane/EtOAc = 4/1) provided **2i** (41.7 mg, 54% yield) as a white solid.
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.88–1.94 (m, 2H), 2.19-2.29 (m, 2H), 3.52 (q, J = 3.3 Hz, 2H), 6.20 (s, 1H), 7.27 (td, J_1 = 1.8 Hz, J_2 = 7.7 Hz, 1H), 7.35 (td, J_1 = 1.2 Hz, J_2 = 7.5 Hz, 1H), 7.50 (dd, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H), 7.58 (dd, J_1 = 1.2 Hz, J_2 = 7.9 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 22.30 (q, J = 2.9 Hz), 31.35 (q, J = 28.7 Hz), 38.73, 119.07, 126.90 (q, J = 276.2 Hz), 127.60, 129.49, 131.35, 133.34, 137.57, 167.85; **^{19}F NMR** (377 MHz, $CDCl_3$) δ –66.13 (t, J = 11.3 Hz); **IR** (neat) ν 3268, 1739, 1643, 1593, 1544, 1438, 1373, 1340, 1310, 1255, 1231, 1149 1030 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{11}H_{11}F_3BrNO$ $[M+Na]^+$ 331.9862, found 331.98628; **M.p.** 73–75 ˚C (recrystallization from CH_2Cl_2/*n*-hexane).

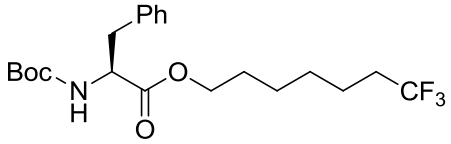
(_S_)-7,7,7-trifluoroheptyl 2-amino-3-phenylpropanoate (2j)



Prepared following general procedure using (*S*)-hex-5-en-1-yl 2-amino-3-phenylpropanoate (86.9 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.7 mg, 0.30 mmol) and MeOH (0.5 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:2) provided **2j** (41.4 mg, 52 % yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25–1.32 (m, 4H), 1.48–1.59 (m, 4H and NH_2), 2.01 (tq, J_1 = 7.8 Hz, J_2 = 11.0 Hz, 2H), 2.83 (dd, J_1 = 7.8 Hz, J_2 = 13.4 Hz, 1H), 3.01 (dd, J_1 = 5.6 Hz, J_2 = 13.4 Hz, 1H), 3.68 (t, J = 5.9 Hz, 1H), 4.04 (t, J = 6.6 Hz, 2H), 7.14 (d, J = 6.8 Hz, 2H), 7.19 (dt, J_1 = 2.4 Hz, J_2 = 7.3 Hz, 1H), 7.24 (d, J = 7.3 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.72 (q, J = 2.8 Hz), 25.49, 28.26, 28.27, 33.61 (q, J = 27.5 Hz), 41.20, 55.84, 64.78, 126.81, 127.20 (q, J = 274.8 Hz), 128.52, 129.25, 137.17, 175.04; **^{19}F NMR** (377 MHz, $CDCl_3$) δ –66.36 (t, J = 12.1 Hz, 3F), **IR** (neat) ν 2944, 1733, 1253, 1178, 1137, 837, 745, 700 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{16}H_{22}F_3NO_2$ $[M+H]^+$ 318.1673 found 318.1675; $[\alpha]_D^{20}$ = 17.4 (c = 0.50, MeOH).

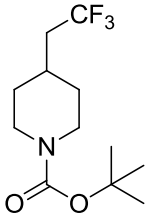
***N*-(*tert*-butoxycarbony) (*S*)-7,7,7-trifluoroheptyl-2-ammino-3-phenylpropanoate (2k)**



Prepared following general procedure using (*S*)-hex-5-en-1-yl 2-amino-3-phenylpropanoate (86.9 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.7 mg, 0.30 mmol) pyridine (15.2 μL, 0.30 mmol) and MeOH (0.5 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:4) provided the title compound (45.7 mg, 44 % yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24–1.40 (m, 4H), 1.40 (s, 9H), 1.51–1.58 (m, 4H), 2.04 (dq, J_1 = 7.9 Hz, J_2 = 11.0 Hz, 1H), 3.05 (d, J = 5.7 Hz, 1H), 3.06 (d, J = 5.4 Hz, 1H), 4.02–4.11 (m, 2H), 4.54 (q, J = 7.6 Hz, 1H), 4.96 (d, J = 7.6 Hz, NH), 7.11 (d, J = 6.9 Hz, 2H), 7.20–7.28 (m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.72 (q, J = 2.9 Hz), 25.44, 28.19, 28.24, 28.27 (q, J = 28.4 Hz), 38.47, 54.46, 65.12, 79.88, 126.97, 127.15 (q, J = 274.8 Hz), 128.49, 129.29, 136.04, 155.05, 172.00; **^{19}F NMR** (377 MHz, $CDCl_3$) δ –66.37 (t, J = 12.1 Hz, 3F), **IR** (neat) ν 2942, 1713, 1497, 1392, 1366, 1252, 1140, 1052, 733, 700 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{21}H_{30}F_3NO_3$ $[M]^+$ 417.2127 found 417.2126; $[\alpha]_D^{20}$ = –4.0 (c = 0.25, MeOH).

***Tert*-Butyl 4-(2,2,2-trifluoroethyl)piperidine-1-carboxylate (2l)**

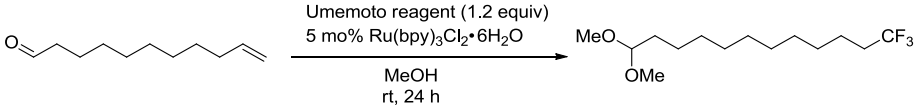


Prepared following general procedure using *tert*-butyl 4-methylenepiperidine-1-carboxylate (41.8 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.7 mg, 0.30 mmol) pyridine (15.2 μL, 0.30 mmol) and MeOH (0.5 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:4)

provided **2l** (45.7 mg, 64 % yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15-1.28 (m, 2H), 1.46 (s, 9H), 1.72-1.90 (m, 3H), 2.04 (qd, J_1 = 11.3 Hz, J_2 = 6.6 Hz, 2H), 2.72 (td, J_1 = 13.4 Hz, J_2 = 2.4 Hz), 4.02-4.17 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 28.40, 30.54 (q, J = 2.3 Hz), 31.87, 40.04 (q, J = 26.7 Hz), 43.50 (br. s.), 79.49, 126.77 (q, J = 277.5 Hz), 154.70; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -63.27 (t, J = 10.9 Hz, 3F); **IR** (neat) ν 2977, 2931, 2856, 1690, 1422, 1234, 1147, 1051; **HRMS** (ESI-TOF) *m/z* Calcd. for $C_{12}H_{20}F_3NO_2$ [M+Na] 290.1338 found 290.1340; **M.p.** 30-32 ^oC.

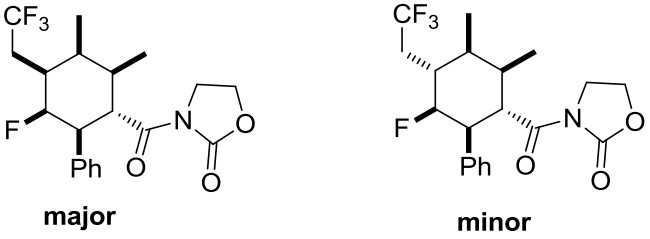
12,12,12-Trifluorododecanal dimethylacetal (2m)



Prepared following general procedure using undecylenic aldehyde (42.1 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (14.9 mg, 0.020 mmol), Umemoto reagent (193.1 mg, 0.48 mmol) and MeOH (0.8 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:4) provided **2m (**39.1 mg, 55% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28–1.36 (m, 14H), 1.52–1.62 (m, 4H), 2.06 (tq, J_1 = 7.9 Hz, J_2 = 11.1 Hz, 2H), 3.32 (s, 6H), 4.36 (t, J = 5.7 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.82 (q, J = 2.8 Hz), 24.57, 24.57, 28.67, 29.14, 29.30, 29.41, 29.43, 29.48, 32.48, 33.71 (q, J = 28.4 Hz), 52.58, 104.55, 127.28 (q, J = 274.8 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ –66.42 (t, J = 12.2 Hz, 3F), **IR** (neat) ν 2927, 2856, 1465, 1387, 1254, 1126, 1053 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{14}H_{27}F_3O_2$ $[M–OMe]^+$ 253,1779 found 253.1815.

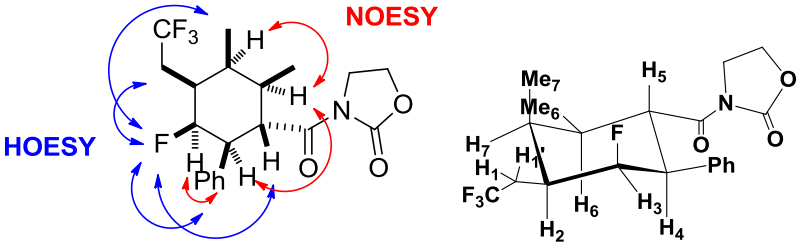
rac-3-[(1S.2S,3S.4S,5S,6S)-3-fluoro-5,6-dimethyl-2-phenyl-4-(2,2,2-trifluoroethyl)cyclohexanecarbonly]oxazolidin-2-one (2n)



Prepared following general procedure using 3-{[(1S,2S,3R,5S,6R)-3-Fluoro-5,6-dimethyl-4-methylene-2-phenylcyclohexyl]carbonyl}-1,3-oxazolidin-2-one (60.0 mg, 0.18 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (6.7 mg, 0.009 mmol), Umemoto reagent (86.9 mg, 0.22 mmol) and MeOH (0.4 mL). The epimeric ratio 3:1 in favor of the CF_3CH_2/F *syn* isomer was determined by ^{19}F NMR analysis of the crude mixture. Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:2) provided the title compound (46.1 mg, 64 % yield, ratio = 4:1) as a colorless oil.

Characterization data for the *major* isomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.05 (d, J = 6.9 Hz, 3H), 1.12 (dd, J_1 = 2.9 Hz, J_2 =7.3 Hz, 3H), 2.00–2.03 (m, 1H), 2.19–2.38 (m, 3H), 2.46–2.56 (m, 1H), 3.16 (ddd, J_1 = 2.5Hz, J_2 = 12.0 Hz, J_3 = 31.0 Hz, 1H), 3.54 (ddd, J_1 = 5.7 Hz, J_2 = 9.2 Hz, J_3 = 11.0 Hz, 1H), 3.84–3.89 (m 1H), 4.00–4.05 (m, 1H), 4.26–4.29 (m, 1H), 4.77 (d, J = 49.2 Hz, 1H), 4.87 (t, J = 11.0 Hz, 1H), 7.25–7.37 (m, 5H); **^{13}C NMR** (125 MHz,

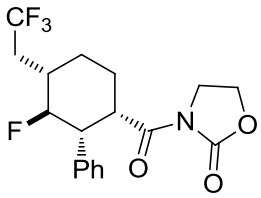
$CDCl_3$) δ 14.11, 16.77, 22.63, 31.58, 34.13 (dq, J_1 = 2.8 Hz, J_2 = 28.4 Hz), 36.90, 40.03, 40.78, 42.12, 51.75 (d, J = 18.0 Hz), 61.55 93.6 (d, J = 181.0 Hz), 127.07 (q, J = 274.8 Hz), 127.34, 128.36, 128.95, 138.96, 153.18, 175.86; **^{19}F {H}NMR** (377 MHz, $CDCl_3$) δ –198.62 (s, 1F), –66.94 (s, 3F); **IR** (neat) ν 2921, 1776, 1692, 1383, 1249, 1195, 1104, 1041, 703 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{20}H_{23}F_4NO_3$ $[M+Na]^+$ 424.1495 found 424.1506; **M.p.** 74–78 °C (recrystallized from $CHCl_3$).



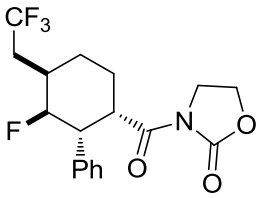
^{1}H NMR δ (H_3)	^{1}H NMR δ (H_4)	^{1}H NMR δ (H_5)	$^2J_{H3-F}$	$^3J_{H4-F}$	$^3J_{H4-H5}$
4.77	3.16	4.87	49.2 Hz	31.0 Hz	12.0 Hz

The characteristic NMR data (key coupling constants: $^3J_{H-F}$ axial/axial = ~ 40 Hz,[5] $^3J_{H-H}$ axial/axial = ~ 10 Hz) allowed assignment of the orientation of F atom, H_4 and H_5 which are axially positioned. NOE and HOESY experiments on the major product indicated that the structure featured a *syn* relationship between the fluorine and trifluoroethyl substituent.

rac-3-[(1S,2R,3S,4S)-3-fluoro-2-phenyl-4-(2,2,2-trifluoroethyl)cyclohexanecarbonyl]oxazolidin-2-one (2o)



major

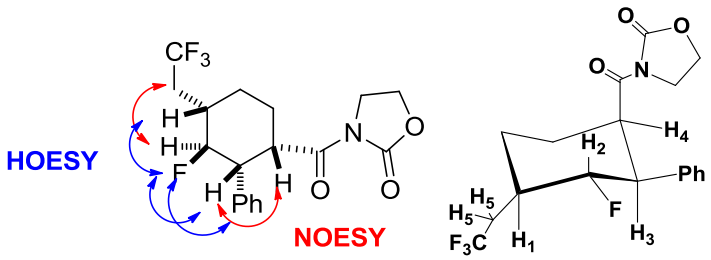


minor

Prepared following general procedure using 3-[(1S,2R,3R)-3-fluoro-4-methylene-2-phenylcyclohexanecarbonyl]oxazolidin-2-one[4] (50.0 mg, 0.17 mmo), $Ru(bpy)_3Cl_2$•$6H_2O$ (6.2 mg, 0.0125 mmol), Umemoto reagent (79.6 mg, 0.19 mmol) and MeOH (0.4 mL). The epimeric ratio 8:1 in favor of the CF_3CH_2/F *anti* isomer was determined by ^{19}F NMR analysis of the crude mixture. Purification by column chromatography on silica gel (AcOEt/*n*-hexane = 1:2) provided the title compound (47.9 mg, 78 % yield, epimeric ratio 9:1) as a white solid.

Characterization data for the *major* isomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.60–1.71 (m, 1H), 1.97–2.21 (m, 5H), 2.79 (quint, J = 12.0 Hz, 1H), 3.18 (dt, J_1 = 5.4 Hz, J_2 = 10.1 Hz, 1H), 3.71–3.77 (m, 1H), 3.85–3.90 (m, 1H), 4.12 (q, J = 8.9 Hz, 1H), 4.29 (dt, J_1 = 6.0 Hz, J_2 = 8.9 Hz, 1H), 4.62–4.69 (m, 1H), 5.50 (dt, J_1 = 10.1 Hz, J_2 = 49.8 Hz, 1H), 7,26–7.35 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 25.78 (d, J = 7.8 Hz), 27.42, 35.62 (dq, J_1 = 2.8 Hz, J_2

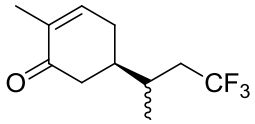
= 27.5 Hz), 38.07 (dq, J_1 = 1.9 Hz, J_2 = 17.0 Hz), 42.39, 45.28 (d, J = 8.5 Hz), 49.88 (d, J = 20.9 Hz), 126.96, 127.05 (q, J = 274.8 Hz), 128.11, 128.35, 138.59, 152.72, 173.54; **IR** (neat) ν 1768, 1691, 1389, 1389, 1278, 1249, 1121, 1089, 1047, 1012, 946, 758, 701 cm^{-1}; **^{19}F {H}NMR** (471 MHz, $CDCl_3$) δ –182.13 (s, 1F), –62.86 (s, 3F); **HRMS** (ESI) *m/z* Calcd for $C_{18}H_{19}F_4NO_3$ $[M+Na]^+$ 396.1183, found 396.1193; **M.p.** 113–121 °C (recrystallized from $CHCl_3$)



^{1}H NMR δ (H_1)	^{1}H NMR δ (H_2)	^{1}H NMR δ (H_3)	$^2J_{H2-F}$	$^3J_{H1-H2}$	$^3J_{H2-H3}$
1.97-2.21	5.50	3.18	49.8 Hz	10.1 Hz	10.1 Hz

The characteristic NMR data (key coupling constants: $^3J_{H-H}$ axial/axial = about 10 Hz) allowed assignment of the orientation of H_1, H_2 and H_3 which are axial position. NOE and HOESY experiments on the major product indicated that the structure featured a *anti* relationship between the fluorine and trifluoroethyl substituent.

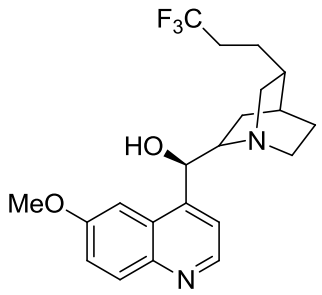
(*R*)-2-methyl-5-(4,4,4-trifluorobutan-2yl)cyclohex-2-enone (2p)



Prepared following general procedure using (*R*)-carvone (50.0 mg, 0.33 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (12.4 mg, 0.0165 mmol), Umemoto reagent (160.2 mg, 0.40 mmol) and MeOH (0.7 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:30) provided **2p** (39.5 mg, 54% yield, dr =1.0) as a colorless oil. The isomeric ratio was determined by ^{19}F NMR analysis.

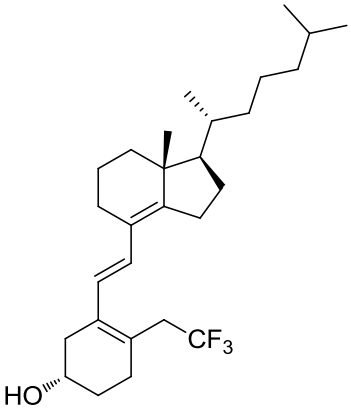
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04–1.06 (m, 3H), 1.79 (s, 3H), 1.90–1.96 (m, 2H), 2.11–2.23 (m, 4H), 2.29–2.33 (m, 1H), 2.44–2.51 (m, 1H), 6.75–6.76 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 15.58, 15.60, 16.14, 16.25, 26,21, 29.83, 31.33 (q, J = 2.9 Hz), 31.40 (q, J = 1.9 Hz), 37.49 (q, J = 22.7 Hz), 37.71 (q, J = 22.7 Hz), 40.07, 40.12, 40.26, 41.86, 127.05 (q, J = 127.05 Hz), 135.57, 135.60, 144.30, 144.39, 199.36, 199.40; **^{19}F NMR** (236 MHz, $CDCl_3$) δ –63.51 (t, J = 11.0 Hz, 1.5F), –63.52 (t, J = 11.0 Hz, 1.5F) **IR** (neat) ν 224,1672, 1367, 1281, 1254, 1154, 1150, 1113, 1052 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{11}H_{15}F_3O$ $[M+Na]^+$ 243.0960, found 243.0967.

(1*R*)-(6-methoxyquinolin-4-yl)((1S,4S,5R)-5-(3,3,3-trifluoropropyl)quinuclidin-2-yl)methanol (2q)



Qunine (81.1 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.7 mg, 0.30 mmol) and MeOH (0.5 mL) were placed in a vial which was equipped with a magnetic stir bar. The vial was exposed to a 14 W fluorescent light bulb at room temperature while stirring for 24 hrs. The reaction mixture was quenched with sat. aq. $NaHCO_3$, and the aqueous phase was extracted with AcOEt (× 2). The combined organic phases were washed with water and brine, then dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by preparative TLC on 18C (AcOEt / MeOH = 9:1) gave **2q** (56.4 mg, 57% yield) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.40–1.54 (m, 4H), 1.65 (br. s, 1H), 1.80–1.82 (m, 1H), 1.87–2.04 (m, 4H), 2.40 (br. d, J = 13.6 Hz, 1H), 2.69–2.75 (m, 1H), 3.11–3.19 (m, 2H), 3.69 (br. s, 1H), 3.81 (s, 3H), 5.73 (br.s, 1H), 7.14 (d, J = 2.6 Hz, 1H), 7.24 (dd, J_1 = 2.6 Hz, J_2 = 9.2 Hz, 1H), 7.52 (d, J = 4.8 Hz, 1H), 7.90 (d, J = 9.2 Hz, 1H), 8.62 (d, J = 4.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 20.36, 25.40, 26.48 (q, J = 1.9 Hz), 27.17, 31.74 (q, J = 29.4 Hz), 34.22, 43.15, 55.83, 57.56, 59.78, 70.40, 100.93, 118.47, 121.58, 126.25 (q, J = 274.8 Hz), 130.13, 144.05, 146.74, 147.35, 157.86; **^{19}F NMR** (236 MHz, $CDCl_3$) δ –66.73 (t, J = 10.8 Hz, 3F), **IR** (neat) ν 2970, 1739, 1434, 1365 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{21}H_{26}F_3N_2O_2$ $[M+H]^+$ 395.1946, found 395.1941. $[\alpha]_D^{20}$ = –96.9 (c = 0.80, MeOH).

CF_3-VitaminD_3 (2r)

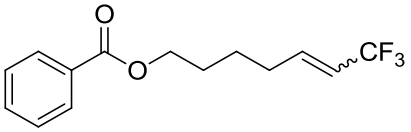


Prepared following general procedure using VitaminD_3 (96.2 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.7 mg, 0.30 mmol) and MeOH (0.5 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:30) provided **2r** (44.2 mg, 39% yield) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.88 (s, 3H), 0.95 (d, J = 6.6 Hz, 3H), 1.04–1.20 (m, 6H), 1.37–1.40 (m, 3H), 1.51–1.56 (m, 2H), 1.65–1.69 (m, 4H), 1.87–1.91 (m, 2H), 1.93–2.07 (m, 4H), 2.13–2.17 (m, 2H), 2.25–2.29 (m, 1H), 2.50 (dd, J_1 = 4.0 Hz, J_2 = 16.7 Hz, 1H), 2.77 (dq, J_1 = 11.4 Hz, J_2 = 14.5 Hz, 1H), 2.87 (dq, J_1 = 11.4 Hz, J_2 = 14.5 Hz, 1H), 3.91–3.98 (m, 1H), 5.80 (d, J = 12.4 Hz, 1H), 5.97 (d, J

= 12.4 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 18.12, 18.93, 19.38, 22.55, 22.79, 23.71, 26.44, 26.97, 27.01, 27.76, 28.01, 30.90, 34.68, 35.86, 36.90, 37.53 (q, *J* = 28.4 Hz), 38.29, 39.51, 43.52, 56.12, 66.66, 122.24 (q, *J* = 1.9 Hz), 125.10, 126.50 (q, *J* = 277.7 Hz), 127.10, 131.53, 134.78, 148.84; **^{19}F NMR** (236 MHz, $CDCl_3$) *δ* –63.31 (t, *J* = 11.3 Hz, 3F), **IR** (neat) ν 3500, 2953, 1717, 1465, 1367, 1256, 1130, 909. 733 cm^{-1}; **HRMS** (ESI) *m/z* Calcd for $C_{28}H_{43}F_3O$ $[M+Na]^+$ 475.3150 found 475.3158; $[\alpha]_D^{20}$ =28.1 (c = 0.42, MeOH).

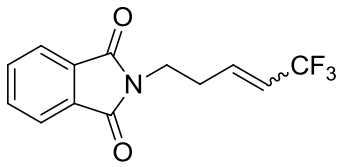
7,7,7-Trifluorohept-5-en-1-yl benzoate (3a)



Prepared following general procedure using 6-benzoyloxy-1-hexyne (50.6 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (18.7 mg, 0.025 mmol), Umemoto reagent (181.0 mg, 0.50 mmol) and MeOH (1 mL). Purification by column chromatography on silica gel (1:99 Et_2O/PET 30/40) provided **3a** (46 mg, 68 % yield) as a colorless oil, in a 3:1 *E*:*Z* ratio.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50–1.66 (m, 2H, *E*, *Z*), 1.69-1.88 (m, 2H, *E*, *Z*), 2.13–2.23 (m, 2H, *E*), 2.28–2.35 (m, 2H, *Z*), 4.25–4.31 (m, 2H, *E*, *Z*), 5.52–5.62 (m, 2H, *E*, *Z*), 5.92 (dt, *J* = 11.5 Hz, 8.0 Hz, 1H, *Z*), 6.31 (dtq, *J* = 16.0 Hz, 7.0 Hz, 2.0 Hz, 1H, *E*), 7.31–7.39 (m, 2H, *E*, *Z*), 7.47–7.50 (m, 1H, *E*, *Z*), 7.96-8.08 (m, 2H, *E*, *Z*); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 24.6 (*E*), 25.4 (*Z*), 28.0 (*Z*), 28.2 (*E*), 28.2 (*Z*), 31.0 (*E*), 64.5 (*E*), 64.5 (*Z*), 118.9 (q, *J* = 33.5 Hz, *E*, *Z*), 123.0 (q, *J* = 267.0 Hz, *E*, *Z*), 128.4 (*E*, *Z*), 129.5 (*E*, *Z*), 130.3 (*E*, *Z*), 132.9 (*Z*), 133.0 (*E*), 140.0 (q, *J* = 6.5 Hz, *E*), 142.3 (q, *J* = 5.5 Hz, *Z*), 166.6 (*E*, *Z*); **^{19}F NMR** (376.5 MHz, CD_3Cl) δ -58.06 (dt, J = 8.0 Hz, 2.0 Hz, *Z*), –63.98 (dq, *J* = 5.5 Hz, 2.0 Hz, *E*); **IR** (neat) ν 1717, 1270, 1113, 711 cm^{-1}; **HRMS** (ESI-TOF) calc. for $C_{14}H_{15}F_3NaO_2$ $[M+Na]^+$ 295.0916, found 295.0911.

2-(5,5,5-Trifluoropent-3-en-1-yl)-1*H*-isoindole-1,3(2*H*)-dione (3b)



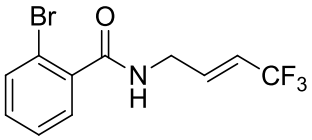
Prepared following general procedure using *N*-(3-butynyl)phthalimide (49.8 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (18.7 mg, 0.025 mmol), Umemoto reagent (181.0 mg, 0.50 mmol) and MeOH (1 mL). Purification by column chromatography on silica gel (1:3 DCM/Hexane) provided **3b** (40 mg, 59 % yield) as a white solid, in a 3:1 *E*:*Z* ratio.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46-2.53 (m, 1H, *E*), 2.61-2.69 (m, 1H, *Z*), 3.74–3.78 (m, 2H, *E*, *Z*), 5.56–5.67 (m, 1H, *E*, *Z*), 5.98 (dt, J = 11.5 Hz, 8.0 Hz, 1H, *Z*), 6.31 (dtq, J = 16.0 Hz, 7.0 Hz, 2.0 Hz, 1H, *E*), 7.63–7.68 (m, 2H, *E*, *Z*), 7.76–7.81 (m, 2H, *E*, *Z*); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 30.6 (*E*, *Z*), 36.2 (*E*), 36. 6 (*Z*), 121.0 (q, *J* = 33.5 Hz, *Z*), 121.1 (q, *J* = 33.5 Hz, *E*), 123.3 (*Z*), 123.4 (*E*), 131.9 (*Z*), 131.9 (*E*), 136.3 (q, *J* = 6.5 Hz, *E*), 138.4 (q, *J* = 6.0 Hz, *Z*), 168.1 (*E*, *Z*); CF_3 carbon was not detected.

^{19}F NMR (376.5 MHz, CD_3Cl) δ –58.25 (dt, *J* = 8.0 Hz, 2.0 Hz, *Z*), –64.46 (dq, *J* = 4.5 Hz, 2.0 Hz, *E*); **IR** (neat) ν

1774, 1707, 1395, 1115, 719 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{13}H_{10}NO_2F_3$ $[M]^+$ 269.0664, found 269.0657.

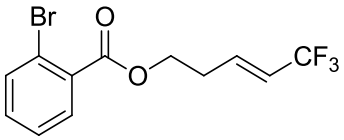
2-Bromo-*N*-[(2*E*)-4,4,4-trifluorobut-2-en-1-yl]benzamide (3c)



Prepared following general procedure using 2-bromo-*N*-(prop-2-yn-1-yl)benzamide (59.5 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (18.7 mg, 0.025 mmol), Umemoto reagent (181.0 mg, 0.50 mmol) and MeOH (1 mL). Purification by column chromatography on silica gel (1:9 EtOAc/PET 30/40) provided **3c** (E/Z = 9: 1, 43 mg, 56 % yield) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10-4.17 (m, 2H), 5.83 (dqt, *J* = 16.0 Hz, 6.5 Hz, 2.0 Hz, 1H), 6.28 (brs, 1H, N*H*), 6.40 (dqt, *J* = 16.0 Hz, 5.0 Hz, 2.0 Hz, 1H), 7.22 (dt, *J* = 8.0 Hz, 2.0 Hz, 1H), 7.30 (dt, *J* = 7.5 Hz, 1.0 Hz, 1H), 7.46 (dd, *J* = 7.5 Hz, 2.0 Hz, 1H), 7.52 (dd, *J* = 8.0 Hz, 1.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 40.0, 119.1, 119.8 (q, *J* = 34.0 Hz), 122.8 (q, *J* = 269.0 Hz), 127.7, 129.2, 131.6, 133.5, 135.9 (q, *J* = 6.5 Hz), 137.0, 167.6; **^{19}F NMR** (377 MHz, CD_3Cl) δ –64.16 (dq, J = 9.0 Hz, 2.0 Hz); **IR** (neat) ν 1646, 1536, 1298, 1272, 1119, 961, 751 cm^{-1}; **HRMS** (CI+) *m/z* Calcd for $C_{11}H_{13}N_2OBrF_3$ $[M+NH_4]^+$ 325.0163, found 325.0160; **Mp** 69–71 °C.

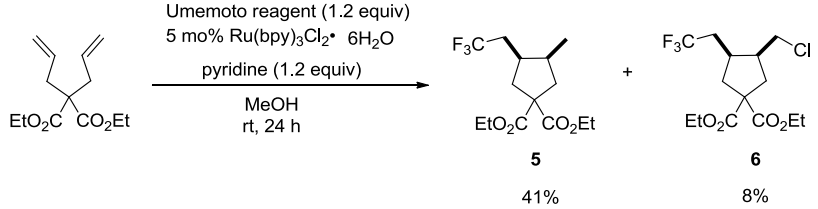
5,5,5-Trifluoropent-3-en-1-yl 2-bromobenzoate (3d)



Prepared following general procedure using but-3-yn-1-yl 2-bromobenzoate (63.3 mg, 0.25 mmol), Ru(bpy)3Cl_2•$6H_2O$ (18.7 mg, 0.025 mmol), Umemoto reagent (181.0 mg, 0.50 mmol) and MeOH (1 mL). Purification by column chromatography on silica gel (1:99 Et_2O/PET 30/40) provided the title compound (48 mg, 59 % yield) yellow oil in a 3:1 *E*:*Z* ratio. Purification by preparative TLC (5:95 Et_2O/PET 30/40) afforded the pure E-**3d** (28 mg, 35 % yield):

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54–2.61 (m, 2H), 4.38 (t, *J* = 6.5 Hz, 2H), 5.71 (dqt, *J* = 16.0 Hz, 6.5 Hz, 1.5 Hz, 1H), 6.39 (dqt, *J* = 16.0 Hz, 7.0 Hz, 2.0 Hz, 1H), 7.24–7.32 (m, 2H), 7.59 (dd, *J* = 7.5 Hz, 2.0 Hz, 1H), 7.68 (dd, *J* = 7.5 Hz, 2.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 30.8, 63.3, 121.1 (q, *J* = 34.0 Hz), 121.6, 122.7 (q, *J* = 269.0 Hz), 127.2, 131.3, 131.9, 132.7, 134.4, 136.1 (q, *J* = 6.5 Hz), 166.0; **^{19}F NMR** (376.5 MHz, CD_3Cl) δ –64.37 (dq, *J* = 5.5 Hz, 2.0 Hz); **IR** (neat) ν 1733, 1290, 1250, 1118, 745 cm^{-1}; **HRMS** (CI+) *m/z* Calcd for $C_{12}H_{10}BrF_3O_2$ $[M+H]^+$ 322.9895, found 322.9893.

Diethyl 3-methyl-4-(2,2,2-trifluoroethyl)cyclopentane-1,1-dicarboxylate (5) and diethyl 3-(chloromethyl)-4-(2,2,2-trifluoroethyl)cyclopentane-1,1-dicarboxylate (6)

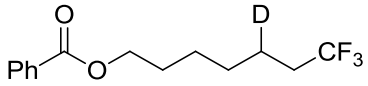


Prepared following general procedure using diethyl 2,2-diallylmalonate (60.1 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.7 mg, 0.30 mmol) pyridine (15.2 μL, 0.30 mmol) and MeOH (0.5 mL). Purification by column chromatography on silica gel (AcOEt /*n*-hexane = 1:20) provided **5** (31.6 mg, 41 % yield, ratio = 13:1) as a colorless oil and **6** (8.0 mg, 8% yield) as a colorless oil.

Characterization data for the *major* isomer of **5** (*major/minor* = 13:1): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 0.91 (d, *J* = 7.0 Hz, 3H), 1.29 (t, *J* = 7.3 Hz, 3H), 1.29 (t, *J* = 7.3 Hz, 3H), 2.06–2.26 (m, 4H), 2.39–2.40 (m, 2H), 2.48–2.54 (m, 2H), 4.23 (q, *J* = 7.3 Hz, 2H), 4.24 (q, *J* = 7.3 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 13.97, 14.86, 34.9 (q, *J* = 28.4 Hz), 35.90, 36.46 (q, *J* = 1.9 Hz), 37.91, 41.14, 58.62, 61.53, 61.55, 127.12 (q, *J* = 274.8 Hz) 172.54, 172.52; **^{19}F NMR** (377 MHz, $CDCl_3$) *δ* –64.63 (t, *J* = 10.4 Hz, 3F), **IR** (neat) ν 2980, 1728, 1249, 1183, 1152, 1117, 856 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{14}H_{21}F_3O_4$ $[M+Na]^+$ 333.1286 found 333.1284.

Characterization data for **6**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.18 (t, *J* =7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.96–2.26 (m, 4H), 2.42–2.51 (m, 4H), 3.37 (dd, J_1 = 7.1 Hz, J_2 = 11.0 Hz, 1H), 3.44 (dd, J_1 = 6.4 Hz, J_2 = 11.0 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 4H); **^{19}F NMR** (377 MHz, $CDCl_3$) *δ* –64.42 (t, *J* = 10.4 Hz, 3F); **HRMS** (ESI) *m/z* Calcd for $C_{14}H_{20}ClF_3O_4$ $[M+Na]^+$ 344.1002 found 344.1008.

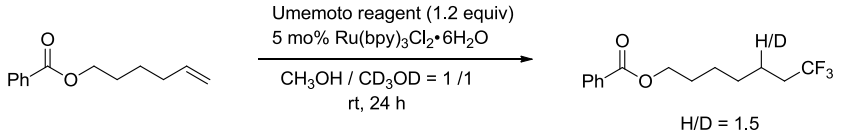
5-deuterio-7,7,7-trifluoroheptyl benzoate [D]-**2a**



A) Prepared following general procedure using hex-5-en-1-yl benzoate (51.1 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.9 mg, 0.30 mmol) and CD_3OD (0.5 mL). Purification by column chromatography on silica gel (Et_2O /*n*-hexane = 1:20) provided the title compound (17.7 mg, 26% yield) as a colorless oil. **^{1}H NMR** (40 MHz, $CDCl_3$) δ 1.42–1.52 (m, 4H), 1.56–1.61 (m, 1H), 1.80 (pent. *J* = 6.6 Hz, 2H), 2.08 (dq, J_1 = 7.8 Hz, J_2= 11.0 Hz, 2H), 4.33 (t, *J* = 6.6 Hz, 2H), 7.46 (t, *J* = 7. 8 Hz, 2H), 7.57 (tt, J_1 = 1.4 Hz, J_2 = 7.4 Hz, 1H), 8.05 (dd, J_1 = 1.4 Hz, J_2 = 8.6 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 21.45 (tq, J_1 = 2.8 Hz, J_2 = 19.0 Hz), 25.69, 28.26, 28.48, 33.55 (q, *J* = 27.9 Hz), 64.78, 127.18 (q, *J* = 273.9 Hz), 128.35, 129.51, 130.61, 132.87, 166.64; **^{19}F NMR** (377 MHz, $CDCl_3$) *δ* –66.37 (t, *J* = 10.4 Hz, 3F), **IR** (neat) ν 2937, 1717, 1270, 1256, 1141, 1111, 710 cm^{-1}; **HRMS** (EI/FI) *m/z* Calcd for $C_{14}H_{16}DF_3O_2$ $[M]^+$ 275.1243, found 275.1240.

B) Prepared following general procedure using hex-5-en-1-yl benzoate (51.1 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.9 mg, 0.30 mmol) and CD_3OH (0.5 mL). Purification by column chromatography on silica gel (Et_2O /*n*-hexane = 1:20) provided the title compound (15.3 mg, 22% yield) as a colorless oil.

Kinetic Isotope effect



Prepared following general procedure using hex-5-en-1-yl benzoate (51.1 mg, 0.25 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (9.4 mg, 0.0125 mmol), Umemoto reagent (120.9 mg, 0.30 mmol), MeOH (0.25 mL) and CD_3OD (0.25 mL). Purification by column chromatography on silica gel (Et_2O /*n*-hexane = 1:20) provided the title compound (28.5 mg, 43% yield) as a colorless oil. The isomeric ratio was determined by ^{19}F NMR analysis (H/D = 1.5).

3. References

[1] Schleicher, K. D.; Jamison, T. F. *Org. Lett.* **2007**, *9*, 875–878.

[2] Dolman, S. J.; Schrock, R. R.; Hoveyda, A. H. *Org. Lett.* **2003**, *5*, 4899–4902.

[3] a] Katritzky, A. R.; Ignatchenko, A. V.; Lang, H. *J. Org. Chem.* **1995**, *60*, 4002–4005. [b] Padwa, A.; Austin, D. J.; Price, A. T.; David Weingarten, M. *Tetrahedron* **1996**, *52*, 3247–3260.

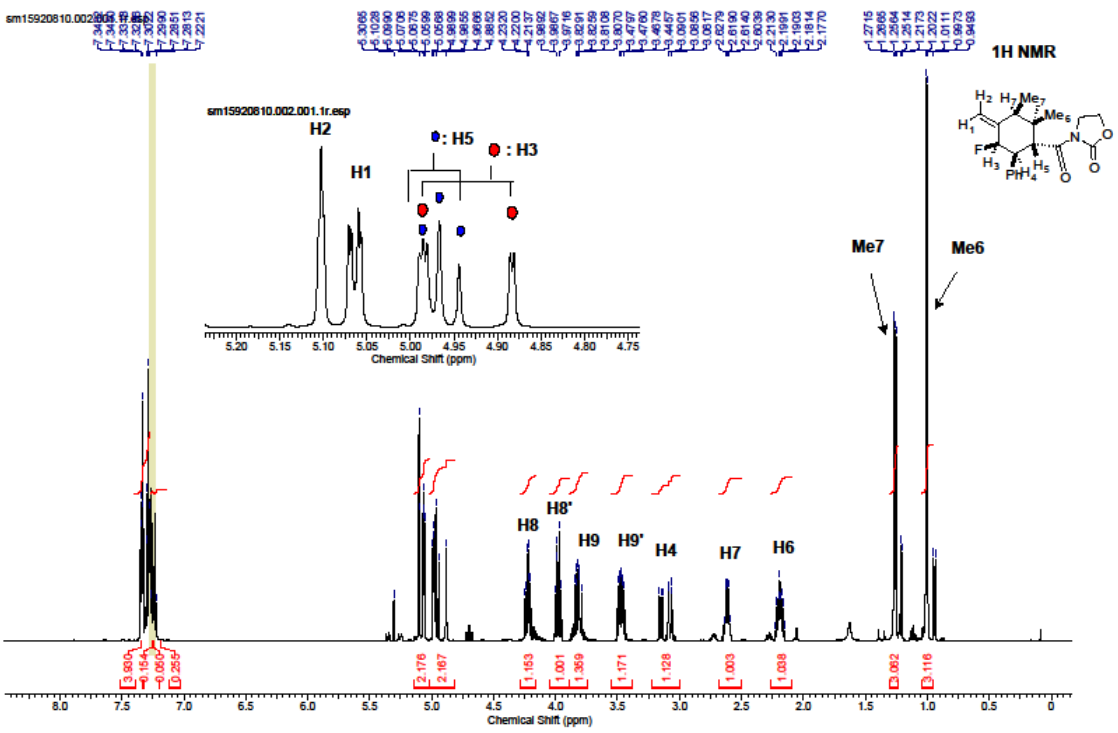
[4] Lam, Y.-H.; Bobbio, C.; Cooper, I. R.; Gouverneur, V. *Angew. Chem., Int. Ed.* **2007**, *46*, 5106–5110.

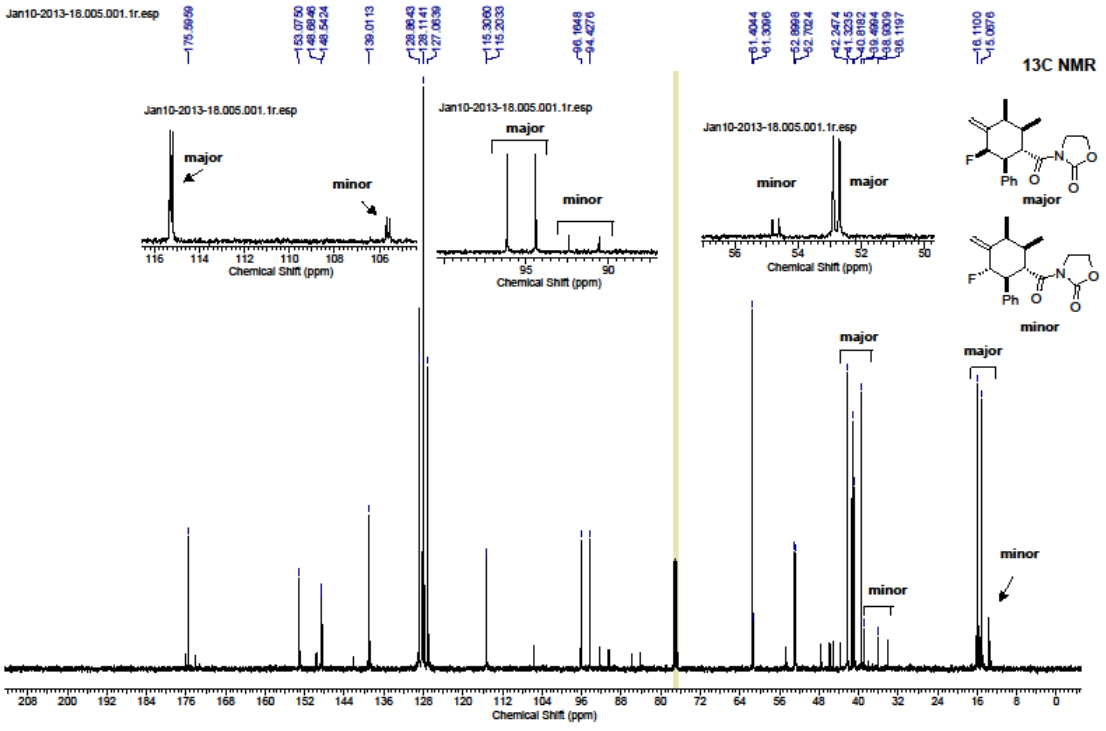
[5] Solladié-Cavallo, A.; Jierry, L.; Bouérat, L.; Schmitt, M. *Tetrahedron* **2002**, *58*, 4195-4199.

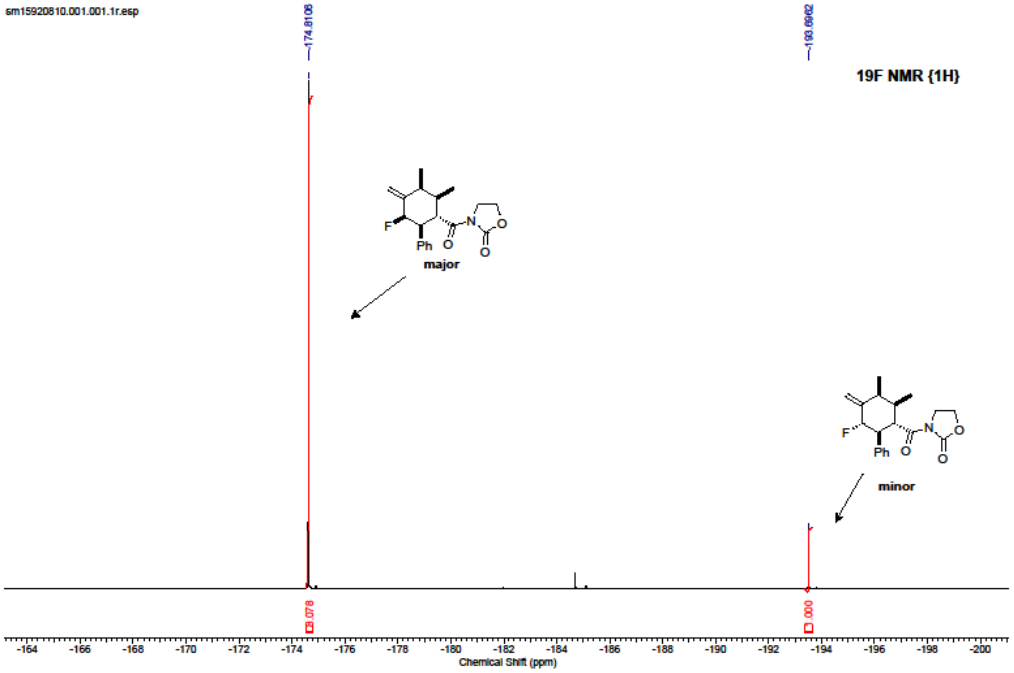
[6] Atobe, S.; Masuno, H.; Sonoda, M.; Suzuki, Y.; Shinohara, H.; Shibata, S.; Ogawa, A. *Tetrahedron Lett.* **2012**, *53*, 1764–1767.

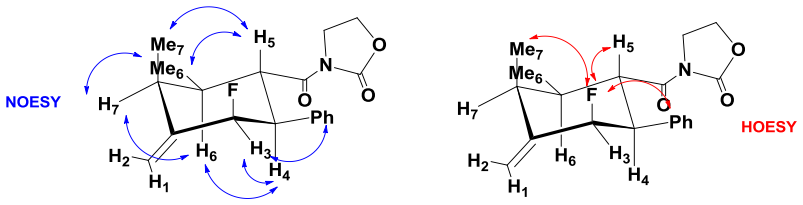
[7] Meng, X.-K.; Tungsten, S. *Org. Biomol. Chem.* **2011**, *9*, 4429–4431.

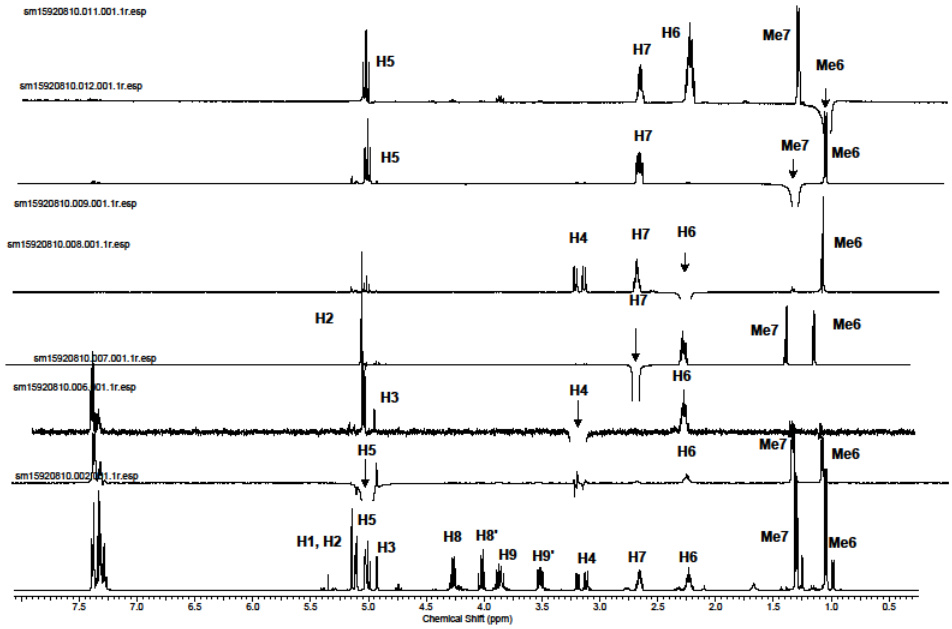
4. NMR Spectra



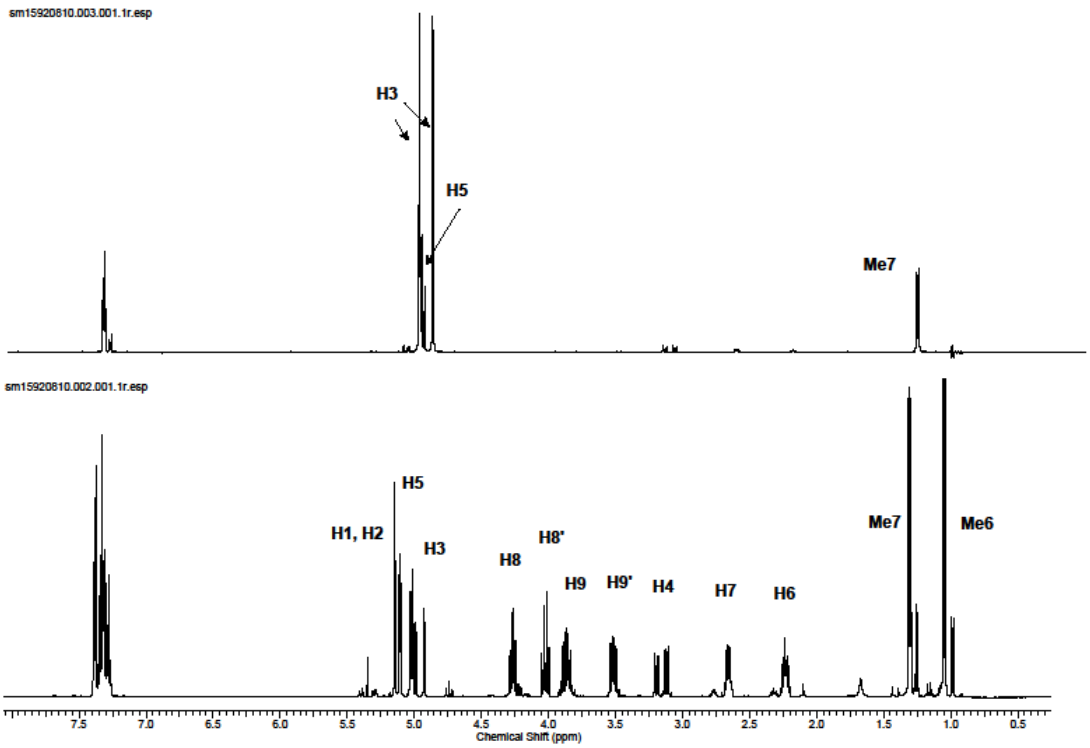




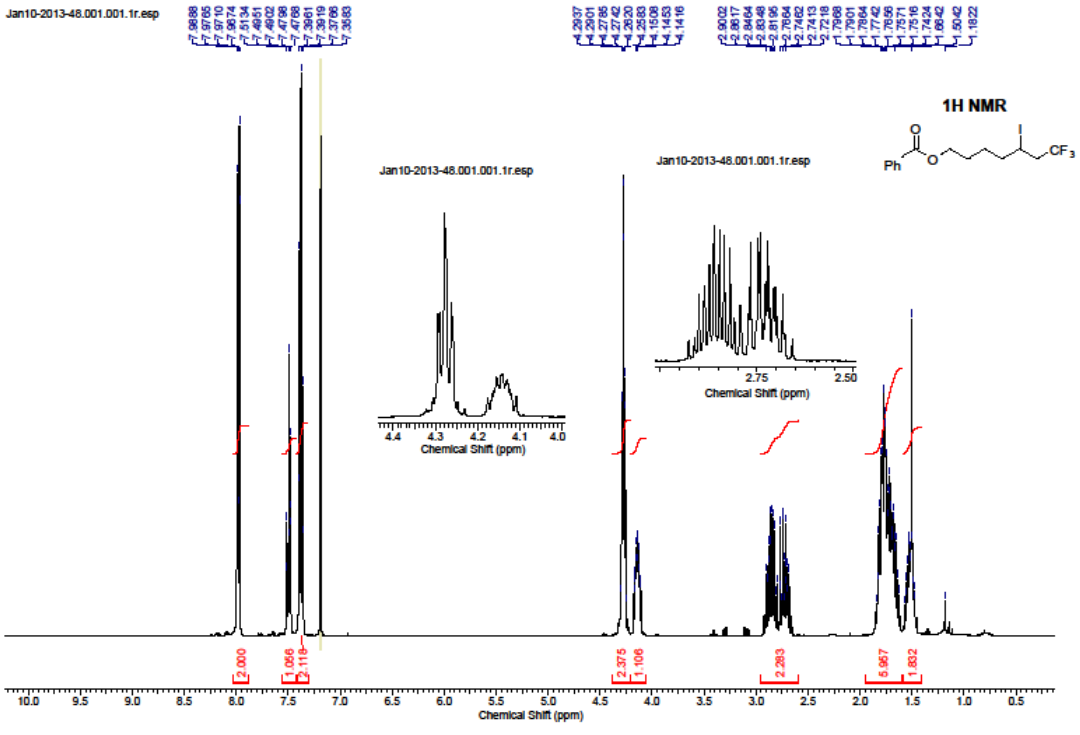


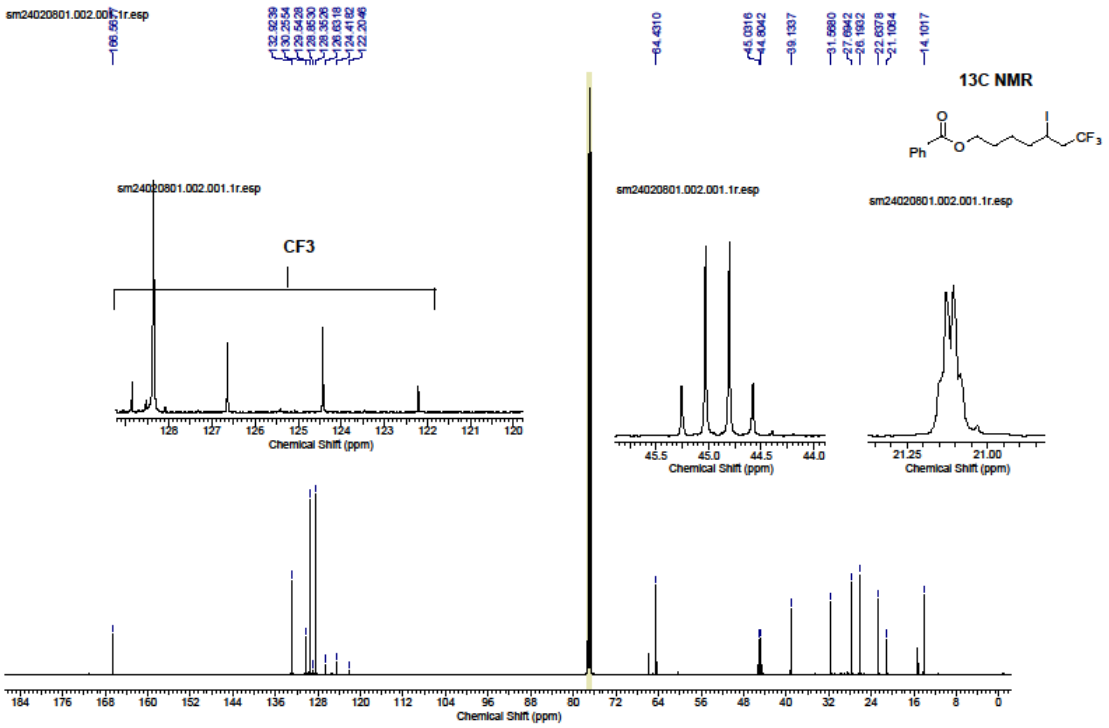


1H TFI probe gradient NOE Tmix = 800msec



19F NMR 1D 19F-1H HOESY TFI probe irradiating signal F at –174 ppm and 1H NMR spectra (bottom).

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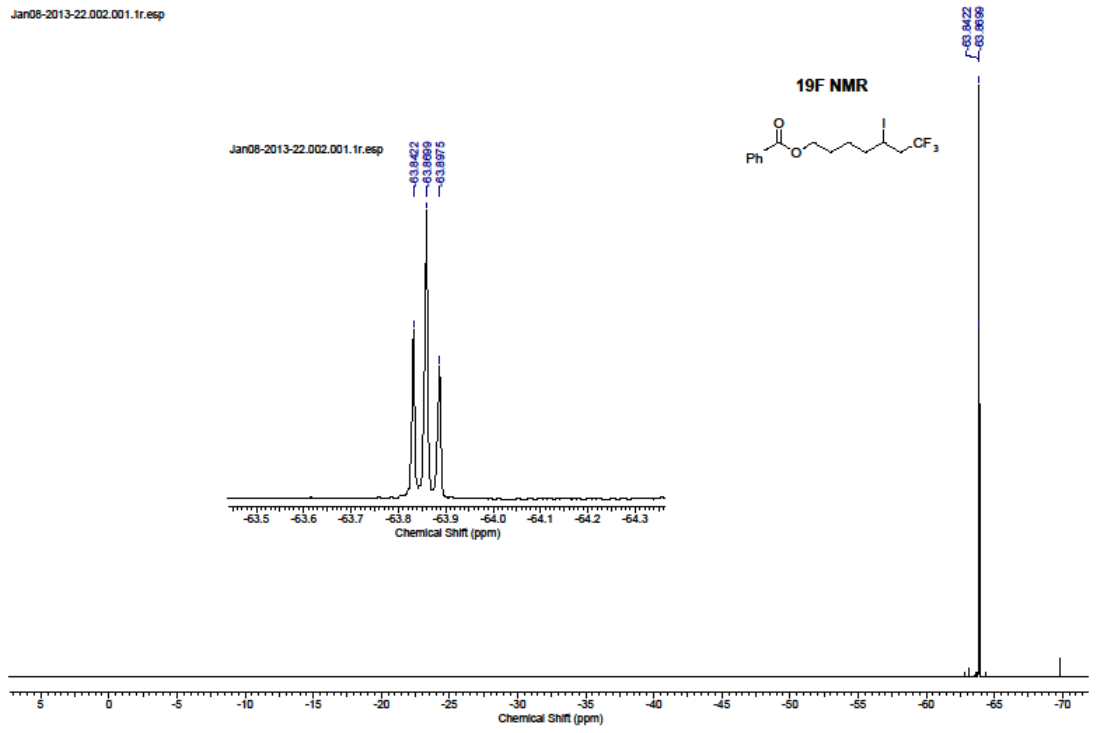
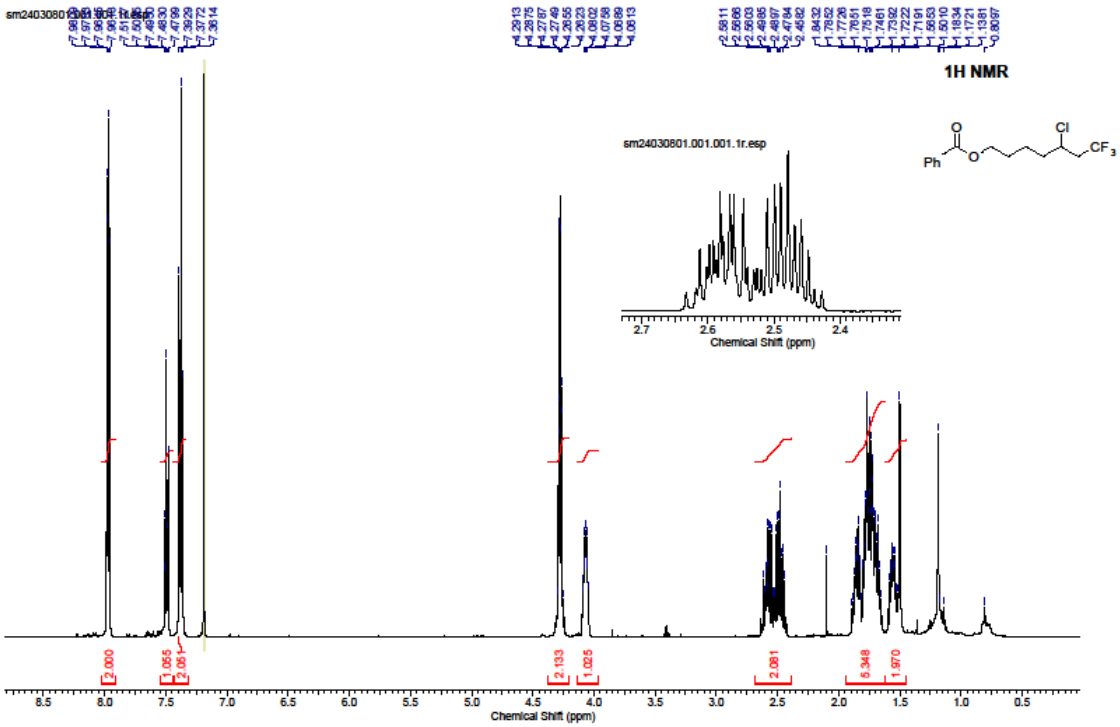
CF3
Chemical Shift (ppm)


19F NMR
Chemical Shift (ppm)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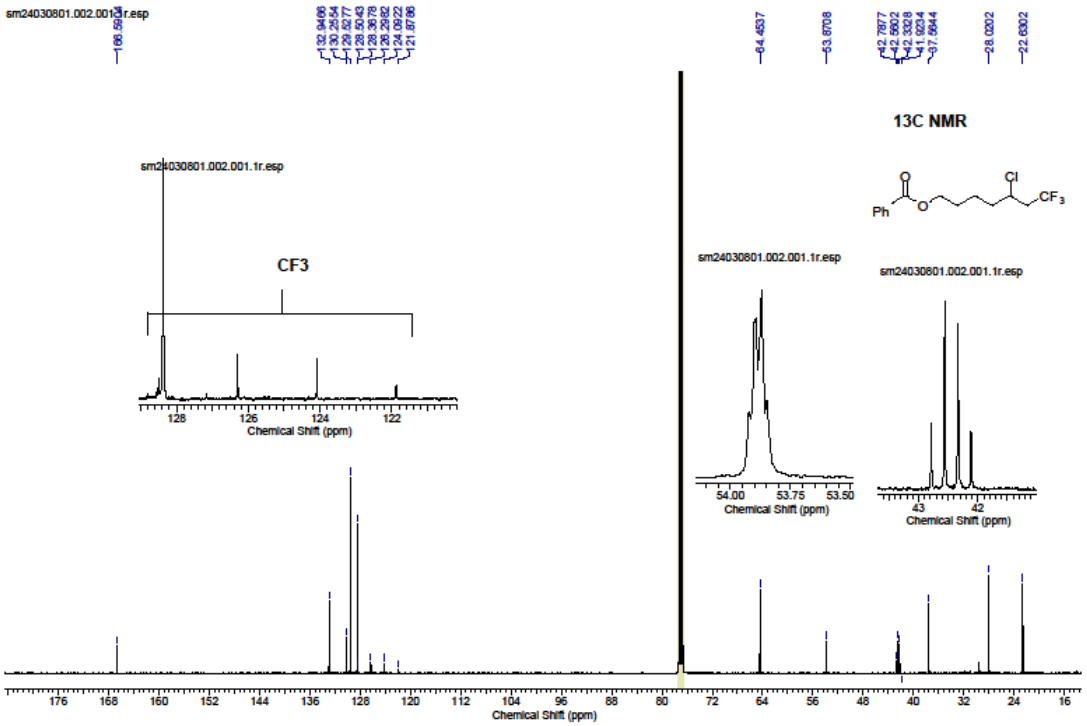
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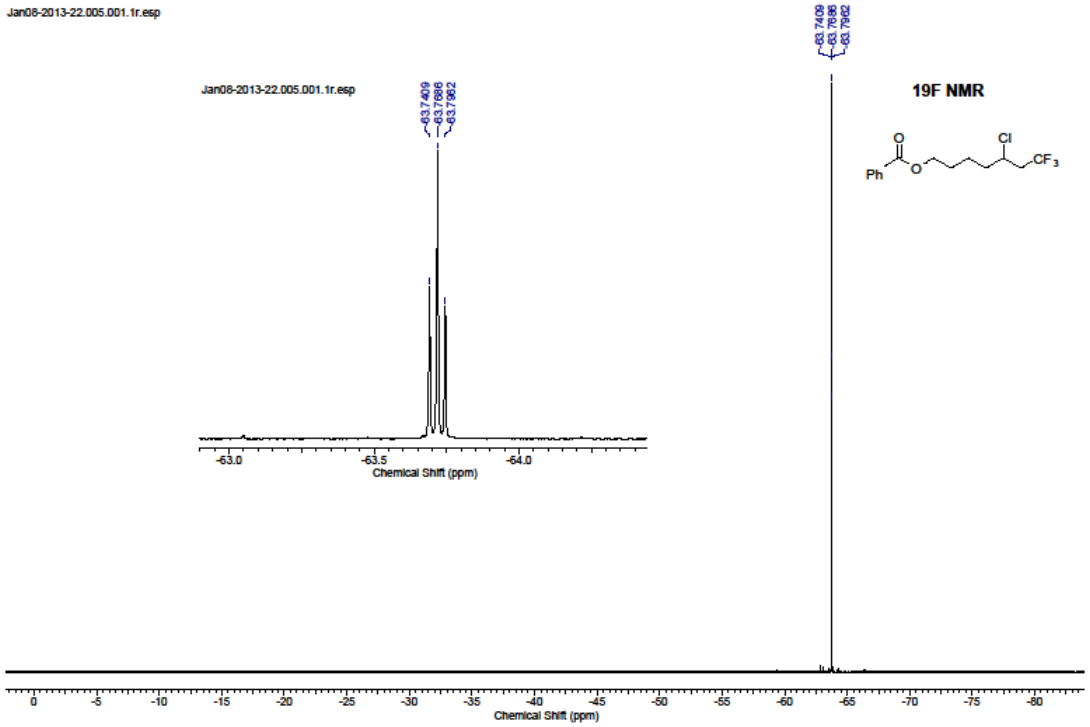
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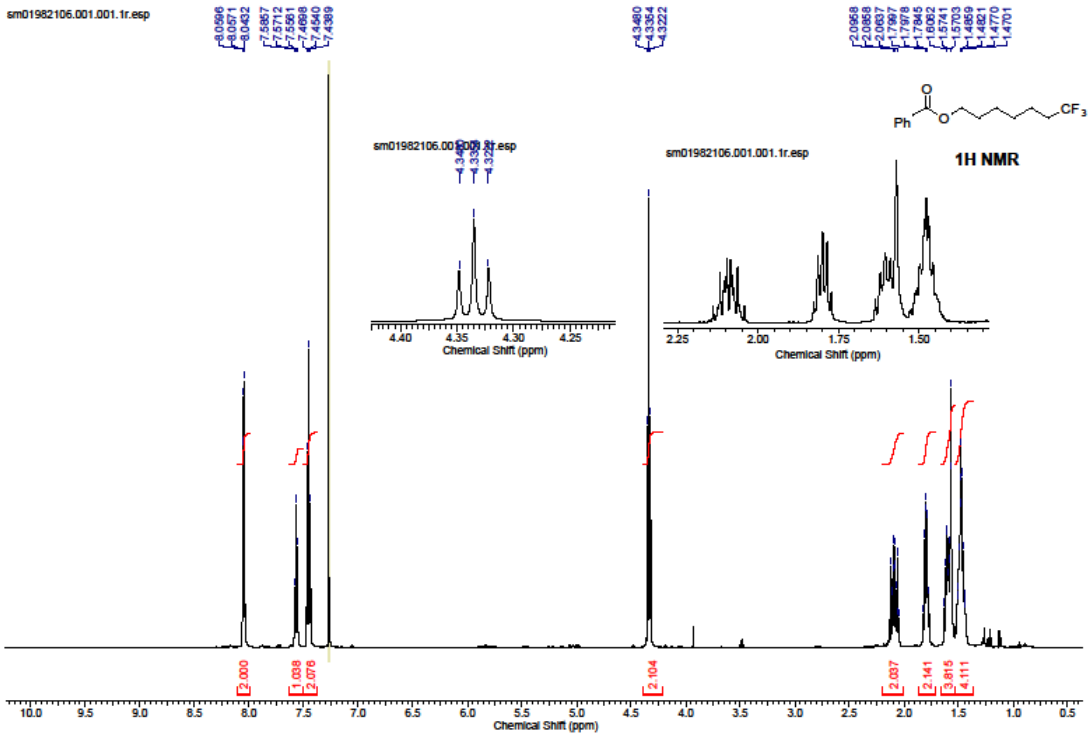
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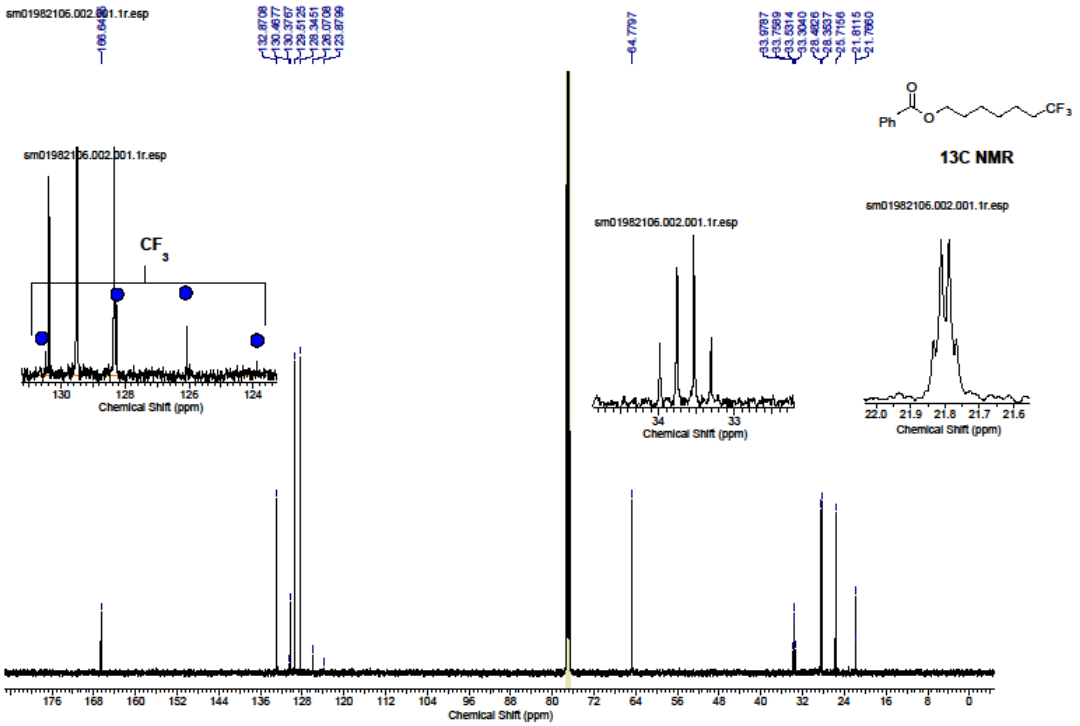
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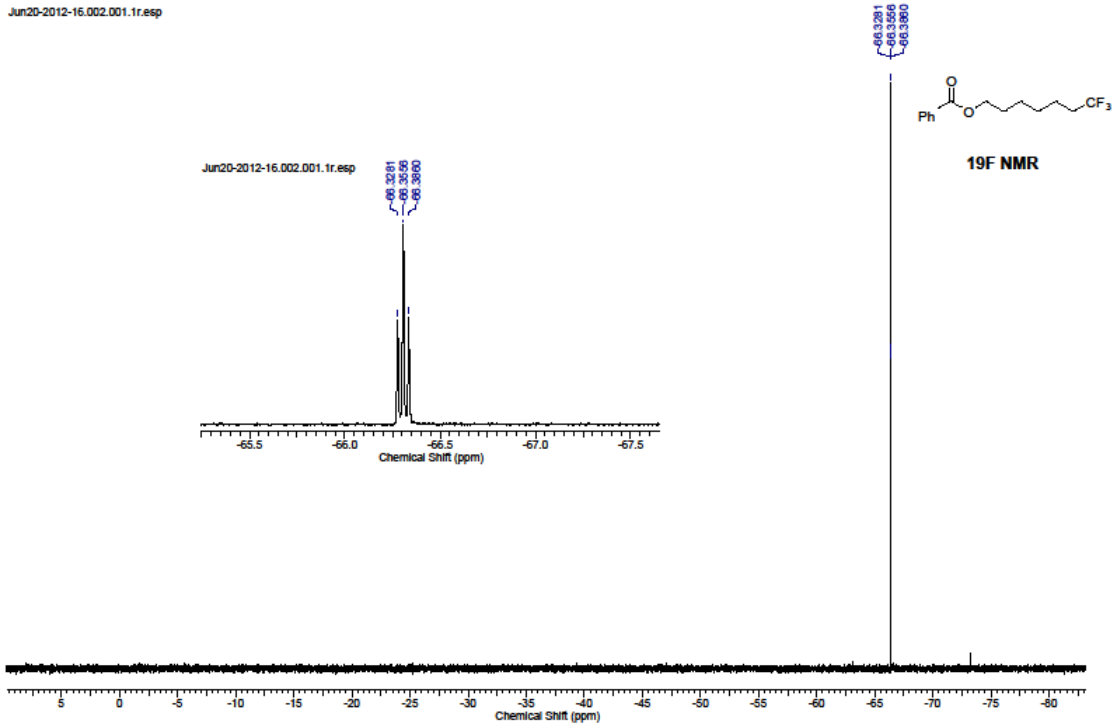
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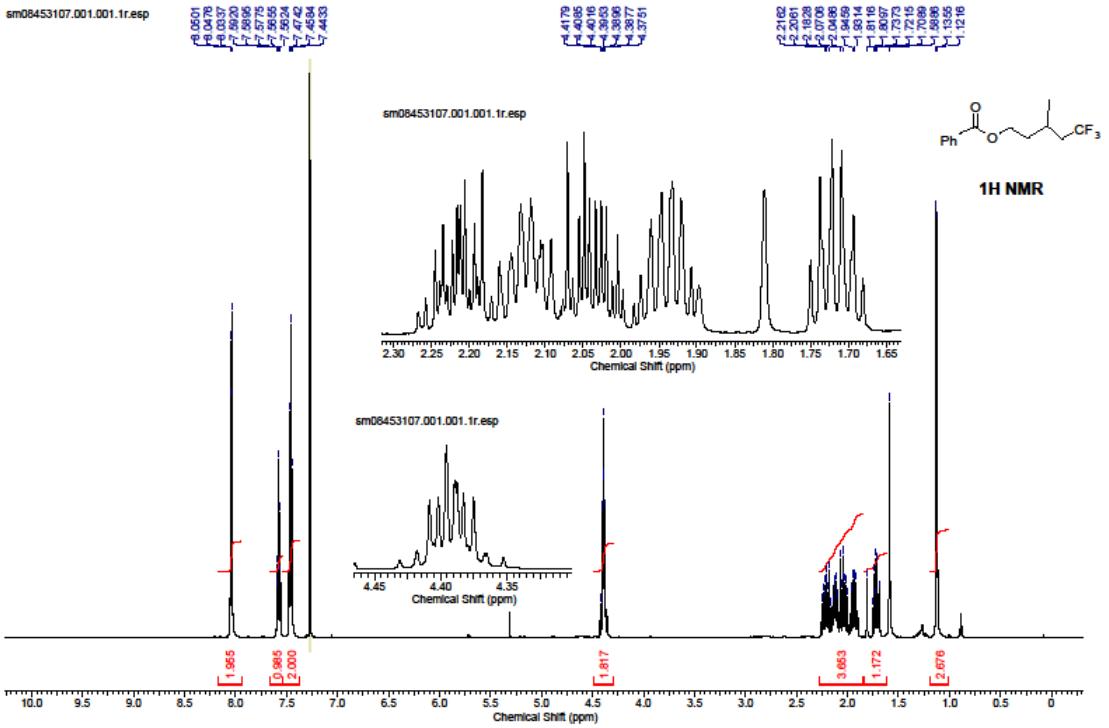
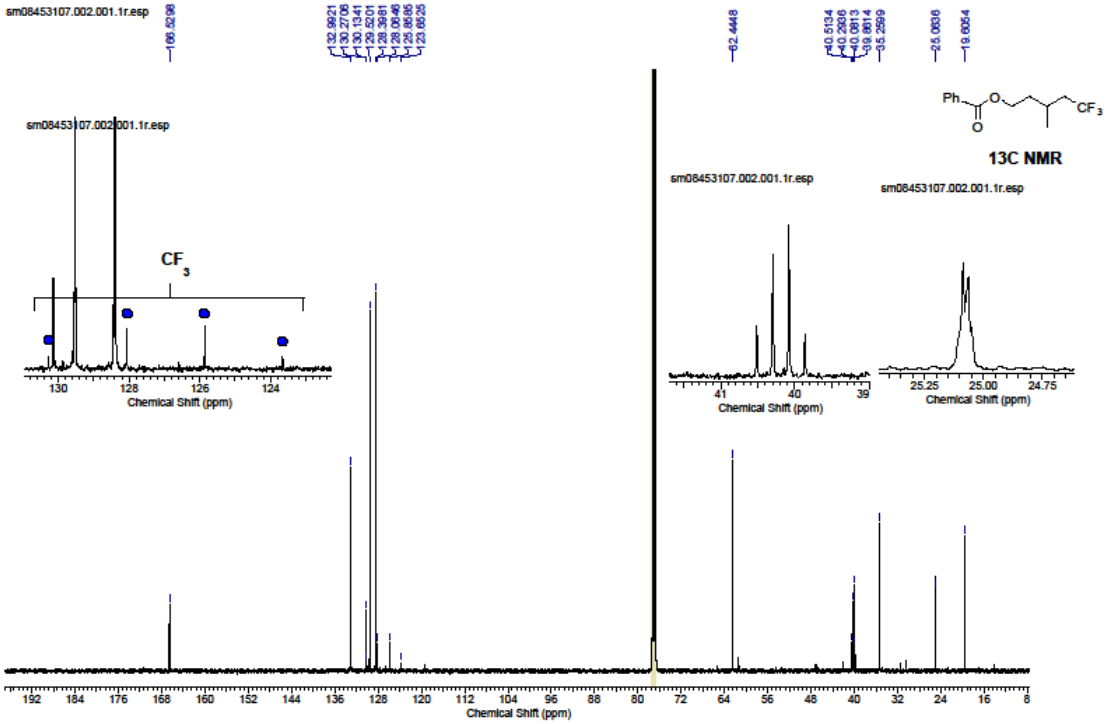
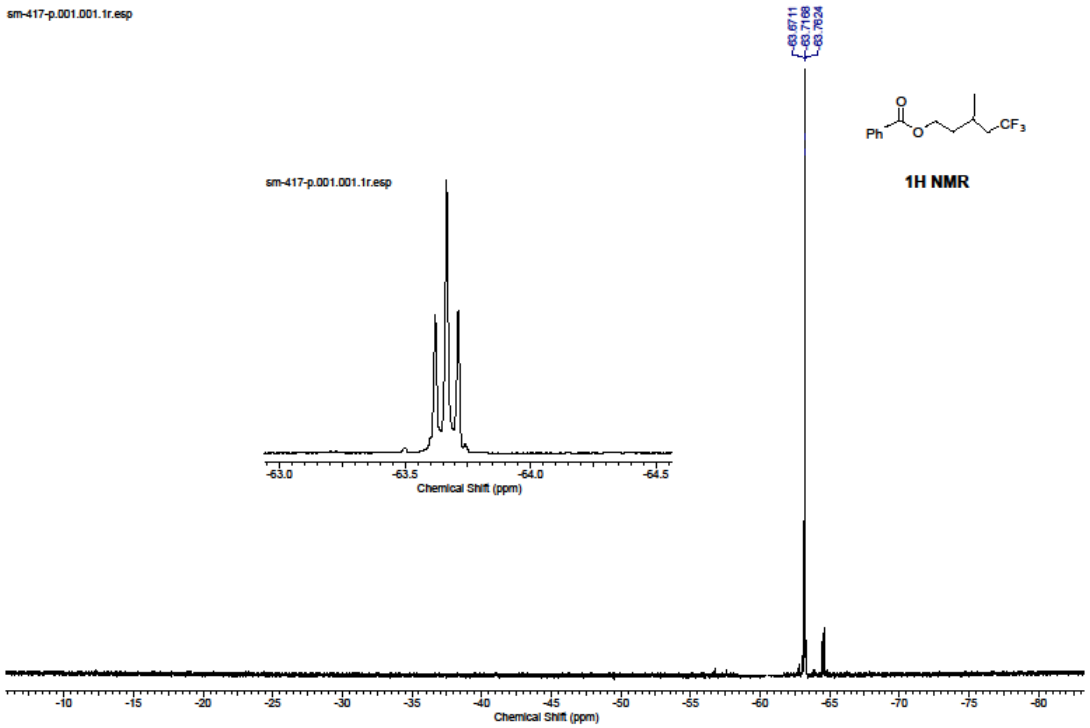
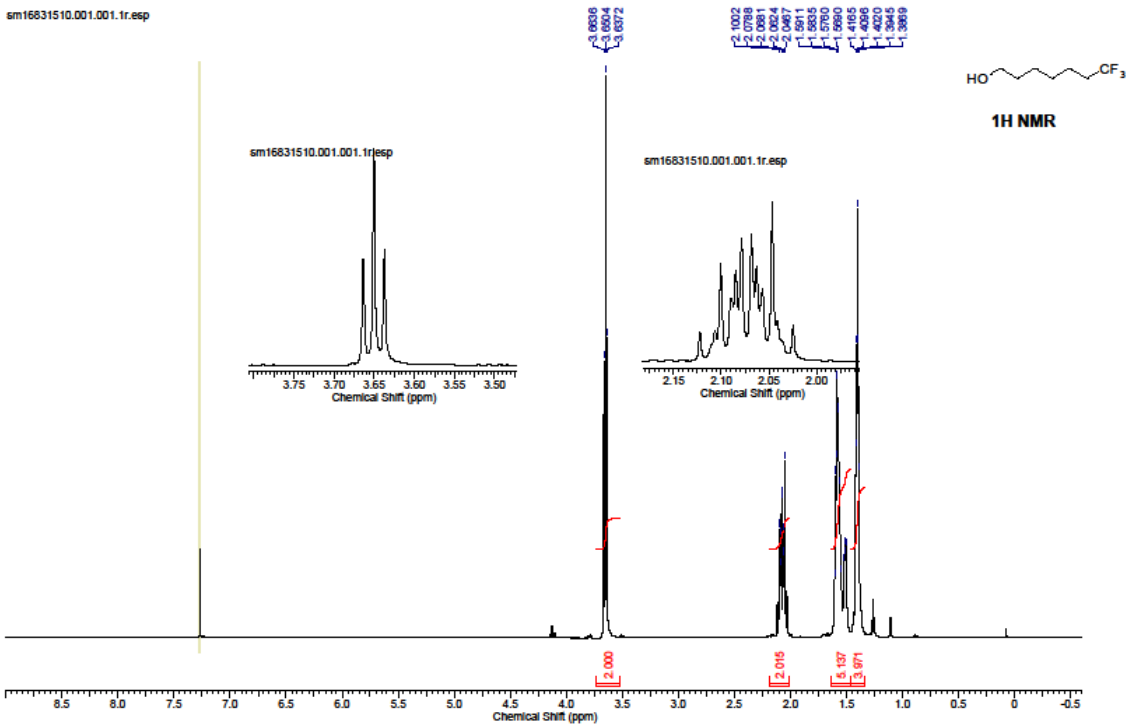
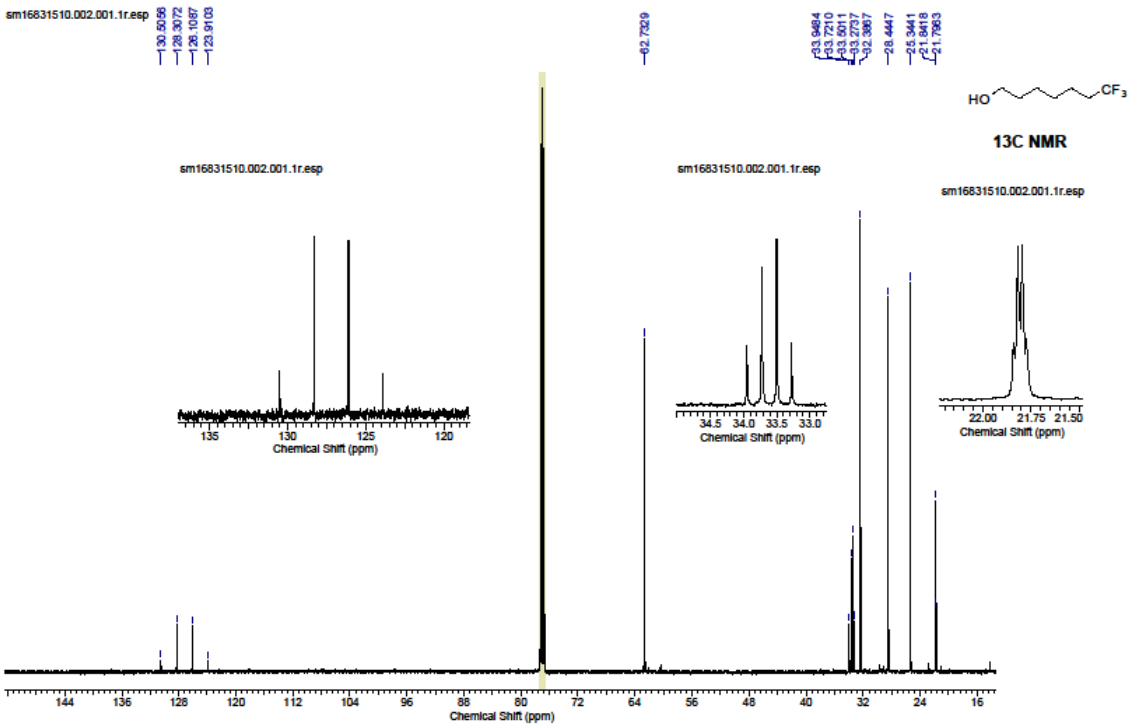
Chemical Shift (ppm)

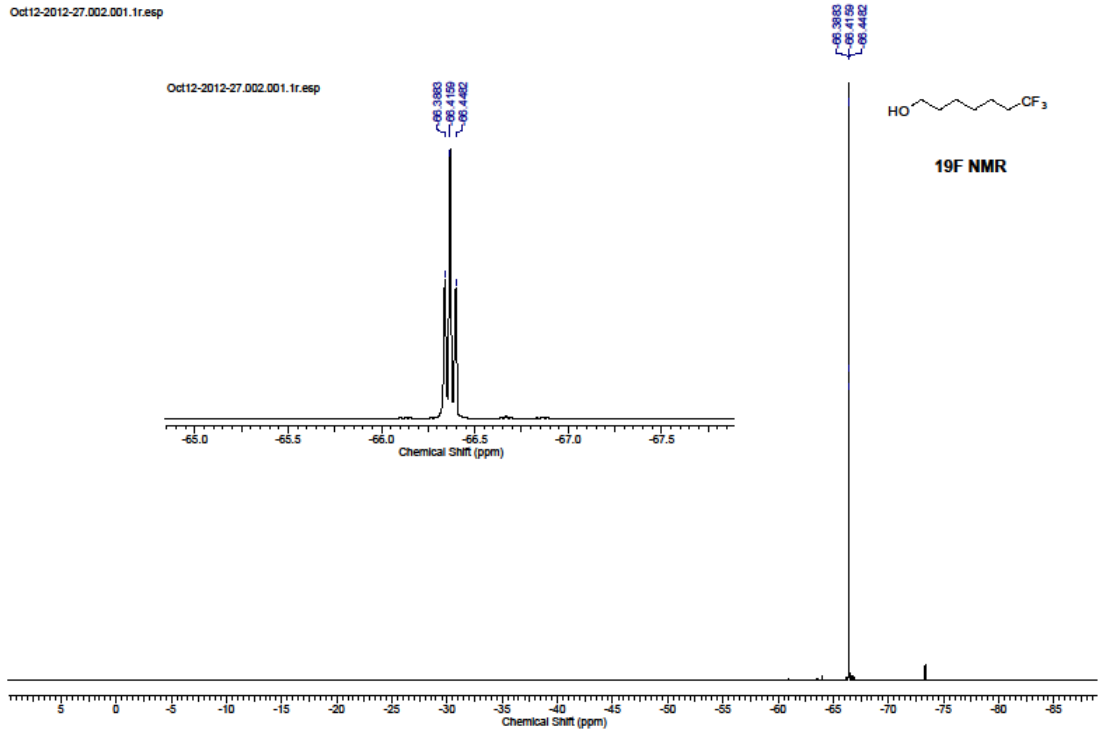

sm08453107.001.001.1r.esp
1H NMR
Chemical Shift (ppm)

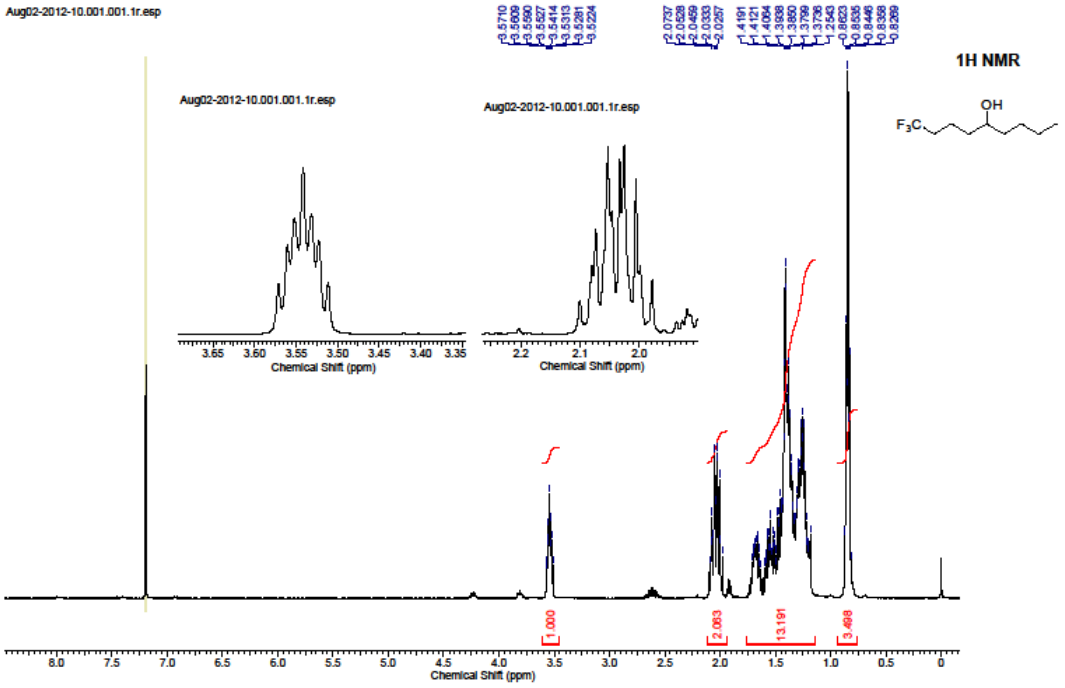

sm08453107.002.001.1r.esp
13C NMR
CF3
Chemical Shift (ppm)

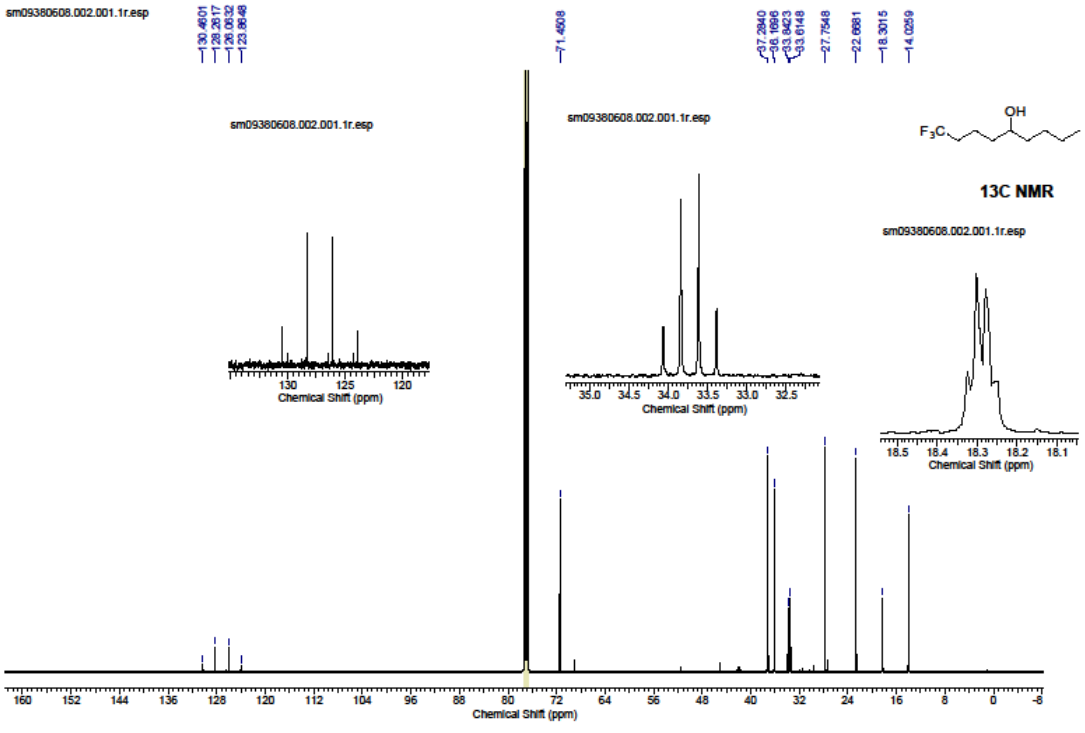

sm-417-p.001.001.1r.esp
-63.6711
-63.7168
-63.7624
Ph
O
O
CF3
1H NMR
sm-417-p.001.001.1r.esp
-63.0
-63.5
-64.0
-64.5
Chemical Shift (ppm)
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
Chemical Shift (ppm)

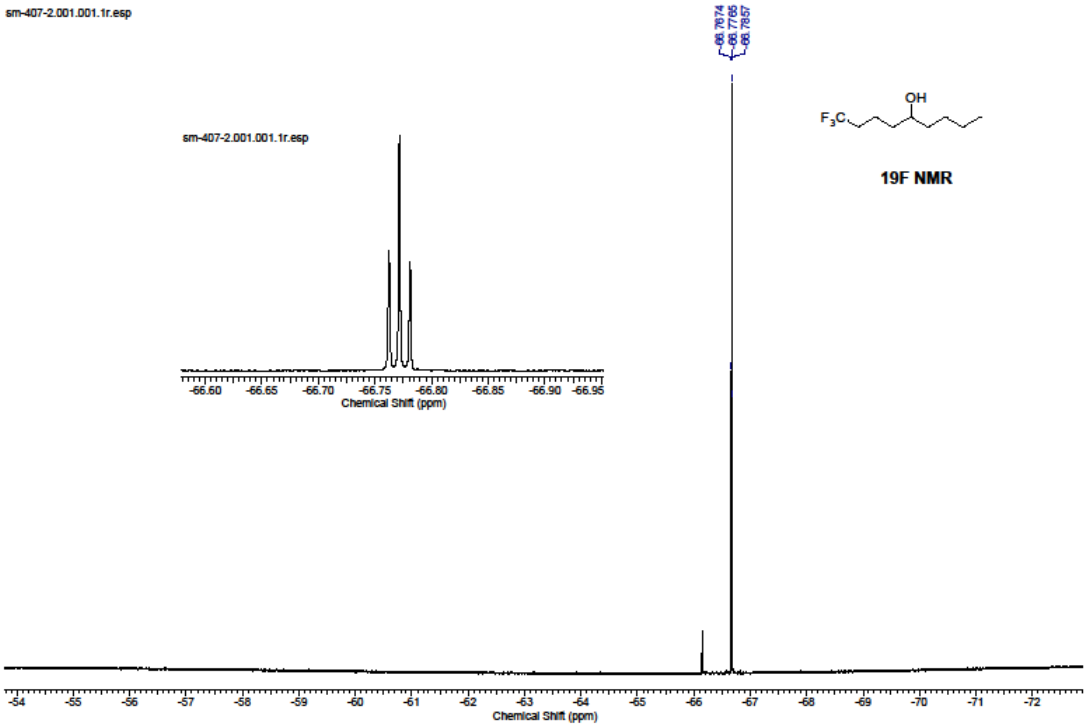

sm16831510.001.001.1r.esp
3.6836
3.6604
3.6372
2.1002
2.0786
2.0681
2.0524
2.0467
1.5911
1.5835
1.5760
1.5660
1.4165
1.4096
1.4020
1.3945
1.3869
HO
CF3
1H NMR
sm16831510.001.001.1r.esp
3.75
3.70
3.65
3.60
3.55
3.50
Chemical Shift (ppm)
sm16831510.001.001.1r.esp
2.15
2.10
2.05
2.00
Chemical Shift (ppm)
2.000
2.015
5.137
3.971
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)

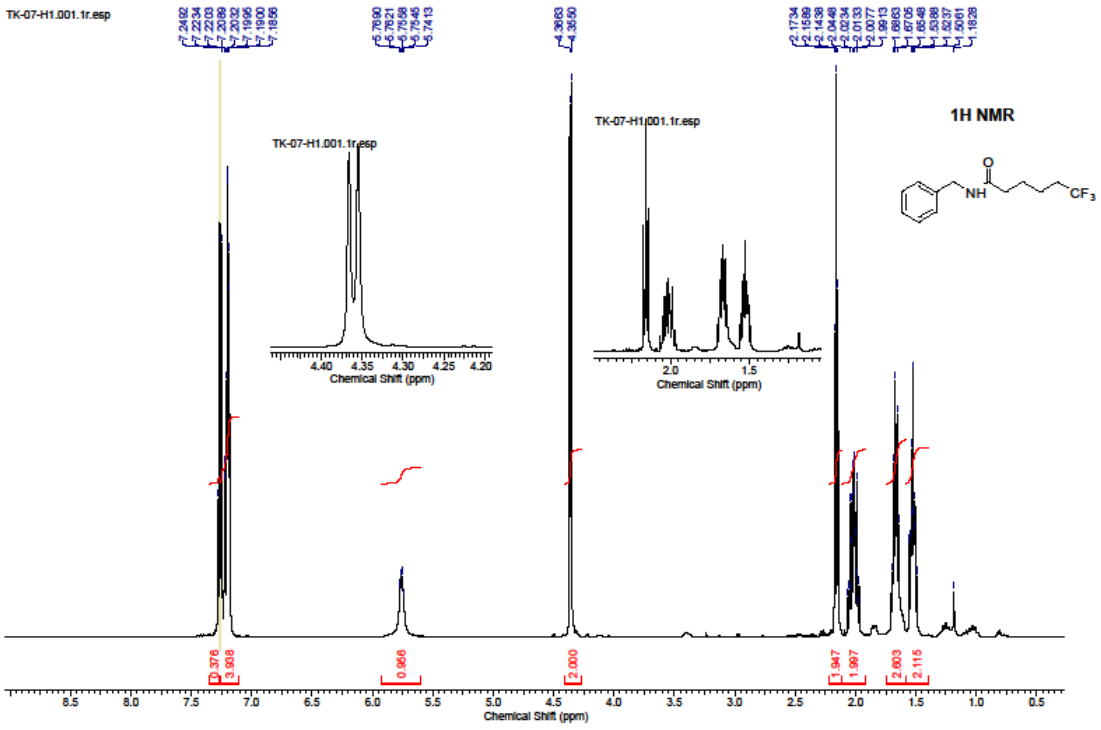

sm16831510.002.001.1r.esp
30.5096
28.3072
26.1067
23.9103
62.7329
33.9484
33.7210
33.5011
33.2737
32.3957
28.4447
25.3441
21.8418
21.7963
HO
CF3
13C NMR
sm16831510.002.001.1r.esp
135
130
125
120
Chemical Shift (ppm)
sm16831510.002.001.1r.esp
34.5
34.0
33.5
33.0
Chemical Shift (ppm)
sm16831510.002.001.1r.esp
22.00
21.75
21.50
Chemical Shift (ppm)
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

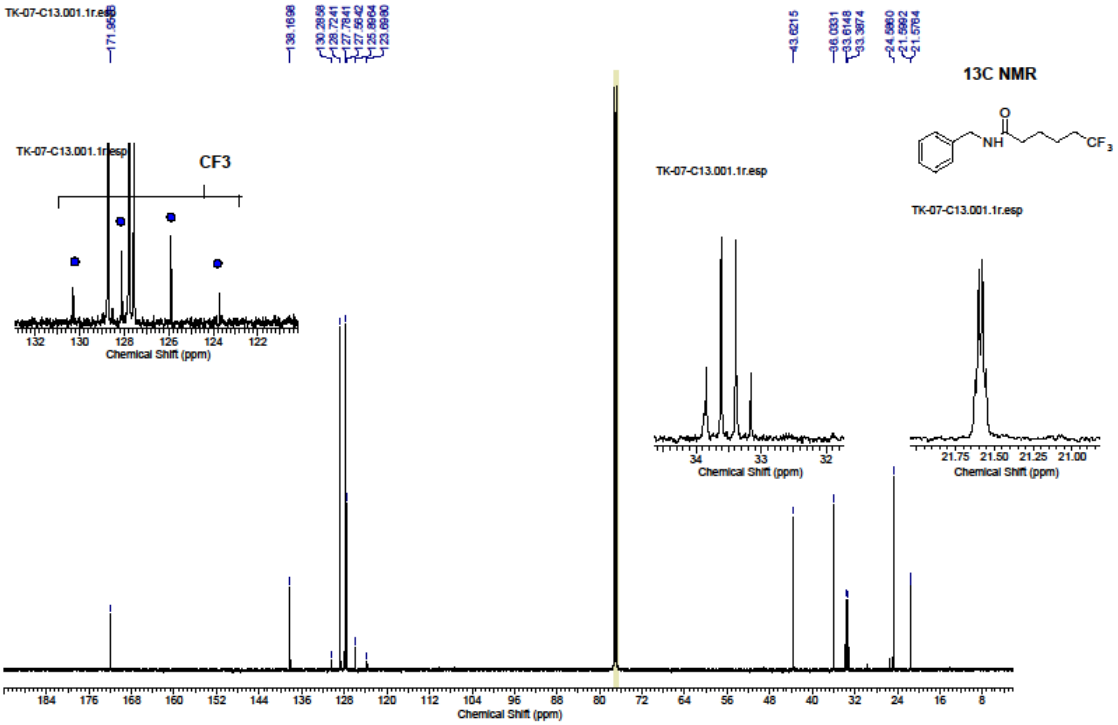

Oct12-2012-27.002.001.1r.esp
66.3883
66.4159
66.4482
Oct12-2012-27.002.001.1r.esp
66.3883
66.4159
66.4482
HO
CF3
19F NMR
-65.0
-65.5
-66.0
-66.5
-67.0
-67.5
Chemical Shift (ppm)
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
Chemical Shift (ppm)

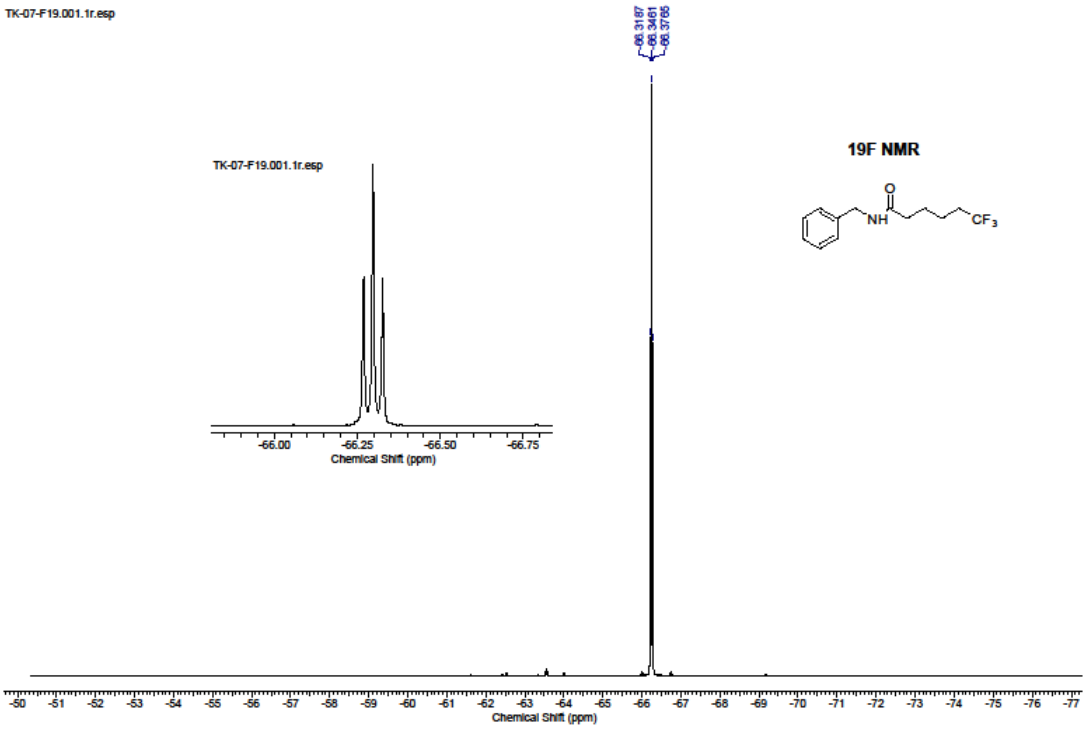

Aug02-2012-10.001.001.1r.esp
1H NMR
Chemical Shift (ppm)

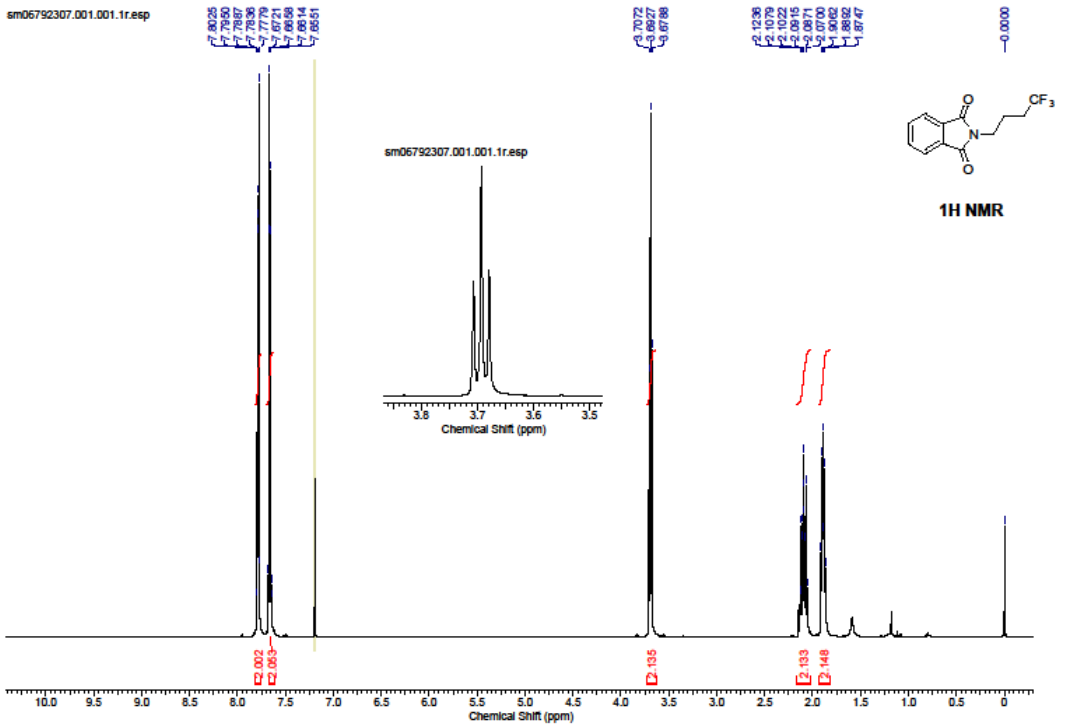

sm09380608.002.001.1r.esp
13C NMR
Chemical Shift (ppm)

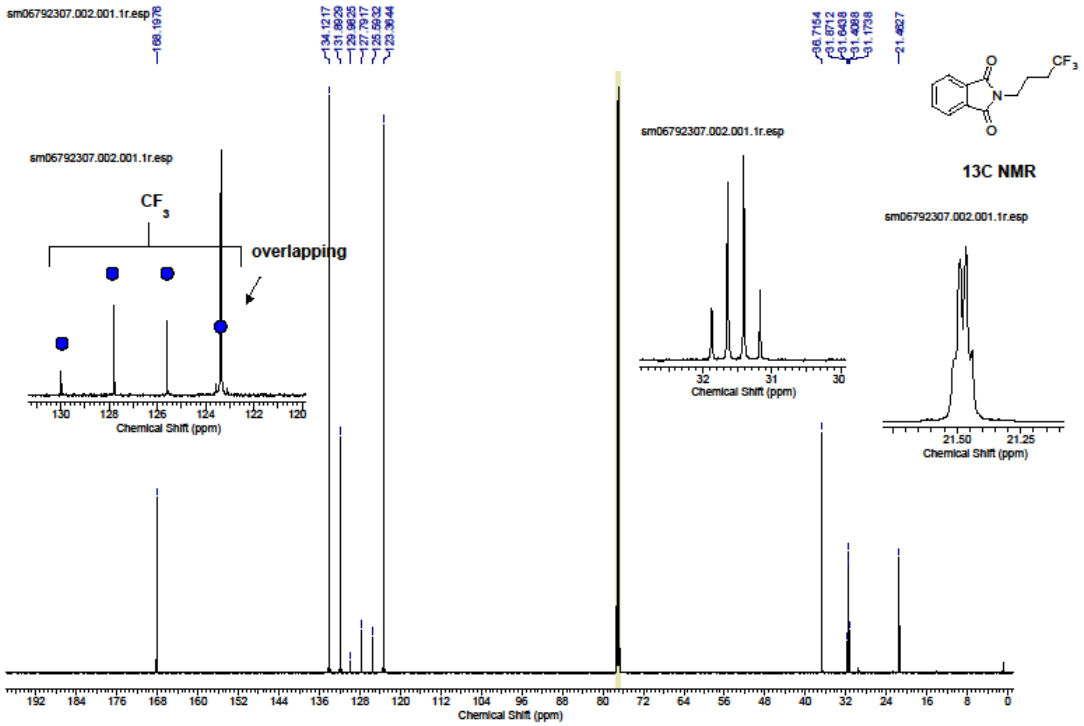

sm-407-2.001.001.1r.esp
-66.7674
-66.7765
-66.7857
OH
F3C
19F NMR
sm-407-2.001.001.1r.esp
-66.60 -66.65 -66.70 -66.75 -66.80 -66.85 -66.90 -66.95
Chemical Shift (ppm)
-54 -55 -56 -57 -58 -59 -60 -61 -62 -63 -64 -65 -66 -67 -68 -69 -70 -71 -72
Chemical Shift (ppm)

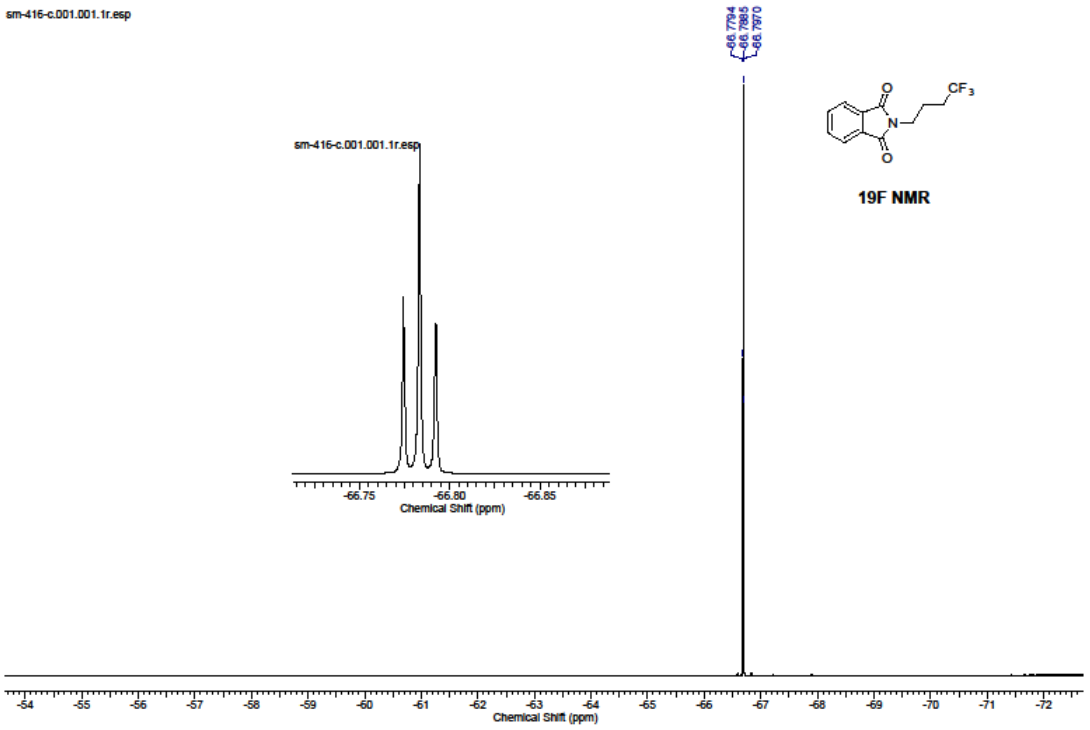

TK-07-H1.001.1r.esp
7.2492
7.2234
7.2203
7.2089
7.2032
7.1995
7.1900
7.1856
6.7690
6.7621
6.7598
6.7545
6.7413
4.3663
4.3650
2.1734
2.1589
2.1438
2.0494
2.0134
2.0133
2.0077
1.9913
1.6863
1.6705
1.6648
1.5388
1.5237
1.5061
1.1828
TK-07-H1.001.1r.esp
4.40 4.35 4.30 4.25 4.20
Chemical Shift (ppm)
TK-07-H1.001.1r.esp
2.0 1.5
Chemical Shift (ppm)
1H NMR
O
NH
CF3
3.376
3.808
0.966
2.000
1.947
1.997
2.003
2.115
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)

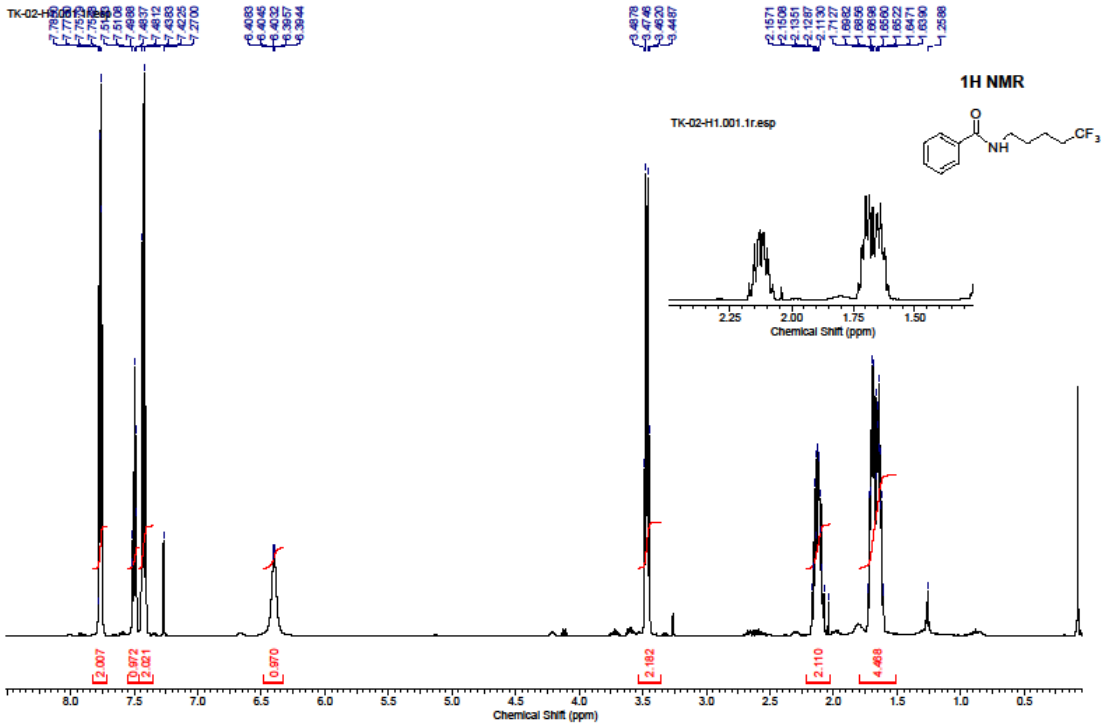

TK-07-C13.001.1r.esp
171.9685
138.1698
130.2859
128.7241
127.7841
127.5642
125.8964
123.6690
43.6215
36.0331
33.6148
33.3874
24.6880
21.5992
21.5764
13C NMR
CF3
Chemical Shift (ppm)

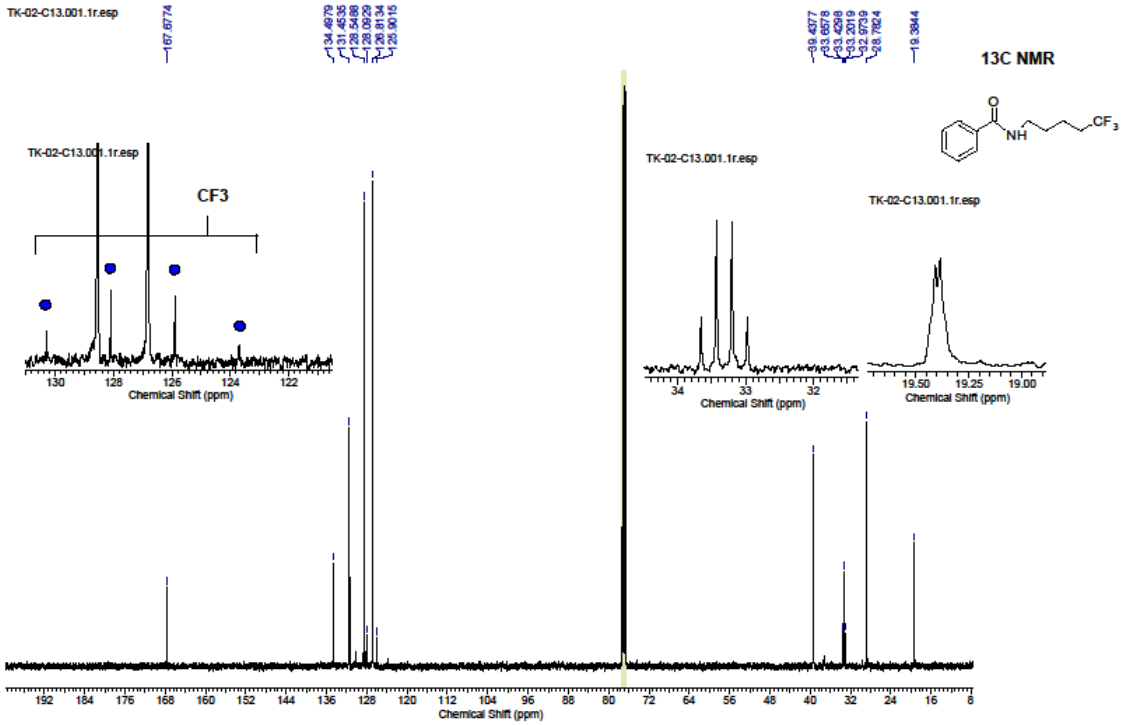

TK-07-F19.001.1r.esp
-66.3187
-66.3461
-66.3766
19F NMR
Chemical Shift (ppm)

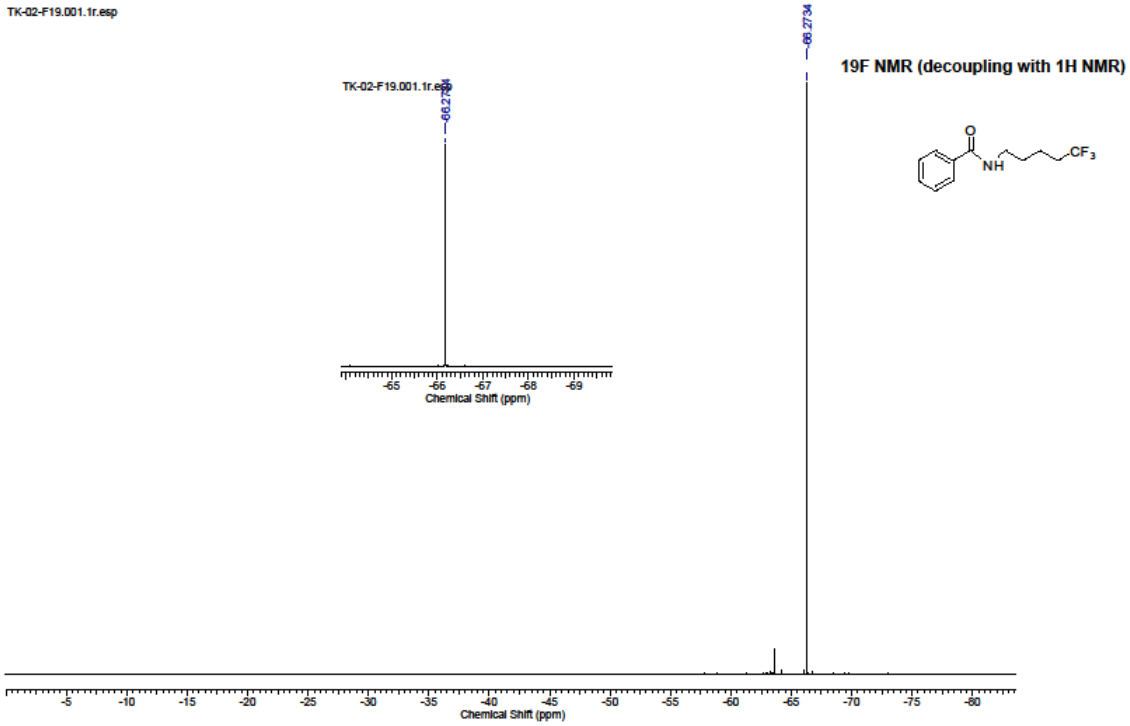

sm06792307.001.001.1r.esp
sm06792307.001.001.1r.esp
Chemical Shift (ppm)
1H NMR
Chemical Shift (ppm)

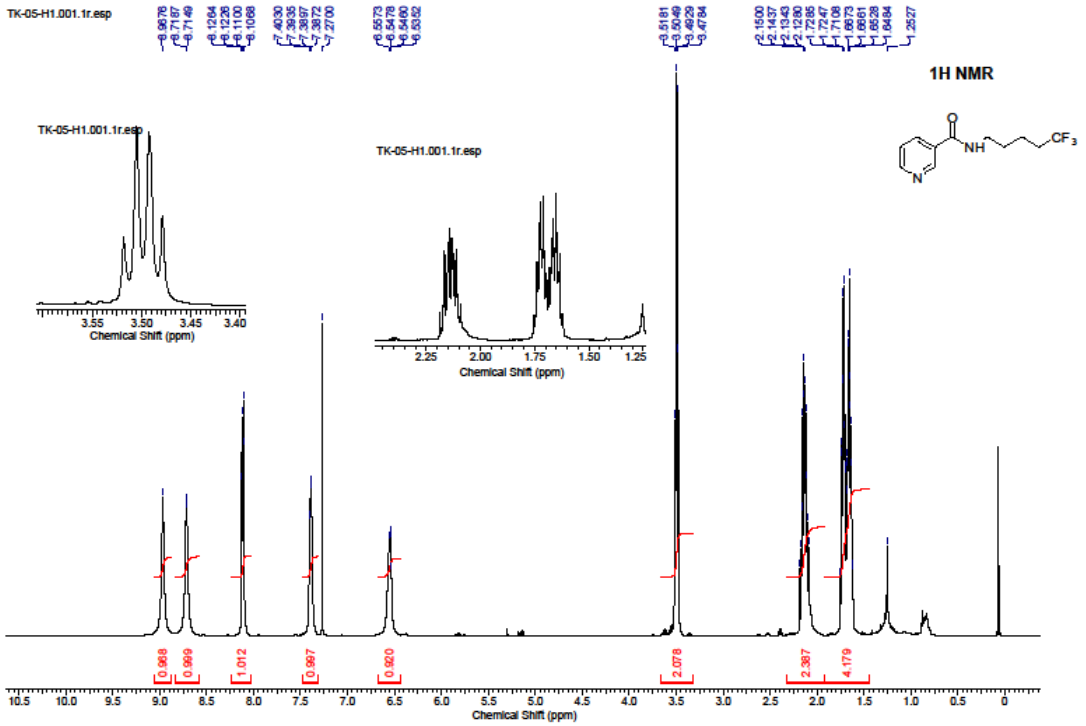

sm06792307.002.001.1r.esp
sm06792307.002.001.1r.esp
CF3
overlapping
Chemical Shift (ppm)
sm06792307.002.001.1r.esp
Chemical Shift (ppm)
13C NMR
sm06792307.002.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)

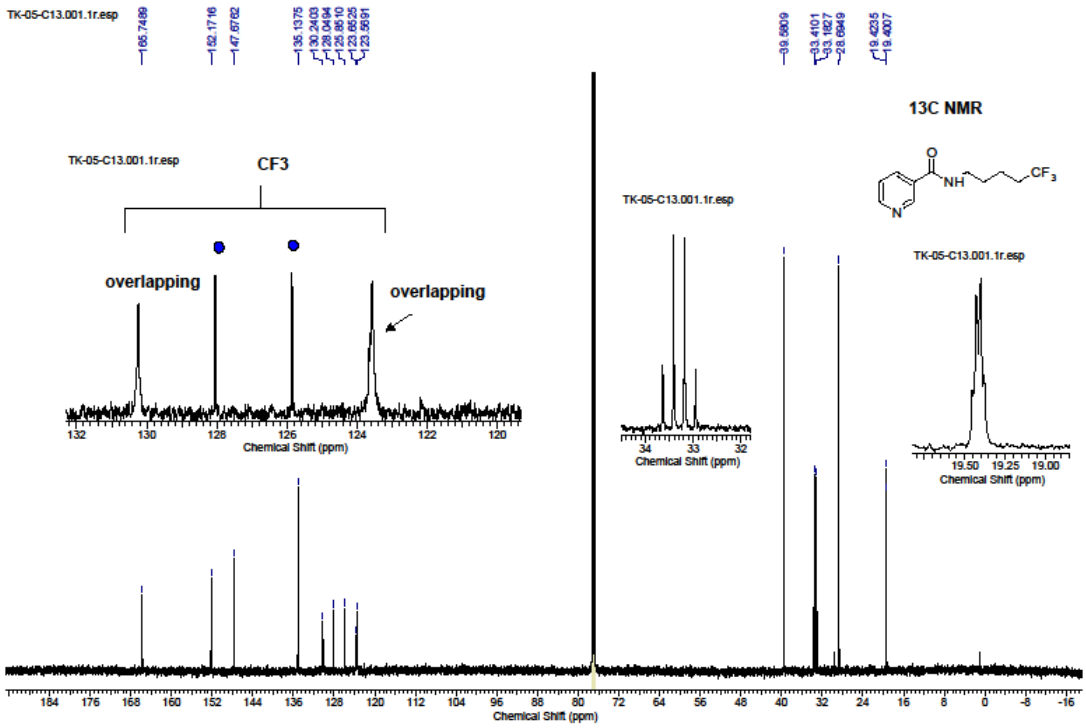

sm-416-c.001.001.1r.esp
-66.7794
-66.7885
-66.7970
sm-416-c.001.001.1r.esp
-66.75
-66.80
-66.85
Chemical Shift (ppm)
19F NMR
-54
-55
-56
-57
-58
-59
-60
-61
-62
-63
-64
-65
-66
-67
-68
-69
-70
-71
-72
Chemical Shift (ppm)

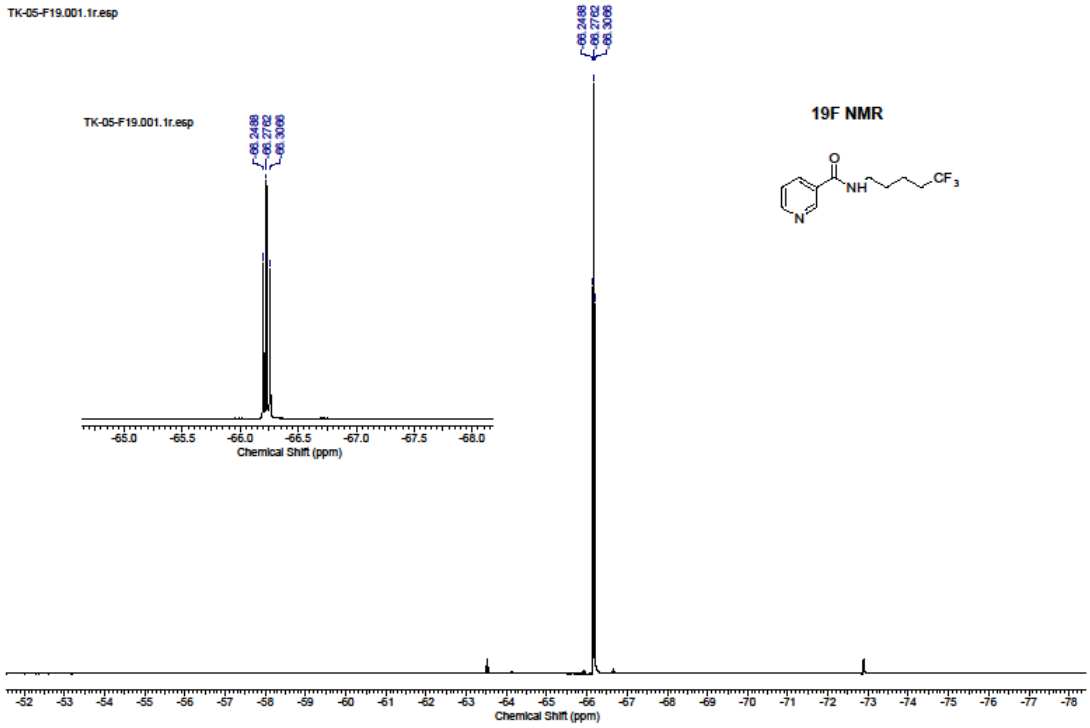

1H NMR
TK-02-H1.001.1r.esp
2.25
2.00
1.75
1.50
Chemical Shift (ppm)
3.007
0.972
2.021
0.970
2.182
2.110
4.468
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

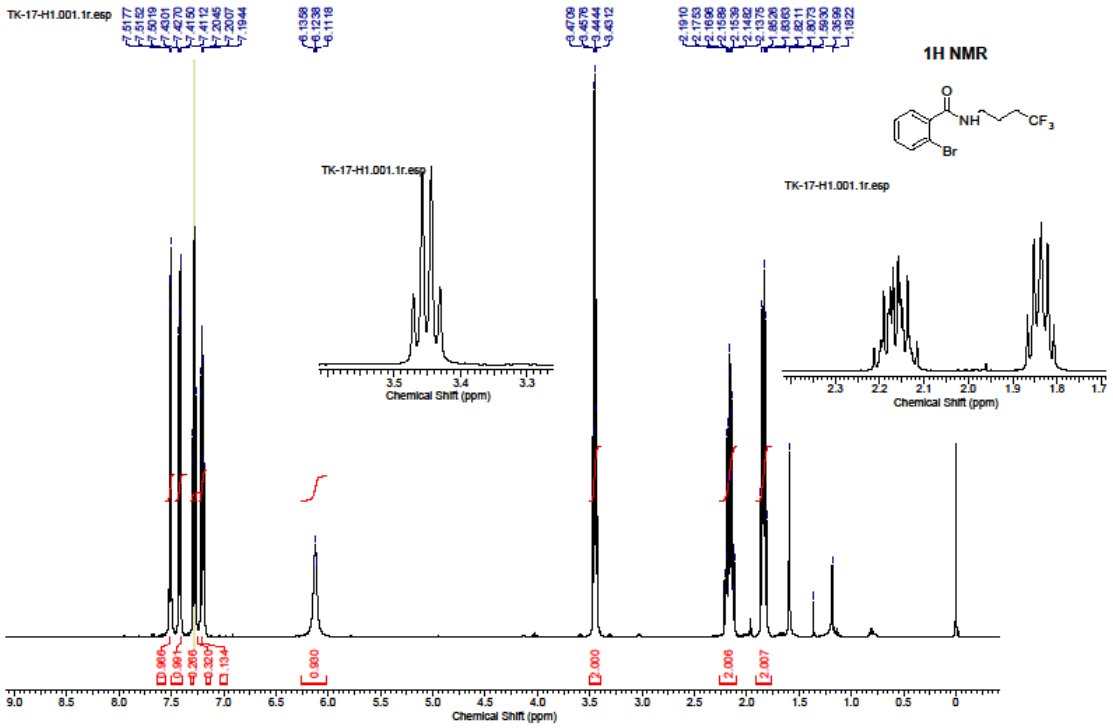

TK-02-C13.001.1r.esp
167.6774
134.4679
131.4535
128.5488
128.0029
126.8734
125.9015
39.4377
33.6578
33.4298
33.2019
32.9739
28.7824
19.3844
13C NMR
CF3
Chemical Shift (ppm)

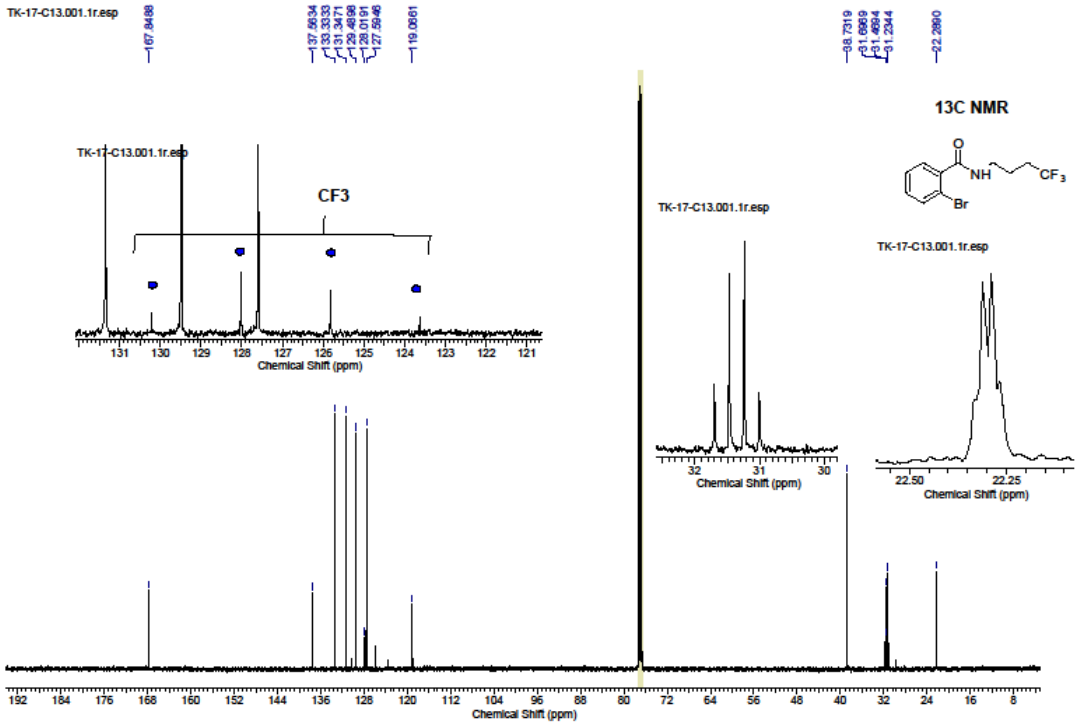

TK-02-F19.001.1r.esp
-66.2734
19F NMR (decoupling with 1H NMR)
Chemical Shift (ppm)

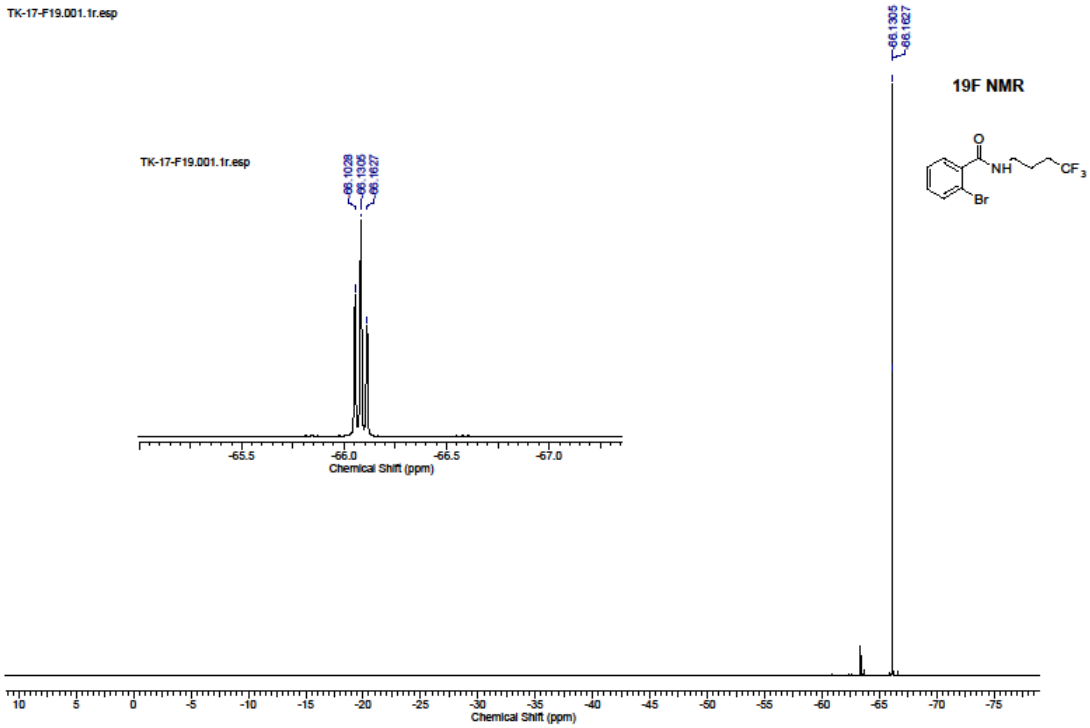

TK-05-H1.001.1r.esp
1H NMR
TK-05-H1.001.1r.esp
TK-05-H1.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)

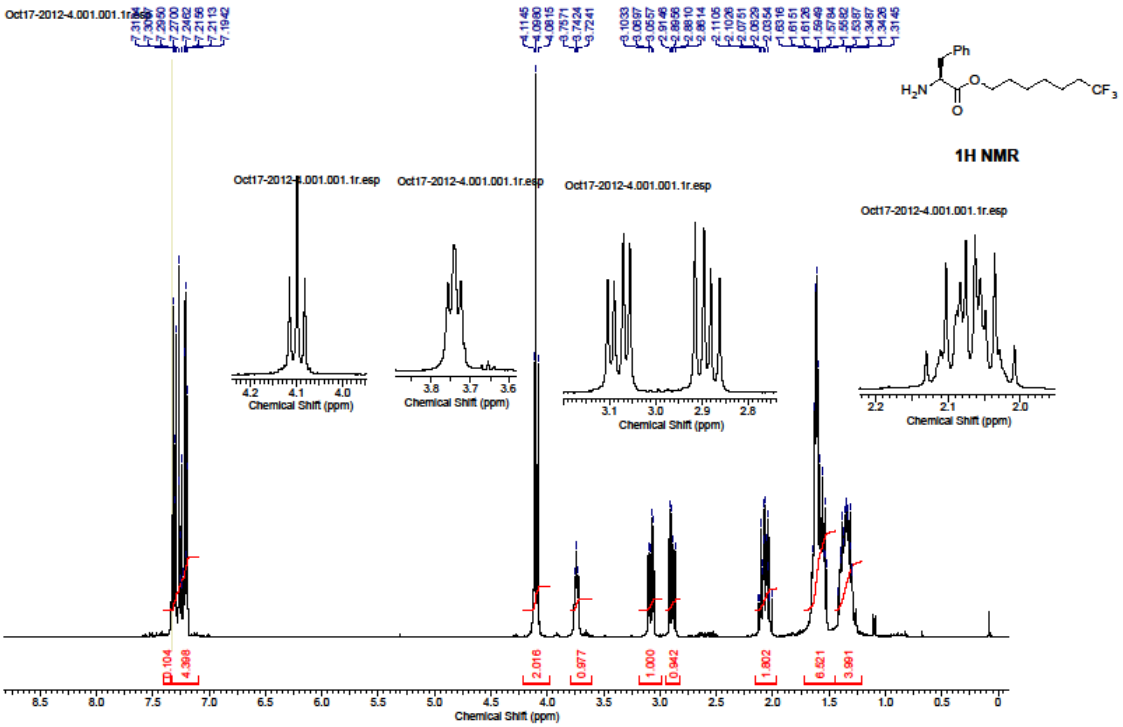

TK-05-C13.001.1r.esp
13C NMR
TK-05-C13.001.1r.esp
CF3
overlapping
overlapping
TK-05-C13.001.1r.esp
TK-05-C13.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)

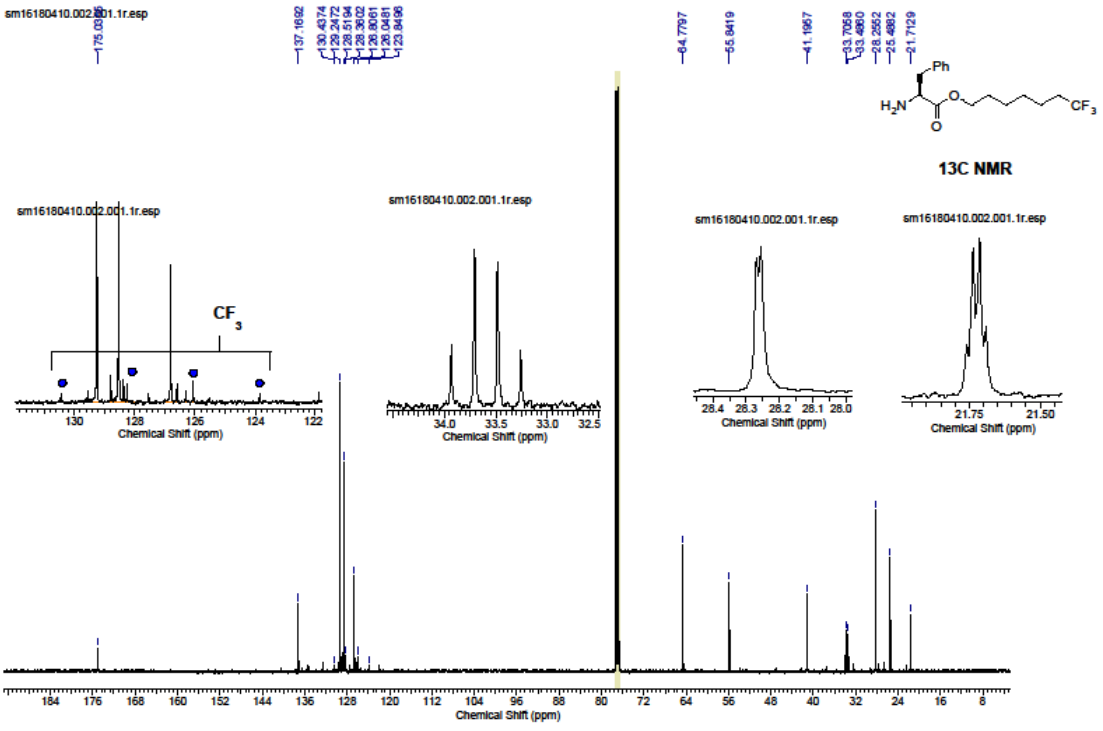

TK-05-F19.001.1r.esp
-66.2488
-66.2762
-66.3066
TK-05-F19.001.1r.esp
19F NMR
O
NH
CF3
N
Chemical Shift (ppm)

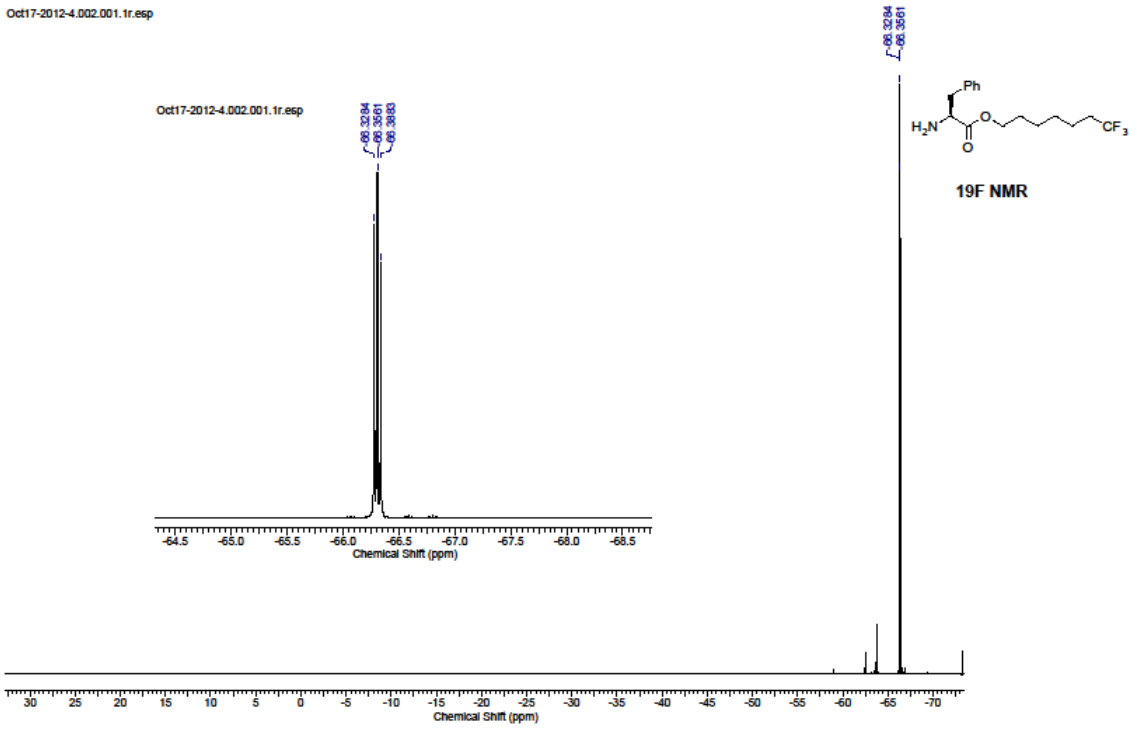

TK-17-H1.001.1r.esp
7.5177
7.5152
7.5019
7.4301
7.4270
7.4150
7.4112
7.2045
7.2007
7.1944
6.1358
6.1238
6.1118
3.4709
3.4576
3.4444
3.4312
2.1910
2.1753
2.1696
2.1589
2.1539
2.1482
2.1375
1.8826
1.8673
1.8611
1.8073
1.5930
1.3699
1.1822
1H NMR
O
NH
CF3
Br
TK-17-H1.001.1r.esp
TK-17-H1.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)

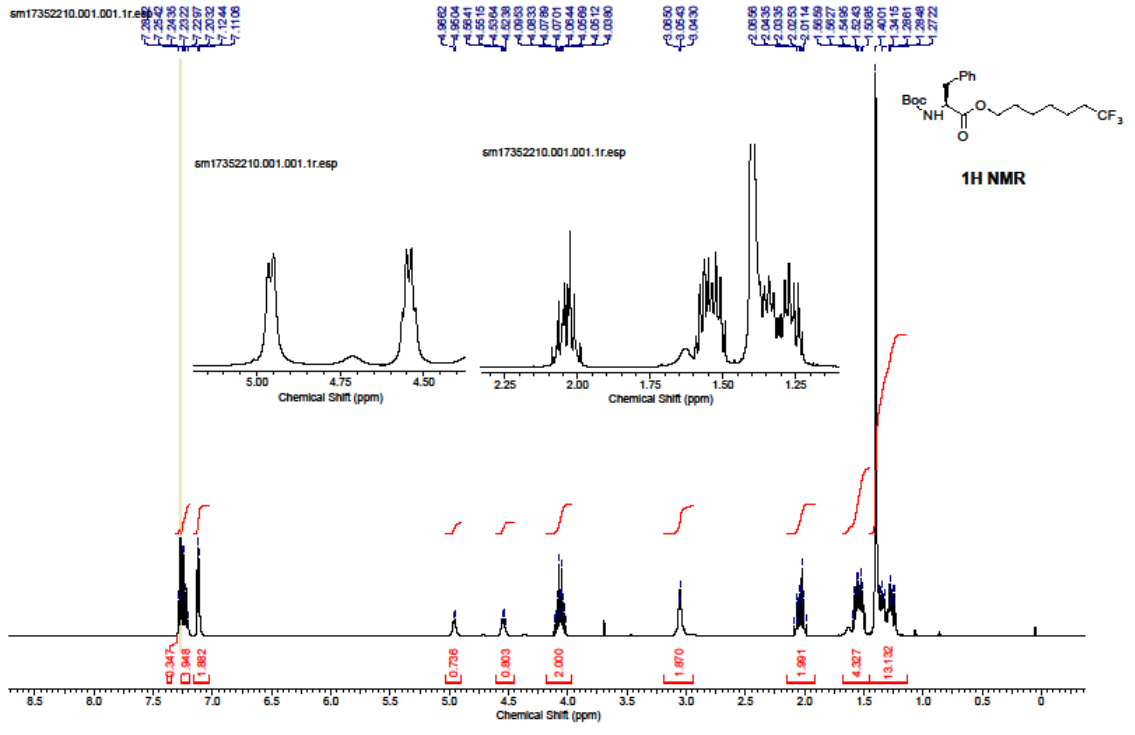

TK-17-C13.001.1r.esp
167.8488
137.5834
133.3333
131.3471
128.8498
128.0191
127.5946
119.0661
38.7319
31.6959
31.4694
31.2344
22.2890
13C NMR
CF3
Chemical Shift (ppm)

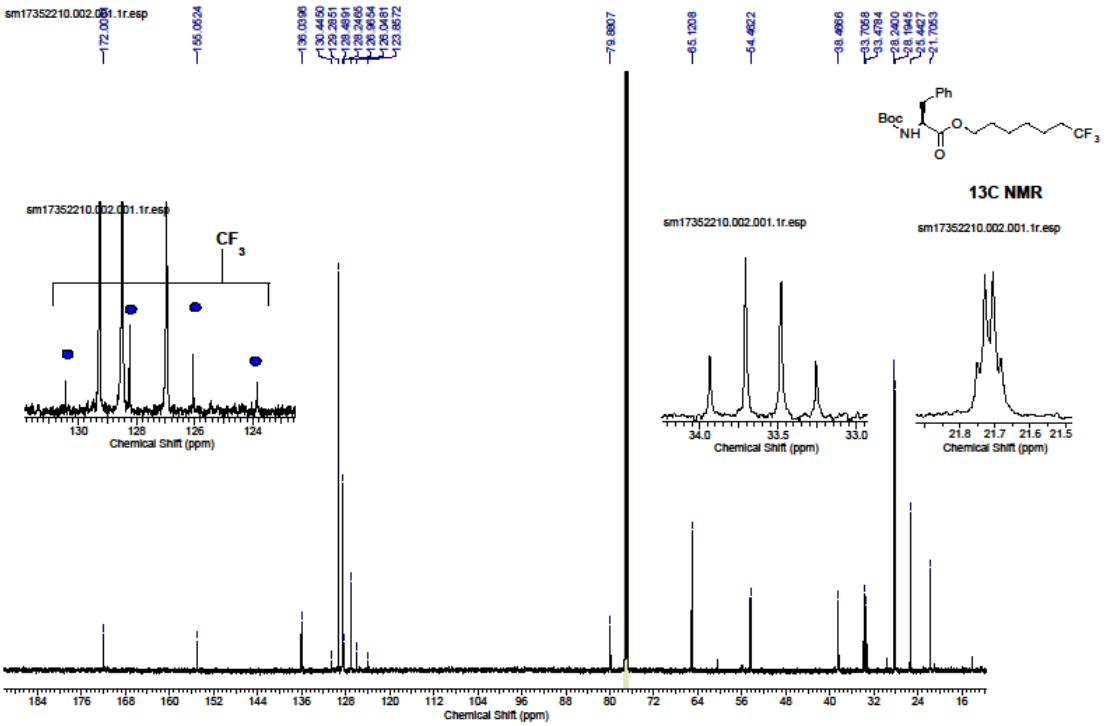

TK-17-F19.001.1r.esp
-66.1305
-66.1627
19F NMR
-66.1028
Chemical Shift (ppm)

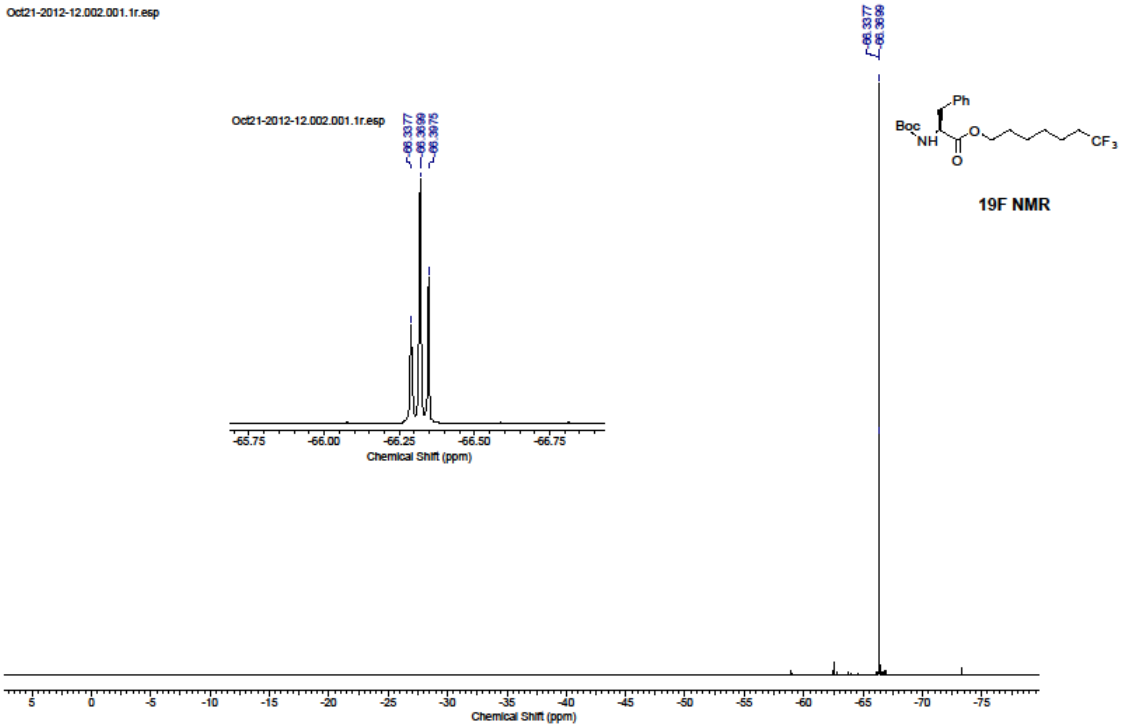

Ph
H_2N
O
O
CF_3
1H NMR
Chemical Shift (ppm)

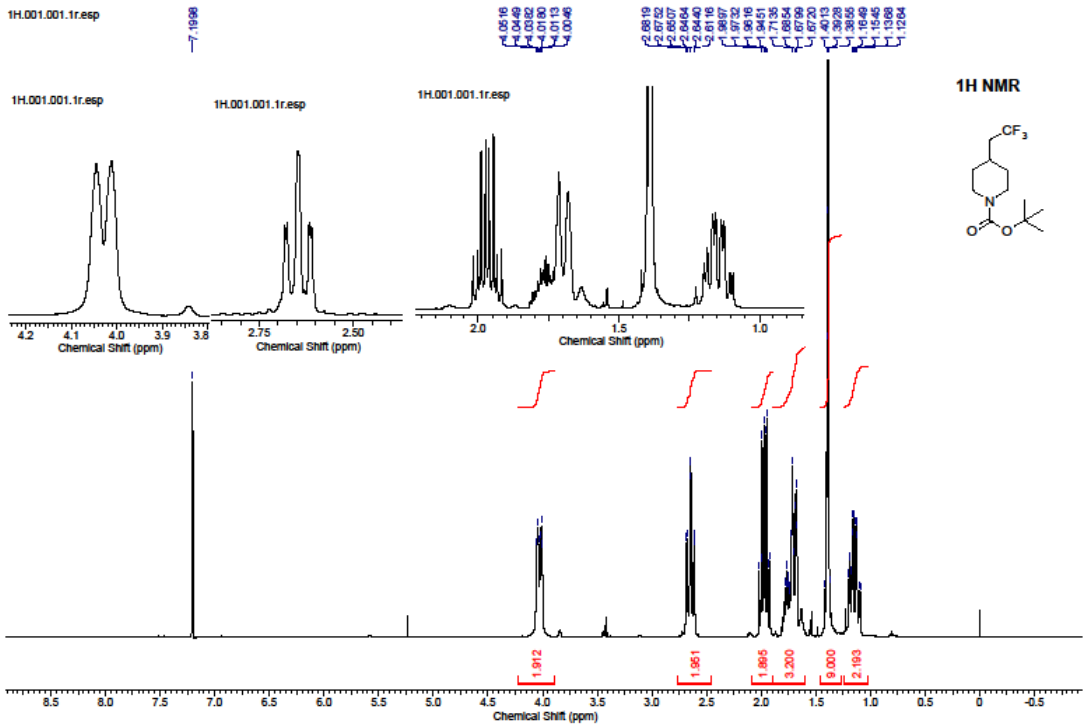

Ph
H_2N
O
O
CF_3
13C NMR
CF_3
Chemical Shift (ppm)

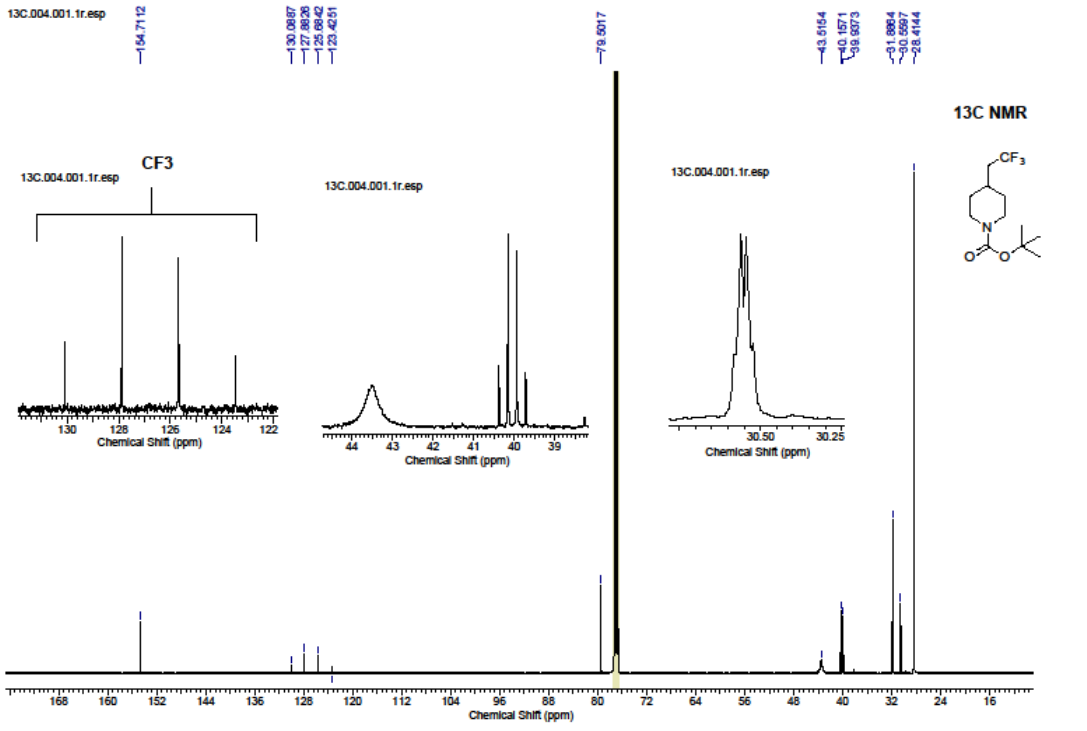

Oct17-2012-4.002.001.1r.esp
Oct17-2012-4.002.001.1r.esp
-66.3294
-66.3561
-66.3883
Chemical Shift (ppm)
Chemical Shift (ppm)
Ph
H2N
O
O
CF3
19F NMR

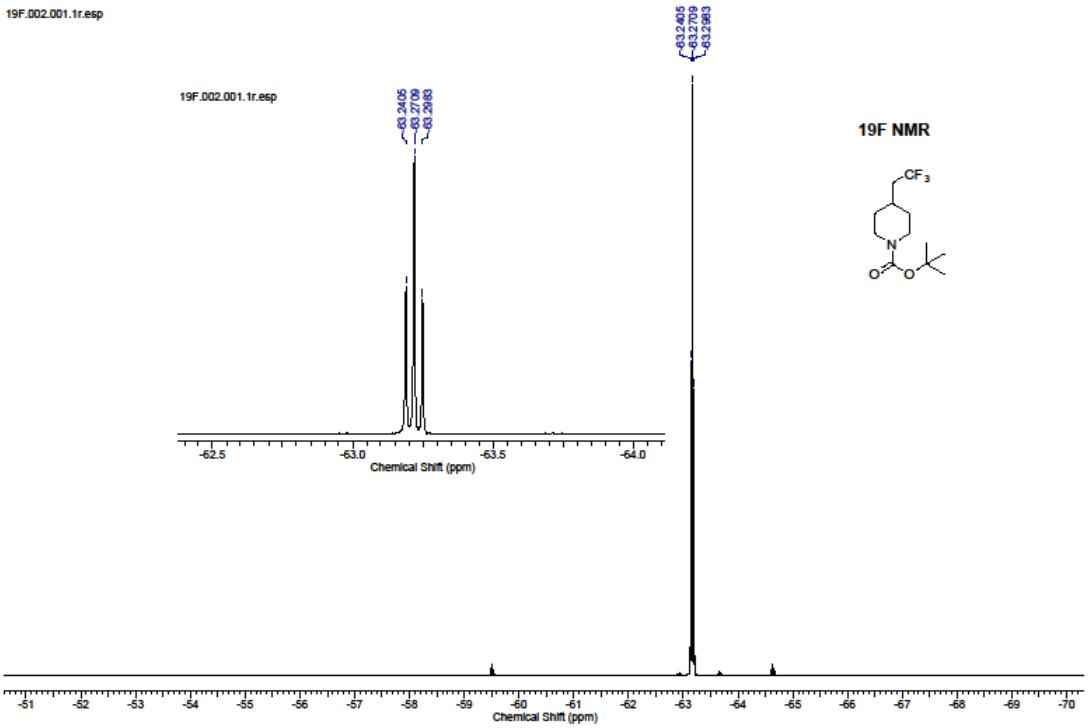

sm17352210.001.001.1r.esp
sm17352210.001.001.1r.esp
sm17352210.001.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
Ph
Boc
NH
O
O
CF3
1H NMR
0.347
0.948
1.882
0.736
0.803
2.000
1.870
1.981
4.327
13.132

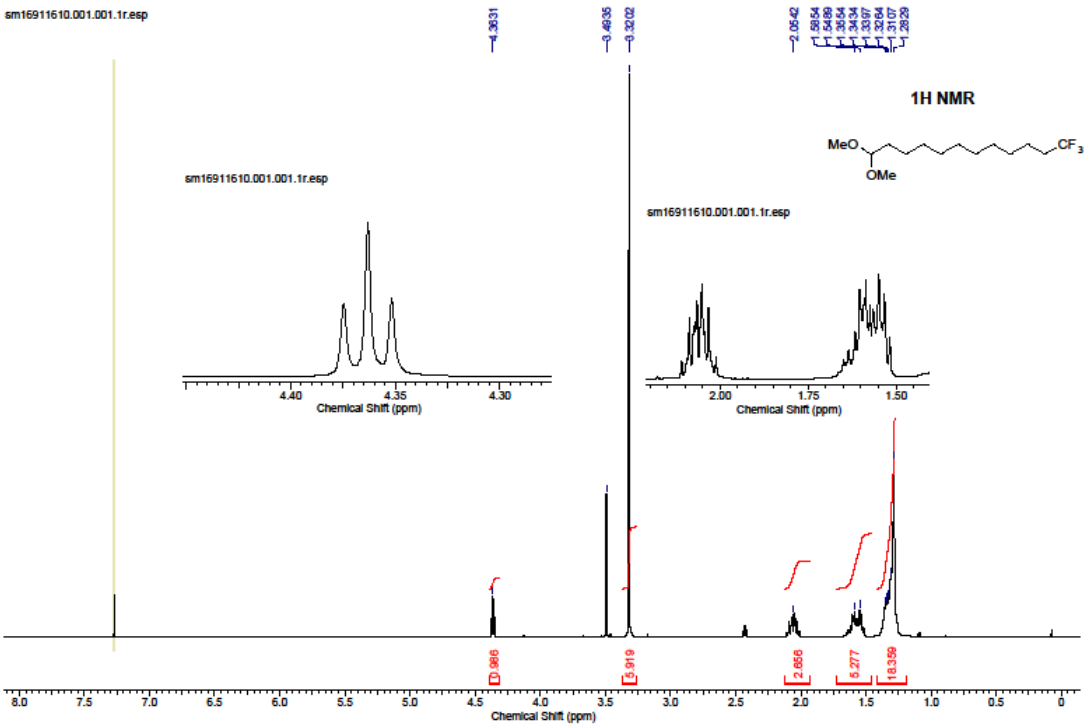

sm17352210.002.001.1r.esp
172.0051
155.0524
136.0396
130.4450
129.2851
128.4891
128.2465
126.9654
126.0481
123.8672
79.8807
65.1208
64.4822
38.4936
33.7058
33.4784
28.3400
28.1945
25.4427
21.7053
Ph
Boc
NH
O
CF3
13C NMR
CF3
130
128
126
124
Chemical Shift (ppm)
34.0
33.5
33.0
21.8
21.7
21.6
21.5
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16

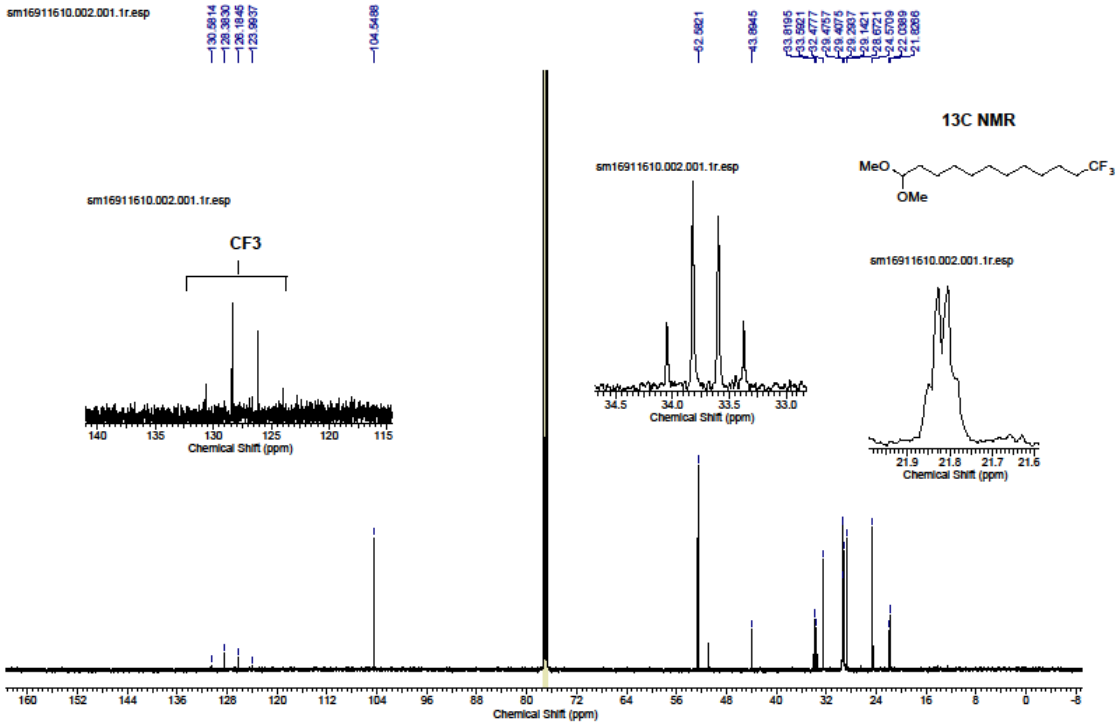

Oct21-2012-12.002.001.1r.esp
66.3377
66.3699
66.3975
Ph
Boc
NH
O
CF3
19F NMR
-65.75
-66.00
-66.25
-66.50
-66.75
Chemical Shift (ppm)
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75

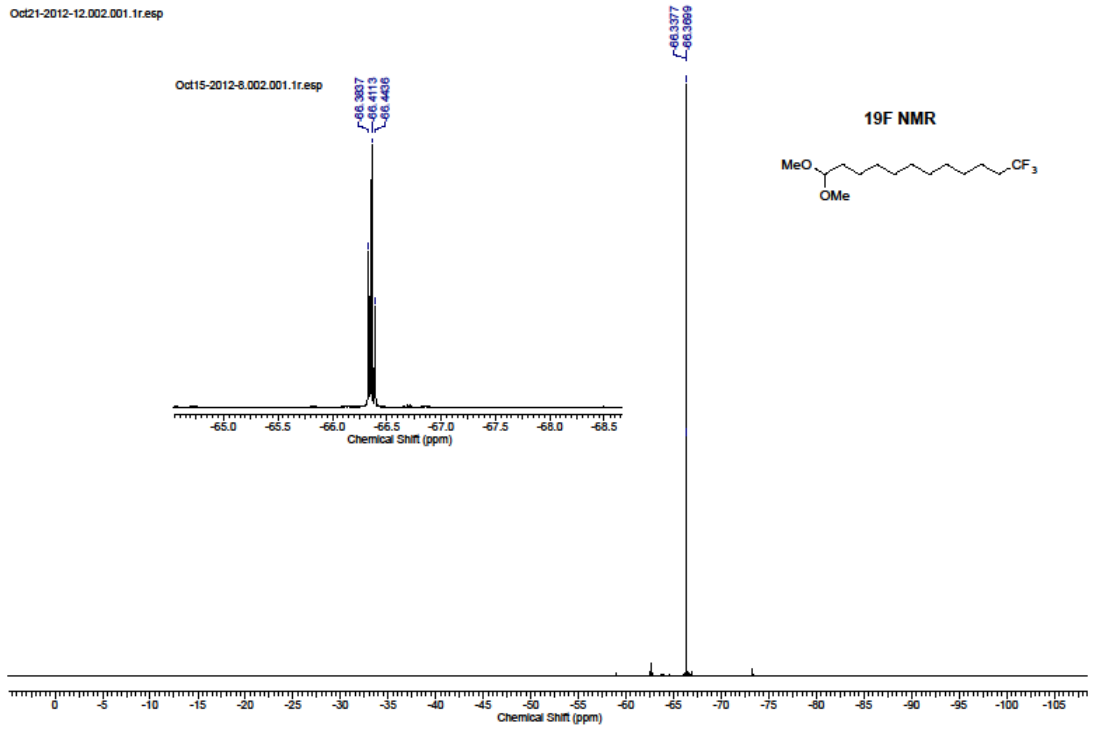

1H.001.001.1r.esp
1H NMR
Chemical Shift (ppm)


13C.004.001.1r.esp
13C NMR
CF3
Chemical Shift (ppm)

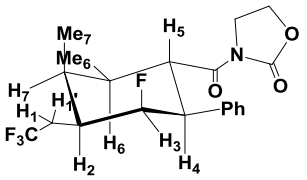

19F.002.001.1r.esp
-63.2405
-63.2709
-63.2983
19F.002.001.1r.esp
-63.2405
-63.2709
-63.2983
19F NMR
CF3
N
O
O
-62.5
-63.0
-63.5
-64.0
Chemical Shift (ppm)
-51
-52
-53
-54
-55
-56
-57
-58
-59
-60
-61
-62
-63
-64
-65
-66
-67
-68
-69
-70
Chemical Shift (ppm)

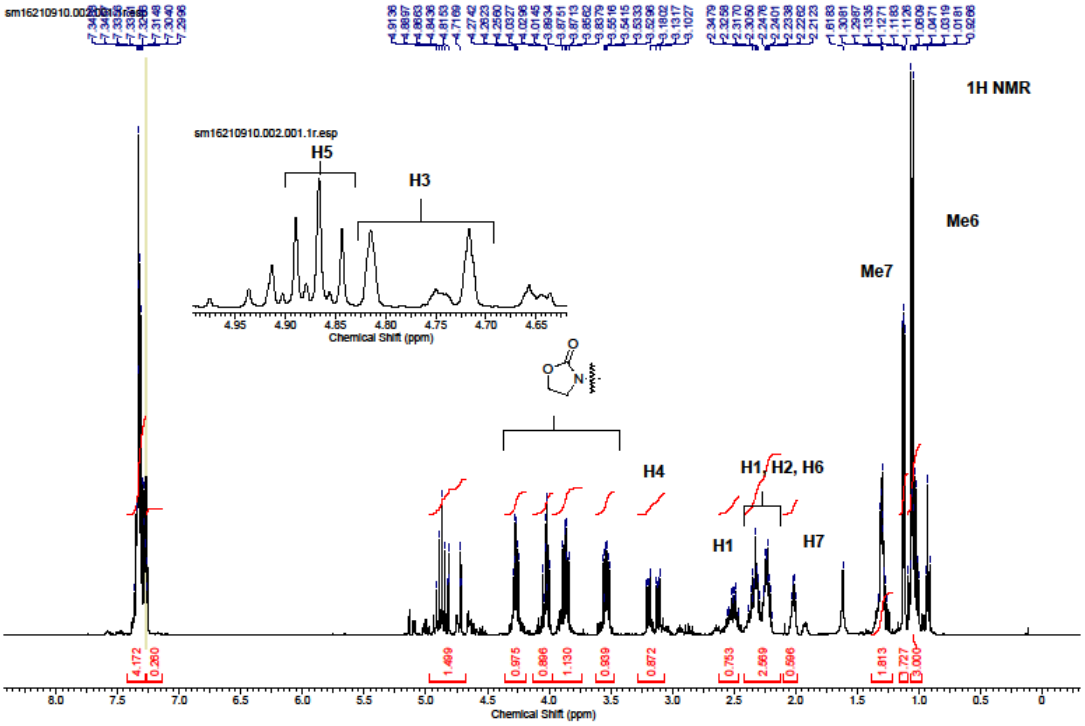

sm16911610.001.001.1r.esp
4.3031
3.4935
3.3202
2.0542
1.5854
1.5488
1.5054
1.4754
1.3097
1.3264
1.3107
1.2929
1H NMR
MeO
OMe
CF3
sm16911610.001.001.1r.esp
sm16911610.001.001.1r.esp
4.40
4.35
4.30
Chemical Shift (ppm)
2.00
1.75
1.50
Chemical Shift (ppm)
0.986
3.919
2.666
5.277
18.359
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

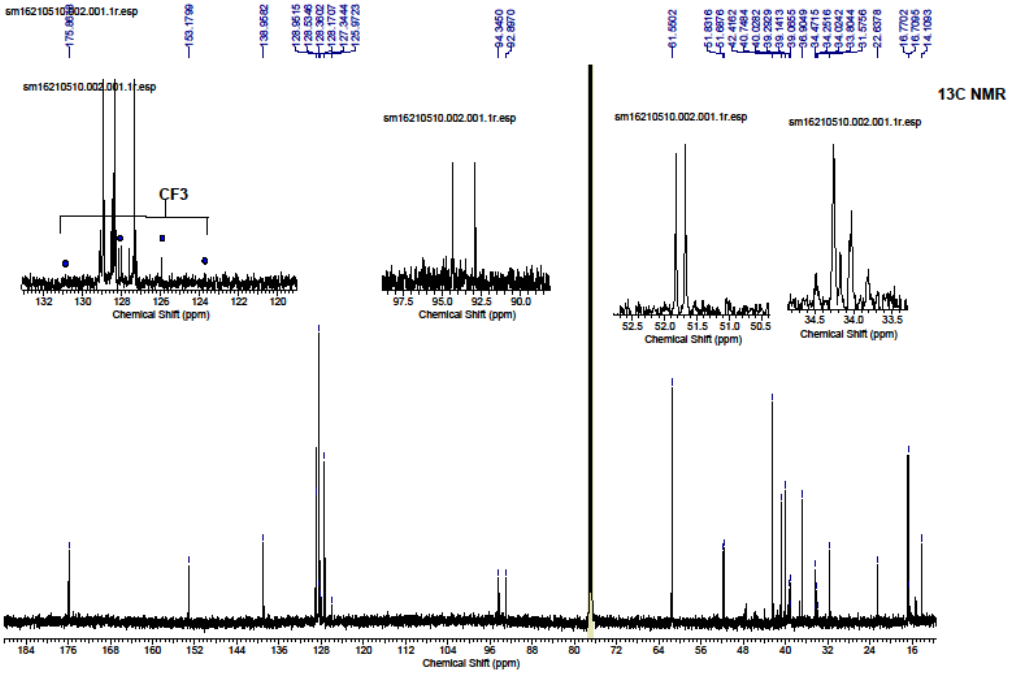

sm16911610.002.001.1r.esp
130.6814
128.3830
128.1945
123.9937
104.5488
52.6821
43.8945
33.6195
33.5921
33.4777
29.4757
29.4075
29.2937
29.1421
28.6721
24.5709
22.0389
21.8266
13C NMR
MeO
CF3
OMe
sm16911610.002.001.1r.esp
CF3
Chemical Shift (ppm)
sm16911610.002.001.1r.esp
Chemical Shift (ppm)
sm16911610.002.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)

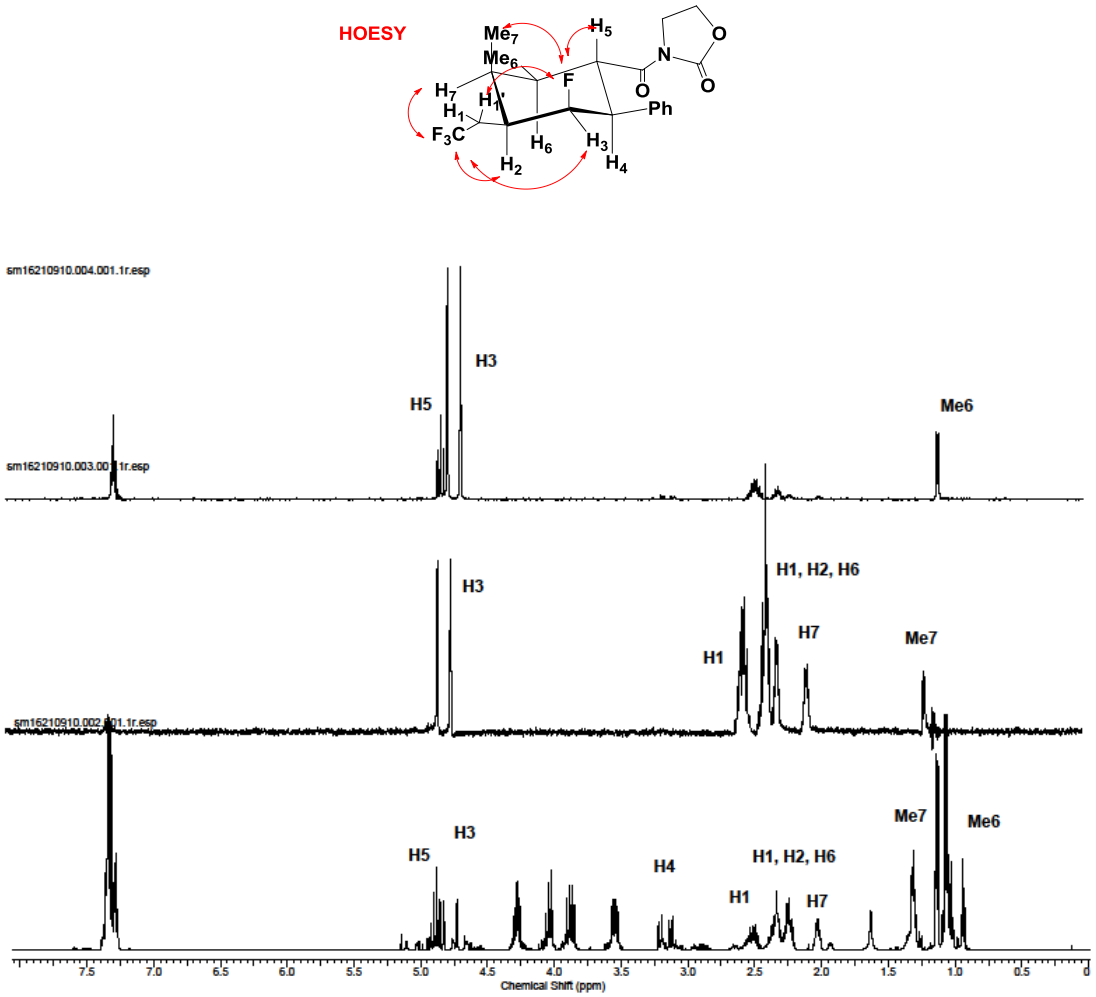

Oct21-2012-12.002.001.1r.esp
Oct15-2012-8.002.001.1r.esp
-66.3837
-66.4113
-66.4436
-66.3377
-66.3669
19F NMR
MeO
CF3
OMe
Chemical Shift (ppm)
Chemical Shift (ppm)

1H NMR & 13C NMR

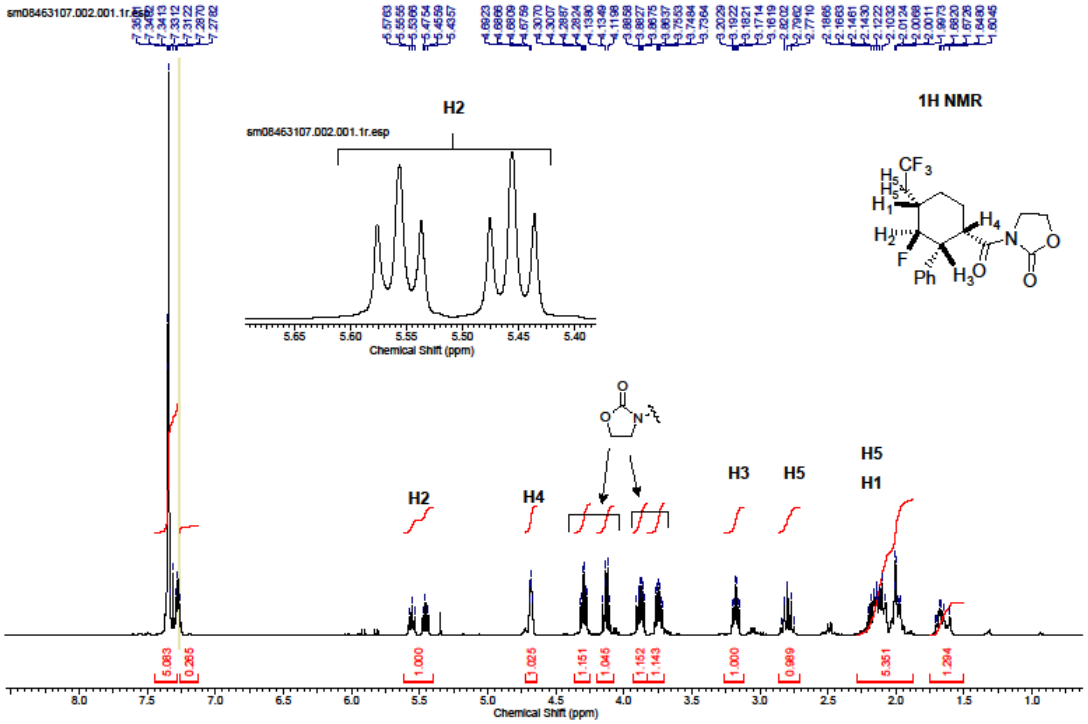


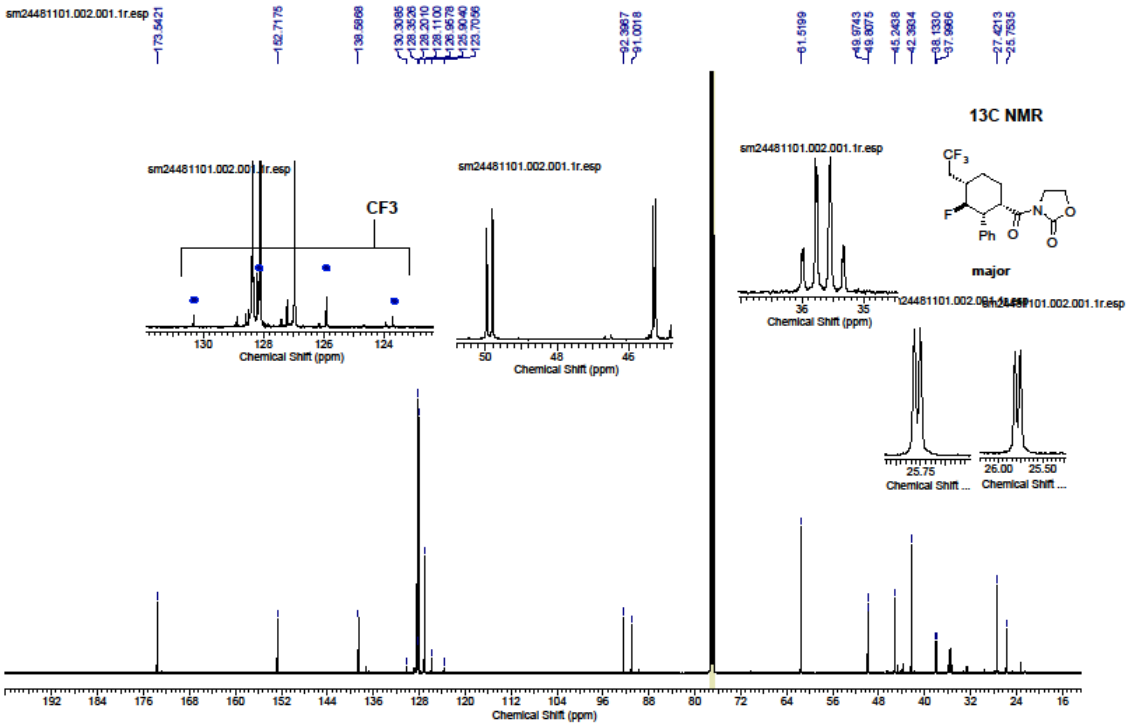


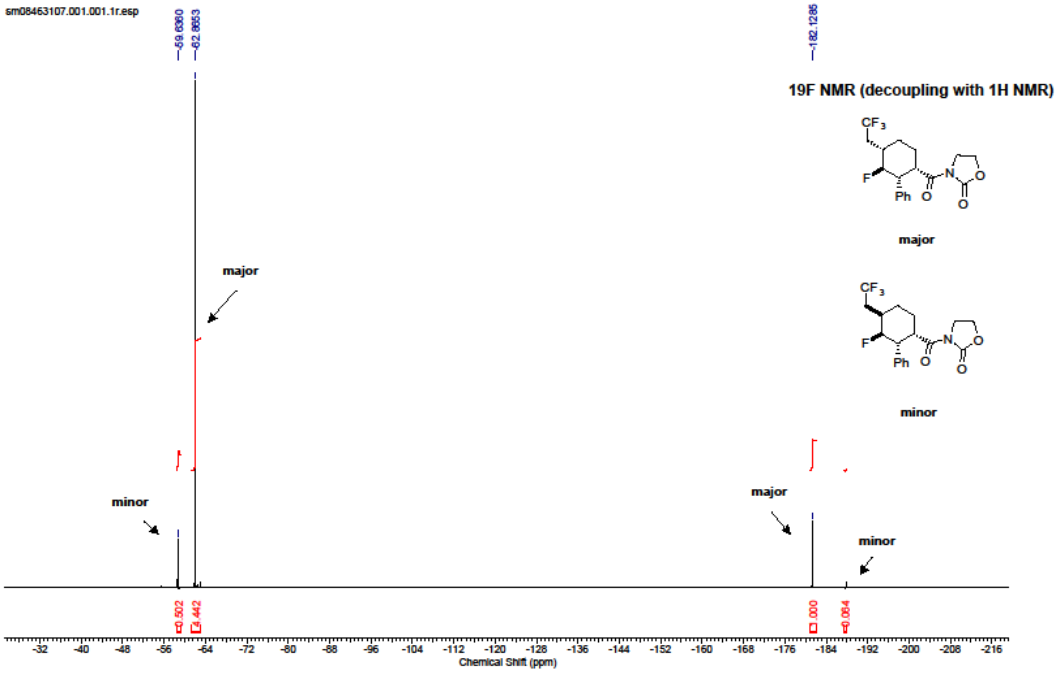


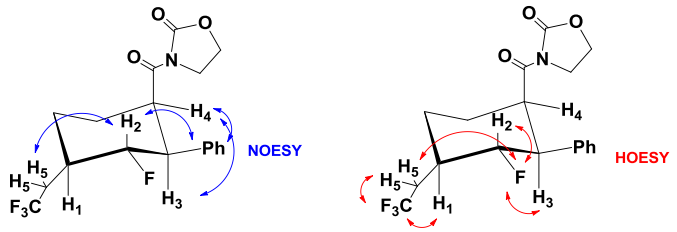


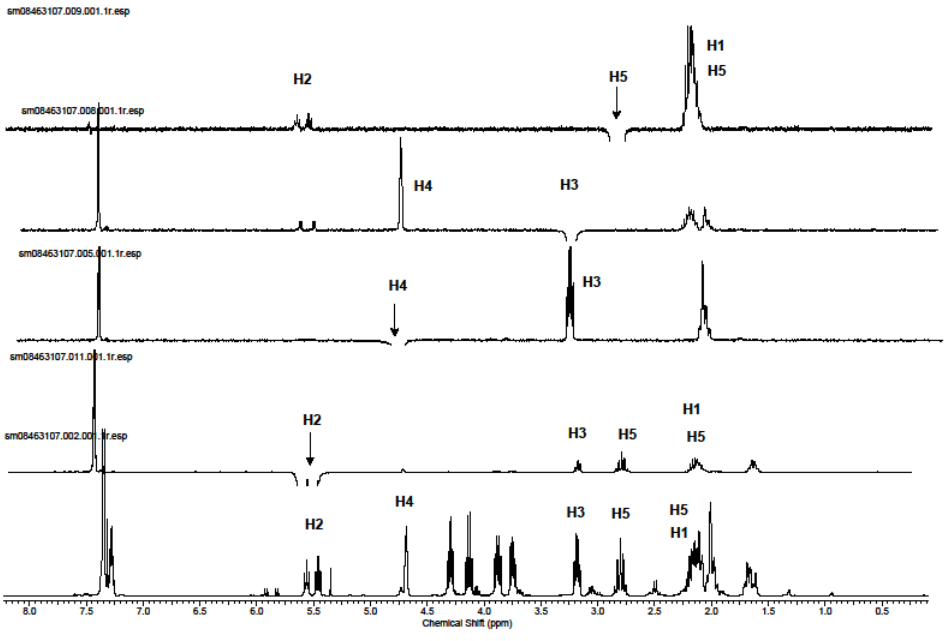
19F NMR 1D 19F-1H HOESY TFI probe irradiating signal F at –198.6 ppm (top), 19F NMR 1D 19F-1H HOESY TFI prove irradiating CF_3 at –63.9 ppm (middle), 1H NMR spectra (bottom).


1H NMR
H2
H4
H3
H5
H1
Chemical Shift (ppm)

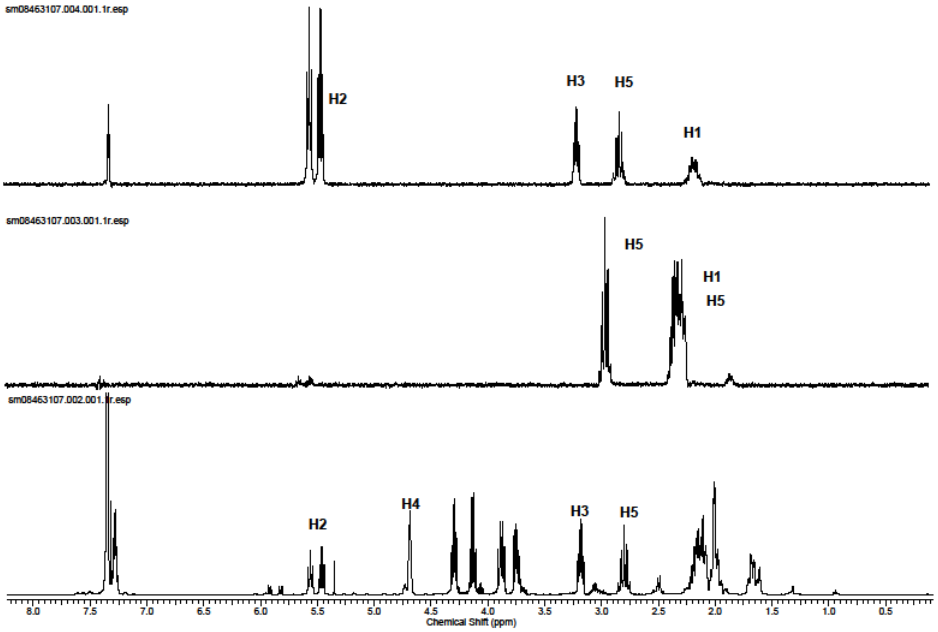

13C NMR
CF3
major
Chemical Shift (ppm)



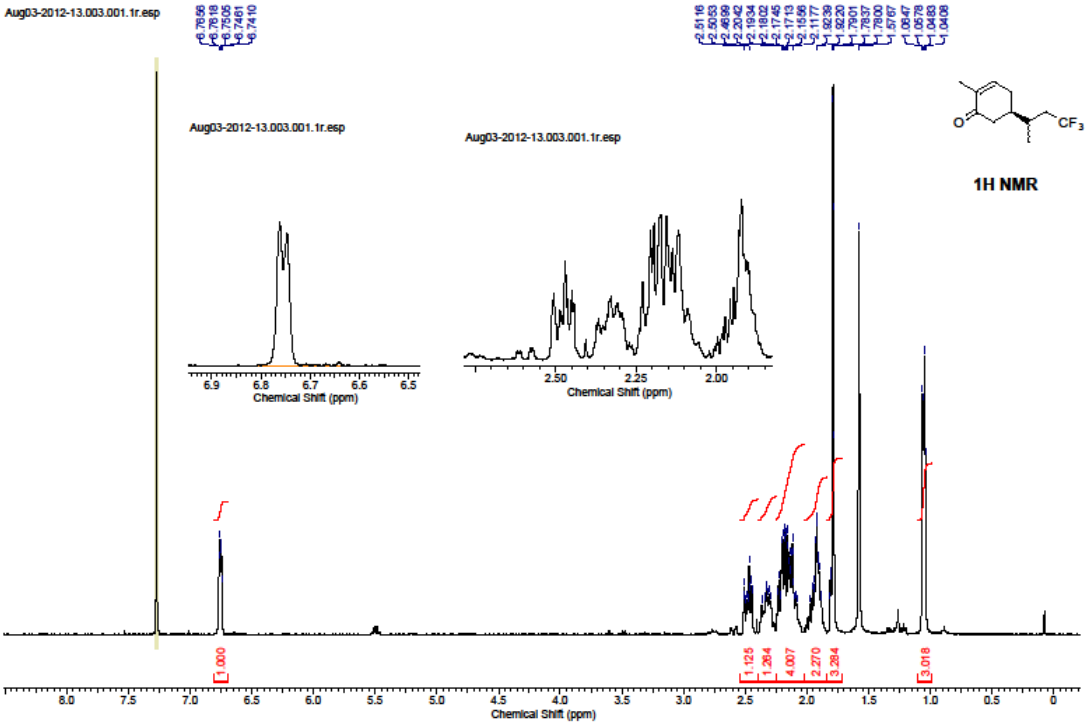


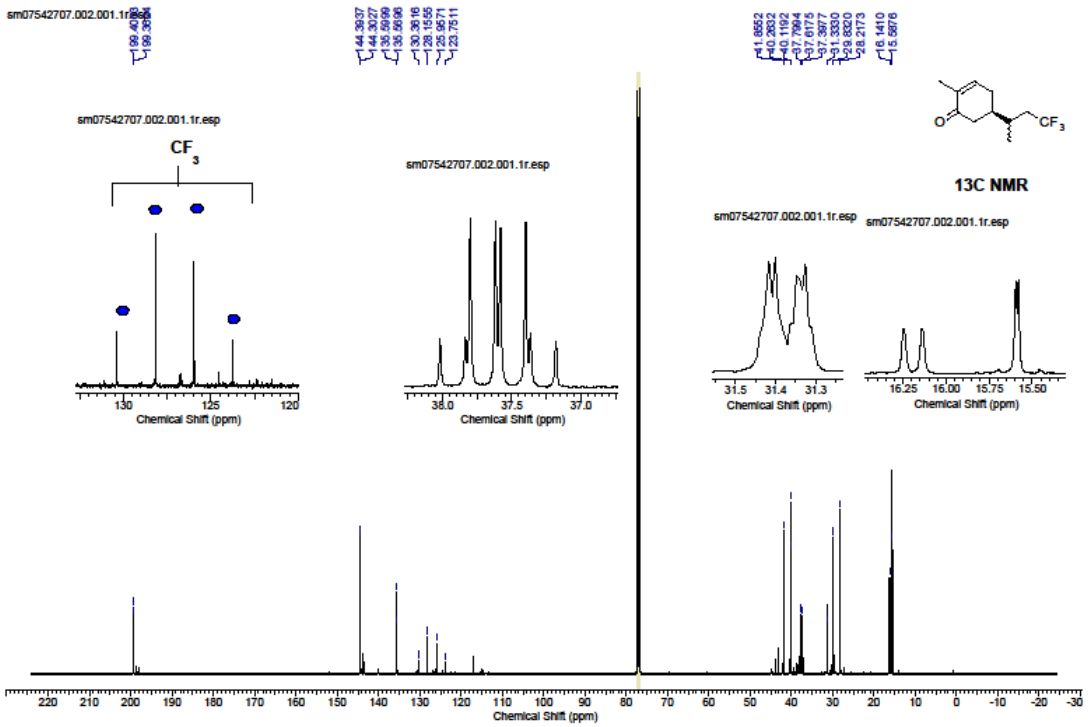


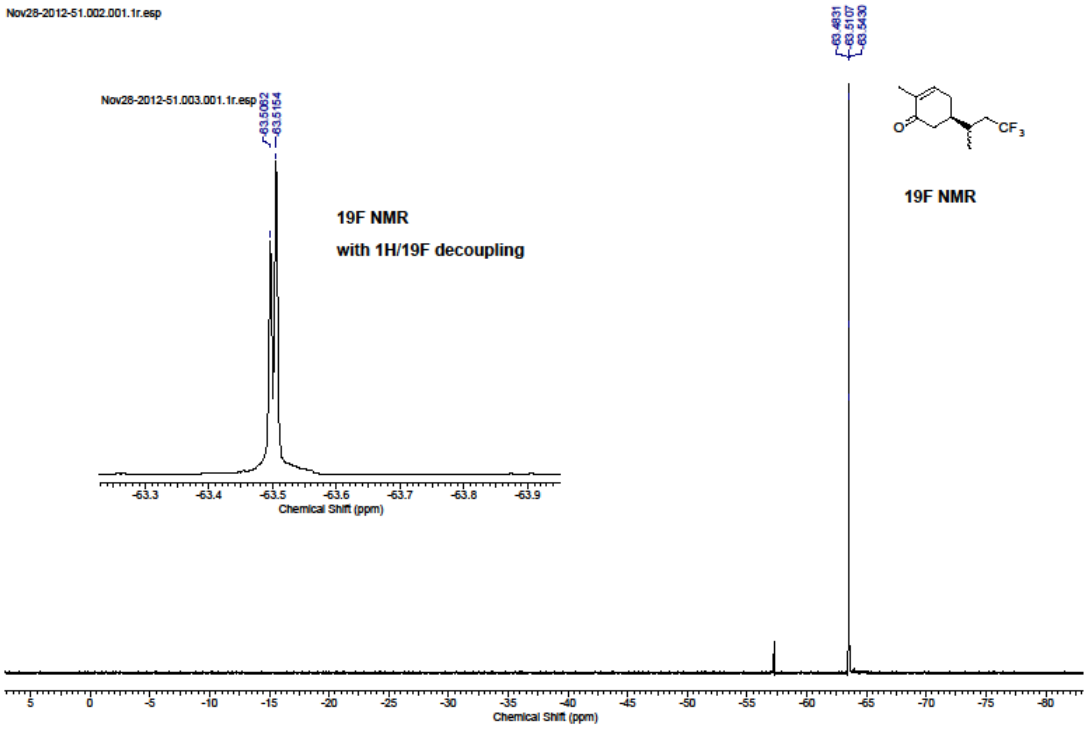
1H TFI probe gradient NOE Tmix = 800msec

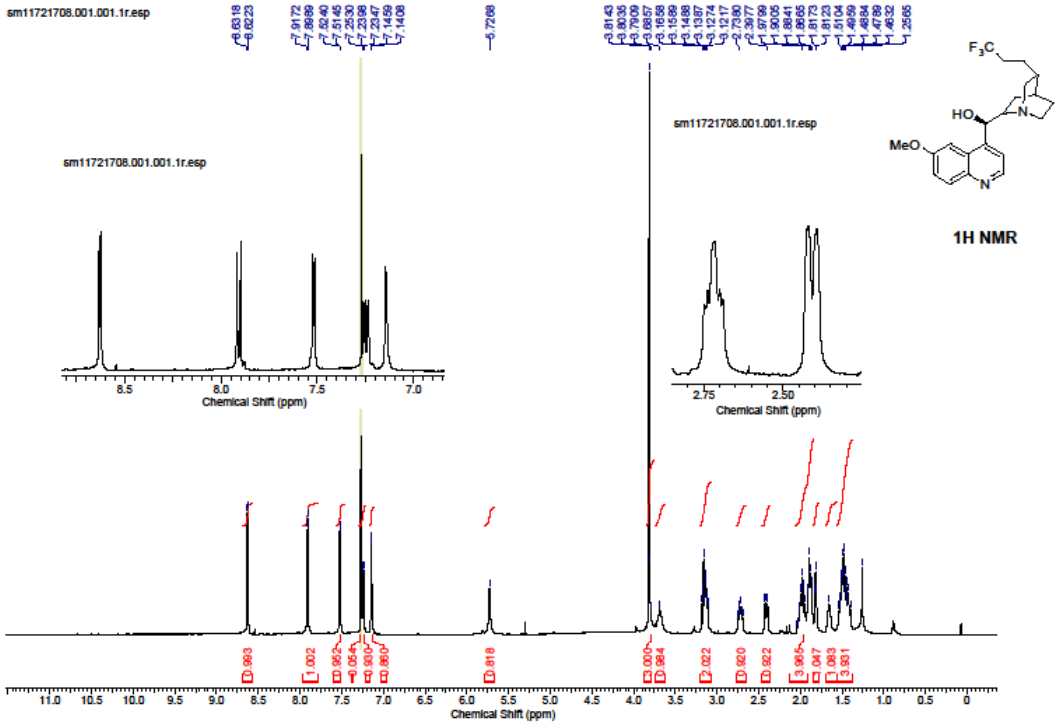


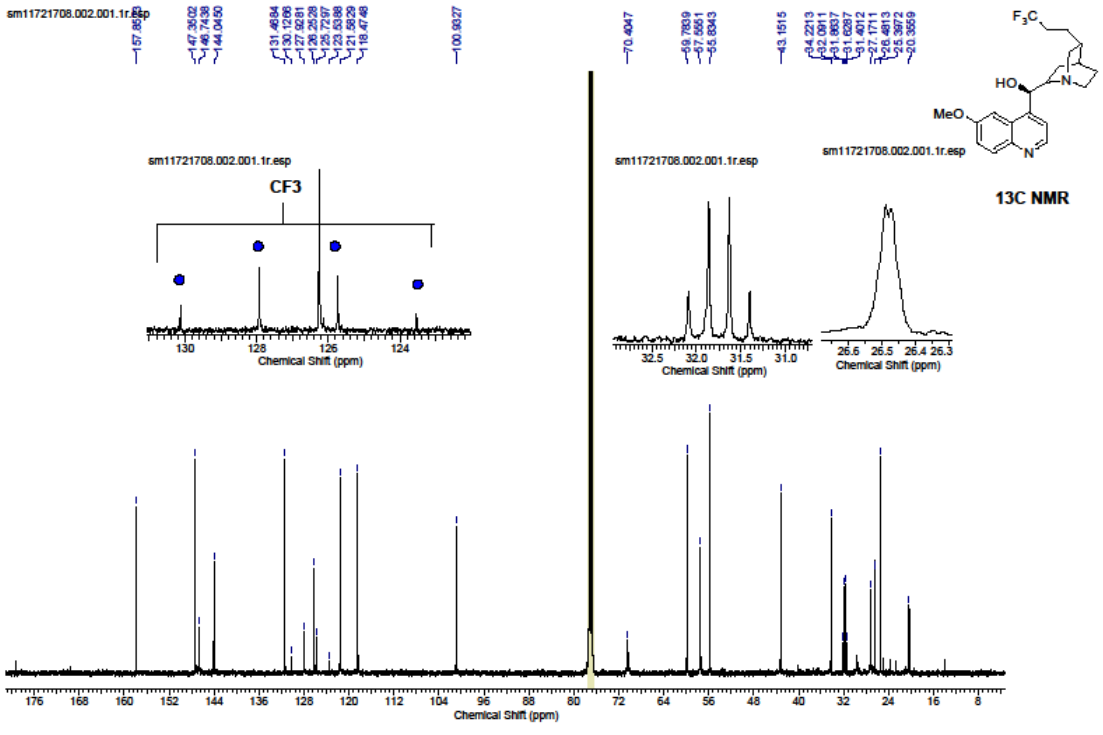
1H TFI probe gradient selective 1-D HOESY Tmix = 800msec; 19F NMR 1D 19F-1H HOESY TFI probe irradiating signal F at –198.6 ppm (top), 19F NMR 1D 19F-1H HOESY TFI prove irradiating CF_3 at –63.9 ppm (middle).

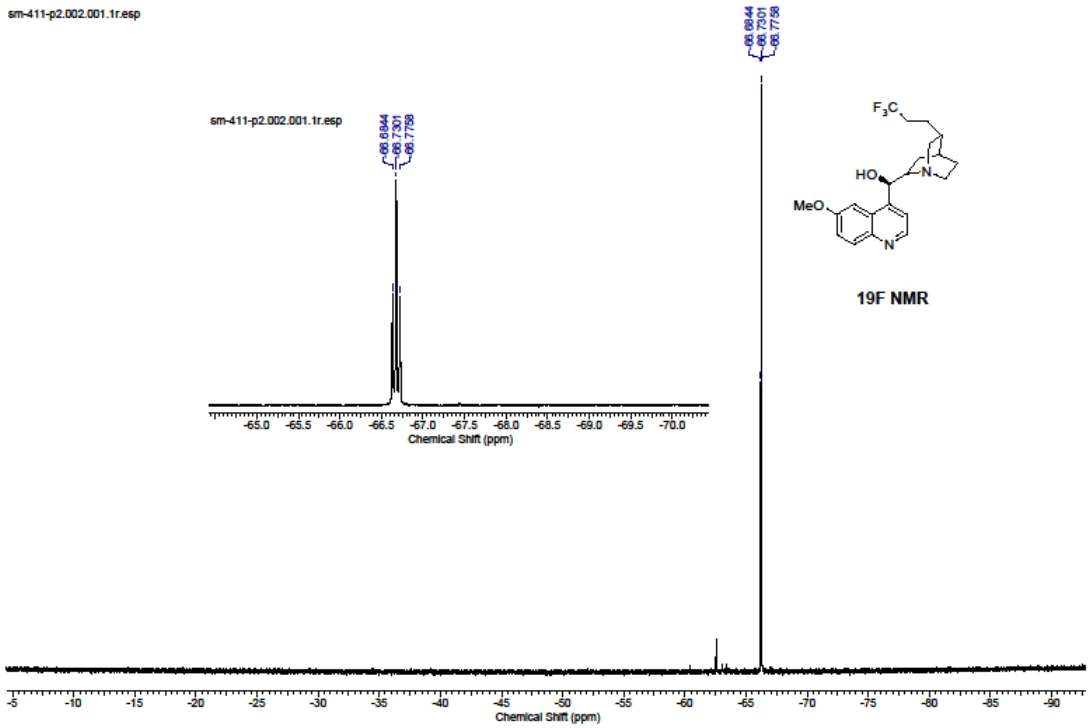


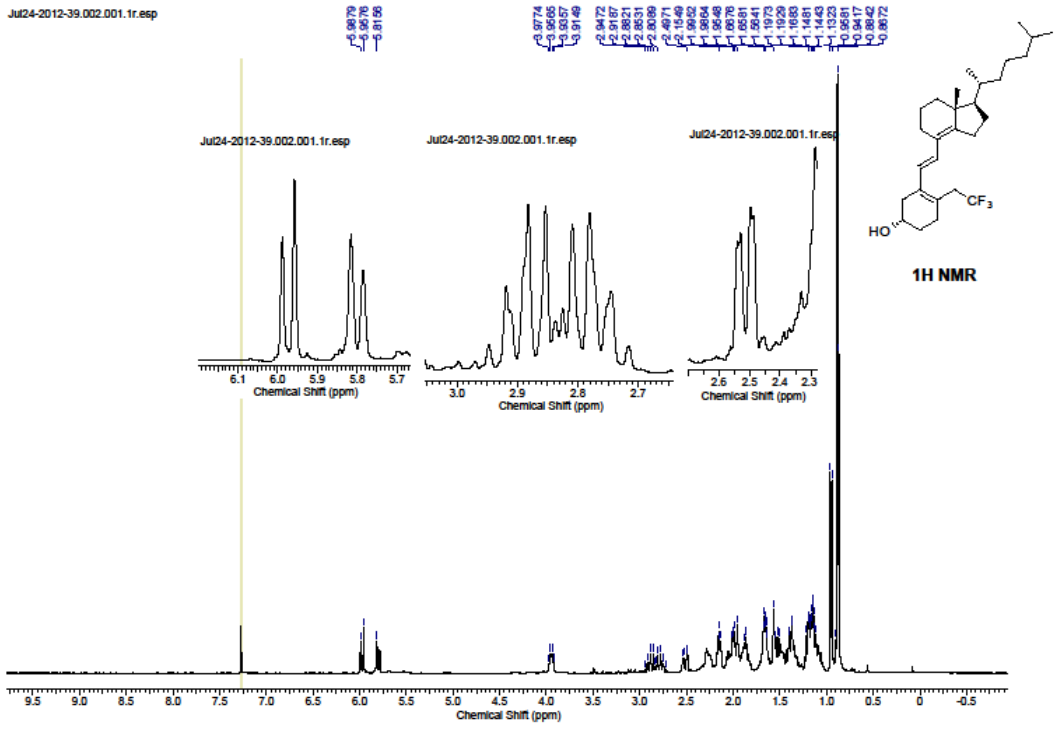

sm07542707.002.001.1r.esp
CF3
sm07542707.002.001.1r.esp
sm07542707.002.001.1r.esp
sm07542707.002.001.1r.esp
13C NMR
Chemical Shift (ppm)

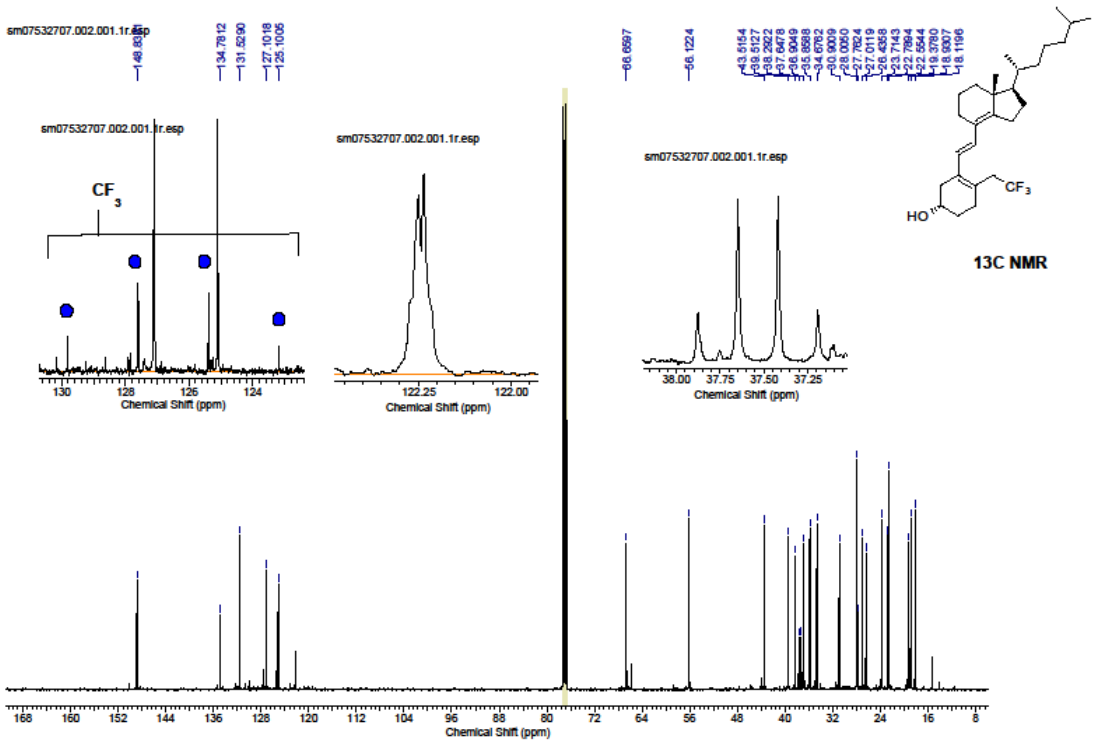

Nov28-2012-51.002.001.1r.esp
Nov28-2012-51.003.001.1r.esp
19F NMR
with 1H/19F decoupling
19F NMR
Chemical Shift (ppm)

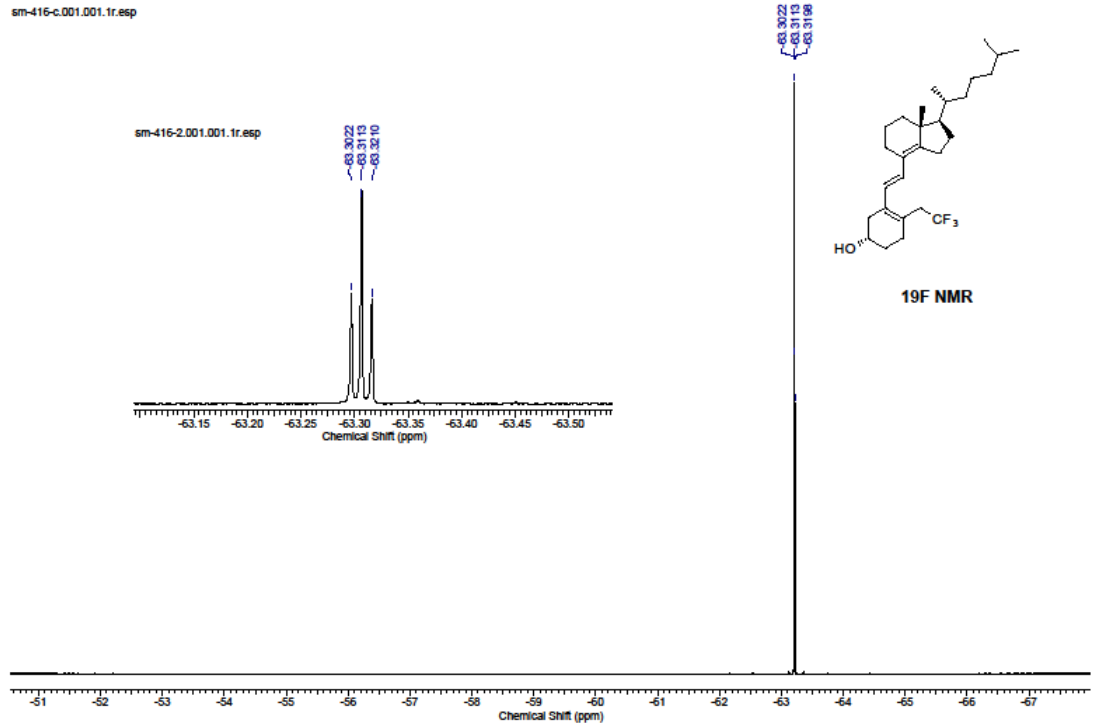

sm11721708.001.001.1r.esp
1H NMR
Chemical Shift (ppm)

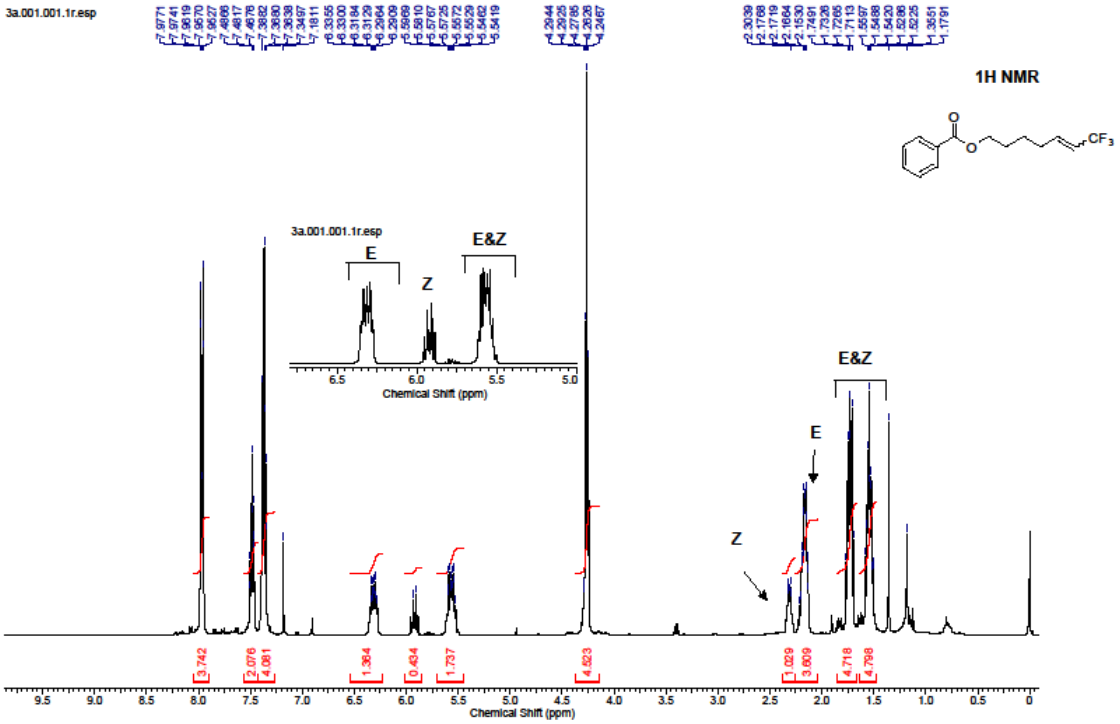

sm11721708.002.001.1r.esp
CF3
13C NMR
Chemical Shift (ppm)

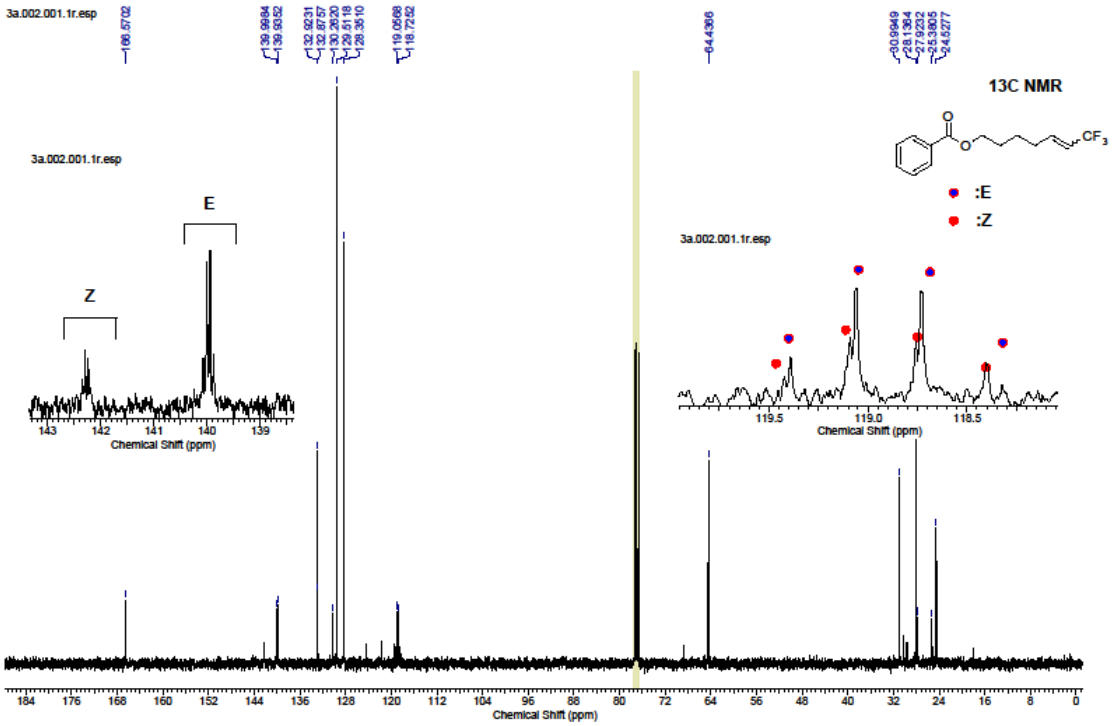

sm-411-p2.002.001.1r.esp
-66.6944
-66.7301
-66.7758
sm-411-p2.002.001.1r.esp
-66.6944
-66.7301
-66.7758
-65.0 -65.5 -66.0 -66.5 -67.0 -67.5 -68.0 -68.5 -69.0 -69.5 -70.0
Chemical Shift (ppm)
F3C
HO
N
MeO
N
19F NMR
-5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90
Chemical Shift (ppm)

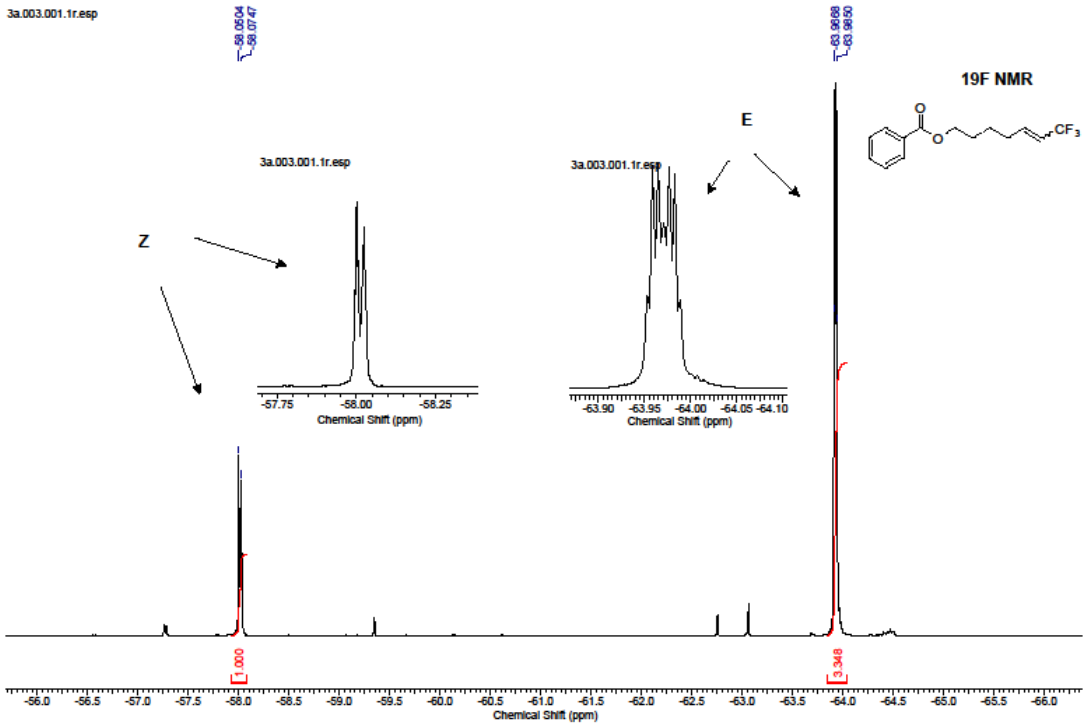

Jul24-2012-39.002.001.1r.esp
5.9879
5.9676
5.8156
3.9774
3.9565
3.9357
3.9149
2.9472
2.9167
2.8821
2.8531
2.8089
2.4971
2.1549
1.9952
1.9864
1.9648
1.9576
1.6591
1.5941
1.1973
1.1929
1.1683
1.1481
1.1443
1.1323
0.9561
0.9417
0.9347
0.9172
Jul24-2012-39.002.001.1r.esp
6.1 6.0 5.9 5.8 5.7
Chemical Shift (ppm)
Jul24-2012-39.002.001.1r.esp
3.0 2.9 2.8 2.7
Chemical Shift (ppm)
Jul24-2012-39.002.001.1r.esp
2.6 2.5 2.4 2.3
Chemical Shift (ppm)
CF3
HO
1H NMR
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)

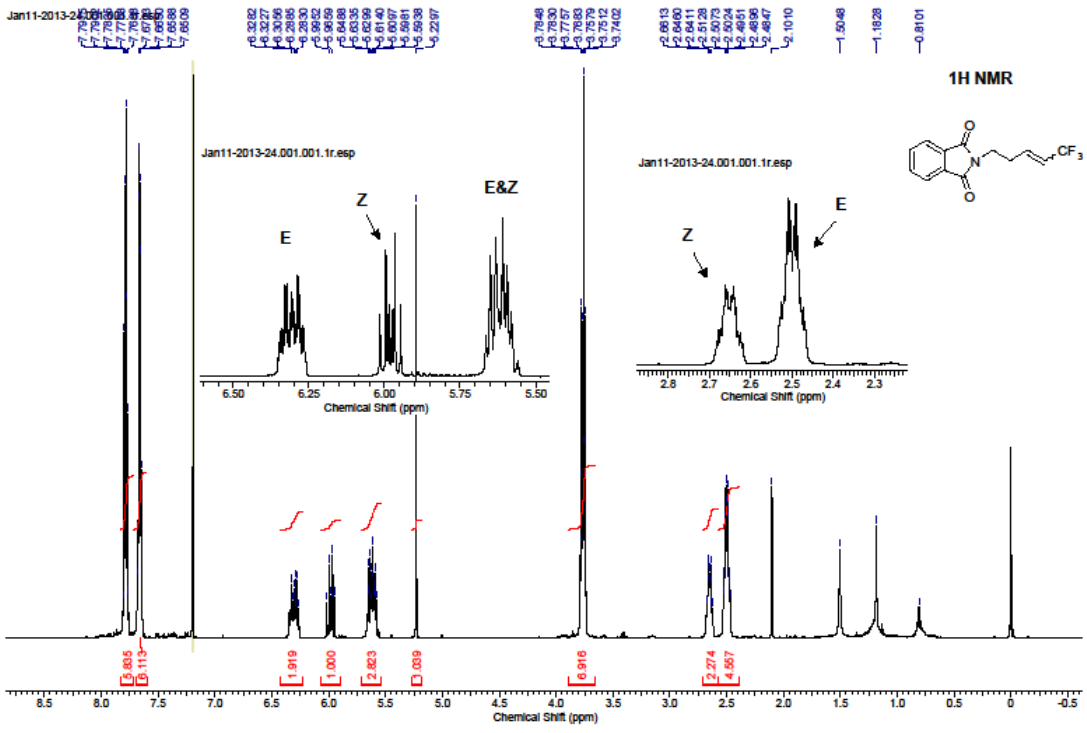

sm07532707.002.001.1r.esp
CF3
HO
13C NMR
Chemical Shift (ppm)

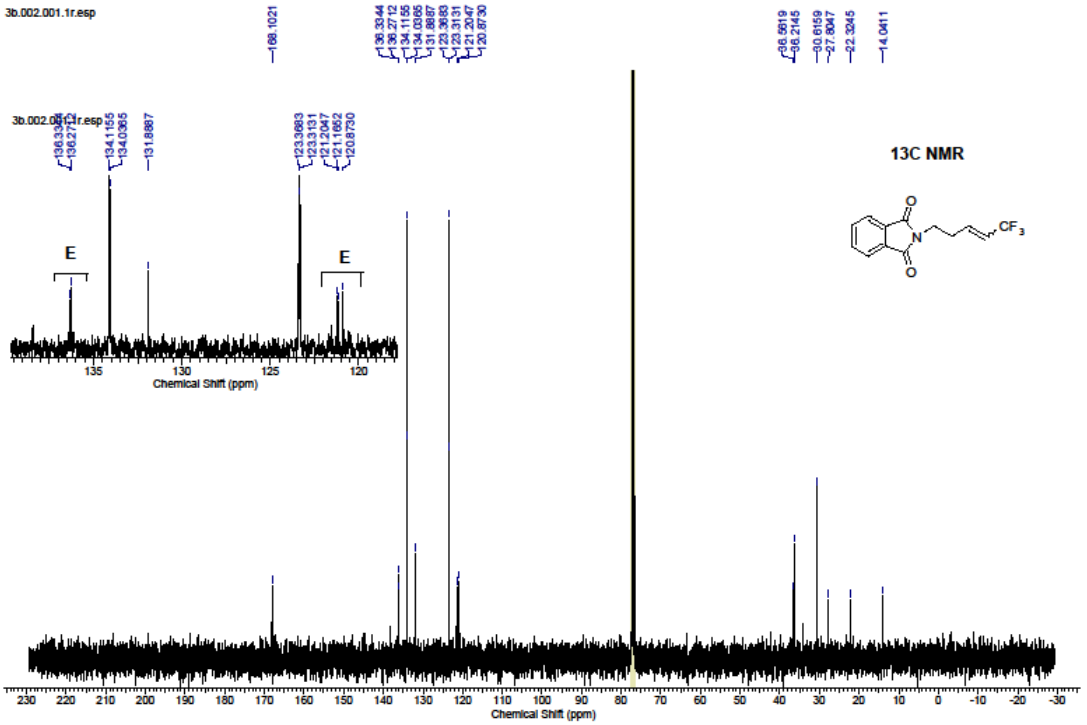

sm-416-c.001.001.1r.esp
sm-416-2.001.001.1r.esp
63.3022
63.3113
63.3198
63.3210
CF3
HO
19F NMR
Chemical Shift (ppm)


3a.001.001.1r.esp
1H NMR
E
Z
E&Z
Chemical Shift (ppm)


3a.002.001.1r.esp
13C NMR
E
Z
:E
:Z
Chemical Shift (ppm)


3a.003.001.1r.esp
19F NMR
E
Z
3a.003.001.1r.esp
3a.003.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)


1H NMR
Jan11-2013-24.001.001.1r.esp
Jan11-2013-24.001.001.1r.esp
E
Z
E&Z
Z
E
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)


3b.002.001.1r.esp
168.1021
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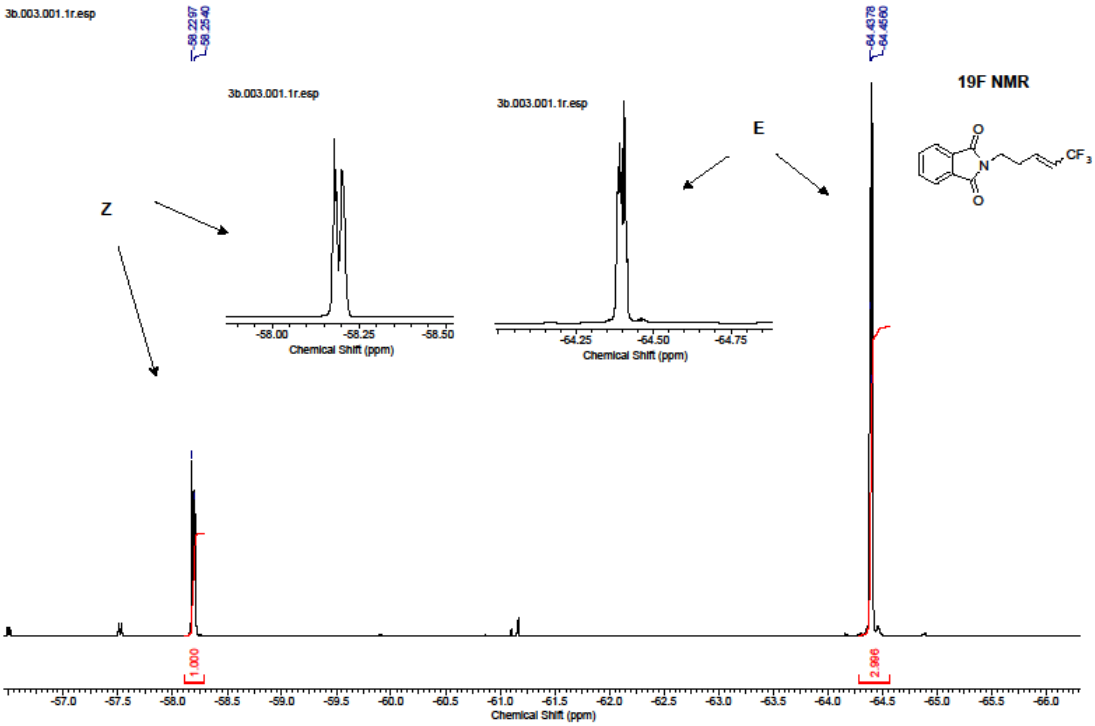
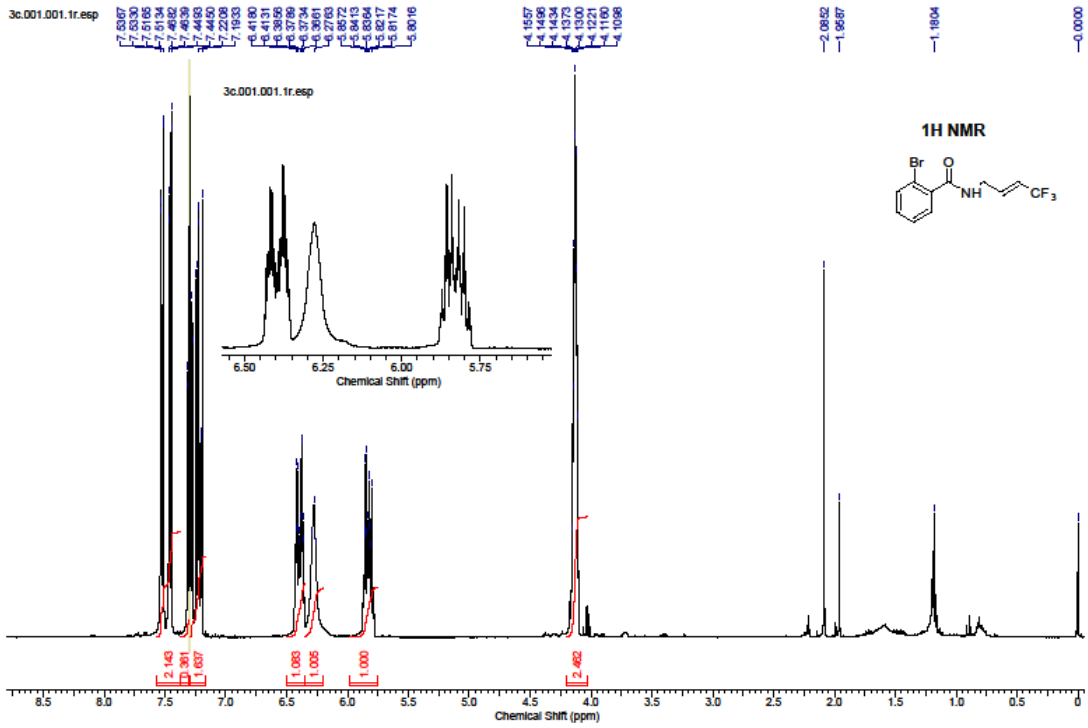
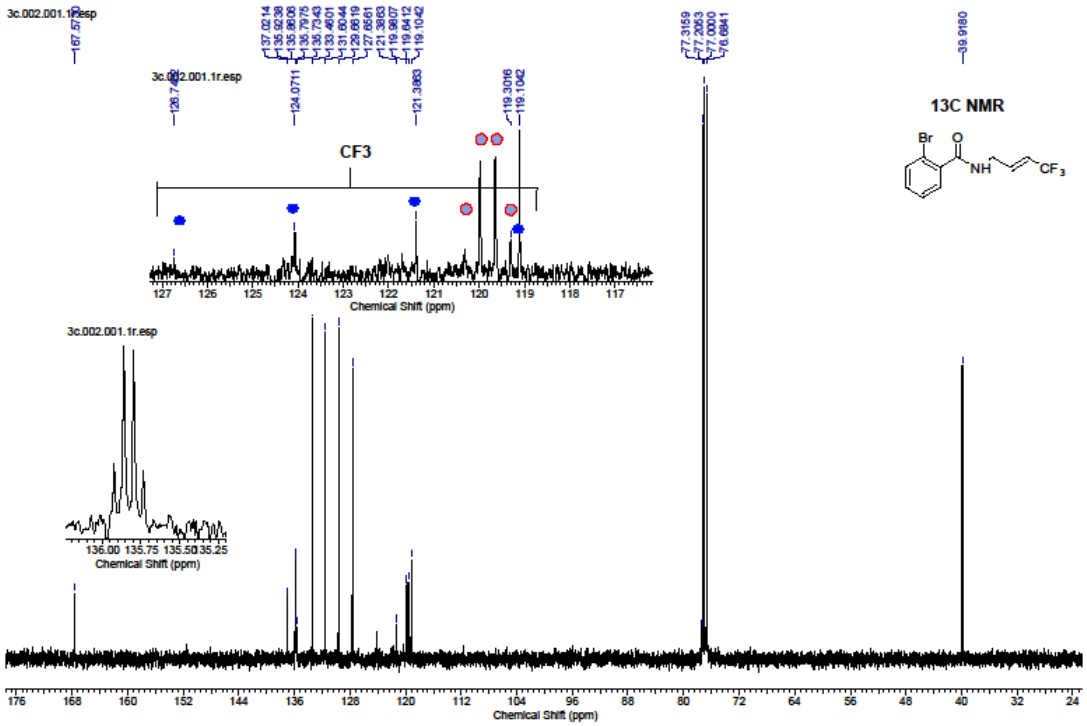
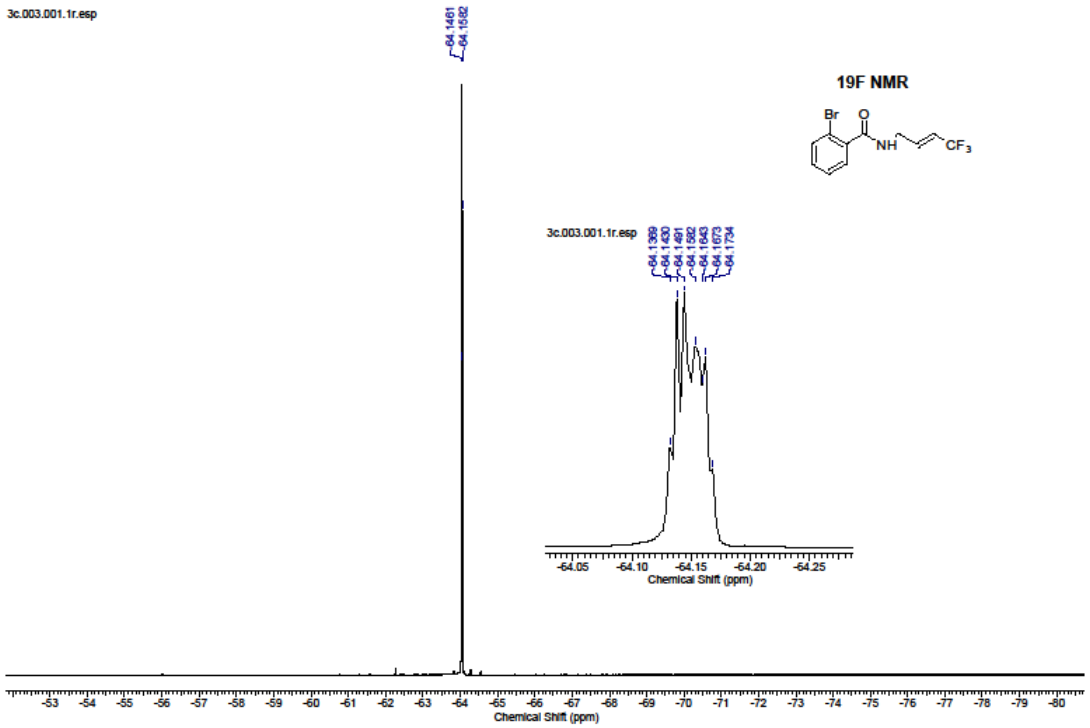
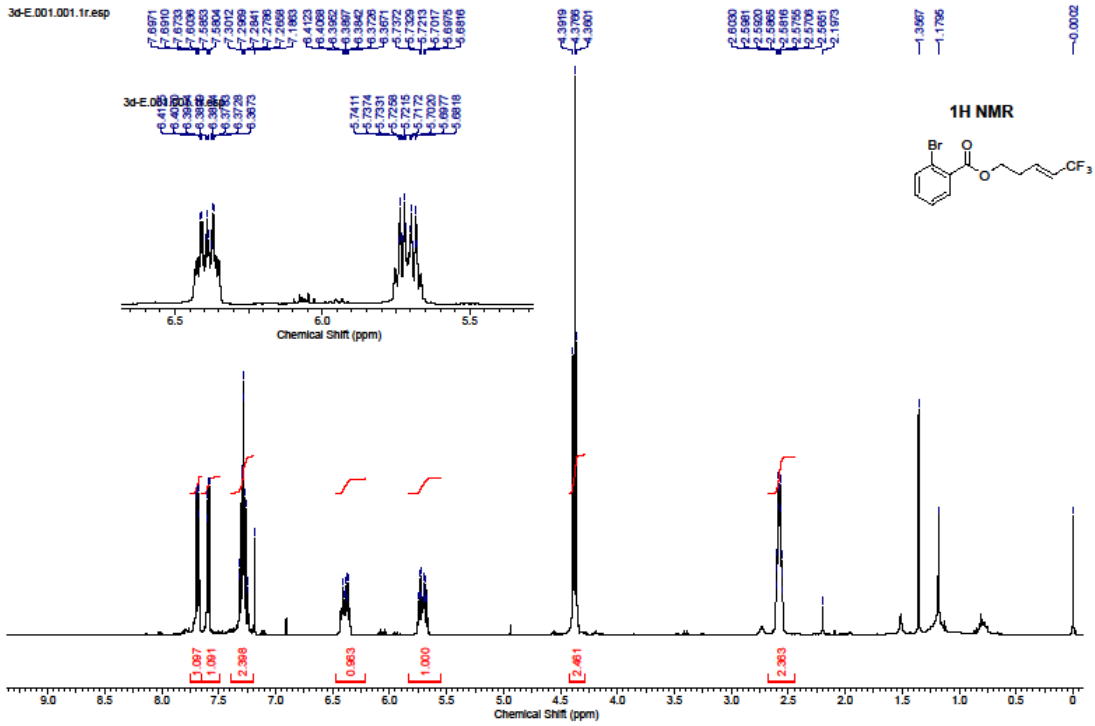
136.2712
134.1155
134.0365
131.8887
123.3683
123.3131
121.2047
121.1662
120.8730
86.5619
86.2145
30.6159
27.8047
22.3245
14.0411
E
E
13C NMR
Chemical Shift (ppm)

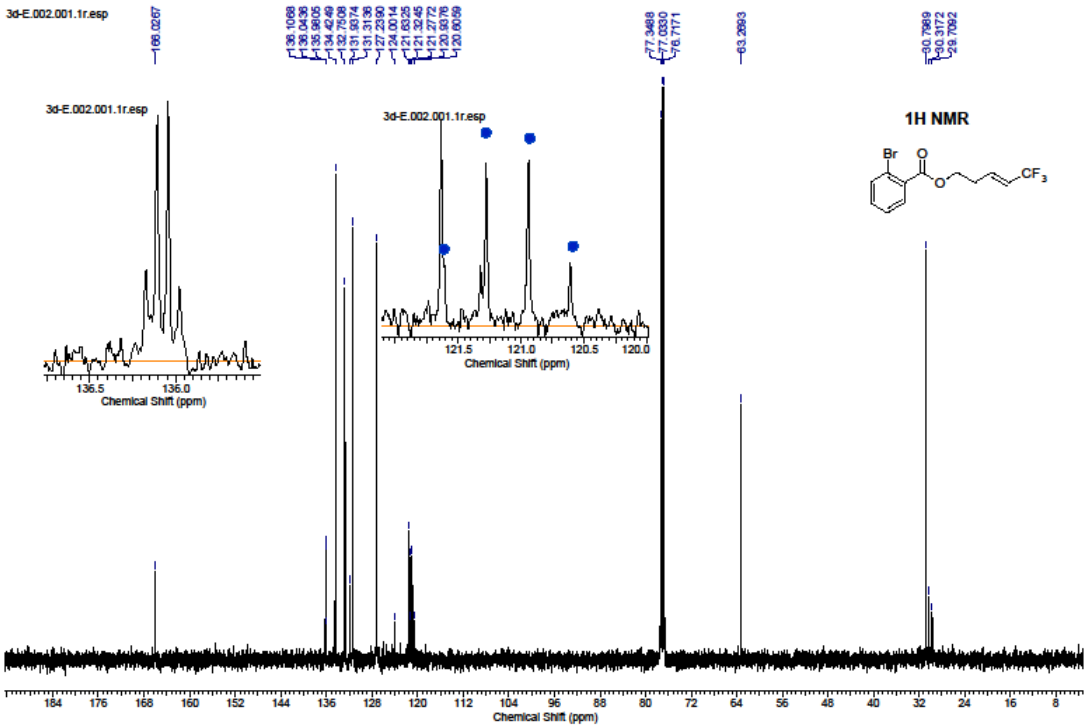

3b.003.001.1r.esp
-58.2297
-58.2540
-64.4378
-64.4660
Z
E
19F NMR
1.000
2.996
Chemical Shift (ppm)

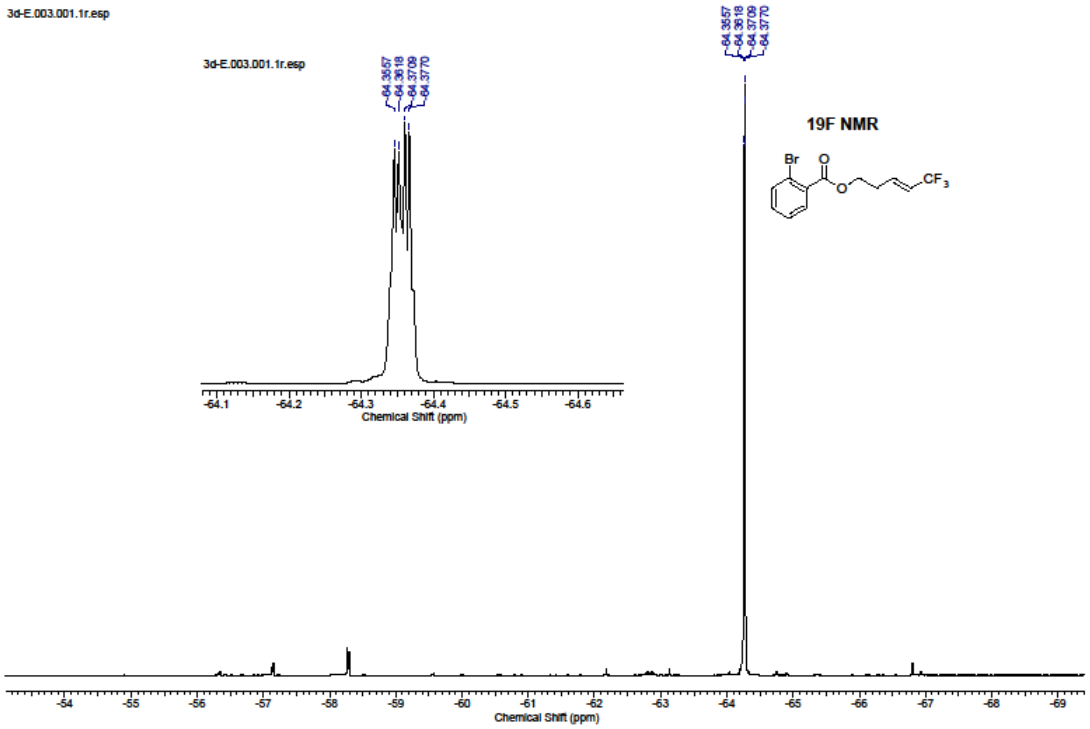

3c.001.001.1r.esp
1H NMR
Br
O
NH
CF3
Chemical Shift (ppm)

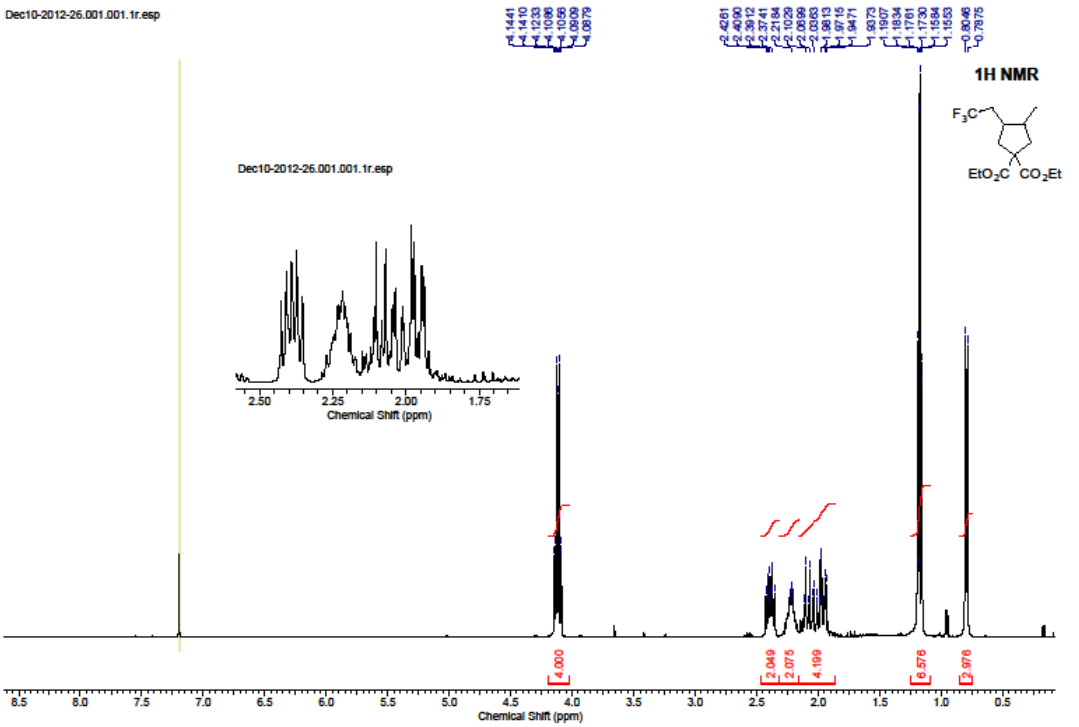

3c.002.001.1r.esp
13C NMR
CF3
Br
O
NH
CF3
Chemical Shift (ppm)

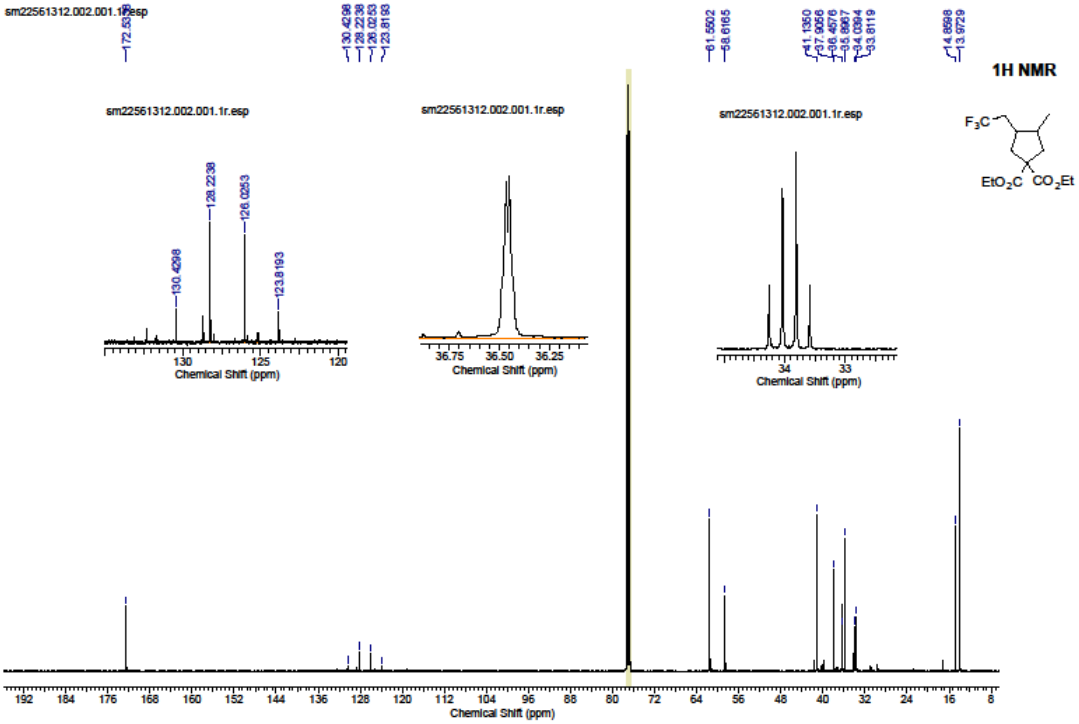

3c.003.001.1r.esp
19F NMR
Br
O
NH
CF3
3c.003.001.1r.esp
Chemical Shift (ppm)
Chemical Shift (ppm)

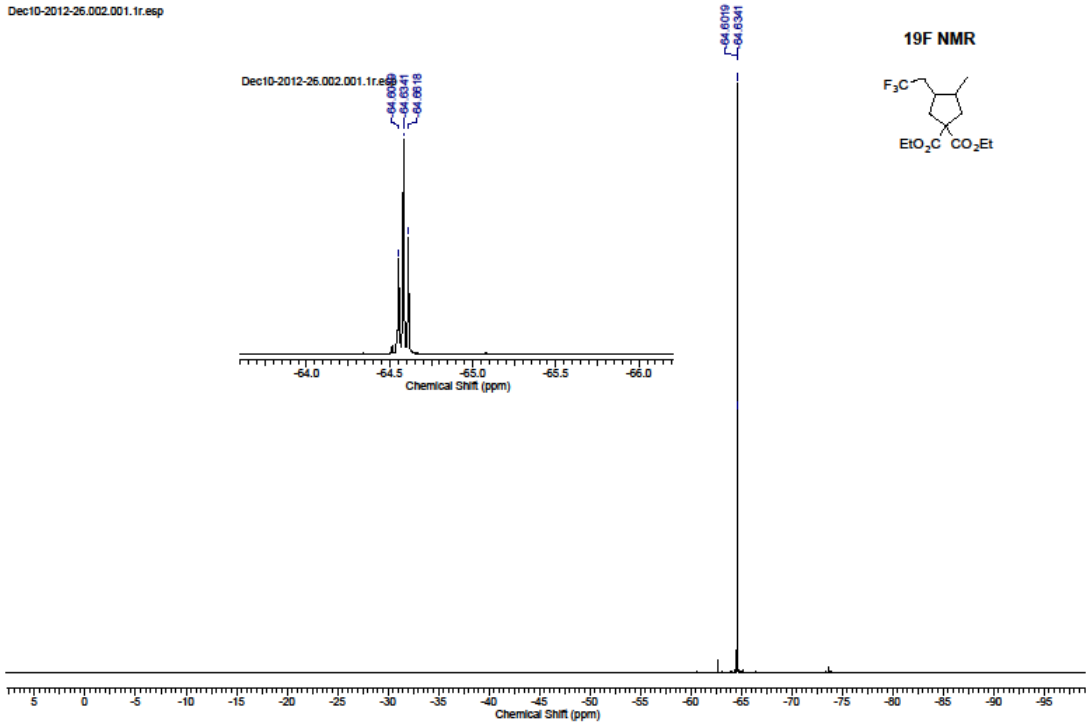

3d-E.001.001.1r.esp
1H NMR
Br
O
O
CF3
Chemical Shift (ppm)
Chemical Shift (ppm)

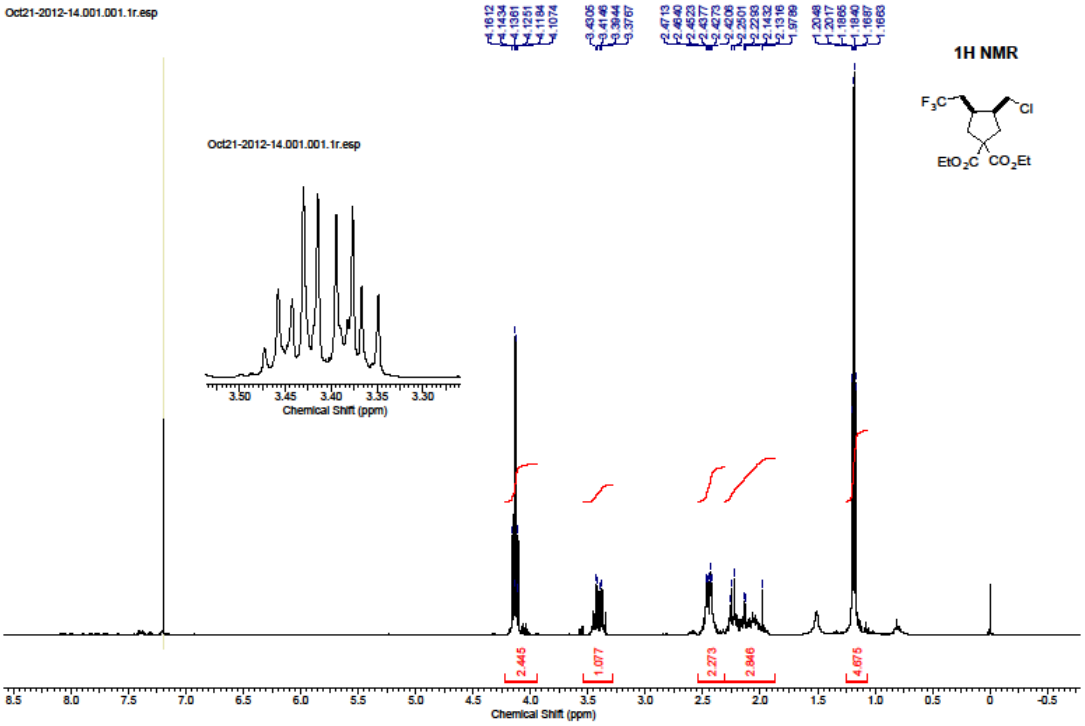

3d-E.002.001.1r.esp
166.0267
138.1068
136.0436
135.9805
134.4249
132.7508
131.9374
131.3136
127.2090
124.0014
121.6525
121.3245
121.2772
120.9376
120.6059
77.3488
77.0330
76.7171
63.2693
30.7989
30.3172
29.7092
1H NMR
Br
O
O
CF3
Chemical Shift (ppm)

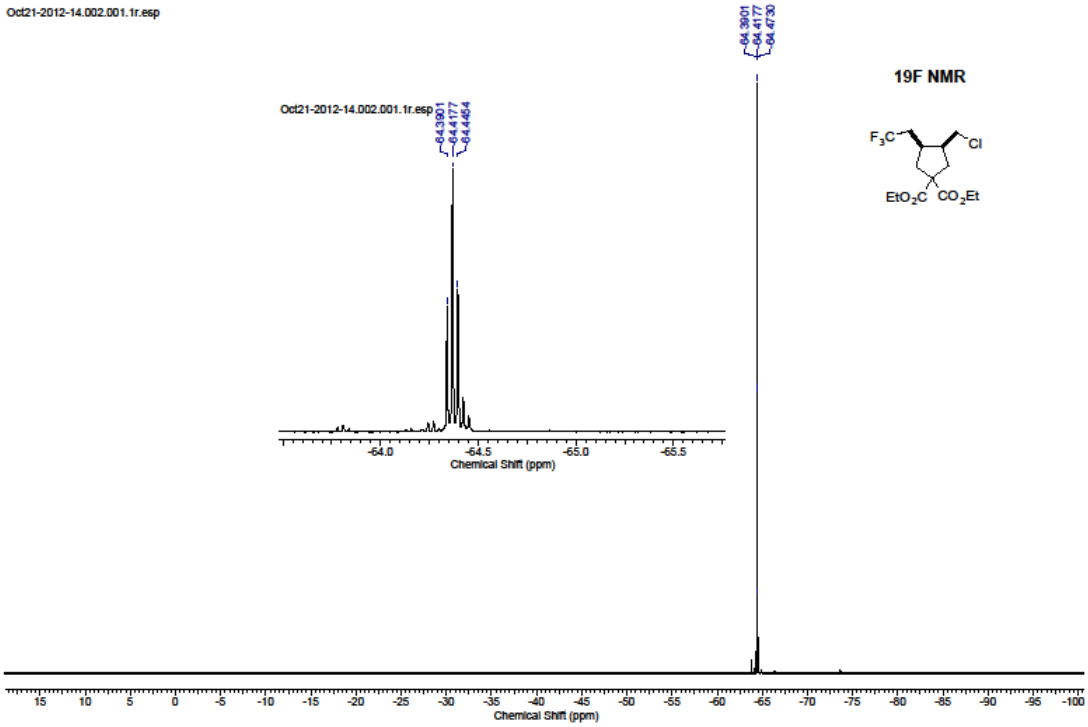

3d-E.003.001.1r.esp
64.3557
64.3618
64.3709
64.3770
19F NMR
Br
O
O
CF3
Chemical Shift (ppm)

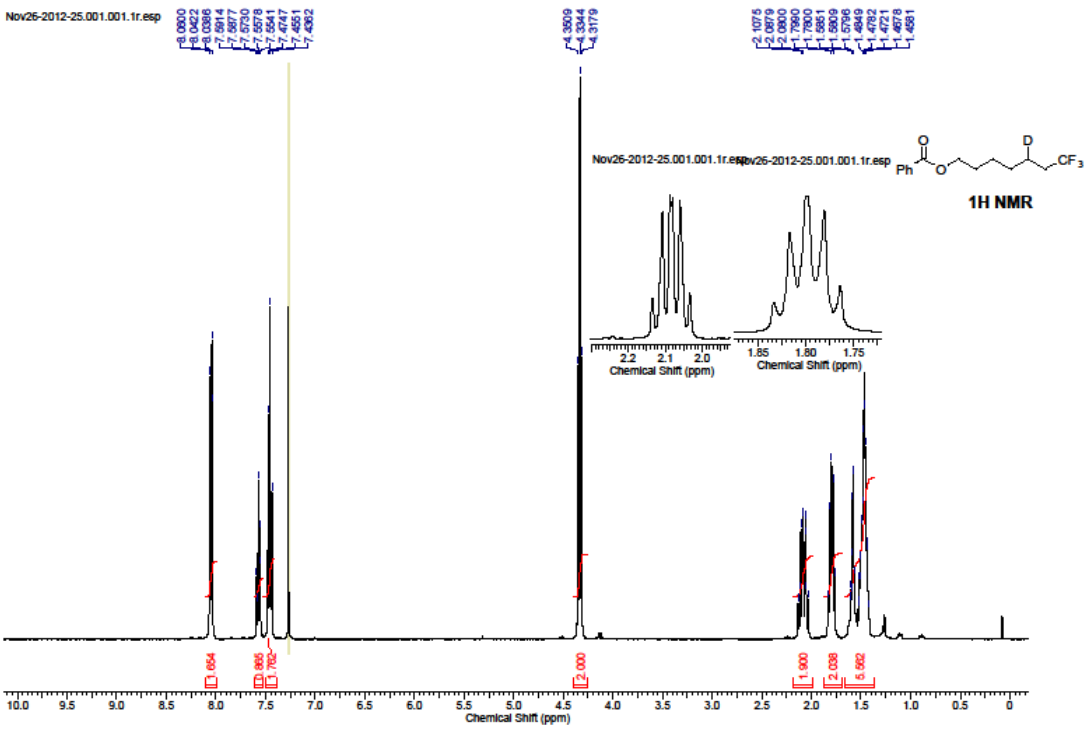

Dec10-2012-26.001.001.1r.esp
1H NMR
Chemical Shift (ppm)

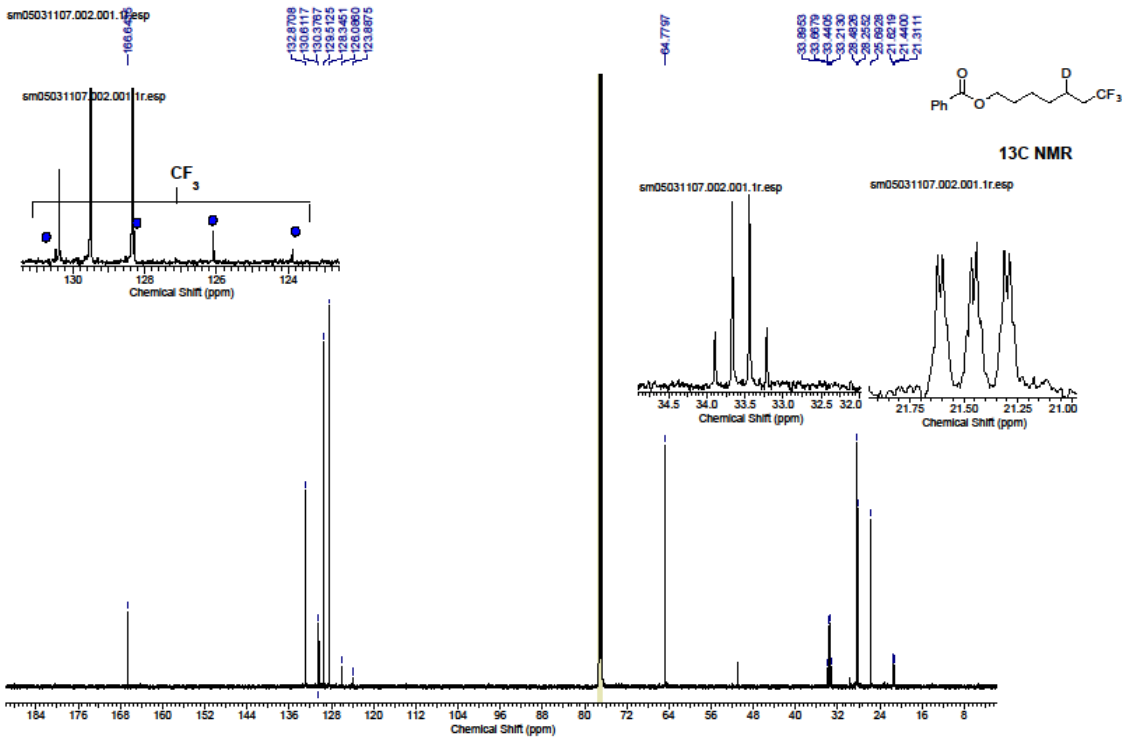

sm22561312.002.001.1r.esp
1H NMR
Chemical Shift (ppm)

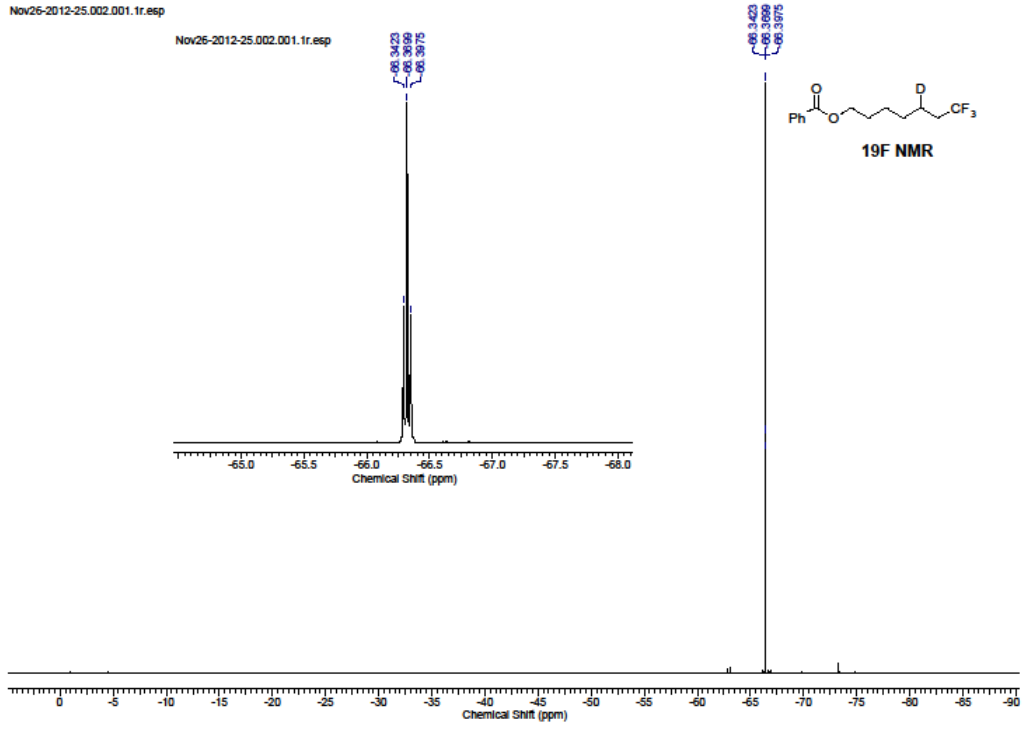

Dec10-2012-26.002.001.1r.esp
19F NMR
Chemical Shift (ppm)

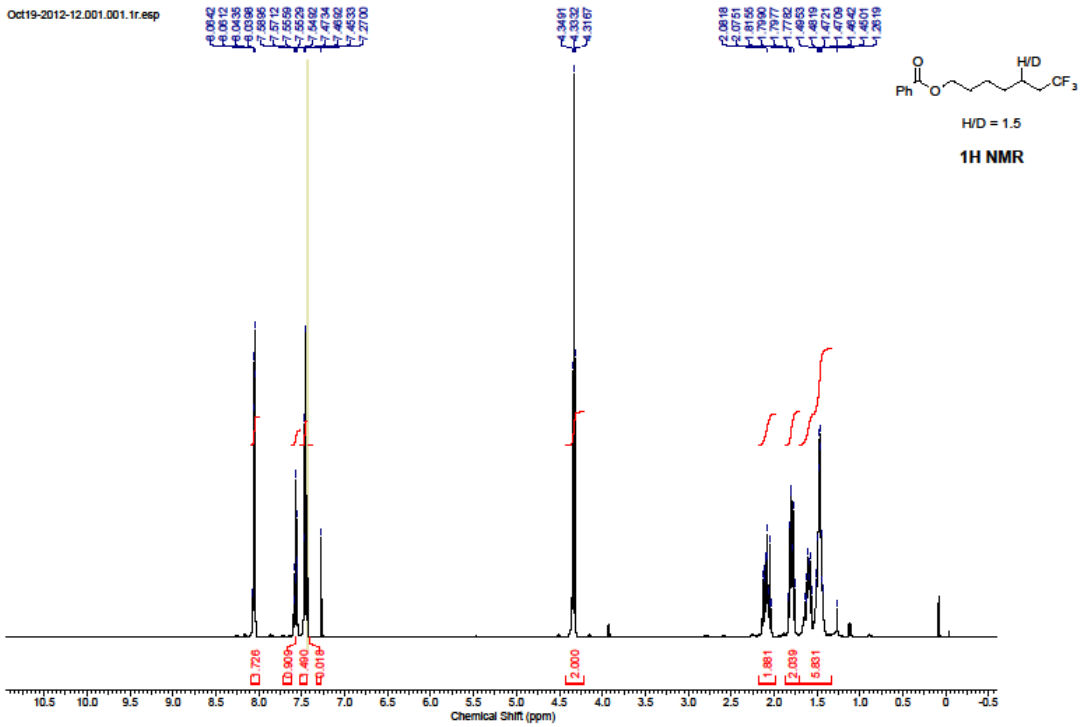

Oct21-2012-14.001.001.1r.esp
1H NMR
Chemical Shift (ppm)

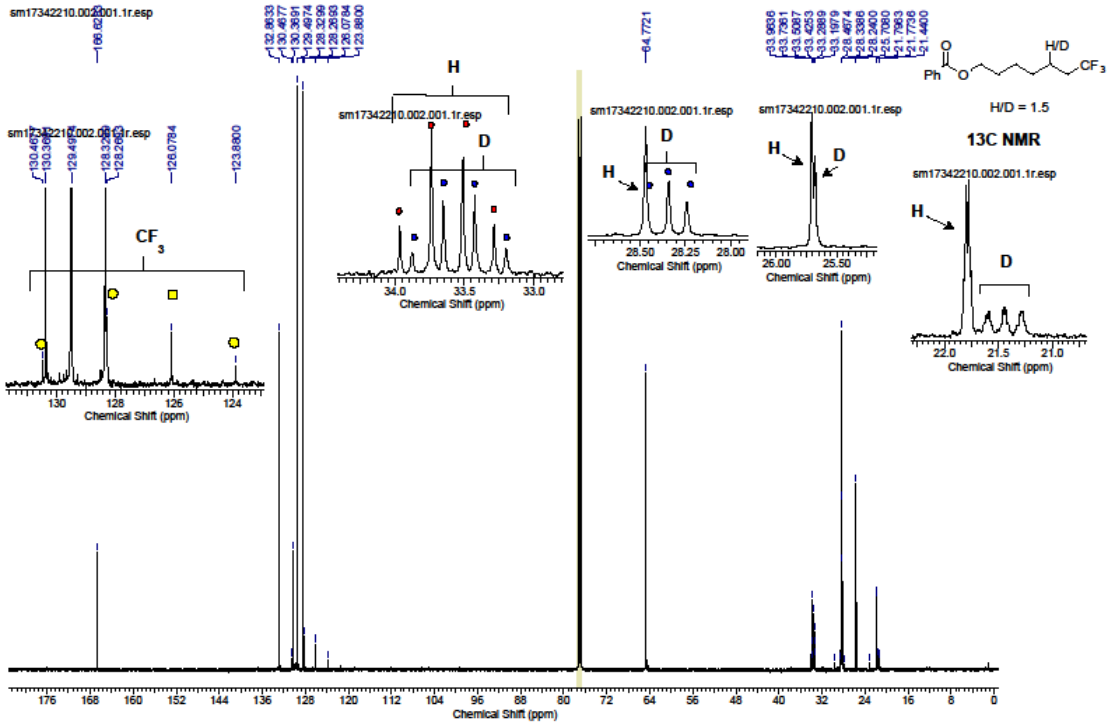

Oct21-2012-14.002.001.1r.esp
-64.3901
-64.4177
-64.4730
19F NMR
Oct21-2012-14.002.001.1r.esp
-64.3901
-64.4177
-64.4464
Chemical Shift (ppm)
Chemical Shift (ppm)

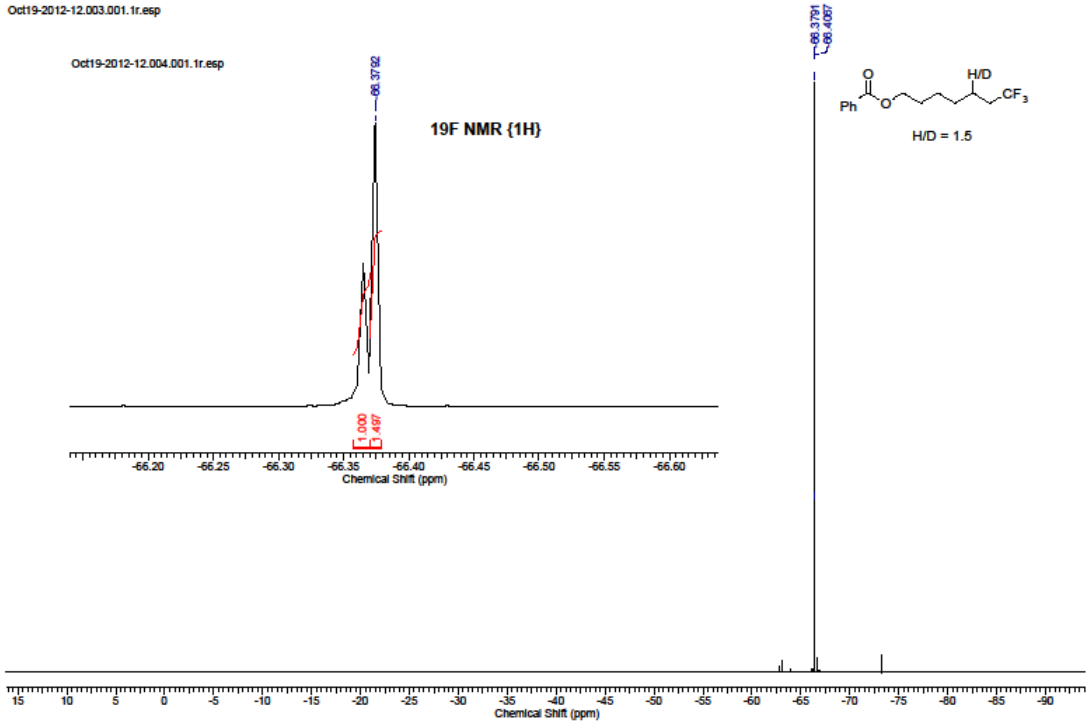

Nov26-2012-25.001.001.1r.esp
8.0900
8.0422
8.0386
7.5914
7.5877
7.5730
7.5578
7.5541
7.4747
7.4551
7.4362
4.3509
4.3344
4.3179
2.1075
2.0979
2.0900
1.7990
1.7900
1.5851
1.5809
1.5796
1.4949
1.4782
1.4721
1.4678
1.4561
Nov26-2012-25.001.001.1r.esp
Nov26-2012-25.001.001.1r.esp
1H NMR
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)


sm05031107.002.001.1r.esp
132.8708
130.6117
130.3767
129.5125
128.3451
126.0860
123.8875
64.7797
33.8953
33.6679
33.4406
33.2130
28.4626
28.2552
25.6928
21.6219
21.4400
21.3111
Ph
O
O
D
CF3
13C NMR
CF3
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)


Nov26-2012-25.002.001.1r.esp
-66.3423
-66.3999
-66.3975
Ph
O
O
D
CF3
19F NMR
Chemical Shift (ppm)
Chemical Shift (ppm)


Oct19-2012-12.001.001.1r.esp
H/D = 1.5
1H NMR
Chemical Shift (ppm)


H/D = 1.5
13C NMR
CF3
H
D
Chemical Shift (ppm)


Oct19-2012-12.003.001.1r.esp
Oct19-2012-12.004.001.1r.esp
19F NMR {1H}
-66.3792
-66.3791
-66.4067
1.000
1.497
Chemical Shift (ppm)
Chemical Shift (ppm)
H/D
CF3
Ph
O
O
H/D = 1.5