Supporting Information

A Versatile Catalyst-free Perfluoroaryl Azide-Aldehyde-Amine Conjugation Reaction

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GENERAL PROCEDURES

All reagents and solvents were used as received from Sigma Aldrich or Alfa Aesar. Thin-layer chromatography was conducted using TLC silica gel 60 F_{254} (Merck Co.), visualized under ultraviolet light. ^{1}H, ^{13}C and ^{19}F NMR data were recorded on Bruker Ascend™ 400 or DMX 500 instruments. Chemical shifts are reported as δ values (ppm) with (residual) solvent internal standard. ^{19}F NMR signals were referenced to hexafluorobenzene (δ = -161.75 in $CDCl_3$ or -162.65 in DMSO-d_6) unless noted otherwise. High resolution electrospray ionization (HRMS-ESI) mass spectrometry data were obtained from Proteoomika tuumiklabor at the University of Tartu, Estonia, or from the Mass Spectrometry Lab at the University of Illinois at Urbana–Champaign. IR spectra were recorded with a ReactIR™ IC10 (Mettler Toledo Co.) for liquid samples, or a SPECTRUM 2000 (Perkin Elmer) for solid samples in the ATR mode.

Fluorescence spectra were recorded on a Varian Cary Eclipse fluorescence spectrophotometer. Particle size measurements were performed on a Malvern Zetasizer Nano ZS with a backscattering angle of 173°. Transmission electron microscopy (TEM) images were obtained on a Phillips EM-400 TEM microscope operating at an accelerating voltage of 100 kV. Thermogravimetric analysis (TGA) was carried on a TA instrument (Q-50 series). Analysis of TGA data followed previously reported method.[1]

XPS spectra were taken on a Surface Science Instruments S-probe spectrometer.[2] This instrument has a monochromatized Al Kα X-ray and a low energy electron flood gun for charge neutralization of non-conducting samples. All samples were then mounted to the sample holder with double sided tape and run as insulators. The X-ray spot size for these acquisitions was approximately 800 μm. Pressure in the analytical chamber during spectral acquisition was less than 5 x 10^{-9} Torr. The pass energy for survey spectra (to calculate composition) was 150 eV and pass energy for high resolution scans was 50 eV. The Service Physics ESCA Hawk data analysis software was used to determine peak areas, to calculate the elemental compositions from peak areas above a linear background, and to peak fit the high resolution spectra. The binding energy scales of the high-resolution spectra were

calibrated by assigning the lowest binding energy of the C1s high-resolution component at 285.0 eV. Three spots were analyzed on each sample.

COMPOUND SYNTHESIS AND CHARACTERIZATION

General procedure for amidine synthesis. To a solution of an aldehyde (0.55 mmol) and an amine (0.55 mmol) in solvent (0.5 mL), the azide (0.50 mmol) in solvent (0.5 mL) was added dropwise while stirring. The reaction was followed by ^{1}H NMR by taking an aliquot (20 µL) of the crude solution and diluted in $CDCl_3$ (500 µL). When NMR indicated full conversion, silica gel (200 mg) was added to the reaction mixture and the mixture was dried under reduced pressure. When DMSO and DMF were used as the reaction solvent, the reaction mixture was added to the column directly. The crude product was further purified by flash column chromatography.

Methyl (*E*)-2,3,5,6-tetrafluoro-4-((2-phenyl-1-(piperidin-1-yl)ethylidene)amino)benzoate (**5a**).[3] White solid (363 mg, 89%). R_f = 0.27 (hexanes/EtOAc = 9:1). ^{1}H NMR (500 MHz, DMSO): δ 1.33 (br, 4H, $CH_2CH_2CH_2$), 1.53 (br, 2H, $CH_2CH_2CH_2$), 3.50 (br, 4H, CH_2NCH_2), 3.76 (s, 2H, Ar-CH_2), 3.85 (s, 3H, OCH_3), 7.14 (d, 2H, Ar-H, J_{HH} = 7.5 Hz), 7.21 (t, 1H, Ar-H, J_{HH} = 7.5 Hz), 7.31 (t, 2H, Ar-H, J_{HH} = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.36, 25.58, 35.64, 46.55 (br, 2C), 52.71, 102.74-103.03 (m), 126.92, 127.64, 127.98, 134.71, 135.29 (m), 139.90 (dm, 2C, J_{CF} = 243.1 Hz), 145.93 (dm, 2C, J_{CF} = 256.7 Hz), 159.85, 161.23; ^{19}F NMR (376 MHz, DMSO-d_6): δ -141.80 (m, 2F), -153.79 (m, 2F); ESI-HRMS: Calcd. for $C_{21}H_{20}F_4N_2O_2$ $[M+H]^+$: 409.1534, found 409.1525.

Methyl (*E*)-2,3,5,6-tetrafluoro-4-((1-morpholino-2-phenylethylidene)amino)benzoate (**5b**).[3] White solid (370 mg, 90%). R_f = 0.25 (Hexanes/EtOAc = 5:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.55 (br, 8H, OCH_2CH_2N), 3.65 (s, 2H, Ar-CH_2), 3.92 (s, 3H, OCH_3), 7.11 (d, 2H, Ar-H, J_{HH} = 7.6 Hz), 7.23 (t, 1H, Ar-H, J_{HH} = 7.4 Hz), 7.31 (t, 2H, Ar-H, J_{HH} = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 35.38, 45.60 (br, 2C), 52.77, 66.40, 103.68 (t, J_{CF} = 15.3 Hz), 127.19, 127.54, 129.15, 134.15, 134.47(m), 139.7 (dm, 2C, J_{CF} = 243.1Hz), 145.79 (dm, 2C, J_{CF} = 255.1 Hz), 160.29, 161.03; ^{19}F NMR (376 MHz, $CDCl_3$): δ -141.07 (m, 2F), -152.97 (m, 2F); ESI-HRMS: Calcd. for $C_{20}H_{18}F_4N_2O_3$ $[M+H]^+$: 411.1326, found 411.13152.

Methyl (*E*)-2,3,5,6-tetrafluoro-4-((2-phenyl-1-(pyrrolidin-1-yl)ethylidene)amino)benzoate (**5c**).[3] White solid (383 mg, 97%). R_f = 0.20 (Hexanes/EtOAc = 9:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.91 (m, 4H, $CH_2CH_2CH_2CH_2$), 3.30 (t, 2H, $CH_2NH_2CH_2$, J_{HH} = 6.1 Hz), 3.66 (t, 2H, $CH_2NH_2CH_2$, J_{HH} = 6.1 Hz), 3.65 (s, 2H, Ar-CH_2), 3.92 (s, 3H, OCH_3), 7.08 (d, 2H, Ar-H, J_{HH} = 7.5 Hz), 7.21 (t, 1H, Ar-H, J_{HH} = 7.4 Hz), 7.27 (t, 2H, Ar-H, J_{HH} = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.48, 26.04, 37.01, 47.72 (d, 2C), 52.65, 102.91-103.14 (m), 126.94, 127.84, 128.92, 134.15, 135.23 (m), 140.14 (dm, 2C, J_{CF} = 240.7 Hz), 145.80 (dm, 2C, J_{CF} = 255.1 Hz), 159.23, 161.20; ^{19}F NMR (376 MHz, $CDCl_3$): δ -141.57 (m, 2F), -153.10 (m, 2F); ESI-HRMS: Calcd. for $C_{20}H_{18}F_4N_2O_2$ $[M+H]^+$: 395.1377, found 395.13652.

Methyl (*E*)-4-((1-(diethylamino)-2-phenylethylidene)amino)-2,3,5,6-tetrafluorobenzoate (**5d**).[3] White-yellow solid (328 mg, 83%). R_f = 0.38 (Hexanes/EtOAc = 5:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.01 (br, 3H, CH_2CH_3), 1.29 (br, 3H, CH_2CH_3), 3.27 (br, 2H, $CH_2NH_2CH_2$), 3.60 (br, 2H, $CH_2NH_2CH_2$), 3.67 (s, 2H, Ar-CH_2), 3.94 (s, 3H, OCH_3), 7.12 (d, 2H, Ar-H, J_{HH} = 7.4 Hz), 7.24 (t, 1H, Ar-H, J_{HH} = 7.5 Hz), 7.31(t, 2H, Ar-H, J_{HH} = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.80, 14.07, 35.50, 42.40-43.46 (br, 2C), 52.62, 102.65-103.88 (m), 126.95, 127.55, 128.96, 134.75, 135.37 (m), 139.02-139.13 and 140.93-141.04 (d, 2C, J_{CF} = 239.9Hz), 144.91 and 146.88 (d, 2C, J_{CF} = 255.8 Hz), 159.49, 161.23; ^{19}F NMR (376 MHz, $CDCl_3$): δ -141.64 (m, 2F), -153.54 (m, 2F); ESI-HRMS: Calcd. for $C_{20}H_{20}F_4N_2O_2$ $[M+H]^+$: 397.1534, found 397.15246.

Methyl (*E*)-2,3,5,6-tetrafluoro-4-((1-(phenethylamino)-2-phenylethylidene)amino)benzoate (**5e**). To a solution of phenylacetaldehyde (2.5 mmol) and azide (2.0 mmol) in MeOH (12 mL), the amine (2.1 mmol) in MeOH (2 mL) was added dropwise at 40 ºC. When NMR indicated full conversion (~ 4 h), silica gel (1.5 g) was added to the reaction mixture and the mixture was dried under reduced pressure. The crude was further purified by flash column chromatography using hexanes/EtOAc 5:1 (R_f = 0.29) as the eluent to provide the title compound as a white solid (671 mg, 91%). ^{1}H NMR (400 MHz, DMSO): δ 3.66 (s, 2H), 2.90 (t, 2H, J_{HH} = 7.2 Hz), 3.49 (br, 2H), 3.55 (dt, 2H, J_{HH} = 6.0, 6.8 Hz), 3.86 (s, 3H, OCH_3), 6.91 (m, 2H), 7.15-7.32 (m, 8H, Ar-H), 8.03 (t, 1H, N*H*, J_{HH} = 5.1 Hz); ^{13}C NMR (100 MHz, DMSO): δ 33.76, 38.44, 42.43, 54.96, 101.92-102.22 (m), 126.42, 126.13, 128.29, 128.33, 128.21, 128.76, 135.26, 135.47 (m), 139.54, 139.58 (dm, 2C, J_{CF} =240.9 Hz), 145.11 (dm, 2C, J_{CF} = 254.0 Hz), 160.25, 160.63; ^{19}F NMR (376 MHz, DMSO): δ -142.28 (m, 2F), -153.13 (m, 2F); ESI-HRMS: Calcd. for $C_{24}H_{21}F_4N_2O_2$ $[M+H]^+$: 444.1534, found 445.1526; IR (ATR) see attached spectra.

(*Z*)-(2-phenyl-1-((2,3,5,6-tetrafluoro-4-(methoxycarbonyl)phenyl)imino)ethyl)-D-alanine (**5f**). To a solution of phenylacetaldehyde (0.75 mmol) and azide (0.50 mmol) in DMSO/H_2O 3:1 (10 mL), alanine (0.75 mmol) was added and the mixture was stirred at 60 ºC. When NMR indicated full conversion (~ 4 h), the mixture was lyophilized. The crude was further purified by flash column chromatography using DCM/MeOH 19:1 (R_f = 0.20) as eluent to provide the title compound as a colorless oil (157 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02 (d, 3H, J_{HH} = 7.0 Hz), 3.51

(s, 2H), 3.93 (s, 3H), 4.63 (Quintet, 1H, J_{HH} = 6.7 Hz), 5.50 (d, 1H, J_{HH} = 6.0 Hz, N*H*), 7.12 (d, 2H, J_{HH} = 6.9 Hz), 7.30 (m, 3H), 7.75 (br, 1H, COO*H*); ^{13}C NMR (100 MHz, DMSO): δ 17.56, 35.80, 51.55, 54.96, 102.3 (m), 126.42, 126.13, 128.31, 128.35, 128.76, 135.26, 135.44, 139.54, 139.54 (dm, 2C, J_{CF} = 240.9 Hz), 145.10 (dm, 2C, J_{CF} = 254.0 Hz), 160.23, 160.56 173.53; ^{19}F NMR (376 MHz, $CDCl_3$): δ -140.97 (m, 2F), -152.00 (m, 2F); ESI-HRMS: Calcd. for $C_{19}H_{17}F_4N_2O_4$ $[M+H]^+$: 413.1124, found 413.1121; IR (ATR) see attached spectra.

Methyl (*E*)-2,3,5,6-tetrafluoro-4-((2-phenyl-1-(phenylamino)ethylidene)amino)benzoate (**5g**). To a solution of phenylacetaldehyde (2.5 mmol) and azide (2.0 mmol) in MeOH (6 mL), aniline (2.5 mmol) in MeOH (2 mL) was added dropwise at 40 °C. When NMR indicated full conversion (~12 h), silica gel (1.3 g) was added to the reaction mixture and the mixture was dried under reduced pressure. The crude product was further purified by flash column chromatography using hexanes/EtOAc 4:1 (R_f = 0.31) as eluent to provide the title compound as a pale yellow solid (337 mg, 81%). ^{1}H NMR(400 MHz, $CDCl_3$): δ 3.66 (s, 2H), 3.96 (s, 3H, O*CH*$_3$), 6.50 (br, 1H, Ph-N*H*), 7.09 (t, 1H, Ar-H, J_{HH} = 7.7 Hz), 7.23-7.39 (m, 7H, Ar-H), 7.48 (d, 2H, Ar-H, J_{HH} = 7.7 Hz); ^{13}C NMR(100 MHz, $CDCl_3$): δ 39.65, 52.99, 104.52 (m), 120.91,124.59, 128.19, 129.01, 129.49, 129.55, 133.67, 138.38, 133.37 (m), 139.55 (dm, 2C, J_{CF} = 243 Hz), 145.18 (dm, 2C, J_{CF} = 254 Hz), 157.32, 161.10; ^{19}F NMR(376 MHz, $CDCl_3$): δ -140.83 (m, 2F), -152.02 (m, 2F); ESI-HRMS: Calcd. for $C_{22}H_{17}F_4N_2O_2$ $[M+H]^+$: 417.1221, found 417.1220; IR (ATR) see attached spectra.

Methyl (*E*)-4-((1-(diphenylamino)-2-phenylethylidene)amino)-2,3,5,6-tetrafluorobenzoate (**5h**). Pale greenish solid (364 mg, 74%). R_f = 0.17 (Hexanes/EtOAc = 9:1). ^{1}H NMR (400 MHz, DMSO): δ 3.77 (s, 2H), 3.84 (s, 3H, O*CH*$_3$), 6.95 (d, 2H, Ar-H, J_{HH} = 7.6 Hz), 7.17-7.24 (m, 9H, Ar-H), 7.35 (t, 4H, J_{HH} = 7.6 Hz); ^{13}C NMR (100 MHz, DMSO): δ 38.22, 52.98, 103.00 (m), 116.70, 119.64, 126.69, 126.98, 127.68, 128.08, 128.73, 129.18, 129.65, 134.87, 133.36 (m), 138.44 (dm, 2C, J_{CF} = 243.6 Hz), 143.41, 144.83 (dm, 2C, J_{CF} = 254.8 Hz), 159.96, 162.23; ^{19}F NMR (376 MHz, DMSO): δ -141.81 (m, 2F), -152.05 (m, 2F); ESI-HRMS: Calcd. for $C_{28}H_{21}F_4N_2O_2$ $[M+H]^+$: 493.1534, found $[M+H]^+$ 493.1515; IR (ATR) see attached spectra.

Methyl (*E*)-2,3,5,6-tetrafluoro-4-((1-(piperidin-1-yl)butylidene)amino)benzoate (**5i**). To a solution of aldehyde (1.2 mmol) and azide (1.0 mmol) in MeOH (6 mL), piperidine (1.1 mmol) in MeOH (2 mL) was added dropwise while stirring at 40 °C. When NMR indicated full conversion (~4 h), silica gel (0.8 g) was added to the reaction mixture. The mixture was dried under reduced pressure. The obtained crude product was further purified by flash column chromatography using hexanes/EtOAc 9:1 (R_f = 0.32) as the eluent to provide the title compounds as a white solid (310 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (t, 3H, J_{HH} = 7.3 Hz), 1.45 (Sextet, 2H, J_{HH} = 7.7 Hz), 1.62 (m, 4H), 1.68 (m, 2H), 2.17 (t, 2H, J_{HH} = 7.7 Hz), 3.55 (m, 4H), 3.93 (s, 3H, O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.89, 20.33, 24.68, 26.10, 31.41, 46.55 (br), 52.79, 102.60 (m), 135.82 (m), 139.73 (dm, 2C, J_{CF} = 240 Hz), 145.92 (dm, 2C, J_{CF} = 254 Hz), 161.50, 162.48; ^{19}F NMR (376 MHz, $CDCl_3$): δ -141.77 (m, 2F), -153.76 (m, 2F); ESI-HRMS: Calcd. for $C_{17}H_{21}F_4N_2O_2$ $[M+H]^+$: 360.1539, found 360.1538; IR (ATR) see attached spectra.

Methyl (*E*)-2,3,5,6-tetrafluoro-4-((3-phenyl-1-(piperidin-1-yl)propylidene)amino)benzoate (**5j**). White solid (299 mg, 71%). R_f = 0.38 (hexanes/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.59 (m, 4H), 1.67 (m, 2H), 2.52 (m, 2H), 2.71 (m, 2H), 3.56 (m, 4H), 3.94 (s, 3H, O*CH*$_3$), 7.03 (dm, 2H, J_{HH} = 7.0 Hz), 7.20 (m, 1H), 7.26 (tm, 2H, J_{HH} = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.58, 25.99, 31.12, 32.94, 46.59, 52.81, 102.80 (m), 126.77, 128.17, 128.78, 135.46 (m), 139.68 (dm, 2C, J_{CF} = 240 Hz), 146.03 (dm, 2C, J_{CF} = 256 Hz), 139.63, 161.41, 161.60; ^{19}F NMR(376 MHz, $CDCl_3$): δ -141.45 (m, 2F), -153.37 (m, 2F); ESI-HRMS: Calcd. for $C_{22}H_{22}F_4N_2O_2$ $[M]^+$: 422.1617, found 422.1617; IR (ATR) see attached spectra.

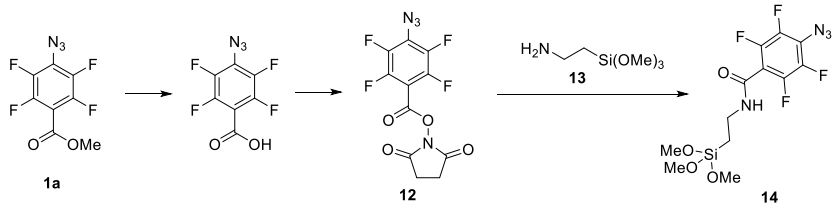
Methyl (*E*)-2,3,5,6-tetrafluoro-4-((2-methyl-1-(piperidin-1-yl)propylidene)amino)benzoate (**5k**). White solid (331 mg, 92%). R_f = 0.30 (hexanes/EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.18 (d, 6H, CH3, J_{HH} = 7.2 Hz), 1.62 (m, 4H), 1.68 (m, 2H), 2.80 (Septet, 1H, J_{HH} = 7.2 Hz), 3.54 (m, 4H), 3.93 (s, 3H, O*CH*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.36, 24.54, 25.87, 31.86, 47.34, 52.63, 101.90 (m), 135.41 (m), 139.14 (dm, 2C, J_{CF} = 239 Hz), 145.76 (dm, 2C, J_{CF} = 260 Hz), 161.42, 165.47; ^{19}F NMR (376 MHz, $CDCl_3$): δ -141.90 (m, 2F), -154.08 (m, 2F); ESI-HRMS: Calcd. for $C_{17}H_{21}F_4N_2O_2$ $[M+H]^+$: 361.1539, found 361.1538; IR (ATR) see attached spectra.

CIP-PFAA. Azide **1** (250 mg, 1.0 mmol), phenylacetaldehyde (132 mg, 1.1 mmol) and ciprofloxacin (183 mg, 0.5 mmol) were mixed in acetone (100 mL), and stirred at r.t. until the solution became clear (~ 3 days). Acetone was removed and the solid was further extracted from 0.5 M HCl using DCM. The organic phase was dried over Na_2SO_4, and the solvent was evaporated. The crude was further purified by flash column chromatography (25:1 DCM/methanol, R_f = 0.25) to provide the title compound as a pale yellow solid (294 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (q, 2H, J = 7.1 Hz), 1.39 (q, 2H, J =7.1 Hz), 3.21 (br, 4H), 3.52 (septet, 1H, J_{HH} = 3.8 Hz), 3.52 (s, 2H), 3.72 (br, 4H), 3.94 (s, 3H, OMe), 7.16 (d, 2H, J_{HH} = 7.3 Hz), 7.24 (t, 1H, J_{HH} = 7.3 Hz), 7.30 (d, 1H, J_{HH} = 6.9 Hz), 7.24 (t, 2H, J_{HH} = 7.3 Hz), 8.03 (d, 1H, J = 13.2 Hz), 8.78 (s, 1H), 14.91 (s, 1H, COOH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.3, 35.4, 35.6, 44.9 (br, 2C), 49.3, 52.9 (OMe), 103.9 (t, 1C, J_{CF} = 15 Hz), 105.0 (d, 1C, J = 3.0 Hz), 108.0,

112.3, 112.5, 119.9, 120.0, 127.4, 127.7, 129.3, 134.2, 134.4 (tt, 1C, J_{CF} = 14, 3 Hz), 139.0, 139.9 (dm, 2C, J_{CF} = 240 Hz), 145.3, 145.4, 145.8 (dm, 2C, J_{CF} = 256 Hz), 147.5, 152.3, 154.8, 160.3, 161.1, 166.9, 177.0 (d, 1C, J = 3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -121.17 (s, 1F), -140.81 (m, 2F), -152.91 (m, 2F); ESI-HRMS: Calcd. for $C_{33}H_{28}F_5N_4O_5$ $[M+H]^+$: 655.1974, found 655.1985. IR (ATR) see attached spectra.

NOR-PFAA. Pentafluorophenyl azide (250 mg, 1.2 mmol), phenylacetaldehyde (132 mg, 2.1 mmol) and norfloxacin (333 mg, 1.0 mmol) were mixed in acetone (60 mL), and stirred at r.t. until it became clear (~ 24 h). Acetone was removed and the crude was extracted from 0.5 M HCl using DCM and the organic phase was dried over Na_2SO_4, and solvent was evaporated. The crude was further purified by flash column chromatography (20:1 DCM/MeOH, R_f = 0.22) to provide the title compound as a pale yellowish solid (495 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.58 (t, 3H, J = 7.2 Hz), 3.21 (br, 4H), 3.71 (s, 2H), 3.85 (br, 4H), 3.80 (br, 4H), 4.30 (quartet, 2H, J = 7.2 Hz), 6.9 (d, 1H, J_{HH} = 6.8 Hz), 7.14 (d, 2H, J_{HH} = 7.4 Hz), 7.25 (t, 1H, J_{HH} = 7.4 Hz), 7.33 (d, 2H, J_{HH} = 7.4 Hz), 8.05 (d, 1H, J_{HH} = 13.0 Hz), 8.66 (s, 1H), 14.96 (s, 1H, -COOH);^{13}C NMR (100 MHz, $CDCl_3$): δ 14.6, 35.2, 45.1 (br, 2C), 49.6, 49.9, 104.1, 108.7, 113.2 (d, 1C, J = 3 Hz), 121.1, 127.4, 127.7, 129.4, 134.3, 136.8, 138.2 (m, 2C, J_{CF} = 264 Hz), 140.2 (m, 2C, J_{CF} = 240 Hz), 145.6 (m, 1C), 147.4, 152.3, 154.7. 161.3, 167.2, 177.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ -120.90 (s, 1F), -152.60 (m, 2F), -164.1 (m, 2F), -165.0 (m, 1F); ESI-HRMS: Calcd. for $C_{31}H_{25}F_6N_4O_3$ $[M+H]^+$: 603.1825, found 603.1830. IR (ATR) see attached spectra.

Synthesis of PFAA-Silane 14[4]



Methyl 4-azido-2,3,5,6-tetrafluorobenzoate (**1a**)[4] (3.86 g, 15.49 mmol) was dissolved in mixture of MeOH (15 mL), aqueous sodium hydroxide solution (20 w%, 3 mL) and water (3 mL). The mixture was stirred until TLC indicated full conversion. The mixture was then acidified with 1 M aqueous HCl and extracted with DCM (3 x 60 mL). The solvent was evaporated under reduced pressure to yield 4-azido-2,3,5,6-tetrafluorobenzoic acid as a white solid (quant.). 4-Azido-2,3,5,6-tetrafluorobenzoic acid (933 mg, 3.97 mmol), *N*-hydroxysuccinimide (502 mg, 4.36 mmol), and EDAC (836 mg, 4.36 mmol) were dissolved in DCM (15 mL) and stirred for 22 h at room temperature. Additional EDAC (433 mg, 2.26 mmol) was added, and the mixture was stirred for another 8 h. When NMR indicated a full conversion, the mixture was diluted with water and extracted twice with DCM. The combined organic phase was washed with water, dried over $MgSO_4$, and evaporated under reduced pressure to give compound **12** as white crystals. A solution of compound **12** (102.8 mg, 3.1 mmol), 3-aminopropyltimethoxysilane **13** (3.7 mmol) in DCM (4 mL) was capped in N_2 and stirred for 5 h at room temperature. Afterwards, the mixture was evaporated and approximately 0.3 g of silica gel was added to the dried residue. This crude was purified by column chromatography on silica gel using 1:3 v/v chloroform/hexanes containing 2% methanol as an eluent. Evaporation of the solvent gave compound **14** as a colorless viscous liquid (98 mg, 88%). ^{1}H NMR ($CDCl_3$): δ 3.56 (s, 9H), 3.47 (q, 2H, J = 12 Hz), 1.76 (m, 2H, J = 15 Hz), 1.61 (s, 1H), 0.72 (t, 2H, J = 16 Hz). ^{19}F NMR ($CDCl_3$): δ -144.0 (m, 2F), -153.8 (m, 2F). IR: 2126 cm^{-1}.

SYNTHESIS OF FUNCTIONALIZED SILICA NANOPARTICLES (SNPs)

PFAA-functionalized SNPs (PFAA-SNPs)

A reported protocol was used to prepare silica nanoparticles (SNPs) of ~50 nm size.[5,6] Ammonium hydroxide (28% in water, 1 mL) and ethanol (95%, 40 mL) were added into a three-necked round-bottom flask at 40 °C, then TEOS (0.5 mL) was added into the flask slowly. After stirring for 48 h, the nanoparticles were isolated by centrifugation. The sediments were redispersed in ethanol and the mixture was centrifuged again. This purification cycle was repeated three times. The obtained nanoparticles were then dried under vacuum.

To prepare 90 nm SNPs,[1,7-9] ammonium hydroxide (28%, 15 mL) was dissolved in ethanol (250 mL) in a three-necked round-bottom flask at 30 °C. A solution of TEOS (10 mL) in ethanol (10 mL) was added dropwise into the flask, and the resulting mixture stirred for 24 h. The reaction mixture was centrifuged at 7500 rpm for 20 min, and the sediments were washed with ethanol. The washing was repeated three times, and the resulting silica nanoparticles were dried under vacuum at 50 °C.

To functionalize SNPs with PFAA,[10] a mixture of PFPA-silane **14** (219 mg, 0.5 mmol) and SNPs (200 mg) for 50 nm (400 mg for 90 nm sized SNPs) in dry toluene (10 mL) was stirred at 70 °C for 16 h. The obtained nanoparticles were collected by centrifugation and washed two times with toluene and ethanol (7500 rpm, 20 min), respectively. The obtained PFPA-SNPs were dried under vacuum.

Fluoroquinolone-functionalized SNPs

Synthesis of CIP-SNPs. PFPA-functioned silica nanoparticles (**PFAA-SNPs**, 100 mg), (88 ± 10 nm by TEM) were sonicated in acetone (20 mL). Ciprofloxacin (10 mg) and phenylacetaldehyde (10 mg) were added and the mixture was first sonicated and then vigorously stirred at room temperature in the dark. To monitor the reaction progress, 400 µL aliquots of the above mixture was diluted to 1.25 mL acetone at defined time point. The mixture was sonicated and then centrifuged at 11000 rpm for 15 minutes to remove the supernatant. The washing protocol was repeated sequentially in acetone, acidic water, acetone, water, acetone and water. The supernatants in every washing cycle were checked with fluorescence spectroscopy and IR to make sure that free ciprofloxacin had been washed off. Surface-modified particles had a much improved dispersibility in water. The reaction process was monitored using the above purified samples by both the fluorescence (emission: 450-470 nm, excitation: 335 nm) and IR spectroscopy (azido peak at 2130 cm^{-1}). After 24 hours, the IR and fluorescence spectra of isolated samples both showed a high degree of conversion. The immobilization was extended up to 7 days. For this specific sample showing in Fig. S6, the workup was done at 100 hours. The purification was done by repeated centrifugation-washing using different solvents above, and the isolated supernatant solutions were checked with fluorescence and IR spectra to ensure the removal of unreacted ciprofloxacin. After drying under vacuum for 2 days, the functionalized particles (**CIP-SNPs**, 80 mg) were collected as a white powder, which showed fluorescence under UV-light.

NOR-SNPs were synthesized in analogy to **CIP-SNPs**.

ANTIBACTERIAL ACTIVITY TESTS

E. coli ORN208 was grown to 0.3 OD_{600} (~10^8 CFU/mL), which was then diluted 100 fold to ~10^6 CFU/mL. The aqueous suspension of samples (compounds, particle samples: **PFAA-SNPs**, **CIP-SNPs** and **NOR-SNPs**) was diluted sequentially to give a concentration series. The suspension (100 µL) was added to the diluted bacteria (100 µL) in a 96 well plate (in triplicates), and incubated at 37 °C for 18 h. Alamar blue dye (20 µL) was added to each sample, which was incubated for an additional 2 h. Fluorescence intensities at 590 nm (excitation: 560 nm) were recorded for the MIC analysis.

CONFOCAL FLUORESCENT IMAGING OF CIP-FSNPs

E. coli ORN208 was incubated overnight in Mueller-Hinton broth at 37 °C with shaking at 110/min (VWR Rocker adjustable double platform). The bacteria were then transferred to new culture medium and cultured for another 3 h, and the OD620 were measured to be 0.209. Afterwards, the bacteria were pelleted (4000 rpm, 15 min) and redispersed in pH 7.4 PBS to an OD_{620} of 0.074 (~10^8 CFU/mL). **CIP-FSNPs** were dispersed in millipore water (0.5 mg/mL) by strong sonication, and then portions of the stock solution were added to a 1.00 mL aliquot of the bacteria suspension. The final concentration of silica nanoparticles were 0.1 mg/ml and 0.01 mg/ml, respectively. The mixtures were further incubated at 37 °C for 4 h while shaking at 100/min. An aliquot of the suspension (0.100 mL) was spread on a glass-bottom dish. Confocal fluorescence microscopy images were acquired using a Zeiss LSM 780 confocal microscope (Carl Zeiss, Jena, Germany) with a C-Apochromat 40x/1.20 W Korr FCS M27 objective. The microscope was focused on the surface of the glass-bottom dish where live bacteria transiently sedimented before they migrated away. 405 and 488 nm excitation sources were used for imaging experiments.

KINETIC ANALYSIS

Estimation of rate constants

The enamine-azide reactions was assumed to proceed in two-steps: cycloaddition followed by decomposition.

$$\mathbf{A} + \mathbf{B} \xrightarrow{k_1} \mathbf{C} \xrightarrow{k_2} \mathbf{D}$$

The cycloaddition rate constant k_1 was estimated through the second-order combined formation of C and D over time (see below), and the decomposition rate constant k_2 was accessed from the first-order formation of D from C. The transformations were followed by ^{19}F and ^{1}H NMR, from which data the constants were estimated through non-linear regression analysis (GraphPad).

Estimation of cycloaddition rate constant k_1

$$\frac{d([C]+[D])}{dt} = k_1[A][B] \quad (1)$$

At $t = 0$: $[A]_0 = a; [B]_0 = b$

At any t: $[A] = a - ([C] + [D]); [B] = b - ([C] + [D])$

This gives:

$$\frac{d([C]+[D])}{dt} = k_1[A][B] = k_1\{a - ([C] + [D])\}\{b - ([C] + [D])\} \quad (2)$$

Rearrangement gives:

$$\frac{d([C]+[D])}{\{a-([C]+[D])\}\{b-([C]+[D])\}} = k_1\, dt \quad (3)$$

Integration of eq. 3:

$$\frac{1}{a-b} ln \frac{b\{a-([C]+[D])\}}{a\{b-([C]+[D])\}} = k_1\, t \quad (4)$$

Solving eq. 4:

$$[C] + [D] = ab\frac{e^{k_1 t(a-b)}-1}{ae^{k_1 t(a-b)}-b} \quad (5)$$

Kinetics of reaction between PFAA 1a and phenylacetaldehyde piperidine enamine in CD_3OD

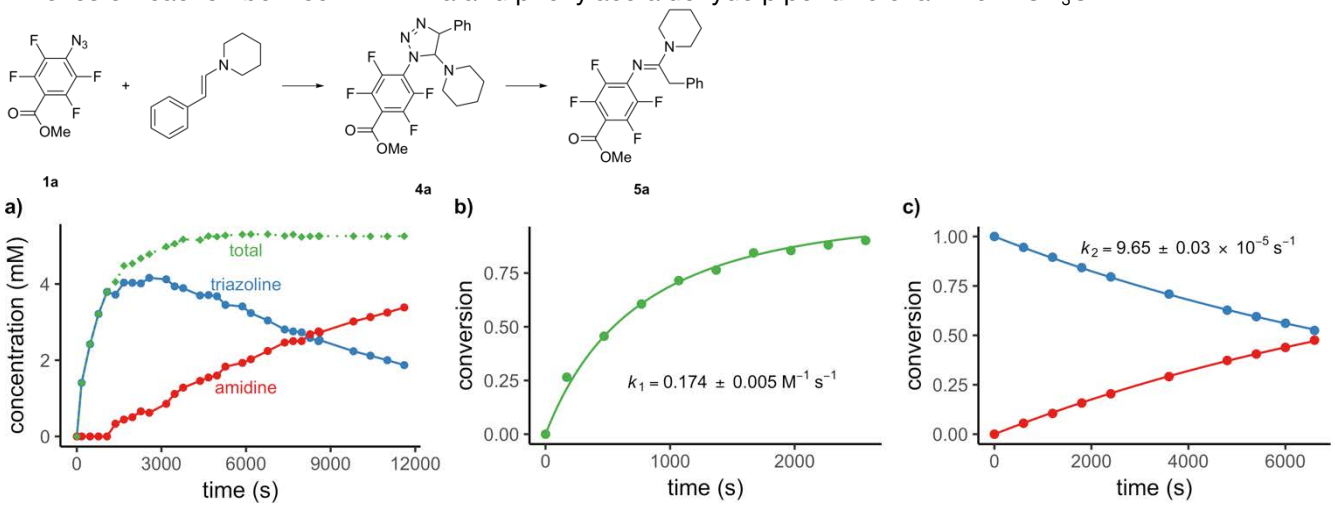


*Figure S1. PFAA **1a** phenylacetaldehyde piperidine enamine cycloaddition and decomposition in CD_3OD (separate experiments),; a) overall profile (3 separate experiments); b) total product formation; c) decomposition; 293 K; determined by ^{19}F and ^{1}H NMR.*

EFFECTS FROM SOLVENT

Perfluoroaryl azide-aldehyde-amine reaction in methanol with different amount of water

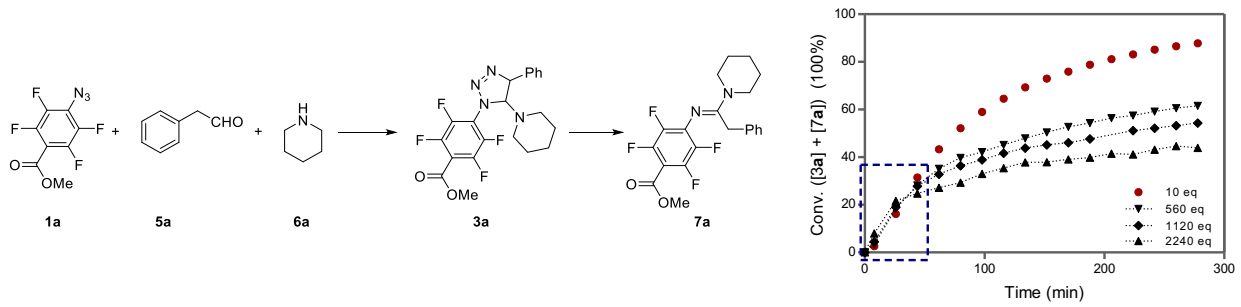


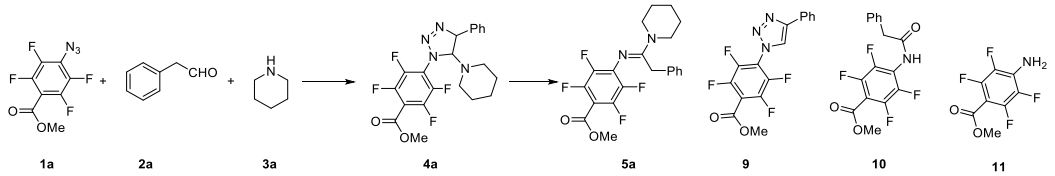
*Figure S2. Perfluoroaryl azide-aldehyde-amine reaction in methanol with different amount of water. Conditions: Compounds **1a** (10 mM), **5a** (11 mM), **6a** (11 mM), in CD_3OD mixed with indicated equivalents of D_2O, monitored by ^{19}F NMR, 21.5 °C. All reactions were homogeneous. 560 equiv. of D_2O is approximately 10 vol% of D_2O in CD_3OD.*

Perfluoroaryl azide-aldehyde-amine reaction under heterogeneous conditions in organic solvent/water mixtures

Reactions in mixed solvents proceeded similar to the corresponding transformations in pure organic solvent.

Figure S3. Appearance of perfluoroaryl azide-aldehyde-amine reaction in organic solvent/water mixtures.

Table S1. Perfluroaryl azide-aldehyde-amine reaction in different solvents.

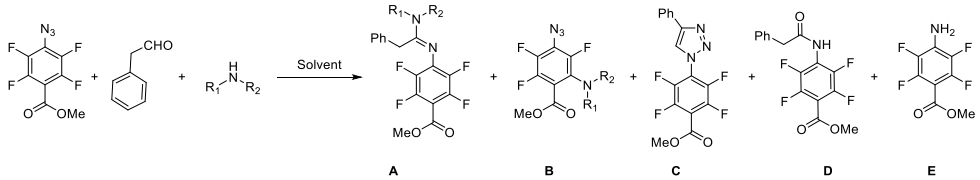


Entry	Solvent	Conv. (%)[b] (3a, 7a)	Yield (%)[c] (7a)	Trace products[e]
1	Acetone	92 (71, 21)	93 (91[c])	**11**
2	Acetone (10 v% H_2O)	81 (67, 13)	93	**9, 10, 11**
3	Acetone (20 v% H_2O)	90 (60, 20)	89 (87[c])	**9, 10, 11**
4	Acetone (30 v% H_2O)	94 (62, 20)	85	**9, 10, 11**
5	Acetone (40 v% H_2O)	94 (61, 24)	90	**9, 10, 11**
6[g]	Acetone (50 v% H_2O)	88 (62, 19)	86	**9, 10, 11**
7	MeOH	91 (75, 16)	90 (91[c])	**9, 11**
8	MeOH (10 v% H_2O)	94 (78, 16)	88	**9, 11**
9[g]	MeOH (60 v% H_2O)	95 (78, 17)	100 (88[c])	-
10[g]	DMSO (50 v% H_2O)	100 (67, 33)	99	**11**
11[g]	DMF (50 v% H_2O)	32 (23, 9)	98	**11**
12[g]	MeCN (40 v% H_2O)	97 (78, 14)	82	**9, 10, 11**
13[g]	THF (40 v% H_2O)	89 (45, 20)	78 (80[c])	**9, 10, 11**
14[d] [g]	Acetone (50 v% H_2O)	100 (66, 34)	92	**9, 10, 11**
15[d]	Acetone (30 v% H_2O)	100(65,35)	87	**9, 10, 11**
16	Toluene	80 (73, 7)	98 (84[c])	**11**
17	DCM	89 (76, 13)	99	**11**
18	Hexane	55 (51, 4)	97	**11**
19	Diethyl ether	80 (42, 19)	92	-
20	THF	84 (66, 18)	94 (87[c])	-
21	EtoAc	87 (73, 14)	95	-
22	Chloroform	88 (82, 6)	98	-
23[f]	MeOH	76 (76, <1)	77[h] (71)	
24[f]	THF	98 (91, <1)	70[h]	
25[f]	MeOH (H_2O, 10 v%)	53 (53, <1)	75[h]	
26[f] [g]	MeOH (H_2O, 60 v%)	56 (56, <1)	81[h]	

[a]Reaction conditions: Compounds **1** (0.1 M), **2a** (0.105 mmol) and **3a** (0.11 mmol) in solvent, at 25 °C. [b]By ^{19}F-NMR, $CDCl_3$, 15 min. [c]8 h, isolated yield at the scale of 1 mmol of azide **1**. [d] Compounds **2a** (0.15 mmol), **3a** (0.2 mmol). [e]Determined by ^{19}F NMR. [f]Aldehyde **2b** was used. [g]As emulsions, see Figure S2. [h]Isolated yields of compound **5i**, 72 h.

REACTIONS WITH DIFFERENT AMINES

Table S2. Reaction with cyclic secondary amines.

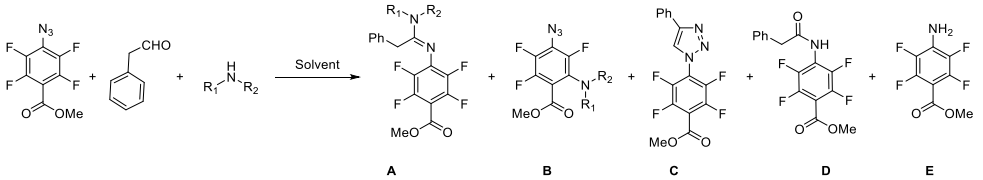


Entry	Amine	Solvent	Environment	Isolated yields(%)				
				A	B	C	D	E
1	Piperidine	DMF	N_2	91	N.D.	Trace	Trace	Trace
2	Morpholine	MeOH (Toluene)	air	87 (88)	Trace	Trace	N.D.	Trace
3	Morpholine	Acetone (20 vol% H_2O)	air	90	N.D.	N.D	Trace	Trace

4	Pyrrolidine	MeOH	air	44	Trace	29	N.D.	N.D.
5	Pyrrolidine	DMF	air	55	Trace	5[a]	12	N.D.
6	Pyrrolidine	MeOH	N_2	81	Trace	6[a]	N.D.	N.D.
7	Pyrrolidine	DMF	N_2	97	N.D.	N.D.	Trace	N.D.
8	Pyrrolidine	Toluene	N_2	96	N.D.	N.D.	Trace	N.D.
9	Pyrrolidine	DMF (10 vol% H_2O)	N_2	33	Trace	4[a]	17	N.D.
10	Ciprofloxacin	Acetone	air	90	N.D.	N.D	4[a]	Trace
11	Ciprofloxacin	DMF	air	4	N.D.	60	Trace	Trace

Reaction conditions: azide (0.50 mmol), phenylacetaldehyde (0.55 mmol), amine (0.55 mmol), solvent (1.0 mL), 25 °C, 8 h. [a]Determined by ^{19}F NMR. N.D.: not detected.

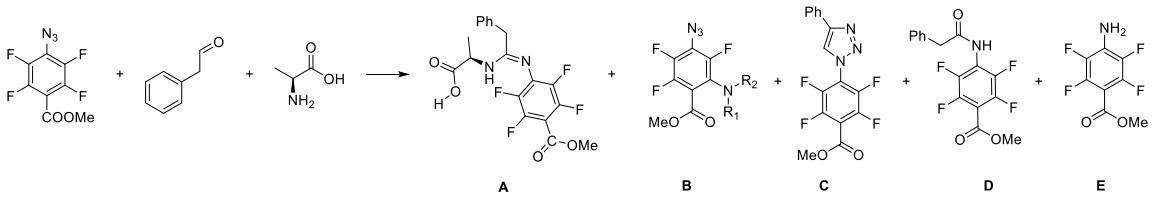
Table S3. Reaction with acyclic secondary amines and primary amines.



Entry	Amine	Solvent	Environ-ment	Isolated yield (%)				
				A	B	C	D	E
1	Diethylamine	MeOH	air	39	Trace	45	Trace	N.D.
2	Diethylamine	DMF	N_2	45	Trace	45	Trace	Trace
3	Diethylamine	Toluene	N_2	77	11	Trace	N.D.	N.D.
4	Diethylamine	THF	N_2	83	Trace	Trace	Trace	N.D.
5	Diethylamine	THF	air	79	Trace	7	N.D.	Trace
6	Diethylamine	THF (20 vol% H_2O)	N_2	45	Trace	19	13	Trace
7	Diethylamine	THF (20 vol% H_2O)	air	53	Trace	23	12	Trace
8[a]	Triethylamine	DMF	air	N.D.	N.D.	35	42	Trace
9[b]	Triethylamine	THF	N_2	N.D.	N.D.	13	39	Trace
10	2-phenylethan-1 amine	THF	N_2	85	N.D.	6[c]	N.D.	5[c]
11	2-phenylethan-1 amine	Acetone (20 vol% H_2O)	air	67	N.D.	Trace	Trace	12
12	Diphenylamine	DMF	air	28[d]	N.D.	N.D.	54[d]	6[c,d]
13	Diphenylamine	THF	N_2	74[e]	N.D.	N.D.	N.D.	8[c,e]

Reaction conditions: azide (0.50 mmol), phenylacetaldehyde (0.55 mmol), amine (0.55 mmol), solvent (1.0 mL), 25 °C, 8 h. [a]Workup at 48 h. Starting azide was recycled in 13%. [b]Determined by ^{19}F NMR at 8 h when starting azide was recycled in ~ 47%. [c]Determined by ^{19}F NMR. [d]48 h, 60 °C. [e]7 d. N.D.: not detected.

Table S4. Reaction with L-alanine.



Entry	Solvent	Temperature	Conversion at 14 h (%)				
			A	B	C	D	E
0.167 M concentration (starting azide)							
1	DMSO	20 °C	59	N.D.	18	N.D.	Trace
0.08 M concentration (starting azide)							
2.1	DMSO	20 °C	60	N.D.	14	N.D.	Trace
2.2	DMSO (10 vol% water)	20 °C	40	N.D.	11	N.D.	Trace
2.3	DMSO (20 vol% water)	20 °C	50	N.D.	4	N.D.	Trace
2.4	DMSO (50 vol% water)	20 °C	Phase separation occurred. Trace products were observed				
2.5	Acetone (20 vol% water)	20 °C	< 3				
0.008 M concentration (starting azide)							
3.1	DMSO	20 °C	50	N.D.	47	N.D.	Trace
3.2	DMSO (10 vol% water)	20 °C	29	N.D.	11	N.D.	Trace
3.3	DMSO (20 vol% water)	20 °C	13	N.D.	<1	N.D.	N.D.
3.4	DMSO (20 vol% water)	37 °C	30	N.D.	<1	N.D.	N.D.
3.5	DMSO (20 vol% water)	50 °C	57	N.D.	<5	N.D.	N.D.
3.6	DMSO (20 vol% water)	70 °C	70	N.D.	<5	N.D.	N.D.

Reaction conditions: To a freshly prepared solution of azide (1 eq) and phenylacetaldhyde (1.3 eq) in DMSO-d_6/D_2O mixture, amine (1.2 eq) in DMSO-d_6/D_2O mixture was added and mixed well. The reaction was monitored by ^{19}F and ^{1}H NMR, and the conversions were based on NMR analysis. N.D.: not detected.

ACID-PROMOTED REARRANGEMENT

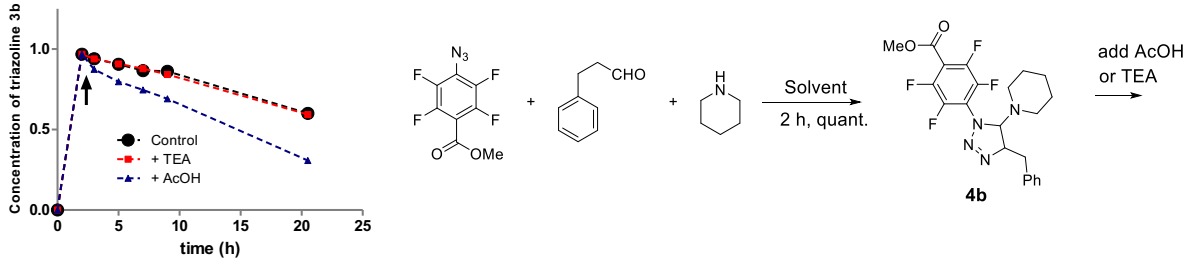


*Figure S4. Acid-promoted rearrangement of triazolines **4b**.*

EFFECTS OF ADDED EQUIVALENTS OF ALDEHYDE AND AMINE

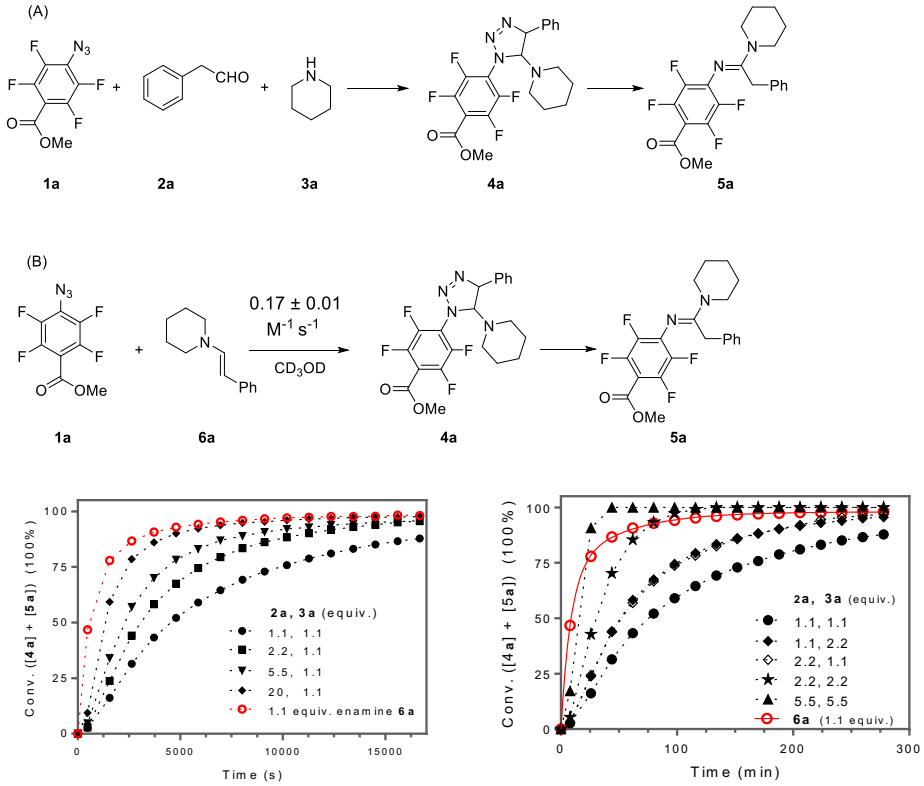


*Figure S5. Conjugation profiles with different equivalents of phenylacetaldehyde and amine. Left: 1.1-20 equiv. aldehyde **2a** with 1.1 equiv. amine **3a**; right: 1.1-5.5 equiv. aldehyde **2a** and amine **3a**. Conditions: Compound **1a** (10 mM, 1 equiv.), CD_3OD, by ^{19}F NMR, 22 °C.*

SIDE REACTIONS

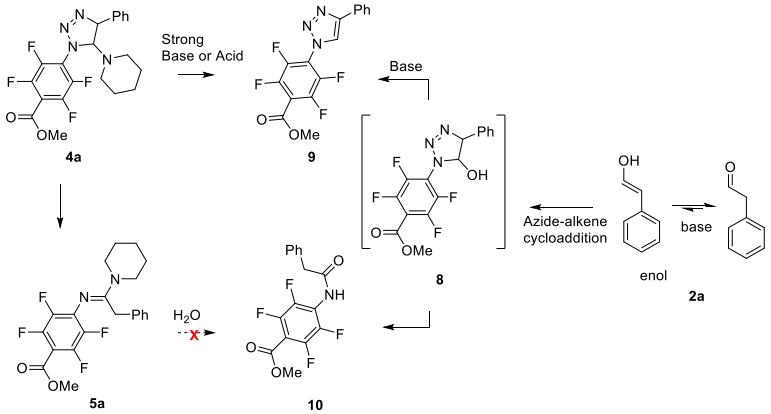


*Figure S6. Side reactions leading to triazole **9** and aryl amide **10**.*[11-13]

FLUORESCENCE OF CIP-SNPs vs REACTION TIME.

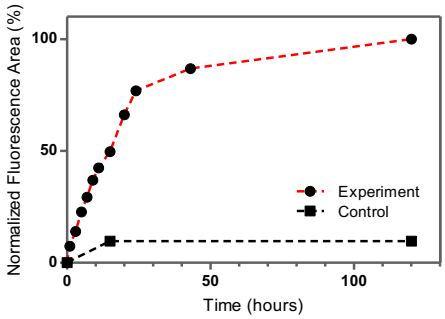


Figure S7. Fluorescence of ciprofloxacin-immobilized SNPs vs. reaction time.

FTIR SPECTRA OF CIP-SNPs

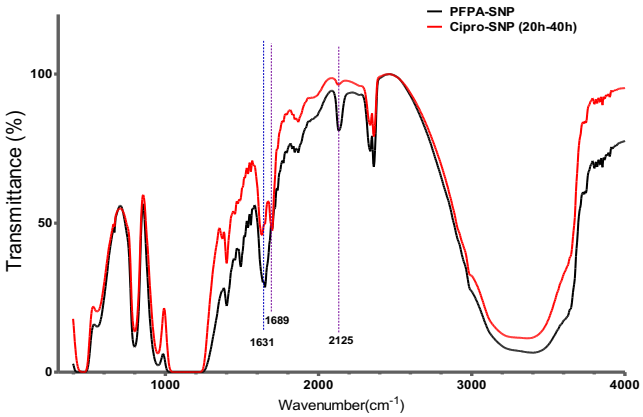


Figure S8. FTIR Spectra of ciprofloxacin-functionalized silica nanoparticles.

DLS MEASUREMENT OF SNPs

CIP-SNPs dispersed well in water or acetone, while **PFPA-SNPs** dispersed well in acetone but not in water.

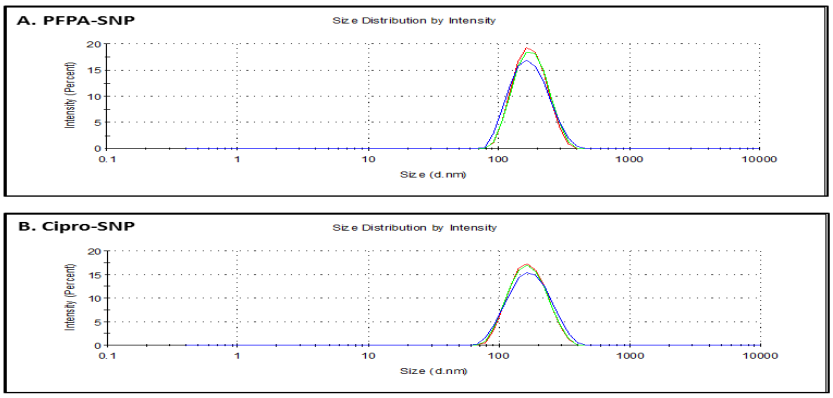


*Figure S9. DLS measurement of SNPs before and after functionalization; (A) **PFAA-SNPs** in acetone; (B) **CIP-SNPs** in water.*

XPS ANALYSIS

PFPA-SNPs

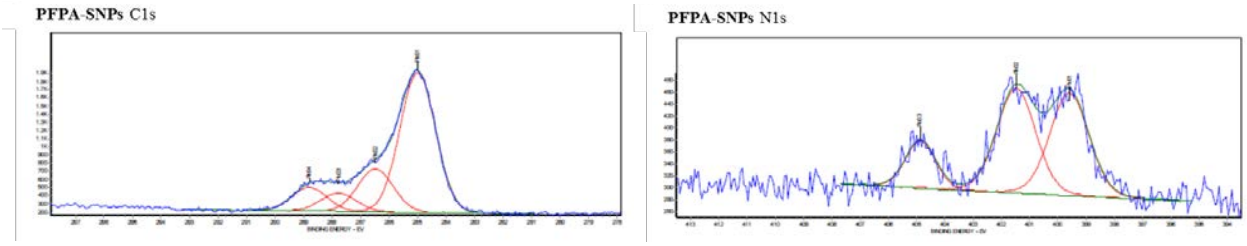


Figure S10. XPS analysis of PFPA-SNPs.

CIP-SNPs.

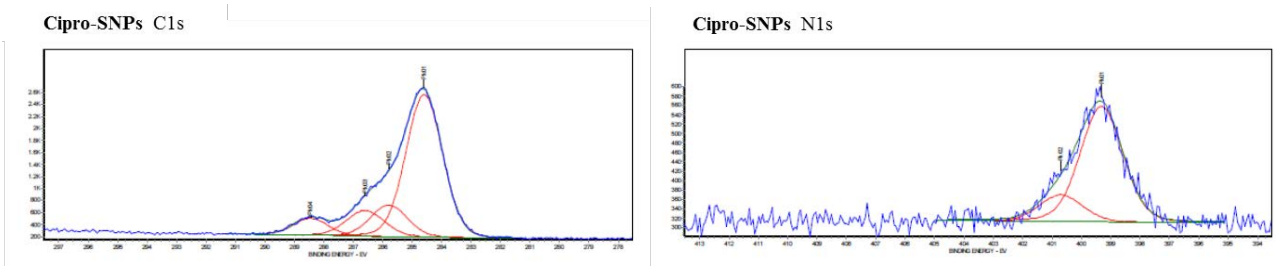


Figure S11. XPS analysis of CIP-SNPs.

Table S5. XPS peak area ratios of functionalized SNPs.[2]

	C 1s				N 1s			
BE (eV)	285.0	286.2	287.0	288.8	399.7	401.1	401.9	405.3
Assignments	C-C, H	C-N,O	O-C-O/C=O/C-F	O-C=O	C(O)NH		R-N=N=N	R-N=N=N
CIP-SNPs	65.6	14.5	12.3	7.6	81.1	18.9	-	-
PFPA-SNPs	62.3	19.1	8.1	10.5	42.1	-	42.8	15.2

Table S6. Surface composition.

	C 1s	N 1s	O 1s	F 1s	Si 2p	C:F	N:F	C:N
CIP-SNPs	57.8	3.0	26.2	2.3	10.7	25.1	1.3 (1)	19.3
PFPA-SNPs	34.4	4.0	37.8	4.9	18.9	7.0	0,81(1)	8.6

TEM OF SNPs

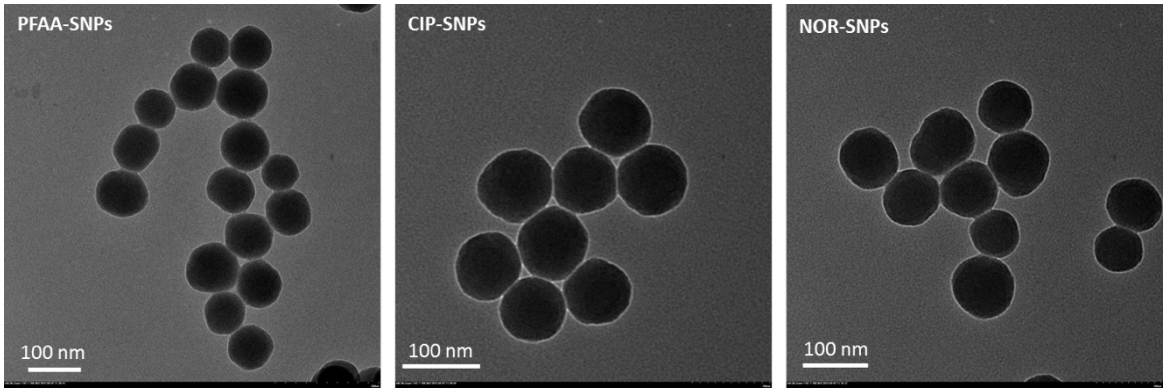


Figure S12. TEM images of silica nanoparticle samples.

ANTIBACTERIAL ACTIVITY

Table S7. MIC of free and conjugated antibiotics against E. coli ORN208.

Entry	Sample	Particle Size (nm)[a]	Drug/SNPs (wt%)[b]	MIC(μg/mL)[c]	Enhancement[d]
1	CIP-SNPs	d = 50 ± 15	2.7 %	54	2.8
2	CIP-SNPs	d = 90 ± 10	1.8 %	180	0.8
3	CIP-PFAA	-	-	150	1
4	NOR-SNPs	d = 50 ± 15	2.1 %	84	6
5	NOR-SNPs	d = 90 ± 10	1.3 %	101	5
6	NOR-PFAA	-	-	500	1
7	PFAA-SNPs	d = 50 ± 15	-	> 2000	-
8	PFAA-SNPs	d = 90 ± 10	-	> 2000	-

[a] Estimated by DLS from the main peak by intensity. [b] Estmimated by TGA. [c] Performed in duplicates or triplicates; calculated based on CIP/NOR. [d] $MIC_{(CIP\text{-}PFAA)}/MIC_{(CIP\text{-}SNPs)}$ or $MIC_{(NOR\text{-}PFAA)}/MIC_{(NOR\text{-}SNPs)}$.

CHARACTERIZATION BY CONFOCAL FLUORESCENCE MICROSCOPY

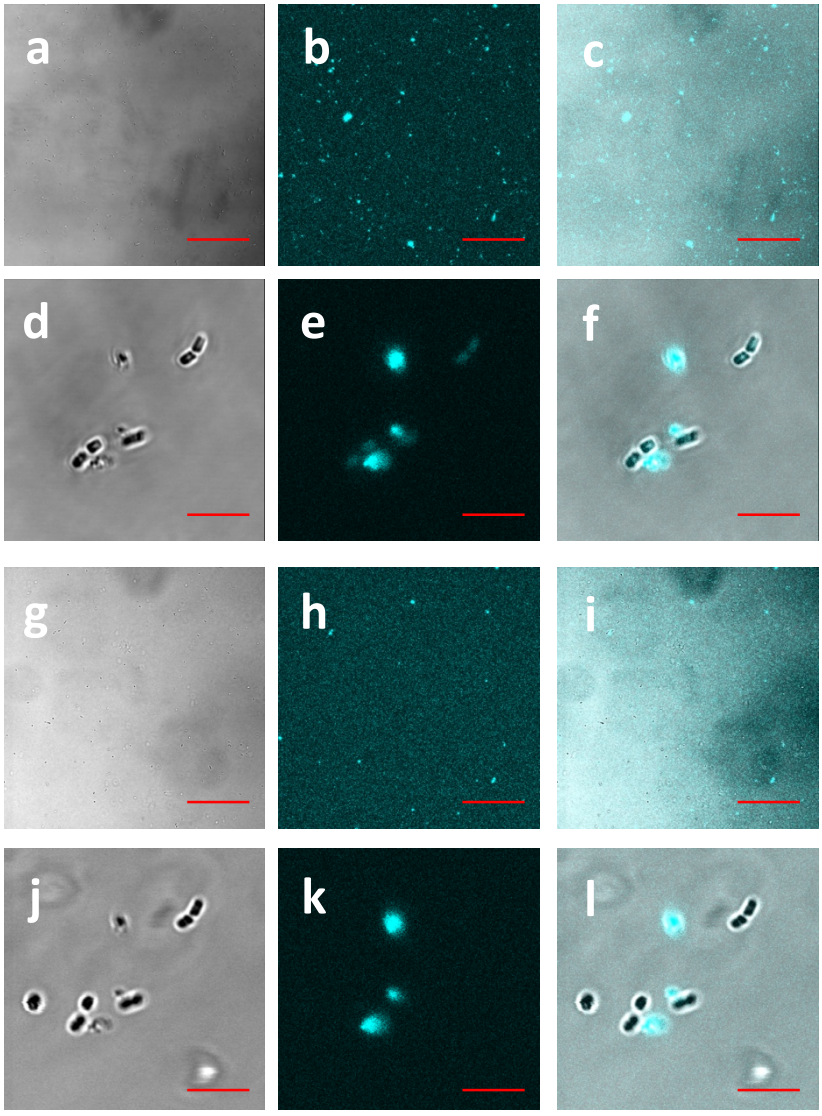
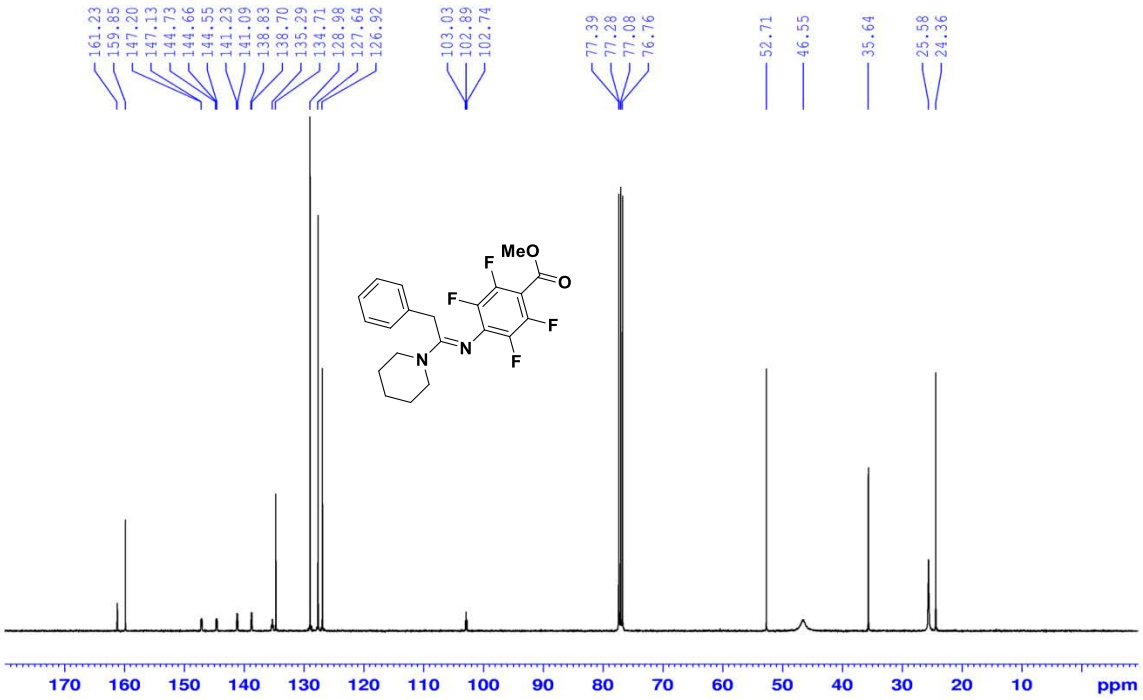
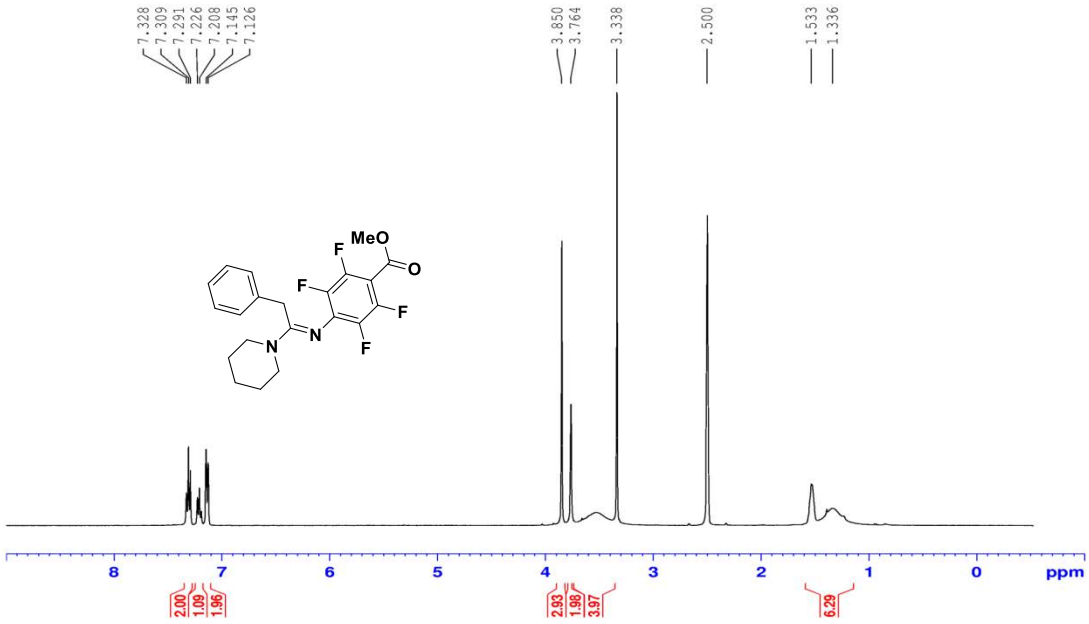
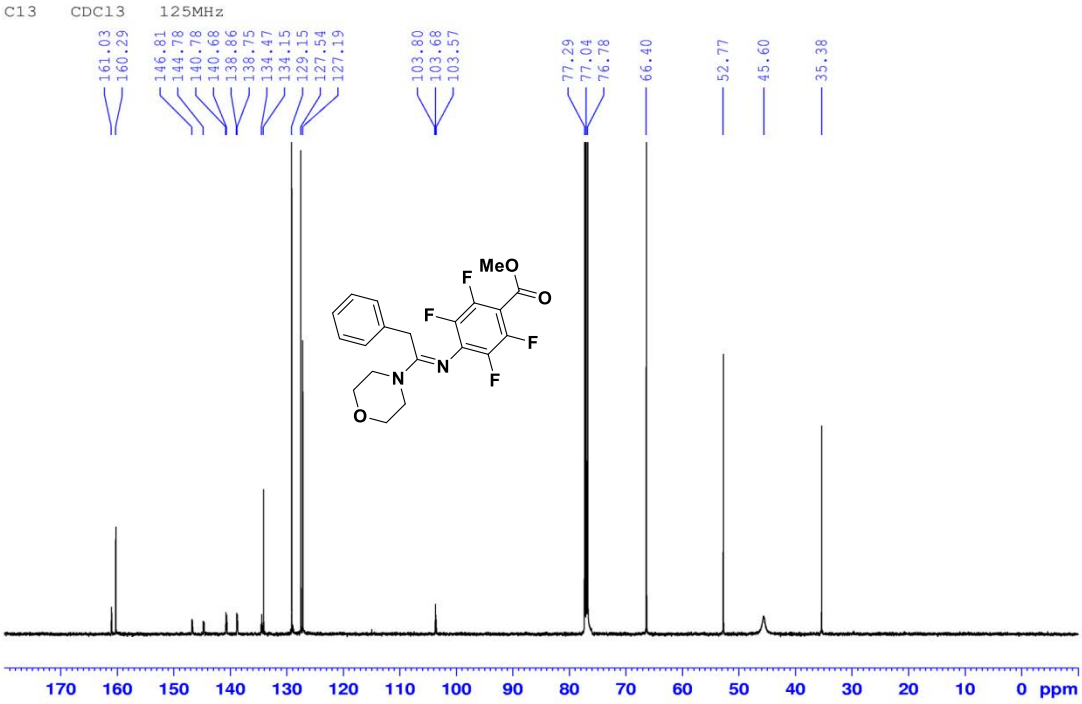


*Figure S13. Confocal fluorescence microscopy images of E. coli ORN208 (~10^8 CFU/mL) incubated with **CIP-FSNPs** of lower concentration (10 μg/mL); a-c, g-i) global view, scale bar: 50 μm; d-f, j-l) Enlarged view, scale bar: 5 μm; b, c, e, f) fluorescence (pseudo color) from Ex: 405 nm; h, i, k, l) fluorescence (pseudo color) from Ex: 488; a, d, g, j) bright field images; c, f, i, l) merged images.*

CHARACTERIZATION SPECTRA



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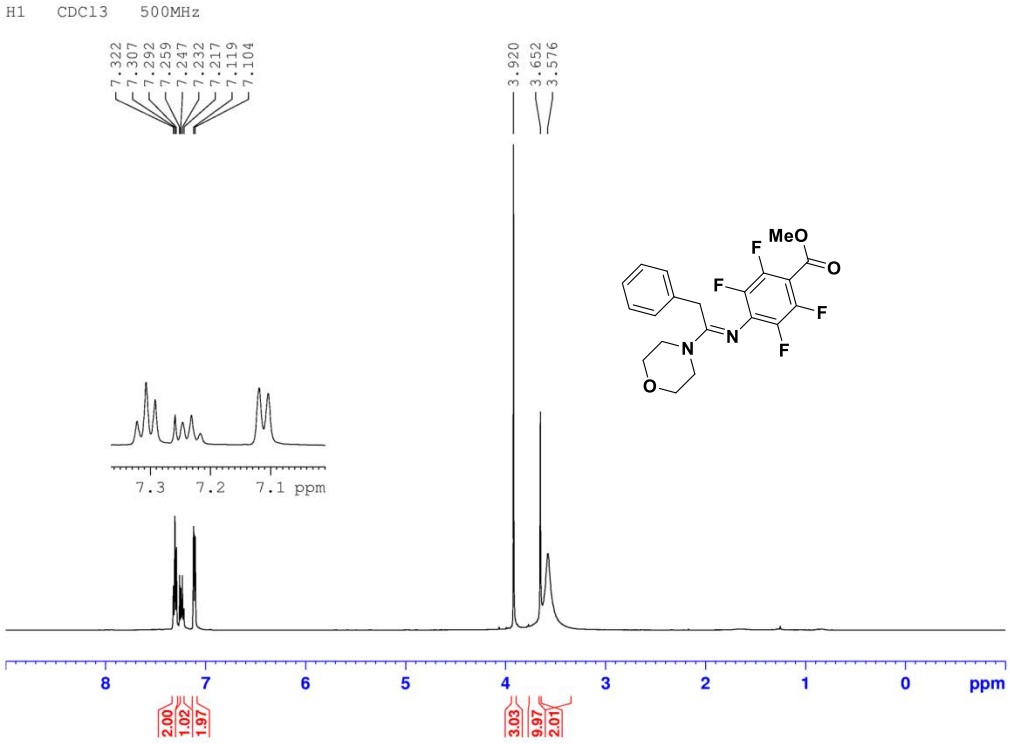
160.29
146.81
144.78
140.78
140.68
138.86
138.75
134.47
134.15
129.15
127.54
127.19
103.80
103.68
103.57
77.29
77.04
76.78
66.40
52.77
45.60
35.38
MeO
O
F
F
F
F
N
N
O
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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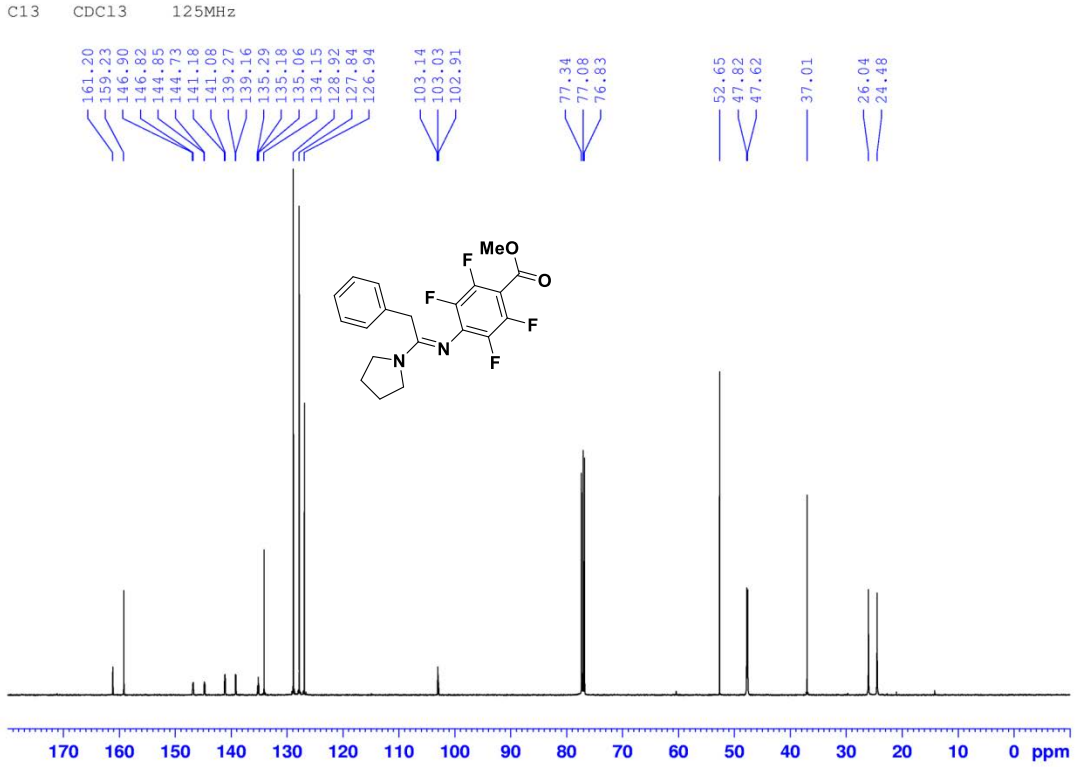
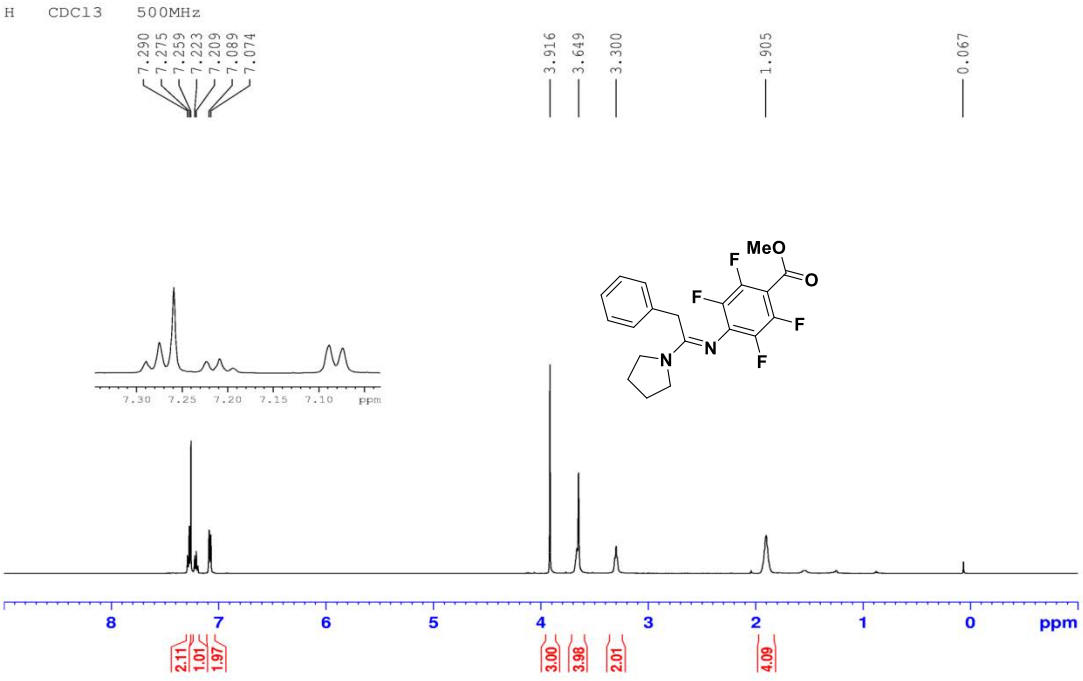
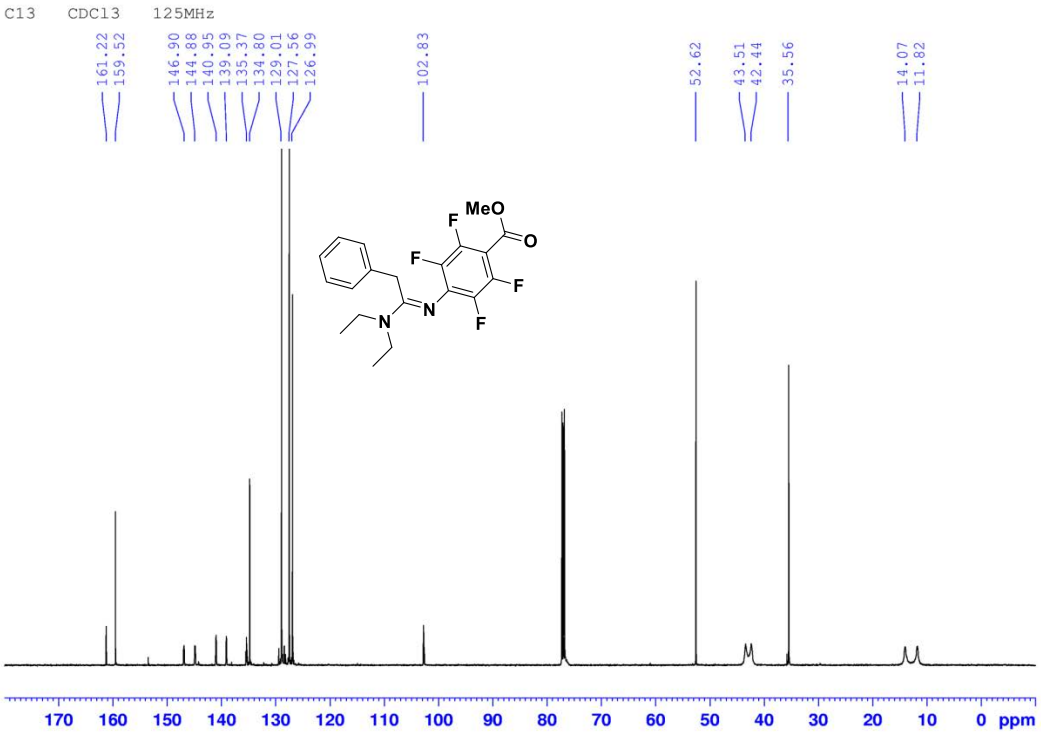
7.322
7.307
7.292
7.259
7.247
7.232
7.217
7.119
7.104
3.920
3.652
3.576
7.3 7.2 7.1 ppm
MeO
O
F
F
F
F
N
N
O
8 7 6 5 4 3 2 1 0 ppm
2.00
1.02
1.97
3.03
9.97
2.01


C13 CDCl3 125MHz
161.20
159.23
146.90
146.82
144.85
144.73
141.18
141.08
139.27
139.16
135.29
135.18
135.06
134.15
128.92
127.84
126.94
103.14
103.03
102.91
77.34
77.08
76.83
52.65
47.82
47.62
37.01
26.04
24.48
MeO
O
F
F
F
F
N
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


H CDCl3 500MHz
7.290
7.275
7.259
7.223
7.209
7.089
7.074
3.916
3.649
3.300
1.905
0.067
MeO
O
F
F
F
F
N
N
7.30 7.25 7.20 7.15 7.10 ppm
8 7 6 5 4 3 2 1 0 ppm
2.11
1.01
1.97
3.00
3.98
2.01
4.09


C13 CDCl3 125MHz
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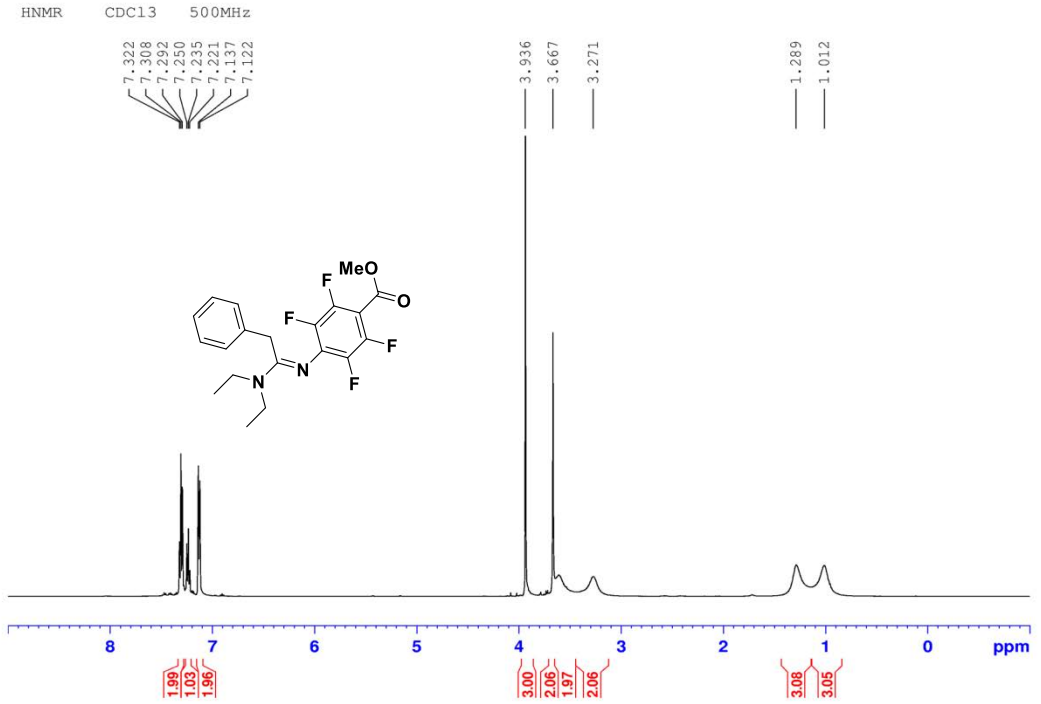
159.52
146.90
144.88
140.95
139.09
135.37
134.80
129.01
127.56
126.99
102.83
52.62
43.51
42.44
35.56
14.07
11.82
MeO
O
F
F
F
F
N
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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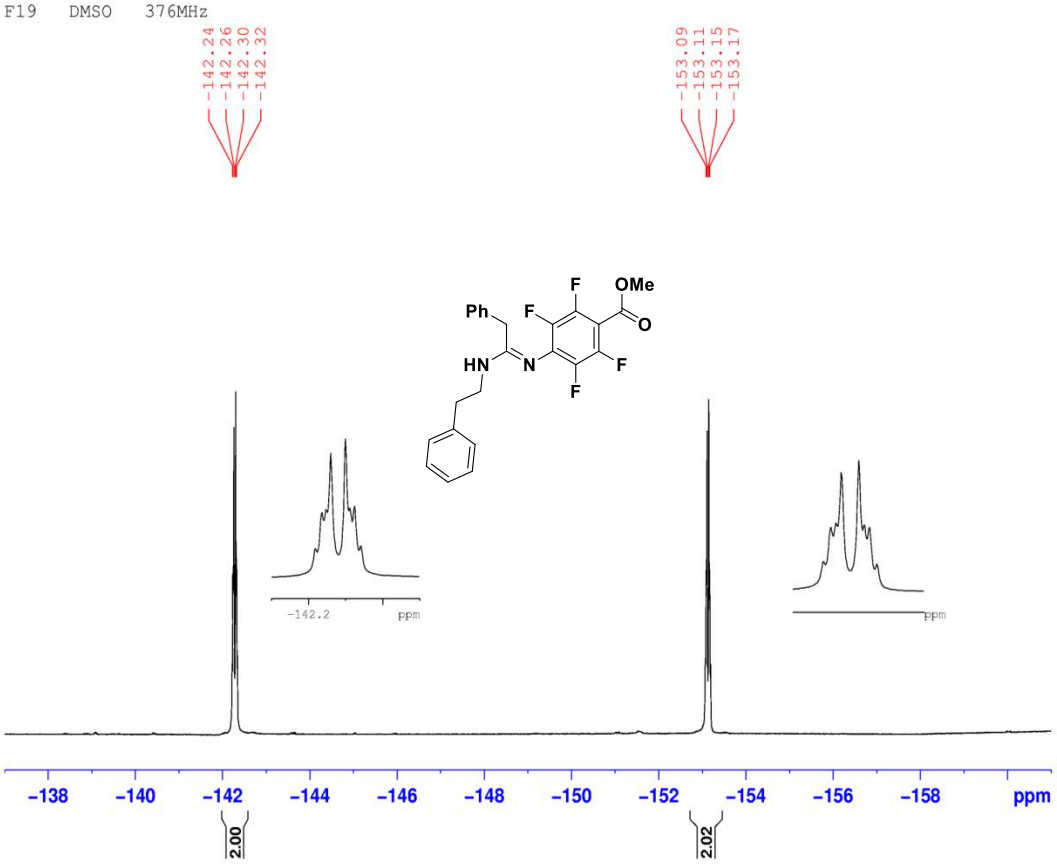
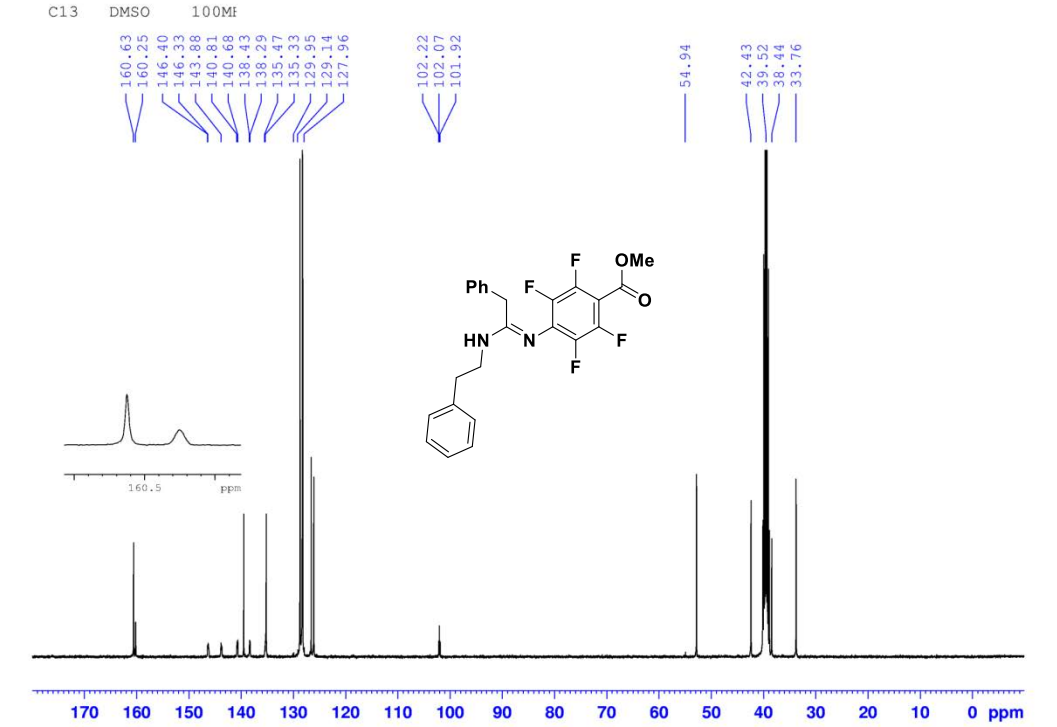
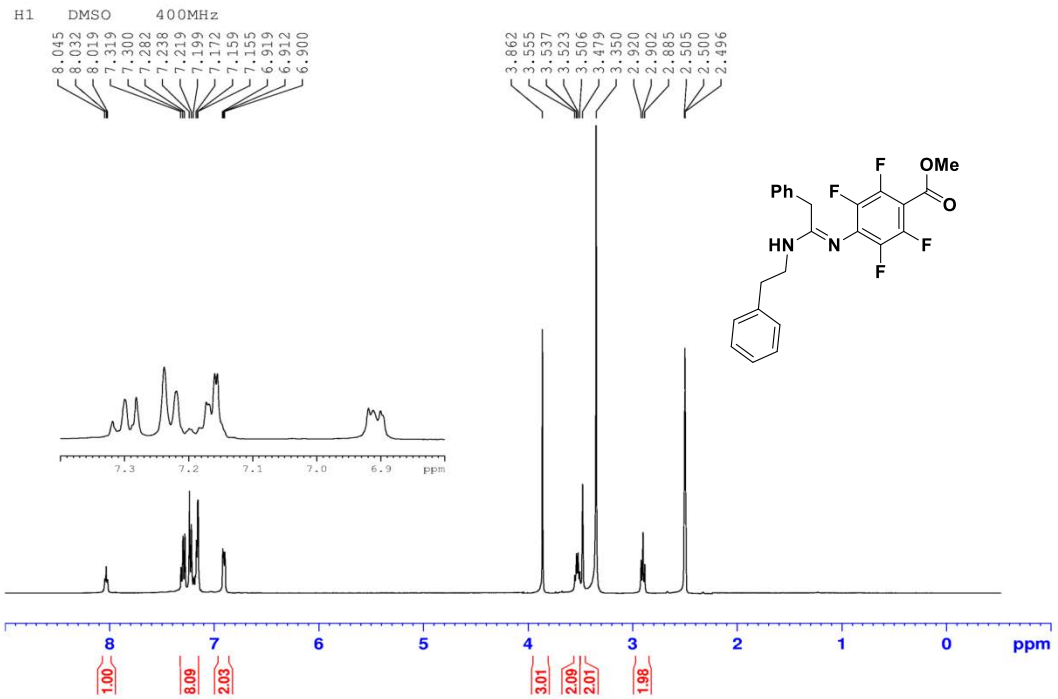
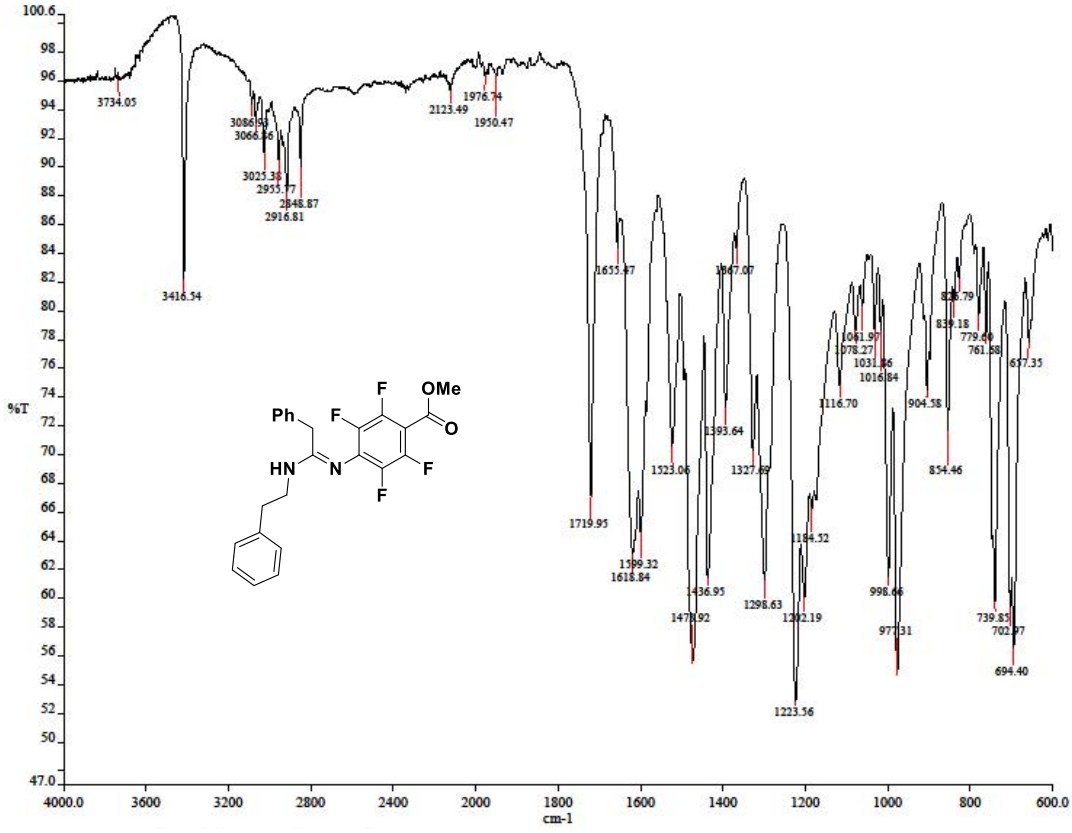
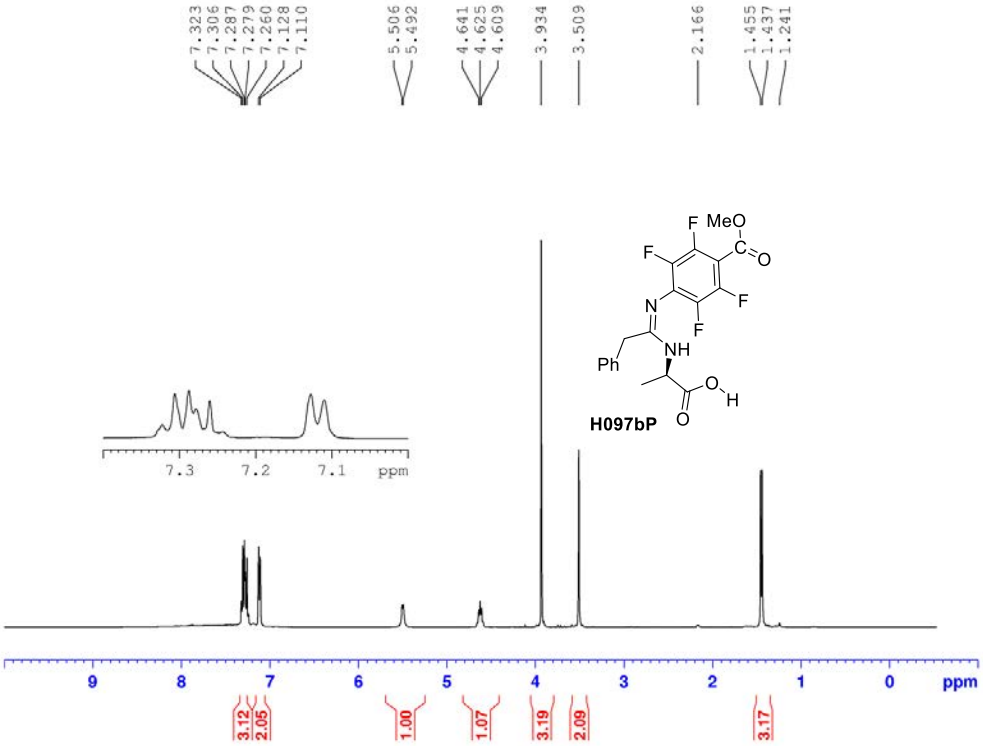
7.308
7.292
7.250
7.235
7.221
7.137
7.122
3.936
3.667
3.271
1.289
1.012
MeO
O
F
F
F
F
N
N
8 7 6 5 4 3 2 1 0 ppm
1.99
1.03
1.96
3.00
2.06
1.97
2.06
3.08
3.05


F19 DMSO 376MHz
-142.24
-142.26
-142.30
-142.32
-153.09
-153.11
-153.15
-153.17
Ph
F
OMe
O
HN
N
F
F
F
-142.2
ppm
ppm
-138
-140
-142
-144
-146
-148
-150
-152
-154
-156
-158
ppm
2.00
2.02


C13 DMSO 100MH
160.63
160.25
146.40
146.33
143.88
140.81
140.68
138.43
138.29
135.47
135.33
129.95
129.14
127.96
102.22
102.07
101.92
54.94
42.43
39.52
38.44
33.76
Ph
F
OMe
O
HN
N
F
F
160.5
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


H1 DMSO 400MHz
8.045
8.032
8.019
7.319
7.300
7.282
7.238
7.219
7.199
7.172
7.159
7.155
6.919
6.912
6.900
3.862
3.555
3.537
3.523
3.506
3.479
3.350
2.920
2.902
2.885
2.505
2.500
2.496
Ph
F
OMe
O
HN
N
F
F
F
7.3
7.2
7.1
7.0
6.9
ppm
8
7
6
5
4
3
2
1
0
ppm
1.00
8.09
2.03
3.01
2.09
2.01
1.98


%T
100.6
98
96
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
47.0
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1
3734.05
3416.54
3066.66
3025.33
2955.77
2848.87
2916.81
2123.49
1976.74
1950.47
1719.95
1655.47
1618.84
1599.32
1523.06
1478.92
1436.95
1393.64
1367.07
1327.69
1298.63
1292.19
1223.56
1184.52
1116.70
1078.27
1061.97
1031.86
1016.84
998.66
977.31
904.58
854.46
839.18
779.69
761.58
739.85
702.97
694.40
Ph
F
OMe
O
HN
N
F
F
F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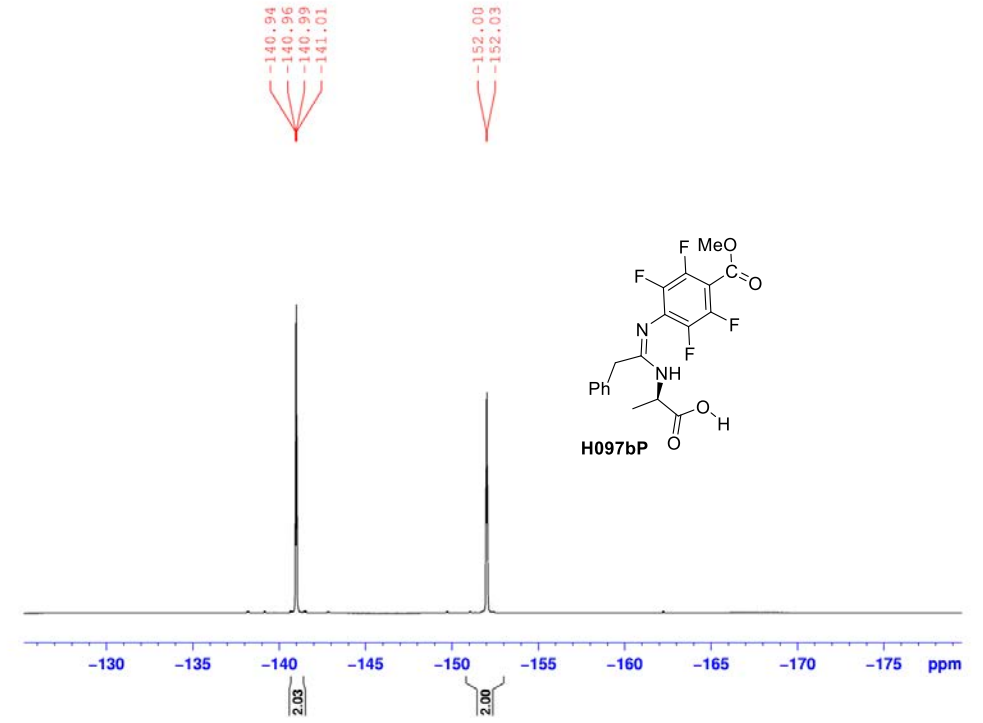
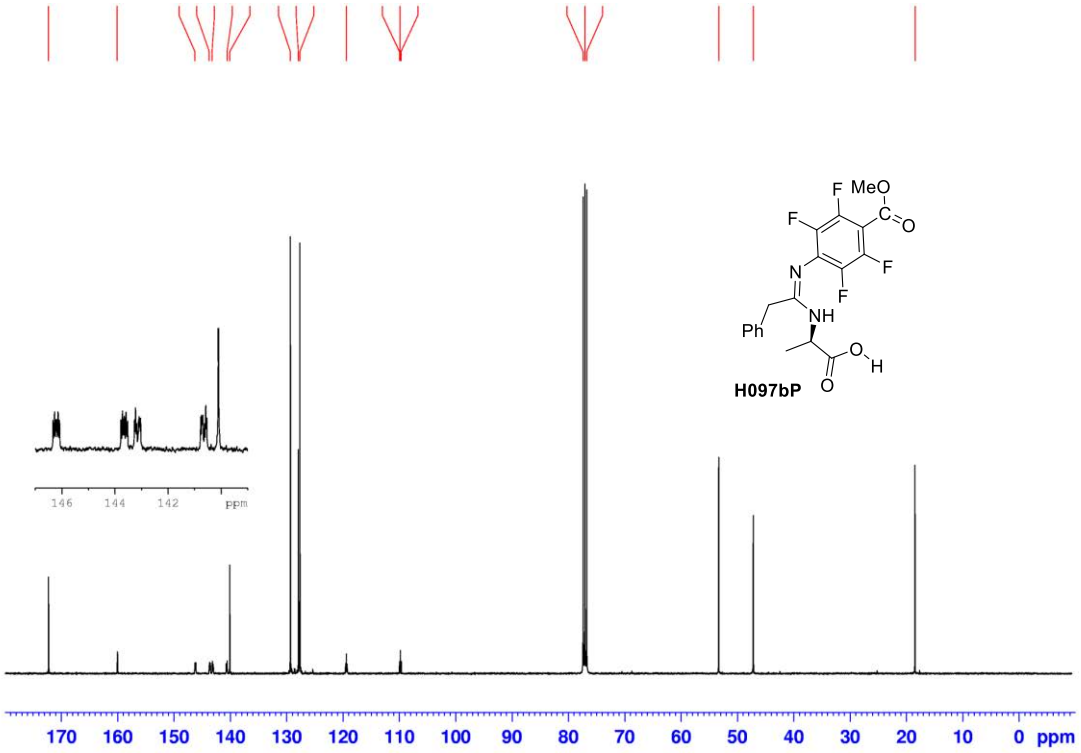
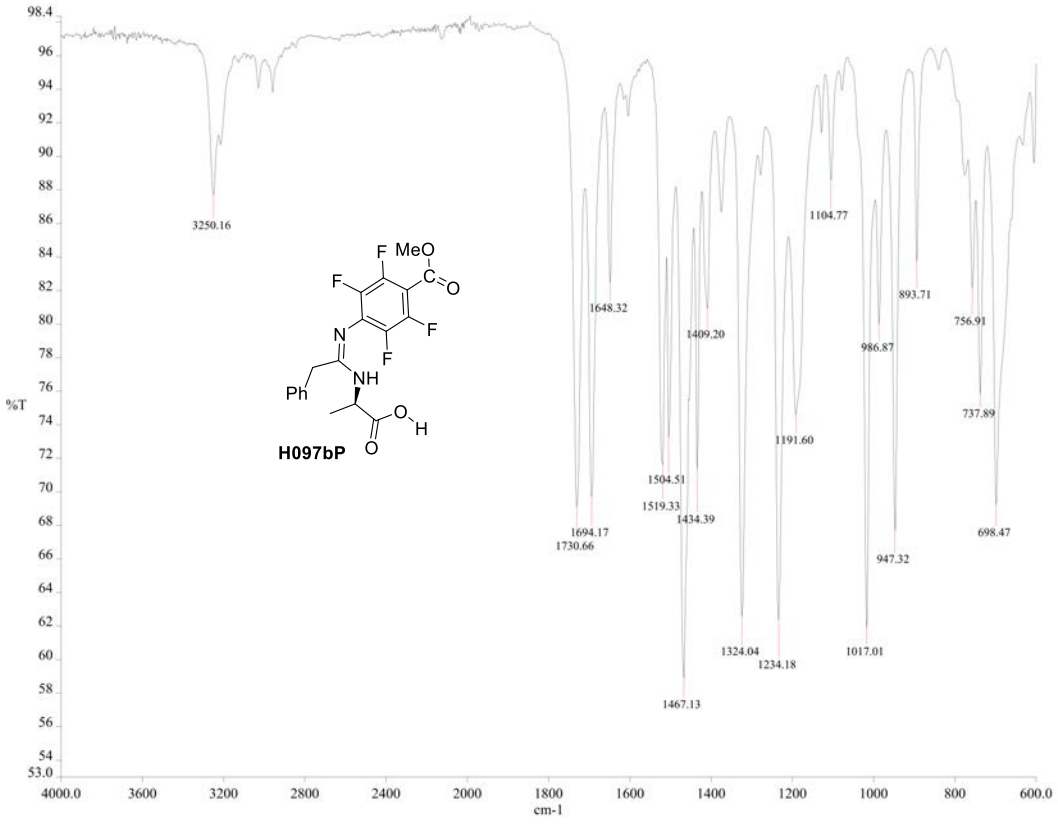
7.306
7.287
7.279
7.260
7.128
7.110
5.506
5.492
4.641
4.625
4.609
3.934
3.509
2.166
1.455
1.437
1.241
F MeO
C=O
F
F
N
F
Ph
NH
O
H
O
H097bP
7.3
7.2
7.1
ppm
9
8
7
6
5
4
3
2
1
0
ppm
3.12
2.05
1.00
1.07
3.19
2.09
3.17

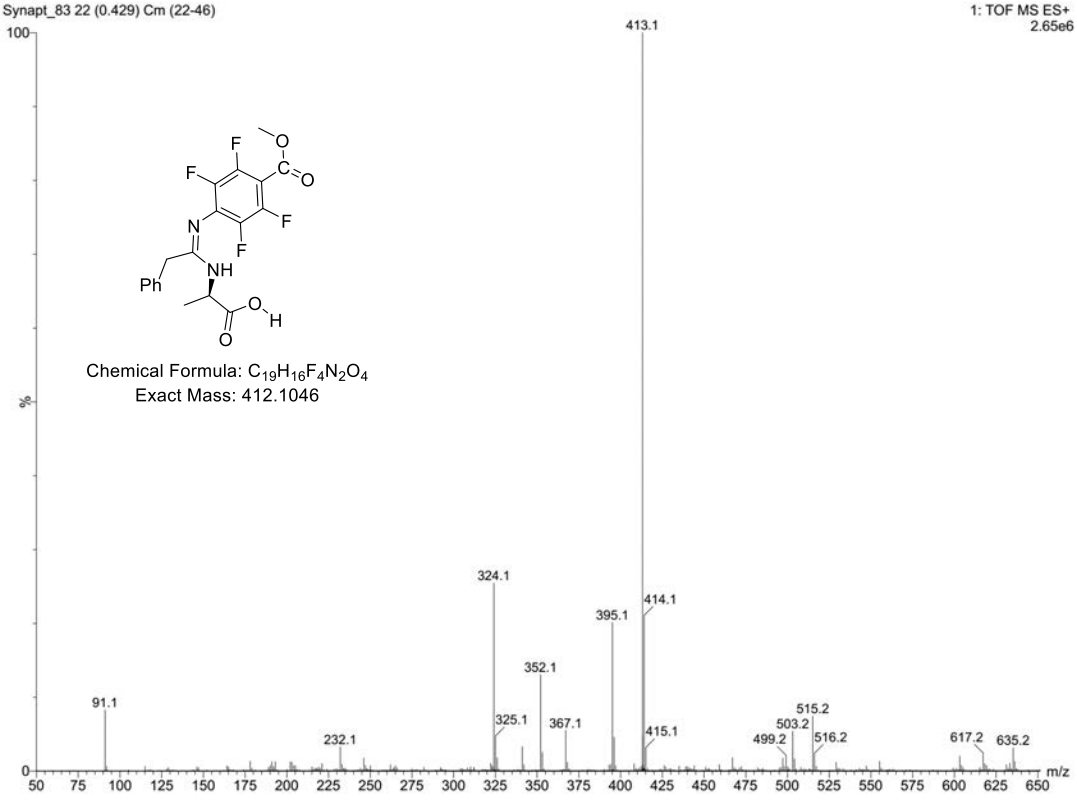

-140.94
-140.96
-140.99
-141.01
-152.00
-152.03
F MeO
C=O
F
F
N
F
Ph
NH
O
H
O
H097bP
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175
ppm
2.03
2.00


F MeO
F
C=O
F
N
F
NH
Ph
O
H
O
H097bP
146
144
142
ppm
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


%T
98.4
96
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
64
62
60
58
56
54
53.0
3250.16
1694.17
1730.66
1648.32
1504.51
1519.33
1434.39
1409.20
1467.13
1324.04
1234.18
1191.60
1104.77
1017.01
986.87
947.32
893.71
756.91
737.89
698.47
F MeO
C=O
F
F
N
F
NH
Ph
O
H
O
H097bP
4000.0 3600 3200 2800 2400 2000 1800 1600 1400 1200 1000 800 600.0
cm-1

H086
Synapt_83 22 (0.429) Cm (22-46)

1: TOF MS ES+
2.65e6



Chemical Formula: $C_{19}H_{16}F_4N_2O_4$
Exact Mass: 412.1046

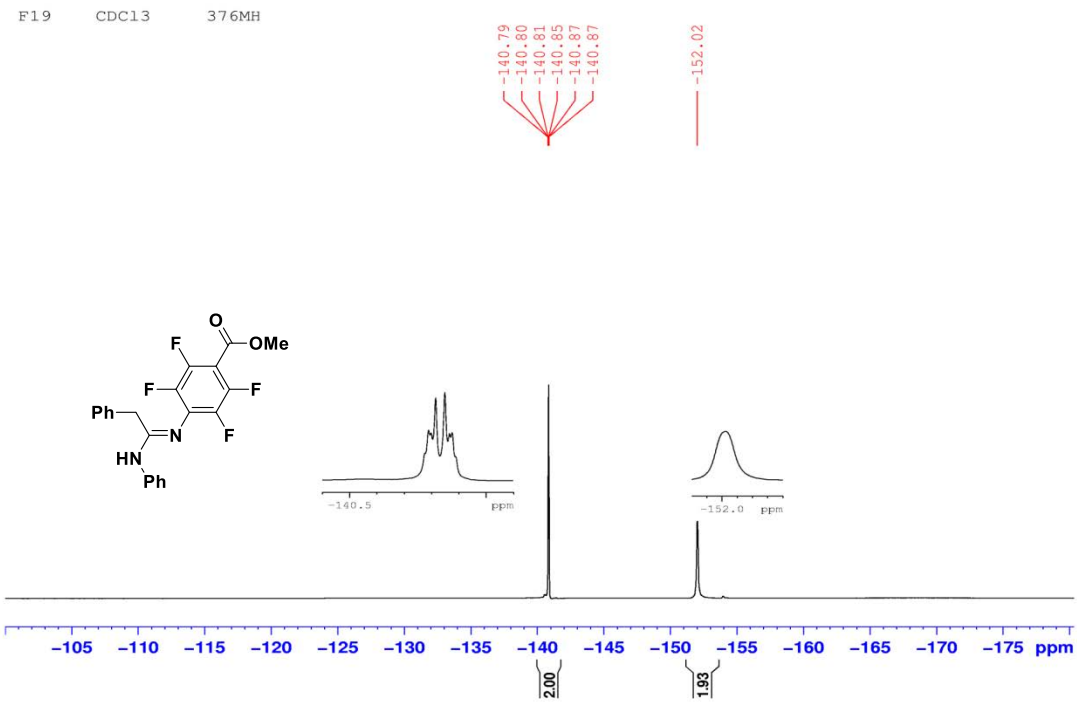
Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
62 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 1-3 O: 1-5 F: 4-4

Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
413.1121	413.1124	-0.3	-0.7	10.5	1568.3	n/a	n/a	C19 H17 N2 O4 F4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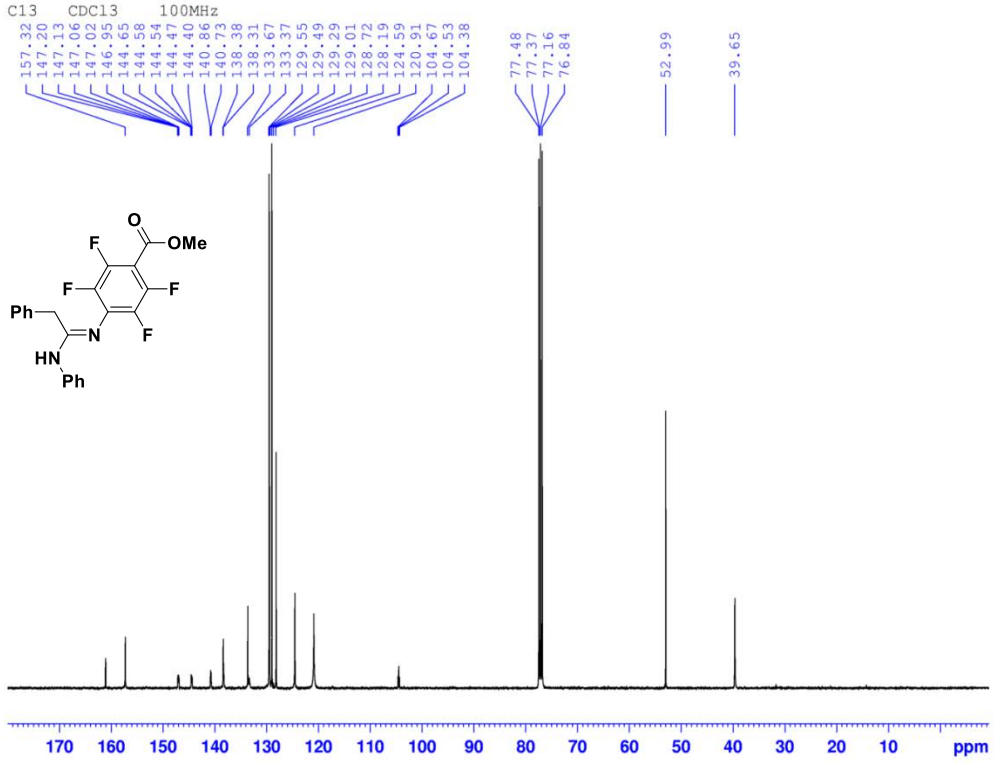
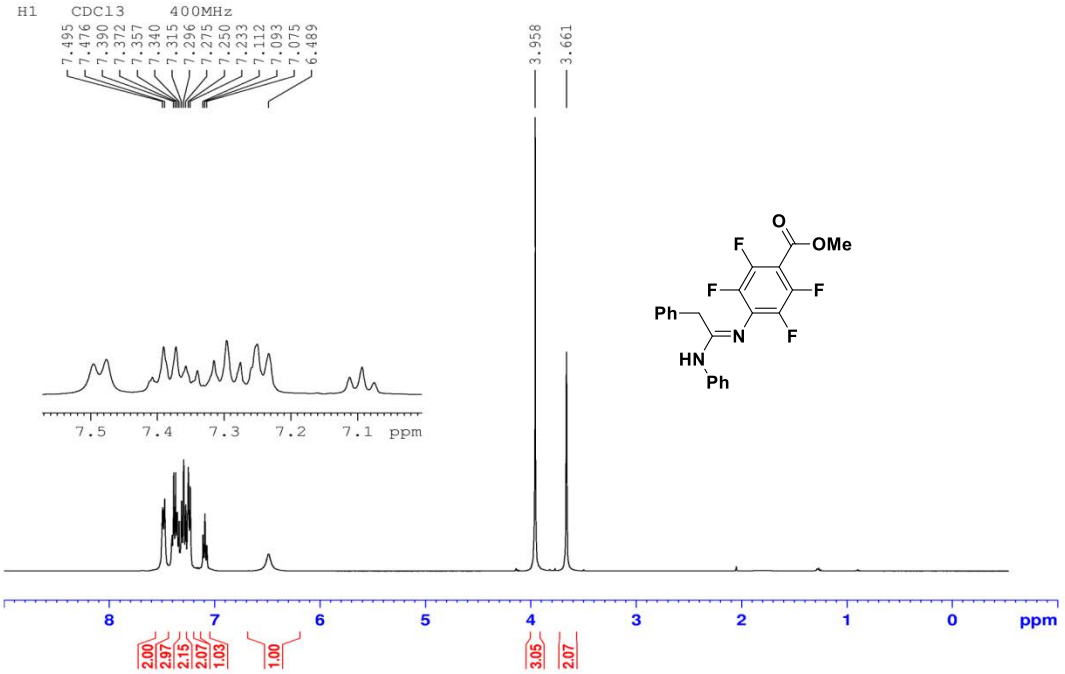
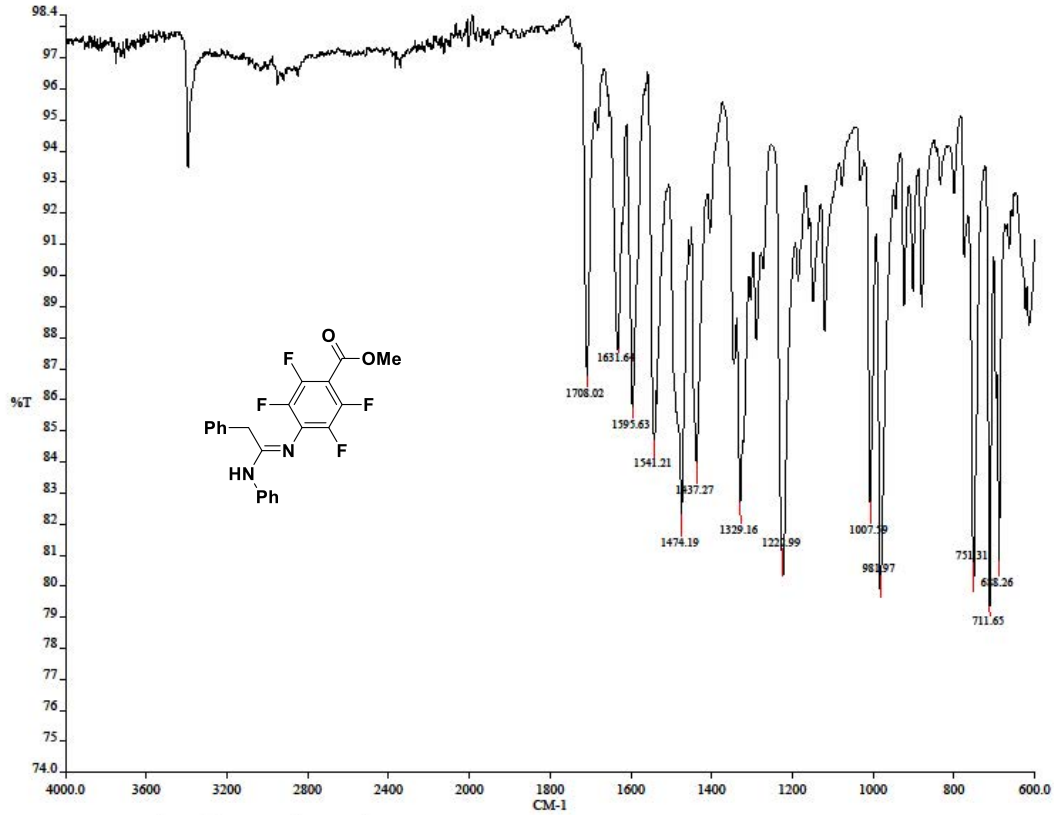
-140.80
-140.81
-140.85
-140.87
-140.87
-152.02
O
OMe
F
F
F
F
Ph
N
HN
Ph
-140.5
ppm
-152.0
ppm
-105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 ppm
2.00
1.93


C13 CDCl3 100MHz
157.32
147.20
147.13
147.06
147.02
146.95
144.65
144.58
144.54
144.47
144.40
140.86
140.73
138.38
138.31
133.67
133.37
129.55
129.49
129.29
129.01
128.72
128.19
124.59
120.91
104.67
104.53
104.38
77.48
77.37
77.16
76.84
52.99
39.65
O
OMe
F
F
F
F
Ph
N
HN
Ph
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


H1 CDC13 400MHz
7.495
7.476
7.390
7.372
7.357
7.340
7.315
7.296
7.275
7.250
7.233
7.112
7.093
7.075
6.489
3.958
3.661
7.5 7.4 7.3 7.2 7.1 ppm
8 7 6 5 4 3 2 1 0 ppm
2.00 2.97 2.15 2.07 1.03 1.00 3.05 2.07
O
OMe
F
F
F
F
Ph
N
HN
Ph


%T
CM-1
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1708.02
1631.64
1595.63
1541.21
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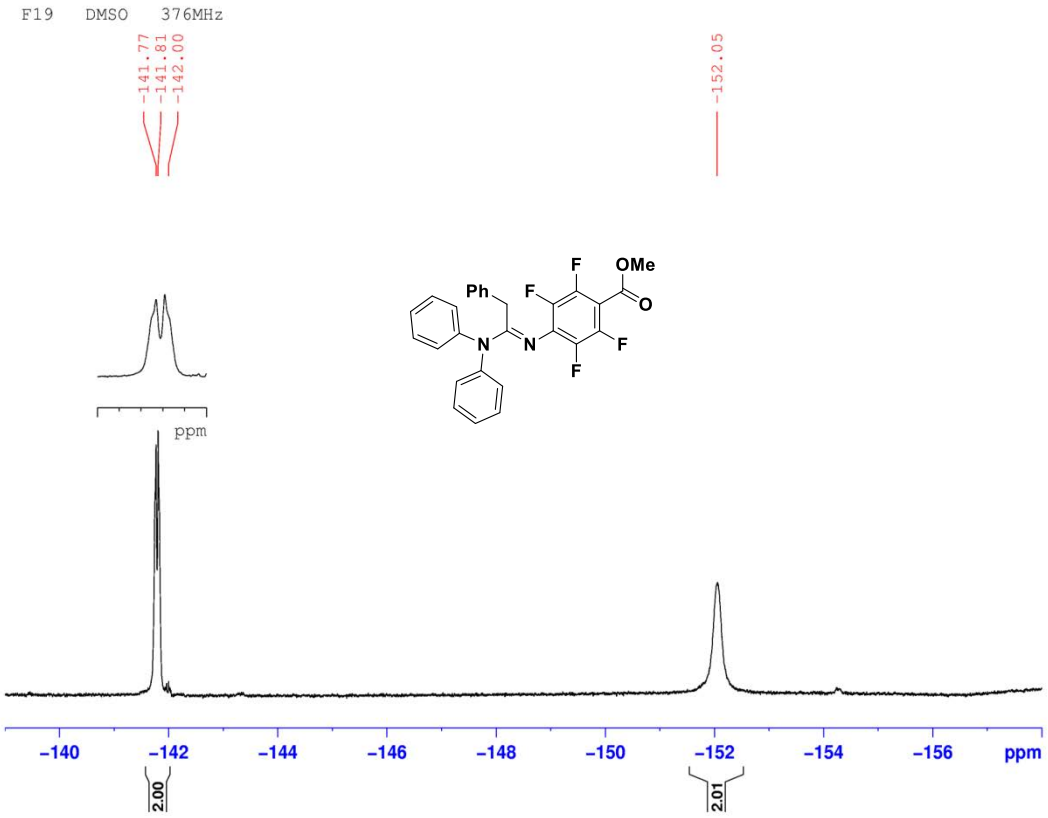
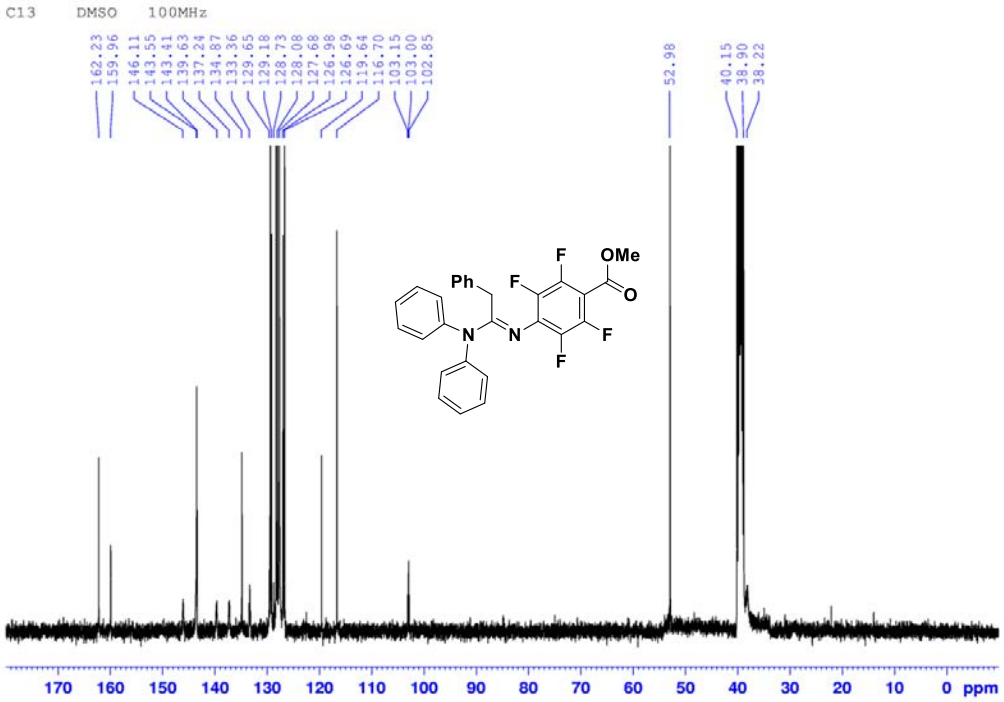
1437.27
1329.16
1222.99
1007.59
981.97
751.31
658.26
711.65
O
OMe
F
F
F
F
Ph
N
HN
Ph


F19 DMSO 376MHz
-141.77
-141.81
-142.00
-152.05
F
OMe
Ph
F
O
N
N
F
F
ppm
-140
-142
-144
-146
-148
-150
-152
-154
-156
ppm
2.00
2.01


C13 DMSO 100MHz
162.23
159.96
146.11
143.55
143.41
139.63
137.24
134.87
133.36
129.65
129.18
128.73
128.08
127.68
126.98
126.69
119.64
116.70
103.15
103.00
102.85
52.98
40.15
38.90
38.22
F
OMe
Ph
F
O
N
N
F
F
170
160
150
140
130
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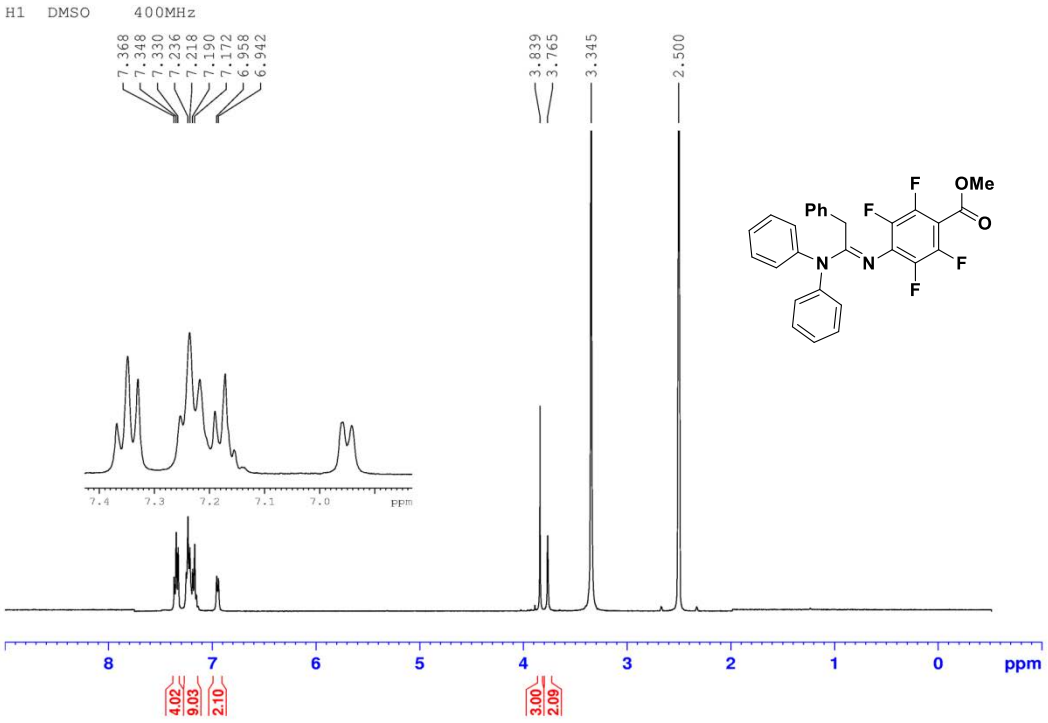
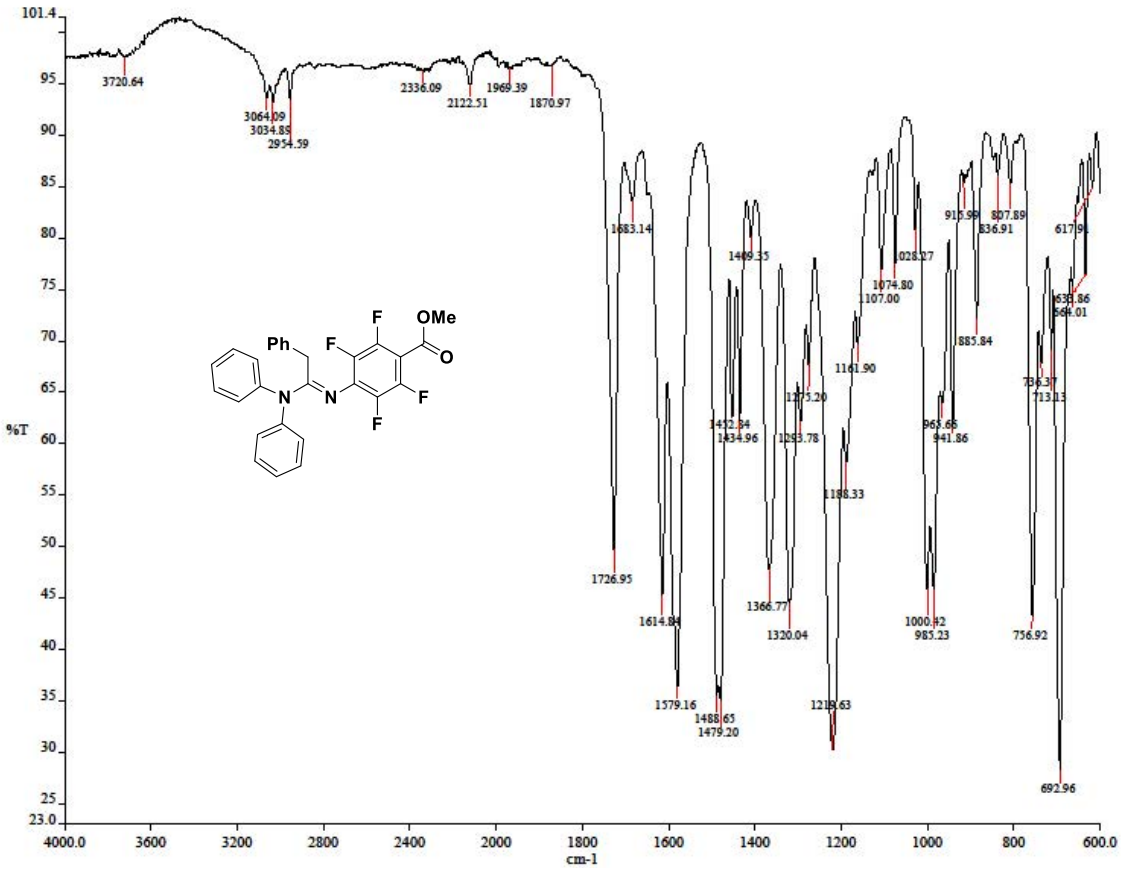
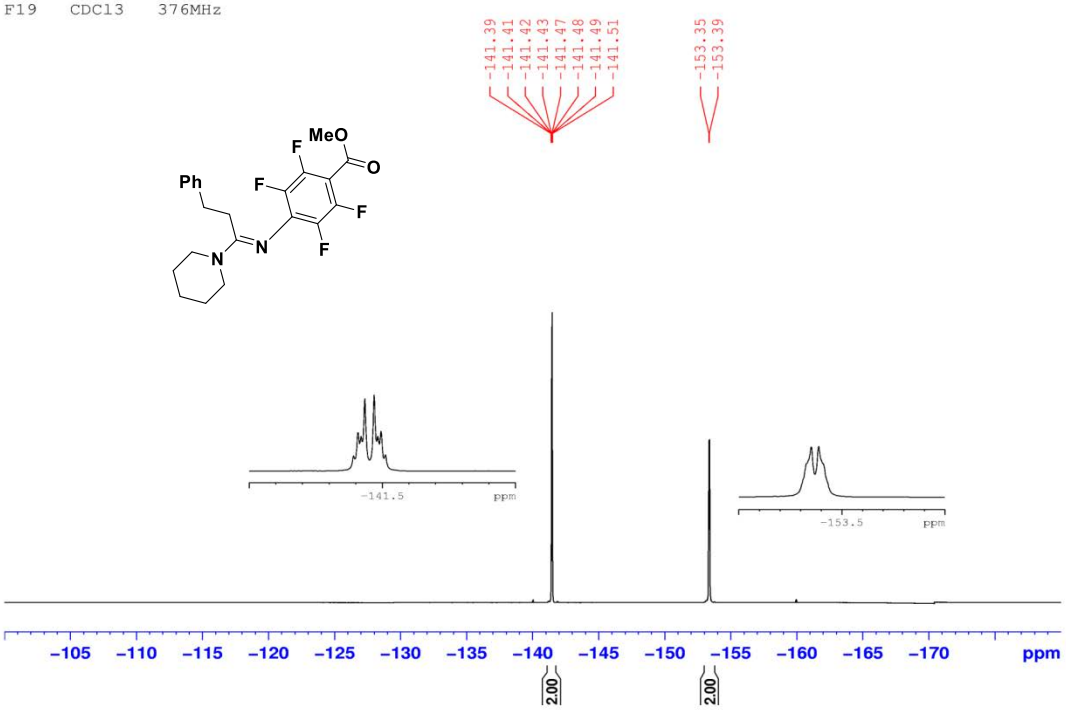
110
100
90
80
70
60
50
40
30
20
10
0 ppm

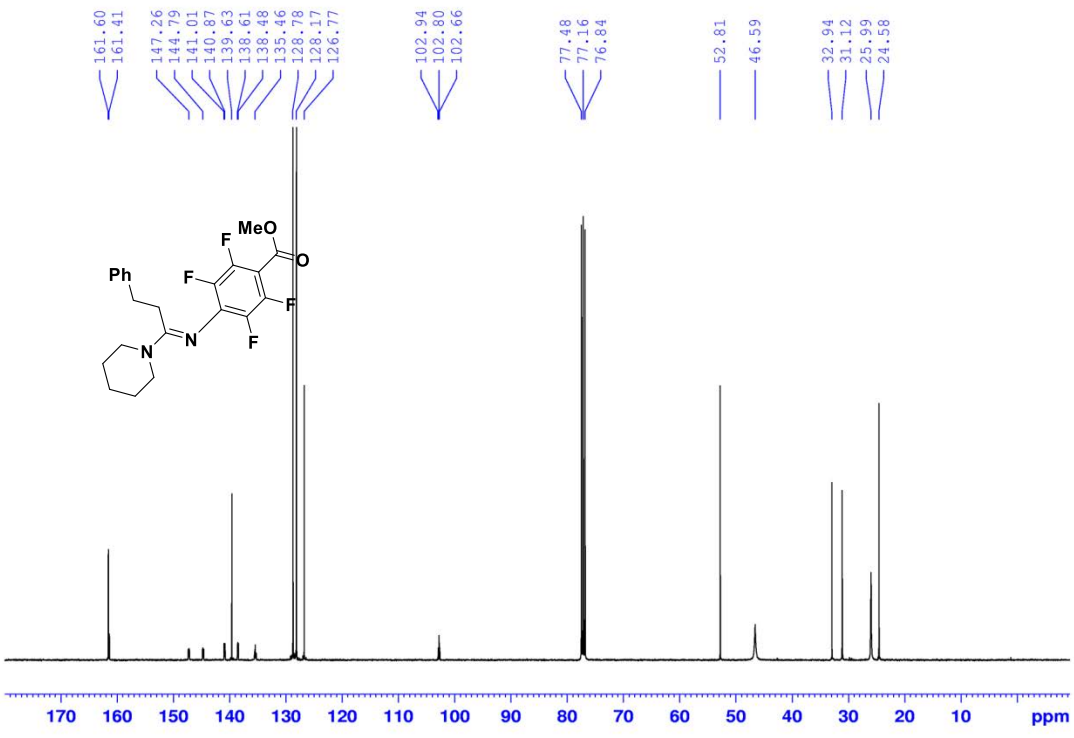

H1 DMSO 400MHz
7.368
7.348
7.330
7.236
7.218
7.190
7.172
6.958
6.942
3.839
3.765
3.345
2.500
F
OMe
Ph
F
O
N
N
F
F
7.4
7.3
7.2
7.1
7.0
ppm
8
7
6
5
4
3
2
1
0
ppm
4.02
9.03
2.10
3.00
2.09

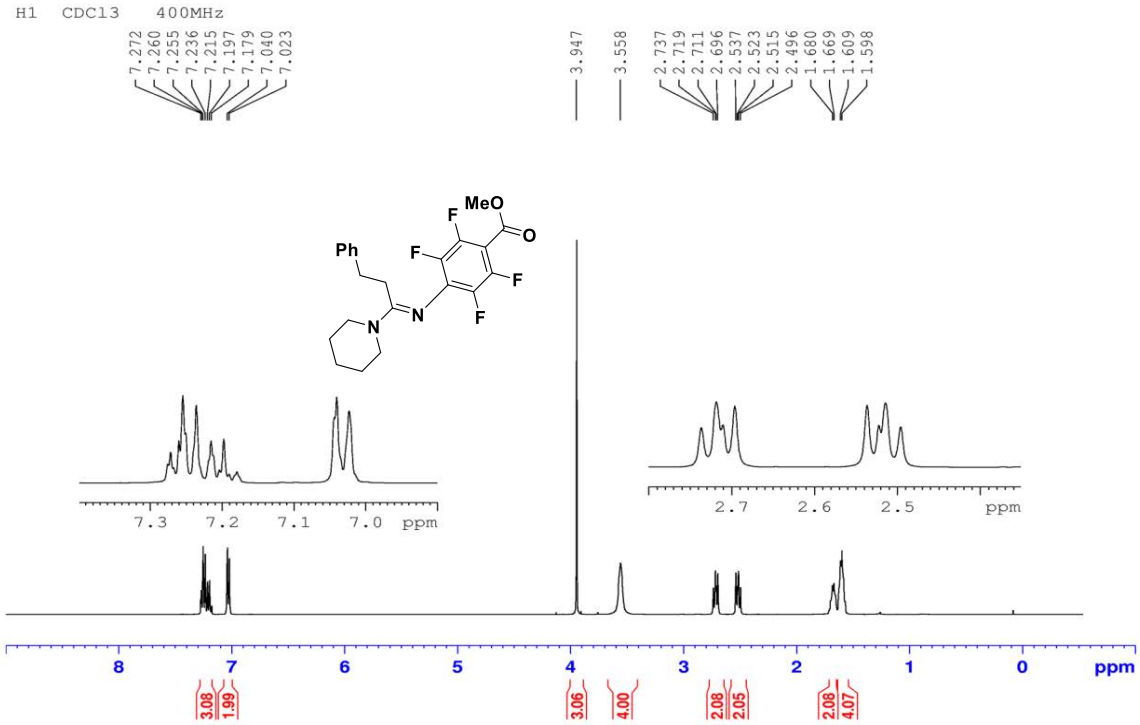

101.4
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
23.0
%T
3720.64
3064.09
3034.85
2954.59
2336.09
2122.51
1969.39
1870.97
1683.14
1726.95
1614.84
1579.16
1488.65
1479.20
1469.35
1434.96
1422.84
1366.77
1320.04
1293.78
1275.20
1218.63
1188.33
1161.90
1107.00
1074.80
1028.27
1000.42
985.23
965.68
941.86
915.98
885.84
836.91
807.89
756.92
736.37
713.13
692.96
617.91
F
OMe
Ph
F
O
N
N
F
F
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1

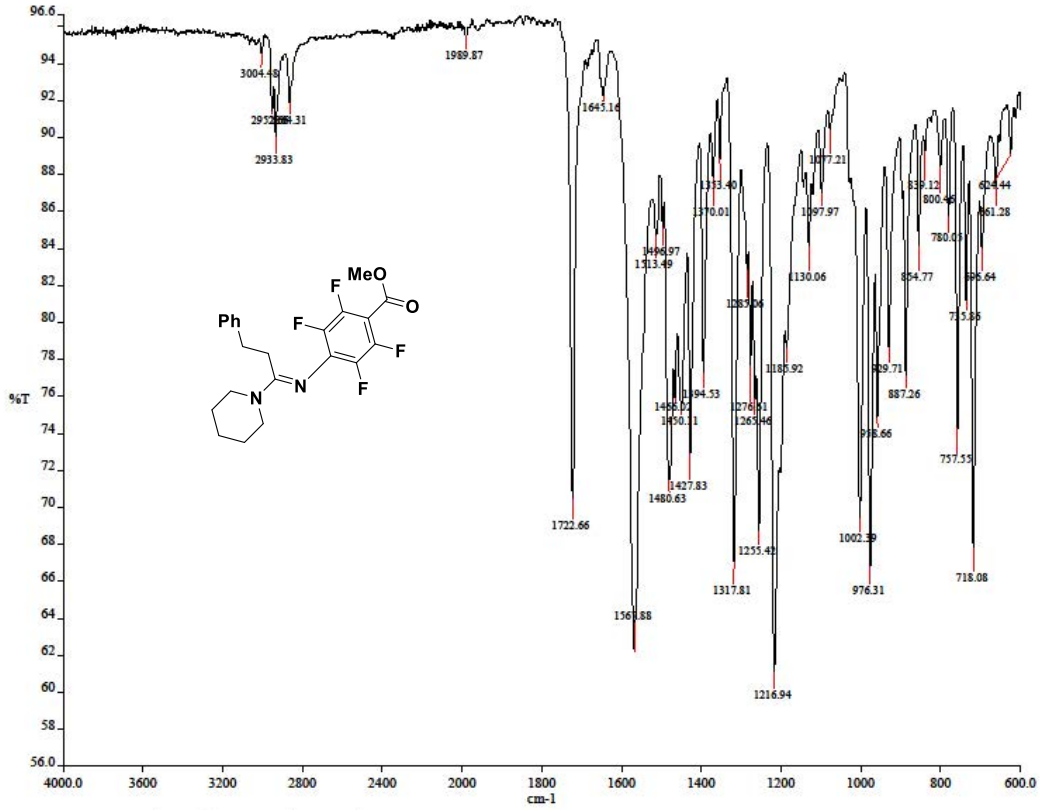
F19 CDCl3 376MHz

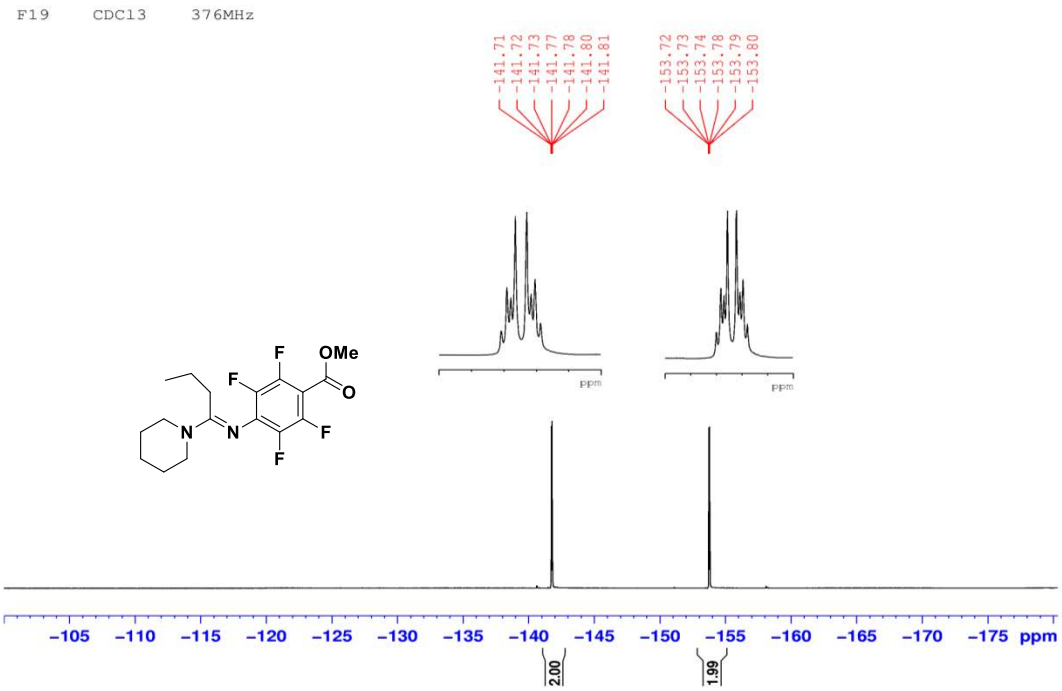


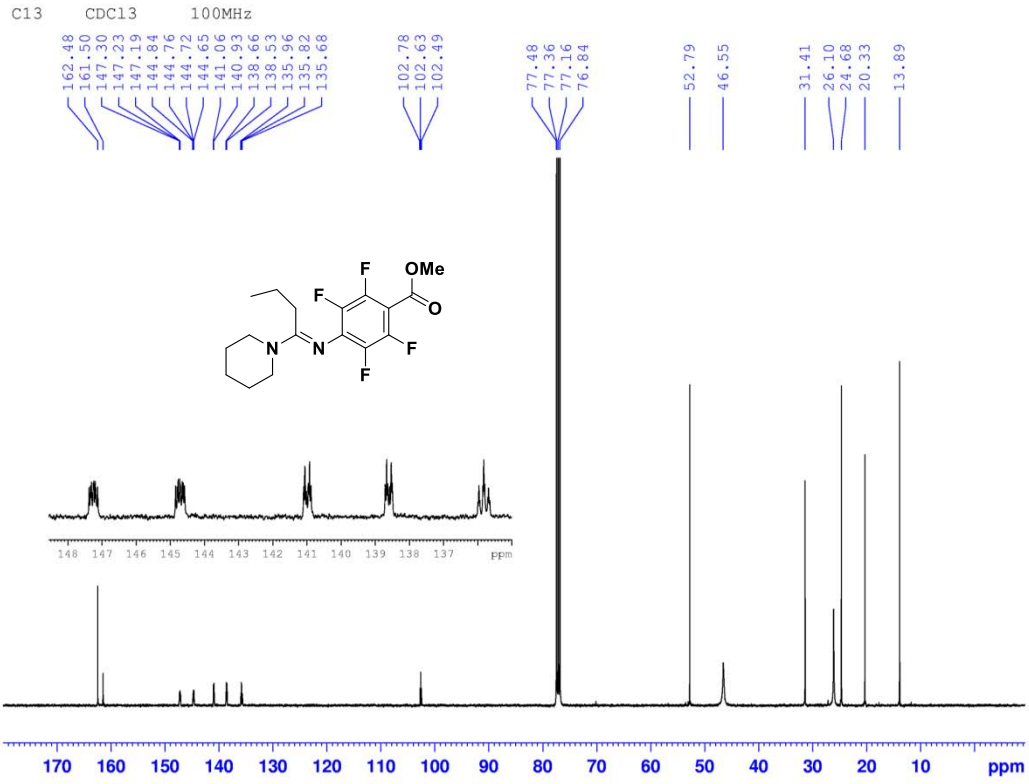
C13 CDCl3 400MHz

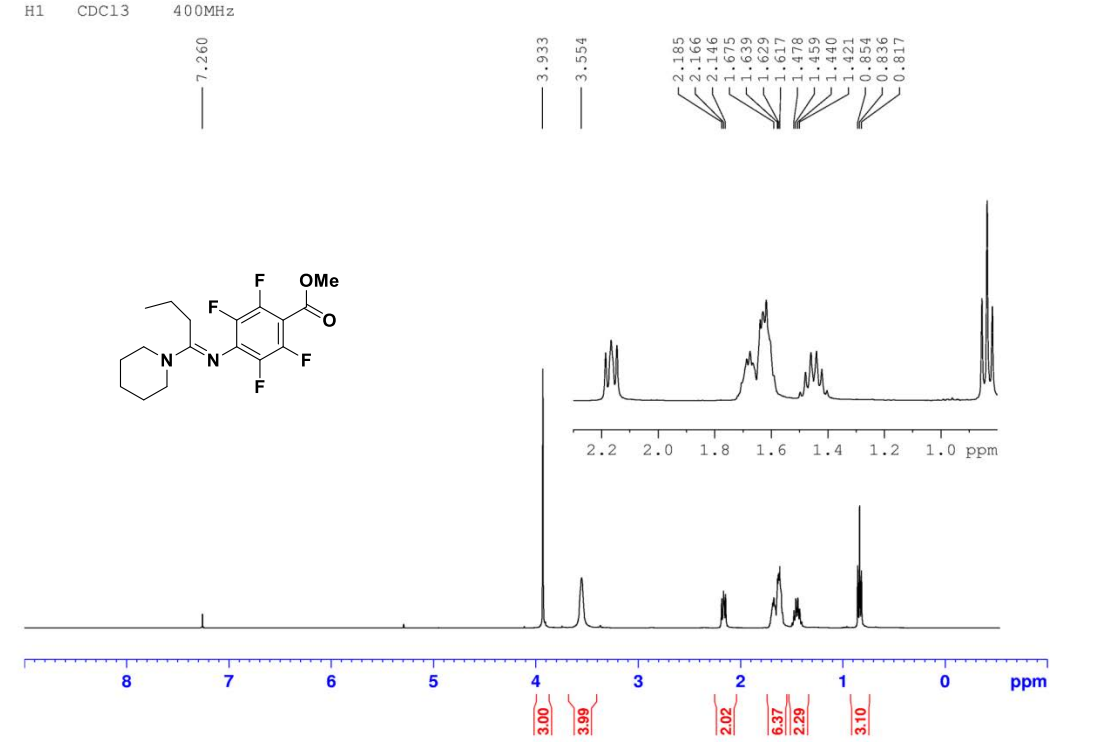


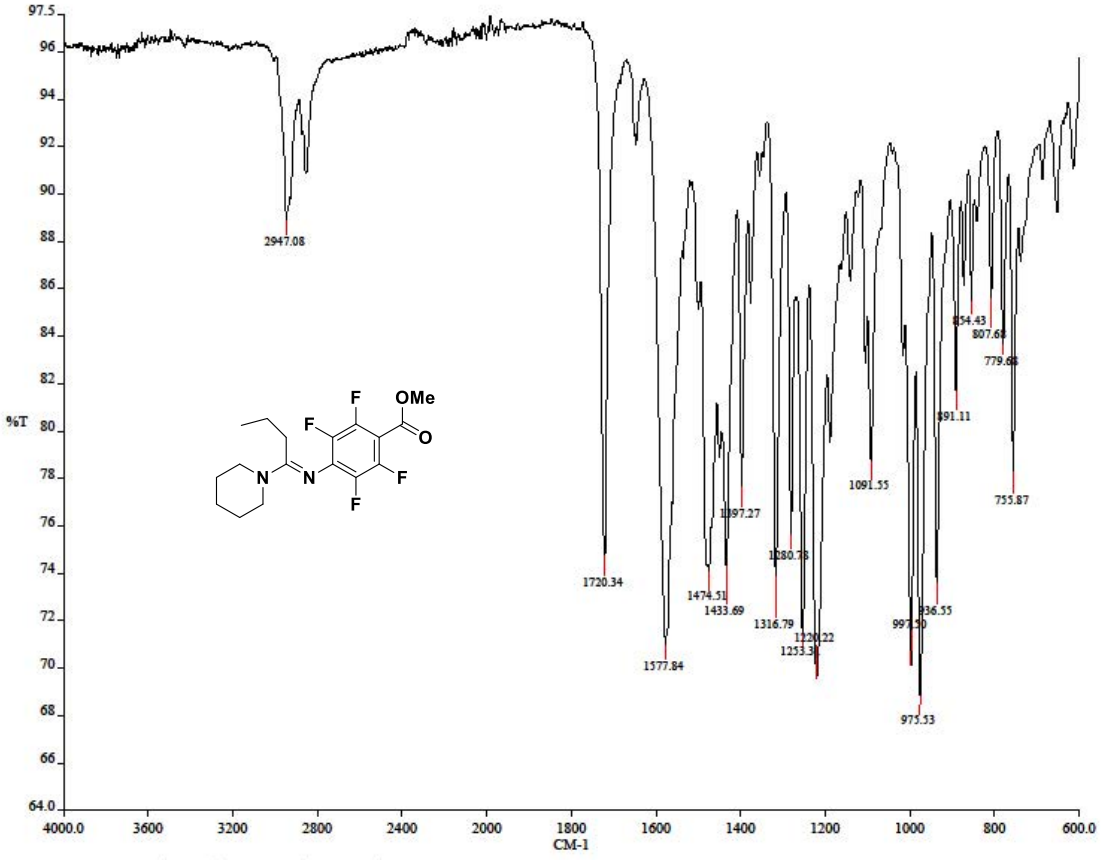

H1 CDC13 400MHz
7.272
7.260
7.255
7.236
7.215
7.197
7.179
7.040
7.023
3.947
3.558
2.737
2.719
2.711
2.696
2.537
2.523
2.515
2.496
1.680
1.669
1.609
1.598
MeO
O
F
F
F
F
Ph
N
N
7.3
7.2
7.1
7.0
ppm
2.7
2.6
2.5
ppm
8
7
6
5
4
3
2
1
0
ppm
3.08
1.99
3.06
4.00
2.08
2.05
2.08
4.07

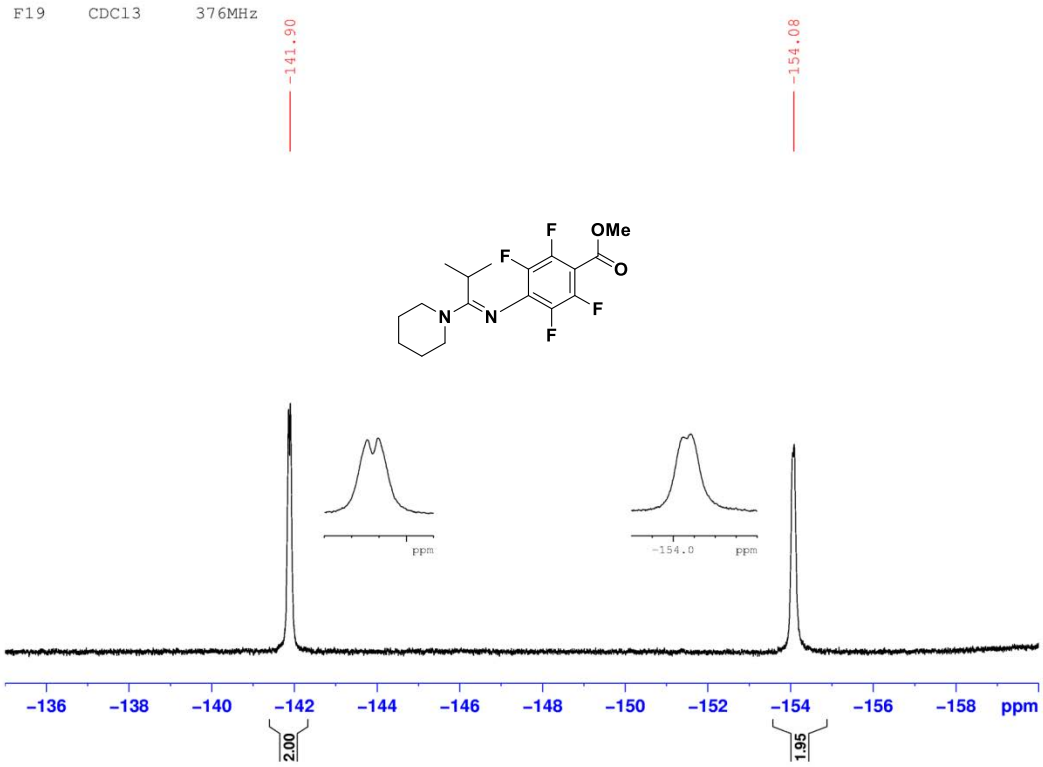

%T
cm-1
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
96.6
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
64
62
60
58
56.0
3004.48
2933.83
1989.87
1645.16
1722.66
1561.88
1480.63
1427.83
1317.81
1216.94
1255.42
1002.39
976.31
718.08
MeO
O
F
F
F
F
Ph
N
N

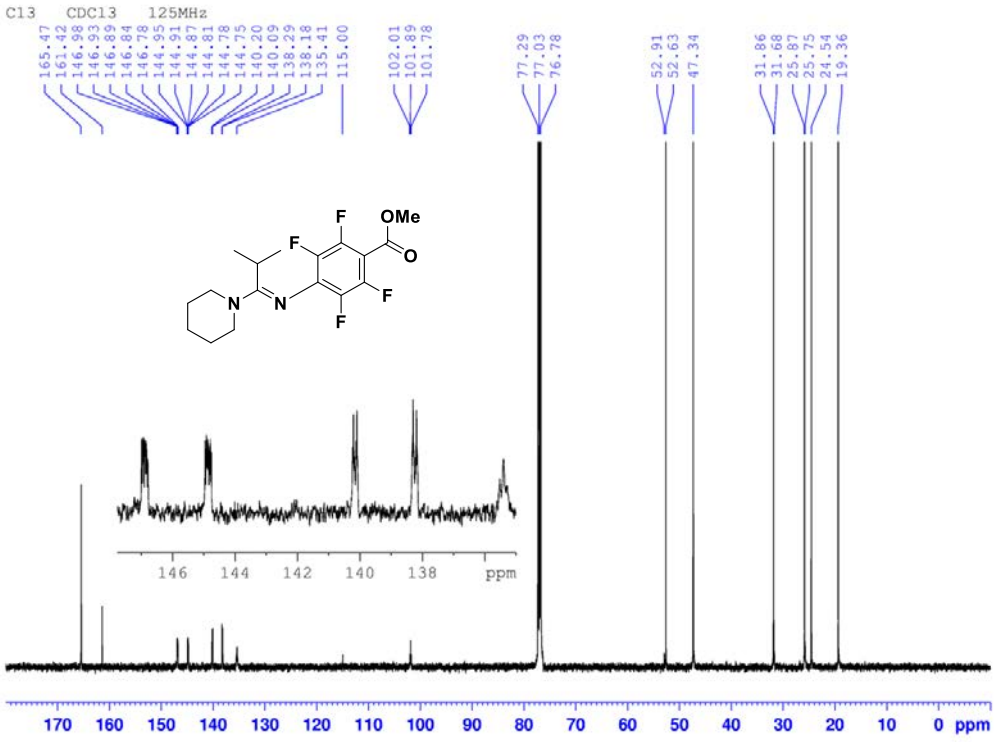

F19 CDC13 376MHz
-141.71
-141.72
-141.73
-141.77
-141.78
-141.80
-141.81
-153.72
-153.73
-153.74
-153.78
-153.79
-153.80
F
OMe
O
N
N
F
F
F
ppm
ppm
-105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 ppm
2.00
1.99

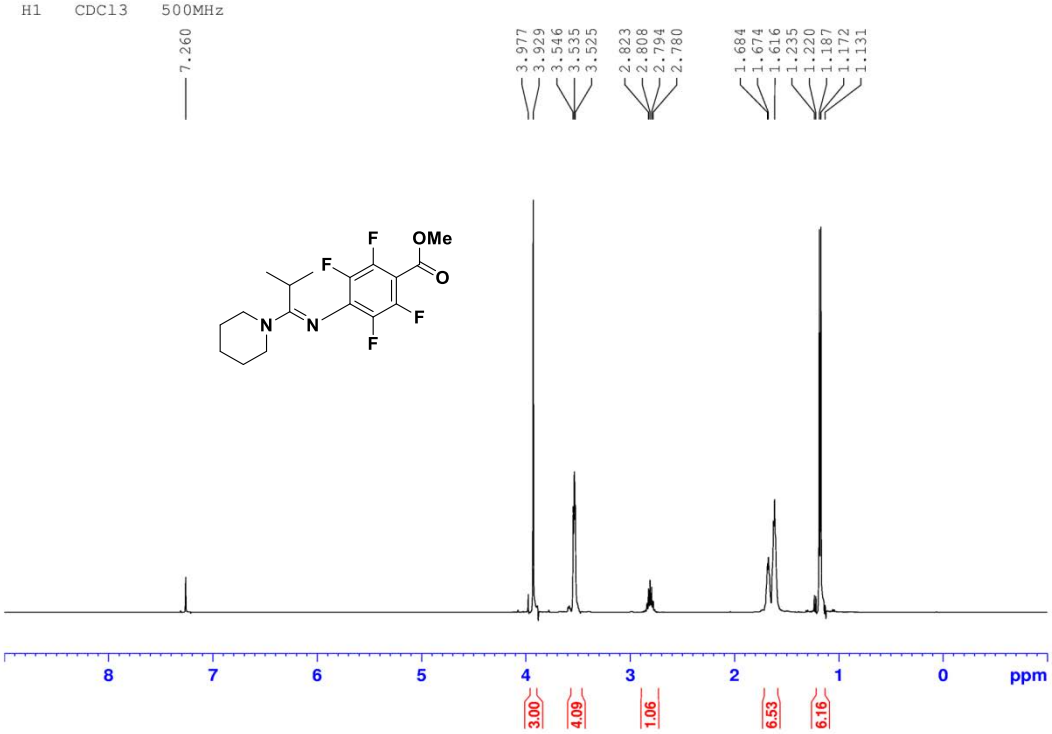

C13 CDC13 100MHz
162.48
161.50
147.30
147.23
147.19
144.84
144.76
144.72
144.65
141.06
140.93
138.66
138.53
135.96
135.82
135.68
102.78
102.63
102.49
77.48
77.36
77.16
76.84
52.79
46.55
31.41
26.10
24.68
20.33
13.89
F
OMe
O
N
N
F
F
F
148 147 146 145 144 143 142 141 140 139 138 137 ppm
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

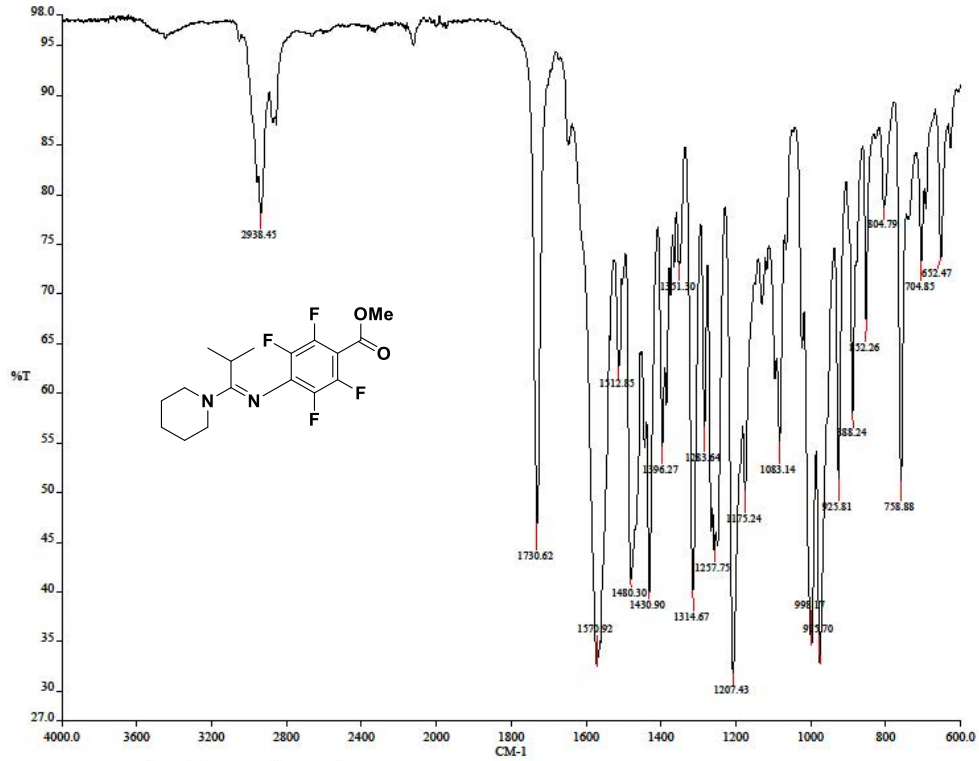

H1 CDCl3 400MHz
7.260
3.933
3.554
2.185
2.166
2.146
1.675
1.639
1.629
1.617
1.478
1.459
1.440
1.421
0.854
0.836
0.817
F
OMe
O
F
N
N
F
F
2.2 2.0 1.8 1.6 1.4 1.2 1.0 ppm
8 7 6 5 4 3 2 1 0 ppm
3.00
3.99
2.02
6.37
2.29
3.10

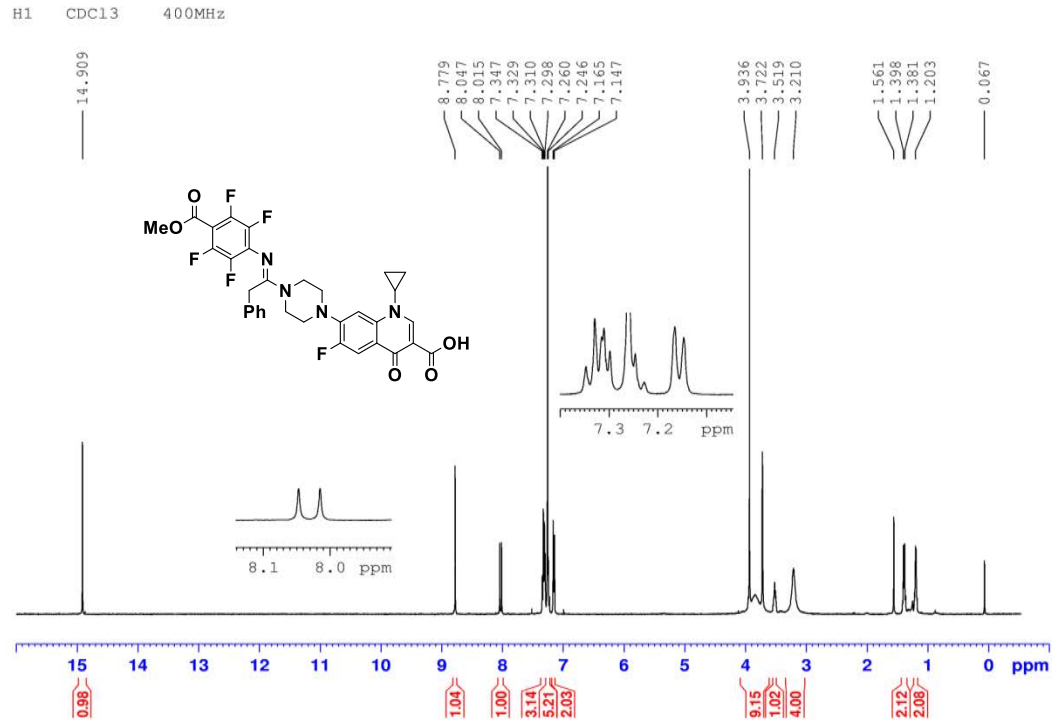

%T
97.5
96
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
64.0
4000.0 3600 3200 2800 2400 2000 1800 1600 1400 1200 1000 800 600.0
CM-1
2947.08
1720.34
1577.84
1474.51
1433.69
1397.27
1316.79
1280.78
1220.22
1253.31
1091.55
975.53
991.11
936.55
997.50
854.43
807.68
779.68
755.87
F
OMe
O
F
N
N
F
F

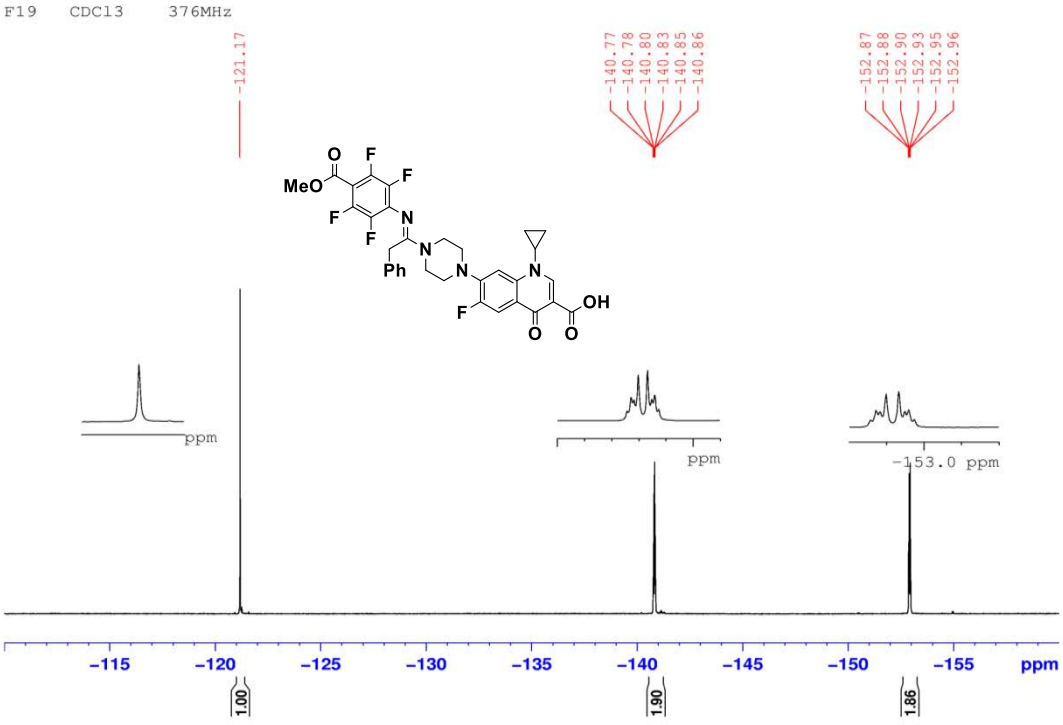

F19 CDCl3 376MHz
-141.90
-154.08
F
OMe
O
F
F
N
N
F
ppm
-154.0
ppm
-136
-138
-140
-142
-144
-146
-148
-150
-152
-154
-156
-158
ppm
2.00
1.95

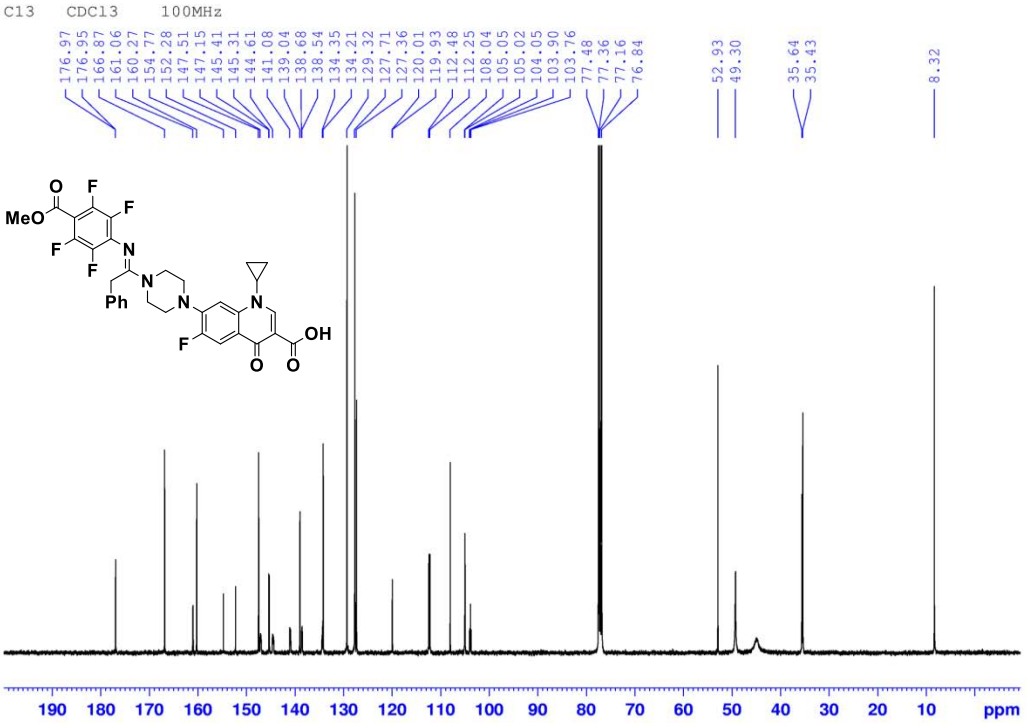

C13 CDCl3 125MHz
165.47
161.42
146.98
146.93
146.89
146.84
146.78
144.95
144.91
144.87
144.81
144.78
144.75
140.20
140.09
138.29
138.18
135.41
115.00
102.01
101.89
101.78
77.29
77.03
76.78
52.91
52.63
47.34
31.86
31.68
25.87
25.75
24.54
19.36
F
OMe
O
F
F
N
N
F
146
144
142
140
138
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

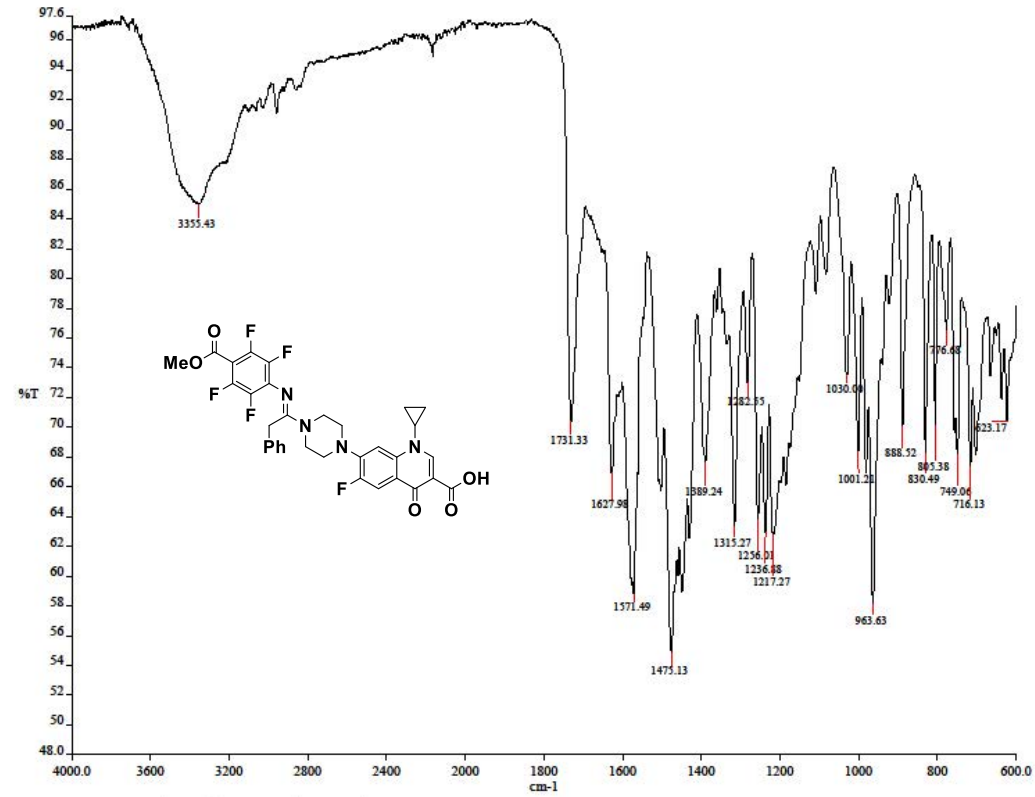

H1 CDCl3 500MHz
7.260
3.977
3.929
3.546
3.535
3.525
2.823
2.808
2.794
2.780
1.684
1.674
1.616
1.235
1.220
1.187
1.172
1.131
F
OMe
F
O
N
N
F
F
8
7
6
5
4
3
2
1
0
ppm
3.00
4.09
1.06
6.53
6.16

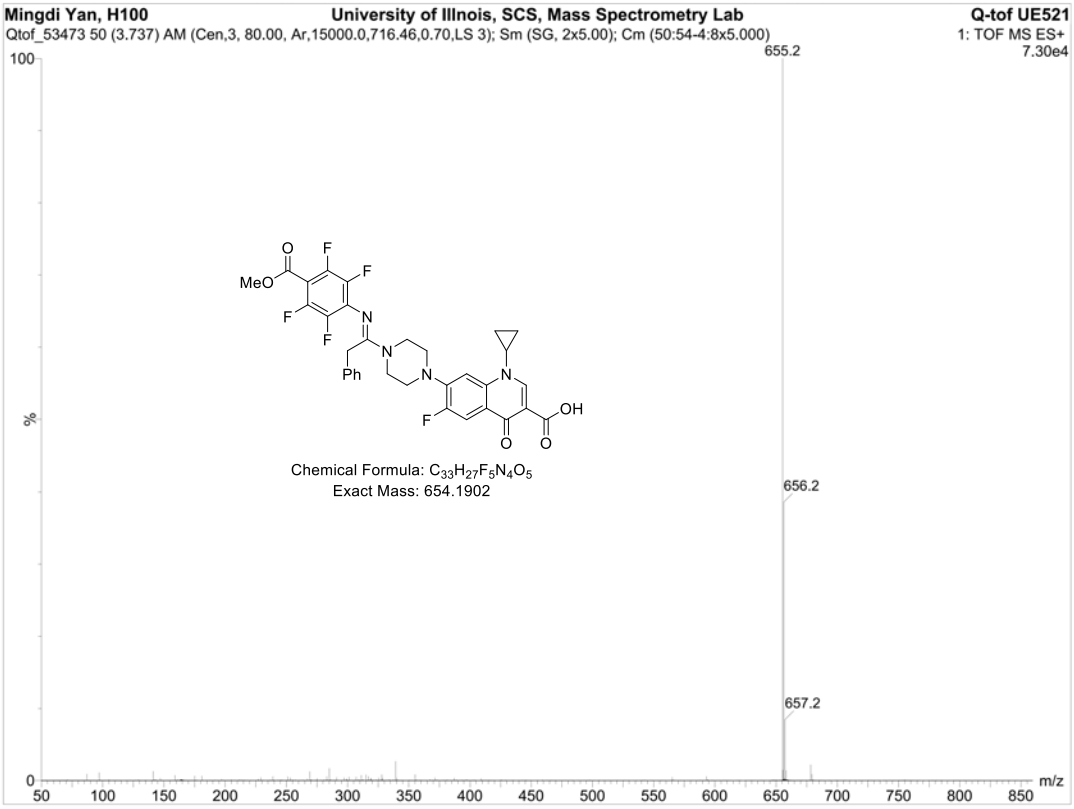

%T
98.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
27.0
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
CM-1
2938.45
1730.62
1570.92
1512.85
1480.30
1430.90
1396.27
1351.30
1314.67
1283.64
1257.75
1207.43
1175.24
1083.14
998.17
915.70
925.81
888.24
852.26
804.79
758.88
704.85
652.47
F
OMe
F
O
N
N
F
F


H1 CDCl3 400MHz
14.909
8.779
8.047
8.015
7.347
7.329
7.310
7.298
7.260
7.246
7.165
7.147
3.936
3.722
3.519
3.210
1.561
1.398
1.381
1.203
0.067
MeO
O
F
F
F
F
N
Ph
N
N
F
OH
O
O
7.3 7.2 ppm
8.1 8.0 ppm
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.98
1.04
1.00
3.14
5.21
2.03
9.15
1.02
4.00
2.12
2.08


F19 CDCl3 376MHz
-121.17
-140.77
-140.78
-140.80
-140.83
-140.85
-140.86
-152.87
-152.88
-152.90
-152.93
-152.95
-152.96
MeO
O
F
F
F
F
N
Ph
N
N
F
OH
O
O
ppm
ppm
-153.0 ppm
-115 -120 -125 -130 -135 -140 -145 -150 -155 ppm
1.00
1.90
1.86


C13 CDCl3 100MHz
176.97
176.95
166.87
161.06
160.27
154.77
152.28
147.51
147.15
145.41
145.31
144.61
141.08
139.04
138.68
138.54
134.35
134.21
129.32
127.71
127.36
120.01
119.93
112.48
112.25
108.04
105.05
105.02
104.05
103.90
103.76
77.48
77.36
77.16
76.84
52.93
49.30
35.64
35.43
8.32
MeO
O
F
F
F
F
N
Ph
N
N
N
F
OH
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


%T
97.6
96
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
48.0
3355.43
1731.33
1627.98
1571.49
1475.13
1389.24
1315.27
1282.55
1256.01
1236.68
1217.27
1030.04
1001.21
963.63
888.52
843.38
830.49
776.68
749.06
716.13
623.17
MeO
O
F
F
F
F
N
Ph
N
N
N
F
OH
O
O
4000.0 3600 3200 2800 2400 2000 1800 1600 1400 1200 1000 800 600.0
cm-1

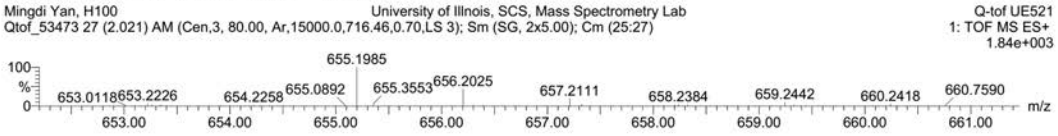


Elemental Composition Report

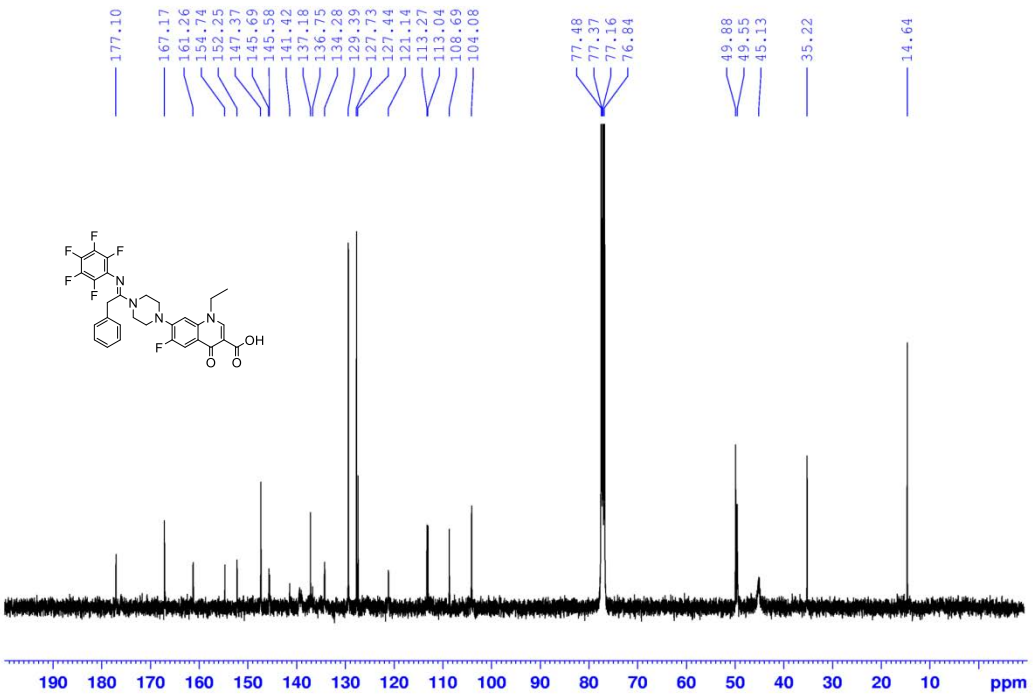
Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 600.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

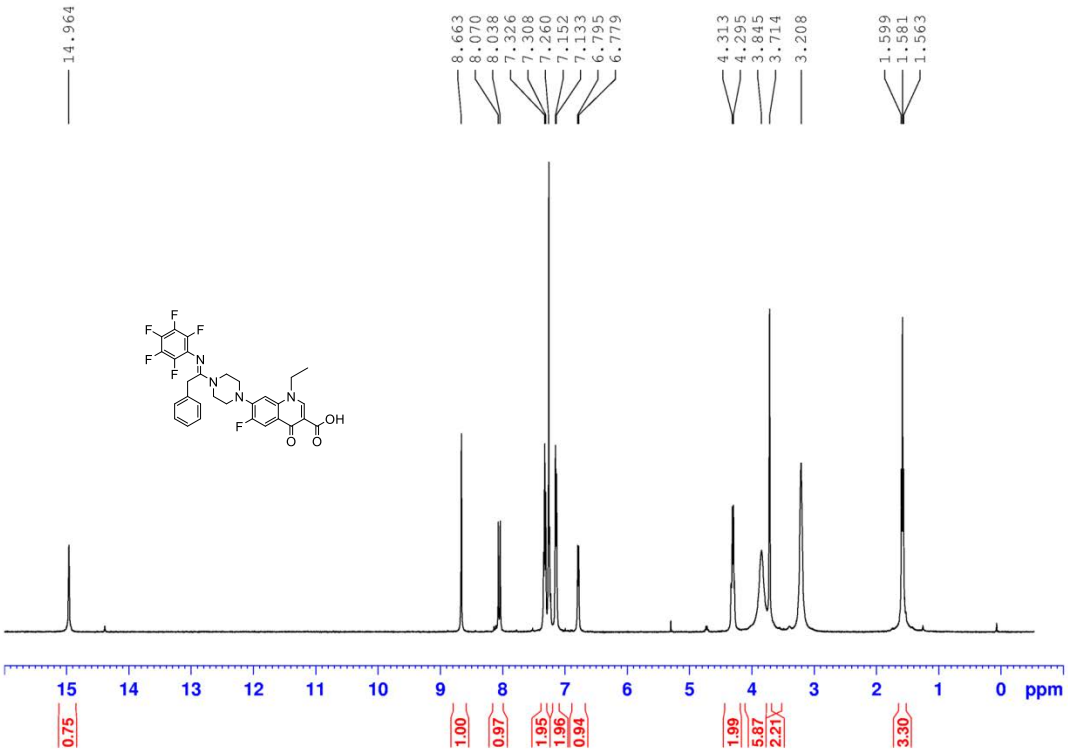
Monoisotopic Mass, Even Electron Ions
541 formula(e) evaluated with 6 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-120 H: 0-180 N: 0-6 O: 0-5 F: 5-6



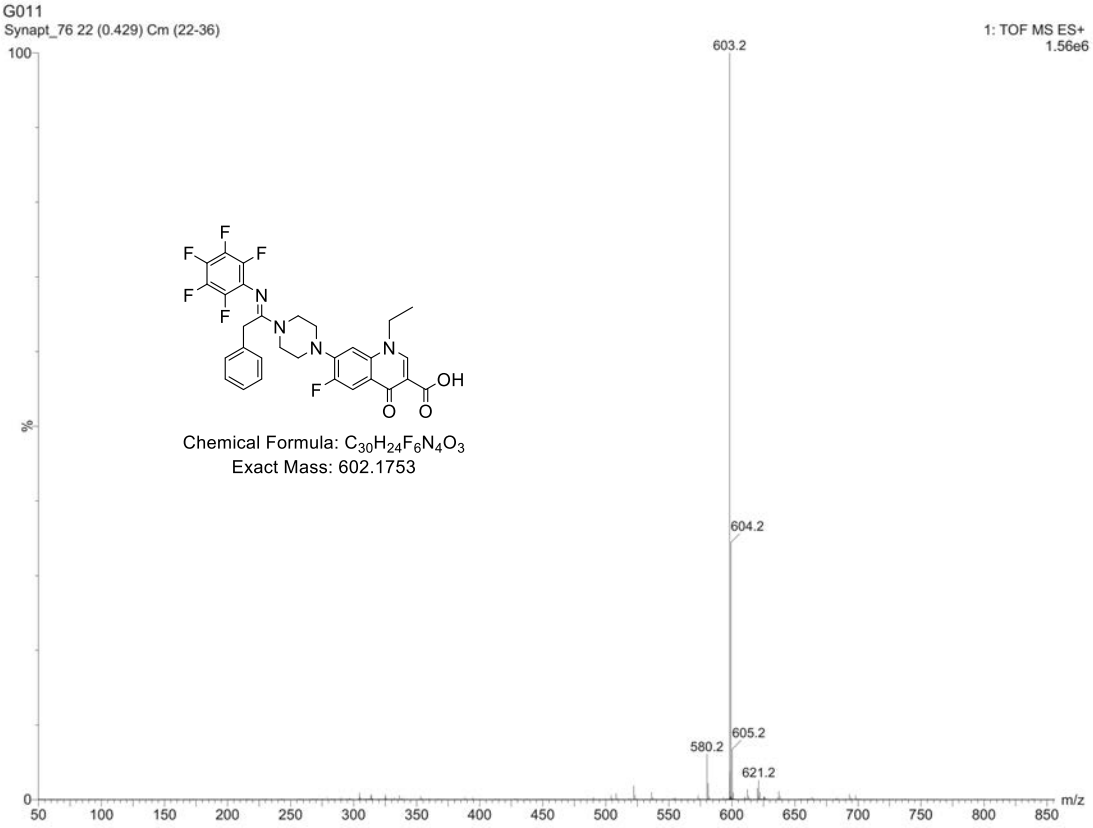
Minimum:		5.0	10.0	-1.5		
Maximum:				600.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
655.1985	655.1980	0.5	0.8	19.5	51.4	C33 H28 N4 O5 F5
	655.2020	-3.5	-5.3	23.5	36.5	C38 H28 N2 O3 F5
	655.2032	-4.7	-7.2	19.5	46.9	C35 H29 N2 O4 F6
	655.1933	5.2	7.9	24.5	42.3	C37 H25 N4 O F6
	655.2045	-6.0	-9.2	24.5	45.4	C36 H25 N6 F6
	655.1921	6.4	9.8	28.5	35.0	C40 H24 N4 F5


177.10
167.17
161.26
154.74
152.25
147.37
145.69
145.58
141.42
137.18
136.75
134.28
129.39
127.73
127.44
121.14
113.27
113.04
108.69
104.08
77.48
77.37
77.16
76.84
49.88
49.55
45.13
35.22
14.64
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

HNMR


14.964
8.663
8.070
8.038
7.326
7.308
7.260
7.152
7.133
6.795
6.779
4.313
4.295
3.845
3.714
3.208
1.599
1.581
1.563
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.75
1.00
0.97
1.95
1.96
0.94
1.99
5.87
2.21
3.30

G011
Synapt_76 22 (0.429) Cm (22-36)



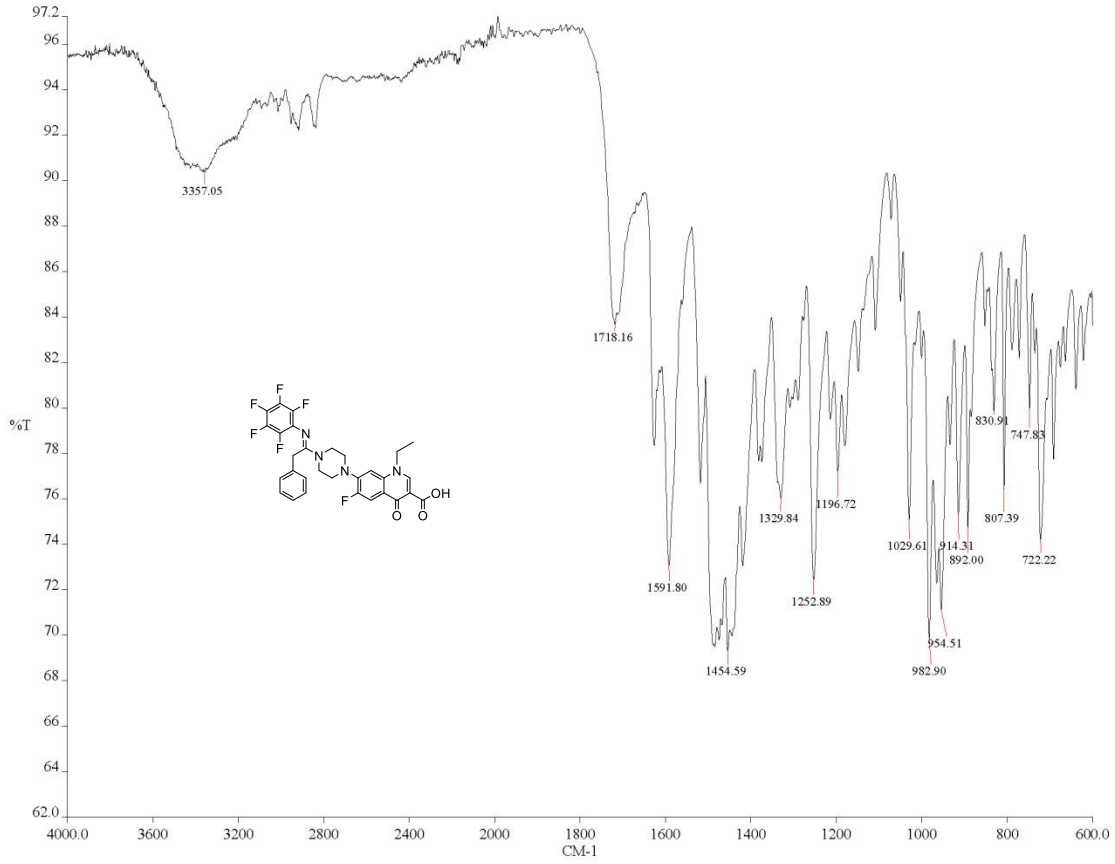
Chemical Formula: $C_{30}H_{24}F_6N_4O_3$
Exact Mass: 602.1753

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
52 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 4-6 O: 2-4 F: 6-6

Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
603.1830	603.1825	0.2	0.3	18.5	1610.6	n/a	n/a	C31 H25 N4 O3 F6



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