Supporting Information

EDA complex mediated [3+2] cyclization for the construction of CF_3-oxadiazoles

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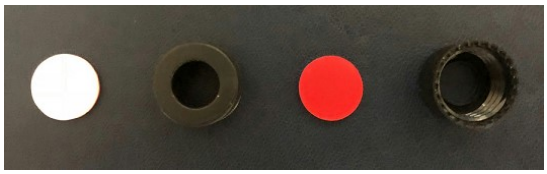
I. General Methods

All reactions were performed in flame-dried glassware with magnetic stirring bar and sealed with a rubber septum. The solvents were distilled by standard methods. Reagents were obtained from commercial suppliers and used without further purification unless otherwise noted. Silica gel column chromatography was carried out using silica Gel 60 (230-400 mesh). Analytical thin layer chromatography (TLC) was done using silica Gel (silica gel 60 F254). TLC plates were analyzed by an exposure to ultraviolet (UV) light and/or submersion in phosphomolybdic acid solution or submersion in $KMnO_4$ solution or in I_2. NMR experiments were measured on a Bruker AVANCE III-400 or 500 spectrometer and carried out in chloroform-*d* ($CDCl_3$) or acetonitrile-d_3 (CD_3CN). ^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz or 500 MHz and 100 MHz or 125 MHz spectrometers, respectively.^{19}F NMR spectra were recorded at 376 MHz or 470 MHz spectrometers. Chemical shifts are reported as δ values relative to internal TMS (δ 0.00 for ^1H NMR), chloroform (δ 7.26 for ^1H NMR), acetonitrile (δ 1.94 for ^1H NMR), chloroform (δ 77.00 for ^{13}C NMR), and acetonitrile (δ 1.32 or 118.26 for ^{13}C NMR) in parts per million (ppm). The following abbreviations are used for the multiplicities: s: singlet, d: doublet, dd: doublet of doublet, t: triplet, q: quadruplet, m: multiplet, br: broad signal for proton spectra; Coupling constants (*J*) are reported in Hertz (Hz). Melting points were uncorrected. Infrared spectra were obtained on agilent Cary630. HRMS were recorded on a Bruker miccOTOF-Q111. GC-MS spectra were performed on Agilent 5977B.

Medium-sized screw-cap test tubes (8 mL) were used for all 0.10 mmol scale reactions: Fisher 13 x 100 mm tubes (Cat. No.1495935C)

Cap with Septa: Thermo Scientific ASM PHN CAP w/PTFE/SIL (Cat. No.03378316)

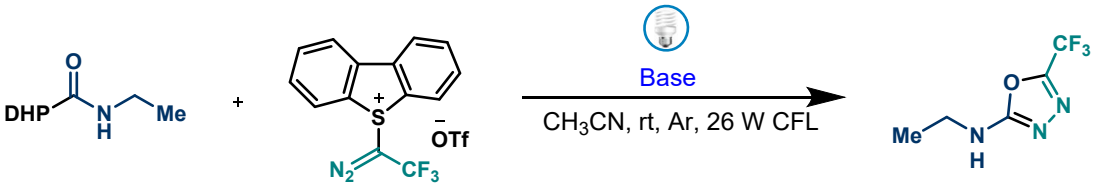


II. Synthesis of Starting Materials

Substrates **2** were prepared according to the literature.[1]
Substrates **S3-21, S27-39** were prepared according to the literature.[2,3]
Substrates **S22-26** were prepared according to the literature.[4]

III. Optimizations of the Reaction Conditions

Table S1: Optimization of base [a]

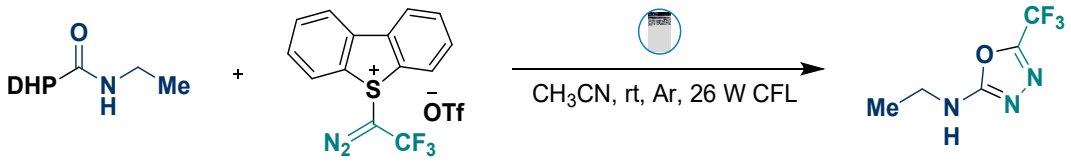


1, 0.1 mmol **2**, 0.1 mmol **3**

Entry	Base	Yield [b]
1	Na_2CO_3	50%
2	K_2CO_3	58%
3	K_3PO_4	43%
4	Et_3N	2%
5	DIPEA	n.d.
6	DBU	n.d.
7	DABCO	5%
8	Bn_2N	26%
9	No Base	85%

[a] All reactions were carried out with **1** (32.5 mg, 0.10 mmol), **2** (0.10 mmol, 1.0 equiv) and Base (0.12 mmol, 1.2 equiv) in CH_3CN (2.0 mL) at rt under Ar and 26 W CFL. [b] Yields determined by ^{19}F NMR spectroscopy using (trifluoromethoxy)benzene as an internal standard. DABCO = Triethylenediamine; DIPEA = N,N-Diisopropylethylamine; DBU = 1,8-Diazabicyclo[5,4,0]-7-Undecene.

Table S2: Optimization of material ratio [a]

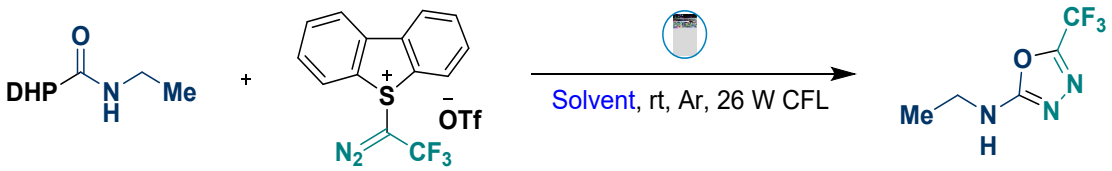


1, 0.1 mmol **2** **3**

Entry	**1** (equiv)	**2** (equiv)	Yield [b]
1	1	1.0	85%
2	1	1.2	82%
3	1	1.5	83%
4	1	1.7	72%
5	1	2.0	74%

[a] All reactions were carried out with **1** (32.5 mg, 0.10 mmol) in CH_3CN (2.0 mL) at rt under Ar and 26 W CFL. [b] Yields determined by ^{19}F NMR spectroscopy using (trifluoromethoxy)benzene as an internal standard.

Table S3: Optimization of solvent [a]



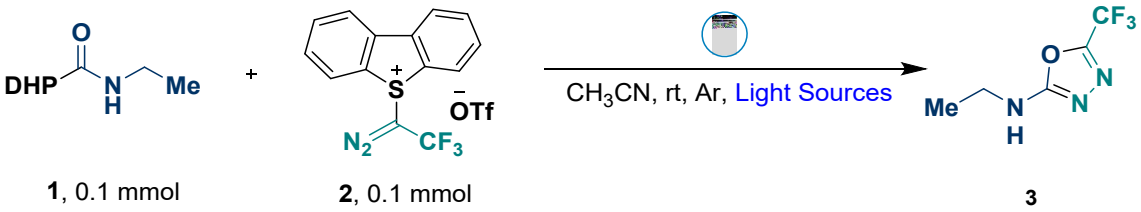
1, 0.1 mmol **2**, 0.1 mmol **3**

Entry	Solvent	Yield [b]
1	DCM	43%
2	MeCN	85%
3	EA	55%
4	THF	48%
5	Toluene	19%

6	DMSO	n.d.
7	MeOH	5%
8	DMF	n.d.

[a] All reactions were carried out with **1** (32.5 mg, 0.10 mmol), **2a** (0.10 mmol, 1.0 equiv) in Solvent (2.0 mL) at rt under Ar and 26 W CFL. [b] Yields determined by ^{19}F NMR spectroscopy using (trifluoromethoxy)benzene as an internal standard.

Table S4: Optimization of light sources [a]



1, 0.1 mmol **2**, 0.1 mmol **3**

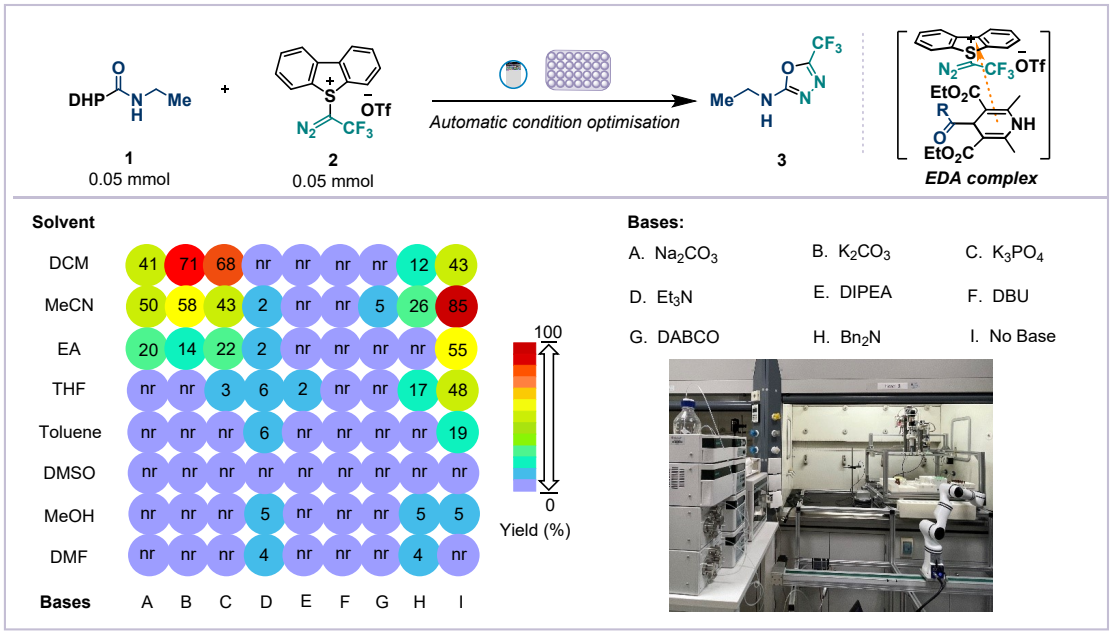
Entry	Light sources	Yield [b]
1	5 W CFL	80%
2	13 W CFL	82%
3	26 W CFL	85%
4	30 W blue LEDs	76%
5	60 W blue LEDs	79%
6	In dark	6%

[a] All reactions were carried out with **1** (32.5 mg, 0.10 mmol), **2** (0.10 mmol, 1.0 equiv) in CH_3CN (2.0 mL) at rt under Ar. [b] Yields determined by ^{19}F NMR spectroscopy using (trifluoromethoxy)benzene as an internal standard.

IV. General Procedure for the Synthesis of the Products 3-39

Condition A: Under argon, to a solution of **2** (0.1 mmol, 1.0 equiv) in CH_3CN (2 mL) was added corresponding dihydropyridine substrates (0.1 mmol) at room temperature. After that, the tube was exposed to a 26 W compact fluorescent light at room temperature about 2 h until the reaction was completed as monitored by TLC analysis. The reaction mixture was evaporated in *vacuo*. The crude products were directly purified by flash chromatography on silica gel to give the desired product.

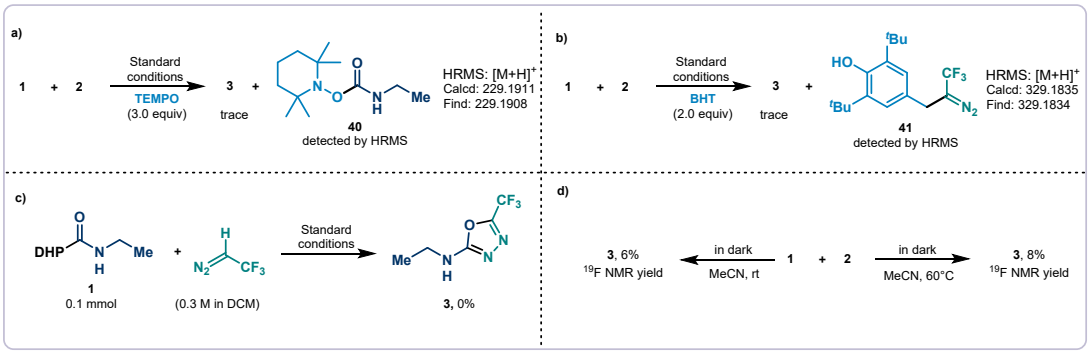
Condition B (Automatic Chemical Systems): Under room temperature, Configure three Stock solutions. Stock solution A: **1**, dissolved in the corresponding solvent (0.1 M); Stock solution B: **2**, dissolved in the corresponding solvent (0.1 M); Stock solution C: Base, dissolved in the corresponding solvent (0.12 M). All the stock solution are prepared and placed into the corresponding position of the Automatic Chemical Systems, and the relevant experimental operations are completed by the robotic arm. After that, the tube was exposed to a 26 W compact fluorescent light at room temperature about 2 h until the reaction was completed as monitored by TLC analysis. Yield determined by ^{19}F NMR spectroscopy using trifluoromethoxybenzene as an internal standard.



Supplementary Figure 1. Optimization of the reaction conditions via Automatic Chemical Systems. [a]All reactions were carried out with Dihydropyridine **1** (0.05 mmol), α-diazo sulfonium triflate **2** (0.05 mmol, 1.0 equiv.) under 26 W CFL for 2 h. Yield determined by ^{19}F NMR spectroscopy using trifluoromethoxybenzene as an internal standard.

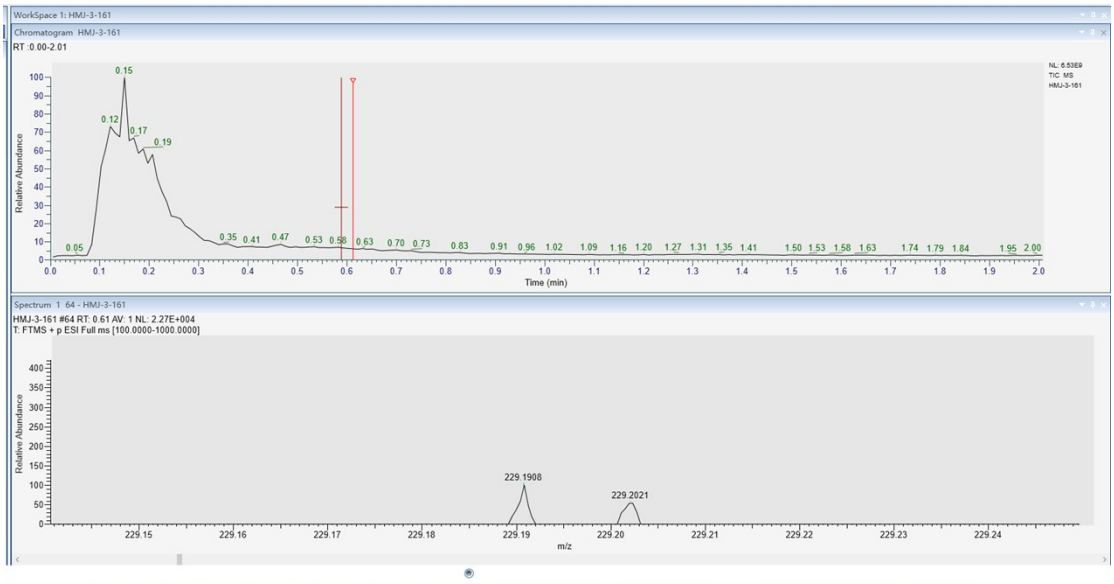
V. Mechanistic studies and green chemistry metrics

V-1. Control Experiment



Control Experiment (a):

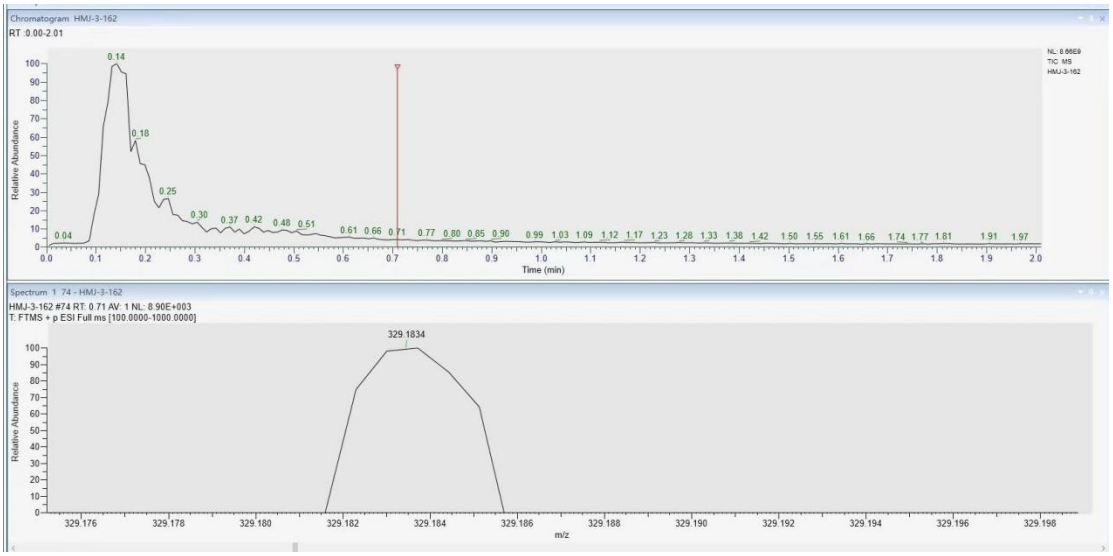
Under argon, to a solution of **2** (0.10 mmol, 1.0 equiv), TEMPO (3.0 equiv) in CH_3CN (2 mL) was added dihydropyridine **1** (0.10 mmol) at room temperature. After that, the tube was exposed to a 26 W compact fluorescent light at room temperature about 2 h until the reaction was completed as monitored by TLC analysis. Subsequently, the reaction mixture was analyzed by GC-MS. GC-MS analysis of this reaction mixture showed that the desired product was not formed and the radical capture product can be monitored by HRMS (ESI): caled for $C_{12}H_{25}N_2O_2^+$ $[M + H]^+$ 229.1911; found 229.1908.



The HRMS spectra of the control experiment (a).

Control Experiment (b):

Under argon, to a solution of **2** (0.10 mmol, 1.0 equiv), BHT (2.0 equiv) in CH_3CN (2 mL) was added dihydropyridine **1** (0.10 mmol) at room temperature. After that, the tube was exposed to a 26 W compact fluorescent light at room temperature about 2 h until the reaction was completed as monitored by TLC analysis. Subsequently, the reaction mixture was analyzed by GC-MS. GC-MS analysis of this reaction mixture showed that the desired product was not formed and the radical capture product can be monitored by HRMS (ESI): caled for $C_{17}H_{24}F_3N_2O^+$ $[M + H]^+$ 329.1835; found 329.1834.



The HRMS spectra of the control experiment (b).

Control Experiment (c):

Under argon, to a solution of Trifluorodiazoethane (0.3 M in DCM), was added dihydropyridine **1** (0.1 mmol) at room temperature. After that, the tube was exposed to a 26 W compact fluorescent light at room temperature about 2 h until the reaction was completed as monitored by TLC analysis. Subsequently, the reaction mixture was analyzed by GC-MS. GC-MS analysis of this reaction mixture showed that the desired product was not formed.

Control Experiment (d):

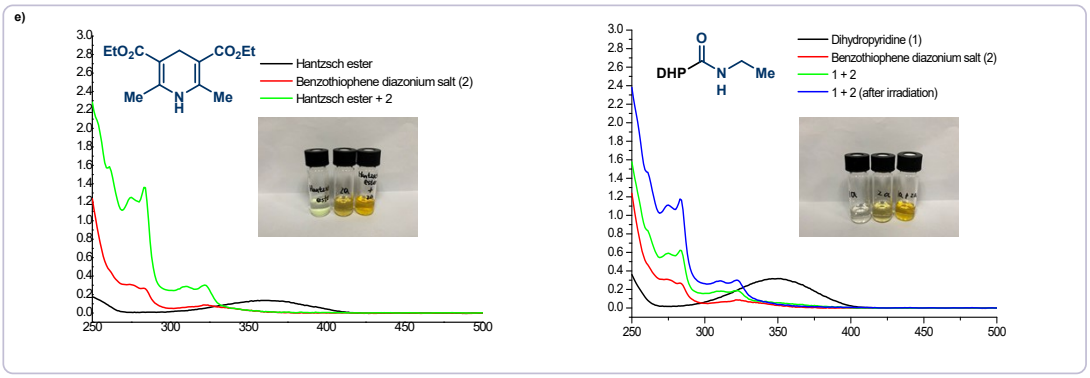
Under argon, to a solution of **2** (0.10 mmol, 1.0 equiv) in CH_3CN (2 mL) was added dihydropyridine **1** (0.1 mmol) at standard conditions. After that, the tube was exposed to a sheltered environment at room temperature about 2 h until the reaction was completed as monitored by TLC analysis. Subsequently, add (trifluoromethoxy)benzene as an internal standard. ^{19}F NMR analysis of this reaction mixture showed that the yield of desired product was 6%; another tube was exposed to a sheltered environment at 60 °C about 2 h until the reaction was completed as monitored by TLC analysis. Subsequently, add (trifluoromethoxy)benzene as an

internal standard. ^{19}F NMR analysis of this reaction mixture showed that the yield of desired product was 8%.

Control Experiment (f):

Under argon, to a solution of **2** (0.10 mmol, 1.0 equiv) in CH_3CN (2 mL) was added dihydropyridine **1** (0.1 mmol) at standard conditions. After that, the tube was irradiated alternately with 60 seconds of exposure to 26 W CFL and 60 seconds of darkness. The yield of product **3** was determined by ^{19}F NMR of the crude reaction mixture using trifluoromethoxybenzene as an internal standard. No product **3** formation was observed in the dark phase, establishing the light-dependent nature of the reaction.

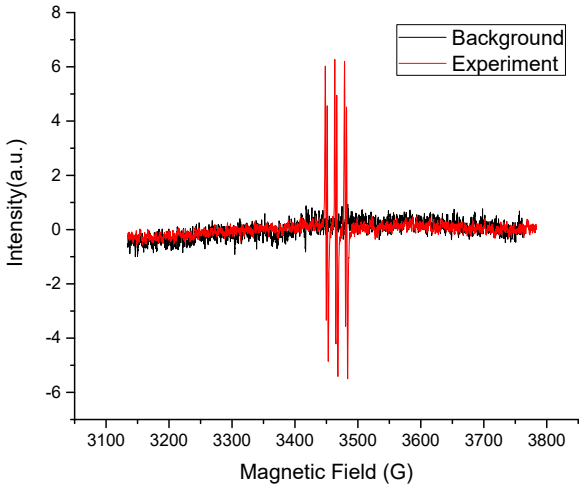
V-2. UV/Vis Absorption Spectra



Supplementary Figure 2. UV/vis absorption spectra of MeCN solutions of Hantzsch Ester ($5x10^{-5}$ M), α-Diazo Sulfonium Triflate ($5x10^{-5}$ M), a mixture of Hantzsch Ester ($5x10^{-5}$ M) and α-Diazo Sulfonium Triflate ($5x10^{-5}$ M), a mixture of Dihydropyridine ($5x10^{-5}$ M) and α-Diazo Sulfonium Triflate ($5x10^{-5}$ M) and a mixture of Dihydropyridine ($5x10^{-5}$ M) and α-Diazo Sulfonium Triflate ($5x10^{-5}$ M) after irradiation.

The UV/vis absorption spectra of MeCN solutions of Hantzsch Ester ($5x10^{-5}$ M), α-Diazo Sulfonium Triflate ($5x10^{-5}$ M), a mixture of Hantzsch Ester ($5x10^{-5}$ M) and α-Diazo Sulfonium Triflate ($5x10^{-5}$ M), a mixture of Dihydropyridine ($5x10^{-5}$ M) and α-Diazo Sulfonium Triflate ($5x10^{-5}$ M) and a mixture of Dihydropyridine ($5x10^{-5}$ M) and α-Diazo Sulfonium Triflate ($5x10^{-5}$ M) after irradiation are shown in Supplementary Figure 2. The strong absorption band of dihydropyridine **1** with a maximum absorption wavelength of 350 nm disappears in the UV absorption spectrum of the mixture [**1**+**2**] and there is a significant redshift relative to the respective absorption may indicate the formation of electron donor-acceptor (EDA) complex.

V-3. EPR Experiments

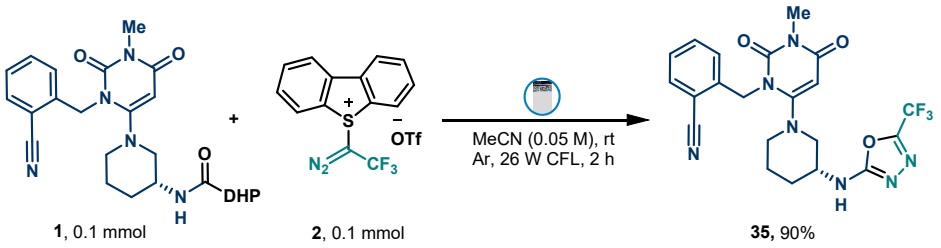


EPR experiment

To demonstrate the possible reaction mechanism, electron paramagnetic resonance (EPR) experiments with *N*-tert-butyl-α-phenylnitrone (PBN) as the electron-spin trapping reagent were carried out. A significant EPR signal was observed when the reaction was run under standard conditions. Combining the above results indicating that the reaction probably proceeded via a radical process.

V-4. Green Chemistry Metrics

We discuss the green chemistry metrics of this method in detail here (including atom economy, carbon efficiency, reaction mass efficiency, E-factor, and EcoScale), take the following reaction as an example:



atom economy (AE): (atom utilization, AU)

$$AU = \frac{molecular\ mass\ of\ 35}{molecular\ mass\ of\ 1\ and\ 2} = \frac{m.w.of\ 35}{\sum(m.w.1+2)} \times 100\% = 45\%$$

carbon efficiency (CE)

$$CE = \frac{number\ of\ carbon\ atoms\ in\ product}{number\ of\ carbon\ atoms\ in\ reactants} \times 100\% = 45\%$$

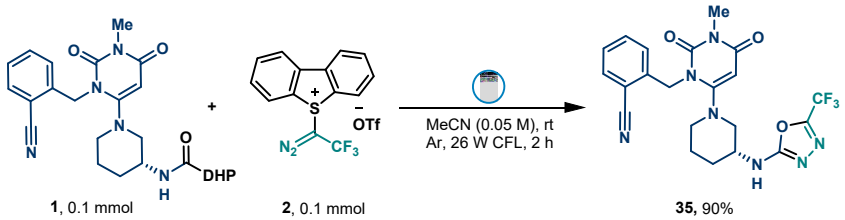
reaction mass efficiency (RME)

$$RME = \frac{actual\ mass\ of\ product}{mass\ of\ reactants} \times 100\% = 41\%$$

Environmental factor (E-factor)

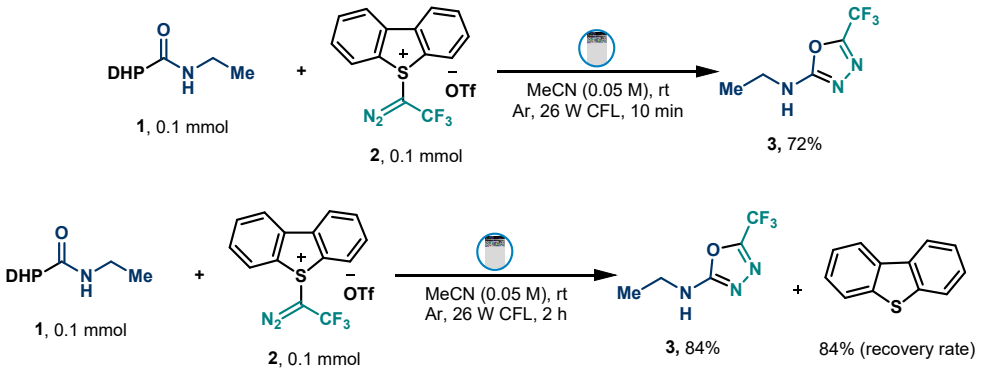
$$E - factor = \frac{mass\ of\ total\ waste}{mass\ of\ product} = 1.01$$

EcoScale[5]:



1, 0.1 mmol **2**, 0.1 mmol **35,** 90%

# 1-6 from reference[1]		Penalty
1	Yield: 90%	5
2	Dihydropyridine **1** (0.1 mmol, 43.5 mg)	0
	α-Diazo Sulfonium Triflate **2** (0.1 mmol, 44.5 mg)	0
3	MeCN (T)	5
	Diazo compounds (E)	10
4	Argon atmosphere	1
5	RT, 2 h	1
6	Removal of MeCN	0
	Silica gel chromatography	10
Penalty points total:		22



In addition, although the atom economy of our reaction less economical, we are sure that our reaction conditions are very mild and green. Notably, no additional base is required, as the dihydropyridine metabolites naturally fulfill this role, and high-value fluorinated oxadiazoles could be obtained efficiently without catalysts. The reaction proceeds rapidly, and the product **3** can be obtained in only 10 minutes with a yield of 72%. we also provide an appropriate solution: we can recycle dibenzothiophene with a recovery rate of 84%, that serves as the starting material for the preparation of the reagent **2**, further enhancing the atom economy of our reaction.

VI. References

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2. N. Alandini, L. Buzzetti, G. Favi, T. Schulte, L. Candish, K. Collins, P. Melchiorre. *Angew. Chem. Int. Ed.* 2020, **59**, 5248-5253.
3. M. Huang, J. Ma, Z. Zou, H. Li, J. Liu, L. Kong, Y. Pan, W. Zhang, Y. Liang, Y. Wang. *Chem. Sci.*, 2022, **13**, 11312-11319.
4. G. Goti, B. Bieszczad, A. Penaloza, and P. Melchiorre. *Angew. Chem. Int. Ed.,* 2019, **58**, 1213-1217.
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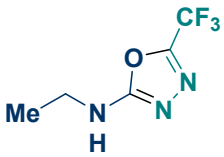
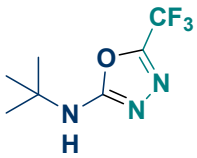
VII. Characteristic Data

N-ethyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (3)



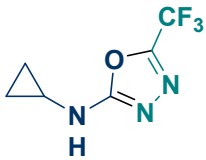
84% (15.2 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (s, 1H), 3.47 (q, J = 8.1 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 148.6 (q, J = 44.1 Hz), 116.2 (q, J = 269.9 Hz), 38.6, 14.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.67. IR (neat) ν (cm^{-1}): 3209.2, 3166.4, 3017.3, 2987.5, 2926.0, 2812.3, 1668.0, 1632.6, 1459.3, 1384.7, 1269.2, 1202.1, 1112.6, 1026.9, 974.7, 821.9, 756.6, 641.1, 534.9; HRMS (ESI): caled for $C_5H_7F_3N_3O^+$ $[M + H]^+$ 182.0536; found 182.0536.

N-(tert-butyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (4)



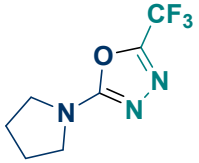
87% (18.2 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69 (s, 1H), 1.46 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1, 148.5 (q, J = 44.2 Hz), 116.3 (q, J = 270.0 Hz), 53.0, 28.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.58. IR (neat) ν (cm^{-1}): 3209.2, 3041.5, 2980.0, 2927.8, 1615.8, 1545.0, 1463.0, 1384.7, 1282.2, 1213.2, 1118.2, 1056.7, 985.9, 933.7, 741.7, 533.0, 471.5; HRMS (ESI): caled for $C_7H_{11}F_3N_3O^+$ $[M + H]^+$ 210.0849; found 210.0849.

N-cyclopropyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (5)



85% (16.4 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (s, 1H), 2.84 – 2.73 (m, 1H), 0.91 – 0.84 (m, 2H), 0.75 – 0.68 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 149.1 (q, J = 45.8 Hz), 116.2 (q, J = 270.1 Hz), 24.6, 7.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.62. IR (neat) ν (cm^{-1}): 3254.0, 3015.4, 1664.3, 1541.3, 1425.7, 1369.8, 1276.6, 1135.0, 1026.9, 836.8, 799.5, 721.2, 516.2; HRMS (ESI): caled for $C_6H_7F_3N_3O^+$ $[M + H]^+$ 194.0536; found 194.0541.

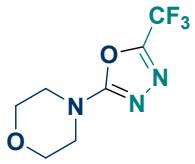
2-(pyrrolidin-1-yl)-5-(trifluoromethyl)-1,3,4-oxadiazole (6)



58% (12.0 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 – 3.53 (m, 4H), 2.09 – 2.01 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 148.5 (q, J = 43.8 Hz), 116.3 (q, J = 269.7 Hz), 47.9, 25.6.

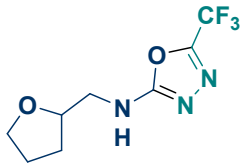
^{19}F NMR (376 MHz, $CDCl_3$) δ -65.59. IR (neat) ν (cm^{-1}):2980.0, 2883.1, 1664.3, 1507.7, 1420.1, 1354.9, 1179.7, 1131.2, 836.8, 799.5, 721.2, 531.1; HRMS (ESI): caled for $C_7H_9F_3N_3O^+$ $[M + H]^+$ 208.0692; found 208.0692.

4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)morpholine (7)



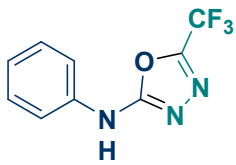
88% (19.6 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 – 3.77 (m, 4H), 3.64 – 3.57 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 149.1(q, J = 44.4 Hz), 116.2 (q, J = 270.1 Hz), 65.8, 45.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.55. IR (neat) ν (cm^{-1}): 2991.2, 2922.2, 2864.5, 1613.9, 1422.0, 1321.3, 1276.6, 1190.9, 1110.7, 1079.1, 976.6, 905.7, 842.4, 736.1, 557.2, 512.5; HRMS (ESI): caled for $C_7H_9F_3N_3O_2^+$ $[M + H]^+$ 224.0642; found 224.0642.

N-((tetrahydrofuran-2-yl)methyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (8)



80% (19.0 mg); white solid; mp 233.7-239.0℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (s, 1H), 4.17 – 4.07 (m, 1H), 3.92 – 3.85 (m, 1H), 3.83 – 3.74 (m, 1H), 3.67 – 3.58 (m, 1H), 3.39 – 3.29 (m, 1H), 2.10 – 2.00 (m, 1H), 1.98 – 1.88 (m, 2H), 1.66 – 1.54 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 148.7 (q, J = 44.3 Hz), 116.2 (q, J = 270.0 Hz), 76.8, 68.2, 47.4, 28.5, 25.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.66. IR (neat) ν (cm^{-1}): 3322.9, 2927.8, 2849.5, 1627.0, 1569.2, 1436.9, 1310.2, 1155.5, 1123.8, 1084.7, 1045.5, 892.7, 741.7, 639.2; HRMS (ESI): caled for $C_8H_{11}F_3N_3O_2^+$ $[M + H]^+$ 238.0798; found 238.0795.

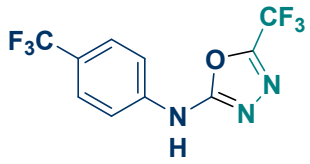
N-phenyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (9)



67% (15.3 mg); white solid; mp 142.1-146.4 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.49 – 7.45 (m, 2H), 7.44 – 7.38 (m, 2H), 7.19 – 7.14 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 148.8 (q, J = 46.8 Hz), 136.4, 129.6, 124.4, 118.3, 116.1 (q, J = 270.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.33. IR (neat) ν (cm^{-1}): 3334.1, 3186.9, 2924.1, 2853.3, 1664.3, 1587.8, 1500.3, 1405.2, 1330.7, 1198.3, 1114.5, 1058.6, 892.7, 810.7, 743.6,

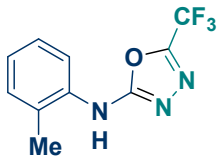
687.7, 626.2, 501.3; HRMS (ESI): caled for $C_9H_7F_3N_3O^+$ $[M + H]^+$ 230.0536; found 230.0536.

5-(trifluoromethyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-amine (10)



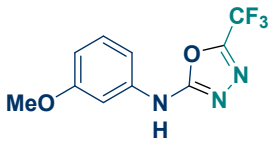
64% (19.0 mg); white solid; mp 190.1-192.5 °C; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 10.43 (s, 1H), 7.90 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8.5 Hz, 2H). ^{13}C NMR (126 MHz, $(CD_3)_2CO$) δ 162.0, 149.5 (q, J = 44.1 Hz), 142.2, 127.4 (q, J = 3.9 Hz), 125.4 (q, J = 270.5 Hz), 125.1 (q, J = 32.5 Hz), 118.7, 117.5 (d, J = 271.6 Hz). ^{19}F NMR (471 MHz, $(CD_3)_2CO$) δ -62.43, -66.38. IR (neat) ν (cm^{-1}): 3270.7, 3136.6, 3073.2, 1612.1, 1548.7, 1422.0, 1332.5, 1209.5, 1112.6, 989.6, 834.9, 754.8, 590.8, 503.2; HRMS (ESI): caled for $C_{10}H_6F_6N_3O^+$ $[M + H]^+$ 298.0410; found 298.0410.

N-(o-tolyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (11)



71% (17.3 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.26 (m, 1H), 7.14 (t, J = 7.4 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 148.8 (q, J = 42.2 Hz), 134.6, 131.0, 128.7, 127.3, 125.5, 120.7, 116.1 (q, J = 270.5 Hz), 17.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.41. IR (neat) ν (cm^{-1}): 3287.5, 3172.0, 3065.7, 2952.1, 1641.9, 1587.8, 1463.0, 1395.9, 1313.9, 1202.1, 1149.9, 1108.9, 1045.5, 864.7, 743.6, 626.2, 549.8, 512.5, 443.6; HRMS (ESI): caled for $C_{10}H_9F_3N_3O^+$ $[M + H]^+$ 244.0692; found 244.0694.

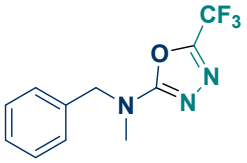
N-(3-methoxyphenyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (12)



60% (15.5 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.29 (t, J = 8.2 Hz, 1H), 7.11 (t, J = 2.3 Hz, 1H), 7.01 (dd, J = 8.2, 2.2 Hz, 1H), 6.70 (dd, J = 8.3, 2.4 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 160.6, 148.8 (q, J = 45.0 Hz), 137.5, 130.4, 116.1 (q, J = 270.6 Hz), 110.5, 109.8, 104.3, 55.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.37. IR (neat) ν (cm^{-1}): 3194.3, 3080.6, 2961.4, 2898.0, 2842.1, 1669.8, 1587.8, 1517.0, 1386.6, 1321.3, 1203.9, 1157.3, 1116.3, 1039.9, 948.6, 838.7, 754.8,

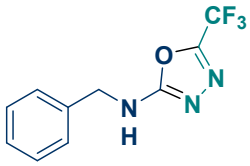
684.0, 551.6, 454.7; HRMS (ESI): caled for $C_{10}H_9F_3N_3O_2^+$ $[M + H]^+$ 260.0642; found 260.0644.

N-benzyl-N-methyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (13)

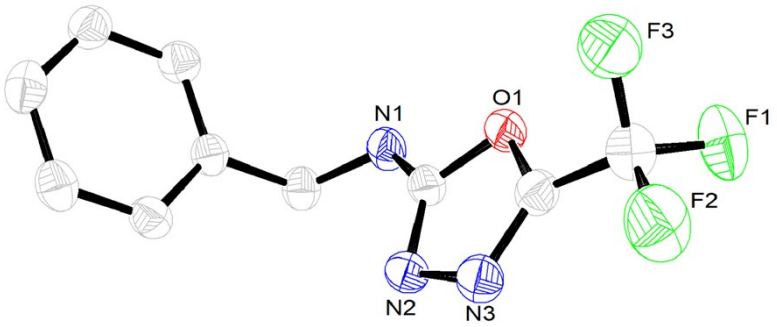


80% (20.6 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 4.65 (s, 2H), 3.08 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4, 148.6 (q, J = 44.2 Hz), 134.9, 128.9, 128.3, 128.0, 116.2 (q, J = 269.9 Hz), 54.5, 35.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.52. IR (neat) ν (cm^{-1}): 3028.5, 1664.3, 1522.6, 1455.5, 1399.6, 1185.3, 1131.2, 836.8, 799.5, 723.1, 698.9, 577.7, 518.1, 458.5; HRMS (ESI): caled for $C_{11}H_{11}F_3N_3O^+$ $[M + H]^+$ 258.0849; found 258.0849.

N-benzyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (14)

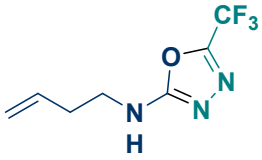


65% (15.8 mg); white solid; mp 105.1-107.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.26 (m, 5H), 6.32 (s, 1H), 4.56 (d, J = 3.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 148.7 (q, J = 44.2 Hz), 136.4, 128.9, 128.2, 127.7, 116.1 (q, J = 270.2 Hz), 47.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.60. IR (neat) ν (cm^{-1}): 3244.6, 3034.1, 2946.5, 1627.0, 1496.5, 1390.3, 1200.2, 1125.7, 1038.1, 933.7, 743.6, 695.1, 590.8, 469.6; HRMS (ESI): caled for $C_{10}H_9F_3N_3O^+$ $[M + H]^+$ 244.0692; found 244.0693.



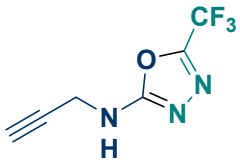
Supplementary Figure 3. X-ray crystallography for **14** (CCDC number: 2264738) (displacement ellipsoids are drawn at the 50% probability level)

N-(but-3-en-1-yl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (15)



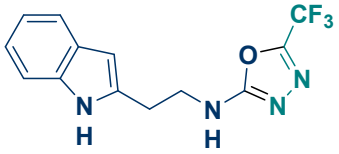
68% (14.1 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 – 5.72 (m, 1H), 5.56 (s, 1H), 5.21 – 5.12 (m, 2H), 3.50 (q, J = 6.4 Hz, 2H), 2.47 – 2.38 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 148.8 (q, J = 46.6 Hz), 134.0, 118.4, 116.2 (q, J = 270.1 Hz), 42.5, 33.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.62. IR (neat) ν (cm^{-1}): 2983.7, 1664.3, 1559.9, 1436.9, 1265.4, 1183.4, 1135.0, 993.3, 918.8, 838.7, 799.5, 723.1, 598.2; HRMS (ESI): caled for $C_7H_9F_3N_3O^+$ $[M + H]^+$ 208.0692; found 208.0693.

N-(prop-2-yn-1-yl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (16)



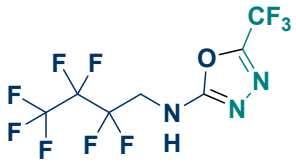
69% (13.2 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (s, 1H), 4.22 (d, J = 2.0 Hz, 2H), 2.36 (t, J = 2.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 149.5 (q, J = 44.4 Hz), 116.1 (q, J = 270.3 Hz), 77.7, 73.3, 33.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.58. IR (neat) ν (cm^{-1}): 3293.1, 3030.3, 2924.1, 1630.7, 1388.4, 1349.3, 1205.8, 1157.3, 1125.7, 1051.1, 985.9, 743.6, 669.1, 635.5, 549.8; HRMS (ESI): caled for $C_6H_5F_3N_3O^+$ $[M + H]^+$ 192.0379; found 192.0377.

N-(2-(1H-indol-2-yl)ethyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (17)



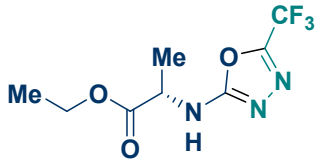
51% (15.1 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.8 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 7.08 (s, 1H), 5.19 (s, 1H), 3.77 (s, 2H), 3.14 (t, J = 6.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.2, 148.8(q, J = 44.9 Hz), 136.5 126.9, 122.5, 122.5, 119.8, 118.5, 116.2 (q, J = 270.3 Hz), 111.6, 111.4, 43.7, 25.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.59. IR (neat) ν (cm^{-1}): 3390.0, 3263.3, 2924.1, 1625.1, 1517.0, 1459.3, 1362.3, 1192.7, 1151.7, 1123.8, 1043.7, 980.3, 812.6, 736.1, 518.1, 421.2; HRMS (ESI): caled for $C_{13}H_{12}F_3N_4O^+$ $[M + H]^+$ 297.0958; found 297.0957.

N-(2,2,3,3,4,4,4-heptafluorobutyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (18)



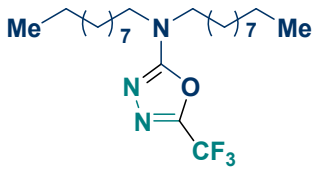
61% (20.5 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (s, 1H), 4.15 (t, *J* = 14.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.9, 149.5 (d, *J* = 43.5 Hz), 121.51 – 105.91 (m, 3C). 115.9 (q, *J* = 270.6 Hz), 43.5 (t, *J* = 24.4 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.70(s, 3F), -80.77 (t, *J* = 9.5 Hz, 3F), -119.66 – -119.76 (m, 2F), -127.57 – -127.62 (m, 2F). IR (neat) ν (cm^{-1}): 3254.0, 3058.3, 1634.4, 1353.0, 1207.7, 1157.3, 1116.3, 1049.2, 1000.8, 959.8, 909.5, 743.6, 527.4; HRMS (ESI): caled for $C_7H_4F_{10}N_3O^+$ $[M + H]^+$ 336.0189; found 336.0188.

ethyl (5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-L-alaninate (19)



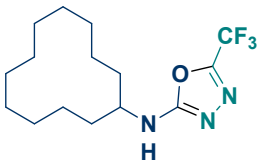
68% (17.2 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.06 (d, *J* = 7.2 Hz, 1H), 4.53 – 4.41 (m, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.58 (d, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 163.1, 148.7 (q, *J* = 44.7 Hz), 116.1 (q, *J* = 270.4 Hz), 62.3, 51.9, 18.2, 14.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.61. IR (neat) ν (cm^{-1}): 3309.9, 2987.5, 1735.1, 1623.3, 1455.5, 1388.4, 1202.1, 1149.9, 1121.9, 1049.2, 862.9, 743.6, 549.8; HRMS (ESI): caled for $C_8H_{11}F_3N_3O_3^+$ $[M + H]^+$ 254.0747; found 254.0746.

N,N-didecyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (20)



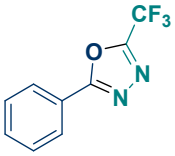
67% (29.0 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 – 3.36 (m, 4H), 1.68 – 1.56 (m, 4H), 1.36 – 1.18 (m, 28H), 0.87 (t, J = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 148.2 (q, *J* = 43.9 Hz), 116.4 (q, J = 269.7 Hz), 49.2, 31.8, 29.5, 29.3, 29.2, 27.6, 26.6, 22.6, 14.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.57. IR (neat) ν (cm^{-1}): 2924.1, 2855.1, 1623.3, 1459.3, 1420.1, 1345.6, 1200.2, 1149.9, 1112.6, 974.7, 752.9; HRMS (ESI): caled for $C_{23}H_{43}F_3N_3O^+$ $[M + H]^+$ 434.3353; found 434.3350.

N-cyclododecyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (21)



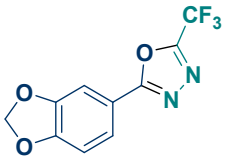
70% (22.3 mg); white solid; mp 173.1-175.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.15 (d, *J* = 8.1 Hz, 1H), 3.89 – 3.80 (m, 1H), 1.81 – 1.70 (m, 2H), 1.59 – 1.50 (m, 2H), 1.49 – 1.28 (m, 18H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 148.5 (q, *J* = 43.3 Hz), 116.2 (q, *J* = 270.2 Hz), 51.7, 30.0, 23.9, 23.8, 23.3, 23.2, 21.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.57. IR (neat) ν (cm^{-1}): 3324.8, 2924.1, 2853.3, 1619.5, 1507.7, 1468.6, 1448.1, 1367.9, 1187.2, 1123.8, 1015.7, 980.3, 739.9, 549.8; HRMS (ESI): caled for $C_{15}H_{25}F_3N_3O^+$ $[M + H]^+$ 320.1944; found 320.1947.

2-phenyl-5-(trifluoromethyl)-1,3,4-oxadiazole (22)



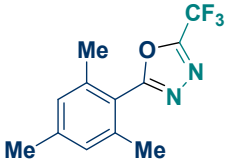
71% (15.2 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.09 (m, 2H), 7.66 – 7.61 (m, 1H), 7.59 – 7.54 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 154.8 (q, *J* = 44.4 Hz), 133.1, 129.3, 127.5, 122.1, 116.3 (q, *J* = 271.6 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.08. IR (neat) ν (cm^{-1}): 3207.4, 2922.2, 2853.3, 1654.9, 1591.6, 1448.1, 1362.3, 1312.0, 1149.9, 1080.9, 969.1, 689.6, 602.0, 542.3; HRMS (ESI): caled for $C_9H_6F_3N_2O^+$ $[M + H]^+$ 215.0427; found 215.0436.

2-(benzo[d][1,3]dioxol-5-yl)-5-(trifluoromethyl)-1,3,4-oxadiazole (23)



75% (19.4 mg); white solid; mp 88.4-89.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.53 (d, *J* = 1.7 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 6.10 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 154.4 (q, *J* = 44.5 Hz), 151.8, 148.6, 123.1, 116.3 (q, *J* = 271.4 Hz), 115.8, 109.1, 107.3, 102.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.11. IR (neat) ν (cm^{-1}): 3112.3, 3022.9, 2927.8, 2797.4, 1610.2, 1559.9, 1451.8, 1397.8, 1356.8, 1265.4, 1244.9, 1166.7, 1140.6, 1038.1, 998.9, 935.6, 885.2, 823.7, 741.7, 596.4, 503.2; HRMS (ESI): caled for $C_{10}H_6F_3N_2O_3^+$ $[M + H]^+$ 259.0325; found 259.0325.

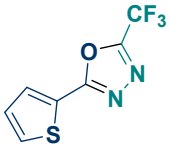
2-mesityl-5-(trifluoromethyl)-1,3,4-oxadiazole (24)



78% (20.0 mg); white solid; mp 100.2-102.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 – 6.99 (m, 2H), 2.35 (s, 3H), 2.28 (s, 6H).

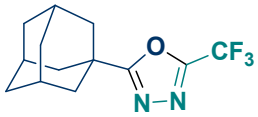
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 155.3 (q, J = 44.1 Hz), 142.2, 139.0, 129.2, 119.1, 116.4 (q, J = 271.6 Hz), 21.3, 20.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.18. IR (neat) ν (cm^{-1}): 2963.2, 2922.2, 2857.0, 1746.3, 1669.8, 1578.5, 1472.3, 1395.9, 1207.7, 1131.2, 1049.2, 1000.8, 954.2, 853.6, 754.8, 596.4, 451.0; HRMS (ESI): caled for $C_{12}H_{12}F_3N_2O^+$ $[M + H]^+$ 257.0896; found 257.0896.

2-(thiophen-2-yl)-5-(trifluoromethyl)-1,3,4-oxadiazole (25)



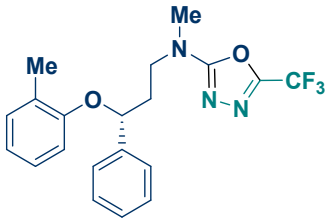
73% (16.1 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.68 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.23 (dd, *J* = 5.0, 3.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 154.1 (q, *J* = 44.5 Hz), 132.3, 131.9, 128.6, 123.1, 116.2 (q, *J* = 271.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.98. IR (neat) ν (cm^{-1}): 3425.4, 3216.7, 3117.9, 3004.2, 2924.1, 2853.3, 1735.1, 1645.6, 1533.8, 1414.5, 1358.6, 1190.9, 1162.9, 1129.4, 1032.5, 909.5, 855.4, 717.5, 518.1; HRMS (ESI): caled for $C_7H_4F_3N_2OS^+$ $[M + H]^+$ 220.9991; found 220.9990.

2-((3r,5r,7r)-adamantan-1-yl)-5-(trifluoromethyl)-1,3,4-oxadiazole (26)



68% (18.5 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 – 2.07 (m, 9H), 1.87 – 1.75 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 154.8 (q, *J* = 44.1 Hz), 116.4 (q, *J* = 272.2 Hz), 39.7, 36.0, 34.7, 29.7, 27.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.18. IR (neat) ν (cm^{-1}): 3315.5, 3190.6, 3037.8, 2905.5, 2853.3, 1654.9, 1507.7, 1451.8, 1345.6, 1200.2, 1162.9, 976.6, 840.5, 725.0, 497.6; HRMS (ESI): caled for $C_{13}H_{16}F_3N_2O^+$ $[M + H]^+$ 273.1209; found 273.1217.

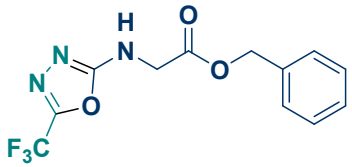
(R)-N-methyl-N-(3-phenyl-3-(o-tolyloxy)propyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (27)



59% (23.1 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 4.3 Hz, 4H), 7.29 – 7.23 (m, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 6.98 – 6.92 (m, 1H), 6.79 (t, *J* = 7.4 Hz, 1H), 6.56 (d, *J* = 8.2 Hz, 1H), 5.24 (dd, *J* = 8.6, 4.0 Hz, 1H), 3.79 – 3.66 (m, 2H), 3.12 (s, 3H), 2.37 – 2.21 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.9, 155.4, 148.6 (q, *J* = 43.9 Hz), 140.9, 130.8, 128.8, 127.8, 126.7, 126.6, 125.5, 120.6, 116.2 (q, *J* = 270.0 Hz), 112.4, 76.7, 48.1, 36.2, 36.1, 16.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.57. IR (neat) ν (cm^{-1}): 3028.5, 2927.8, 1634.4, 1490.9, 1414.5, 1334.4, 1235.6, 1198.3, 1114.5, 1049.2, 974.7, 922.5, 751.1, 700.7,

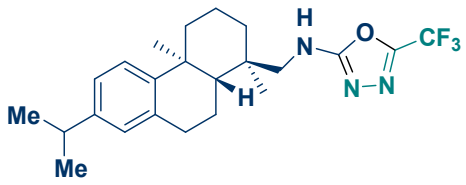
531.1, 441.7; HRMS (ESI): caled for $C_{20}H_{21}F_3N_3O_2^+$ [M + H]$^+$ 392.1581; found 392.1581.

benzyl (5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)glycinate (28)



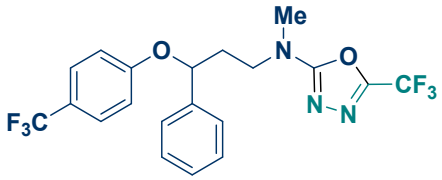
77% (23.2 mg); white solid; mp 82.6-84.7℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 5H), 6.04 (s, 1H), 5.24 (s, 2H), 4.24 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 163.6, 149.4 (q, J = 44.4 Hz), 134.6, 128.8, 128.7, 128.5, 116.0 (q, J = 270.4 Hz), 67.9, 44.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.59. IR (neat) ν (cm^{-1}): 3319.2, 2916.6, 1738.8, 1619.5, 1509.6, 1438.8, 1403.3, 1272.9, 1198.3, 1176.0, 1135.0, 1056.7, 959.8, 749.2, 700.7, 561.0, 484.6; HRMS (ESI): caled for $C_{12}H_{11}F_3N_3O_3^+$ [M + H]$^+$ 302.0747; found 302.0748.

N-(((1R,4aS,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (29)



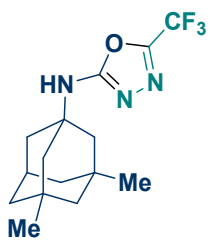
57% (24.0 mg); white solid; mp 126.3-129.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 8.1 Hz, 1H), 7.00 (dd, J = 8.1, 2.0 Hz, 1H), 6.88 (d, J = 2.0 Hz, 1H), 6.06 (q, J = 6.8, 5.7 Hz, 1H), 4.40 (q, J = 7.1 Hz, 1H), 3.40 (dd, J = 13.7, 6.6 Hz, 1H), 3.22 (dd, J = 13.7, 6.6 Hz, 1H), 2.99 – 2.71 (m, 3H), 2.36 – 2.26 (m, 1H), 1.93 – 1.64 (m, 4H), 1.56 – 1.27 (m, 3H), 1.26 – 1.19 (m, 9H), 1.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 148.2 (q, J = 44.0 Hz), 146.8, 145.8, 134.4, 126.9, 124.1, 123.9, 116.2 (q, J = 270.1 Hz), 61.4, 54.6, 44.9, 38.1, 37.6, 37.4, 35.8, 33.4, 29.8, 25.2, 23.9, 19.0, 18.4, 18.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.57. IR (neat) ν (cm^{-1}): 3218.6, 2939.0, 2871.9, 1645.6, 1541.3, 1448.1, 1381.0, 1256.1, 1205.8, 1155.5, 1118.2, 1023.2, 825.6, 739.9, 624.3, 547.9; HRMS (ESI): caled for $C_{23}H_{31}F_3N_3O^+$ [M + H]$^+$ 422.2414; found 422.2414.

N-methyl-N-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (30)



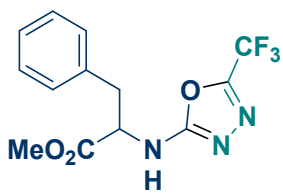
75% (33.4 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.7 Hz, 2H), 7.37 – 7.26 (m, 5H), 6.86 (d, *J* = 8.5 Hz, 2H), 5.26 (dd, *J* = 9.0, 3.8 Hz, 1H), 3.82 – 3.63 (m, 2H), 3.14 (s, 3H), 2.45 – 2.13 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 159.8, 148.6 (q, *J* = 44.1 Hz), 140.0, 129.0, 128.2, 126.8 (q, *J* = 3.8 Hz), 125.5, 124.2 (q, *J* = 271.0 Hz), 123.2 (q, *J* = 32.7 Hz), 116.1 (q, *J* = 269.9 Hz), 115.5, 77.7, 48.1, 36.2, 35.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.71, -65.62. IR (neat) ν (cm^{-1}): 2926.0, 1638.2, 1517.0, 1418.3, 1323.2, 1246.8, 1153.6, 1107.0, 1067.9, 1008.2, 834.9, 754.8, 700.7, 637.4, 592.6, 512.5; HRMS (ESI): caled for $C_{20}H_{18}F_6N_3O_2^+$ $[M + H]^+$ 446.1298; found 446.1298.

N-((1r,3R,5S,7r)-3,5-dimethyladamantan-1-yl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (31)



70% (22.1 mg); white solid; mp 125.1-126.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (s, 1H), 2.25 – 2.19 (m, 1H), 1.87 (d, *J* = 2.5 Hz, 2H), 1.72 – 1.61 (m, 4H), 1.45 – 1.29 (m, 4H), 1.24 – 1.14 (m, 2H), 0.89 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 148.4 (q, *J* = 45.1 Hz), 116.3 (q, *J* = 270.1 Hz), 54.9, 50.2, 47.5, 42.3, 40.1, 32.6, 30.1, 29.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.51. IR (neat) ν (cm^{-1}): 3192.5, 3021.0, 2926.0, 2849.5, 1612.1, 1537.5, 1455.6, 1358.6, 1205.8, 1151.7, 1120.1, 1030.6, 933.7, 745.5, 654.1, 553.5, 475.2; HRMS (ESI): caled for $C_{15}H_{21}F_3N_3O^+$ $[M + H]^+$ 316.1631; found 316.1631.

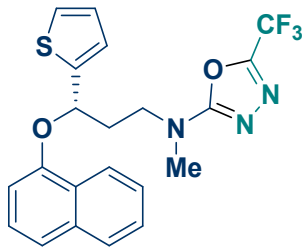
methyl (5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)phenylalaninate (32)



58% (18.3 mg); white solid; mp 219.4-221.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.24 (m, 3H), 7.15 – 7.09 (m, 2H), 5.79 (d, *J* = 8.0 Hz, 1H), 4.80 – 4.70 (m, 1H), 3.79 (s, 3H), 3.35 – 3.15 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

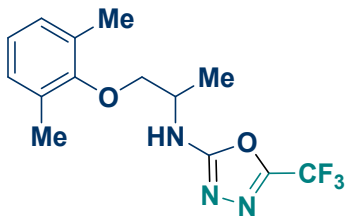
171.0, 163.1, 149.2 (q, J = 44.8 Hz), 134.7, 129.2, 128.8, 127.6, 116.0 (q, J = 270.4 Hz), 57.0, 52.9, 37.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.55. IR (neat) ν (cm^{-1}): 3326.6, 3213.0, 3028.5, 2927.8, 1763.0, 1709.0, 1541.3, 1442.5, 1313.9, 1161.1, 1084.7, 972.8, 900.2, 752.9, 698.9, 624.3, 490.1, 439.8; HRMS (ESI): caled for $C_{13}H_{13}F_3N_3O_3^+$ $[M + H]^+$ 316.0904; found 316.0904.

(S)-N-methyl-N-(3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (33)



74% (32.0 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 – 8.30 (m, 1H), 7.82 – 7.77 (m, 1H), 7.54 – 7.47 (m, 2H), 7.42 (d, J = 8.3 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.23 (dd, J = 5.0, 1.0 Hz, 1H), 7.08 (d, J = 3.4 Hz, 1H), 6.94 (dd, J = 5.0, 3.6 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 5.75 (dd, J = 8.2, 4.5 Hz, 1H), 3.86 – 3.69 (m, 2H), 3.13 (s, 3H), 2.66 – 2.56 (m, 1H), 2.51 – 2.42 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.9, 152.7, 148.7 (q, J = 43.9 Hz), 143.9, 134.6, 127.6, 126.7, 126.4, 125.9, 125.6, 125.4, 125.1, 124.9, 121.7, 121.1, 116.2 (q, J = 270.1 Hz), 106.8, 73.7, 48.1, 36.5, 36.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.55. IR (neat) ν (cm^{-1}): 3052.7, 2931.6, 1735.1, 1641.9, 1576.7, 1384.7, 1276.6, 1198.3, 1142.4, 1082.8, 1015.7, 773.4, 700.7, 572.1, 527.4, 421.2; HRMS (ESI): caled for $C_{21}H_{19}F_3N_3O_2S^+$ $[M + H]^+$ 434.1145; found 434.1144.

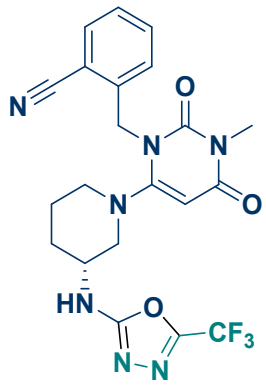
N-(1-(2,6-dimethylphenoxy)propan-2-yl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (34)



89% (28.0 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, J = 7.4 Hz, 2H), 6.94 (dd, J = 8.2, 6.6 Hz, 1H), 5.89 (d, J = 7.8 Hz, 1H), 4.25 – 4.17 (m, 1H), 3.93 (dd, J = 9.4, 4.1 Hz, 1H), 3.81 (dd, J = 9.4, 4.3 Hz, 1H), 2.24 (s, 6H), 1.54 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.9, 154.5, 148.9 (q, J = 43.5 Hz), 130.6, 129.1, 124.4, 116.2 (q, J = 270.1 Hz), 73.1, 50.4, 17.5, 16.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.6. IR (neat) ν (cm^{-1}): 3024.7, 2978.1, 2920.4, 1623.3, 1476.0, 1388.3, 1263.6, 1198.3, 1153.6, 1120.1, 1026.9, 982.2, 767.8,

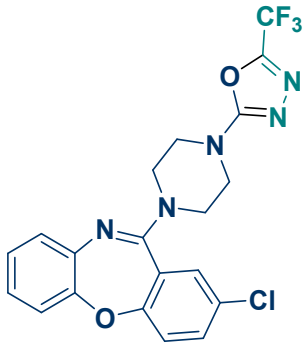
747.3, 549.8, 503.2; HRMS (ESI): caled for $C_{14}H_{17}F_3N_3O_2^+$ $[M + H]^+$ 316.1268; found 316.1268.

(R)-2-((3-methyl-2,4-dioxo-6-(3-((5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)amino)piperidin-1-yl)-3,4-dihydropyrimidin-1(2H)-yl)methyl)benzonitrile (35)



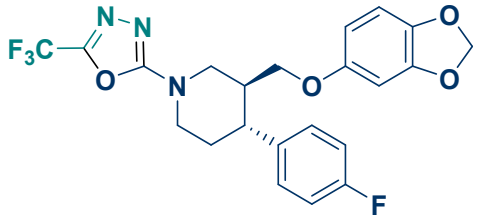
90% (42.8 mg); white solid; mp 166.0-170.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.7 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.9 Hz, 1H), 6.34 (s, 1H), 5.39 (s, 1H), 5.27 (s, 2H), 3.92 (s, 1H), 3.28 (s, 3H), 3.19 (s, 1H), 2.87 (s, 2H), 2.11 – 1.60 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 162.9, 159.4, 152.3, 148.6 (q, *J* = 44.0 Hz), 140.4, 133.3, 133.2, 128.2, 127.6, 117.3, 116.1 (q, *J* = 270.1 Hz), 110.5, 90.9, 54.8, 52.7, 49.3, 46.3, 28.7, 28.0, 21.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.44. IR (neat) ν (cm^{-1}): 3265.1, 2935.3, 2849.5, 2225.2, 1701.5, 1619.5, 1436.9, 1367.9, 1202.1, 1149.9, 1120.1, 1053.0, 915.1, 808.8, 728.7, 520.0; HRMS (ESI): caled for $C_{21}H_{21}F_3N_7O_3^+$ $[M + H]^+$ 476.1653; found 476.1652.

2-chloro-11-(4-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)piperazin-1-yl)dibenzo[b,f][1,4]oxazepine (36)



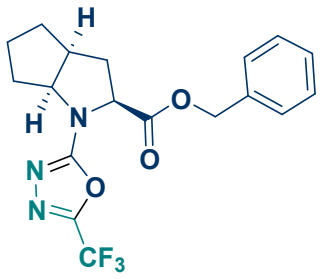
72% (32.3 mg); white solid; mp 194.0-196.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.33 (d, *J* = 2.6 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.18 – 7.14 (m, 1H), 7.13 – 7.08 (m, 2H), 7.06 – 7.01 (m, 1H), 3.81 – 3.59 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 159.4, 158.5, 151.7, 149.1 (q, *J* = 44.3 Hz), 139.5, 133.0, 130.5, 128.7, 127.1, 125.9, 125.3, 124.5, 122.9, 120.2, 116.2 (q, *J* = 270.4 Hz), 46.5, 45.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.48. IR (neat) ν (cm^{-1}): 2991.2, 2924.1, 2873.8, 2847.7, 1615.8, 1559.9, 1423.8, 1323.2, 1241.2, 1198.3, 1125.7, 1013.8, 978.4, 903.9, 829.3, 752.9, 577.7, 523.7, 456.6; HRMS (ESI): caled for $C_{20}H_{16}ClF_3N_5O_3^+$ $[M + H]^+$ 450.0939; found 450.0940.

2-((3S,4R)-3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)piperidin-1-yl)-5-(trifluoromethyl)-1,3,4-oxadiazole (37)



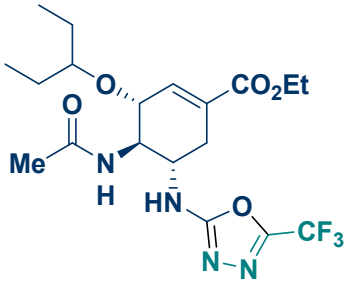
78% (36.3 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 – 7.12 (m, 2H), 7.04 – 6.96 (m, 2H), 6.63 (d, *J* = 8.5 Hz, 1H), 6.37 (d, *J* = 2.5 Hz, 1H), 6.15 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.89 (s, 2H), 4.43 – 4.34 (m, 1H), 4.27 – 4.19 (m, 1H), 3.65 (dd, *J* = 9.5, 2.8 Hz, 1H), 3.51 (dd, *J* = 9.5, 6.3 Hz, 1H), 3.31 – 3.19 (m, 2H), 2.88 – 2.78 (m, 1H), 2.27 – 2.15 (m, 1H), 2.02 – 1.84 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 162.7, 160.8, 153.9, 148.8 (q, *J* = 44.1 Hz), 148.2, 141.9, 137.9 (d, *J* = 3.3 Hz), 128.7 (d, *J* = 7.8 Hz), 116.2 (q, *J* = 270.1 Hz), 115.8, 115.6, 107.9, 105.6, 101.2, 98.0, 68.2, 49.5, 46.8, 43.1, 41.3, 32.9. ^{19}F{H} NMR (471 MHz, $CDCl_3$) δ -65.48 , -115.40. IR (neat) ν (cm^{-1}): 2922.2, 1735.1, 1487.2, 1422.0, 1336.3, 1181.6, 1108.9, 1036.2, 930.0, 831.2, 752.9, 613.1, 521.8, 428.6; HRMS (ESI): caled for $C_{22}H_{20}F_4N_3O_4^+$ $[M + H]^+$ 466.1385; found 466.1385.

Benzyl (2S,3aS,6aS)-1-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl) octahydrocyclopenta [b] pyrrole-2-carboxylate (38)



92% (35.1 mg); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 5.20 (d, *J* = 1.0 Hz, 2H), 4.59 (dd, *J* = 9.7, 4.1 Hz, 1H), 4.45 – 4.36 (m, 1H), 2.90 – 2.77 (m, 1H), 2.64 – 2.51 (m, 1H), 2.14 – 1.96 (m, 3H), 1.85 – 1.66 (m, 2H), 1.64 – 1.48 (m, 1H), 1.37 – 1.24 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 162.7, 149.1 (q, *J* = 44.0 Hz), 135.1, 128.6, 128.5, 128.3, 116.2 (q, *J* = 270.0 Hz), 67.4, 67.2, 62.2, 43.2, 35.4, 32.8, 31.9, 25.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.42. IR (neat) ν (cm^{-1}): 2955.8, 2871.9, 1746.3, 1619.5, 1420.1, 1198.3, 1148.0, 1121.9, 1021.3, 974.7, 913.2, 736.1, 697.0, 492.0; HRMS (ESI): caled for $C_{18}H_{19}F_3N_3O_3^+$ $[M + H]^+$ 382.1373; found 382.1372.

Ethyl (3R,4R,5S)-4-acetamido-3-(pentan-3-yloxy)-5-((5-(trifluoromethyl)-1,3,4-oxadiazol -2-yl) amino)cyclohex-1-ene-1-carboxylate (39)



84% (37.6 mg); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.0 Hz, 1H), 6.81 (s, 1H), 6.34 (d, *J* = 7.2 Hz, 1H), 4.26 – 4.07 (m, 5H), 3.45 – 3.36 (m, 1H), 2.96 (dd, *J* = 17.9, 4.8 Hz, 1H), 2.55 – 2.44 (m, 1H), 1.93 (s, 3H), 1.57 – 1.44 (m, 4H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.89 (q, *J* = 7.5 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 165.6, 164.1, 148.7 (q, *J* = 43.6 Hz), 136.7, 129.0, 116.1 (q, *J* = 270.3 Hz), 82.2, 74.8, 61.1, 54.1, 53.0, 30.1, 26.2, 25.6, 23.1, 14.1, 9.4, 9.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.68. IR (neat) ν (cm^{-1}): 3276.3, 2967.0, 2931.6, 1720.2, 1625.1, 1558.0, 1377.3, 1248.7, 1192.7, 1166.7, 1127.5, 1045.5, 1013.8, 939.3, 751.1, 602.0, 438.0; HRMS (ESI): caled for $C_{19}H_{28}F_3N_4O_5^+$ $[M + H]^+$ 449.2007; found 449.2009.

VIII. X-ray crystallography data for 14

Table S5 Crystal data and structure refinement

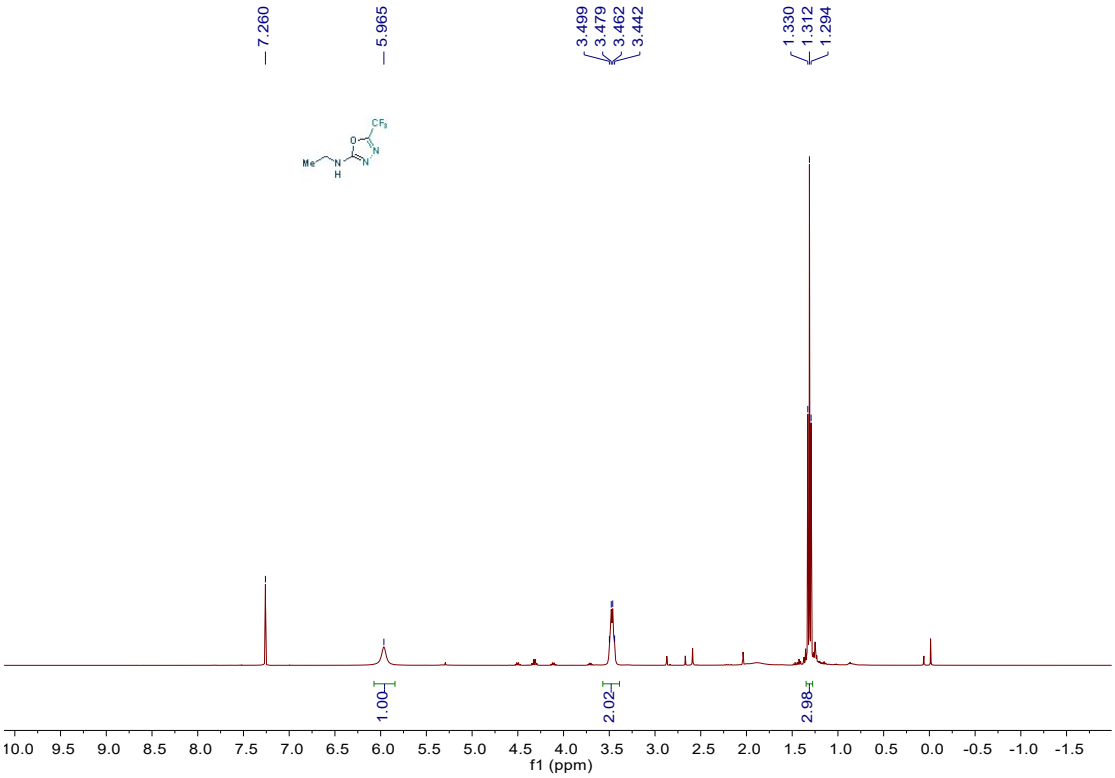
Identification code	**14**
Empirical formula	$C_{10}H_8F_3N_3O$
Formula weight	243.06
Temperature/K	193.0
Crystal system	monoclinic
Space group	P21/n
a/Å	5.900(3)
b/Å	12.748(6)
c/Å	28.745(15)
α/°	90
β/°	95.113(19)
γ/°	90
Volume/Å3	2153.3(19)
Z	4
ρcalcg/cm3	1.500
μ/mm-1	0.766
F(000)	992.0
Crystal size/mm3	0.1 × 0.1 × 0.1
Radiation	GaKα (λ = 1.34139)
2Θ range for data collection/°	5.37 to 107.944
Index ranges	$-7 \leq h \leq 7$, $-15 \leq k \leq 15$, $-34 \leq l \leq 34$

Reflections collected	26562
Independent reflections	3932 [Rint = 0.0995, Rsigma = 0.0935]
Data/restraints/parameters	3932/0/307
Goodness-of-fit on F2	1.024
Final R indexes [I>=2σ (I)]	R1 = 0.0641, wR2 = 0.1601
Final R indexes [all data]	R1 = 0.1061, wR2 = 0.1915
Largest diff. peak/hole / e Å-3	0.28/-0.29

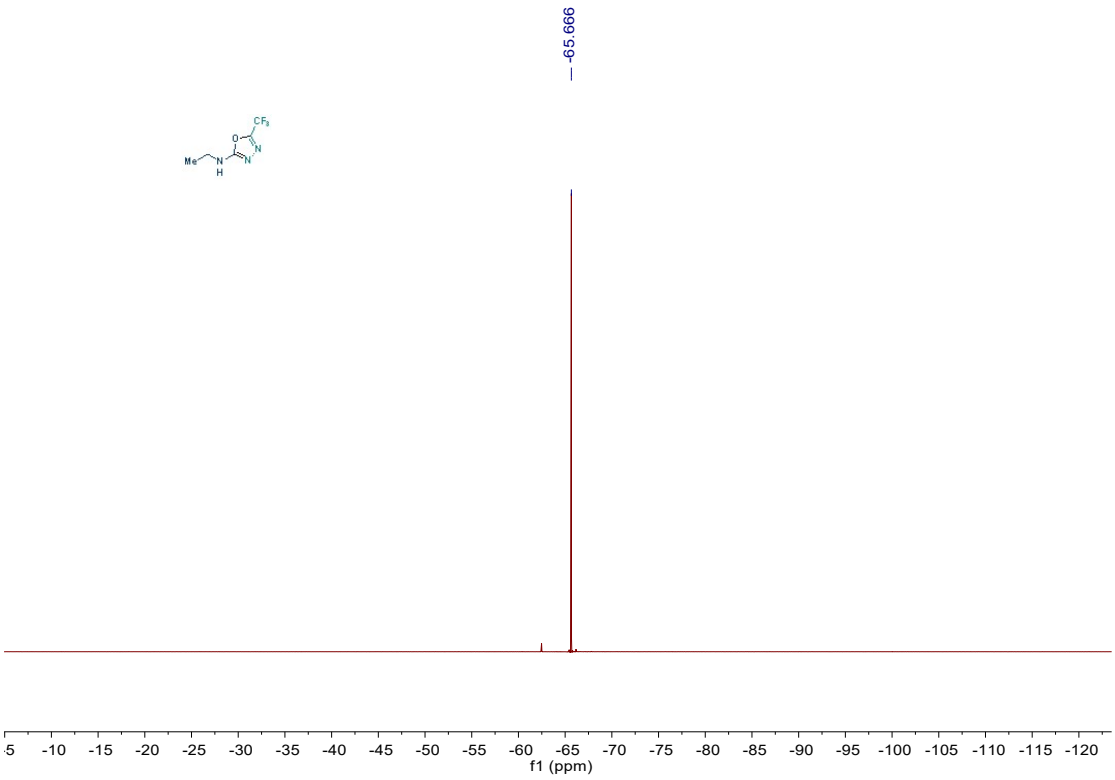
Crystal structure determination of 14

Crystal Data for $C_{10}H_8F_3N_3O$ (M =486.39 g/mol): monoclinic, space group P21/n (no. 14), a = 5.900(3) Å, b = 12.748(6) Å, c = 28.745(15) Å, β = 95.113(19)°, V = 2153.3(19) Å3, Z = 4, T = 193.0 K, μ(GaKα) = 0.766 mm-1, Dcalc = 1.500 g/cm3, 26562 reflections measured (5.37° ≤ 2Θ ≤ 107.944°), 3932 unique (Rint = 0.0995, Rsigma = 0.0935) which were used in all calculations. The final R1 was 0.0641 (I > 2σ(I)) and wR2 was 0.1915 (all data).

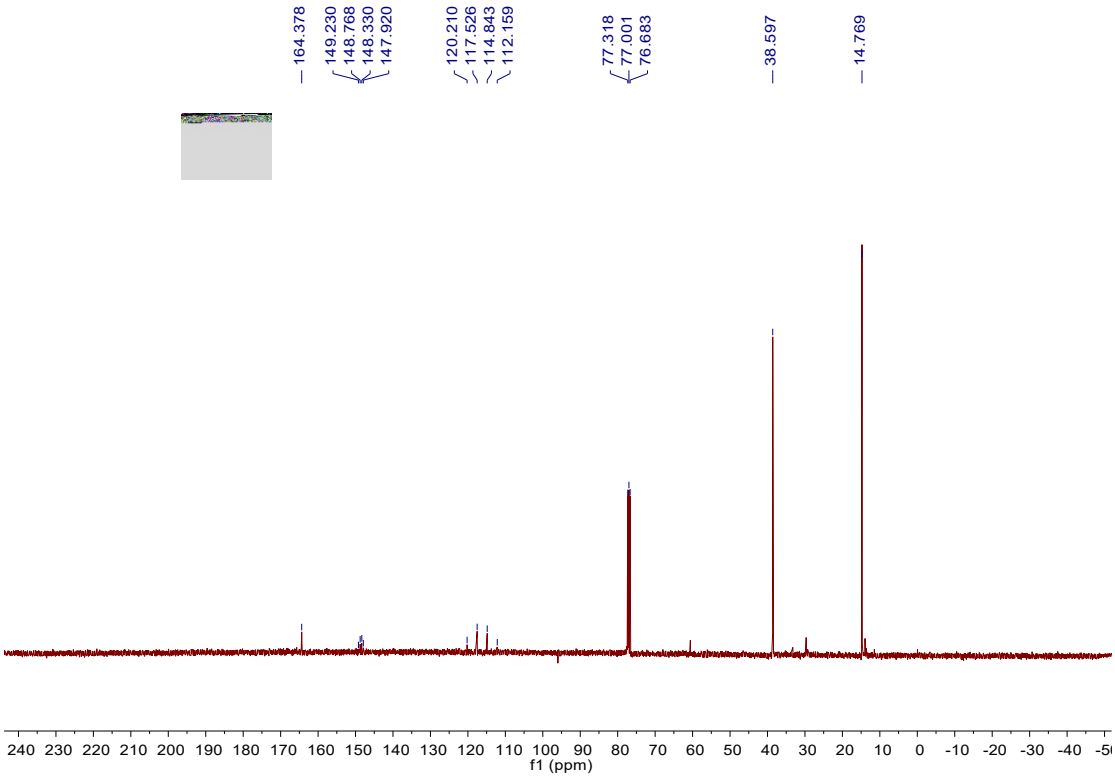
IX. NMR Spectra for compounds 3-39



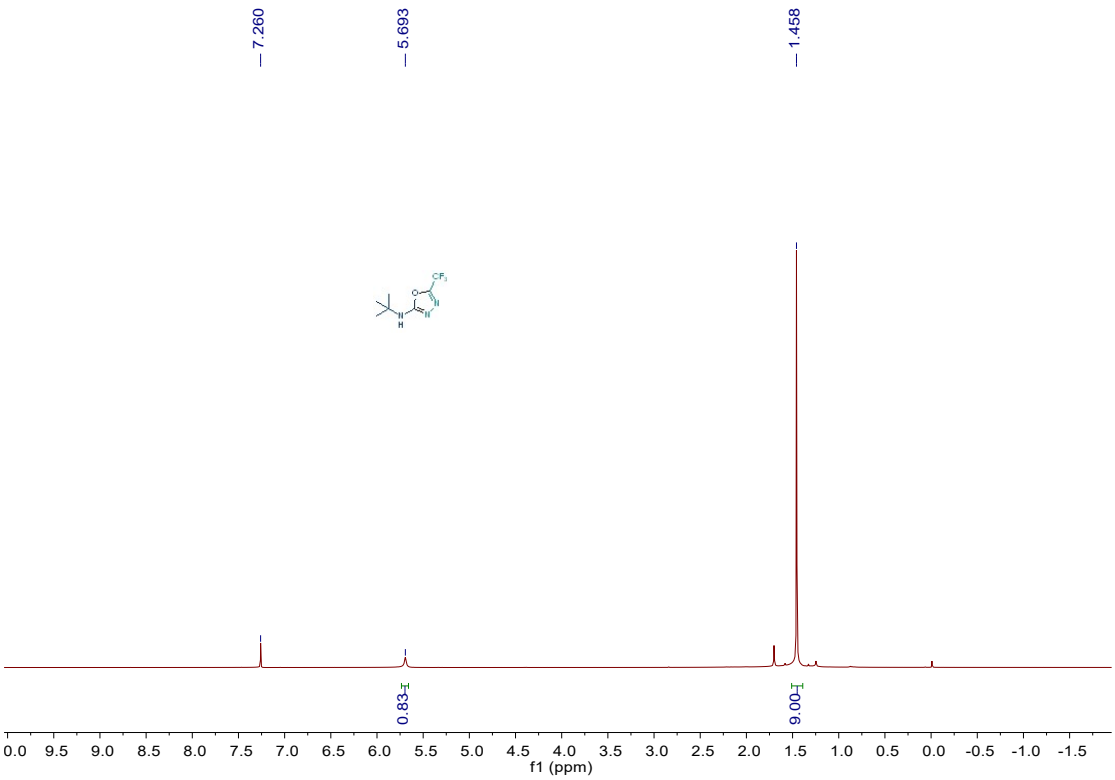
Supplementary Figure 4. ^{1}H NMR spectra of product **3**



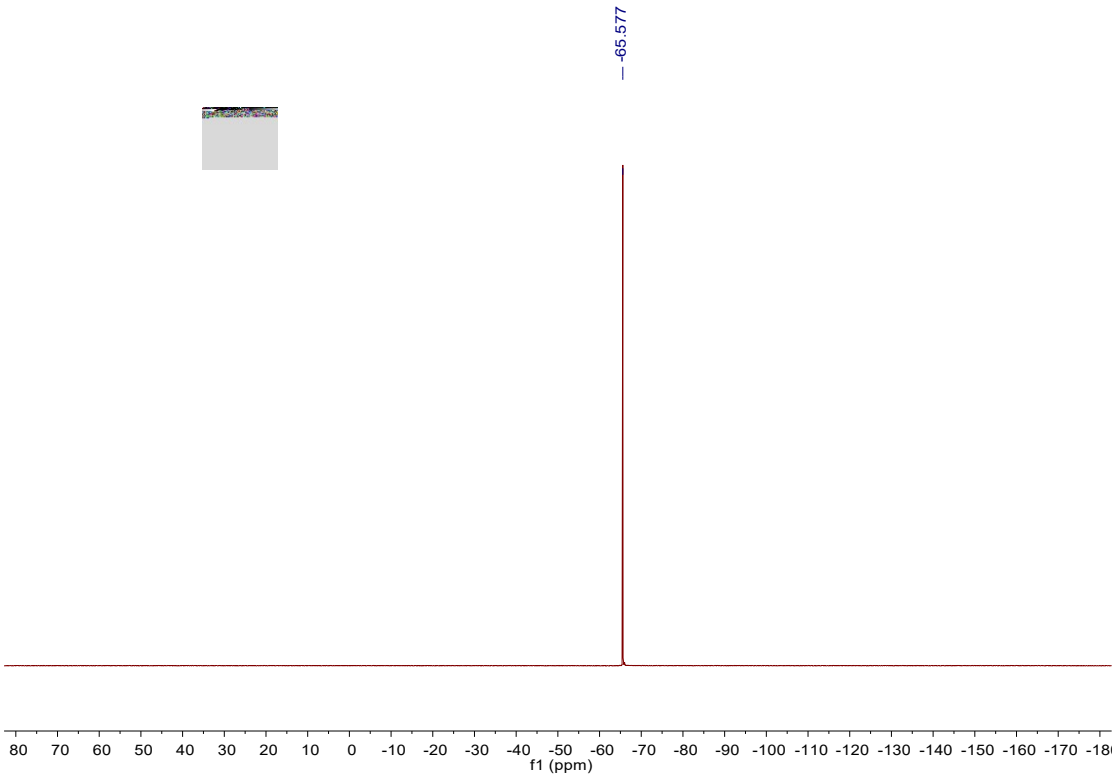
Supplementary Figure 5. ^{19}F NMR spectra of product **3**



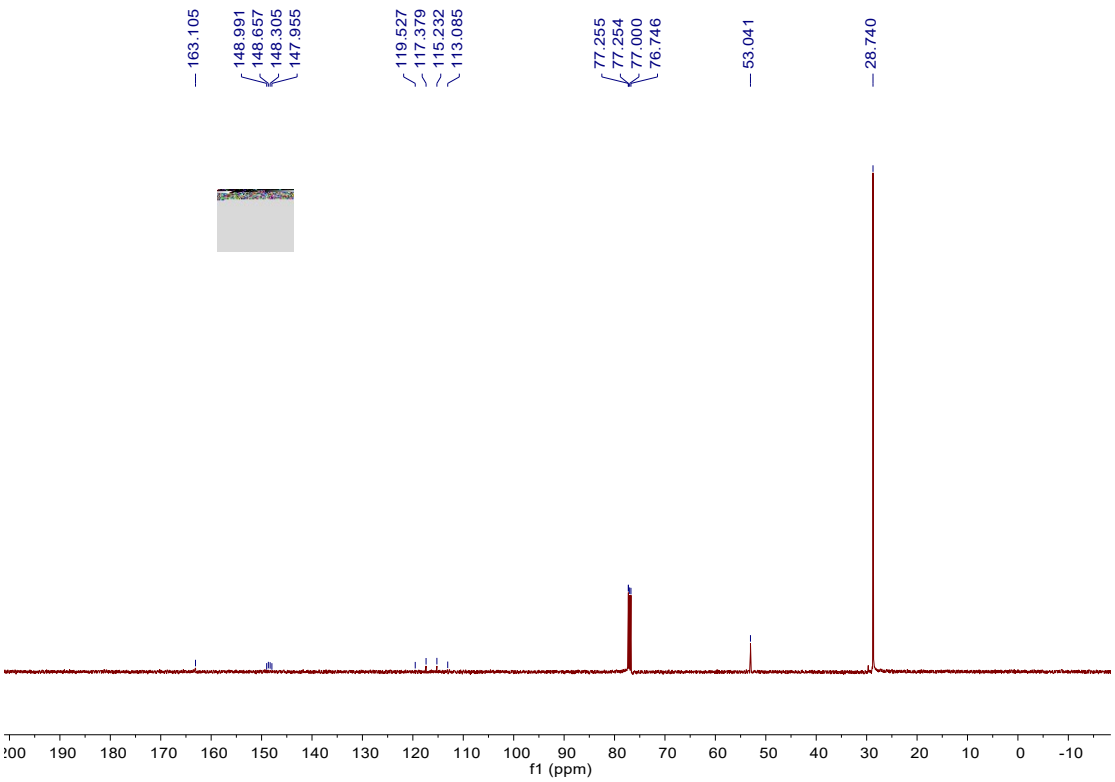
Supplementary Figure 6. ^{13}C NMR spectra of product **3**



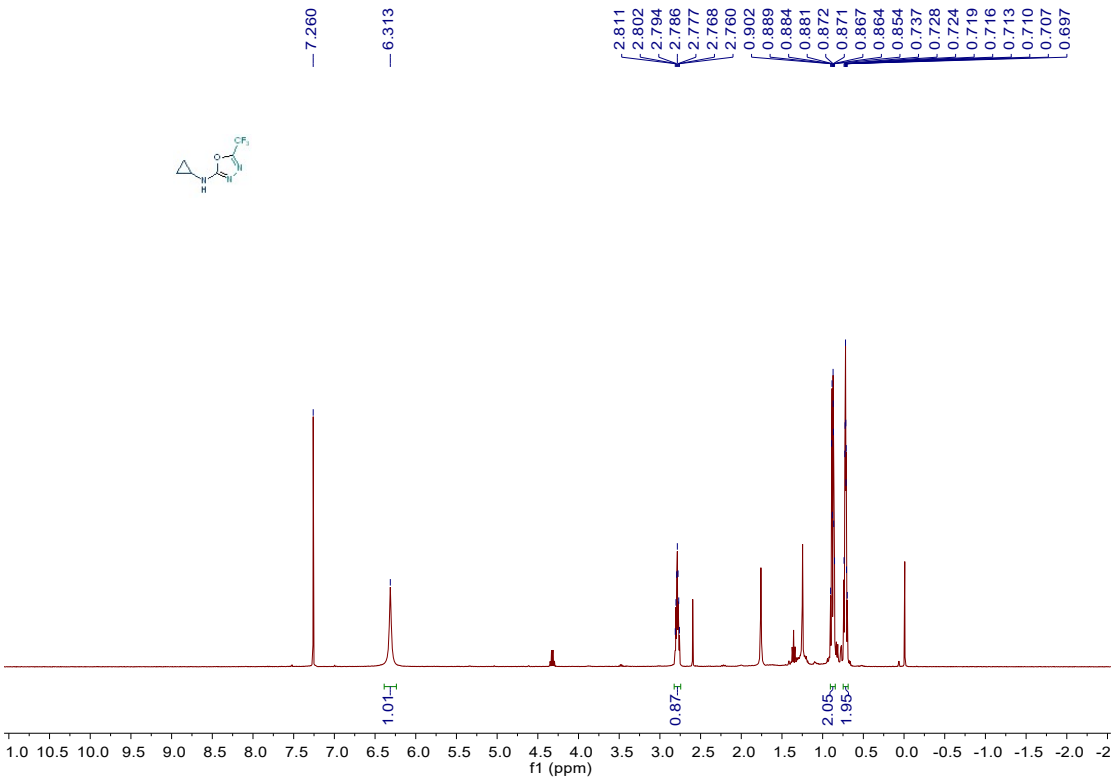
Supplementary Figure 7. ^{1}H NMR spectra of product **4**



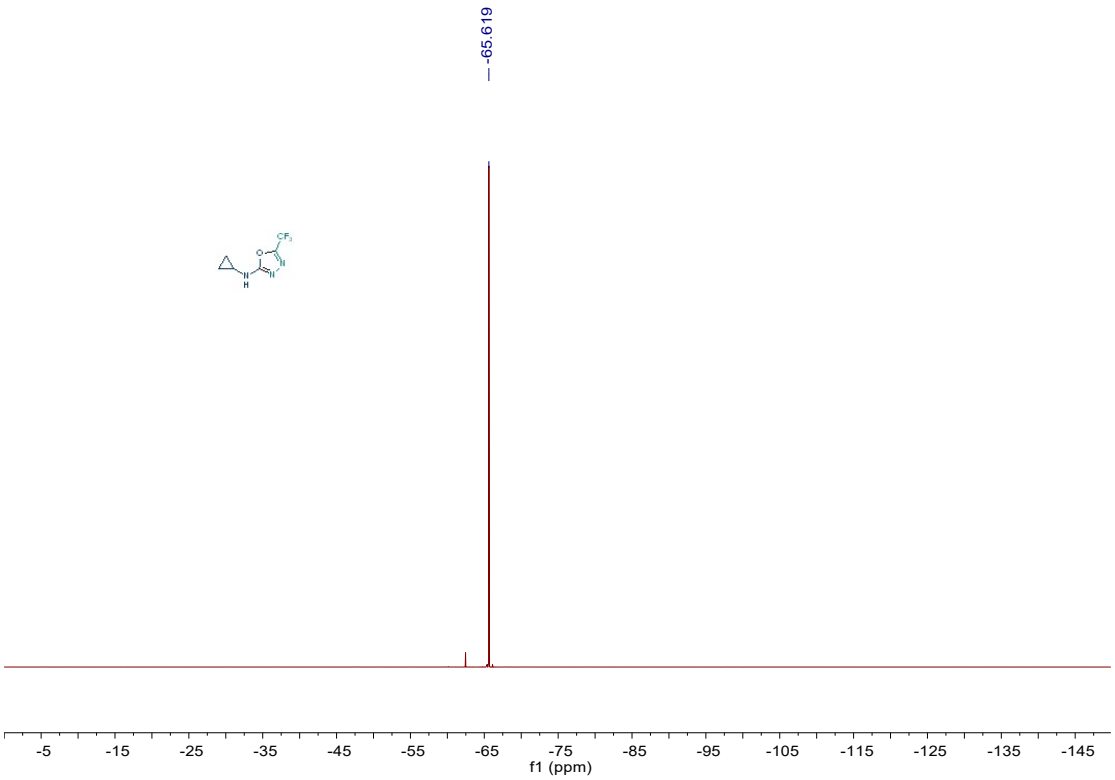
Supplementary Figure 8. ^{19}F NMR spectra of product **4**



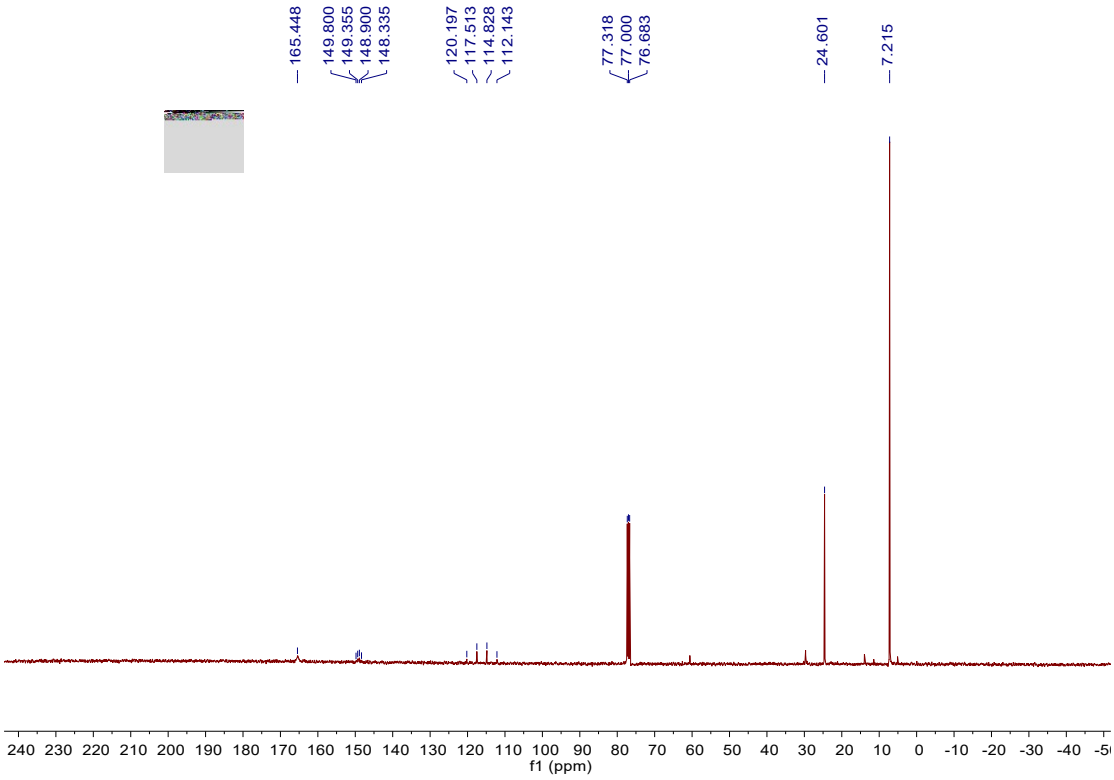
Supplementary Figure 9. ^{13}C NMR spectra of product **4**



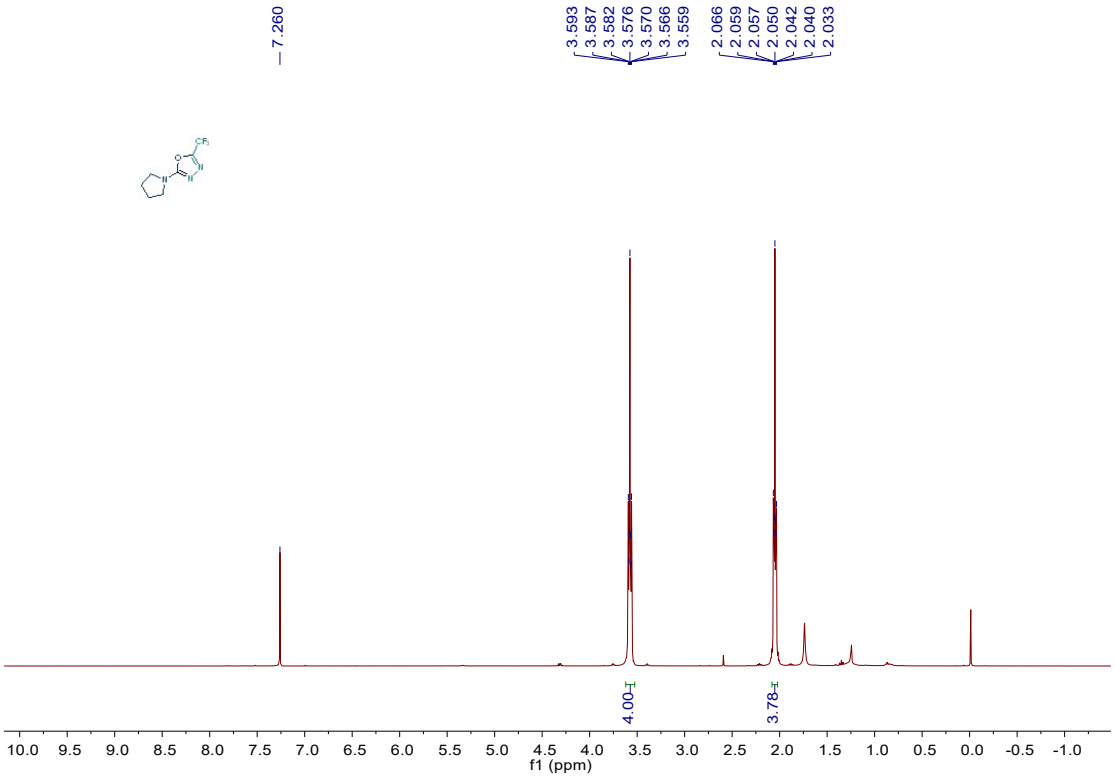
Supplementary Figure 10. ^{1}H NMR spectra of product **5**



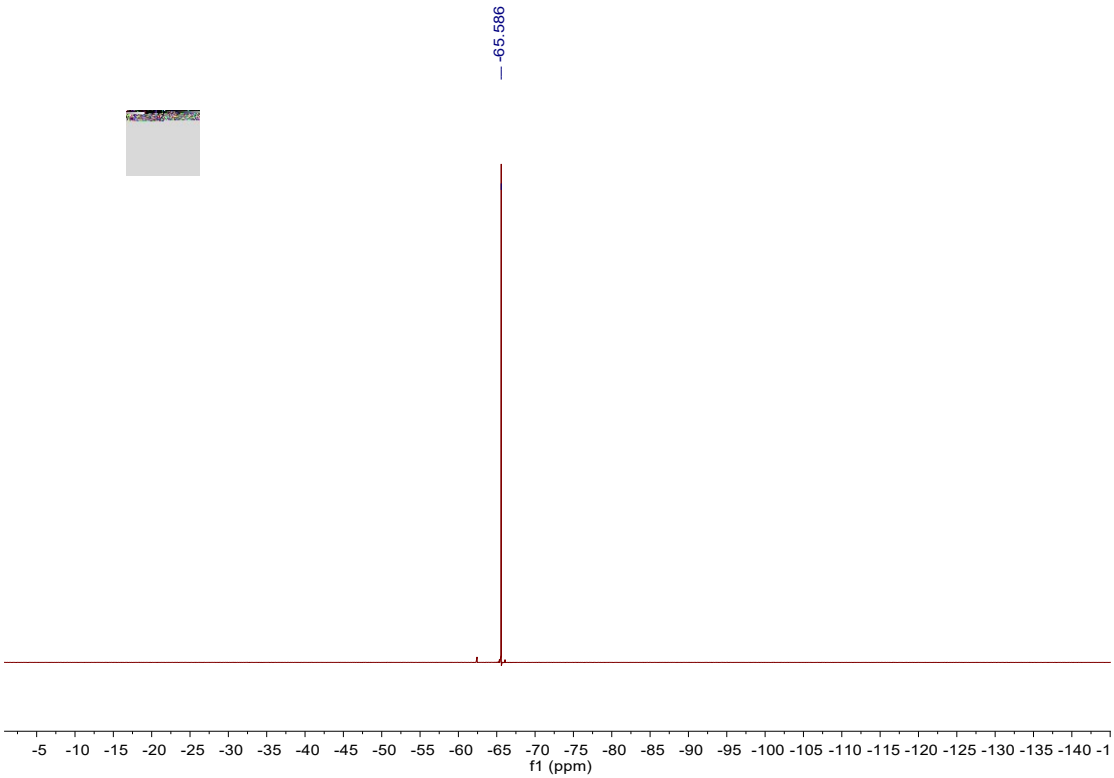
Supplementary Figure 11. ^{19}F NMR spectra of product **5**



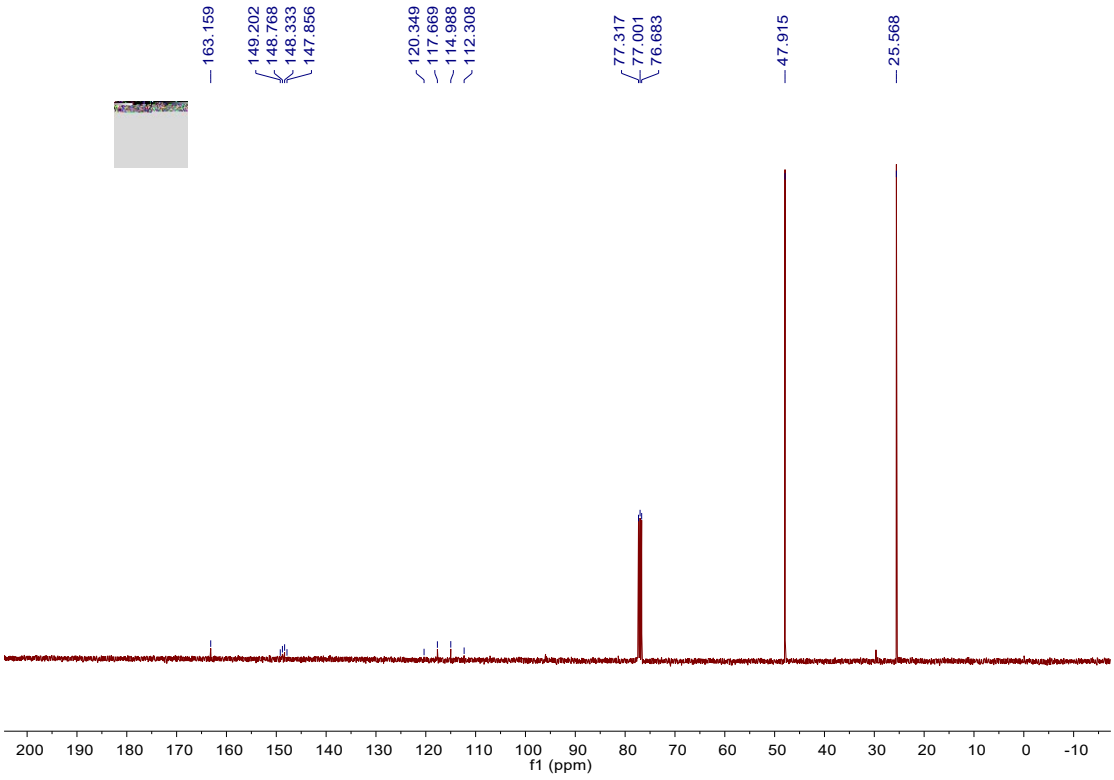
Supplementary Figure 12. ^{13}C NMR spectra of product **5**



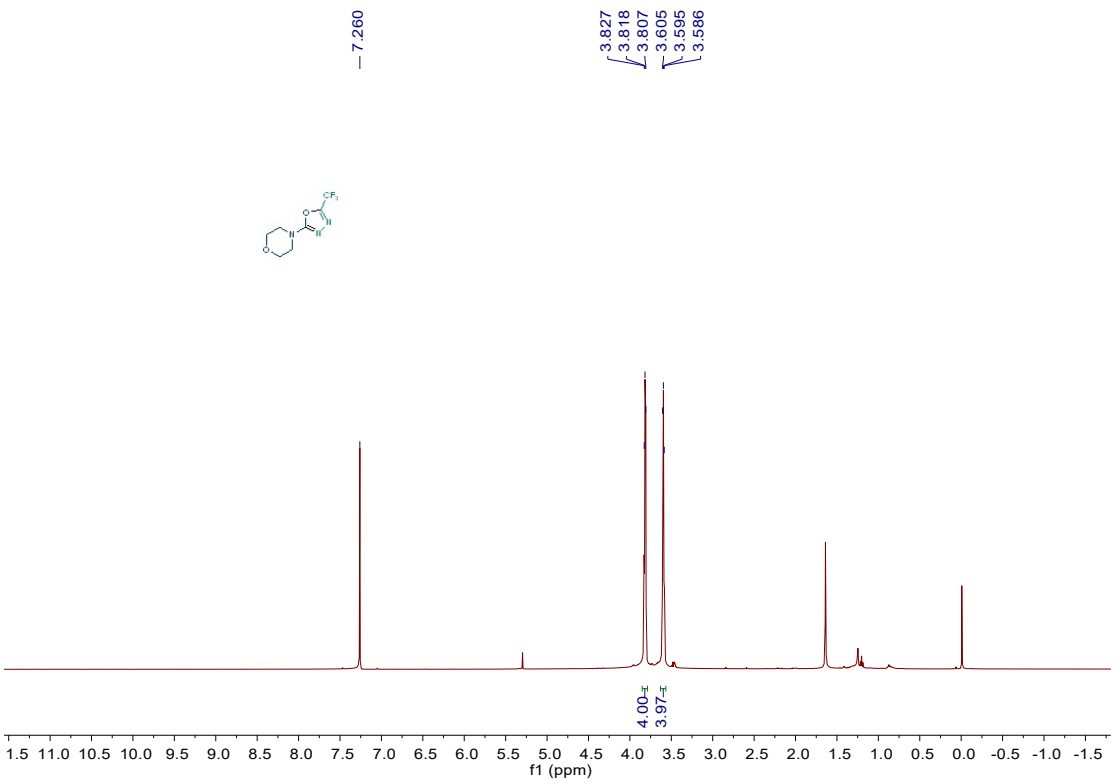
Supplementary Figure 13. ^{1}H NMR spectra of product **6**



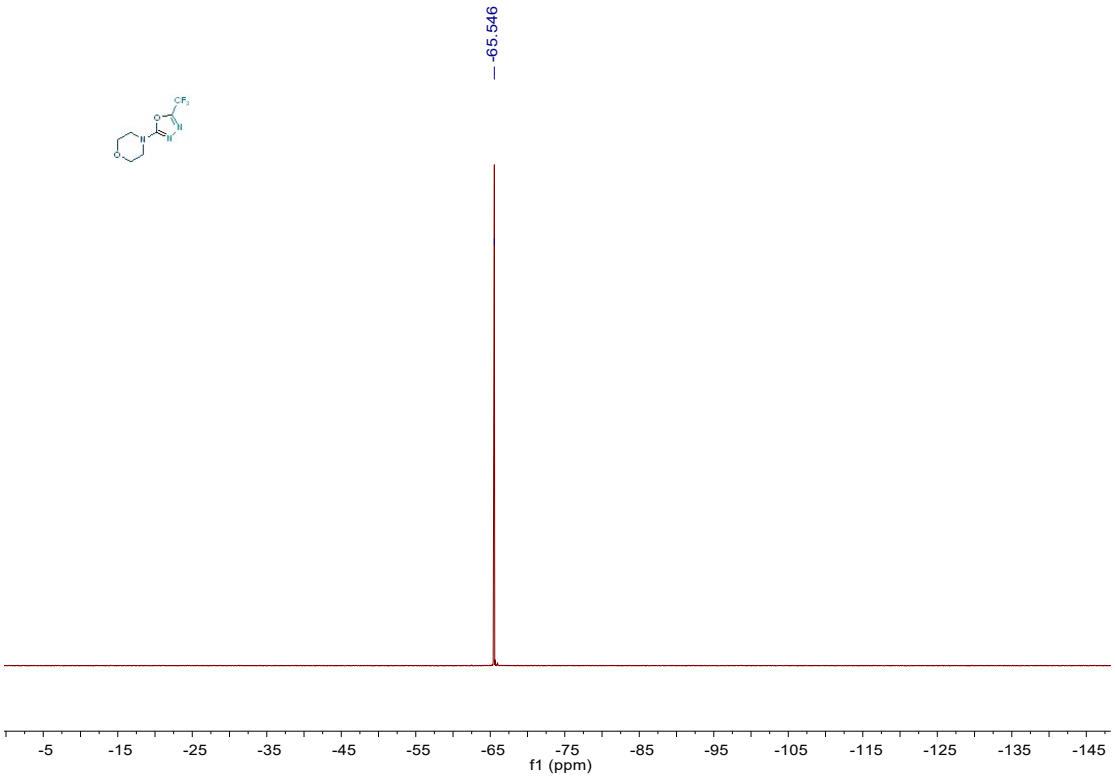
Supplementary Figure 14. ^{19}F NMR spectra of product **6**



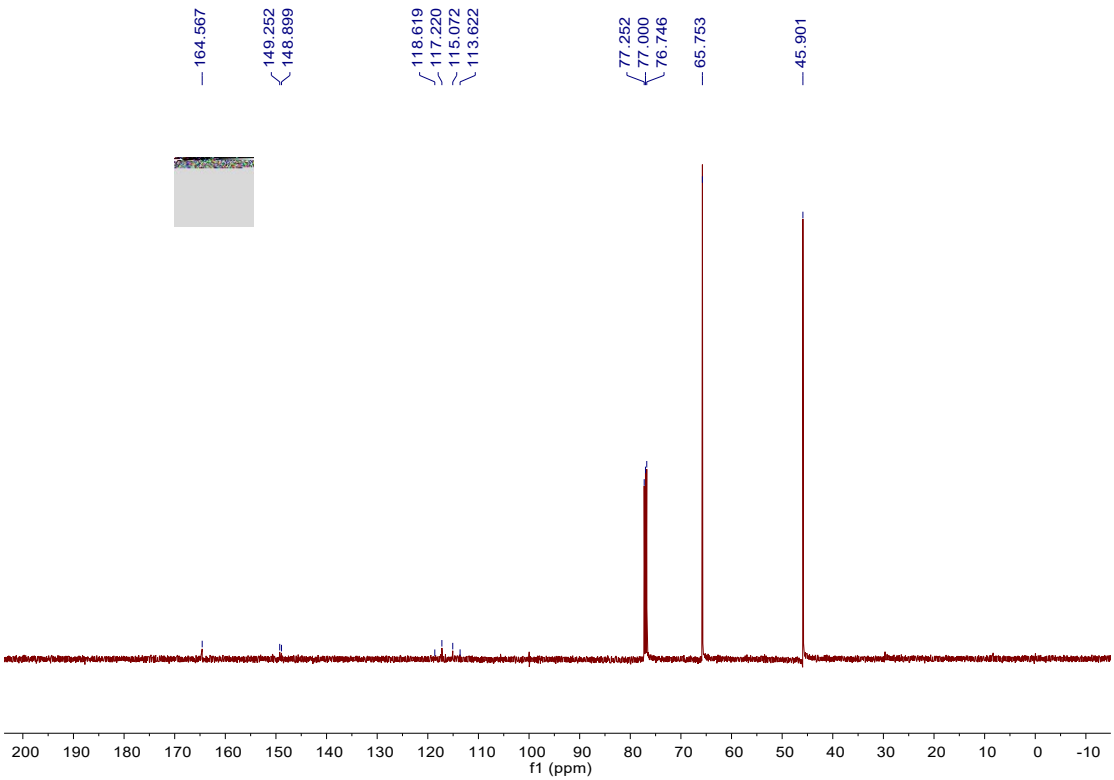
Supplementary Figure 15. ^{13}C NMR spectra of product **6**



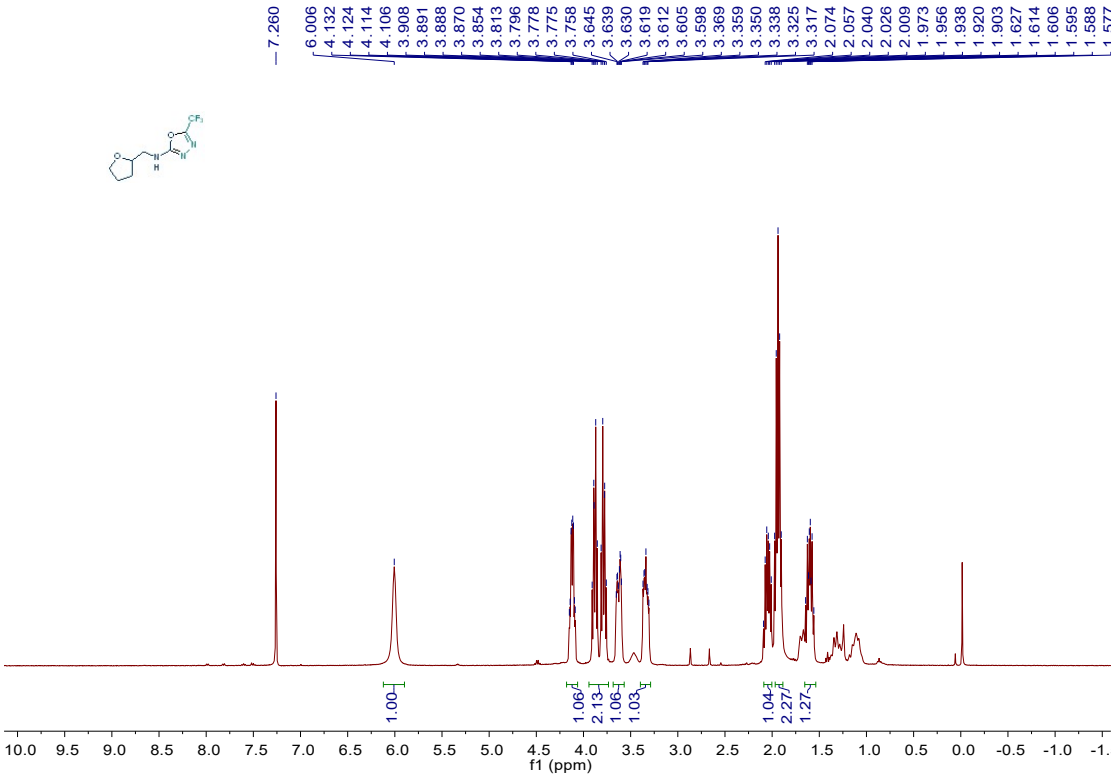
Supplementary Figure 16. ^{1}H NMR spectra of product **7**



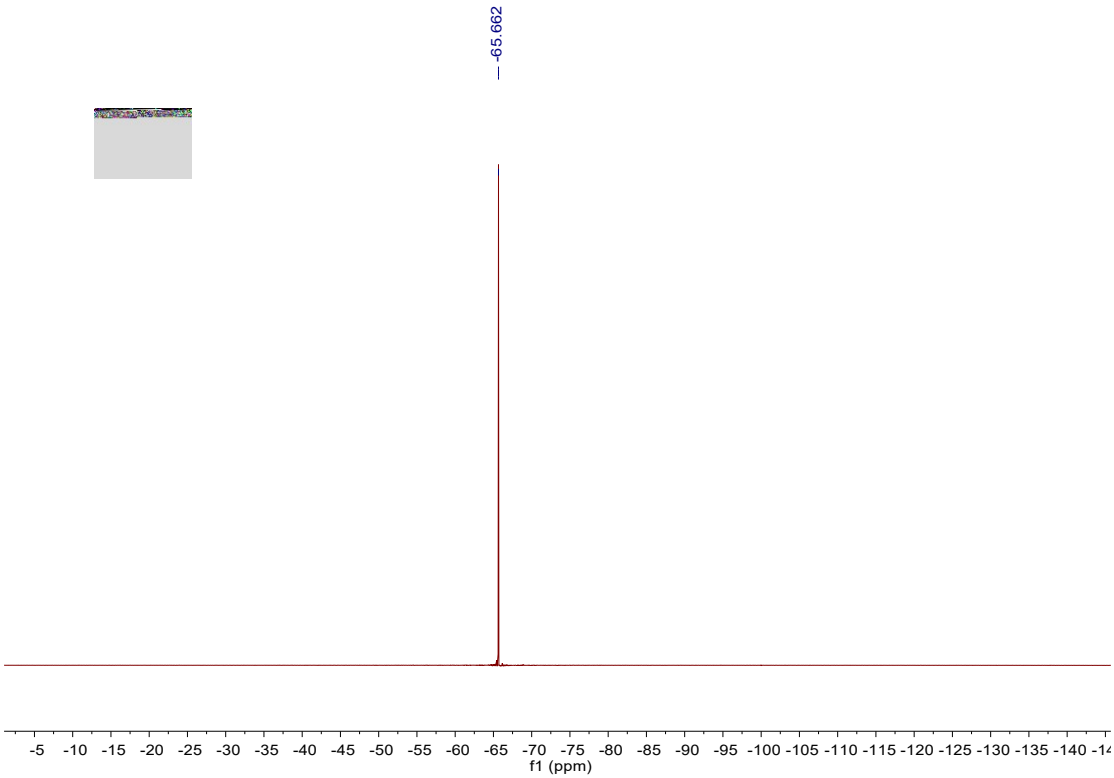
Supplementary Figure 17. ^{19}F NMR spectra of product **7**



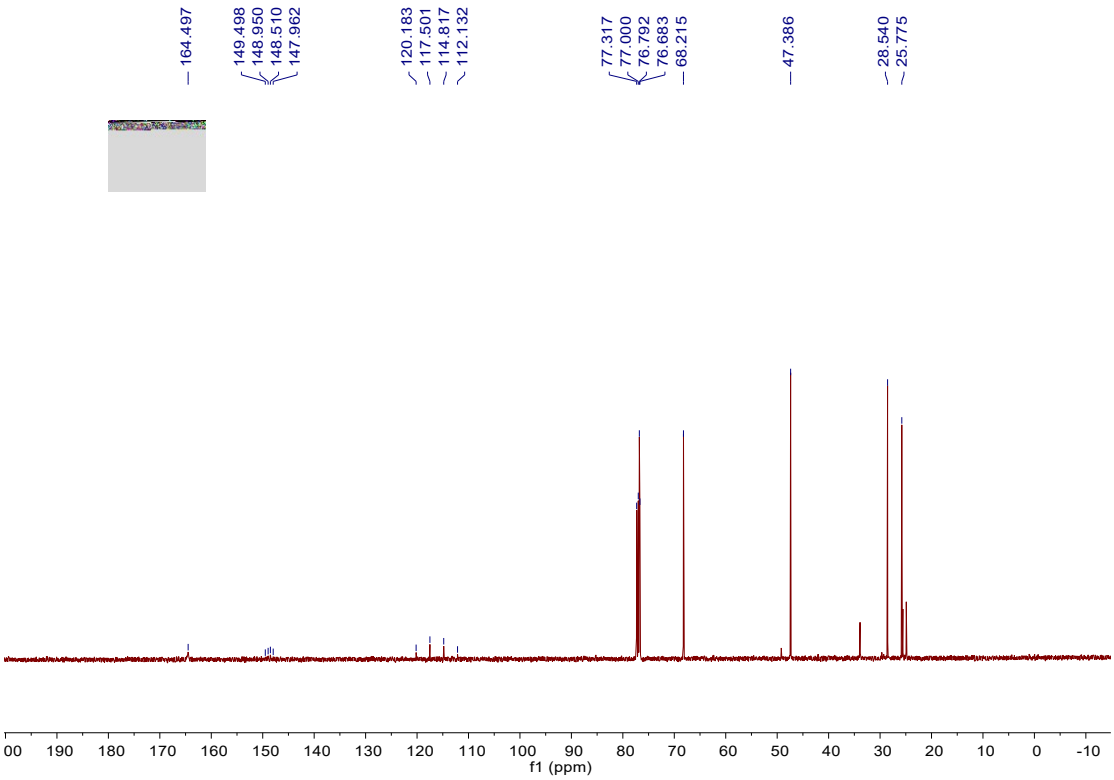
Supplementary Figure 18. ^{13}C NMR spectra of product **7**



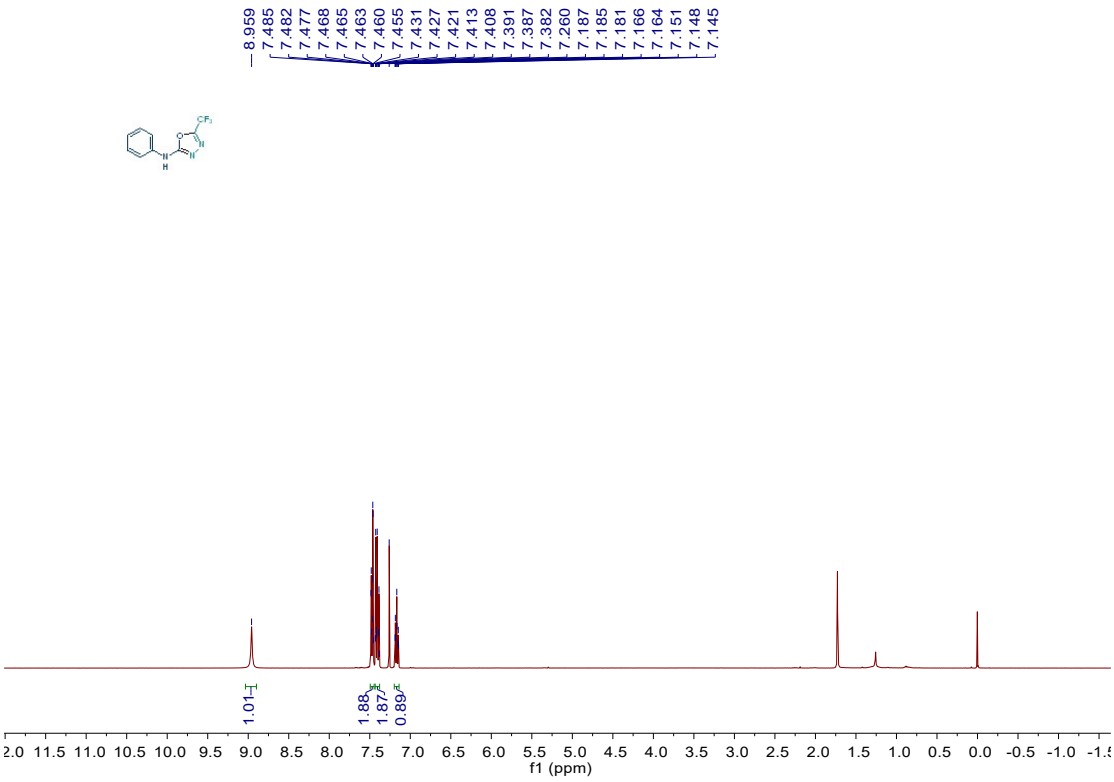
Supplementary Figure 19. ^{1}H NMR spectra of product **8**



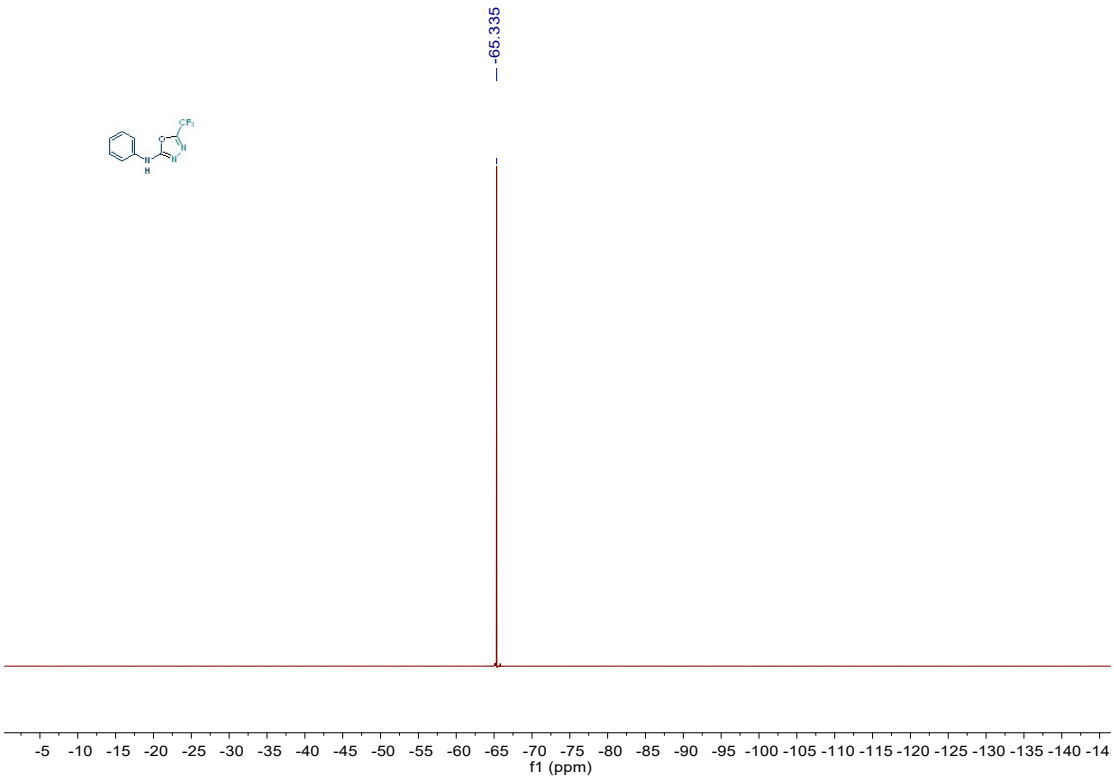
Supplementary Figure 20. ^{19}F NMR spectra of product **8**



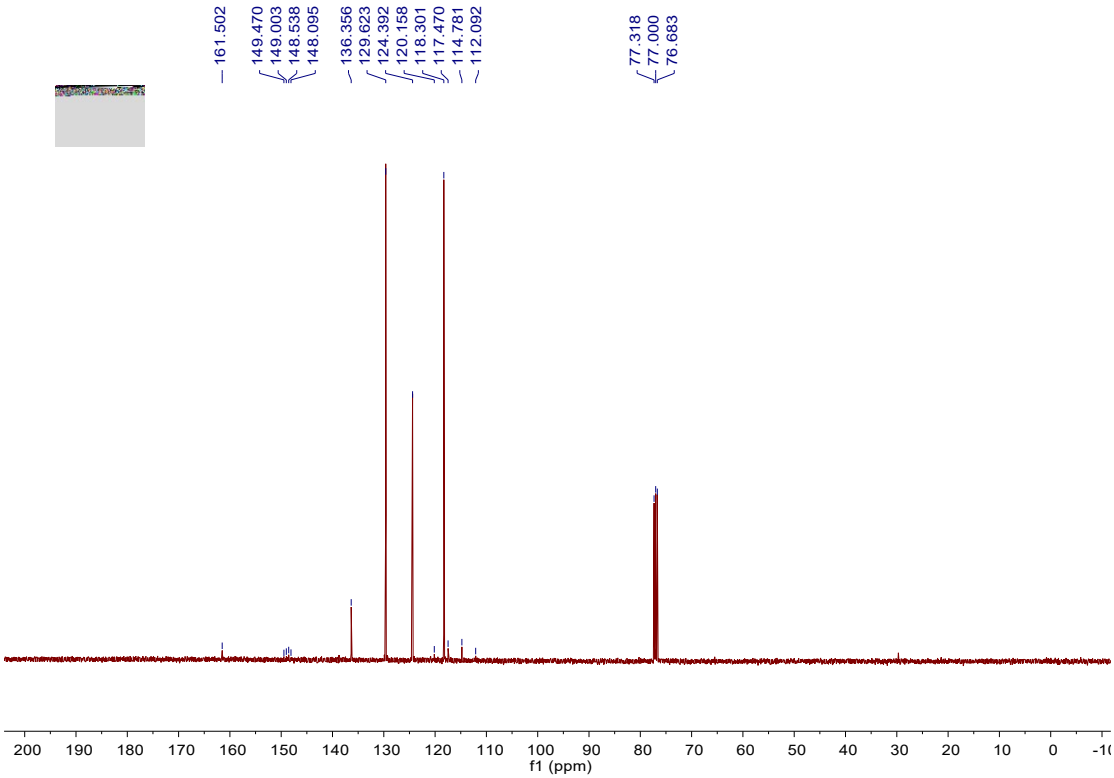
Supplementary Figure 21. ^{13}C NMR spectra of product **8**



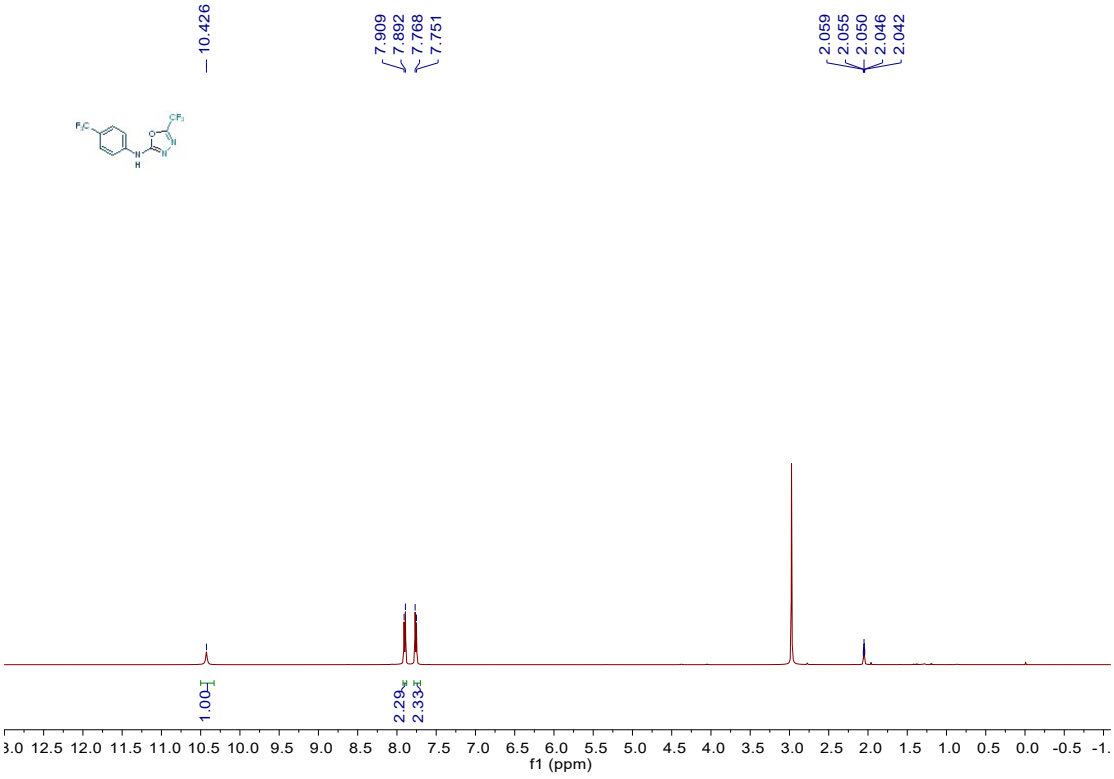
Supplementary Figure 22. ^{1}H NMR spectra of product **9**



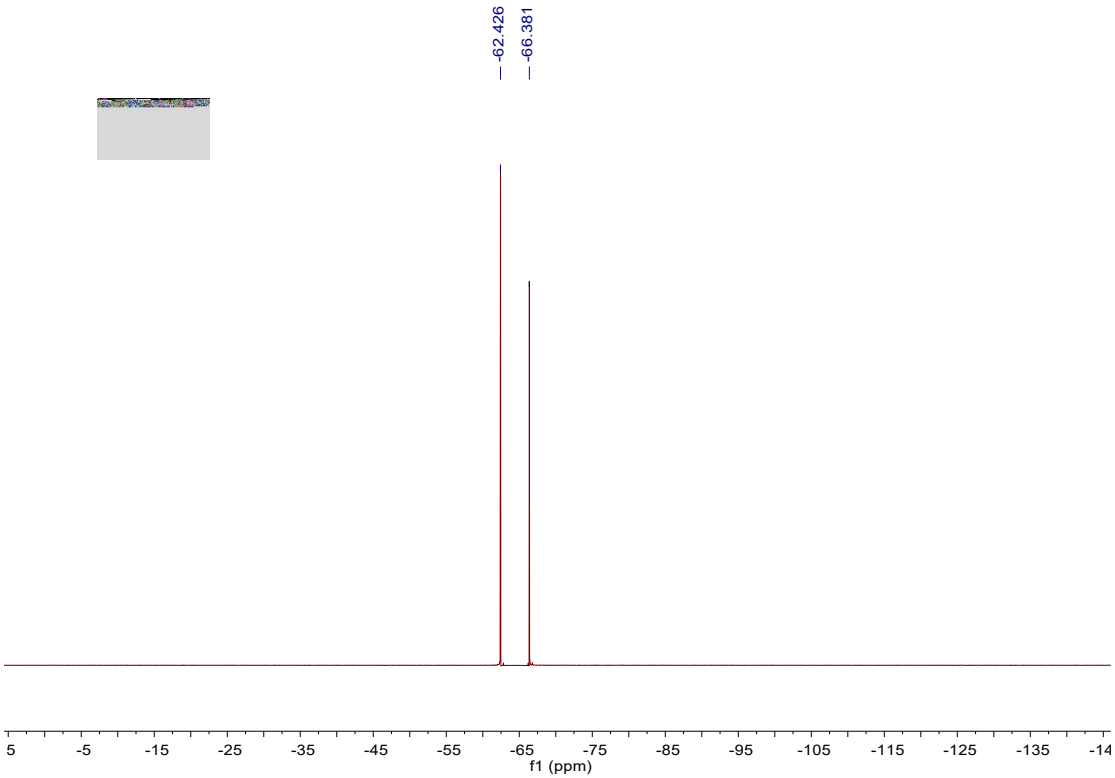
Supplementary Figure 23. ^{19}F NMR spectra of product **9**



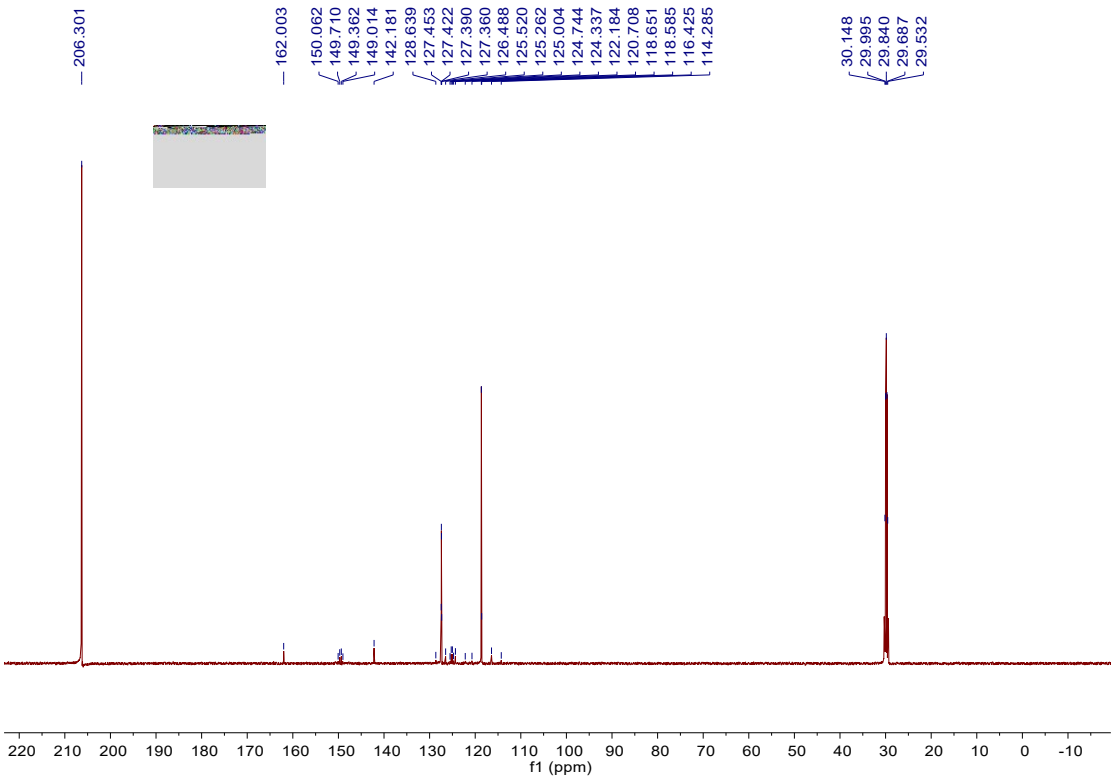
Supplementary Figure 24. ^{13}C NMR spectra of product **9**



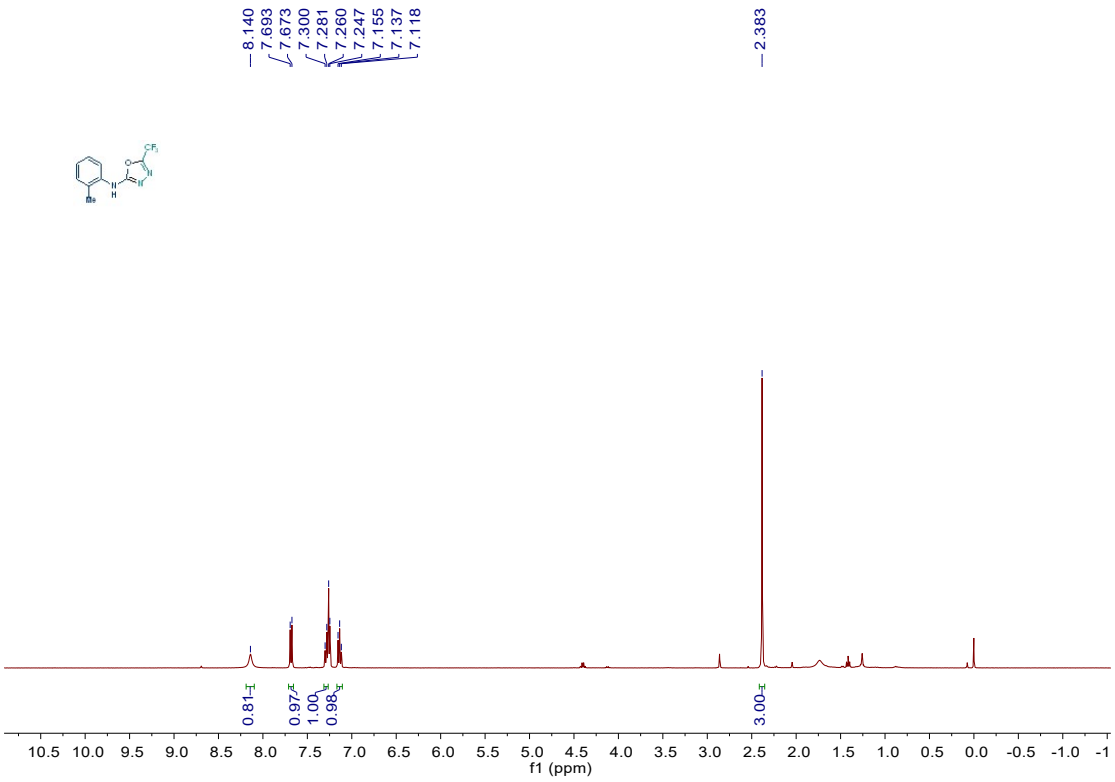
Supplementary Figure 25. ^{1}H NMR spectra of product **10**



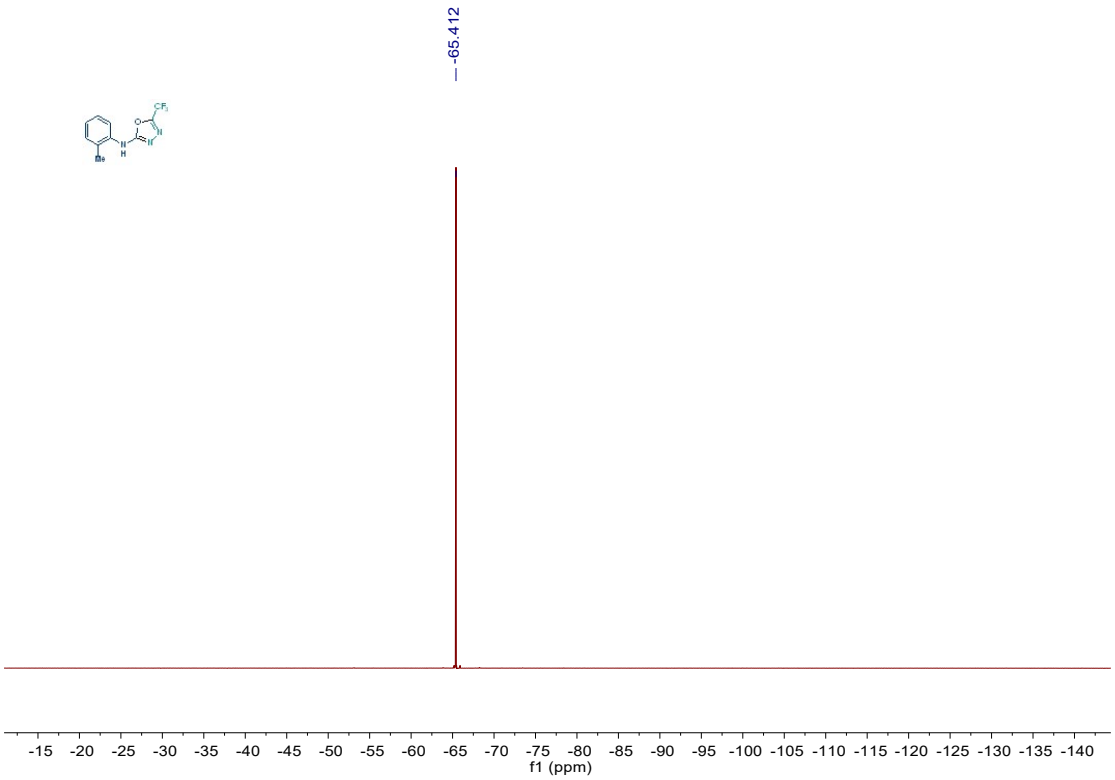
Supplementary Figure 26. ^{19}F NMR spectra of product **10**



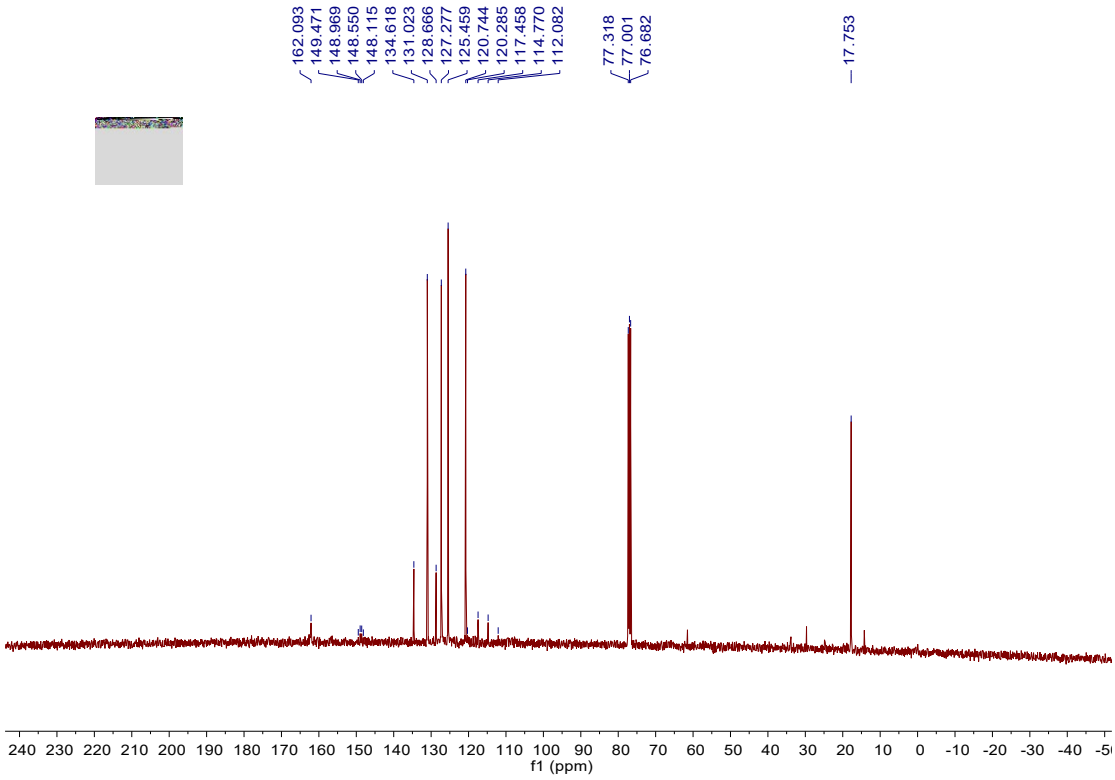
Supplementary Figure 27. ^{13}C NMR spectra of product **10**



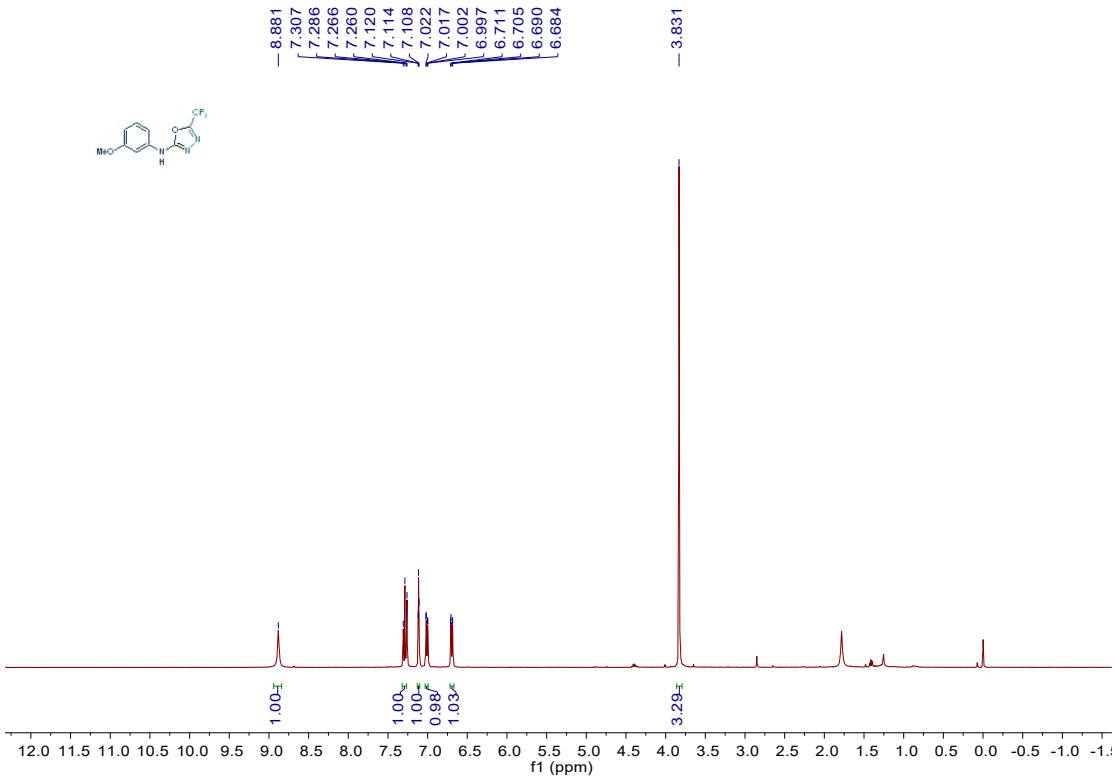
Supplementary Figure 28. ^{1}H NMR spectra of product **11**



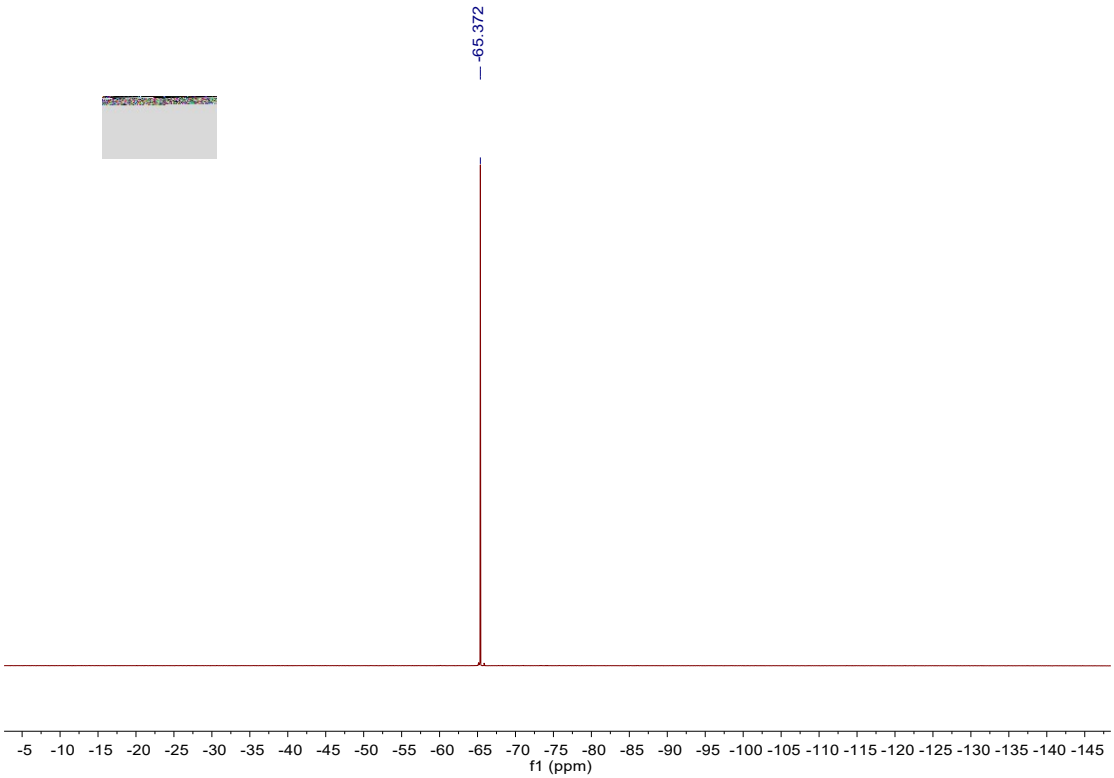
Supplementary Figure 29. ^{19}F NMR spectra of product **11**



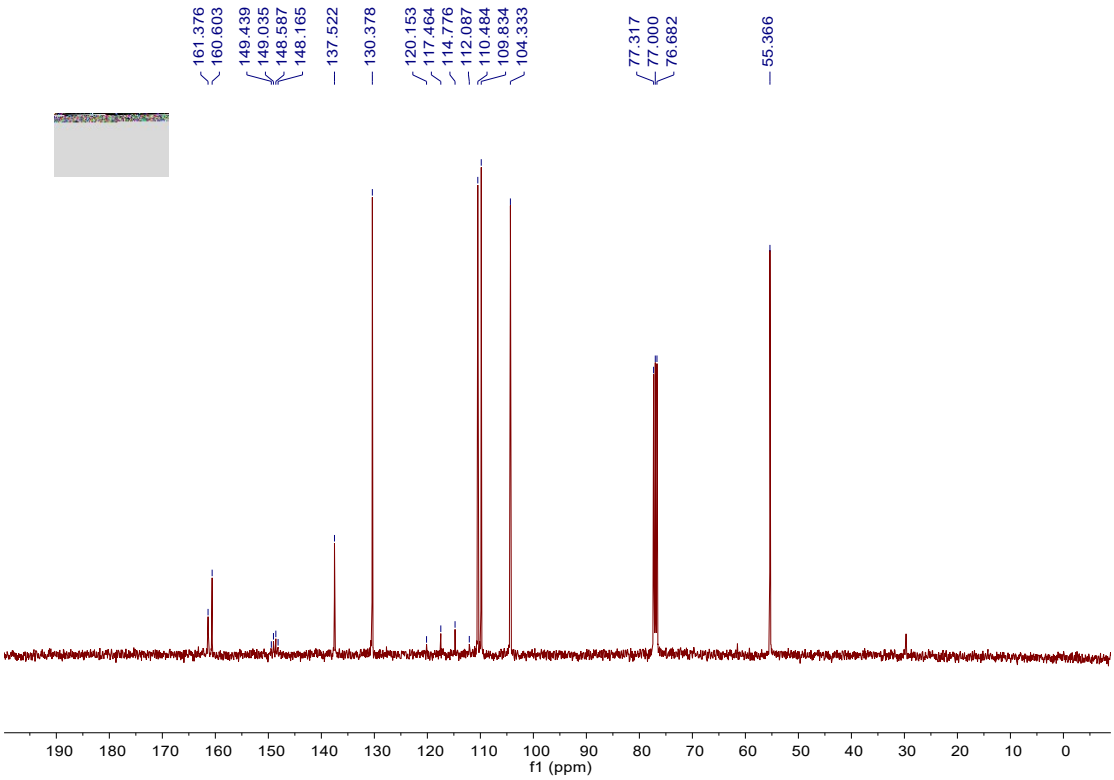
Supplementary Figure 30. ^{13}C NMR spectra of product **11**



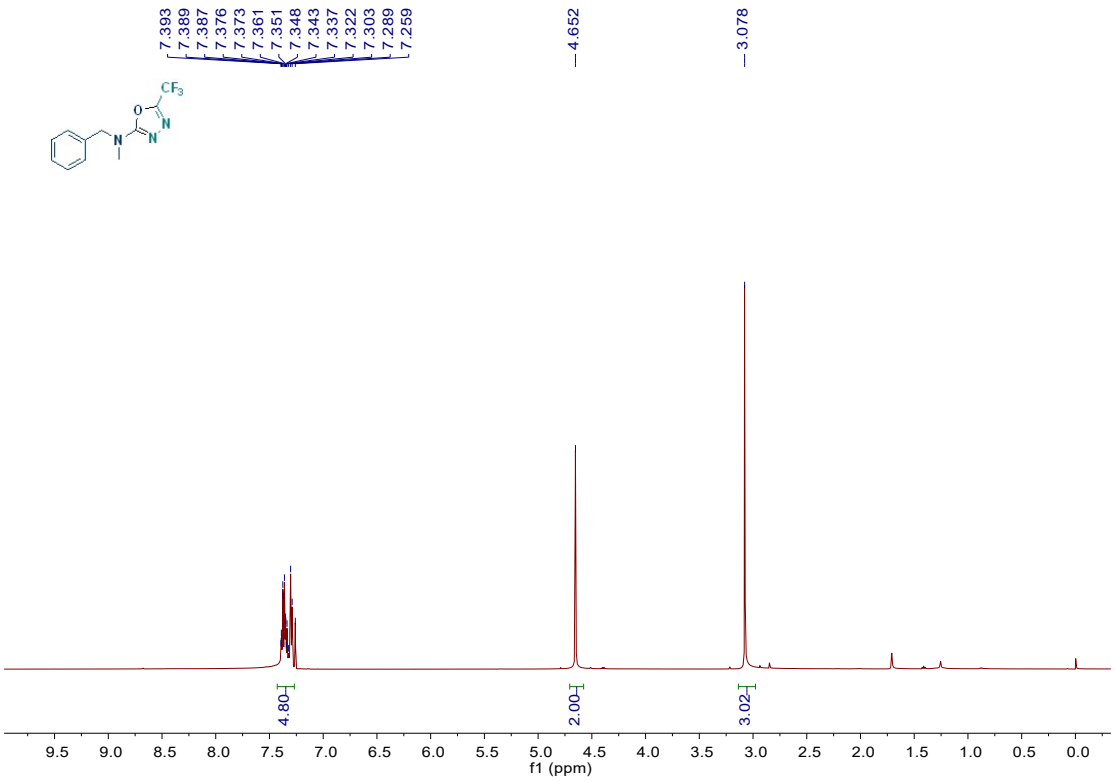
Supplementary Figure 31. ^{1}H NMR spectra of product **12**



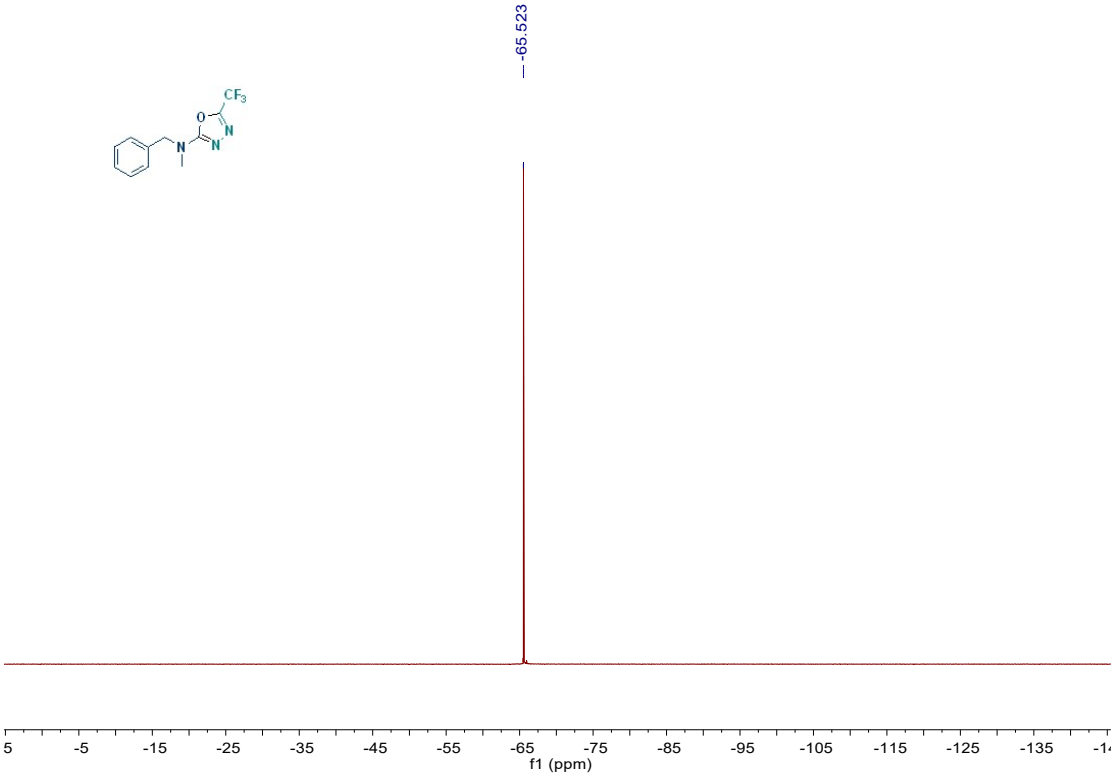
Supplementary Figure 32. ^{19}F NMR spectra of product **12**



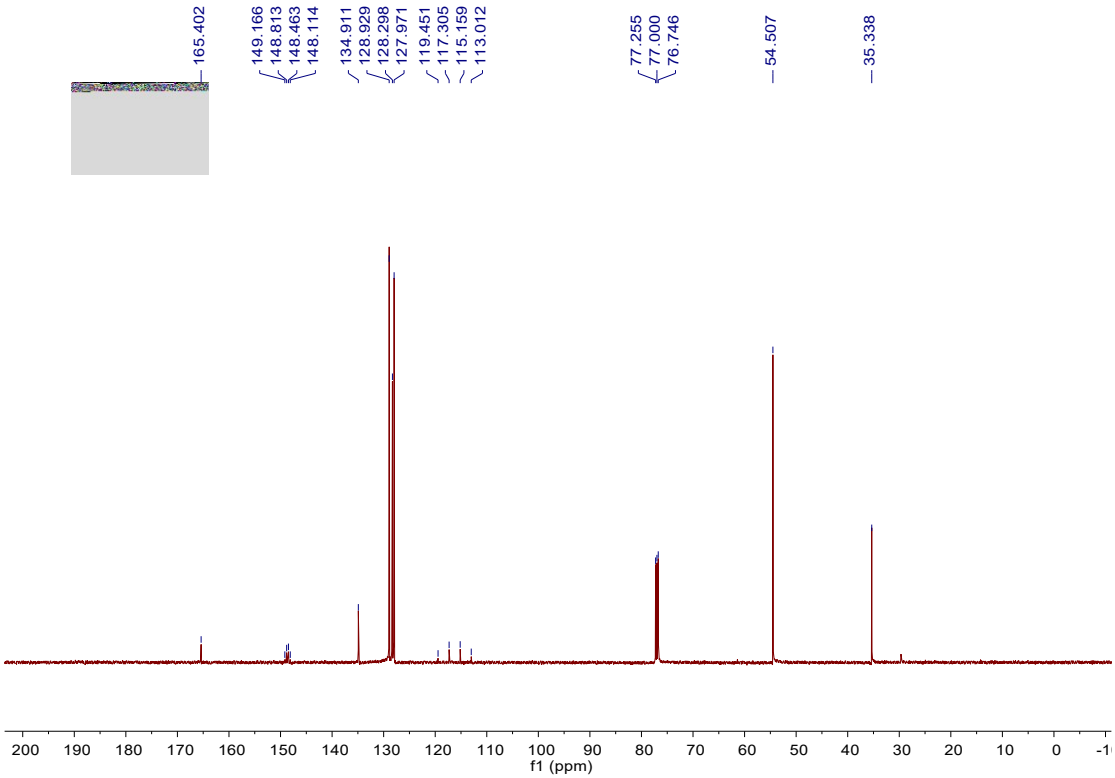
Supplementary Figure 33. ^{13}C NMR spectra of product **12**



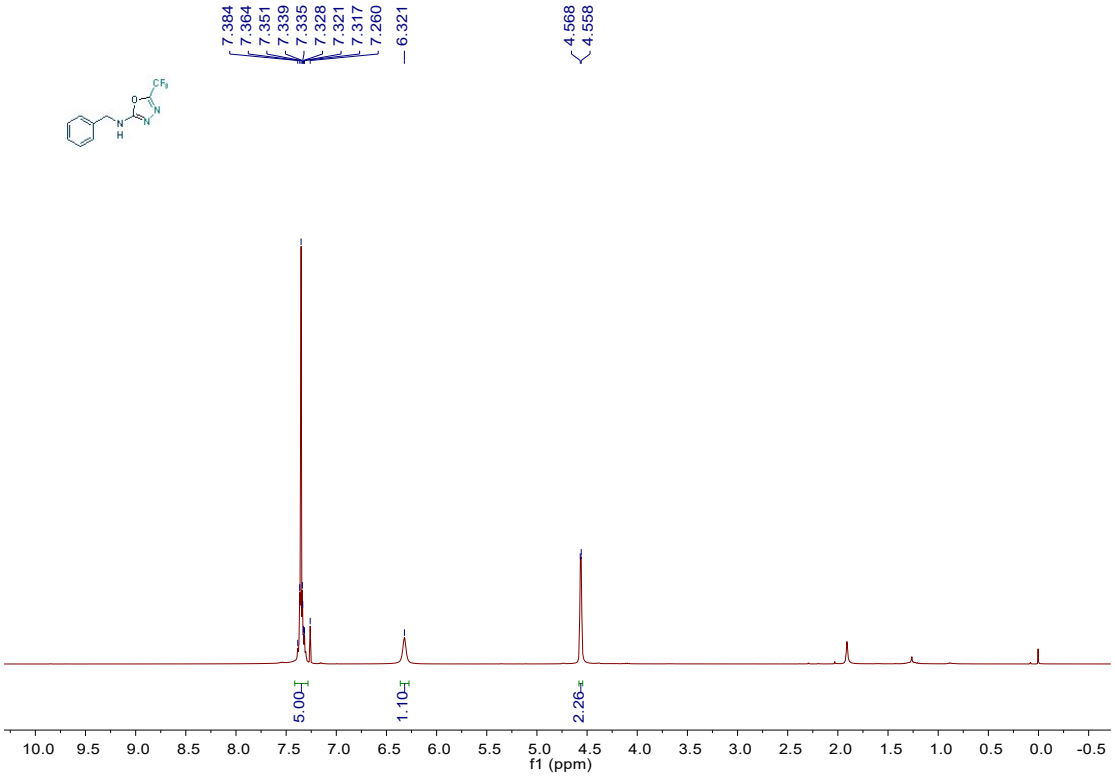
Supplementary Figure 34. ^{1}H NMR spectra of product **13**



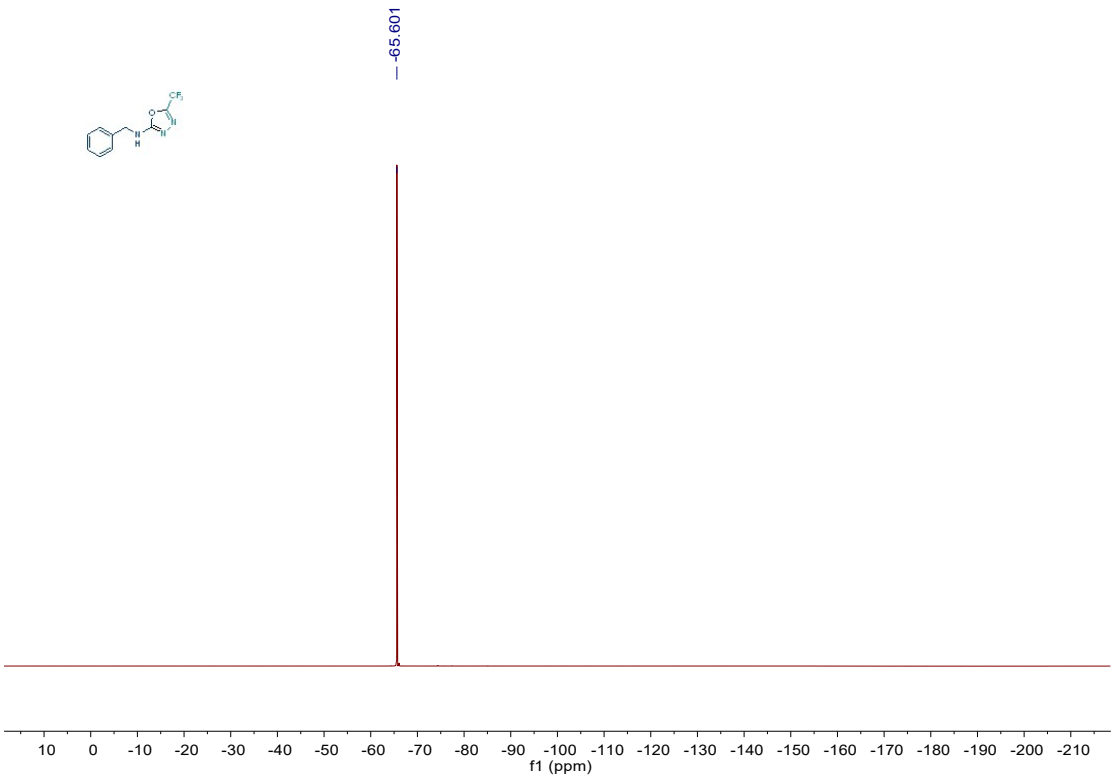
Supplementary Figure 35. ^{19}F NMR spectra of product **13**



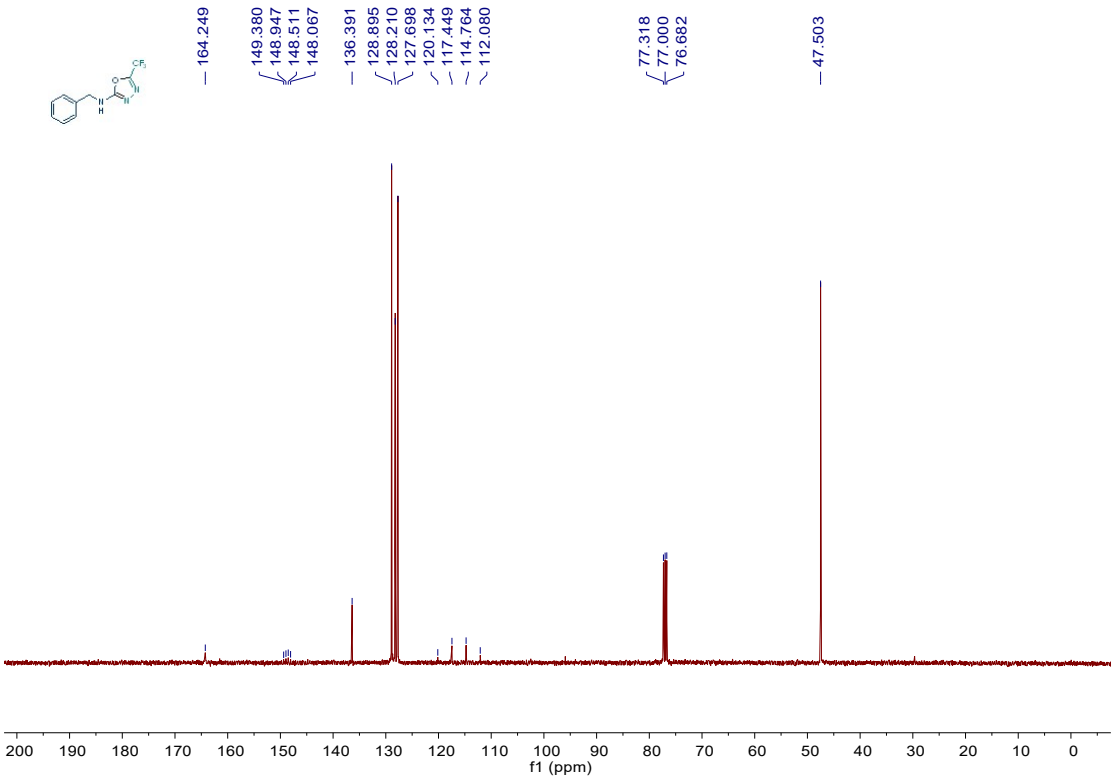
Supplementary Figure 36. ^{13}C NMR spectra of product **13**



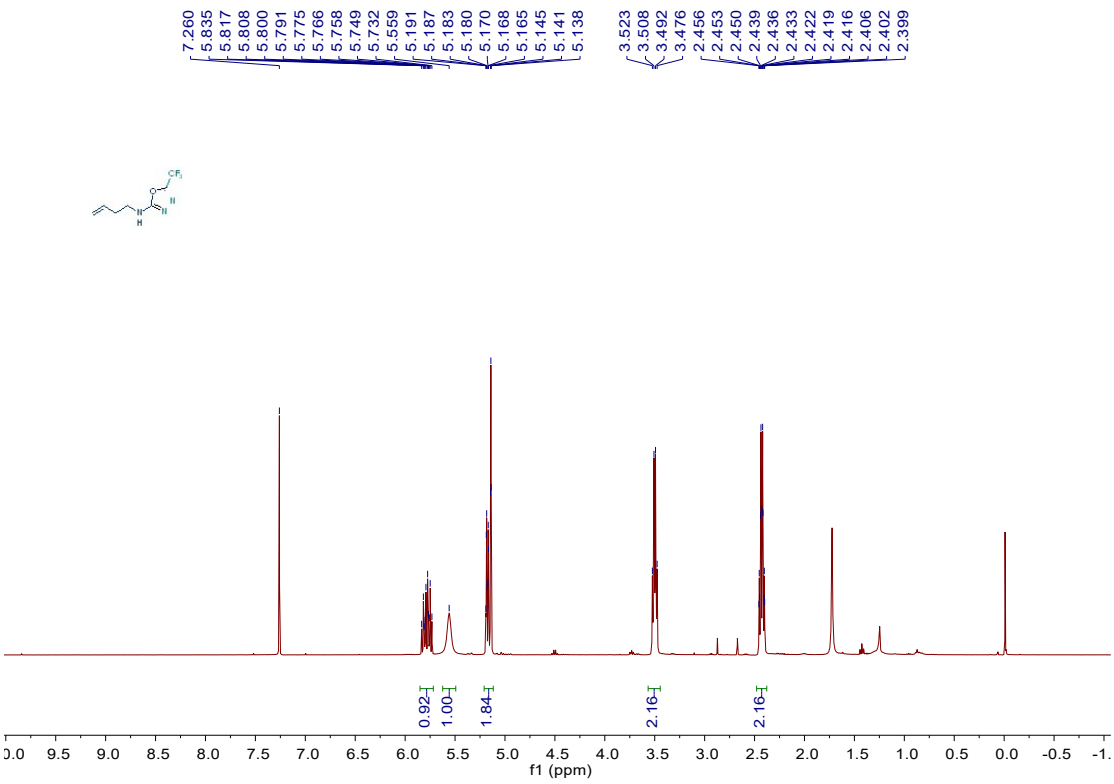
Supplementary Figure 37. ^{1}H NMR spectra of product **14**



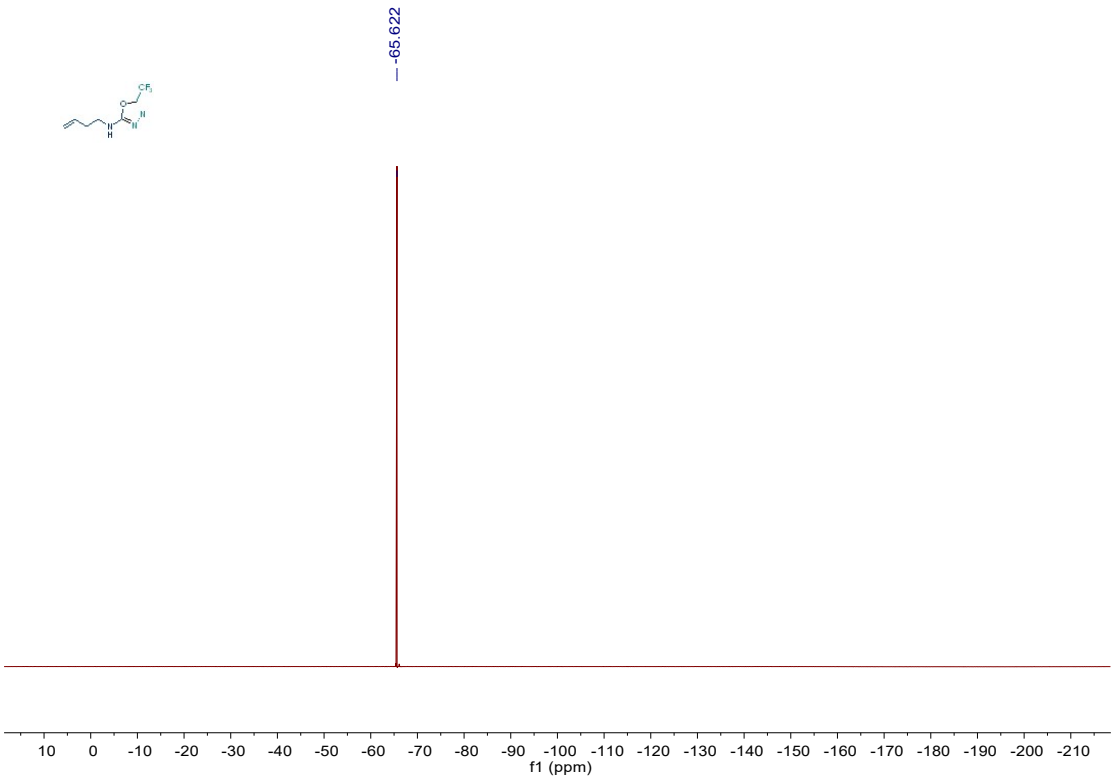
Supplementary Figure 38. ^{19}F NMR spectra of product **14**



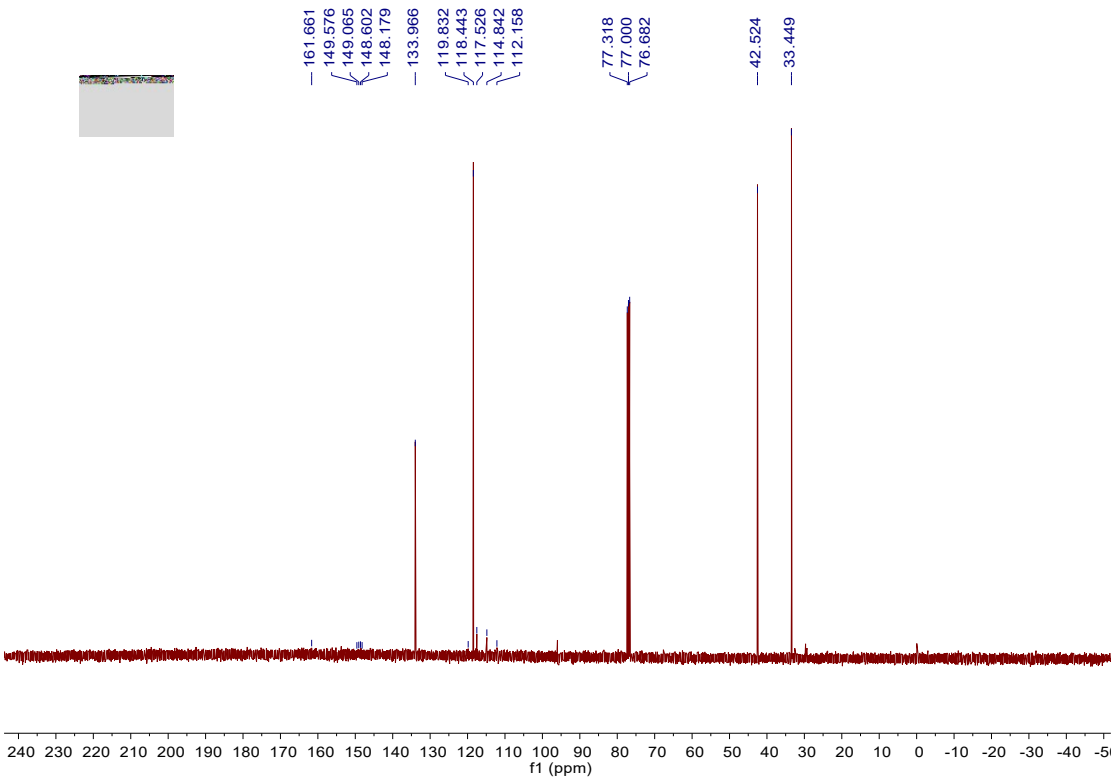
Supplementary Figure 39. ^{13}C NMR spectra of product **14**



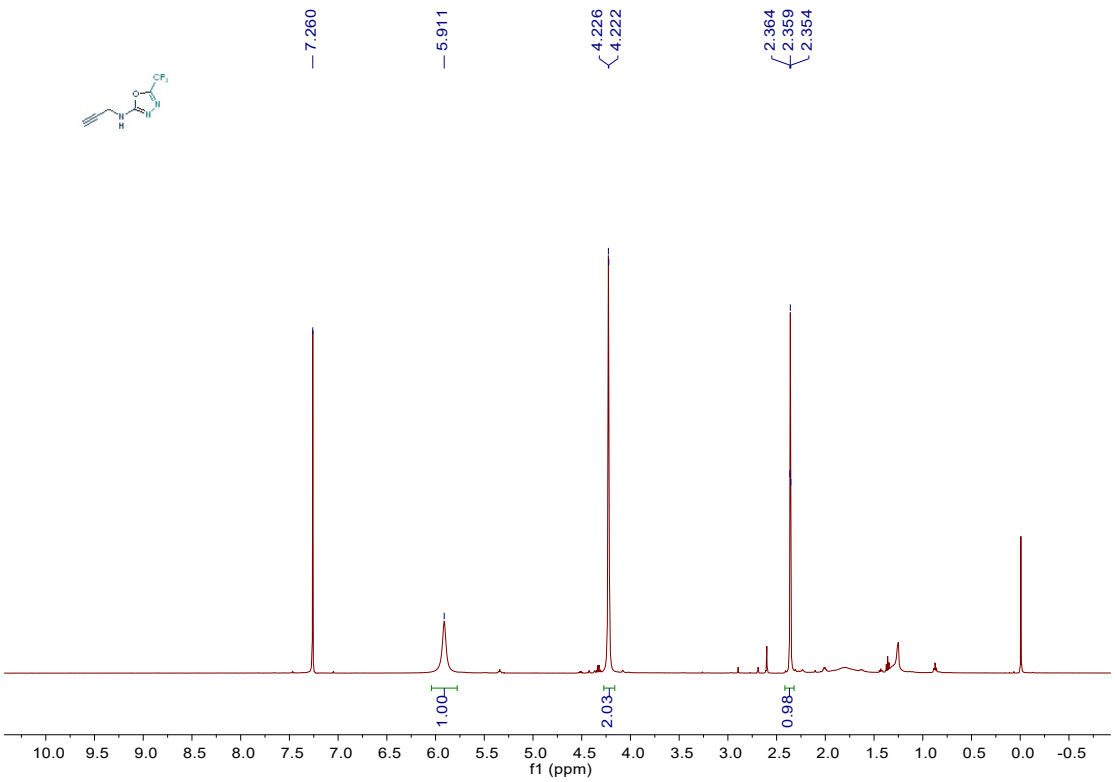
Supplementary Figure 40. ^{1}H NMR spectra of product **15**



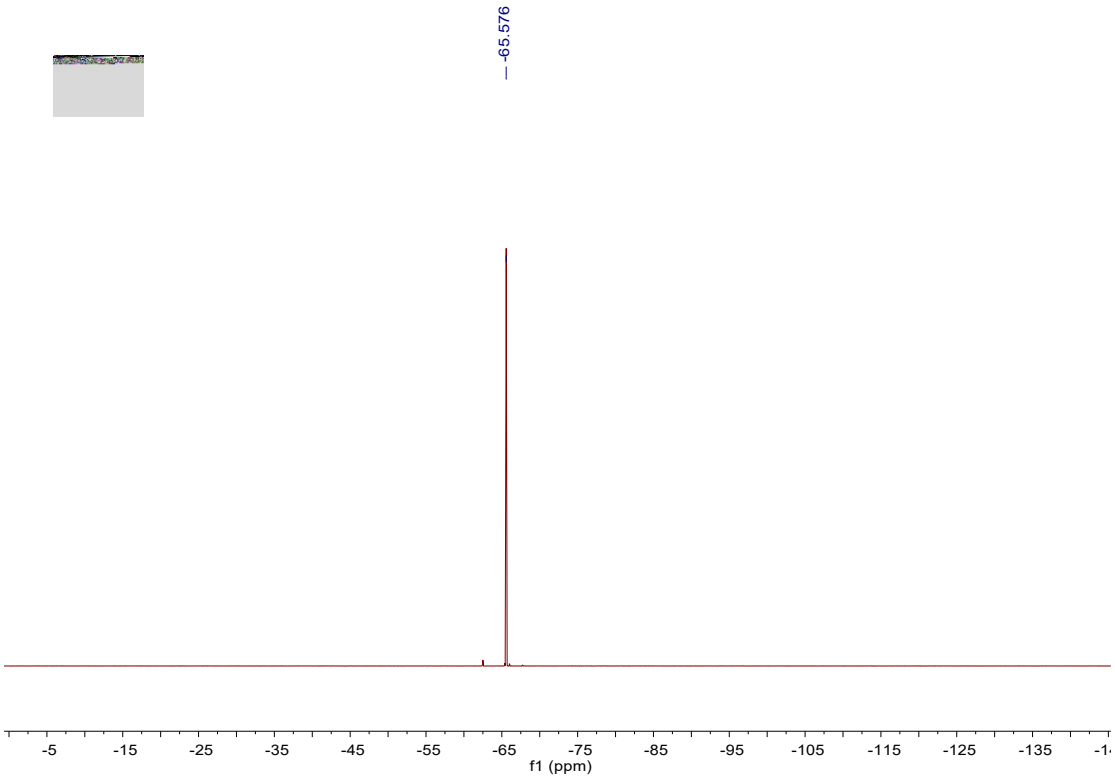
Supplementary Figure 41. ^{19}F NMR spectra of product **15**



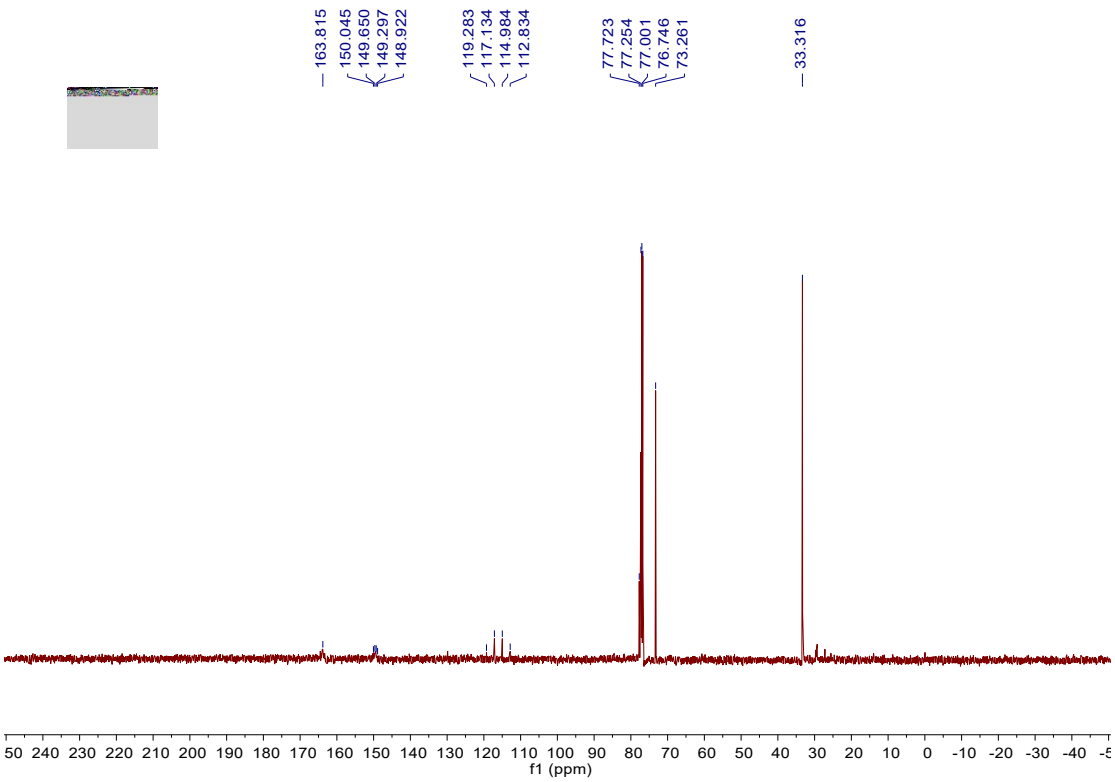
Supplementary Figure 42. ^{13}C NMR spectra of product **15**



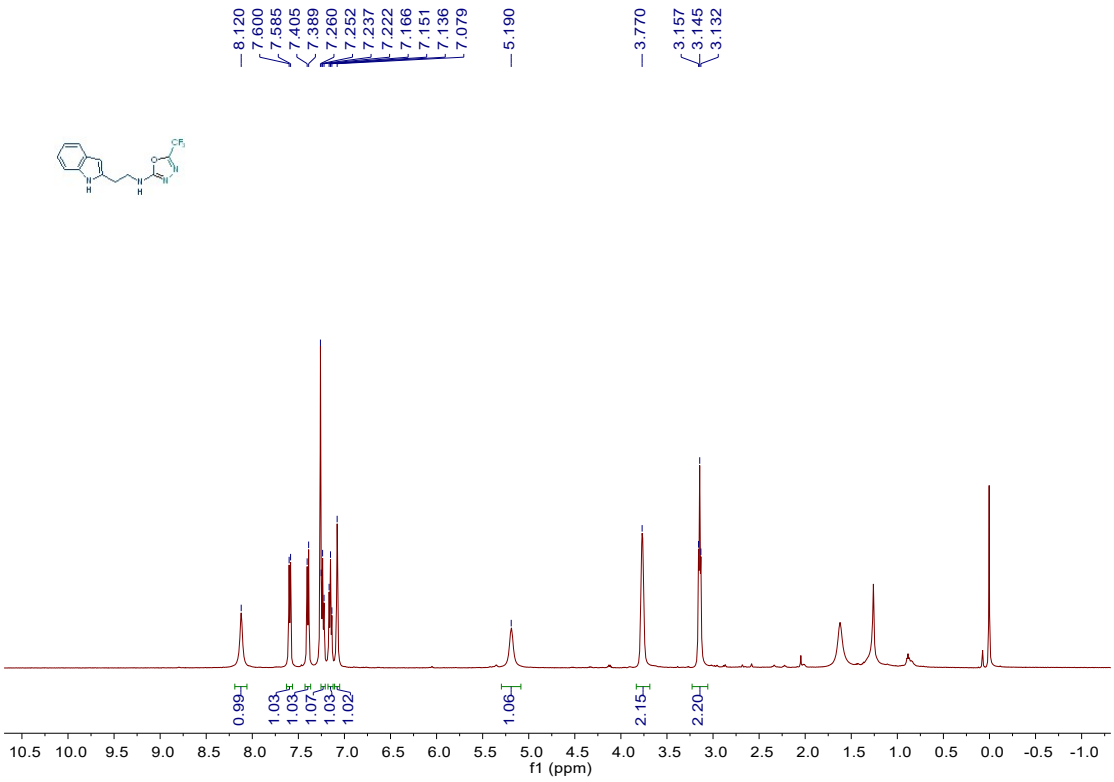
Supplementary Figure 43. ^{1}H NMR spectra of product **16**



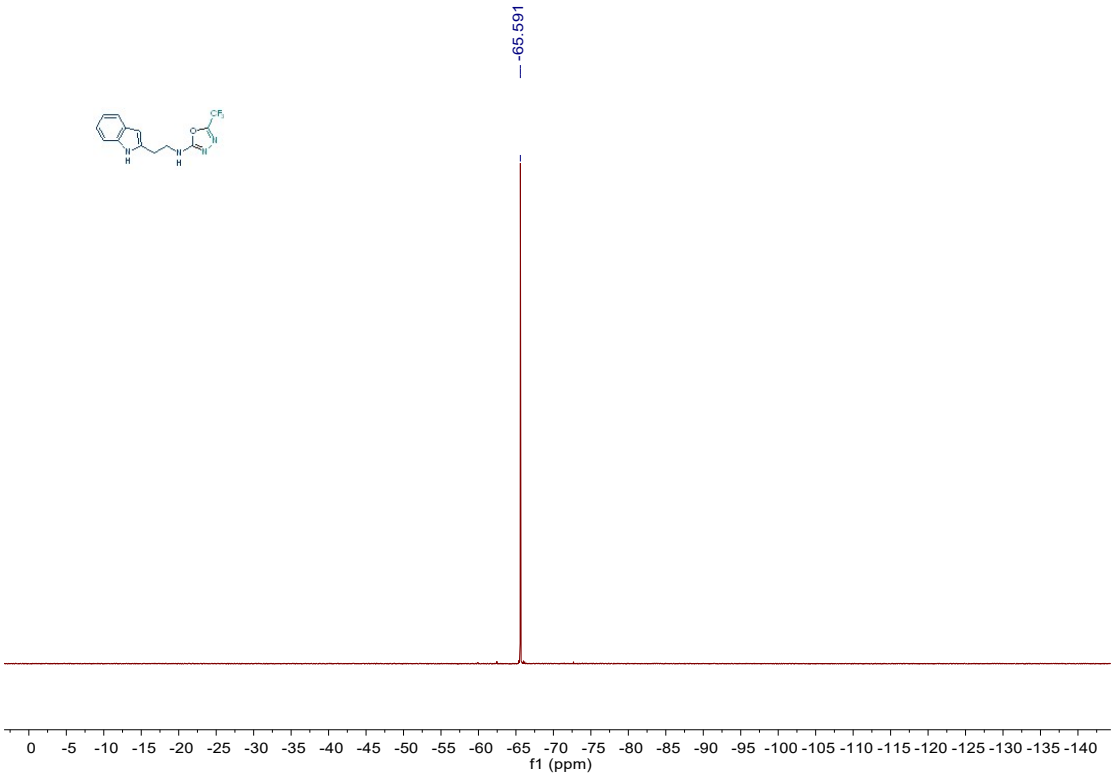
Supplementary Figure 44. ^{19}F NMR spectra of product **16**



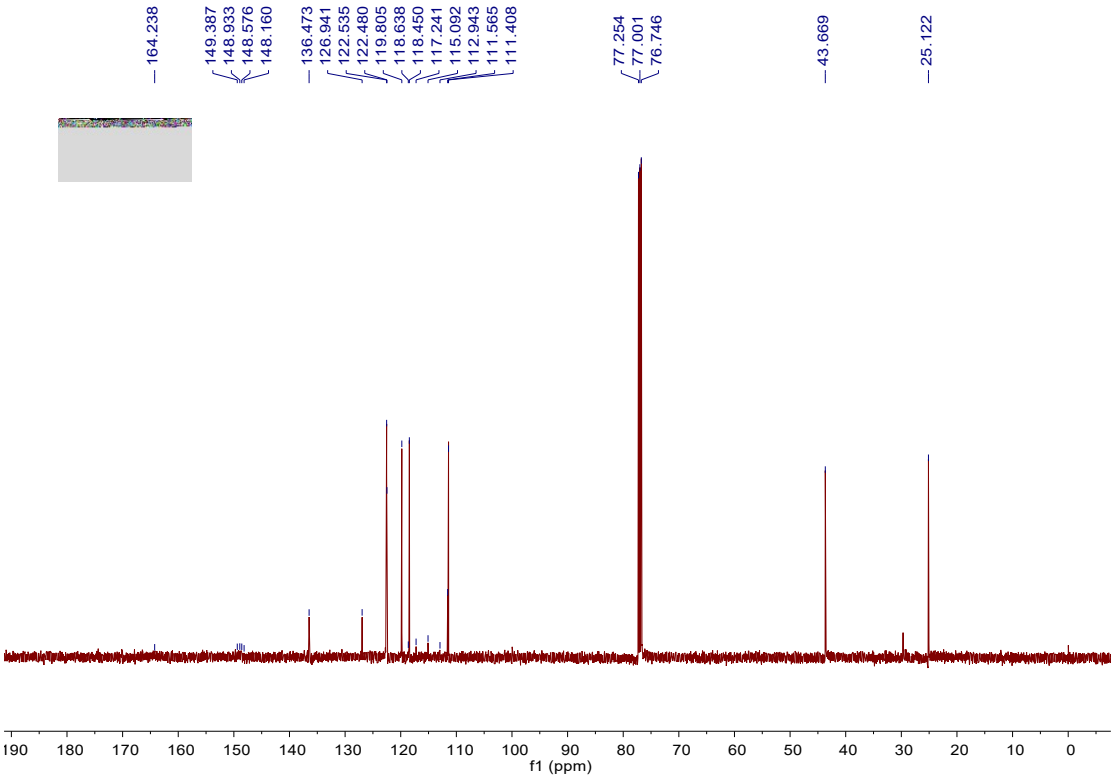
Supplementary Figure 45. ^{13}C NMR spectra of product **16**



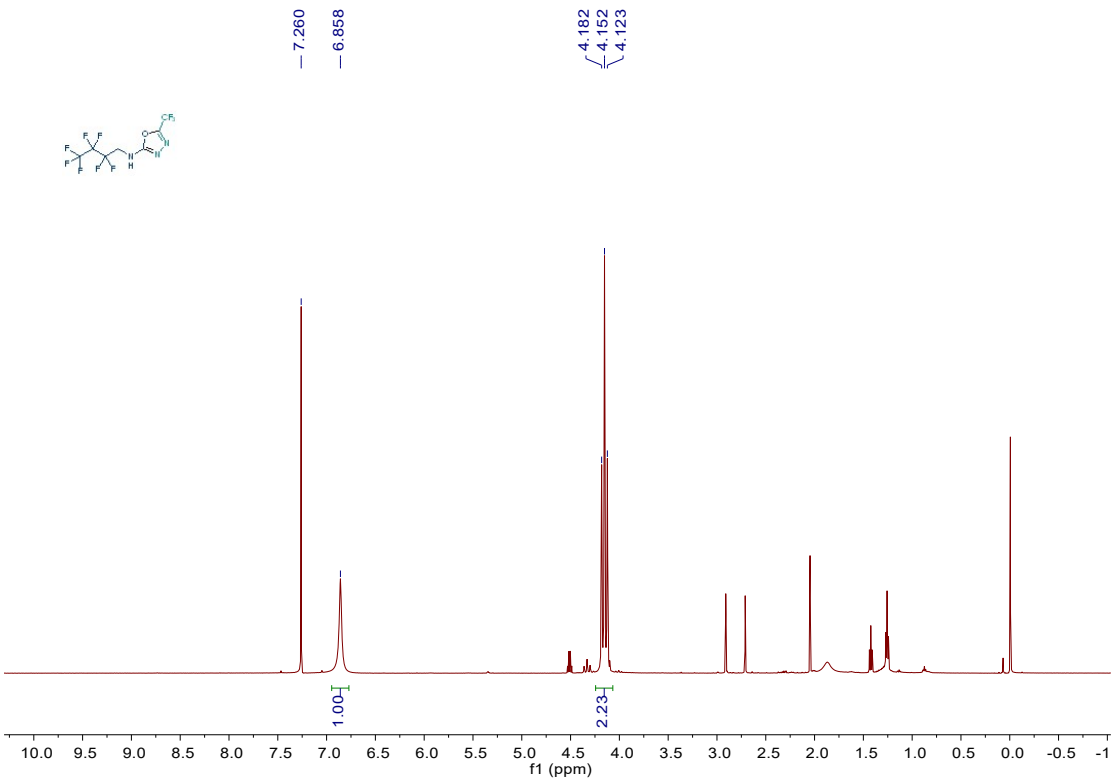
Supplementary Figure 46. ^{1}H NMR spectra of product **17**



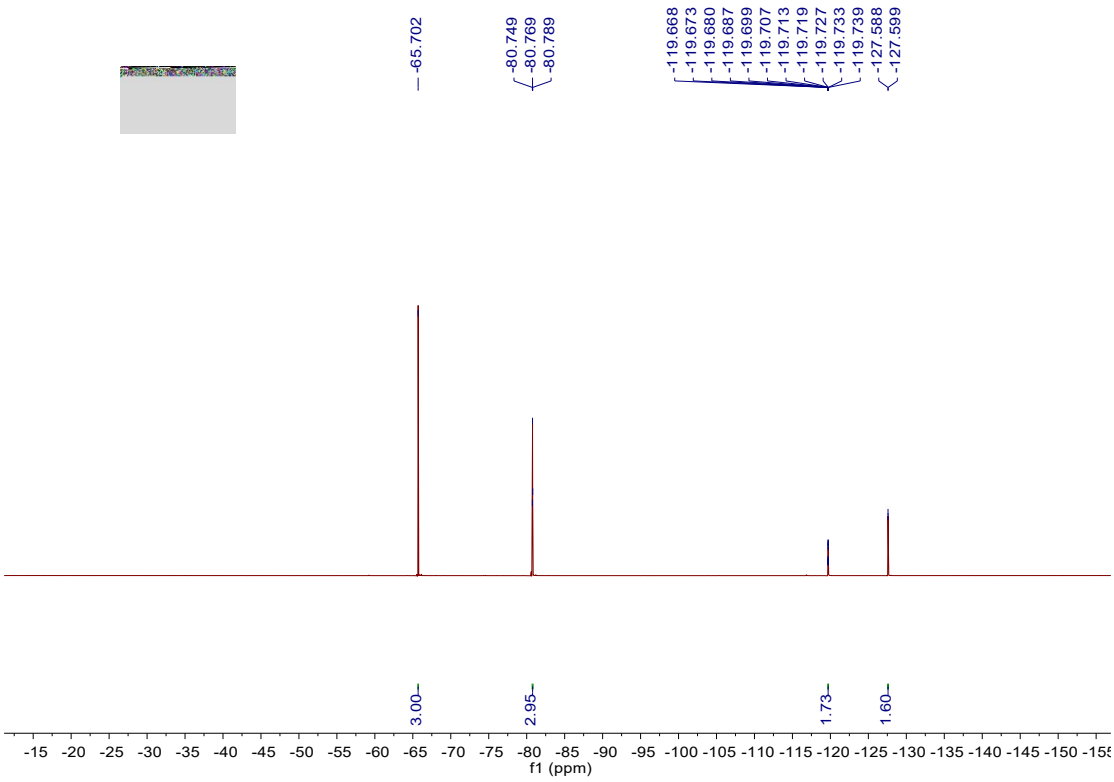
Supplementary Figure 47. ^{19}F NMR spectra of product **17**



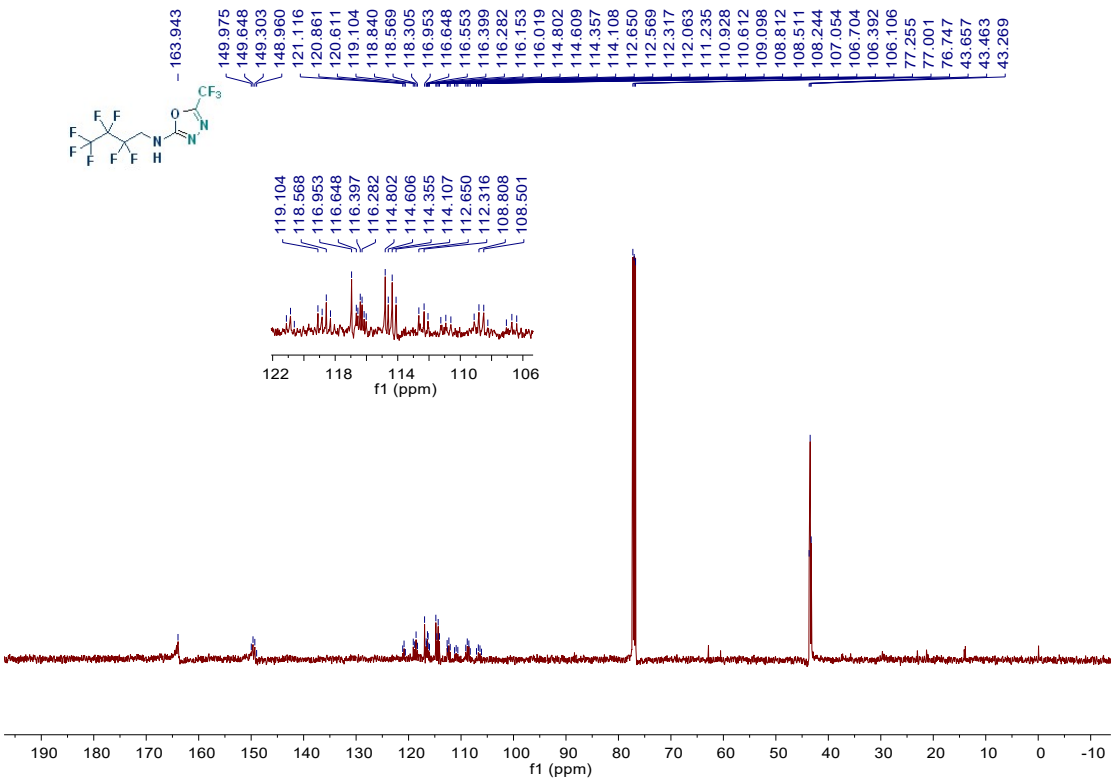
Supplementary Figure 48. ^{13}C NMR spectra of product **17**



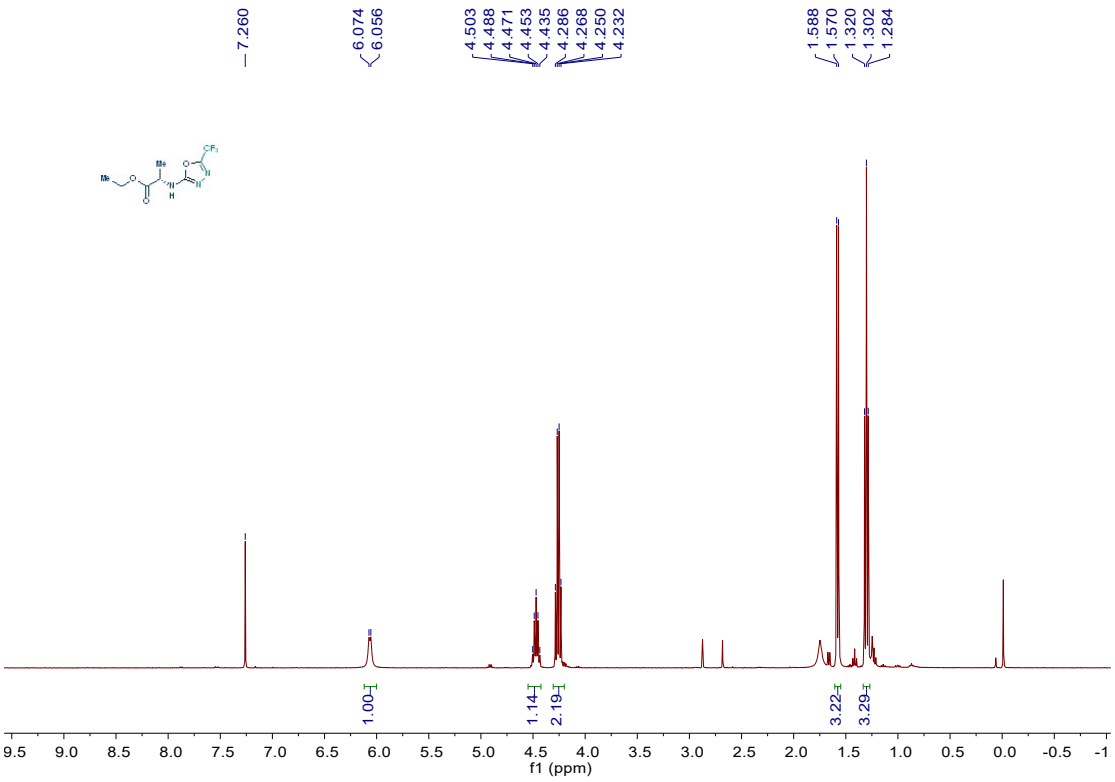
Supplementary Figure 49. ^{1}H NMR spectra of product **18**



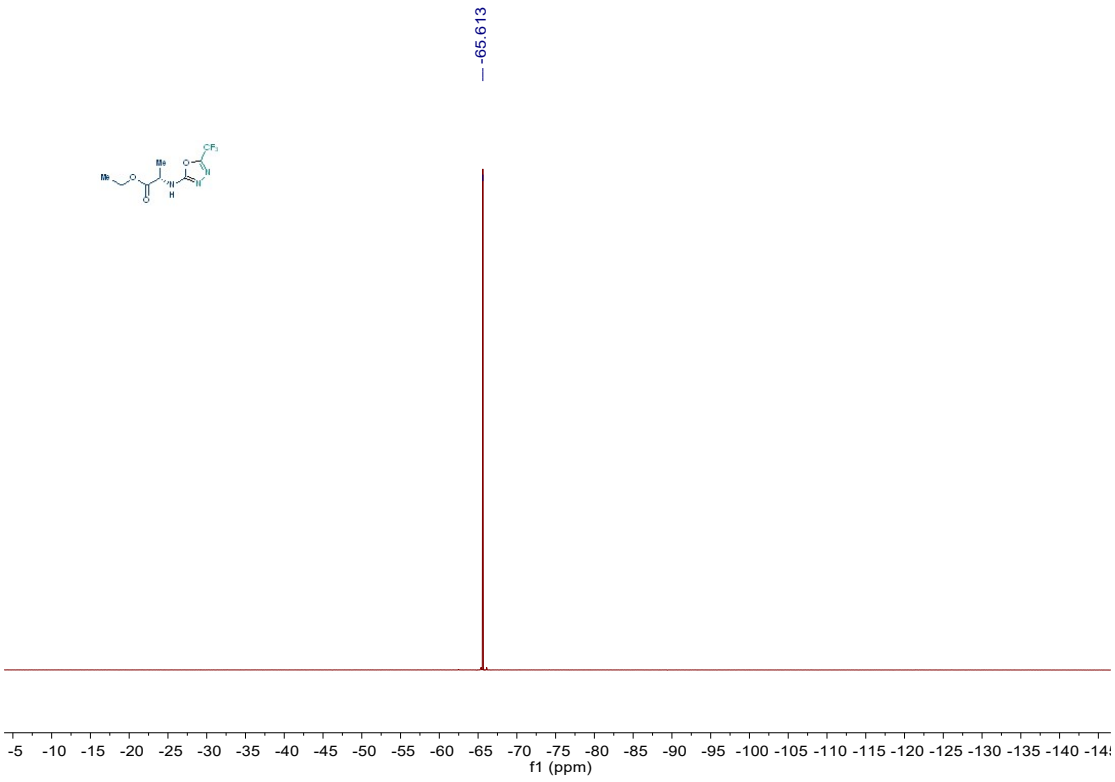
Supplementary Figure 50. ^{19}F NMR spectra of product **18**



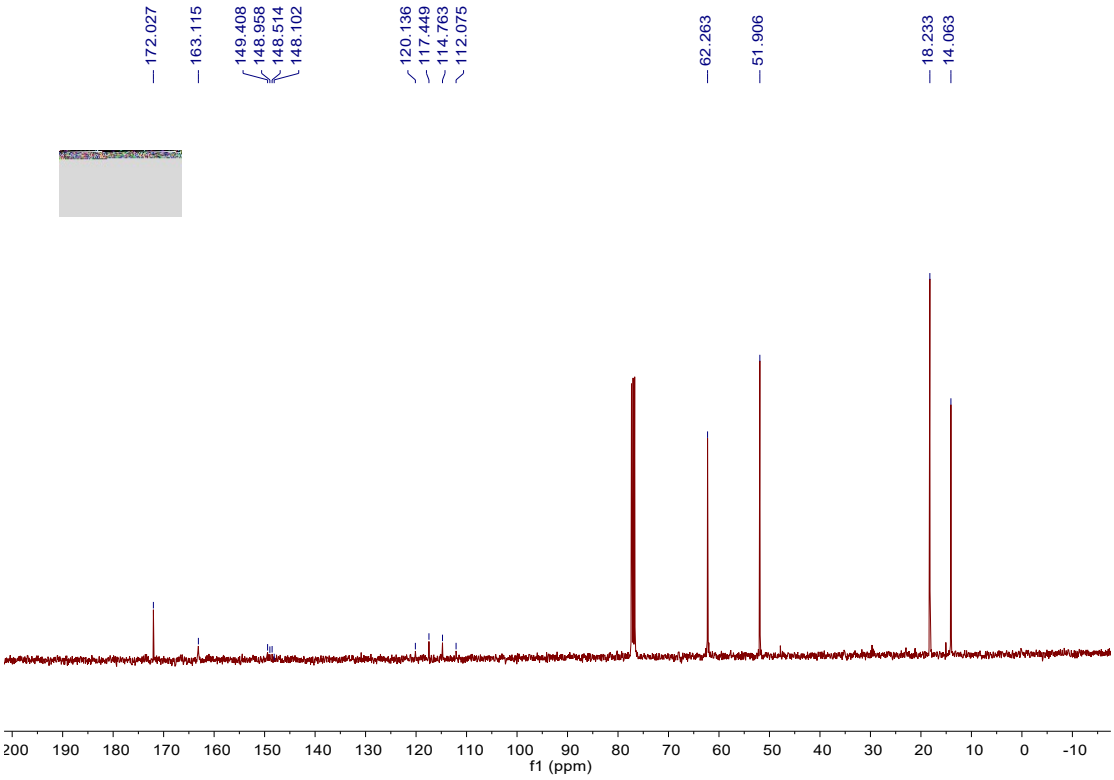
Supplementary Figure 51. ^{13}C NMR spectra of product **18**



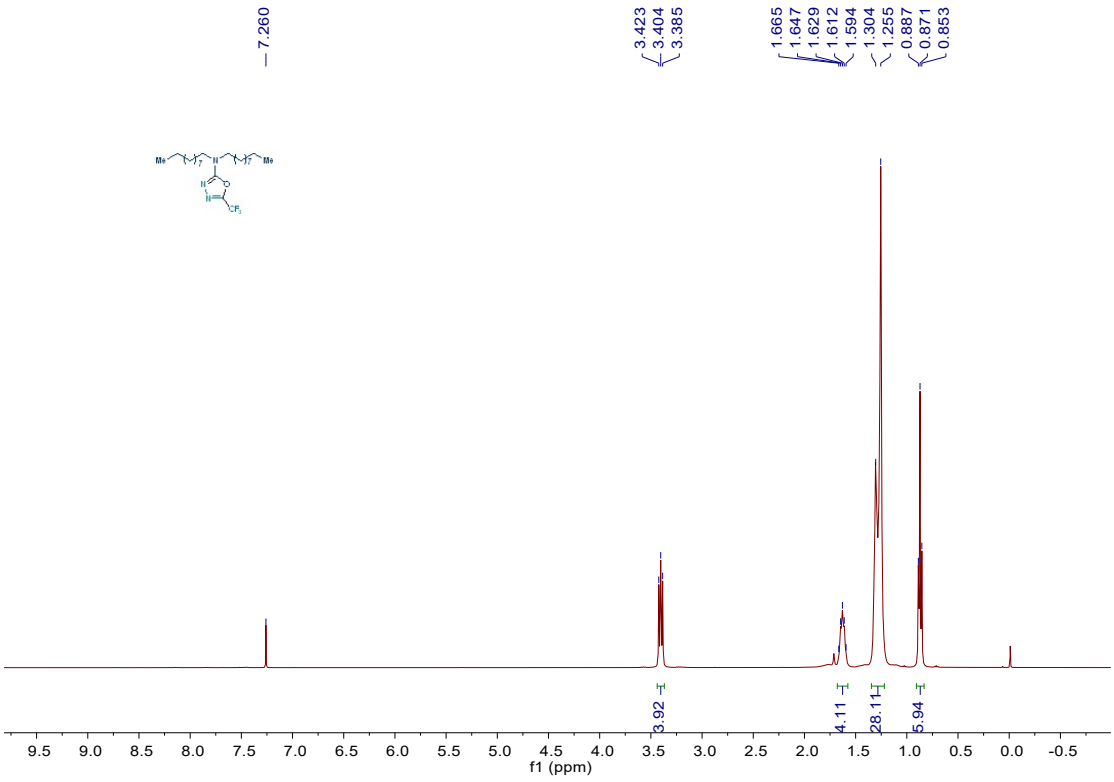
Supplementary Figure 52. ^{1}H NMR spectra of product **19**



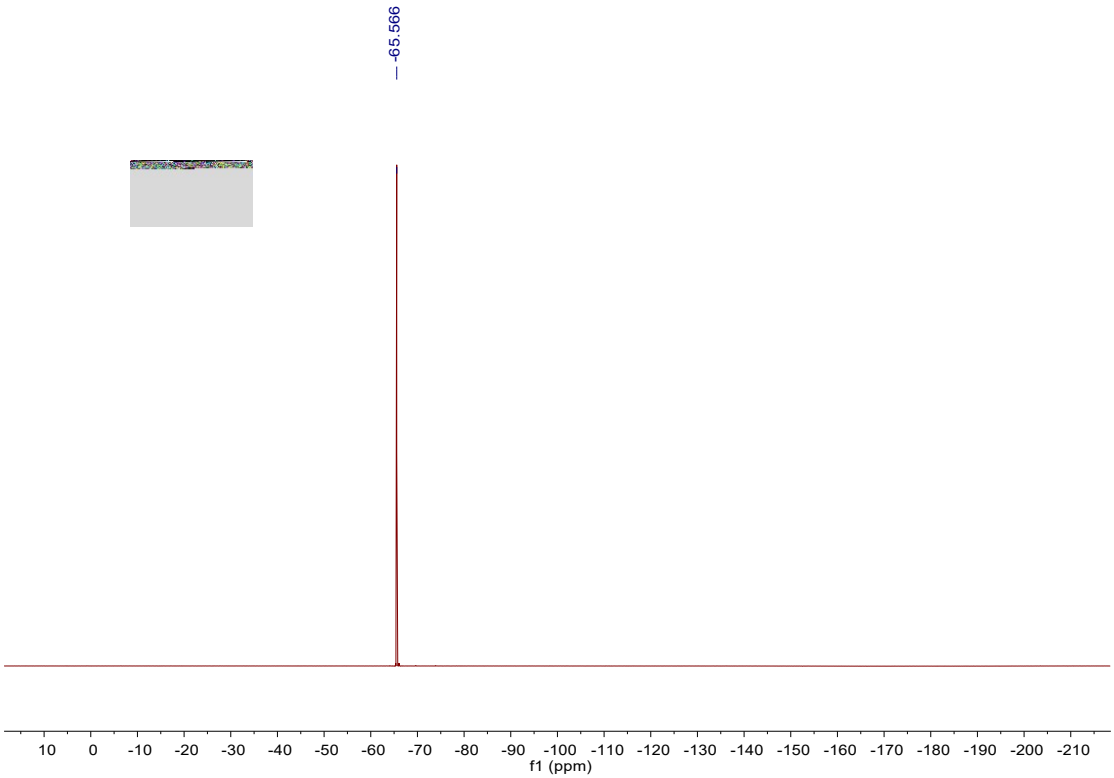
Supplementary Figure 53. ^{19}F NMR spectra of product **19**



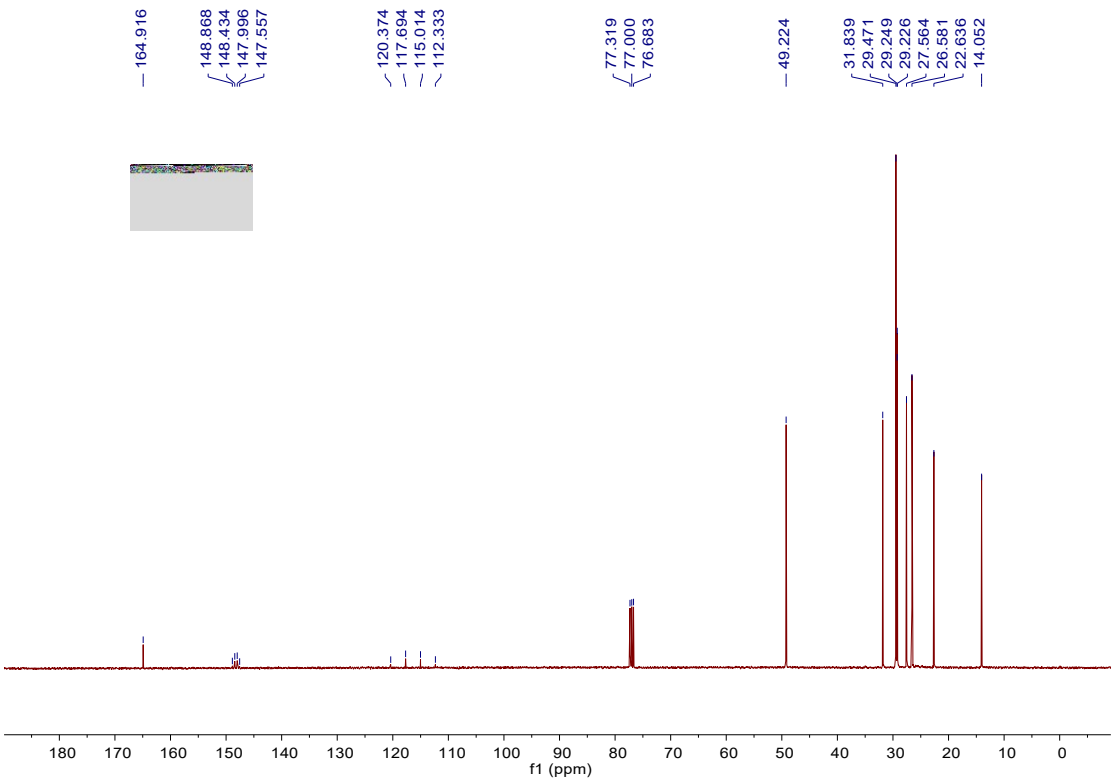
Supplementary Figure 54. ^{13}C NMR spectra of product **19**



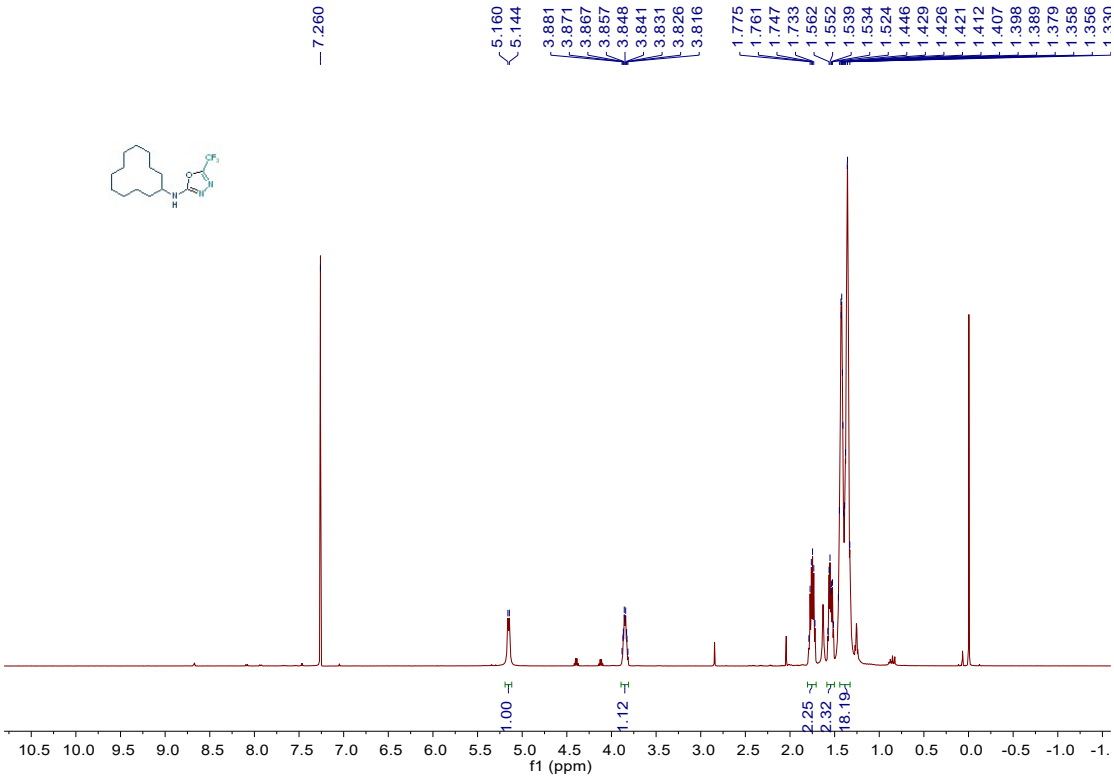
Supplementary Figure 55. ^{1}H NMR spectra of product **20**



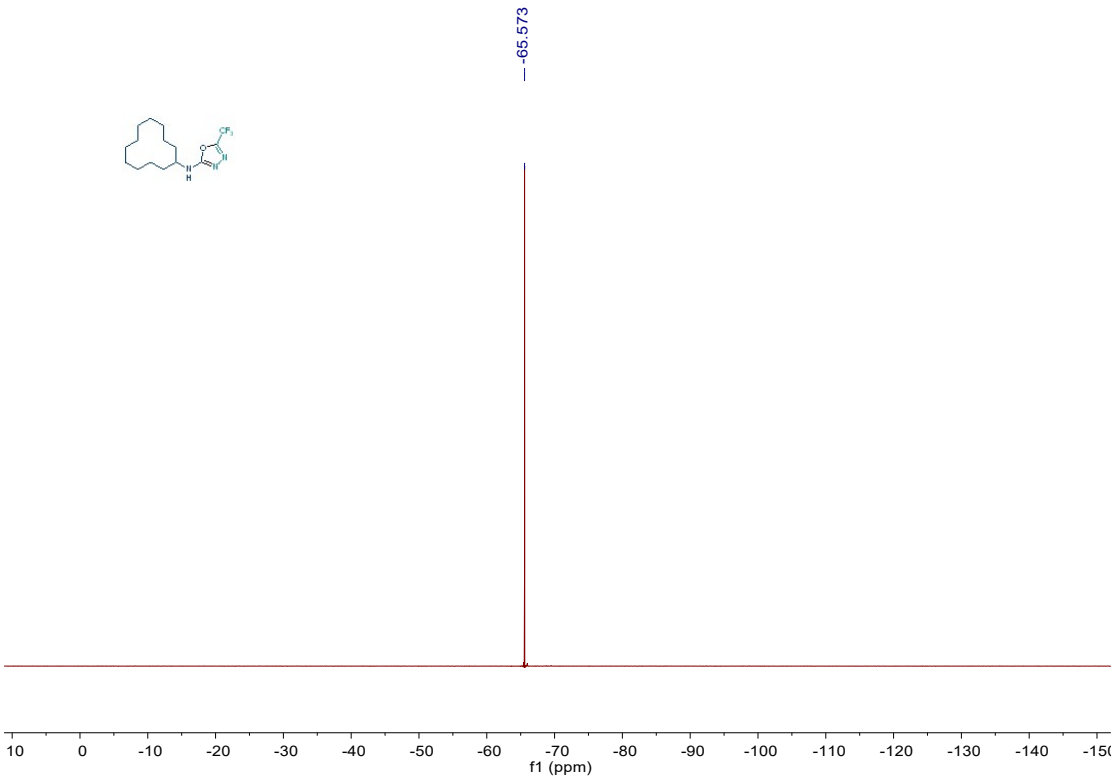
Supplementary Figure 56. ^{19}F NMR spectra of product **20**



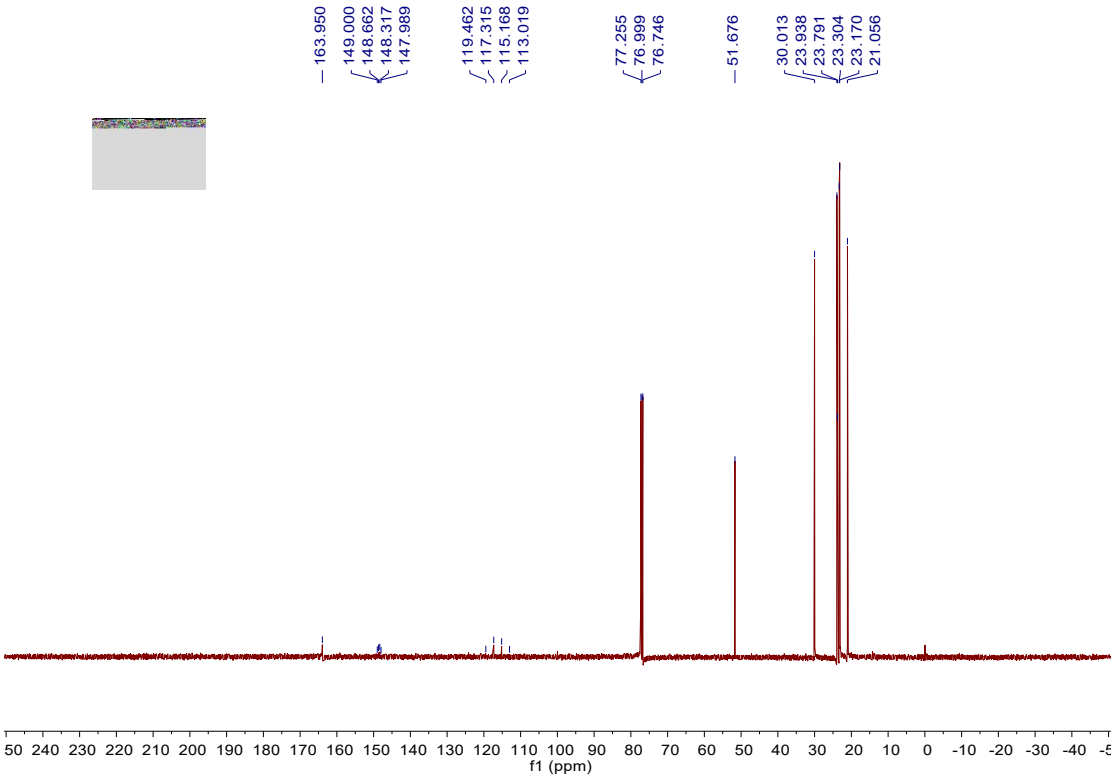
Supplementary Figure 57. ^{13}C NMR spectra of product **20**



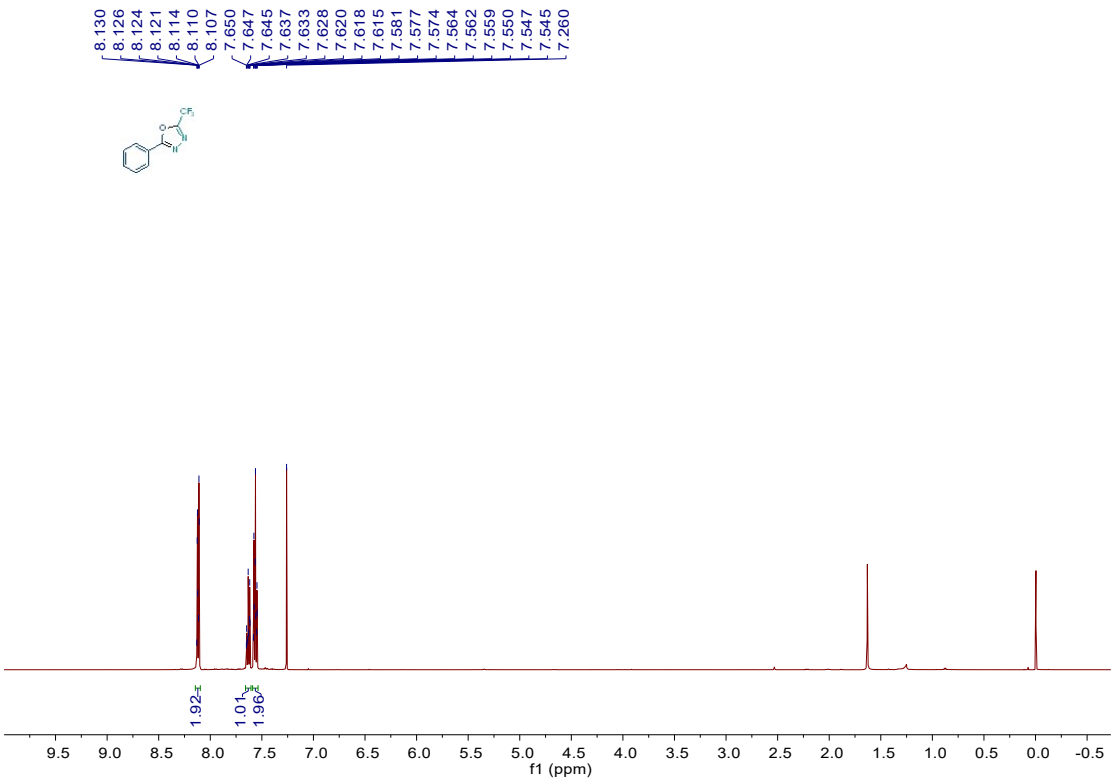
Supplementary Figure 58. ^{1}H NMR spectra of product **21**



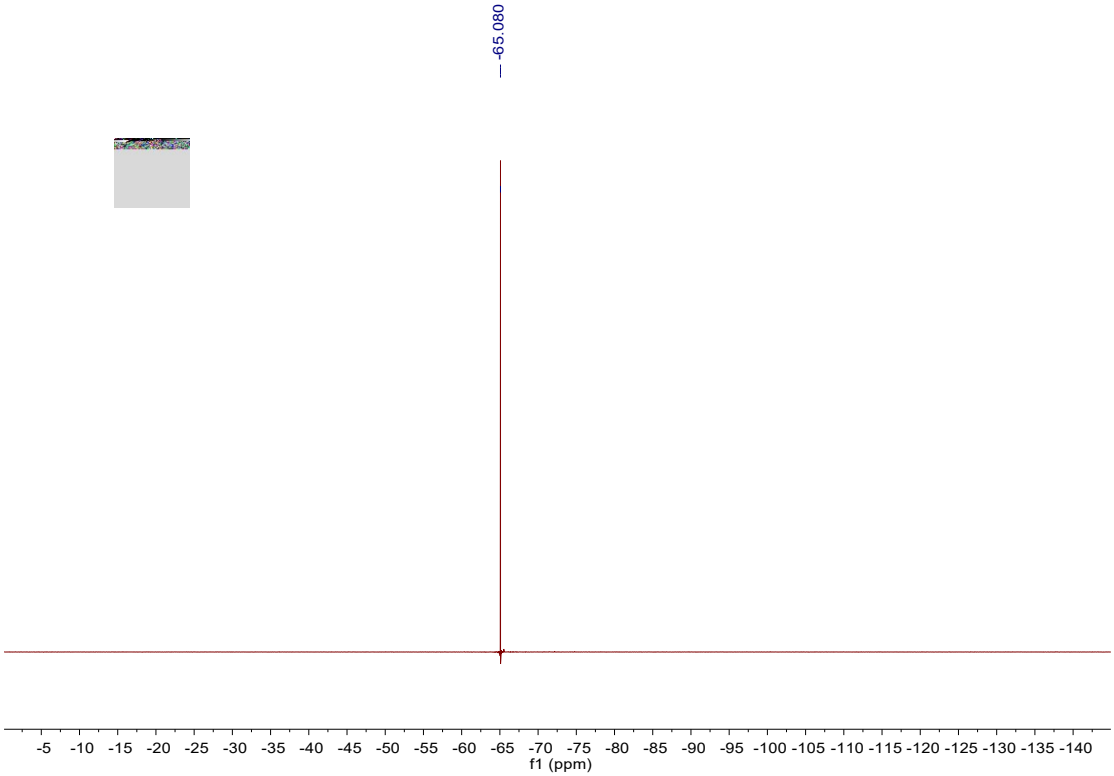
Supplementary Figure 59. ^{19}F NMR spectra of product **21**



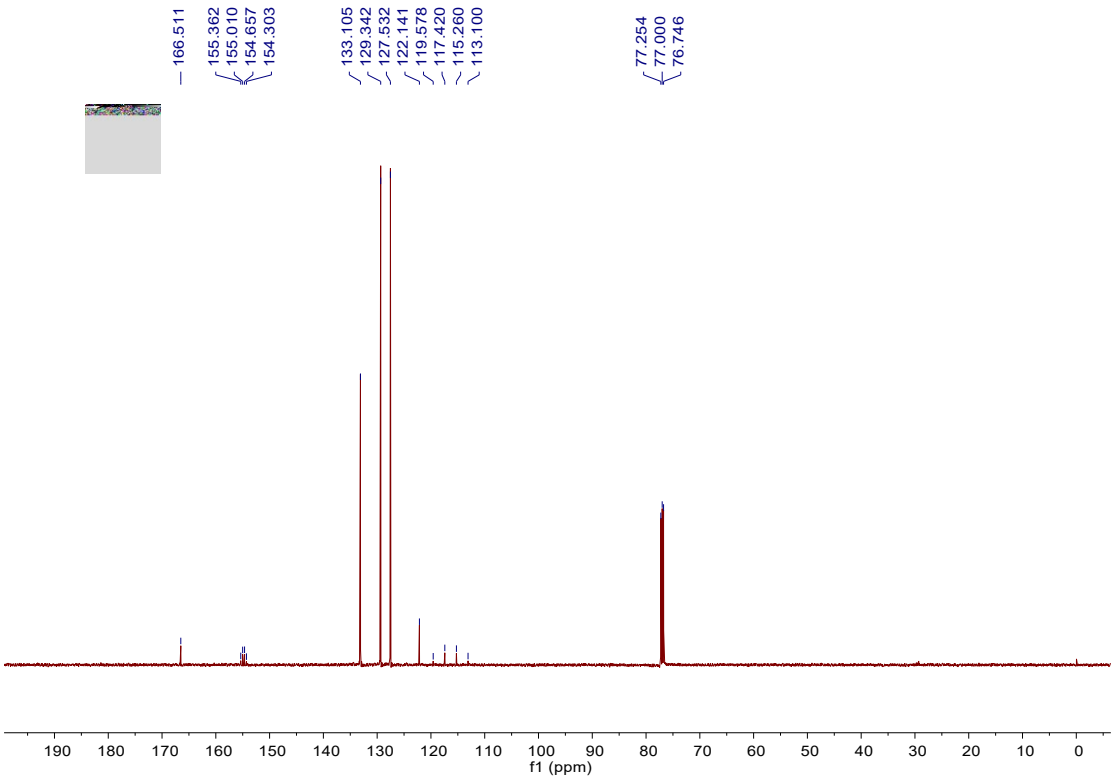
Supplementary Figure 60. ^{13}C NMR spectra of product **21**



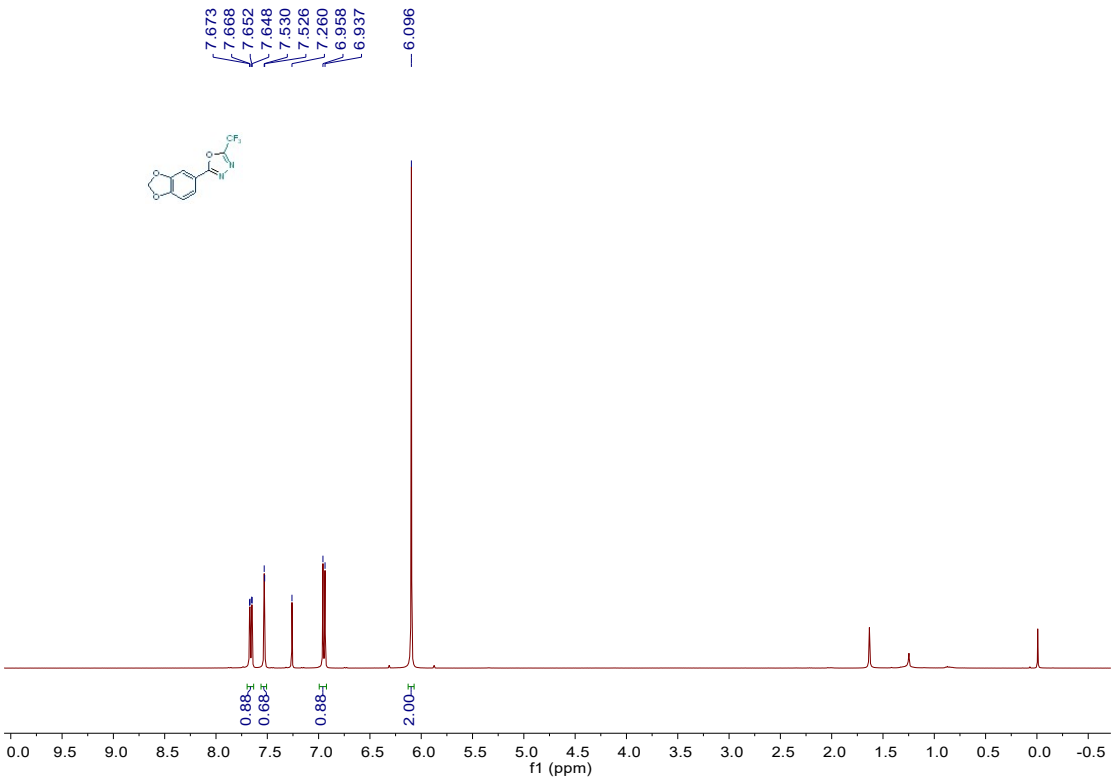
Supplementary Figure 61. ^{1}H NMR spectra of product **22**



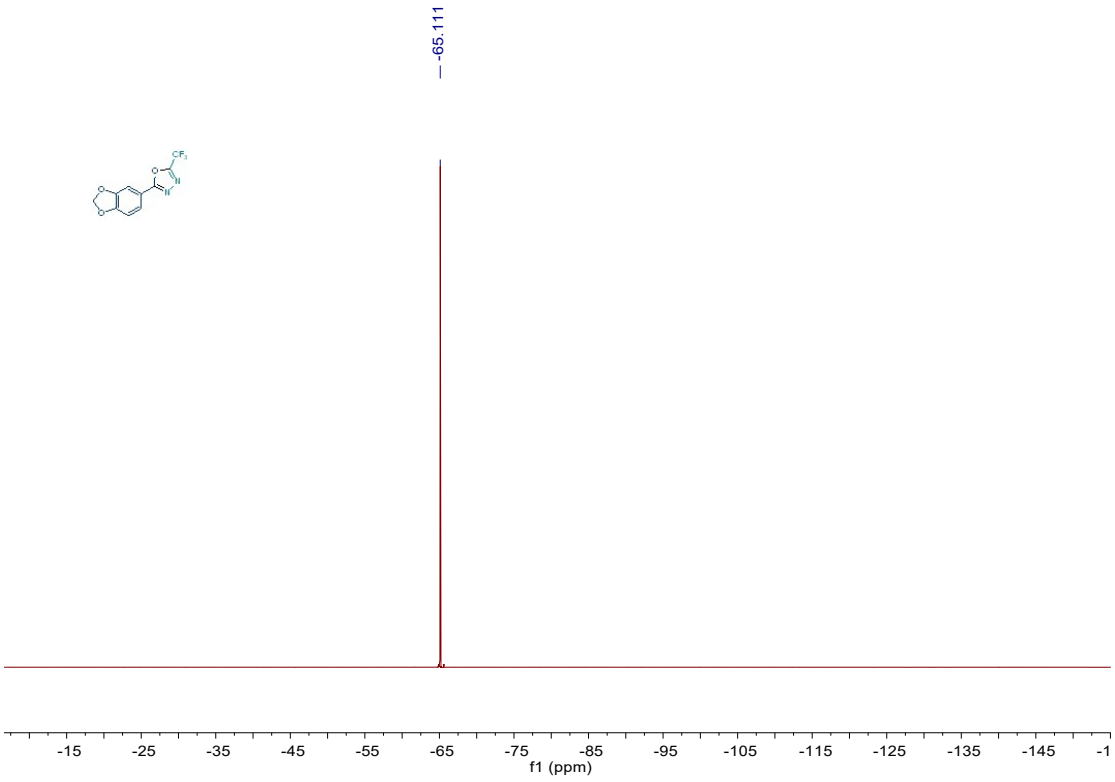
Supplementary Figure 62. ^{19}F NMR spectra of product **22**



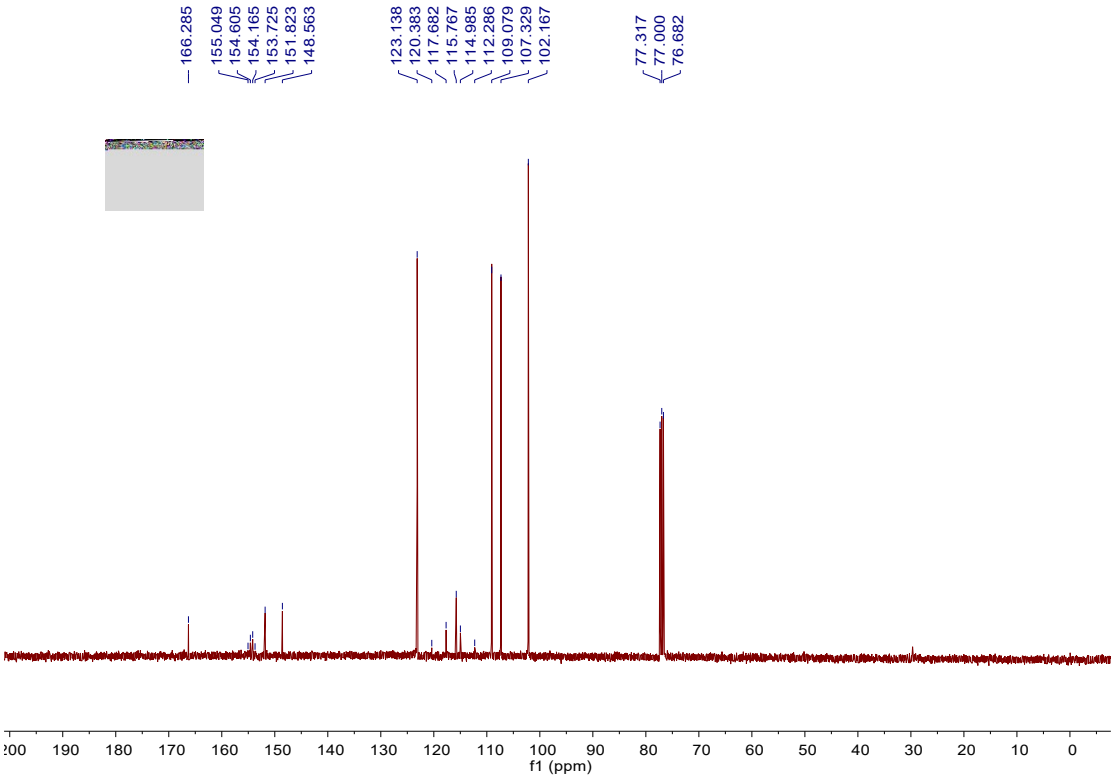
Supplementary Figure 63. ^{13}C NMR spectra of product **22**



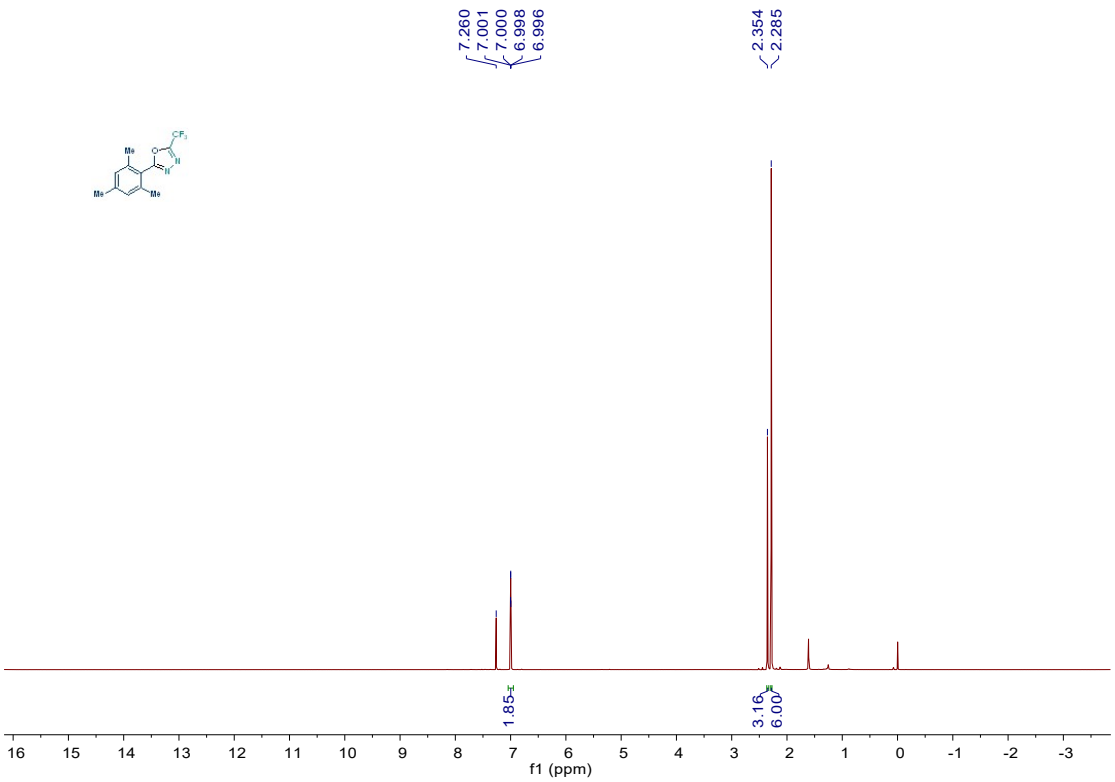
Supplementary Figure 64. ^{1}H NMR spectra of product **23**



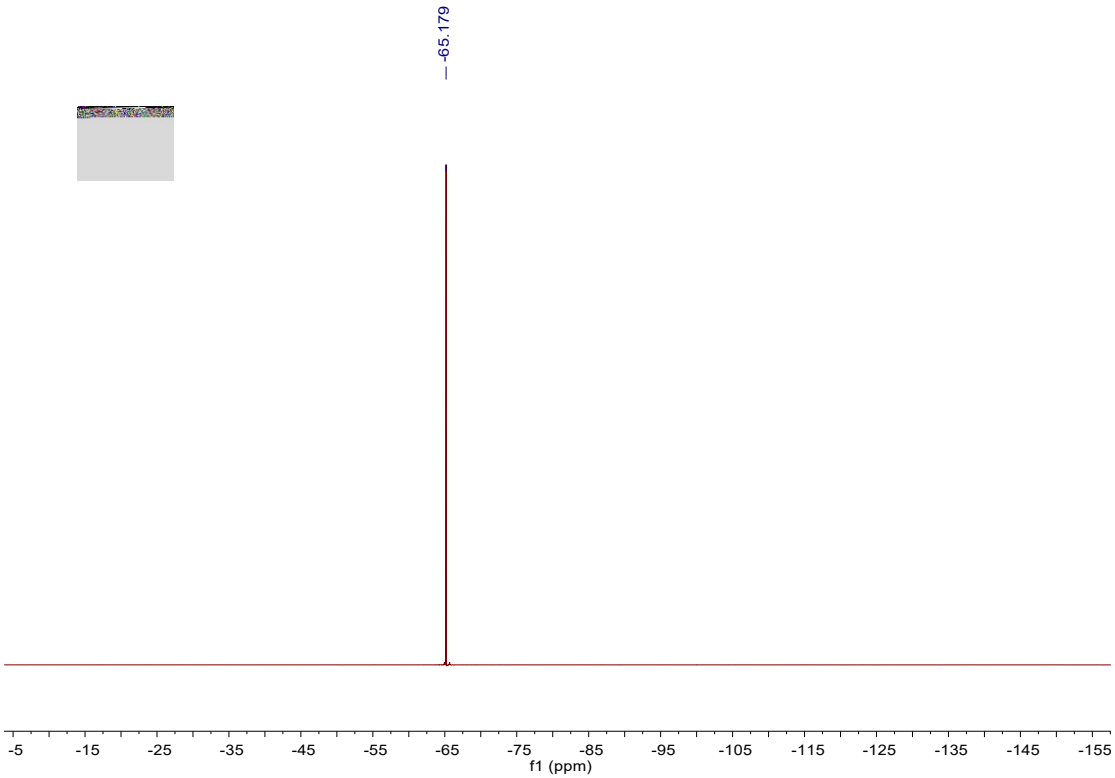
Supplementary Figure 65. ^{19}F NMR spectra of product **23**



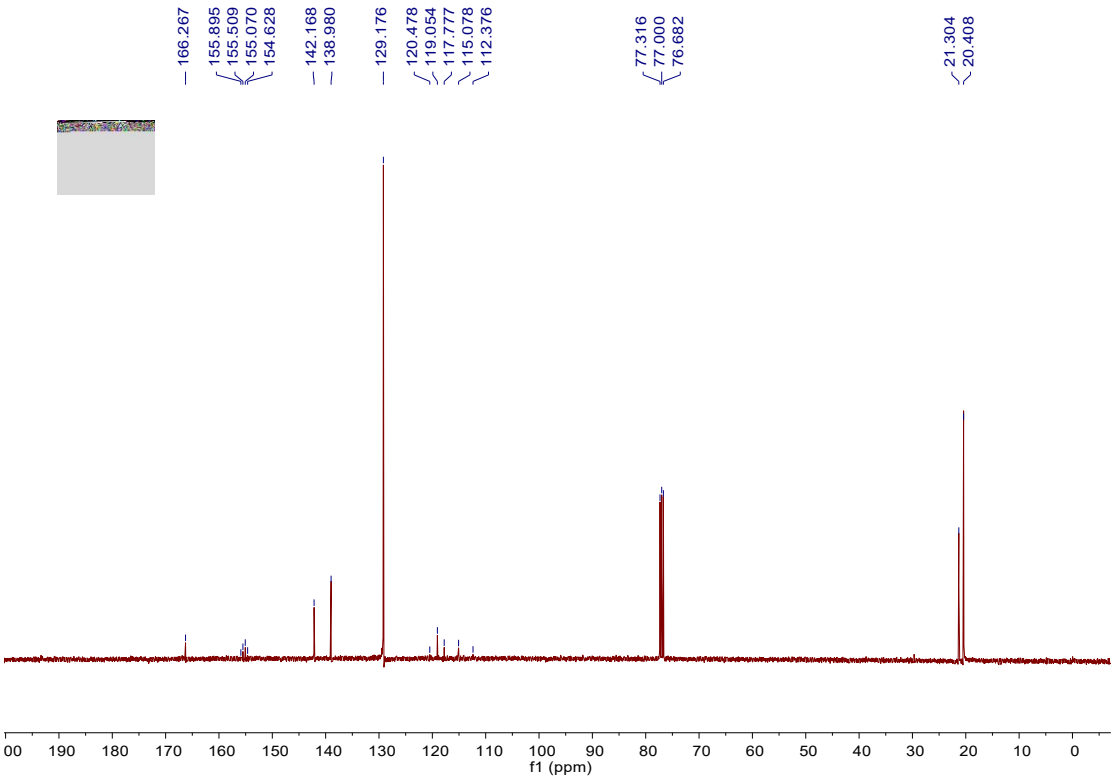
Supplementary Figure 66. ^{13}C NMR spectra of product **23**



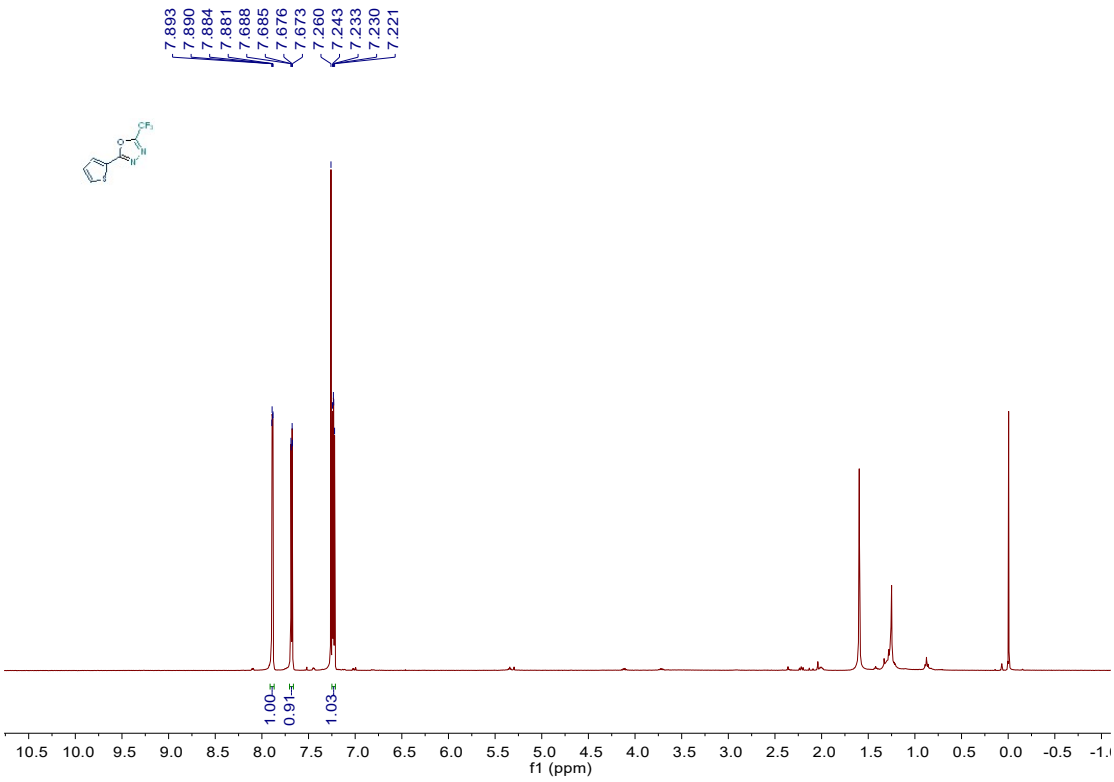
Supplementary Figure 67. ^{1}H NMR spectra of product **24**



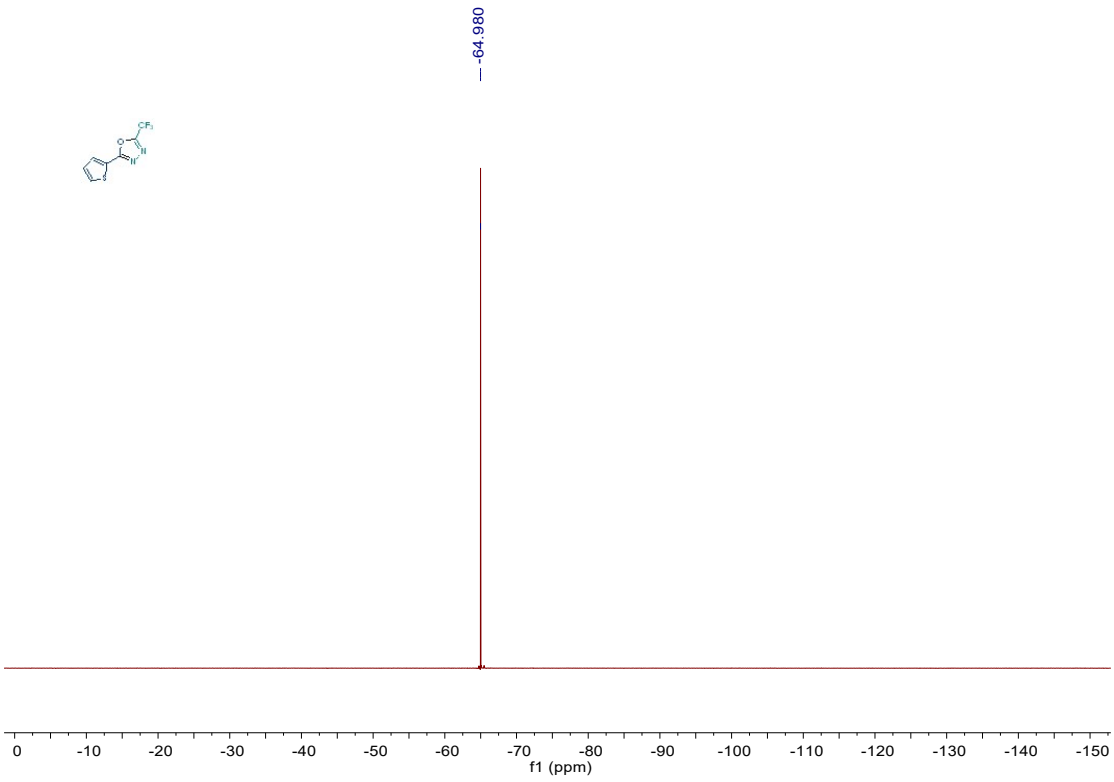
Supplementary Figure 68. ^{19}F NMR spectra of product **24**



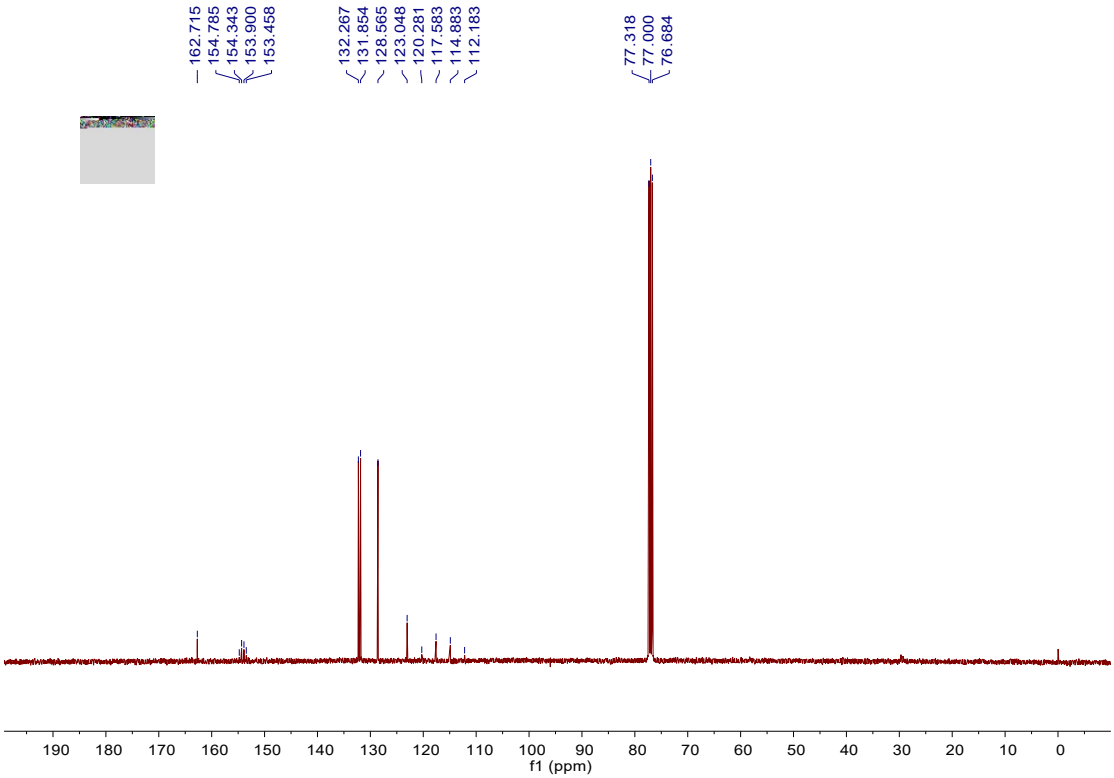
Supplementary Figure 69. ^{13}C NMR spectra of product **24**



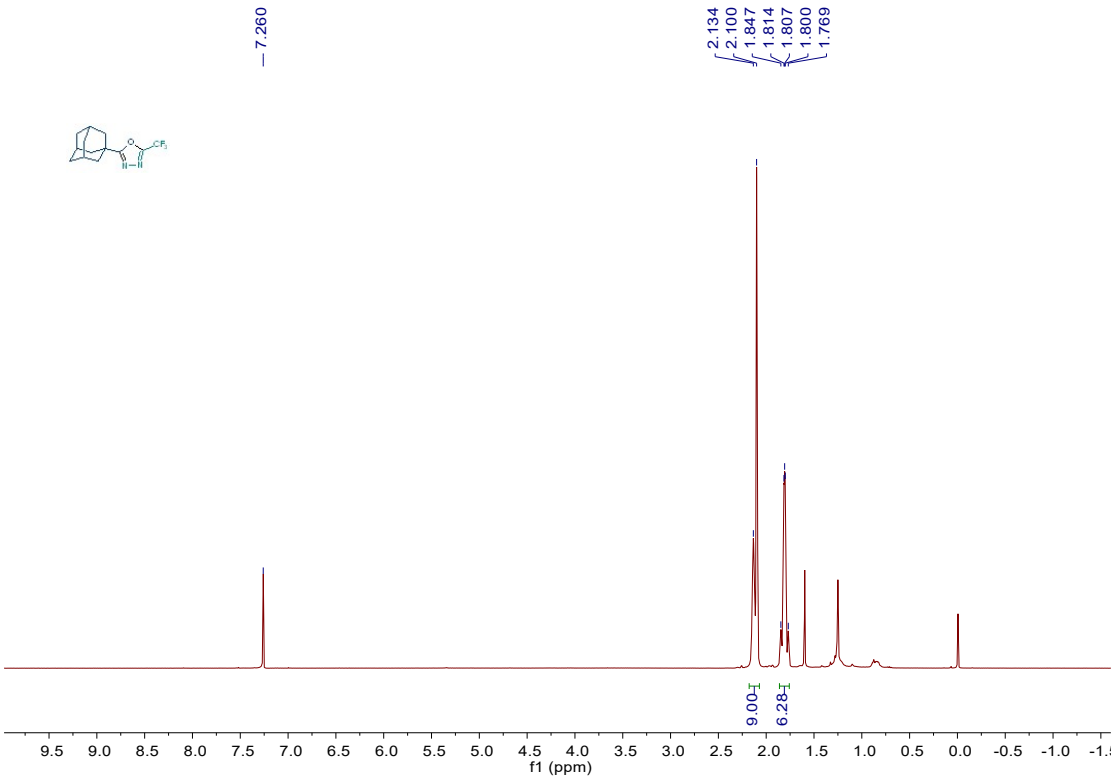
Supplementary Figure 70. ^{1}H NMR spectra of product **25**



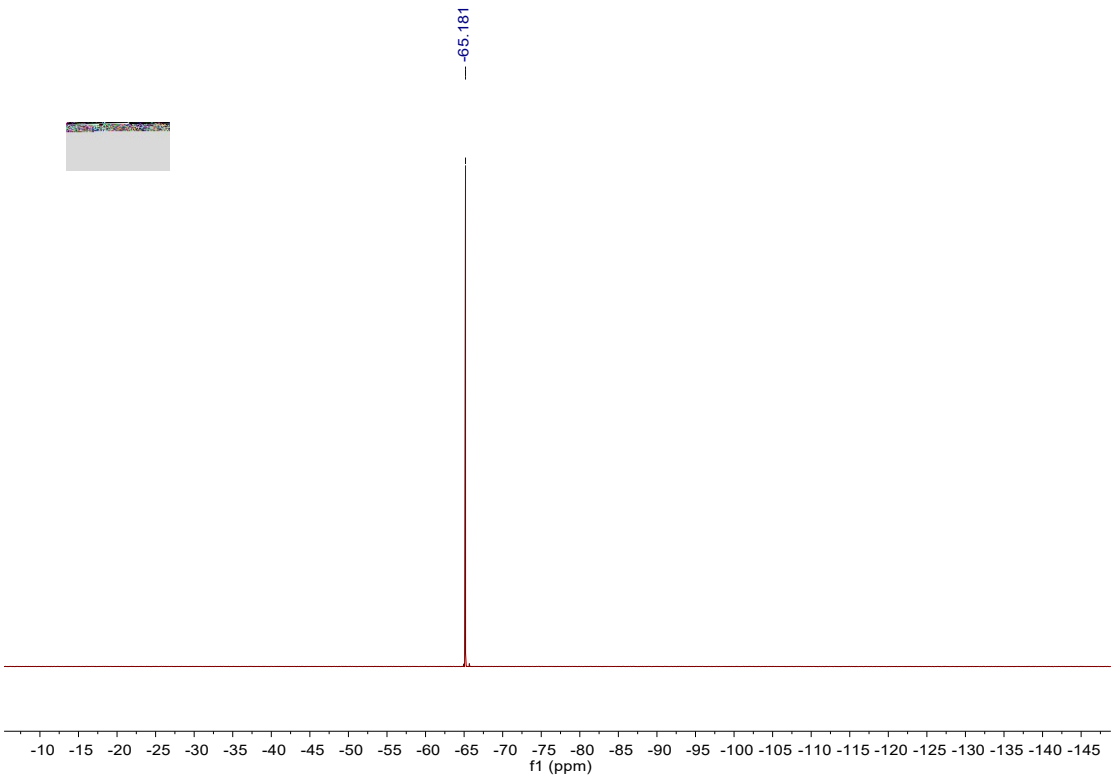
Supplementary Figure 71. ^{19}F NMR spectra of product **25**



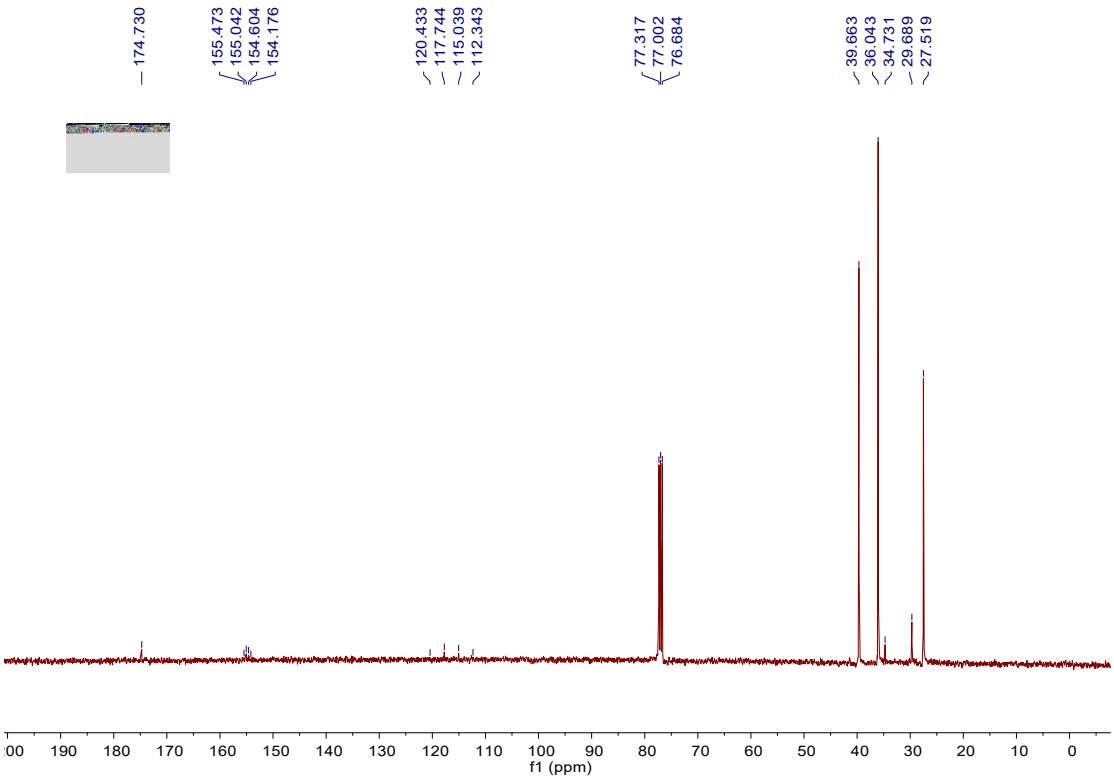
Supplementary Figure 72. ^{13}C NMR spectra of product **25**



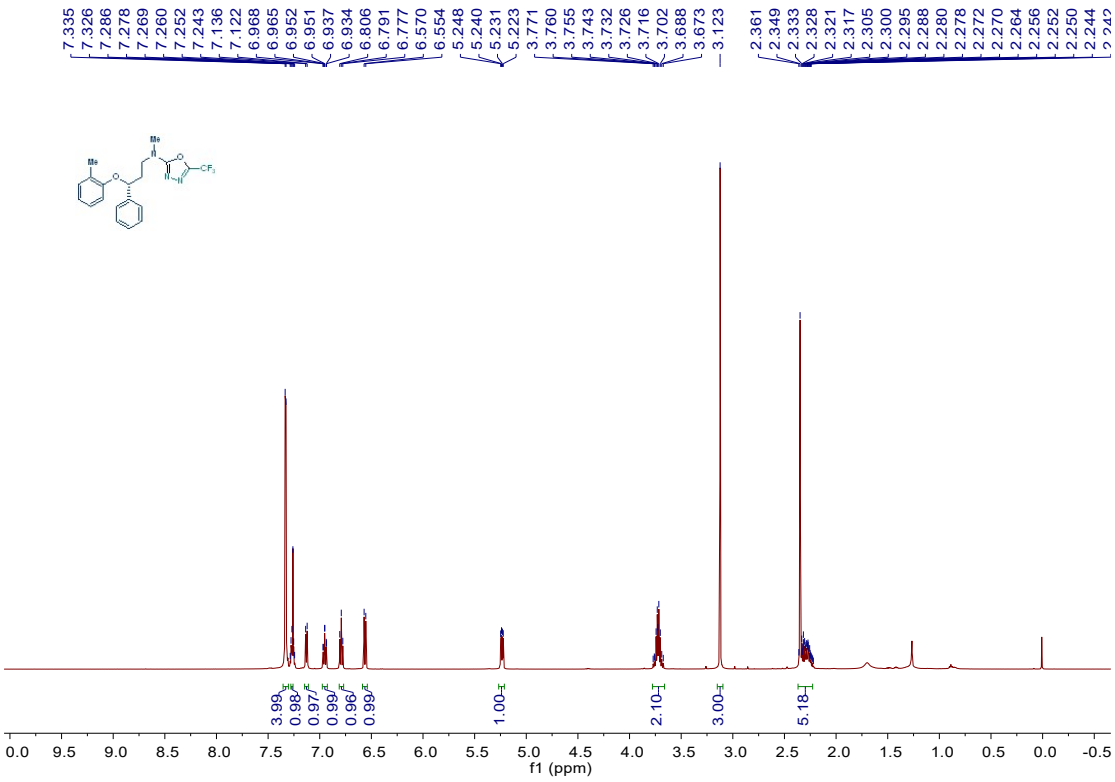
Supplementary Figure 73. ^{1}H NMR spectra of product **26**



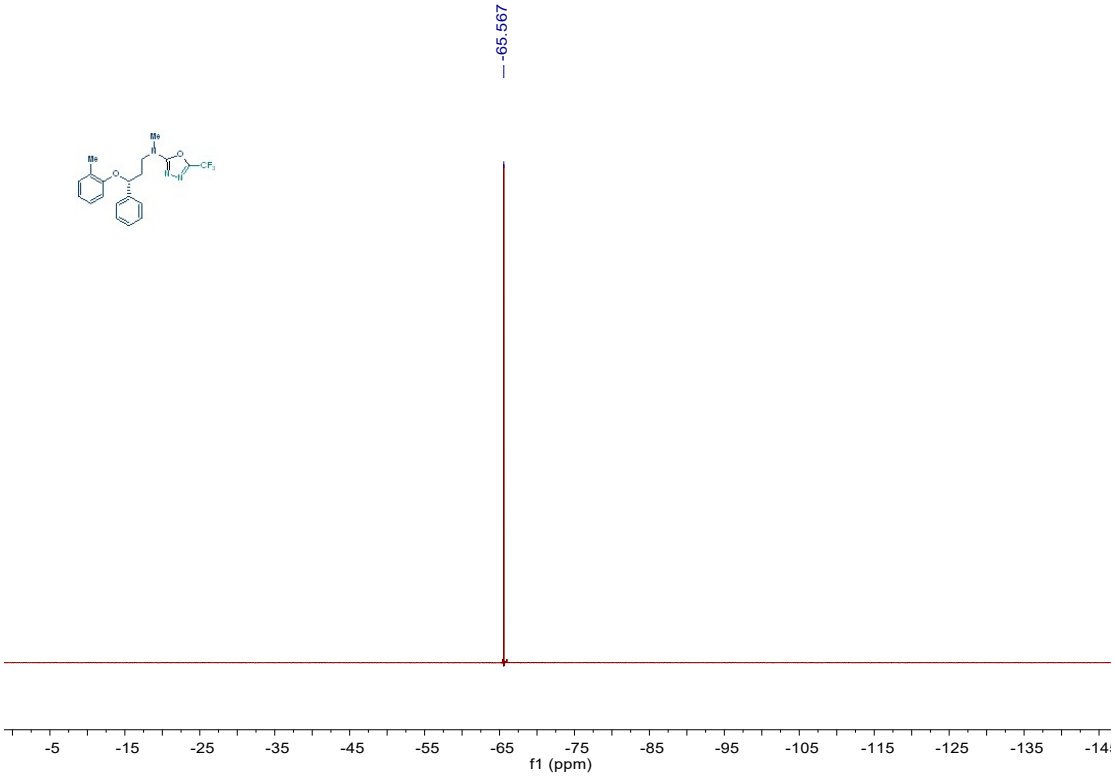
Supplementary Figure 74. ^{19}F NMR spectra of product **26**



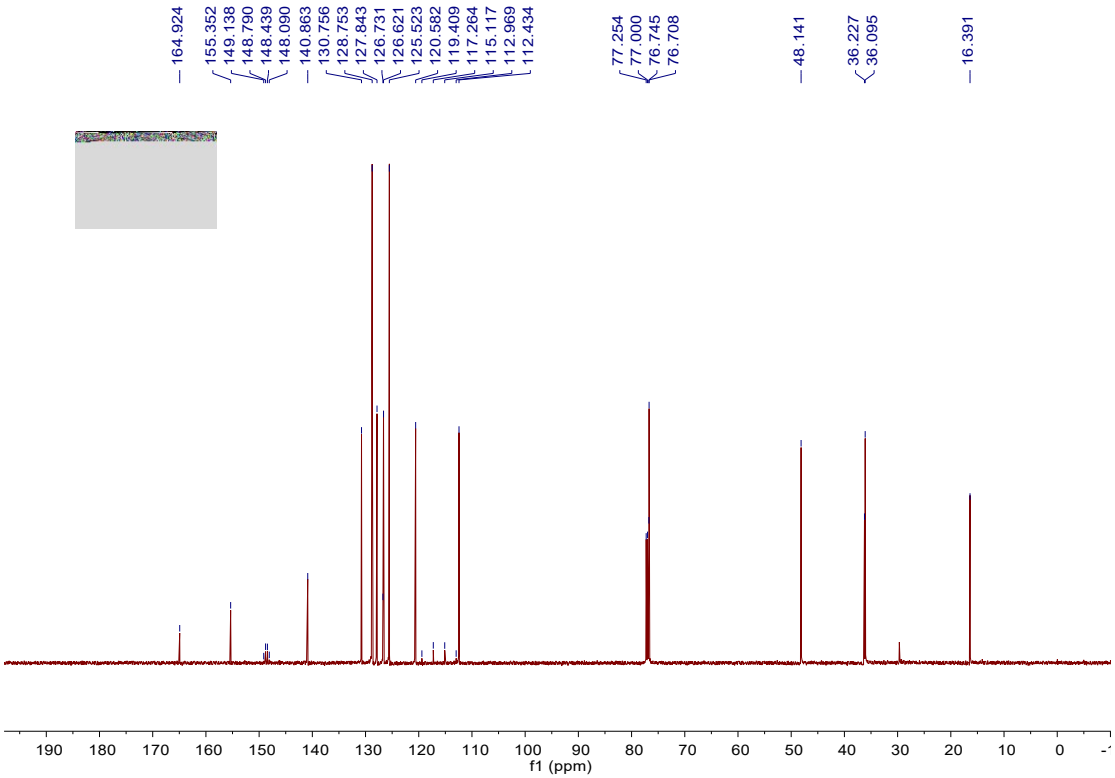
Supplementary Figure 75. ^{13}C NMR spectra of product **26**



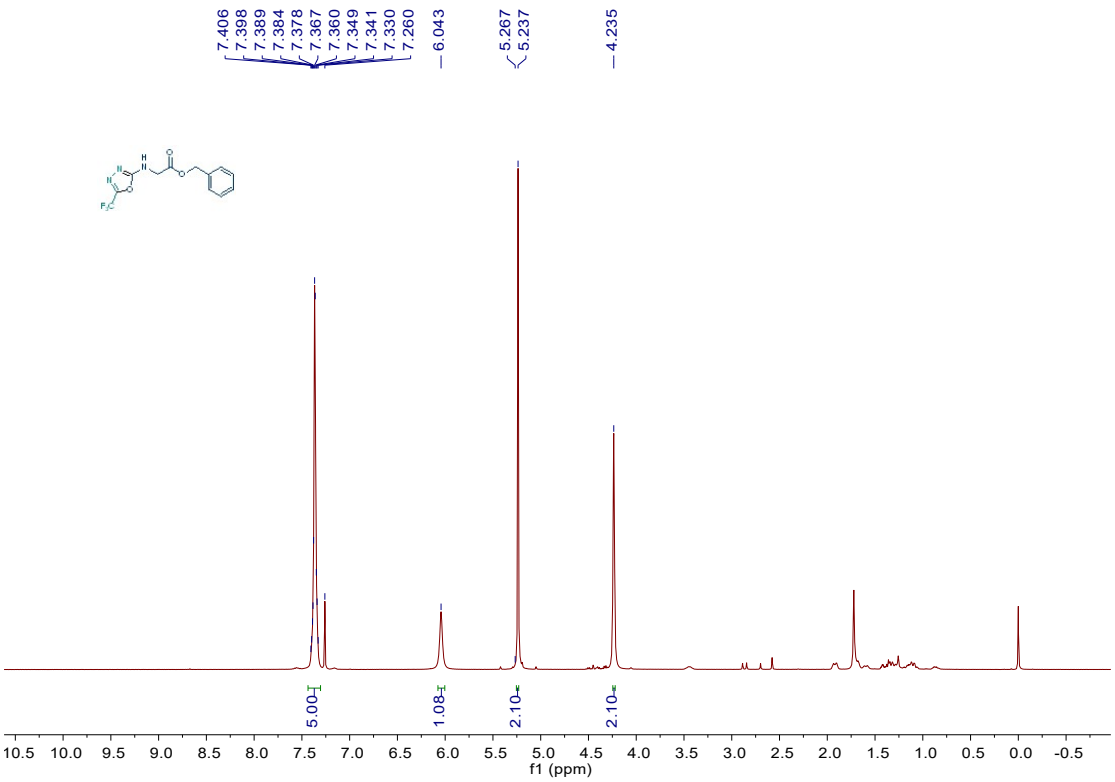
Supplementary Figure 76. ^{1}H NMR spectra of product **27**



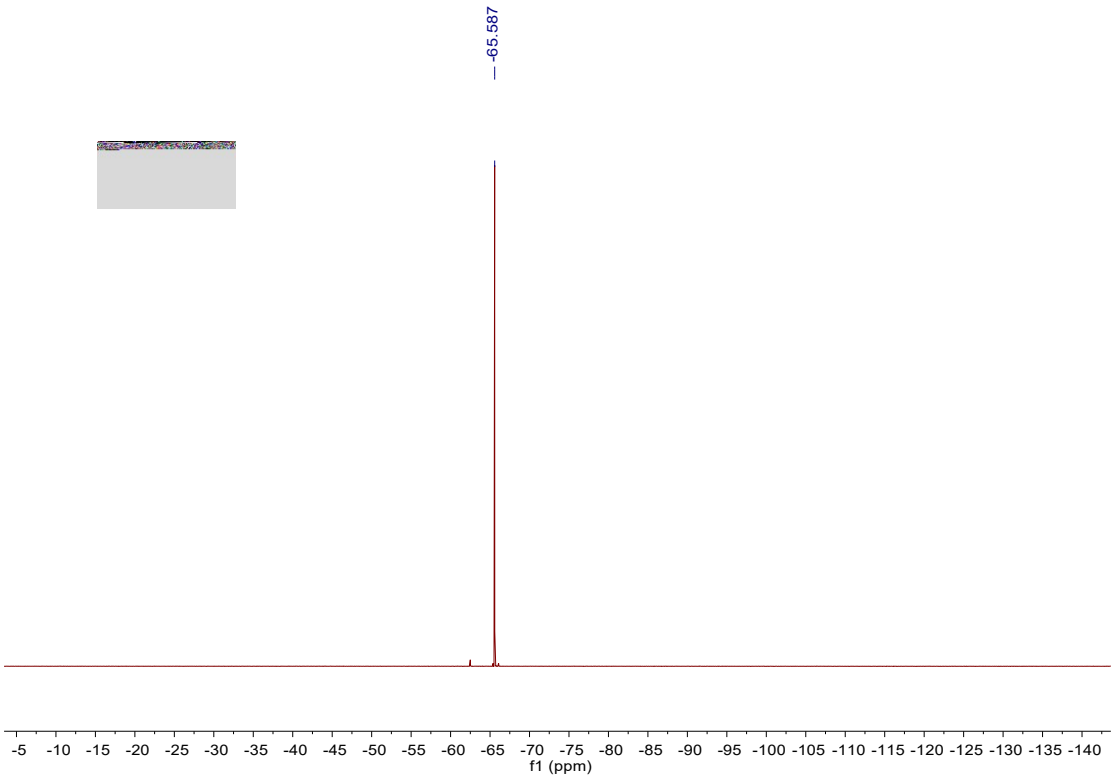
Supplementary Figure 77. ^{19}F NMR spectra of product **27**



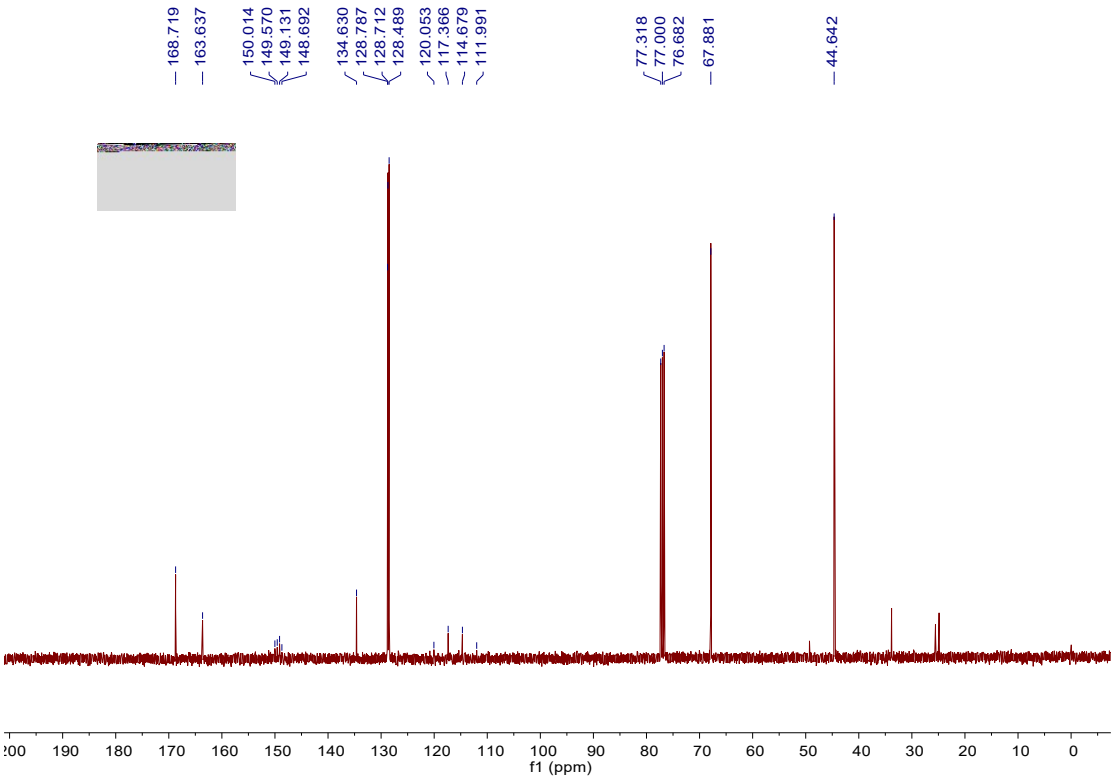
Supplementary Figure 78. ^{13}C NMR spectra of product **27**



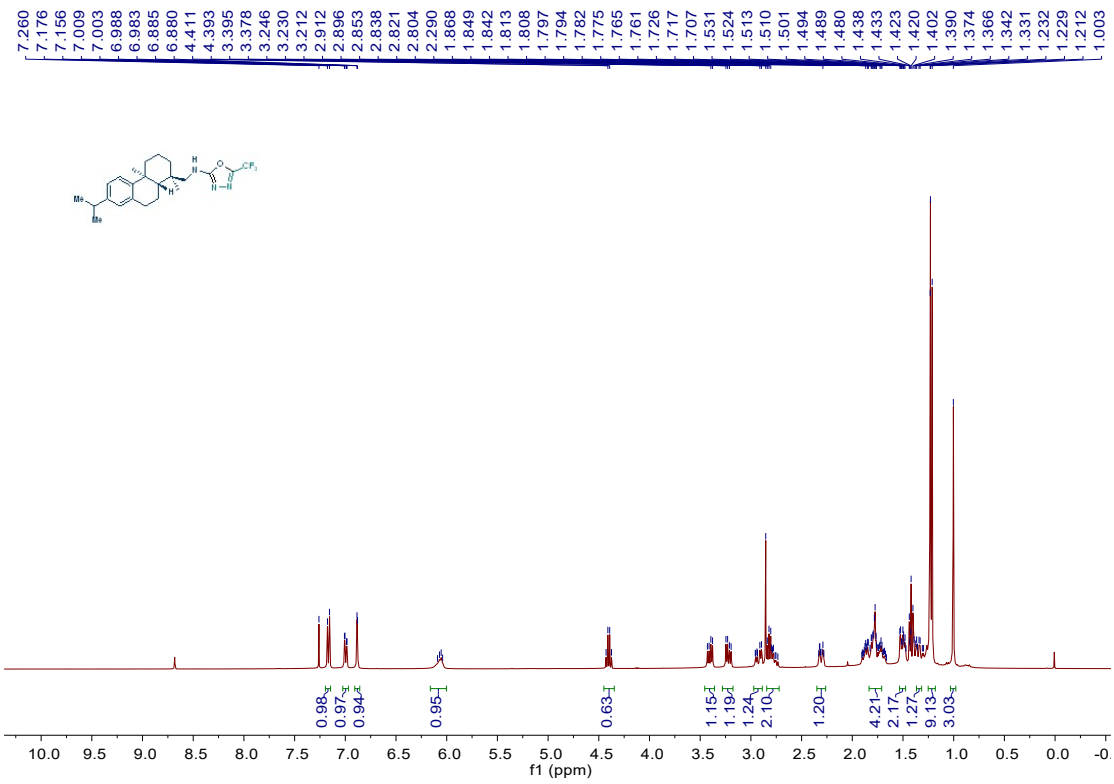
Supplementary Figure 79. ^{1}H NMR spectra of product **28**



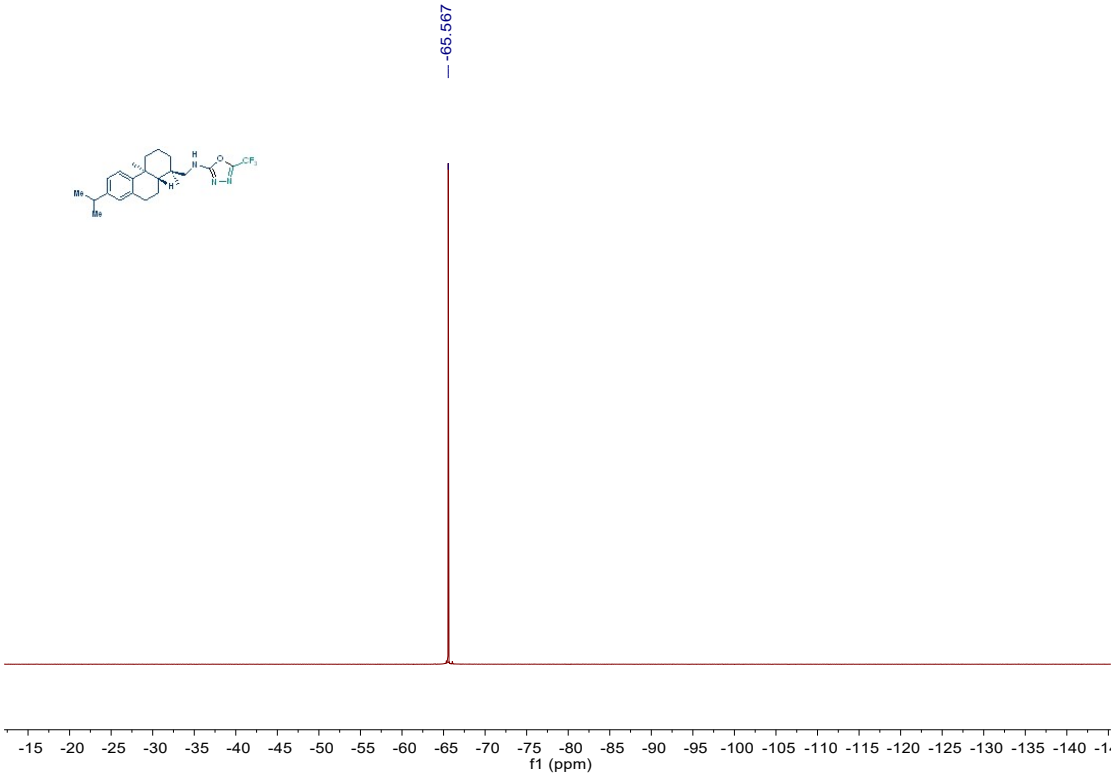
Supplementary Figure 80. ^{19}F NMR spectra of product **28**



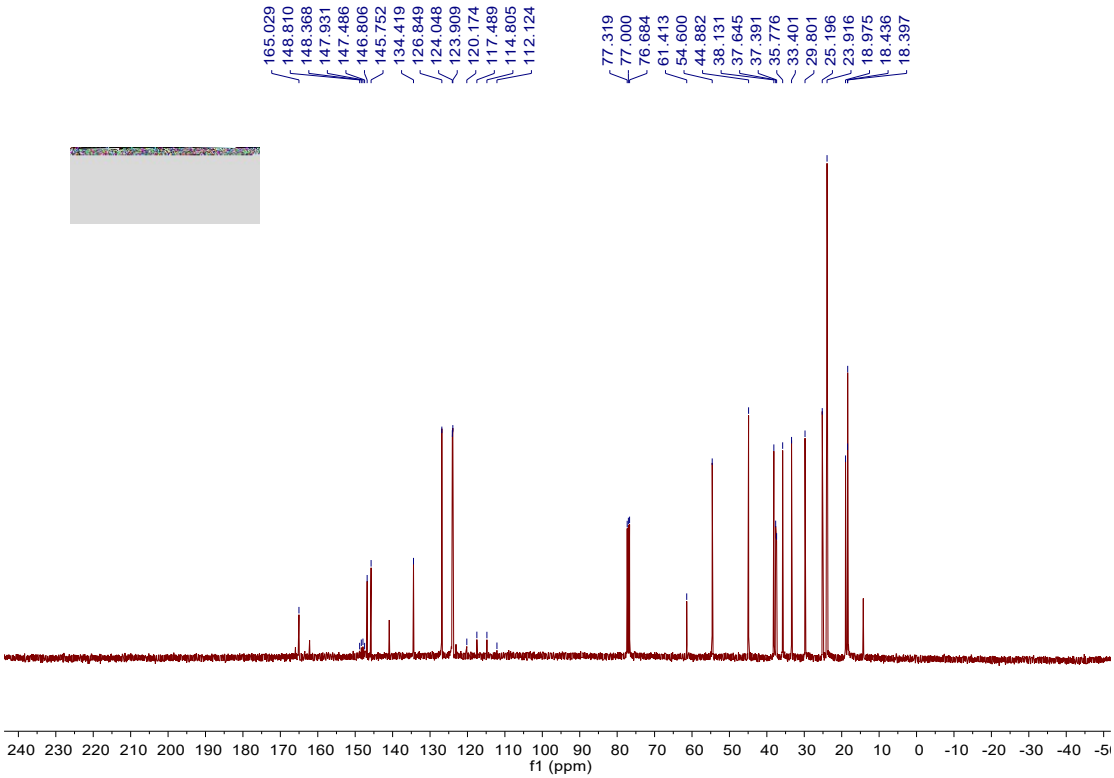
Supplementary Figure 81. ^{13}C NMR spectra of product **28**



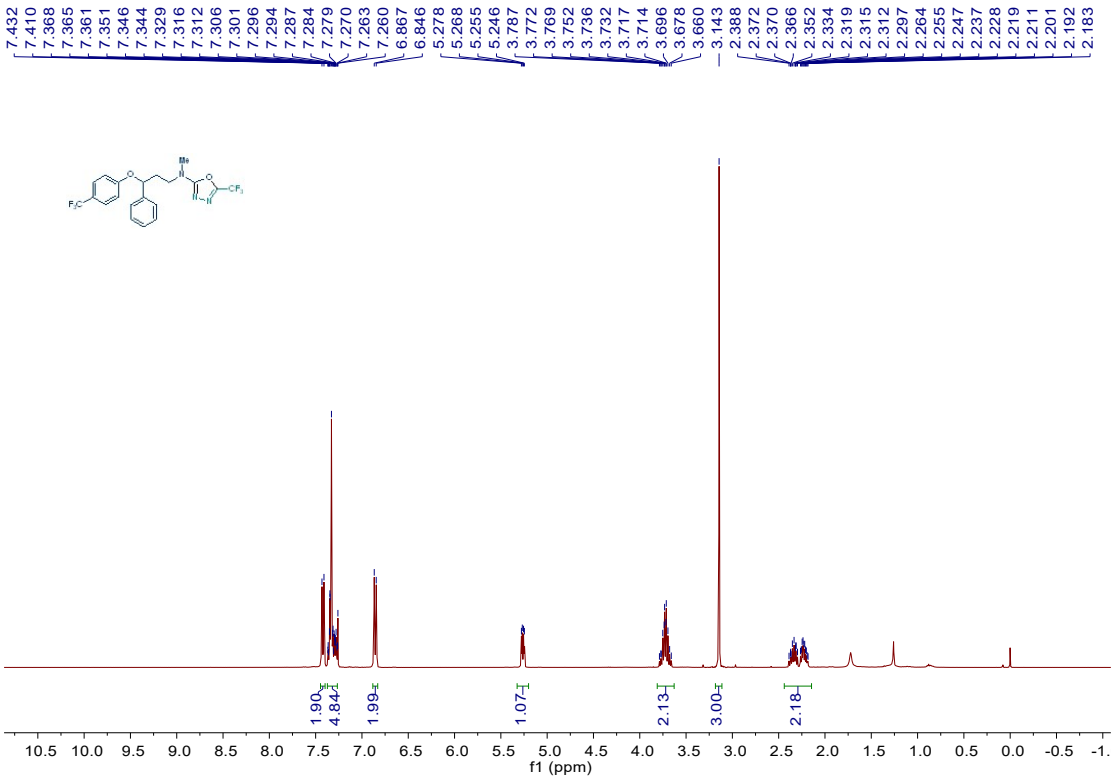
Supplementary Figure 82. ^{1}H NMR spectra of product **29**



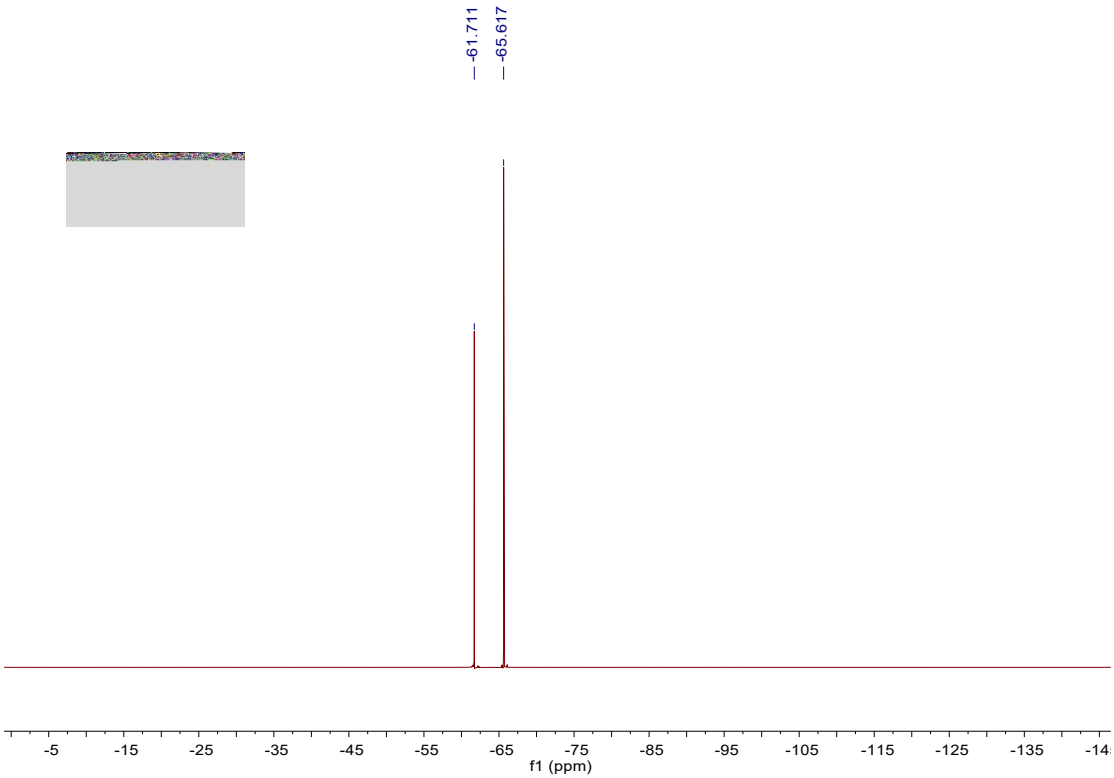
Supplementary Figure 83. ^{19}F NMR spectra of product **29**



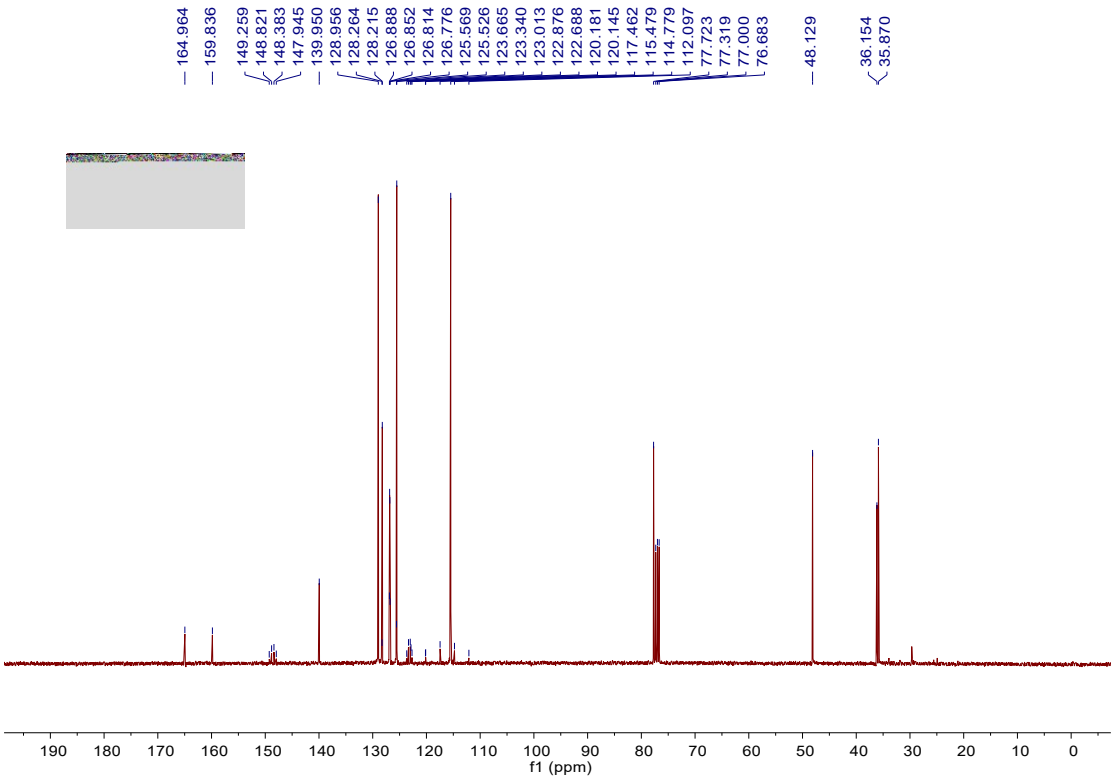
Supplementary Figure 84. ^{13}C NMR spectra of product **29**



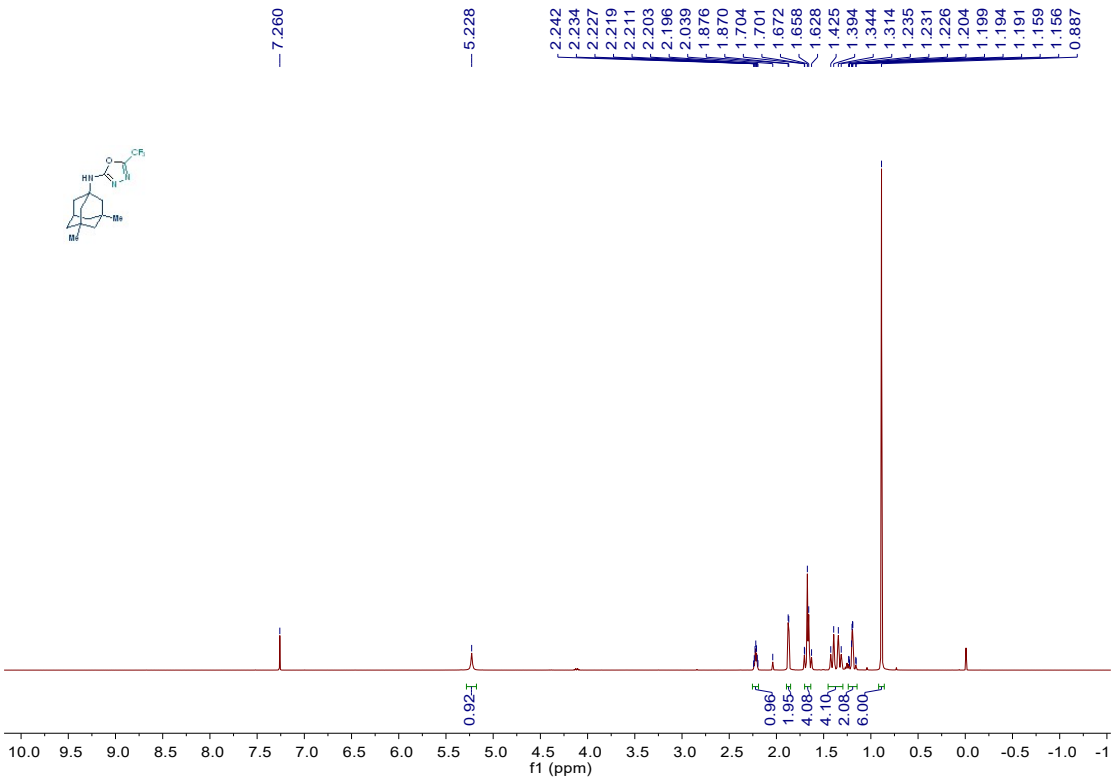
Supplementary Figure 85. ^{1}H NMR spectra of product **30**



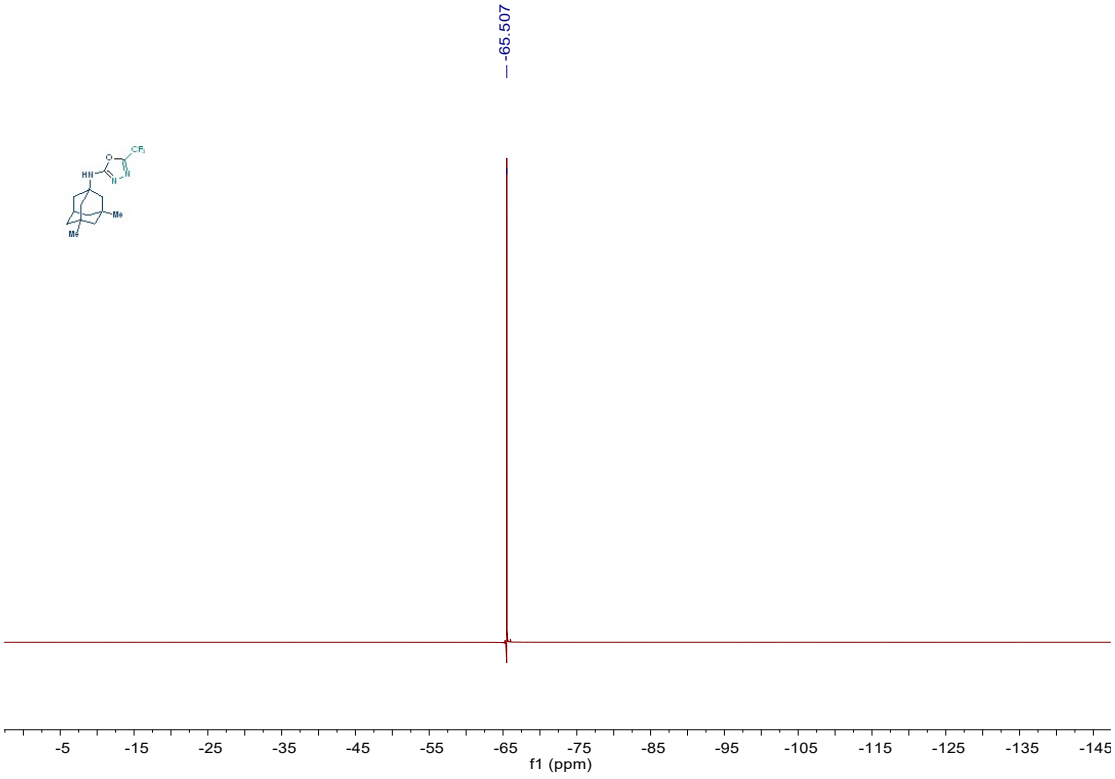
Supplementary Figure 86. ^{19}F NMR spectra of product **30**



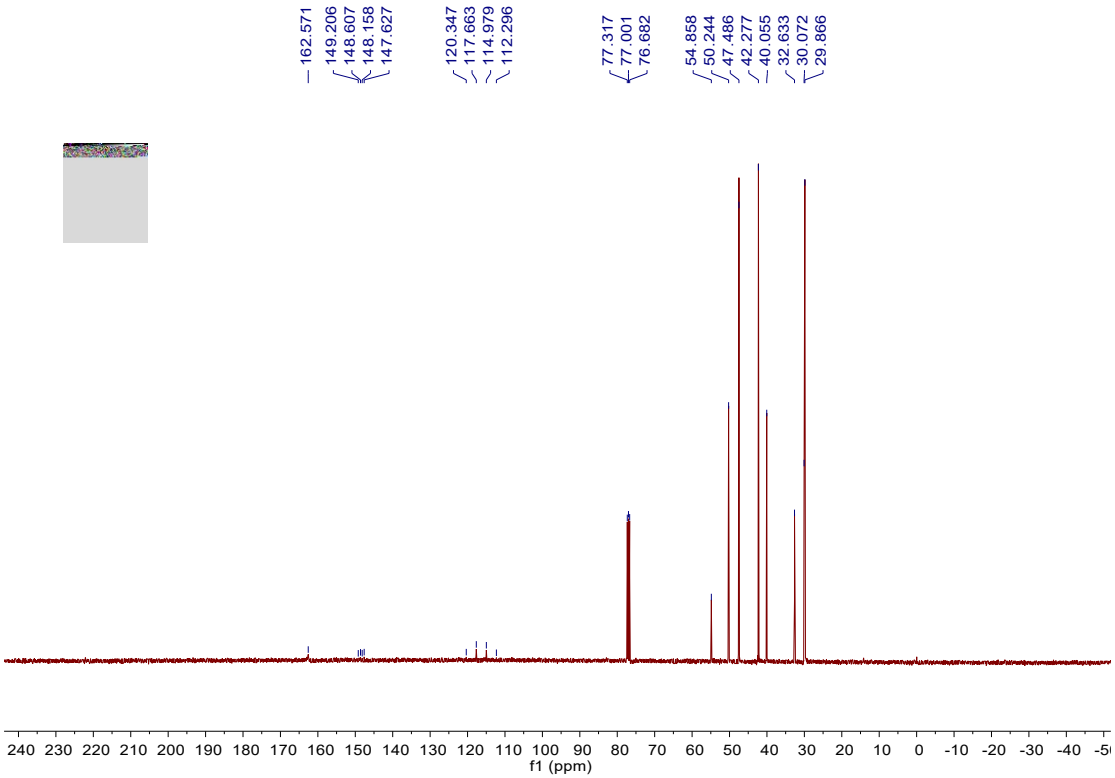
Supplementary Figure 87. ^{13}C NMR spectra of product **30**



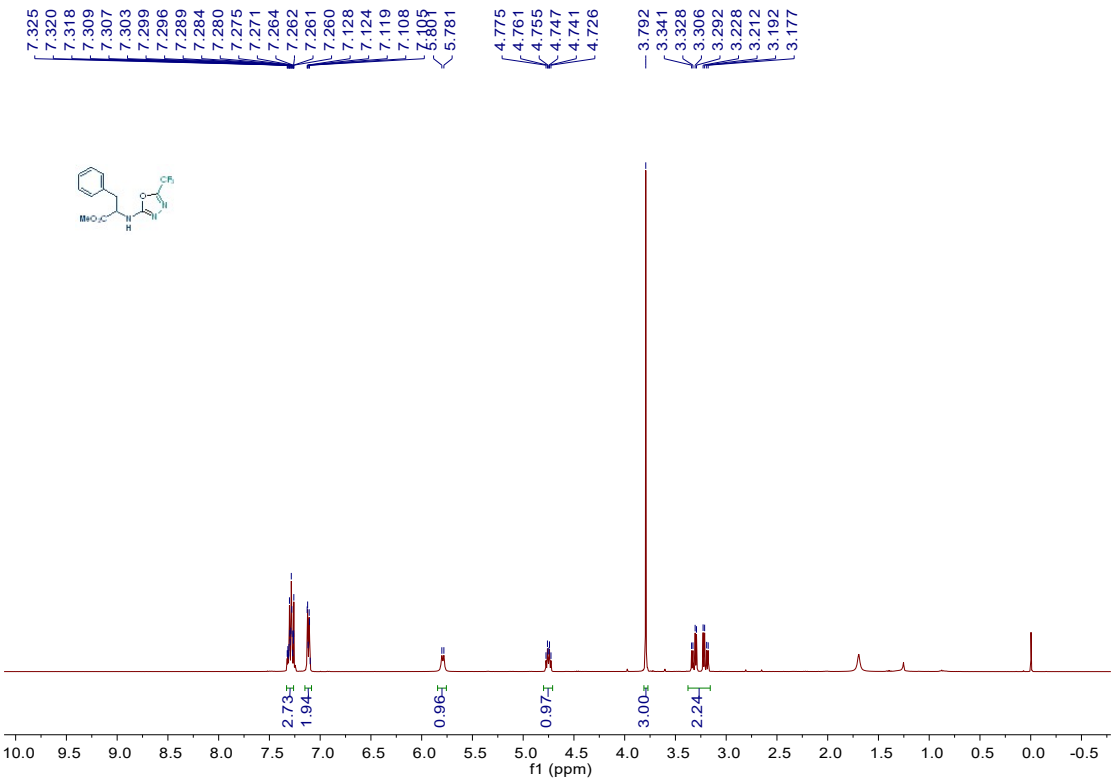
Supplementary Figure 88. ^{1}H NMR spectra of product **31**



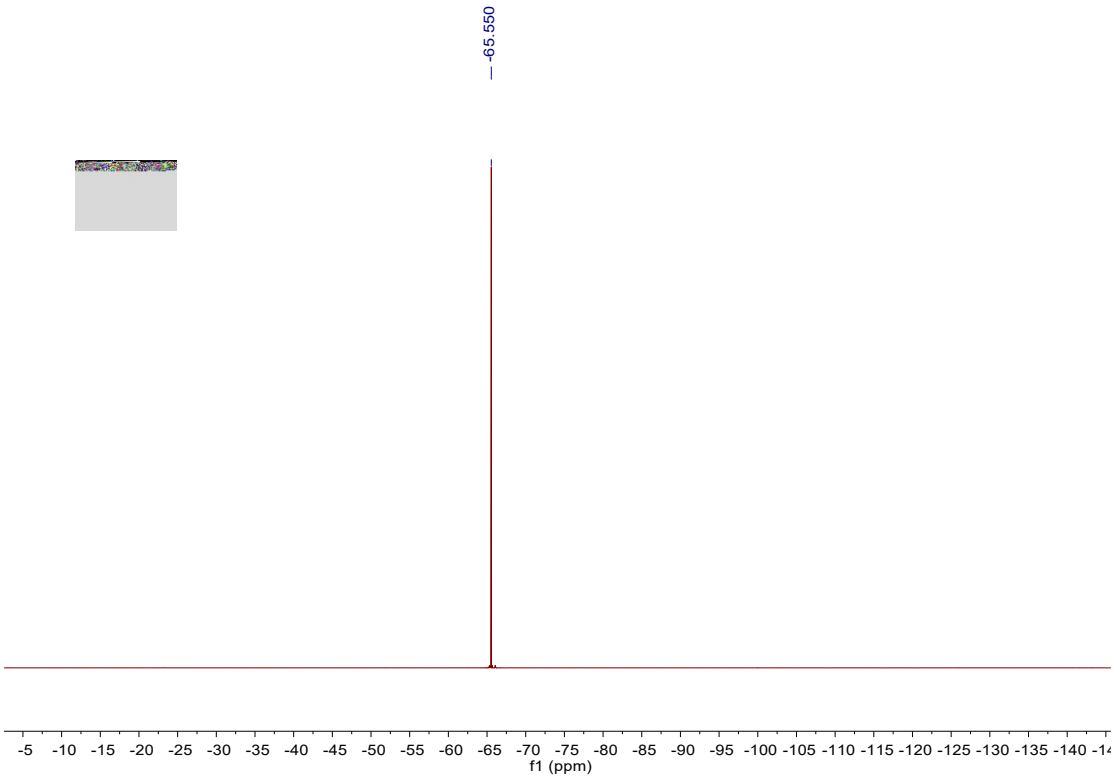
Supplementary Figure 89. ^{19}F NMR spectra of product **31**



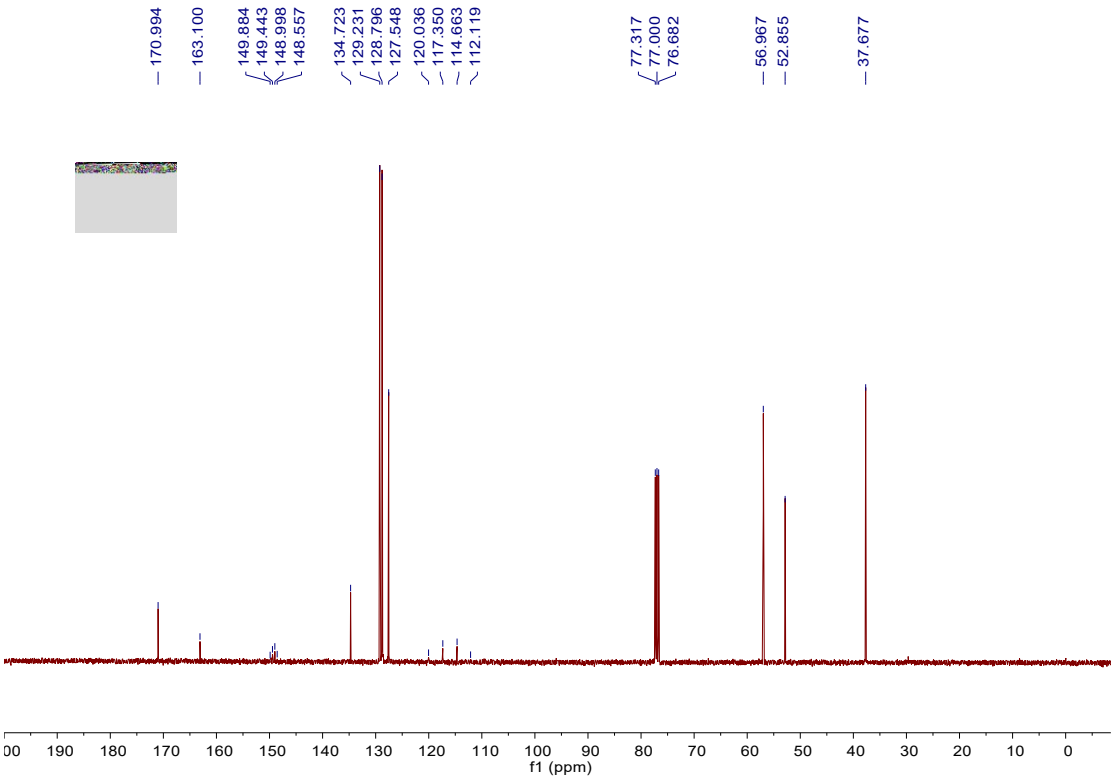
Supplementary Figure 90. ^{13}C NMR spectra of product **31**



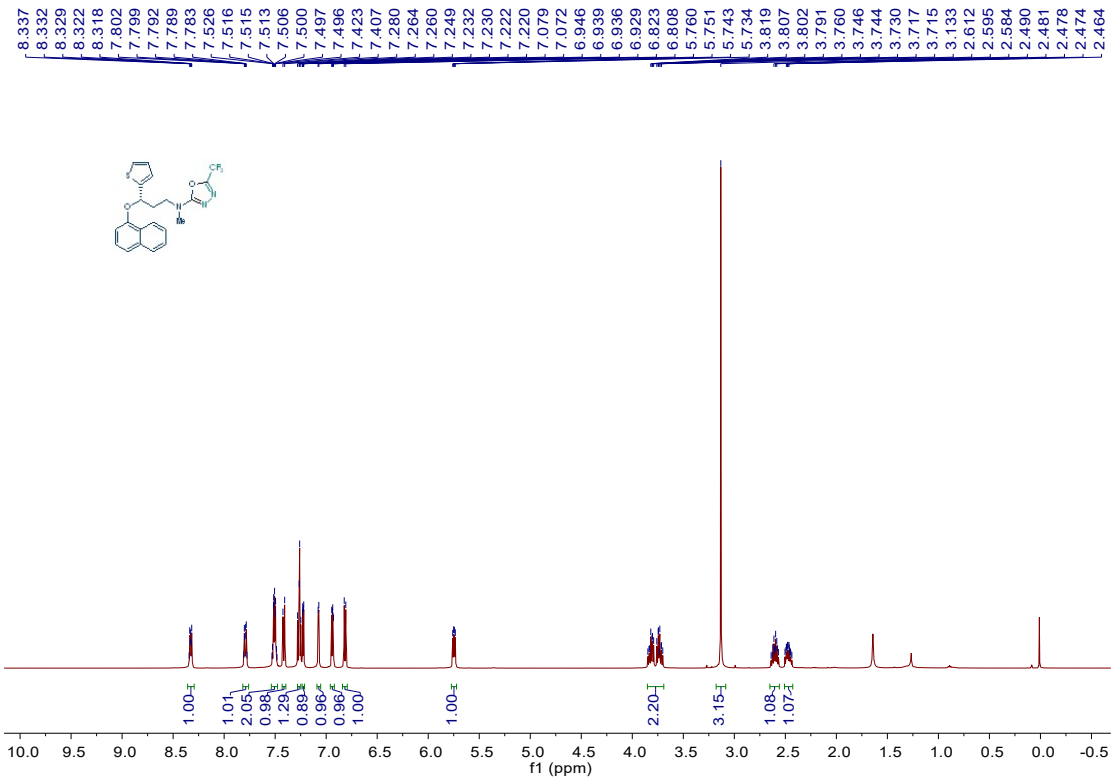
Supplementary Figure 91. ^{1}H NMR spectra of product **32**



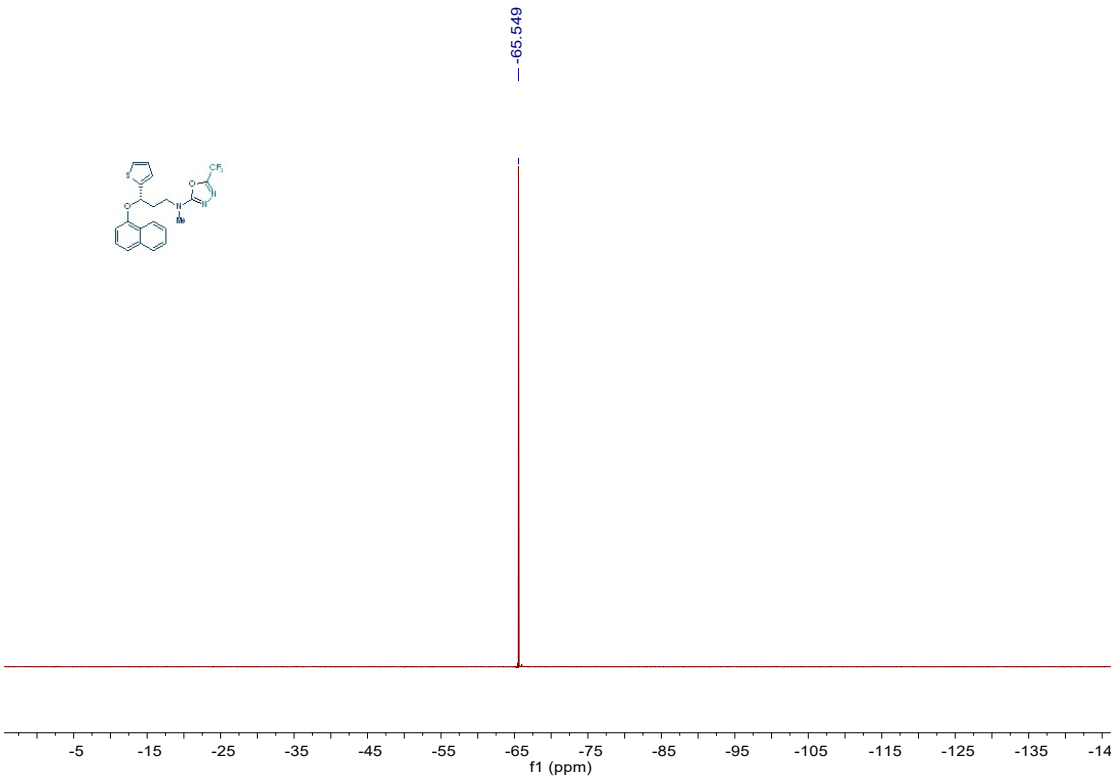
Supplementary Figure 92. ^{19}F NMR spectra of product **32**



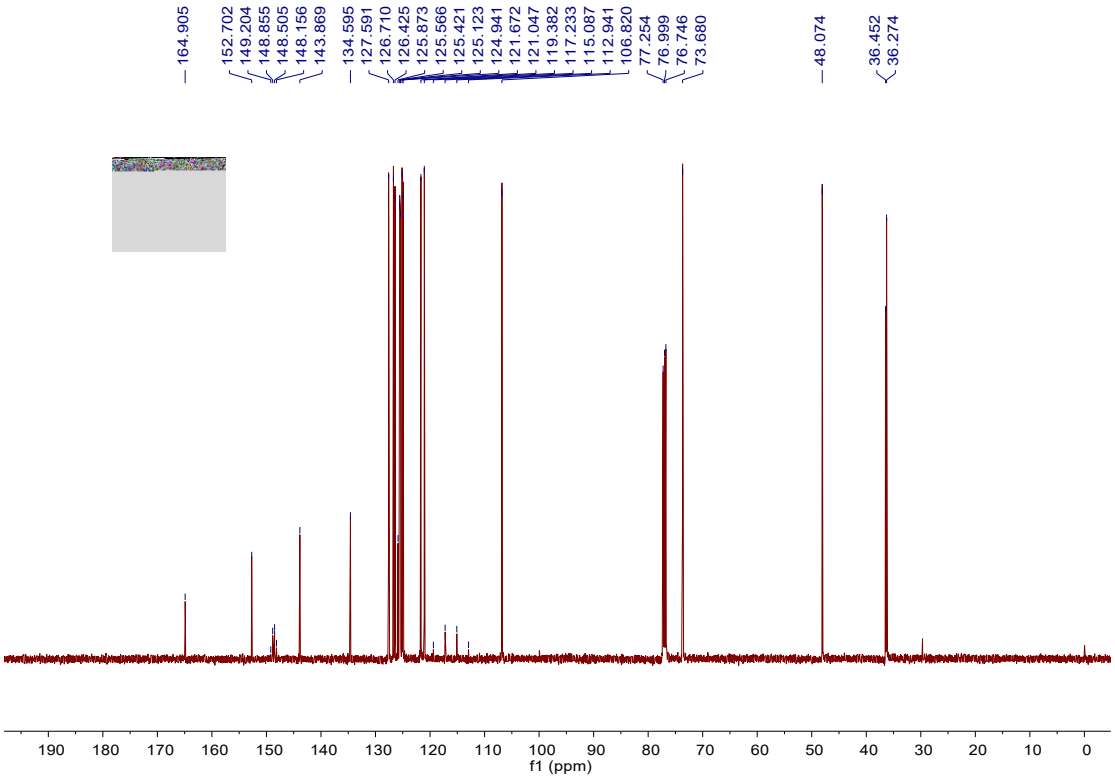
Supplementary Figure 93. ^{13}C NMR spectra of product **32**



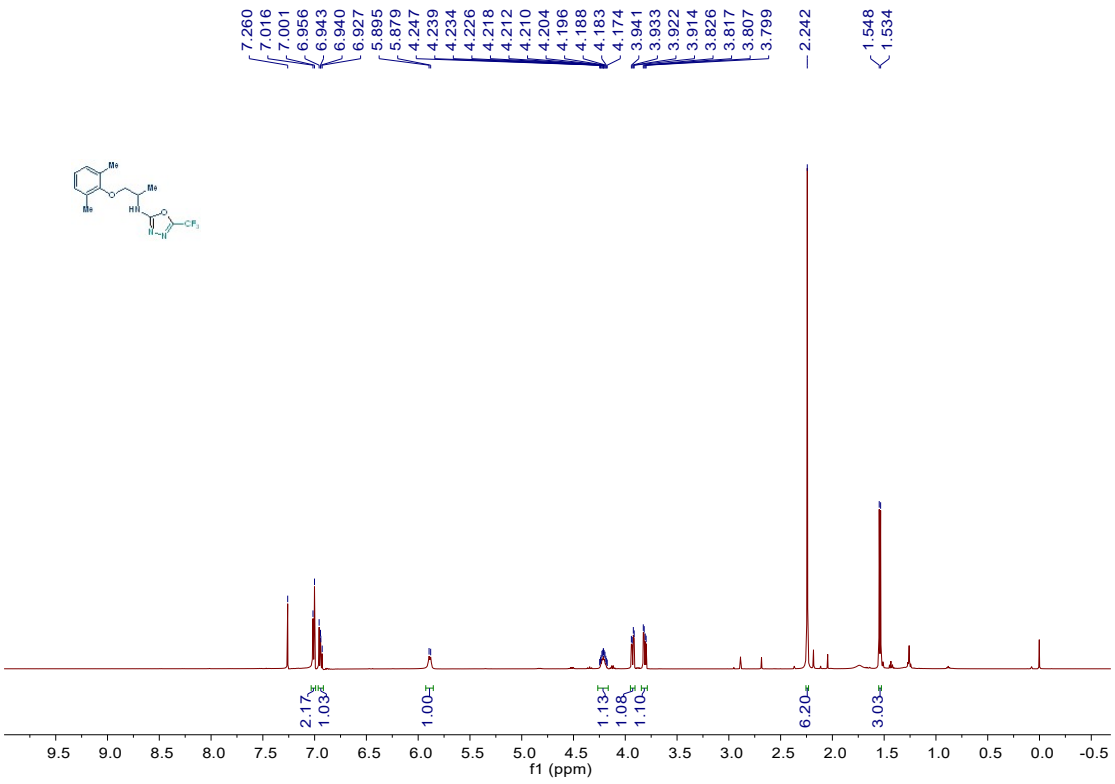
Supplementary Figure 94. ^{1}H NMR spectra of product **33**



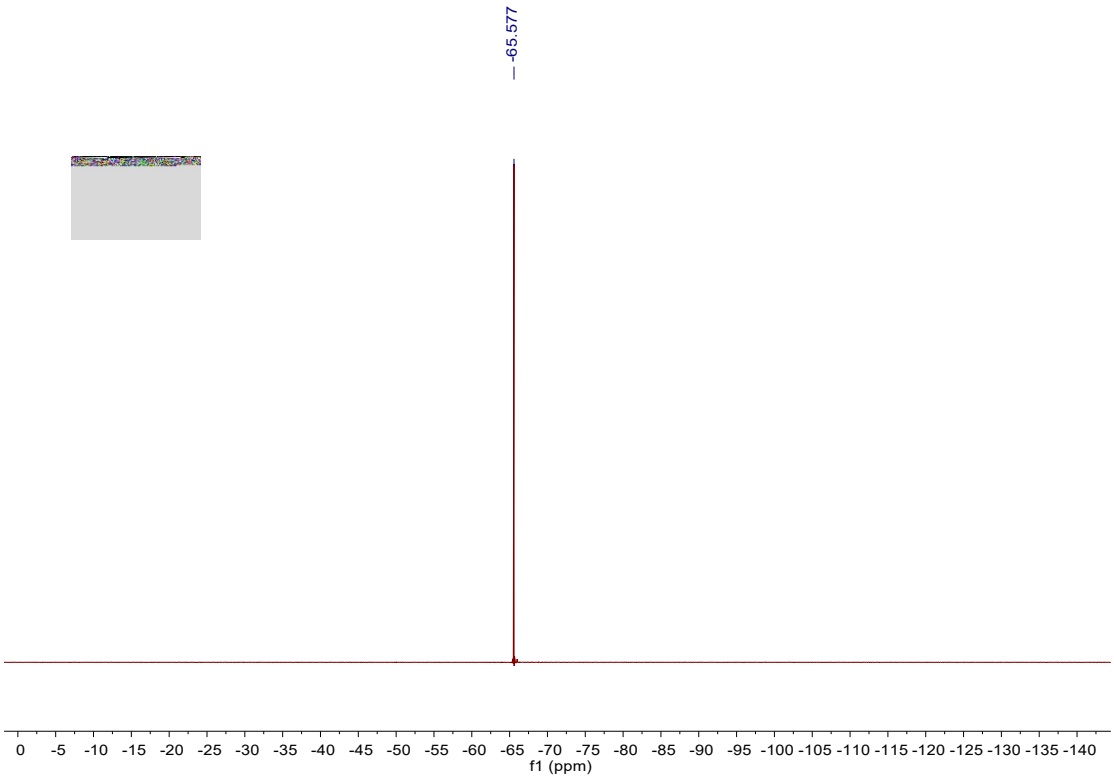
Supplementary Figure 95. ^{19}F NMR spectra of product **33**



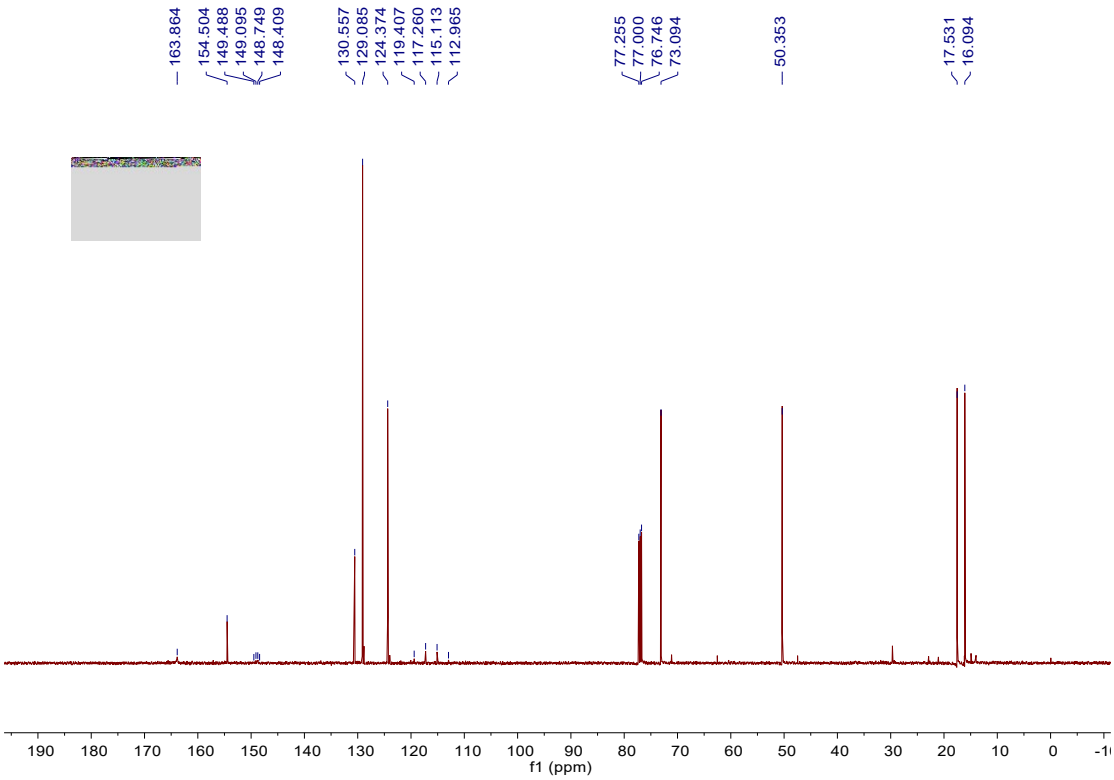
Supplementary Figure 96. ^{13}C NMR spectra of product **33**



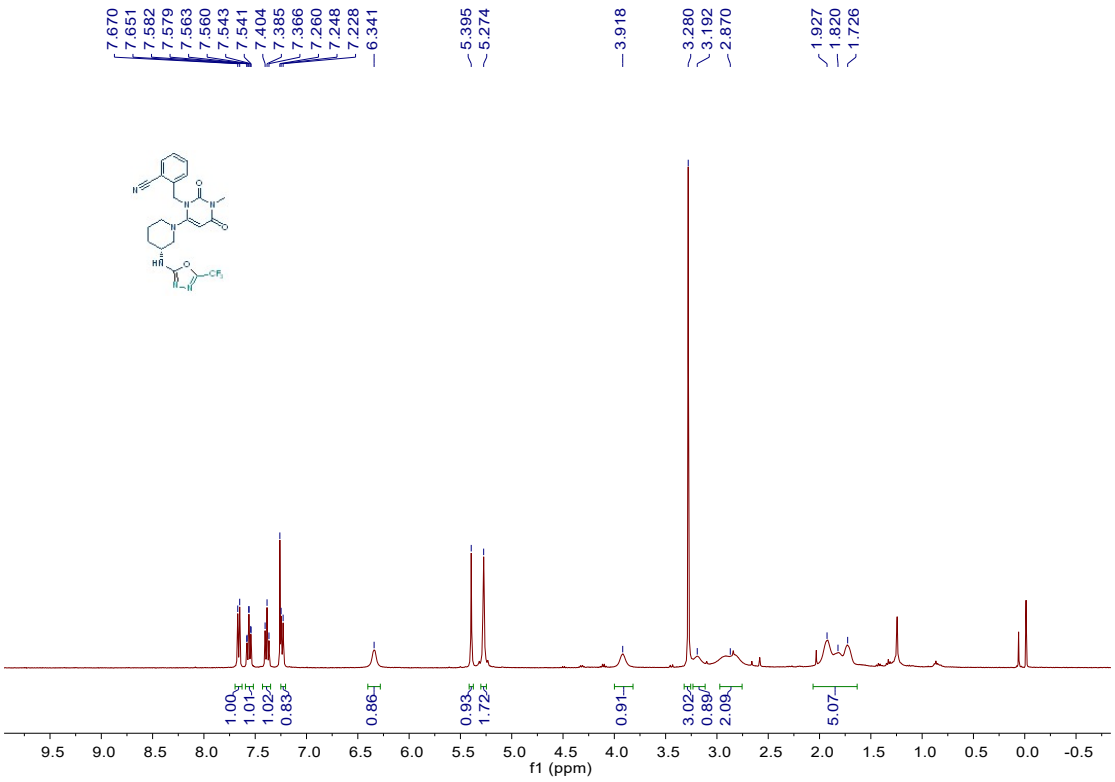
Supplementary Figure 97. ^{1}H NMR spectra of product **34**



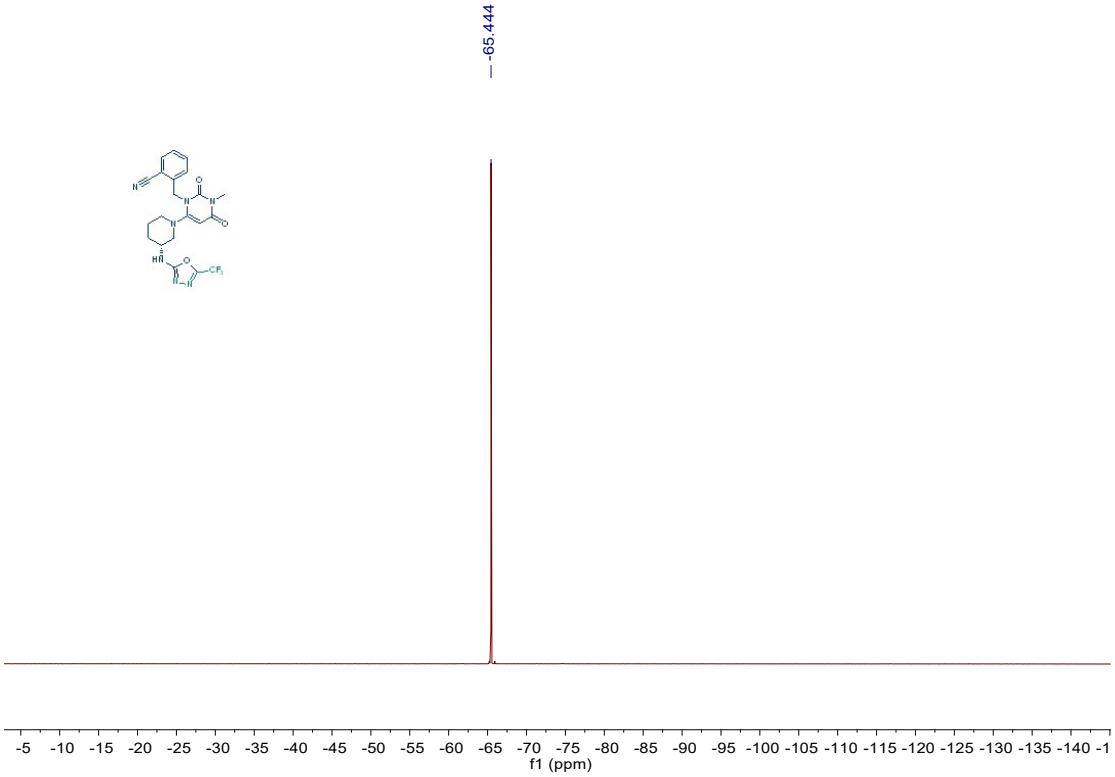
Supplementary Figure 98. ^{19}F NMR spectra of product **34**



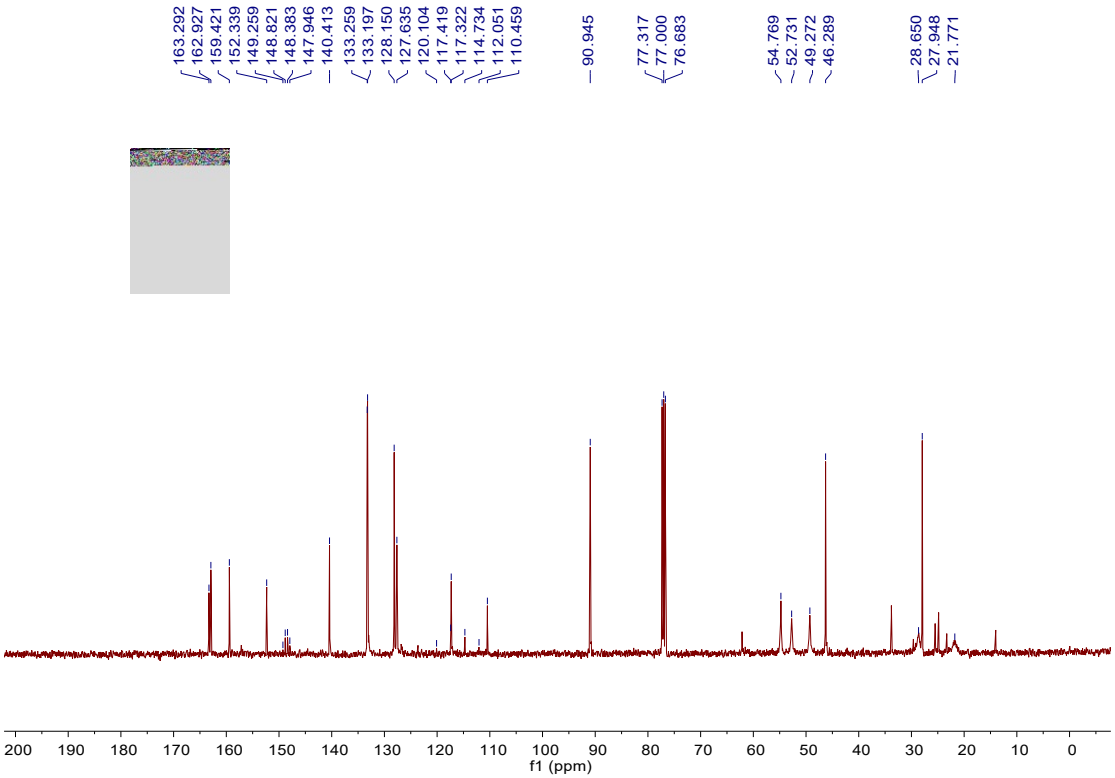
Supplementary Figure 99. ^{13}C NMR spectra of product **34**



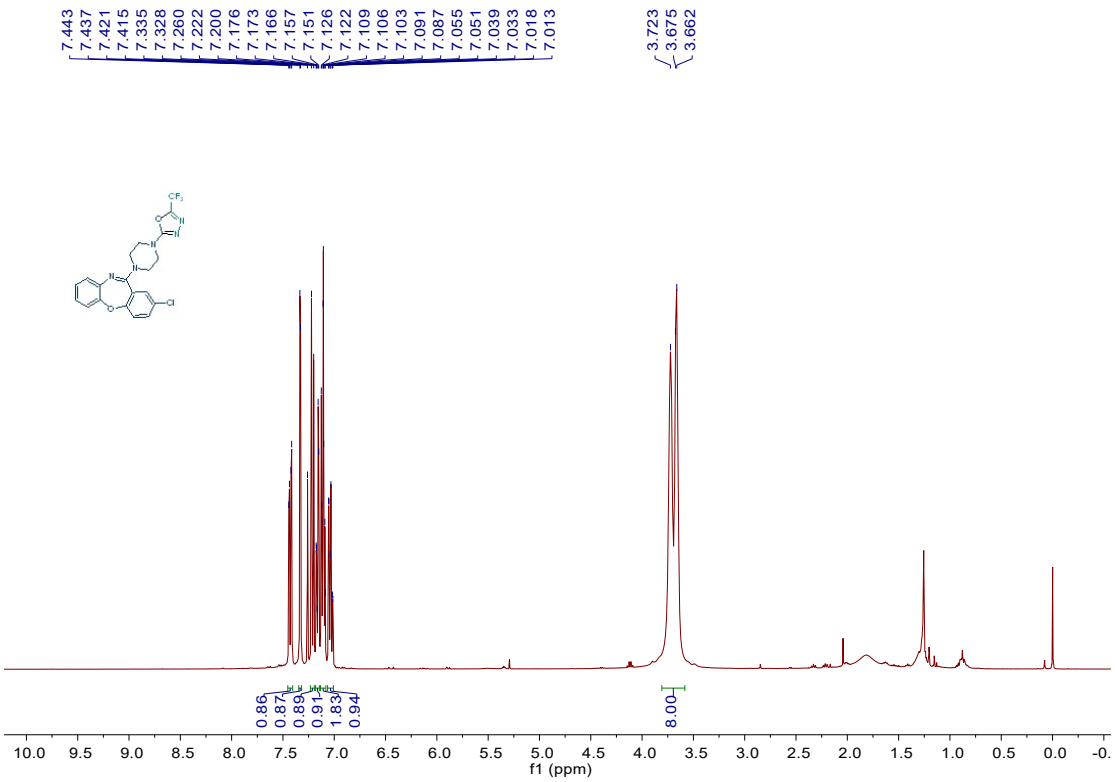
Supplementary Figure 100. ^{1}H NMR spectra of product **35**



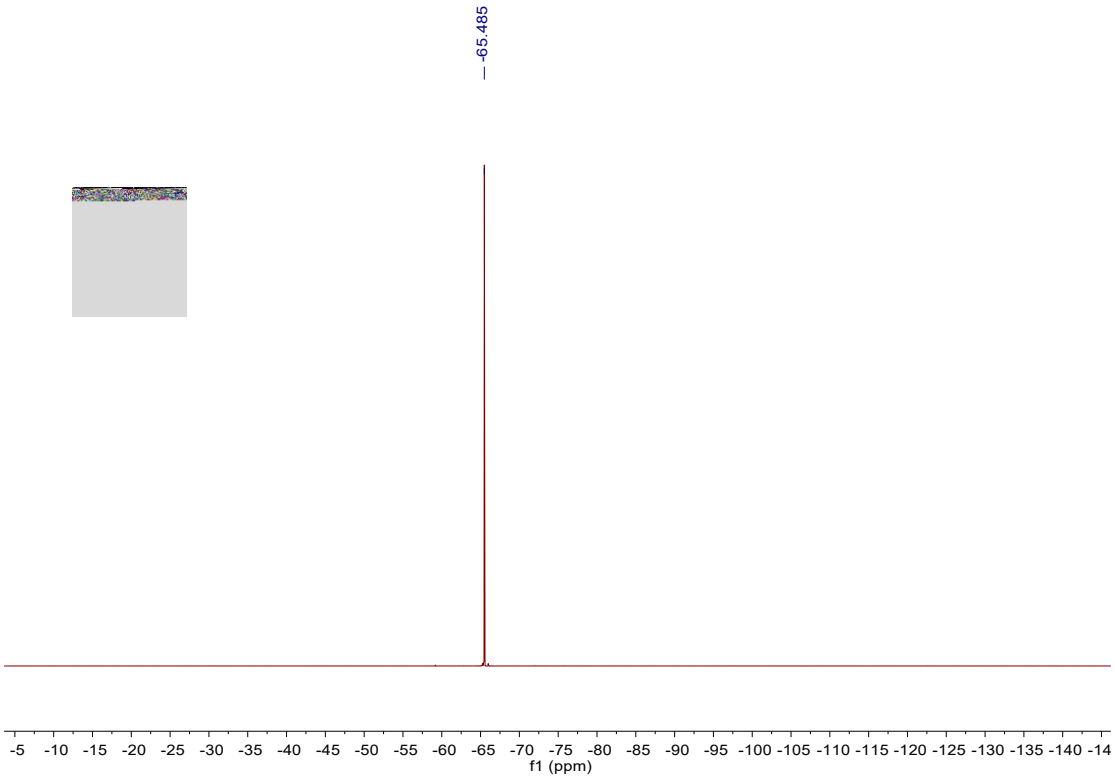
Supplementary Figure 101. ^{19}F NMR spectra of product **35**



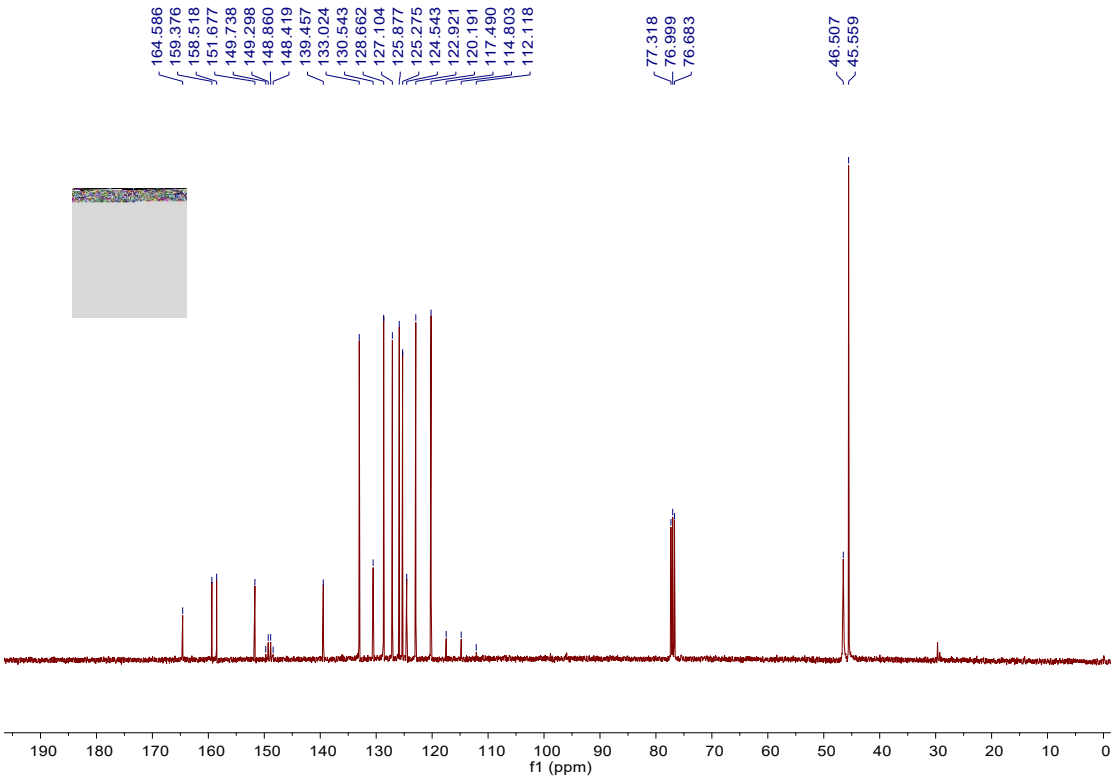
Supplementary Figure 102. ^{13}C NMR spectra of product **35**



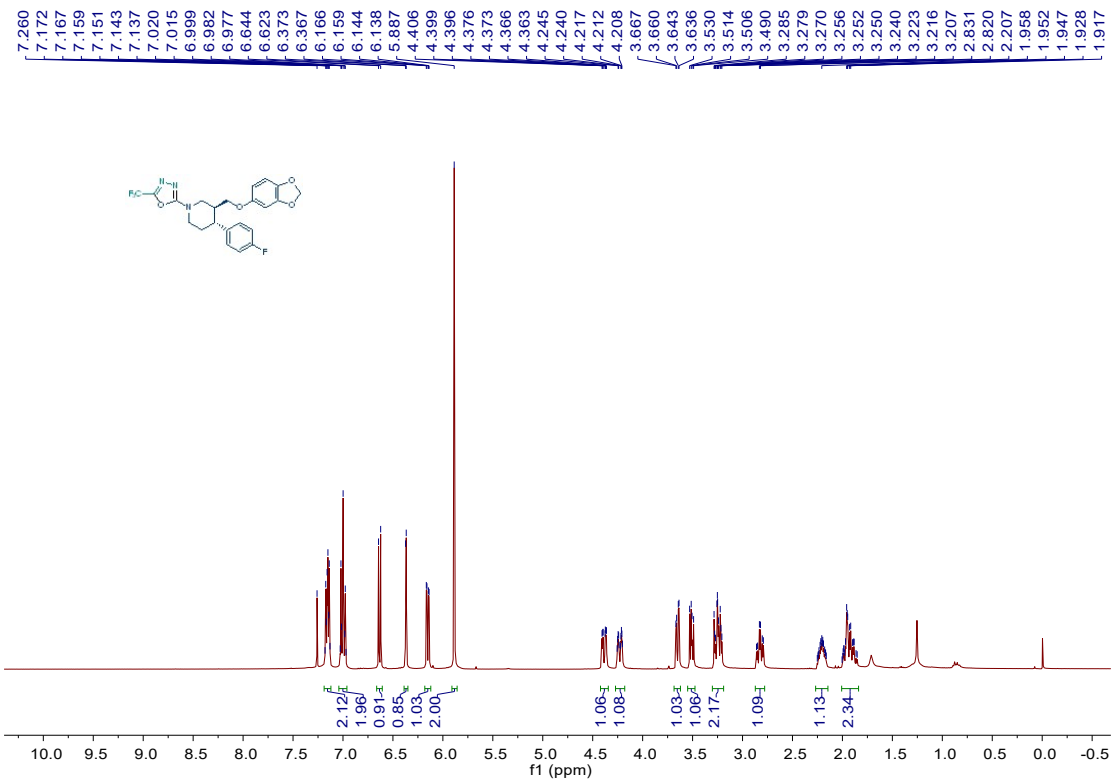
Supplementary Figure 103. ^{1}H NMR spectra of product **36**



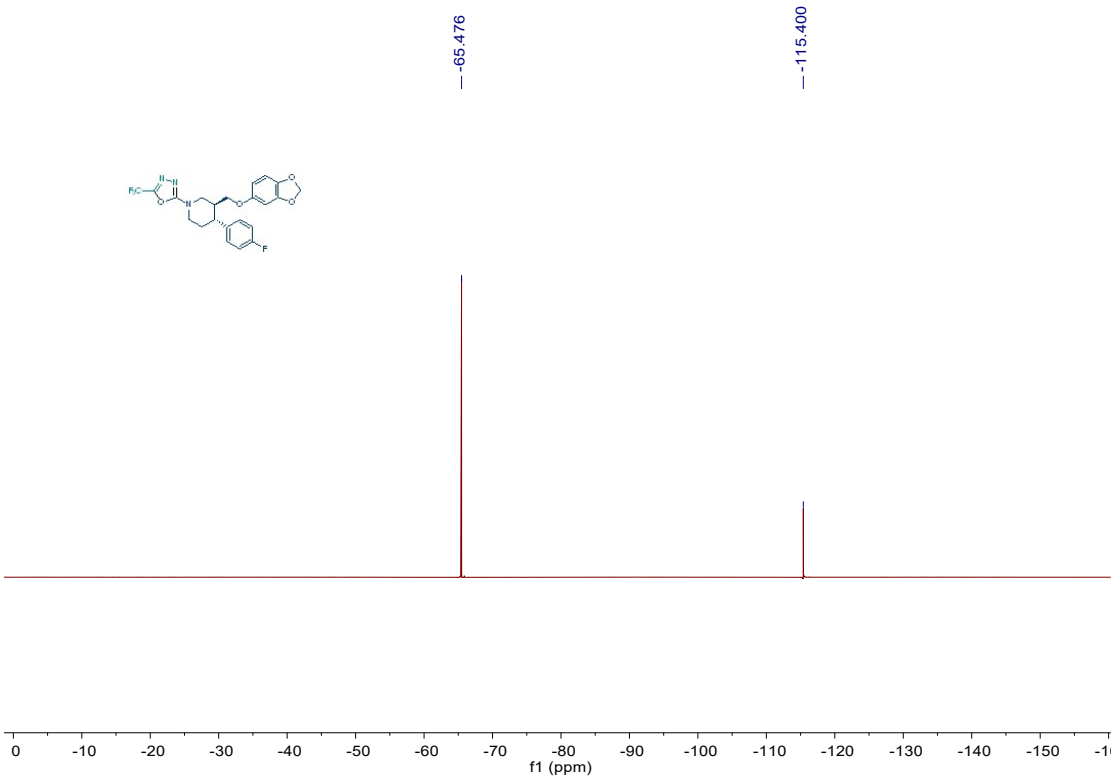
Supplementary Figure 104. ^{19}F NMR spectra of product **36**



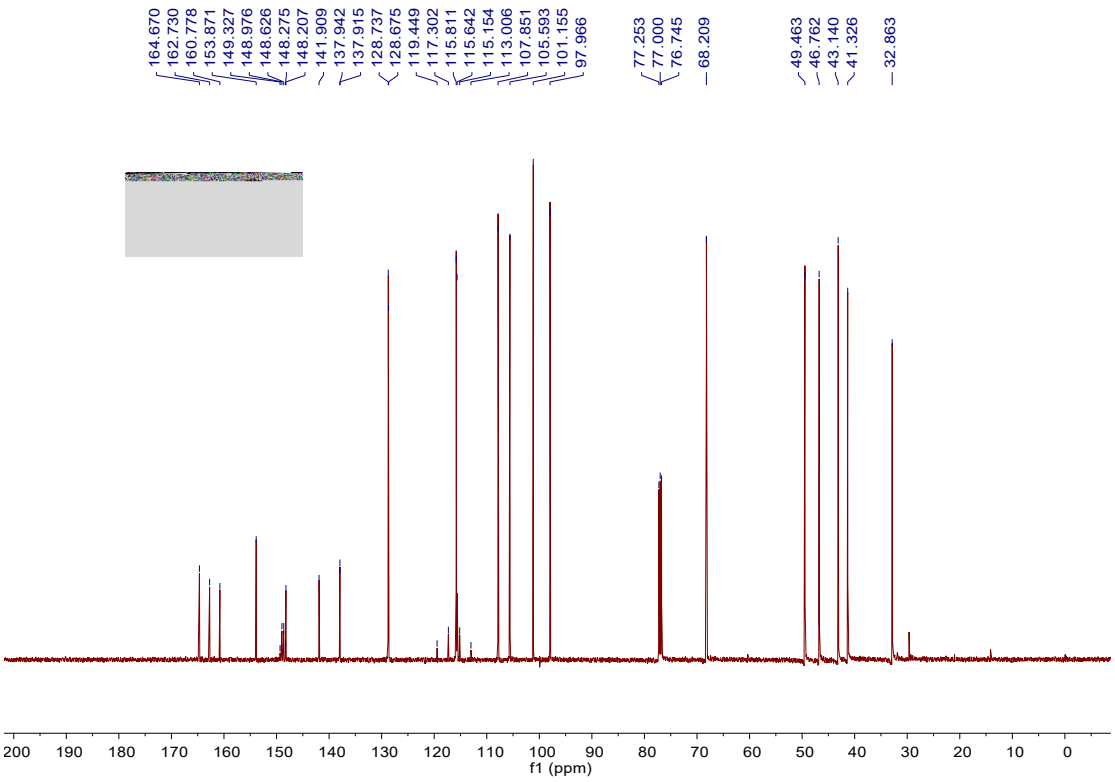
Supplementary Figure 105. ^{13}C NMR spectra of product **36**



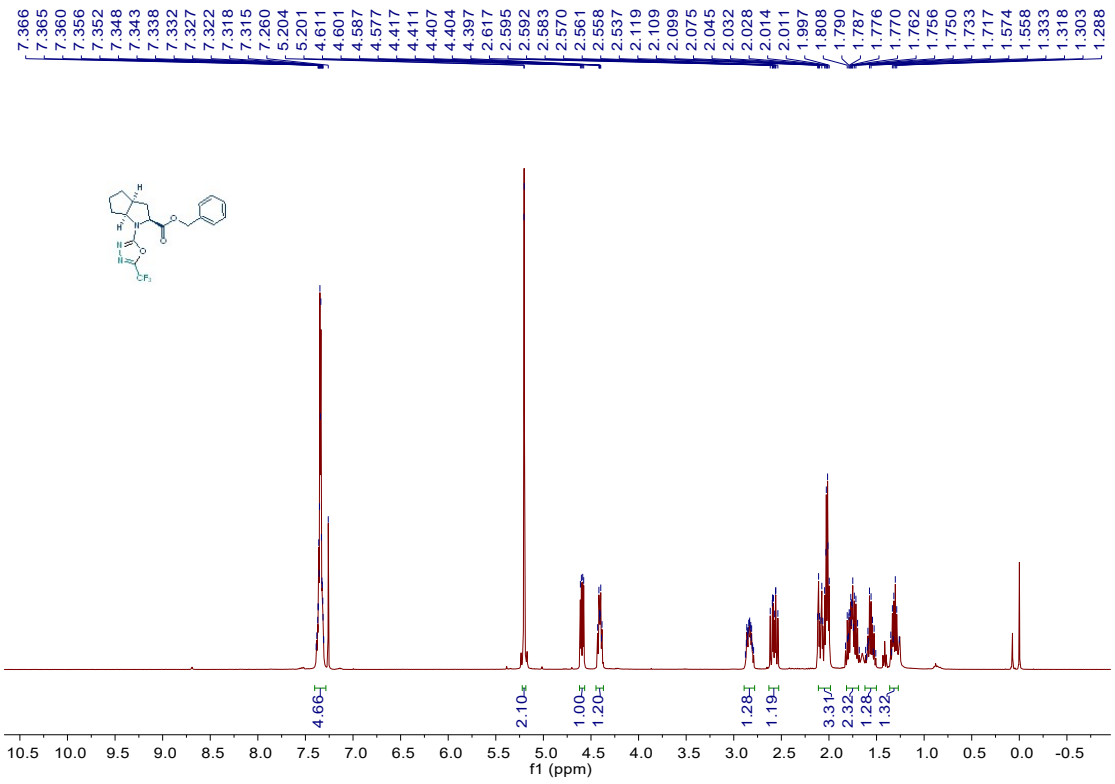
Supplementary Figure 106. ^{1}H NMR spectra of product **37**



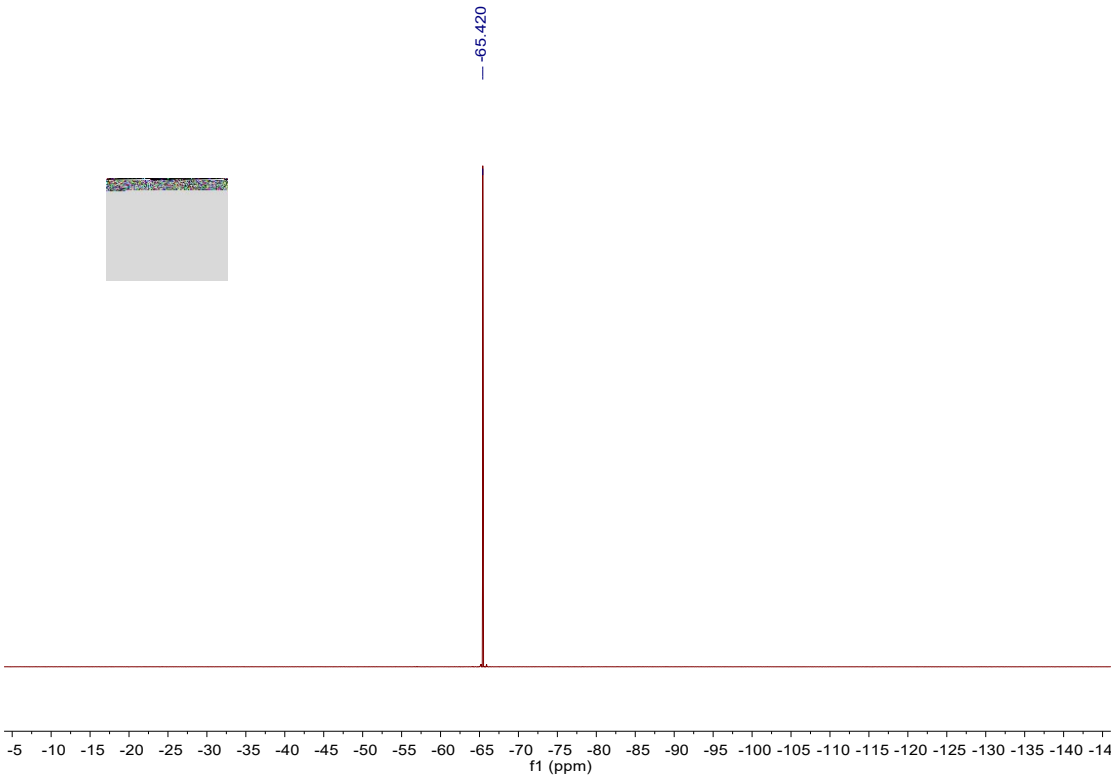
Supplementary Figure 107. ^{19}F NMR spectra of product **37**



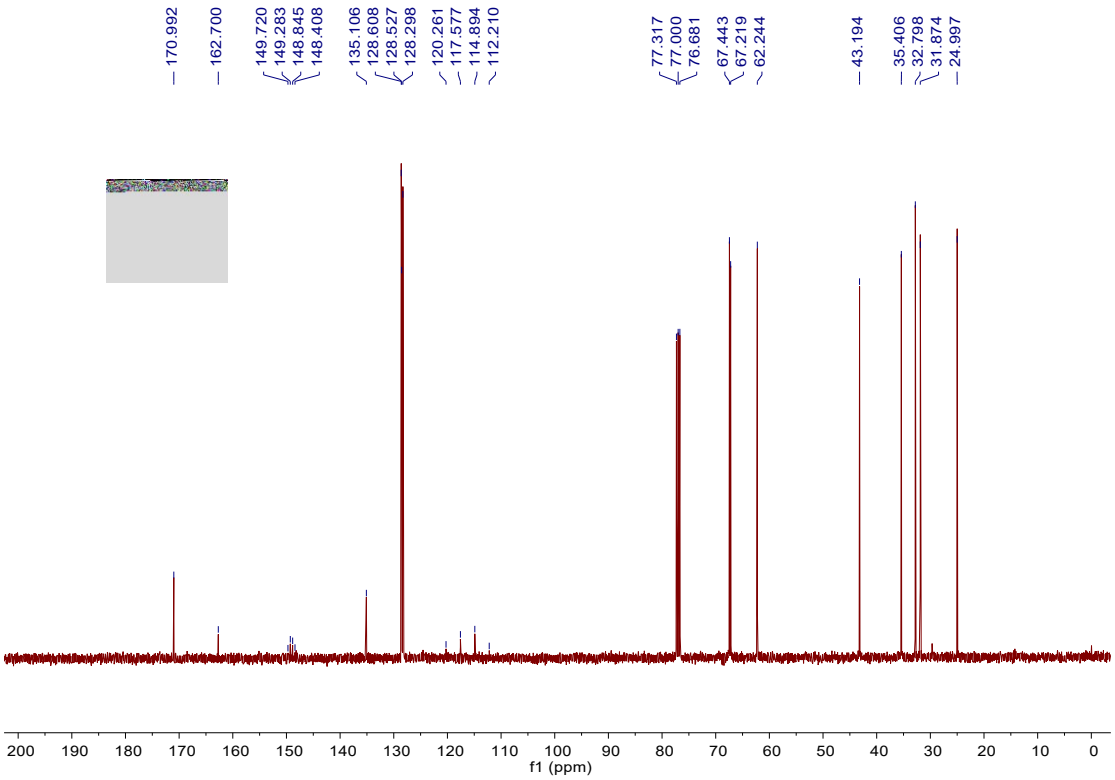
Supplementary Figure 108. ^{13}C NMR spectra of product **37**



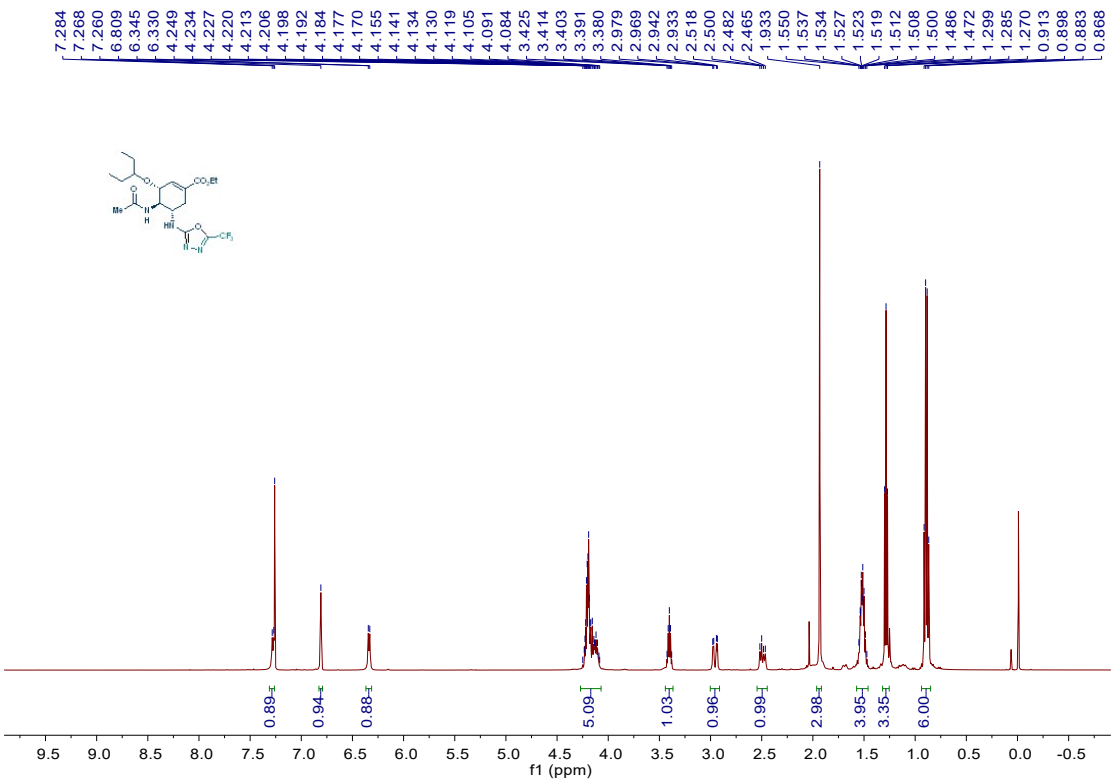
Supplementary Figure 109. ^{1}H NMR spectra of product **38**



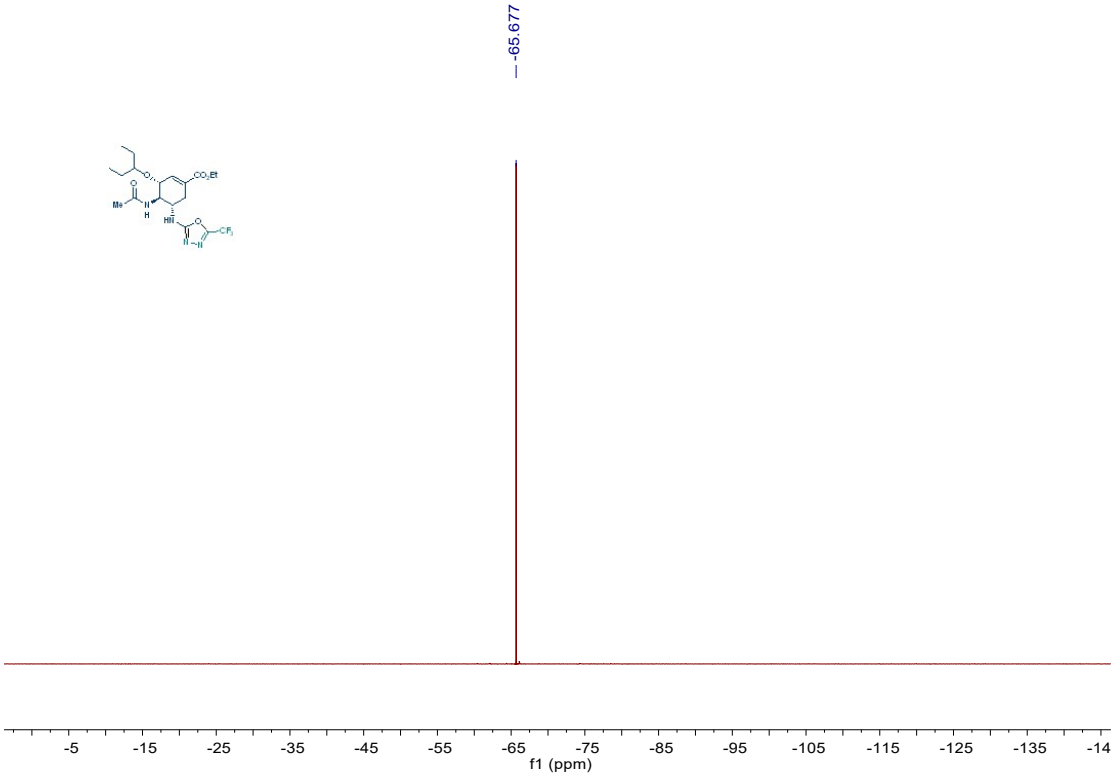
Supplementary Figure 110. ^{19}F NMR spectra of product **38**



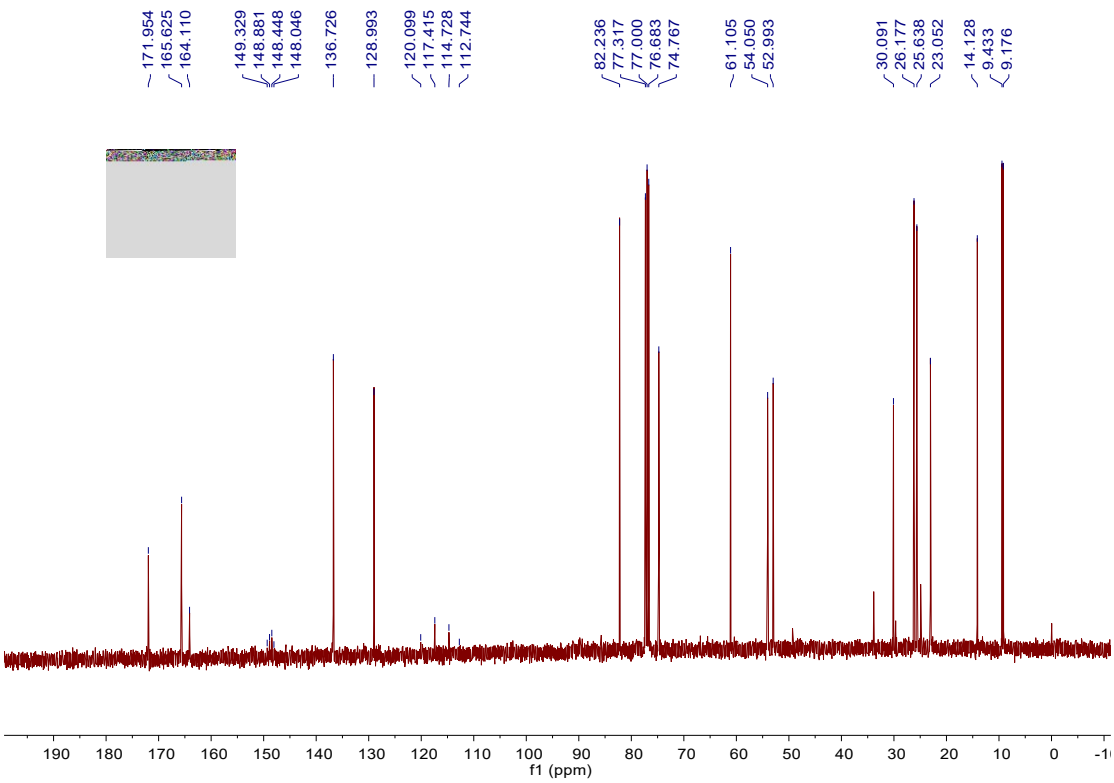
Supplementary Figure 111. ^{13}C NMR spectra of product **38**



Supplementary Figure 112. ^{1}H NMR spectra of product **39**



Supplementary Figure 113. ^{19}F NMR spectra of product **39**



Supplementary Figure 114. ^{13}C NMR spectra of product **39**