Supplementary Information

Novel strategy for non-aqueous bioconjugation of substituted Phenyl-1,2,4-triazole-3,5-dione analogues

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Table S1: Isolated yields of N-({phenyl carbamoyl}amino)ethoxyformamide derivatives (**3a-f**)

3	**R =**	**Yield (%)**
a	SF_5	88
b	CF_3	78
c	F	79
d	H	81
e	Me	51
f	OMe	43

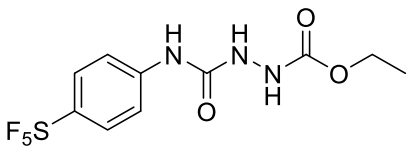
Table S2: Isolated yields of N-phenyl-1,2,4-triazolidine-3,5-dione derivatives (**4a-f**)

4	**R =**	**Yield (%)**
a	SF_5	90
b	CF_3	82
c	F	65
d	H	78
e	Me	73
f	OMe	67

General procedure for the synthesis of N-({phenyl carbamoyl}amino)ethoxyformamide derivatives (3a-f):

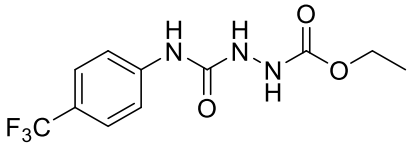
1,1'-Carbonyldiimidazole (450 mg, 2.765 mmol) was suspended in anhydrous dichloromethane (10 mL) under nitrogen. The para substituted aniline (2 mmol) was added and the reaction mixture was refluxed at 50°C for 18 hr. Ethyl hydrazinecarboxylate (209 mg; 2 mmol) dropwise to the solution and the reaction was stirred at 50°C for 45 min and a further 2 hr under nitrogen flow. The precipitate was collected by vacuum filtration and washed with cold dichloromethane, the crude product was further dried *in vacuo*

*N-({[4-(pentafluoro-λ⁶-sulfanyl)phenyl]carbamoyl}amino)ethoxyformamide (**3a**)*



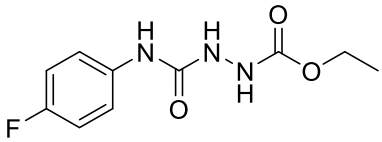
Compound **3a** was obtained as a white solid (620 mg, 1.78 mmol, 88%). Calcd for $C_{10}H_{13}F_5N_3O_3S$ $[M+H]^+$ 350.0597, $[M+H]^+$ Found 350.0592; **^{1}H-NMR (DMSO**): δ 7.75 (d, J = 9.5 Hz, 2H), 7.65 (d, J = 8.5 Hz , 2H), 4.05 (q, J = 7, 14 Hz), 1.2 (t, J = 6.5 Hz) **^{13}C-NMR (DMSO):** 157.05, 155.50, 146.22, 146.06, 143.43, 126.79, 117.98, 60.80, 14.71; **^{19}F-NMR (DMSO):** δ 89.39 (q, J = 150.62, 1F), 64.20 (d, J = 150.62, Hz, 4F); **IR (KBr):** 3315 (w), 1703 (w), 1673 (w), 1565 (m), 1507 (w), 1237 (w), 1105 (w), 840 (m), 810 (s) cm^{-1}

*N-({[4-(trifluoromethyl)phenyl]carbamoyl}amino)ethoxyformamide (**3b**)*



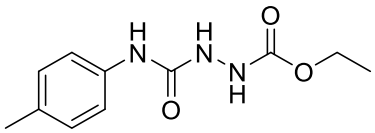
Compound **3b** was obtained as a white solid (462 mg, 1.59 mmol, 78%). **HRMS (EI)** Calcd for $C_{11}H_{13}F_3N_3O_3$ $[M+H]^+$ 292.0909, $[M+H]^+$ Found 292.0903; **^{1}H-NMR (DMSO**): δ 7.67 (br s, 2H), 7.59 (d, 2H, J = 10 Hz); **^{13}C-NMR (DMSO):** δ 156.91, 155.40, 143.55, 128.55, 125.92, 125.88, 123.23, 122.29, 121.98, 121.66, 121.34, 120.54, 118.15, 60.60, 14.53; **^{19}F-NMR (DMSO):** δ -60.13 (s); **IR (KBr):** 3302 (w), 1701 (w), 1671 (w), 1612 (w), 1559 (w), 1509 (w), 1410 (w), 1325 (m), 1231 (m), 1159 (m), 1108 (s), 1067 (s), 1012 (w), 844 (s) cm^{-1}

*N-({[4-fluorophenyl]carbamoyl}amino)ethoxyformamide (**3c**)*



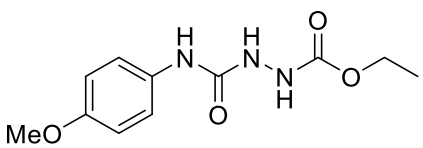
Compound **3c** was obtained as a white solid (382 mg, 1.59 mmol, 79%). **HRMS (EI)** Calcd for $C_{10}H_{13}FN_3O_3$ $[M+H]^+$ 242.0940, $[M+H]^+$ Found 242.0938; **^{1}H-NMR (DMSO**): δ 7.47 (d, J = 3.5 Hz , 2H); 7.08 (d, J = 8.5 Hz, 2H), 4.06 (q, J = 7, 14 Hz, 2H), 1.19 (t, J = 7 Hz, 3H); **^{13}C-NMR (DMSO):** δ 158.48, 156.92, 156.13, 155.68, 152.70, 136.03, 136.01, 135.97, 120.23, 120.02, 119.94, 115.34, 115.12, 114.91, 60.49, 14.52; **^{19}F-NMR (DMSO):** δ -121.61; **IR (KBr):** 3274 (s), 2983 (w), 1735 (s) 1682 (s) 1559 (s), 1505 (s), 1410 (w), 1320 (w), 1233 (s), 1207 (s), 1053 (w), 1023 (w), 848 (s), 788 (m) cm^{-1}

*N-({phenyl carbamoyl}amino)ethoxyformamide (**3d**)*



Compound **3d** was obtained as a tan brown solid (362 mg, 1.62 mmol, 81%). **HRMS (EI)** Calcd for $C_{10}H_{14}N_3O_3$ $[M+H]^+$ 224.1035, $[M+H]^+$ Found 224.1031 **^{1}H-NMR (DMSO**): δ 7.45 (d, J = 7.5 Hz, 2H), 7.24 (t, 7.5 Hz, 2H), 6.94 (t, J = 7.5 Hz, 2H), 4.06 (q, 7, 14 Hz, 3H), 1.19 (t, J = 6.5 Hz, 3H); **^{13}C-NMR (DMSO):** δ 157.13, 155.75, 139.86, 128.95, 128.76, 121.97, 118.62, 118.43, 60.67, 14.72; **IR (KBr):** 3300 (m), 3259 (m), 2980 (s), 1744 (s), 1595 (s), 1554 (s), 1442 (m), 1317 (w), 1226 (s), 1202 (s), 1053 (m), 741 (s), 695 (s) cm^{-1}

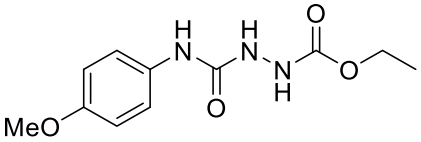
*N-({[4-methylphenyl]carbamoyl}amino)ethoxyformamide (**3e**)*



Compound **3e** was obtained as a white solid (245 mg, 1.03 mmol, 51%). **HRMS (EI)** Calcd for $C_{11}H_{16}N_3O_3$ $[M+H]^+$ 238.1191, $[M+H]^+$ Found 238.1192; **^{1}H-NMR (DMSO**): δ 7.33 (d, J = 8 Hz, 2H), 7.04 (d, J = 8 Hz, 2H), 4.05 (q, J = 7.5, 14.5 Hz, 2H), 2.22 (s, 3H), 1.19 (t, J = 6.5 Hz, 3H); **^{13}C-NMR (DMSO):** δ 157.15, 155.78, 137.27, 130.75, 129.15, 118.74, 60.65, 20.48, 14.73; **IR (KBr):**

3315 (m), 3267 (m), 2987 (w), 2905 (w), 1742 (s), 1682 (m), 1640 (m), 1597 (s), 1550 (s), 1515 (s) 1304 (m), 1202 (s), 825 (s), 663 (s) cm^{-1}

*N-({[4-methoxyphenyl]carbamoyl}amino)ethoxyformamide (**3f**)*

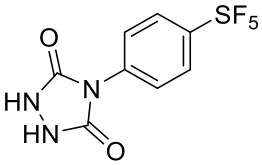


Compound **3f** was obtained as a white solid (219 mg, 0.86 mmol, 43%). **HRMS (EI)** Calcd for $C_{11}H_{16}N_3O_4$ $[M+H]^+$ 254.1140, $[M+H]^+$ Found 254.1131; **^{1}H-NMR (DMSO**): δ 7.35 (d, J = 9 Hz, 2H), 6.83 (d, J = 7 Hz, 2H), 4.04 (q, J = 10, 20 Hz, 2H), 3.70 (s, 3H), 1.19 (t, J = 6.5 Hz, 3H); **^{13}C-NMR (DMSO):** 156.98, 155.80, 154.41, 132.72, 120.72, 120.28, 113.78, 60.47, 55.13, 14.55; **IR (KBr):** 3278 (m), 2978 (m), 1736 (s), 1682 (m), 1640 (m), 1597 (s), 1556 (s), 1513 (s), 1455 (w), 1295 (m) 1231 (s), 1187 (s), 834 (s), 756 (m), 665 (m) cm^{-1}

General procedure for synthesis of phenyl-1,2,4-triazolidine-3,5-dione's derivatives (4a-f)

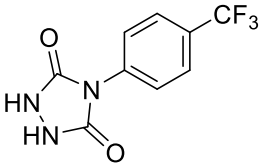
A 100mL RBF is charged 4M potassium hydroxide (10mL) and *N*-({[4-(pentafluoro-λ⁶-sulfanyl)phenyl]carbamoyl}amino)ethoxyformamide **(**517 mg, 1.5 mmol). The suspension was refluxed at 100^{o}C until the solid had completely dissolved, at which point the reaction was left for an additional hour and the solution was filtered. Upon cooling to room temperature, the solution was acidified *via* the dropwise addition of concentrated hydrochloric acid. The precipitate was isolated *via* vacuum filtration and the mother liquor was concentrated *in vaccuo*. The subsequent residue was extracted twice with hot ethanol (2x10 mL) and the combined organic layers were then filtered, concentrated *in vaccuo* and lyophilised.

*4-[4-(pentafluoro-λ⁶-sulfanyl)phenyl]-1,2,4-triazolidine-3,5-dione (**4a**)*



Compound **4a** was obtained as a white solid (410 mg, 1.34 mmol, 90%). **HRMS (EI)** Calcd for $C_8H_7N_3O_2SF_5$ $[M+H]^+$ 304.0179, $[M+H]^+$ Found 304.0178; **^{1}H-NMR (DMSO**): δ 8.04 (d, J = 7.5 Hz, 2H), 7.81 (d, J = 9 Hz, 2H); **^{13}C-NMR (DMSO):** δ 152.58, 150.92, 150.76, 135.67, 126.75, 126.71, 125.79; **^{19}F-NMR (DMSO):** δ 86.95 (q, J = 86.48, 1F), 64.27 (d, J = 150.4 Hz, 4F); **IR (KBr):** 3052 (w), 1697 (m), 1507 (w), 1220 (w), 1107 (m), 834 (s), 747 (s)

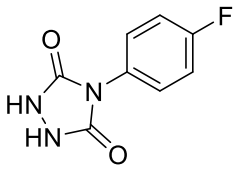
*4-[4-(trifluoromethyl)phenyl]-1,2,4-triazolidine-3,5-dione (**4b**)*



Compound **4d** was obtained as a pale yellow solid (304 mg, 1.24 mmol, 82%). **HRMS (EI)** Calcd for $C_9H_7F_3N_3O_2$ $[M+H]^+$ 246.0490, $[M+H]^+$ Found 246.0496; **^{1}H-NMR (DMSO**): δ 7.86 (d, 2H, J = 10 Hz), 7.77 (d, 2H, J = 10 Hz); **^{13}C-NMR (DMSO):** δ 152.77, 135.92, 127.82, 126.07, 125.98,

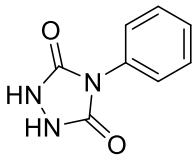
122.82; **^{19}F-NMR (DMSO):** δ 60.96 (s, 1F) ; **IR (KBr):** 3063 (w), 1697 (s, br), 1615 (w), 1420 (s), 1319 (s) 1174 (s), 1120 (s), 1069 (m), 1021 (w), 848 (m), 790 (w), 762 (m) cm^{-1}

*4-[4-(fluoro)phenyl]-1,2,4-triazolidine-3,5-dione (**4c**)*



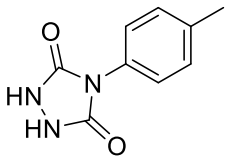
Compound **4c** was obtained as a white solid (190 mg, 0.97 mmol, 65%). **HRMS (EI)** Calcd for $C_8H_7FN_3O_2$ $[M+H]^+$ 196.0522, $[M+H]^+$ Found 196.0527; **^{1}H-NMR (DMSO**): δ 7.49 (br s, 2H), 7.31 (t, J = 10.5, 20.5 Hz, 2H); **^{13}C-NMR (DMSO):** δ 162.23, 159.91, 153.46, 128.40, 115.98; **^{19}F-NMR (DMSO):** δ -114.04; **IR (KBr):** 3207 (w), 3160 (w), 3088 (w), 1682 (s), 1602 (w), 1511 (s), 1436 (m), 1215 (s), 1155 (w), 1116 (w), 1086 (w), 844 (s), 790 (s), 758 (s) cm^{-1}

*4-phenyl-1,2,4-triazolidine-3,5-dione (**4d**)*



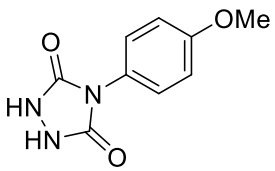
Compound **4d** was obtained as a brown crystalline solid (133 mg, 0.78 mmol, 78%). **HRMS (EI)** Calcd for $C_8H_8N_3O_2$ $[M+H]^+$ 178.0617, $[M+H]^+$ Found 178.0614; **^{1}H-NMR (DMSO**): δ 7.50-7.36 (5H); **^{13}C-NMR (DMSO):** δ 153.53, 132.09, 128.97, 127.78, 126.24; **IR (KBr):** 3151 (w), 3103 (w) 3054 (w), 1777 (s, br), 1679 (w), 1597 (m), 1504 (m), 1436 (w), 1220 (s), 1177 (s), 1116 (m), 911 (w), 892 (m), 756 (m), 689 (s, br) cm^{-1}.

*4-[4-(methyl)phenyl]-1,2,4-triazolidine-3,5-dione (**4e**)*



Compound **4e** was obtained as a white crystalline solid (209 mg, 1.1 mmol, 73%). **HRMS (EI)** Calcd for $C_9H_{10}N_3O_2$ $[M+H]^+$ 192.0773, $[M+H]^+$ Found 192.0773; **^{1}H-NMR (DMSO**): δ 7.31 (d, 8 Hz, 2H), 7.27 (d, 8.5 Hz, 2H), 2.34 (s, 3H); **^{13}C-NMR (DMSO):** δ 153.75, 137.30, 129.47, 129.44, 126.14, 20.86; **IR (KBr):** 3097 (w), 3170 (w), 3062 (w), 1697 (s), 1615 (w), 1522 (w), 1420 (br m), 1321 (s), 1174 (s), 1120 (s), 848 (m), 792 (m), 762 (m) cm^{-1}

*4-[4-(methoxy)phenyl]-1,2,4-triazolidine-3,5-dione (**4f**)*



Compound **4f** was obtained as a brown crystalline solid (208 mg, 1 mmol, 67%). **HRMS (EI)** Calcd for $C_9H_9N_3O_3$ $[M+H]^+$ 208.0722, $[M+H]^+$ Found 208.0726; **^{1}H-NMR (DMSO)**: δ 6.52 (d, J = 10 Hz, 2H), 6.22 (d, J = 10 Hz, 2H), 3.02 (s, 3H); **^{13}C-NMR (DMSO):** δ 158.49, 153.75, 127.64, 124.48, 114.04, 53.37; **IR (KBr):** 3227 (br s), 1766 (w), 1673 (br s), 1608 (m), 1507 (s), 1444 (m), 1241 (m), 1215 (w), 1170 (w), 1116 (w), 834 (s), 786 (s), 762 (s) cm^{-1}.

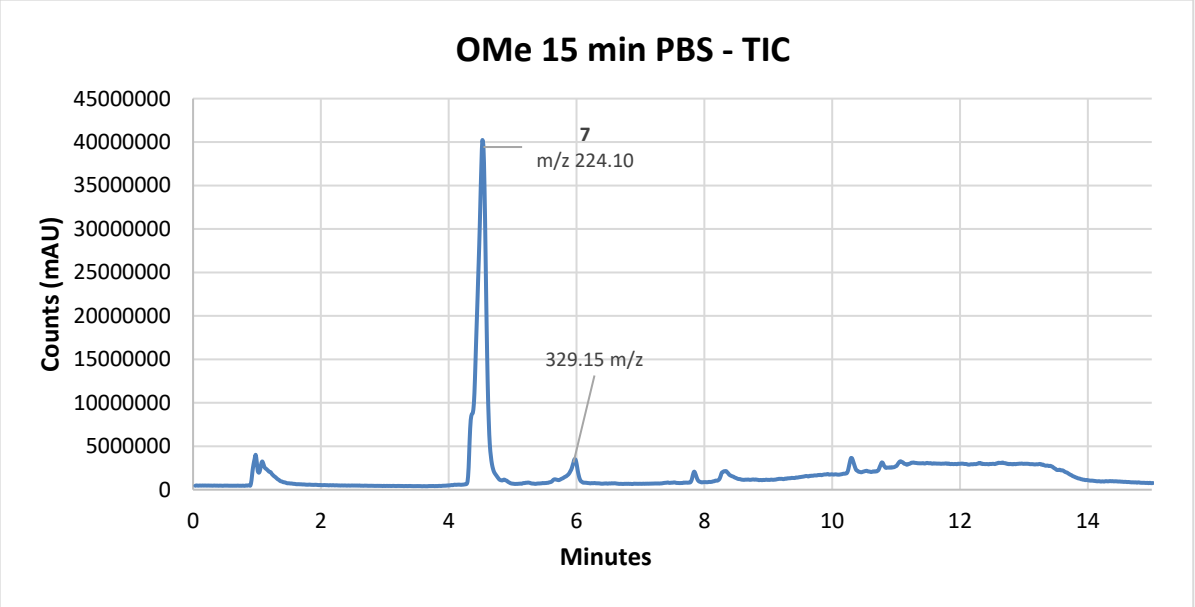


Figure S1. TIC chromatogram of **6f** after 15 minutes reaction time in phosphate-buffered saline, representative of the reaction being performed under aqueous conditions as previously reported in the literature

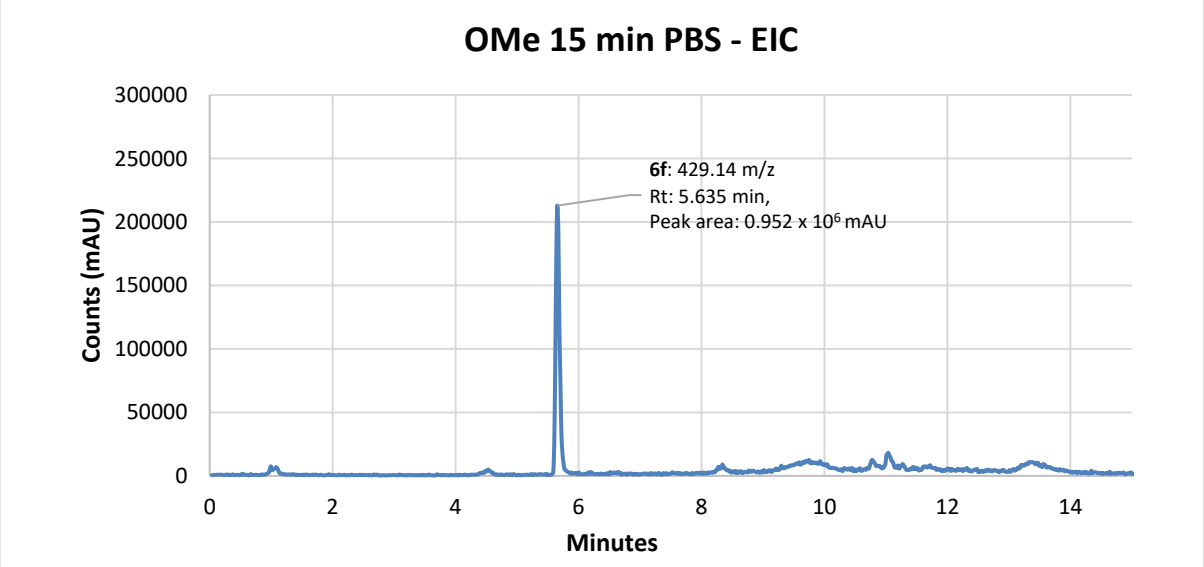


Figure S2. EIC chromatogram of **6f** after 15 minutes reaction time in phosphate-buffered saline, representative of the reaction being performed under aqueous conditions as previously reported in the literature with relatively low conversion

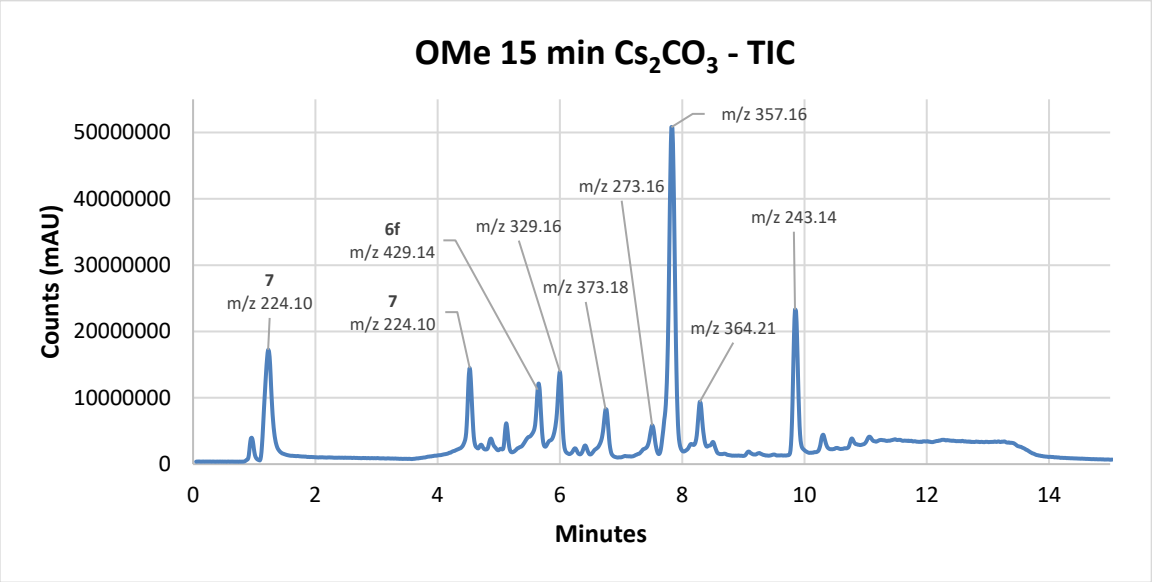


Figure S3. TIC chromatogram of **6f** after 15 minutes reaction time in acetonitrile and caesium carbonate (2 equiv.), representative of synthetic scale reaction performed under Condition **A**

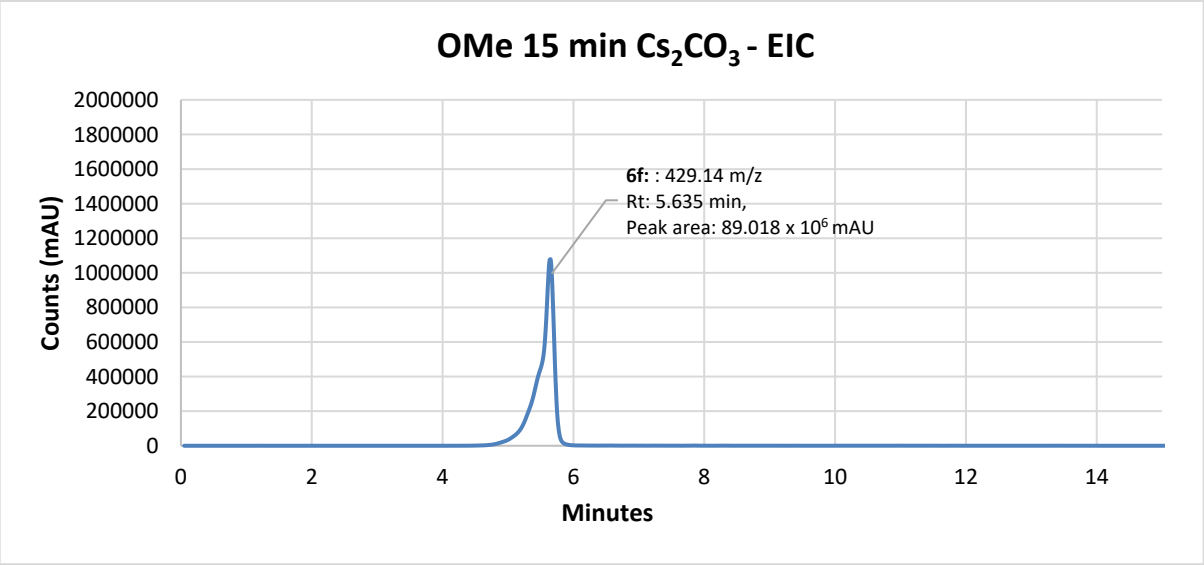


Figure S4. TIC chromatogram of **6f** after 15 minutes reaction time in acetonitrile and caesium carbonate (2 equiv.), representative of synthetic scale reaction performed under Condition **A.** Despite obtaining the highest mAU reading in the LC-MS catalytic study, this reaction gave numerous by-products and >5% **6f** on a synthetic scale.

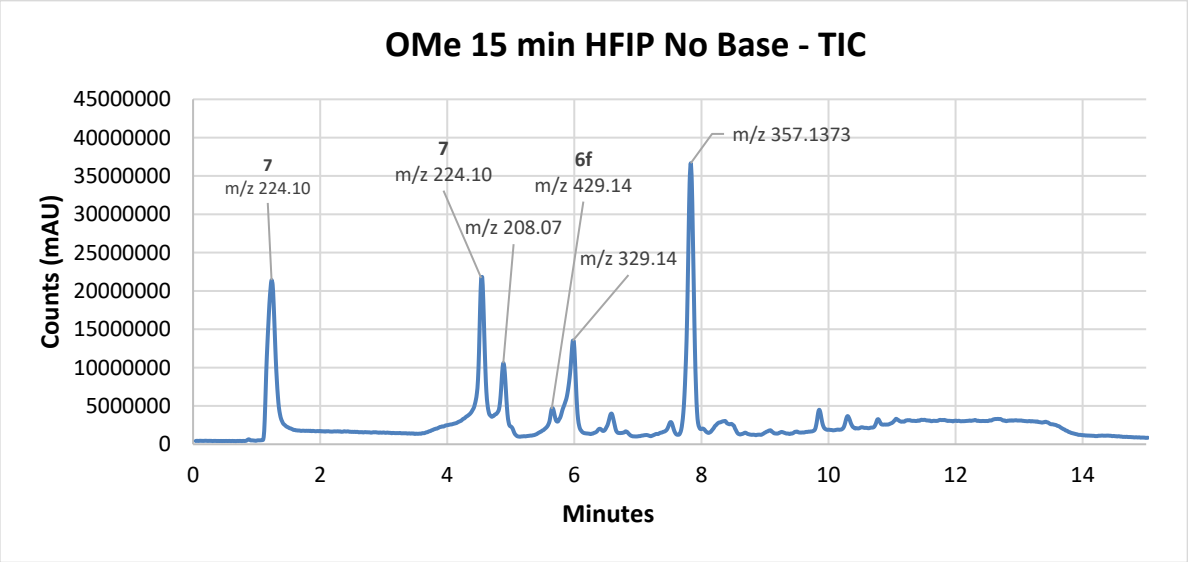


Figure S5. TIC chromatogram of **6f** after 15 minutes reaction time in acetonitrile and HFIP (2 equiv.), representative of synthetic scale reaction performed under Condition **A.** Despite obtaining the highest mAU reading in the LC-MS catalytic study, this reaction proceeded slowly on a synthetic scale.

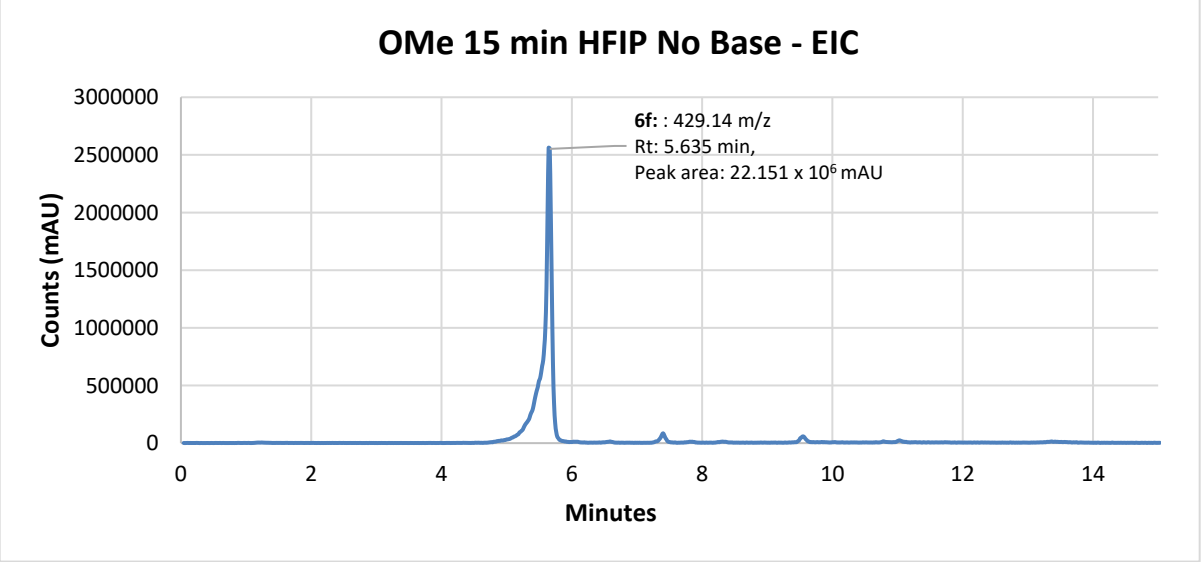


Figure S6. EIC chromatogram of **6f** after 15 minutes reaction time in acetonitrile and HFIP (2 equiv.), representative of synthetic scale reaction performed under Condition **A.** Despite obtaining a relatively high mAU reading in the LC-MS catalytic study, this reaction proceeded slowly on a synthetic scale.

Table S3: The three conditions tested on a synthetic scale based on results obtained from LC-MS catalytic experiments. Condition A: **5a** decomposed rapidly to give numerous by-products and < 5% yield of **6a**, Condition B: Reaction was very slow (> 12 hrs), rendering it unsuitable for the purposes of bioconjugation, Condition C: Reaction proceeded rapidly with minimal by-product formation.

Reaction (6a)	Conditions	Yield (%)
A	MeCN, Cs_2CO_3 (2 equiv.)	< 5
B	MeCN, HFIP (2 equiv.)	No reaction
C	DCM, HFIP (2 equiv.)	54

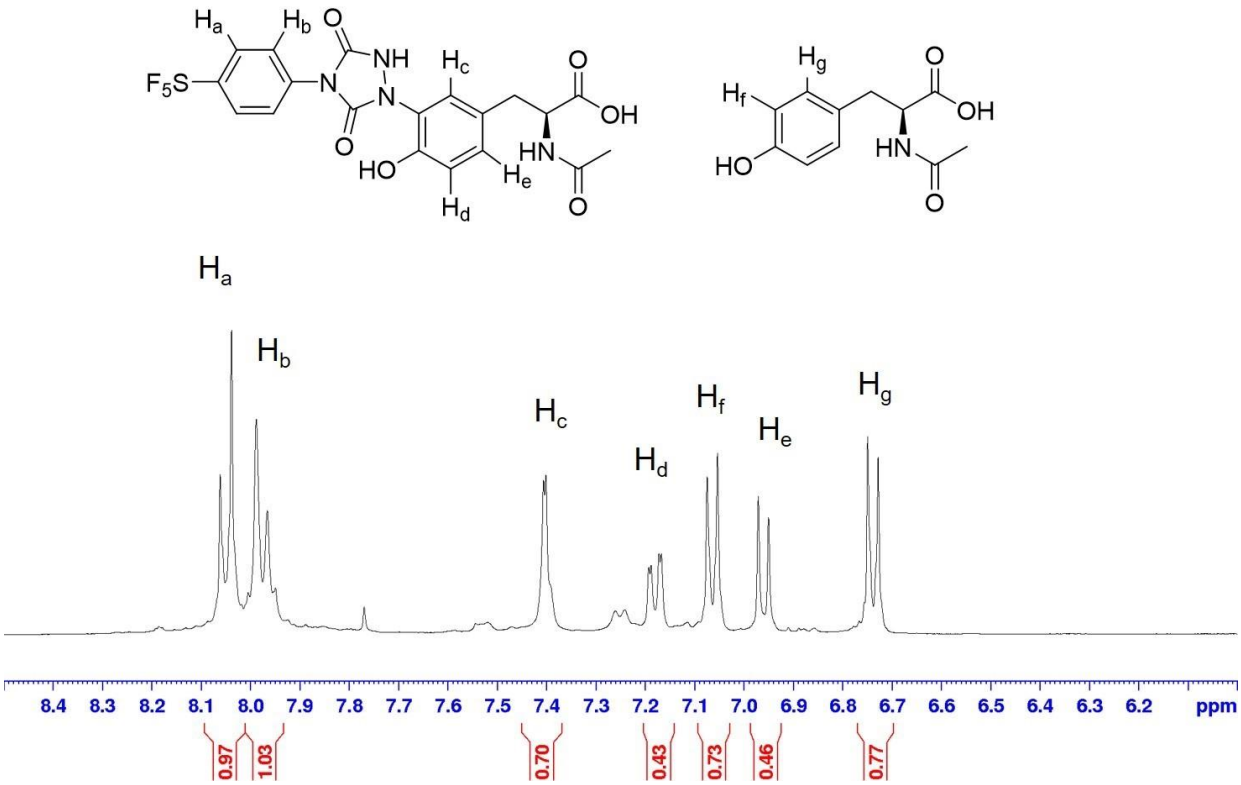
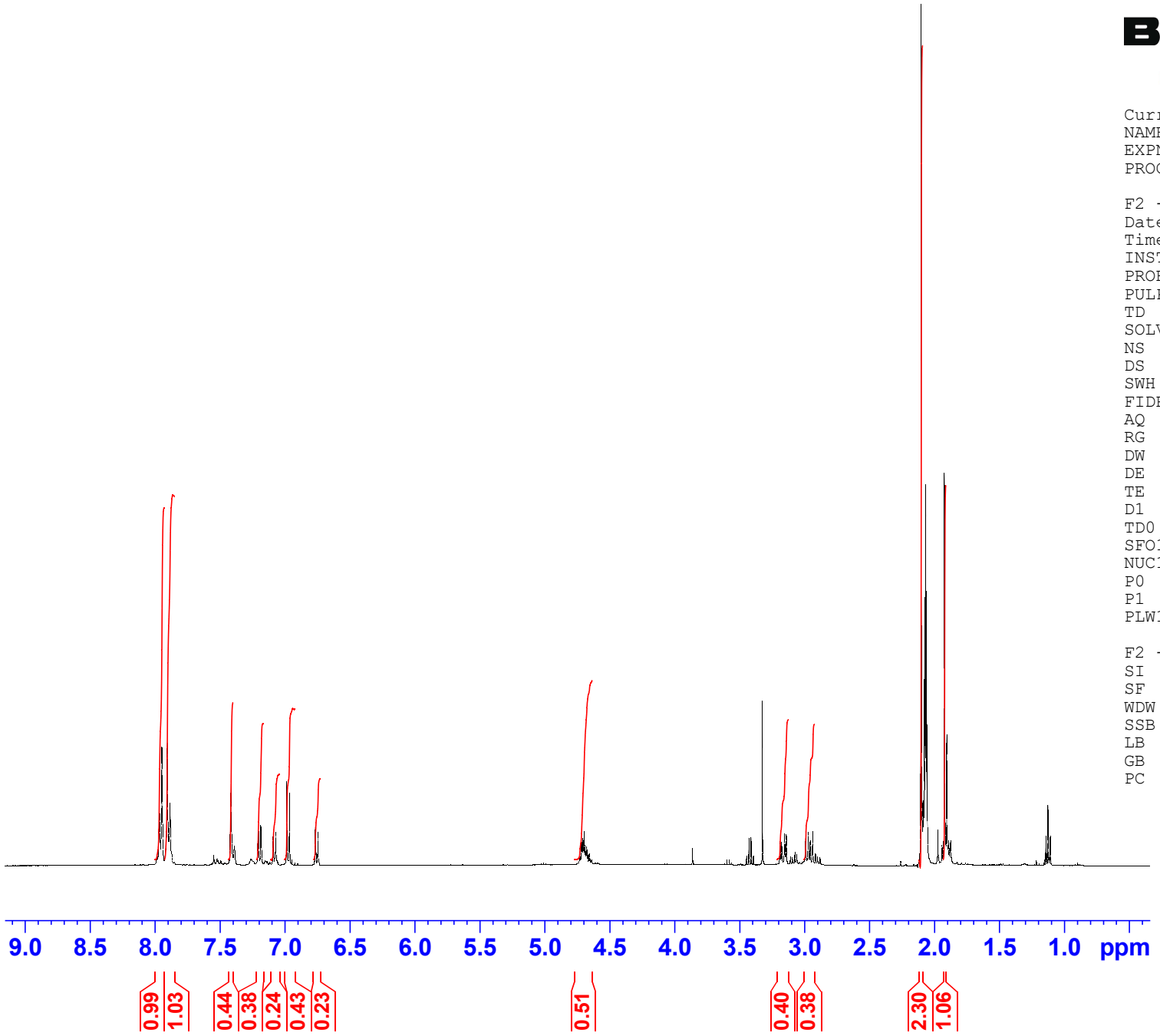


Figure S7: Example ^{1}H-NMR spectra of the crude product **6a** used for calculation of molar conversion using relative integration of aromatic peaks (H_e/H_g)

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TE                298.0 K
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P1                10.00 usec
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F2 - Processing parameters
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WDW                   EM
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GB                     0
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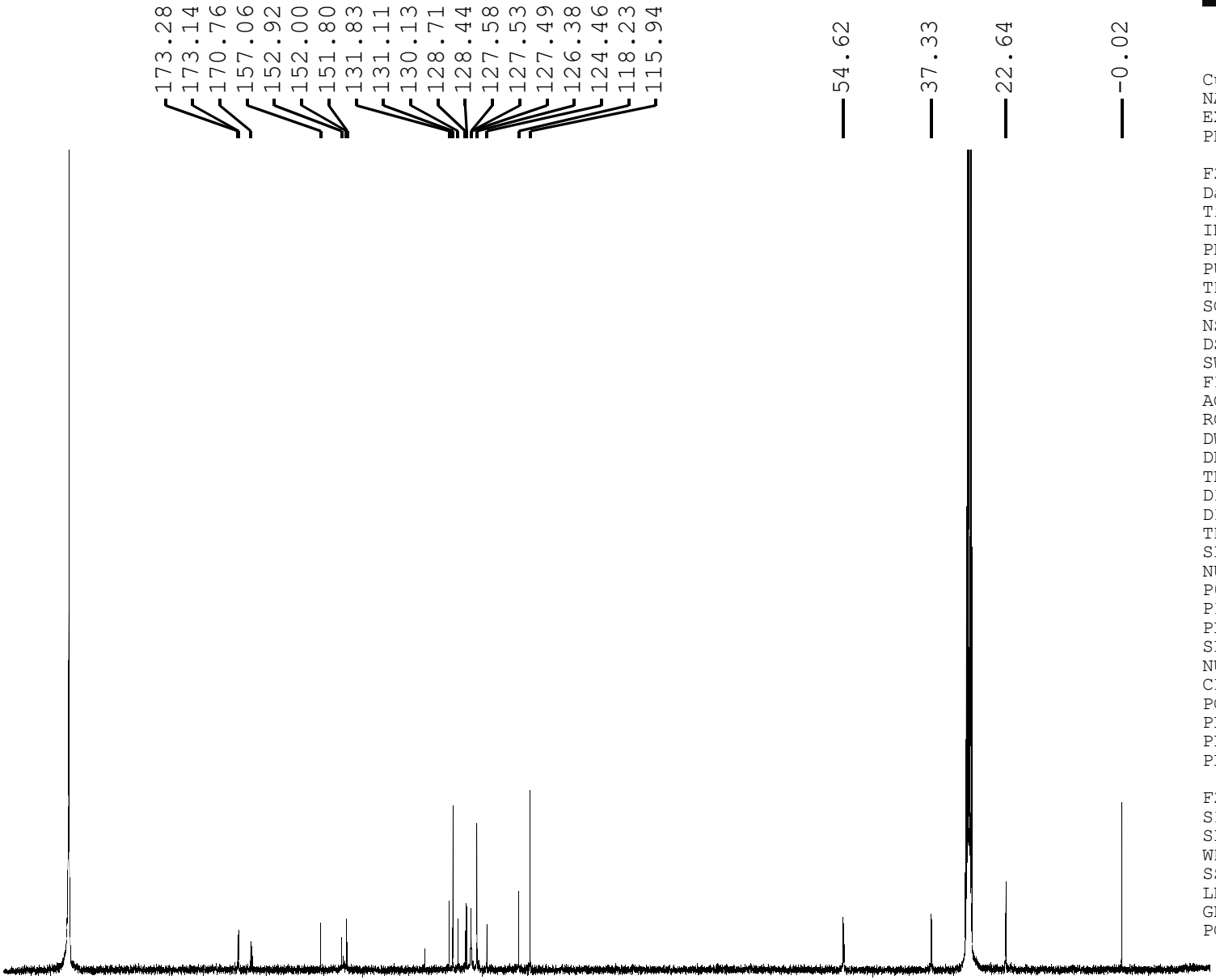
Figure S8. The ^{1}H NMR (400 MHz, $(CD_3)_2CO$) of compound **6a**

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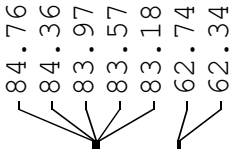
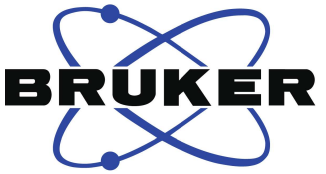
TD0                   1
SFO1        100.6278593 MHz
NUC1                13C
P0                3.33 usec
P1               10.00 usec
PLW1         58.38199997 W
SFO2         400.1516006 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2         19.63299942 W
PLW12         0.24237999 W
PLW13         0.12192000 W

F2 - Processing parameters
SI                 32768
SF          100.6177093 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

Figure S9. The ^{13}C NMR (100 MHz, $(CD_3)_2CO$) of compound **6a.**






```
Current Data Parameters
NAME          Jul04-2022
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220707
Time               1.38 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG              zg
TD               131072
SOLVENT         Acetone
NS                   128
DS                     4
SWH           147058.828 Hz
FIDRES          2.243940 Hz
AQ              0.4456448 sec
RG                   101
DW                 3.400 usec
DE                 6.50 usec
TE                 298.0 K
D1            1.00000000 sec
TD0                    1
SFO1         376.5171850 MHz
NUC1                 19F
P1                12.00 usec
PLW1         45.00000000 W

F2 - Processing parameters
SI                 65536
SF           376.5171850 MHz
WDW                  EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

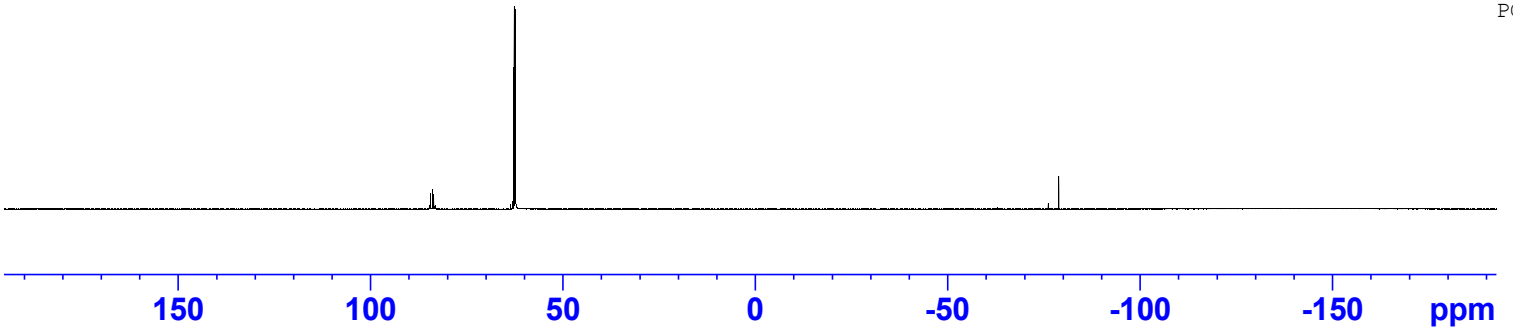
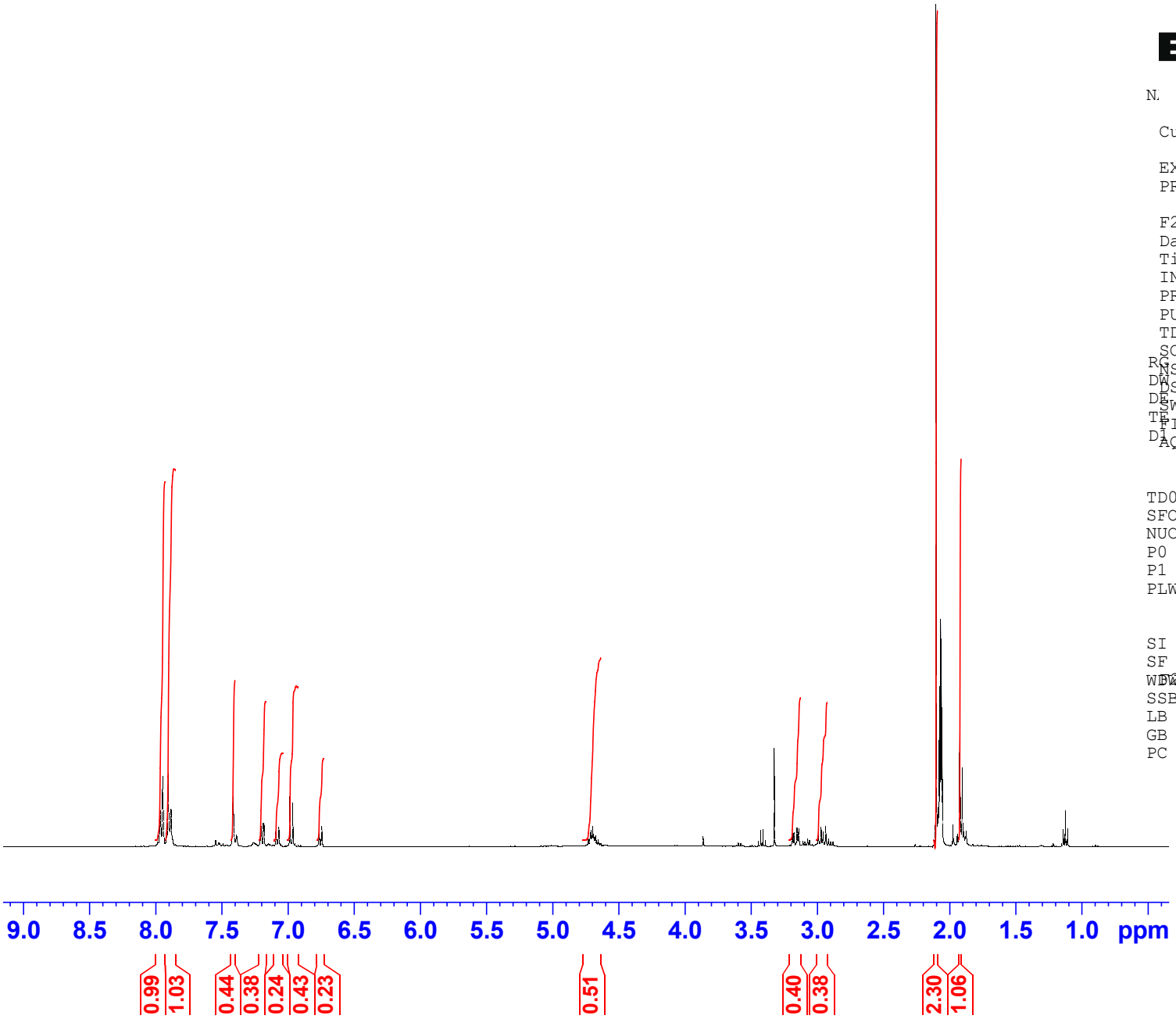


Figure S10. The ^{19}F NMR (376.5 MHz, $(CD_3)_2CO$) of compound **6a**.

CF3 PTAD Conj. - 20% HFIP/DCM

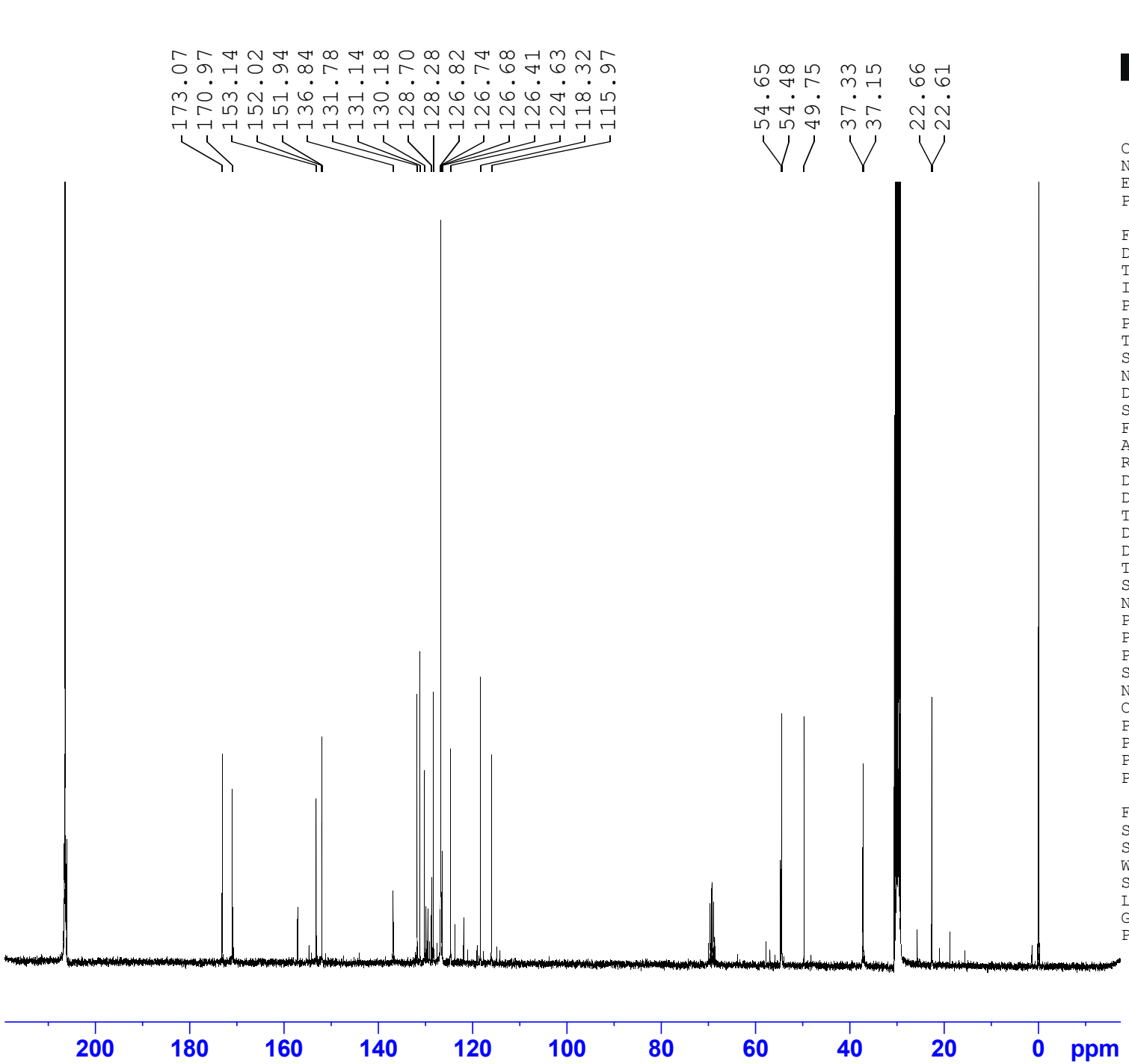



```
N.

 Current Data Parameters
              Jul04-2022
 EXPNO                15
 PROCNO                1

 F2 - Acquisition Parameters
 Date_          20220705
 Time               9.30 h
 INSTRUM           AVNEO
 PROBHD   Z175272_0008 (
 PULPROG            zg30
 TD               131072
 SOLVENT         Acetone
RG
 NS                   32
DW
 DS                    2
DE
 SWH            8196.722 Hz
TE
 FIDRES         0.125072 Hz
D1
 AQ             7.9953918 sec
                     101
                61.000 usec
TD0                13.54 usec
SFO1               298.0 K
NUC1           1.00000000 sec
P0                    1
P1             400.1524709 MHz
PLW1                 1H
                3.33 usec
               10.00 usec
SI             19.63299942 W
SF
WDW - Processing parameters
SSB                65536
LB             400.1500000 MHz
GB                    EM
PC                    0
                0.30 Hz
                      0
                   1.00
```

Figure S11. The ^{1}H NMR (400 MHz, $(CD_3)_2CO$) of compound **6b**

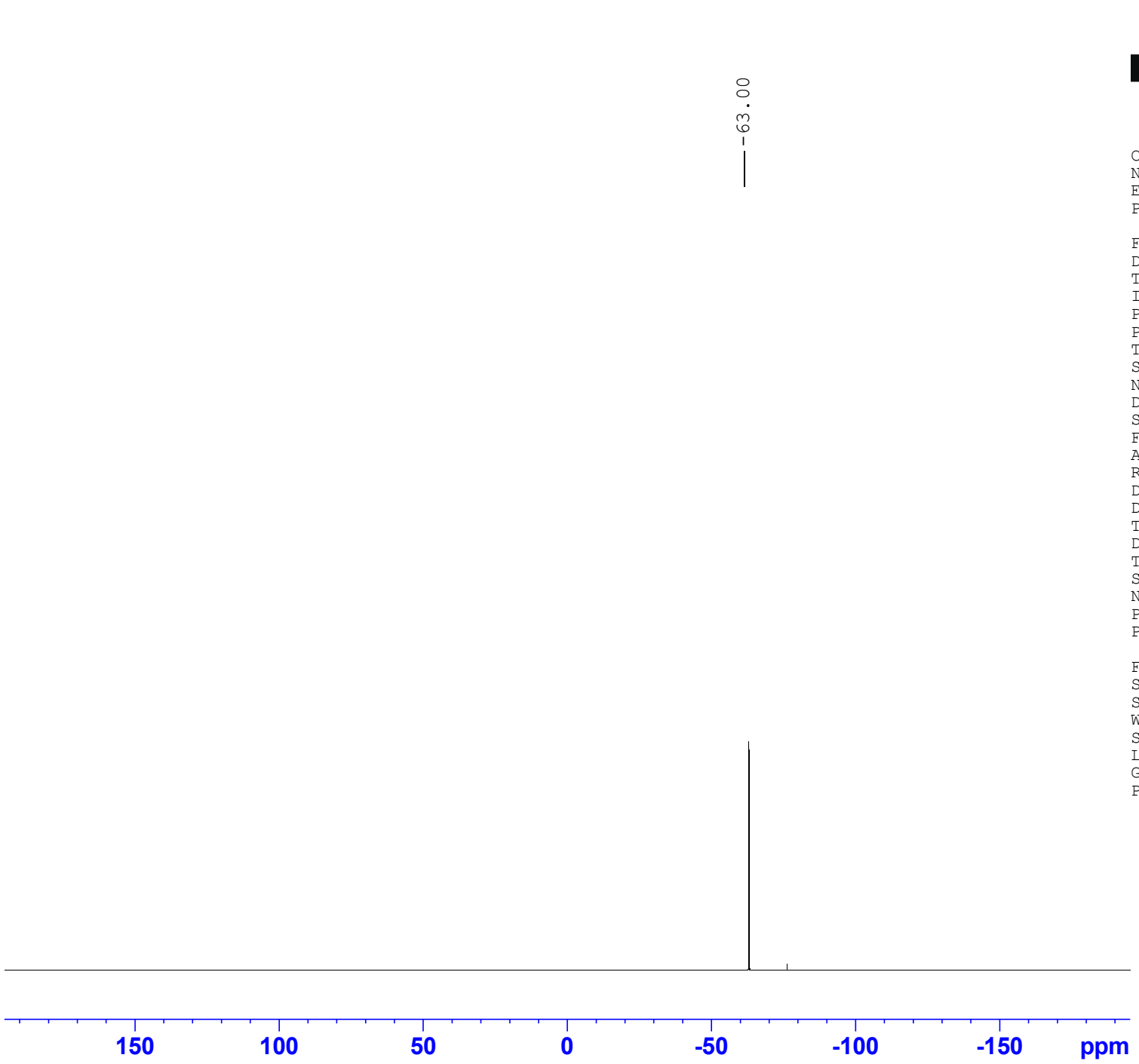



```
Current Data Parameters
NAME          Jun30-2022
EXPNO                  8
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220702
Time                7.26 h
INSTRUM             AVNEO
PROBHD   Z175272_0008 (
PULPROG           zgpg30
TD                131072
SOLVENT          Acetone
NS                  3600
DS                     4
SWH            23809.523 Hz
FIDRES          0.363304 Hz
AQ              2.7525120 sec
RG                   101
DW                21.000 usec
DE                 6.50 usec
TE                298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1         100.6278593 MHz
NUC1                13C
P0                 3.33 usec
P1                10.00 usec
PLW1          58.38199997 W
SFO2         400.1516006 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2          19.63299942 W
PLW12          0.24237999 W
PLW13          0.12192000 W

F2 - Processing parameters
SI                 32768
SF           100.6177078 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

Figure S12. The ^{13}C NMR (100.6 MHz, $(CD_3)_2CO$) of compound **6b**



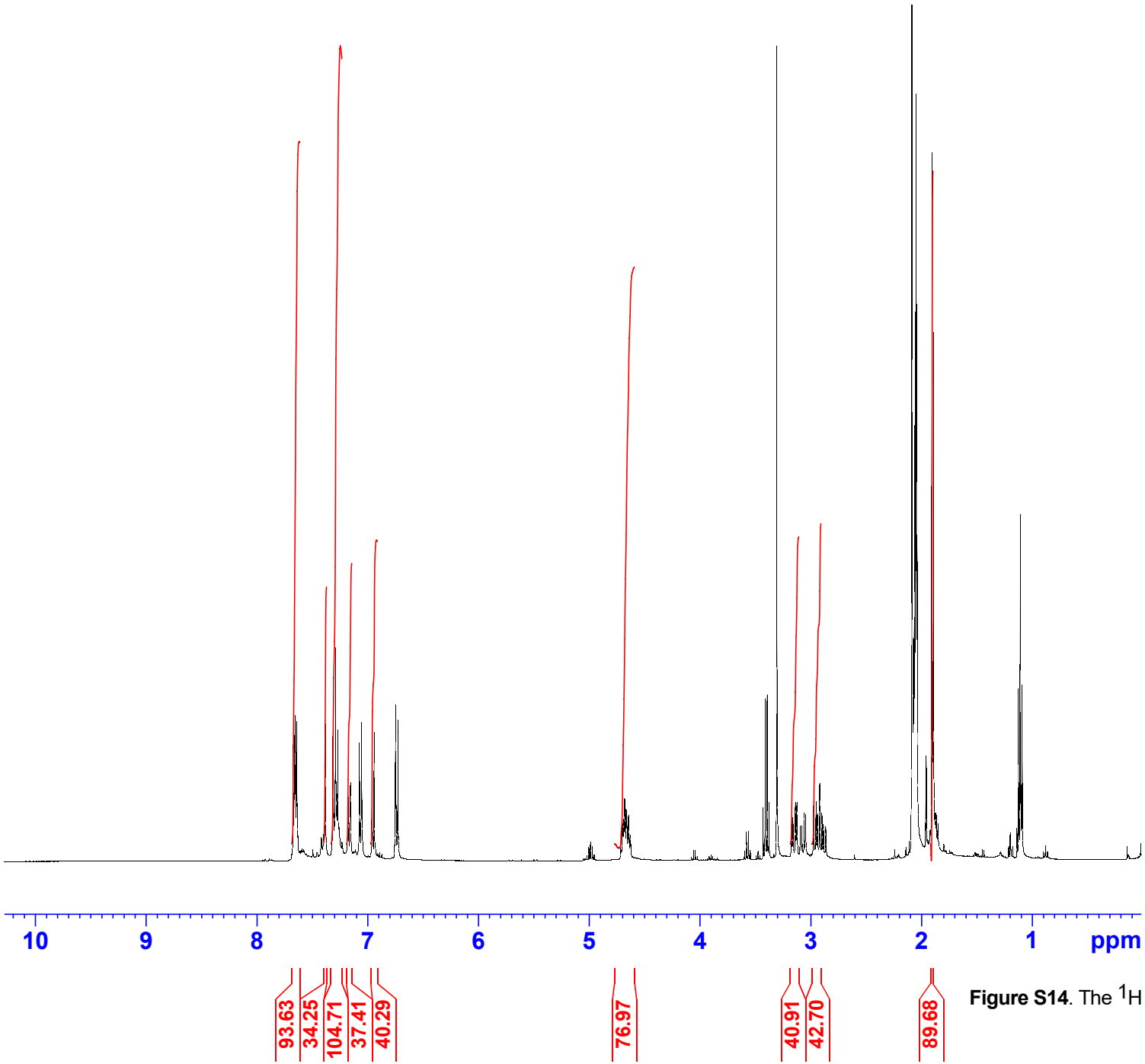

```
Current Data Parameters
NAME          Jul04-2022
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220706
Time               5.11 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG              zg
TD               131072
SOLVENT         Acetone
NS                   128
DS                     4
SWH           147058.828 Hz
FIDRES          2.243940 Hz
AQ              0.4456448 sec
RG                   101
DW                 3.400 usec
DE                 6.50 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1
SFO1          376.5171850 MHz
NUC1                 19F
P1                12.00 usec
PLW1          45.00000000 W

F2 - Processing parameters
SI                 65536
SF          376.5171850 MHz
WDW                  EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                 1.00
```

Figure S13 The ^{19}F NMR (376.5 MHz, $(CD_3)_2CO$) of compound **6b**.

F PTAD Conj. - 20% HFIP/DCM



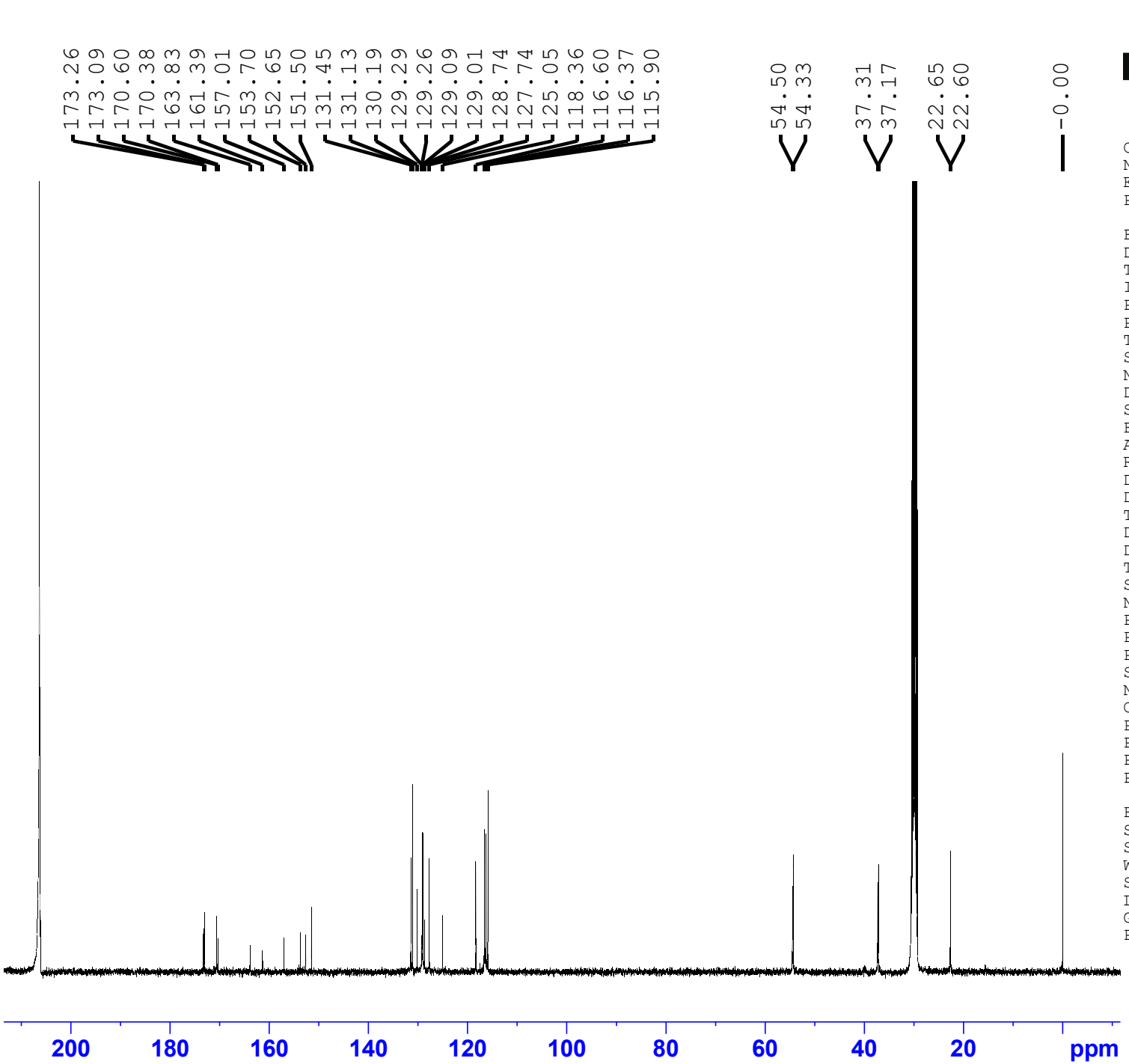

```
Current Data Parameters
NAME          Jul04-2022
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220705
Time               9.19 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG             zg30
TD                131072
SOLVENT          Acetone
NS                    32
DS                     2
SWH             8196.722 Hz
FIDRES          0.125072 Hz
AQ             7.9953918 sec
RG                   101
DW                61.000 usec
DE                13.54 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1524709 MHz
NUC1                1H
P0                 3.33 usec
P1                10.00 usec
PLW1         19.63299942 W

F2 - Processing parameters
SI                 65536
SF           400.1500067 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

Figure S14. The ^{1}H NMR (400 MHz, $(CD_3)_2CO$) of compound **6c**

F PTAD Conj.

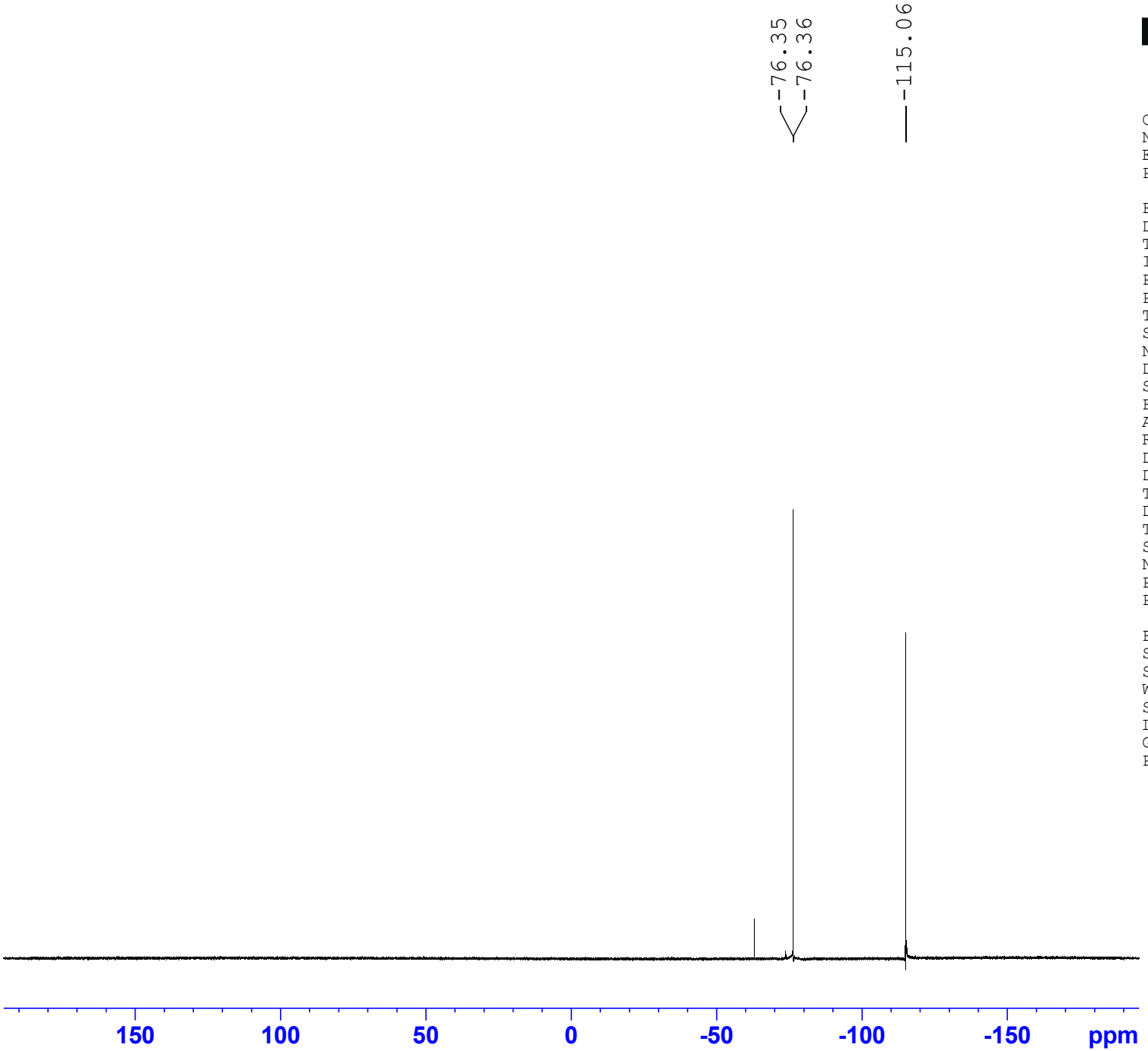



```
Current Data Parameters
NAME          Aug22-2022
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220823
Time               3.41 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG           zgpg30
TD                65536
SOLVENT          H2O+D2O
NS                 3000
DS                    4
SWH           23809.523 Hz
FIDRES         0.726609 Hz
AQ            1.3762560 sec
RG                  101
DW               21.000 usec
DE                6.50 usec
TE                298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6278593 MHz
NUC1                13C
P0                3.33 usec
P1               10.00 usec
PLW1         58.38199997 W
SFO2         400.1516006 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2         19.63299942 W
PLW12         0.24237999 W
PLW13         0.12192000 W

F2 - Processing parameters
SI                 32768
SF          100.6179757 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                  1.40
```

Figure S15. The ^{13}C NMR (100.6 MHz, $(CD_3)_2CO$) of compound **6c**



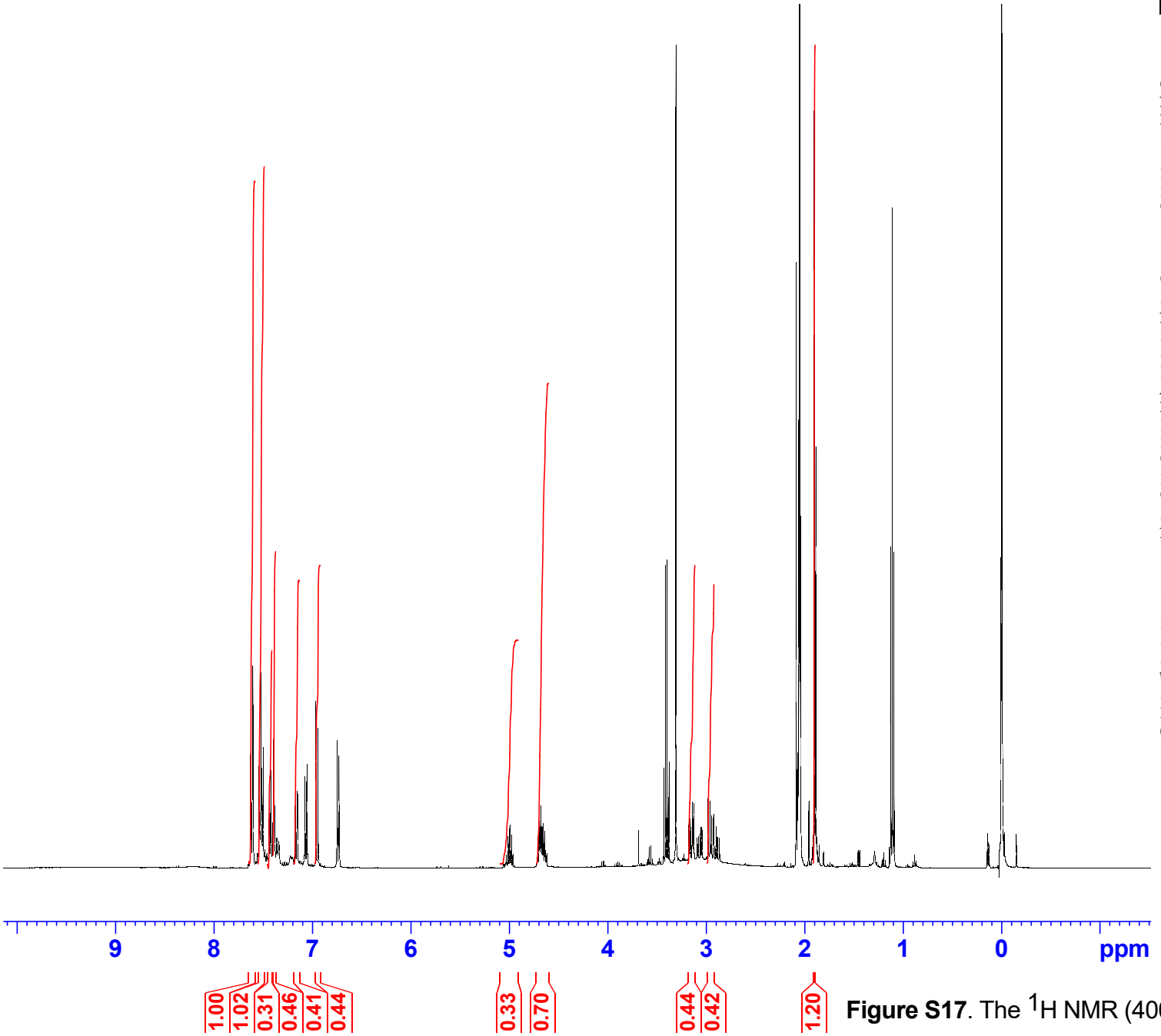

```
Current Data Parameters
NAME          Jul04-2022
EXPNO                 14
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220706
Time               1.49 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG              zg
TD               131072
SOLVENT         Acetone
NS                   128
DS                     4
SWH           147058.828 Hz
FIDRES          2.243940 Hz
AQ              0.4456448 sec
RG                   101
DW                 3.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1         376.5171850 MHz
NUC1                 19F
P1                12.00 usec
PLW1         45.00000000 W

F2 - Processing parameters
SI                 65536
SF           376.5171957 MHz
WDW                  EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Figure S16. The ^{19}F NMR (376.5 MHz, $(CD_3)_2CO$) of compound **6c**

H PTAD Conj. - 20% HFIP/DCM



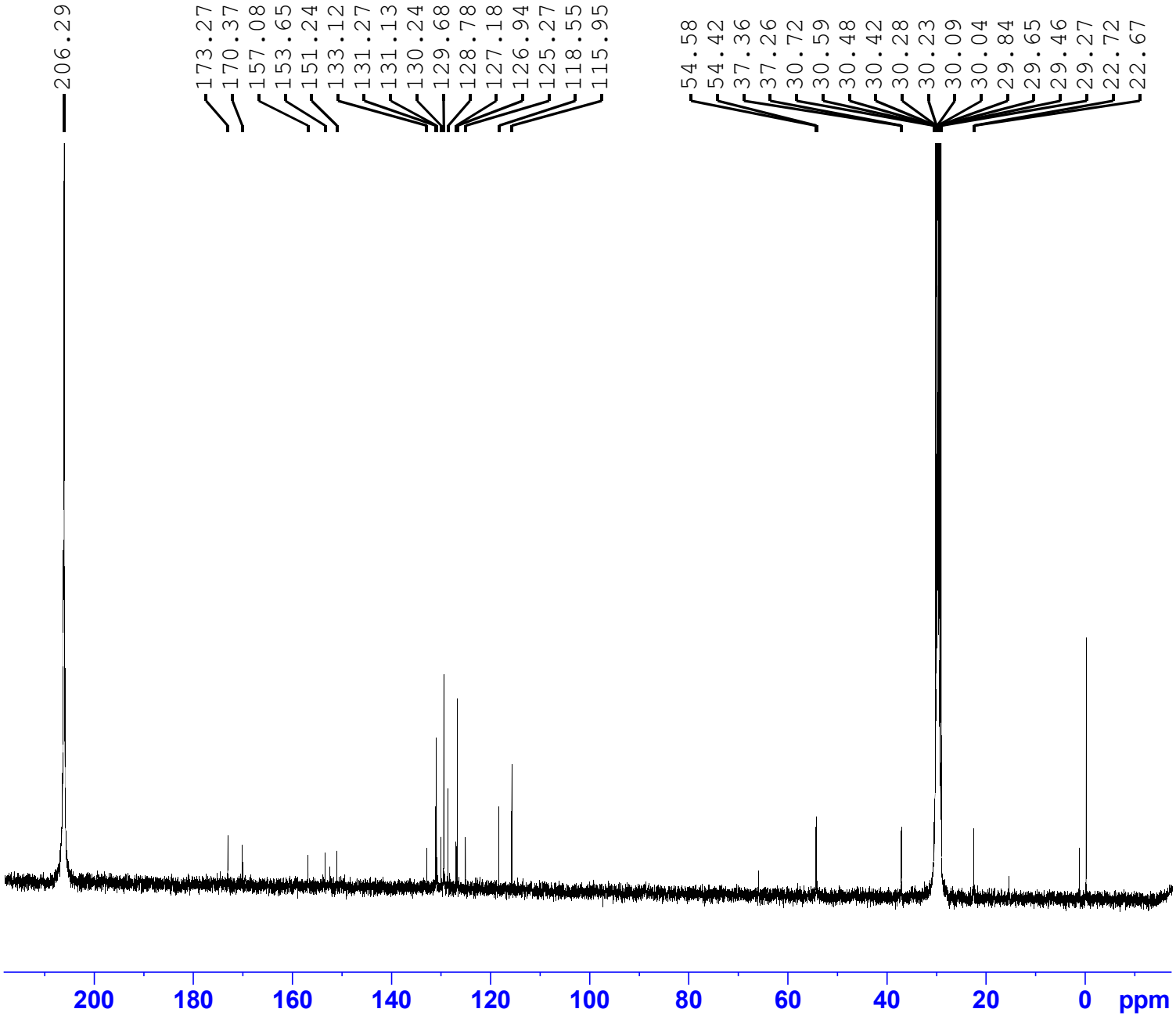
Current Data Parameters
NAME Jul04-2022
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220705
Time 9.08 h
INSTRUM AVNEO
PROBHD Z175272_0008 (
PULPROG zg30
TD 131072
SOLVENT Acetone
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.125072 Hz
AQ 7.9953918 sec
RG 101
DW 61.000 usec
DE 13.54 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1524709 MHz
NUC1 1H
P0 3.33 usec
P1 10.00 usec
PLW1 19.63299942 W

F2 - Processing parameters
SI 65536
SF 400.1500067 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Figure S17. The ^{1}H NMR (400 MHz, $(CD_3)_2CO$) of compound **6d**

H PTAD Conj.

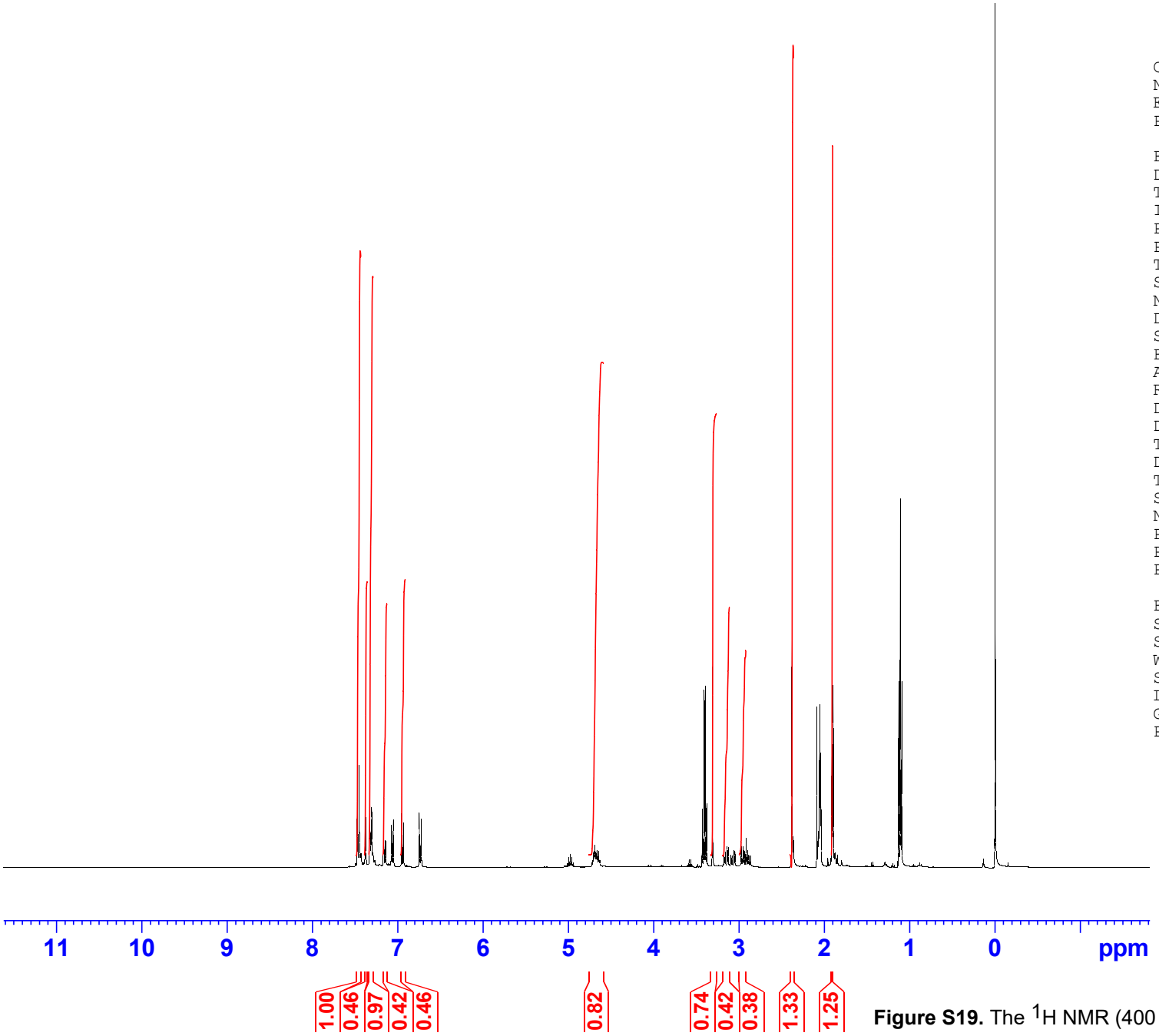



```
Current Data Parameters
NAME          Aug22-2022
EXPNO                  9
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220825
Time               4.48 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG          zgpg30
TD                65536
SOLVENT         Acetone
NS                 3600
DS                    4
SWH           23809.523 Hz
FIDRES         0.726609 Hz
AQ             1.3762560 sec
RG                  101
DW               21.000 usec
DE                6.50 usec
TE                298.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1        100.6278593 MHz
NUC1                13C
P0                3.33 usec
P1               10.00 usec
PLW1         58.38199997 W
SFO2        400.1516006 MHz
NUC2                1H
CPDPRG[2        waltz65
PCPD2             90.00 usec
PLW2         19.63299942 W
PLW12         0.24237999 W
PLW13         0.12192000 W

F2 - Processing parameters
SI                32768
SF          100.6177074 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

Figure S18. The ^{13}C NMR (100.6 MHz, $(CD_3)_2CO$) of compound **6d**



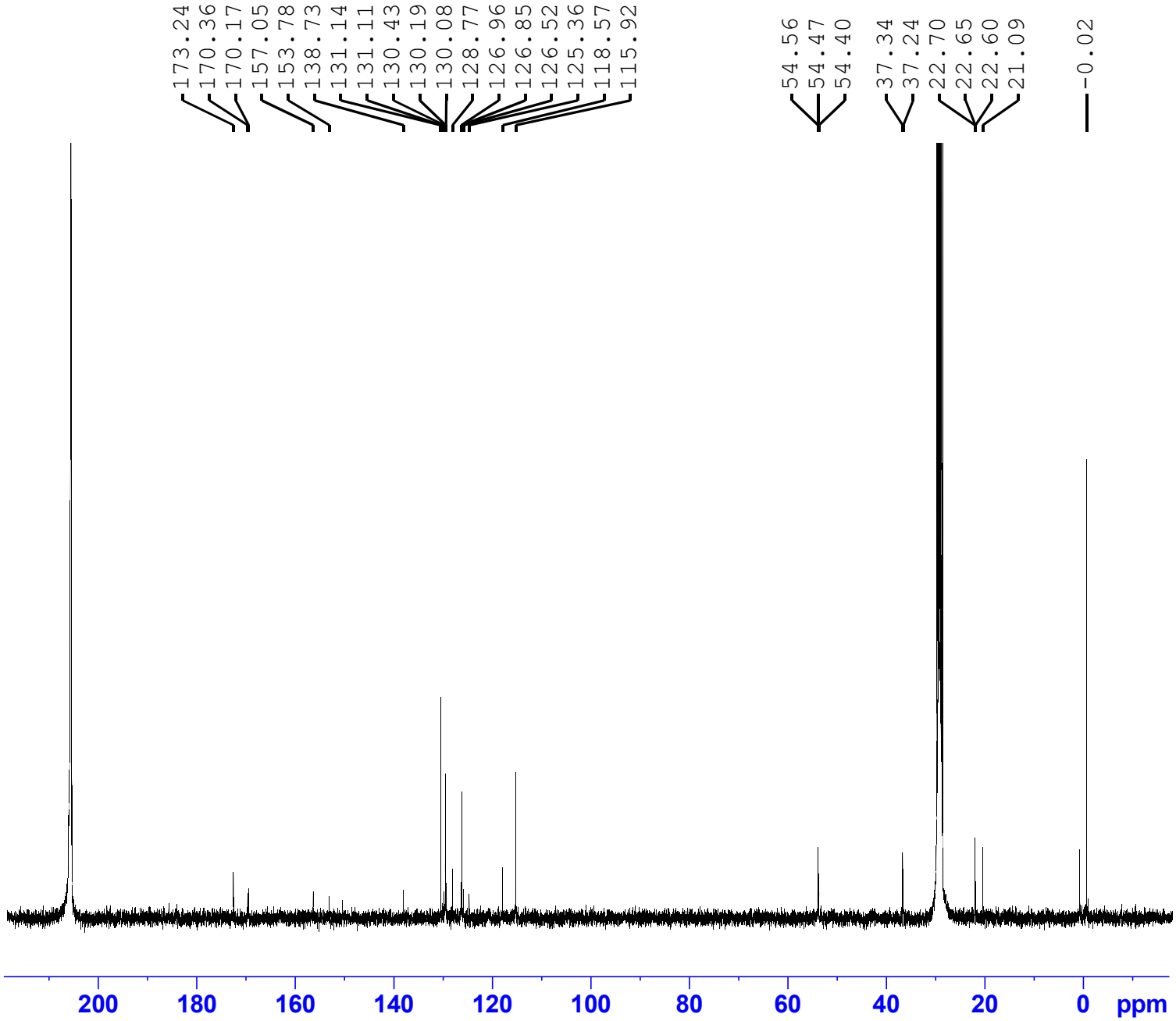

```
Current Data Parameters
NAME          Jul04-2022
EXPNO                  8
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220705
Time              19.13 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG             zg30
TD                131072
SOLVENT          Acetone
NS                    32
DS                     2
SWH             8196.722 Hz
FIDRES          0.125072 Hz
AQ             7.9953918 sec
RG                  71.8
DW                61.000 usec
DE                13.54 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1524709 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         19.63299942 W

F2 - Processing parameters
SI                 65536
SF           400.1500067 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Figure S19. The ^{1}H NMR (400 MHz, $(CD_3)_2CO$) of compound **6e**

CH3 PTAD Conj.

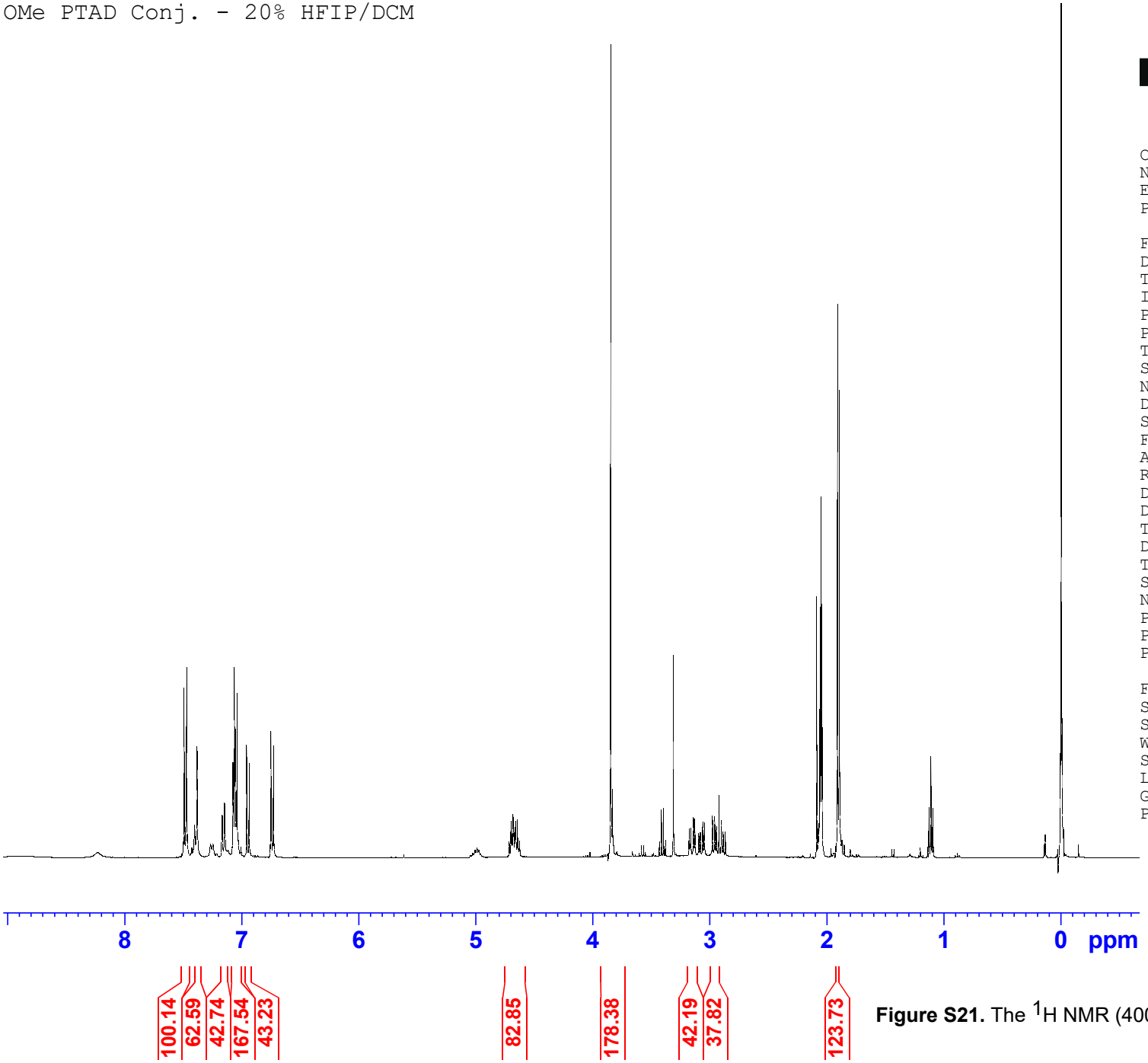



```
Current Data Parameters
NAME          Aug22-2022
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220823
Time              21.59 h
INSTRUM             AVNEO
PROBHD   Z175272_0008 (
PULPROG           zgpg30
TD                65536
SOLVENT          Acetone
NS                 3000
DS                    4
SWH           23809.523 Hz
FIDRES         0.726609 Hz
AQ            1.3762560 sec
RG                  101
DW               21.000 usec
DE                6.50 usec
TE                298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6278593 MHz
NUC1                13C
P0                3.33 usec
P1               10.00 usec
PLW1         58.38199997 W
SFO2        400.1516006 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2         19.63299942 W
PLW12         0.24237999 W
PLW13         0.12192000 W

F2 - Processing parameters
SI                 32768
SF          100.6177093 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

Figure S20. The ^{13}C NMR (100.6 MHz, $(CD_3)_2CO$) of compound **6e**



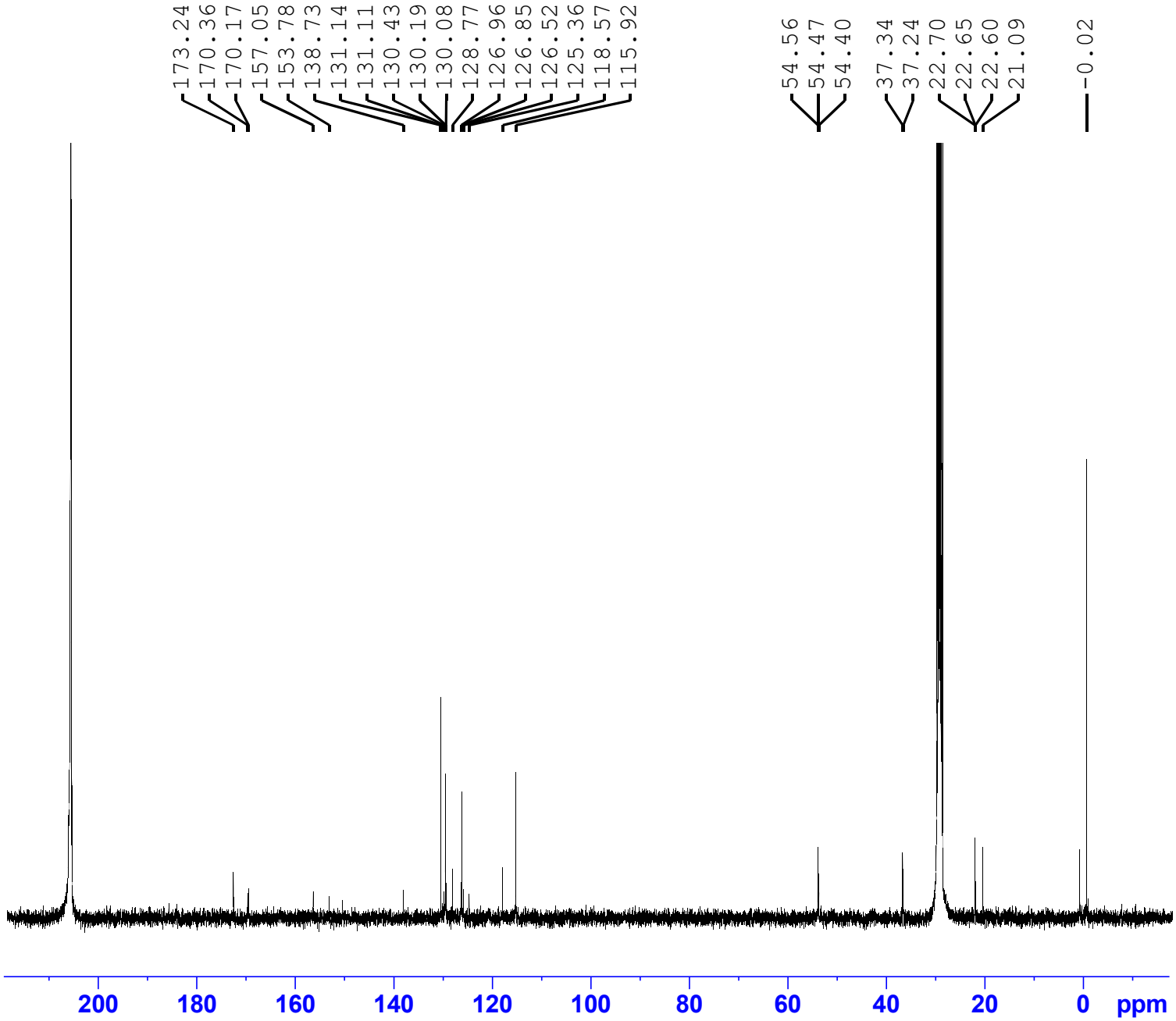

```
Current Data Parameters
NAME          Jul04-2022
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220705
Time               8.44 h
INSTRUM            AVNEO
PROBHD   Z175272_0008 (
PULPROG             zg30
TD                131072
SOLVENT          Acetone
NS                    32
DS                     2
SWH             8196.722 Hz
FIDRES          0.125072 Hz
AQ             7.9953918 sec
RG                   101
DW                61.000 usec
DE                13.54 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1524709 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         19.63299942 W

F2 - Processing parameters
SI                 65536
SF           400.1500067 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

Figure S21. The ^{1}H NMR (400 MHz, $(CD_3)_2CO$) of compound **6f**

CH3 PTAD Conj.




```
Current Data Parameters
NAME          Aug22-2022
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220823
Time              21.59 h
INSTRUM             AVNEO
PROBHD   Z175272_0008 (
PULPROG           zgpg30
TD                65536
SOLVENT          Acetone
NS                 3000
DS                    4
SWH           23809.523 Hz
FIDRES         0.726609 Hz
AQ            1.3762560 sec
RG                  101
DW               21.000 usec
DE                6.50 usec
TE                298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6278593 MHz
NUC1                13C
P0                3.33 usec
P1               10.00 usec
PLW1         58.38199997 W
SFO2        400.1516006 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2         19.63299942 W
PLW12         0.24237999 W
PLW13         0.12192000 W

F2 - Processing parameters
SI                 32768
SF          100.6177093 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

Figure S22. The ^{13}C NMR (100.6 MHz, $(CD_3)_2CO$) of compound **6e**