# Design, synthesis, and biological evaluation of quinoline-8-sulfonamides as inhibitors of the tumor cell specific M2 isoform of pyruvate kinase

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**Table S1.** Interaction of compounds **9a–e** with target proteins

| Protein | | Ligand | | Interaction | |
|---|---|---|---|---|---|
| Name | Residue | Name | Residue | Type | Distance [Å] |
| **G1N** | A:Tyr390 | **9a** | Sulfonamide oxygen | Conventional hydrogen bond | 1.76 |
| | B:Lys311 | | Triazole nitrogen | Conventional hydrogen bond | 2.67 |
| | A:Leu353 | | Sulfonamide nitrogen | Conventional hydrogen bond | 2.42 |
| | A:Ile389 | | Sulfonamide oxygen | Carbon hydrogen bond | 2.75 |
| | A:Asp354 | | Pyridine ring C2 | Carbon hydrogen bond | 2.29 |
| | B:Asp354 | | Pyridine ring C2′ | Carbon hydrogen bond | 2.82 |
| | A:Met30 | | Triazole ring | π-Sulfur | 4.07 |
| | A:Phe26 | | Benzene ring | π-Sulfur | 5.89 |
| | A:Phe26 | | Benzene ring | π-π- Stacked | 5.36 |
| | A:Phe26 | | Pyridine ring | π-π T-shaped | 5.94 |
| | A:Phe26 | | Benzene ring | π-π T-shaped | 4.53 |
| | A:Phe26 | | Benzene ring | π-π T-shaped | 5.18 |
| | A:Phe26 | | Pyridine ring | π-π T-shaped | 5.13 |
| | A:Leu27 | | Chlorine atom | Alkyl | 4.42 |
| | B:Leu394 | | Chlorine atom | Alkyl | 5.43 |
| | A:Leu394 | | Benzene ring | π-Alkyl | 4.44 |
| | A:Leu394 | | Pyridine ring | π-Alkyl | 4.87 |
| | B:Leu27 | | Pyridine ring | π-Alkyl | 5.36 |
| | B:Met30 | | Pyridine ring | π-Alkyl | 5.49 |
| | A:Leu353 | | Triazole ring | π-Alkyl | 4.41 |
| | A:Met30 | | Benzene ring | π-Alkyl | 5.13 |
| | A:Met30 | | Pyridine ring | π-Alkyl | 4.12 |
| | A:Tyr390 | **9b** | Sulfonamide oxygen | Conventional hydrogen bond | 1.97 |
| | A:Leu353 | | Sulfonamide oxygen | Carbon hydrogen bond | 2.58 |
| | A:Ile389 | | Sulfonamide oxygen | Carbon hydrogen bond | 2.35 |
| | A:Leu353 | | Pyridine ring C2 | Carbon hydrogen bond | 2.70 |
| | A:Asp354 | | Pyridine ring C2 | Carbon hydrogen bond | 2.27 |
| | B:Leu353 | | Ethyl group | Carbon hydrogen bond | 2.73 |
| | A:Phe26 | | Sulfonamide sulfur | π-Sulfur | 5.16 |
| | B:Phe26 | | Benzene ring | π-π T-shaped | 5.45 |
| | B:Phe26 | | Pyridine ring | π-π T-shaped | 5.14 |
| | B:Leu394 | | Ethyl group | Alkyl | 4.66 |
| | B:Leu394 | | Ethyl group | Alkyl | 4.87 |
| | A:Leu394 | | Benzene ring | π-Alkyl | 4.48 |
| | A:Leu394 | | Pyridine ring | π-Alkyl | 5.20 |
| | A:Met30 | | Triazole ring | π-Alkyl | 4.59 |
| | A:Leu353 | | Triazole ring | π-Alkyl | 5.44 |
| | B:Lys311 | | Triazole ring | π-Alkyl | 4.86 |
| | B:Lys311 | **9c** | Sulfonamide oxygen | Conventional hydrogen bond | 1.95 |
| | B:Leu394 | | Ester carbonyl oxygen | Carbon hydrogen bond | 2.42 |
| | A:Leu353 | | Benzene ring | π -Sigma | 2.47 |
| | A:Met30 | | Triazole ring | π -Sulfur | 4.82 |
| | A:Phe26 | | Triazole ring | π-π-Stacked | 3.16 |
| | A:Phe26 | | Benzene ring | π-π T-shaped | 4.80 |
| | B:Phe26 | | Triazole ring | π-π T-shaped | 5.38 |
| | A:Leu27 | | Ethyl group | Alkyl | 4.64 |

| | | | | | |
|---|---|---|---|---|---|
| | B:Leu394 | | Ethyl group | Alkyl | 5.44 |
| | A:Leu353 | | Pyridine ring | π-Alkyl | 3.97 |
| | B:Lys311 | **9d** | Sulfonamide oxygen | Conventional Hydrogen Bond | 1.83 |
| | A:Met30 | | Triazole ring | π-Sulfur | 4.95 |
| | A:Phe26 | | Triazole ring | π-π-Stacked | 3.33 |
| | A:Phe26 | | Benzene ring | π-π T-shaped | 5.01 |
| | A:Phe26 | | Pyridine ring | π-π T-shaped | 5.21 |
| | B:Phe26 | | Triazole ring | π-π T-shaped | 5.37 |
| | B:Ile389 | | Butyl group | Alkyl | 4.77 |
| | B:Leu394 | | Butyl group | Alkyl | 4.07 |
| | A:Leu353 | | Benzene ring | π-Alkyl | 3.79 |
| | A:Leu353 | | Pyridine ring | π-Alkyl | 4.37 |
| | A:Lys311 | **9e** | Ester carbonyl oxygen | Conventional hydrogen bond | 1.55 |
| | A:Leu353 | | Betuline C29′* | Carbon hydrogen bond | 2.01 |
| | A:Leu353 | | Betuline C29′ | Carbon hydrogen bond | 1.87 |
| | B:Asn350 | | Betuline C28′ | Carbon hydrogen bond | 2.16 |
| | A:Gln393 | | Sulfonamide methyl group | Carbon hydrogen bond | 2.32 |
| | A:Leu394 | | Pyridine ring | π-Sigma | 2.26 |
| | B:Met30 | | Triazole ring | π-Sulfur | 5.70 |
| | B:Met30 | | Benzene ring | π-Sulfur | 4.13 |
| | B:Met30 | | Pyridine ring | π-Sulfur | 5.67 |
| | B:Phe26 | | Sulfonamide sulfur | π-Sulfur | 5.76 |
| | B:Leu353 | | Betuline C15′ | Alkyl | 5.29 |
| | B:Leu394 | | Betuline C1′ | Alkyl | 5.45 |
| | A:Leu353 | | Betuline C21′ | Alkyl | 4.30 |
| | A:Leu27 | | Betuline C23′ | Alkyl | 4.84 |
| | B:Leu394 | | Betuline C23′ | Alkyl | 3.82 |
| | B:Leu394 | | Betuline C24′ | Alkyl | 3.02 |
| | B:Leu353 | | Betuline C25′ | Alkyl | 4.79 |
| | A:Met30 | | Betuline C27′ | Alkyl | 4.61 |
| | A:Leu353 | | Betuline C30′ | Alkyl | 3.44 |
| | A:Phe26 | | Betuline C1′ | π-Alkyl | 4.90 |
| | A:Phe26 | | Betuline C11′ | π-Alkyl | 4.81 |
| | B:Phe26 | | Betuline C12′ | π-Alkyl | 4.72 |
| | B:Phe26 | | Betuline C25′ | π-Alkyl | 4.35 |
| | B:Phe26 | | Betuline C26′ | π-Alkyl | 4.76 |
| | A:Leu394 | | Benzene ring | π-Alkyl | 4.88 |
| | B:Leu27 | | Benzene ring | π-Alkyl | 5.08 |
| **4FXF** | A:Arg120 | **9a** | Sulfonamide oxygen | Conventional hydrogen bond | 2.82 |
| | A:Arg120 | | Sulfonamide oxygen | Conventional hydrogen bond | 1.67 |
| | A:Lys207 | | Triazole nitrogen | Conventional hydrogen bond | 2.10 |
| | A:His78 | | Sulfonamide nitrogen | Conventional hydrogen bond | 2.73 |
| | A:Asp177 | | Pyridine ring C2 | Carbon hydrogen bond | 2.65 |
| | A:Asp178 | | Benzene ring | π-Anion | 3.21 |
| | A:Asp178 | | Pyridine ring | π-Anion | 2.64 |
| | A:His78 | | Sulfonamide sulfur | π-Sulfur | 5.74 |
| | A:His78 | | Triazole ring | π-π-Stacked | 3.29 |
| | A:His78 | | Pyridine ring | π-π-Stacked | 4.47 |
| | A:His78 | | Benzene ring | π-π-Stacked | 4.43 |
| | A:Tyr83 | | Chlorine atom | π-Alkyl | 4.41 |
| | A:Pro53 | | Pyridine ring | π-Alkyl | 5.19 |
| | A:Ala366 | | Pyridine ring | π-Alkyl | 4.66 |

| | | | | |
|---|---|---|---|---|
| A:Pro53 | | Benzene ring | π-Alkyl | 4.93 |
| A:Arg73 | **9b** | Phosphonate oxygen | Conventional hydrogen bond | 1.81 |
| A:Arg73 | | Phosphonate oxygen | Conventional hydrogen bond | 3.09 |
| A:Ser205 | | Sulfonamide oxygen | Conventional hydrogen bond | 3.03 |
| A:Ser205 | | Sulfonamide oxygen | Conventional hydrogen bond | 2.63 |
| A:Lys207 | | Sulfonamide oxygen | Carbon hydrogen bond | 2.15 |
| A:Arg120 | | Triazole ring | π-Cation | 4.00 |
| A:His78 | | Pyridine ring | π-π-Stacked | 3.62 |
| A:His78 | | Benzene ring | π-π-Stacked | 3.57 |
| A:His78 | | Triazole ring | π-π-Stacked | 5.30 |
| A:Ala293 | | Ethyl | Alkyl | 4.06 |
| A:Ala327 | | Ethyl | Alkyl | 4.34 |
| A:Met291 | | Ethyl | Alkyl | 4.76 |
| A:Met360 | | Ethyl | Alkyl | 5.24 |
| A:Phe244 | | Ethyl | π-Alkyl | 5.26 |
| A:Pro53 | | Pyridine ring | π-Alkyl | 5.44 |
| A:Ala366 | | Benzene ring | π-Alkyl | 4.83 |
| A:Arg73 | **9c** | Ester carbonyl oxygen | Conventional hydrogen bond | 2.09 |
| A:Arg73 | | Triazole nitrogen | Conventional hydrogen bond | 1.65 |
| A:Arg73 | | Ester carbonyl oxygen | Conventional hydrogen bond | 2.86 |
| A:Arg120 | | Ester oxygen | Conventional hydrogen bond | 2.73 |
| A:Lys207 | | Sulfonamide oxygen | Conventional hydrogen bond | 2.38 |
| A:His78 | | Sulfonamide nitrogen | Conventional hydrogen bond | 2.86 |
| A:Asn75 | | Ethyl group | Carbon hydrogen bond | 2.15 |
| A:Asp113 | | Ethyl group | Carbon hydrogen bond | 3.07 |
| A:Asp113 | | Ethyl group | Carbon hydrogen bond | 2.63 |
| A:His78 | | Sulfonamide sulfur | π-Sulfur | 4.43 |
| A:His78 | | Pyridine ring | π-π-Stacked | 3.97 |
| A:His78 | | Benzene ring | π-π-Stacked | 4.93 |
| A:Pro53 | | Pyridine ring | π-Alkyl | 5.19 |
| A:Pro53 | | Benzene ring | π-Alkyl | 4.62 |
| A:Ala366 | | Pyridine ring | π-Alkyl | 5.23 |
| A:Arg73 | **9d** | Triazole nitrogen | Conventional hydrogen bond | 2.70 |
| A:Arg73 | | Triazole nitrogen | Conventional hydrogen bond | 2.05 |
| A:Lys207 | | Sulfonamide oxygen | Conventional hydrogen bond | 1.72 |
| A:His78 | | Sulfonamide nitrogen | Conventional hydrogen bond | 2.02 |
| A:His78 | | Sulfonamide oxygen | Carbon hydrogen bond | 2.95 |
| A:His78 | | Methylene linker | Carbon hydrogen bond | 2.92 |
| A:His78 | | Benzene ring | π-π-Stacked | 3.14 |
| A:His78 | | Pyridine ring | π-π-Stacked | 3.80 |
| A:Phe244 | | Butyl group | π-Alkyl | 5.39 |
| A:Ala366 | | Pyridine ring | π-Alkyl | 4.77 |
| A:Lys367 | **9e** | Triazole nitrogen | Conventional hydrogen bond | 2.22 |
| B:Lys337 | | Sulfonamide oxygen | Carbon hydrogen bond | 2.89 |
| A:Thr129 | | Betuline C33′ | Carbon hydrogen bond | 2.20 |
| A:Lys367 | | Triazole nitrogen | Carbon hydrogen bond | 2.53 |
| A:Asp177 | | Betuline C29′ | Carbon hydrogen bond | 2.82 |
| A:Glu332 | | Betuline C29′ | Carbon hydrogen bond | 3.07 |
| A:Asp178 | | Betuline C28′ | Carbon hydrogen bond | 2.64 |
| A:Glu332 | | Triazole carbon | Carbon hydrogen bond | 2.71 |
| B:Lys337 | | Benzene ring | π-Cation | 3.55 |
| B:Lys337 | | Pyridine ring | π-Cation | 3.99 |

| | | | | |
|---|---|---|---|---|
| | A:His78 | Betuline C6′ | π-Sigma | 2.09 |
| | A:Pro53 | Betuline C1′ | Alkyl | 4.93 |
| | A:Ala366 | Betuline C27′ | Alkyl | 3.82 |
| | A:Lys367 | Betuline C1′ | Alkyl | 4.80 |
| | A:Lys367 | Betuline C10′ | Alkyl | 5.44 |
| | A:Lys367 | Betuline C11′ | Alkyl | 4.80 |
| | A:Pro53 | Betuline C23′ | Alkyl | 3.90 |
| | A:Ile335 | Betuline C30′ | Alkyl | 4.04 |
| | A:His78 | Betuline C5′ | π-Alkyl | 4.85 |
| | A:His78 | Betuline C24′ | π-Alkyl | 3.86 |
| | A:His78 | Betuline C25′ | π-Alkyl | 3.36 |
| | A:His78 | Betuline C26′ | π-Alkyl | 3.33 |
| | A:Ile335 | Triazole ring | π-Alkyl | 4.94 |
| | B:Lys337 | Benzene ring | π-Alkyl | 5.08 |
| | B:Lys336 | Pyridine ring | π-Alkyl | 4.84 |

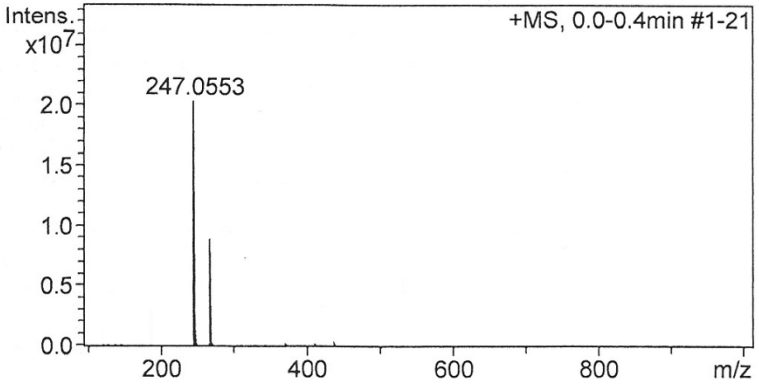
# Compound Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\Service_20220831\8QSAProp2.d | Acquisition Date | 9/13/2022 1:13:51 PM |
| Method | low_mass.m | Operator | KM |
| Sample Name | tune_poshigh_test1 | Instrument | impact II 1825265.10082 |
| Comment | | | |

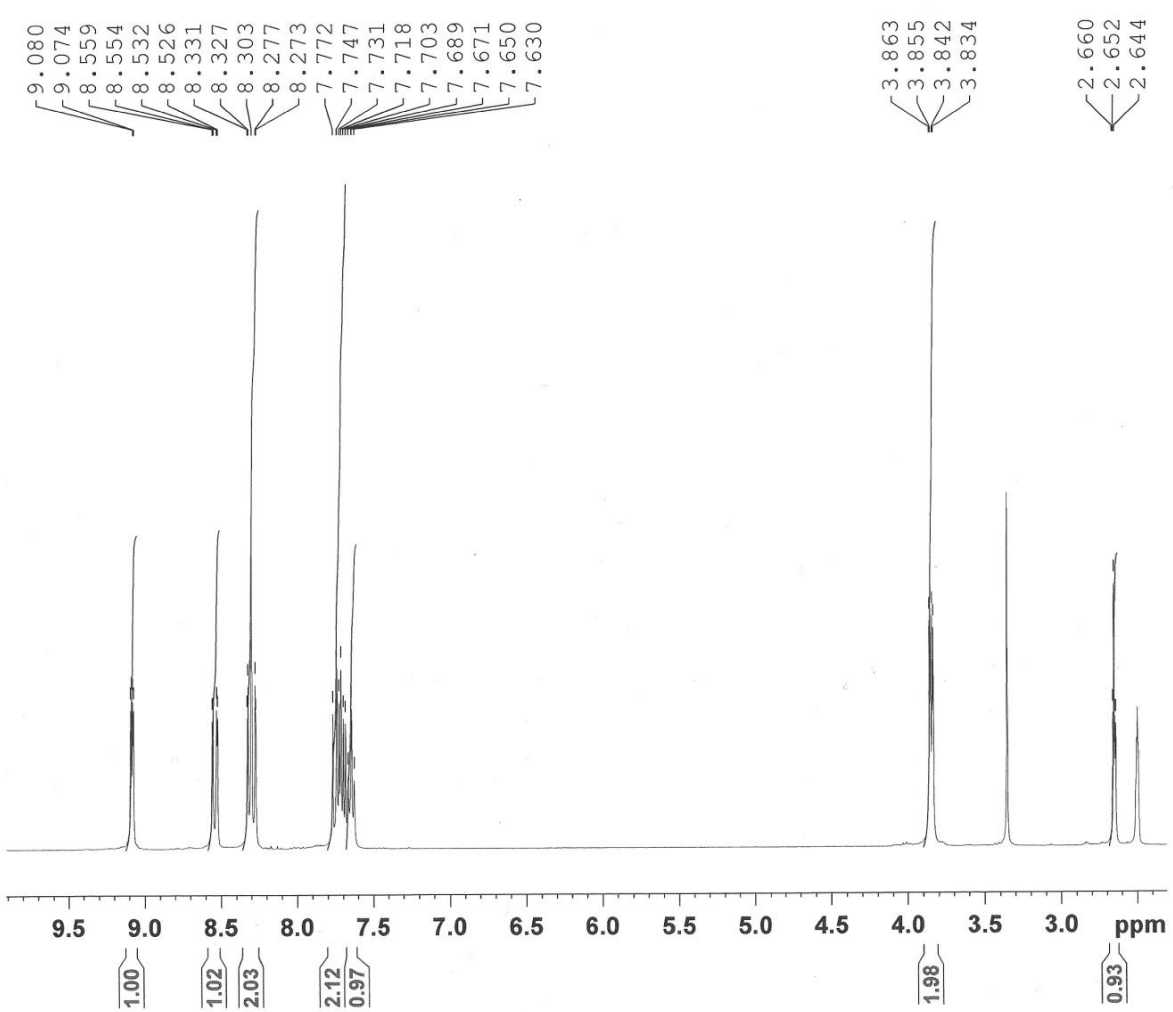
**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 4000 V | Set Dry Heater | 200 °C |
| Scan Begin | 100 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 3.0 l/min |
| Scan End | 1000 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




| # | m/z | Res. | S/N | I | I % | FWHM |
|---|---|---|---|---|---|---|
| 1 | 247.0553 | 15207 | 81856.7 | 20377568 | 100.0 | 0.0162 |
| 2 | 269.0362 | 36498 | 31220.0 | 8915149 | 43.7 | 0.0074 |

**Figure S1**. HR MS spectra of 8-*N*-(prop-2-ynyl)quinolinesulfonamide **(8a)**

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EXPNO                      3
PROCNO                     1

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PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                        16
DS                         2
SWH                6103.516 Hz
FIDRES            0.093132 Hz
AQ                5.3687091 sec
RG                   31.623
DW                   81.920 usec
DE                    6.50 usec
TE                   295.2 K
D1              1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
SFO1           300.1818537 MHz
NUC1                     1H
P1                    8.50 usec
PLW1           44.00000000 W

F2 - Processing parameters
SI                    65536
SF             300.1800000 MHz
WDW                      EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
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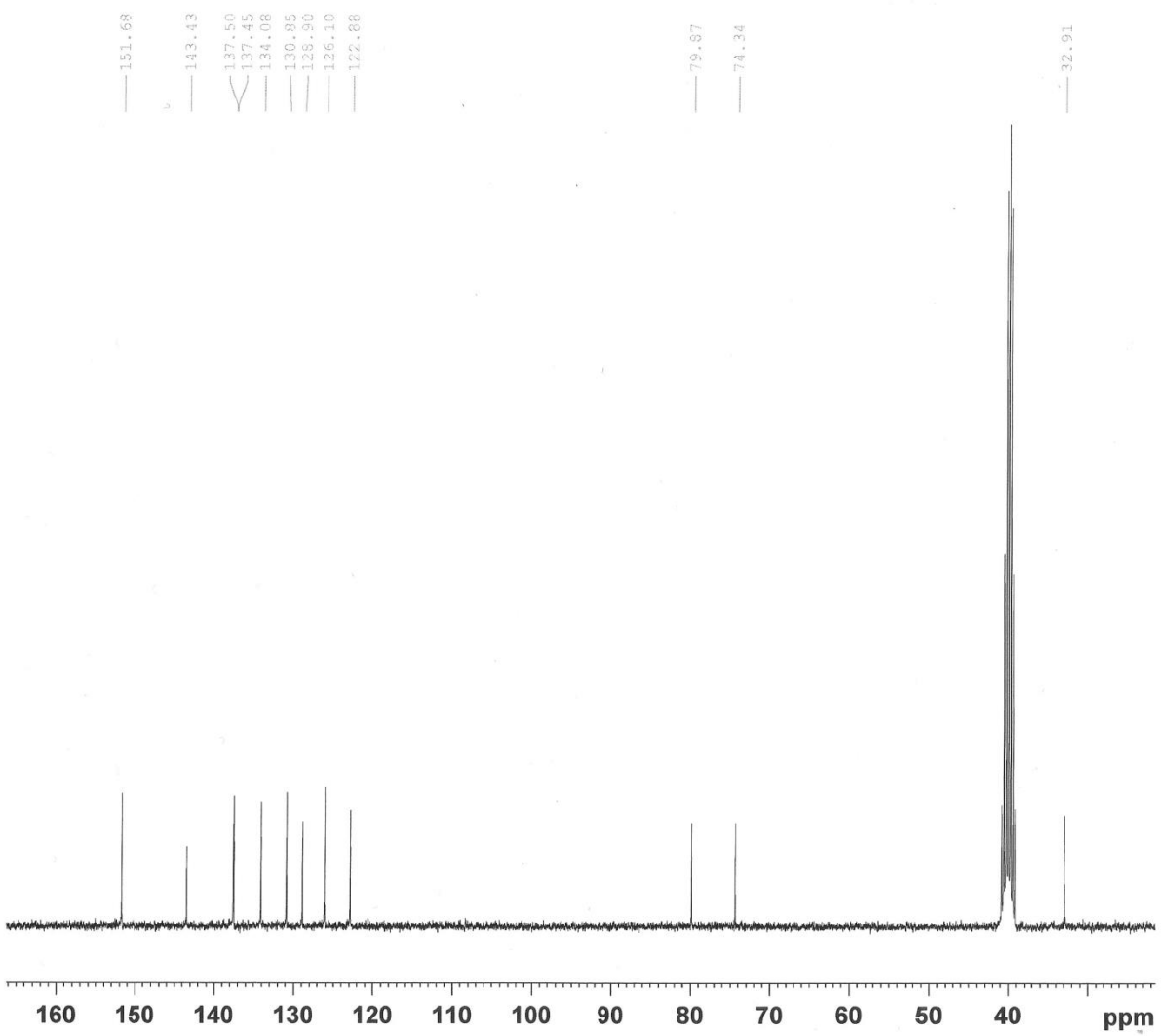
**Figure S2.** $^{1}$H NMR spectra of 8-*N*-(prop-2-ynyl)quinolinesulfonamide **(8a)**

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EXPNO                  3
PROCNO                 1

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Time               12.50
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PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           24414.063 Hz
FIDRES         0.372529 Hz
AQ            1.3421773 sec
RG              501.187
DW               20.480 usec
DE                6.50 usec
TE               295.3 K
D1           2.00000000 sec
D11          0.03000000 sec
D31          0.00000950 sec
D40          0.03008300 sec
L4                   40
L5                   57
P32               90.00 usec
TD0                   1

======== CHANNEL f1 ========
SFO1         75.4878687 MHz
NUC1                13C
P1                 9.50 usec
PLW1        50.00000000 W

======== CHANNEL f2 ========
SFO2        300.1812007 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2        44.00000000 W
PLW12        0.39247000 W
PLW13        0.31790000 W

F2 - Processing parameters
SI                 32768
SF           75.4803210 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

**Figure S3**. $^{13}$C NMR spectra of 8-*N*-(prop-2-ynyl)quinolinesulfonamide (**8a**)

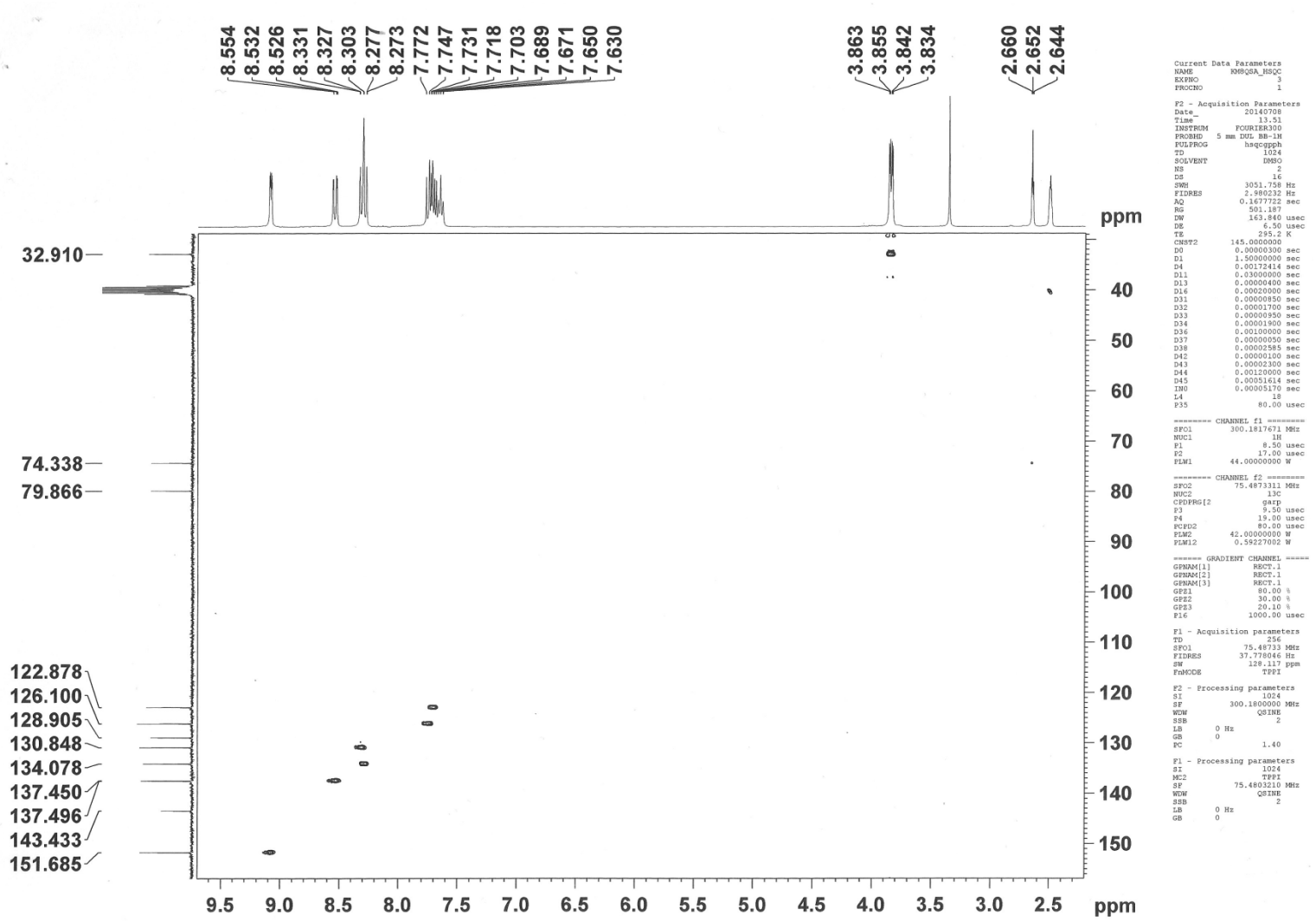


**Figure S4**. HSQC spectra of 8-*N*-(prop-2-ynyl)quinolinesulfonamide (**8a**)

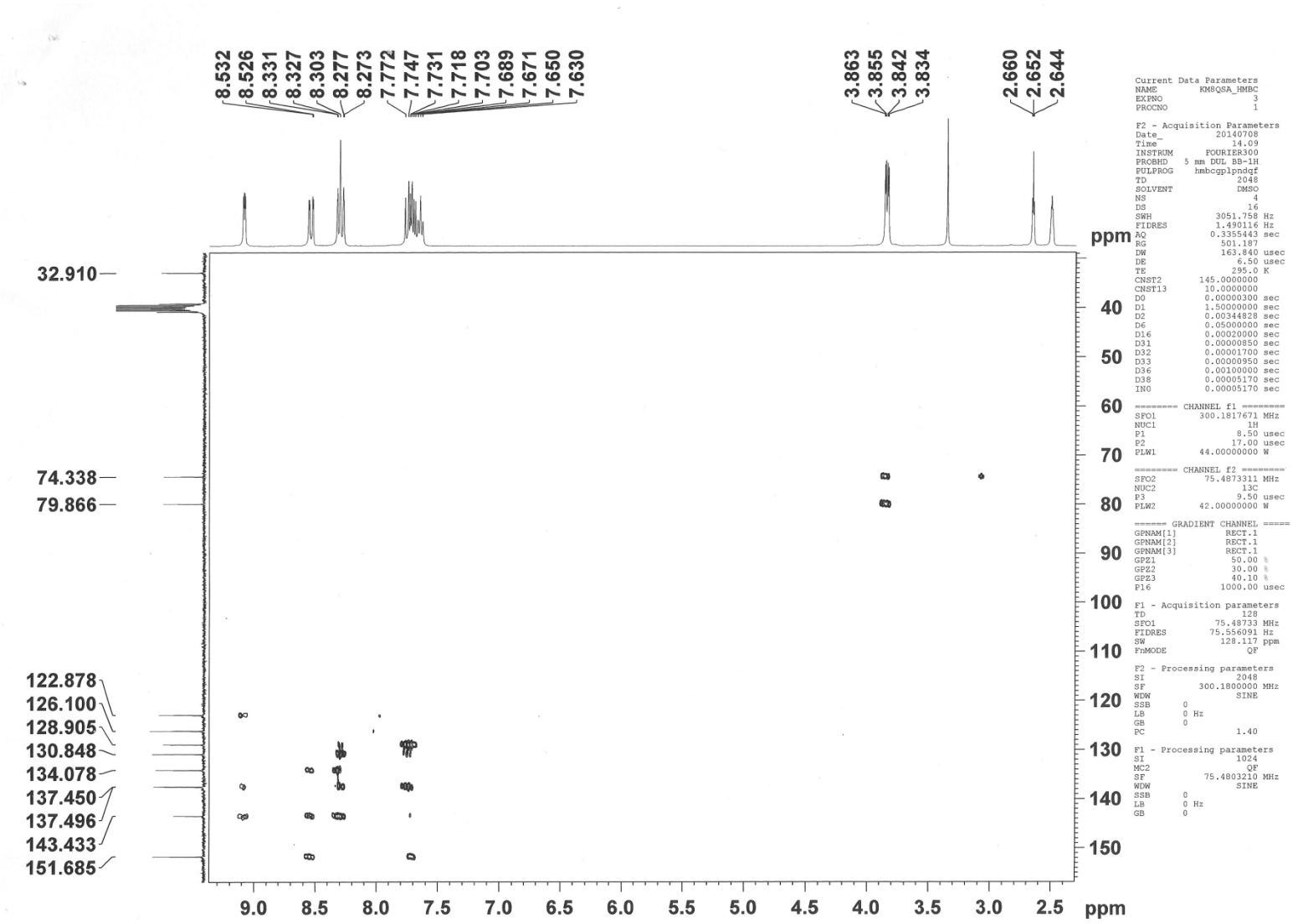


**Figure S5**. HMBC spectra of 8-*N*-(prop-2-ynyl)quinolinesulfonamide (**8a**)

# Compound Spectrum List Report

**Analysis Info**

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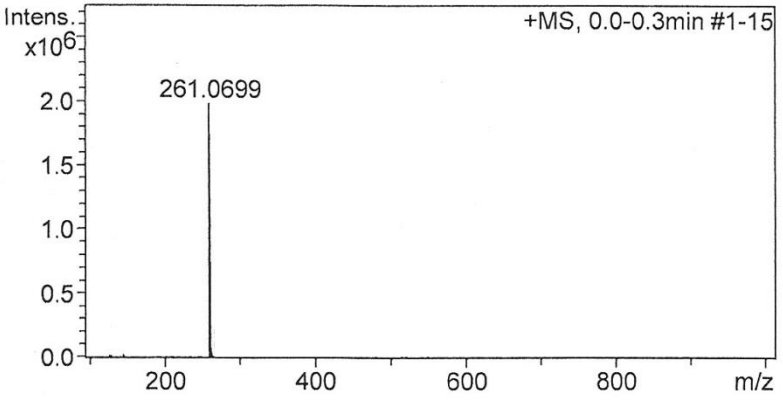
|---|---|---|---|
| Analysis Name | D:\Data\Service_20220831\8QSAProp.d | Acquisition Date | 9/13/2022 1:03:48 PM |
| Method | low_mass.m | Operator | KM |
| Sample Name | tune_poshigh_test1 | Instrument | impact II 1825265.10082 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 4000 V | Set Dry Heater | 200 °C |
| Scan Begin | 100 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 3.0 l/min |
| Scan End | 1000 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




| # | m/z | Res. | S/N | I | I % | FWHM |
|---|---|---|---|---|---|---|
| 1 | 261.0699 | 32410 | 60509.1 | 1975905 | 100.0 | 0.0081 |

**Figure S6**. HR MS spectra of 8-*N*-methyl-*N*-(prop-2-ynyl)quinolinesulfonamide (**8b)**

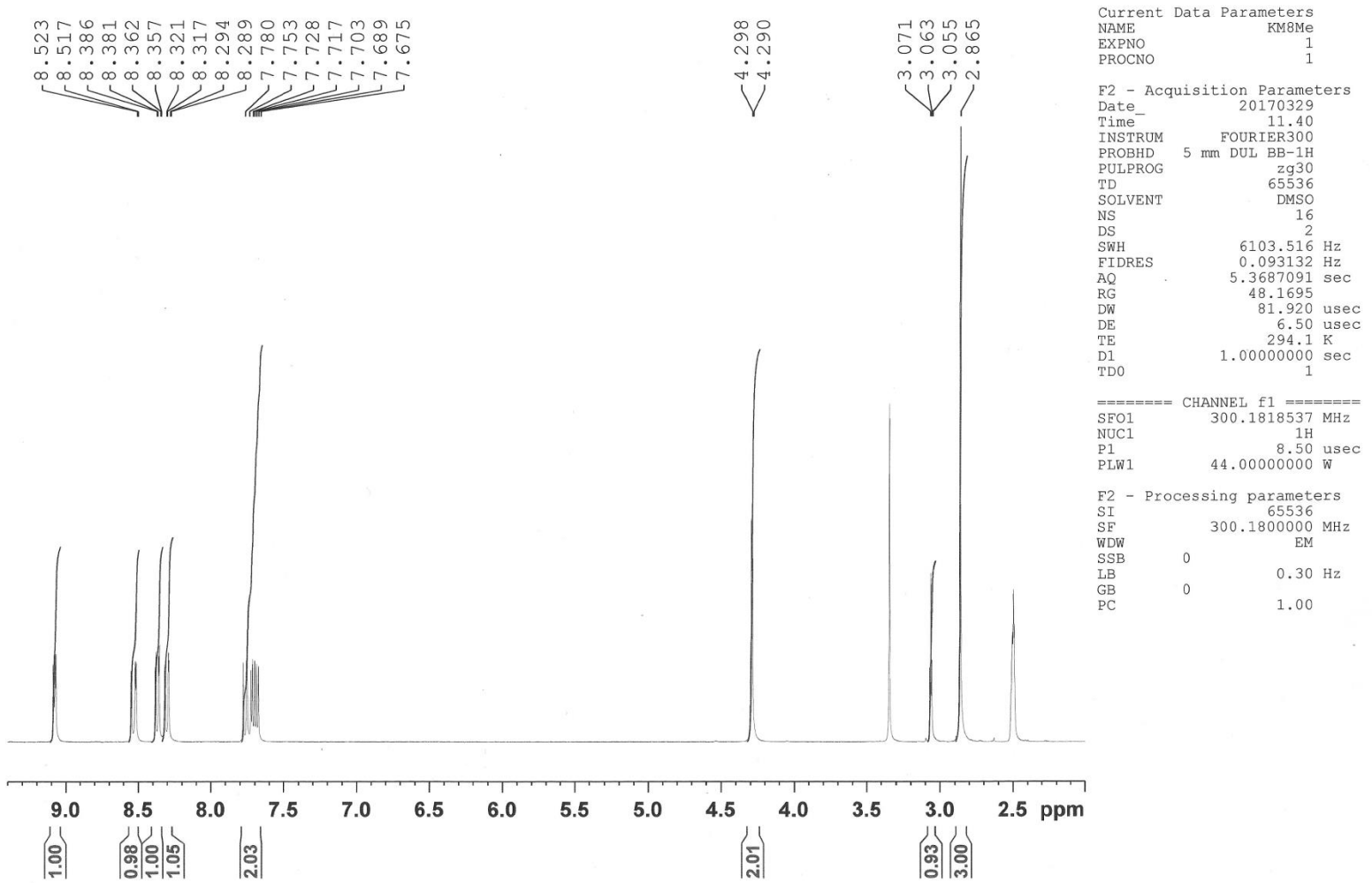
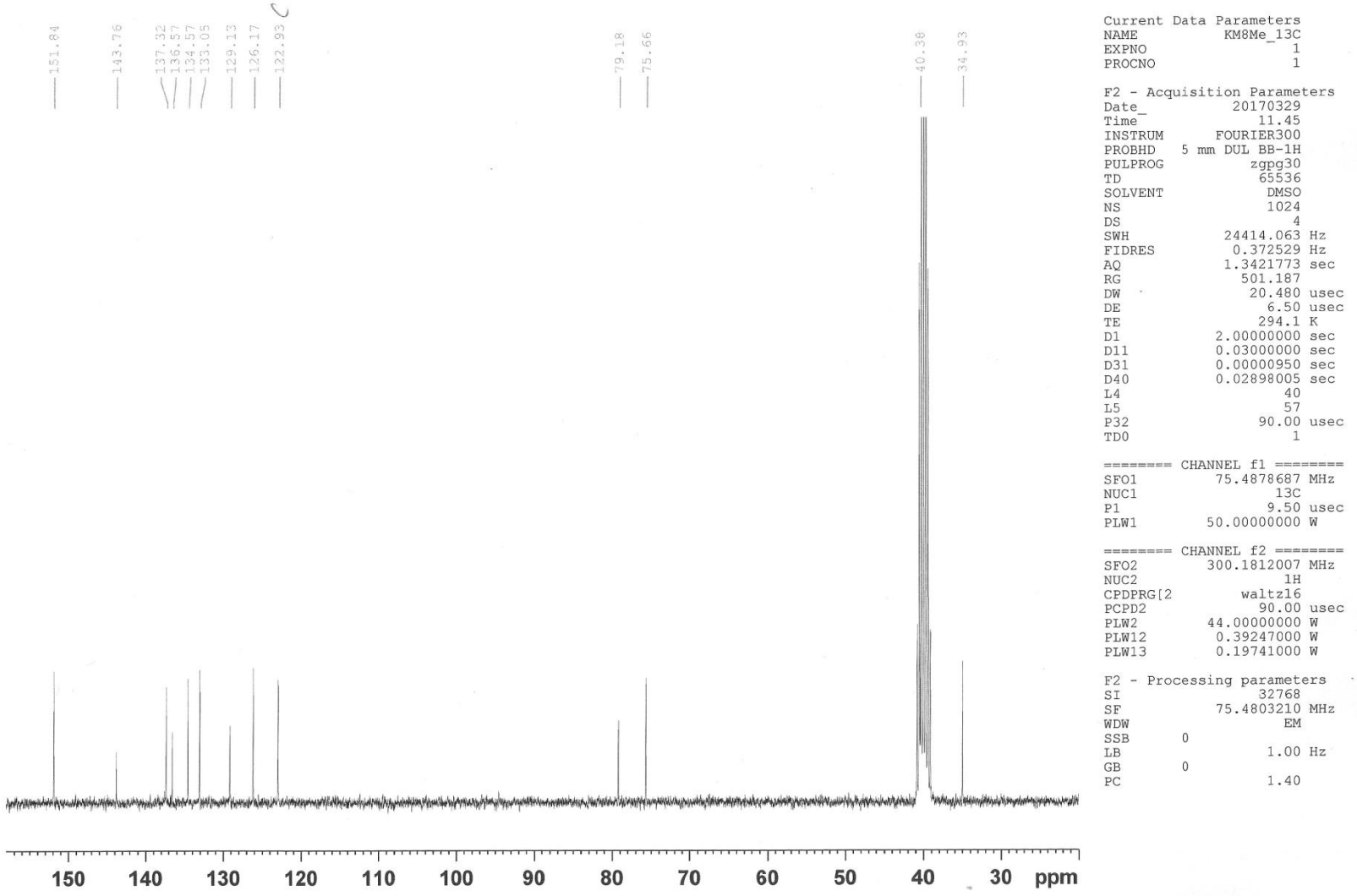



**Figure S7.** $^{1}$H NMR spectra of 8-*N*-methyl-*N*-(prop-2-ynyl)quinolinesulfonamide (**8b)**

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EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
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Time                      11.45
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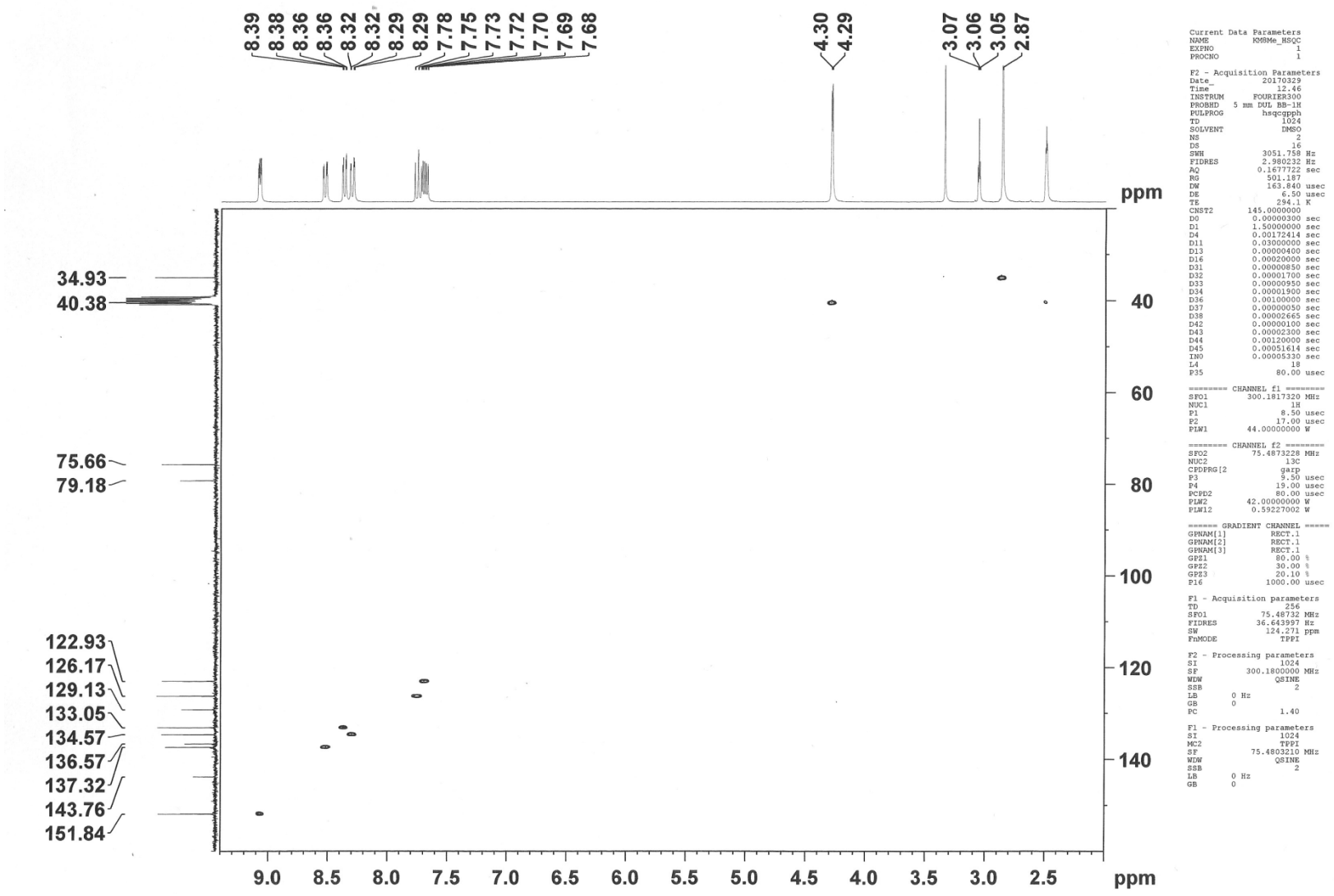
PULPROG                 zgpg30
TD                       65536
SOLVENT                   DMSO
NS                        1024
DS                           4
SWH                  24414.063 Hz
FIDRES                0.372529 Hz
AQ                    1.3421773 sec
RG                      501.187
DW                     20.480 usec
DE                      6.50 usec
TE                      294.1 K
D1                   2.00000000 sec
D11                  0.03000000 sec
D31                  0.00000950 sec
D40                  0.02898005 sec
L4                           40
L5                           57
P32                    90.00 usec
TD0                           1

======== CHANNEL f1 ========
SFO1                75.4878687 MHz
NUC1                        13C
P1                       9.50 usec
PLW1               50.00000000 W

======== CHANNEL f2 ========
SFO2               300.1812007 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                   90.00 usec
PLW2               44.00000000 W
PLW12               0.39247000 W
PLW13               0.19741000 W

F2 - Processing parameters
SI                       32768
SF                  75.4803210 MHz
WDW                         EM
SSB          0
LB                       1.00 Hz
GB           0
PC                       1.40
```

**Figure S8**. $^{13}$C NMR spectra of 8-*N*-methyl-*N*-(prop-2-ynyl)quinolinesulfonamide (**8b**)

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Current Data Parameters
NAME            KM8Me_HSQC
EXPNO                    1
PROCNO                   1

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Time                 12.46
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PROBHD    5 mm DUL BB-1H
PULPROG           hsqcgpph
TD                   1024
SOLVENT              DMSO
NS                      2
DS                     16
SWH              3051.758 Hz
FIDRES           2.980232 Hz
AQ               0.1677722 sec
RG                  501.187
DW                  163.840 usec
DE                    6.50 usec
TE                   294.1 K
CNST2           145.0000000
D0              0.00000300 sec
D1              1.50000000 sec
D4              0.00172414 sec
D11             0.03000000 sec
D13             0.00000400 sec
D16             0.00020000 sec
D31             0.00000850 sec
D32             0.00001700 sec
D33             0.00000950 sec
D34             0.00001900 sec
D36             0.00100000 sec
D37             0.00000050 sec
D38             0.00002665 sec
D42             0.00000100 sec
D43             0.00002300 sec
D44             0.00120000 sec
D45             0.00051614 sec
IN0             0.00005330 sec
L4                      18
P35                  80.00 usec

======== CHANNEL f1 ========
SFO1            300.1817320 MHz
NUC1                    1H
P1                    8.50 usec
P2                   17.00 usec
PLW1            44.00000000 W

======== CHANNEL f2 ========
SFO2             75.4873228 MHz
NUC2                   13C
CPDPRG[2               garp
P3                    9.50 usec
P4                   19.00 usec
PCPD2                80.00 usec
PLW2            42.00000000 W
PLW12            0.59227002 W

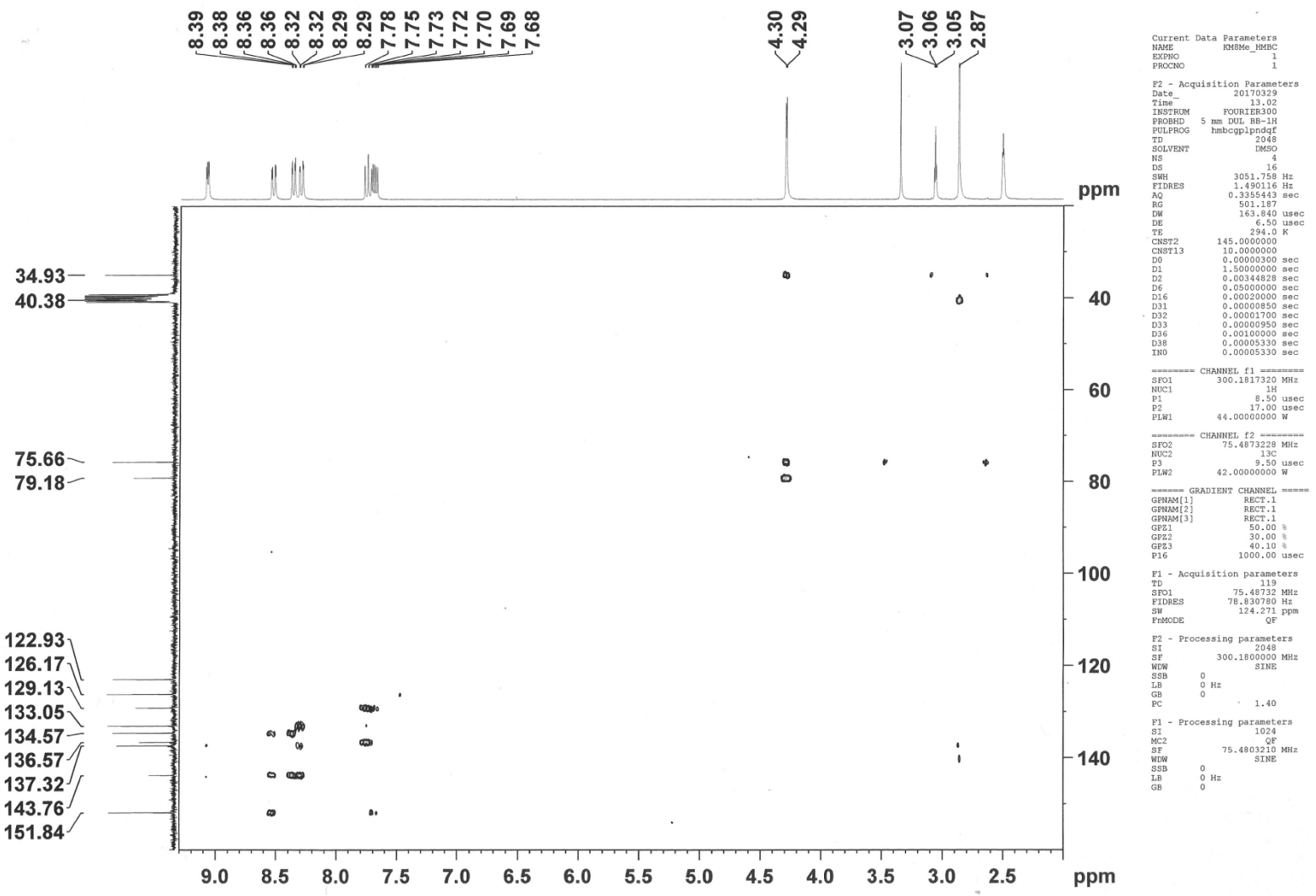
====== GRADIENT CHANNEL =====
GPNAM[1]             RECT.1
GPNAM[2]             RECT.1
GPNAM[3]             RECT.1
GPZ1                 80.00 %
GPZ2                 30.00 %
GPZ3                 20.10 %
P16                1000.00 usec

F1 - Acquisition parameters
TD                      256
SFO1             75.48732 MHz
FIDRES          36.643997 Hz
SW                 124.271 ppm
FnMODE                TPPI

F2 - Processing parameters
SI                     1024
SF              300.1800000 MHz
WDW                   QSINE
SSB                       2
LB          0 Hz
GB          0
PC                     1.40

F1 - Processing parameters
SI                     1024
MC2                    TPPI
SF               75.4803210 MHz
WDW                   QSINE
SSB                       2
LB          0 Hz
GB          0
```

**Figure S9**. HSQC spectra of 8-*N*-methyl-*N*-(prop-2-ynyl)quinolinesulfonamide (**8b**)




```
Current Data Parameters
NAME          KM8Me_HMBC
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170329
Time              13.02
INSTRUM       FOURIER300
PROBHD   5 mm DUL BB-1H
PULPROG    hmbcgplpndqf
TD                 2048
SOLVENT            DMSO
NS                    4
DS                   16
SWH           3051.758 Hz
FIDRES        1.490116 Hz
AQ            0.3355443 sec
RG              501.187
DW              163.840 usec
DE                6.50 usec
TE              294.0 K
CNST2         145.0000000
CNST13         10.0000000
D0            0.00000300 sec
D1            1.50000000 sec
D2            0.00344828 sec
D6            0.05000000 sec
D16           0.00020000 sec
D31           0.00000850 sec
D32           0.00001700 sec
D33           0.00000950 sec
D36           0.00100000 sec
D38           0.00005330 sec
IN0           0.00005330 sec

======== CHANNEL f1 ========
SFO1         300.1817320 MHz
NUC1                   1H
P1                  8.50 usec
P2                 17.00 usec
PLW1          44.00000000 W

======== CHANNEL f2 ========
SFO2          75.4873228 MHz
NUC2                  13C
P3                  9.50 usec
PLW2          42.00000000 W

====== GRADIENT CHANNEL =====
GPNAM[1]           RECT.1
GPNAM[2]           RECT.1
GPNAM[3]           RECT.1
GPZ1                50.00 %
GPZ2                30.00 %
GPZ3                40.10 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                   119
SFO1          75.48732 MHz
FIDRES        78.830780 Hz
SW              124.271 ppm
FnMODE                QF

F2 - Processing parameters
SI                  2048
SF          300.1800000 MHz
WDW                 SINE
SSB       0
LB        0 Hz
GB        0
PC                  1.40

F1 - Processing parameters
SI                  1024
MC2                   QF
SF          75.4803210 MHz
WDW                 SINE
SSB       0
LB        0 Hz
GB        0
```

**Figure S10**. HMBC spectra of 8-*N*-methyl-*N*-(prop-2-ynyl)quinolinesulfonamide (**8b**)

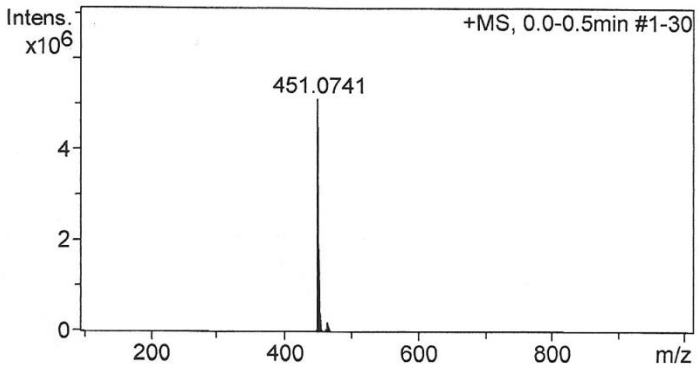
# Compound Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\KM7QCI.d | | |
| Method | low_mass.m | Operator | KM |
| Sample Name | TM Low concentration | Instrument | impact II 1825265.10082 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 4000 V | Set Dry Heater | 240 °C |
| Scan Begin | 100 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 1000 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




| # | m/z | Res. | S/N | I | I % | FWHM |
|---|---|---|---|---|---|---|
| 1 | 451.0741 | 46889 | 14570.0 | 5115211 | 100.0 | 0.0096 |
| 2 | 453.0711 | 42091 | 5173.1 | 1821962 | 35.6 | 0.0108 |
| 3 | 473.0557 | 37315 | 1641.0 | 630401 | 12.3 | 0.0127 |
| 4 | 475.0531 | 31446 | 613.5 | 237045 | 4.6 | 0.0151 |

**Figure S11.** HR MS spectra of 8-*N*-{[1-(7-chloroquinolin-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9a**)

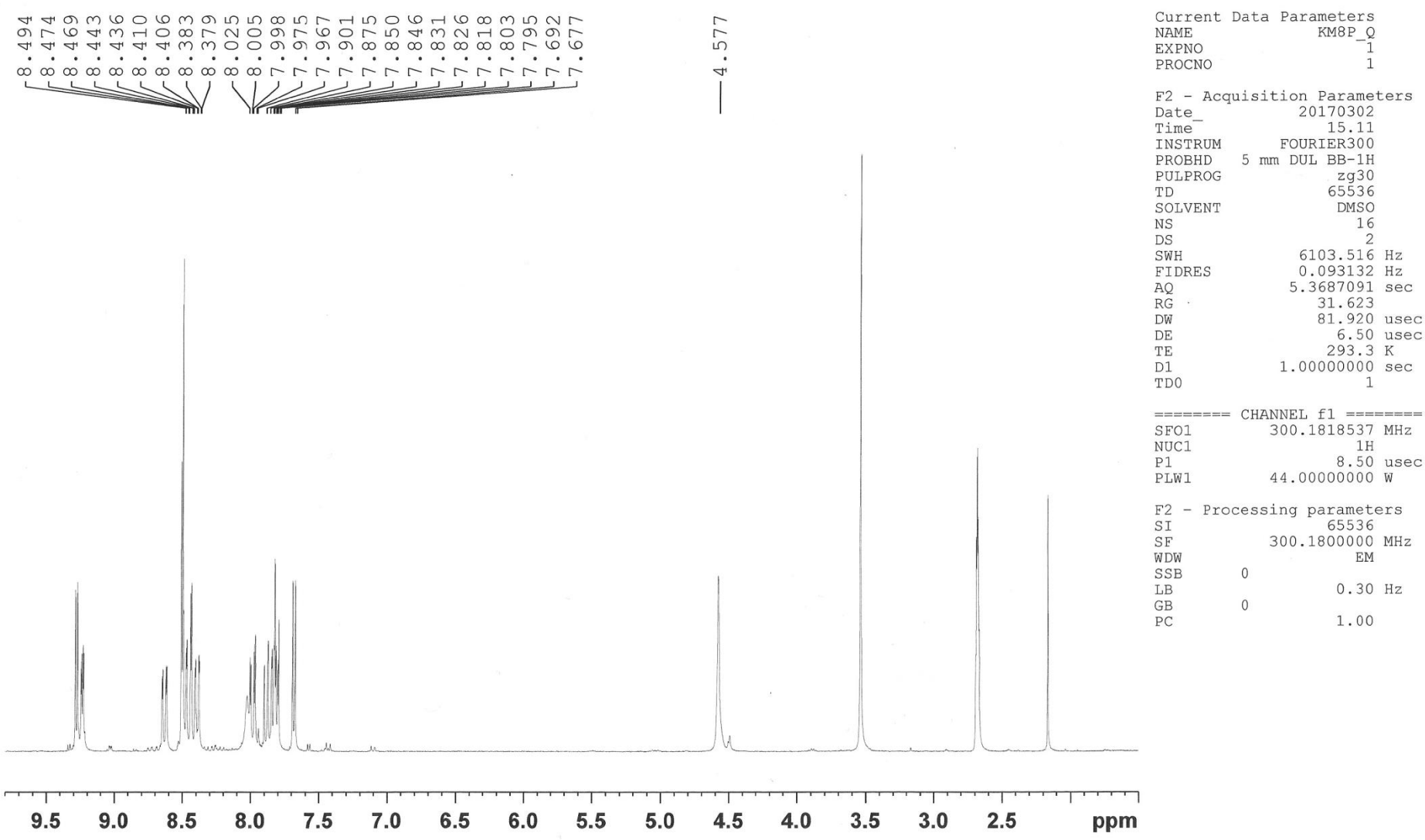
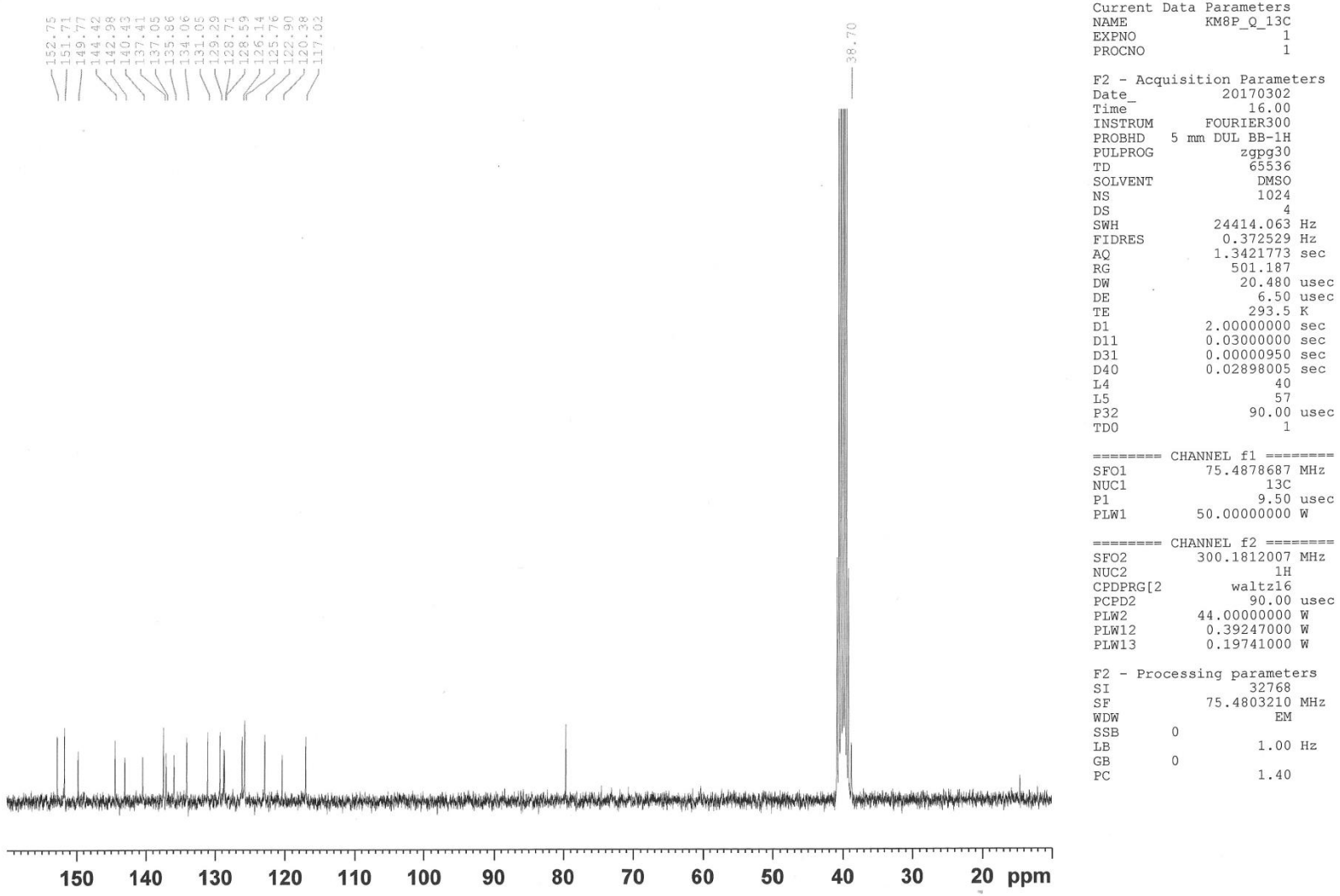



**Figure S12**. [1]H NMR spectra of 8-*N*-{[1-(7-chloroquinolin-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9a**)

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Current Data Parameters
NAME          KM8P_Q_13C
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170302
Time              16.00
INSTRUM       FOURIER300
PROBHD   5 mm DUL BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                  1024
DS                     4
SWH           24414.063 Hz
FIDRES         0.372529 Hz
AQ             1.3421773 sec
RG               501.187
DW                20.480 usec
DE                 6.50 usec
TE                293.5 K
D1           2.00000000 sec
D11          0.03000000 sec
D31          0.00000950 sec
D40          0.02898005 sec
L4                    40
L5                    57
P32               90.00 usec
TD0                    1

======== CHANNEL f1 ========
SFO1         75.4878687 MHz
NUC1                13C
P1                 9.50 usec
PLW1        50.00000000 W

======== CHANNEL f2 ========
SFO2        300.1812007 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2        44.00000000 W
PLW12        0.39247000 W
PLW13        0.19741000 W

F2 - Processing parameters
SI                 32768
SF           75.4803210 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

**Figure S13**. $^{13}$C NMR spectra of 8-*N*-{[1-(7-chloroquinolin-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9a**)

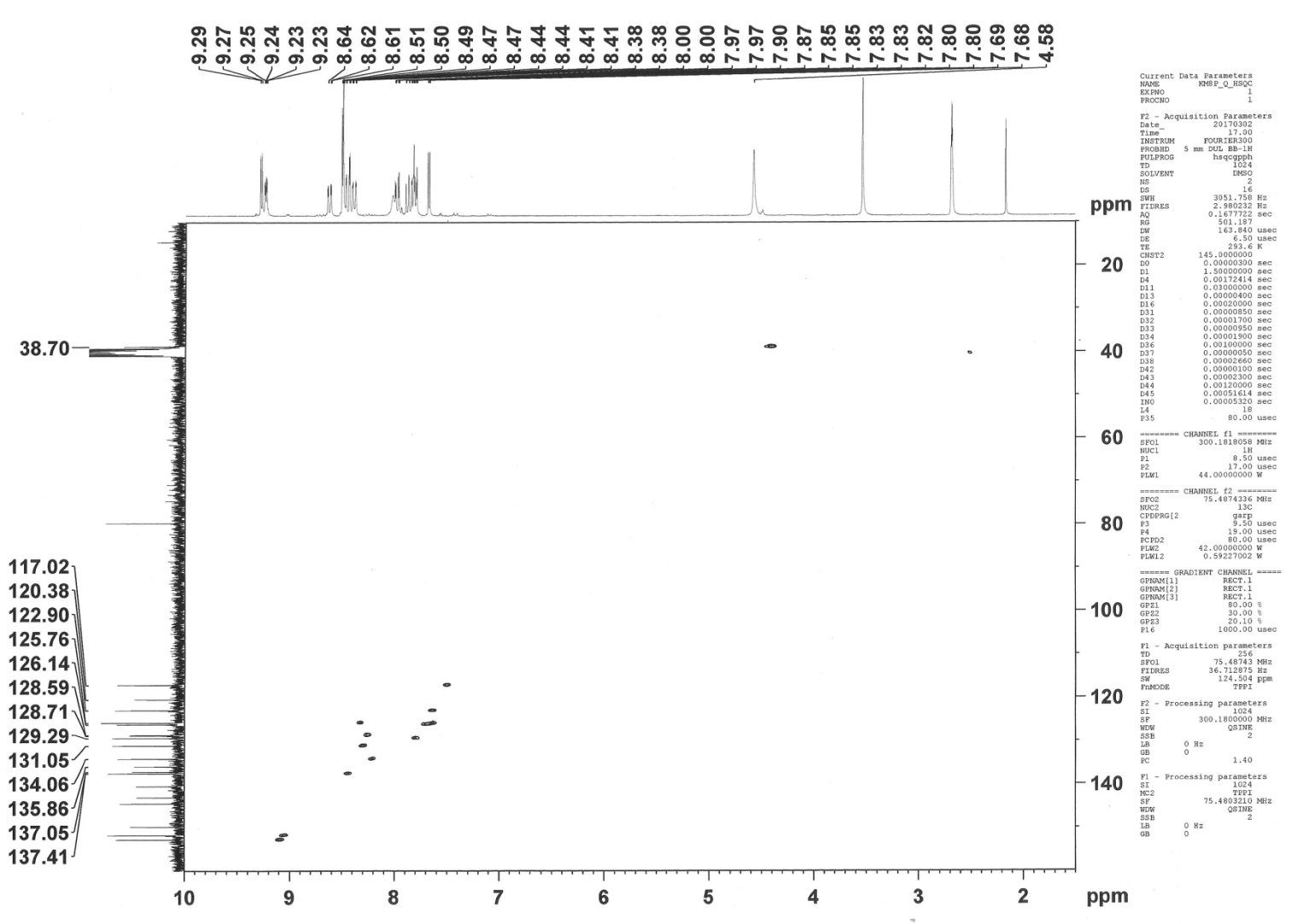
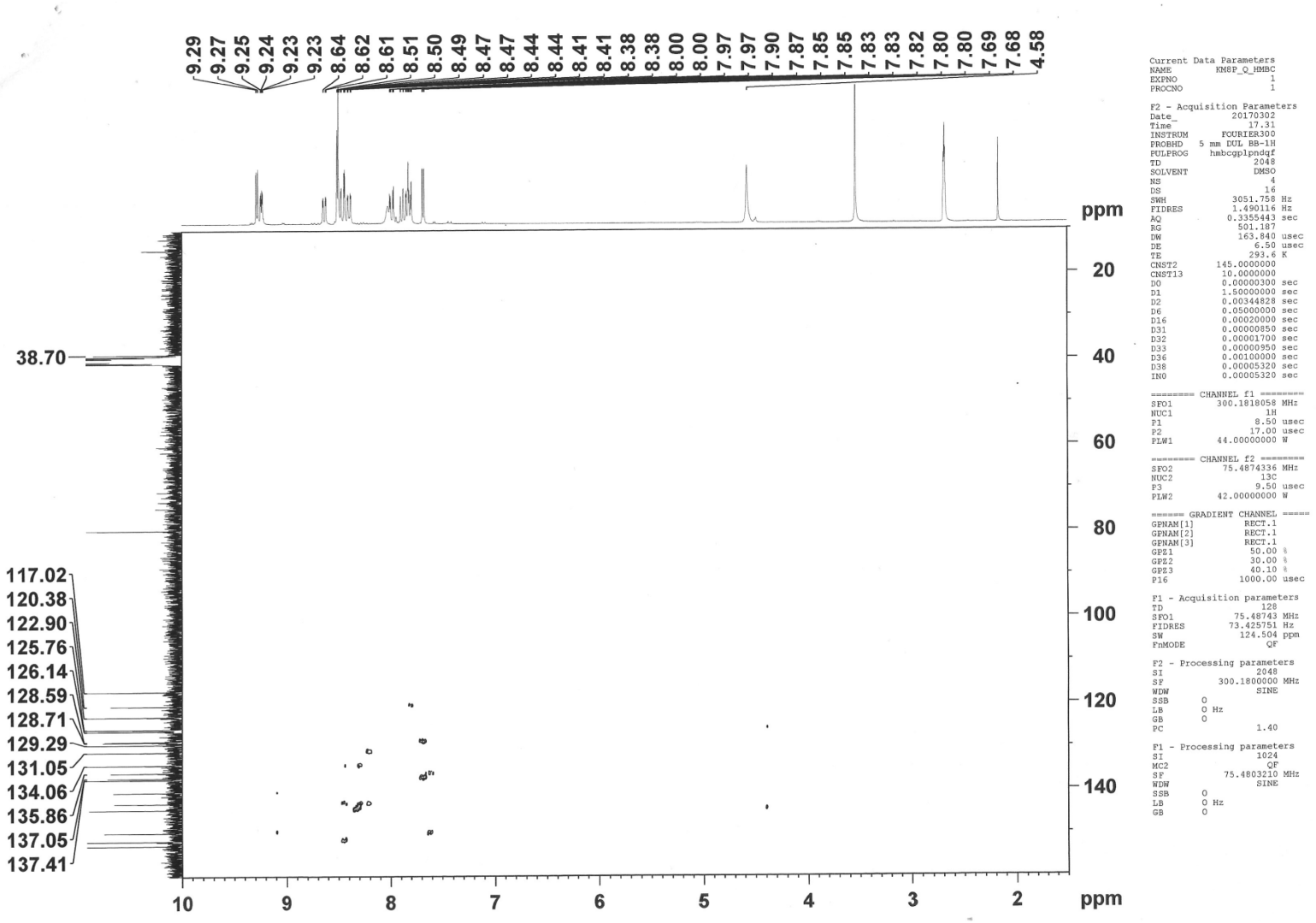



**Figure S14**. HSQC spectra of 8-*N*-{[1-(7-chloroquinolin-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9a**)




```
Current Data Parameters
NAME                  KM8P_Q_HMBC
EXPNO                           1
PROCNO                          1

F2 - Acquisition Parameters
Date_                    20170302
Time                        17.31
INSTRUM                FOURIER300
PROBHD    5 mm DUL BB-1H
PULPROG             hmbcgplpndqf
TD                          2048
SOLVENT                     DMSO
NS                             4
DS                            16
SWH                     3051.758 Hz
FIDRES                  1.490116 Hz
AQ                      0.3355443 sec
RG                        501.187
DW                        163.840 usec
DE                          6.50 usec
TE                        293.6 K
CNST2                145.0000000
CNST13                10.0000000
D0                    0.00000300 sec
D1                    1.50000000 sec
D2                    0.00344828 sec
D6                    0.05000000 sec
D16                   0.00020000 sec
D31                   0.00000850 sec
D32                   0.00001700 sec
D33                   0.00000950 sec
D36                   0.00100000 sec
D38                   0.00005320 sec
IN0                   0.00005320 sec

======== CHANNEL f1 ========
SFO1                  300.1818058 MHz
NUC1                          1H
P1                          8.50 usec
P2                         17.00 usec
PLW1                  44.00000000 W

======== CHANNEL f2 ========
SFO2                   75.4874336 MHz
NUC2                          13C
P3                          9.50 usec
PLW2                  42.00000000 W

====== GRADIENT CHANNEL =====
GPNAM[1]                   RECT.1
GPNAM[2]                   RECT.1
GPNAM[3]                   RECT.1
GPZ1                       50.00 %
GPZ2                       30.00 %
GPZ3                       40.10 %
P16                      1000.00 usec

F1 - Acquisition parameters
TD                            128
SFO1                   75.48743 MHz
FIDRES                 73.425751 Hz
SW                       124.504 ppm
FnMODE                        QF

F2 - Processing parameters
SI                           2048
SF                    300.1800000 MHz
WDW                         SINE
SSB          0
LB           0 Hz
GB           0
PC                           1.40

F1 - Processing parameters
SI                           1024
MC2                           QF
SF                    75.4803210 MHz
WDW                         SINE
SSB          0
LB           0 Hz
GB           0
```

**Figure S15**. HMBC spectra of 8-*N*-{[1-(7-chloroquinolin-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9a**)

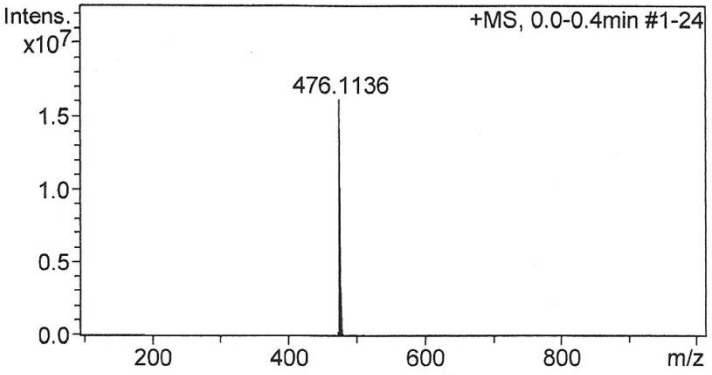
# Compound Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\KMFosf.d | | |
| Method | low_mass.m | Operator | KM |
| Sample Name | TM Low concentration | Instrument | impact II 1825265.10082 |
| Comment | | | |

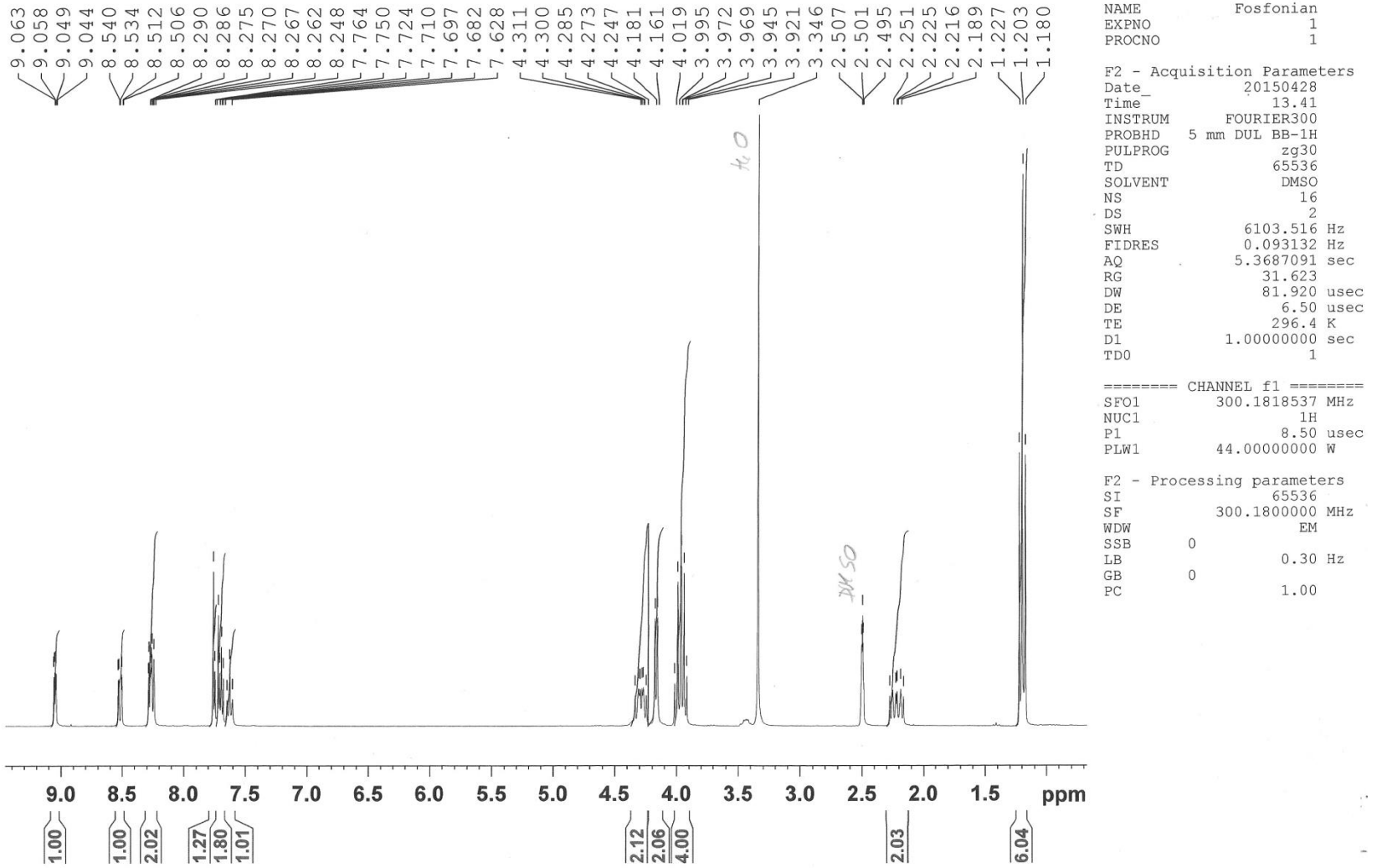
**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 4000 V | Set Dry Heater | 240 °C |
| Scan Begin | 100 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 1000 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




| # | m/z | Res. | S/N | I | I % | FWHM |
|---|---|---|---|---|---|---|
| 1 | 476.1136 | 48479 | 36474.8 | 16198640 | 100.0 | 0.0098 |

**Figure S16.** HR MS spectra of diethyl 2-{4-[methyl-(8-sulfamoylquinolyl)-1*H*-1,2,3-triazol-1-yl]}ethylphosphonate (**9b**)



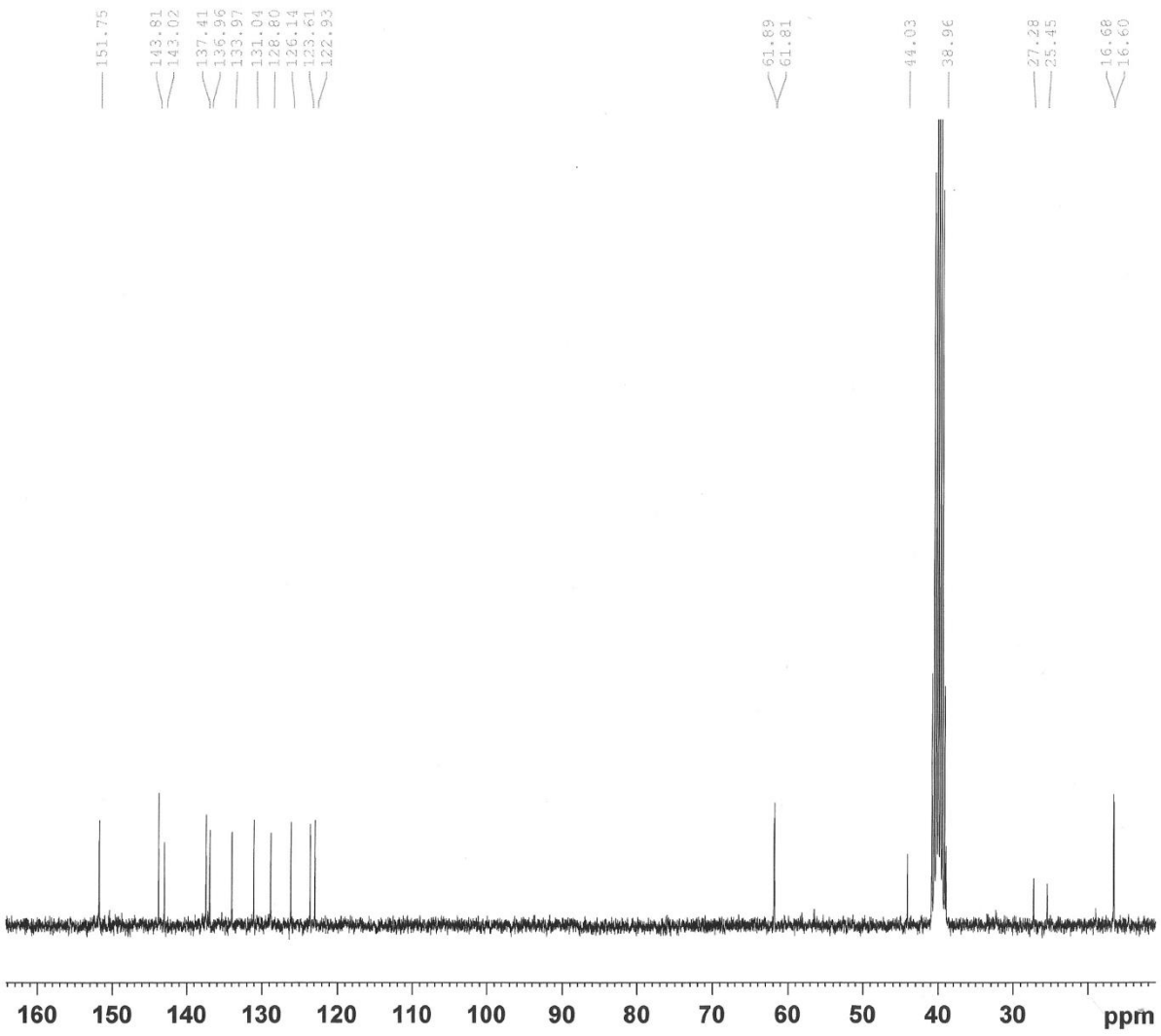

```
Current Data Parameters
NAME                  Fosfonian
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20150428
Time                      13.41
INSTRUM              FOURIER300
PROBHD    5 mm DUL BB-1H
PULPROG                    zg30
TD                        65536
SOLVENT                    DMSO
NS                           16
DS                            2
SWH                   6103.516 Hz
FIDRES                0.093132 Hz
AQ                    5.3687091 sec
RG                       31.623
DW                       81.920 usec
DE                        6.50 usec
TE                       296.4 K
D1                    1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                300.1818537 MHz
NUC1                        1H
P1                        8.50 usec
PLW1                44.00000000 W

F2 - Processing parameters
SI                        65536
SF                  300.1800000 MHz
WDW                         EM
SSB                  0
LB                        0.30 Hz
GB                   0
PC                        1.00
```

**Figure S17**. $^{1}$H NMR spectra of diethyl 2-{4-[methyl-(8-sulfamoylquinolyl)-1*H*-1,2,3-triazol-1-yl]}ethylphosphonate (**9b**)




```
Current Data Parameters
NAME       Fosfonian_13C
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150428
Time              13.51
INSTRUM       FOURIER300
PROBHD   5 mm DUL BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                 1024
DS                    4
SWH           24414.063 Hz
FIDRES         0.372529 Hz
AQ             1.3421773 sec
RG               501.187
DW                20.480 usec
DE                 6.50 usec
TE                296.6 K
D1           2.00000000 sec
D11          0.03000000 sec
D31          0.00000950 sec
D40          0.03008300 sec
L4                   40
L5                   57
P32               90.00 usec
TD0                   1

======== CHANNEL f1 ========
SFO1         75.4878687 MHz
NUC1                13C
P1                 9.50 usec
PLW1        50.00000000 W

======== CHANNEL f2 ========
SFO2        300.1812007 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2              90.00 usec
PLW2        44.00000000 W
PLW12        0.39247000 W
PLW13        0.31790000 W

F2 - Processing parameters
SI                 32768
SF           75.4803210 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

**Figure S18**. $^{13}$C NMR spectra of diethyl 2-{4-[methyl-(8-sulfamoylquinolyl)-1*H*-1,2,3-triazol-1-yl]}ethylphosphonate (**9b**)

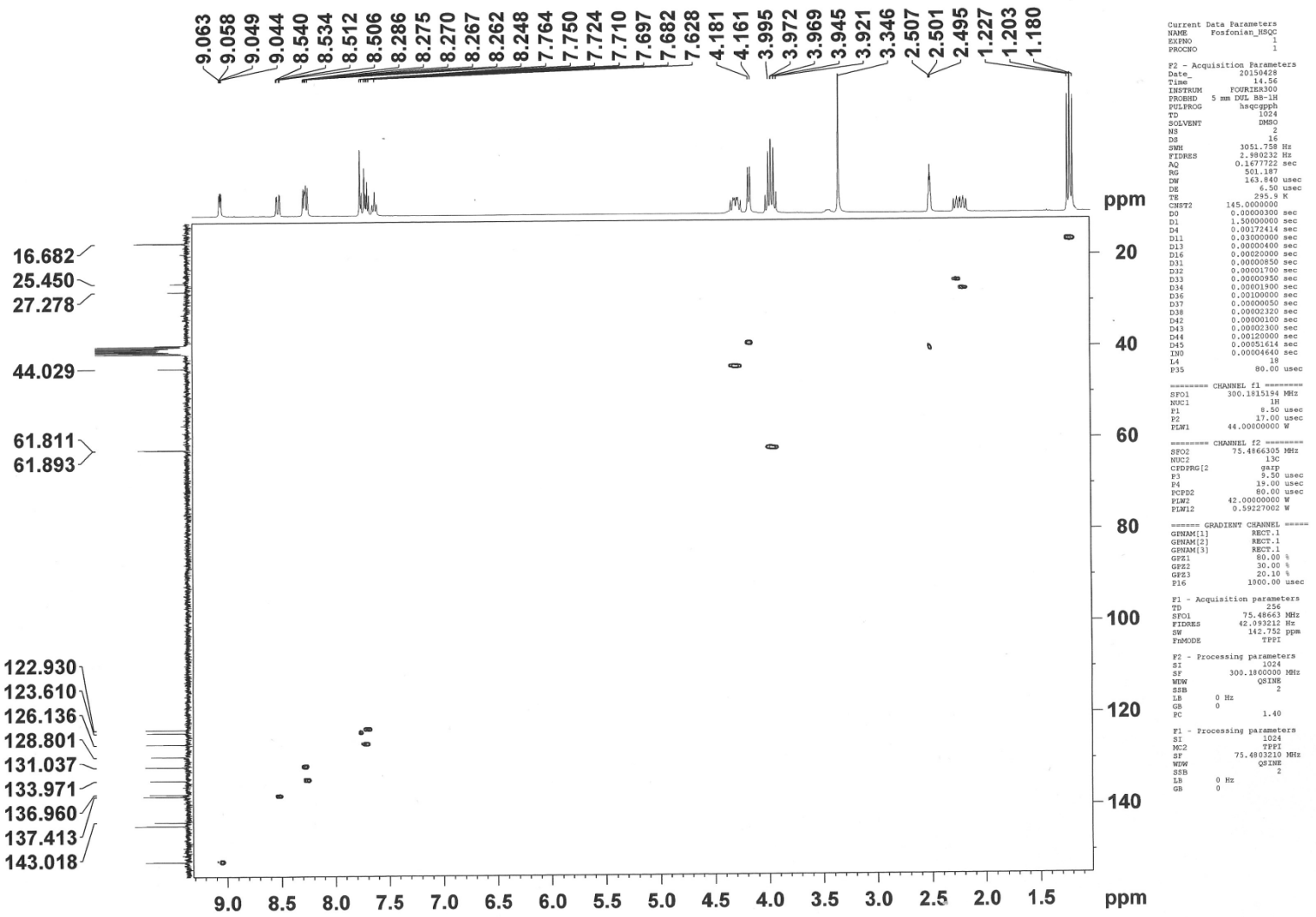
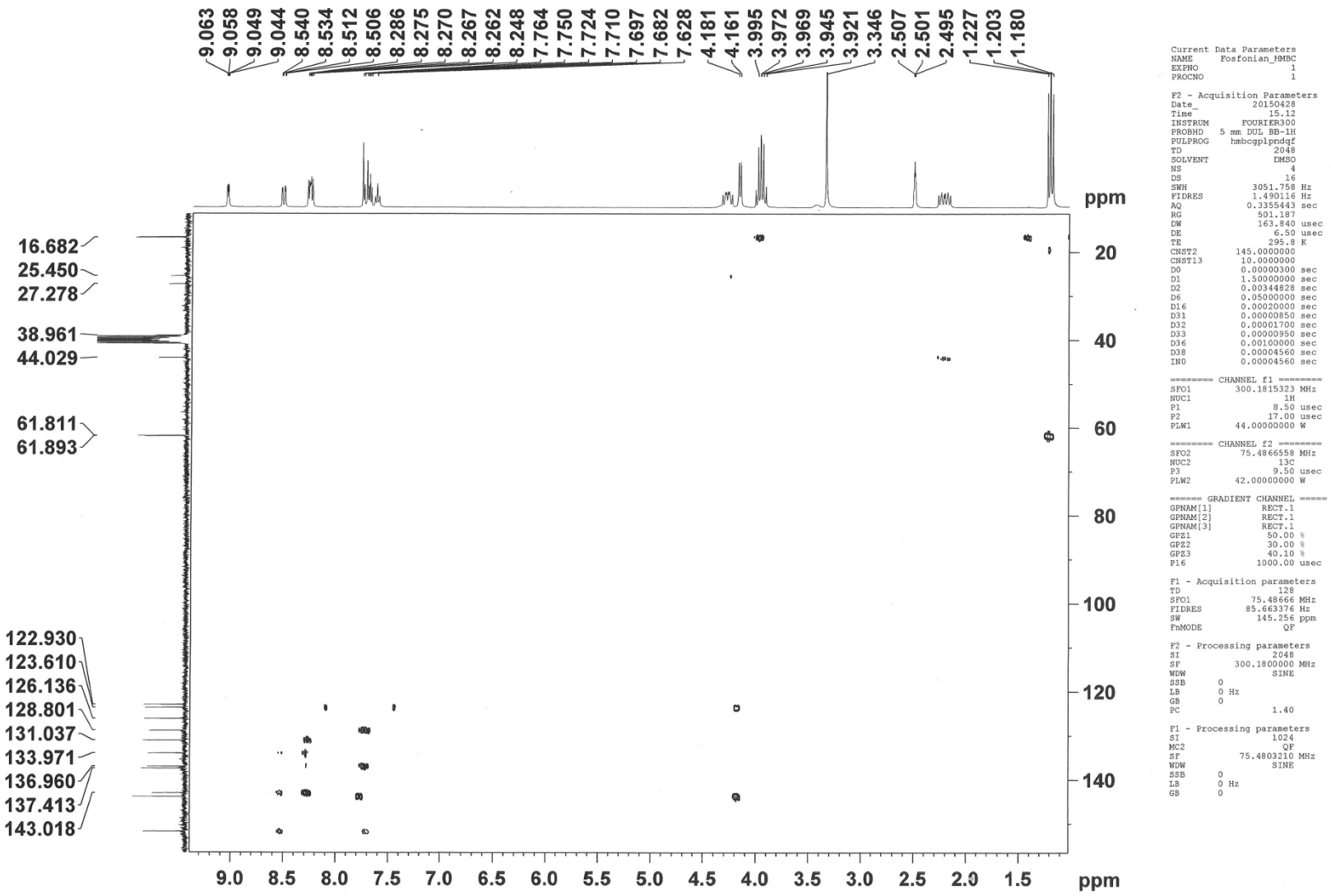



**Figure S19**. HSQC spectra diethyl 2-{4-[methyl-(8-sulfamoylquinolyl)-1*H*-1,2,3-triazol-1-yl]}ethylphosphonate (**9b**)




```
Current Data Parameters
NAME      Fosfonian_HMBC
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150428
Time              15.12
INSTRUM       FOURIER300
PROBHD   5 mm DUL BB-1H
PULPROG    hmbcgplpndqf
TD                 2048
SOLVENT            DMSO
NS                    4
DS                   16
SWH           3051.758 Hz
FIDRES        1.490116 Hz
AQ            0.3355443 sec
RG              501.187
DW              163.840 usec
DE                6.50 usec
TE              295.8 K
CNST2       145.0000000
CNST13       10.0000000
D0          0.00000300 sec
D1          1.50000000 sec
D2          0.00344828 sec
D6          0.05000000 sec
D16         0.00020000 sec
D31         0.00000850 sec
D32         0.00001700 sec
D33         0.00000950 sec
D36         0.00100000 sec
D38         0.00004560 sec
IN0         0.00004560 sec

======== CHANNEL f1 ========
SFO1        300.1815323 MHz
NUC1               1H
P1                8.50 usec
P2               17.00 usec
PLW1        44.00000000 W

======== CHANNEL f2 ========
SFO2         75.4866558 MHz
NUC2               13C
P3                9.50 usec
PLW2        42.00000000 W

====== GRADIENT CHANNEL =====
GPNAM[1]          RECT.1
GPNAM[2]          RECT.1
GPNAM[3]          RECT.1
GPZ1               50.00 %
GPZ2               30.00 %
GPZ3               40.10 %
P16              1000.00 usec

F1 - Acquisition parameters
TD                  128
SFO1         75.48666 MHz
FIDRES       85.663376 Hz
SW             145.256 ppm
FnMODE              QF

F2 - Processing parameters
SI                 2048
SF          300.1800000 MHz
WDW                SINE
SSB       0
LB        0 Hz
GB        0
PC                 1.40

F1 - Processing parameters
SI                 1024
MC2                 QF
SF          75.4803210 MHz
WDW                SINE
SSB       0
LB        0 Hz
GB        0
```

**Figure S20**. HMBC spectra diethyl 2-{4-[methyl-(8-sulfamoylquinolyl)-1*H*-1,2,3-triazol-1-yl]}ethylphosphonate (**9b**)

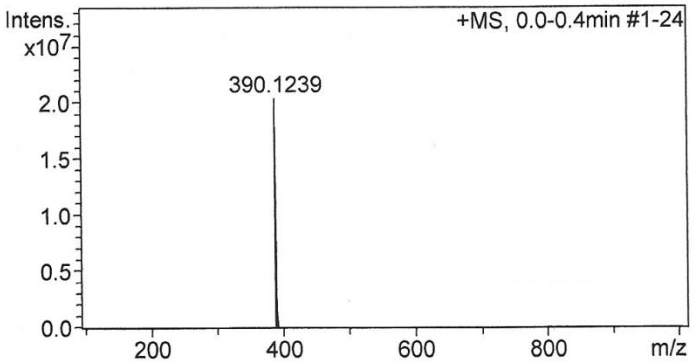
# Compound Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\KMEster.d | | |
| Method | low_mass.m | Operator | KM |
| Sample Name | TM Low concentration | Instrument | impact II 1825265.10082 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 4000 V | Set Dry Heater | 240 °C |
| Scan Begin | 100 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 1000 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




| # | m/z | Res. | S/N | I | I % | FWHM |
|---|---|---|---|---|---|---|
| 1 | 390.1239 | 22292 | 75359.1 | 20377458 | 100.0 | 0.0175 |

**Figure S21 .** HR MS spectra of ethyl 3-{[4-(8-sulfamoylquinolyl)methyl]-1*H*-1,2,3-triazol-1-yl}propanoate (**9c**)

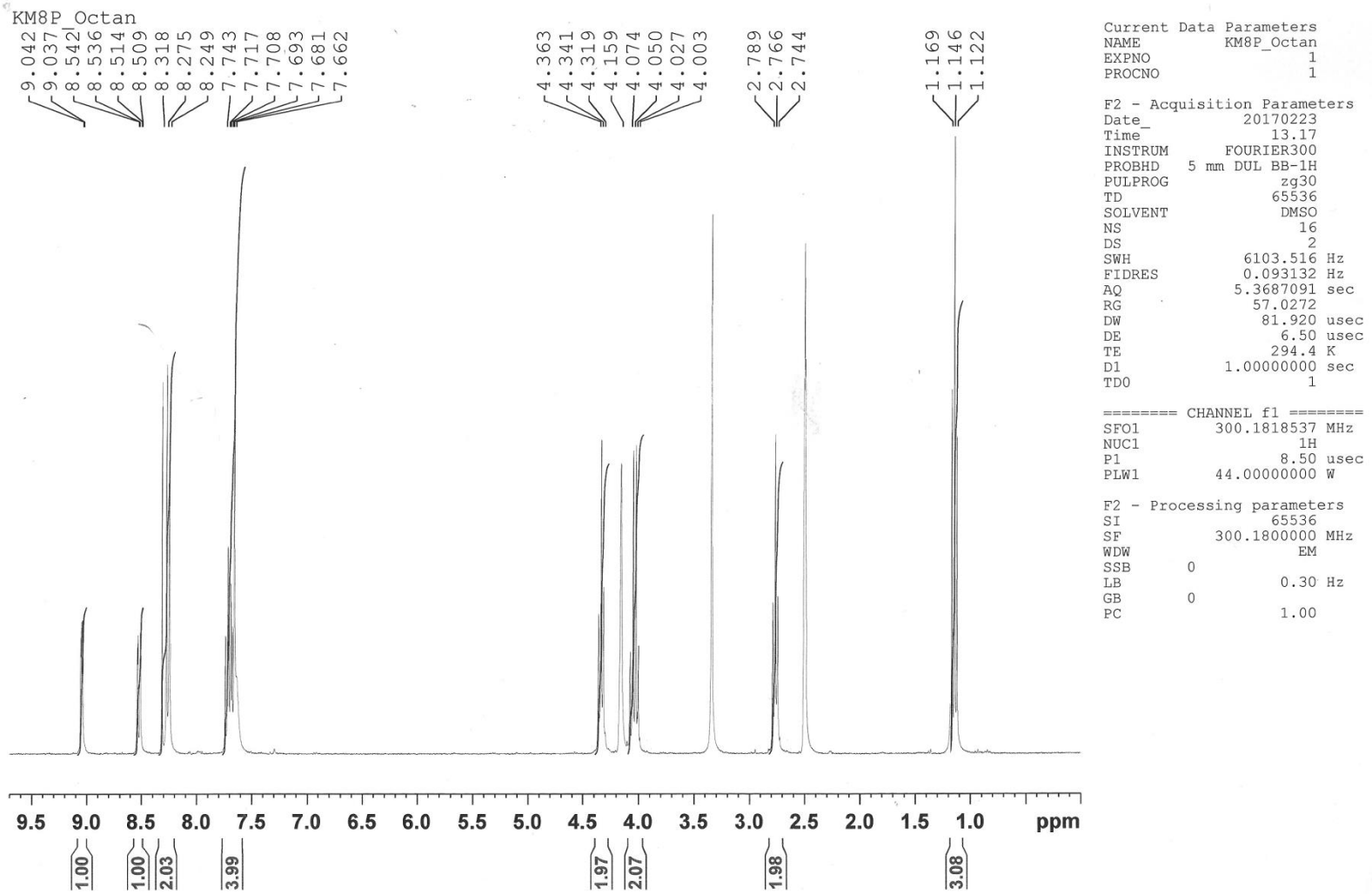
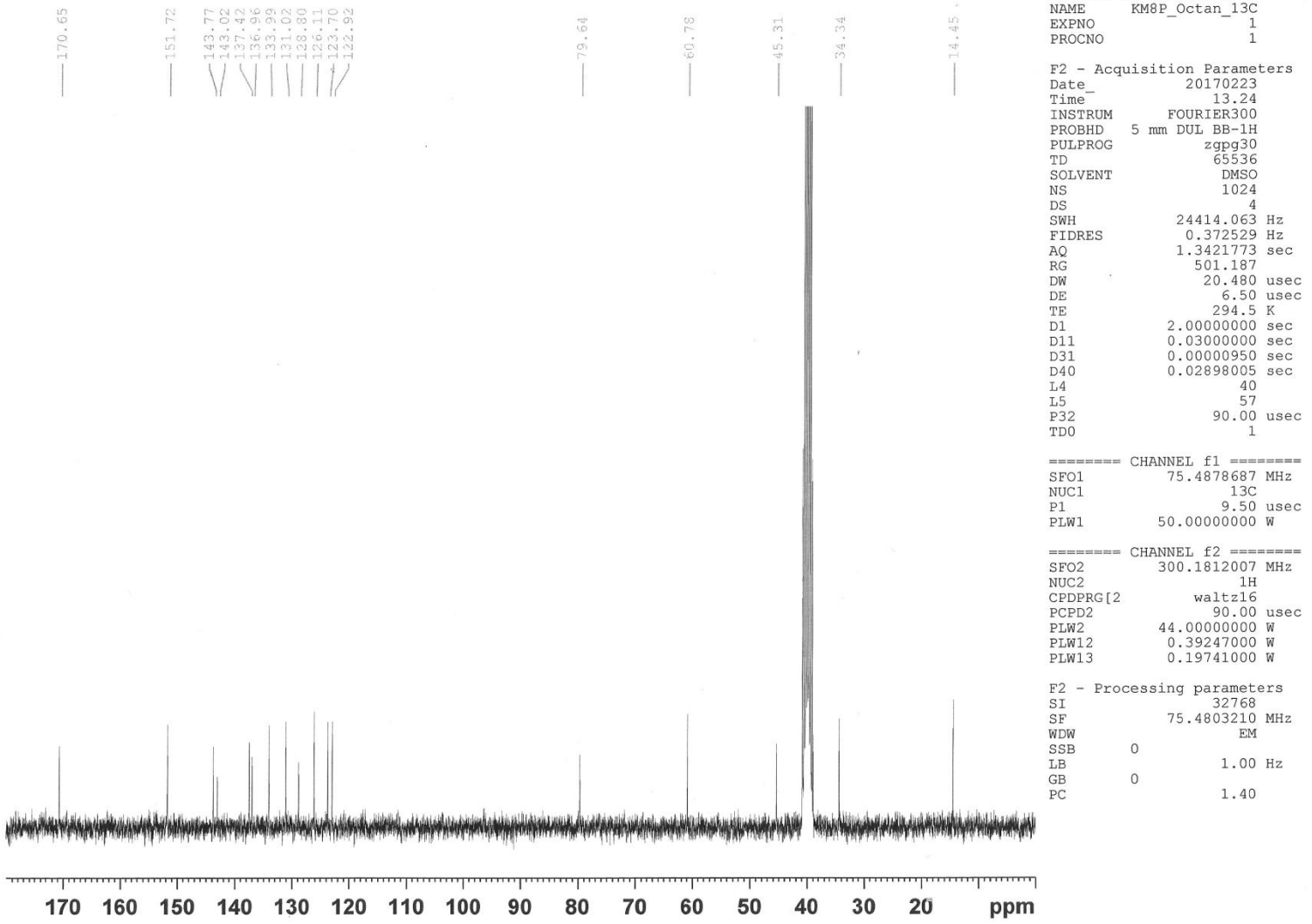



**Figure S22 .** $^{1}$H NMR spectra of ethyl 3-{[4-(8-sulfamoylquinolyl)methyl]-1*H*-1,2,3-triazol-1-yl}propanoate (**9c**)

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Current Data Parameters
NAME      KM8P_Octan_13C
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20170223
Time              13.24
INSTRUM       FOURIER300
PROBHD   5 mm DUL BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                  1024
DS                     4
SWH           24414.063 Hz
FIDRES         0.372529 Hz
AQ             1.3421773 sec
RG               501.187
DW                20.480 usec
DE                 6.50 usec
TE                294.5 K
D1           2.00000000 sec
D11          0.03000000 sec
D31          0.00000950 sec
D40          0.02898005 sec
L4                    40
L5                    57
P32                90.00 usec
TD0                    1

======== CHANNEL f1 ========
SFO1         75.4878687 MHz
NUC1                13C
P1                 9.50 usec
PLW1        50.00000000 W

======== CHANNEL f2 ========
SFO2        300.1812007 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2              90.00 usec
PLW2        44.00000000 W
PLW12        0.39247000 W
PLW13        0.19741000 W

F2 - Processing parameters
SI                 32768
SF          75.4803210 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

**Figure S23 .** $^{13}$C NMR spectra of ethyl 3-{[4-(8-sulfamoylquinolyl)methyl]-1*H*-1,2,3-triazol-1-yl}propanoate (**9c**)

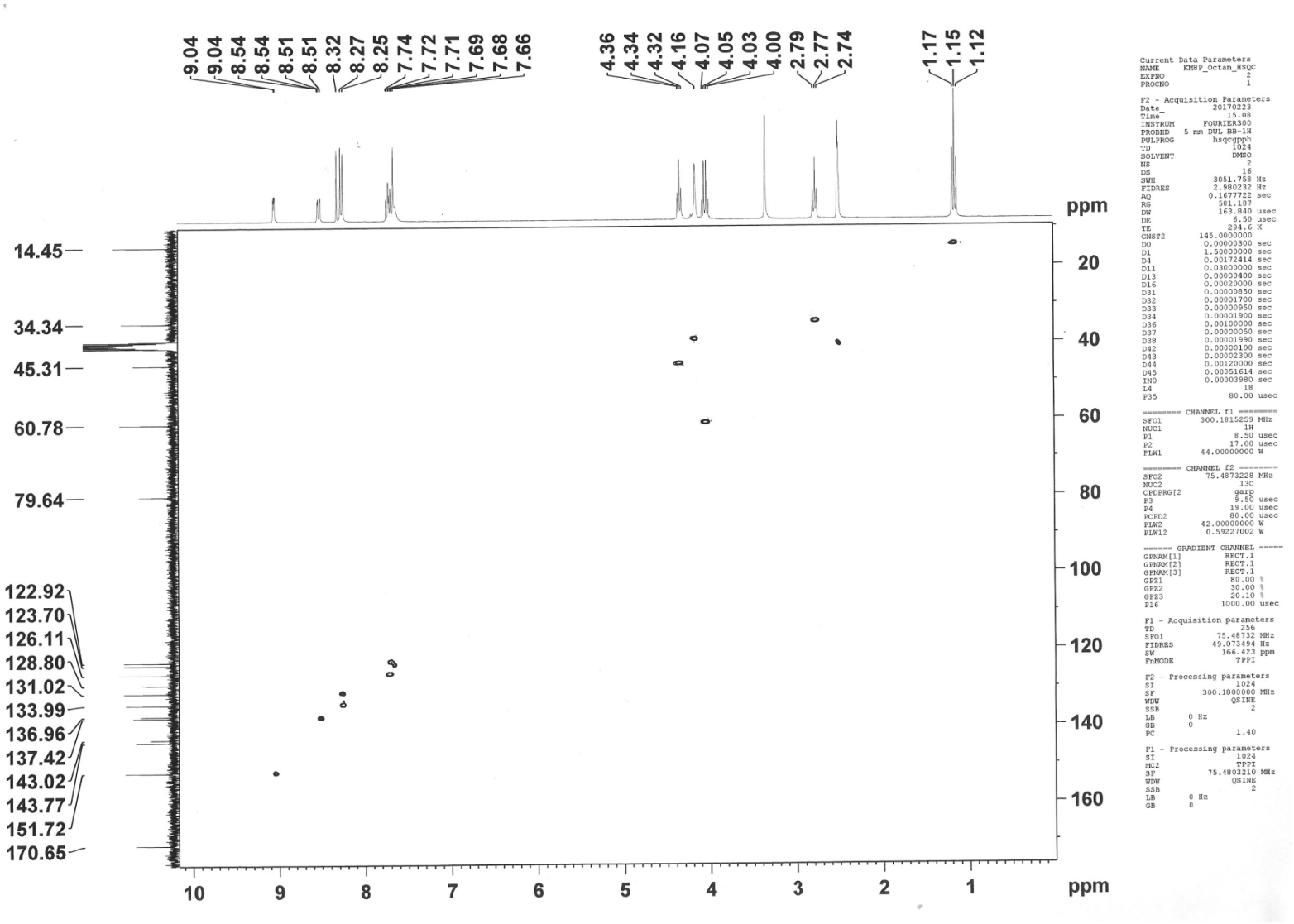



**Figure S24 .** $^{1}$HSQC spectra of ethyl 3-{[4-(8-sulfamoylquinolyl)methyl]-1*H*-1,2,3-triazol-1-yl}propanoate (**9c**)

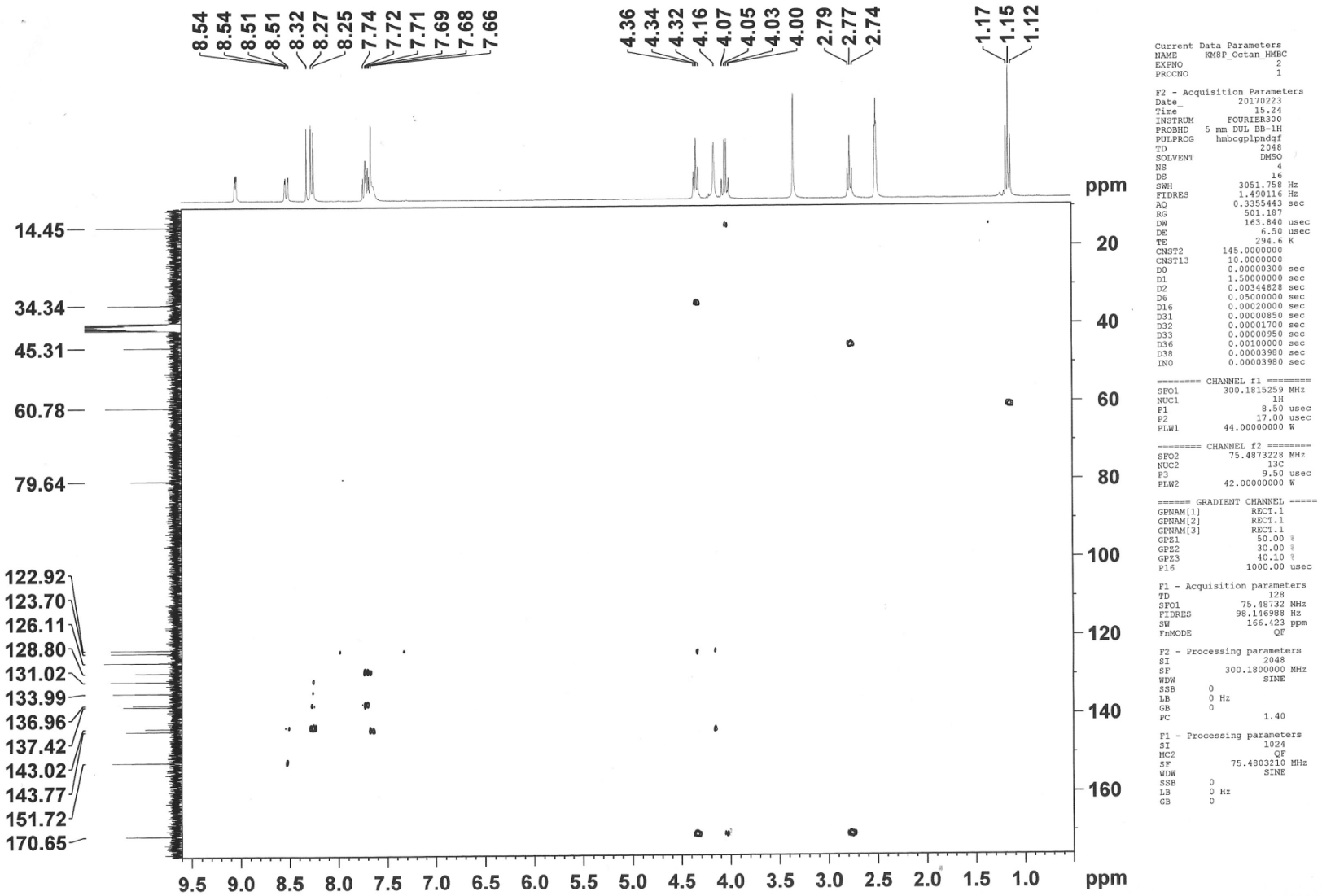



**Figure S25 .** [1]HMBC spectra of ethyl 3-{[4-(8-sulfamoylquinolyl)methyl]-1*H*-1,2,3-triazol-1-yl}propanoate (**9c**)

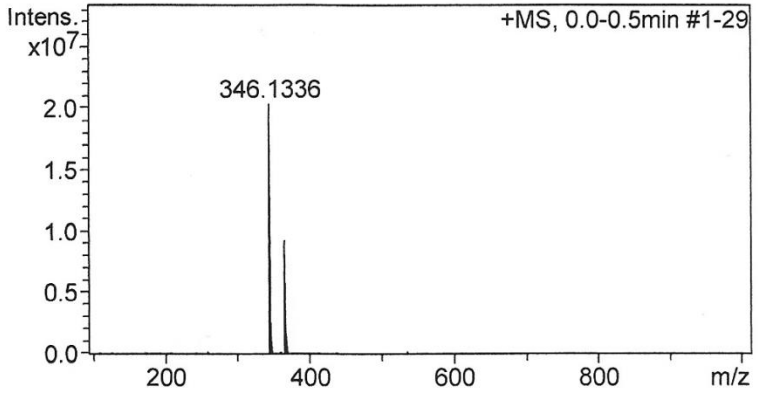
# Compound Spectrum List Report

**Analysis Info**

| | | | | | |
|---|---|---|---|---|---|
| Analysis Name | D:\Data\KMBuyl.d | | | | |
| Method | low_mass.m | | | Operator | KM |
| Sample Name | TM Low concentration | | | Instrument | impact II 1825265.10082 |
| Comment | | | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 4000 V | Set Dry Heater | 240 °C |
| Scan Begin | 100 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 1000 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




| # | m/z | Res. | S/N | I | I % | FWHM |
|---|---|---|---|---|---|---|
| 1 | 346.1336 | 20957 | 86756.1 | 20377468 | 100.0 | 0.0165 |
| 2 | 368.1154 | 43608 | 36143.5 | 9331787 | 45.8 | 0.0084 |

**Figure S26 .** HR MS spectra of 8-*N*-{[1-(1-butyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9d**)

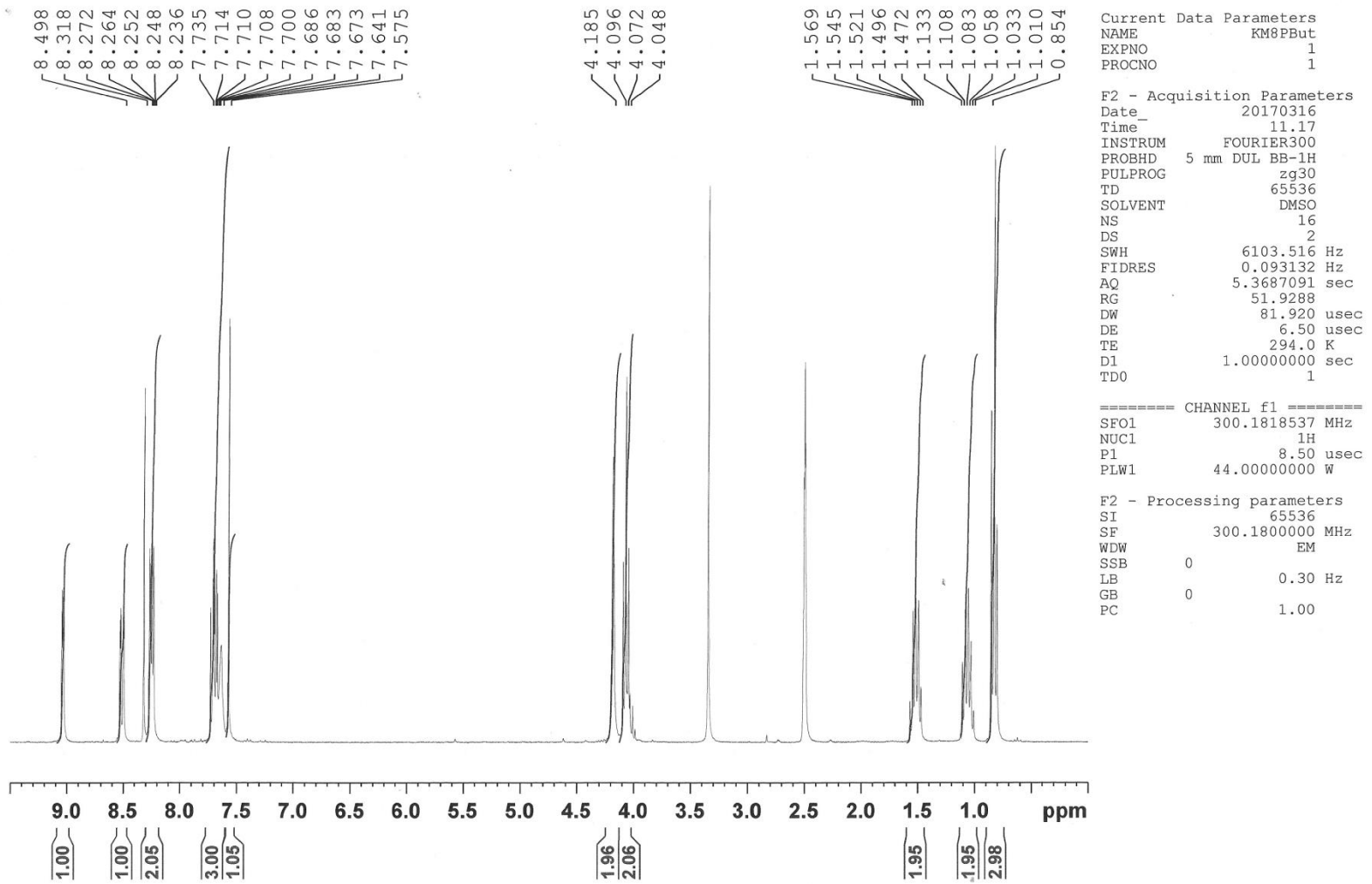



**Figure S27 .** $^{1}$H NMR spectra of 8-*N*-{[1-(1-butyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9d**)

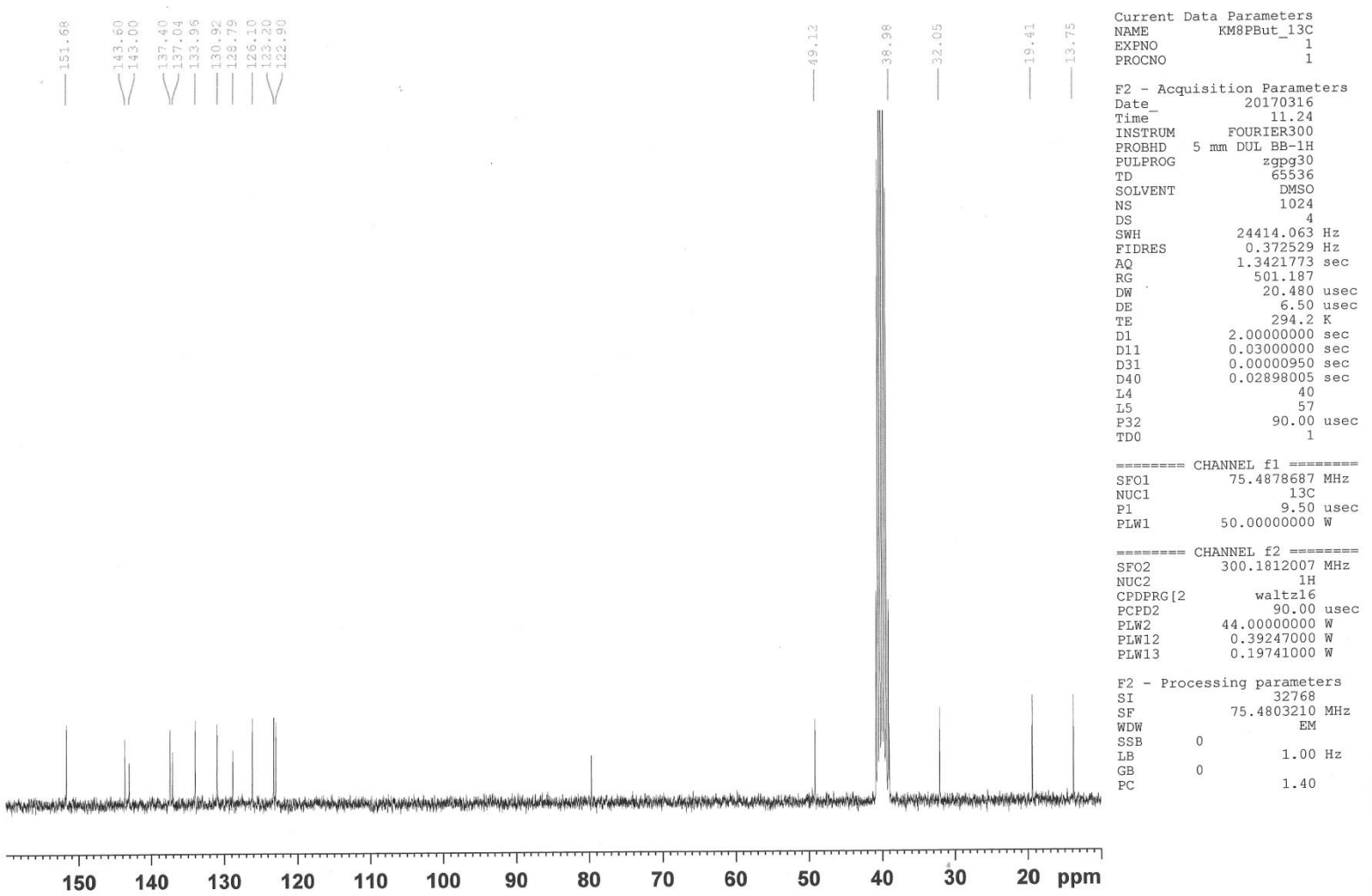



**Figure S28**. $^{13}$C NMR spectra of 8-*N*-{[1-(1-butyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9d**)

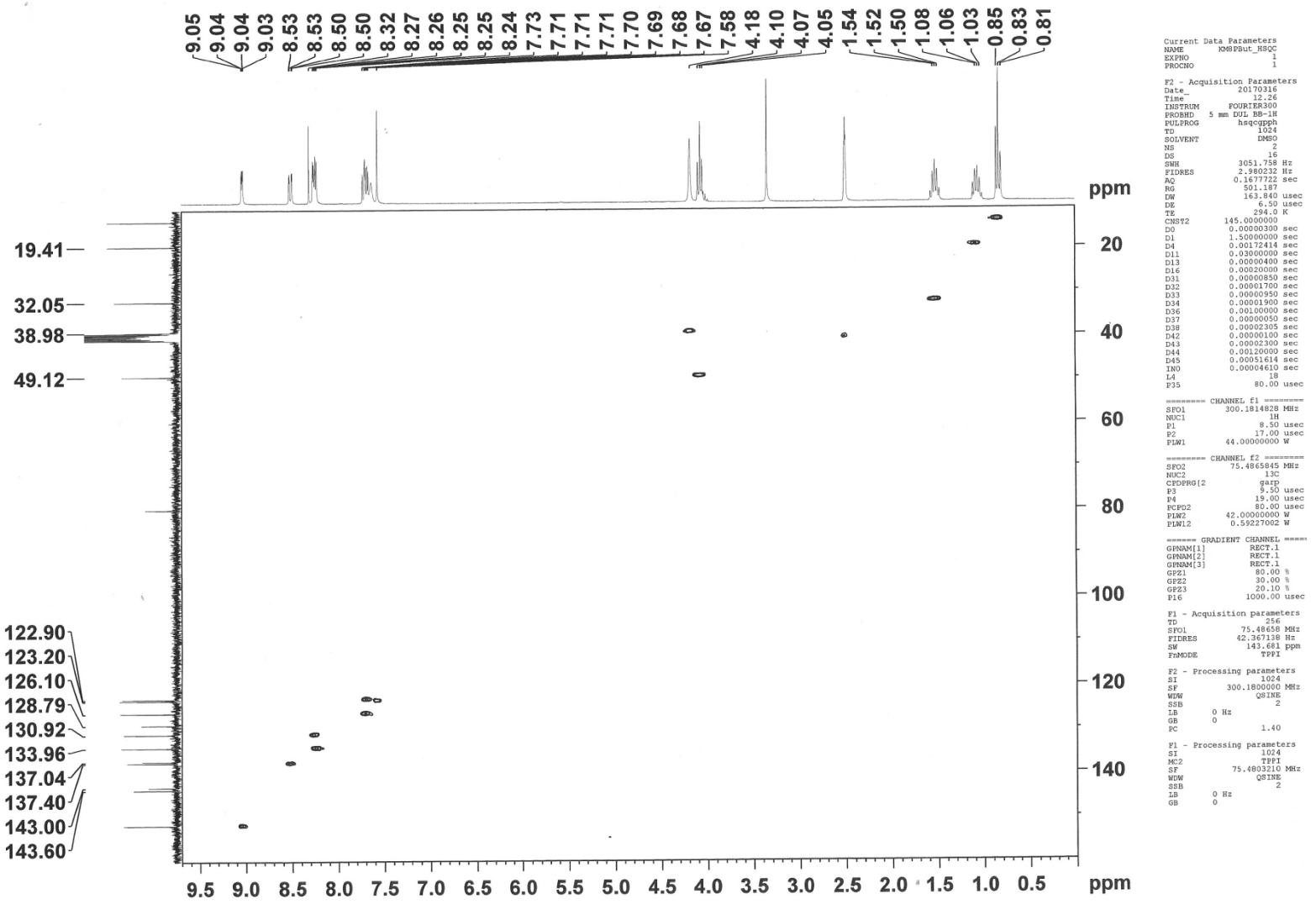



**Figure S29**. HSQC spectra of 8-*N*-{[1-(1-butyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9d**)

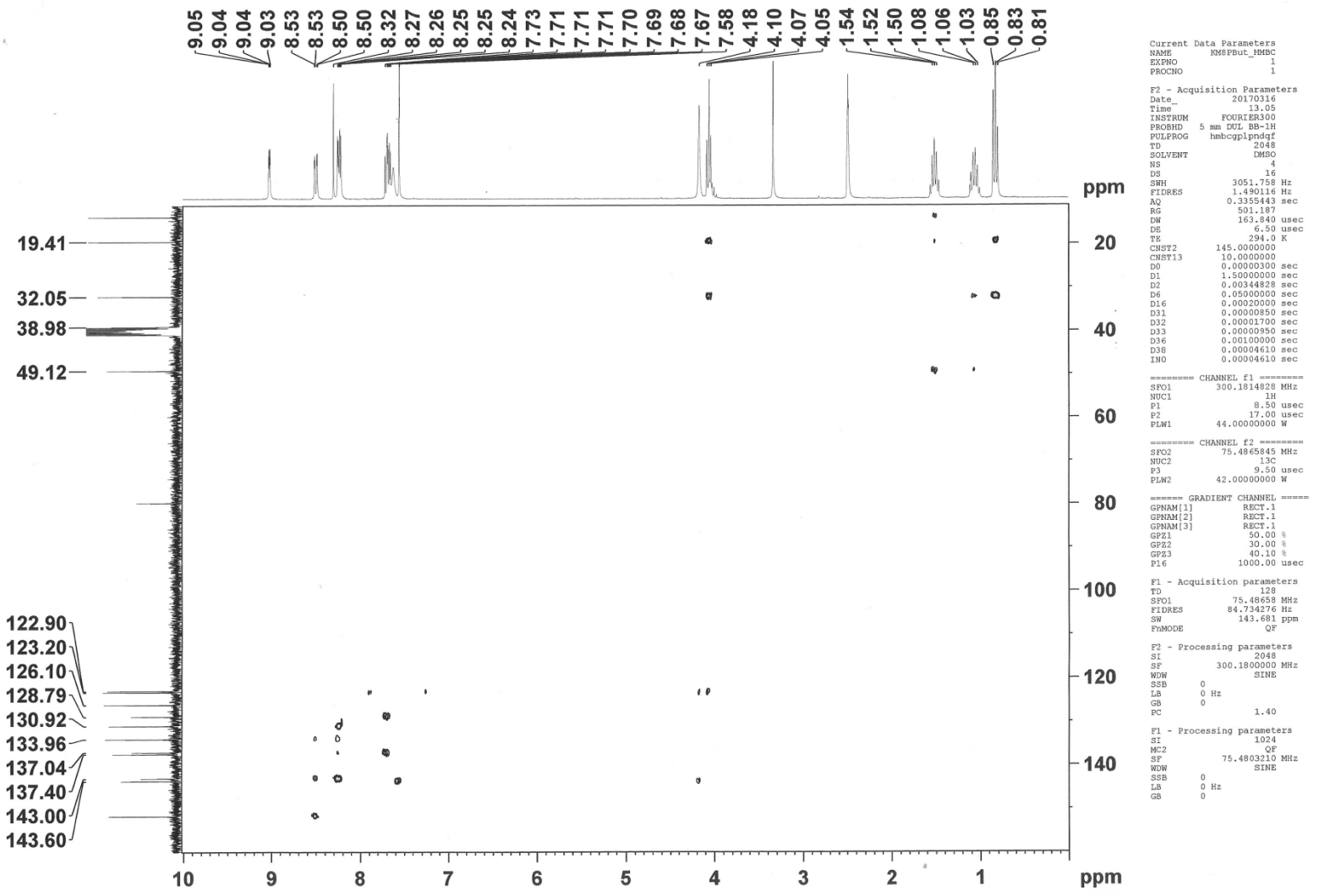



**Figure S30**. HMBC spectra of 8-*N*-{[1-(1-butyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9d**)

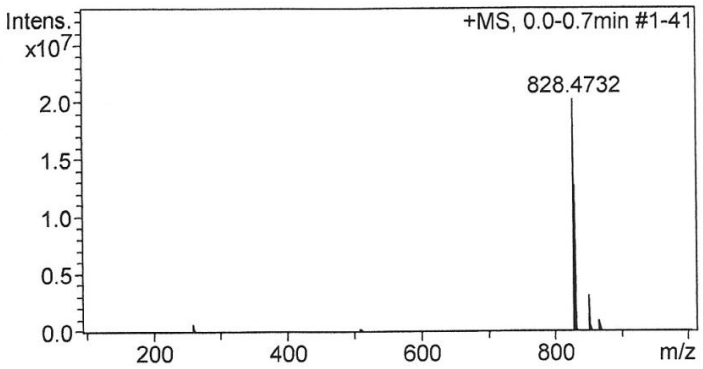
# Compound Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\KMMeBetulinaPositive.d | | |
| Method | low_mass.m | Operator | KM |
| Sample Name | TM Low concentration | Instrument | impact II 1825265.10082 |
| Comment | | | |

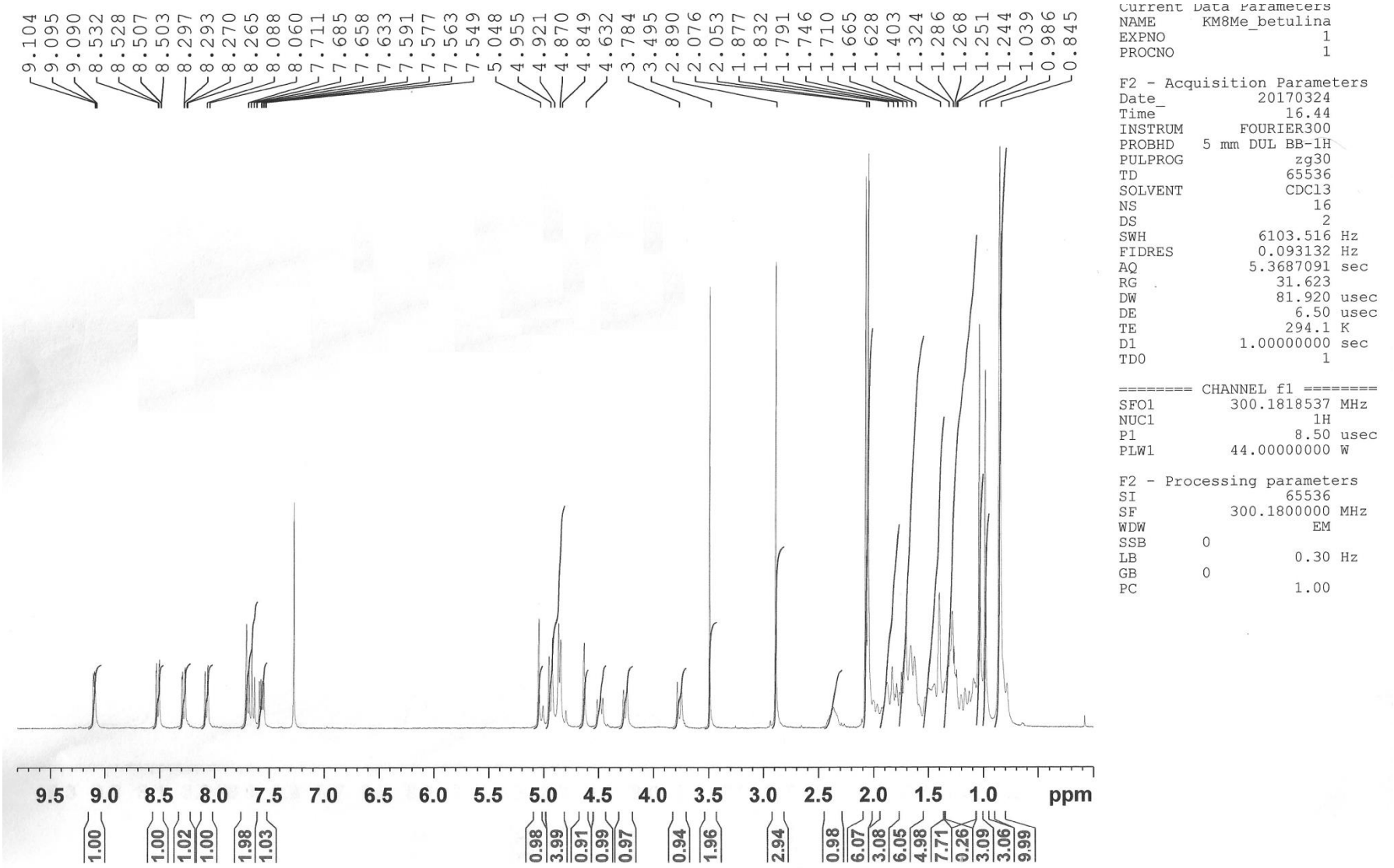
**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 4000 V | Set Dry Heater | 240 °C |
| Scan Begin | 100 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 1000 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




| # | m/z | Res. | S/N | I | I % | FWHM |
|---|---|---|---|---|---|---|
| 1 | 828.4732 | 36740 | 57187.3 | 20214546 | 100.0 | 0.0225 |
| 2 | 850.4540 | 54137 | 9022.8 | 3173013 | 15.7 | 0.0157 |
| 3 | 866.4274 | 43927 | 2836.8 | 980902 | 4.9 | 0.0197 |

**Figure S31.** HR MS spectra of 8-*N*-methyl-*N*-({1-[3β, 28-diacetoxylup-20(29)-en-30-yl]-1*H*-1,2,3-triazol-4-yl}methyl)-quinolinesulfonamide (**9e**)




```
Current Data Parameters
NAME      KM8Me_betulina
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170324
Time               16.44
INSTRUM       FOURIER300
PROBHD   5 mm DUL BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           6103.516 Hz
FIDRES        0.093132 Hz
AQ            5.3687091 sec
RG               31.623
DW               81.920 usec
DE                6.50 usec
TE               294.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.1818537 MHz
NUC1                 1H
P1                 8.50 usec
PLW1        44.00000000 W

F2 - Processing parameters
SI                 65536
SF           300.1800000 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

**Figure S32** . $^{1}$H NMR spectra of 8-*N*-methyl-*N*-({1-[3β, 28-diacetoxylup-20(29)-en-30-yl]-1*H*-1,2,3-triazol-4-yl}methyl)-quinolinesulfonamide (**9e**)

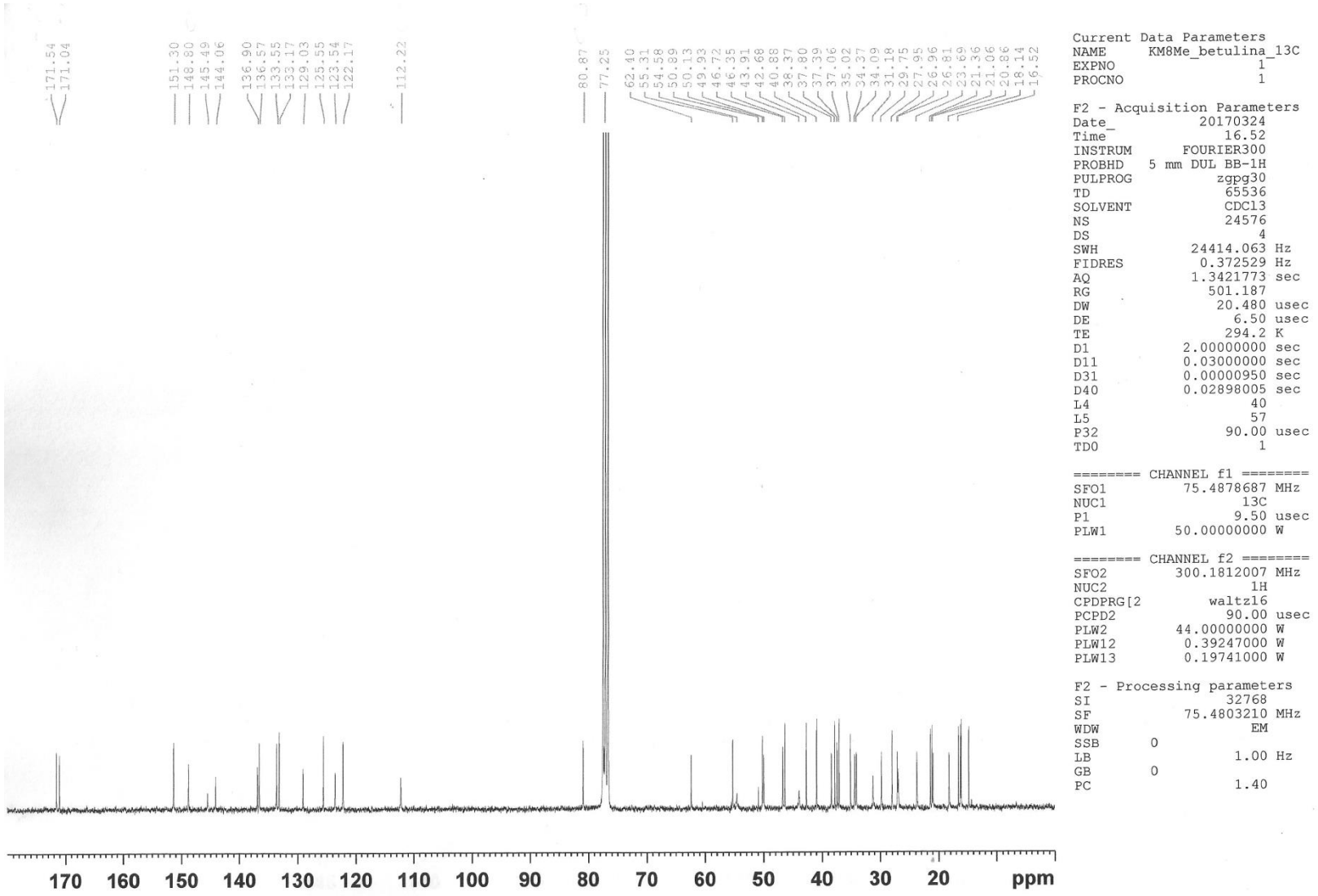



**Figure S33** . $^{13}$C NMR spectra of 8-*N*-methyl-*N*-({1-[3β, 28-diacetoxylup-20(29)-en-30-yl]-1*H*-1,2,3-triazol-4-yl}methyl)-quinolinesulfonamide (**9e**)

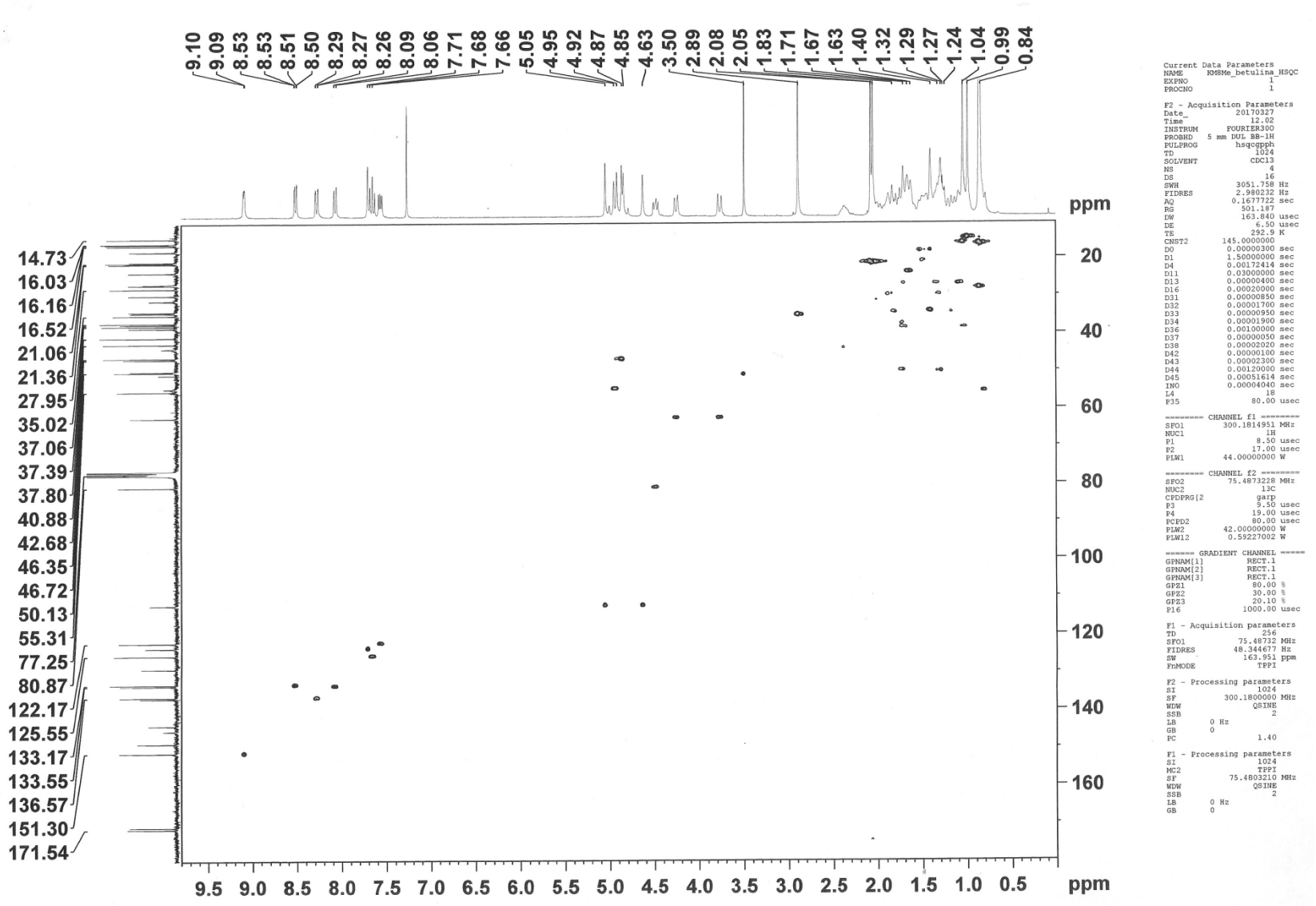



**Figure S34** . HSQC spectra of 8-*N*-methyl-*N*-({1-[3β, 28-diacetoxylup-20(29)-en-30-yl]-1*H*-1,2,3-triazol-4-yl}methyl)-quinolinesulfonamide (**9e**)

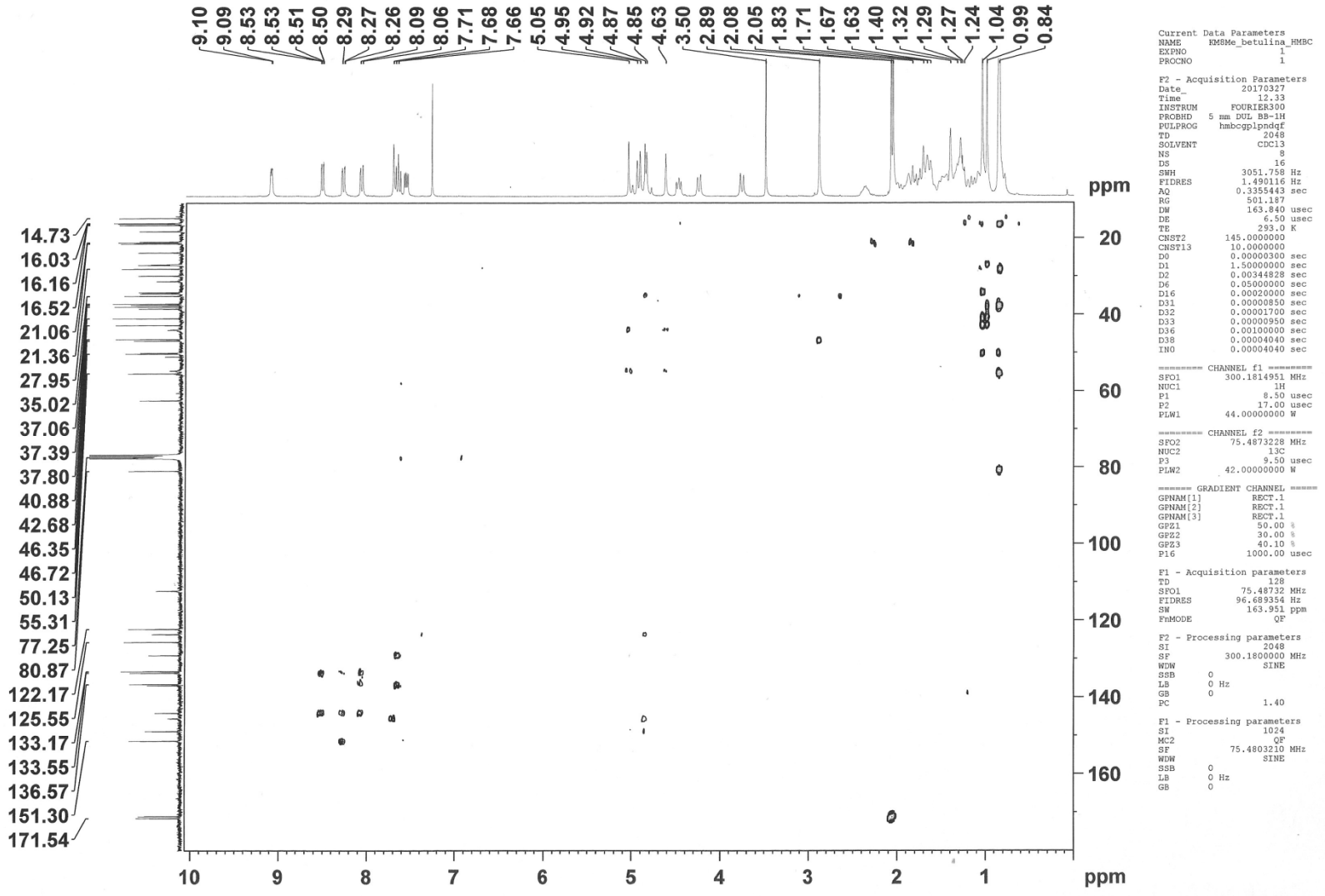


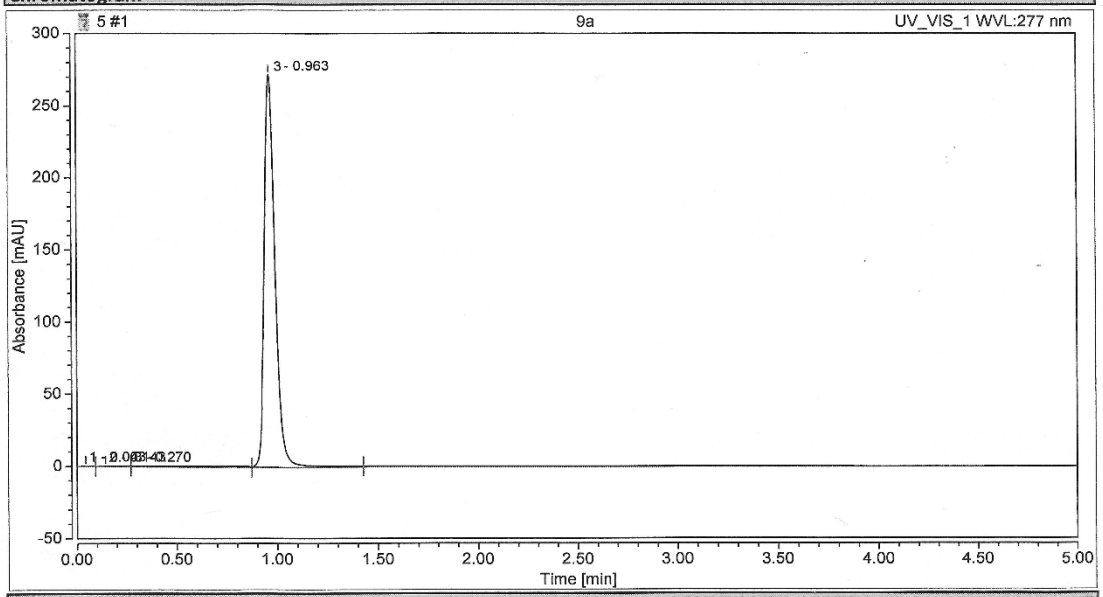

**Figure S35** . HMBC spectra of 8-*N*-methyl-*N*-({1-[3β, 28-diacetoxylup-20(29)-en-30-yl]-1*H*-1,2,3-triazol-4-yl}methyl)-quinolinesulfonamide (**9e**)

## Chromatogram and Results

### Injection Details

| | | | |
|---|---|---|---|
| *Injection Name:* | **9a** | *Run Time (min):* | **5.00** |
| *Vial Number:* | **RA1** | *Injection Volume:* | **5.00** |
| *Injection Type:* | **Unknown** | *Channel:* | **UV_VIS_1** |
| *Calibration Level:* | | *Wavelength:* | **277.0** |
| *Instrument Method:* | **ACN 80 HCOOH** | *Bandwidth:* | **2** |
| *Processing Method:* | **LC MS** | *Dilution Factor:* | **1.0000** |
| *Injection Date/Time:* | **15/Feb/23 15:05** | *Sample Weight:* | **1.0000** |

### Chromatogram




### Integration Results

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Relative Height % | Amount n.a. |
|---|---|---|---|---|---|---|---|
| 1 | | 0.043 | 0.012 | 0.186 | 0.06 | 0.07 | n.a. |
| 2 | | 0.143 | 0.047 | 0.242 | 0.25 | 0.09 | n.a. |
| 3 | | 0.963 | 17.259 | 272.469 | 99.69 | 99.85 | n.a. |
| **Total:** | | | **17.318** | **272.897** | **100.00** | **100.00** | |



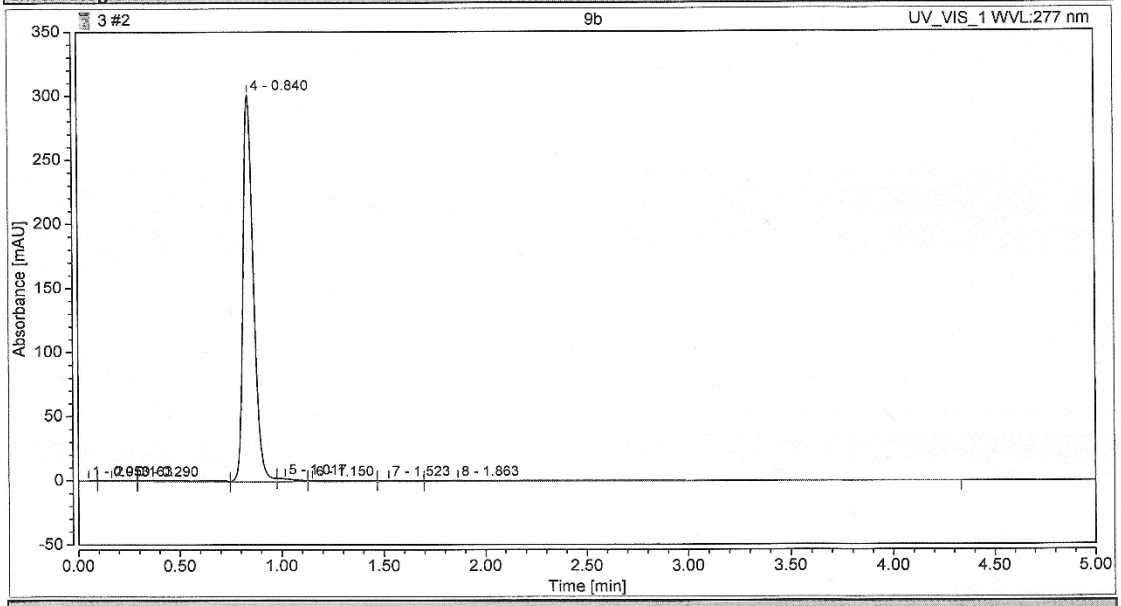
**Figure S36**. HPLC analysis of 8-*N*-{[1-(7-chloroquinolin-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (**9a**)

## Chromatogram and Results

### Injection Details

| | | | |
|---|---|---|---|
| *Injection Name:* | **9b** | *Run Time (min):* | **5.00** |
| *Vial Number:* | **RA2** | *Injection Volume:* | **5.00** |
| *Injection Type:* | **Unknown** | *Channel:* | **UV_VIS_1** |
| *Calibration Level:* | | *Wavelength:* | **277.0** |
| *Instrument Method:* | **ACN 80 HCOOH** | *Bandwidth:* | **2** |
| *Processing Method:* | **LC MS** | *Dilution Factor:* | **1.0000** |
| *Injection Date/Time:* | **15/Feb/23 14:36** | *Sample Weight:* | **1.0000** |

### Chromatogram




### Integration Results

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Relative Height % | Amount n.a. |
|---|---|---|---|---|---|---|---|
| 1 | | 0.050 | 0.012 | 0.186 | 0.06 | 0.06 | n.a. |
| 2 | | 0.163 | 0.056 | 0.275 | 0.29 | 0.09 | n.a. |
| 3 | | 0.290 | 0.261 | 0.376 | 1.33 | 0.12 | n.a. |
| 4 | | 0.840 | 17.635 | 301.871 | 90.15 | 98.19 | n.a. |
| 5 | | 1.017 | 0.253 | 2.218 | 1.29 | 0.72 | n.a. |
| 6 | | 1.150 | 0.282 | 0.965 | 1.44 | 0.31 | n.a. |
| 7 | | 1.523 | 0.170 | 0.832 | 0.87 | 0.27 | n.a. |
| 8 | | 1.863 | 0.892 | 0.724 | 4.56 | 0.24 | n.a. |
| **Total:** | | | **19.562** | **307.447** | **100.00** | **100.00** | |



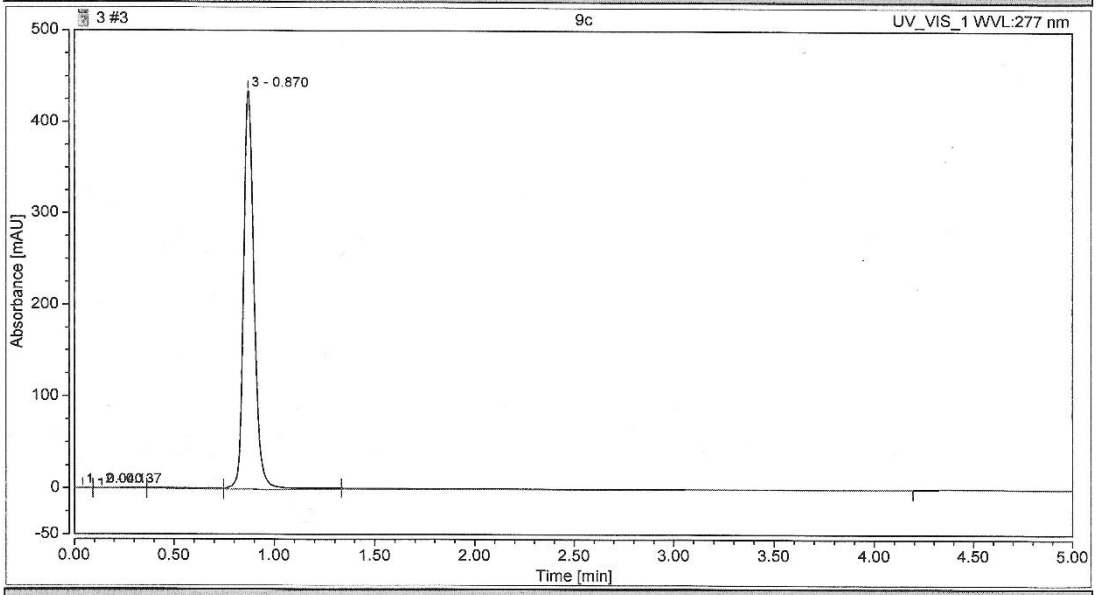
**Figure S37.** diethyl 2-{4-[methyl-(8-sulfamoylquinolyl)-1*H*-1,2,3-triazol-1-yl]}ethylphosphonate (**9b**)

## Chromatogram and Results

### Injection Details

| | | | |
|---|---|---|---|
| *Injection Name:* | **9c** | *Run Time (min):* | **5.00** |
| *Vial Number:* | **RA3** | *Injection Volume:* | **5.00** |
| *Injection Type:* | **Unknown** | *Channel:* | **UV_VIS_1** |
| *Calibration Level:* | | *Wavelength:* | **277.0** |
| *Instrument Method:* | **ACN 80 HCOOH** | *Bandwidth:* | **2** |
| *Processing Method:* | **LC MS** | *Dilution Factor:* | **1.0000** |
| *Injection Date/Time:* | **15/Feb/23 14:42** | *Sample Weight:* | **1.0000** |

### Chromatogram




### Integration Results

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Relative Height % | Amount n.a. |
|---|---|---|---|---|---|---|---|
| 1 | | 0.040 | 0.013 | 0.193 | 0.05 | 0.04 | n.a. |
| 2 | | 0.137 | 0.084 | 0.243 | 0.30 | 0.05 | n.a. |
| 3 | | 0.870 | 0.229 | 0.841 | 99.65 | 99.40 | n.a. |
| **Total:** | | | **25.842** | **435.180** | **100.00** | **100.00** | |



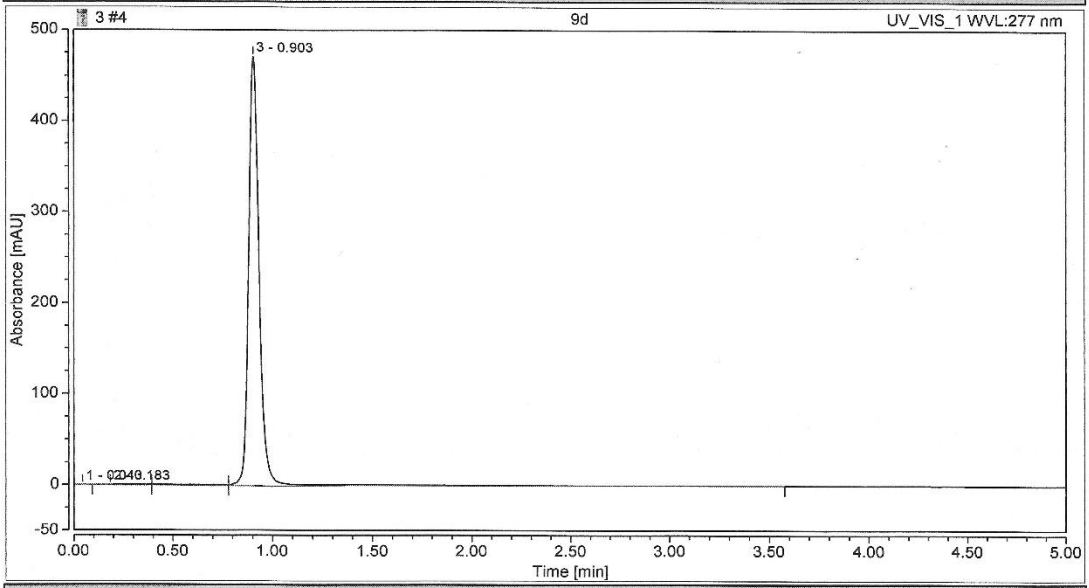
**Figure S3**8. ethyl 3-{[4-(8-sulfamoylquinolyl)methyl]-1*H*-1,2,3-triazol-1-yl}propanoate (**9c**)

## Chromatogram and Results

### Injection Details

| | | | |
|---|---|---|---|
| *Injection Name:* | **9d** | *Run Time (min):* | **5.00** |
| *Vial Number:* | **RA4** | *Injection Volume:* | **5.00** |
| *Injection Type:* | **Unknown** | *Channel:* | **UV_VIS_1** |
| *Calibration Level:* | | *Wavelength:* | **277.0** |
| *Instrument Method:* | **ACN 80 HCOOH** | *Bandwidth:* | **2** |
| *Processing Method:* | **LC MS** | *Dilution Factor:* | **1.0000** |
| *Injection Date/Time:* | **15/Feb/23 14:48** | *Sample Weight:* | **1.0000** |

### Chromatogram




### Integration Results

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Relative Height % | Amount n.a. |
|---|---|---|---|---|---|---|---|
| 1 | | 0.043 | 0.007 | 0.131 | 0.02 | 0.03 | n.a. |
| 2 | | 0.183 | 0.087 | 0.263 | 0.30 | 0.05 | n.a. |
| 3 | | 0.903 | 28.102 | 471.386 | 99.68 | 99.92 | n.a. |
| **Total:** | | | **28.196** | **471.780** | **100.00** | **100.00** | |



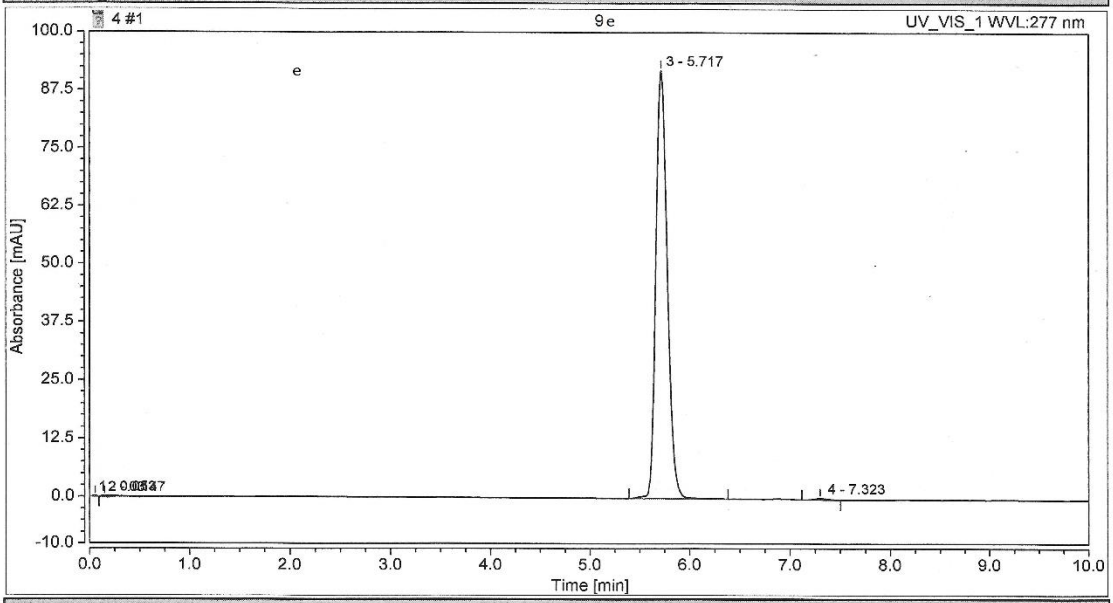
**Figure S39.** 8-*N*-{[1-(1-butyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinolinesulfonamide (9d)

## Chromatogram and Results

### Injection Details

| | | | |
|---|---|---|---|
| *Injection Name:* | **9e** | *Run Time (min):* | **10.00** |
| *Vial Number:* | **RA5** | *Injection Volume:* | **5.00** |
| *Injection Type:* | **Unknown** | *Channel:* | **UV_VIS_1** |
| *Calibration Level:* | | *Wavelength:* | **277.0** |
| *Instrument Method:* | **ACN 80 FA 20 10 min** | *Bandwidth:* | **2** |
| *Processing Method:* | **LC MS** | *Dilution Factor:* | **1.0000** |
| *Injection Date/Time:* | **15/Feb/23 14:54** | *Sample Weight:* | **1.0000** |

### Chromatogram




### Integration Results

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Relative Height % | Amount n.a. |
|---|---|---|---|---|---|---|---|
| 1 | | 0.053 | 0.006 | 0.122 | 0.04 | 0.08 | n.a. |
| 2 | | 0.147 | 0.092 | 0.221 | 0.54 | 0.14 | n.a. |
| 3 | | 5.717 | 12.133 | 92.096 | 97.96 | 99.46 | n.a. |
| 4 | | 7.323 | 0.248 | 0.486 | 1.46 | 0.32 | n.a. |
| **Total:** | | | **12.479** | **92.925** | **100.00** | **100.00** | |



**Figure S40.** 8-*N*-methyl-*N*-({1-[3β, 28-diacetoxylup-20(29)-en-30-yl]-1*H*-1,2,3-triazol-4-yl}methyl)-quinolinesulfonamide (**9e**)