

Sulfonyl fluorides as alternative to sulfonyl chlorides in parallel synthesis of aliphatic sulfonamides

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Figure S1. Parallel synthesis set-up.

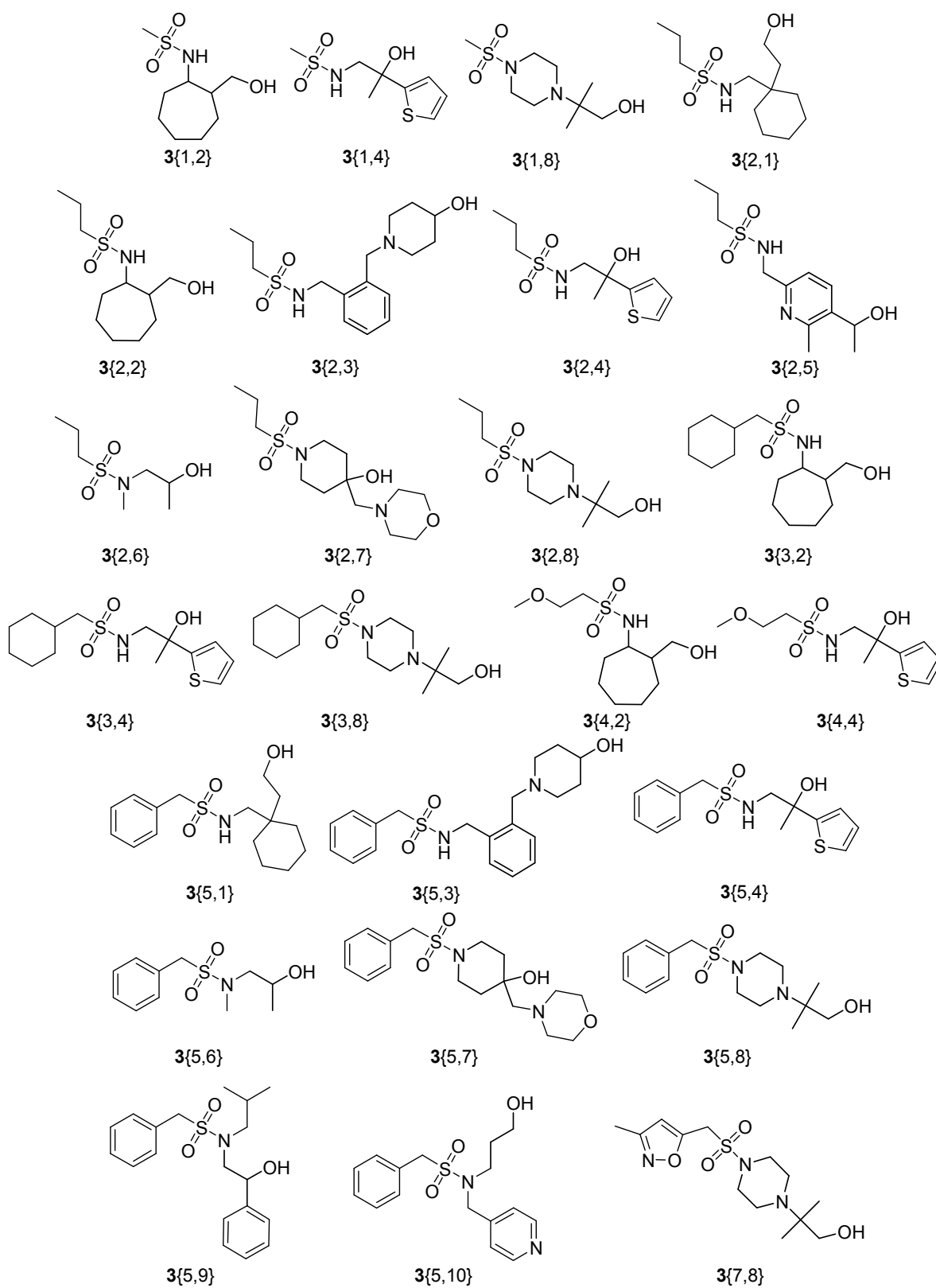


Figure S2. List of sulfonamides synthesized from amines of subgroup Ia.

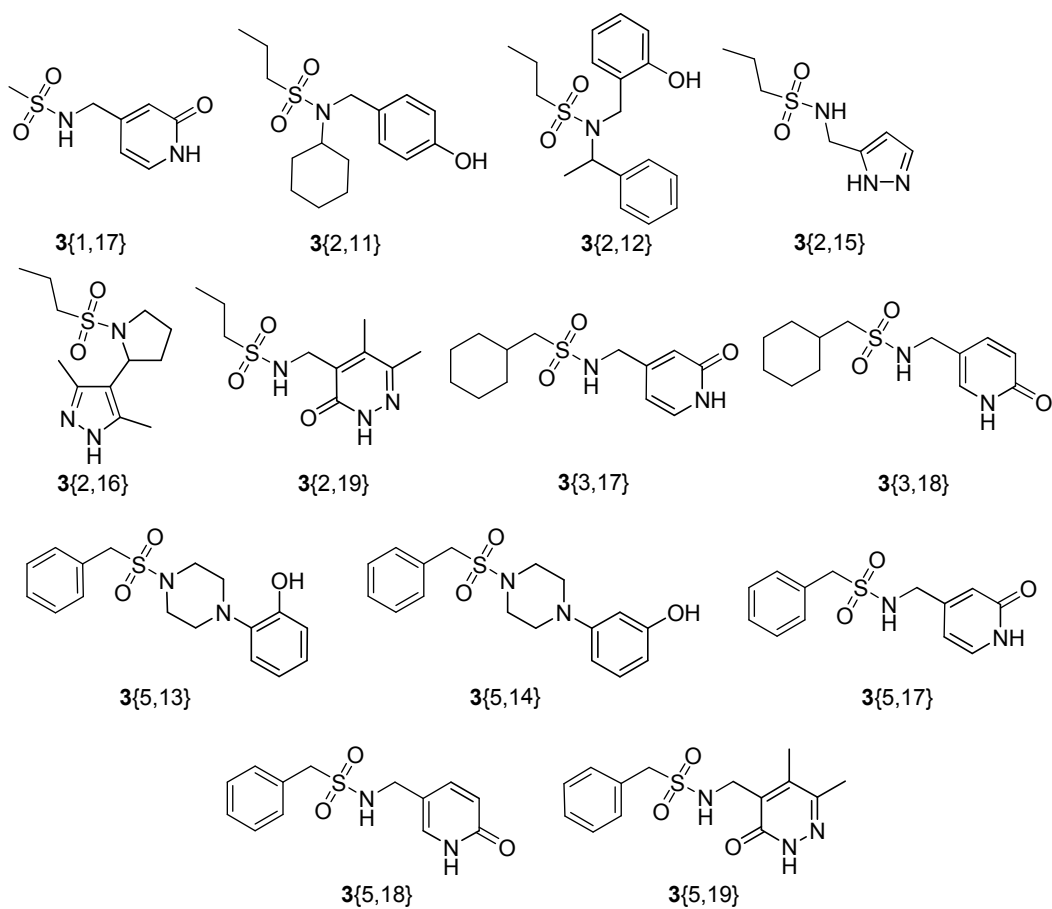


Figure S3. List of sulfonamides synthesized from amines of subgroup Ib.

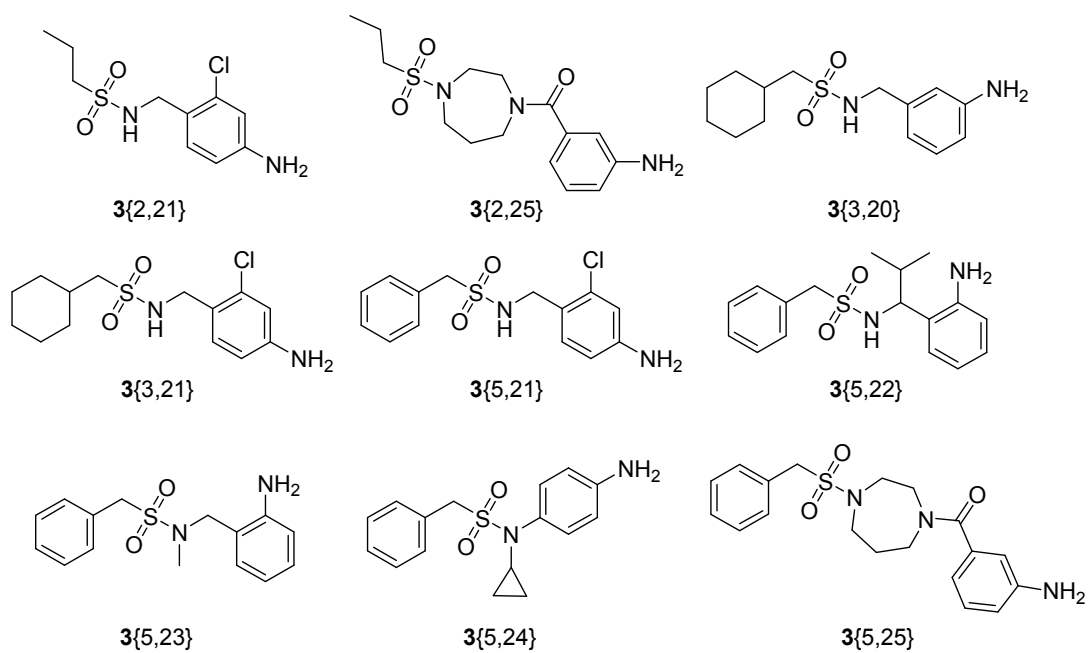


Figure S4. List of sulfonamides synthesized from amines of subgroup Ic.

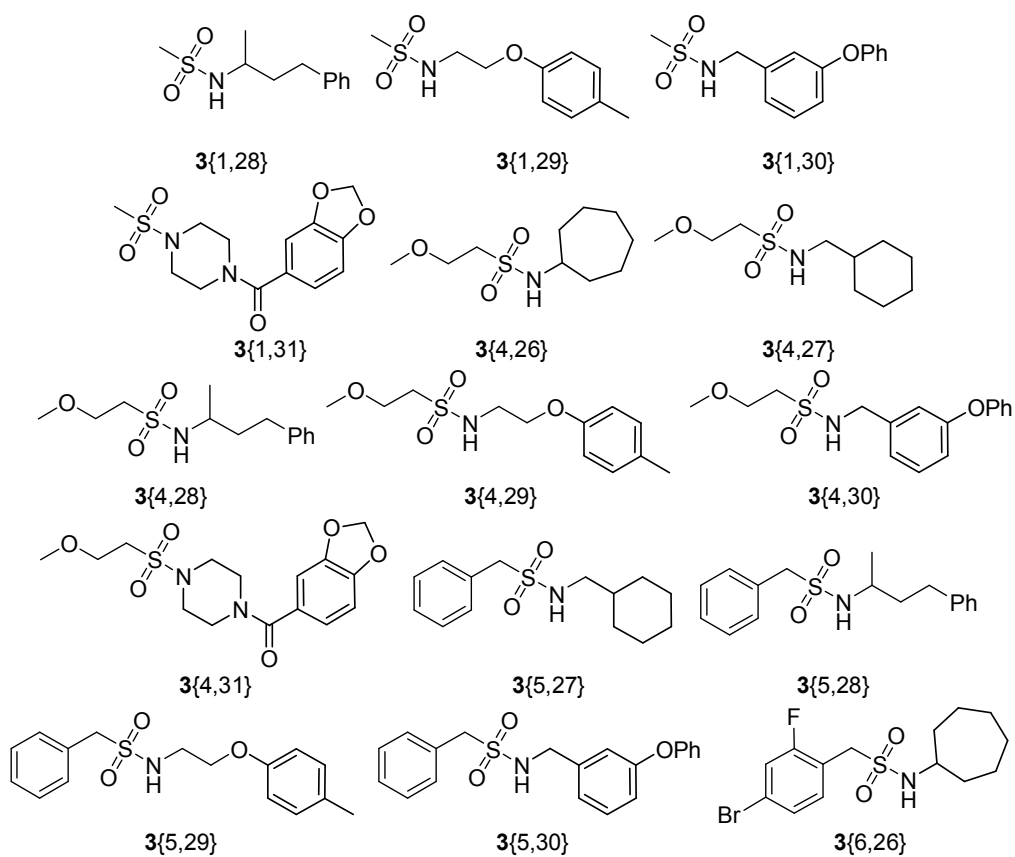


Figure S5. List of sulfonamides synthesized from amines of group II.

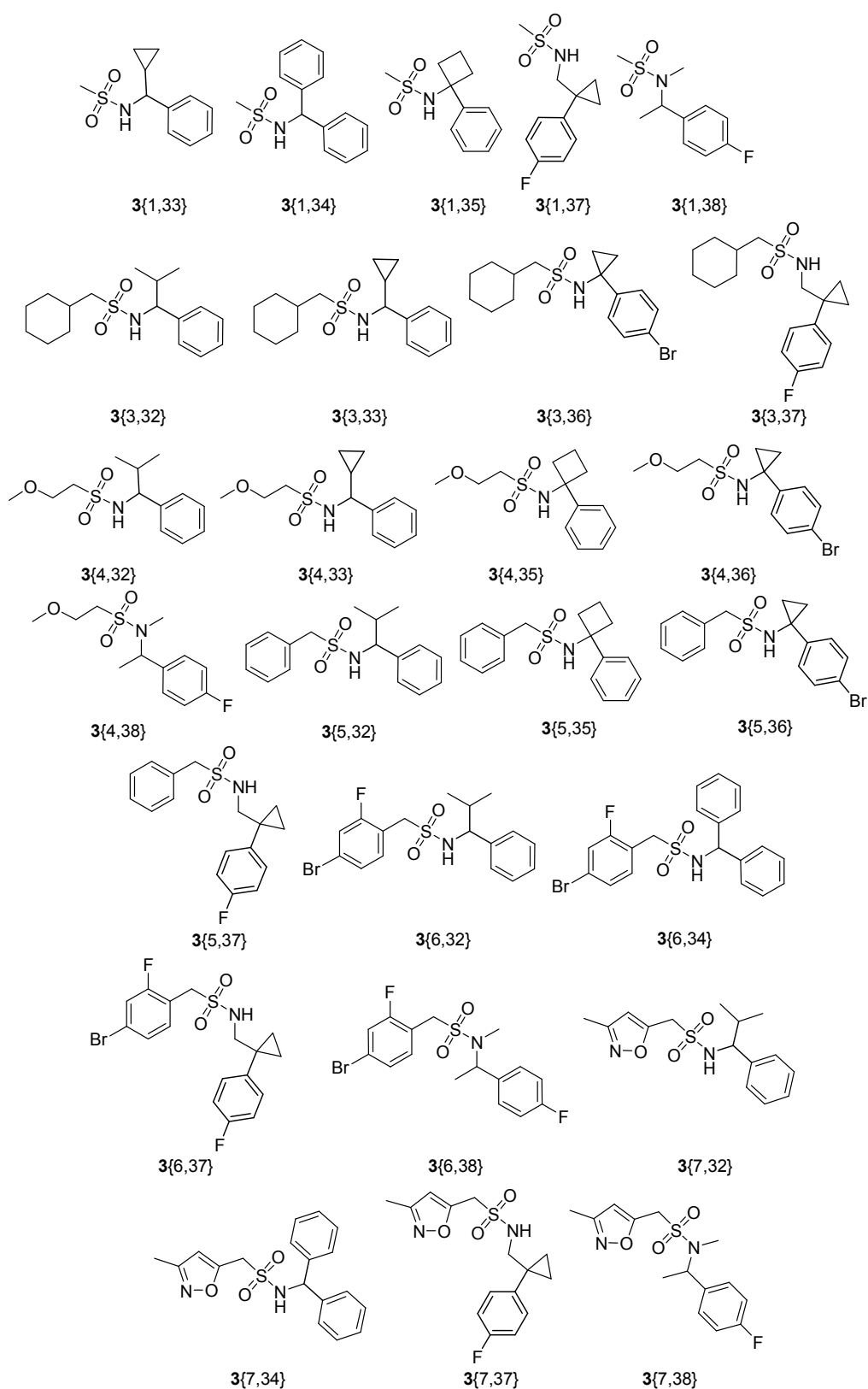
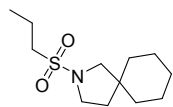


Figure S6. List of sulfonamides synthesized from amines of group **III**.

Representative examples of the identified side products.

Compound **3**{2,1} (Figure S1).

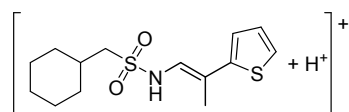


[2-Phenylmethanesulfonyl]-2-aza-spiro[4.5]decane

NMR spectrum is shown in Figure S28 (p. S20).

Compound **3**{3,4} (Figure S1).

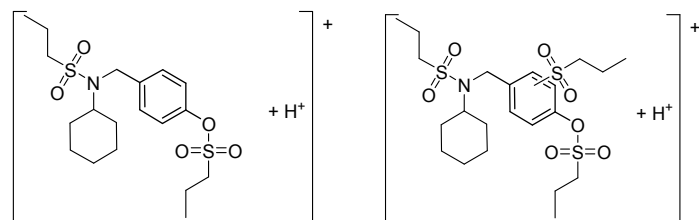
Suggested structure



H₂O-eliminated side product with m/z $[M+H]^+ = 300.1$, Figure S10 (p. S10).

Compound **3**{2,11} (Figure S2).

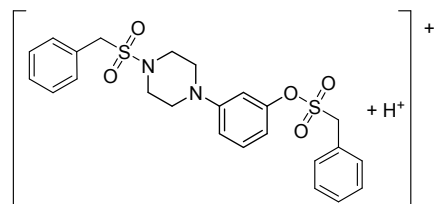
Suggested structures



Di- and trisulfonylated side products with m/z $[M+H]^+ = 418.2$ and 524.2 , respectively, Figure S14 (p. S13).

Compound **3**{5,14} (Figure S2).

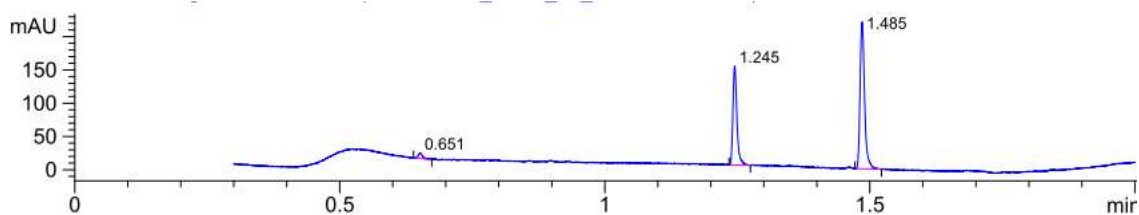
Suggested structure



Disulfonylated side product with m/z $[M+H]^+ = 487.2$, Figure S16 (p. S15).

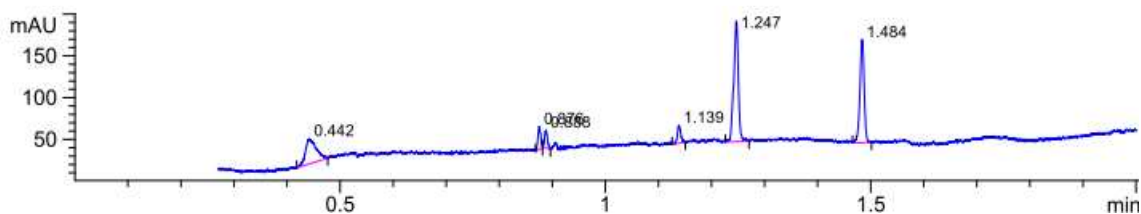
Comparison of LC-MS traces of the selected crude mixtures analyzed after completion of the synthesis (Figures S7-S21).

3{5a,1}



Peaks were assigned to the **product** (1.25 min, 37%), side product - [2-Phenylmethanesulfonyl-2-aza-spiro[4.5]decane (1.48 min, 61%).*.*

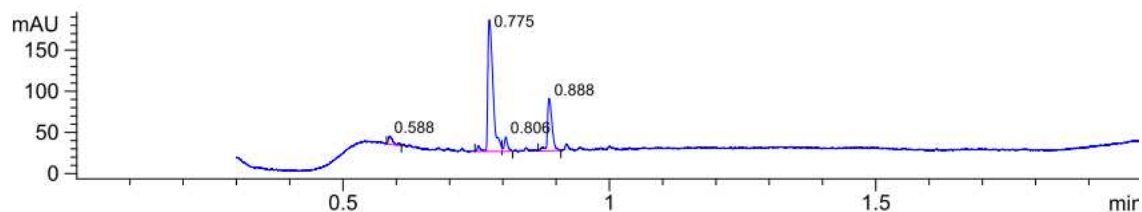
3{5b,1}



Peaks were assigned to the **product** (1.25 min, 39%), [5.6] bicyclo side product (1.48 min, 30%).*.*

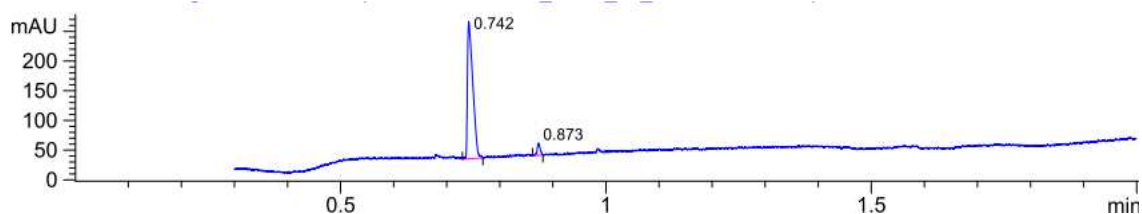
Figure S7

3{2a,3}



Peaks were assigned to the **product** (0.78 min, 67%), trisulfonylated side product (0.89 min, 24%).*

3{2b,3}

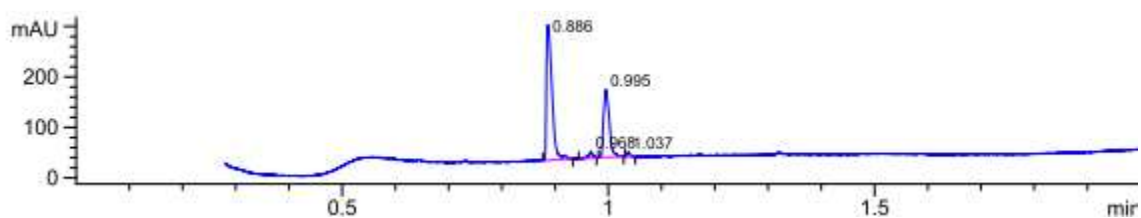


Peaks were assigned to the **product** (0.74 min, 95%), trisulfonylated side product (0.87 min, 5%).*

Figure S8

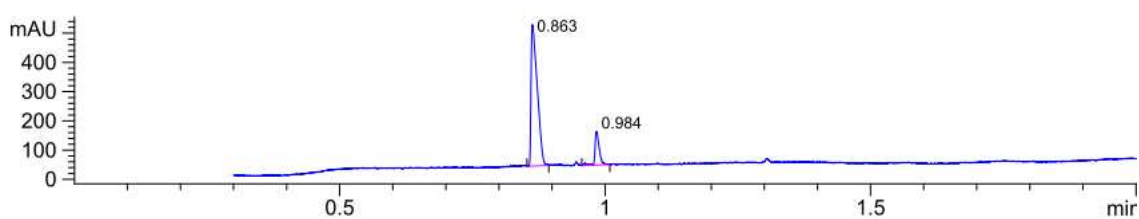
* - assignment is based on the MS data; ** - assignment is based on the NMR data.

3{5a,3}



Peaks were assigned to the **product** (RT 0.89 min, 64%), trisulfonylated side product (1.0 min, 33%).*

3{5b,3}



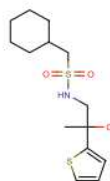
Peaks were assigned to the **product** (0.86 min, 86%), trisulfonylated side product (0.98 min, 14%).*

Figure S9

* - assignment is based on the MS data.

3{3a,4}

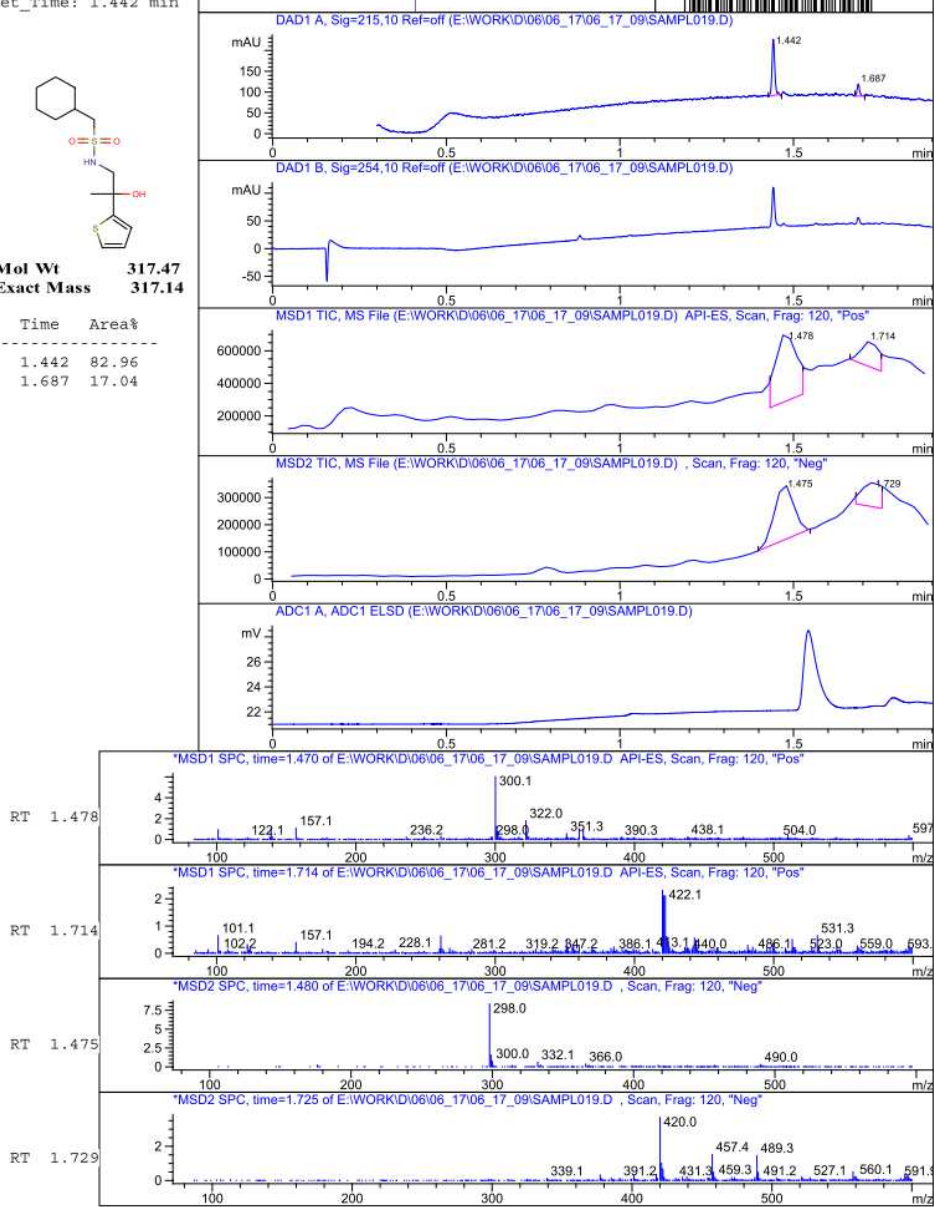
MaxPeak: 82.96%
Ret_Time: 1.442 min



Mol Wt 317.47
Exact Mass 317.14

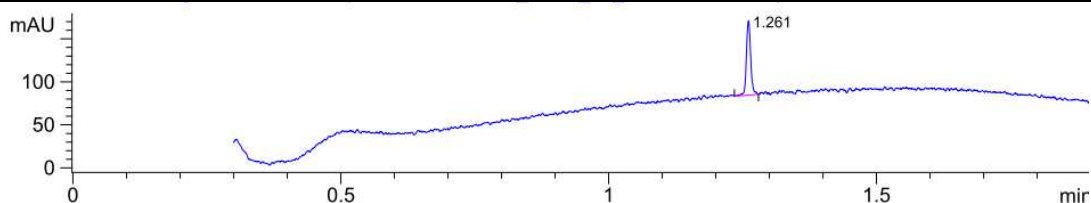
#	Time	Area%
1	1.442	82.96
2	1.687	17.04

6242367



Peak of the **product** was not found, H₂O-eliminated side product (alkene) (1.44 min, 83%).*

3{3b,4}

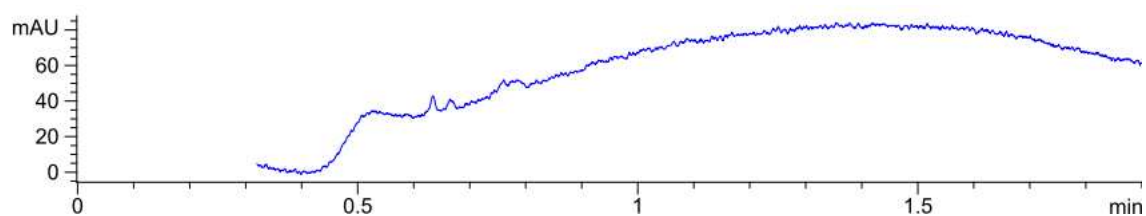


Peak was assigned to the **product** (1.26 min, 100%).*

Figure S10

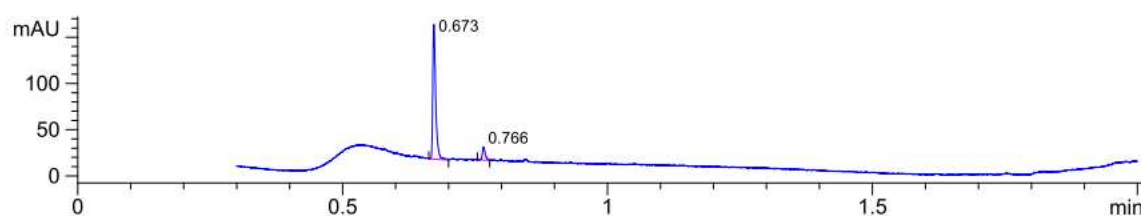
* - assignment is based on the MS data.

3{2a,5}



Peak was assigned to the **product** (0.66 min, 25%).*

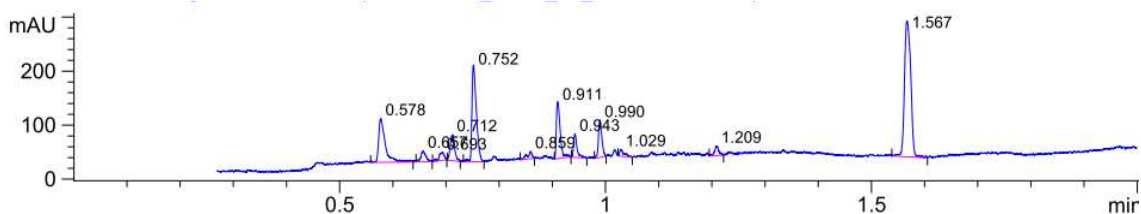
3{2b,5}



Peak was assigned to the **product** (0.67 min, 91%).*

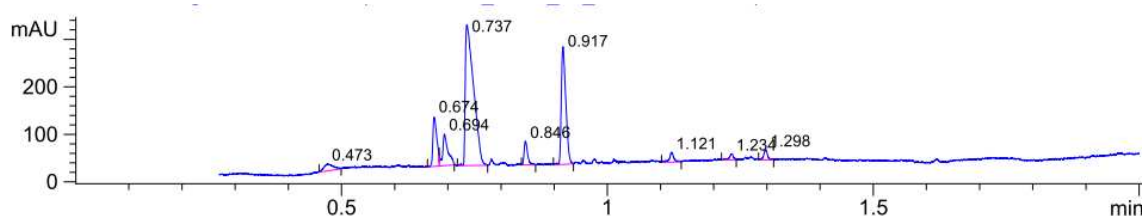
Figure S11

3{5a,8}



Peaks were assigned to disulfonlated side product (0.71 min, 5 %), the **product** (0.75 min, 18%), O-sulfonlated side product (1.57 min, 37%).*

3{5b,8}

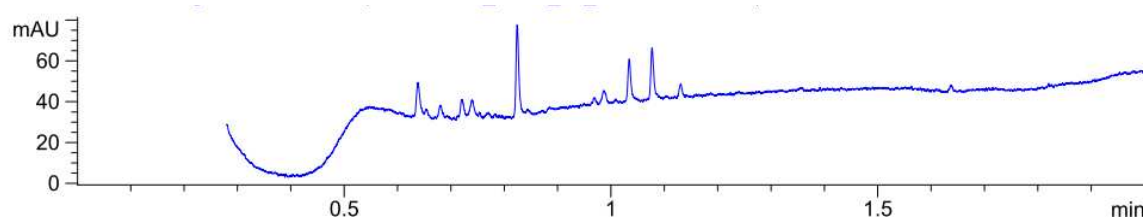


Peaks were assigned to disulfonlated side product (0.69 min, 7 %), the **product** (0.74 min, 50%).*

Figure S12

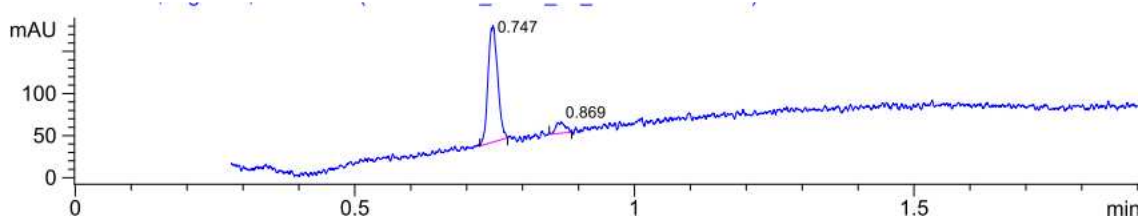
* - assignment is based on the MS data.

3{5a,10}



Peaks were assigned to the **product** (0.84 min, 35%), side product (OH repaced with Cl) (1.05 min, 20%).*

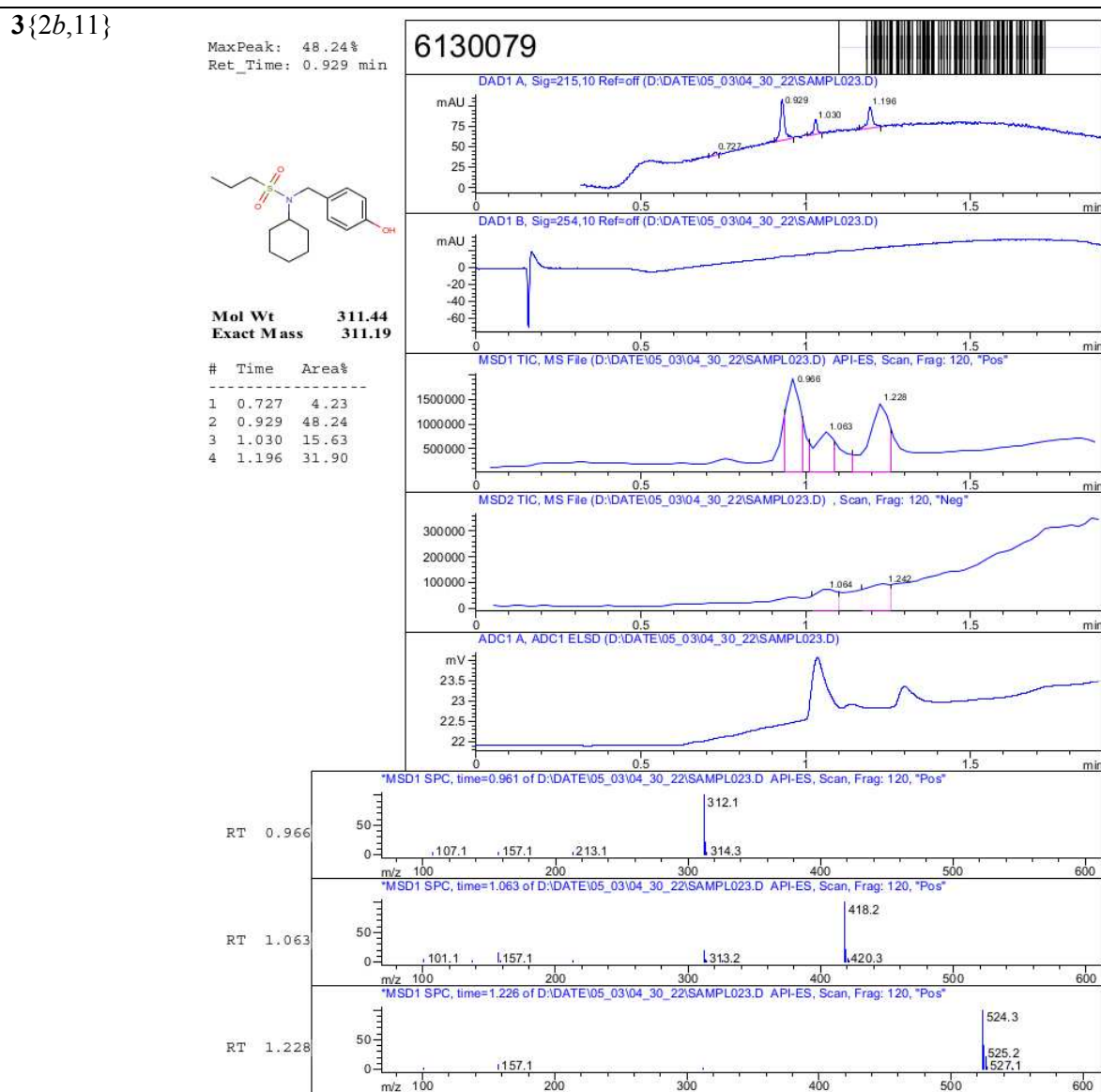
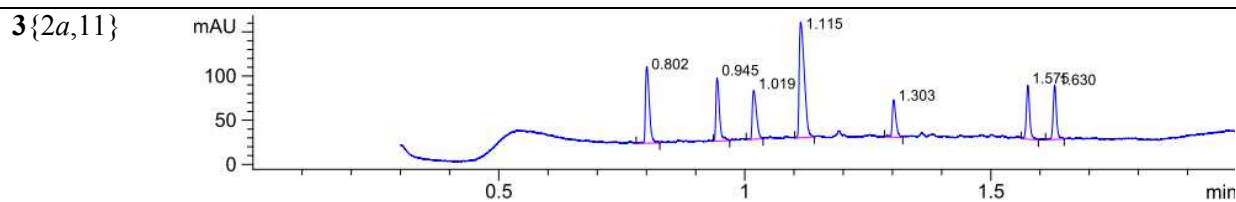
3{5b,10}



Peak was assigned to the **product** (0.75 min, 91%).*

Figure S13

* - assignment is based on the MS data.

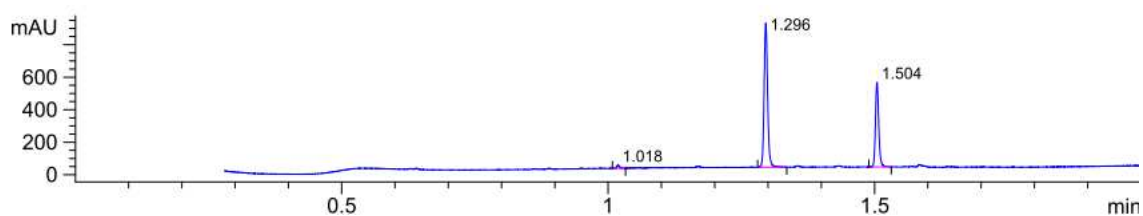


Peaks were assigned the **product** (0.93 min, 48%), disulfonylated side product (1.03 min, 16%), trisulfonylated side product (1.2 min, 32%).*

Figure S14

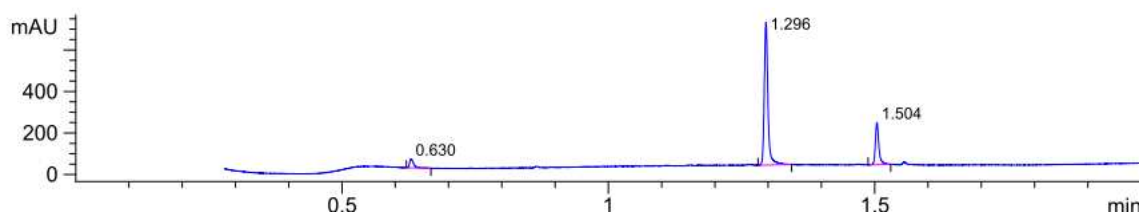
* - assignment is based on the MS data.

3{5a,13}



Peaks were assigned to O-sulfonylated side product (1.02 1%), the **product** (1.3 min, 64%), disulfonylated side product (1.5 min, 35%).*

3{5b,13}



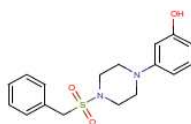
Peaks were assigned the **product** (1.3 min, 74%), disulfonylated side product (1.5 min, 21%).*

Figure S15

* - assignment is based on the MS data.

3{5a,14}

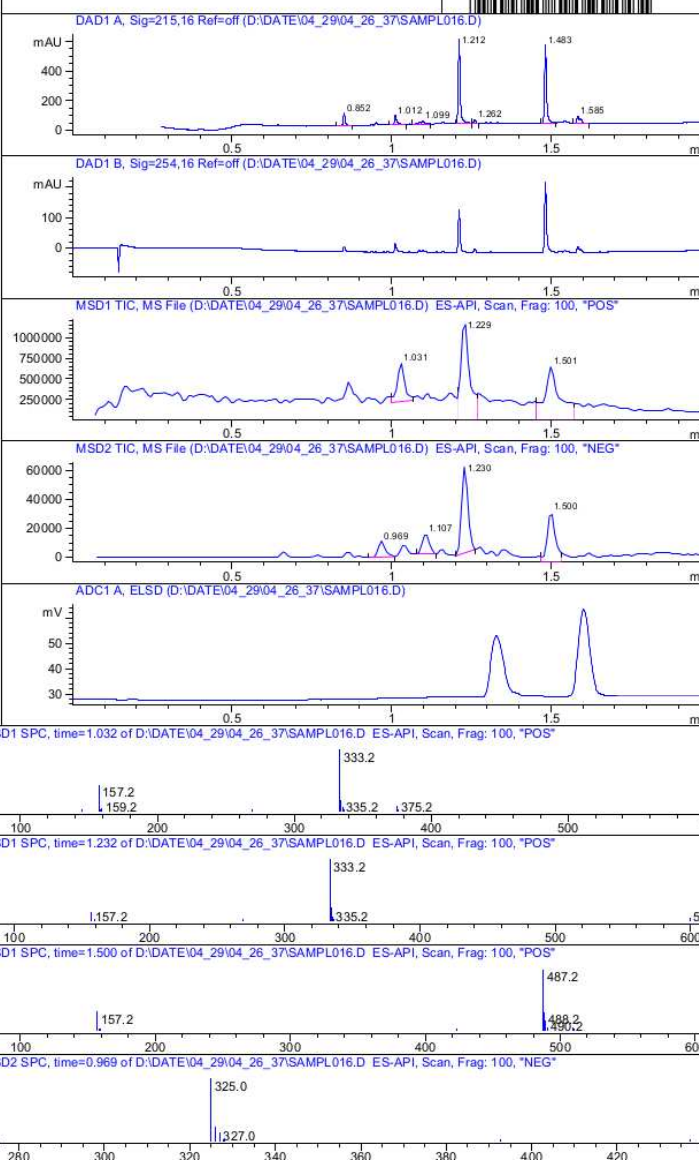
MaxPeak: 40.58%
Ret_Time: 1.212 min



Mol Wt 332.42
Exact Mass 332.14

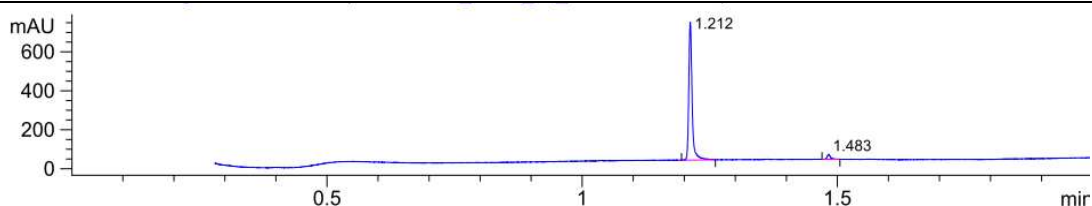
#	Time	Area%
1	0.852	5.61
2	1.012	5.31
3	1.099	3.69
4	1.212	40.58
5	1.262	1.74
6	1.483	37.38
7	1.585	5.69

6130252



Peaks were assigned to O-sulfonylated side product (1.01 5%), the **product** (1.2 min, 41%), disulfonylated side product (1.48 min, 37%).*

3{5b,14}

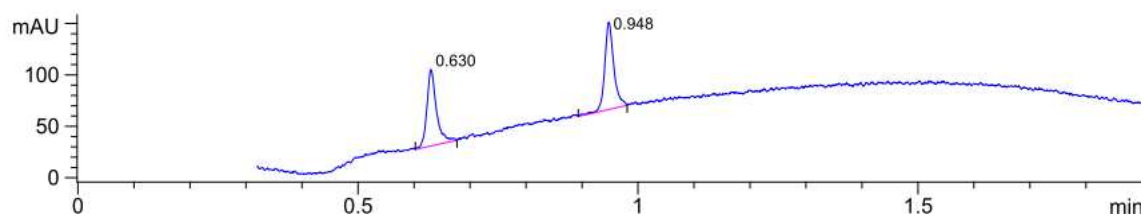


Peaks were assigned the **product** (1.2 min, 96%), disulfonylated side product (1.48 min, 4%).*

Figure S16

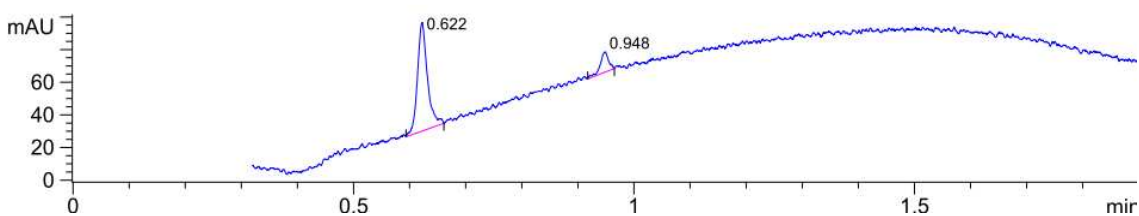
* - assignment is based on the MS data.

3{2a,15}



Peaks were assigned to the **product** (0.63 min, 48%), disulfonylated side product (0.95 min, 52%).*

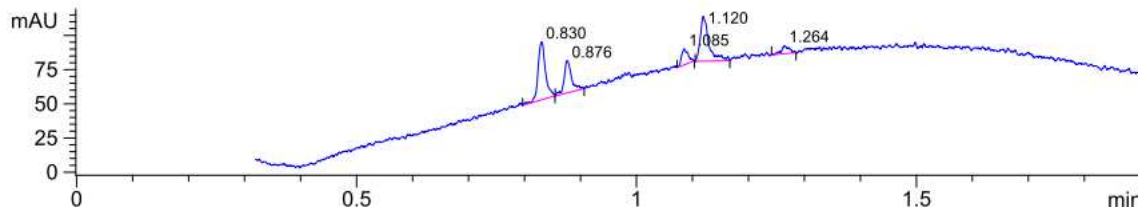
3{2b,15}



Peaks were assigned the **product** (0.62 min, 86%), disulfonylated side product (0.95 min, 14%).*

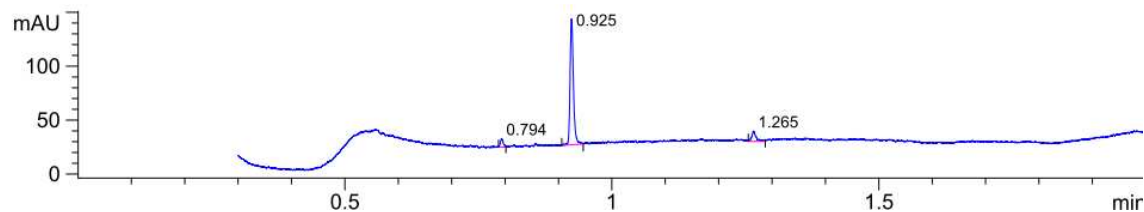
Figure S17

3{2a,16}



Peaks were assigned to N_{pz} sulfonylated side product (0.83 min, 35%), the **product** (0.88 min, 20%), disulfonylated side product (1.12, 1.26 min, 32%).*

3{2b,16}

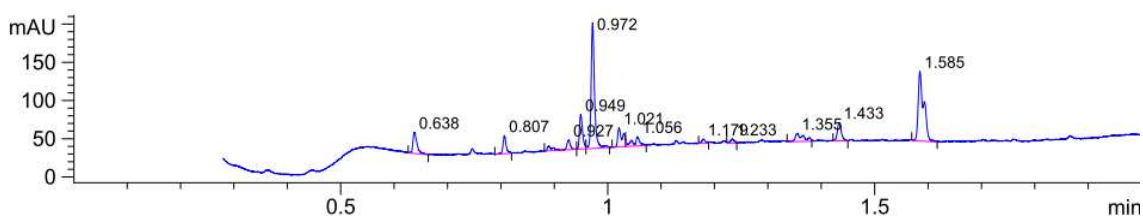


Peaks were assigned to N_{pz} sulfonylated side product (0.79 min, 5%); the **product** (0.93 min, 85%), disulfonylated side product (1.27 min, 10%).*

Figure S18

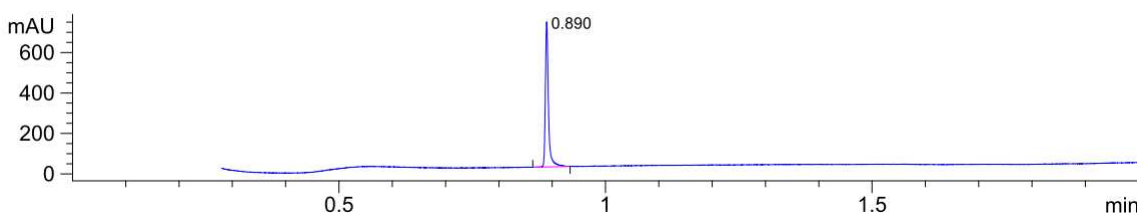
* - assignment is based on the MS data.

3{5a,17}



Peak was assigned to O-sulfonylated side product (0.97 min, 29%), peak of the **product** was not found.*

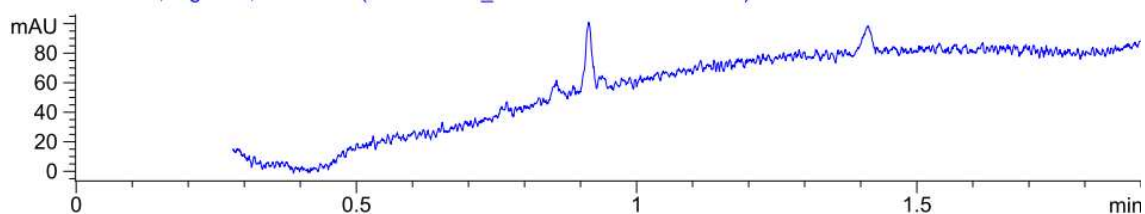
3{5b,17}



Peak was assigned to the **product** (0.89 min, 100%).*

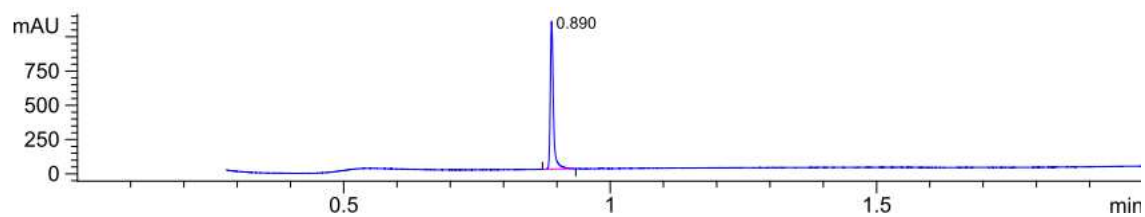
Figure S19

3{5a,18}



Peak of the **product** was not found.

3{5b,18}

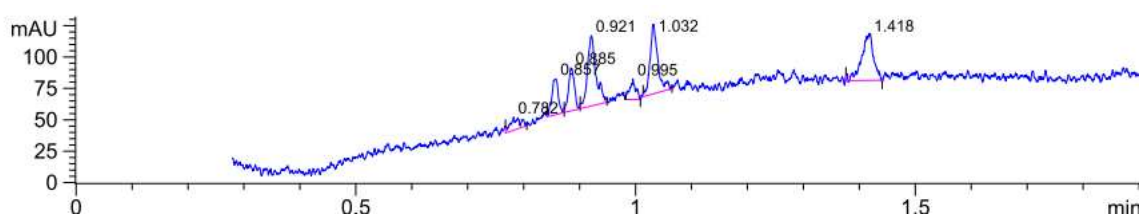


Peak was assigned to the **product** (0.89 min, 100 %).*

Figure S20

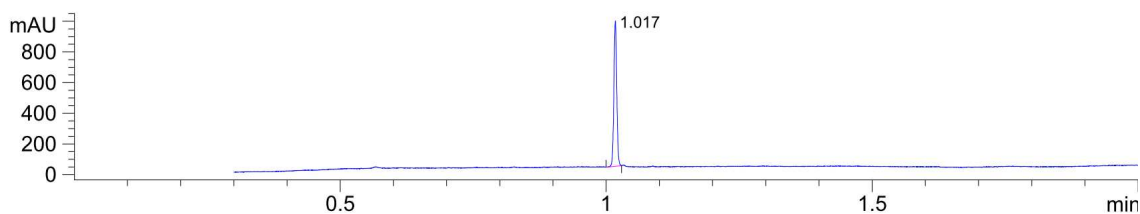
* - assignment is based on the MS data.

3{5a,19}



Peaks were assigned to O-sulfonylated side product (0.92 min, 25%), the **product** (1.03 min, 22%).*

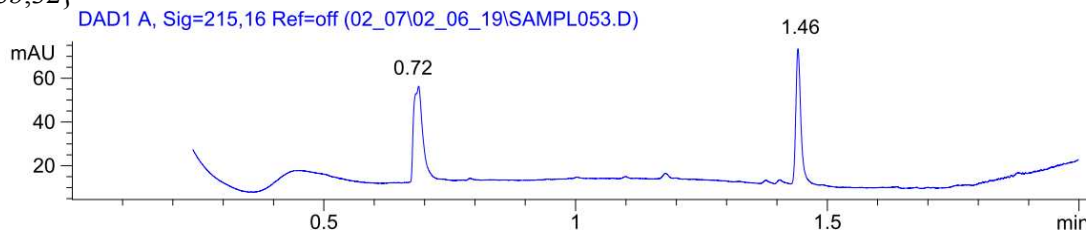
3{5b,19}



Peak was assigned to the **product** (1.02 min, 100%).*

Figure S21

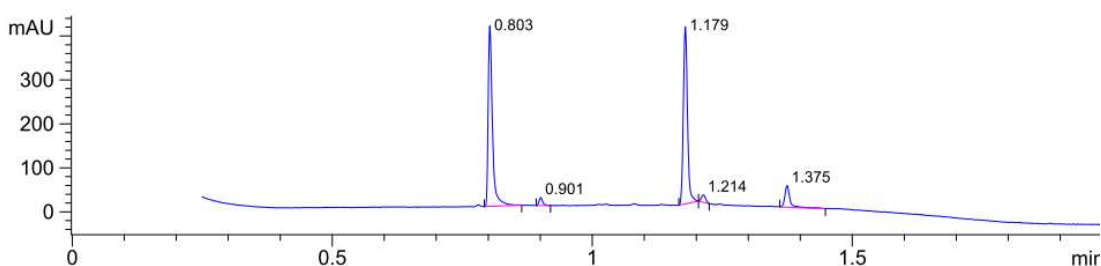
3{3b,32}



Peaks were assigned to side product, cyclohexylmethanesulfonic acid (0.72 min, 54%) and the **product** (1.46 min, 46%).*

Figure S22

3{7b,34}

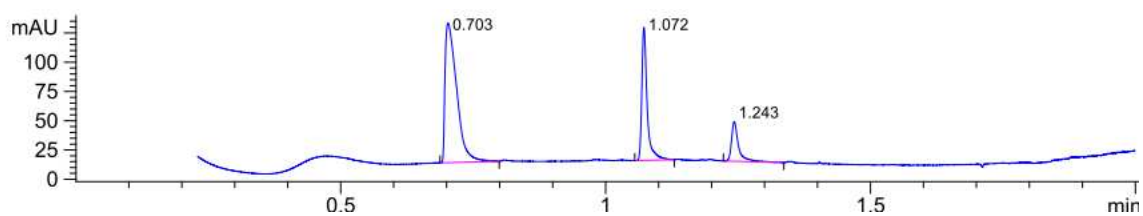


Peak was assigned to the **product** (1.18 min, 46%).*

Figure S23

* - assignment is based on the MS data.

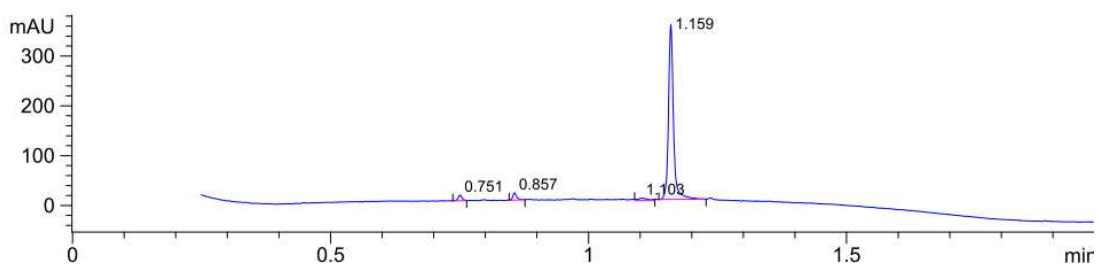
3{1b,36}



Peaks were assigned to amine **2**{36} (0.70 min, 62%) and the **product** (1.07 min, 27%).*

Figure S24

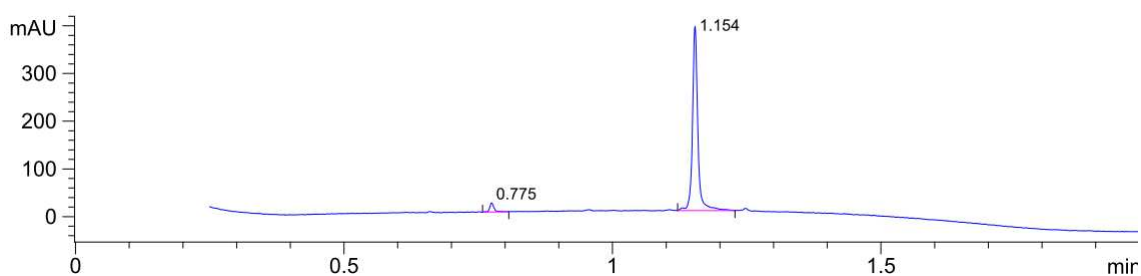
3{7b,32}



Peak was assigned to the **product** (1.16 min, 92%).*

Figure S25

3{7b,38}



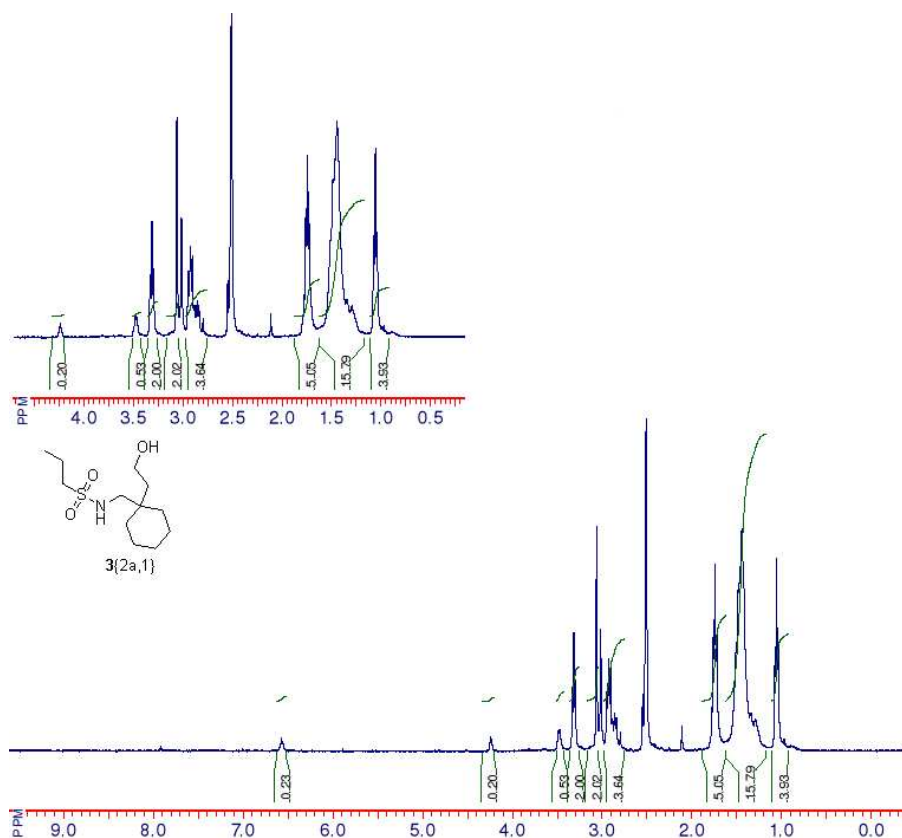
Peak was assigned to the **product** (1.15 min, 96%).*

Figure S26

* - assignment is based on the MS data.

Comparison of NMR spectra of the selected crude mixtures analyzed after completion of the synthesis (Figures S22-S31).

3{2a,1}, purity 20%



3{2b,1}, purity 20%

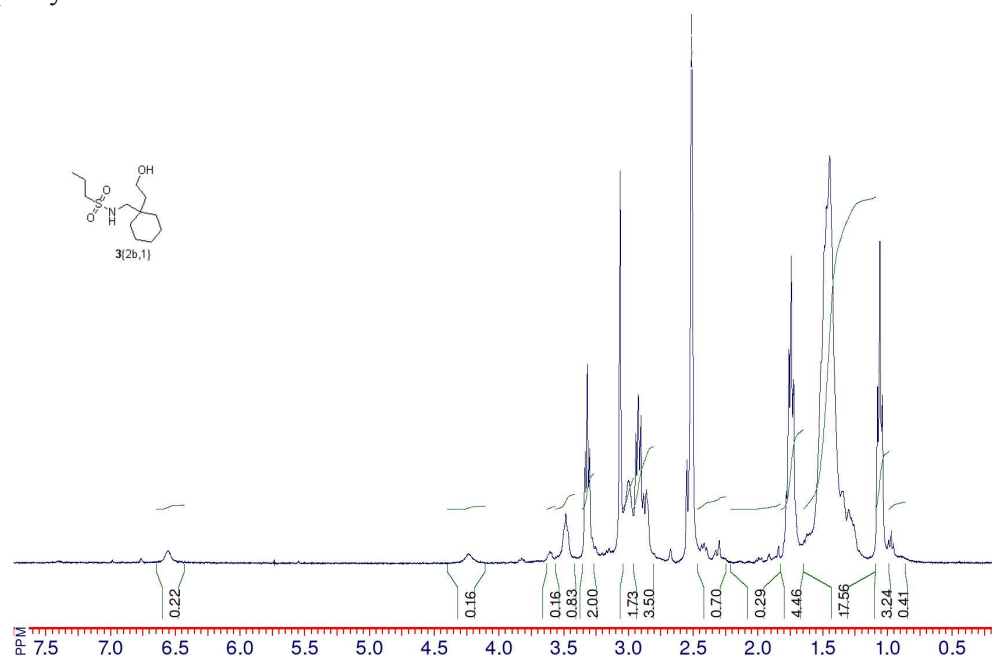


Figure S27

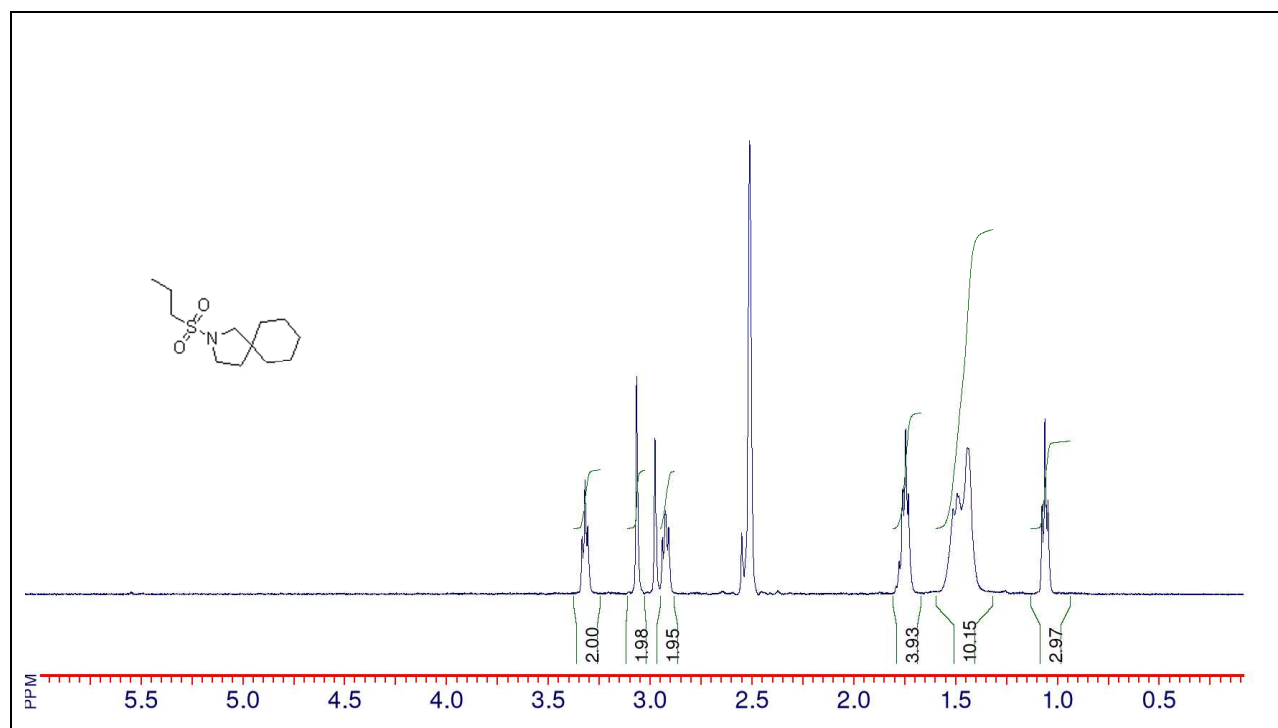
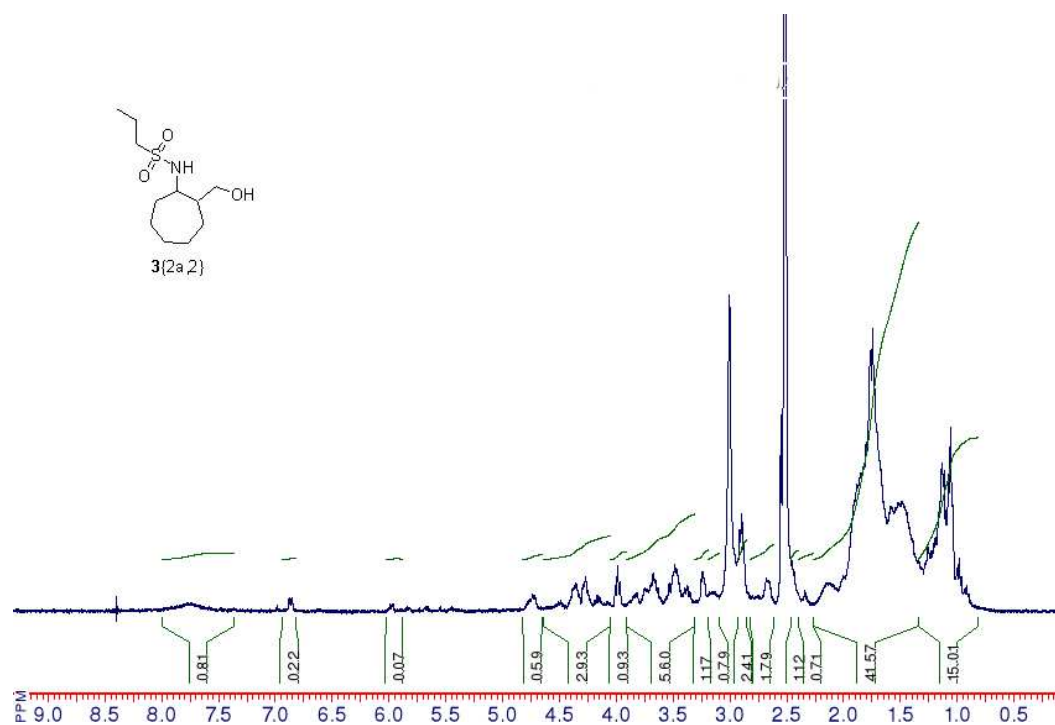


Figure S28. ^1H NMR spectrum of 2-(Propane-1-sulfonyl)-2-aza-spiro[4.5]decane (side product).

3{2a,2}, purity 15%



3{2b,2}, purity >90%

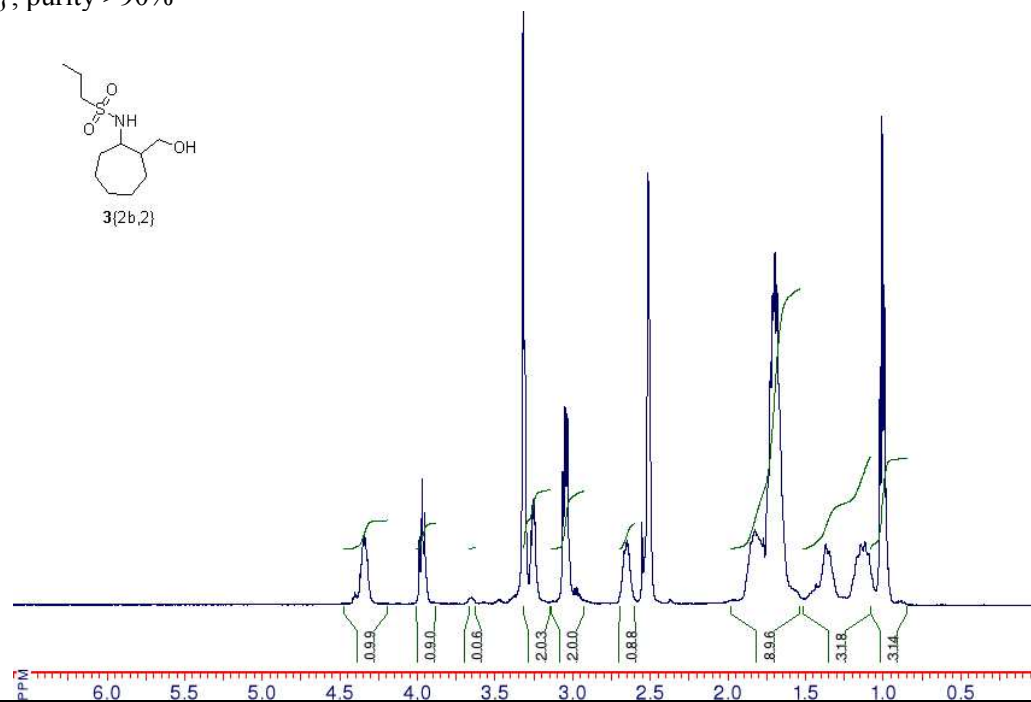
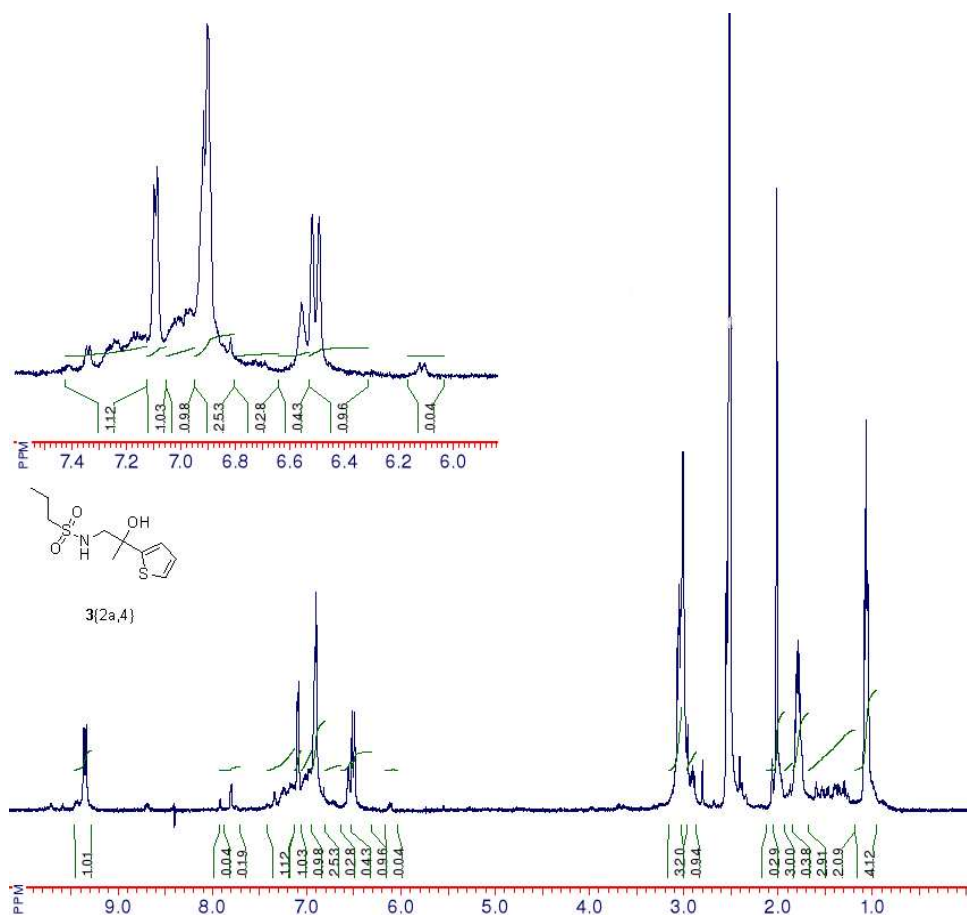


Figure S29

3{2a,4}, purity 5%



3{2b,4}, purity >90%

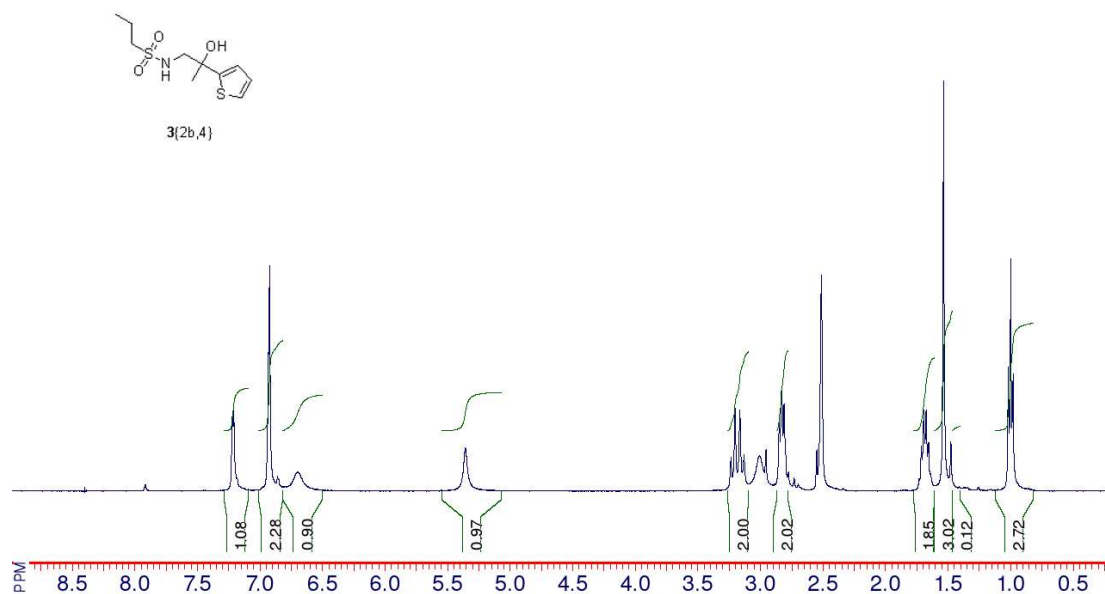
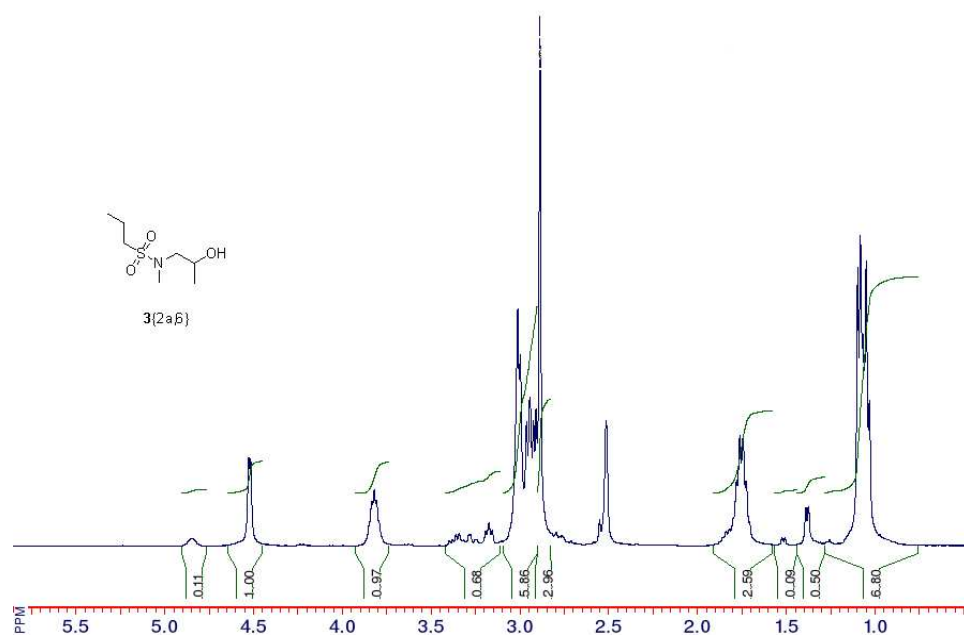


Figure S30

3{2*a*,6}, purity 80%



3{2*b*,6}, purity >90%

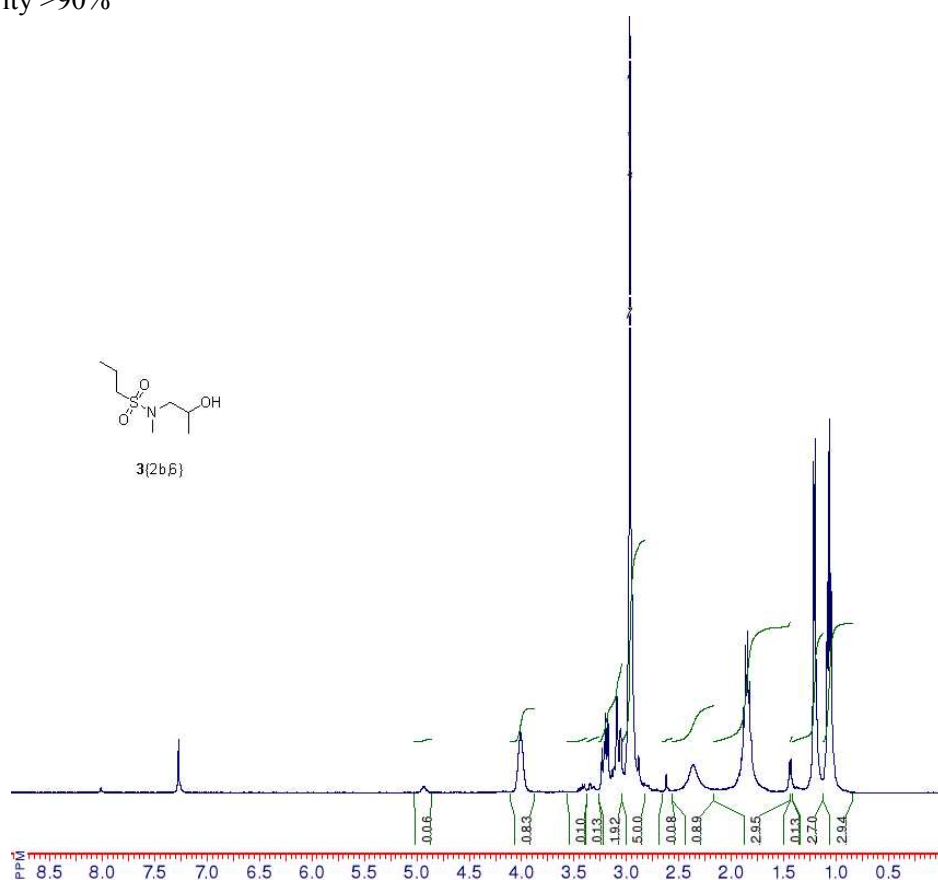
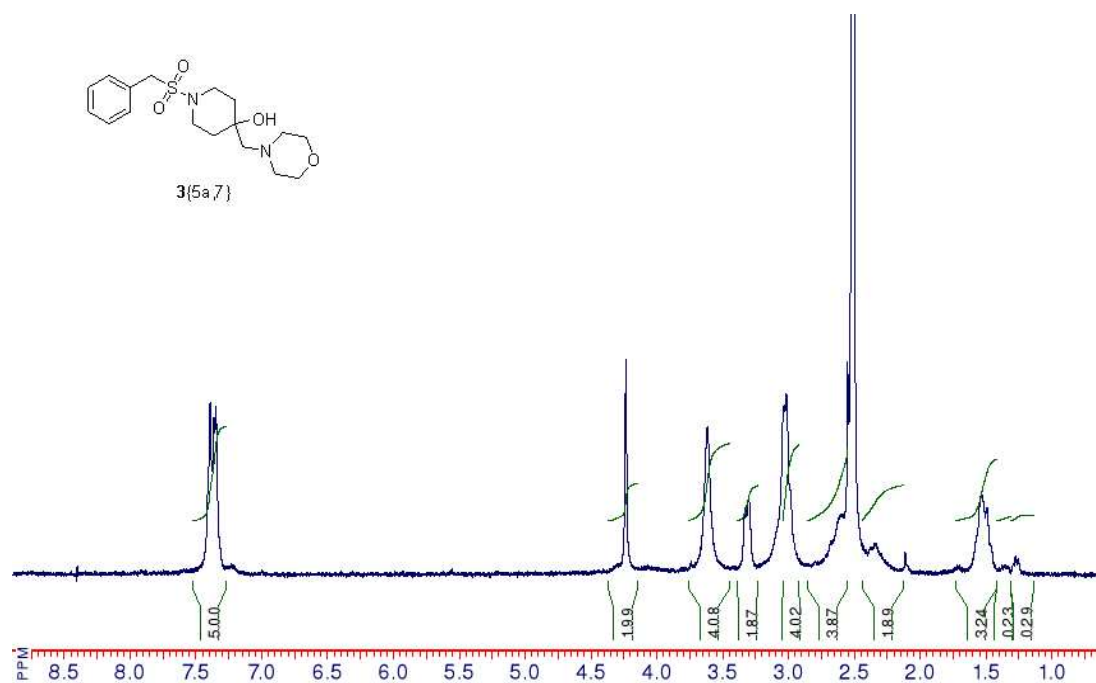


Figure S31

3{5a,7}, purity 85%



3{5b,7}, purity >95%

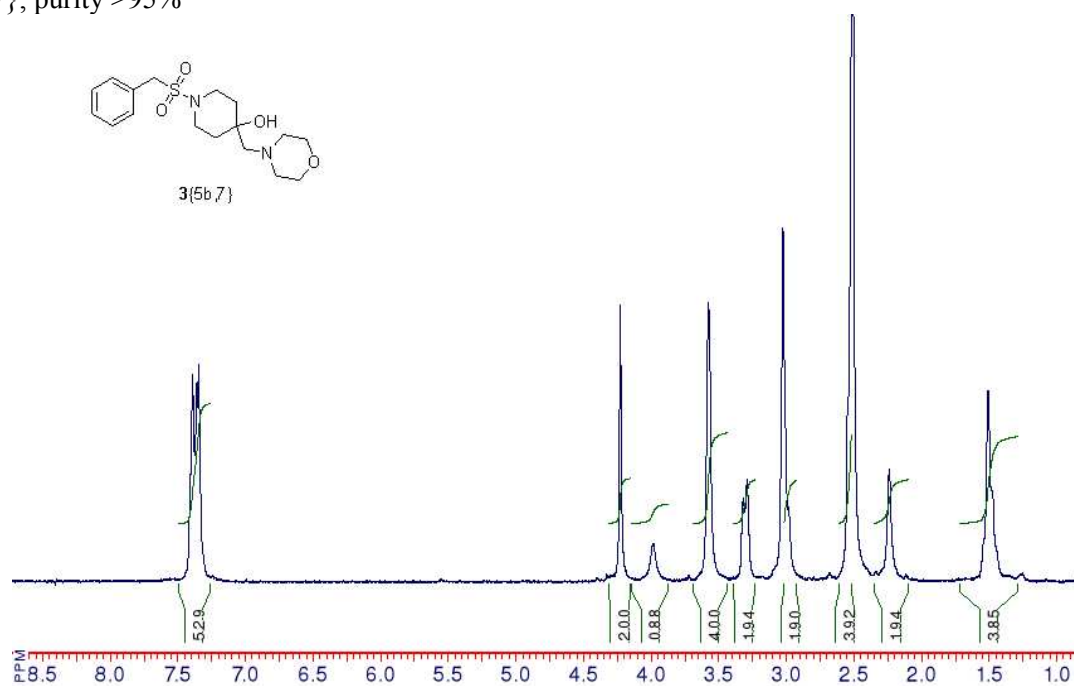
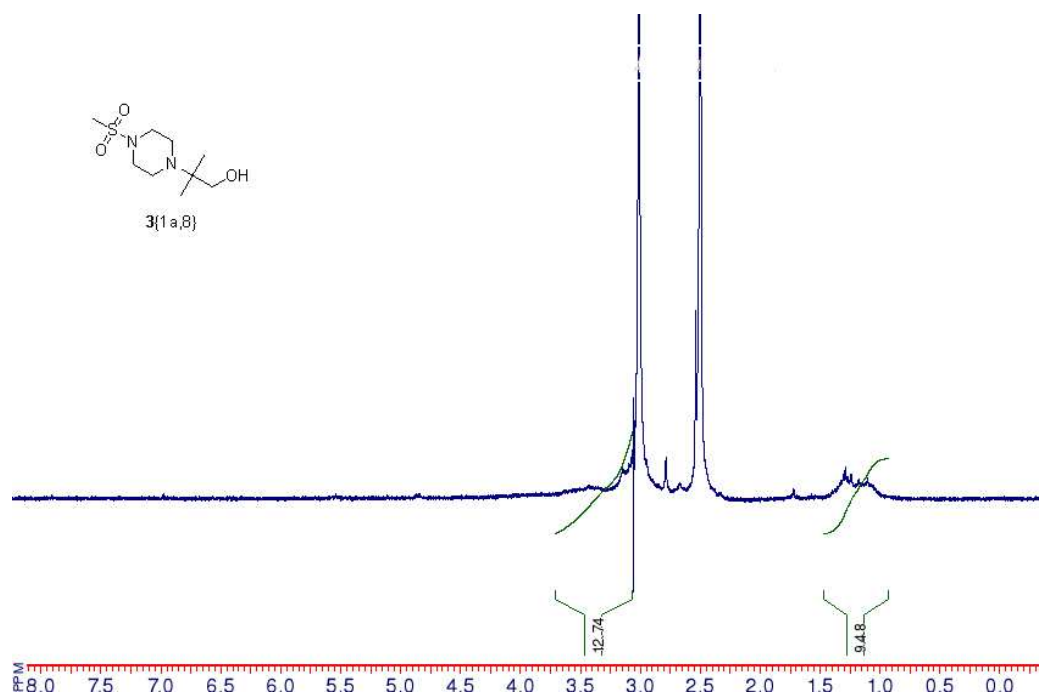


Figure S32

3{1*a*,8}, purity 5%



3{1*b*,8}, purity >90%

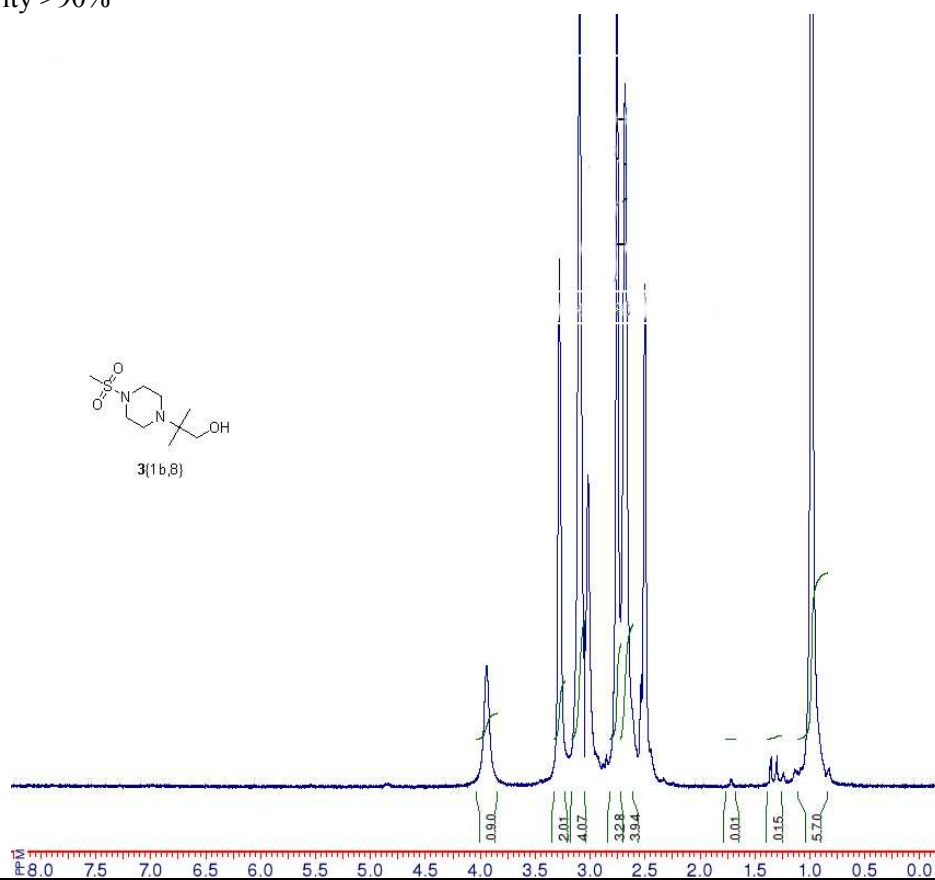
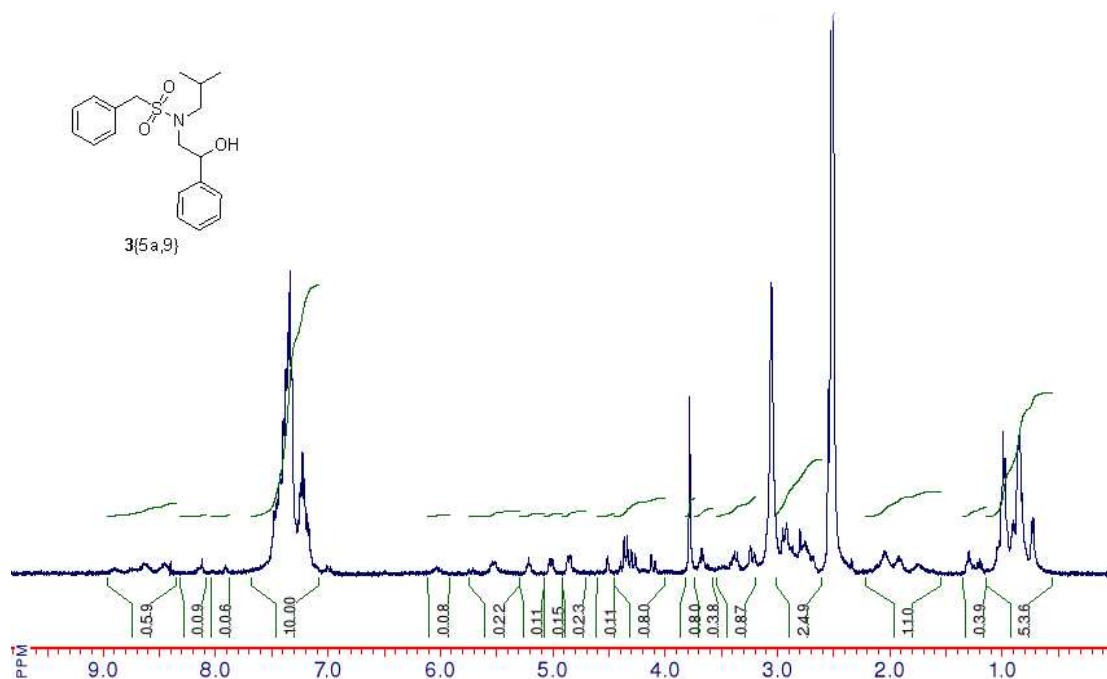


Figure S33

3{5a,9}, purity 10%



3{5b,9}, purity >75%

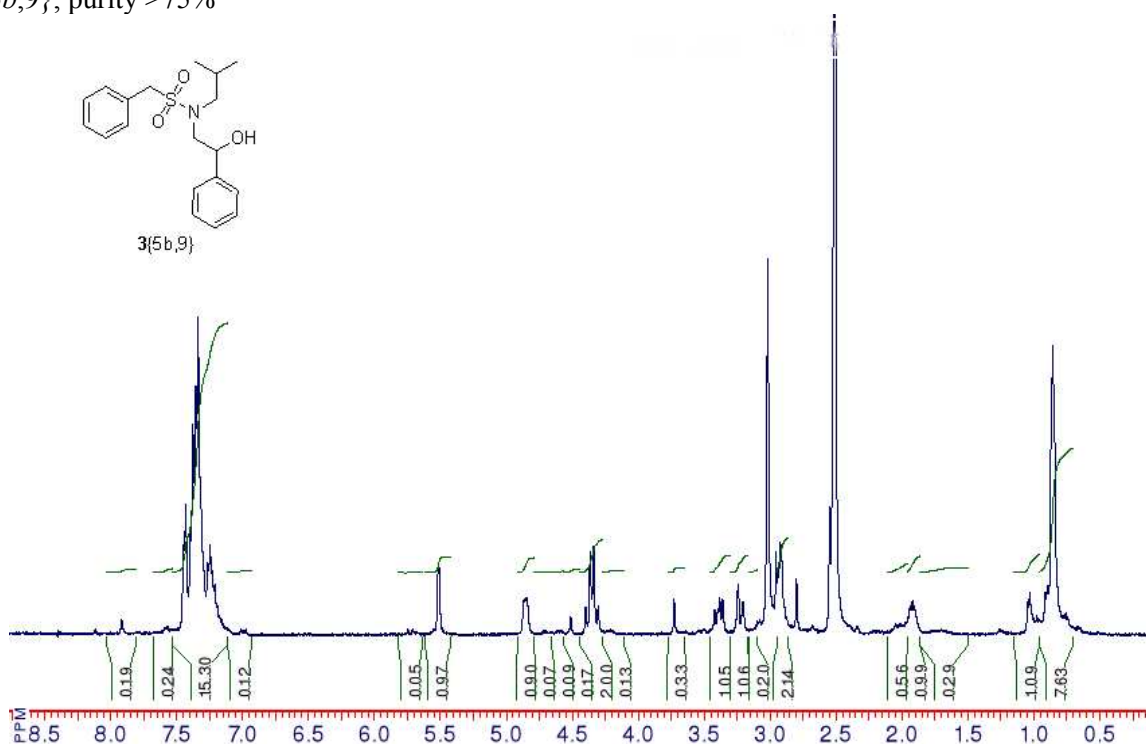
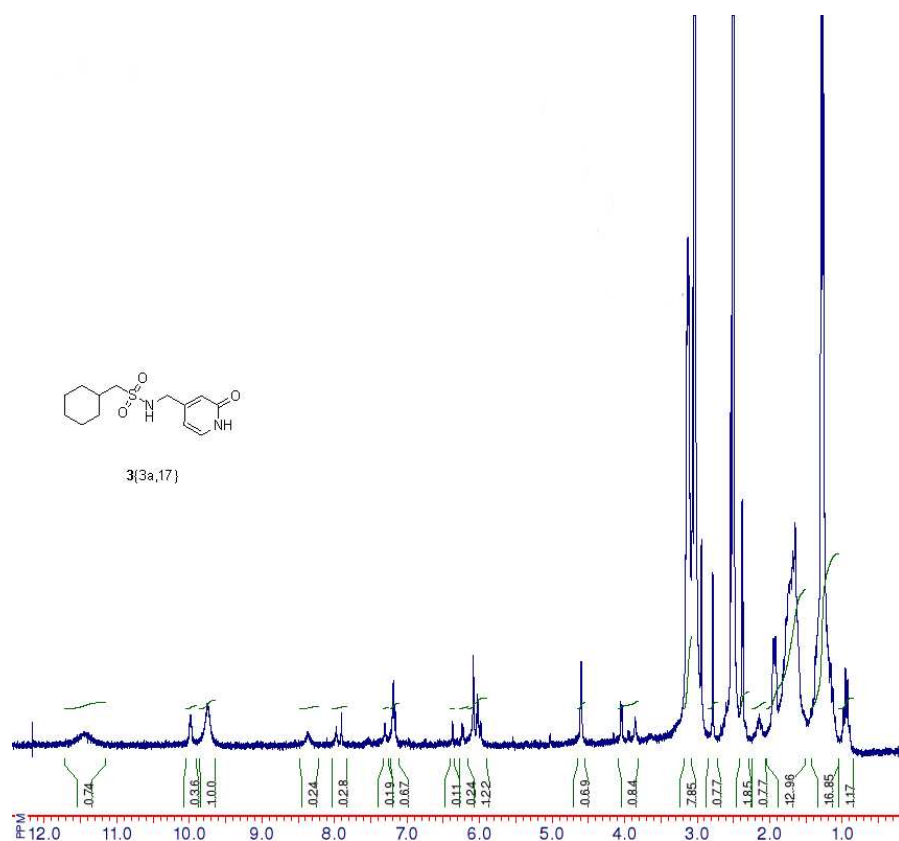


Figure S34

3{3a,17}, purity 20%



3{3b,17}, purity 85%

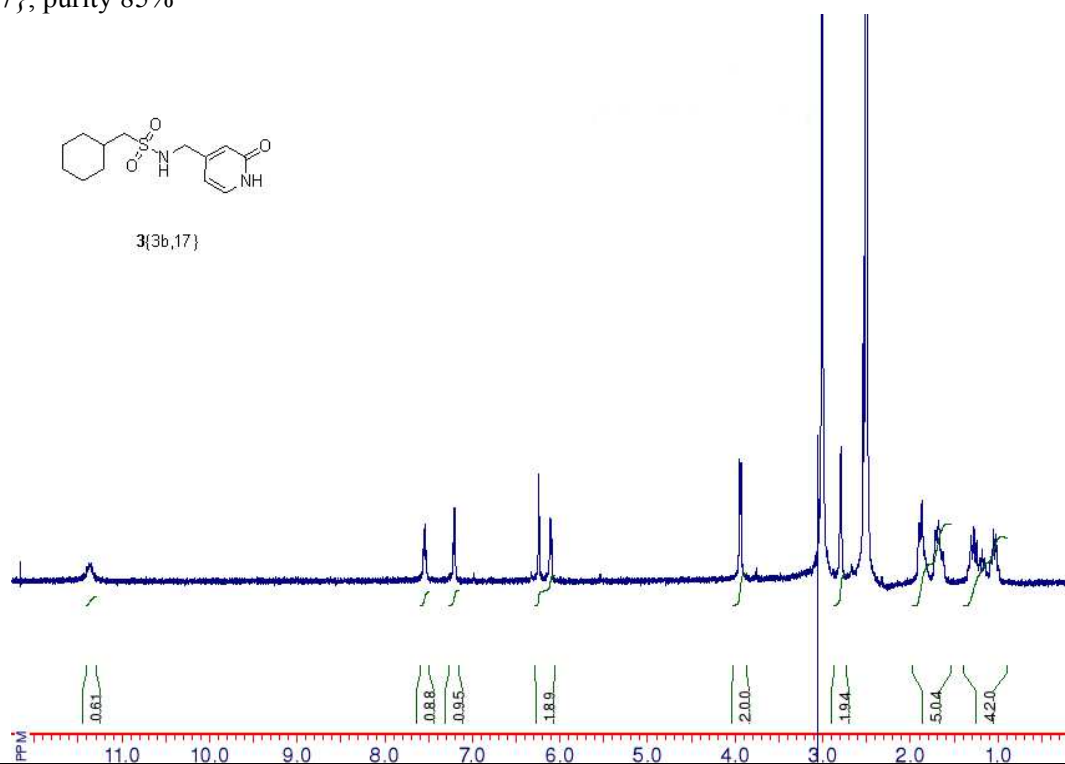
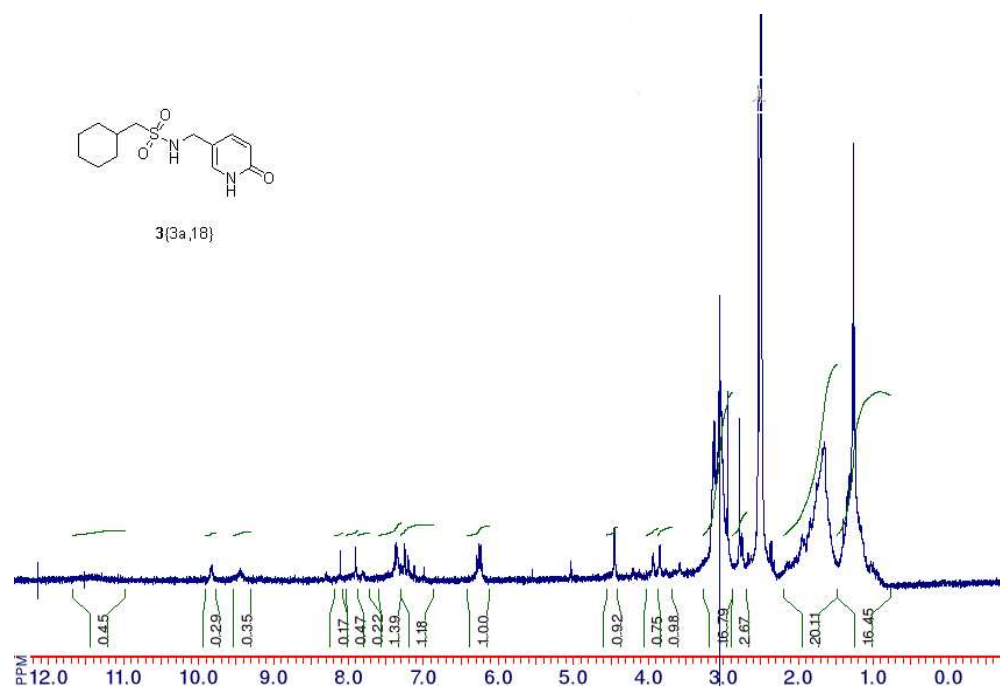


Figure S35

3{3a,18}, purity 25%



3{3b,18}, purity 90%

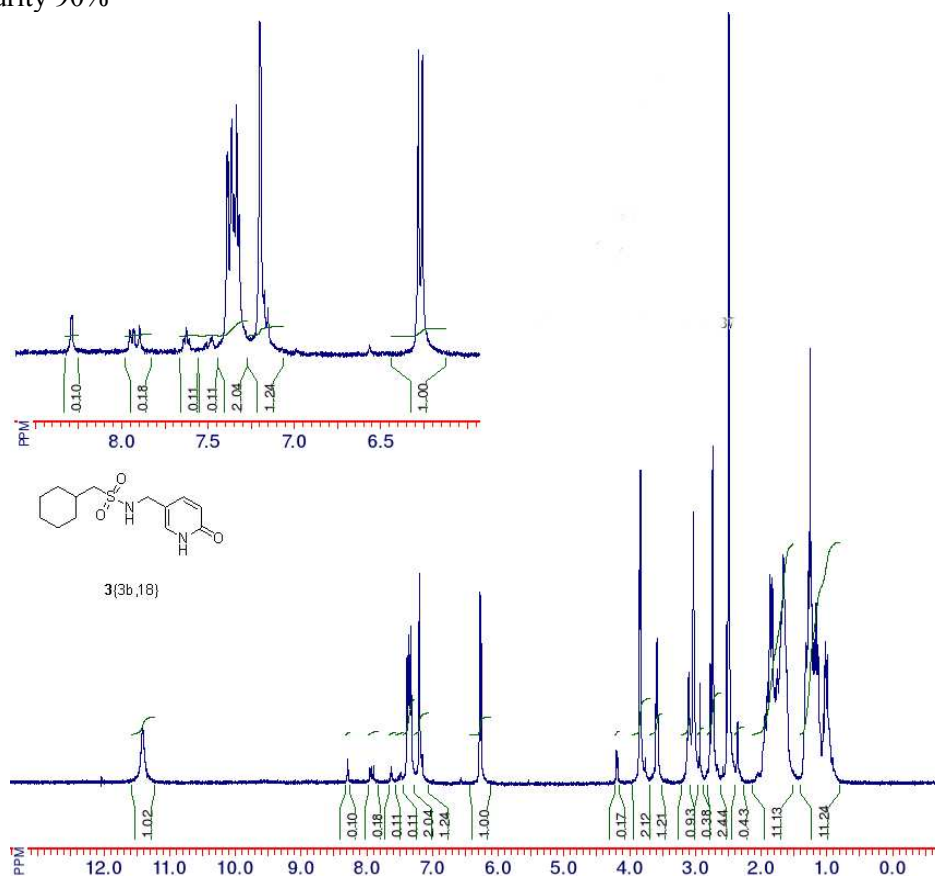
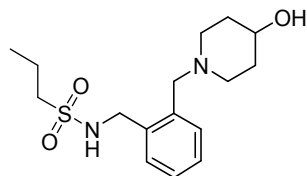


Figure S36

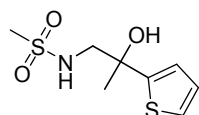
Spectral data for the selected compounds.

Propane-1-sulfonic acid 2-(4-hydroxy-piperidin-1-ylmethyl)-benzylamide (3{2,3})



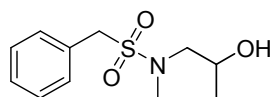
Whitish solid, mp 80-82°C; **FTIR** (KBr): ν_{\max} (cm⁻¹) 3360 (OH+NH), 3080, 3055, 2981, 2905 (CH), 1139 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 0.86 (t, J = 8.0 Hz, 3H, CH₃), 1.35 (m, 2H, CH₂), 1.52 (m, 2H, CH₂), 1.66 (m, 2H, CH₂), 2.10 (m, 2H, CH₂), 2.64 (m, 2H, CH₂), 2.89 (t, J = 7.7 Hz, 2H, CH₂), 3.49 (br s, 3H, CH₂ + CH), 4.23 (s, 2H, CH₂), 4.58 (br s, 1H, OH), 7.25 (m, 2H, Ar), 7.29 (m, 1H, Ar), 7.39 (d, J = 6.6 Hz, 1H, Ar), 8.36 (br s, 1H, NH).; **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 12.7, 16.9, 34.0, 44.8, 50.4, 53.3, 60.2, 65.9, 127.4, 127.8, 129.5, 131.2, 136.6, 137.9; **MS** (APCI) m/z calculated for C₁₆H₂₇N₂O₃S 327.2 [M+H]⁺, found 327.1.

N-(2-Hydroxy-2-thiophen-2-yl-propyl)-methanesulfonamide (3{1,4})



Yellow oil; **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 1.15 (s, 3H, CH₃), 2.81 (s, 3H, CH₃), 3.11 (d, J = 13 Hz, 1H, CH₂), 3.17 (d, J = 13 Hz, 1H, CH₂), 5.64 (s, 1H, OH), 6.91 (s, 1H, NH), 6.95 (2, 2H, Het), 7.36 (d, J = 4.5 Hz, 1H, Het); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 27.5, 54.4, 72.1, 122.8, 124.2, 126.8, 152.5, 162.4; **MS** (APCI) m/z calculated for C₈H₁₄NO₃S₂ 236.1 [M+H]⁺, found 236.2.

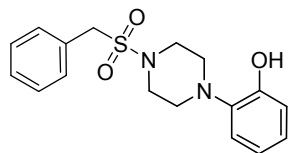
N-(2-Hydroxy-propyl)-N-methyl-C-phenyl-methanesulfonamide (3{5,6})



Yellowish solid, mp 55-57°C; **FTIR** (KBr): ν_{\max} (cm⁻¹) 3375 (OH), 3088, 3063, 3034, 2979, 2915 (CH), 1146 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 1.00 (d, J = 6.3 Hz, 3H, CH₃), 2.76 (s, 3H, CH₃), 2.86 (d, J = 6.3 Hz, 2H, CH₂), 3.74 (six, J = 5.8 Hz, 1H, CH), 4.40 (s, 2H, CH₂), 4.73 (d, J = 5.8 Hz,

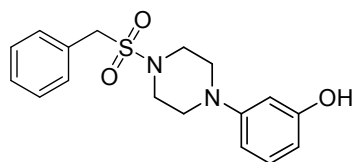
1H, OH), 7.37 (m, 5H, Ar); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 21.1, 36.3, 54.7, 57.1, 65.0, 128.2, 128.4, 130.0, 131.0; **MS** (APCI) m/z calculated for C₁₁H₁₈NO₃S 244.1 [M+H]⁺, found 244.0.

2-(4-Phenylmethanesulfonyl-piperazin-1-yl)-phenol (3{5,13})



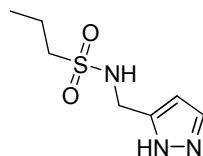
Whitish solid, mp 136-138°C; **FTIR** (KBr): ν_{max} (cm⁻¹) 3421 (OH), 3063, 3042, 2960, 2928, 2888, 2842 (CH), 1155 (SO₂); ¹H NMR (500 MHz, DMSO-d₆): δ (ppm) 2.93 (m, 4H, 2CH₂), 3.26 (m, 4H, 2CH₂), 4.45 (s, 2H, CH₂), 6.73 (t, J = 7.4 Hz, 1H, Ar), 6.80 (d, J = 8.0 Hz, 1H, Ar), 6.85 (t, J = 8.5 Hz, 2H, Ar), 7.39 (m, 3H, Ar), 7.44 (m, 2H, Ar), 9.06 (s, 1H, OH); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 45.8, 50.1, 54.3, 115.8, 119.1, 119.5, 123.4, 128.3, 128.5, 128.8, 129.6, 131.1, 139.3, 150.2; **MS** (APCI) m/z calculated for C₁₇H₂₁N₂O₃S 333.1 [M+H]⁺, found 333.1.

3-(4-Phenylmethanesulfonyl-piperazin-1-yl)-phenol (3{5,14})



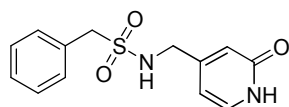
Brownish solid, mp 170-172°C; **FTIR** (KBr): ν_{max} (cm⁻¹) 3158 (OH), 3058, 3036, 2978, 2930, 2849 (CH), 1160 (SO₂); ¹H NMR (500 MHz, DMSO-d₆): δ (ppm) 3.08 (m, 4H, 2CH₂), 3.22 (m, 4H, 2CH₂), 4.45 (s, 2H, CH₂), 6.26 (dd, J = 1.8; 8.1 Hz, 1H, Ar), 6.31 (m, 1H, Ar), 6.38 (dd, J = 1.9; 8.2 Hz, 1H, Ar), 6.99 (t, J = 8.2 Hz, 1H, Ar), 7.38 (m, 3H, Ar), 7.42 (m, 2H, Ar), 9.18 (s, 1H, OH); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 45.5, 48.6, 54.4, 103.2, 107.0, 107.3, 128.3, 128.5, 129.5, 129.7, 131.0, 152.0, 158.2; **MS** (APCI) m/z calculated for C₁₇H₂₁N₂O₃S 333.1 [M+H]⁺, found 333.2.

Propane-1-sulfonic acid (2H-pyrazol-3-ylmethyl)-amide (3{2,15})



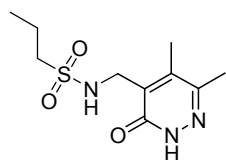
Whitish solid, mp 82-84°C; **FTIR** (KBr): ν_{max} (cm⁻¹) 3260 (NH), 3000, 2950, 2880 (CH), 1138 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 0.87 (t, J = 7.1 Hz, 3H, CH₃), 1.57 (m, 2H, CH₂), 2.85 (t, J = 8.0 Hz, 2H, CH₂), 4.11 (s, 2H, CH₂), 6.22 (s, 1H, CH, Ar), 7.43 (m, 1H, CH, Ar), 7.64 (m, 1H, NH), 12.65 (br s, 1H, NH); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 12.7, 16.9, 53.4, 103.6, 129.2, 148.8; **MS** (APCI) m/z calculated for C₇H₁₄N₃O₂S 204.1 [M+H]⁺, found 204.0.

N-(2-Oxo-1,2-dihydro-pyridin-4-ylmethyl)-C-phenyl-methanesulfonamide (3{5,17})



White solid, mp 202-204°C; **FTIR** (KBr): ν_{max} (cm⁻¹) 3238 (NH), 3108, 3077, 3013, 2878 (CH), 1136 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.91 (d, J = 6.4 Hz, 2H, CH₂), 4.37 (s, 2H, CH₂), 6.10 (d, J = 6.9 Hz, 1H, CH, Py), 6.23 (s, 1H, CH, Py), 7.30 (d, J = 6.7 Hz, 1H, CH, Py), 7.36 (m, 5H, Ar), 7.69 (t, J = 6.3 Hz, 1H, NH), 11.44 (s, 1H, OH); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 45.2, 57.7, 104.4, 116.8, 128.2, 128.4, 130.3, 130.9, 135.0, 144.3, 152.6, 162.5; **MS** (APCI) m/z calculated for C₁₃H₁₅N₂O₃S 279.1 [M+H]⁺, found 279.2.

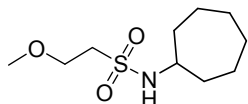
Propane-1-sulfonic acid (5,6-dimethyl-3-oxo-2,3-dihydro-pyridazin-4-ylmethyl)-amide (3{2,19})



Yellowish solid, mp 135-137°C; **FTIR** (KBr): ν_{max} (cm⁻¹) 3307, 3254 (NH), 2997, 2964, 2940, 2881 (CH), 1138 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 0.94 (t, J = 7.4 Hz, 3H, CH₃), 1.63 (m, 2H, CH₂), 2.17 (s, 3H, CH₃), 2.20 (s, 3H, CH₃), 3.04 (t, J = 7.8 Hz, 2H, CH₂), 4.05 (d, J = 5.6 Hz, 2H, CH₂), 7.12 (t, J = 5.6 Hz, 1H, NH), 12.7 (s, 1H, OH); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 12.8, 15.3,

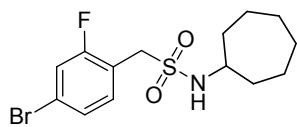
17.0, 19.7, 36.9, 52.6, 133.5, 141.8, 145.3, 160.5; **MS** (APCI) m/z calculated for $C_{10}H_{18}N_3O_3S$ 260.1 $[M+H]^+$, found 260.2.

2-Methoxy-ethanesulfonic acid cycloheptylamide (3{4,26})



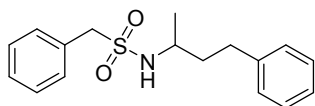
Yellowish solid, mp 37-39°C; **FTIR** (KBr): ν_{\max} (cm^{-1}) 3260 (NH), 2931, 2859 (CH), 1160 (SO_2); **1H NMR** (500 MHz, $DMSO-d_6$): δ (ppm) 1.46 (m, 10H, $5CH_2$), 1.84 (m, 2H, CH_2), 3.25 (m, 6H, CH + CH_2 + OCH_3), 3.63 (t, $J = 6.3$ Hz, 2H, CH_2), 7.01 (d, $J = 7.0$ Hz, 1H, NH); **^{13}C NMR** (125.75 MHz, $DMSO-d_6$): δ (ppm) 23.3, 27.8, 35.9, 51.9, 54.2, 58.1, 66.3; **MS** (APCI) m/z calculated for $C_{10}H_{22}NO_3S$ 236.1 $[M+H]^+$, found 236.1.

C-(4-Bromo-2-fluoro-phenyl)-N-cycloheptyl-methanesulfonamide (3{6,26})



Whitish solid, mp 120-122°C; **FTIR** (KBr): ν_{\max} (cm^{-1}) 3260 (NH), 3110, 3089, 3047, 2933, 2908, 2858, 2822 (CH), 1160 (SO_2); **1H NMR** (500 MHz, $DMSO-d_6$): δ (ppm) 1.34 (m, 2H, CH_2), 1.47 (m, 8H, $4CH_2$), 1.85 (m, 2H, CH_2), 3.27 (m, 1H, CH), 4.31 (s, 2H, CH_2), 7.22 (d, $J = 7.5$ Hz, 1H, Ar), 7.4 (t, 1H, Ar), 7.46 (d, $J = 8$ Hz, 1H, Ar), 7.59 (d, $J = 9$ Hz, 1H, NH); **^{13}C NMR** (125.75 MHz, $DMSO-d_6$): δ (ppm) 23.4, 27.8, 35.8, 51.3, 54.6, 117.8 (d, $J_{C,F} = 15$ Hz), 118.9 (d, $J_{C,F} = 25$ Hz), 121.9 (d, $J_{C,F} = 10$ Hz), 127.6 (d, $J_{C,F} = 3.8$ Hz), 134.6 (d, $J_{C,F} = 3.8$ Hz), 160.8 (d, $J_{C,F} = 252$ Hz); **MS** (APCI) m/z calculated for $C_{14}H_{20}BrFNO_2S$ 265.1 $[M+H]^+$, found 365.5.

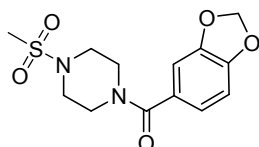
N-(1-Methyl-3-phenyl-propyl)-C-phenyl-methanesulfonamide (3{5,28})



Whitish solid, mp 108-110°C; **FTIR** (KBr): ν_{\max} (cm^{-1}) 3293 (NH), 3087, 3062, 3031, 2973, 2943, 2925, 2860 (CH), 1164 (SO_2); **1H NMR** (500 MHz, $DMSO-d_6$): δ (ppm) 1.13 (d, $J = 6.7$ Hz, 3H, CH_3),

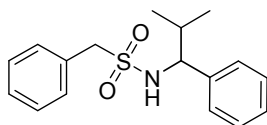
1.66 (m, 2H, CH₂), 2.58 (m, 2H, CH₂), 3.30 (m, 1H, CH), 4.30 (d, J = 2.9 Hz, 2H, CH₂), 7.10 (d, J = 7.8 Hz, 1H, NH), 7.17 (m, 3H, Ar), 7.27 (m, 2H, Ar), 7.36 (m, 5H, Ar); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 22.0, 31.7, 52.3, 58.7, 125.8, 128.0, 128.3, 128.3, 128.4, 130.7, 130.9, 142.0; MS (APCI) m/z calculated for C₁₇H₂₂NO₂S 304.1 [M+H]⁺, found 304.2.

Benzo[1,3]dioxol-5-yl-(4-methanesulfonyl-piperazin-1-yl)-methanone (3{1,31})



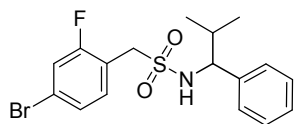
Yellowish solid, mp 200-202°C; FTIR (KBr): ν_{max} (cm⁻¹) 3028, 3014, 3000, 2925, 2912, 2893, 2866 (CH), 1154 (SO₂); ¹H NMR (500 MHz, DMSO-d₆): δ (ppm) 2.89 (s, 3H, CH₃), 3.14 (m, 4H, 2CH₂), 3.56 (m, 4H, 2CH₂), 6.07(s, 2H, CH₂), 6.93 (d, J = 7.8 Hz, 1H, Ar), 6.98 (d, J = 7.8 Hz, 1H, Ar), 6.99 (s, 1H, Ar); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 34.2, 45.4, 101.6, 107.8, 108.3, 121.6, 129.1, 147.3, 148.5, 168.8; MS (APCI) m/z calculated for C₁₃H₁₇N₂O₅S 313.4 [M+H]⁺, found 313.0.

N-(2-Methyl-1-phenyl-propyl)-C-phenyl-methanesulfonamide (3{5,32})



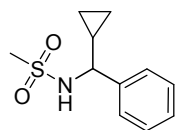
Whitish solid, mp 87-89°C; FTIR (KBr): ν_{max} (cm⁻¹) 3264 (NH), 3061, 3039, 2972, 2959, 2928, 2905, 2870 (CH), 1167 (SO₂); ¹H NMR (500 MHz, DMSO-d₆): δ (ppm) 0.67 (d, J = 6.9 Hz, 3H, CH₃), 0.97 (d, J = 6.6 Hz, 3H, CH₃), 1.92 (m, 1H, CH), 3.84 (s, 2H, CH₂), 4.0 (t, J = 9.1 Hz, 1H, CH), 6.98 (d, J = 6.9 Hz, 2H, Ar), 7.24 (m, 3H, Ar), 7.29 (m, 1H, Ar), 7.36 (m, 4H, Ar), 7.78 (d, J = 9.6 Hz, 1H, NH); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 19.6, 19.7, 33.8, 58.9, 63.9, 127.2, 127.5, 127.9, 128.1, 128.3, 130.1, 130.7, 142.3; MS (APCI) m/z calculated for C₁₇H₂₂NO₂S 304.1 [M+H]⁺, found 304.2.

***C*-(4-Bromo-2-fluoro-phenyl)-*N*-(2-methyl-1-phenyl-propyl)-methanesulfonamide (3{6,32})**



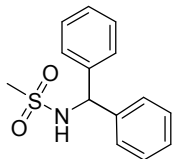
White solid, mp 120-122°C; **FTIR** (KBr): ν_{\max} (cm⁻¹) 3261 (NH), 2979, 2965, 2938, 2874 (CH), 1160 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 0.68 (d, J=6.5 Hz, 3H, CH₃), 0.96 (d, J=6.5 Hz, 3H, CH₃), 1.9 (m, 1H, CH), 3.82 (d, J=13.5 Hz, 1H, CH₂), 3.91 (d, J=13.5 Hz, 1H, CH₂), 3.99 (t, J = 8.5 Hz, 1H, CH), 6.99 (t, J = 8.5 Hz, 1H, Ar), 7.31 (m, 6H, Ar), 7.42 (d, J = 9.5 Hz, 1H, Ar), 7.99 (d, J=9 Hz, 1H, NH); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 19.5, 33.9, 51.9, 64.0, 117.1 (d, J_{C,F} = 14 Hz), 118.8 (d, J_{C,F} = 25 Hz), 121.9 (d, J_{C,F} = 10 Hz), 127.2, 127.3, 128.4 (d, J_{C,F} = 3.8 Hz), 134.1 (d, J_{C,F} = 3.8 Hz), 141.9, 160.6 (d, J_{C,F} = 253 Hz). **MS** (APCI) m/z calculated for C₁₇H₂₀BrFNO₂S 401.0 [M+H]⁺, found 401.0.

***N*-(Cyclopropyl-phenyl-methyl)-methanesulfonamide (3{1,33})**



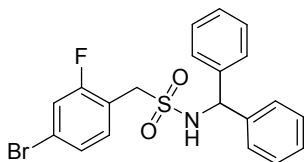
Whitish solid, mp 70-72°C; **FTIR** (KBr): ν_{\max} (cm⁻¹) 3302 (NH), 3087, 3065, 3034, 3005, 2930 (CH), 1157 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 0.32 (m, 1H, CH₂), 0.42 (m, 2H, CH₂), 0.55 (m, 1H, CH₂), 1.13 (m, 1H, CH), 2.59 (s, 3H, CH₃), 3.70 (t, J = 7.7 Hz, 1H, CH), 7.25 (t, J = 7.1 Hz, 1H, Ar), 7.34 (t, J = 7.4 Hz, 2H, Ar), 7.40 (d, J = 7.4 Hz, 2H, Ar), 7.82 (d, J = 6.9 Hz, 1H, NH); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 3.8, 4.8, 18.3, 41.5, 61.4, 126.9, 127.2, 128.4, 142.9; **MS** (APCI) m/z calculated for C₁₁H₁₆NO₂S 226.1 [M+H]⁺, found 226.3.

N-Benzhydryl-methanesulfonamide (3{1,34})



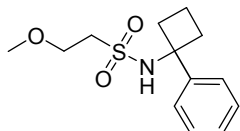
Yellowish solid, mp 133-135°C; **FTIR** (KBr): ν_{\max} (cm⁻¹) 3300 (NH), 3087, 3065, 3021, 2925, 2862 (CH), 1152 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.63 (s, 3H, CH₃), 5.63 (d, J = 9.7 Hz, 1H, CH), 7.24 (t, J = 7.3 Hz, 2H, Ar), 7.34 (t, J = 7.8 Hz, 4H, Ar), 7.4 (d, J = 7.5 Hz, 4H, Ar), 8.33 (d, J = 9.6 Hz, 1H, NH); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 41.4, 60.5, 127.2, 127.3, 128.6, 142.3; **MS** (APCI) m/z calculated for C₁₄H₁₄NO₂S 260.1 [M-H]⁻, found 260.0.

N-Benzhydryl-C-(4-bromo-2-fluoro-phenyl)-methanesulfonamide (3{6,34})



White solid, mp 125-127°C; **FTIR** (KBr): ν_{\max} (cm⁻¹) 3235 (NH), 3089, 3068, 3032, 2935 (CH), 1154 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 4.13 (s, 2H, CH₂), 5.61 (s, 1H, CH), 7.06 (t, J=8.5 Hz, 1H, Ar), 7.25 (m, 2H, Ar), 7.29 (d, J= 8.0 Hz, 1H, Ar), 7.34 (m, 8H, Ar), 7.42 (dd, J= 1.6, 9.6 Hz, 1H, Ar), 8.62 (br s, 1H, NH); **¹³C NMR** (125.75 MHz, DMSO-d₆): δ (ppm) 52.0, 60.7, 117.0 (d, J_{C,F} = 15 Hz), 118.9 (d, J_{C,F} = 25 Hz), 122.0 (d, J_{C,F} = 10 Hz), 127.2, 127.3, 127.4 (d, J_{C,F} = 3.8 Hz), 128.5, 134.1 (d, J_{C,F} = 3.8 Hz), 142.4, 160.7 (d, J_{C,F} = 252 Hz); **MS** (APCI) m/z calculated for C₂₀H₁₈BrFNO₂S 235.1 [M+H]⁺, found 435.2.

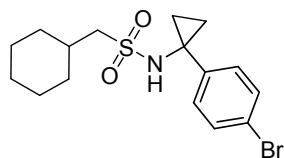
2-Methoxy-ethanesulfonic acid (1-phenyl-cyclobutyl)-amide (3{4,35})



Yellowish solid, mp 52-54°C; **FTIR** (KBr): ν_{\max} (cm⁻¹) 3266 (NH), 3088, 3060, 3032, 2998, 2983, 2939, 2901, 2883, (CH), 1149 (SO₂); **¹H NMR** (500 MHz, DMSO-d₆): δ (ppm) 1.64 (m, 1H, CH₂), 2.02

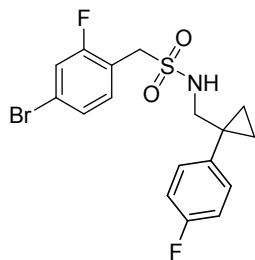
(m, 1H, CH₂), 2.35 (t, J = 6.9 Hz, 2H, CH₂), 2.46 (m, 2H, CH₂), 2.54 (m, 2H, CH₂), 3.07 (s, 3H, OCH₃), 3.37 (t, J = 7.0 Hz, 2H, CH₂), 7.28 (t, J = 7.2 Hz, 1H, Ar), 7.38 (t, J = 7.5 Hz, 2H, Ar), 7.43 (d, J = 7.2 Hz, 2H, Ar), 7.90 (s, 1H, NH); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 15.3, 34.5, 52.8, 57.8, 60.7, 65.7, 126.5, 127.2, 128.2; **MS** (APCI) m/z calculated for C₁₃H₂₀NO₃S 270.1 [M+H]⁺, found 270.0.

***N*-[1-(4-Bromo-phenyl)-cyclopropyl]-C-cyclohexyl-methanesulfonamide (3{3,36})**



Yellowish solid, mp 70-72°C; **FTIR** (KBr): ν_{max} (cm⁻¹) 3251 (NH), 3009, 2947, 2922, 2851 (CH), 1148 (SO₂); ¹H NMR (500 MHz, DMSO-d₆): δ (ppm) 0.85 (m, 2H, CH₂), 1.11 (m, 5H, 2CH₂ + CH), 1.26 (m, 2H, CH₂), 1.56 (m, 6H, 3CH₂), 2.52 (d, J = 5.5 Hz, 2H, CH₂), 7.34 (d, J = 8.5 Hz, 2H, Ar), 7.50 (d, J = 8.5 Hz, 2H, Ar), 8.23 (s, 1H, NH); ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 16.0, 25.4, 25.6, 32.2, 33.0, 36.7, 60.3, 119.7, 129.2, 131.1, 142.6; **MS** (APCI) m/z calculated for C₁₆H₂₃BrNO₂S 373.1 [M+H]⁺, found 373.0.

***C*-(4-Bromo-2-fluoro-phenyl)-*N*-[1-(4-fluoro-phenyl)-cyclopropylmethyl]-methanesulfonamide (3{6,37})**



Whitish solid, mp 104-106°C; **FTIR** (KBr): ν_{max} (cm⁻¹) 3269 (NH), 3102, 3091, 3071, 3054, 3036, 3005, 2922, 2861 (CH), 1156 (SO₂); ¹H NMR (500 MHz, DMSO-d₆): δ (ppm) 0.73 (t, J = 5.4 Hz, 2H, CH₂), 0.86 (t, J = 5.4 Hz, 2H, CH₂), 3.16 (d, J = 6.0 Hz, 2H, CH₂), 4.21 (s, 2H, CH₂), 7.10 (t, J = 8.8 Hz, 2H, Ar), 7.27 (t, J = 8.2 Hz, 1H, Ar), 7.34 (q, J = 5.8 Hz, 2H, Ar), 7.4 (m, 2H, Ar), 7.56 (d, J = 9.3 Hz, 1H, NH). ¹³C NMR (125.75 MHz, DMSO-d₆): δ (ppm) 11.8, 24.6, 50.2, 51.0, 114.8 (d, J_{C,F} = 20 Hz), 117.3 (d, J_{C,F} = 15 Hz), 118.9 (d, J_{C,F} = 25 Hz), 121.9 (d, J_{C,F} = 10 Hz), 127.6 (d, J_{C,F} = 2.5 Hz), 130.7 (d, J_{C,F} =

7.5 Hz), 134.6 (d, $J_{\text{C,F}} = 3.8$ Hz), 139.2 (d, $J_{\text{C,F}} = 2.5$ Hz), 160.8 (d, $J_{\text{C,F}} = 252$ Hz), 160.9 (d, $J_{\text{C,F}} = 243$ Hz); **MS** (APCI) m/z calculated for $\text{C}_{17}\text{H}_{17}\text{BrF}_2\text{NO}_2\text{S}$ 417.0 $[\text{M}+\text{H}]^+$, found 417.1.

NMR spectra of the selected compounds.

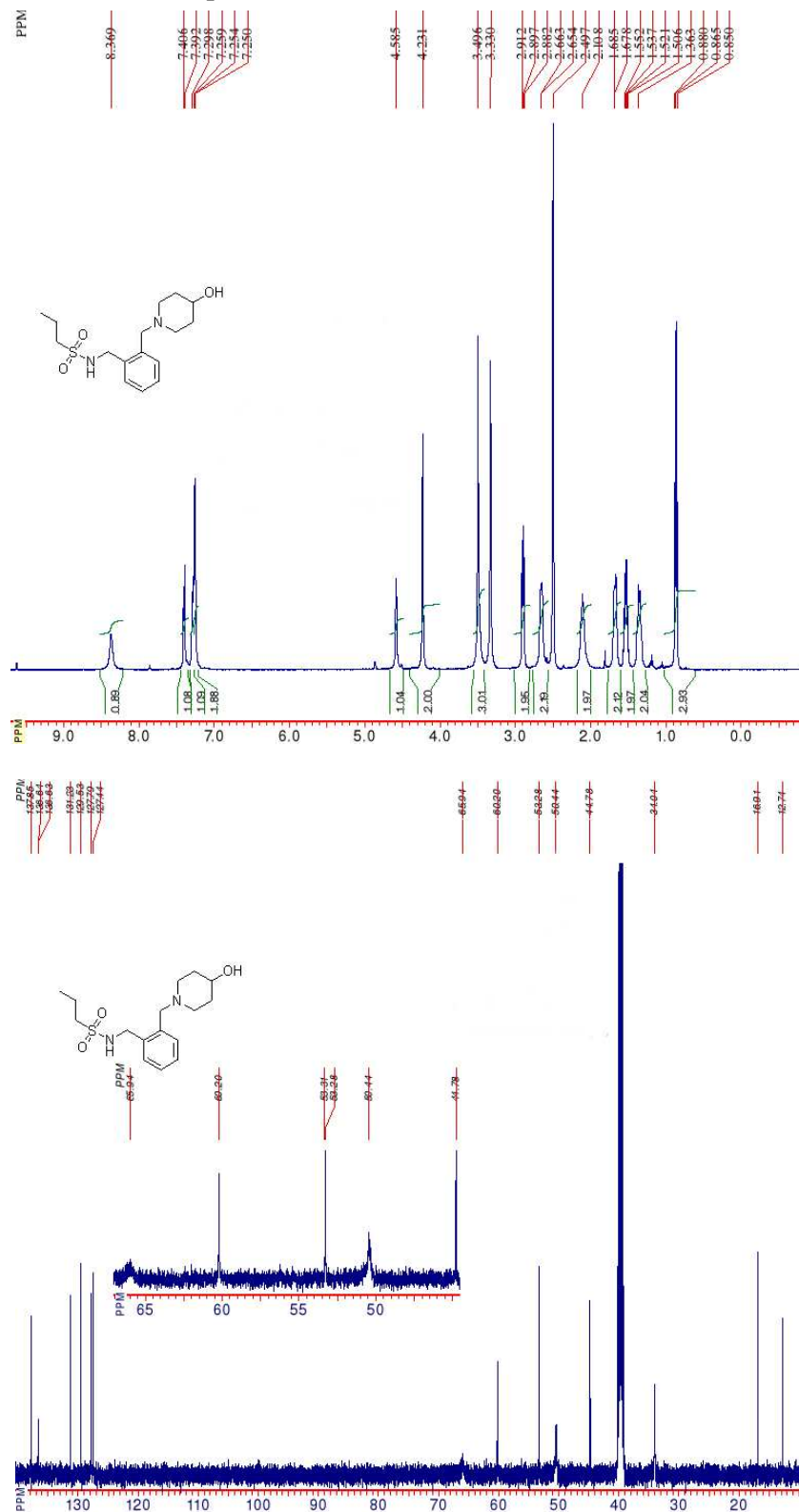


Figure S37

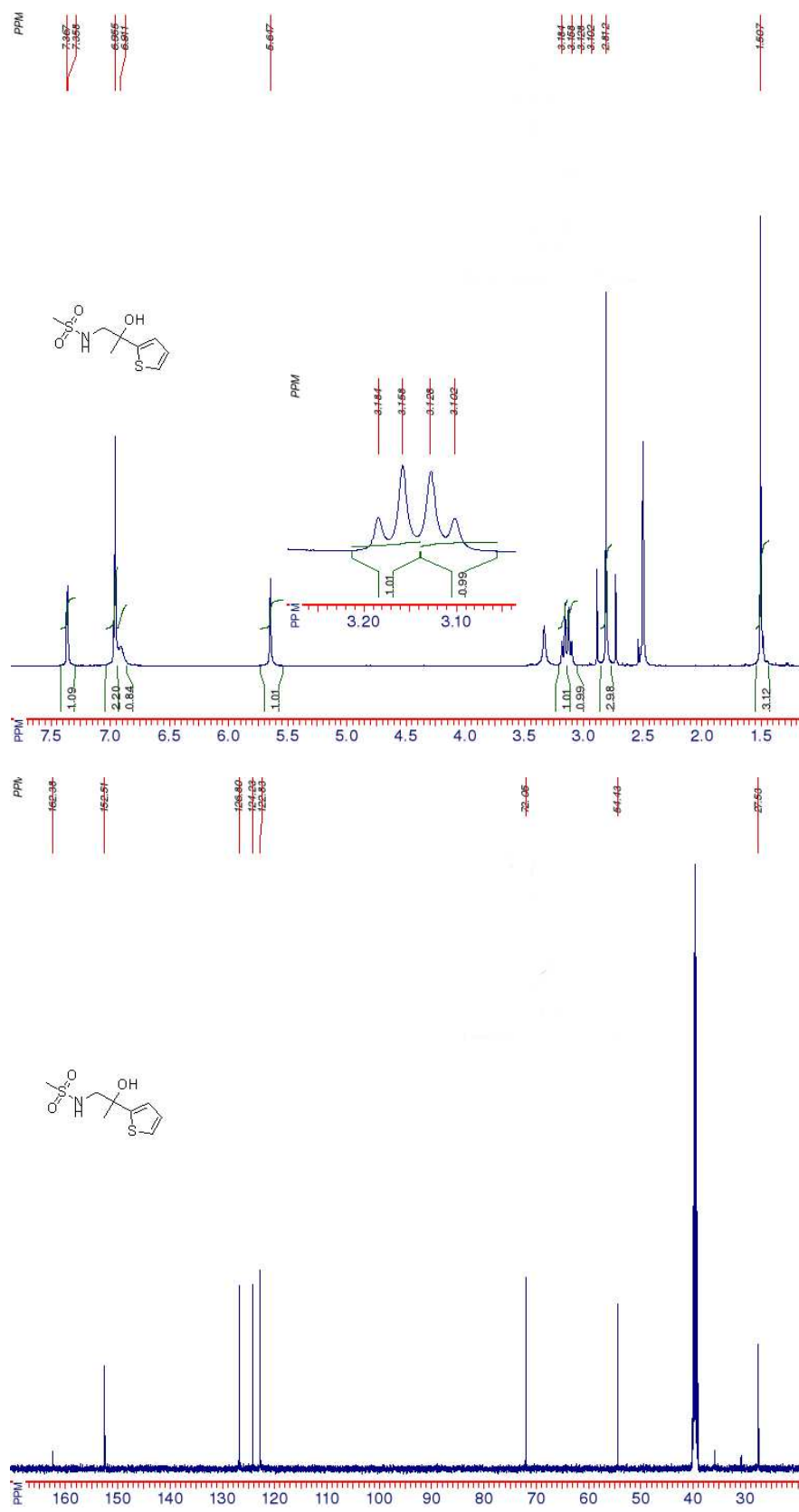


Figure S38

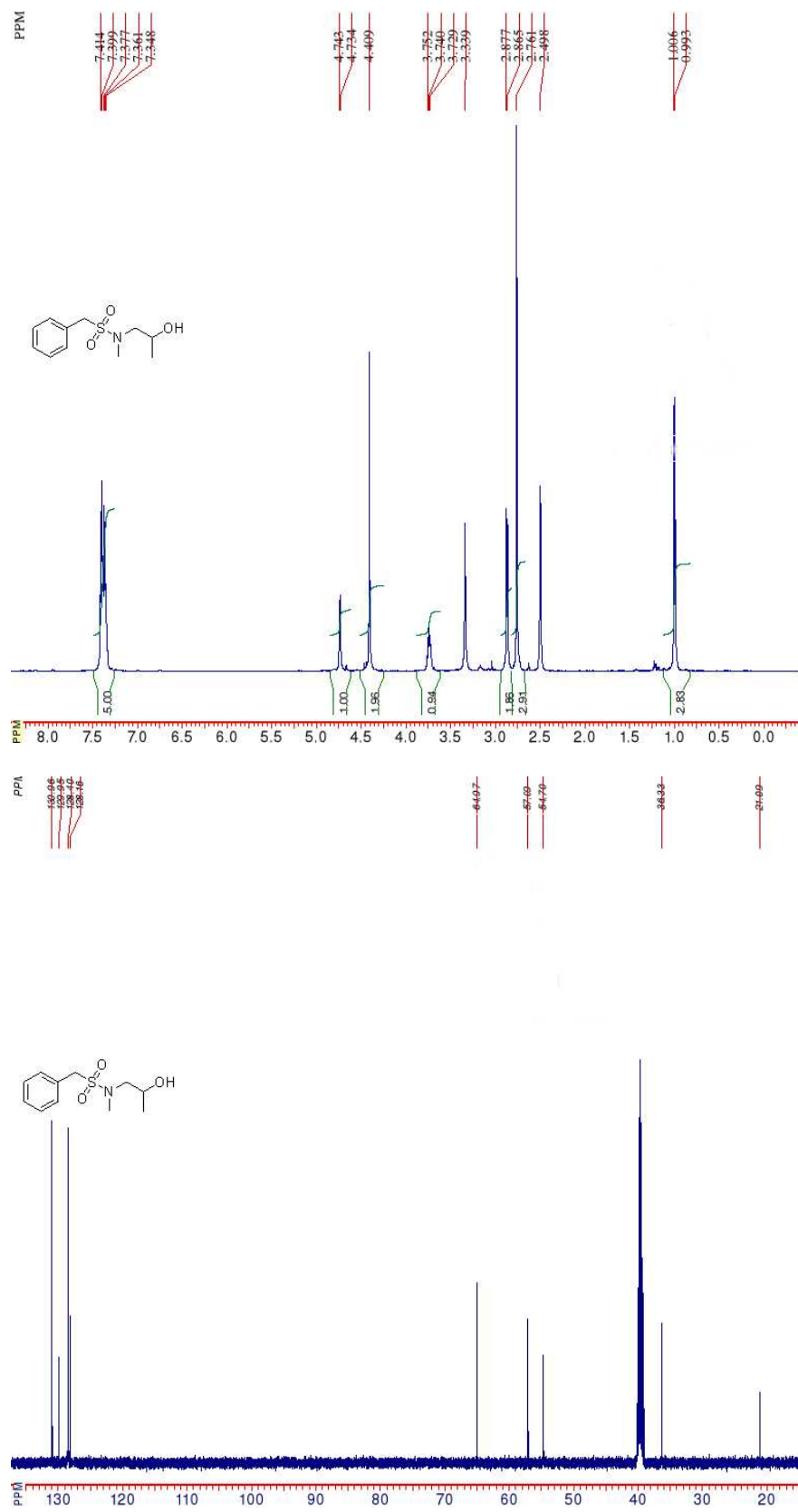


Figure S39

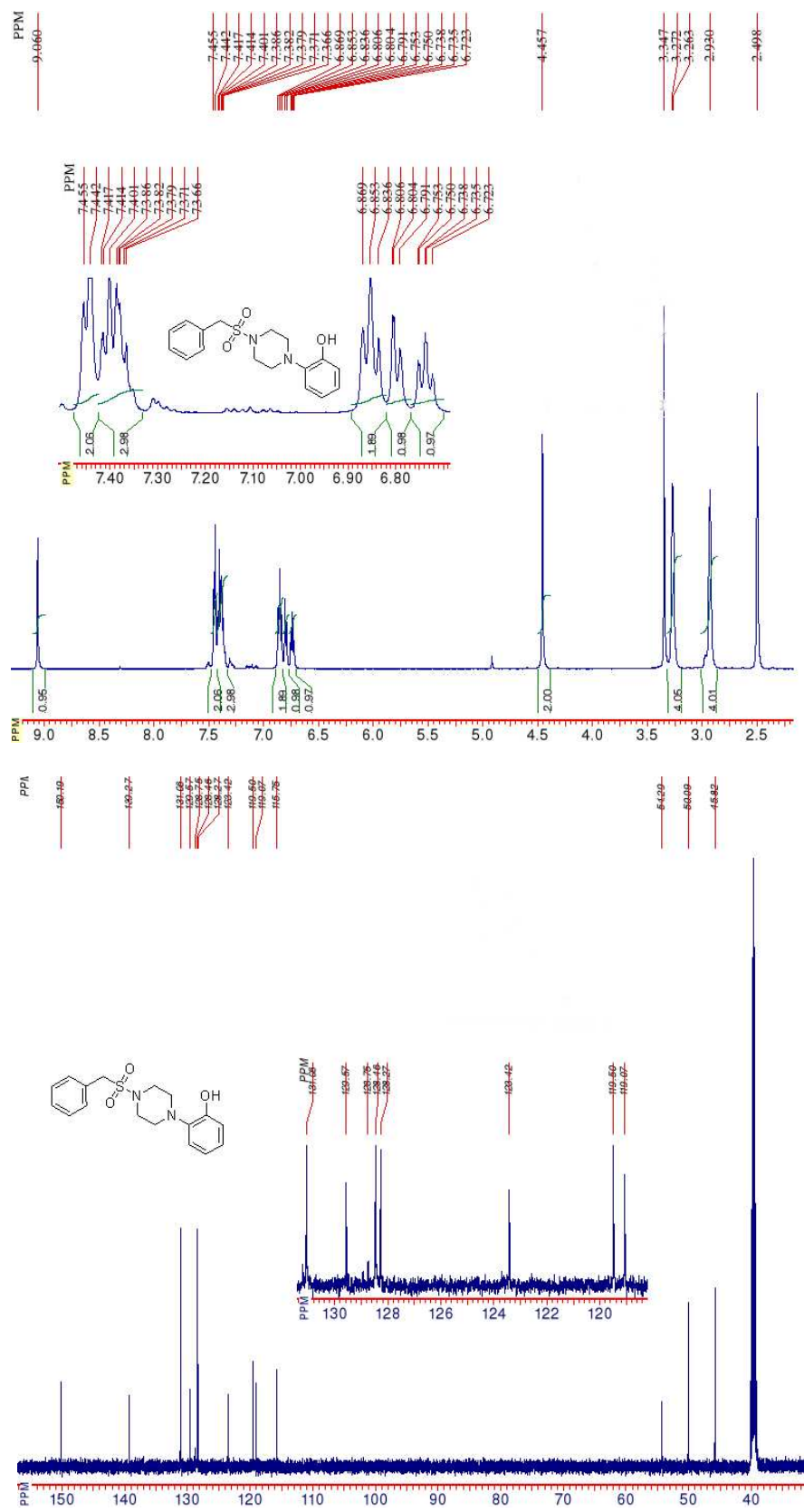


Figure S40

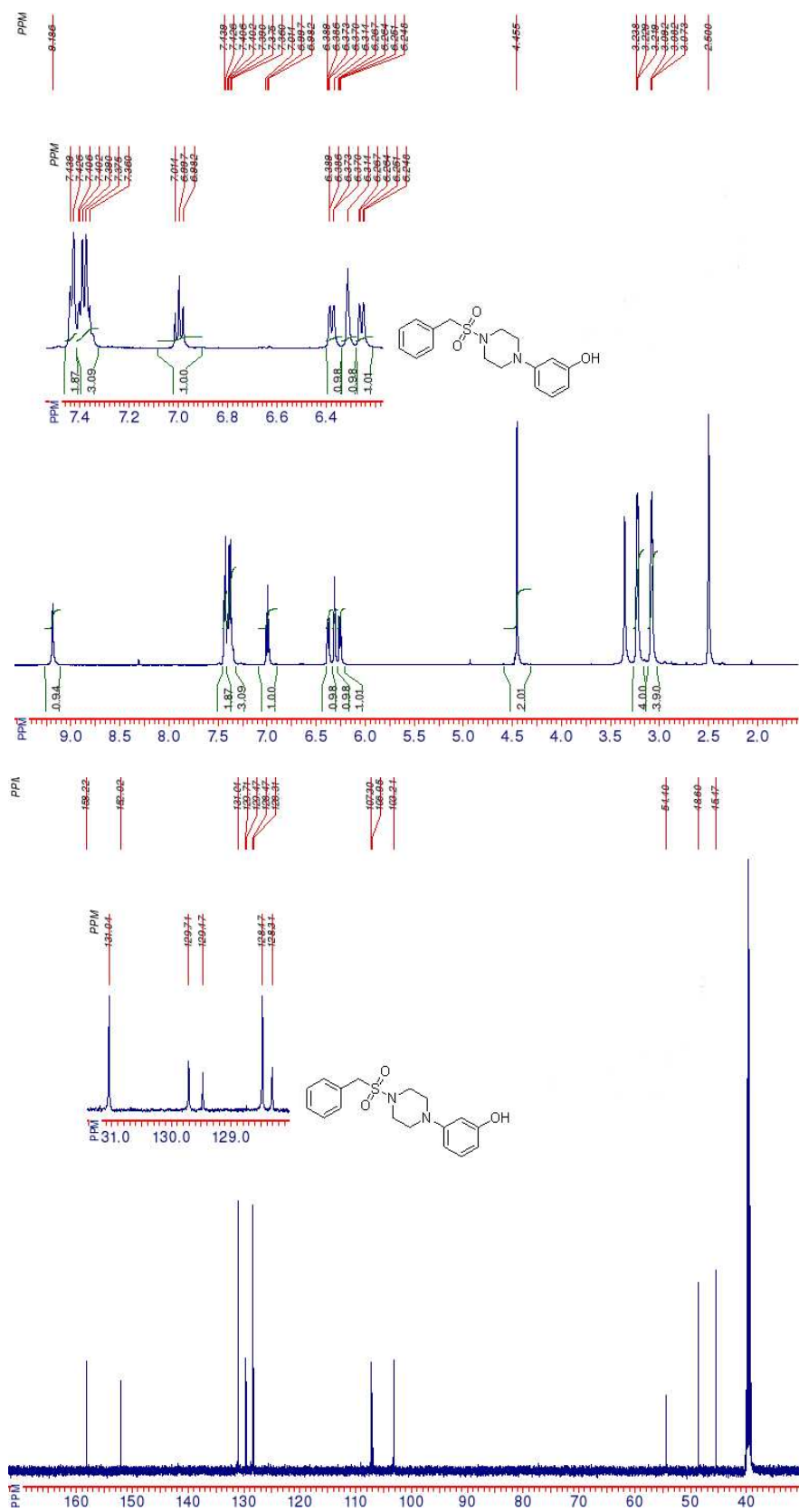


Figure S41

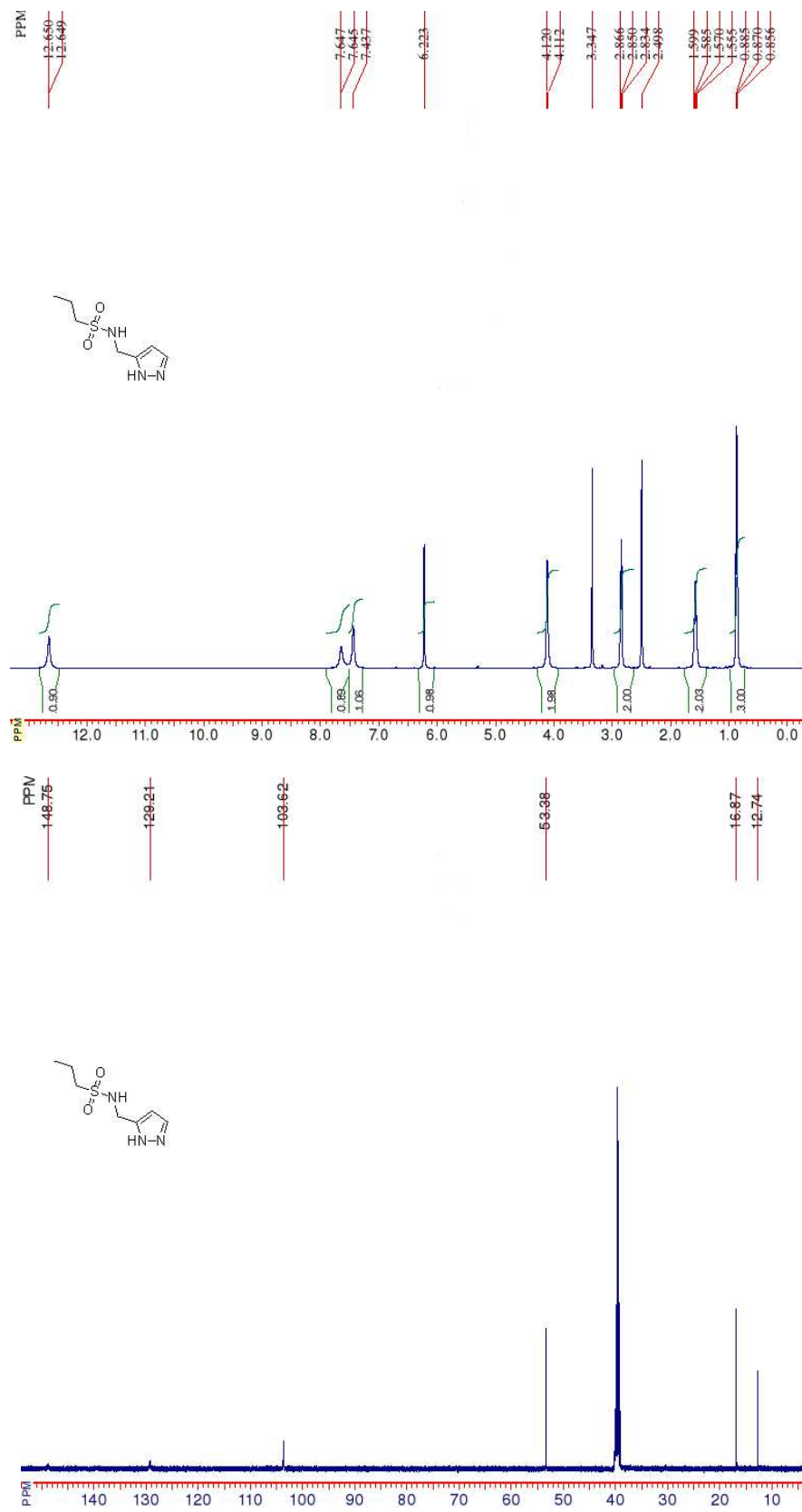


Figure S42

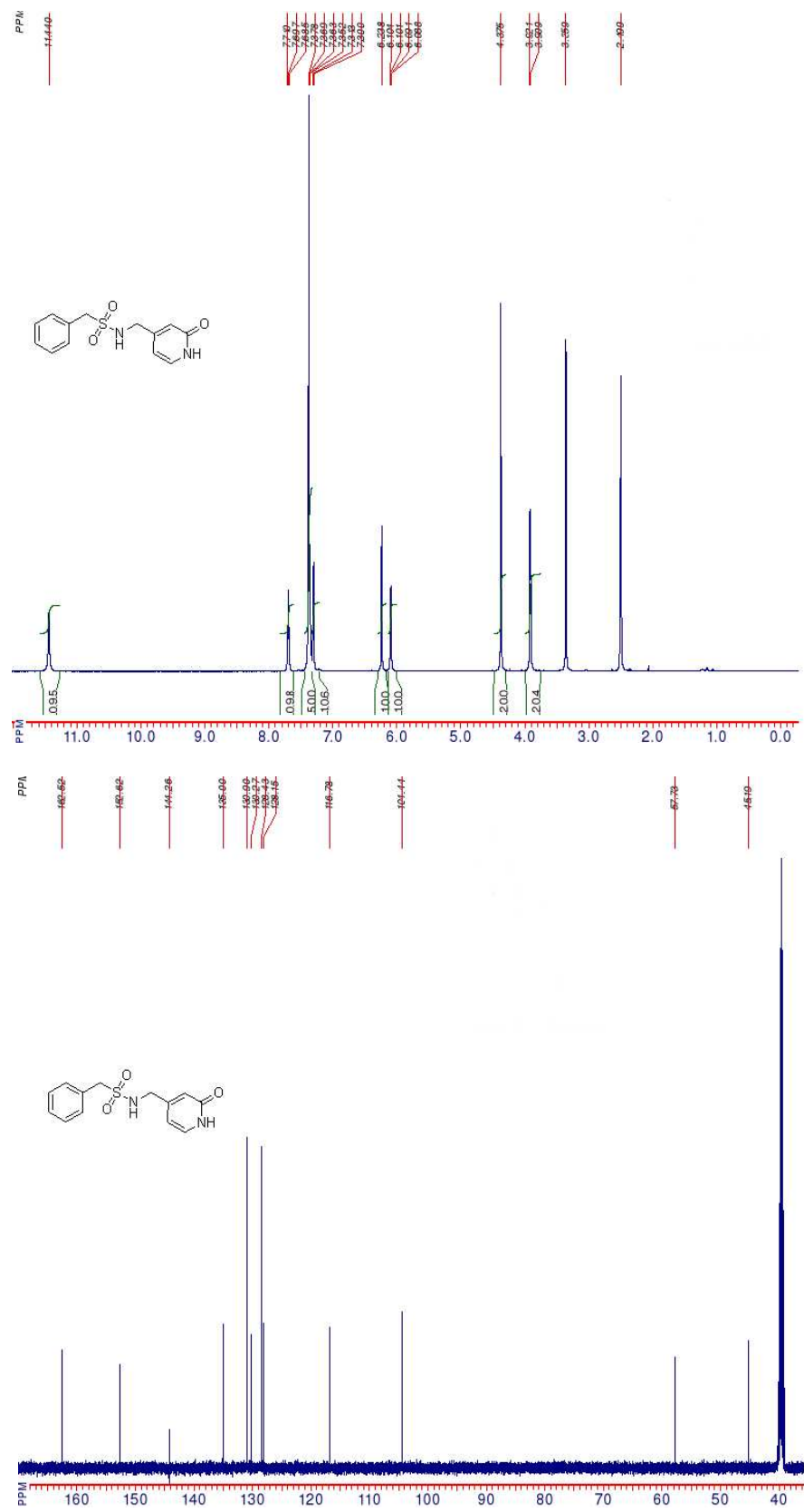


Figure S43

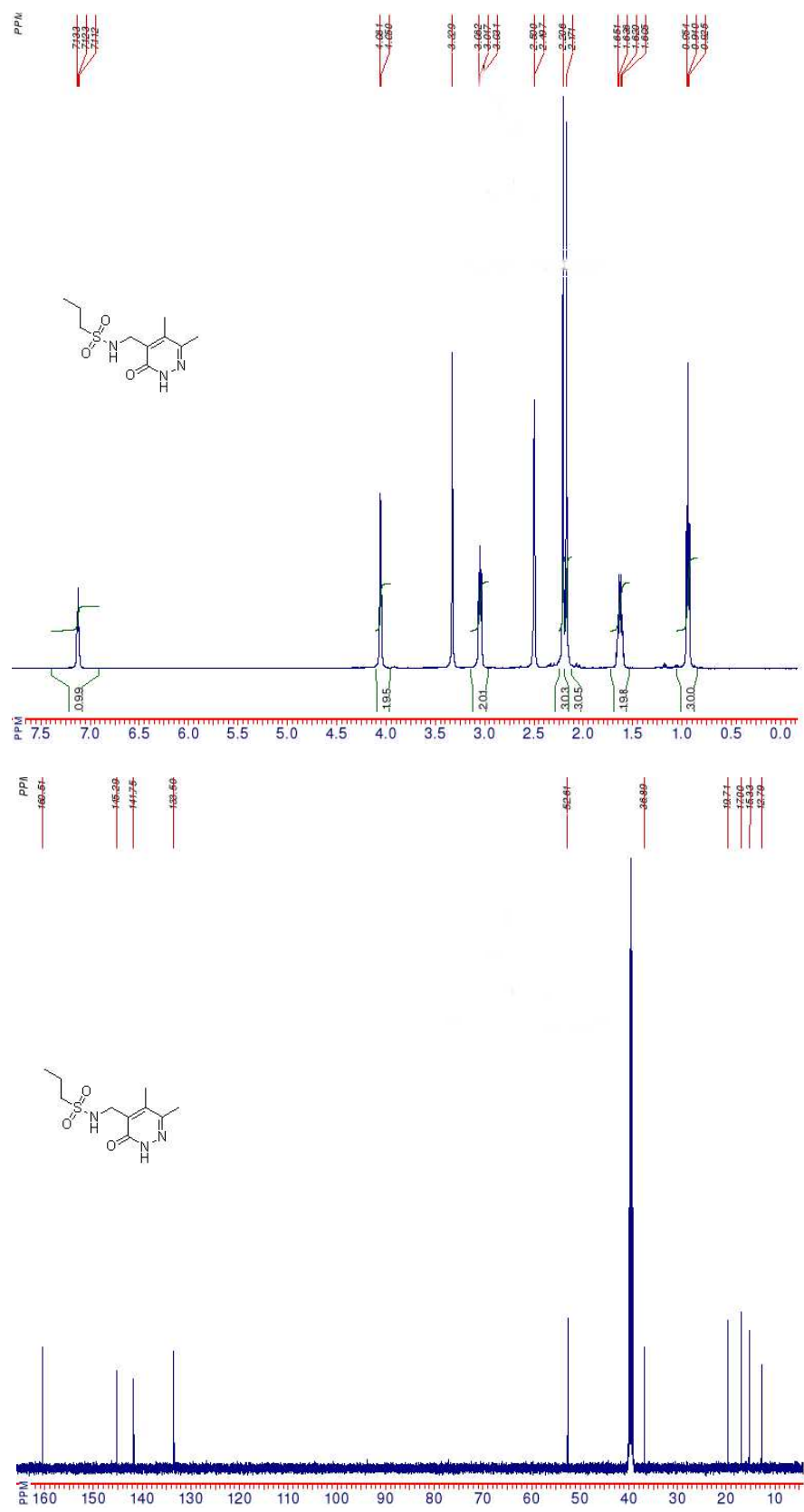


Figure S44

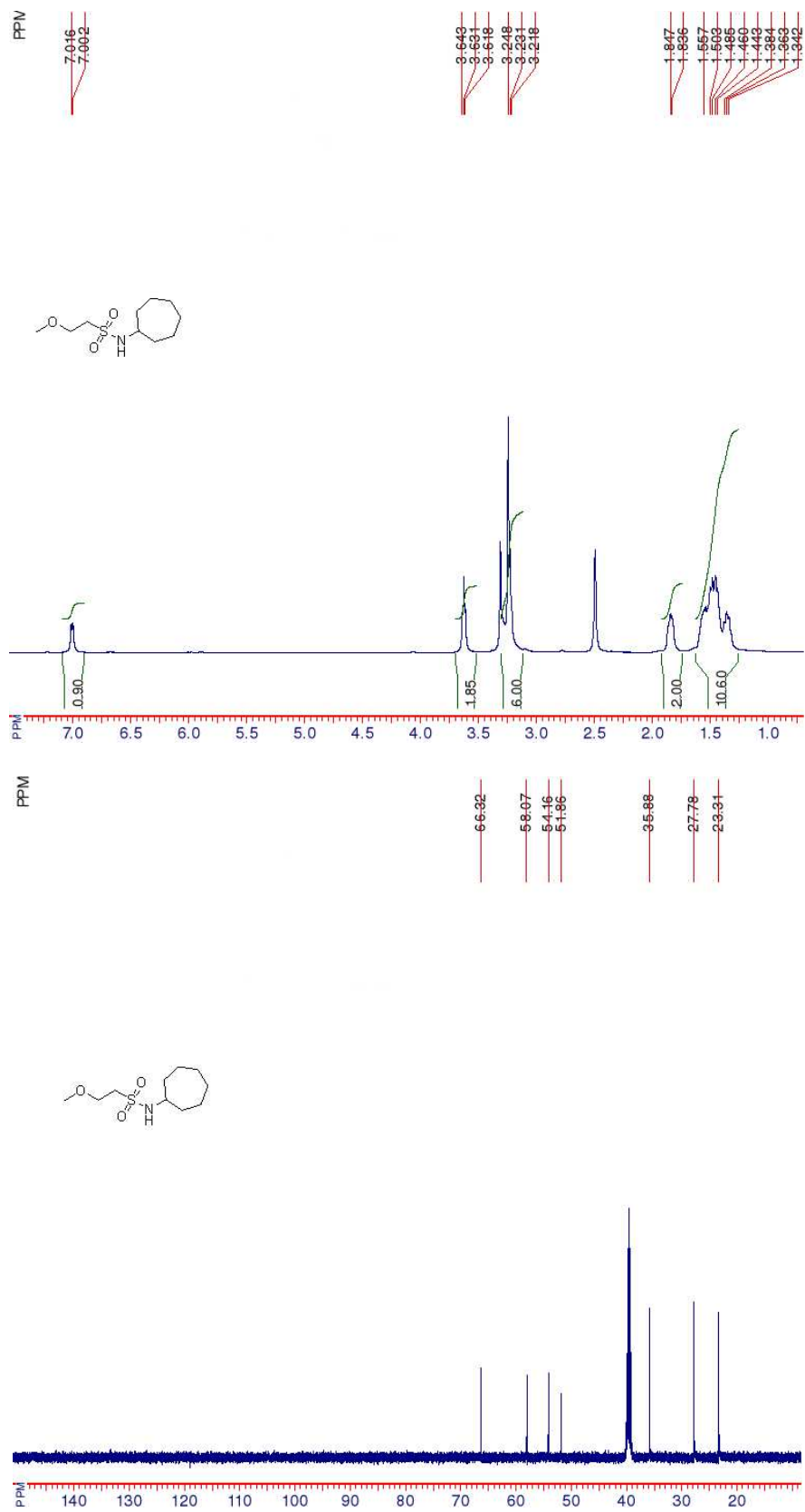
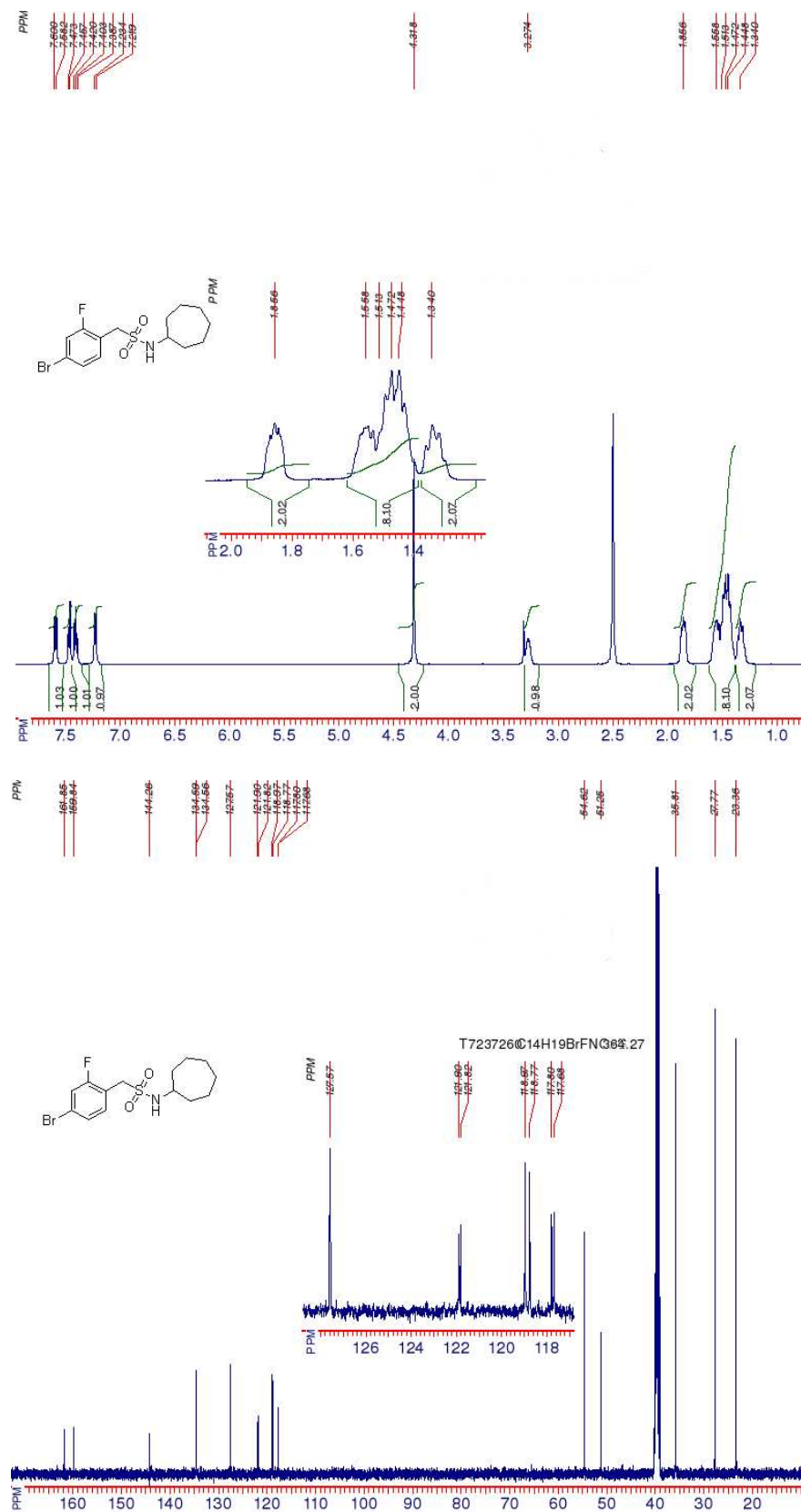


Figure S45



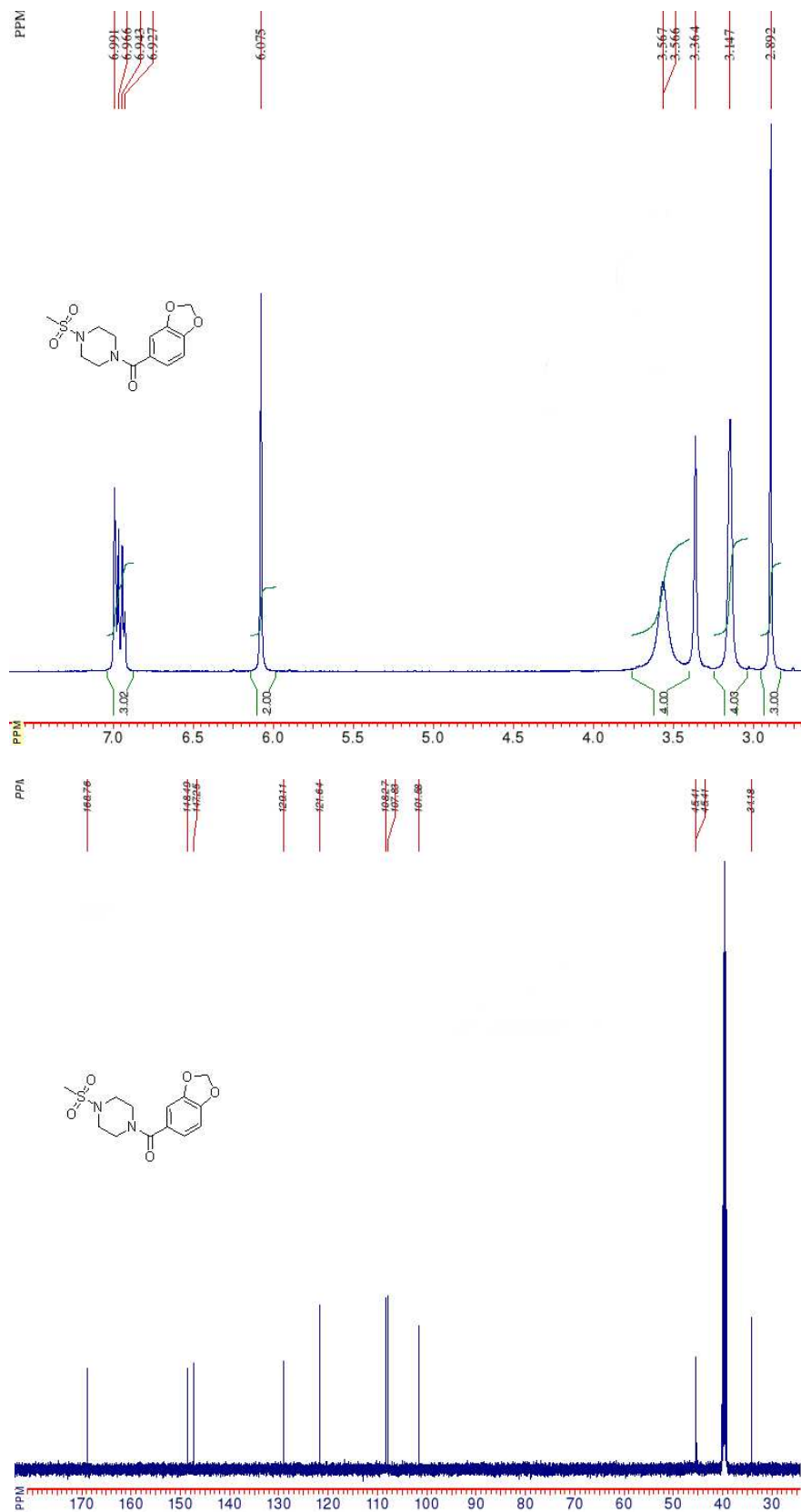


Figure S48

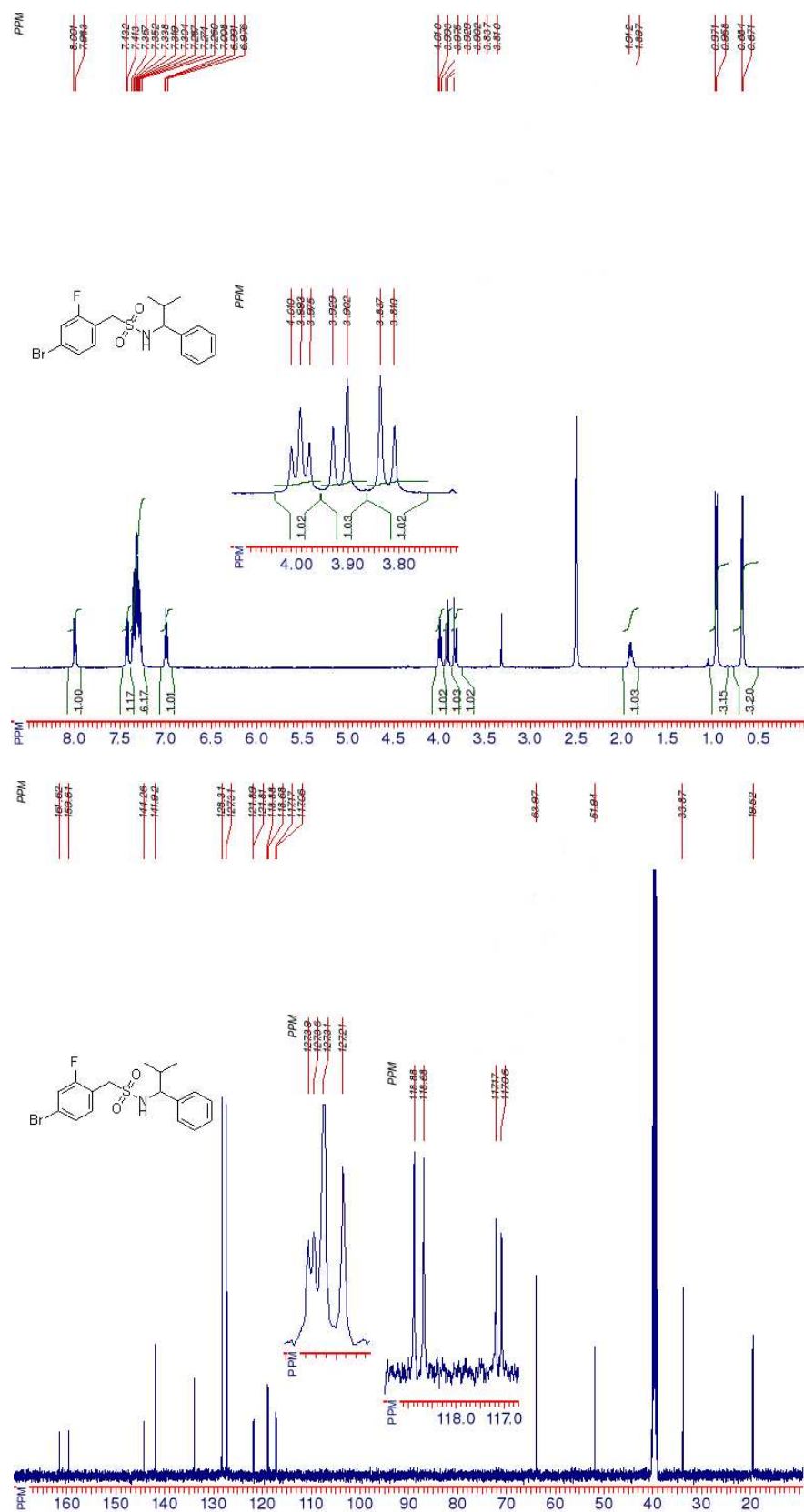


Figure S50

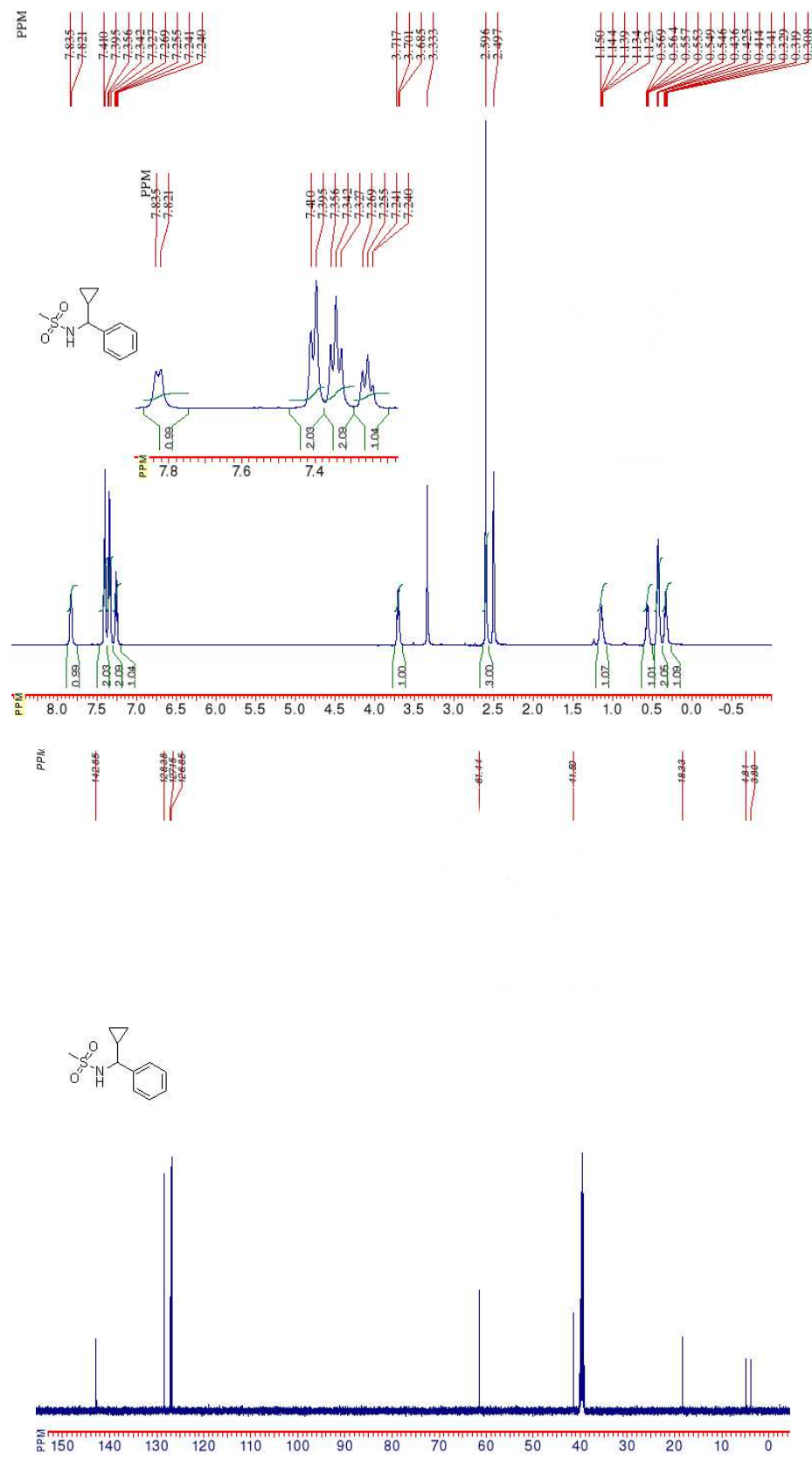


Figure S51

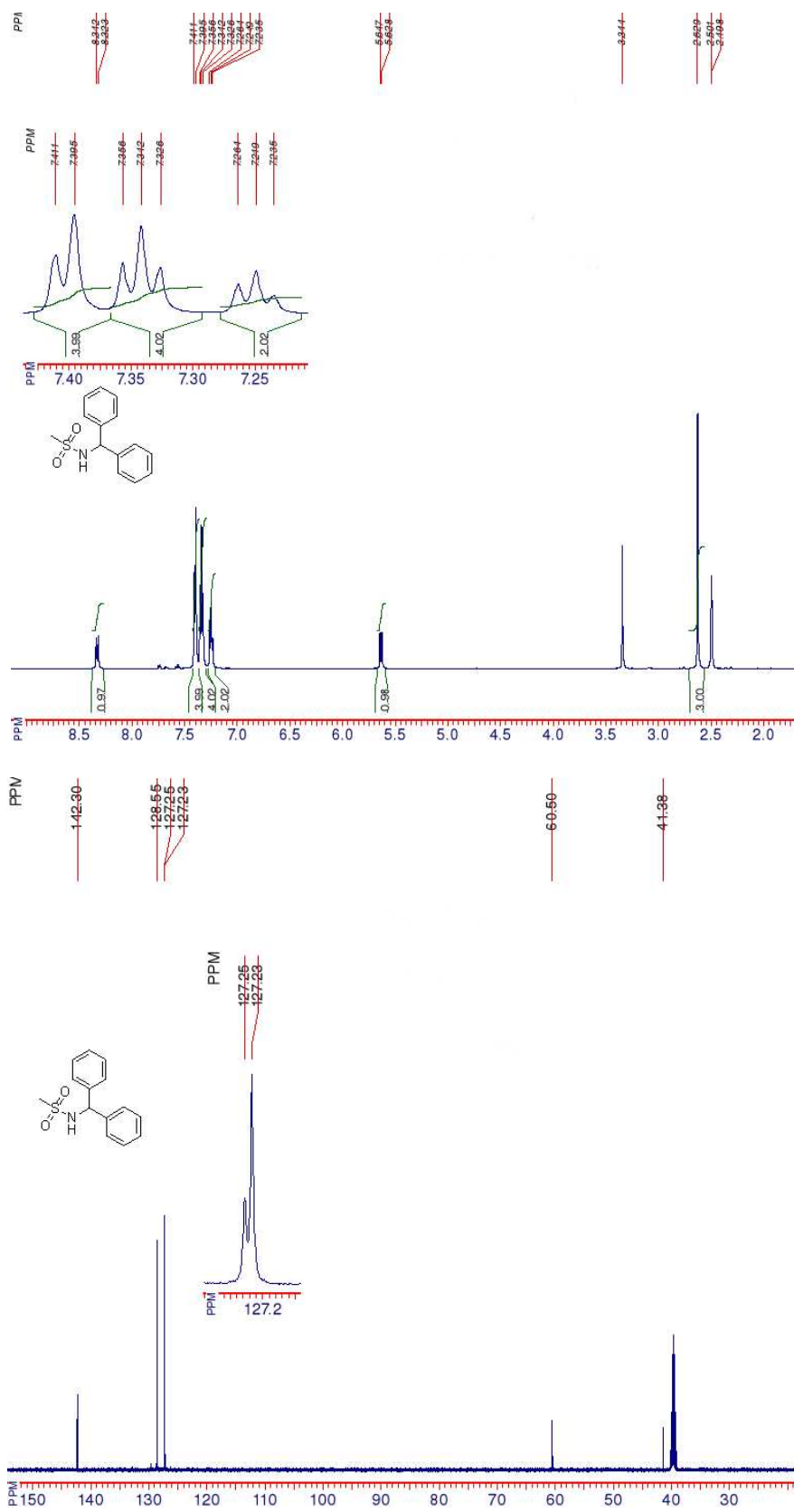
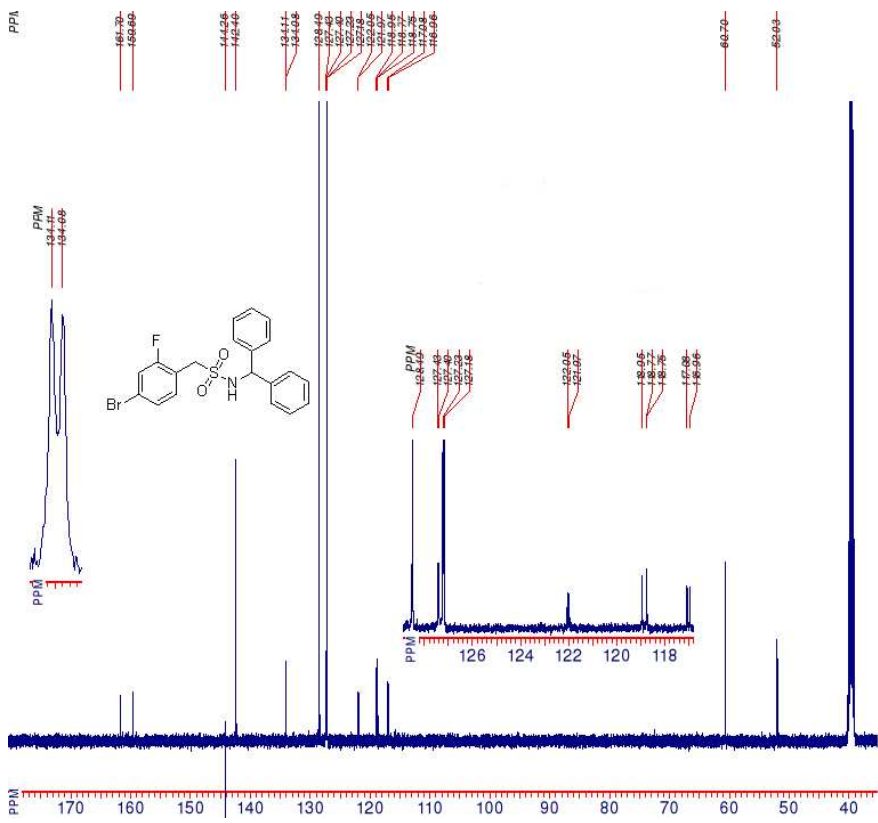


Figure S52



S56

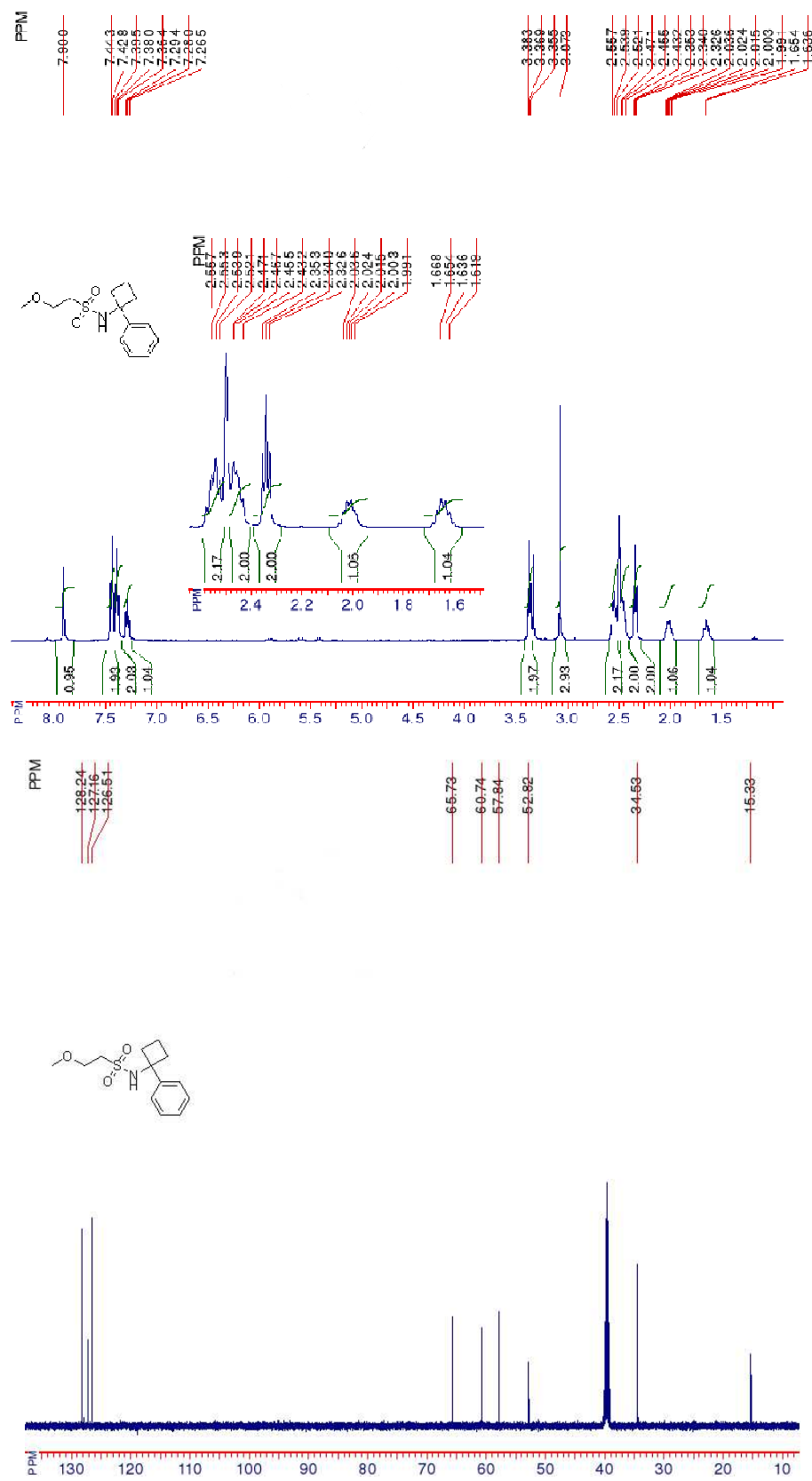


Figure S54

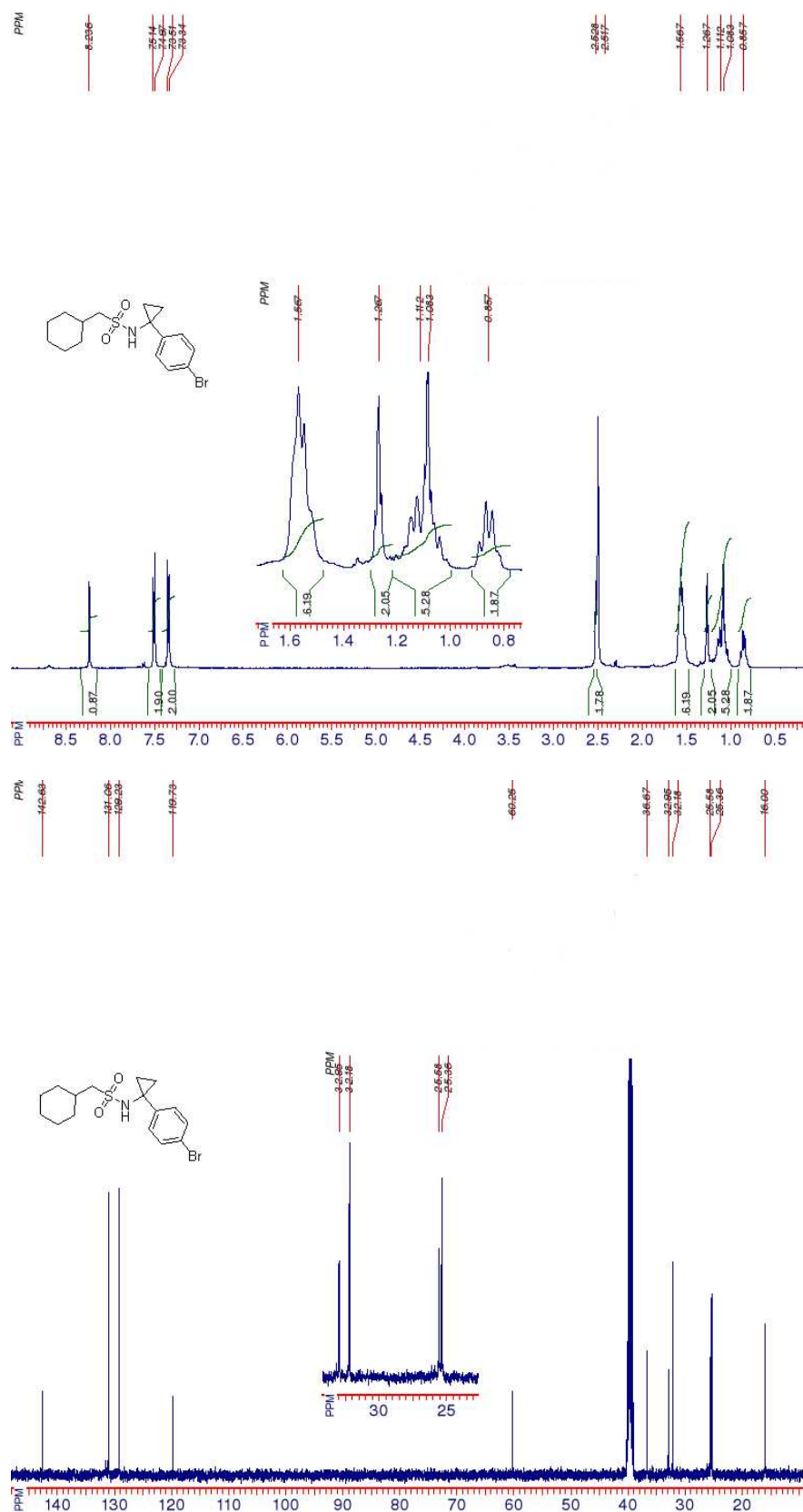


Figure S55

