Electronic Supplementary Material (ESI) for Chemical Communications

SUPPORTING INFORMATION

New superacid synthesized (fluorinated) tertiary benzenesulfonamides acting as selective hCA IX inhibitors: toward a new mode of carbonic anhydrases inhibition by sulfonamides.

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A. GENERAL METHOD

The authors draw the reader's attention to the dangerous features of superacidic chemistry. Handling of hydrogen fluoride and antimony pentafluoride must be done by experienced chemists with all the necessary safety arrangements in place.

Reactions performed in superacid were carried out in a sealed Teflon® flask with a magnetic stirrer. No further precautions have to be taken to prevent mixture from moisture (test reaction worked out in anhydrous conditions leads to the same results as expected).

Yields refer to isolated pure products.

^{1}H, ^{13}C and ^{19}F NMR were recorded on a 400 MHz Bruker Advance DPX spectrometer using $CDCl_3$ as solvent. COSY ^{1}H-^{1}H and ^{1}H-^{13}C experiments were used to confirm the NMR peaks assignments.

Melting points were determined in a capillary tube with a device Büchi melting point B-545 and were uncorrected.

Mass Spectra (MS) were performed with a Liquid Chromatography–Coupled *Tandem* Mass Spectrometry *(electronic impact).*

All separations were done under flash-chromatography conditions on silica gel (15-40 µm).

High Resolution Mass Spectrometry (HRMS) spectra were performed at the Institut Lavoisier de Versailles of the University of Versailles St Quentin, France.

B. *N*-ALLYL-*N*-ARYLBENZENESULFONAMIDE

Procedure A: optimized procedure for *N*-sulfonylation of anilines

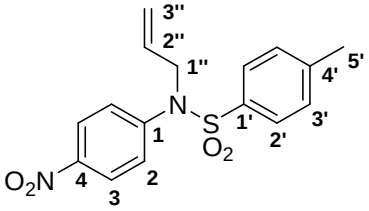
Into a round bottom flask cooled to 0°C, aniline de rivative (1 eq), sulfonyl chloride (1.2 eq) and dichloromethane were introduced. Mixture was stirred under nitrogen's atmosphere. Pyridine (3 eq) was slowly added. The mixture was magnetically stirred at room temperature for 48 hours. The reaction mixture was then neutralized with water-sodium carbonate solution (100 mL), extracted with dichloromethane (x 3). The combined organic layers were washed with hydrochloric acid 2M (x 4), dried over magnesium sulphate, filtered and concentrated *in vacuo*.

Procedure B: optimized procedure for *N*-allylation of *N*-arylbenzenesulfonamides

Into a round bottom flask at room temperature, *N*-arylbenzenesulfonamide derivative (1 eq), acetonitrile (60 mL) and potassium carbonate (10 eq) were introduced. Allyl bromide (3 eq) was slowly added. The mixture was magnetically stirred under nitrogen atmosphere at 80°C for 16 hours. The reaction mixture was then concentrated *in vacuo*, washed with water (x 1), dried over magnesium sulphate, filtered and concentrated *in vacuo*.

Products were isolated by column chromatography over silica gel.

Formation of compound 3a:



***N*-allyl-4-methyl-*N*-(4-nitrophenyl)benzenesulfonamide**

This compound was obtained from 4-methyl-*N*-(4-nitrophenyl)benzenesulfonamide (1.38 g, 10.0 mmol) following the general procedure B. The reaction crude (without further purification) gave compound **3a** (1.73 g, 98 %).

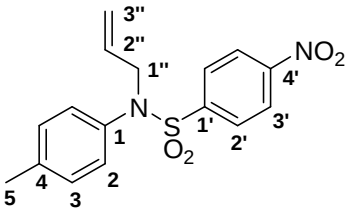
Aspect: Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 8.15 (d, 2 H, J = 9.1 Hz, **H_3**), 7.47 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.29 - 7.25 (m, 4 H, **H_2** and **$H_{3'}$**), 5.70 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.3 Hz, J = 6.2 Hz, **$H_{2''}$**), 5.15 - 5.09 (dm, 1 H, J_{trans} = 17.2 Hz, **$H_{3''}$**), 5.12 - 5.08 (dm, 1 H, J_{cis} = 10.1 Hz, **$H_{3''}$**), 4.27 - 4.24 (dm, 2 H, J = 6.2 Hz, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 148.0 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 145.0 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 144.3 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 134.5 (**$C_{1'}$** or **$C_{4'}$**), 131.8 (CH, **$C_{2''}$**), 129.7 (CH, **C_2** or **$C_{3'}$**), 128.1 (CH, **C_2** or **$C_{3'}$**), 127.4 (CH, **$C_{2'}$**), 124.1 (CH, **C_3**), 119.7 (CH_2, **$C_{3''}$**), 52.7 (CH_2, **$C_{1''}$**), 21.5 (CH_3, **$C_{5'}$**).

HRMS (MALDI/TOF, ES$^+$, CH_3CN): m/z calc for $C_{16}H_{16}N_2O_4S$ $[M+H]^+$: 333.0909, m/z found: 333.0905.

Formation of compound 3b:



***N*-allyl-*N*-(4-methylphenyl)-4-nitrobenzenesulfonamide**

This compound was obtained from 4-methylaniline (536 mg, 5.0 mmol) following the general procedure A then B. The reaction crude was filtered over silica gel with the eluent ethyl acetate, thereby obtaining compound **3b** (1.61 g, 97 % for two steps).

Aspect: Orange powder.

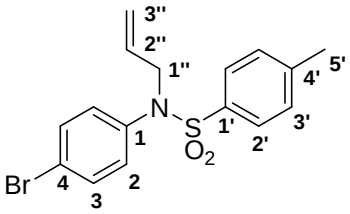
Mp: 125.3 - 126.2 ℃.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 8.31 (d, 2 H, J = 9.0 Hz, **$H_{3'}$**), 7.78 (d, 2 H, J = 9.0 Hz, **$H_{2'}$**), 7.10 (d, 2 H, J = 8.0 Hz, **H_2** or **H_3**), 6.90 (d, 2 H, J = 8.3 Hz, **H_2** or **H_3**), 5.73 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.2 Hz, J = 6.3 Hz, **$H_{2''}$**), 5.13 - 5.07 (dm, 1 H, J_{trans} = 17.1 Hz, **$H_{3''}$**), 5.09 - 5.05 (dm, 1 H, J_{cis} = 10.1 Hz, **$H_{3''}$**), 4.20 (ddd, 2 H, J = 6.3 Hz, J = 1.2 Hz, J = 1.2 Hz, **$H_{1''}$**), 2.32 (s, 3 H, **H_5**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 149.9 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 144.2 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 138.4 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 135.4 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 132.1 (CH, **$C_{2''}$**), 129.8 (CH, **C_2** or **C_3** or **$C_{2'}$**), 128.7 (CH, **C_2** or **C_3** or **$C_{2'}$**), 128.5 (CH, **C_2** or **C_3** or **$C_{2'}$**), 123.9 (CH, **$C_{3'}$**), 119.3 (CH_2, **$C_{3''}$**), 53.9 (CH_2, **$C_{1''}$**), 21.0 (CH_3, **$C_{5'}$**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{16}H_{16}N_2O_4S$ $[M+H]^+$: 333.0909, m/z found: 333.0906.

Compound 3c:



***N*-allyl-*N*-(4-bromophenyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-(4-bromophenyl)-4-methylbenzenesulfonamide (879 mg, 2.7 mmol) following the general procedure B. The reaction crude was filtered over silica gel with the eluent ethyl acetate, thereby obtaining compound **3c** (987 mg, 99 %).

Aspect: White powder.

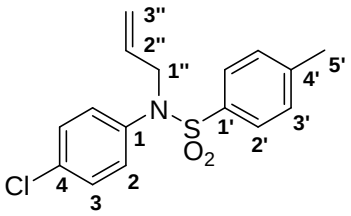
Mp: 64.8 - 65.5 ℃.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.50 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.42 (d, 2 H, J = 8.8 Hz, **H_3**), 7.28 (d, 2 H, J = 8.0 Hz, **$H_{3'}$**), 6.95 (d, 2 H, J = 8.8 Hz, **H_2**), 5.72 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.2 Hz, J = 6.3 Hz, **$H_{2''}$**), 5.12 - 5.06 (dm, 1 H, J_{trans} = 17.1 Hz, **$H_{3''}$**), 5.09 - 5.04 (dm, 1 H, J_{cis} = 10.1 Hz, **$H_{3''}$**), 4.17 (ddd, 2 H, J = 6.3 Hz, J = 1.3 Hz, J = 1.3 Hz, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 143.6 (**$C_{1'}$** or **$C_{4'}$**), 138.0 (**C_1**), 134.7 (**$C_{1'}$** or **$C_{4'}$**), 132.2 (CH, **$C_{2''}$**), 131.8 (CH, **C_3**), 130.2 (CH, **C_2**), 129.4 (CH, **$C_{3'}$**), 127.4 (CH, **$C_{2'}$**), 121.4 (**C_4**), 119.0 (CH_2, **$C_{3''}$**), 53.1 (CH_2, **$C_{1''}$**), 21.3 (CH_3, **$C_{5'}$**).

Already described in: Studies on the amido-Claisen rearrangement. VII. Synthesis of N-mesyl- and N-tosylo-allylanilines by amido-claisen rearrangement ; Inada Seisaku, Hirabayashi Shigeto,Taguchi Kazuhiro, Okazaki Mitsuo ; *Nippon Kagaku Kaishi*, **1978**, (1), 86-92.

Compound 3d:



***N*-allyl-*N*-(4-chlorophenyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-(4-chlorophenyl)-4-methylbenzenesulfonamide (1.08 g, 3.8 mmol) following the general procedure B. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 90/10, thereby obtaining compound **3d** (1.21 g, 98 %).

Aspect: White powder.

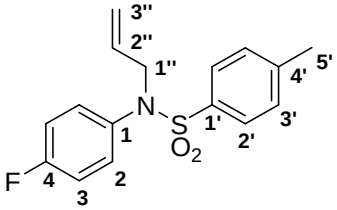
Mp: 49.1 - 50.0 °C.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.51 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.30 - 7.26 (m, 4 H, **H_3** and **$H_{3'}$**), 7.03 (d, 2 H, J = 8.8 Hz, **H_2**), 5.73 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.2 Hz, J = 6.3 Hz, **$H_{2''}$**), 5.13 - 5.05 (m, 2 H, **$H_{3''}$**), 4.21 - 4.18 (dm, 2 H, J = 6.3 Hz, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 143.5 (**$C_{1'}$** or **$C_{4'}$**), 137.4 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 134.6 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 133.1 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 132.1 (CH, **$C_{2''}$**), 129.8 (CH, **C_2**), 129.3 (CH, **C_3** or **$C_{3'}$**), 128.7 (CH, **C_3** or **$C_{3'}$**), 127.3 (CH, **$C_{2'}$**), 118.8 (CH_2, **$C_{3''}$**), 53.0 (CH_2, **$C_{1''}$**), 21.2 (CH_3, **$C_{5'}$**).

Already described in: Studies on the amido-Claisen rearrangement. VII. Synthesis of N-mesyl- and N-tosylo-allylanilines by amido-claisen rearrangement ; Inada Seisaku, Hirabayashi Shigeto,Taguchi Kazuhiro, Okazaki Mitsuo ; *Nippon Kagaku Kaishi*, **1978**, (1), 86-92.

Compound 3e:



***N*-allyl-*N*-(4-fluorophenyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-(4-fluorophenyl)-4-methylbenzenesulfonamide (1.06 g, 4.0 mmol) following the general procedure B. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 90/10, thereby obtaining compound **3e** (1.20 g, 98 %).

Aspect: White solid.

Mp: 62.4 - 63.3 °C.

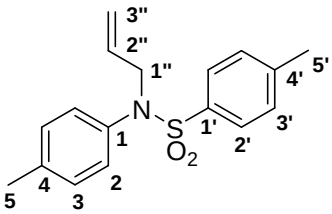
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.51 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.28 (d, 2 H, J = 8.0 Hz, **$H_{3'}$**), 7.06 - 6.95 (m, 4 H, **H_2** and **H_3**), 5.74 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.1 Hz, J = 6.3 Hz, **$H_{2''}$**), 5.12 - 5.06 (dm, 1 H, J_{trans} = 17.1 Hz, **$H_{3''}$**), 5.08 - 5.04 (dm, 1 H, J_{cis} = 10.1 Hz, **$H_{3''}$**), 4.18 (ddd, 2 H, J = 6.3 Hz, J = 1.3 Hz, J = 1.3 Hz, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 161.8 (d, J = 248.0 Hz, **C_4**), 143.8 (**$C_{1'}$** or **$C_{4'}$**), 135.1 (**$C_{1'}$** or **$C_{4'}$**), 134.9 (d, J = 3.1 Hz, **C_1**), 132.6 (CH, **$C_{2''}$**), 130.7 (d, CH, J = 8.7 Hz, **C_2**), 129.5 (CH, **$C_{3'}$**), 127.7 (CH, **$C_{2'}$**), 119.0 (CH_2, **$C_{3''}$**), 115.7 (d, CH, J = 22.6 Hz, **C_3**), 53.7 (CH_2, **$C_{1''}$**), 21.5 (CH_3, **$C_{5'}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -113.28 (**F_4**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{16}H_{16}FNO_2S$ $[M+H]^+$: 306.0964, m/z found: 306.0961.

Compound 3f:



***N*-allyl-4-methyl-*N*-(4-methylphenyl)benzenesulfonamide**

This compound was obtained from 4-methyl-*N*-(4-methylphenyl)benzenesulfonamide (1.05 g, 4.0 mmol) following the general procedure B. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 92/8, thereby obtaining compound **3f** (1.18 mg, 98 %).

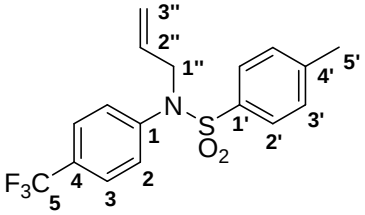
Aspect: Pale yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.48 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.23 (d, 2 H, J = 7.9 Hz, **$H_{3'}$**), 7.06 (d, 2 H, J = 8.0 Hz, **H_2** or **H_3**), 6.91 (d, 2 H, J = 8.3 Hz, **H_2** or **H_3**), 5.72 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.2 Hz, J = 6.2 Hz, **$H_{2''}$**), 5.09 - 5.03 (dm, 1 H, J_{trans} = 17.1 Hz, **$H_{3''}$**), 5.03 - 4.99 (dm, 1 H, J_{cis} = 10.2 Hz, **$H_{3''}$**), 4.15 (ddd, 2 H, J = 6.2 Hz, J = 1.3 Hz, J = 1.3 Hz, **$H_{1''}$**), 2.39 (s, 3 H, **$H_{5'}$**), 2.29 (s, 3 H, **H_5**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 143.2 (**$C_{1'}$** or **$C_{4'}$**), 137.4 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 135.2 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 134.2 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 132.7 (CH, **$C_{2''}$**), 129.3 (CH, **C_2** or **C_3** or **$C_{3'}$**), 129.2 (CH, **C_2** or **C_3** or **$C_{3'}$**), 128.4 (CH, **C_2** or **C_3** or **$C_{3'}$**), 127.4 (CH, **$C_{2'}$**), 118.4 (CH_2, **$C_{3''}$**), 53.3 (CH_2, **$C_{1''}$**), 21.3 (CH_3, **C_5** or **$C_{5'}$**), 20.8 (CH_3, **C_5** or **$C_{5'}$**).

Already described in: Studies on the amido-Claisen rearrangement. VII. Synthesis of N-mesyl- and N-tosylo-allylanilines by amido-claisen rearrangement ; Inada Seisaku, Hirabayashi Shigeto,Taguchi Kazuhiro, Okazaki Mitsuo ; *Nippon Kagaku Kaishi*, **1978**, (1), 86-92.

Compound 3g:



***N*-allyl-*N*-(4-trifluoromethylphenyl)-4-methylbenzenesulfonamide**

This compound was obtained from 4-trifluoromethylaniline (645 mg, 4.0 mmol) following the general procedure A then B. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 92/8, thereby obtaining compound **3g** (1.46 g, 99 % for two steps).

Aspect: Pale yellow oil.

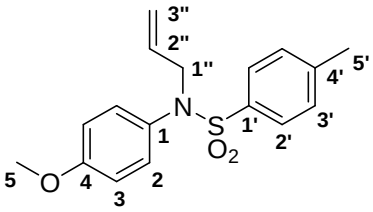
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.55 (d, 2 H, J = 8.3 Hz, **H_3**), 7.48 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.27 (d, 2 H, J = 8.3 Hz, **$H_{3'}$**), 7.19 (d, 2 H, J = 8.2 Hz, **H_2**), 5.72 (ddt, 1 H, J_{trans} = 16.9 Hz, J_{cis} = 10.3 Hz, J = 6.3 Hz, **$H_{2''}$**), 5.12 - 5.05 (dm, 1 H, J_{trans} = 16.9 Hz, **$H_{3''}$**), 5.10 - 5.05 (dm, 1 H, J_{cis} = 10.4 Hz, **$H_{3''}$**), 4.20 (ddd, 2 H, J = 6.2 Hz, J = 1.3 Hz, J = 1.3 Hz, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 143.9 (**$C_{1'}$** or **$C_{4'}$**), 142.4 (**C_1**), 134.9 (**$C_{1'}$** or **$C_{4'}$**), 132.2 (CH, **$C_{2''}$**), 129.9 (q, J = 32.9 Hz, **C_4**), 129.6 (CH, **$C_{3'}$**), 128.6 (CH, **C_2**), 127.6 (CH, **$C_{2'}$**), 125.9 (q, CH, J = 3.7 Hz, **C_3**), 123.8 (q, J = 272.8 Hz, **C_5**), 119.4 (CH_2, **$C_{3''}$**), 53.1 (CH_2, **$C_{1''}$**), 21.5 (CH_3, **$C_{5'}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -62.52 (**F_5**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{17}H_{16}F_3NO_2S$ $[M+H]^+$: 356.0932, m/z found: 356.0934.

Compound 3h:



***N*-allyl-*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide (1.11 g, 4.0 mmol) following the general procedure B. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 90/10, thereby obtaining compound **3h** (769 mg, 61 %).

Aspect: Brown solid.

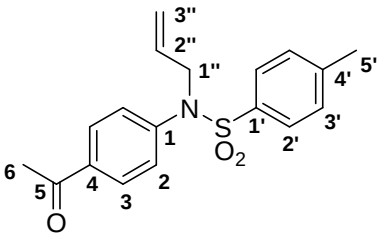
Mp: 53.7 - 54.9 ℃.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.49 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.25 (d, 2 H, J = 8.1 Hz, **$H_{3'}$**), 6.92 (d, 2 H, J = 9.1 Hz, **H_2**), 6.79 (d, 2 H, J = 9.1 Hz, **H_3**), 5.73 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.2 Hz, J = 6.3 Hz, **$H_{2''}$**), 5.09 - 5.03 (dm, 1 H, J_{trans} = 17.1 Hz, **$H_{3''}$**), 5.06 - 5.02 (dm, 1 H, J_{cis} = 10.1 Hz, **$H_{3''}$**), 4.14 - 4.11 (dm, 2 H, J = 6.3 Hz, **$H_{1''}$**), 3.79 (s, 3 H, **H_5**), 2.43 (s, 3 H, **$H_{5'}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 158.9 (**C_4**), 143.3 (**$C_{1'}$** or **$C_{4'}$**), 135.5 (**$C_{1'}$** or **$C_{4'}$**), 132.9 (CH, **$C_{2''}$**), 131.6 (**C_1**), 130.2 (CH, **C_2**), 129.4 (CH, **$C_{3'}$**), 127.3 (CH, **$C_{2'}$**), 118.7 (CH_2, **$C_{3''}$**), 114.0 (CH, **C_3**), 55.3 (CH_3, **C_5**), 53.8 (CH_2, **$C_{1''}$**), 21.5 (CH_3, **$C_{5'}$**).

Already described in: Studies on the amido-Claisen rearrangement. VII. Synthesis of N-mesyl- and N-tosylo-allylanilines by amido-claisen rearrangement ; Inada Seisaku, Hirabayashi Shigeto,Taguchi Kazuhiro, Okazaki Mitsuo ; *Nippon Kagaku Kaishi*, **1978**, (1), 86-92.

Compound 3i:



***N*-(4-acetylphenyl)-*N*-allyl-4-methylbenzenesulfonamide**

This compound was obtained from 4-acetylaniline (541 mg, 4.0 mmol) following the general procedure A then B. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 80/20, thereby obtaining compound **3i** (1.23 mg, 93 % for two steps).

Aspect: Brown solid.

Mp: 60.9 - 61.7 ℃.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.88 (d, 2 H, J = 8.8 Hz, **H_3**), 7.47 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.26 (d, 2 H, J = 7.9 Hz, **$H_{3'}$**), 7.17 (d, 2 H, J = 8.8 Hz, **H_2**), 5.71 (ddt, 1 H, J_{trans} = 17.1 Hz, J_{cis} = 10.2 Hz, J = 6.2 Hz, **$H_{2''}$**), 5.12 - 5.06 (dm, 1 H, J_{trans} = 17.1 Hz, **$H_{3''}$**), 5.09 - 5.04 (dm, 1 H, J_{cis} = 10.2 Hz, **$H_{3''}$**), 4.21 (ddd, 2 H, J = 6.2 Hz, J = 1.4 Hz, J = 1.4 Hz, **$H_{1''}$**), 2.59 (s, 3 H, **H_5**), 2.43 (s, 3 H, **$H_{5'}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 197.2 (**C_5**), 143.9 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 143.5 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 135.7 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 135.0 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 132.3 (CH, **$C_{2''}$**), 129.6 (CH, **$C_{3'}$**), 128.9 (CH, **C_3**), 128.1 (CH, **C_2**), 127.6 (CH, **$C_{2'}$**), 119.3 (CH_2, **$C_{3''}$**), 52.9 (CH_2, **$C_{1''}$**), 26.6 (CH_3, **C_6**), 21.6 (CH_3, **$C_{5'}$**).

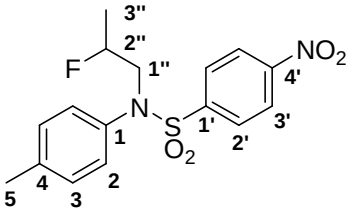
Already described in: Studies on the amido-Claisen rearrangement. VII. Synthesis of N-mesyl- and N-tosylo-allylanilines by amido-claisen rearrangement ; Inada Seisaku, Hirabayashi Shigeto,Taguchi Kazuhiro, Okazaki Mitsuo ; *Nippon Kagaku Kaishi*, **1978**, (1), 86-92.

C. HYDROFLUORINATION REACTION

Procedure C: optimized procedure in superacid media

To a mixture of hydrofluoric acid and antimony pentafluoride (8 mL, 3.8 mol% antimony pentafluoride) maintained at -65 °C, was added *N*-allyl-*N*-arylbenzenesulfonamide derivative. The mixture was magnetically stirred at the same temperature during 10 minutes. The reaction mixture was then neutralized with water-ice-sodium carbonate solution, extracted with dichloromethane (x 3). The combined organic phases were dried over magnesium sulphate, filtered and concentrated *in vacuo*. Products were isolated by column chromatography over silica gel.

Compound 4b:



***N*-(2-fluoropropyl)-*N*-(4-methylphenyl)-4-nitrobenzenesulfonamide**

This compound was obtained from *N*-allyl-*N*-(4-methylphenyl)-4-nitrobenzenesulfonamide **3b** (133 mg, 0.400 mmol) following the general procedure C. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 90/10, thereby obtaining compound **4b** (47 mg, 33 %).

Aspect: Yellow viscous oil.

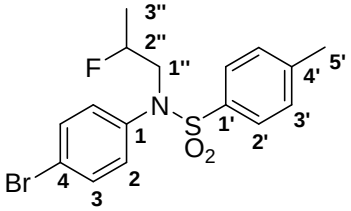
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 8.23 (d, 2 H, J = 9.0 Hz, **$H_{3'}$**), 7.72 (d, 2 H, J = 9.0 Hz, **$H_{2'}$**), 7.07 (d, 2 H, J = 8.0 Hz, **H_2** or **H_3**) 6.87 (d, 2 H, J = 8.3 Hz, **H_2** or **H_3**), 4.73 - 4.53 (dm, 1 H, J = 48.8 Hz, **$H_{2''}$**), 3.82 (td, 1 H, J = 14.4 Hz, J = 6.7 Hz, **$H_{1''}$**), 3.54 (ddd, 1 H, J = 25.4 Hz, J = 14.4 Hz, J = 3.8 Hz, **$H_{1''}$**), 2.28 (s, 3 H, **H_5**), 1.27 (dd, 3 H, J = 23.6 Hz, J = 6.3 Hz, **$H_{3''}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 150.0 (**C_1** or **C_4**), 144.4 (**$C_{1'}$** or **$C_{4'}$**), 139.0 (**C_1** or **C_4**), 135.9 (**$C_{1'}$** or **$C_{4'}$**), 130.2 (CH, **C_2** or **C_3**), 128.9 (CH, **C_2** or **C_3** or **$C_{2'}$**), 128.8 (CH, **C_2** or **C_3** or **$C_{2'}$**), 124.0 (CH, **$C_{3'}$**), 88.1 (d, CH, J = 171.4 Hz, **$C_{2''}$**), 56.3 (d, CH_2, J = 24.2 Hz, **$C_{1''}$**), 21.1 (CH_3, **C_5**), 18.3 (d, CH_3, J = 21.8 Hz, **$C_{3''}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -178.28 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{16}H_{17}FN_2O_4S$ $[M+H]^+$: 353.0971, m/z found: 353.0977.

Compound 4c:



***N*-(4-bromophenyl)-*N*-(2-fluoropropyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-allyl-*N*-(4-bromophenyl)-4-methylbenzenesulfonamide **3c** (90 mg, 0.256 mmol) following the general procedure C. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 92/8, thereby obtaining compound **4c** (10 mg, 11 %).

Aspect: Colourless viscous oil.

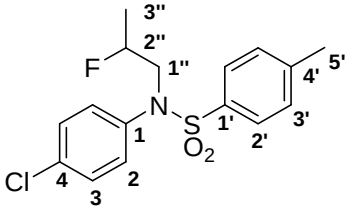
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.46 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.43 (d, 2 H, J = 8.8 Hz, **H_3**), 7.26 (d, 2 H, J = 7.9 Hz, **$H_{3'}$**), 6.94 (d, 2 H, J = 8.8 Hz, **H_2**), 4.84 - 4.63 (dm, 1 H, J = 48.7 Hz, **$H_{2''}$**), 3.71 (td, 1 H, J = 14.5 Hz, J = 6.9 Hz, **$H_{1''}$**), 3.63 (ddd, 1 H, J = 23.1 Hz, J = 14.4 Hz, J = 4.2 Hz, **$H_{1''}$**), 2.42 (s, 3 H, **$H_{5'}$**), 1.34 (dd, 3 H, J = 23.7 Hz, J = 6.3 Hz, **$H_{3''}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 143.9 (**$C_{1'}$** or **$C_{4'}$**), 139.0 (**C_1**), 135.0 (**$C_{1'}$** or **$C_{4'}$**), 132.3 (CH, **C_3**), 130.5 (CH, **C_2**), 129.6 (CH, **$C_{3'}$**), 127.6 (CH, **$C_{2'}$**), 122.0 (**C_4**), 88.8 (d, CH, J = 170.8 Hz, **$C_{2''}$**), 55.8 (d, CH_2, J = 24.3 Hz, **$C_{1''}$**), 21.5 (CH_3, **$C_{5'}$**), 18.4 (d, CH_3, J = 21.7 Hz, **$C_{3''}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -177.81 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{16}H_{17}BrFNO_2S$ $[M+H]^+$: 386.0226, m/z found: 386.0225.

Compound 4d:



***N*-(4-chlorophenyl)-*N*-(2-fluoropropyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-allyl-*N*-(4-chlorophenyl)-4-methylbenzenesulfonamide **3d** (103 mg, 0.320 mmol) following the general procedure C. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 92/8, thereby obtaining compound **4d** (53 mg, 48 %).

Aspect: Colourless viscous oil.

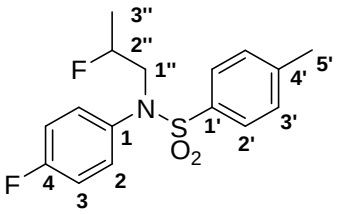
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.46 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.28 - 7.24 (m, 4 H, **H_3** and **$H_{3'}$**), 7.01 (d, 2 H, J = 8.8 Hz, **H_2**), 4.84 - 4.63 (dm, 1 H, J = 48.6 Hz, **$H_{2''}$**), 3.72 (td, 1 H, J = 14.5 Hz, J = 6.9 Hz, **$H_{1''}$**), 3.63 (ddd, 1 H, J = 23.3 Hz, J = 14.4 Hz, J = 4.2 Hz, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**), 1.34 (dd, 3 H, J = 23.7 Hz, J = 6.3 Hz, **$H_{3''}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 143.8 (**$C_{1'}$** or **$C_{4'}$**), 138.4 (**C_1** or **C_4**), 135.0 (**$C_{1'}$** or **$C_{4'}$**), 133.9 (**C_1** or **C_4**), 130.2 (CH, **C_2**), 129.5 (CH, **C_3** or **$C_{3'}$**), 129.3 (CH, **C_3** or **$C_{3'}$**), 127.6 (CH, **$C_{2'}$**), 88.8 (d, CH, J = 170.9 Hz, **$C_{2''}$**), 55.9 (d, CH_2, J = 24.3 Hz, **$C_{1''}$**), 21.5 (CH_3, **$C_{5'}$**), 18.4 (d, CH_3, J = 21.9 Hz, **$C_{3''}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -177.86 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES$^+$, CH_3CN): m/z calc for $C_{16}H_{17}ClFNO_2S$ $[M+Na]^+$: 364.0550, m/z found: 364.0553.

Compound 4e:



***N*-(4-fluorophenyl)-*N*-(2-fluoropropyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-allyl-*N*-(4-fluorophenyl)-4-methylbenzenesulfonamide **3e** (191 mg, 0.625 mmol) following the general procedure C. The reaction crude was filtered over silica gel with the eluent ethyl acetate, thereby obtaining compound **4e** (185 mg, 97 %).

Aspect: Brown solid.

MP: 88.9 - 90.3 ℃.

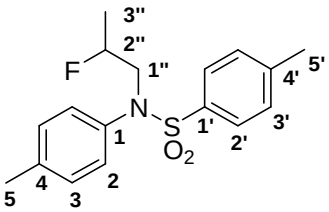
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.47 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.26 (d, 2 H, J = 7.9 Hz, **$H_{3'}$**), 6.96 - 7.06 (m, 4 H, **H_2** and **H_3**), 4.84 - 4.63 (dm, 1 H, J = 48.6 Hz, **$H_{2''}$**), 3.72 (td, 1 H, J = 14.4 Hz, J = 7.0 Hz, **$H_{1''}$**), 3.63 (ddd, 1 H, J = 23.4 Hz, J = 14.4 Hz, J = 4.2 Hz, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**), 1.35 (dd, 3 H, J = 23.7 Hz, J = 6.3 Hz, **$H_{3''}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 161.8 (d, J = 248.5 Hz, **C_4**), 143.7 (**$C_{1'}$** or **$C_{4'}$**), 135.7 (d, J = 3.1 Hz, **C_1**), 135.0 (**$C_{1'}$** or **$C_{4'}$**), 130.8 (d, CH, J = 8.8 Hz, **C_2**), 129.5 (CH, **$C_{3'}$**), 127.6 (CH, **$C_{2'}$**), 115.9 (d, CH, J = 22.7 Hz, **C_3**), 88.6 (d, CH, J = 170.8 Hz, **$C_{2''}$**), 56.0 (d, CH_2, J = 24.2 Hz, **$C_{1''}$**), 21.4 (CH_3, **$C_{5'}$**), 18.3 (d, CH_3, J = 21.8 Hz, **$C_{3''}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -112.77 (**F_4**), -178.03 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES$^+$, CH_3CN): m/z calc for $C_{16}H_{17}F_2NO_2S$ $[M+H]^+$: 326.1026, m/z found: 326.1024.

Compound 4f:



***N*-(2-fluoropropyl)-*N*-(4-methylphenyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-allyl-4-methyl-*N*-(4-methylphenyl)benzenesulfonamide **3f** (150 mg, 0.498 mmol) following the general procedure C. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 92/8, thereby obtaining compound **4f** (52 mg, 33 %).

Aspect: white solid.

MP: 62.9 - 63.7 °C.

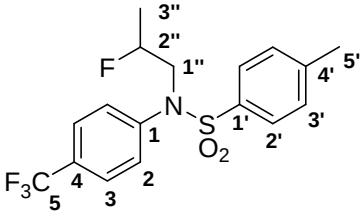
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.48 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.24 (d, 2 H, J = 8.0 Hz, **$H_{3'}$**), 7.10 (d, 2 H, J = 8.0 Hz, **H_3**), 6.94 (d, 2 H, J = 8.3 Hz, **H_2**), 4.81 - 4.60 (dm, 1 H, J = 48.5 Hz, H2''), 3.75 (td, 1 H, J = 14.1 Hz, J = 6.9 Hz, **$H_{1''}$**), 3.60 (ddd, 1 H, J = 22.4 Hz, J = 14.2 Hz, J = 4.6 Hz, **$H_{1''}$**), 2.42 (s, 3 H, **$H_{5'}$**), 2.33 (s, 3 H, **H_5**), 1.34 (dd, 3 H, J = 23.7 Hz, J = 6.3 Hz, **$H_{3''}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 143.5 (**$C_{1'}$** or **$C_{4'}$**), 138.1 (**C_1** or **C_4**), 137.1 (**C_1** or **C_4**), 135.4 (**$C_{1'}$** or **$C_{4'}$**), 129.7 (CH, **C_3**), 129.4 (CH, **$C_{3'}$**), 128.7 (CH, **C_2**), 127.7 (CH, **$C_{2'}$**), 88.6 (d, CH, J = 170.4 Hz, **$C_{2''}$**), 55.9 (d, CH_2, J = 25.1 Hz, **$C_{1''}$**), 21.5 (CH_3, **C_5** or **$C_{5'}$**), 21.1 (CH_3, **C_5** or **$C_{5'}$**), 18.5 (d, CH_3, J = 21.7 Hz, **$C_{3''}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -178.19 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{17}H_{20}FNO_2S$ $[M+Na]^+$: 344.1096, m/z found: 344.1095.

Compound 4g:



***N*-(2-fluoropropyl)-4-methyl-*N*-(4-trifluoromethylphenyl)benzenesulfonamide**

This compound was obtained from *N*-allyl-4-methyl-*N*-(4-trifluoromethylphenyl)benzenesulfonamide **3g** (91 mg, 0.256 mmol) following the general procedure C. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 92/8, thereby obtaining compound **4g** (93 mg, 97 %).

Aspect: White solid.

MP: 89.4 - 90.0 °C.

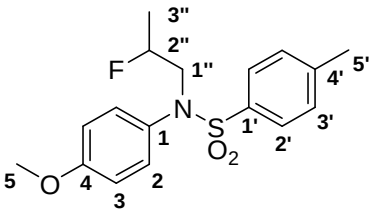
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.57 (d, 2 H, J = 8.4 Hz, **H_3**), 7.46 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.27 (d, 2 H, J = 8.0 Hz, **$H_{3'}$**), 7.22 (d, 2 H, J = 8.3 Hz, **H_2**), 4.87 - 4.66 (dm, 1 H, J = 48.6 Hz, **$H_{2''}$**), 3.80 - 3.64 (m, 2 H, **$H_{1''}$**), 2.43 (s, 3 H, **$H_{5'}$**), 1.35 (dd, 3 H, J = 23.6 Hz, J = 6.3 Hz, **$H_{3''}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 144.1 (**C_1** or **$C_{1'}$** or **$C_{4'}$**), 143.3 (**C_1** or **$C_{1'}$** or **$C_{4'}$**), 134.9 (**$C_{1'}$** or **$C_{4'}$**), 129.9 (q, J = 32.9 Hz, **C_4**), 129.6 (CH, **$C_{3'}$**), 129.1 (CH, **C_2**), 127.5 (CH, **$C_{2'}$**), 126.2 (q, CH, J = 3.7 Hz, **C_3**), 123.7 (q, J = 272.2 Hz, **C_5**), 88.9 (d, CH, J = 171.0 Hz, **$C_{2''}$**), 55.7 (d, CH_2, J = 24.0 Hz, **$C_{1''}$**), 21.5 (CH_3, **$C_{5'}$**), 18.3 (d, CH_3, J = 21.9 Hz, **$C_{3''}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -62.55 (**F_5**), -177.68 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{17}H_{17}F_4NO_2S$ $[M+H]^+$: 376.0994, m/z found: 376.0997.

Compound 4h:



***N*-(2-fluoropropyl)-*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-allyl-*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide **3h** (124 mg, 0.391 mmol) following the general procedure C. The reaction crude was filtered over silica gel with the eluent ethyl acetate, thereby obtaining compound **4h** (127 mg, 96 %).

Aspect: Colourless viscous oil.

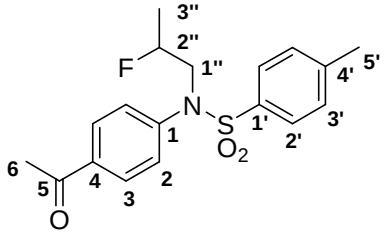
^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.47 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.23 (d, 2 H, J = 8.0 Hz, **$H_{3'}$**), 6.95 (d, 2 H, J = 9.0 Hz, **H_2**), 6.79 (d, 2 H, J = 9.0 Hz, **H_3**), 4.79 - 4.59 (dm, 1 H, J = 48.6 Hz, **$H_{2''}$**), 3.76 (s, 3 H, **H_5**), 3.73 (td, 1 H, J = 14.1 Hz, J = 7.1 Hz, **$H_{1''}$**), 3.57 (ddd, 1 H, J = 23.2 Hz, J = 14.2 Hz, J = 4.4 Hz, **$H_{1''}$**), 2.40 (s, 3 H, **$H_{5'}$**), 1.32 (dd, 3 H, J = 23.7 Hz, J = 6.3 Hz, **$H_{3''}$**).

^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 159.0 (**C_4**), 143.4 (**$C_{1'}$** or **$C_{4'}$**), 135.3 (**$C_{1'}$** or **$C_{4'}$**), 132.1 (**C_1**), 130.1 (CH, **C_2**), 129.3 (CH, **$C_{3'}$**), 127.6 (CH, **$C_{2'}$**), 114.2 (CH, **C_3**), 88.4 (d, CH, J = 170.5 Hz, **$C_{2''}$**), 56.1 (d, CH_2, J = 24.9 Hz, **$C_{1''}$**), 55.3 (CH_3, **C_5**), 21.4 (CH_3, **$C_{5'}$**), 18.3 (d, CH_3, J = 21.9 Hz, **$C_{3''}$**).

^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -178.28 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{17}H_{20}FNO_3S$ $[M+Na]^+$: 360.1046, m/z found: 360.1042.

Compound 4i:



***N*-(4-acetylphenyl)-*N*-(2-fluoropropyl)-4-methylbenzenesulfonamide**

This compound was obtained from *N*-(4-acetylphenyl)-*N*-allyl-4-methylbenzenesulfonamide **3i** (110 mg, 0.334 mmol) following the general procedure C. The reaction crude was purified over silica gel with the eluent petroleum ether/ethyl acetate: 80/20, thereby obtaining compound **4i** (104 mg, 89 %).

Aspect: White solid.

MP: 92.9 - 94.3 °C.

^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 7.89 (d, 2 H, J = 8.7 Hz, **H_3**), 7.43 (d, 2 H, J = 8.3 Hz, **$H_{2'}$**), 7.24 (d, 2 H, J = 8.0 Hz, **$H_{3'}$**), 7.19 (d, 2 H, J = 9.0 Hz, **H_2**), 4.85 - 4.65 (dm, 1 H, J = 48.5 Hz, **$H_{2''}$**), 3.76 (td, 1 H, J = 14.6 Hz, J = 6.7 Hz, **$H_{1''}$**), 3.69 (ddd, 1 H, J = 22.8 Hz, J = 14.5 Hz, J = 4.2 Hz, **$H_{1''}$**), 2.58 (s, 3 H, **H_6**), 2.41 (s, 3 H, **$H_{5'}$**), 1.34 (dd, 3 H, J = 23.7 Hz, J = 6.3 Hz, **$H_{3''}$**).

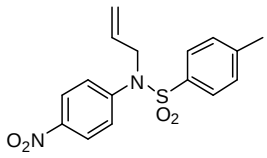
^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 197.1 (**C_5**), 144.3 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 143.0 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 136.1 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 134.9 (**C_1** or **C_4** or **$C_{1'}$** or **$C_{4'}$**), 129.6 (CH, **$C_{3'}$**), 129.2 (CH, **C_3**), 128.6 (CH, **C_2**), 127.5 (CH, **$C_{2'}$**), 88.9 (d, CH, J = 171.0 Hz, **$C_{2''}$**), 55.5 (d, CH_2, J = 24.3 Hz, **$C_{1''}$**), 26.6 (CH_3, **C_6**), 21.5 (CH_3, **$C_{5'}$**), 18.4 (d, CH_3, J = 21.9 Hz, **$C_{3''}$**).

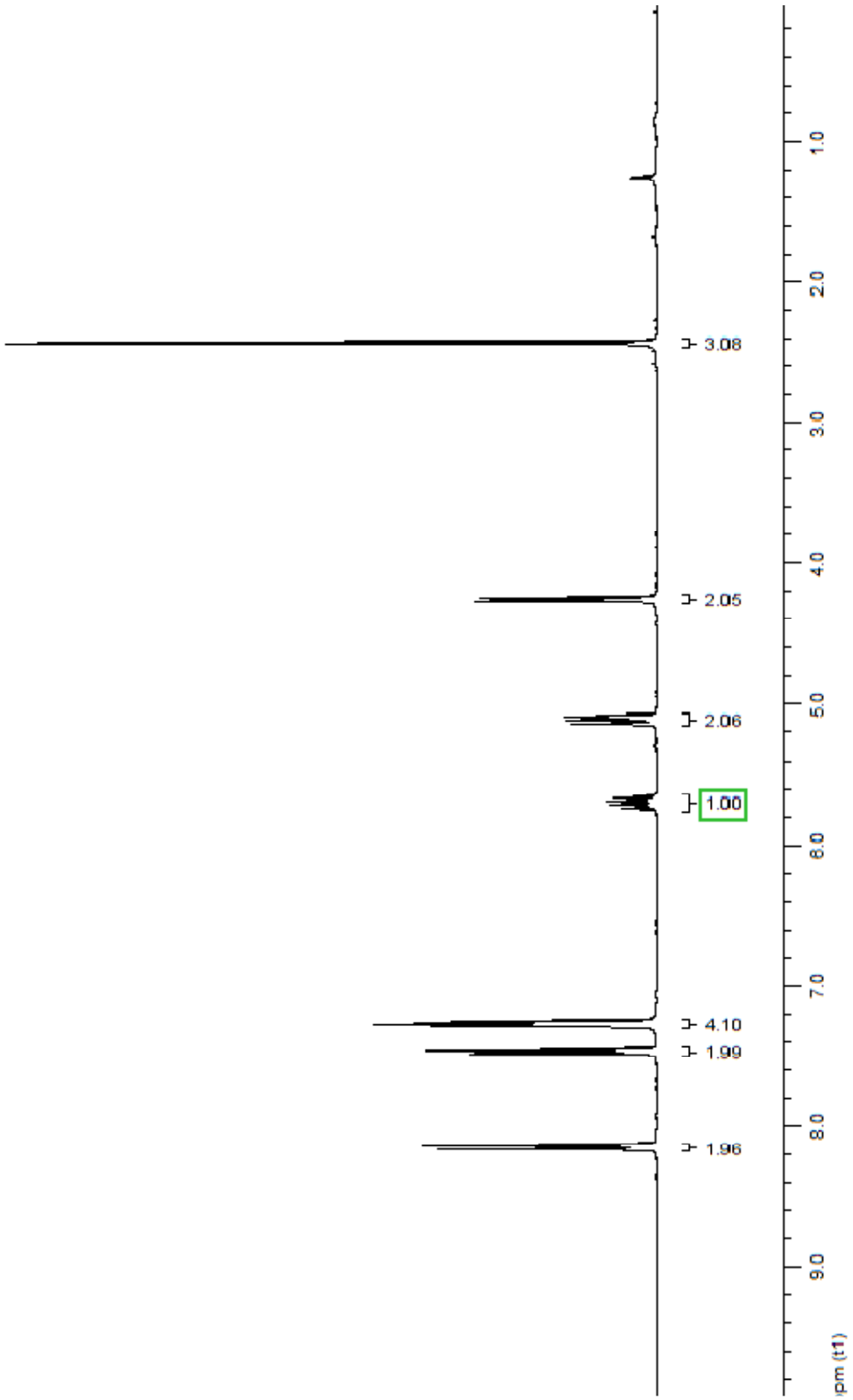
^{19}F {1H} NMR ($CDCl_3$, 376 MHz, ppm) δ: -177.52 (**$F_{2''}$**).

HRMS (MALDI/TOF, ES^+, CH_3CN): m/z calc for $C_{18}H_{20}FNO_3S$ $[M+H]^+$: 350.1226, m/z found: 350.1230.

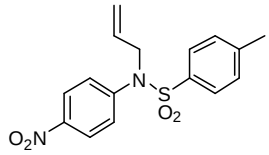
D. NMR SPECTRA:

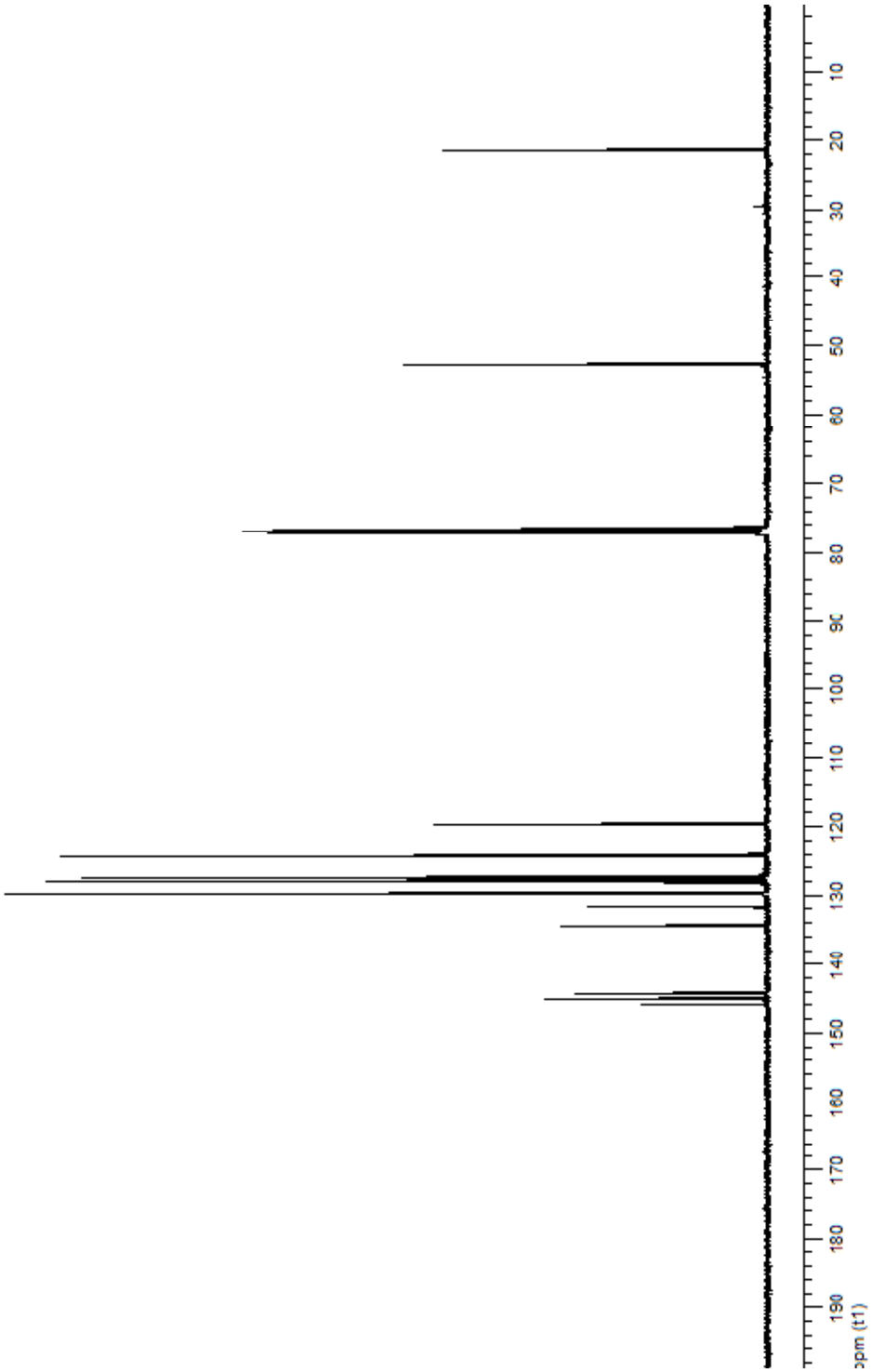
Compound 3a: ^{1}H NMR



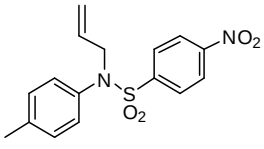


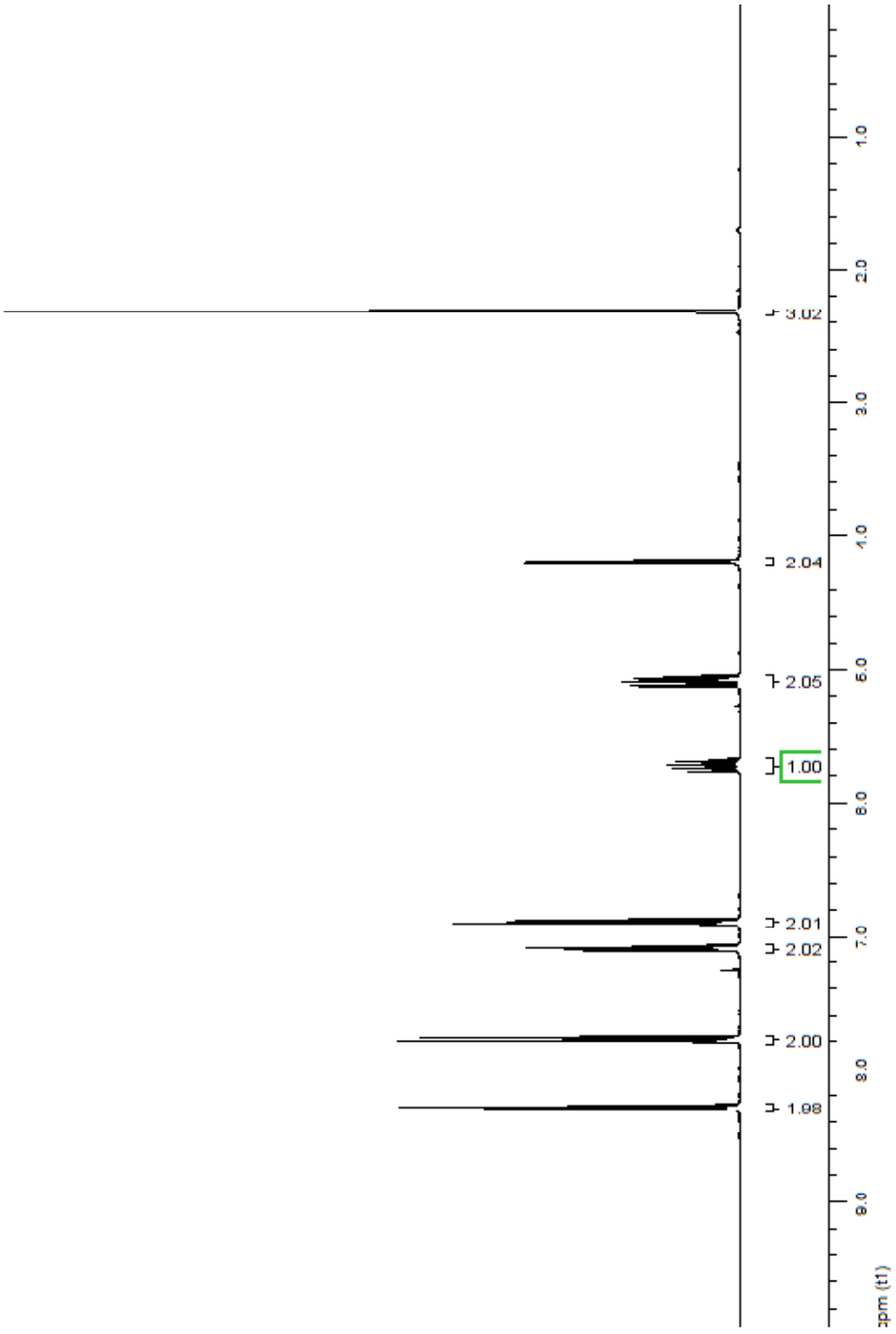
Compound 3a: ^{13}C NMR



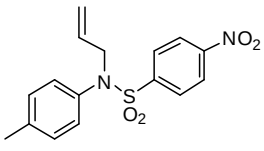


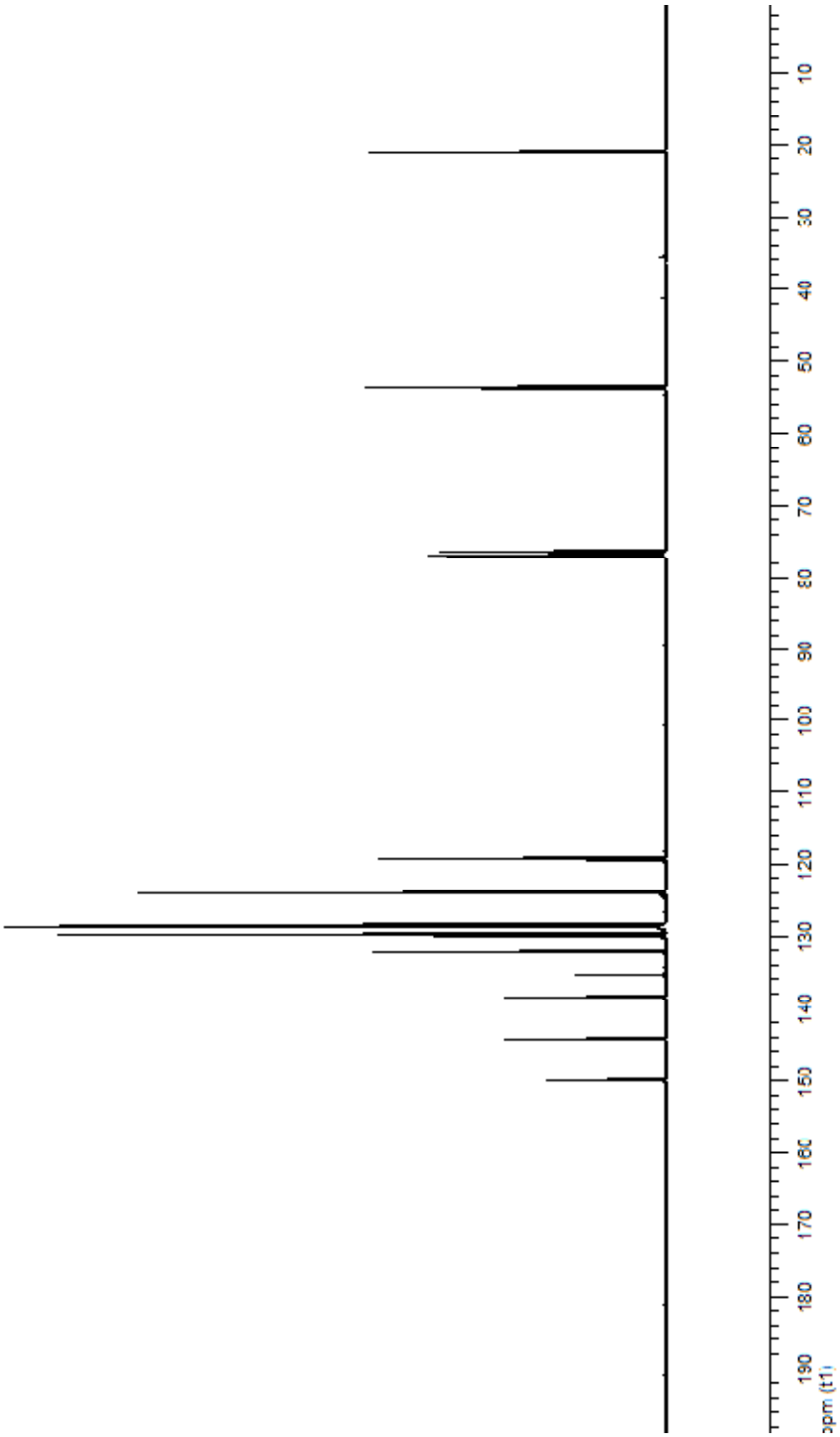
Compound 3b: ^{1}H NMR



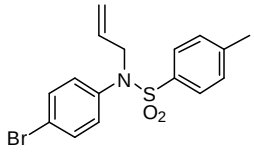


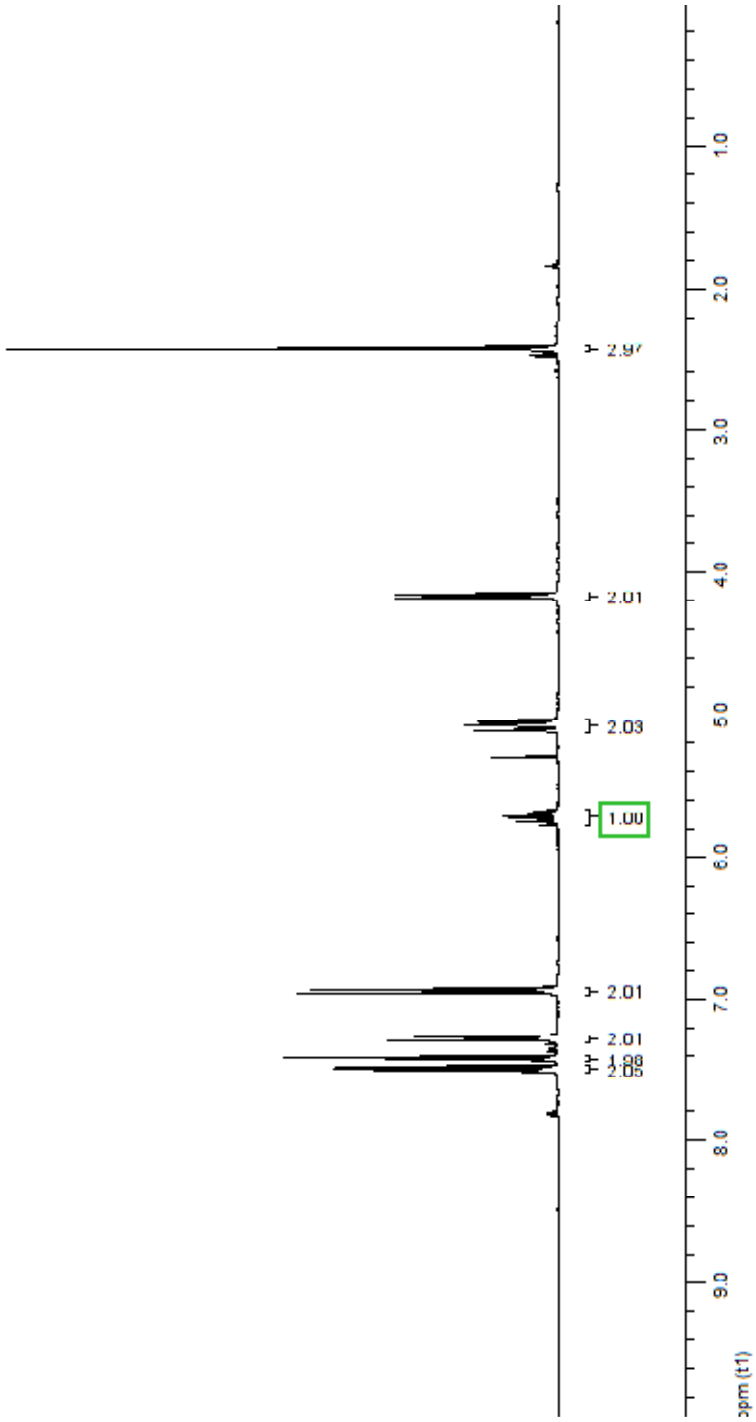
Compound 3b: ^{13}C NMR



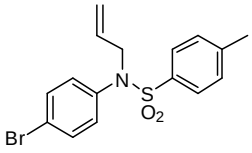


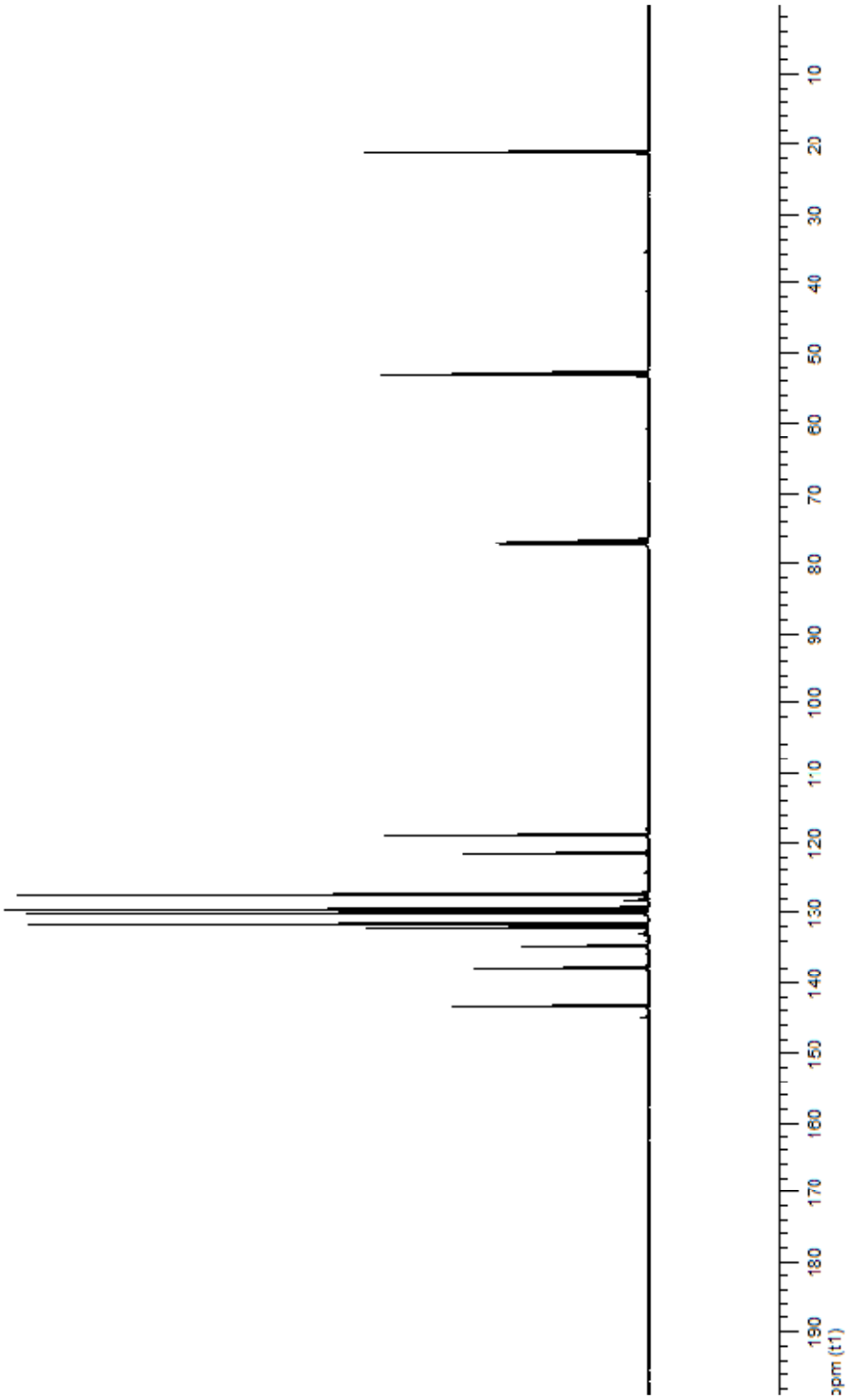
Compound 3c: ^{1}H NMR



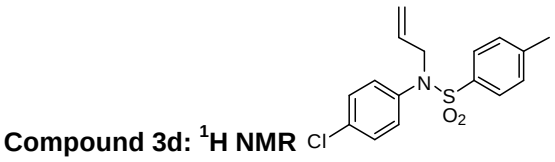


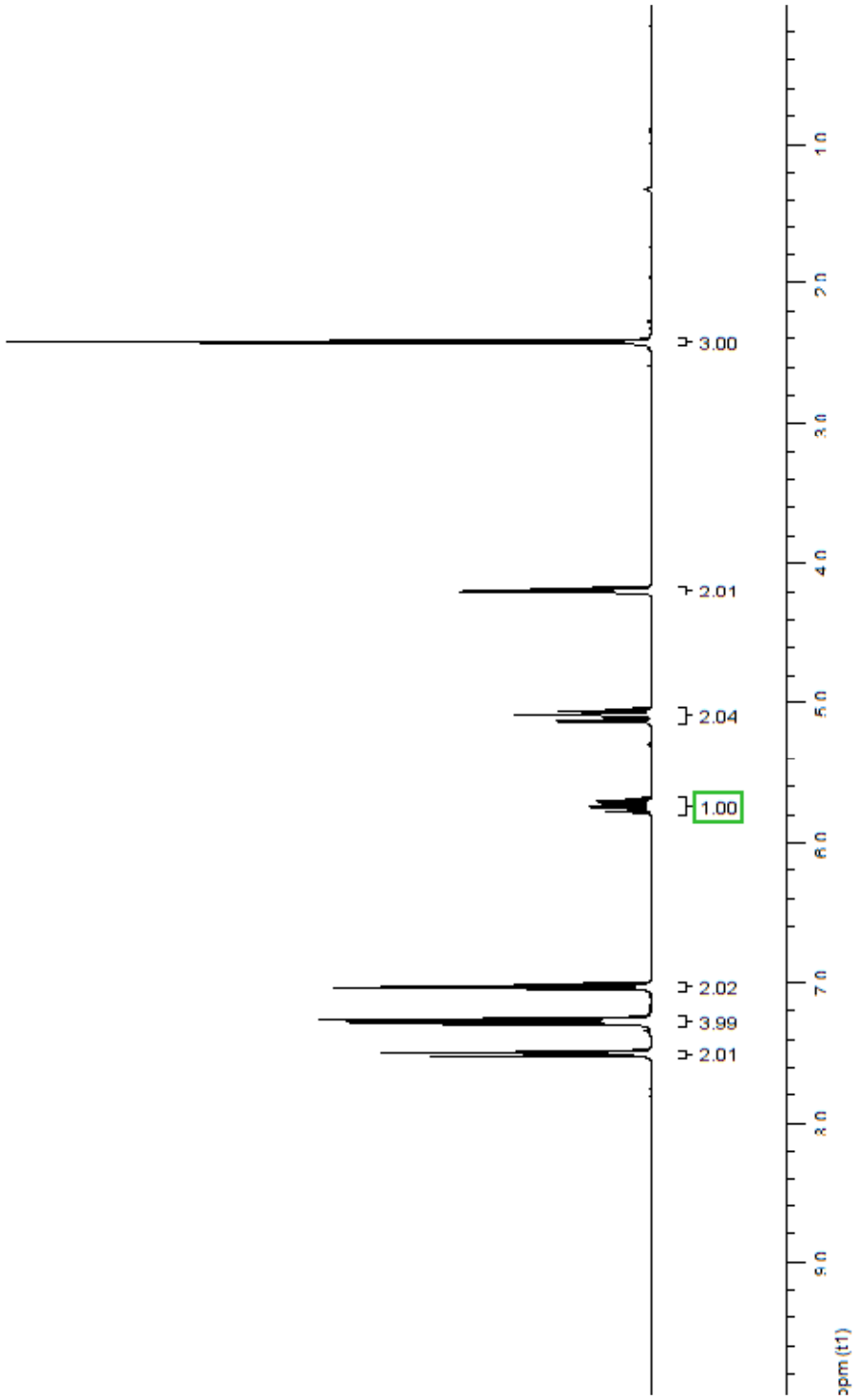
Compound 3c: ^{13}C NMR



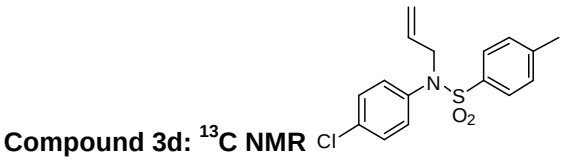


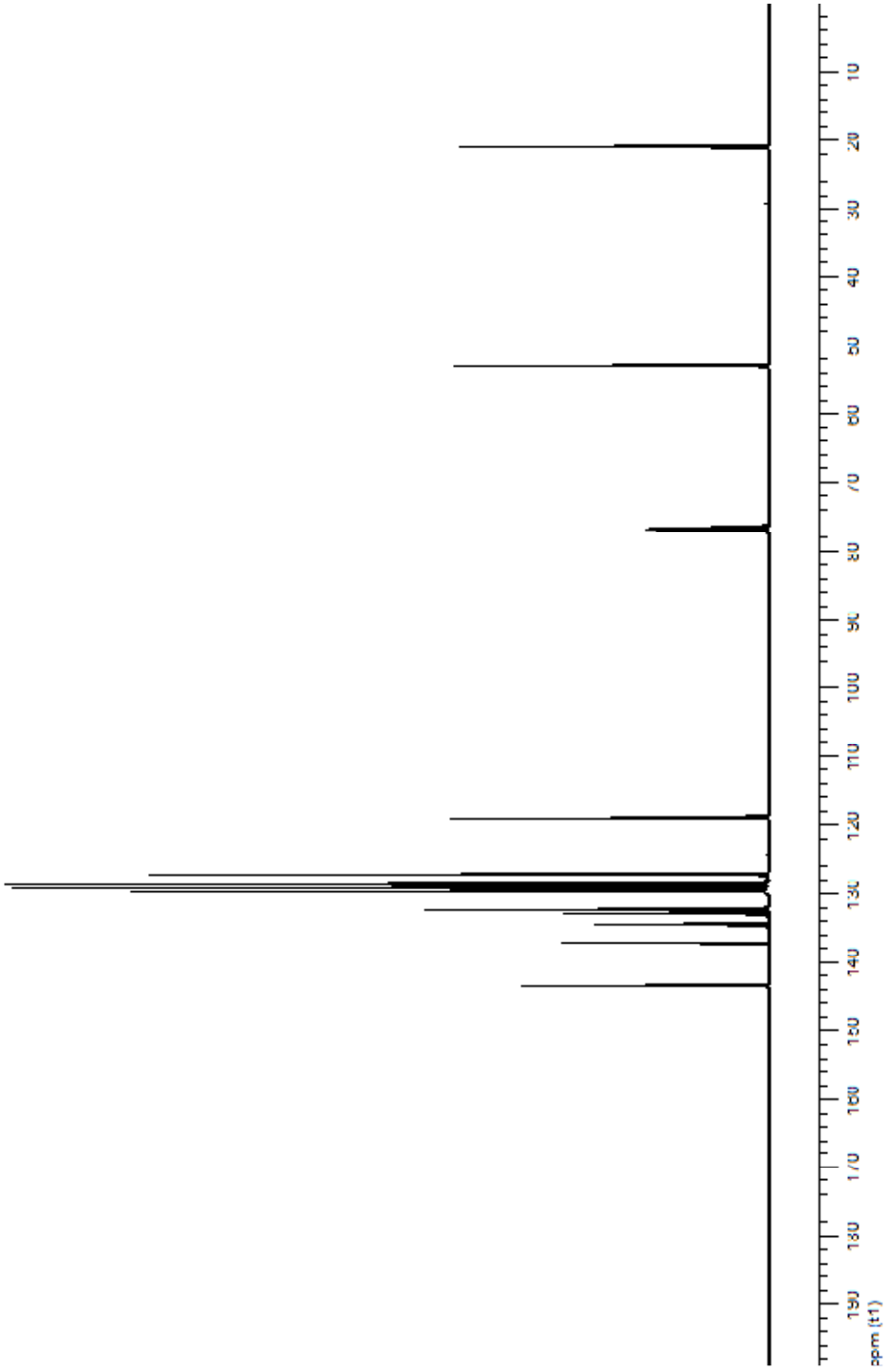
Compound 3d: ^{1}H NMR



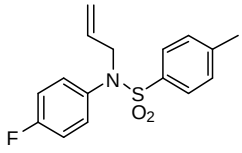


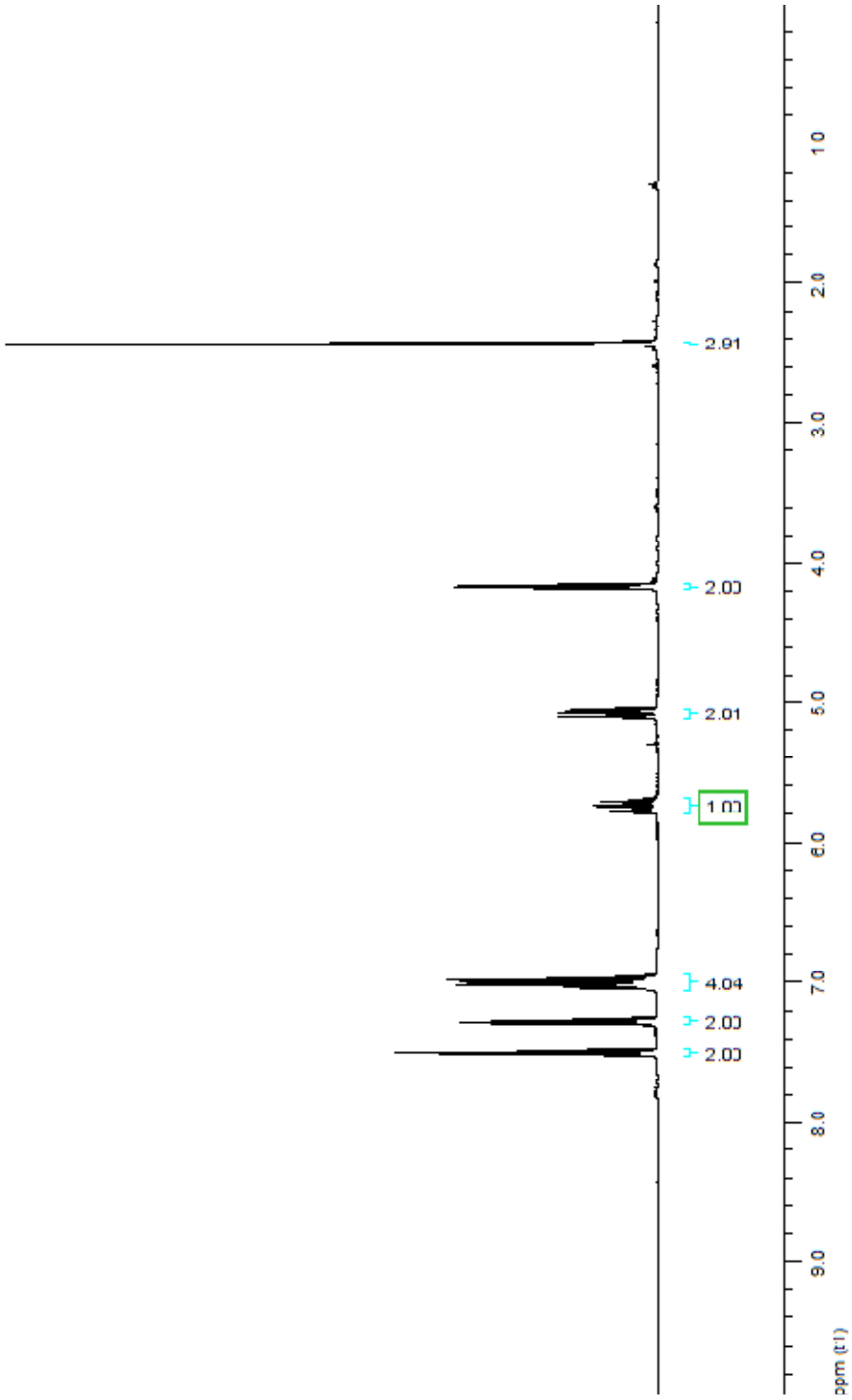
Compound 3d: ^{13}C NMR





Compound 3e: ^{1}H NMR





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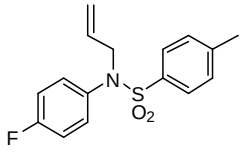

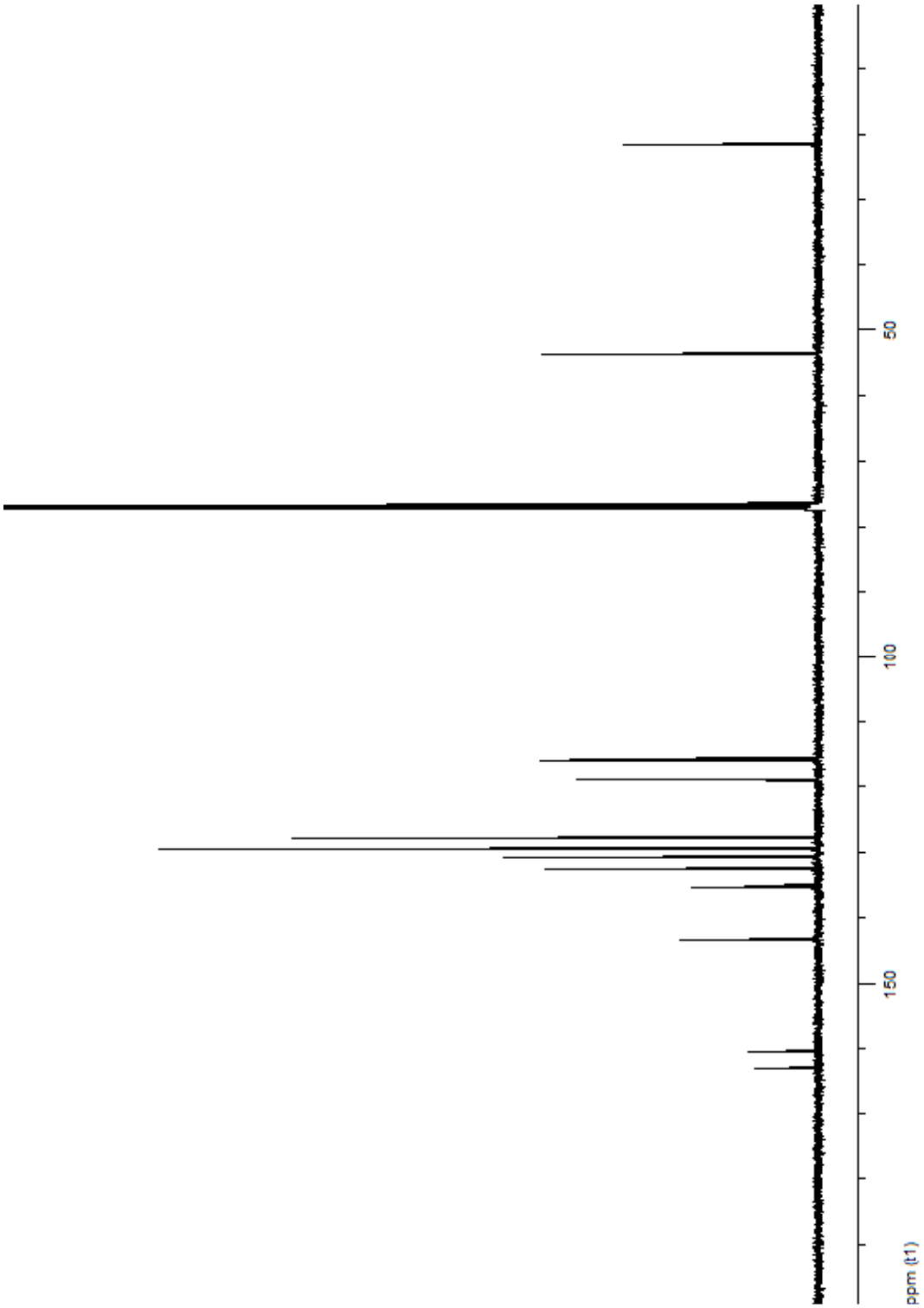

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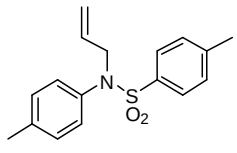
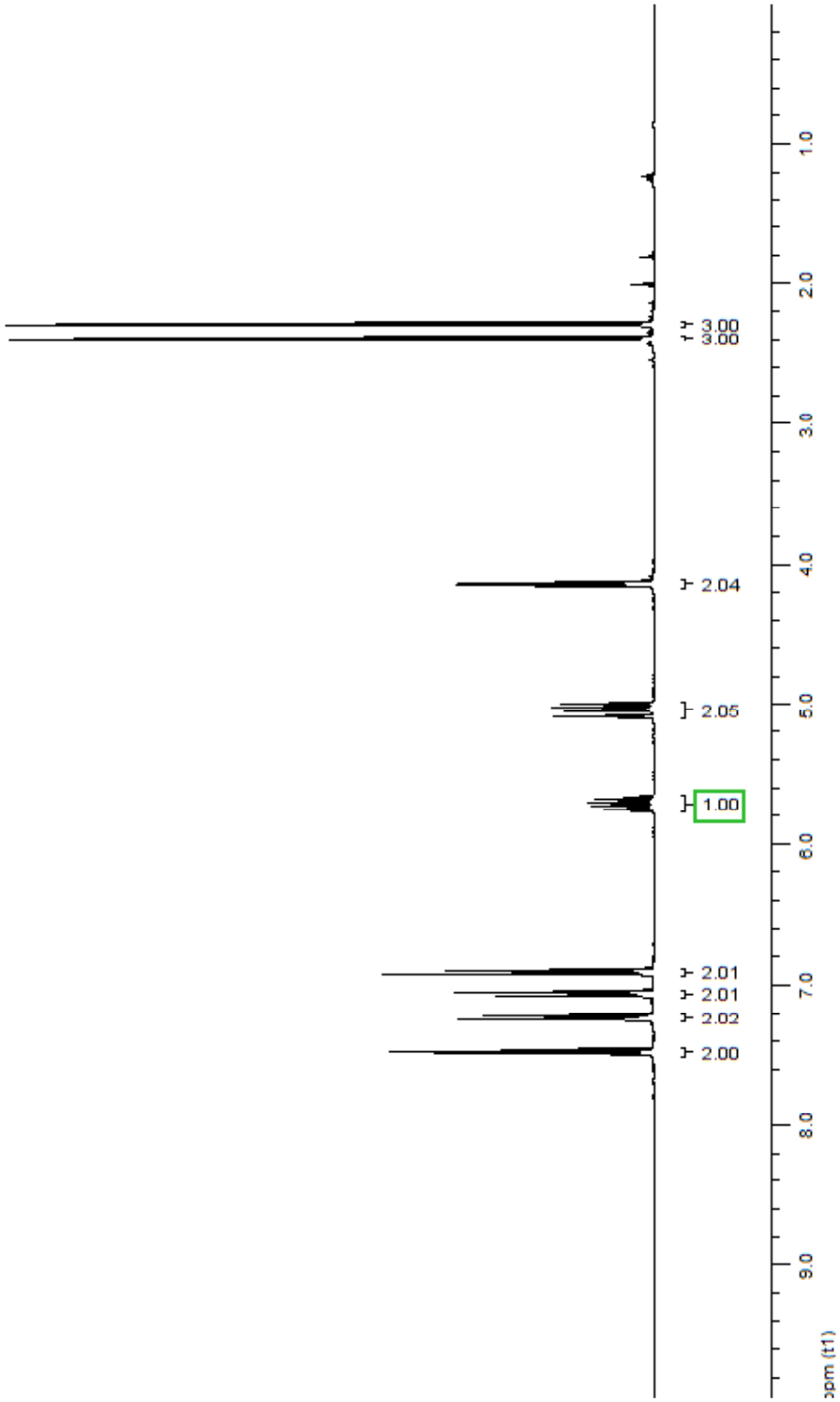
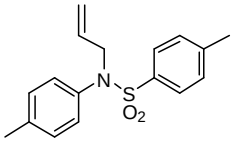
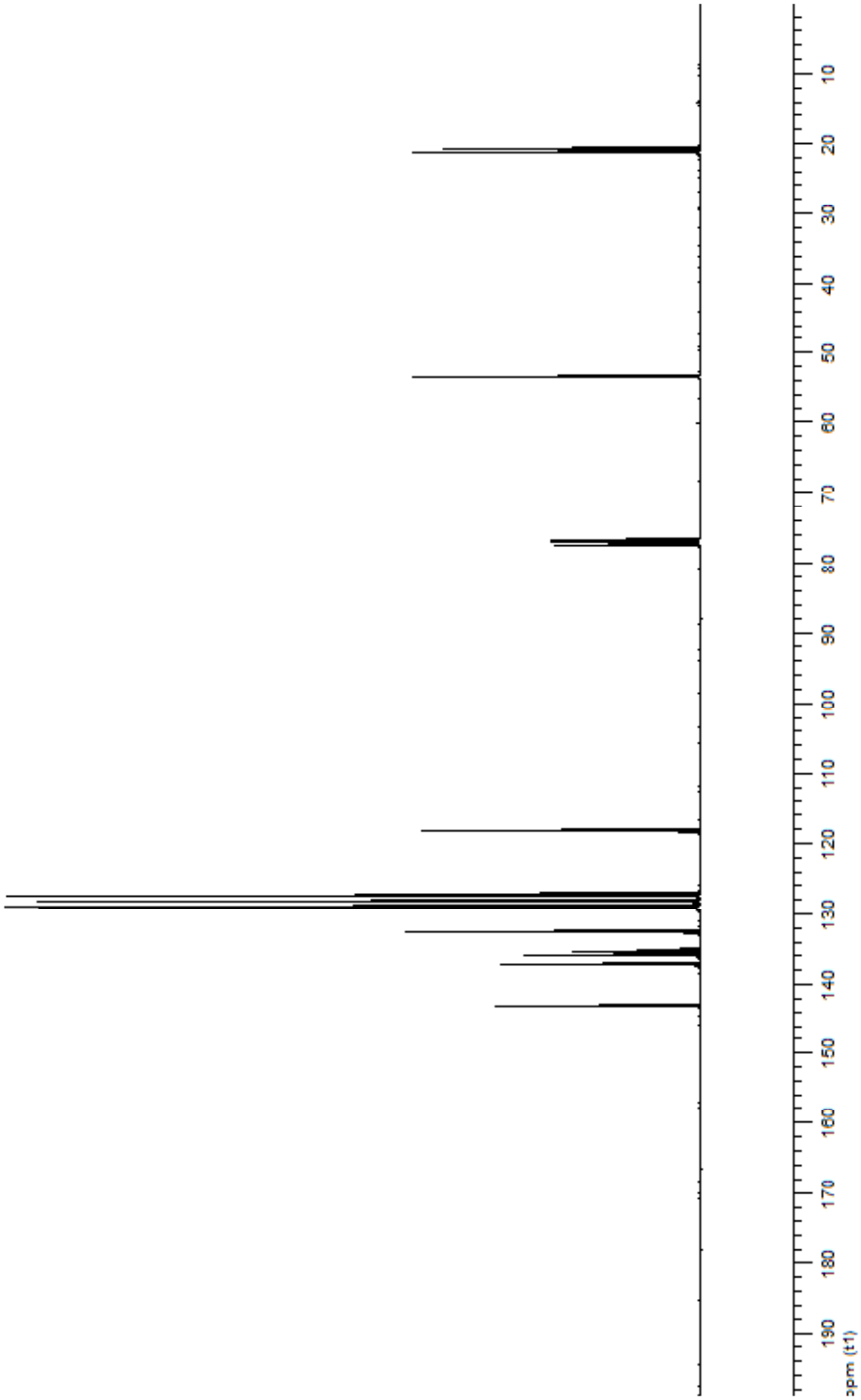


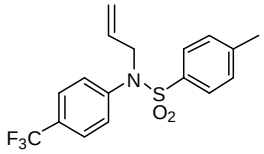


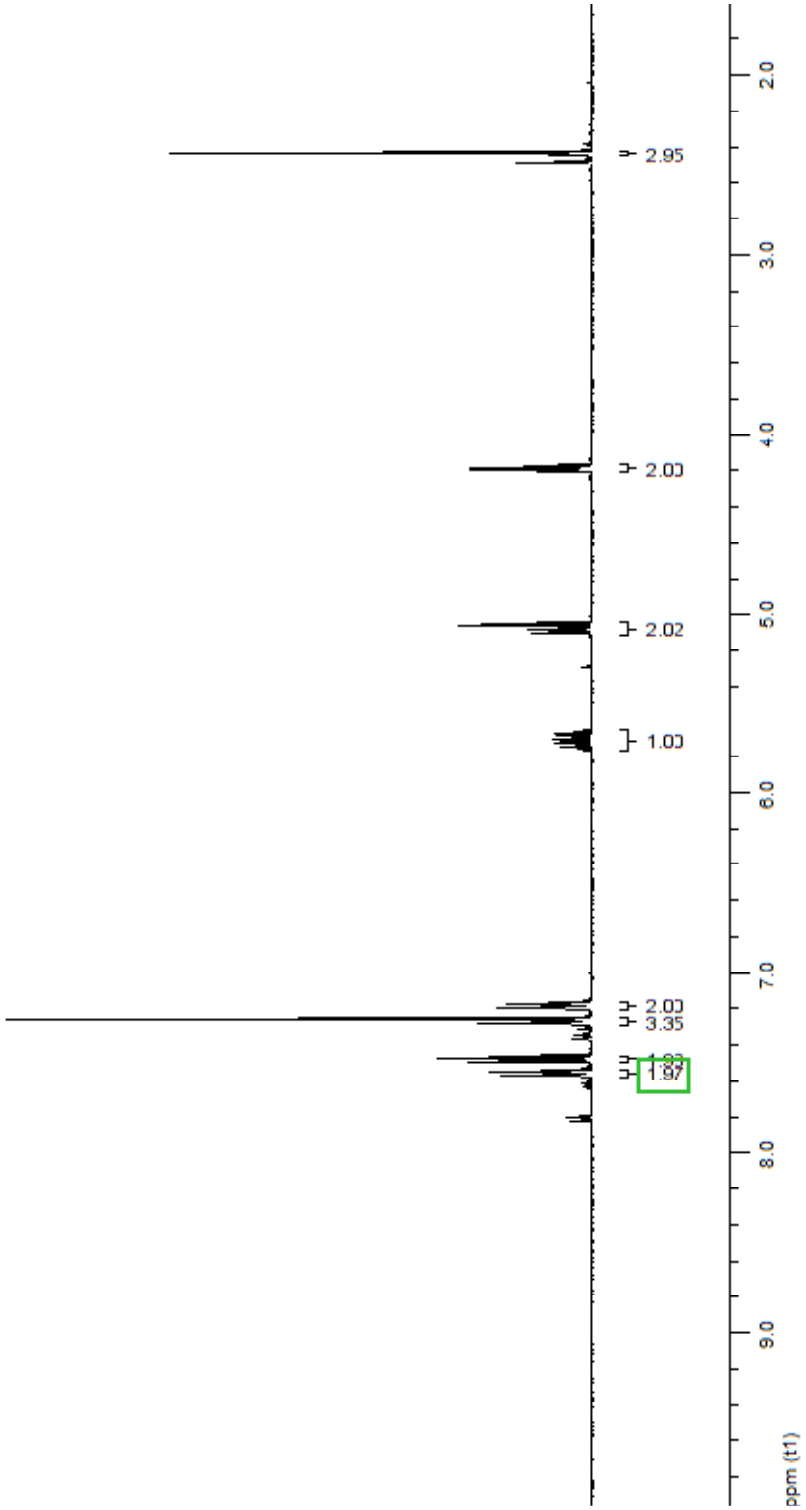
Compound 3f: ^{13}C NMR



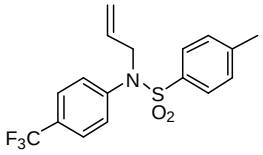


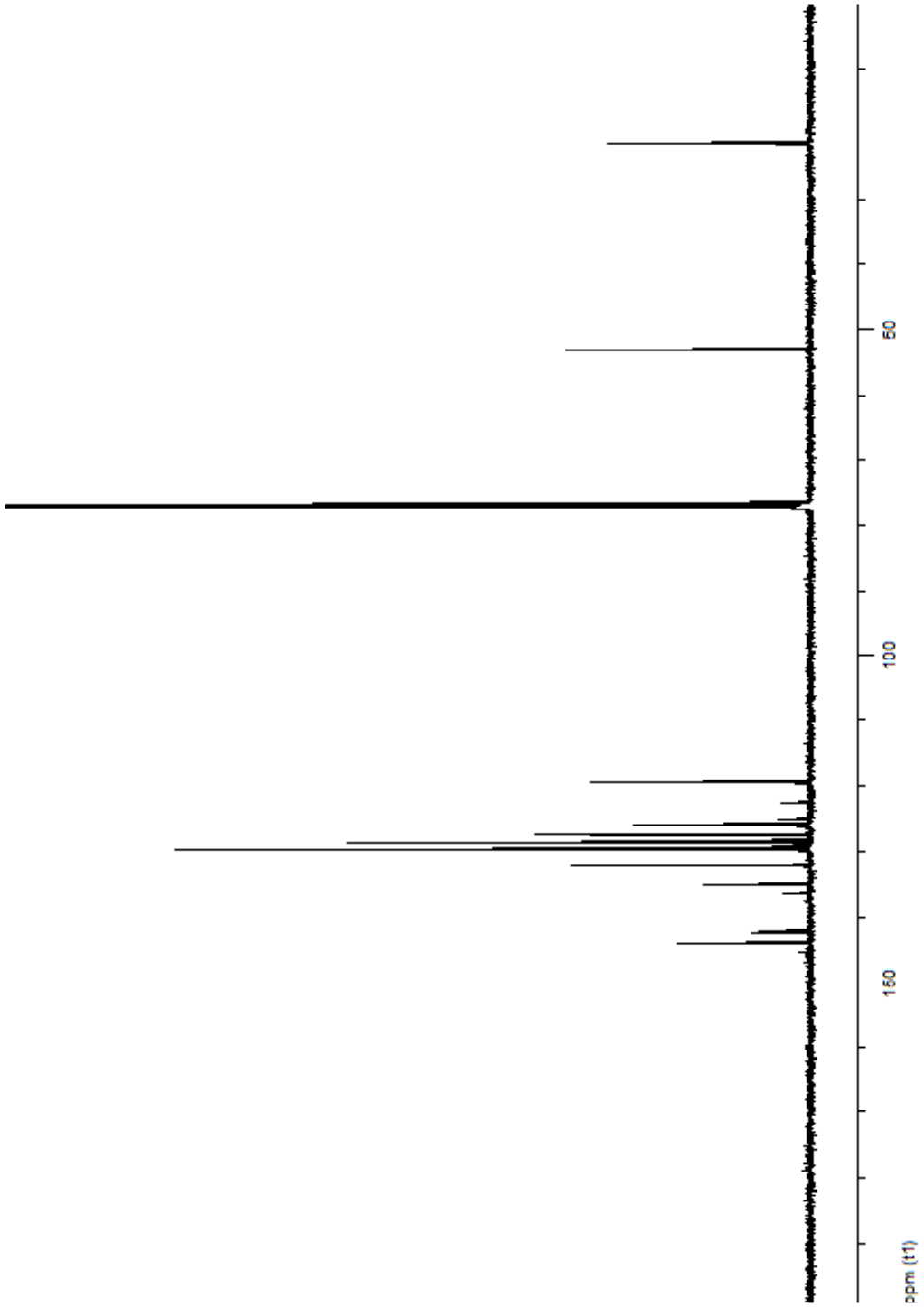
Compound 3g: ^{1}H NMR



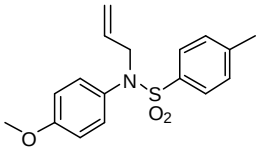


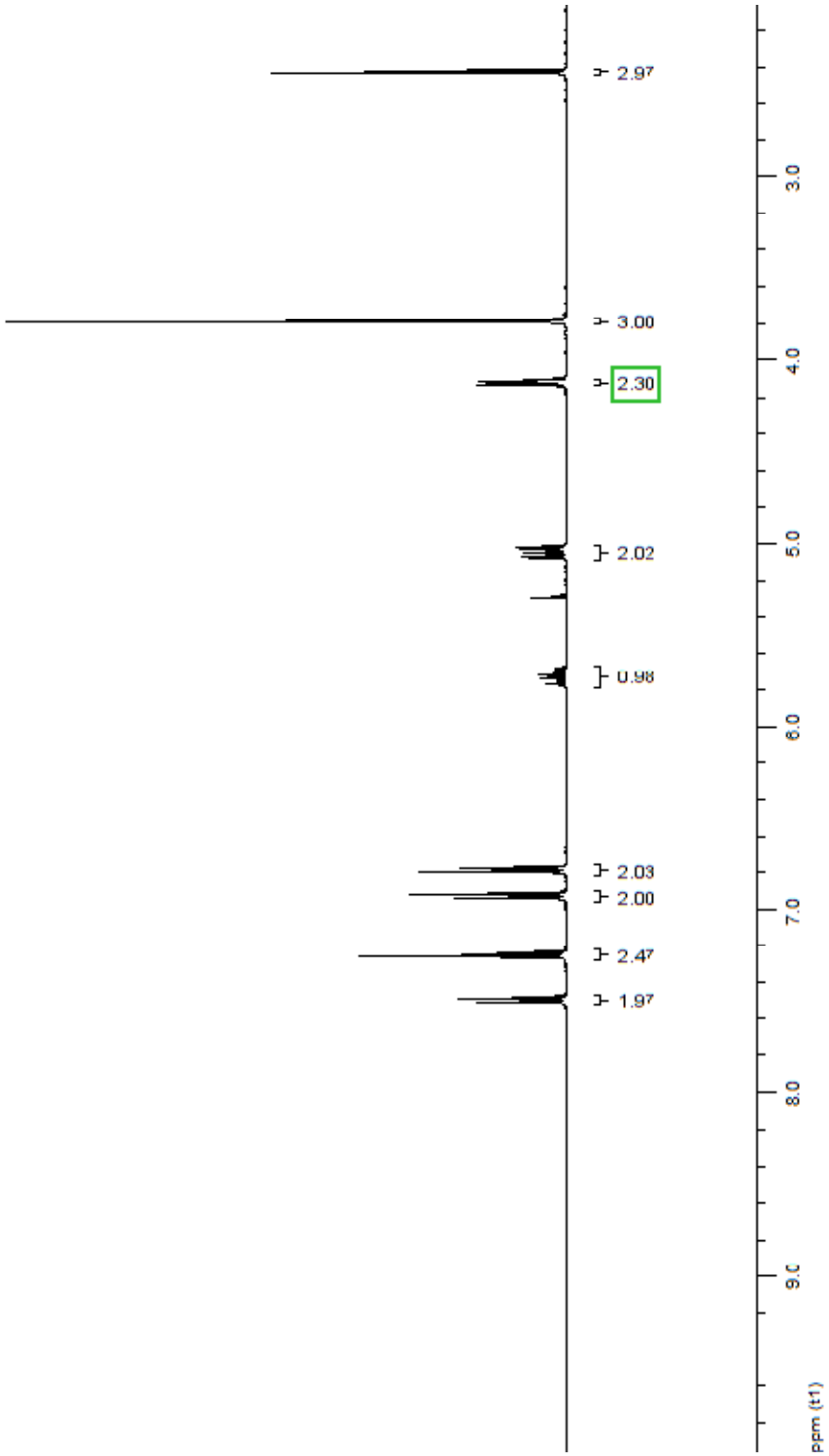
Compound 3g: ^{13}C NMR



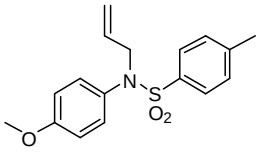


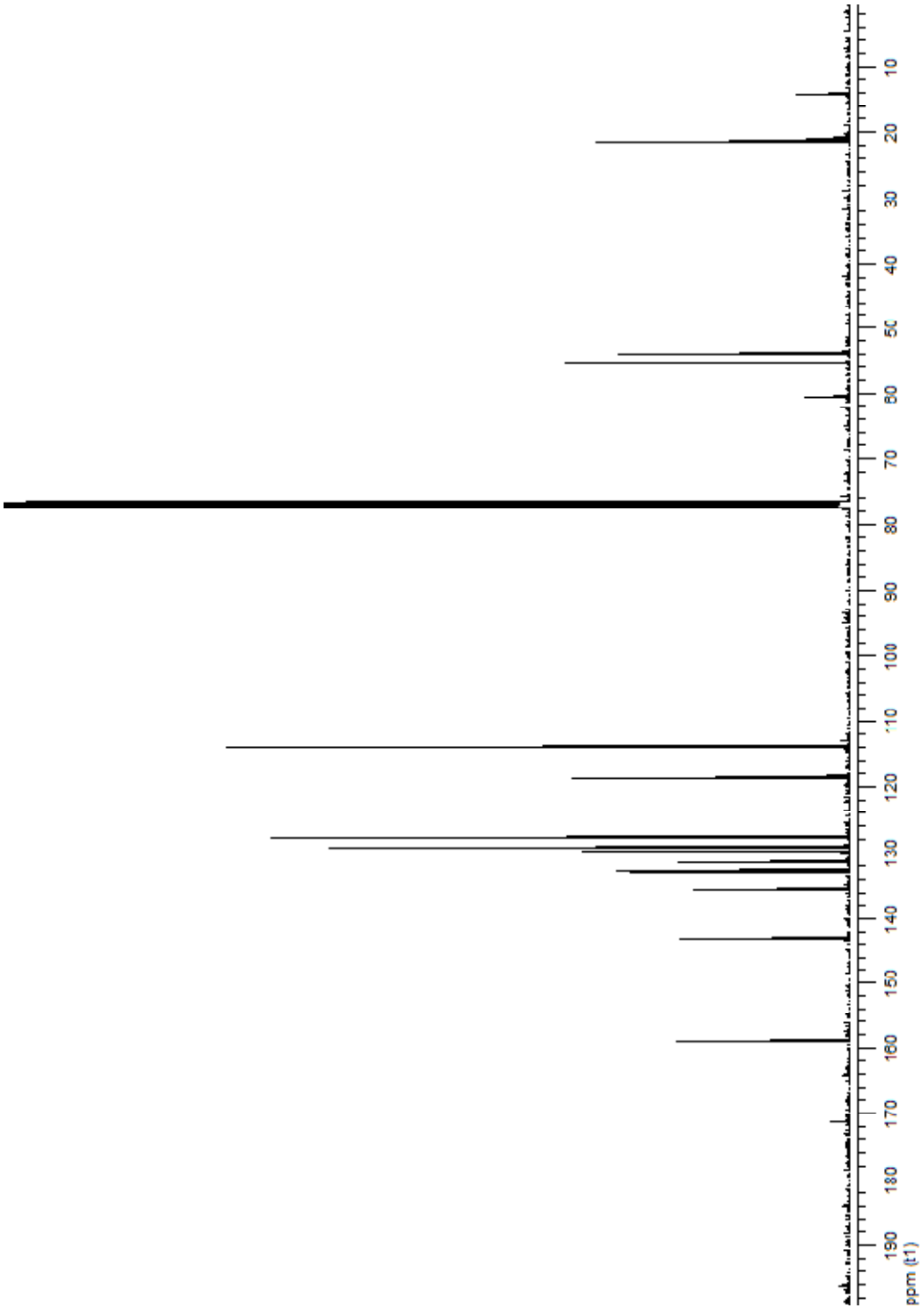
Compound 3h: ^{1}H NMR

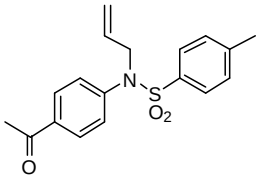




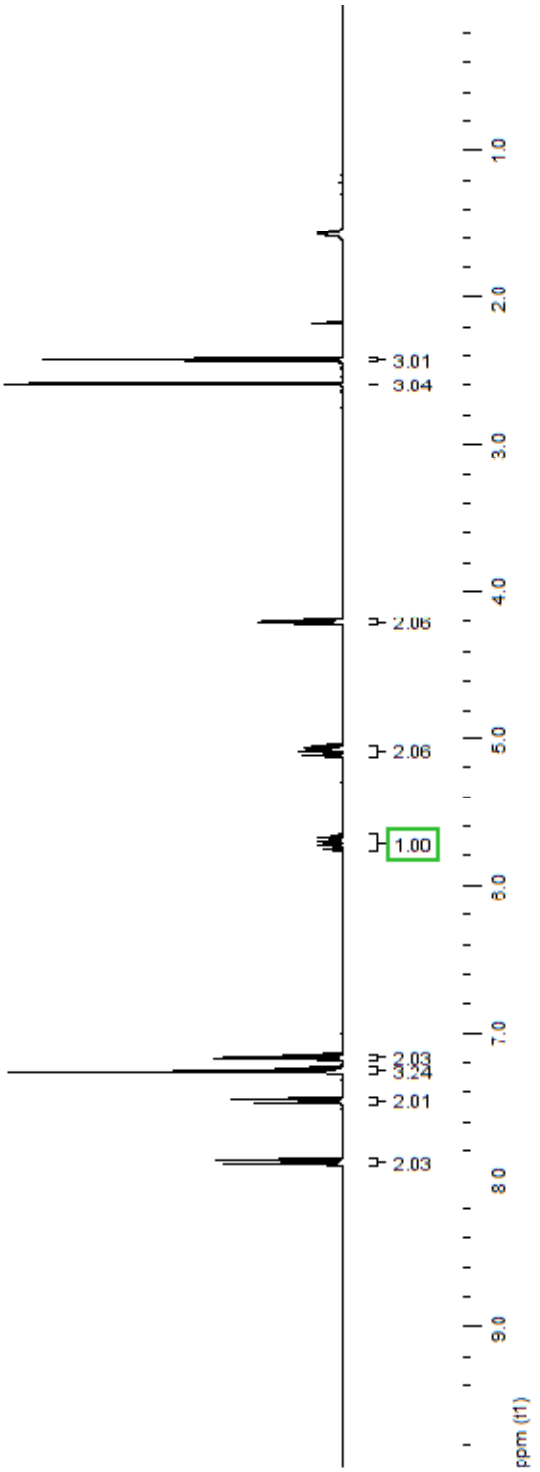
Compound 3h: ^{1}H NMR

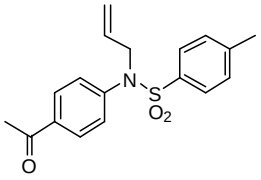




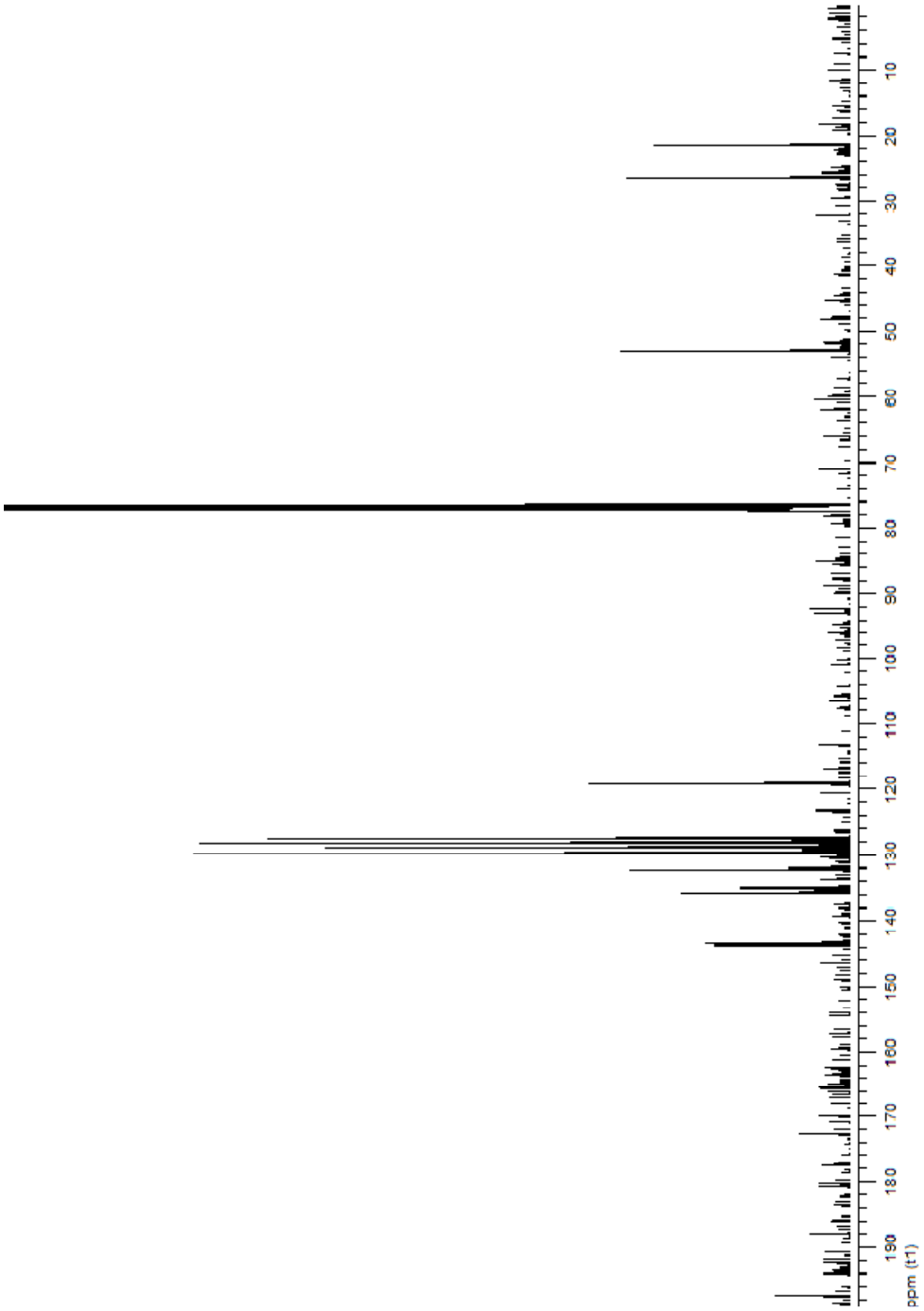


Compound 3i: ^{1}H NMR

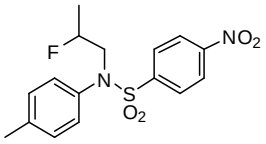


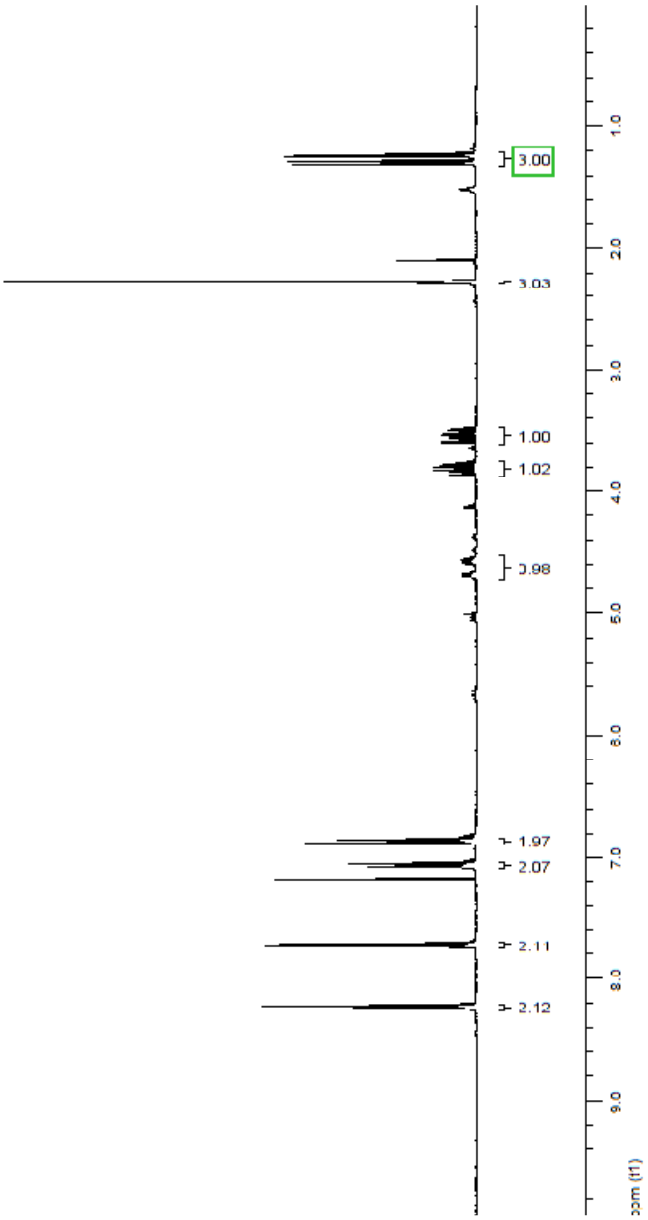


Compound 3i: ^{13}C NMR

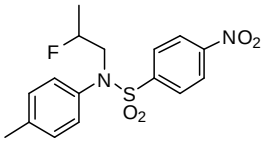


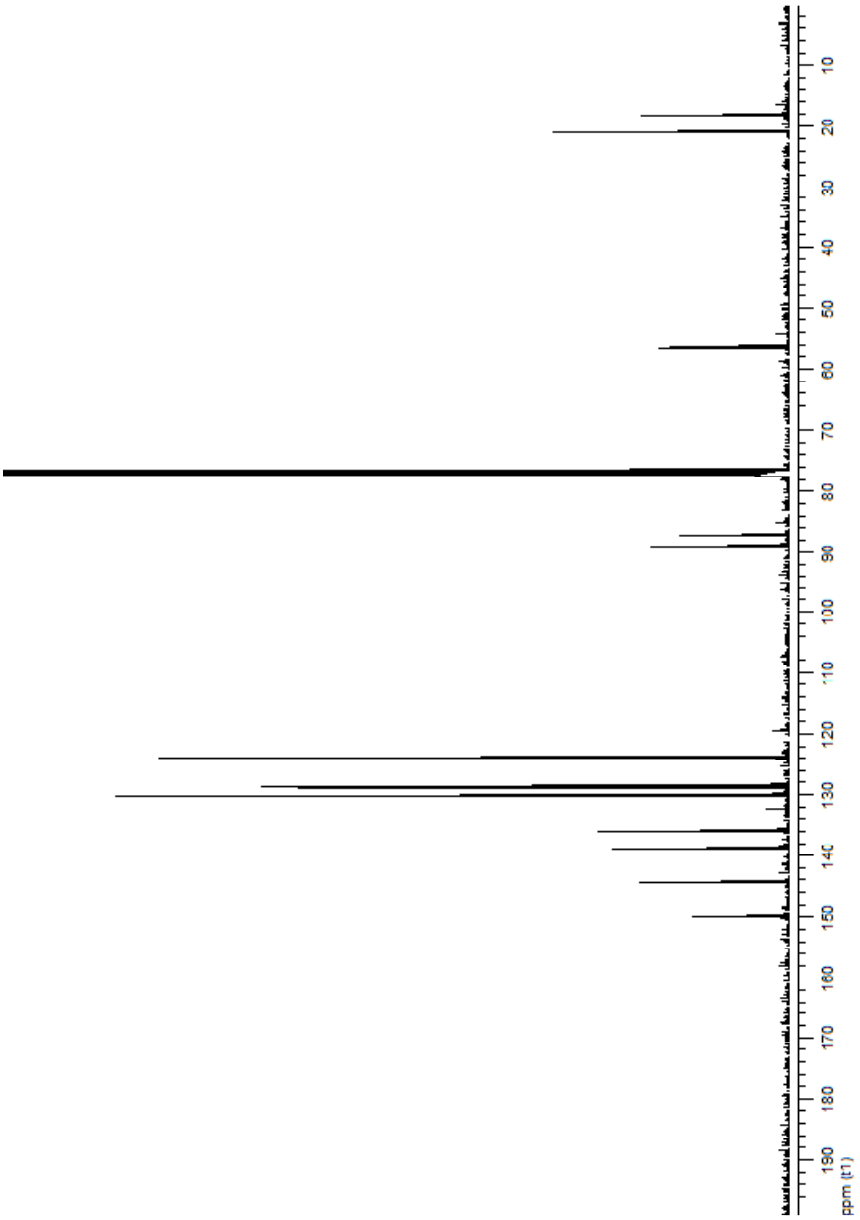
Compound 4b: ^{1}H NMR



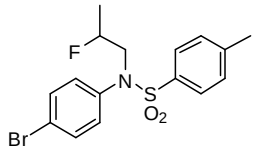


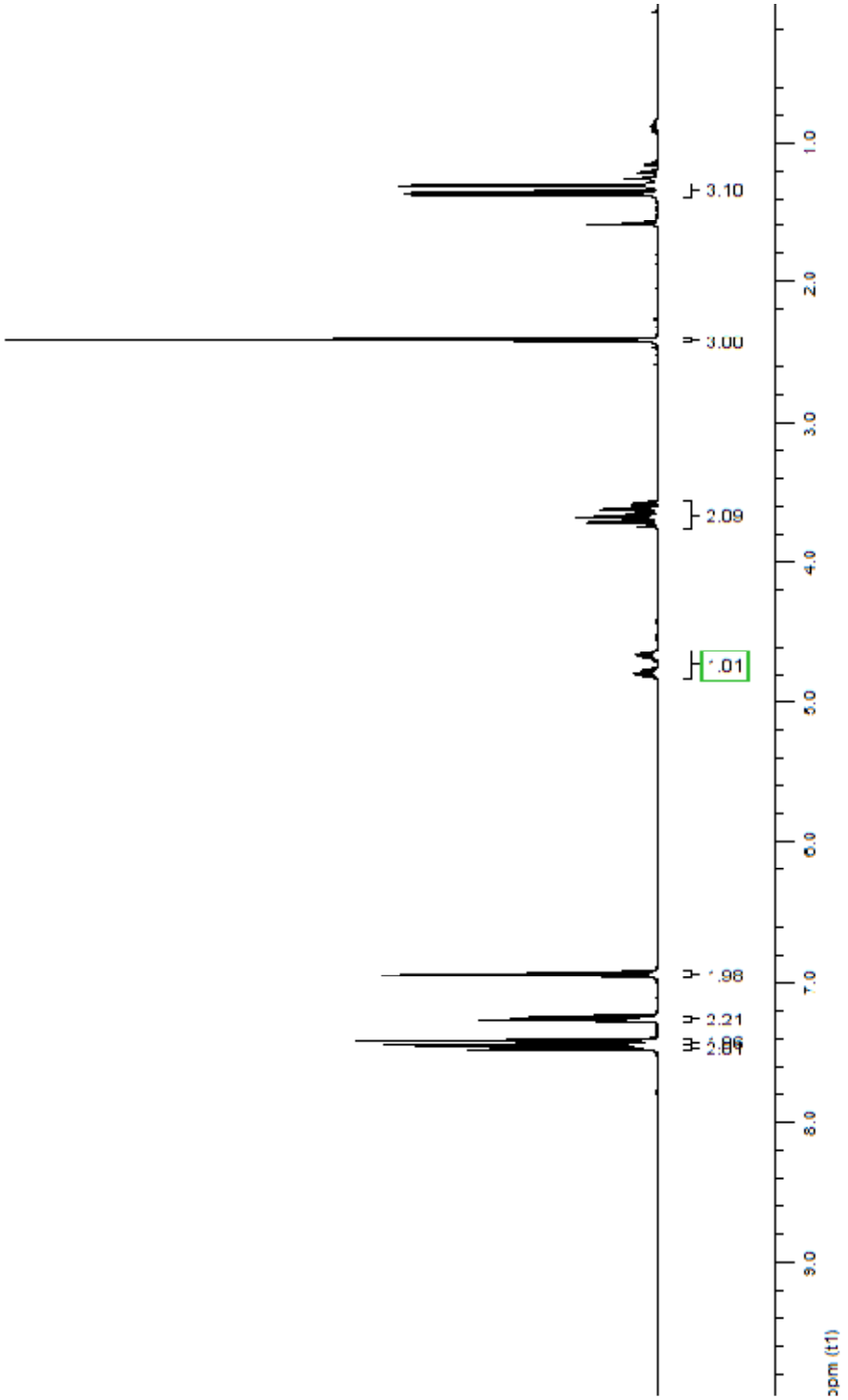
Compound 4b: ^{13}C NMR



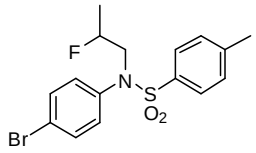


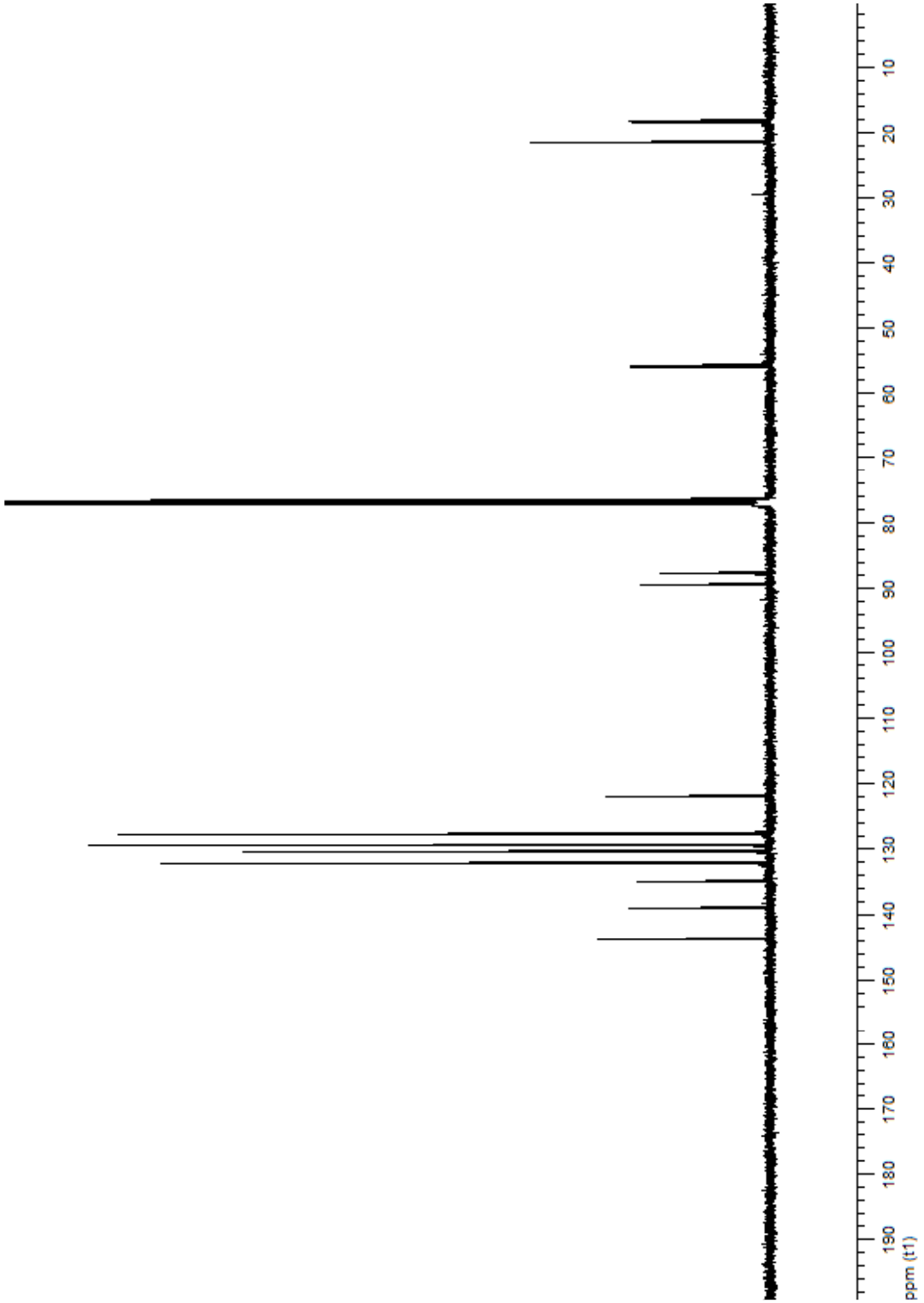
Compound 4c: ^{1}H NMR



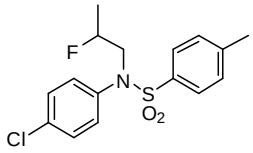


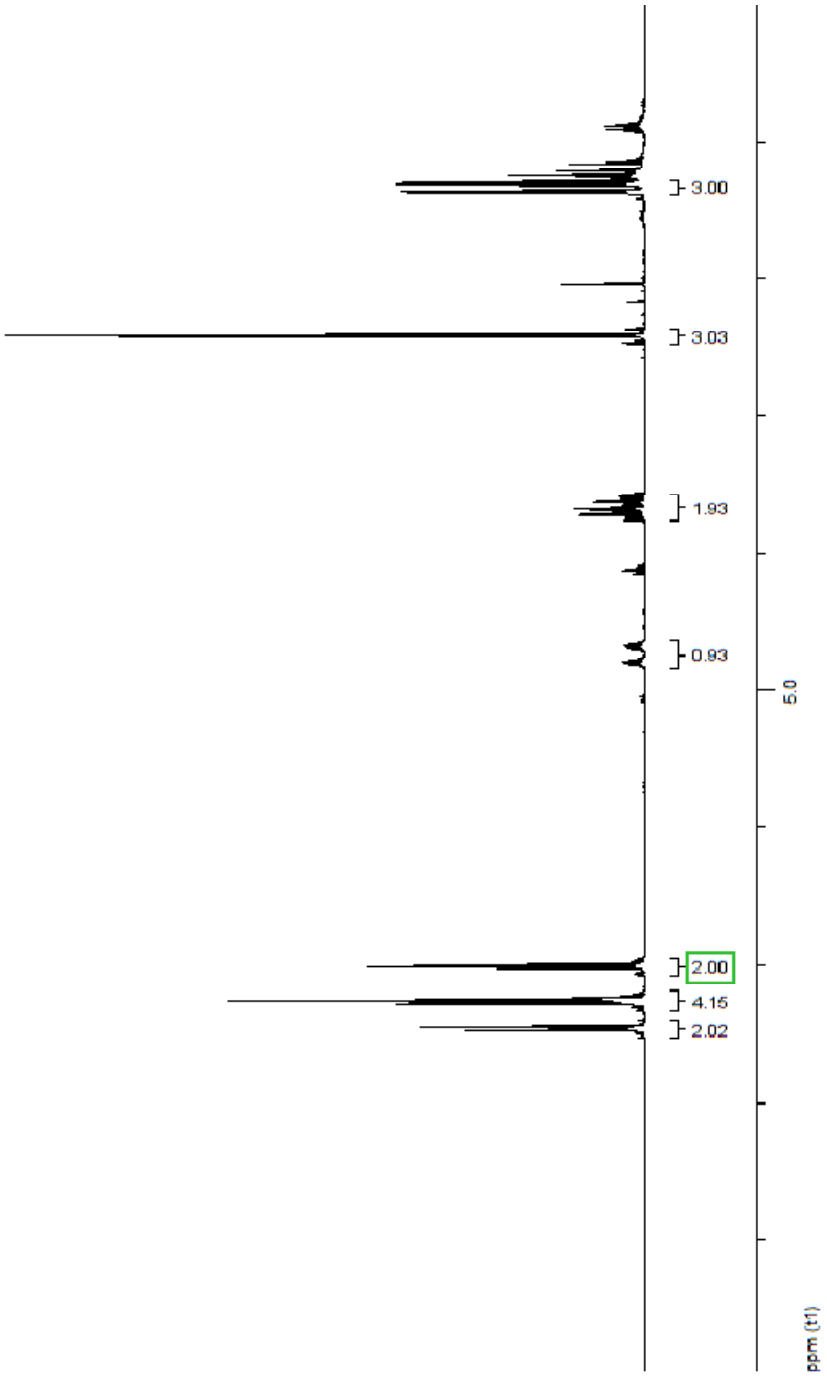
Compound 4c: ^{13}C NMR



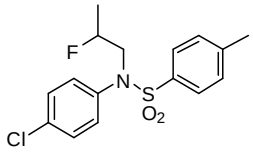


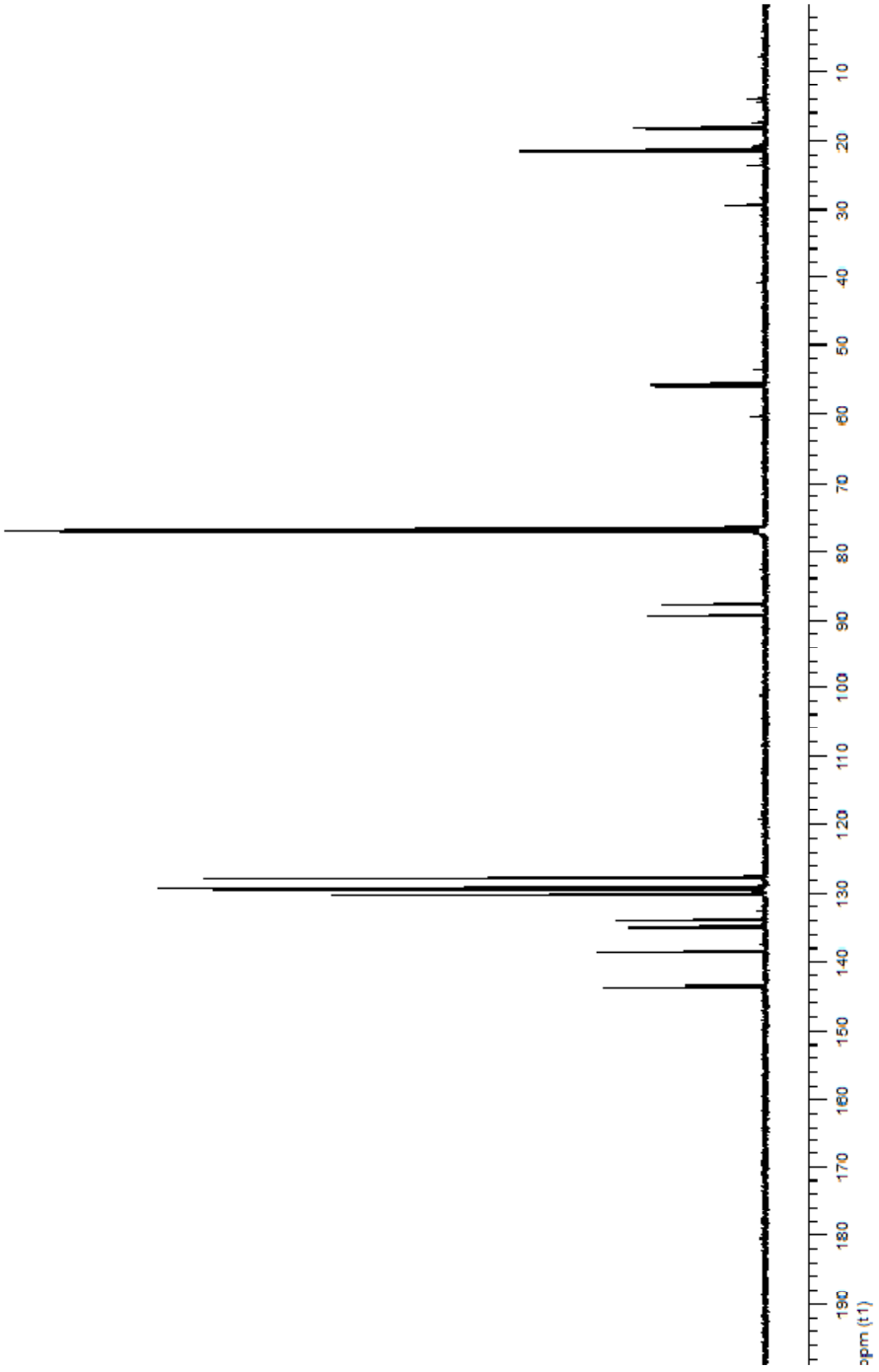
Compound 4d: ^{1}H NMR



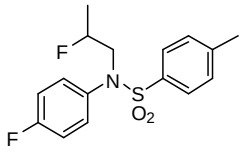


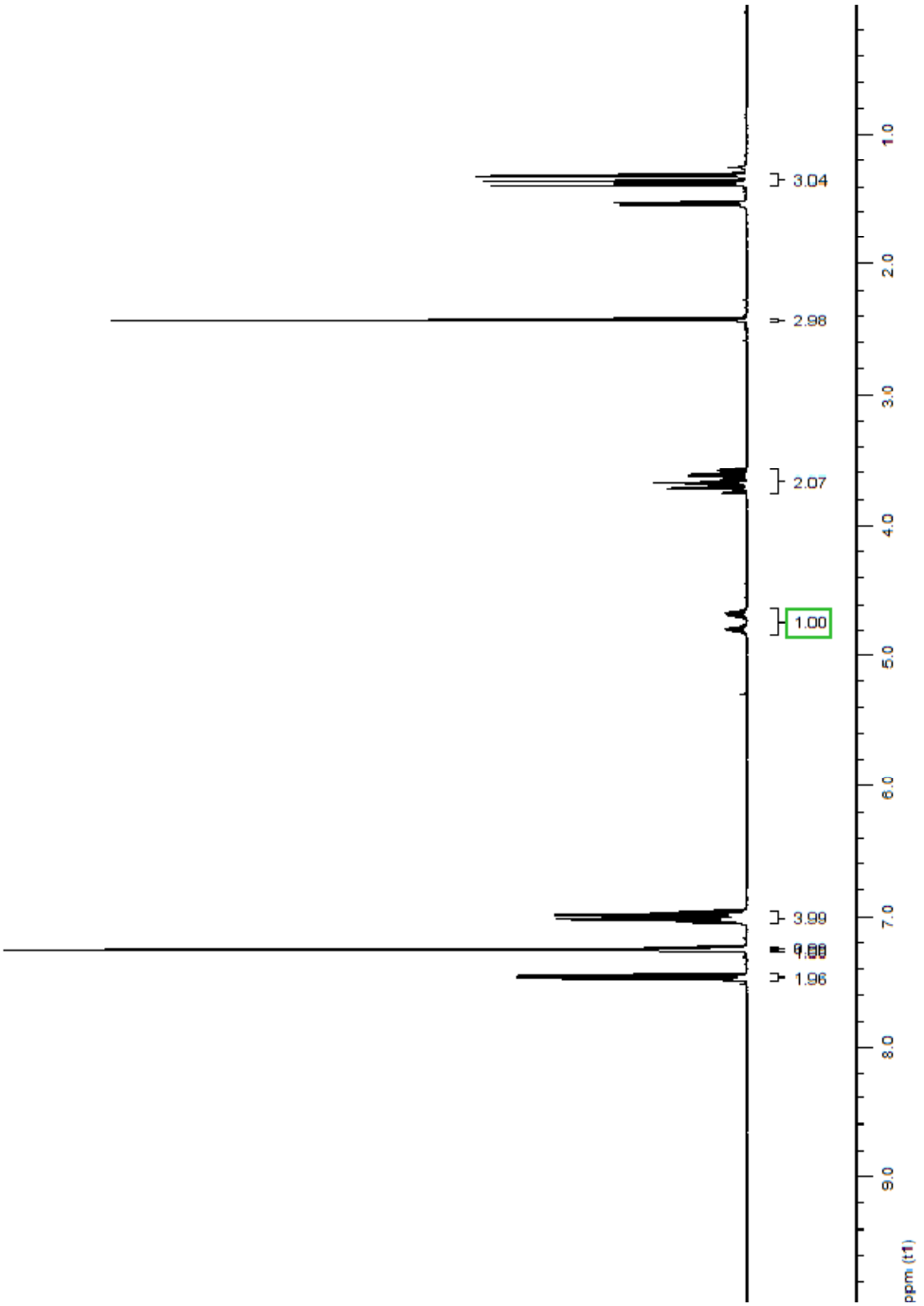
Compound 4d: ^{13}C NMR



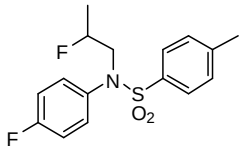


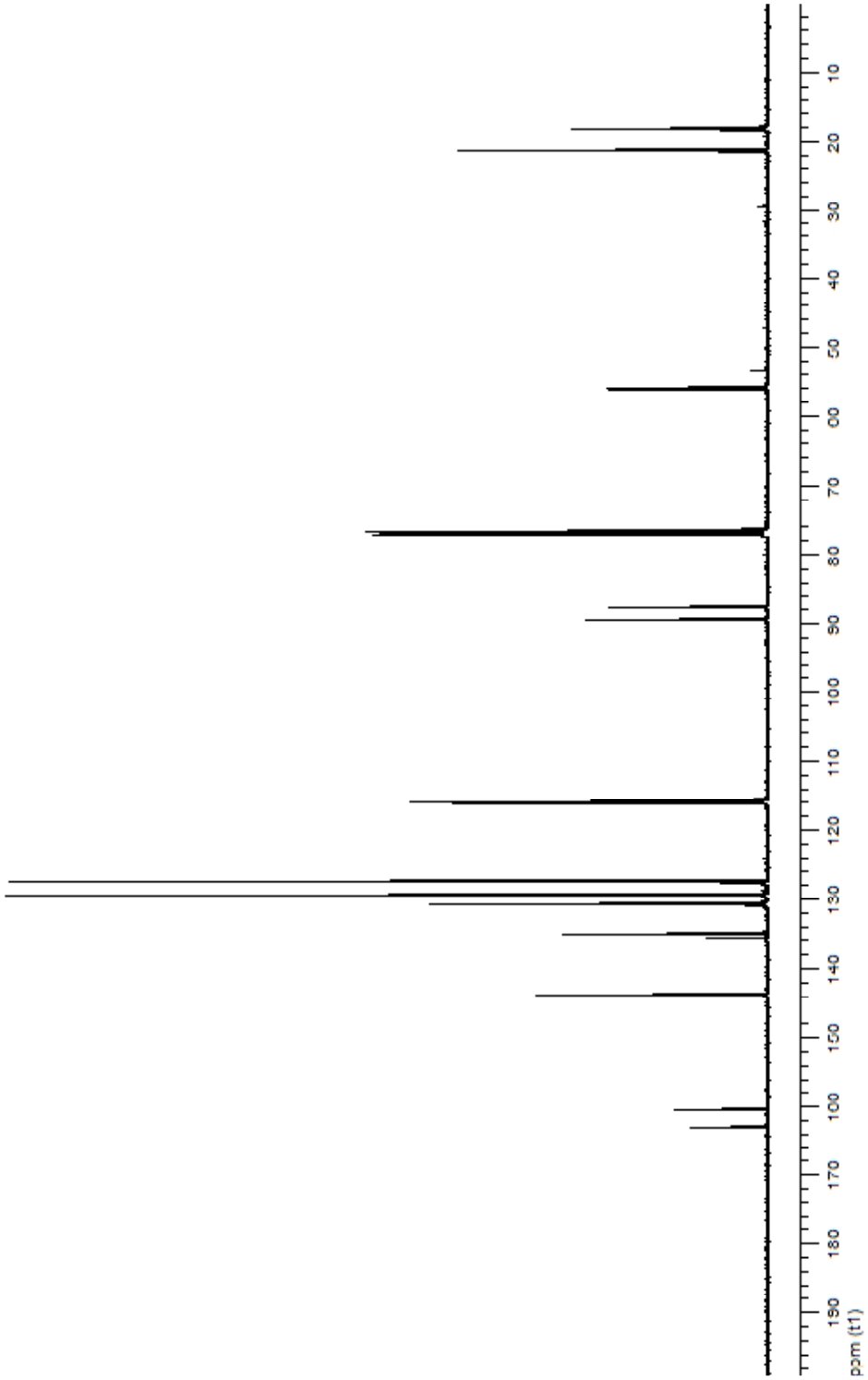
Compound 4e: ^{1}H NMR



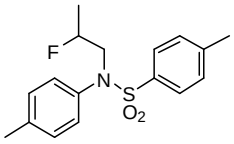


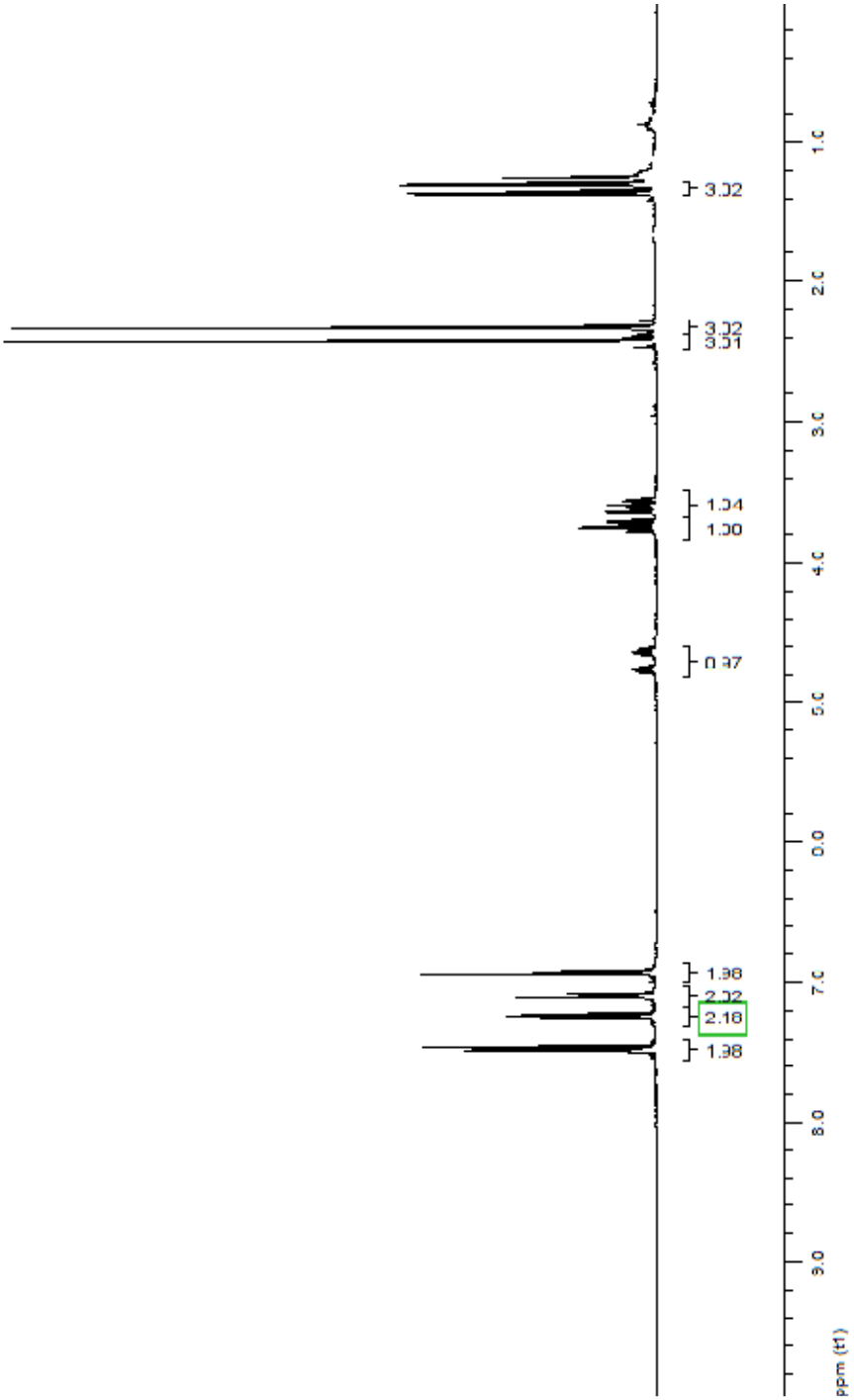
Compound 4e: ^{13}C NMR



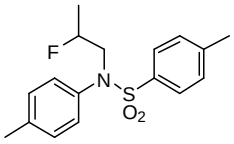


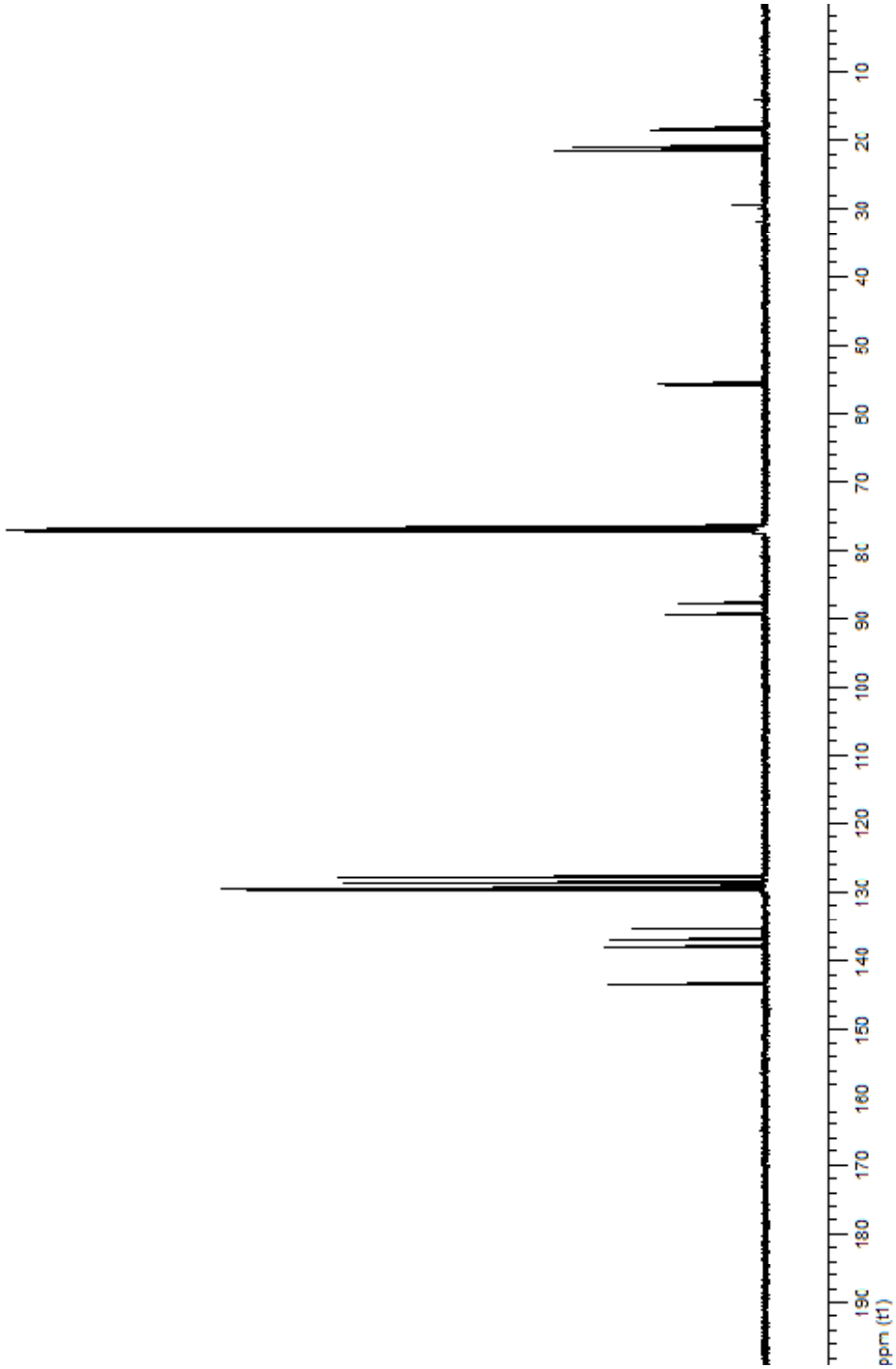
Compound 4f: ^{1}H NMR



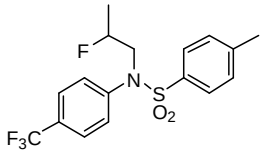


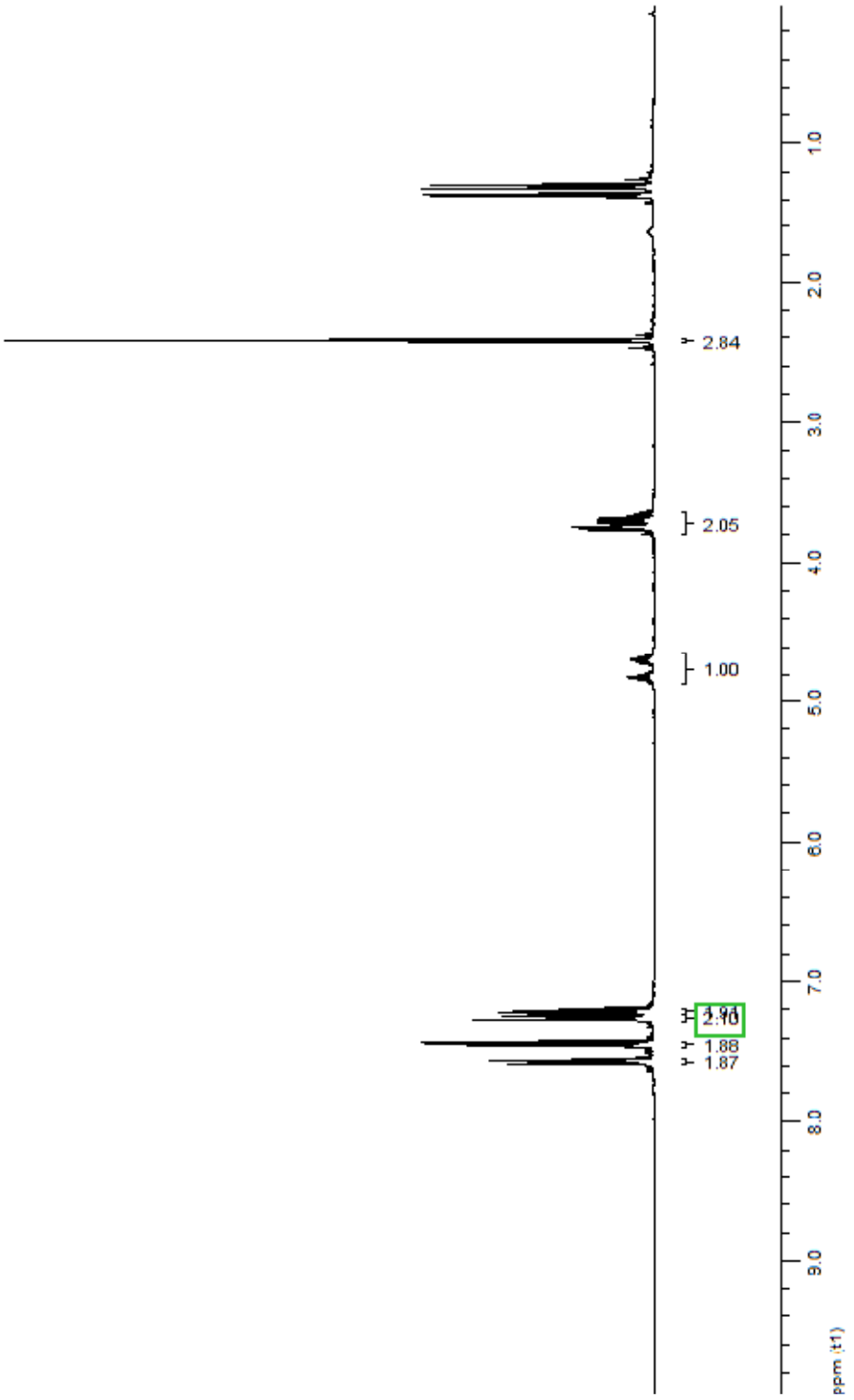
Compound 4f: ^{13}C NMR



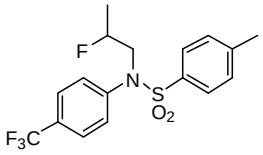


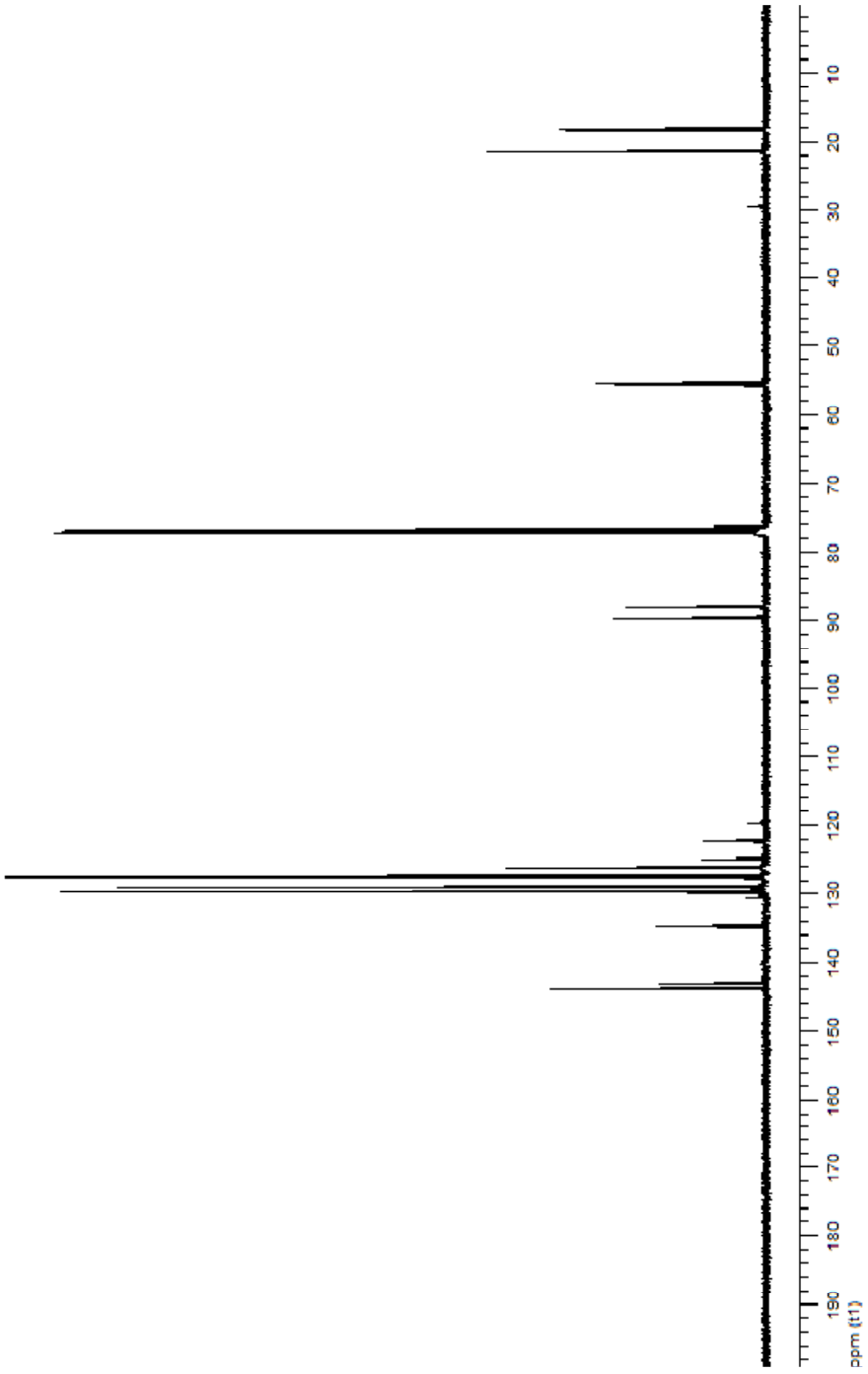
Compound 4g: ^{1}H NMR



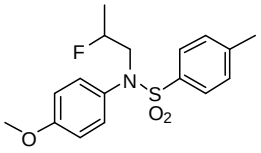


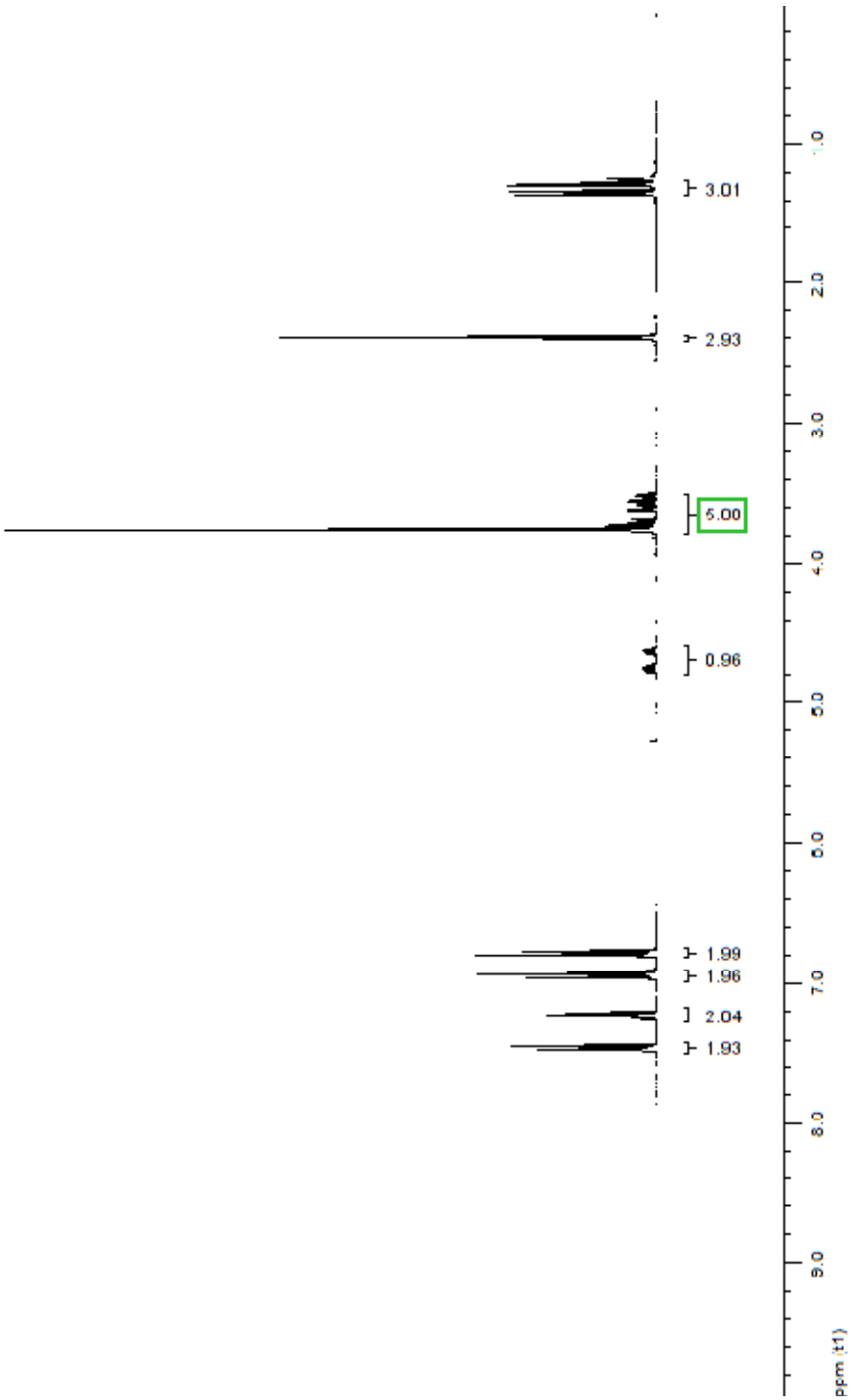
Compound 4g: ^{13}C NMR



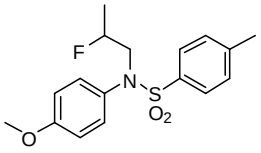


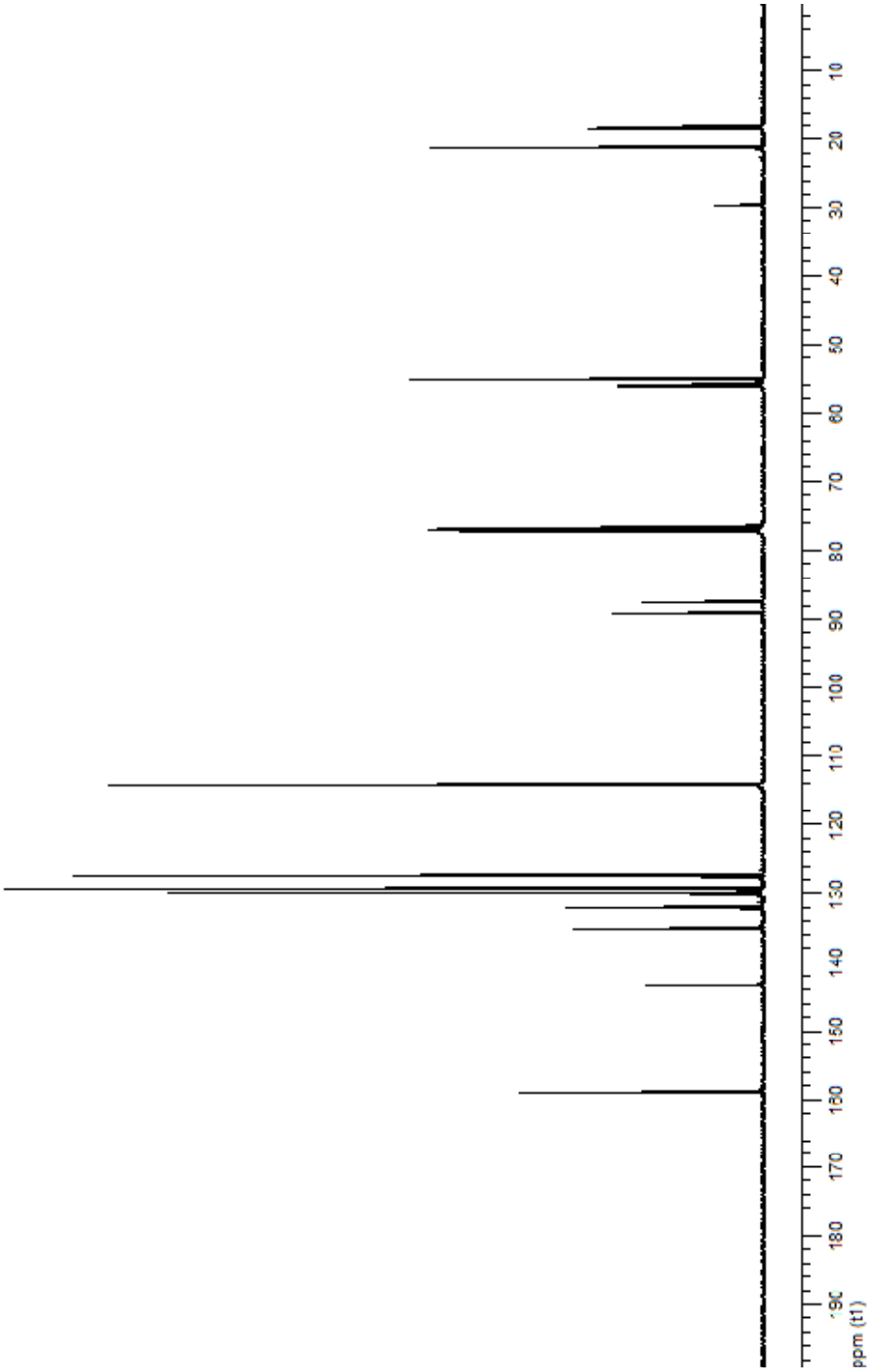
Compound 4h: ^{1}H NMR

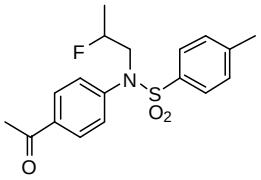




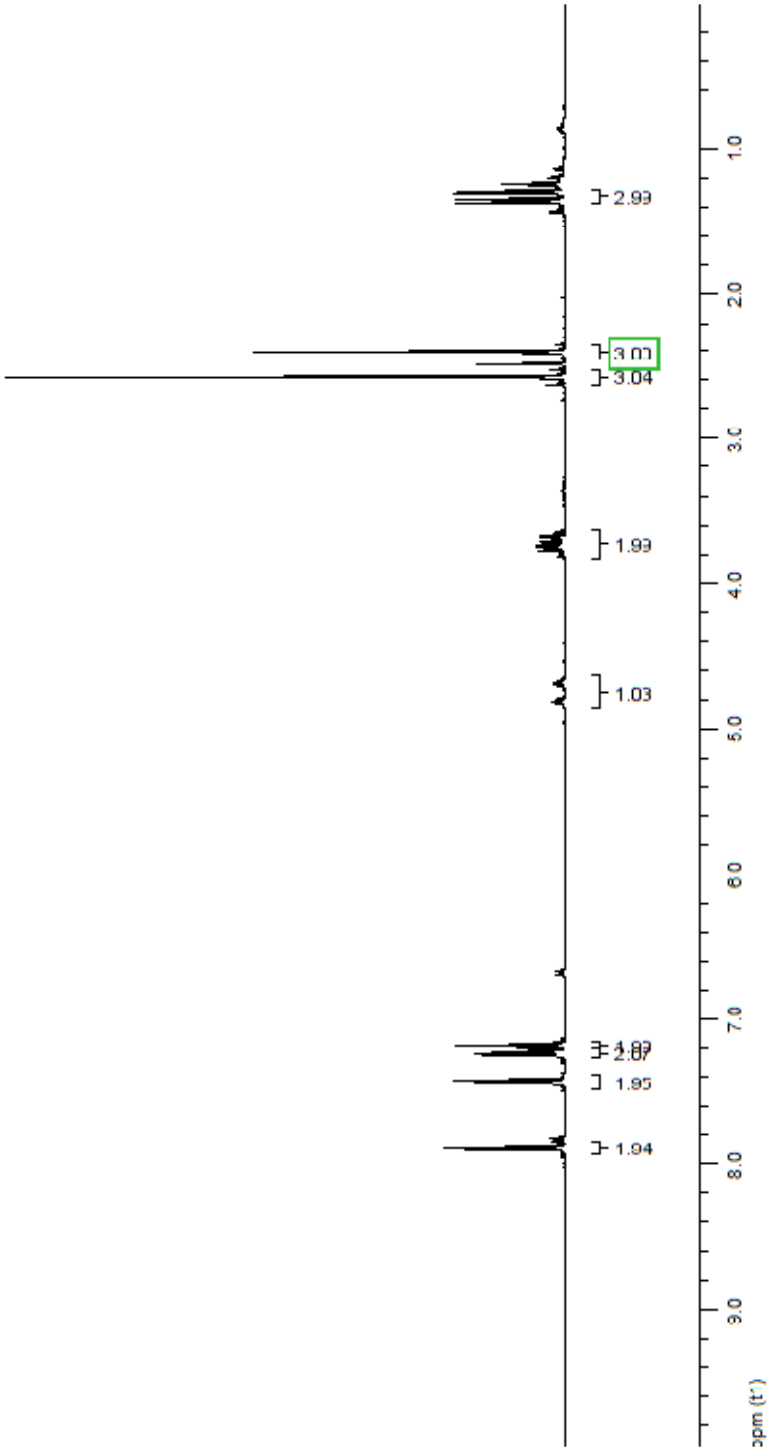
Compound 4h: ^{13}C NMR

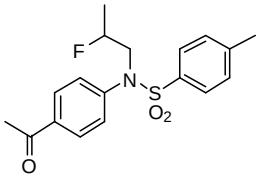




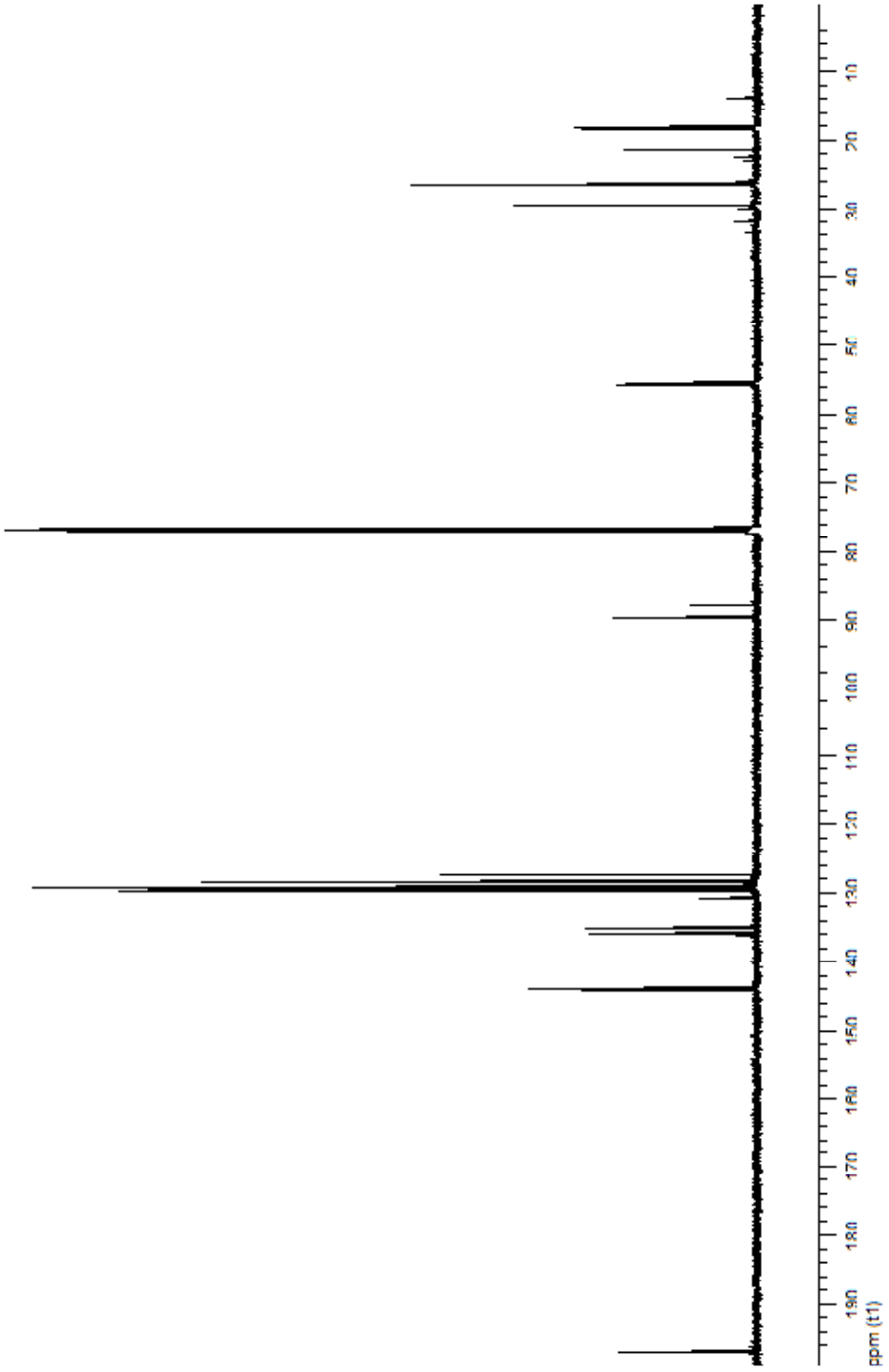


Compound 4i: ^{1}H NMR





Compound 4i: ^{13}C NMR



A. CA INHIBITION ASSAY

An Applied Photophysics stopped-flow instrument has been used for assaying the CA catalysed CO_2 hydration activity.[1] Phenol red (at a concentration of 0.2 mM) has been used as indicator, working at the absorbance maximum of 557 nm, with 20 mM Hepes (pH 7.5) as buffer, and 20 mM Na_2SO_4 (for maintaining constant the ionic strength), following the initial rates of the CA-catalyzed CO_2 hydration reaction for a period of 10-100 s. The CO_2 concentrations ranged from 1.7 to 17 mM for the determination of the kinetic parameters and inhibition constants. For each inhibitor at least six traces of the initial 5-10% of the reaction have been used for determining the initial velocity. The uncatalyzed rates were determined in the same manner and subtracted from the total observed rates. Stock solutions of inhibitor (0.1 mM) were prepared in distilled-deionized water and dilutions up to 0.01 nM were done thereafter with the assay buffer. Inhibitor and enzyme solutions were preincubated together for 15 min – 6 h at room temperature (15 min) 0r 4 ℃ (6h) prior to assay, in order to allow for the formation of the E-I complex. The inhibition constants were obtained by non-linear least-squares methods using PRISM 3, as reported earlier,[2] and represent the mean from at least three different determinations. All CA isofoms were recombinant ones obtained in-house as reported earlier.[3,4]

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