Supporting Information

Palladium-catalyzed *N*-(2-Pyridyl)sulfonyl-directed C(sp^3)–H γ-arylation of amino acid derivatives

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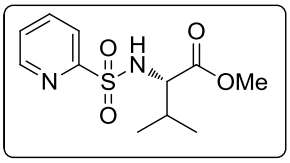
1. General Information. Chromatography: silica gel Merck-60 (230-400 mesh). TLC: silica gel Merck 60 (0.25 mm). Visualization of the chromatograms was performed by UV lamp and phosphomolibdic acid staining. Mass spectra were recorded on Waters AutoSpec mass spectrometer (FAB+) or Agilent LC/MSD TOF mass spectrometer (ESI+). ^{1}H and ^{13}C NMR were recorded on a Bruker (300 or 500 and 75.4 or 125 MHz, respectively) when indicated, using $CDCl_3$ or CD_3OD as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26 for ^{1}H, δ 77.0 for ^{13}C; CD_3OD: δ 3.34 for ^{1}H, δ 49.7 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (bs = broad single, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, m = multiplet), coupling constants (Hz), and integration. Melting points were recorded on a Buchi Melting Point B-540 apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241MC polarimeter using a 10 cm cell with the solvent and concentration stated, at 589 nm sodium lamp. Enantioselectivities were determined by HPLC analysis, carried out on Agilent 1100 Series with a diode array detector. All starting amino acids were purchased from Sigma-Aldrich or Bachem and used without further purification. The starting hydrochlorides 2-methyl-DL-valine ethyl ester, DL-alloisoleucine methyl ester and DL-β-leucine methyl ester were prepared following the procedure described in the literature.[1] The 2-pyridylsulfonyl chloride was synthesized form 2-mercaptopyridine following the procedure described in the literature.[2]

[1] J. Solà, S. P. Fletcher, A. Castellanos, J. Clayden, *Angew. Chem.* **2010**, *122*, 6988-6991; *Angew. Chem. Int. Ed.* **2010**, *49*, 6836-6839.
[2] A. García-Rubia, B. Urones, R. Gómez Arrayás, J. C. Carretero, *Angew. Chem.* **2011**, *123*, 11119-11123; *Angew. Chem. Int. Ed*. **2011**, *50*, 10927-1093.

2. General procedure for the synthesis of *N*-(2-pyridylsulfonyl) amino acid derivatives. *N*-(2-Pyridylsulfonyl) amino acid derivatives were prepared following a procedure described in the literature for similar derivatives.[3] The appropriate amino acid hydrochloride ester (3.3 mmol, 1.0 equiv) was weighed into a round bottom flask, then anhydrous CH_3CN (20 mL), 2-pyridylsulfonyl chloride (643 mg, 4.0 mmol, 1.2 equiv) and *N,N,N',N'*-tetramethylethylenediamine (2.9 mL, 20.0 mmol, 6.0 equiv) were successively added under nitrogen. The mixture was stirred overnight at room temperature and then the solvent was removed under reduced pressure. The crude was dissolved with EtOAc (20 mL), washed with 1 M HCl (aq) solution (x 2) and the aqueous phase was extracted with EtOAc (x 2). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified if necessary as specified for each example to afford the corresponding *N*-(2-pyridylsulfonyl) amino acid ester.

Methyl *N*-(2-pyridylsulfonyl)-L-valinate (**1**)



Compound **1** was obtained from L-valine methyl ester hydrochloride following the general procedure as a white solid (870 mg, yield 97%). The title compound was used without further purification.

$[\alpha]_D$ = +17 (c = 1, CH_2Cl_2).

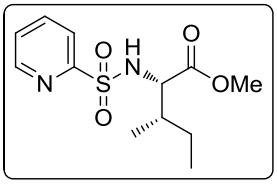
m.p.: 108-109 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, *J* = 4.8 Hz, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 7.89 (td, *J* = 7.5, 1,5 Hz, 1H), 7.51 (ddd, *J* = 7.5, 4.7, 1.5 Hz, 1H), 5.32 (d, *J* = 9.6 Hz, NH), 4.16 (dd, *J* = 9.6, 4.8 Hz, 1H), 3.61 (s, 3H), 2.10 - 2.01 (m, 1H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.8, 157.9, 149.7, 137.9, 162.6, 121.7, 62.1, 52.2, 31.8, 18.9, 17.4.

MS (ESI) *m/z*: 213 [(M^+ - 60), 273 (M^+ + H), 295 (M^+ + Na) (100), 567 ($2M^+$ + Na); HRMS calcd for $C_{11}H_{17}N_2O_4S$ (M^+ + H): 273.0903, found: 273.0914.

Methyl *N*-(2-pyridylsulfonyl)-L-isoleucinate (**4**)



Compound **4** was obtained from L-isoleucine methyl ester hydrochloride following the general procedure as a white solid (793 mg, yield 84%). The title compound was used without further purification.

$[\alpha]_D$ = +25 (c = 1, CH_2Cl_2).

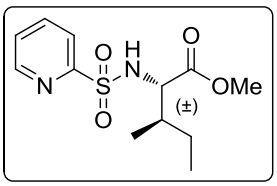
m.p.: 97-99 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (d, *J* = 4.8 Hz, 1H), 7.95 (d, *J* = 7.3 Hz, 1H), 7.89 (t, *J* = 7.1 Hz, 1H), 7.42 (t, *J* = 5.9 Hz, 1H), 5.36 (d, *J* = 9.7 Hz, NH), 4.18 (m, 1H), 3.51 (s, 3H), 1.84 (m, 1H), 1.47-1.29 (m, 1H), 1.22-1.01 (m, 1H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.82 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.7, 157.8, 149.6, 137.9, 126.6, 121.7, 61.2, 52.1, 38.6, 24.6, 15.3, 11.2.

MS (ESI) *m/z*: 227 (M^+ - 60), 287 (M^+ + H), 309 (M^+ + Na) (100); 595 ($2M^+$ + Na); HRMS calcd for $C_{12}H_{19}N_2O_4S$ (M^+ + H): 287.1060, found: 287.1060.

Methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**6**)



Compound **6** was obtained from DL-alloisoleucine methyl ester hydrochloride following the general procedure, after purification by trituration (hexane/CH_2Cl_2), as a white solid (924 mg, yield 98%).

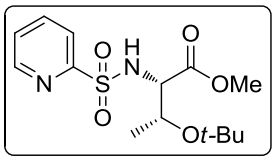
m.p.: 111-113 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, *J* = 4.4 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.87 (td, *J* = 7.6, 1.5 Hz, 1H), 7.45 (m, 1H), 5.39 (d, *J* = 9.8 Hz, NH), 4.30 (dd, *J* = 9.8, 4.0 Hz,1H), 3.54 (s, 3H), 1.82 (m, 1H), 1.54-1.44 (m, 1H), 1.31-1.15 (m, 1H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 172.0, 157.8, 149.6, 137.9, 126.5, 121.6, 121.6, 60.1, 52.1, 38.0, 25.8, 14.1, 11.4.

MS (FAB) *m/z*: 287 (M^+ + H); HRMS calcd for $C_{12}H_{19}N_2O_4S$ (M^+ + H): 287.1066, found: 287.1066.

Methyl *O*-(*tert*-butyl)-*N*-(2-pyridylsulfonyl)-L-threoninate (**8**)



Compound **8** was obtained from *O-tert*-Butyl-L-threonine methyl ester hydrochloride following the general procedure, after purification by trituration (hexane/Et_2O), as a white solid (1.013 g, yield 93%).

$[\alpha]_D$ = -17 (c = 1, CH_2Cl_2).

[3] M. Pattarozzi, C. Zonta, Q. B. Broxterman, B. Kaptein, R. De Zorzi, L. Randaccio, P. Scrimin, G. Licini. *Org. Lett.* **2007**, *9*, 2365-2368.

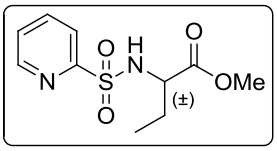
m.p.: 118-120 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (d, *J* = 4.4 Hz, 1H), 7.95 (d, *J* = 7.2 Hz, 1H), 7.84 (dt, *J* = 7.2, 1.6 Hz, 1H), 7.45 (dd,d *J* = 7.2, 4.8, 1.3 Hz, 1H), 5.48 (d, *J* = 10.2 Hz ,NH), 4.21 (dd, *J* = 10.1, 2.0 Hz, 1H), 4.14 (dd, *J* = 6.1, 1.9 Hz, 1H), 3.51 (s, 3H), 1.27 (d, *J* = 6.2 Hz, 3H), 1.06 (s, 9H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.7, 158.2, 149.6, 137.8, 126.4, 121.4, 74.1, 67.9, 62.5, 52.1, 28.2, 20.7.

MS (ESI) *m/z*: 215 (M^+ - 60), 275 (M^+ - 55) (100), 331 (M^+ + H); 353 (M^+ + Na); 683 ($2M^+$ + Na); HRMS calcd for $C_{14}H_{23}N_2O_5S$ (M^+ + H): 331.1312, found: 331.1308.

Methyl *N*-(2-pyridylsulfonyl)-DL-homoalalinate (**10**)



Compound **10** was obtained from DL-homoalanine methyl ester hydrochloride following the general procedure, after purification by column chromatography (hexane\EtOAc 1:1), as a white solid (715 mg, yield 84%).

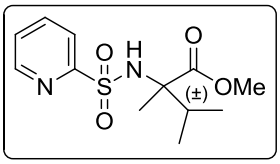
m.p.: 81-83 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (d, *J* = 4.7 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.89 (td, *J* = 7.5, 1.6 Hz, 1H), 7.51 (ddd, *J* = 7.6, 4.7, 1.3 Hz, 1H), 5.42 (d, *J* = 8.6 Hz, NH), 4.27 (ddd, *J* = 8.7, 7.0, 5.3 Hz, 1H), 3.61 (s, 3H), 1.98-1.59 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 172.1, 157.9, 149.7, 137.9, 126.6, 121.7, 57.8, 52.4, 27.0, 9.3.

MS (ESI) *m/z*: 199 (M^+ - 60), 259 (M^+ + H), 281 (M^+ + Na) (100); HRMS calcd for $C_{10}H_{15}N_2O_4S$ (M^+ + H): 259.0747, found: 259.0759.

Methyl 2-methyl-*N*-(2-pyridylsulfonyl)-DL-valinate (**12**)



Compound **12** was obtained from 2-methyl-DL-valine methyl ester hydrochloride following the general procedure, after purification by column chromatography (hexane\EtOAc 1:1), as a yellow solid (537 mg, yield 57%).

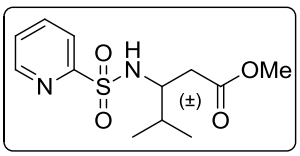
m.p.: 125-128 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (ddd, *J* = 4.7, 1.8, 1.0 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.88 (dt, *J* = 7.7, 1.7 Hz, 1H), 7.41 (ddd, *J* = 7.5, 4.7, 1.3 Hz, 1H), 5.49 (bs, NH), 3.61 (s, 3H), 2.02 (sept, *J* = 13.6, 6.8 Hz, 1H), 1.39 (s, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 173.5, 159.0, 149.8, 137.9, 126.4, 121.6, 65.8, 52.4, 37.1, 17.3, 16.9, 16.8.

MS (ESI) *m/z*: 287 (M^+ + H) (100), 573 ($2M^+$ + H); HRMS calcd for $C_{12}H_{19}N_2O_4S$ (M^+ + H): 287.1066, found: 287.1061.

Methyl *N*-(2-pyridylsulfonyl)-DL-β-leucinate (**14**)



Compound **14** was obtained from DL-β-leucine methyl ester hydrochloride following the general procedure, after purification by column chromatography (hexane\EtOAc 1:1), as a white solid (727 mg, yield 77%).

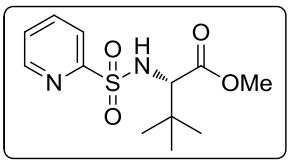
m.p.: 67-69 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.66 (d, *J* = 3.9 Hz, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.88 (t, *J* = 7.5 Hz, 1H), 7.46 (m, 1H), 5.60 (d, *J* = 8.8 Hz, NH), 3.59 (m,1H), 3.54 (s, 3H), 2.48 (d, *J* = 5.4 Hz, 2H), 1.81 (m, 1H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.8, 158.4, 149.9, 137.9, 126.5, 121.9, 56.7, 51.7, 36.5, 31.9, 18.9, 18.4.

MS (FAB) *m/z*: 287 (M^+ + H) (100); HRMS calcd for $C_{12}H_{19}N_2O_4S$ (M^+ + H): 287.1066, found: 287.1069.

Methyl *N*-(2-pyridylsulfonyl)-L-*tert*-leucinate (**22**)



Compound **22** was obtained from L-*tert*-leucine methyl ester hydrochloride following the general procedure as a white solid (840 mg, yield 89%). The title compound was used without further purification.

$[\alpha]_D$ = +26 (c = 1, CH_2Cl_2).

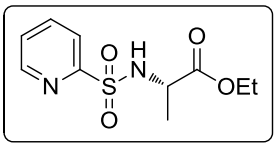
m.p.: 121-123 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (ddd, *J* = 4.7, 1.8, 1.0 Hz, 1H), 7.96 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.88 (td, *J* = 7.7, 1,8 Hz, 1H), 7.46 (ddd, *J* = 7.6, 4.7, 1.3 Hz, 1H), 5.36 (d, *J* = 10.1 Hz, NH), 3.95 (d, *J* = 10.1Hz, 1H) 3.53 (s, 3H), 0.99 (s, 9H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.3, 157.8, 149.6, 137.9, 126.6, 121.9, 65.2, 51.8, 34.8, 26.3.

MS (ESI) *m/z*: 227 (M^+ - 60), 287 (M^+ + H), 309 (M^+ + Na) (100), 595 ($2M^+$ + Na); HRMS calcd for $C_{12}H_{19}N_2O_4S$ (M^+ + H): 287.1060, found: 287.1061.

Ethyl *N*-(2-pyridylsulfonyl)-L-alaninate (**28**)



Compound **28** was obtained from L-alanine ethyl ester hydrochloride following the general procedure as a white solid (511 mg, yield 98%). The title compound was used without further purification.

$[\alpha]_D$ = +5 (c = 1, CH_2Cl_2).

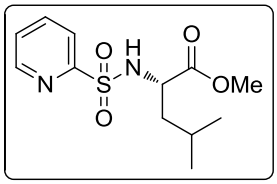
m.p.: 118-121 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (ddt, *J* = 4.6, 1.6, 0.8 Hz, 1H), 7.97 (d, *J* = 7.8, 1H), 7.89 (dt, *J* = 7.7, 1.7, 1H), 7.47 (ddd, *J* = 7.3, 4.9, 1.5 Hz, 1H), 5.49 (d, *J* = 8.1 Hz, NH), 4.35 (quint, *J* = 4.3 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 1.45 (d, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 172.2, 158.0, 149.8, 137.9, 126.7, 121.7, 61.7, 52.5, 20.3, 14.0.

MS (ESI) *m/z*: 259 (M^+ + H) (100), 517 ($2M^+$ + H); HRMS calcd for $C_{10}H_{15}N_2O_4S$ (M^+ + H): 259.0753, found: 259.0759.

Methyl *N*-(2-pyridylsulfonyl)-L-leucinate (**29**)



Compound **29** was prepared from L-leucine methyl ester hydrochloride following the general procedure, after purification by crystallisation (hexane/CH_2Cl_2), as a white solid (566 mg, yield 60%).

$[\alpha]_D$ = 0 (c = 1, CH_2Cl_2).

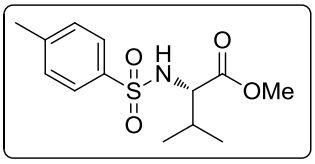
m.p.: 81-83 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (d, *J* = 4.6 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.88 (t, *J* = 7.8 Hz, 1H), 7.46 (m, 1H), 5.40 (bs, NH), 4.29 (m,1H), 3.55 (s, 3H), 1.82 (sept, *J* = 6.7 Hz, 1H), 1.54 (t, *J* = 6.7 Hz, 2H), 0.94-0.90 (m, 6H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.7, 158.2, 149.6, 137.9, 126.5, 121.5, 74.1, 67.9, 62.5, 52.1, 28.2, 20.6.

MS (ESI) *m/z*: 227 (M^+ - 60), 287 (M^+ + H), 309 (M^+ + Na) (100); 595 ($2M^+$ + Na); HRMS calcd for $C_{12}H_{19}N_2O_4S$ (M^+ + H): 287.1060, found: 287.1051.

3. Synthesis of methyl *N*-(tosyl)-L-valinate (**26**)



L-Valine methyl ester hydrochloride (300 mg, 1.8 mmol) was weighed into a round bottom flask, then anhydrous CH_3CN (6.5 mL), tosyl chloride (412 mg, 2.17 mmol) and *N,N,N′,N′*-tetramethylethylenediamine (1.3 mL, 9.0 mmol) were successively added under nitrogen. The mixture was stirred overnight at room temperature. EtOAc was added and the organic phase was then washed with 1 M HCl (aq) solution, sat.aq. solution of $NaHCO_3$ and brine. The combined organic phases were dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to give methyl *N*-(tosyl)-L-valinate **26**, after purification by crystallisation (hexane/Et_2O), as a white solid (492 mg, yield 96%).

$[\alpha]_D$ = -2 (c = 1, CH_3OH).

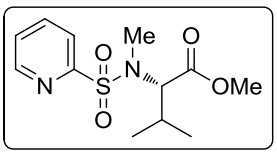
m.p.: 68-71 ºC

^{1}H NMR (300 MHz, CD_3OD) δ 7.64 (d, *J* = 7.4 Hz, 2H), 7.21 (d, *J* = 7.2 Hz, 2H), 3.66 (bs, 1H), 3.38 (s, 3H), 2.24 (s, 3H), 1.95 (m, 1H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (75.4 MHz, CD_3OD): δ 171.6, 143.2, 137.6, 129.0, 126.8, 61.6, 50.7, 31.0, 19.9, 17.9, 17.0.

MS (ESI) *m/z* 286 (M^+ + H) (100); HRMS calcd for $C_{13}H_{20}NO_4S$ (M^+ + H):287.1113, found: 286.1118.

4. Synthesis of methyl *N*-methyl-*N*-(2-pyridylsulfonyl)-L-valinate (**27**)



Compound **27** was prepared following the procedure described in the literature for a similar derivative.[4] Methyl *N*-(2-pyridylsulfonyl)-L-valinate **1** (50 mg, 0.18 mmol, 1.0 equiv) was dissolved in anhydrous DMF (0.7 mL). Next, methyl iodide (34 µL, 0.55 mmol, 3.0 equiv) and NaH (60% dispersion in mineral oil, 5 mg, 0.2 mmol, 1.1 equiv) were added and the mixture was stirred at room temperature overnight. CH_2Cl_2 was added and the organic phase was washed with brine, dried over $MgSO_4$ and filtered. The volatiles were removed under reduced pressure to give methyl *N*-methyl-*N*-(2-pyridylsulfonyl)-L-valinate **27** as yellow oil (42 mg, yield 82%).

[4] T. M. Krülle, J. C. H. M. Wijkmans, *Tetrahedron* **2001**, *57*, 7021.

$[\alpha]_D$ = -18 (c = 1, CH_2Cl_2).

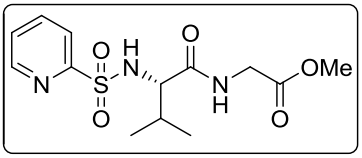
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.8 Hz, 1H), 7.92 (d. *J* = 7.2 Hz, 1H), 7.90 (d, *J* = 7.3, 1.6 Hz, 1H), 7.50-7.43 (m, 1H), 4.16 (d, *J* = 10.2 Hz, NH), 3.43 (s, 3H), 3.07 (s, 3H), 2.18-2.11 (m, 1H), 1.02 (d, *J* = 6.7Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.5, 157.5, 149.7, 137.6, 126.4, 122.4, 65.2, 51.4, 31.1, 27.7, 19.2, 19.1.

MS (ESI) *m/z*: 287 (M^+ + H) (100); HRMS calcd for $C_{12}H_{19}N_2O_4S$ (M^+ + H): 287.1066, found: 287.1064.

5. General procedure for the preparation of peptides 18 and 20. [5,6] 2 M LiOH·H_2O (44 mg, 1.047 mmol, 3.0 equiv) was added to a solution of methyl *N*-(2-pyridylsulfonyl) ester **1** or **6** (0.349 mmol) in THF/H_2O/MeOH (0.3/0.1/0.1 mL), and the reaction mixture was stirred at room temperature for 24 h. After this time, 1 M HCl (aq) solution was added until pH = 3 and the solution was extracted with EtOAc (x 3). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the corresponding acid as a white solid. To the resulting white solid, HOBt·H_2O (54 mg, 0.349 mmol, 1.1 equiv), EDC·HCl (67 mg, 0.349 mmol, 1.1 equiv), and glycine methyl ester hydrochloride (40 mg, 0.317 mmol, 1.0 equiv) were added, the mixture was suspended in anhydrous CH_2Cl_2 (0.2 M) and Et_3N (87 µL, 0.63 mmol, 2.0 equiv) was added. The solution was stirred at room temperature overnight. The reaction mixture was then diluted with EtOAc, transferred to a separatory funnel and sequentially washed with 0.5 M (aq) citric acid solution (x 4) and with sat.aq. $NaHCO_3$ solution. The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified, as specified for each example, to obtain the desired peptide **18** or **20**.

Methyl *N*-(2-pyridylsulfonyl)-L-valylglycinate (**18**)



Compound **18** was obtained from methyl *N*-(2-pyridylsulfonyl)-L-valinate **1** following the general procedure, after purification by column chromatography (hexane\EtOAc 1:5), as a white solid (66 mg, yield 63%, two steps).

$[\alpha]_D$ = + 12 (c = 1, CH_2Cl_2).

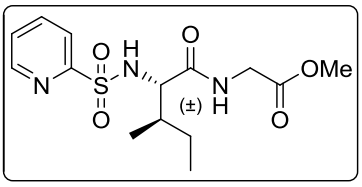
m.p.: 118-120 ºC

^{1}H NMR(300 MHz, $CDCl_3$): δ 8.66 (d, *J* = 4.7 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.86 (t, *J* = 7.7 Hz, 1H), 7.44 (dd, *J* = 7.7, 4.5 Hz, 1H), 7.22 (bs, NH), 6.26 (d, *J* = 8.5 Hz, NH), 3.97-3.82 (m, 3H), 3.67 (s, 3H), 2.12 (m, 1H), 0.85 (dd, *J* = 6.7, 3.4 Hz, 6H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.0, 157.4, 149.9, 138.2, 126.8, 122.3, 62.8, 52.3, 41.1, 31.2, 18.9, 17.3.

MS (FB) *m/z*: 213 (M^+ - 117), 330 (M^+ + H) (100); HRMS calcd for $C_{13}H_{20}N_3O_5S$ (M^+ + H): 330.1124; found: 330.1125.

Methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucylglycinate (**20**)



Compound **20** was obtained from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** following the general procedure, after purification by trituration (hexane/CH_2Cl_2), as a white solid (87 mg, yield 80%, two steps).

m.p.: 154 -156 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, *J* = 4.4 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.90 (td, *J* = 7.6, 1.5 Hz, 1H), 7.48 (m, 1H), 7.00 (bs, NH), 5.62 (d, *J* = 7.9 Hz, NH), 4.10 (dd, *J* = 8.2, 3.9 Hz,1H), 4.00 (dd, *J* = 18.1, 5.5 Hz, 1H), 3.88 (dd, *J* = 18.1, 5.1 Hz, 1H), 3.73 (s, 3H), 1.98 (m, 1H), 1.43-1.15 (m, 2H), 0.88-0.81 (m, 6H).

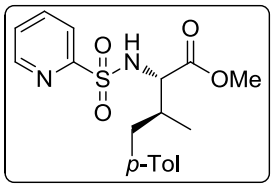
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.1, 169.8, 157.5, 149.8, 138.1, 126.8, 122.2, 60.9, 52.3, 41.2, 37.9, 26.0, 13.9, 11.5.

MS (FB) *m/z*: 344 (M^+ + H) (100); HRMS calcd for $C_{14}H_{22}N_3O_5S$ (M^+ + H): 344.1280; found: 344.1281.

6. General procedure for Pd(II)-catalyzed C(sp^3)–H arylation of *N*-(2-pyridylsulfonyl) amino acid esters. An oven dried Ace Pressure tube with Teflon stir bar was charged with the appropriate *N*-(2-pyridylsulfonyl) amino acid ester (0.25 mmol, 1.0 equiv), $Pd(OAc)_2$ (6 mg, 0.025 mmol, 10 mol%), AgOAc (62 mg, 0.375 mmol, 1.5 equiv), aryl iodide (0.625 mmol, 2.5 equiv) and 1,1,1,3,3,3-hexaflouro-2-propranol (0.25 mL). The pressure tube was then sealed with a screw-cap and the reaction was placed in a preheated oil bath at the temperature and over the time period indicated for each example. At this point, the reaction mixture was removed from the oil bath and allowed to cool to room temperature. The reaction mixture was then diluted with CH_2Cl_2, filtered through a pad of Celite® and concentrated under reduced pressure. The residue was purified by column chromatography using mixtures of toluene/EtOAc or hexane/EtOAc as eluent to afford the corresponding arylated amino acid derivative.

[5] D. Hernádez, E. Riego, A. Francesch, C. Cuevas, F. Albericio, M. Alvarez, *Tetrahedron* **2007,** *63*, 9862-9870.
[6] F. Kolundzic, M. N. Noshi, M. Tjandra, M. Movassaghi, S. J. Miller, *J. Am. Chem. Soc.* **2011**, *133*, 9104-9111.

Methyl (3*S*)-4-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-L-valinate (**2a**)



Compound **2a** was prepared from methyl *N*-(2-pyridylsulfonyl)-L-valinate **1** (68 mg, 0.25 mmol) and 4-iodotoluene (136 mg, 0.625 mmol) following the general procedure, after heating at 140 ºC for 4 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 5:1), as yellow oil (63 mg, yield 70%).

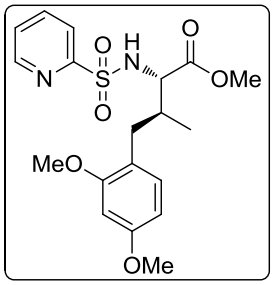
$[\alpha]_D$ = + 69 (c = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (d, *J* = 4.6 Hz, 1H), 7.98-7.77 (m, 2H), 7.49-7.43 (m, 1H), 7.09-6.96 (m, 4H), 5.56 (d, *J* = 9.4 Hz, NH), 4.23 (dd, *J* = 9.3, 4.5 Hz, 1H), 3.55 (s, 3H), 2.76 (dd, *J* = 12.8, 4.0 Hz, 1H), 2.34-2.20 (m, 5H), 0.92 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.6, 157.9, 149.8, 138.1, 136.3, 135.8, 129.1, 126.8, 122.0, 61.3, 52,4, 39.1, 38.0, 21,1, 16.0.

MS (FAB) *m/z*: 363 (M^+ + H) (100); HRMS calcd for $C_{18}H_{23}N_2O_4S$ (M^+ + H): 363.1379; found: 363.1381.

Methyl (3*S*)-4-(2,4-dimethoxyphenyl)-*N*-(2-pyridylsulfonyl)-L-valinate (**2b**)



Compound **2b** was prepared from methyl *N*-(2-pyridylsulfonyl)-L-valinate **1** (68 mg, 0.25 mmol) and 2,4-dimethoxy-iodobencene (165 mg, 0.625 mmol) following the general procedure, after heating at 150 ºC for 3 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 5:1), as a white solid (69 mg, yield 68%).

$[\alpha]_D$ = + 46 (c = 1, CH_2Cl_2).

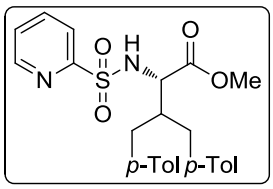
m.p.: 56-58 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (d, *J* = 3,8, Hz, 1H), 7.98-7.90 (m, 1H), 7.89-7.81 (m, 1H), 7.43 (ddd, *J* = 7.4, 4.7, 1.3 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 1H), 6.41-6.34 (m, 2H), 5.74 (d, *J* = 9.5 Hz, NH), 4.19 (dd, *J* = 9.6, 3.9 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.35 (s, 3H), 2.72 (dd, *J* = 13.2, 6.3 Hz, 1H), 2.43-2.30 (m, 1H), 2.29-2.18 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.7, 159.7, 158.3, 158.2, 149.8, 137.9, 131.5, 126.6, 121.8, 119.9, 104.2, 98.5, 61.1, 55.5, 55.4, 52.1, 37.4, 31.8, 17.4.

MS (FAB) *m/z*: 409 (M^+ + H) (100); HRMS calcd for $C_{19}H_{25}N_2O_6S$ (M^+ + H): 409.1433; found: 409.1436.

Methyl 4,4'-[bis-(4-methylphenyl)]-*N*-(2-pyridylsulfonyl)-L-valinate (**3a**)



Compound **3a** was prepared from methyl *N*-(2-pyridylsulfonyl)-L-valinate **1** (68 mg, 0.25 mmol) following the general procedure but using 3.0 equiv of AgOAc (125 mg, 0.75 mmol) and 5.0 equiv of 4-iodotoluene (273 mg, 1.25 mmol), after heating at 150 ºC for 4 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 5:1), as a white solid (104 mg, yield 92%).

$[\alpha]_D$ = + 80 (c = 0.5, CH_2Cl_2) (≥99% *ee*).

Ee determination by chiral HPLC analysis, Chiralpak IB column, Heptane:*i*-PrOH 90:10, flow rate: 0.7 mL/min, retention times: 25.9 min (L), 32.0 min (D).

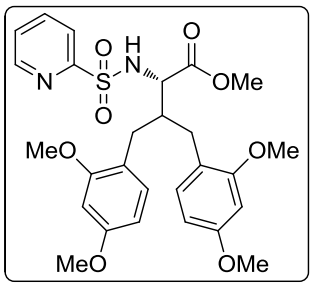
m.p.: 142-145 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.60 (d, *J* = 4.5 Hz, 1H), 7.96-7.76 (m, 2H), 7.43 (dt, *J* = 6.7, 3.6, 1H), 7.10-7.00 (m, 6H), 7.00-6.93 (m, 2H), 5.37 (d, *J* = 9.3 Hz, NH), 4.33 (d, *J* = 8.6 Hz, 1H), 3.38 (s, 3H), 2.81 (t, *J* = 7.5 Hz, 1H), 2.64-2.47 (m, 4H), 2.30 (d, *J* = 5.2 Hz, 6H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.7, 157.8, 149.9, 137.8, 136.4, 135.9, 135.8, 158.7, 129.2, 129.1, 129.0, 126.6, 121.9, 58.2, 52.3, 45.9, 36.2, 35.1, 21.1, 21.0.

MS (FAB) *m/z*: 452 (M^+ + H) (100); HRMS calcd for $C_{25}H_{29}N_2O_4S$ (M^+ + H): 453.1848; found: 453.1840.

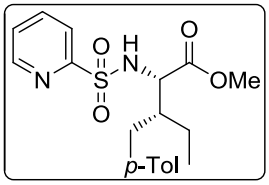
Methyl 4,4'-[bis-(2,4-dimethoxyphenyl)]-*N*-(2-pyridylsulfonyl)-L-valinate (**3b**)



Compound **3b** was prepared from methyl *N*-(2-pyridylsulfonyl)-L-valinate **1** (68 mg, 0.25 mmol) and 2,4-dimethoxy-iodobencene (165 mg, 0.625 mmol) following the general procedure, after heating at 150 ºC for 3 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 5:1), as yellow oil (23 mg, yield 17%). Compound **3b** was identified by HRMS.

MS (FAB) *m/z*: 544 (M^+ + H) (100); HRMS calcd for $C_{39}H_{29}N_2O_8S$ (M^+ + H): 545.1958; found: 545.1946.

Methyl 4´-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-L-isoleucinate (**5**)



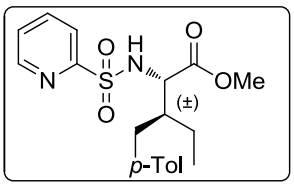
Compound **5** was prepared from methyl *N*-(2-pyridylsulfonyl)-L-isoleucinate **4** (72 mg, 0.25 mmol) and 4-iodotoluene (136 mg, 0.625 mmol) following the general procedure, after heating at 150 ºC for 4 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 2:1), as yellow solid (24 mg, yield 25%) (86% purity, measured by ^{1}H NMR).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (d, *J* = 4.5 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.4, 1.6 Hz, 1H), 7.48 (ddd, *J* = 7.3, 4.6, 1.4 Hz, 1H), 7.10 (s, 4H), 5.40 (d, *J* = 9.8 Hz, NH), 4.34 (dd, *J* = 9.8, 3.6 Hz,1H), 3.51 (s, 3H), 2.71 (dd, *J* = 14.1, 7.5 Hz, 1H), 2.56 (dd, *J* = 14.1, 7.5 Hz, 1H), 2.32 (s, 3H), 2.06 (m, 1H), 1.43-1.21 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.9, 157.8, 149.7, 137.9, 136.6, 135.6, 129.1, 129.0, 126.6, 121.7, 58.4, 52.2, 45.8, 35.8, 21.9, 21.0, 11.5.

MS (FAB) *m/z*: 377 (M^+ + H) (100); HRMS calcd for $C_{19}H_{25}N_2O_4S$ (M^+ + H): 377.1535; found: 377.1537.

Methyl 4´-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**7a**)



Compound **7a** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** (72 mg, 0.25 mmol) and 4-iodotoluene (136 mg, 0.625 mmol) following the general procedure, after heating at 150 ºC for 4 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 2:1), as a white solid (68 mg, yield 72%).

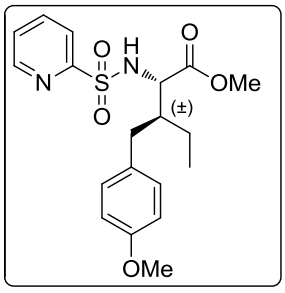
m.p.: 113-116 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (dt *J* = 4.6, 1.7 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.86 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.45 (ddd, *J* = 7.7, 4.6, 1.5 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 7.8 Hz, 2H), 5.40 (d, *J* = 9.4 Hz, NH), 4.43 (dd, *J* = 9.5 , 3.4 Hz, 1H), 3.48 (s, 3H), 2.51 (m, 2H), 2.30 (s, 3H), 2.15-2.02 (m, 1H), 1.50 (m, 1H), 1.34 (m, 1H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.9, 157.7, 149.7, 137.9, 136.2, 135.6, 129.1, 129.0, 126.6, 121.8, 58.2, 52.3, 45.4, 35.4, 22.9, 20.9, 11.5.

MS (FAB) *m/z*: 377 (M^+ + H) (100); HRMS calcd for $C_{19}H_{25}N_2O_4S$ (M^+ + H): 377.1535; found: 377.1539.

Methyl 4´-(4-methoxyphenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**7b**)



Compound **7b** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** (72 mg, 0.25 mmol) and 4-iodoanisole (146 mg, 0.625 mmol) following the general procedure, after heating at 150 ºC for 4 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 3:1), as a white solid (73 mg, yield 75%).

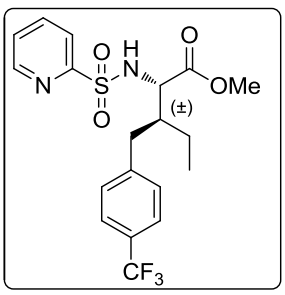
m.p.: 113-117 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (d, *J* = 4.7 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.86 (dt, *J* = 7.7 Hz, 1.3 Hz, 1H), 7.45 (ddd, *J* = 7.7, 4.6, 1.2 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.5 Hz, 2H), 5.46 (d, *J* = 9.4 Hz, NH), 4.41 (dd, *J* = 9.4, 3.5 Hz, 1H), 3.76 (s, 3H), 3.47 (s, 3H), 3.47 (t, *J* = 7.8 Hz, 2H), 2.15-1-96 (m, 1H), 1.51 (m, 1H), 1.30 (m, 1H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.9, 158.0, 157.7, 149.7, 137.9, 131.3, 130.1, 126.6, 121.8, 113.7, 58.1, 55.2, 52.3, 45.6, 34.9, 22.9, 11.5.

MS (FAB) *m/z*: 392 (M^+ + H) (100); HRMS calcd for $C_{19}H_{25}N_2O_5S$ (M^+ + H): 392.1539; found: 392.1543.

Methyl 4´-(3- trifluoromethylphenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**7c**)



Compound **7c** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** (72 mg, 0.25 mmol) and 4-iodobenzotrifluoride (92 µL, 0.625 mmol), following the general procedure, after heating at 150 ºC for 4 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 3:1), as a white solid (77 mg, yield 72%).

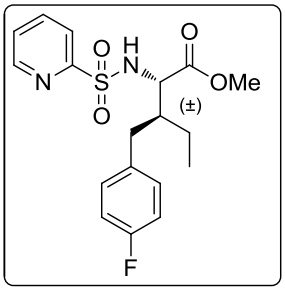
m.p.: 128-131 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, *J* = 4.6 Hz, 1H), 7.96-7.78 (m, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.49-7.40 (m, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 5.45 (d, *J* = 9.1 Hz, NH), 4.38 (dd, *J* = 9.1, 3.5 Hz, 1H), 3.51 (s, 3H), 2.63 (dd, *J* = 7.3, 4.6 Hz, 2H), 2.13 (m, 1H), 1.59 (m, 1H), 1.29 (m, 1H), 0.97 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.7, 157.6, 149.7, 143.7, 137.9, 129.5, 126.7, 125.2, 121.8, 58.0, 52.4, 45.3, 35.7, 22.8, 11.4.

MS (FAB) *m/z*: 431 (M^+ + H) (100); HRMS calcd for $C_{19}H_{22}F_3N_2O_4S$ (M^+ + H):431.1252; found: 431.1251.

Methyl 4´-(4-fluorophenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**7d**)



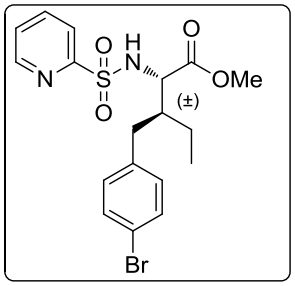
Compound **7d** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** (72 mg, 0.25 mmol) and fluoro-4-iodobenzene (72 µL, 0.625 mmol) following the general procedure, after heating at 150 ºC for 6 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 3:1), as yellow oil (67 mg, yield 71%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (dt, *J* = 4.6, 1.5 Hz, 1H), 7.98-7.80 (m, 2H), 7.46 (ddd, *J* = 6.9, 4.7, 1.9 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.6 Hz, 2H), 5.37 (d, *J* = 9.2 Hz, NH), 4.40 (dd, *J* = 9.3, 3.4 Hz, 1H), 3.49 (s, 3H), 2.52 (dd, *J* = 7.3, 5.1 Hz, 2H), 2.15-2.01 (m, 1H), 1.53 (m, 1H), 1.30 (m, 1H), 0.96 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.8, 163.0 (d, $J_{F,C}$ = 244 Hz), 157.7, 149.7, 137.9, 135.0 (d, $J_{F,C}$ = 3.2 Hz), 130.5 (d, $J_{F,C}$ = 7.8 Hz), 126.7, 121.8, 115.2 (d, $J_{F,C}$ = 21.1 Hz), 58.0, 52.3, 45.6, 35.0, 22.8, 11.4.

MS (FAB) *m/z*: 381 (M^+ + H) (100); HRMS calcd for $C_{18}H_{22}FN_2O_4S$ (M^+ + H):381.1284; found: 381.1293.

Methyl 4´-(4-bromophenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**7e**)



Compound **7e** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** (72 mg, 0.25 mmol) and bromo-4-iodobenzene (177 mg, 0.625 mmol) following the general procedure, after heating at 150 ºC for 4 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 3:1), as a white solid (78 mg, yield 71%).

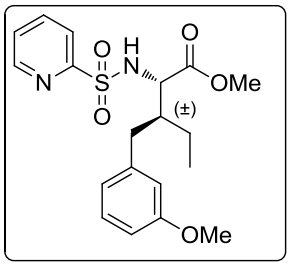
m.p.: 137-139 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (dd, *J* = 4.6 Hz, 1H), 8.00-7.79 (m, 2H), 7.46 (ddd, *J* = 6.5, 4.9, 1.7 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 5.49 (d, *J* = 9.3 Hz, NH), 4.36 (dd, *J* = 9.2 , 3.5 Hz, 1H), 3.50 (s, 3H), 2.51 (dd, *J* = 7.3, 4.6 Hz, 2H), 2.14-1.97 (bs, 1H), 1.63-1.43 (m, 1H), 1.38-1.09 (m, 1H), 0.95 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.7, 157.6, 149.7, 138.5, 137.9, 131.4, 130.9, 126.7, 121.9, 120.0, 58.0, 52.4, 45.4, 35.3, 22.8, 11.5.

MS (FAB) *m/z*: 441 (M^+ + H) (100); HRMS calcd for $C_{18}H_{22}BrN_2O_4S$ (M^+ + H): 441.0484; found: 441.0487.

Methyl 4´-(3-methoxyphenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**7f**)



Compound **7f** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** (72 mg, 0.25 mmol) and 3-iodoanisole (74 µL, 0.625 mmol), following the general procedure, after heating at 150 ºC for 8 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 3:1), as a white solid (70 mg, yield 71%).

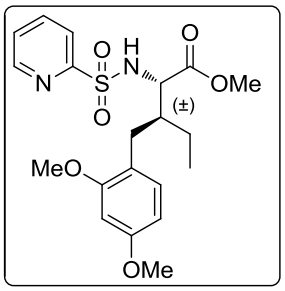
m.p.: 112-115 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (dd, *J* = 4.7, 1.7 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.87 (dt, *J* = 7.2 Hz, 1.8 Hz, 1H), 7.45 (ddd, *J* = 7.2, 4.7, 1.6 Hz, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.77-6.59 (m, 3H), 5.36 (d, *J* = 9.3 Hz, NH), 4.42 (dd, *J* = 9.3, 3.4 Hz, 1H), 3.78 (s, 3H), 3.50 (s, 3H), 2.54 (m, 2H), 2.20-2.01 (bs, 1H), 1.52 (m, 1H), 1.31 (m, 1H), 0.96 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.9, 159.6, 157.7, 149.7, 141.0, 137.9, 129.3, 126.6, 121.8, 121.6, 114.9, 111.5, 58.2, 55.2, 52.3, 45.3, 36.9, 22.9, 11.5.

MS (FAB) *m/z*: 393 (M^+ + H) (100); HRMS calcd for $C_{19}H_{25}N_2O_5S$ (M^+ + H): 393.1484; found: 393.1482.

Methyl 4´-(2,4-dimethoxyphenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucinate (**7g**)



Compound **7g** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucinate **6** (72 mg, 0.25 mmol) and 2,4-dimethoxy-iodobenzene (72 µL, 0.625 mmol), following the general procedure, after heating at 150 ºC for 8 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 3:1), as a white solid (76 mg, yield 72%).

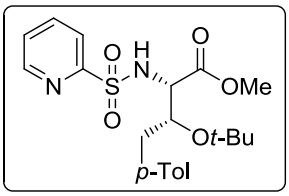
m.p.: 123-126 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.55 (dt, *J* = 4.6, 1.5 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.78 (dt, *J* = 7.5, 1.5 Hz, 1H), 7.36 (ddd, *J* = 7.4, 4.7, 1.4 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 1H), 6.39-6.14 (m, 2H), 5.78 (d, *J* = 9.6 Hz, NH), 4.28 (dd, *J* = 9.8, 2.7 Hz, 1H), 3.74 (s, 3H), 3.68 (s, 3H), 3.14 (s, 3H), 2.54 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.28 (dd, *J* = 13.9, 6.7 Hz, 1H), 2.18-2.02 (m, 1H), 1.55-1.23 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.8, 159.5, 158.1, 149.7, 137.8, 131.5, 126.4, 121.5, 119.5, 104.3, 98.3, 57.8, 55.3, 55.2, 51.9, 44.3, 29.4, 24.5, 11.7.

MS (FAB) *m/z*: 423 (M^+ + H) (100); HRMS calcd for $C_{20}H_{27}N_2O_6S$ (M^+ + H): 423.1590; found: 423.1581.

Methyl *O*-(*tert*-butyl)-4-(4-methylphenyl*)-N*-(2-pyridylsulfonyl)-L-threoninate (**9**)



Compound **9** was prepared from methyl methyl *O*-(*tert*-butyl)-*N*-(2-pyridylsulfonyl)-L-threoninate **8** (83 mg, 0.25 mmol) and 4-iodotoluene (136 mg, 0.625 mmol) following the general procedure but using 1.2 mL of 1,1,1,3,3,3-hexaflouro-2-propranol (0.2 M), after heating at 120 ºC for 4 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 2:1), as yellow oil (74 mg, yield 70%).

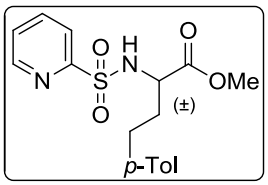
$[\alpha]_D$ = +21 (c = 1, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (d, *J* = 4.5 Hz, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.81 (t, *J* = 7.3, 1H), 7.45 (ddd, *J* = 7.5, 4.6, 1.4 Hz, 1H), 7.16 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 5.59 (d, *J* = 10.4 Hz, NH), 4.23 (d, *J* = 10.5, 1H), 4.07 (ddd, *J* = 10.0, 3.9, 1.4, 1H), 3.41 (s, 3H), 3.06 (dd, *J* = 13.8, 10.0 Hz, 1H), 2.79 (dd, *J* = 13.8, 10.0 Hz, 1H), 2.32 (s, 3H), 1.09 (s, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.2, 158.1, 149.7, 137.8, 136.1, 134.2, 129.5, 129.4, 126.5, 121.6, 74.9, 74.1, 58.4, 52.1, 39.6, 28.2, 21.1.

MS (FAB) *m/z*: 365 (M^+ - 55), 421 (M^+ + H); HRMS calcd for $C_{21}H_{29}N_2O_5S$ (M^+ + H): 421.1797; found: 421.1789.

Methyl 4-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-DL-homoalaninate (**11**)



Compound **11** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-homoalalinate **10** (65 mg, 0.25 mmol) and 4-iodotoluene (136 mg, 0.625 mmol) following the general procedure but using 20 mol% of $Pd(OAc)_2$ (11 mg, 0.05 mmol) and 3.0 equiv of AgOAc (136 mg, 0.625 mmol), after heating at 150 ºC for 16 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 1:1), as a white solid (38 mg, yield 44%).

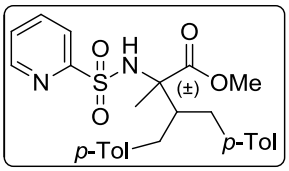
m.p.: 113-115 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (d, *J* = 4.6 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.6, 1.6 Hz, 1H), 7.49 (ddd, *J* = 7.5, 4.7, 1.3 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 5.45 (d, *J* = 8.8 Hz, NH), 4.28 (m, 1H), 3.50 (s, 3H), 2.61 (t, *J* = 7.9 Hz, 2H), 2.23 (s, 3H), 2.08-1.80 (m, 2H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 172.1, 157.9, 149.8, 138.0, 137.3, 135.6, 129.1, 128.3, 126.7, 121.7, 56.4, 52.4, 35.3, 30.7, 20.9.

MS (FAB) *m/z*: 349 (M^+ + H) (100); HRMS calcd for $C_{17}H_{21}N_2O_4S$ (M^+ + H): 349.1222; found: 349.1229.

Methyl 4,4'-[bis-(4-methylphenyl)]-2-methyl-*N*-(2-pyridylsulfonyl)-DL-isoleucinate (**13**)



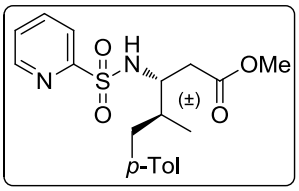
Compound **13** was prepared from methyl 2-methyl *N*-(2-pyridylsulfonyl)-DL-isoleucinate **12** (72 mg, 0.25 mmol) following the general procedure, after heating at 150 ºC for 8 h, but using 2.0 equiv of AgOAc (83 mg, 0.50 mmol) and 3.0 equiv of 4-iodotoluene (175 mg, 0.75 mmol). The title compound was obtained, after purification by column chromatography (hexane/EtOAc 2:1), as colourless oil (70 mg, yield 60%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, *J* = 4.4 Hz, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.88 (dt, *J* = 7.5, 1,5 Hz, 1H), 7.45 (ddd, *J* = 7.2, 4.5, 1.1 Hz, 1H), 7.09-6.78 (m, 8H), 5.6 (bs, NH), 3.27 (s, 3H), 2.95-2.68 (m, 2H), 2.59-2-40 (m, 2H), 2.26 (s, 6H), 1.49 (s, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 174.5, 160.4, 151.2, 139.4, 138.3, 137.0, 136.9, 130.5, 130.4, 127.7, 123.1, 67.1, 53.7, 52.4, 36.7, 36.5, 22.3, 19.6.

MS (ESI) *m/z*: 467 (M^+ + H) (100); 933 ($2M^+$ + H); HRMS calcd for $C_{26}H_{31}N_2O_4S$ (M^+ + H): 467.2005, found:467.2012.

Methyl (4*S*)-5-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-DL-β-leucinate (**15**)



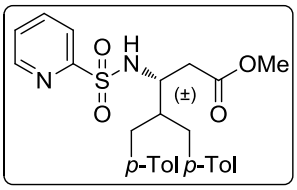
Compound **15** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-β-leucinate **14** (72 mg, 0.25 mmol) and 4-iodotoluene (136 mg, 0.625 mmol) following the general procedure, after heating at 150 ºC for 6 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 2:1), as colourless oil (40 mg, yield 43%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.68 (d, *J* = 4.4 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.88 (td, *J* = 7.6, 1.7 Hz, 1H), 7.46 (ddd, *J* = 7.6, 4.7, 1.3 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 5.63 (d, *J* = 8.9 Hz, NH), 3.68 (m,1H), 3.60 (s, 3H), 2.90 (dd, *J* = 13.3, 4.2 Hz, 1H), 2.60 (dd, *J* = 16.0, 5.1 Hz, 1H), 2.53 (dd, *J* = 16.1, 5.6 Hz, 1H), 2.31 (s, 3H), 2.14 (m, 1H), 2.00 (m, 1H), 0.77 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.8, 168.2, 149.9, 137.9, 136.9, 135.4, 129.0, 128.9, 126.5, 122.0, 55.7, 51.7, 39.2, 38.8, 35.9, 20.9, 15.2.

MS (FAB) *m/z*: 377 (M^+ + H) (100); HRMS calcd for $C_{19}H_{25}N_2O_4S$ (M^+ + H): 377.1535; found: 377.1541.

Methyl 5,5'-[bis-(4-methylphenyl)]-*N*-(2-pyridylsulfonyl)-DL-β-leucinate (**16**)



Compound **16** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-β-leucinate **14** (72 mg, 0.25 mmol) following the general procedure but using 3.0 equiv of AgOAc (125 mg, 0.75 mmol) and 5.0 equiv of 4-iodotoluene (273 mg, 1.25 mmol), after heating at 150 ºC for 6 h. The title compound was obtained, after purification by column chromatography (toluene/EtOAc 2:1), as a white solid (74 mg, yield 64%).

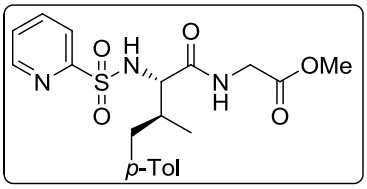
m.p.: 92-94 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, *J* = 3.6 Hz, 1H), 7.80 (d, *J* = 3.4 Hz, 2H), 7.45 (q, *J* = 4.4 Hz, 1H), 7.05 (d, *J* =7.9, 2 Hz, 4H), 6.94 (dd, *J* = 7.8, 2.0 Hz, 4H), 5.47 (d, *J* = 8.4 Hz, NH),3.79 (m,1H), 3.49 (s, 3H), 2.69 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.59-2.37 (m, 6H), 2.31 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.2, 157.6, 149.9, 137.7, 136.7, 136.4, 135.4, 129.0, 128.9, 128.8, 128.7, 126.4, 122.2, 52.8, 51.6, 46.2, 36.6, 35.6, 35.3, 20.9, 20.9.

MS (FAB) *m/z*: 467 (M^+ + H) (100); HRMS calcd for $C_{26}H_{31}N_2O_4S$ (M^+ + H): 467.2005; found: 467.2000.

Methyl (3*S*)-4-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-L-valylglycinate (**19**)



Compound **19** was prepared from methyl *N*-(2-pyridylsulfonyl)-L-valylglycinate **18** (66 mg, 0.2 mmol) following the general procedure but using 3.0 equiv of AgOAc (100 mg, 0.6 mmol), after heating at 150 ºC for 8 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 1:1), as a white solid (50 mg, yield 60%).

$[\alpha]_D$ = +31 (c = 1, CH_2Cl_2).

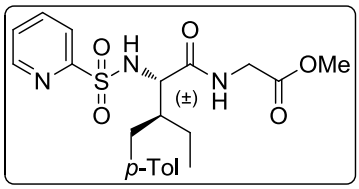
m.p.: 114-117 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.87 (td, *J* = 7.5, 1.5 Hz, 1H), 7.47 (ddd, *J* = 7.5, 4.7, 1.3 Hz, 1H), 7.10–6.95 (m, 4H), 6.82 (bs, NH), 5.48 (d, *J* = 8.1 Hz, NH), 4.03 (dd, *J* = 8.1, 4.2 Hz, 1H), 3.96 (d, *J* = 5.4 Hz, 2H), 3.75 (s, 3H), 2.84 (d, *J* = 8.4 Hz, 1H), 2.30 (s, 5H), 0.88 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.4, 169.7, 157.4, 149.9, 138.1, 136.3, 135.6, 129.0, 129.0, 126.8, 122.2, 61.5, 52.4, 41.2, 38.7, 37.7, 20.9, 15.6.

MS (FB) *m/z*: 420 (M^+ + H) (100); HRMS calcd for $C_{20}H_{25}N_3O_5S$ (M^+ + H): 420.1515; found: 420.1581.

Methyl 4´-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-DL-alloisoleucylglycinate (**21**)



Compound **21** was prepared from methyl *N*-(2-pyridylsulfonyl)-DL-alloisoleucylglycinate **20** (86 mg, 0.25 mmol) following the general procedure but using 3.0 equiv of AgOAc (125 mg, 0.75 mmol), after heating at 150 ºC for 8 h. The title compound was obtained, after purification by column chromatography (hexane/EtOAc 3:1), as a white solid (47 mg, yield 43%).

m.p.: 152 -154 ºC

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.2 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.86 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.47 (ddd, *J* = 7.4, 5.0, 1.4 Hz, 1H), 7.15 (bs, NH), 6.99 (m, 4H), 5.81 (dd, *J* = 8.1 Hz, 1H), 4.18 (dd, *J* = 8.1, 3.5 Hz,1H), 3.93 (dq, *J* = 18.1, 5.3 Hz, 2H), 3.73 (s, 3H), 2.70 (dd, *J* = 13.7, 5.3 Hz, 1H), 2.38 (m, 1H), 2.29 (s, 3H), 2.12 (bs, 1H), 1.35 (m, 2H), 0.78 (t, *J* = 7.3 Hz, 3H).

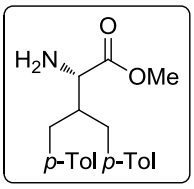
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.9, 169.8, 157.2, 149.9, 138.2, 136.5, 135.5, 129.0, 128.9, 126.8, 122.3, 58.5, 52.3, 45.3, 41.3, 35.2, 22.1, 20.9, 11.5.

MS (FB) *m/z*: 434 (M^+ + H) (100); HRMS calcd for $C_{21}H_{27}N_3O_5S$ (M^+ + H): 434.1750; found: 434.1751.

7. Preparative-scale synthesis of methyl 4,4'-[bis-(4-methylphenyl)]-*N*-(2-pyridylsulfonyl)-L-valinate (3a). An oven dried Ace Pressure tube with Teflon stir bar was charged with methyl *N*-(2-pyridylsulfonyl)-L-valinate (**1**) (545 mg, 2.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (90 mg, 0.2 mmol, 10 mol%), AgOAc (1.14 g, 6.0 mmol, 3.0 equiv), 4-iodotoluene (4.36 g, 20.0 mmol, 5.0 equiv) and 1,1,1,3,3,3-hexafluoro-2-propranol (2.0 mL). The pressure tube was then sealed with a screw-cap and the reaction was placed in a preheated oil bath at 150 ºC and stirring for 4 h. At this point, the reaction mixture was removed from the oil bath and allowed to cool to room temperature. The reaction mixture was then diluted with EtOAc (2.0 mL), filtered through a pad of Celite® and concentrated under reduced pressure. The residue was purified by column chromatography using a mixture of hexane/EtOAc (10:1) as eluent to afford **3a** in 98% yield (879 mg).

8. Procedure for the cleavage of the 2-pyridylsulfonyl directing group. An oven dried, nitrogen-flushed vial was charged with methyl 4,4'-[bis-(4-methylphenyl)]-*N*-(2-pyridylsulfonyl)-L-valinate **3a** (45 mg, 0.1 mmol) and zinc powder (327 mg, 5.0 mmol). Under an atmosphere of nitrogen, a mixture of THF/NH_4Cl (aq) (1:1) was added by syringe (5.0 mL) and the resulting mixture was stirred at 60 ºC for 16 h. After reaction was complete, the mixture was cooled to room temperature and the volatiles were removed in vacuo. The crude was then diluted with EtOAc (2.0 mL), washed with water and brine, dried over $MgSO_4$ and filtered. The volatiles were removed in vacuo and the residue was purified by column chromatography on silica gel (hexane/EtOAc 5:1), yielding **17a** as colourless oil in 73% yield (23 mg).

Methyl 4,4'-[bis-(4-methylphenyl)]-L-valinate (**17a**)



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.06 (s, 8H), 3.58 (s, 3H), 3.39 (d, *J* = 2.3 Hz, 1H), 2.68-2.44 (m, 5H), 2.31 (s, 6H).

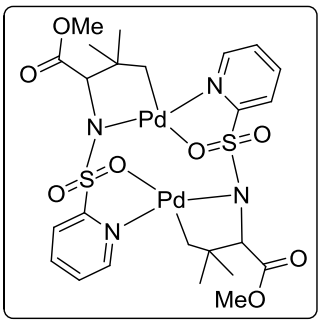
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 176.2, 137.2, 136.9, 135.5, 129.2, 129.1, 129.0, 128.9, 54.7, 51.8, 45.9, 36.3, 35.1, 21.0.

MS (FAB) *m/z*: 311 (M^+) (100); HRMS calcd for $C_{20}H_{25}NO_2$ (M^+): 311.1885; found: 311.1882.

$[\alpha]_D$ = +8 (c = 1, CH_2Cl_2) (98% *ee*).

Ee determination by chiral HPLC analysis, Chiralpak IC column Hexane:*i*-PrOH 95:5, flow rate: 1.0 mL/min, retention times: 16.1 min (L) and 20.1 min (D).

9a. Preparation of the bimetallic complex $C_{24}H_{32}N_4O_8Pd_2S_2$ (23).



An oven dried Ace Pressure tube with Teflon stir bar was charged with the methyl *N*-(2-pyridylsulfonyl)-L-*tert*-leucinate **22** (30 mg, 0.1 mmol), $Pd(OAc)_2$ (22 mg, 0.1 mmol) and anhydrous acetonitrile (0.1 mL). The pressure tube was then sealed with a screw-cap and the reaction was placed in a preheated oil bath at 60 ºC and stirring for 90 min. At this point, the reaction mixture was removed from the oil bath and allowed to cool to room temperature. The reaction mixture was then diluted with CH_2Cl_2, filtered through a pad of Celite® and concentrated under reduced pressure. The residue was purified by crystallisation (hexane/CH_2Cl_2) to afford the bimetallic complex **23** as yellow solid (62 mg, yield 80%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (d, J = 5.2 Hz, 2H), 8.03-7.88 (m, 4H), 7.44 (m, 2H), 3.82 (s, 6H), 3.30 (s, 3H), 3.20 (d, J = 6.3 Hz, 4H), 2.15 (d, J = 6.6 Hz, 2H), 0.91 (s, 6H), 0.85 (s, 6H)

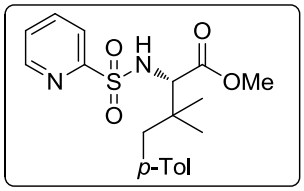
MS (ESI) *m/z*: 780 (M^+ + H) (100); HRMS calcd for $C_{24}H_{33}N_4O_8Pd_2S_2$ (M^+ + H): 780.9803; found: 780.9761

9b. Reactivity of the bimetallic complex $C_{24}H_{32}N_4O_8Pd_2S_2$ (23).

An oven dried Ace Pressure tube with Teflon stir bar was charged with the bimetallic complex **23** (10 mg, 0.0128 mmol, 1.0 equiv), 4-iodotoluene (14 mg, 0.064 mmol, 2.5 equiv respect to Pd) and 1,1,1,3,3,3-hexaflouro-2-propranol (0.1 mL). The pressure tube was then sealed with a screw-cap and the reaction was placed in a preheated oil bath at 60 ºC and stirring for 13 h. At this point, the reaction

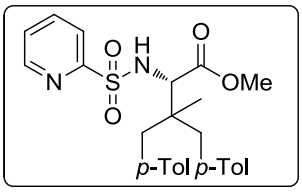
mixture was removed from the oil bath and allowed to cool to room temperature. the reaction mixture was allowed to cool to room temperature. The reaction mixture was then diluted with CH_2Cl_2, filtered through a pad of Celite® and concentrated under reduced pressure. ^{1}H NMR analysis of the crude material showed the formation of two arylated products **24** and **25** in a ratio 54:46, which were purified by column chromatography using a mixture of hexane/EtOAc (3:1) (79% yield). Both products were separated by preparative TLC in toluene/EtOAc (3:1).

Methyl 4-(4-methylphenyl)-*N*-(2-pyridylsulfonyl)-L-*tert*-leucinate (**24**)



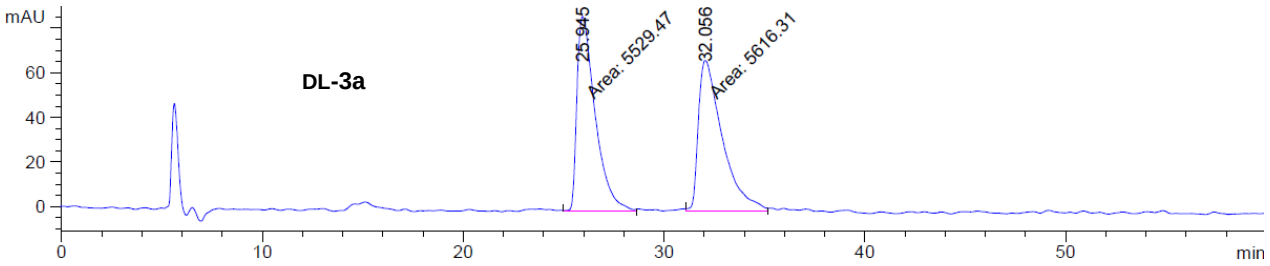
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.3 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.92 (m, 1H), 7.48 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 5.44 (d, *J* = 10.3 Hz, NH), 4.08 (d, *J* = 10.3 Hz, 1H), 3.54 (s, 3H), 2.69 (d, *J* = 13.2 Hz, 1H), 2.55 (d, *J* = 13.2 Hz, 1H), 0.92 (s, 3H), 0.88 (s, 3H).
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.2, 157.7, 149.6, 137.9, 136.7, 134.1, 130.7, 128.5, 126.6, 121.9, 64.8, 51.8, 43.9, 38.4, 23.2, 22.6, 20.9.
MS (ESI) *m/z*: 227 [(M^+ - 60), 377 (M^+ + H), 399 (M^+ + Na) (100), 775 ($2M^+$ + Na); HRMS calcd for $C_{19}H_{25}N_2O_4S$ (M^+ + H): 377.1538, found: 377.1529.

Methyl 4,4'-[bis-(4-methylphenyl)]-*N*-(2-pyridylsulfonyl)-L-*tert*-leucinate (**25**)

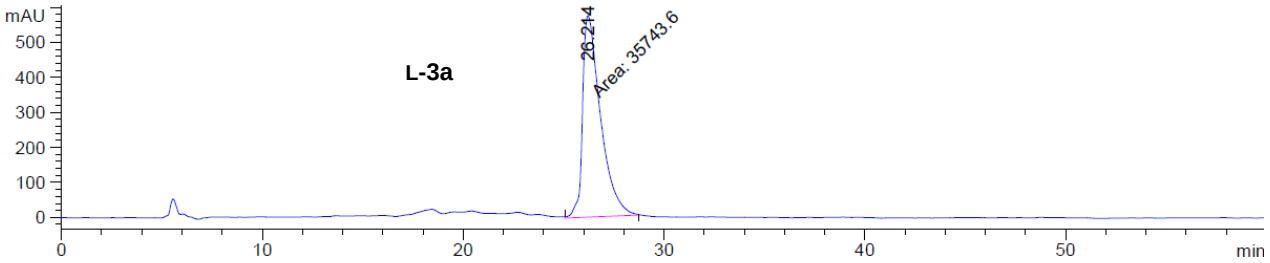


^{1}H NMR (500 MHz, $CDCl_3$): δ 8.66 (d, *J* = 4.4 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.87 (td, *J* = 7.6, 1,5 Hz, 1H), 7.47 (ddd, *J* = 7.6, 4.5, 1.5 Hz, 1H), 7.12-7.02 (m, 8H), 5.44 (d, *J* = 10.6 Hz, NH), 4.20 (d, *J* = 10.6 Hz, 1H), 3.47 (s, 3H), 2.87 (d, *J* = 13.5, 1H), 2.80 (d, *J* = 13.4, 1H), 2.65 (d, *J* = 13.3, 1H), 2.53 (d, *J* = 13.5, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 0.76 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 157.4, 149.8, 137.8, 136.0, 135.9, 133.8, 133.7, 131.1, 131.0, 128.7, 128.6, 126.6, 122.0, 62.0, 51.8, 41.9, 41.1, 41.0, 21.8, 21.0.
MS (ESI) *m/z*: 467 (M^+ + H) (100); HRMS calcd for $C_{26}H_{31}N_2O_4S$ (M^+ + H): 467.2005, found: 467.2009.

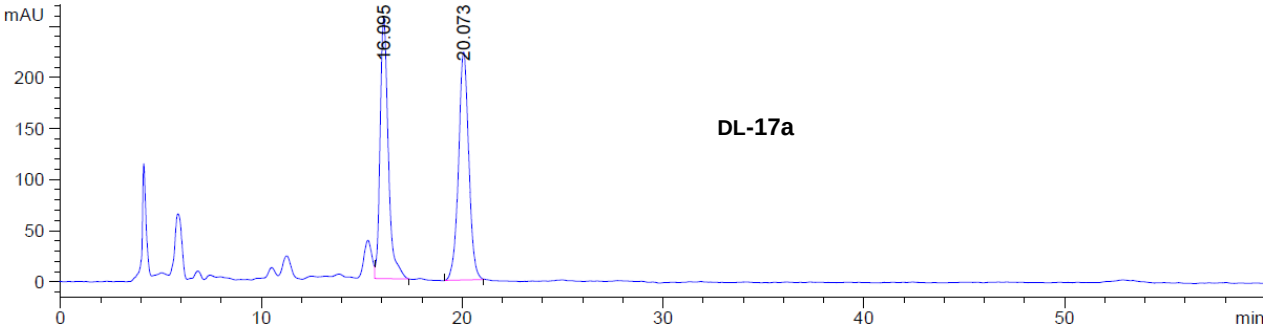
10. HPLC Chromatograms



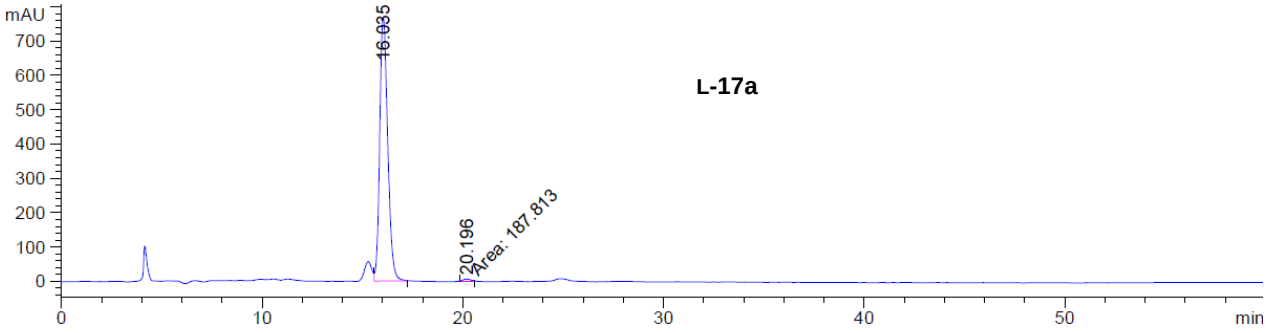
	Time	Area	Height	Width	Area %
1	25.945	5529.5	87.2	1.1	49.6105
2	32.056	5616.3	67.4	1.4	50.3895



	Time	Area	Height	Width	Area %
1	26.214	35743	575.7	1.1	100

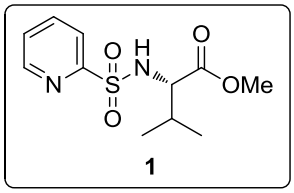


	Time	Area	Height	Width	Area %
1	16.095	7248.2	255.4	0.4	47.8005
2	20.073	7915.2	223.1	0.5	52.1995



	Time	Area	Height	Width	Area %
1	16.035	21235.3	767.8	0.4	99.1233
2	20.196	187.8	6.4	0.5	0.8767

11. NMR spectra



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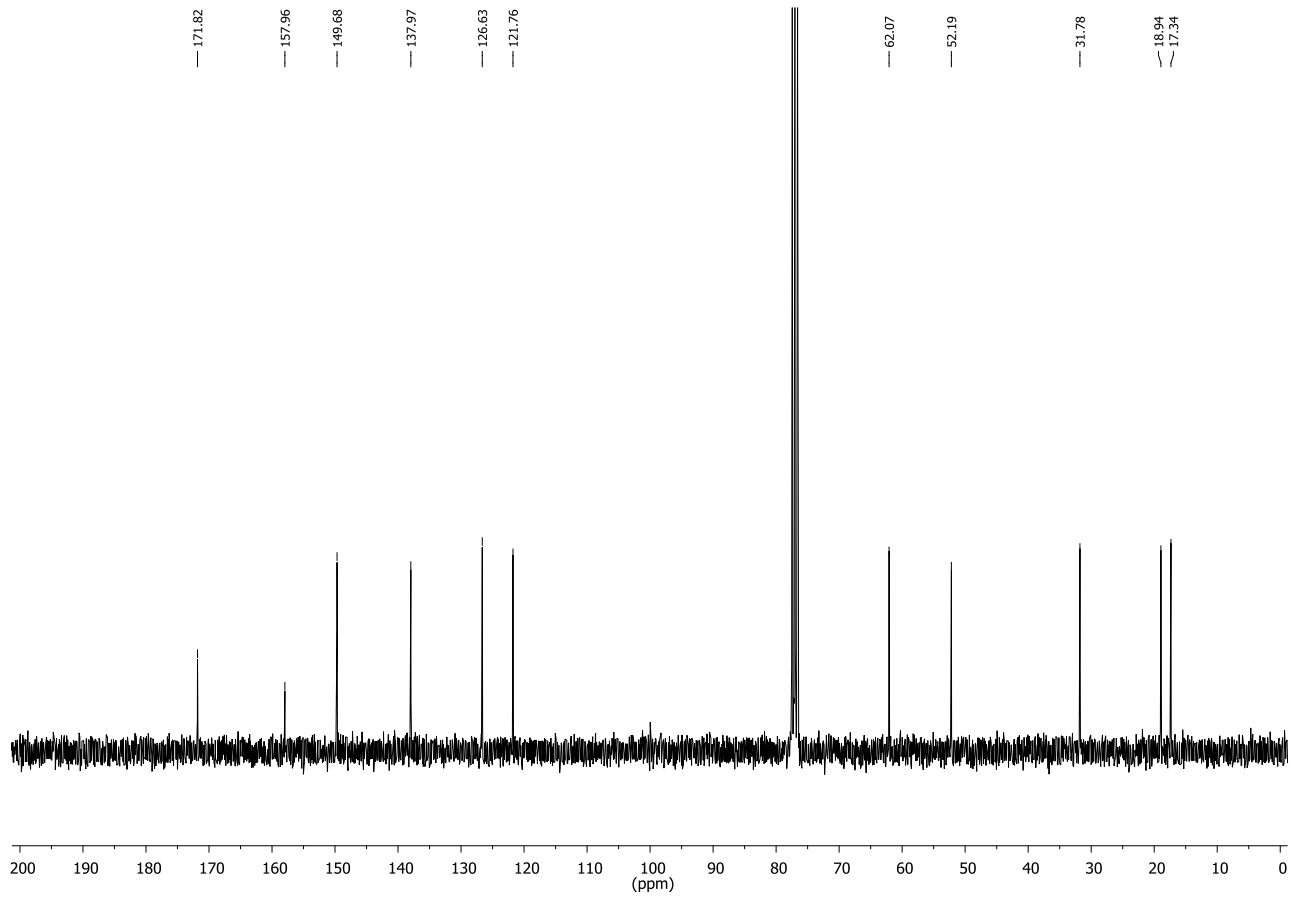

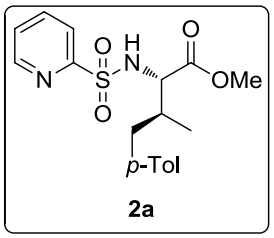

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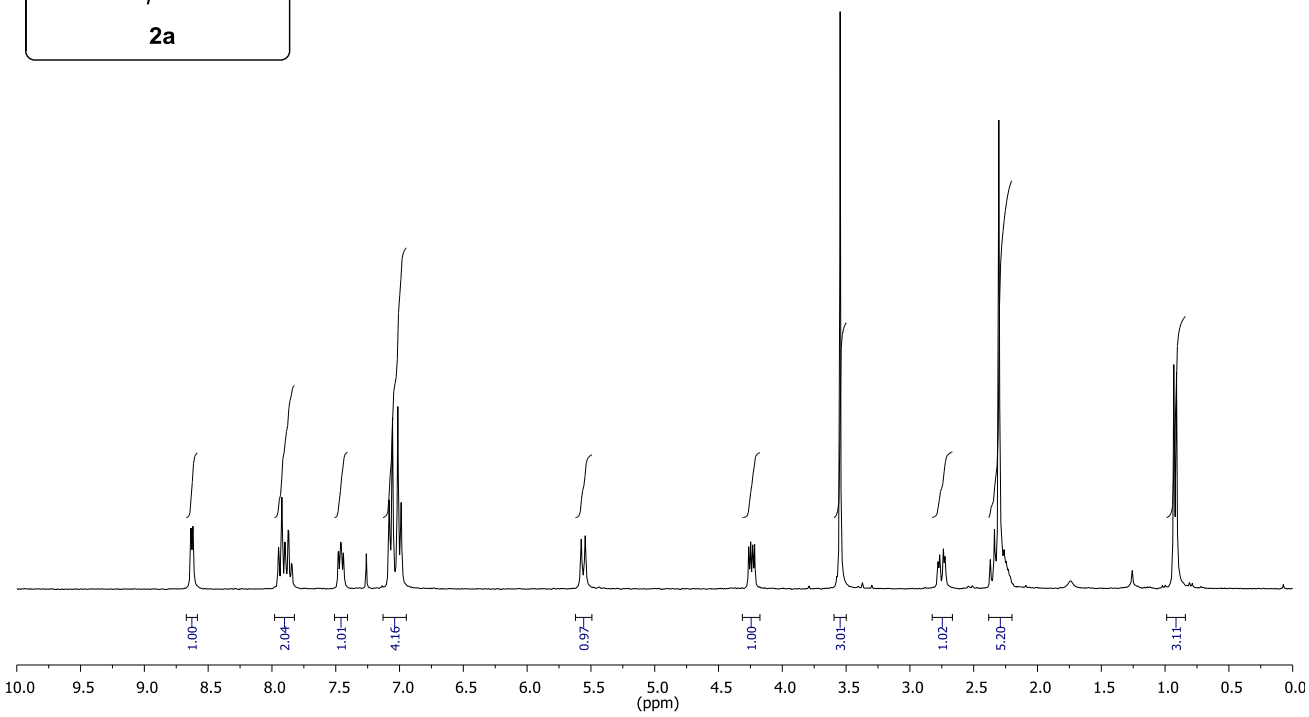

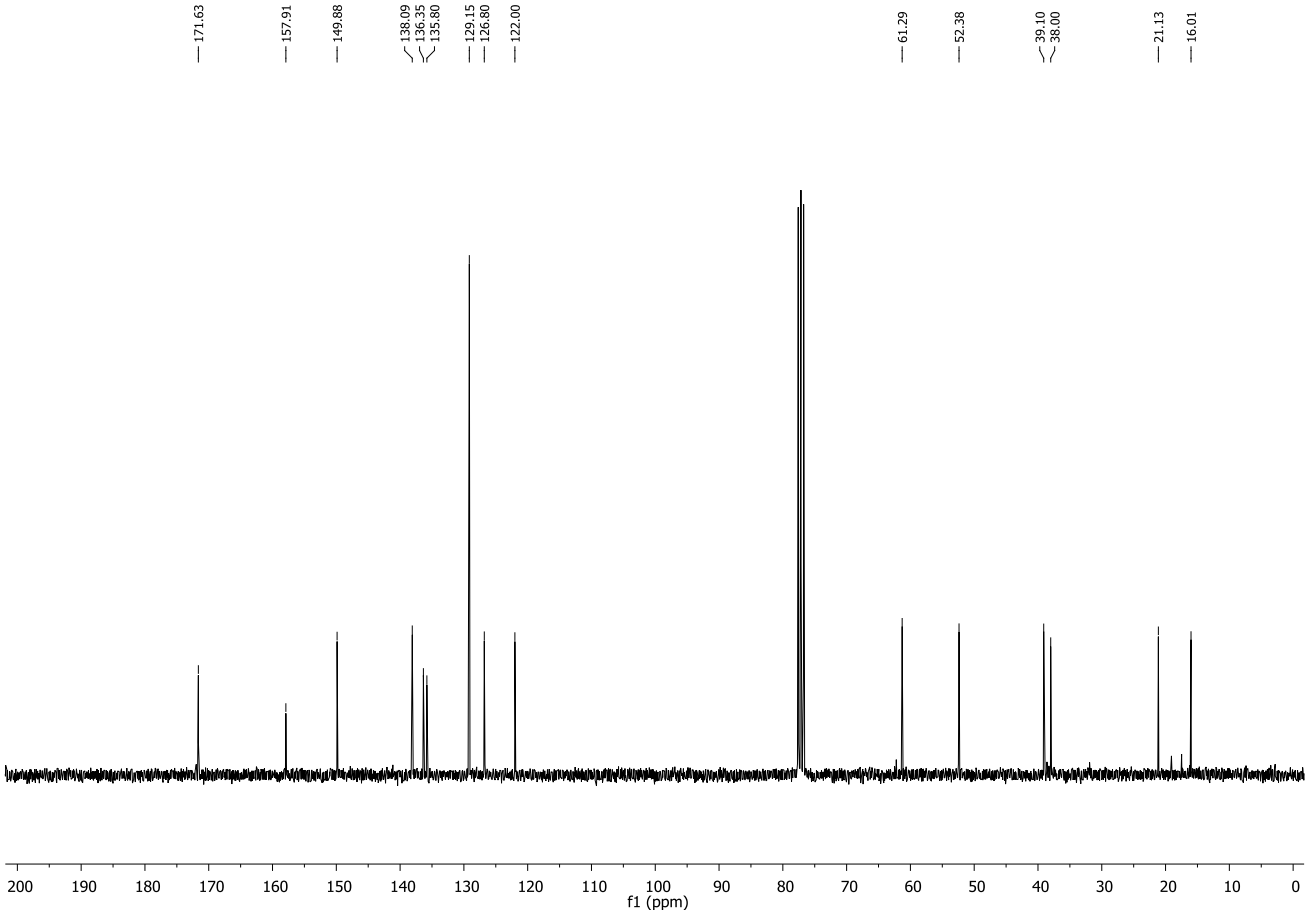

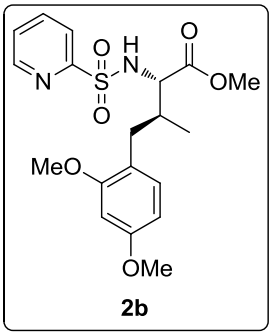

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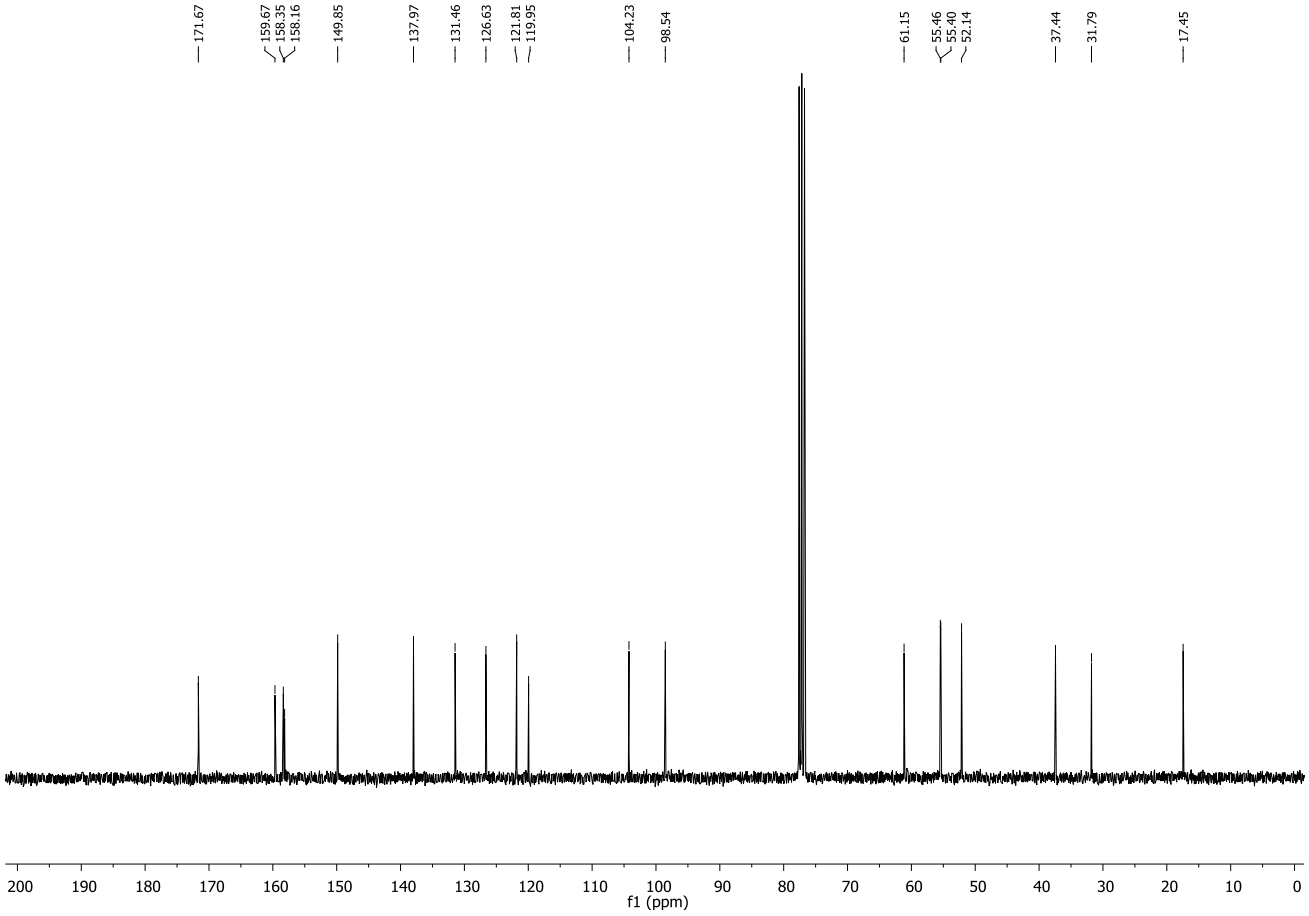

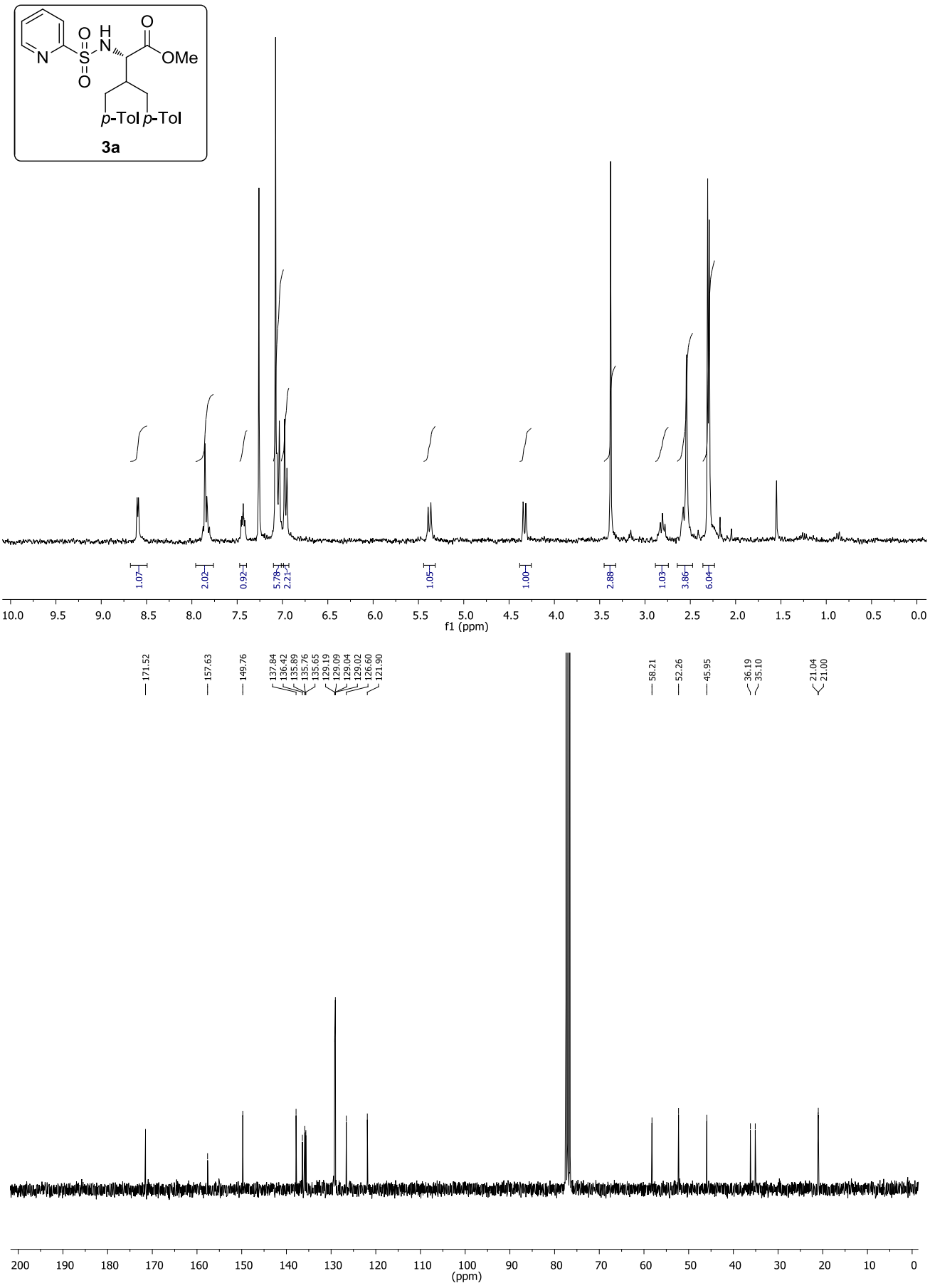

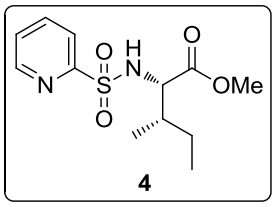

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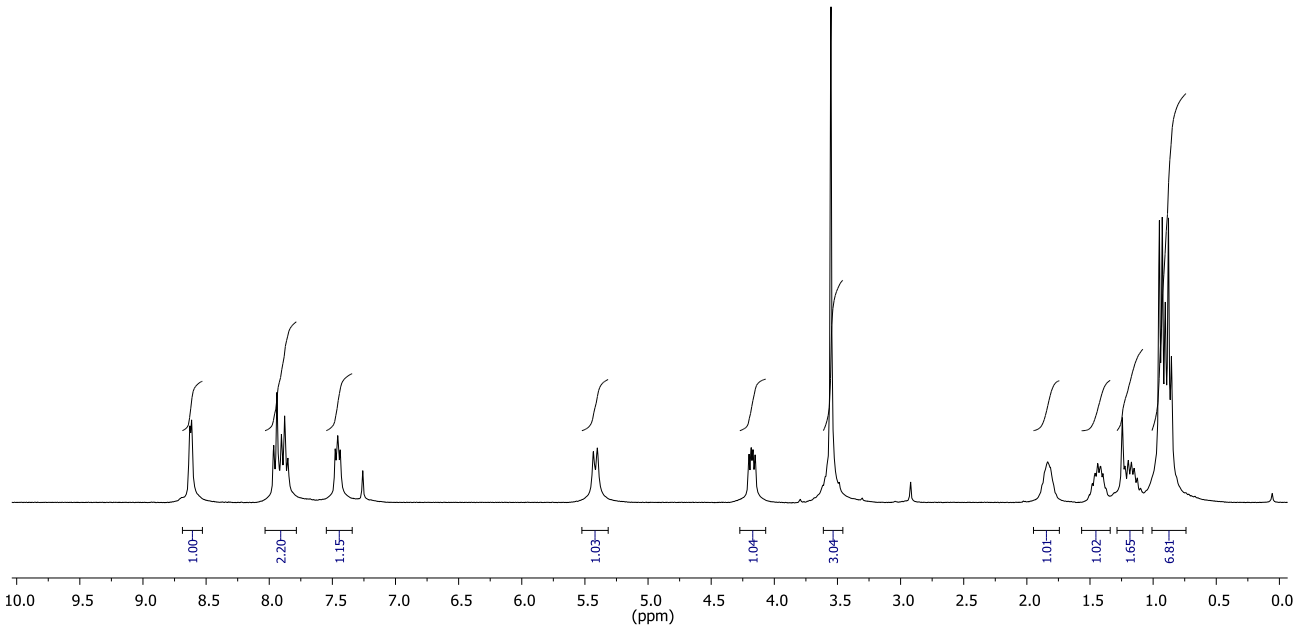

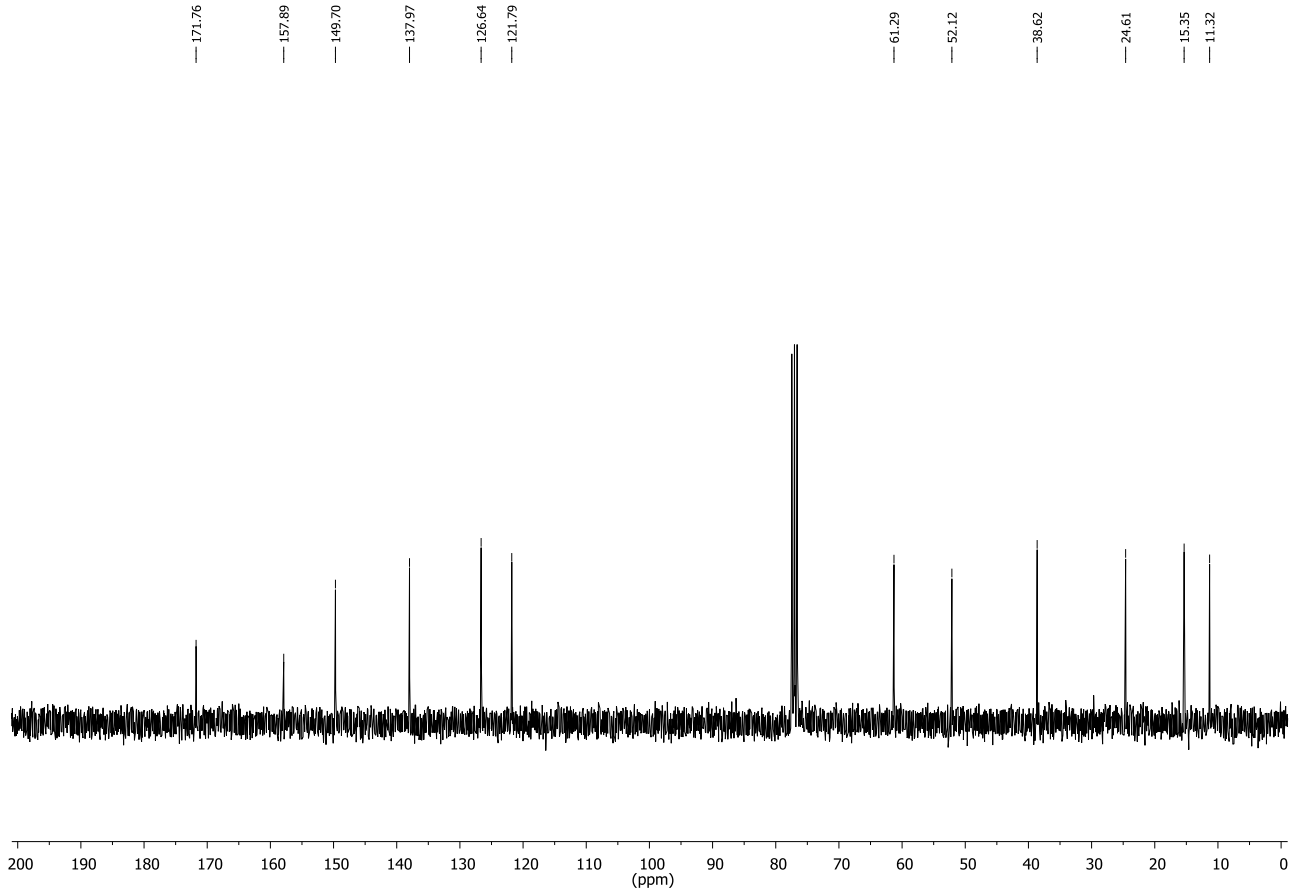

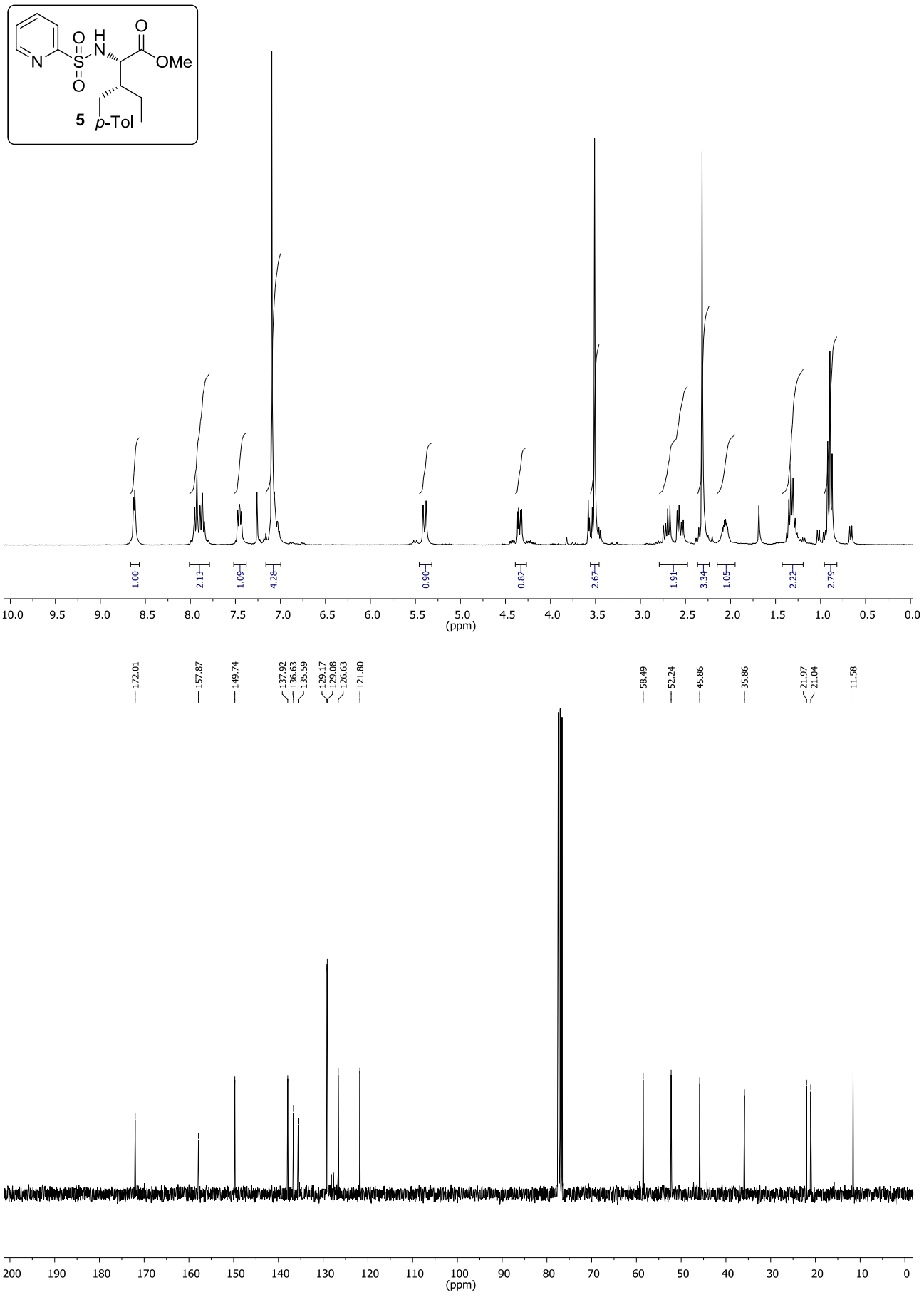

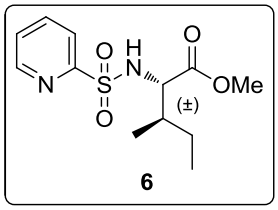

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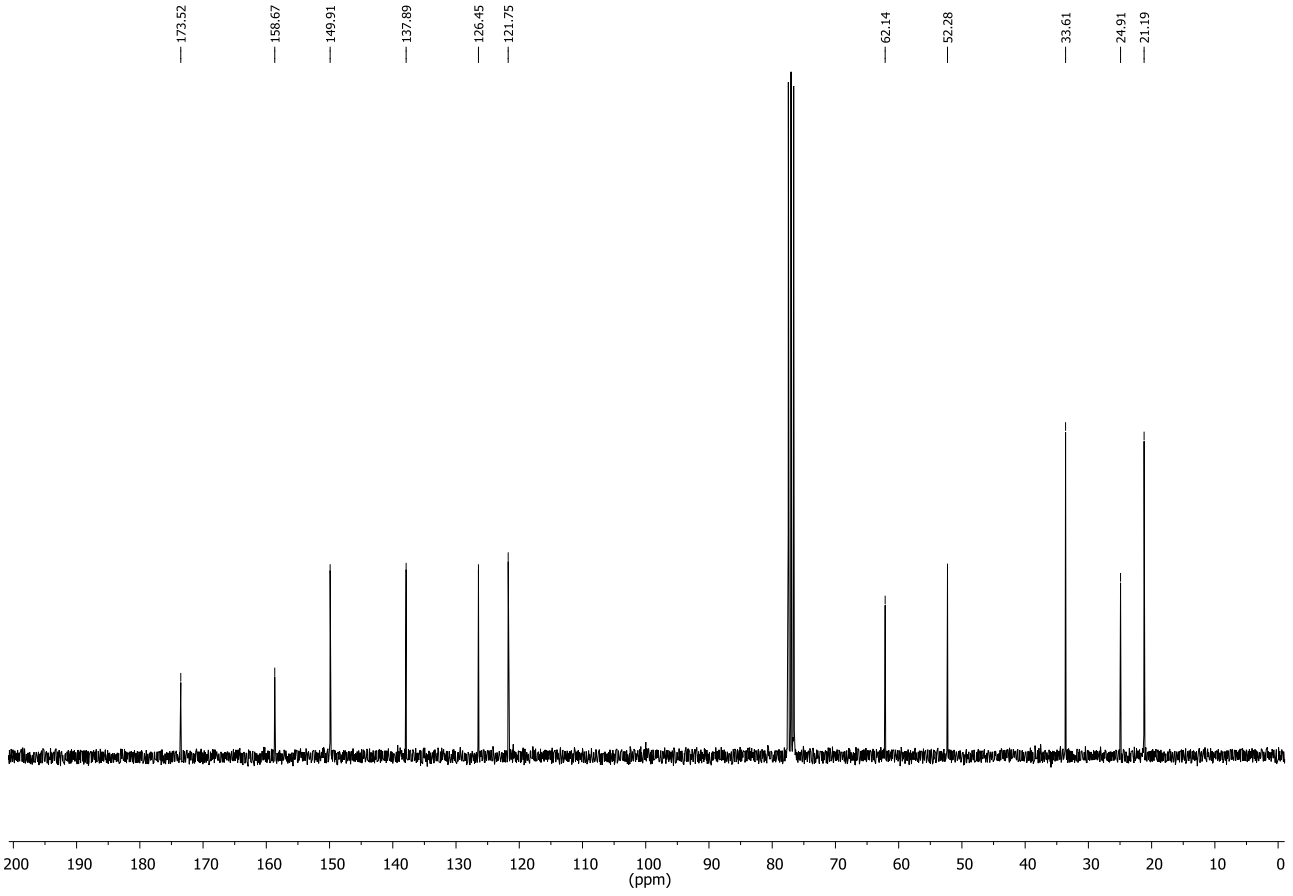

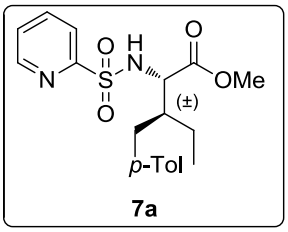
O
H
N
O
N
S
O
OMe
(±)
p-Tol

7a

1.00
2.04
1.05
4.26
0.95
0.92
2.92
2.19
3.27
1.03
1.01
1.08
2.85
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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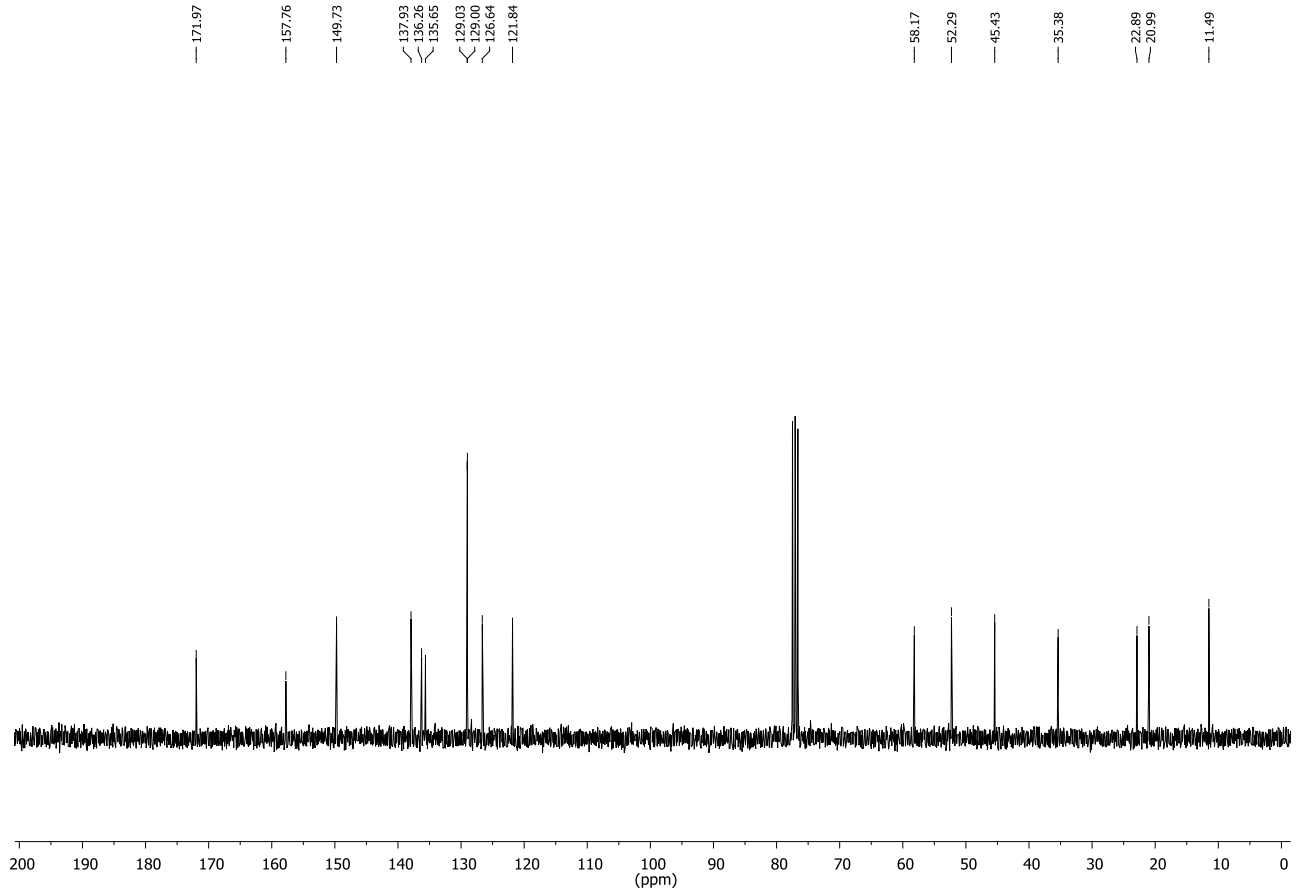
2.5
2.0
1.5
1.0
0.5
0.0
(ppm)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121.84
58.17
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11.49
200
190
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0
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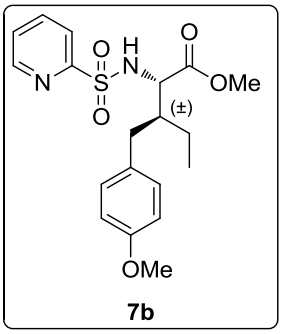

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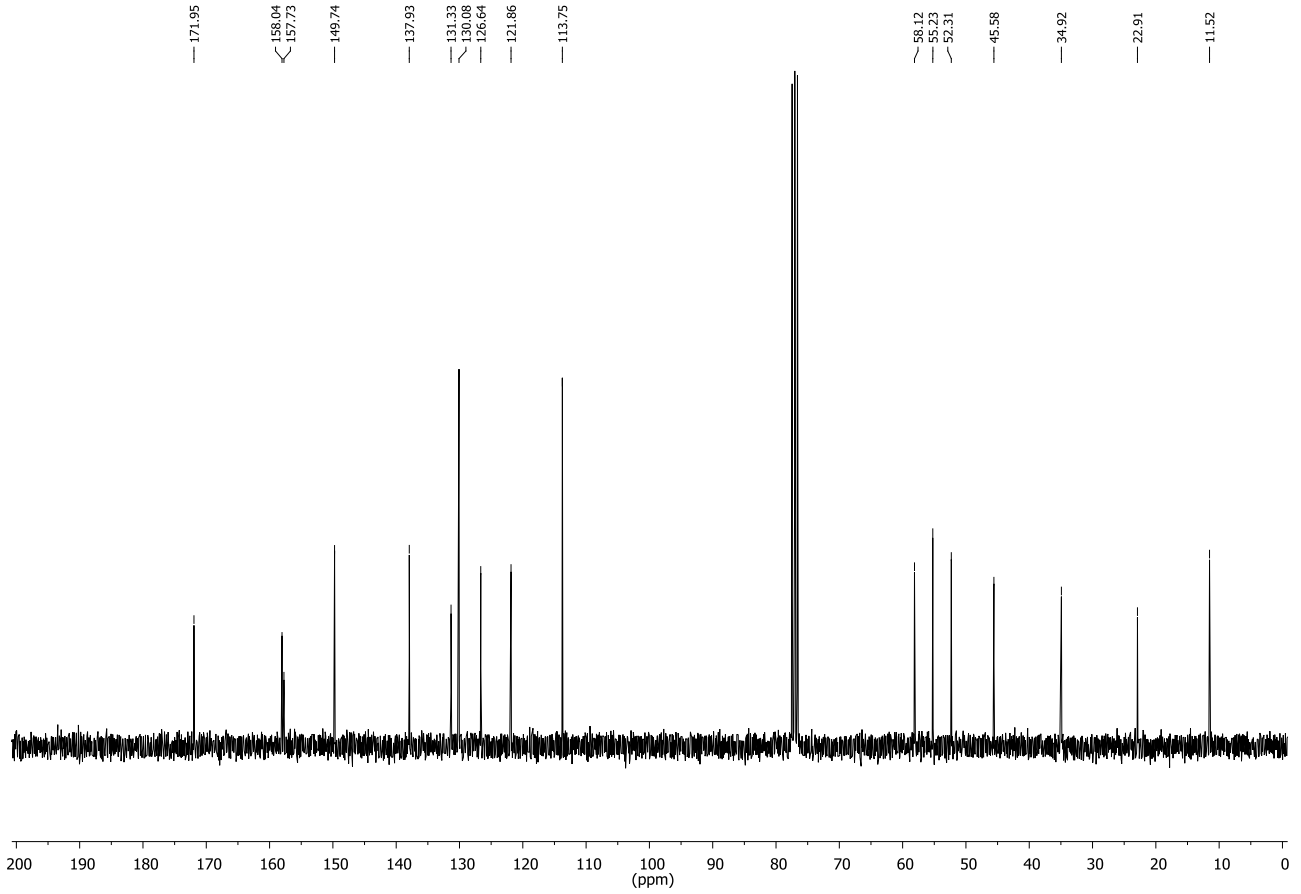

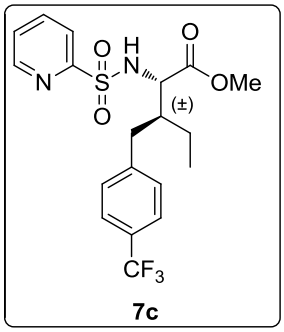

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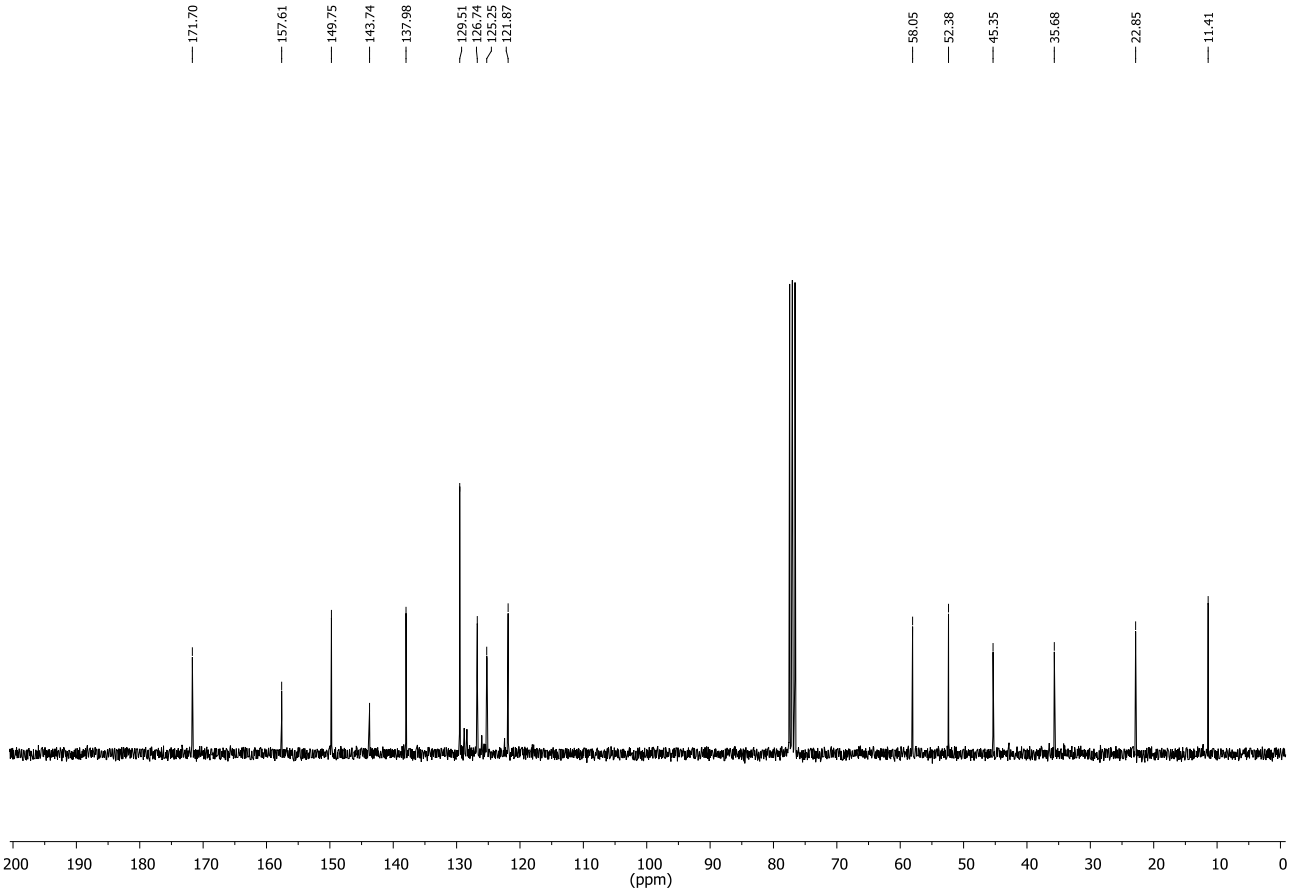

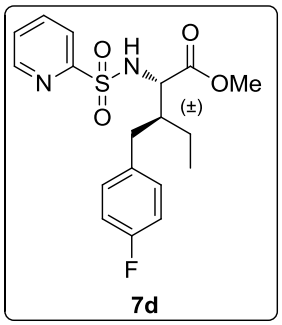

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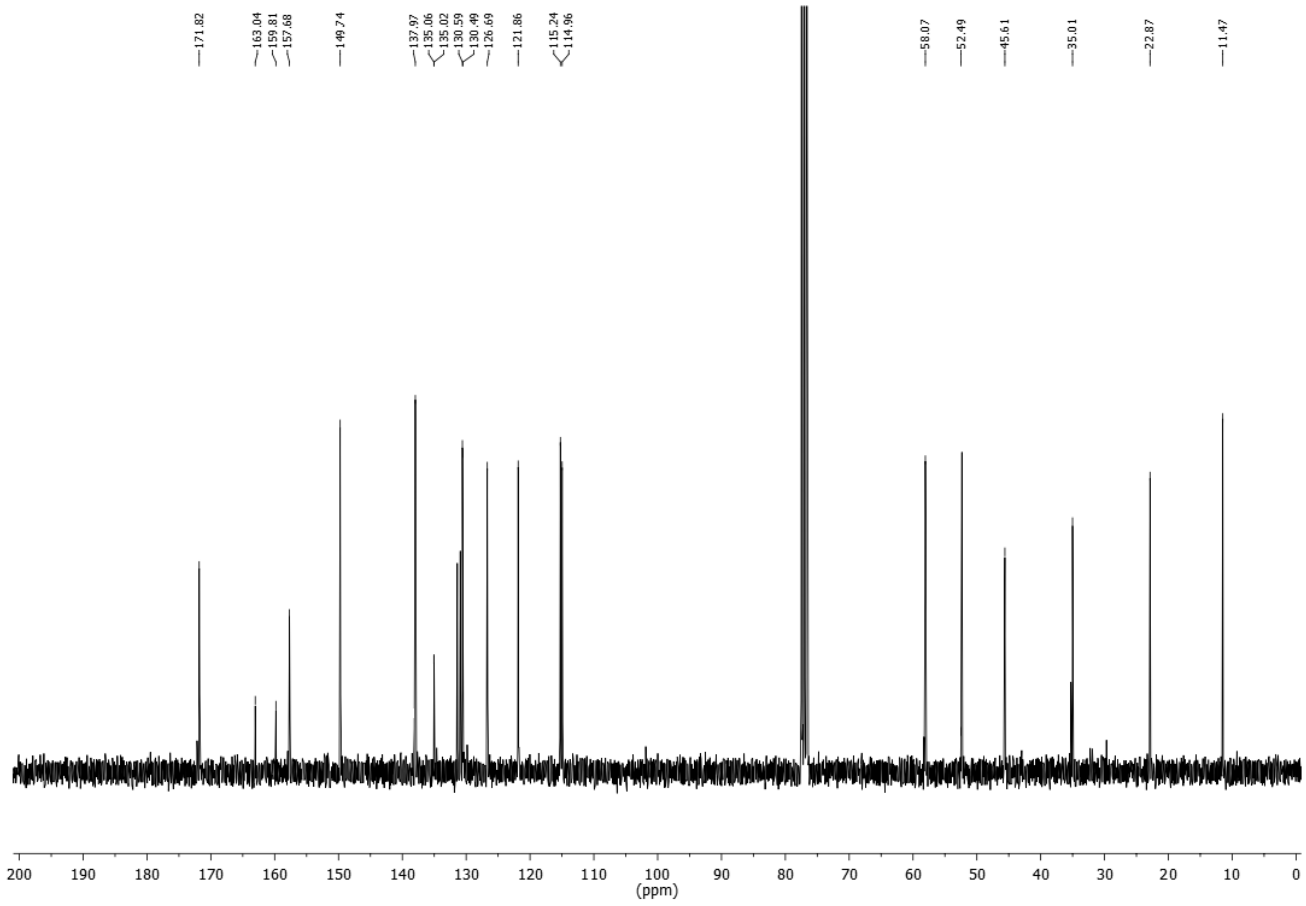

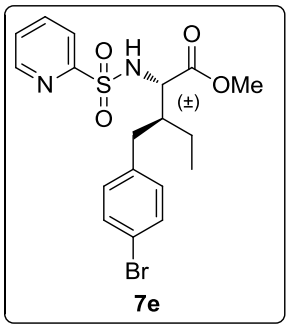

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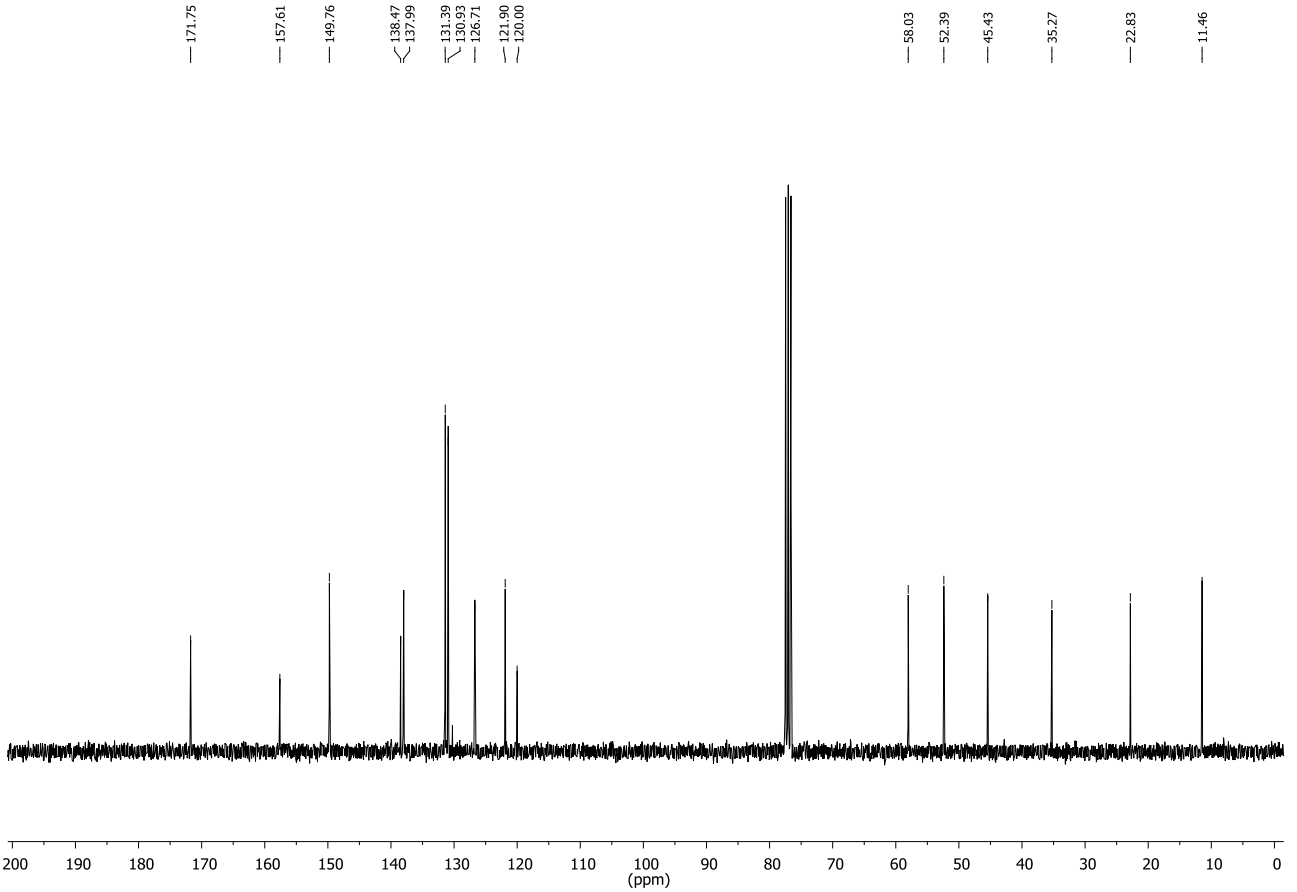

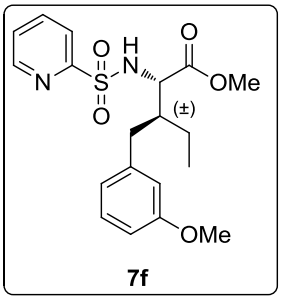

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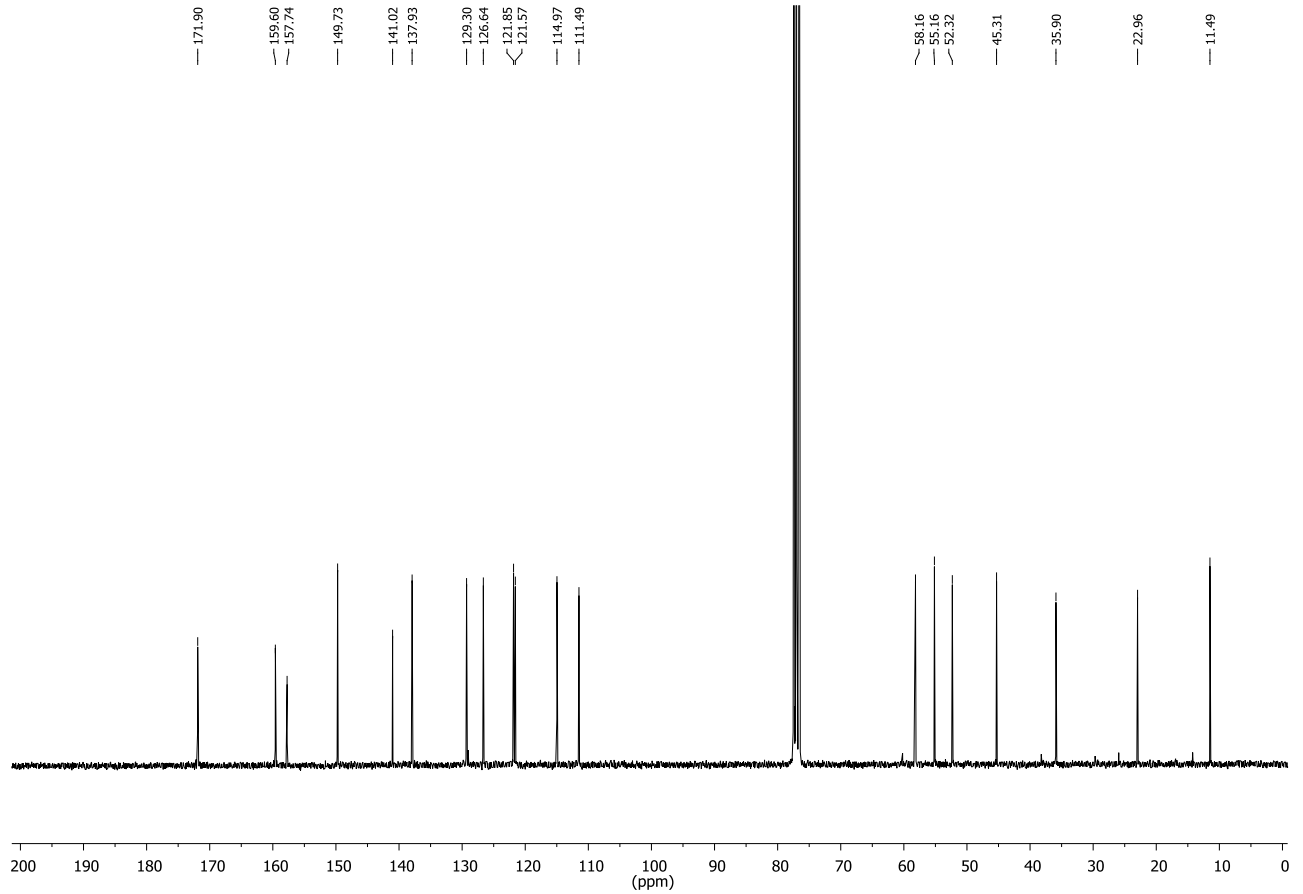

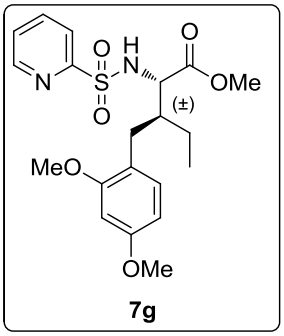

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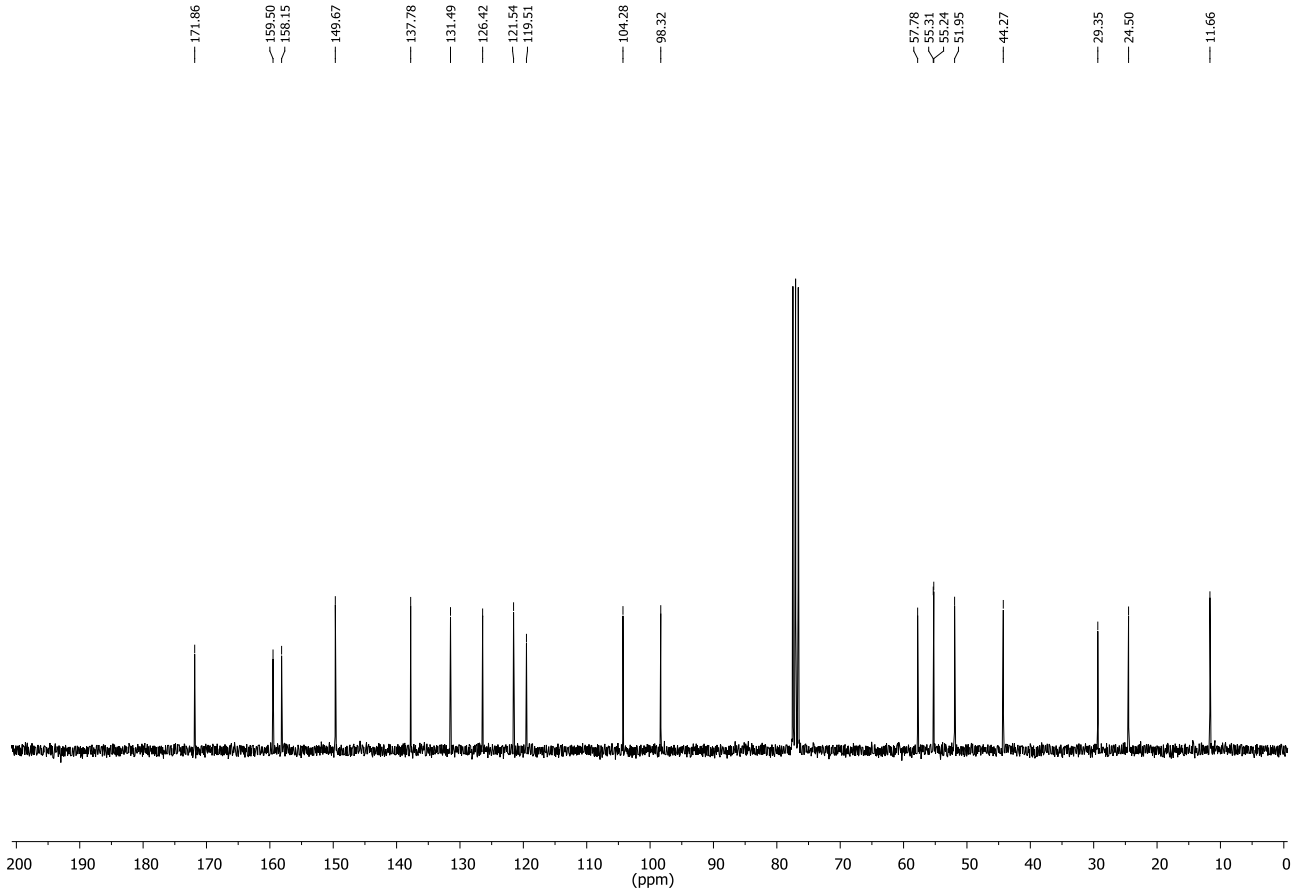

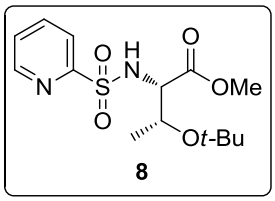

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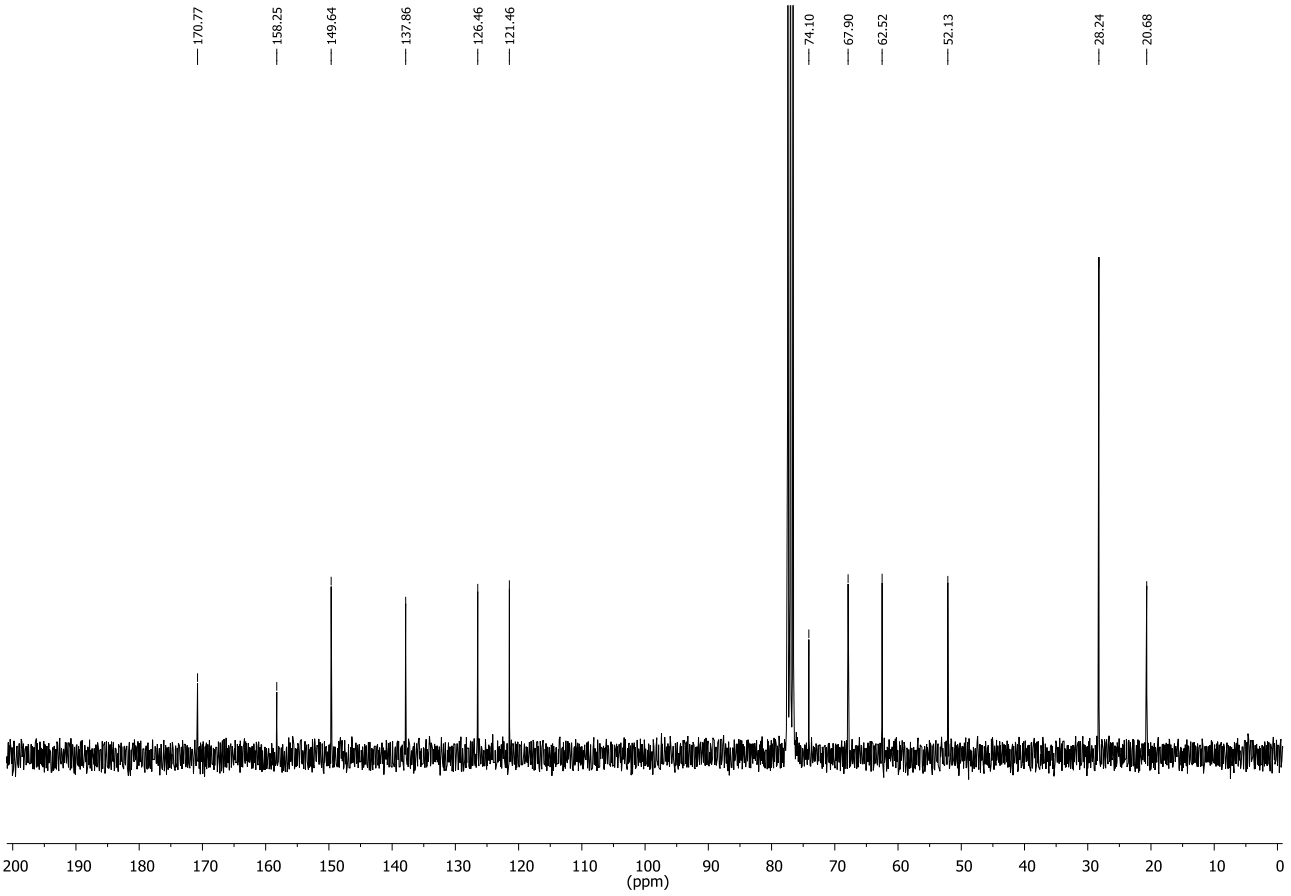

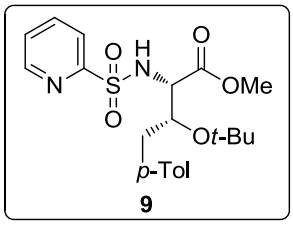

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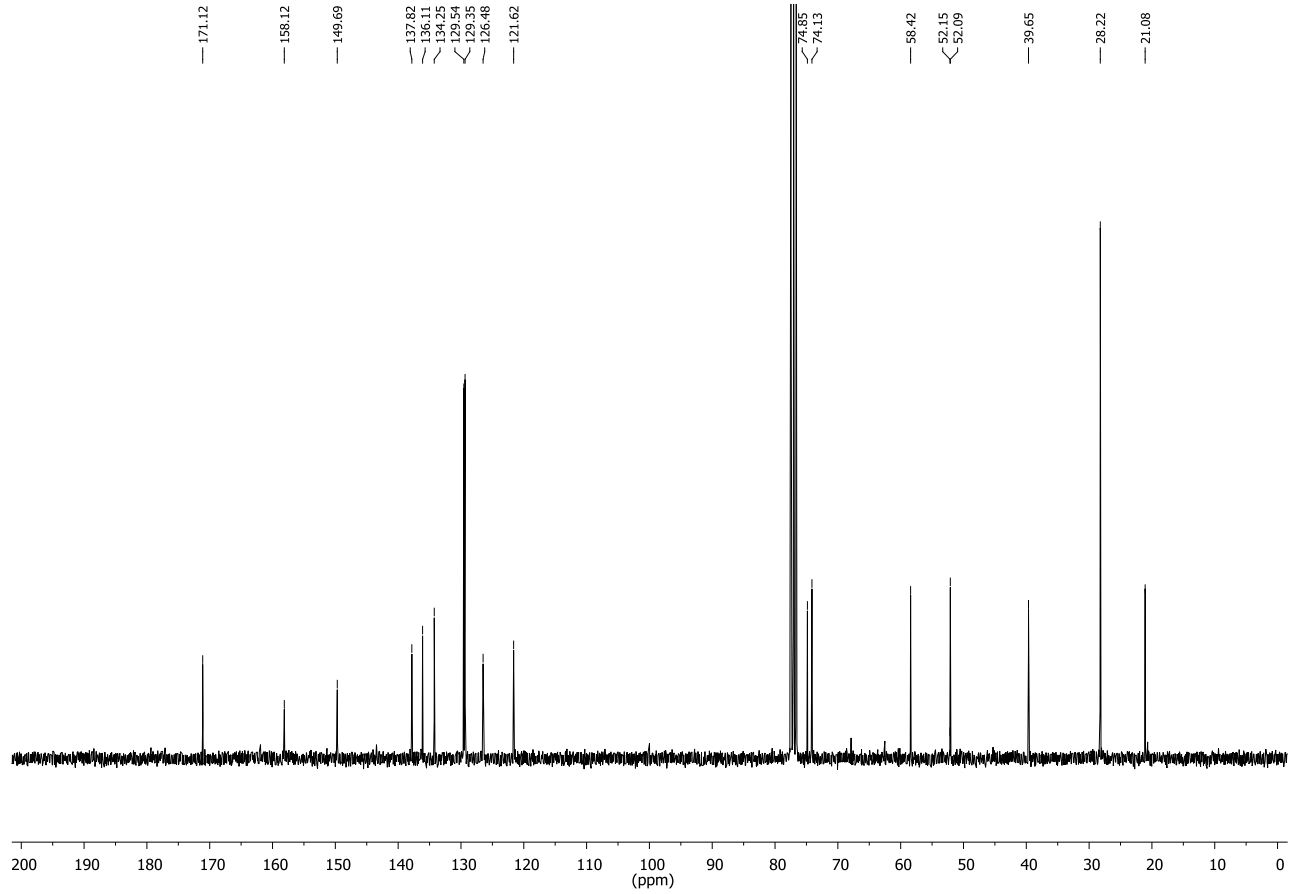

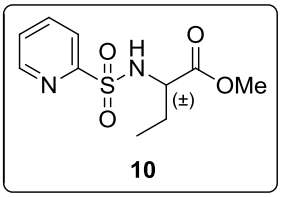

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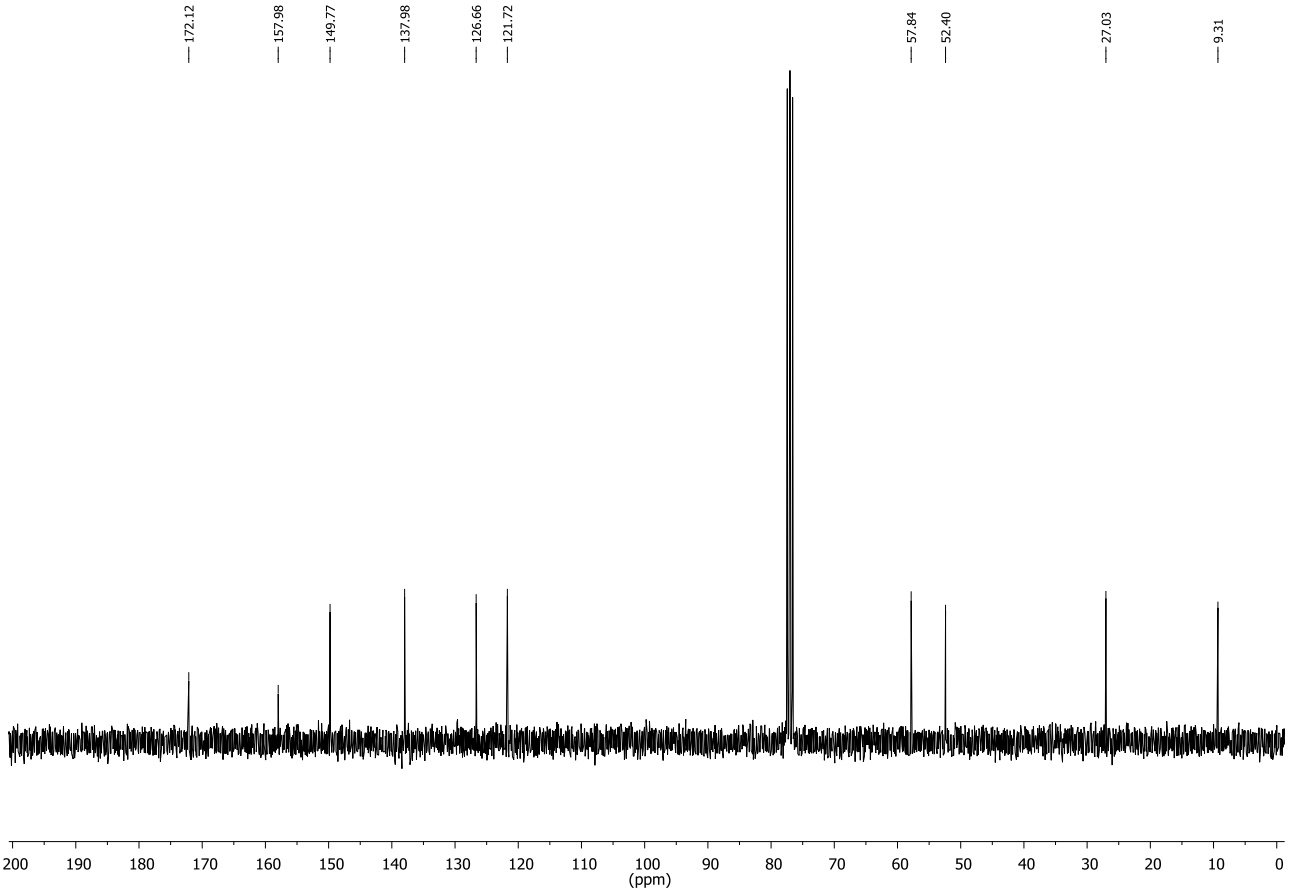

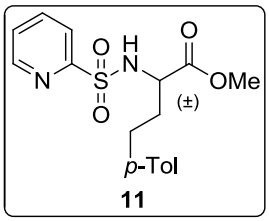

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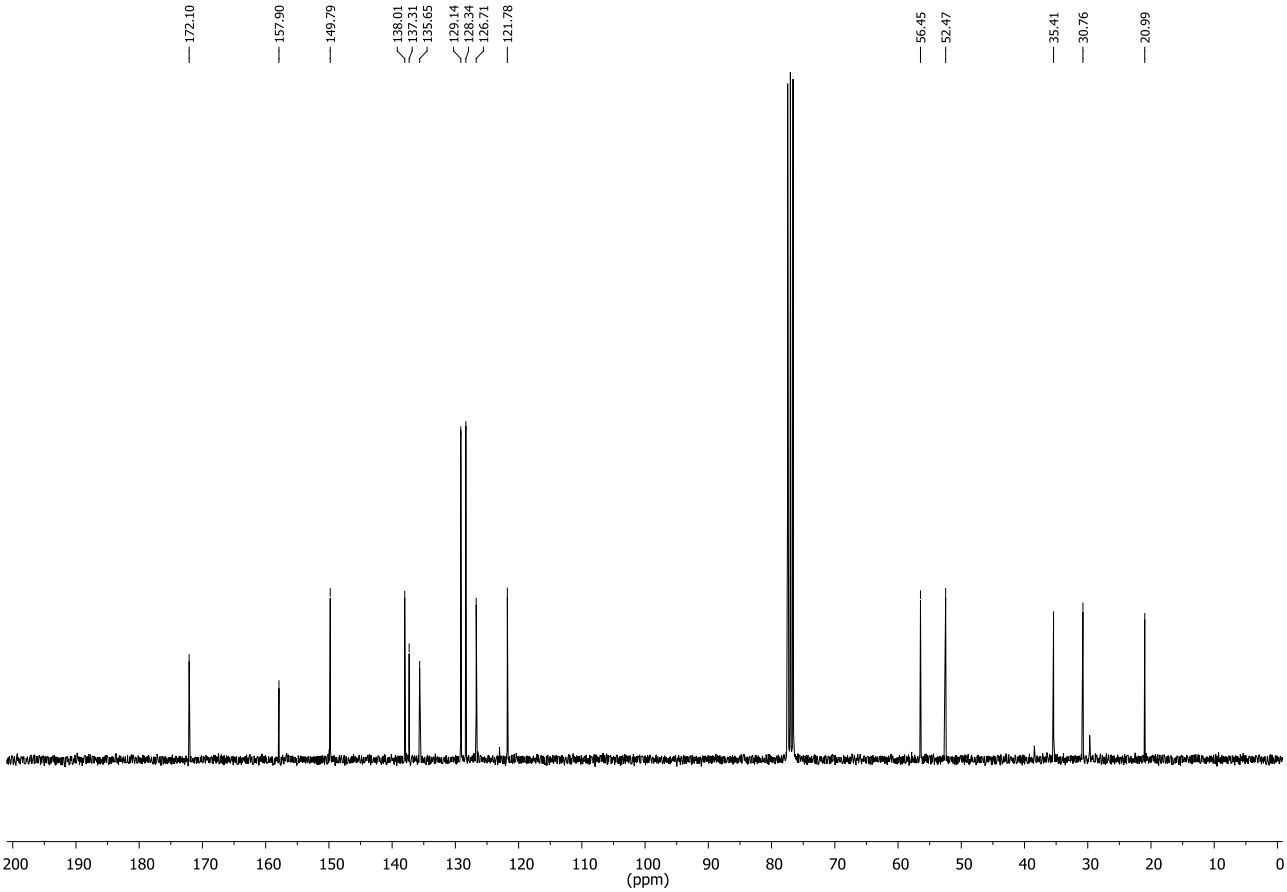

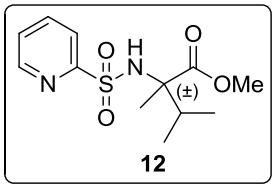

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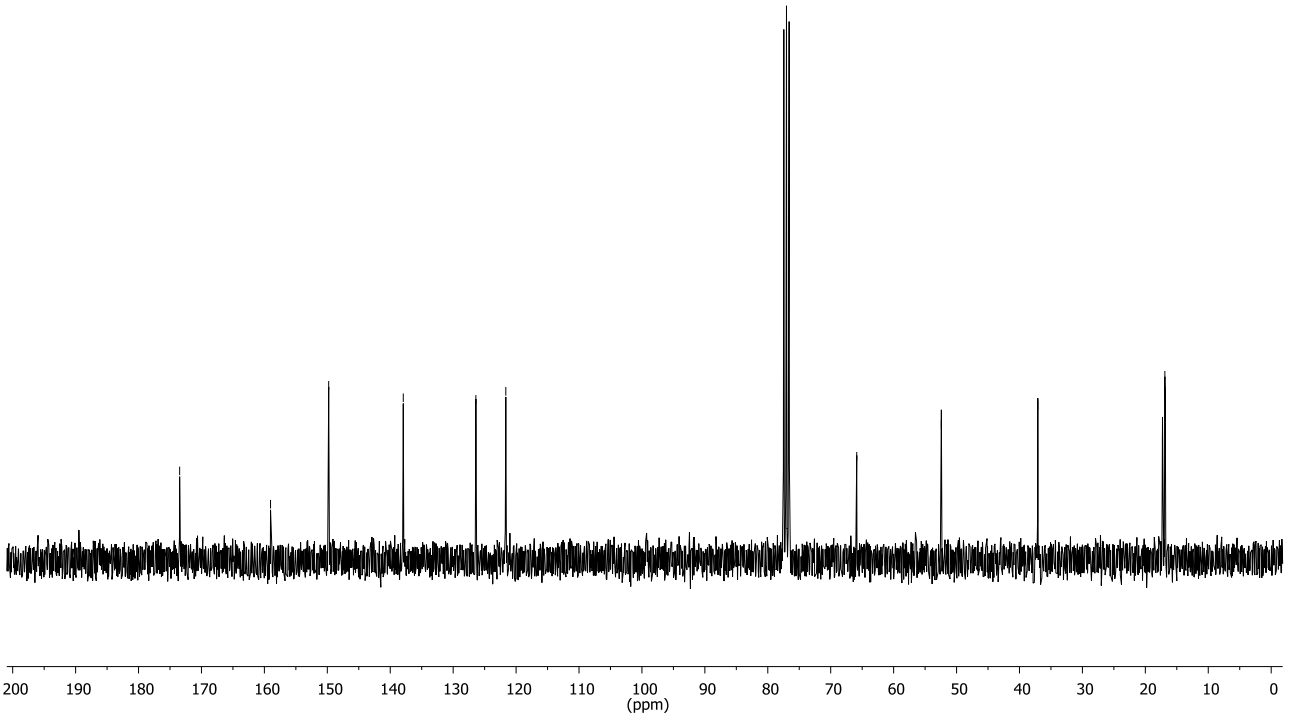
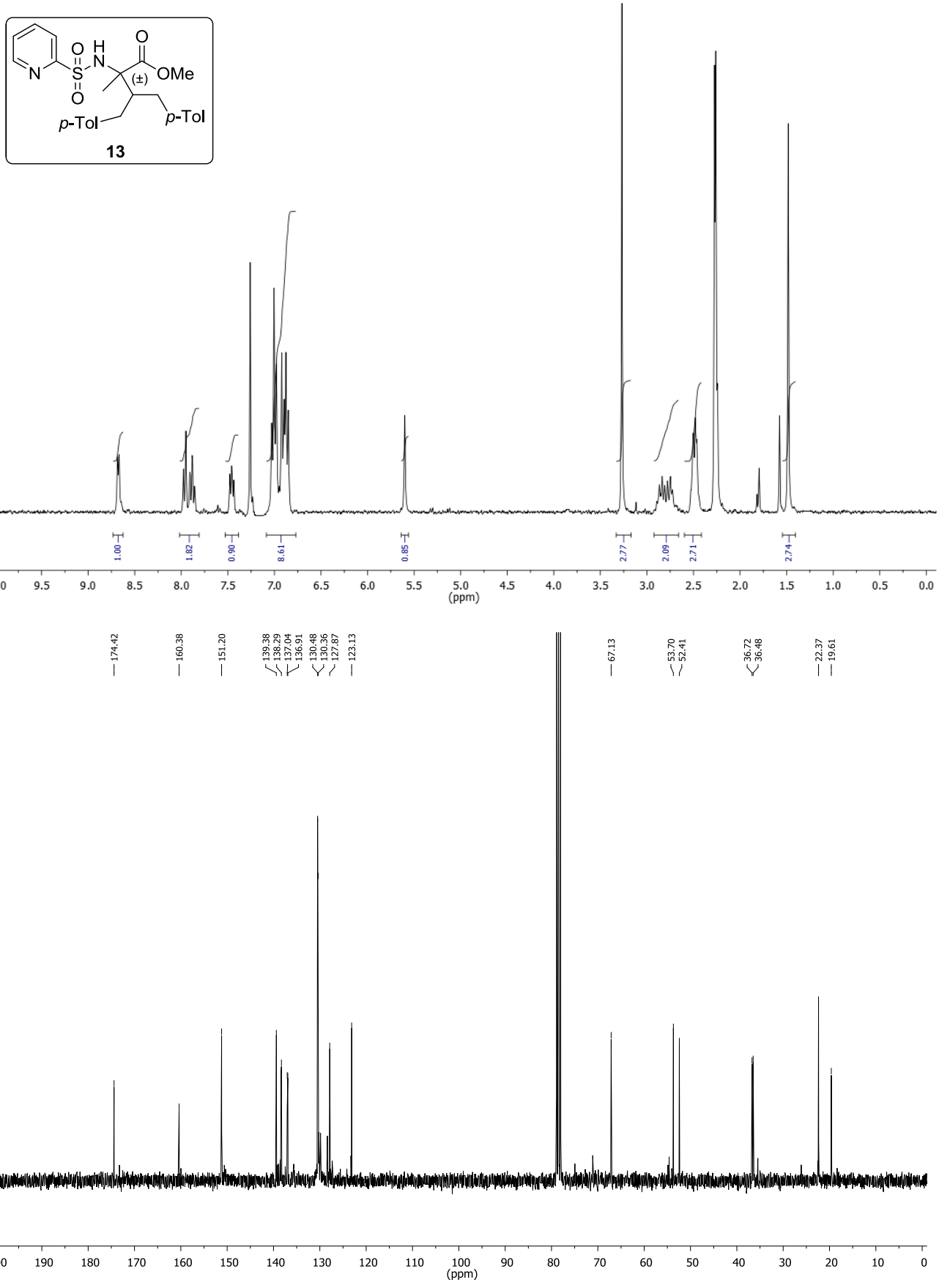
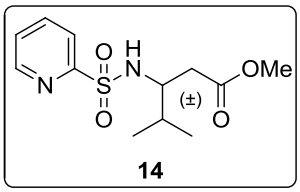



13
p-Tol
p-Tol
OMe
(±)
1.00
1.82
0.90
8.61
0.85
2.77
2.09
2.71
2.74
(ppm)
174.42
160.38
151.20
139.38
138.29
137.04
136.91
130.48
130.36
127.87
123.13
67.13
53.70
52.41
36.72
36.48
22.37
19.61
(ppm)



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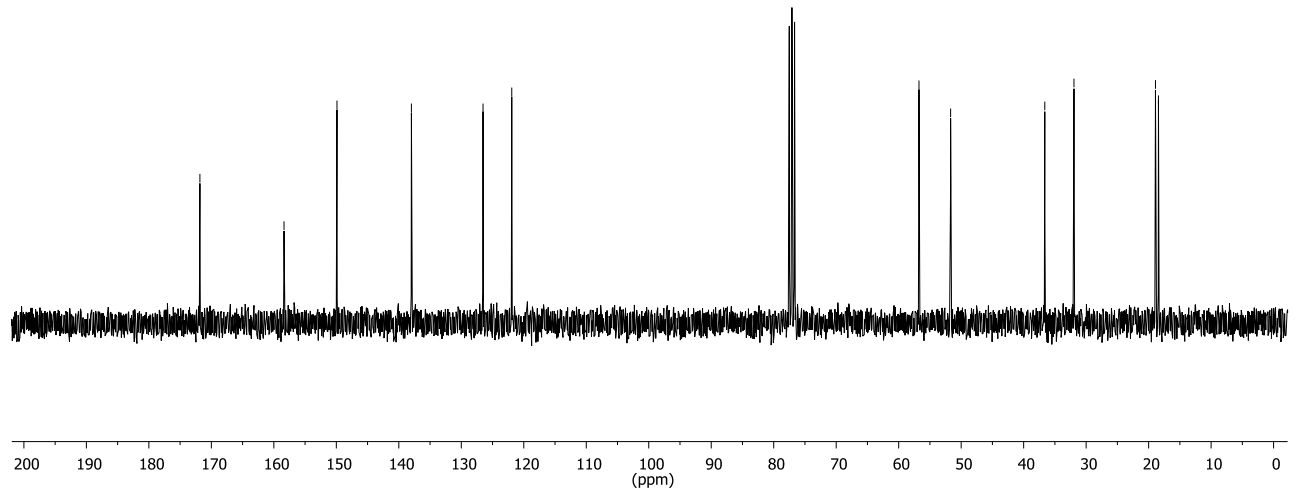

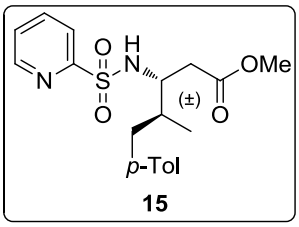

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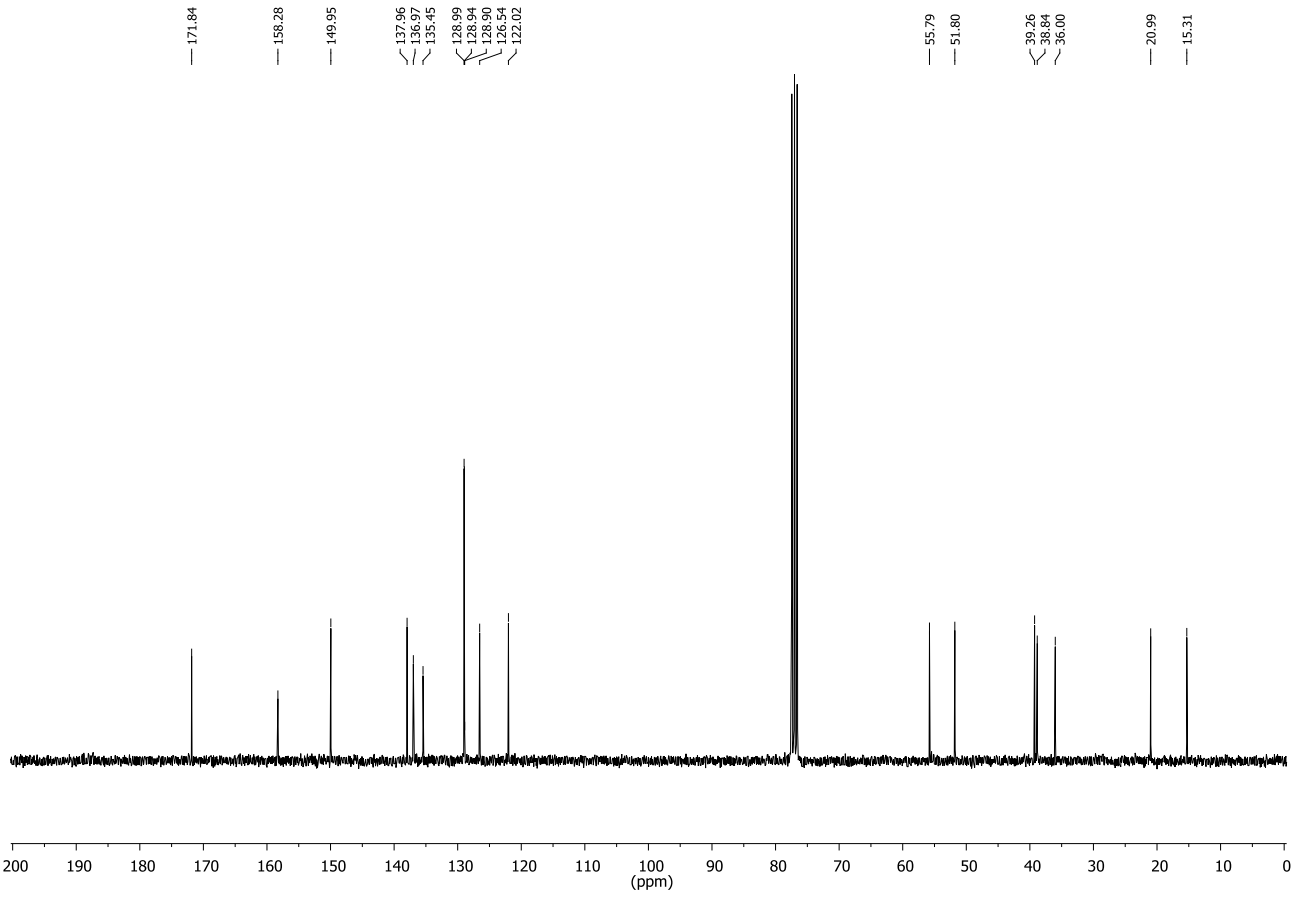

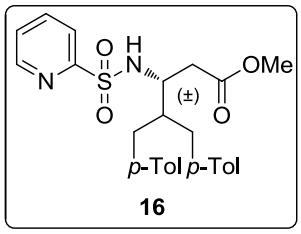

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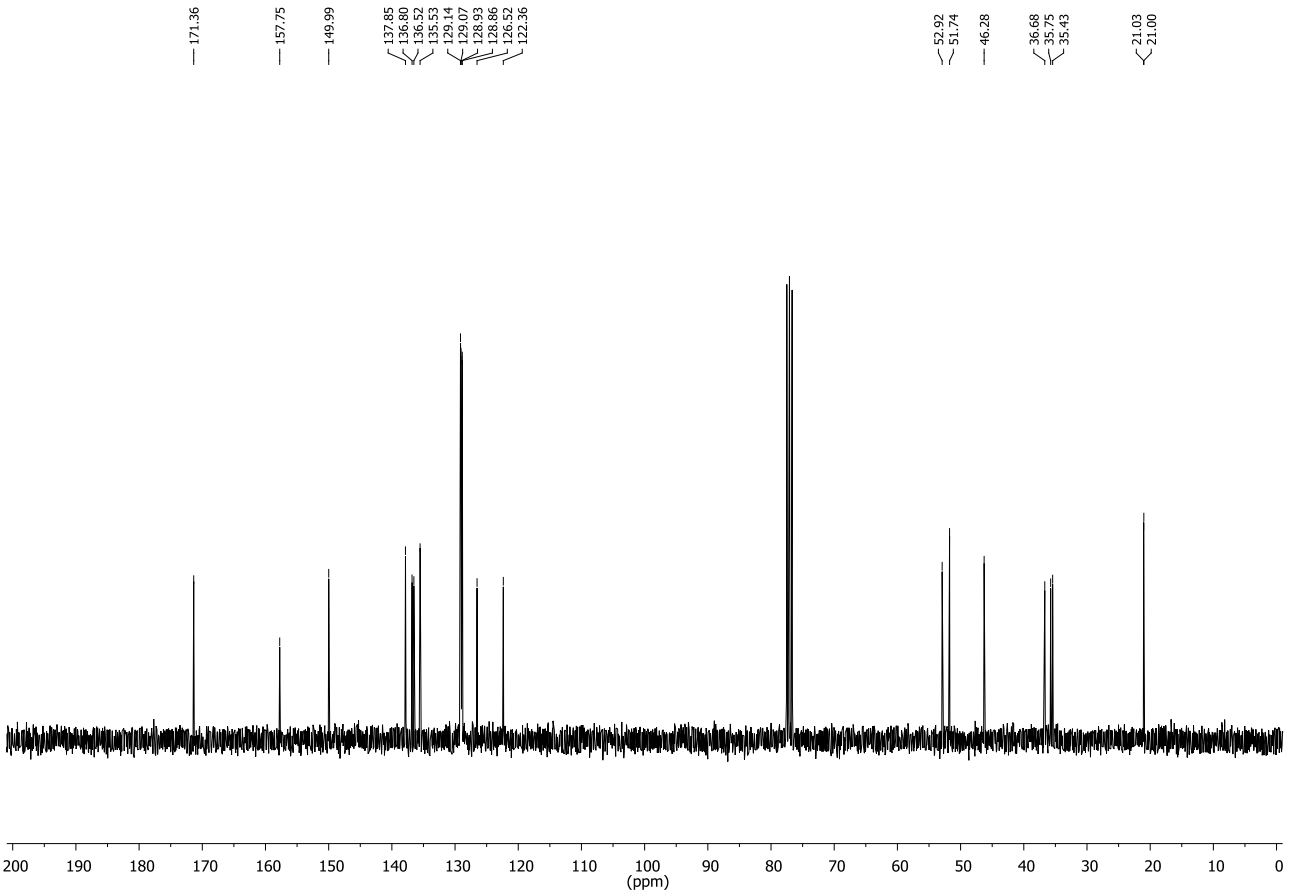

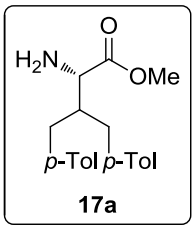

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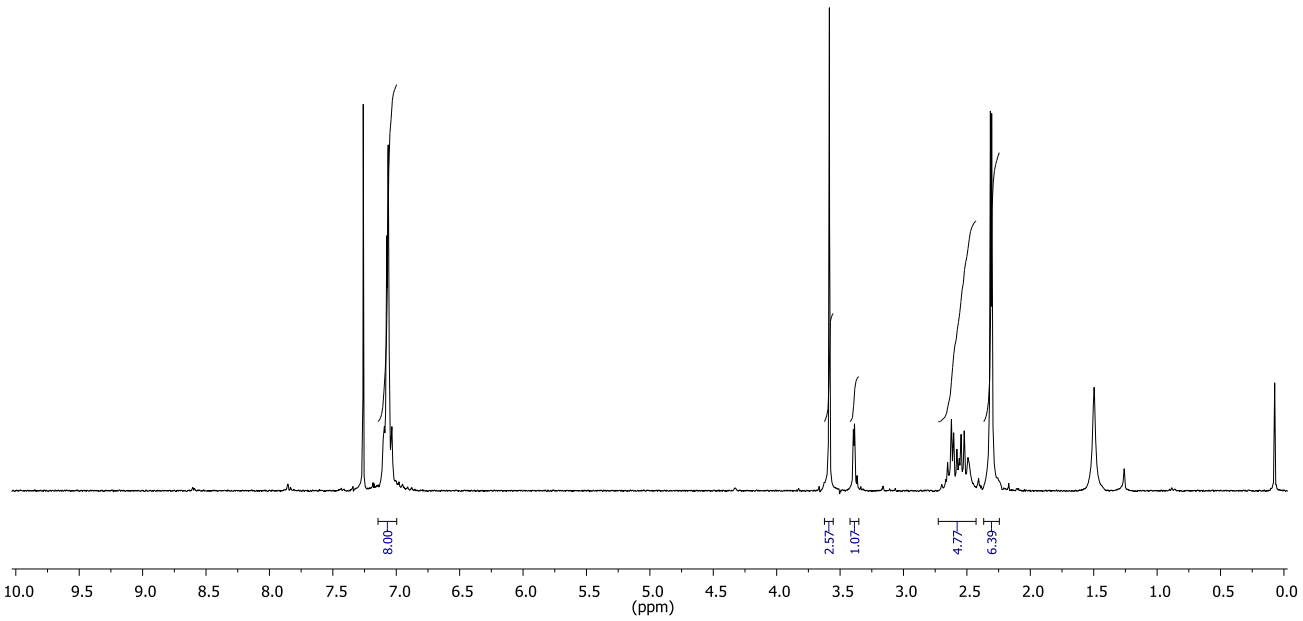

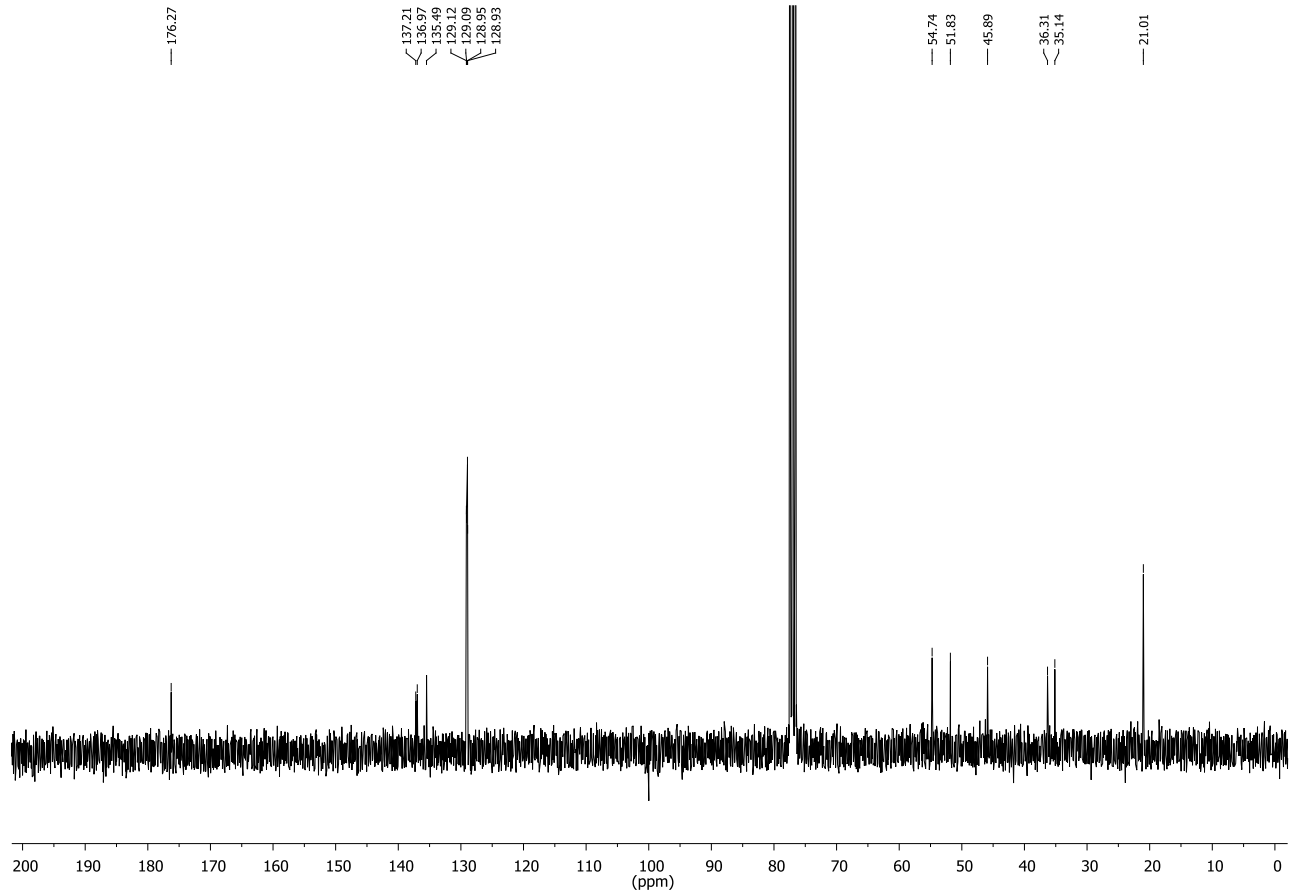

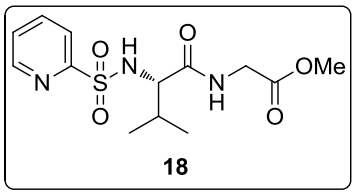

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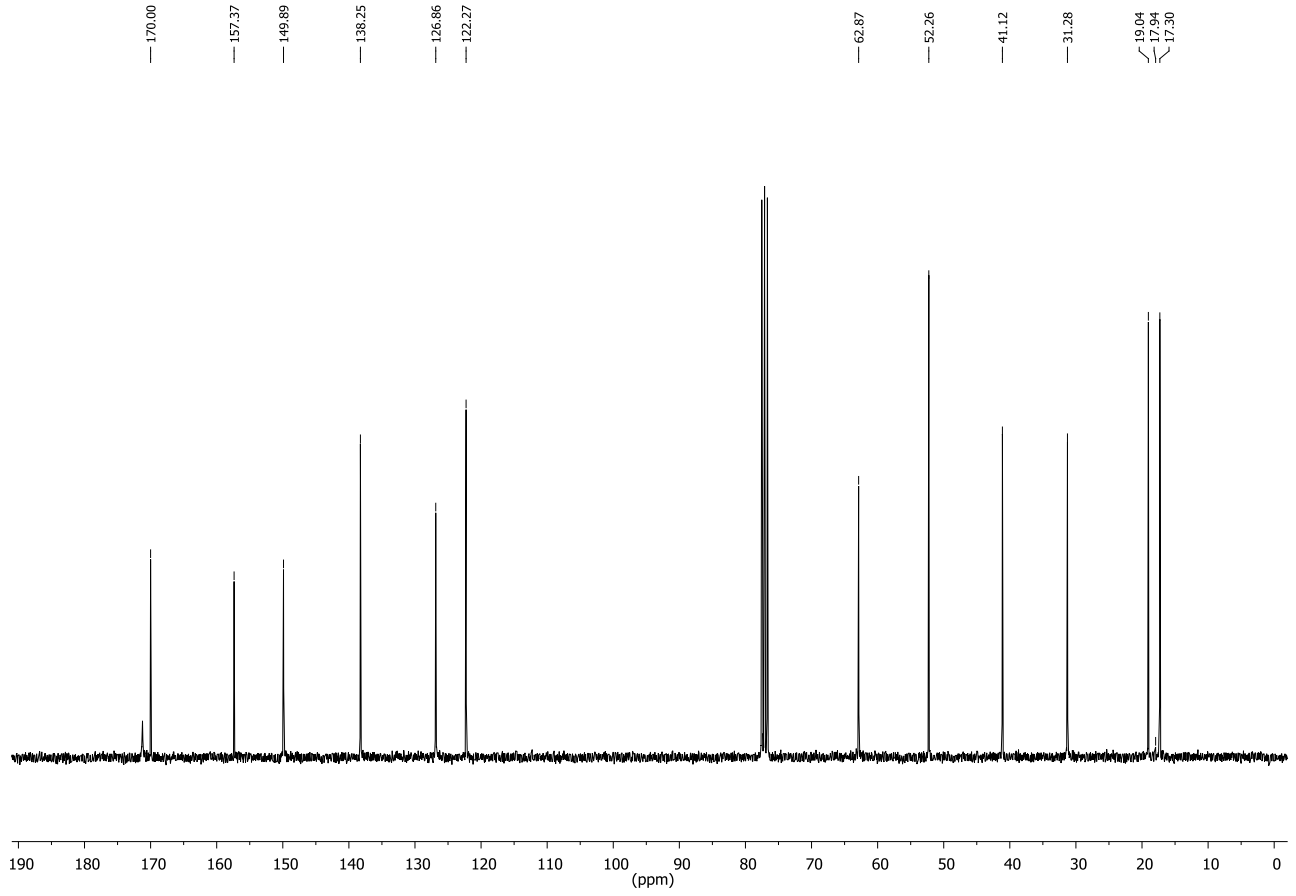

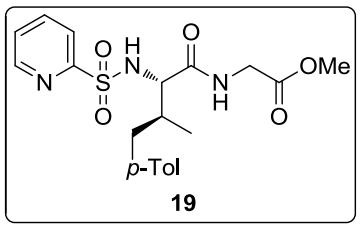

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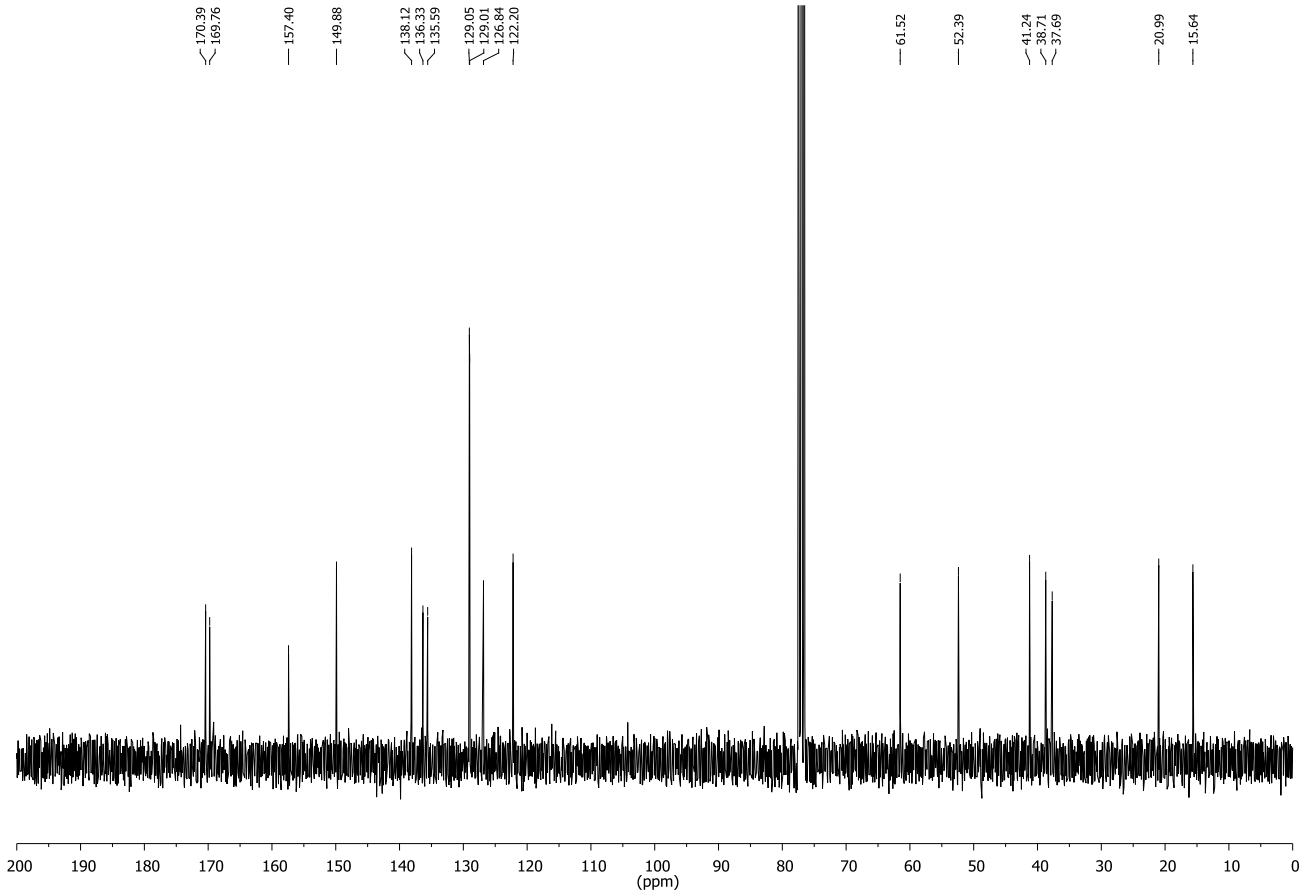

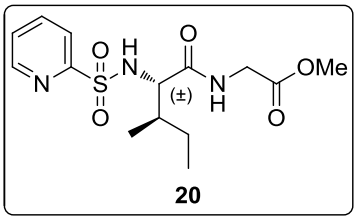

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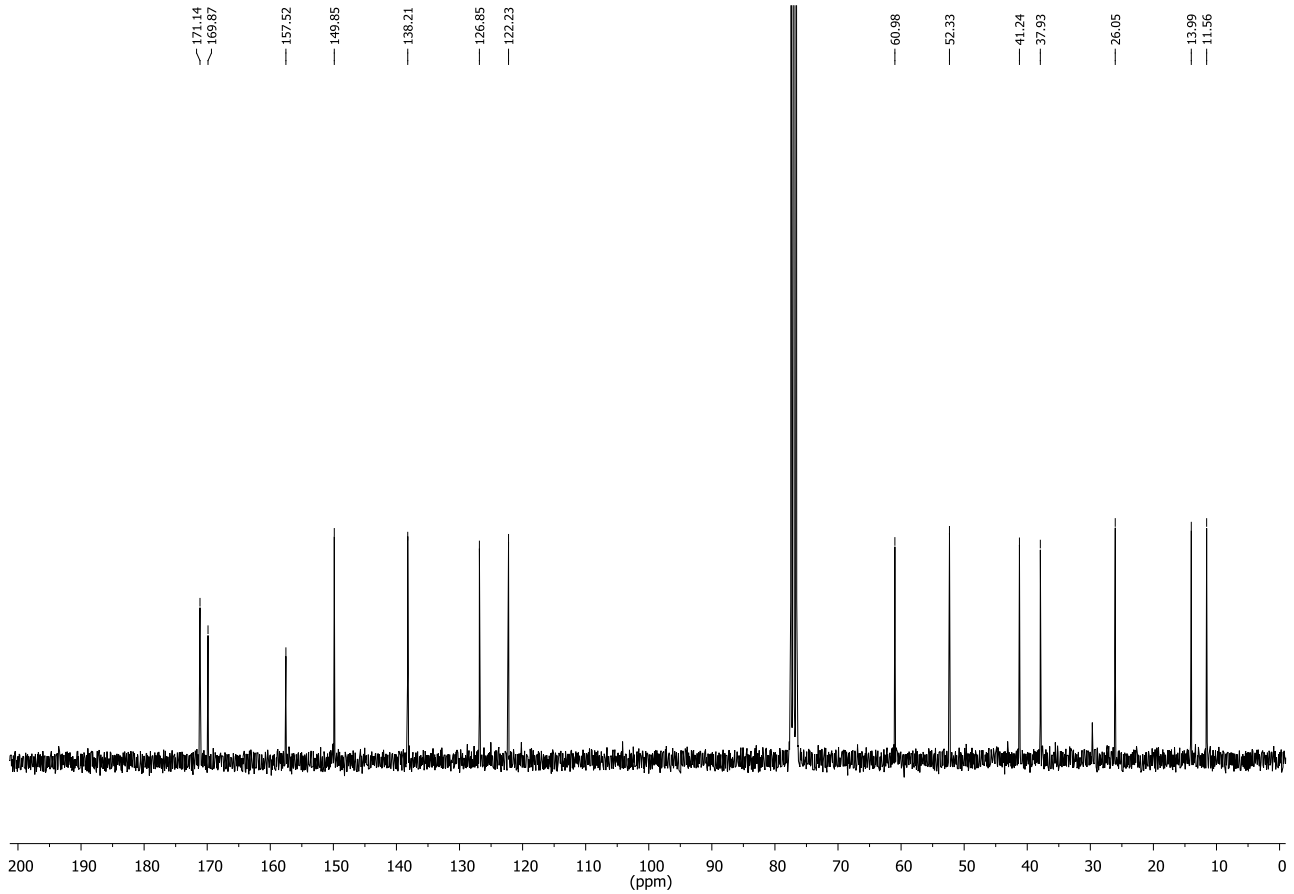

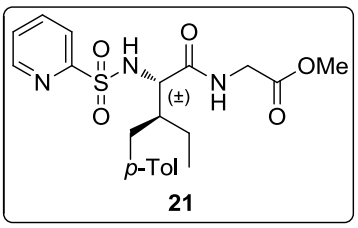

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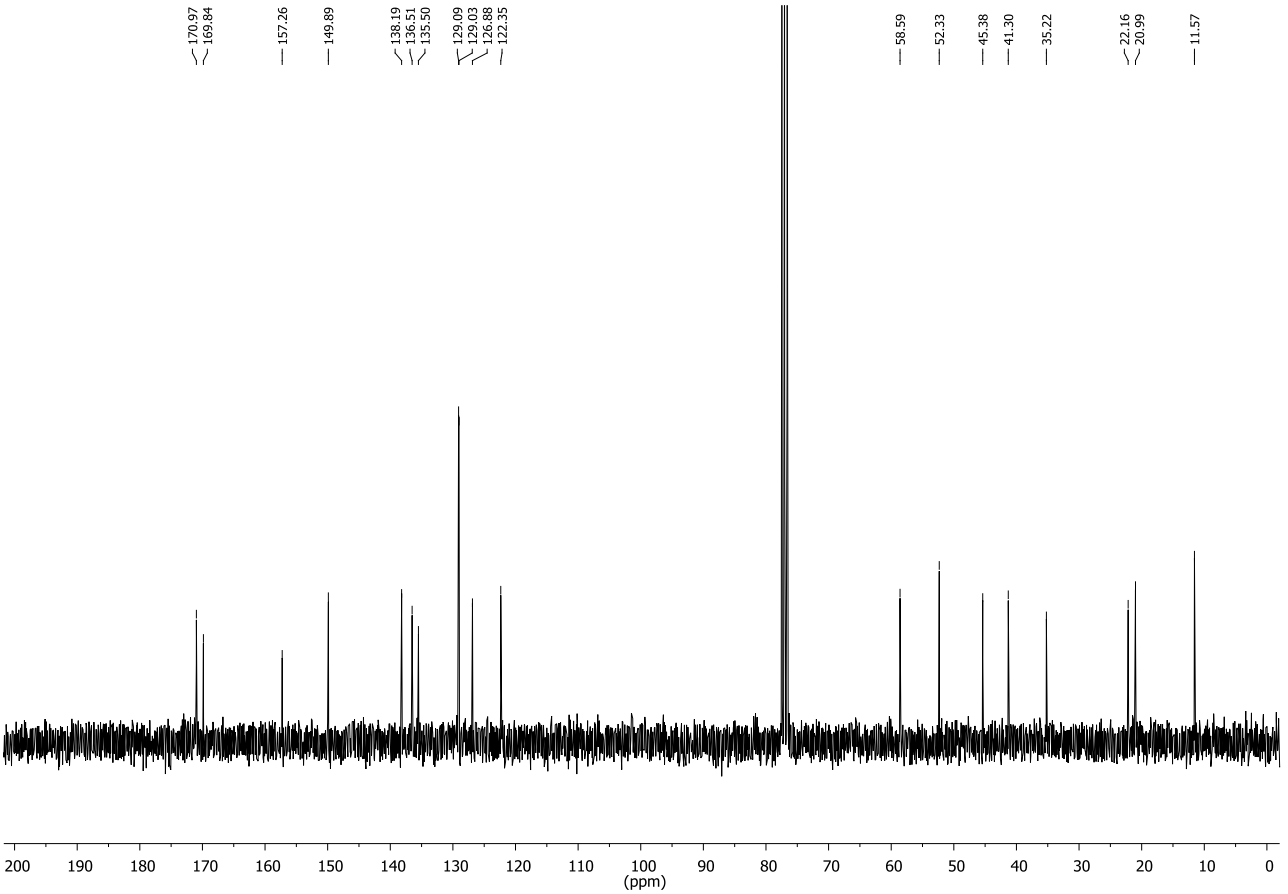

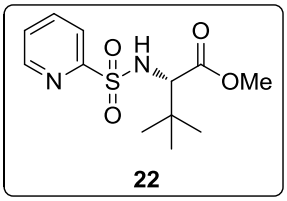

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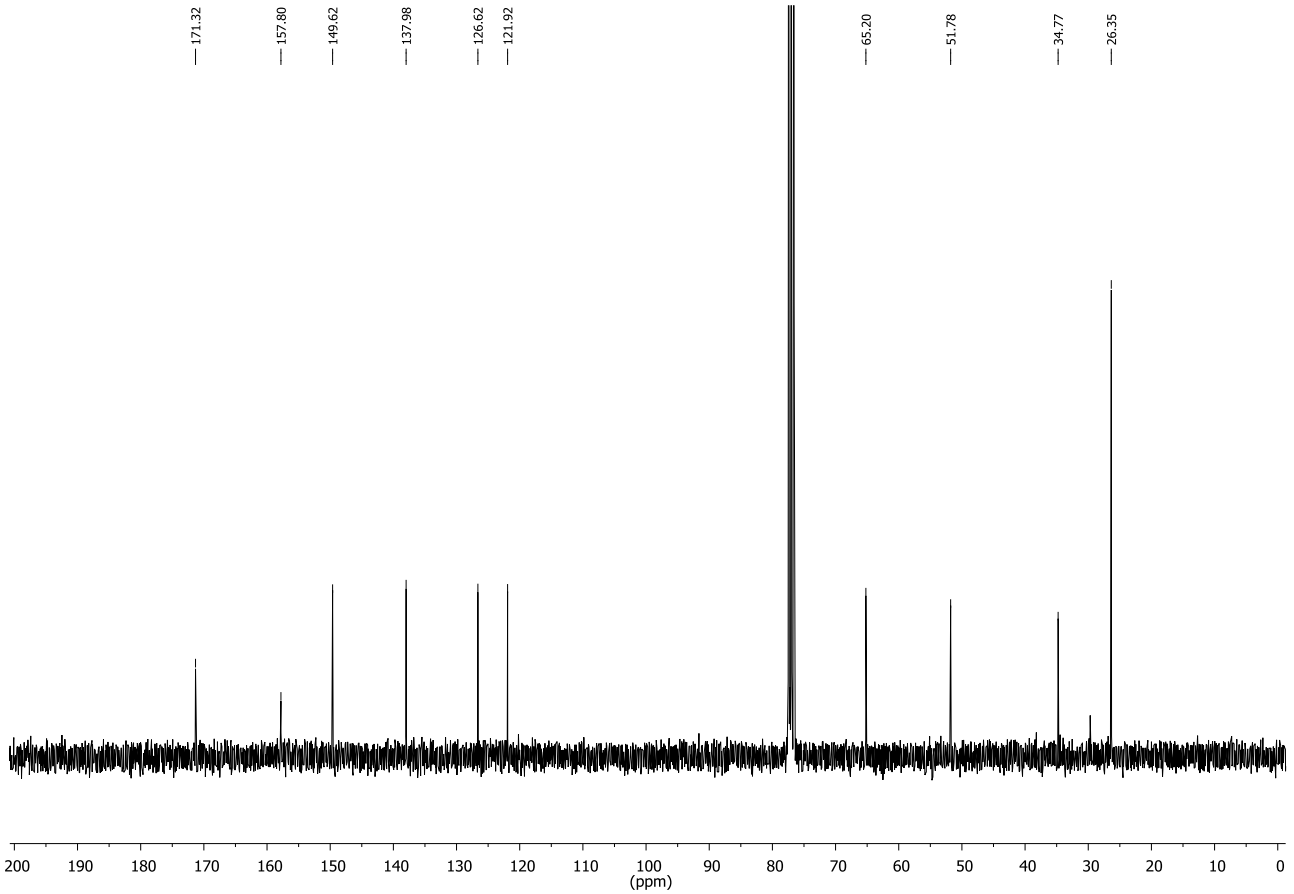

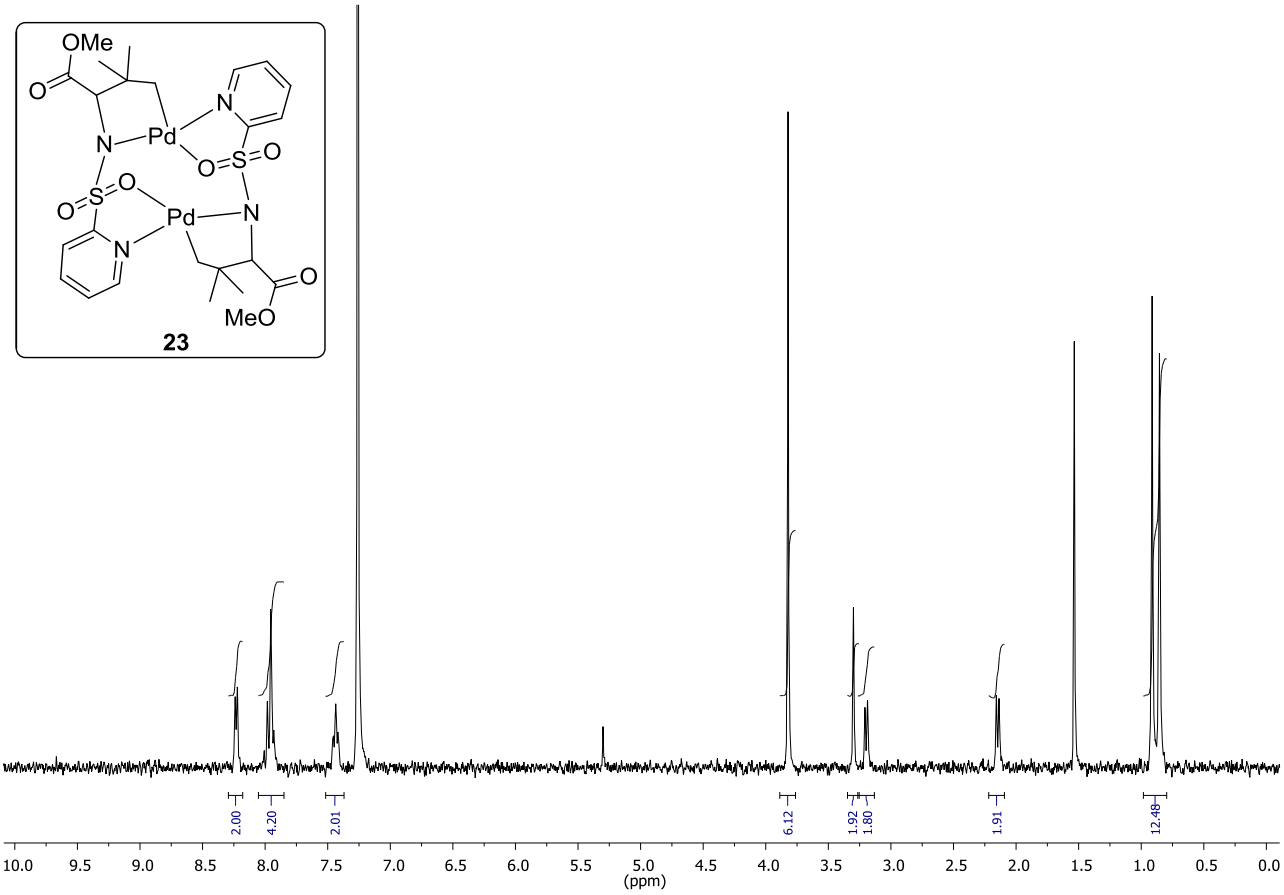

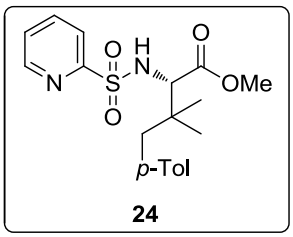

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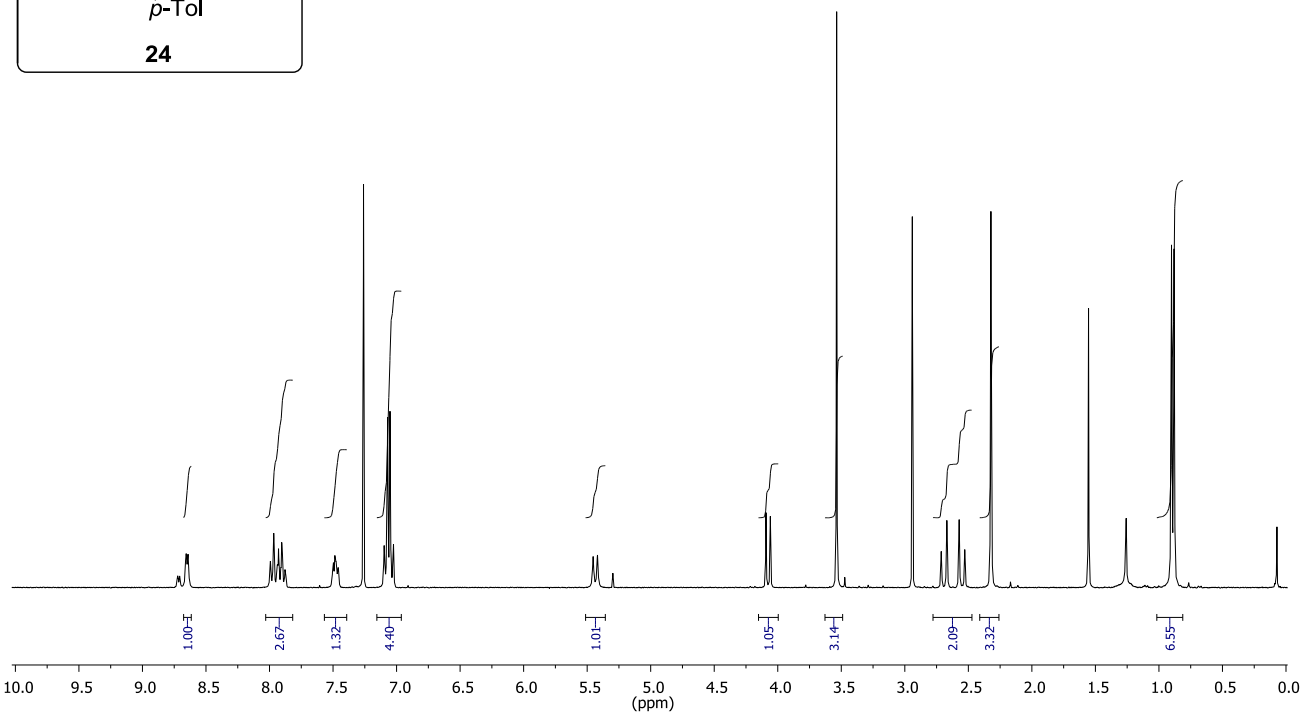

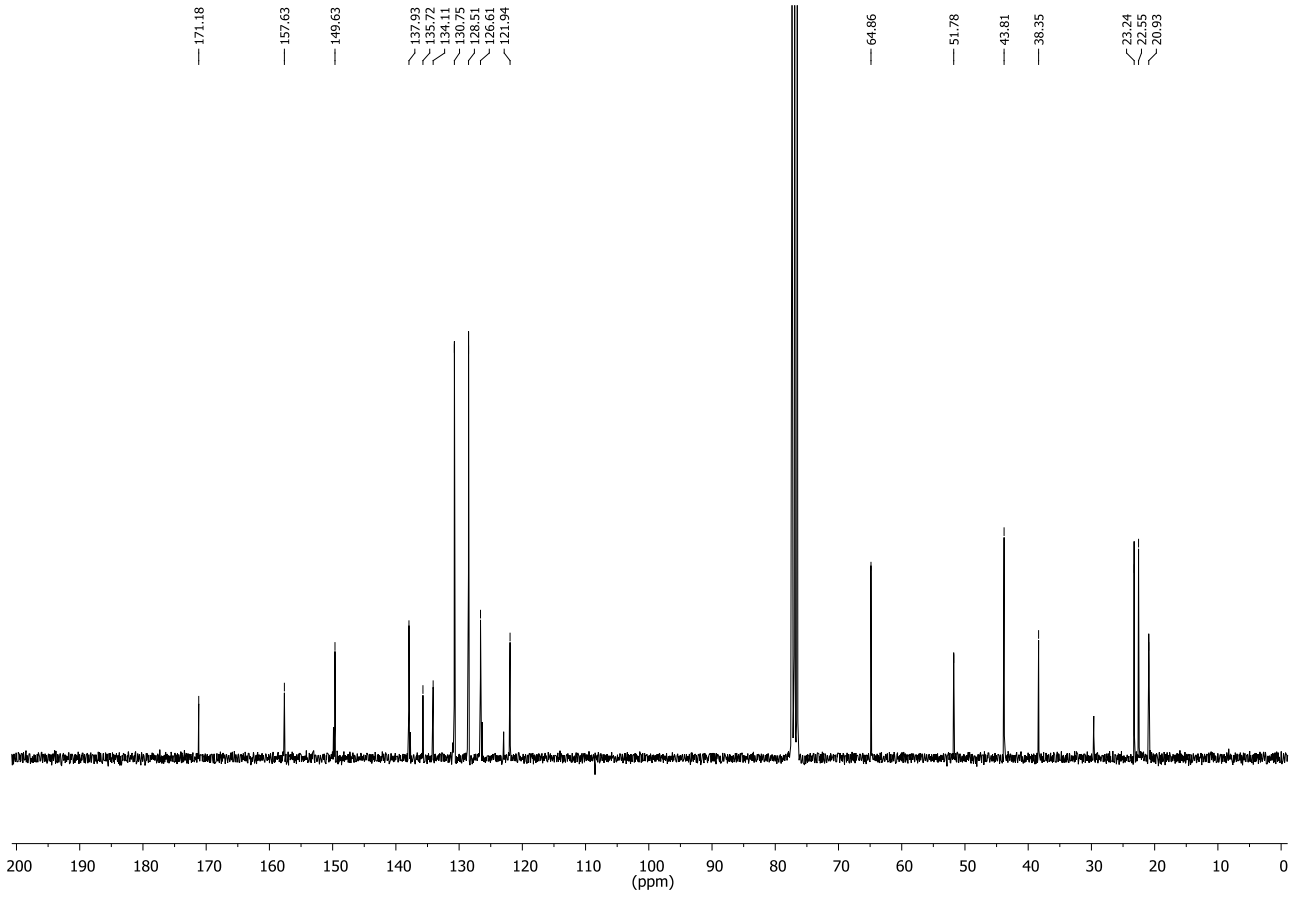

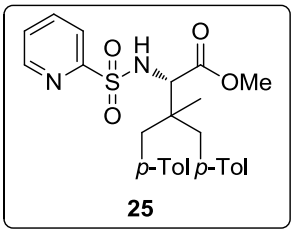

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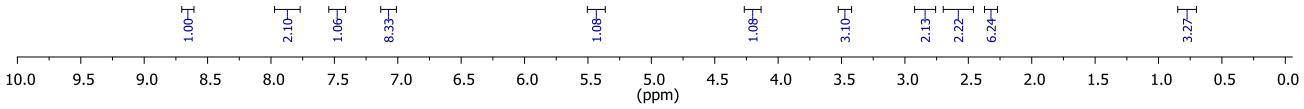

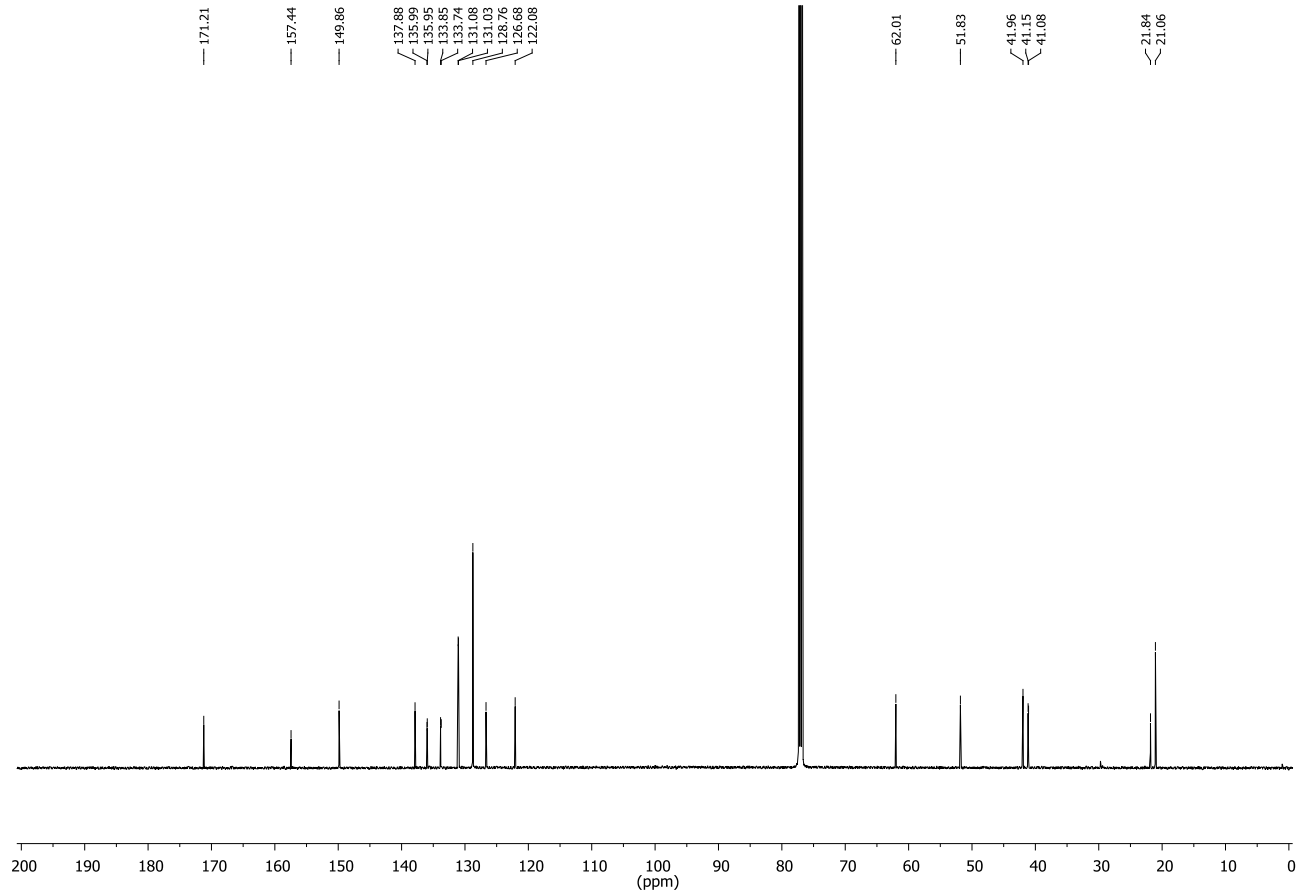

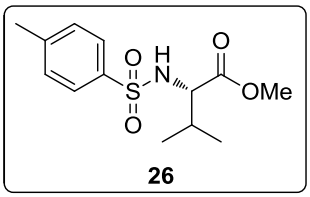

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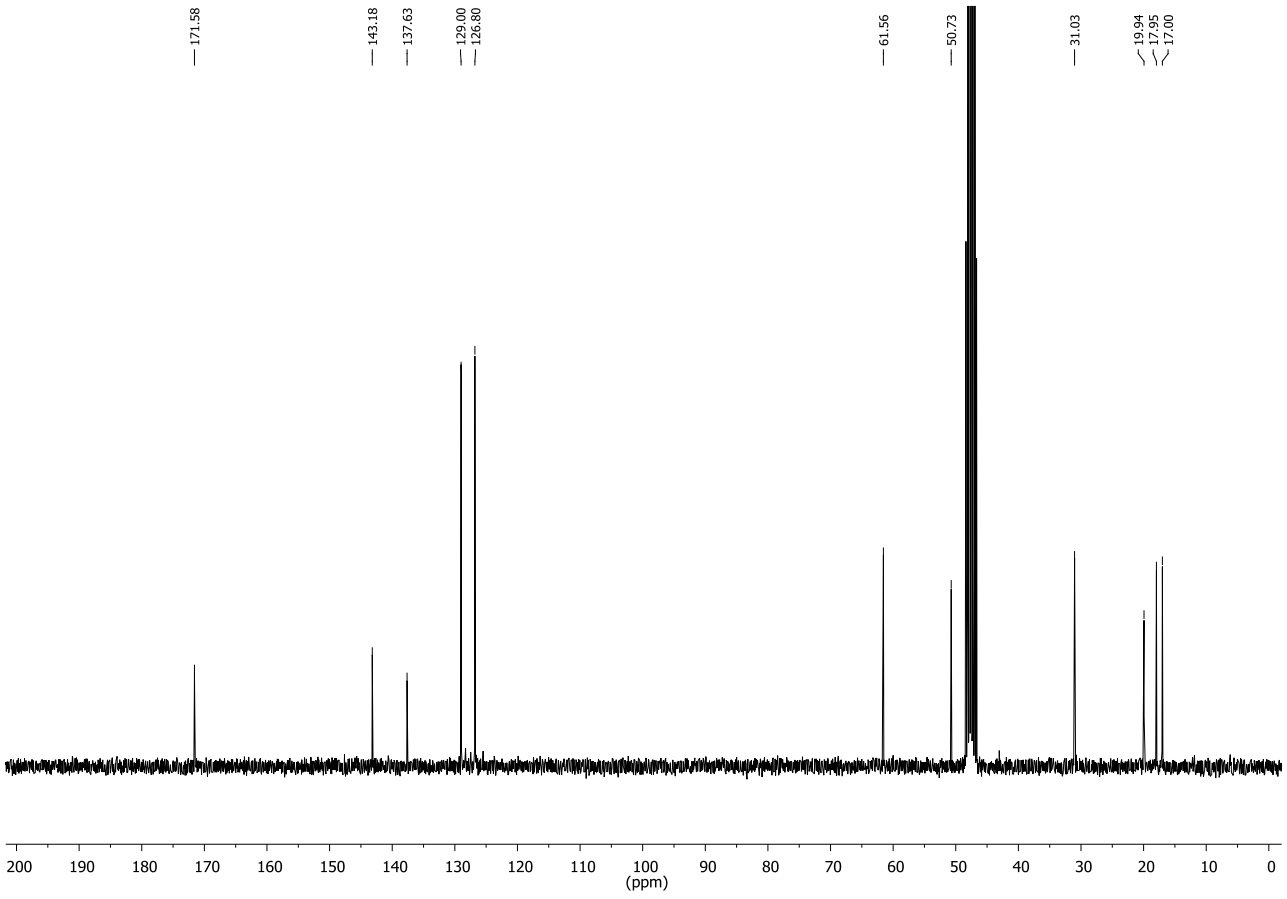

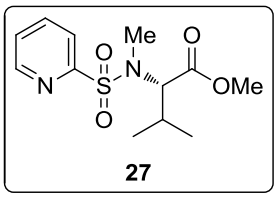

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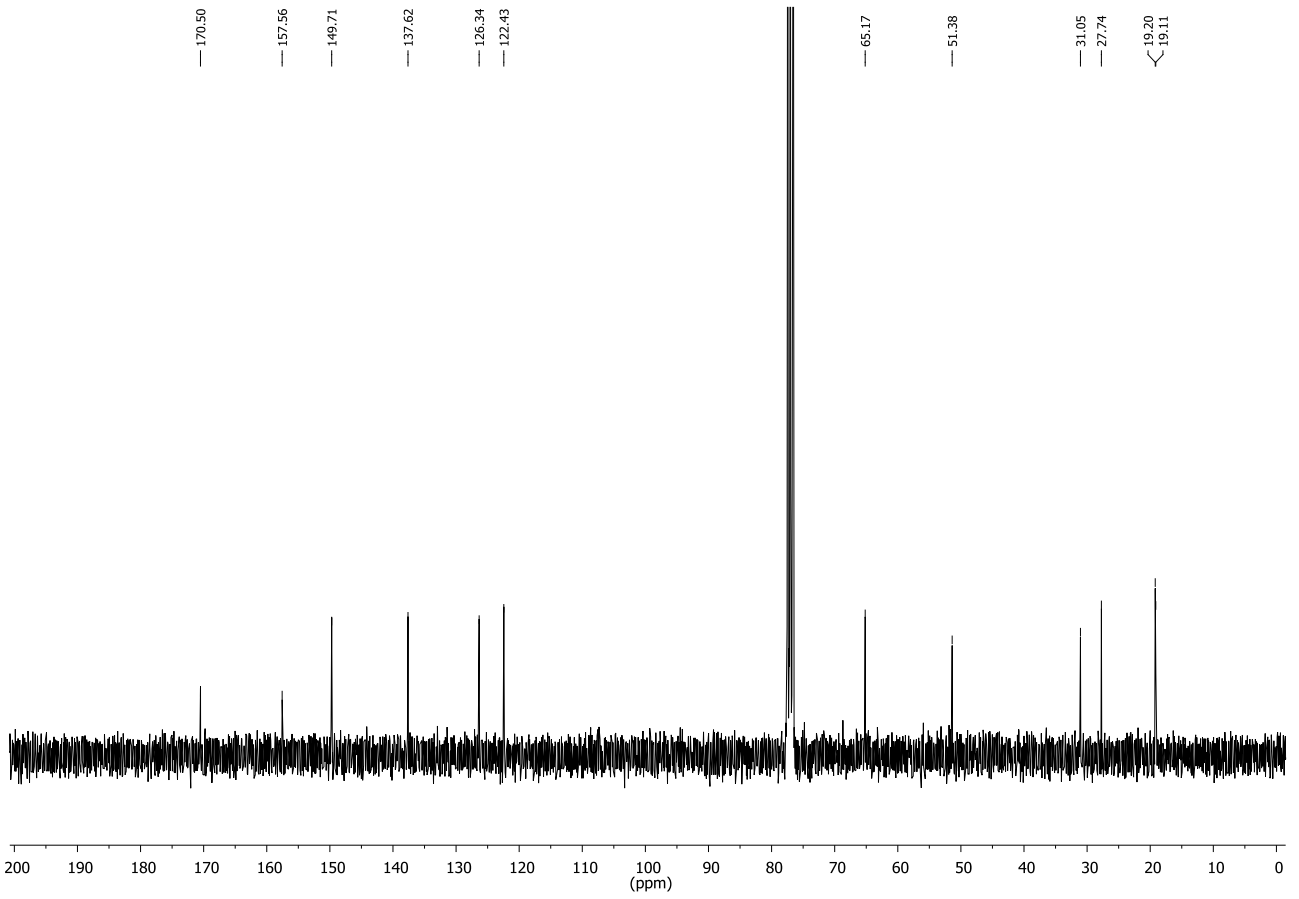

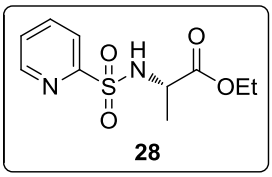

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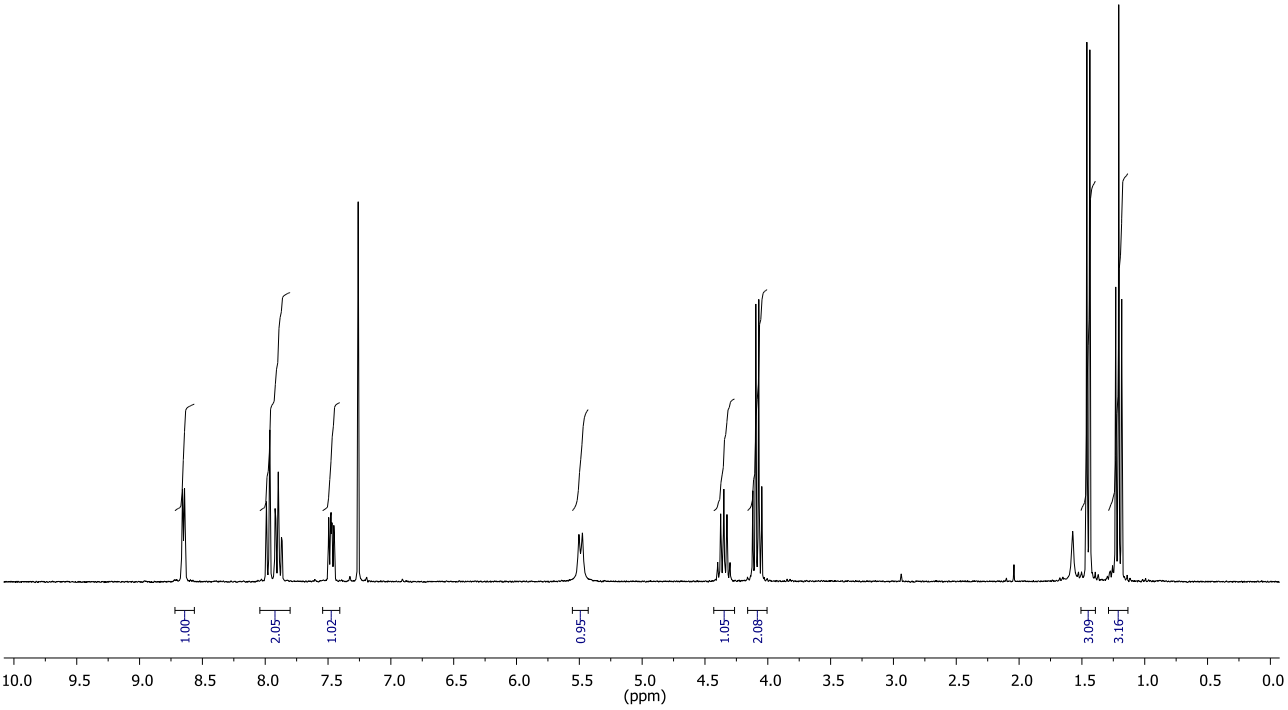

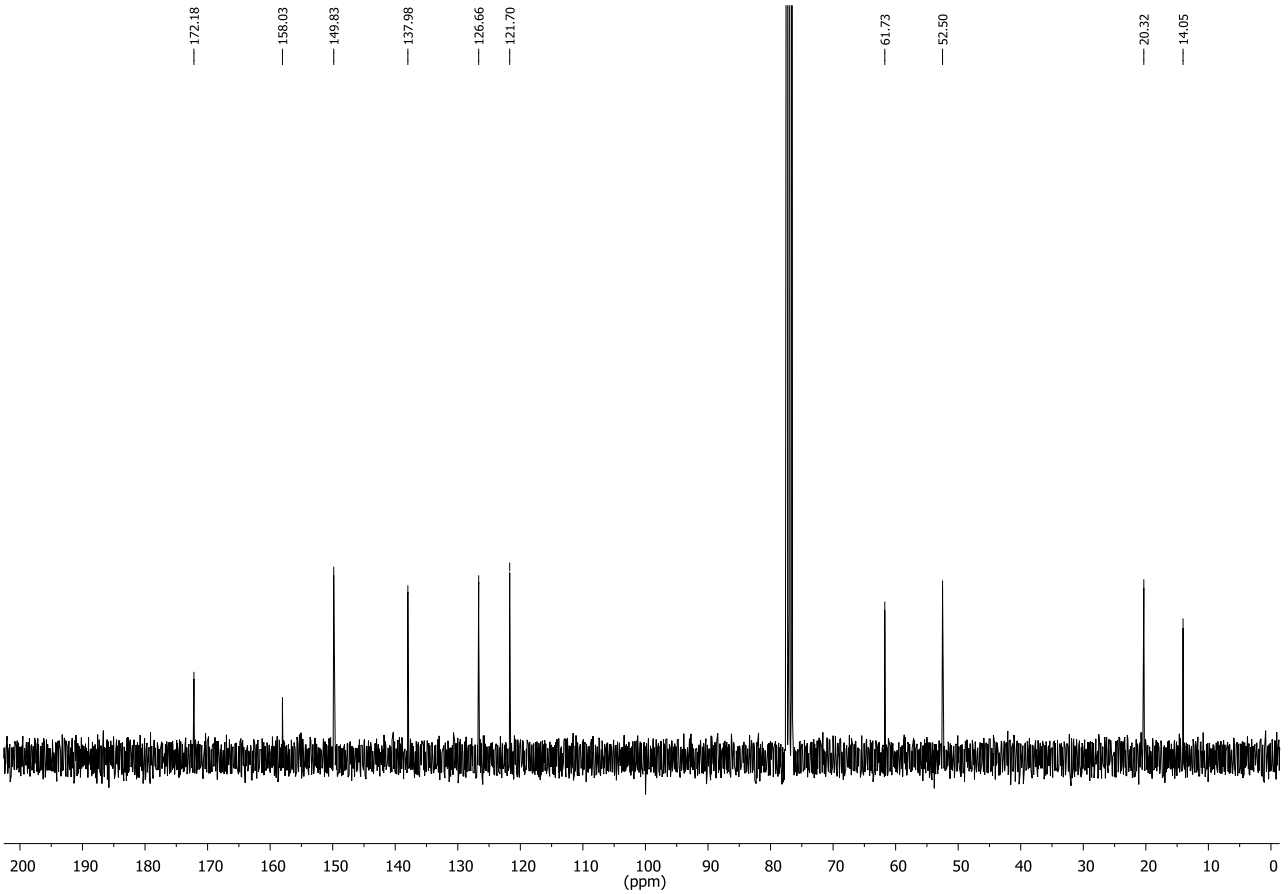

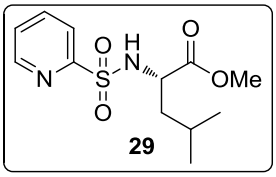

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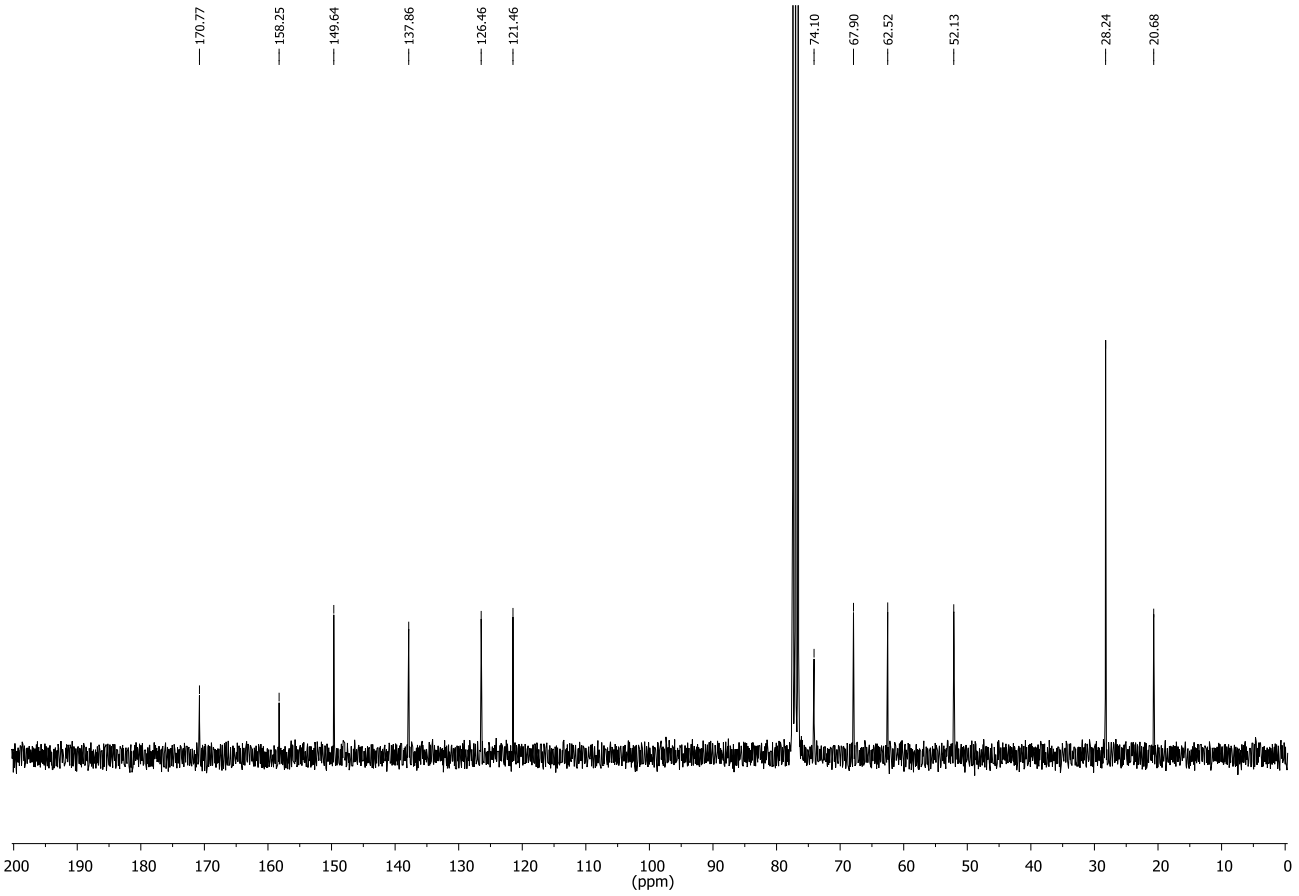
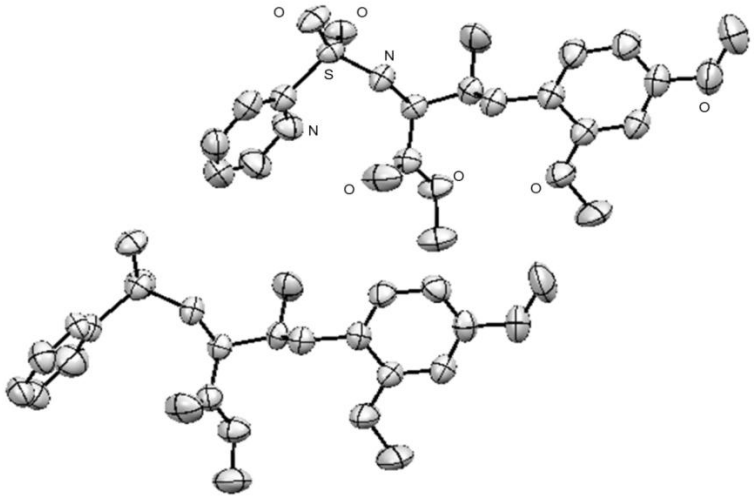


12a. X-Ray Data of enantiopure 2b



Crystal data

Chemical formula sum: $C_{19}H_{24}N_2O_6S$

Chemical formula weight: 408.46

Symmetry cell: Orthorhombic

Symmetric space group name: *P*2(1)2(1)2(1)

Cell volume: 4086.8 (3) $Å^3$

Cell formula units: $Z = 8$

Cell length a: 9.8306 (5) Å

Cell length b: 17.0929 (8) Å

Cell length c: 24.3215(12) Å

Cell measurement temperature: 298(2) K

Cell measurement reflections: 19517

Cell measurement theta (θ): 3.63 - 66.56 °

Mo *K*α radiation, λ = 1.54178 Å

$\mu = 1.735\ mm^{-1}$

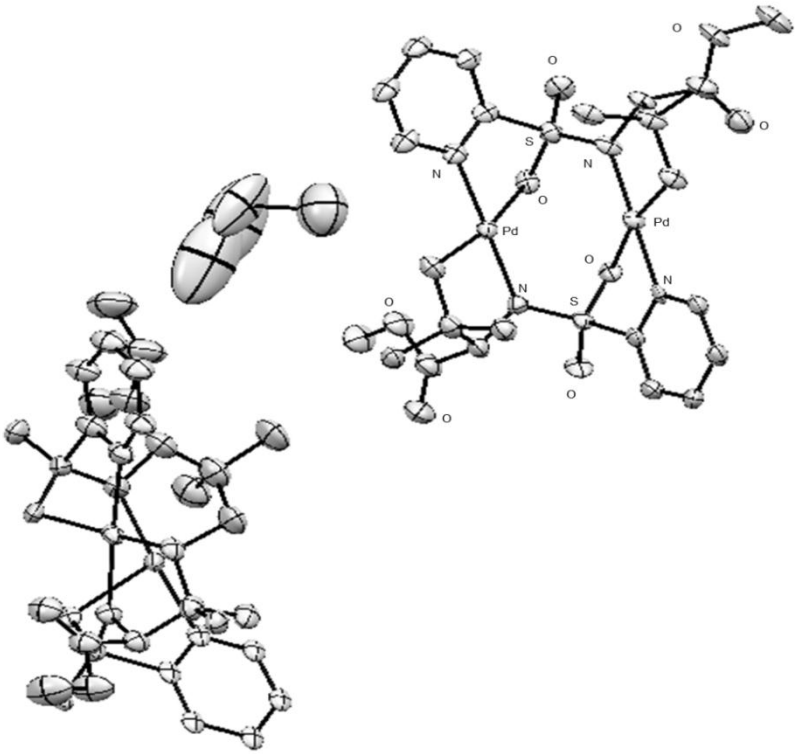
$D_x = 1.328\ Mgm^{-3}$

Crystal F(000): 1728

Crystal size (max, mid, min): 0.15 x 0.10 x 0.08 mm

12b. X-Ray Data of compound 23

The system has crystallized with a chiral space group and with a large metric due to the presence of two structurally independent complex molecules which are chemically equivalent.



Crystal data

Chemical formula sum: $2(C_{24}H_{32}N_4O_8Pd_2S_2)\cdot CH_2Cl_2$

Chemical formula weight: 1647.88

Symmetry cell: Orthorhombic

Symmetric space group name: *P*2(1)2(1)2(1)

Cell volume: 6045.2 (6) $Å^3$

Cell formula units: $Z = 4$

Cell length a: 8.4525 (4) Å

Cell length b: 15.486 (1) Å

Cell length c: 46.184 (3) Å

Cell measurement temperature: 100 K

Cell measurement reflections: 12340

Cell measurement theta (θ): 2.2–20.9°

Mo *K*α radiation, λ = 0.7107 Å

$\mu = 1.47\ mm^{-1}$

D_x=1.811 Mgm^{-3}

Crystal F(000): 404

Crystal Description: Prism

Crystal Colour: Colourless

Crystal size (max, mid, min): 0.2 × 0.11 × 0.04 mm