Supporting information for:

"Efficient synthesis of carbon-11 labeled acylsulfonamides using [^{11}C]CO carbonylation chemistry"

Berend van der Wildt, Bin Shen, Frederick T. Chin

Stanford University, School of Medicine, Department of Radiology, Molecular Imaging Program at Stanford (MIPS), 1201 Welch Road, PS049, Stanford, CA, 4305-5484, USA.

Table of Contents:

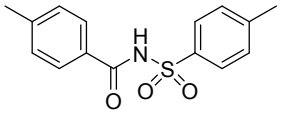
1. General synthethic conditions, materials and equipment

All chemical reagents and solvents were obtained from commercial suppliers and used as received. Tasisulam was obtained from Selleckchem (Houston, TX, USA), **ABT-199** was obtained from Cayman Chemicals (Ann Arbor, MI, USA). Microwave reactions were performed on a CEM Discover Legacy (Matthews, NC, USA). Reaction monitoring was performed by thin layer chromatography on pre-coated silica 60 F254 aluminium plates (Merck, Darmstadt, Germany). Spots were visualized with UV light (254 nm), $KMnO_4$ or ninhydrin staining. NMR spectroscopy was performed using an Agilent 400 MR (Agilent Technologies, Santa Clara, CA, USA) with chemical shifts (δ) reported in parts per million (ppm) relative to the solvent ($CDCl_3$ ^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm; DMSO-d_6 ^{1}H: 2.50 ppm, ^{13}C 39.52 ppm; CD_3OD ^{1}H: 3.31 ppm, ^{13}C: 49.00 ppm). High resolution mass spectrometry was performed on a Bruker Daltonics - apex-Qe (Bruker, Billerica, MA, USA) in either positive or negative ion mode. Carbon-11 was prepared by the ^{14}N(p,α)^{11}C nuclear reaction on a GE PETtrace 880 cyclotron using a irradiation for 5 minutes with 5 μA beam current and was delivered as [^{11}C]CO_2 using helium as a carrier gas to the experimental set up (GE TRACERlab FX-C Pro, Boston, MA, USA). Collecting and dispensing of radioactivity was performed using a Genie Plus syringe pump (Kent Scientific, Torrington, CT, USA) equipped with a disposable sterile 10 mL Luer-slip Norm-Ject syringe (VWR, Radnor, PA, USA). Radioactivity levels were measured using a Capintec CRC-15 dose calibrator (Florham Park, NJ, USA). Analytical HPLC was performed on an Agilent Technologies 1200 HPLC system (Agilent Technologies, Santa Clara, CA , USA) connected to a Raytest GABI* radiodetector (Elisia Raytest GmbH, Straubenhardt, Germany, sensitivity 370 Bq (10 nCi)) using a Luna 5u C18 column (250 x 4.6 mm, 5 μm particle size) using a mixture of A) H_2O + 0.1% TFA and B) MeCN + 0.1% TFA as a mobile phase according to the following scheme: 0 min, 50% B; 15 min, 70% B; 15.1 min, 95% B; 17 min, 95% B; 17.1 min, 50% B; 17.1-20.0 min 50% B. Preparative HPLC was performed on a Dionex Ultimate 3000 pump connected to a Dionex UVD340-U UV-Vis detector (Sunnyvale, CA, USA) and a Carroll and Ramsey Associates model 105s radiodetector (Berkeley, CA, USA) equipped with a Phenomenex Gemini HPLC column (Torrance, CA, USA, particle size 5u, 250 x 10 mm) using a mixture of A)) H_2O + 0.1% TFA and B) MeCN + 0.1% TFA as a mobile phase according to the following scheme: 0 min, 50% B; 15 min, 70% B; 15.1 min, 95% B; 17 min, 95% B; 17.1 min, 50% B; 17.1-20.0 min, 50% B.

2. General procedure and detailed synthesis towards unlabeled acylsulfonamides

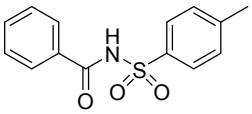
General procedure 'A' for the synthesis of acylsulfonamides: A solution of aryl halide (0.40 mmol), sulfonamide (0.40 mmol), $Mo(CO)_6$ (0.11 g, 0.40 mmol), $Pd(OAc)_2$ (9 mg, 0.04 mmol), and DBU (0.18 mL, 1.2 mmol) in dioxane (1.0 mL) was heated in a closed reaction vial for 15 minutes at 115 ^{o}C by microwave irradiation. After cooling to room temperature, the resulting reaction mixture was diluted with MeOH (10 mL), filtered and concentrated *in vacuo*. Purification by flash column chromatography (DCM –> 3% MeOH in DCM) afforded the desired acylsulfonamides.

4-methyl-*N*-tosylbenzamide (**1**):



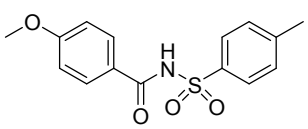
Using 'General Method A' (87 mg of 1-iodo-4-methylbenzene, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (107 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (br s, 1H), 8.04 (d, 2H, *J* = 8.0 Hz), 7.71 (d, 2H, *J* = 8.0 Hz), 7.34 (d, 2H, *J* = 8.0 Hz), 7.21 (d, 2H, *J* = 7.9 Hz), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.41, 145.30, 144.55, 135.52, 129.72, 129.68, 128.73, 128.30, 128.01, 21.86 ,21.76; ESI-HRMS *m*/*z* calculated for $C_{15}H_{15}NO_3S$ 289.0773, found 312.0664 $[M + Na]^+$.

N-tosylbenzamide (**2**):



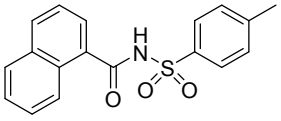
Using 'General Method A' (82 mg of iodobenzene and 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (110 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (bs, 1H), 8.05 (d, 2H, *J* = 8.4 Hz), 7.76 (d, 2H, *J* = 7.2 Hz), 7.58 (t, 1H, *J* = 7.4 Hz), 7.45 (t, 2H, *J* = 7.9 Hz), 7.36 (d, 2H, *J* = 8.6 Hz), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.62, 145.31, 135.66, 133.54, 131.37, 129.74, 129.00, 128.75, 127.98, 21.83; ESI-HRMS *m*/*z* calculated for $C_{14}H_{13}NO_3S$ 275.0616, found 298.0509 $[M + Na]^+$.

4-methoxy-*N*-tosylbenzamide (**3**):



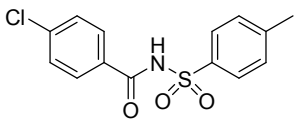
Using 'General Method A' (94 mg of 1-iodo-4-methoxybenzene, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (108 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (br s, 1H), 8.04 (d, 2H, *J* = 8.3 Hz), 7.80 (d, 2H, *J* = 8.8 Hz), 7.35 (d, 2H, *J* = 8.3 Hz), 6.89 (d, 2H, *J* = 8.8 Hz), 3.82 (s, 3H), 2.43 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.92, 163.83, 145.24, 135.65, 130.16, 129.72, 128.70, 123.28, 114.22, 55.66, 21.86; ESI-HRMS *m*/*z* calculated for $C_{15}H_{15}NO_4S$ 305.0722, found 328.0616 $[M + Na]^+$.

N-tosyl-1-naphthamide (**4**):



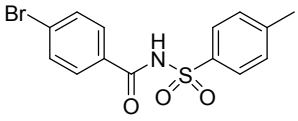
Using 'General Method A' (102 mg of 1-iodonaphthalene, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (96 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (bs, 1H), 8.20 (m, 1H), 8.07 (d, 2H, *J* = 8.2 Hz), 7.97 (d, 1H, *J* = 8.2 Hz), 7.85 (m, 1H), 7.68 (d, 1H, *J* = 7.1 Hz), 7.52 (m, 2H), 7.44 (t, 1H, *J* = 8.2 Hz), 7.38 (d, 2H, *J* = 7.8 Hz), 2.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.94, 145.43, 135.64, 133.86, 133.04, 130.26, 130.08, 129.81, 128.80, 128.67, 128.11, 127.02, 126.60, 124.97, 124.54, 21.89; ESI-HRMS *m*/*z* calculated for $C_{18}H_{15}NO_3S$ 325.0773, found 348.0666 $[M + Na]^+$.

4-chloro-*N*-tosylbenzamide (**5**):



Using 'General Method A' (77 mg of 1-bromo-4-chlorobenzene, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (97 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98, bs, 1H), 8.03 (d, 2H, *J* = 8.5 Hz), 7.73 (d, 2H, *J* = 8.7 Hz), 7.42 (d, 2H, *J* = 8.7 Hz), 7.36 (d, 2H, *J* = 8.5 Hz), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.32, 145.59, 140.22, 135.40, 129.82, 129.75, 129.44, 129.30, 128.86, 21.88. ESI-HRMS *m*/*z* calculated for $C_{14}H_{12}ClNO_3S$ 309.0226, found 332.0120 $[M + Na]^+$.

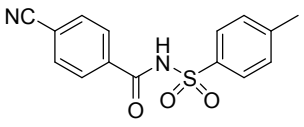
4-bromo-*N*-tosylbenzamide (**6**):



Using 'General Method A' (113 mg of 1-bromo-4-iodobenzene, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (86 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (bs, 1H), 8.03 (d, 2H, *J* = 8.4 Hz), 7.67 (d, 2H, *J* = 8.4 Hz), 7.57 (d, 2H, *J* = 8.4 Hz), 7.36 (d, 2H, *J* = 8.6 Hz), 2.44 (s, 3H); ^{13}C NMR

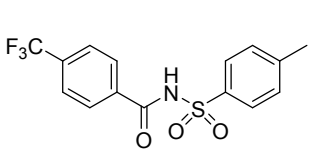
(101 MHz, $CDCl_3$) δ 163.70, 145.59, 135.39, 132.37, 130.19, 129.82, 129.48, 128.80, 128.78, 21.87; ESI-HRMS *m/z* calculated for $C_{14}H_{12}BrNO_3S$ 352.9721, found 375.9615 $[M + Na]^+$.

4-cyano-*N*-tosylbenzamide (**7**):



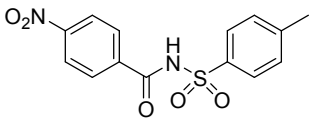
Using 'General Method A' (92 mg of 4-iodobenzonitrile, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (98 mg, 82%). ^1H NMR ($CDCl_3$) δ 8.05 (d, 2H, *J* = 8.3 Hz), 7.94 (d, 2H, *J* = 8.1 Hz), 7.70 (d, 2H, *J* = 7.9 Hz), 7.38 (d, 2H, *J* = 7.8 Hz), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.22, 145.60, 134.71, 134.44, 129.70, 128.67, 128.33, 125.94, 121.91, 21.71.

N-tosyl-4-(trifluoromethyl)benzamide (**8**):



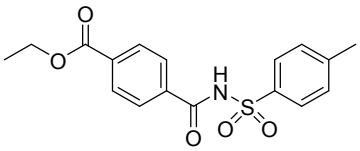
Using 'General Method A' (109 mg of 1-iodo-4-(trifluoromethyl)benzene, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (85 mg, 62%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, 2H, *J* = 8.4 Hz), 7.90 (d, 2H, *J* = 8.7 Hz), 7.75 (d, 2H, *J* = 8.7 Hz), 7.38 (d, 2H, *J* = 8.7 Hz), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.55, 145.75, 135.02, 134.89, 132.69, 129.73, 128.76, 128.35, 117.38, 116.94, 21.74; ESI-HRMS *m/z* calculated for $C_{15}H_{12}F_3NO_3S$ 343.0490, found 366.0390 $[M + Na]^+$.

4-nitro-*N*-tosylbenzamide (**9**):



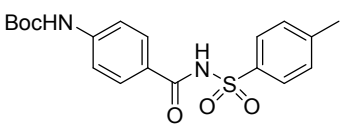
To solution of *p*-toluenesulfonamide (69 mg, 0.40 mmol) and TEA (0.11 mL, 0.80 mmol) in DMF (5 mL) was added 4-nitrobenzoyl chloride (74 mg, 0.40 mmol) and the resulting solution was stirred at 50 °C for 2 h. After concentration *in vacuo*, the resulting mixture was purified by flash column chromatography (2% MeOH in DCM) to afford the product as a white solid (45 mg, 35%). ^1H NMR (400 MHz, CD_3OD) δ 8.32 (d, 2H, *J* = 8.7 Hz), 8.01 (m, 4H), 7.42 (d, 2H, *J* = 8.2 Hz), 2.45 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 164.53, 150.41, 144.99, 137.56, 136.26, 129.18, 129.12, 128.10, 123.34, 20.14; ESI-HRMS *m/z* calculated for $C_{14}H_{12}N_2O_5S$ 320.0467, found 343.0361 $[M + Na]^+$.

Ethyl 4-(tosylcarbamoyl)benzoate (**10**):



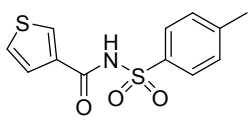
Using 'General Method A' (110 mg of ethyl 4-iodobenzoate, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (97 mg, 70%). ^1H NMR (400 MHz, DMSO-d_6) δ 9.70 (bs, 1H), 8.04 (m, 2H), 7.89 (m, 2H), 7.34 (d, 2H, *J* = 8.0 Hz), 4.37 (q, 2H, *J* = 7.1 Hz), 2.43 (s, 3H), 1.38 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.56, 164.00, 145.57, 135.36, 134.96, 134.73, 130.04, 129.8, 128.79, 128.05, 61.74, 21.83, 14.35; ESI-HRMS *m/z* calculated for $C_{17}H_{17}NO_5S$ 347.0827, found 370.0720 $[M + Na]^+$.

tert-butyl (4-(tosylcarbamoyl)phenyl)carbamate (**11**):



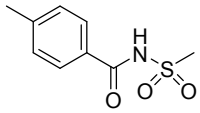
Using 'General Method A' (128 mg of *tert*-butyl (4-iodophenyl)carbamate, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (101 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.91 (bs, 1H), 8.03 (d, 2H, *J* = 8.4 Hz), 7.73 (d, 2H, *J* = 8.8 Hz), 7.42 (d, 2H, *J* = 8.9 Hz), 7.34 (d, 2H, *J* = 8.6 Hz), 6.72 (bs, 1H), 2.43 (s, 3H), 1.51 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 163.56, 152.17, 145.27, 143.44, 135.74, 129.73, 129.32, 128.81, 125.18, 117.84, 81.72, 28.38, 21.85; ESI-HRMS *m/z* calculated for $C_{19}H_{22}N_2O_5S$ 390.1249, found 413.1143 $[M + Na]^+$.

N-tosylthiophene-3-carboxamide (**12**):



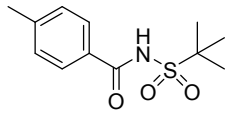
Using 'General Method A' (84 mg of 3-iodothiophene, 69 mg of *p*-toluenesulfonamide) the product was obtained as a white solid (106 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (bs, 1H), 8.11 (dd, 1H, *J* = 1.4, 3.0 Hz), 8.04 (d, 2H, *J* = 8.3 Hz), 7.47 (dd, 1H, *J* = 1.4, 5.2 Hz), 7.35 (d, 2H, *J* = 8.0 Hz), 7.30 (dd, 1H, *J* = 3.0, 5.2 Hz), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.72, 145.43, 135.59, 134.45, 132.03, 129.80, 128.71, 127.24, 126.91, 21.84; ESI-HRMS *m*/*z* calculated for $C_{12}H_{11}NO_3S_2$ 281.0180, found 304.0073 $[M + Na]^+$.

4-methyl-*N*-(methylsulfonyl)benzamide (**13**):



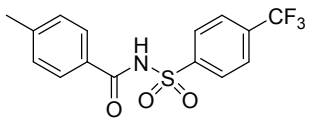
Using 'General Method A' (87 mg of 1-iodo-4-methylbenzene, 38 mg of methanesulfonamide) the product was obtained as a white solid (77 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (bs, 1H), 7.76 (d, 2H, *J* = 8.3 Hz), 7.29 (d, 2H, *J* = 7.9 Hz), 3.43 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 144.96, 129.88, 128.26, 128.07, 41.93, 21.82; ESI-HRMS *m*/*z* calculated for $C_9H_{11}NO_3S$ 213.0460, found 236.0353 $[M + Na]^+$.

N-(*tert*-butylsulfonyl)-4-methylbenzamide (**14**):



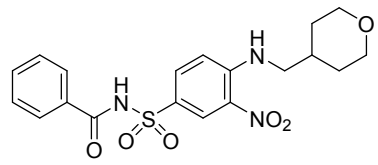
Using 'General Method A' (87 mg of 1-iodo-4-methylbenzene, 55 mg of 2-methylpropane-2-sulfonamide) the product was obtained as a white solid (82 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (bs, 1H), 7.74 (d, 2H, *J* = 8.1 Hz), 7.29 (d, 2H, *J* = 8.2 hz), 2.42 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.69, 144.53, 129.80, 129.24, 128.04, 62.86, 24.74, 21.76; ESI-HRMS *m*/*z* calculated for $C_{12}H_{17}NO_3S$ 255.0929, found 278.0821 $[M + Na]^+$.

4-methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)benzamide (**15**):



Using 'General Method A' (87 mg of 1-iodo-4-methylbenzene, 99 mg of 4-(trifluoromethyl)benzenesulfonamide) the product was obtained as a white solid (100 mg, 73%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 (d, 2H, *J* = 8.2 Hz), 7.92 (d, 2H, *J* = 8.3 Hz), 7.72 (d, 2H, *J* = 8.3 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 2.38 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 166.35, 144.30, 143.46, 134.45 (q, *J* = 32.8 Hz), 129.01, 128.85, 128.79, 128.03, 123.40 (q, *J* = 272.2 Hz), 125.68 (q, *J* = 3.8 Hz), 20.14; ESI-HRMS *m*/*z* calculated for $C_{15}H_{12}F_3NO_3S$ 343.0490, found 366.0384 $[M + Na]^+$.

N-((3-nitro-4-(((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide (**16**):

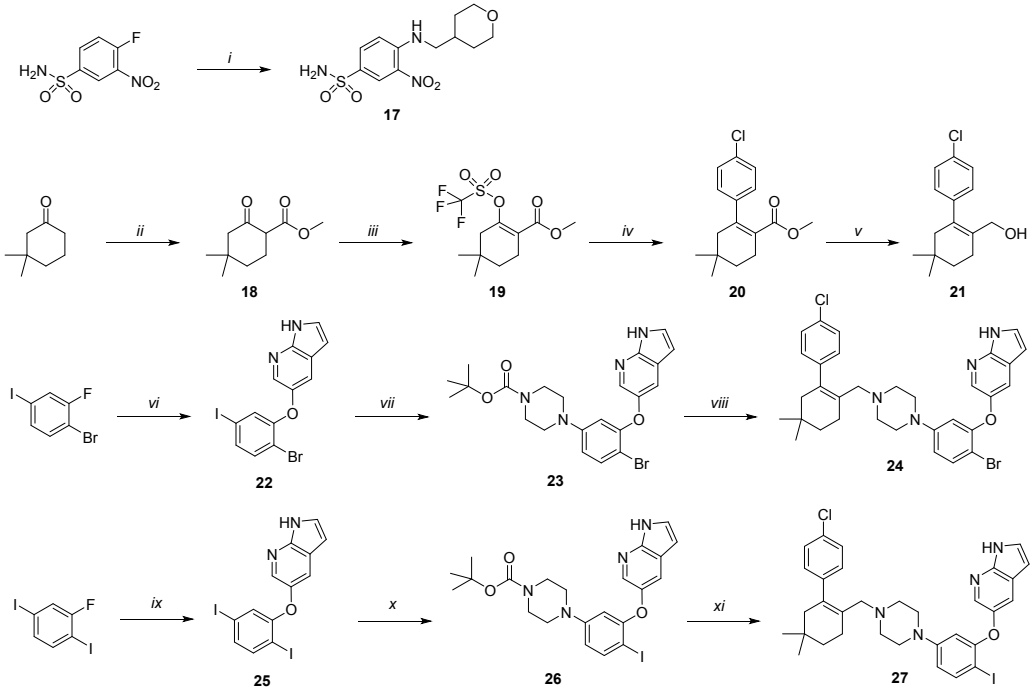


A solution of 3-nitro-4-(((tetrahydro-2H-pyran-4-yl)methyl)amino)benzenesulfonamide (0.16 g, 0.50 mmol), benzoic acid (61 mg, 0.50 mmol), EDC (0.12 g, 0.60 mmol) and DMAP (73 mg, 0.60 mmol) in DCM/THF (4 mL, 1:1) was stirred at ambient temperature for 16 h. The solution was diluted with EA (50 mL) and washed with sat. $NaHCO_3$ (3 x 50 mL), 1 M HCl (3 x 50 mL) and brine (50 mL). After drying on Na_2SO_4, filtration and concentration *in vacuo* the product was obtained as a yellow solid (80 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, 1H, *J* = 2.3 Hz), 8.55 (t, 1H, *J* = 5,4 Hz), 8.19 (dd, 1H, *J* = 2.3, 9.2 Hz), 7.82 (d, 2H, *J* = 7.2 Hz), 7.56 (t, 1H, *J* = 7.5 Hz), 7.41 (t, 2H, *J* = 7.8 Hz), 6.96 (d, 1H, *J* = 9.4 Hz), 4.01 (dd, 2H, *J* = 3.1, 11.5 Hz), 3.41 (dt, 2H, *J* = 1.9, 11.8 Hz), 3.27 (t, 2H, *J* = 6.2 Hz), 1.97 (m, 1H), 1.72 (d, 2H, *J* = 12.9 Hz), 1.44 (dq, 2H, *J* = 4.4, 12.1 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.06, 148.22, 135.54, 133.66, 131.25, 130.87, 129.35, 129.00, 128.01, 124.60, 114.17, 67.51, 49.27, 34.73, 30.85; ESI-HRMS *m*/*z* calculated for $C_{19}H_{21}N_3O_6S$ 419.1151, found: 442.1045 $[M + Na]^+$.

3. Synthesis scheme and procedures for precursors towards [^{11}C]ABT199

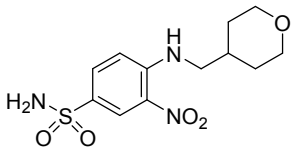
The synthesis route towards precursors **17**, **24** and **27** was derived from the reported literature procedures and is depicted below.[1,2] Sulfonamide precursor **17** was obtained in a single step by nucleophilic substitution with aminomethyltetrahydropyran. For the aryl halide, efforts were focused on using the aryl bromide precursor **24**, rather than its corresponding aryl iodide analogue, due to the increased ease of synthesis. Precursor **24** was synthesized in a convergent fashion from the key building blocks aryl bromide **23** and alcohol **21**. Briefly, alkylation of dimethylcyclohexanone with dimethylcarbonate resulted in β-ketoester **18**. Following triflation of the enol tautomer of **18**, triflate **19** was obtained, which was directly subjected to a Suzuki reaction with chlorophenylboronoic acid to afford the methyl ester **20**. Subsequent reduction with $LiBH_4$ resulted in alcohol **21** in an overall yield of 48% over 4 steps. Aryl bromide **23** was obtained after nucleophilic aromatic substitution of bromo-fluoro-iodobenzene with hydroxyl-azaindole followed by Buchwald Hartwig amination with boc-piperazine, which proceeded selectively at the aryl iodide position. Finally, combining Boc-deprotected **23** and mesyl chloride activated **21** under basic conditions resulted in precursor aryl bromide **24** in total of 8 reactions with 5 steps being the longest linear sequence and corresponding to a 19% yield. In an analogous fashion as **24**, precursor **27** was obtained.

1) M. Bruncko, D. Hong, G. A. Doherty, S. W. Elmore, L. Hasvold, L. Hexamer, A. R. Kunzer, R. A. Mantei, W. J. McClellan, C. H. Park, C. M. Park, A. M. Petros, X. Song, A. J. Souers, G. M. Sullivan, Z. F. Tao, G. T. Wang, L. Wang, X. Wang, M. D. Wendt and T. M. Hansen, US 20100298321, 2010.
2) R. J. Giedt, M. M. Sprachman, K. S. Yang and R. Weissleder, Bioconjugate Chem., 2014, 25, 2081–2085.



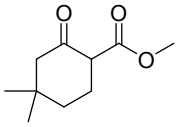
Synthesis of sulfonamide **17**, aryl bromide precursor **24**, aryl iodide precursor **27**. Reagents and conditions: *i*) 4-aminomethyltetrahydropyran, TEA, THF, rt, 16 h, 78%; *ii*) Dimethylcarbonate, NaH, THF, reflux, 2 h, 80%; *iii*) Triflic anhydride, NaH, DCM, -78 °C to rt, 16 h; *iv*) (4-chlorophenyl)boronic acid, $Pd(PPh_3)_4$, CsF, MeOH/DME, 70 °C, 16 h, 70% over two steps; *v*) $LiBH_4$, THF/MeOH, rt, 24 h, 85%; *vi*) 5-hydroxy-7-azaindole, K_2CO_3, 120 °C, 16 h, 58%; *vii*) Boc-piperazine, Pd_2dba_3, xantphos, KOtBu, THF/dioxane, 80 °C, 16 h, 58%; *viii*) 1) Compound **23**, DCM/TFA 1:1, 1 h, rt, quant.; 2) Compound **21**, MsCl, TEA, DCM, 1h, rt; 3) Solution of 1) and 2) in DCM, rt, 16 h, 40%; *ix*) 5-hydroxy-7-azaindole, K_2CO_3, 120 °C, 16 h, 48%; *x*) Boc-piperazine, Pd_2dba_3, xantphos, KOtBu, THF/dioxane, 80 °C, 16 h, 23%; *xi*) 1) Compound **26**, DCM/TFA 1:1, 1 h, rt, quant.; 2) Compound **21**, MsCl, TEA, DCM, 1h, rt; 3) Solution of 1) and 2) in DCM, rt, 16 h, 38%.

3-nitro-4-(((tetrahydro-2H-pyran-4-yl)methyl)amino)benzenesulfonamide (**17**):



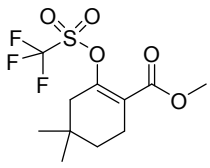
A solution of 4-fluoro-3-nitrobenzenesulfonamide (1.1 g, 5.0 mmol), (tetrahydro-2H-pyran-4-yl)methanamine (0.60 g, 4.5 mmol) and TEA (0.56 g, 5.5 mmol) in THF (20 mL) was reacted for 16 h at ambient temperature. After concentration *in vacuo* and dilution with DCM (100 mL) the solids were filtered, washed with DCM and dried to yield the product as a yellow solid (1.1 g, 78%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (t, 1H, *J* = 5.9 Hz), 8.45 (d, 1H, *J* = 2.3 Hz), 7.81 (dd, 1H, *J* = 2.2, 9.2 Hz), 7.30 (s, 2H), 7.29 (d, 1H, *J* = 9.3 Hz), 3.84 (dd, 2H, *J* = 2.9, 11.3 Hz), 3.34 (t, 2H, *J* = 6.7 Hz), 3.25 (t, 2H, *J* = 11.7 Hz), 1.90 (m, 1H), 1.61 (m, 2H), 1.26 (dq, 2H, *J* = 4.4, 12.0 Hz); ^{13}C NMR (101 MHz, DMSO-d_6) δ 146.67, 132.71, 130.00, 129.39, 124.73, 115.66, 66.64, 47.82, 33.94, 30.15; ESI-HRMS *m/z* calculated for $C_{12}H_{17}N_3O_5S$ 315.0889, found 338.0784 $[M + Na]^+$.

Methyl 4,4-dimethyl-2-oxocyclohexane-1-carboxylate (**18**):



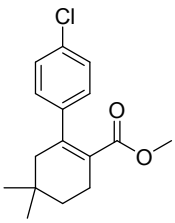
To a mixture of dimethylcarbonate (15.5 mL, 160 mmol) and NaH (1.9 g, 80 mmol) in THF (60 mL) was added 3,3-dimethylcyclohexan-1-one (5.0 g, 40 mmol) dropwise. The resulting mixture was reacted at reflux temperature for 2 h. The mixture was poured into H_2O (100 mL) and extracted with Et_2O (3 x 100 mL). After concentration *in vacuo*, the residue was purified using flash column chromatography (EA/hexanes 1:9) to obtain the product as a colorless oil (5.9 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.10 (s, 1H), 3.75 (s, 3H), 2.24 (m, 2H), 2.04 (s, 2H), 1.37 (t, 2H, *J* = 6.5 Hz), 0.95 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.94, 171.36, 96.08, 51.29, 42.54, 35.05, 29.61, 27.91, 19.94; ESI-HRMS *m/z* calculated for $C_{10}H_{16}O_3$ 184.1099, found 391.2098 $[2M + Na]^+$.

Methyl 4,4-dimethyl-2-(((trifluoromethyl)sulfonyl)oxy)cyclohex-1-ene-1-carboxylate (**19**):



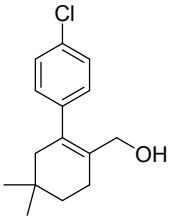
A suspension of **18** (3.0 g, 16 mmol) and NaH (0.78 g, 32 mmol) in DCM (100 mL) was reacted for 1 h at 0 °C. After cooling to -78 C, Tf_2O (3.0 mL, 18 mmol) was added dropwise and the mixture was allowed to reach room temperature and stirred overnight. The mixture was diluted with brine (150 mL) and extracted with DCM (3 x 100 mL). The organic fractions were combined and dried on Na_2SO_4, filtered and concentrated to obtain a purple oil that was directly used in the subsequent reaction (5.1 g, quant.). ESI-HRMS: *m/z* calculated for $C_{11}H_{15}F_3O_5S$ 316.0592, found 339.0491 $[M + Na]^+$.

Methyl 4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-carboxylate (**20**):



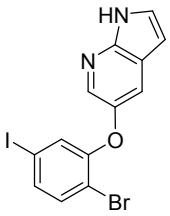
A solution of **19** (4.8 g, 15 mmol), (4-chlorophenyl)boronic acid (2.4 g, 15 mmol), $Pd(PPh_3)_4$ (0.52 g, 0.45 mmol) and CsF (4.6 g, 30 mmol) in MeOH/DME (1:1, 60 mL) was heated to 70 °C and reacted for 16 h. The mixture was concentrated and resuspended in EA (100 mL) and washed with sat. $NaHCO_3$ (100 mL), 1 M HCl (100 mL) and brine (100 mL). The organic fractions was dried on Na_2SO_4, filtered and concentrated. After flash column chromatography (3% EA in hexane) the product was obtained as a colorless oil (2.9 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, 2H, *J* = 8.1 Hz), 7.03 (d, 2H, *J* = 8.2 Hz), 3.46 (s, 3H), 2.46 (m, 2H), 2.12 (s, 2H), 1.48 (t, 2H, *J* = 6.4 Hz), 0.99 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.68, 144.46, 142.11, 132.79, 128.30, 128.23, 126.80, 51.38, 46.96, 34.67, 29.23, 28.05, 24.67; ESI-HRMS *m/z* calculated for $C_{16}H_{19}ClO_2$ 278.1074, found 301.0966 $[M + Na]^+$.

(4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methanol (**21**):



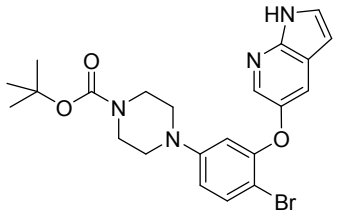
To a solution of **20** (0.56 g, 2.0 mmol) and $LiBH_4$ (0.13 g, 6.0 mmol) in THF (5 mL) was added MeOH (0.23 mL, 6.0 mmol) dropwise and the resulting mixture was stirred for 24 h at ambient temperature. The mixture was quenched with 1 M HCl (20 mL) and extracted with chloroform (3 x 50 mL). The organic fractions were combined and concentrated *in vacuo*. After flash column chromatography (10% EA in hexane) the product was obtained as a colorless oil (0.43 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (m, 2H), 7.06 (m, 2H), 3.92 (s, 2H), 2.28 (m, 2H), 2.03 (s, 2H), 1.48 (m, 2H), 1.37 (bs, 1H), 0.97 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.54, 134.85, 132.43, 131.87, 129.61, 128.40, 63.67, 46.31, 35.34, 29.33, 28.18, 25.02.

5-(2-bromo-5-iodophenoxy)-1H-pyrrolo[2,3-b]pyridine (**22**):



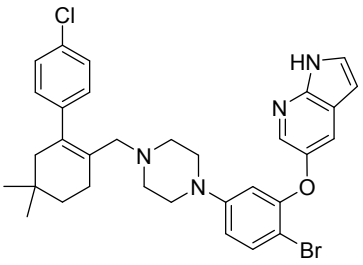
A mixture of 1-bromo-2-fluoro-4-iodobenzene (1.5 g, 5.0 mmol), 1H-pyrrolo[2,3-b]pyridin-5-ol (0.67 g, 5.0 mmol) and K_2CO_3 (0.69 g, 5.0 mmol) in DMF (10 mL) was heated at 120 °C for 16 h. The mixture was filtered and the filtrate was concentrated *in vacuo*. After addition of hexane/EA (20 mL) the precipitates were filtered and washed with additional ethyl acetate. After drying the precipitate the product was obtained as a white solid (1.2 g, 58%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.09 (d, 1H, *J* = 2.6 Hz), 7.70 (d, 1H, *J* = 2.7 Hz), 7.56 (m, 1H), 7.52 (d, 1H, *J* = 8.3 Hz), 7.41 (dd, 1H, *J* = 1.9, 8.3 Hz), 7.07 (d, 1H, *J* = 1.9 Hz), 6.46 (dd, 1H, *J* = 1.6, 3.4 Hz); ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.62, 146.01, 145.80, 135.22, 135.20, 133.21, 128.14, 126.26, 119.98, 118.54, 112.51, 100.11, 93.76; ESI-HRMS *m/z* calculated for $C_{13}H_8BrIN_2O$ 413.8865, found 414.8942 $[M + H]^+$.

tert-butyl 4-(3-((1H-pyrrolo[2,3-b]pyridin-5-yl)oxy)-4-bromophenyl)piperazine-1-carboxylate (**23**):



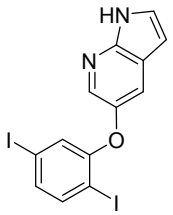
To a solution of **22** (1.0 g, 2.4 mmol), boc-piperazine (0.50 g, 2.7 mmol), $Pd_2(dba)_3$ (0.11 g, 0.12 mmol) and Xantphos (0.21 g, 0.36 mmol) in dioxane (4 mL) was added KOtBu (1.0 M in THF, 3.6 mL, 0.36 mmol) and the resulting mixture was heated at 80 °C for 16 h. After filtration the filtrate was concentrated *in vacuo* and purified by flash column chromatography (1% MeOH in DCM), affording the product as a yellow solid (0.59 g, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (bs, 1H), 8.04 (m, 1H), 7.97 (m, 1H), 7.37 (dd, 1H, *J* = 2.4, 3.5 Hz), 7.02 (m, 2H), 6.61 (dd, 1H, *J* = 2.1, 3.6 Hz), 3.64 (t, 4H, *J* = 5.2 Hz), 3.30 (t, 4H, *J* = 5.1 Hz), 1.50 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) 155.68, 154.69, 152.09, 147.94, 145.66, 136.04, 133.89, 126.71, 120.64, 118.89, 112.59, 107.28, 103.61, 101.22, 80.16, 49.04, 28.53.

5-(2-bromo-5-(4-((4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)piperazin-1-yl)phenoxy)-1H-pyrrolo[2,3-b]pyridine (**24**):



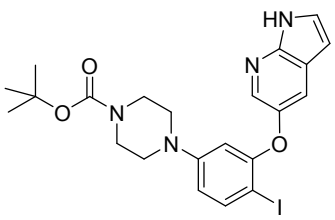
Compound **23** (0.50 mmol, 0.24 g) was dissolved in DCM/TFA (1:1, 5 mL) and stirred for 1 h at room temperature. After concentration *in vacuo* and co-evaporation with toluene (2 x 5 mL) an orange solid was obtained, which was taken up in DCM (2 mL) and TEA (0.40 mL, 3 mmol). A solution of compound **21** (0.13 g, 0.50 mmol), MsCl (69 mg, 0.60 mmol) and TEA (0.10 mL, 0.75 mmol) in DCM (10 mL) were reacted for 1 h at rt. The solution was diluted with DCM (40 mL) and washed with 1 M HCl (3 x 50 mL). The organic fraction was dried on Na_2SO_4, filtered and concentrated *in vacuo* to obtain a colorless oil. This oil was dissolved in the previously obtained orange solution containing deprotected **23** and this solution was stirred overnight at ambient temperature. After concentration *in vacuo* and flash column chromatography (n-hexane/EA 3:1) the product was obtained as a white solid (0.12 g, 40%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.68 (s, 1H), 8.02 (d, 1H, *J* = 2.6), 7.50 (m, 2H), 7.45 (d, 1H, *J* = 8.9 Hz), 7.33 (m, 2H), 7.05 (m, 2H), 6.65 (dd, 1H, *J* = 2.6, 8.9 Hz), 6.45 (d, 1H, *J* = 2.6 Hz), 6.40 (m, 1H), 2.96 (m, 4H), 2.72 (s, 2H), 2.19 (m, 6H), 1.95 (s, 2H), 1.38 (t, 2H, *J* = 6.3 Hz), 0.92 (s, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.37, 151.69, 147.24, 145.15, 141.97, 134.43, 133.87, 133.14, 130.64, 129.85, 129.03, 127.87, 127.53, 119.70, 116.64, 111.90, 106.29, 101.10, 99.79, 59.60, 52.10, 47.59, 46.23, 34.77, 28.74, 27.77, 25.10; ESI-HRMS *m/z* calculated for $C_{32}H_{34}BrClN_4O$ 604.1605, found: 605.1687 $[M + H]^+$.

5-(2,5-diiodophenoxy)-1*H*-pyrrolo[2,3-*b*]pyridine (**25**):



A mixture of 2-fluoro-1,4-diiodobenzene (1.7 g, 5.0 mmol), 1H-pyrrolo[2,3-b]pyridin-5-ol (0.67 g, 5.0 mmol) and K_2CO_3 (0.69 g, 5.0 mmol) in DMF (10 mL) was heated at 120 °C for 16 h. The resulting mixture was cooled to room temperature, diluted with EA (10 mL) and filtered. The filtrate was concentrated *in vacuo* and diluted with MeOH/EA 1:1. The precipitate was collected and dried. The title compound was obtained as a white solid (1.1 g, 48%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.80 (bs, 1H), 8.07 (d, 1H, *J* = 2.6 Hz), 7.67 (m, 2H), 7.57 (m, 1H), 7.25 (dd, 1H, *J* = 1.9, 8.2 Hz), 6.98 (d, 1H, *J* = 1.8 Hz), 6.45 (dd, 1H, *J* = 1.8, 3.4 Hz); ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.41, 146.30, 145.74, 141.08, 135.28, 133.67, 128.11, 125.38, 119.97, 118.50, 100.10, 94.72, 87.83; ESI-HRMS *m/z* calculated for $C_{13}H_8I_2N_2O$ 461.8726, found 460.9653 $[M - H]^-$.

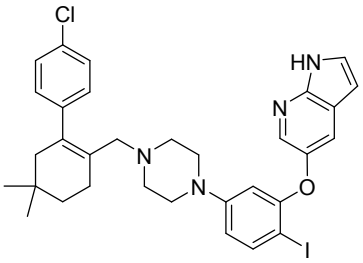
Tert-butyl 4-(3-((1H-pyrrolo[2,3-b]pyridin-5-yl)oxy)-4-iodophenyl)piperazine-1-carboxylate (**26**):



To a solution of **25** (0.46 g, 1.0 mmol), *boc*-piperazine (0.20 g, 1.1 mmol), $Pd_2(dba)_3$ (46 mg, 50 µmol), xantphos (87 mg, 0.15 mmol) in THF (2 mL) under N_2 atmosphere was added KOtBu (1.5 mL of a 1.0 M solution in THF, 1.5 mmol) and the resulting solution was heated at reflux temperature for 16 hours. After concentration *in vacuo*, the residue was purified using flash column chromatography (EA/hexanes 1:3). The product was obtained as a yellow solid (0.12 g, 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.26 (s, 1H), 8.20 (d, 1H, *J* = 2.5 Hz), 7.67 (d, 1H, *J* = 8.7 Hz), 7.59 (d, 1H, *J* = 2.4 Hz), 7.42 (m, 1H), 6.46 (m, 2H), 6.36 (d, 1H, *J* = 2.7 Hz), 3.48 (m, 4H), 3.00 (m, 4H), 1.44 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.44, 154.53, 152.88, 147.62, 145.80, 139.62, 135.59, 127.00, 120.77, 119.15, 113.06, 106.12, 100.77, 80.00, 75.07, 48.67, 28.39. ESI-HRMS calculated for $C_{22}H_{25}IN_4O_3$ 520.0971, found 519.0901 $[M - H]^-$.

5-(5-(4-((4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)piperazin-1-yl)-2-iodophenoxy)-1H-pyrrolo[2,3-b]pyridine (**27**):

Compound **26** (0.10 g, 0.20 mmol) was dissolved in DCM/TFA (1:1, 5 mL) and stirred for 1 h at room temperature. After concentration *in vacuo* and co-evaporation with toluene (2 x 5 mL) an orange solid was obtained, which was taken up in DCM (2 mL) and TEA (0.40 mL, 3 mmol). A solution of compound **21** (50 mg, 0.24 mmol), MsCl (27 mg, 0.24 mmol) and TEA (80 mg, 0.40 mmol) in DCM (4 mL) were reacted for 1 h at rt. The solution was diluted with DCM (40 mL) and washed with 1 M HCl (3 x 50 mL). The organic fraction was dried on Na_2SO_4, filtered and concentrated *in vacuo* to obtain a colorless oil. This oil was dissolved in the previously obtained orange solution containing deprotected **27** and this solution was stirred overnight at ambient temperature. After concentration *in vacuo* and flash column chromatography (hexane/EA 3:1) the product was obtained as a white solid (50 mg, 38%). ^{1}H NMR (400 MHz, CDCl3) δ 10.44 (bs, 1H), 8.19 (s, 1H), 7.62 (d, 1H, *J* = 8.8 Hz), 7.57 (d, 1H, *J* = 2.4 Hz), 7.40 (m, 1H), 7.24 (m, 2H), 6.94 (d, 2H, *J* = 8.5 Hz), 6.47 (dd, 1H, *J* = 1.9, 3.4 Hz), 6.43 (dd, 1H, *J* = 2.7, 8.8 Hz), 6.33 (d, 1H, *J* = 2.7 Hz), 2.99 (m, 4H), 2.77 (m, 2H), 2.18 (m, 8H), 1.42 (m, 2H), 0.94 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.22, 153.01, 147.84, 145.63, 142.17, 139.43, 135.76, 135.05, 131.86, 129.72, 129.26, 128.18, 126.70, 120.65, 119.01, 112.60, 105.64, 100.91, 74.08, 60.38, 52.53, 48.49, 46.98, 35.35, 29.20, 28.18, 25.63; ESI-HRMS calculated for $C_{32}H_{34}ClIN_4O$ 652.1466, found 651.1400 $[M - H]^-$.



4. General procedures towards carbon-11 labeled acylsulfonamides

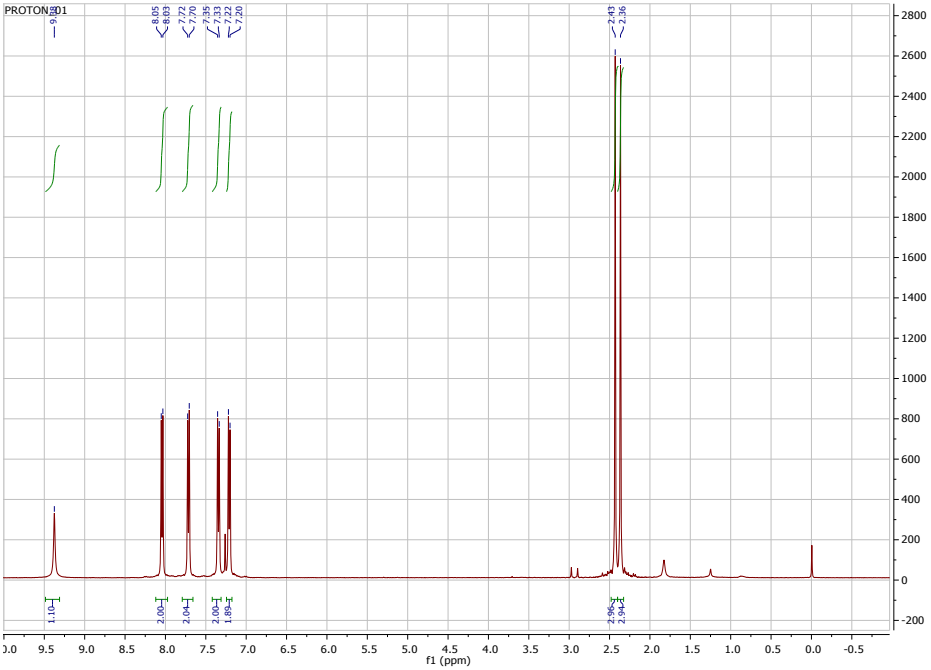
Carbon-11 was prepared by the ^{14}N(*p*,α)^{11}C nuclear reaction on a GE PETtrace cyclotron using a 5 minute irradiation with 5 microampere beam current and was delivered as $[^{11}C]CO_2$ using helium as a carrier gas to the experimental set up. $[^{11}C]CO_2$ was accumulated on a molecular sieve trap at room temperature. The molecular sieve trap was heated to 350 °C and $[^{11}C]CO_2$ was released with a 10 mL·min-1 He-flow and passed through a Zn/silica column heated at 485 °C. Residual $[^{11}C]CO_2$ was trapped on an Ascarite column, while [^{11}C]CO was trapped on silica (100 mg, cooled to -196 °C using liquid nitrogen). Radioactivity in the [^{11}C]CO trap was measured in a dose calibrator and allowed to decay to approximately 0.5 GBq. The trap was warmed to room temperature for 1 min and activity was transferred to the pump-mounted collection syringe with a He-flow of 10 mL·min^{-1} while the pump was set at 'withdraw' at a speed of 10 mL·min^{-1}. Then, the syringe pump was set at 'continuous infusion' at a 10 mL·min^{-1} flow rate. Each vial was charged with [^{11}C]CO manually for 4 seconds prior to closing the dispensing line and transferring the needle to the next reaction vial (taking appr. 2 seconds). Each subsequent vial was similarly charged with [^{11}C]CO until all 10 vials were charged with [^{11}C]CO. The radiochemical reactions were performed by adding [^{11}C]CO (1-50 MBq) to a solution of aryl halide (20 µmol), sulfonamide (20 µmol), Pd-source (1 µmol of Pd), Xantphos (2.9 mg, 5 µmol), DBU (3.0 uL, 20 µmol) in THF (0.7 mL) in a closed conical vial (1.0 mL, Alltech). The resulting solution was heated for 5 minutes at 100 °C. After cooling to 50 °C an exhaust needle was applied to the vial and the solution was left for 5 minutes to allow unreacted [^{11}C]CO and other radioactive volatiles to escape from the reaction solution. Subsequently, an aliquot (50-100 uL) of the reaction solution was diluted with 1.0 mL of H_2O/MeCN (1:1) and analyzed by HPLC. The identity of the product as observed by radioHPLC was confirmed by comparing the retention times of the carbon-11 labeled acylsulfonamides with retention time (UV detection) of the unlabeled reference standards, where because of serial installation of detectors the UV signal precedes the radioactivity signal by approximately 0.5 minutes. The amount of radioactivity in the reaction vial was measured prior to heating, after the 5

minute reaction and after removal of volatile radioactivity to determine the leakage and trapping efficiency, respectively. Only reactions with <5% leakage were included in the results. The results are expressed as trapping efficiency (% of non-volatile radioactive products after reaction), radiochemical purity (% of radioactive product AUC relative to the total AUC), and radiochemical yield (the product of trapping efficiency and radiochemical yield). All experiments were conducted at least in triplicate and are expressed as average ± standard deviation.

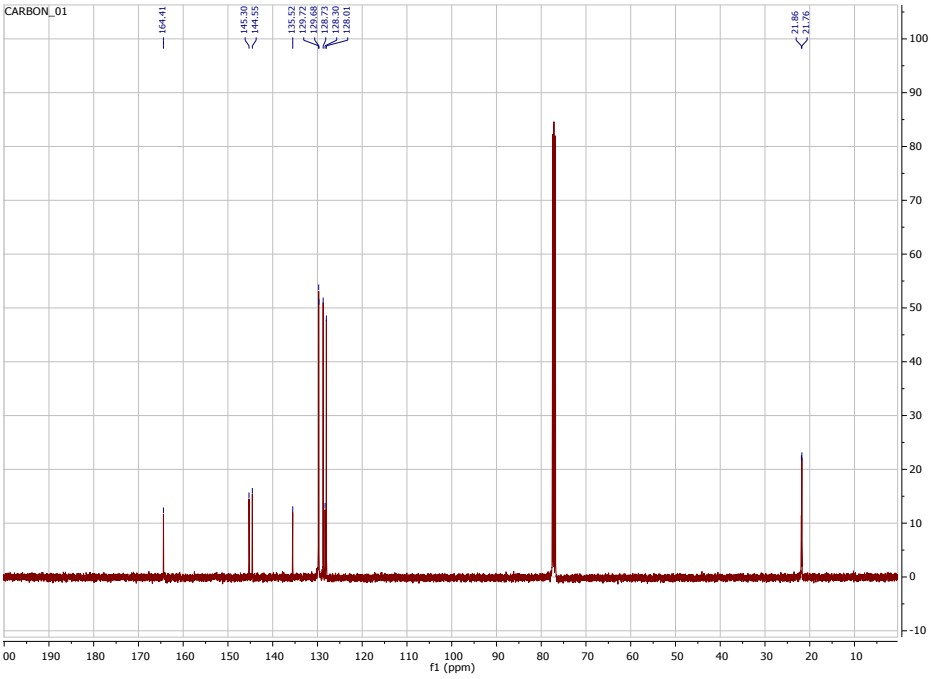
5. Spectra and chromatograms

4-methyl-*N*-tosylbenzamide (**1**):

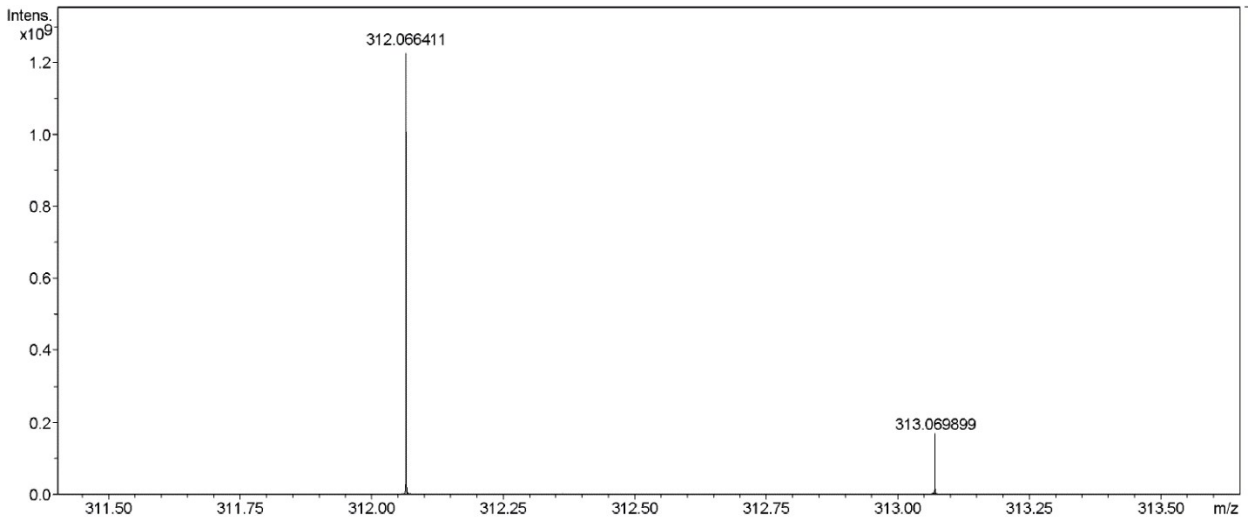
^{1}H NMR:



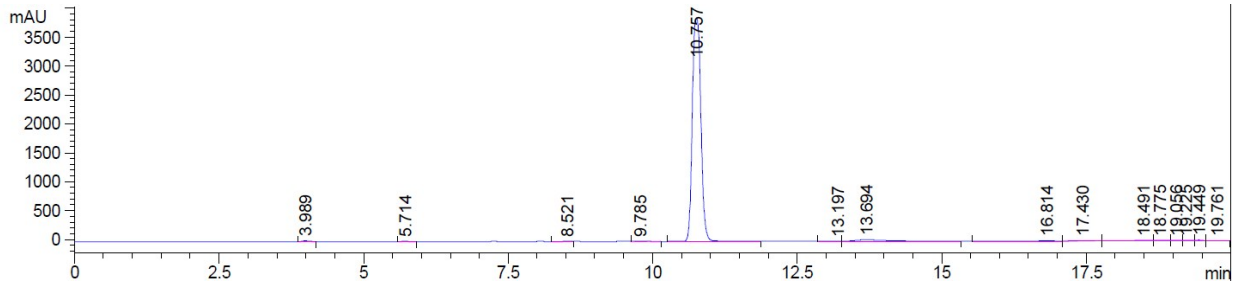
^{13}C NMR:



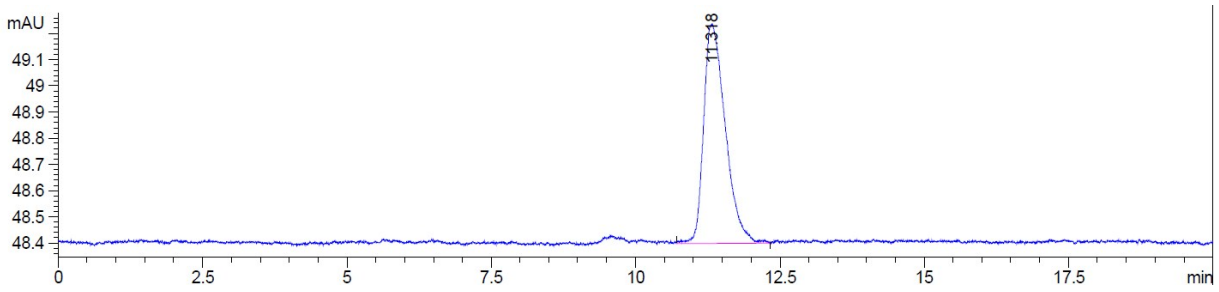
ESI-HRMS:



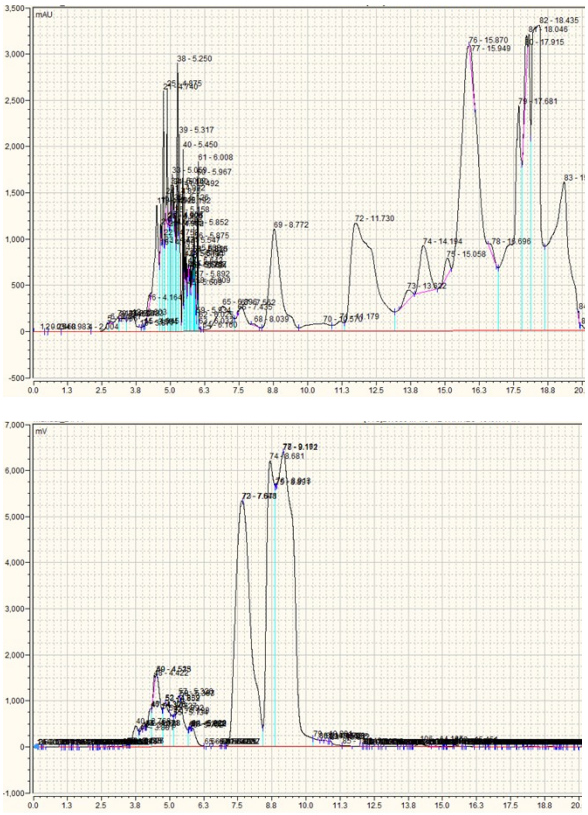
HPLC chromatogram - UV-detection (254 nm):



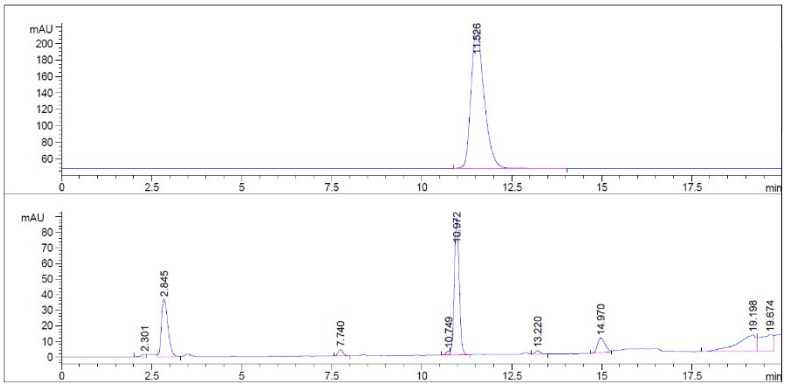
HPLC chromatogram - radioactivity-detection:



HPLC chromatogram of crude reaction mixture on preparative HPLC – UV-detection (upper chromatogram, 254 nm) and radio-detection (lower chromatogram):

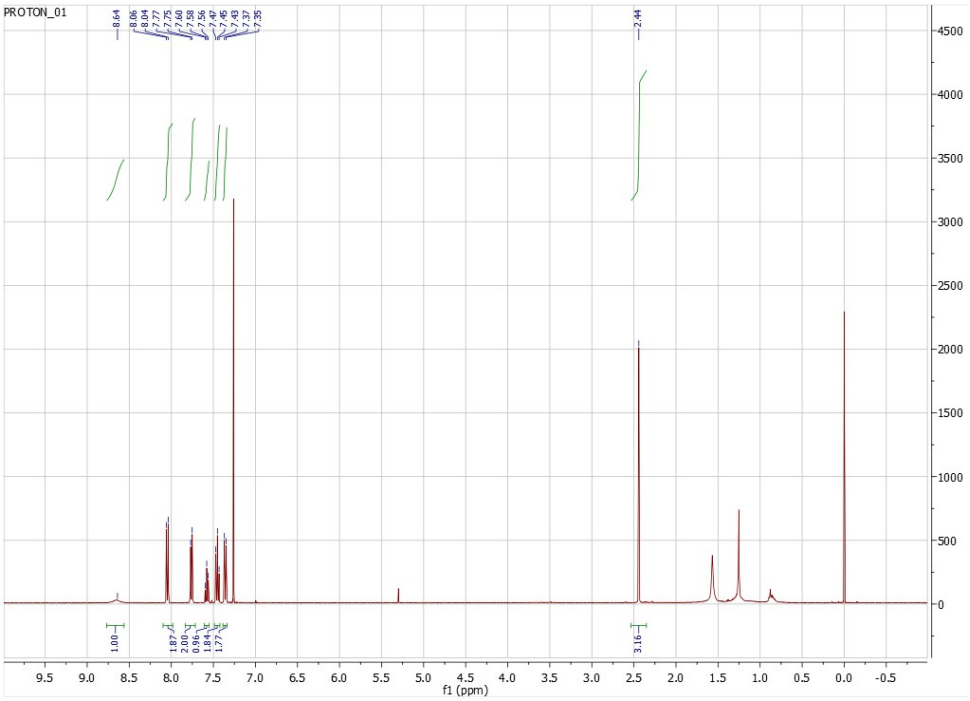


HPLC chromatogram of purified [^{11}C]**1**. Upper chromatogram represents radiodetection, lower chromatogram represents UV-detection at 254 nm.

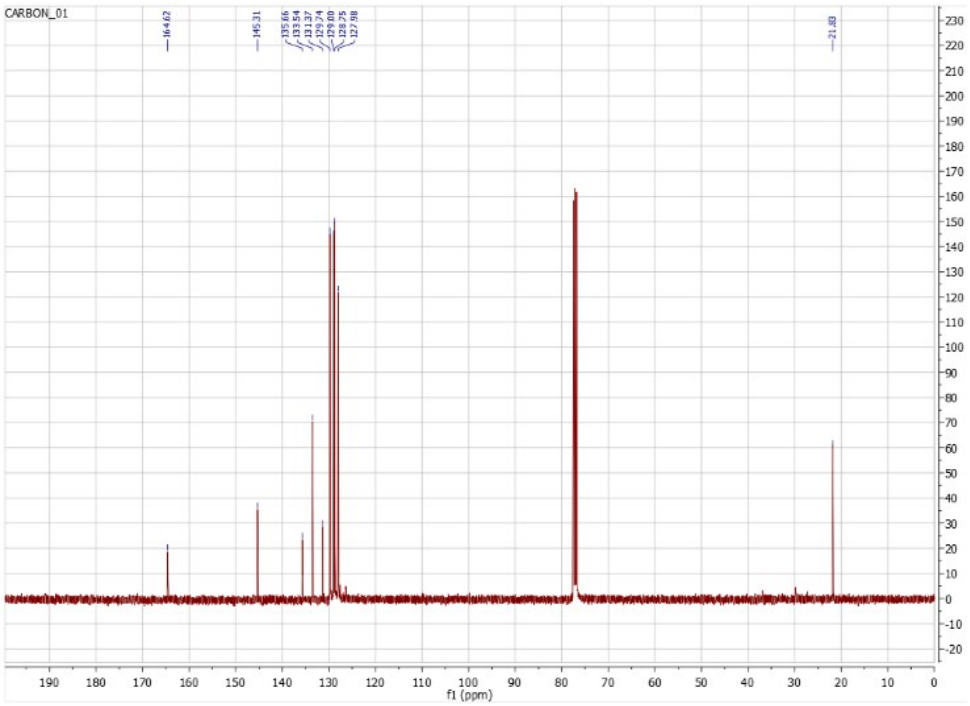


N-tosylbenzamide (**2**):

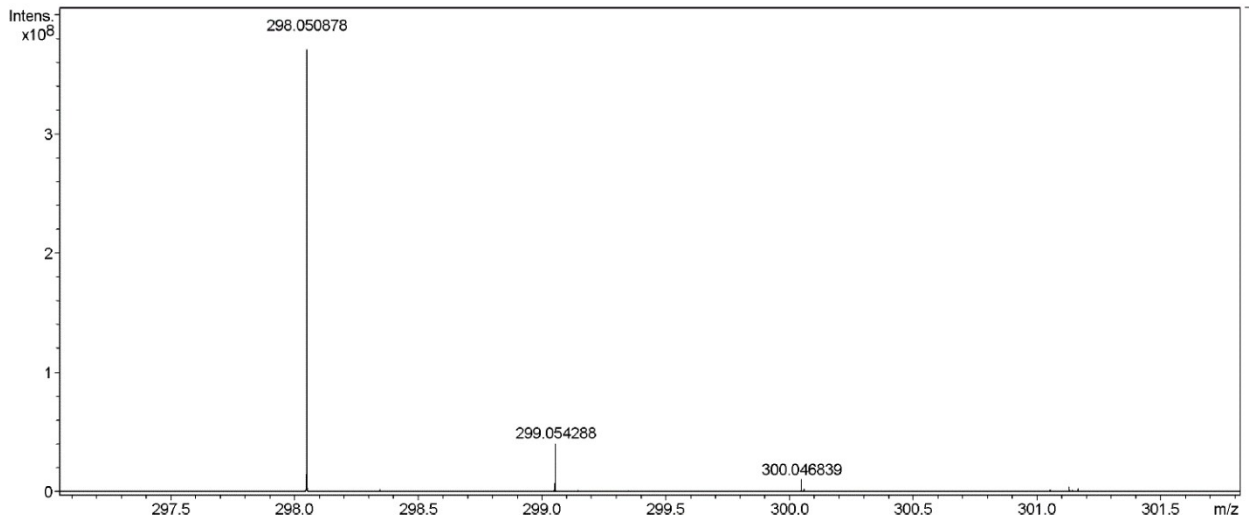
^{1}H NMR:



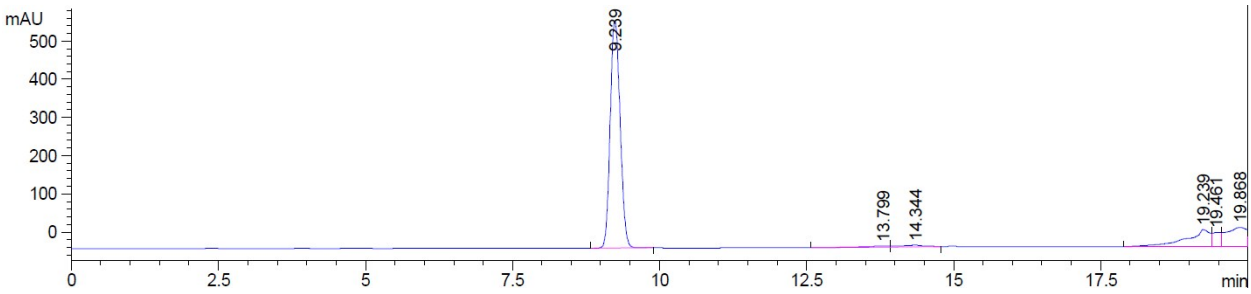
^{13}C NMR:



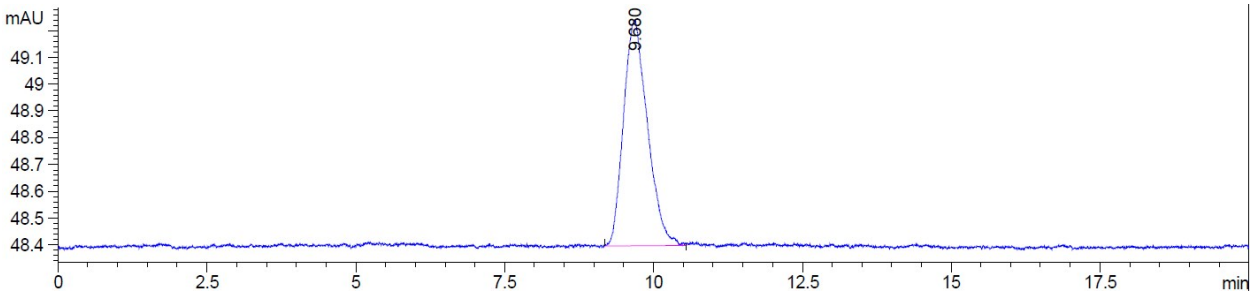
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

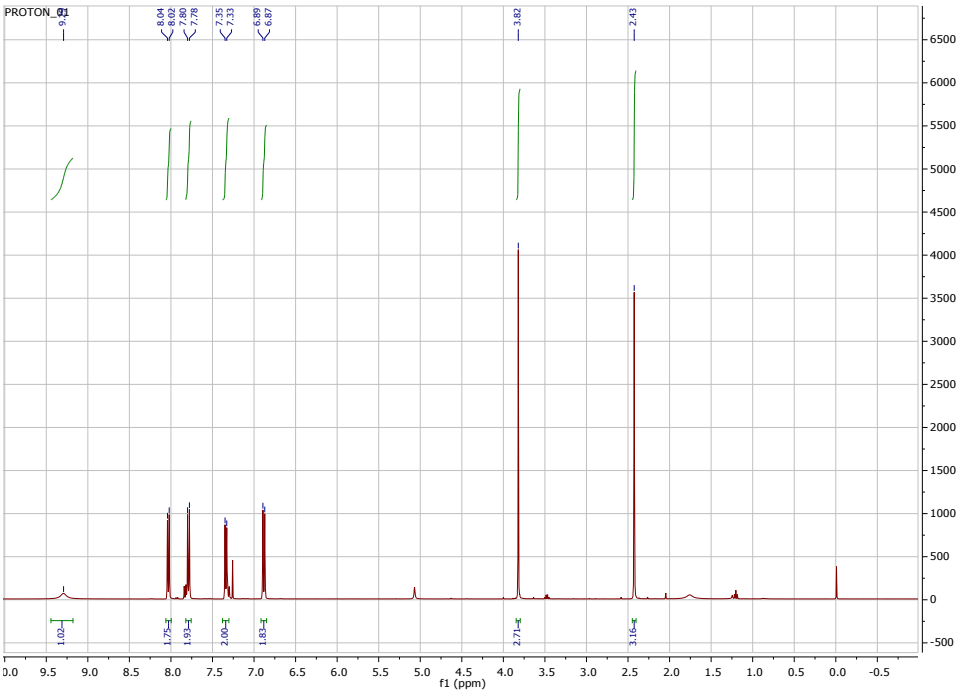


HPLC chromatogram - radioactivity-detection:

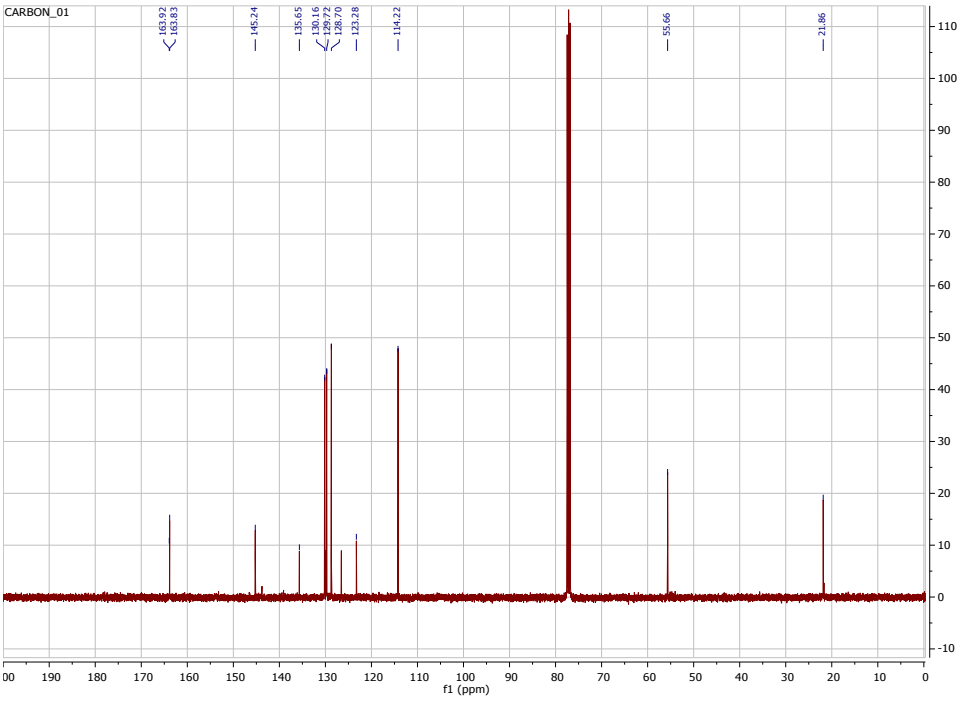


4-methoxy-*N*-tosylbenzamide (**3**):

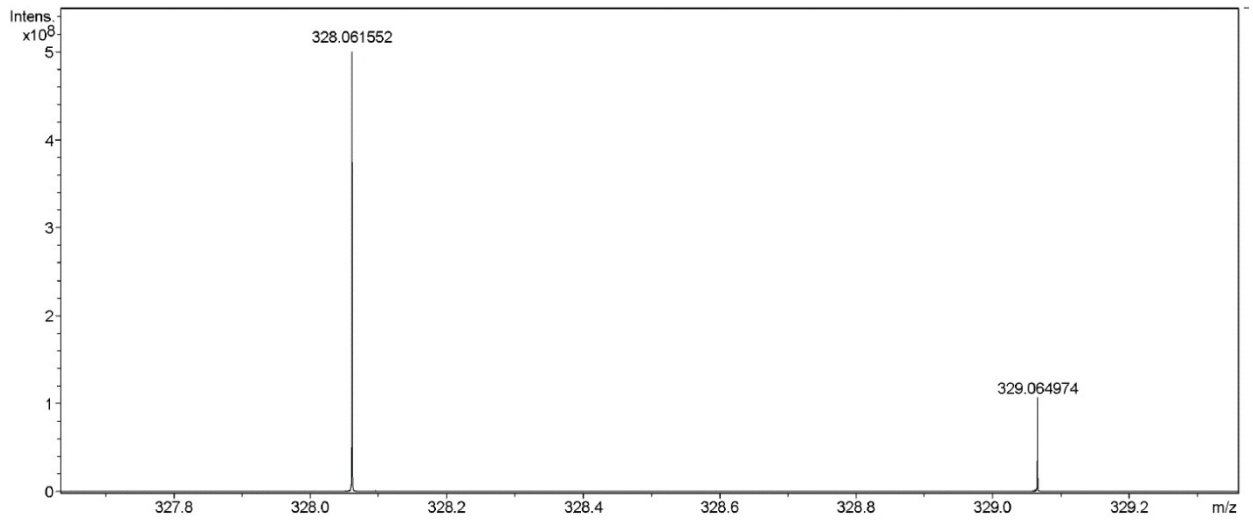
^{1}H NMR:



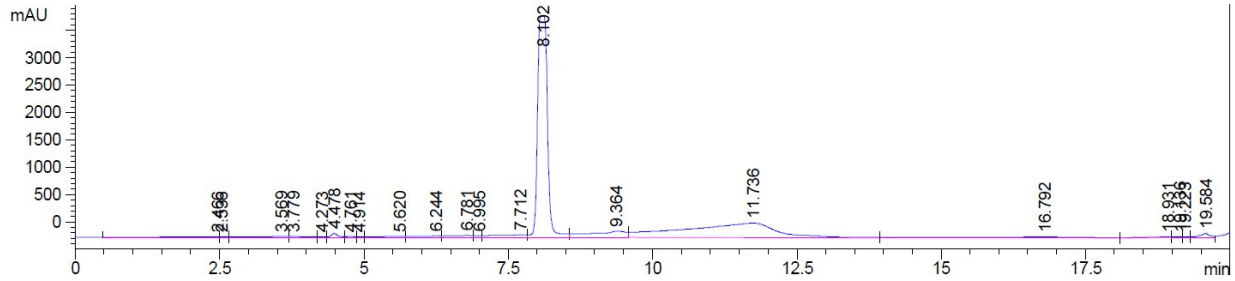
^{13}C NMR:



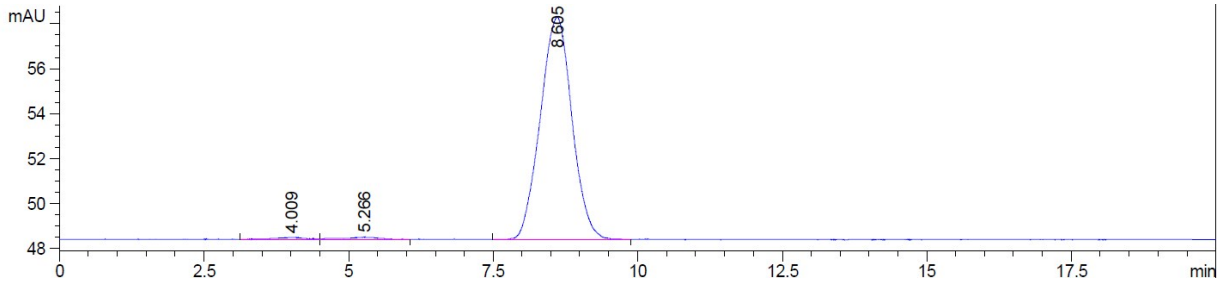
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

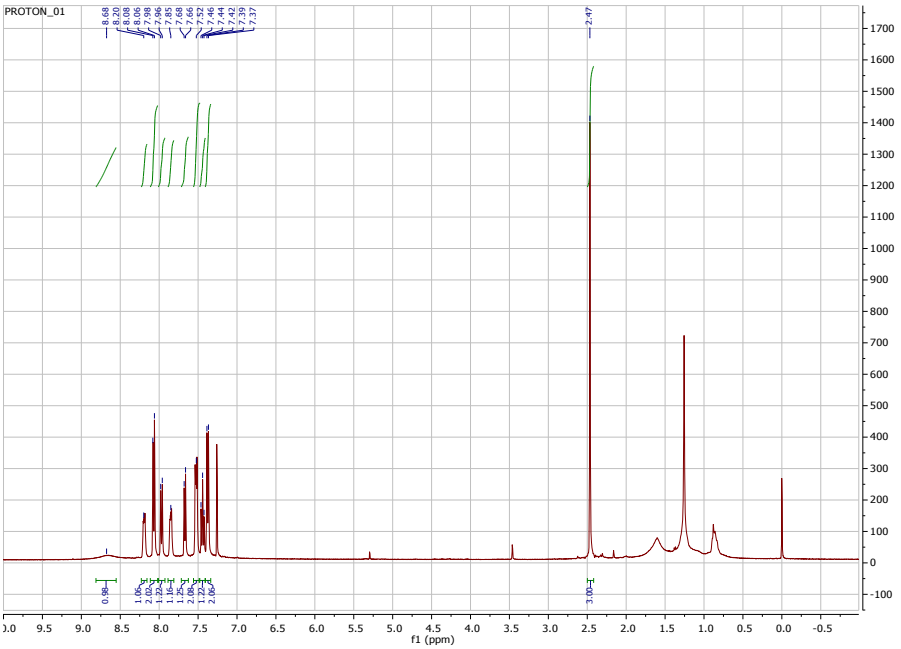


HPLC chromatogram - radioactivity-detection:

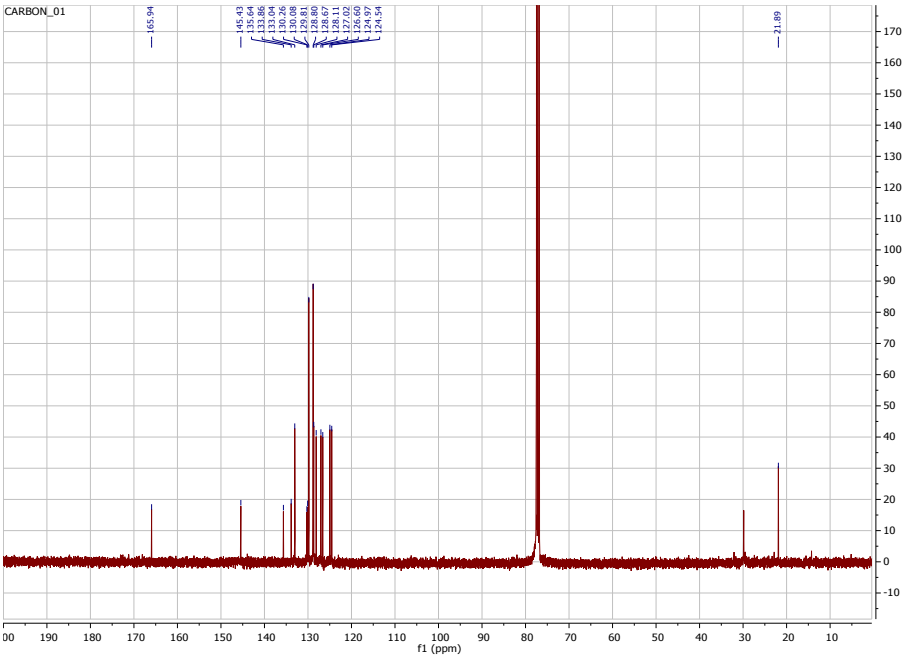


N-tosyl-1-naphthamide (**4**):

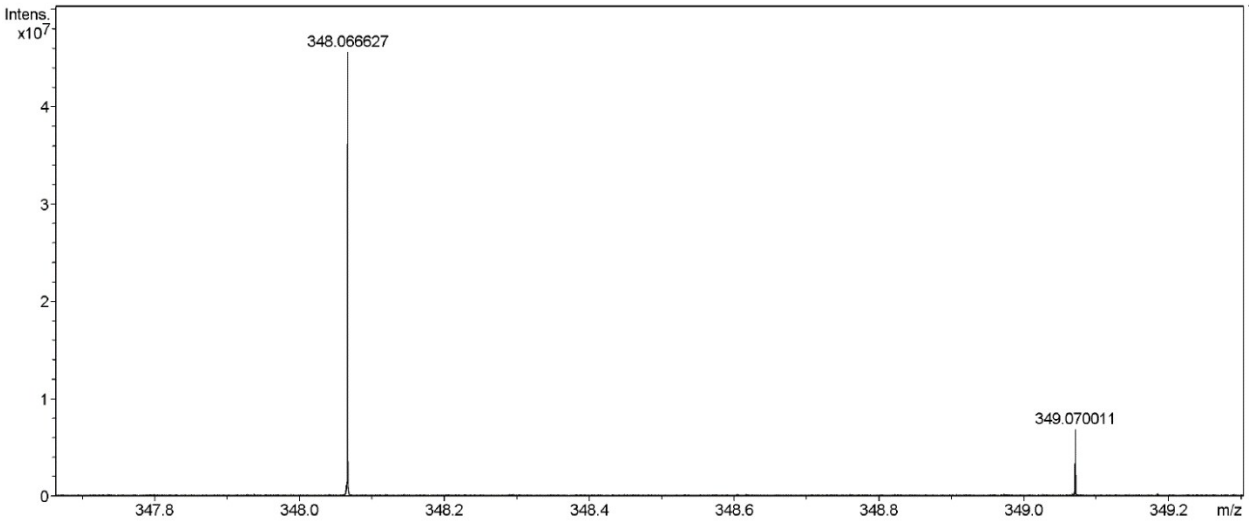
^{1}H NMR:



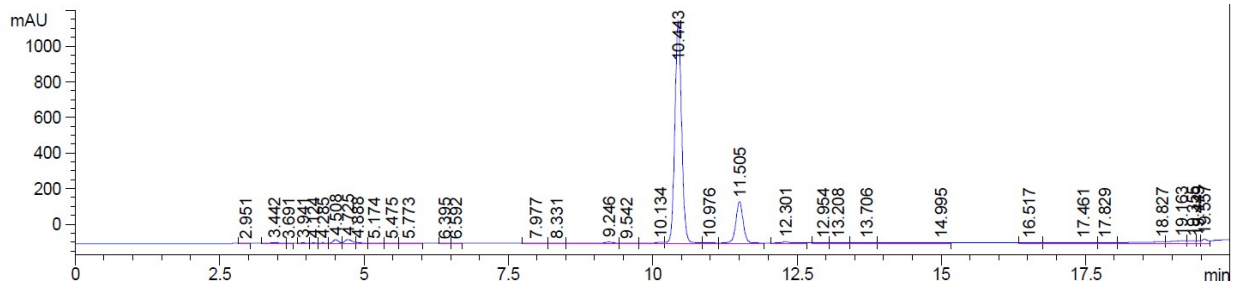
^{13}C NMR:



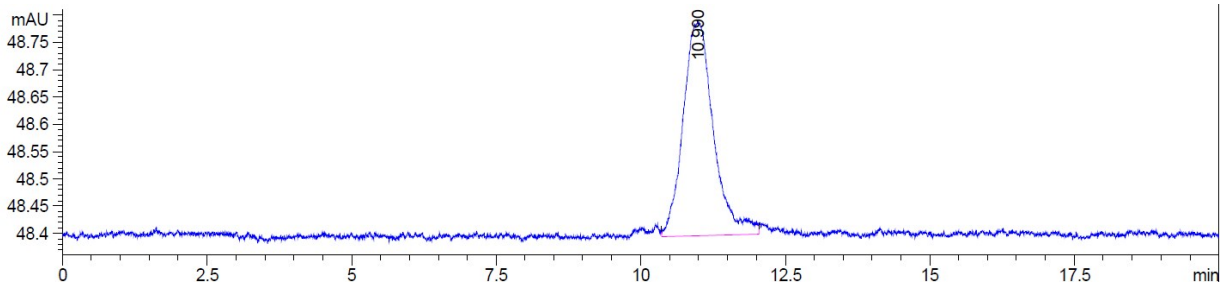
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

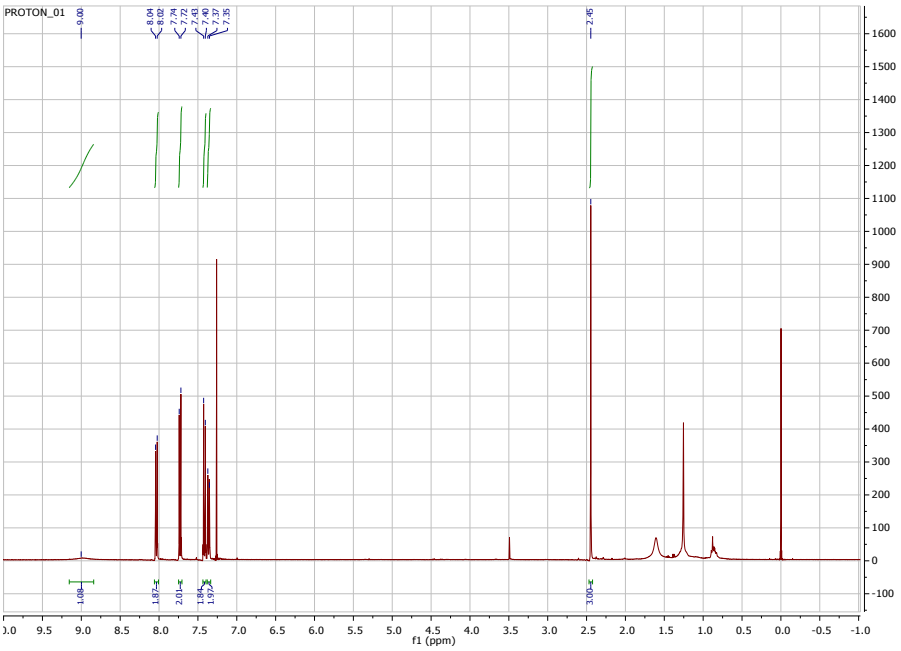


HPLC chromatogram - radioactivity-detection:

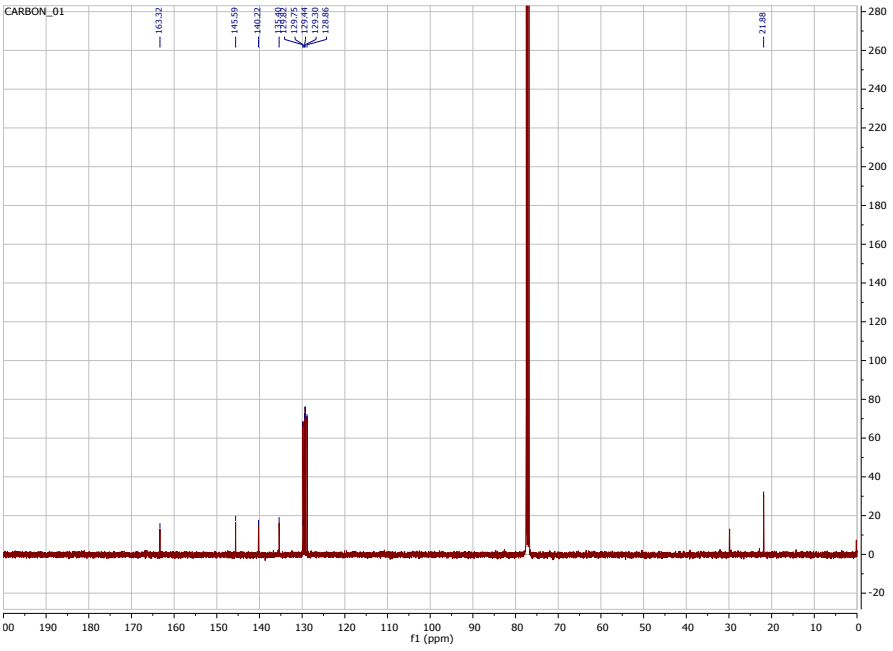


4-chloro-*N*-tosylbenzamide **(5)**:

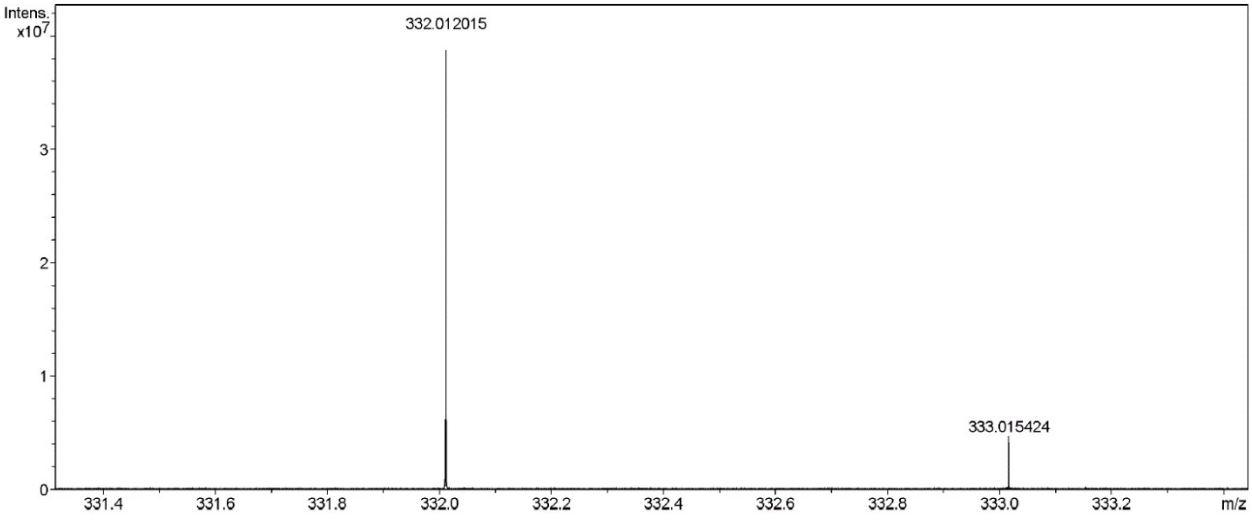
^{1}H NMR:



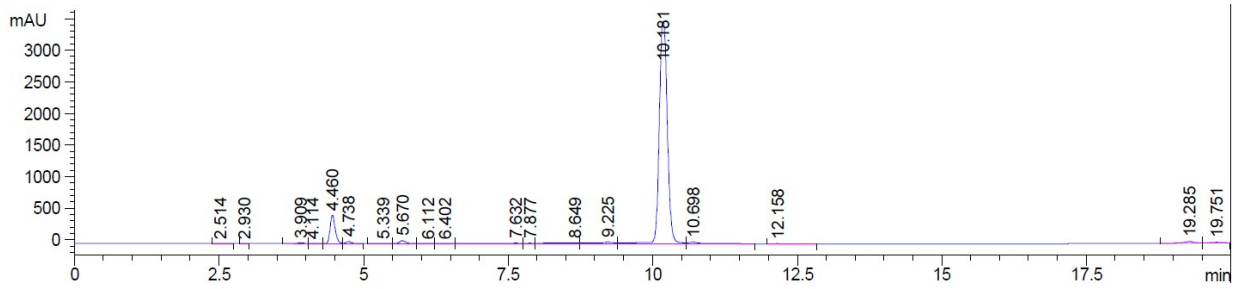
^{13}C NMR:



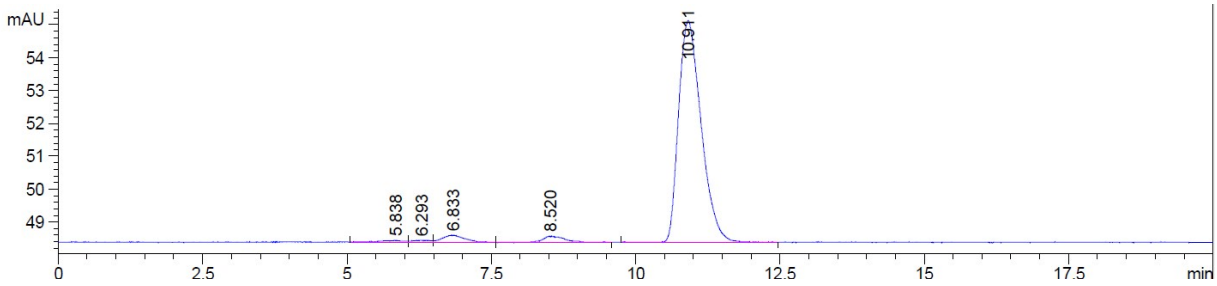
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

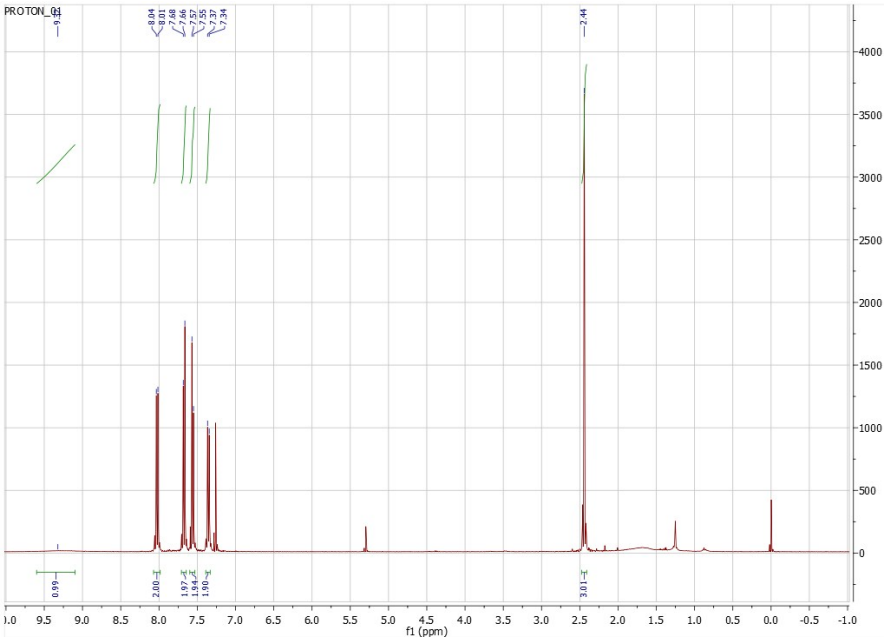


HPLC chromatogram - radioactivity-detection:

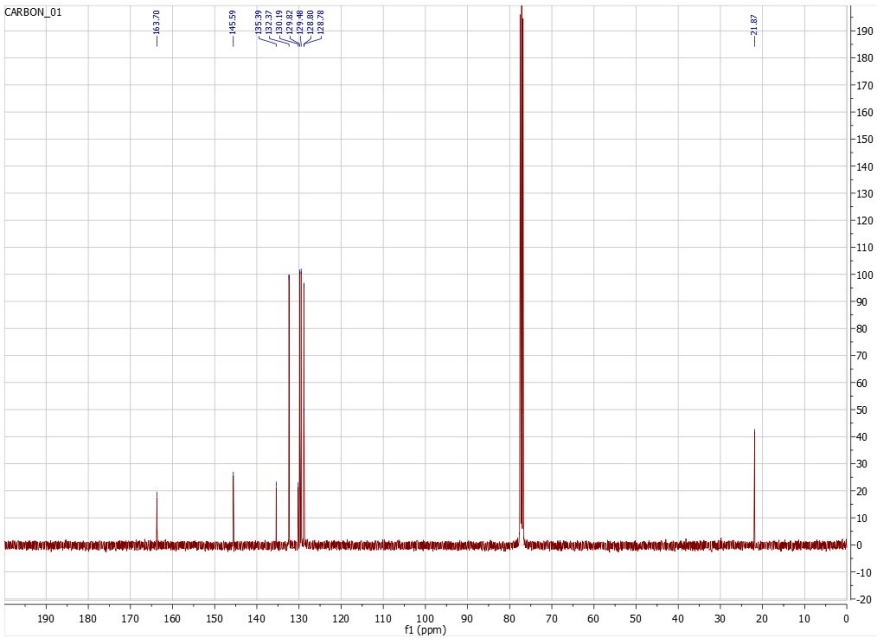


(4-bromo-*N*-tosylbenzamide) (**6**):

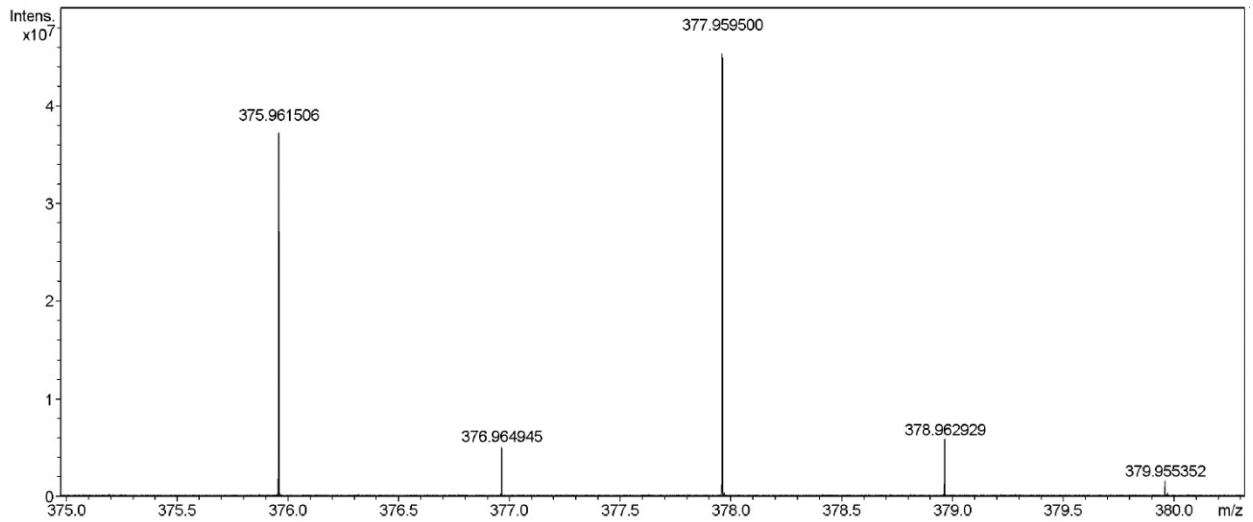
^{1}H NMR:



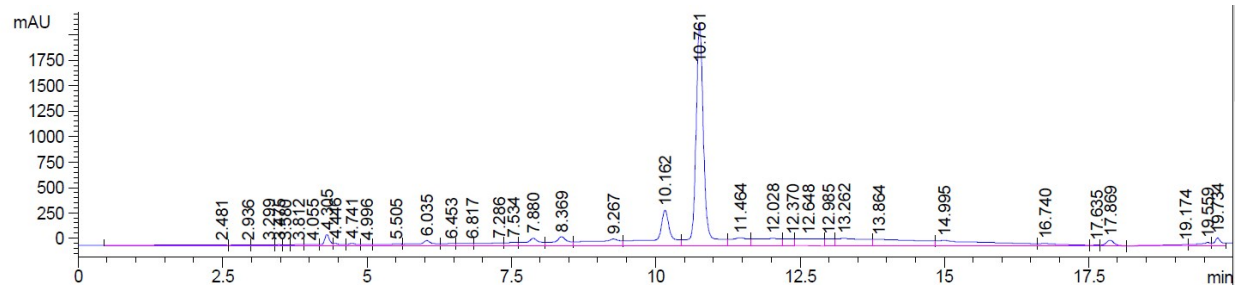
^{13}C NMR:



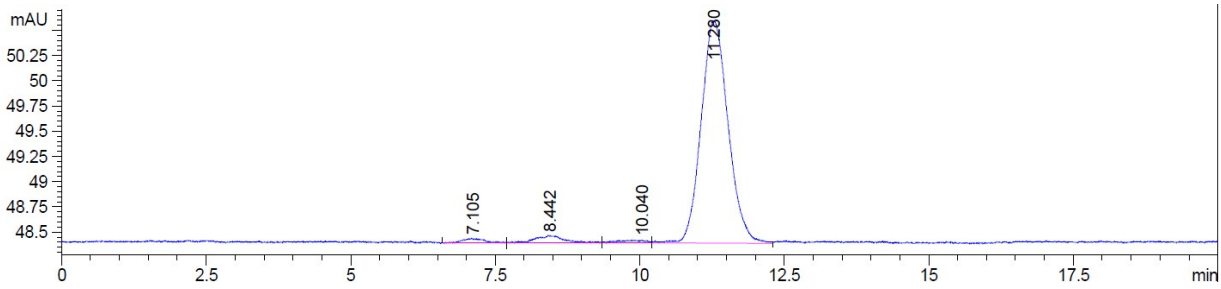
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

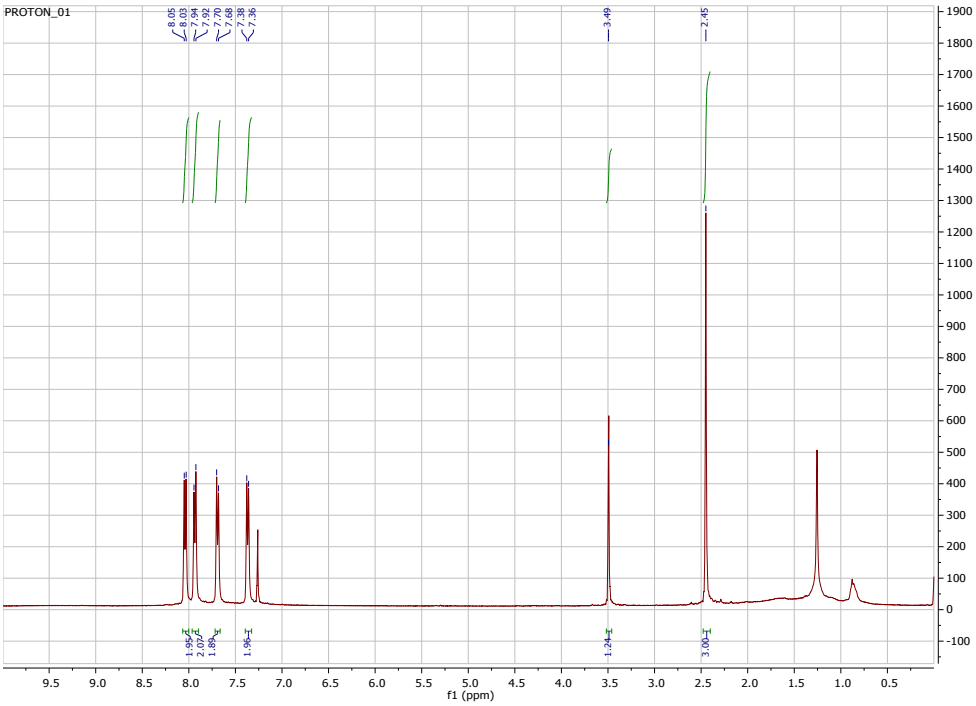


HPLC chromatogram - radioactivity-detection:

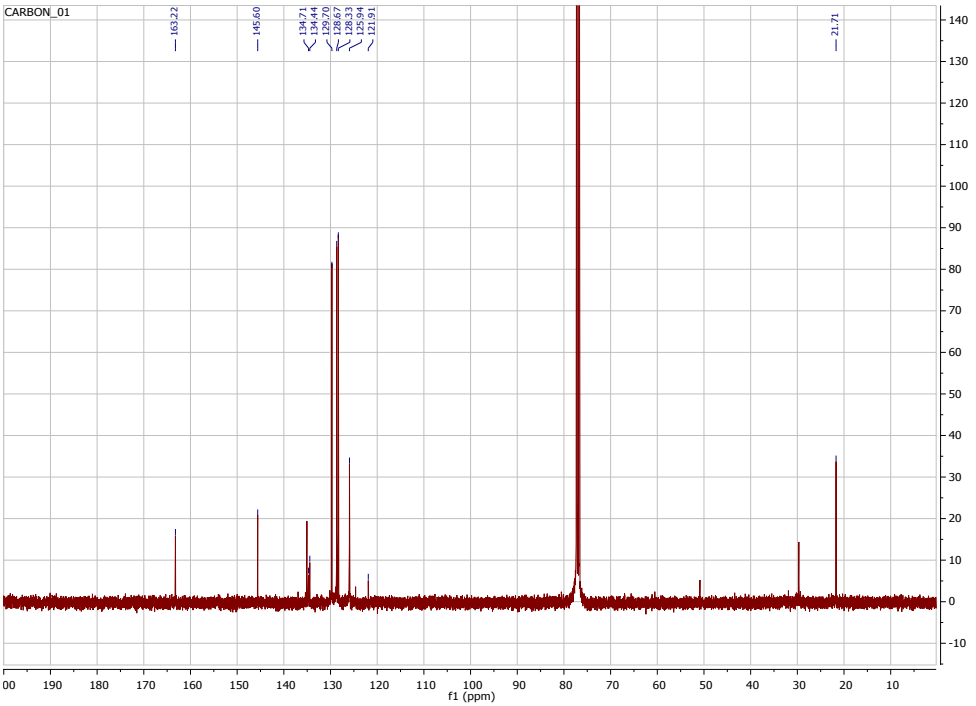


4-cyano-*N*-tosylbenzamide (**7**):

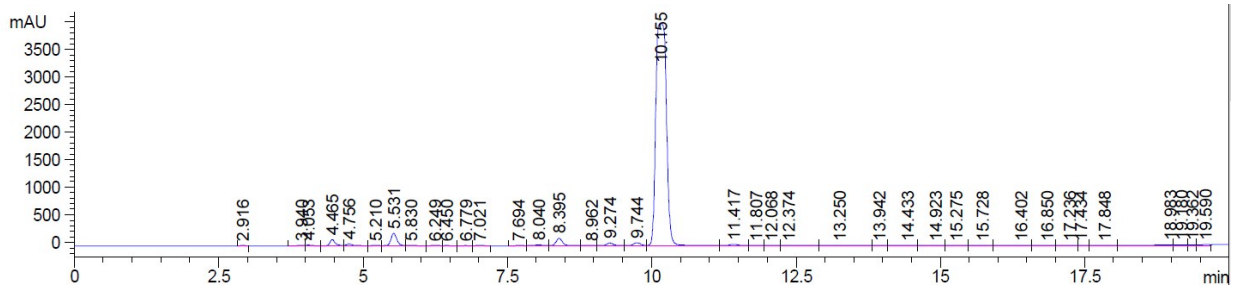
^{1}H NMR:



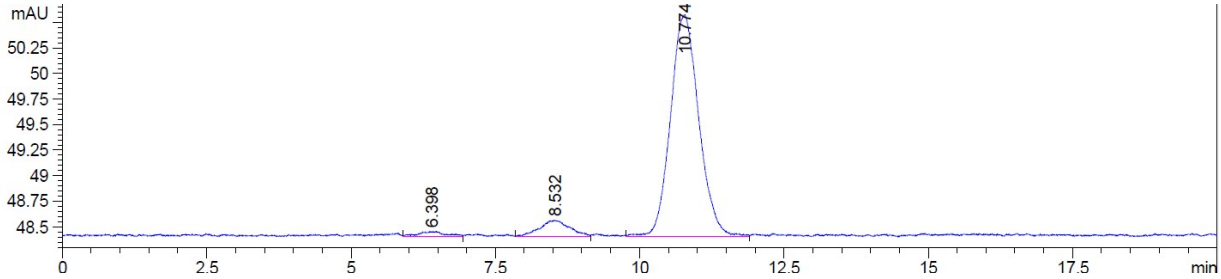
^{13}C NMR:



HPLC chromatogram - UV-detection (254 nm):

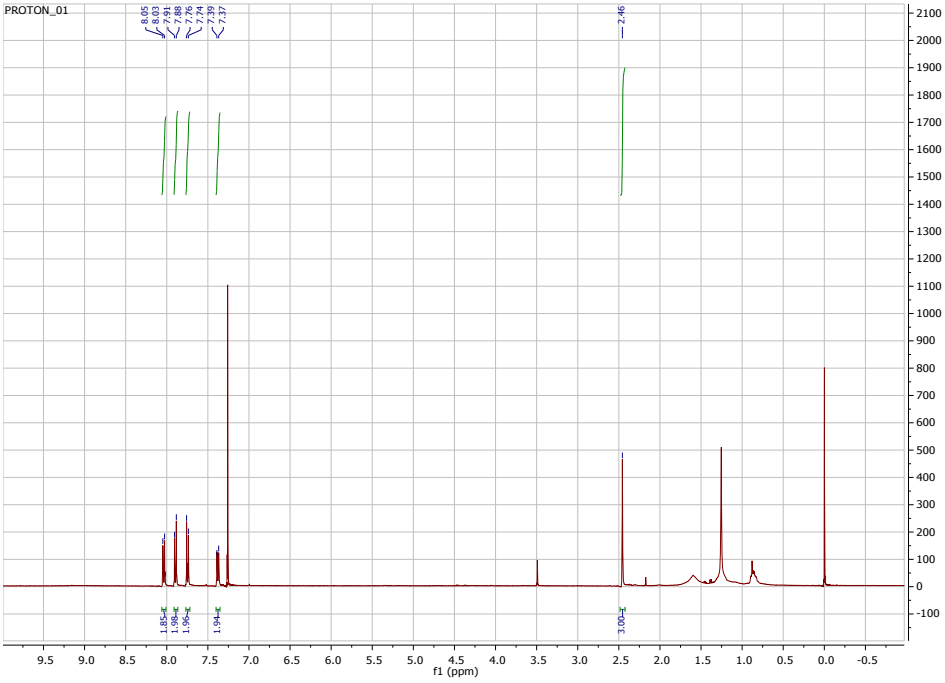


HPLC chromatogram - radioactivity-detection:

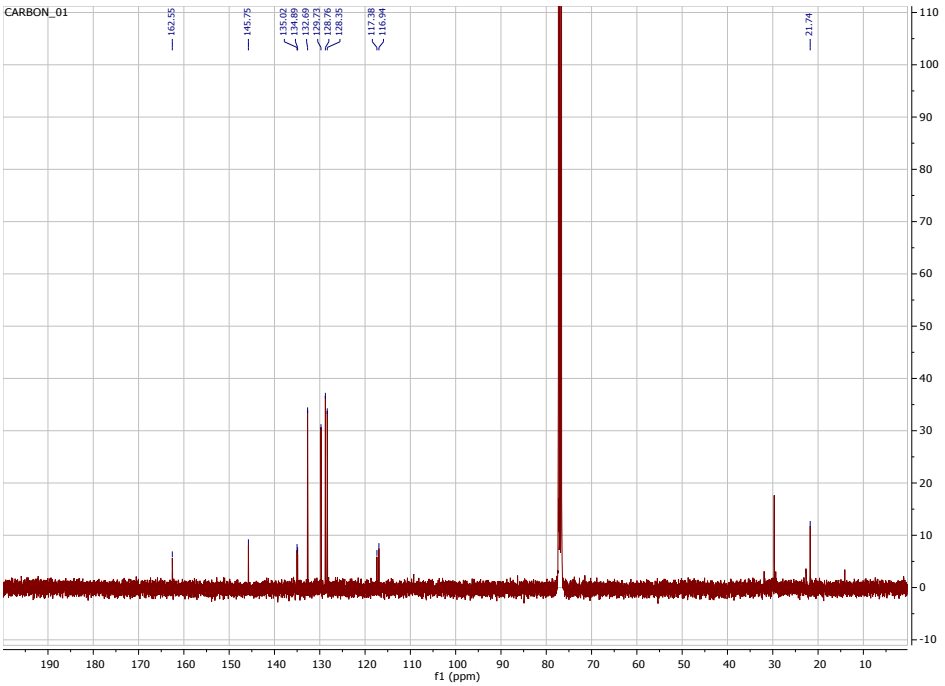


N-tosyl-4-(trifluoromethyl)benzamide (**8**):

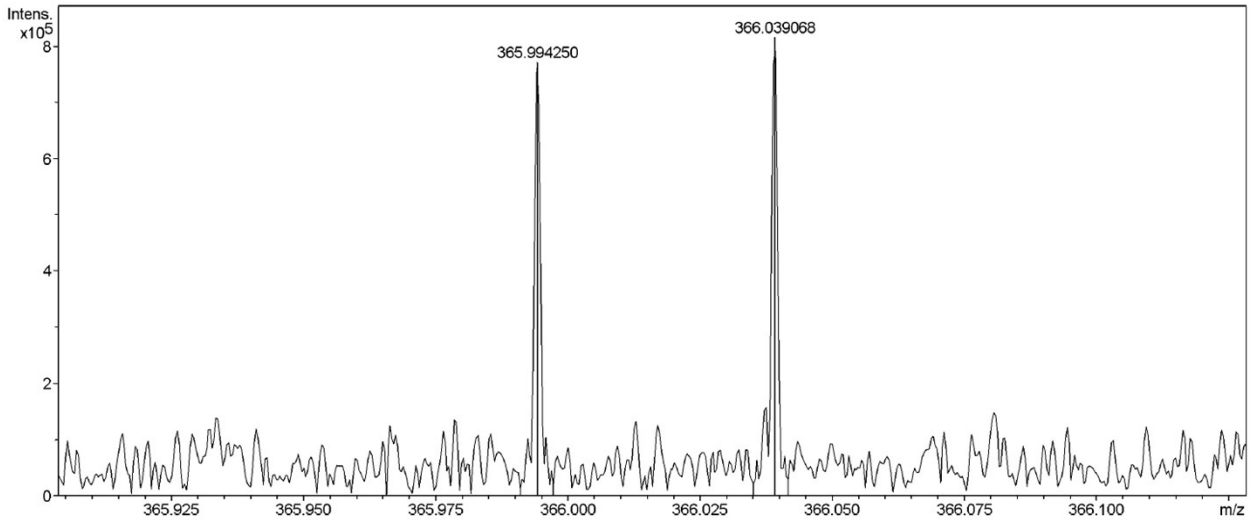
^{1}H NMR:



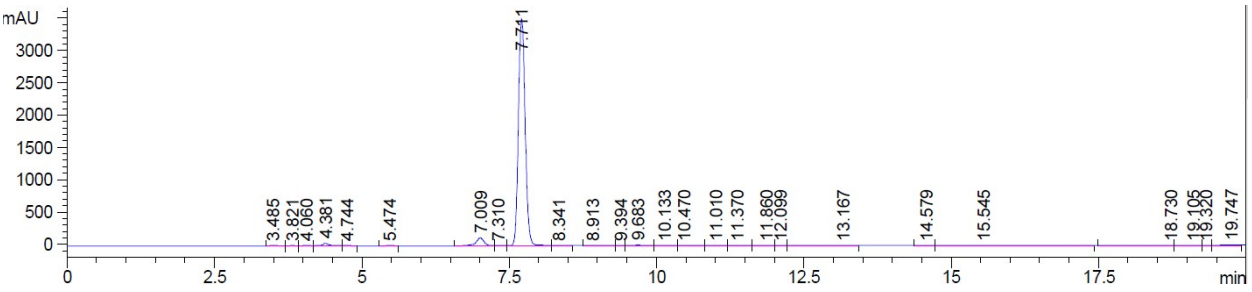
^{13}C NMR:



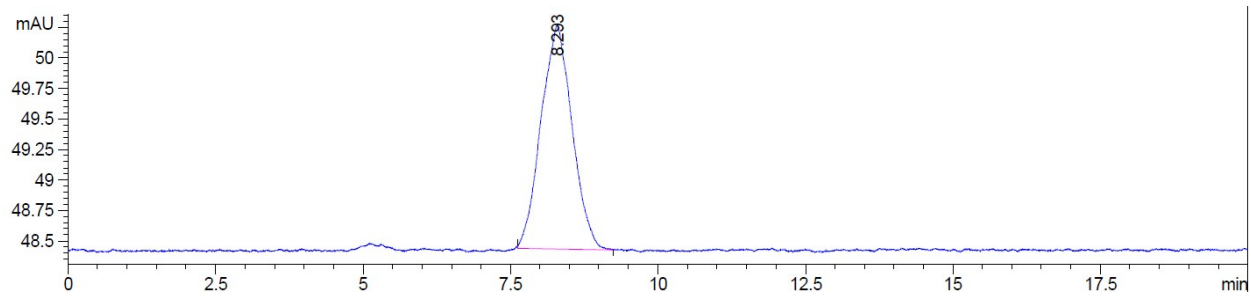
ESI-HRMS



HPLC chromatogram - UV-detection (254 nm):

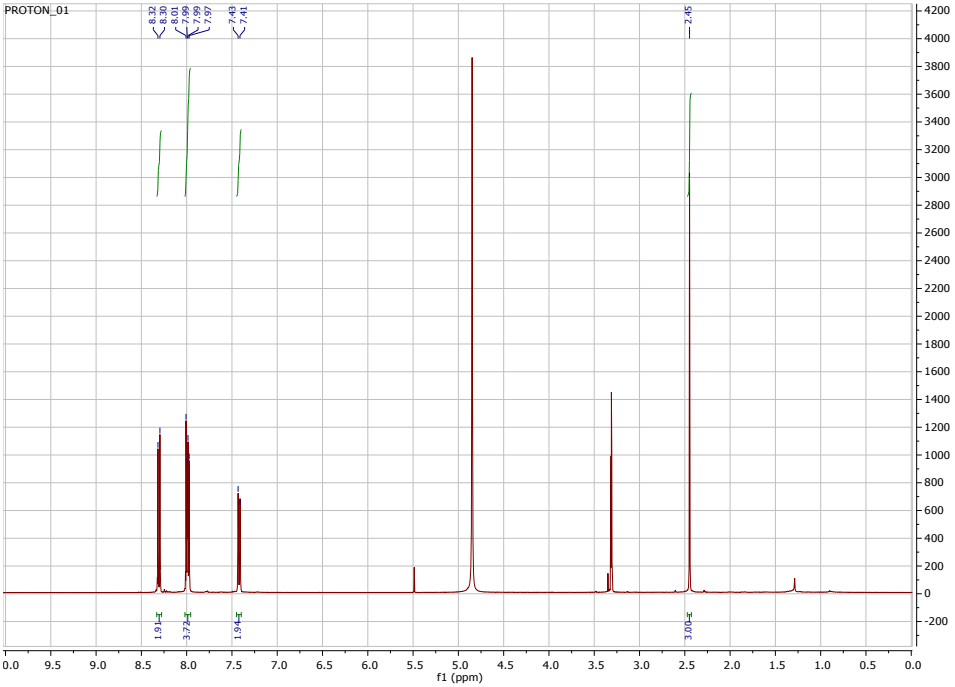


HPLC chromatogram - radioactivity-detection:

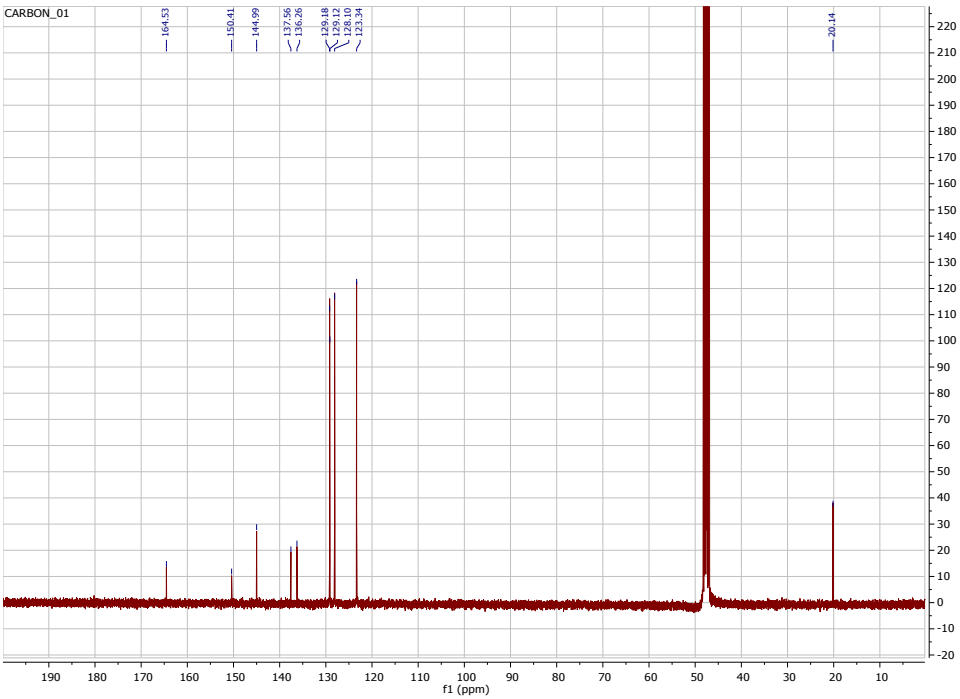


4-nitro-*N*-tosylbenzamide (**9**):

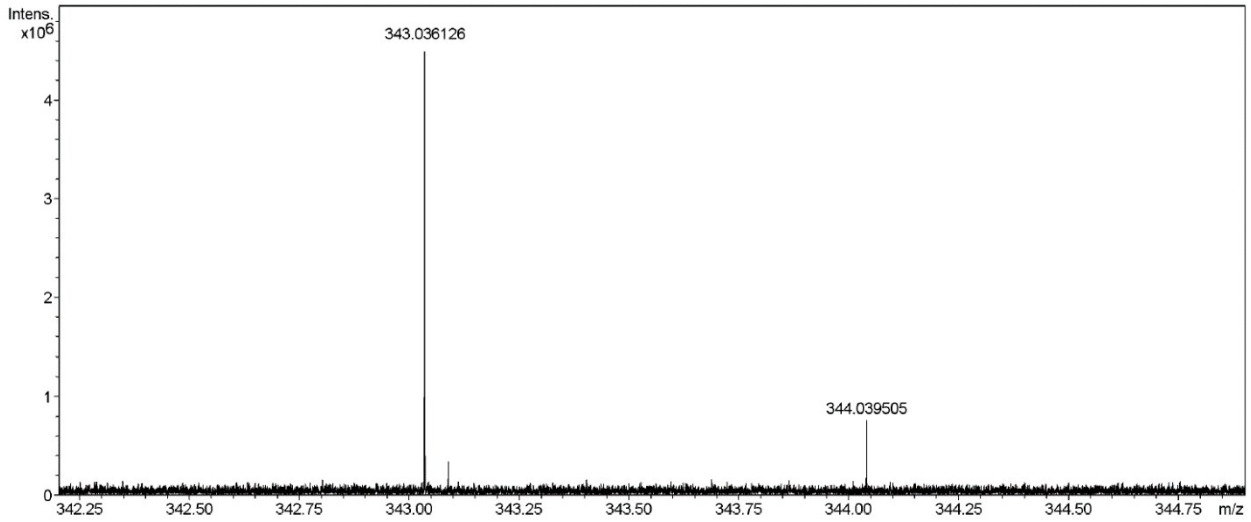
^{1}H NMR:



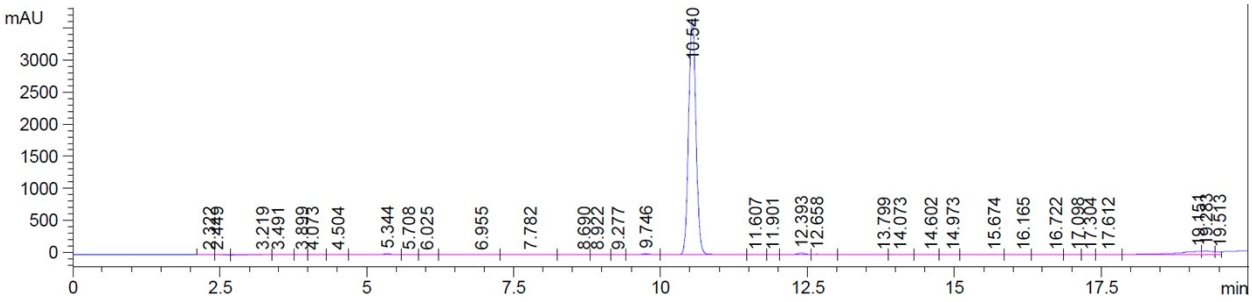
^{13}C NMR:



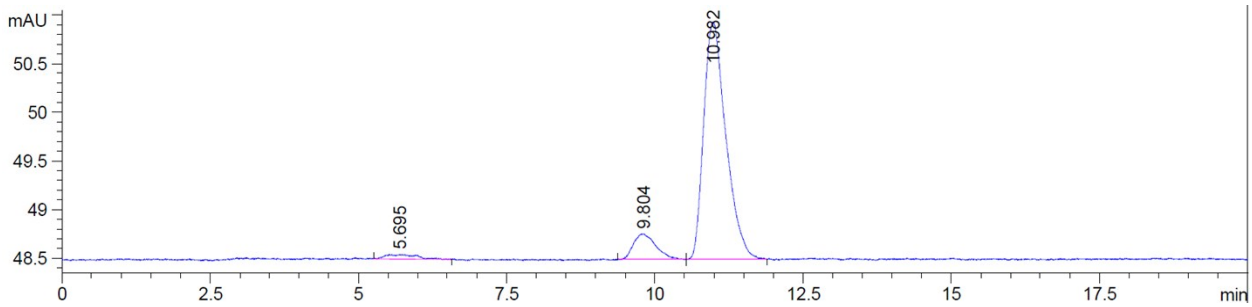
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

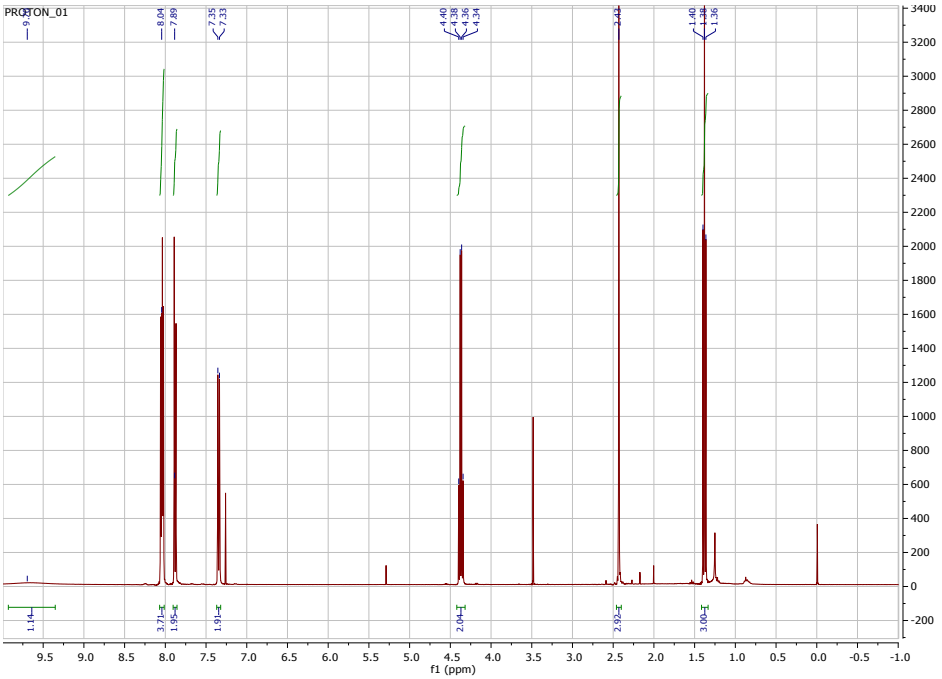


HPLC chromatogram - radioactivity-detection:

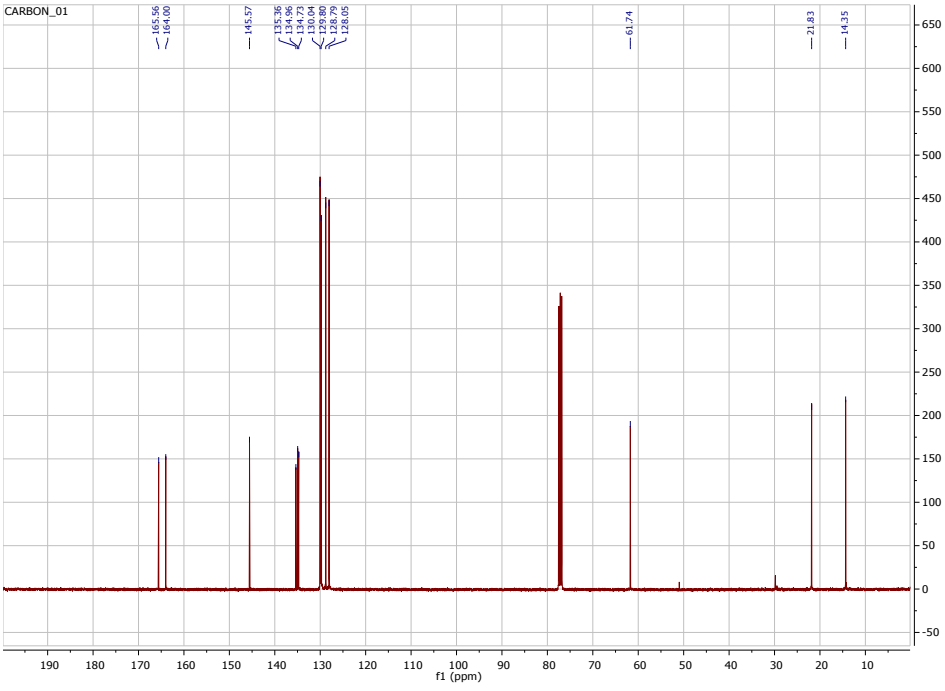


Ethyl 4-(tosylcarbamoyl)benzoate) (**10**):

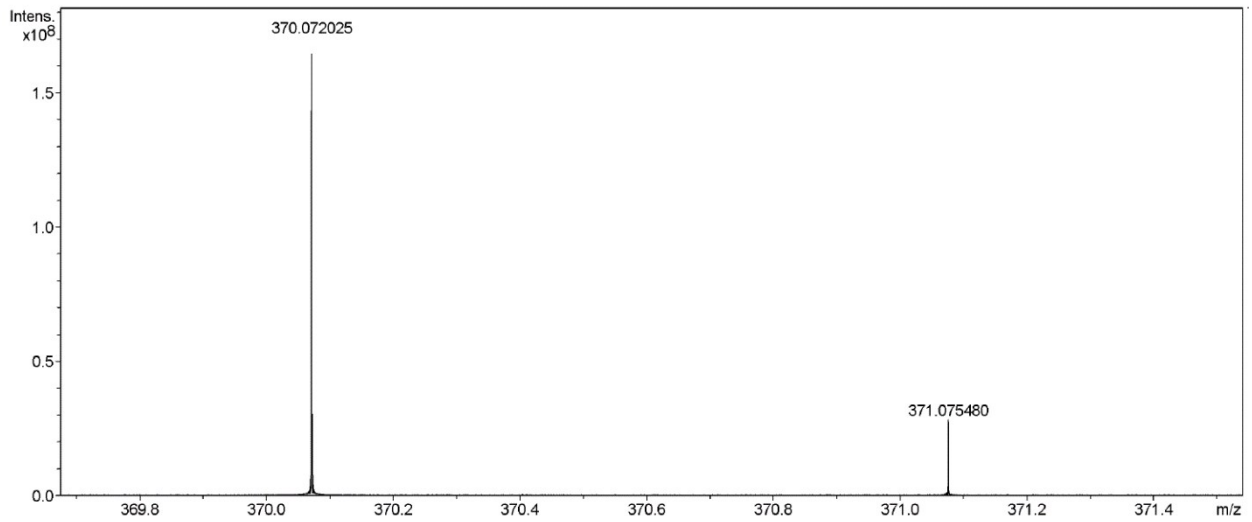
^{1}H NMR:



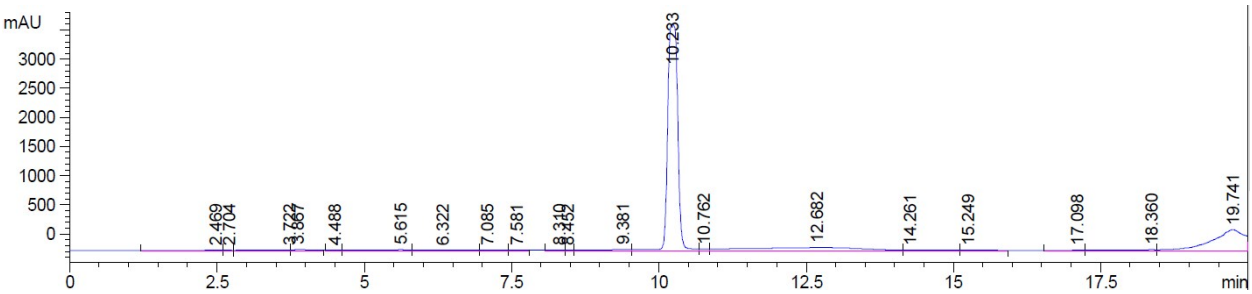
^{13}C NMR:



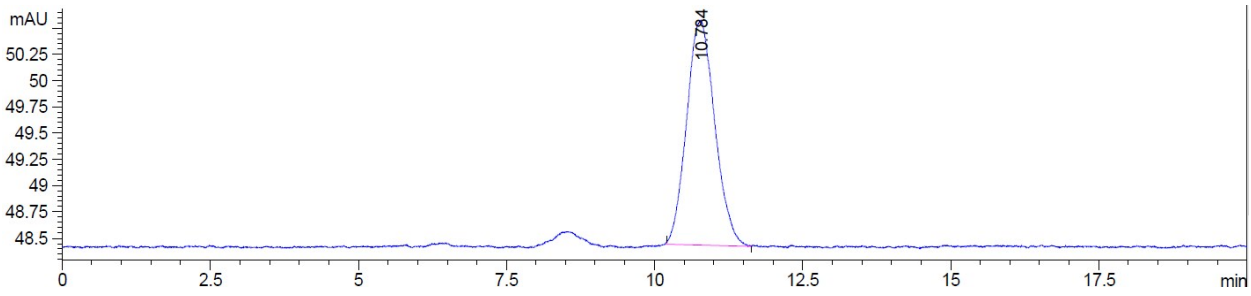
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

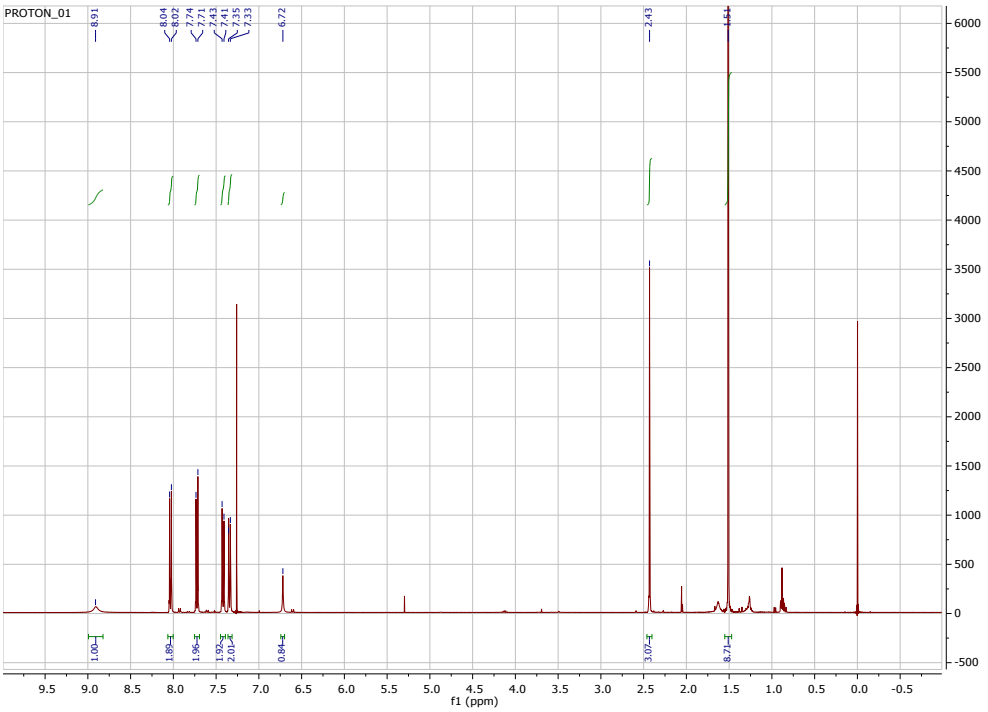


HPLC chromatogram - radioactivity-detection:

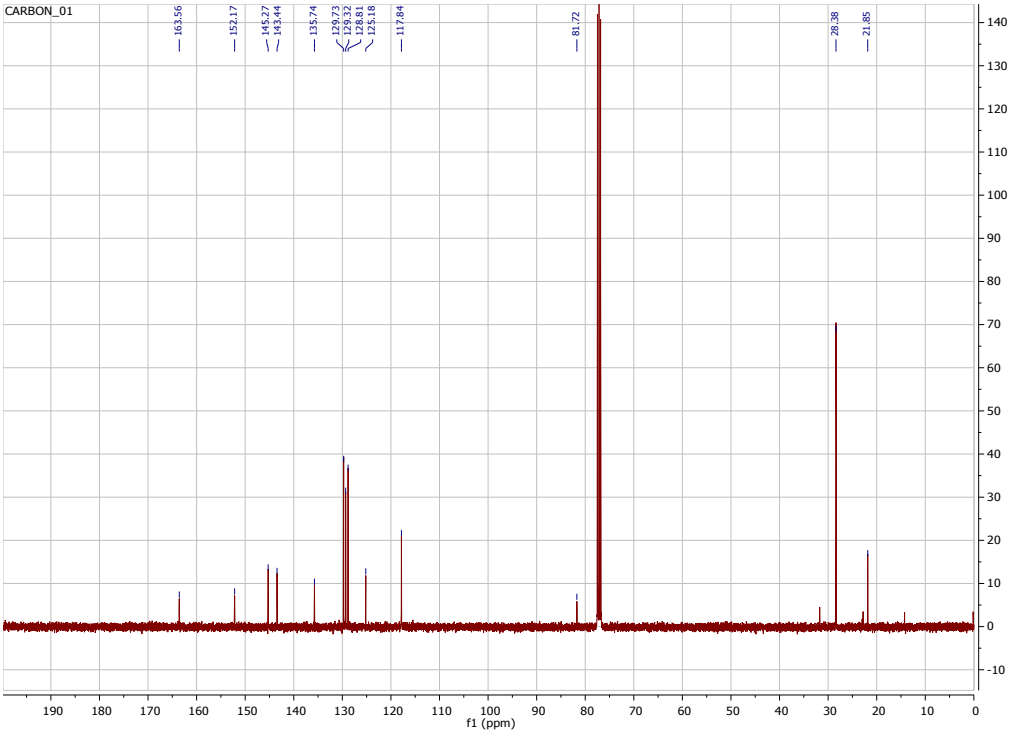


Tert-butyl (4-(tosylcarbamoyl)phenyl)carbamate) (**11**):

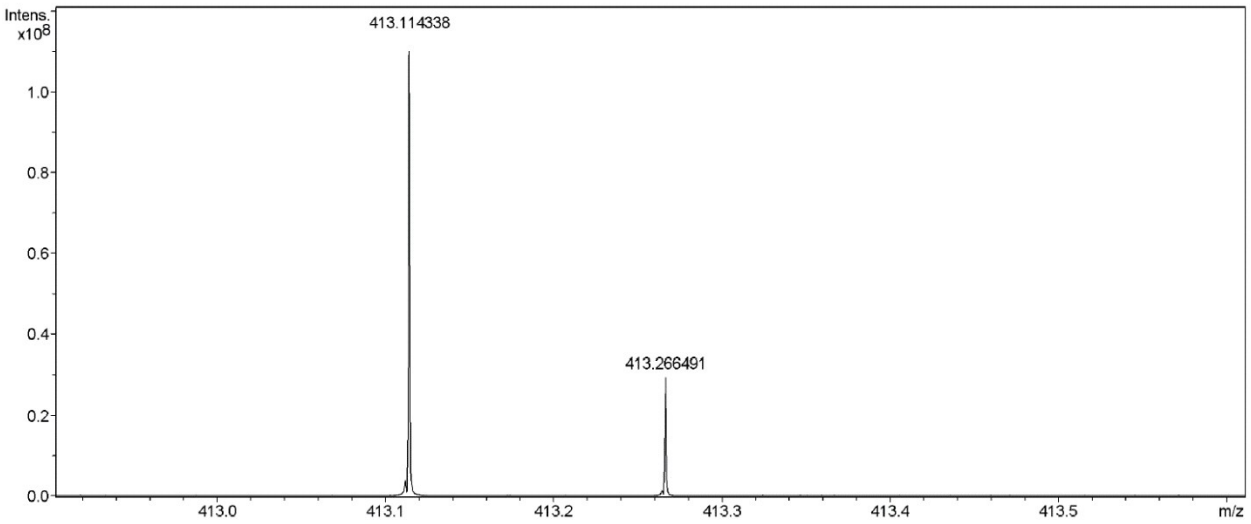
^{1}H NMR:



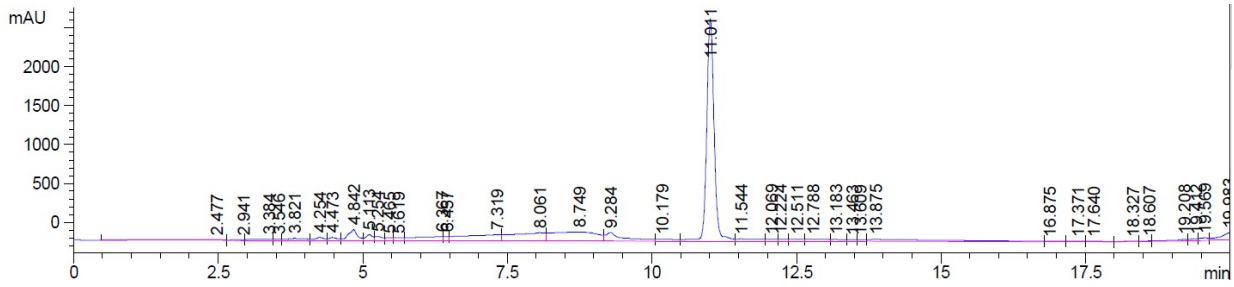
^{13}C NMR:



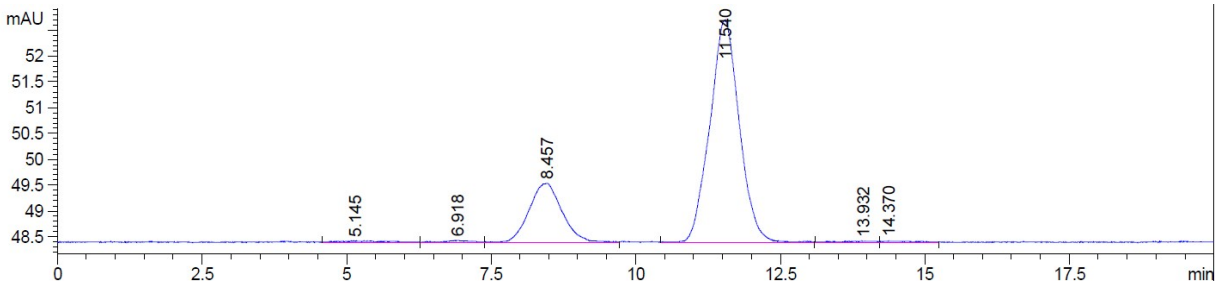
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

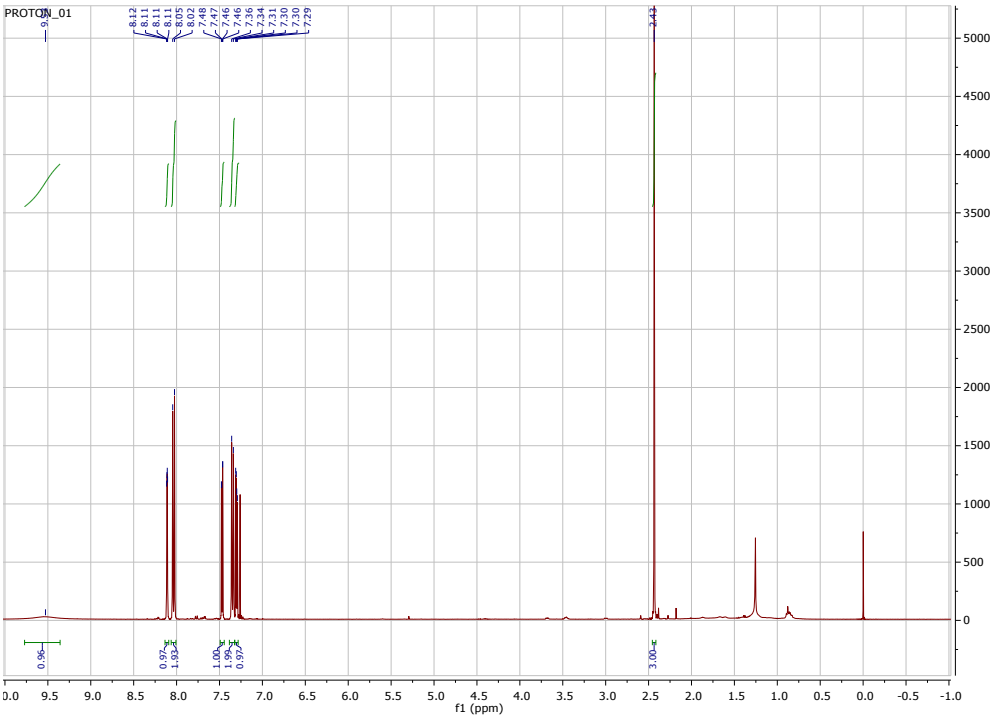


HPLC chromatogram - radioactivity-detection:

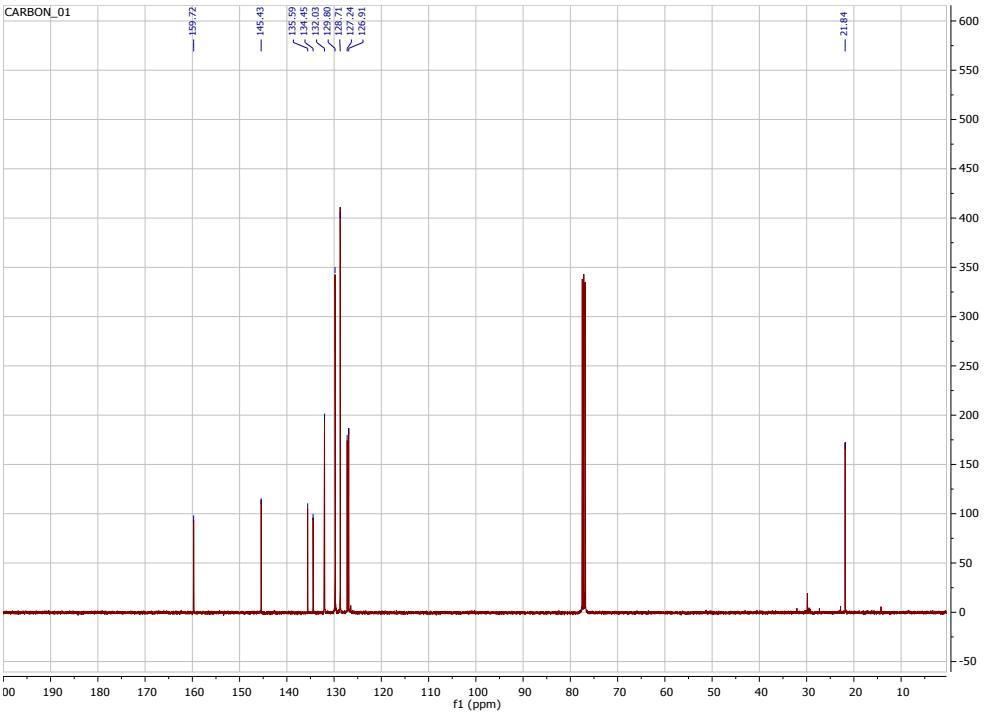


N-tosylthiophene-3-carboxamide (**12**):

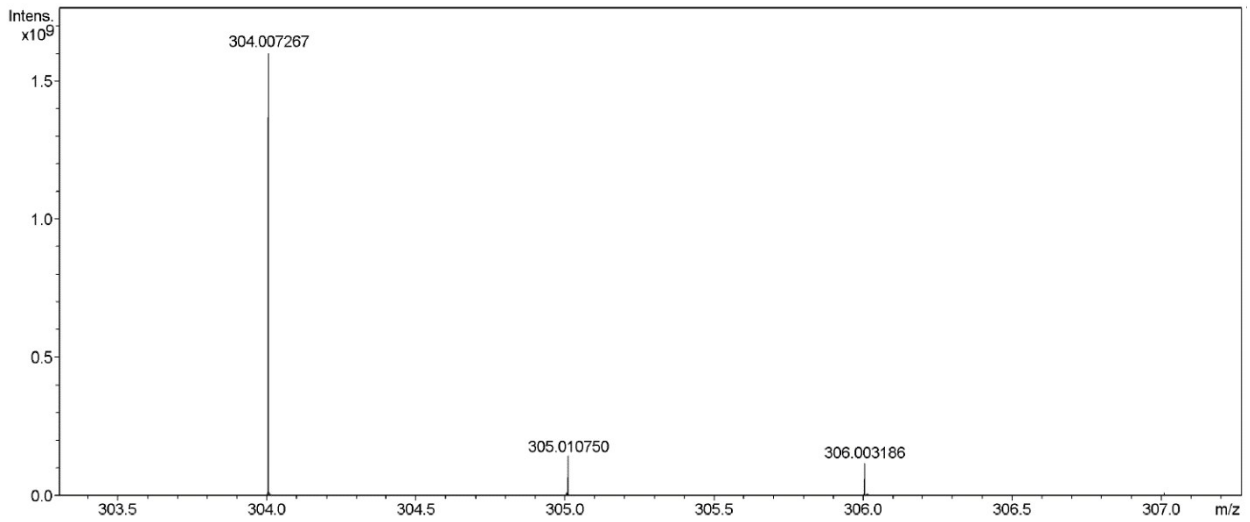
^{1}H NMR:



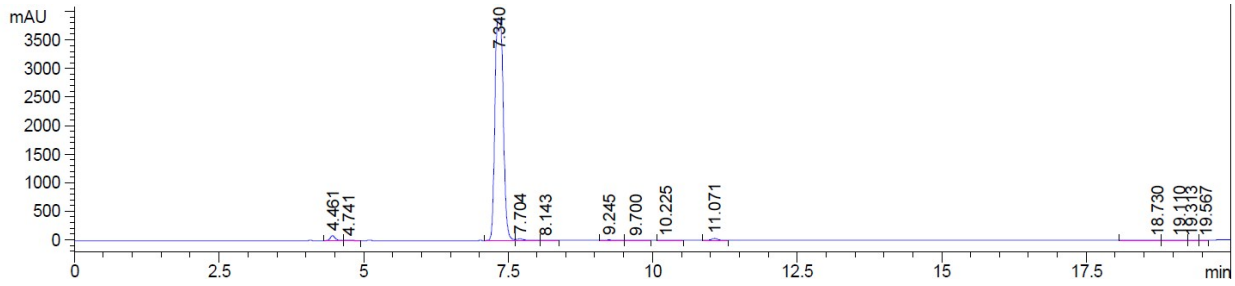
^{13}C NMR:



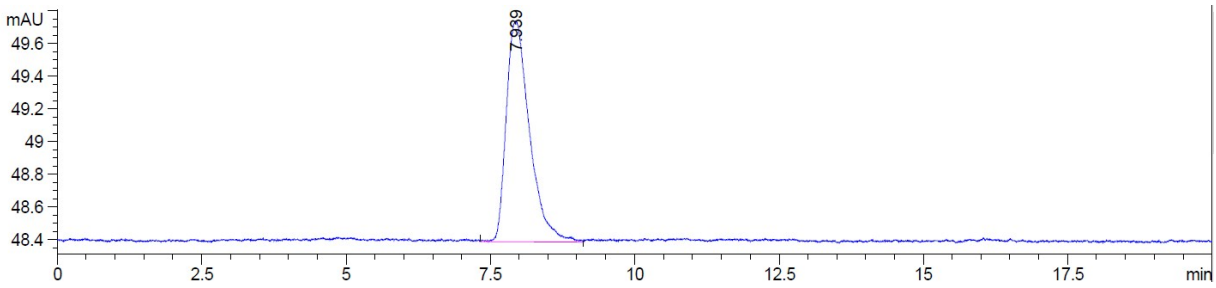
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

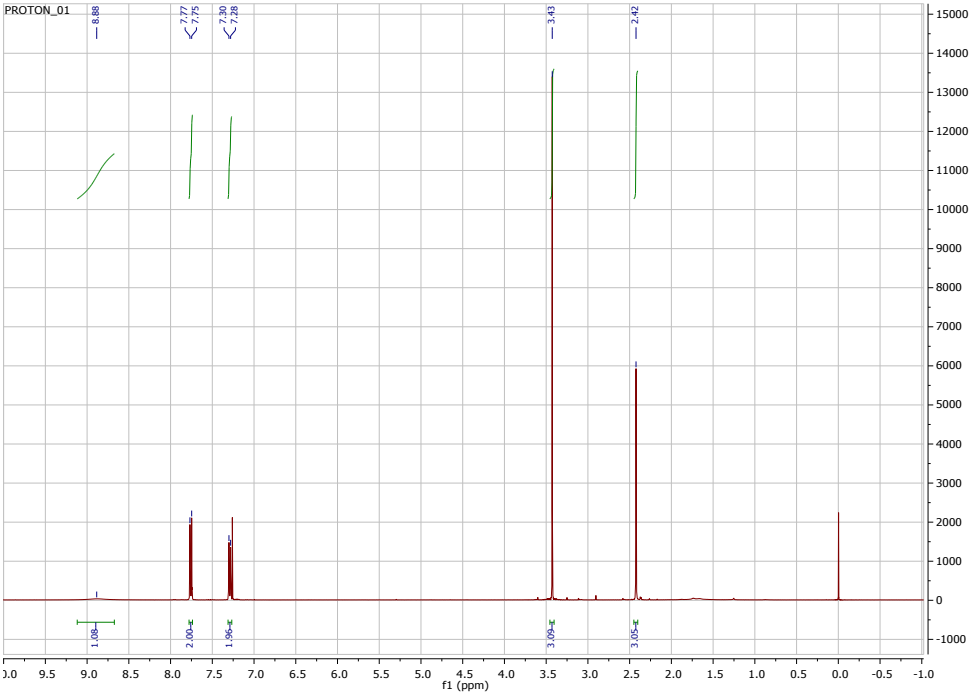


HPLC chromatogram - radioactivity-detection:

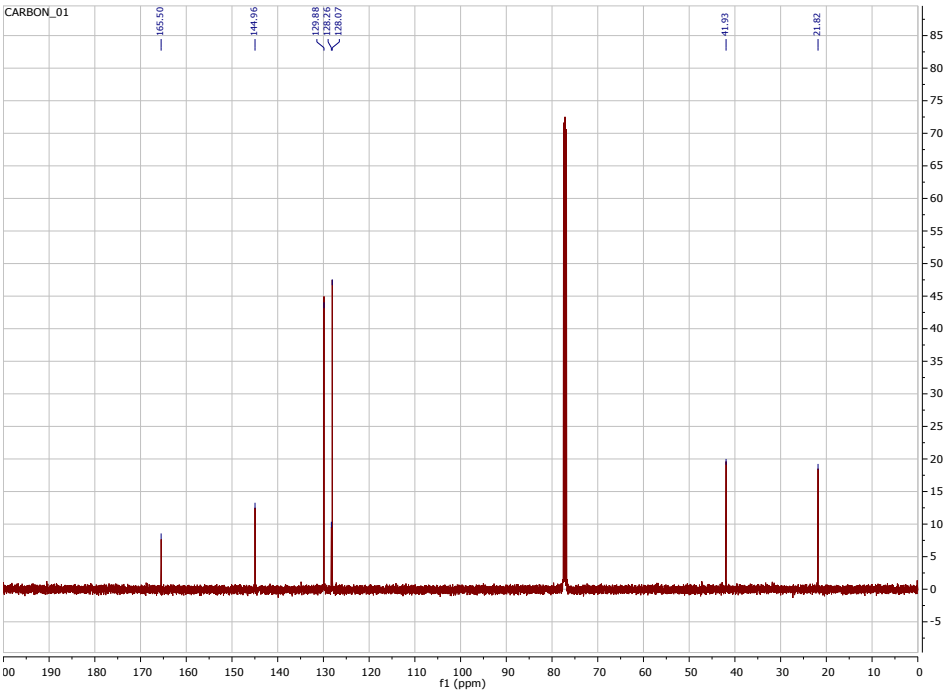


4-methyl-*N*-(methylsulfonyl)benzamide) (**13**):

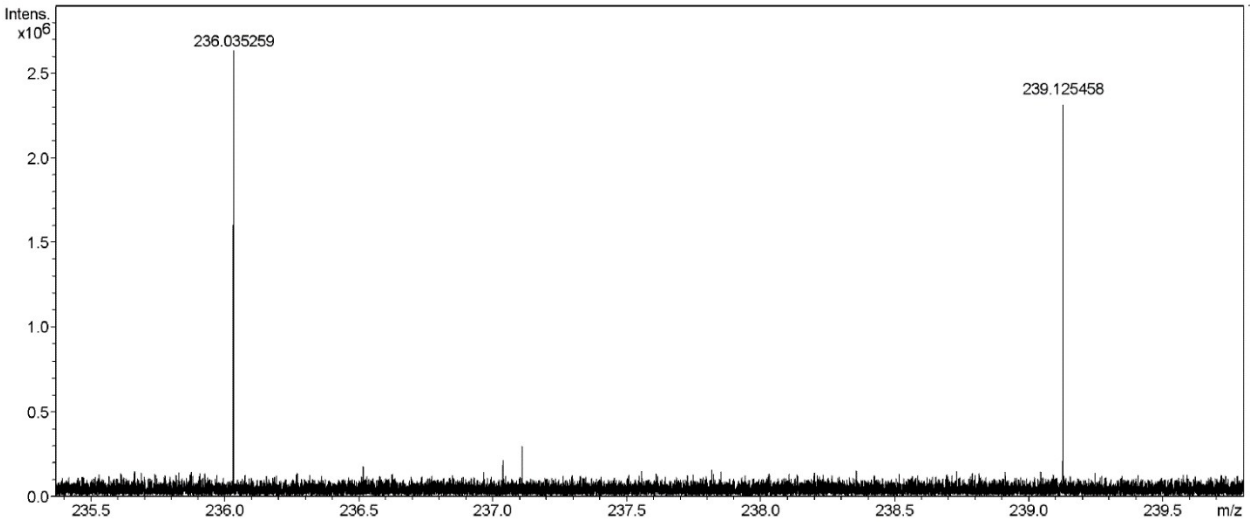
^{1}H NMR:



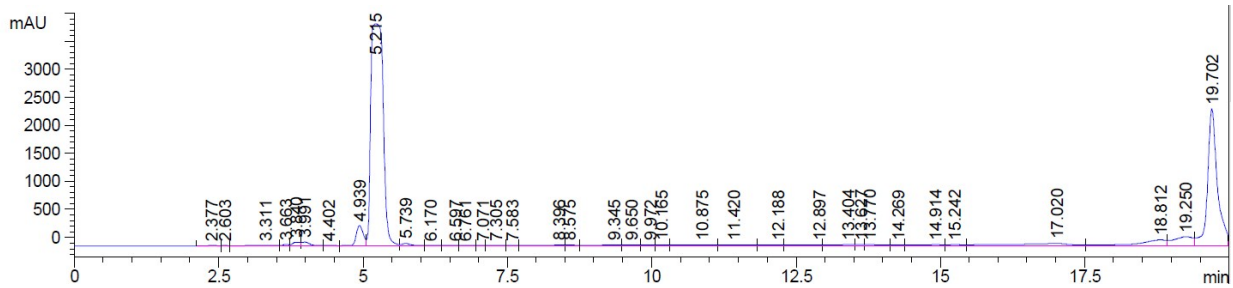
^{13}C NMR:



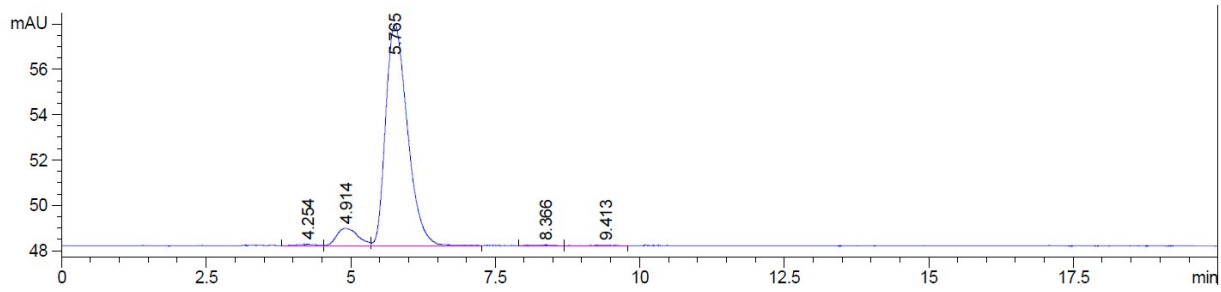
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

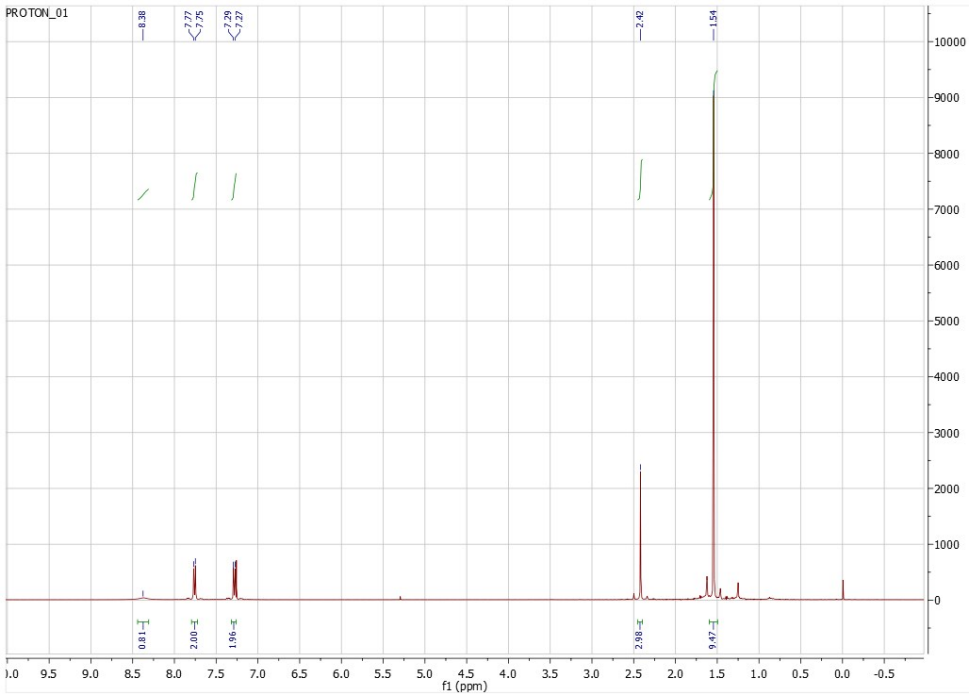


HPLC chromatogram - radioactivity-detection:

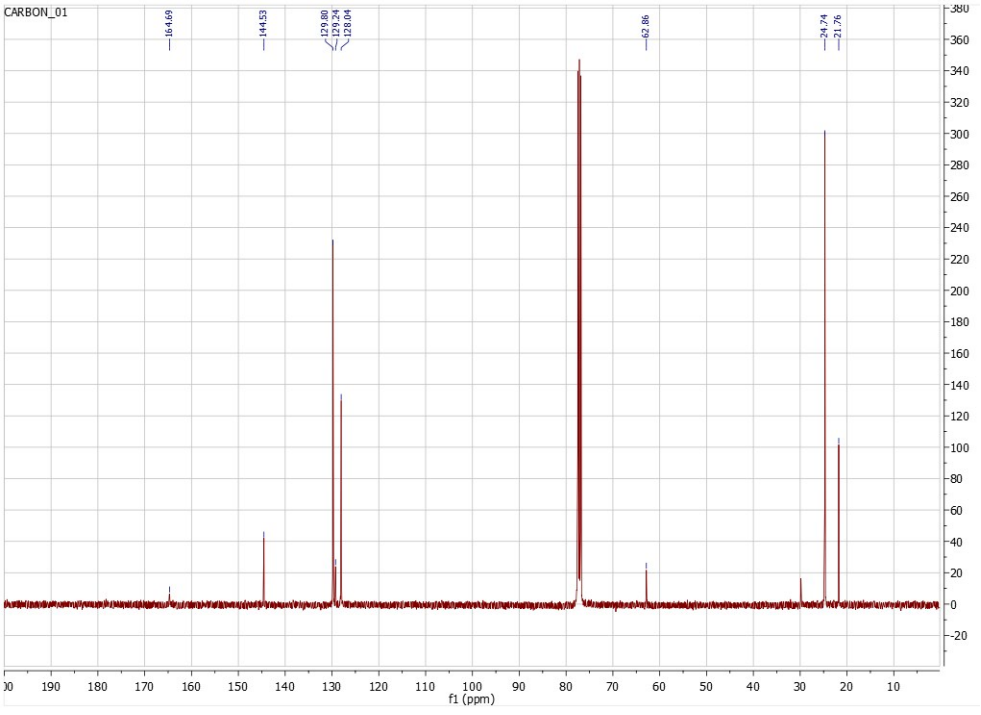


N-(*tert*-butylsulfonyl)-4-methylbenzamide (**14**):

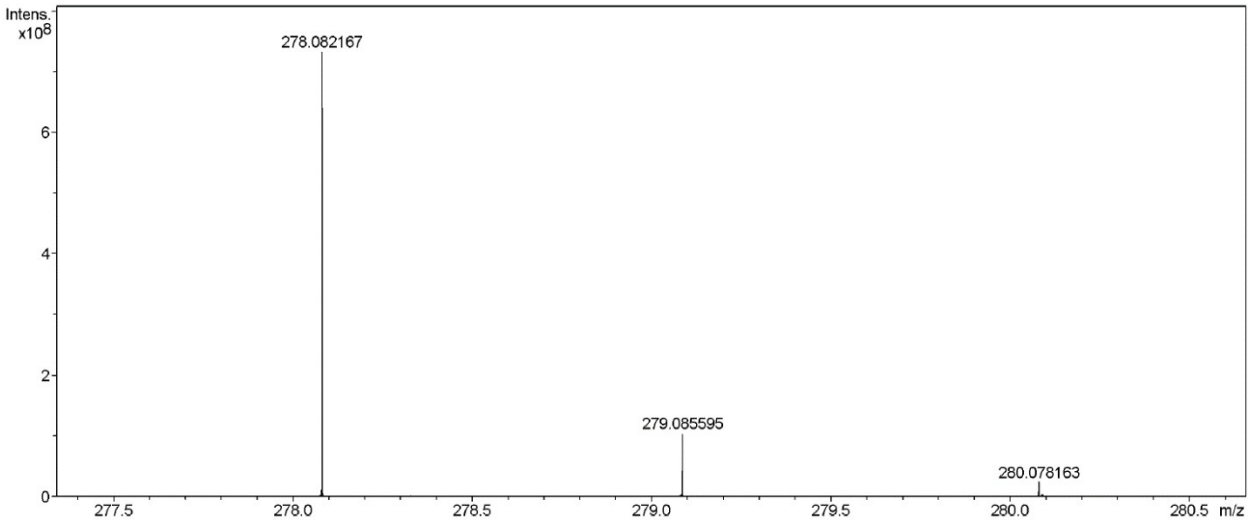
^{1}H NMR:



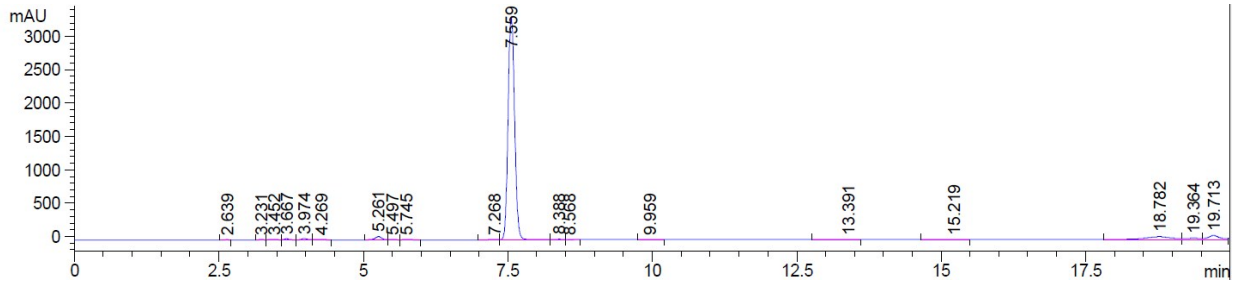
^{13}C NMR:



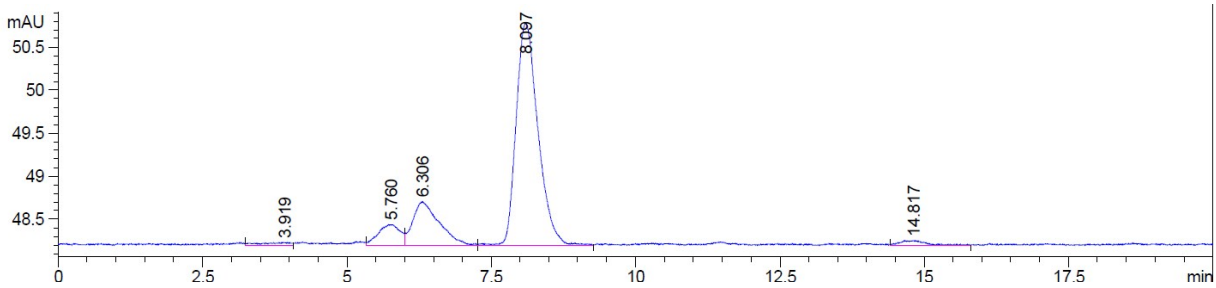
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

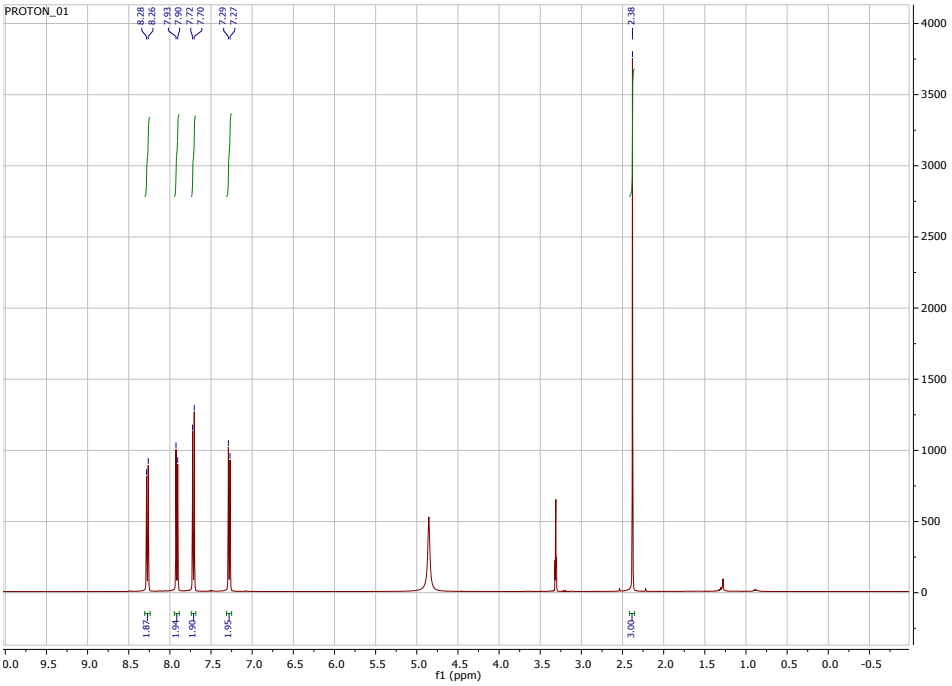


HPLC chromatogram - radioactivity-detection:

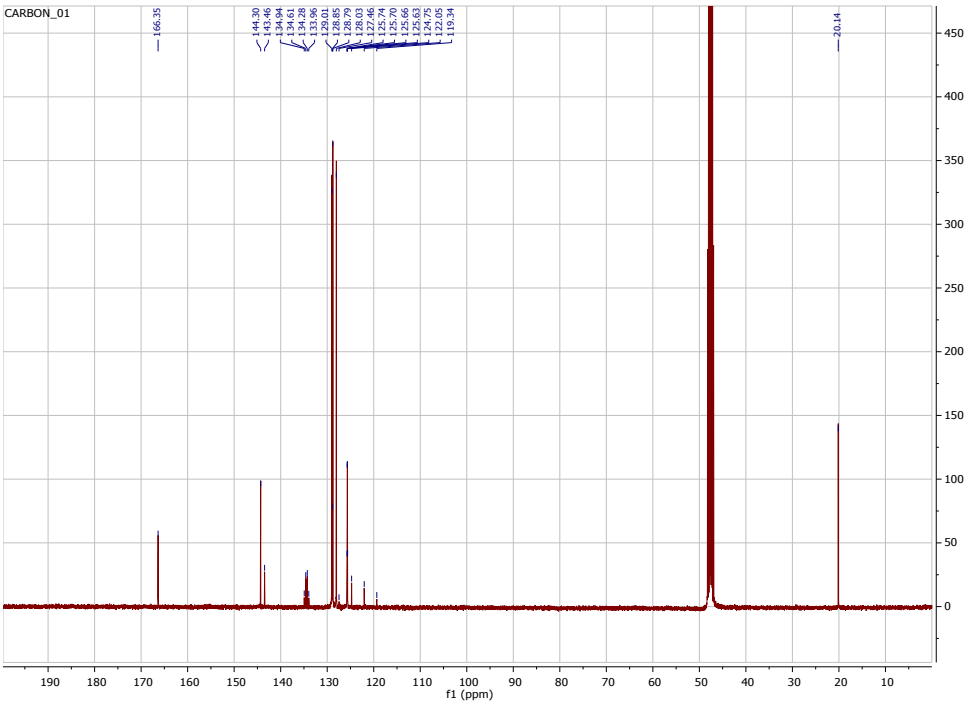


4-methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)benzamide (**15**):

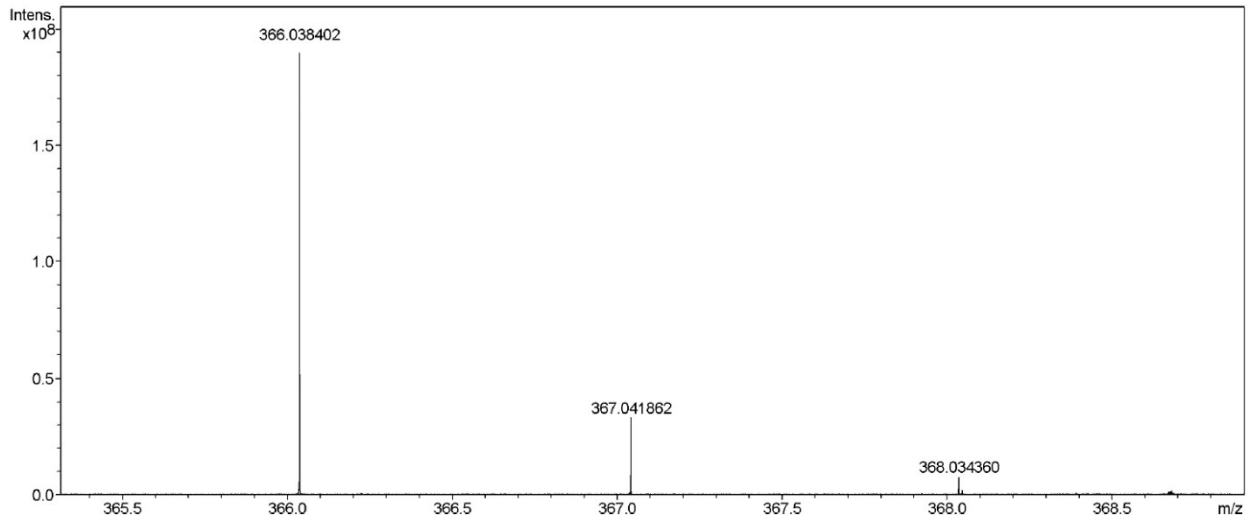
^{1}H NMR:



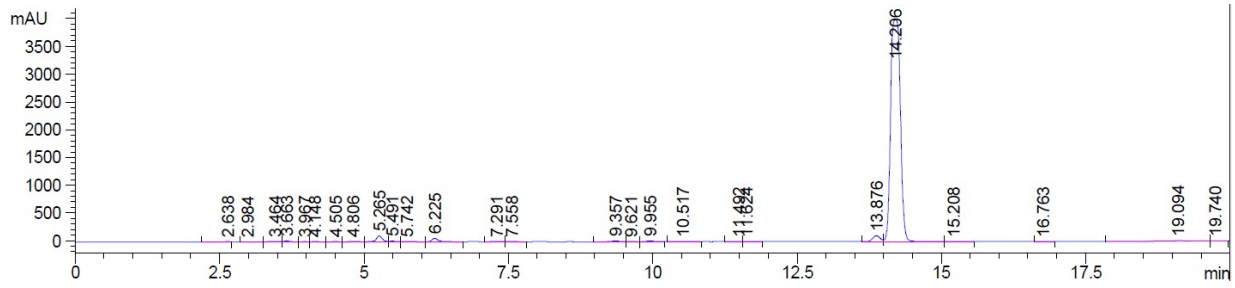
^{13}C NMR:



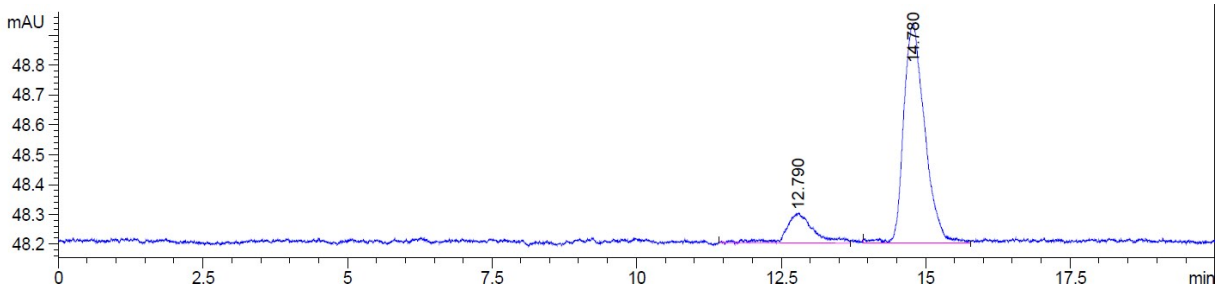
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

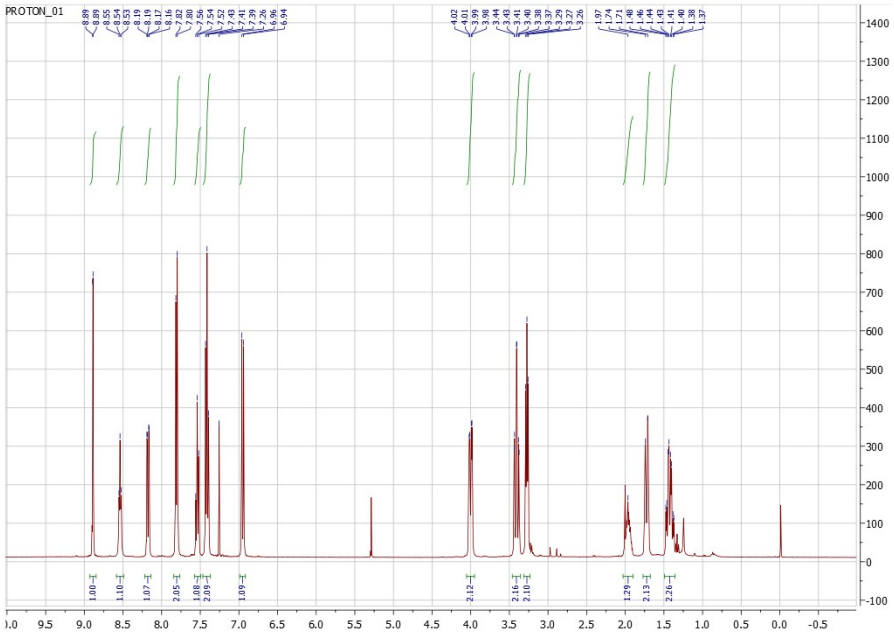


HPLC chromatogram - radioactivity-detection:

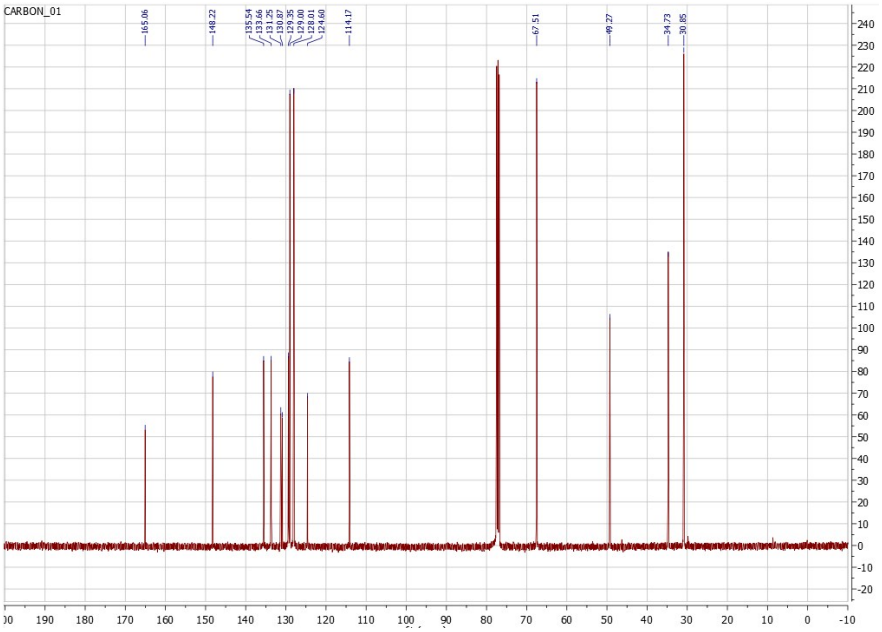


N-((3-nitro-4-(((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide (**16**):

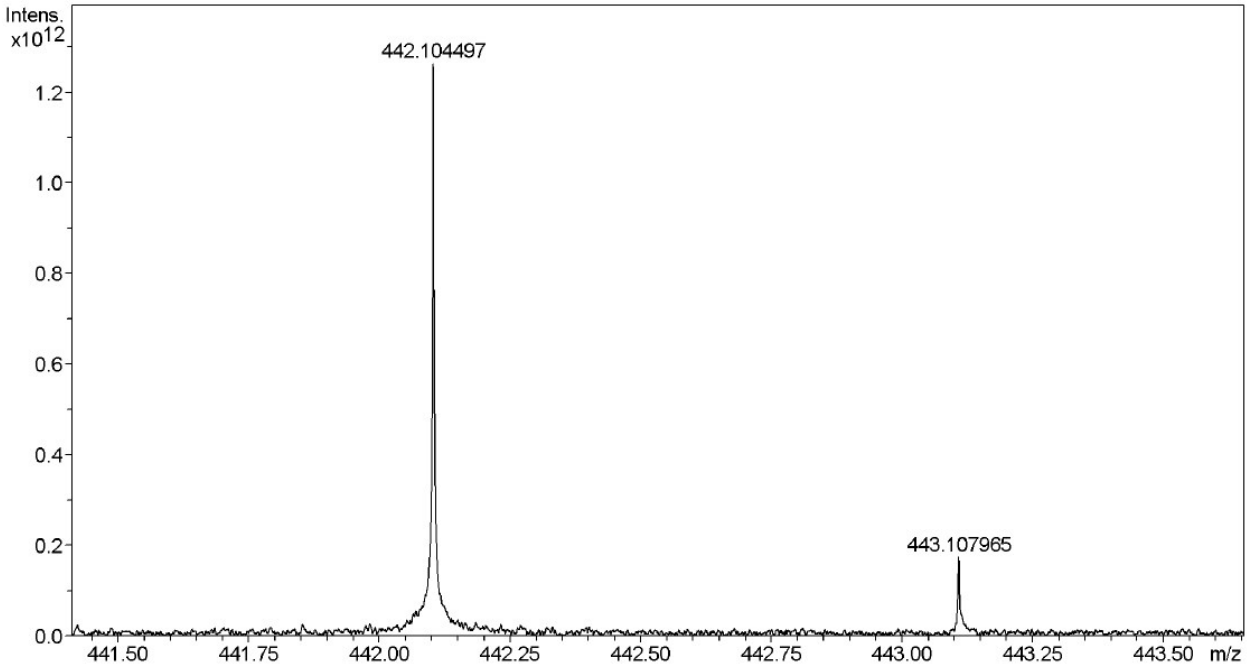
^{1}H NMR:



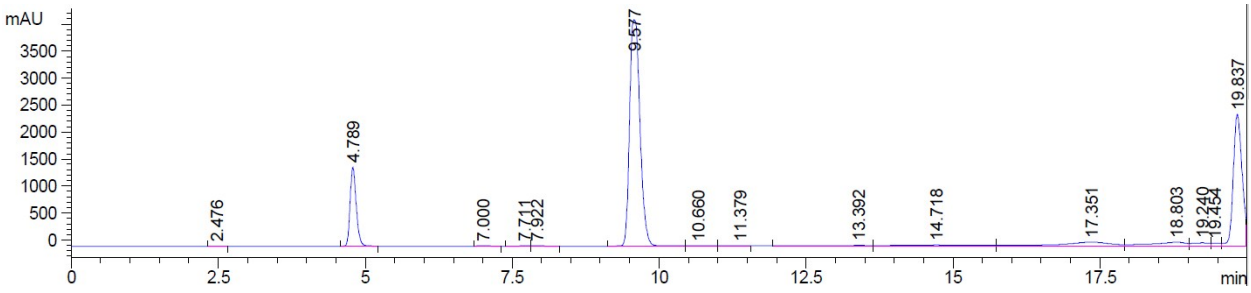
^{13}C NMR:



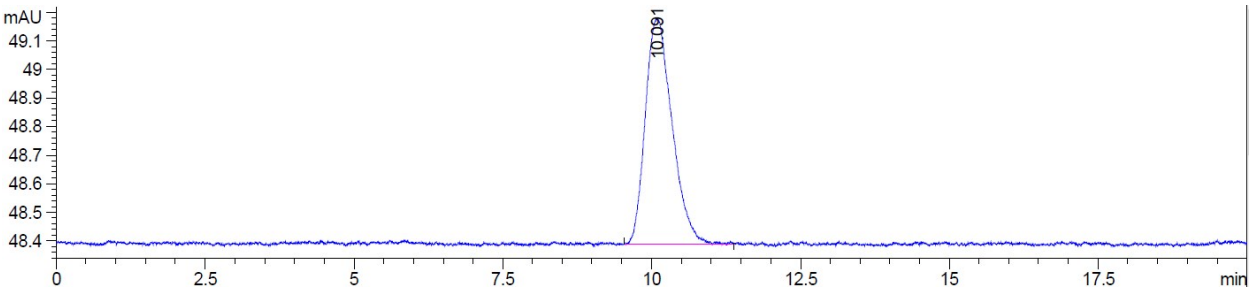
ESI-HRMS:



HPLC chromatogram - UV-detection (254 nm):

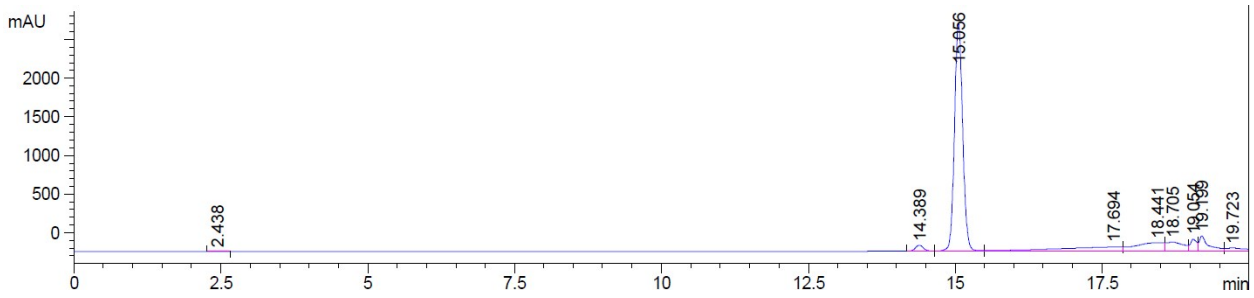


HPLC chromatogram - radioactivity-detection:

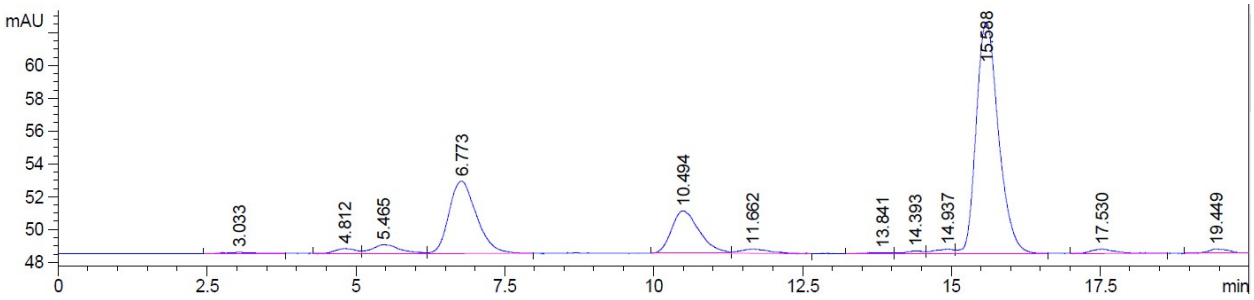


Tasisulam

HPLC chromatogram - UV-detection (254 nm):

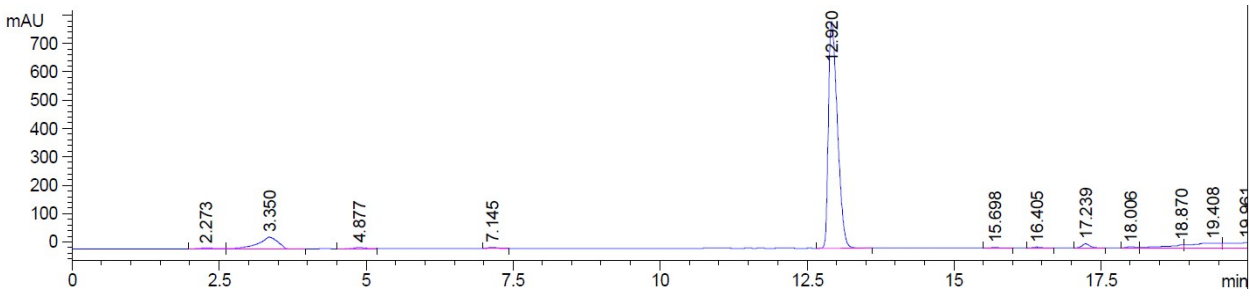


HPLC chromatogram - radioactivity-detection:

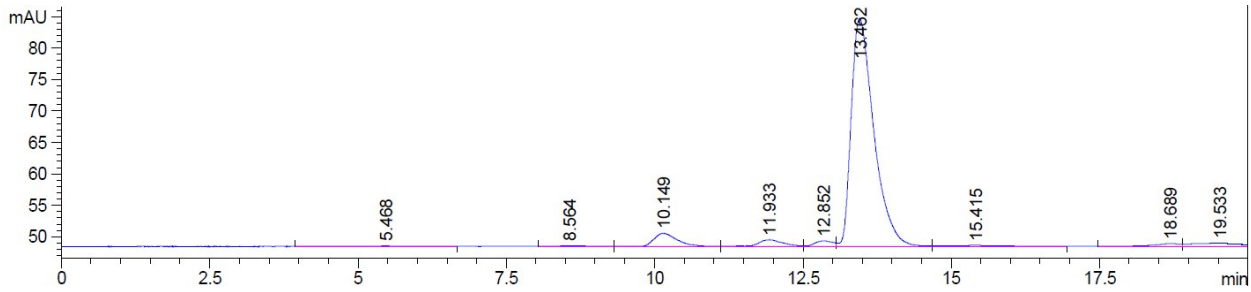


ABT-199

HPLC chromatogram - UV-detection (254 nm):

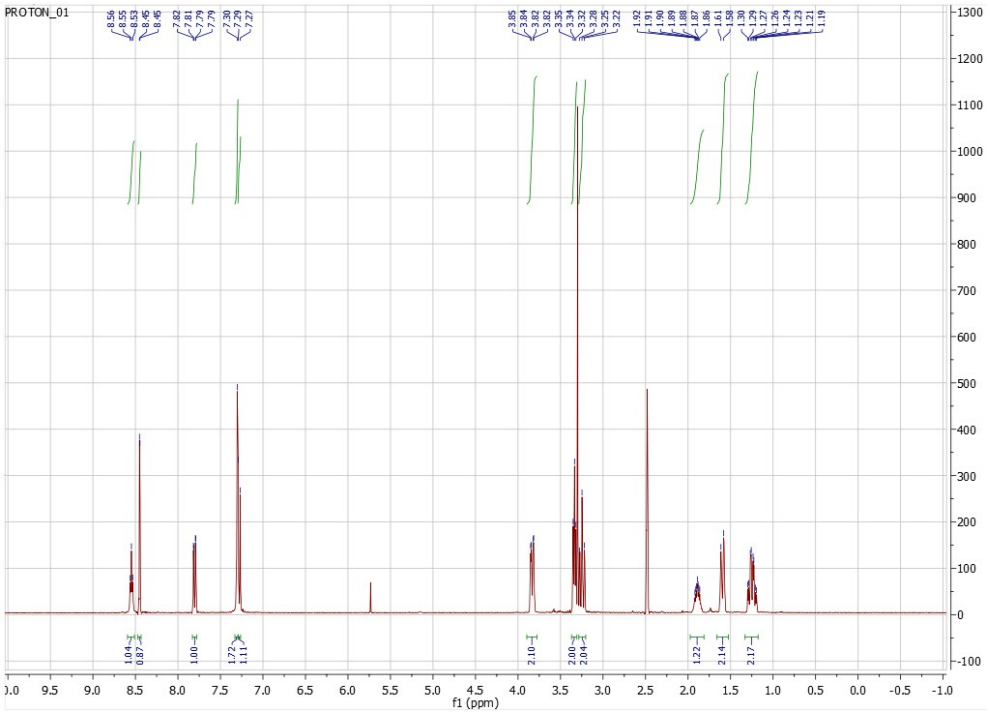


HPLC chromatogram - radioactivity-detection:

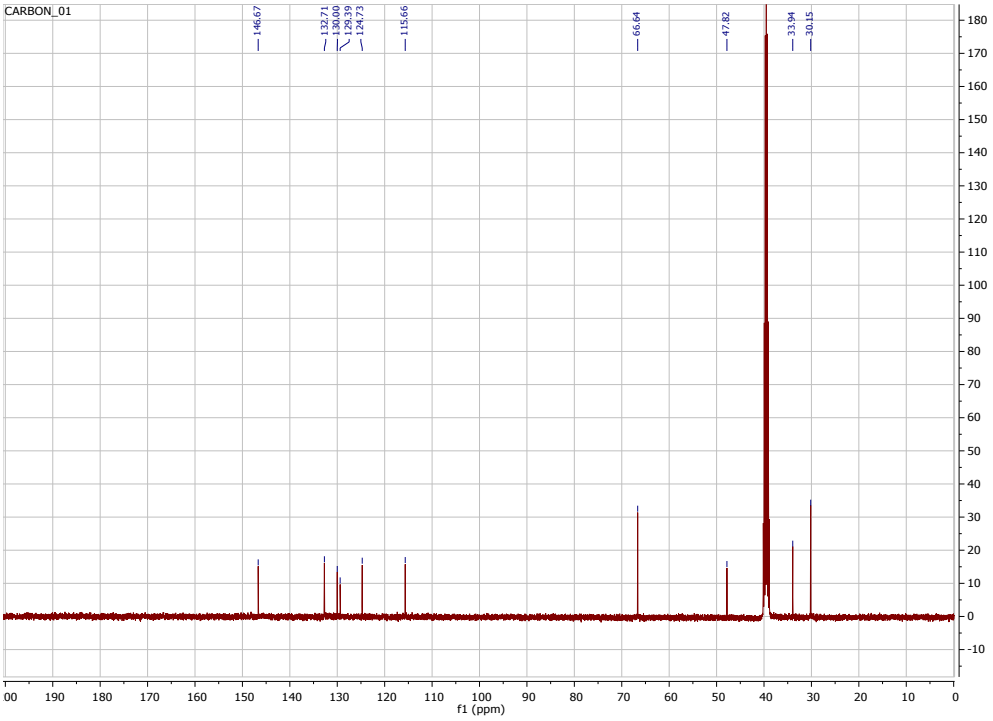


3-nitro-4-(((tetrahydro-2H-pyran-4-yl)methyl)amino)benzenesulfonamide (**17**):

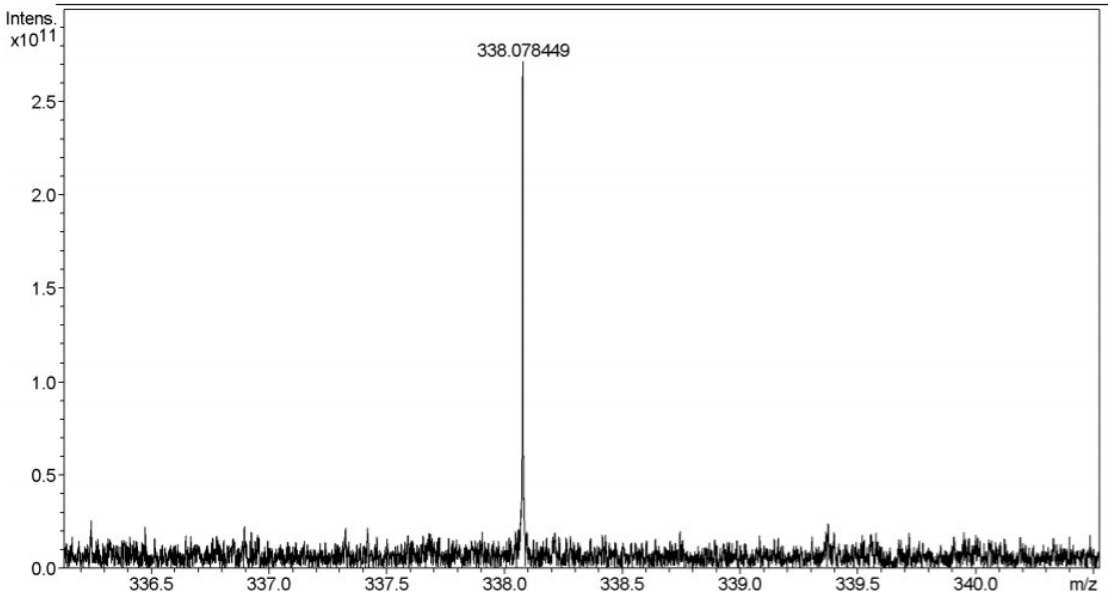
^{1}H NMR:



^{13}C NMR:

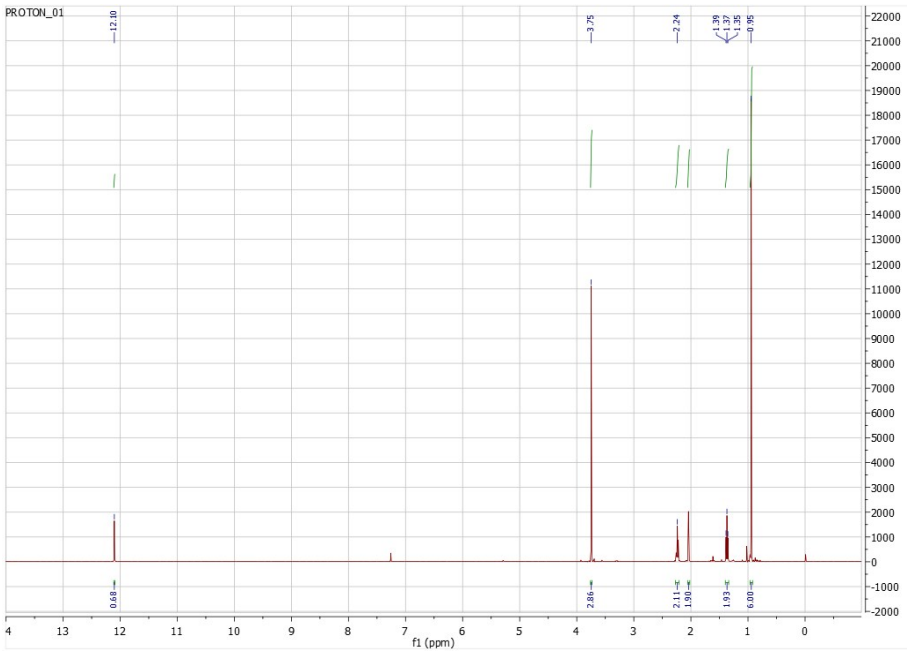


ESI-HRMS:

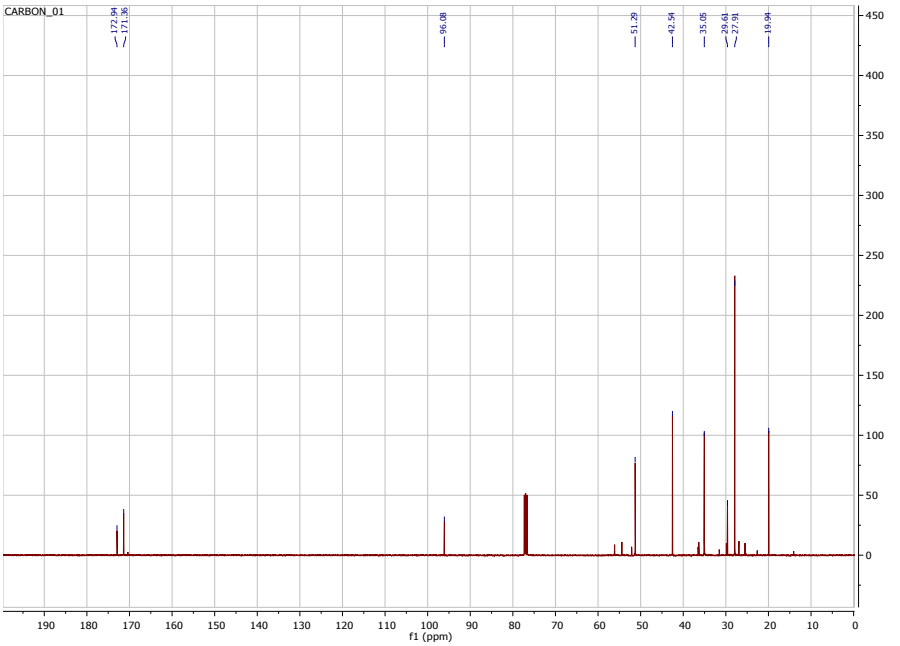

Intens.
x10^11
338.078449
2.5
2.0
1.5
1.0
0.5
0.0
336.5
337.0
337.5
338.0
338.5
339.0
339.5
340.0
m/z

Methyl 4,4-dimethyl-2-oxocyclohexane-1-carboxylate (**18**):

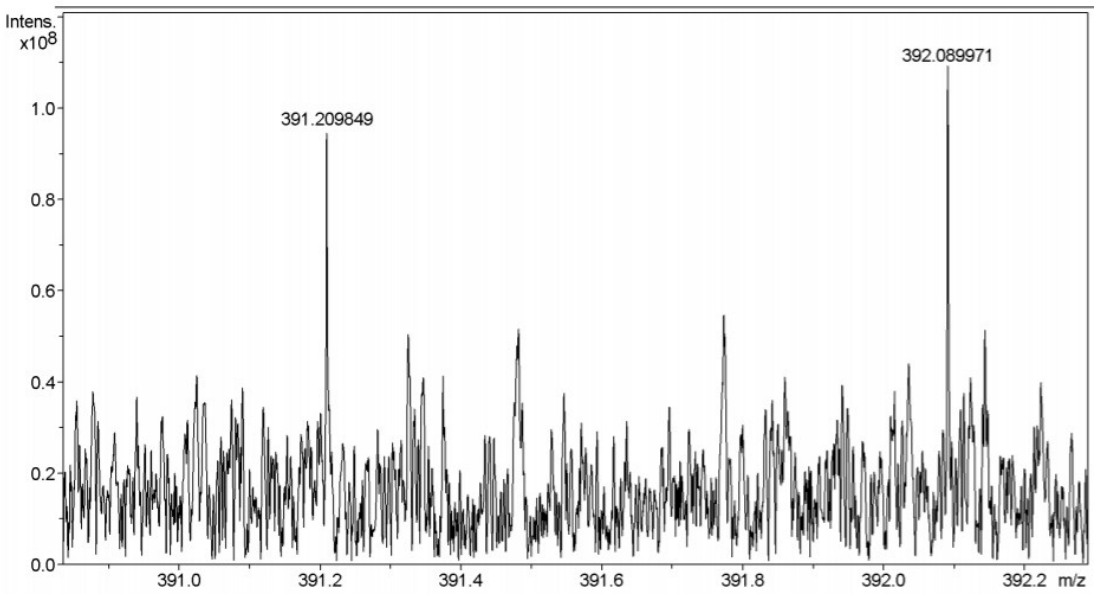
^{1}H NMR:



^{13}C NMR:

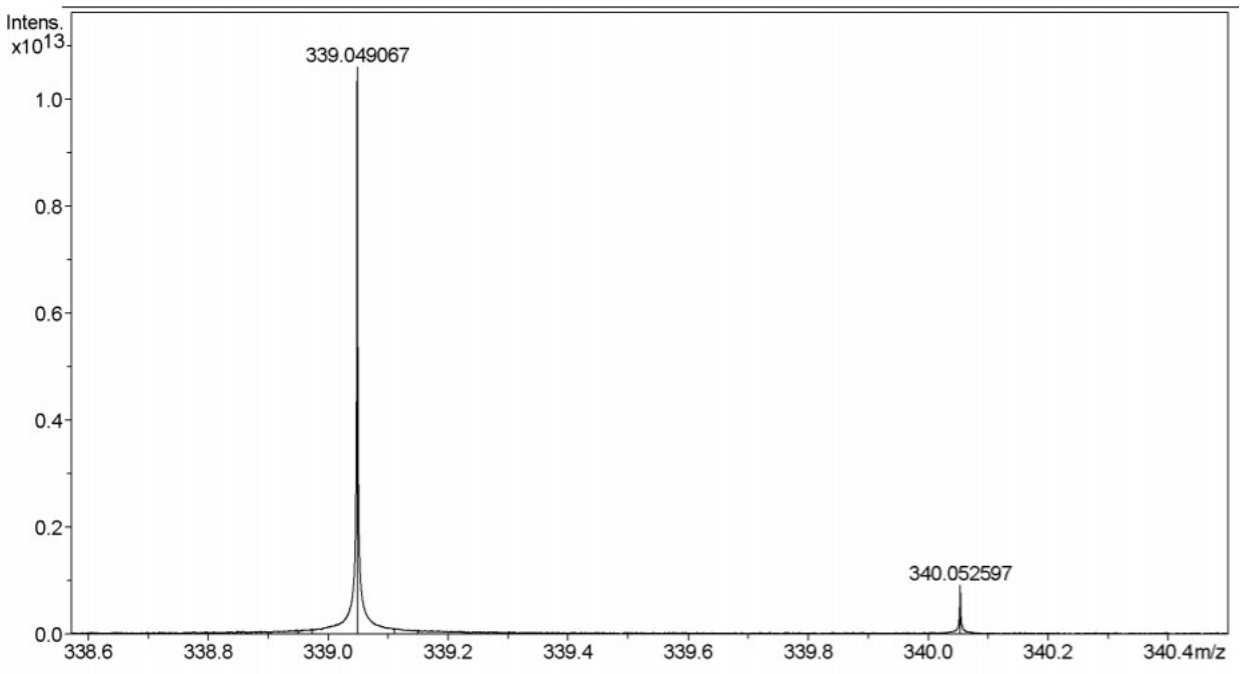


ESI-HRMS:


Intens.
x10^8
1.0
0.8
0.6
0.4
0.2
0.0
391.209849
392.089971
391.0
391.2
391.4
391.6
391.8
392.0
392.2
m/z

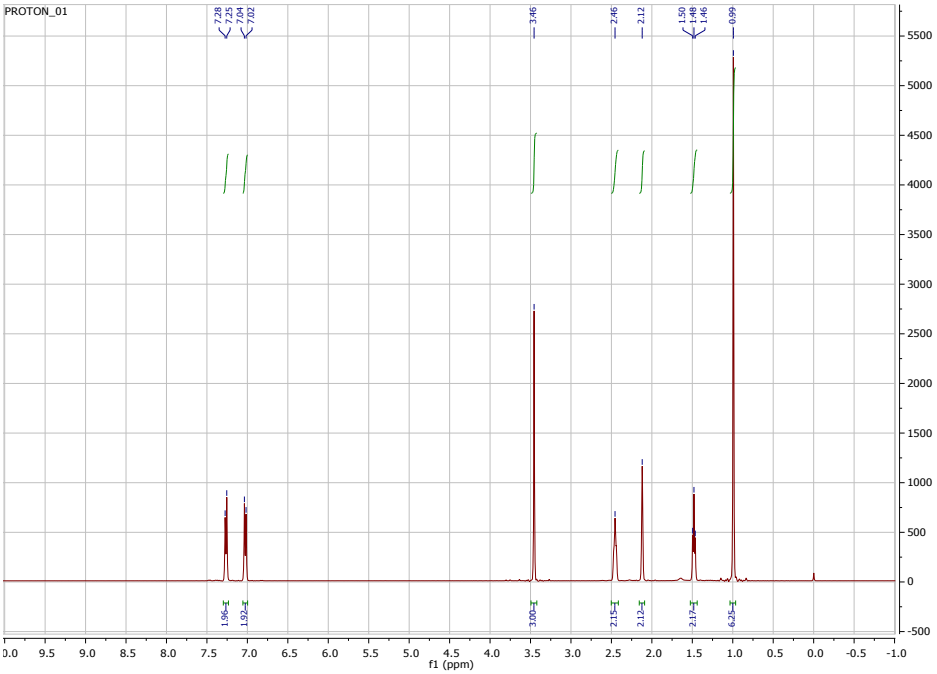
Methyl 4,4-dimethyl-2-(((trifluoromethyl)sulfonyl)oxy)cyclohex-1-ene-1-carboxylate) (**19**):

ESI-HRMS:

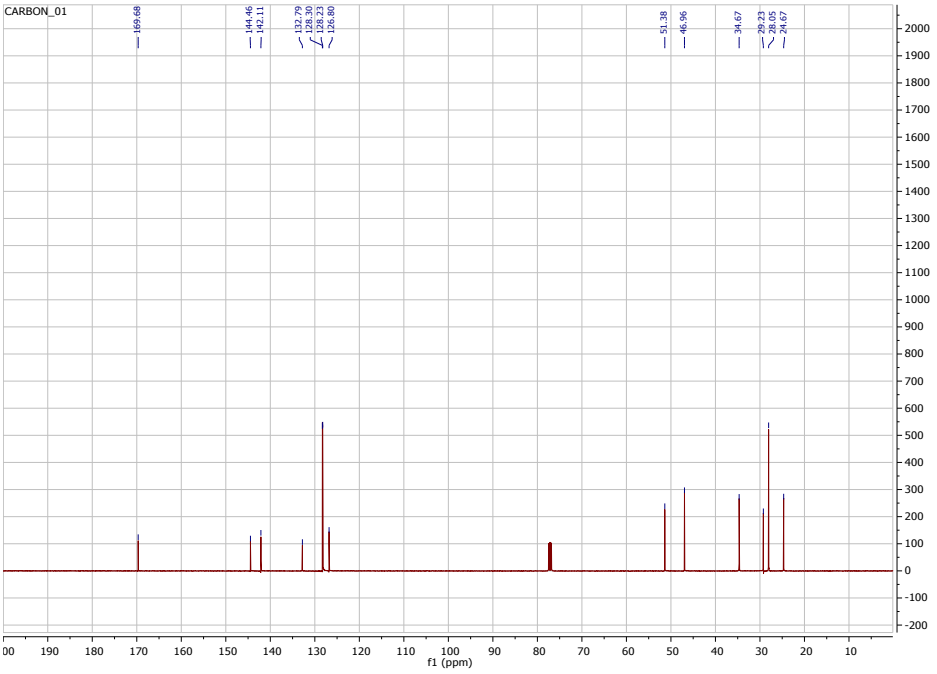


Methyl 4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-carboxylate) (**20**):

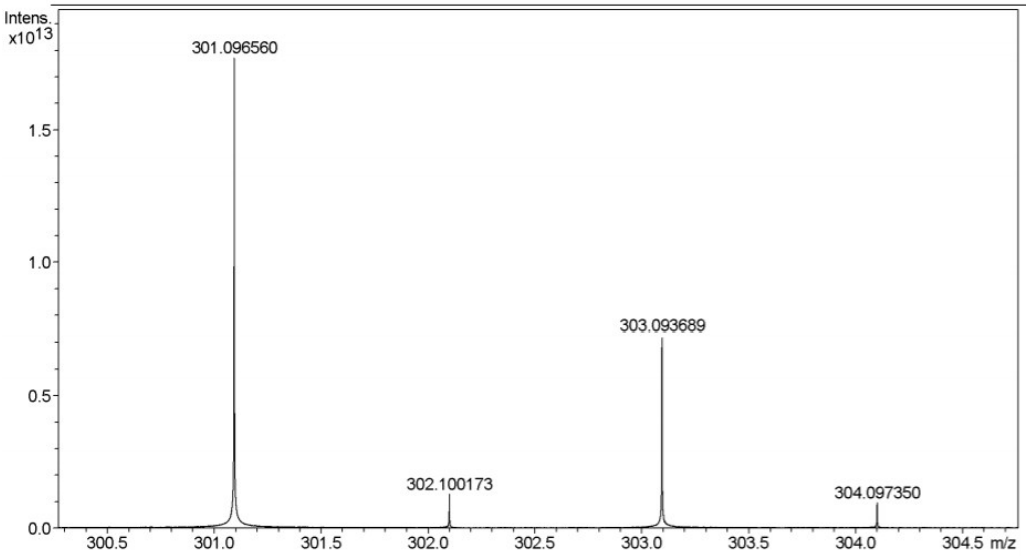
^{1}H NMR:



^{13}C NMR:

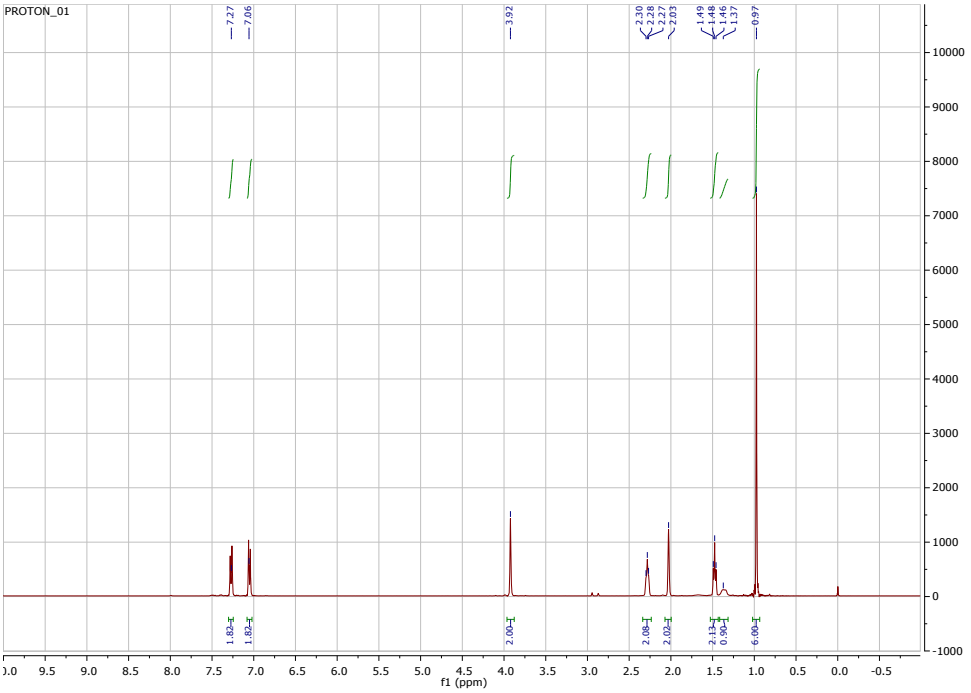


ESI-HRMS:

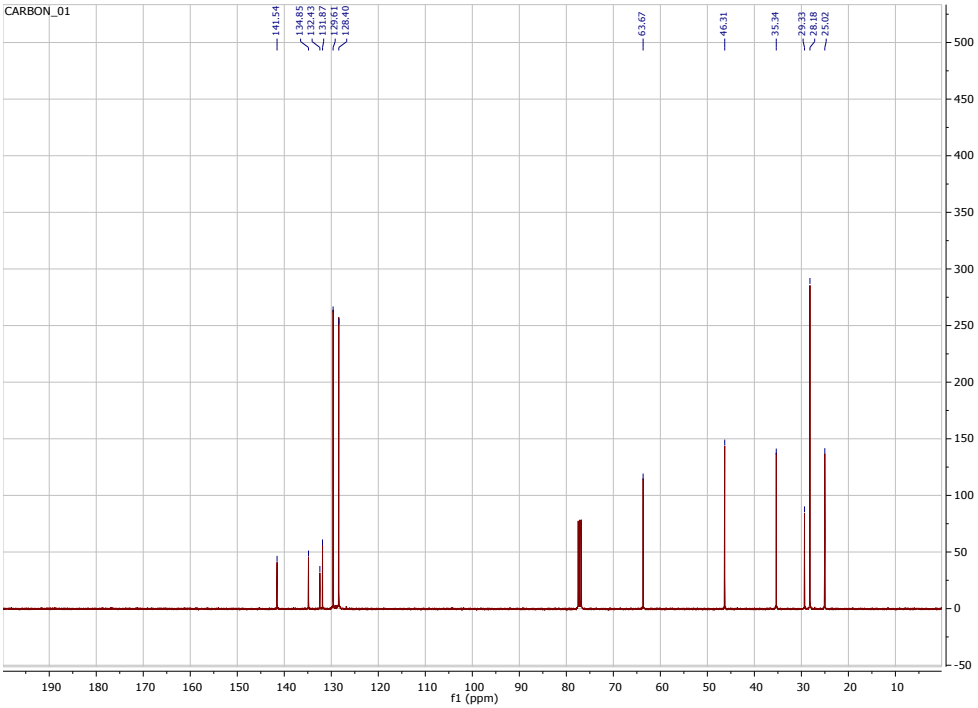

Intens.
x10^13
1.5
1.0
0.5
0.0
301.096560
303.093689
302.100173
304.097350
300.5
301.0
301.5
302.0
302.5
303.0
303.5
304.0
304.5 m/z

(4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methanol (**21**):

^{1}H NMR:

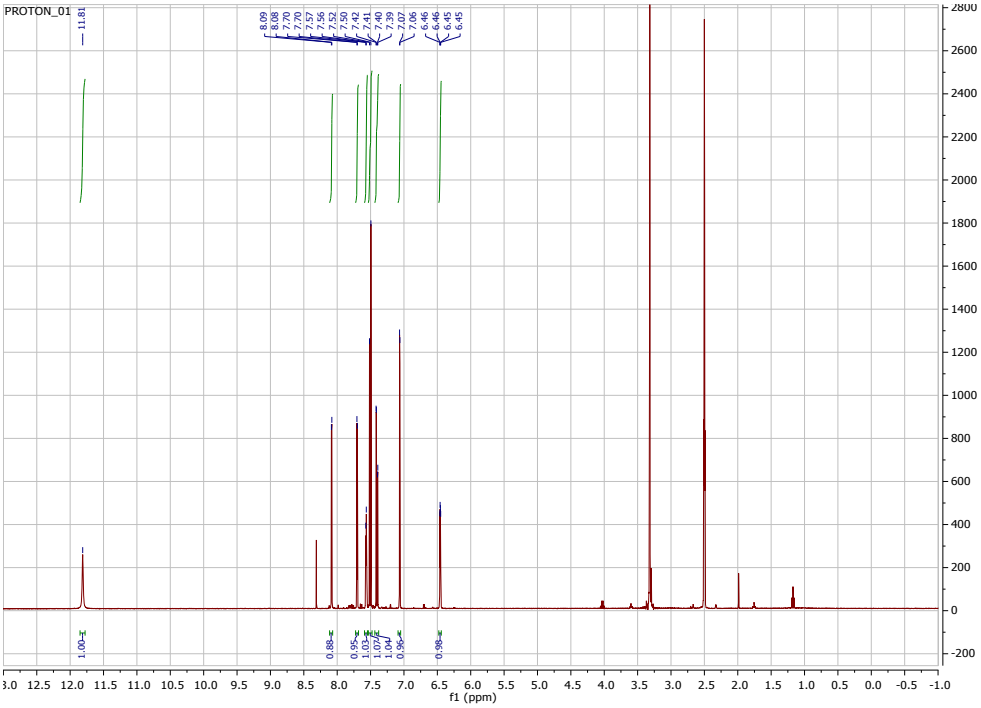


^{13}C NMR:

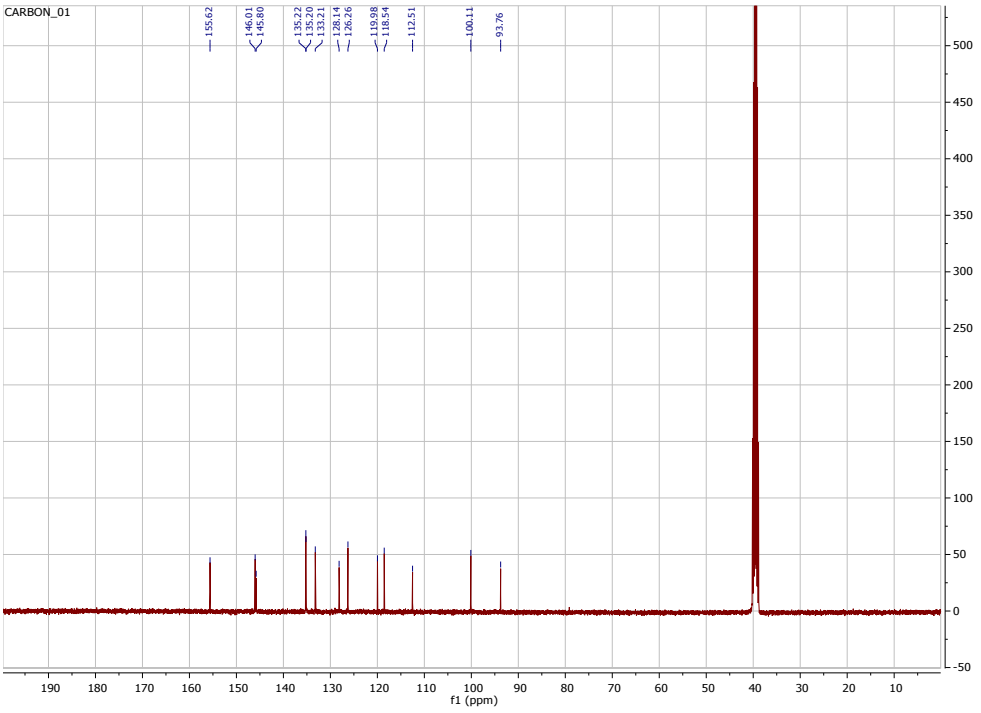


5-(2-bromo-5-iodophenoxy)-1H-pyrrolo[2,3-b]pyridine (**22**):

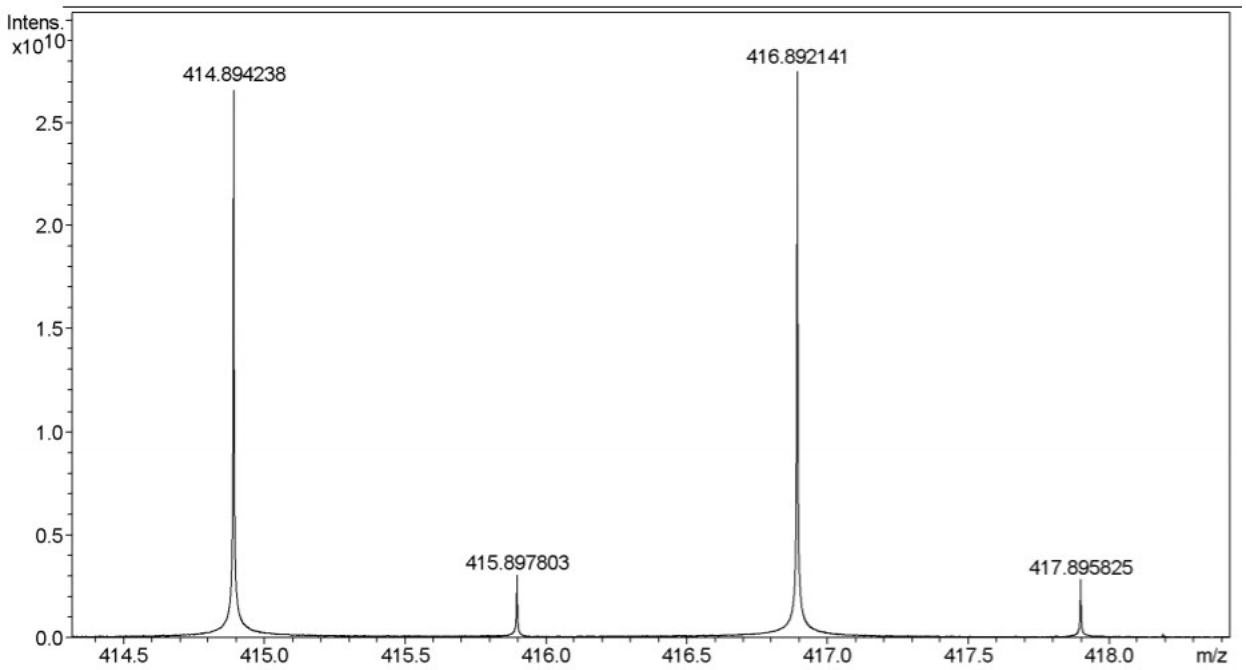
^{1}H NMR:



^{13}C NMR:

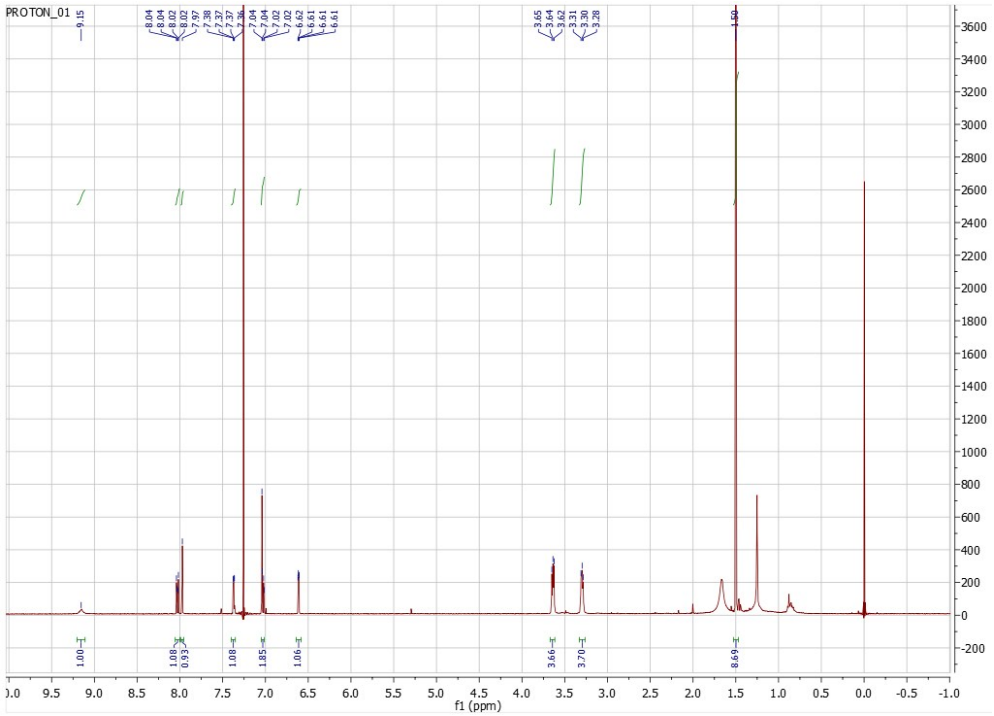


ESI-HRMS:

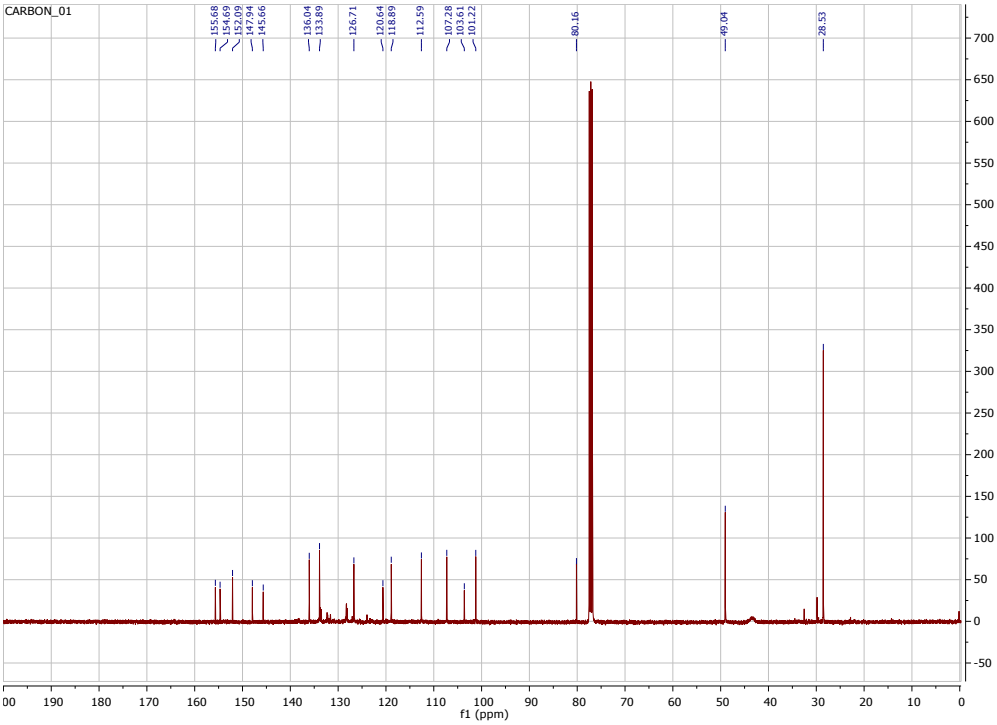

Intens.
x10^10
2.5
2.0
1.5
1.0
0.5
0.0
414.894238
415.897803
416.892141
417.895825
414.5
415.0
415.5
416.0
416.5
417.0
417.5
418.0
m/z

Tert-butyl 4-(3-((1H-pyrrolo[2,3-b]pyridin-5-yl)oxy)-4-bromophenyl)piperazine-1-carboxylate) (**23**):

^{1}H NMR:

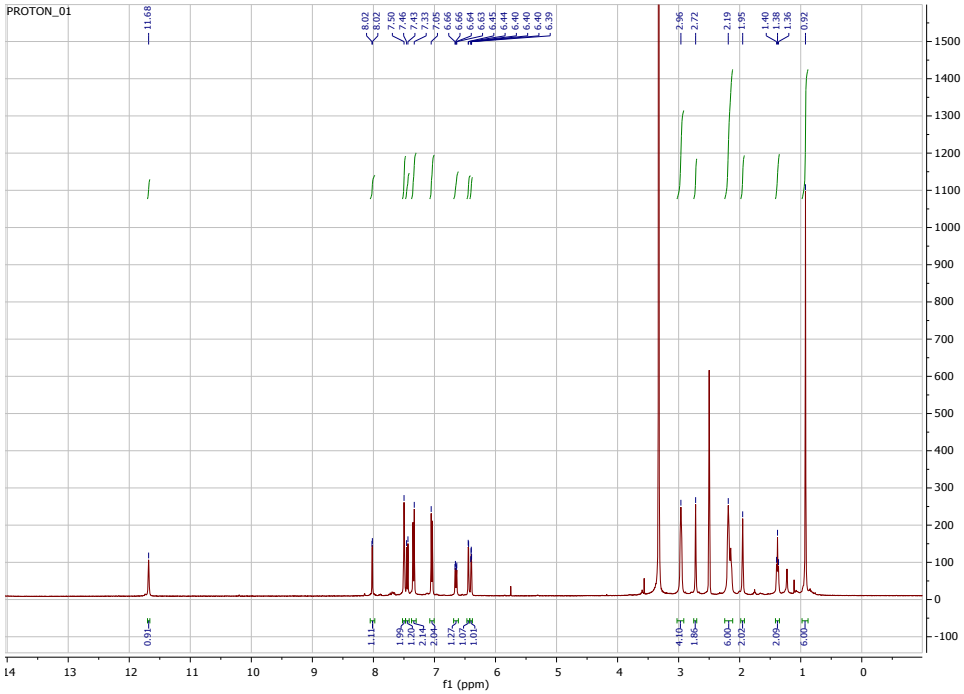


^{13}C NMR:

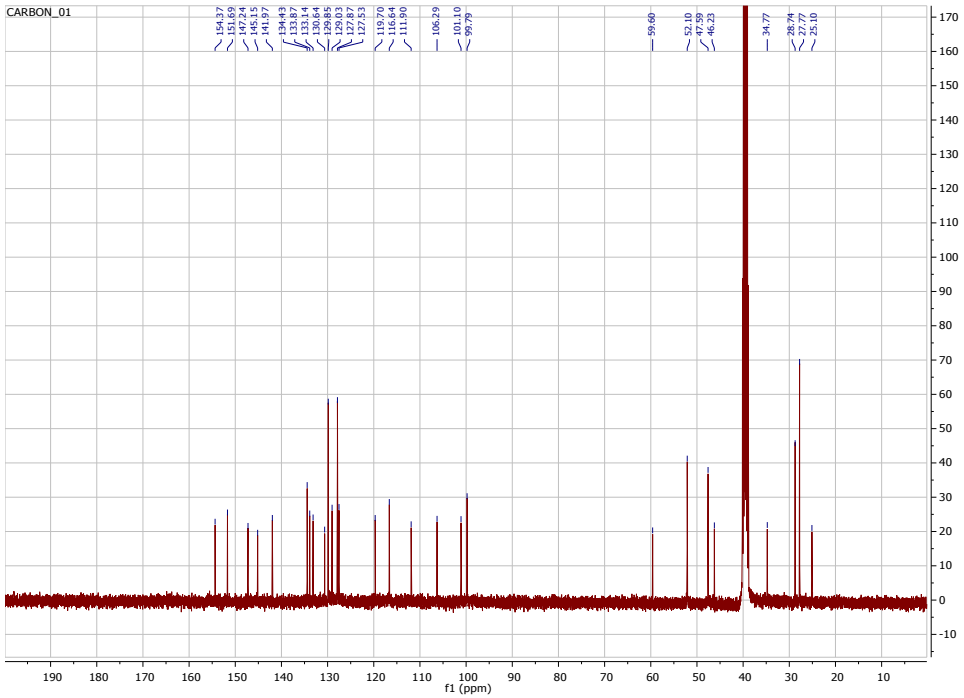


5-(2-bromo-5-(4-((4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)piperazin-1-yl)phenoxy)-1H-pyrrolo[2,3-b]pyridine (**24**):

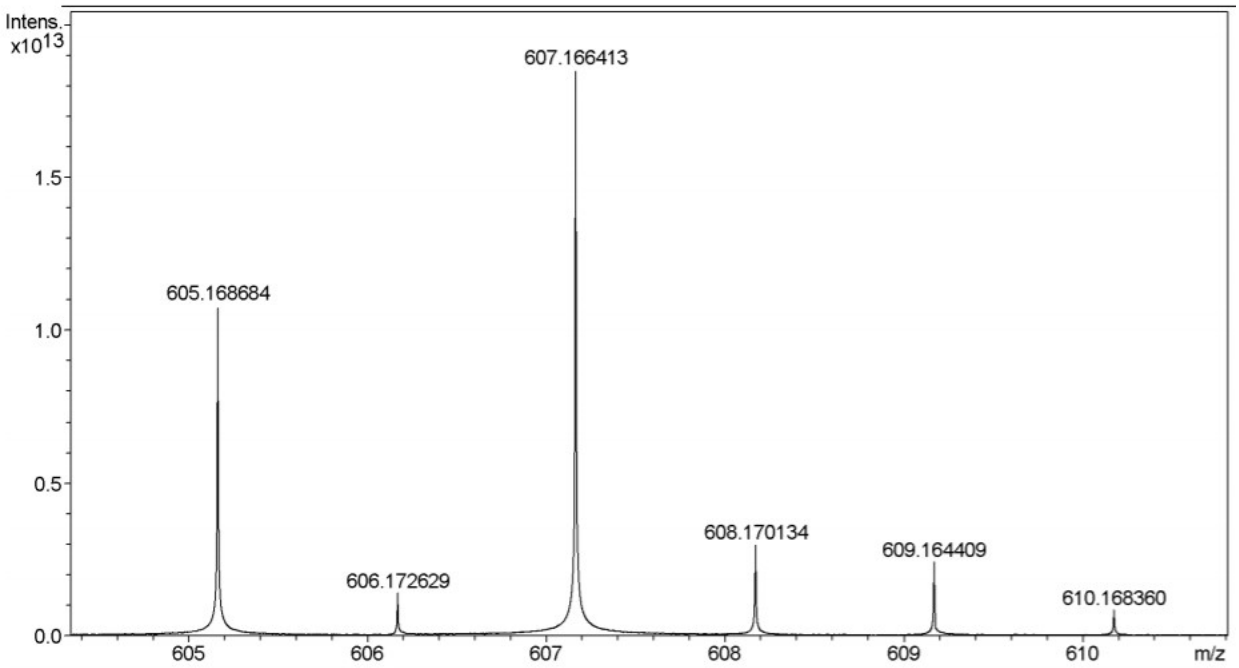
^{1}H NMR:



^{13}C NMR:

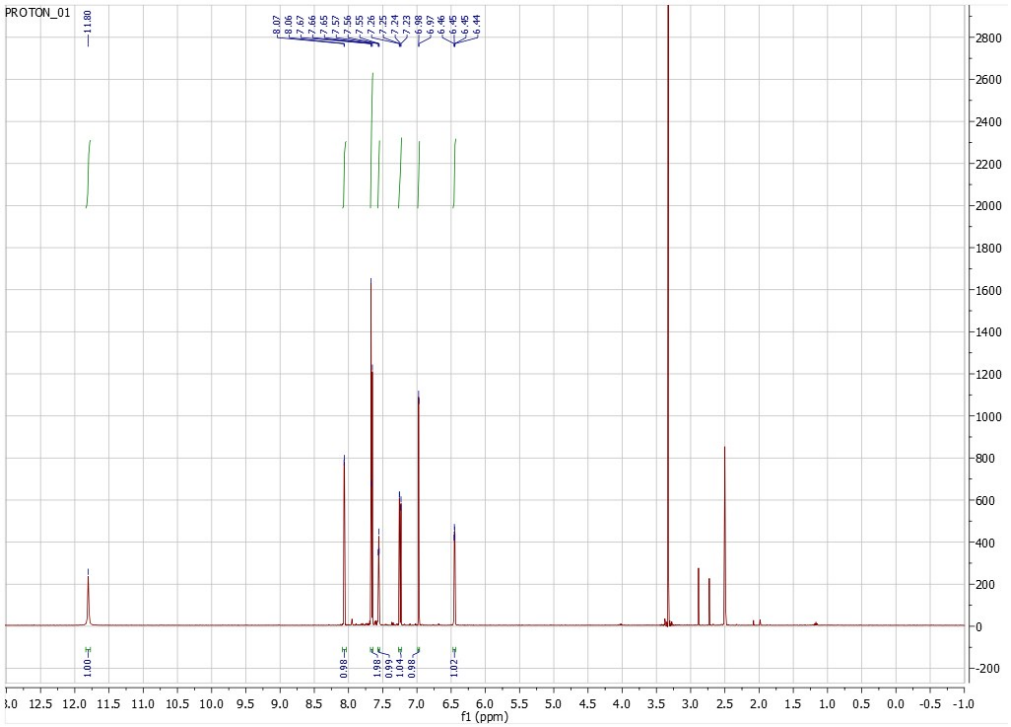


ESI-HRMS:

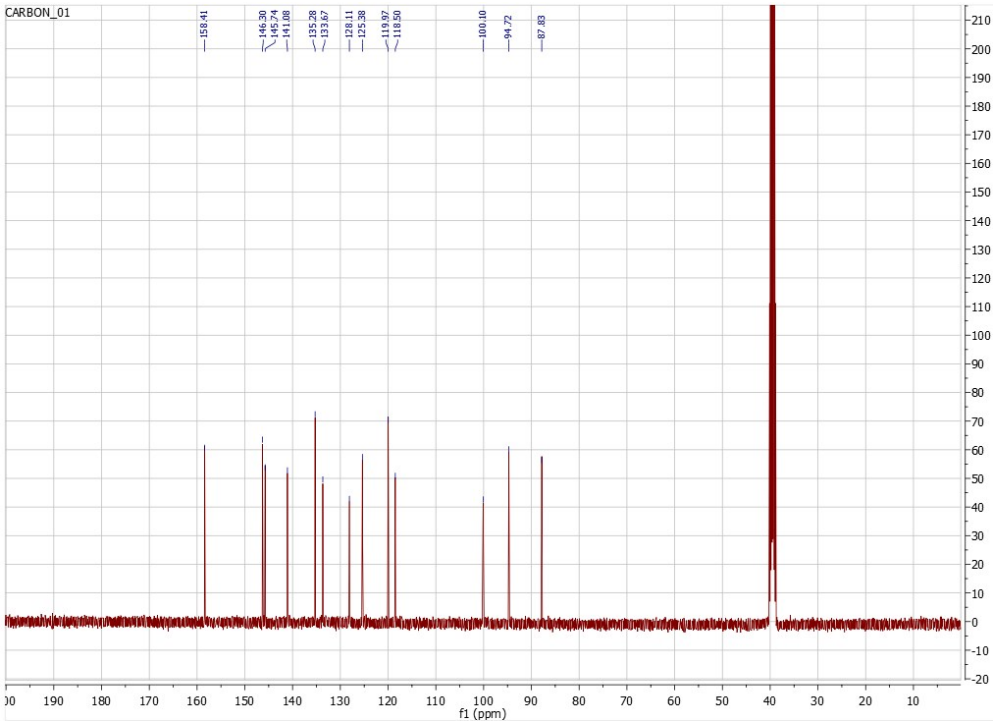

Intens.
x10^13
1.5
1.0
0.5
0.0
605.168684
606.172629
607.166413
608.170134
609.164409
610.168360
605
606
607
608
609
610
m/z

5-(2,5-diiodophenoxy)-1*H*-pyrrolo[2,3-*b*]pyridine (**25**):

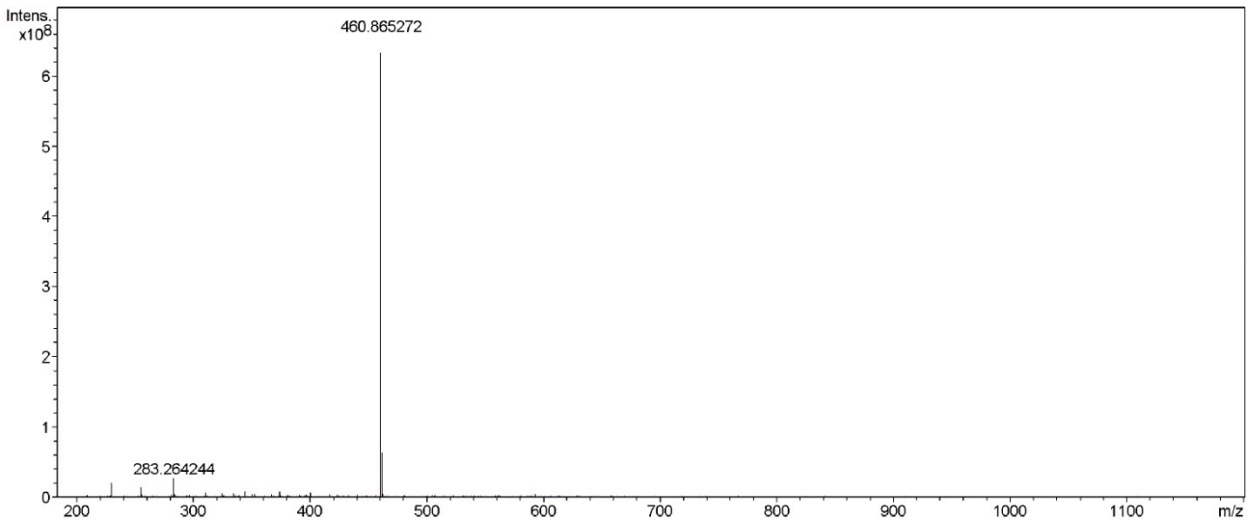
^{1}H NMR:



^{13}C NMR:

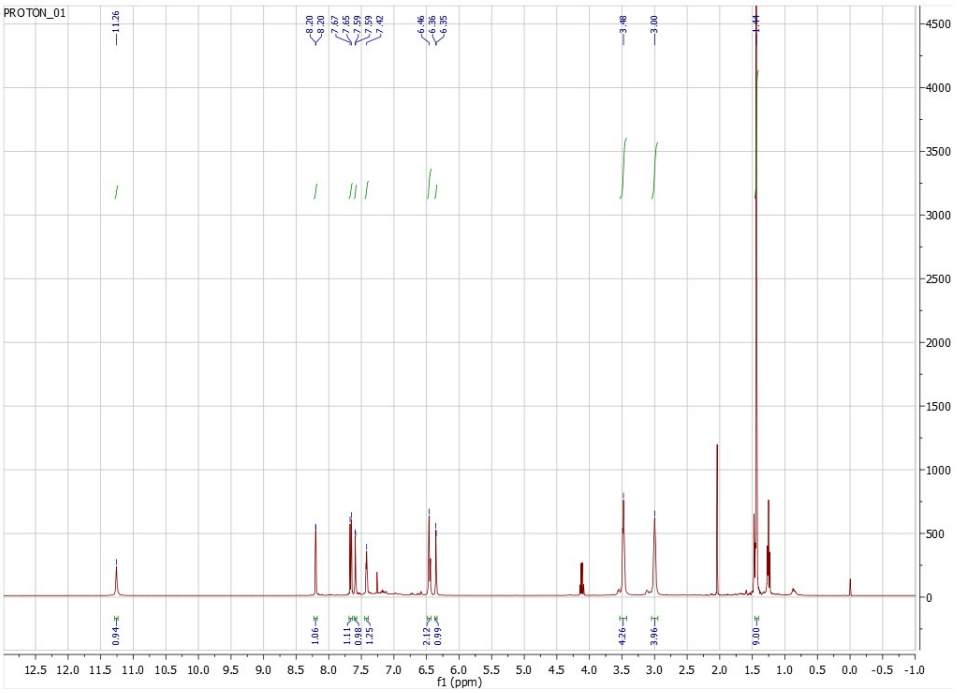


ESI-HMRS:

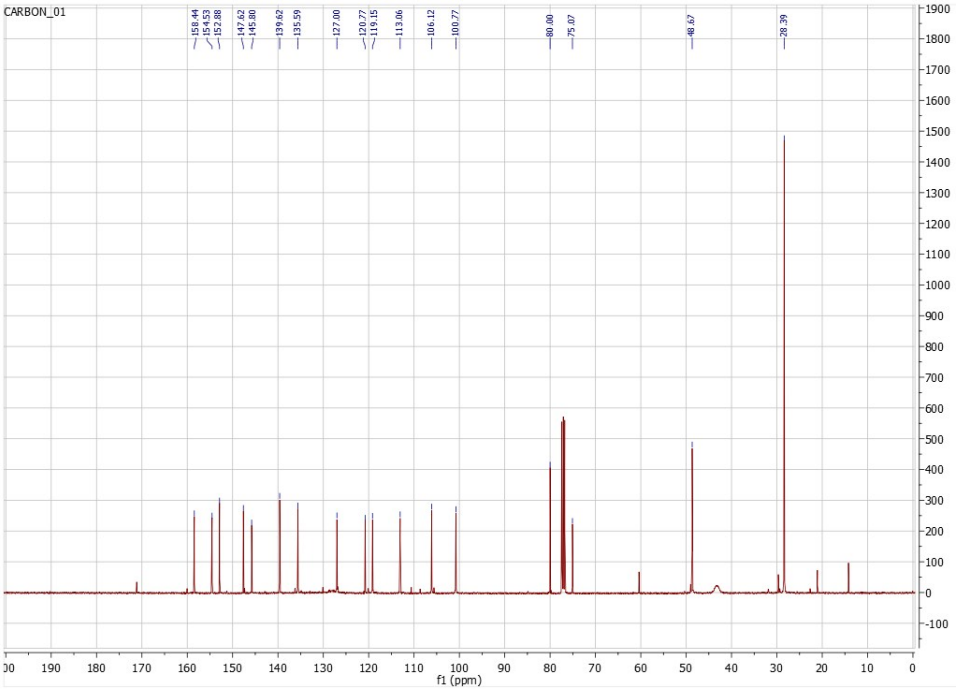


Tert-butyl 4-(3-((1H-pyrrolo[2,3-b]pyridin-5-yl)oxy)-4-iodophenyl)piperazine-1-carboxylate (**26**):

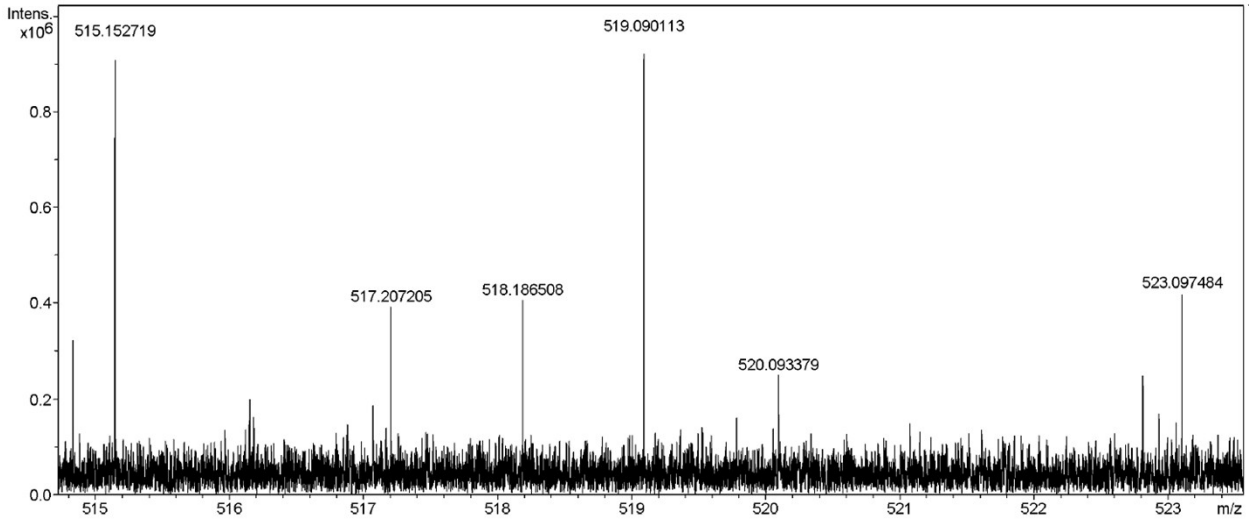
^{1}H NMR



^{13}C NMR

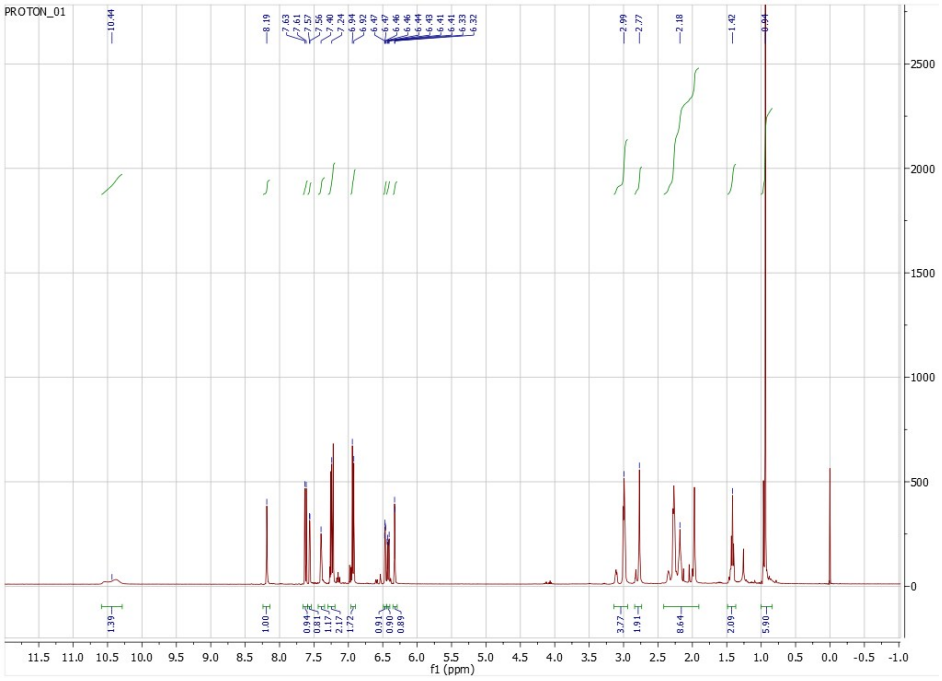


ESI-HMRS:

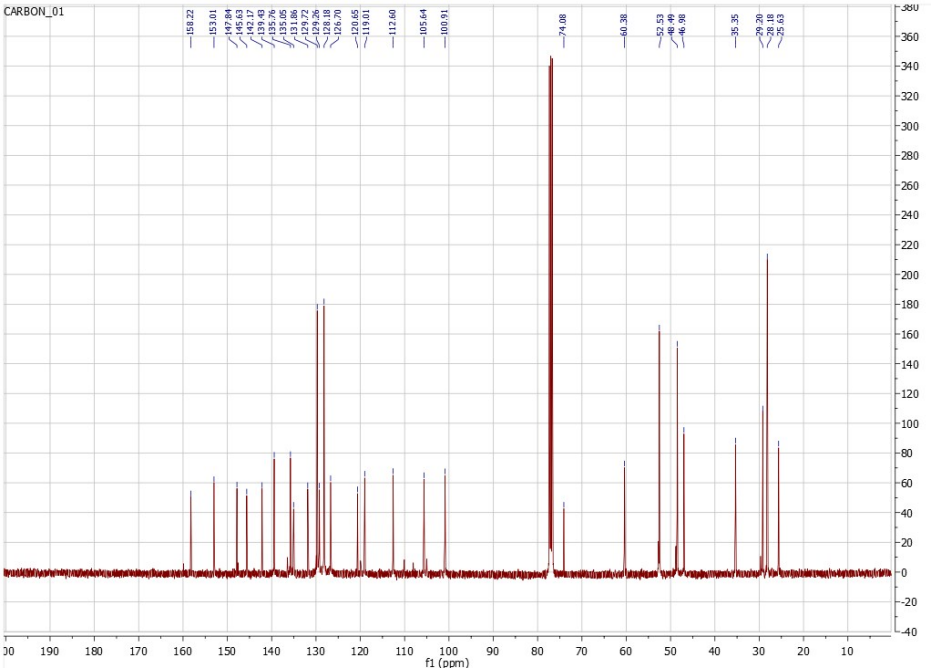

Intens.
x10^6
0.8
0.6
0.4
0.2
0.0
515.152719
517.207205
518.186508
519.090113
520.093379
523.097484
515
516
517
518
519
520
521
522
523
m/z

5-(5-(4-((4'-chloro-5,5-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)piperazin-1-yl)-2-iodophenoxy)-1H-pyrrolo[2,3-b]pyridine (**27**):

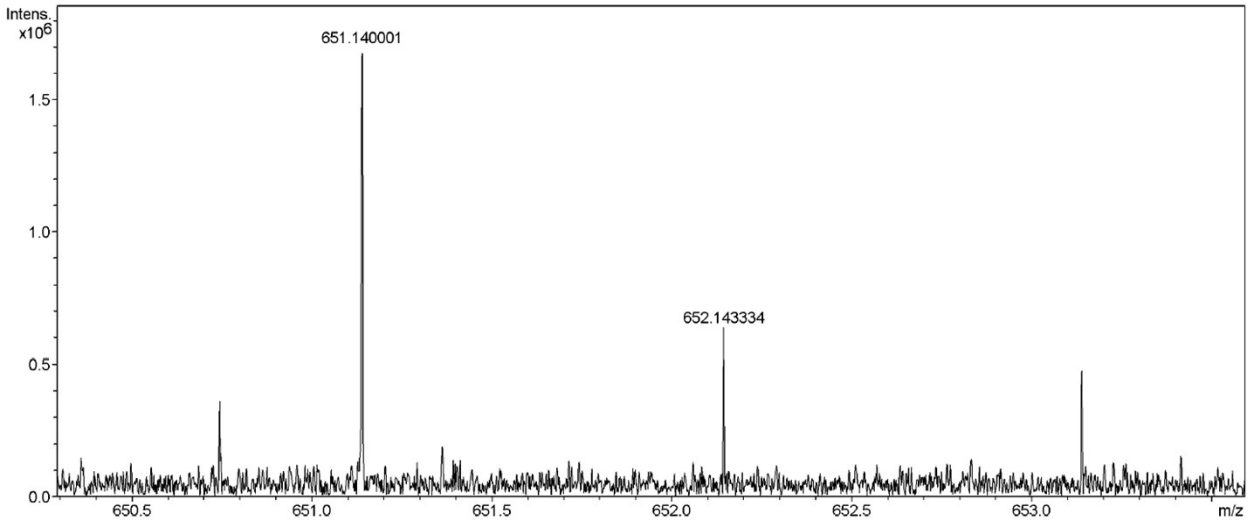
^{1}H NMR



^{13}C NMR



ESI-HRMS:


Intens.
x10^6
1.5
1.0
0.5
0.0
651.140001
652.143334
650.5
651.0
651.5
652.0
652.5
653.0
m/z