# SUPPLEMENTARY INFORMATION

# New *N*-phenylpyrrolamide inhibitors of DNA gyrase with improved antibacterial activity

Andrej Emanuel Cotman, [a] Federica Fulgheri, [a,'] Martina Piga, [a] Peter Peršolja, [a] Davide Benedetto Tiz, [a] Žiga Skok, [a] Martina Durcik, [a] Maša Sterle, [a] Jaka Dernovšek, [a] Cristina D. Cruz, [b] Päivi Tammela, [b] Petra Éva Szili, [c] Lejla Daruka, [c] Csaba Pál, [c] Anamarija Zega, [a] Lucija Peterlin Mašič, [a] Janez Ilaš, [a] Tihomir Tomašič, [a] Danijel Kikelj, [a] Nace Zidar [*a]

[a] *University of Ljubljana, Faculty of Pharmacy, Aškerčeva cesta 7, 1000 Ljubljana, Slovenia*

[b] *Drug Research Program, Division of Pharmaceutical Biosciences, Faculty of Pharmacy, University of Helsinki, P.O. Box 56, Viikinkaari 5E, Helsinki 00014, Finland*

[c] *Synthetic and Systems Biology Unit, Institute of Biochemistry, Biological Research Centre of the Hungarian Academy of Sciences, Szeged, H-6726, Hungary*

*' Current address: Department of Life and Environmental Sciences, University of Cagliari, University Campus, S.P., Monserrato, 09042 Cagliari, Italy*

* Corresponding author.

*E-mail address*: nace.zidar@ffa.uni-lj.si

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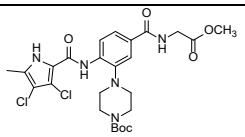
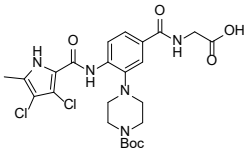
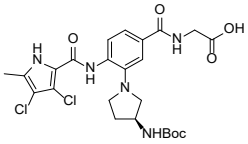
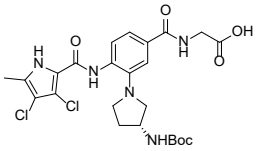
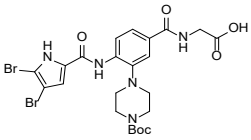
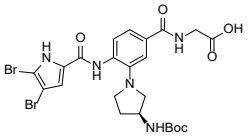
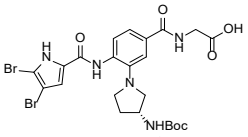
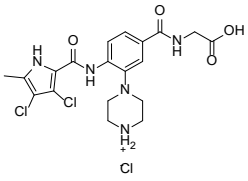
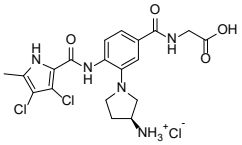
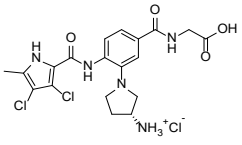
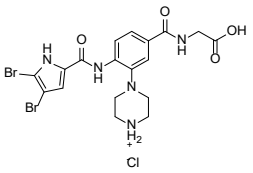
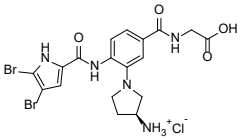
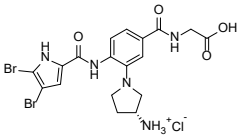
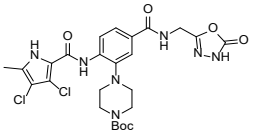
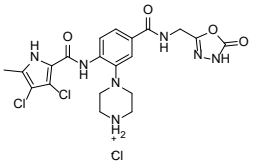
## 1. Minimum inhibitory concentrations of compounds 6-14

**Table 1S.** Minimum inhibitory concentrations (MICs) of compounds **6-14** against selected gram-positive and gram-negative bacteria.

| Comp. | Structure | MIC (μg/mL)[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | ***P. aeruginosa ATCC 27853*** | ***A. baumannii (ATCC 19606)*** | ***K. pneumoniae (ATCC 700603)*** | ***E. coli ATCC 25922*** | ***S. aureus ATCC 29213*** | ***E. faecium* (ATCC3 5667)** | ***K. aerogenes (ATCC 13408)*** |
| **6a** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **8a** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **8b** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **8c** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **9a** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **9b** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **9c** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **10a** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **10b** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **10c** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **11a** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **11b** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **11c** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |
| **13** |  | >32 | >32 | >32 | >32 | **1** | **32** | >32 |
| **14** |  | >32 | >32 | >32 | >32 | >32 | >32 | >32 |

[a] Minimum inhibitory concentration.

## 2. Inhibitory activities of 23b against DNA gyrase from *A. baumannii* and *P. aeruginosa*

**Table 2S.** Inhibitory activities of compound **23b** against DNA gyrase from *A. baumannii* and *P. aeruginosa*

| **Compound** | **$IC_{50}$[a]** | |
|---|---|---|
| | ***A. baumannii* gyrase** | ***P. aeruginosa* gyrase** |
| **23b** | 15.3 nM | 3.63 nM |
| **novobiocin** | 16.0 nM | 22.8 nM |

[a] Concentration of compound that inhibits the enzyme activity by 50%.

## 3. Heatmap showing the antibacterial activities (MICs) of the tested compounds

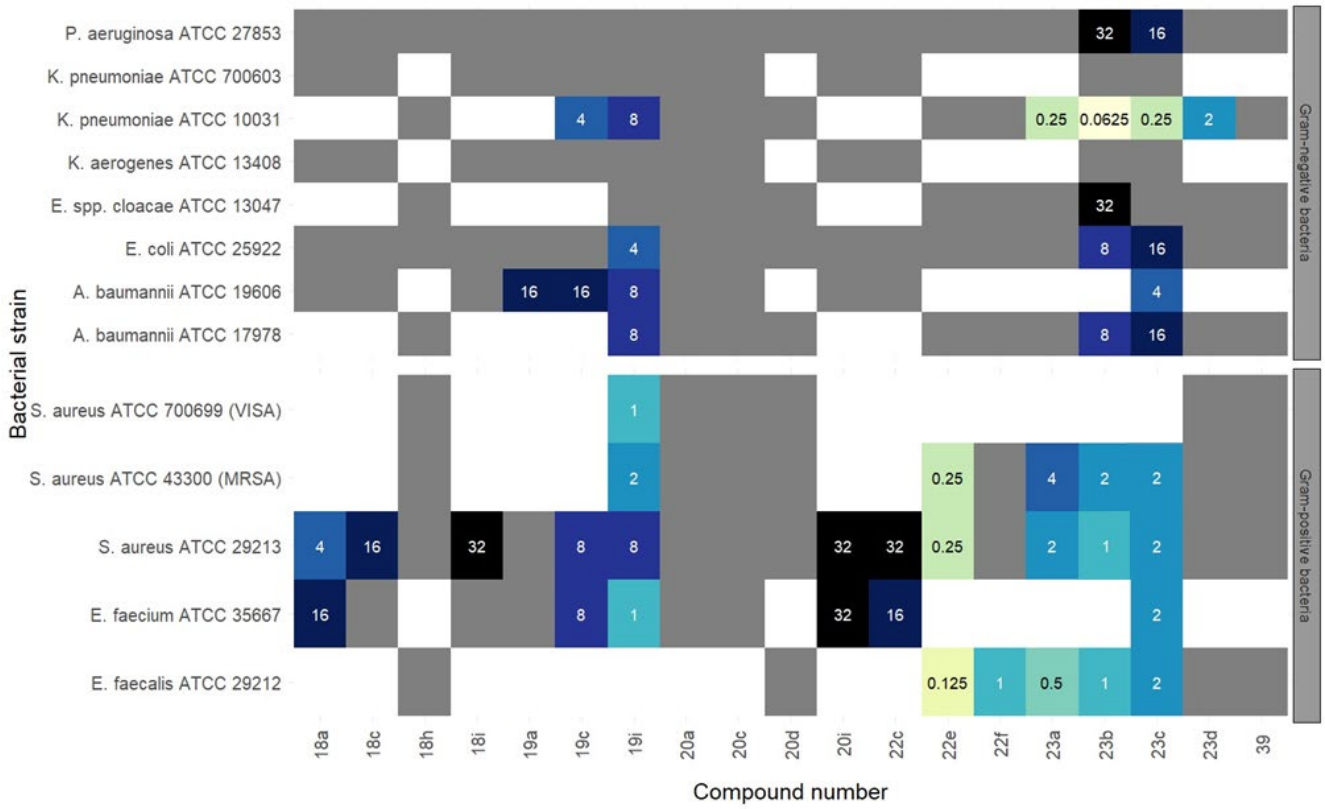



**Figure 1S. Minimum inhibitory concentrations (MICs) of compounds 20i-39 against selected gram-positive and gram-negative bacteria.** The heatmap shows the minimum inhibitory concentration values in µg/mL measured by the broth microdilution method according to the Clinical and Laboratory Standards Institute guidelines. White tiles indicate missing experimental data, while grey tiles represent data points where the MIC values were outside the range of the experiments (>32 µg/mL or >64 µg/mL).

## 4. Spontaneous frequency of resistance table

**Table 3S.** Spontaneous frequency of resistance of **23a**, **23c** and novobiocin in *S. aureus* ATCC 29213 and *K. pneumoniae* ATCC 10031.

| Species | Repli-cate | 23a | | | 23c | | | Novobiocin | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 2×MIC | 4×MIC | 8×MIC | 2×MIC | 4×MIC | 8×MIC | 2×MIC | 4×MIC | 8×MIC |
| *S. aureus* ATCC 29213 | 1 | 3.61E-07 | 3.28E-07 | 2.21E-07 | 9.48E-08 | 6.19E-08 | 2.19E-09 | 1.00E-06 | 1.00E-06 | 1.00E-06 |
| *S. aureus* ATCC 29213 | 2 | 2.39E-07 | 2.15E-07 | 1.62E-07 | 1.45E-07 | 8.29E-08 | 2.00E-10 | 1.00E-06 | 1.00E-06 | 1.00E-06 |
| *S. aureus* ATCC 29213 | 3 | 3.71E-07 | 3.95E-07 | 3.05E-07 | 1.49E-07 | 1.17E-07 | 1.00E-12 | 1.00E-06 | 1.00E-06 | 1.00E-06 |
| *K. pneumoniae* ATCC 10031 | 1 | 5.70E-10 | 1.27E-10 | 1.90E-10 | 3.31E-11 | 1.00E-12 | 1.00E-12 | 1.00E-06 | 8.48E-08 | 1.36E-07 |
| *K. pneumoniae* ATCC 10031 | 2 | 5.34E-10 | 1.00E-12 | 9.71E-11 | 2.75E-10 | 1.00E-12 | 1.00E-12 | 1.00E-06 | 1.67E-08 | 3.85E-09 |
| *K. pneumoniae* ATCC 10031 | 3 | 3.55E-09 | 1.00E-12 | 5.81E-11 | 1.09E-10 | 1.00E-12 | 1.00E-12 | 1.00E-06 | 7.65E-08 | 7.87E-08 |

Values of 1.00E-06 indicate that the plates contained an uncountable amount of colonies (i.e. the frequency of resistance is above the detection limit), while 1.00E-12 indicate that no colonies were observed under the experimental conditions (the frequency of resistance is below the detection limit).

## 5. Minimum inhibitory concentrations of 23a and 23c adapted lines

**Table 4S.** Minimum inhibitory concentrations of **23a** and **23c** adapted lines.

| Species | Comp. | Replicate | MIC (μg/mL)[a] |
|---|---|---|---|
| *S. aureus* ATCC 29213 | **23a** | 1 | >64 |
| | | 2 | >64 |
| | | 3 | >64 |
| | **23c** | 1 | 8 |
| | | 2 | 8 |
| | | 3 | 8 |
| *K. pneumoniae* ATCC 10031 | **23a** | 1 | 16 |
| | | 2 | 16 |
| | | 3 | 16 |
| | **23c** | 1 | 16 |
| | | 2 | 16 |
| | | 3 | 16 |

[a] Minimum inhibitory concentration. Up to 10 independent colonies were collected from the frequency of resistance plates at the highest concentration at which the bacteria could still grow. The collected colonies were pooled and their MIC was measured as described in the experimental section.

## 6. Synthetic procedures and analytical data

**General procedure A. Synthesis of *tert*-butyl 4-(5-(methoxycarbonyl)-2-nitrophenyl)piperazine-1-carboxylate (2a).** To a suspension of methyl 3-fluoro-4-nitrobenzoate (**1**, 5.00 g, 25.0 mmol) and potassium carbonate (4.16 g, 30.0 mmol) in DMF (100 mL), piperazine N1-Boc protected (4.68 g, 25.0 mmol) was added. The mixture was heated at 70 °C for 15 h. The solvent was evaporated under reduced pressure. EtOAc (150 mL) and $H_2O$ (75 mL) were added and the compound was extracted to the organic layer. The organic phase was washed with water (50 mL) and brine (2 × 50 mL), dried over $Na_2SO_4$, filtered and the solvent removed under reduced pressure to obtain **2a** as yellow solid. Yield 7.56 g (83%); yellow solid; mp 88 – 90 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.96 (d, 1H, $J$ = 8.4 Hz, ArH), 7.80 (d, 1H, $J$ = 1.6 Hz, ArH), 7.68 (dd, 1H, $J$ = 8.4, 1.7 Hz, ArH), 3.90 (s, 3H, $CH_3$), 3.40 – 3.50 (m, 4H, 2 × $CH_2$), 2.98 – 3.08 (m, 4H, 2 × $CH_2$), 1.43 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 164.8, 153.8, 145.4, 144.9, 133.8, 125.9, 122.6, 122.3, 79.1, 52.8, 50.8, 42.8, 28.0 ppm.

**Methyl (*S*)-3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-nitrobenzoate (2b).** Synthesised according to *General procedure A* from **1** (1.00 g, 5.03 mmol), (3*S*)-Boc-3-aminopyrrolidine (0.938 g, 5.03 mmol) and $K_2CO_3$ (0.835 g, 6.04 mmol). Yield 84% (1.62 g); pale orange solid; mp 120 – 124 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.84 (d, 1H, $J$ = 8.4 Hz, ArH), 7.51 (d, 1H, $J$ = 1.7 Hz, ArH), 7.28 (dd, 1H, $J$ = 8.4, 1.7 Hz, ArH), 7.24 (d, 1H, $J$ = 6.4 Hz, NH), 4.07 – 4.14 (m, 1H, CH), 3.89 (s, 3H, $CH_3$), 3.39 – 3.45 (m, 1H, CH), 3.27 – 3.33 (m, 2H, 2 × CH), 2.87 – 2.92 (m, 1H, CH), 2.07 – 2.16 (m, 1H, CH), 1.88 – 1.95 (m, 1H, CH), 1.38 (s, 9H) ppm. IR (ATR): ν 3120, 3066, 2964, 2361, 1727, 1598,

1520, 1486, 1421, 1357, 1281, 1225, 1155, 1111, 1079, 986, 905, 839, 798, 772, 737, 685, 592, 563 $cm^{-1}$. $[\alpha]_D^{25}$ 0,54 (*c* 0,287 DMF). MS (ESI) *m/z* = 388.2 ($[M+Na]^+$).

**Methyl (*R*)-3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-nitrobenzoate (2c).** Synthesised according to *General procedure A* from **1** (1.07 g, 5.4 mmol), (3*R*)-3-aminopyrrolidine 3-Boc protected (1.00 g, 5.4 mmol) and $K_2CO_3$ (0.890 g, 6.4 mmol). The crude product was purified with flash column chromatography using ethyl acetate/petroleum ether (1:3) as mobile phase, to obtain **2c** (1.64 g) as yellow solid. Yield 84% (1.64 g); yellow solid; mp 113 – 118 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.77 (d, 1H, *J* = 8.5 Hz Ar-H-5), 7.61 (d, *J* = 1.6 Hz, 1H, Ar-H-2), 7.40 (dd, 1H, *J* = 8.5, 1.6 Hz, Ar-H-6), 4.63 – 4.77 (m, 1H, CH/NH), 4.32 – 4.43 (m, 1H, CH/NH), 3.96 (s, 3H, $CH_3$), 3.47 – 3.53 (m, 2H, 2 × CH), 3.27 – 3.36 (m, 1H, CH), 3.11 – 3.15 (m, 1H, CH), 2.24 – 2.32 (m, 1H, CH), 1.97 – 2.07 (m, 1H, CH), 1.47 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.3, 155.2, 141.6, 138.4, 133.3, 126.7, 117.1, 115.4, 77.9, 55.3, 52.7, 49.9, 48.0, 30.2, 28.2 ppm. IR (ATR): ν 3361, 2985, 2958, 1721, 1682, 1609, 1523, 1441, 1364, 1272, 1252, 1116, 1016, 866, 825, 798, 739, 642 $cm^{-1}$. $[\alpha]_D^{25}$ -4.2 (*c* 0.208, MeOH). MS (ESI) *m/z* = 388.04 ($[M+Na]^+$).

**3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-nitrobenzoic acid (3a).** To the solution of **2a** (200 mg, 0.55 mmol) in methanol (10 mL) 1 M NaOH (0.81 mL, 0.82 mmol) was added and the reaction mixture was stirred for 15 h at rt. 1 M HCl was added dropwise until pH 7 and solvent was removed under reduce pressure. To the crude residue were added 1 M HCl until pH 4, water (20 mL) and ethyl acetate (25 mL). The phases were separated and organic phase was washed with water (20 mL) and brine (20 mL), dried over $Na_2SO_4$, filtered and evaporated, to obtain 171 mg of product as orange crystals. Yield 171 mg (89%); orange crystals; mp 170 – 175 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.73 – 7.75 (m, 2H, ArH-2, ArH-5), 7.58 (dd, 1H, *J* = 6.2, 1.4 Hz, ArH-6), 3.41 – 3.47 (m, 4H, 2 × $CH_2$), 2.93 – 2.95 (m, 4H, 2 × $CH_2$), 1.42 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.6, 153.8, 153.6, 144.7, 144.4, 125.2, 123.0, 122.1, 79.1, 51.1, 42.8, 28.0 ppm. IR (ATR): ν 2976, 2931, 1686, 1570, 1419, 1365, 1231, 1160, 1126, 966, 749 $cm^{-1}$. MS (ESI) *m/z* = 350.13 ($[M-H]^-$).

**(*S*)-3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-nitrobenzoic acid (3b).** To the solution of **2b** (6.90 g, 18.9 mmol) in a mixture of methanol (200 mL) and tetrahydrofuran (40 mL) 1 M NaOH (28.4 mL, 28 mmol) was added and the reaction mixture was stirred for 15 h at rt. 1 M HCl was added dropwise until pH 7 and solvent was removed under reduce pressure. To the crude residue were added 1 M HCl until pH 4, water (100 mL) and ethyl acetate (100 mL). The phases were separated and organic phase was washed with water (50 mL) and brine (50 mL), dried over $Na_2SO_4$, filtered and evaporated, to obtain **3b** (6.61 g) as orange crystals. Yield 6.61 g (99%); orange crystals; mp 153 – 163 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.47 (br s, 1H, COOH), 7.81 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.52 (d, 1H, *J* = 1.6 Hz, ArH-2), 7.23 – 7.28 (m, 2H, ArH-6, NH), 4.08 – 4.12 (m, 1H, CH), 3.27 – 3.44 (m, 3H, 3 × CH, overlapping with the signal for water), 2.86 – 2.90 (m, 1H, CH), 2.07 – 2.15 (m, 1H, CH), 1.87 – 1.95

(m, 1H, CH), 1.38 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.3, 155.2, 141.6, 138.3, 134.6, 126.5, 117.3, 115.7, 77.9, 55.3, 49.9, 47.9, 30.2, 28.1 ppm. IR (ATR): ν 3340, 2976, 1724, 1682, 1611, 1541, 1504, 1254, 1160, 736 cm$^{-1}$. $[\alpha]_D^{25}$ +12.8 (*c* 0.133, MeOH). MS (ESI) *m/z* = 374.03 ($[M+Na]^+$).

**(*R*)-3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-nitrobenzoic acid (3c).** To the solution of **2c** (1.49 g, 4.0 mmol) in a mixture of methanol (50 mL) and tetrahydrofuran (10 mL) 1 M NaOH (8.00 mL, 8.0 mmol) was added and the reaction mixture was stirred for 15 h at rt. 1 M HCl was added dropwise until pH 7 and solvent was removed under reduce pressure. To the crude residue were added 1 M HCl until pH 4, water (100 mL) and ethyl acetate (100 mL). The phases were separated and organic phase was washed with water (100 mL) and brine (100 mL), dried over $Na_2SO_4$, filtered and evaporated, to obtain **3c** (1.35 g) as orange crystals. Yield 1.35 g (94%); orange crystals; mp 158 – 162 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.47 (br s, 1H, COOH), 7.81 (d, 1H, *J* = 8.5 Hz, Ar-H-5), 7.52 (d, 1H, *J* = 1.6 Hz, Ar-H-2), 7.23 – 7.28 (m, 2H, Ar-H-6, NH), 4.08 – 4.12 (m, 1H, CH), 3.27 – 3.44 (m, 3H, 3 × CH, overlapping with the signal for water), 2.86 – 2.90 (m, 1H, CH), 2.07 – 2.15 (m, 1H, CH), 1.87 – 1.95 (m, 1H, CH), 1.38 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.3, 155.2, 141.6, 138.3, 134.6, 126.5, 117.3, 115.7, 77.9, 55.3, 49.9, 47.9, 30.2, 28.2 ppm. IR (ATR): ν 3331, 2976, 2935, 1687, 1610, 1572, 1504, 1443, 1336, 1263, 1161, 872, 829, 772, 739 cm$^{-1}$. $[\alpha]_D^{25}$ -11.7 (*c* 0.180, MeOH). MS (ESI) *m/z* = 374.01 ($[M+Na]^+$).

***tert*-Butyl 4-(5-((2-methoxy-2-oxoethyl)carbamoyl)-2-nitrophenyl)piperazine-1-carboxylate (4a).** To the solution of **3a** (0.900 g, 2.4 mmol) and TBTU (1.01 g, 3.1 mmol) in DMF (20 mL) NMM (0.53 mL, 4.8 mmol) was added and the solution was stirred for 30 min at rt. Glycine methyl ester hydrochloride (333 mg, 2.7 mmol) was added and reaction mixture was stirred at rt for 20 h. Solvent was removed under reduced pressure, the residue was dissolved in ethyl acetate (20 mL) and washed with water (2 × 20 mL), saturated solutions of $NaHCO_3$ (2 × 20 mL) and brine (20 mL), then organic phase was dried over $Na_2SO_4$, filtered and evaporated. The crude product was purified with flash column chromatography using ethyl acetate/petroleum ether 1:1 as mobile phase to obtain **4a** as orange oil (0.852 g). Yield 0.852 g (84%); orange oil. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.22 (t, 1H, *J* = 5.8 Hz, NH), 7.94 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.76 (d, 1H, *J* = 1.7 Hz, ArH-2), 7.59 (dd, 1H, *J* = 8.5, 1.7 Hz, ArH-6), 4.05 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.67 (s, 3H, $CH_3$), 3.43 – 3.48 (m, 4H, 2 × $CH_2$, overlapped with the signal of water), 3.00 – 3.03 (m, 4H, 2 × $CH_2$), 1.42 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.1, 165.0, 153.8, 144.9, 144.4, 137.8, 125.7, 121.1, 120.8, 79.1, 51.8, 51.0, 43.7, 41.3, 28.0 ppm. IR (ATR): ν 3324, 2978, 1750, 1691, 1668, 1521, 1418, 1365, 1229, 1209, 1661, 1000, 834, 744 cm$^{-1}$. MS (ESI) *m/z* = 445.01 ($[M+Na]^+$).

**Methyl (*S*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-nitrobenzoyl)glycinat*e* (4b).** To the solution of **3b** (3.00 g, 8.5 mmol) and TBTU (3.57 g, 11.1 mmol) in DMF (100 mL) NMM (2.82

mL, 25.6 mmol) was added and the solution was stirred for 30 min at rt. Glycine methyl ester hydrochloride (1.18 g, 9.4 mmol) was added and reaction mixture was stirred at rt for 20 h. Solvent was removed under reduced pressure, the residue was dissolved in ethyl acetate (50 mL) and washed with water (2 × 20 mL), saturated solutions of $NaHCO_3$ (2 × 20 mL) and brine (20 mL), then organic phase was dried over $Na_2SO_4$, filtered and evaporated. The crude product was recrystallized from ethyl acetate. The solvent of the mother liquor was evaporated and the residue was recrystallized from ethanol. The pure products were combined to obtain **4b** as yellow solid (2.98 g). Yield 2.98 g (84%); yellow solid, mp 133 – 138 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.17 (t, 1H, *J* = 5.8 Hz, NH), 7.82 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.45 (d, 1H, *J* = 1.6 Hz, ArH-2), 7.26 (d, 1H, *J* = 6.0 Hz, NH), 7.20 (dd, 1H, *J* = 8.5, 1.6 Hz, ArH-6), 4.08 – 4.13 (m, 1H, CH), 4.04 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.67 (s, 3H, $CH_3$), 3.24 – 3.36 (m, 3H, 3 × CH, overlapping with the signal for water), 2.90 – 2.94 (m, 1H, CH), 2.06 – 2.15 (m, 1H, CH), 1.89 – 1.96 (m, 1H, CH), 1.38 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.2, 165.5, 155.2, 141.8, 137.5, 137.3, 126.5, 115.4, 114.1, 77.9, 55.5, 51.8, 49.9, 48.1, 41.3, 30.2, 28.2 ppm. IR (ATR): ν 3343, 2983, 1748, 1675, 1648, 1572, 1529, 1509, 1492, 1310, 1165, 869, 831, 741 cm$^{-1}$. $[\alpha]_D^{25}$ +5.3 (*c* 0.133, MeOH). MS (ESI) *m/z* = 445.00 ($[M+Na]^+$).

**Methyl (*R*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-nitrobenzoyl)glycinat*e* (4c).**To the solution of **3c** (1.26 g, 3.6 mmol) and TBTU (1.50 g, 4.7 mmol) in DMF (30 mL) NMM (1.19 mL, 10.8 mmol) was added and the solution was stirred for 30 min at rt. Glycine methyl ester hydrochloride (496 mg, 4.0 mmol) was added and reaction mixture was stirred at rt for 20 h. Solvent was removed under reduced pressure, the residue was dissolved in ethyl acetate (50 mL) and washed with water (2 × 20 mL), saturated solutions of $NaHCO_3$ (2 × 20 mL) and brine (20 mL), then organic phase was dried over $Na_2SO_4$, filtered and evaporated. The crude product was purified with flash column chromatography using ethyl acetate/petroleum ether (1:1) as mobile phase to obtain **4c** as yellow solid (1.22 g). Yield 1.22 g (80%); yellow solid, mp 130 – 134 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.17 (t, 1H, *J* = 5.8 Hz, NH), 7.82 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.45 (d, 1H, *J* = 1.6 Hz, ArH-2), 7.26 (d, 1H, *J* = 6.0 Hz, NH), 7.20 (dd, 1H, *J* = 8.5, 1.6 Hz, ArH-6), 4.08 – 4.13 (m, 1H, CH), 4.04 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.67 (s, 3H, $CH_3$), 3.24 – 3.36 (m, 3H, 3 × CH, overlapping with the signal for water), 2.90 – 2.94 (m, 1H, CH), 2.06 – 2.15 (m, 1H, CH), 1.89 – 1.96 (m, 1H, CH), 1.38 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.2, 165.5, 155.2, 141.8, 137.5, 137.3, 126.5, 115.4, 114.1, 77.9, 55.5, 51.8, 49.9, 48.1, 41.3, 30.2, 28.2 ppm. IR (ATR): ν 3344, 2982, 2972, 1748, 1676, 1648, 1529, 1509, 1492, 1209, 1166, 831, 742 cm$^{-1}$. $[\alpha]_D^{25}$ -6.4 (*c* 0.220, MeOH). MS (ESI) *m/z* = 444.99 ($[M+Na]^+$).

***tert*-Butyl 4-(2-amino-5-((2-methoxy-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (5a).** The solution of **4a** (2.51 g, 5.9 mmol) in methanol (90 mL) was stirred for 15 min under an argon atmosphere. Pd/C (0.500 g) was added, the solution was saturated with hydrogen and the reaction mixture was stirred for 4 h under hydrogen atmosphere. The catalyst was filtered off and the solvent was

evaporated. The crude product was purified with flash column chromatography using ethyl acetate/petroleum ether 2:1 as mobile phase, to obtain 2.08 g of **5a** as white crystals. Yield 2.08 g (90%); white crystals; mp 80 – 84 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 8.59 (t, 1H, *J* = 5.8 Hz, NH), 7.53 (d, 1H, *J* = 1.9 Hz, ArH-6), 7.48 (dd, 1H, *J* = 8.4, 1.9 Hz, ArH-4), 6.74 (d, 1H, *J* = 8.4 Hz, ArH-3), 4.58 – 6.07 (br s, 2H, $NH_2$), 3.99 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.69 (s, 3H, $CH_3$), 3.51 – 3.63 (m, 4H, 2 × $CH_2$, overlapped with the signal of water), 2.75 – 2.85 (m, 4H, 2 × $CH_2$), 1.49 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.8, 166.5, 153.9, 145.8, 136.7, 124.5, 121.0, 119.1, 113.1, 78.8, 51.6, 50.6, 43.2, 41.1, 28.1 ppm. IR (ATR): ν 3479, 3367, 3308, 2935, 1743, 1693, 1610, 1504, 1415, 1365, 1248, 1205, 1163, 1119, 768 cm$^{-1}$. MS (ESI) *m/z* = 415.07 ([M+Na]$^{+}$).

**Methyl (*S*)-(4-amino-3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)benzoyl)glycinate (5b).** The solution of **4b** (2.41 g, 5.7 mmol) in methanol (90 mL) was stirred for 15 min under an argon atmosphere. Pd/C (483 mg) was added, the solution was saturated with hydrogen and the reaction mixture was stirred for 5 h under hydrogen atmosphere. The catalyst was filtered off and the solvent was evaporated. The crude product was purified with flash column chromatography using ethyl acetate/petroleum ether (2:1) as mobile phase, to obtain **5b** (2.23 g) as grey crystals. Yield 2.23 g (99%); grey crystals; mp 78 – 81 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 8.52 (t, 1H, *J* = 5.8 Hz, NH), 7.39 (d, 1H, *J* = 1.9 Hz, ArH-2), 7.36 (dd, 1H, *J* = 8.3, 1.9 Hz, ArH-6), 7.22 (d, 1H, *J* = 7.9 Hz, NH), 6.64 (d, 1H, *J* = 8.3 Hz, ArH-5), 4.91 – 5.80 (br s, 2H, $NH_2$), 4.06 – 4.15 (m, 1H, CH), 3.93 (d, 1H, *J* = 5.8 Hz, $CH_2$), 3.63 (s, 3H, $CH_3$), 3.06 – 3.17 (m, 2H, 2 × CH), 2.77 – 2.85 (m, 2H, 2 × CH), 2.17 – 2.25 (m, 1H, CH), 1.65 – 1.73 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.8, 166.6, 155.1, 145.7, 134.7, 123.3, 120.9, 117.5, 113.1, 77.6, 56.5, 51.6, 49.2, 48.7, 41.1, 31.3, 28.3 ppm. IR (ATR): ν 3333, 2979, 1751, 1707, 1685, 1621, 1525, 1500, 1367, 1313, 1160, 1066, 973, 1119, 766 cm$^{-1}$. $[\alpha]_D^{25}$ -18.3 (*c* 0.131, MeOH). MS (ESI) *m/z* = 415.05 ([M+Na]$^{+}$).

**Methyl (*R*)-(4-amino-3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)benzoyl)glycinate (5c).** The solution of **4c** (1.20 g, 2.8 mmol) in methanol (40 mL) was stirred for 15 min under an argon atmosphere. Pd/C (239 mg) was added, the solution was saturated with hydrogen and the reaction mixture was stirred for 4 h under hydrogen atmosphere. The catalyst was filtered off and the solvent was evaporated. The crude product was purified with flash column chromatography using ethyl acetate/petroleum ether (3:1) as mobile phase, to obtain **5c** (1.10 g) as pink crystals. Yield 1.10 g (99%); pink crystals; mp 77 – 80 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 8.52 (t, 1H, *J* = 5.8 Hz, NH), 7.39 (d, 1H, *J* = 1.9 Hz, ArH), 7.36 (dd, 1H, *J* = 8.3, 1.9 Hz, ArH-4), 7.22 (d, 1H, *J* = 7.9 Hz, NH), 6.64 (d, 1H, *J* = 8.3 Hz, ArH-3), 5.44 (br s, 2H, $NH_2$), 4.06 – 4.15 (m, 1H, CH), 3.93 (d, 1H, *J* = 5.8 Hz, $CH_2$), 3.63 (s, 3H, $CH_3$), 3.06 – 3.17 (m, 2H, 2 × CH), 2.77 – 2.85 (m, 2H, 2 × CH), 2.17 – 2.25 (m, 1H, CH), 1.65 – 1.73 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.8, 166.6, 155.1, 145.7, 134.7, 123.3, 120.9, 117.5, 113.1, 77.6, 56.5, 51.6, 49.2, 48.7, 41.1, 31.3, 28.3 ppm. IR (ATR): ν

3332, 2975, 1743, 1687, 1613, 1502, 1365, 1206, 1163, 1074, 974, 767 $cm^{-1}$. $[\alpha]_D^{25}$ +18.7 (*c* 0.167, MeOH). MS (ESI) *m/z* = 415.06 ($[M+Na]^+$).

**General procedure B. 4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-((2-methoxy-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (6a).** To a solution of 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.178 g, 0.92 mmol) in anhydrous dichloromethane (10 mL), oxalyl chloride (0.31 mL, 3.7 mmol) was added dropwise and the solution was stirred at rt for 15 h under argon atmosphere. The solvent was evaporated under reduced pressure. Fresh anhydrous dichloromethane (5 mL), **5a** (0.300 g, 0.76 mmol) and pyridine (2 mL) were added and the reaction mixture was stirred under argon atmosphere at rt for 15 h. Solvent was removed under reduced pressure, the residue was dissolved in ethyl acetate (15 mL) and washed with $H_2O$ (10 mL), HCl 1 M solution (15 mL) and brine (2 × 15 mL). During the extraction the product precipitated and was filtered off. The crude product was triturated with water and the undissolved solid was filtered off. The product was then triturated with diethyl ether and the undissolved solid was filtered off to give **6a** as grey solid. Yield 246 mg (57%); grey solid; mp 194 – 197 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.43 (s, 1H, NH), 9.79 (s, 1H, NH), 8.93 (t, 1H, *J* = 5.7 Hz, NH), 8.48 (d, 1H, *J* = 8.4 Hz, ArH-3), 7.91 (d, 1H, *J* = 1.9 Hz, ArH-6), 7.75 (dd, 1H, *J* = 8.6, 1.9 Hz, ArH-4), 4.02 (d, 2H, *J* = 5.7 Hz, $CH_2$), 3.67 (s, 3H, $CH_3$), 3.50 – 3.57 (m, 4H, 2 × $CH_2$), 2.82 – 2.85 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.44 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.5, 165.6, 156.5, 153.7, 141.0, 136.7, 129.8, 128.4, 125.3, 121.0, 118.8, 118.6, 109.7, 108.6, 79.1, 52.1, 51.7, 41.2, 28.0, 10.8 ppm. One peak not seen. IR (ATR): ν 3299, 2978, 1757, 1672, 1647, 1621, 1510, 1410, 1367, 1250, 1201, 1170, 1122, 947, 761 $cm^{-1}$. MS (ESI) *m/z* = 566 ($[M-H]^-$). HRMS for $C_{25}H_{30}Cl_2N_5O_6$: calculated 566.1573, found 566.1572. HPLC: Agilent Eclipse Plus C18 column (5 µm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 µL; $t_R$: 14.083 min (96.1% at 280 nm).

**Methyl (*S*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (6b).** Synthesised according to *General procedure B* from **5b** (300 mg, 0.76 mmol), 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (178 mg, 0.92 mmol) and oxalyl chloride (0.31 mL, 3.7 mmol). The crude product was triturated with diethyl ether and the undissolved solid was filtered off to give **6b** as beige solid (245 mg). Yield 245 mg (57%); beige solid; mp 206 – 209 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.38 (s, 1H, NH), 9.49 (s, 1H, NH), 8.94 (t, 1H, *J* = 5.6 Hz, NH), 8.27 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.76 (d, 1H, *J* = 1.8 Hz, ArH-2), 7.63 (dd, 1H, *J* = 8.5, 1.8 Hz, ArH-6), 7.19 (d, 1H, *J* = 6.4 Hz, NH), 4.05 – 4.13 (m, 1H, CH), 4.01 (d, 2H, *J* = 5.6 Hz, $CH_2$), 3.29 – 3.33 (m, 1H, CH, overlapping with the signal for water), 3.14 – 3.20 (m, 1H, CH), 3.00 – 3.06 (m, 1H, CH), 2.89 – 2.94 (m, 1H, CH), 2.15 – 2.24 (m, 4H, CH, $CH_3$), 1.81 – 1.89 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.5, 166.0, 156.6, 155.2, 139.8, 135.4, 129.5, 129.0,

123.1, 119.8, 119.2, 118.8, 110.1, 108.6, 77.8, 57.5, 51.7, 50.8, 49.8, 41.2, 31.3, 28.2, 10.8 ppm. IR (ATR): ν 3369, 3347, 2985, 2849, 1719, 1671, 1635, 1519, 1251, 1174, 968, 761, 1170, 1122, 947, 761 $cm^{-1}$. $[\alpha]_D^{25}$ -15.7 (*c* 0.153, MeOH). MS (ESI) *m/z* = 566.0 ($[M-H]^-$). HRMS for $C_{25}H_{30}Cl_2N_5O_6$: calculated 566.1573, found 566.1573. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 12.870 min (96.5% at 280 nm).

**Methyl (*R*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (6c).** Synthesised according to *General procedure B* from **5c** (450 mg, 1.1 mmol), 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.266 g, 1.4 mmol) and oxalyl chloride (0.47 mL, 5.5 mmol). Yield 470 mg (72%); grey solid; mp 204 – 208 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.38 (s, 1H, NH), 9.49 (s, 1H, NH), 8.94 (t, 1H, *J* = 5.6 Hz, NH), 8.27 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.76 (d, 1H, *J* = 1.8 Hz, ArH-2), 7.63 (dd, 1H, *J* = 8.5, 1.8 Hz, ArH-6), 7.19 (d, 1H, *J* = 6.4 Hz, NH), 4.05 – 4.13 (m, 1H, CH), 4.01 (d, 2H, *J* = 5.6 Hz, $CH_2$), 3.29 – 3.33 (m, 1H, CH, overlapping with the signal for water), 3.14 – 3.20 (m, 1H, CH), 3.00 – 3.06 (m, 1H, CH), 2.89 – 2.94 (m, 1H, CH), 2.15 – 2.24 (m, 4H, CH, $CH_3$), 1.81 – 1.89 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.5, 166.0, 156.6, 155.2, 139.8, 135.4, 129.5, 129.0, 123.1, 119.8, 119.2, 118.8, 110.1, 108.6, 77.8, 57.5, 51.7, 50.8, 49.8, 41.2, 31.3, 28.2, 10.8 ppm. IR (ATR): ν 3371, 3347, 3297, 2984, 1719, 1672, 1635, 1519, 1373, 1221, 1174, 761 $cm^{-1}$. $[\alpha]_D^{25}$ +14.2 (*c* 0.120, MeOH). MS (ESI) *m/z* = 566.0 ($[M-H]^-$). HRMS for $C_{25}H_{30}Cl_2N_5O_6$: calculated 566.1573, found 566.1576. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 12.870 min (95.5% at 280 nm).

***tert*-Butyl 4-(2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)-5-((2-methoxy-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (7a).** Synthesised according to *General procedure B* from **5a** (0.600 g, 1.5 mmol), 4,5-dibromo-1*H*-pyrrole-2 carboxylic acid (493 mg, 1.8 mmol) and oxalyl chloride (0.629 mL, 7.3 mmol). The precipitate that was formed during the extraction was filtered off to obtain crude product 1. The two phases of the mother liquor were separated and organic phase was washed with water (20 mL), saturated solution of $NaHCO_3$ (2 × 20 mL) and brine (2 × 20 mL), dried over $Na_2SO_4$, filtered and the solvent evaporated to obtain crude product 2. The combined crude products were triturated with diethyl ether and the undissolved solid was filtered off and dried to give **7a** (801 mg) as grey solid. Yield 801 mg (83%); grey solid; mp 140 – 143 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.08 (d, 1H, *J* = 2.7 Hz, NH), 9.19 (s, 1H, NH), 8.93 (t, 1H, *J* = 5.7 Hz, NH), 8.10 (d, 1H, *J* = 8.4 Hz, ArH-3), 7.75 (d, 1H, *J* = 1.9 Hz, ArH-6), 7.68 (dd, 1H, *J* = 8.4, 1.9 Hz, ArH-4), 7.17 (d, 1H, *J* = 2.7 Hz, ArH), 4.05 – 4.13 (m, 1H, CH), 4.01 (d, 2H, *J* = 5.7 Hz, $CH_2$), 3.67 (s, 3H, $CH_3$), 3.52 – 3.57 (m, 4H, 2 × $CH_2$), 2.81 – 2.83 (m, 4H, 2 × $CH_2$), 1.43 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz,

DMSO-$d_6$): δ 170.5, 165.9, 156.9, 153.8, 142.7, 135.1, 129.2, 127.5, 123.9, 121.1, 119.8, 113.5, 106.8, 98.7, 79.0, 51.7, 51.4, 41.2, 28.0 ppm. One peak not seen. IR (ATR): ν 3201, 2950, 1755, 1736, 1645, 1549, 1516, 1430, 1250, 1204, 1168, 937, 759, 680 $cm^{-1}$. MS (ESI) *m/z* = 640.0 ([M-H]$^-$). HRMS for $C_{24}H_{28}Br_2N_5O_6$: calculated 640.0406, found 640.0403.

**Methyl (*S*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (7b).** Synthesised according to *General procedure B* from **5b** (0.600 g, 1.5 mmol), 4,5-dibromo-1*H*-pyrrole-2 carboxylic acid (493 mg, 1.8 mmol) and oxalyl chloride (0.629 mL, 7.3 mmol). The precipitate that was formed during the extraction was filtered off to obtain crude product 1. The two phases of the mother liquor were separated and organic phase was washed with water (20 mL), saturated solution of $NaHCO_3$ (2 × 20 mL) and brine (2 × 20 mL), dried over $Na_2SO_4$, filtered and the solvent evaporated to obtain crude product 2. The combined crude products were triturated with diethyl ether and the undissolved solid was filtered off and dried to give **7b** (782 mg) as grey solid. Yield 797 mg (81%); brown solid; mp 213 – 217 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.89 (d, 1H, *J* = 2.7 Hz, NH), 9.53 (s, 1H, NH), 8.91 (t, 1H, *J* = 5.8 Hz, NH), 7.35 – 7.29 (m, 3H, 3 × ArH), 7.17 – 7.14 (m, 2H, NH, ArH), 4.07 – 3.99 (m, 3H, CH, $CH_2$), 3.66 (s, 3H, $CH_3$), 3.43 – 3.31 (m, 2H, 2 × CH), 3.27 – 3.21 (m, 1H, CH), 3.08 – 3.04 (m, 1H, CH), 2.11 – 2.03 (m, 1H, CH), 1.84 – 1.76 (m, 1H, CH), 1.36 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.5, 166.5, 157.6, 155.2, 144.4, 131.5, 128.4, 127.9, 127.8, 117.5, 114.5, 113.5, 105.8, 98.2, 77.8, 55.9, 51.7, 49.8, 48.3, 41.2, 30.5, 28.2 ppm. IR (ATR): ν 3416, 3343, 3229, 2981, 1722, 1677, 1651, 1499, 1468, 1214, 1174, 1093, 760 $cm^{-1}$. $[\alpha]_D^{25}$ -26.5 (*c* 0.147, MeOH). MS (ESI) *m/z* = 640 ([M-H]$^-$). HRMS for $C_{24}H_{28}Br_2N_5O_6$: calculated 640.0406, found 640.0414. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 10.593 min (95.1% at 280 nm).

**Methyl (*R*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (7c).** Synthesised according to *General procedure B* from **5c** (0.500 g, 1.3 mmol), 4,5-dibromo-1*H*-pyrrole-2 carboxylic acid (411 mg, 1.5 mmol) and oxalyl chloride (0.52 mL, 6.1 mmol). The precipitate that was formed during the extraction was filtered off to obtain crude product 1. The two phases of the mother liquor were separated and organic phase was washed with water (20 mL), saturated solution of $NaHCO_3$ (2 × 20 mL) and brine (2 × 20 mL), dried over $Na_2SO_4$, filtered and the solvent evaporated to obtain crude product 2. The combined crude products were triturated with diethyl ether and the undissolved solid was filtered off and dried to give **7c** (778 mg) as grey solid. Yield 778 mg (93%); brown solid; mp 203 – 208 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.89 (d, 1H, *J* = 2.7 Hz, NH), 9.53 (s, 1H, NH), 8.94 (t, 1H, *J* = 5.8 Hz, NH), 7.35 – 7.29 (m, 3H, 3 × ArH), 7.17 – 7.14 (m, 2H, NH, ArH), 4.06 – 3.99 (m, 3H, CH, $CH_2$), 3.66 (s, 3H, $CH_3$), 3.45 – 3.31 (m, 2H, 2 × CH), 3.27 – 3.21 (m, 1H, CH), 3.07 – 3.04 (m, 1H, CH), 2.10 – 2.03 (m, 1H, CH), 1.85 – 1.75 (m, 1H, CH), 1.36 (s,

9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 170.5, 166.5, 157.6, 155.2, 144.5, 131.5, 128.4, 127.9, 127.8, 117.5, 114.5, 113.5, 105.8, 98.2, 77.8, 55.9, 51.7, 49.8, 48.3, 41.2, 30.5, 28.2 ppm. IR (ATR): ν 3415, 3340, 3230, 2979, 2840, 1721, 1677, 1652, 1498, 1214, 1172, 1094, 972, 759 cm$^{-1}$. $[\alpha]_D^{25}$ +25.0 (*c* 0.120, MeOH). MS (ESI) *m/z* = 640.0 ([M-H]$^-$). HRMS for $C_{24}H_{28}Br_2N_5O_6$: calculated 640.0406, found 640.0403. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 10.593 min (95.4% at 280 nm).

**(3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8a).** To the solution of **6a** (0.160 g, 0.28 mmol) in methanol (10 mL) 1 M NaOH (0.84 mL, 0.84 mmol) was added and the mixture was stirred at rt for 15 h. The mixture was neutralized with 1 M HCl and methanol was removed under reduced pressure. The pH was adjusted to 4 with 1 M HCl, ethyl acetate was added and the precipitate that formed was filtered off and dried to obtain **8a** as grey solid. Yield 138 mg (89%); grey solid; mp > 300 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.63 (br s, 1H, COOH), 12.43 (s, 1H, NH), 9.79 (s, 1H, NH), 8.81 (t, 1H, *J* = 5.7 Hz, NH), 8.48 (d, 1H, *J* = 8.6 Hz, ArH-5), 7.91 (d, 1H, *J* = 1.9 Hz, ArH-2), 7.75 (dd, 1H, *J* = 8.6, 1.9 Hz, ArH-6), 3.93 (d, 2H, *J* = 5.7 Hz, $CH_2$), 3.58 – 3.50 (m, 4H, 2 × $CH_2$), 2.85 – 2.82 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.44 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 165.5, 156.5, 153.7, 140.9, 136.6, 129.8, 128.6, 125.3, 121.0, 118.8, 118.5, 109.7, 108.6, 79.1, 52.1, 41.1, 28.0, 10.8 ppm. One peak not seen. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 125.8, 121.5, 119.1, 52.6, 41.7, 28.5, 11.2 ppm. One peak not seen. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 125.8, 121.5, 119.0, 52.6 (negative), 41.7 (negative), 28.5, 11.2 ppm. One peak not seen. IR (ATR): ν 3369, 3287, 3108, 2973, 1748, 1632, 1505, 1481, 1409, 1366, 1253, 1170, 1138, 1083, 759, 621 cm$^{-1}$. MS (ESI) *m/z* = 552.0 ([M-H]$^-$). HRMS for $C_{24}H_{28}Cl_2N_5O_6$: calculated 552.1417, found 552.1411. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 12.420 min (98.1% at 280 nm).

**(*S*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8b).** To the solution of **6b** (155 mg, 0.27 mmol) in a mixture of methanol (10 mL) and tetrahydrofuran (2 mL) 1 M NaOH (1.09 mL, 1.09 mmol) was added and the mixture was stirred at rt for 15 h. To the mixture 1M HCl was added to reach pH 7 and methanol was removed under reduced pressure. 1M HCl was added to the aqueous residue to reach pH 4 upon which ethyl acetate (15 mL) was added. The undissolved precipitate was filtered off and dried to give **8b** (81 mg). Mother liquid was poured into a separating funnel and the two phases were separated. Organic phase was washed with brine (2 × 10 mL), dried with $Na_2SO_4$, filtered and evaporated. Diethyl ether was added to the residue, the obtained suspension was sonicated and the precipitate filtered off and dried (26 mg). The pure products were combined to obtain **8b** (107 mg) as brown crystals. Yield 107 mg

(71%); brown crystals; mp 210 – 215 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.57 (br s, 1H, COOH), 12.38 (s, 1H, NH), 9.50 (s, 1H, NH), 8.82 (t, 1H, *J* = 5.8 Hz, NH), 8.27 (d, 1H, *J* = 8.5 Hz, Ar-H-5), 7.76 (d, 1H, *J* = 1.8 Hz, Ar-H-2), 7.63 (dd, 1H, *J* = 8.5, 1.8 Hz, Ar-H-6), 7.19 (d, 1H, *J* = 6.5 Hz, NH), 4.07 – 4.14 (m, 1H, CH), 3.92 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.33 – 3.27 (m, 1H, CH, overlapping with the signal for water), 3.19 – 3.14 (m, 1H, CH), 3.06 – 3.00 (m, 1H, CH), 2.94 – 2.89 (m, 1H, CH), 2.24 – 2.15 (m, 4H, CH, $CH_3$), 1.89 – 1.81 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 165.9, 156.6, 155.2, 139.8, 135.3, 129.5, 129.2, 123.1, 119.7, 119.2, 118.8, 110.1, 108.6, 77.8, 57.5, 50.9, 49.8, 41.2, 31.3, 28.2, 10.8 ppm. IR (ATR): ν 3311, 3177, 2976, 1710, 1694, 1634, 1585, 1506, 1331, 1169, 860, 765 cm$^{-1}$. $[\alpha]_D^{25}$ -12.0 (*c* 0.125, MeOH). MS (ESI) *m/z* = 552.0 ($[M-H]^-$). HRMS for $C_{24}H_{28}Cl_2N_5O_6$: calculated 552.1417, found 552.1412. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 11.366 min (97.0% at 280 nm).

**(*R*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8c).** To the solution of **6c** (200 mg, 0.35 mmol) in a mixture of methanol (8 mL) and tetrahydrofuran (3 mL) 1 M NaOH (1.41 mL, 1.4 mmol) was added and the mixture was stirred at rt for 15 h. To the mixture water (10 mL) was added and the pH was adjusted to 4 with 1 M HCl upon which the obtained precipitate was filtered off and dried to obtain **8c** (91 mg) as grey solid. Yield 91 mg (47%); grey solid; mp 210 – 214 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.57 (br s, 1H, COOH), 12.38 (s, 1H, NH), 9.50 (s, 1H, NH), 8.81 (t, 1H, *J* = 5.8 Hz, NH), 8.27 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.76 (d, 1H, *J* = 1.8 Hz, ArH-2), 7.63 (dd, 1H, *J* = 8.5, 1.8 Hz, ArH-6), 7.19 (d, 1H, *J* = 6.5 Hz, NH), 4.07 – 4.14 (m, 1H, CH), 3.92 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.33 – 3.27 (m, 1H, CH, overlapping with the signal for water), 3.19 – 3.14 (m, 1H, CH), 3.06 – 3.00 (m, 1H, CH), 2.94 – 2.89 (m, 1H, CH), 2.24 – 2.15 (m, 4H, CH, $CH_3$), 1.89 – 1.81 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 166.1, 156.6, 155.4, 139.9, 135.1, 129.6, 129.3, 122.9, 120.0, 119.0, 118.7, 110.2, 108.7, 78.0, 57.4, 50.7, 49.7, 41.5, 31.2, 28.1, 10.7 ppm. IR (ATR): ν 3440, 3292, 2977, 2931, 2840, 1733, 1687, 1636, 1506, 1403, 1244, 1063, 1041, 764, 605 cm$^{-1}$. $[\alpha]_D^{25}$ +11.8 (*c* 0.187, MeOH). MS (ESI) *m/z* = 552.1 ($[M-H]^-$). HRMS for $C_{24}H_{28}Cl_2N_5O_6$: calculated 552.1417, found 552.1414. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 11.366 min (96.9% at 280 nm).

**(3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9a).** To the solution of **7a** (200 mg, 0.32 mmol) in methanol (10 mL) 1 M NaOH (1.24 mL, 1.2 mmol) was added and the mixture was stirred at rt for 15 h. The mixture was neutralized with 1 M HCl and methanol was removed under reduced pressure. Water (10 mL) was added, the pH was adjusted to 4 with 1 M HCl, ethyl acetate (20 mL) was added, and the organic phase was

washed with water (10 mL) and brine (2 × 10 mL), dried over $Na_2SO_4$, filtered and the solvent removed. To the residue diethyl ether was added, the obtained suspension was sonicated and the precipitate was filtered to obtain **9a** (115 mg) as grey solid. Yield 115 mg (59%); grey solid; mp > 300 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.08 (s, 1H, NH), 12.59 (br s, 1H, COOH), 9.20 (s, 1H, NH), 8.81 (t, 1H, *J* = 5.8 Hz, NH), 8.10 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.76 (d, 1H, *J* = 1.9 Hz, ArH-2), 7.68 (dd, 1H, *J* = 8.5, 1.9 Hz, ArH-6), 7.17 (d, 1H, *J* = 2.8 Hz, ArH), 3.93 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.57 – 3.51 (m, 4H, 2 × $CH_2$), 2.83 – 2.81 (m, 4H, 2 × $CH_2$), 1.43 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 165.7, 156.9, 153.8, 142.6, 135.0, 129.4, 127.6, 123.9, 121.0, 119.8, 113.5, 106.8, 98.7, 79.0, 51.4, 41.2, 28.0 ppm. One peak not seen. IR (ATR): ν 3101, 3053, 2972, 1745, 1630, 1505, 1406, 1368, 1172, 1140, 830, 756, 631 cm$^{-1}$. MS (ESI) *m/z* = 626.0 ([M-H]$^-$). HRMS for $C_{23}H_{26}Br_2N_5O_6$: calculated 626.0250, found 626.0255. HPLC: Agilent Eclipse Plus C18 column (5 µm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 µL; $t_R$: 11.169 min (95.8% at 280 nm).

**(*S*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9b).** To the solution of **7b** (250 mg, 0.38 mmol) in methanol (10 mL) 1 M NaOH (1.52 mL, 1.52 mmol) was added and the mixture was stirred at rt for 15 h. The mixture was neutralized with 1 M HCl and methanol was removed under reduced pressure. The pH was adjusted to 4 with 1 M HCl, ethyl acetate was added, and the organic phase was washed with water (10 mL) and brine (2 × 10 mL), dried over $Na_2SO_4$, filtered and the solvent removed. To the residue diethyl ether was added, the obtained suspension was sonicated and the precipitate was filtered to obtain **9b** (188 mg) as grey solid. Yield 188 mg (77%); grey solid; mp 219 – 223 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.89 (s, 1H, NH), 12.47 (br s, 1H, COOH), 9.52 (s, 1H, NH), 8.80 (t, 1H, *J* = 5.8 Hz, NH), 7.35 – 7.29 (m, 3H, 3 × ArH), 7.20 – 7.13 (m, 1H, ArH), 4.06 – 4.01 (m, 1H, CH), 3.91 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.43 – 3.31 (m, 2H, 2 × CH, overlapping with the signal for water), 3.27 – 3.21 (m, 1H, CH), 3.08 – 3.04 (m, 1H, CH), 2.11 – 2.03 (m, 1H, CH), 1.84 – 1.75 (m, 1H, CH), 1.37 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 166.3, 157.6, 155.2, 144.4, 131.7, 128.3, 127.8, 117.5, 114.5, 113.4, 105.7, 98.2, 77.8, 55.9, 49.8, 48.3, 41.2, 30.5, 28.2 ppm. IR (ATR): ν 3376, 3276, 3104, 1735, 1692, 1666, 1628, 1509, 1399, 1383, 1236, 1153, 976, 767 cm$^{-1}$. $[\alpha]_D^{25}$ -37.3 (*c* 0.126, MeOH). MS (ESI) *m/z* = 626.0 ([M-H]$^-$). HRMS for $C_{23}H_{26}Br_2N_5O_6$: calculated 626.0250, found 626.0239. HPLC: Agilent Eclipse Plus C18 column (5 µm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 µL; $t_R$: 9.325 min (98.6% at 280 nm).

**(*R*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9c).** To the solution of **7c** (300 mg, 0.47 mmol) in a mixture of methanol (10 mL) and tetrahydrofuran (1 mL) 1 M NaOH (1.86 mL, 1.8 mmol) was added and the mixture was stirred at rt for 15 h. The mixture was neutralized with 1 M HCl and methanol was removed under

reduced pressure. Water (10 mL) was added and the pH was adjusted to 4 with 1 M HCl. The precipitate was filtered off and dried to obtain **9c** (234 mg) as grey solid. Yield 234 mg (80%); grey solid; mp 218 – 223 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.89 (s, 1H, NH), 12.47 (br s, 1H, COOH), 9.52 (s, 1H, NH), 8.80 (t, 1H, *J* = 5.8 Hz, NH), 7.35 – 7.29 (m, 3H, 3 × ArH), 7.20 – 7.13 (m, 2H, NH, ArH), 4.06 – 4.01 (m, 1H, CH), 3.91 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.44 – 3.39 (m, 2H, 2 × CH, overlapping with the signal for water), 3.26 – 3.20 (m, 1H, CH), 3.07 – 3.04 (m, 1H, CH), 2.10 – 2.03 (m, 1H, CH), 1.84 – 1.75 (m, 1H, CH), 1.37 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 166.3, 157.6, 155.2, 147.9, 144.3, 131.7, 128.0, 117.5, 114.5, 113.5, 105.8, 98.2, 77.8, 55.9, 49.8, 48.3, 41.2, 30.5, 28.2 ppm. Signal for one aromatic carbon not seen. IR (ATR): ν 3376, 3276, 3104, 1735, 1692, 1666, 1628, 1509, 1399, 1383, 1236, 1153, 976, 767 cm$^{-1}$. $[\alpha]_D^{25}$ +35.3 (*c* 0.133, MeOH). MS (ESI) *m/z* = 626.0 ([M-H]$^-$). HRMS for $C_{23}H_{26}Br_2N_5O_6$: calculated 626.0250, found 626.0252. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 9.325 min (95.1% at 280 nm).

**4-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (10a).** Compound **8a** (50 mg, 0.09 mmol) was suspended in 4 M HCl in 1,4-dioxane (5 mL) and THF (2 mL), and the mixture was stirred at rt for 1 h. The solvents were evaporated, to the solid residue diethyl ether was added, the obtained suspension was sonicated and the solid was filtered off to give **10a** (39 mg) as grey solid. Yield 39 mg (89%); grey solid; mp 262 – 265 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.59 (br s, 1H, COOH), 12.49 (s, 1H, NH), 9.59 (s, 1H, NH), 9.23 (br s, 2H, $NH_2^+$), 8.96 (t, 1H, *J* = 5.7 Hz, NH), 8.45 (d, 1H, *J* = 8.6 Hz, ArH-3), 7.83 (d, 1H, *J* = 1.8 Hz, ArH-6), 7.79 (dd, 1H, *J* = 8.6, 1.8 Hz, ArH-4), 3.93 (d, 2H, *J* = 5.7 Hz, $CH_2$), 3.31 – 3.24 (m, 4H, 2 × $CH_2$), 3.12 – 3.09 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 165.5, 156.6, 140.3, 136.4, 129.7, 128.9, 125.3, 120.7, 118.9, 118.8, 110.0, 108.6, 48.9, 43.4, 41.2, 10.8 ppm. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 125.7, 121.2, 119.4, 49.5, 44.0, 41.7, 11.2 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 125.7, 121.2, 119.4, 49.5 (negative), 44.0 (negative), 41.7 (negative), 11.2 ppm. IR (ATR): ν 3402, 3307, 3240, 2834, 1734, 1645, 1588, 1504, 1412, 1211, 1040, 920, 763 cm$^{-1}$. MS (ESI) *m/z* = 452.0 ([M-H]$^-$). HRMS for $C_{19}H_{20}Cl_2N_5O_4$: calculated 452.0892, found 452.0891. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 20-40% of acetonitrile in phosphate buffer (pH = 6.8) in 16 min, 40% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 9.087 min (99.6% at 280 nm).

**(*S*)-1-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (10b).** The solution of **8b** (40 mg, 0.072 mmol) in a mixture of 4 M HCl in 1,4-dioxane (1 mL) and THF (1 mL) was stirred at rt for 2 h. The solvent was removed, to the residue diethyl ether was added, the obtained suspension was sonicated and the undissolved solid was filtered off and dried to give **10b** (34 mg) as beige solid. Yield 24 mg (97%);

beige solid; mp 216 – 220 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.6 (s, 1H, NH), 9.47 (s, 1H, NH), 8.92 (t, 1H, *J* = 5.8 Hz, NH), 8.43 (s, 3H, $NH_3^+$), 8.17 (d, 1H, *J* = 8.5 Hz, ArH-3), 7.79 (d, 1H, *J* = 1.8 Hz, ArH-6), 7.65 (dd, 1H, *J* = 8.5, 1.8 Hz, ArH-4), 3.92 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.71 – 3.66 (m, 1H, CH, overlapping with the signal for water), 3.52 – 3.47 (m, 1H, CH, overlapping with the signal for water), 3.42 – 3.36 (m, 1H, CH), 3.12 – 3.08 (m, 1H, CH), 3.00 – 2.95 (m, 1H, CH), 2.34 – 2.24 (m, 4H, CH, $CH_3$), 2.06 – 1.96 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 165.8, 156.7, 139.3, 134.8, 129.5, 129.1, 122.9, 121.0, 119.2, 118.7, 111.2, 108.7, 55.1, 49.0, 41.2, 29.6, 10.8 ppm. IR (ATR): ν 3365, 3263, 2937, 1729, 1640, 1509, 1507, 1410, 1317, 1259, 1222, 1041, 762 cm$^{-1}$. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 175.7, 173.2, 123.4, 121.4, 119.8, 55.6, 50.8, 49.5, 41.7, 30.1, 11.2 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 123.4, 121.4, 119.8, 55.6 (negative), 50.8, 49.5 (negative), 41.7, 30.1 (negative), 11.2 (negative) ppm. $[\alpha]_D^{25}$ -11.9 (*c* 0.117, MeOH). MS (ESI) *m/z* = 452.0 ([M-H]$^-$). HRMS for $C_{19}H_{20}Cl_2N_5O_4$: calculated 452.0892, found 452.0881. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 20-40% of acetonitrile in phosphate buffer (pH = 6.8) in 16 min, 40% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 9.252 min (99.3% at 280 nm).

**(*R*)-1-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (10c).** Solution of **8c** (35 mg, 0.063 mmol) in 4 M HCl in 1,4-dioxane (5 mL) was stirred at rt for 2 h. The solvent was removed, to the residue diethyl ether was added, the obtained suspension was sonicated and the undissolved solid was filtered off and dried to give **10c** (22 mg) as grey solid. Yield 22 mg (71%); grey solid; mp 217 – 221 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.6 (s, 1H, NH), 9.47 (s, 1H, NH), 8.92 (t, 1H, *J* = 5.8 Hz, NH), 8.43 (s, 3H, $NH_3^+$), 8.17 (d, 1H, *J* = 8.5 Hz, ArH-3), 7.79 (d, 1H, *J* = 1.8 Hz, ArH-6), 7.65 (dd, 1H, *J* = 8.5, 1.8 Hz, ArH-4), 3.92 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.71 – 3.66 (m, 1H, CH, overlapping with the signal for water), 3.52 – 3.47 (m, 1H, CH, overlapping with the signal for water), 3.42 – 3.36 (m, 1H, CH), 3.12 – 3.08 (m, 1H, CH), 3.00 – 2.95 (m, 1H, CH), 2.34 – 2.24 (m, 4H, CH, $CH_3$), 2.06 – 1.96 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 165.8, 156.7, 139.3, 134.8, 129.5, 129.1, 122.9, 121.0, 119.2, 118.7, 111.2, 108.7, 55.1, 49.0, 41.2, 29.6, 10.8 ppm. IR (ATR): ν 3348, 3235, 3017, 2922, 1733, 1636, 1602, 1509, 1410, 1317, 1042, 764, 607 cm$^{-1}$. $[\alpha]_D^{25}$ +11.0 (*c* 0.100, MeOH). MS (ESI) *m/z* = 452.1 ([M-H]$^-$). HRMS for $C_{19}H_{20}Cl_2N_5O_4$: calculated 452.0892, found 452.0898. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 20-40% of acetonitrile in phosphate buffer (pH = 6.8) in 16 min, 40% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 9.252 min (99.4% at 280 nm).

**4-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (11a).** Compound **9a** (50 mg, 0.079 mmol) was dissolved in 4 M HCl in 1,4-dioxane (4 mL) and THF (1 mL), and the solution was stirred at rt for 2 h. The solvents were evaporated, to the solid residue diethyl ether was added, the obtained suspension was

sonicated and the solid was filtered off to give **11a** (45 mg) as beige solid. Yield 45 mg (100%); beige solid; mp 225 – 228 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.19 (d, 1H, *J* = 2.8 Hz, NH), 12.52 (br s, 1H, COOH), 9.24 (br s, 2H, $NH_2^+$), 9.19 (s, 1H, NH), 8.95 (t, 1H, *J* = 5.8 Hz, NH), 8.06 (d, 1H, *J* = 9.0 Hz, ArH-3), 7.72 – 7.69 (m, 2H, ArH-4,6), 7.29 (d, 1H, *J* = 2.8 Hz, ArH), 3.93 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.36 – 3.27 (m, 4H, 2 × $CH_2$), 3.10 – 3.08 (m, 4H, 2 × $CH_2$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 165.7, 156.9, 142.2, 134.9, 129.7, 127.5, 123.9, 121.9, 119.5, 114.0, 106.7, 98.6, 48.2, 43.0, 41.2 ppm. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 124.4, 122.5, 120.1, 114.5, 48.7, 43.6, 41.7 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 124.4, 122.4, 120.1, 114.5, 48.7 (negative), 43.6 (negative), 41.7 (negative) ppm. IR (ATR): ν 3326, 3199, 2798, 2719, 1730, 1655, 1507, 1406, 1305, 1178, 950, 746 $cm^{-1}$. MS (ESI) *m/z* = 526.0 ([M-H]$^-$). HRMS for $C_{18}H_{18}Br_2N_5O_4$: calculated 525.9726, found 525.9727. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 20-40% of acetonitrile in phosphate buffer (pH = 6.8) in 16 min, 40% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 6.884 min (98.4% at 280 nm).

**(*S*)-1-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (11b).** Suspension of **9b** (70 mg, 0.11 mmol) in 4 M HCl in 1,4-dioxane (5 mL) was stirred at rt for 2 h. The precipitate was filtered off and washed with diethyl ether and dried to obtain **11b** (48 mg) as grey solid. Yield 48 mg (76%); grey solid; mp 209 – 212 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.01 (d, 1H, *J* = 2.4 Hz, NH), 12.38 (br s, 1H, COOH), 9.61 (s, 1H, NH), 8.84 (t, 1H, *J* = 5.8 Hz, NH), 8.22 (s, 3H, $NH_3^+$), 7.50 – 7.52 (m, 1H, ArH), 7.41 – 7.43 (m, 2H, 2 × ArH), 7.36 (d, 1H, *J* = 2.4 Hz, ArH), 3.91 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.88 (s, 1H, CH, overlapping with the signal for water), 3.49 – 3.53 (m, 2H, 2 × CH), 3.20 – 3.23 (m, 1H, CH), 3.01 – 3.07 (m, 1H, CH), 2.20 – 2.29 (m, 1H, CH), 1.94 – 2.04 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.4, 166.2, 157.4, 142.6, 131.1, 129.7, 127.8, 127.0, 119.0, 115.9, 114.4, 105.8, 98.4, 53.6, 49.4, 47.7, 41.2, 29.1 ppm. IR (ATR): ν 3374, 3188, 2943, 1725, 1630, 1507, 1411, 1389, 1328, 1221, 1180, 974, 868, 755 $cm^{-1}$. $[\alpha]_D^{25}$ -11.1 (*c* 0.189, MeOH). MS (ESI) *m/z* = 526.0 ([M-H]$^-$). HRMS for $C_{18}H_{18}Br_2N_5O_4$: calculated 525.9726, found 525.9726. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 20-40% of acetonitrile in phosphate buffer (pH = 6.8) in 16 min, 40% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 5.908 min (95.2% at 280 nm).

**(*R*)-1-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (11c).** Solution of **9c** (70 mg, 0.11 mmol) in a mixture of 1,4-dioxane (10 mL) and 4 M HCl in 1,4-dioxane (5 mL) was stirred at rt for 2 h. The solvent was removed under reduced pressure, to the residue diethyl ether was added, the obtained suspension was sonicated, the precipitate was filtered off, washed with diethyl ether and dried to obtain **11c** (62 mg) as grey solid. Yield 62 mg (98%); grey solid; mp 209 – 214 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.01 (d, 1H, *J* = 2.4 Hz, NH), 12.38 (br s, 1H, COOH), 9.61 (s, 1H, NH), 8.84 (t, 1H, *J* = 5.8 Hz, NH), 8.22

(s, 3H, $NH_3^+$), 7.50 – 7.52 (m, 1H, ArH), 7.41 – 7.43 (m, 2H, 2 × ArH), 7.36 (d, 1H, *J* = 2.4 Hz, ArH), 3.74 – 3.94 (m, 3H, CH, $CH_2$ overlapping with the signal for water), 3.49 – 3.53 (m, 2H, 2 × CH), 3.20 – 3.23 (m, 1H, CH), 3.01 – 3.07 (m, 1H, CH), 2.20 – 2.29 (m, 1H, CH), 1.94 – 2.04 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 171.7, 167.6, 157.9, 143.0, 131.1, 129.2, 127.3, 127.2, 119.0, 115.8, 114.0, 106.4, 98.8, 53.4, 49.4, 47.9, 41.2, 28.9 ppm. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 127.3, 119.6, 116.5, 114.8, 54.2, 49.9, 48.3, 41.7, 29.6 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 127.3, 119.6, 116.5, 114.8, 54.2 (negative), 49.9, 48.3 (negative), 41.7 (negative), 29.6 (negative) ppm. IR (ATR): ν 3418, 3313, 2954, 2875, 1725, 1632, 1506, 1411, 1388, 1211, 1180, 974, 757 $cm^{-1}$. $[\alpha]_D^{25}$ +10.8 (*c* 0.120, MeOH). MS (ESI) *m/z* = 526.0 ($[M-H]^-$). HRMS for $C_{18}H_{18}Br_2N_5O_4$: calculated 525.9726, found 525.9727. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 20-40% of acetonitrile in phosphate buffer (pH = 6.8) in 16 min, 40% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 5.908 min (95.1% at 280 nm).

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-((2-hydrazineyl-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (12).** To the solution of compound **6c** (0.589 g, 1.0 mmol) in a mixture of methanol (10 mL) and THF (10 mL) hydrazine hydrate solution (80%, 0.50 mL, 10.2 mmol) was added and the mixture was stirred under reflux for 20 h. The solvent was removed under reduced pressure, to the residue ethanol was added and the obtained suspension was sonicated, the undissolved solid was filtered off and dried to obtain **12** (430 mg) as white solid. Yield 430 mg (76%); white solid; mp 156 – 160 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.43 (s, 1H, NH), 9.79 (s, 1H, NH), 9.23 (br s, 1H, NH), 8.71 (t, 1H, *J* = 5.8 Hz, NH), 8.46 (d, 1H, *J* = 8.6 Hz, ArH-3), 7.92 (d, 1H, *J* = 1.8 Hz, ArH-6), 7.75 (dd, 1H, *J* = 8.6, 1.8 Hz, ArH-4), 4.67 (br s, 2H, $NH_2$), 3.84 (d, 2H, *J* = 5.8 Hz, $CH_2$), 3.49 – 3.57 (m, 4H, 2 × $CH_2$), 2.82 – 2.85 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.44 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 168.4, 165.6, 156.5, 153.7, 140.8, 136.4, 129.8, 128.9, 125.4, 121.2, 118.8, 118.4, 109.7, 108.6, 79.1, 52.1, 41.3, 28.0, 10.8 ppm. Signal for one aliphatic carbon not seen. IR (ATR): ν 3263, 1690, 1641, 1509, 1410, 1262, 1245, 1168, 1132, 1040, 713 $cm^{-1}$. MS (ESI) *m/z* = 566.0 ($[M-H]^-$). HRMS for $C_{24}H_{30}Cl_2N_7O_5$: calculated 566.1685, found 566.1682. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 10.065 min (96.3% at 280 nm).

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(((5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)carbamoyl)phenyl)piperazine-1-carboxylate (13).** The solution of **12** (392 mg, 0.69 mmol) and CDI (224 mg, 1.38 mmol) in a mixture of 1,4-dioxane (15 mL) and DMF (5 mL) was stirred at 101°C for 20 h. The solvent was removed and the residue was purified with flash column chromatography using dichloromethane/methanol (10:1) as the eluent, to obtain **13** (70 mg) as white solid. Yield 70 mg (17%); white solid; mp 147 – 151 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.43

(s, 1H, NH), 12.29 (s, 1H, NH), 9.79 (s, 1H, NH), 9.03 (t, 1H, *J* = 5.8 Hz, NH), 8.47 (d, 1H, *J* = 8.6 Hz, ArH-3), 7.90 (d, 1H, *J* = 1.9 Hz, ArH-6), 7.76 (dd, 1H, *J* = 8.6, 1.9 Hz, ArH-4), 4.39 (d, 2H, *J* = 5.6 Hz, $CH_2$), 3.45 (4H, 2 × $CH_2$, overlapping with the signal for water), 2.81 – 2.85 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.43 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.5, 156.5, 154.9, 154.5, 153.7, 141.0, 136.8, 129.9, 128.1, 125.4, 121.0, 118.8, 118.6, 109.8, 108.6, 79.1, 52.0, 30.8, 28.0, 10.7 ppm. Signal for one aliphatic carbon not seen. IR (ATR): ν 3262, 2979, 2935, 1776, 1644, 1506, 1411, 1247, 1165, 1130, 1091, 1041, 762 cm$^{-1}$. MS (ESI) *m/z* = 592.0 ([M-H]$^-$). HRMS for $C_{25}H_{28}Cl_2N_7O_6$: calculated 592.1478, found 592.1474. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 30-90% of acetonitrile in TFA (0.1%) in 16 min, 90% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 12.838 min (97.1% at 280 nm).

**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(((5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)carbamoyl)phenyl)piperazin-1-ium chloride (14).** The solution of **13** (65 mg, 0.12 mmol) in a mixture of 1,4-dioxane (10 mL) and 4 M HCl in 1,4-dioxane (6 mL) was stirred for 2 h at rt. The precipitate was filtered off and dried to obtain **14** (46 mg) as grey solid. Yield 46 mg (79%); grey solid; mp 258 – 262 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.46 (s, 1H, NH), 12.34 (s, 1H, NH), 9.60 (s, 1H, NH), 9.18 (t, 1H, *J* = 5.6 Hz, NH), 9.02 (br s, 2H, $NH_2^+$), 8.46 (d, 1H, *J* = 8.6 Hz, ArH-3), 7.84 (d, 1H, *J* = 1.9 Hz, ArH-6), 7.78 (dd, 1H, *J* = 8.6, 1.8 Hz, ArH-4), 4.39 (d, 2H, *J* = 5.6 Hz, $CH_2$), 3.24 – 3.31 (m, 4H, 2 × $CH_2$), 3.06 – 3.12 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.7, 156.6, 154.9, 154.4, 140.3, 136.6, 129.9, 128.3, 125.4, 120.9, 118.9, 118.8, 110.0, 108.7, 48.8, 43.5, 35.1, 10.7 ppm. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 125.9, 121.3, 119.4, 49.3, 43.9, 35.6, 11.2 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 125.9, 121.3, 119.4, 49.3 (negative), 43.9 (negative), 35.6 (negative) ppm. IR (ATR): ν 3245, 2956, 2797, 1773, 1639, 1507, 1460, 1309, 1258, 922, 842, 730 cm$^{-1}$. MS (ESI) *m/z* = 492.1 ([M-H]$^-$). HRMS for $C_{20}H_{20}Cl_2N_7O_4$: calculated 492.0954, found 492.0959. HPLC: Agilent Eclipse Plus C18 column (5 μm, 4.6 × 150 mm); mobile phase: 20-40% of acetonitrile in phosphate buffer (pH = 6.8) in 16 min, 40% acetonitrile to 20 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 13.668 min (96.7% at 280 nm).

**Methyl (*S*)-3-(3-((tert-butoxycarbonyl)amino)piperidin-1-yl)-4-nitrobenzoate (15c).** Synthesised according to *General procedure A* from **1** (1.07 g, 5.39 mmol), (3*S*)-3-aminopiperidine 3-Boc protected (1.00 g, 5.35 mmol) and $K_2CO_3$ (0.894 g, 6.47 mmol). Yield 87% (1.78 g); orange solid; mp 120 – 124 °C. $^1$H NMR (400 MHz, CDCl3): δ 7.83 (d, 1H, *J* = 1.5 Hz, Ar-H-2), 7.77 (d, 1H, *J* = 8.4 Hz, Ar-H-5), 7.71 (dd, 1H, *J* = 8.4, 1.5 Hz, ArH-6), 5.05 – 5.15 (m, 1H, NH), 3.97 (s, 3H, $CH_3$), 3.88 – 3.97 (m, 1H, CH), 3.26 – 3.30 (m, 1H, CH), 2.92 – 3.12 (m, 3H, CH, $CH_2$), 1.84 – 1.93 (m, 1H, CH), 1.64 – 1.80 (m, 3H, CH, $CH_2$), 1.48 (s, 9H, tBu) ppm. IR (ATR): ν 3444, 3122, 3067, 2966, 1727, 1616, 1598, 1521, 1487, 1438, 1421, 1358, 1282, 1227, 1188, 1156, 1111, 1080, 987, 917, 905, 851, 840, 799, 772, 738, 686 cm$^{-1}$.

***tert*-Butyl 4-((5-(methoxycarbonyl)-2-nitrophenyl)amino)piperidine-1-carboxylate (15d).** Synthesised according to *General procedure A* from **1** (400 mg, 2.01 mmol), *tert*-butyl 4-aminopiperidine-1-carboxylate (483 mg, 2.41 mmol) and $K_2CO_3$ (555 mg, 4.02 mmol). The crude product was purified with flash column chromatography using ethyl acetate/hexane (1:6) as eluent, to obtain **15d** (212 mg) as red solid. Yield 28% (212 mg); red solid; mp 94 – 97 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 8.19 (d, 1H, *J* = 8.8 Hz, ArH), 7.89 (d, 1H, *J* = 7.9 Hz, NH), 7.60 (d, 1H, *J* = 1.7 Hz, ArH), 7.17 (dd, 1H, *J* = 1.7, 8.8 Hz, ArH), 3.83 – 3.99 (m, 6H, CH, $CH_2$, $CH_3$), 3.03 (s, 2H, $CH_2$), 1.90 – 1.99 (m, 2H, $CH_2$), 1.43 – 1.55 (m, 2H, $CH_2$), 1.42 (s, 9H, tBu) ppm. IR (ATR): ν 2846, 2039, 1985, 1764, 1723, 1684, 1438, 1340, 1211, 1146, 1091, 1044, 1007, 952, 890, 765, 740, 695, 645 cm$^{-1}$. MS (ESI) *m/z* = 401.9 ([M+Na]$^+$).

**Methyl 3-morpholino-4-nitrobenzoate (15e).** Synthesised according to *General procedure A* from **1** (3.30 g, 16.6 mmol), morpholine (1.45 mL, 16.6 mmol) and $K_2CO_3$ (2.75 g, 19.9 mmol). Yield 94% (4.15 g); orange solid; mp 72 – 78 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.94 (d, 1H, *J* = 8.4 Hz, ArH), 7.78 (d, 1H, *J* = 1.7 Hz, ArH), 7.66 (dd, 1H, *J* = 8.4, 1.7 Hz, ArH), 3.89 (s, 3H, $CH_3$), 3.67 – 3.72 (m, 4H, 2 × $CH_2$), 3.00 – 3.06 (m, 4H, 2 × $CH_2$) ppm.

**Methyl 3-(2-methylmorpholino)-4-nitrobenzoate (15f).** Synthesised according to *General procedure A* from **1** (1.77 g, 8.90 mmol), 2-methylmorpholine (0.90 mL, 8.90 mmol) and $K_2CO_3$ (1.48 g, 10.7 mmol). Yield 93% (2.32 g); orange solid; mp 62 – 65 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.94 (d, 1H, *J* = 8.4 Hz, ArH), 7.77 (s, 1H, ArH), 7.65 (d, 1H, *J* = 8.4 Hz, ArH), 3.90 (s, 3H, $CH_3$), 3.81 – 3.88 (m, 1H, CH), 3.55 – 3.67 (m, 2H, 2 × CH), 3.07 – 3.13 (m, 1H, CH), 2.99 – 3.05 (m, 1H, CH), 2.89 – 2.96 (m, 1H, CH), 2.62 – 2.68 (m, 1H, CH), 1.11 (d, 3H, *J* = 6.2 Hz, $CH_3$) ppm.

**Methyl 3-(2,6-dimethylmorpholino)-4-nitrobenzoate (15g).** Synthesised according to *General procedure A* from **1** (2.00 g, 10.0 mmol), 2,6-dimethylmorpholine (1.24 mL, 10.0 mmol) and $K_2CO_3$ (1.66 g, 12.1 mmol). Yield 99% (2.91 g); orange solid; mp 72 – 77 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.95 (d, 1H, *J* = 8.5 Hz, ArH), 7.77 (d, 1H, *J* = 1.8 Hz, ArH), 7.64 (dd, 1H, *J* = 8.3, 1.7 Hz, ArH), 3.90 (s, 3H, $CH_3$), 3.62 – 3.75 (m, 2H, 2 × CH), 3.07 – 3.11 (m, 2H, 2 × CH), 2.54 – 2.62 (m, 2H, 2 × CH), 1.11 (d, 6H, *J* = 6.2 Hz, 2 × $CH_3$) ppm.

**Methyl 4-nitro-3-(4-phenylpiperazin-1-yl)benzoate (15h).** Synthesised according to *General procedure A* from **1** (500 mg, 2.51 mmol), 1-phenylpiperazine (460 µL, 2.92 mmol) and potassium carbonate (0.694 g, 5.02 mmol). Yield: 76% (650 mg); orange solid; mp 86 – 88 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.96 (d, 1H, *J* = 8.4 Hz, ArH), 7.82 (d, 1H, *J* = 1.7 Hz, ArH), 7.66 (dd, 1H, *J* = 1.7, 8.4 Hz, ArH), 7.29 – 7.20 (m, 2H, 2 × ArH), 7.00 – 6.94 (m, 2H, 2 × ArH), 6.86 – 6.78 (m, 1H, ArH), 3.90 (s, 3H, $CH_3$), 3.22 – 3.30 (m, 4H, 2 × $CH_2$), 3.17 – 3.22 (m, 4H, 2 × $CH_2$) ppm. IR (ATR): **ν** 2998, 2950, 2842, 1723, 1673, 1600, 1577, 1511, 1438, 1384, 1345, 1303, 1271, 1242, 1226, 1191, 1154, 1118, 1084, 1043, 1005, 951, 914, 891, 858, 828, 762, 691, 644 cm$^{-1}$. MS (ESI) *m/z* = 342.0 ([M+H]$^+$).

**Methyl 3-(3-(((*tert*-butoxycarbonyl)amino)methyl)piperidin-1-yl)-4-nitrobenzoate (15i).** Synthesised according to *General procedure A* from **1** (1.50 g, 7.53 mmol), 3-(Boc-aminomethyl)piperidine (1.61 g, 7.53 mmol) and potassium carbonate (1.46 g, 10.54 mmol). The crude product was triturated with diethyl ether, the undissolved solid was filtered off and dried to afford **15i** (2.10 g) as orange solid. Yield 71% (2.10 g); orange solid; mp 88 – 89 °C. $^{1}$H NMR (400 MHz, CDCl3): δ 7.81 (d, 1H, *J* = 1.5 Hz, Ar-H-2), 7.75 (d, 1H, *J* = 8.4 Hz, Ar-H-5), 7.64 (dd, 1H, *J* = 8.4, 1.5 Hz, Ar-H-6), 4.68 (t, 1H, *J* = 5.3 Hz, NHBoc), 3.18 – 3.27 (m, 2H, 2 × CH), 3.05 – 3.14 (m, 2H, 2 × CH), 2.83 – 2.89 (m, 1H, CH), 2.63 – 2.68 (m, 1H, CH), 1.88 – 2.00 (m, 1H, CH), 1.67 – 1.87 (m, 3H, 3 × CH), 1.46 (s, 9H, tBu), 1.16 – 1.28 (m, 1H, CH), 3.96 (s, 3H, $COOCH_3$) ppm. $^{13}$C NMR (100 MHz, CDCl3): δ 165.6 (COOMe), 156.15, 146.39, 145.51, 134.16, 125.70, 122.79, 121.99, 79.31 ($CCH_3$), 55.82, 52.78, 52.70, 46.64, 37.08, 28.39 (3 × $CH_3$), 27.85, 24.58 ppm. IR (ATR): ν 3394, 2937, 1724, 1679, 1605, 1513, 1434, 1338, 1366, 1342, 1271, 1237, 1222, 1130, 1109, 1003, 980, 882, 837, 745, 627 cm$^{-1}$. MS (ESI) *m/z* = 394.0 ([M+H]$^{+}$).

***tert*-Butyl 4-(2-amino-5-(methoxycarbonyl)phenyl)piperazine-1-carboxylate (16a).** To the solution of compound **2a** (5.44 g, 16.0 mmol) in a mixture of methanol (200 mL) and tetrahydrofuran (90 mL) under an argon atmosphere Pd-C (1.00 g) was added, the mixture was saturated with hydrogen and stirred under a hydrogen atmosphere at rt for 4 h. The catalyst was filtered off and the solvent was removed under reduced pressure to afford **16a** (4.87 g) as white solid. Yield 90% (4.87 g); white solid; mp 135 – 137 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 7.49 (dd, 1H, *J* = 8.4, 1.9 Hz, ArH), 7.44 (d, 1H, *J* = 1.9 Hz, ArH), 6.70 (d, 1H, *J* = 8.4 Hz, ArH), 5.73 (br s, 2H, $NH_2$), 3.74 (s, 3H, $CH_3$), 3.44 – 3.59 (m, 4H, 2 × $CH_2$), 2.68 – 2.84 (m, 4H, 2 × $CH_2$), 1.43 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.3, 153.9, 147.6, 136.7, 126.8, 120.6, 116.4, 113.1, 78.8, 51.2, 50.4, 43.2, 28.0 ppm. IR (ATR): ν 3412, 3319, 2977, 2811, 1685, 1614, 1579, 1510, 1477, 1440, 1417, 1362, 1323, 1302, 1261, 1248, 1218, 1157, 1133, 1107, 1066, 1052, 1039, 993, 945, 930, 908, 870, 843, 829, 811, 769, 649, 624 cm$^{-1}$. MS (ESI) m/z = 336.2 ([M+H]$^{+}$). HRMS for $C_{17}H_{26}O_3N_4$: calculated 336.1923, found 336.1924.

**Methyl (*S*)-4-amino-3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)benzoate (16b).** To the solution of compound **2b** (1.62 g, 4.43 mmol) in a mixture of methanol (65 mL) and tetrahydrofuran (15 mL) under an argon atmosphere Pd-C (500 mg) was added, the mixture was saturated with hydrogen and stirred under a hydrogen atmosphere at rt for 4 h. The catalyst was filtered off and the solvent was removed under reduced pressure. The crude product was purified with flash column chromatography (ethyl acetate/petroleum ether = 1:3 to 1:1) to afford **16b** (1.78 g) as pink solid. Yield 87% (1.78 g); pink solid; mp 105 – 107 °C. $^{1}$H NMR (400 MHz, CDCl3): δ 7.49 (m, 2H, 2 × ArH), 7.37 (d, 1H, *J* = 7.9 Hz, NHBoc), 6.64 (d, 1H, *J* = 8.2 Hz, ArH), 5.69 (s, 2H, $NH_2$), 4.07 – 4.15 (m, 1H, CH), 3.73 (s, 3H, $CH_3$), 3.04 – 3.13 (m, 2H, 2 × CH), 2.78 – 2.82 (m, 2H, 2 × CH), 2.15 – 2.27 (m, 1H, CH), 1.63 – 1.70 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. IR (ATR): ν 3413, 3360, 3330, 2975, 2844, 2361, 1684, 1667, 1616, 1583,

1527, 1512, 1441, 1391, 1367, 1314, 1291, 1269, 1243, 1169, 1107, 1043, 1021, 1008, 958, 894, 857, 826, 808, 767, 745, 697, 654, 630, 548 $cm^{-1}$. $[\alpha]_D^{25}$ 0.073 (*c* 0.418, DMF). MS (ESI) m/z = 336.3 ($[M+H]^+$).

**Methyl (*S*)-4-amino-3-(3-((*tert*-butoxycarbonyl)amino)piperidin-1-yl)benzoate (16c).** To the solution of compound **15c** (1.78 g, 4.69 mmol) in a mixture of methanol (65 mL) and tetrahydrofuran (25 mL) under an argon atmosphere Pd-C (500 mg) was added, the mixture was saturated with hydrogen and stirred under a hydrogen atmosphere at rt for 4 h. The catalyst was filtered off and the solvent was removed under reduced pressure to afford **16c** (1.56 g) as white solid. Yield 88% (1.56 g); white solid; mp 112 – 114 °C. $^1$H NMR (400 MHz, CDCl3): δ 7.47 (dd, *J* = 8.3, 1.9 Hz, Ar-H-6), 7.42 (d, *J* = 1.9 Hz, Ar-H-2), 6.93 – 7.05 (m, 1H, NH), 6.68 (d, *J* = 8.3 Hz, Ar-H-5), 5.71 (br s, 2H, $NH_2$), 3.74 (s, 3H, $CH_3$), 3.60 – 3.69 (m, 1H, CH), 2.96 – 3.00 (m, 1H, CH), 2.70 – 2.81 (m, 1H, CH), 2.36 – 2.50 (m, 1H, $CH_2$), 1.71 – 1.87 (m, 1H, $CH_2$), 1.57 – 1.75 (m, 1H, CH), 1.39 (s, 9H, tBu), 1.27 – 1.37 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.3, 154.9, 147.9, 137.4, 126.6, 120.7, 116.3, 113.0, 77.6, 56.3, 51.4, 51.2, 47.0, 29.7, 28.2 ppm. IR (ATR): ν 3440, 3403, 3363, 2935, 2850, 2361, 2048, 1979, 1698, 1681, 1674, 1651, 1584, 1522, 1510, 1439, 1389, 1366, 1302, 1279, 1260, 1243, 1222, 1165, 1104, 1053, 1032, 1005, 945, 910, 899, 868, 827, 807, 768, 745, 698, 648, 635, 622 $cm^{-1}$. MS (ESI) m/z = 350.2 ($[M+H]^+$). HRMS for $C_{18}H_{28}N_3O_4$: calculated 350.2080, found 350.2072.

***tert*-Butyl 4-((2-amino-5-(methoxycarbonyl)phenyl)amino)piperidine-1-carboxylate (16d).** Compound **15d** (200 mg, 0.527 mmol) was dissolved in methanol (50 mL) and flushed with argon. Pd/C (10%, 20 mg) was added and the reaction mixture was then stirred at rt under hydrogen atmosphere for 1 h. The catalyst was filtered off and the solvent removed *in vacuo*. Yield 100% (184 mg); light brown solid; mp: 140 – 143 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.14 (dd, *J* = 1.9, 8.1 Hz, ArH), 7.05 (d, *J* = 1.9 Hz, ArH), 6.55 (d, *J* = 8.1 Hz, ArH), 5.45 (s, 2H, $NH_2$), 4.40 (d, 1H, *J* = 7.6 Hz, NH), 3.89 (d, 2H, *J* = 13.0 Hz, $CH_2$), 3.72 (s, 3H, $CH_3$), 3.39 – 3.51 (m, 1H, CH), 2.95 (s, 2H, $CH_2$), 1.85 – 1.97 (m, 2H, $CH_2$), 1.41 (s, 9H, tBu), 1.20 – 1.34 (m, 2H, $CH_2$) ppm. IR (ATR): **ν** 3366, 3266, 2932, 1765, 1688, 1662, 1588, 1522, 1497, 1472, 1415, 1364, 1206, 1173, 1145, 1091, 1041, 944, 826, 854, 767, 708, 629 $cm^{-1}$. MS (ESI) *m/z* = 372.0 ($[M+Na]^+$).

**Methyl 4-amino-3-morpholinobenzoate (16e).** To the solution of compound **15e** (4.00 g, 15.0 mmol) in a mixture of methanol (190 mL) and tetrahydrofuran (80 mL) under an argon atmosphere Pd-C (400 mg) was added, the mixture was saturated with hydrogen and stirred under a hydrogen atmosphere at rt for 3 h. The catalyst was filtered off and the solvent was removed under reduced pressure to obtain **16e** (3.51 g) as white solid. Yield 99% (3.51 g); white solid; mp 122 – 124 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.48 (dd, *J* = 8.2, 1.9 Hz, ArH), 7.45 (d, *J* = 2.0 Hz, ArH), 6.70 (d, *J* = 8.3 Hz, ArH), 5.68 (s, 2H, $NH_2$), 3.75 – 3.81 (m, 7H, 2 × $CH_2$, $CH_3$), 2.74 – 2.82 (m, 4H, 2 × $CH_2$) ppm.

**Methyl 4-amino-3-(2-methylmorpholino)benzoate (16f).** To the solution of compound **15f** (2.10 g, 7.49 mmol) in a mixture of methanol (90 mL) and tetrahydrofuran (40 mL) under an argon atmosphere Pd-C (210 mg) was added, the mixture was saturated with hydrogen and stirred under a hydrogen atmosphere at rt for 5 h. The catalyst was filtered off and the solvent was removed under reduced pressure to obtain **16f** (1.80 g) as white solid. Yield 96% (1.80 g); white solid; mp 111 – 114 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.46 – 7.52 (m, 1H, ArH), 7.44 (s, 1H, ArH), 6.70 (d, *J* = 8.3 Hz, ArH), 5.68 (s, 2H, $NH_2$), 3.80 – 3.87 (m, 1H, CH), 3.74 (s, 5H, 2 × CH, $CH_3$), 2.84 – 2.94 (m, 2H, 2 × CH), 2.57 (td, *J* = 11.3, 3.3 Hz, CH), 2.32 (t, *J* = 10.5 Hz, CH), 1.10 (d, *J* = 6.2 Hz, $CH_3$) ppm.

**Methyl 4-amino-3-(2,6-dimethylmorpholino)benzoate (16g).** To the solution of compound **15g** (2.50 g, 8.49 mmol) in a mixture of methanol (90 mL) and tetrahydrofuran (40 mL) under an argon atmosphere Pd-C (250 mg) was added, the mixture was saturated with hydrogen and stirred under a hydrogen atmosphere at rt for 3 h. The catalyst was filtered off and the solvent was removed under reduced pressure and the crude product was recrystallized from EtOAc to obtain **16g** (0.628 g) as white solid. Yield 28% (0.628 g); white solid; mp 137 – 142 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.47 (dd, 1H, *J* = 8.3, 1.9 Hz, ArH), 7.42 (d, 1H, *J* = 1.9 Hz, ArH), 6.69 (d, 1H, *J* = 8.3 Hz, ArH), 5.66 (s, 2H, $NH_2$), 3.77 – 3.85 (m, 2H, 2 × CH), 3.74 (s, 3H, $CH_3$), 2.89 – 2.95 (m, 2H, 2 × CH), 2.17 – 2.27 (m, 2H, 2 × CH), 1.10 (d, 6H, *J* = 6.2 Hz, 2 × $CH_3$) ppm.

**Methyl 4-amino-3-(4-phenylpiperazin-1-yl)benzoate (16h).** Compound **15h** (0.600 g, 1.93 mmol) was dissolved in methanol and tetrahydrofuran (3:1, 80 mL) and flushed with argon. Pd/C (10%, 60 mg) was added and the reaction mixture was then stirred at rt under hydrogen atmosphere for 3 h. The catalyst was filtered off and the solvent removed *in vacuo*. The crude product was suspended in diethyl ether, sonicated, filtered off and dried. Yield 59% (320 mg); grey solid; mp 124 – 129 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.47 – 7.52 (m, 2H, 2 × ArH), 7.19 – 7.29 (m, 2H, 2 × ArH), 6.95 – 7.03 (m, 2H, 2 × ArH), 6.76 – 6.85 (m, 1H, ArH), 6.73 (d, 1H, *J* = 8.8 Hz, ArH), 5.69 (s, 2H, $NH_2$), 3.75 (s, 3H, $CH_3$), 3.32 (4H, overlapped with the signal for water, 2 × $CH_2$), 2.95 (t, 4H, *J* = 4.9 Hz, 2 × $CH_2$) ppm. IR (ATR): **ν** 3424, 3335, 2954, 2820, 1689, 1600, 1510, 1493, 1439, 1375, 1320, 1283, 1183, 1139, 1105, 1048, 986, 945, 909, 831, 692, 648 cm$^{-1}$. MS (ESI) *m/z* = 312.0 ([M+H]$^+$).

**Methyl 4-amino-3-(3-(((*tert*-butoxycarbonyl)amino)methyl)piperidin-1-yl)benzoate (16i).** To the solution of compound **15i** (2.10 g, 5.34 mmol) in methanol (150 mL) under an argon atmosphere Pd-C (210 mg) was added, the mixture was saturated with hydrogen and stirred under a hydrogen atmosphere at rt for 4 h. The catalyst was filtered off and the solvent was removed under reduced pressure. The crude product was purified with flash column chromatography using ethyl acetate/petroleum ether (1/2) as an eluent to give **16i** (1.60 g) as pink solid. Yield 82% (1.60 g); pink solid; mp 119 – 121 °C. $^1$H NMR (400 MHz, CDCl3): δ 7.67 (d, 1H, *J* = 1.9 Hz, Ar-H-2), 7.64 (dd, 1H, *J* = 8.4, 1.9 Hz, Ar-H-6), 6.68 (d, 1H, *J* = 8.4 Hz, Ar-H-5), 4.66 (t, 1H, *J* = 5.9 Hz, NHBoc), 4.41 (s, 2H, $NH_2$), 3.85 (s, 3H, $COOCH_3$), 3.19 –

2.95 (m, 4H, CH), 2.66 – 2.51 (m, 1H, CH), 2.50 – 2.33 (m, 1H, CH), 1.95 – 1.73 (m, 3H, CH), 1.72 – 1.59 (m, 1H, CH), 1.43 (s, 9H, tBu), 1.23 – 1.04 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 167.4 (COOMe), 156.1, 146.5, 139.1, 127.2, 122.0, 119.4, 113.6, 79.2 ($CCH_3$), 55.8, 52.5, 51.6, 44.1, 37.6, 28.4 (3 × $CH_3$), 28.2, 25.5 ppm. IR (ATR): ν 3425, 3398, 3309, 2977, 2931, 2850, 1700, 1622, 1514, 1436, 1392, 1365, 1291, 1260, 1216, 1165, 1108, 1003, 884, 832, 765, 697, 635 cm$^{-1}$. MS (ESI) *m/z* = 364.22 ([M+H]$^+$).

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperazine-1-carboxylate (17a).** Synthesised according to *General procedure B* from 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.850 g, 4.38 mmol) and **16a** (1.62 g, 4.82 mmol). During the extraction the product precipitated and was filtered off. The crude product was sequentially triturated with methanol and tetrahydrofuran, and the undissolved solid was filtered off and dried, to obtain **17a** (0.589 g) as white solid. Yield 25% (0.589 g); white solid; mp 132 – 136 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.45 (s, 1H, NH), 9.79 (s, 1H, NH), 8.51 (d, 1H, *J* = 8.6 Hz, ArH), 7.78 – 7.89 (m, 2H, 2 × ArH), 3.84 (s, 3H, $CH_3$), 3.52 (br s, 4H, 2 × $CH_2$), 2.78 – 2.87 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.44 (s, 9H, tBu) ppm. IR (ATR): ν 3252, 2975, 2892, 2364, 1722, 1686, 1639, 1593, 1524, 1488, 1455, 1410, 1378, 1365, 1332, 1273, 1258, 1245, 1218, 1194, 1164, 1131, 1116, 1098, 1079, 1041, 998, 980, 939, 894, 860, 844, 818, 748, 740, 711, 664, 650, 632, 622, 611 cm$^{-1}$. MS (ESI) m/z = 511.2 ([M+H]$^+$). HRMS for $C_{23}H_{29}N_4O_5Cl_2$: calculated 511.1515, found 511.1524. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 μm, 4.6 × 150 mm): $t_r$ 16.803 min (98.3% at 280 nm).

**Methyl (*S*)-3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoate (17b).** Synthesised according to *General procedure B* from 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.446 g, 2.30 mmol) and **16b** (0.700 g, 2.09 mmol). The crude product obtained after the extraction was triturated with methanol, and the undissolved solid was filtered off and dried, to obtain **17b** (391 mg) as brown solid. Yield 60% (0.965 g); white solid; mp 113 – 116 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.41 (s, 1H, NH), 9.60 (s, 1H, NH), 8.36 (d, 1H, *J* = 8.5 Hz, ArH), 7.81 (d, 1H, *J* = 2.0 Hz, ArH), 7.74 (dd, 1H, *J* = 8.5, 2.0 Hz, ArH), 7.19 (d, 1H, *J* = 6.7 Hz, NHBoc), 4.07 – 4.15 (m, 1H, CH), 3.29 – 3.34 (m, 1H, CH), 3.12 – 3.19 (m, 1H, CH), 3.01 – 3.07 (m, 1H, CH), 2.88 – 2.92 (m, 1H, CH), 2.24 (s, 3H, $CH_3$), 2.14 – 2.23 (m, 1H, CH), 1.78 – 1.89 (m, 1H, CH), 1.40 (s, 9H, tBu), 3.85 (s, 3H, $CH_3$) ppm. IR (ATR): ν 3301, 2973, 2361, 2340, 1716, 1684, 1646, 1591, 1519, 1489, 1439, 1409, 1365, 1324, 1302, 1254, 1179, 1129, 1100, 1060, 1042, 1017, 954, 883, 838, 761, 737, 650, 628, 606, 562, 527 cm$^{-1}$. $[\alpha]_D^{25}$ 0,953 (*c* 0,270, DMF). MS (ESI) m/z = 511.2 ([M+H]$^+$).

**Methyl (*S*)-3-(3-((*tert*-butoxycarbonyl)amino)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoate (17c).** Synthesised according to *General procedure B* from 3,4-

dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.590 g, 3.07 mmol) and **16c** (1.00 g, 2.98 mmol). During the extraction part of the product precipitated and was filtered off. The crude product was sequentially triturated with diethyl ether and methanol, and the undissolved solid was filtered off and dried, to obtain **17c** (0.965 g) as white solid. Yield 64% (0.965 g); white solid; mp 188 – 191 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.45 (s, 1H, NH), 9.83 (s, 1H, NH), 8.51 (d, 1H, *J* = 8.9 Hz, ArH), 7.81 – 7.83 (m, 2H, 2 × ArH), 6.88 (d, 1H, *J* = 7.2 Hz, NH), 3.85 (s, 3H, $CH_3$), 3.54 – 3.66 (m, 1H, CH), 2.91 – 3.01 (m, 1H, CH), 2.78 – 2.88 (m, 1H, CH), 2.53 – 2.62 (m, 2H, $CH_2$), 2.25 (s, 3H, $CH_3$), 1.76 – 1.94 (m, 1H, $CH_2$), 1.60 – 1.73 (m, 1H, CH), 1.35 (s, 9H, tBu), 1.22 – 1.30 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.6, 156.6, 154.8, 141.6, 138.3, 130.0, 127.1, 124.4, 122.6, 118.7, 110.0, 108.7, 77.7, 57.5, 53.0, 52.0, 47.5, 29.4, 28.2, 24.4, 10.8 ppm. Signal for one aromatic carbon not seen. IR (ATR): ν 3328, 3103, 2958, 2363, 2204, 2049, 1990, 1719, 1687, 1639, 1590, 1521, 1490, 1436, 1408, 1365, 1354, 1319, 1288, 1263, 1231, 1197, 1176, 1160, 1122, 1105, 1083, 1069, 1054, 1039, 1026, 997, 938, 927, 863, 836, 812, 762, 773, 733, 669, 650, 624, 609 cm$^{-1}$. $[\alpha]^{20}_{D}$ = + 0.30° (c 0.375, THF). MS (ESI) m/z = 525.2 ($[M+H]^+$). HRMS for $C_{24}H_{31}N_4O_5Cl_2$: calculated 525.1672, found 525.1681. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4,6 × 150 mm): $t_r$ 16.404 min (98.7% at 280 nm).

***tert*-Butyl 4-((2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)amino)piperidine-1-carboxylate (17d).** To a suspension of 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (113 mg, 0.584 mmol) in anhydrous dichloromethane (10 mL), oxalyl chloride (209 µL, 2.43 mmol) was added dropwise and the reaction mixture was stirred at rt under argon atmosphere overnight. The solvent was evaporated under reduced pressure, **16d** (170 mg, 0.487 mmol), anhydrous pyridine (2 mL) and anhydrous dichloromethane (10 mL) were added and the reaction mixture was stirred at rt under argon atmosphere overnight. The solvent was removed *in vacuo*, to the residue ethyl acetate and water were added and the formed precipitate was filtered off and dried. Yield 63% (160 mg); white solid; mp 210 – 212 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.30 (s, 1H, NH), 8.94 (s, 1H, NH), 7.84 (d, 1H, *J* = 8.2 Hz, ArH), 7.32 – 7.47 (m, 2H, 2 × ArH), 5.11 (d, 1H, *J* = 6.9 Hz, NH), 3.87 (s, 1H, CH), 3.83 (s, 3H, $CH_3$), 3.38 – 3.48 (m, 2H, $CH_2$), 2.97 (s, 2H, $CH_2$), 2.24 (s, 3H, $CH_3$), 1.80 – 1.94 (m, 2H, $CH_2$), 1.40 (s, 9H, tBu), 1.23 – 1.37 (m, 2H, $CH_2$) ppm. IR (ATR): **ν** 3324, 3244, 2945, 1685, 1641, 1556, 1533, 1495, 1425, 1291, 1260, 1215, 1171, 1138, 1110, 1045, 979, 950, 912, 814, 763, 733, 705, 670, 613 cm$^{-1}$. MS (ESI) *m/z* = 522.9 ($[M-H]^-$).

**Methyl 4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-3-morpholinobenzoate (17e).** To the 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.65 g, 3.38 mmol) $SOCl_2$ (8.28 mL, 114.15 mmol) was added and the mixture was stirred at 75 °C for 1 h under argon atmosphere. The solvent was was removed *in vacuo*, then toluene (50 mL) and **16e** (0.66 g, 2.81 mmol) were added. The reaction mixture was stirred for 15 h at 130 °C under argon atmosphere. The solvent was evaporated under

reduced pressure, the crude residue was suspended in EtOAc and filtered off to obtain a brown solid. The solid was suspended again in MeOH, filtered off and dried to obtain **17e** as a light-brown solid. Yield 70% (0.811 g); light-brown solid; mp 274 – 280 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.45 (s, 1H, NH), 9.82 (s, 1H, NH), 8.52 (d, 1H, *J* = 8.6 Hz, ArH), 7.87 – 7.93 (m, 1H, ArH), 7.80 – 7.87 (m, 1H, ArH), 3.85 (s, 3H, $CH_3$), 3.79 (t, 4H, *J* = 4.4 Hz, 2 × $CH_2$), 2.87 (t, 4H, *J* = 4.5 Hz, 2 × $CH_2$), 2.25 (s, 3H, $CH_3$) ppm.

**Methyl 4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-3-(2-methylmorpholino)benzoate (17f).** Synthesised according to *General procedure B* from 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.82 g, 4.20 mmol) and **16f** (0.700 g, 2.80 mmol). The suspension formed in the reaction mixture was filtered off and the solvent of the filtrate was evaporated under reduced pressure. The crude product was suspended in EtOAc (6 mL) and water (6 mL), filtered off and washed with EtOAc to obtain **17f** (227 mg) as a pale-brown solid. Yield 19% (227 mg); white solid; mp 232 – 235 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.45 (s, 1H, NH), 9.83 (s, 1H, NH), 8.53 (d, 1H, *J* = 8.6 Hz, ArH), 7.80 – 7.89 (m, 2H, 2 × ArH), 3.90 (d, 1H, *J* = 11.3 Hz, CH), 3.85 (s, 3H, $CH_3$), 3.68 – 3.80 (m, 2H, 2 × CH), 2.89 (d, 1H, *J* = 11.1 Hz, CH), 2.76 – 2.85 (m, 2H, 2 × CH), 2.52 – 2.58 (m, 1H, CH), 2.24 (s, 3H, $CH_3$), 1.12 (d, 3H, *J* = 6.1 Hz, $CH_3$) ppm.

**Methyl 4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-3-(2,6-dimethylmorpholino)benzoate (17g).** Synthesised according to *General procedure B* from 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (220 mg, 1.13 mmol) and **16g** (200 mg, 0.760 mmol). The suspension formed in the reaction mixture was filtered off, washed with dichloromethane and dried to obtain **17g** (288 mg) as a white solid. Yield 86% (288 mg); white solid; mp 277 – 279 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.46 (s, 1H, NH), 9.84 (s, 1H, NH), 8.54 (d, 1H, *J* = 8.5 Hz, ArH), 7.85 (d, 1H, *J* = 2.0 Hz, ArH), 7.83 (dd, 1H, *J* = 8.6, 2.0 Hz, ArH), 3.85 (s, 3H, $CH_3$), 3.78 – 3.84 (m, 2H, 2 × CH), 2.85 – 2.89 (m, 2H, 2 × CH), 2.42 – 2.47 (m, 2H, 2 × CH), 2.24 (s, 3H, $CH_3$), 1.12 (d, 6H, *J* = 6.3 Hz, 2 × $CH_3$) ppm.

**Methyl 4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-3-(4-phenylpiperazin-1-yl)benzoate (17h).** To a suspension of 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (224 mg, 1.16 mmol) in anhydrous dichloromethane (15 mL), oxalyl chloride (413 µL, 4.82 mmol) was added dropwise and the reaction mixture was stirred at rt under argon atmosphere overnight. The solvent was evaporated under reduced pressure, **16h** (300 mg, 0.963 mmol), anhydrous pyridine (2 mL) and anhydrous dichloromethane (15 mL) were added and the reaction mixture was stirred at rt under argon atmosphere for 15 h. The solvent was removed *in vacuo*, to the residue ethyl acetate and water were added and the formed precipitate was filtered off, washed with methanol and dried. Yield 32% (150 mg); light grey solid; mp 218 – 221 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.48 (s, 1H, NH), 9.88 (s, 1H, NH), 8.54 (d, 1H, *J* = 8.6 Hz, ArH), 7.92 (d, 1H, *J* = 2.0 Hz, ArH), 7.85 (dd, 1H, *J* = 2.0, 8.6 Hz, ArH),

7.30 – 7.23 (m, 2H, 2 × ArH), 7.05 – 6.99 (m, 2H, 2 × ArH), 6.84 (t, 1H, $J$ = 7.2 Hz, ArH), 3.86 (s, 3H, $CH_3$), 3.40 (4H, overlapped with the signal for water, 2 × $CH_2$), 3.04 (t, 4H, $J$ = 4.9 Hz, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$) ppm. IR (ATR): **ν** 3804, 3679, 3633, 3307, 2181, 2106, 2046, 2010, 1951, 1860, 1689, 1629, 1560, 1511, 1434, 1188, 1101, 1055, 990, 945, 882, 841, 771, 731, 668 $cm^{-1}$.

**Methyl 3-(3-(((*tert*-butoxycarbonyl)amino)methyl)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoate (17i).** Synthesised according to *General procedure B* from 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (695 mg, 3.58 mmol) and **16i** (1.24 g, 3.41 mmol). The solid was purified with flash column chromatography using dichloromethane/methanol (50/1) as an eluent to give **17i** (0.450 g) as white solid. Yield 24% (0.450 g); white solid; mp 192 – 194 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.47 (s, 1H, NH), 9.91 (s, 1H, NH), 8.56 (d, 1H, $J$ = 8.4 Hz, Ar-H-5), 7.91 (d, 1H, $J$ = 1.9 Hz, Ar-H-2), 7.85 (dd, 1H, $J$ = 8.4, 1.9 Hz, Ar-H-6), 6.93 (t, 1H, $J$ = 5.7 Hz, NHBoc), 3.89 (s, 3H, $COOCH_3$), 2.87 – 3.02 (m, 3H, 3 × CH), 2.76 – 2.85 (m, 1H, CH), 2.64 – 2.69 (m, 1H, CH), 2.39 – 2.45 (m, 1H, CH), 2.28 (s, 3H, $CH_3$), 1.87 – 1.99 (m, 1H, CH), 1.77 – 1.86 (m, 2H, 2 × CH), 1.62 – 1.75 (m, 1H, CH), 1.36 (s, 9H, tBu), 1.05 – 1.13 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.7 (COOMe), 156.6, 155.6, 142.4, 138.3, 130.0, 126.9, 124.3, 122.4, 118.7, 118.4, 110.0, 109.8, 108.7, 77.4 ($CCH_3$), 57.1, 53.3, 52.0, 43.6, 37.3, 28.1, 27.6, 25.4, 10.7 ppm. IR (ATR): ν 3381, 3292, 2933, 1696, 1648, 1592, 1518, 1491, 1437, 1414, 1365, 1260, 1169, 1109, 1007, 973, 944, 891, 760, 687 $cm^{-1}$. MS (ESI) *m/z* = 539.18 ($[M+H]^+$). HRMS for $C_{25}H_{33}Cl_2N_4O_5$: calculated 539.1815, found 539.1823. HPLC: Agilent Zorbax 80Å Extend-C18 (3.5 μm, 4.6 × 150 mm); mobile phase: 5% acetonitrile in 0.1% TFA to 8 min, 5-95% of acetonitrile from 8 to 15 min, 95% acetonitrile from 15 to 16 min, 95-5% of acetonitrile from 16 to 18 min, 5% of acetonitrile from 18 to 21 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 15.577 min (99.6% at 254 nm).

**3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18a).** To a solution of compound **17a** (201 mg, 0.391 mmol) in a mixture of methanol (10 mL) and tetrahydrofuran (7 mL) 1 M NaOH (1.56 mL, 1.56 mmol) was added and the mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure, to the residue water (10 mL) was added and the mixture was acidified to pH 4 with 1 M HCl. The water phase was extracted with ethyl acetate (20 mL), the organic phase was washed with brine (10 mL), dried over $Na_2SO_4$ and the solvent was removed under reduced pressure. The crude product was triturated with diethyl ether and the undissolved solid was filtered off and dried to obtain **18a** as pale pink solid (70 mg). Yield 35% (70 mg); pale pink solid; mp 260 – 262 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.87 (s, 1H, COOH), 12.45 (s, 1H, NH), 9.78 (s, 1H, NH), 8.49 (d, 1H, $J$ = 8.6 Hz, ArH), 7.77 – 7.88 (m, 2H, 2 × ArH), 3.42 – 3.63 (m, 4H, 2 × $CH_2$), 2.75 – 2.91 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.44 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.7, 156.6, 153.8, 141.1, 137.8, 129.9, 127.3, 125.7, 122.6, 118.7, 118.7, 109.8, 108.6, 79.1, 51.9, 28.0, 10.8 ppm. One peak not seen. IR (ATR): ν 3261, 2980, 2363, 1713,

1644, 1609, 1594, 1523, 1489, 1456, 1429, 1410, 1376, 1366, 1338, 1280, 1248, 1211, 1199, 1169, 1137, 1105, 1088, 1042, 1005, 956, 897, 865, 833, 800, 765, 724, 700, 646, 629, 619, 609 $cm^{-1}$. MS (ESI) m/z = 495.1 ($[M-H]^-$). HRMS for $C_{22}H_{25}N_4O_5Cl_2$: calculated 495.1202, found 495.1206. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 14.030 min (96.3% at 280 nm).

**(*S*)-3-(3-((*tert*-Butoxycarbonyl)amino)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18c).** To a solution of compound **17c** (203 mg, 0.391 mmol) in a mixture of methanol (5 mL) and tetrahydrofuran (4 mL) 1 M NaOH (3.13 mL, 3.13 mmol) was added and the mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure, to the residue water (10 mL) was added and the mixture was acidified to pH 4 with 1 M HCl. The water phase was extracted with ethyl acetate (20 mL), the organic phase was washed with brine (10 mL), dried over $Na_2SO_4$ and the solvent was removed under reduced pressure to obtain **18c** (101 mg) as pale-yellow solid. Yield 50% (101 mg); pale yellow solid; mp 231 – 233 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.89 (br s, 1H, COOH), 12.46 (s, 1H, NH), 9.83 (s, 1H, NH), 8.49 (d, 1H, *J* = 8.5 Hz, ArH-5), 7.75 – 7.91 (m, 2H, 2 × ArH), 6.80 – 6.99 (m, 1H, NHBoc), 3.55 – 3.67 (m, 1H, CH), 2.91 – 3.03 (m, 1H, CH), 2.78 – 2.88 (m, 1H, CH), 2.53 – 2.62 (m, 2H, $CH_2$), 2.25 (s, 3H, $CH_3$), 1.75 – 1.96 (m, 2H, $CH_2$), 1.60 – 1.74 (m, 1H, CH), 1.36 (s, 9H, tBu), 1.23 – 1.30 (m, 1H, CH) ppm. IR (ATR): ν 3326, 2959, 2362, 2163, 2032, 2001, 1969, 1717, 1686, 1639, 1588, 1519, 1490, 1437, 1405, 1365, 1318, 1289, 1262, 1173, 1122, 1107, 1082, 1068, 1038, 1026, 997, 960, 928, 877, 864, 839, 805, 765, 731, 676, 648, 625, 608 $cm^{-1}$. $[\alpha]^{20}_D$ = + 0.44° (c 0.297, THF). MS (ESI) m/z = 511.2 ($[M+H]^+$). HRMS for $C_{23}H_{29}N_4O_5Cl_2$: calculated 511.1515, found 511.1512. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 13.706min (97.7% at 280 nm).

**3-((1-(*tert*-Butoxycarbonyl)piperidin-4-yl)amino)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18d).** To a solution of **17d** (40 mg, 0.076 mmol) in methanol, 1 M NaOH (0.761 mL, 0.761 mmol) was added and the reaction mixture was stirred at 60 °C for 15 h. The solvent was evaporated *in vacuo* and the residue was neutralised with 1 M HCl to pH 7. The precipitate that formed was filtered off and dried to obtain **18d** (30 mg) as light brown solid. Yield 77% (30 mg); light brown solid. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.60 (br s, 1H, COOH), 12.30 (s, 1H, NH), 8.93 (s, 1H, NH), 7.80 (d, 1H, *J* = 8.3 Hz, ArH), 7.33 – 7.43 (m, 2H, 2 × ArH), 5.07 (d, 1H, *J* = 6.9 Hz, NH), 3.86 (d, 2H, *J* = 13.6 Hz, $CH_2$), 3.48 (d, 1H, *J* = 9.7 Hz, CH), 2.97 (s, 2H, $CH_2$), 2.24 (s, 3H, $CH_3$), 1.88 (d, 2H, *J* = 12.7 Hz, $CH_2$), 1.40 (s, 9H, tBu), 1.25 – 1.38 (m, 2H, $CH_2$) ppm.

**4-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-3-(4-phenylpiperazin-1-yl)benzoic acid (18h).** To a solution of **17h** (30 mg, 0.062 mmol) in methanol, 1 M NaOH (0.616 mL, 0.616 mmol) was added and the reaction mixture was stirred at 60 °C for 15 h. The solvent was evaporated *in vacuo* and the residue was neutralised with 1 M HCl to pH 7. The precipitate that formed was filtered off to afford

**17h** (28.8 mg) as light brown solid. Yield 99% (28.8 mg); light brown solid; mp >300 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.90 (s, 1H, COOH), 12.47 (s, 1H, NH), 9.87 (s, 1H, NH), 8.51 (d, 1H, *J* = 8.8 Hz, ArH), 7.91 (s, 1H, ArH), 7.84 (s, 1H, ArH), 7.27 (s, 2H, 2 × ArH), 7.03 (s, 2H, 2 × ArH), 6.84 (s, 1H, ArH), 3.33 (4H, overlapped with the signal for water, 2 × $CH_2$), 3.04 (s, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$) ppm. IR (ATR): ν 3257, 3176, 3132, 3073, 2961, 2883, 2825, 1749, 1680, 1632, 1586, 1557, 1518, 1492, 1438, 1409, 1375, 1289, 1271, 1254, 1234, 1154, 1134, 1091, 1044, 966, 922, 883, 767 cm$^{-1}$. HRMS (ESI$^+$) *m/z* for $C_{23}H_{23}Cl_2N_4O_3$ ([M+H]$^+$): calculated 473.1142, found 473.1138. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Extend-C18 column: 3.5 ***μ***m, 4.6 × 150 mm): $t_r$ 15.437 min (95.50 % at 254 nm).

**3-(3-(((*tert*-Butoxycarbonyl)amino)methyl)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18i).** To a solution of compound **17i** (180 mg, 0.33 mmol) in a mixture of methanol (10 mL) and tetrahydrofuran (10 mL) 1 M NaOH (1.32 mL, 1.32 mmol) was added and the mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure, EtOAc (10 mL) and 1 M HCl (10 mL) were added to the residue. The phases were separated, the organic phase was washed with brine (2 × 10 mL), dried over $Na_2SO_4$, filtered and the solvent removed under reduced pressure to afford **18i** (160 mg) as white solid. Yield 92% (160 mg); white solid; mp 221 – 224 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.86 (br s, 1H, COOH), 12.44 (s, 1H, NH), 9.86 (s, 1H, NHAr), 8.49 (d, 1H, *J* = 8.4 Hz, Ar-H-5), 7.86 (d, 1H, *J* = 1.8 Hz, Ar-H-2), 7.78 (dd, 1H, *J* = 8.4, 1.8 Hz, Ar-H-6), 6.90 (t, 1H, *J* = 5.8 Hz, NHBoc), 2.81 – 2.98 (m, 3H, 3 × CH), 2.69 – 2.80 (m, 1H, CH), 2.59 – 2.69 (m, 1H, CH), 2.35 – 2.40 (m, 1H, CH), 2.24 (s, 3H, $CH_3$), 1.83 – 1.93 (m, 1H, CH), 1.72 – 1.82 (m, 2H, 2 × CH), 1.59 – 1.71 (m, 1H, CH), 1.31 (s, 9H, tBu), 0.99 – 1.09 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.9, 156.6, 155.6, 142.3, 137.8, 129.9, 126.9, 125.7, 122.6, 118.7, 118.3, 109.9, 108.6, 77.4, 57.2, 53.3, 43.6, 37.3, 28.1, 27.6, 25.4, 10.7 ppm. IR (ATR): ν 3271, 2959, 2808, 1709, 1675, 1641, 1603, 1519, 1487, 1435, 1300, 1254, 1166, 1091, 728, 594 cm$^{-1}$. MS (ESI) *m/z* = 525.17 ([M+H]$^+$). HRMS for $C_{24}H_{31}Cl_2N_4O_5$: calculated 525.1666, found 525.1662. HPLC: Agilent Zorbax 80Å Extend-C18 (3.5 μm, 4.6 × 150 mm); mobile phase: 5% acetonitrile in 0.1% TFA to 8 min, 5-95% of acetonitrile from 8 to 15 min, 95% acetonitrile from 15 to 16 min, 95-5% of acetonitrile from 16 to 18 min, 5% of acetonitrile from 18 to 21 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 13.587 min (99.4% at 254 nm).

**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperazin-1-ium chloride (19a).** Compound **17a** (102 mg, 0.200 mmol) was dissolved in 1 M HCl solution in acetic acid (5 mL) and the mixture was stirred at rt for 5 h. The solvent was removed under reduced pressure, the solid residue was sequentially triturated with diethyl ether and water, and the undissolved solid was filtered off and dried to obtain **19a** (71 mg) as white solid. Yield 35% (71 mg); white solid; mp 244 – 248 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.51 (s, 1H,

NH), 9.67 (s, 1H, NH), 9.07 (s, 2H, $NH_2^+$), 8.53 (d, 1H, *J* = 8.6 Hz, ArH), 7.87 (dd, 1H, *J* = 8.6, 1.9 Hz, ArH), 7.82 (d, 1H, *J* = 1.9 Hz, ArH), 3.86 (s, 3H, $COOCH_3$), 3.22 – 3.31 (m, 4H, 2 × $CH_2$), 3.05 – 3.14 (m, 4H, 2 × $CH_2$), 2.25 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.5, 156.7, 140.4, 138.2, 130.0, 127.6, 124.5, 122.3, 119.1, 118.7, 110.2, 108.7, 52.1, 48.7, 43.5, 10.8 ppm. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 128.1, 122.7, 119.6, 52.6, 49.3, 43.9, 11.2 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 128.1, 122.7, 119.6, 52.6, 49.3 (negative), 43.9 (negative), 11.2 ppm. IR (ATR): ν 3357, 3291, 3162, 3124, 2954, 2853, 2773, 2720, 2607, 2451, 2363, 1767, 1710, 1632, 1615, 1592, 1573, 1525, 1491, 1446, 1405, 1375, 1355, 1324, 1313, 1284, 1272, 1254, 1225, 1192, 1132, 1120, 1104, 1091, 1043, 1017, 1001, 983, 962, 947, 894, 859, 817, 761, 730, 711, 655, 639, 615 $cm^{-1}$. MS (ESI) m/z = 411.1 ($[M-H]^-$). HRMS for $C_{18}H_{21}N_4O_3Cl_2$: calculated 411.0991, found 411.0998. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 6.367 min (100% at 280 nm).

**(*S*)-1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperidin-3-aminium chloride (19c).** Compound **17c** (102 mg, 0.209 mmol) was dissolved in 1 M HCl solution in acetic acid (5 mL) and the mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure, the solid residue was triturated with diethyl ether, and the undissolved solid was filtered off and dried to obtain **19c** (79 mg) as brown solid. Yield 74% (79 mg); brown solid; mp 201 – 203 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.55 (s, 1H, NH), 9.64 (s, 1H, NH), 8.47 (d, *J* = 8.5 Hz, ArH), 8.16 (br s, 3H, $NH_3^+$), 7.79 – 7.90 (m, 2H, 2 × ArH), 3.86 (s, 3H, $CH_3$), 3.26 – 3.36 (m, 1H, CH), 3.14 – 3.23 (m, 1H, CH), 2.86 – 2.94 (m, 1H, CH), 2.65 – 2.79 (m, 2H, $CH_2$), 2.25 (s, 3H, $CH_3$), 2.05 – 2.16 (m, 1H, CH), 1.85 – 1.92 (m, 1H, CH), 1.63 – 1.79 (m, 1H, CH), 1.43 – 1.58 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.6, 156.6, 141.3, 137.8, 129.9, 127.0, 124.5, 122.1, 119.3, 118.6, 110.3, 108.7, 54.7, 52.3, 52.1, 47.5, 27.5, 23.6, 10.7 ppm. IR (ATR): ν 2949, 2153, 2013, 1987, 1970, 1712, 1636, 1589, 1515, 1489, 1438, 1414, 1376, 1318, 1287, 1257, 1204, 1105, 1041, 994, 941, 873, 844, 765, 731, 657, 608 $cm^{-1}$. $[\alpha]^{20}_D$ = – 0.72° (c 0.337, THF). MS (ESI) m/z = 425.1 ($[M+H]^+$). HRMS for $C_{19}H_{23}N_4O_3Cl_2$: calculated 425.1147, found 425.1145. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 7.370 min (98.9% at 280 nm).

**(1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperidin-3-yl)methanaminium chloride (19i).** Compound **17i** (100 mg, 0.851 mmol) was dissolved in 4 M HCl solution in dioxane (10 mL) and the mixture was stirred for 4 h. After the completion of the reaction the solvent was removed under reduced pressure and the obtained solid was washed with diethyl ether (2 × 5 mL) to give **19i** (70 mg) as beige solid. Yield 79% (70 mg); beige solid; mp 194 – 198 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.53 (s, 1H, NH), 9.93 (s, 1H, NH), 8.58 (d, 1H, *J* = 8.4 Hz, Ar-H-3), 8.02 (br s, 3H, $NH_3^+$), 7.94 (d, 1H, *J* = 1.8 Hz Ar-H-6), 7.89 (dd, 1H,

*J* = 8.4, 1.8 Hz, Ar-H-4), 3.91 (s, 3H, $COOCH_3$), 3.08 – 3.14 (m, 1H, CH), 2.89 – 2.98 (m, 1H, CH), 2.76 – 2.87 (m, 2H, 2 × CH), 2.58 – 2.68 (m, 2H, 2 × CH), 2.30 (s, 3H, $CH_3$), 2.07 – 2.19 (m, 1H, CH), 1.90 – 2.00 (m, 1H, CH), 1.80 – 1.89 (m, 1H, CH), 1.68 – 1.79 (m, 1H, CH), 1.16 – 1.25 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.7, 156.6, 142.1, 138.4, 130.1, 127.1, 124.3, 122.7, 118.7, 118.5, 110.0, 108.7, 55.5, 53.5, 52.1, 41.8, 34.9, 27.1, 25.0, 10.8 ppm. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 127.6, 123.2, 119.0, 56.1, 54.0, 52.5, 42.3, 35.4, 27.6, 25.5, 11.3 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 127.6, 123.2, 119.0, 56.1 (negative), 54.0 (negative), 52.5, 42.3 (negative), 35.4, 27.6 (negative), 25.5 (negative), 11.3 ppm. IR (ATR): ν 2948, 1717, 1640, 1590, 1517, 1488, 1414, 1289, 1257, 1199, 1121, 1036, 1007, 764 cm$^{-1}$. MS (ESI) *m/z* = 439.13 ([M+H]$^+$). HRMS for $C_{20}H_{25}Cl_2N_4O_3$: calculated 439.1293, found 439.1298. HPLC: Agilent Zorbax 80Å Extend-C18 (3.5 µm, 4.6 × 150 mm); mobile phase: 5% acetonitrile in 0.1% TFA to 8 min, 5-95% of acetonitrile from 8 to 15 min, 95% acetonitrile from 15 to 16 min, 95-5% of acetonitrile from 16 to 18 min, 5% of acetonitrile from 18 to 21 min; flow rate 1.0 mL/min; injection volume: 10 µL; $t_R$: 9.373 min (95.6% at 254 nm).

**4-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (20a).** Compound **18a** (50 mg, 0.100 mmol) was dissolved in a mixture of 1 M HCl solution in acetic acid (5 mL), tetrahydrofuran (2 mL) and dichloromethane (4 mL) and the mixture was stirred at rt for 5 h. The solvent was removed under reduced pressure, the solid residue was sequentially triturated with diethyl ether and water, and the undissolved solid was filtered off and dried to obtain **20a** (16 mg) as pale pink solid. Yield 32% (16 mg); pale pink solid; mp 258 – 261 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.50 (s, 1H, NH), 9.68 (s, 1H, NH), 8.50 (d, 1H, *J* = 8.4 Hz, ArH), 7.76 – 7.92 (m, 2H, 2 × ArH), 3.22 – 3.29 (m, 4H, 2 × $CH_2$), 3.03-3.11 (m, 4H, 2 × $CH_2$), 2.25 (s, 3H, $CH_3$) ppm. Signal for $NH_2^+$ is overlapping with the signal for water. Signal for COOH proton not seen. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 183.4, 178.3, 166.7, 156.6, 140.4, 137.8, 129.9, 127.7, 122.4, 118.8, 110.1, 108.7, 49.0, 43.6, 10.8 ppm. IR (ATR): ν 3293, 3005, 2822, 2470, 2363, 1684, 1651, 1588, 1529, 1488, 1457, 1406, 1374, 1316, 1285, 1229, 1192, 1142, 1120, 1089, 1047, 963, 923, 885, 849, 787, 771, 726, 704, 647, 634, 606 cm$^{-1}$. MS (ESI) m/z = 395.1 ([M-H]$^-$). HRMS for $C_{17}H_{17}N_4O_3Cl_2$: calculated 395.0678, found 395.0670. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 4.769 min (98.1% at 280 nm).

**(*S*)-1-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperidin-3-aminium chloride (20c).** Compound **18c** (70 mg, 0.14 mmol) was dissolved in 1 M HCl solution in acetic acid (5 mL) and the mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure, the solid residue was triturated with diethyl ether, and the undissolved solid was filtered off and dried to obtain **20c** (64 mg) as pale-yellow solid. Yield 91% (64 mg); pale yellow solid; mp 240 – 244 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.54 (br s, 1H, NH), 9.63 (s, 1H, NH), 8.45 (d, *J* = 9.1 Hz, ArH), 7.77 – 7.85 (m, 2H, 2 × ArH), 3.28 – 3.33 (m, 1H, CH), 3.14 – 3.21 (m, 1H, CH), 2.85 – 2.93 (m,

1H, CH), 2.64 – 2.78 (m, 2H, $CH_2$), 2.25 (s, 3H, $CH_3$), 2.04 – 2.14 (m, 1H, CH), 1.84 – 1.92 (m, 1H, CH), 1.63 – 1.76 (m, 1H, CH), 1.44 – 1.58 (m, 1H, CH) ppm. Signals for COOH and $NH_3^+$ protons not seen. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.7, 156.6, 141.2, 137.4, 129.8, 127.1, 125.8, 122.2, 119.2, 118.7, 110.3, 108.7, 54.8, 52.3, 47.6, 27.5, 23.6, 10.7 ppm. IR (ATR): ν 2926, 2154, 2050, 1992, 1682, 1634, 1589, 1518, 1490, 1406, 1322, 1249, 1201, 1125, 1107, 1090, 1043, 1017, 960, 942, 836, 766, 743, 728, 649, 608 cm$^{-1}$. $[\alpha]^{20}_D$ = – 0.55° (c 0.264, THF). MS (ESI) m/z = 411.1 ($[M+H]^+$). HRMS for $C_{18}H_{21}N_4O_3Cl_2$: calculated 411.0991, found 411.1002. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 μm, 4.6 × 150 mm): $t_r$ 5.947 min (99.7% at 280 nm).

**4-((5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)amino)piperidin-1-ium chloride (20d).** To a suspension of **18d** (30 mg, 0.059 mmol) in 1,4-dioxane (1 mL), 4 M HCl in 1,4-dioxane (4 mL) was added and the reaction mixture was stirred at rt for 4 h. The precipitate that formed was filtered off, washed with diethyl ether and dried. Yield 94% (24.7 mg); pale yellow solid; mp 260 – 265 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.52 (s, 2H, NH, COOH), 9.14 (s, 1H, NH), 8.79 (s, 1H, NH), 8.65 (s, 1H, NH), 7.83 (d, 1H, *J* = 8.1 Hz, ArH), 7.35 – 7.44 (m, 2H, 2 × ArH), 3.64 (1H, overlapped with the signal for water, CH), 3.25 – 3.35 (m, 3H, CH, $CH_2$), 3.05 (q, 2H, *J* = 10.6, 11.3 Hz, $CH_2$), 2.25 (s, 3H, $CH_3$), 2.05 (d, 2H, *J* = 13.9 Hz, $CH_2$), 1.60 – 1.75 (m, 2H, $CH_2$) ppm. Signal for one NH proton not seen. IR (ATR): **ν** 3117, 2955, 2786, 2323, 1722, 1657, 1620, 1581, 1519, 1500, 1471, 1402, 1371, 1335, 1311, 1282, 1218, 1179, 1135, 1117, 1090, 1076, 1055, 1031, 992, 965, 933, 901, 872, 846, 803, 763, 748, 725, 638, 606 cm$^{-1}$. HRMS ($ESI^+$) *m/z* for $C_{18}H_{21}Cl_2N_4O_3$ ($[M+H]^+$): calculated 411.0985, found 411.0980. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Extend-C18 column: 3.5 ***μ***m, 4.6 × 150 mm): $t_r$ 12.480 min (95.11% at 254 nm).

**(1-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperidin-3-yl)methanaminium chloride (20i).** Compound **18i** (59 mg, 0.11 mmol) was dissolved in 4 M HCl solution in 1,4-dioxane (8 mL). The mixture was stirred for 12 h. The solvent was removed under reduced pressure and the solid was washed with diethyl ether (2 × 5 mL) to obtain **20i** (49 mg) as white solid. Yield 96% (49 mg); white solid; mp 234 – 238 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.48 (s, 1H, NH), 9.87 (s, 1H, NH), 8.50 (d, 1H, *J* = 8.4 Hz, Ar-H-3), 7.97 (br s, 3H, $NH_3^+$), 7.88 (d, 1H, *J* = 1.8 Hz, Ar-H-6), 7.81 (dd, 1H, *J* = 8.4, 1.8 Hz, Ar-H-4), 3.03 – 3.10 (m, 1H, CH), 2.83 – 2.92 (m, 1H, CH), 2.71 – 2.80 (m, 2H, 2 × CH), 2.54 – 2.63 (m, 3H, *J* = 9.0 Hz, 3 × CH), 2.25 (s, 3H, $CH_3$), 2.02 – 2.13 (m, 1H, CH), 1.85 – 1.95 (m, 1H, CH), 1.75 – 1.83 (m, 1H, CH), 1.63 – 1.73 (m, 1H, CH), 1.09 – 1.19 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 166.7, 156.6, 141.9, 137.9, 129.9, 127.1, 125.6, 122.8, 118.7, 118.4, 110.0, 108.6, 55.6, 53.6, 41.8, 34.8, 27.2, 25.0, 10.8 ppm. IR (ATR): ν 3446, 3070, 2888, 1722, 1635, 1605, 1521, 1422, 1378, 1219, 1201, 1140, 1041, 837, 814, 752, 730, 660, 546 cm$^{-1}$.

MS (ESI) *m/z* = 425.11 ([M+H]$^+$). HRMS for $C_{19}H_{23}Cl_2N_4O_3$: calculated 425.1142, found 425.1137. HPLC: Agilent Zorbax 80Å Extend-C18 (3.5 μm, 4.6 × 150 mm); mobile phase: 5% acetonitrile in 0.1% TFA to 8 min, 5-95% of acetonitrile from 8 to 15 min, 95% acetonitrile from 15 to 16 min, 95-5% of acetonitrile from 16 to 18 min, 5% of acetonitrile from 18 to 21 min; flow rate 1.0 mL/min; injection volume: 10 μL; $t_R$: 8.557 min (99.2% at 254 nm).

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(hydrazinecarbonyl)phenyl)piperazine-1-carboxylate (21a).** To the solution of **17a** (0.71 g, 1.38 mmol) in a mixture of MeOH (20 mL) and THF (10 mL) in a high-pressure tube hydrazine hydrate (64%, 4.71 mL, 96.8 mmol) was added. The tube was sealed and reaction mixture was stirred at 120 °C for 15 h. The tube was cooled down to rt and the precipitate was filtered off and dried, to obtain **21a** (0.579 g) as white solid. Yield 82% (0.579 g); white solid; mp 277 – 280 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.42 (s, 1H, NH), 9.74 (s, 1H, NH), 9.71 (s, 1H, NH), 8.43 (d, 1H, *J* = 8.6 Hz, ArH), 7.84 (s, 1H, ArH), 7.70 (d, 1H, *J* = 8.6 Hz, ArH), 4.47 (s, 2H, $NH_2$), 3.47 – 3.57 (m, 4H, 2 × $CH_2$), 2.77 – 2.85 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.44 (s, 9H, tBu) ppm.

***tert*-Butyl (*S*)-(1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(hydrazinecarbonyl)phenyl)pyrrolidin-3-yl)carbamate (21b).** To a solution of **17b** (540 mg, 1.06 mmol) in a mixture of MeOH (11 mL) and THF (8 mL) in a high-pressure tube hydrazine hydrate (64%, 5.14 mL, 0.106 mol) was added. The tube was sealed and reaction mixture was stirred at 120 °C for 15 h. The tube was cooled down to rt, the solvent was removed under reduced pressure and the solid residue was triturated with methanol, the undissolved solid was filtered off and dried, to obtain **21b** (390 mg) as white solid. Yield 72% (390 mg); white solid; mp 224 – 228 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.37 (s, 1H, NH), 9.72 (s, 1H, NH), 9.47 (s, 1H, NH), 8.22 (d, 1H, *J* = 8.5 Hz, ArH), 7.71 (d, 1H, *J* = 2.0 Hz, ArH), 7.56 (dd, 1H, *J* = 8.5, 2.0 Hz, ArH), 7.17 (d, 1H, *J* = 6.6 Hz, NHBoc), 4.46 (s, 2H, $NH_2$), 4.05 – 4.14 (m, 1H, CH), 3.27 – 3.33 (m, 1H, CH), 3.12 – 3.19 (m, 1H, CH), 2.99 – 3.05 (m, 1H, CH), 2.80 – 2.92 (m, 1H, CH), 2.23 (s, 3H, $CH_3$), 2.14 – 2.21 (m, 1H, CH), 1.80 – 1.88 (m, 1H, CH), 1.39 (s, 9H, tBu) ppm. IR (ATR): ν 3342, 3307, 2980, 2847, 2361, 1721, 1681, 1643, 1620, 1602, 1512, 1491, 1416, 1366, 1329, 1276, 1215, 1172, 1118, 1086, 1036, 1004, 958, 897, 833, 761, 730, 656, 624, 609, 571 cm$^{-1}$. $[\alpha]_D^{25}$ – 0,314 (c 0,373, DMF). MS (ESI) m/z = 511.3 ([M+H]$^+$).

***tert*-Butyl (*S*)-(1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(hydrazinecarbonyl)phenyl)piperidin-3-yl)carbamate (21c).** To a solution of **17c** (295 mg, 0.561 mmol) in a mixture of MeOH (6 mL) and THF (5 mL) in a high-pressure tube hydrazine hydrate (64%, 2.72 mL, 56.1 mmol) was added. The tube was sealed and reaction mixture was stirred at 120 °C for 15 h. The tube was cooled down to rt, the solvent was removed under reduced pressure and the solid residue was triturated with methanol, the undissolved solid was filtered off and dried, to obtain **21c** (295 mg) as yellow solid. Yield 66% (295 mg); yellow solid; mp 224 – 228 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ

9.75 (s, 2H, 2 × NH), 8.42 (d, *J* = 8.6 Hz, 1H, ArH), 7.79 (d, *J* = 2.0 Hz, 1H, ArH), 7.68 (dd, *J* = 8.6, 2.0 Hz, 1H, ArH), 6.91 (d, *J* = 7.5 Hz, 1H, NHBoc), 4.47 (s, 2H, $NH_2$), 3.57 – 3.68 (m, 1H, CH), 2.90 – 2.99 (m, 1H, CH), 2.76 – 2.84 (m, 1H, CH), 2.55 – 2.64 (m, 1H, CH), 2.24 (s, 3H, $CH_3$), 1.74 – 1.94 (m, 2H, $CH_2$), 1.59 – 1.73 (m, 1H, CH), 1.36 (s, 9H, tBu), 1.20 – 1.29 (m, 1H, CH) ppm. Signals for one CH and one NH proton not seen. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.2, 156.6, 154.8, 141.4, 136.2, 129.7, 128.2, 124.4, 120.7, 118.9, 118.4, 109.7, 108.5, 77.7, 57.7, 53.0, 47.6, 29.4, 28.2, 24.5, 10.8 ppm. IR (ATR): ν 3309, 3198, 2968, 1708, 1641, 1509, 1415, 1367, 1307, 1236, 1163, 1040, 946, 838, 766, 637, 612 cm$^{-1}$. $[\alpha]^{20}_D$ = – 0.70° (c 0.321, THF). MS (ESI) m/z = 523.2 ($[M-H]^-$). HRMS for $C_{23}H_{29}N_6O_4Cl_2$: calculated 523.1627, found 523.1627. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 μm, 4.6 × 150 mm): $t_r$ 7.883 min (95.8% at 254 nm).

***tert*-Butyl 4-((2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(hydrazinecarbonyl)phenyl)amino)piperidine-1-carboxylate (21d).** To a suspension of **17d** (110 mg, 0.209 mmol) in a mixture of methanol and THF (2:1, 15 mL), hydrazine monohydrate (419 μL, 8.37 mmol) was added and the reaction mixture was stirred in a pressure tube at 120 °C for 48 h. The precipitate that was formed was filtered off and dried. Yield 64% (70 mg); white solid; mp 247 – 250 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.25 (s, 1H, NH), 9.69 (s, 1H, NH), 8.80 (s, 1H, NH), 7.63 (d, *J* = 8.3 Hz, 1H, ArH), 7.27 (d, *J* = 1.9 Hz, 1H, ArH), 7.20 (dd, *J* = 1.9, 8.3 Hz, ArH), 5.02 (d, 1H, *J* = 7.2 Hz, NH), 4.45 (s, 2H, $NH_2$), 3.89 (d, 2H, *J* = 13.4 Hz, $CH_2$), 2.96 (s, 2H, $CH_2$), 2.42 (s, 1H, CH), 2.23 (s, 3H, $CH_3$), 1.84 – 1.96 (m, 2H, $CH_2$), 1.40 (s, 9H, tBu), 1.32 (t, 2H, *J* = 11.7 Hz, $CH_2$) ppm. IR (ATR): **ν** 3324, 2200, 2184, 1978, 1871, 1682, 1635, 1561, 1513, 1462, 1431, 1364, 1307, 1274, 1213, 1130, 1099, 1056, 989, 945, 887, 841, 773, 729, 670, 651 cm$^{-1}$.

**3,4-Dichloro-*N*-(4-(hydrazinecarbonyl)-2-morpholinophenyl)-5-methyl-1*H*-pyrrole-2-carboxamide (21e).** To the solution of **17e** (0.70 g, 1.70 mmol) in a mixture of MeOH (15 mL) and THF (10 mL) in a high-pressure tube hydrazine hydrate (64%, 5.77 mL, 119 mmol) was added. The tube was sealed and the reaction mixture was stirred at 120 °C for 15 h. The tube was cooled to rt and the precipitate was filtered off and dried. The crude product was triturated with methanol, the undissolved solid was filtered off and dried, to obtain **21e** (0.519 g) as an off-white solid. Yield 74% (0.519 g); off-white solid; mp 281 – 283 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.42 (s, 1H, NH), 9.76 (s, 1H, NH), 9.74 (s, 1H, NH), 8.44 (d, *J* = 8.5 Hz, 1H, ArH), 7.85 (d, *J* = 1.9 Hz, 1H, ArH), 7.69 (dd, *J* = 8.5, 1.9 Hz, ArH), 4.47 (s, 2H, $NH_2$), 3.77 – 3.82 (m, 4H, 2 × $CH_2$), 2.84 – 2.89 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$) ppm.

**3,4-Dichloro-*N*-(4-(hydrazinecarbonyl)-2-(2-methylmorpholino)phenyl)-5-methyl-1*H*-pyrrole-2-carboxamide (21f).** To the solution of **17f** (420 mg, 0.985 mmol) in a mixture of MeOH (15 mL) and THF (10 mL) in a high-pressure tube hydrazine hydrate (64%, 3.34 mL, 68.6 mmol) was added. The tube was sealed and the reaction mixture was stirred at 120 °C for 15 h. The tube was cooled to rt and

the precipitate was filtered off and dried, to obtain **21f** (311 mg) as a white solid. Yield 74% (311 mg); white solid; mp 282 – 284 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.42 (s, 1H, NH), 9.76 (s, 1H, NH), 9.74 (s, 1H, NH), 8.44 (d, *J* = 8.6 Hz, 1H, ArH), 7.84 (s, 1H, ArH), 7.69 (d, *J* = 8.6 Hz, 1H, ArH), 4.47 (s, 2H, $NH_2$), 3.98 – 3.87 (m, 1H, CH), 3.79 – 3.69 (m, 2H, 2 × CH), 2.92 – 2.74 (m, 3H, 3 × CH), 2.60 – 2.53 (m, 1H, CH), 2.24 (s, 3H, $CH_3$), 1.12 (d, *J* = 6.1 Hz, 3H, $CH_3$) ppm.

**3,4-Dichloro-*N*-(4-(hydrazinecarbonyl)-2-morpholinophenyl)-5-methyl-1*H*-pyrrole-2-carboxamide (21g).** To the solution of **17g** (329 mg, 0.747 mmol) in a mixture of MeOH (10 mL) and THF (7 mL) in a high-pressure tube hydrazine hydrate (64%, 2.54 mL, 52.3 mmol) was added. The tube was sealed and the reaction mixture was stirred at 120 °C for 15 h. The tube was cooled to rt and the precipitate was filtered off and dried, to obtain **21g** (244 mg) as a white solid. Yield 70% (244 mg); white solid; mp > 300 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.37 (s, 1H, NH), 9.78 (s, 1H, NH), 9.73 (s, 1H, NH), 8.46 (d, *J* = 8.6 Hz, 1H, ArH), 7.83 (d, *J* = 2.0 Hz, 1H, ArH), 7.69 (dd, *J* = 8.7, 1.9 Hz, 1H, ArH), 4.47 (s, 2H, $NH_2$), 3.85 – 3.77 (m, 2H, 2 × CH), 2.86 – 2.82 (m, 2H, 2 × CH), 2.48 – 2.44 (m, 2H, 2 × CH), 2.24 (s, 3H, $CH_3$), 1.12 (d, *J* = 6.2 Hz, 6H, 2 × $CH_3$) ppm.

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperazine-1-carboxylate (22a).** To a solution of compound **21a** (0.500 g, 0.980 mmol) in a mixture of DMF (30 mL) and 1,4-dioxane (15 mL) 1,1'-carbonyldiimidazole (0.640 g, 3.93 mmol) was added and the reaction mixture was stirred at 101 °C for 15 h. The solvent was removed under reduce pressure, the crude product was sequentially triturated with acetonitrile, water and THF, the undissolved solid was filtered off and dried. The crude product was crystallized from DMF and dried to obtain **22a** (226 mg) as a white solid. Yield 43% (226 mg); white solid; mp 260 – 263 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.50 (s, 1H, NH), 12.45 (s, 1H, NH), 9.73 (s, 1H, NH), 8.53 (d, *J* = 8.6 Hz, 1H, ArH), 7.69 (s, 1H, ArH), 7.64 (d, *J* = 8.5 Hz, 1H, ArH), 3.52 (s, 4H, 2 × $CH_2$), 2.88 – 2.80 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$), 1.44 (s, 9H, tBu) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 157.0, 154.9, 154.2, 154.0, 153.9, 142.3, 136.9, 130.4, 123.5, 120.1, 119.5, 119.2, 109.1, 79.6, 52.2, 44.3, 28.5, 11.2 ppm. Peaks of two aromatic carbons overlapping. HRMS for $C_{23}H_{27}O_5N_6Cl_2$ ($[M+H]^+$): calculated 537.14099, found 537.14145. HPLC (0–10 min, 10–90% ACN in 0.1% TFA, 10–11 min, 90% ACN in 0.1% TFA, Waters Acquity UPLC HSS C18 column: 1.8 μm, 2.1 × 50 mm): $t_r$ 6.560 min (97.45% at 254 nm, 96.79% at 280 nm).

***tert*-Butyl (*S*)-(1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)pyrrolidin-3-yl)carbamate (22b).** To a solution of compound **21b** (100 mg, 0.192 mmol) in a mixture of DMF (2.5 mL) and 1,4-dioxane (5 mL) 1,1'-carbonyldiimidazole (94 mg, 0.576 mmol) was added and the reaction mixture was stirred at 101 °C for 15 h. The solvent was removed under reduce pressure, the crude product was sequentially triturated with acetonitrile and methanol, the undissolved solid was filtered off and dried to obtain **22b** (24 mg) as pale-yellow solid.

Yield 23% (24 mg); pale yellow solid; mp 260 – 263 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.40 (br s, 2H, 2 × NH), 9.50 (s, 1H, NH), 8.32 (d, *J* = 8.6 Hz, 1H, ArH), 7.60 (s, 1H, ArH), 7.53 (d, *J* = 8.6 Hz, 1H, ArH), 7.20 (d, 1H, NHBoc), 4.15 – 4.07 (m, 1H, CH), 3.33 – 3.24 (m, 1H, CH), 3.24 – 3.17 (m, 1H, CH), 3.12 – 3.04 (m, 1H, CH), 2.96 – 2.91 (m, 1H, CH), 2.25 (s, 3H, $CH_3$), 2.22 – 2.16 (m, 1H, CH), 1.90 – 1.80 (m, 1H, CH), 1.40 (s, 9H, tBu) ppm. IR (ATR): ν 3342, 2980, 2850, 2361, 1721, 1681, 1643, 1620, 1602, 1512, 1491, 1416, 1366, 1329, 1275, 1216, 1171, 1118, 1086, 1037, 1003, 958, 897, 833, 761, 731, 657, 625, 608, 571 cm$^{-1}$. $[\alpha]^{20}_D$ = 0.035 (*c* 0.255, DMF). HRMS for $C_{23}H_{27}Cl_2N_6O_5$: calculated 537.1414, found 537.1416.

***tert*-Butyl (*S*)-(1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperidin-3-yl)carbamate (22c).** To a solution of compound **21c** (240 mg, 0.449 mmol) in a mixture of DMF (5 mL) and 1,4-dioxane (10 mL) 1,1'-carbonyldiimidazole (219 mg, 1.35 mmol) was added and the reaction mixture was stirred at 101 °C for 15 h. The solvent was removed under reduce pressure, the crude product was triturated with a mixture of acetonitrile and methanol (20 mL, 1:1), the undissolved solid was filtered off and dried to obtain **22c** (202 mg) as brown solid. Yield 84% (202 mg); brown solid; mp 260 – 263 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.55 (s, 1H, NH), 12.44 (s, 1H, NH), 9.76 (s, 1H, NH), 8.53 (d, *J* = 8.6 Hz, 1H, ArH), 7.62 – 7.64 (m, 2H, 2 × ArH), 6.89 (d, *J* = 7.5 Hz, 1H, NHBoc), 3.54 – 3.70 (m, 1H, CH), 2.91 – 3.05 (m, 1H, CH), 2.77 – 2.91 (m, 1H, CH), 2.54 – 2.70 (m, 2H, $CH_2$), 2.24 (s, 3H, $CH_3$), 1.75 – 1.99 (m, 2H, $CH_2$), 1.58 – 1.74 (m, 1H, CH), 1.36 (s, 9H, tBu), 1.17 – 1.27 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 156.6, 154.8, 154.4, 153.5, 142.2, 136.5, 129.9, 122.8, 119.4, 118.9, 118.7, 118.7, 108.6, 109.9, 77.7, 57.4, 52.9, 47.6, 29.3, 28.2, 24.4, 10.8 ppm. IR (ATR): ν 3317, 2963, 2360, 1778, 1687, 1634,1582, 1514, 1491, 1403, 1362, 1326, 1251, 1170, 1125, 1072, 1034, 945, 913, 827, 747 cm$^{-1}$. $[\alpha]^{20}_D$ = – 0.73° (c 0.318, THF). MS (ESI) m/z = 549.1 ([M-H]$^-$). HRMS for $C_{24}H_{27}N_6O_5Cl_2$: calculated 549.1420, found 549.1436. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 11.960 min (95.1% at 280 nm).

***tert*-Butyl 4-((2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)amino)piperidine-1-carboxylate (22d).** To a suspension of **21d** (60 mg, 0.114 mmol) in a mixture of 1,4-dioxane and DMF (2:1, 15 mL), 1,1'-carbonyldiimidazole (55.6 mg, 0.343 mmol) was added and the reaction mixture was stirred 101 °C for 24 h. The solvent was evaporated *in vacuo*, the residue was suspended in acetonitrile, sonicated, filtered off and dried. Yield 56% (35 mg); yellow solid; mp 168 – 171 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.49 (s, 1H, NH), 12.26 (s, 1H, NH), 8.84 (s, 1H, NH), 7.74 – 7.78 (m, 1H, ArH), 7.14 – 7.19 (m, 2H, 2 × ArH), 5.19 (d,1H, *J* = 7.1 Hz, NH), 3.79 – 3.92 (m, 2H, $CH_2$), 3.53 (s, 1H, CH), 2.93 (m, 2H, $CH_2$), 2.23 (s, 3H, $CH_3$), 1.89 (d, 2H, *J* = 9.7 Hz, $CH_2$), 1.40 (s, 9H, tBu), 1.25 – 1.37 (m, 2H, $CH_2$) ppm. IR (ATR): ν 3347, 3328, 3265, 3122, 2974, 2931, 2852, 1767, 1660, 1590, 1533, 1496, 1478, 1417, 1366, 1322, 1241, 1212, 1175, 1143, 1093,

1074, 1043, 939, 860, 823, 734 $cm^{-1}$. HRMS for $C_{24}H_{29}Cl_2N_6O_5$: calculated 551.15710, found 551.15704.

**3,4-Dichloro-5-methyl-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (22e).** To a solution of compound **21e** (400 mg, 0.970 mmol) in a mixture of DMF (20 mL) and 1,4-dioxane (20 mL) 1,1'-carbonyldiimidazole (310 mg, 1.94 mmol) was added and the reaction mixture was stirred at 101 °C for 15 h. The solvent was removed under reduce pressure, the crude product was sequentially triturated with acetonitrile, water and MeOH, and the undissolved solid was filtered off and dried. The crude product was crystallized from DMF and dried to obtain **22e** (42.9 mg) as a white solid. Yield 11% (42.9 mg); white solid; mp 304 – 305 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.54 (s, 1H, NH), 12.44 (s, 1H, NH), 9.75 (s, 1H, NH), 8.54 (d, 1H, *J* = 8.6 Hz, ArH), 7.70 (d, 1H, *J* = 2.0 Hz, ArH), 7.64 (dd, 1H, *J* = 8.5, 1.9 Hz, ArH), 3.72 – 3.84 (m, 4H, 2 × $CH_2$), 2.84 – 2.95 (m, 4H, 2 × $CH_2$), 2.24 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 157.0, 154.9, 153.9, 142.4, 137.0, 130.4, 123.4, 120.1, 119.6, 119.2, 118.9, 109.1, 110.3, 67.0, 52.6, 11.2 ppm. HRMS for $C_{18}H_{18}O_4N_5Cl_2$ ($[M+H]^+$): calculated 438.07237, found 438.07304. HPLC (0–10 min, 10–90% ACN in 0.1% TFA, 10–11 min, 90% ACN in 0.1% TFA, Waters Acquity UPLC HSS C18 column: 1.8 μm, 2.1 × 50 mm): $t_r$ 5.333 min (97.38% at 254 nm, 97.45% at 280 nm).

**3,4-Dichloro-5-methyl-*N*-(2-(2-methylmorpholino)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (22f).** To a solution of compound **21f** (310 mg, 0.703 mmol) in a mixture of DMF (20 mL) and 1,4-dioxane (10 mL) 1,1'-carbonyldiimidazole (456 mg, 2.81 mmol) was added and the reaction mixture was stirred at 101 °C for 15 h. The solvent was removed under reduce pressure, the solid residue was sequentially triturated with acetonitrile, water and THF, and the undissolved solid was filtered off and dried. The crude product was crystallized from DMF and dried to obtain **22f** (169 mg) as a white solid. Yield 53% (169 mg); white solid; mp 302 – 303 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.56 (s, 1H, NH), 12.44 (s, 1H, NH), 9.75 (s, 1H, NH), 8.55 (d, 1H, *J* = 8.6 Hz, ArH), 7.68 (d, 1H, *J* = 2.0 Hz, ArH), 7.64 (dd, 1H, *J* = 8.6, 2.0 Hz, ArH), 3.88 – 3.93 (m, 1H, CH), 3.69 – 3.81 (m, 2H, 2 × CH), 2.78 – 2.94 (m, 3H, 3 × CH), 2.55 – 2.61 (m, 1H, CH), 2.24 (s, 3H, $CH_3$), 1.12 (d, 3H, *J* = 6.2 Hz, $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 157.0, 154.9, 153.9, 142.2, 137.1, 130.4, 123.4, 120.0, 119.5, 119.2, 119.0, 109.1, 110.3, 72.1, 66.7, 58.6, 52.1, 19.3, 11.2 ppm. DEPT 45 NMR (100 MHz, DMSO-$d_6$) δ 123.4, 120.0, 119.0, 72.2, 66.7, 58.6, 52.1, 19.3, 11.2 ppm. DEPT 135 NMR (100 MHz, DMSO-$d_6$) δ 123.4, 120.0, 119.0, 72.2, 66.7 (negative), 58.6 (negative), 52.1 (negative), 19.3, 11.2 ppm. HRMS for $C_{19}H_{18}O_4N_5Cl_2$ ($[M-H]^-$): calculated 450.07428, found 450.07413. HPLC (0–10 min, 10–90% ACN in 0.1% TFA, 10–11 min, 90% ACN in 0.1% TFA, Waters Acquity UPLC HSS C18 column: 1.8 μm, 2.1 × 50 mm): $t_r$ 5.703 min (95.50% at 254 nm, 95.08% at 280 nm).

**3,4-Dichloro-*N*-(2-(2,6-dimethylmorpholino)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-5-methyl-1*H*-pyrrole-2-carboxamide (22g).** To the solution of compound **21g** (217 mg, 0.492 mmol) in a mixture of DMF (8 mL) and 1,4-dioxane (15 mL) 1,1'-carbonyldiimidazole (319 mg, 1.97 mmol) was added and the reaction mixture was stirred at 101 °C for 15 h. The solvent was removed under reduce pressure, the solid residue was sequentially triturated with acetonitrile, MeOH and THF, and the undissolved solid was filtered off and dried. The crude product was crystallized from DMF and dried to obtain **22g** (112 mg) as a white solid. Yield 49% (112 mg); white solid; mp 301 – 303 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.57 (s, 1H, NH), 12.45 (s, 1H, NH), 9.79 (s, 1H, NH), 8.57 (d, 1H, *J* = 8.6 Hz, ArH), 7.61 – 7.71 (m, 2H, 2 × ArH), 3.77 – 3.86 (m, 2H, 2 × CH), 2.86 – 2.93 (m, 2H, 2 × CH), 2.43 – 2.48 (m, 2H, 2 × CH), 2.24 (s, 3H, $CH_3$), 1.12 (d, 6H, *J* = 6.1 Hz, 2 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 157.0, 154.9, 153.9, 141.9, 137.1, 130.4, 123.4, 119.9, 119.5, 119.3, 119.1, 109.1, 110.2, 72.0, 58.1, 19.3, 11.2 ppm. HRMS for $C_{20}H_{22}O_4N_5Cl_2$ ([M+H]$^+$): calculated 466.10399, found 466.10434. HPLC (0–10 min, 10–90% ACN in 0.1% TFA, 10–11 min, 90% ACN in 0.1% TFA, Waters Acquity UPLC HSS C18 column: 1.8 μm, 2.1 × 50 mm): $t_r$ 6.077 min (98.33% at 254 nm, 98.27% at 280 nm).

**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperazin-1-ium chloride (23a).** To a solution of **22a** (60.0 mg, 0.110 mmol) in DMF (6 mL) 4 M HCl in 1,4-dioxane (6 mL) was added and the reaction mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure and the solid residue was triturated with acetonitrile, the undissolved solid was filtered off and dried, to obtain **23a** (47.4 mg) as a white solid. Yield 91% (47.4 mg); white solid; mp 287 – 289 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.63 (s, 1H, NH), 12.51 (s, 1H, NH), 9.60 (s, 1H, NH), 9.17 (s, 2H, $NH_2^+$), 8.53 (dd, 1H, *J* = 8.7, 1.3 Hz, ArH), 7.68 (d, 1H, *J* = 8.5 Hz, ArH), 7.62 (s, 1H, ArH), 3.23 – 3.31 (m, 4H, 2 × $CH_2$), 3.08 – 3.15 (m, 4H, 2 × $CH_2$), 2.25 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 157.1, 154.9, 153.8, 141.5, 136.9, 130.4, 123.9, 120.4, 119.6, 119.2, 118.8, 110.7, 109.2, 49.2, 43.9, 11.2 ppm. HRMS for C18H19O3N6Cl2 ([M+H]$^+$): calculated 437.08880, found 437.08902. HPLC (0–10 min, 10–90% ACN in 0.1% TFA, 10–11 min, 90% ACN in 0.1% TFA, Waters Acquity UPLC HSS C18 column: 1.8 μm, 2.1 × 50 mm): tr 3.107 min (96.56% at 254 nm, 95.85% at 280 nm).

**(*S*)-1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)pyrrolidin-3-aminium chloride (23b).** To a solution of compound **22b** (24 mg, 0.045 mmol) in DMF (1 mL) 4 M HCl in 1,4-dioxane (3 mL) was added and the reaction mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure and the solid residue was sequentially triturated with diethyl ether and acetonitrile, the undissolved solid was filtered off and dried, to obtain **23b** (13 mg) as off-white solid. Yield 60% (13 mg); off-white solid; mp > 230 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$): δ 12.63 (s, 1H, NH), 12.58 (s, 1H, NH), 9.50 (s, 1H, NH), 8.32 (br s, 3H, $NH_3^+$),

8.25 (d, 1H, *J* = 8.5 Hz, ArH), 7.61 (d, 1H, *J* = 1.9 Hz, ArH), 7.55 (dd, 1H, *J* = 8.5, 1.9 Hz, ArH), 3.87 – 3.97 (s, 1H, CH), 3.50 – 3.57 (m, 1H, CH), 3.37 – 3.45 (m, 1H, CH), 3.02 – 3.14 (m, 2H, 2 × CH), 2.26 – 2.32 (m, 1H, CH), 1.98 – 2.06 (m, 1H, CH), 2.25 (s, 3H, $CH_3$) ppm. IR (ATR): ν 2969, 2360, 2341, 2187, 1994, 1768, 1637, 1584, 1519, 1490, 1360, 1311, 1257, 1179, 1091, 1040, 958, 927, 832, 707 $cm^{-1}$. $[\alpha]_D^{25}$ 1.25 (*c* 0.271, DMF). HRMS for $C_{18}H_{19}Cl_2N_6O_3$: calculated 437.0890, found 437.0890. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 3.523 min (96.05% at 254 nm).

**(*S*)-1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperidin-3-aminium chloride (23c).** To a solution of compound **22c** (133 mg, 0.241 mmol) in DMF (2 mL) 4 M HCl in 1,4-dioxane (6 mL) was added and the reaction mixture was stirred at rt for 15 h. The solvent was removed under reduced pressure and the solid residue was sequentially triturated with diethyl ether and acetonitrile, the undissolved solid was filtered off and dried, to obtain **23c** (71 mg) as off-white solid. Yield 60% (71 mg); off-white solid; mp > 230 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.64 (s, 1H, NH), 12.57 (s, 1H, NH), 9.58 (s, 1H, NH), 8.46 (d, *J* = 8.4 Hz, 1H, ArH), 8.27 (br s, 3H, $NH_3^+$), 7.63 – 7.66 (m, 2H, 2 × ArH), 3.26 – 3.40 (s, 1H, CH), 3.16 – 3.25 (m, 1H, CH), 2.83 – 2.94 (m, 1H, CH), 2.65 – 2.81 (m, 2H, $CH_2$), 2.25 (s, 3H, $CH_3$), 2.05 – 2.13 (m, 1H, CH), 1.83 – 1.93 (m, 1H, CH), 1.62 – 1.77 (m, 1H, CH), 1.44 – 1.62 (m, 1H, CH) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 156.6, 154.4, 153.4, 141.9, 136.0, 129.8, 122.8, 120.3, 119.2, 118.7, 118.2, 110.3, 108.7, 54.7, 52.1, 47.5, 27.5, 23.6, 10.8 ppm. IR (ATR): ν 3100, 2361, 1766, 1650, 1613, 1511, 1488, 1408, 1373, 1333, 1255, 1204, 1125, 1086, 1039, 945, 919, 836, 749, 708 $cm^{-1}$. MS (ESI) m/z = 449.1 ($[M-H]^-$). HRMS for $C_{19}H_{19}N_6O_3Cl_2$: calculated 449.0896, found 449.0890. HPLC (0–16 min, 30–90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Eclipse Plus C18: 5 µm, 4.6 × 150 mm): $t_r$ 4.633 min (95.8% at 280 nm).

**4-((2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)amino)piperidin-1-ium chloride (23d).** To a suspension of **22d** (25 mg, 0.045 mmol) in 1,4-dioxane (7 mL), 4 M HCl in 1,4-dioxane (3 mL) was added and the reaction mixture was stirred at rt for 3 h. The precipitate that formed was filtered off, washed with diethyl ether and dried to obtain **23d** as a pale yellow solid. Yield 100% (22 mg); pale yellow solid; mp 212 – 217 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.55 (s, 1H, NH), 12.53 (s, 1H, NH), 9.10 (s, 1H, NH), 8.72 (s, 2H, $NH_2^+$), 7.79 (d, 1H, *J* = 8.2 Hz, ArH), 7.17 (m, 2H, 2 × ArH), 3.67 – 3.72 (m, 1H, CH), 3.25 – 3.35 (m, 2H, $CH_2$), 3.01 – 3.11 (m, 2H, $CH_2$), 2.24 (s, 3H, $CH_3$), 2.06 (dd, 2H, *J* = 13.2, 2.8 Hz, $CH_2$), 1.65 – 1.72 (m, 2H, $CH_2$) ppm. Signal for one NH proton not seen. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 167.9, 157.6, 138.7, 130.9, 128.9, 127.7, 123.5, 120.3, 119.6, 115.3, 112.1, 109.1, 47.3, 42.1, 28.6, 11.2 ppm. HRMS ($ESI^+$) *m/z* for $C_{19}H_{21}Cl_2N_6O_3$ ($[M+H]^+$): calculated 451.1047, found 451.1040. HPLC (0–16 min, 30–

90% ACN in 0.1% TFA, 16–20 min, 90% ACN in 0.1% TFA, Agilent Extend-C18 column: 3.5 $\mu$m, 4.6 × 150 mm): $t_r$ 12.587 min (92.82 % at 254 nm).

**Methyl 4-(methylamino)-3-morpholinobenzoate (24).** To a solution of methyl 4-amino-3-morpholinobenzoate (**16e**, 1.50 g, 6.35 mmol) and sodium methoxide (0.48 g, 8.89 mmol) in MeOH (35 mL) paraformaldehyde (0.48 g, 15.9 mmol) was added in one portion. The reaction mixture was heated to 40 °C and stirred for 15 h. Solid $NaBH_4$ (0.48 g, 12.7 mmol) was added to the reaction mixture and stirred at 40 °C for 5 h. Additional 2.00 equivalents of solid $NaBH_4$ (0.48 g, 12.7 mmol) was added and the mixture was stirred at 40 °C for 15 h. The reaction mixture was quenched with 80 mL of saturated aqueous $NaHCO_3$ and then diluted with 80 mL of ethyl acetate. The phases were separated and the aqueous layer was washed with ethyl acetate (3 × 45 mL). The organic layers were combined, washed with brine (2 × 50 mL) and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography using ethyl acetate/hexane (2:3) as eluent. The crude product was purified by washing the solid with ethyl acetate to give **24** (413 mg) as a white solid. Yield 26% (413 mg); white solid; mp 125 – 126 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.63 (d, $J$ = 8.5 Hz, 1H, ArH), 7.47 (s, 1H, ArH), 6.56 (d, $J$ = 8.4 Hz, 1H, ArH), 5.86 (q, $J$ = 4.8 Hz, 1H, NH), 3.73 – 3.80 (m, 7H, 2 × $CH_2$, $COOCH_3$), 2.81 (d, $J$ = 4.9 Hz, 3H, $NCH_3$), 2.72 – 2.79 (m, 4H, 2 × $CH_2$) ppm.

**Methyl 4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)-3-morpholinobenzoate (25a).** To a solution of 4,5-dibromo-1*H*-pyrrole-2-carboxylic acid (0.500 g, 1.86 mmol) in anhydrous dichloromethane (20 mL) oxalyl chloride (0.80 mL, 9.30 mmol) was added and the mixture was stirred for 15 h at room temperature under an argon atmosphere. The solvent was evaporated under reduced pressure, anhydrous dichloromethane (15 mL), **16e** (293 mg, 1.24 mmol) and pyridine (1.5 mL) were added, and the reaction mixture was stirred for 15 h under argon atmosphere at room temperature. The product was filtered off and dried to give **25a** as a pale brown solid. Yield 84% (0.507 g); pale brown solid; mp 270 – 274 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.13 (s, 1H, NH), 9.28 (s, 1H, CONH), 8.15 (d, $J$ = 8.3 Hz, 1H, ArH), 7.71 – 7.80 (m, 2H, 2 × ArH), 7.15 (s, 1H, ArH), 3.85 (s, 3H, $COOCH_3$), 3.75 – 3.82 (m, 4H, 2 × $CH_2$), 2.82 – 2.90 (m, 4H, 2 × $CH_2$) ppm.

**Methyl 4-(3,4-dichloro-*N*,5-dimethyl-1*H*-pyrrole-2-carboxamido)-3-morpholinobenzoate (25b).** To a solution of 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.500 g, 2.58 mmol) in anhydrous dichloromethane (25 mL), oxalyl chloride (1.10 mL, 12.9 mmol) was added and the mixture was stirred at room temperature for 15 h under argon atmosphere. The solvent was evaporated under reduced pressure, anhydrous dichloromethane (20 mL), **24** (0.431 g, 1.72 mmol) and pyridine (1.72 mL) were added, and the reaction mixture was stirred for 15 h under an argon atmosphere at room temperature. The undissolved solid was filtered off and the mother liquor was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (30 mL) and $NaHCO_3$ (20 mL) and the phases were separated. The organic phase was washed with $NaHCO_3$ (20 mL), 1 M HCl (4 × 20 mL) and brine (2 × 30 mL),

dried over $Na_2SO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified with flash column chromatography using ethyl acetate/hexane (1:1) as eluent. The crude product was purified by washing the solid with ethyl acetate to give **25b** as an off-white solid. Yield 70% (0.511 g); off-white solid; mp 187 – 190 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.88 (s, 1H, NH), 7.68 (d, $J$ = 8.3 Hz, 1H, ArH), 7.52 (s, 1H, ArH), 7.46 (d, $J$ = 8.2 Hz, 1H, ArH), 3.84 (s, 3H, $COOCH_3$), 3.61 – 3.74 (m, 4H, 2 × $CH_2$), 3.37 (s, 3H, $NCH_3$), 2.69 – 2.96 (m, 4H, 2 × $CH_2$), 2.13 (s, 3H, $CH_3$) ppm.

**4,5-Dibromo-*N*-(4-(hydrazinecarbonyl)-2-morpholinophenyl)-1*H*-pyrrole-2-carboxamide (26a).** To a solution of **25a** (485 mg, 1.00 mmol) in MeOH (15 mL) and THF (10 mL) in a pressure tube hydrazine monohydrate (3.40 mL, 69.8 mmol) was added and the reaction mixture was stirred at 120 °C for 15 h. The precipitate was filtered off and dried. The solvent of the mother liquor was evaporated under reduced pressure, MeOH (1 mL) was added to the crude residue, the undissolved solid was filtered off and combined with the precipitate from the first filtration. Yield 54% (263 mg); pale brown solid; mp 258 – 261 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 13.08 (s, 1H, NH), 9.75 (s, 1H, NH), 9.22 (s, 1H, NH), 8.01 (d, $J$ = 8.3 Hz, 1H, ArH), 7.68 (s, 1H, ArH), 7.61 (d, $J$ = 8.5 Hz, 1H, ArH), 7.13 (s, 1H, ArH), 4.40 – 4.62 (m, 2H, $NH_2$), 3.72 – 3.85 (m, 4H, 2 × $CH_2$), 2.81 – 2.90 (m, 4H, 2 × $CH_2$) ppm.

**3,4-Dichloro-*N*-(4-(hydrazinecarbonyl)-2-morpholinophenyl)-*N*,5-dimethyl-1*H*-pyrrole-2-carboxamide (26b).** To a solution of **25b** (179 mg, 0.420 mmol) in MeOH (5 mL) and THF (4 mL) in a pressure tube hydrazine monohydrate (1.44 mL, 29.6 mmol) was added and the reaction mixture was stirred at 120 °C for 15 h. The precipitate was filtered off and dried to give **26b** as a white solid. Yield 41% (73 mg); white solid; mp 246 – 249 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.83 (s, 1H, NH), 9.78 (s, 1H, NH), 7.55 (d, $J$ = 8.2 Hz, 1H, ArH), 7.45 (s, 1H, ArH), 7.37 (d, $J$ = 8.1 Hz, 1H, ArH), 4.47 (s, 2H, $NH_2$), 3.60 – 3.75 (m, 4H, 2 × $CH_2$), 2.70 – 2.95 (m, 4H, 2 × $CH_2$), 2.12 (s, 3H, $CH_3$) ppm. The peak for $NCH_3$ overlaps with the peak of water.

**4,5-Dibromo-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (27a).** To a solution of **26a** (248 mg, 0.510 mmol) in 1,4-dioxane (10 mL) and DMF (20 mL) 1,1'-carbonyldiimidazole (336 mg, 2.07 mmol) was added, and the reaction mixture was stirred at 101 °C for 15 h. The solvent was evaporated under reduced pressure and the solid was washed successively with acetonitrile, water, and diethyl ether. The crude product was recrystallized from DMF and washed with THF to give **27a** as a pale yellow solid. Yield 51% (133 mg); pale yellow solid; mp >300 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.52 (br s, 2H, 2 × NH), 9.35 (s, 1H, NH), 8.17 (d, $J$ = 8.3 Hz, 1H, ArH), 7.51 – 7.62 (m, 2H, 2 × ArH), 7.11 (s, 1H, ArH), 3.77 – 3.86 (m, 4H, 2 × $CH_2$), 2.83 – 2.93 (m, 4H, 2 × $CH_2$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 157.4, 154.9, 154.1, 144.2, 135.4, 128.1, 123.0, 122.0, 120.4, 117.5, 114.1, 107.4, 99.1, 66.9, 52.0 ppm. HRMS for $C_{17}H_{16}O_4N_5Br_2$ $[M+H]^+$: calculated 511.95626, found 511.95636. HPLC (0–10 min, 10–90% ACN in 0.1% TFA, 10–11 min,

90% ACN in 0.1% TFA, Waters Acquity UPLC HSS C18 column: 1.8 μm, 2.1 × 50 mm): $t_r$ 4.900 min (95.01% at 254, 95.00% at 280 nm).

**3,4-Dichloro-*N*,5-dimethyl-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (27b).** To a solution of **26b** (63.9 mg, 0.150 mmol) in 1,4-dioxane (3 mL) and DMF (5 mL) 1,1'-carbonyldiimidazole (73.0 g, 0.450 mmol) was added, and the reaction mixture was stirred at 101 °C for 15 h. The solvent was evaporated under reduced pressure and the solid was washed successively with acetonitrile, water, 1,4-dioxane, and methanol to afford **27b** as a pale yellow solid. Yield 15% (10 mg); pale yellow solid; mp 257 – 259 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.52 (s, 1H, NH), 11.89 (s, 1H, NH), 7.49 (s, 2H, 2 × ArH), 7.32 (s, 1H, ArH), 3.68 (s, 4H, 2 × $CH_2$), 3.37 (s, 3H, $NCH_3$), 2.71 – 3.00 (m, 4H, 2 × $CH_2$), 2.13 (s, 3H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 162.4, 154.9, 153.8, 148.4, 140.6, 130.6, 127.6, 123.3, 121.4, 120.9, 117.1, 108.9, 107.2, 66.0, 51.5, 37.5, 11.1 ppm. HRMS for $C_{19}H_{18}O_4N_5Cl_2$ [M-H]$^-$: calculated 450.07394, found 450.07413. HPLC (0–10 min, 10–90% ACN in 0.1% TFA, 10–11 min, 90% ACN in 0.1% TFA, Waters Acquity UPLC HSS C18 column: 1.8 μm, 2.1 × 50 mm): $t_r$ 4.243 min (99.49% at 254, 99.82% at 280 nm).

**Methyl 4-aminobenzoate (29).** The solution of **28** (3.77 g, 20.8 mmol) in a mixture of MeOH and THF (100 mL) was stirred for 15 min under an argon atmosphere. Pd/C (0.913 g) was added, the solution was saturated with hydrogen and the reaction mixture was stirred for 3 h under hydrogen atmosphere. The catalyst was filtered off and the solvent was evaporated to obtain **29** (2.62 g) as pale brown solid. Yield 2.62 g (83%); pale brown solid; mp 90 – 93 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.64 (d, 2H, $J$ = 8.8 Hz, 2 × ArH), 6.57 (d, 2H, $J$ = 8.8 Hz, 2 × ArH), 5.85 (s, 2H, $NH_2$), 3.73 (s, 3H, $CH_3$) ppm. IR (ATR): ν 3407, 3330, 3226, 3044, 2988, 2944, 2845, 1681, 1635, 1596, 1574, 1513, 1433, 1313, 1283, 1199, 1175, 1117, 1078, 973, 851, 842, 767, 697, 638 cm$^{-1}$.

**Methyl 4-(benzylamino)benzoate (30).** To the solution of **29** (2.07 g, 13.7 mmol, 1 eq.) in $CH_2Cl_2$ (70 mL) benzaldehyde (3.9 mL, 38.9 mmol) was added and the mixture was stirred at rt for 10 min, after which $Na_2SO_4$ (7.76 g, 54.6 mmol) was added and the mixture was stirred at reflux for 15 h. The mixture was cooled to rt, filtered and the solvent was removed under reduced pressure. The residue was dissolved in MeOH and cooled on an ice bath, after which $NaBH_4$ (1.03 g, 27.3 mmol) was added in small portions. The reaction mixture was stirred at rt for 15 h. Few mL of water were added and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc (160 mL) and water (80 mL), the phases were separated and the organic phase was washed with brine (2 × 80 mL), dried over $Na_2SO_4$, filtered and the solvent evaporated. The crude product was purified with flash column chromatography using dichloromethane as the eluent. The fractions that contained the product were combined, the solvent was removed under reduced pressure and the solid residue was triturated with hexane and the undissolved solid was filtered off and dried to obtain **30** (0.959 g) as white solid. Yield 0.959 g (29%); white solid; mp 107 – 109 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.66 (d, 2H, $J$ = 8.8 Hz, 2 × ArH), 7.29 – 7.39 (m,

4H, 4 × ArH), 7.20 – 7.28 (m, 1H, ArH), 7.14 (t, 1H, *J* = 6.0 Hz, NH), 6.61 (d, 2H, *J* = 8.8 Hz, 2 × ArH), 4.34 (d, 2H, *J* = 6.0 Hz, $CH_2$), 3.72 (s, 3H, $CH_3$) ppm. IR (ATR): ν 3416, 3027, 3005, 2952, 1686, 1598, 1569, 1529, 1494, 1456, 1432, 1419, 1344, 1312, 1275, 1236, 1186, 1172, 1111, 1064, 1027, 1003, 962, 909, 834, 767, 738, 700, 644, 618 $cm^{-1}$.

**Methyl 4-(*N*-benzyl-3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoate (31).** To a suspension of 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.775 g, 4.00 mmol) in anhydrous dichloromethane (55 mL), oxalyl chloride (1.39 mL, 16.0 mmol) was added dropwise and the reaction mixture was stirred at rt under argon atmosphere for 15 h. The solvent was evaporated under reduced pressure, **30** (0.959 g, 3.97 mmol), anhydrous pyridine (8 mL) and anhydrous $CH_2Cl_2$ (30 mL) were added and the reaction mixture was stirred at rt under argon atmosphere overnight. The solvent was removed *in vacuo*, and to the residue EtOAc (55 mL) and water (45 mL) were added. The phases were separated, organic phase was washed with 1 M HCl (35 ml), saturated solution of $NaHCO_3$ (35 mL) and brine (2 × 20 mL), dried over $Na_2SO_4$, filtered and solvent removed *in vacuo*. The crude product was purified with flash column chromatography using EtOAc/hexane (1:7 to 1:3) as eluent to obtain **31** (0.925 g) as brown solid. Yield 0.925 g (56%); brown solid; mp 135 – 140 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.19 (s, 1H, NH), 7.79 (d, *J* = 8.7 Hz, 2H, 2 × ArH), 7.19 – 7.31 (m, 5H, 5 × ArH), 7.19 (d, *J* = 8.7 Hz, 2H, 2 × ArH), 5.16 (s, 2H, $CH_2$), 3.79 (s, 3H, $COOCH_3$), 2.15 (s, 3H, pyrrole-$CH_3$) ppm. IR (ATR): ν 3265, 3140, 3034, 2950, 1709, 1626, 1600, 1575, 1509, 1483, 1456, 1436, 1412, 1376, 1356, 1314, 1280, 1217, 1180, 1117, 1100, 1067, 1016, 977, 861, 764, 749, 733, 701, 669, 640, 613 $cm^{-1}$. HRMS for $C_{21}H_{19}O_3N_2Cl_2$ ($[M+H]^+$): calculated 417.07672, found 417.07615.

***N*-Benzyl-3,4-dichloro-*N*-(4-(hydrazinecarbonyl)phenyl)-5-methyl-1*H*-pyrrole-2-carboxamide (32).** To the solution of **31** (308 mg, 0.738 mmol) in a mixture of MeOH (10 mL) and THF (6 mL) in a high-pressure tube hydrazine hydrate (64%, 1.80 mL, 36.9 mmol) was added. The tube was sealed and the reaction mixture was stirred at 100 °C for 2 d. The tube was cooled down to rt, the solvent was removed under reduced pressure and to the residue water was added to obtain a white suspension. The solid was filtered off and dried. The crude product was triturated with acetonitrile and the undissolved solid was filtered off and dried, to obtain the first part of **32** (145 mg). The filtrate was concentrated under reduced pressure and the residue was purified with flash column chromatography using $CH_2Cl_2$/MeOH (50:1 to 25:1) as eluent to obtain the second part of **32** (125 mg). Both fractions of the product were combined. Yield 88% (270 mg); white solid; mp 144 – 147 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.07 (s, 1H, pyrrole-NH), 9.70 (s, 1H, NH), 7.66 (d, *J* = 8.7 Hz, 2H, 2 × ArH), 7.20 – 7.32 (m, 5H, 5 × ArH), 7.12 (d, 2H, *J* = 8.6 Hz, 2 × ArH), 5.14 (s, 2H, $CH_2$), 4.47 (s, 2H, $NH_2$), 2.14 (s, 3H, pyrrole-$CH_3$) ppm. $^{13}$C NMR (101 MHz, DMSO-$d_6$): δ 165.4, 161.9, 145.3, 137.7, 130.6, 128.8, 128.2, 128.1, 128.1, 127.8, 127.6, 126.0, 120.6, 110.2, 107.7, 52.8, 11.3 ppm. IR (ATR): ν 3313, 3236, 2986, 2856, 1655, 1599, 1572, 1540, 1487, 1454, 1426, 1379, 1329, 1286, 1228, 1202, 1103, 1069,

1029, 978, 861, 697, 625 $cm^{-1}$. HRMS for $C_{20}H_{19}O_2N_4Cl_2$ ($[M+H]^+$): calculated 417.08796, found 417.08769.

***N*-Benzyl-3,4-dichloro-5-methyl-*N*-(4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (33).** The solution of **32** (245 mg, 0.590 mmol) and CDI (352 mg, 2.17 mmol) in 1,4-dioxane (10 mL) was stirred for 15 h at 101°C. The solvent was removed under reduced pressure and the residue was purified with flash column chromatography, starting with dichloromethane and continuing with dichloromethane/methanol (50:1) as eluent, to obtain **33** (43 mg) as a pale yellow solid. Yield 43 mg (17%); pale yellow solid; mp 202 – 204 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.54 (s, 1H, NH), 12.13 (s, 1H, NH), 7.64 (d, *J* = 8.6 Hz, 2H, 2 × ArH), 7.19 – 7.32 (m, 7H, 7 × ArH), 5.15 (s, 2H, $CH_2$), 2.14 (s, 3H, pyrrole-$CH_3$) ppm. $^{13}$C NMR (101 MHz, DMSO-$d_6$): δ 161.8, 154.9, 153.7, 145.6, 137.6, 128.9, 128.5, 128.1, 127.7, 126.9, 126.1, 121.4, 120.4, 110.3, 107.8, 52.8, 11.3 ppm. IR (ATR): ν 3202, 2840, 1769, 1597, 1578, 1510, 1481, 1427 1407, 1381, 1351, 1275, 1209, 1182, 1075, 1031, 955, 925, 841, 750, 696, 667, 645, 613 $cm^{-1}$. HRMS for $C_{21}H_{17}O_3N_4Cl_2$ ($[M+H]^+$): calculated 443.06722, found 443.06693. HPLC: Waters Acquity UPLC BEH C18 (1,7 µm, 2.1 × 50 mm); mobile phase: 10-90% of acetonitrile in TFA (0.1%) in 10 min; flow rate 0.4 mL/min; injection volume: 1.75 µL; $t_R$: 5.163 min (95.23% at 254 nm, 95.38% at 280 nm).

**Methyl 3-(benzyloxy)-4-nitrobenzoate (35).** To a stirred suspension of methyl 3-hydroxy-4-nitrobenzoate (**34**, 500 mg, 2.53 mmol) and potassium carbonate (699 mg, 5.06 mmol) in acetonitrile (10 mL) benzyl bromide (0.30 mL, 2.53 mmol) was added and the mixture was stirred at 60 °C for 3 h. The solvent was removed under reduced pressure and to the residue ethyl acetate (20 mL) and water (20 mL) were added, and separated. The organic phase was washed with brine (2 × 20 mL), dried over $Na_2SO_4$, filtered and the solvent removed under reduced pressure to afford **35** (620 mg) as yellow solid. Yield 85% (620 mg); yellow solid; mp 90 – 93 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 8.03 (d, *J* = 8.4 Hz, Ar-H), 7.90 (d, *J* = 1.2 Hz, Ar-H), 7.70 (dd, *J* = 8.4, 1.2 Hz, Ar-H), 7.35 – 7.48 (m, 5H, 5 × Ar-H), 5.41 (s, 2H, $CH_2$), 3.92 (s, 3H, $COOCH_3$) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 165.2, 150.9, 143.0, 136.1, 134.7, 129.0, 128.7, 127.9, 125.7, 122.0, 116.2, 71.2, 53.4 ppm. IR (ATR): ν $cm^{-1}$. MS (ESI) m/z = 310.1 ($[M+Na]^+$).

**3-(Benzyloxy)-4-nitrobenzohydrazide (36).** To a solution of **35** (4.60 g, 16.3 mmol) in MeOH (100 mL) and THF (100 mL), hydrazine monohydrate 80% solution (7.95 mL, 163 mmol) was added. The reaction mixture was stirred at 65 °C for 15 h and the solvent was removed under reduced pressure. The residue was suspended in ethanol and the flask was left in the fridge for 1 h. Precipitate was filtered off, suspended in water, the suspension was sonicated, the solid filtered off and dried to give 1.44 g of **36**. Ethanol from the mother liquor of the previous filtration was removed and the residue was purified with flash column chromatography (dichloromethane/methanol 10/1) to give 2.09 of **36**. Yield 77% (3.54 g). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 10.06 (s, 1H, NH), 7.97 (d, *J* = 8.4 Hz, ArH), 7.83 (d, *J* = 1.5 Hz,

ArH), 7.54 (dd, *J* = 8.4, 1.6 Hz, ArH), 7.40 – 7.48 (m, 4H, 4 × ArH), 7.34 – 7.38 (m, 1H, ArH), 5.37 (s, 2H, $CH_2$), 4.63 (s, 2H, $NH_2$) ppm. MS (ESI) m/z = 285.9 ($[M-H]^-$).

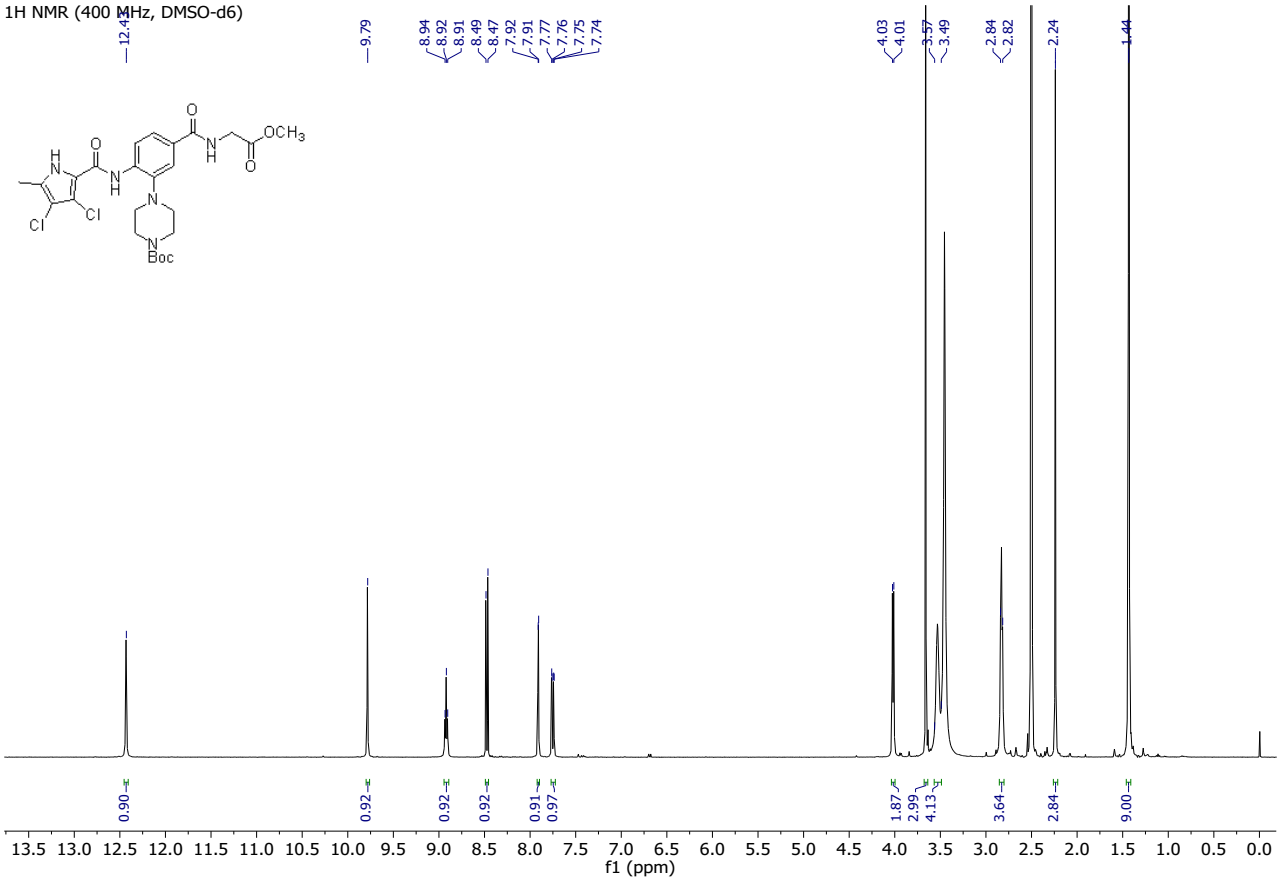
**5-(3-(Benzyloxy)-4-nitrophenyl)-1,3,4-oxadiazol-2(3*H*)-one (37).** To a solution of compound **30** (3.50 g, 12.2 mmol) in 1,4-dioxane (175 mL) 1,1'-carbonyldiimidazole (2.96 g, 18.3 mmol) was added and the reaction mixture was stirred at 101 °C for 15 h. The solvent was removed under reduce pressure, the residue was suspended in methanol, the suspension was sonicated, heated and the solid filtered off to give 3.22 g of **37**. Mother liquor was evaporated and purified with flash column chromatography (dichloromethane/methanol 30/1). The purified product was combined with the product after filtration. Yield 98% (3.74 g). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.91 (s, 1H, NH), 8.06 (d, *J* = 8.4 Hz, ArH), 7.73 (d, *J* = 1.6 Hz, ArH), 7.54 (dd, *J* = 8.4, 1.6 Hz, ArH), 7.33 – 7.50 (m, 5H, 5 × ArH), 5.43 (s, 2H, $CH_2$) ppm. MS (ESI) m/z = 312.0 ($[M-H]^-$).

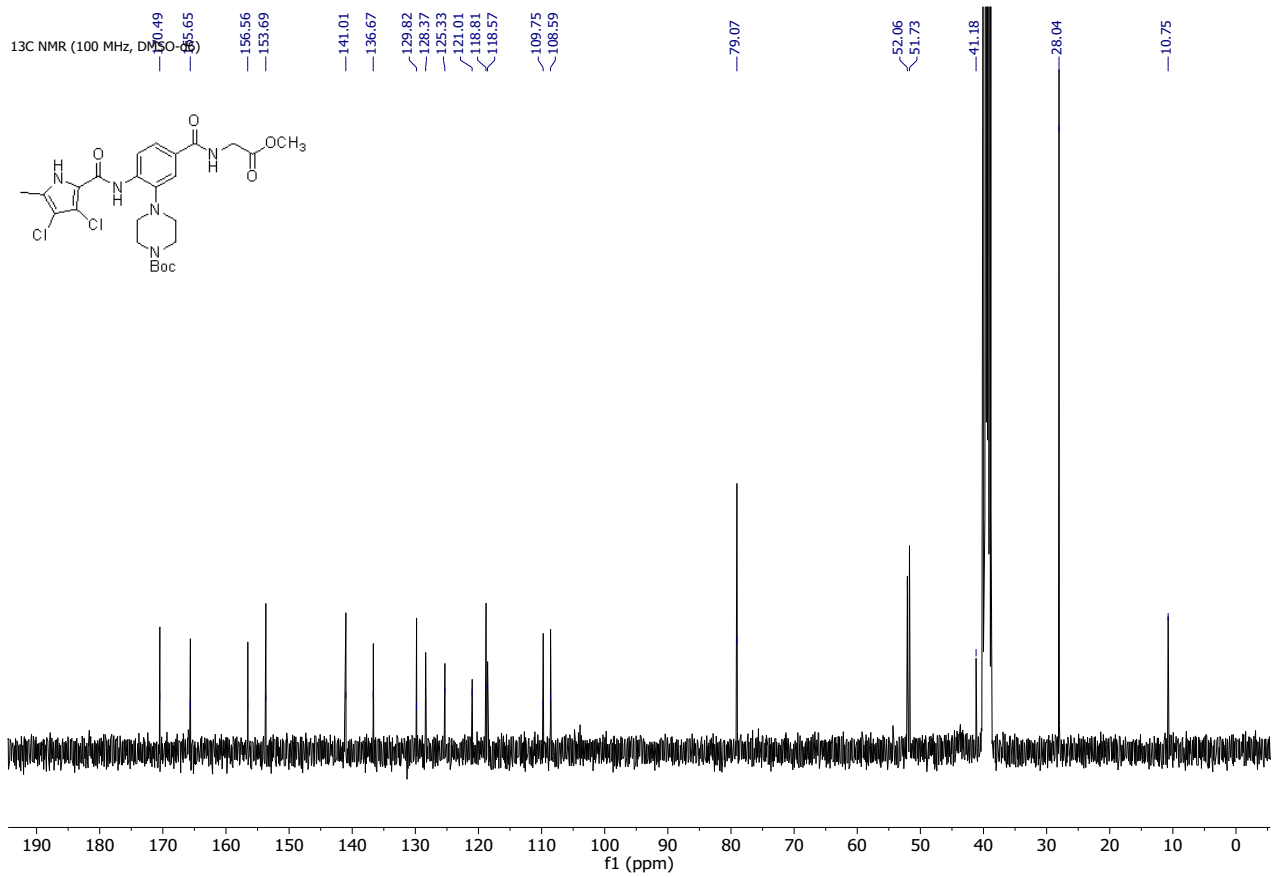
**5-(4-Amino-3-(benzyloxy)phenyl)-1,3,4-oxadiazol-2(3*H*)-one (38).** Compound **37** (523 mg, 1.67 mmol) was suspended in acetic acid (25 mL), iron (932 mg, 16.7 mmol) was added and the reaction mixture was stirred at rt for 90 min. Water was added and iron was filtered over Celite. The flask was left on an ice bath for 1 h upon which the product in the mother liquor crystalized. The product was filtered off and dried. Yield 57% (269 mg). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.22 (s, 1H, NH), 7.51 (d, *J* = 7.0 Hz, 2 × Ar-H), 7.40 (s, 2H, 2 × Ar-H), 7.33 (s, 1H, ArH), 7.21 (d, *J* = 1.8 Hz, ArH), 7.16 (dd, *J* = 8.2, 1.8 Hz, ArH), 6.73 (d, *J* = 8.2 Hz, ArH), 5.54 (s, 2H, $NH_2$), 5.18 (s, 2H, $CH_2$) ppm. MS (ESI) m/z = 283.9 ($[M+H]^+$).

***N*-(2-(Benzyloxy)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamide (39).** Synthesised according to *General procedure B* from 3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxylic acid (0.123 g, 0.71 mmol) and **38** (0.150 g, 0.53 mmol). During the extraction the product precipitated and was filtered off. The crude product was sequentially triturated with acetonitrile, methanol, diethyl ether and the undissolved solid was filtered off. The crude product was purified by crystallization from DMF to afford **39** (0.113 g) as white solid. Yield 47% (0.113 g); white solid; mp 293 – 295 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 12.59 (s, 1H, NH), 12.42 (s, 1H, NH), 9.20 (s, 1H, NH), 8.56 (d, *J* = 8.5 Hz, ArH), 7.51 – 7.62 (m, 3H, 3 × Ar-H), 7.42 – 7.49 (m, 4H, 4 × Ar-H), 5.30 (s, 2H, $CH_2$), 2.20 (s, 3H, $CH_3$) ppm. HRMS for $C_{21}H_{15}O_4N_4Cl_2$ ($[M-H]^-$): calculated 457.04758, found 457.04776. HPLC (30-90% ACN in 0.1% TFA in 10 min, UPLC): $t_r$ 5.430 min (98.87% at 254 nm, 98.66% at 280 nm).

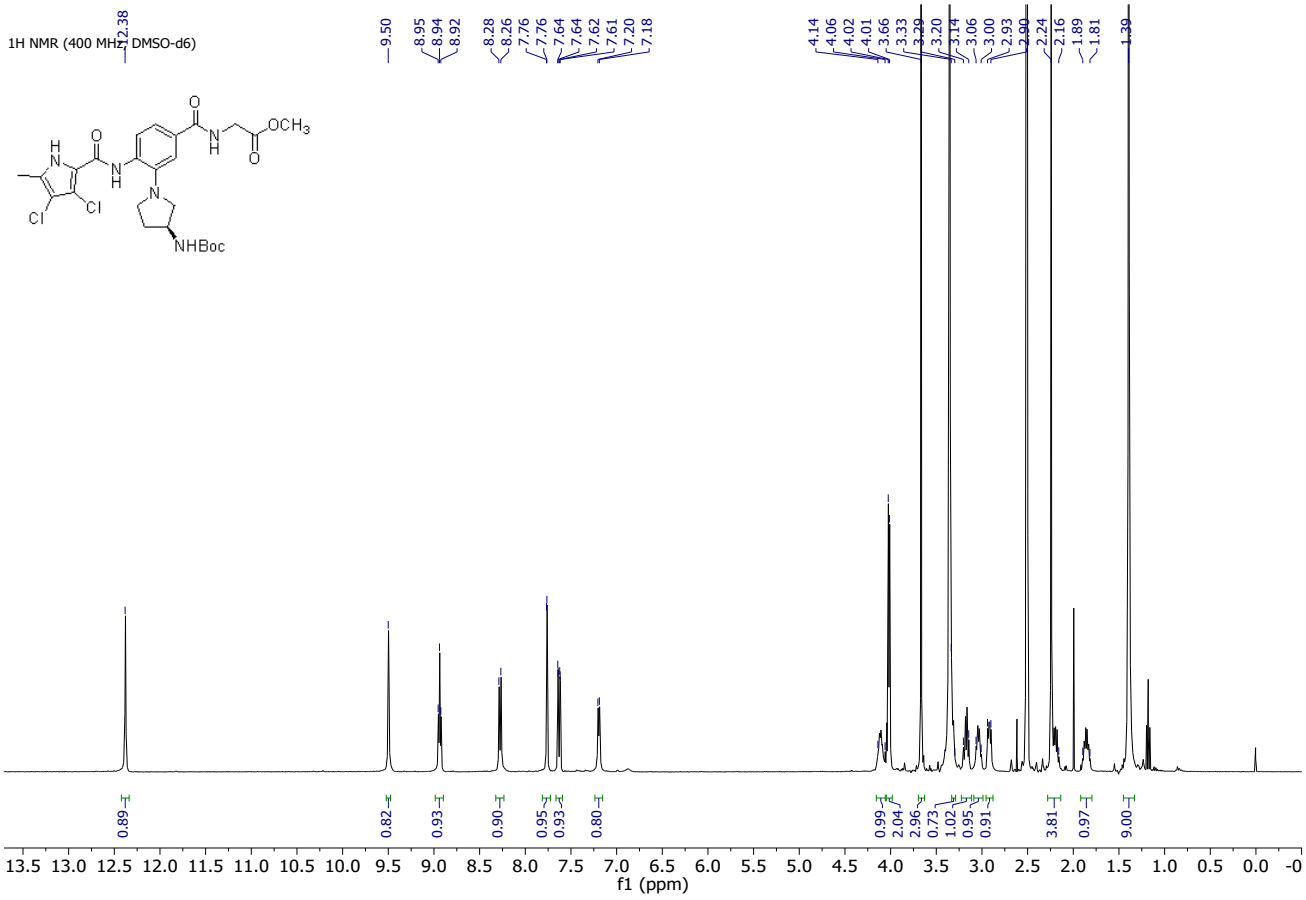
## 7. $^{1}H$ and $^{13}C$ NMR spectra of the representative compounds

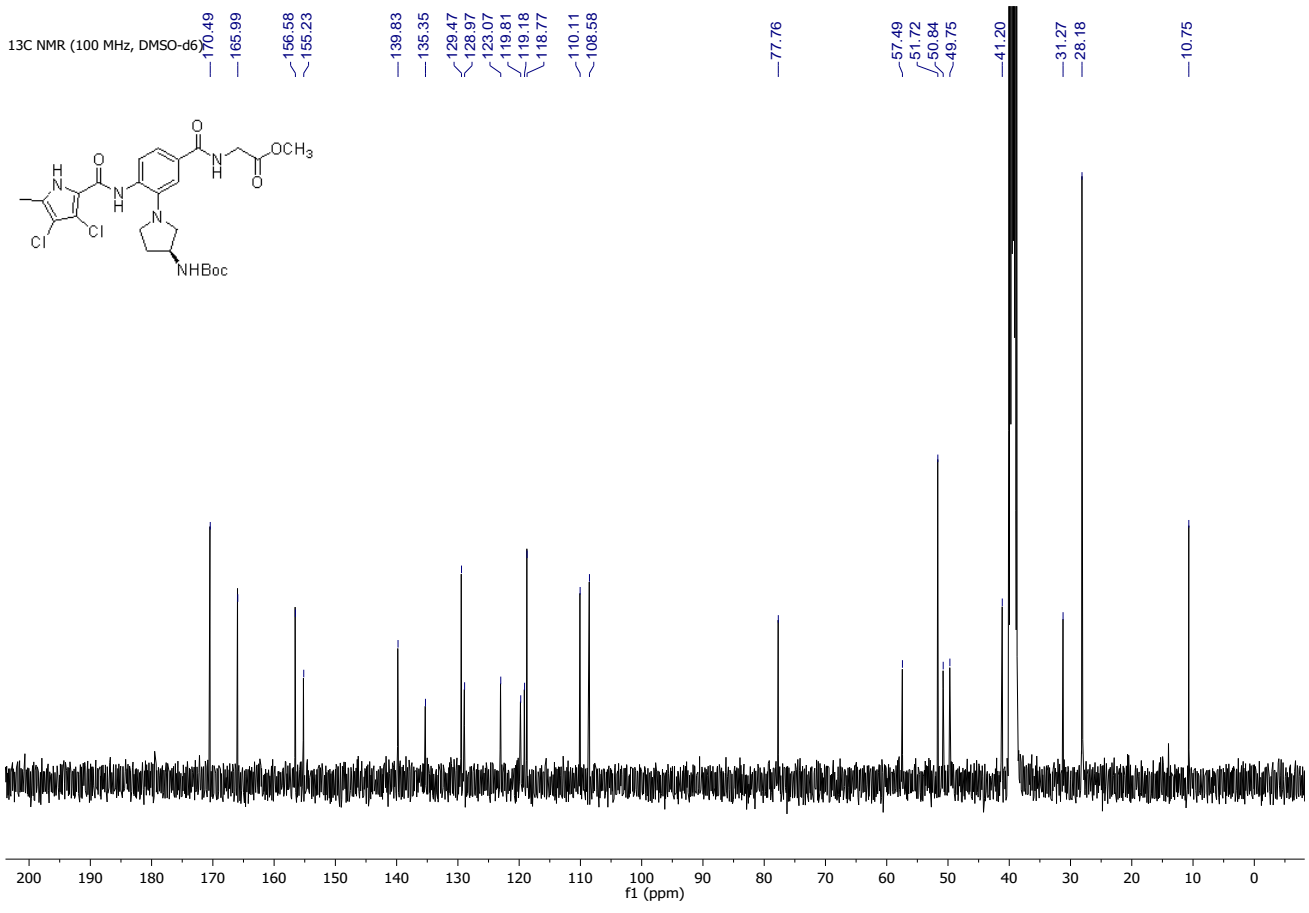
### 4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-((2-methoxy-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (6a)



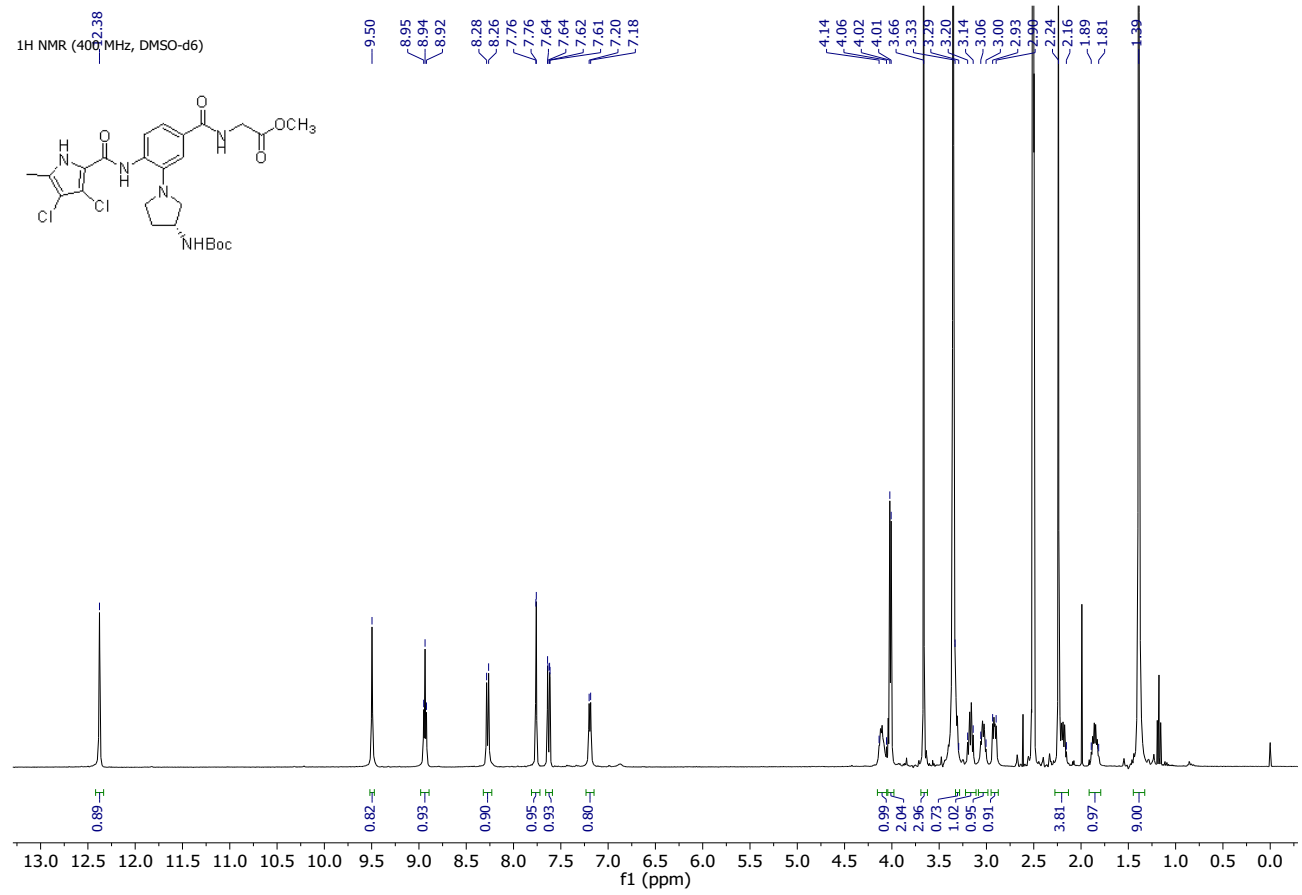



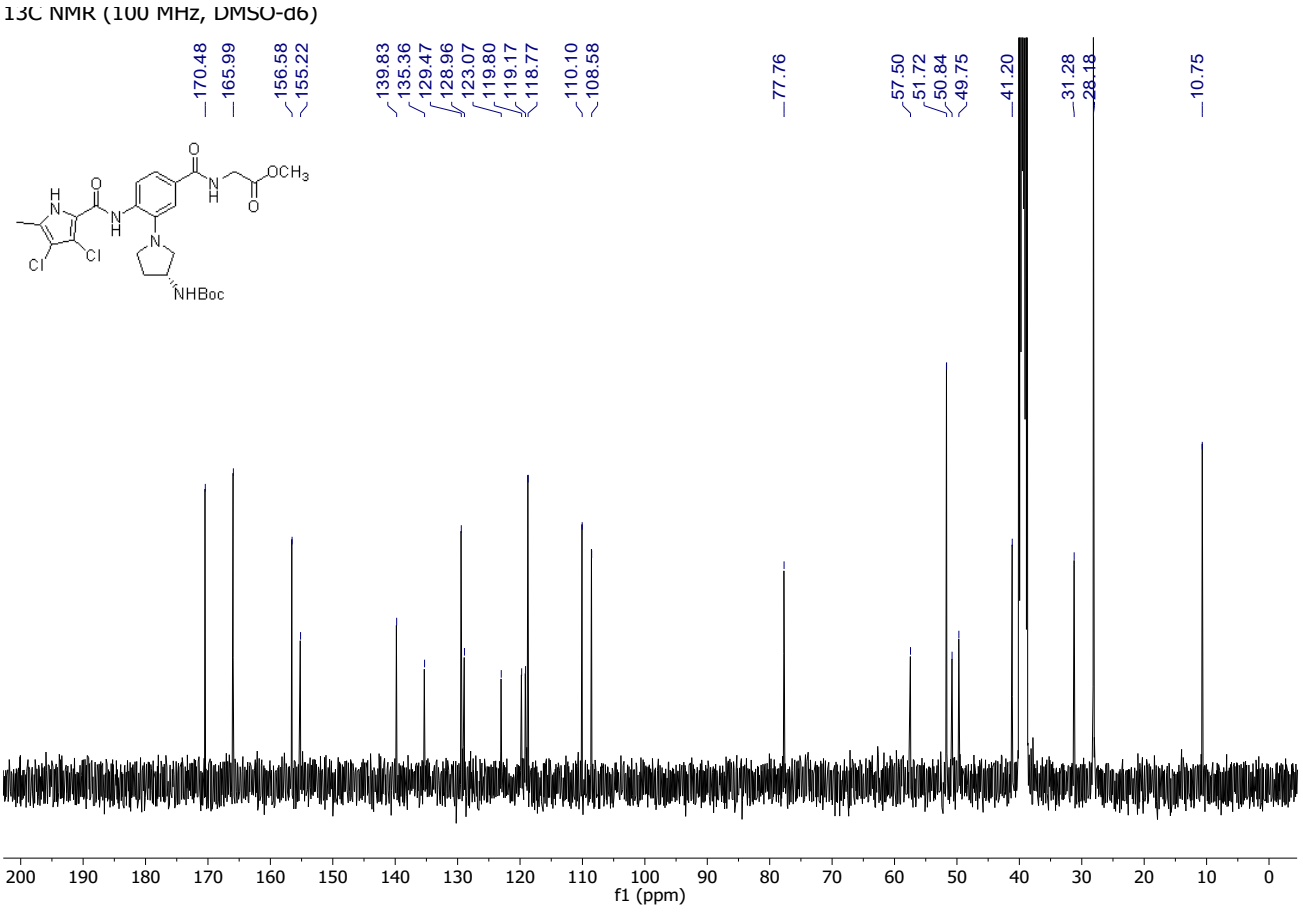
**Methyl (*S*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (6b)**



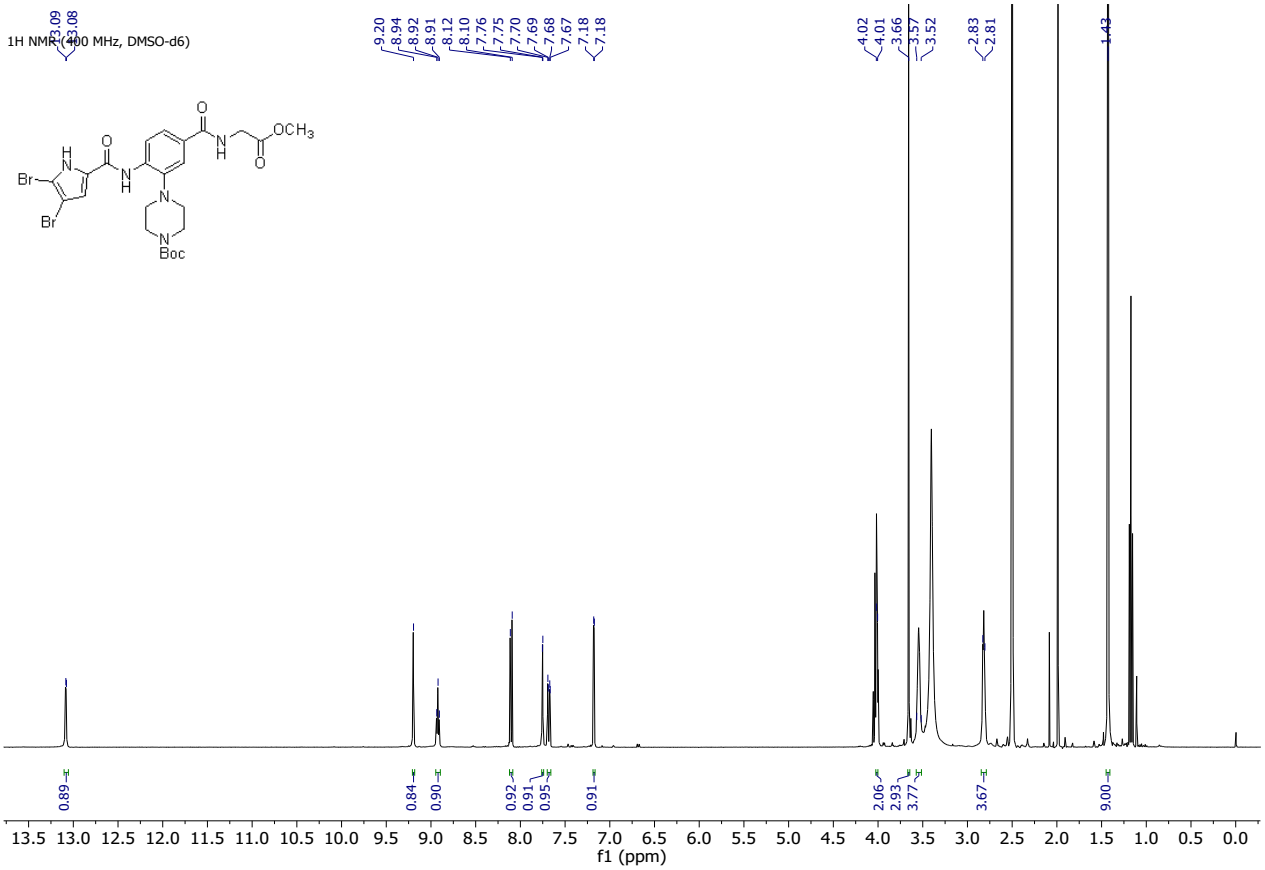



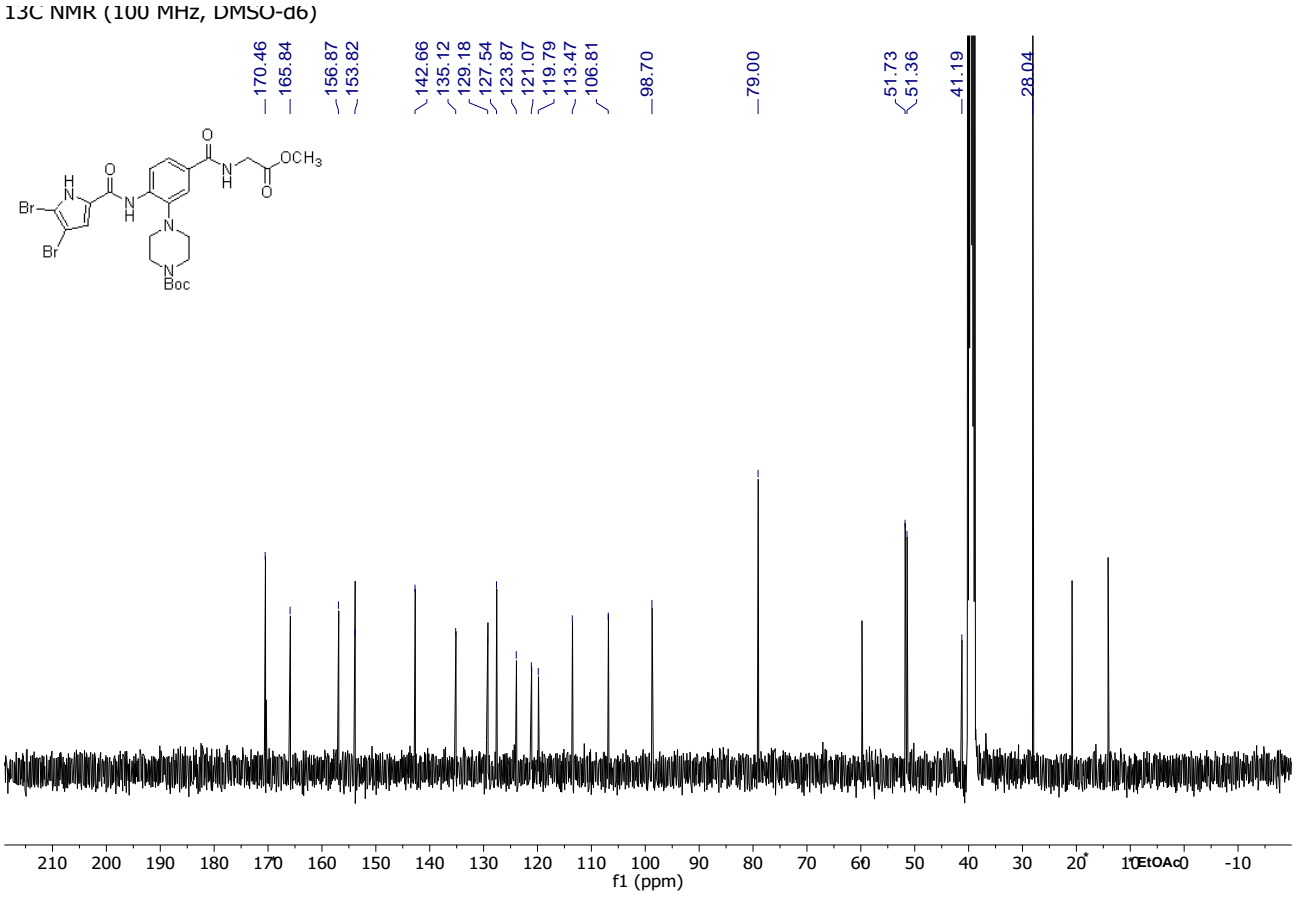
**Methyl (*R*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (6c)**



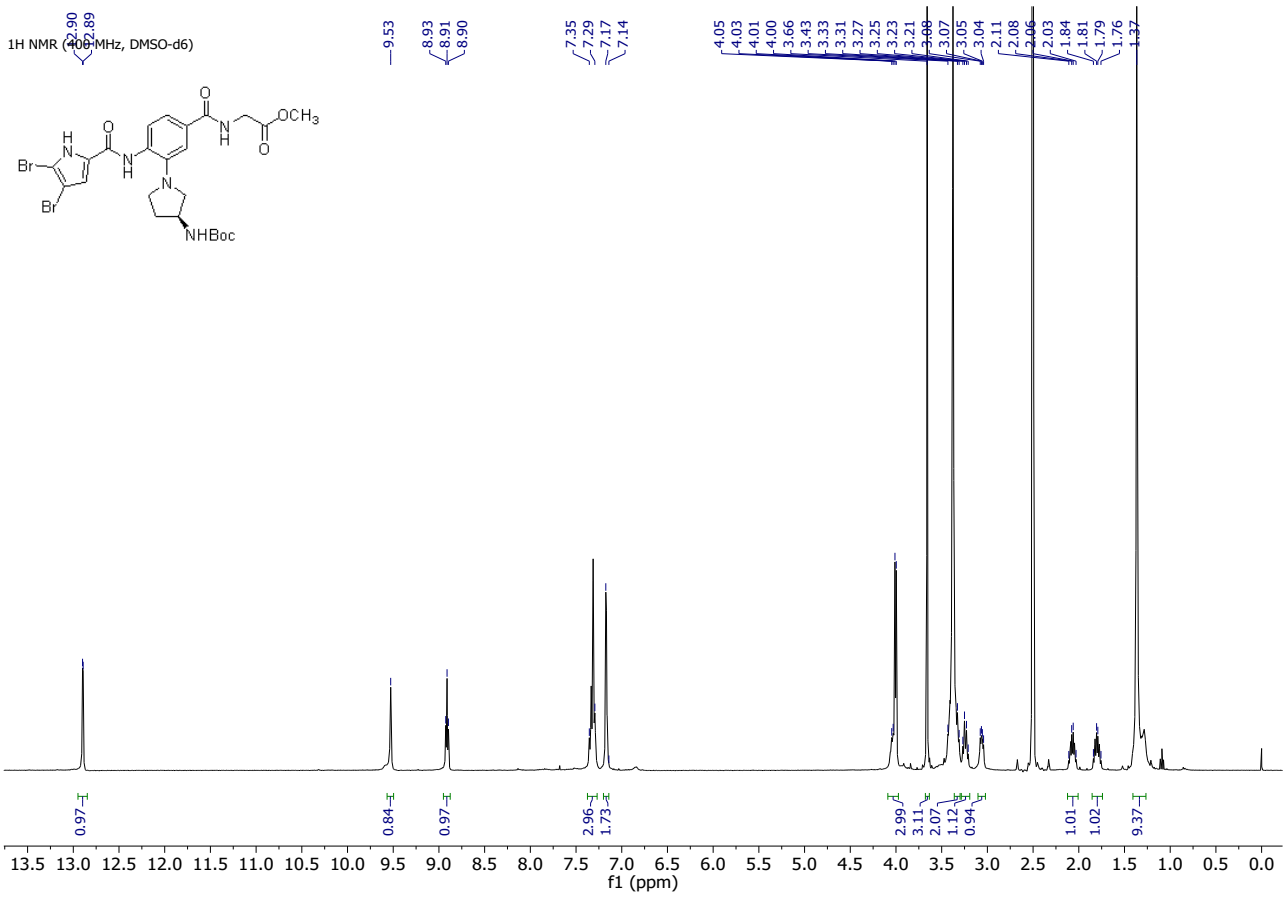



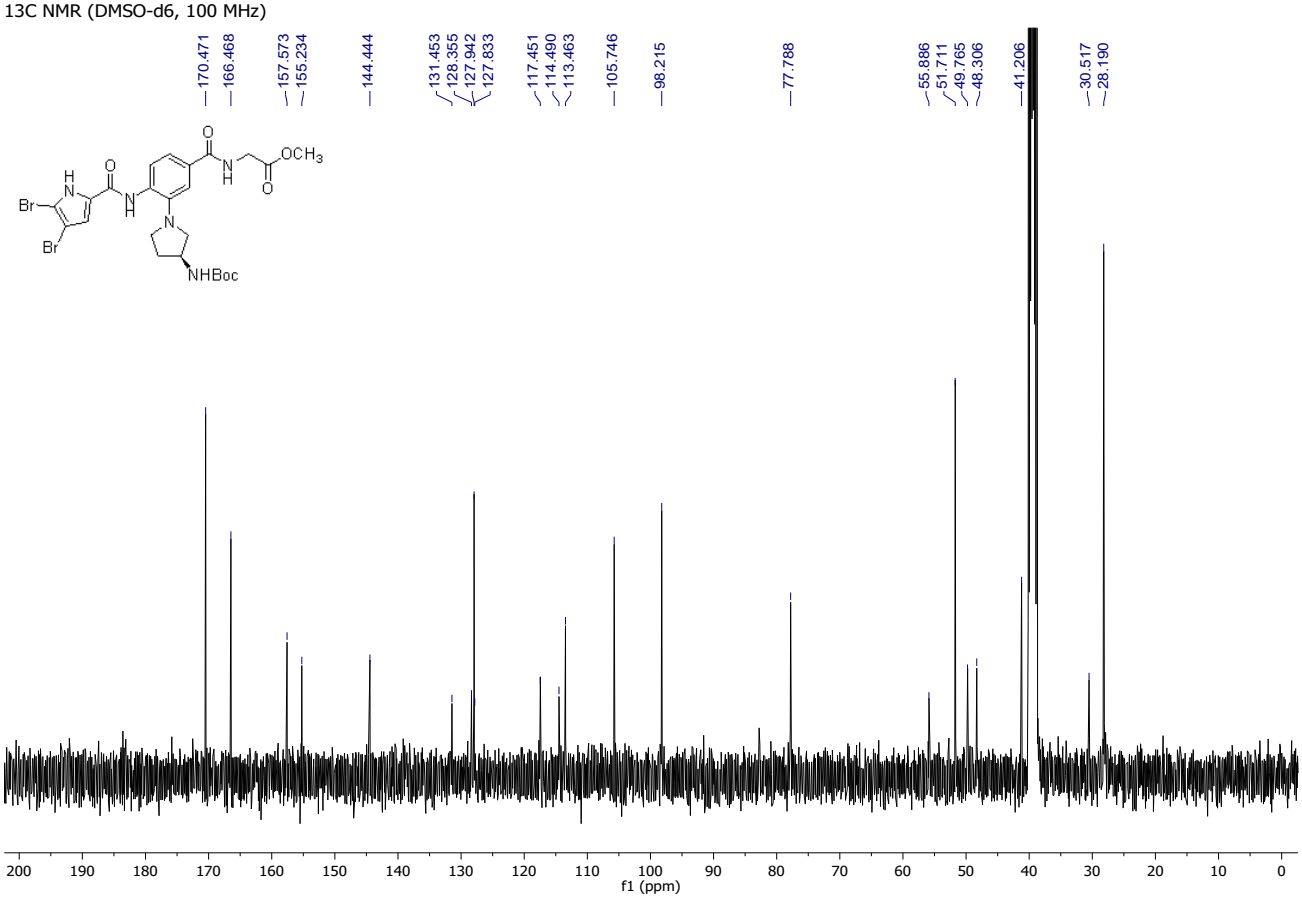
**_tert_-Butyl 4-(2-(4,5-dibromo-1_H_-pyrrole-2-carboxamido)-5-((2-methoxy-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (7a)**



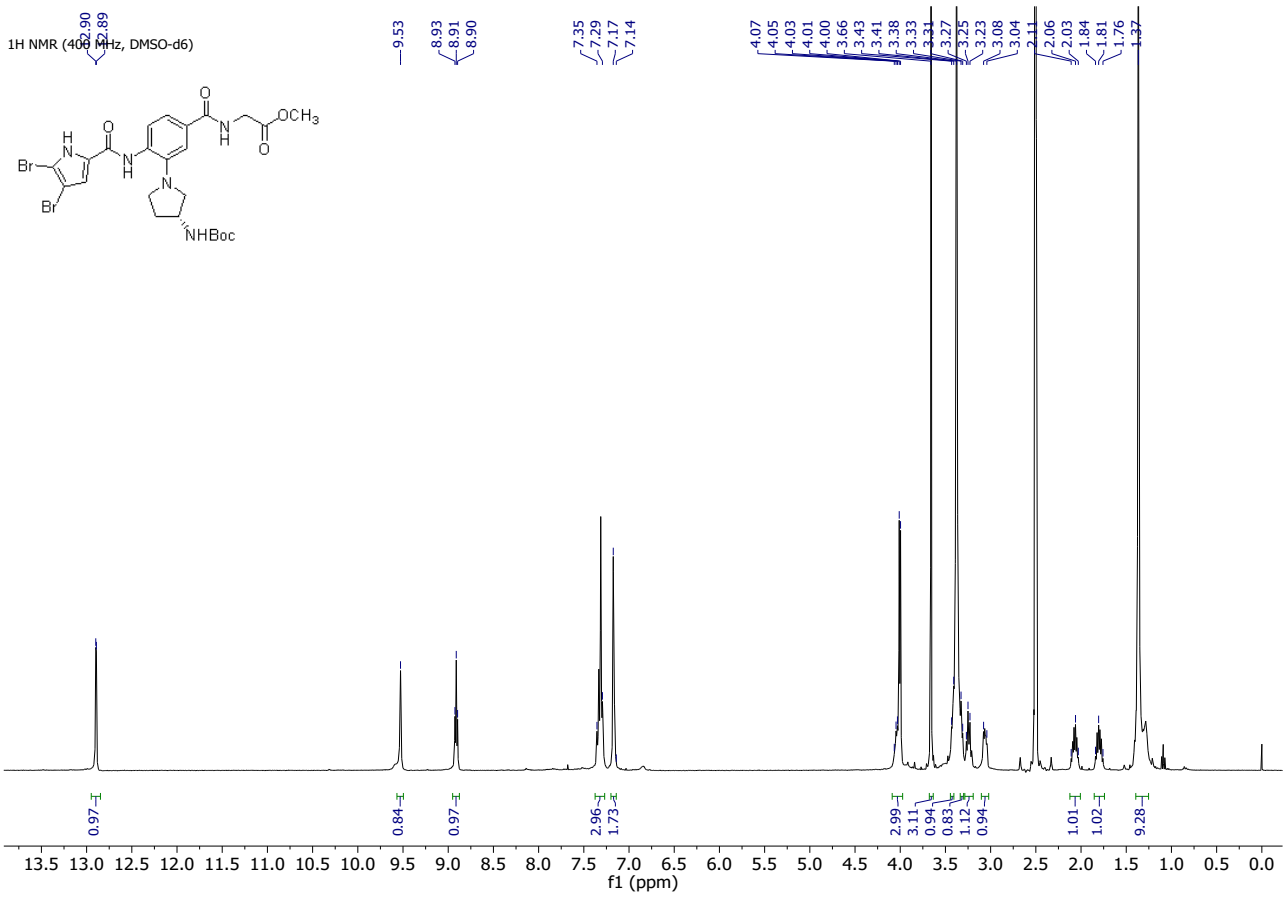



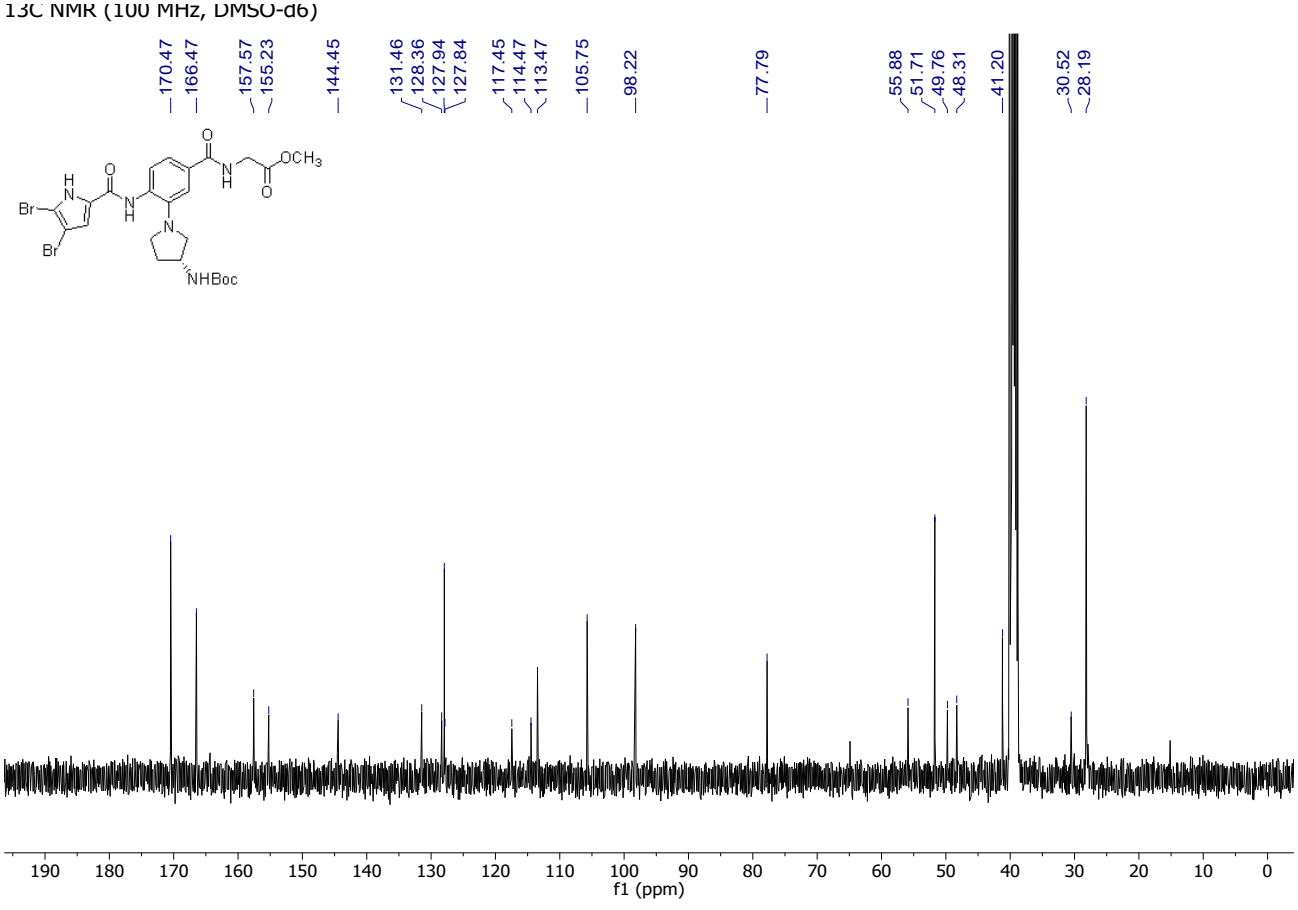
**Methyl (*S*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (7b)**



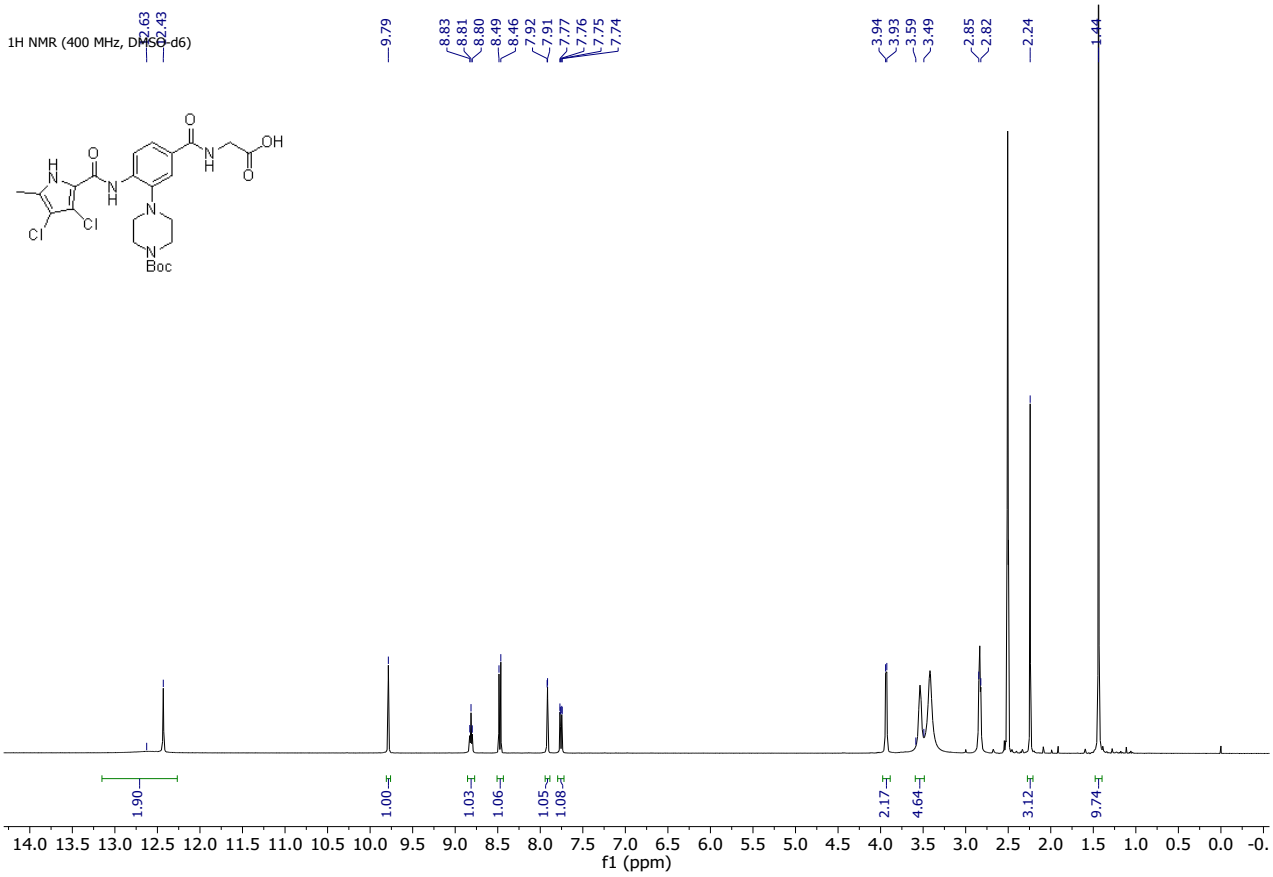



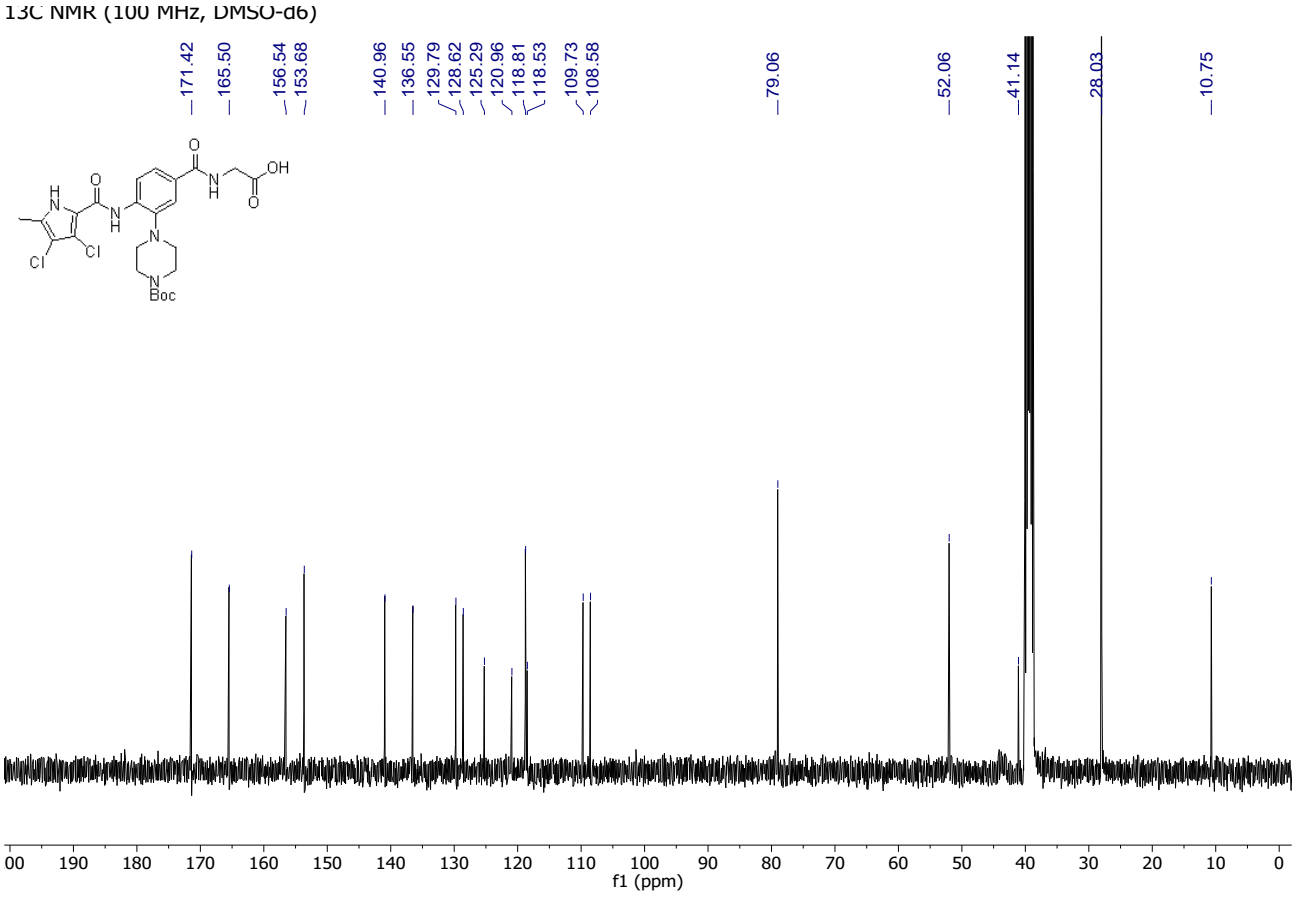
**Methyl (*R*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (7c)**



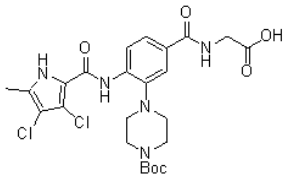



**(3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8a)**



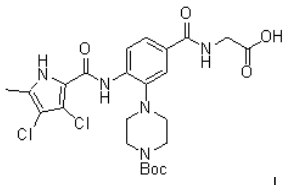



DEPT 45 NMR (100 MHz, DMSO-d6)

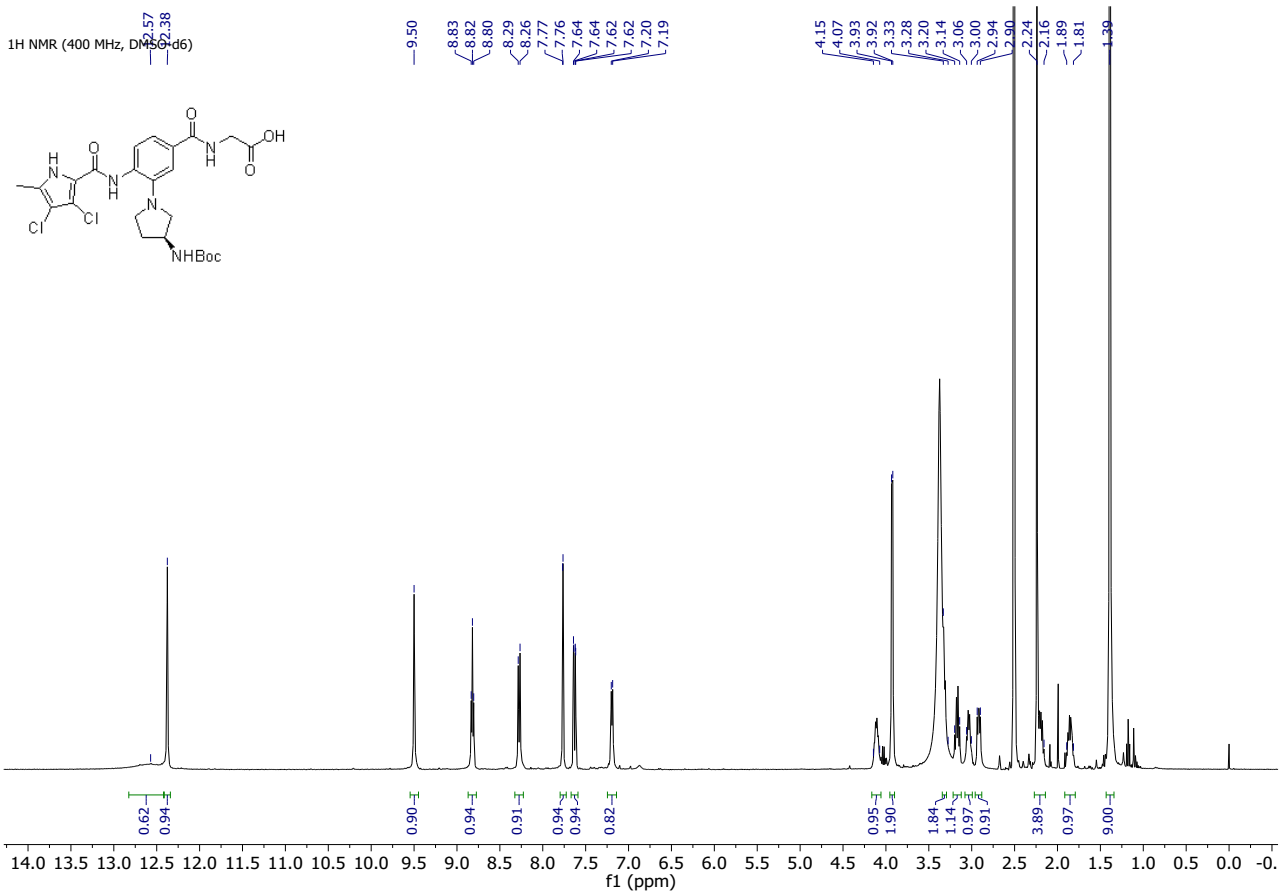


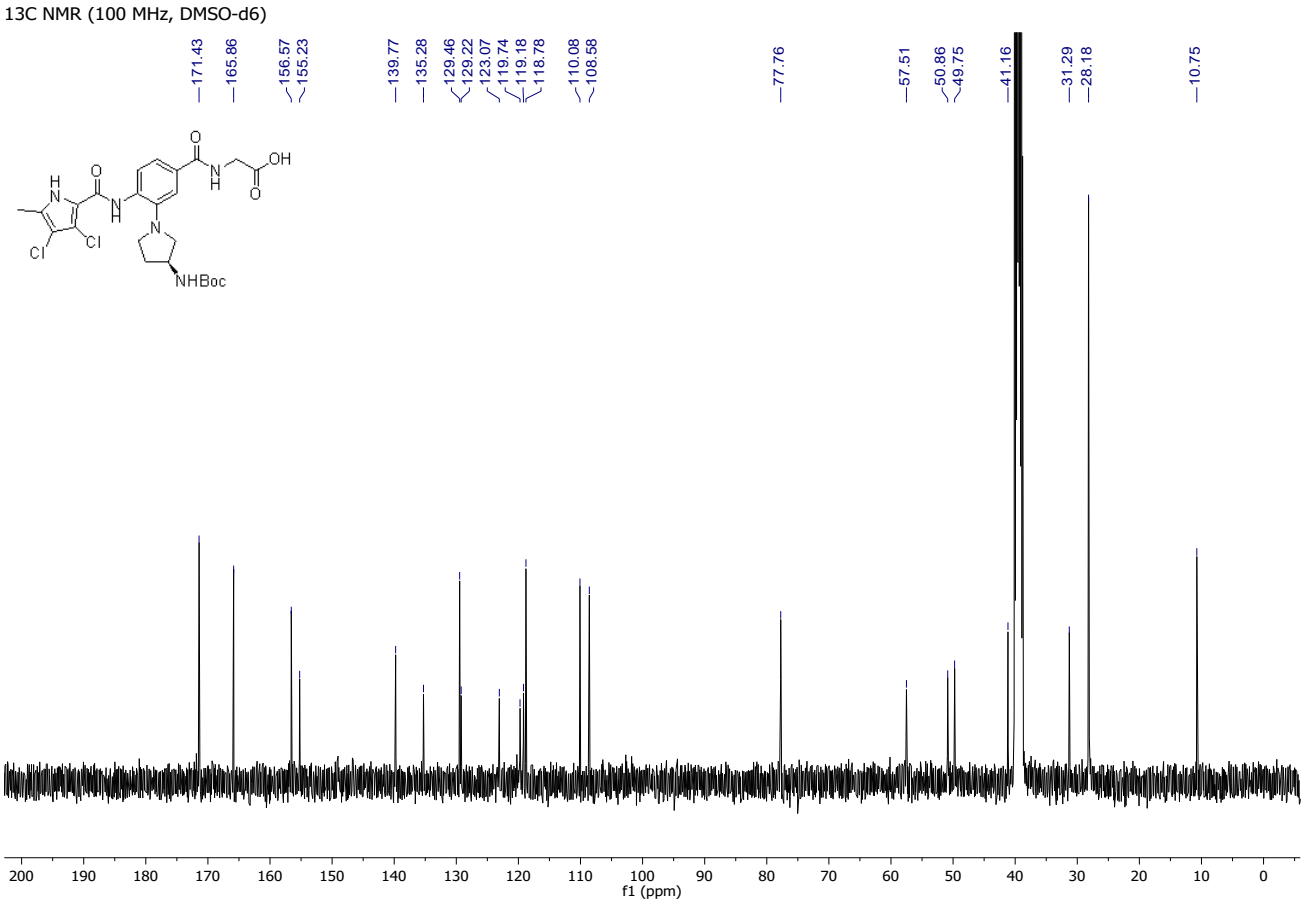



DEPT 135 NMR (100 MHz, DMSO-d6)

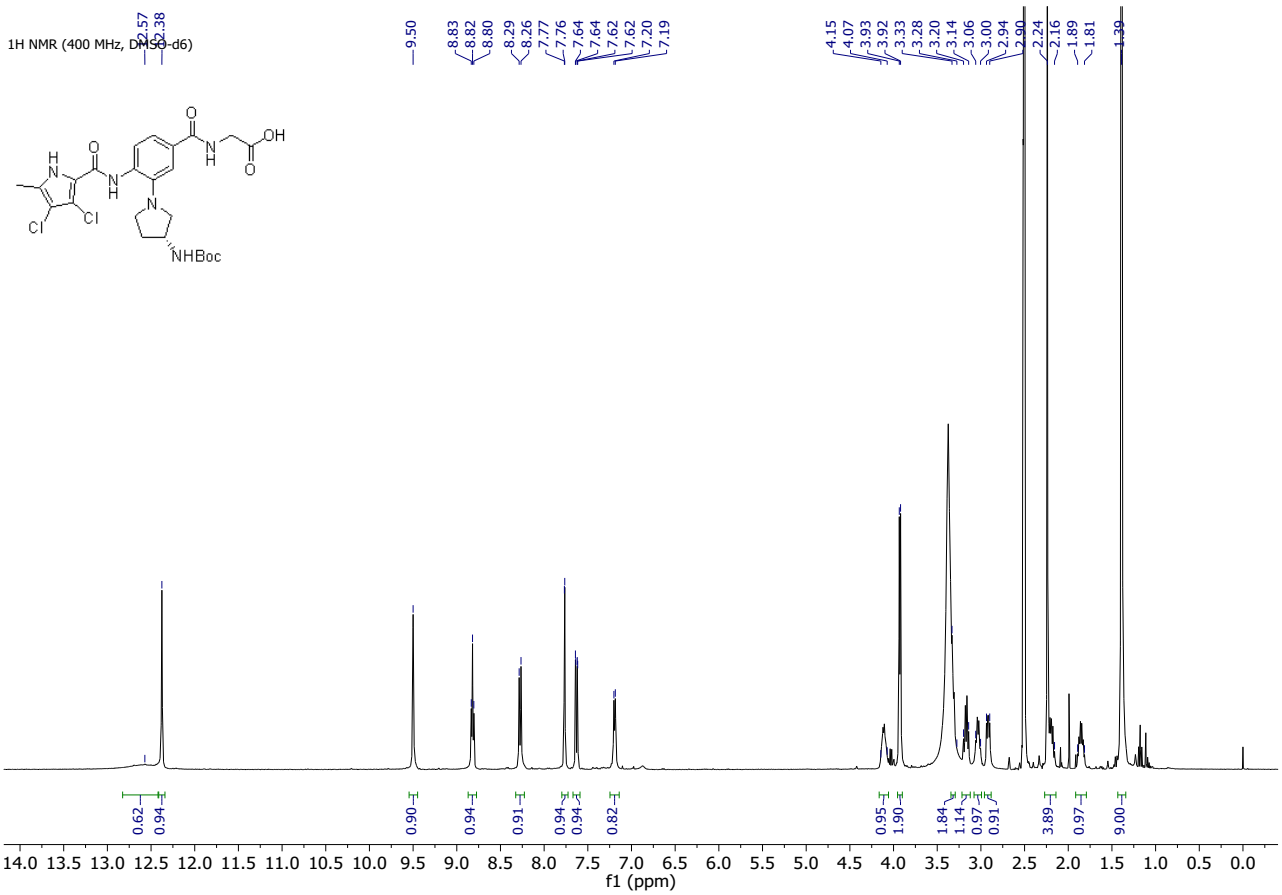


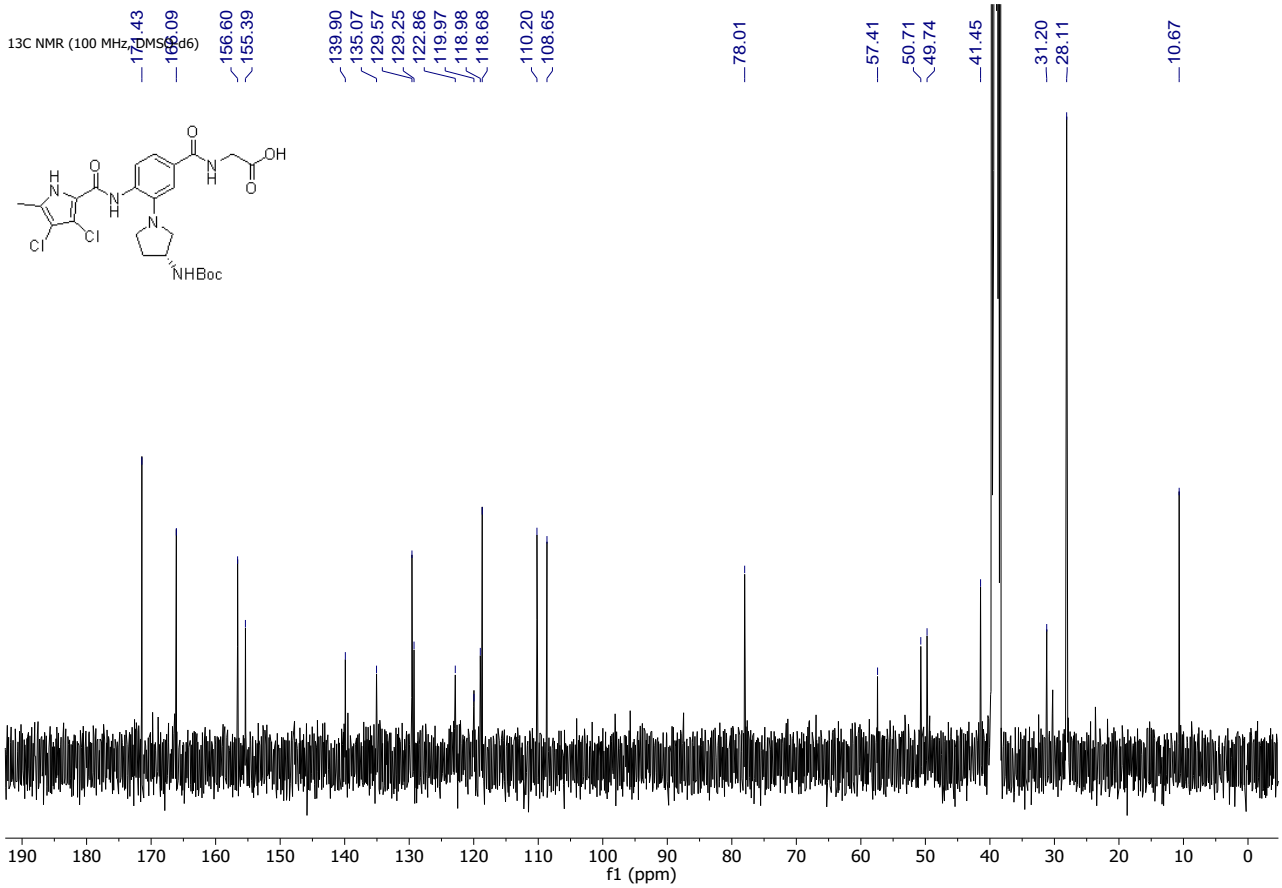
**(*S*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8b)**



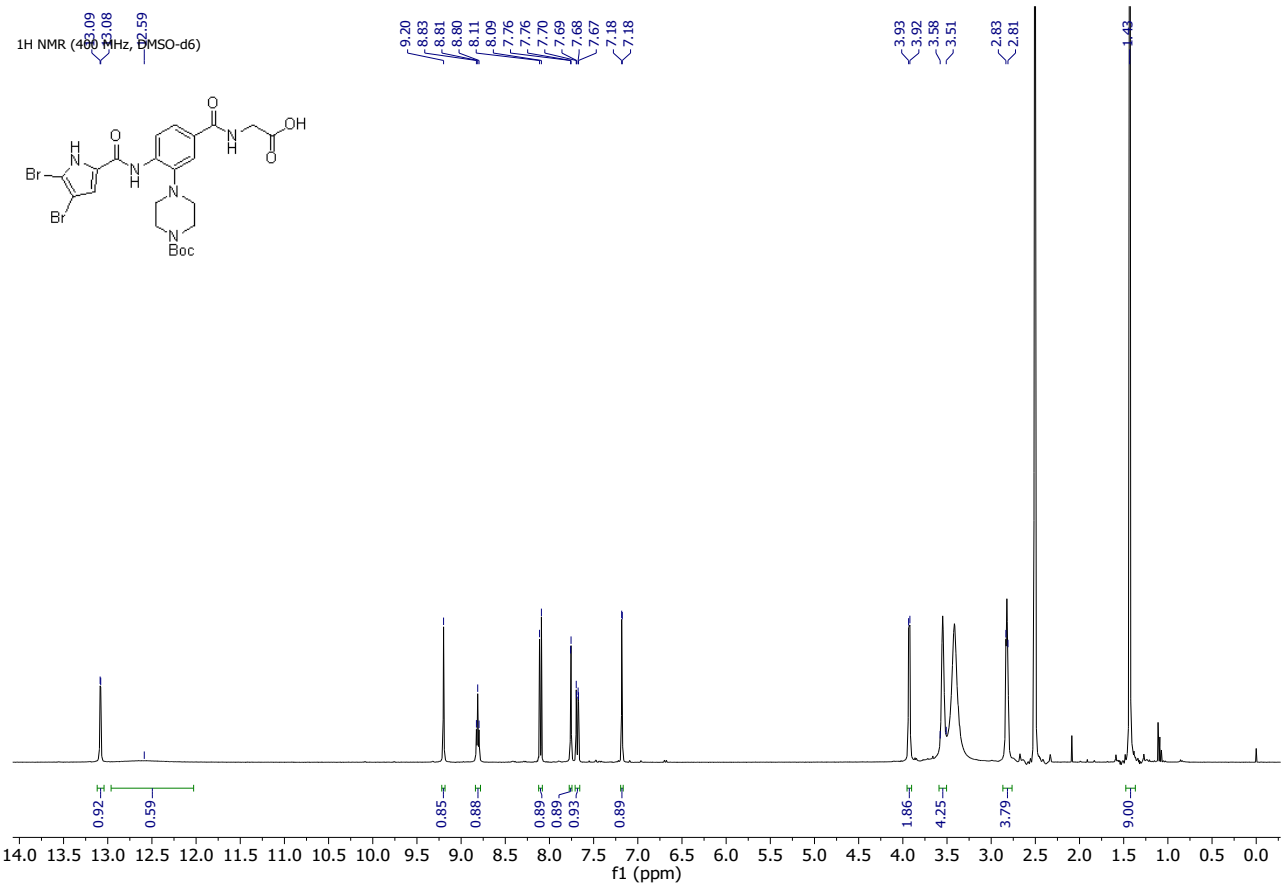



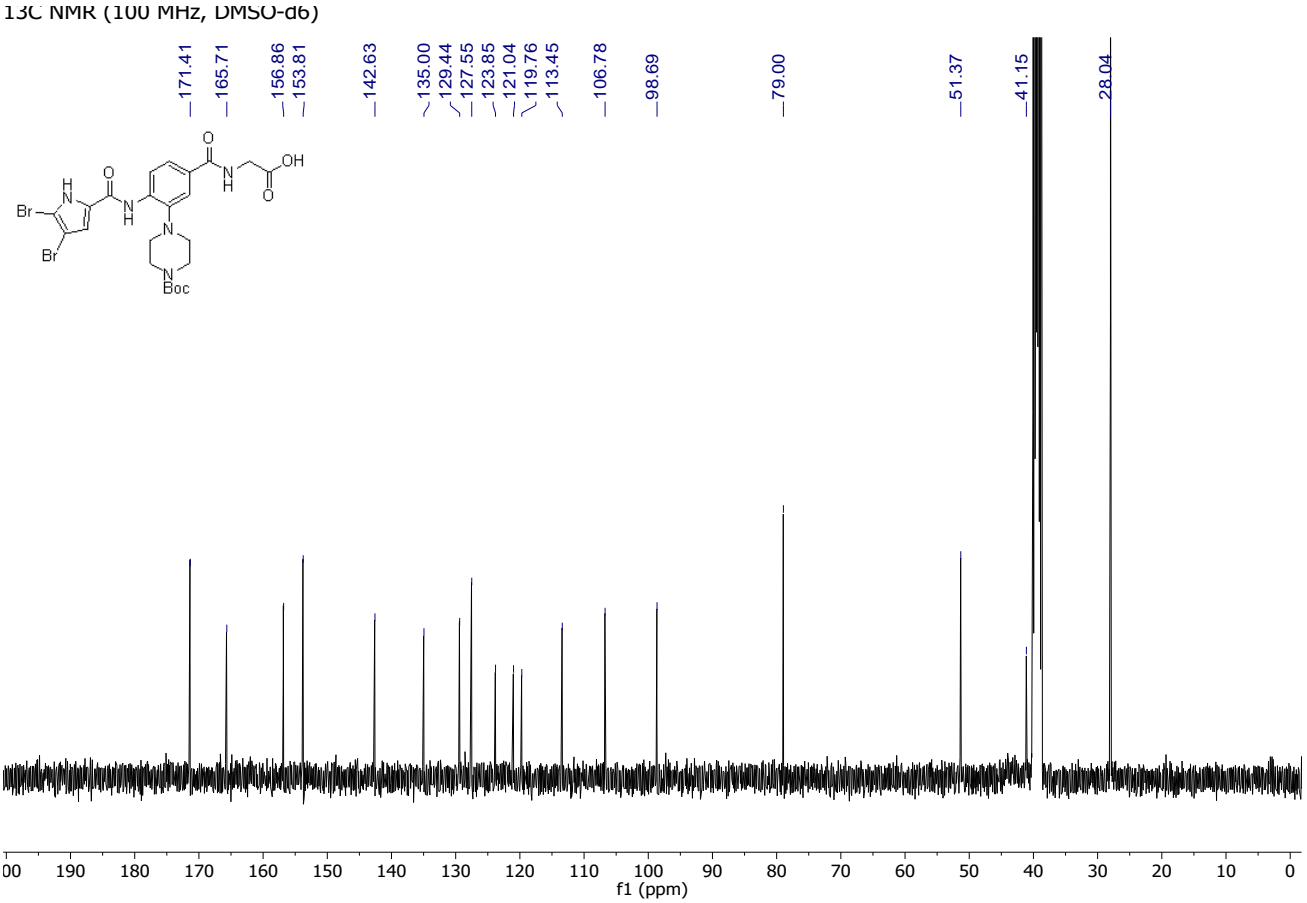
**(*R*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8c)**



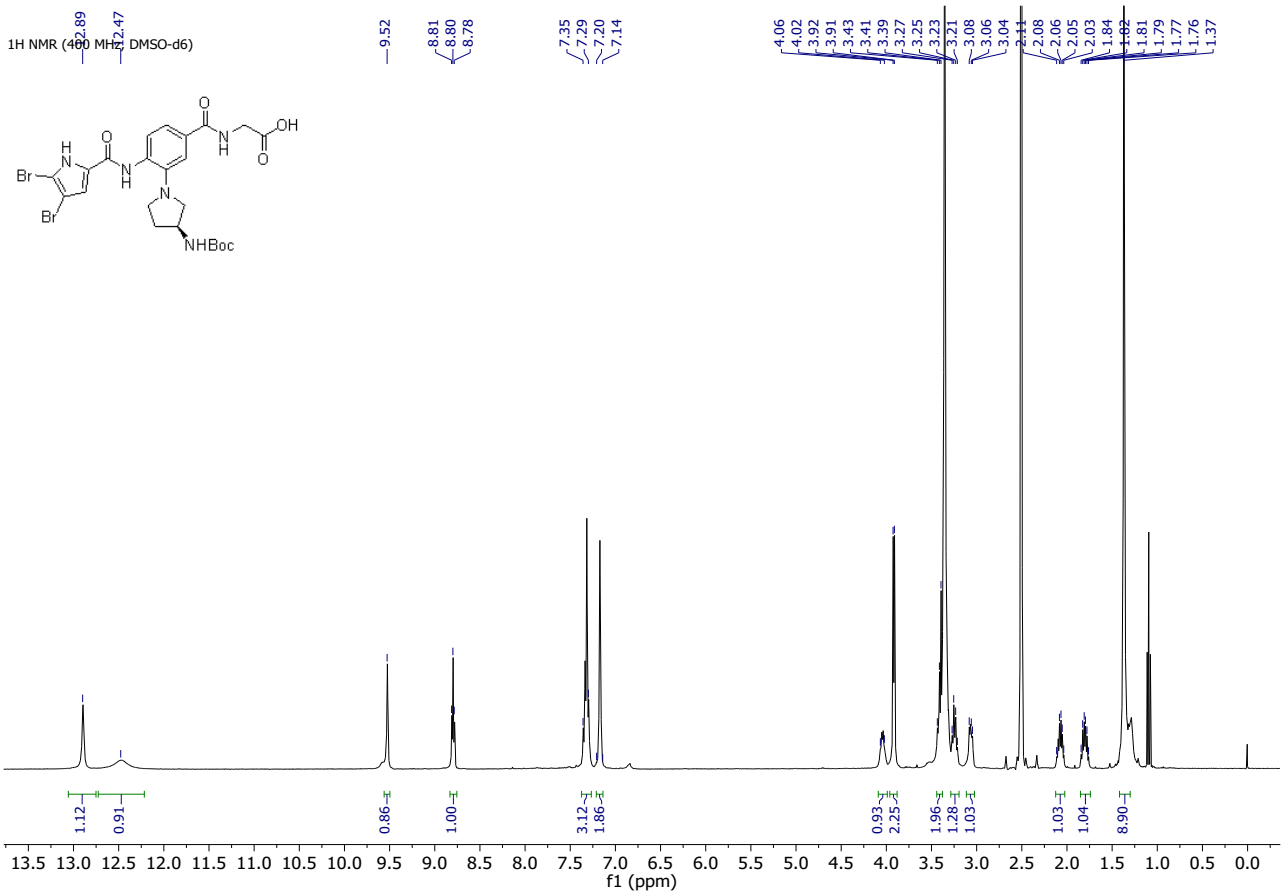



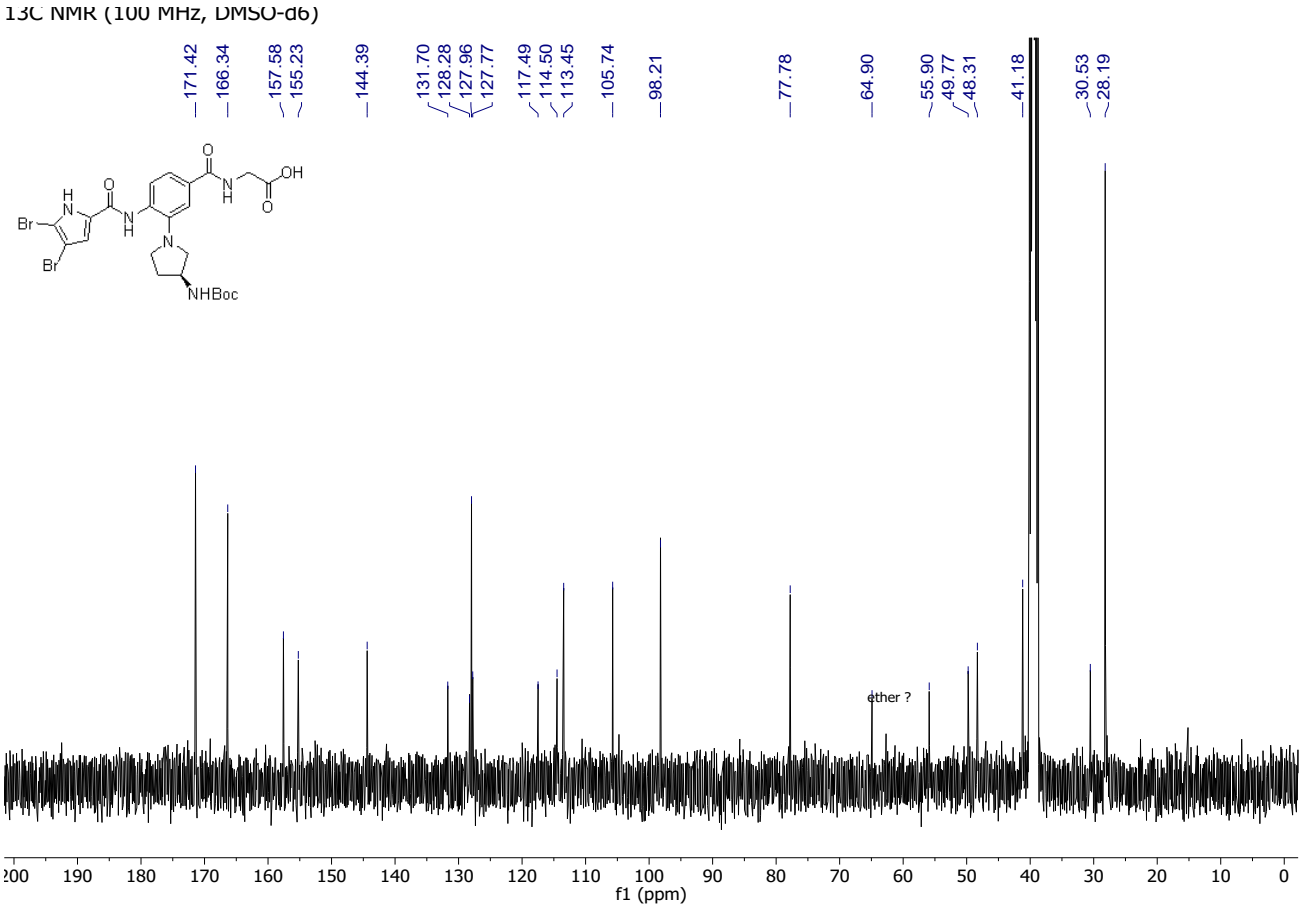
**(3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9a)**



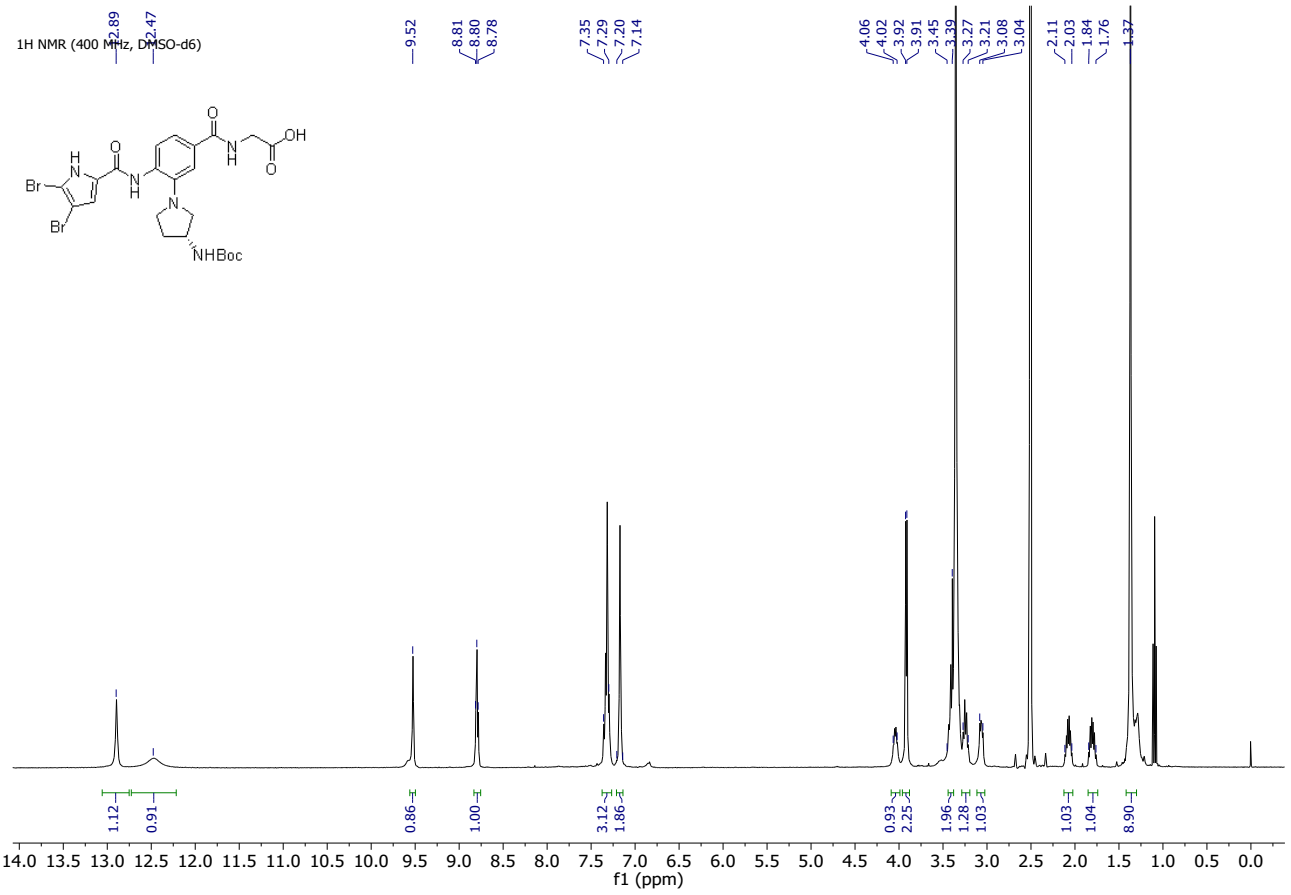



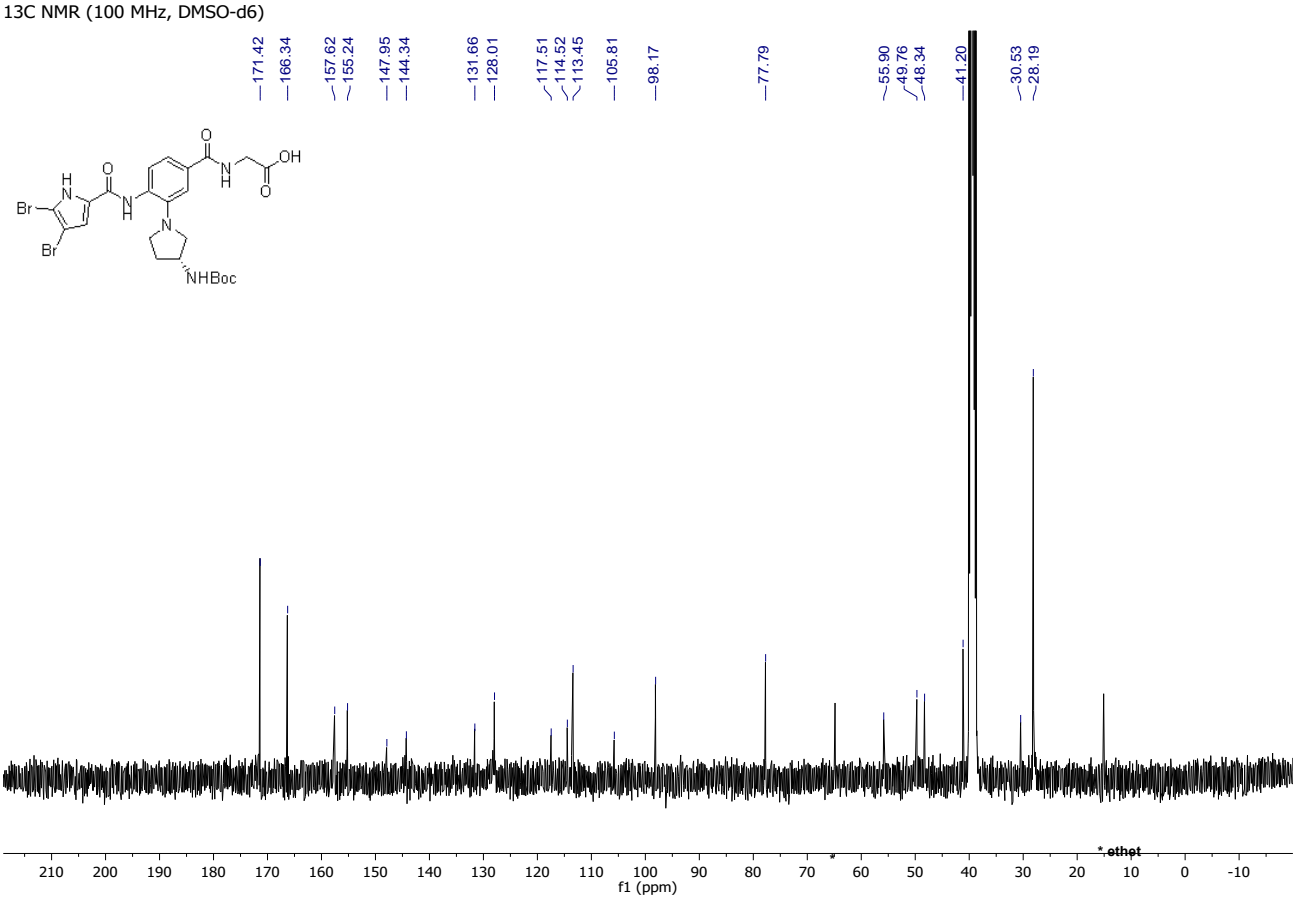
**(*S*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9b)**



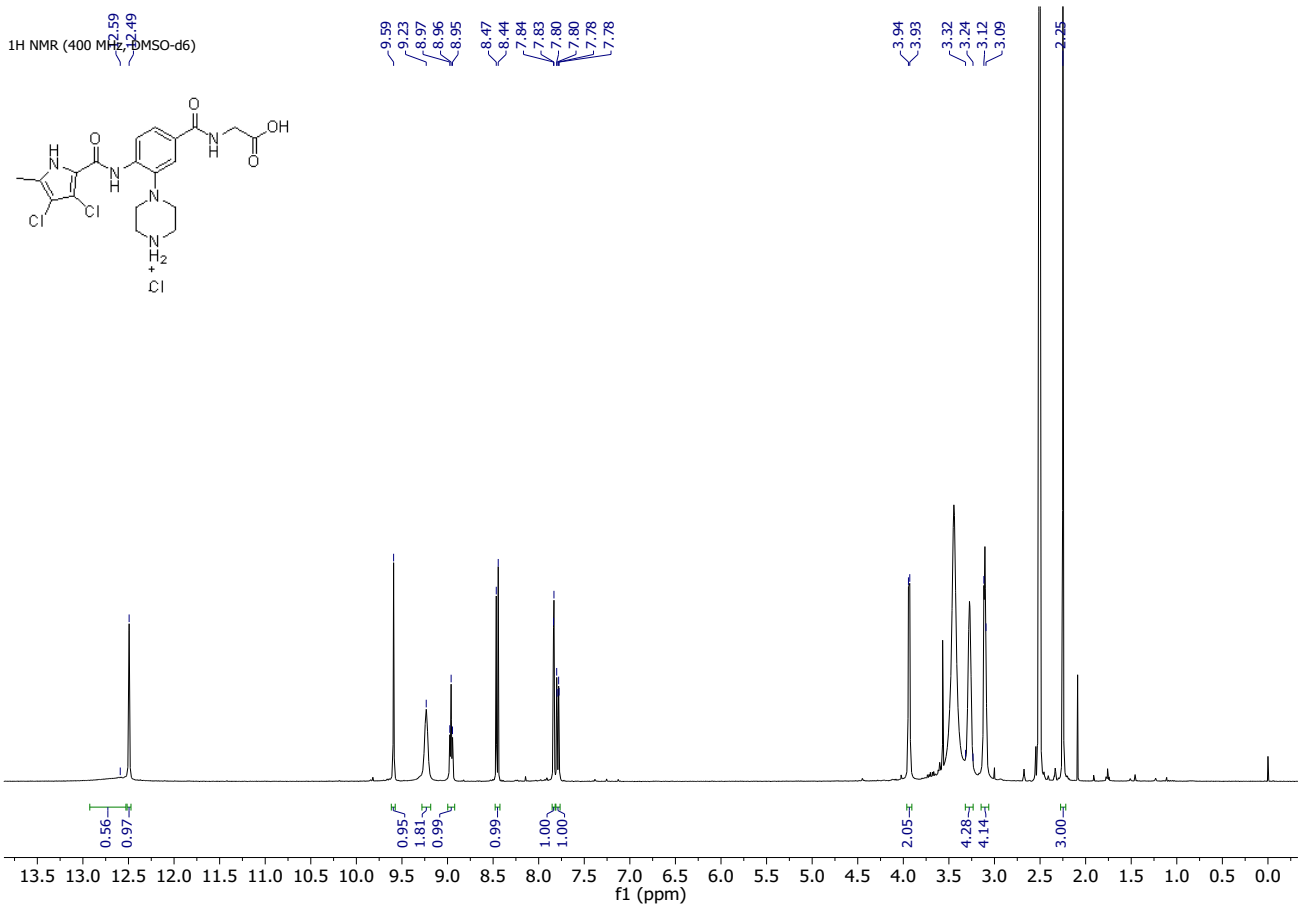



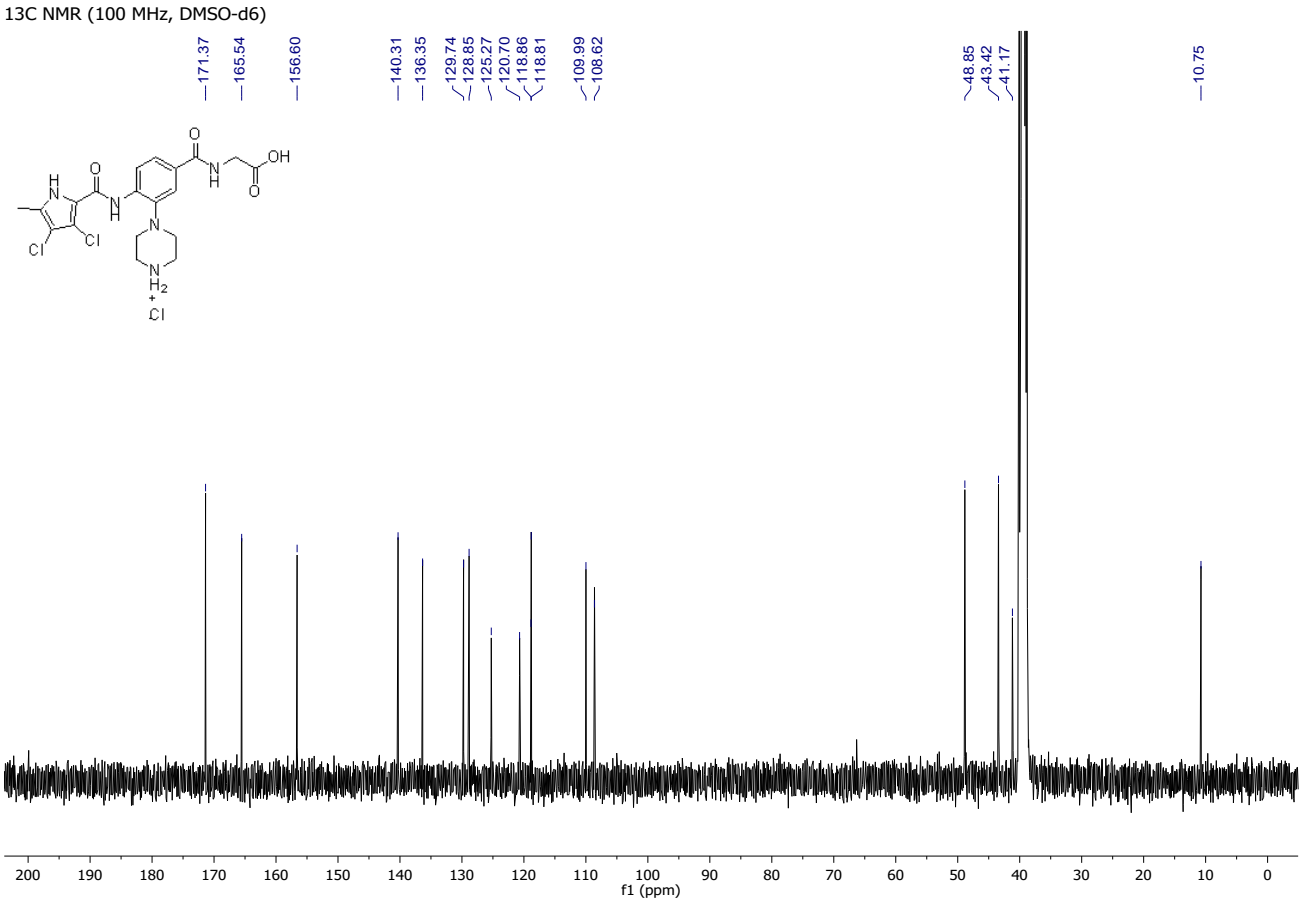
**(*R*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9c)**



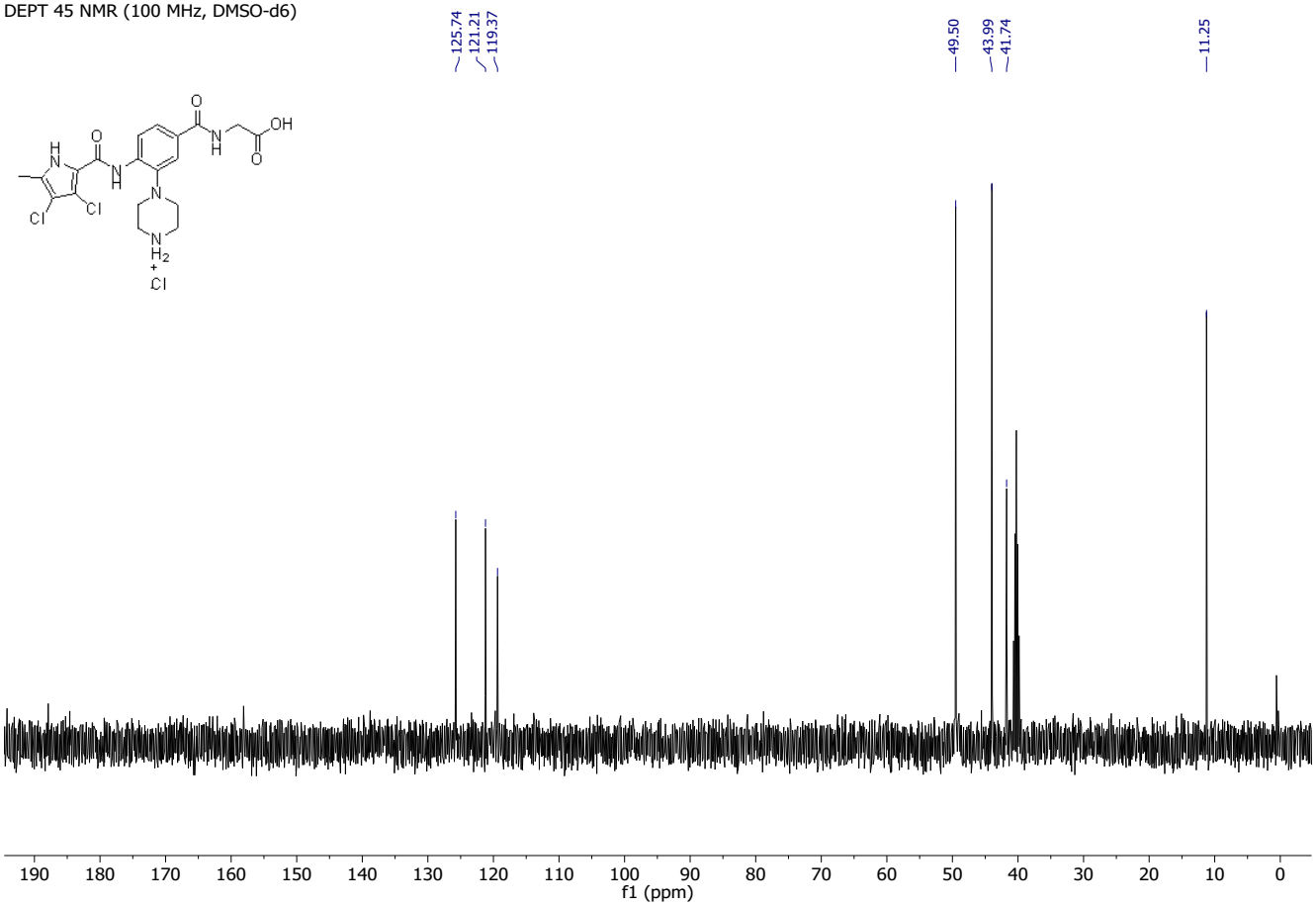



**4-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (10a)**

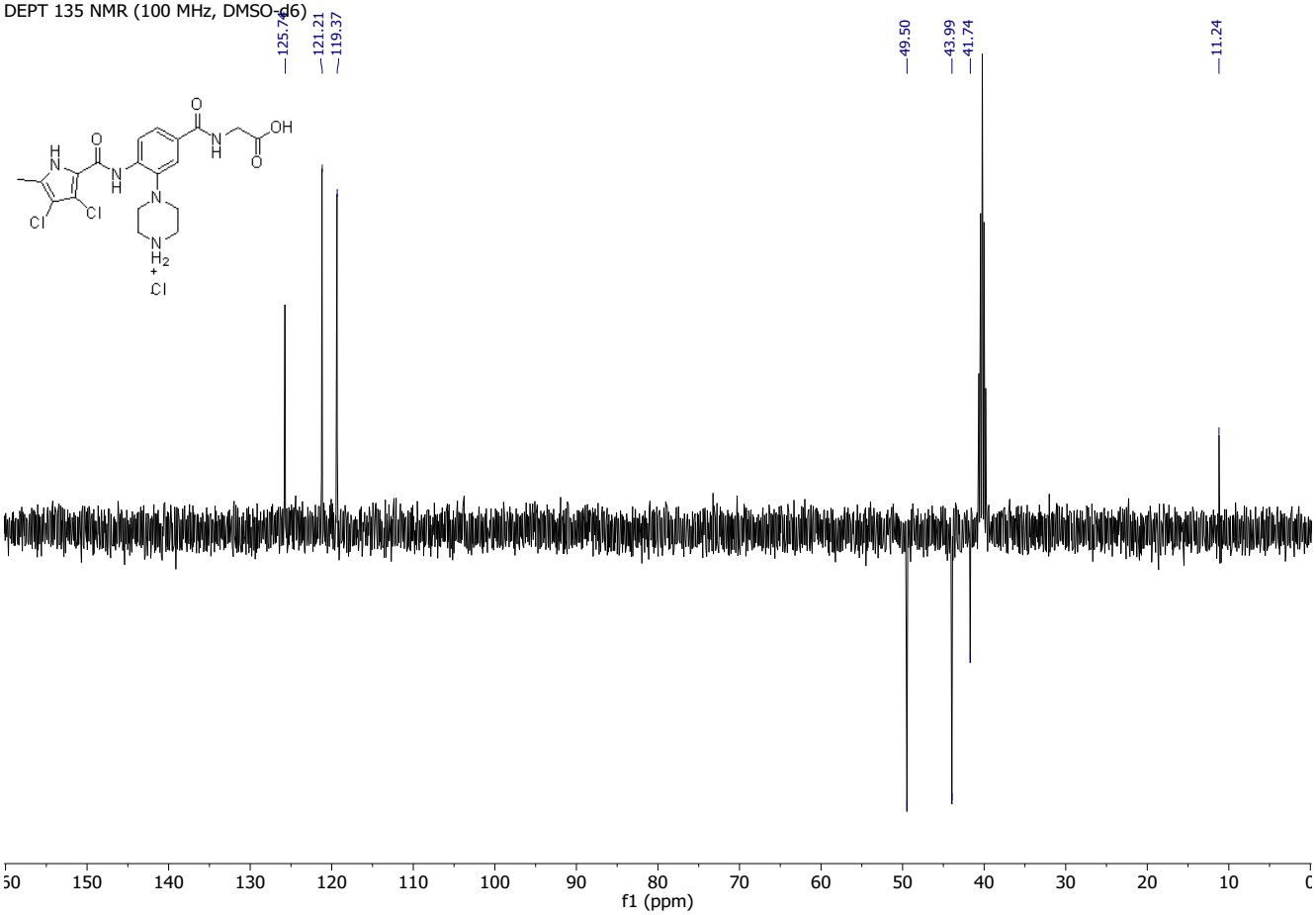


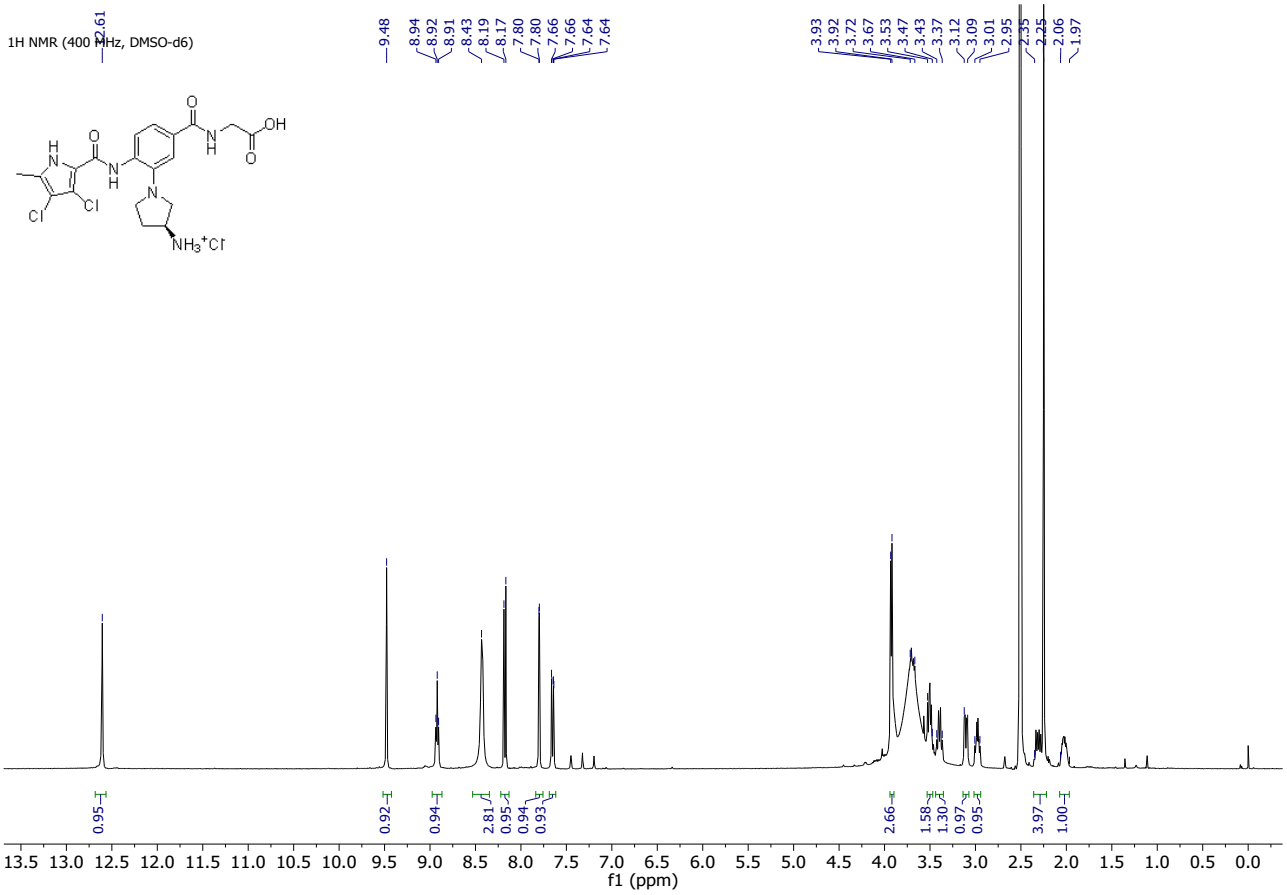
DEPT 45 NMR (100 MHz, DMSO-d6)

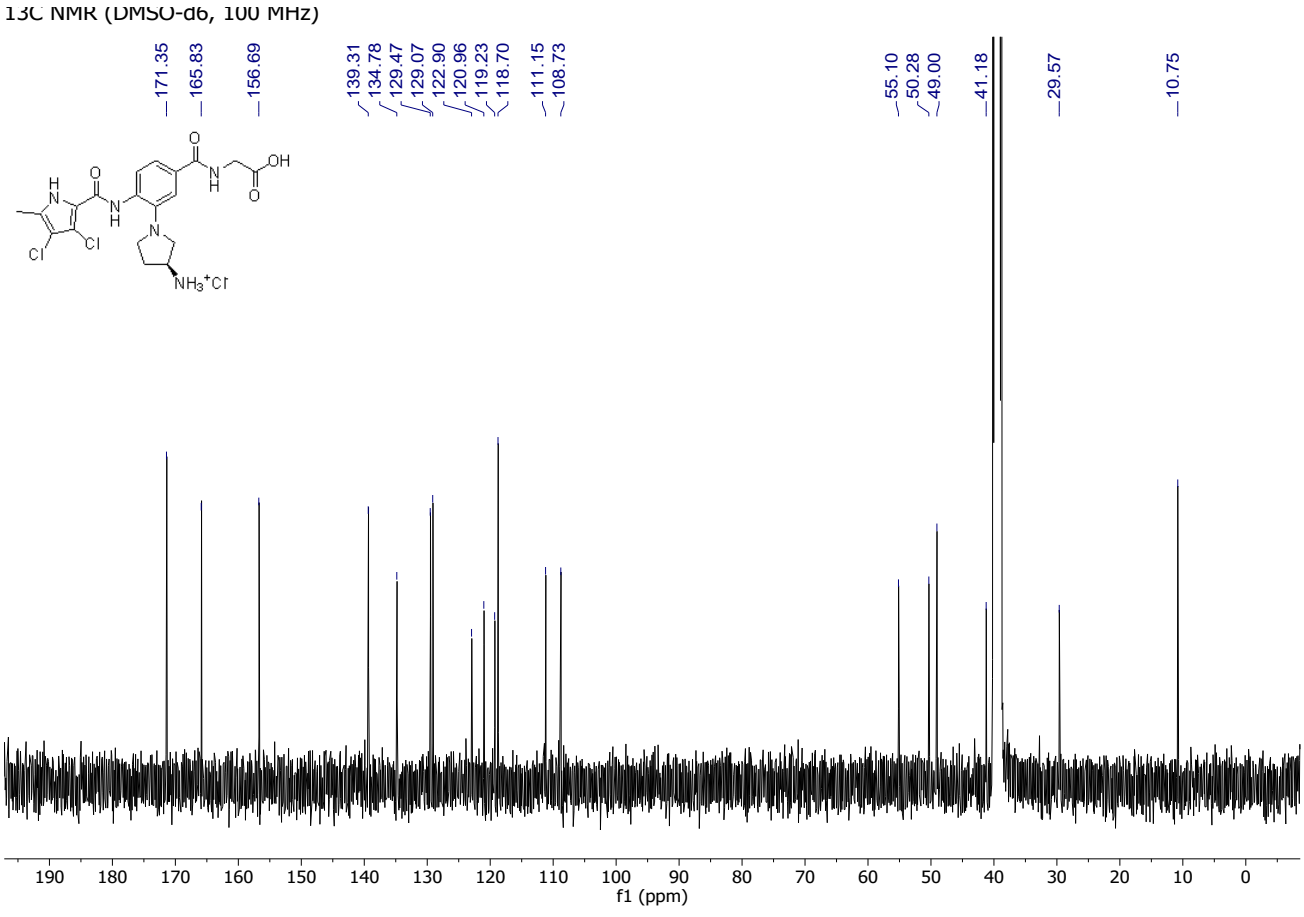



DEPT 135 NMR (100 MHz, DMSO-d6)

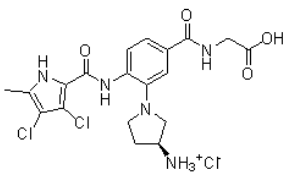


**(*S*)-1-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (10b)**



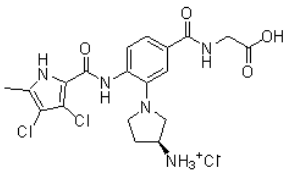



DEPT 45 NMR (100 MHz, DMSO-d6)

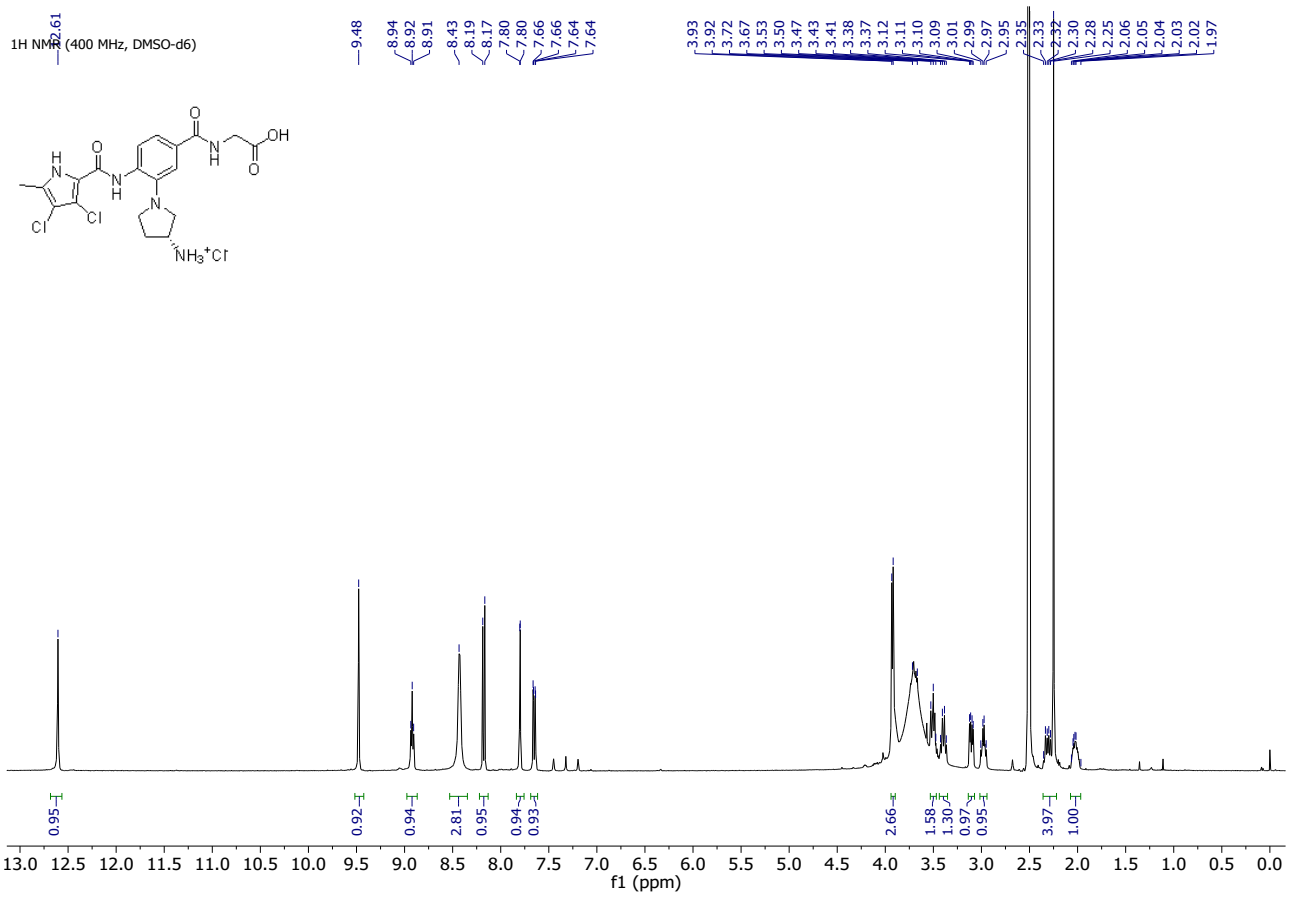




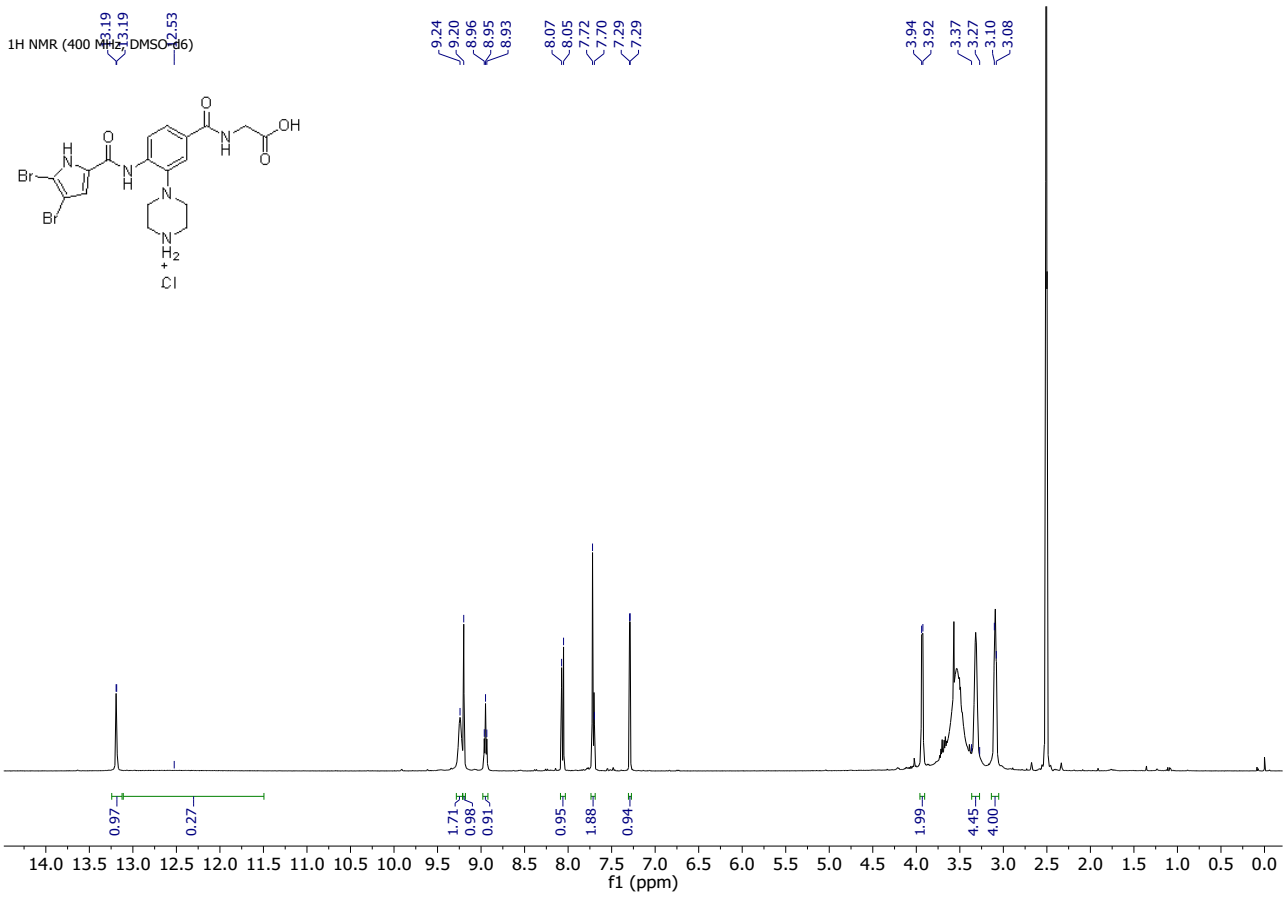

DEPT 135 NMR (100 MHz, DMSO-d6)

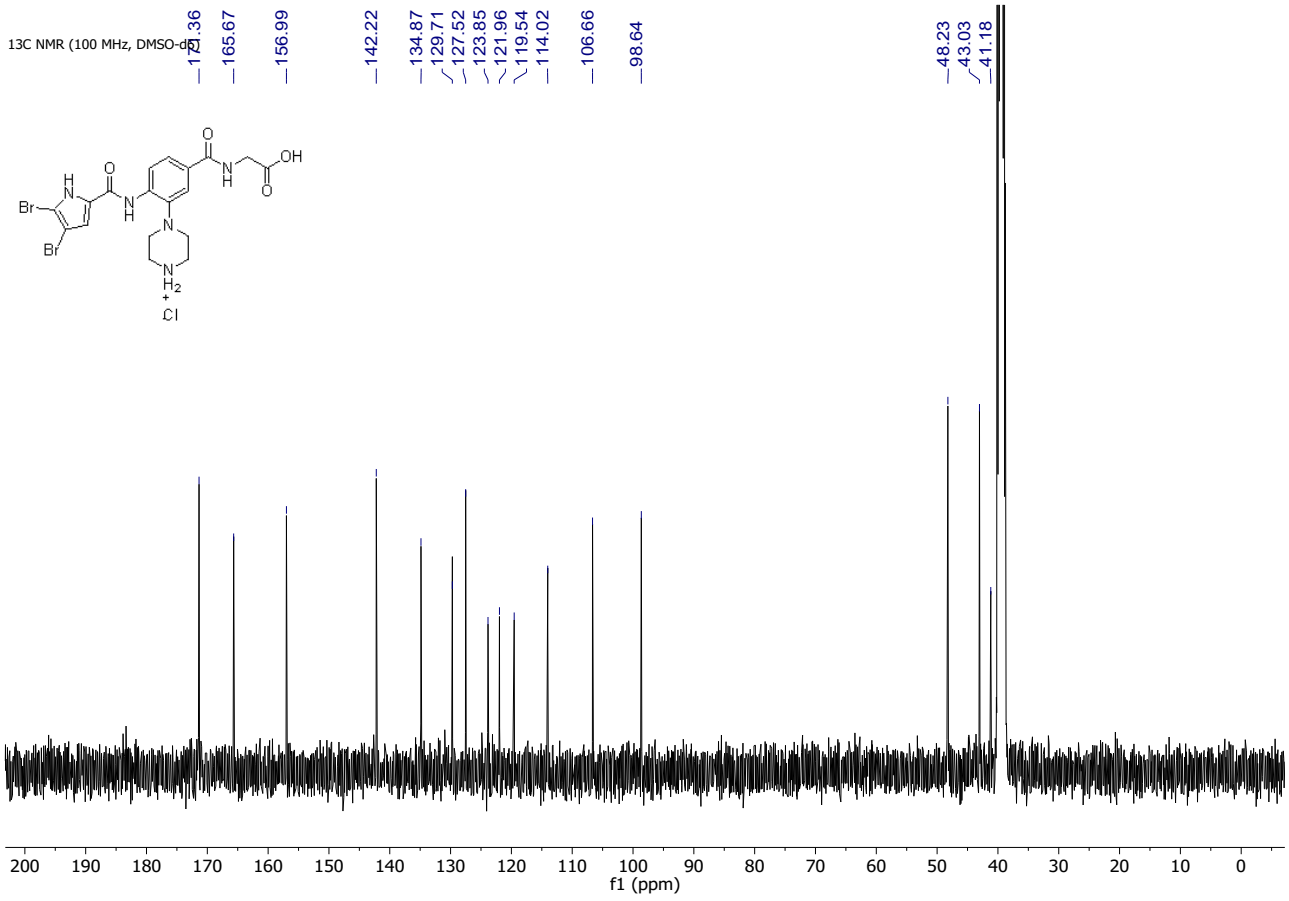


**(*R*)-1-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (10c)**

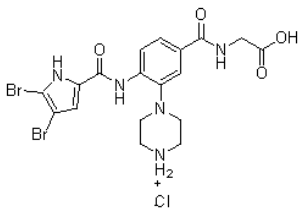


**4-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (11a)**



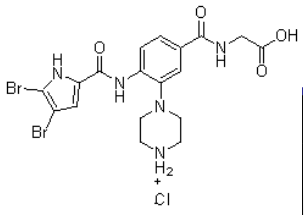
DEPT 45 NMR (100 MHz, DMSO-d6)



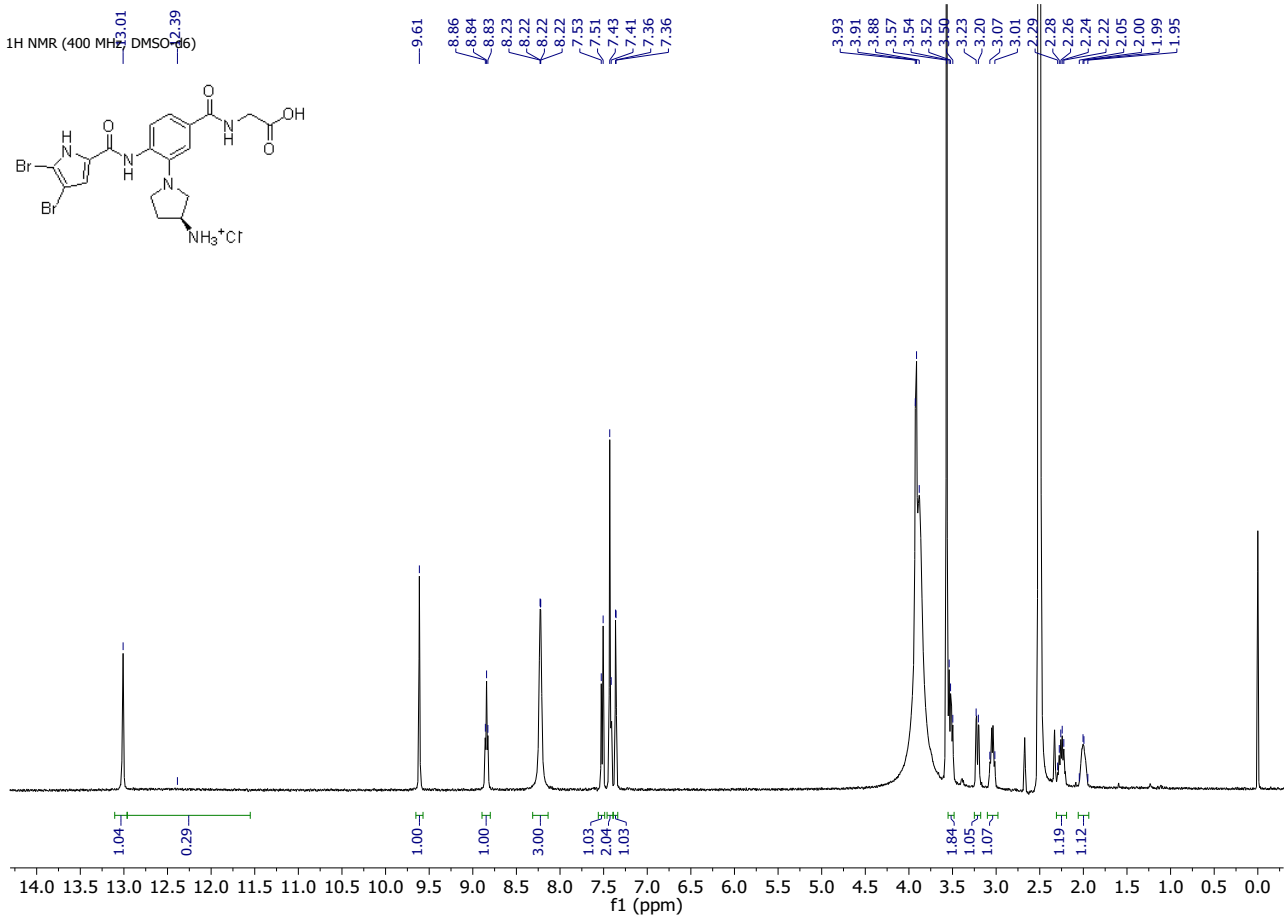


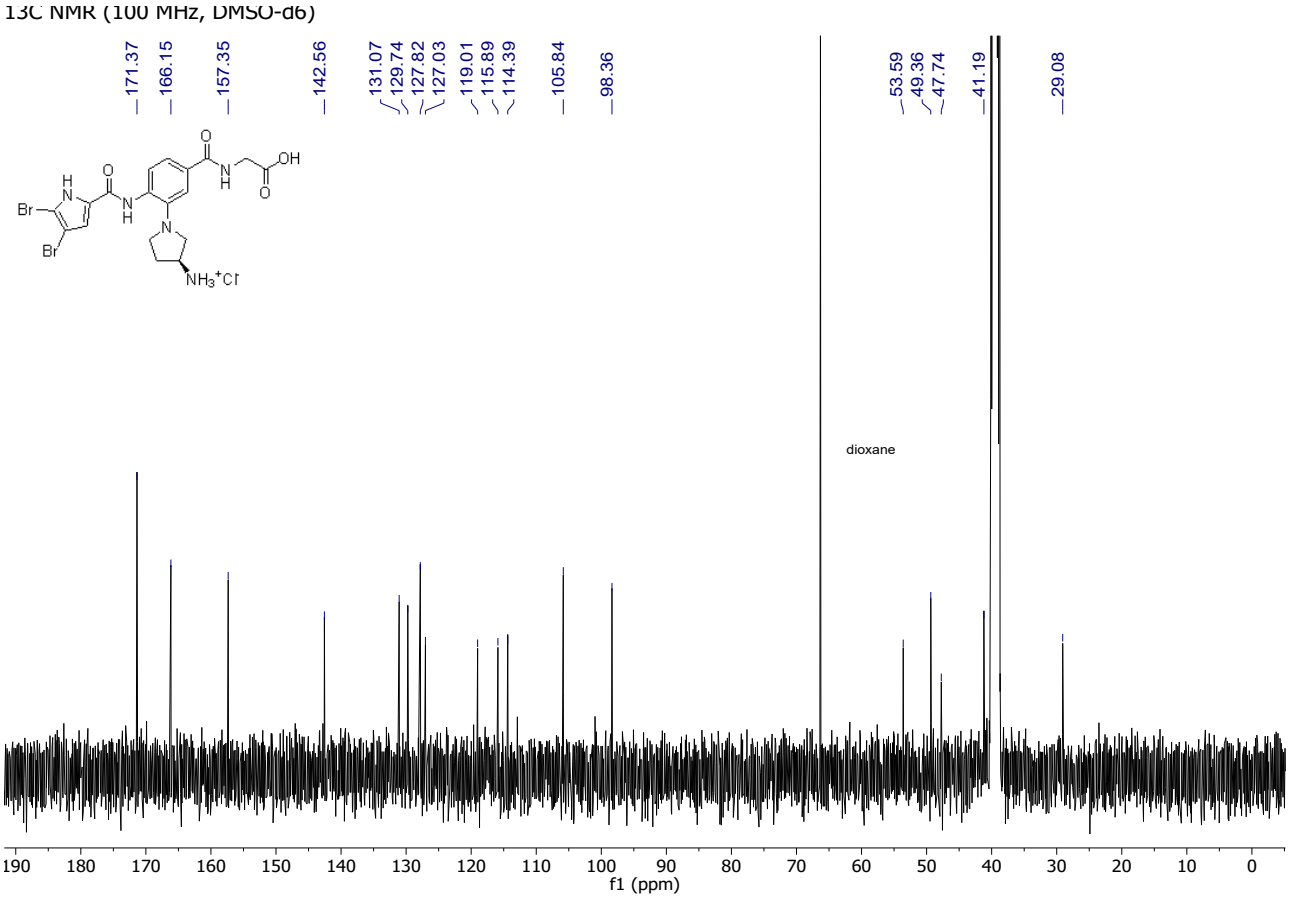


DEPT 135 NMR (100 MHz, DMSO-d6)

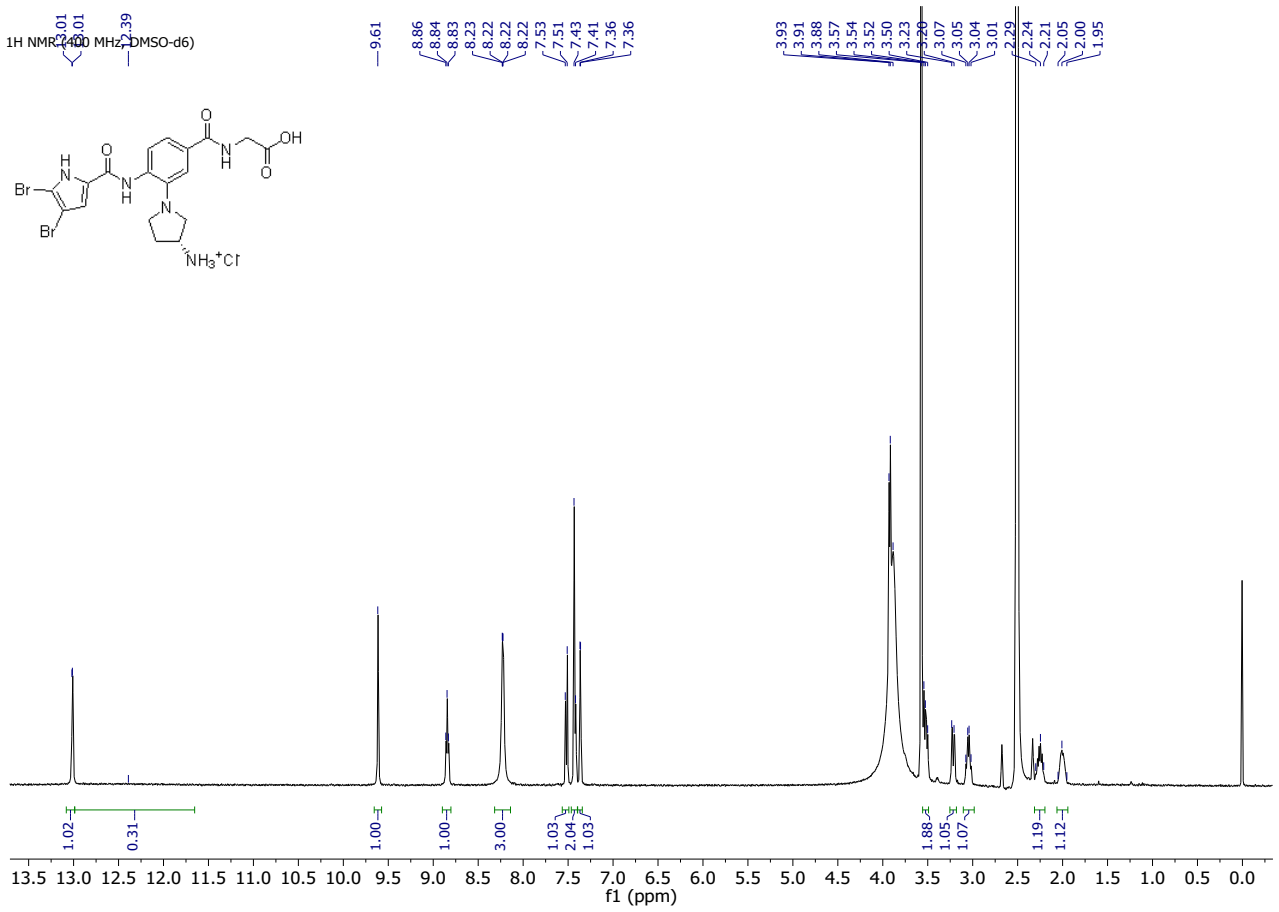


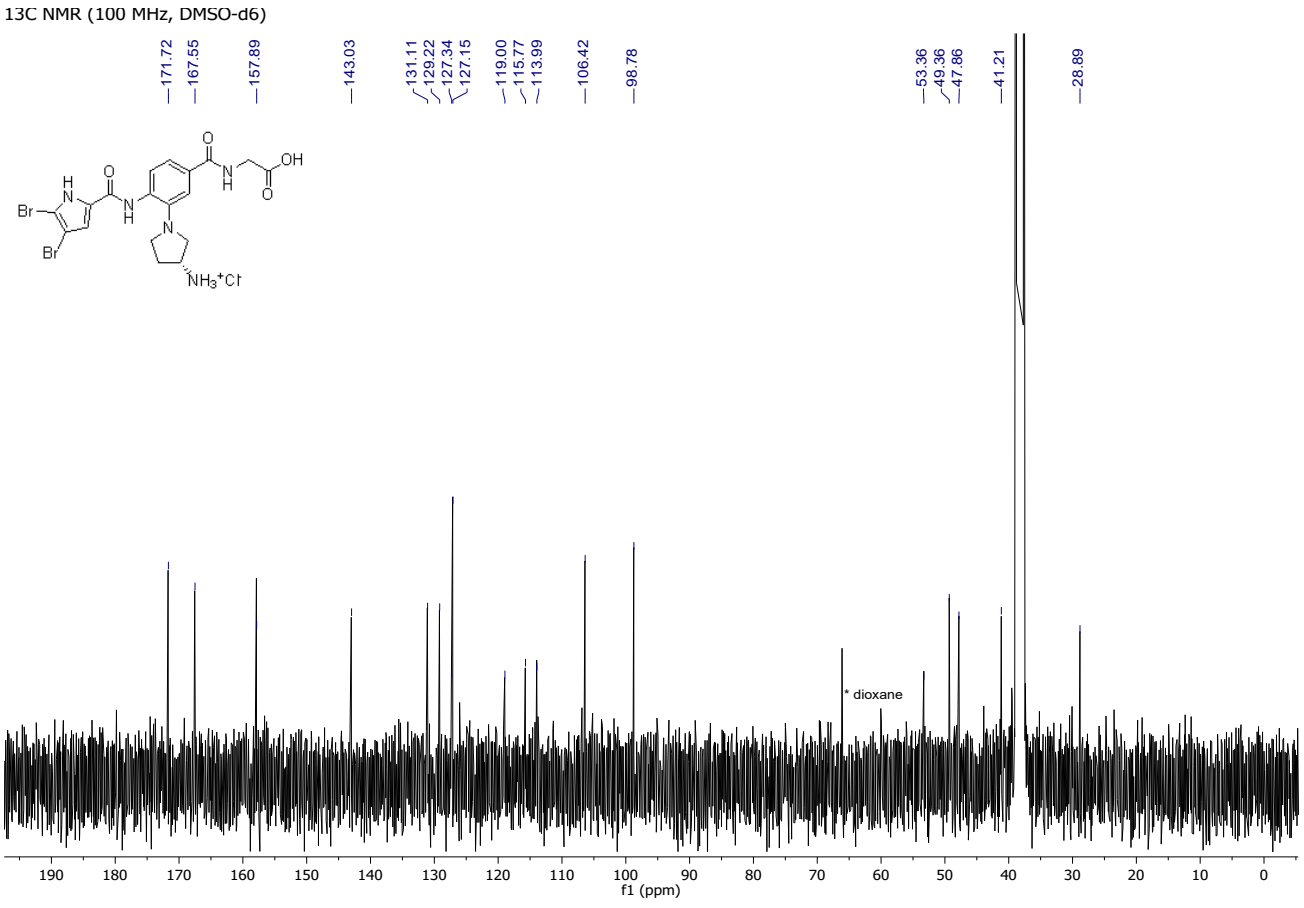
**(*S*)-1-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (11b)**



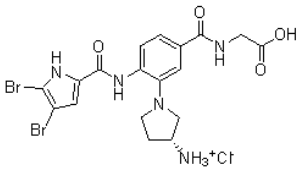



**(*R*)-1-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (11c)**



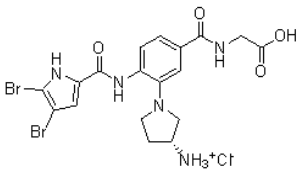



DEPT 45 NMR (100 MHz, DMSO-d6)

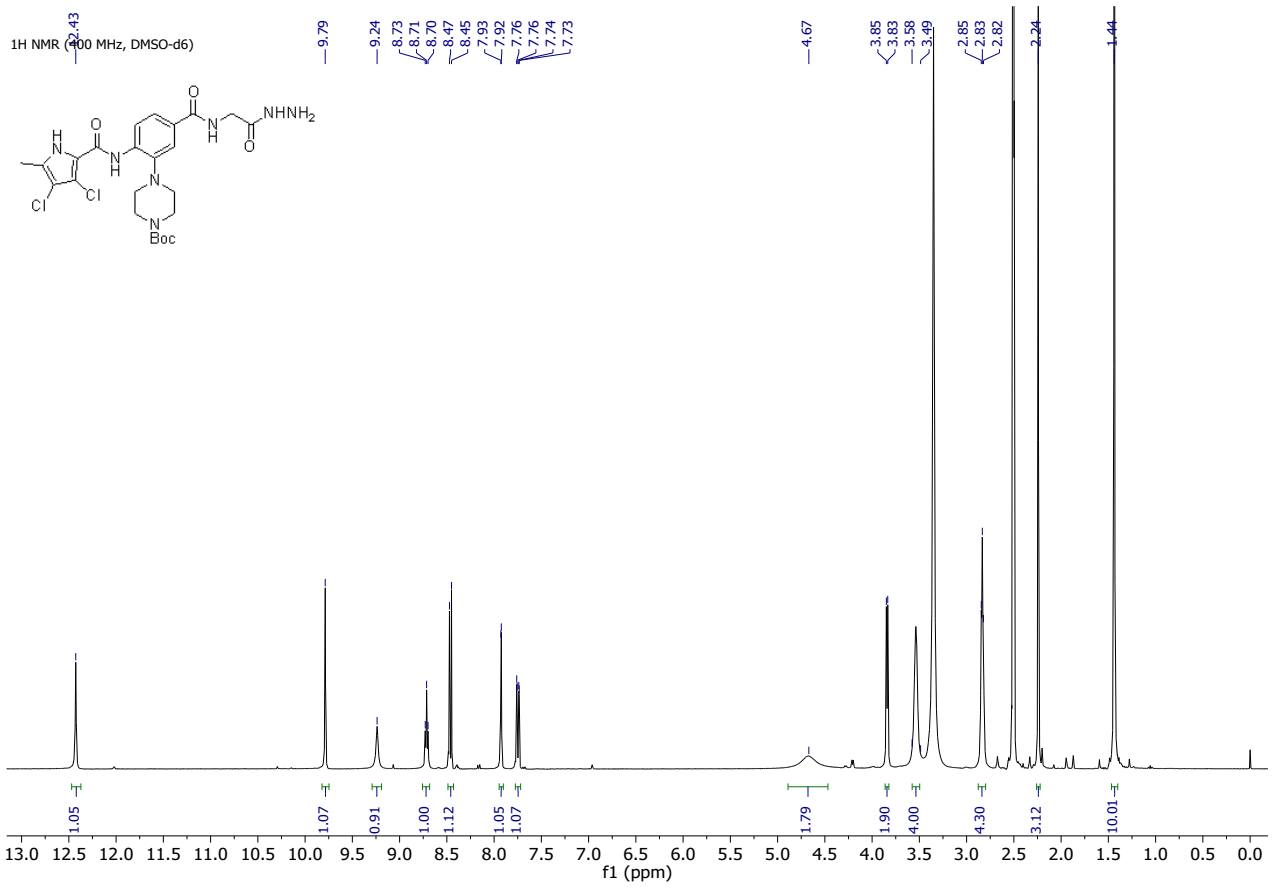


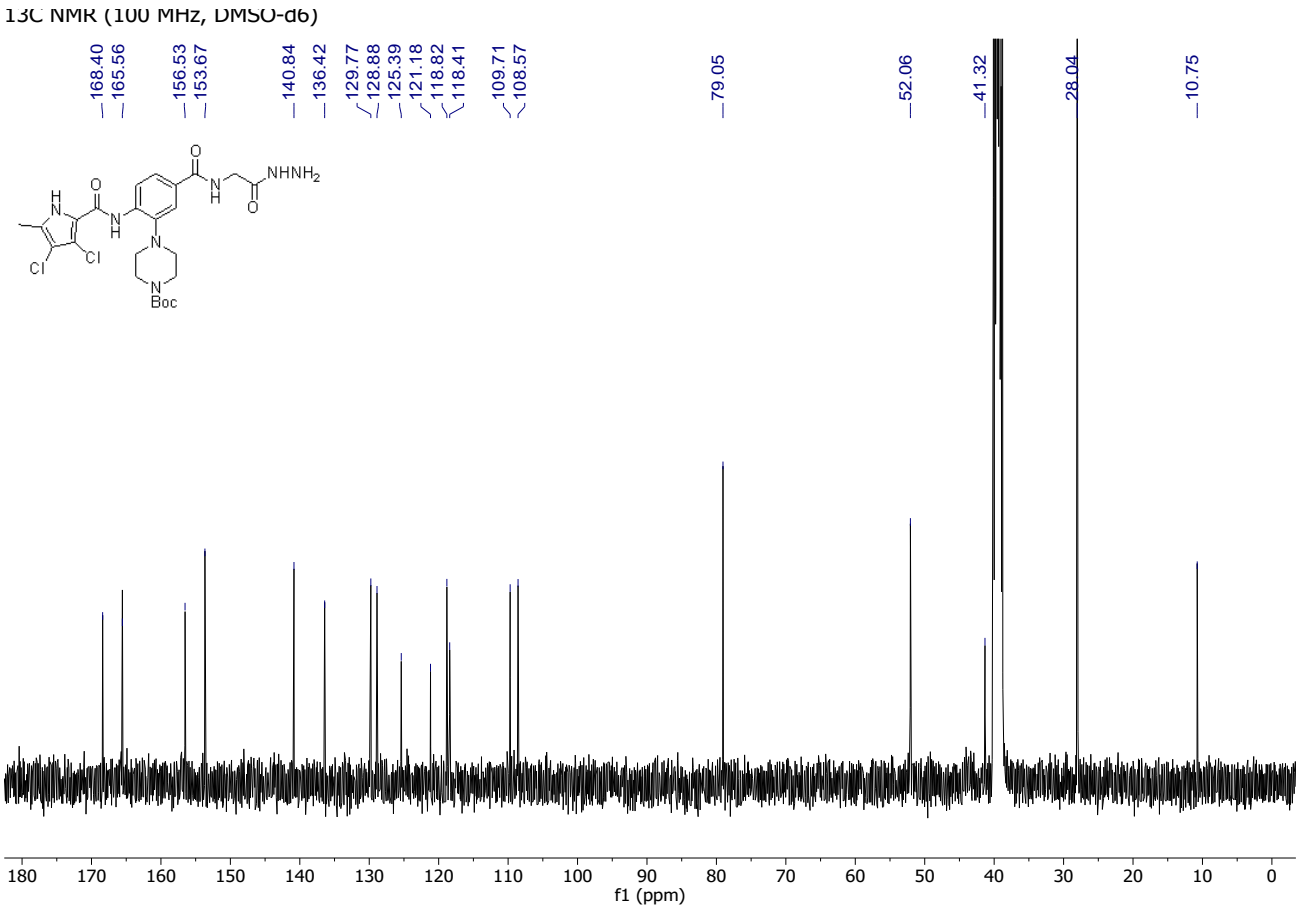



DEPT 135 NMR (100 MHz, DMSO-d6)

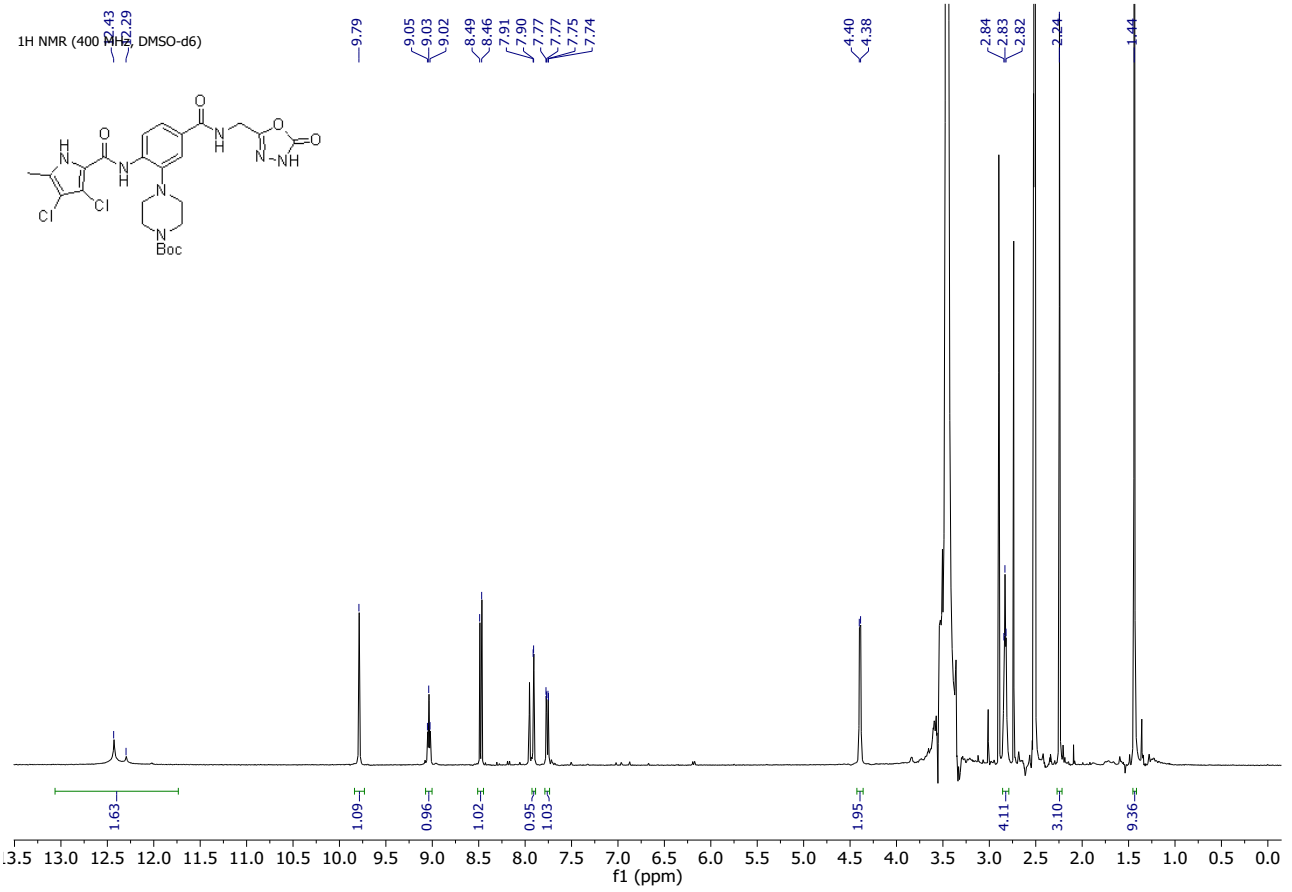


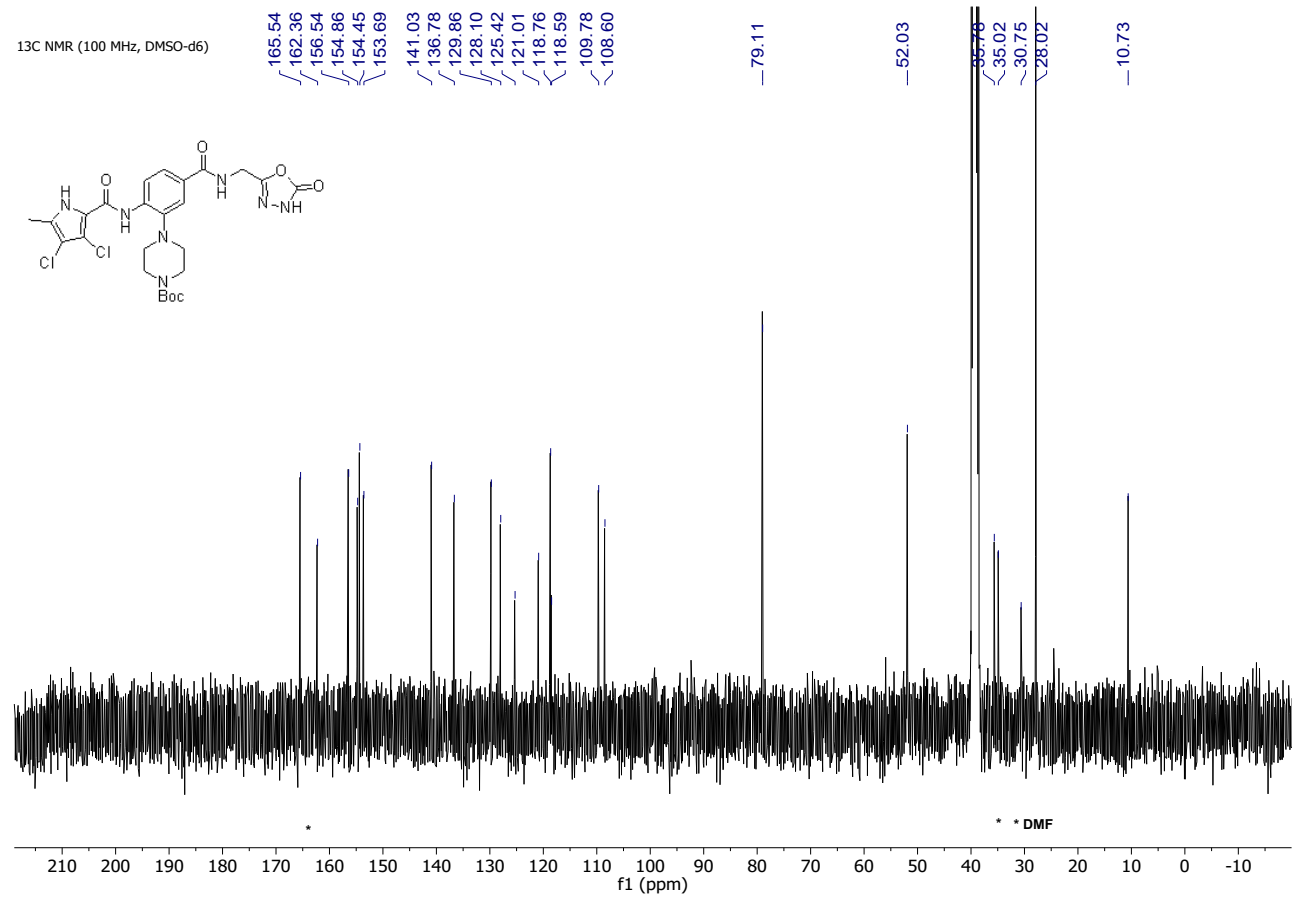
**_tert_-Butyl 4-(2-(3,4-dichloro-5-methyl-1_H_-pyrrole-2-carboxamido)-5-((2-hydrazineyl-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (12)**



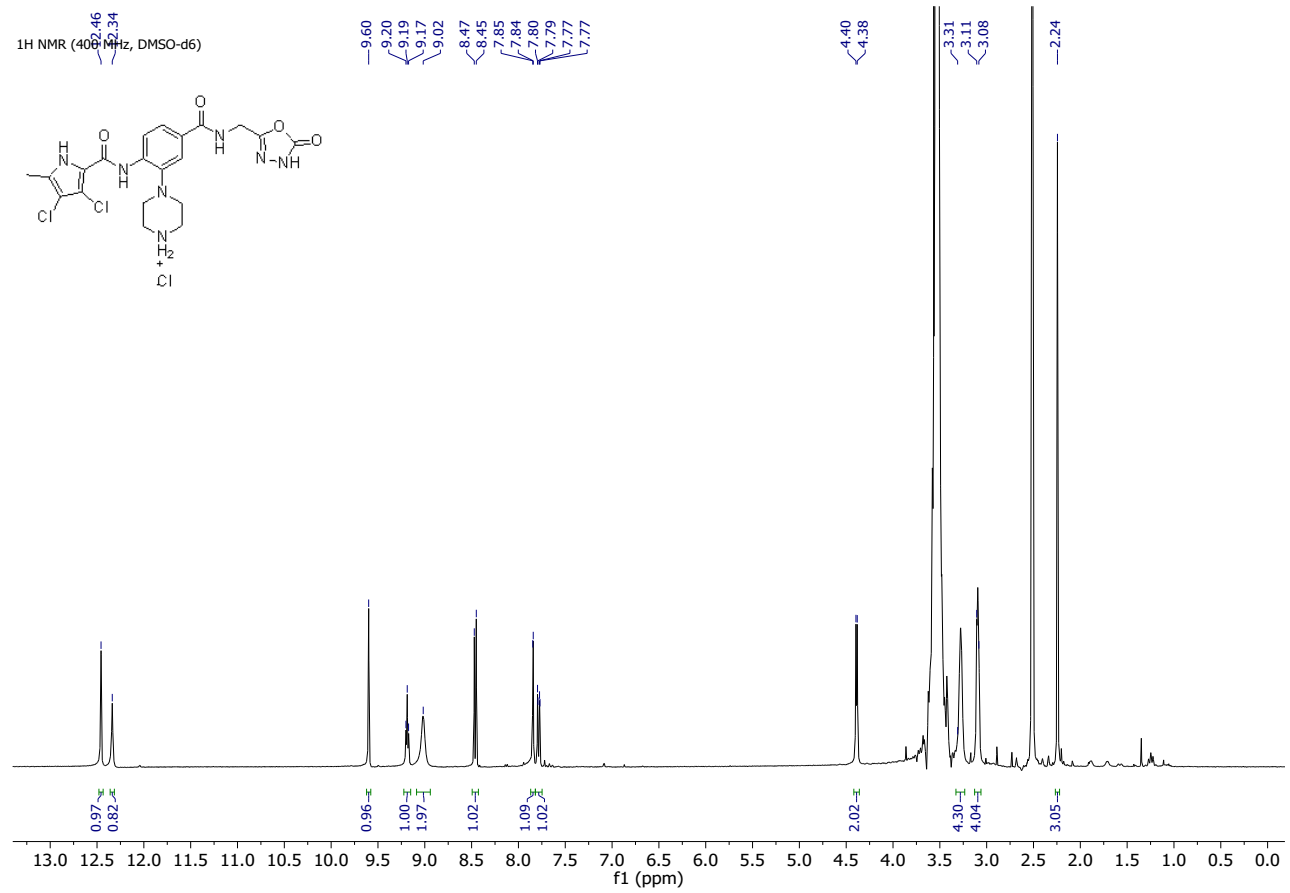



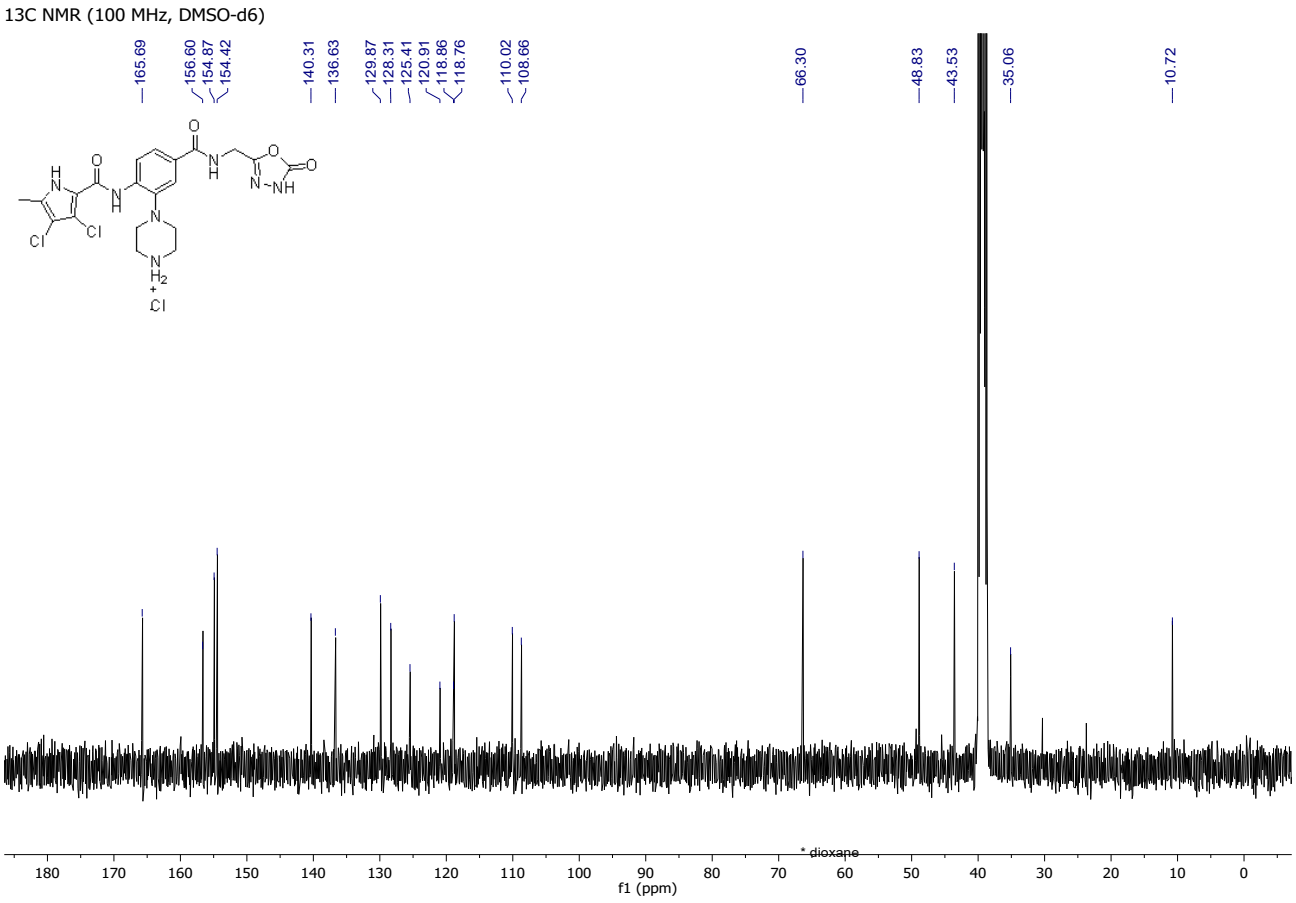
**_tert_-Butyl 4-(2-(3,4-dichloro-5-methyl-1_H_-pyrrole-2-carboxamido)-5-(((5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)carbamoyl)phenyl)piperazine-1-carboxylate (13)**



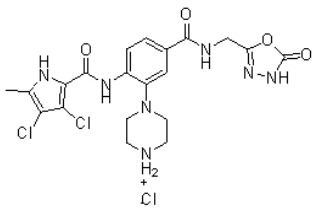



**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(((5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)carbamoyl)phenyl)piperazin-1-ium chloride (14)**



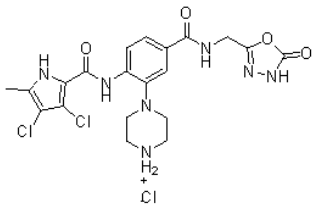



DEPT 45 NMR (100 MHz, DMSO-d6)

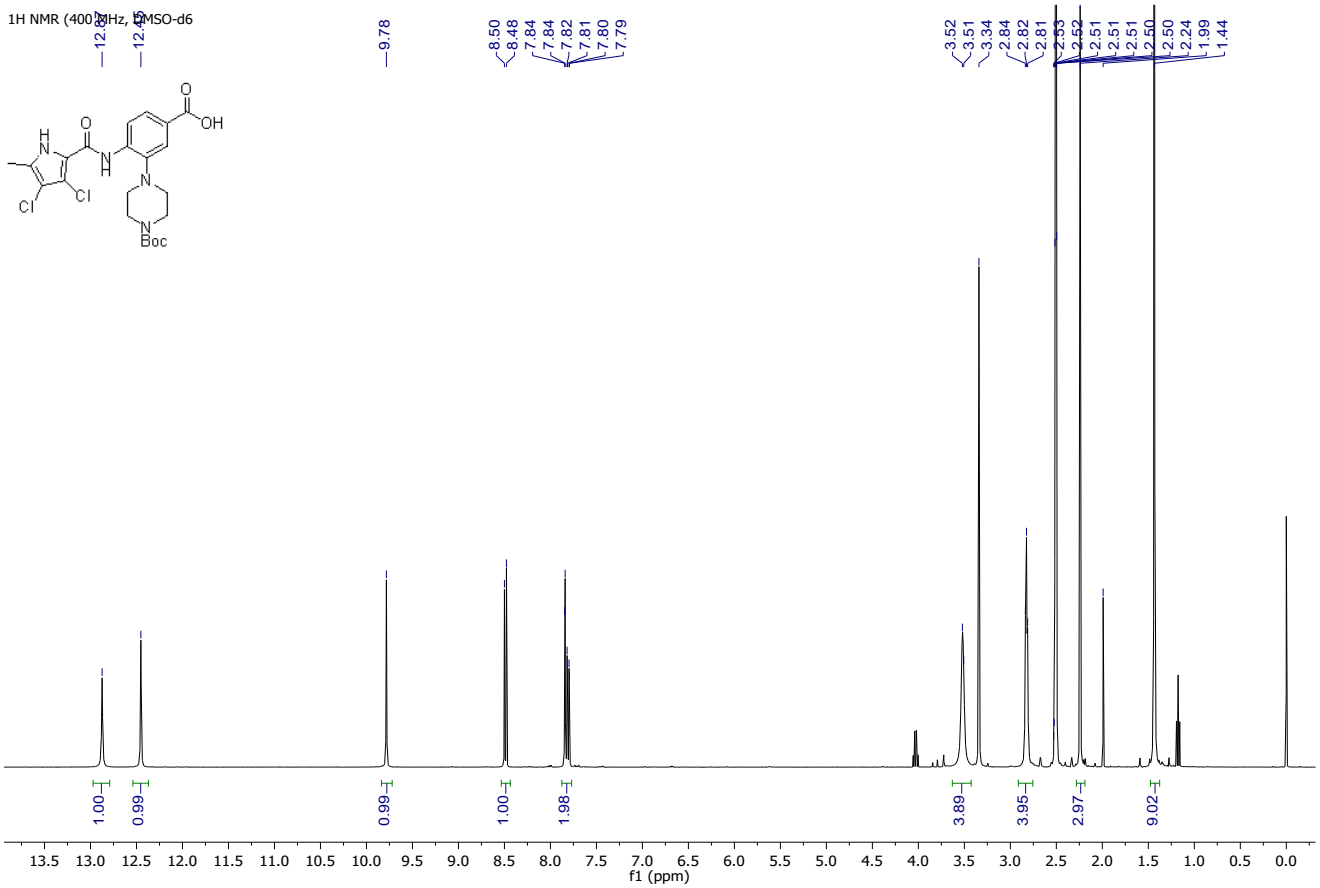


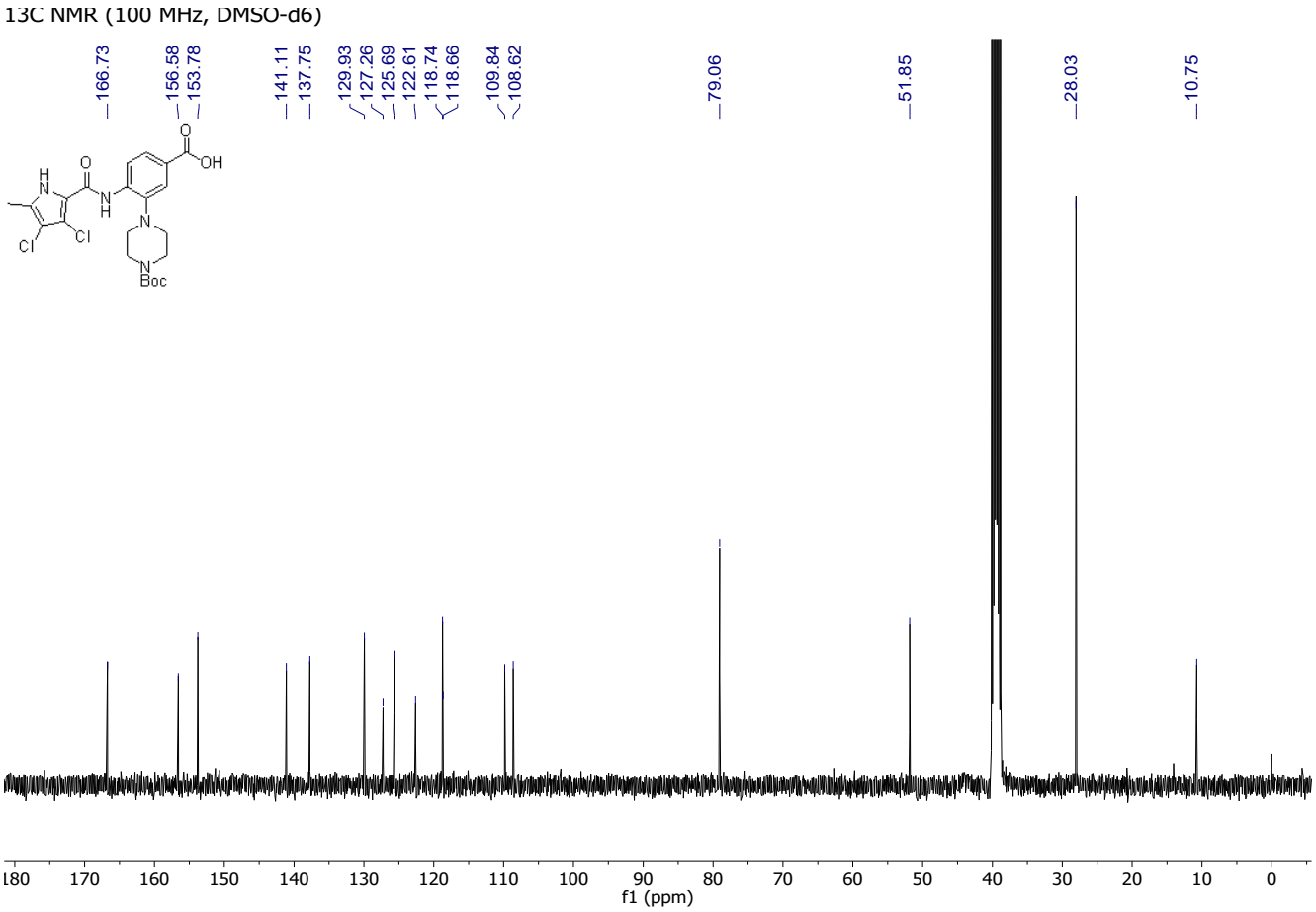



DEPT 135 NMR (100 MHz, DMSO-d6)

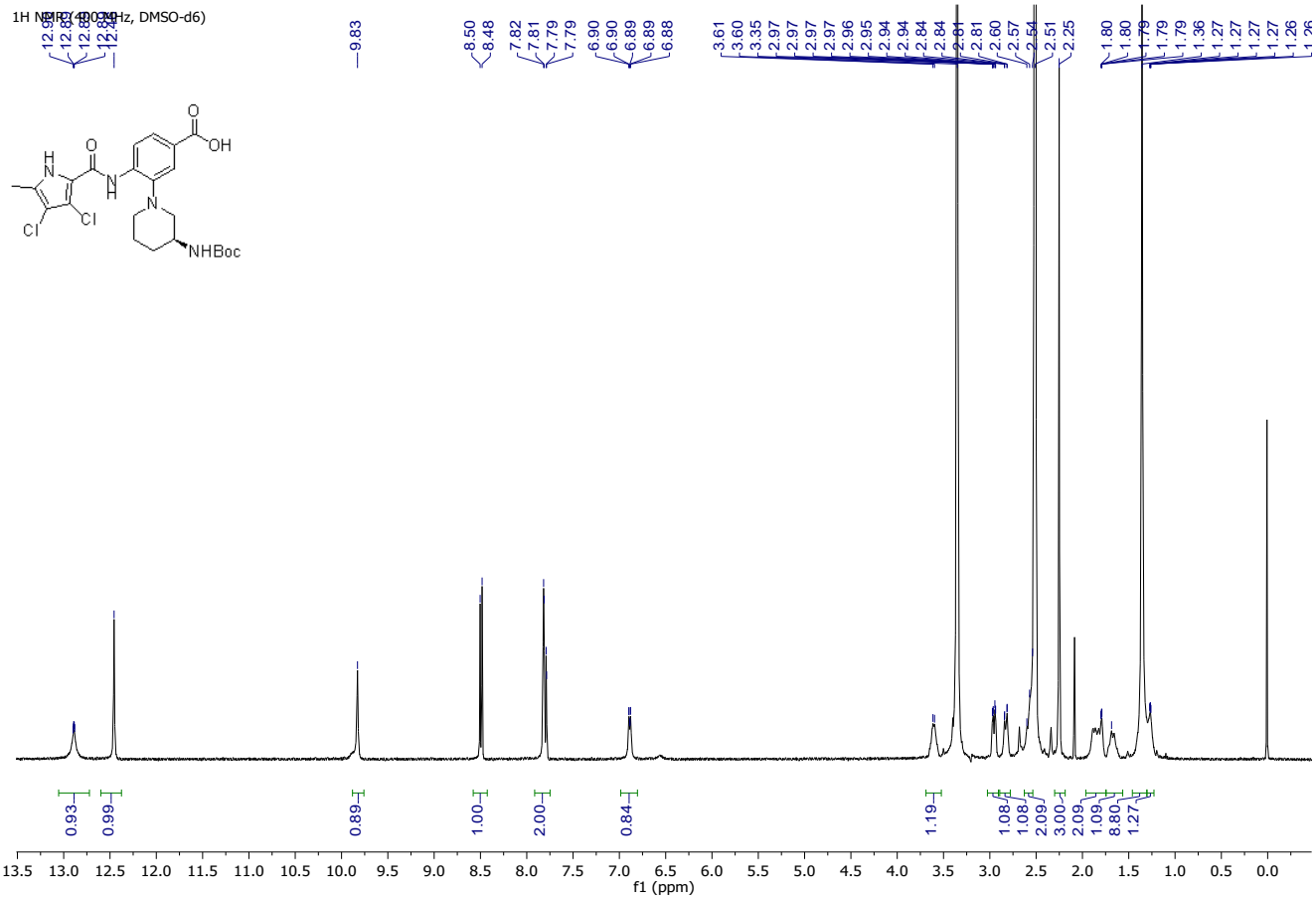


**3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18a)**

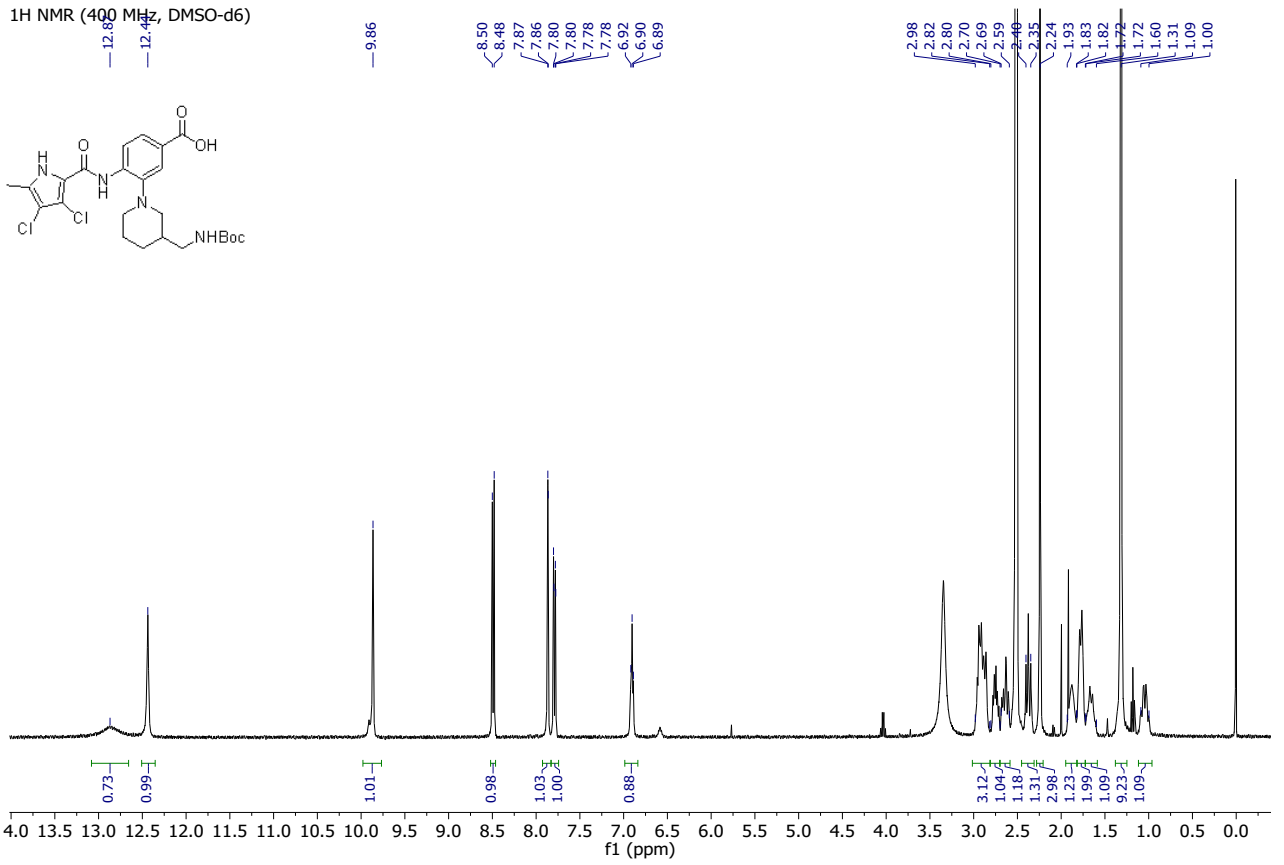


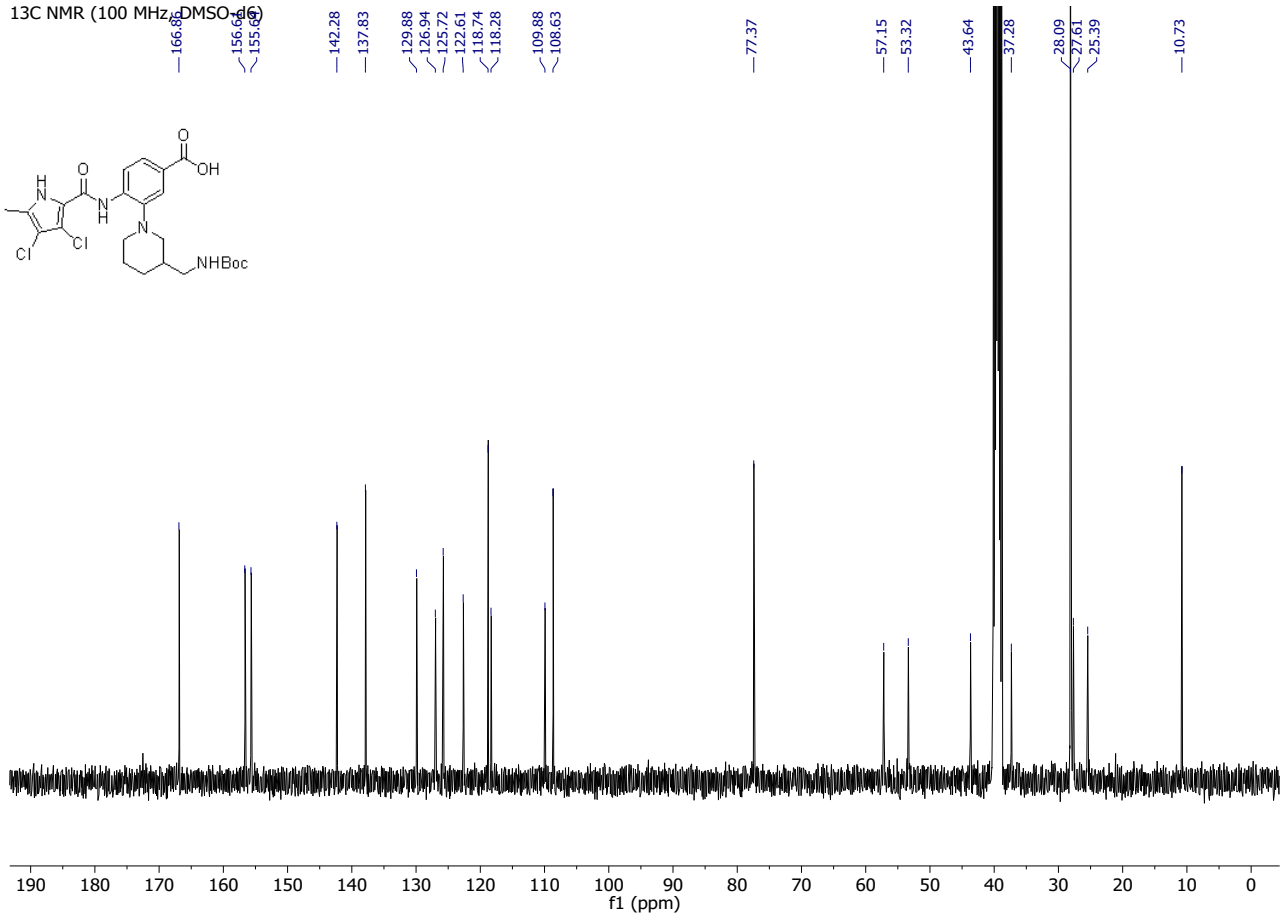



**(*S*)-3-(3-((*tert*-Butoxycarbonyl)amino)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18c)**

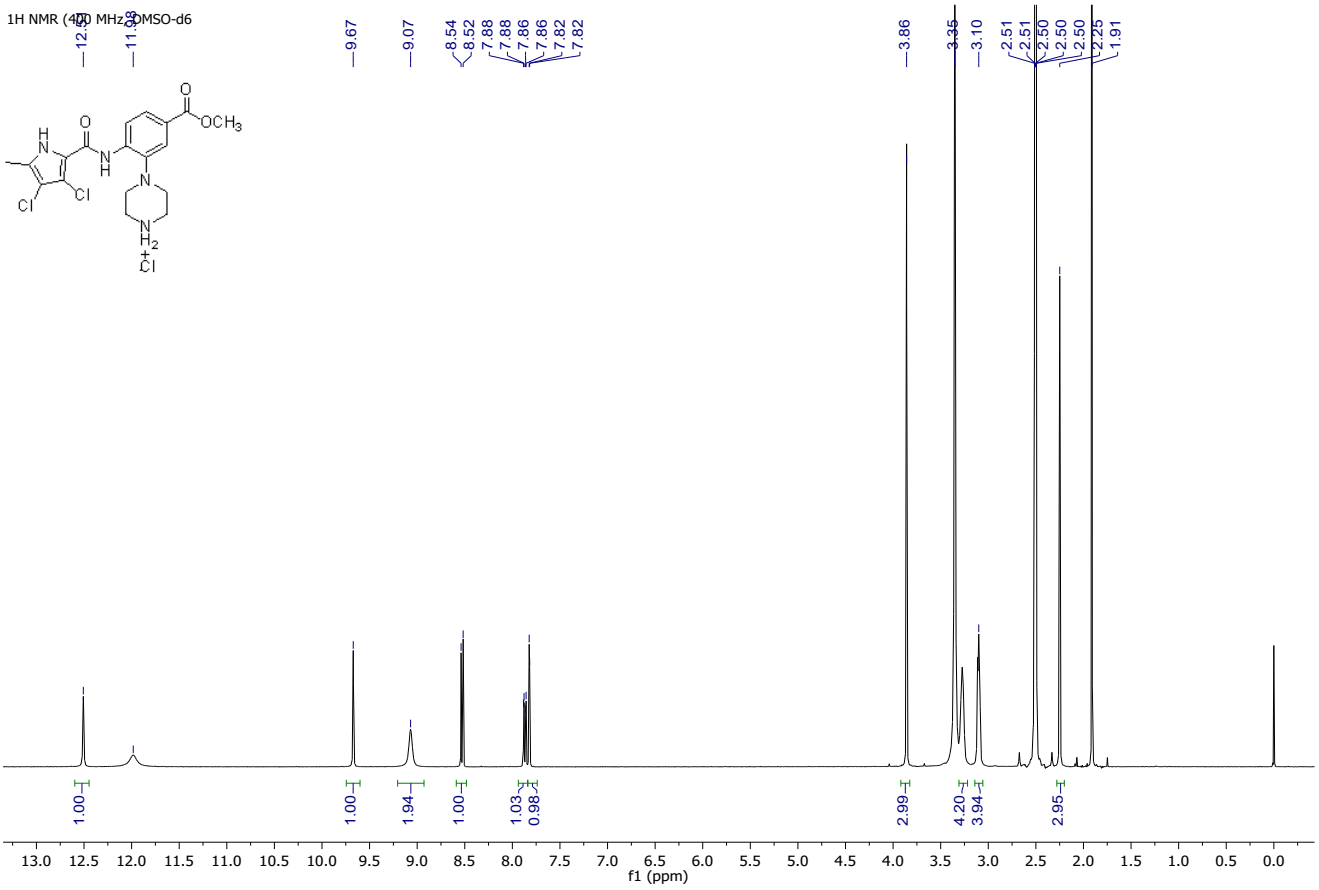


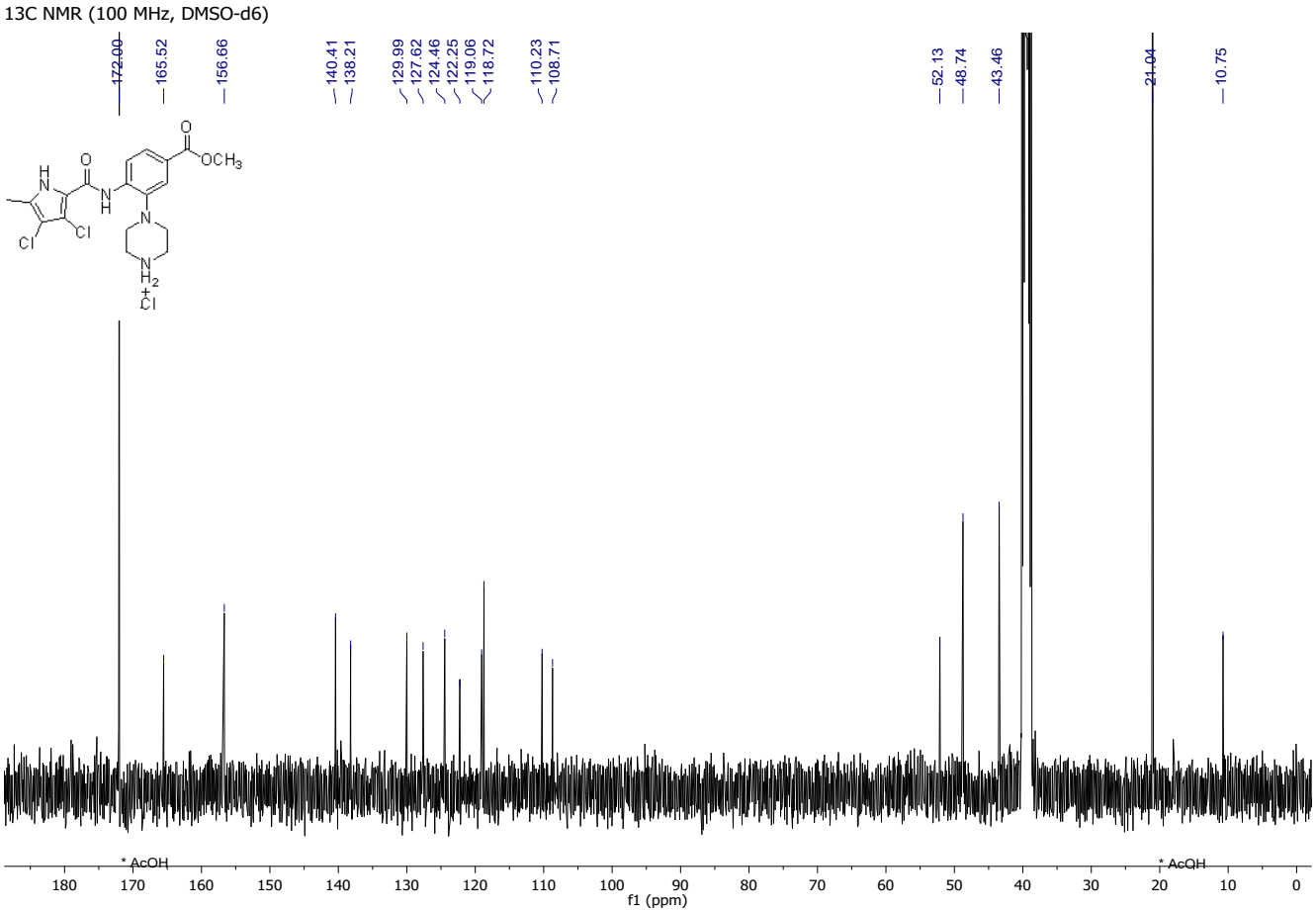
**3-(3-(((*tert*-Butoxycarbonyl)amino)methyl)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18i)**



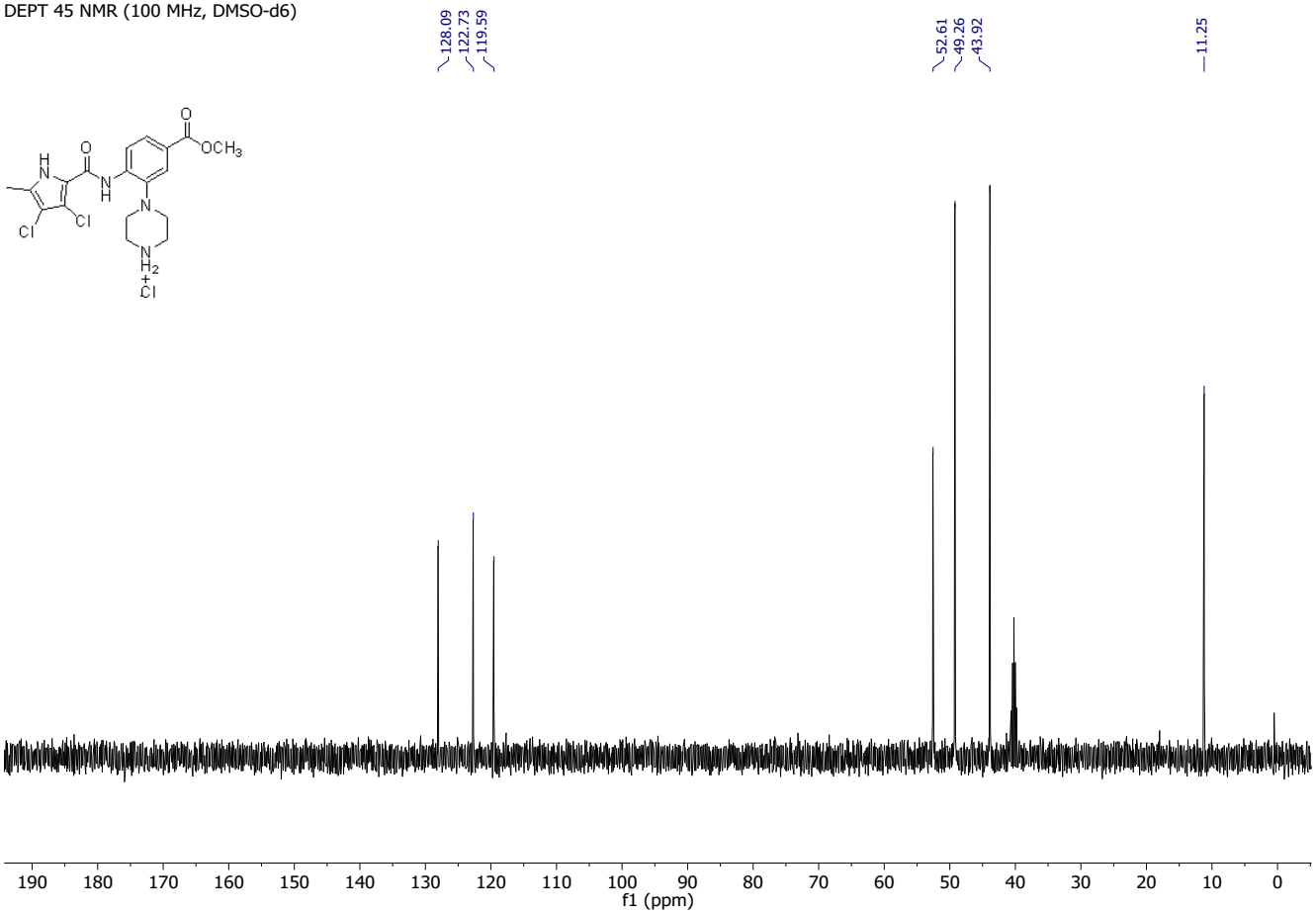



**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperazin-1-ium chloride (19a)**

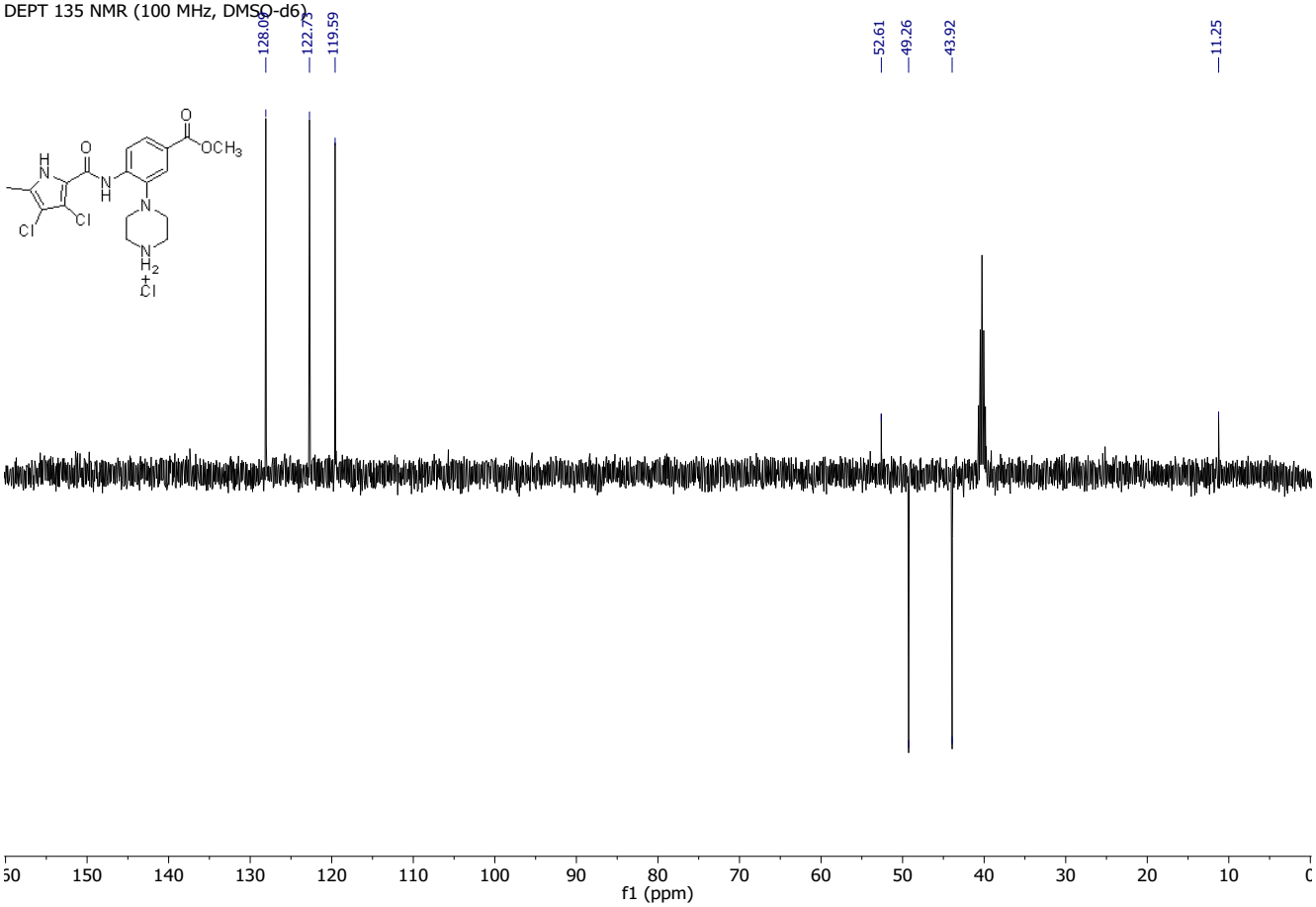


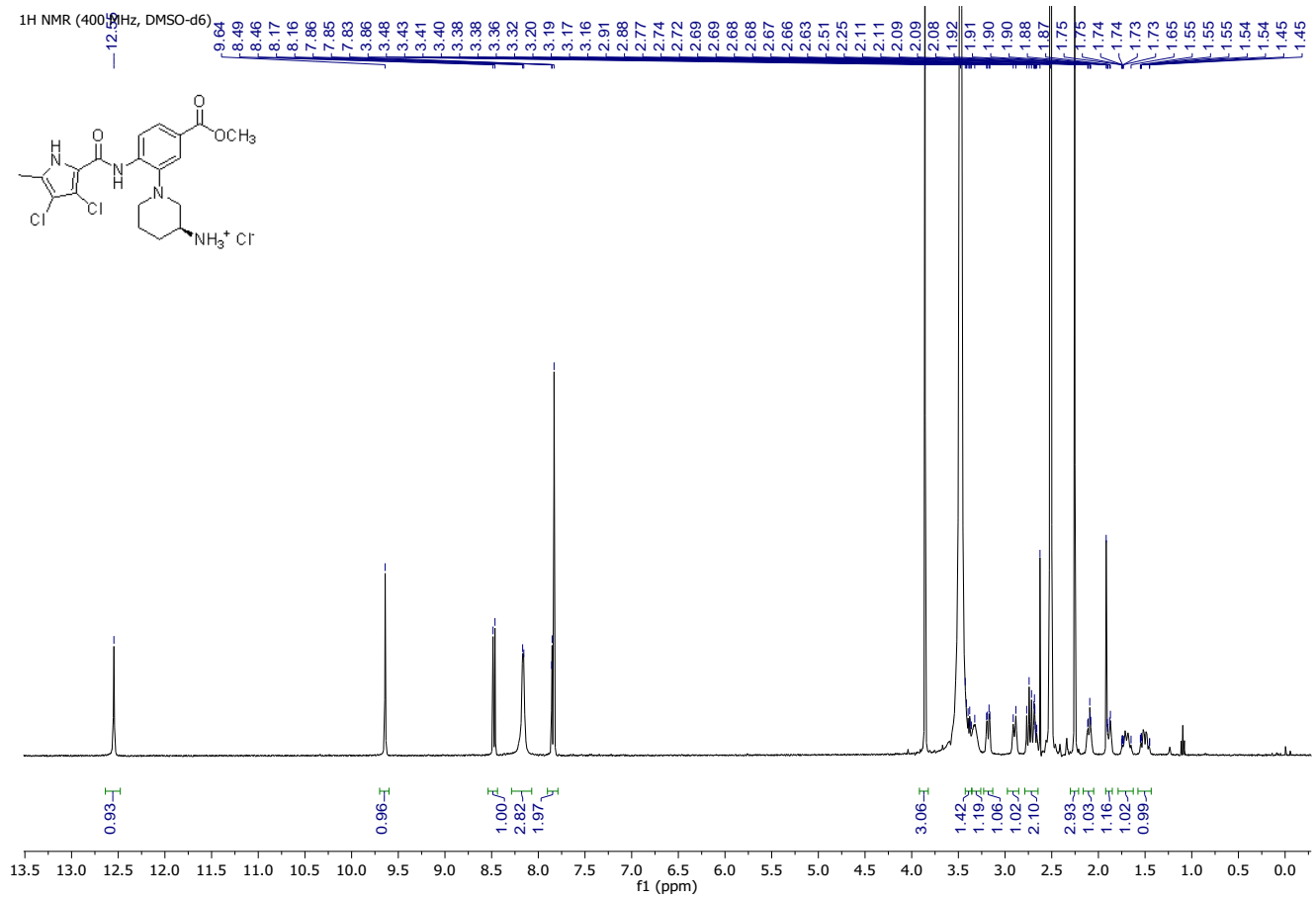
DEPT 45 NMR (100 MHz, DMSO-d6)

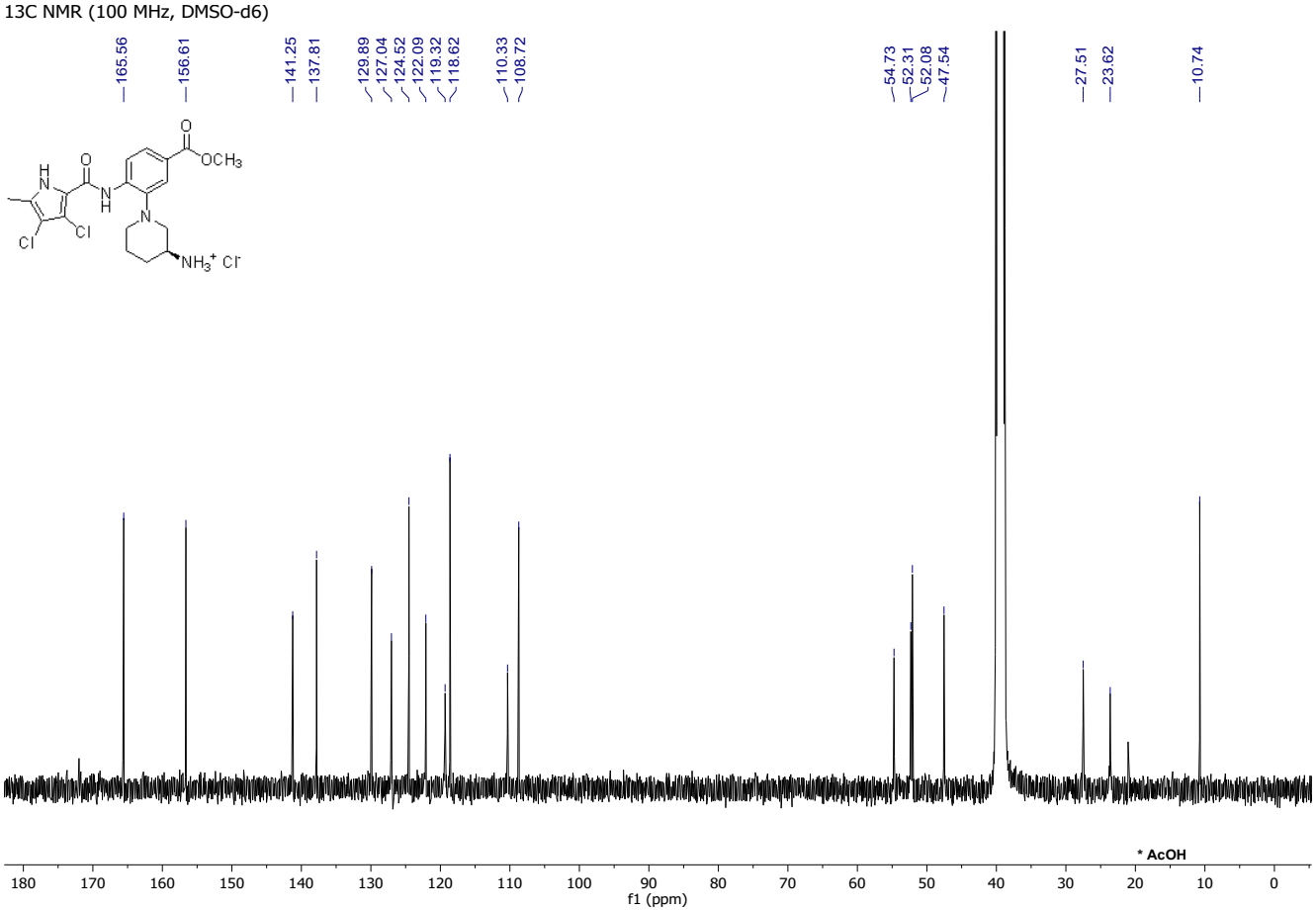



DEPT 135 NMR (100 MHz, DMSO-d6)

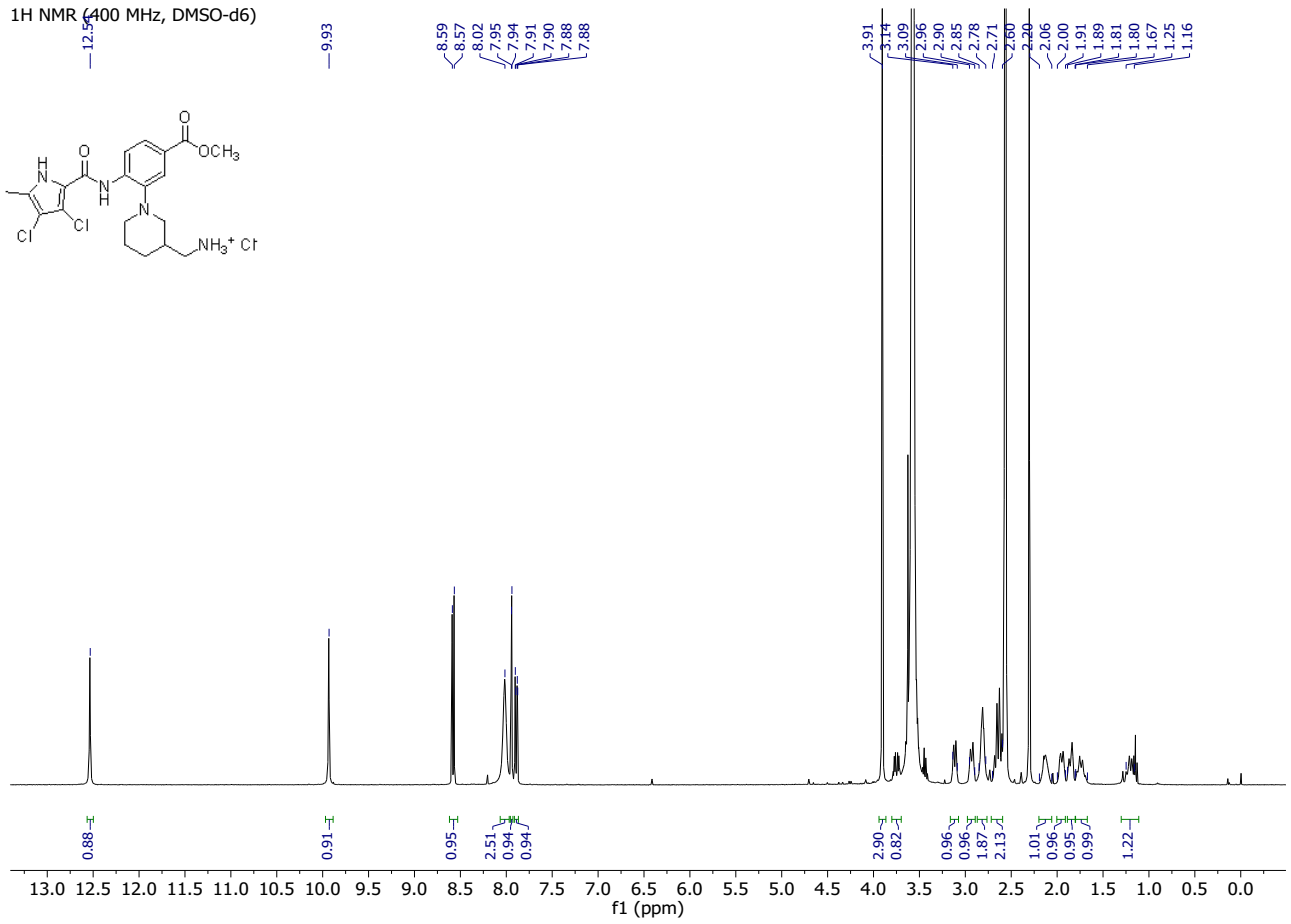


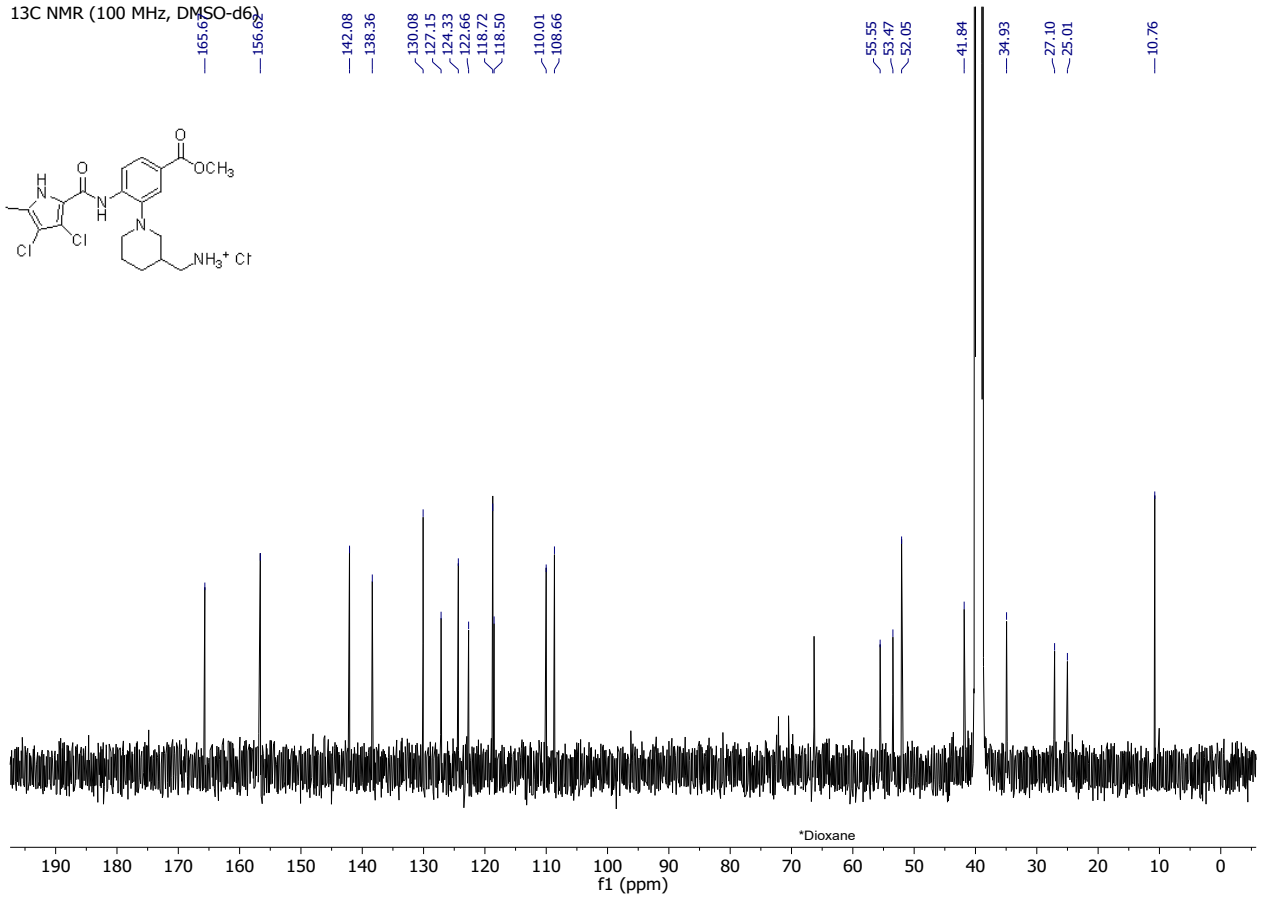
**(*S*)-1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperidin-3-aminium chloride (19c)**



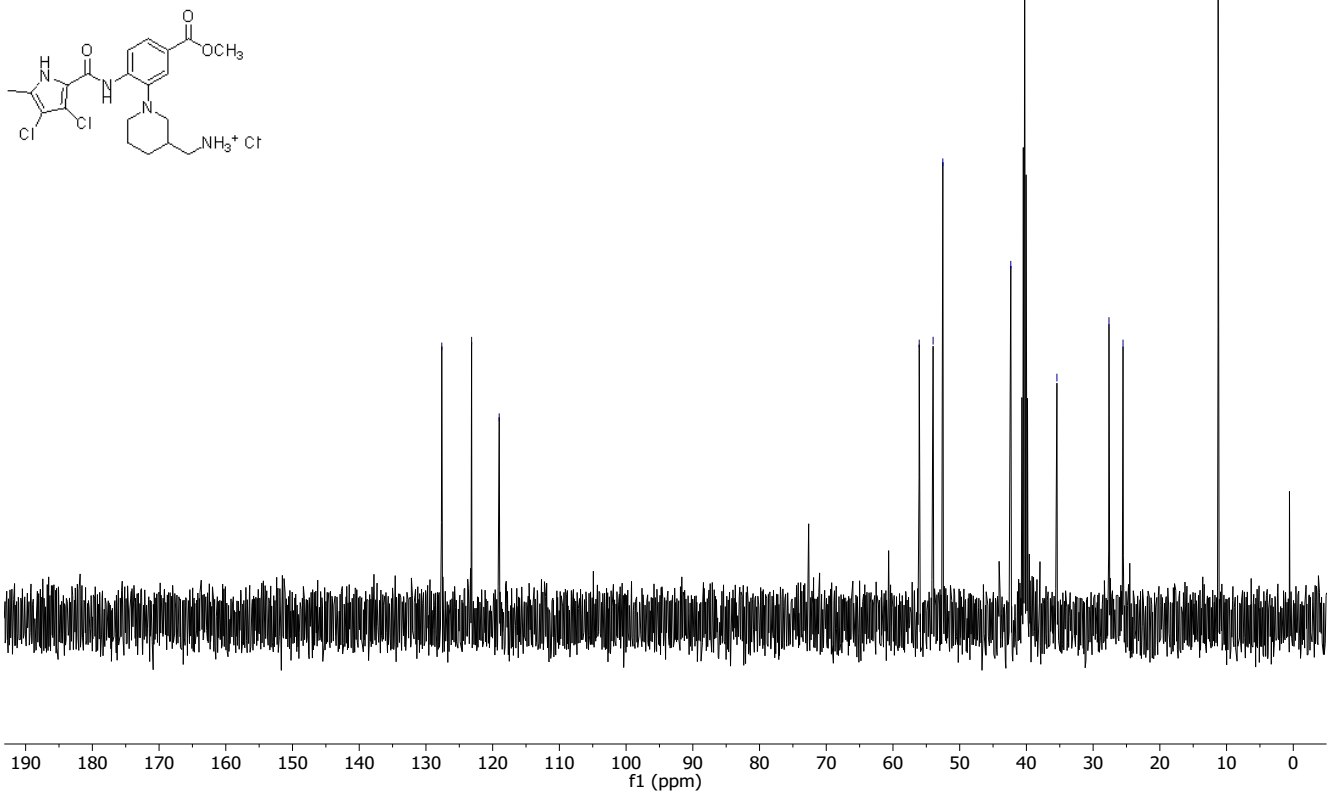



**(1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperidin-3-yl)methanaminium chloride (19i)**

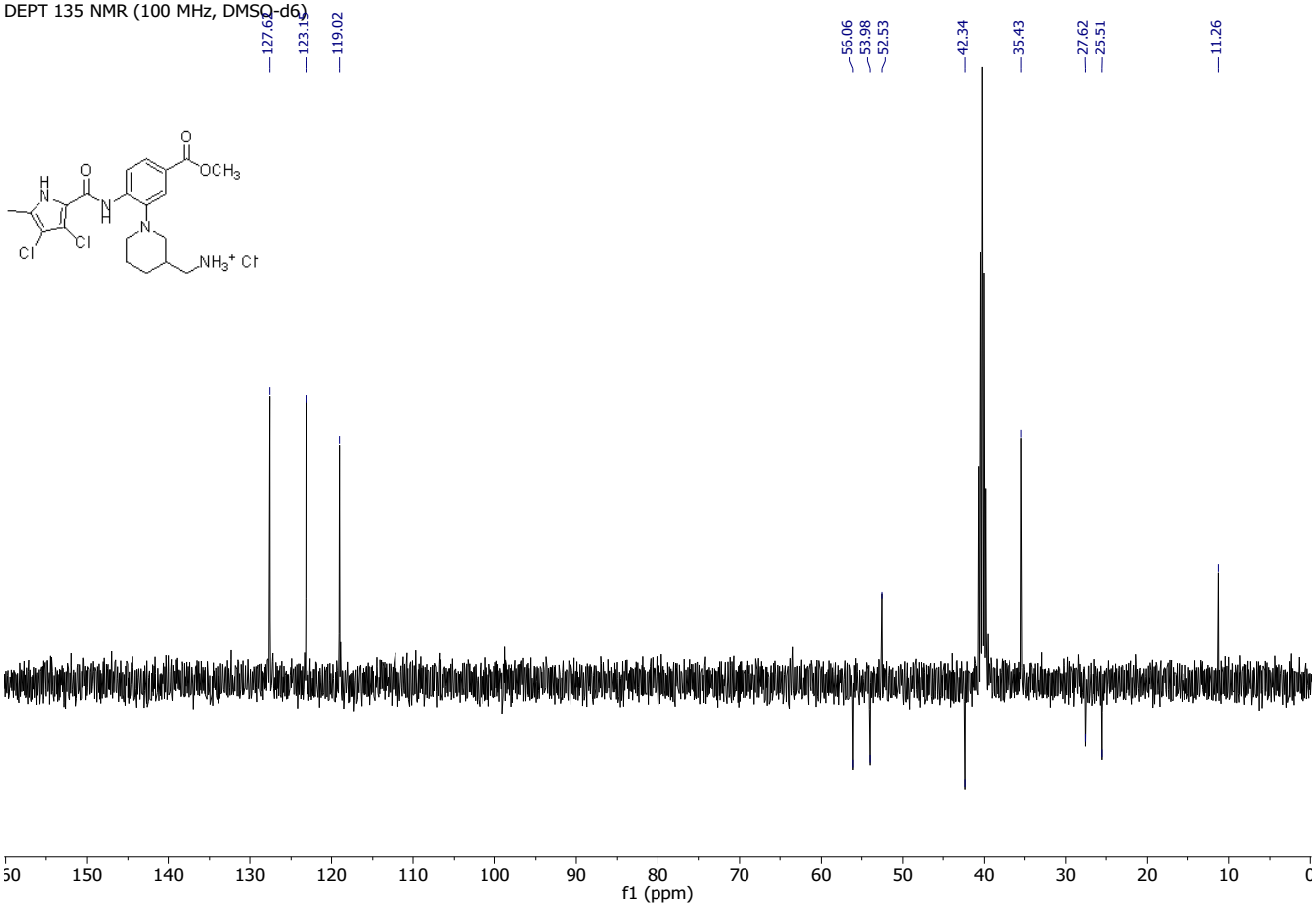


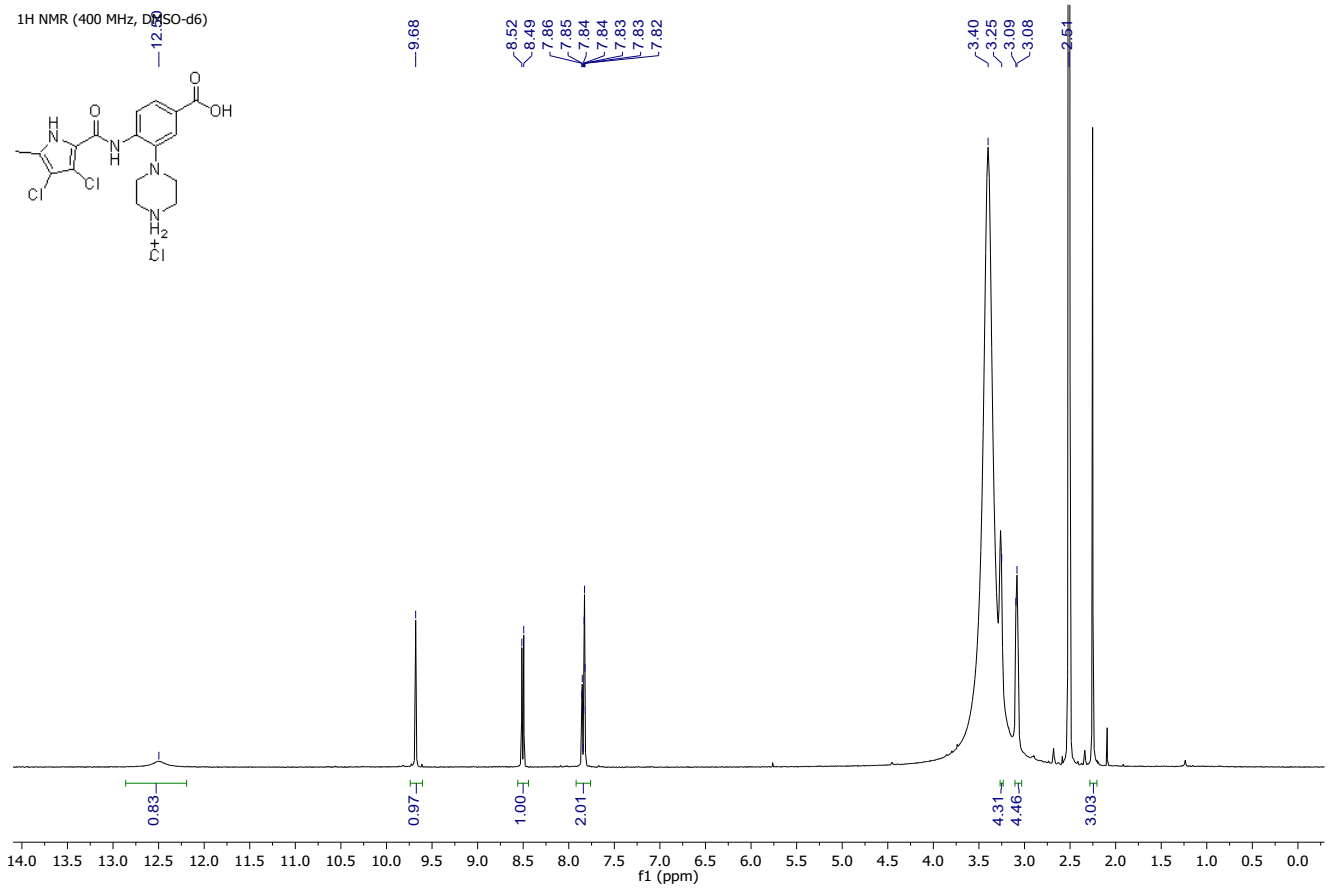
DEPT 45 NMR (100 MHz, DMSO-d6)

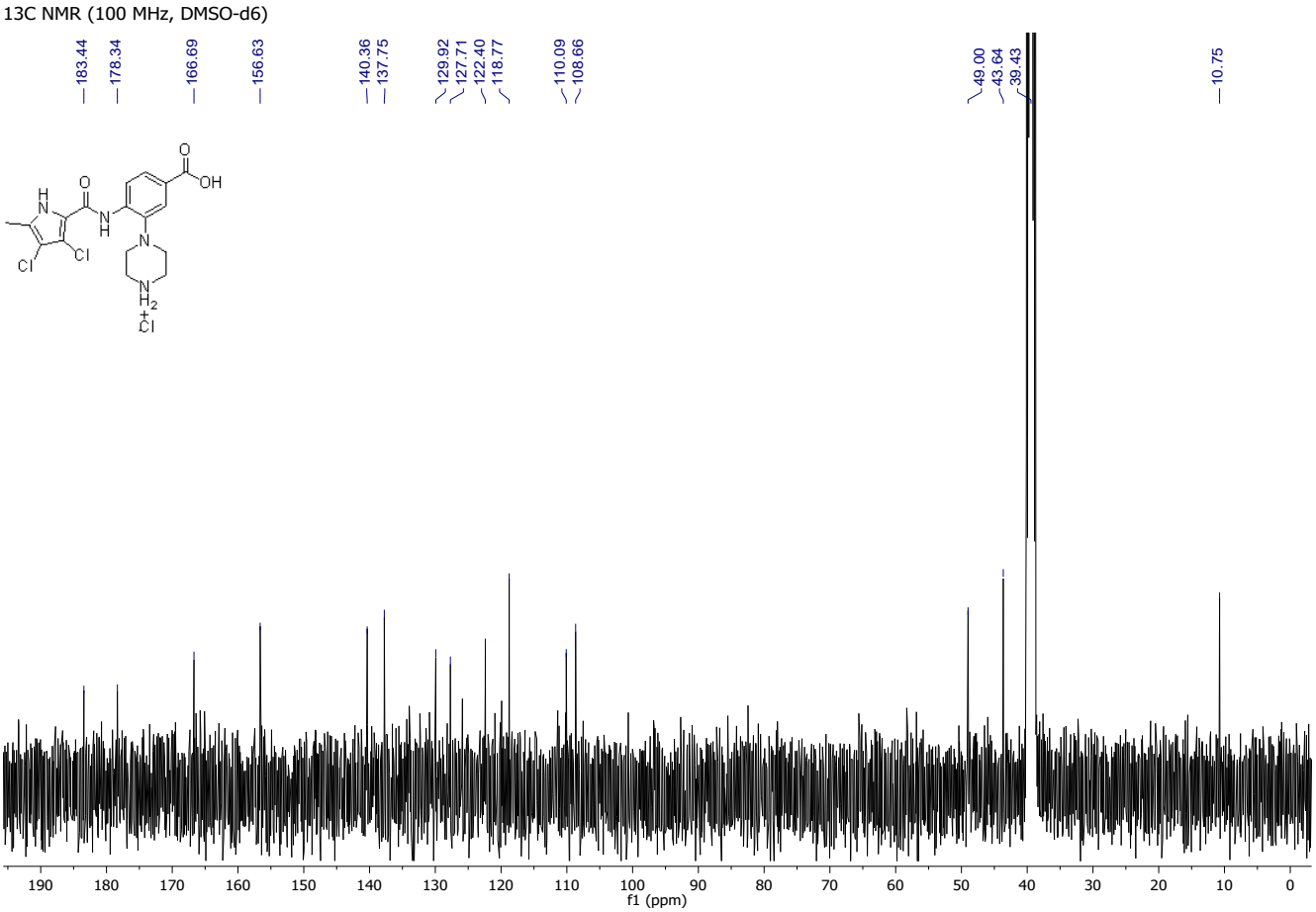



DEPT 135 NMR (100 MHz, DMSO-d6)

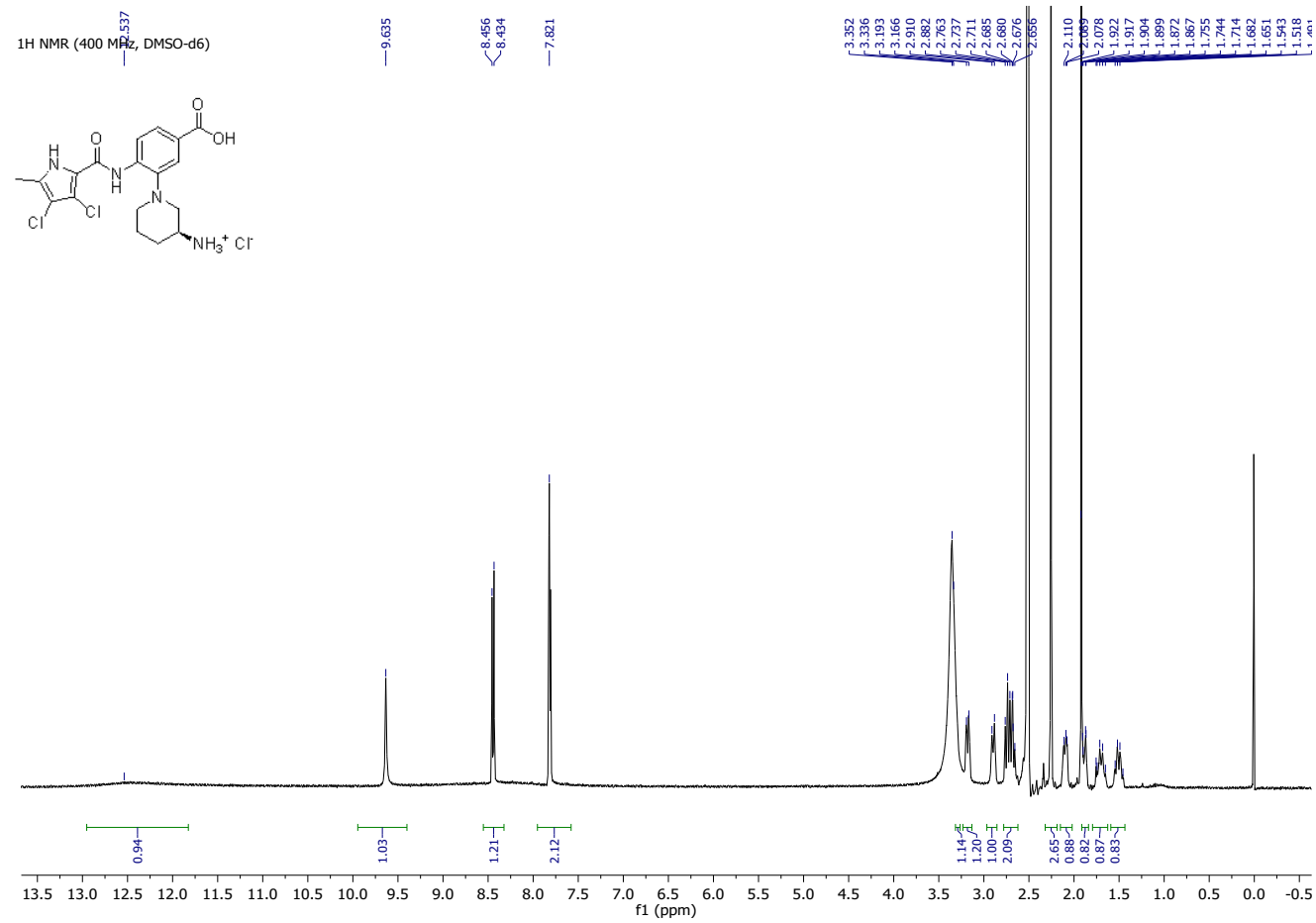


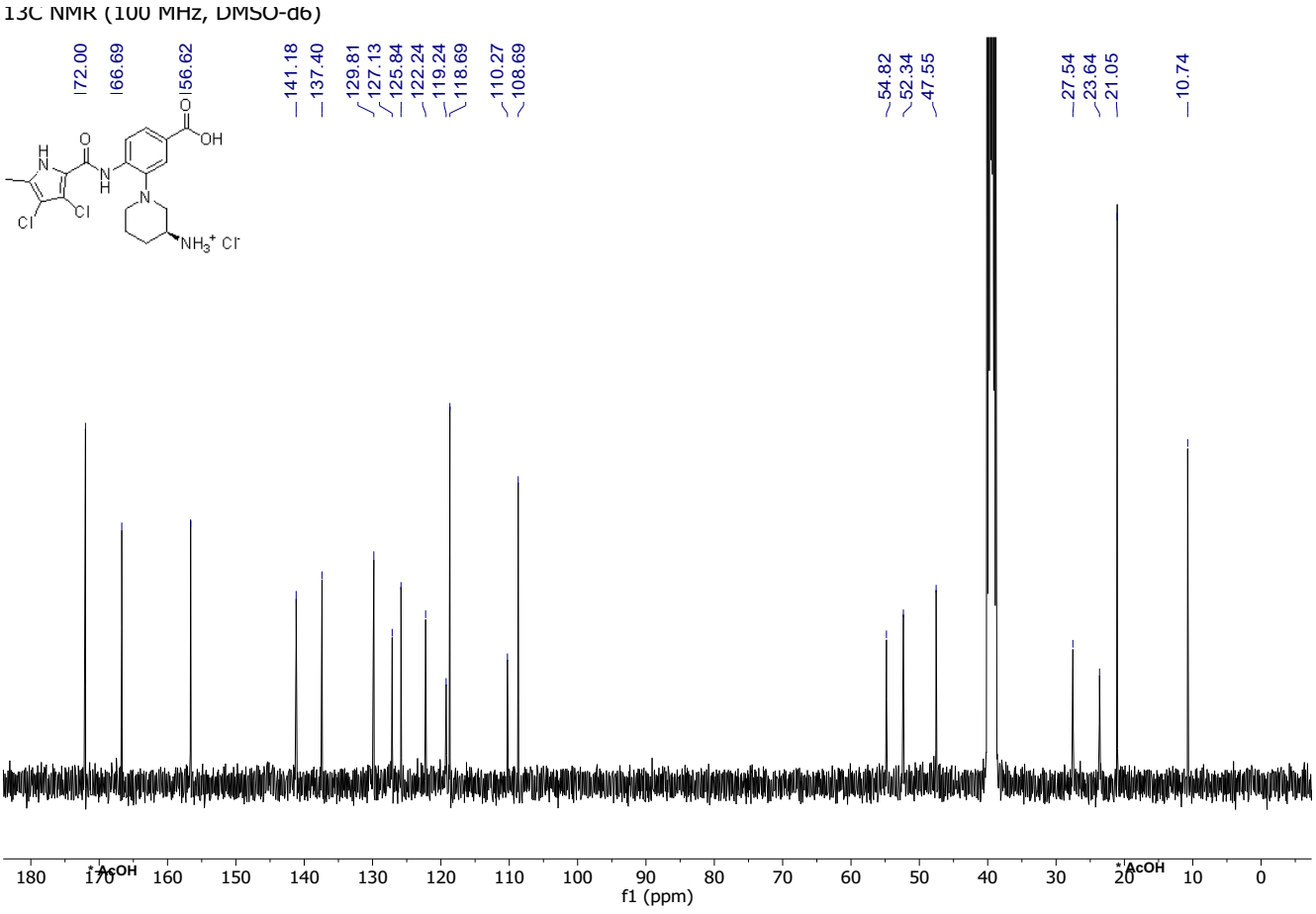
**4-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (20a)**



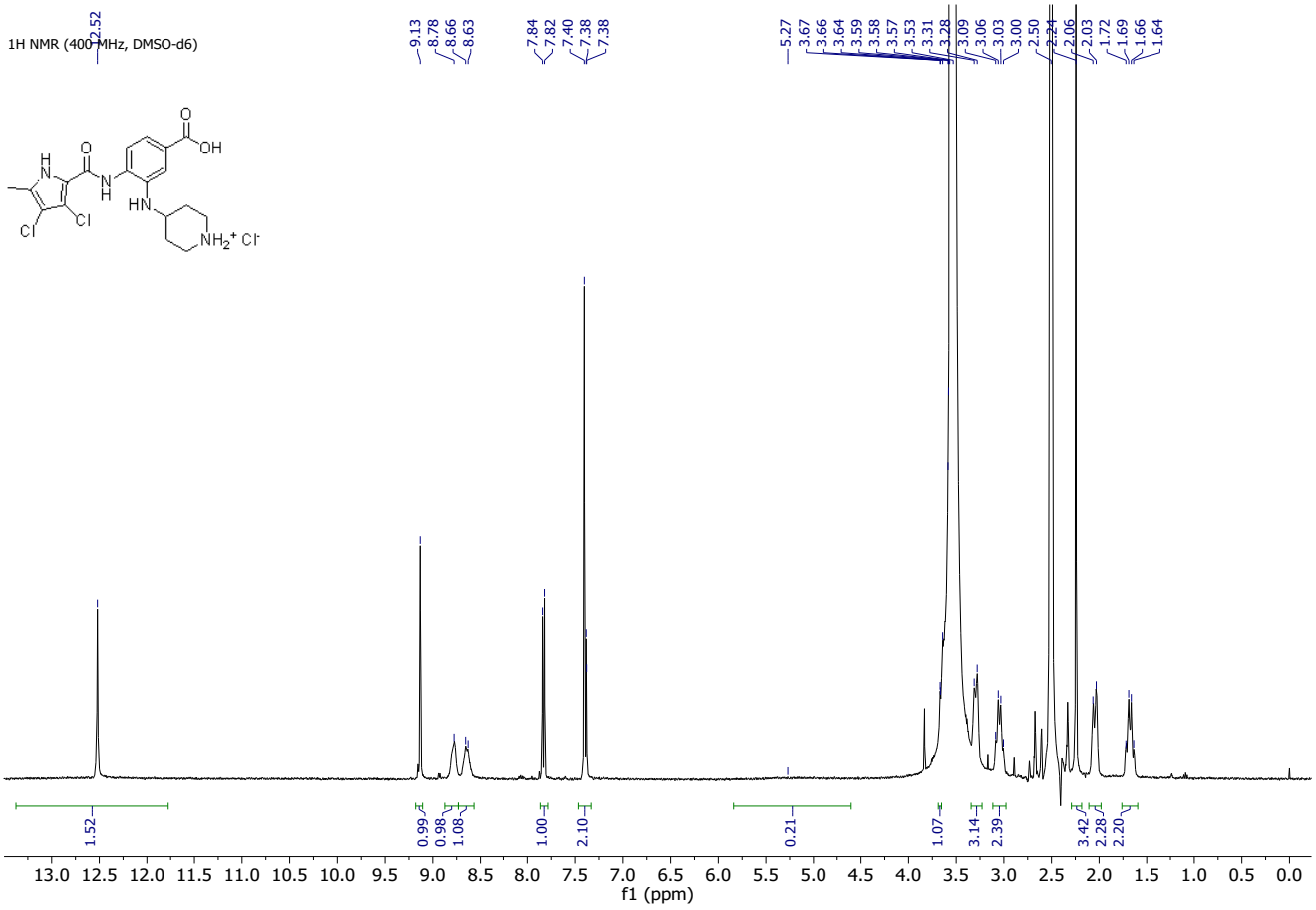



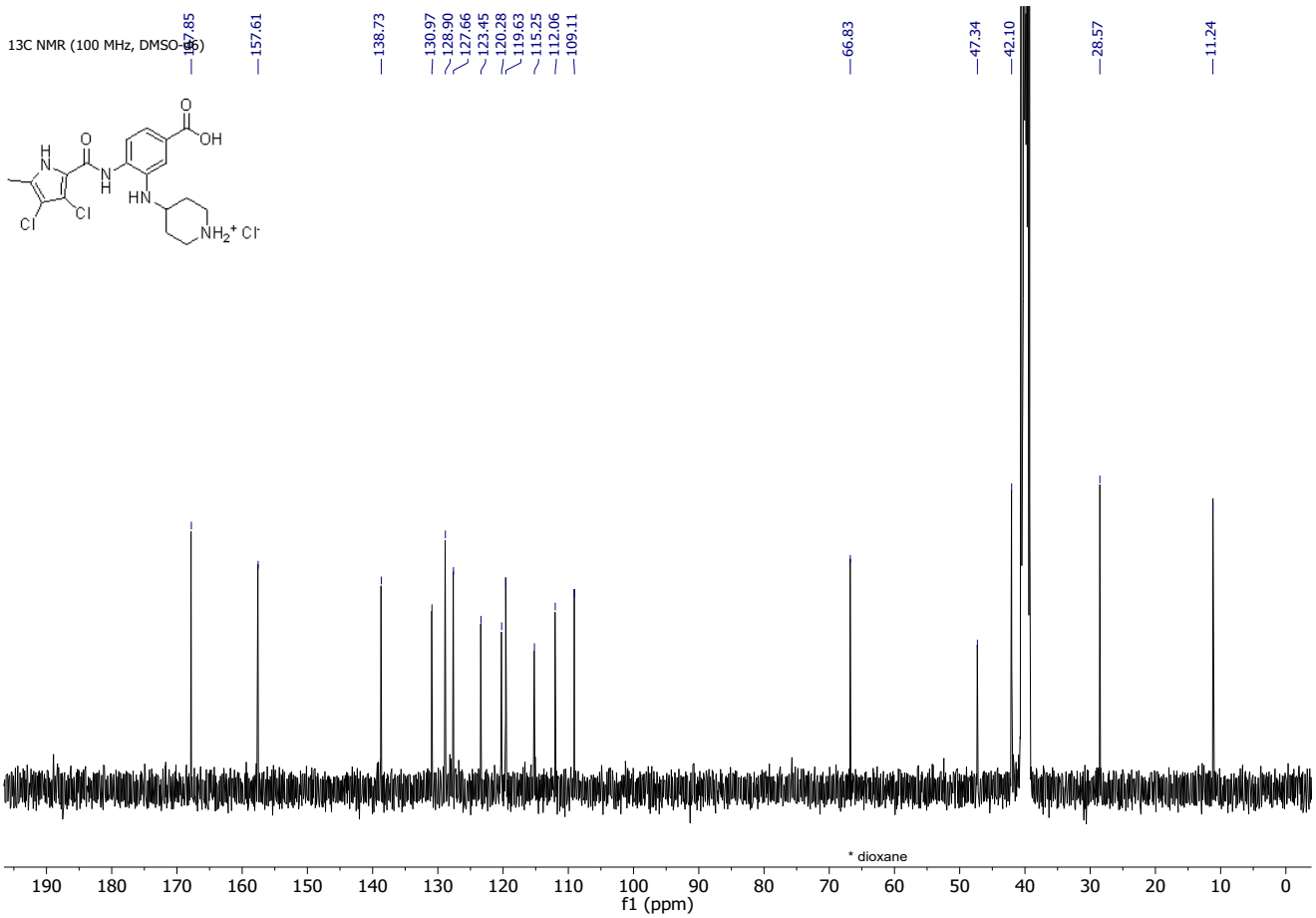
**(*S*)-1-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperidin-3-aminium chloride (20c)**



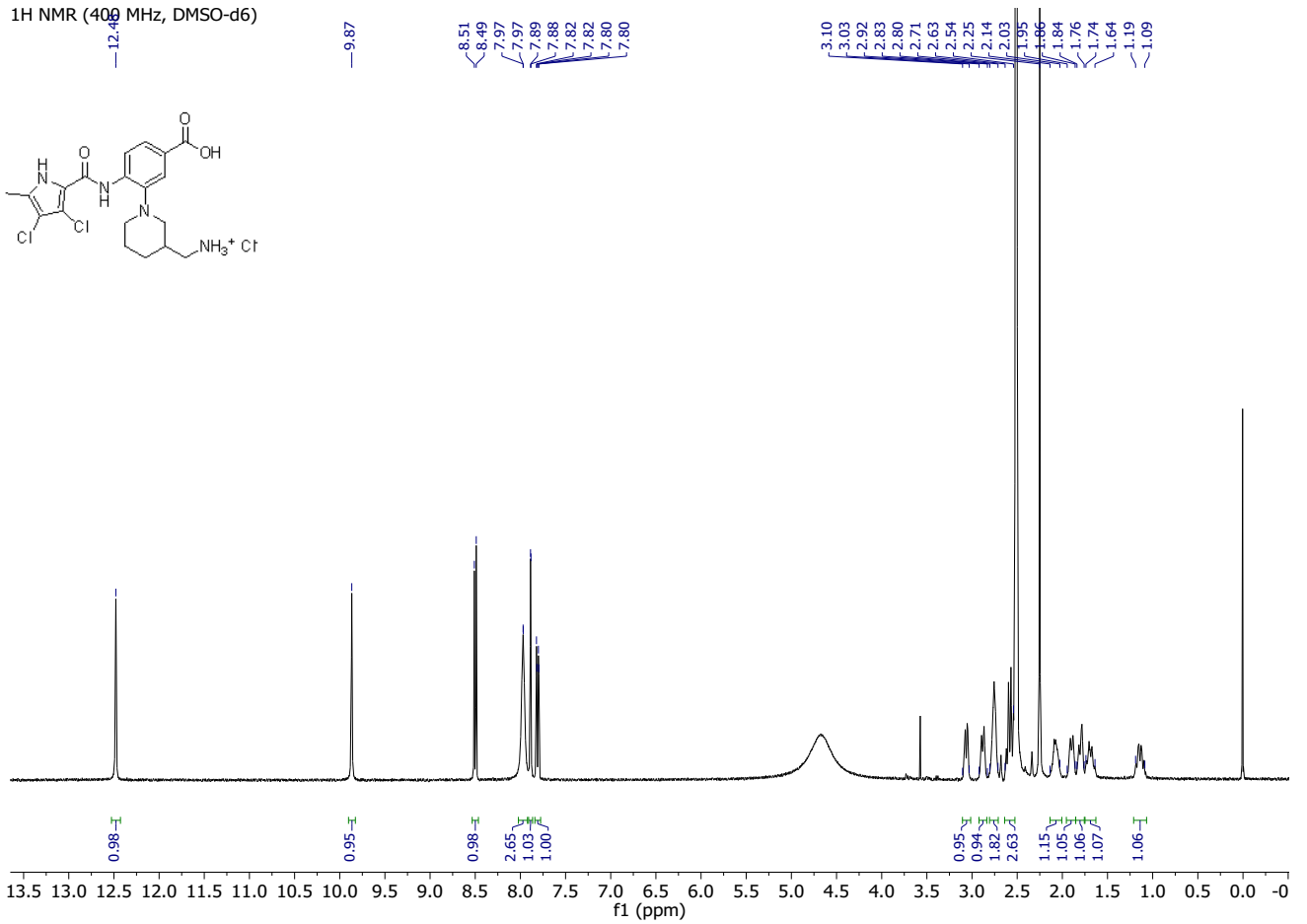



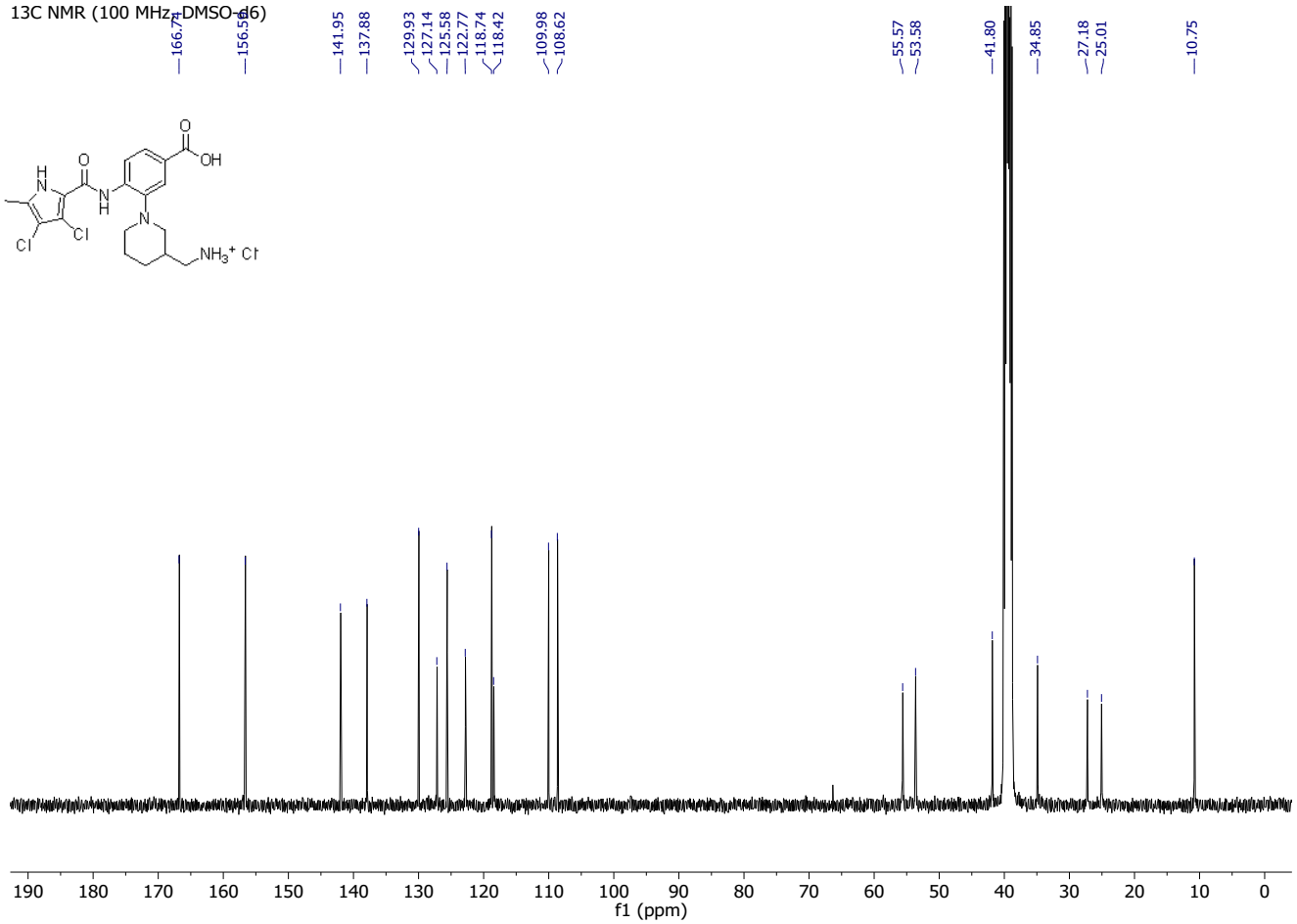
**4-((5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)amino)piperidin-1-ium chloride (20d)**



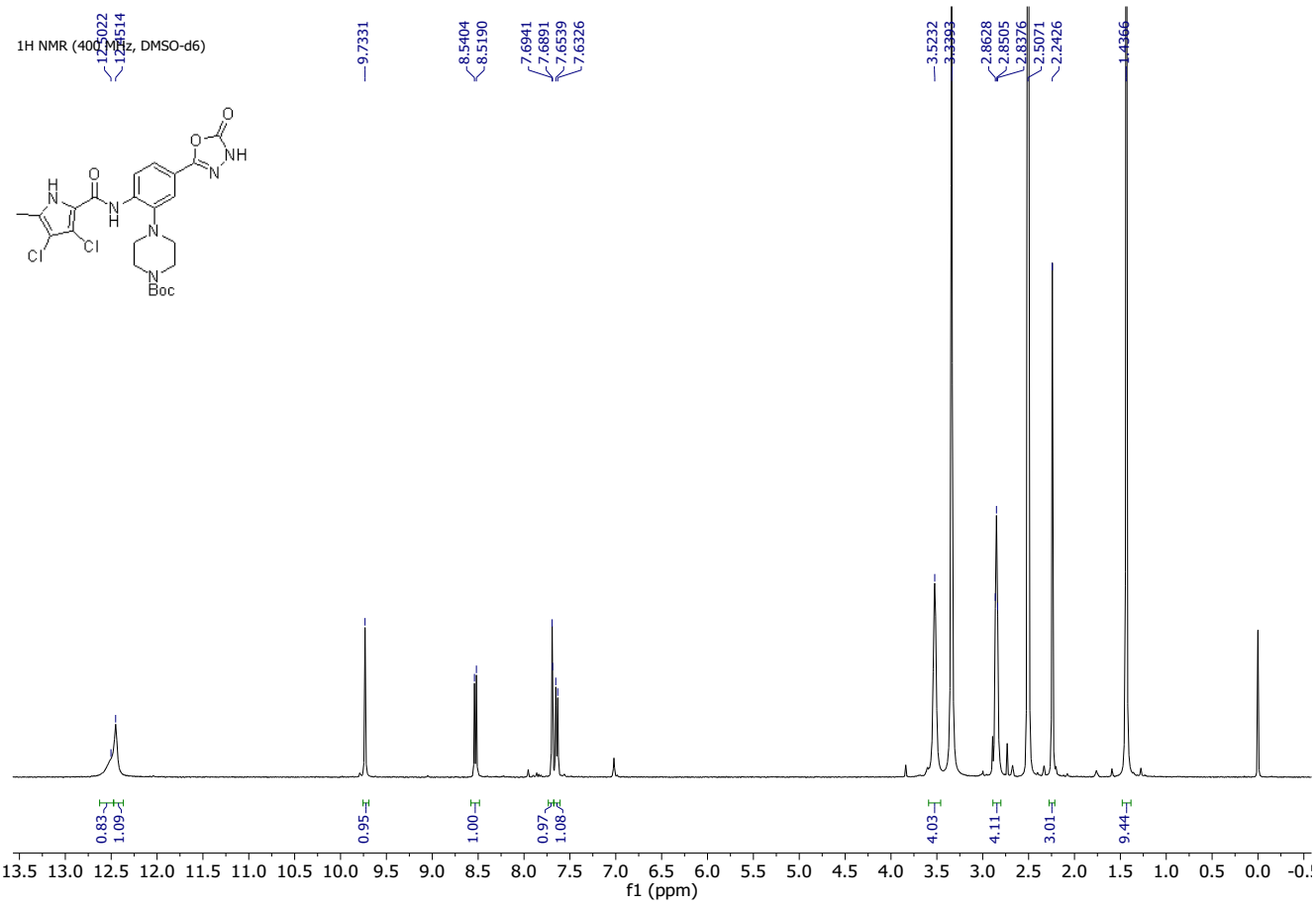



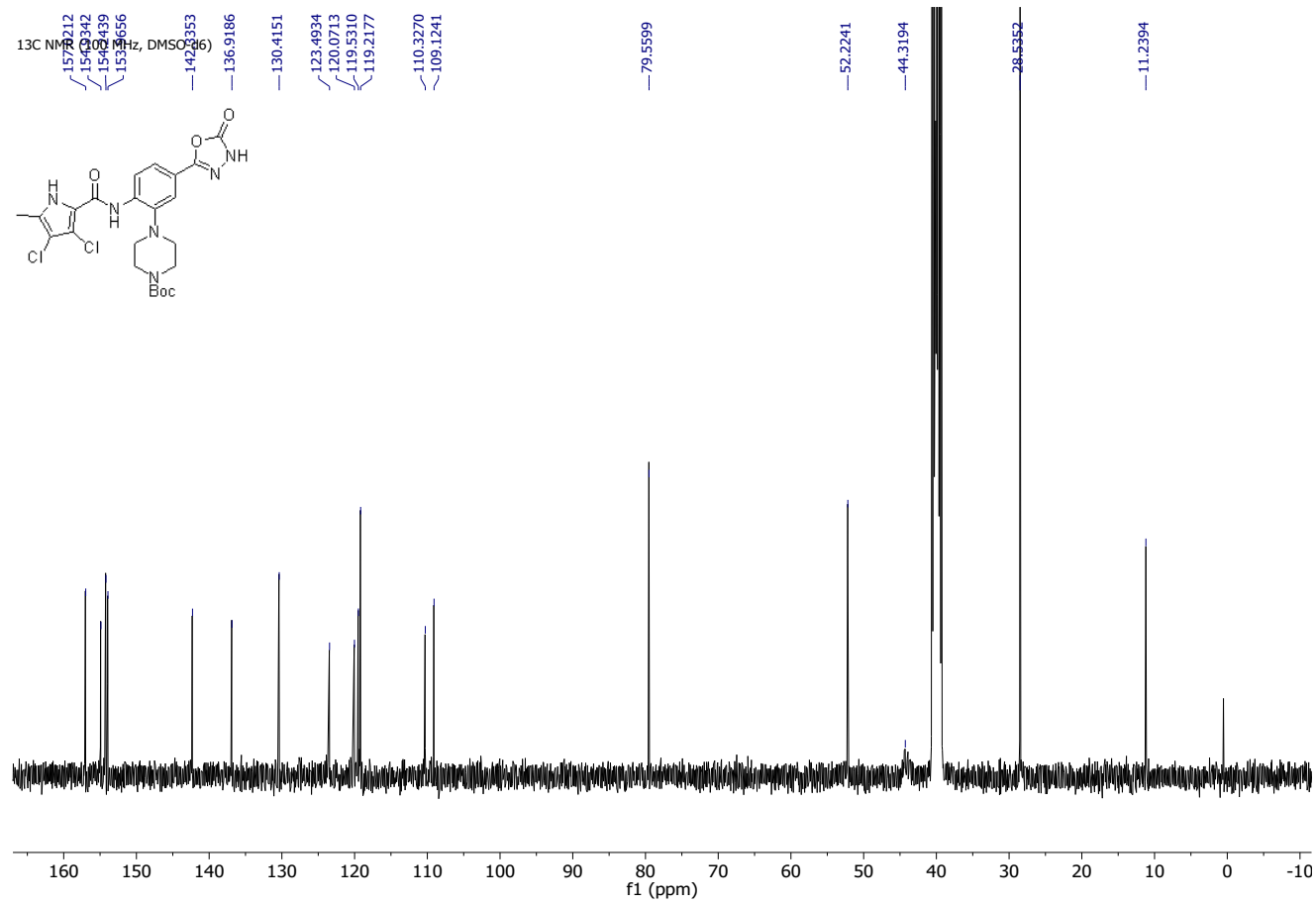
**(1-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperidin-3-yl)methanaminium chloride (20i)**



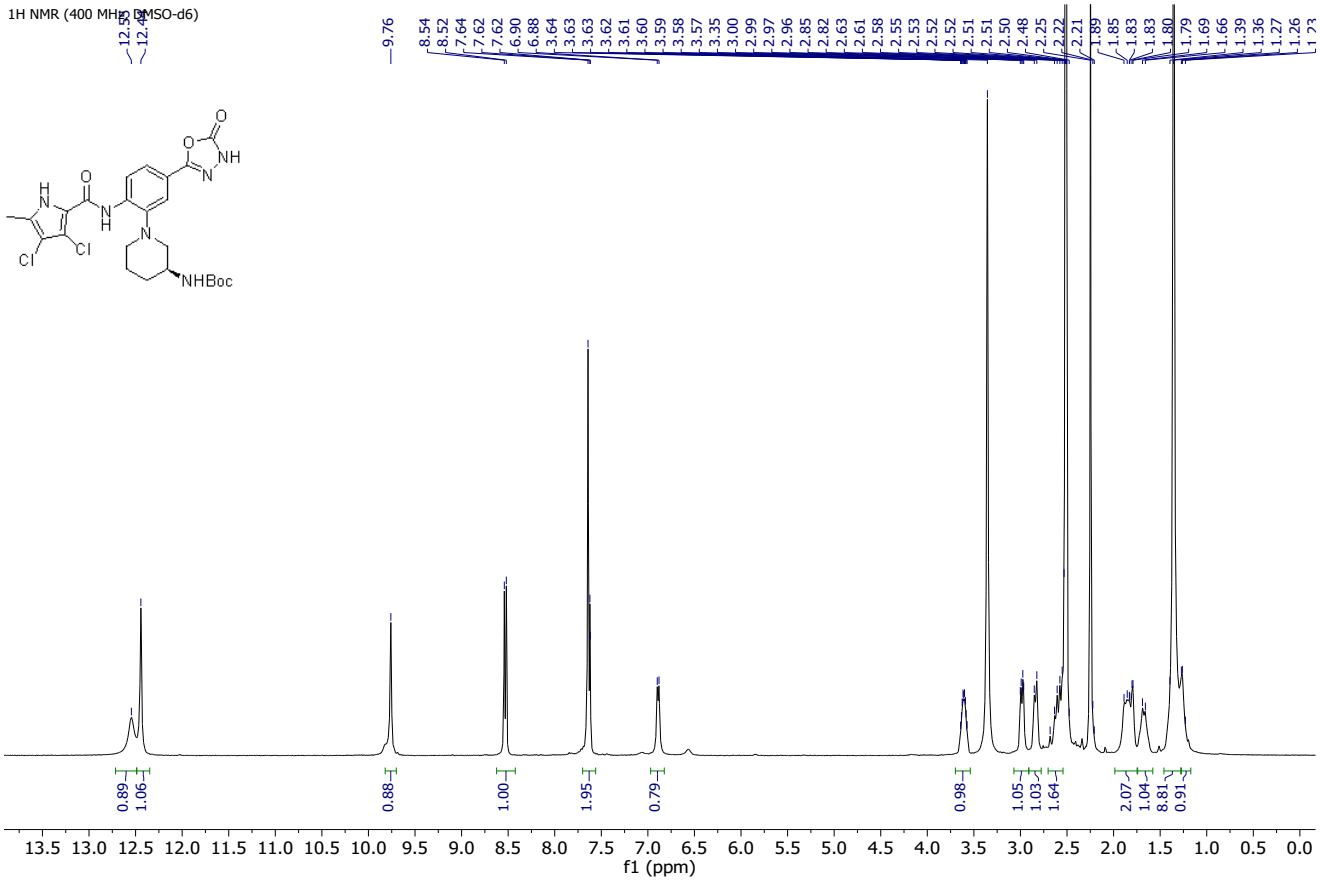



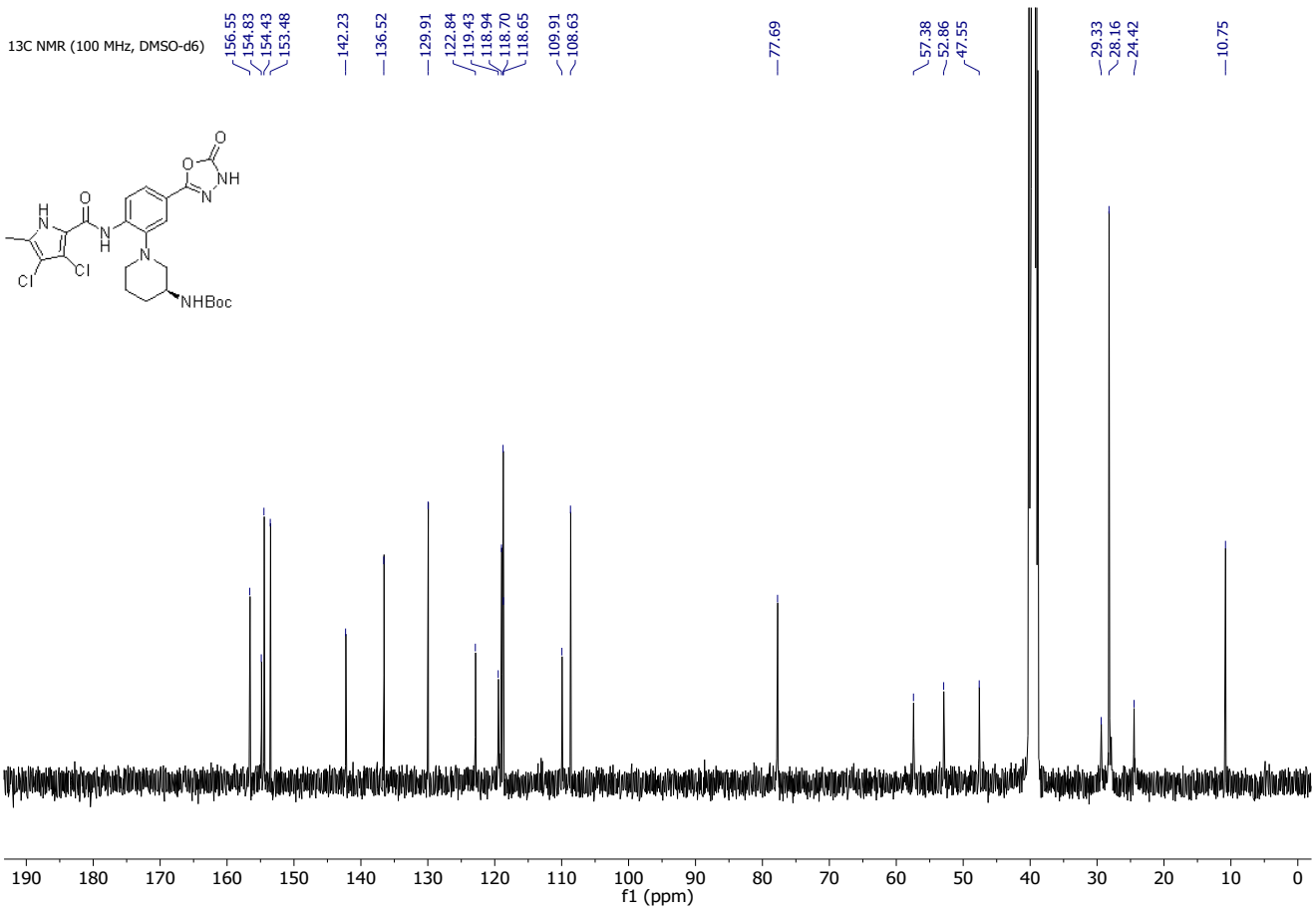
***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperazine-1-carboxylate (22a)**



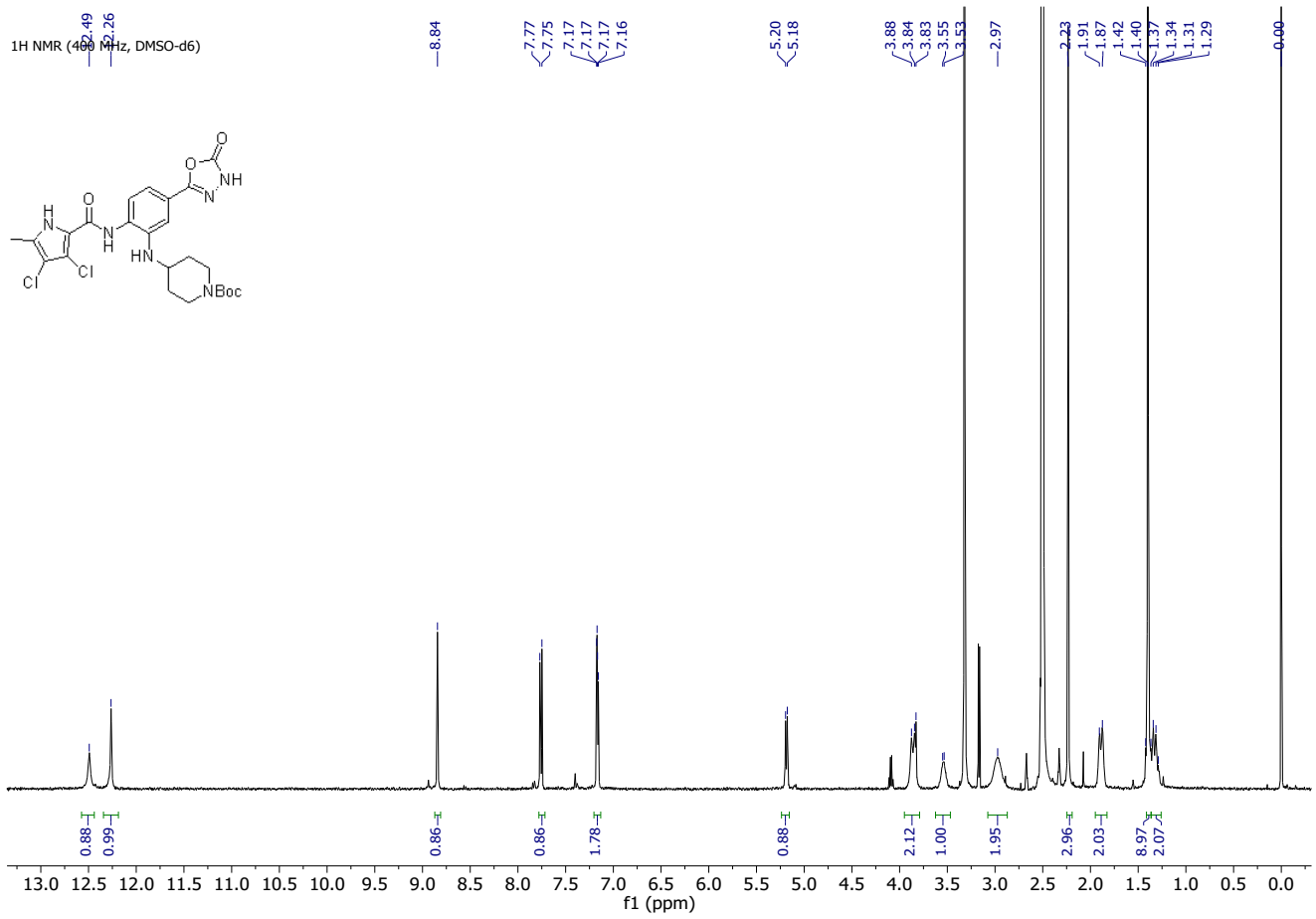



**_tert_-Butyl (_S_)-(1-(2-(3,4-dichloro-5-methyl-1_H_-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperidin-3-yl)carbamate (22c)**

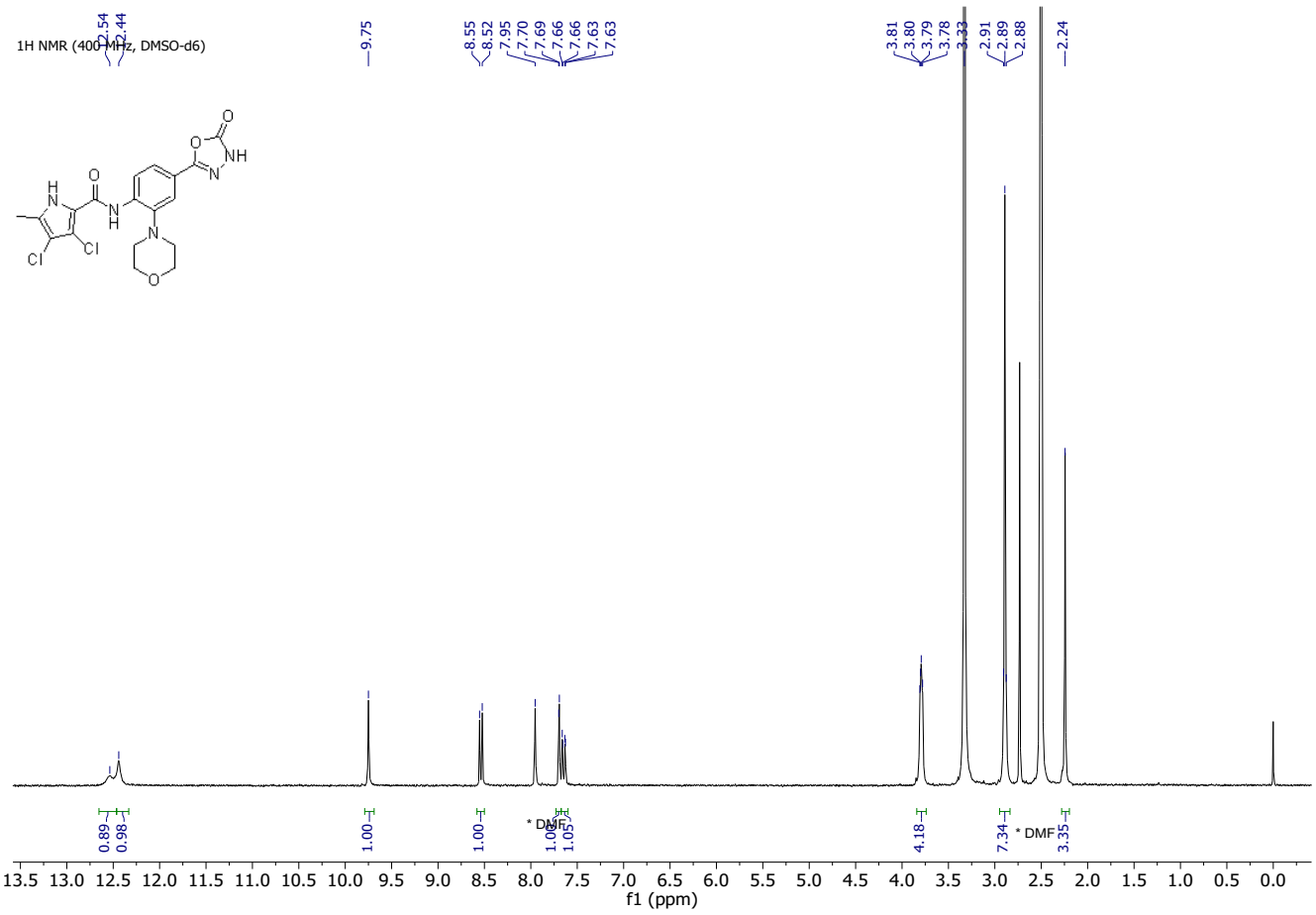


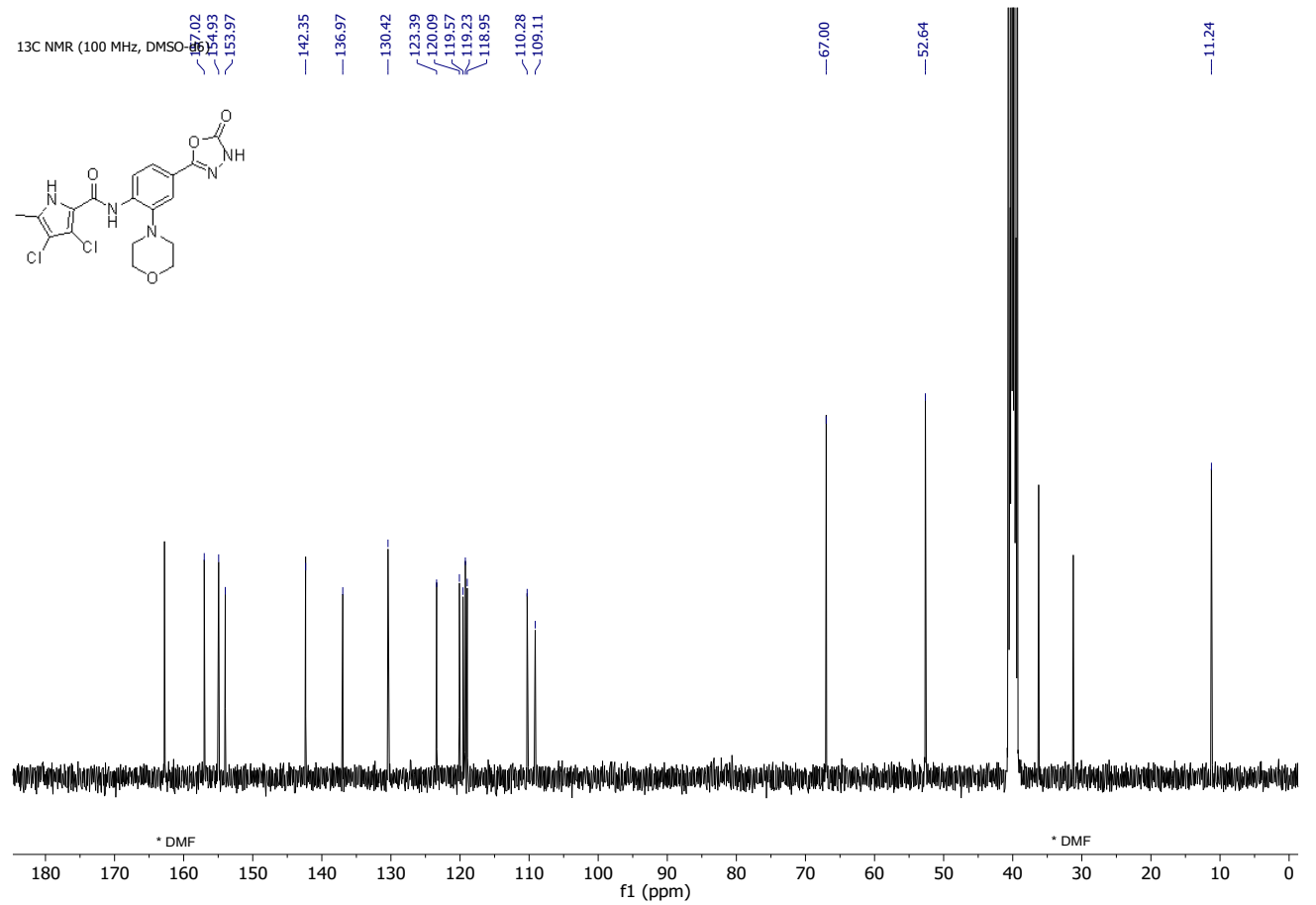



***tert*-Butyl 4-((2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)amino)piperidine-1-carboxylate (22d)**

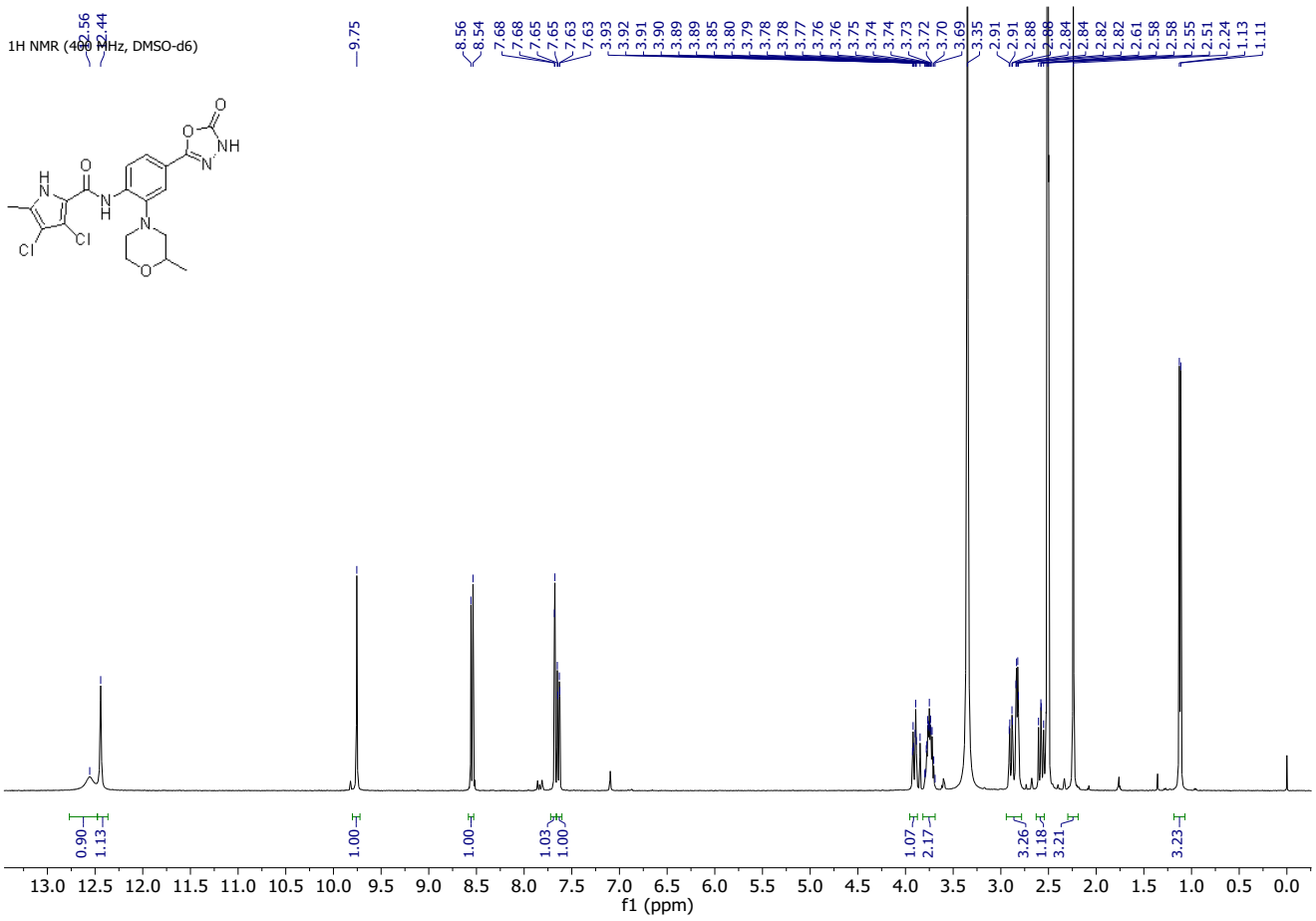


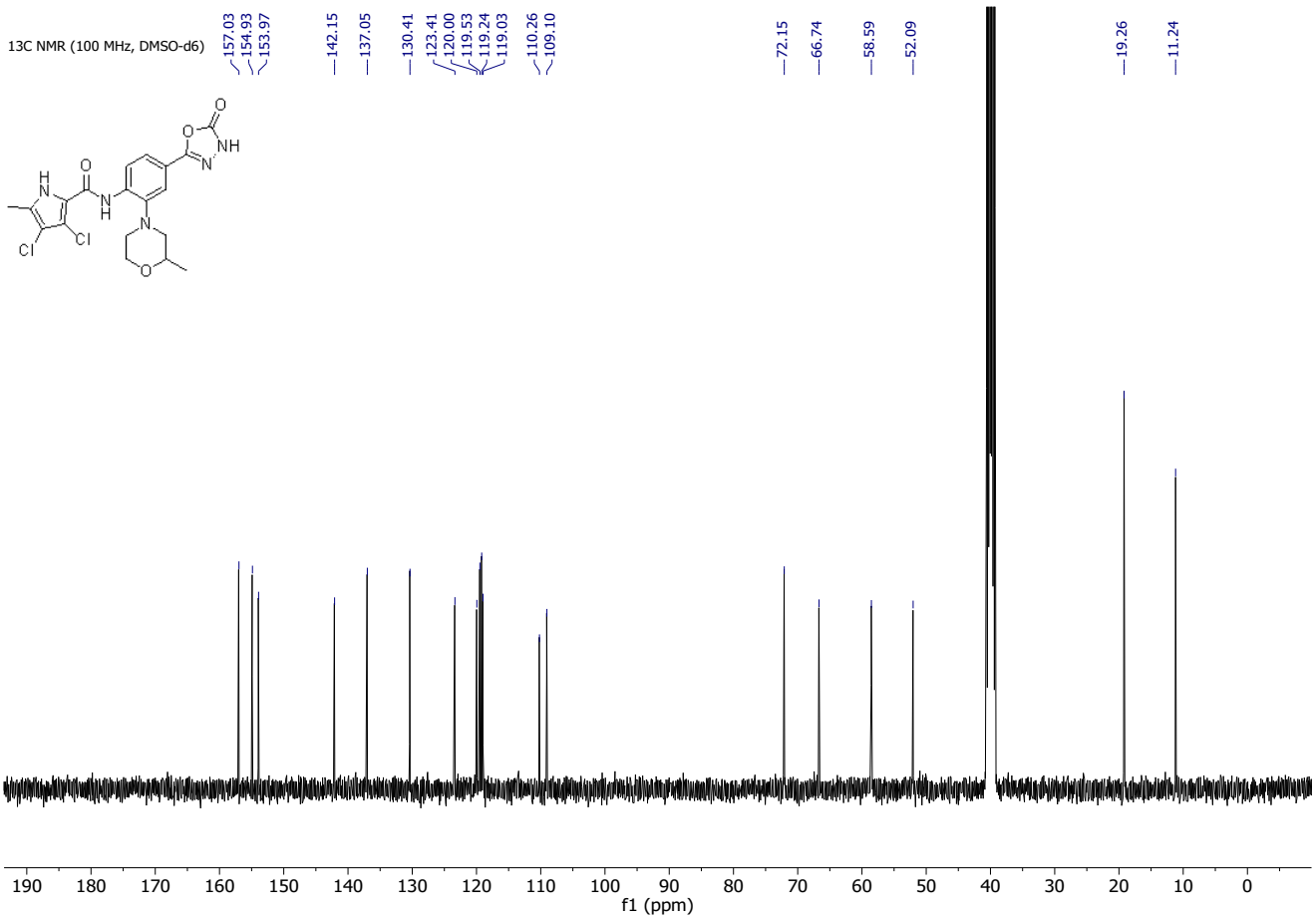
**3,4-Dichloro-5-methyl-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (22e)**



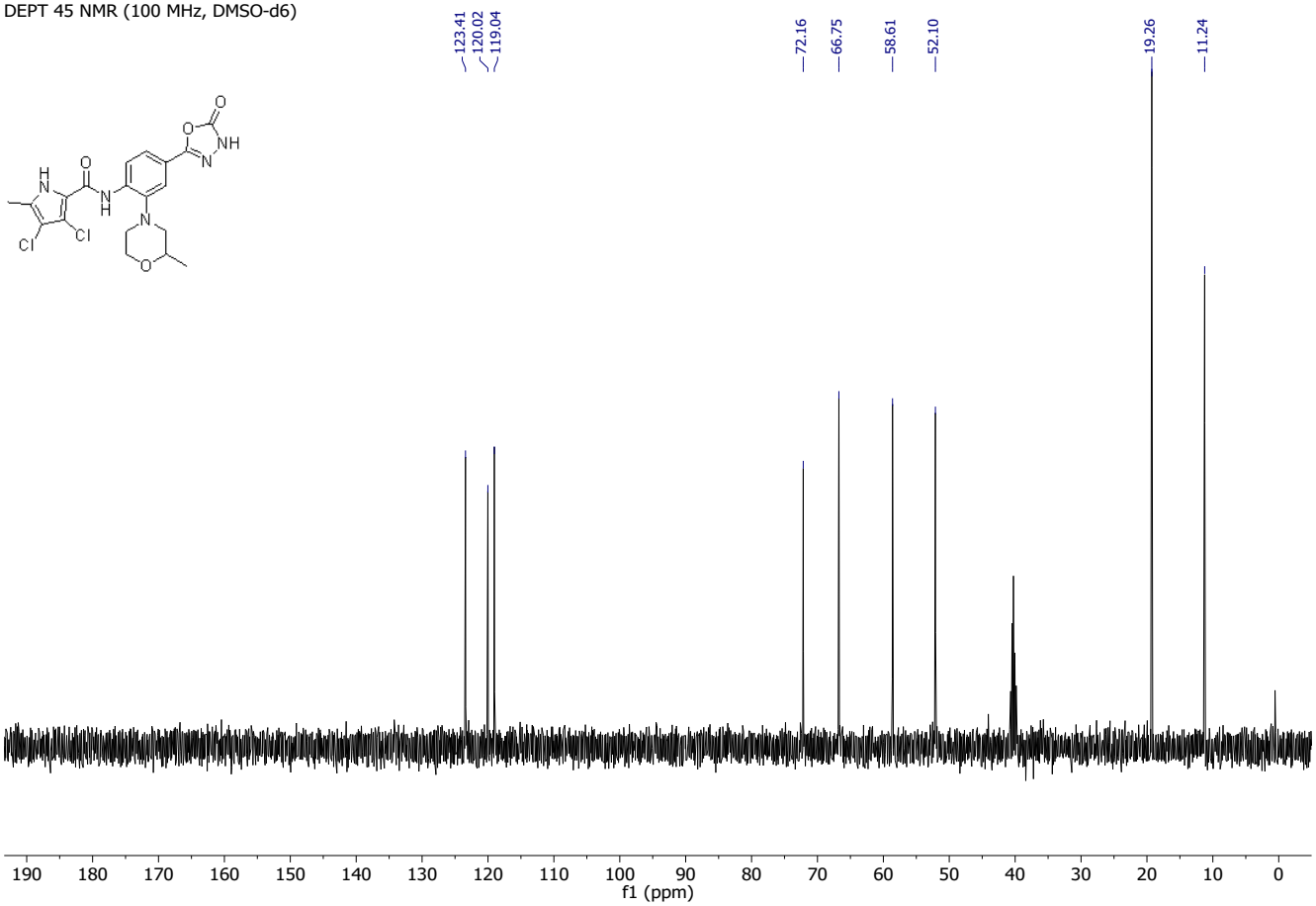



**3,4-Dichloro-5-methyl-*N*-(2-(2-methylmorpholino)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (22f)**

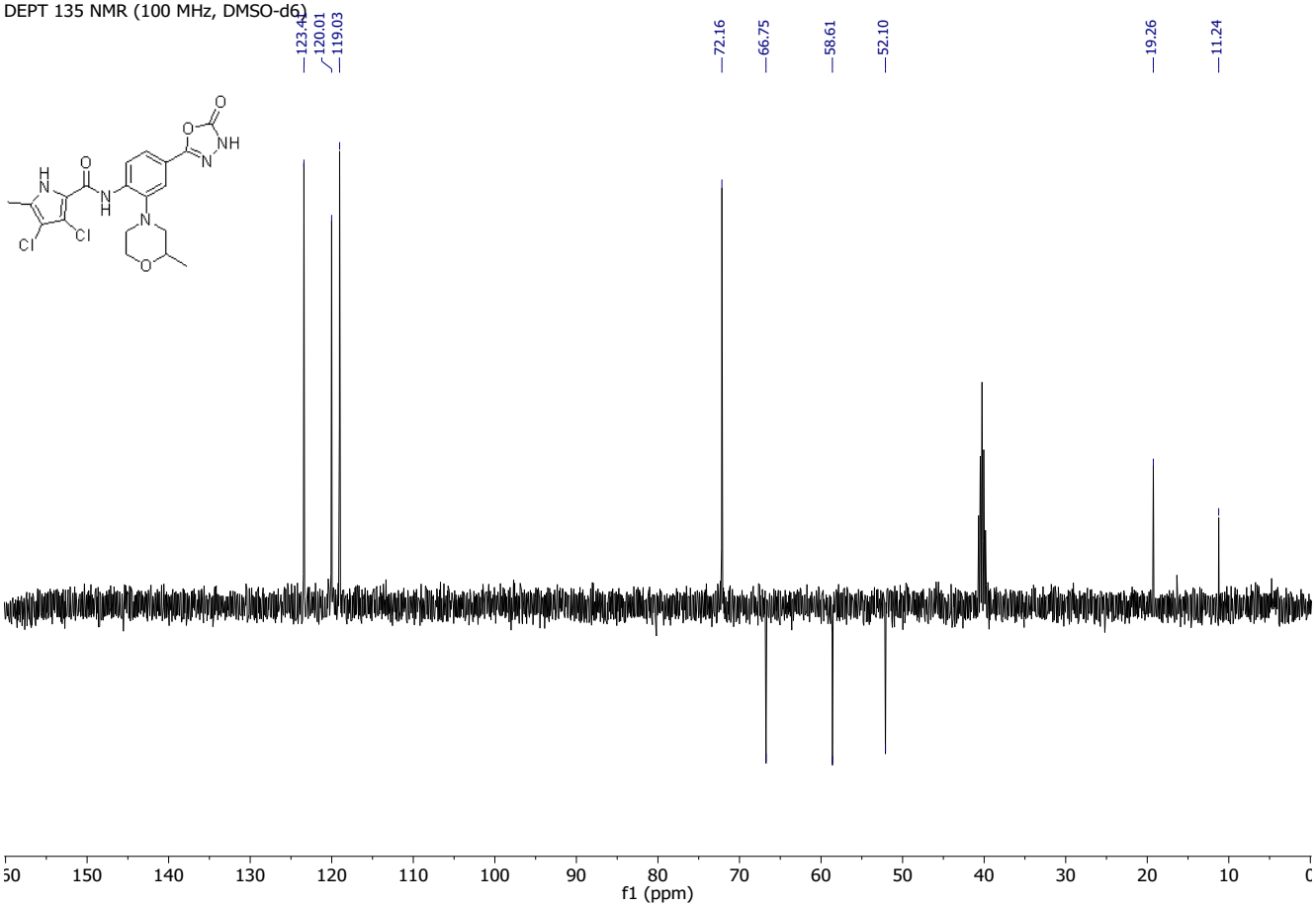


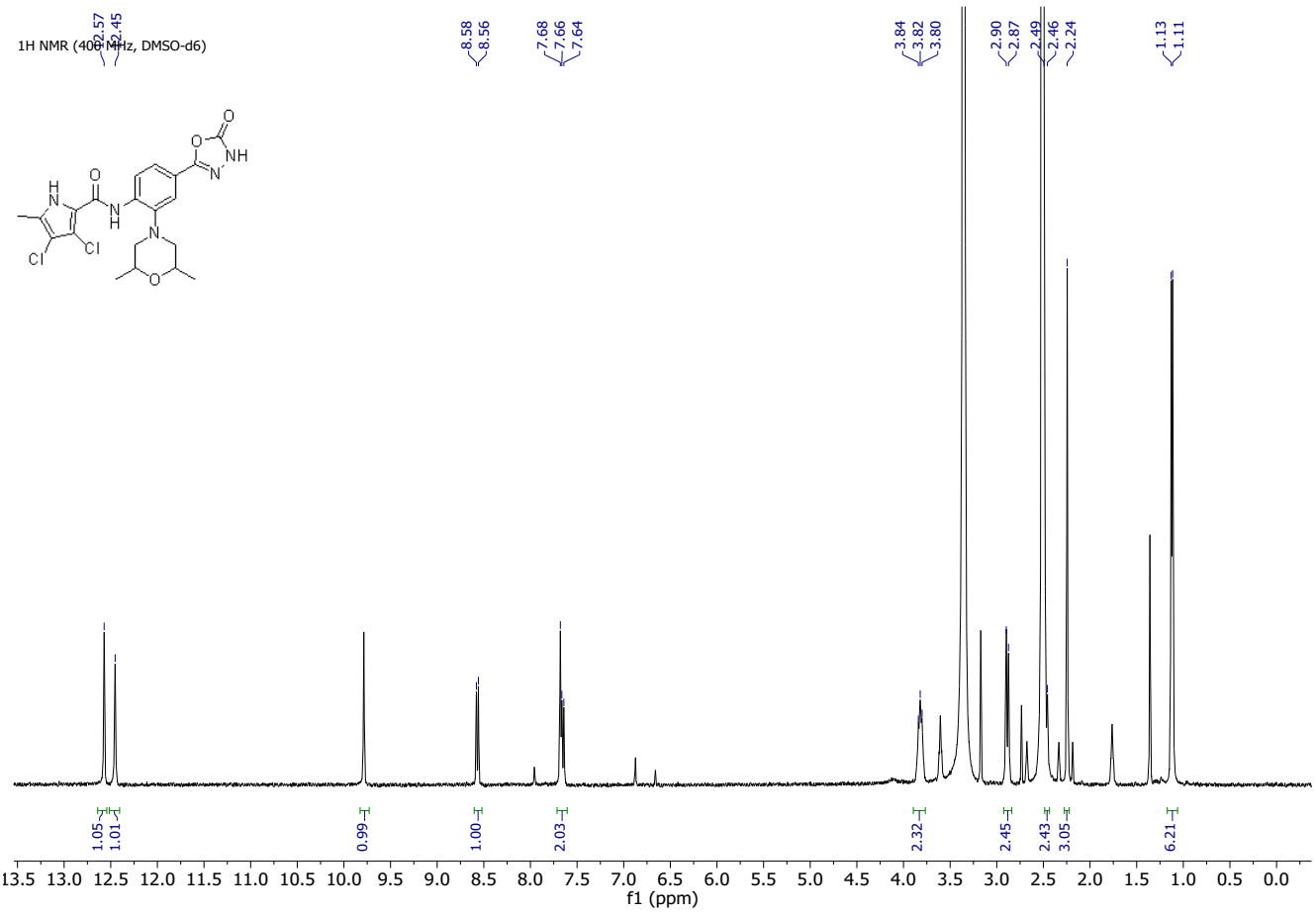
DEPT 45 NMR (100 MHz, DMSO-d6)

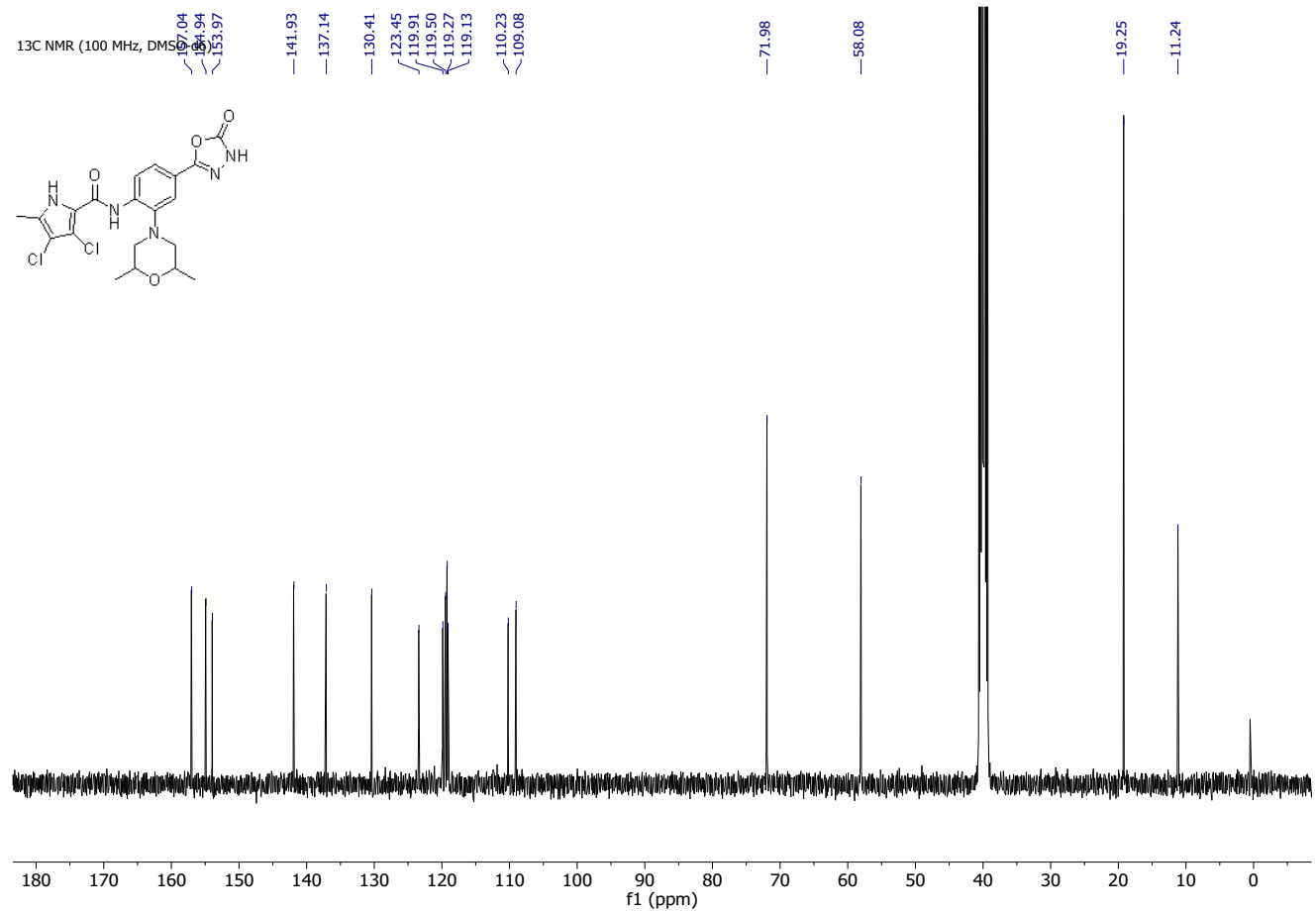



DEPT 135 NMR (100 MHz, DMSO-d6)

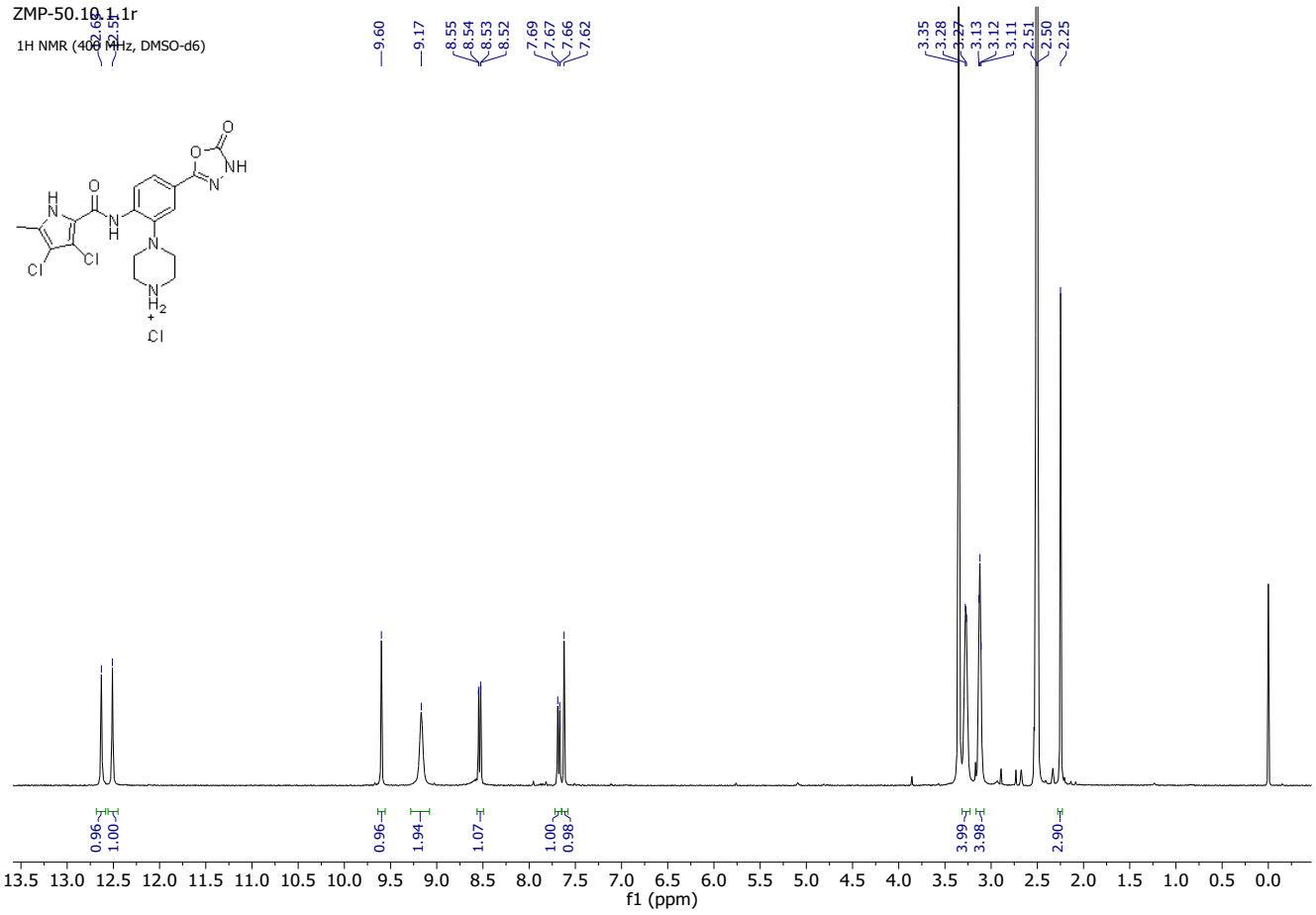


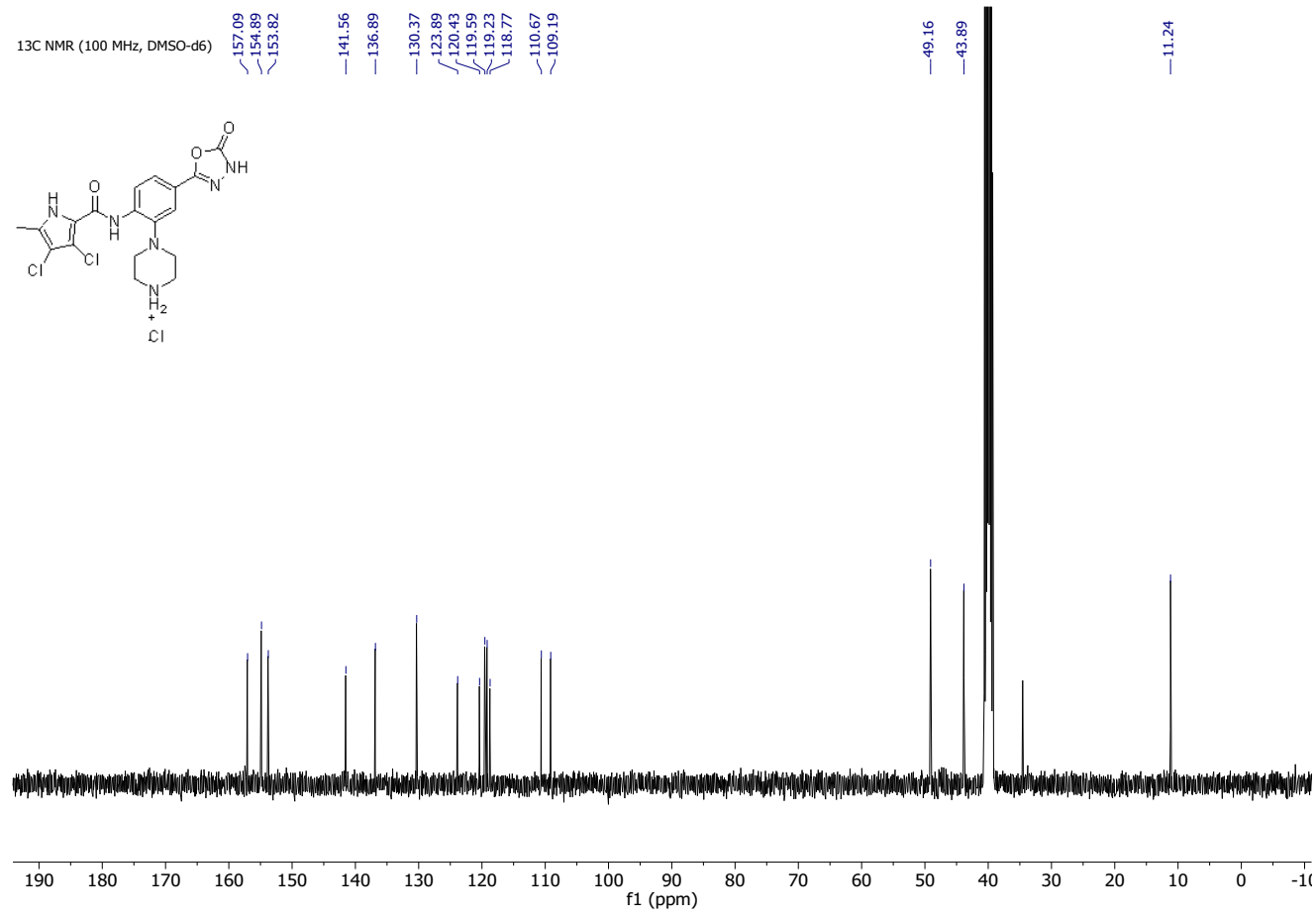
**3,4-Dichloro-*N*-(2-(2,6-dimethylmorpholino)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-5-methyl-1*H*-pyrrole-2-carboxamide (22g)**



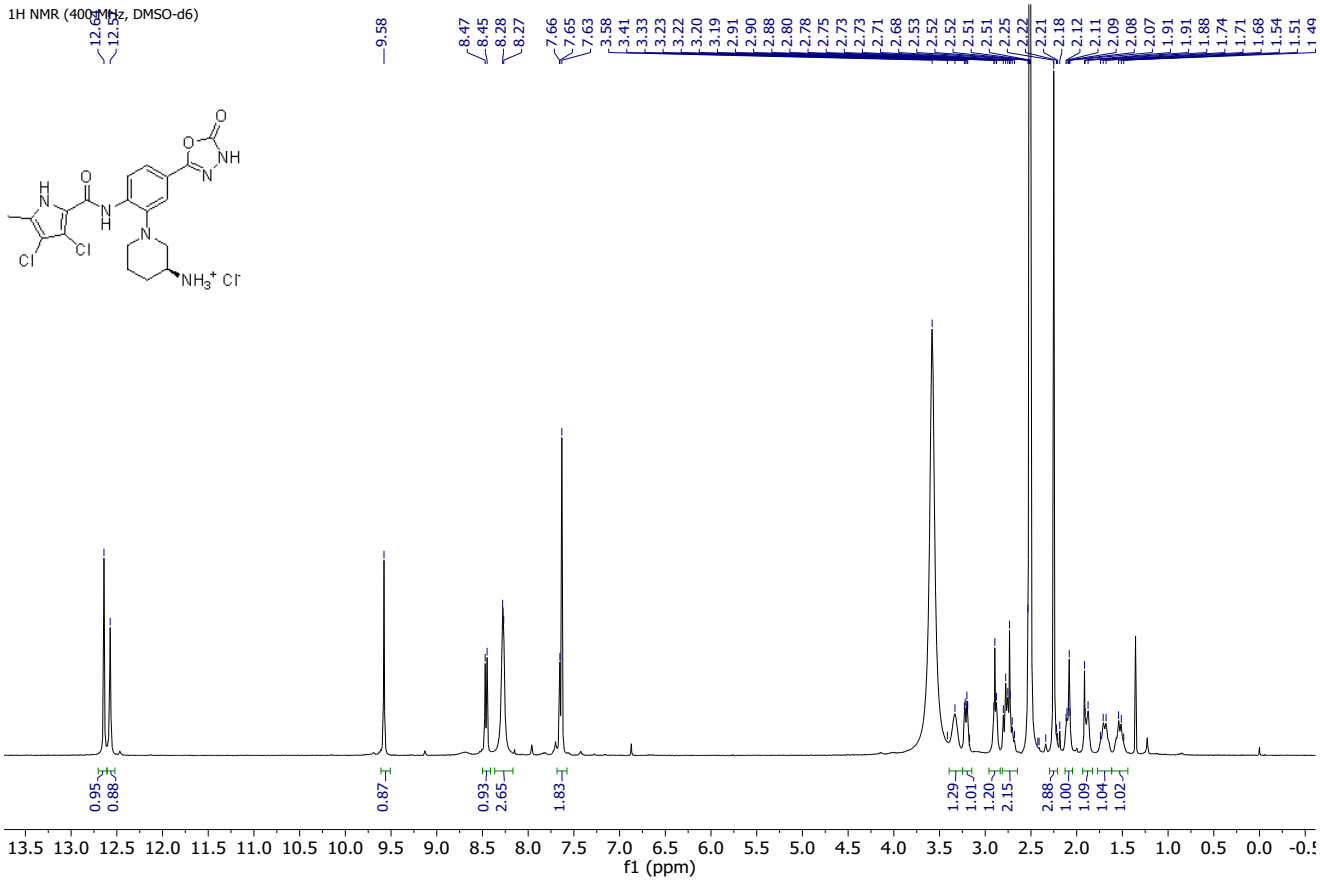



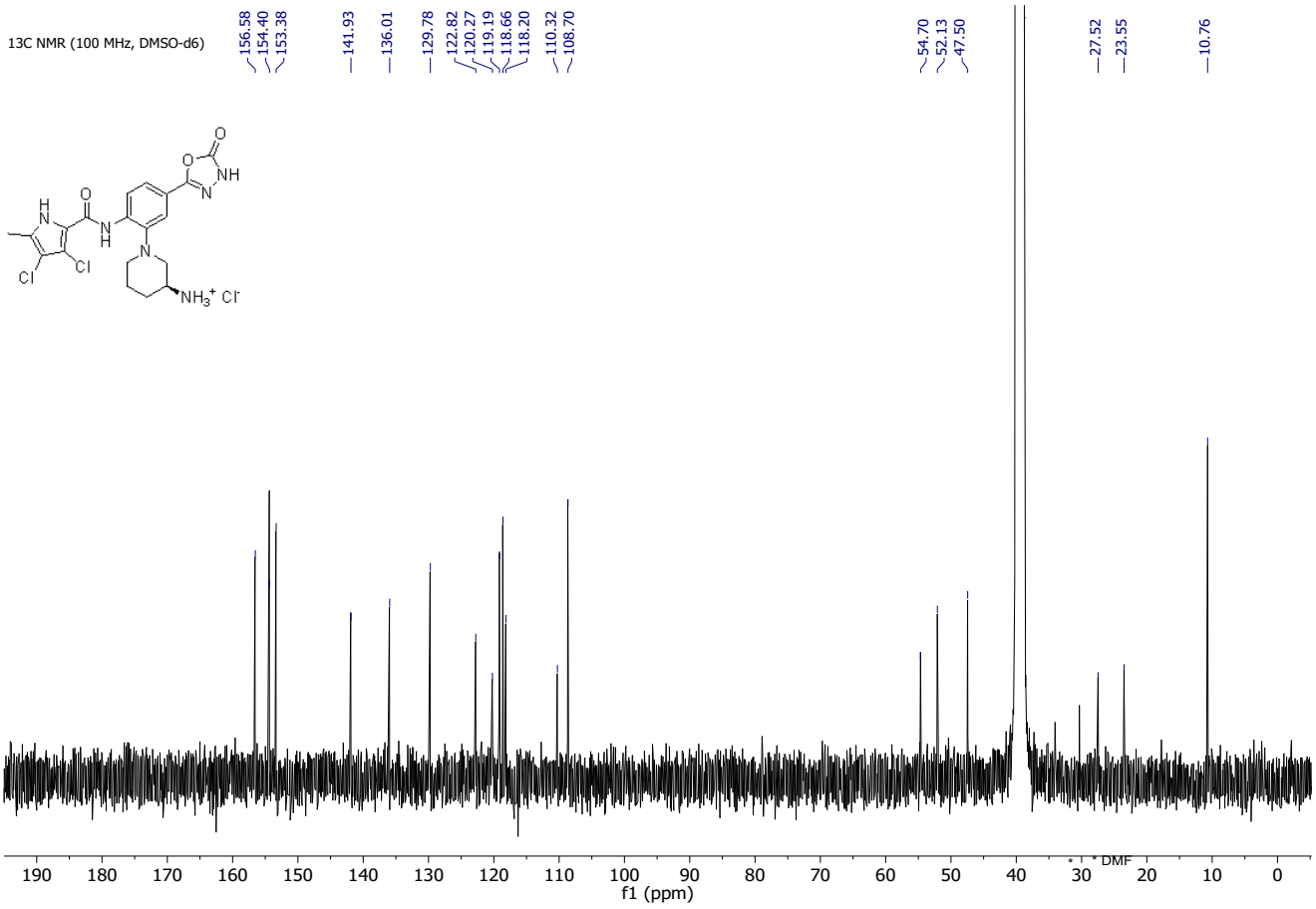
**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperazin-1-ium chloride (23a)**



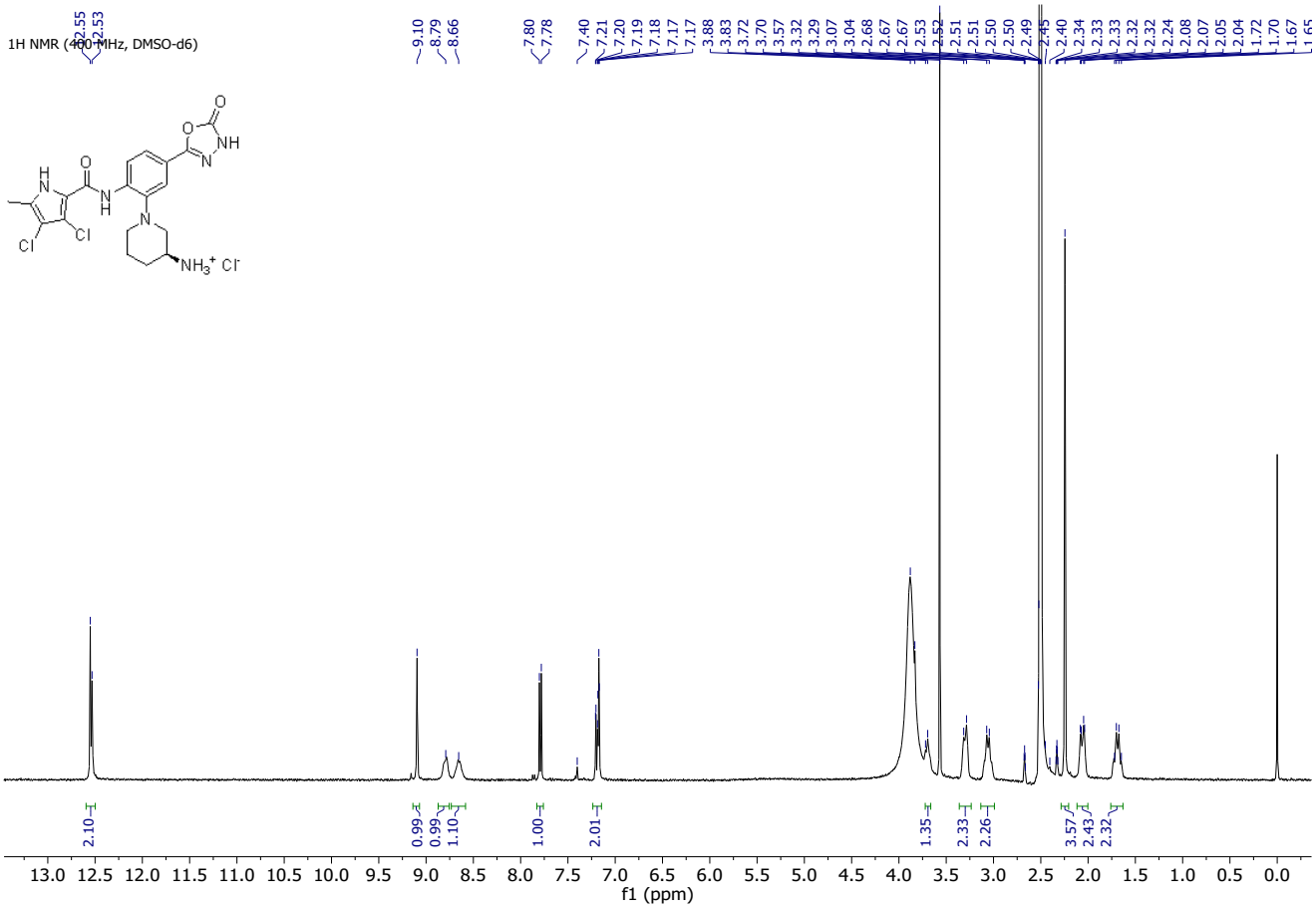



**(*S*)-1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperidin-3-aminium chloride (23c)**

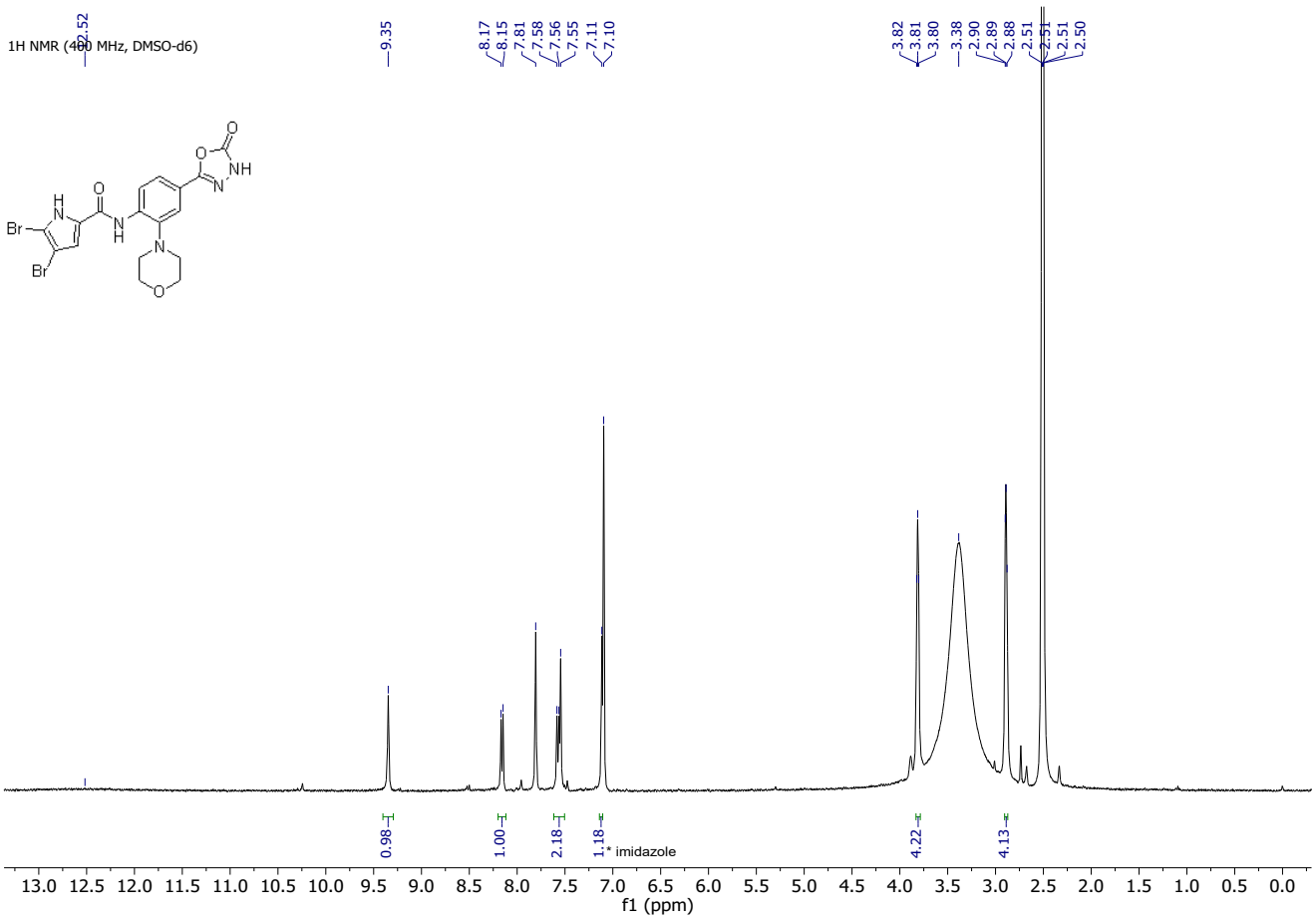


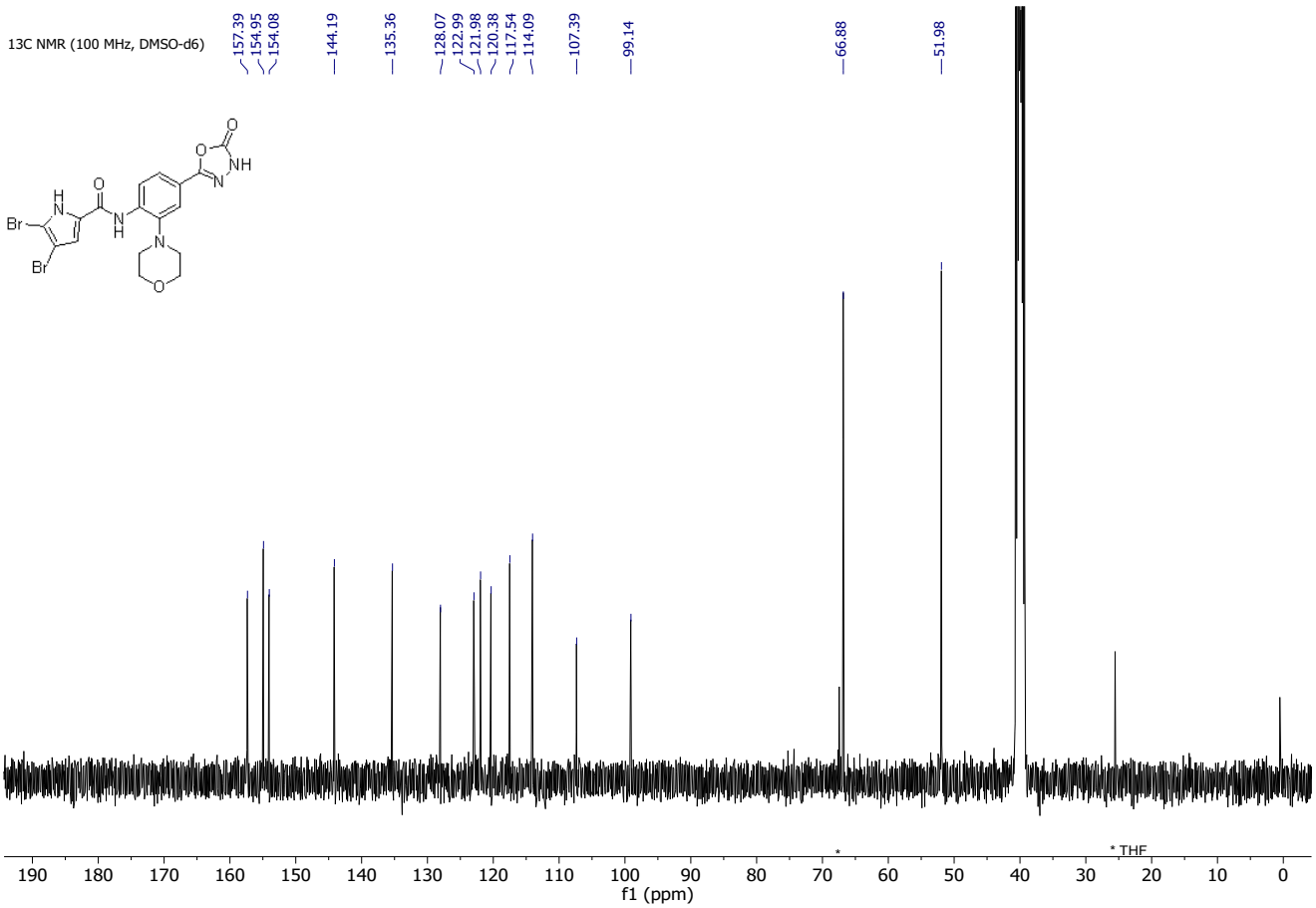



**4-((2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)amino)piperidin-1-ium chloride (23d)**

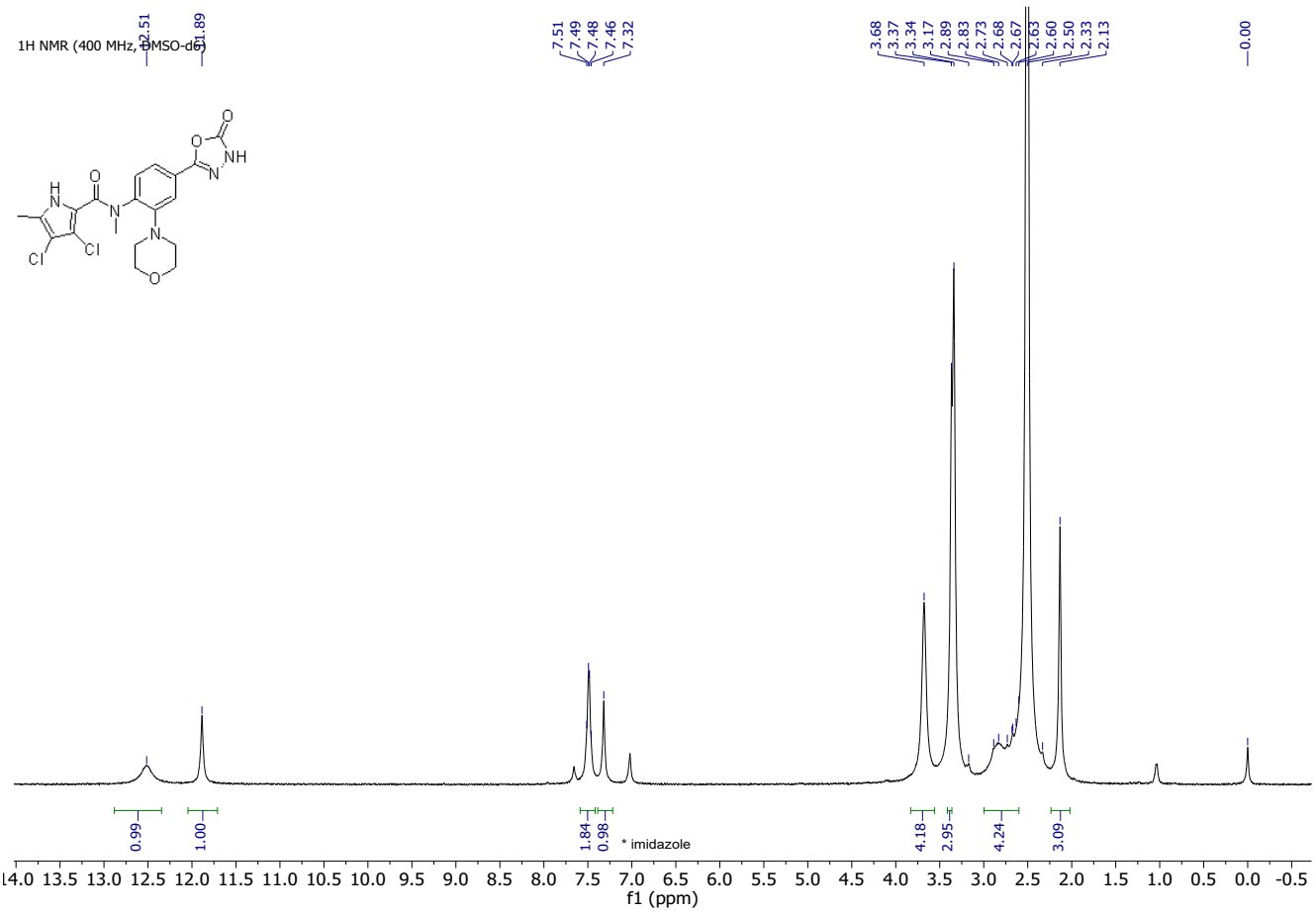


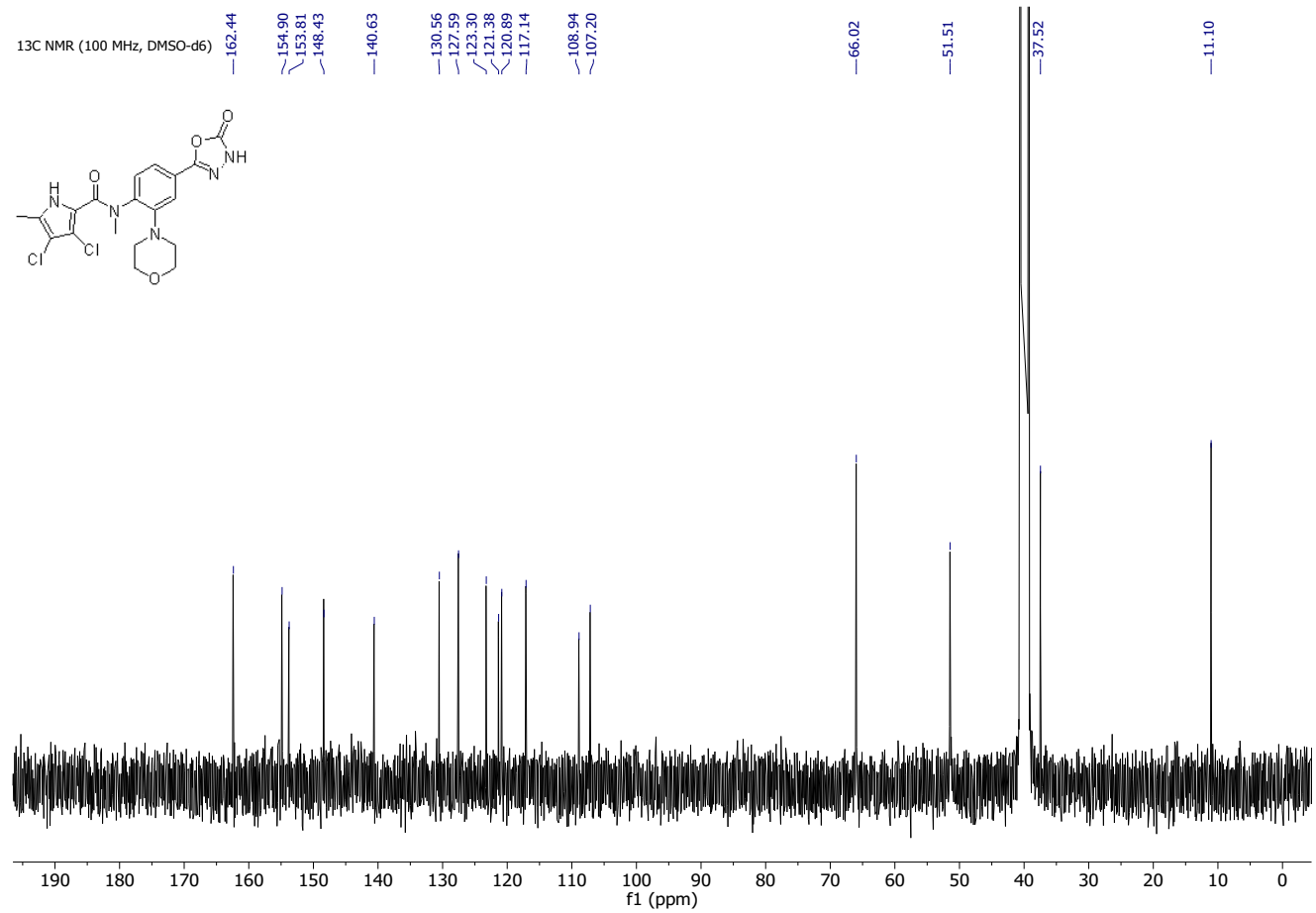
**4,5-Dibromo-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (27a)**



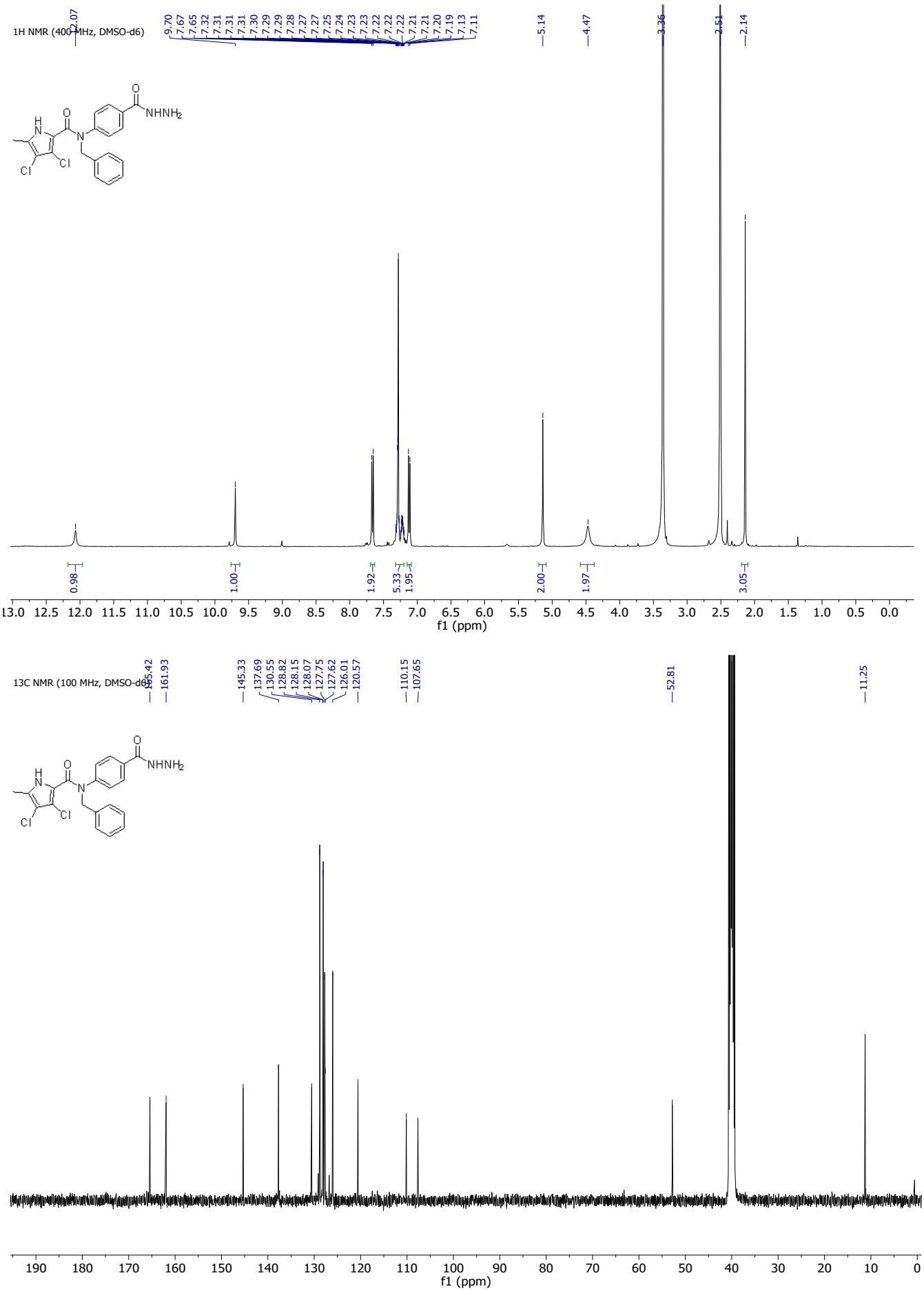



**3,4-Dichloro-*N*,5-dimethyl-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (27b)**

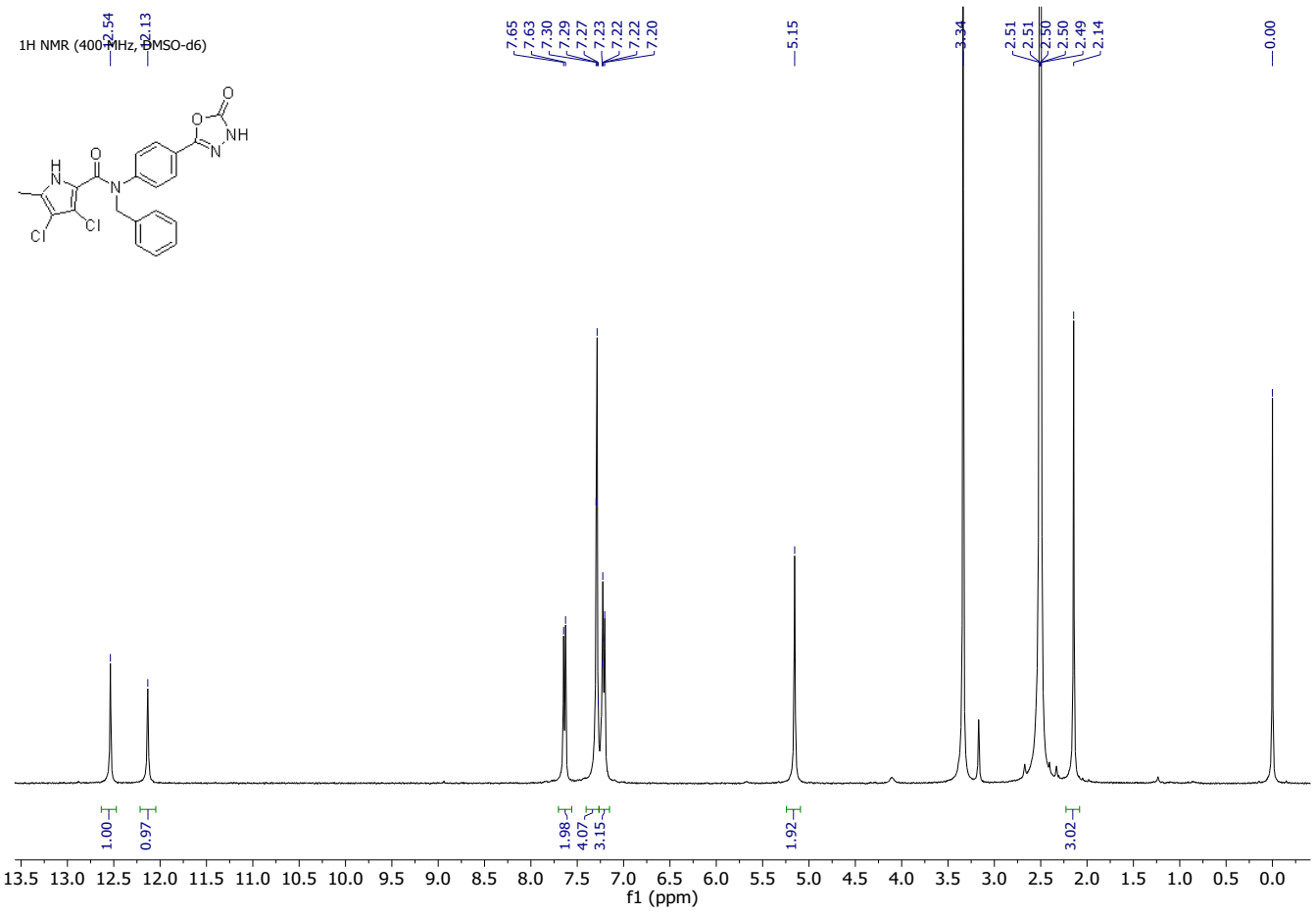


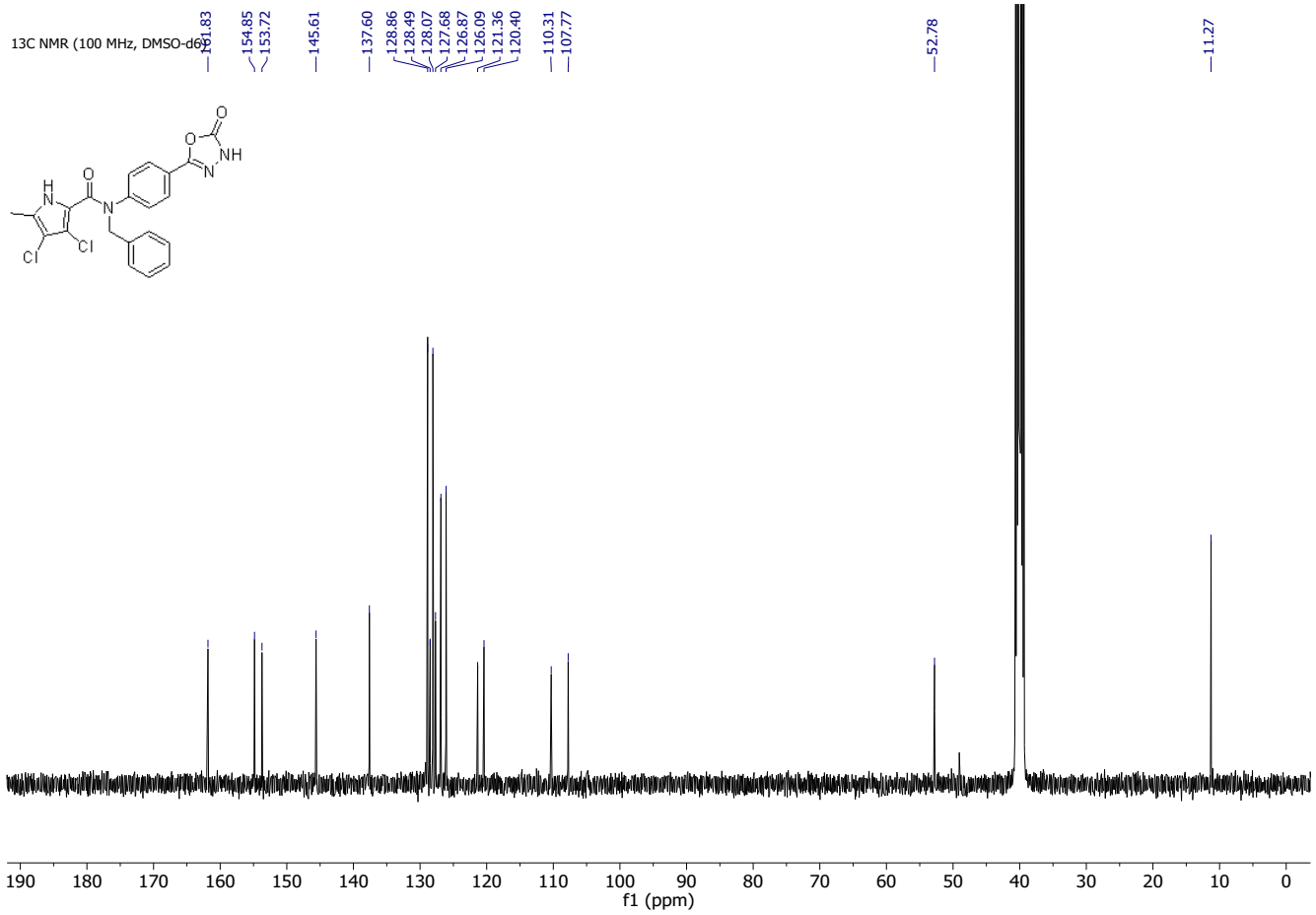



**_N_-Benzyl-3,4-dichloro-_N_-(4-(hydrazinecarbonyl)phenyl)-5-methyl-1_H_-pyrrole-2-carboxamide (32)**

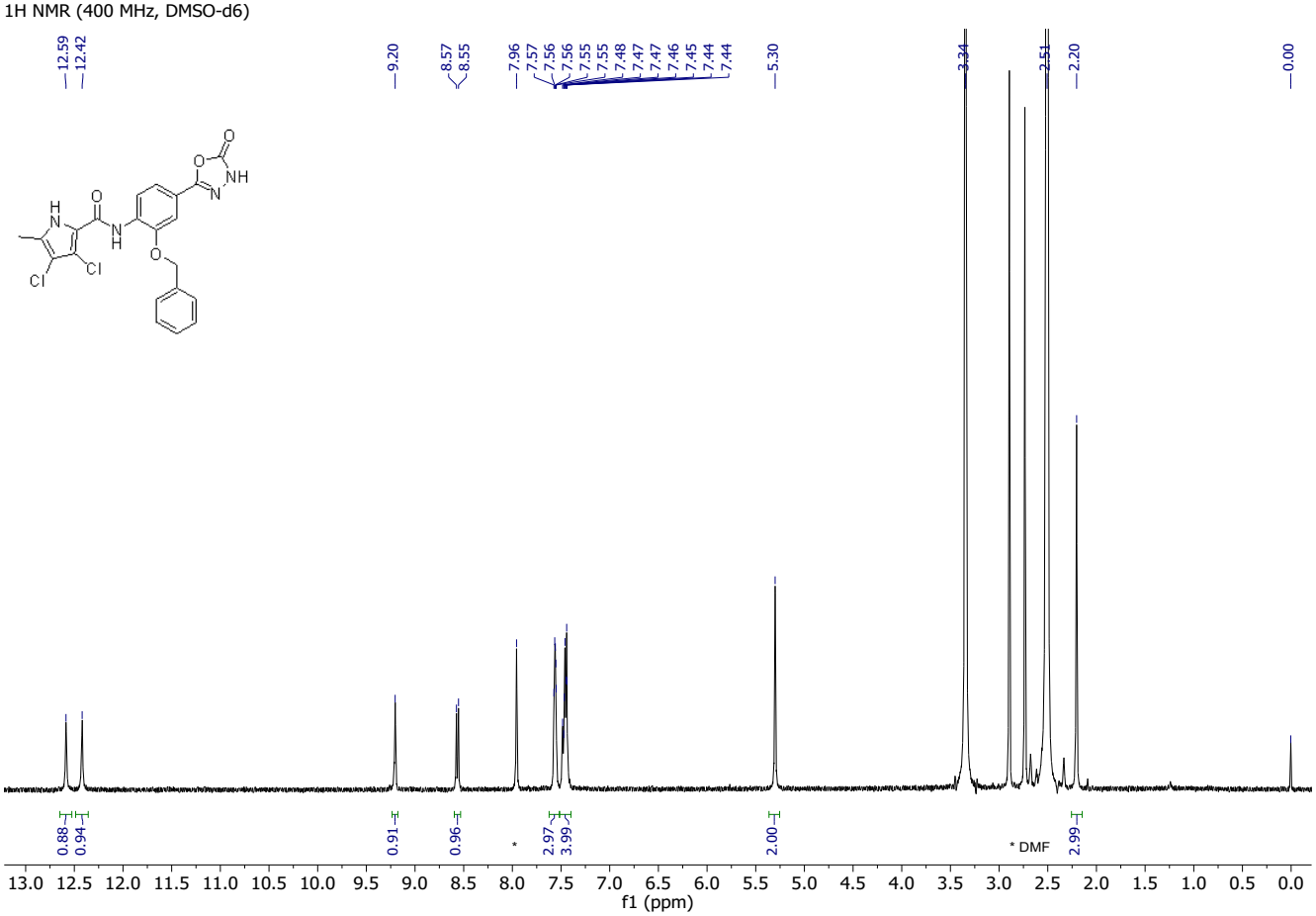


**_N_-Benzyl-3,4-dichloro-5-methyl-_N_-(4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1_H_-pyrrole-2-carboxamide (33)**






## *N*-(2-(Benzyloxy)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamide (39)



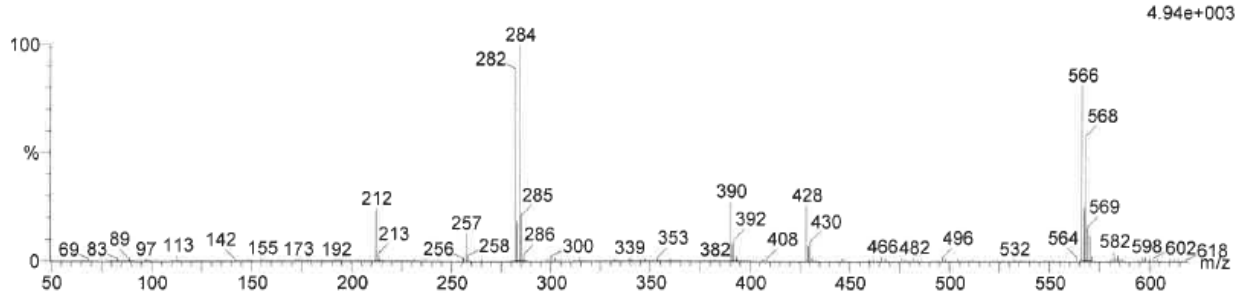
## 8. HRMS spectra of the representative compounds

### 4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-((2-methoxy-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (6a)

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1647 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-20 41 (1.680) Cm (41)
1: TOF MS ES-



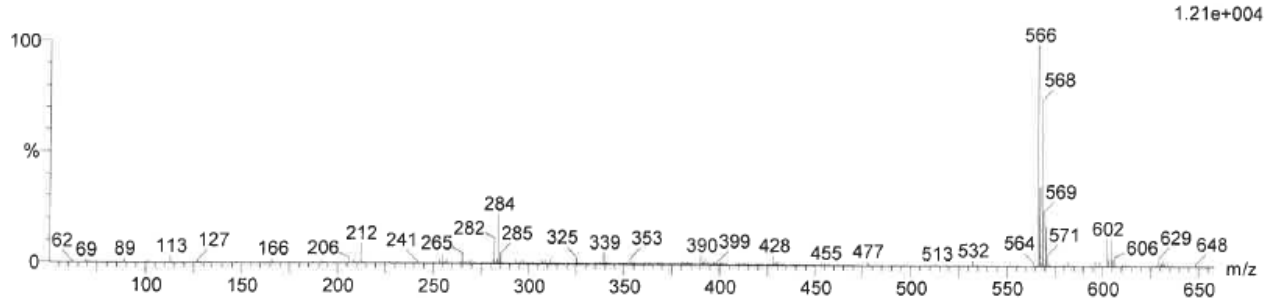

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 566.1572 | 566.1573 | -0.1 | -0.2 | 12.5 | 74.7 | 0.2 | C25 H30 N5 O6 Cl2 ✓ M-H |
| | 566.1560 | 1.2 | 2.1 | 7.5 | 76.7 | 2.3 | C24 H34 N O10 Cl2 |
| | 566.1560 | 1.2 | 2.1 | 18.5 | 77.4 | 2.9 | C22 H22 N15 Cl2 |
| | 566.1587 | -1.5 | -2.6 | 17.5 | 77.4 | 3.0 | C26 H26 N9 O2 Cl2 |
| | 566.1546 | 2.6 | 4.6 | 13.5 | 79.1 | 4.7 | C21 H26 N11 O4 Cl2 |
| | 566.1592 | -2.0 | -3.5 | -0.5 | 83.6 | 9.1 | C13 H34 N7 O13 Cl2 |
| | 566.1578 | -0.6 | -1.1 | 5.5 | 84.7 | 10.3 | C10 H26 N17 O7 Cl2 |
| | 566.1565 | 0.7 | 1.2 | 0.5 | 85.8 | 11.4 | C9 H30 N13 O11 Cl2 |

**Methyl (*S*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (6b)**

**emental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1647 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-21 45 (1.828) Cm (44:45)
1: TOF MS ES-



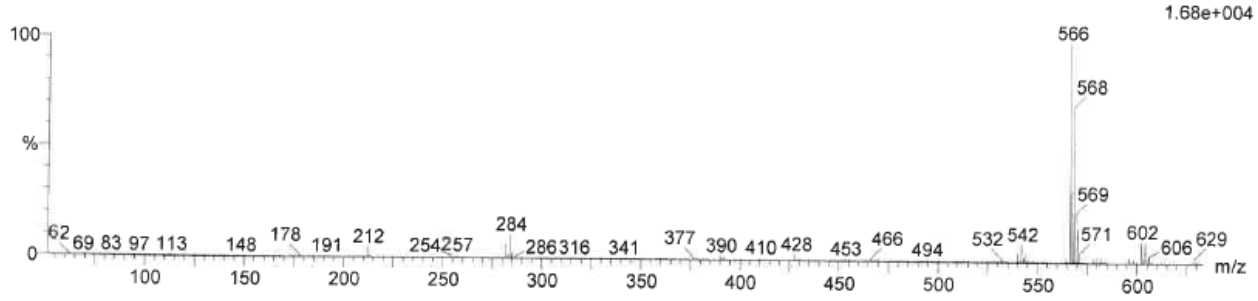

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 566.1573 | 566.1573 | 0.0 | 0.0 | 12.5 | 163.4 | 2.0 | C25 H30 N5 O6 Cl2 |
| | 566.1578 | -0.5 | -0.9 | 5.5 | 163.6 | 2.2 | C10 H26 N17 O7 Cl2 |
| | 566.1565 | 0.8 | 1.4 | 0.5 | 163.6 | 2.2 | C9 H30 N13 O11 Cl2 |
| | 566.1560 | 1.3 | 2.3 | 7.5 | 163.4 | 2.0 | C24 H34 N O10 Cl2 |
| | 566.1560 | 1.3 | 2.3 | 18.5 | 163.3 | 2.0 | C22 H22 N15 Cl2 |
| | 566.1587 | -1.4 | -2.5 | 17.5 | 163.5 | 2.1 | C26 H26 N9 O2 Cl2 |
| | 566.1592 | -1.9 | -3.4 | -0.5 | 163.7 | 2.3 | C13 H34 N7 O13 Cl2 |
| | 566.1546 | 2.7 | 4.8 | 13.5 | 163.3 | 1.9 | C21 H26 N11 O4 Cl2 |

**Methyl (*R*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (6c)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1647 formula(e) evaluated with 7 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-36 33 (1.348) Cm (32:34)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 566.1576 | 566.1578 | -0.2 | -0.4 | 5.5 | 181.7 | 11.5 | C10 H26 N17 O7 Cl2 |
| | 566.1573 | 0.3 | 0.5 | 12.5 | 172.8 | 2.6 | C25 H30 N5 O6 Cl2 |
| | 566.1565 | 1.1 | 1.9 | 0.5 | 182.7 | 12.4 | C9 H30 N13 O11 Cl2 |
| | 566.1587 | -1.1 | -1.9 | 17.5 | 170.4 | 0.1 | C26 H26 N9 O2 Cl2 |
| | 566.1592 | -1.6 | -2.8 | -0.5 | 180.7 | 10.4 | C13 H34 N7 O13 Cl2 |
| | 566.1560 | 1.6 | 2.8 | 7.5 | 176.5 | 6.3 | C24 H34 N O10 Cl2 |
| | 566.1560 | 1.6 | 2.8 | 18.5 | 173.9 | 3.7 | C22 H22 N15 Cl2 |

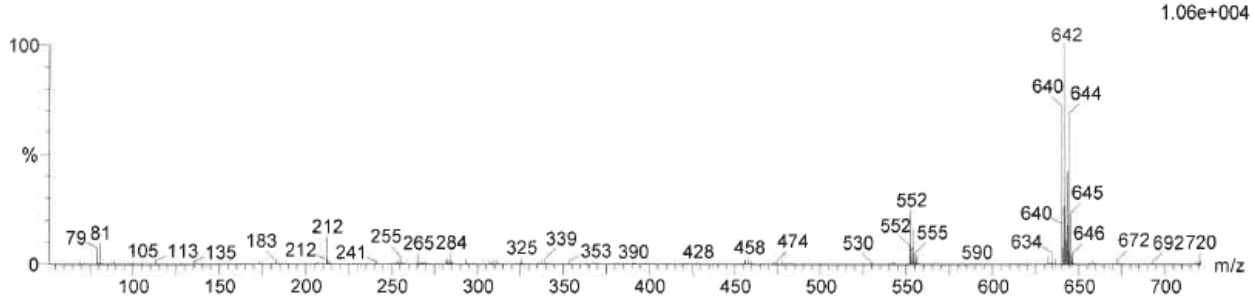
***tert*-Butyl 4-(2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)-5-((2-methoxy-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (7a)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1562 formula(e) evaluated with 9 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Br: 2-2

NFF-27 42 (1.717) Cm (42:46)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 640.0403 | 640.0406 | -0.3 | -0.5 | 12.5 | 214.7 | 1.9 | C24 H28 N5 O6 Br2 ✓ M-H- |
| | 640.0398 | 0.5 | 0.8 | 0.5 | 215.9 | 3.0 | C8 H28 N13 O11 Br2 |
| | 640.0411 | -0.8 | -1.2 | 5.5 | 215.9 | 3.0 | C9 H24 N17 O7 Br2 |
| | 640.0393 | 1.0 | 1.6 | 18.5 | 214.6 | 1.7 | C21 H20 N15 Br2 |
| | 640.0393 | 1.0 | 1.6 | 7.5 | 214.8 | 1.9 | C23 H32 N O10 Br2 |
| | 640.0420 | -1.7 | -2.7 | 17.5 | 214.7 | 1.8 | C25 H24 N9 O2 Br2 |
| | 640.0425 | -2.2 | -3.4 | -0.5 | 216.0 | 3.1 | C12 H32 N7 O13 Br2 |
| | 640.0379 | 2.4 | 3.7 | 13.5 | 214.6 | 1.8 | C20 H24 N11 O4 Br2 |
| | 640.0371 | 3.2 | 5.0 | 1.5 | 215.9 | 3.1 | C4 H24 N19 O9 Br2 |

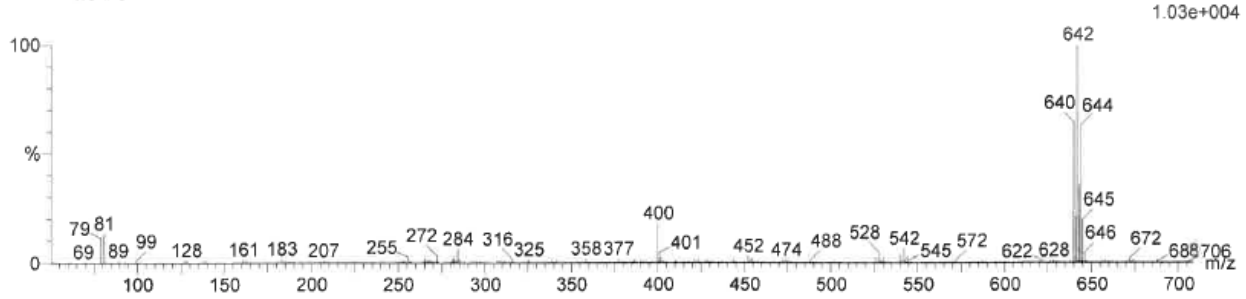
**Methyl (*S*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (7b)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1562 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Br: 2-2

NFF-34 49 (1.997) Cm (49:50-28:34)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 640.0414 | 640.0420 | -0.6 | -0.9 | 17.5 | 118.0 | 1.4 | C25 H24 N9 O2 Br2 |
| | 640.0393 | 2.1 | 3.3 | 18.5 | 118.1 | 1.5 | C21 H20 N15 Br2 |
| | 640.0406 | 0.8 | 1.2 | 12.5 | 118.1 | 1.5 | C24 H28 N5 O6 Br2 |
| | 640.0393 | 2.1 | 3.3 | 7.5 | 118.3 | 1.7 | C23 H32 N O10 Br2 |
| | 640.0438 | -2.4 | -3.7 | 4.5 | 120.2 | 3.5 | C13 H28 N11 O9 Br2 |
| | 640.0425 | -1.1 | -1.7 | -0.5 | 120.3 | 3.6 | C12 H32 N7 O13 Br2 |
| | 640.0411 | 0.3 | 0.5 | 5.5 | 120.4 | 3.8 | C9 H24 N17 O7 Br2 |
| | 640.0398 | 1.6 | 2.5 | 0.5 | 120.6 | 4.0 | C8 H28 N13 O11 Br2 |

$M-H^-$

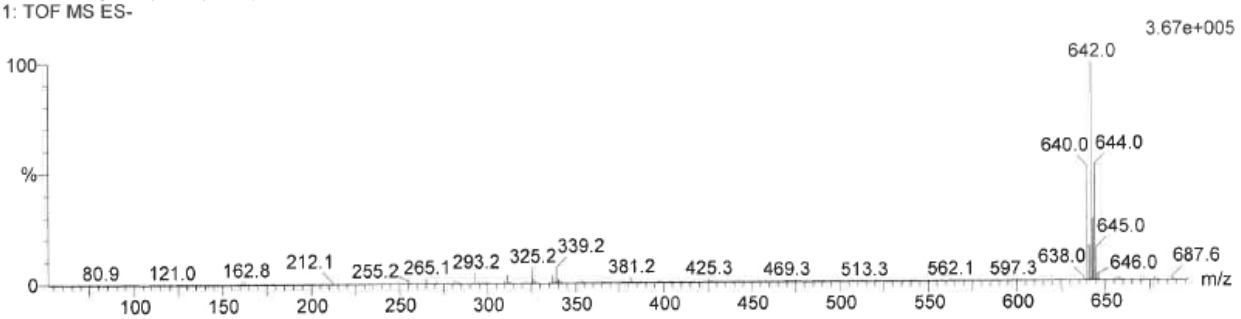
**Methyl (*R*)-(3-(3-((*tert*-butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycinate (7c)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1562 formula(e) evaluated with 9 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Br: 2-2

NFF-40 35 (1.422) Cm (34:38)
1: TOF MS ES-



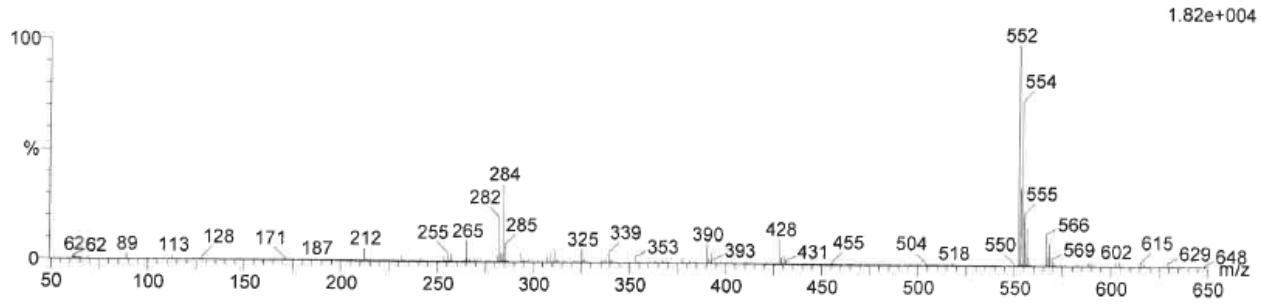

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 5.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 640.0403 | 640.0420 | -1.7 | -2.7 | 17.5 | 322.2 | 0.3 | C25 H24 N9 O2 Br2 |
| | 640.0406 | -0.3 | -0.5 | 12.5 | 323.6 | 1.7 | C24 H28 N5 O6 Br2 |
| | 640.0393 | 1.0 | 1.6 | 18.5 | 325.4 | 3.5 | C21 H20 N15 Br2 |
| | 640.0393 | 1.0 | 1.6 | 7.5 | 325.9 | 4.0 | C23 H32 N O10 Br2 |
| | 640.0379 | 2.4 | 3.7 | 13.5 | 328.3 | 6.4 | C20 H24 N11 O4 Br2 |
| | 640.0425 | -2.2 | -3.4 | -0.5 | 331.5 | 9.6 | C12 H32 N7 O13 Br2 |
| | 640.0411 | -0.8 | -1.2 | 5.5 | 333.3 | 11.4 | C9 H24 N17 O7 Br2 |
| | 640.0398 | 0.5 | 0.8 | 0.5 | 333.8 | 11.9 | C8 H28 N13 O11 Br2 |
| | 640.0371 | 3.2 | 5.0 | 1.5 | 336.7 | 14.7 | C4 H24 N19 O9 Br2 |

**(3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8a)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1562 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-22 56 (2.075) Cm (56:58)
TOF MS ES-



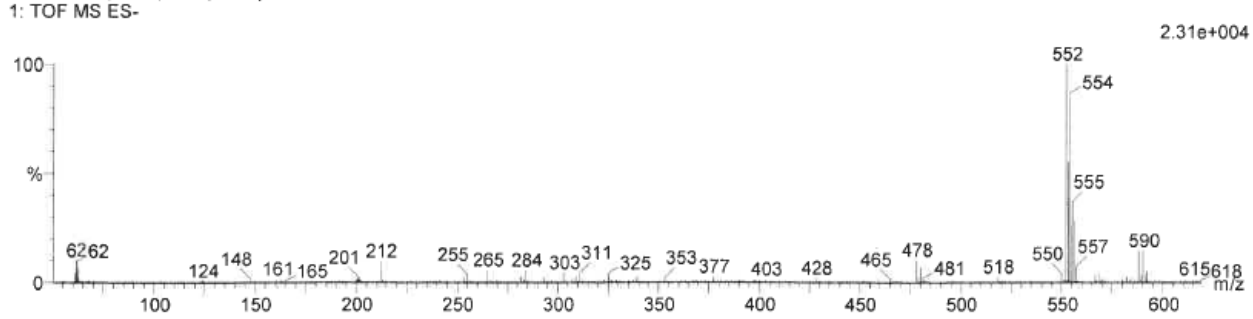

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 552.1411 | 552.1408 | 0.3 | 0.5 | 0.5 | 233.7 | 2.6 | C8 H28 N13 O11 Cl2 |
| | 552.1417 | -0.6 | -1.1 | 12.5 | 233.1 | 1.9 | C24 H28 N5 O6 Cl2 |
| | 552.1403 | 0.8 | 1.4 | 7.5 | 233.0 | 1.9 | C23 H32 N O10 Cl2 |
| | 552.1403 | 0.8 | 1.4 | 18.5 | 232.9 | 1.8 | C21 H20 N15 Cl2 |
| | 552.1422 | -1.1 | -2.0 | 5.5 | 233.7 | 2.6 | C9 H24 N17 O7 Cl2 |
| | 552.1430 | -1.9 | -3.4 | 17.5 | 233.1 | 2.0 | C25 H24 N9 O2 Cl2 |
| | 552.1390 | 2.1 | 3.8 | 13.5 | 232.9 | 1.7 | C20 H24 N11 O4 Cl2 |
| | 552.1435 | -2.4 | -4.3 | -0.5 | 233.8 | 2.7 | C12 H32 N7 O13 Cl2 |

**(*S*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8b)**



**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1562 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-25 38 (1.551) Cm (38:42)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 552.1412 | 552.1430 | -1.8 | -3.3 | 17.5 | 202.0 | 1.4 | C25 H24 N9 O2 Cl2 |
| | 552.1417 | -0.5 | -0.9 | 12.5 | 202.2 | 1.6 | C24 H28 N5 O6 Cl2 |
| | 552.1403 | 0.9 | 1.6 | 18.5 | 202.3 | 1.7 | C21 H20 N15 Cl2 |
| | 552.1403 | 0.9 | 1.6 | 7.5 | 202.5 | 1.9 | C23 H32 N O10 Cl2 |
| | 552.1390 | 2.2 | 4.0 | 13.5 | 202.6 | 2.0 | C20 H24 N11 O4 Cl2 |
| | 552.1435 | -2.3 | -4.2 | -0.5 | 204.2 | 3.6 | C12 H32 N7 O13 Cl2 |
| | 552.1422 | -1.0 | -1.8 | 5.5 | 204.3 | 3.7 | C9 H24 N17 O7 Cl2 |
| | 552.1408 | 0.4 | 0.7 | 0.5 | 204.4 | 3.8 | C8 H28 N13 O11 Cl2 |

M-H⁻

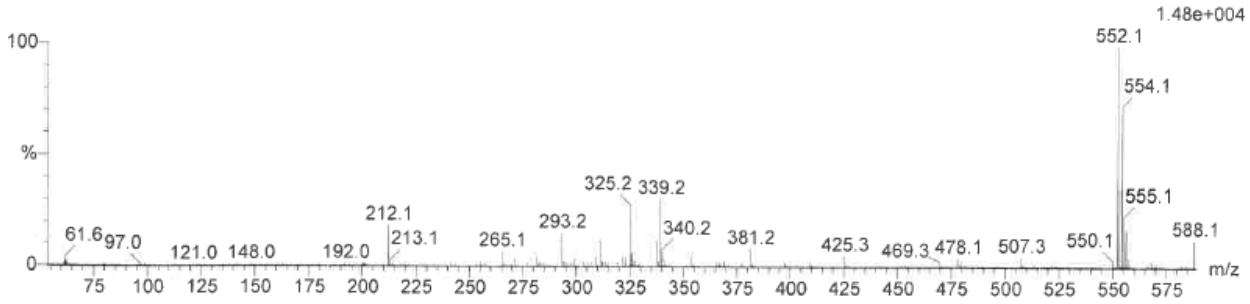
**(*R*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (8c)**

Elemental Composition Report



**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1562 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NFF-41 33 (1.348) Cm (31:33)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 5.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 552.1414 | 552.1430 | -1.6 | -2.9 | 17.5 | 169.5 | 0.5 | C25 H24 N9 O2 Cl2 |
| | 552.1417 | -0.3 | -0.5 | 12.5 | 170.9 | 1.9 | C24 H28 N5 O6 Cl2 ✓M-H⁻ |
| | 552.1403 | 1.1 | 2.0 | 18.5 | 171.2 | 2.2 | C21 H20 N15 Cl2 |
| | 552.1403 | 1.1 | 2.0 | 7.5 | 171.9 | 2.9 | C23 H32 N O10 Cl2 |
| | 552.1390 | 2.4 | 4.3 | 13.5 | 172.3 | 3.2 | C20 H24 N11 O4 Cl2 |
| | 552.1435 | -2.1 | -3.8 | -0.5 | 175.9 | 6.9 | C12 H32 N7 O13 Cl2 |
| | 552.1422 | -0.8 | -1.4 | 5.5 | 176.2 | 7.2 | C9 H24 N17 O7 Cl2 |
| | 552.1408 | 0.6 | 1.1 | 0.5 | 176.5 | 7.5 | C8 H28 N13 O11 Cl2 |

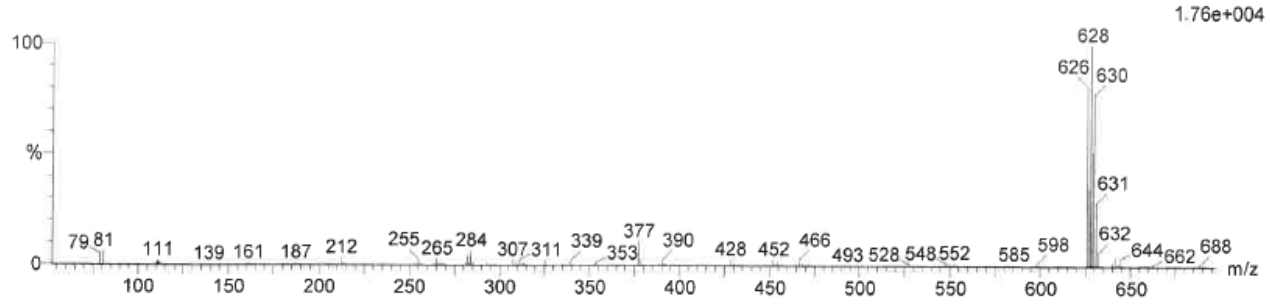
**(3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9a)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1482 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Br: 2-2

NFF-30 40 (1.625) Cm (38:40)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 626.0255 | 626.0255 | 0.0 | 0.0 | 5.5 | 147.7 | 2.7 | C8 H22 N17 O7 Br2 |
| | 626.0250 | 0.5 | 0.8 | 12.5 | 146.7 | 1.7 | C23 H26 N5 O6 Br2 |
| | 626.0263 | -0.8 | -1.3 | 17.5 | 146.6 | 1.6 | C24 H22 N9 O2 Br2 |
| | 626.0268 | -1.3 | -2.1 | -0.5 | 147.6 | 2.6 | C11 H30 N7 O13 Br2 |
| | 626.0241 | 1.4 | 2.2 | 0.5 | 147.8 | 2.8 | C7 H26 N13 O11 Br2 |
| | 626.0236 | 1.9 | 3.0 | 7.5 | 146.8 | 1.8 | C22 H30 N O10 Br2 |
| | 626.0236 | 1.9 | 3.0 | 18.5 | 146.7 | 1.7 | C20 H18 N15 Br2 |
| | 626.0282 | -2.7 | -4.3 | 4.5 | 147.6 | 2.6 | C12 H26 N11 O9 Br2 |

$M-H^-$

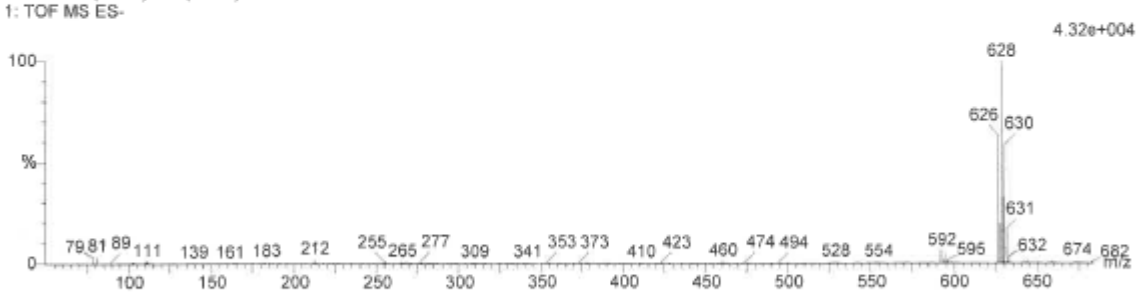
**(*S*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9b)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1482 formula(e) evaluated with 21 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Br: 2-2

NFF-38 39 (1.587) Cm (38:39)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 5.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 626.0239 | 626.0241 | -0.2 | -0.3 | 0.5 | 162.5 | 3.2 | C7 H26 N13 O11 Br2 |
| | 626.0241 | -0.2 | -0.3 | 6.0 | 162.5 | 3.2 | C6 H20 N20 O6 Br2 |
| | 626.0236 | 0.3 | 0.5 | 13.0 | 162.3 | 3.0 | C21 H24 N8 O5 Br2 |
| | 626.0236 | 0.3 | 0.5 | 7.5 | 162.4 | 3.0 | C22 H30 N O10 Br2 |
| | 626.0236 | 0.3 | 0.5 | 18.5 | 162.3 | 3.0 | C20 H18 N15 Br2 |
| | 626.0245 | -0.6 | -1.0 | 25.0 | 162.2 | 2.8 | C37 H24 Br2 |
| | 626.0250 | -1.1 | -1.8 | 12.5 | 162.4 | 3.0 | C23 H26 N5 O6 Br2 |
| | 626.0250 | -1.1 | -1.8 | 18.0 | 162.4 | 3.0 | C22 H20 N12 O Br2 |
| | 626.0228 | 1.1 | 1.8 | 1.0 | 162.5 | 3.1 | C5 H24 N16 O10 Br2 |
| | 626.0223 | 1.6 | 2.6 | 8.0 | 162.3 | 2.9 | C20 H28 N4 O9 Br2 |
| | 626.0255 | -1.6 | -2.6 | 0.0 | 162.6 | 3.3 | C9 H28 N10 O12 Br2 |
| | 626.0255 | -1.6 | -2.6 | 5.5 | 162.6 | 3.2 | C8 H22 N17 O7 Br2 |
| | 626.0223 | 1.6 | 2.6 | 13.5 | 162.3 | 2.9 | C19 H22 N11 O4 Br2 |
| | 626.0263 | -2.4 | -3.8 | 17.5 | 162.4 | 3.1 | C24 H22 N9 O2 Br2 |
| | 626.0215 | 2.4 | 3.8 | 1.5 | 162.4 | 3.0 | C3 H22 N19 O9 Br2 |
| | 626.0263 | -2.4 | -3.8 | 12.0 | 162.5 | 3.1 | C25 H28 N2 O7 Br2 |
| | 626.0210 | 2.9 | 4.6 | 8.5 | 162.2 | 2.9 | C18 H26 N7 O8 Br2 |
| | 626.0210 | 2.9 | 4.6 | 14.0 | 162.2 | 2.8 | C17 H20 N14 O3 Br2 |
| | 626.0268 | -2.9 | -4.6 | 5.0 | 162.7 | 3.3 | C10 H24 N14 O8 Br2 |
| | 626.0268 | -2.9 | -4.6 | -0.5 | 162.7 | 3.3 | C11 H30 N7 O13 Br2 |
| | 626.0210 | 2.9 | 4.6 | 3.0 | 162.2 | 2.9 | C19 H32 O13 Br2 |

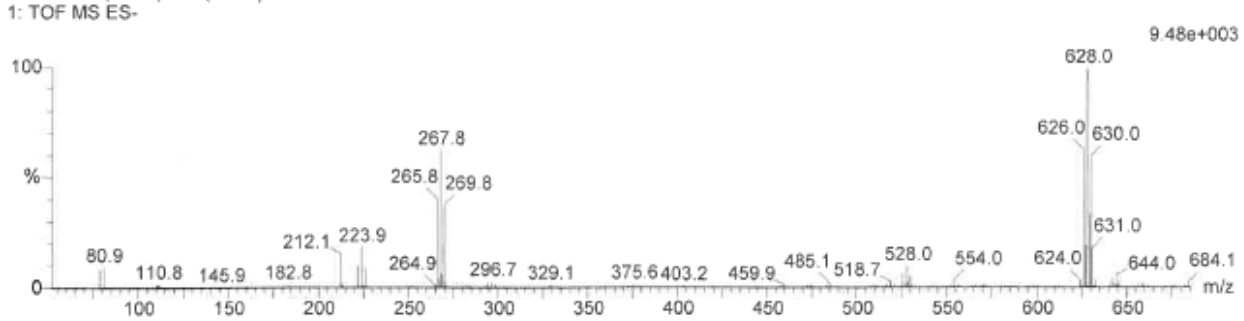
**(*R*)-(3-(3-((*tert*-Butoxycarbonyl)amino)pyrrolidin-1-yl)-4-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)benzoyl)glycine (9c)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1482 formula(e) evaluated with 21 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Br: 2-2

NFF-46 27 (1.108) Cm (25:27)
1: TOF MS ES-



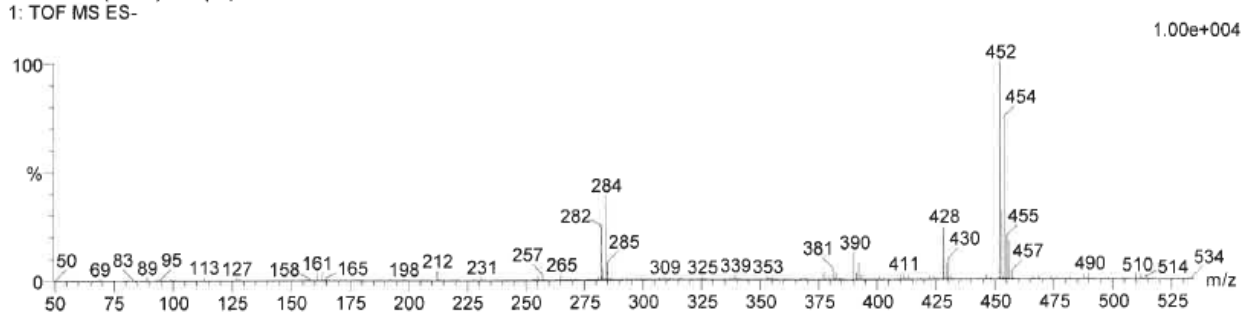

| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 5.0 | 50.0 | | | |
| 626.0252 | 626.0250 | 0.2 | 0.3 | 18.0 | 129.7 | 2.4 | C22 H20 N12 O Br2 |
| | 626.0250 | 0.2 | 0.3 | 12.5 | 129.9 | 2.5 | C23 H26 N5 O6 Br2 ✓M-H⁻ |
| | 626.0255 | -0.3 | -0.5 | 0.0 | 132.5 | 5.1 | C9 H28 N10 O12 Br2 |
| | 626.0255 | -0.3 | -0.5 | 5.5 | 132.4 | 5.1 | C8 H22 N17 O7 Br2 |
| | 626.0245 | 0.7 | 1.1 | 25.0 | 129.5 | 2.1 | C37 H24 Br2 |
| | 626.0263 | -1.1 | -1.8 | 17.5 | 129.9 | 2.5 | C24 H22 N9 O2 Br2 |
| | 626.0241 | 1.1 | 1.8 | 0.5 | 132.5 | 5.2 | C7 H26 N13 O11 Br2 |
| | 626.0241 | 1.1 | 1.8 | 6.0 | 132.5 | 5.2 | C6 H20 N20 O6 Br2 |
| | 626.0263 | -1.1 | -1.8 | 12.0 | 130.0 | 2.7 | C25 H28 N2 O7 Br2 |
| | 626.0236 | 1.6 | 2.6 | 13.0 | 129.8 | 2.4 | C21 H24 N8 O5 Br2 |
| | 626.0268 | -1.6 | -2.6 | -0.5 | 132.5 | 5.1 | C11 H30 N7 O13 Br2 |
| | 626.0268 | -1.6 | -2.6 | 5.0 | 132.4 | 5.0 | C10 H24 N14 O8 Br2 |
| | 626.0236 | 1.6 | 2.6 | 18.5 | 129.7 | 2.3 | C20 H18 N15 Br2 |
| | 626.0236 | 1.6 | 2.6 | 7.5 | 129.9 | 2.6 | C22 H30 N O10 Br2 |
| | 626.0228 | 2.4 | 3.8 | 1.0 | 132.7 | 5.3 | C5 H24 N16 O10 Br2 |
| | 626.0277 | -2.5 | -4.0 | 17.0 | 130.0 | 2.7 | C26 H24 N6 O3 Br2 |
| | 626.0223 | 2.9 | 4.6 | 8.0 | 129.9 | 2.5 | C20 H28 N4 O9 Br2 |
| | 626.0223 | 2.9 | 4.6 | 13.5 | 129.8 | 2.4 | C19 H22 N11 O4 Br2 |
| | 626.0282 | -3.0 | -4.8 | -1.0 | 132.5 | 5.2 | C13 H32 N4 O14 Br2 |
| | 626.0282 | -3.0 | -4.8 | 10.0 | 132.3 | 4.9 | C11 H20 N18 O4 Br2 |
| | 626.0282 | -3.0 | -4.8 | 4.5 | 132.4 | 5.1 | C12 H26 N11 O9 Br2 |

**4-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (10a)**

**emental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
979 formula(e) evaluated with 6 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-23 41 (1.680) Cm (41)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 452.0891 | 452.0892 | -0.1 | -0.2 | 11.5 | 127.3 | 1.4 | C19 H20 N5 O4 Cl2 |
| | 452.0897 | -0.6 | -1.3 | 4.5 | 132.2 | 6.2 | C4 H16 N17 O5 Cl2 |
| | 452.0884 | 0.7 | 1.5 | -0.5 | 132.5 | 6.5 | C3 H20 N13 O9 Cl2 |
| | 452.0879 | 1.2 | 2.7 | 6.5 | 128.1 | 2.1 | C18 H24 N O8 Cl2 |
| | 452.0906 | -1.5 | -3.3 | 16.5 | 126.4 | 0.5 | C20 H16 N9 Cl2 |
| | 452.0911 | -2.0 | -4.4 | -1.5 | 131.7 | 5.8 | C7 H24 N7 O11 Cl2 |

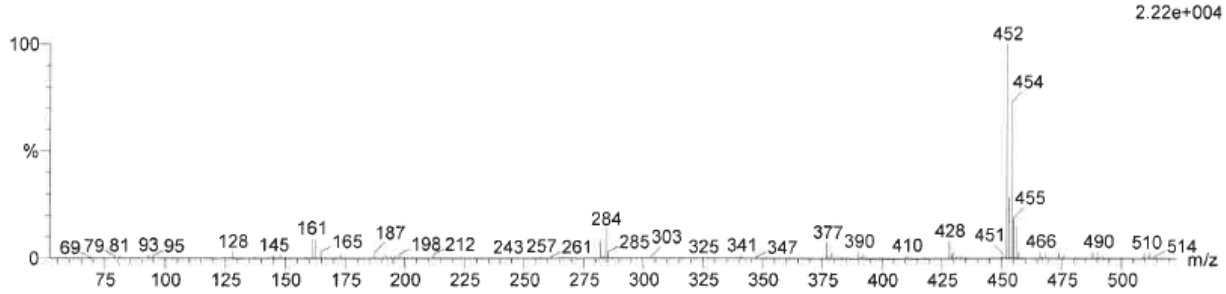
M-H⁻

**(*S*)-1-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (10b)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
979 formula(e) evaluated with 5 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-33 46 (1.886) Cm (45:47)
1: TOF MS ES-




| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| 452.0881 | 452.0892 | -1.1 | -2.4 | 11.5 | 192.9 | 0.3 | C19 H20 N5 O4 Cl2 |
| | 452.0879 | 0.2 | 0.4 | 6.5 | 194.2 | 1.7 | C18 H24 N O8 Cl2 |
| | 452.0865 | 1.6 | 3.5 | 12.5 | 195.1 | 2.5 | C15 H16 N11 O2 Cl2 |
| | 452.0897 | -1.6 | -3.5 | 4.5 | 199.2 | 6.7 | C4 H16 N17 O5 Cl2 |
| | 452.0884 | -0.3 | -0.7 | -0.5 | 199.8 | 7.3 | C3 H20 N13 O9 Cl2 |

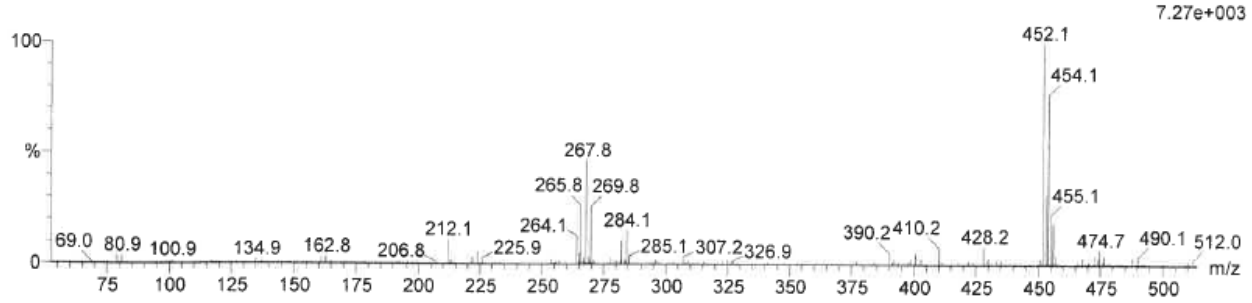
$M-H^-$

**(*R*)-1-(5-((Carboxymethyl)carbamoyl)-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (10c)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
979 formula(e) evaluated with 6 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NFF-47 42 (1.716) Cm (41:42)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 5.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 452.0898 | 452.0906 | -0.8 | -1.8 | 16.5 | 156.9 | 0.6 | C20 H16 N9 Cl2 |
| | 452.0892 | 0.6 | 1.3 | 11.5 | 157.5 | 1.2 | C19 H20 N5 O4 Cl2 |
| | 452.0879 | 1.9 | 4.2 | 6.5 | 158.0 | 1.8 | C18 H24 N O8 Cl2 |
| | 452.0911 | -1.3 | -2.9 | -1.5 | 161.7 | 5.4 | C7 H24 N7 O11 Cl2 |
| | 452.0897 | 0.1 | 0.2 | 4.5 | 161.9 | 5.6 | C4 H16 N17 O5 Cl2 |
| | 452.0884 | 1.4 | 3.1 | -0.5 | 162.1 | 5.8 | C3 H20 N13 O9 Cl2 |

M-H⁻

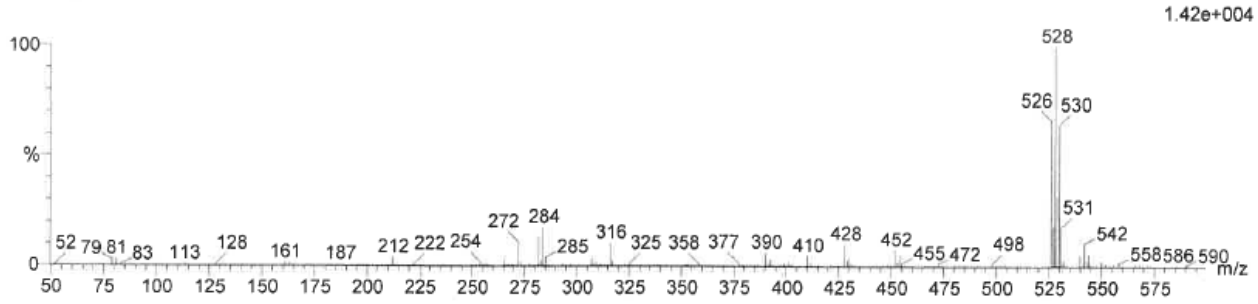
**4-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (11a)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
905 formula(e) evaluated with 6 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Br: 2-2

NFF-32 40 (1.627) Cm (38:40)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 525.9727 | 525.9739 | -1.2 | -2.3 | 16.5 | 172.1 | 1.1 | C19 H14 N9 Br2 |
| | 525.9726 | 0.1 | 0.2 | 11.5 | 172.2 | 1.2 | C18 H18 N5 O4 Br2 |
| | 525.9712 | 1.5 | 2.9 | 6.5 | 172.3 | 1.3 | C17 H22 N O8 Br2 |
| | 525.9744 | -1.7 | -3.2 | -1.5 | 174.6 | 3.6 | C6 H22 N7 O11 Br2 |
| | 525.9731 | -0.4 | -0.8 | 4.5 | 174.9 | 3.8 | C3 H14 N17 O5 Br2 |
| | 525.9717 | 1.0 | 1.9 | -0.5 | 175.0 | 4.0 | C2 H18 N13 O9 Br2 |

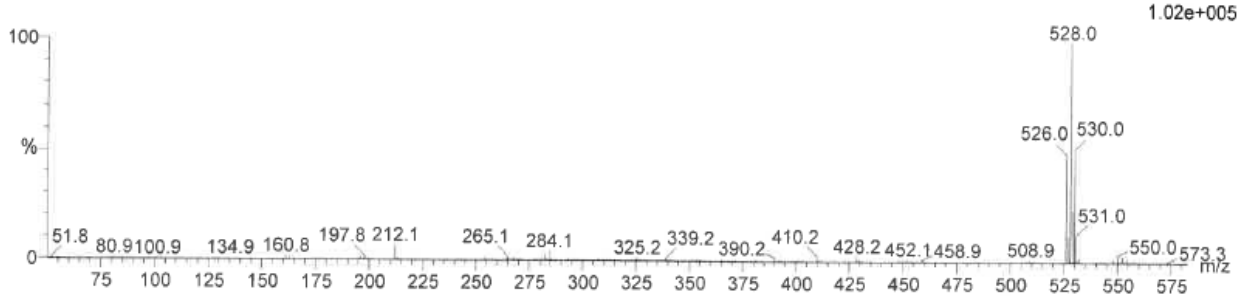
**(*S*)-1-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (11b)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
905 formula(e) evaluated with 11 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Br: 2-2

NFF-43 29 (1.182) Cm (28:32)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 525.9726 | 525.9726 | 0.0 | 0.0 | 11.5 | 255.0 | 0.1 | C18 H18 N5 O4 Br2 |
| | 525.9739 | -1.3 | -2.5 | 16.5 | 257.9 | 3.0 | C19 H14 N9 Br2 |
| | 525.9712 | 1.4 | 2.7 | 6.5 | 259.6 | 4.7 | C17 H22 N O8 Br2 |
| | 525.9699 | 2.7 | 5.1 | 12.5 | 261.2 | 6.3 | C14 H14 N11 O2 Br2 |
| | 525.9766 | -4.0 | -7.6 | 15.5 | 261.4 | 6.4 | C23 H18 N3 O2 Br2 |
| | 525.9685 | 4.1 | 7.8 | 7.5 | 263.7 | 8.8 | C13 H18 N7 O6 Br2 |
| | 525.9771 | -4.5 | -8.6 | 8.5 | 266.2 | 11.3 | C8 H14 N15 O3 Br2 |
| | 525.9744 | -1.8 | -3.4 | -1.5 | 266.6 | 11.7 | C6 H22 N7 O11 Br2 |
| | 525.9757 | -3.1 | -5.9 | 3.5 | 266.6 | 11.7 | C7 H18 N11 O7 Br2 |
| | 525.9731 | -0.5 | -1.0 | 4.5 | 269.5 | 14.6 | C3 H14 N17 O5 Br2 |
| | 525.9717 | 0.9 | 1.7 | -0.5 | 270.2 | 15.3 | C2 H18 N13 O9 Br2 |

**(*R*)-1-(5-((Carboxymethyl)carbamoyl)-2-(4,5-dibromo-1*H*-pyrrole-2-carboxamido)phenyl)pyrrolidin-3-aminium chloride (11c)**

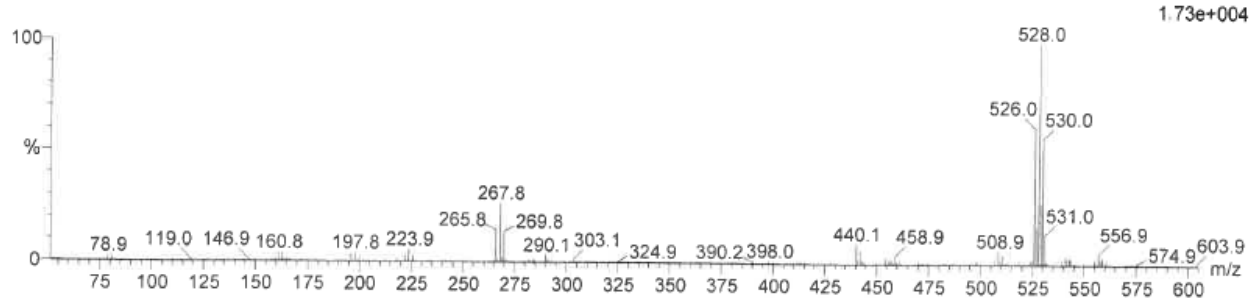
Elemental Composition Report



**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
905 formula(e) evaluated with 11 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Br: 2-2

NFF-48 55 (2.238) Cm (54:56)
1: TOF MS ES-



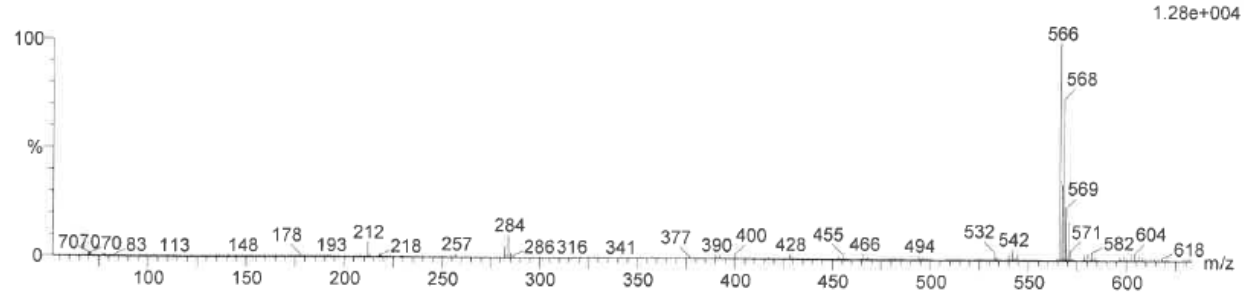

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 525.9727 | 525.9712 | 1.5 | 2.9 | 6.5 | 138.2 | 1.2 | C17 H22 N O8 Br2 |
| | 525.9726 | 0.1 | 0.2 | 11.5 | 138.7 | 1.7 | C18 H18 N5 O4 Br2 |
| | 525.9699 | 2.8 | 5.3 | 12.5 | 138.9 | 1.9 | C14 H14 N11 O2 Br2 |
| | 525.9685 | 4.2 | 8.0 | 7.5 | 138.9 | 1.9 | C13 H18 N7 O6 Br2 |
| | 525.9739 | -1.2 | -2.3 | 16.5 | 138.9 | 1.9 | C19 H14 N9 Br2 |
| | 525.9766 | -3.9 | -7.4 | 15.5 | 139.7 | 2.7 | C23 H18 N3 O2 Br2 |
| | 525.9744 | -1.7 | -3.2 | -1.5 | 142.5 | 5.5 | C6 H22 N7 O11 Br2 |
| | 525.9757 | -3.0 | -5.7 | 3.5 | 142.8 | 5.9 | C7 H18 N11 O7 Br2 |
| | 525.9771 | -4.4 | -8.4 | 8.5 | 143.0 | 6.0 | C8 H14 N15 O3 Br2 |
| | 525.9731 | -0.4 | -0.8 | 4.5 | 144.0 | 7.0 | C3 H14 N17 O5 Br2 |
| | 525.9717 | 1.0 | 1.9 | -0.5 | 144.2 | 7.2 | C2 H18 N13 O9 Br2 |

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-((2-hydrazineyl-2-oxoethyl)carbamoyl)phenyl)piperazine-1-carboxylate (12)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1646 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-35 29 (1.184) Cm (27:29)
1: TOF MS ES-



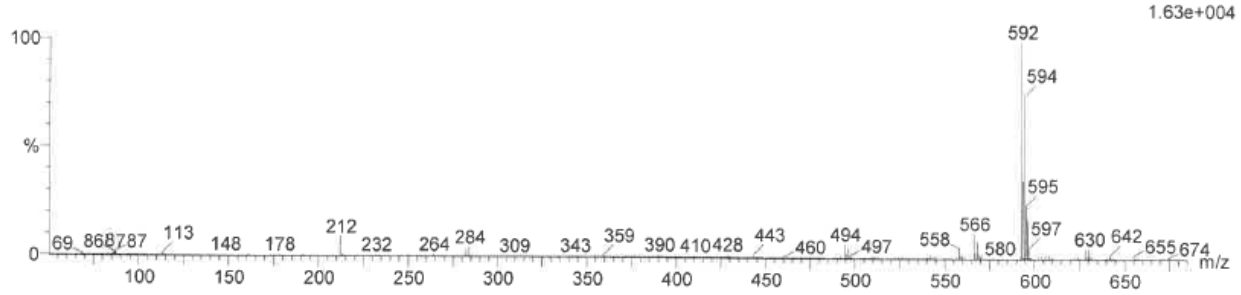

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 566.1682 | 566.1685 | -0.3 | -0.5 | 12.5 | 152.1 | 2.0 | C24 H30 N7 O5 Cl2 |
| | 566.1677 | 0.5 | 0.9 | 0.5 | 158.1 | 8.0 | C8 H30 N15 O10 Cl2 |
| | 566.1691 | -0.9 | -1.6 | 5.5 | 157.8 | 7.7 | C9 H26 N19 O6 Cl2 |
| | 566.1672 | 1.0 | 1.8 | 7.5 | 153.1 | 3.0 | C23 H34 N3 O9 Cl2 |
| | 566.1699 | -1.7 | -3.0 | 17.5 | 150.9 | 0.8 | C25 H26 N11 O Cl2 |
| | 566.1704 | -2.2 | -3.9 | -0.5 | 157.6 | 7.5 | C12 H34 N9 O12 Cl2 |
| | 566.1659 | 2.3 | 4.1 | 13.5 | 153.5 | 3.3 | C20 H26 N13 O3 Cl2 |
| | 566.1654 | 2.8 | 4.9 | 20.5 | 151.2 | 1.1 | C35 H30 N O2 Cl2 |

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(((5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)carbamoyl)phenyl)piperazine-1-carboxylate (13)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1798 formula(e) evaluated with 9 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-80 H: 0-110 N: 0-20 O: 0-20 Cl: 2-2
NFF-37 39 (1.587) Cm (37:40)
1: TOF MS ES-



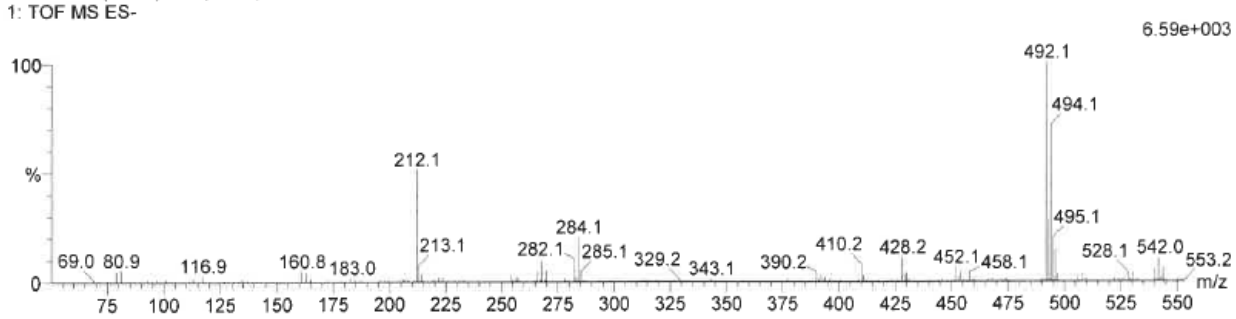

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 10.0 | 5.0 | 100.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 592.1474 | 592.1478 | -0.4 | -0.7 | 14.5 | 186.2 | 1.9 | C25 H28 N7 O6 Cl2 ✓ M-H⁻ |
| | 592.1470 | 0.4 | 0.7 | 2.5 | 192.2 | 7.9 | C9 H28 N15 O11 Cl2 |
| | 592.1483 | -0.9 | -1.5 | 7.5 | 191.9 | 7.6 | C10 H24 N19 O7 Cl2 |
| | 592.1465 | 0.9 | 1.5 | 20.5 | 186.6 | 2.3 | C22 H20 N17 Cl2 |
| | 592.1465 | 0.9 | 1.5 | 9.5 | 187.4 | 3.0 | C24 H32 N3 O10 Cl2 |
| | 592.1491 | -1.7 | -2.9 | 19.5 | 185.0 | 0.7 | C26 H24 N11 O2 Cl2 |
| | 592.1497 | -2.3 | -3.9 | 1.5 | 191.6 | 7.3 | C13 H32 N9 O13 Cl2 |
| | 592.1451 | 2.3 | 3.9 | 15.5 | 187.7 | 3.4 | C21 H24 N13 O4 Cl2 |
| | 592.1446 | 2.8 | 4.7 | 22.5 | 186.0 | 1.7 | C36 H28 N O3 Cl2 |

**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(((5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)carbamoyl)phenyl)piperazin-1-ium chloride (14)**



**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1209 formula(e) evaluated with 7 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NFF-49 25 (1.015) Cm (23:26)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 5.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 492.0959 | 492.0959 | 0.0 | 0.0 | 6.5 | 174.3 | 9.3 | C5 H16 N19 O5 Cl2 |
| | 492.0954 | 0.5 | 1.0 | 13.5 | 167.3 | 2.4 | C20 H20 N7 O4 Cl2 |
| | 492.0967 | -0.8 | -1.6 | 18.5 | 165.9 | 1.0 | C21 H16 N11 Cl2 |
| | 492.0972 | -1.3 | -2.6 | 0.5 | 174.6 | 9.6 | C8 H24 N9 O11 Cl2 |
| | 492.0945 | 1.4 | 2.8 | 1.5 | 174.3 | 9.4 | C4 H20 N15 O9 Cl2 |
| | 492.0940 | 1.9 | 3.9 | 8.5 | 168.6 | 3.7 | C19 H24 N3 O8 Cl2 |
| | 492.0981 | -2.2 | -4.5 | 12.5 | 165.6 | 0.7 | C24 H24 N O6 Cl2 |

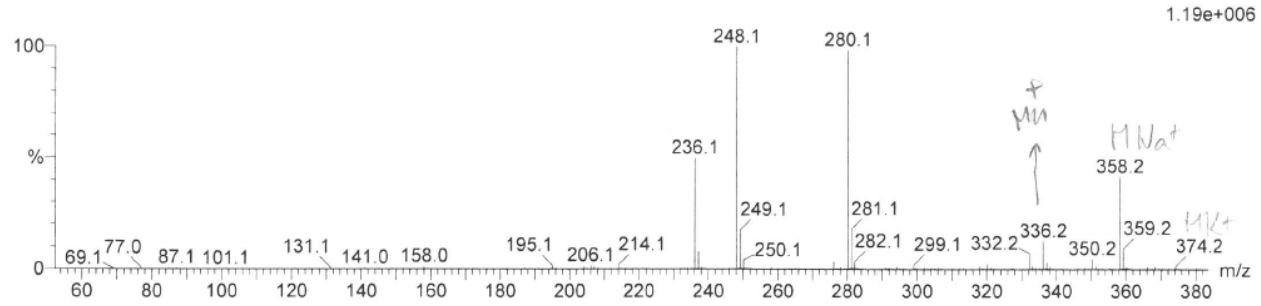
$M-H^-$

## *tert*-Butyl 4-(2-amino-5-(methoxycarbonyl)phenyl)piperazine-1-carboxylate (16a)

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
771 formula(e) evaluated with 6 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20
NBH-51 19 (0.775) Cm (19:22)
1: TOF MS ES+



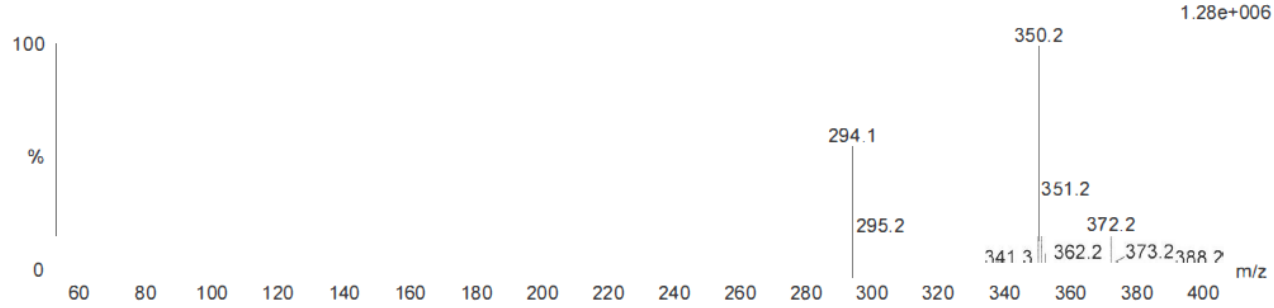

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 336.1924 | 336.1923 | 0.1 | 0.3 | 6.5 | 491.5 | 0.9 | C17 H26 N3 O4 |
| | 336.1937 | -1.3 | -3.9 | 11.5 | 491.6 | 1.0 | C18 H22 N7 |
| | 336.1896 | 2.8 | 8.3 | 7.5 | 492.6 | 2.0 | C13 H22 N9 O2 |
| | 336.1955 | -3.1 | -9.2 | -1.5 | 493.6 | 3.0 | C6 H26 N9 O7 |
| | 336.1928 | -0.4 | -1.2 | -0.5 | 494.6 | 4.0 | C2 H22 N15 O5 |
| | 336.1942 | -1.8 | -5.4 | 4.5 | 495.1 | 4.5 | C3 H18 N19 O |

**Methyl (*S*)-4-amino-3-(3-((*tert*-butoxycarbonyl)amino)piperidin-1-yl)benzoate (16c)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
843 formula(e) evaluated with 6 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20
NBH-3 10 (0.406) Cm (7 10)
1: TOF MS ES+




| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula | | | |
| 350.2072 | 350.2093 | -2.1 | -6.0 | 11.5 | 617.6 | 0.9 | C19 | H24 | N7 | O4 |
| | 350.2080 | -0.8 | -2.3 | 6.5 | 617.7 | 0.9 | C18 | H28 | N3 | O4 |
| | 350.2053 | 1.9 | 5.4 | 7.5 | 619.1 | 2.4 | C14 | H24 | N9 | O2 |
| | 350.2040 | 3.2 | 9.1 | 2.5 | 619.3 | 2.6 | C13 | H28 | N5 | O6 |
| | 350.2085 | -1.3 | -3.7 | -0.5 | 621.8 | 5.1 | C3 | H24 | N15 | O5 |
| | 350.2098 | -2.6 | -7.4 | 4.5 | 622.1 | 5.3 | C4 | H20 | N19 | O |

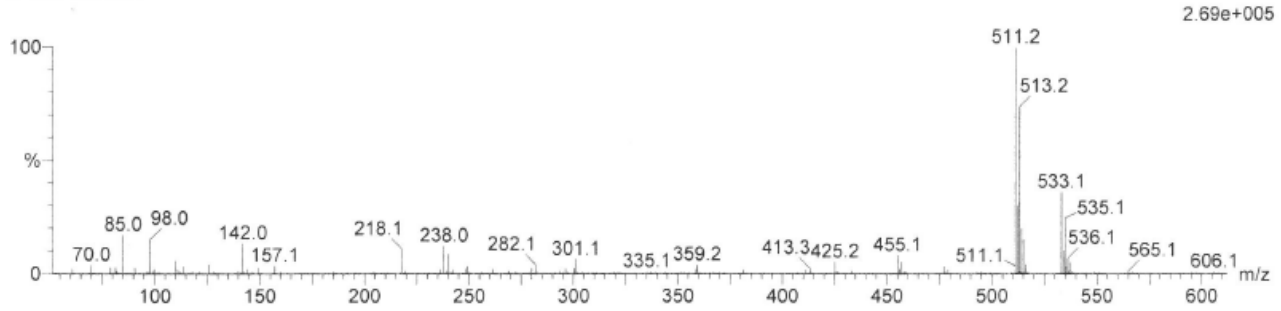
$MH^+$

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperazine-1-carboxylate (17a)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1346 formula(e) evaluated with 14 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-53 14 (0.573) Cm (12:15-2:7)
1: TOF MS ES+



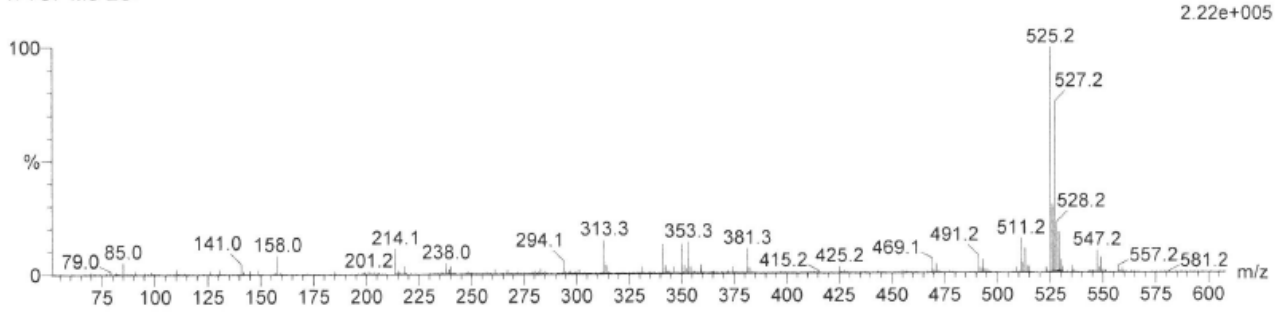

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 511.1524 | 511.1528 | -0.4 | -0.8 | 15.5 | 333.4 | 0.8 | C24 H25 N8 O Cl2 |
| | 511.1515 | 0.9 | 1.8 | 10.5 | 333.5 | 0.9 | C23 H29 N4 O5 Cl2 |
| | 511.1555 | -3.1 | -6.1 | 14.5 | 335.4 | 2.8 | C28 H29 N2 O3 Cl2 |
| | 511.1502 | 2.2 | 4.3 | 5.5 | 335.9 | 3.2 | C22 H33 O9 Cl2 |
| | 511.1488 | 3.6 | 7.0 | 11.5 | 338.2 | 5.6 | C19 H25 N10 O3 Cl2 |
| | 511.1475 | 4.9 | 9.6 | 6.5 | 340.2 | 7.5 | C18 H29 N6 O7 Cl2 |
| | 511.1574 | -5.0 | -9.8 | 1.5 | 341.0 | 8.4 | C16 H33 N4 O10 Cl2 |
| | 511.1547 | -2.3 | -4.5 | 2.5 | 341.3 | 8.6 | C12 H29 N10 O8 Cl2 |
| | 511.1574 | -5.0 | -9.8 | 12.5 | 341.3 | 8.7 | C14 H21 N18 Cl2 |
| | 511.1560 | -3.6 | -7.0 | 7.5 | 341.5 | 8.8 | C13 H25 N14 O4 Cl2 |
| | 511.1533 | -0.9 | -1.8 | 8.5 | 343.7 | 11.1 | C9 H21 N20 O2 Cl2 |
| | 511.1520 | 0.4 | 0.8 | 3.5 | 344.2 | 11.5 | C8 H25 N16 O6 Cl2 |
| | 511.1507 | 1.7 | 3.3 | -1.5 | 344.5 | 11.9 | C7 H29 N12 O10 Cl2 |
| | 511.1480 | 4.4 | 8.6 | -0.5 | 347.7 | 15.1 | C3 H25 N18 O8 Cl2 |

**Methyl (*S*)-3-(3-((*tert*-butoxycarbonyl)amino)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoate (17c)**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1432 formula(e) evaluated with 14 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-5 14 (0.572) Cm (13:15)
1: TOF MS ES+




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 525.1681 | 525.1712 | -3.1 | -5.9 | 14.5 | 363.0 | 0.9 | C29 H31 N2 O3 Cl2 |
| | 525.1672 | 0.9 | 1.7 | 10.5 | 363.4 | 1.3 | C24 H31 N4 O5 Cl2 ✓ $MH^+$ |
| | 525.1685 | -0.4 | -0.8 | 15.5 | 363.7 | 1.6 | C25 H27 N8 O Cl2 |
| | 525.1658 | 2.3 | 4.4 | 5.5 | 364.7 | 2.7 | C23 H35 O9 Cl2 |
| | 525.1730 | -4.9 | -9.3 | 1.5 | 365.6 | 3.6 | C17 H35 N4 O10 Cl2 |
| | 525.1645 | 3.6 | 6.9 | 11.5 | 366.0 | 3.9 | C20 H27 N10 O3 Cl2 |
| | 525.1730 | -4.9 | -9.3 | 12.5 | 366.4 | 4.4 | C15 H23 N18 Cl2 |
| | 525.1717 | -3.6 | -6.9 | 7.5 | 367.2 | 5.1 | C14 H27 N14 O4 Cl2 |
| | 525.1631 | 5.0 | 9.5 | 6.5 | 367.4 | 5.4 | C19 H31 N6 O7 Cl2 |
| | 525.1703 | -2.2 | -4.2 | 2.5 | 368.0 | 5.9 | C13 H31 N10 O8 Cl2 |
| | 525.1690 | -0.9 | -1.7 | 8.5 | 369.5 | 7.5 | C10 H23 N20 O2 Cl2 |
| | 525.1677 | 0.4 | 0.8 | 3.5 | 370.3 | 8.3 | C9 H27 N16 O6 Cl2 |
| | 525.1663 | 1.8 | 3.4 | -1.5 | 371.0 | 9.0 | C8 H31 N12 O10 Cl2 |
| | 525.1636 | 4.5 | 8.6 | -0.5 | 373.1 | 11.1 | C4 H27 N18 O8 Cl2 |

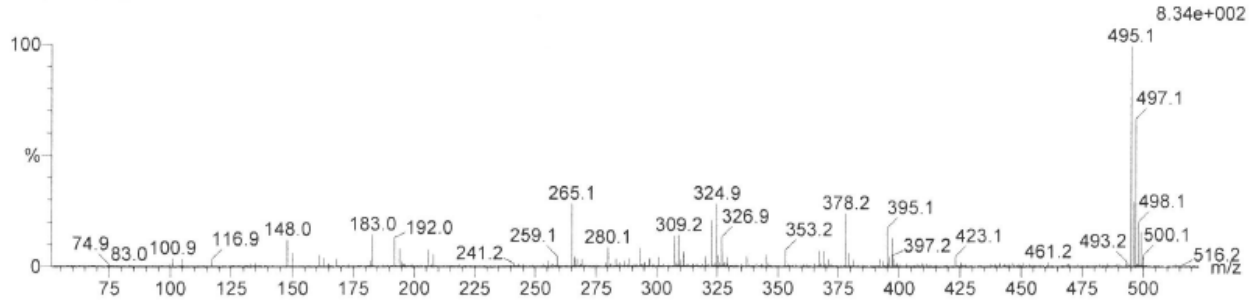
**3-(4-(*tert*-Butoxycarbonyl)piperazin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18a)**

Elemental Composition Report



**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1251 formula(e) evaluated with 13 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-54 NEG 33 (1.347) Cm (32:34-6:18)
1: TOF MS ES-




| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| 495.1206 | 495.1215 | -0.9 | -1.8 | 16.5 | 38.6 | 1.1 | C23 H21 N8 O Cl2 |
| | 495.1202 | 0.4 | 0.8 | 11.5 | 39.0 | 1.5 | C22 H25 N4 O5 Cl2 |
| | 495.1175 | 3.1 | 6.3 | 12.5 | 39.3 | 1.8 | C18 H21 N10 O3 Cl2 |
| | 495.1242 | -3.6 | -7.3 | 15.5 | 39.4 | 2.0 | C27 H25 N2 O3 Cl2 |
| | 495.1189 | 1.7 | 3.4 | 6.5 | 39.9 | 2.5 | C21 H29 O9 Cl2 |
| | 495.1162 | 4.4 | 8.9 | 7.5 | 40.2 | 2.8 | C17 H25 N6 O7 Cl2 |
| | 495.1247 | -4.1 | -8.3 | 8.5 | 43.9 | 6.4 | C12 H21 N14 O4 Cl2 |
| | 495.1220 | -1.4 | -2.8 | 9.5 | 44.0 | 6.6 | C8 H17 N20 O2 Cl2 |
| | 495.1167 | 3.9 | 7.9 | 0.5 | 44.2 | 6.8 | C2 H21 N18 O8 Cl2 |
| | 495.1207 | -0.1 | -0.2 | 4.5 | 44.4 | 6.9 | C7 H21 N16 O6 Cl2 |
| | 495.1234 | -2.8 | -5.7 | 3.5 | 44.4 | 7.0 | C11 H25 N10 O8 Cl2 |
| | 495.1194 | 1.2 | 2.4 | -0.5 | 44.6 | 7.2 | C6 H25 N12 O10 Cl2 |
| | 495.1221 | -1.5 | -3.0 | -1.5 | 44.8 | 7.4 | C10 H29 N6 O12 Cl2 |

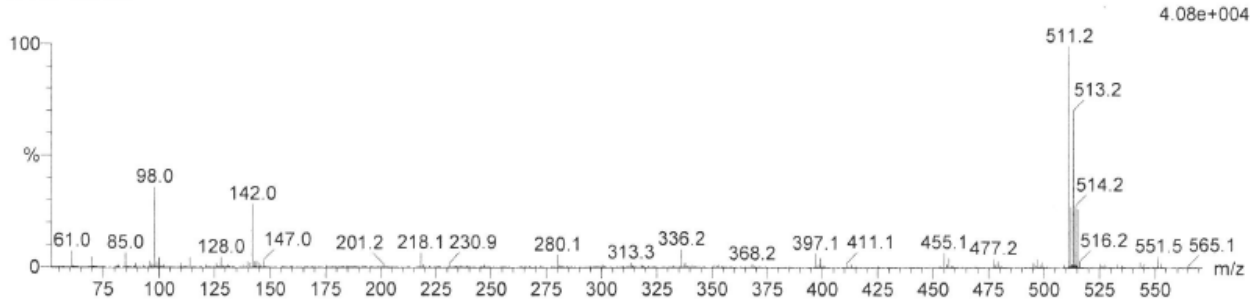
M-H-

**(*S*)-3-(3-((*tert*-Butoxycarbonyl)amino)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18c)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

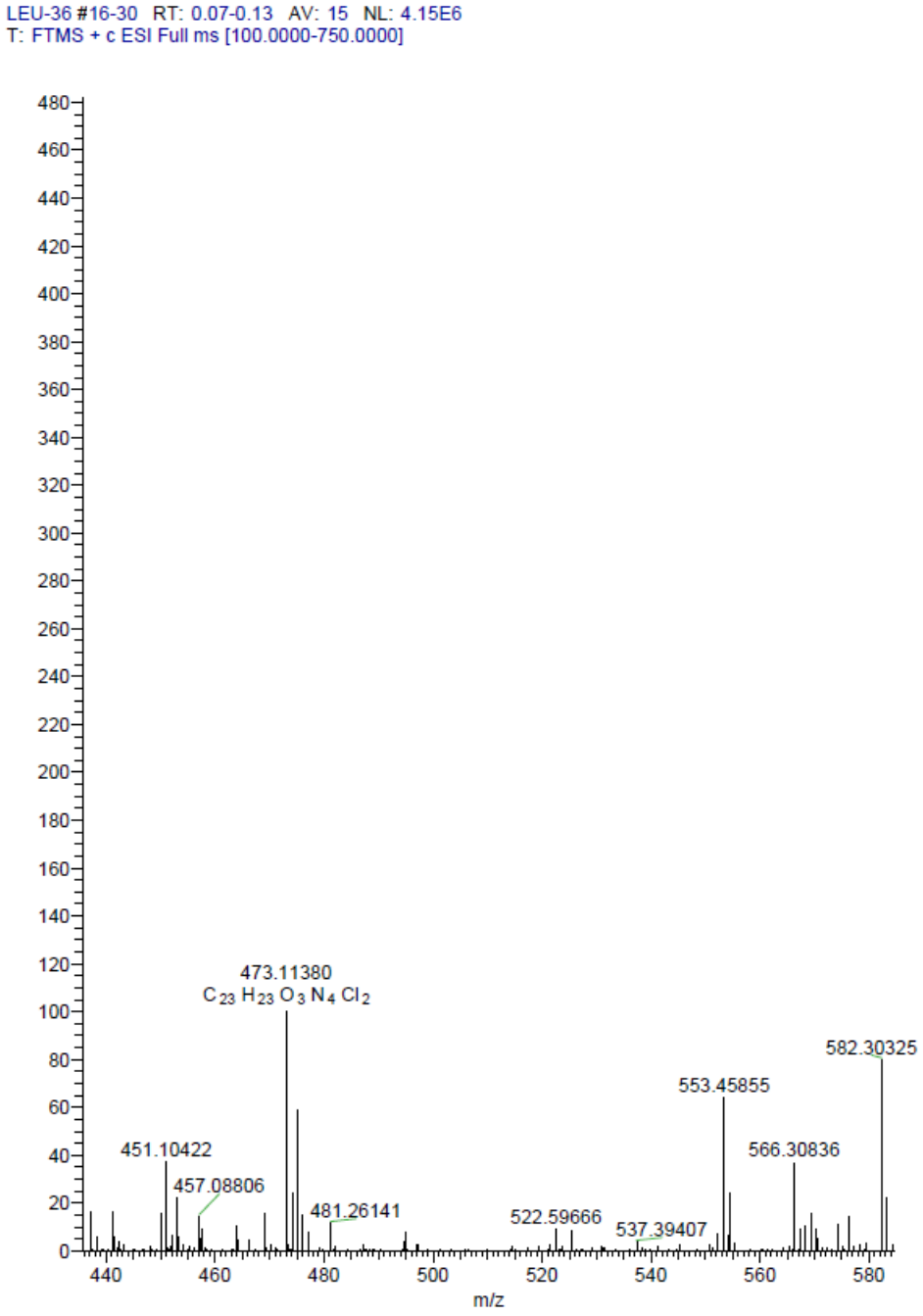
Monoisotopic Mass, Even Electron Ions
1346 formula(e) evaluated with 14 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-6 17 (0.701) Cm (16:17-1:8)
1: TOF MS ES+




| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| 511.1512 | 511.1515 | -0.3 | -0.6 | 10.5 | 216.1 | 0.2 | C23 H29 N4 O5 Cl2 |
| | 511.1502 | 1.0 | 2.0 | 5.5 | 217.9 | 2.0 | C22 H33 O9 Cl2 |
| | 511.1488 | 2.4 | 4.7 | 11.5 | 219.3 | 3.3 | C19 H25 N10 O3 Cl2 |
| | 511.1528 | -1.6 | -3.1 | 15.5 | 219.9 | 4.0 | C24 H25 N8 O Cl2 |
| | 511.1555 | -4.3 | -8.4 | 14.5 | 221.5 | 5.5 | C28 H29 N2 O3 Cl2 |
| | 511.1475 | 3.7 | 7.2 | 6.5 | 221.8 | 5.9 | C18 H29 N6 O7 Cl2 |
| | 511.1461 | 5.1 | 10.0 | 12.5 | 222.8 | 6.9 | C15 H21 N16 O Cl2 |
| | 511.1461 | 5.1 | 10.0 | 1.5 | 223.6 | 7.7 | C17 H33 N2 O11 Cl2 |
| | 511.1560 | -4.8 | -9.4 | 7.5 | 224.1 | 8.1 | C13 H25 N14 O4 Cl2 |
| | 511.1547 | -3.5 | -6.8 | 2.5 | 224.9 | 9.0 | C12 H29 N10 O8 Cl2 |
| | 511.1533 | -2.1 | -4.1 | 8.5 | 225.9 | 9.9 | C9 H21 N20 O2 Cl2 |
| | 511.1520 | -0.8 | -1.6 | 3.5 | 226.6 | 10.7 | C8 H25 N16 O6 Cl2 |
| | 511.1507 | 0.5 | 1.0 | -1.5 | 227.3 | 11.4 | C7 H29 N12 O10 Cl2 |
| | 511.1480 | 3.2 | 6.3 | -0.5 | 229.2 | 13.3 | C3 H25 N18 O8 Cl2 |

$MH^+$

**4-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-3-(4-phenylpiperazin-1-yl)benzoic acid (18h)**

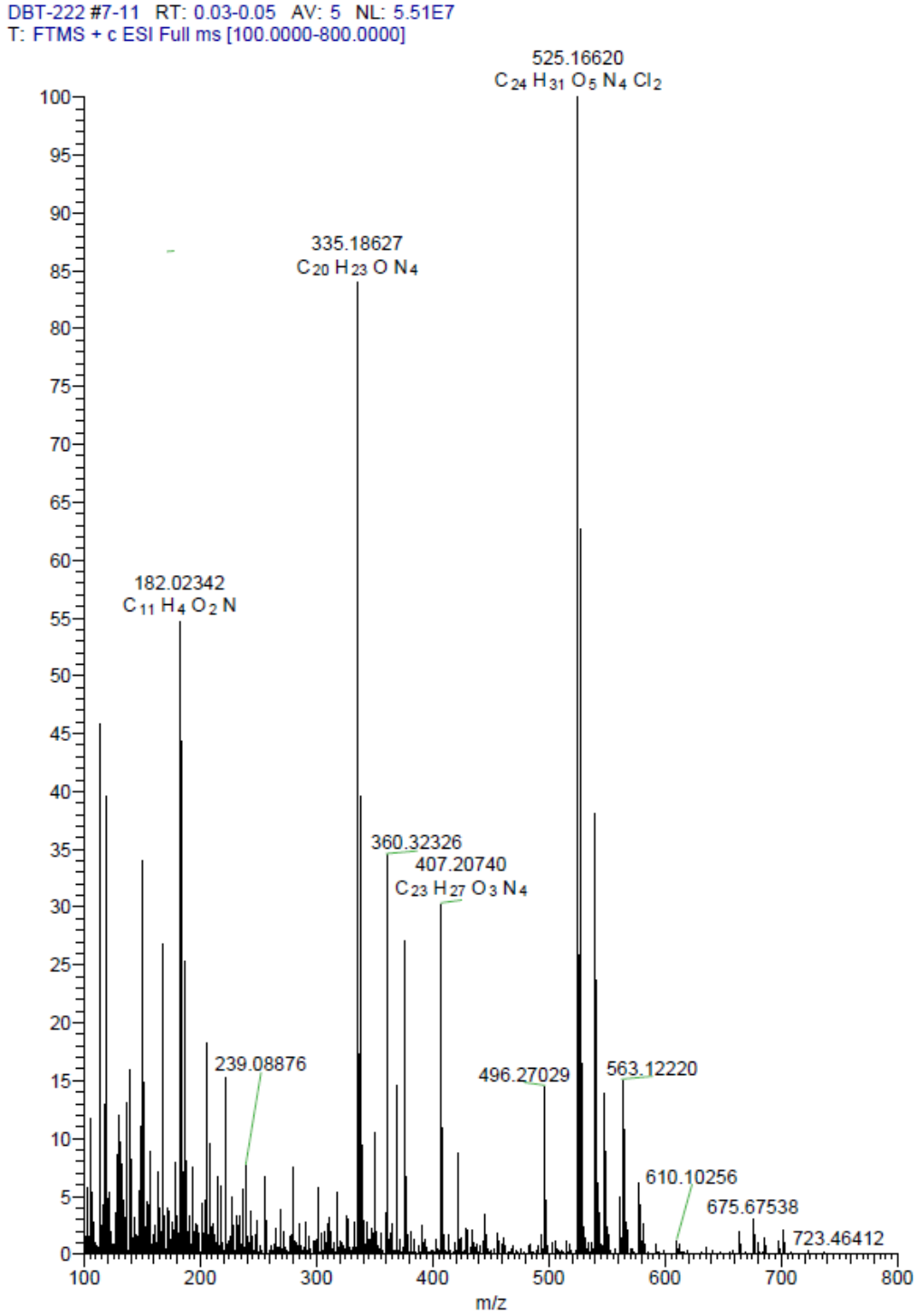



Elemental composition search on mass 473.11380

m/z= 468.11380-478.11380

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 473.11380 | 473.11417 | -0.79 | 13.5 | $C_{23}H_{23}O_3N_4Cl_2$ |

**3-(3-(((*tert*-Butoxycarbonyl)amino)methyl)piperidin-1-yl)-4-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoic acid (18i)**




Elemental composition search on mass 525.16620

m/z= 520.16620-530.16620

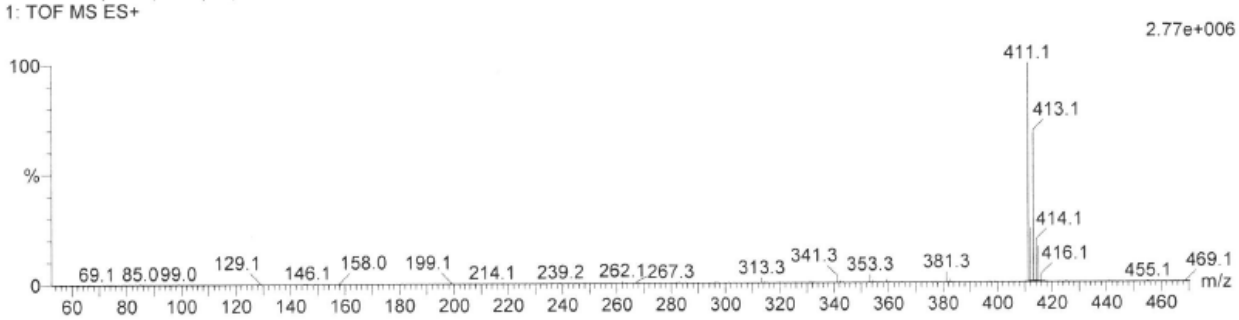
| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 525.16620 | 525.16660 | -0.77 | 10.5 | $C_{24}H_{31}O_5N_4Cl_2$ |

**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperazin-1-ium chloride (19a)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
779 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-56 7 (0.295) Cm (6:8)
1: TOF MS ES+



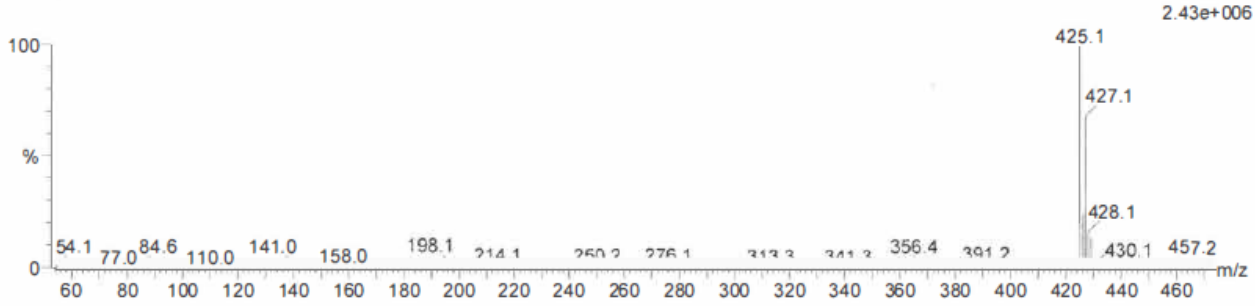

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 411.0998 | 411.1031 | -3.3 | -8.0 | 13.5 | 438.2 | 0.6 | C23 H21 N2 O Cl2 |
| | 411.0991 | 0.7 | 1.7 | 9.5 | 438.7 | 1.0 | C18 H21 N4 O3 Cl2 |
| | 411.0977 | 2.1 | 5.1 | 4.5 | 441.1 | 3.4 | C17 H25 O7 Cl2 |
| | 411.0964 | 3.4 | 8.3 | 10.5 | 441.7 | 4.0 | C14 H17 N10 O Cl2 |
| | 411.1036 | -3.8 | -9.2 | 6.5 | 444.9 | 7.3 | C8 H17 N14 O2 Cl2 |
| | 411.1023 | -2.5 | -6.1 | 1.5 | 445.7 | 8.0 | C7 H21 N10 O6 Cl2 |
| | 411.1009 | -1.1 | -2.7 | 7.5 | 446.5 | 8.9 | C4 H13 N20 Cl2 |
| | 411.0996 | 0.2 | 0.5 | 2.5 | 447.3 | 9.6 | C3 H17 N16 O4 Cl2 |

**(*S*)-1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperidin-3-aminium chloride (19c)**

**Elemental Composition Report** **Page 1**

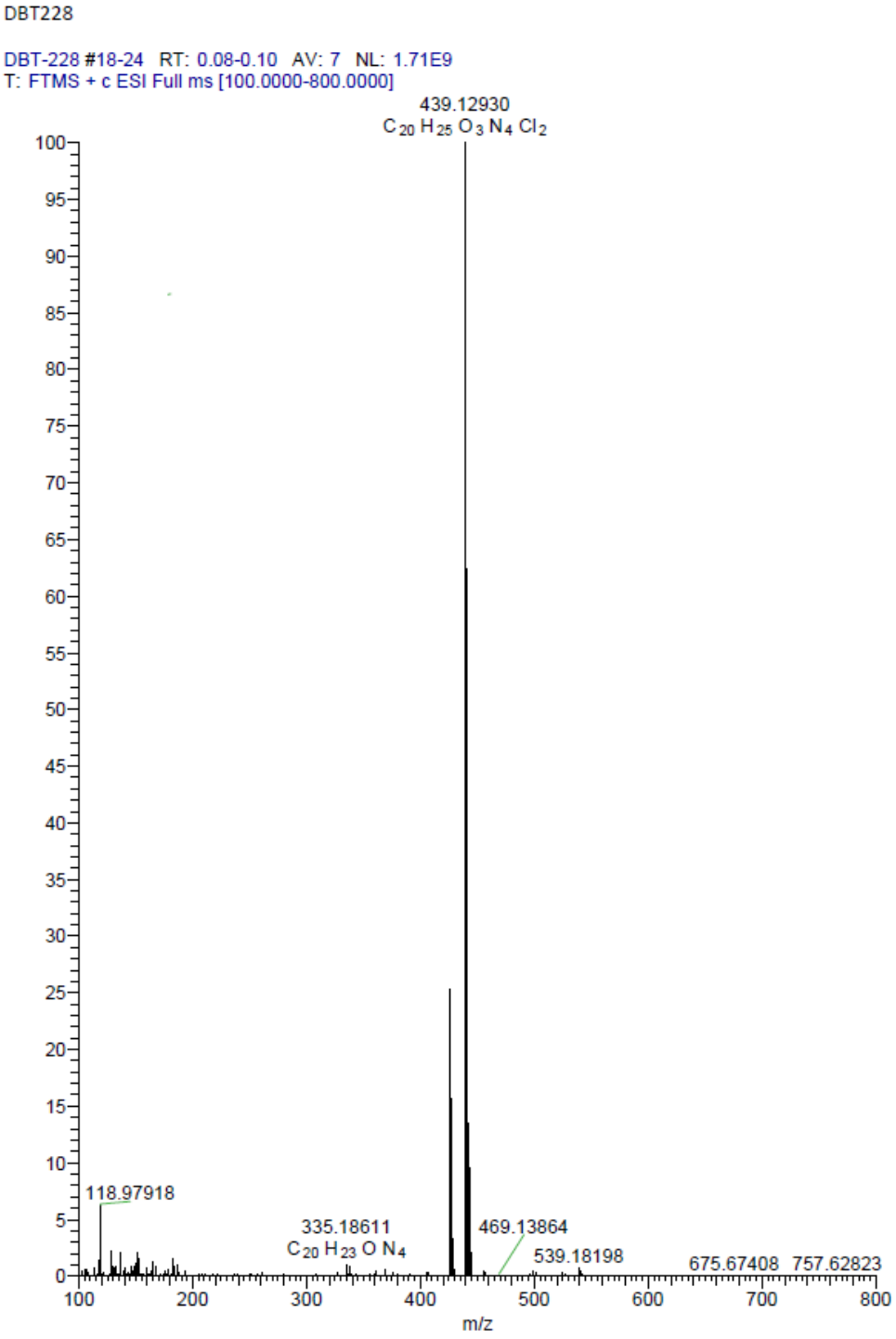
**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
856 formula(e) evaluated with 7 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-9 13 (0.536) Cm (11:13)
1: TOF MS ES+




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 425.1145 | 425.1147 | -0.2 | -0.5 | 9.5 | 524.3 | 0.0 | C19 H23 N4 O3 Cl2 |
| | 425.1134 | 1.1 | 2.6 | 4.5 | 528.0 | 3.7 | C18 H27 O7 Cl2 |
| | 425.1120 | 2.5 | 5.9 | 10.5 | 529.0 | 4.7 | C15 H19 N10 O Cl2 |
| | 425.1107 | 3.8 | 8.9 | 5.5 | 530.9 | 6.7 | C14 H23 N6 O5 Cl2 |
| | 425.1179 | -3.4 | -8.0 | 1.5 | 533.5 | 9.2 | C8 H23 N10 O6 Cl2 |
| | 425.1166 | -2.1 | -4.9 | 7.5 | 534.7 | 10.4 | C5 H15 N20 Cl2 |
| | 425.1152 | -0.7 | -1.6 | 2.5 | 535.5 | 11.2 | C4 H19 N16 O4 Cl2 |

**(1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(methoxycarbonyl)phenyl)piperidin-3-yl)methanaminium chloride (19i)**




Elemental composition search on mass 439.12930

m/z= 434.12930-444.12930

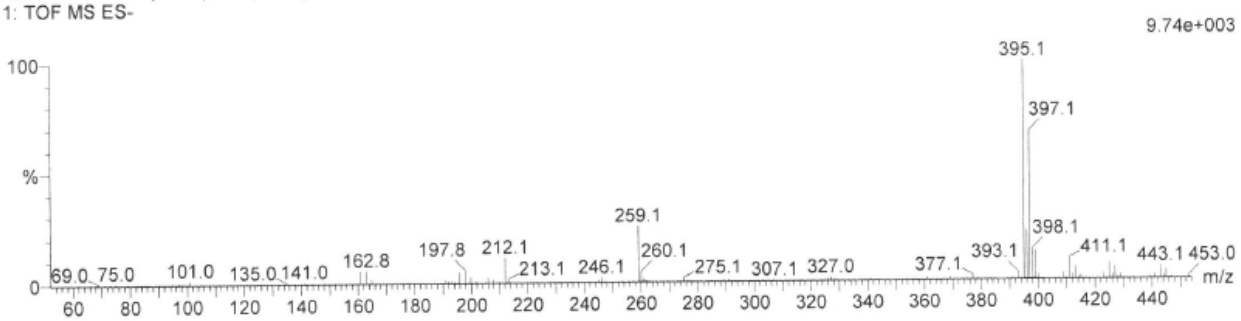
| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 439.12930 | 439.12982 | -1.19 | 9.5 | $C_{20}H_{25}O_3N_4Cl_2$ |

**4-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperazin-1-ium chloride (20a)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
698 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-55 NEG 47 (1.920) Cm (46:48)
1: TOF MS ES-




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 395.0670 | 395.0678 | -0.8 | -2.0 | 10.5 | 182.1 | 0.1 | C17 H17 N4 O3 Cl2 |
| | 395.0651 | 1.9 | 4.8 | 11.5 | 185.0 | 3.0 | C13 H13 N10 O Cl2 |
| | 395.0664 | 0.6 | 1.5 | 5.5 | 185.5 | 3.5 | C16 H21 O7 Cl2 |
| | 395.0637 | 3.3 | 8.4 | 6.5 | 185.9 | 3.9 | C12 H17 N6 O5 Cl2 |
| | 395.0710 | -4.0 | -10.1 | 2.5 | 192.6 | 10.6 | C6 H17 N10 O6 Cl2 |
| | 395.0696 | -2.6 | -6.6 | 8.5 | 192.9 | 10.9 | C3 H9 N20 Cl2 |
| | 395.0683 | -1.3 | -3.3 | 3.5 | 193.5 | 11.5 | C2 H13 N16 O4 Cl2 |
| | 395.0669 | 0.1 | 0.3 | -1.5 | 193.9 | 12.0 | C H17 N12 O8 Cl2 |

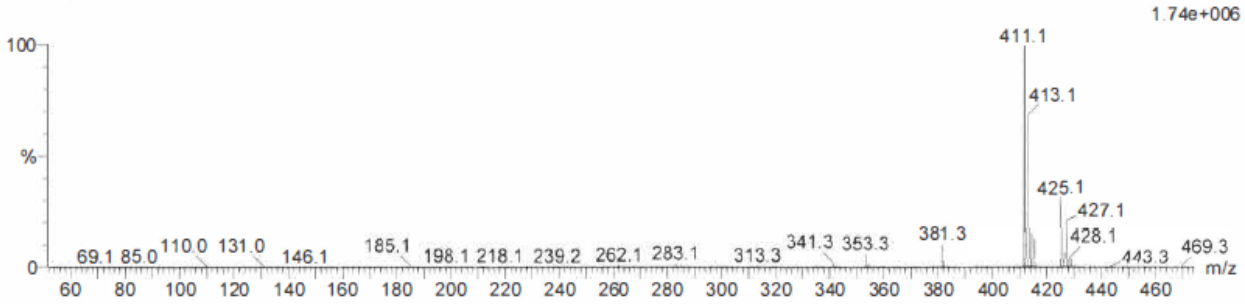
$M-H^-$

**(*S*)-1-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperidin-3-aminium chloride (20c)**

**Elemental Composition Report** Page 1

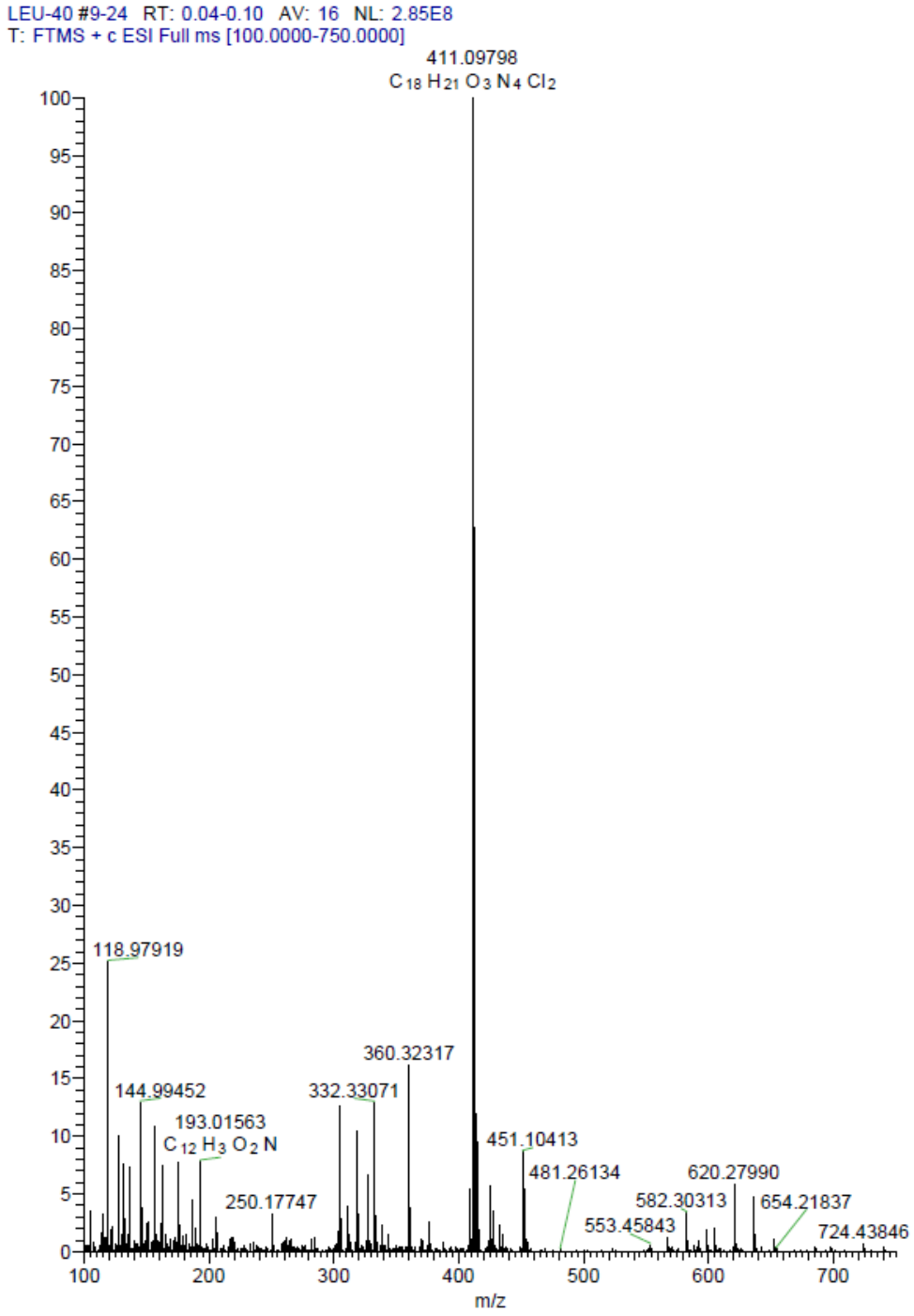
**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
779 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH-7 15 (0.609) Cm (15:16-1:9)
1: TOF MS ES+




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
| 411.1002 | 411.1031 | -2.9 | -7.1 | 13.5 | 383.2 | 0.3 | C23 H21 N2 O Cl2 |
| | 411.0991 | 1.1 | 2.7 | 9.5 | 384.4 | 1.5 | C18 H21 N4 O3 Cl2 |
| | 411.0977 | 2.5 | 6.1 | 4.5 | 386.9 | 4.0 | C17 H25 O7 Cl2 |
| | 411.0964 | 3.8 | 9.2 | 10.5 | 387.9 | 5.0 | C14 H17 N10 O Cl2 |
| | 411.1036 | -3.4 | -8.3 | 6.5 | 391.0 | 8.1 | C8 H17 N14 O2 Cl2 |
| | 411.1023 | -2.1 | -5.1 | 1.5 | 391.7 | 8.8 | C7 H21 N10 O6 Cl2 |
| | 411.1009 | -0.7 | -1.7 | 7.5 | 393.0 | 10.1 | C4 H13 N20 Cl2 |
| | 411.0996 | 0.6 | 1.5 | 2.5 | 393.7 | 10.8 | C3 H17 N16 O4 Cl2 |

**4-((5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)amino)piperidin-1-ium chloride (20d)**

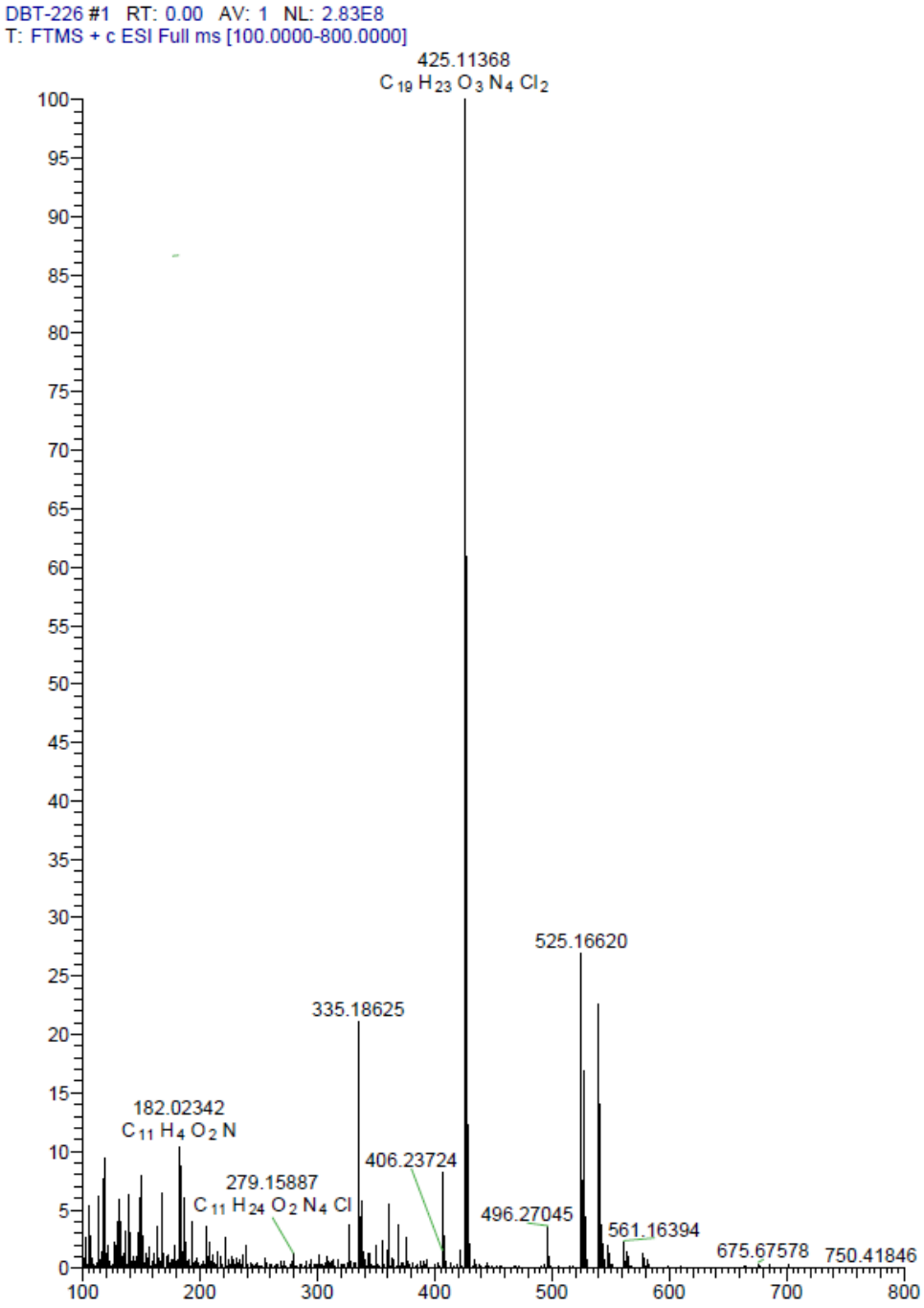



Elemental composition search on mass 411.09798

m/z= 406.09798-416.09798

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 411.09798 | 411.09852 | -1.32 | 9.5 | $C_{18}H_{21}O_3N_4Cl_2$ |

**(1-(5-Carboxy-2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)phenyl)piperidin-3-yl)methanaminium chloride (20i)**

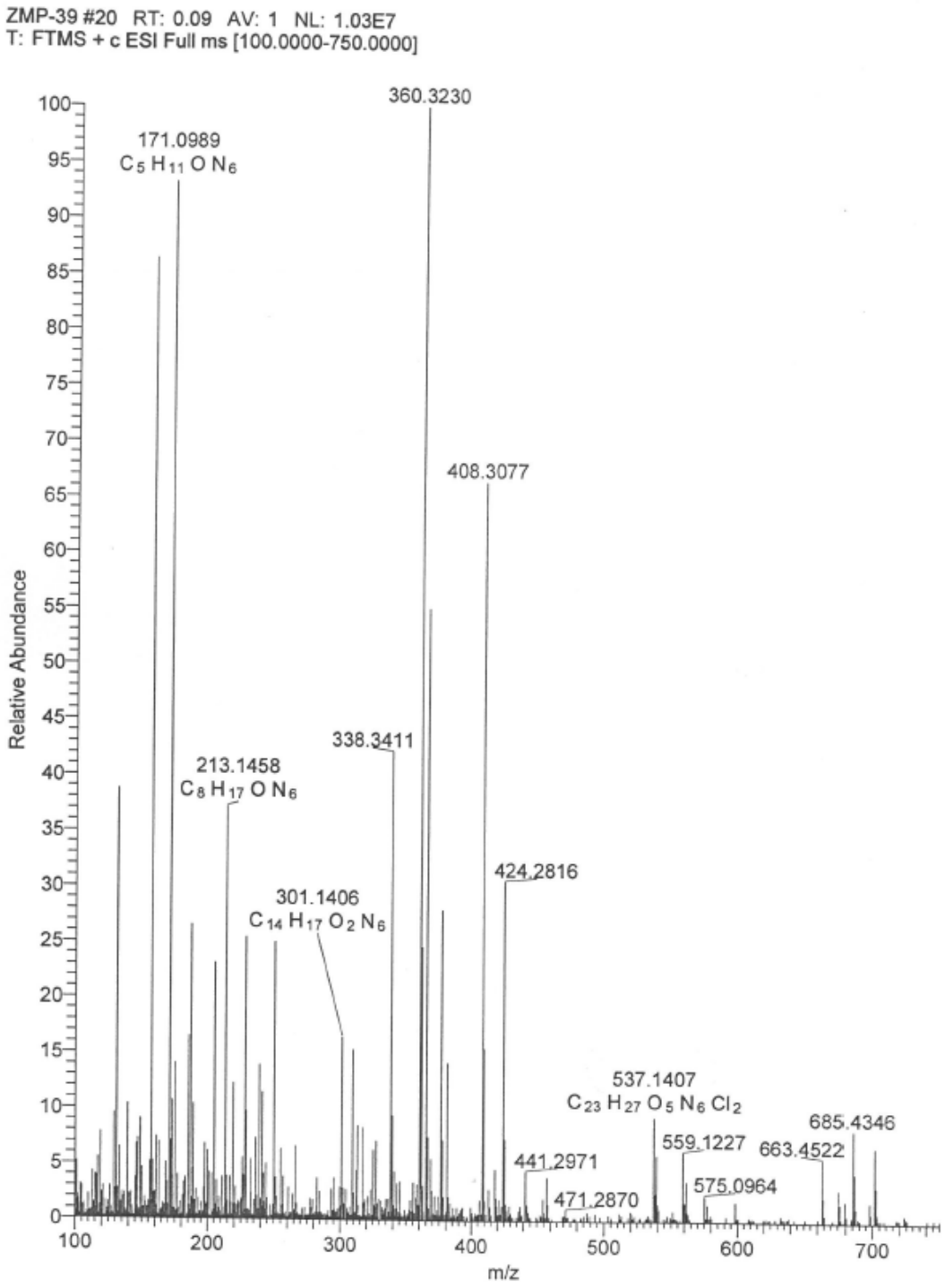



Elemental composition search on mass 425.11368

m/z= 420.11368-430.11368

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 425.11368 | 425.11417 | -1.16 | 9.5 | $C_{19}H_{23}O_3N_4Cl_2$ |

***tert*-Butyl 4-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperazine-1-carboxylate (22a)**

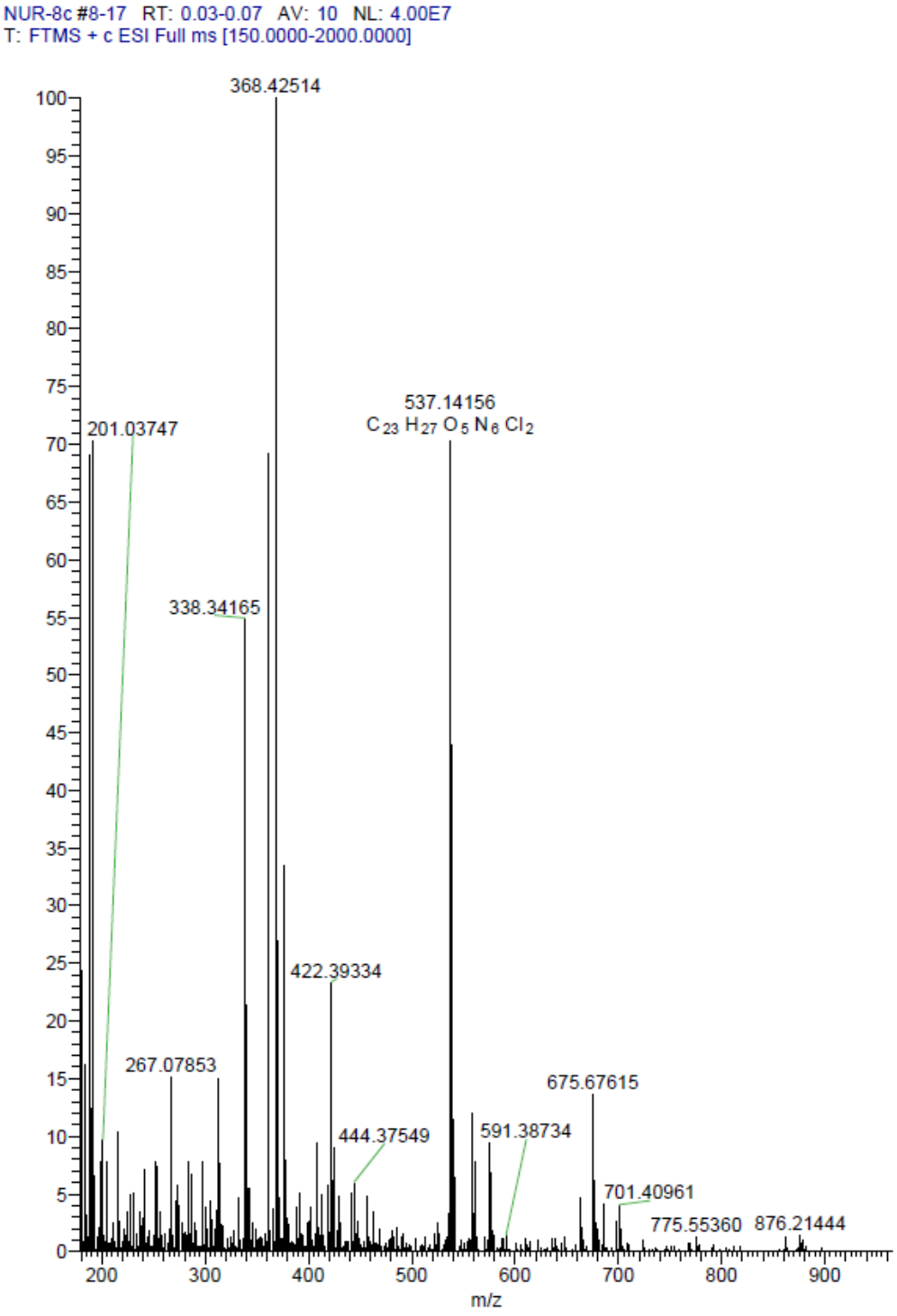



Elemental composition search on mass 537.14075

m/z= 532.14075-542.14075

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 537.14075 | 537.14145 | -1.30 | 12.5 | $C_{23}H_{27}O_5N_6Cl_2$ |

***tert*-Butyl (*S*)-(1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)pyrrolidin-3-yl)carbamate (22b)**




Elemental composition search on mass 537.14156

m/z= 532.14156-542.14156

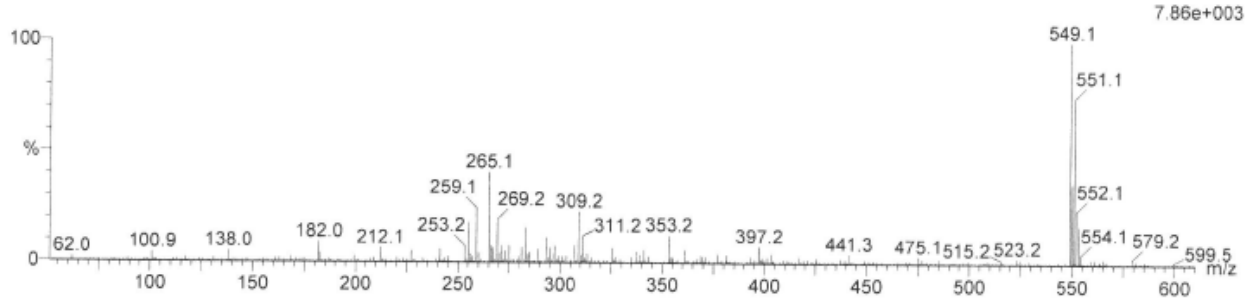
| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 537.14156 | 537.14145 | 0.21 | 12.5 | $C_{23}H_{27}O_5N_6Cl_2$ |

***tert*-Butyl (*S*)-(1-(2-(3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperidin-3-yl)carbamate (22c)**

**Elemental Composition Report** Page 1

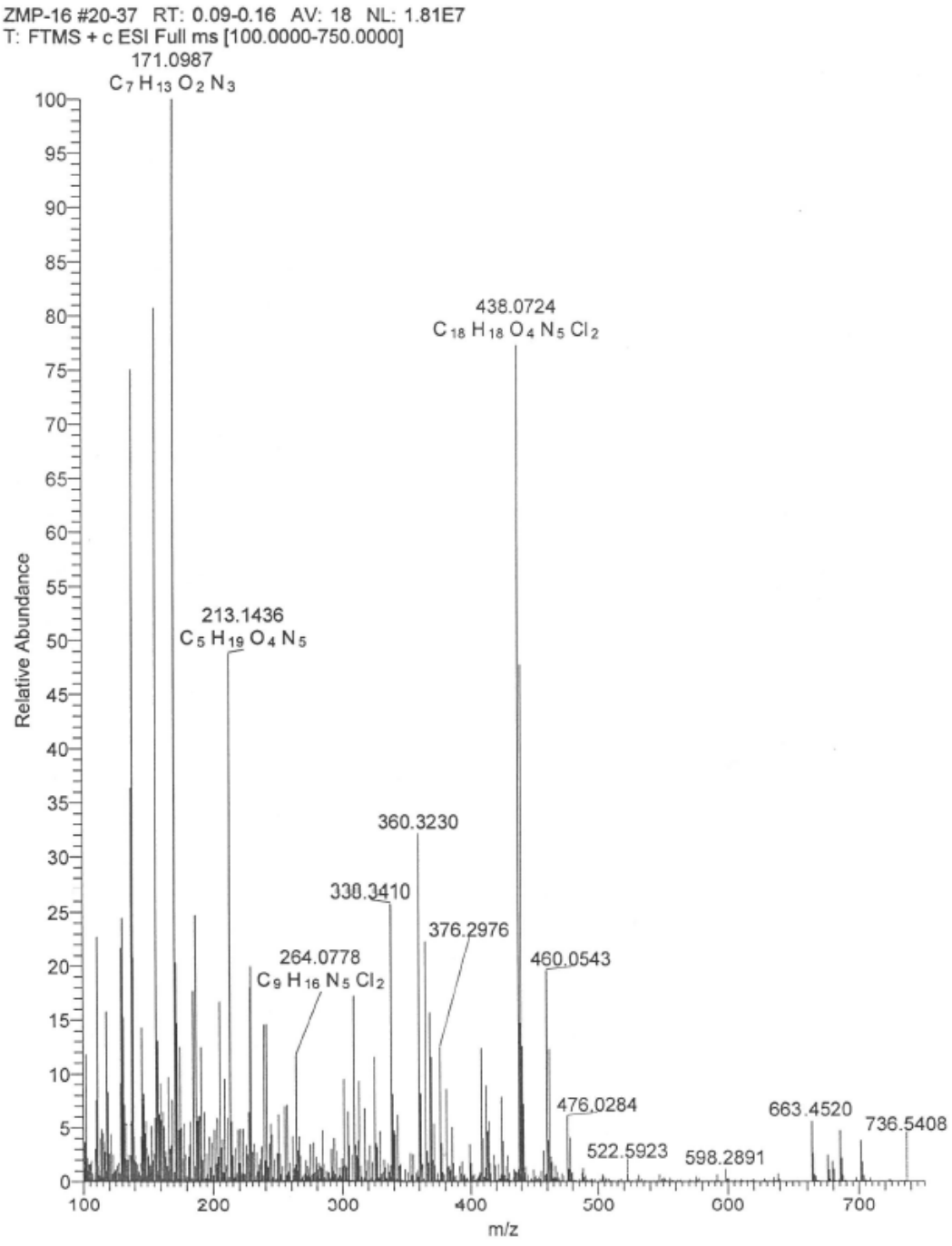
**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1576 formula(e) evaluated with 16 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH 11 48 (1.956) Cm (47:48)
1: TOF MS ES-




| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| 549.1436 | 549.1438 | -0.2 | -0.4 | 0.5 | 113.1 | 8.6 | C12 H31 N8 O12 Cl2 |
| | 549.1433 | 0.3 | 0.5 | 18.5 | 107.0 | 2.5 | C25 H23 N10 O Cl2 |
| | 549.1447 | -1.1 | -2.0 | 12.5 | 106.5 | 2.0 | C28 H31 O7 Cl2 |
| | 549.1425 | 1.1 | 2.0 | 6.5 | 113.6 | 9.1 | C9 H23 N18 O6 Cl2 |
| | 549.1420 | 1.6 | 2.9 | 13.5 | 108.3 | 3.8 | C24 H27 N6 O5 Cl2 |
| | 549.1452 | -1.6 | -2.9 | 5.5 | 112.7 | 8.2 | C13 H27 N12 O8 Cl2 |
| | 549.1412 | 2.4 | 4.4 | 1.5 | 113.9 | 9.4 | C8 H27 N14 O10 Cl2 |
| | 549.1460 | -2.4 | -4.4 | 17.5 | 105.1 | 0.6 | C29 H27 N4 O3 Cl2 |
| | 549.1465 | -2.9 | -5.3 | 10.5 | 112.3 | 7.8 | C14 H23 N16 O4 Cl2 |
| | 549.1465 | -2.9 | -5.3 | -0.5 | 112.4 | 7.9 | C16 H35 N2 O14 Cl2 |
| | 549.1407 | 2.9 | 5.3 | 8.5 | 109.2 | 4.7 | C23 H31 N2 O9 Cl2 |
| | 549.1393 | 4.3 | 7.8 | 14.5 | 109.7 | 5.2 | C20 H23 N12 O3 Cl2 |
| | 549.1479 | -4.3 | -7.8 | 15.5 | 111.8 | 7.2 | C15 H19 N20 Cl2 |
| | 549.1479 | -4.3 | -7.8 | 4.5 | 112.0 | 7.5 | C17 H31 N6 O10 Cl2 |
| | 549.1388 | 4.8 | 8.7 | 21.5 | 106.2 | 1.7 | C35 H27 O2 Cl2 |
| | 549.1385 | 5.1 | 9.3 | 2.5 | 115.0 | 10.5 | C4 H23 N20 O8 Cl2 |

**3,4-Dichloro-5-methyl-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (22e)**

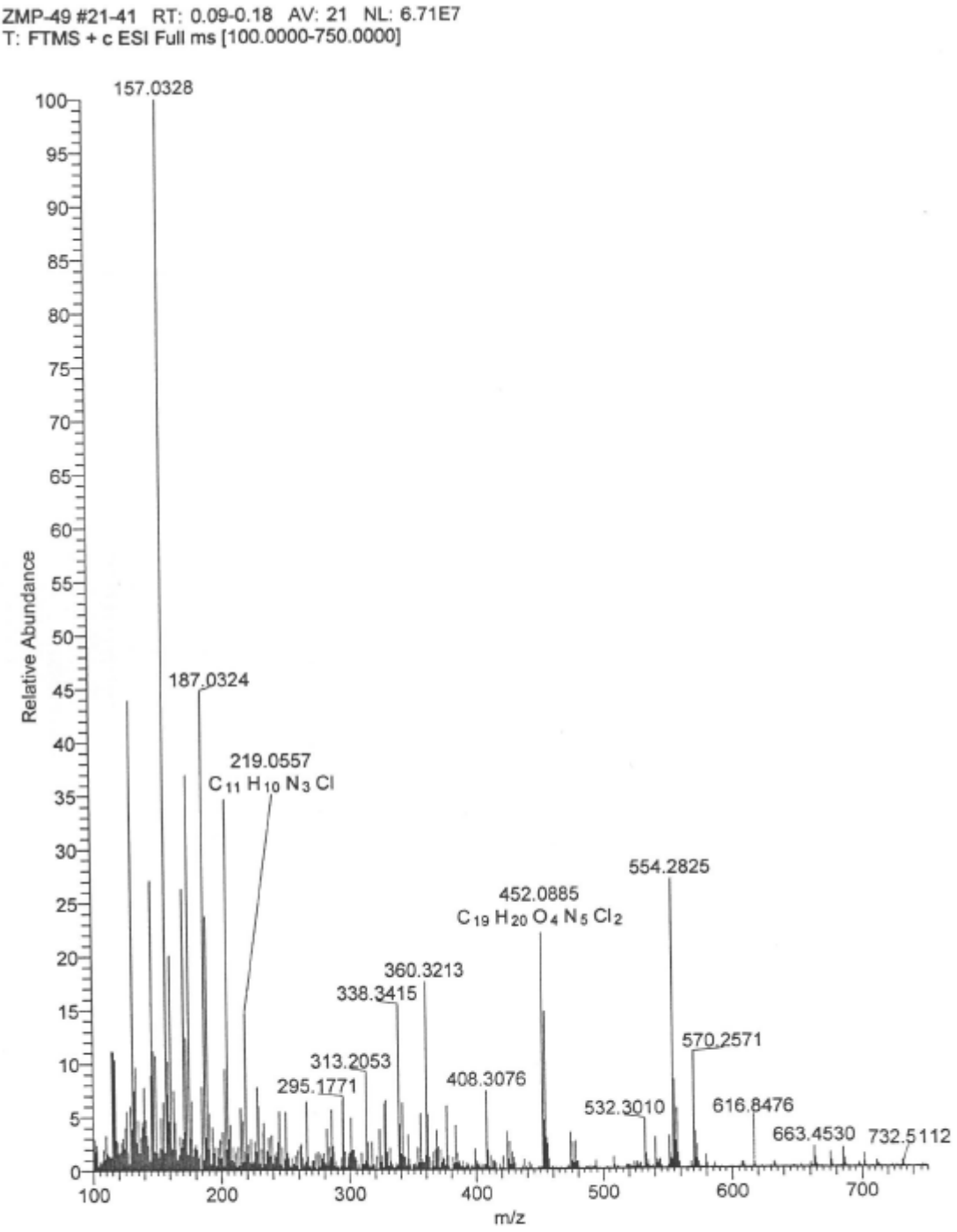



Elemental composition search on mass 438.07237

m/z= 433.07237-443.07237

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 438.07237 | 438.07304 | -1.52 | 11.5 | $C_{18}H_{18}O_4N_5Cl_2$ |

**3,4-Dichloro-5-methyl-*N*-(2-(2-methylmorpholino)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (22f)**

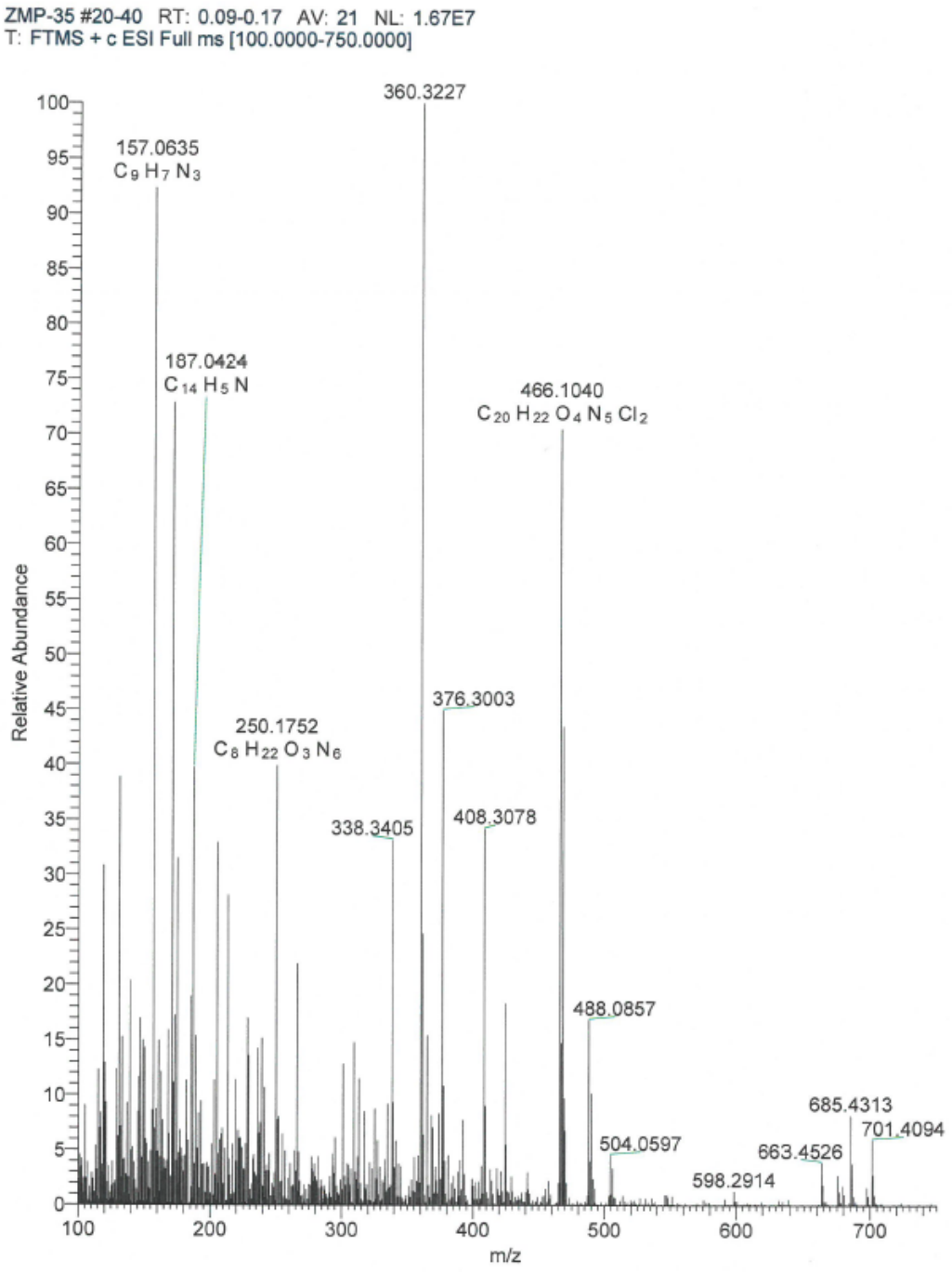



Elemental composition search on mass 452.08846

m/z= 447.08846-457.08846

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 452.08846 | 452.08869 | -0.50 | 11.5 | $C_{19}H_{20}O_4N_5Cl_2$ |

**3,4-Dichloro-*N*-(2-(2,6-dimethylmorpholino)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-5-methyl-1*H*-pyrrole-2-carboxamide (22g)**

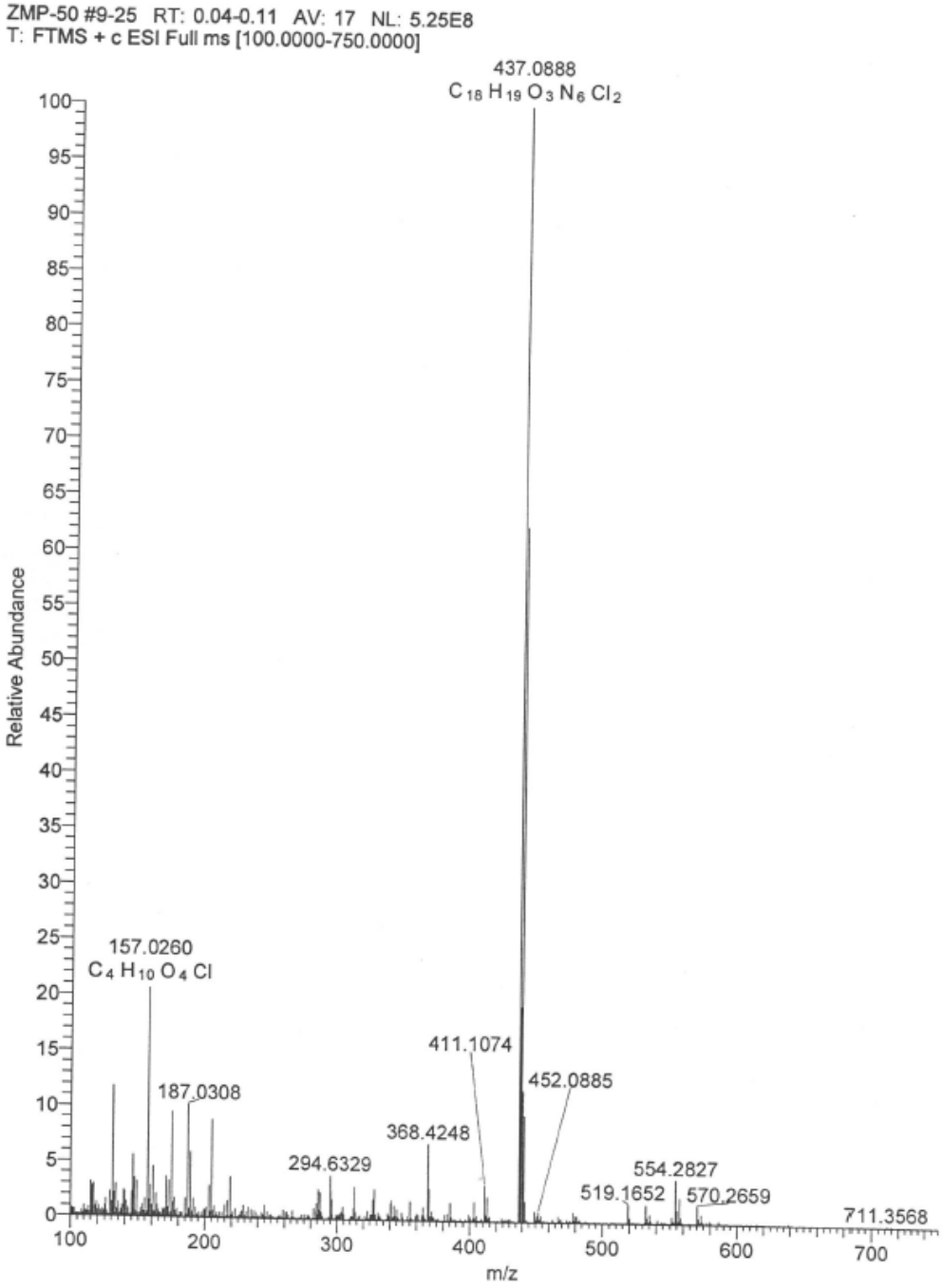



Elemental composition search on mass 466.10399

m/z= 461.10399-471.10399

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 466.10399 | 466.10434 | -0.74 | 11.5 | $C_{20}H_{22}O_4N_5Cl_2$ |

**4-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperazin-1-ium chloride (23a)**




Elemental composition search on mass 437.08880

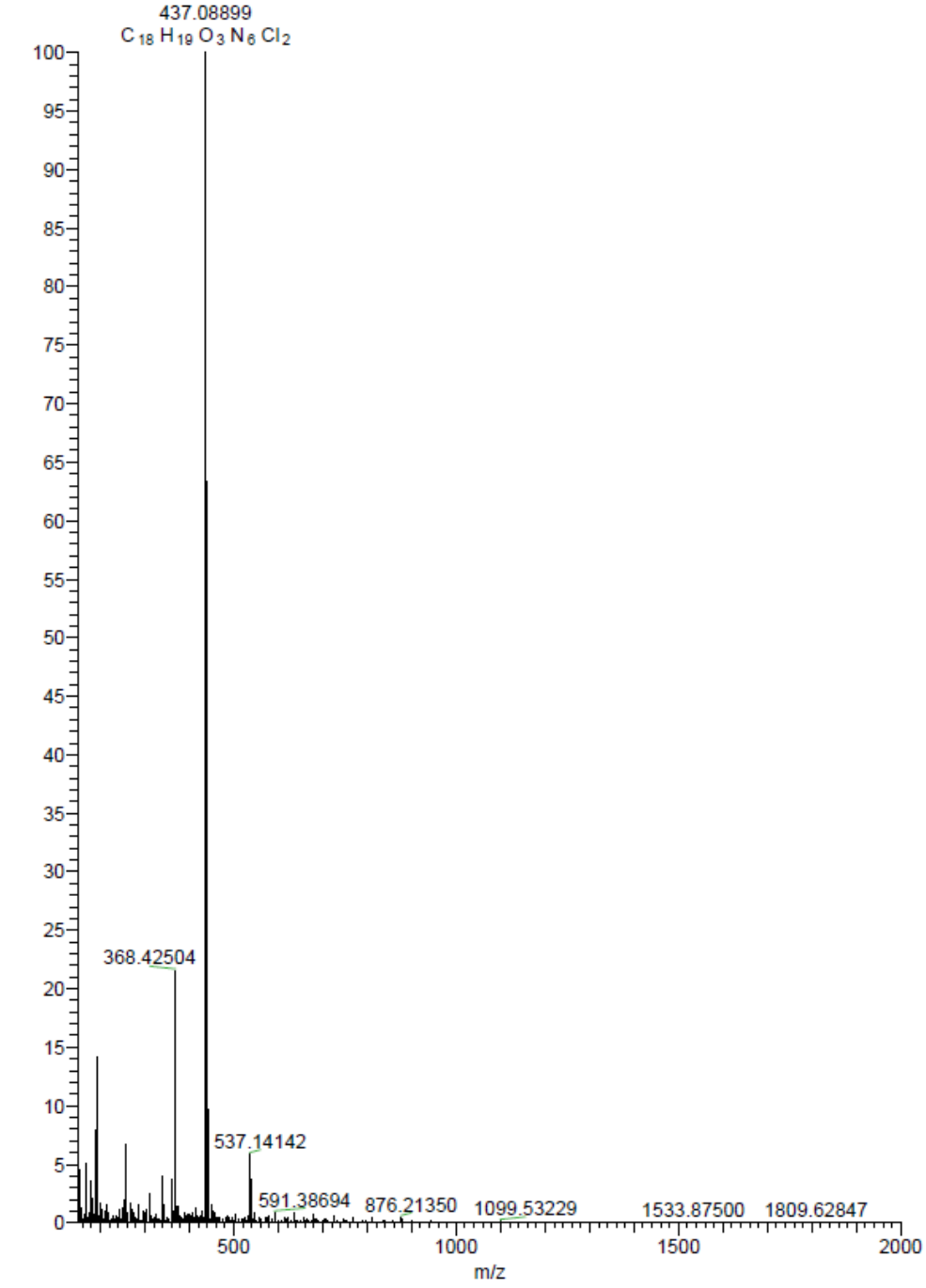
m/z= 432.08880-442.08880

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 437.08880 | 437.08902 | -0.50 | 11.5 | $C_{18}H_{19}O_3N_6Cl_2$ |

**(*S*)-1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)pyrrolidin-3-aminium chloride (23b)**

NUR-10

NUR-10 #9-15 RT: 0.04-0.07 AV: 7 NL: 5.10E8
T: FTMS + c ESI Full ms [150.0000-2000.0000]




Elemental composition search on mass 437.08899

m/z= 432.08899-442.08899

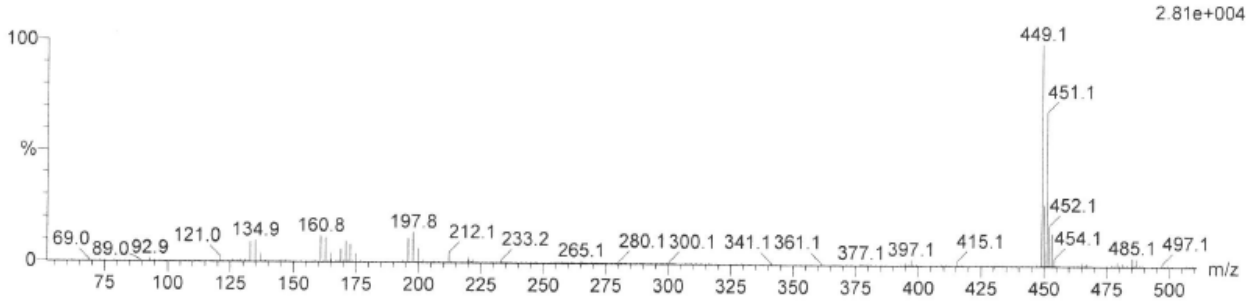
| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 437.08899 | 437.08902 | -0.07 | 11.5 | $C_{18}H_{19}O_3N_6Cl_2$ |

**(*S*)-1-(2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)piperidin-3-aminium chloride (23c)**

**Elemental Composition Report** Page 1

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

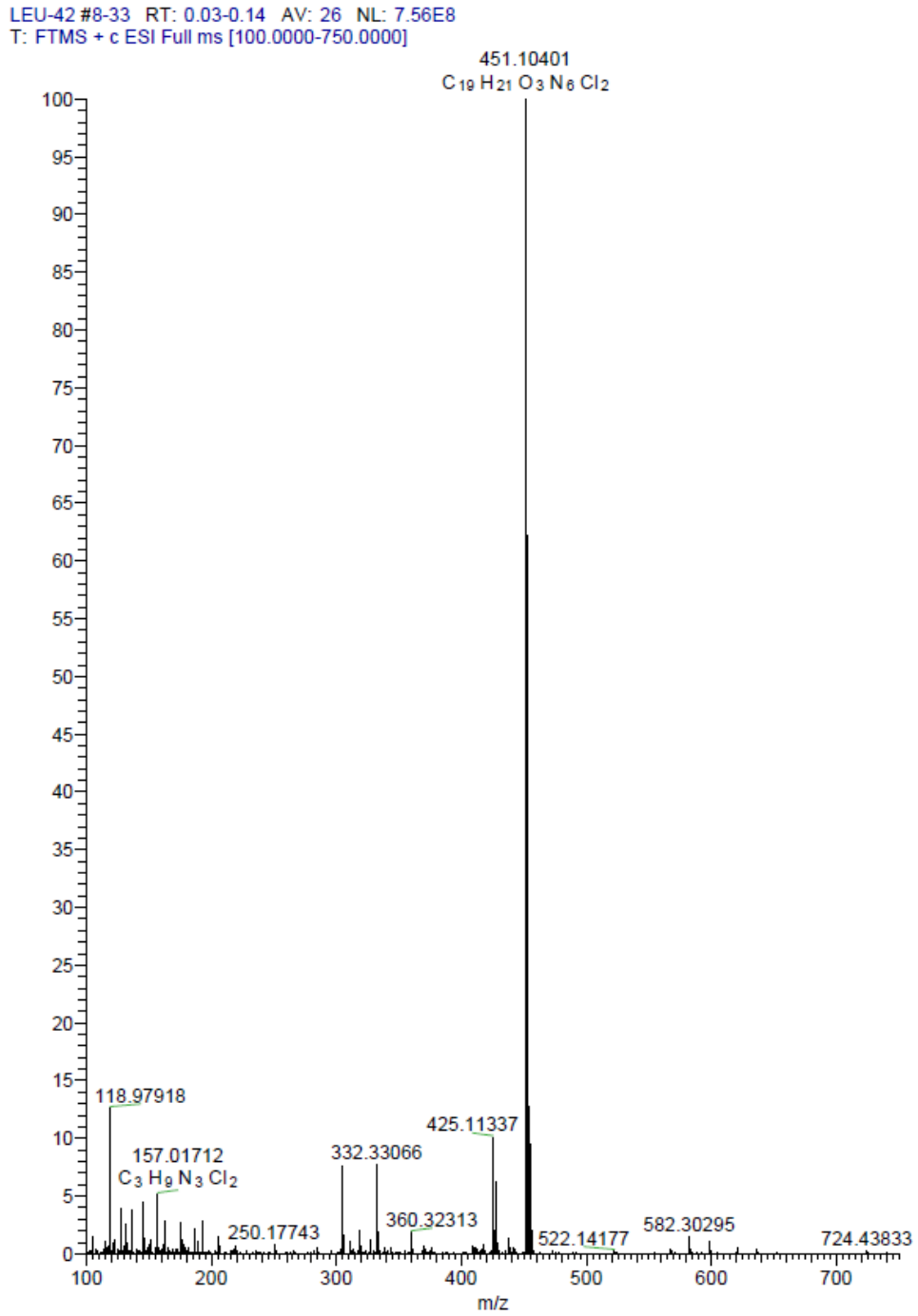
Monoisotopic Mass, Even Electron Ions
989 formula(e) evaluated with 10 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-20 O: 0-20 Cl: 2-2
NBH 12 30 (1.219) Cm (29:30)
1: TOF MS ES-




| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula |
|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | | |
| 449.0890 | 449.0923 | -3.3 | -7.3 | 11.5 | 173.1 | 0.0 | C23 H23 O5 Cl2 |
| | 449.0896 | -0.6 | -1.3 | 12.5 | 177.3 | 4.2 | C19 H19 N6 O3 Cl2 |
| | 449.0864 | 2.6 | 5.8 | 20.5 | 178.6 | 5.5 | C30 H19 Cl2 |
| | 449.0882 | 0.8 | 1.8 | 7.5 | 178.9 | 5.8 | C18 H23 N2 O7 Cl2 |
| | 449.0869 | 2.1 | 4.7 | 13.5 | 179.9 | 6.8 | C15 H15 N12 O Cl2 |
| | 449.0855 | 3.5 | 7.8 | 8.5 | 181.0 | 7.9 | C14 H19 N8 O5 Cl2 |
| | 449.0928 | -3.8 | -8.5 | 4.5 | 183.9 | 10.8 | C8 H19 N12 O6 Cl2 |
| | 449.0914 | -2.4 | -5.3 | -0.5 | 184.2 | 11.1 | C7 H23 N8 O10 Cl2 |
| | 449.0901 | -1.1 | -2.4 | 5.5 | 185.4 | 12.3 | C4 H15 N18 O4 Cl2 |
| | 449.0887 | 0.3 | 0.7 | 0.5 | 185.9 | 12.8 | C3 H19 N14 O8 Cl2 |

M-H⁻

**4-((2-(3,4-Dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)-5-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)amino)piperidin-1-ium chloride (23d)**

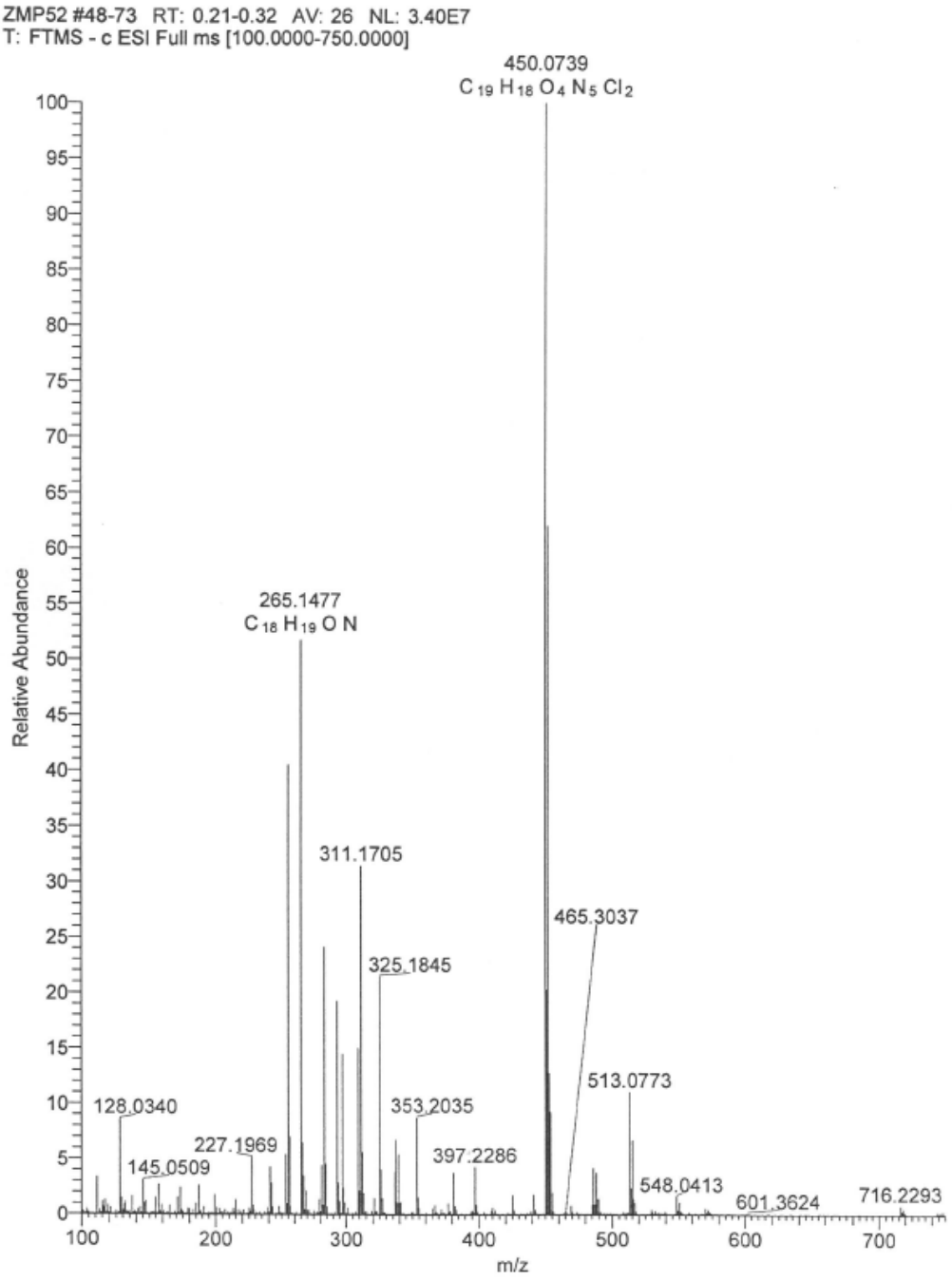



Elemental composition search on mass 451.10401

m/z= 446.10401-456.10401

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 451.10401 | 451.10467 | -1.46 | 11.5 | $C_{19}H_{21}O_3N_6Cl_2$ |

**4,5-Dibromo-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (27a)**

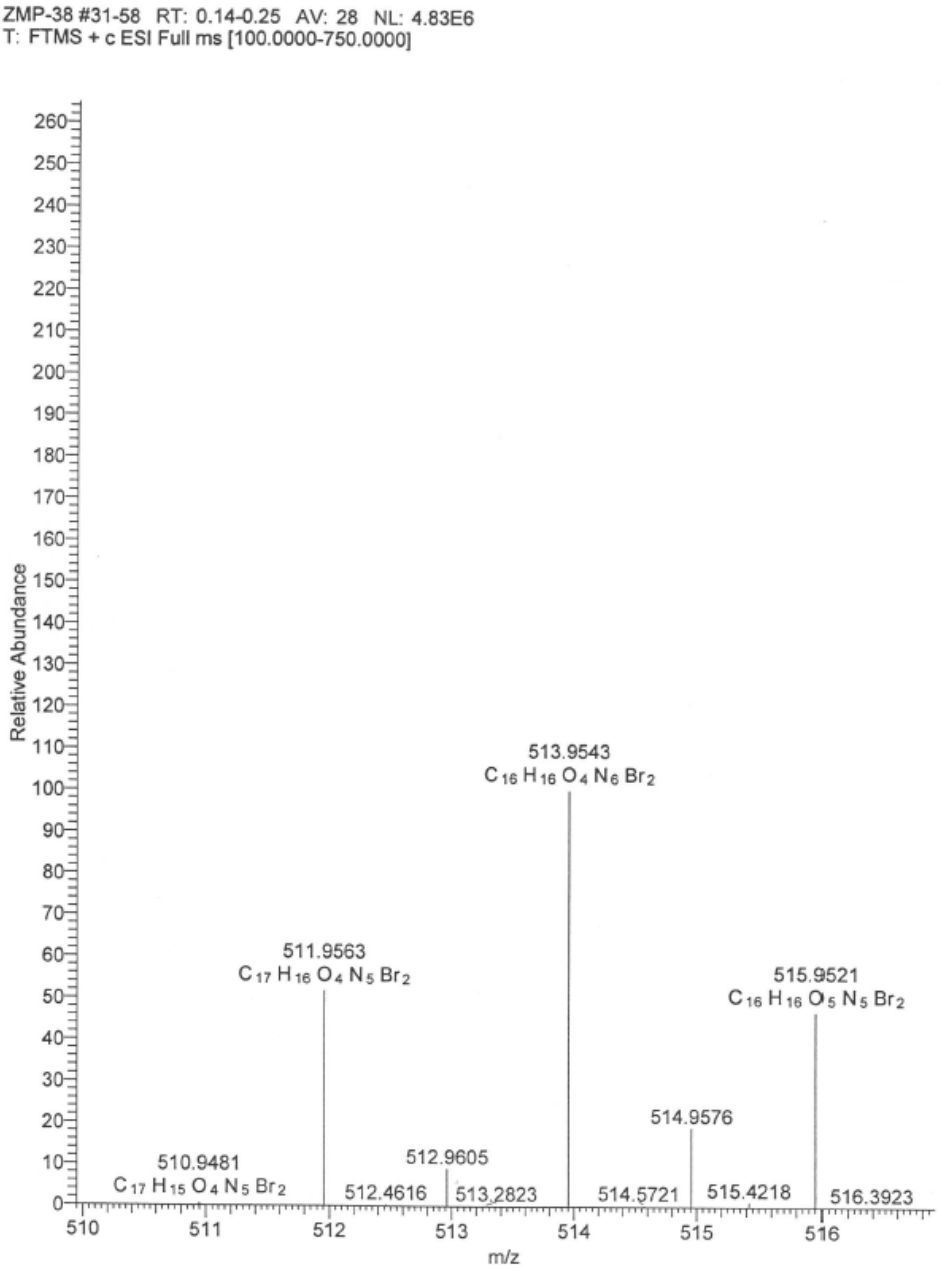



Elemental composition search on mass 450.07394

m/z= 445.07394-455.07394

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 450.07394 | 450.07413 | -0.43 | 12.5 | $C_{19}H_{18}O_4N_5Cl_2$ |
| | 450.07173 | 4.92 | 9.5 | $C_{17}H_{19}O_4N_5Cl_2Na$ |

**3,4-Dichloro-*N*,5-dimethyl-*N*-(2-morpholino-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1*H*-pyrrole-2-carboxamide (27b)**

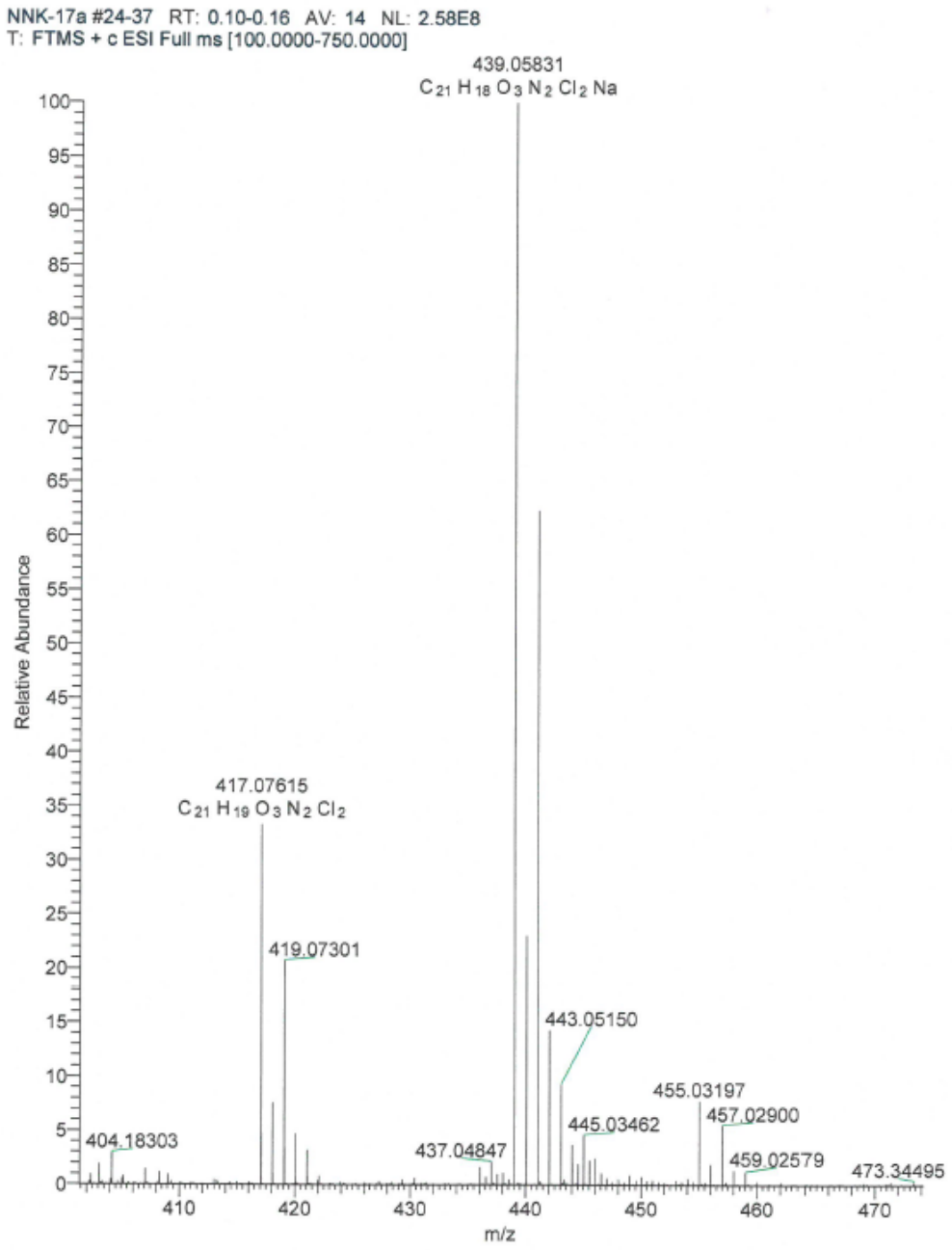



Elemental composition search on mass 511.95626

m/z= 506.95626-516.95626

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 511.95626 | 511.95636 | -0.19 | 11.5 | $C_{17}H_{16}O_4N_5Br_2$ |

**Methyl 4-(*N*-benzyl-3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamido)benzoate (31)**

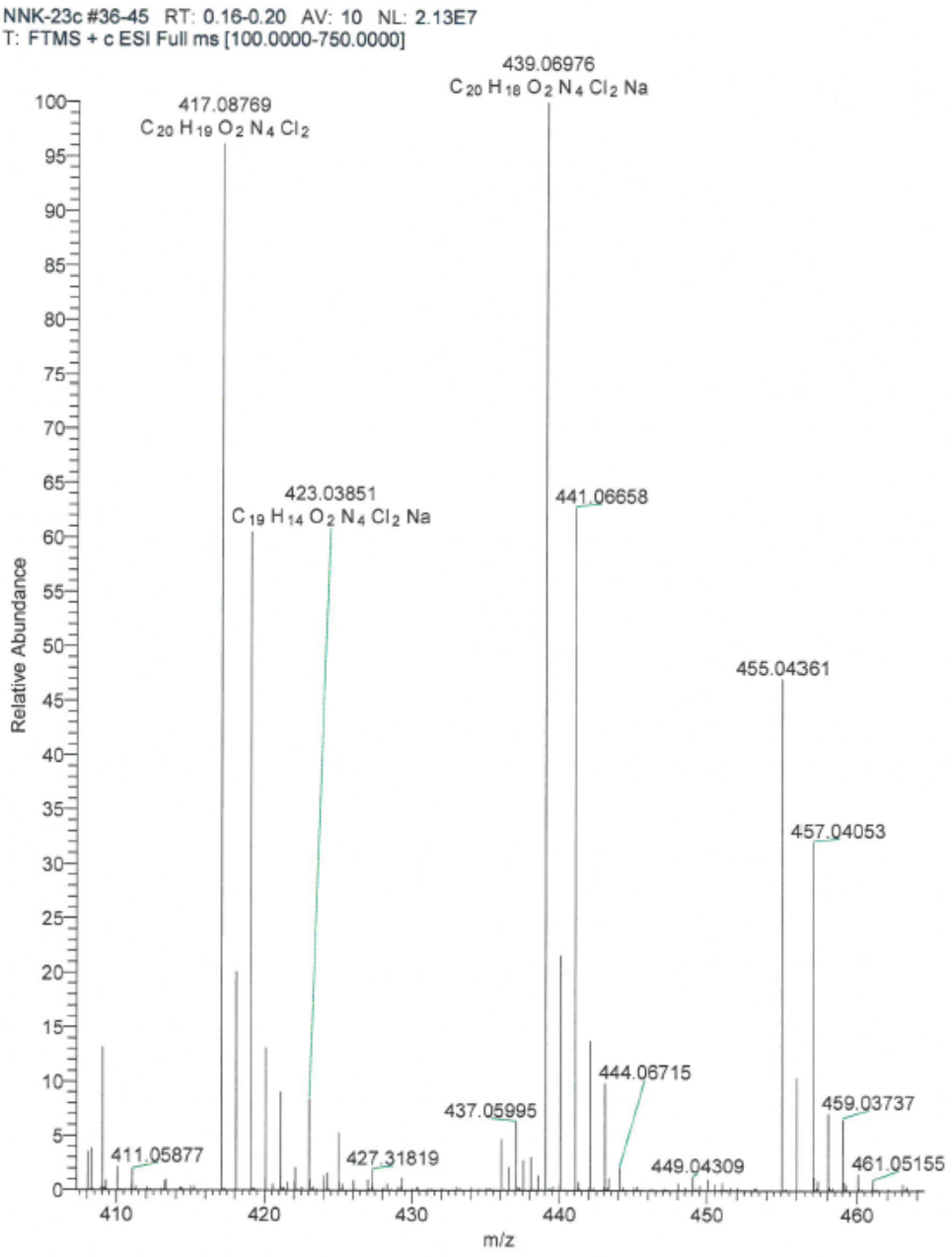



Elemental composition search on mass 417.07615

m/z= 412.07615-422.07615

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 417.07615 | 417.07672 | -1.38 | 12.5 | $C_{21}H_{19}O_3N_2Cl_2$ |
| | 417.07249 | 8.78 | 14.5 | $C_{20}H_{15}O_3N_4ClNa$ |

**_N_-Benzyl-3,4-dichloro-_N_-(4-(hydrazinecarbonyl)phenyl)-5-methyl-1_H_-pyrrole-2-carboxamide (32)**

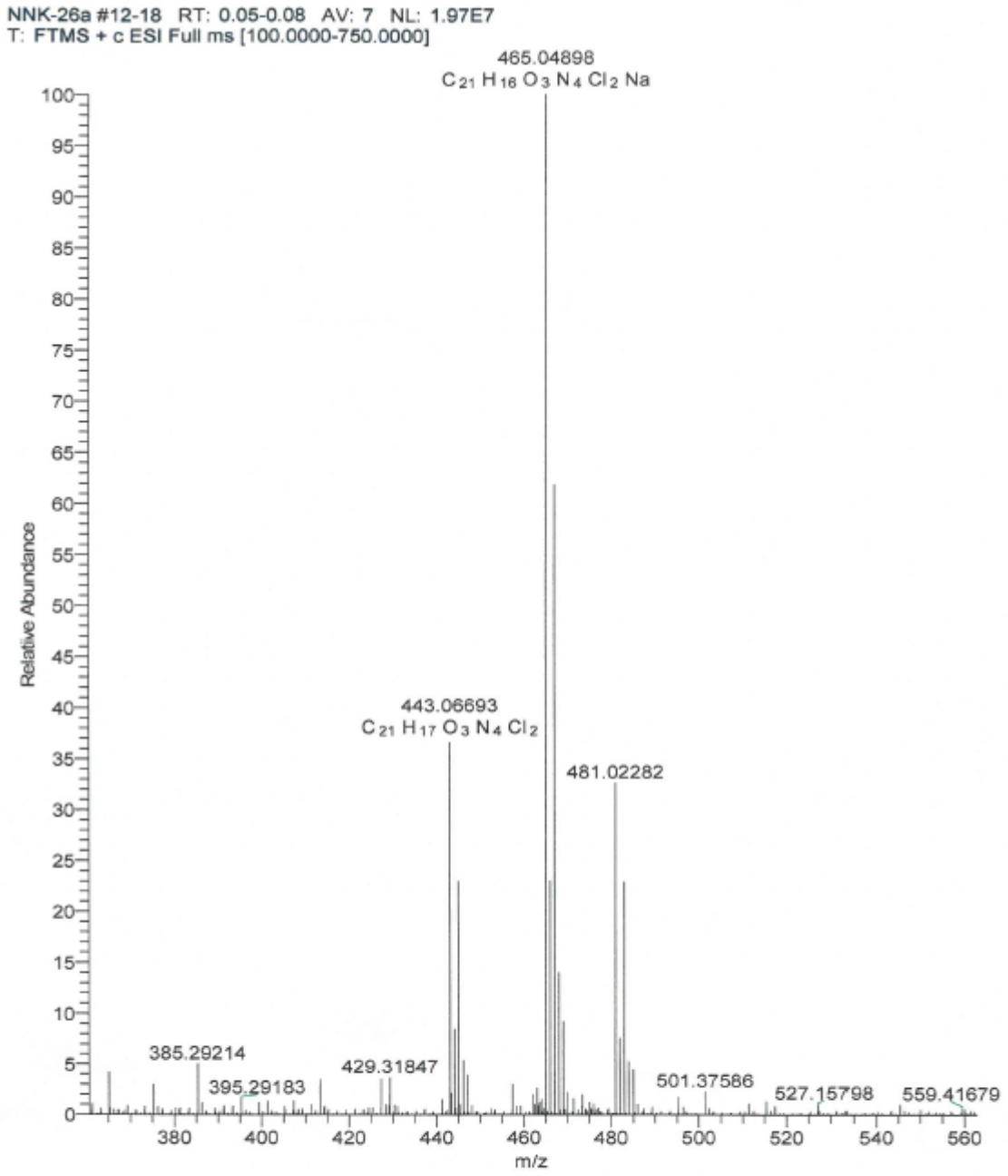



Elemental composition search on mass 417.08769

m/z= 412.08769-422.08769

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 417.08769 | 417.08796 | -0.64 | 12.5 | $C_{20}H_{19}O_2N_4Cl_2$ |

**_N_-Benzyl-3,4-dichloro-5-methyl-_N_-(4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-1_H_-pyrrole-2-carboxamide (33)**

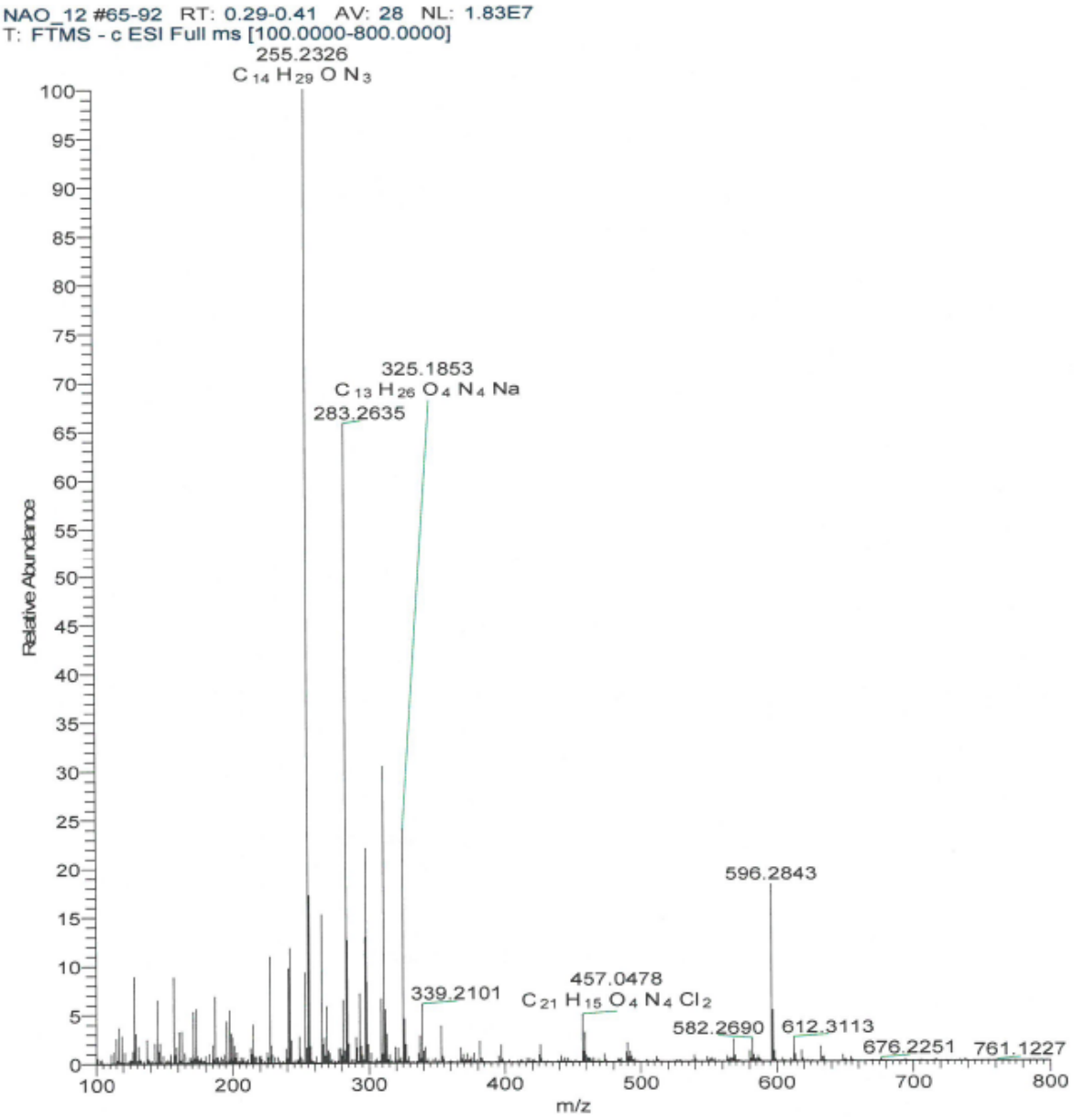



Elemental composition search on mass 443.06693

m/z= 438.06693-448.06693

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 443.06693 | 443.06722 | -0.66 | 14.5 | $C_{21}H_{17}O_3N_4Cl_2$ |

***N*-(2-(Benzyloxy)-4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl)-3,4-dichloro-5-methyl-1*H*-pyrrole-2-carboxamide (39)**




Elemental composition search on mass 457.0478

m/z= 452.0478-462.0478

| m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition |
|---|---|---|---|---|
| 457.04776 | 457.04758 | 0.39 | 15.5 | $C_{21}H_{15}O_4N_4Cl_2$ |
| | 457.04801 | -0.55 | 12.0 | $C_{19}H_{18}O_2N_5Cl_2K$ |
| | 457.04695 | 1.78 | 8.5 | $C_{19}H_{21}O_3N_2Cl_2KNa$ |