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## Supplemental Information

# Generating Multibillion Chemical Space of Readily Accessible Screening Compounds

**Oleksandr O. Grygorenko, Dmytro S. Radchenko, Igor Dziuba, Alexander Chuprina, Kateryna E. Gubina, and Yurii S. Moroz**

**Figure S1.** The parallel reactions set up (related to Scheme 1 and Table 1). Reprinted with permission from: Bogolubsky, A. V., Moroz, Y. S. et al. (2018) *ACS Comb. Sci.* 20, 35−43. 


**Figure S2.** A laboratory oven with a shaker (related to Scheme 1 and Table 1). Reprinted with permission from: Bogolubsky, A. V., Moroz, Y. S. et al. (2018) *ACS Comb. Sci.* 20, 35−43. 

**Table S3.** Data used to build the diagrams in Figure 6.

| MW | Method ***A*** | | Method ***E*** | | Total | |
|---|---|---|---|---|---|---|
| | No. of cpds | % of cpds | No. of cpds | % of cpds | No. of cpds | % of cpds |
| <150 | 0 | 0 | 0 | 0 | 0 | 0 |
| 150 | 81 | 0.000 | 2 | 0.000 | 83 | 0.000 |
| 200 | 24865 | 0.000 | 1506 | 0.000 | 26371 | 0.000 |
| 250 | 2928095 | 0.011 | 146677 | 0.009 | 3074772 | 0.011 |
| 300 | 126840477 | 0.465 | 4818124 | 0.308 | 131658601 | 0.456 |
| 350 | 1690324822 | 6.192 | 45585024 | 2.915 | 1735909846 | 6.015 |
| 400 | 7949008636 | 29.120 | 182488242 | 11.670 | 8131496878 | 28.178 |
| 450 | 11893243921 | 43.569 | 354039102 | 22.640 | 12247283023 | 42.440 |
| 500 | 4975547385 | 18.227 | 405752895 | 25.947 | 5381300280 | 18.647 |
| 550 | 644594878 | 2.361 | 312759436 | 20.000 | 957354314 | 3.317 |
| 600 | 14483114 | 0.053 | 170017630 | 10.872 | 184500744 | 0.639 |
| 650 | 400282 | 0.001 | 66893317 | 4.278 | 67293599 | 0.233 |
| >650 | 1088 | 0.000 | 18214639 | 1.165 | 18215727 | 0.063 |
| All | 27297397644 | 100 | 1560716594 | 100 | 28858114238 | 100 |

| sLogP | Method ***A*** | | Method ***E*** | | Total | |
|---|---|---|---|---|---|---|
| | No. of cpds | % of cpds | No. of cpds | % of cpds | No. of cpds | % of cpds |
| <–2 | 9680365 | 0.035 | 151552 | 0.010 | 9680365 | 0.034 |
| –2 | 71464639 | 0.262 | 1726477 | 0.110 | 73191116 | 0.254 |
| –1 | 387167997 | 1.418 | 12021028 | 0.769 | 399189025 | 1.384 |
| 0 | 1439959065 | 5.275 | 51921069 | 3.320 | 1491880134 | 5.171 |
| 1 | 3783279941 | 13.859 | 151434129 | 9.684 | 3934714070 | 13.638 |
| 2 | 6666422497 | 24.421 | 298753963 | 19.105 | 6965176460 | 24.142 |
| 3 | 7536160005 | 27.608 | 399412101 | 25.542 | 7935572106 | 27.505 |
| 4 | 5124595911 | 18.773 | 354665763 | 22.680 | 5479261674 | 18.991 |
| 5 | 1906945290 | 6.986 | 201575452 | 12.890 | 2108520742 | 7.308 |
| 6 | 344499995 | 1.262 | 72158367 | 4.614 | 416658362 | 1.444 |
| >6 | 27221939 | 0.100 | 19932715 | 1.275 | 47154654 | 0.163 |
| All | 27287717279 | 100 | 1563601064 | 100 | 28851318343 | 100 |

| HAcc | Method ***A*** | | Method ***E*** | | Total | |
|---|---|---|---|---|---|---|
| | No. of cpds | % of cpds | No. of cpds | % of cpds | No. of cpds | % of cpds |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 572147399 | 2.096 | 0 | 0 | 572147399 | 1.982 |
| 3 | 2747814751 | 10.066 | 0 | 0 | 2747814751 | 9.521 |
| 4 | 5737303319 | 21.018 | 9610832 | 0.615 | 5746914151 | 19.912 |
| 5 | 7004112548 | 25.659 | 81854862 | 5.235 | 7085967410 | 24.552 |
| 6 | 5696047963 | 20.867 | 232148220 | 14.846 | 5928196183 | 20.540 |
| 7 | 3345554738 | 12.256 | 369738217 | 23.644 | 3715292955 | 12.873 |
| 8 | 1493257821 | 5.470 | 372963949 | 23.851 | 1866221770 | 6.466 |
| 9 | 520065936 | 1.905 | 265014059 | 16.947 | 785079995 | 2.720 |
| 10 | 143470151 | 0.526 | 143570857 | 9.181 | 287041008 | 0.995 |
| >10 | 37623018 | 0.138 | 88851620 | 5.682 | 126474638 | 0.438 |
| All | 27297397644 | 100 | 1563752616 | 100 | 28861150260 | 100 |

| HDon | Method ***A*** | | Method ***E*** | | Total | |
|---|---|---|---|---|---|---|
| | No. of cpds | % of cpds | No. of cpds | % of cpds | No. of cpds | % of cpds |
| 0 | 3187748954 | 11.6778 | 313693134 | 20.06028 | 3501442088 | 12.26534 |
| 1 | 11514063585 | 42.1801 | 661866465 | 42.32552 | 12175930050 | 42.65154 |
| 2 | 8814595589 | 32.2910 | 436524642 | 27.9152 | 9251120231 | 32.40611 |
| 3 | 3107816412 | 11.3850 | 129777225 | 8.299089 | 3237593637 | 11.34109 |
| 4 | 602113896 | 2.2058 | 20101362 | 1.285457 | 622215258 | 2.179582 |
| 5 | 66845429 | 0.2449 | 1703616 | 0.108944 | 68549045 | 0.240123 |
| >5 | 4213779 | 0.0154 | 86172 | 0.005511 | 4299951 | 0.015062 |
| All | 27297397644 | 100 | 1250059482 | 100 | 28547457126 | 100 |

| RotB | Method ***A*** | | Method ***E*** | | Total | |
|---|---|---|---|---|---|---|
| | No. of cpds | % of cpds | No. of cpds | % of cpds | No. of cpds | % of cpds |
| 0 | 29957 | 0.000 | 0 | 0.000 | 29957 | 0.000 |
| 1 | 6028530 | 0.022 | 104 | 0.000 | 6028634 | 0.021 |
| 2 | 317910606 | 1.165 | 92306 | 0.006 | 318002912 | 1.118 |
| 3 | 1508875367 | 5.528 | 14538387 | 0.930 | 1523413754 | 5.356 |
| 4 | 3381280817 | 12.387 | 59564079 | 3.809 | 3440844896 | 12.096 |
| 5 | 4774360963 | 17.490 | 133246511 | 8.521 | 4907607474 | 17.253 |
| 6 | 5056521442 | 18.524 | 207941672 | 13.298 | 5264463114 | 18.507 |
| 7 | 4374782280 | 16.026 | 250341558 | 16.009 | 4625123838 | 16.259 |
| 8 | 3246990992 | 11.895 | 247807164 | 15.847 | 3494798156 | 12.286 |
| 9 | 2131540056 | 7.809 | 210797401 | 13.480 | 2342337457 | 8.234 |
| 10 | 1255491384 | 4.599 | 159490637 | 10.199 | 1414982021 | 4.974 |
| 11 | 670246782 | 2.455 | 109918272 | 7.029 | 780165054 | 2.743 |
| 12 | 326795259 | 1.197 | 70088476 | 4.482 | 396883735 | 1.395 |
| 13 | 146403645 | 0.536 | 42137017 | 2.695 | 188540662 | 0.663 |
| 14 | 61249058 | 0.224 | 24518316 | 1.568 | 85767374 | 0.302 |
| 15 | 24370304 | 0.089 | 14243016 | 0.911 | 38613320 | 0.136 |
| >15 | 14520202 | 0.053 | 19027700 | 1.217 | 33547902 | 0.118 |
| All | 27297397644 | 100 | 1148369557 | 100 | 28445767201 | 100 |

| F$sp^3$ | Method ***A*** | | Method ***E*** | | Total | |
|---|---|---|---|---|---|---|
| | No. of cpds | % of cpds | No. of cpds | % of cpds | No. of cpds | % of cpds |
| 0 | 602496 | 0.002 | 1442908 | 0.092 | 2045404 | 0.007 |
| 0.1 | 47724123 | 0.175 | 20483171 | 1.310 | 68207294 | 0.236 |
| 0.2 | 453879381 | 1.663 | 79048294 | 5.055 | 532927675 | 1.847 |
| 0.3 | 1904676513 | 6.978 | 185528454 | 11.864 | 2090204967 | 7.242 |
| 0.4 | 4954266113 | 18.149 | 303197434 | 19.389 | 5257463547 | 18.216 |
| 0.5 | 5884585398 | 21.557 | 299512055 | 19.153 | 6184097453 | 21.427 |
| 0.6 | 5967794224 | 21.862 | 334194659 | 21.371 | 6301988883 | 21.836 |
| 0.7 | 4483237975 | 16.424 | 173555288 | 11.099 | 4656793263 | 16.135 |
| 0.8 | 2213453075 | 8.109 | 123783792 | 7.916 | 2337236867 | 8.098 |
| 0.9 | 1387178346 | 5.082 | 43006561 | 2.750 | 1430184907 | 4.955 |
| All | 27297397644 | 100 | 1563752616 | 100 | 28861150260 | 100 |

**Table S4.** Data used to build the diagram in Figure 7.

| % of the initial synthon set | Database size | | | |
|---|---|---|---|---|
| | Selection 1 | Selection 2 | Selection 3 | Average |
| 0 | 0 | 0 | 0 | 0 |
| 5 | 3403925 | 3428214 | 3390057 | 3407399 |
| 10 | 27110556 | 27394230 | 27186189 | 27230325 |
| 15 | 91840658 | 91732904 | 91402990 | 91658851 |
| 20 | 218527689 | 218963333 | 218703739 | 218731587 |
| 25 | 425632157 | 426936973 | 426736465 | 426435198 |
| 30 | 738353634 | 737414660 | 738647994 | 7381387637 |
| 35 | 1167189585 | 1170624550 | 1171458018 | 1169757384 |
| 40 | 1747577364 | 1747527058 | 1740846423 | 1745316948 |
| 45 | 2480899801 | 2486719501 | 2487750229 | 2485123177 |
| 50 | 3417793869 | 3416799399 | 3419592448 | 3418061905 |
| 55 | 4537339006 | 4550268732 | 4543764987 | 4543790908 |
| 60 | 5906370545 | 5900799500 | 5911540359 | 5906236801 |
| 65 | 7486457003 | 7501975505 | 7499292741 | 7495908416 |
| 70 | 9357690180 | 9370507250 | 9356875950 | 9361691127 |
| 75 | 11508760458 | 11507498938 | 11504122179 | 11506793858 |
| 80 | 13948650520 | 13949995515 | 13962963245 | 13953869760 |
| 85 | 16773978528 | 16766934320 | 16776040301 | 16772317716 |
| 90 | 19909715437 | 19905994815 | 19912856421 | 19909522224 |
| 95 | 23416800942 | 23390466947 | 23412827679 | 23406698523 |
| 100 | 27297397644 | 27297397644 | 27297397644 | 27297397644 |

**Table S5.** Data used to build the diagrams in Figure 8.

| Synthon MW cut-off | Database size |
|---|---|
| 100 | 1619048 |
| 125 | 159135441 |
| 150 | 2880024222 |
| 175 | 16838150263 |
| 200 | 26512675168 |
| 225 | 27163855694 |
| 250 | 27287325628 |
| 275 | 27297397644 |
| 300 | 27297397644 |

| Database member MW | % of the database with the synthon MW cut-off | | | |
|---|---|---|---|---|
| | <100 | <150 | <200 | <300 |
| <150 | 0 | 0 | 0 | 0 |
| 150 | 0.005 | 0.000 | 0.000 | 0.000 |
| 200 | 1.229 | 0.001 | 0.000 | 0.000 |
| 250 | 47.054 | 0.101 | 0.011 | 0.011 |
| 300 | 51.712 | 4.027 | 0.478 | 0.465 |
| 350 | 0 | 37.191 | 6.375 | 6.192 |
| 400 | 0 | 55.673 | 29.960 | 29.120 |
| 450 | 0 | 3.006 | 44.520 | 43.569 |
| 500 | 0 | 0 | 17.388 | 18.227 |
| 550 | 0 | 0 | 1.267 | 2.361 |
| 600 | 0 | 0 | 0.000 | 0.053 |
| >600 | 0 | 0 | 0 | 0.001 |

| Database member LogP | % of the database with the synthon MW cut-off | | | |
|---|---|---|---|---|
| | <100 | <150 | <200 | <300 |
| <–2 | 0.063 | 0.065 | 0.035 | 0.035 |
| –2 | 0.904 | 0.534 | 0.259 | 0.262 |
| –1 | 6.737 | 2.978 | 1.417 | 1.418 |
| 0 | 25.170 | 10.439 | 5.299 | 5.275 |
| 1 | 41.718 | 23.251 | 13.966 | 13.859 |
| 2 | 23.541 | 30.885 | 24.615 | 24.421 |
| 3 | 1.866 | 22.663 | 27.724 | 27.608 |
| 4 | 0 | 8.073 | 18.662 | 18.773 |
| 5 | 0 | 1.075 | 6.780 | 6.986 |
| 6 | 0 | 0.036 | 1.160 | 1.262 |
| >6 | 0 | 0.000 | 0.082 | 0.100 |

## Transparent methods

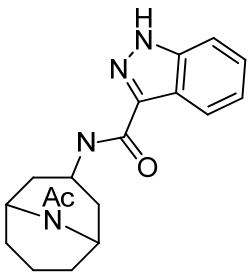
**General.** All chemicals and solvents were obtained from Enamine Ltd. and used without further purification. $^{1}$H, $^{13}$C, and $^{19}$F NMR spectra were acquired on Bruker Advance DRX 400, Bruker Avance DRX 500, and Agilent ProPulse 600 spectrometers using DMSO-$d_6$ as a solvent (unless noted otherwise). Melting points were determined on a Buchi melting point apparatus. LCMS data were recorded on Agilent 1100 HPLC equipped with diode-matrix and mass-selective detector Agilent LC/MSD SL instrument, column: Zorbax SB-C18, 4.6 mm × 15 mm; eluent, A, acetonitrile – water with 0.1% of TFA (95:5), B, water with 0.1% of TFA; flow rate: 1.8 mL/min. Elemental analyses were performed at the Laboratory of Organic Analysis, Department of Chemistry, Kyiv National Taras Shevchenko University.

The transformation of the reagents into the synthons was performed by our proprietary software; this can be also easily done using an open-source software e.g. ChemAxon tools (www.chemaxon.com). Virtual coupling, InChi key generation and duplicate removal, calculation of descriptor values, filtering by physico-chemical parameters and structural features were performed using RDKit (www.rdkit.org) in Python (www.python.org).

Syntheses of the libraries were typically performed in 8 mL vials (Figure S1); loading of the reagents, as well as work-up of the reaction mixtures was performed manually in a parallel fashion. If any of the reagents **1–10** was used as a salt, an additional amount of *i*-$Pr_2$NEt (0.55 mmol per each equivalent of acid was added to the reaction mixture to convert the reagent into a free form at the corresponding step of the procedure indicated by an asterisk (*). The reactions were performed in ultrasonic baths or laboratory ovens with a shaker (Figure S2); up to 1,000 vials could be used simultaneously. Centrifugal evaporators were used to remove the solvents from the vials in a parallel fashion.

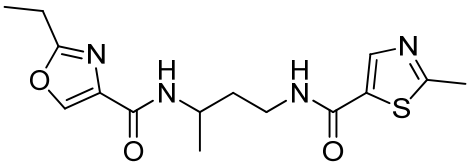
**General procedure for the reaction sequence *A*.** *N*-Boc-diamine **1** (0.5 mmol), carboxylic acid **4** (0.6 mmol), *i*-$Pr_2$NEt (1.25 mmol*), and 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxide hexafluorophosphate (HATU) (0.575 mmol) were mixed in dry DMSO (appr. 1.4 mL). The reaction mixture was sealed and left at ambient temperature for 16 h, then evaporated under reduced pressure. Then the cleavage cocktail containing trifluoroacetic acid, triisopropylsilane, and water (93:5:2) (appr. 2 mL) was added in one portion. The mixture was stirred at ambient temperature for 6 h and evaporated under reduced pressure. The residue was taken up in DMSO (appr. 1.4 mL). Carboxylic acid **5** (0.6 mmol), *i*-$PrNEt_2$ (3 mmol*), and HATU (0.6 mmol) were added in one portion, the reaction mixture was sealed and left at ambient temperature for 16 h, then cooled and evaporated under reduced pressure. The residue was dissolved in DMSO (appr. 1 mL), filtered, analyzed by LCMS, and transferred for the HPLC purification.

***N*-(9-Acetyl-9-azabicyclo[3.3.1]nonan-3-yl)-1*H*-indazole-3-carboxamide (11{*52*,*55*,*23*})**



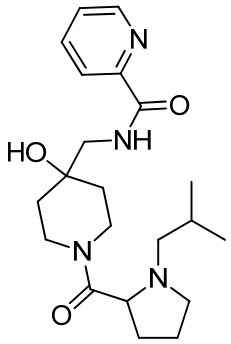
Beige solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 13.56 (s, 1H), 8.24 (d, $J$ = 8.8 Hz, 1H), 8.16 (d, $J$ = 8.1 Hz, 1H), 7.60 (d, $J$ = 8.4 Hz, 1H), 7.40 (t, $J$ = 7.2 Hz, 1H), 7.23 (t, $J$ = 7.5 Hz, 1H), 4.97 – 4.74 (m, 1H), 4.34 – 4.07 (m, 1H), 3.93 – 3.59 (m, 1H), 2.36 – 2.04 (m, 3H), 2.03 (s, 3H), 1.72 – 1.58 (m, 2H), 1.58 – 1.18 (m, 5H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.0, 162.0, 141.6, 138.8, 126.9, 122.4, 122.1, 122.0, 111.1, 47.8, 41.9, 40.9, 32.0, 31.5, 31.0, 21.5, 13.9. LC/MS (CI): *m/z* = 327 $[M+H]^+$. Anal. calcd. for $C_{18}H_{22}N_4O_2$: C 66.24; H 6.79; N 17.17. Found: C 65.89; H 6.97; N 16.96.

**2-Ethyl-*N*-(4-(2-methylthiazole-5-carboxamido)butan-2-yl)oxazole-4-carboxamide (11{*25*,*19*,*9*})**



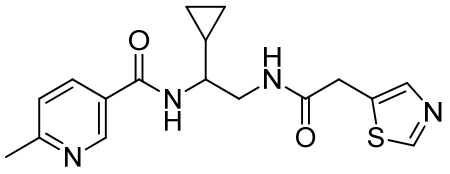
Yellowish oil. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.48 (t, $J$ = 5.5 Hz, 1H), 8.42 (s, 1H), 8.12 (s, 1H), 7.95 (d, $J$ = 8.8 Hz, 1H), 4.07 – 3.98 (m, 1H), 3.28 – 3.20 (m, 1H), 3.19 – 3.12 (m, 1H), 2.76 (q, $J$ = 7.6 Hz, 2H), 2.63 (s, 3H), 1.81 – 1.67 (m, 2H), 1.23 (t, $J$ = 7.6 Hz, 3H), 1.14 (d, $J$ = 6.5 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 169.7, 165.6, 160.2, 160.0, 142.9, 141.7, 136.5, 135.5, 42.9, 37.1, 35.8, 21.4, 20.9, 19.6, 11.4. LC/MS (CI): *m/z* = 337 $[M+H]^+$. Anal. calcd. for $C_{15}H_{20}N_4O_3S$: C 53.56; H 5.99; N 16.65; S 9.53. Found: C 53.80; H 5.91; N 16.65; S 9.32.

***N*-((4-Hydroxy-1-(isobutylprolyl)piperidin-4-yl)methyl)picolinamide (11{*24*,*21*,*10*})**



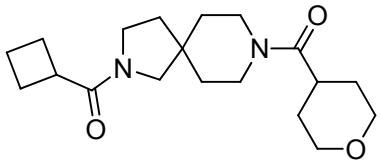
Yellowish solid. The compound existed as a ca. 1:1 mixture of rotamers. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.63 (d, $J$ = 4.7 Hz, 1H), 8.58 (q, $J$ = 7.1, 6.5 Hz, 1H), 8.03 (d, $J$ = 7.6 Hz, 1H), 7.98 (td, $J$ = 7.6, 1.7 Hz, 1H), 7.59 (ddd, $J$ = 6.9, 4.8, 1.5 Hz, 1H), 4.86 (s, 1H), 4.10 – 3.78 (m, 2H), 3.33 (s, 2H), 3.31 – 3.10 (m, 3H), 3.09 – 2.86 (m, 2H), 2.37 – 1.81 (m, 4H), 1.75 – 1.54 (m, 3H), 1.52 – 1.25 (m, 4H), 0.79 (t, $J$ = 6.9 Hz, 3H), 0.74 (d, $J$ = 5.7 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 170.9, 164.3, 150.1, 148.9, 138.3, 127.0, 122.3, 69.4 and 69.3, 67.1 and 66.7, 63.0 and 63.0, 52.9 and 52.8, 49.1, 41.1 and 40.8, 38.2 and 37.9, 35.7 and 35.6, 35.0 and 34.8, 28.4 and 28.3, 27.4, 23.0, 21.5 and 21.4, 21.0. LC/MS (CI): *m/z* = 389 $[M+H]^+$. Anal. calcd. for $C_{21}H_{32}N_4O_3$: C 64.92; H 8.3; N 14.42. Found: C 64.84; H 8.02; N 14.25.

***N*-(1-Cyclopropyl-2-(2-(thiazol-5-yl)acetamido)ethyl)-6-methylnicotinamide (11{*30*,*17*,*13*})**



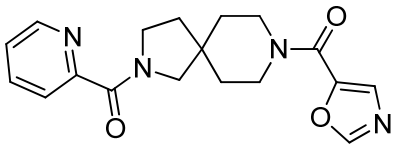
Beige solid. The compound existed as a ca. 3:1 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 9.12 – 8.61 (m, 2H), 8.53 (t, *J* = 5.7 Hz, 0.25H) and 8.35 (d, *J* = 8.3 Hz, 0.75H) and 8.23 (t, *J* = 5.7 Hz, 0.75H) and 8.14 (d, *J* = 8.3 Hz, 0.25H), 8.01 (dd, *J* = 8.1, 2.2 Hz, 0.75H) and 7.96 (dd, *J* = 8.1, 2.2 Hz, 0.25H), 7.64 (s, 0.25H) and 7.62 (s, 0.75H), 7.36 – 7.23 (m, 1H), 3.68 (s, 2H), 3.51 – 3.36 (m, 2H), 3.32 – 3.21 (m, 1H), 2.49 – 2.47 (m, 3H), 0.98 – 0.85 (m, 1H), 0.50 – 0.38 (m, 1H), 0.38 – 0.29 (m, 1H), 0.29 – 0.12 (m, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 169.4 and 168.9, 165.5 and 165.1, 161.0, 154.0, 148.4 and 148.3, 141.9 and 141.8, 135.7 and 135.5, 132.8 and 132.6, 127.8 and 127.8, 123.0 and 122.9, 53.9 and 53.2, 43.7 and 43.2, 33.8 and 33.6, 24.5, 14.1 and 14.0, 3.7, 2.7 and 2.4. LC/MS (CI): *m/z* = 345 $[M+H]^+$. Anal. calcd. for $C_{17}H_{20}N_4O_2S$: C 59.28; H 5.85; N 16.27; S 9.31. Found: C 59.64; H 5.7; N 16.05; S 9.62.

**(2-(Cyclobutanecarbonyl)-2,8-diazaspiro[4.5]decan-8-yl)(tetrahydro-2*H*-pyran-4-yl)methanone (11{*50*,*64*,*26*})**



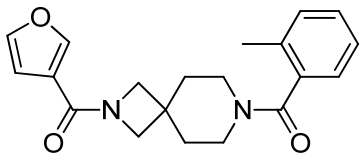
Beige solid. The compound existed as a ca. 1:1 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 3.82 (dt, *J* = 10.7, 3.2 Hz, 2H), 3.61 – 3.33 (m, 8H), 3.26 – 3.15 (m, 3H), 2.86 (ddt, *J* = 11.3, 7.4, 3.6 Hz, 1H), 2.18 – 2.01 (m, 4H), 1.88 (dtd, *J* = 17.4, 8.9, 5.8 Hz, 1H), 1.82 – 1.66 (m, 3H), 1.64 – 1.53 (m, 2H), 1.53 – 1.28 (m, 6H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 172.6 and 172.5, 172.5 and 172.4, 66.8, 55.3, 44.0 and 43.9, 42.8 and 42.6, 41.5, 39.1 and 39.1, 37.9 and 37.6, 36.7, 35.9, 35.4 and 35.1, 34.2 and 34.0, 34.0, 29.5, 24.6, 18.0 and 17.9. LC/MS (CI): *m/z* = 335 $[M+H]^+$. Anal. calcd. for $C_{19}H_{30}N_2O_3$: C 68.23; H 9.04; N 8.38. Found: C 67.86; H 8.77; N 8.41.

**Oxazol-5-yl(2-picolinoyl-2,8-diazaspiro[4.5]decan-8-yl)methanone (11{*50*,*69*,*10*})**



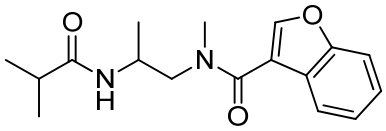
Yellowish oil. The compound existed as a ca. 1:1 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.58 (t, *J* = 4.2 Hz, 1H), 8.53 (s, 0.5H) and 8.50 (s, 0H), 7.93 – 7.89 (m, 0.5H), 7.72 – 7.68 (m, 1H), 7.67 (s, 0.5H) and 7.63 (s, 0.5H), 7.47 (ddd, *J* = 7.9, 4.9, 1.5 Hz, 1H), 3.73 – 3.56 (m, 6H), 3.51 (s, 1H) and 3.45 (s, 1H), 1.86 – 1.80 (m, 2H), 1.66 – 1.45 (m, 5H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 166.3 and 166.2, 157.1 and 154.5, 154.5 and 153.4, 148.6 and 148.5, 144.8 and 144.7, 137.7 and 137.6, 130.3 and 130.2, 125.4 and 123.8, 58.6, 56.3, 47.2, 45.2, 41.8, 39.3, 36.2, 33.1. LC/MS (CI): *m/z* = 341 $[M+H]^+$. Anal. calcd. for $C_{18}H_{20}N_4O_3$: C 63.52; H 5.92; N 16.46. Found: C 63.52; H 6.20; N 16.36.

**(2-(Furan-3-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)(*o*-tolyl)methanone (11{*60*,*73*,*32*})**



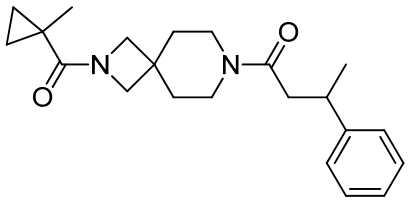
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.10 (s, 1H), 7.73 (d, $J$ = 1.6 Hz, 1H), 7.33 – 7.17 (m, 3H), 7.13 (d, $J$ = 7.5 Hz, 1H), 6.73 – 6.64 (m, 1H), 4.15 – 4.07 (m, 1H), 4.07 – 3.99 (m, 1H), 3.77 – 3.69 (m, 2H), 3.68 – 3.43 (m, 2H), 3.13 – 3.00 (m, 2H), 2.18 (s, 3H), 1.77 (t, $J$ = 5.6 Hz, 2H), 1.67 – 1.53 (m, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.9, 163.2, 145.5, 144.3, 137.0, 134.0, 130.6, 129.0, 126.2, 125.9, 120.8, 110.1, 61.3, 58.0, 43.8, 38.3, 35.5, 34.9, 34.4, 19.0. LC/MS (CI): *m/z* = 339 $[M+H]^+$. Anal. calcd. for $C_{20}H_{22}N_2O_3$: C 70.99; H 6.55; N 8.28. Found: C 71.16; H 6.62; N 8.56.

**_N_-(2-Isobutyramidopropyl)-_N_-methylbenzofuran-3-carboxamide (11{*67*,*81*,*37*})**



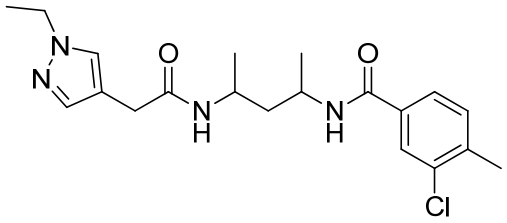
Brownish oil. The compound existed as a ca. 3:2 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.49 (d, $J$ = 1.6 Hz, 0.4H) and 8.44 (d, $J$ = 1.6 Hz, 0.6H), 8.17 (d, $J$ = 8.7 Hz, 0.4H) and 8.08 – 7.99 (m, 1.6H), 7.64 – 7.57 (m, 1H), 7.39 – 7.28 (m, 2H), 4.37 – 4.29 (m, 1H), 3.51 (ddd, $J$ = 13.4, 8.8, 1.6 Hz, 0.6H) and 3.48 – 3.42 (m, 0.4H), 3.30 (dd, $J$ = 5.5, 1.6 Hz, 0.6H) and 3.27 (dd, $J$ = 5.5, 1.6 Hz, 0.4H), 3.03 (d, $J$ = 1.6 Hz, 1.6H) and 3.02 – 2.96 (m, 0.4H) and 2.83 (d, $J$ = 1.6 Hz, 1.2H) and 2.78 – 2.73 (m, 0.6H), 1.17 (dd, $J$ = 6.8, 1.6 Hz, 1.2H) and 1.10 (dd, $J$ = 6.7, 1.6 Hz, 1.8H), 0.97 (dd, $J$ = 6.8, 1.6 Hz, 1.2H) and 0.93 (dd, $J$ = 6.7, 1.6 Hz, 1.8H), 0.86 (dd, $J$ = 6.7, 1.6 Hz, 1.2H) and 0.80 (dd, $J$ = 6.8, 1.6 Hz, 1.8H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 176.8 and 176.6, 162.0 and 161.9, 155.1, 147.7 and 147.5, 125.6 and 125.6, 125.6 and 125.4, 124.2 and 124.1, 122.4 and 122.4, 117.6 and 117.4, 112.0 and 111.9, 54.3 and 52.3, 43.9 and 43.3, 36.0 and 34.6, 29.8 and 29.3, 20.2 and 20.1 and 19.6 and 19.5, 18.5 and 18.3. LC/MS (CI): *m/z* = 303 $[M+H]^+$. Anal. calcd. for $C_{17}H_{22}N_2O_3$: C 67.53; H 7.33; N 9.26. Found: C 67.61; H 7.22; N 8.97.

**1-(2-(1-Methylcyclopropane-1-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-phenylbutan-1-one (11{*60*,*102*,*51*})**



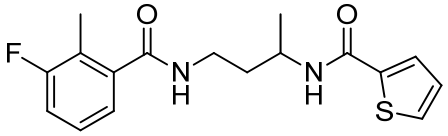
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.32 – 7.19 (m, 4H), 7.18 – 7.09 (m, 1H), 4.10 – 3.88 (m, 2H), 3.67 – 3.33 (m, 5H), 3.19 – 3.12 (m, 1H), 2.59 (dd, $J$ = 17.7, 6.5 Hz, 1H), 2.52 (dd, $J$ = 15.2, 7.8 Hz, 1H), 1.80 – 1.31 (m, 5H), 1.20 (s, 3H), 1.18 (d, $J$ = 7.0 Hz, 3H), 0.90 – 0.79 (m, 2H), 0.48 – 0.38 (m, 2H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 174.5, 169.7, 147.1, 128.7, 127.3, 126.4, 42.7, 40.7, 38.7, 36.5, 35.7, 35.0, 33.9, 22.4, 20.5, 19.2, 14.2. LC/MS (CI): *m/z* = 355 $[M+H]^+$. Anal. calcd. for $C_{22}H_{30}N_2O_2$: C 74.54; H 8.53; N 7.90. Found: C 74.67; H 8.87; N 7.65.

**3-Chloro-_N_-(4-(2-(1-ethyl-1_H_-pyrazol-4-yl)acetamido)pentan-2-yl)-4-methylbenzamide (11{*70*,*84*,*38*})**



Yellowish solid. The compound existed as a ca. 3:2 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.27 (d, $J$ = 8.2 Hz, 0.6H) and 8.20 (d, $J$ = 8.2 Hz, 0.4H), 7.91 – 7.83 (m, 1H), 7.81 (d, $J$ = 8.2 Hz, 0.6H) and 7.74 – 7.64 (m, 1.4H), 7.52 (s, 0.6H) and 7.48 (s, 0.4H), 7.44 – 7.37 (m, 1H), 7.24 (s, 0.6H) and 7.22 (s, 0.4H), 4.20 – 3.97 (m, 3H), 3.83 – 3.74 (m, 1H), 3.16 (s, 1.2H) and 3.14 (s, 0.8H), 2.35 (s, 3H), 1.69 – 1.46 (m, 2H), 1.30 (t, $J$ = 7.3 Hz, 3H), 1.09 (d, $J$ = 6.6 Hz, 3H), 1.02 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 169.9 and 169.9, 164.5 and 164.3, 139.0 and 138.9, 138.6 and 138.6, 134.8 and 134.6, 133.6 and 133.6, 131.5 and 131.4, 128.3, 127.9 and 127.9, 126.5, 115.1 and 115.1, 46.4, 43.4 and 43.0, 43.0 and 42.4, 42.4 and 42.3, 32.1, 21.5 and 21.4 and 21.2 and 21.2, 20.0, 16.0. LC/MS (CI): $m/z$ = 391 $[M+H]^+$. Anal. calcd. for $C_{20}H_{27}ClN_4O_2$: C 61.45; H 6.96; N 14.33; Cl 9.07. Found: C 61.47; H 6.62; N 14.39; Cl 9.02.

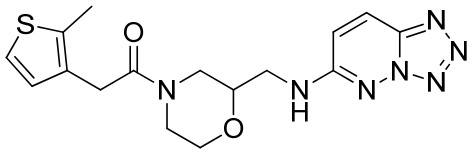
***N*-(4-(3-Fluoro-2-methylbenzamido)butan-2-yl)thiophene-2-carboxamide (11{*83*,*105*,*54*})**



Beige solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.30 (t, $J$ = 5.5 Hz, 1H), 8.26 (d, $J$ = 8.3 Hz, 1H), 7.77 (d, $J$ = 3.6 Hz, 1H), 7.71 (d, $J$ = 4.9 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.22 – 7.16 (m, 1H), 7.16 – 7.04 (m, 2H), 4.11 – 4.01 (m, 1H), 3.30 – 3.18 (m, 2H), 2.19 (d, $J$ = 2.2 Hz, 3H), 1.80 – 1.67 (m, 2H), 1.17 (d, $J$ = 6.6 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.1 (d, $J$ = 3.1 Hz), 161.0 (d, $J$ = 243 Hz), 160.9, 140.8, 140.3 (d, $J$ = 3.8 Hz), 131.0, 128.2, 128.2, 127.6 (d, $J$ = 8.6 Hz), 123.3 (d, $J$ = 3.2 Hz), 122.5 (d, $J$ = 17.7 Hz), 116.1 (d, $J$ = 22.8 Hz), 43.4, 36.9, 36.1, 21.0, 11.5 (d, $J$ = 4.8 Hz). $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –116.9. LC/MS (CI): $m/z$ = 335 $[M+H]^+$. Anal. calcd. for $C_{17}H_{19}FN_2O_2S$: C 61.06; H 5.73; N 8.38; S 9.59. Found: C 60.95; H 6.11; N 8.16; S 9.98.

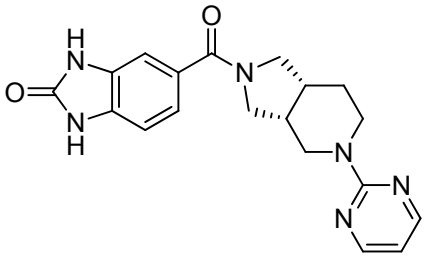
**General procedure for the reaction sequence *B*.** *N*-Boc-diamine **1** (0.5 mmol), carboxylic acid **4** (0.6 mmol), and *i*-$Pr_2NEt$ (1.25 mmol*), and HATU (0.575 mmol) were mixed in dry DMSO (appr. 1.4 mL). The reaction mixture was sealed and left at ambient temperature for 16 h, then evaporated under reduced pressure. Then the cleavage cocktail containing trifluoroacetic acid, triisopropylsilane, and water (93:5:2) (appr. 2 mL) was added in one portion. The mixture was stirred at ambient temperature for 6 h and evaporated under reduced pressure. The residue was taken up in *N*-methyl-2-pyrrolidone (NMP) (appr. 2 mL). Aryl halide **6** (0.6 mmol) and *i*-$PrNEt_2$ (3 mmol*) were added in one portion, the reaction mixture was sealed and heated at 100 °C for 16 h, then cooled and evaporated under reduced pressure. The residue was dissolved in DMSO (appr. 1 mL), filtered, analyzed by LCMS, and transferred for the HPLC purification.

**2-(2-Methylthiophen-3-yl)-1-(2-((tetrazolo[1,5-*b*]pyridazin-6-ylamino)methyl)morpholino)ethanone (12{*140*,*239*,*35*})**



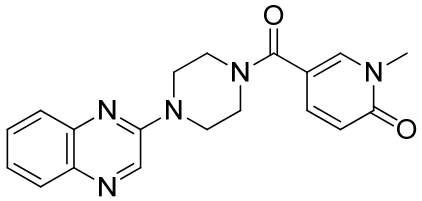
Brownish solid. The compound existed as a *ca.* 1:1 mixture of rotamers. $^{1}$H NMR (600 MHz, DMSO-$d_6$) δ 8.22 (t, *J* = 9.5 Hz, 1H), 8.06 – 7.95 (m, 1H), 7.26 – 7.16 (m, 1H), 7.14 (d, *J* = 5.2 Hz, 0.5H) and 7.05 (d, *J* = 5.2 Hz, 0.5H), 6.77 (dd, *J* = 9.4, 5.2 Hz, 1H), 4.32 (d, *J* = 13.3 Hz, 0.5H) and 4.16 (d, *J* = 13.3 Hz, 0.5H), 3.95 – 3.85 (m, 1H), 3.83 (d, *J* = 11.4 Hz, 0.5H) and 3.76 (d, *J* = 13.3 Hz, 0.5H), 3.65 – 3.32 (m, 6H), 3.16 – 3.10 (m, 0.5H) and 2.95 (dd, *J* = 13.3, 10.3 Hz, 0.5H), 2.72 (dt, *J* = 14.0, 7.1 Hz, 0.5H) and 2.57 – 2.52 (m, 0.5H), 2.28 (s, 1.5H) and 2.28 (s, 1.5H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 169.2 and 169.2, 156.2, 140.5, 134.4 and 134.3, 131.5 and 131.4, 129.7 and 129.5, 123.6, 121.9 and 121.8, 121.2, 73.4, 66.2, 48.7 and 45.8, 44.5 and 43.6, 43.3 and 41.6, 33.2 and 33.1, 13.2. LC/MS (CI): *m/z* = 374 $[M+H]^+$. Anal. calcd. for $C_{16}H_{19}N_7O_2S$: C 51.46; H 5.13; N 26.26; S 8.59. Found: C 51.20; H 5.08; N 26.20; S 8.89.

**_rac_-5-((3a*R*,7a*R*)-5-(Pyrimidin-2-yl)octahydro-1*H*-pyrrolo[3,4-*c*]pyridine-2-carbonyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (12{*17*,*14*,*5*})**



Yellowish solid. The compound existed as a *ca.* 3:2 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 10.79 (s, 1H), 10.70 (d, *J* = 20.3 Hz, 1H), 8.32 (dd, *J* = 16.6, 4.7 Hz, 2H), 7.17 – 7.00 (m, 2H), 6.95 – 6.85 (m, 1H), 6.58 (s, 1H), 4.17 – 3.74 (m, 2H), 3.68 – 3.54 (m, 2H), 3.47 (dd, *J* = 12.0, 7.8 Hz, 1H), 3.25 – 3.15 (m, 1H), 2.45 – 2.30 (m, 2H), 1.82 – 1.69 (m, 0.4H) and 1.68 – 1.41 (m, 1H) and 1.32 – 1.17 (m, 0.6H), 1.03 (d, *J* = 6.1 Hz, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 169.7 and 169.5, 162.0 and 161.9, 158.4, 158.4, 155.8, 131.6 and 131.5, 129.7 and 129.7, 129.6 and 129.4, 120.8 and 120.7, 110.2 and 110.1, 108.3 and 108.1, 108.1, 62.5, 53.9, 50.9 and 47.8, 42.7 and 41.3, 37.5 and 36.7, 35.6 and 34.5, 26.0 and 25.0. LC/MS (CI): *m/z* = 365 $[M+H]^+$. Anal. calcd. for $C_{19}H_{20}N_6O_2$: C 62.62; H 5.53; N 23.06. Found: C 62.69; H 5.23; N 23.24.

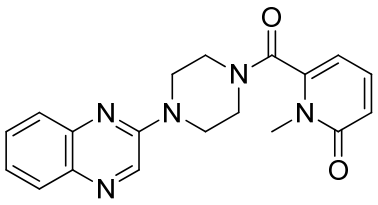
**1-Methyl-5-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (12{*9*,*26*,*3*})**



Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.84 (s, 1H), 8.05 (d, *J* = 2.5 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.71 – 7.59 (m, 2H), 7.55 (dd, *J* = 9.3, 2.5 Hz, 1H), 7.42 (ddd, *J* = 8.2, 6.0, 2.5 Hz, 1H), 6.43 (d, *J* = 9.3 Hz, 1H), 3.85 (dd, *J* = 6.7, 3.8 Hz, 4H), 3.69 (dd, *J* = 6.7, 3.8 Hz, 4H), 3.48 (s, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 166.8, 161.9, 152.3, 141.9, 141.4, 139.5, 137.4,

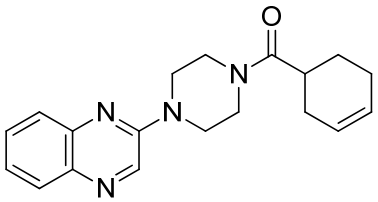
136.8, 130.5, 128.9, 126.5, 125.1, 118.7, 113.2, 44.6, 40.3, 37.6. LC/MS (CI): *m/z* = 350 $[M+H]^+$. Anal. calcd. for $C_{19}H_{19}N_5O_2$: C 65.32; H 5.48; N 20.04. Found: C 64.95; H 5.33; N 19.74.

**1-Methyl-6-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (12{*9*,*27*,*3*})**



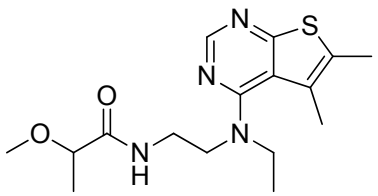
Yellowish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.83 (s, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.45 (dd, *J* = 9.1, 6.8 Hz, 1H), 7.43 – 7.39 (m, 1H), 6.46 (dd, *J* = 9.1, 1.4 Hz, 1H), 6.29 (dd, *J* = 6.8, 1.4 Hz, 1H), 3.96 – 3.88 (m, 2H), 3.86 – 3.73 (m, 4H), 3.53 – 3.43 (m, 2H), 3.32 (s, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 162.4, 161.9, 152.2, 143.8, 141.2, 139.5, 137.4, 136.8, 130.6, 128.8, 126.5, 125.2, 120.2, 104.1, 46.3 and 44.7, 44.1 and 41.4, 33.0. LC/MS (CI): *m/z* = 350 $[M+H]^+$. Anal. calcd. for $C_{19}H_{19}N_5O_2$: C 65.32; H 5.48; N 20.04. Found: C 65.69; H 5.28; N 19.64.

**Cyclohex-3-en-1-yl(4-(quinoxalin-2-yl)piperazin-1-yl)methanone (12{*9*,*28*,*3*})**



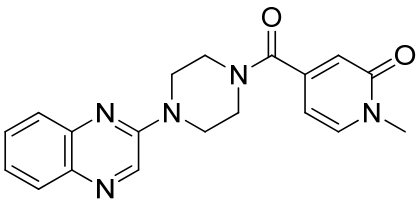
Brownish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.83 (s, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.67 – 7.57 (m, 2H), 7.42 (ddd, *J* = 8.3, 6.2, 2.2 Hz, 1H), 5.77 – 5.63 (m, 2H), 3.88 – 3.74 (m, 4H), 3.72 – 3.58 (m, 4H), 2.93 – 2.80 (m, 1H), 2.24 – 2.01 (m, 4H), 1.77 (dd, *J* = 12.1, 4.7 Hz, 1H), 1.59 – 1.46 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 174.0, 152.3, 141.4, 137.3, 136.8, 130.5, 128.9, 126.9, 126.5, 126.3, 125.0, 45.0 and 44.9, 44.5 and 41.3, 35.7, 28.1, 25.9, 24.8. LC/MS (CI): *m/z* = 323 $[M+H]^+$. Anal. calcd. for $C_{19}H_{22}N_4O$: C 70.78; H 6.88; N 17.38. Found: C 70.99; H 7.03; N 17.44.

***N*-(2-((5,6-Dimethylthieno[2,3-*d*]pyrimidin-4-yl)(ethyl)amino)ethyl)-2-methoxypropanamide (12{*45*,*44*,*24*})**



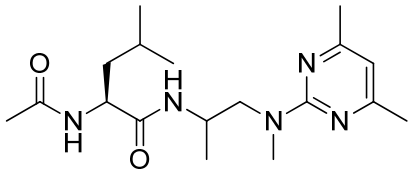
Yellowish oil. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.39 (s, 1H), 7.73 (t, *J* = 5.9 Hz, 1H), 3.56 – 3.48 (m, 3H), 3.42 (qd, *J* = 6.9, 2.3 Hz, 2H), 3.30 – 3.22 (m, 2H), 3.13 (s, 3H), 2.40 (s, 3H), 2.34 (s, 3H), 1.06 (d, *J* = 6.7 Hz, 3H), 1.01 (t, *J* = 6.9 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 172.6, 166.8, 161.7, 151.1, 131.1, 125.4, 121.6, 77.8, 57.2, 48.1, 46.5, 36.6, 18.5, 14.1, 14.0, 12.6. LC/MS (CI): *m/z* = 337 $[M+H]^+$. Anal. calcd. for $C_{16}H_{24}N_4O_2S$: C 57.12; H 7.19; N 16.65; S 9.53. Found: C 57.29; H 7.35; N 16.50; S 9.59.

**1-Methyl-4-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (12{*9*,*48*,*3*})**



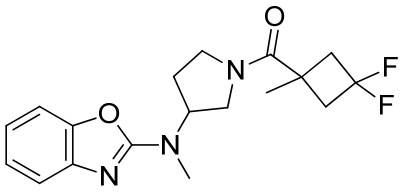
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.81 (s, 1H), 7.83 (d, $J$ = 8.2 Hz, 1H), 7.79 (d, $J$ = 6.8 Hz, 1H), 7.68 – 7.53 (m, 2H), 7.40 (ddd, $J$ = 8.2, 5.8, 2.4 Hz, 1H), 6.38 (d, $J$ = 1.6 Hz, 1H), 6.22 (dt, $J$ = 6.8, 1.6 Hz, 1H), 4.04 – 3.60 (m, 6H), 3.57 – 3.46 (m, 2H), 3.44 (s, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 166.8, 161.9, 152.3, 147.4, 141.3, 141.2, 137.3, 136.7, 130.5, 128.8, 126.5, 125.1, 116.6, 103.5, 46.6 and 44.7, 44.1 and 41.4, 37.3. LC/MS (CI): *m/z* = 350 $[M+H]^+$. Anal. calcd. for $C_{19}H_{19}N_5O_2$: C 65.32; H 5.48; N 20.04. Found: C 65.27; H 5.56; N 19.93.

**(2*S*)-2-Acetamido-*N*-(1-((4,6-dimethylpyrimidin-2-yl)(methyl)amino)propan-2-yl)-4-methylpentanamide (12{*68*,*82*,*32*})**



Beige solid. The compound existed as a *ca.* 11:9 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.89 – 7.79 (m, 1.45H) and 7.67 (d, $J$ = 8.3 Hz, 0.55H), 6.35 (s, 0.45H) and 6.33 (s, 0.55H), 4.20 (q, $J$ = 7.9 Hz, 0.45H) and 4.17 – 4.06 (m, 1.55H), 3.81 – 3.69 (m, 1H), 3.44 (dd, $J$ = 13.7, 5.0 Hz, 0.55H) and 3.39 (dd, $J$ = 13.7, 7.5 Hz, 0.45H), 3.05 (s, 1.35H) and 3.03 (s, 1.65H), 2.24 – 2.18 (m, 6H), 1.80 (s, 1.35H) and 1.78 (s, 1.65H), 1.57 – 1.47 (m, 0.45H) and 1.46 – 1.38 (m, 0.55H), 1.34 (t, $J$ = 7.3 Hz, 1H), 1.19 (ddd, $J$ = 14.7, 10.3, 5.1 Hz, 0.55H) and 1.03 (d, $J$ = 6.6 Hz, 2H) and 0.99 – 0.95 (m, 1.45H), 0.86 (d, $J$ = 6.6 Hz, 1.35H) and 0.81 (d, $J$ = 6.6 Hz, 1.35H) and 0.74 (d, $J$ = 2.6 Hz, 1.65H) and 0.73 (d, $J$ = 2.6 Hz, 1.65H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 172.0 and 171.8, 169.3, 166.7 and 166.7, 162.2 and 162.1, 108.5 and 108.5, 53.4 and 53.2, 51.6 and 51.3, 44.3 and 43.8, 41.6 and 41.4, 36.2 and 35.8, 24.7 and 24.5, 24.3 and 24.3, 23.4 and 23.4, 22.9 and 22.9, 22.2 and 21.9, 18.7 and 18.6. LC/MS (CI): *m/z* = 350 $[M+H]^+$. Anal. calcd. for $C_{18}H_{31}N_5O_2$: C 61.86; H 8.94; N 20.04. Found: C 61.64; H 8.82; N 19.94.

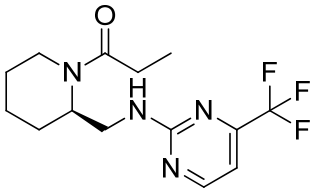
**(3-(Benzo[*d*]oxazol-2-yl(methyl)amino)pyrrolidin-1-yl)(3,3-difluoro-1-methylcyclobutyl)methanone (12{*81*,*39*,*30*})**



Brownish solid. The compound existed as a *ca.* 1:1 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.39 (dd, $J$ = 7.8, 2.5 Hz, 1H), 7.27 (dd, $J$ = 7.8, 2.5 Hz, 1H), 7.16 – 7.10 (m, 1H), 6.99 (t, $J$ = 7.7 Hz, 1H), 4.92 – 4.78 (m, 1H), 3.70 – 3.51 (m, 2H), 3.49 – 3.33 (m, 2H), 3.17 – 2.90 (m, 5H), 2.48 – 2.41 (m, 2H), 2.25 – 2.14 (m, 1H), 2.09 (q, $J$ = 7.7 Hz, 1H), 1.40 (d, $J$ = 10.6 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 172.8 and 172.8, 162.7 and 162.5, 148.7, 143.4 and 143.4, 124.4, 120.8 and 120.8, 116.1 and 116.1, 109.3 and 109.3, 57.3 and 55.0, 48.0 and 47.3, 45.5 and 45.1, 45.0 – 44.0 (m), 33.5 (t, $J$ = 15.3 Hz) and 33.5 (t, $J$ = 15.3 Hz), 31.0 and 30.8, 29.1, 25.8, 23.2. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –83.3 (dd, $J$ = 194, 30.4 Hz), –91.7 (dd,

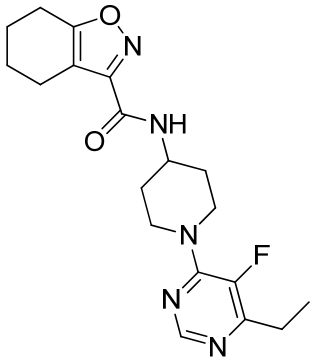
*J* = 194, 17.3 Hz). LC/MS (CI): *m/z* = 350 $[M+H]^+$. Anal. calcd. for $C_{18}H_{21}F_2N_3O_2$: C 61.88; H 6.06; N 12.03. Found: C 61.86; H 5.8; N 12.24.

**(*R*)-1-(2-(((4-(Trifluoromethyl)pyrimidin-2-yl)amino)methyl)piperidin-1-yl)propan-1-one (12{*84*,*40*,*34*})**



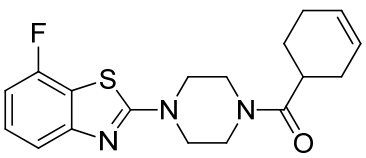
Yellowish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.70 (t, *J* = 6.4 Hz, 1H), 6.88 (d, *J* = 4.8 Hz, 1H), 5.01 – 4.86 (m, 1H), 4.54 (d, *J* = 13.7 Hz, 1H), 3.42 – 3.31 (m, 1H), 3.29 – 3.20 (m, 1H), 3.02 (td, *J* = 14.2, 13.7, 2.6 Hz, 1H), 1.87 (q, *J* = 7.6 Hz, 2H), 1.75 – 1.58 (m, 3H), 1.56 – 1.42 (m, 2H), 1.35 – 1.25 (m, 1H), 0.80 (t, *J* = 7.6 Hz, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 173.2, 161.7, 161.4, 154.9 (q, *J* = 34.6 Hz), 121.1 (q, *J* = 275 Hz), 104.3 (d, *J* = 2.9 Hz), 49.9, 39.0, 37.5, 28.8, 26.0, 25.3, 19.3, 10.2. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –70.0. LC/MS (CI): *m/z* = 317 $[M+H]^+$. Anal. calcd. for $C_{14}H_{19}F_3N_4O$: C 53.16; H 6.05; N 17.71. Found: C 52.90; H 5.91; N 18.09.

***N*-(1-(6-Ethyl-5-fluoropyrimidin-4-yl)piperidin-4-yl)-4,5,6,7-tetrahydrobenzo[*d*]isoxazole-3-carboxamide (12{*79*,*130*,*39*})**



Yellowish oil. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.57 (d, *J* = 8.2 Hz, 1H), 8.27 (d, *J* = 2.5 Hz, 1H), 4.36 (d, *J* = 13.4 Hz, 2H), 4.14 – 3.97 (m, 1H), 3.11 (t, *J* = 12.8 Hz, 2H), 2.70 (t, *J* = 6.3 Hz, 2H), 2.64 (qd, *J* = 7.5, 4.7 Hz, 2H), 2.57 – 2.52 (m, 2H), 1.89 – 1.82 (m, 2H), 1.81 – 1.72 (m, 2H), 1.71 – 1.65 (m, 2H), 1.65 – 1.51 (m, 2H), 1.17 (t, *J* = 7.5 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 170.1, 159.3, 156.1, 156.0 (d, *J* = 15.2 Hz), 152.9 (d, *J* = 9.7 Hz), 151.2 (d, *J* = 4.6 Hz), 144.4 (d, *J* = 257 Hz), 113.0, 46.6, 45.6, 45.5, 31.5, 23.6, 22.4, 22.2, 21.9, 20.0, 12.3. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –146.5. LC/MS (CI): *m/z* = 374 $[M+H]^+$. Anal. calcd. for $C_{19}H_{24}FN_5O_2$: C 61.11; H 6.48; N 18.75. Found: C 61.26; H 6.60; N 18.78.

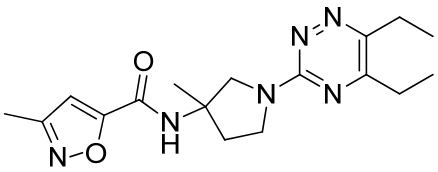
**Cyclohex-3-en-1-yl(4-(7-fluorobenzo[*d*]thiazol-2-yl)piperazin-1-yl)methanone (12{*9*,*28*,*43*})**



Yellowish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 7.38 – 7.29 (m, 2H), 7.02 – 6.93 (m, 1H), 5.73 – 5.63 (m, 2H), 3.73 – 3.53 (m, 8H), 2.92 – 2.79 (m, 1H), 2.22 – 1.99 (m, 4H), 1.83 – 1.70 (m,

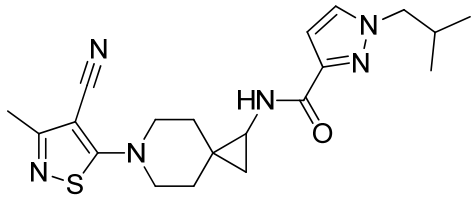
1H), 1.51 (qd, *J* = 12.0, 5.6 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 174.0, 168.7, 156.6 (d, *J* = 245 Hz), 155.8 (d, *J* = 2.7 Hz), 127.8 (d, *J* = 8.0 Hz), 126.9, 126.2, 116.7 (d, *J* = 15.8 Hz), 115.4, 107.8 (d, *J* = 18.7 Hz), 49.0 and 48.5, 44.6 and 40.9, 35.7, 28.1, 25.9, 24.8. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –113.7. LC/MS (CI): *m/z* = 346 $[M+H]^+$. Anal. calcd. for $C_{18}H_{20}FN_3OS$: C 62.59; H 5.84; N 12.16; S 9.28. Found: C 62.36; H 6.05; N 12.29; S 9.35.

**_N_-(1-(5,6-Diethyl-1,2,4-triazin-3-yl)-3-methylpyrrolidin-3-yl)-3-methylisoxazole-5-carboxamide (12{*49*,*150*,*31*})**



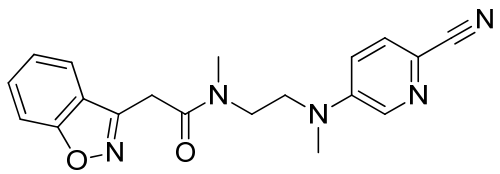
Yellowish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.76 (s, 1H), 6.92 (s, 1H), 4.05 (d, *J* = 11.6 Hz, 1H), 3.78 – 3.47 (m, 3H), 2.76 (q, *J* = 7.4 Hz, 2H), 2.66 (q, *J* = 7.4 Hz, 2H), 2.58 – 2.52 (m, 1H), 2.27 (s, 3H), 2.22 – 1.96 (m, 1H), 1.51 (s, 3H), 1.28 – 1.16 (m, 6H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 163.7, 162.0, 160.8, 159.1, 156.4, 150.6, 107.6, 59.3, 56.8, 44.9, 36.7, 26.5, 24.6, 23.0, 13.2, 11.4, 11.2. LC/MS (CI): *m/z* = 345 $[M+H]^+$. Anal. calcd. for $C_{17}H_{24}N_6O_2$: C 59.28; H 7.02; N 24.4. Found: C 59.68; H 6.97; N 24.11.

**_N_-(6-(4-Cyano-3-methylisothiazol-5-yl)-6-azaspiro[2.5]octan-1-yl)-1-isobutyl-1*H*-pyrazole-3-carboxamide (12{*31*,*29*,*13*})**



Yellowish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.14 (d, *J* = 3.4 Hz, 1H), 7.78 (d, *J* = 1.5 Hz, 1H), 6.63 (d, *J* = 1.5 Hz, 1H), 3.95 (d, *J* = 7.3 Hz, 2H), 3.74 – 3.64 (m, 2H), 3.61 – 3.52 (m, 1H), 3.44 (ddd, *J* = 12.6, 9.0, 3.6 Hz, 1H), 2.69 (dt, *J* = 8.3, 4.2 Hz, 1H), 2.29 (s, 3H), 2.14 (hept, *J* = 6.5 Hz, 1H), 1.74 – 1.61 (m, 2H), 1.52 – 1.41 (m, 2H), 0.90 (t, *J* = 5.1 Hz, 1H), 0.88 – 0.81 (m, 6H), 0.79 (dd, *J* = 8.3, 5.5 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 179.4, 167.9, 163.8, 146.4, 132.5, 116.6, 106.1, 84.9, 59.3, 51.2, 51.0, 33.5, 33.3, 29.6, 28.4, 22.3, 20.1, 20.0, 19.2, 16.5. LC/MS (CI): *m/z* = 399 $[M+H]^+$. Anal. calcd. for $C_{20}H_{26}N_6O_S$: C 60.28; H 6.58; N 21.09; S 8.04. Found: C 60.10; H 6.71; N 21.17; S 8.35.

**2-(Benzo[*d*]isoxazol-3-yl)-*N*-(2-((6-cyanopyridin-3-yl)(methyl)amino)ethyl)-*N*-methylacetamide (12{*2*,*23*,*11*})**

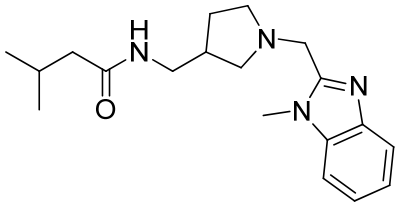


Brownish solid. The compound existed as a *ca.* 3:1 mixture of rotamers. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.27 (d, *J* = 2.9 Hz, 0.25H) and 8.18 (d, *J* = 2.9 Hz, 0.75H), 7.78 – 7.47 (m, 4H), 7.38 – 7.28 (m, 1H), 7.18 (dd, *J* = 9.0, 3.0 Hz, 0.25H) and 7.08 (dd, *J* = 9.0, 3.0 Hz, 0.75H), 4.10 (s, 2H), 3.77 (t, *J* = 6.3 Hz, 0.5H) and 3.66 (t, *J* = 6.3 Hz, 0.5H) and 3.58 (t, *J* = 6.5 Hz, 1.5H)

and 3.48 (t, *J* = 6.5 Hz, 1.5H), 3.14 (s, 2.25H) and 3.06 (s, 0.75H), 2.98 (s, 2.25H) and 2.89 (s, 0.75H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.3 and 167.5, 162.6, 155.0 and 154.8, 147.1 and 146.9, 136.0 and 135.8, 130.5, 129.8 and 129.6, 123.9 and 123.8, 123.1, 122.2 and 122.1, 119.5 and 119.4, 118.3 and 117.8, 117.4 and 117.0, 109.9, 49.4 and 48.4, 47.1 and 45.0, 38.5 and 38.1, 36.6 and 34.1, 30.6 and 30.1. LC/MS (CI): *m/z* = 350 $[M+H]^+$. Anal. calcd. for $C_{19}H_{19}N_5O_2$: C 65.32; H 5.48; N 20.04. Found: C 65.53; H 5.42; N 20.16.

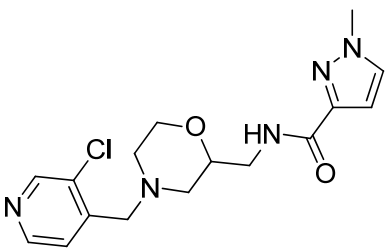
**General procedure for the reaction sequence *C*.** *N*-Boc-diamine **1** (0.5 mmol), carboxylic acid **4** (0.6 mmol), *i*-$Pr_2$NEt (1.25 mmol*), and HATU (0.575 mmol) were mixed in dry DMSO (appr. 1.4 mL). The reaction mixture was sealed and left at ambient temperature for 16 h, then evaporated under reduced pressure. Then the cleavage cocktail containing trifluoroacetic acid, triisopropylsilane, and water (93:5:2) (appr. 2 mL) was added in one portion. The mixture was stirred at ambient temperature for 6 h and evaporated under reduced pressure. The residue was taken up in DMF (appr. 2 mL). Alkylating agent **7** (0.6 mmol) and *i*-PrN$Et_2$ (3 mmol*) were added in one portion, the reaction mixture was sealed and heated at 80 °C for 16 h, then cooled and evaporated under reduced pressure. The residue was dissolved in DMSO (appr. 1 mL), filtered, analyzed by LCMS, and transferred for the HPLC purification.

**3-Methyl-*N*-((1-((1-methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)pyrrolidin-3-yl)methyl)butanamide (13{*125*,*197*,*36*}).**



Brownish oil. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 7.76 (t, *J* = 5.7 Hz, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 3.81 (d, *J* = 2.5 Hz, 2H), 3.79 (s, 3H), 3.02 – 2.93 (m, 2H), 2.57 – 2.50 (m, 2H), 2.46 – 2.42 (m, 1H), 2.26 – 2.18 (m, 2H), 1.91 – 1.85 (m, 3H), 1.84 – 1.77 (m, 1H), 1.39 – 1.32 (m, 1H), 0.79 (d, *J* = 6.3 Hz, 3H), 0.77 (d, *J* = 6.3 Hz, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 171.8, 152.6, 142.3, 136.5, 122.3, 121.6, 119.1, 110.2, 58.0, 53.8, 52.4, 45.2, 43.3, 37.6, 30.2, 28.4, 25.9, 22.7, 22.6. LC/MS (CI): *m/z* = 329 $[M+H]^+$. Anal. calcd. for $C_{19}H_{28}N_4O$: C 69.48; H 8.59; N 17.06. Found: C 69.29; H 8.87; N 17.07.

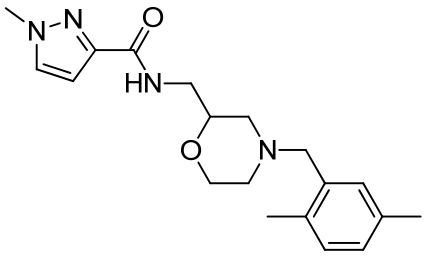
***N*-((4-((3-Chloropyridin-4-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (13{*74*,*107*,*20*})**



Yellowish oil. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.55 (s, 1H), 8.46 (d, *J* = 4.9 Hz, 1H), 7.93 (t, *J* = 6.0 Hz, 1H), 7.73 (d, *J* = 2.3 Hz, 1H), 7.50 (d, *J* = 4.9 Hz, 1H), 6.58 (dt, *J* = 2.3, 1.0 Hz, 1H), 3.86 (s, 3H), 3.79 (d, *J* = 11.3 Hz, 1H), 3.64 – 3.59 (m, 1H), 3.57 (s, 2H), 3.50 (td, *J* = 11.3, 2.5 Hz, 1H), 3.26 (t, *J* = 5.7 Hz, 2H), 2.73 (d, *J* = 11.3 Hz, 1H), 2.59 (d, *J* = 11.3 Hz, 1H), 2.17 (td, *J* = 11.3, 3.2 Hz, 1H), 1.95 (t, *J* = 10.5 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 161.8, 149.2,

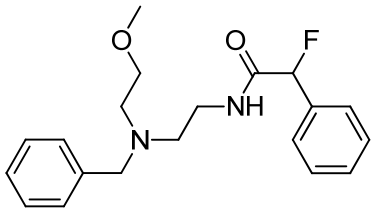
148.5, 146.5, 145.0, 133.0, 131.6, 125.2, 106.4, 74.5, 66.2, 58.2, 56.6, 53.1, 41.5, 39.4. LC/MS (CI): *m/z* = 350/352 $[M+H]^+$. Anal. calcd. for $C_{16}H_{20}ClN_5O_2$: C 54.94; H 5.76; N 20.02; Cl 10.13. Found: C 54.60; H 6.14; N 20.35; Cl 9.80.

**_N_-((4-(2,5-Dimethylbenzyl)morpholin-2-yl)methyl)-1-methyl-1_H_-pyrazole-3-carboxamide (13{*74*,*107*,*21*}).**



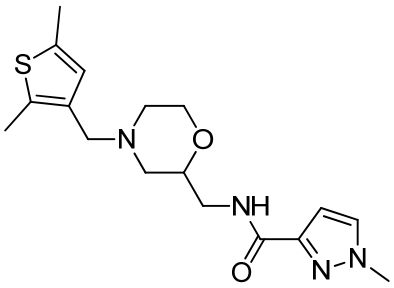
Yellowish oil. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 7.90 (t, *J* = 6.0 Hz, 1H), 7.73 (d, *J* = 2.2 Hz, 1H), 7.06 – 6.96 (m, 2H), 6.92 (d, *J* = 7.7 Hz, 1H), 6.57 (d, *J* = 2.2 Hz, 1H), 3.86 (s, 3H), 3.75 (d, *J* = 11.3 Hz, 1H), 3.57 – 3.50 (m, 1H), 3.47 – 3.33 (m, 3H), 3.24 (t, *J* = 6.2 Hz, 2H), 2.68 (d, *J* = 11.3 Hz, 1H), 2.55 – 2.50 (m, 1H), 2.23 (s, 3H), 2.20 (s, 3H), 2.04 (td, *J* = 11.3, 3.1 Hz, 1H), 1.82 (t, *J* = 10.6 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 161.8, 146.5, 136.0, 134.6, 134.4, 133.0, 130.9, 130.5, 128.0, 106.4, 74.6, 66.3, 61.0, 56.8, 53.2, 41.6, 39.3, 21.1, 18.9. LC/MS (CI): *m/z* = 343 $[M+H]^+$. Anal. calcd. for $C_{19}H_{26}N_4O_2$: C 66.64; H 7.65; N 16.36. Found: C 67.03; H 7.45; N 16.05.

**_N_-(2-(Benzyl(2-methoxyethyl)amino)ethyl)-2-fluoro-2-phenylacetamide (13{*107*,*152*,*23*})**



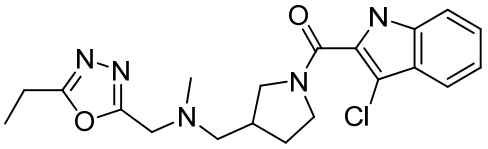
Yellowish oil. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.23 (t, *J* = 5.7 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.41 – 7.35 (m, 3H), 7.32 – 7.23 (m, 4H), 7.23 – 7.18 (m, 1H), 5.84 (d, *J* = 47.8 Hz, 1H), 3.59 (s, 2H), 3.33 (t, *J* = 5.8 Hz, 2H), 3.28 – 3.20 (m, 2H), 3.17 (s, 3H), 2.64 – 2.52 (m, 4H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.0 (d, *J* = 23.0 Hz), 139.9, 136.3 (d, *J* = 19.4 Hz), 129.6 (d, *J* = 2.4 Hz), 129.0, 128.9, 128.5, 127.4 (d, *J* = 5.9 Hz), 127.2, 91.4 (d, *J* = 183 Hz), 70.9, 58.8, 58.5, 53.2, 52.7, 36.9. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –175.2. LC/MS (CI): *m/z* = 345 $[M+H]^+$. Anal. calcd. for $C_{20}H_{25}FN_2O_2$: C 69.74; H 7.32; N 8.13. Found: C 69.47; H 7.39; N 8.50.

**_N_-((4-((2,5-Dimethylthiophen-3-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1_H_-pyrazole-3-carboxamide (13{*74*,*107*,*27*})**



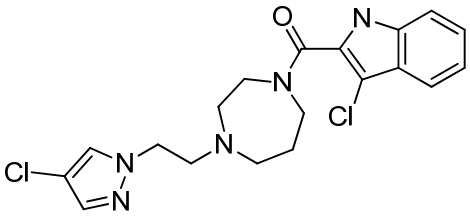
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.91 (t, *J* = 6.1 Hz, 1H), 7.74 (d, *J* = 2.5 Hz, 1H), 6.64 – 6.54 (m, 1H), 6.53 (s, 1H), 3.87 (s, 3H), 3.74 (d, *J* = 11.3 Hz, 1H), 3.51 (ddt, *J* = 8.7, 6.2, 3.7 Hz, 1H), 3.41 (td, *J* = 11.3, 2.5 Hz, 1H), 3.28 – 3.20 (m, 4H), 2.67 (d, *J* = 11.3 Hz, 1H), 2.53 (d, *J* = 11.3 Hz, 1H), 2.29 (s, 3H), 2.24 (s, 3H), 1.98 (td, *J* = 11.3, 3.2 Hz, 1H), 1.76 (t, *J* = 10.6 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 161.8, 146.5, 134.6, 133.8, 133.3, 133.0, 128.4, 106.4, 74.5, 66.3, 56.5, 55.4, 52.9, 41.6, 39.4, 15.2, 13.1. LC/MS (CI): *m/z* = 349 $[M+H]^+$. Anal. calcd. for $C_{17}H_{24}N_4O_2S$: C 58.6; H 6.94; N 16.08; S 9.20. Found: C 58.40; H 7.17; N 16.13; S 9.47.

**(3-Chloro-1*H*-indol-2-yl)(3-((((5-ethyl-1,3,4-oxadiazol-2-yl)methyl)(methyl)amino)methyl)-pyrrolidin-1-yl)methanone (13{*44*,*129*,*33*})**



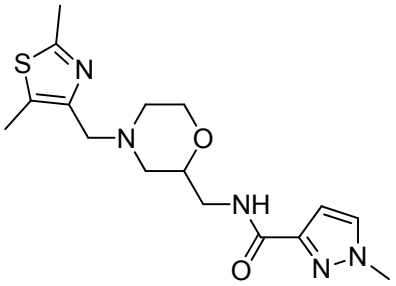
Yellowish oil. The compound existed as a ca. 11:9 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 11.83 (s, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.36 (m, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.17 – 7.10 (m, 1H), 3.82 (s, 0.95H) and 3.72 (s, 1.1H), 3.65 – 3.46 (m, 3H), 3.27 – 3.20 (m, 1H), 2.83 (q, *J* = 7.7 Hz, 0.9H) and 2.71 (q, *J* = 7.7 Hz, 1.1H), 2.47 – 2.29 (m, 3H), 2.27 (s, 1.35H) and 2.17 (s, 1.65H), 2.04 – 1.91 (m, 1H), 1.63 – 1.54 (m, 1H), 1.24 (t, *J* = 7.7 Hz, 1.35H) and 1.15 (t, *J* = 7.7 Hz, 1.65H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.4 and 168.3, 164.1 and 164.0, 161.0 and 160.9, 134.8, 129.2 and 129.1, 124.8, 124.4, 121.0, 118.4, 112.9, 103.2 and 103.1, 59.3 and 58.8, 52.1 and 51.0, 50.9 and 50.4, 47.2 and 45.6, 42.5, 37.1 and 35.4, 29.9 and 28.2, 18.8 and 18.7, 10.9 and 10.8. LC/MS (CI): *m/z* = 402/404 $[M+H]^+$. Anal. calcd. for $C_{20}H_{24}ClN_5O_2$: C 59.77; H 6.02; N 17.43; Cl 8.82. Found: C 59.95; H 5.71; N 17.12; Cl 8.47.

**(3-Chloro-1*H*-indol-2-yl)(4-(2-(4-chloro-1*H*-pyrazol-1-yl)ethyl)-1,4-diazepan-1-yl)methanone (13{*23*,*129*,*34*})**



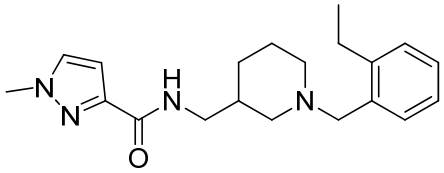
Yellowish oil. The compound existed as a ca. 1:1 mixture of rotamers.$^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 11.88 (s, 1H), 7.97 (s, 0.5H) and 7.87 (s, 0.5H) and 7.61 – 7.41 (m, 2H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 4.16 (t, *J* = 6.5 Hz, 1H) and 4.08 (t, *J* = 6.5 Hz, 1H), 3.68 – 3.55 (m, 2H), 3.54 – 3.43 (m, 2H), 2.86 (t, *J* = 6.5 Hz, 1H) and 2.84 – 2.73 (m, 2H) and 2.71 – 2.62 (m, 2H) and 2.62 – 2.55 (m, 1H), 1.86 – 1.77 (m, 1H) and 1.70 – 1.60 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 162.6, 137.1, 134.8, 128.9, 128.8, 128.8, 124.6, 124.1, 120.9, 118.2, 112.9, 108.0, 56.3 and 55.7, 55.2 and 55.0, 53.9 and 53.8, 50.7, 49.3 and 47.6, 45.9 and 44.9, 28.5 and 26.7. LC/MS (CI): *m/z* = 406/408 $[M+H]^+$. Anal. calcd. for $C_{19}H_{21}Cl_2N_5O$: C 56.17; H 5.21; N 17.24; Cl 17.45. Found: C 56.21; H 5.58; N 17.12; Cl 17.35.

***N*-((4-((2,5-Dimethylthiazol-4-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (13{*74*,*107*,*35*})**



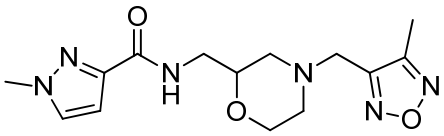
Brownish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.91 (t, $J$ = 5.3 Hz, 1H), 7.74 (t, $J$ = 2.3 Hz, 1H), 6.58 (q, $J$ = 2.3 Hz, 1H), 3.87 (s, 3H), 3.76 – 3.71 (m, 1H), 3.55 – 3.48 (m, 1H), 3.45 – 3.35 (m, 4H), 3.26 – 3.19 (m, 2H), 2.72 – 2.66 (m, 1H), 2.60 – 2.54 (m, 1H), 2.49 – 2.46 (m, 2H), 2.31 (s, 3H), 2.07 (t, $J$ = 11.0 Hz, 1H), 1.83 (t, $J$ = 10.3 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 161.8, 160.9, 147.7, 146.6, 133.0, 130.1, 106.4, 74.5, 66.3, 56.4, 55.5, 52.9, 41.6, 39.4, 19.0, 11.4. LC/MS (CI): $m/z$ = 350 $[M+H]^+$. Anal. calcd. for $C_{16}H_{23}N_5O_2S$: C 54.99; H 6.63; N 20.04; S 9.17. Found: C 55.01; H 6.41; N 19.89; S 9.53.

**_N_-((1-(2-Ethylbenzyl)piperidin-3-yl)methyl)-1-methyl-1_H_-pyrazole-3-carboxamide (13{*102*,*107*,*29*})**



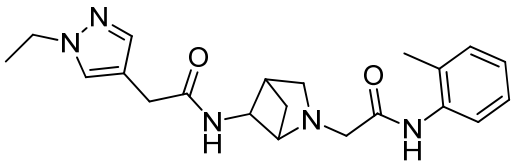
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.01 (t, $J$ = 6.2 Hz, 1H), 7.72 (d, $J$ = 2.2 Hz, 1H), 7.19 (d, $J$ = 7.5 Hz, 1H), 7.17 – 7.10 (m, 2H), 7.07 (td, $J$ = 6.9, 2.5 Hz, 1H), 6.55 (d, $J$ = 1.7 Hz, 1H), 3.95 – 3.77 (m, 3H), 3.44 – 3.34 (m, 2H), 3.13 – 3.02 (m, 2H), 2.75 – 2.67 (m, 1H), 2.64 (q, $J$ = 7.5 Hz, 2H), 2.60 – 2.53 (m, 1H), 1.90 (t, $J$ = 10.9 Hz, 1H), 1.80 – 1.70 (m, 2H), 1.64 – 1.54 (m, 2H), 1.38 – 1.29 (m, 1H), 1.12 (t, $J$ = 7.5 Hz, 3H), 0.98 – 0.88 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 161.8, 146.9, 143.4, 136.5, 132.9, 130.2, 128.8, 127.5, 125.7, 106.3, 60.9, 58.5, 54.2, 42.6, 39.3, 36.8, 28.6, 25.2, 24.9, 15.8. LC/MS (CI): $m/z$ = 341 $[M+H]^+$. Anal. calcd. for $C_{20}H_{28}N_4O$: C 70.56; H 8.29; N 16.46. Found: C 70.80; H 7.94; N 16.15.

**1-Methyl-_N_-((4-((4-methyl-1,2,5-oxadiazol-3-yl)methyl)morpholin-2-yl)methyl)-1_H_-pyrazole-3-carboxamide (13{*74*,*107*,*38*})**



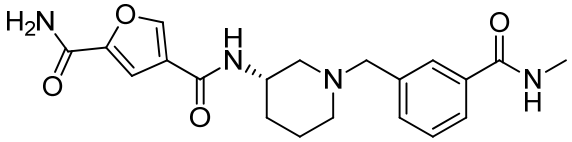
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.95 (t, $J$ = 6.0 Hz, 1H), 7.74 (d, $J$ = 1.8 Hz, 1H), 6.57 (d, $J$ = 1.8 Hz, 1H), 3.87 (s, 3H), 3.79 – 3.72 (m, 1H), 3.70 (s, 2H), 3.59 – 3.49 (m, 1H), 3.43 (td, $J$ = 11.4, 2.1 Hz, 1H), 3.25 (t, $J$ = 6.1 Hz, 2H), 2.74 – 2.63 (m, 1H), 2.58 – 2.51 (m, 1H), 2.36 (s, 3H), 2.14 (td, $J$ = 11.2, 3.2 Hz, 1H), 1.92 (t, $J$ = 10.5 Hz, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 161.7, 152.4, 152.4, 146.4, 133.0, 106.4, 74.4, 66.1, 56.2, 52.7, 50.0, 41.3, 39.3, 8.4. LC/MS (CI): $m/z$ = 321 $[M+H]^+$. Anal. calcd. for $C_{14}H_{20}N_6O_3$: C 52.49; H 6.29; N 26.23. Found: C 52.83; H 6.22; N 26.56.

**2-(1-Ethyl-1_H_-pyrazol-4-yl)-_N_-(2-(2-oxo-2-(_o_-tolylamino)ethyl)-2-azabicyclo[2.1.1]hexan-5-yl)acetamide (13{*7*,*7*,*1*})**



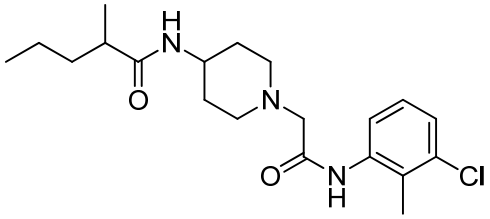
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 9.58 (s, 1H), 7.94 (d, $J$ = 7.6 Hz, 1H), 7.55 (d, $J$ = 7.9 Hz, 1H), 7.50 (s, 1H), 7.36 – 7.21 (m, 2H), 7.19 (t, $J$ = 7.6 Hz, 1H), 7.09 (t, $J$ = 7.4 Hz, 1H), 4.03 (q, $J$ = 7.3 Hz, 2H), 3.85 – 3.77 (m, 1H), 3.46 – 3.39 (m, 2H), 3.31 – 3.24 (m, 3H), 3.12 (d, $J$ = 8.4 Hz, 1H), 2.68 – 2.61 (m, 1H), 2.34 (d, $J$ = 8.4 Hz, 1H), 2.20 (s, 3H), 1.31 (t, $J$ = 7.3 Hz, 3H), 1.28 (s, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 170.8, 169.4, 138.6, 136.5, 131.8, 130.7, 128.4, 126.6, 125.6, 125.0, 114.8, 66.1, 58.9, 52.9, 52.6, 46.4, 43.1, 31.5, 28.7, 18.1, 16.0. LC/MS (CI): $m/z$ = 382 $[M+H]^+$. Anal. calcd. for $C_{21}H_{27}N_5O_2$: C 66.12; H 7.13; N 18.36. Found: C 66.18; H 6.91; N 18.38.

**(*S*)-*N*$^4$-(1-(3-(Methylcarbamoyl)benzyl)piperidin-3-yl)furan-2,4-dicarboxamide (13{*139*,*243*,*50*})**



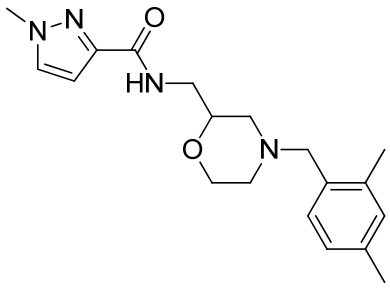
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.39 (q, $J$ = 4.4 Hz, 1H), 8.24 (s, 1H), 8.01 (d, $J$ = 7.9 Hz, 1H), 7.85 (s, 1H), 7.74 (s, 1H), 7.71 – 7.66 (m, 1H), 7.46 (s, 1H), 7.44 – 7.39 (m, 2H), 7.37 (t, $J$ = 7.5 Hz, 1H), 3.91 – 3.82 (m, 1H), 3.51 (s, 2H), 2.84 – 2.78 (m, 1H), 2.76 (d, $J$ = 4.4 Hz, 3H), 2.70 – 2.65 (m, 1H), 1.90 (t, $J$ = 10.7 Hz, 1H), 1.83 (t, $J$ = 10.2 Hz, 1H), 1.80 – 1.74 (m, 1H), 1.70 – 1.62 (m, 1H), 1.54 – 1.45 (m, 1H), 1.25 (qd, $J$ = 11.9, 4.0 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 167.1, 160.7, 159.4, 148.8, 146.8, 138.8, 134.9, 131.9, 128.5, 128.0, 126.1, 124.6, 112.8, 62.3, 58.5, 53.2, 46.4, 30.3, 26.7, 24.3. LC/MS (CI): $m/z$ = 385 $[M+H]^+$. Anal. calcd. for $C_{20}H_{24}N_4O_4$: C 62.49; H 6.29; N 14.57. Found: C 62.30; H 5.97; N 14.95.

***N*-(1-(2-((3-Chloro-2-methylphenyl)amino)-2-oxoethyl)piperidin-4-yl)-2-methylpentanamide (13{*79*,*95*,*11*})**



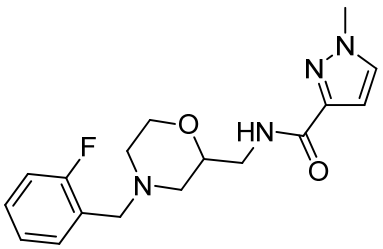
Beige solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 9.53 (s, 1H), 7.75 – 7.58 (m, 2H), 7.28 – 7.12 (m, 2H), 3.59 – 3.49 (m, 1H), 3.10 (s, 2H), 2.91 – 2.74 (m, 2H), 2.42 – 2.04 (m, 6H), 1.81 – 1.63 (m, 2H), 1.58 – 1.36 (m, 3H), 1.30 – 1.09 (m, 3H), 0.94 (d, $J$ = 6.7 Hz, 3H), 0.83 (t, $J$ = 6.8 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 175.3, 168.9, 138.1, 134.0, 128.1, 127.5, 125.6, 122.3, 62.1, 52.8, 45.6, 39.7, 36.6, 32.3, 32.1, 20.5, 18.4, 14.9, 14.4. LC/MS (CI): $m/z$ = 380 $[M+H]^+$. Anal. calcd. for $C_{20}H_{30}ClN_3O_2$: C 63.23; H 7.96; N 11.06; Cl 9.33. Found: C 63.4; H 7.92; N 10.70; Cl 8.97.

***N*-((4-(2,4-Dimethylbenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (13{*74*,*107*,*12*})**



Yellowish oil. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 7.91 (t, *J* = 6.0 Hz, 1H), 7.73 (d, *J* = 2.2 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.93 (s, 1H), 6.91 – 6.87 (m, 1H), 6.63 – 6.50 (m, 1H), 3.86 (d, *J* = 1.0 Hz, 3H), 3.77 – 3.72 (m, 1H), 3.54 – 3.49 (m, 1H), 3.40 (td, *J* = 11.2, 2.5 Hz, 1H), 3.36 – 3.33 (m, 2H), 3.23 (td, *J* = 6.2, 2.5 Hz, 2H), 2.66 (d, *J* = 11.2 Hz, 1H), 2.51 (d, *J* = 3.2 Hz, 1H), 2.20 (s, 3H), 2.02 (td, *J* = 11.3, 3.2 Hz, 1H), 1.80 (t, *J* = 10.6 Hz, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 161.7, 146.5, 137.4, 136.4, 133.2, 133.0, 131.3, 130.2, 126.3, 106.3, 74.5, 66.3, 60.7, 56.7, 53.1, 41.5, 39.3, 21.0, 19.2. LC/MS (CI): *m/z* = 343 $[M+H]^+$. Anal. calcd. for $C_{19}H_{26}N_4O_2$: C 66.64; H 7.65; N 16.36. Found: C 66.76; H 7.99; N 16.46.

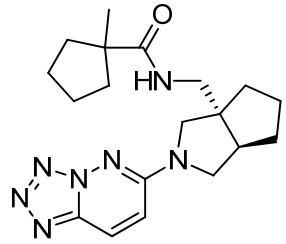
**_N_-((4-(2-Fluorobenzyl)morpholin-2-yl)methyl)-1-methyl-1_H_-pyrazole-3-carboxamide (13{*74*,*107*,*25*})**



Brownish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 7.91 (t, *J* = 6.0 Hz, 1H), 7.73 (d, *J* = 2.2 Hz, 1H), 7.38 (td, *J* = 7.7, 1.8 Hz, 1H), 7.33 – 7.25 (m, 1H), 7.19 – 7.08 (m, 2H), 6.66 – 6.53 (m, 1H), 3.86 (s, 3H), 3.79 – 3.70 (m, 1H), 3.61 – 3.37 (m, 4H), 3.23 (td, *J* = 6.2, 2.3 Hz, 2H), 2.71 (d, *J* = 11.3 Hz, 1H), 2.56 (d, *J* = 11.3 Hz, 1H), 2.06 (td, *J* = 11.3, 3.2 Hz, 1H), 1.84 (t, *J* = 10.6 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 161.7, 161.2 (d, *J* = 245 Hz), 146.5, 133.0, 132.0 (d, *J* = 4.6 Hz), 129.6 (d, *J* = 8.3 Hz), 124.6 (d, *J* = 14.5 Hz), 124.6 (d, *J* = 3.4 Hz), 115.6 (d, *J* = 21.9 Hz), 106.3, 74.5, 66.2, 56.4, 55.3, 52.8, 41.5, 39.3. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –118.6. LC/MS (CI): *m/z* = 333 $[M+H]^+$. Anal. calcd. for $C_{17}H_{21}FN_4O_2$: C 61.43; H 6.37; N 16.86. Found: C 61.60; H 6.62; N 16.65.

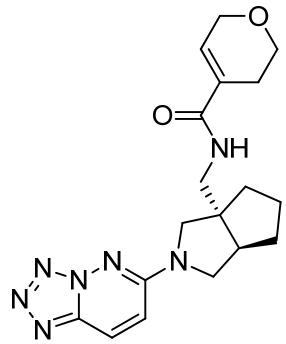
**General procedure for the reaction sequence *D*.** *N*-Boc-diamine **1** (0.5 mmol), aryll halide **6** (0.6 mmol), and *i*-$Pr_2NEt$ (1.25 mmol*), were mixed in dry NMP (appr. 2 mL). The reaction mixture was sealed and heated at 100 °C for 16 h, then evaporated under reduced pressure. Then the cleavage cocktail containing trifluoroacetic acid, triisopropylsilane, and water (93:5:2) (appr. 2 mL) was added in one portion. The mixture was stirred at ambient temperature for 6 h and evaporated under reduced pressure. The residue was taken up in DMSO (appr. 1.4 mL). Carboxylic acid **5** (0.6 mmol), *i*-$PrNEt_2$ (3 mmol*), and HATU (0.6 mmol) were added in one portion, the reaction mixture was sealed and left at ambient temperature for 16 h, then cooled and evaporated under reduced pressure. The residue was dissolved in DMSO (appr. 1 mL), filtered, analyzed by LCMS, and transferred for the HPLC purification.

***rac*-1-Methyl-*N*-(((3*aR*,6*aS*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3*a*(1*H*)-yl)methyl)cyclopentane-1-carboxamide (14{*19*,*35*,*360*})**



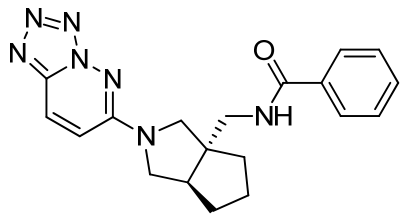
Brownish solid. $^{1}$H NMR (600 MHz, DMSO-$d_6$) δ 8.32 (d, $J$ = 9.9 Hz, 1H), 7.62 (t, $J$ = 6.3 Hz, 1H), 7.32 (d, $J$ = 9.9 Hz, 1H), 3.79 – 3.70 (m, 1H), 3.66 (d, $J$ = 11.6 Hz, 1H), 3.32 – 3.26 (m, 3H), 3.12 (dd, $J$ = 13.5, 5.9 Hz, 1H), 2.55 – 2.50 (m, 1H), 1.95 – 1.84 (m, 3H), 1.73 – 1.55 (m, 4H), 1.54 – 1.39 (m, 5H), 1.38 – 1.22 (m, 2H), 1.08 (s, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 178.3, 154.5, 140.0, 123.6, 119.3, 56.5, 55.8, 53.8, 50.1, 45.6, 45.2, 37.5, 37.4, 35.2, 32.2, 25.6, 24.5, 24.5. LC/MS (CI): $m/z$ = 370 $[M+H]^+$. Anal. calcd. for $C_{19}H_{27}N_7O$: C 61.77; H 7.37; N 26.54. Found: C 62.11; H 7.24; N 26.69.

**_rac_-_N_-(((3a_R_,6a_S_)-2-(Tetrazolo[1,5-_b_]pyridazin-6-yl)hexahydrocyclopenta[_c_]pyrrol-3a(1_H_)-yl)methyl)-3,6-dihydro-2_H_-pyran-4-carboxamide (14{_19_,_35_,_361_})**



Brownish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.34 (d, $J$ = 9.9 Hz, 1H), 7.99 (t, $J$ = 6.2 Hz, 1H), 7.35 (d, $J$ = 9.7 Hz, 1H), 6.51 (s, 1H), 4.18 – 4.03 (m, 2H), 3.78 (t, $J$ = 9.8 Hz, 1H), 3.70 – 3.59 (m, 3H), 3.48 – 3.37 (m, 2H), 3.25 (dd, $J$ = 13.5, 6.0 Hz, 1H), 2.57 – 2.51 (m, 2H), 2.25 – 2.14 (m, 2H), 1.95 – 1.84 (m, 1H), 1.77 – 1.60 (m, 4H), 1.56 – 1.49 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 167.4, 154.6, 140.0, 131.3, 131.1, 123.7, 119.3, 64.7, 63.6, 56.5, 55.8, 53.7, 45.7, 45.0, 35.1, 31.9, 24.8, 24.4. LC/MS (CI): $m/z$ = 370 $[M+H]^+$. Anal. calcd. for $C_{18}H_{23}N_7O_2$: C 58.52; H 6.28; N 26.54. Found: C 58.61; H 6.13; N 26.42.

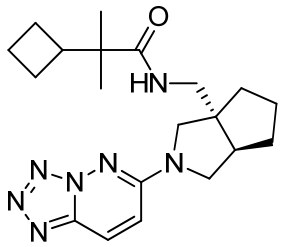
**_rac_-_N_-(((3a_R_,6a_S_)-2-(Tetrazolo[1,5-_b_]pyridazin-6-yl)hexahydrocyclopenta[_c_]pyrrol-3a(1_H_)-yl)methyl)benzamide (14{_19_,_35_,_367_})**



Yellowish solid. $^{1}$H NMR (600 MHz, DMSO-$d_6$) δ 8.58 (t, $J$ = 6.3 Hz, 1H), 8.30 (d, $J$ = 9.8 Hz, 1H), 7.87 – 7.71 (m, 2H), 7.46 (t, $J$ = 7.4 Hz, 1H), 7.39 (t, $J$ = 7.4 Hz, 2H), 7.32 (d, $J$ = 10.1 Hz, 1H), 3.84 – 3.76 (m, 1H), 3.74 (d, $J$ = 11.6 Hz, 1H), 3.49 – 3.35 (m, 4H), 2.59 (tt, $J$ = 8.5, 4.8 Hz, 1H), 1.96 – 1.88 (m, 1H), 1.86 – 1.72 (m, 2H), 1.71 – 1.59 (m, 2H), 1.56 – 1.48 (m, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 167.5, 154.6, 140.0, 135.0, 131.6, 128.6, 127.7, 123.6, 119.3,

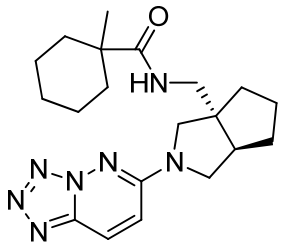
56.5, 55.8, 53.7, 45.7, 45.4, 35.2, 31.9, 24.4. LC/MS (CI): *m/z* = 364 $[M+H]^+$. Anal. calcd. for $C_{19}H_{21}N_7O$: C 62.79; H 5.82; N 26.98. Found: C 63.02; H 5.99; N 27.26.

**_rac_-2-Cyclobutyl-2-methyl-_N_-(((3a_R_,6a_S_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)hexahydrocyclopenta[_c_]pyrrol-3a(1_H_)-yl)methyl)propanamide (14{_19_,_35_,_369_})**



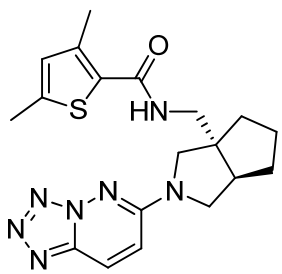
Brownish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.33 (d, *J* = 9.9 Hz, 1H), 7.43 (t, *J* = 6.3 Hz, 1H), 7.32 (d, *J* = 9.9 Hz, 1H), 3.73 (dd, *J* = 11.1, 8.3 Hz, 1H), 3.64 (d, *J* = 11.6 Hz, 1H), 3.31 – 3.29 (m, 1H), 3.26 (dd, *J* = 13.5, 6.6 Hz, 1H), 3.11 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.51 (td, *J* = 8.3, 4.2 Hz, 1H), 2.44 (d, *J* = 8.9 Hz, 1H), 1.91 – 1.83 (m, 1H), 1.83 – 1.50 (m, 10H), 1.51 – 1.26 (m, 2H), 0.93 (s, 3H), 0.92 (s, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 177.1, 154.5, 140.0, 123.7, 119.2, 56.5, 55.8, 53.8, 45.5, 44.9, 43.7, 43.3, 35.2, 32.0, 24.4, 23.4, 23.3, 22.1, 22.1, 16.9. LC/MS (CI): *m/z* = 384 $[M+H]^+$. Anal. calcd. for $C_{20}H_{29}N_7O$: C 62.64; H 7.62; N 25.57. Found: C 62.93; H 7.43; N 25.31.

**_rac_-1-Methyl-_N_-(((3a_R_,6a_S_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)hexahydrocyclopenta[_c_]pyrrol-3a(1_H_)-yl)methyl)cyclohexane-1-carboxamide (14{19,35,373})**



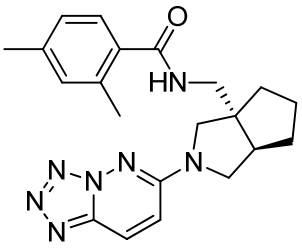
Brownish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.32 (d, *J* = 9.8 Hz, 1H), 7.59 (t, *J* = 6.3 Hz, 1H), 7.32 (d, *J* = 9.8 Hz, 1H), 3.75 (t, *J* = 9.6 Hz, 1H), 3.68 (d, *J* = 11.6 Hz, 1H), 3.38 – 3.34 (m, 1H), 3.32 – 3.26 (m, 2H), 3.11 (dd, *J* = 13.5, 5.8 Hz, 1H), 2.54 (tt, *J* = 8.5, 4.6 Hz, 1H), 1.96 – 1.82 (m, 3H), 1.74 – 1.56 (m, 4H), 1.52 – 1.45 (m, 1H), 1.40 – 1.31 (m, 2H), 1.27 – 1.04 (m, 6H), 0.95 (s, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 177.5, 154.5, 139.9, 123.7, 119.2, 56.6, 55.9, 53.8, 45.6, 45.1, 42.6, 35.5, 35.4, 32.2, 27.2, 25.8, 24.5, 23.1. LC/MS (CI): *m/z* = 384 $[M+H]^+$. Anal. calcd. for $C_{20}H_{29}N_7O$: C 62.64; H 7.62; N 25.57. Found: C 62.77; H 7.37; N 25.52.

**_rac_-3,5-Dimethyl-_N_-(((3a_R_,6a_S_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)octahydrocyclopenta[_c_]-pyrrol-3a-yl)methyl)thiophene-2-carboxamide (14{_19_,_35_,_375_})**



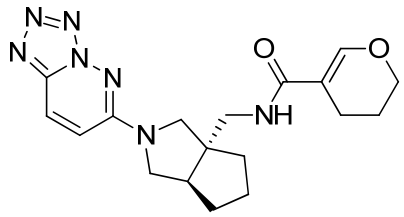
Brownish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.31 (d, *J* = 9.9 Hz, 1H), 7.94 (t, *J* = 6.3 Hz, 1H), 7.33 (d, *J* = 9.8 Hz, 1H), 6.58 (s, 1H), 3.78 (dd, *J* = 11.2, 8.1 Hz, 1H), 3.71 (d, *J* = 11.5 Hz, 1H), 3.45 – 3.34 (m, 3H), 3.32 – 3.28 (m, 1H), 2.56 (tt, *J* = 8.4, 4.9 Hz, 1H), 2.32 (s, 3H), 2.25 (s, 3H), 1.95 – 1.87 (m, 1H), 1.81 – 1.58 (m, 4H), 1.54 – 1.47 (m, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 163.4, 154.6, 140.9, 140.2, 140.0, 130.5, 129.5, 123.6, 119.3, 56.5, 55.7, 53.8, 45.7, 45.3, 35.3, 32.1, 24.5, 15.7, 15.3. LC/MS (CI): *m/z* = 398 $[M+H]^+$. Anal. calcd. for $C_{19}H_{23}N_7OS$: C 57.41; H 5.83; N 24.67; S 8.07. Found: C 57.16; H 5.53; N 24.47; S 8.13.

**_rac_-2,4-Dimethyl-_N_-(((3a_R_,6a_S_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)octahydrocyclopenta[_c_]-pyrrol-3a-yl)methyl)benzamide (14{_19_,_35_,_377_})**



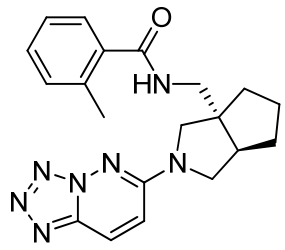
Brownish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.36 (t, *J* = 6.3 Hz, 1H), 8.33 (d, *J* = 9.9 Hz, 1H), 7.34 (d, *J* = 9.9 Hz, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.99 (s, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 3.86 – 3.76 (m, 1H), 3.73 (d, *J* = 11.6 Hz, 1H), 3.43 – 3.36 (m, 3H), 3.32 – 3.28 (m, 1H), 2.58 (tt, *J* = 8.5, 4.7 Hz, 1H), 2.23 (s, 6H), 1.95 – 1.86 (m, 1H), 1.79 – 1.71 (m, 2H), 1.71 – 1.63 (m, 2H), 1.57 – 1.48 (m, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 170.2, 154.6, 140.0, 139.1, 135.5, 134.8, 131.4, 127.5, 126.3, 123.7, 119.3, 56.6, 55.6, 53.8, 45.7, 45.3, 35.4, 32.1, 24.5, 21.2, 19.8. LC/MS (CI): *m/z* = 392 $[M+H]^+$. Anal. calcd. for $C_{21}H_{25}N7O$: C 64.43; H 6.44; N 25.05. Found: C 64.66; H 6.12; N 24.75.

**_N_-(((3a_S_,6a_R_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)octahydrocyclopenta[_c_]pyrrol-3a-yl)methyl)-3,4-dihydro-2_H_-pyran-5-carboxamide (14{_19_,_35_,_378_})**



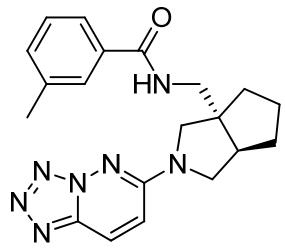
Brownish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.31 (d, *J* = 9.9 Hz, 1H), 7.57 (t, *J* = 6.0 Hz, 1H), 7.31 (d, *J* = 9.9 Hz, 1H), 7.25 (s, 1H), 3.86 (t, *J* = 5.2 Hz, 2H), 3.74 (dd, *J* = 11.2, 8.3 Hz, 1H), 3.65 (d, *J* = 11.6 Hz, 1H), 3.35 (s, 1H), 3.32 – 3.26 (m, 2H), 3.20 (dd, *J* = 13.6, 6.1 Hz, 1H), 2.53 – 2.49 (m, 1H), 2.13 – 2.06 (m, 2H), 1.92 – 1.84 (m, 1H), 1.77 – 1.67 (m, 4H), 1.65 – 1.56 (m, 2H), 1.51 – 1.45 (m, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 167.9, 154.5, 150.4, 140.0, 123.6, 119.3, 109.3, 66.0, 56.5, 55.8, 53.6, 45.6, 44.7, 35.1, 31.8, 24.4, 21.2, 19.6. LC/MS (CI): *m/z* = 370 $[M+H]^+$. Anal. calcd. for $C_{18}H_{23}N_7O_2$: C 58.52; H 6.28; N 26.54. Found: C 58.67; H 6.26; N 26.86.

**_rac_-2-Methyl-_N_-(((3a_R_,6a_S_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)octahydrocyclopenta[_c_]pyrrol-3a-yl)methyl)benzamide (14{_19_,_35_,_384_})**



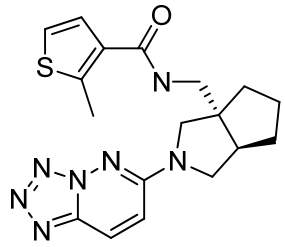
Brownish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.47 (s, 1H), 8.36 (d, *J* = 9.7 Hz, 1H), 7.37 (d, *J* = 9.7 Hz, 1H), 7.32 – 7.24 (m, 2H), 7.23 – 7.15 (m, 2H), 3.84 (dd, *J* = 10.4, 8.9 Hz, 1H), 3.76 (d, *J* = 11.6 Hz, 1H), 3.50 – 3.36 (m, 4H), 2.66 – 2.59 (m, 1H), 2.29 (s, 3H), 2.01 – 1.90 (m, 1H), 1.83 – 1.75 (m, 2H), 1.73 – 1.65 (m, 2H), 1.60 – 1.52 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 170.2, 154.7, 140.0, 137.8, 135.4, 130.8, 129.6, 127.4, 125.9, 123.8, 119.3, 56.7, 55.7, 53.8, 45.8, 45.4, 35.5, 32.1, 24.6, 19.8. LC/MS (CI): *m/z* = 378 $[M+H]^+$. Anal. calcd. for $C_{20}H_{23}N_7O$: C 63.64; H 6.14; N 25.98. Found: C 63.82; H 5.97; N 25.76.

**_rac_-3-Methyl-_N_-(((3a_R_,6a_S_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)octahydrocyclopenta[_c_]pyrrol-3a-yl)methyl)benzamide (14{*19*,*35*,*171*})**



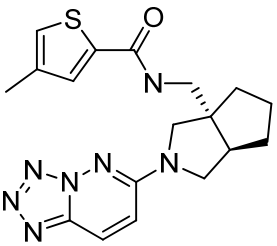
Brownish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.52 (t, *J* = 6.2 Hz, 1H), 8.30 (d, *J* = 9.9 Hz, 1H), 7.69 – 7.47 (m, 2H), 7.32 (d, *J* = 9.9 Hz, 1H), 7.29 – 7.22 (m, 2H), 3.83 – 3.71 (m, 2H), 3.48 – 3.34 (m, 4H), 2.59 (tt, *J* = 8.5, 4.7 Hz, 1H), 1.96 – 1.88 (m, 1H), 1.79 – 1.72 (m, 2H), 1.69 – 1.61 (m, 2H), 1.55 – 1.48 (m, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 167.6, 154.5, 140.0, 137.9, 135.0, 132.1, 128.5, 128.1, 124.8, 123.6, 119.3, 56.5, 55.8, 53.7, 45.8, 45.4, 35.2, 31.9, 24.4, 21.3. LC/MS (CI): *m/z* = 378 $[M+H]^+$. Anal. calcd. for $C_{20}H_{23}N_7O$: C 63.64; H 6.14; N 25.98. Found: C 63.34; H 5.86; N 25.60.

**_rac_-2-Methyl-_N_-(((3a_R_,6a_S_)-2-(tetrazolo[1,5-_b_]pyridazin-6-yl)octahydrocyclopenta[_c_]pyrrol-3a-yl)methyl)thiophene-3-carboxamide (14{*19*,*35*,*390*})**



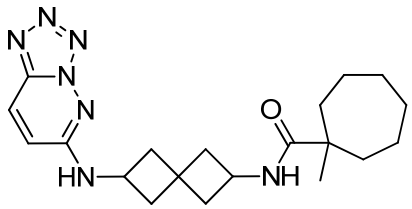
Brownish solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ 8.31 (d, *J* = 9.8 Hz, 1H), 8.22 (t, *J* = 6.3 Hz, 1H), 7.33 (d, *J* = 9.8 Hz, 1H), 7.21 (s, 2H), 3.78 (dd, *J* = 11.1, 8.2 Hz, 1H), 3.71 (d, *J* = 11.6 Hz, 1H), 3.44 – 3.35 (m, 3H), 3.32 – 3.27 (m, 1H), 2.57 (tt, *J* = 8.6, 4.7 Hz, 1H), 2.47 (s, 3H), 1.97 – 1.86 (m, 1H), 1.81 – 1.71 (m, 2H), 1.69 – 1.60 (m, 2H), 1.55 – 1.47 (m, 1H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 164.8, 154.6, 143.3, 140.0, 133.0, 127.7, 123.6, 122.3, 119.3, 56.5, 55.7, 53.7, 45.7, 45.0, 35.3, 31.9, 24.4, 14.9. LC/MS (CI): *m/z* = 384 $[M+H]^+$. Anal. calcd. for $C_{18}H_{21}N_7OS$: C 56.38; H 5.52; N 25.57; S 8.36. Found: C 55.99; H 5.81; N 25.78; S 8.00.

***rac*-4-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)thiophene-2-carboxamide (14{*19*,*35*,*394*})**



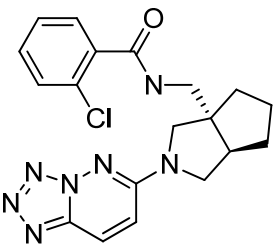
Brownish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.51 (t, *J* = 6.3 Hz, 1H), 8.33 (d, *J* = 9.9 Hz, 1H), 7.56 (s, 1H), 7.34 (d, *J* = 9.9 Hz, 1H), 7.29 (s, 1H), 3.80 (dd, *J* = 11.2, 8.1 Hz, 1H), 3.73 (d, *J* = 11.6 Hz, 1H), 3.50 – 3.38 (m, 3H), 3.35 – 3.31 (m, 1H), 2.59 (tt, *J* = 8.4, 4.6 Hz, 1H), 2.17 (s, 3H), 1.99 – 1.88 (m, 1H), 1.83 – 1.73 (m, 2H), 1.71 – 1.63 (m, 2H), 1.57 – 1.50 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 162.3, 154.6, 140.0, 139.8, 138.1, 130.5, 126.5, 123.7, 119.3, 56.5, 55.8, 53.7, 45.8, 45.3, 35.2, 31.8, 24.4, 15.8. LC/MS (CI): *m/z* = 384 $[M+H]^+$. Anal. calcd. for $C_{18}H_{21}N_7OS$: C 56.38; H 5.52; N 25.57; S 8.36. Found: C 56.09; H 5.52; N 25.53; S 8.13.

**1-Methyl-*N*-(6-(tetrazolo[1,5-*b*]pyridazin-6-ylamino)spiro[3.3]heptan-2-yl)cycloheptane-carboxamide (14{*114*,*35*,*399*})**



Brownish solid. $^{1}$H NMR (600 MHz, DMSO-$d_6$) δ 8.17 (d, *J* = 9.7 Hz, 1H), 8.10 (d, *J* = 6.4 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 1H), 7.03 (d, *J* = 9.7 Hz, 1H), 4.14 – 4.05 (m, 2H), 2.54 – 2.50 (m, 1H), 2.39 – 2.32 (m, 2H), 2.15 (ddd, *J* = 12.0, 7.5, 4.9 Hz, 1H), 2.05 (dd, *J* = 10.7, 8.8 Hz, 1H), 2.00 – 1.90 (m, 5H), 1.45 – 1.36 (m, 8H), 1.29 – 1.24 (m, 2H), 0.99 (s, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 177.1, 155.1, 140.4, 123.5, 121.1, 45.0, 42.5, 42.4, 42.4, 42.3, 41.9, 37.9, 37.9, 31.4, 29.9, 27.7, 23.7. LC/MS (CI): *m/z* = 384 $[M+H]^+$. Anal. calcd. for $C_{20}H_{29}N_7O$: C 62.64; H 7.62; N 25.57. Found: C 62.79; H 7.70; N 25.75.

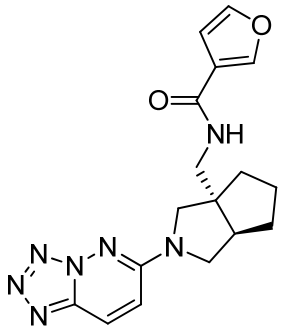
***rac*-2-Chloro-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (14{*19*,*35*,*408*})**



Brownish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.67 (t, *J* = 5.9 Hz, 1H), 8.36 (d, *J* = 9.7 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.39 – 7.33 (m, 3H), 3.84 (dd, *J* = 10.6, 8.5 Hz, 1H), 3.75 (d, *J* = 11.7 Hz, 1H), 3.50 – 3.36 (m, 4H), 2.68 – 2.61 (m, 1H), 2.00 – 1.91 (m, 1H), 1.82 – 1.67 (m, 4H), 1.58 – 1.52 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 167.5, 154.7, 140.0, 137.6, 131.1, 130.1, 130.0, 129.2, 127.5, 123.8, 119.3, 56.7, 55.6, 53.8, 45.7, 45.4, 35.6,

32.2, 24.6. LC/MS (CI): *m/z* = 398/400 $[M+H]^+$. Anal. calcd. for $C_{19}H_{20}ClN_7O$: C 57.36; H 5.07; N 24.64; Cl 8.91. Found: C 57.48; H 4.96; N 24.62; Cl 8.64.

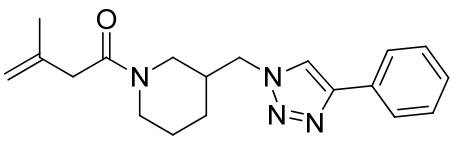
***rac*-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)furan-3-carboxamide (14{*19*,*35*,*32*})**



Brownish solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.34 (d, *J* = 9.9 Hz, 1H), 8.29 (t, *J* = 6.3 Hz, 1H), 8.16 (s, 1H), 7.68 (d, *J* = 2.0 Hz, 1H), 7.35 (d, *J* = 9.8 Hz, 1H), 6.83 (d, *J* = 2.0 Hz, 1H), 3.79 (dd, *J* = 11.4, 8.1 Hz, 1H), 3.70 (d, *J* = 11.4 Hz, 1H), 3.47 – 3.36 (m, 4H), 2.61 – 2.54 (m, 1H), 1.97 – 1.89 (m, 1H), 1.81 – 1.73 (m, 2H), 1.70 – 1.62 (m, 2H), 1.57 – 1.50 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 162.7, 154.6, 145.6, 144.4, 140.0, 123.7, 123.1, 119.3, 109.5, 56.5, 55.7, 53.7, 45.7, 44.7, 35.2, 31.8, 24.4. LC/MS (CI): *m/z* = 354 $[M+H]^+$. Anal. calcd. for $C_{17}H_{19}N_7O_2$: C 57.78; H 5.42; N 27.75. Found: C 58.07; H 5.29; N 28.08.

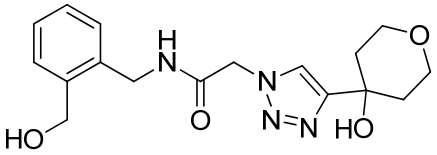
**General procedure for the reaction sequence *E*.** Amine **2** or **9** (0.5 mmol), carboxylic acid **8** or **3** (0.6 mmol), *i*-$Pr_2NEt$ (1.25 mmol*), and 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo-[4,5-*b*]pyridinium 3-oxide hexafluorophosphate (HATU) (0.575 mmol) were mixed in dry DMF (appr. 1.4 mL). The reaction mixture was sealed and left at ambient temperature for 16 h, Alkyne **10** (0.6 mmol), *i*-$PrNEt_2$ (1.5 mmol*), and $Cu(OAc)_2$ (0.05 mmol) were added in one portion, the reaction mixture was sealed and heated at 80 °C for 16 h, then cooled and evaporated under reduced pressure. The residue was dissolved in DMSO (appr. 1 mL), filtered, analyzed by LCMS, and transferred for the HPLC purification.

**3-Methyl-1-(3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)piperidin-1-yl)but-3-en-1-one (15{*5*,*7*,*7*})**



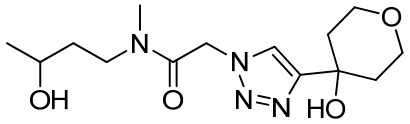
Yellowish liquid. The compound existed as a *ca.* 11:9 mixture of rotamers. $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.56 (d, *J* = 7.1 Hz, 1H), 7.87 – 7.78 (m, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 1H), 4.81 (s, 0.55H) and 4.69 (s, 0.55H) and 4.68 (s, 0.45H) and 4.48 (s, 0.45H), 4.37 – 4.27 (m, 2H), 4.19 – 4.10 (m, 1H), 3.70 – 3.63 (m, 0.55H) and 3.58 – 3.53 (m, 0.45H), 3.09 – 2.93 (m, 2H), 2.91 – 2.80 (m, 1H), 2.66 – 2.60 (m, 0.45H) and 2.55 (dd, *J* = 12.9, 10.2 Hz, 0.55H), 2.04 – 1.92 (m, 1H), 1.72 – 1.52 (m, 5H), 1.37 – 1.19 (m, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.6 and 168.4, 146.9 and 146.7, 140.7 and 140.3, 131.2, 129.3, 128.3, 125.6 and 125.6, 122.2 and 122.2, 113.1 and 113.0, 52.8 and 52.5, 49.2 and 46.4, 44.6 and 43.0, 42.8 and 41.9, 37.7 and 36.9, 28.0 and 27.9, 25.0 and 24.4, 22.9 and 22.7. LC/MS (CI): *m/z* = 325 $[M+H]^+$. Anal. calcd. for $C_{19}H_{24}N_4O$: C 70.34; H 7.46; N 17.27. Found: C 70.63; H 7.43; N 17.24.

***N*-(2-(Hydroxymethyl)benzyl)-2-(4-(4-hydroxytetrahydro-2*H*-pyran-4-yl)-1*H*-1,2,3-triazol-1-yl)acetamide (15{*3*,*17*,*38*})**



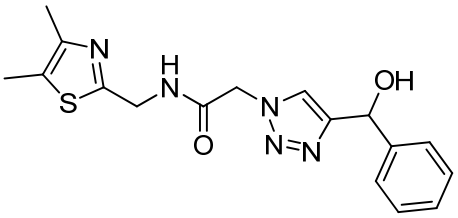
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.68 (t, *J* = 5.6 Hz, 1H), 7.91 (s, 1H), 7.43 – 7.37 (m, 1H), 7.29 – 7.20 (m, 3H), 5.23 (s, 1H), 5.15 (s, 1H), 5.13 (s, 2H), 4.56 (s, 2H), 4.36 (d, *J* = 5.5 Hz, 2H), 3.75 (td, *J* = 11.0, 2.5 Hz, 2H), 3.67 – 3.56 (m, 2H), 2.05 (ddd, *J* = 14.3, 10.5, 4.5 Hz, 2H), 1.74 – 1.63 (m, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 165.9, 155.1, 140.3, 136.1, 128.3, 127.7, 127.4, 127.3, 123.1, 66.1, 63.5, 61.0, 52.0, 40.0, 38.4.LC/MS (CI): *m/z* = 347 $[M+H]^+$. Anal. calcd. for $C_{17}H_{22}N_4O_4$: C 58.95; H 6.4; N 16.17. Found: C 59.25; H 6.19; N 16.43.

***N*-(3-Hydroxybutyl)-2-(4-(4-hydroxytetrahydro-2*H*-pyran-4-yl)-1*H*-1,2,3-triazol-1-yl)-*N*-methylacetamide (Z4180225403)**



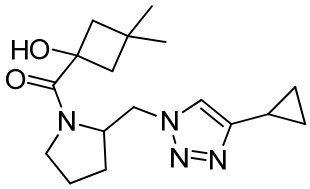
Yellowish solid. The compound existed as a *ca.* 11:9 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.81 (s, 0.45H) and 7.78 (s, 0.55H), 5.59 – 5.38 (m, 1H), 5.35 (s, 1H), 5.19 (s, 1H), 4.64 (d, *J* = 4.8 Hz, 0.45H) and 4.43 (d, *J* = 4.8 Hz, 0.55H), 3.77 – 3.69 (m, 2H), 3.67 – 3.50 (m, 3H), 3.50 – 3.33 (m, 2H), 3.02 (s, 1.65H) and 2.81 (s, 1.35H), 2.03 (ddd, *J* = 14.2, 10.4, 4.3 Hz, 2H), 1.74 – 1.65 (m, 2.2H) and 1.60 – 1.42 (m, 1.8H), 1.11 (d, *J* = 6.2 Hz, 1.35H) and 1.04 (d, *J* = 6.2 Hz, 1.65H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 165.9 and 165.7, 154.9 and 154.9, 123.3 and 123.2, 66.1 and 66.0, 64.2 and 63.7, 63.5, 51.1 and 50.7, 45.8 and 45.4, 38.5, 37.1 and 36.7, 34.6 and 33.4, 24.4 and 24.1. LC/MS (CI): *m/z* = 313 $[M+H]^+$. Anal. calcd. for $C_{14}H_{24}N_4O_4$: C 53.83; H 7.74; N 17.94. Found: C 53.81; H 7.50; N 17.56.

***N*-((4,5-Dimethylthiazol-2-yl)methyl)-2-(4-(hydroxy(phenyl)methyl)-1*H*-1,2,3-triazol-1-yl)-acetamide (15{*3*,*21*,*37*})**



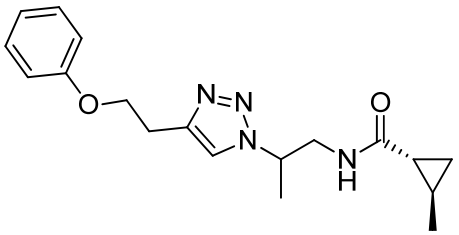
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 9.09 (t, *J* = 6.1 Hz, 1H), 7.81 (s, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 6.9 Hz, 1H), 5.99 (d, *J* = 3.9 Hz, 1H), 5.82 (d, *J* = 4.7 Hz, 1H), 5.11 (s, 2H), 4.46 (d, *J* = 5.9 Hz, 2H), 2.28 (s, 3H), 2.21 (s, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 166.2, 163.3, 151.7, 147.6, 144.6, 128.5, 127.5, 126.9, 126.6, 124.0, 68.4, 51.9, 40.8, 14.9, 11.3. LC/MS (CI): *m/z* = 358 $[M+H]^+$. Anal. calcd. for $C_{17}H_{19}N_5O_2S$: C 57.13; H 5.36; N 19.59; S 8.97. Found: C 56.82; H 5.03; N 19.58; S 9.24.

**(2-((4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)methyl)pyrrolidin-1-yl)(1-hydroxy-3,3-dimethyl-cyclobutyl)methanone (15{*1*,*6*,*6*})**



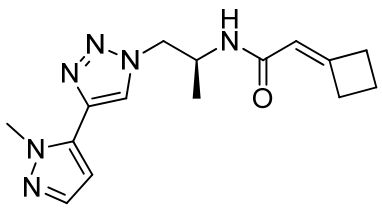
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.63 (s, 1H), 5.71 (s, 1H), 4.44 (d, *J* = 4.5 Hz, 2H), 4.22 (dq, *J* = 8.6, 4.5 Hz, 1H), 3.46 (dt, *J* = 10.8, 6.8 Hz, 1H), 3.16 – 3.07 (m, 1H), 2.47 – 2.42 (m, 1H), 2.36 (dd, *J* = 12.8, 2.6 Hz, 1H), 1.89 (tt, *J* = 8.6, 5.0 Hz, 1H), 1.85 – 1.68 (m, 3H), 1.65 – 1.52 (m, 2H), 1.33 – 1.23 (m, 1H), 1.17 (s, 3H), 0.98 (s, 3H), 0.92 – 0.81 (m, 2H), 0.71 – 0.59 (m, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 172.7, 149.6, 121.8, 70.5, 57.3, 50.4, 47.0, 45.8, 31.1, 29.8, 27.0, 26.9, 24.1, 8.2, 8.1, 7.0. LC/MS (CI): *m/z* = 319 $[M+H]^+$. Anal. calcd. for $C_{17}H_{26}N_4O_2$: C 64.12; H 8.23; N 17.60. Found: C 64.07; H 8.13; N 17.64.

**rac-(1*R*,2*R*)-2-Methyl-*N*-(2-(4-(2-phenoxyethyl)-1*H*-1,2,3-triazol-1-yl)propyl)cyclopropane-carboxamide (15{*4*,*4*,*4*})**



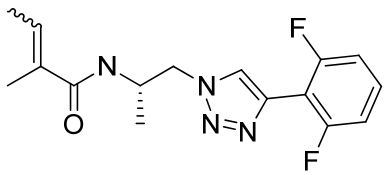
Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.09 (q, *J* = 5.5 Hz, 1H), 7.95 (d, *J* = 3.0 Hz, 1H), 7.26 (t, *J* = 7.9 Hz, 2H), 7.00 – 6.80 (m, 3H), 4.75 – 4.64 (m, 1H), 4.19 (t, *J* = 6.8 Hz, 2H), 3.50 – 3.35 (m, 2H), 3.06 (t, *J* = 6.8 Hz, 2H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.21 (dq, *J* = 7.9, 3.9 Hz, 1H), 1.12 – 1.01 (m, 1H), 0.97 (dd, *J* = 6.0, 2.2 Hz, 3H), 0.85 – 0.76 (m, 1H), 0.42 (ddd, *J* = 8.8, 5.8, 3.4 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 173.1, 158.8, 143.5, 129.9, 121.8, 121.1, 114.9, 66.9, 56.2, 56.2, 44.6, 26.1, 22.4, 19.0, 19.0, 18.0, 14.9, 14.9, 14.9, 14.9. LC/MS (CI): *m/z* = 329 $[M+H]^+$. Anal. calcd. for $C_{18}H_{24}N_4O_2$: C 65.83; H 7.37; N 17.06. Found: C 65.75; H 7.34; N 16.96.

**(*S*)-2-Cyclobutylidene-*N*-(1-(4-(1-methyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)acetamide (15{*6*,*11*,*11*})**



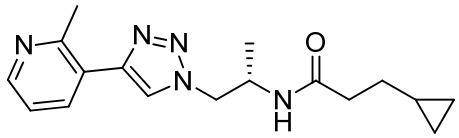
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.42 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 1.8 Hz, 1H), 6.54 (d, *J* = 1.5 Hz, 1H), 5.55 – 5.45 (m, 1H), 4.50 – 4.34 (m, 2H), 4.31 – 4.21 (m, 1H), 4.01 (d, *J* = 1.3 Hz, 3H), 3.01 – 2.85 (m, 2H), 2.70 (t, *J* = 7.9 Hz, 2H), 2.02 – 1.86 (m, 2H), 1.06 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 165.4, 160.3, 138.5, 137.7, 133.7, 124.2, 114.9, 105.6, 54.3, 44.7, 38.7, 33.4, 32.1, 18.2, 18.1. LC/MS (CI): *m/z* = 301 $[M+H]^+$. Anal. calcd. for $C_{15}H_{20}N_6O$: C 59.98; H 6.71; N 27.98. Found: C 60.18; H 6.75; N 27.72.

**(*S*)-*N*-(1-(4-(2,6-Difluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-2-methylbut-2-enamide (15{*6*,*1*,*8*})**



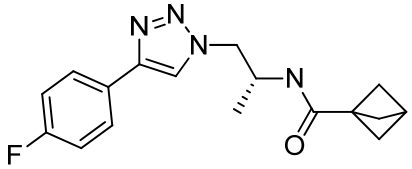
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.33 (d, $J$ = 1.5 Hz, 1H), 7.71 (d, $J$ = 8.4 Hz, 1H), 7.46 (tt, $J$ = 8.4, 6.4 Hz, 1H), 7.21 (t, $J$ = 8.4 Hz, 2H), 6.20 (q, $J$ = 6.4 Hz, 1H), 4.53 (dd, $J$ = 13.6, 5.4 Hz, 1H), 4.47 (dd, $J$ = 13.6, 7.9 Hz, 1H), 4.38 – 4.28 (m, 1H), 1.91 – 1.39 (m, 6H), 1.11 (d, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 168.7, 159.8 (dd, $J$ = 251, 7.1 Hz), 135.1 (t, $J$ = 2.7 Hz), 132.3, 130.6 (t, $J$ = 10.5 Hz), 129.6, 126.2 (t, $J$ = 4.2 Hz), 112.6 (dd, $J$ = 20.7, 5.0 Hz), 108.8 (t, $J$ = 17.4 Hz), 53.9, 45.5, 18.3, 14.0, 12.7. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –111.9. LC/MS (CI): $m/z$ = 321 $[M+H]^+$. Anal. calcd. for $C_{16}H_{18}F_2N_4O$: C 59.99; H 5.66; N 17.49. Found: C 59.81; H 5.97; N 17.62.

**(*S*)-3-Cyclopropyl-*N*-(1-(4-(2-methylpyridin-3-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)propanamide (15{*6*,*27*,*27*})**



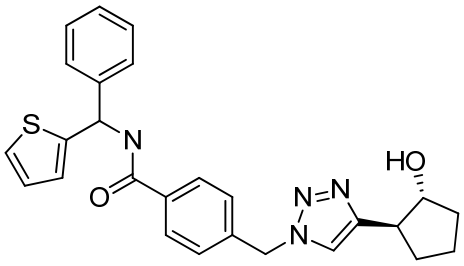
Beige solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.51 – 8.42 (m, 1H), 8.38 (d, $J$ = 1.5 Hz, 1H), 8.08 (dd, $J$ = 7.9, 1.8 Hz, 1H), 7.86 (d, $J$ = 8.1 Hz, 1H), 7.32 (dd, $J$ = 7.9, 4.8 Hz, 1H), 4.49 (dd, $J$ = 13.6, 5.2 Hz, 1H), 4.40 (dd, $J$ = 13.6, 7.5 Hz, 1H), 4.35 – 4.25 (m, 1H), 2.63 (s, 3H), 2.08 (t, $J$ = 7.4 Hz, 2H), 1.39 – 1.24 (m, 2H), 1.10 (d, $J$ = 6.7 Hz, 3H), 0.60 – 0.49 (m, 1H), 0.32 – 0.22 (m, 2H), –0.04 – –0.13 (m, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 172.1, 155.0, 148.5, 144.0, 135.8, 126.0, 124.8, 121.9, 54.2, 45.0, 36.0, 30.7, 24.7, 18.2, 10.8, 4.7, 4.7. LC/MS (CI): $m/z$ = 314 $[M+H]^+$. Anal. calcd. for $C_{17}H_{23}N_5O$: C 65.15; H 7.40; N 22.35. Found: C 65.41; H 7.03; N 22.24.

**(*R*)-*N*-(1-(4-(4-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)bicyclo[1.1.1]pentane-1-carboxamide (15{*2*,*2*,*2*})**



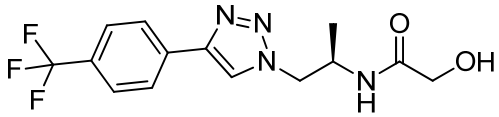
Colorless soild. $^{1}$H NMR (600 MHz, DMSO-$d_6$) δ 8.35 (s, 1H), 7.84 (dd, $J$ = 8.7, 5.6 Hz, 2H), 7.63 (d, $J$ = 8.4 Hz, 1H), 7.26 (t, $J$ = 8.7 Hz, 2H), 4.42 (dd, $J$ = 13.6, 5.6 Hz, 1H), 4.33 (dd, $J$ = 13.6, 7.4 Hz, 1H), 4.24 – 4.15 (m, 1H), 2.33 (s, 1H), 1.84 (s, 6H), 1.06 (d, $J$ = 6.8 Hz, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 168.9, 162.1 (d, $J$ = 244 Hz), 145.5, 127.8 (d, $J$ = 3.1 Hz), 127.5 (d, $J$ = 8.2 Hz), 122.1, 116.2 (d, $J$ = 21.7 Hz), 53.9, 50.8, 45.0, 44.6, 26.7, 18.0. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –114.8. LC/MS (CI): $m/z$ = 315 $[M+H]^+$. Anal. calcd. for $C_{17}H_{19}FN_4O$: C 64.95; H 6.09; N 17.82. Found: C 65.06; H 6.17; N 17.48.

***rac*-4-((4-((1*R*,2*S*)-2-Hydroxycyclopentyl)-1*H*-1,2,3-triazol-1-yl)methyl)-N-(phenyl(thiophen-2-yl)methyl)benzamide (15{*1*,*2*,*17*})**



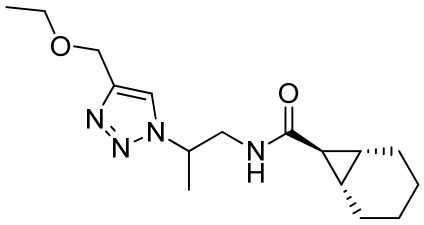
Beige solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 9.46 (d, $J$ = 8.7 Hz, 1H), 7.98 – 7.87 (m, 3H), 7.48 (d, $J$ = 7.4 Hz, 2H), 7.46 – 7.42 (m, 1H), 7.42 – 7.34 (m, 4H), 7.31 (t, $J$ = 7.4 Hz, 1H), 6.97 (t, $J$ = 4.2 Hz, 1H), 6.87 – 6.79 (m, 1H), 6.58 (d, $J$ = 8.7 Hz, 1H), 5.60 (s, 2H), 4.74 (d, $J$ = 4.8 Hz, 1H), 4.08 – 3.98 (m, 1H), 2.98 – 2.89 (m, 1H), 2.12 – 2.02 (m, 1H), 1.88 – 1.80 (m, 1H), 1.76 – 1.60 (m, 3H), 1.55 – 1.48 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 165.8, 150.4, 146.7, 142.2, 140.0, 134.3, 128.8, 128.6, 128.2, 127.9, 127.9, 127.3, 126.1, 125.9, 122.1, 78.0, 52.8, 52.8, 45.2, 34.4, 30.5, 22.1. LC/MS (CI): $m/z$ = 459 $[M+H]^+$. Anal. calcd. for $C_{26}H_{26}N_4O_2S$: C 68.10; H 5.72; N 12.22; S 6.99. Found: C 68.08; H 5.56; N 11.84; S 6.92.

**(*R*)-2-Hydroxy-*N*-(1-(4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)acetamide (15{*2*,*30*,*29*})**



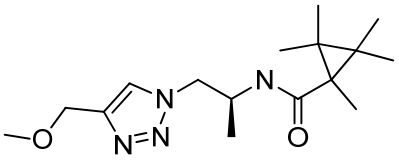
Beige solid. $^{1}$H NMR (600 MHz, DMSO-$d_6$) δ 8.63 (s, 1H), 8.04 (d, $J$ = 8.2 Hz, 2H), 7.84 (d, $J$ = 8.6 Hz, 1H), 7.78 (d, $J$ = 8.2 Hz, 2H), 5.47 (t, $J$ = 5.8 Hz, 1H), 4.53 – 4.44 (m, 2H), 4.37 – 4.31 (m, 1H), 3.78 – 3.67 (m, 2H), 1.10 (d, $J$ = 6.8 Hz, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 172.0, 145.2, 135.2, 128.4 (q, $J$ = 31.7 Hz), 126.3 (q, $J$ = 4.0 Hz), 126.1, 124.7 (q, $J$ = 272 Hz), 123.5, 61.7, 54.1, 44.7, 18.1. $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ –61.5. LC/MS (CI): $m/z$ = 329 $[M+H]^+$. Anal. calcd. for $C_{26}H_{26}N_4O_2S$: C 68.10; H 5.72; N 12.22; S 6.99. Found: C 68.08; H 5.56; N 11.84; S 6.92.

**(1*R*,6*S*,7*r*)-*N*-(2-(4-(Ethoxymethyl)-1*H*-1,2,3-triazol-1-yl)propyl)bicyclo[4.1.0]heptane-7-carboxamide (15{*4*,*15*,*14*})**



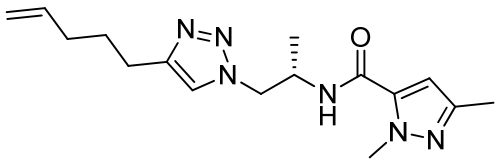
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.08 (s, 1H), 8.01 (t, $J$ = 5.0 Hz, 1H), 4.77 – 4.67 (m, 1H), 4.47 (s, 2H), 3.53 – 3.41 (m, 4H), 1.86 – 1.76 (m, 2H), 1.53 (s, 2H), 1.43 (d, $J$ = 6.9 Hz, 3H), 1.32 – 1.17 (m, 5H), 1.17 – 1.04 (m, 5H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 173.4, 144.3, 122.8, 65.3, 63.7, 56.4, 44.5, 26.6, 22.8, 21.2, 19.5, 19.5, 19.1, 15.5. LC/MS (CI): $m/z$ = 307 $[M+H]^+$. Anal. calcd. for $C_{16}H_{26}N_4O_2$: C 62.72; H 8.55; N 18.29. Found: C 62.96; H 8.58; N 18.06.

**(*S*)-*N*-(1-(4-(Methoxymethyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-1,2,2,3,3-pentamethylcyclopropanecarboxamide (15{*6*,*14*,*13*})**



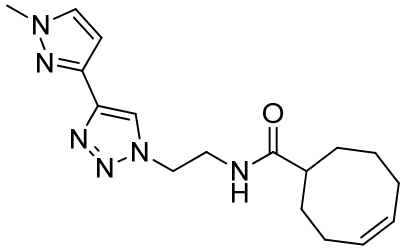
Yellowish oil. $^{1}$H NMR (600 MHz, DMSO-$d_6$) δ 7.95 (s, 1H), 7.33 (d, $J$ = 8.4 Hz, 1H), 4.38 (s, 2H), 4.35 – 4.29 (m, 2H), 4.26 – 4.20 (m, 1H), 3.20 (d, $J$ = 1.2 Hz, 3H), 1.02 (d, $J$ = 6.7 Hz, 3H), 0.98 (s, 3H), 0.89 (s, 6H), 0.87 (s, 3H), 0.84 (s, 3H). $^{13}$C NMR (151 MHz, DMSO-$d_6$) δ 172.8, 143.9, 124.6, 65.3, 57.6, 53.8, 44.8, 34.6, 23.6, 23.6, 20.9, 20.9, 18.4, 18.1, 17.9, 15.6. LC/MS (CI): *m/z* = 309 $[M+H]^+$. Anal. calcd. for $C_{16}H_{28}N_4O_2$: C 62.31; H 9.15; N 18.17. Found: C 61.98; H 8.85; N 18.51.

**(*S*)-1,3-Dimethyl-*N*-(1-(4-(pent-4-en-1-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-1*H*-pyrazole-5-carboxamide (15{*6*,*9*,*9*})**



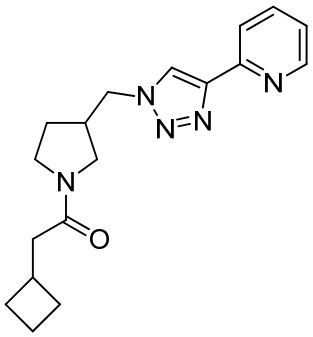
Yellowish solid. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.26 (d, $J$ = 7.3 Hz, 1H), 7.77 (s, 1H), 6.53 (s, 1H), 5.78 (ddt, $J$ = 17.0, 10.3, 6.6 Hz, 1H), 4.96 (t, $J$ = 13.9 Hz, 2H), 4.50 – 4.30 (m, 3H), 3.87 (s, 3H), 2.58 (t, $J$ = 7.5 Hz, 2H), 2.00 (q, $J$ = 7.2 Hz, 2H), 1.62 (p, $J$ = 7.5 Hz, 2H), 1.14 (d, $J$ = 5.9 Hz, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 159.4, 146.8, 145.7, 138.8, 136.1, 122.9, 115.5, 106.9, 53.7, 45.5, 38.7, 32.9, 28.6, 24.8, 18.1, 13.5. LC/MS (CI): *m/z* = 317 $[M+H]^+$. Anal. calcd. for $C_{16}H_{24}N_6O$: C 60.74; H 7.65; N 26.56. Found: C 60.46; H 7.62; N 26.76.

***N*-(2-(4-(1-Methyl-1*H*-pyrazol-3-yl)-1*H*-1,2,3-triazol-1-yl)ethyl)cyclooct-4-enecarboxamide (15{*3*,*3*,*3*})**

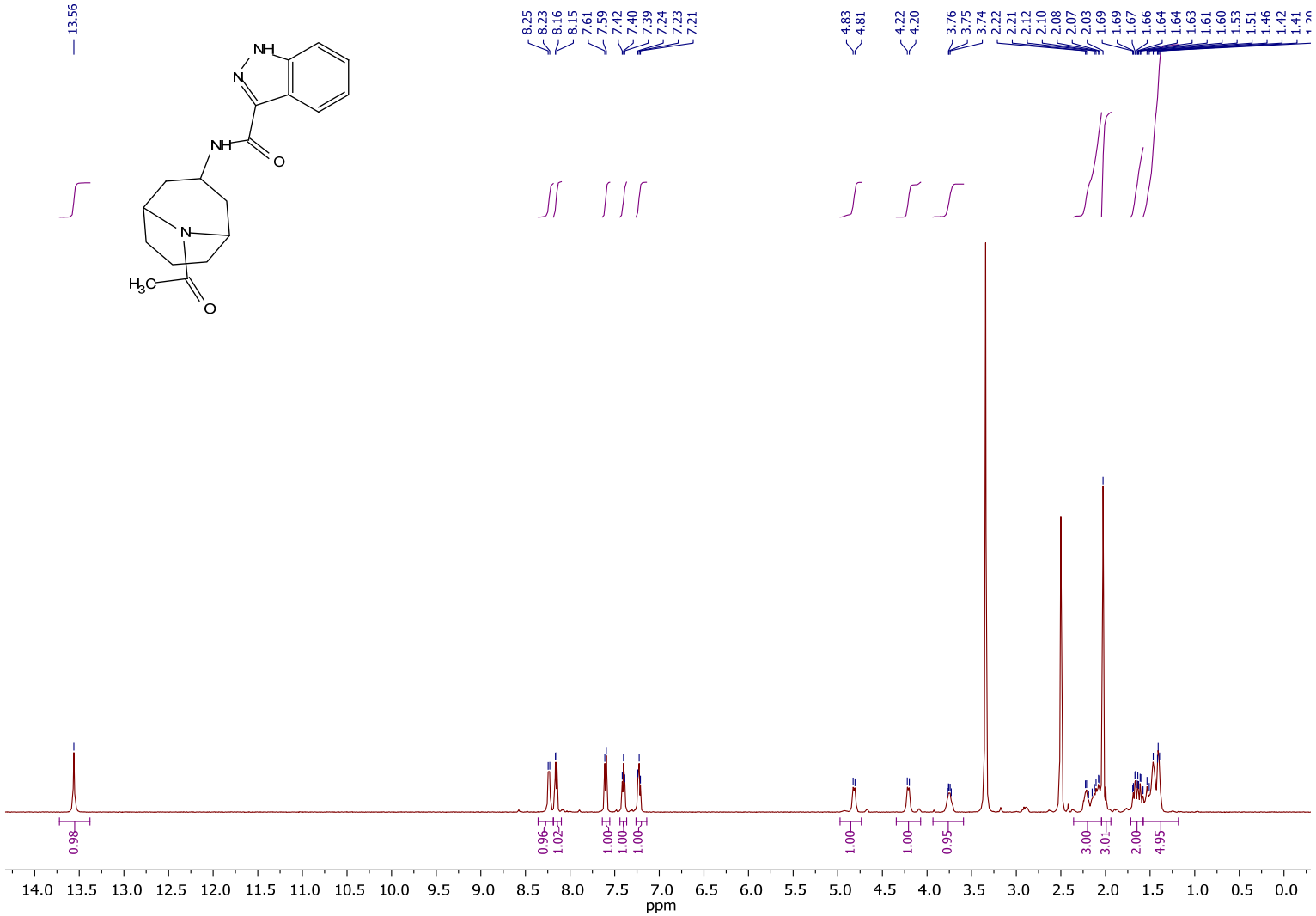


Yellowish oil. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.21 (s, 1H), 7.84 (t, $J$ = 5.7 Hz, 1H), 7.71 (d, $J$ = 2.3 Hz, 1H), 6.54 (dd, $J$ = 2.3, 0.8 Hz, 1H), 5.66 – 5.49 (m, 2H), 4.40 (t, $J$ = 6.0 Hz, 2H), 3.84 (s, 3H), 3.54 – 3.38 (m, 2H), 2.30 – 2.21 (m, 1H), 2.13 (ddd, $J$ = 11.5, 6.9, 4.1 Hz, 1H), 2.10 – 2.00 (m, 2H), 2.00 – 1.89 (m, 1H), 1.66 (dt, $J$ = 14.6, 4.1 Hz, 1H), 1.62 – 1.34 (m, 4H), 1.31 – 1.21 (m, 1H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 177.6, 143.5, 142.0, 132.3, 130.4, 130.2, 121.4, 103.3, 49.3, 44.3, 39.1, 39.0, 32.4, 30.2, 27.9, 25.9, 24.4. LC/MS (CI): *m/z* = 329 $[M+H]^+$. Anal. calcd. for $C_{17}H_{24}N_6O$: C 62.17; H 7.37; N 25.59. Found: C 62.28; H 7.23; N 25.23.

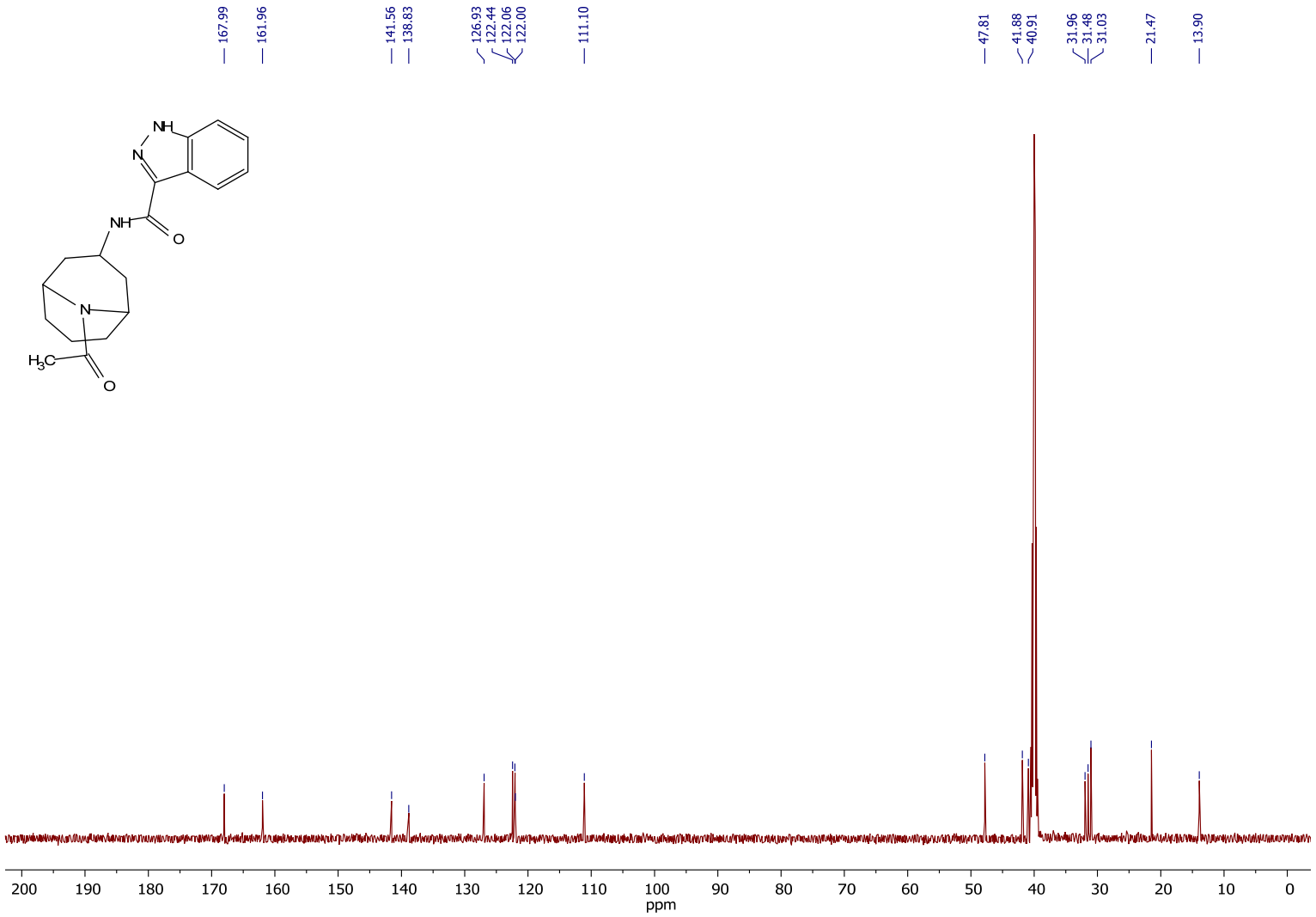
**2-Cyclobutyl-1-(3-((4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)methyl)pyrrolidin-1-yl)ethanone (15{*8*,*10*,*10*})**



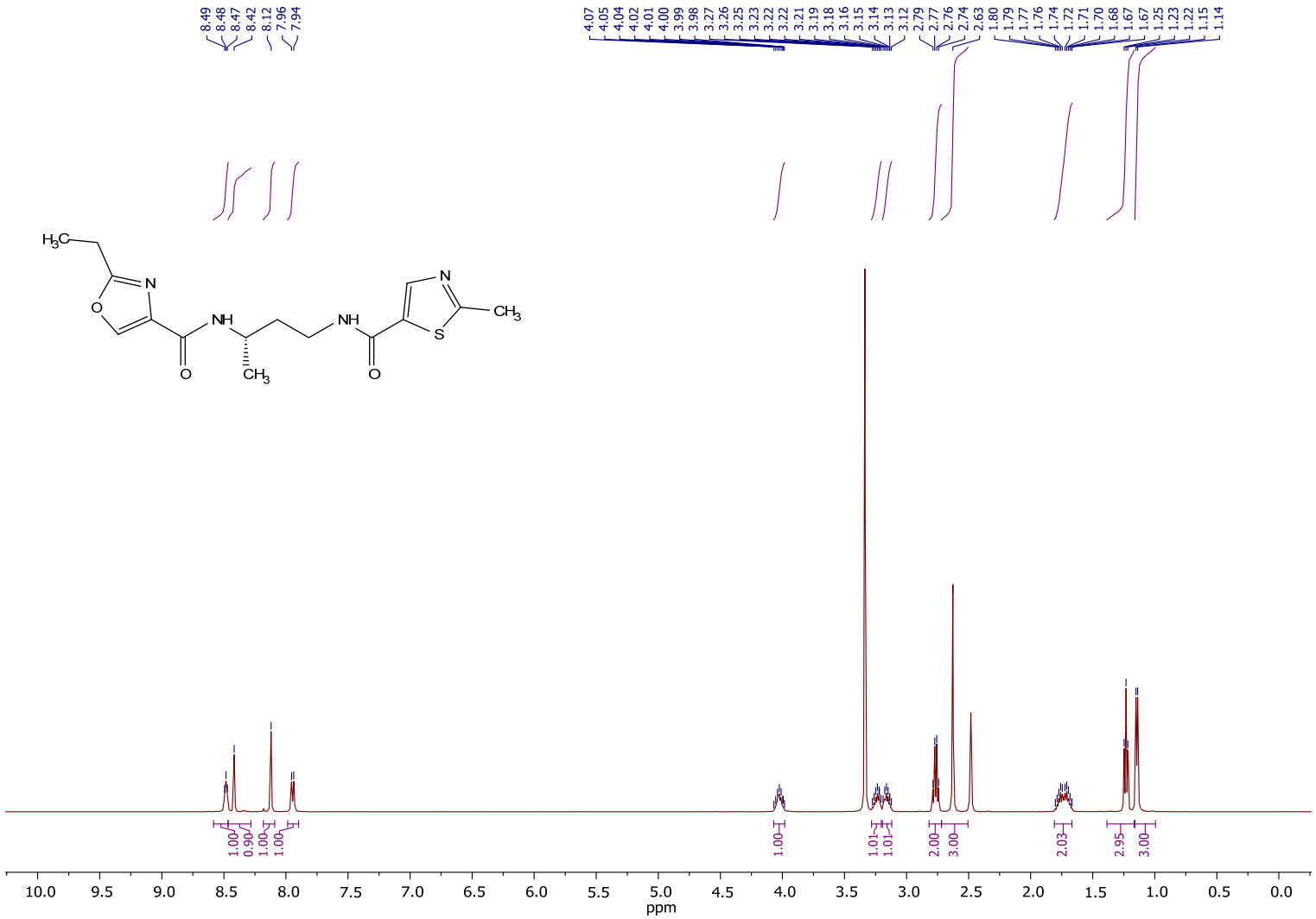
Brownish solid. The compound existed as a ca. 1:1 mixture of rotamers. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 8.76 – 8.64 (m, 1H), 8.60 (s, 1H), 8.04 (s, 1H), 7.89 (t, *J* = 7.8 Hz, 1H), 7.35 (s, 1H), 4.54 – 4.47 (m, 2H), 3.58 – 3.49 (m, 1H), 3.46 – 3.37 (m, 1.5H) and 3.28 – 3.17 (m, 1H) and 3.09 (dd, *J* = 11.8, 7.1 Hz, 0.5H), 2.90 – 2.79 (m, 0.5H) and 2.77 – 2.70 (m, 0.5H), 2.63 – 2.54 (m, 1H), 2.39 – 2.27 (m, 2H), 2.05 – 1.95 (m, 2.5H) and 1.94 – 1.85 (m, 0.5H), 1.83 – 1.70 (m, 2.5H) and 1.66 – 1.56 (m, 2.5H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 170.1 and 170.0, 150.5, 150.0, 147.7, 137.6, 124.1, 123.5, 119.9, 52.0 and 52.0, 49.5 and 48.6, 45.6 and 44.7, 41.1 and 40.9, 38.1, 32.1 and 32.1, 29.4, 28.4 and 28.4, 28.4, 27.8, 18.8. LC/MS (CI): *m/z* = 326 $[M+H]^+$. Anal. calcd. for $C_{18}H_{23}N_5O$: C 66.44; H 7.12; N 21.52. Found: C 66.43; H 7.34; N 21.40.



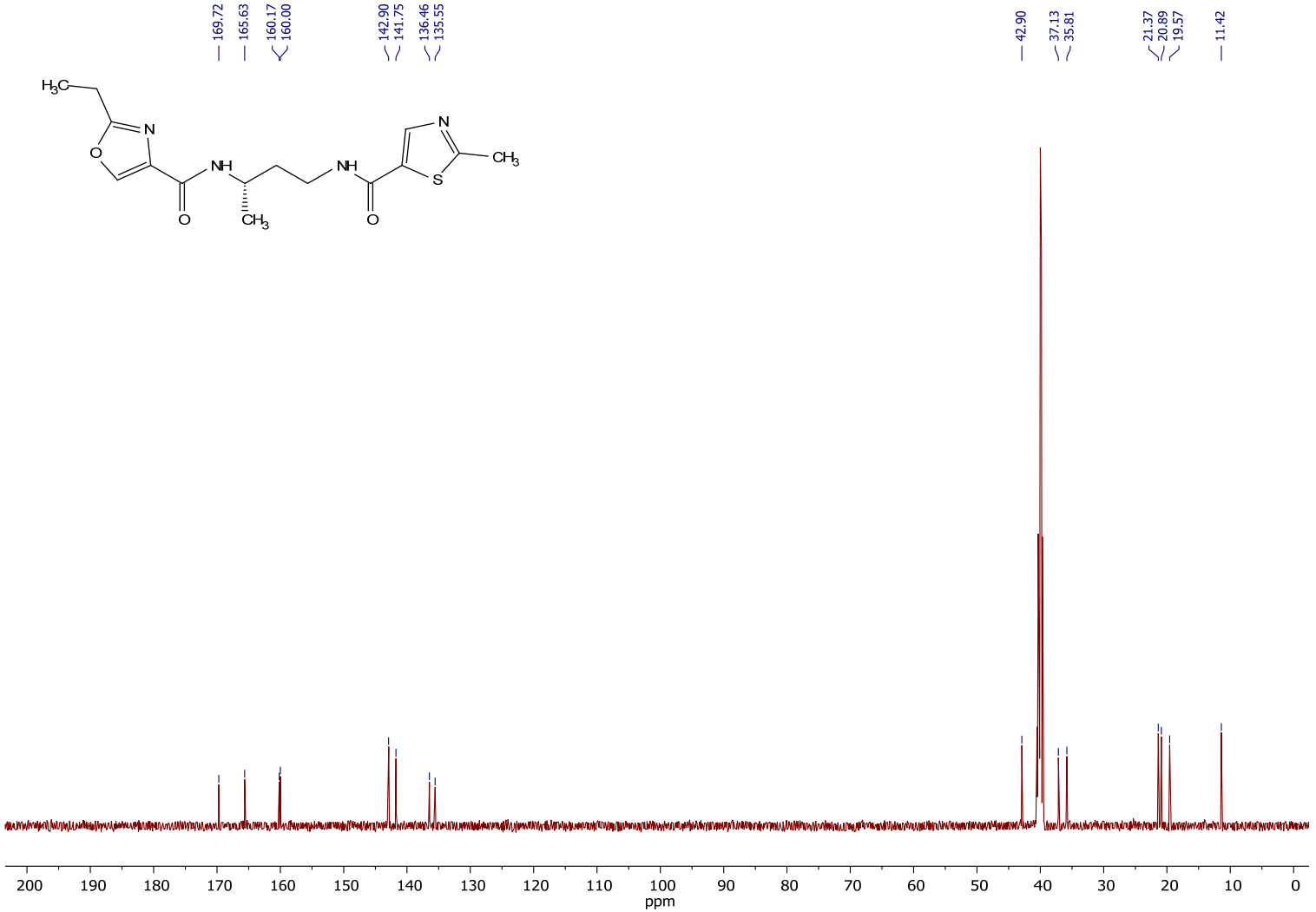

*N*-(9-Acetyl-9-azabicyclo[3.3.1]nonan-3-yl)-1*H*-indazole-3-carboxamide (**11**{*52*,*55*,*23*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



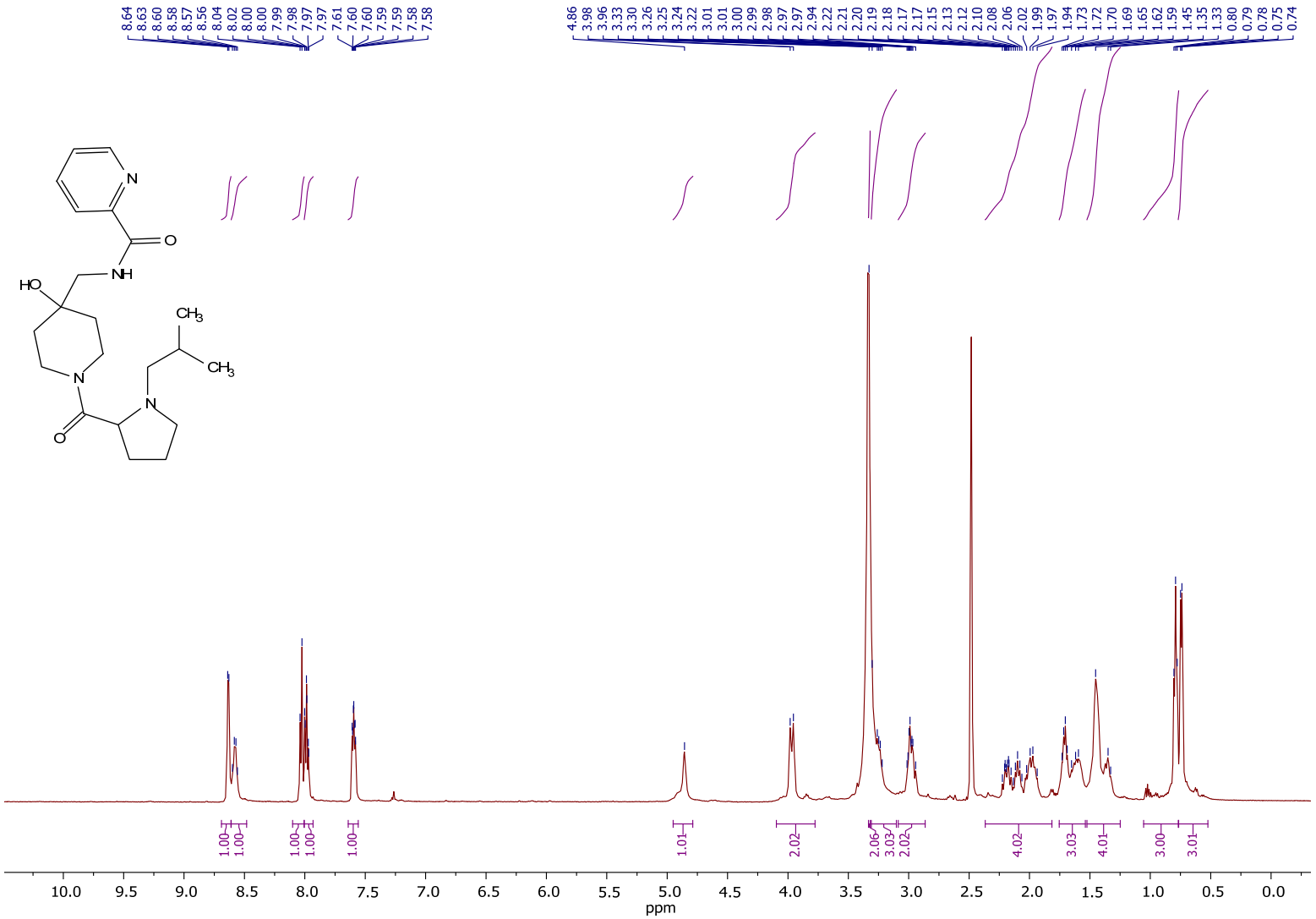

*N*-(9-Acetyl-9-azabicyclo[3.3.1]nonan-3-yl)-1*H*-indazole-3-carboxamide (**11**{*52*,*55*,*23*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



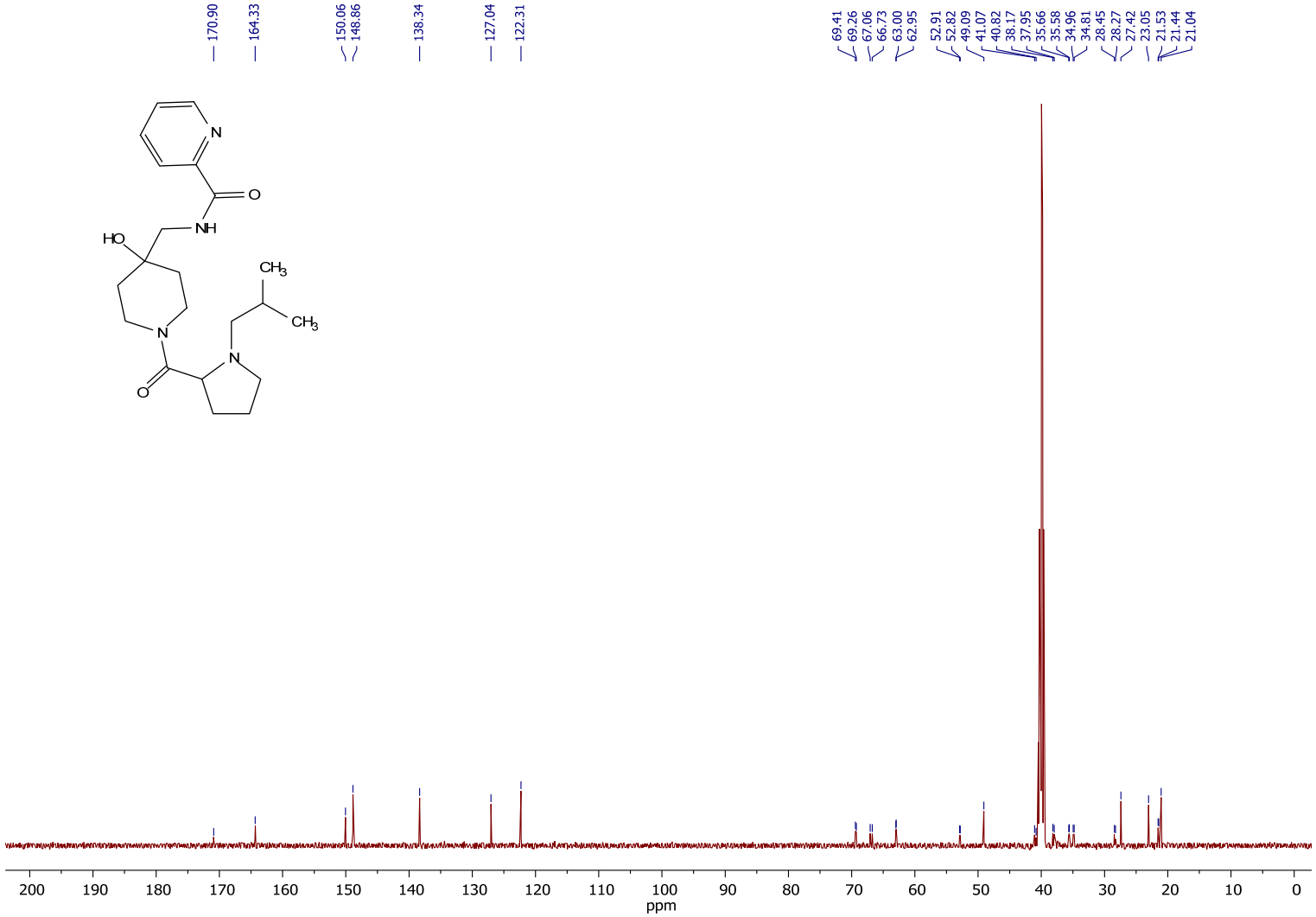

(*S*)-2-Ethyl-*N*-(4-(2-methylthiazole-5-carboxamido)butan-2-yl)oxazole-4-carboxamide (**11**{*25*,*19*,*9*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



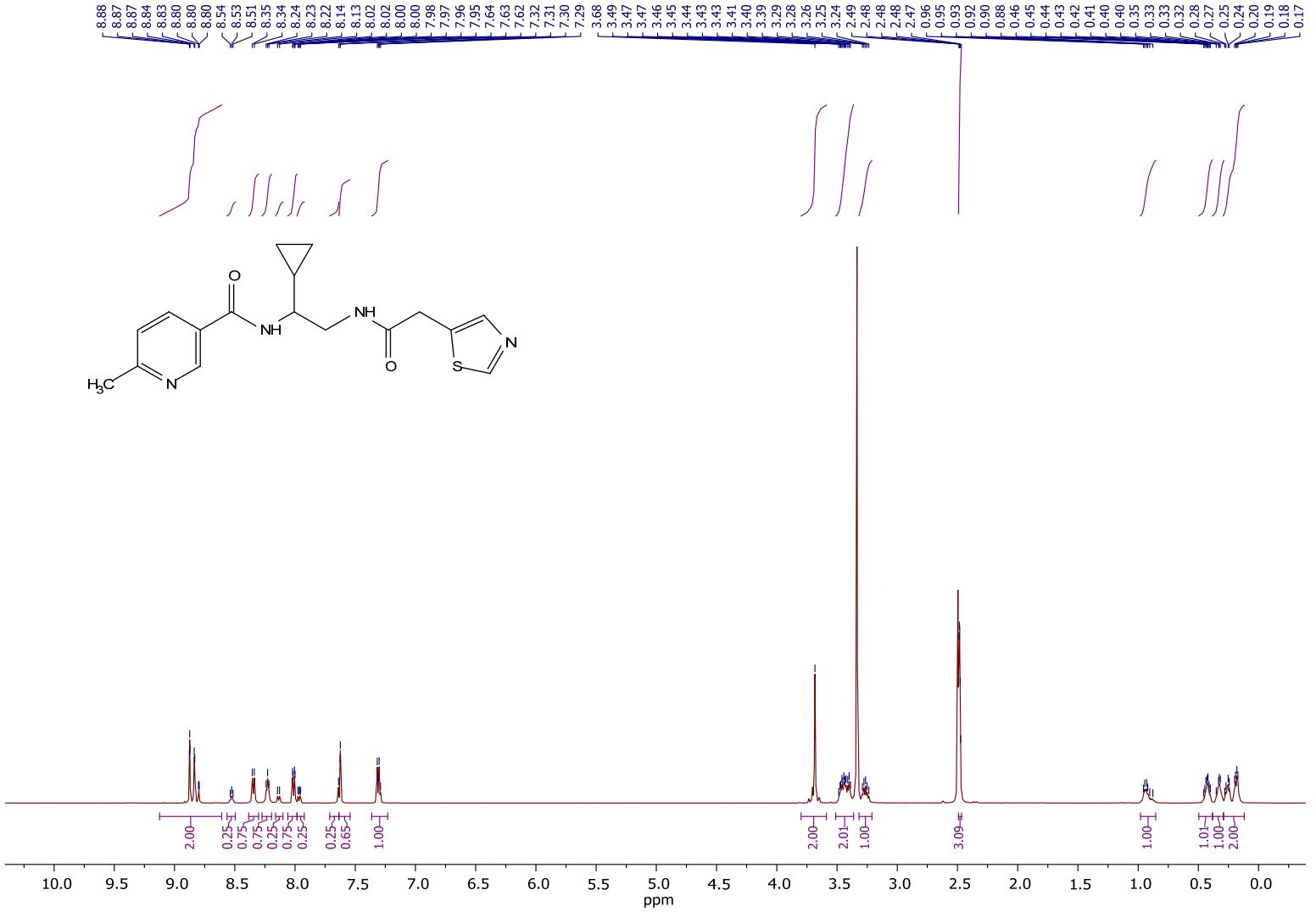

(*S*)-2-Ethyl-*N*-(4-(2-methylthiazole-5-carboxamido)butan-2-yl)oxazole-4-carboxamide (**11**{*25*,*19*,*9*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



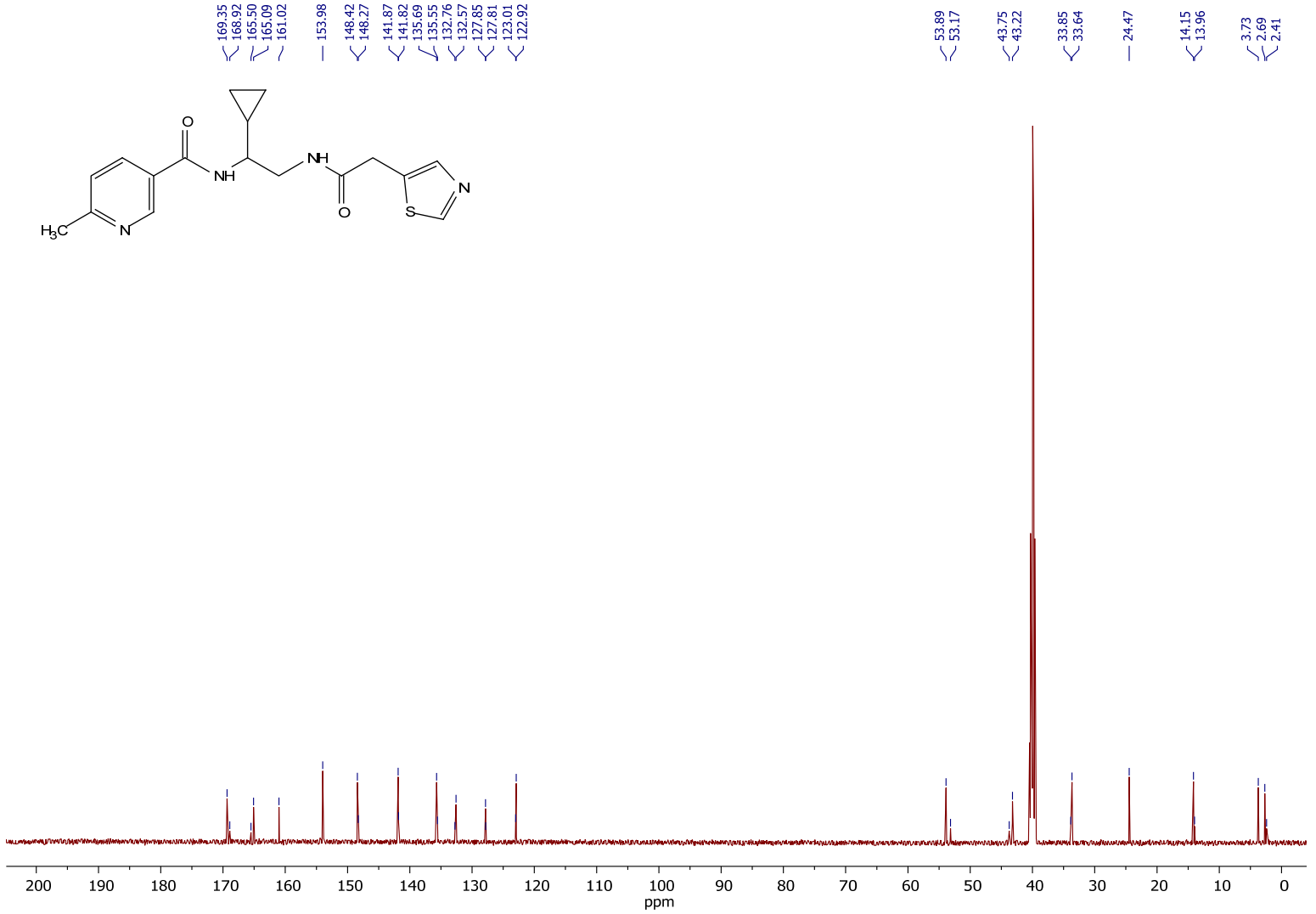

*N*-((4-Hydroxy-1-(isobutylprolyl)piperidin-4-yl)methyl)picolinamide (**11**{*24*,*21*,*10*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



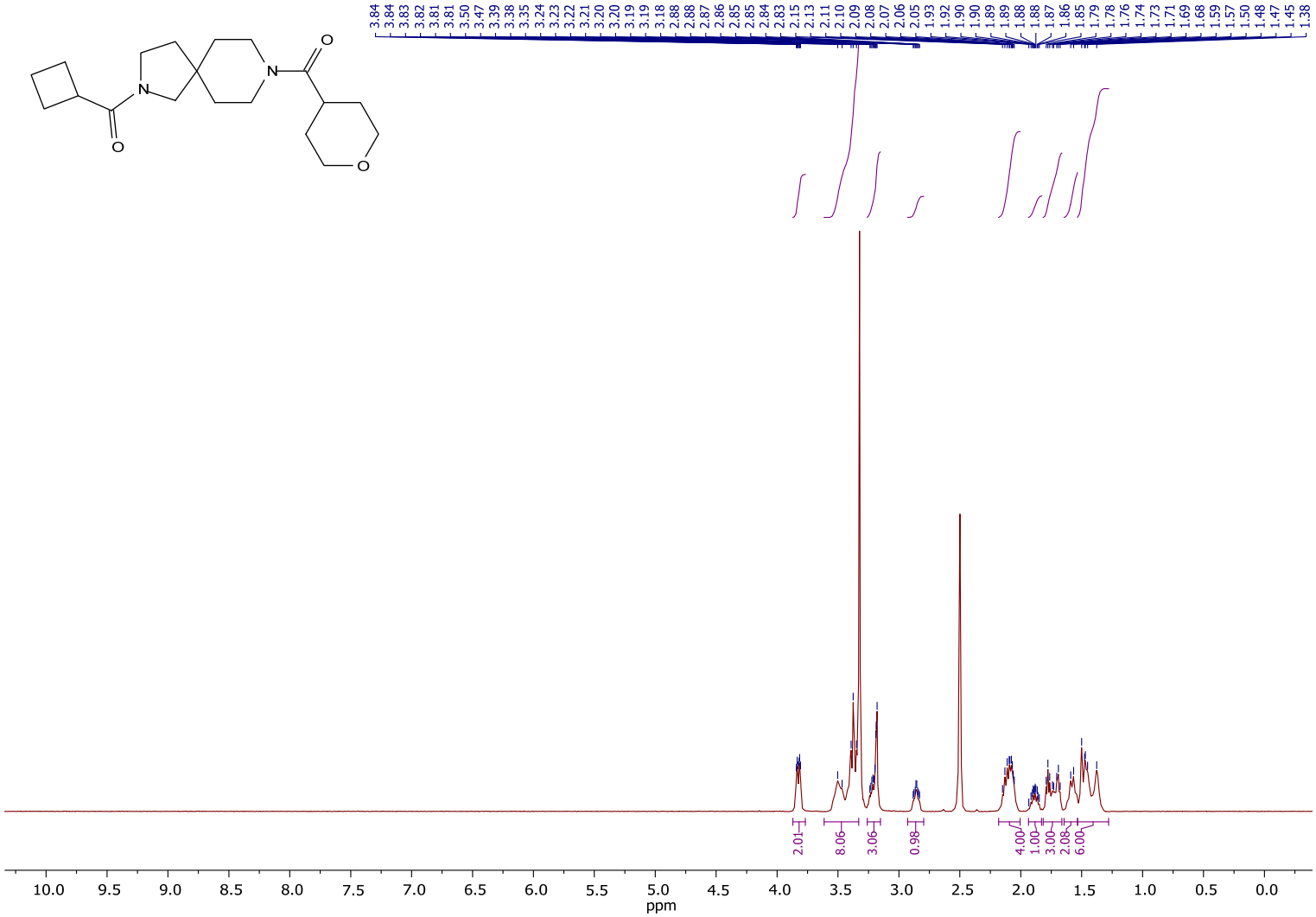

*N*-((4-Hydroxy-1-(isobutylprolyl)piperidin-4-yl)methyl)picolinamide (**11**{*24*,*21*,*10*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



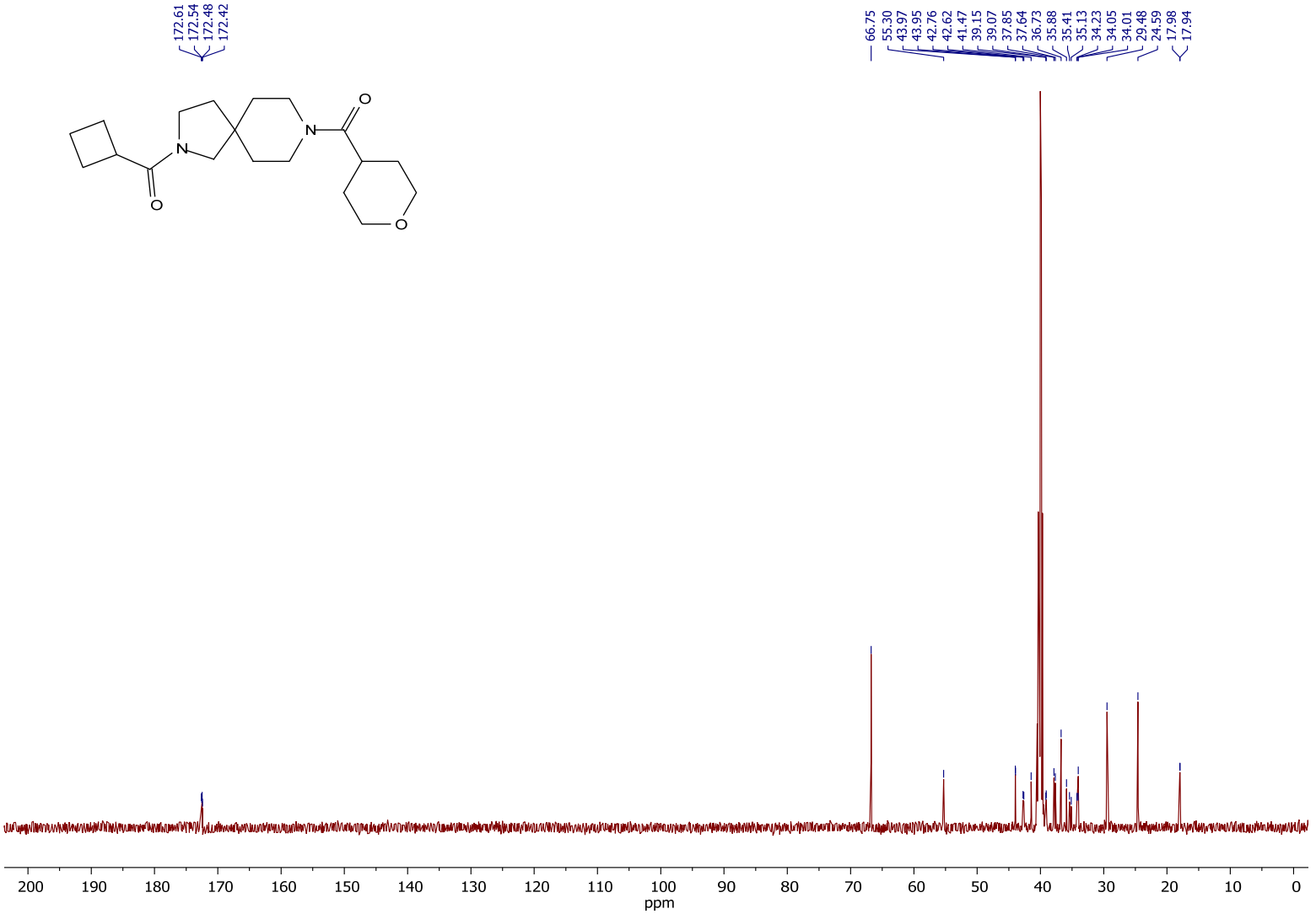

*N*-(1-Cyclopropyl-2-(2-(thiazol-5-yl)acetamido)ethyl)-6-methylnicotinamide (**11**{*30*,*17*,*13*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



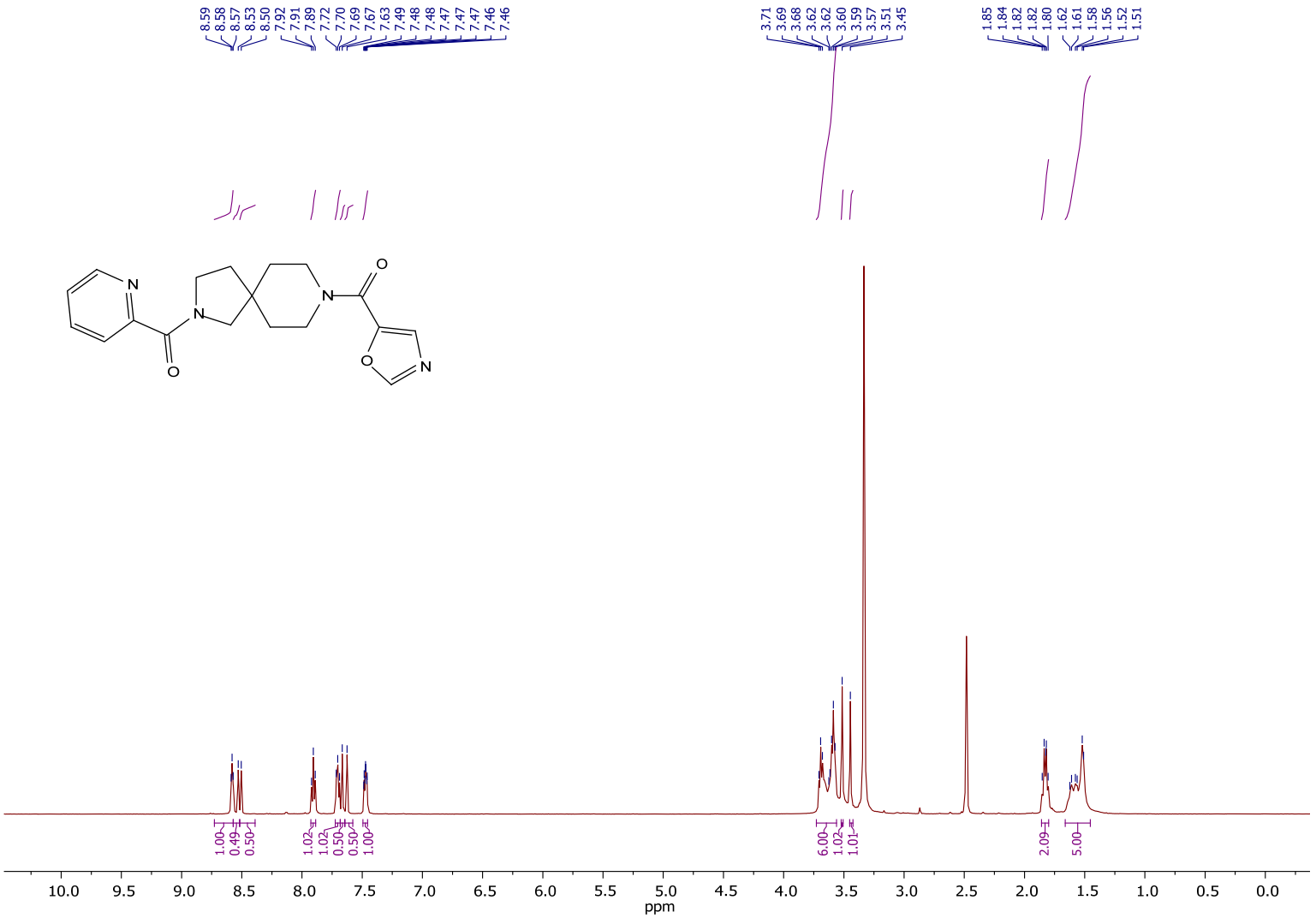

*N*-(1-Cyclopropyl-2-(2-(thiazol-5-yl)acetamido)ethyl)-6-methylnicotinamide (**11**{*30*,*17*,*13*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



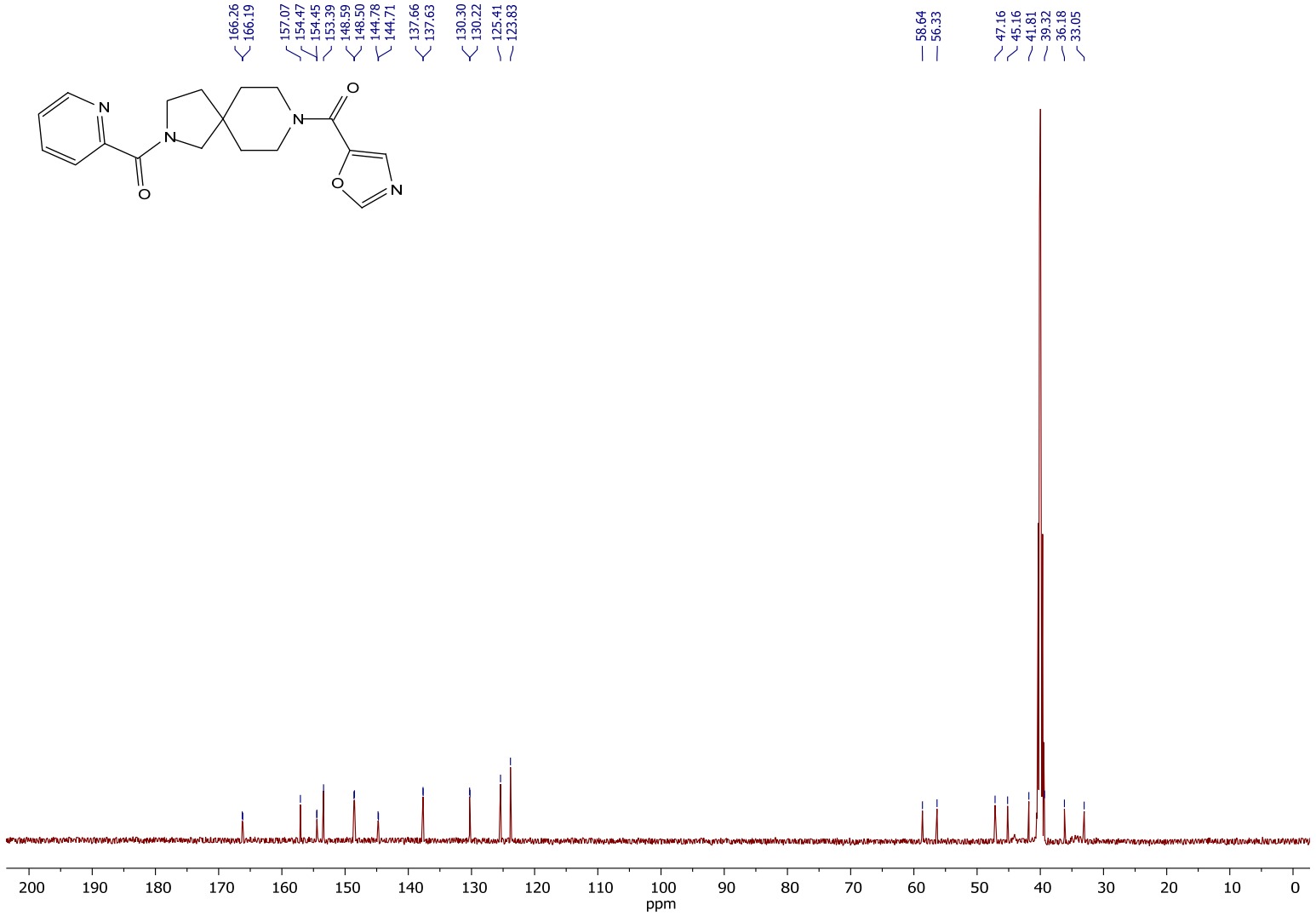

(2-(Cyclobutanecarbonyl)-2,8-diazaspiro[4.5]decan-8-yl)(tetrahydro-2*H*-pyran-4-yl)methanone (**11**{*50*,*64*,*26*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



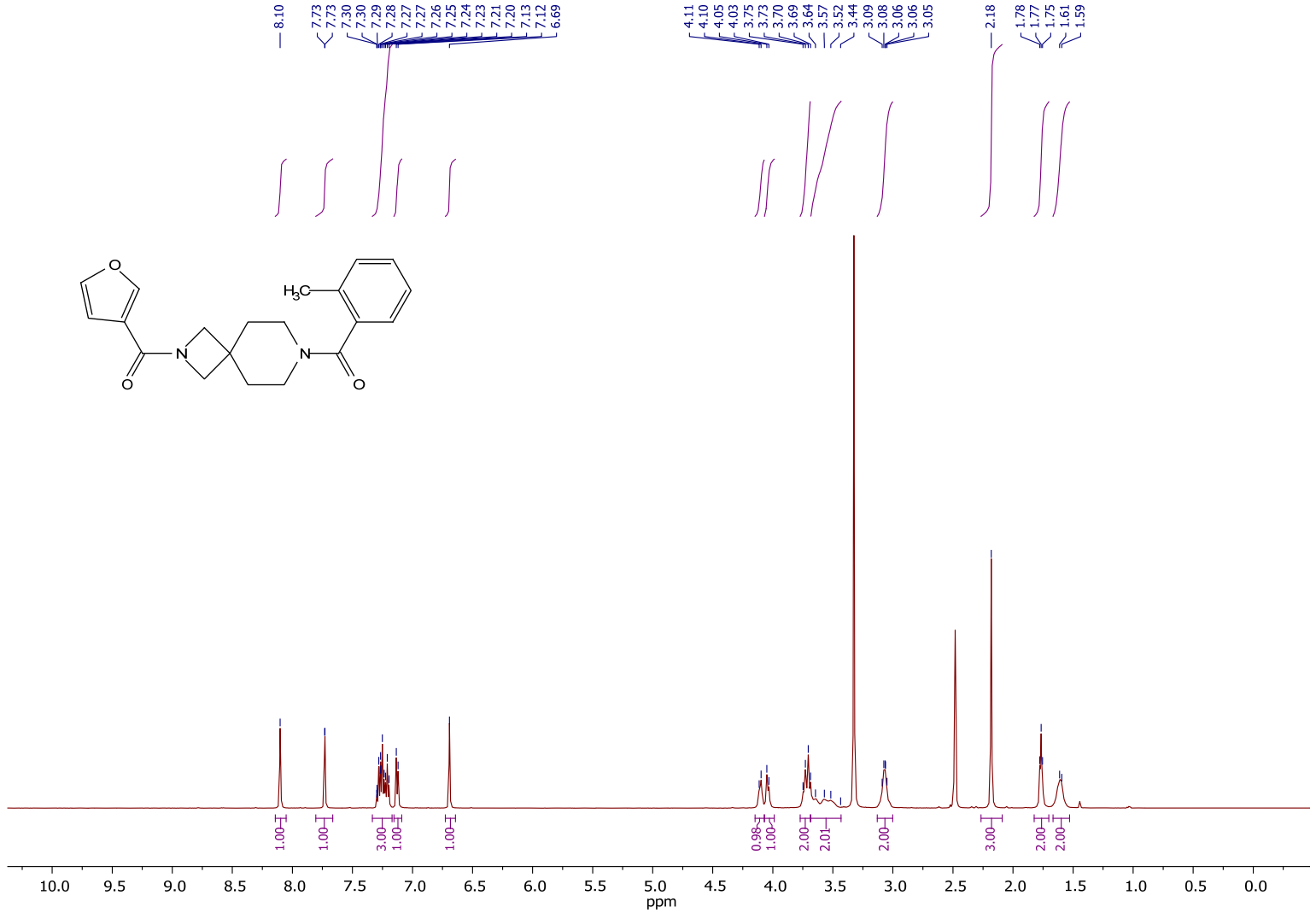

(2-(Cyclobutanecarbonyl)-2,8-diazaspiro[4.5]decan-8-yl)(tetrahydro-2*H*-pyran-4-yl)methanone (**11**{*50*,*64*,*26*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



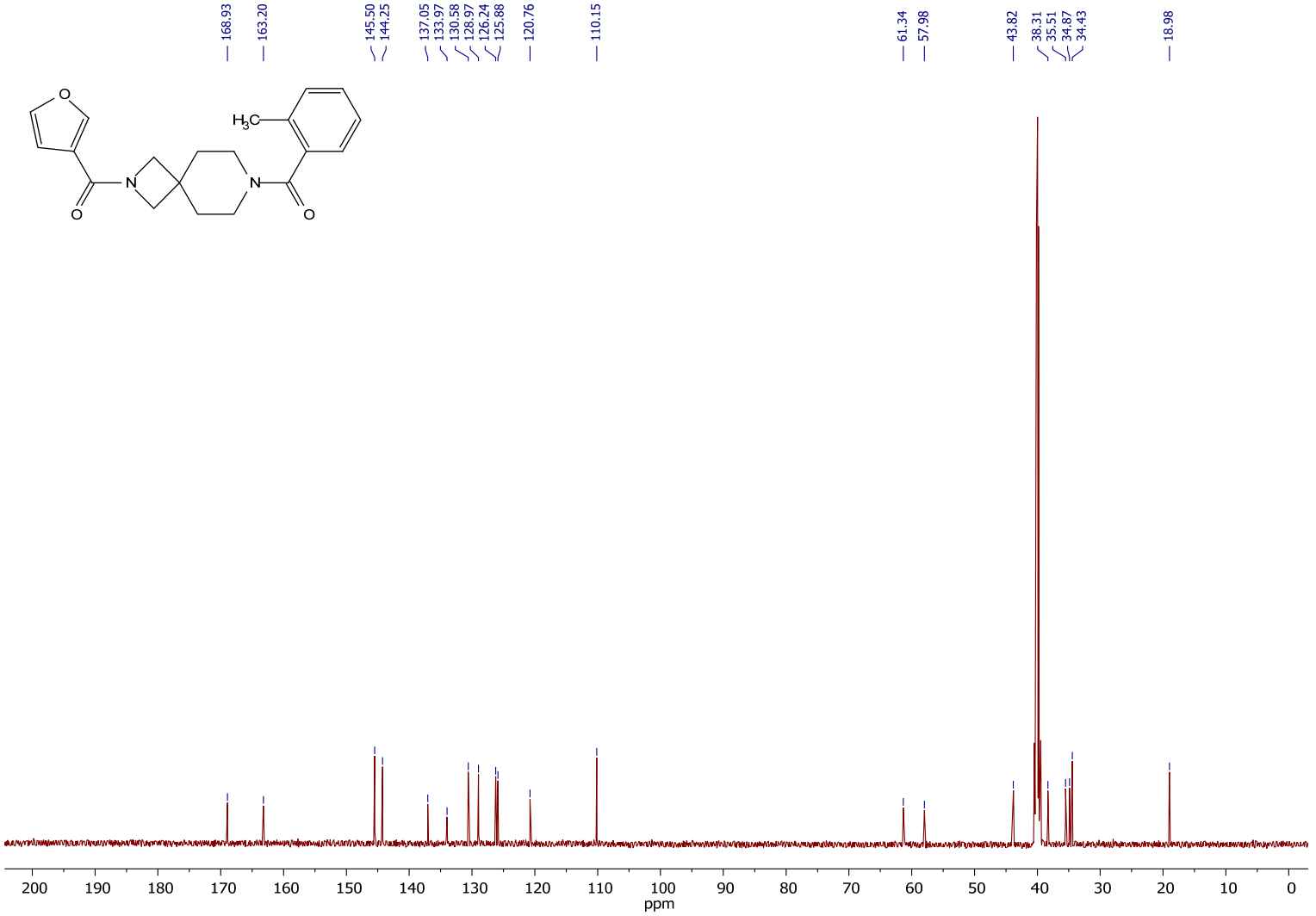

Oxazol-5-yl(2-picolinoyl-2,8-diazaspiro[4.5]decan-8-yl)methanone (**11**{*50*,*69*,*10*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



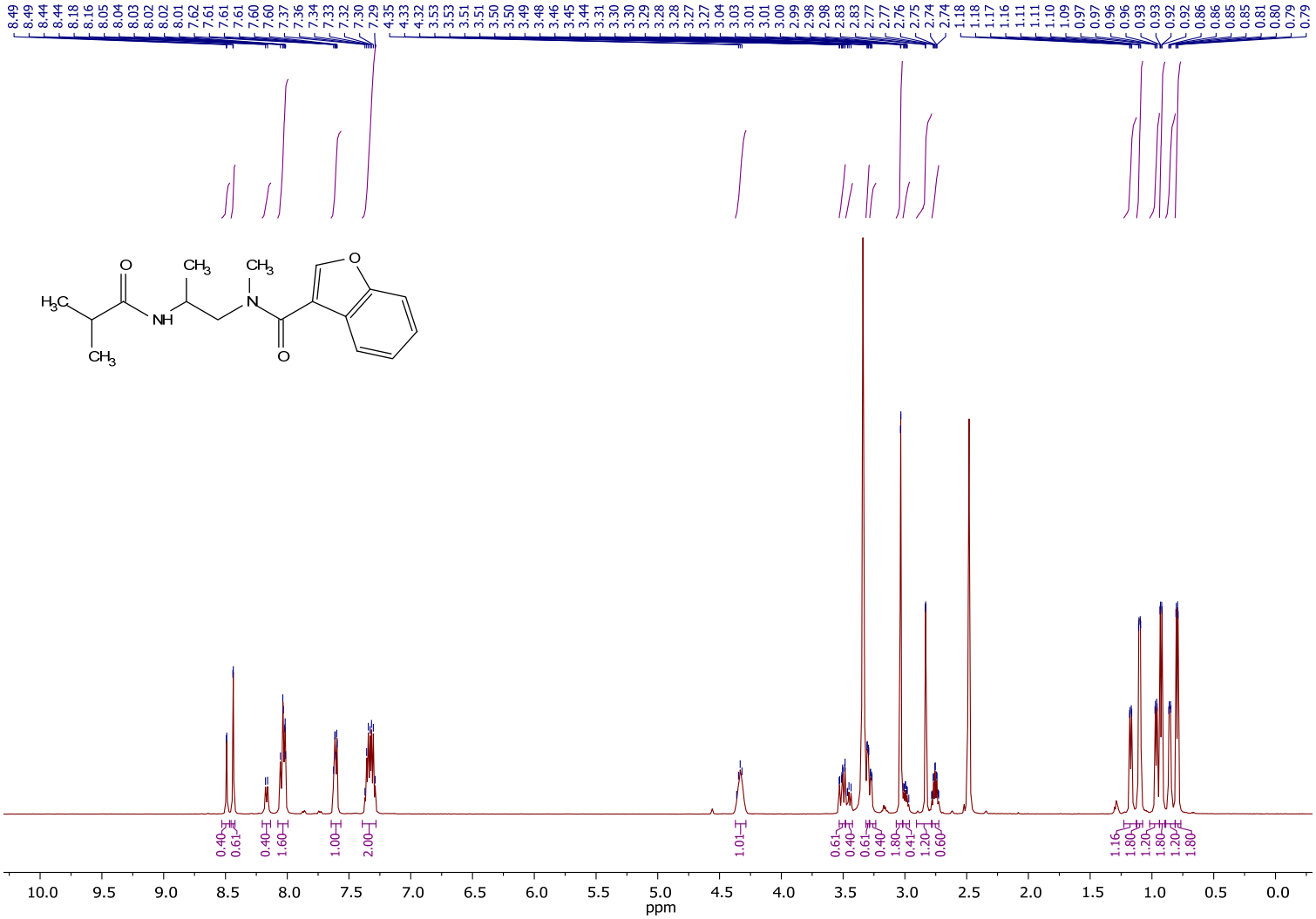

Oxazol-5-yl(2-picolinoyl-2,8-diazaspiro[4.5]decan-8-yl)methanone (**11**{*50*,*69*,*10*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



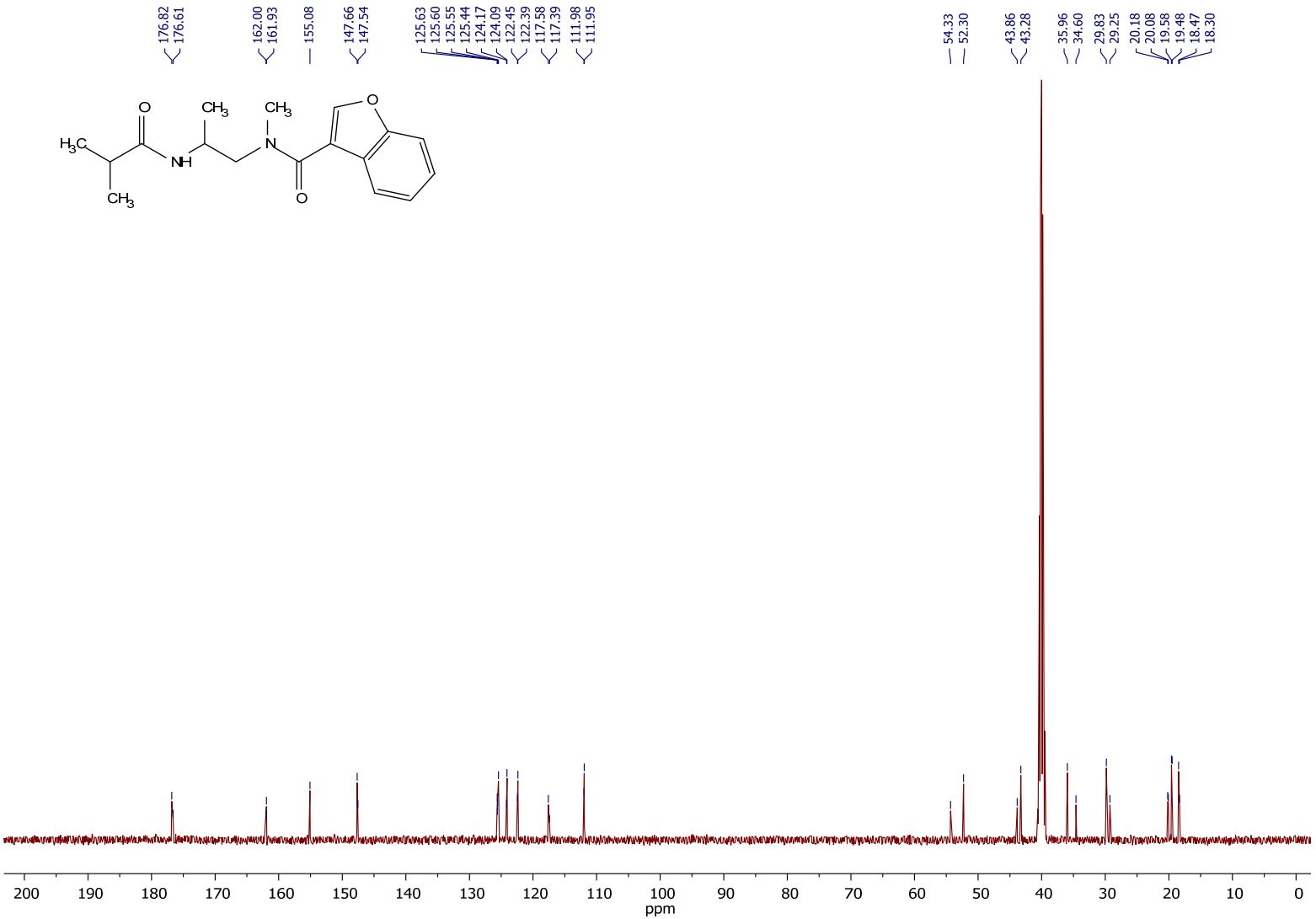

(2-(Furan-3-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)(*o*-tolyl)methanone (**11**{*60*,*73*,*32*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



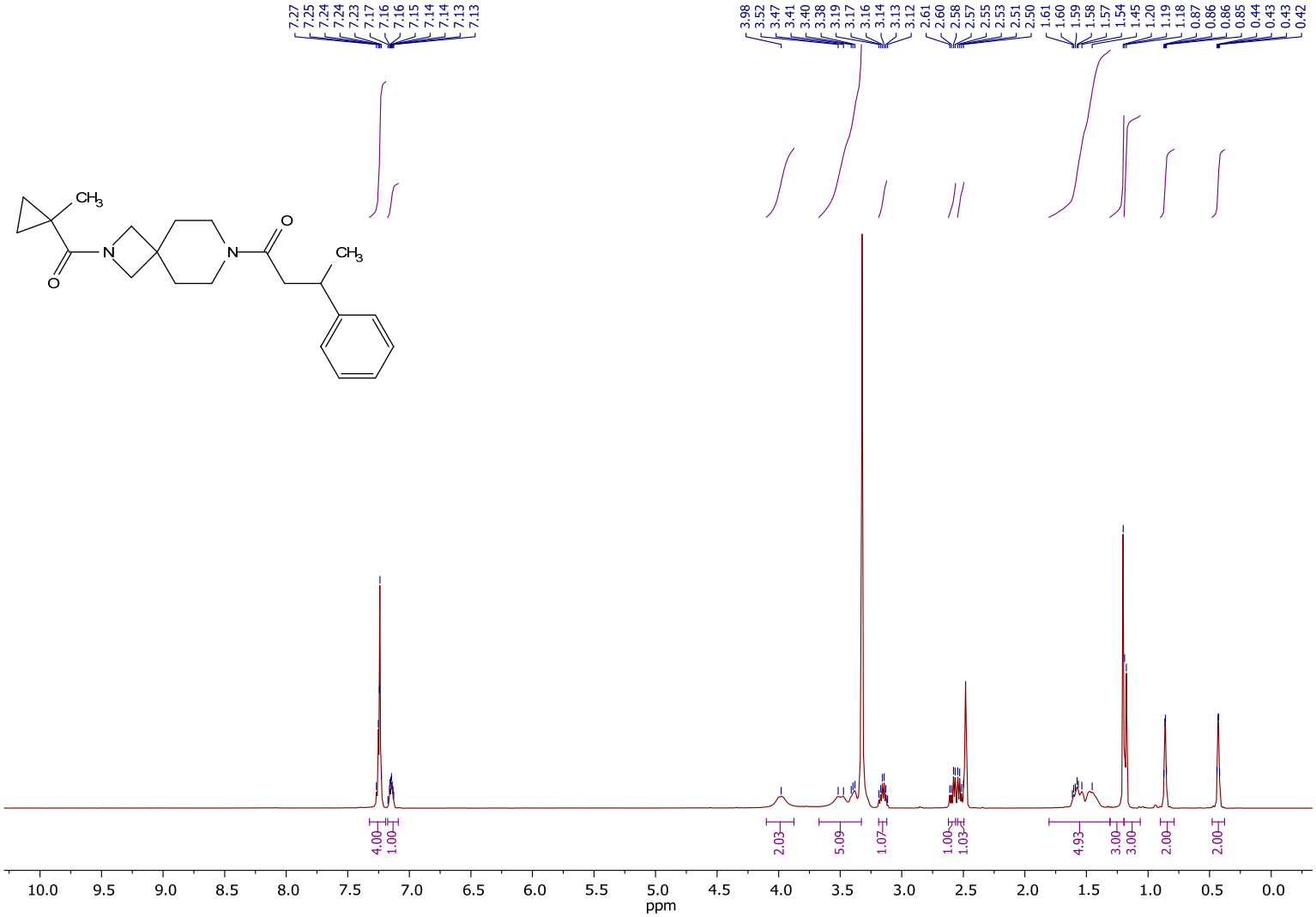

(2-(Furan-3-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)(*o*-tolyl)methanone (**11**{*60*,*73*,*32*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



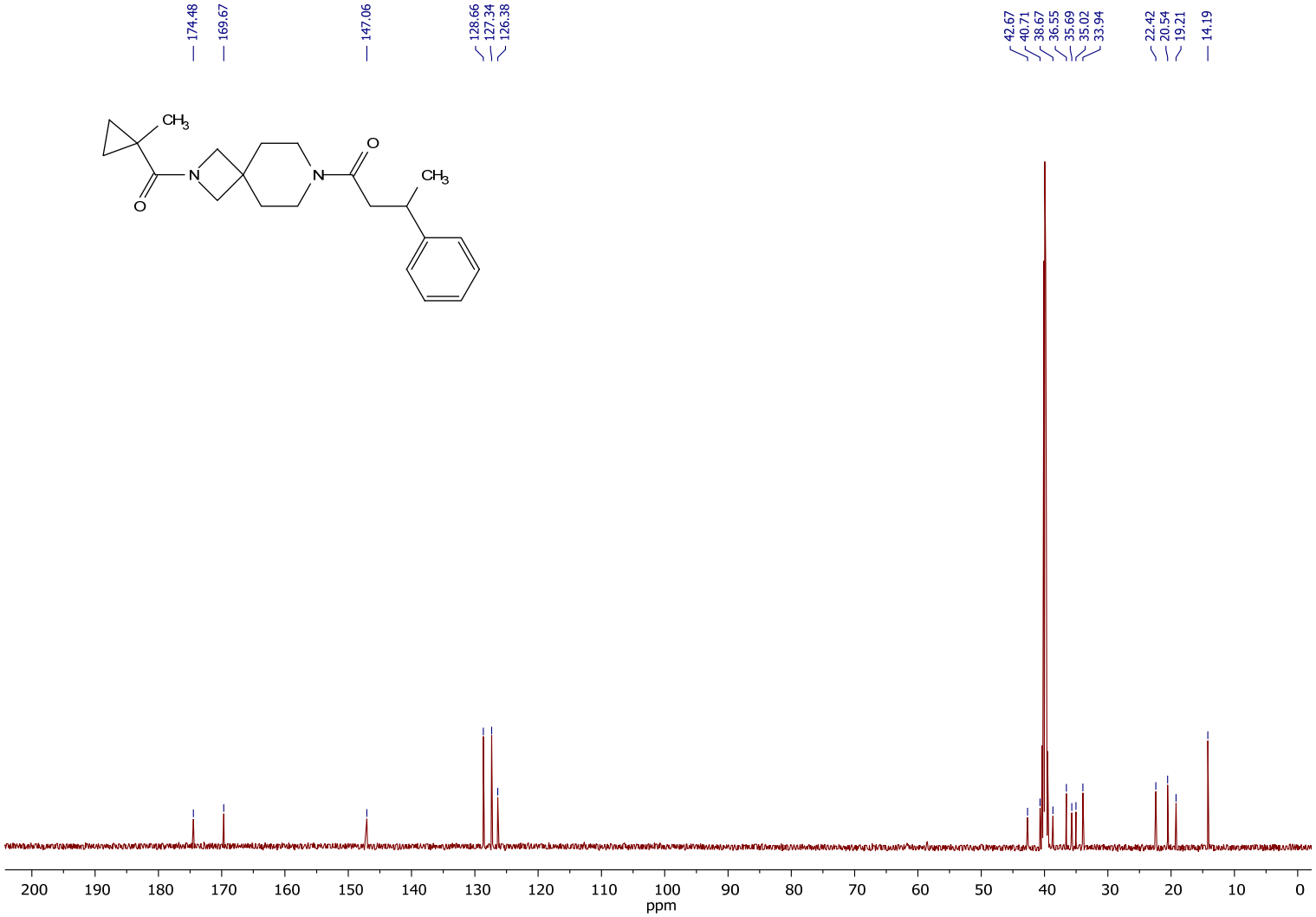

*N*-(2-Isobutyramidopropyl)-*N*-methylbenzofuran-3-carboxamide (**11**{*67*,*81*,*37*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



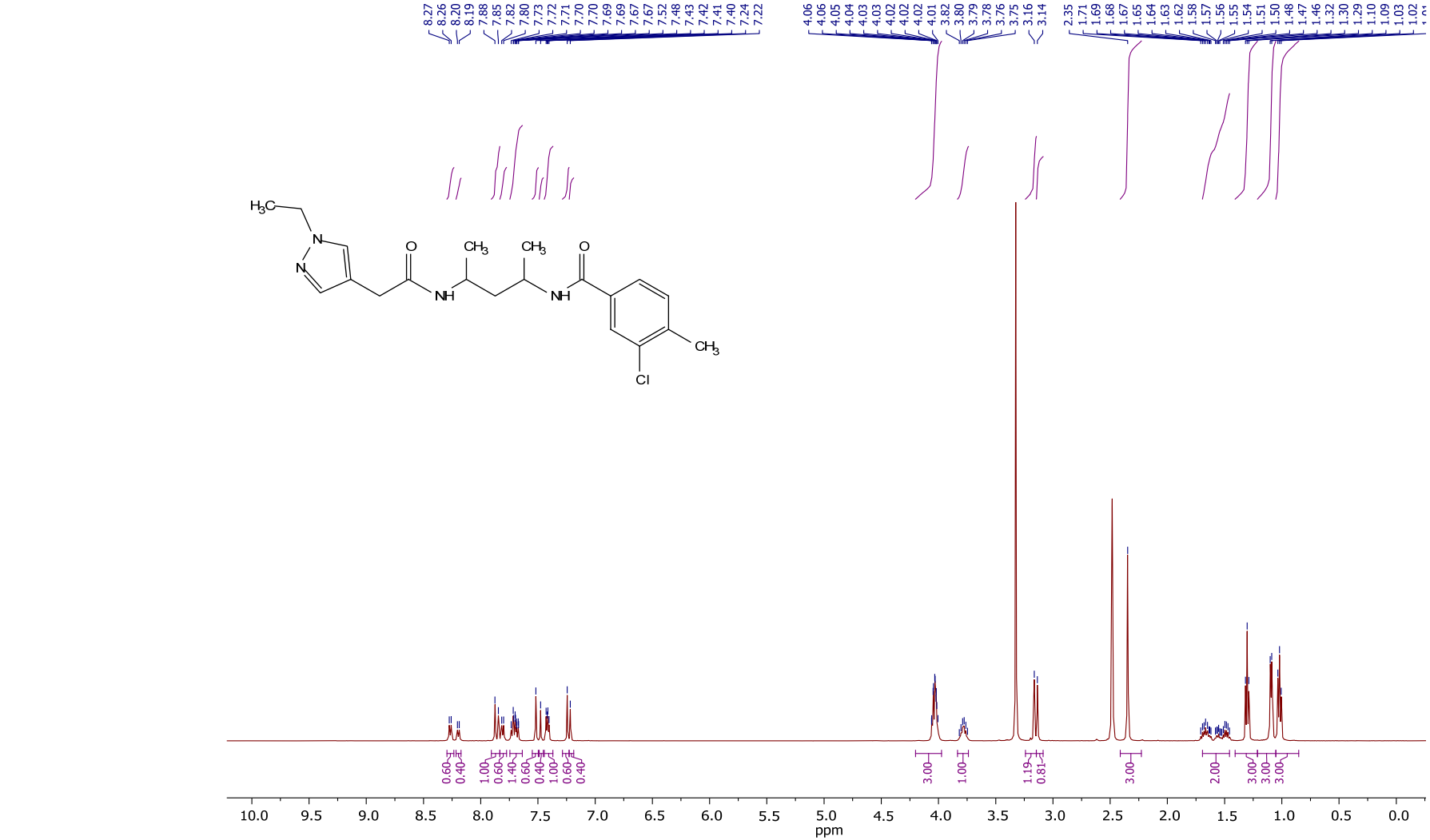

*N*-(2-Isobutyramidopropyl)-*N*-methylbenzofuran-3-carboxamide (**11**{*67*,*81*,*37*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



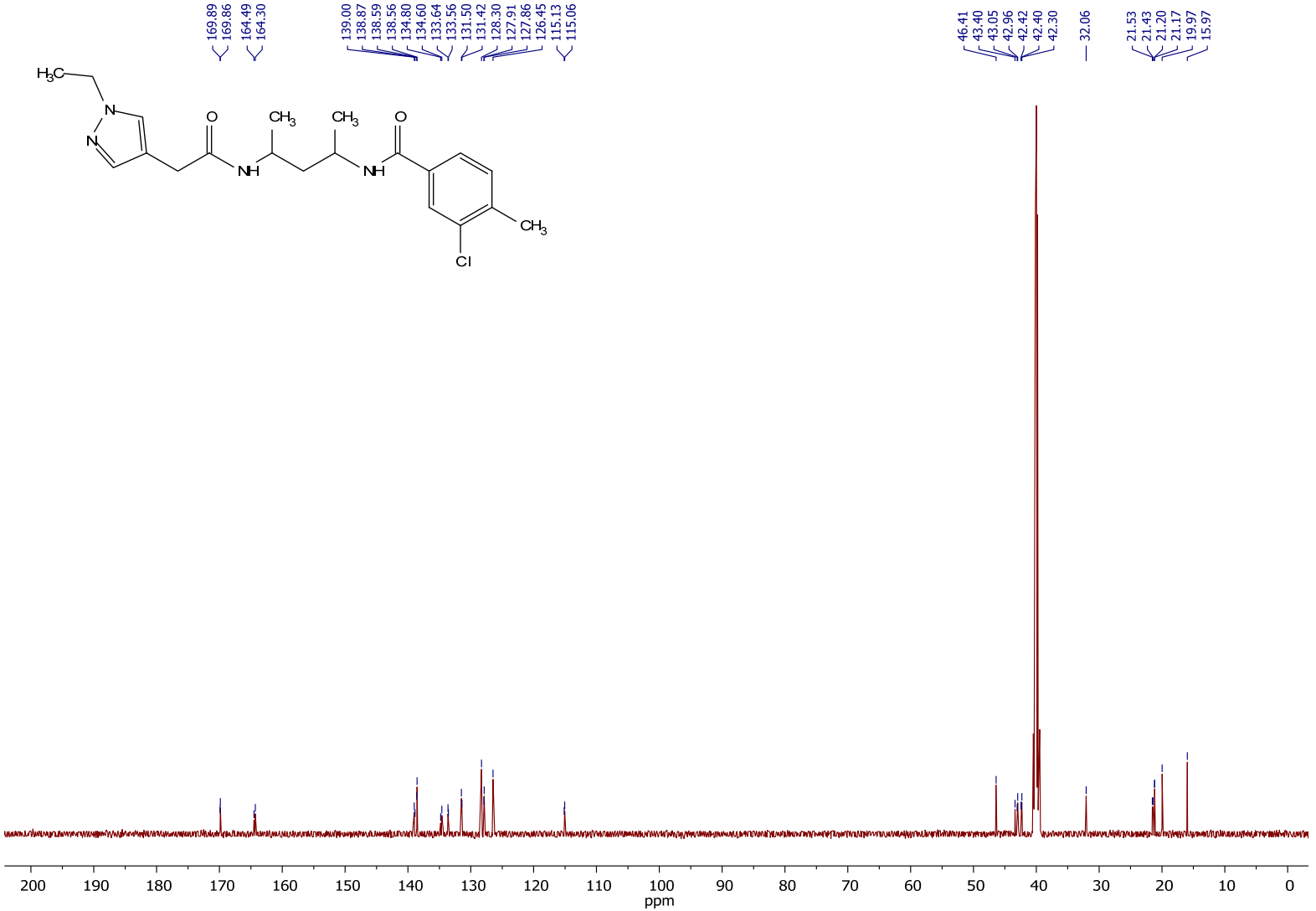

1-(2-(1-Methylcyclopropane-1-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-phenylbutan-1-one (**11**{*60*,*102*,*51*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



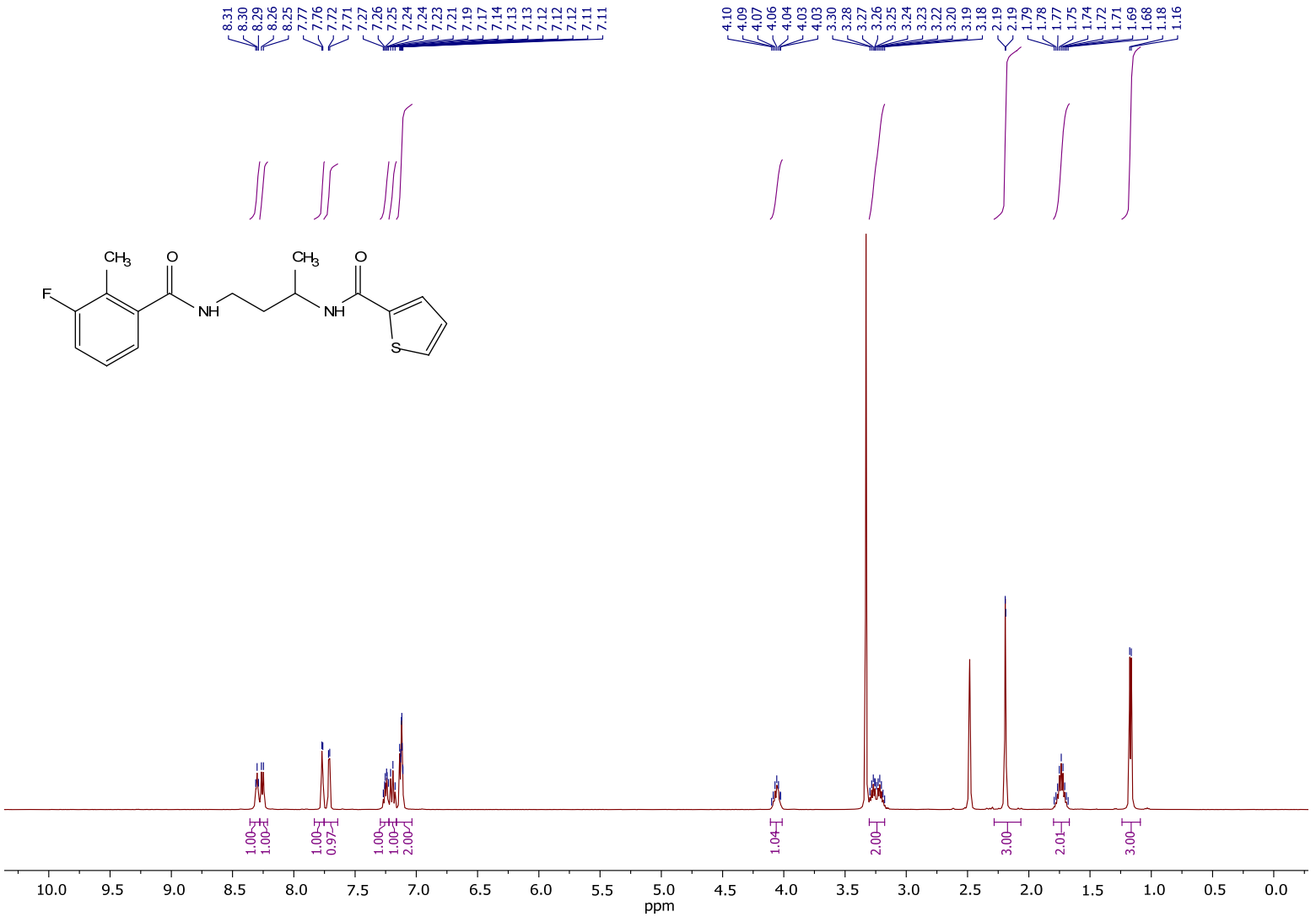

1-(2-(1-Methylcyclopropane-1-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-phenylbutan-1-one (**11**{*60*,*102*,*51*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



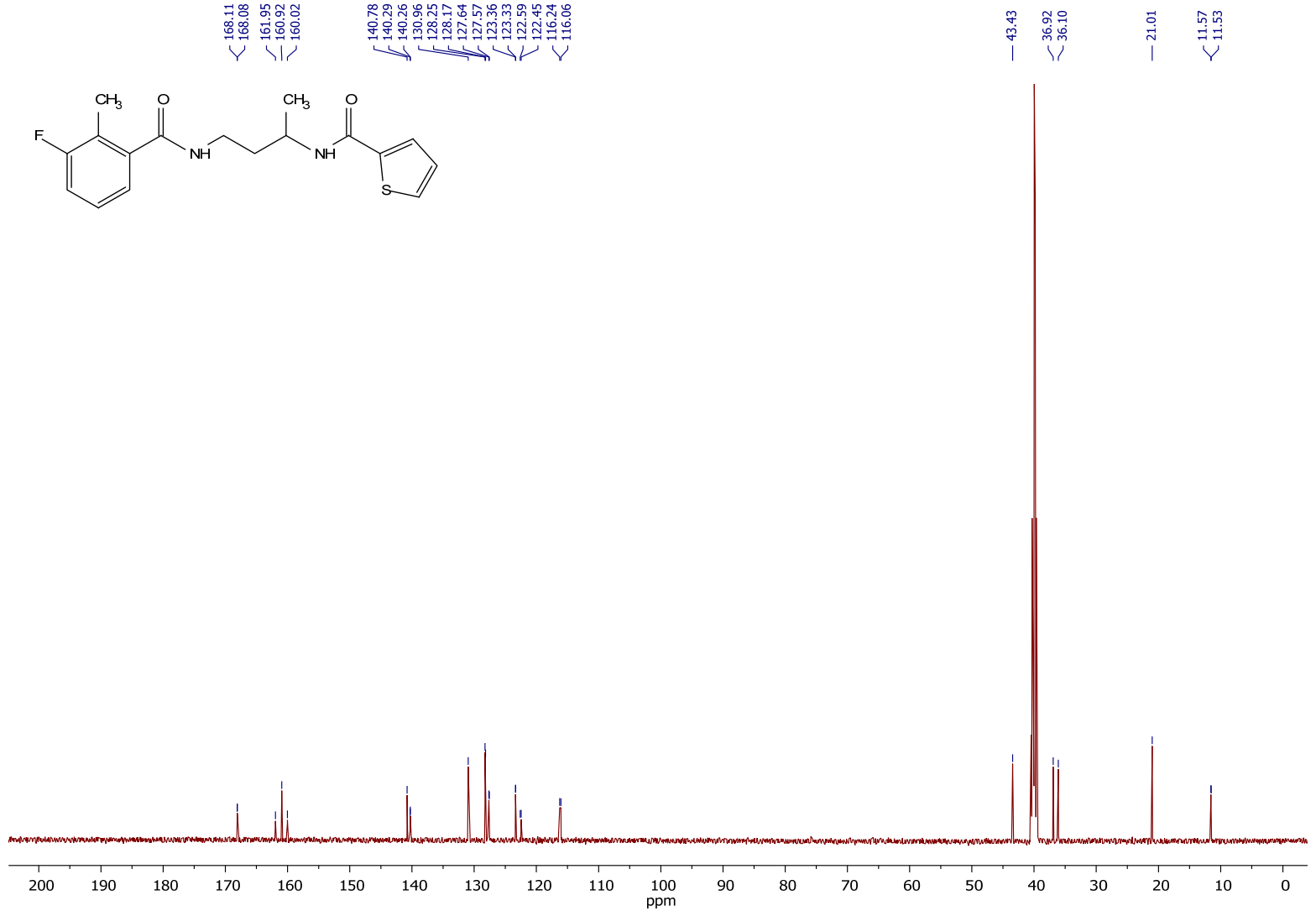

3-Chloro-*N*-(4-(2-(1-ethyl-1*H*-pyrazol-4-yl)acetamido)pentan-2-yl)-4-methylbenzamide (**11**{*70*,*84*,*38*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



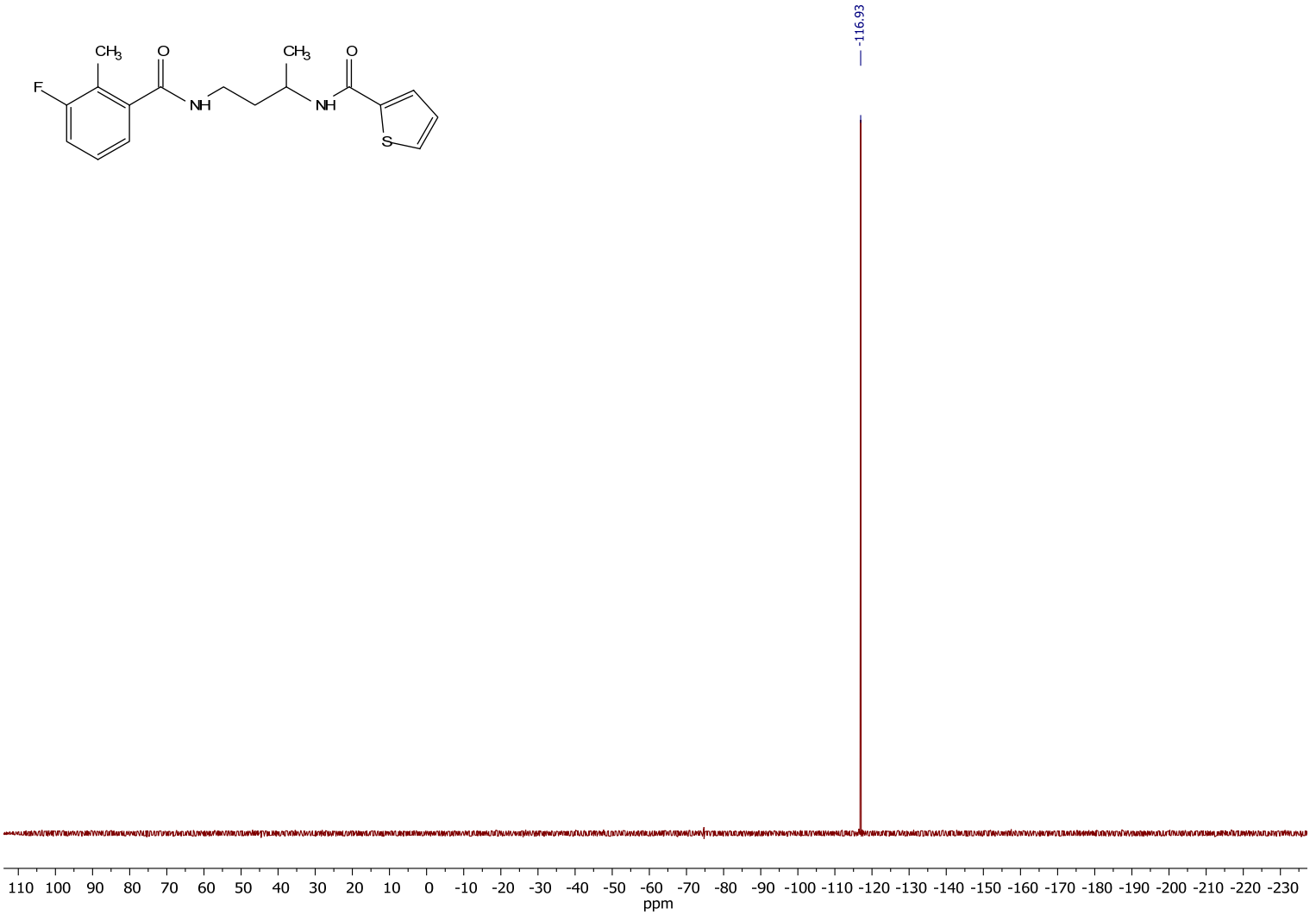

3-Chloro-*N*-(4-(2-(1-ethyl-1*H*-pyrazol-4-yl)acetamido)pentan-2-yl)-4-methylbenzamide (**11**{*70*,*84*,*38*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$



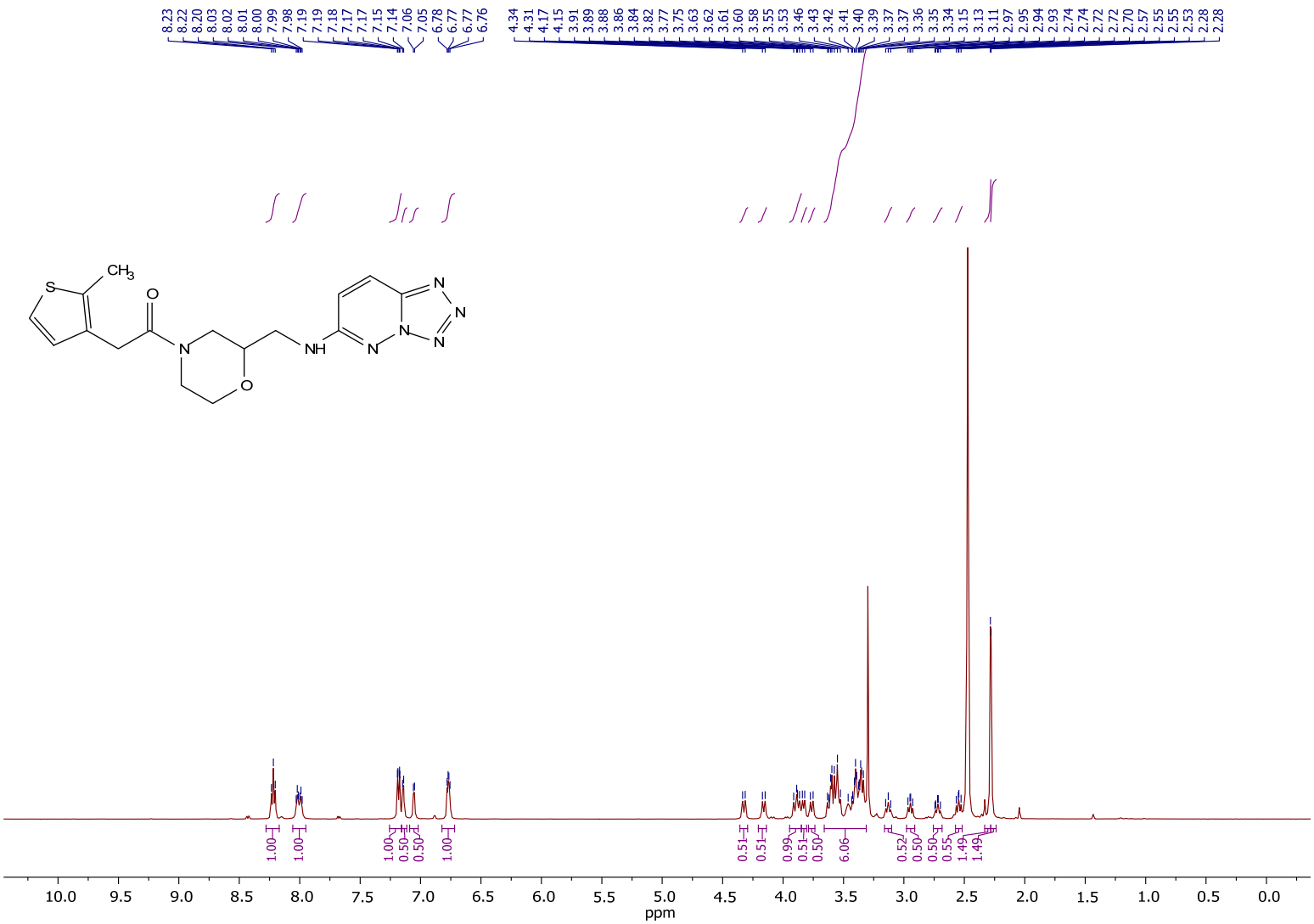

*N*-(4-(3-Fluoro-2-methylbenzamido)butan-2-yl)thiophene-2-carboxamide (**11**{*83*,*105*,*54*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



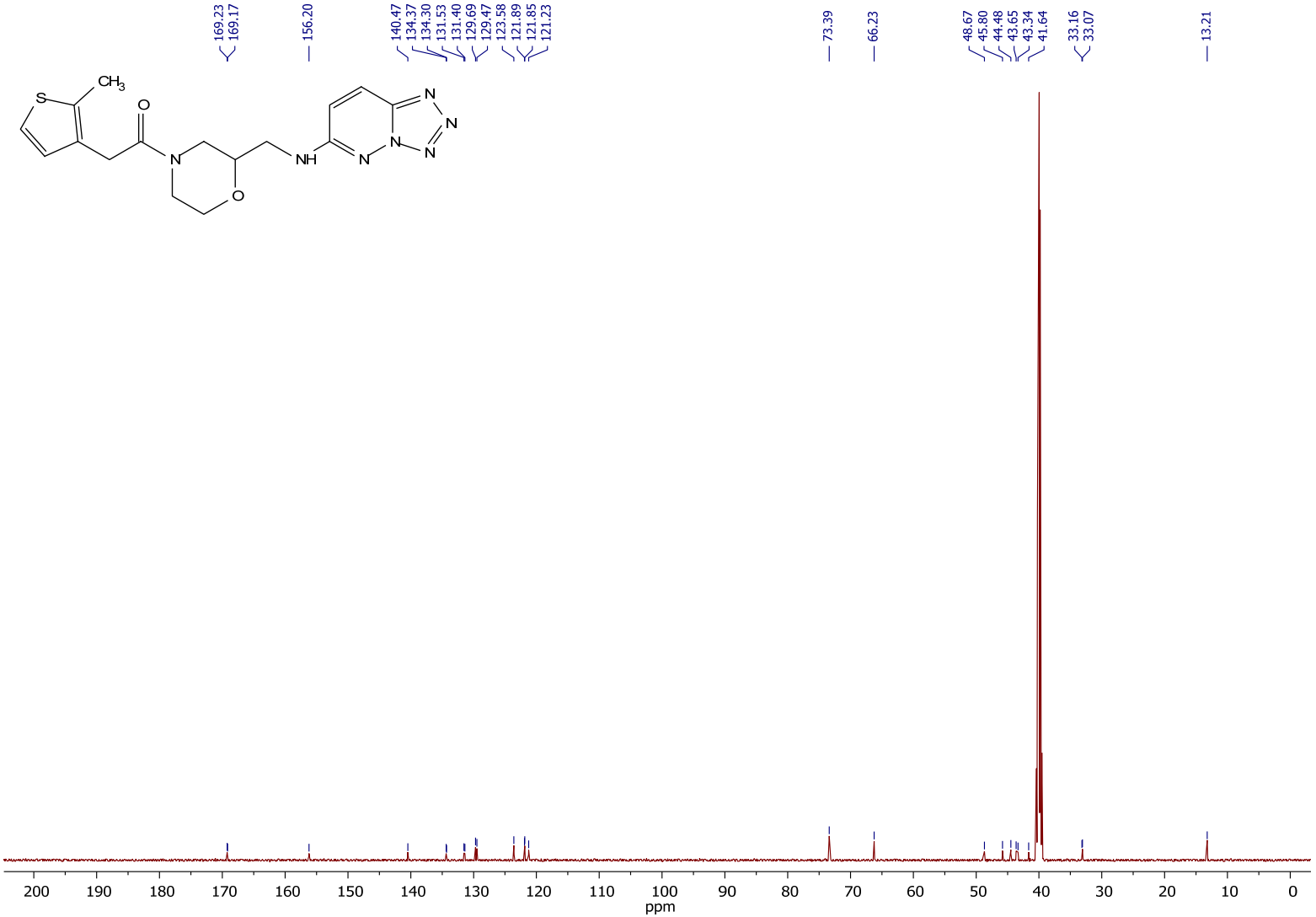

*N*-(4-(3-Fluoro-2-methylbenzamido)butan-2-yl)thiophene-2-carboxamide (**11**{*83*,*105*,*54*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



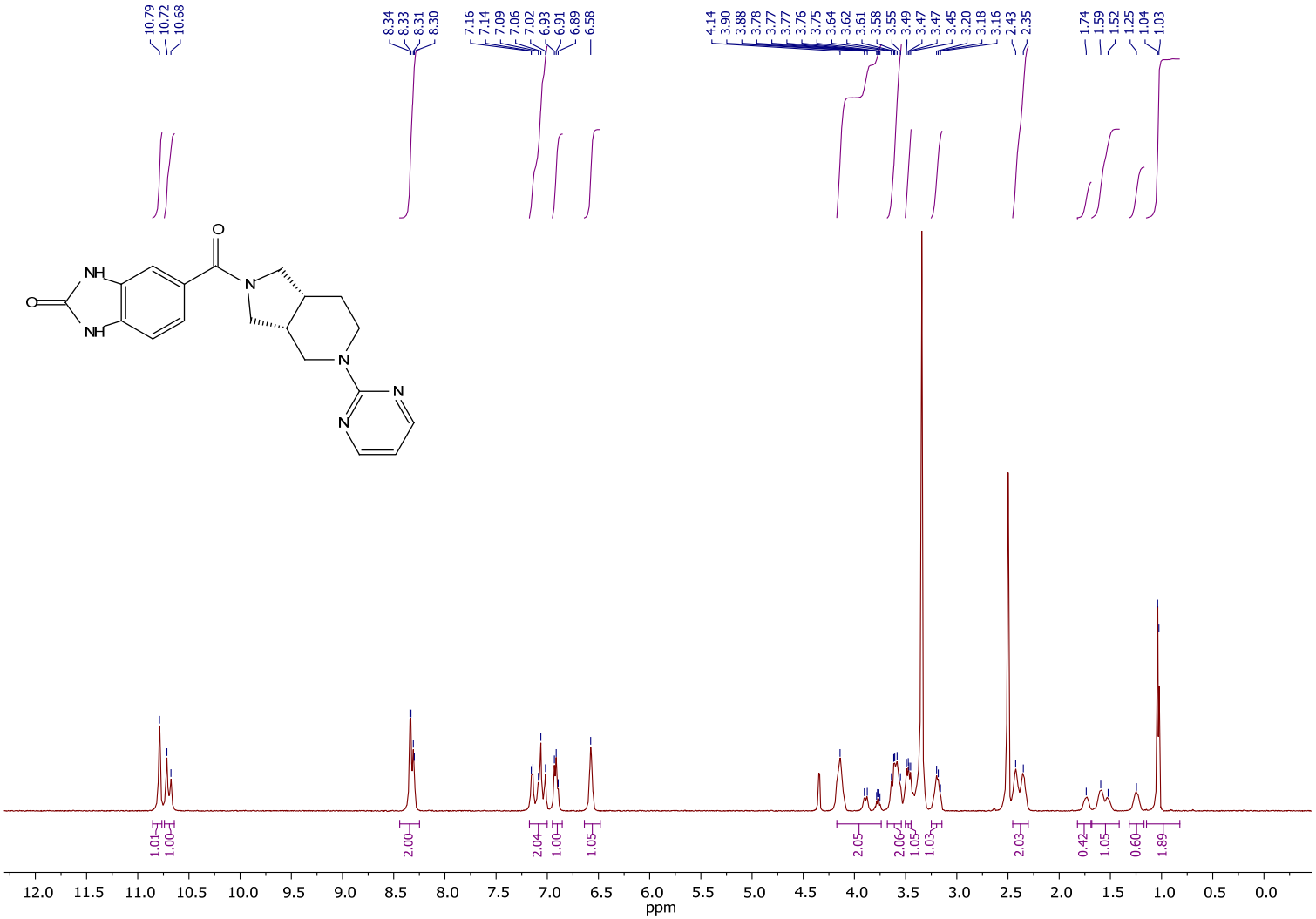

*N*-(4-(3-Fluoro-2-methylbenzamido)butan-2-yl)thiophene-2-carboxamide (**11**{*83*,*105*,*54*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$)



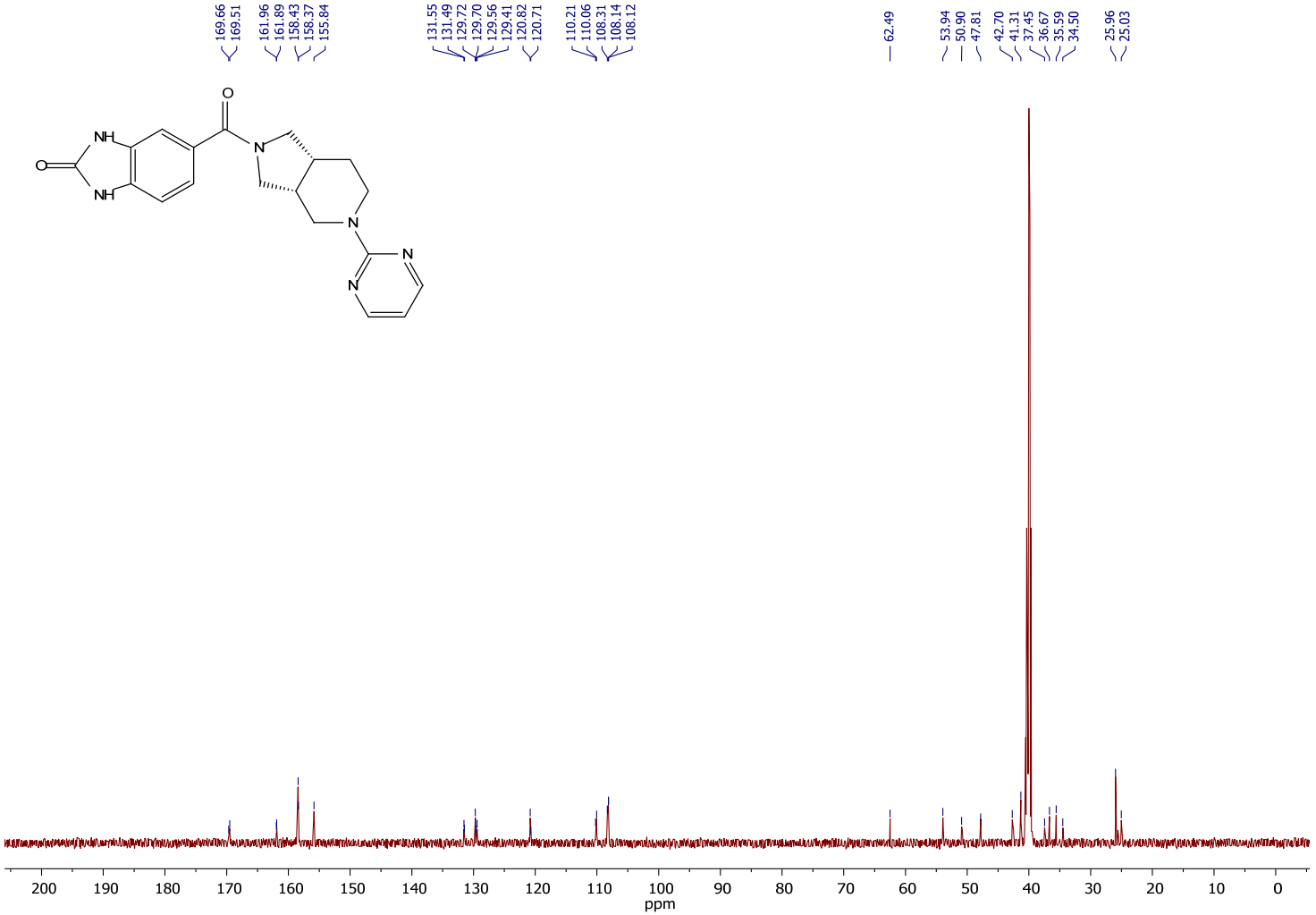

2-(2-Methylthiophen-3-yl)-1-(2-((tetrazolo[1,5-*b*]pyridazin-6-ylamino)methyl)morpholino)ethanone (**12**{*140*,*239*,*35*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



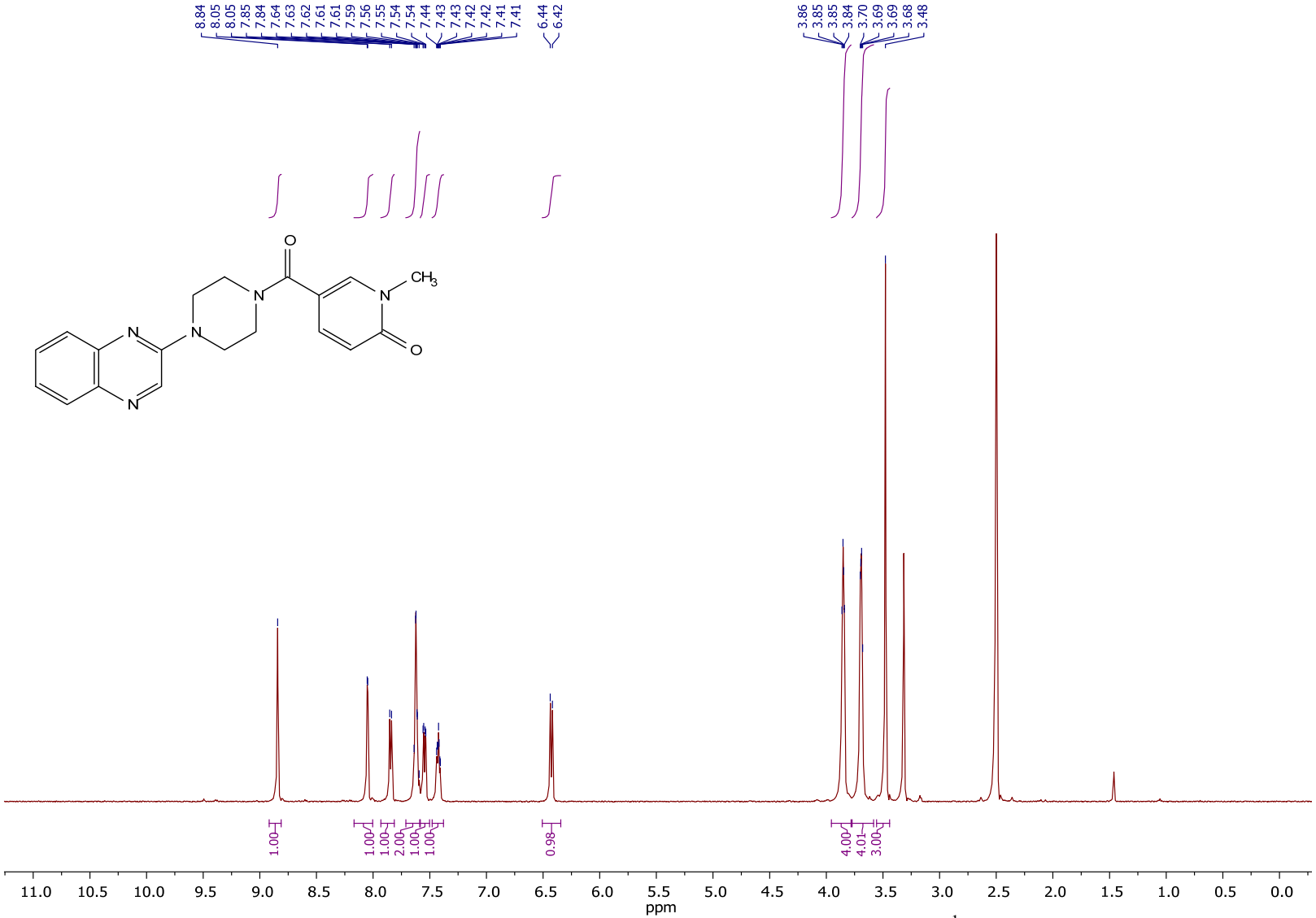

2-(2-Methylthiophen-3-yl)-1-(2-((tetrazolo[1,5-*b*]pyridazin-6-ylamino)methyl)morpholino)ethanone (**12**{*140*,*239*,*35*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



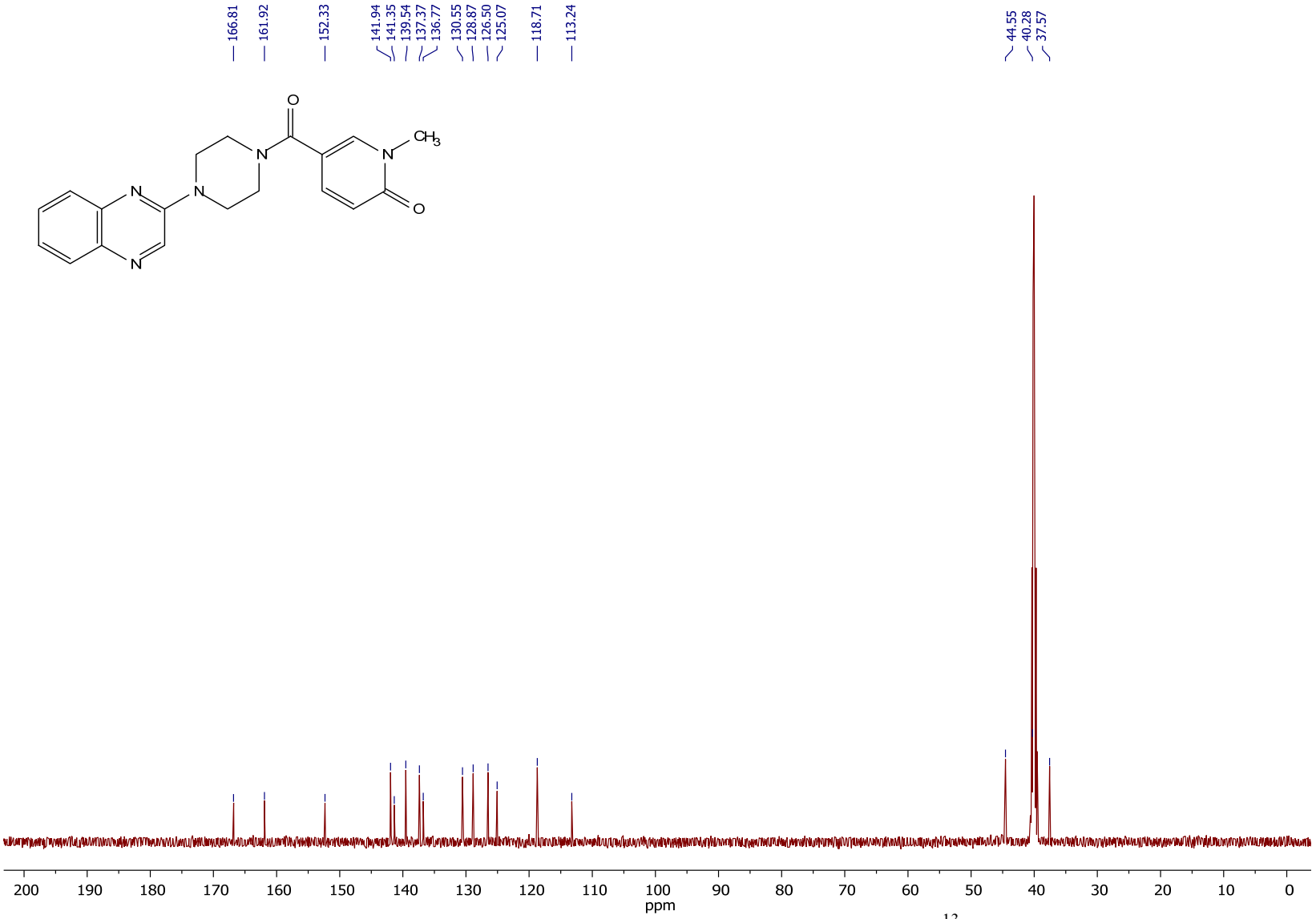

*rac*-5-((3a*R*,7a*R*)-5-(Pyrimidin-2-yl)octahydro-1*H*-pyrrolo[3,4-*c*]pyridine-2-carbonyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (**12**{*17*,*14*,*5*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



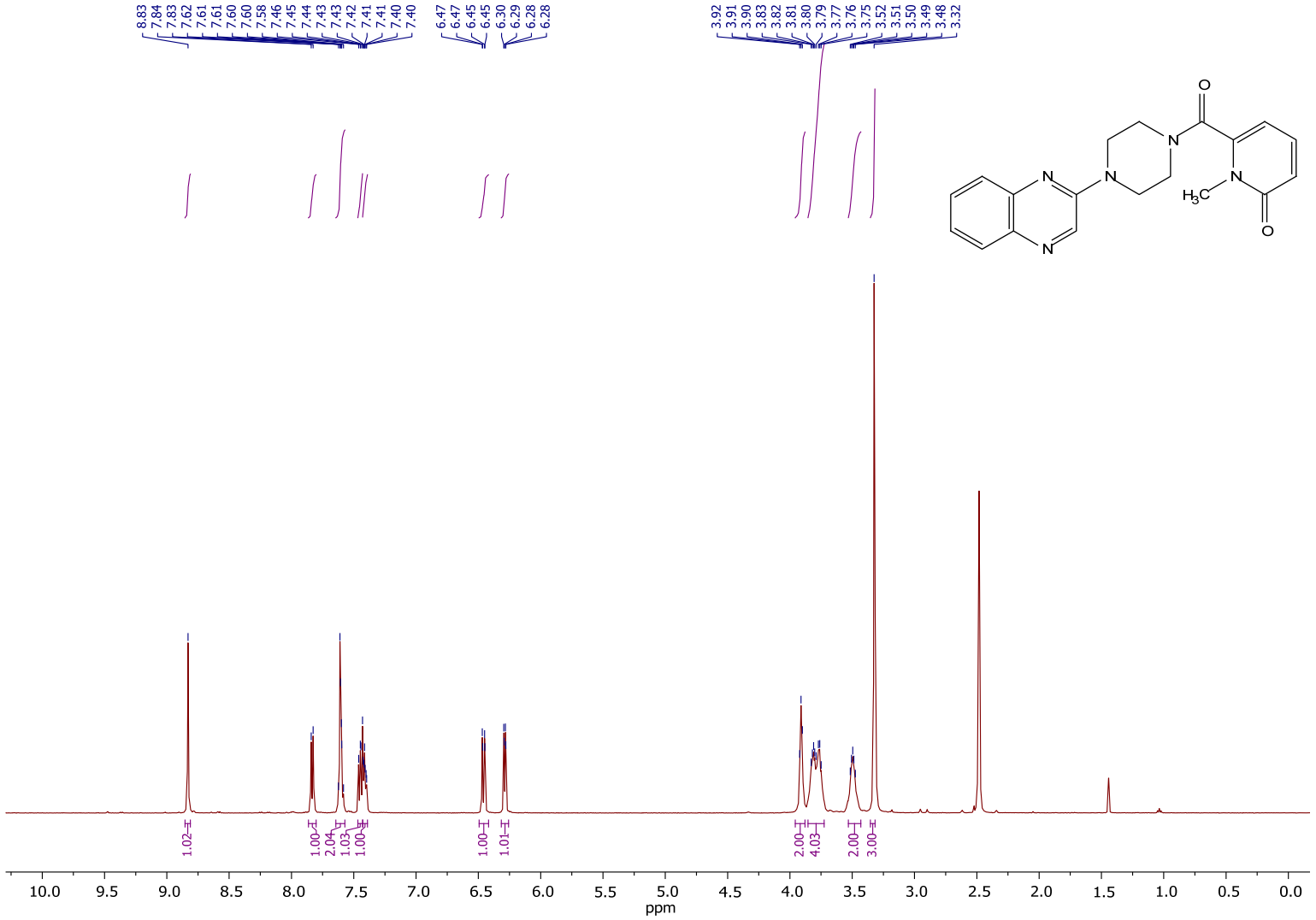

*rac*-5-((3a*R*,7a*R*)-5-(Pyrimidin-2-yl)octahydro-1*H*-pyrrolo[3,4-*c*]pyridine-2-carbonyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (**12**{*17*,*14*,*5*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



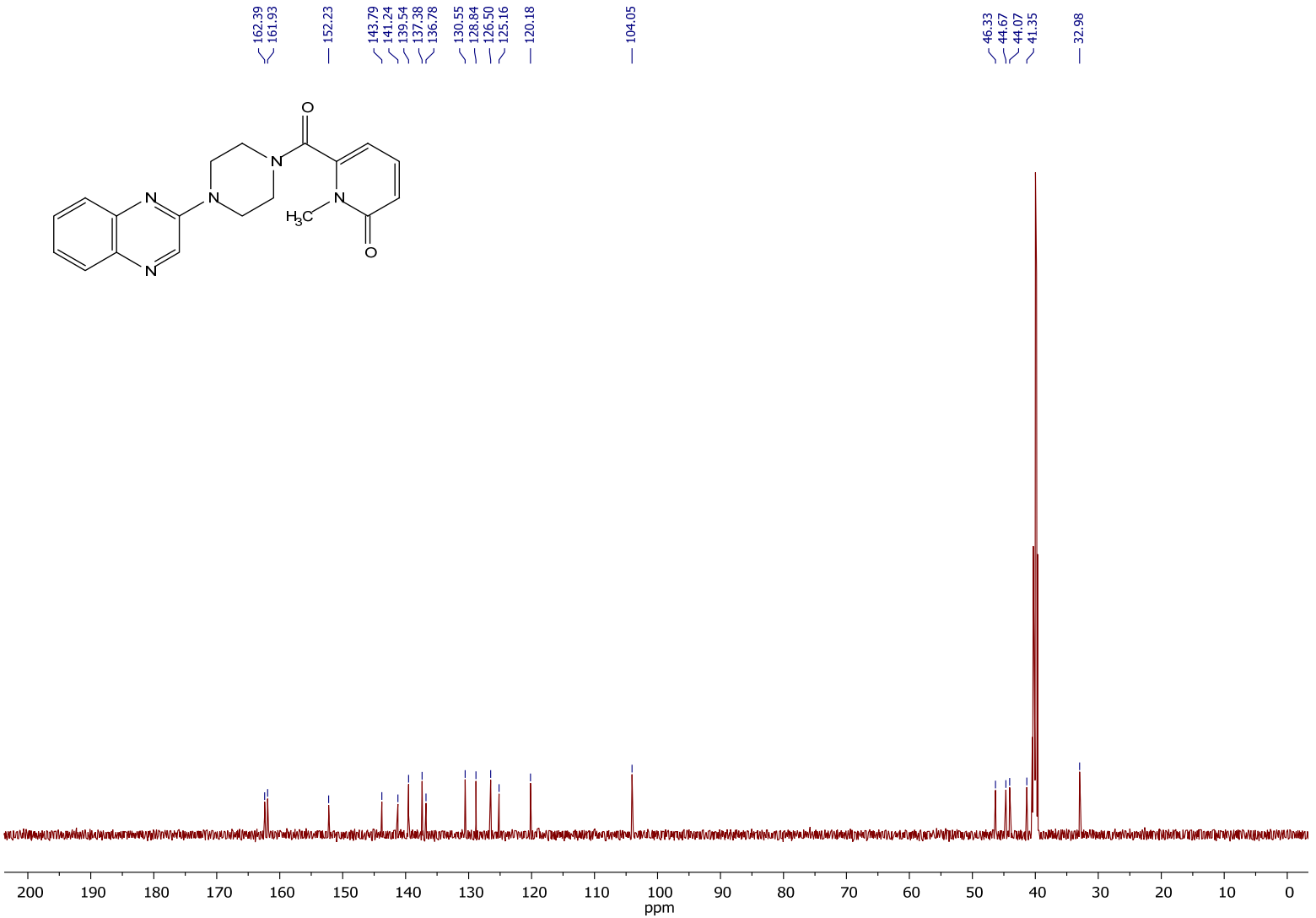

1-Methyl-5-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (**12**{*9*,*26*,*3*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



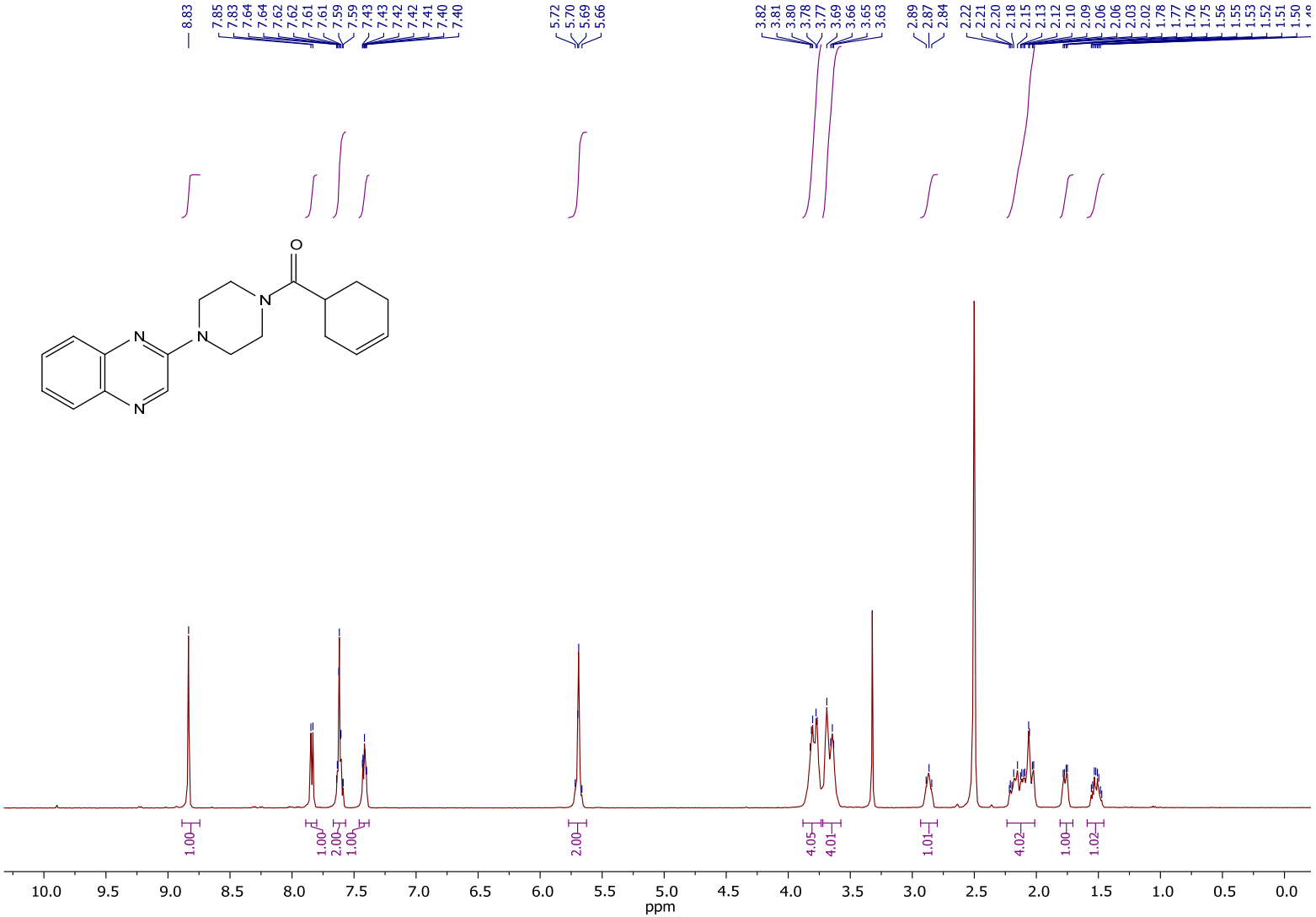

1-Methyl-5-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (**12**{*9*,*26*,*3*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



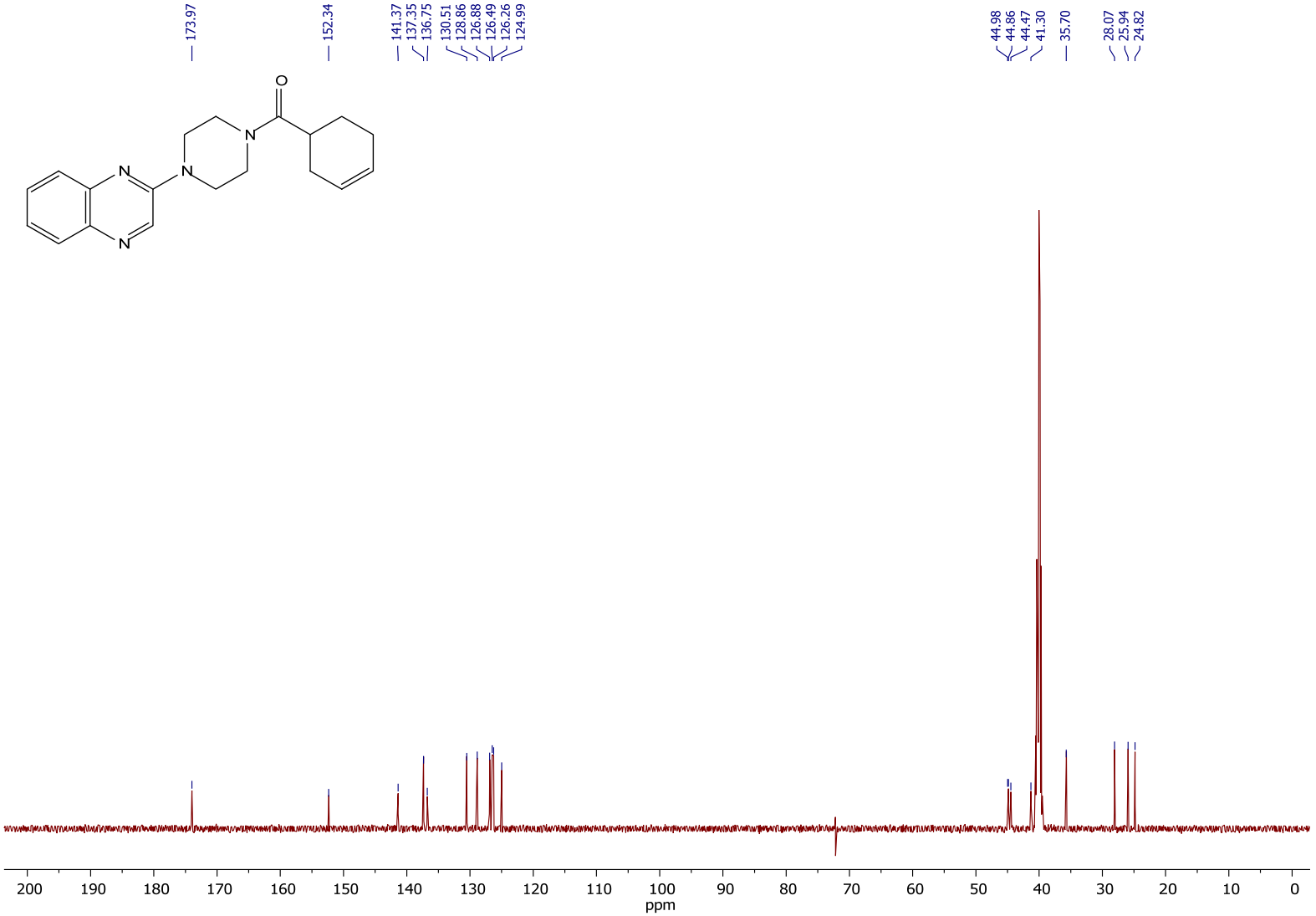

1-Methyl-6-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (**12**{*9*,*27*,*3*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



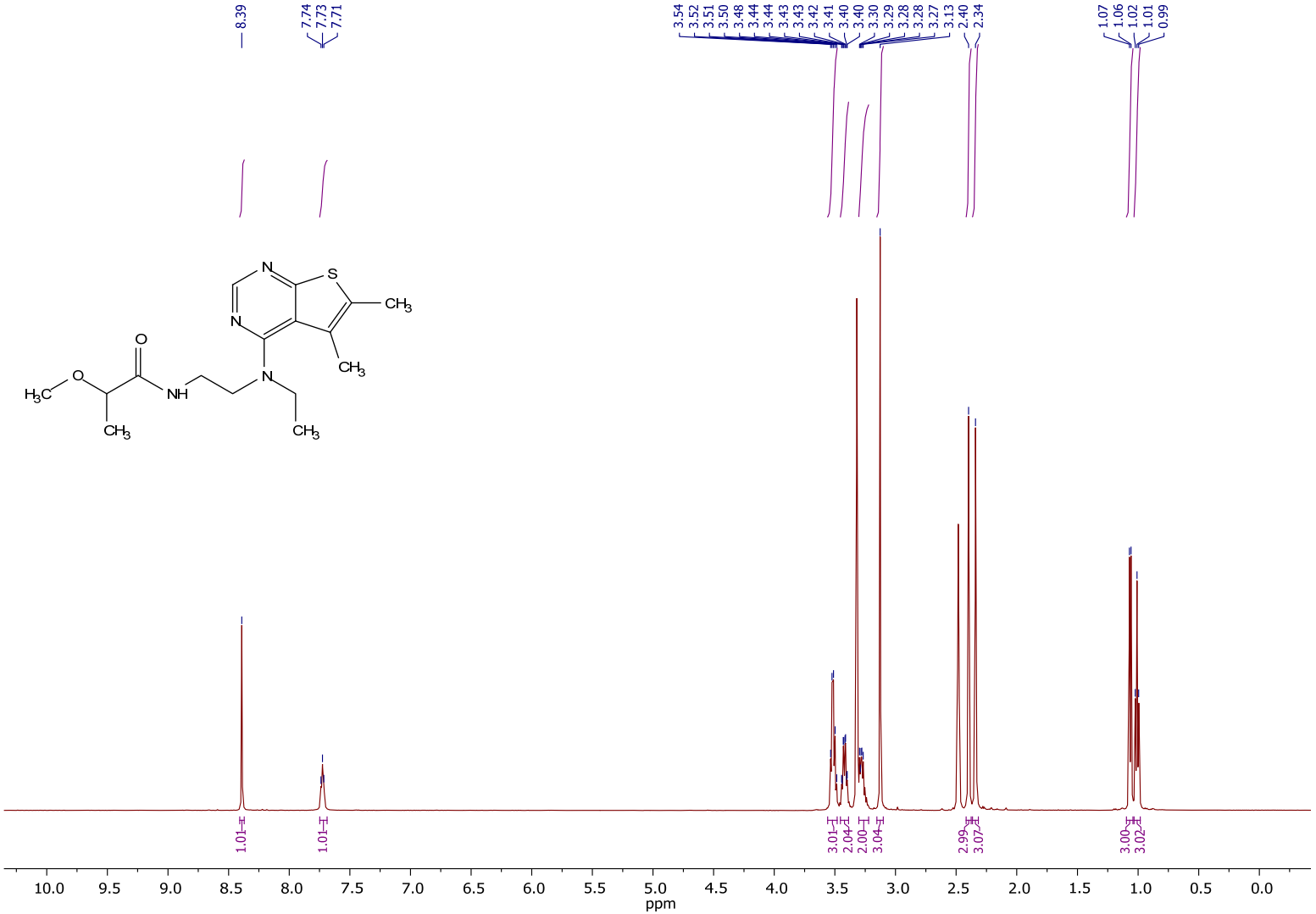

1-Methyl-6-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (**12**{*9*,*27*,*3*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



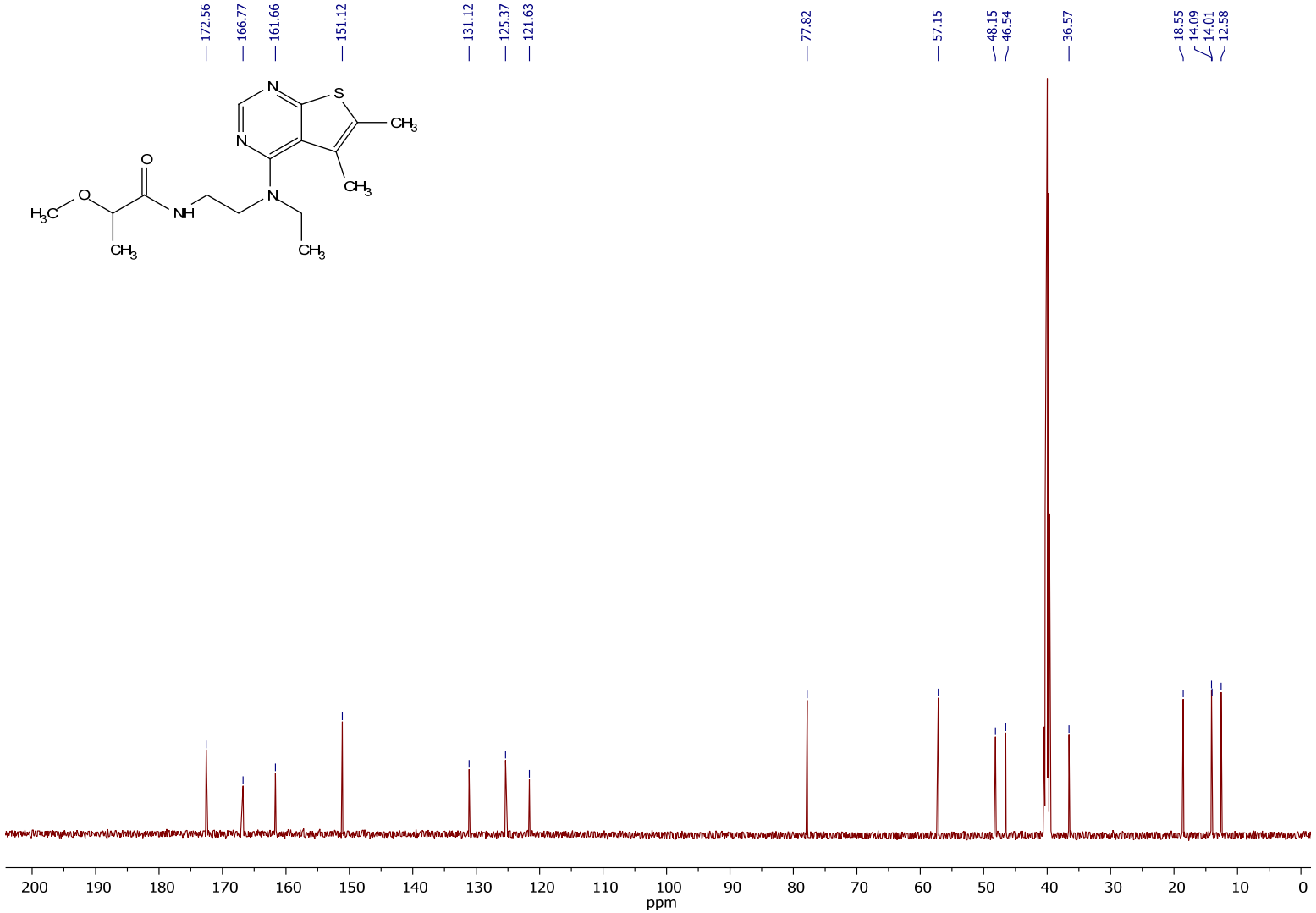

Cyclohex-3-en-1-yl(4-(quinoxalin-2-yl)piperazin-1-yl)methanone (**12**{*9*,*28*,*3*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



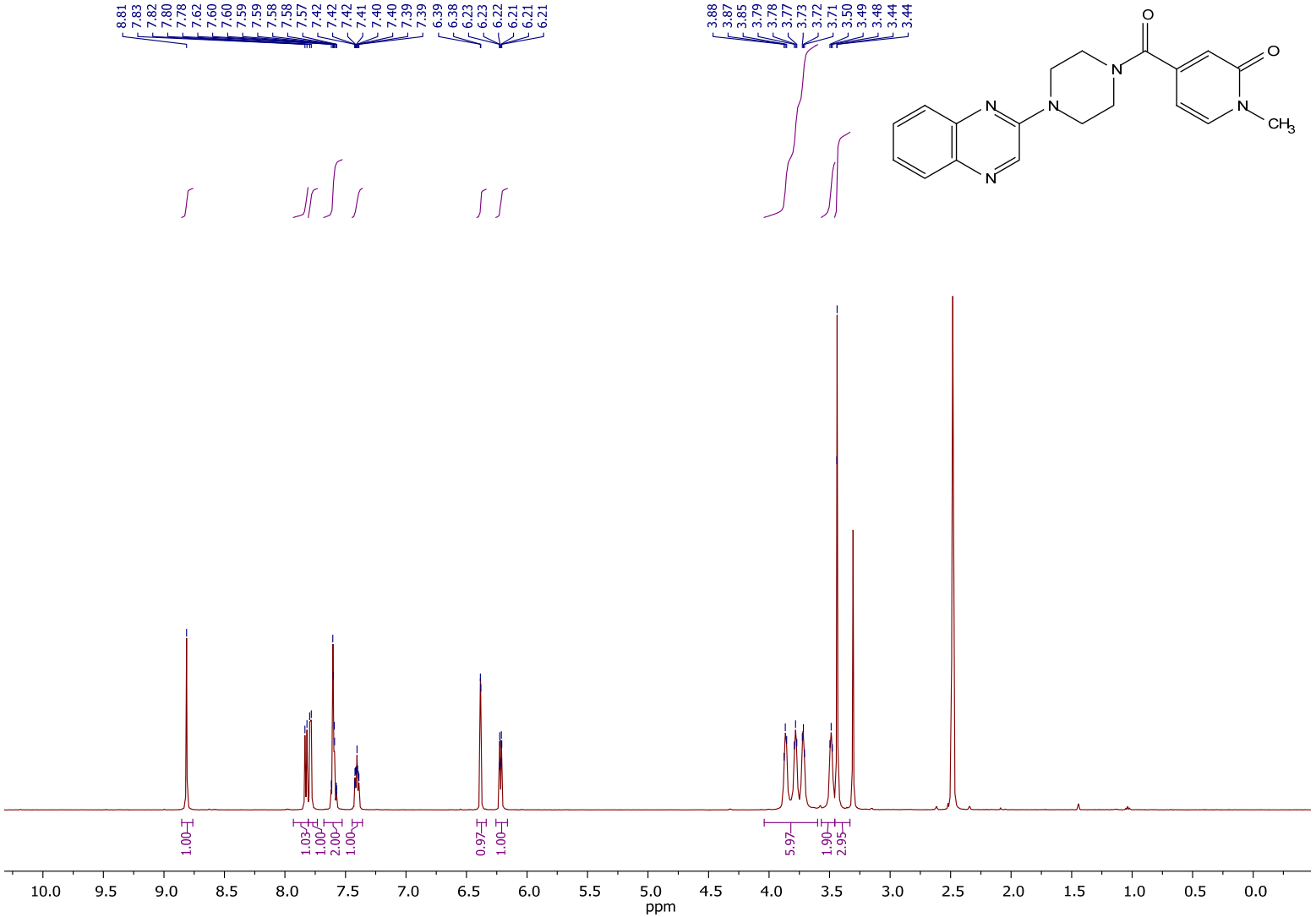

Cyclohex-3-en-1-yl(4-(quinoxalin-2-yl)piperazin-1-yl)methanone (**12**{*9*,*28*,*3*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



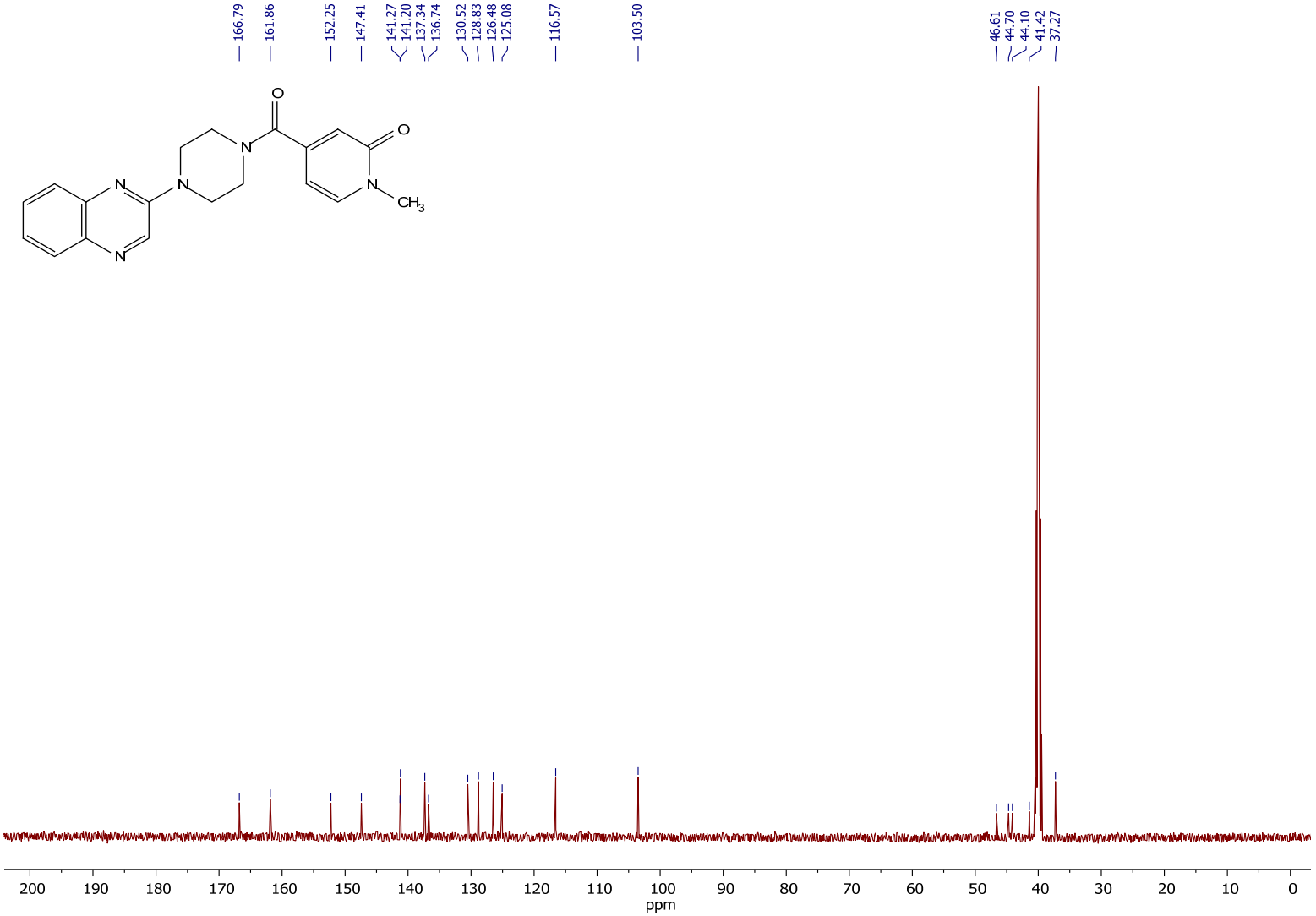

*N*-(2-((5,6-Dimethylthieno[2,3-*d*]pyrimidin-4-yl)(ethyl)amino)ethyl)-2-methoxypropanamide (**12**{*45*,*44*,*24*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



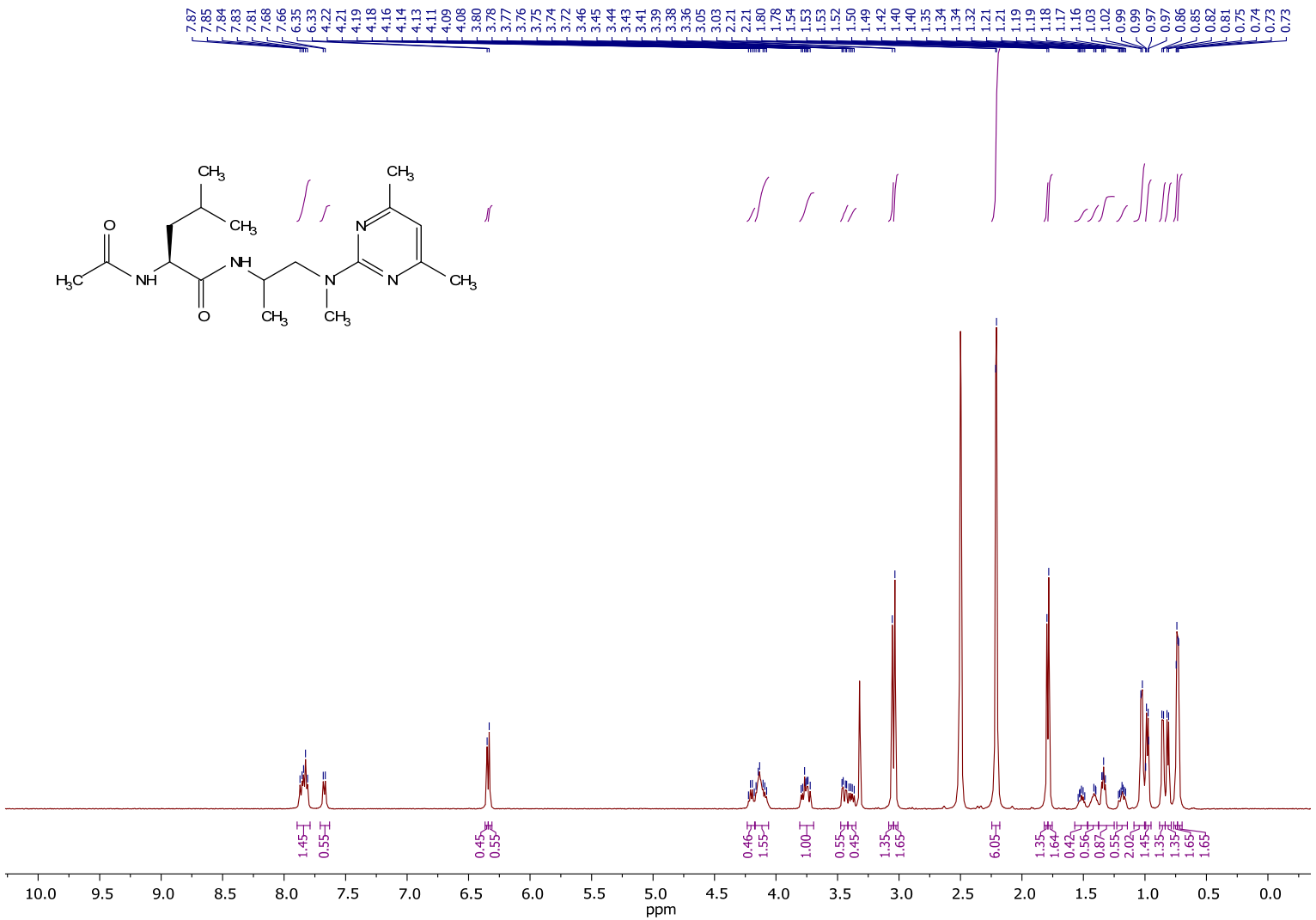

*N*-(2-((5,6-Dimethylthieno[2,3-*d*]pyrimidin-4-yl)(ethyl)amino)ethyl)-2-methoxypropanamide (**12**{*45*,*44*,*24*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



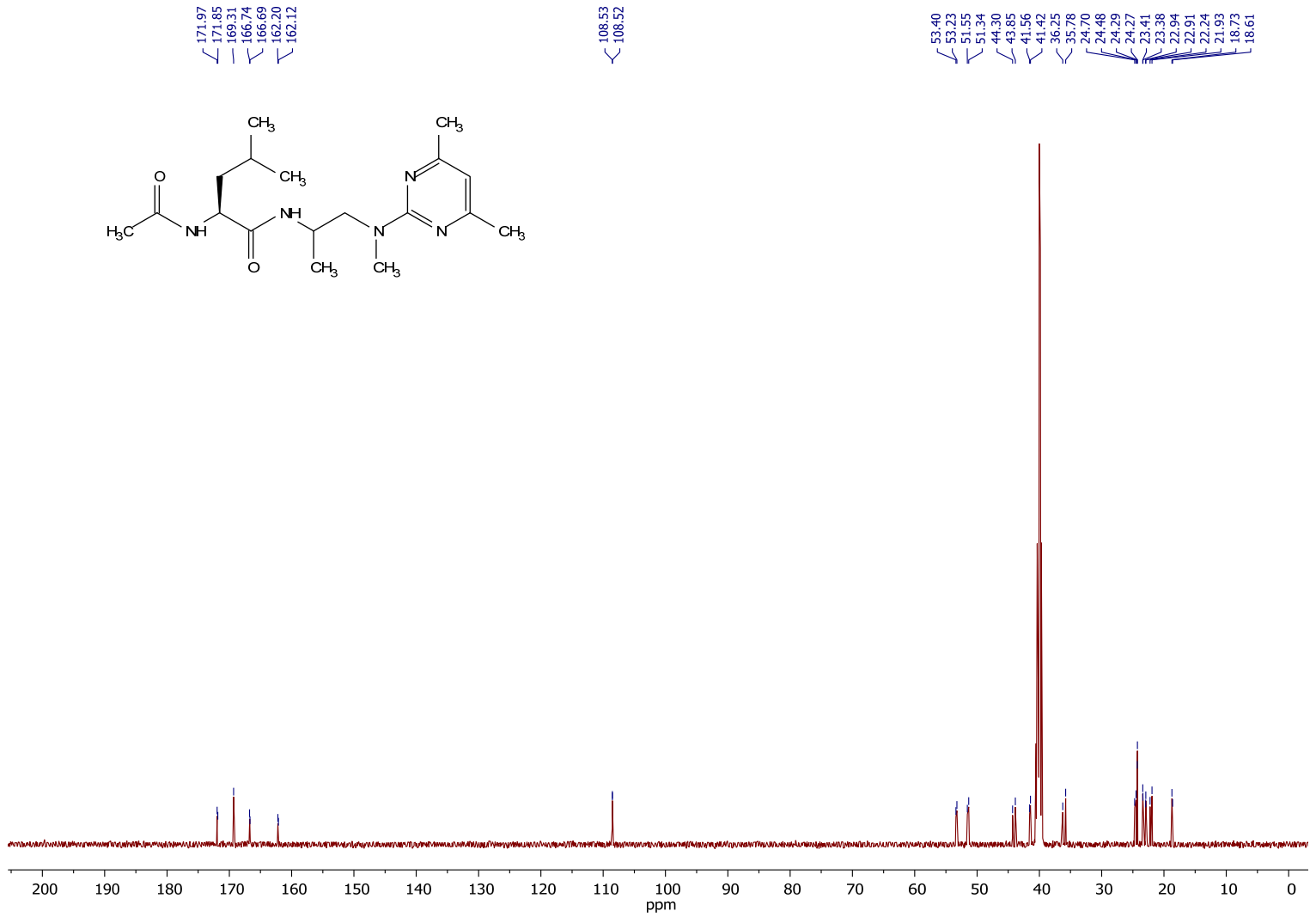

1-Methyl-4-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (**12**{*9*,*48*,*3*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



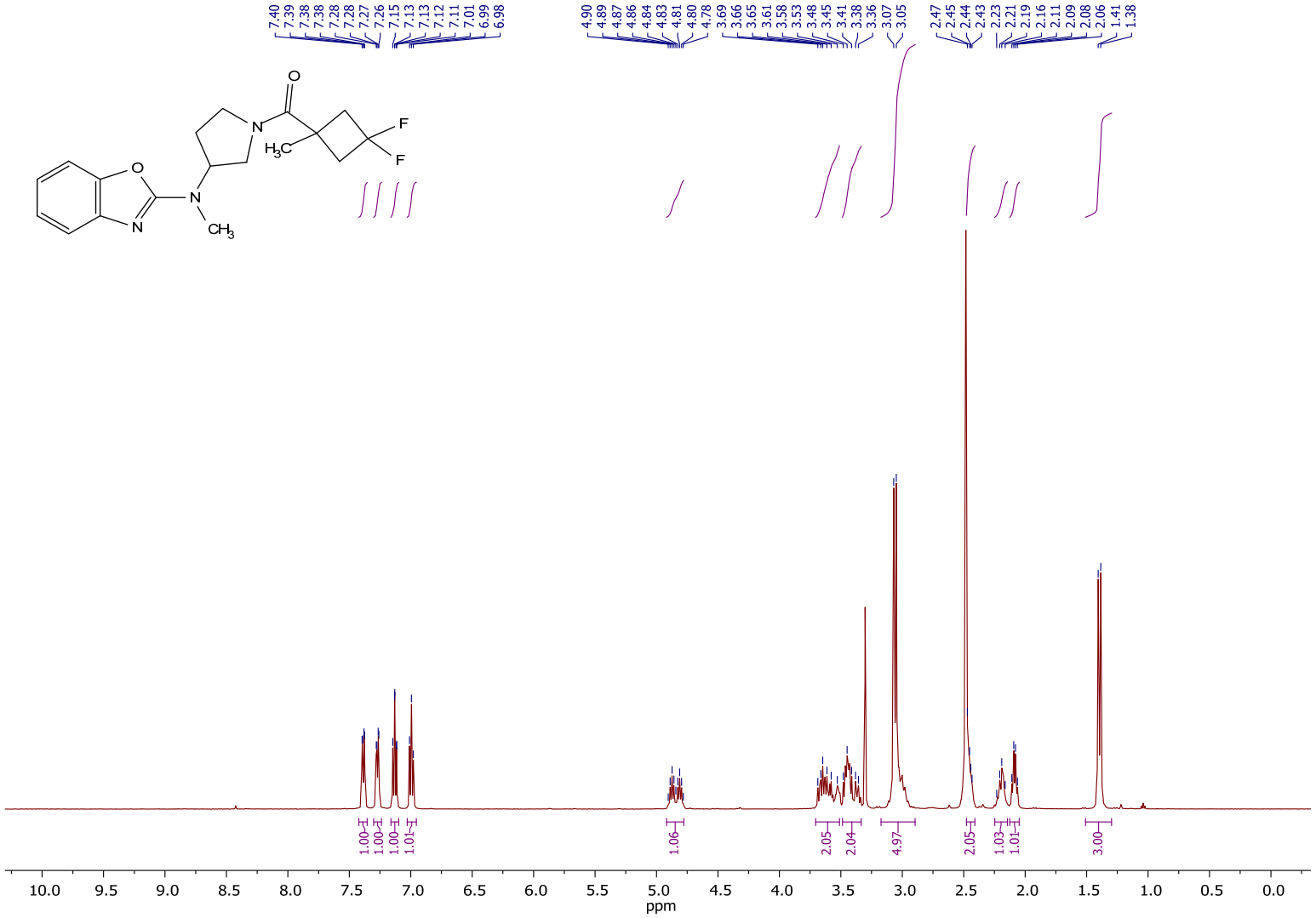

1-Methyl-4-(4-(quinoxalin-2-yl)piperazine-1-carbonyl)pyridin-2(1*H*)-one (**12**{*9*,*48*,*3*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



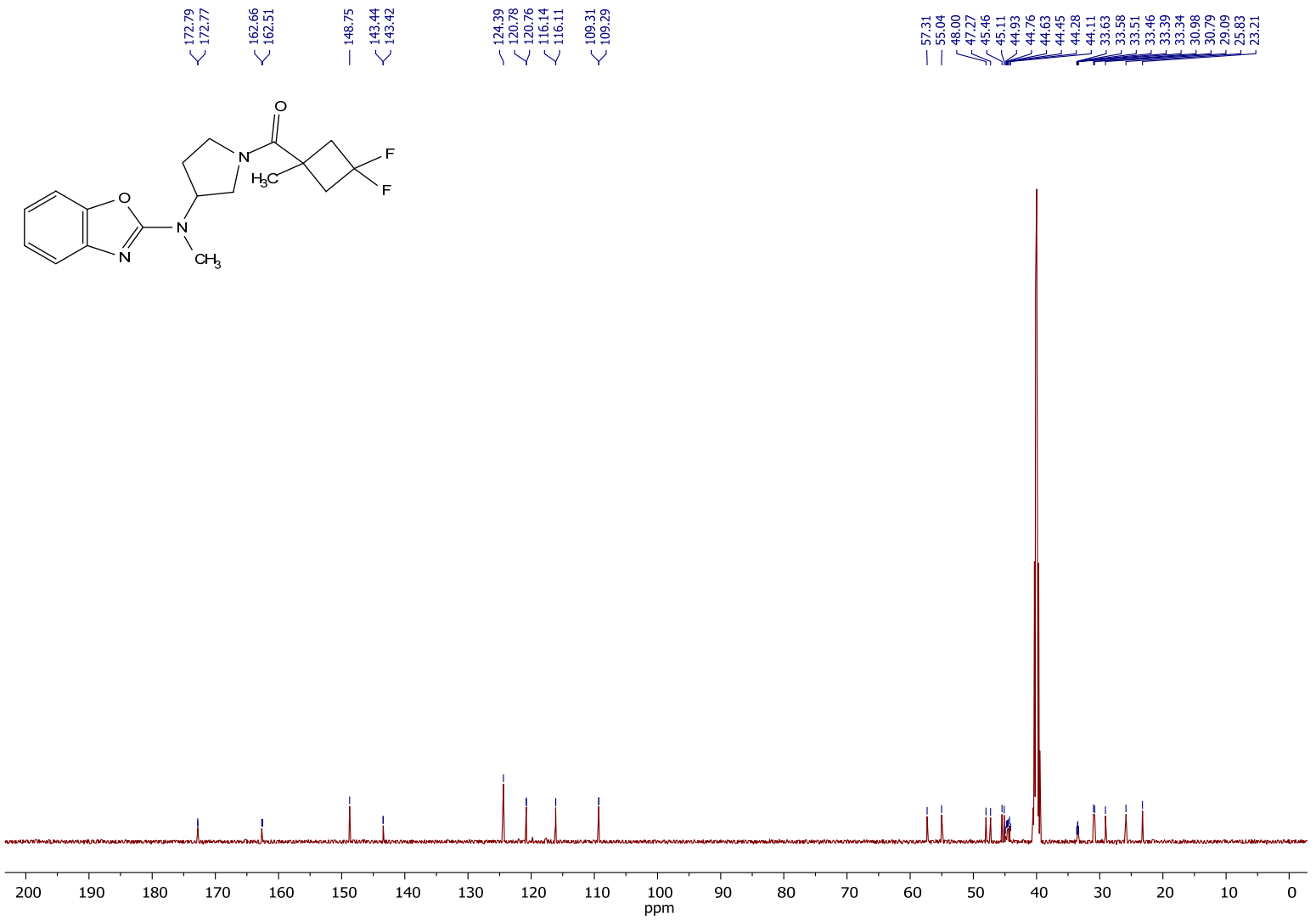

(2*S*)-2-Acetamido-*N*-(1-((4,6-dimethylpyrimidin-2-yl)(methyl)amino)propan-2-yl)-4-methylpentanamide (**12**{*68*,*82*,*32*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



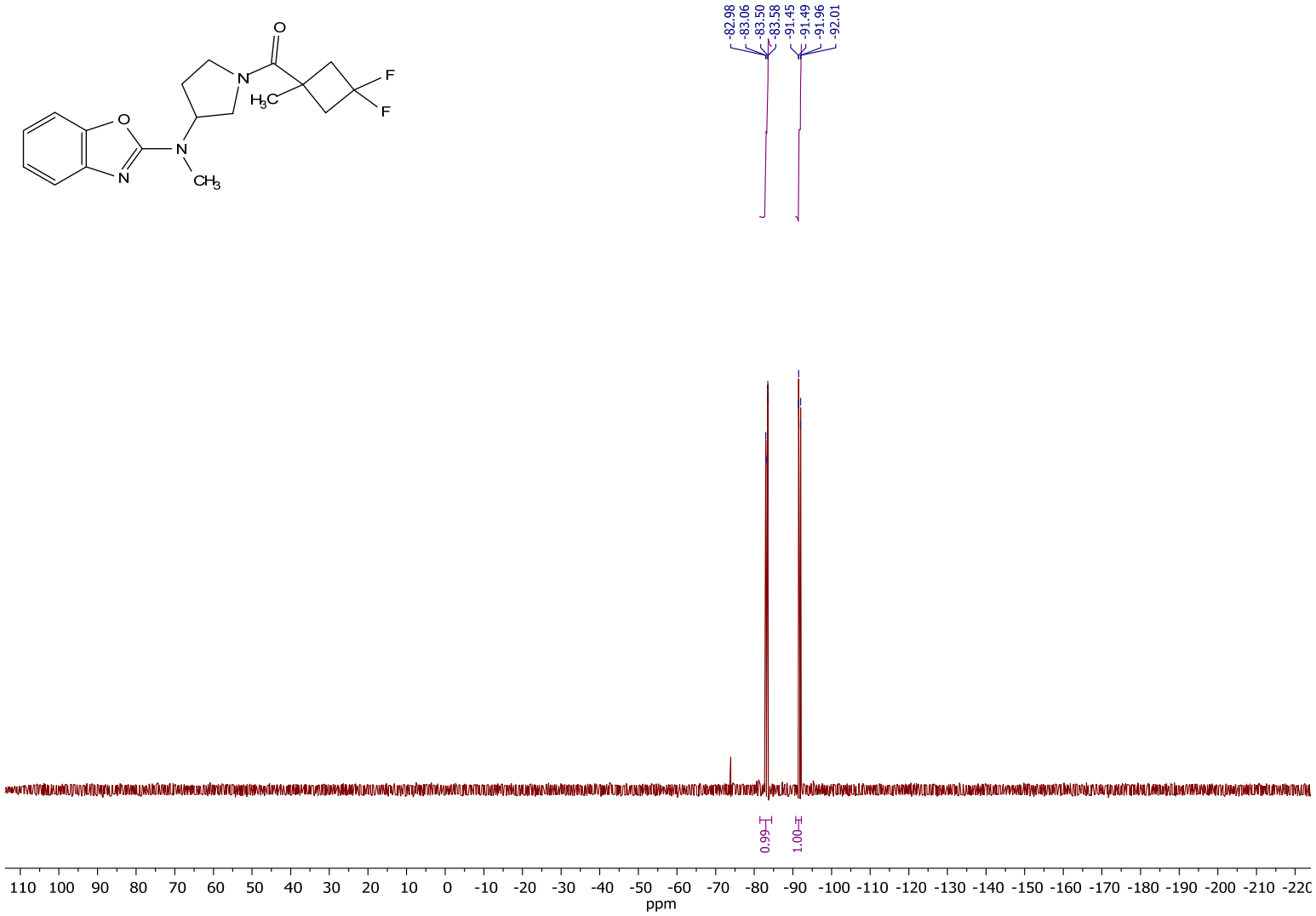

(2*S*)-2-Acetamido-*N*-(1-((4,6-dimethylpyrimidin-2-yl)(methyl)amino)propan-2-yl)-4-methylpentanamide (**12**{*68*,*82*,*32*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



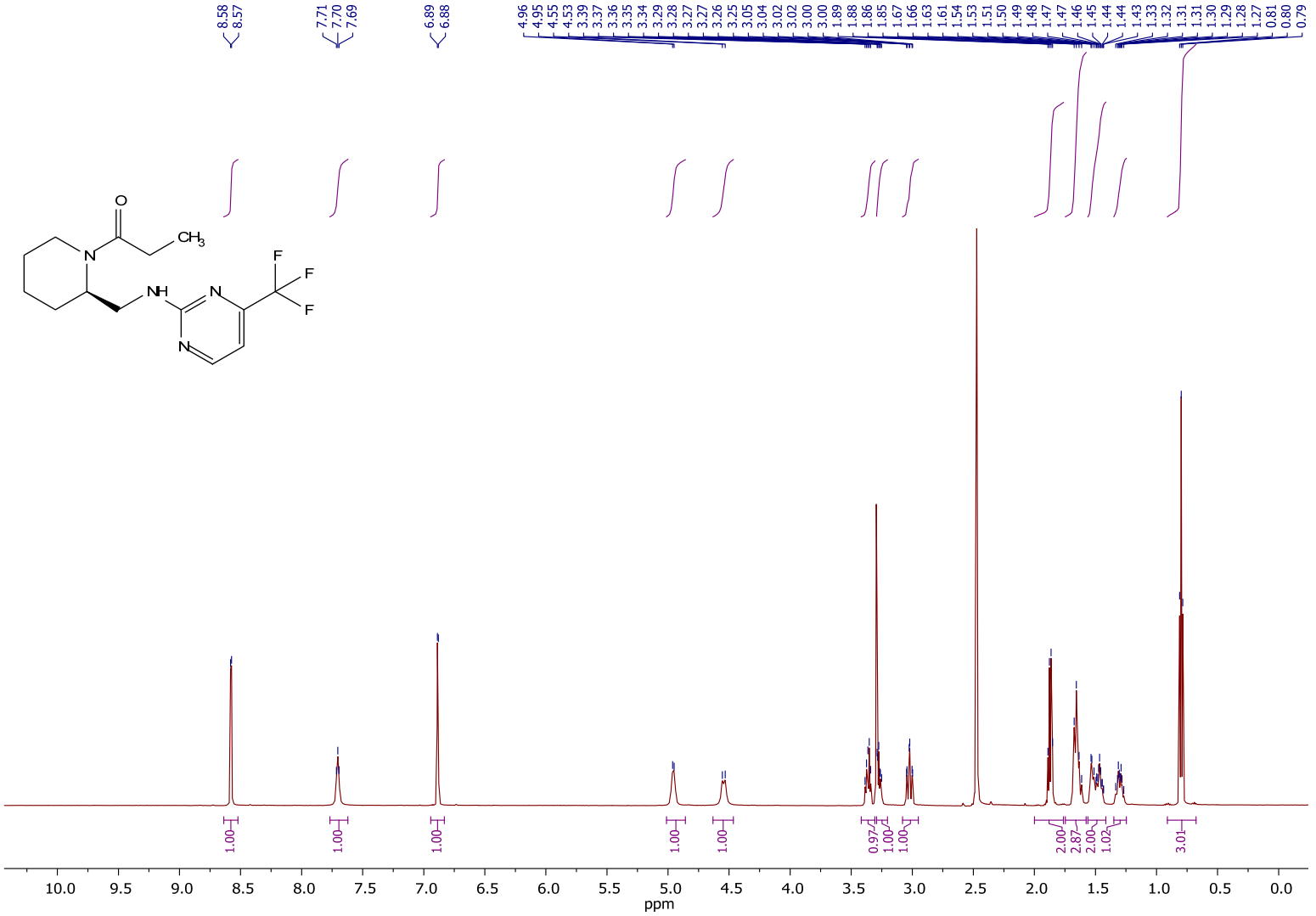

(3-(Benzo[*d*]oxazol-2-yl(methyl)amino)pyrrolidin-1-yl)(3,3-difluoro-1-methylcyclobutyl)methanone (**12**{*81*,*39*,*30*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



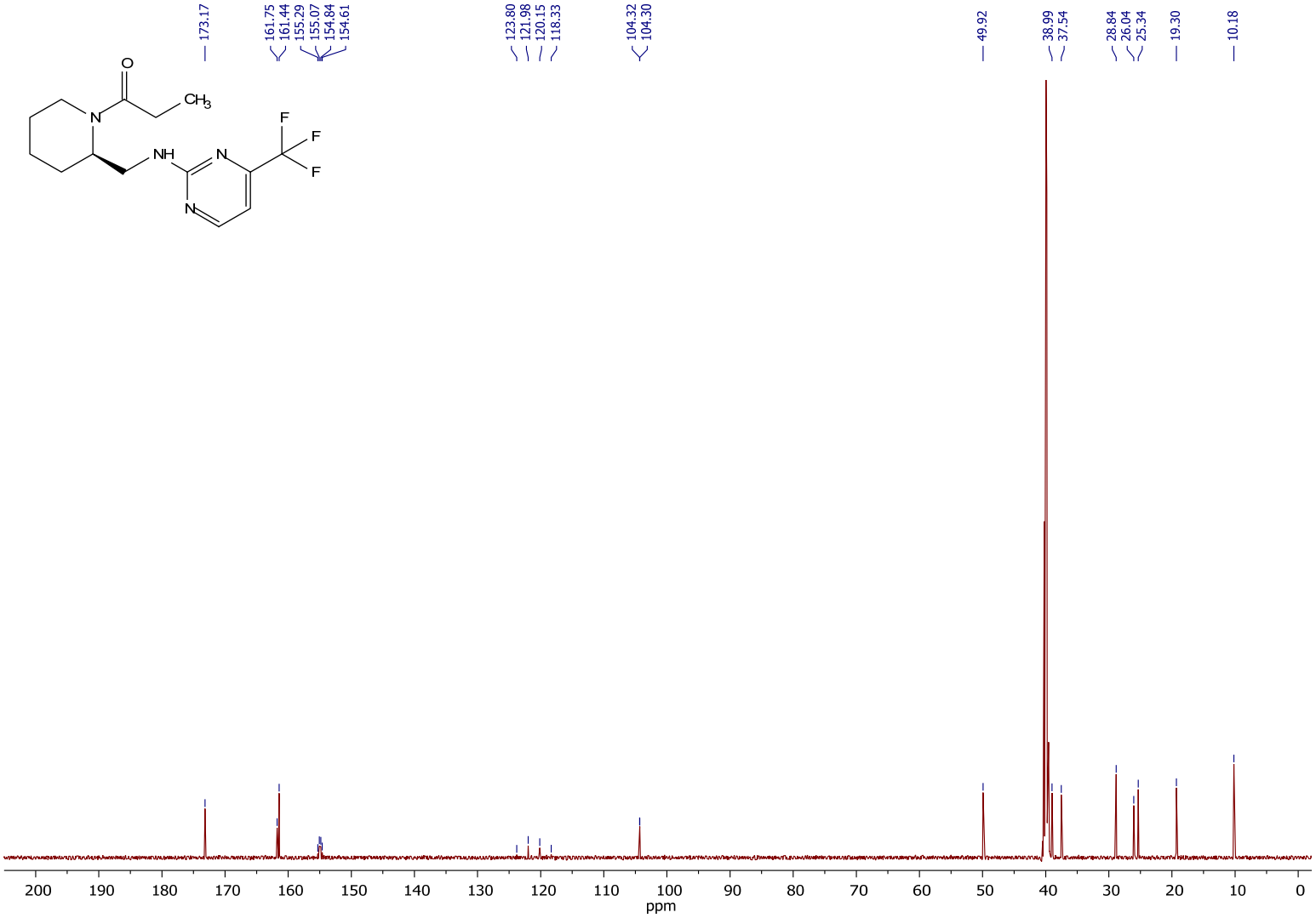

(3-(Benzo[*d*]oxazol-2-yl(methyl)amino)pyrrolidin-1-yl)(3,3-difluoro-1-methylcyclobutyl)methanone (**12**{*81*,*39*,*30*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



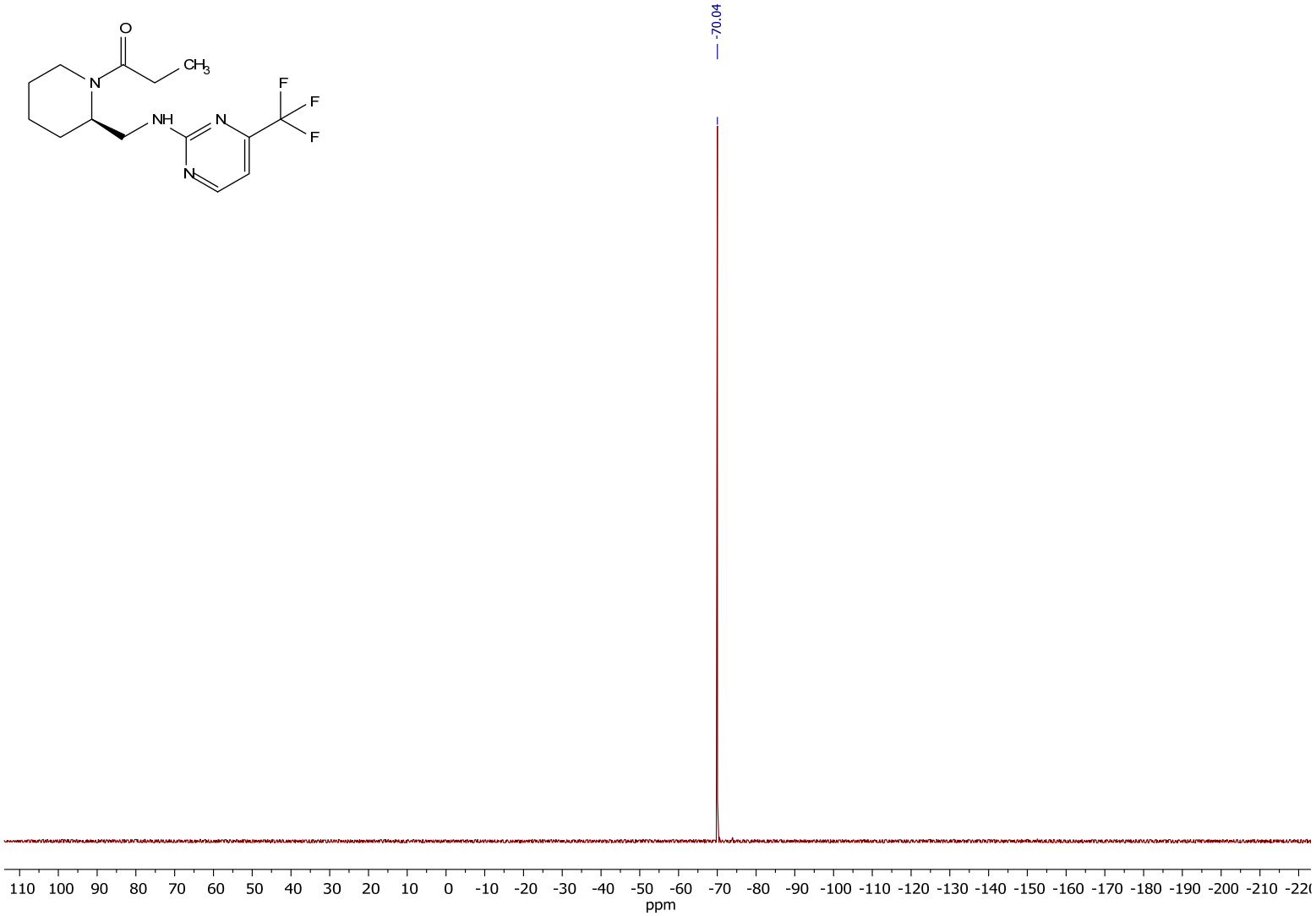

(3-(Benzo[*d*]oxazol-2-yl(methyl)amino)pyrrolidin-1-yl)(3,3-difluoro-1-methylcyclobutyl)methanone (**12**{*81*,*39*,*30*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$)



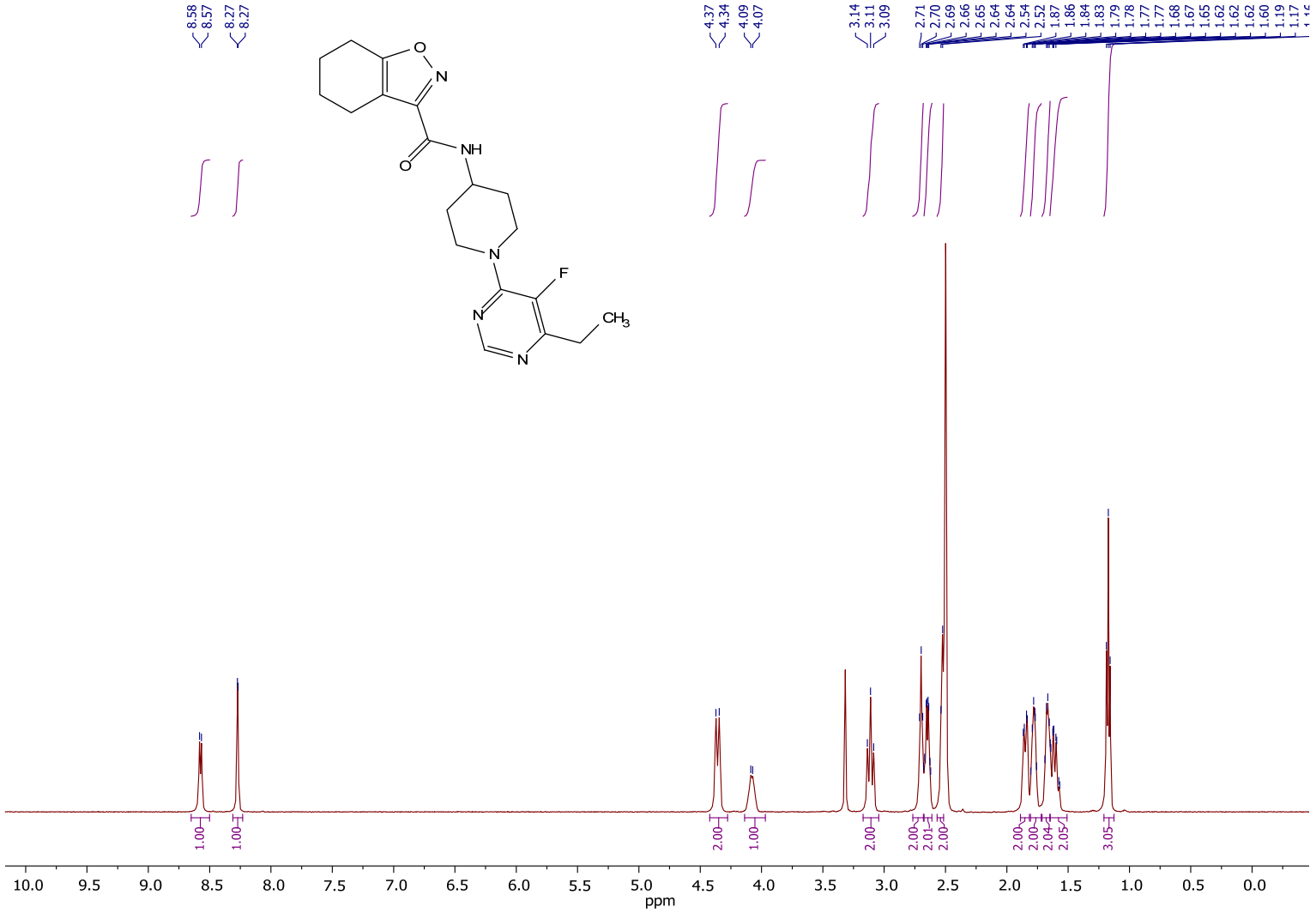

(*R*)-1-(2-(((4-(Trifluoromethyl)pyrimidin-2-yl)amino)methyl)piperidin-1-yl)propan-1-one (**12**{*84*,*40*,*34*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



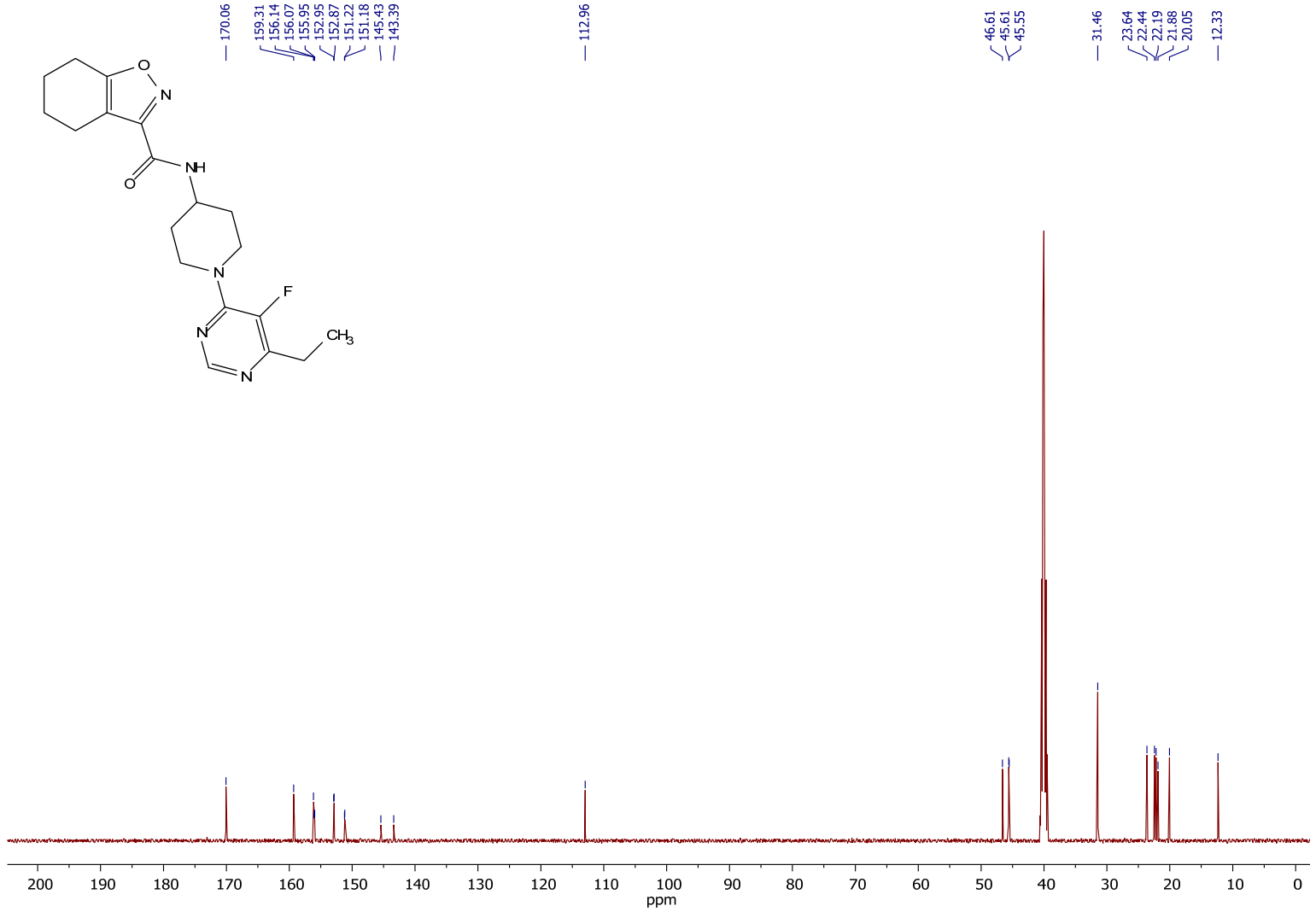

(*R*)-1-(2-(((4-(Trifluoromethyl)pyrimidin-2-yl)amino)methyl)piperidin-1-yl)propan-1-one (**12**{*84*,*40*,*34*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



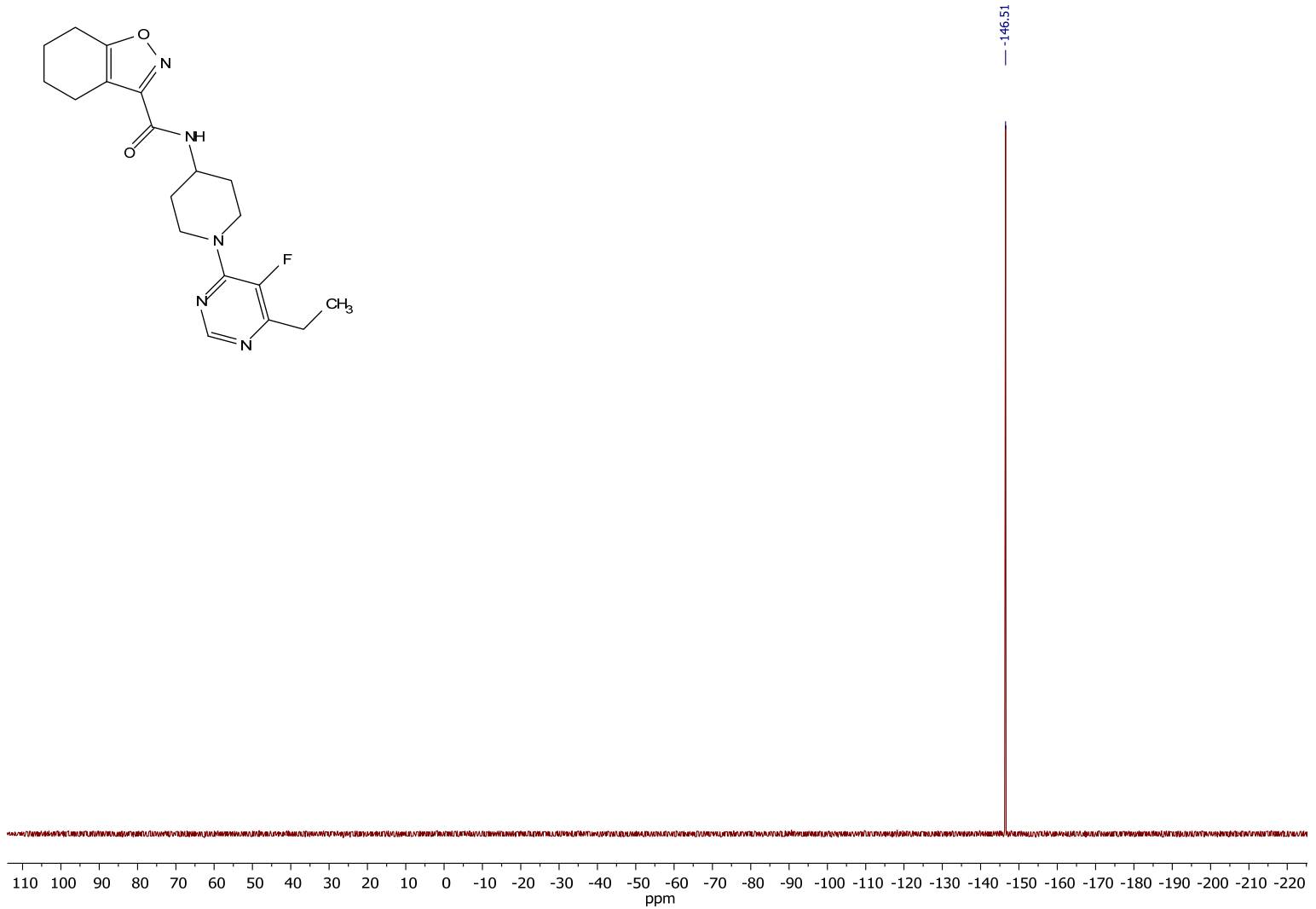

(*R*)-1-(2-(((4-(Trifluoromethyl)pyrimidin-2-yl)amino)methyl)piperidin-1-yl)propan-1-one (**12**{*84*,*40*,*34*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$)



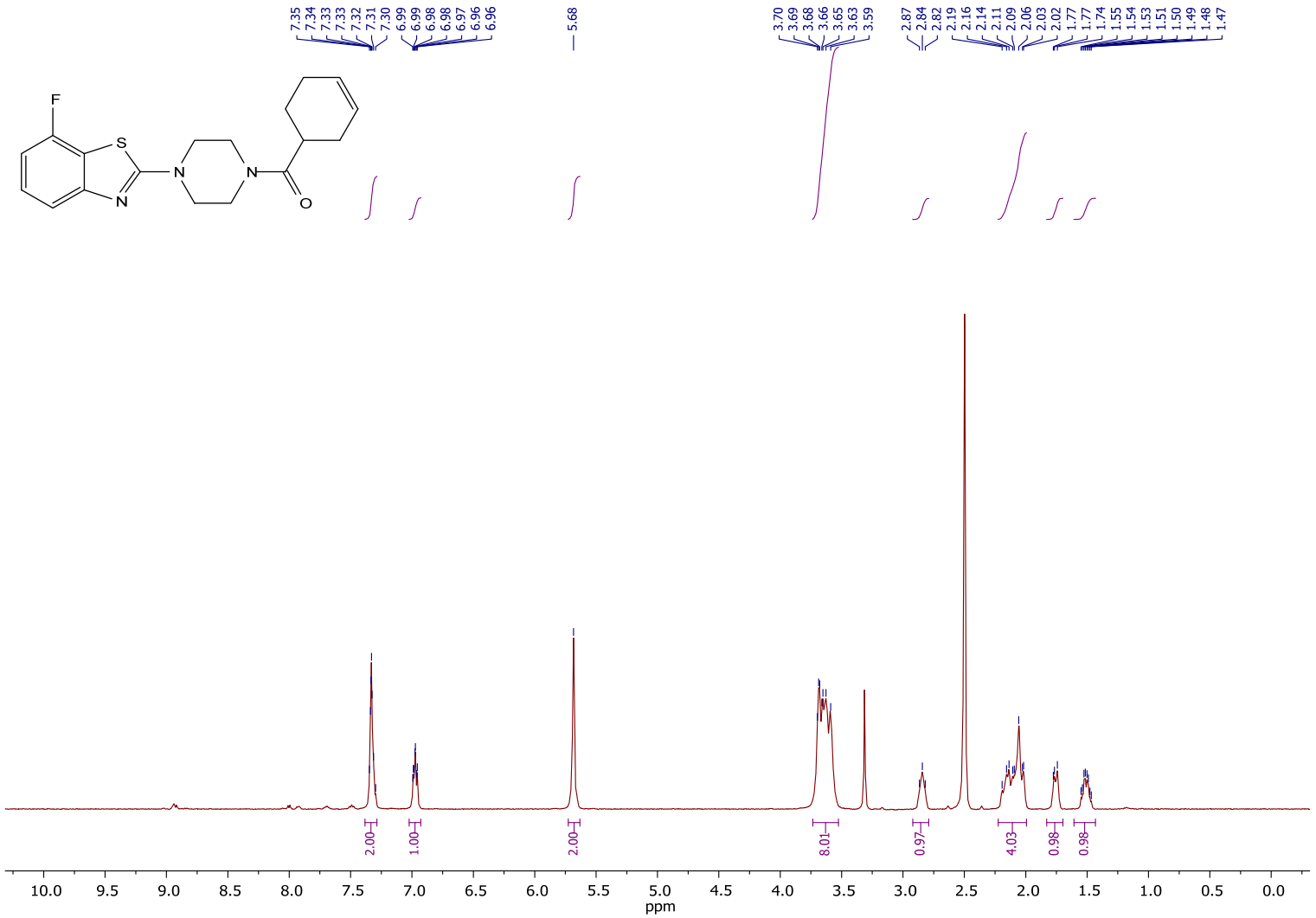

*N*-(1-(6-Ethyl-5-fluoropyrimidin-4-yl)piperidin-4-yl)-4,5,6,7-tetrahydrobenzo[*d*]isoxazole-3-carboxamide (**12**{*79*,*130*,*39*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



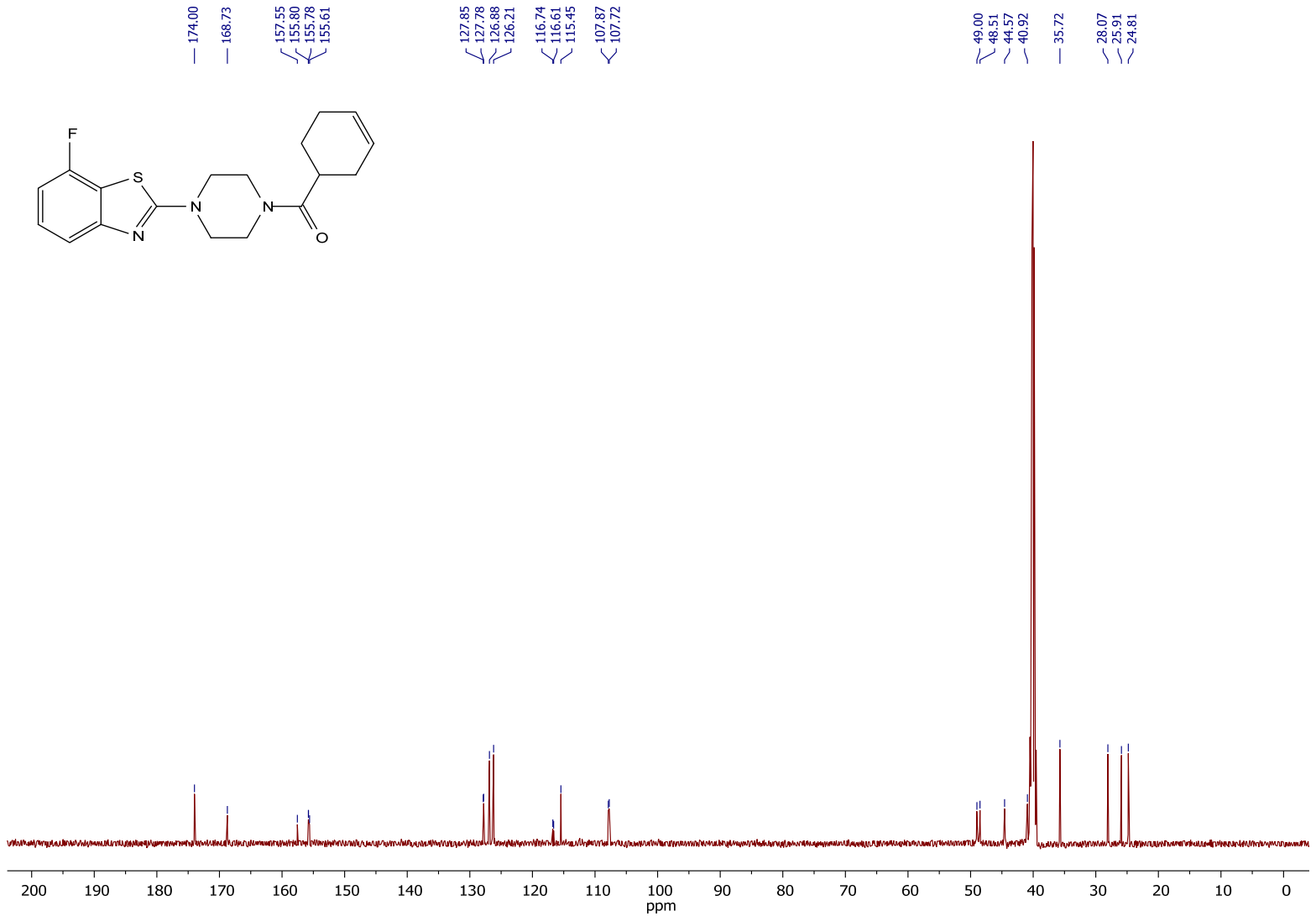

*N*-(1-(6-Ethyl-5-fluoropyrimidin-4-yl)piperidin-4-yl)-4,5,6,7-tetrahydrobenzo[*d*]isoxazole-3-carboxamide (**12**{*79*,*130*,*39*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



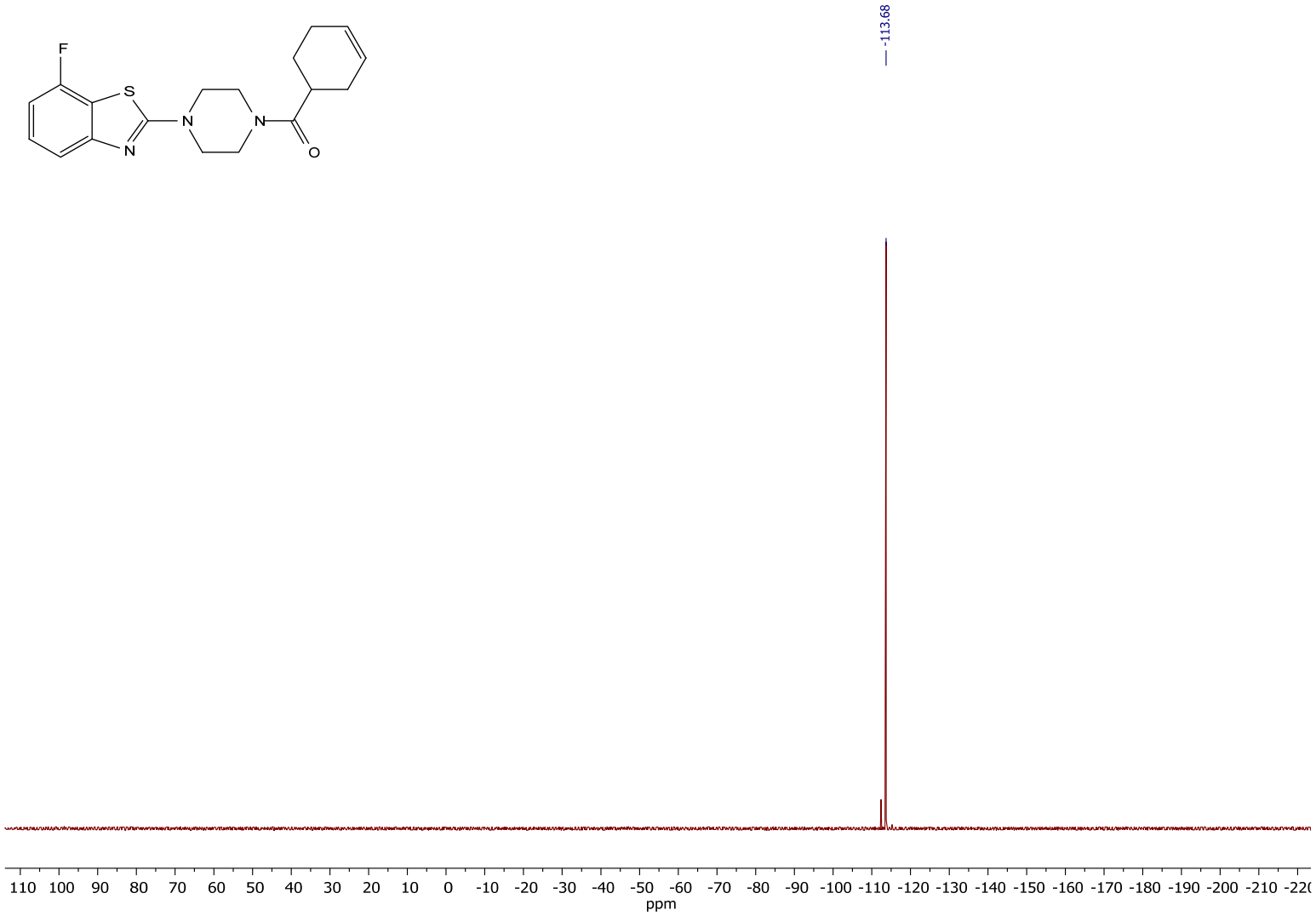

*N*-(1-(6-Ethyl-5-fluoropyrimidin-4-yl)piperidin-4-yl)-4,5,6,7-tetrahydrobenzo[*d*]isoxazole-3-carboxamide (**12**{*79*,*130*,*39*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$



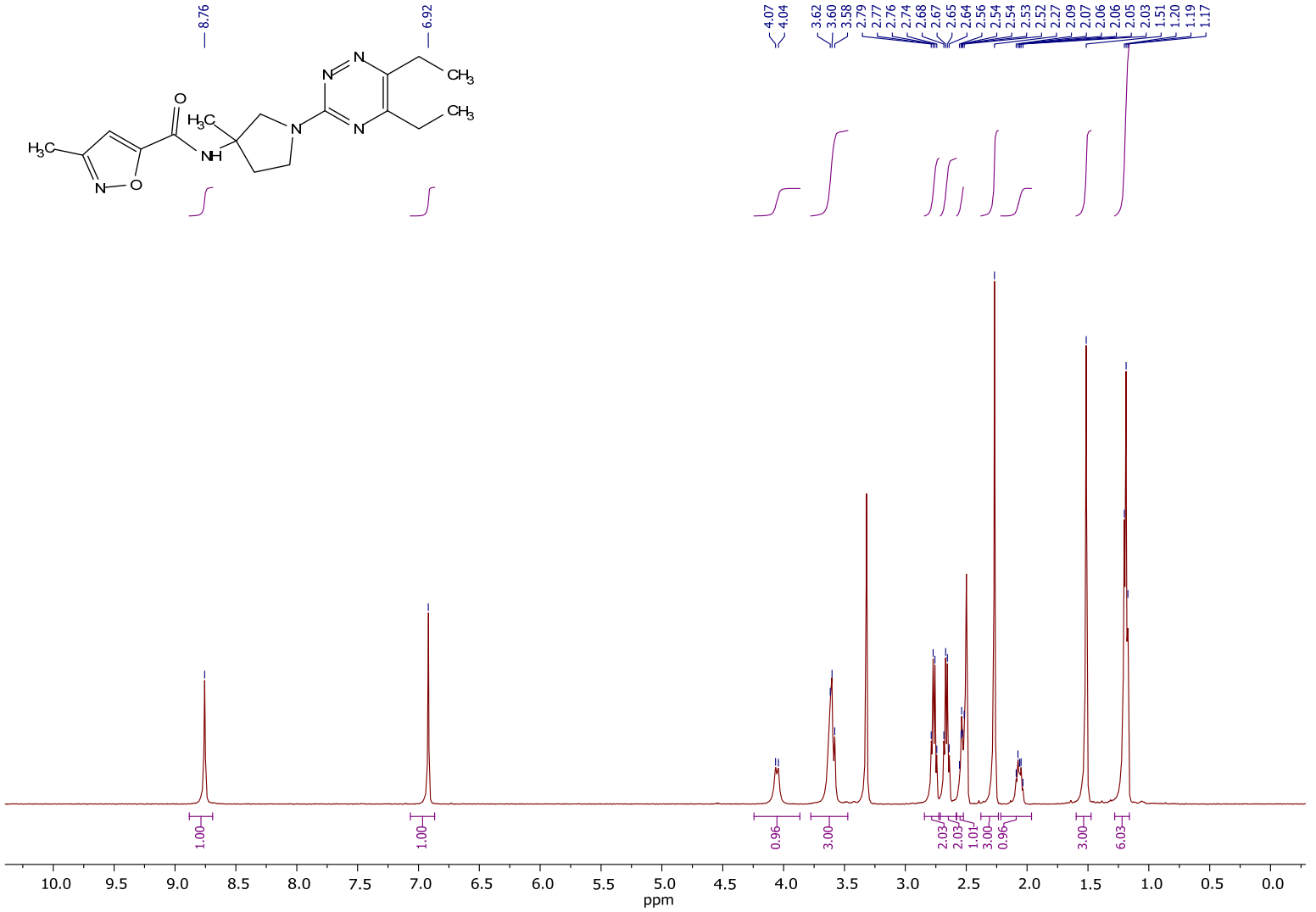

Cyclohex-3-en-1-yl(4-(7-fluorobenzo[*d*]thiazol-2-yl)piperazin-1-yl)methanone (**12**{*9*,*28*,*43*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



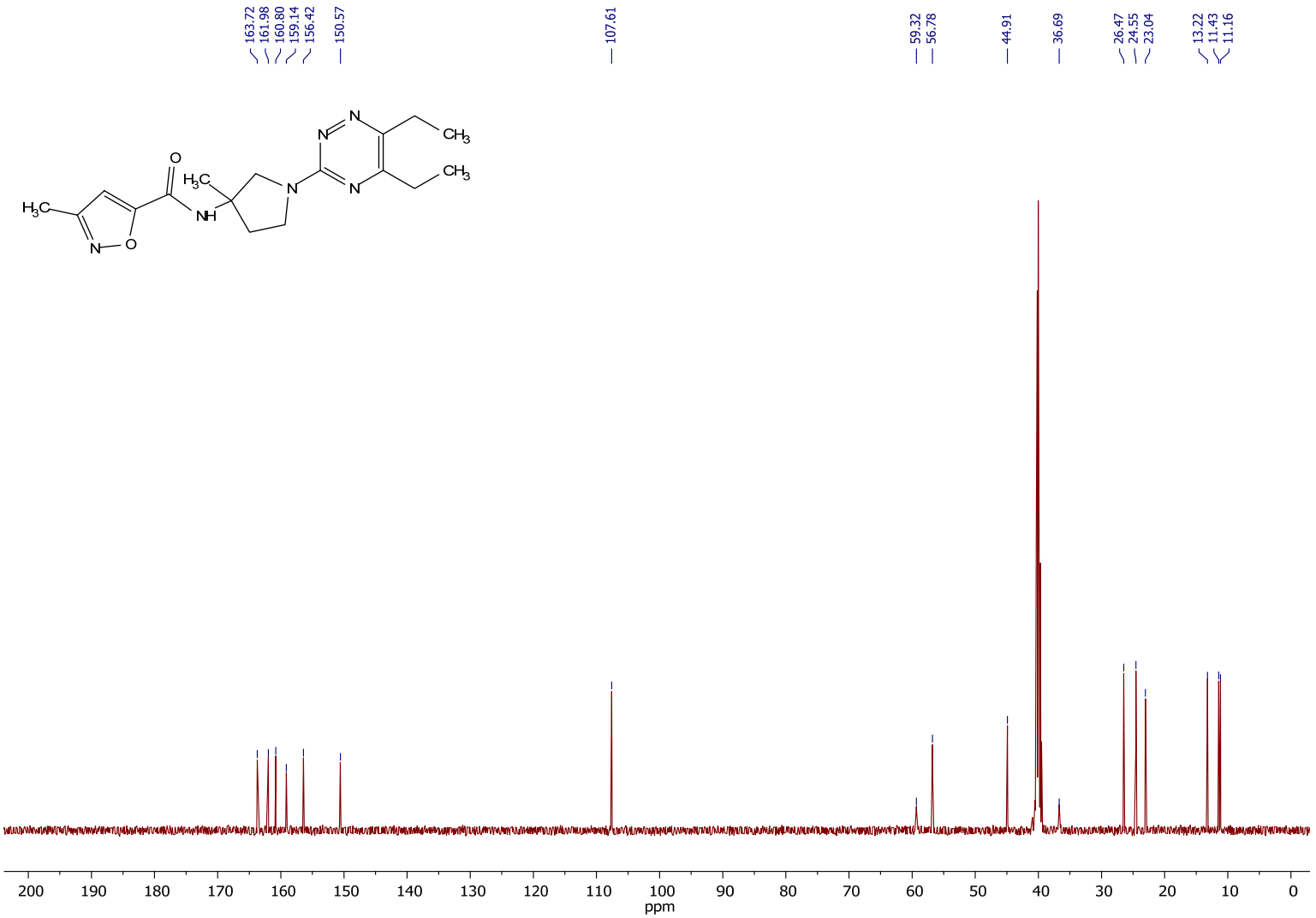

Cyclohex-3-en-1-yl(4-(7-fluorobenzo[*d*]thiazol-2-yl)piperazin-1-yl)methanone (**12**{*9*,*28*,*43*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



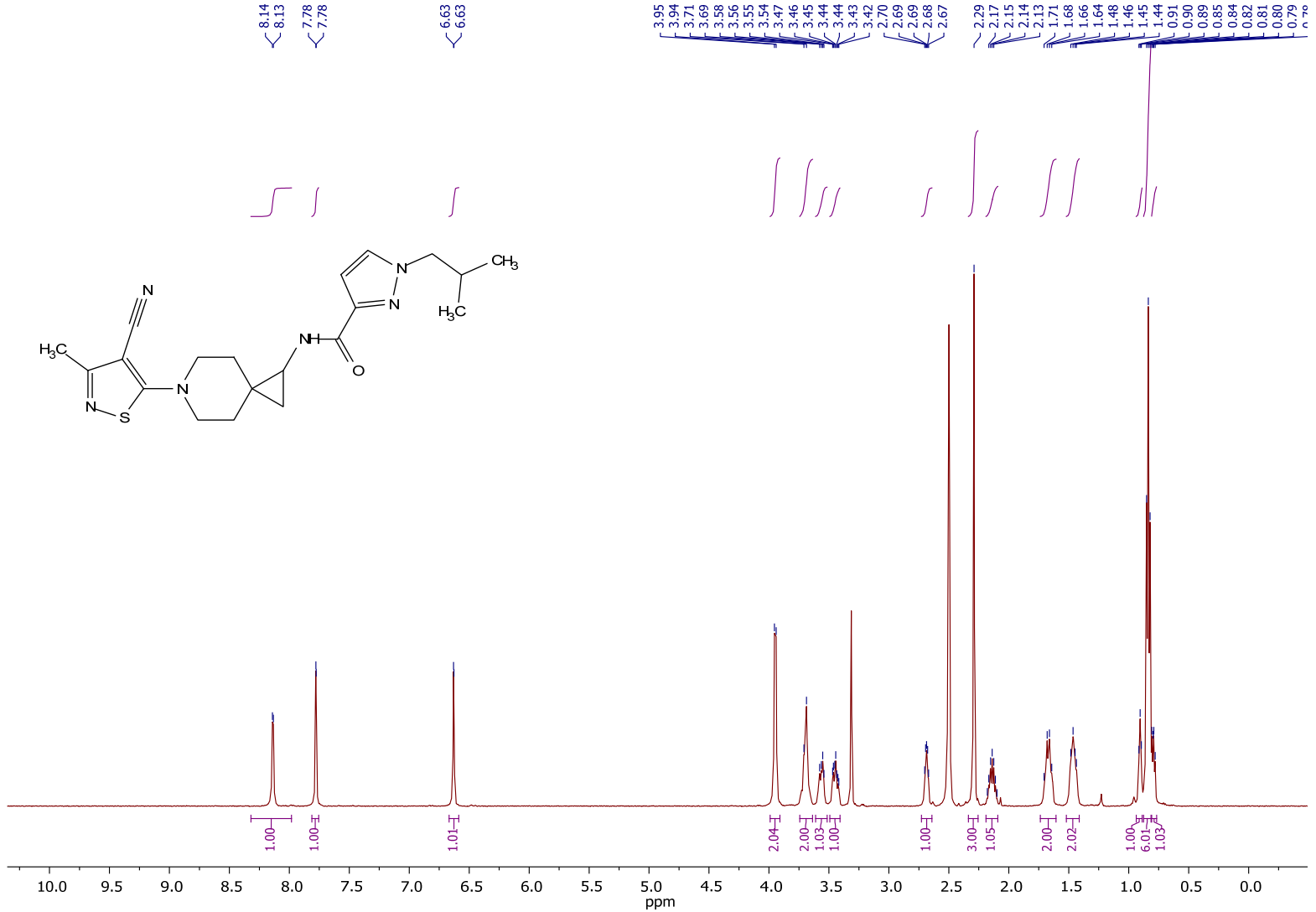

Cyclohex-3-en-1-yl(4-(7-fluorobenzo[*d*]thiazol-2-yl)piperazin-1-yl)methanone (**12**{*9*,*28*,*43*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$)



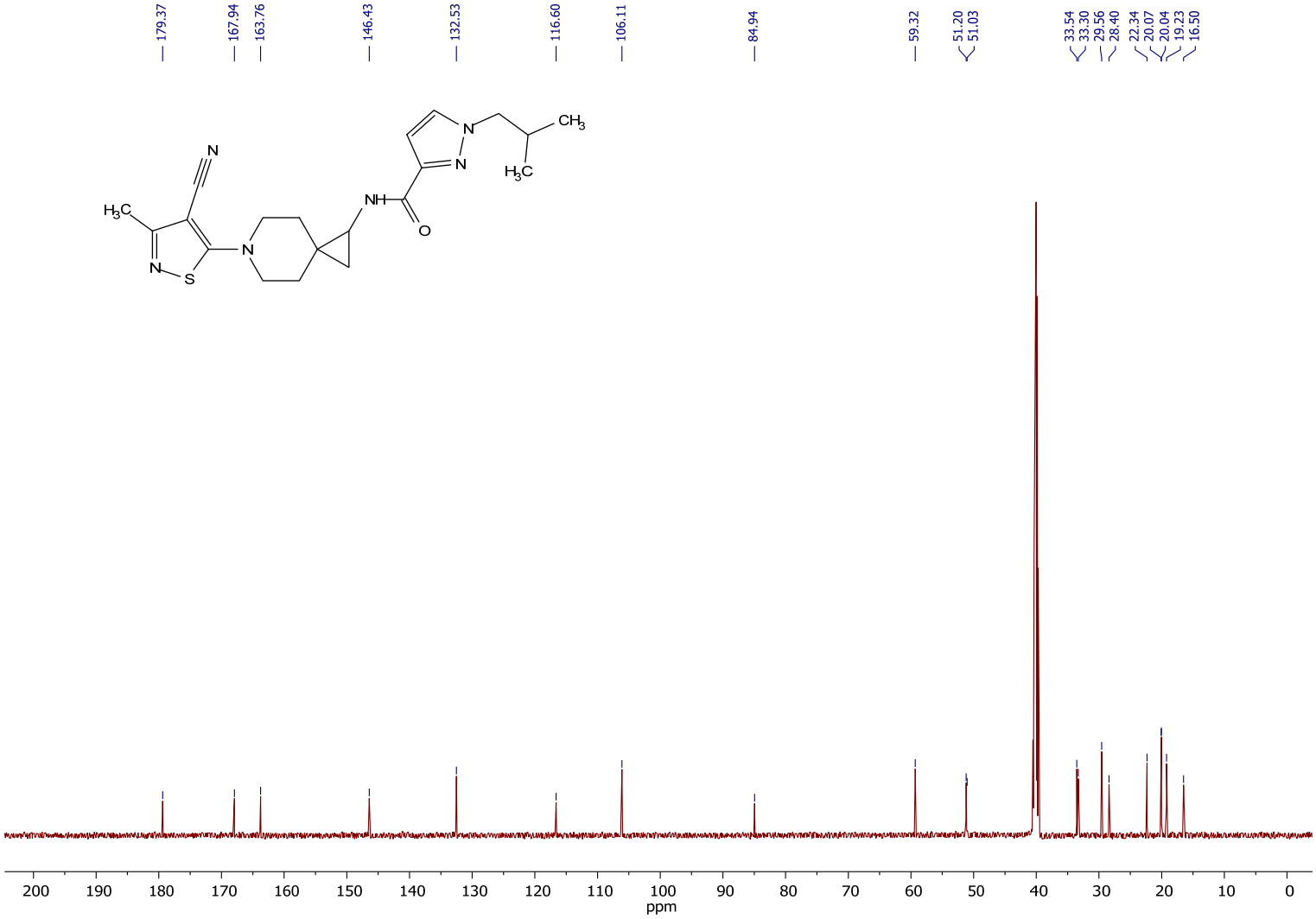

*N*-(1-(5,6-Diethyl-1,2,4-triazin-3-yl)-3-methylpyrrolidin-3-yl)-3-methylisoxazole-5-carboxamide **12**{*49*,*150*,*31*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



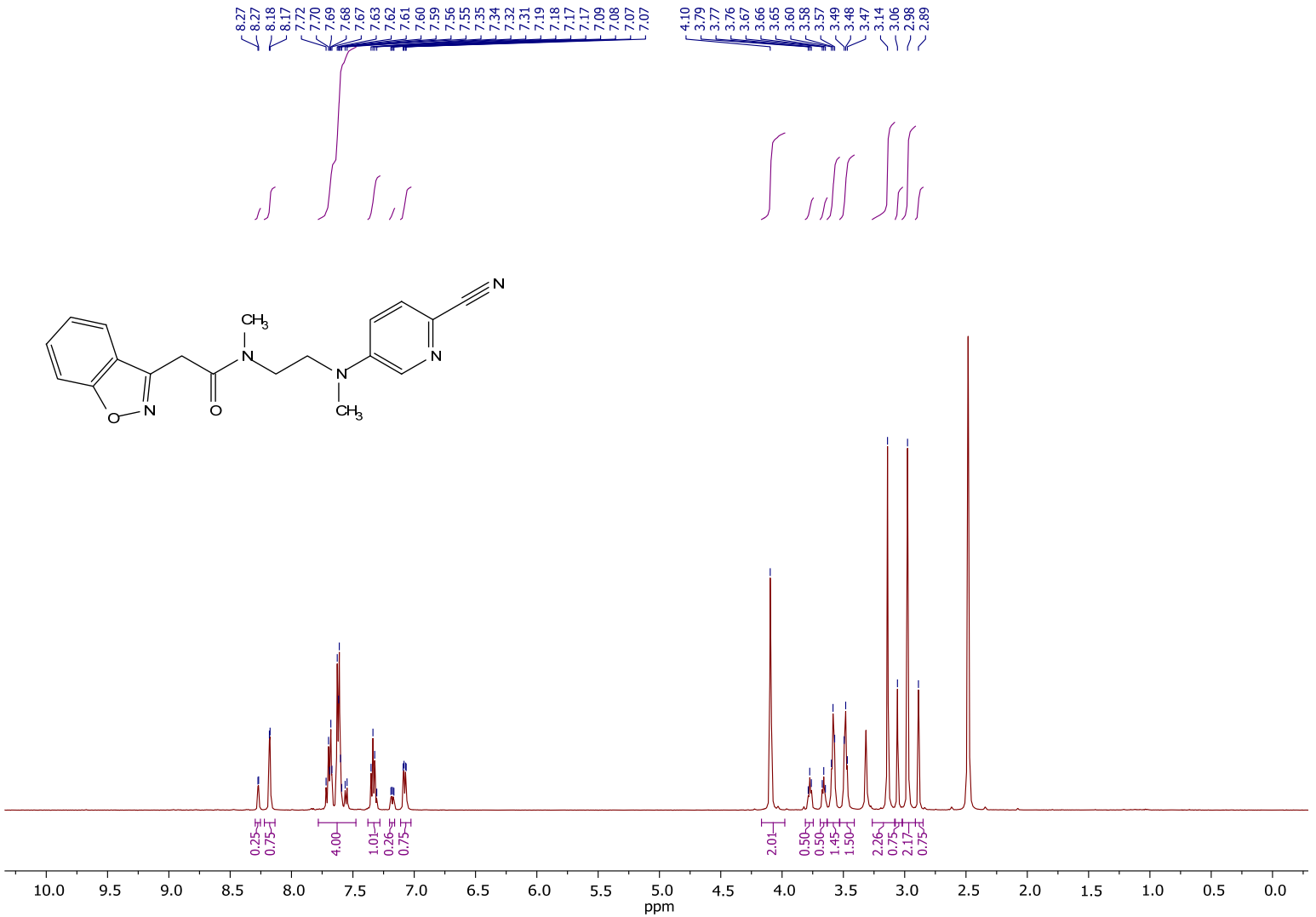

*N*-(1-(5,6-Diethyl-1,2,4-triazin-3-yl)-3-methylpyrrolidin-3-yl)-3-methylisoxazole-5-carboxamide (**12**{*49*,*150*,*31*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



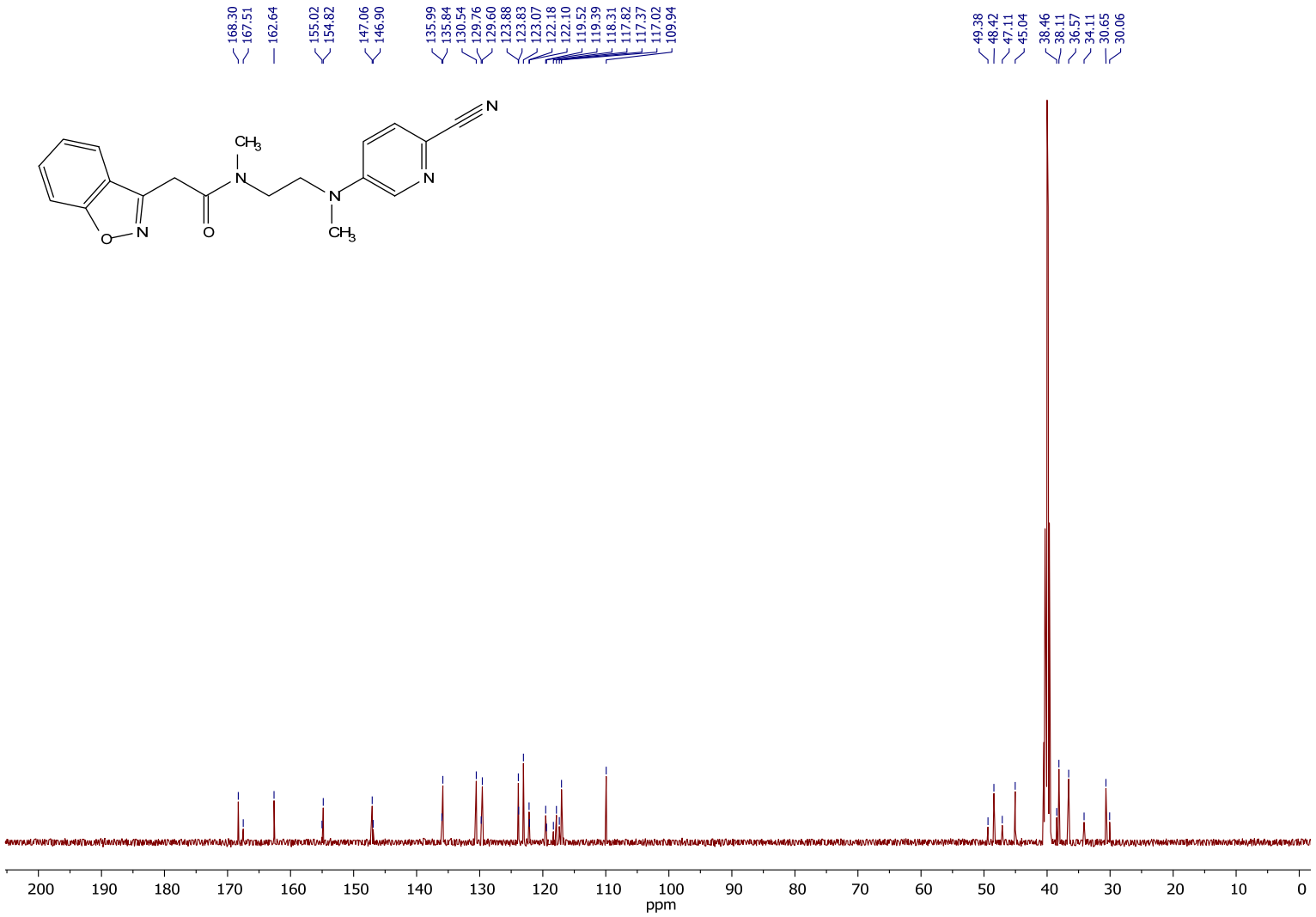

*N*-(6-(4-Cyano-3-methylisothiazol-5-yl)-6-azaspiro[2.5]octan-1-yl)-1-isobutyl-1*H*-pyrazole-3-carboxamide (**12**{*31*,*29*,*13*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



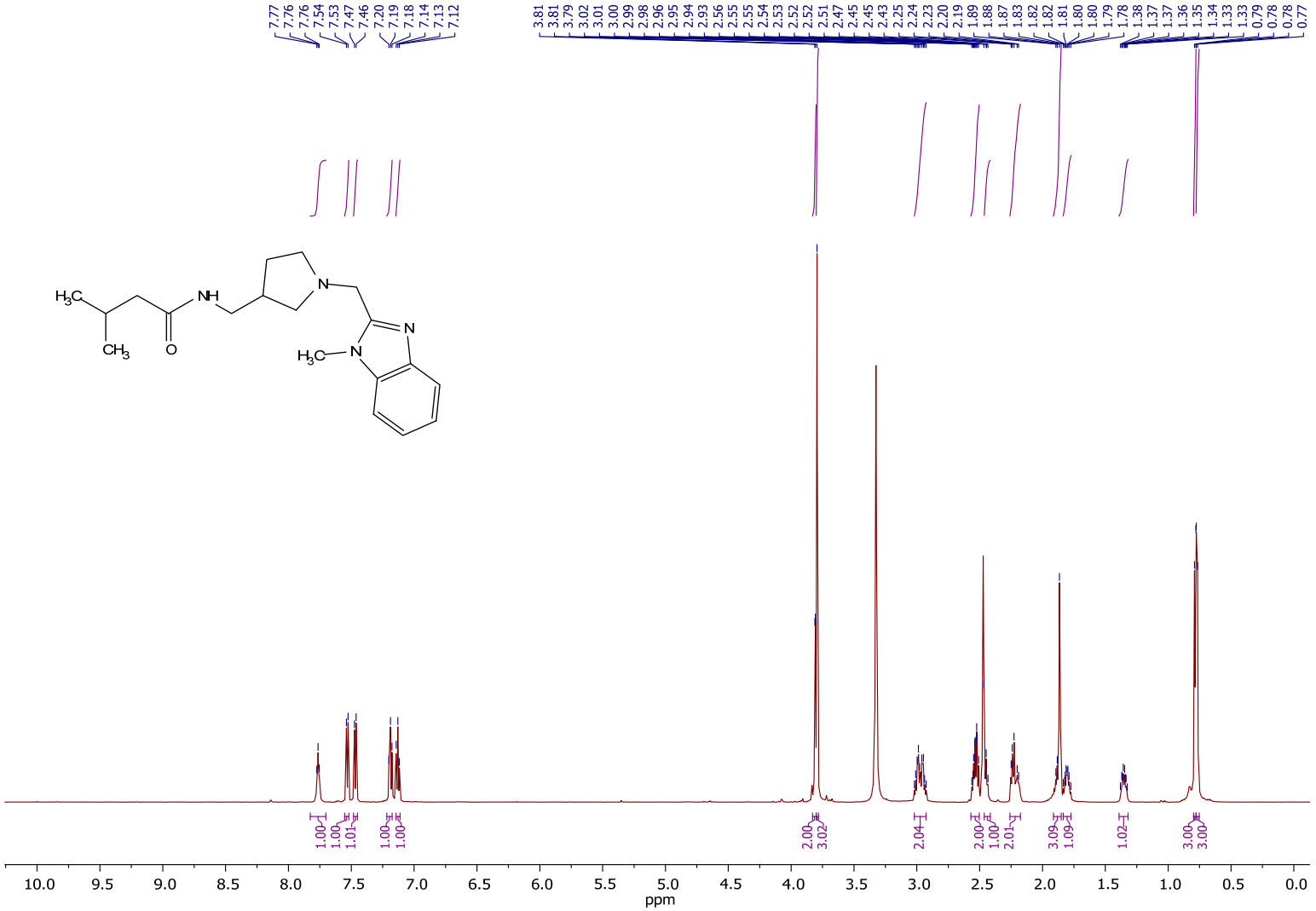

*N*-(6-(4-Cyano-3-methylisothiazol-5-yl)-6-azaspiro[2.5]octan-1-yl)-1-isobutyl-1*H*-pyrazole-3-carboxamide (**12**{*31*,*29*,*13*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



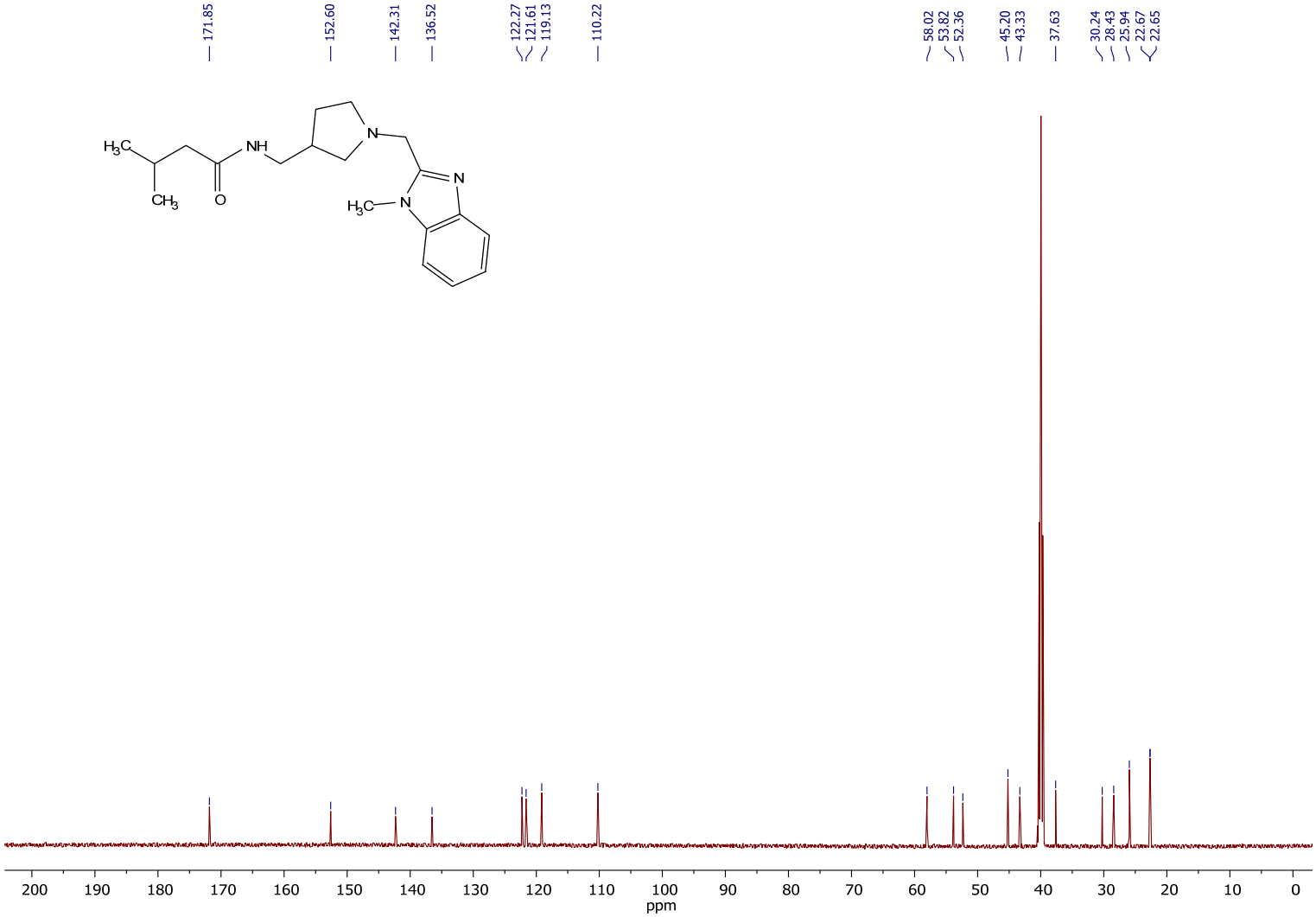

2-(Benzo[*d*]isoxazol-3-yl)-*N*-(2-((6-cyanopyridin-3-yl)(methyl)amino)ethyl)-*N*-methylacetamide (**12**{*2*,*23*,*11*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



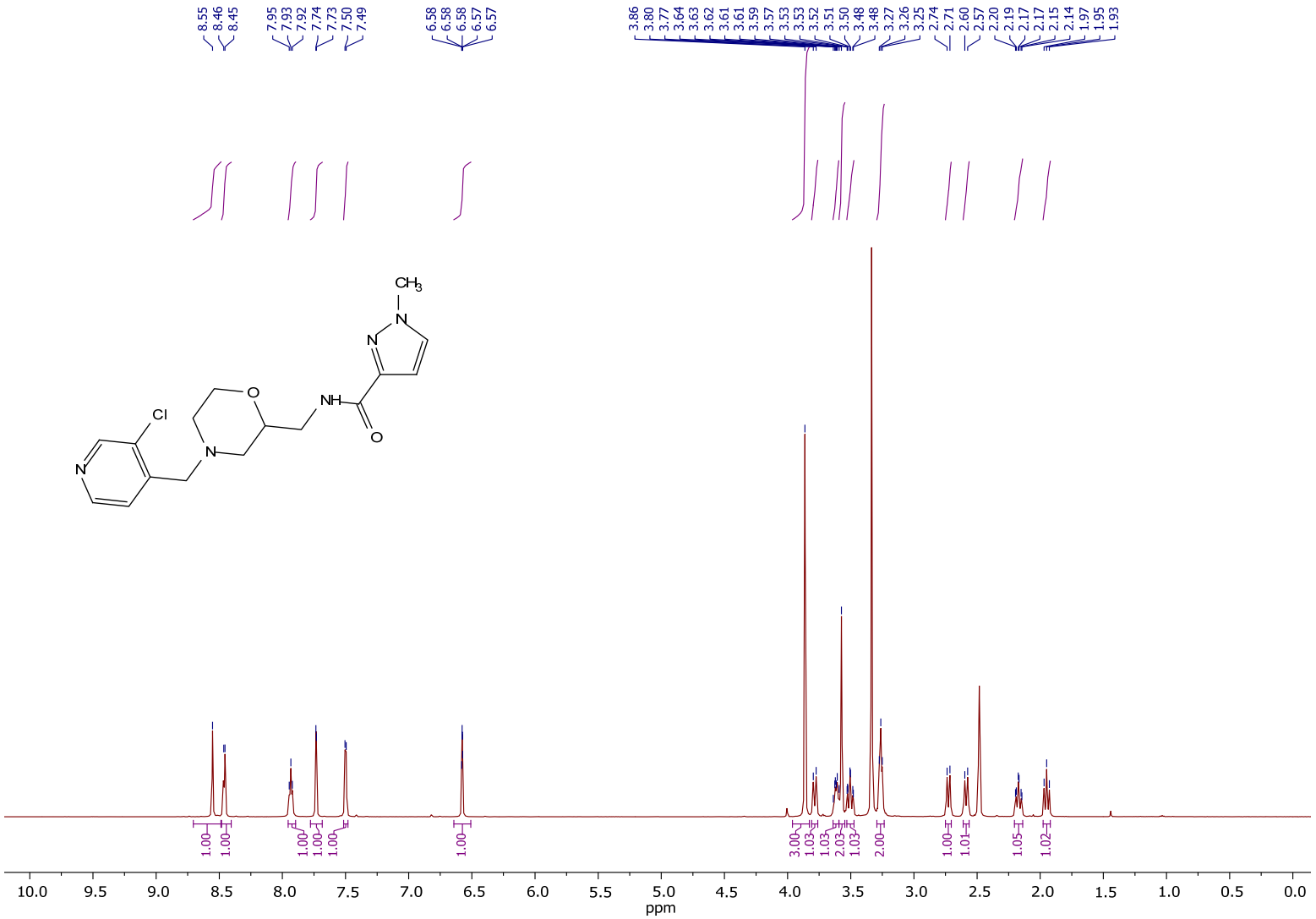

2-(Benzo[*d*]isoxazol-3-yl)-*N*-(2-((6-cyanopyridin-3-yl)(methyl)amino)ethyl)-*N*-methylacetamide (**12**{*2*,*23*,*11*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



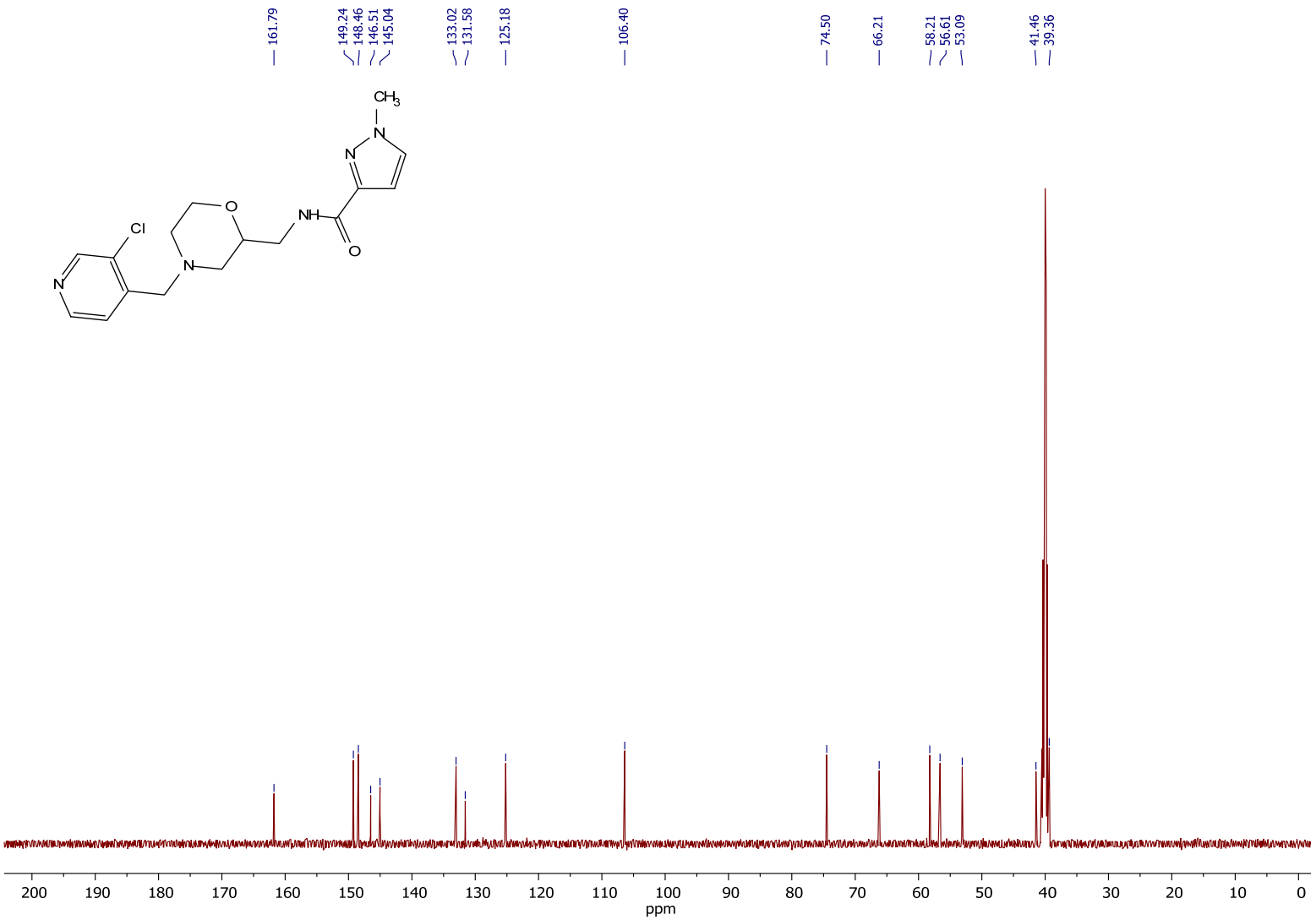

3-Methyl-*N*-((1-((1-methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)pyrrolidin-3-yl)methyl)butanamide (**13**{*85*,*113*,*14*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



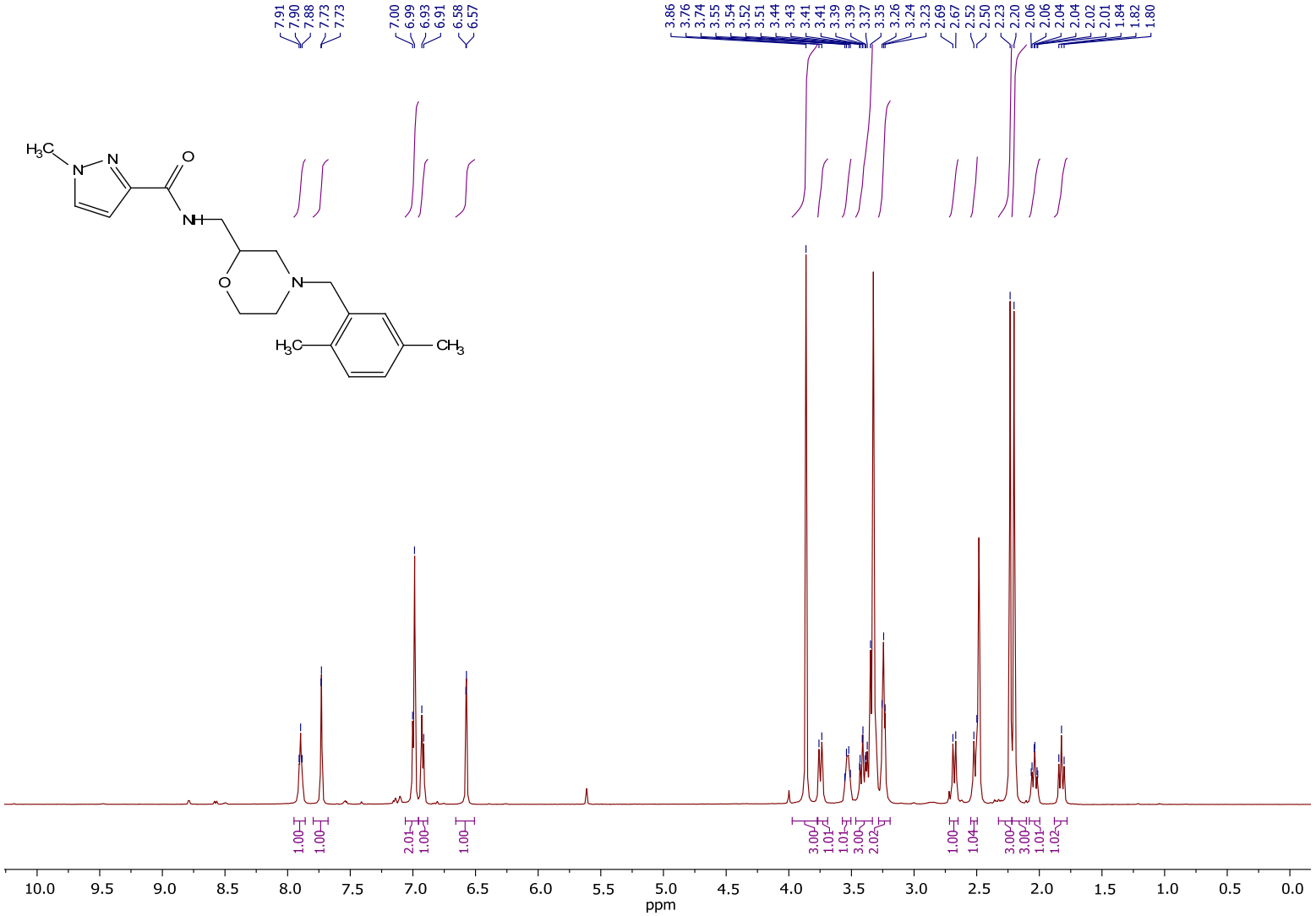

3-Methyl-*N*-((1-((1-methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)pyrrolidin-3-yl)methyl)butanamide (**13**{*85*,*113*,*14*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



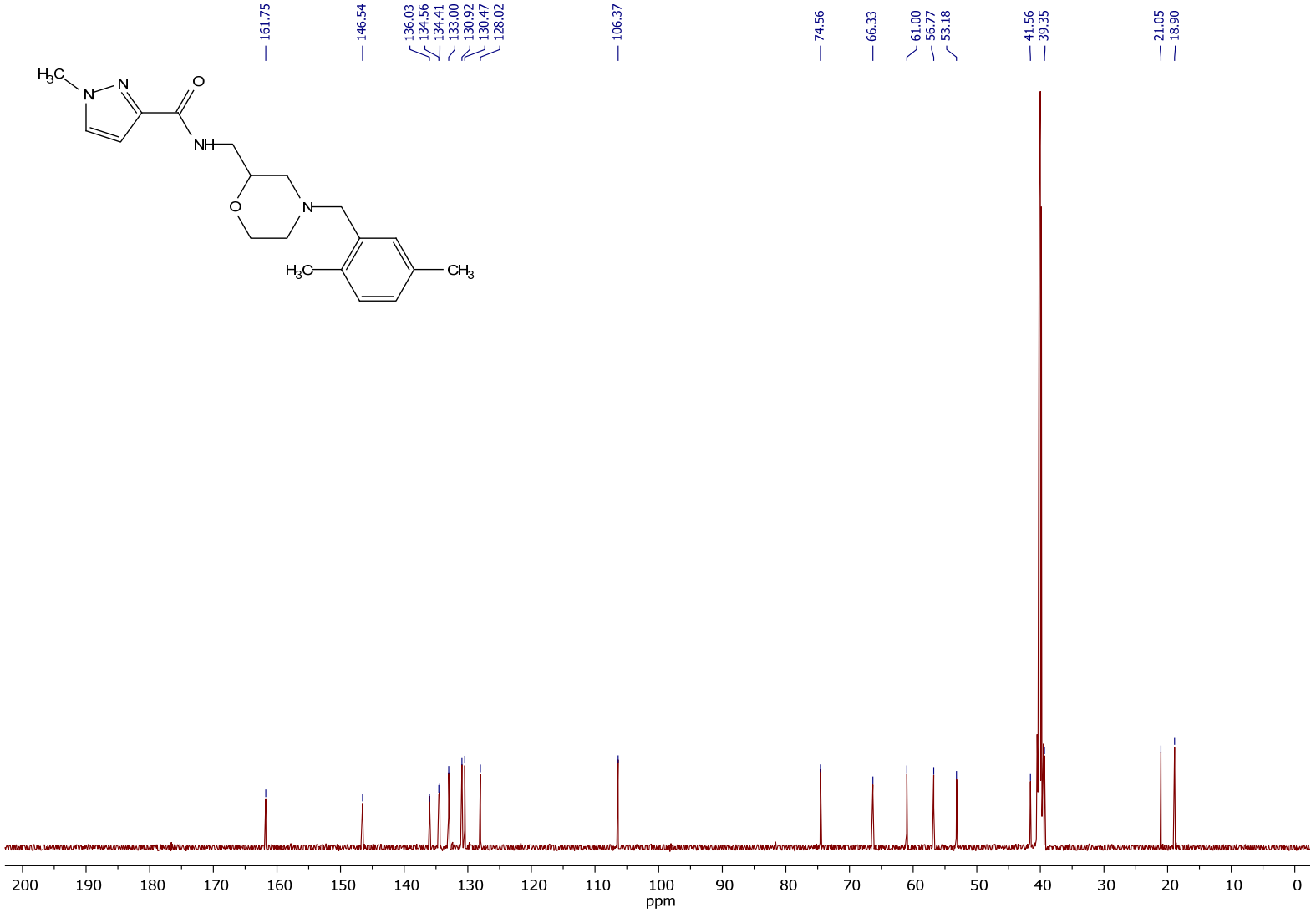

*N*-((4-((3-Chloropyridin-4-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*20*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



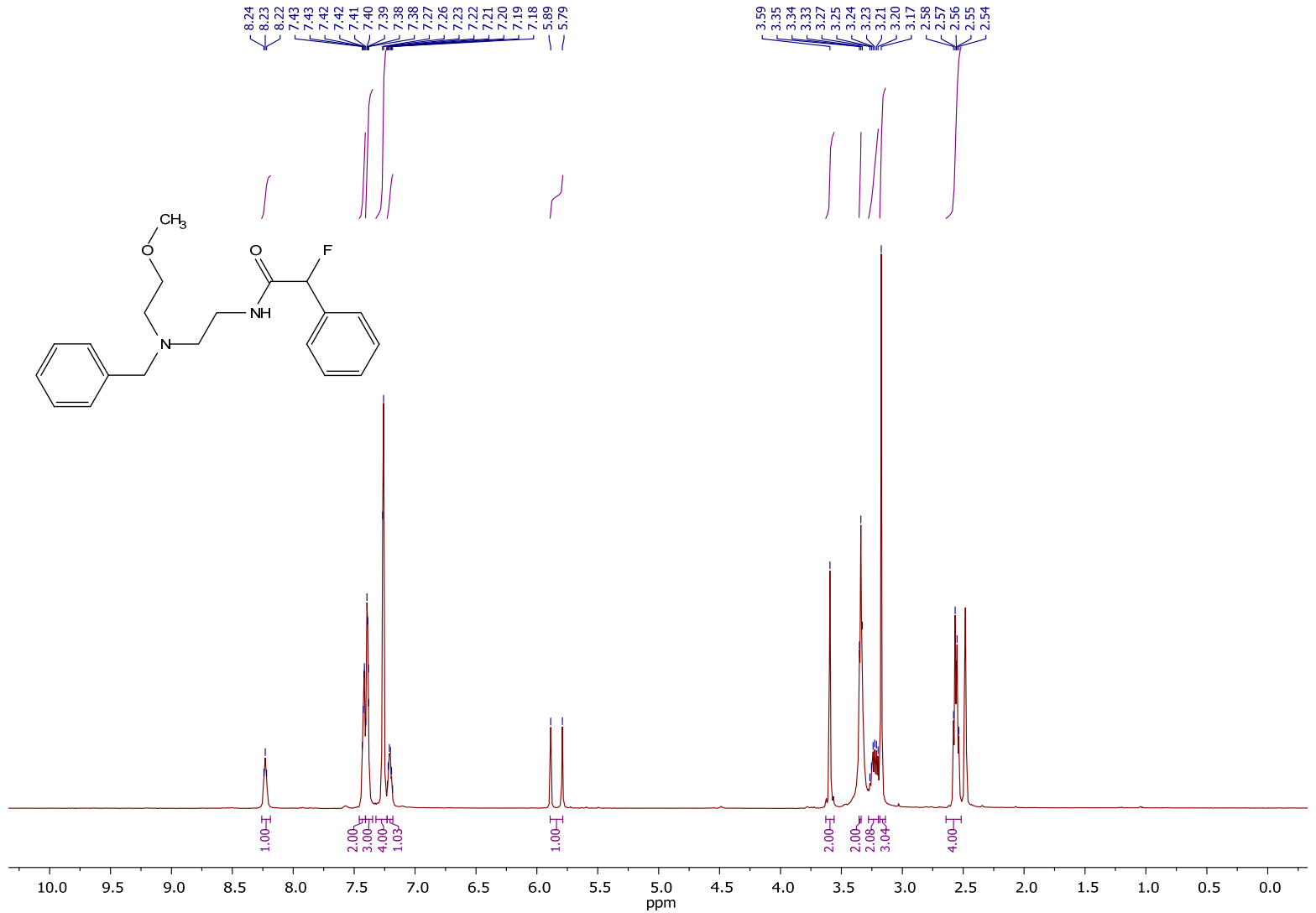

*N*-((4-((3-Chloropyridin-4-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*20*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



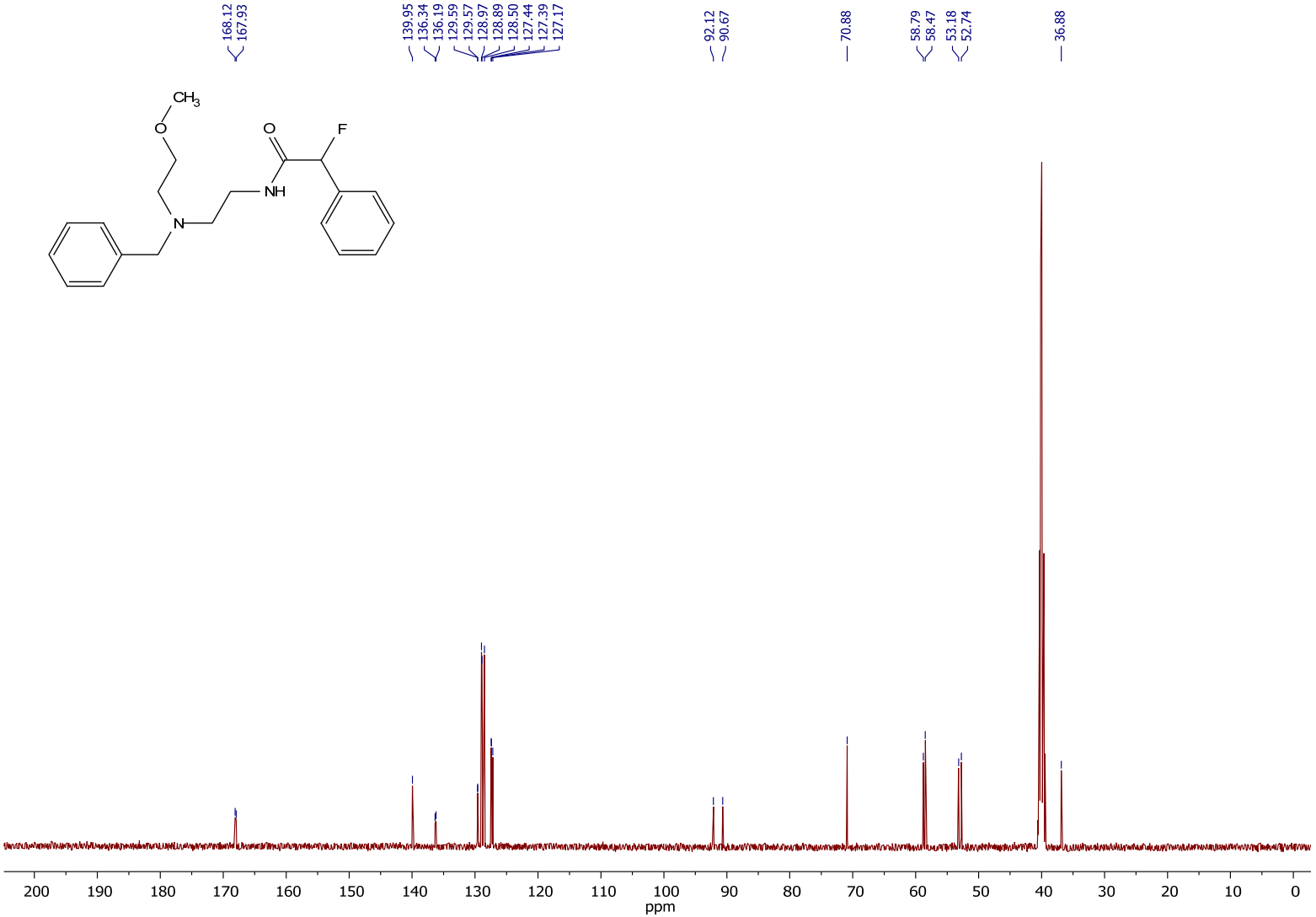

*N*-((4-(2,5-Dimethylbenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*21*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



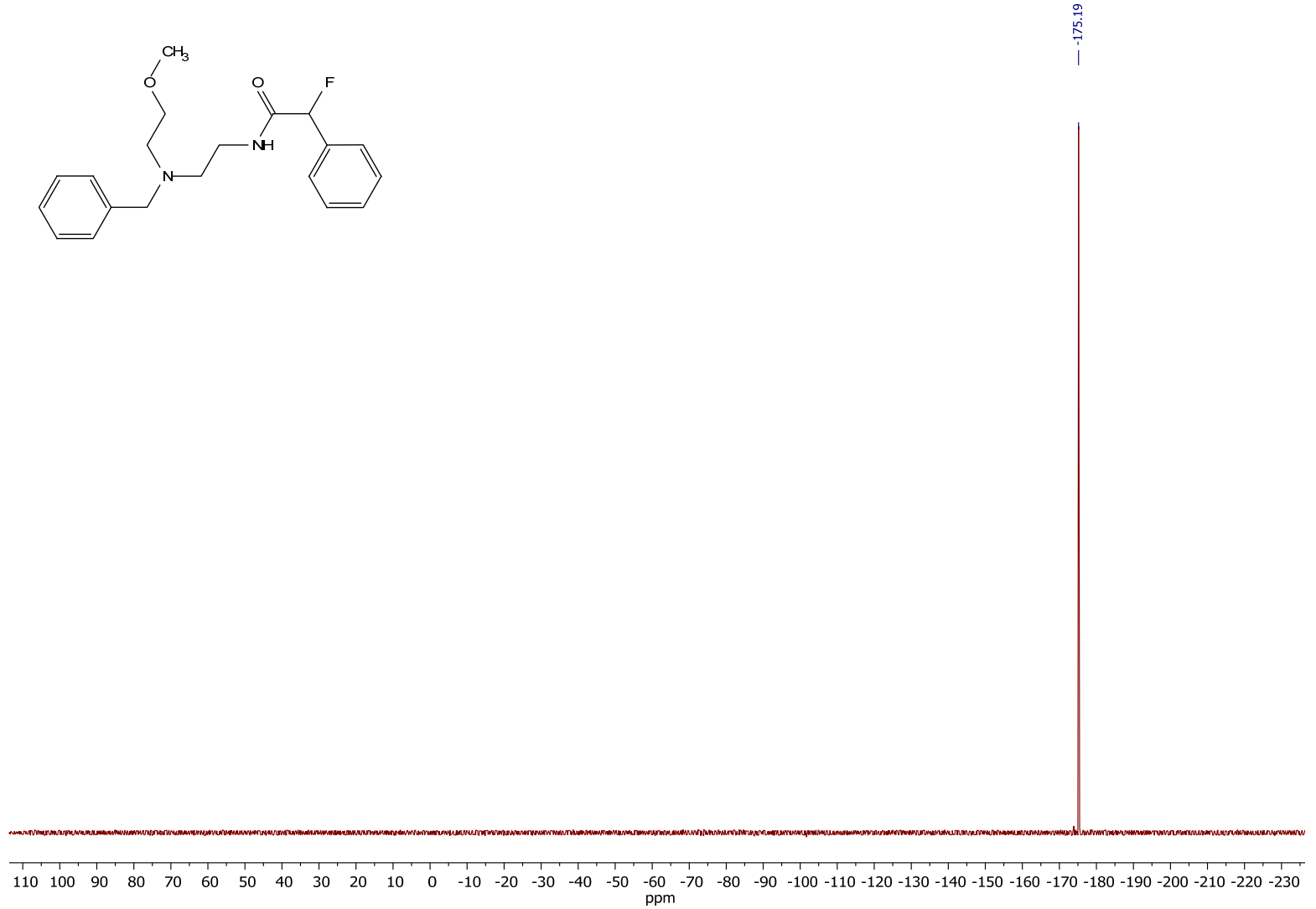

*N*-((4-(2,5-Dimethylbenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*21*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



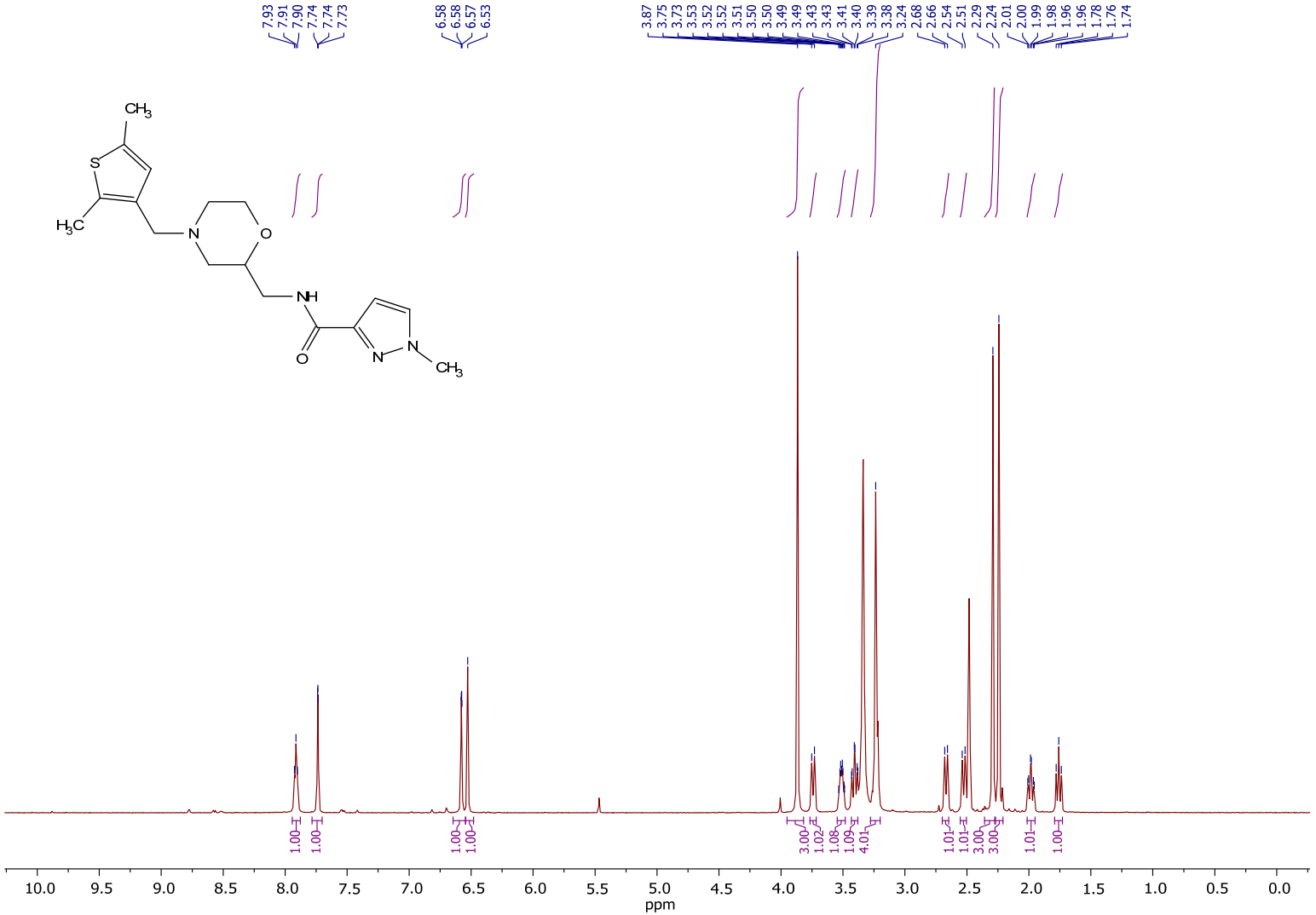

*N*-(2-(Benzyl(2-methoxyethyl)amino)ethyl)-2-fluoro-2-phenylacetamide (**13**{*107*,*152*,*23*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$



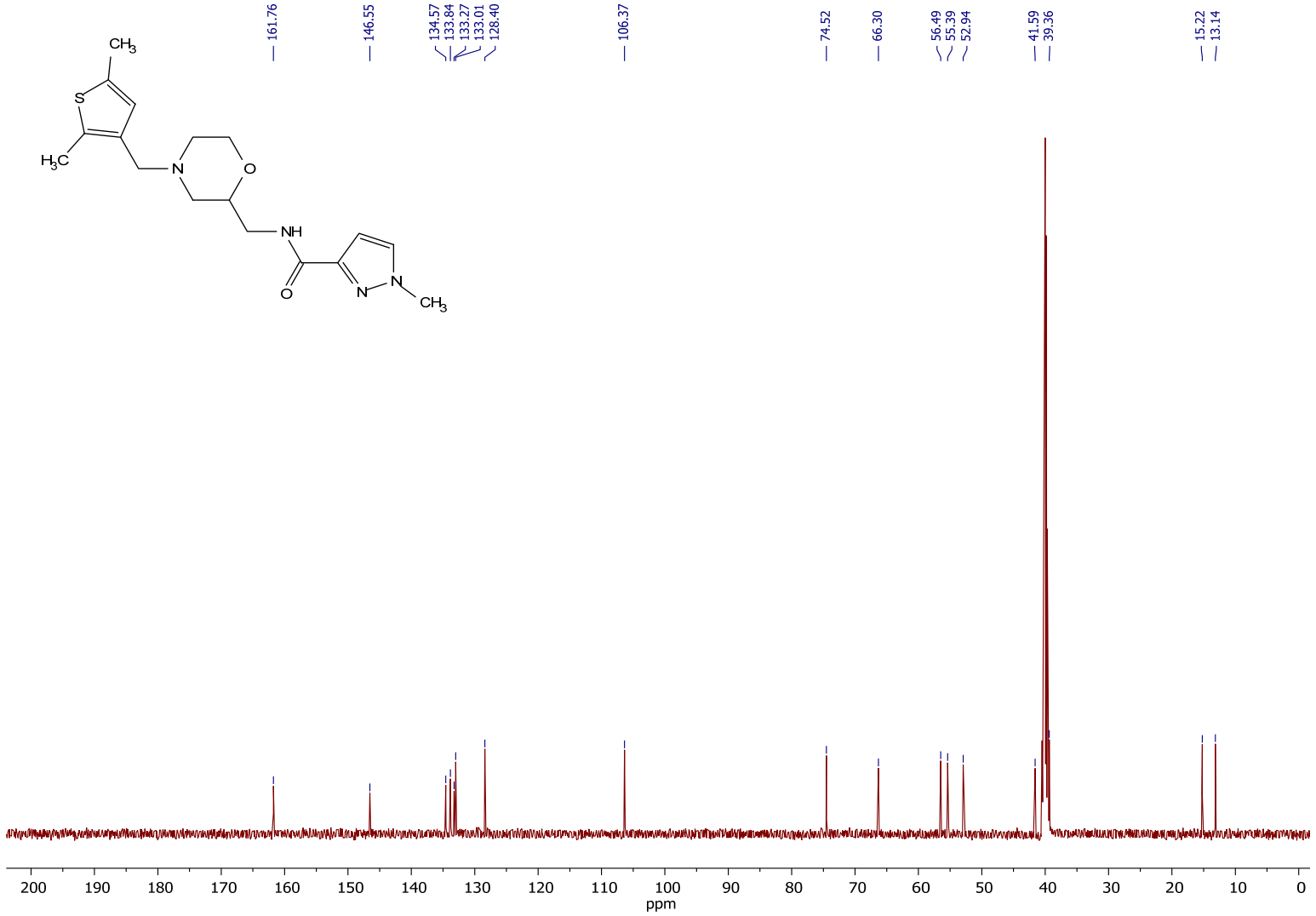

*N*-(2-(Benzyl(2-methoxyethyl)amino)ethyl)-2-fluoro-2-phenylacetamide (**13**{*107*,*152*,*23*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



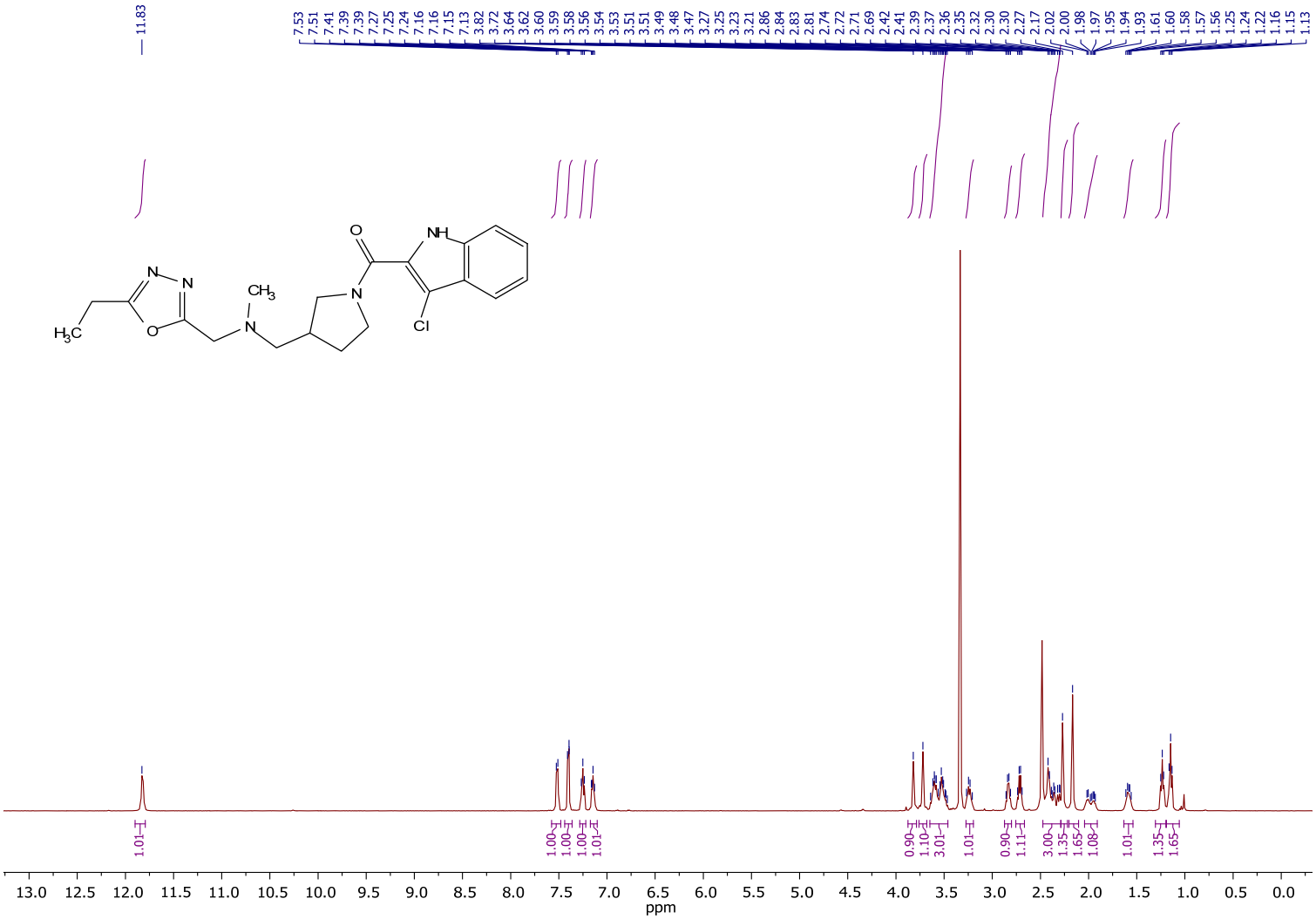

*N*-(2-(Benzyl(2-methoxyethyl)amino)ethyl)-2-fluoro-2-phenylacetamide (**13**{*107*,*152*,*23*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$)



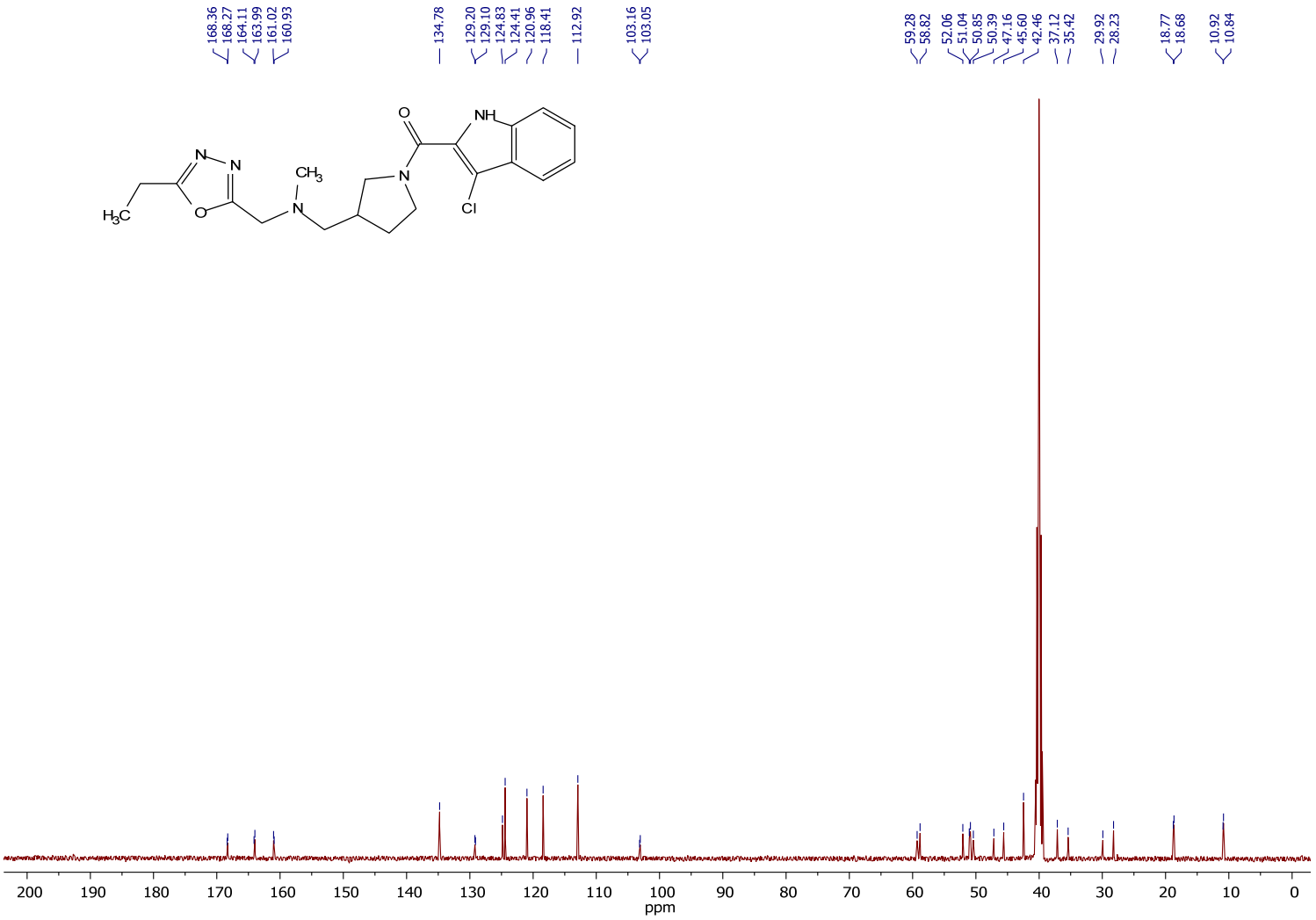

*N*-((4-((2,5-Dimethylthiophen-3-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*27*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



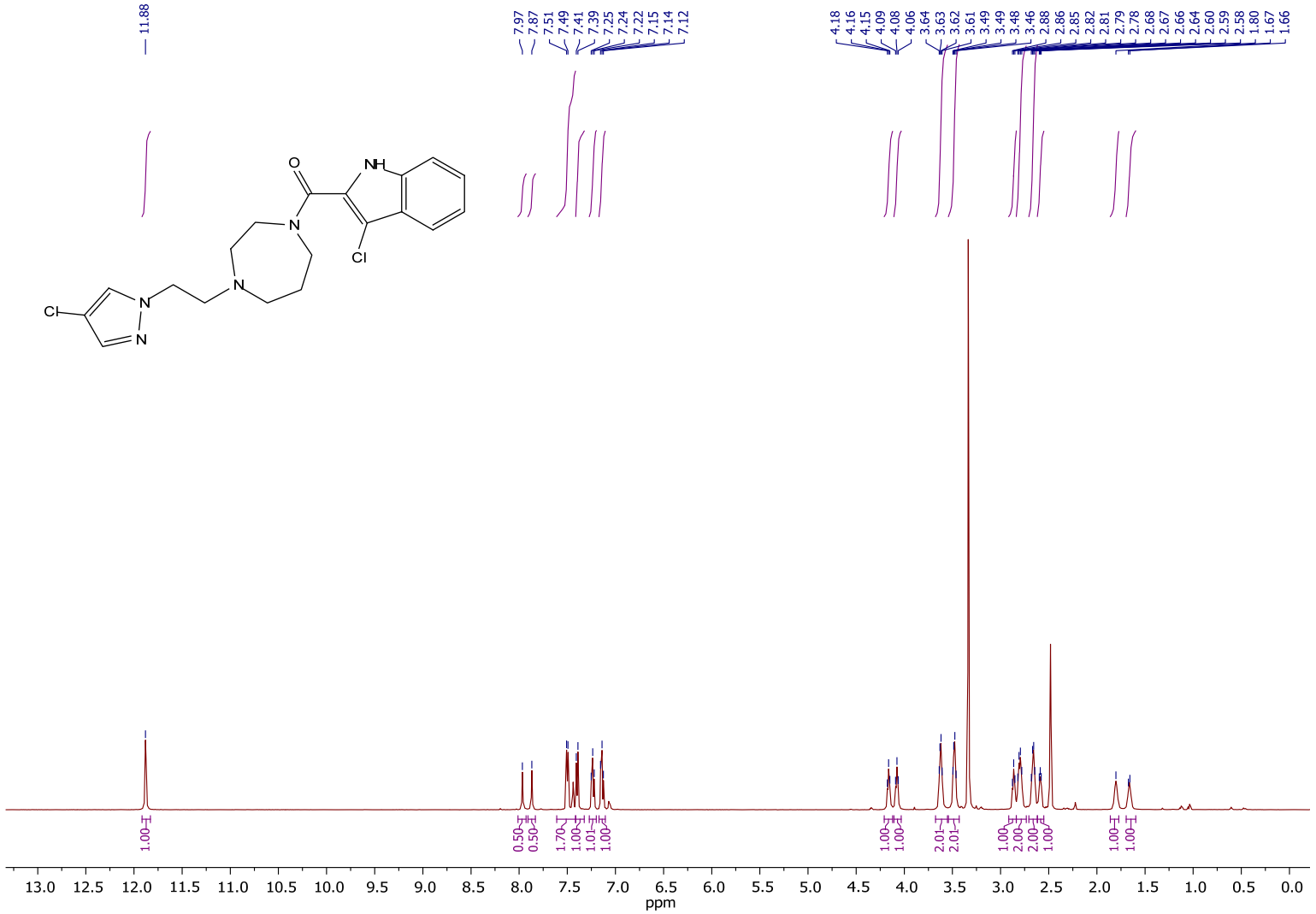

*N*-((4-((2,5-Dimethylthiophen-3-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*27*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



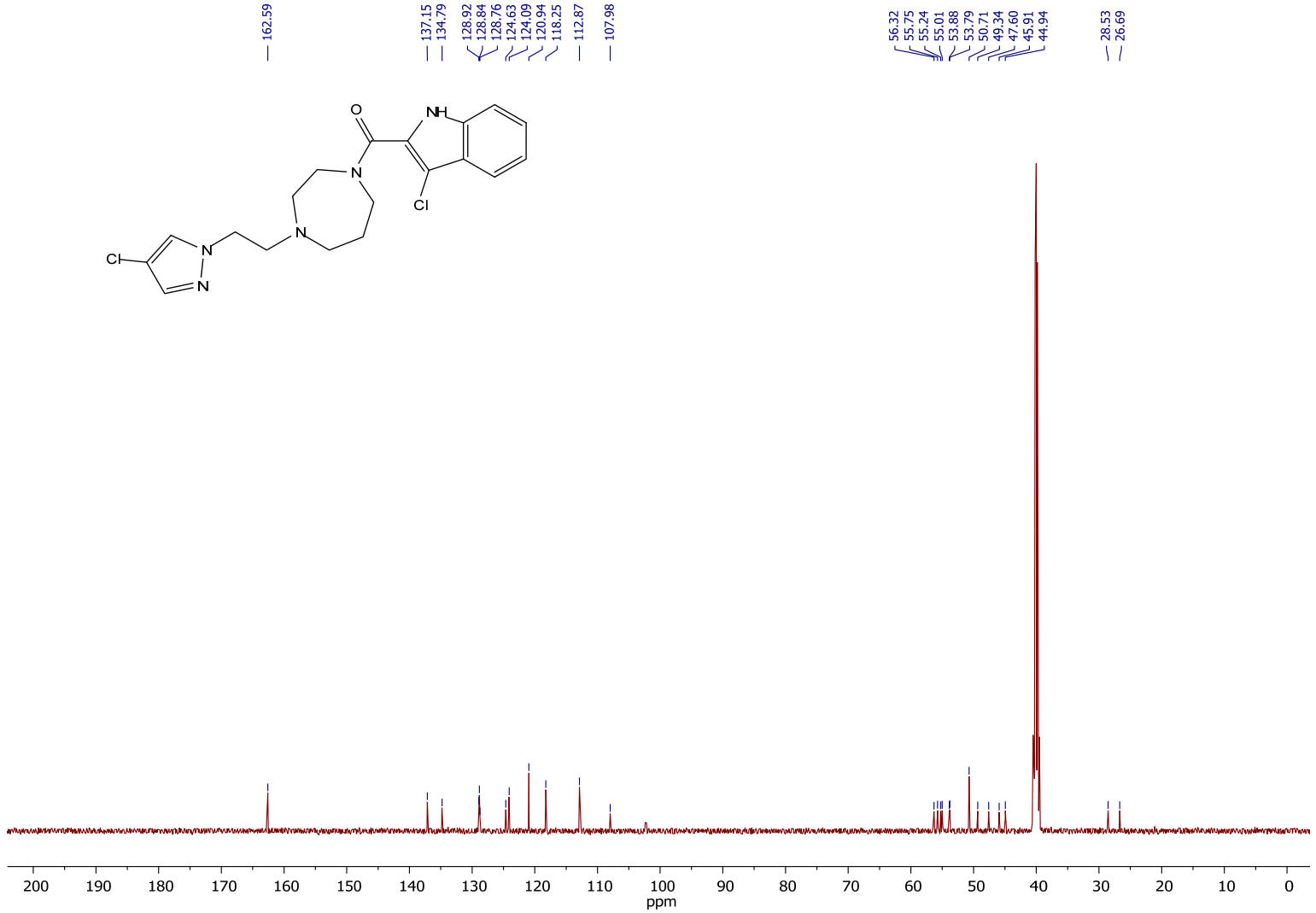

(3-Chloro-1*H*-indol-2-yl)(3-((((5-ethyl-1,3,4-oxadiazol-2-yl)methyl)(methyl)amino)methyl)pyrrolidin-1-yl)methanone (**13**{*44*,*129*,*33*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



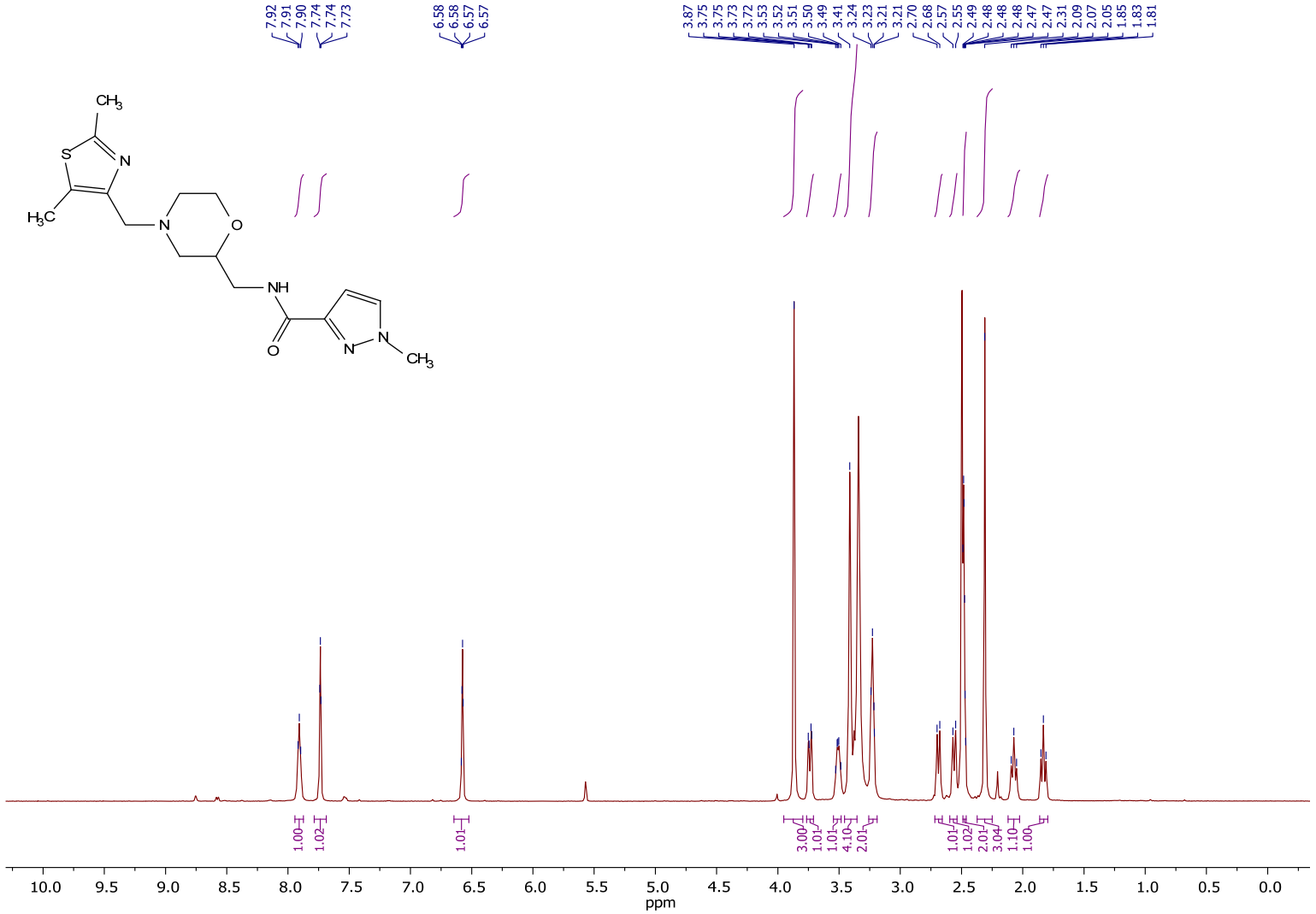

(3-Chloro-1*H*-indol-2-yl)(3-((((5-ethyl-1,3,4-oxadiazol-2-yl)methyl)(methyl)amino)methyl)pyrrolidin-1-yl)methanone (**13**{*44*,*129*,*33*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



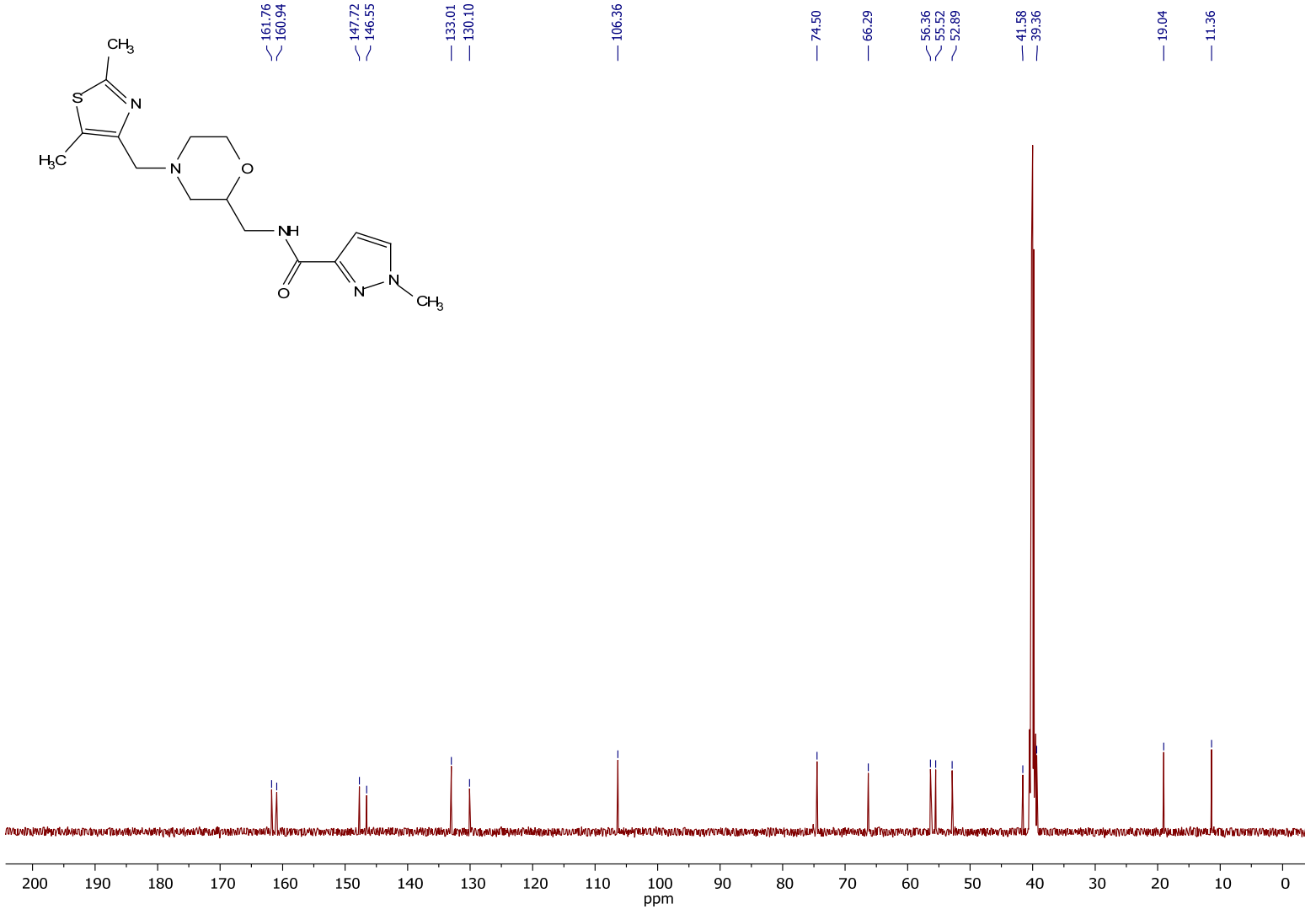

(3-Chloro-1*H*-indol-2-yl)(4-(2-(4-chloro-1*H*-pyrazol-1-yl)ethyl)-1,4-diazepan-1-yl)methanone (**13**{*23*,*129*,*34*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



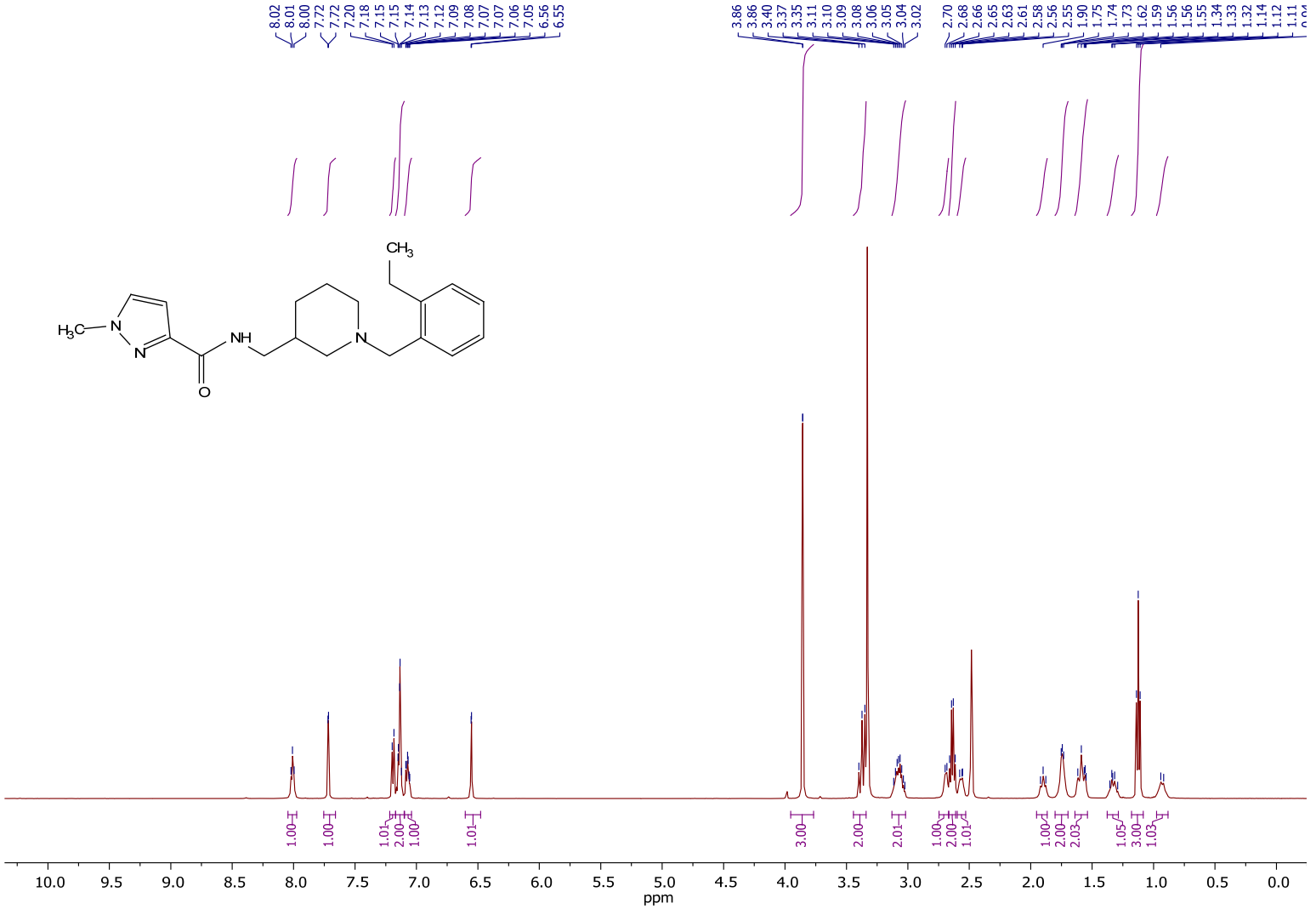

(3-Chloro-1*H*-indol-2-yl)(4-(2-(4-chloro-1*H*-pyrazol-1-yl)ethyl)-1,4-diazepan-1-yl)methanone (**13**{*23*,*129*,*34*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



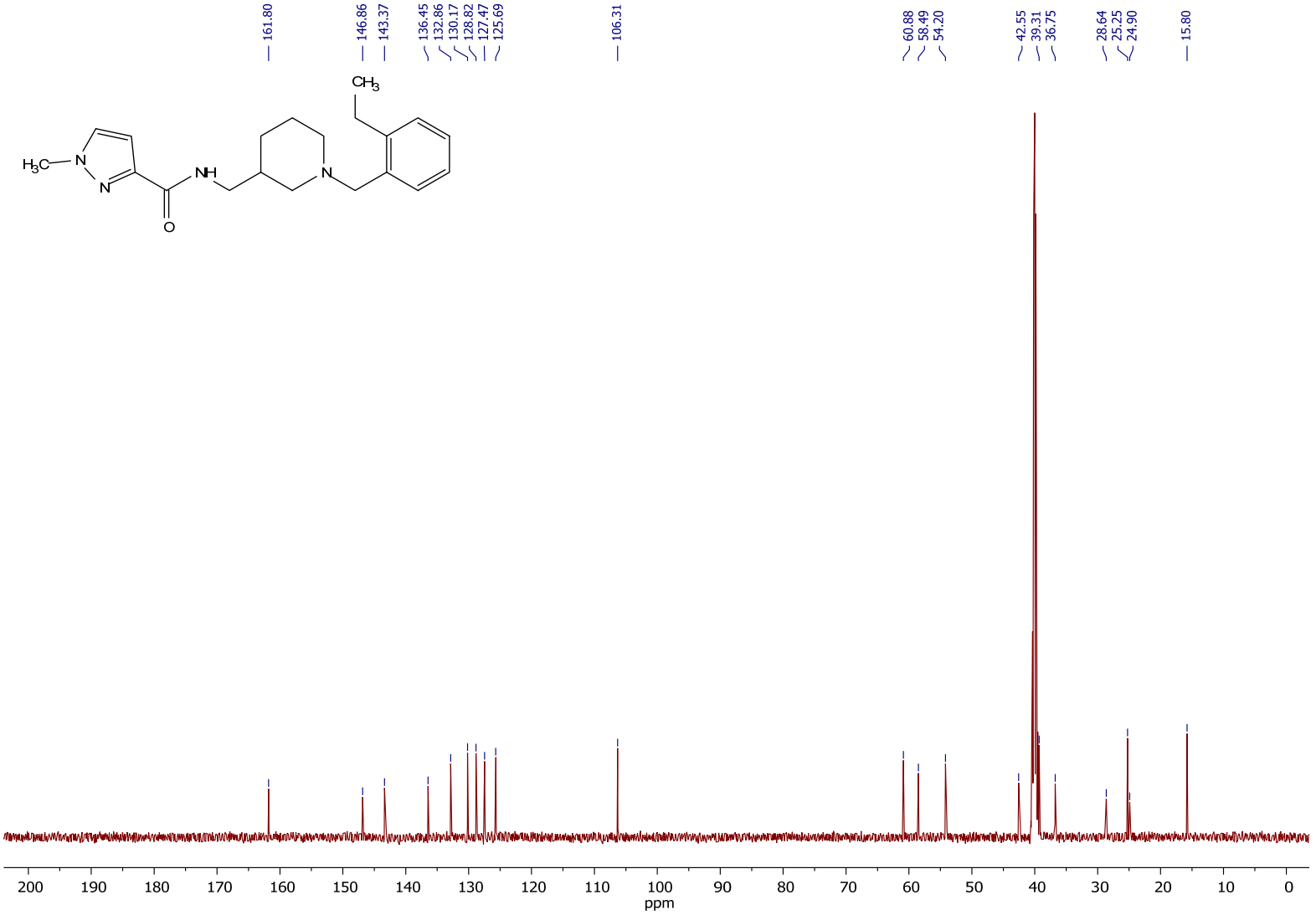

*N*-((4-((2,5-Dimethylthiazol-4-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*35*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



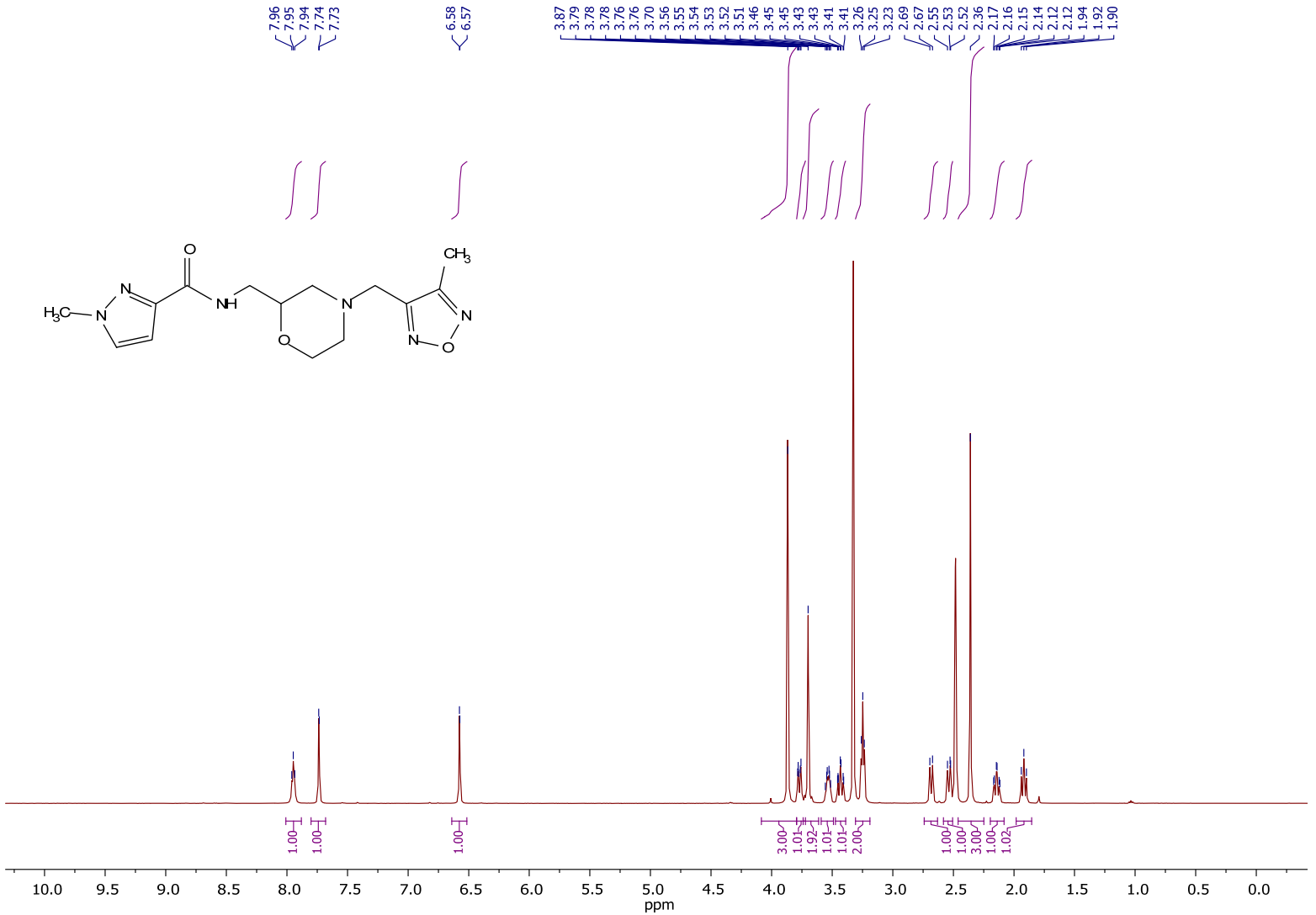

*N*-((4-((2,5-Dimethylthiazol-4-yl)methyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*35*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



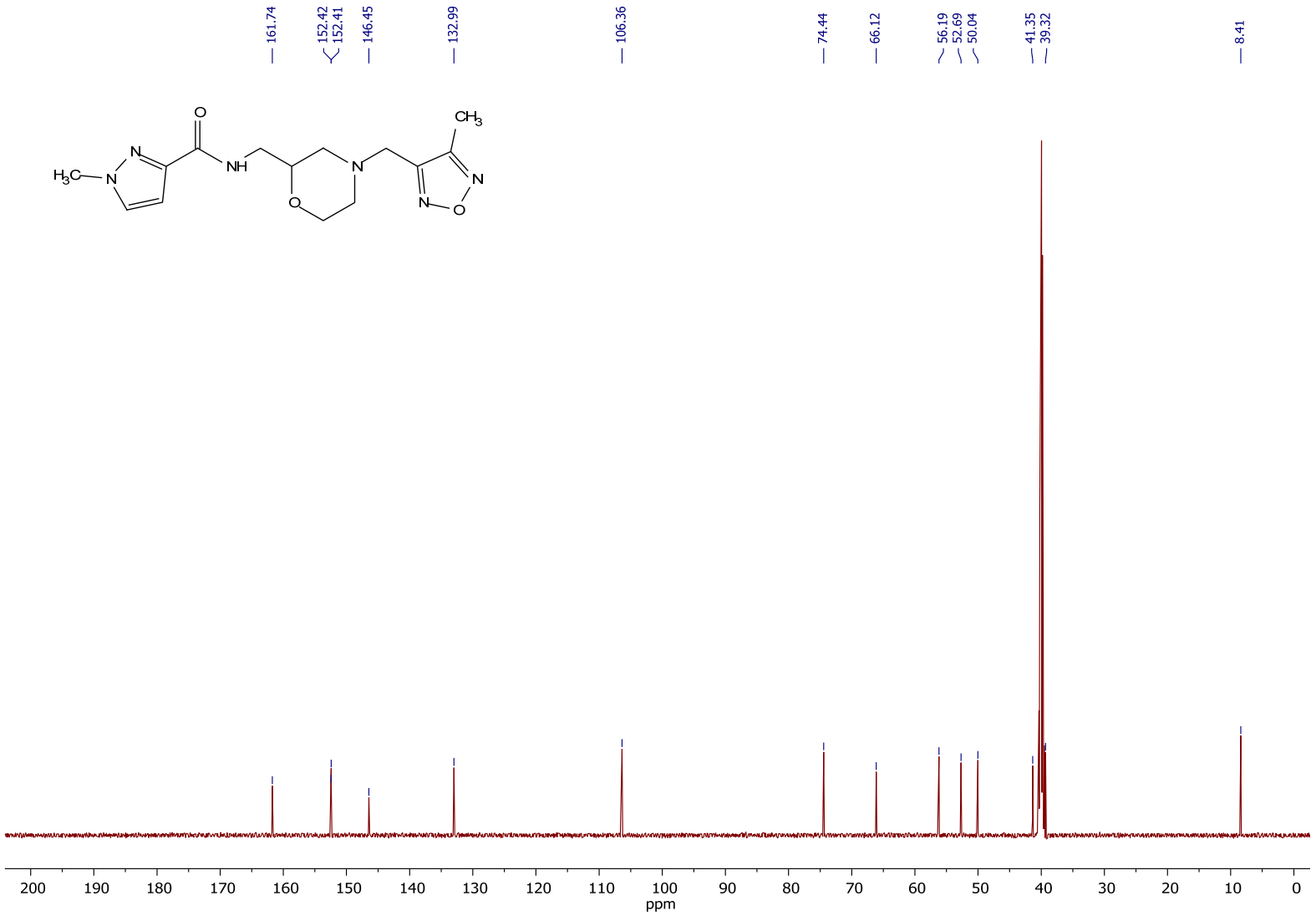

*N*-((1-(2-Ethylbenzyl)piperidin-3-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*102*,*107*,*29*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



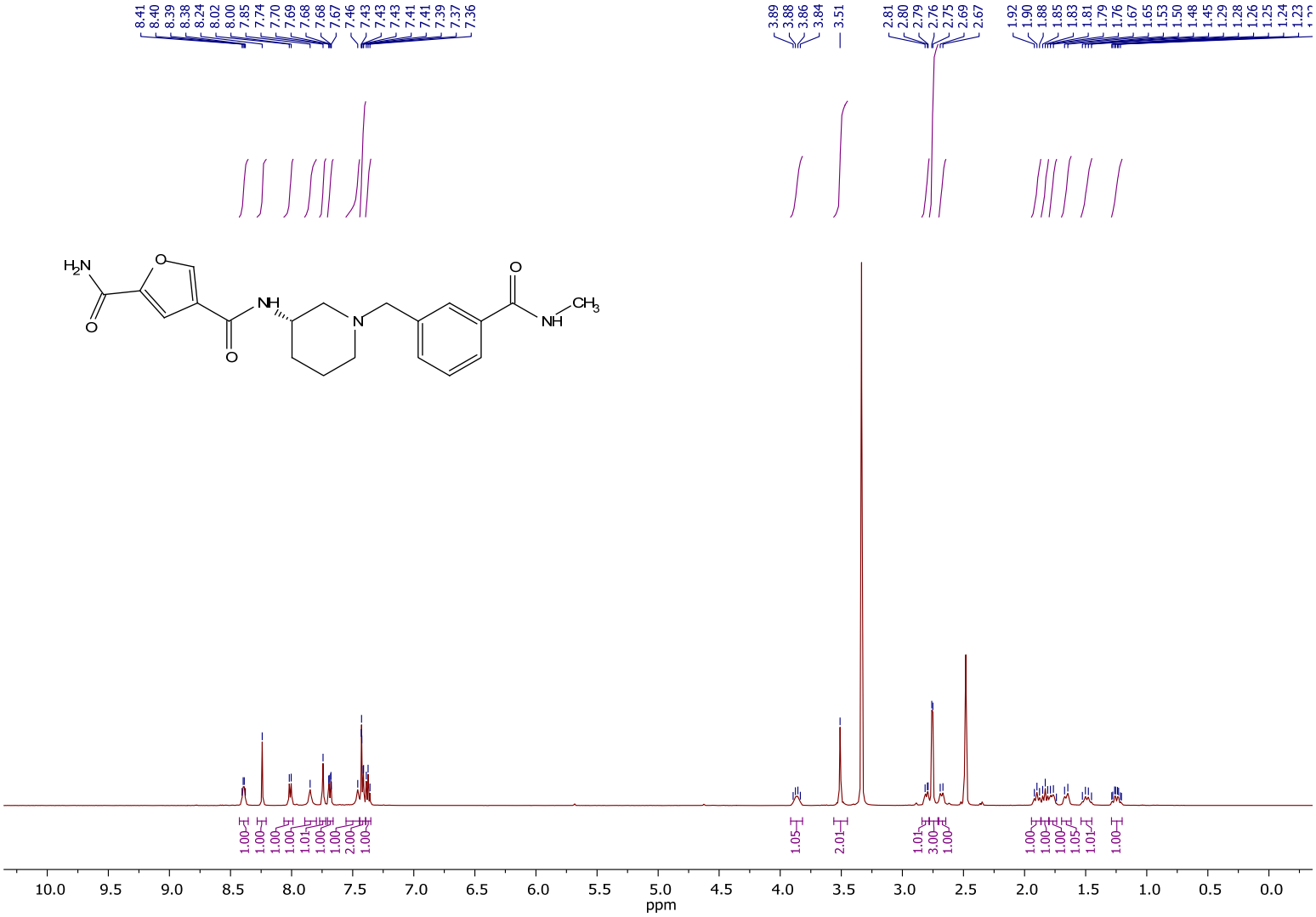

*N*-((1-(2-Ethylbenzyl)piperidin-3-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*102*,*107*,*29*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



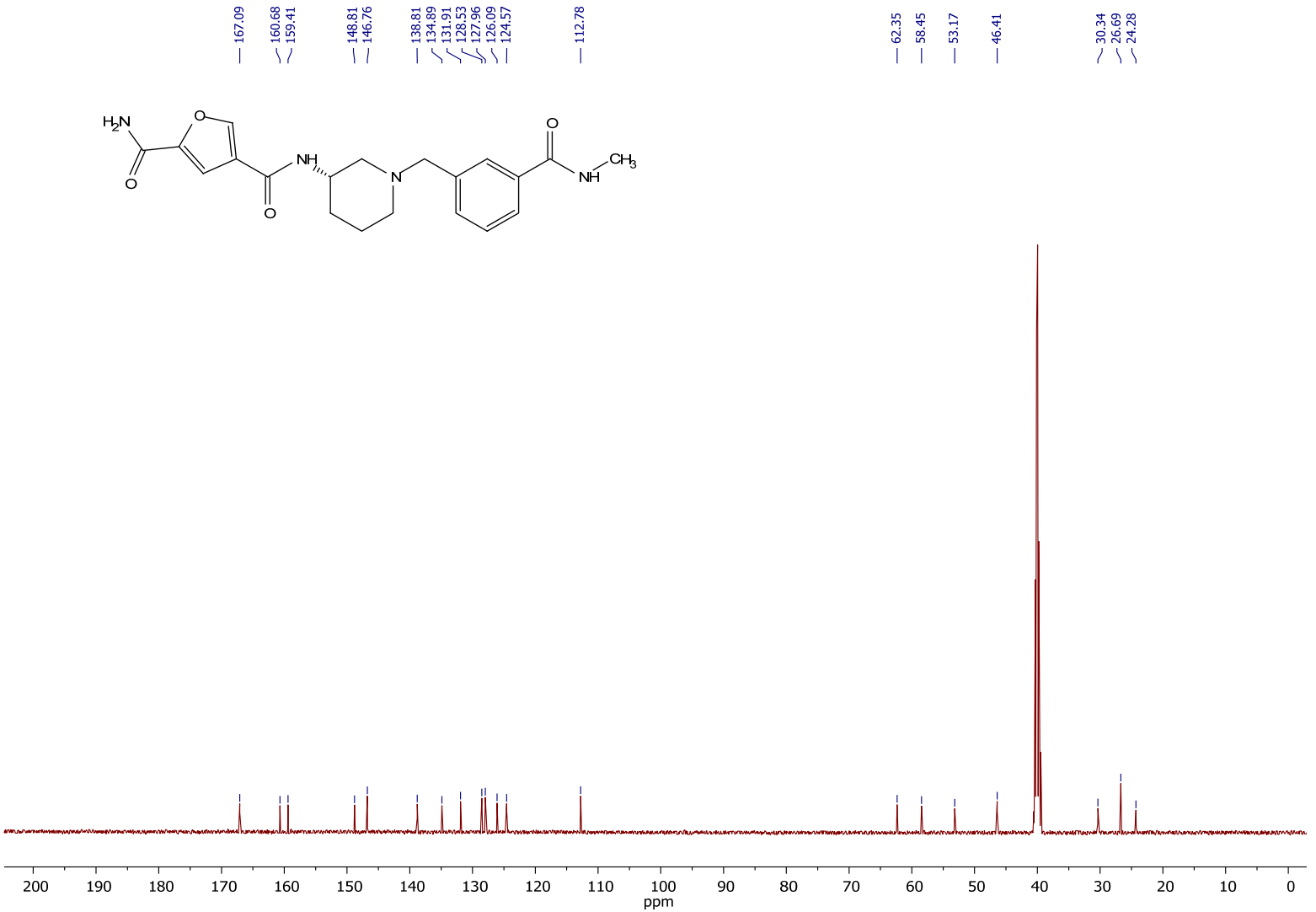

1-Methyl-*N*-((4-((4-methyl-1,2,5-oxadiazol-3-yl)methyl)morpholin-2-yl)methyl)-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*38*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



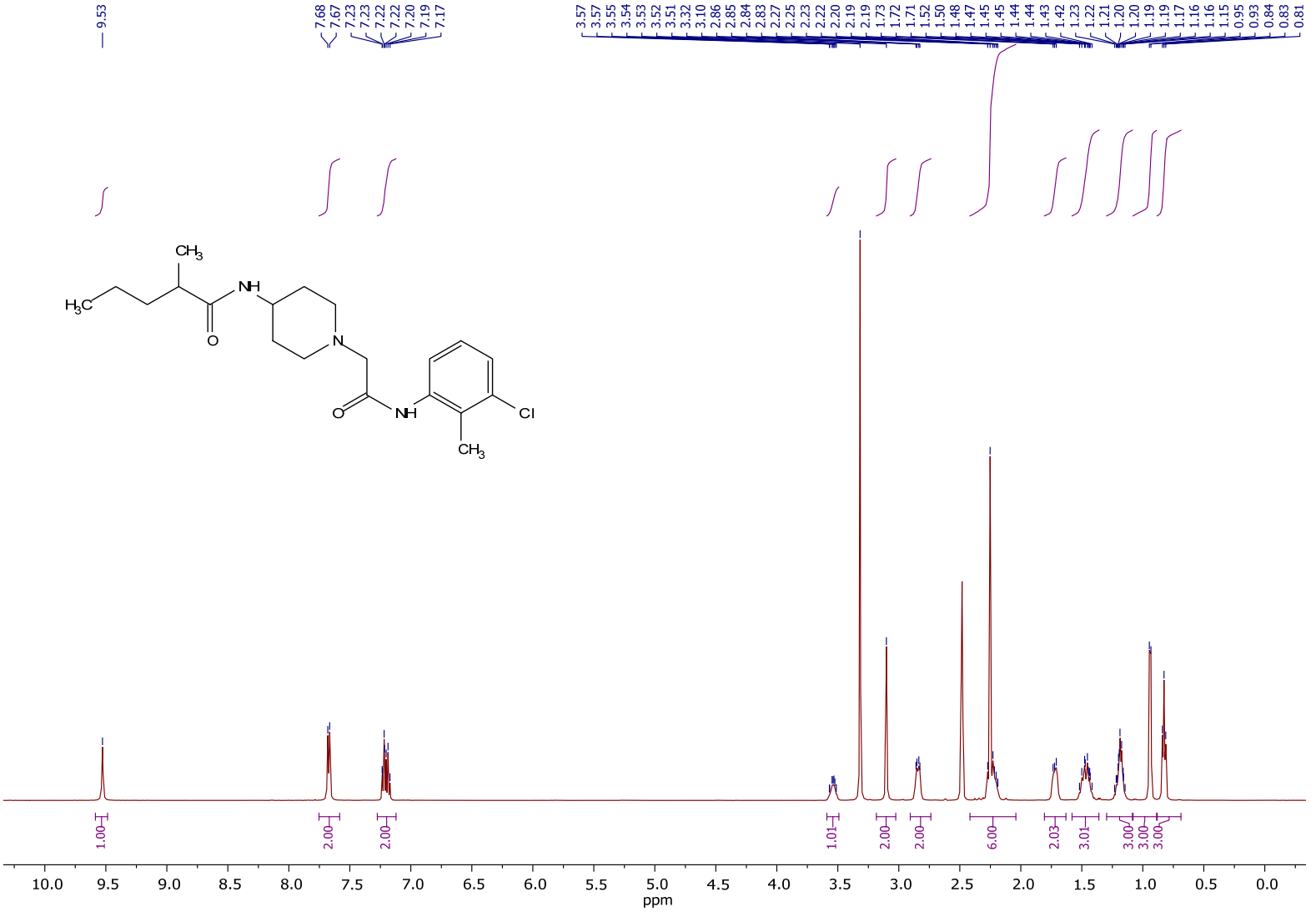

1-Methyl-*N*-((4-((4-methyl-1,2,5-oxadiazol-3-yl)methyl)morpholin-2-yl)methyl)-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*38*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



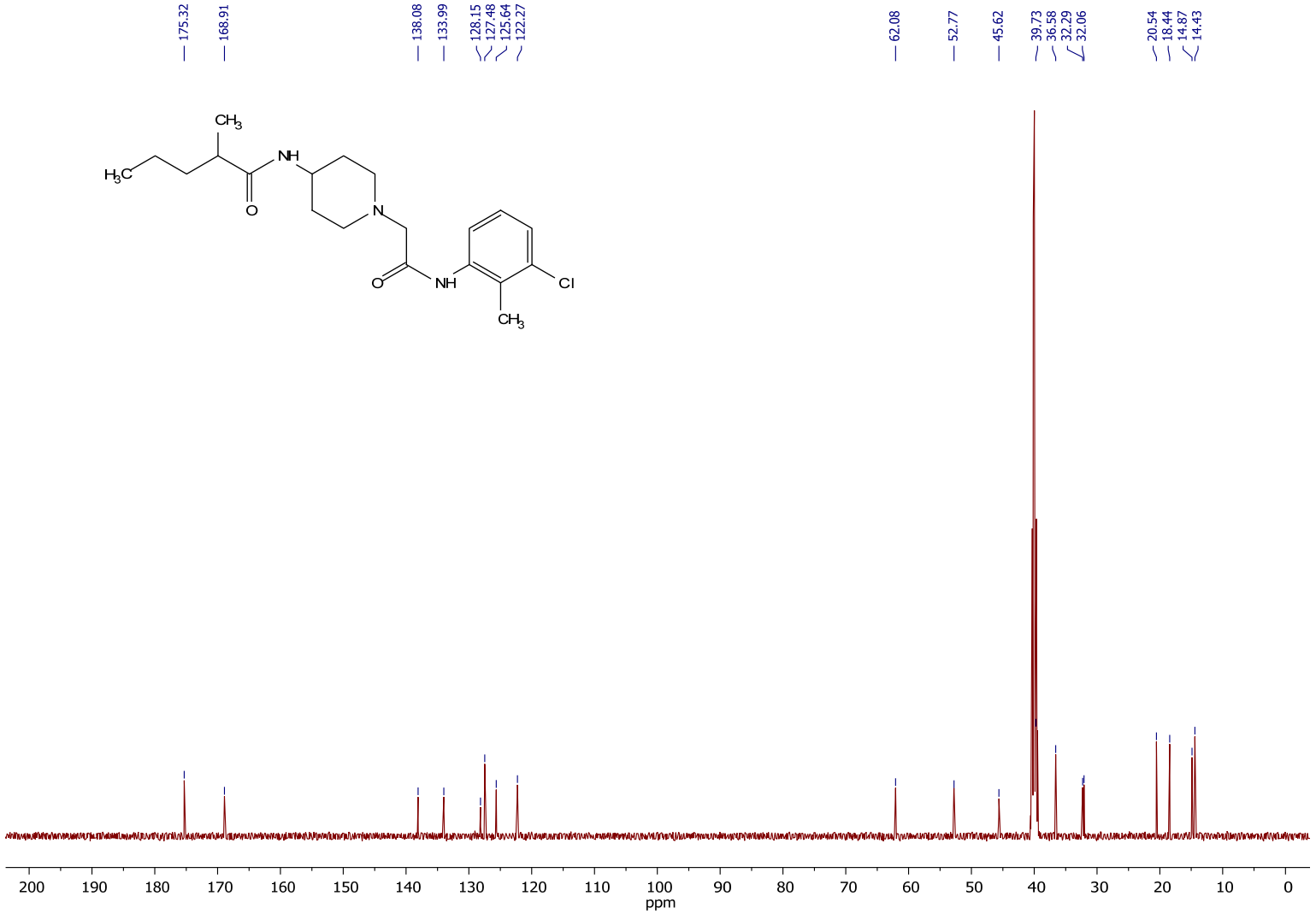

(*S*)-$N^4$-(1-(3-(Methylcarbamoyl)benzyl)piperidin-3-yl)furan-2,4-dicarboxamide (**13**{*139*,*243*,*50*}), $^1$H NMR (500 MHz, DMSO-$d_6$)



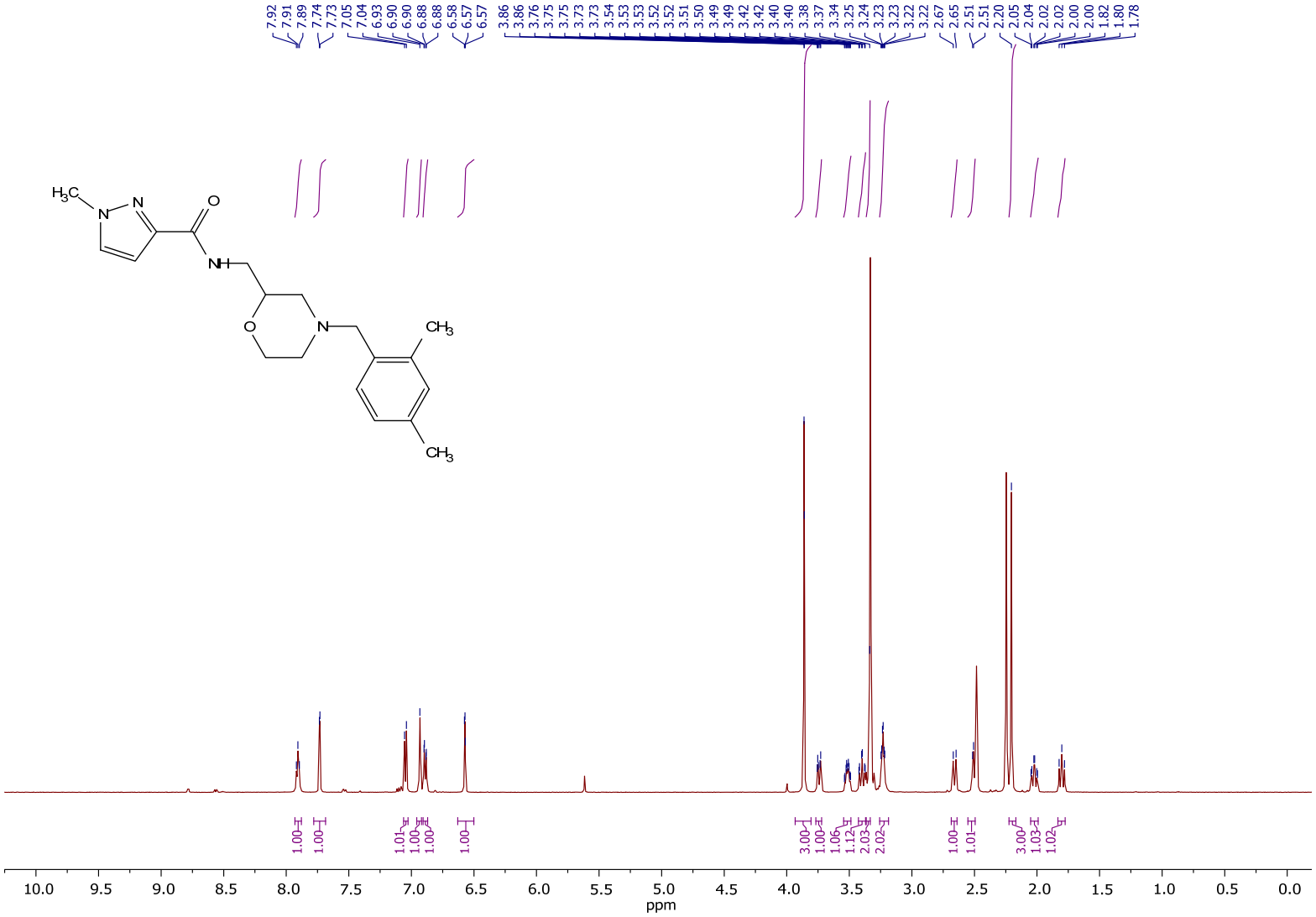

(*S*)-*N*$^4$-(1-(3-(Methylcarbamoyl)benzyl)piperidin-3-yl)furan-2,4-dicarboxamide (**13**{*139*,*243*,*50*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



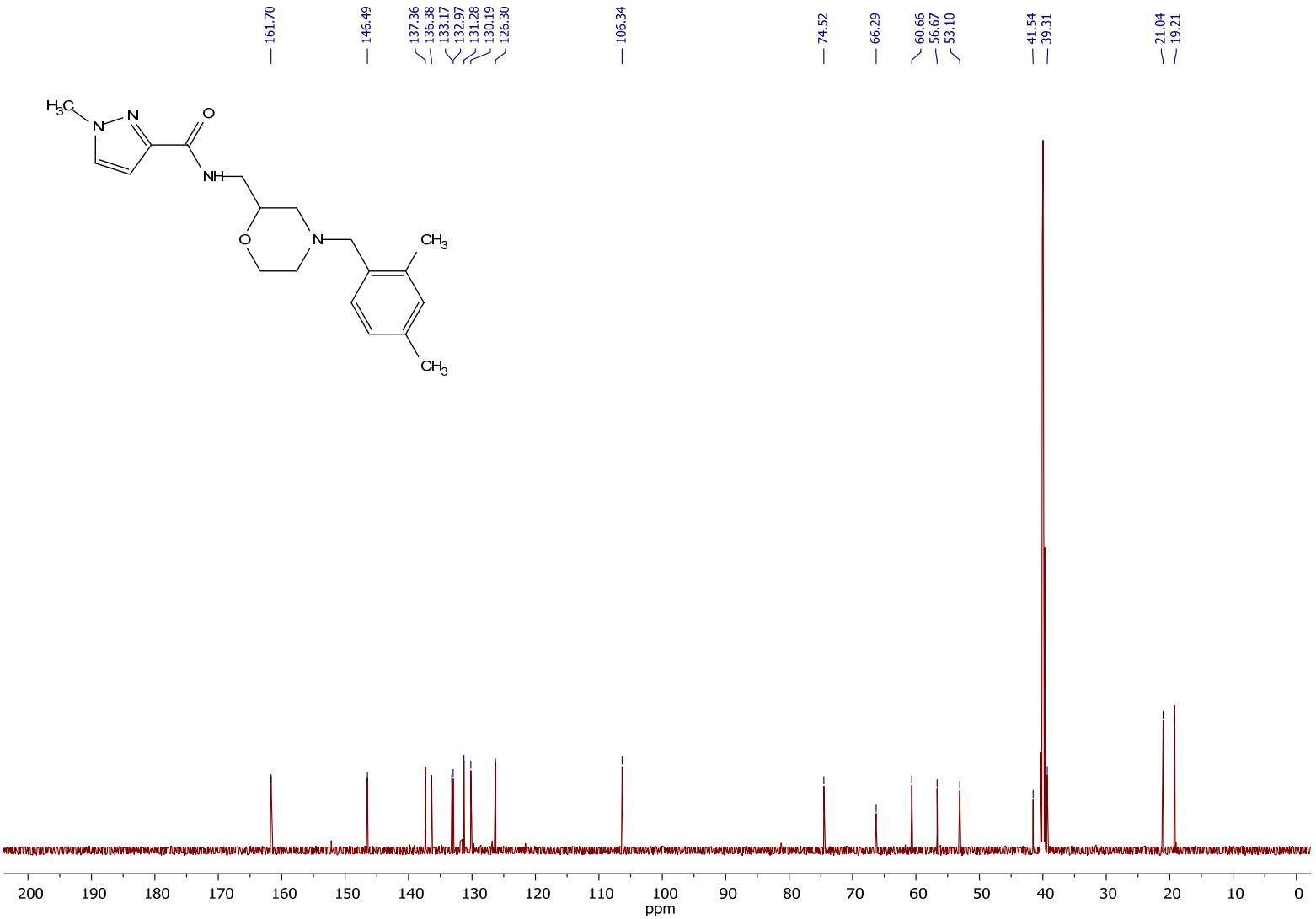

*N*-(1-(2-((3-Chloro-2-methylphenyl)amino)-2-oxoethyl)piperidin-4-yl)-2-methylpentanamide (**13**{*79*,*95*,*11*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



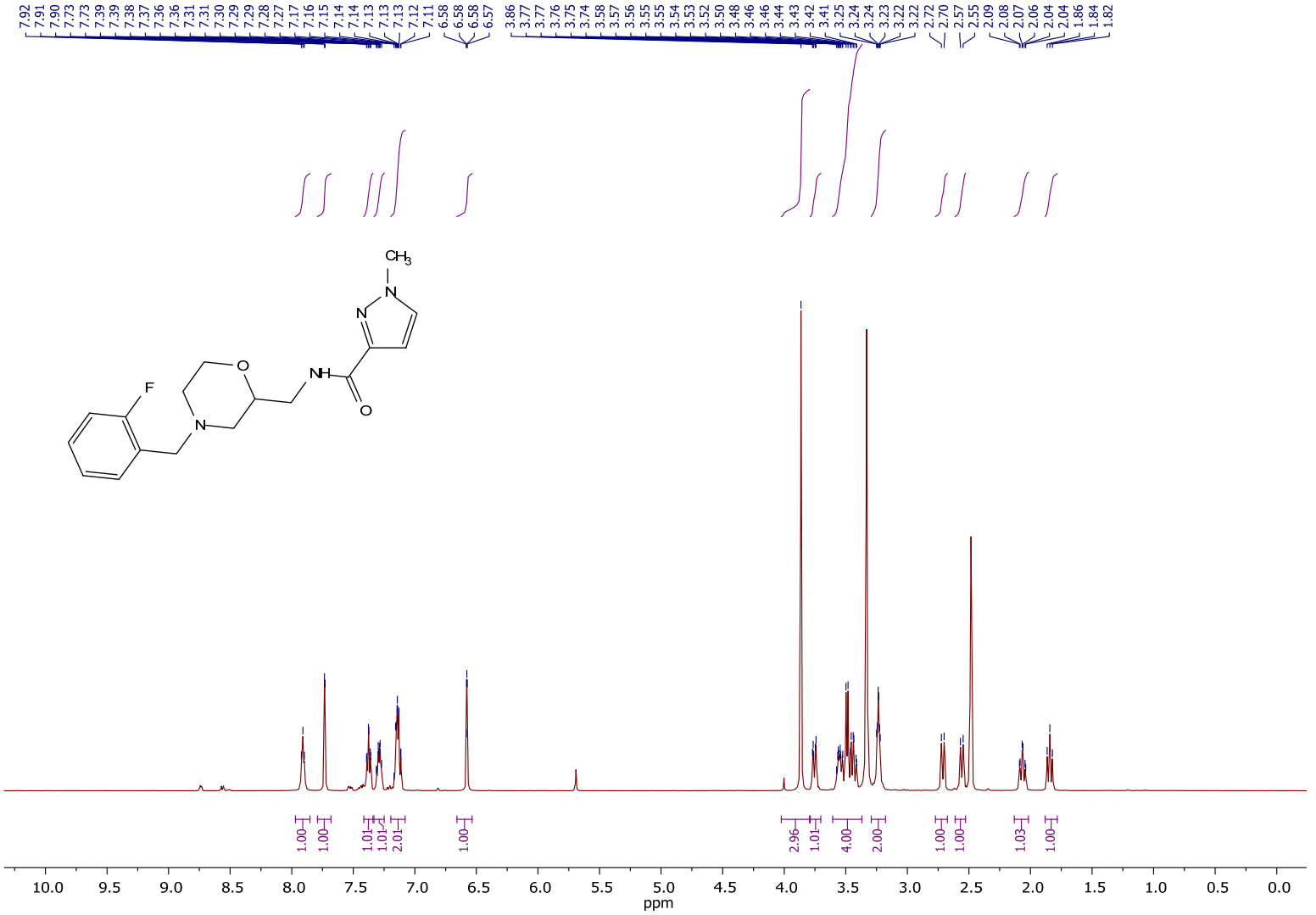

*N*-(1-(2-((3-Chloro-2-methylphenyl)amino)-2-oxoethyl)piperidin-4-yl)-2-methylpentanamide (**13**{*79*,*95*,*11*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



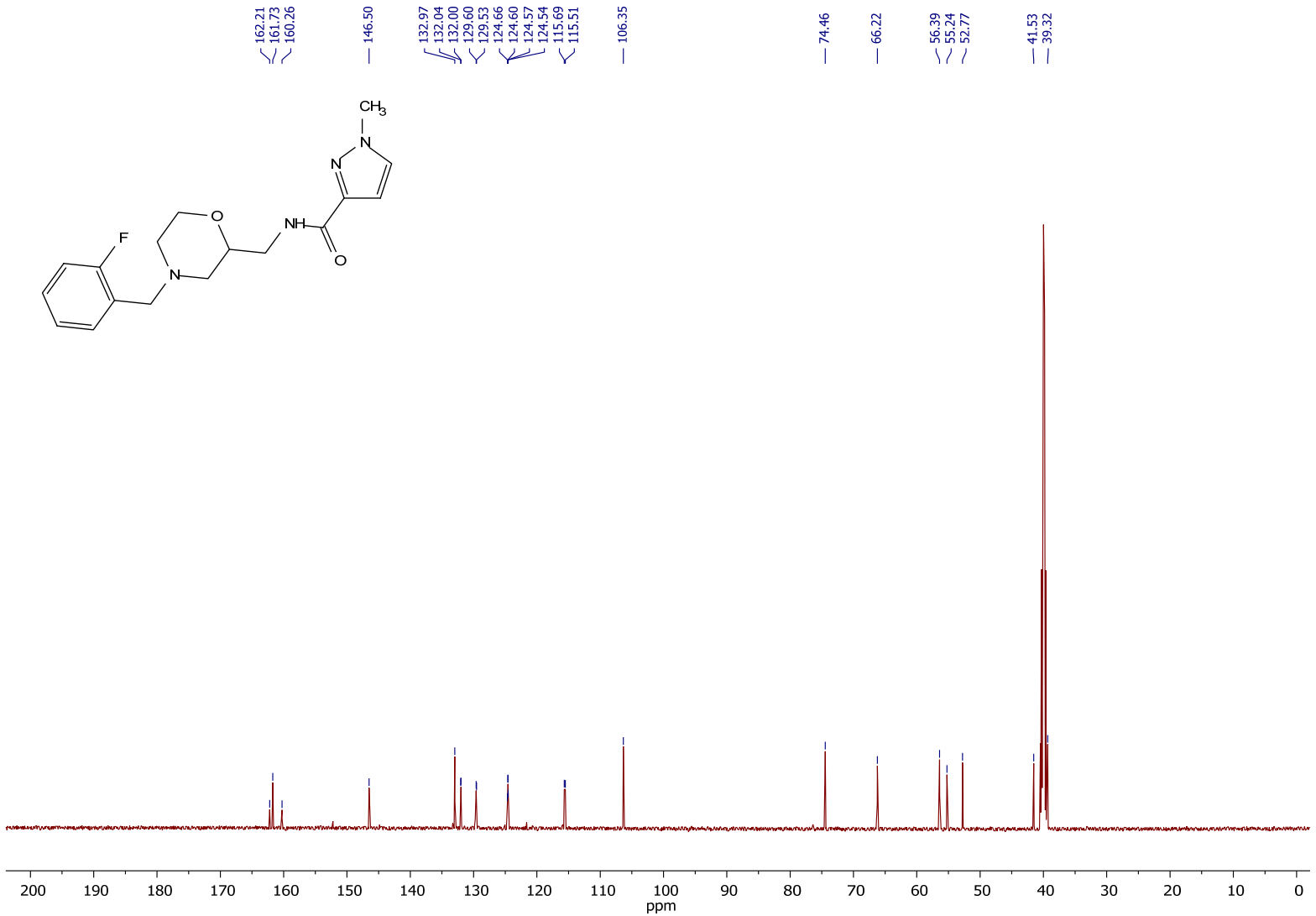

*N*-((4-(2,4-Dimethylbenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*12*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



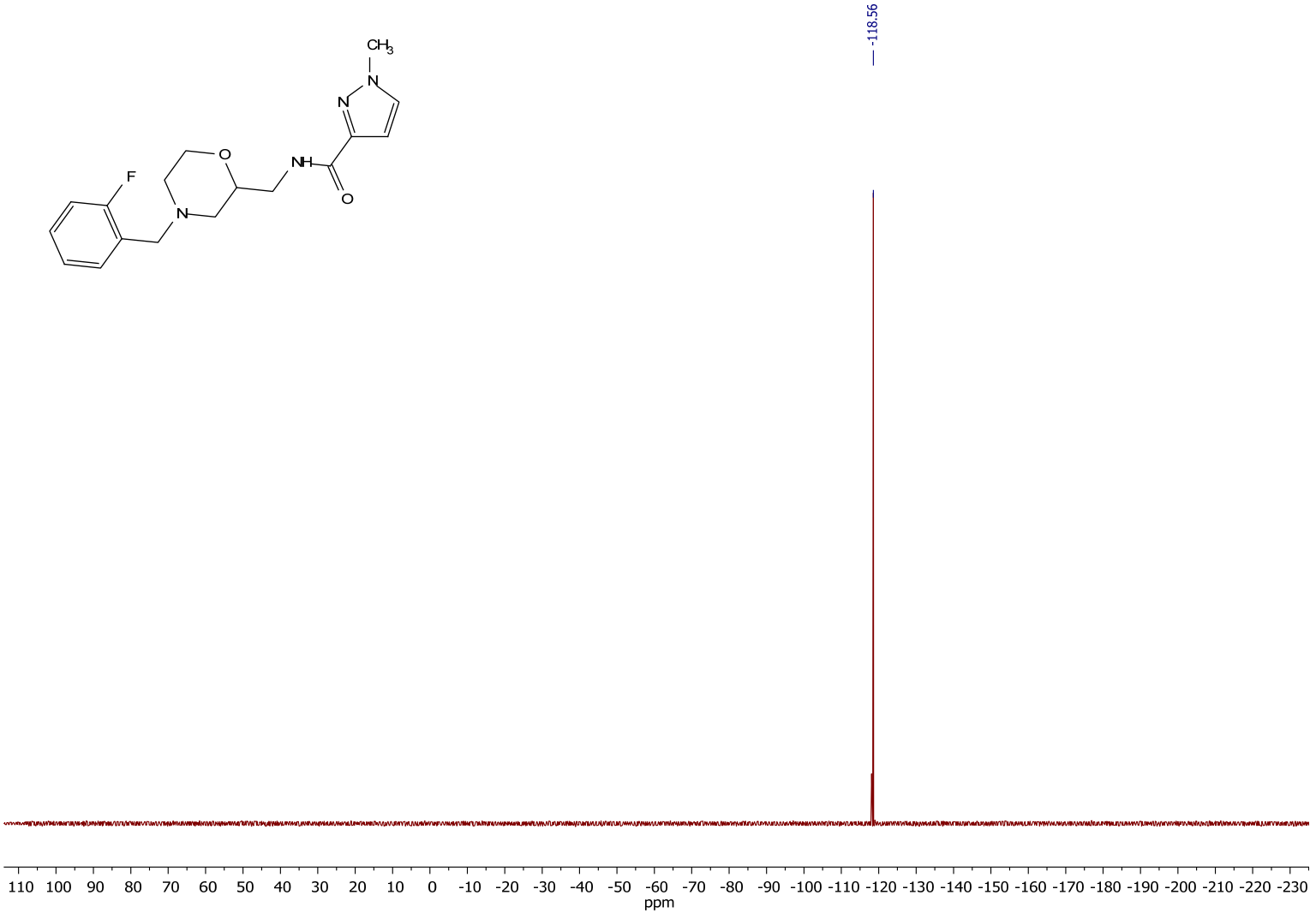

*N*-((4-(2,4-Dimethylbenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*12*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



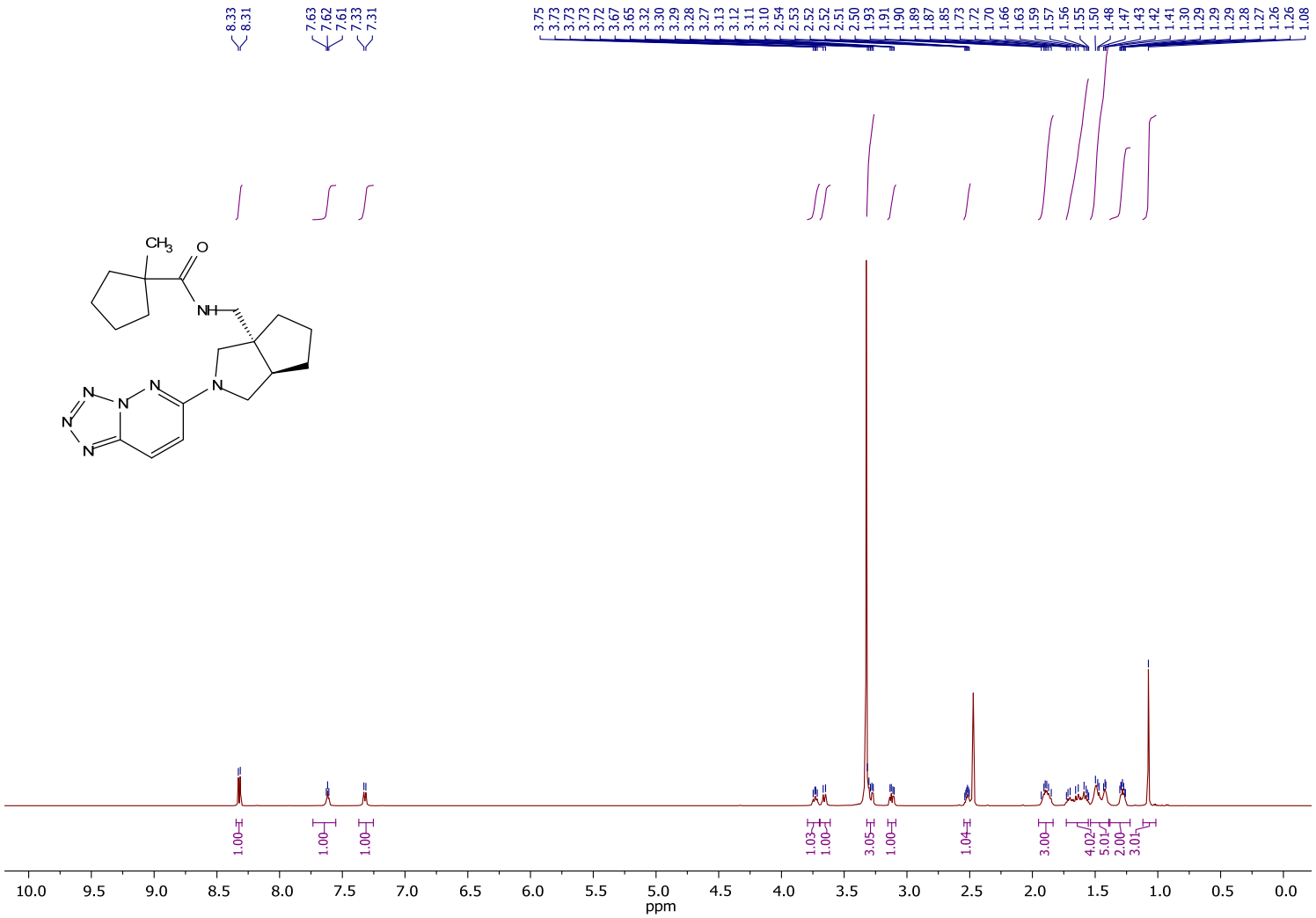

*N*-((4-(2-Fluorobenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*25*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



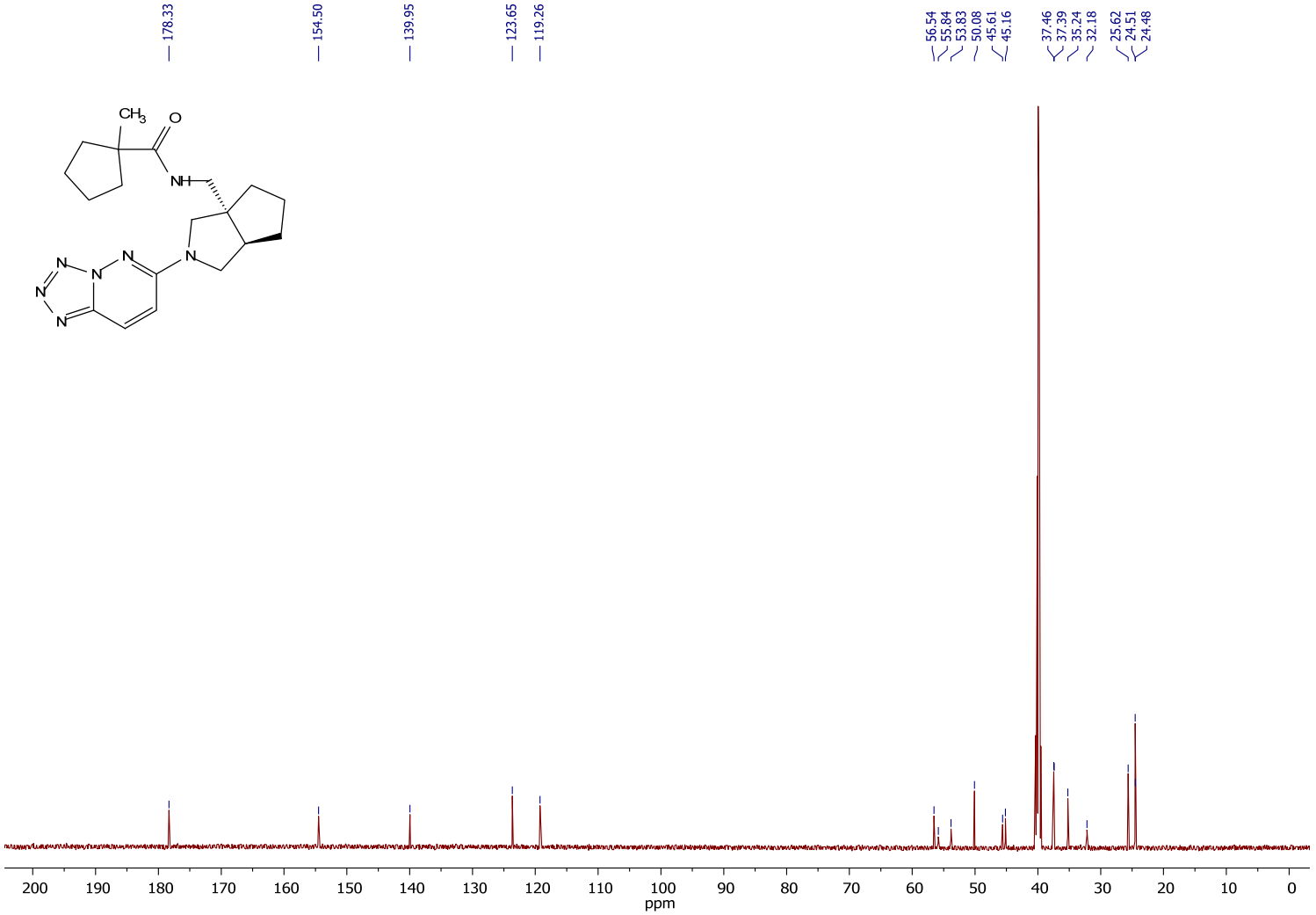

*N*-((4-(2-Fluorobenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*25*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



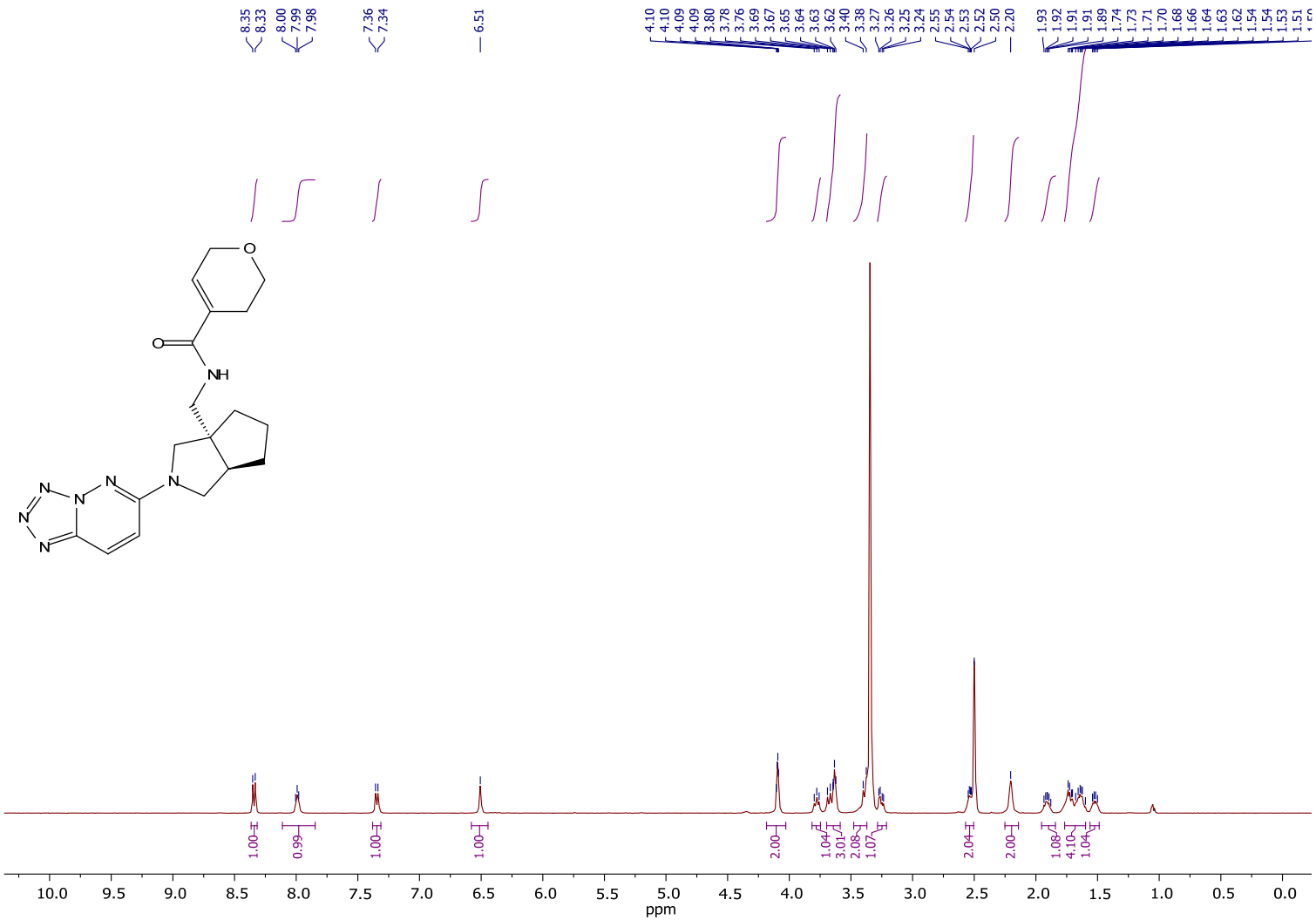

*N*-((4-(2-Fluorobenzyl)morpholin-2-yl)methyl)-1-methyl-1*H*-pyrazole-3-carboxamide (**13**{*74*,*107*,*25*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$)



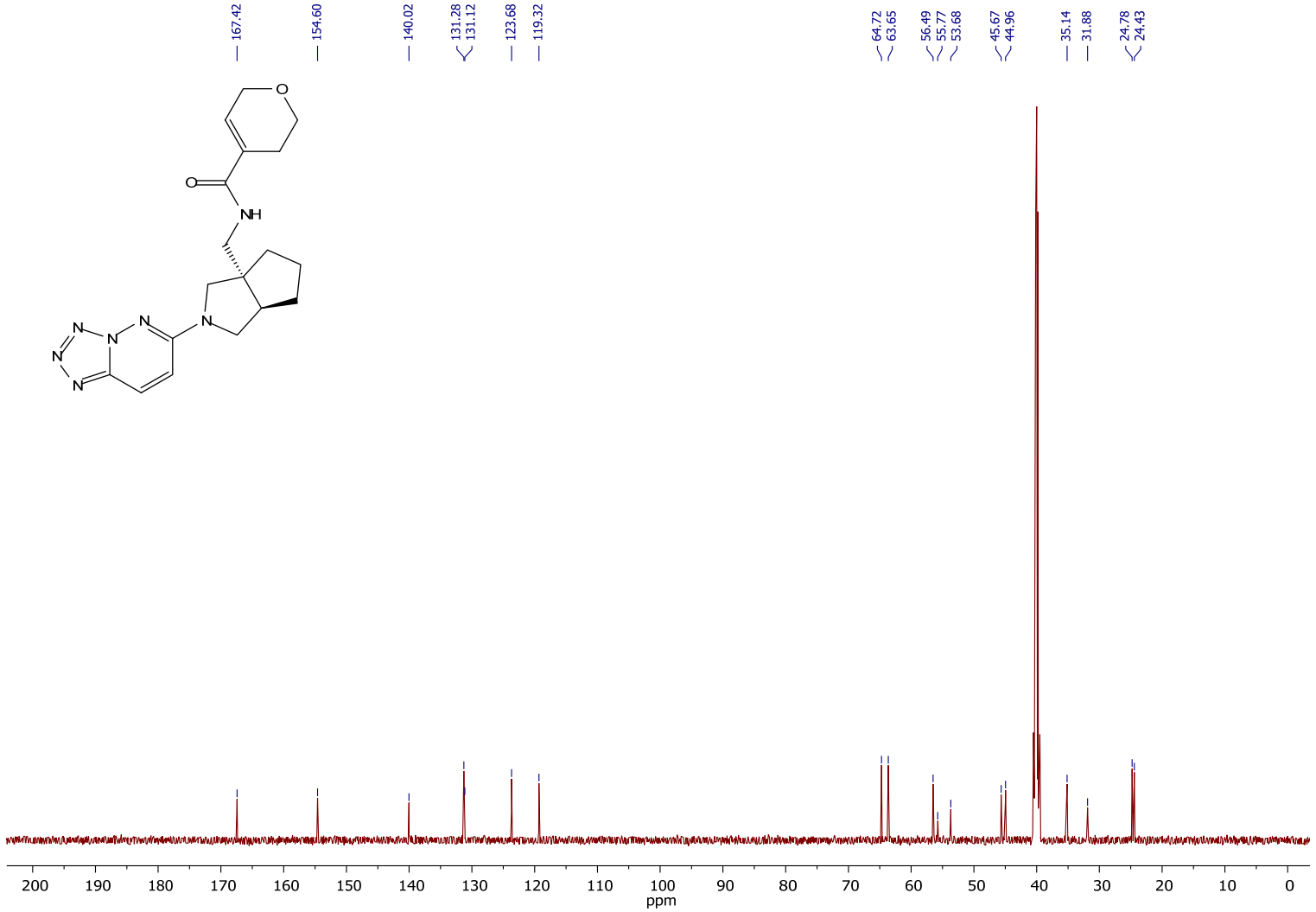

*rac*-1-Methyl-*N*-(((3*aR*,6*aS*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3*a*(1*H*)-yl)methyl)cyclopentane-1-carboxamide (**14**{*19*,*35*,*360*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



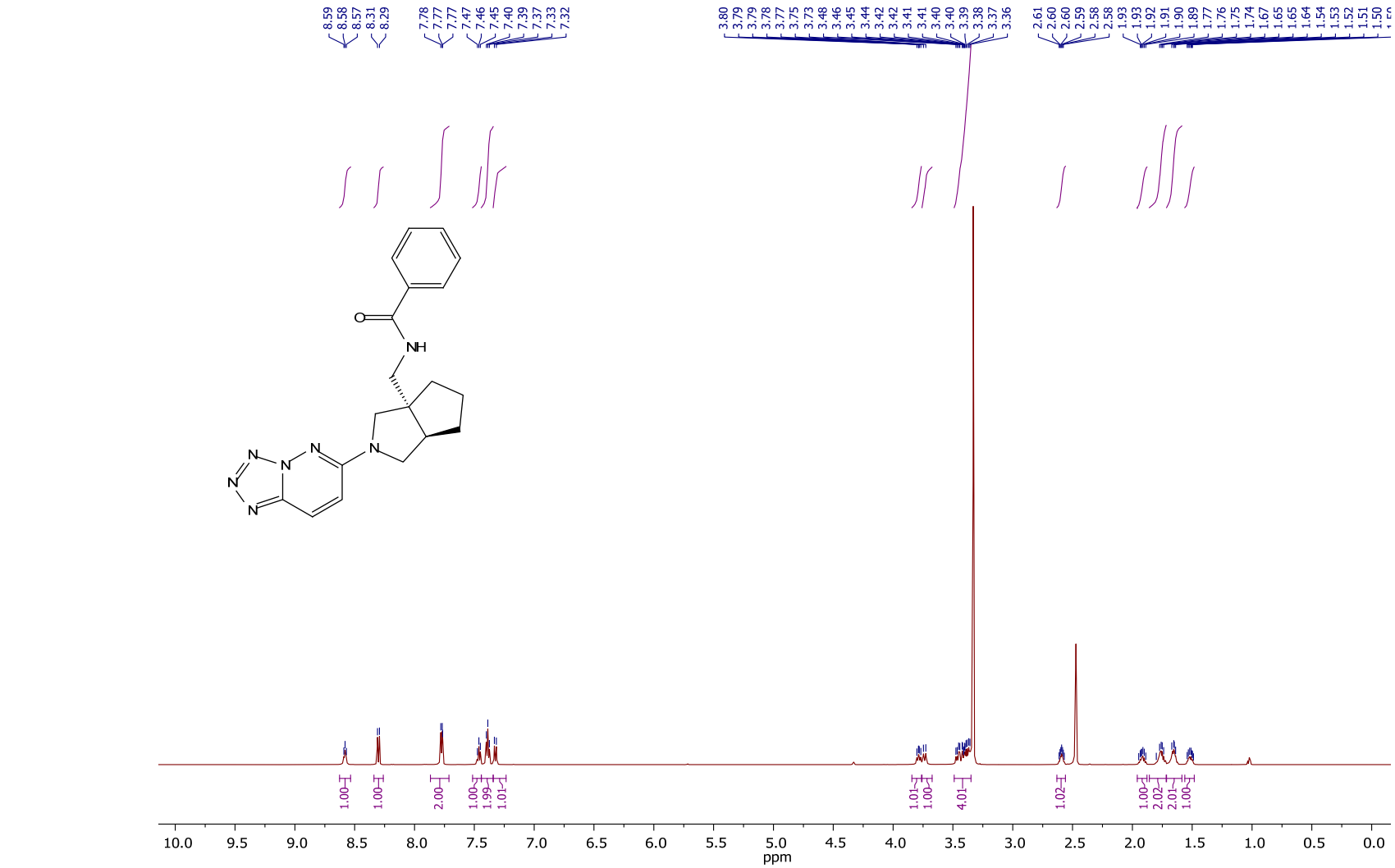

*rac*-1-Methyl-*N*-(((3*aR*,6*aS*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3*a*(1*H*)-yl)methyl)cyclopentane-1-carboxamide (**14**{*19*,*35*,*360*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



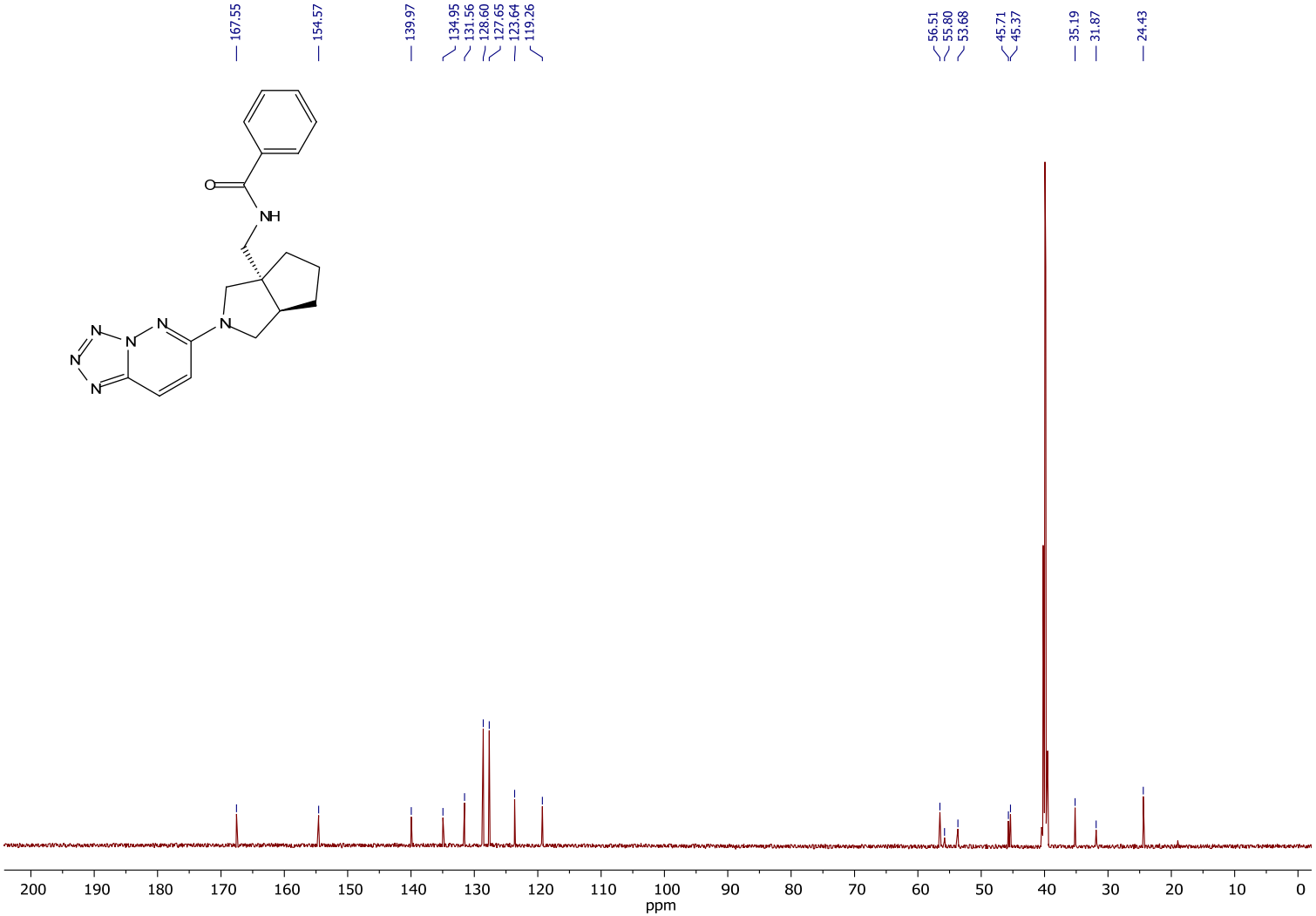

*rac*-*N*-(((3a*R*,6a*S*)-2-(Tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)-3,6-dihydro-2*H*-pyran-4-carboxamide (**14**{*19*,*35*,*361*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



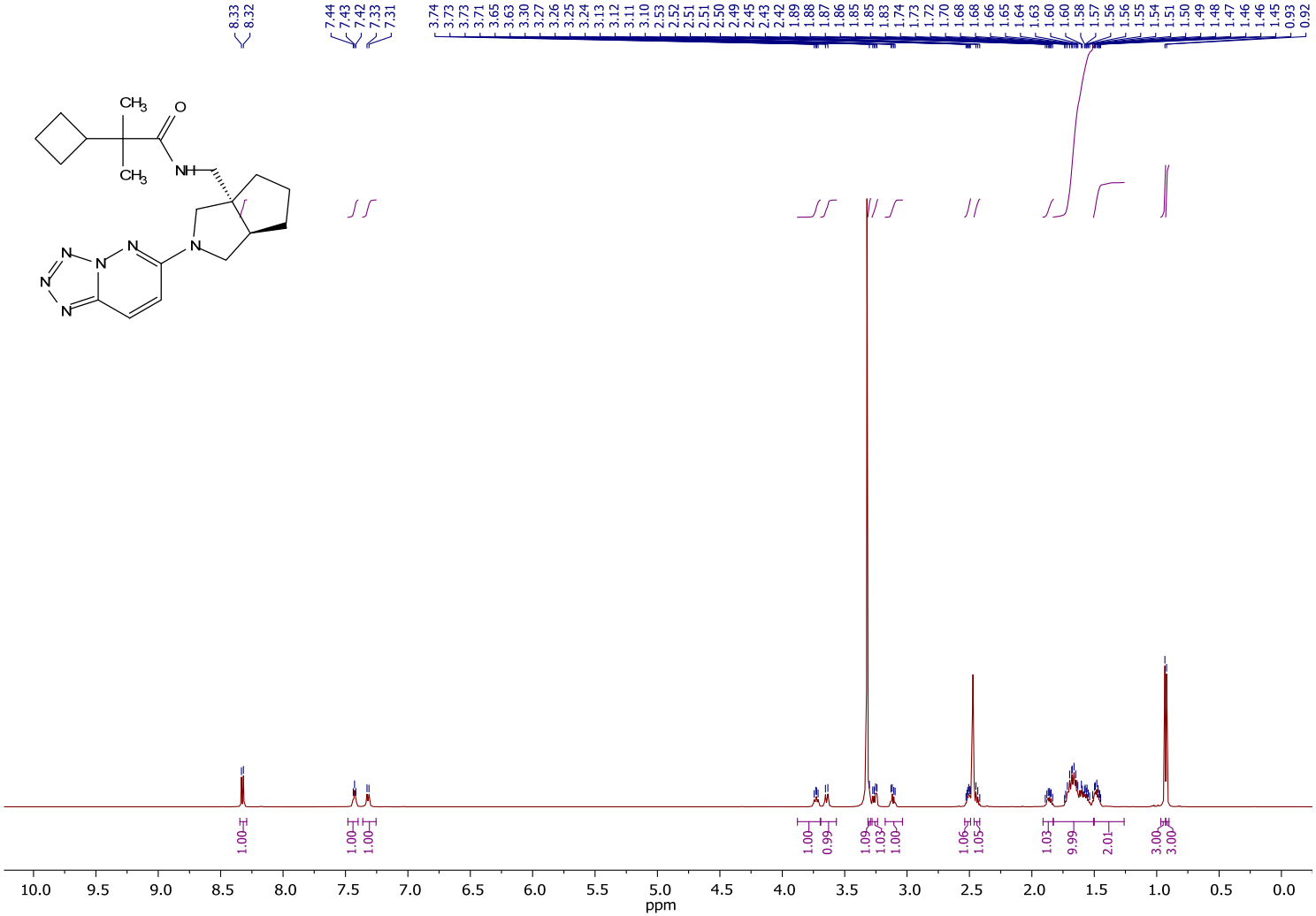

*rac*-*N*-(((3a*R*,6a*S*)-2-(Tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)-3,6-dihydro-2*H*-pyran-4-carboxamide (**14**{*19*,*35*,*361*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



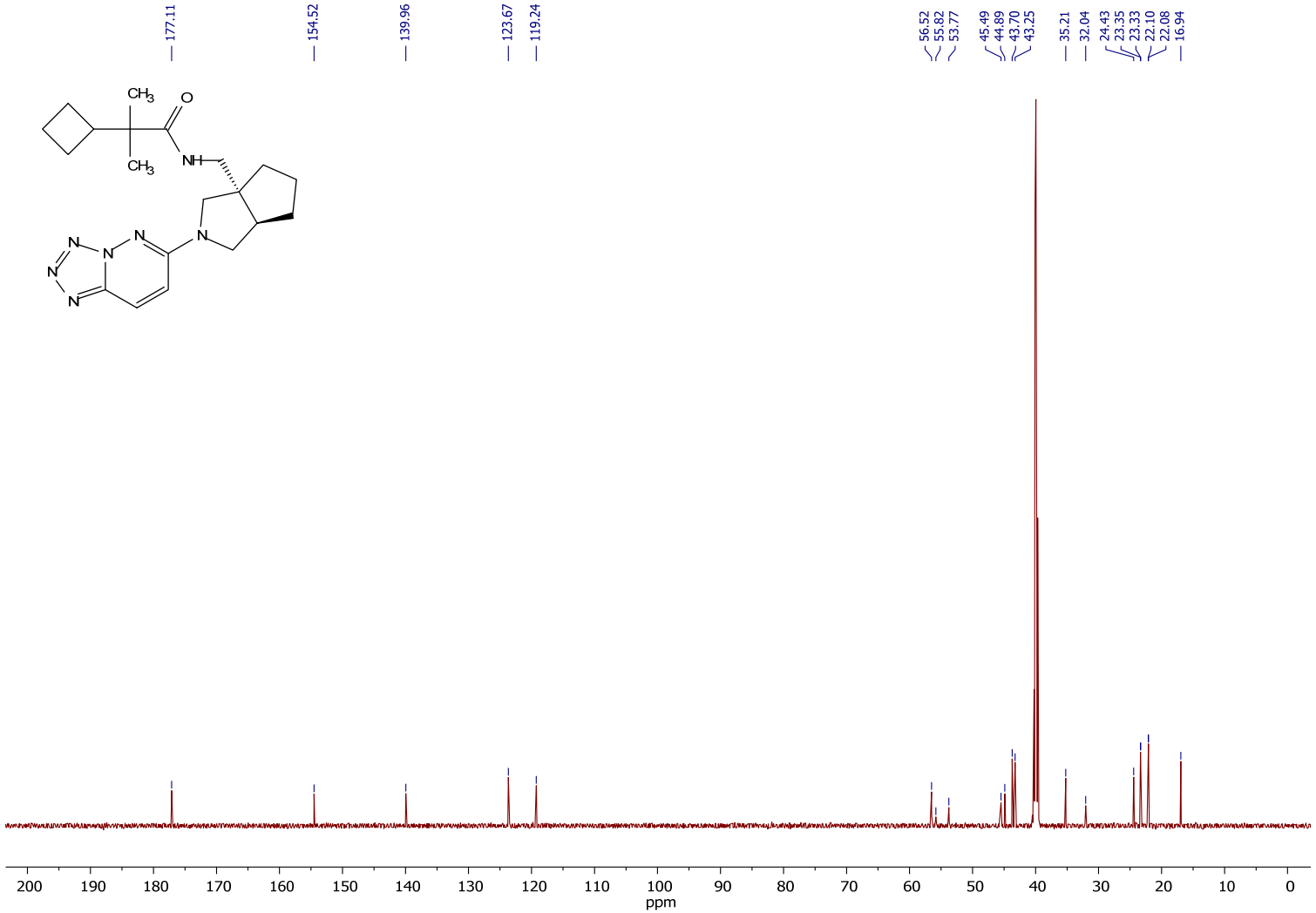

*rac*-*N*-(((3a*R*,6a*S*)-2-(Tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)benzamide (**14**{*19*,*35*,*367*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



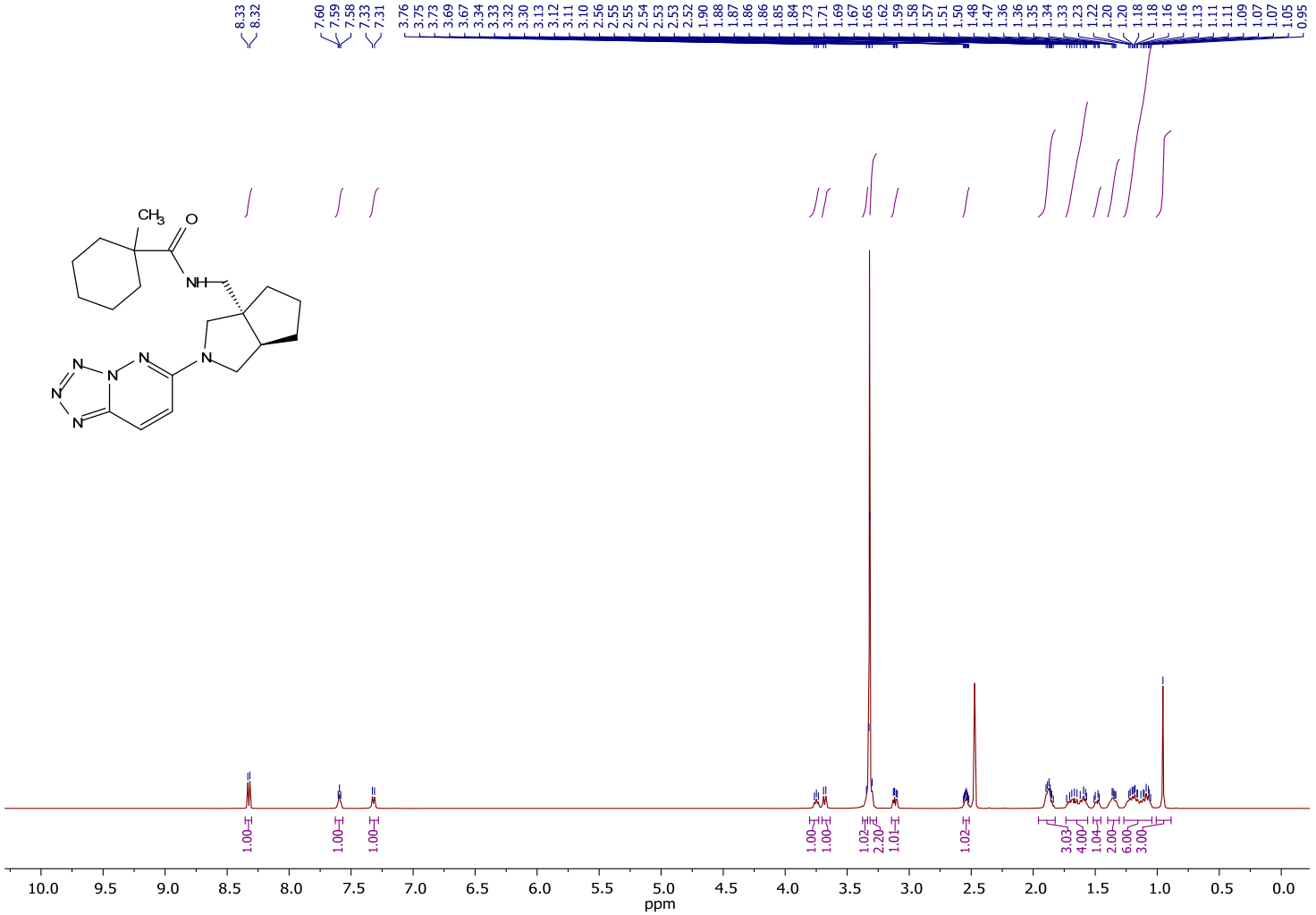

*rac*-*N*-(((3a*R*,6a*S*)-2-(Tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)benzamide (**14**{*19*,*35*,*367*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



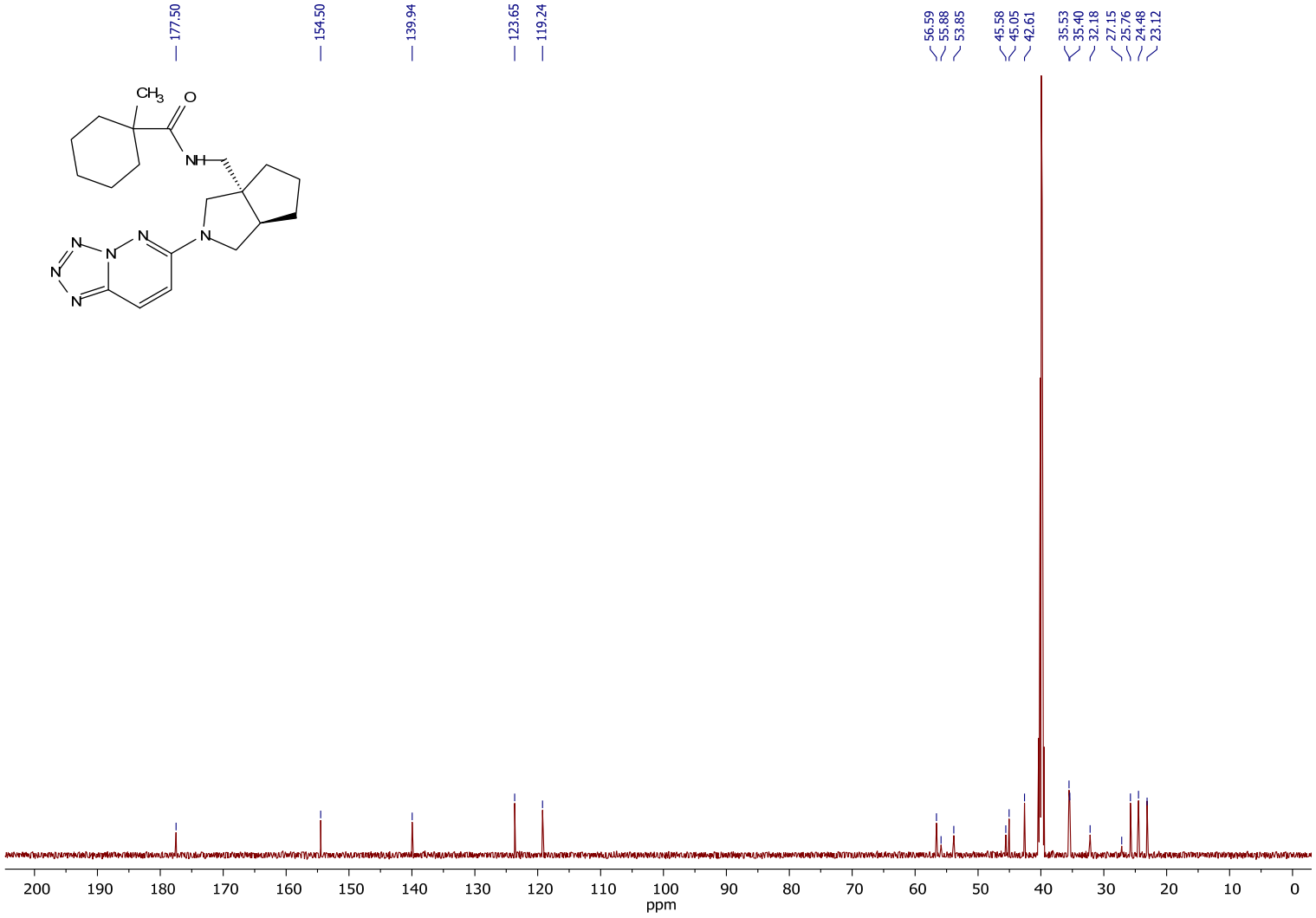

*rac*-2-Cyclobutyl-2-methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)propanamide (**14**{*19*,*35*,*369*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



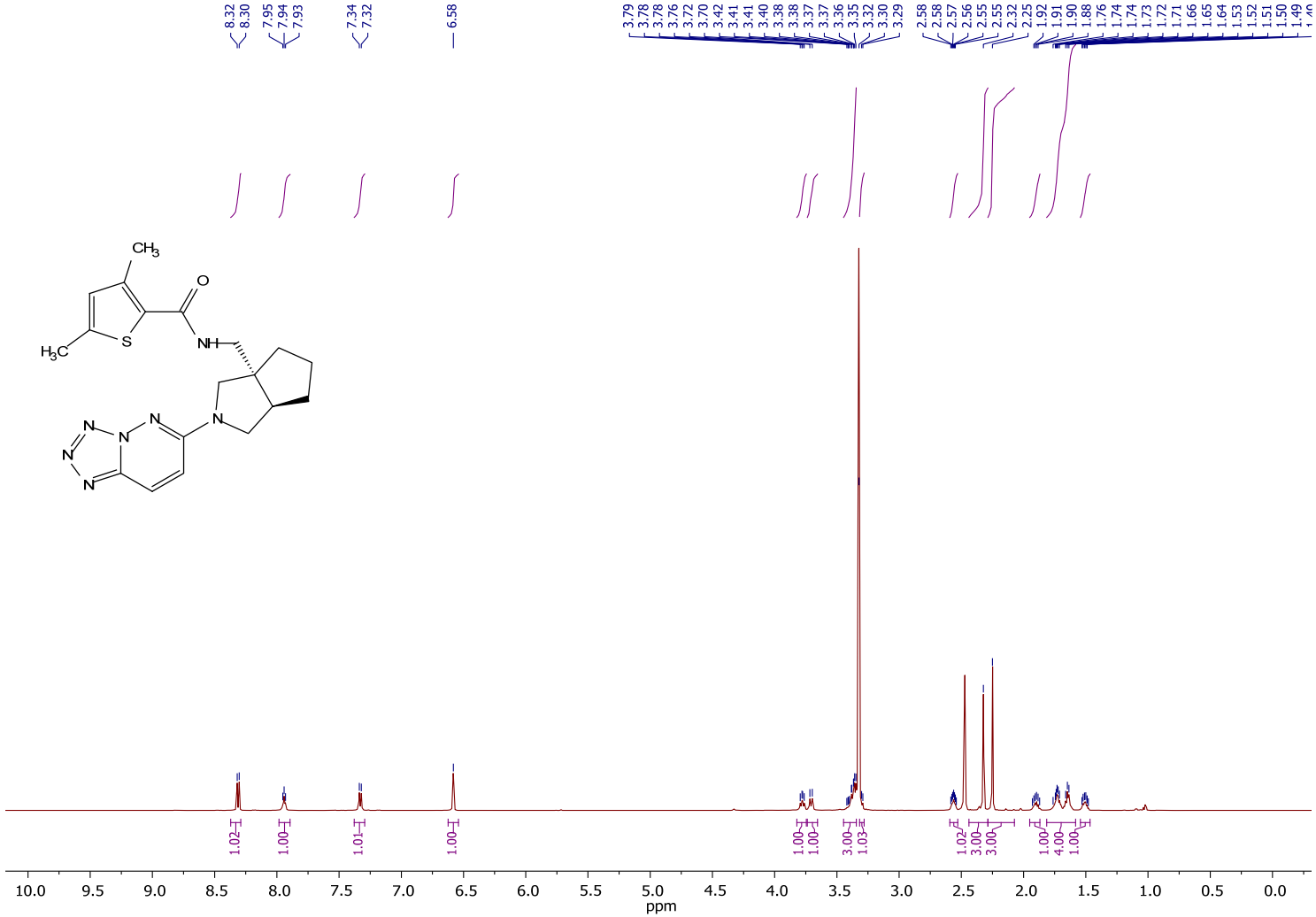

*rac*-2-Cyclobutyl-2-methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)propanamide (**14**{*19*,*35*,*369*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



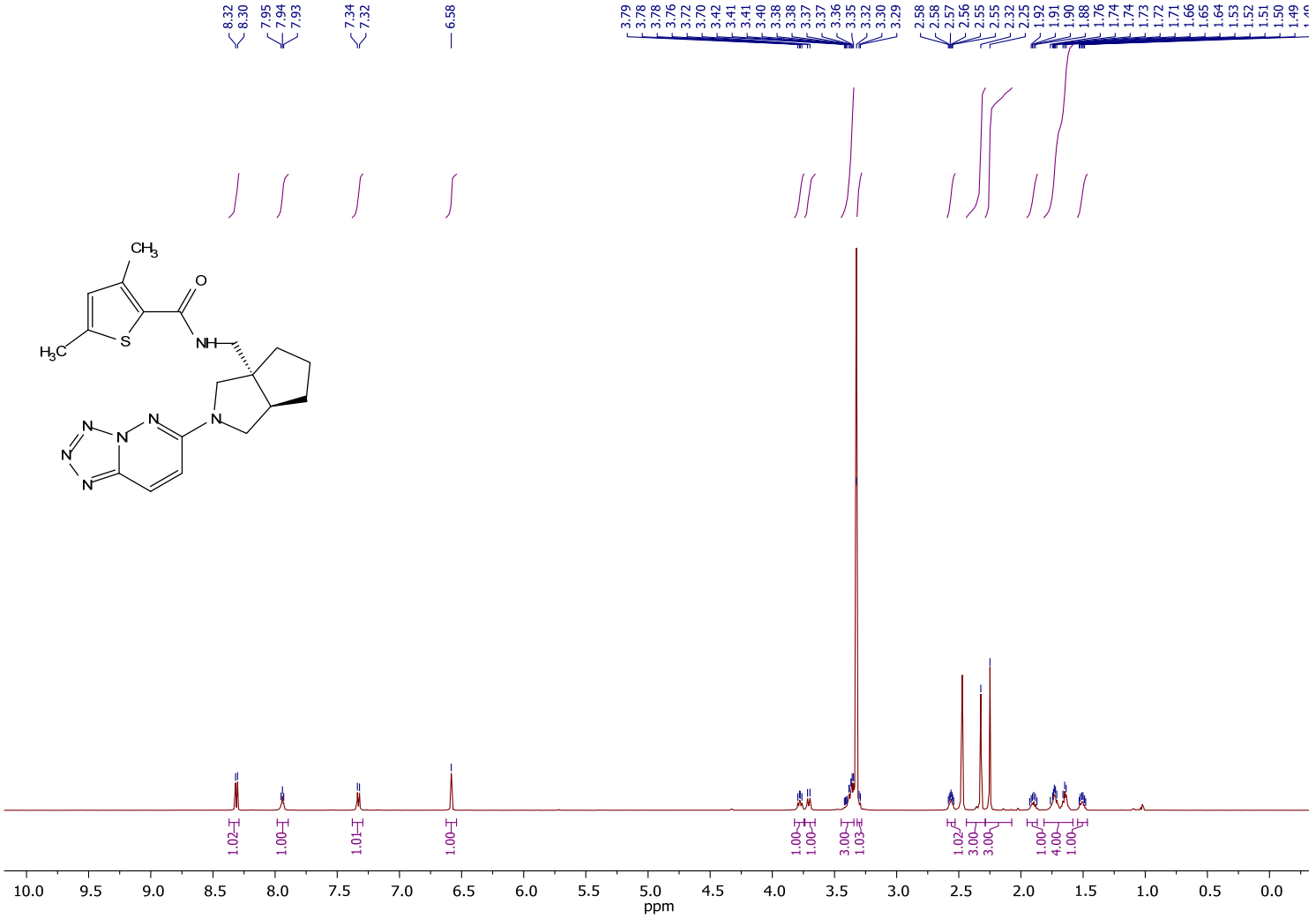

*rac*-1-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)cyclohexane-1-carboxamide (**14**{*19*,*35*,*373*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



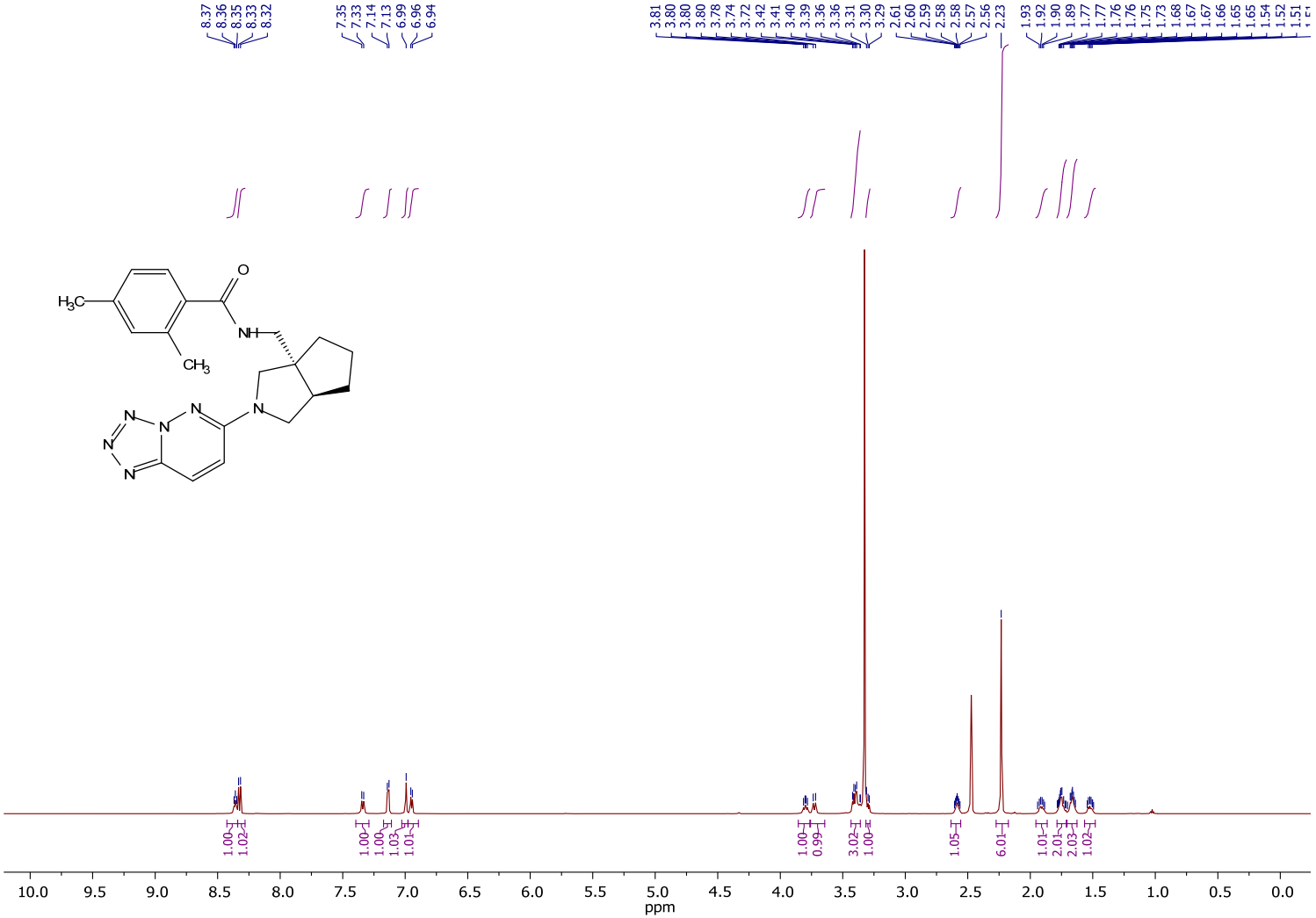

*rac*-1-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)hexahydrocyclopenta[*c*]pyrrol-3a(1*H*)-yl)methyl)cyclohexane-1-carboxamide (**14**{*19*,*35*,*373*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



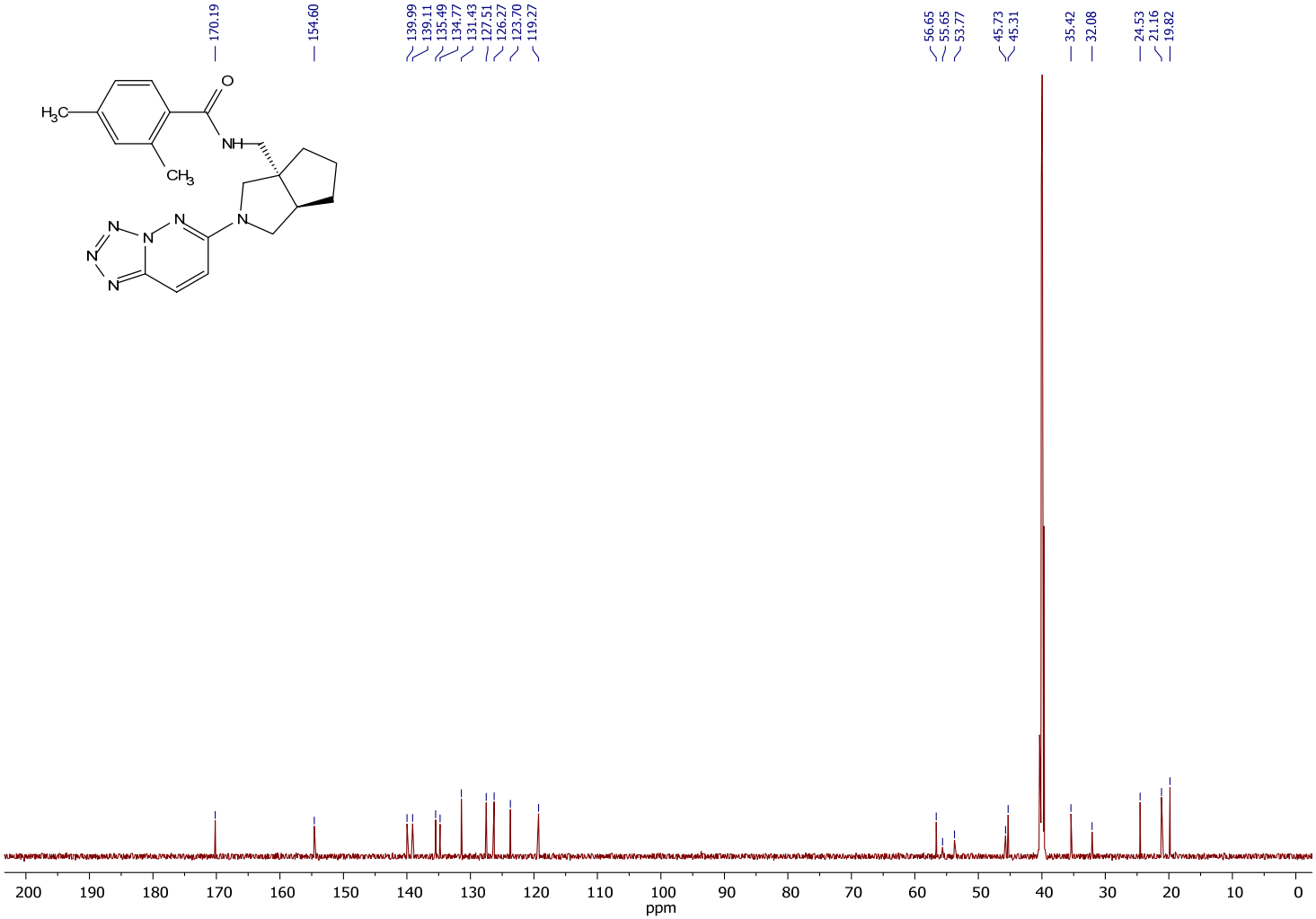

*rac*-3,5-Dimethyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)thiophene-2-carboxamide (**14**{*19*,*35*,*375*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



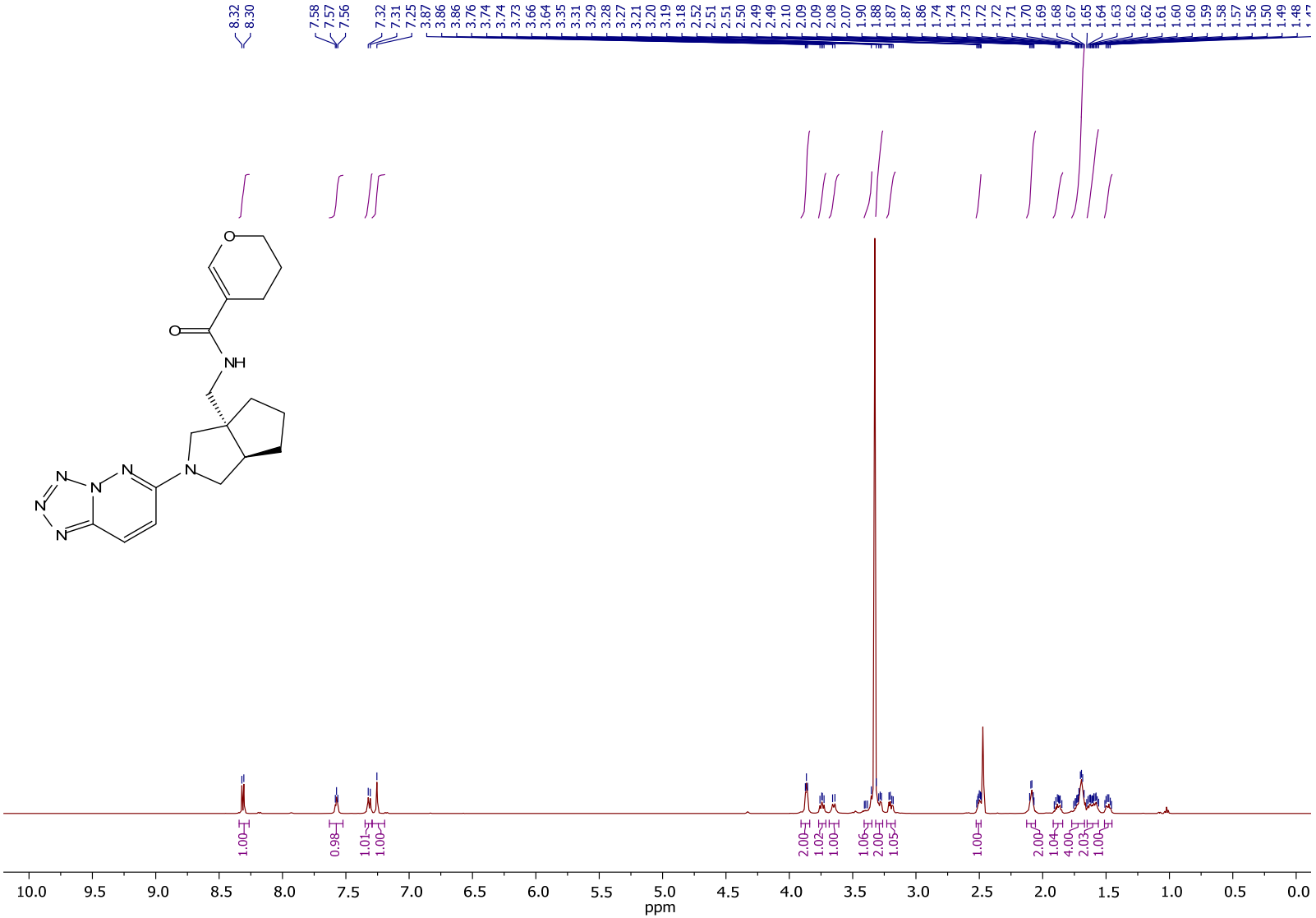

*rac*-3,5-Dimethyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)thiophene-2-carboxamide (**14**{*19*,*35*,*375*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



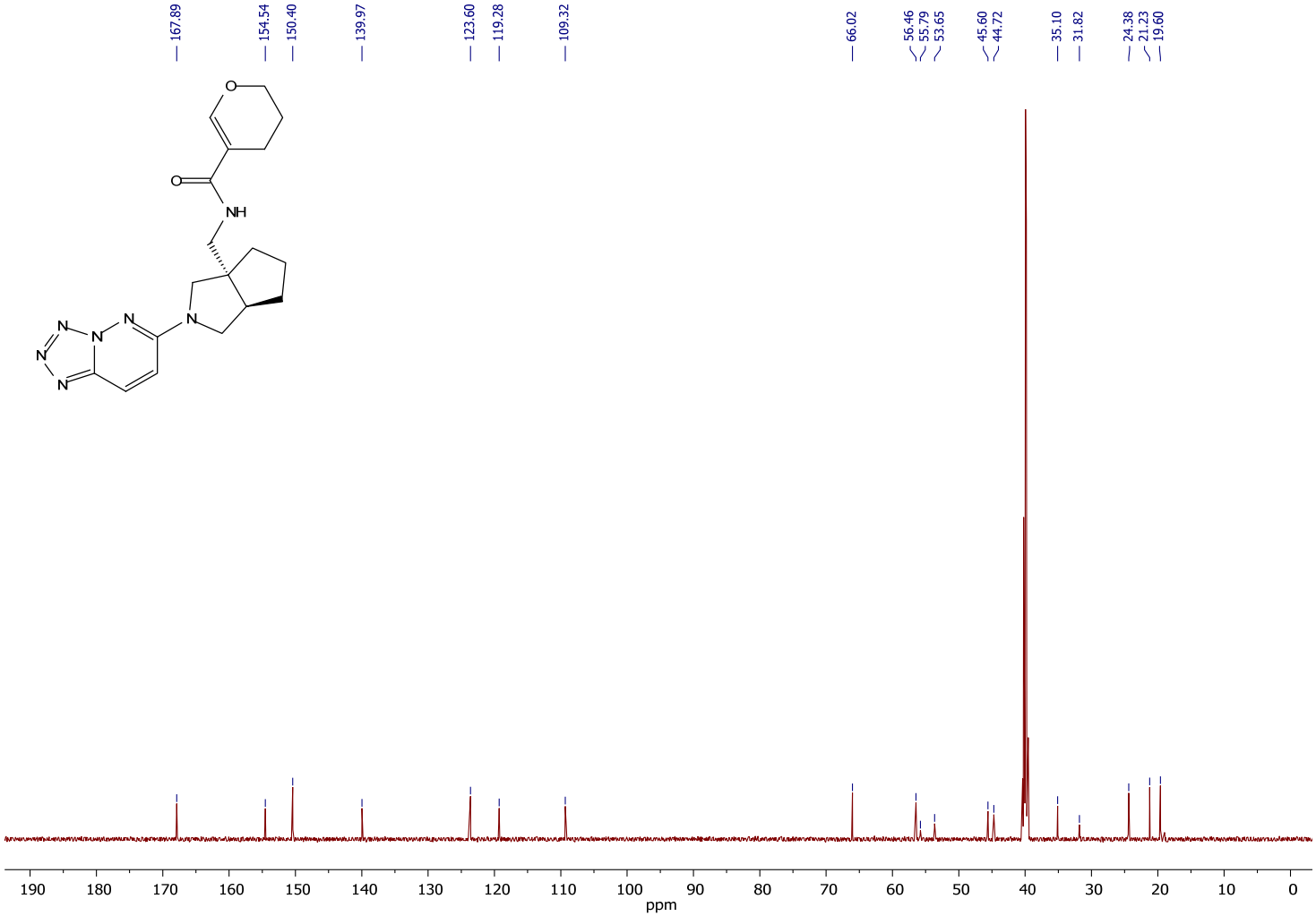

*rac*-2,4-Dimethyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*377*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



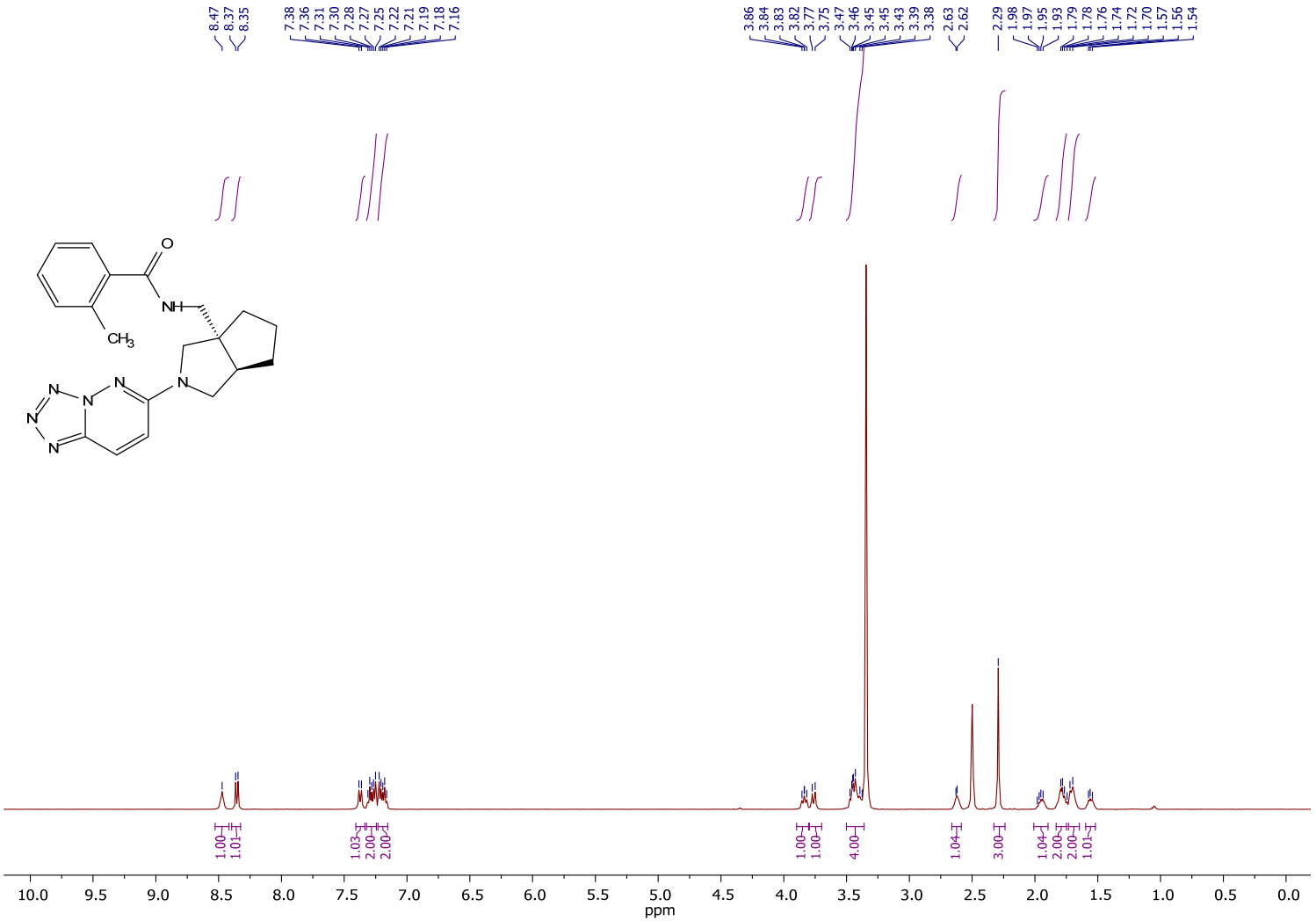

*rac*-2,4-Dimethyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*377*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



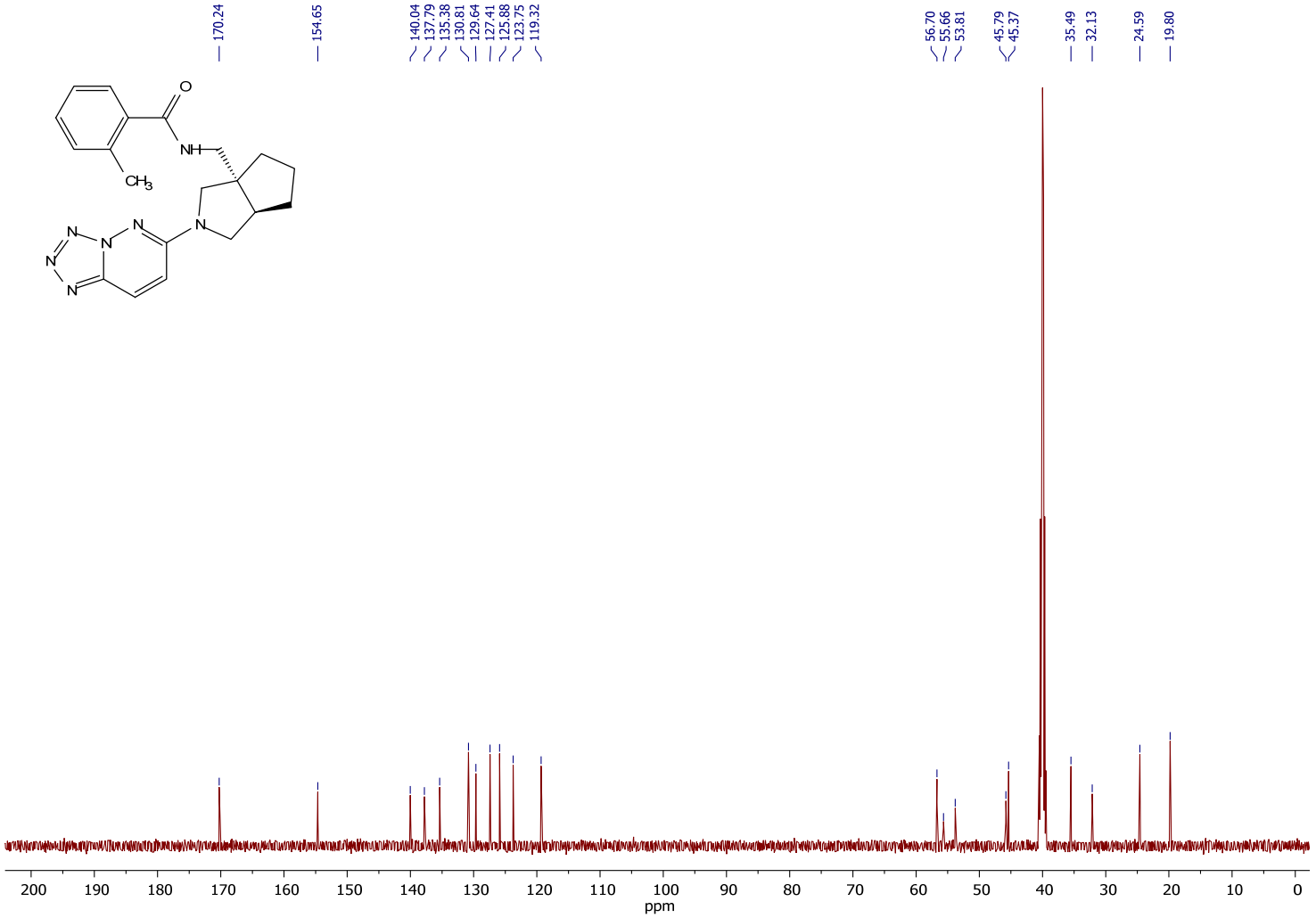

*N*-(((3a*S*,6a*R*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)-3,4-dihydro-2*H*-pyran-5-carboxamide (**14**{*19*,*35*,*378*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



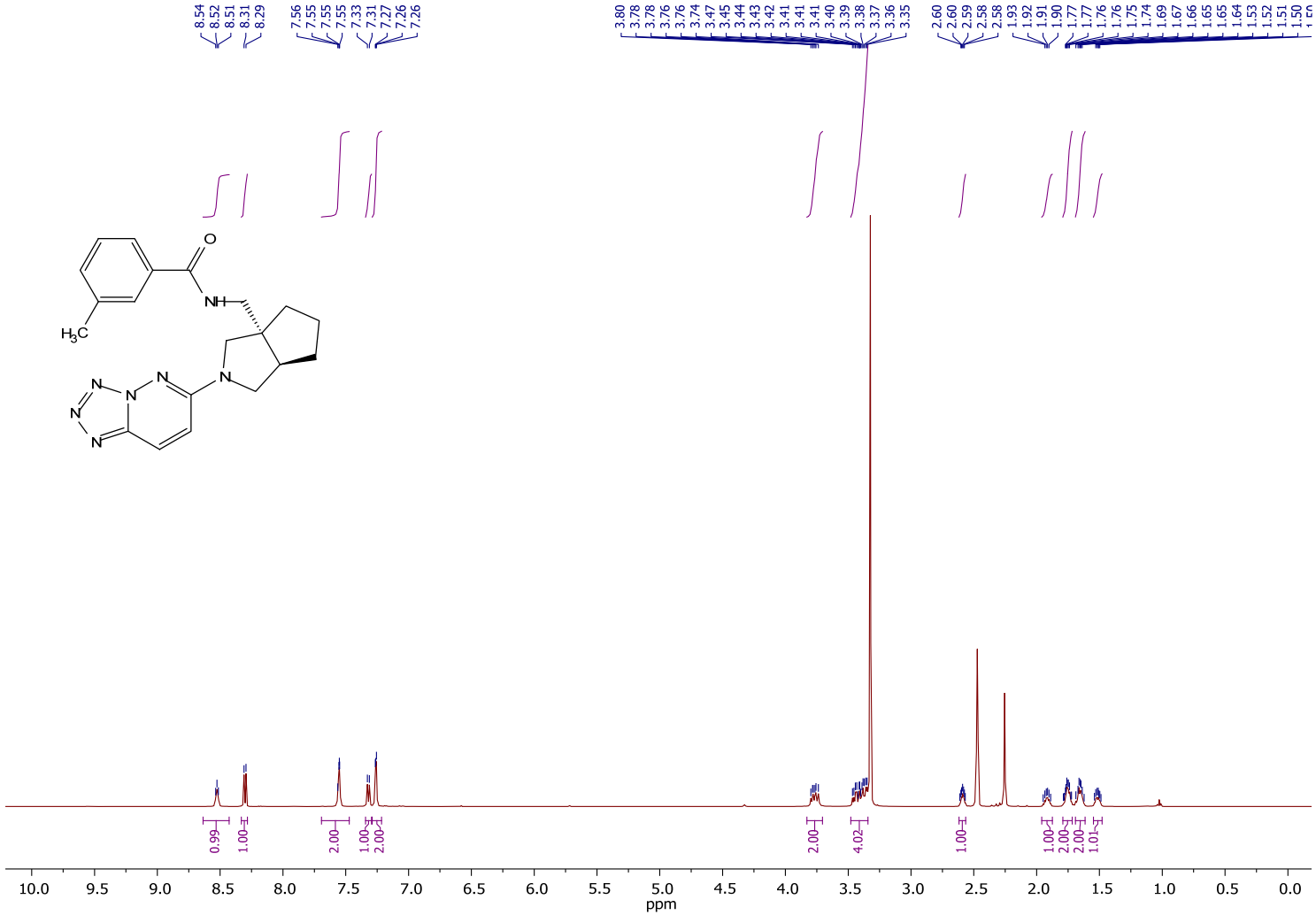

*N*-(((3a*S*,6a*R*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)-3,4-dihydro-2*H*-pyran-5-carboxamide (**14**{*19*,*35*,*378*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



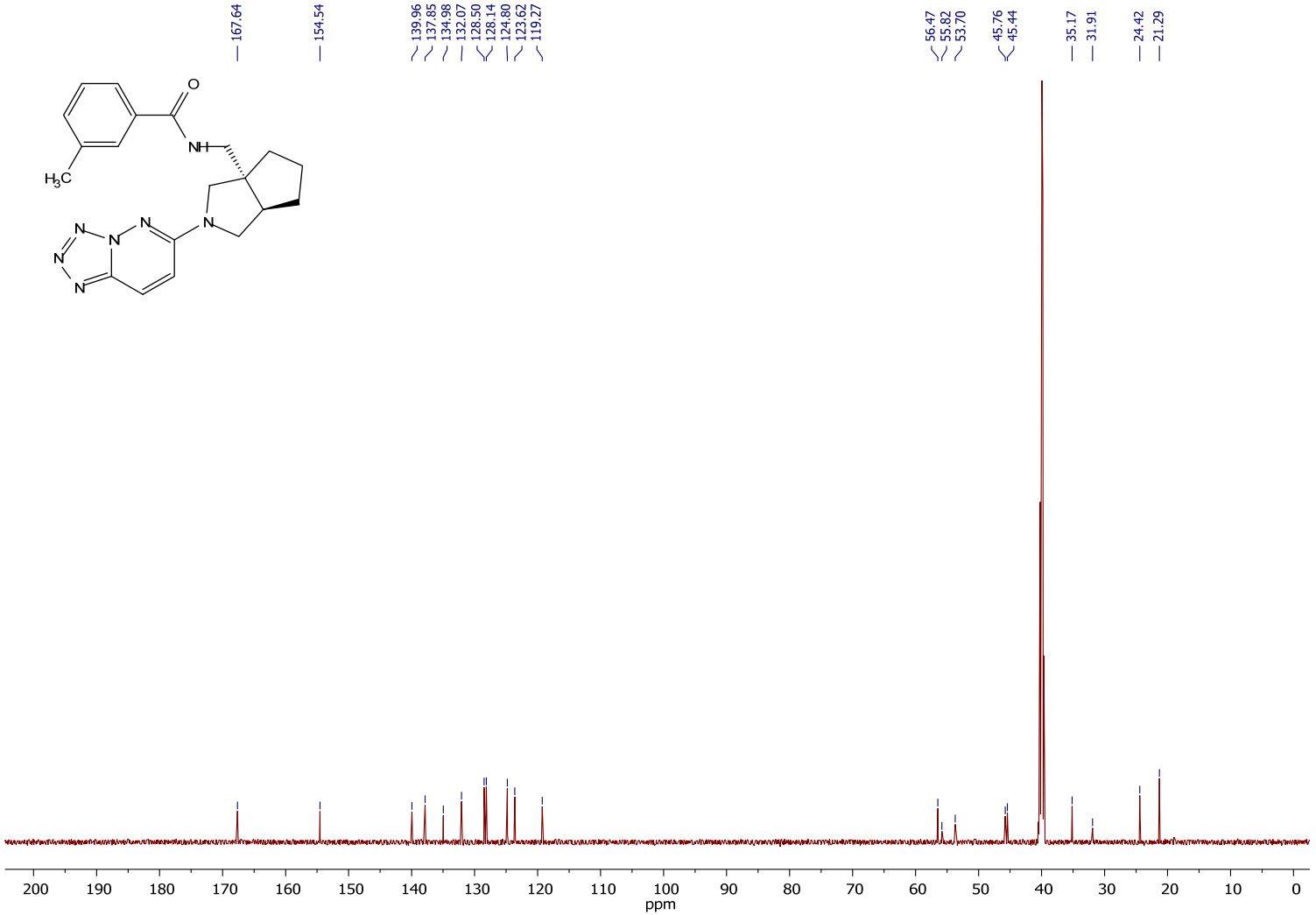

*rac*-2-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*384*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



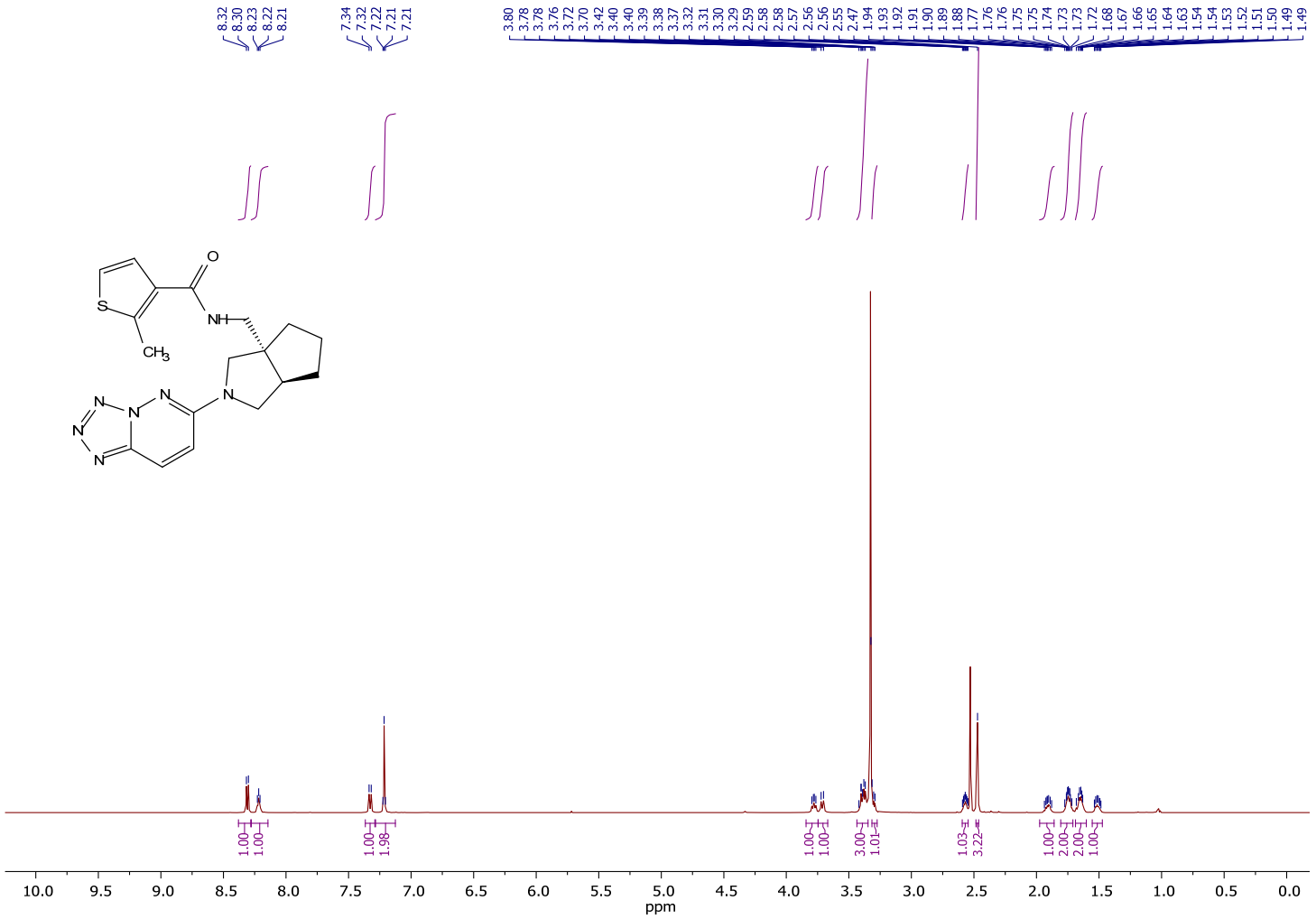

*rac*-2-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*384*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$



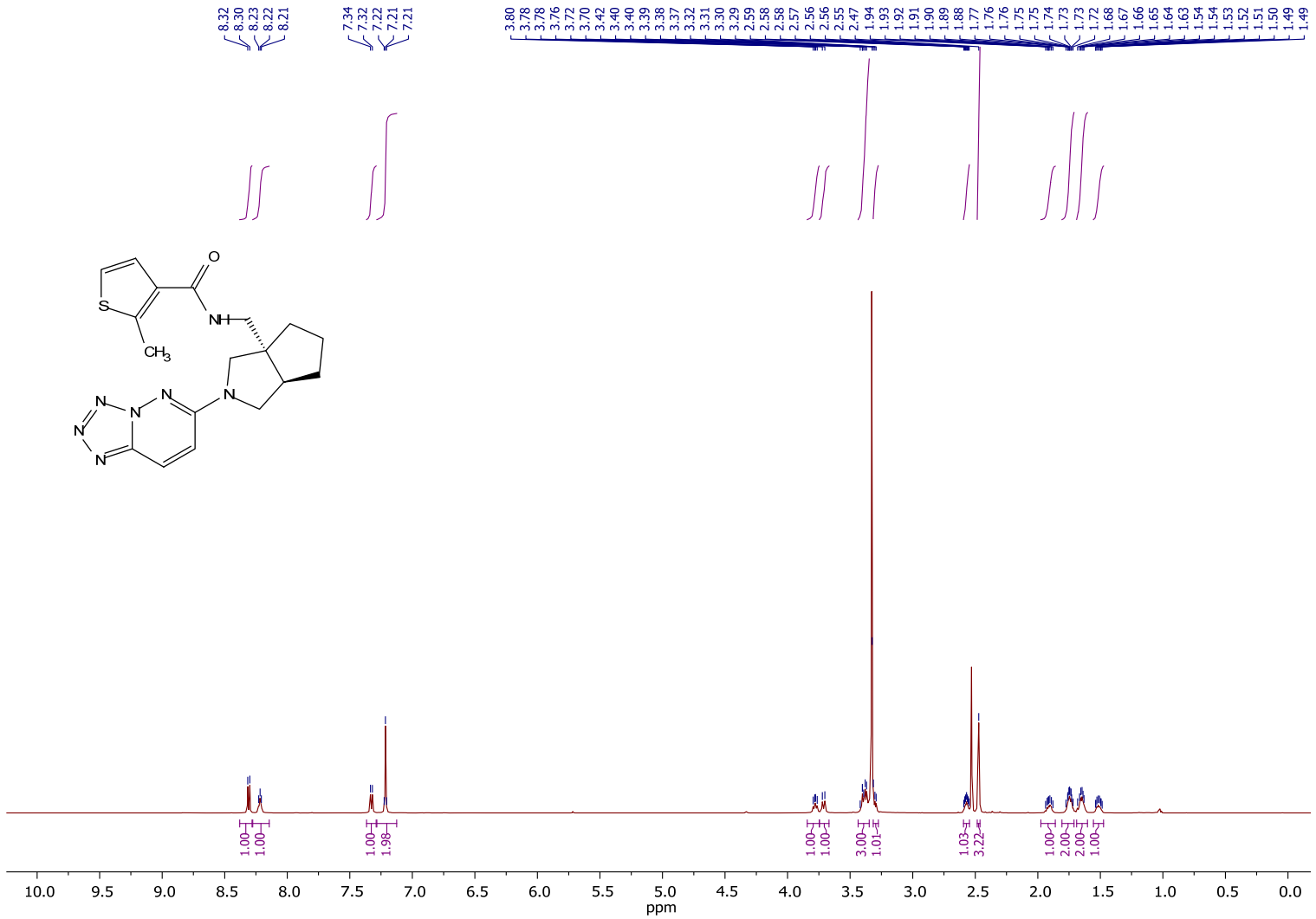

*rac*-3-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*171*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



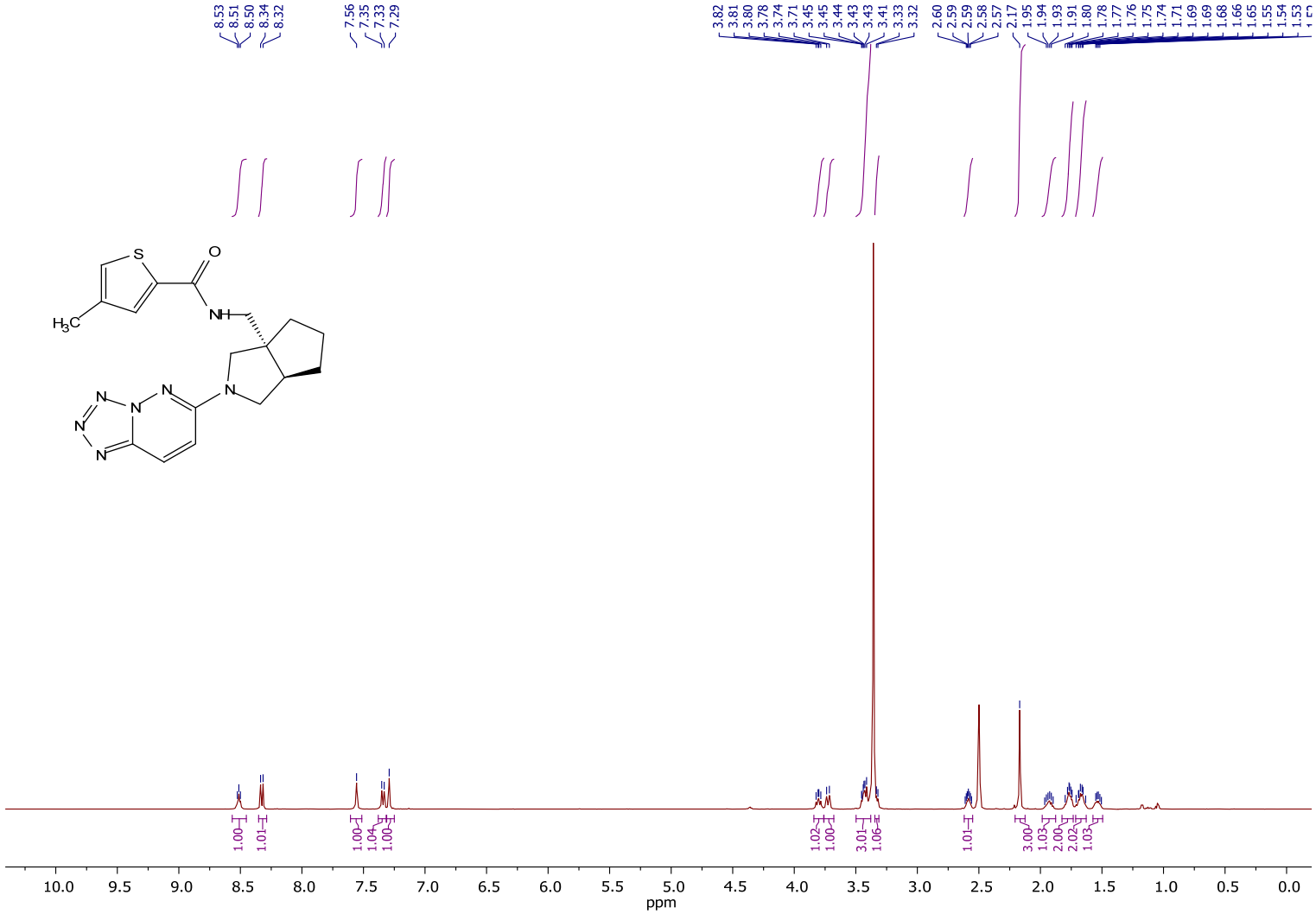

*rac*-3-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*171*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



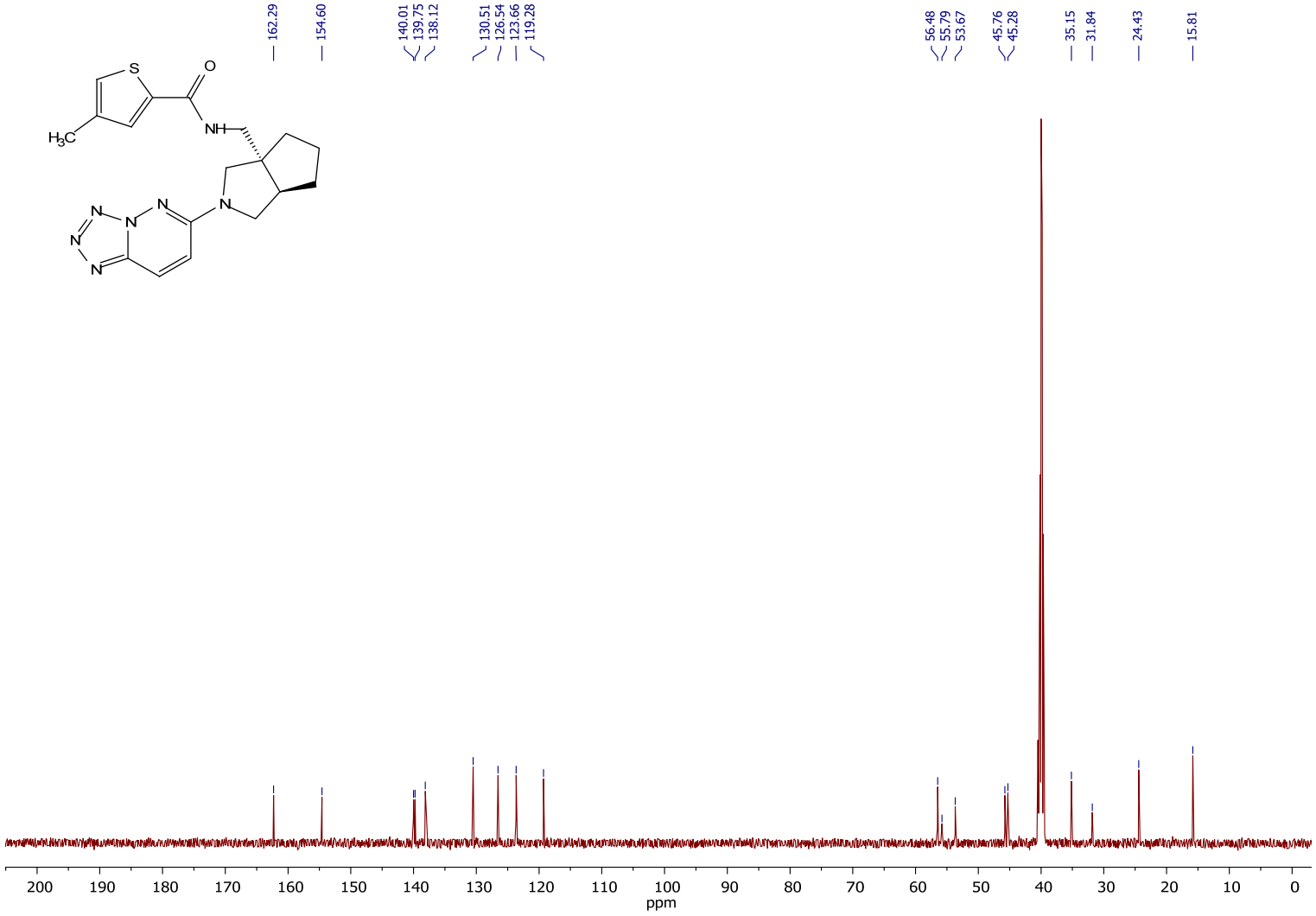

*rac*-2-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)thiophene-3-carboxamide **14**{*19*,*35*,*390*}, $^{1}$H NMR (600 MHz, DMSO-$d_6$)



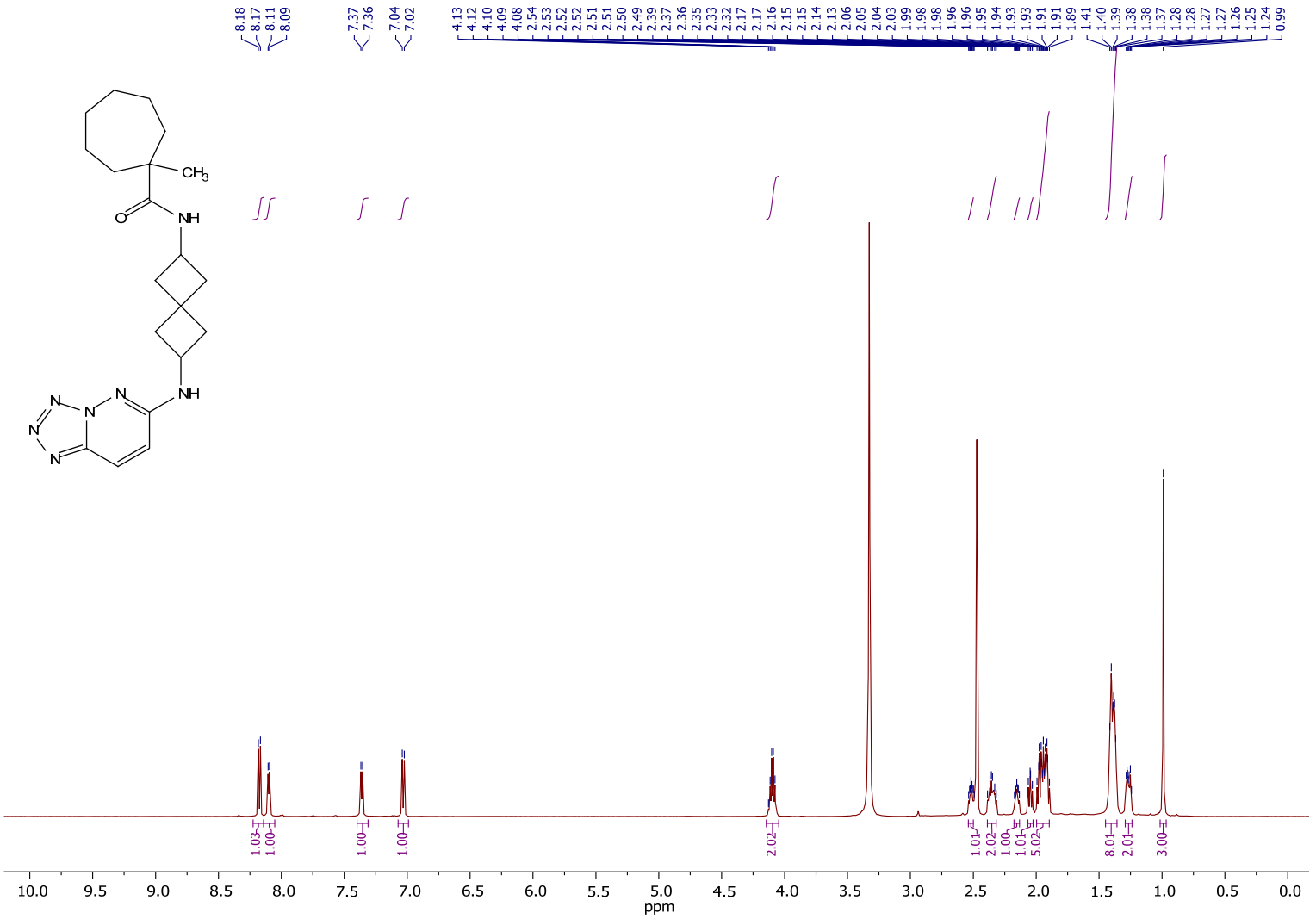

*rac*-2-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)thiophene-3-carboxamide **14**{*19,35,390*}, $^{13}$C NMR (151 MHz, DMSO-$d_6$)



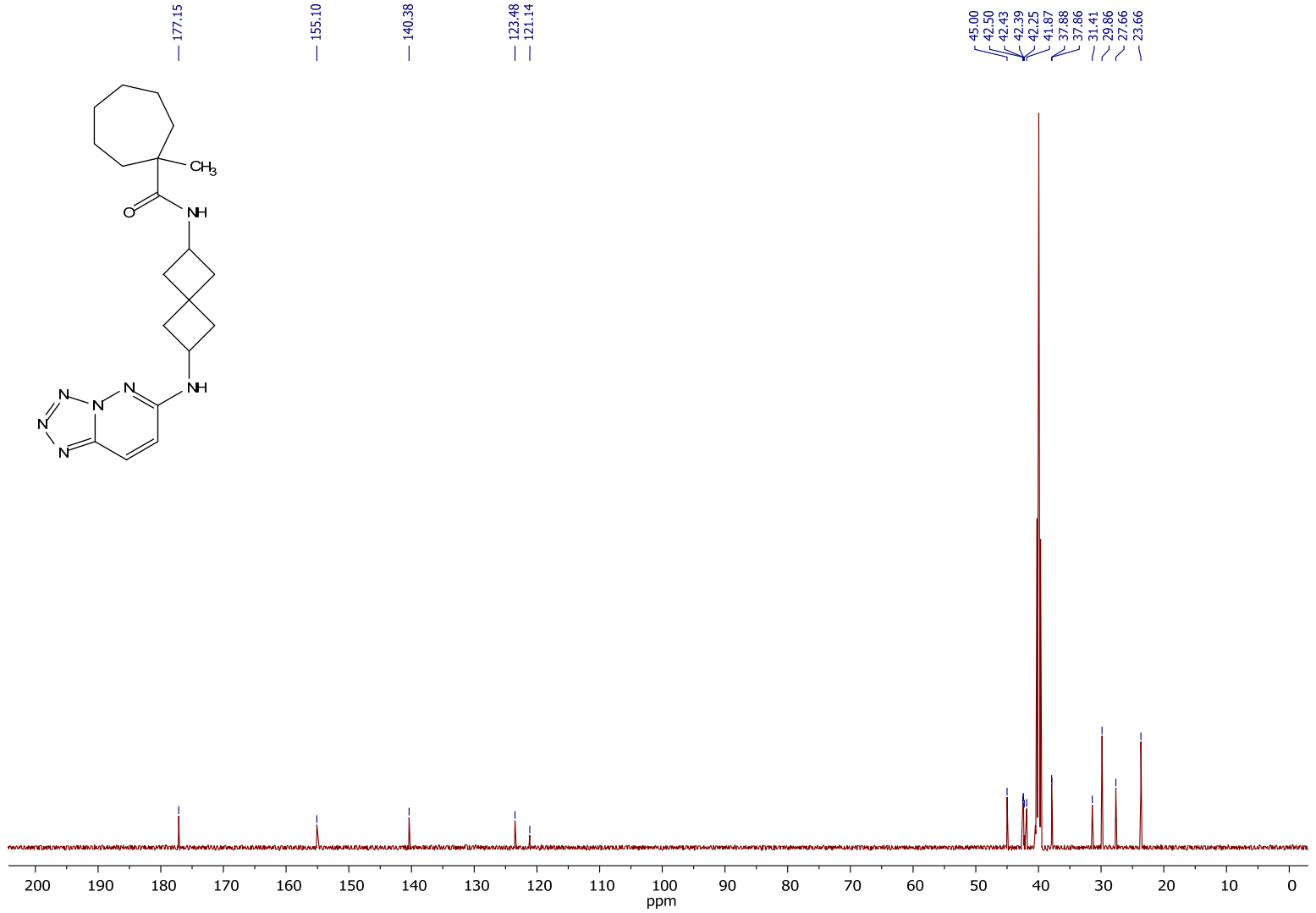

*rac*-4-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)thiophene-2-carboxamide (**14**{*19*,*35*,*394*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



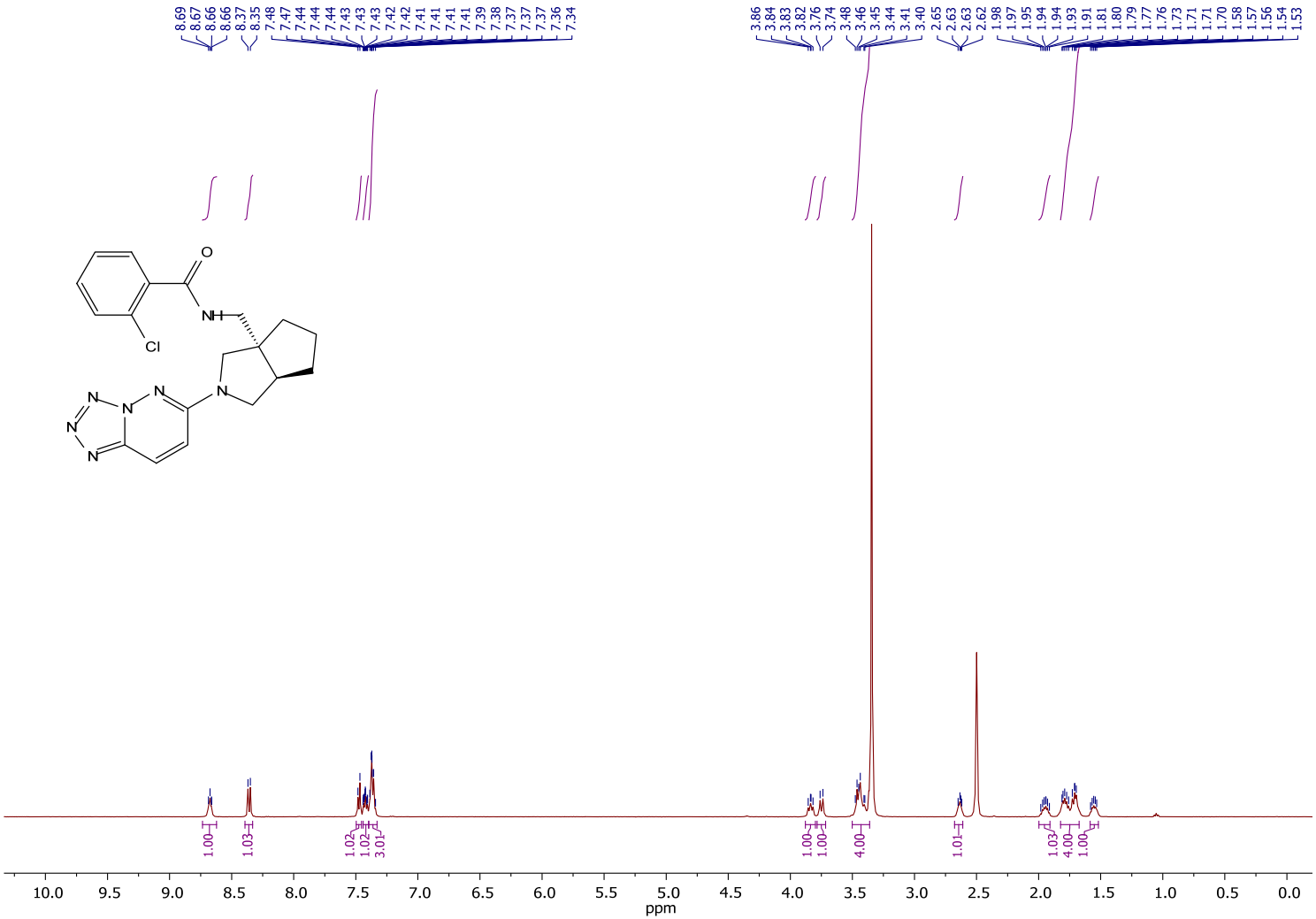

*rac*-4-Methyl-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)thiophene-2-carboxamide (**14**{*19*,*35*,*394*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



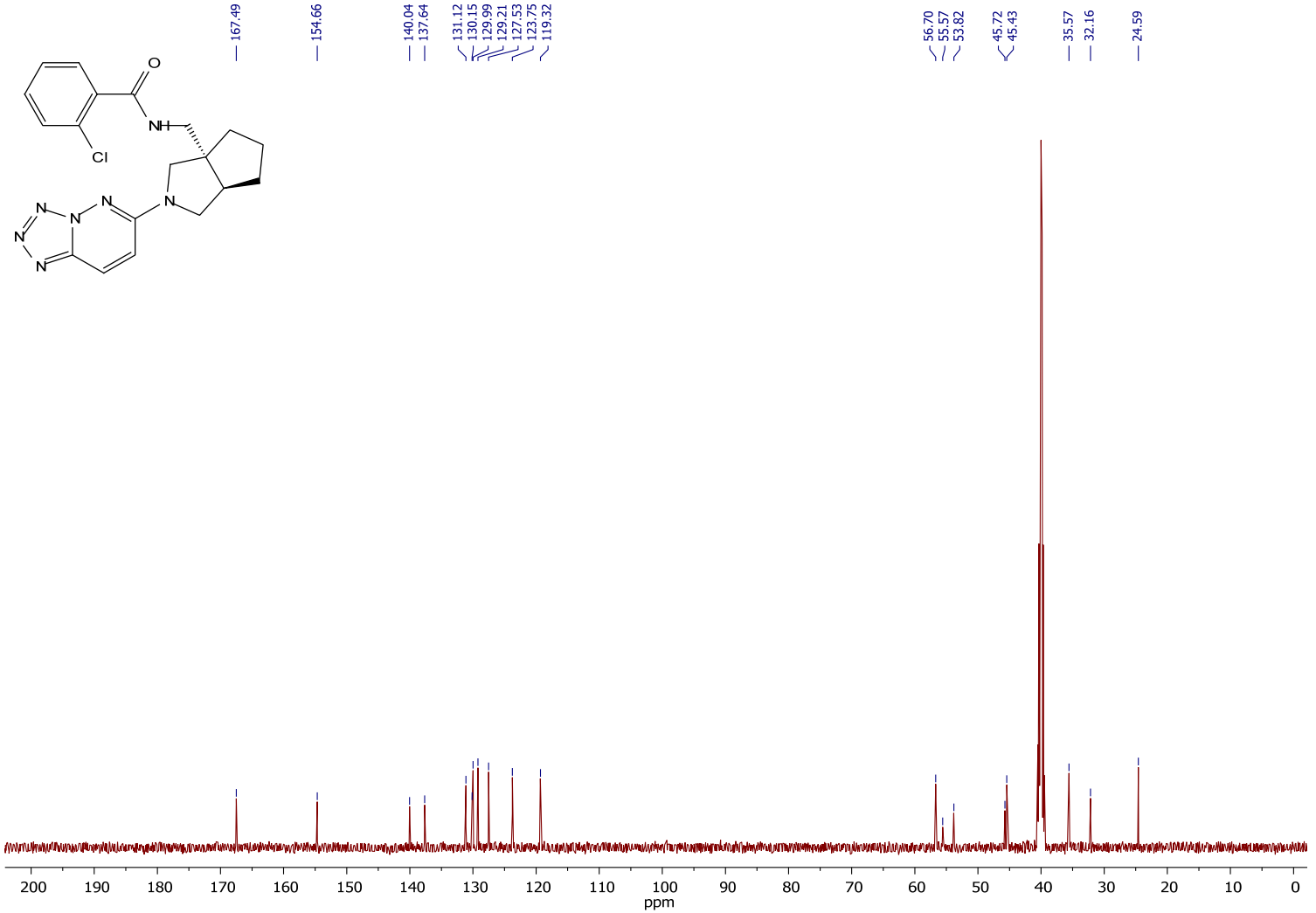

1-Methyl-*N*-(6-(tetrazolo[1,5-*b*]pyridazin-6-ylamino)spiro[3.3]heptan-2-yl)cycloheptanecarboxamide (**14**{*114*,*35*,*399*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



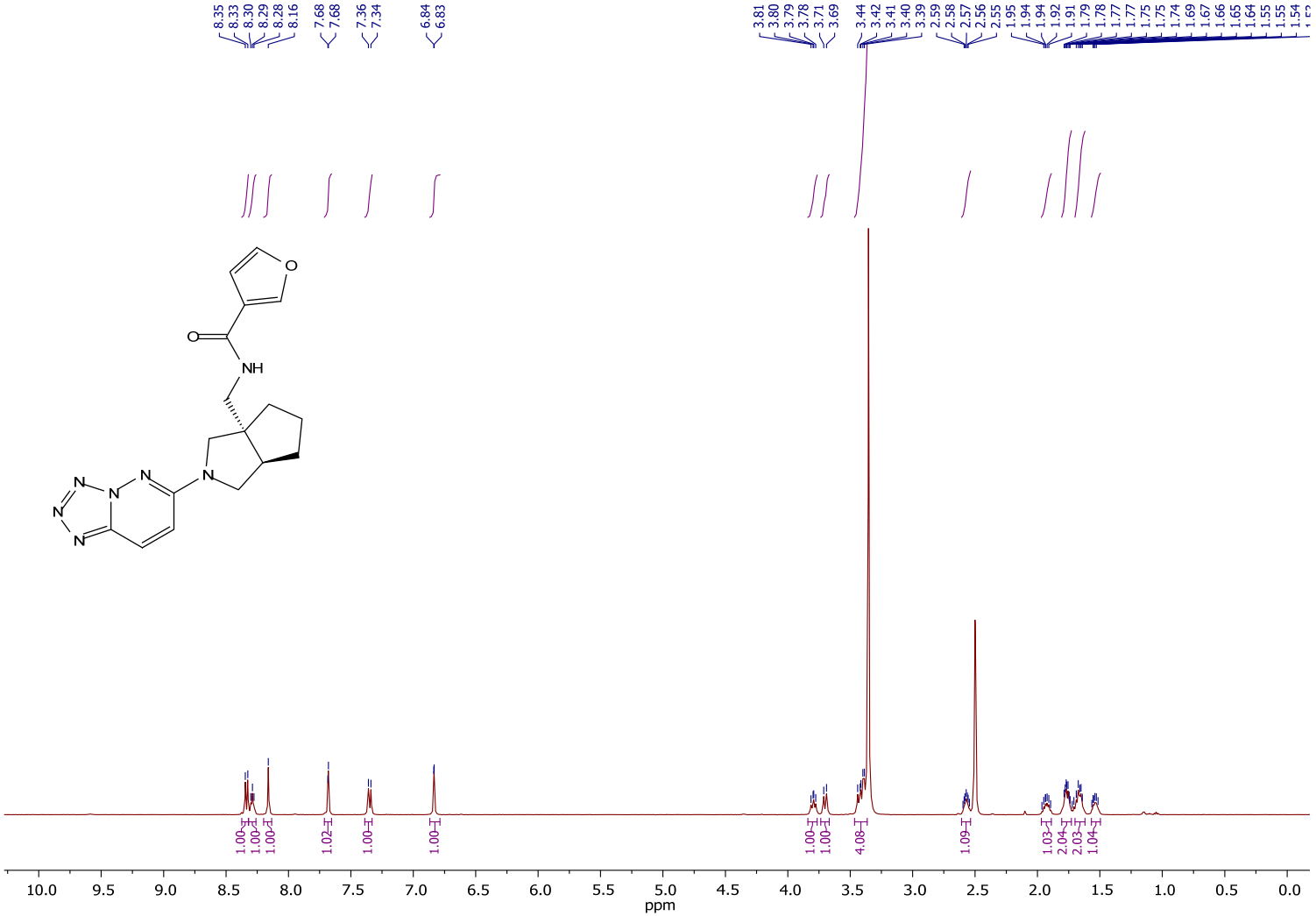

1-Methyl-*N*-(6-(tetrazolo[1,5-*b*]pyridazin-6-ylamino)spiro[3.3]heptan-2-yl)cycloheptanecarboxamide (**14**{*114*,*35*,*399*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



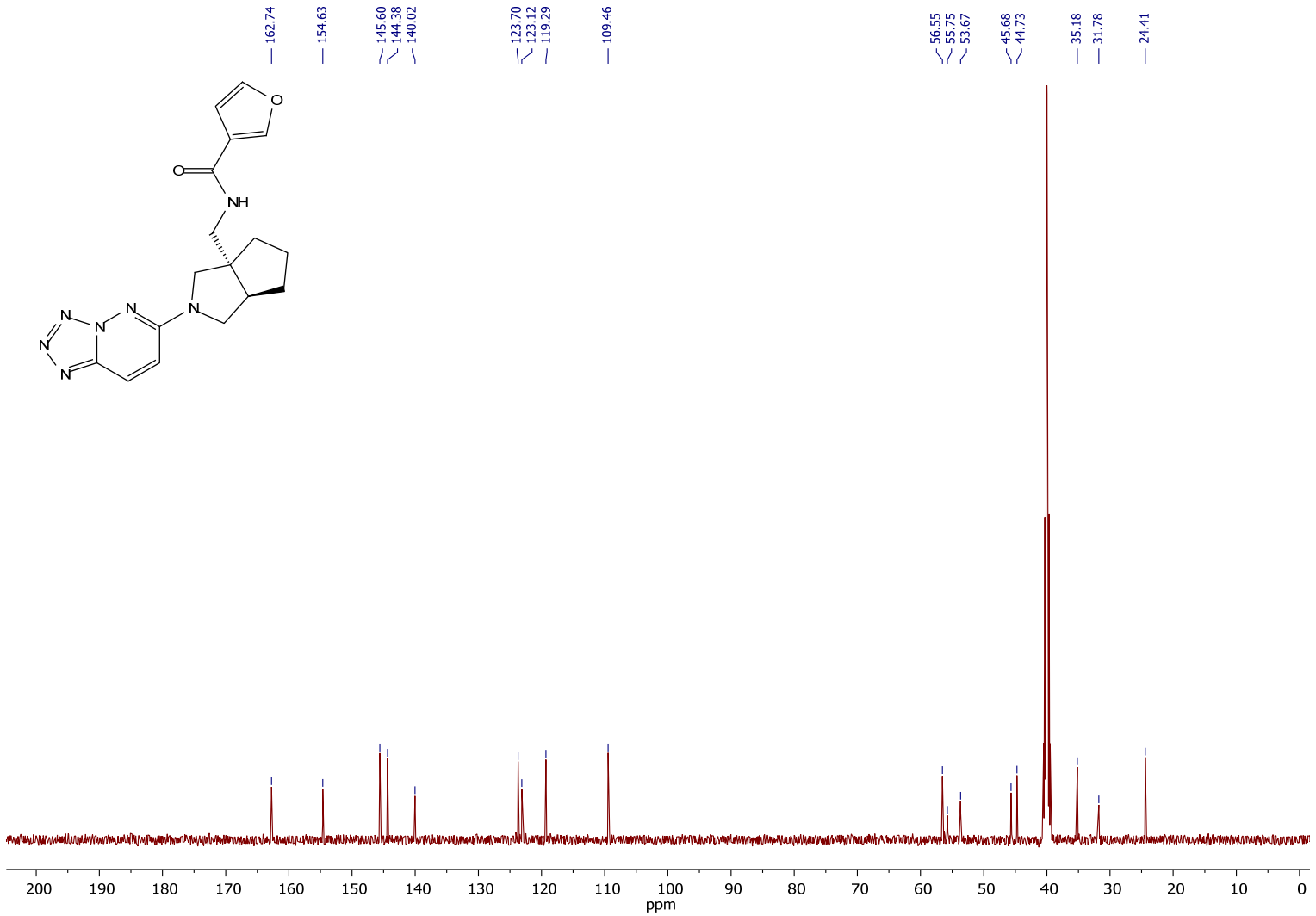

*rac*-2-Chloro-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*408*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



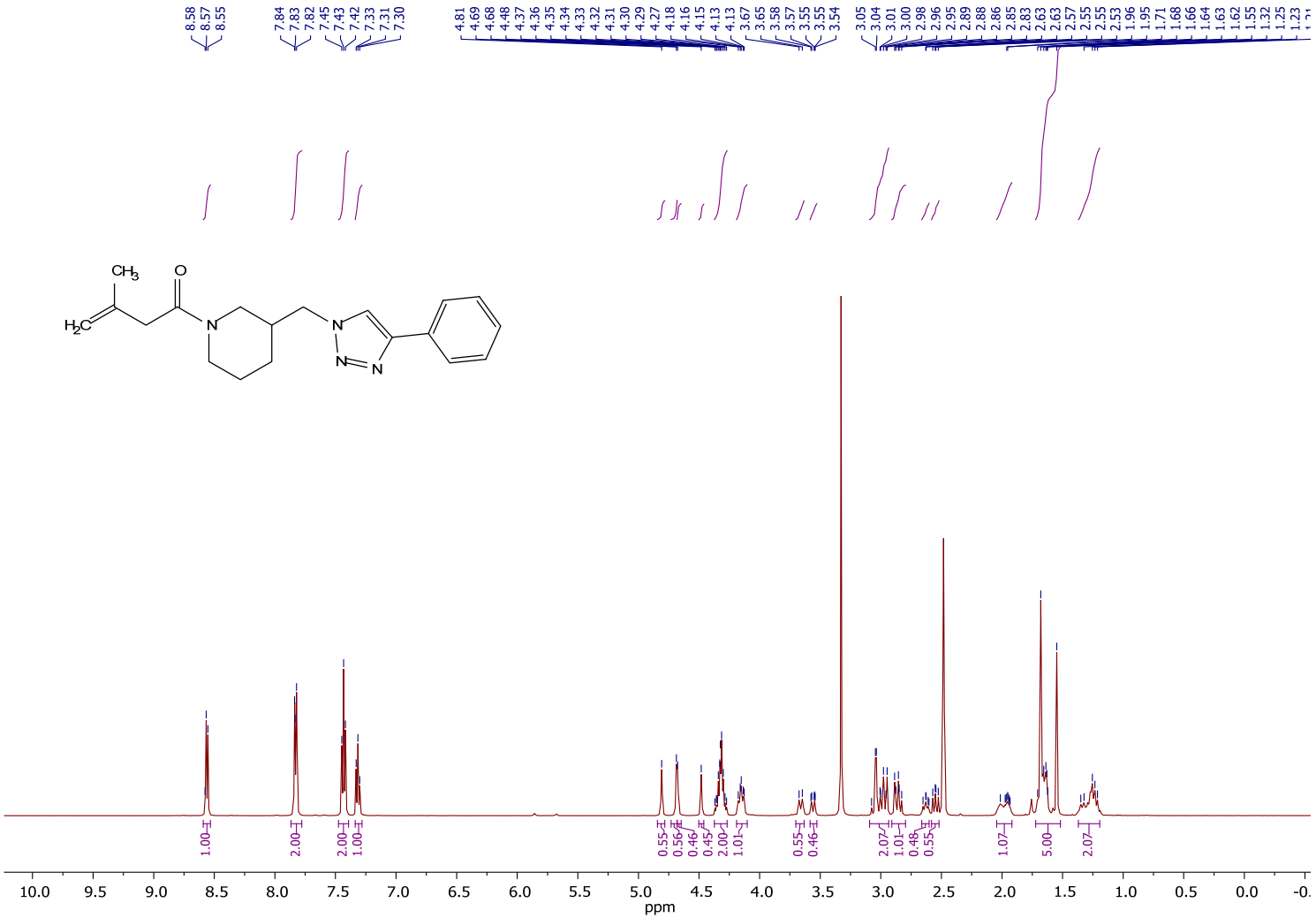

*rac*-2-Chloro-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)benzamide (**14**{*19*,*35*,*408*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



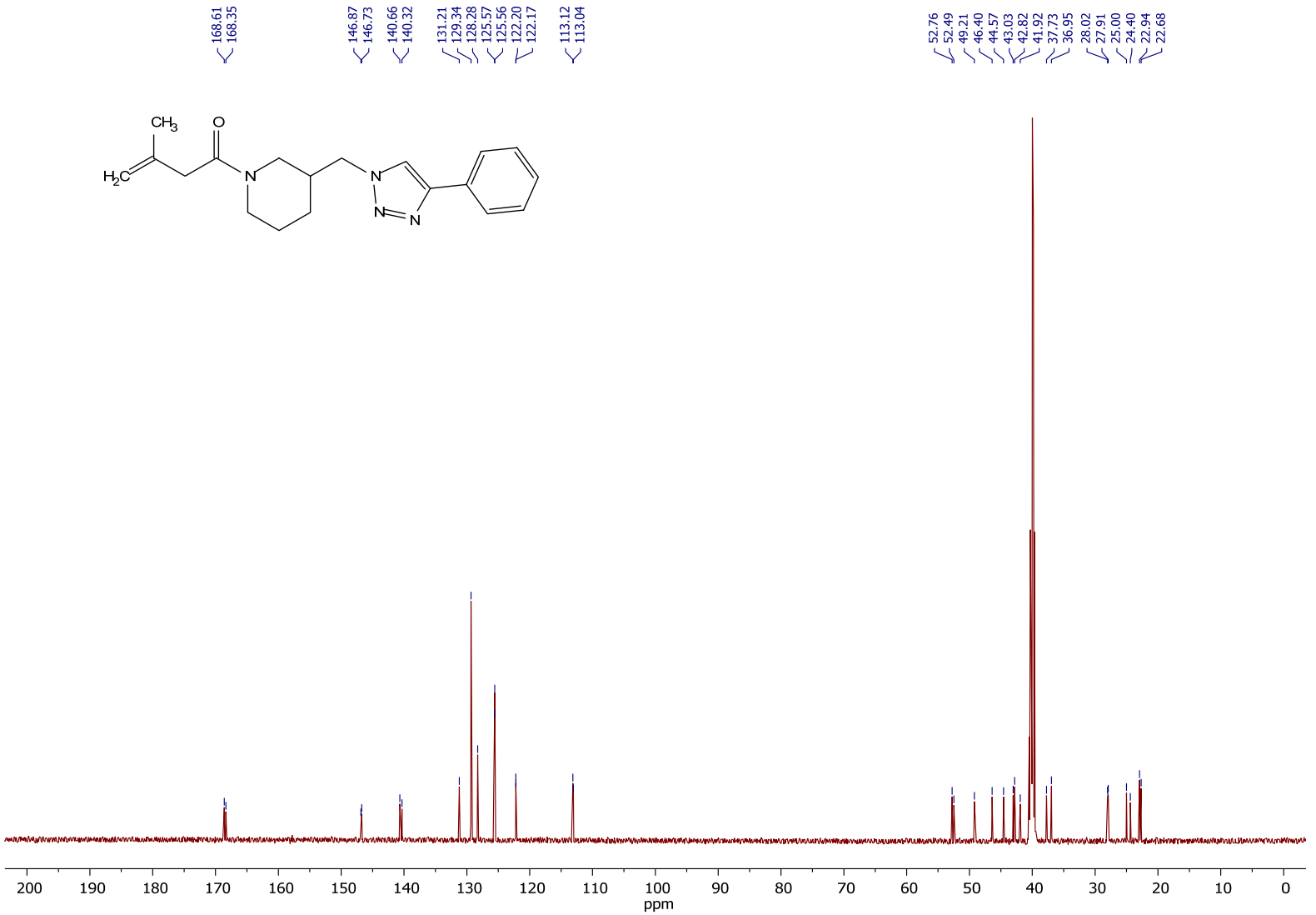

*rac*-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)furan-3-carboxamide (**14**{*19*,*35*,*32*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



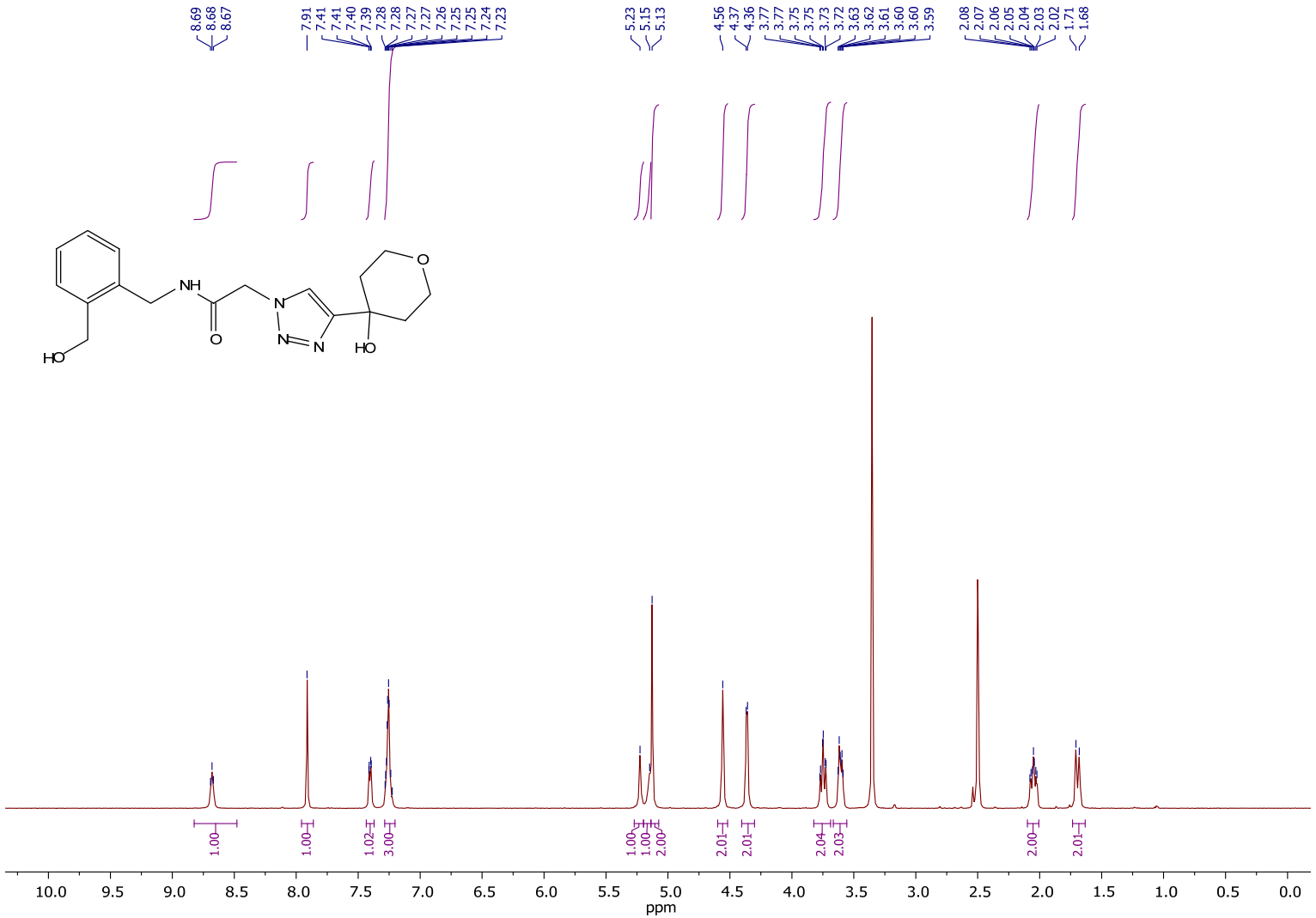

*rac*-*N*-(((3a*R*,6a*S*)-2-(tetrazolo[1,5-*b*]pyridazin-6-yl)octahydrocyclopenta[*c*]pyrrol-3a-yl)methyl)furan-3-carboxamide (**14**{*19*,*35*,*32*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



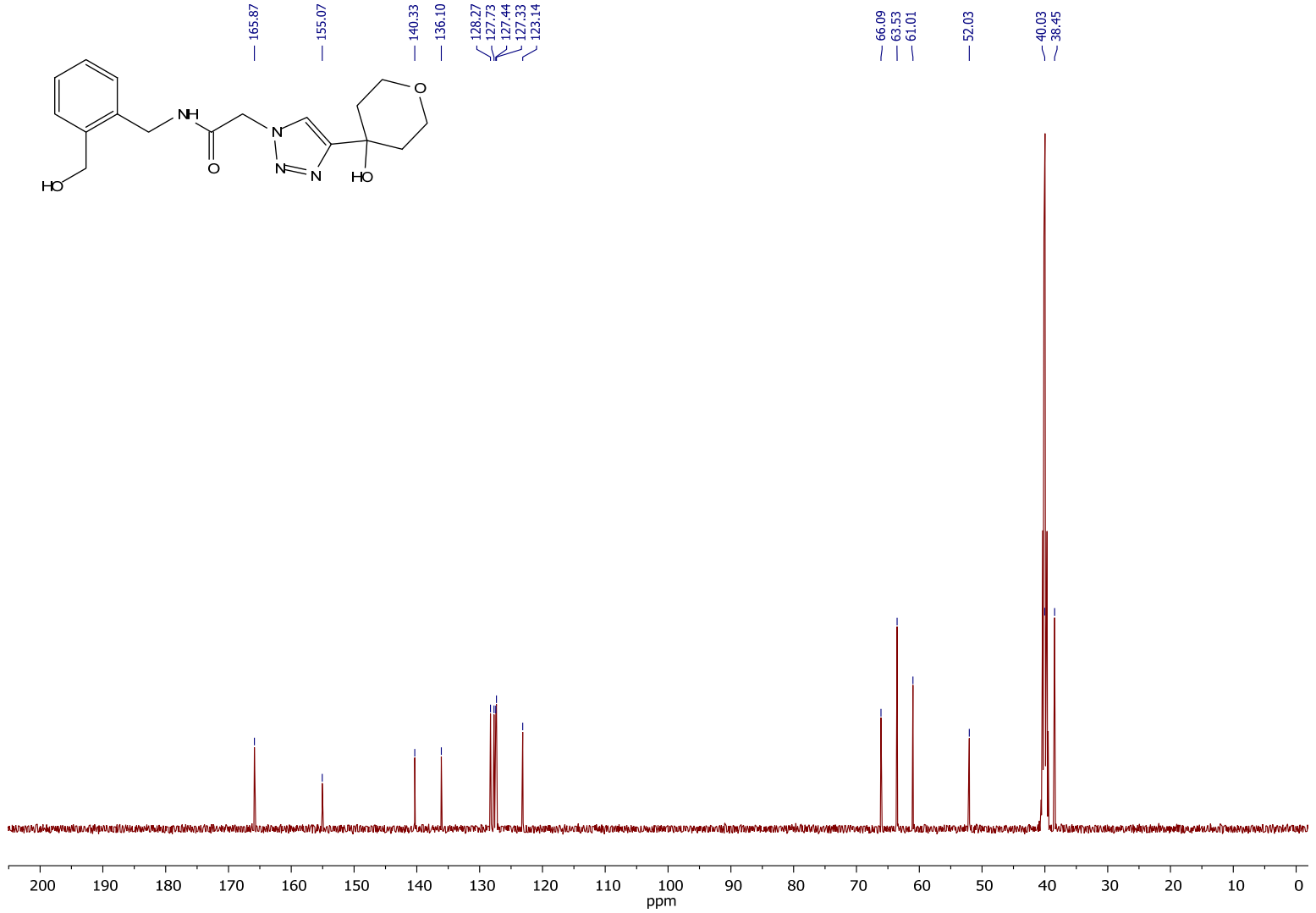

3-Methyl-1-(3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)piperidin-1-yl)but-3-en-1-one (**15**{*5*,*7*,*7*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



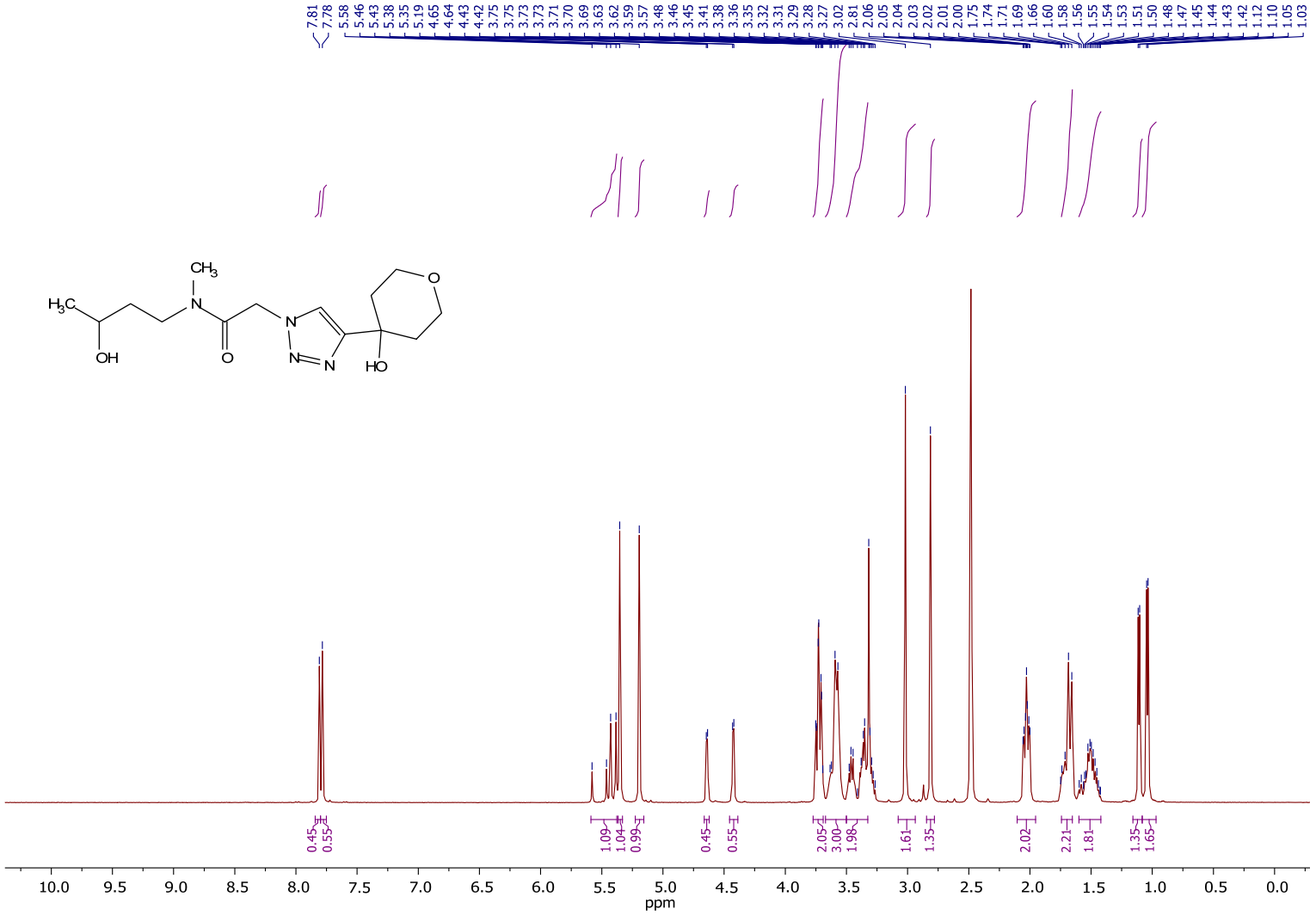

3-Methyl-1-(3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)piperidin-1-yl)but-3-en-1-one (**15**{*5*,*7*,*7*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



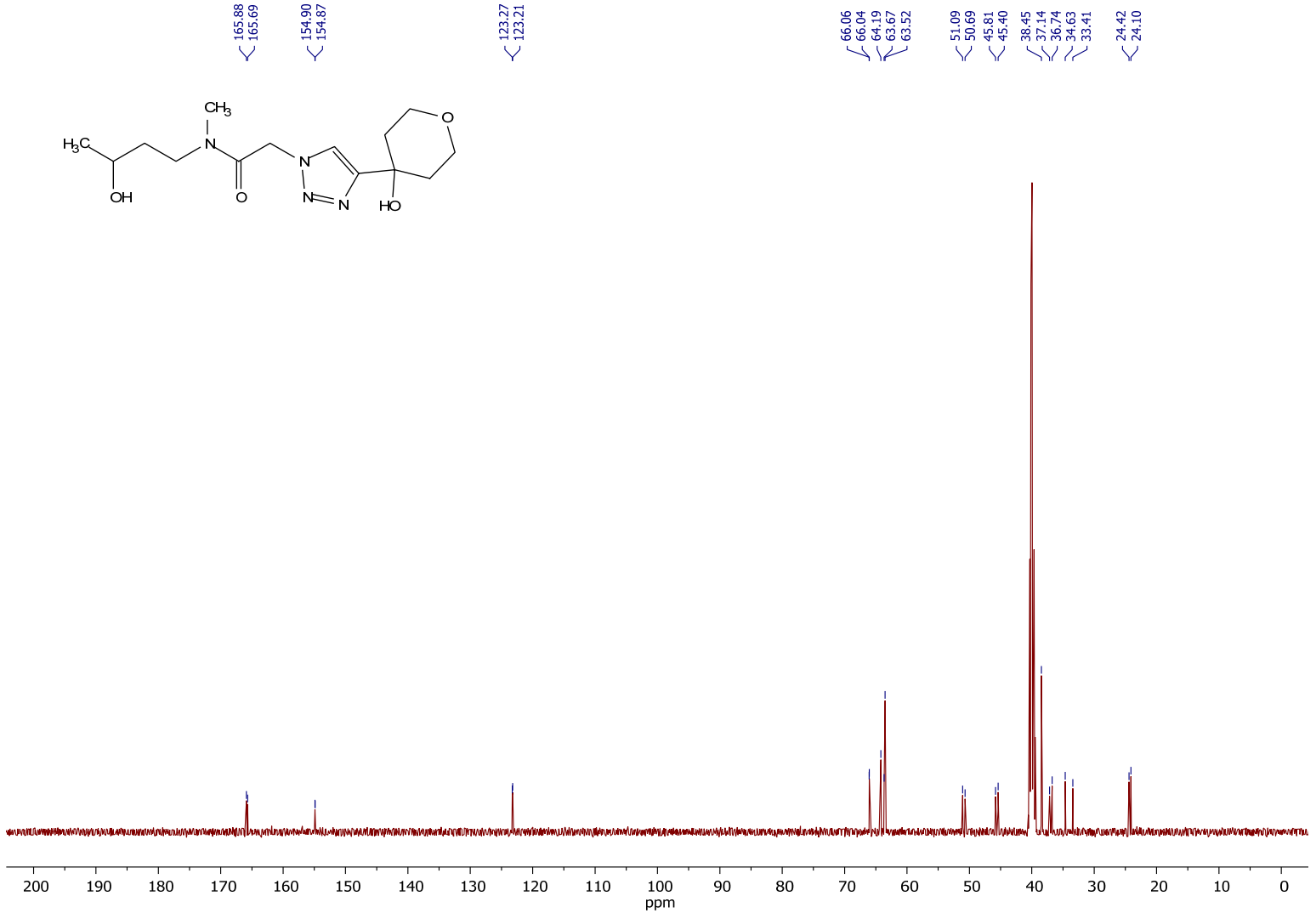

*N*-(3-Hydroxybutyl)-2-(4-(4-hydroxytetrahydro-2*H*-pyran-4-yl)-1*H*-1,2,3-triazol-1-yl)-*N*-methylacetamide (**15**{*3*,*20*,*38*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



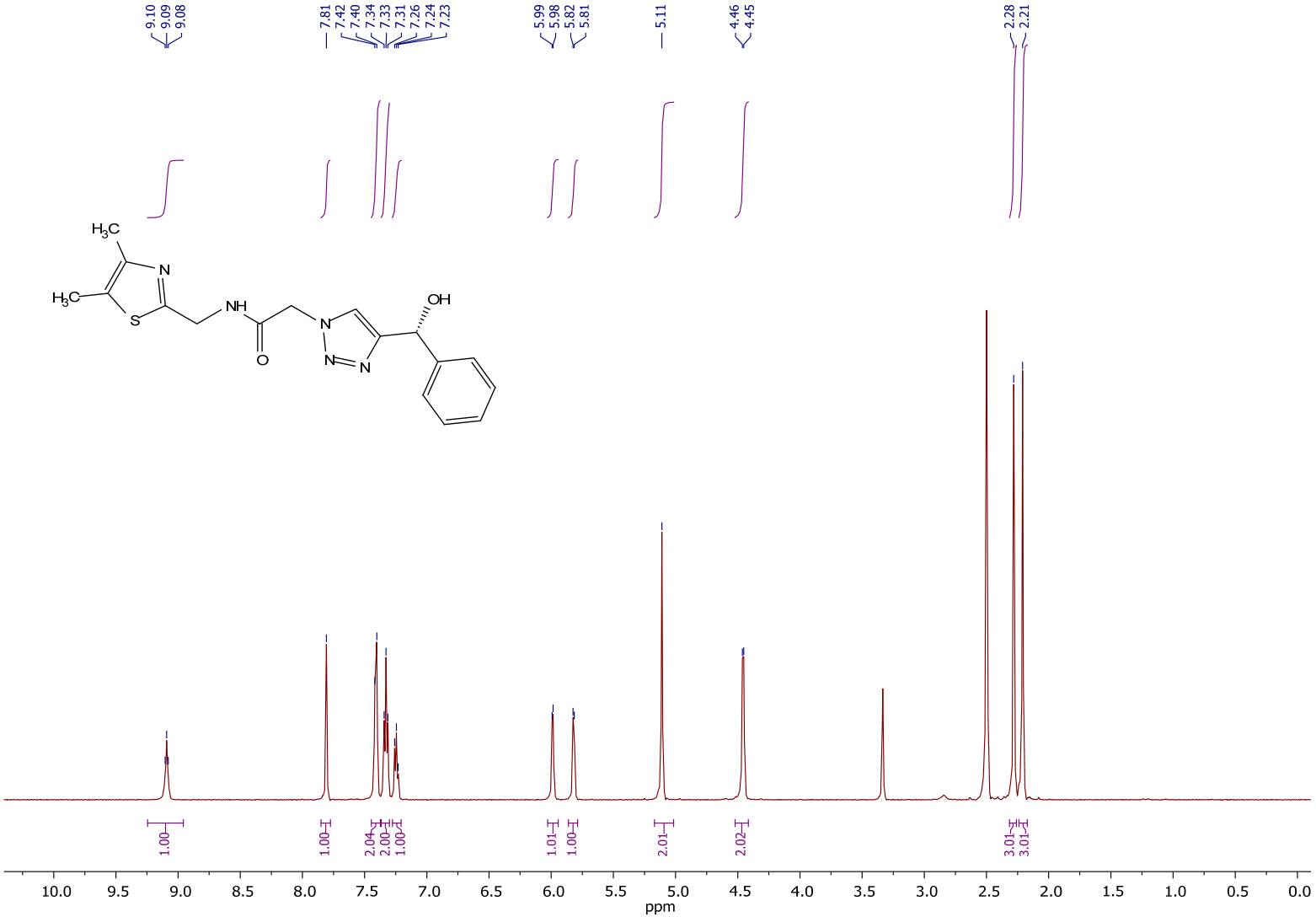

*N*-(3-Hydroxybutyl)-2-(4-(4-hydroxytetrahydro-2*H*-pyran-4-yl)-1*H*-1,2,3-triazol-1-yl)-*N*-methylacetamide (**15**{*3*,*20*,*38*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



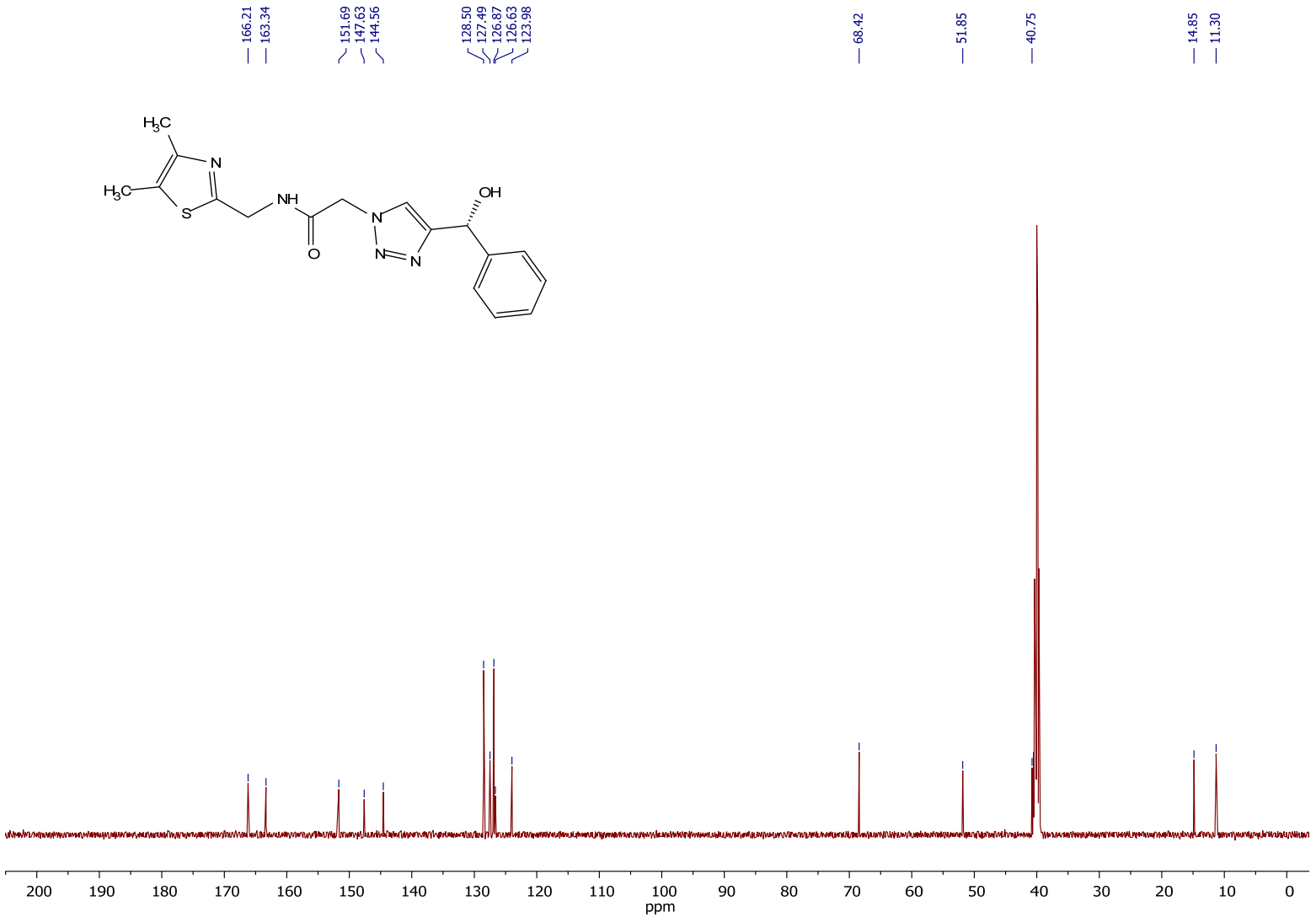

*N*-(3-Hydroxybutyl)-2-(4-(4-hydroxytetrahydro-2*H*-pyran-4-yl)-1*H*-1,2,3-triazol-1-yl)-*N*-methylacetamide (**15**{*3*,*20*,*38*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



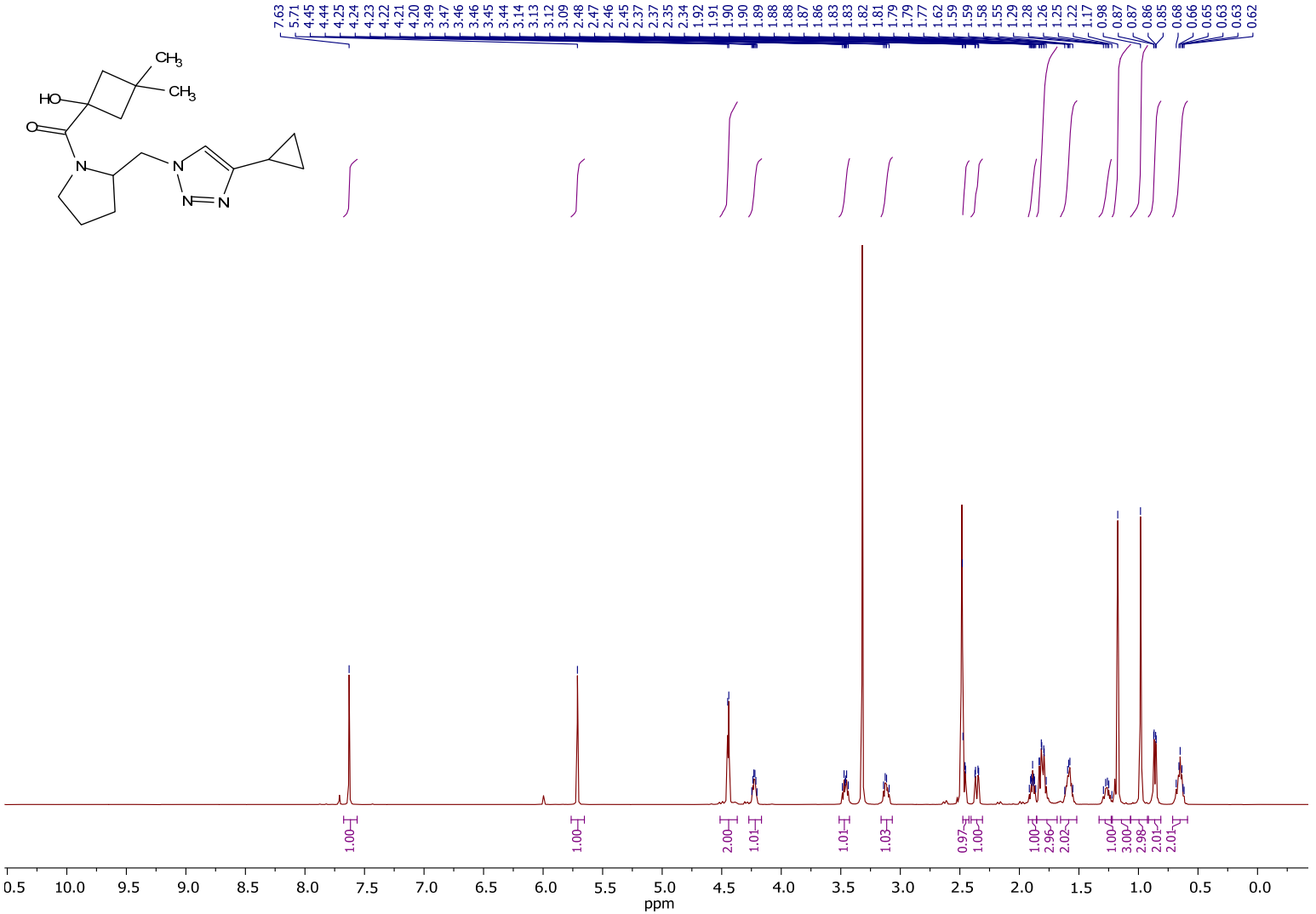

*N*-(3-Hydroxybutyl)-2-(4-(4-hydroxytetrahydro-2*H*-pyran-4-yl)-1*H*-1,2,3-triazol-1-yl)-*N*-methylacetamide (**15**{*3*,*20*,*38*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



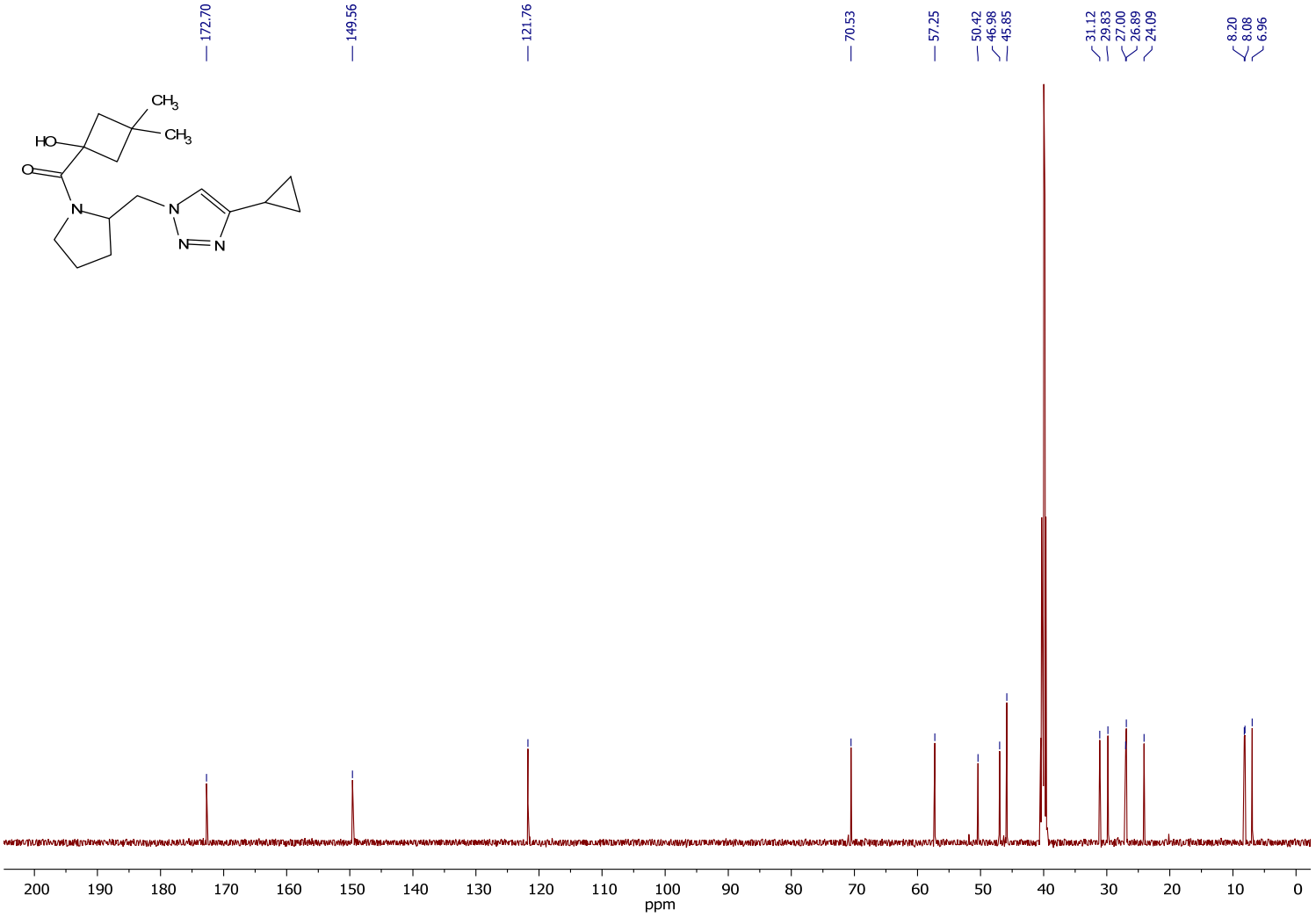

*N*-((4,5-Dimethylthiazol-2-yl)methyl)-2-(4-(hydroxy(phenyl)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (**15**{*3*,*21*,*37*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



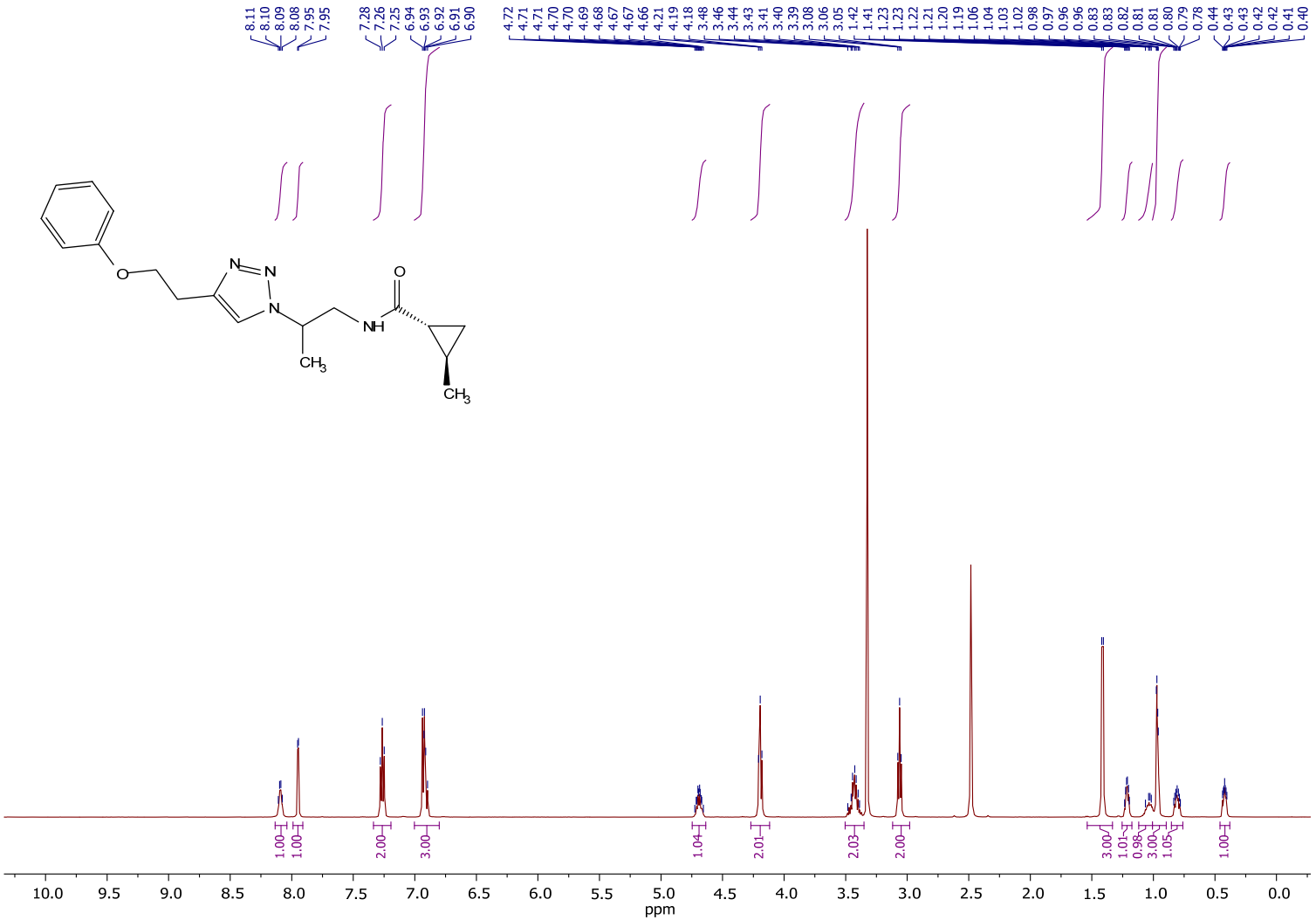

(*N*-((4,5-Dimethylthiazol-2-yl)methyl)-2-(4-(hydroxy(phenyl)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (**15**{*3*,*21*,*37*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



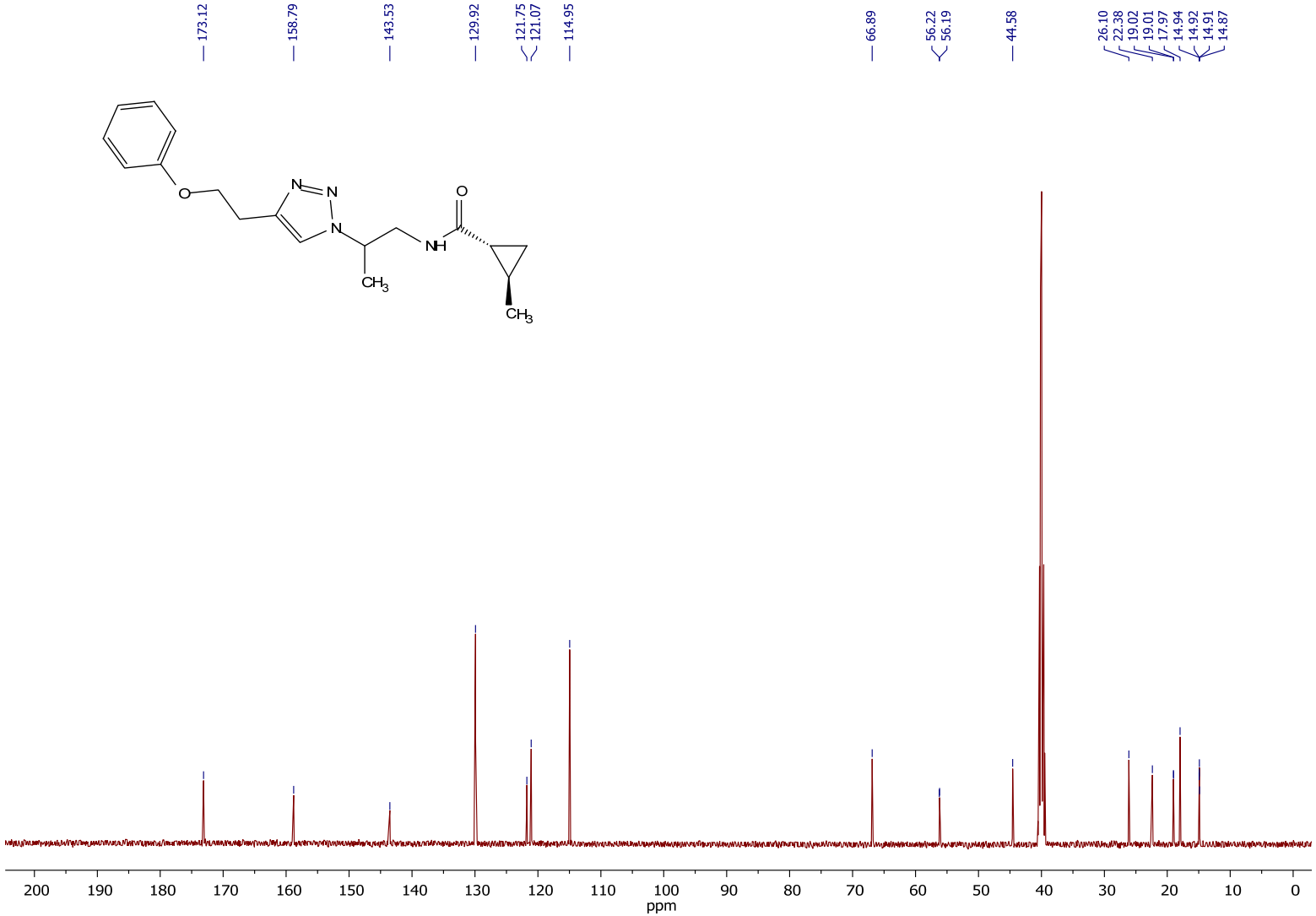

(2-((4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)methyl)pyrrolidin-1-yl)(1-hydroxy-3,3-dimethylcyclobutyl)methanone (**15**{*1*,*6*,*6*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



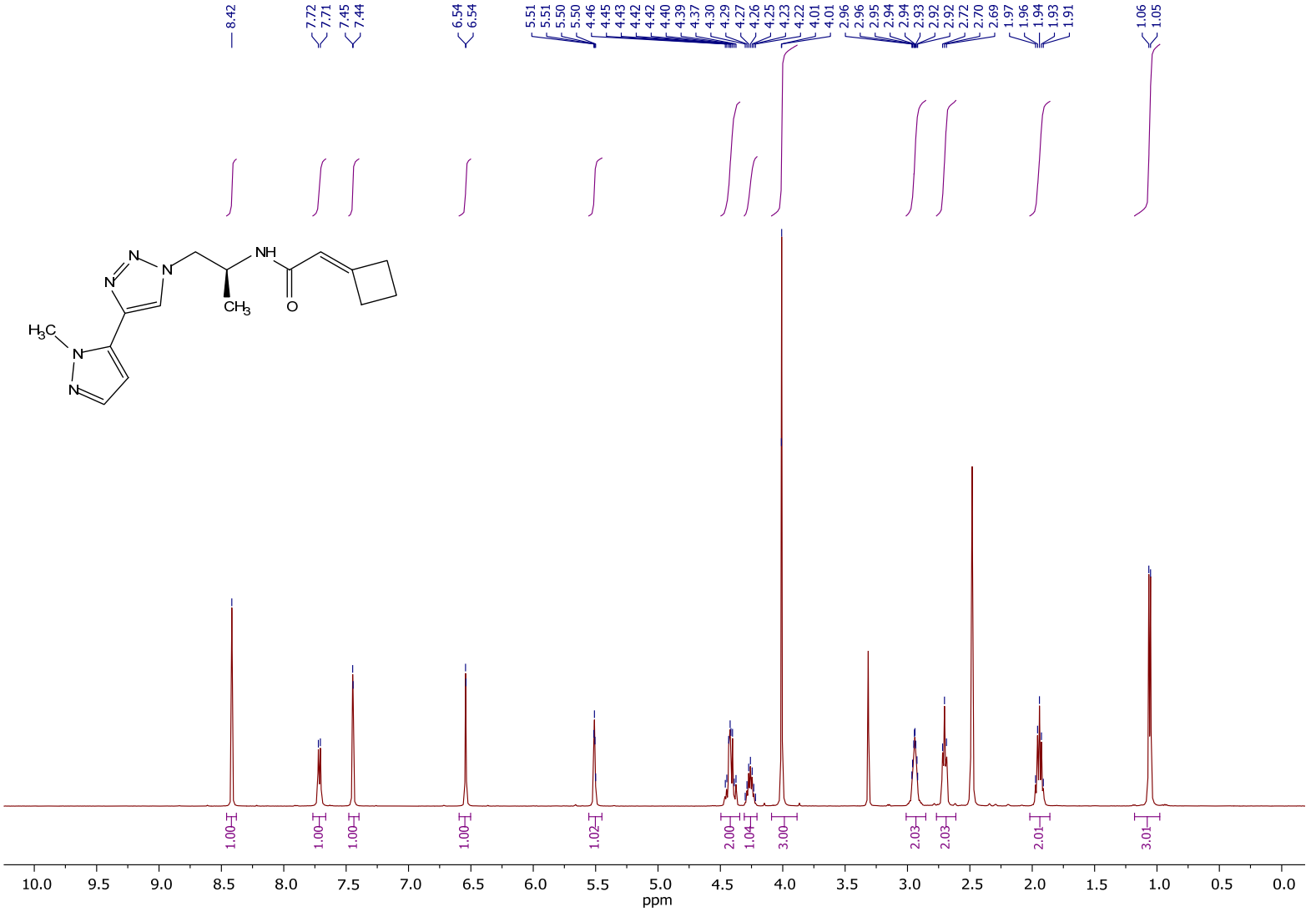

(2-((4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)methyl)pyrrolidin-1-yl)(1-hydroxy-3,3-dimethylcyclobutyl)methanone (**15**{*1*,*6*,*6*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



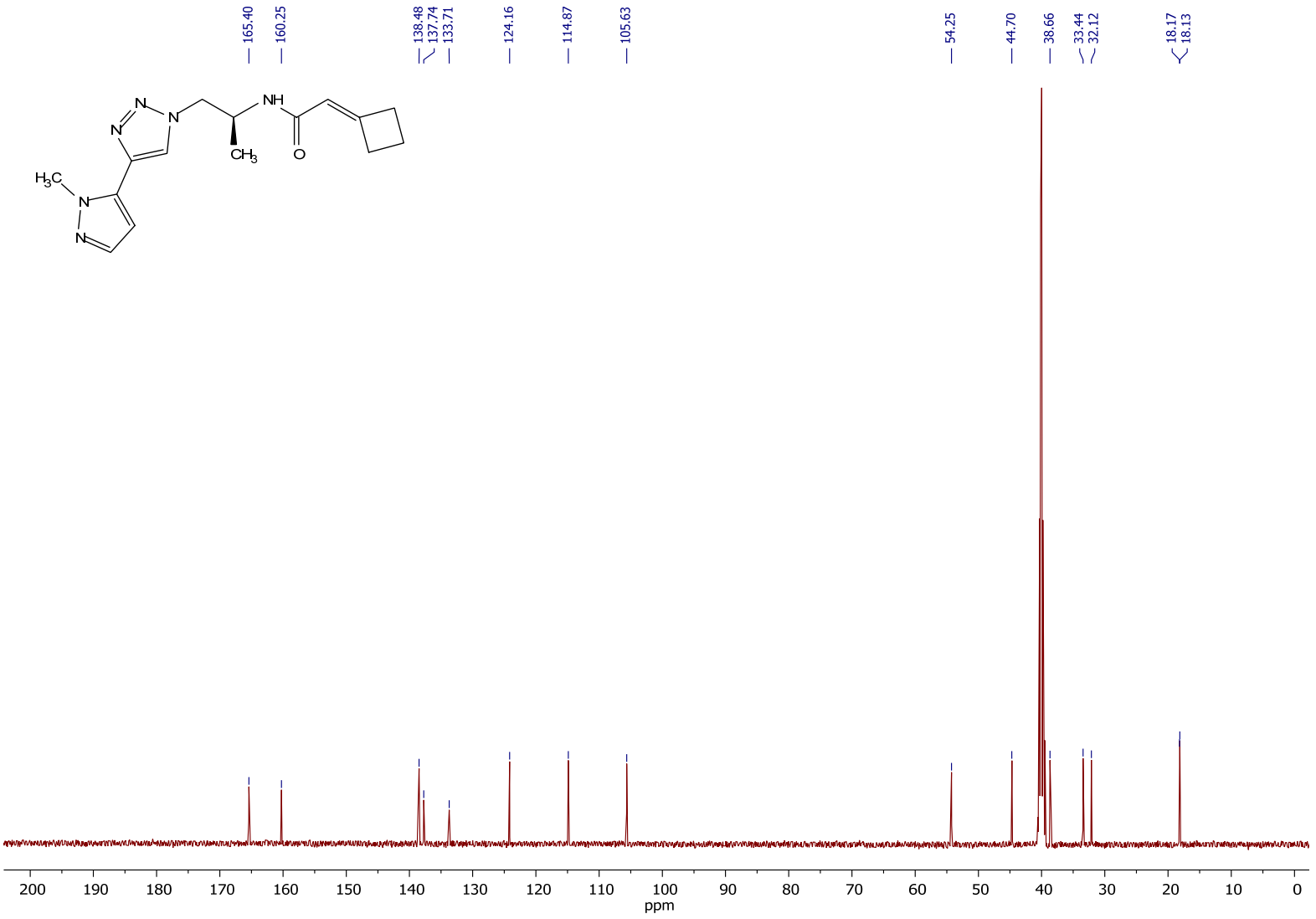

*rac*-(1*R*,2*R*)-2-Methyl-*N*-(2-(4-(2-phenoxyethyl)-1*H*-1,2,3-triazol-1-yl)propyl)cyclopropanecarboxamide (**15**{*4*,*4*,*4*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



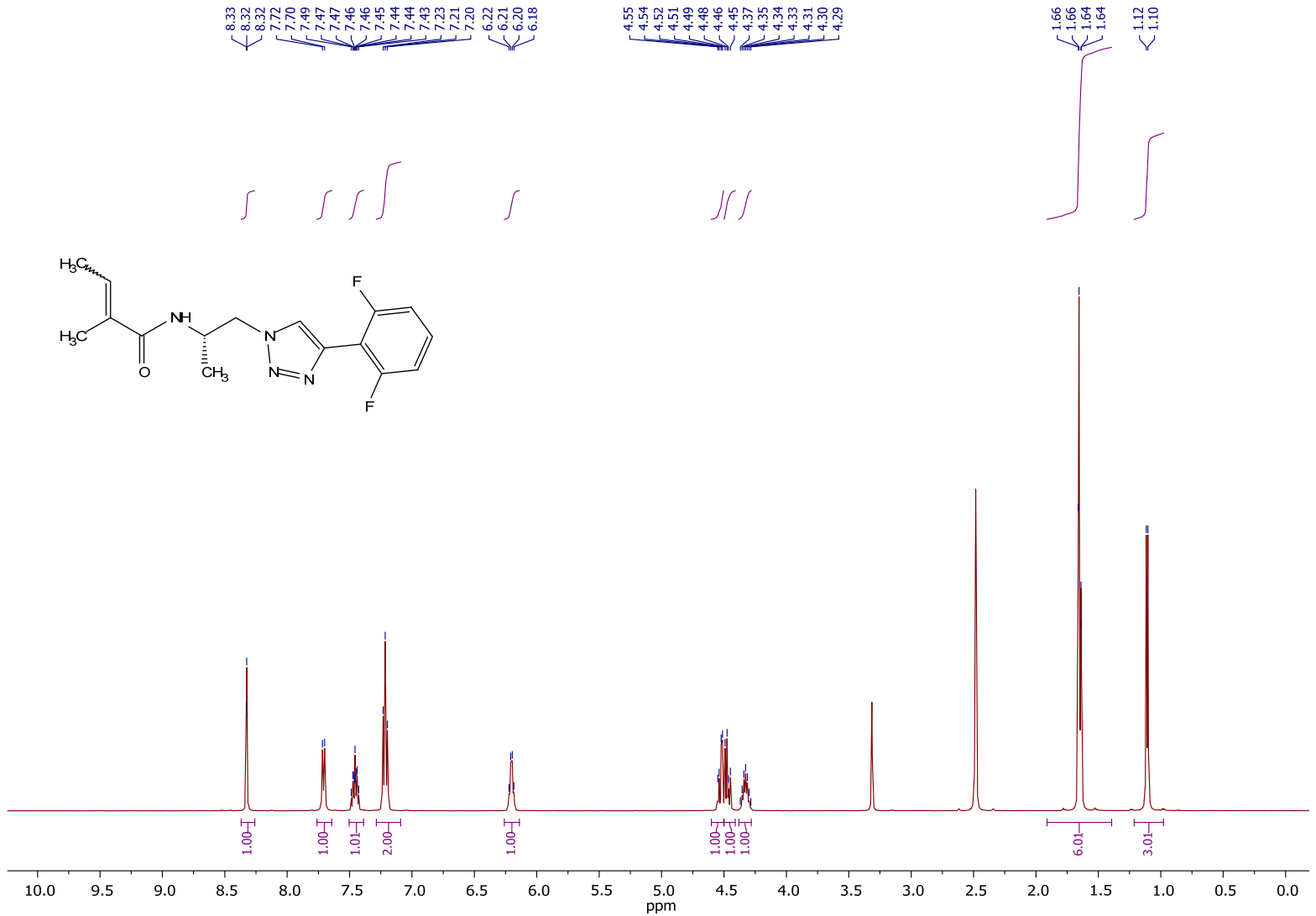

*rac*-(1*R*,2*R*)-2-Methyl-*N*-(2-(4-(2-phenoxyethyl)-1*H*-1,2,3-triazol-1-yl)propyl)cyclopropanecarboxamide (**15**{*4*,*4*,*4*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



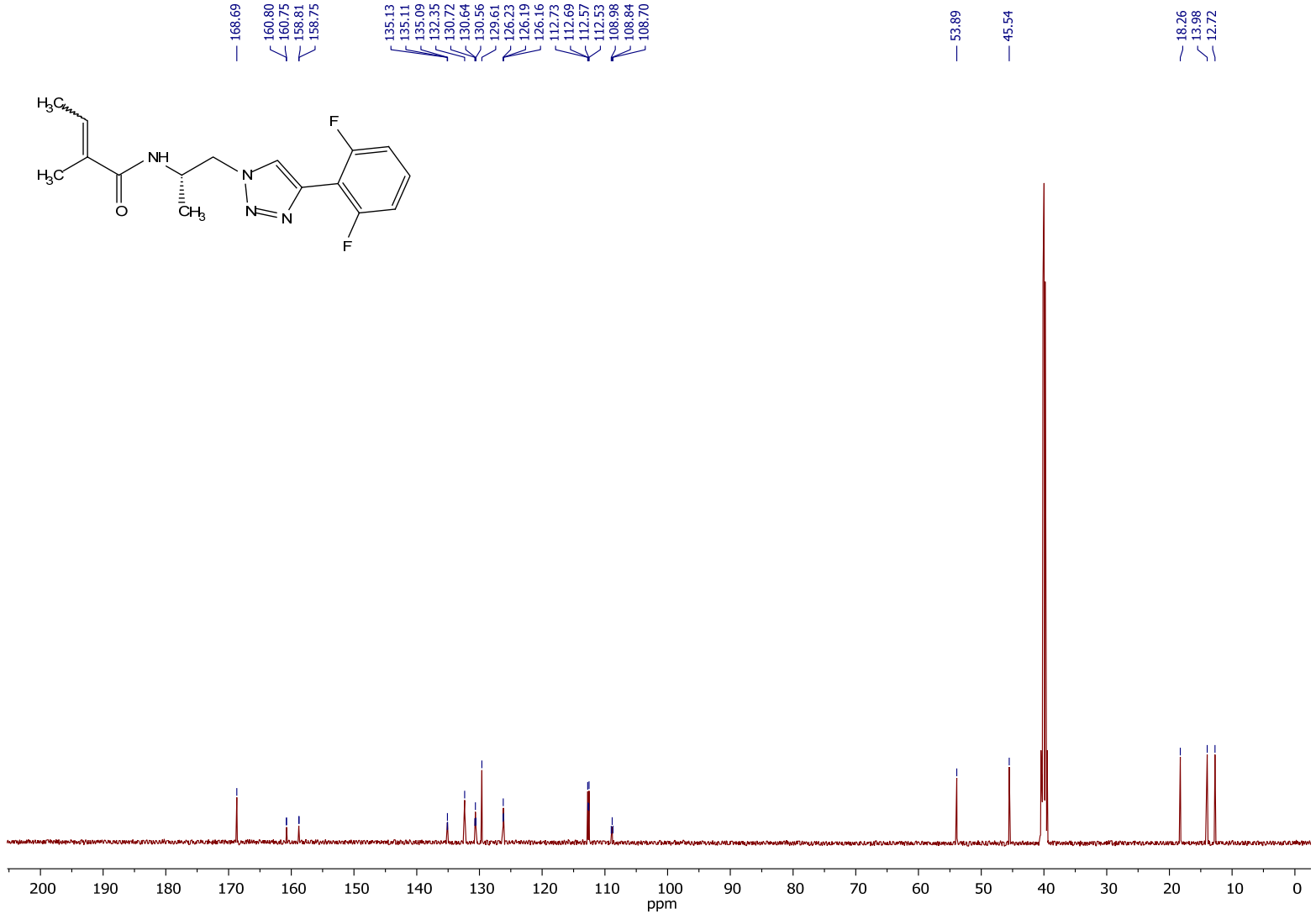

(*S*)-2-Cyclobutylidene-*N*-(1-(4-(1-methyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)acetamide **15**{*6*,*11*,*11*}, $^{1}$H NMR (500 MHz, DMSO-$d_6$)



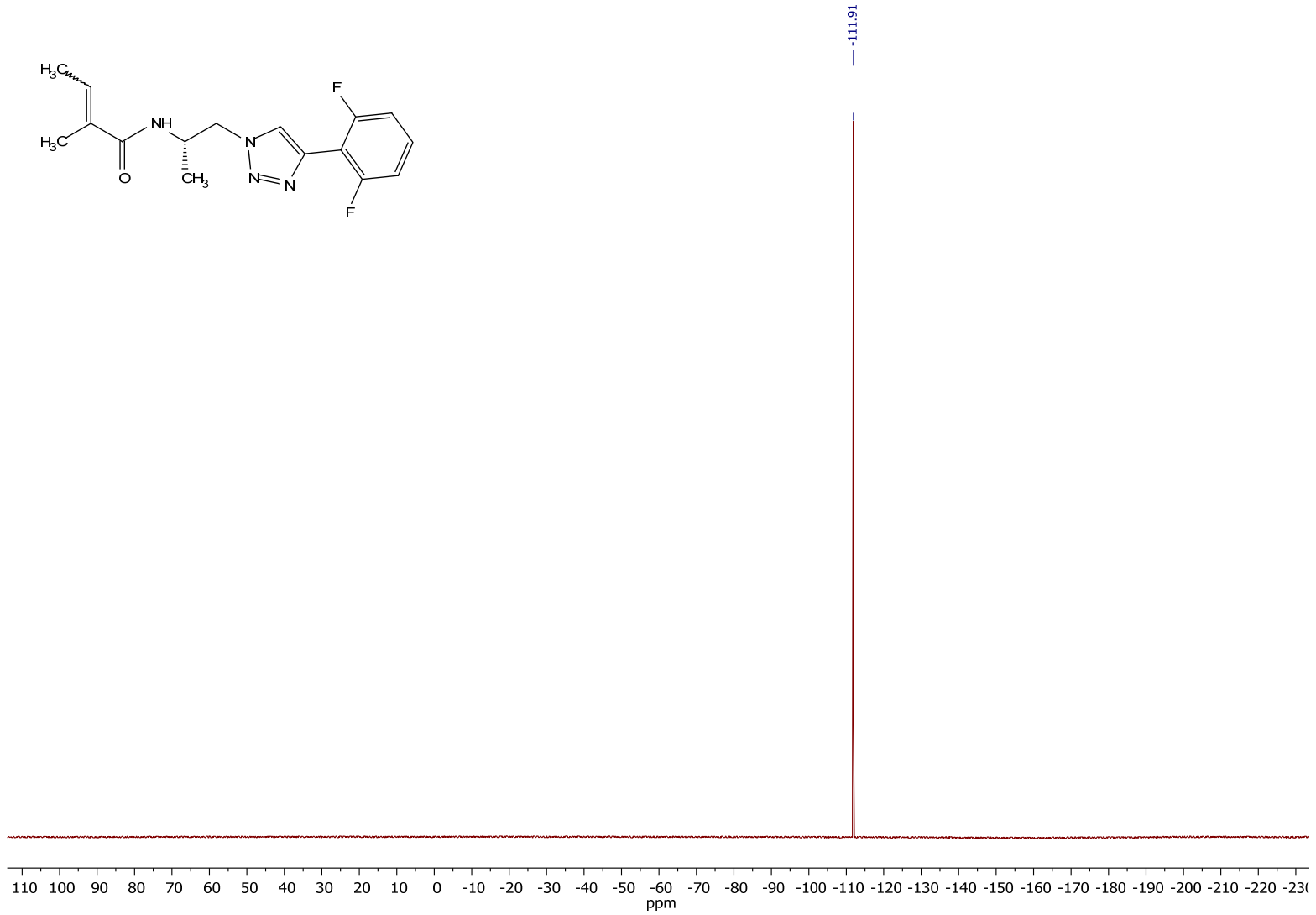

(*S*)-2-Cyclobutylidene-*N*-(1-(4-(1-methyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)acetamide **15**{*6*,*11*,*11*}, $^{13}$C NMR (126 MHz, DMSO-$d_6$)



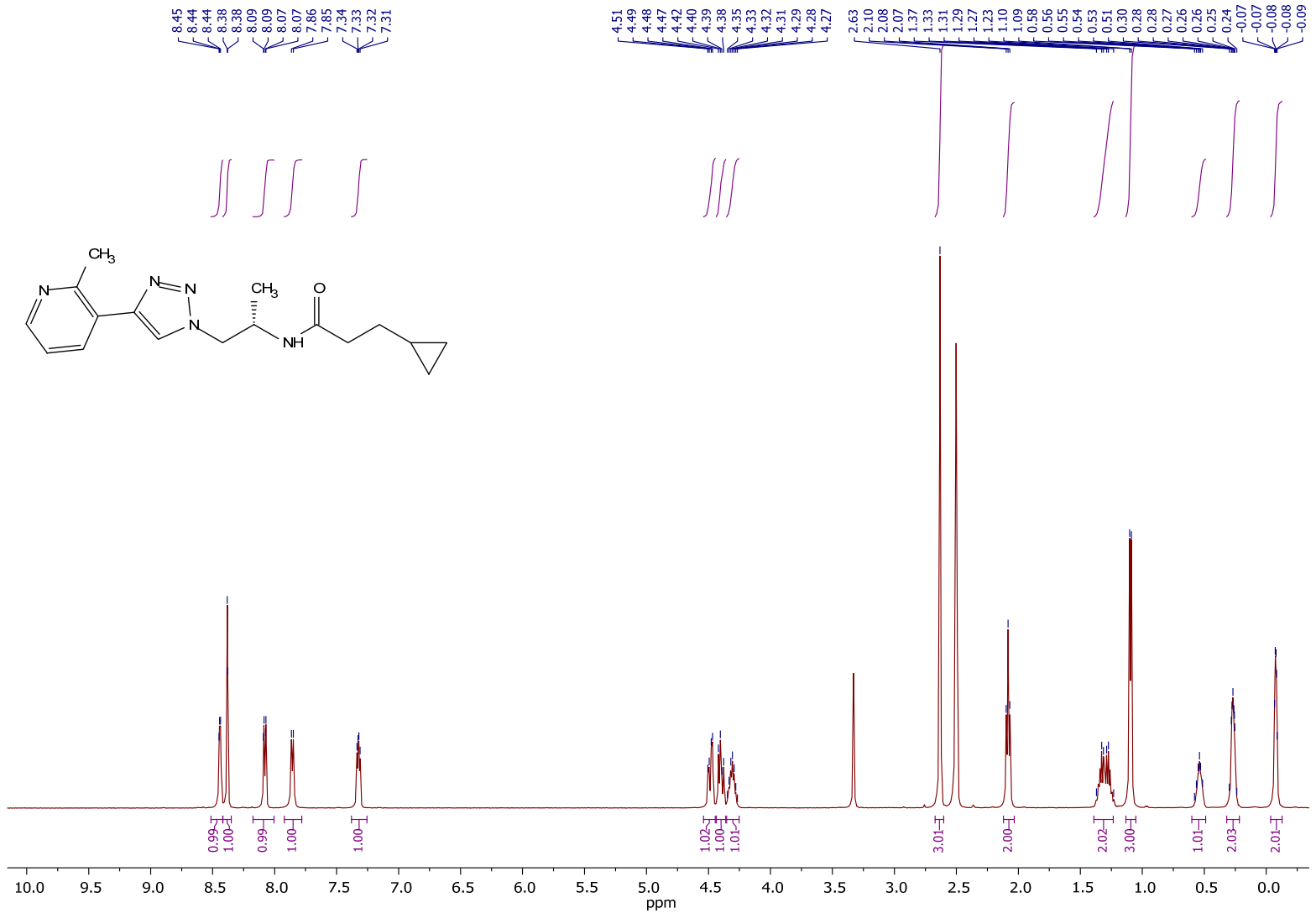

(*S*)-*N*-(1-(4-(2,6-Difluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-2-methylbut-2-enamide (**15**{*6*,*1*,*8*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



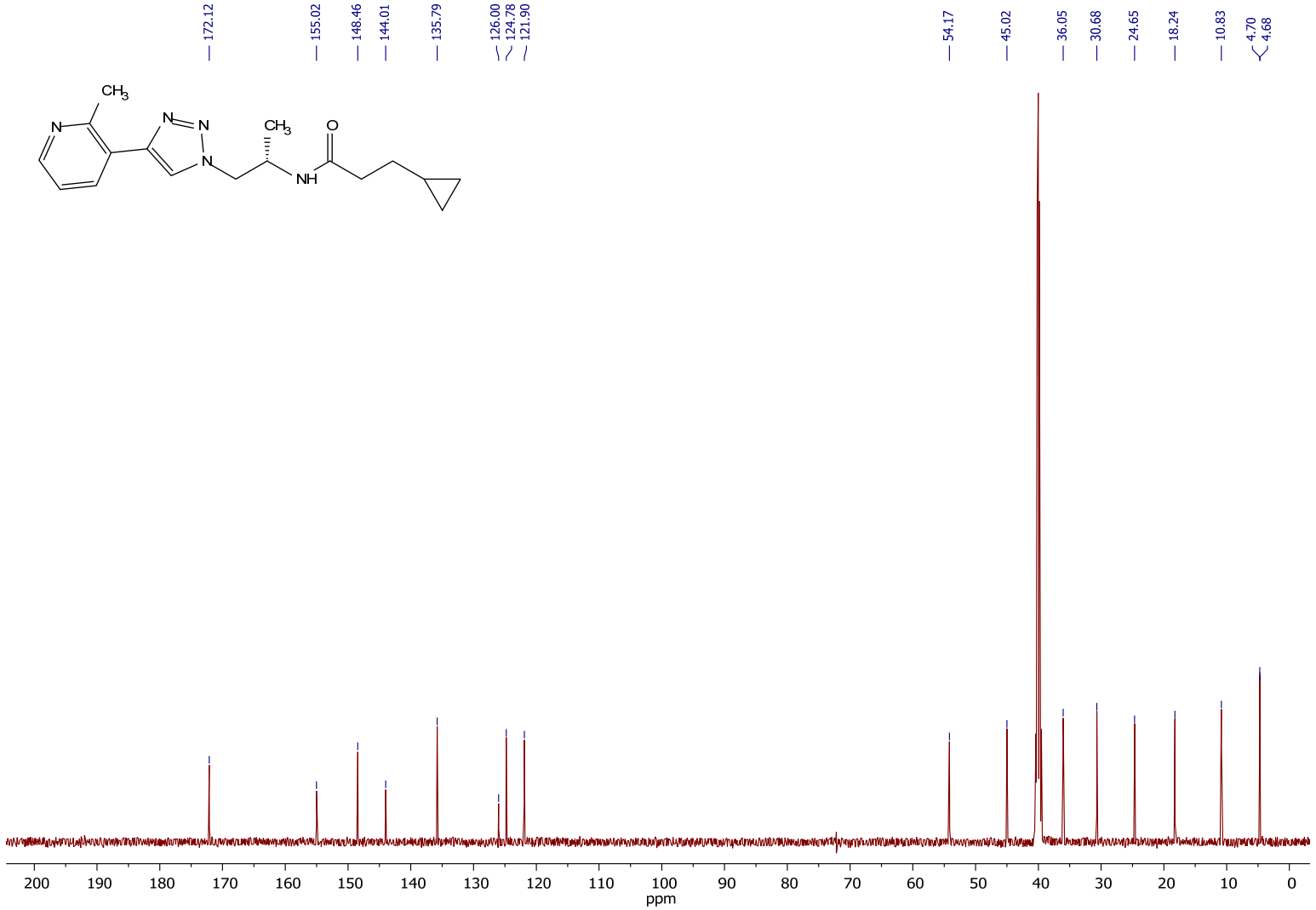

(*S*)-*N*-(1-(4-(2,6-Difluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-2-methylbut-2-enamide (**15**{*6*,*1*,*8*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



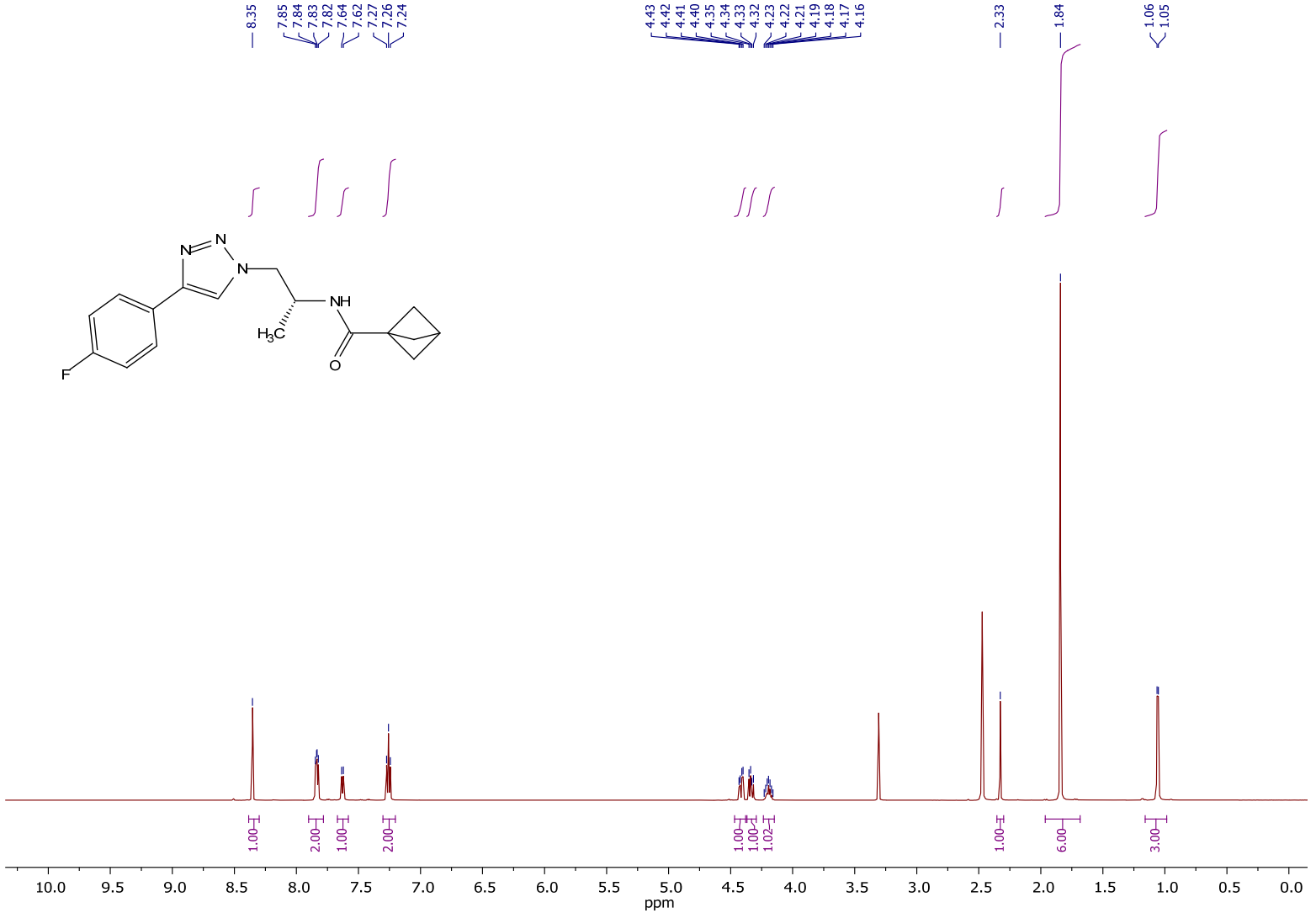

(*S*)-*N*-(1-(4-(2,6-Difluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-2-methylbut-2-enamide (**15**{*6*,*1*,*8*}), $^{19}$F NMR (376 MHz, DMSO-$d_6$)



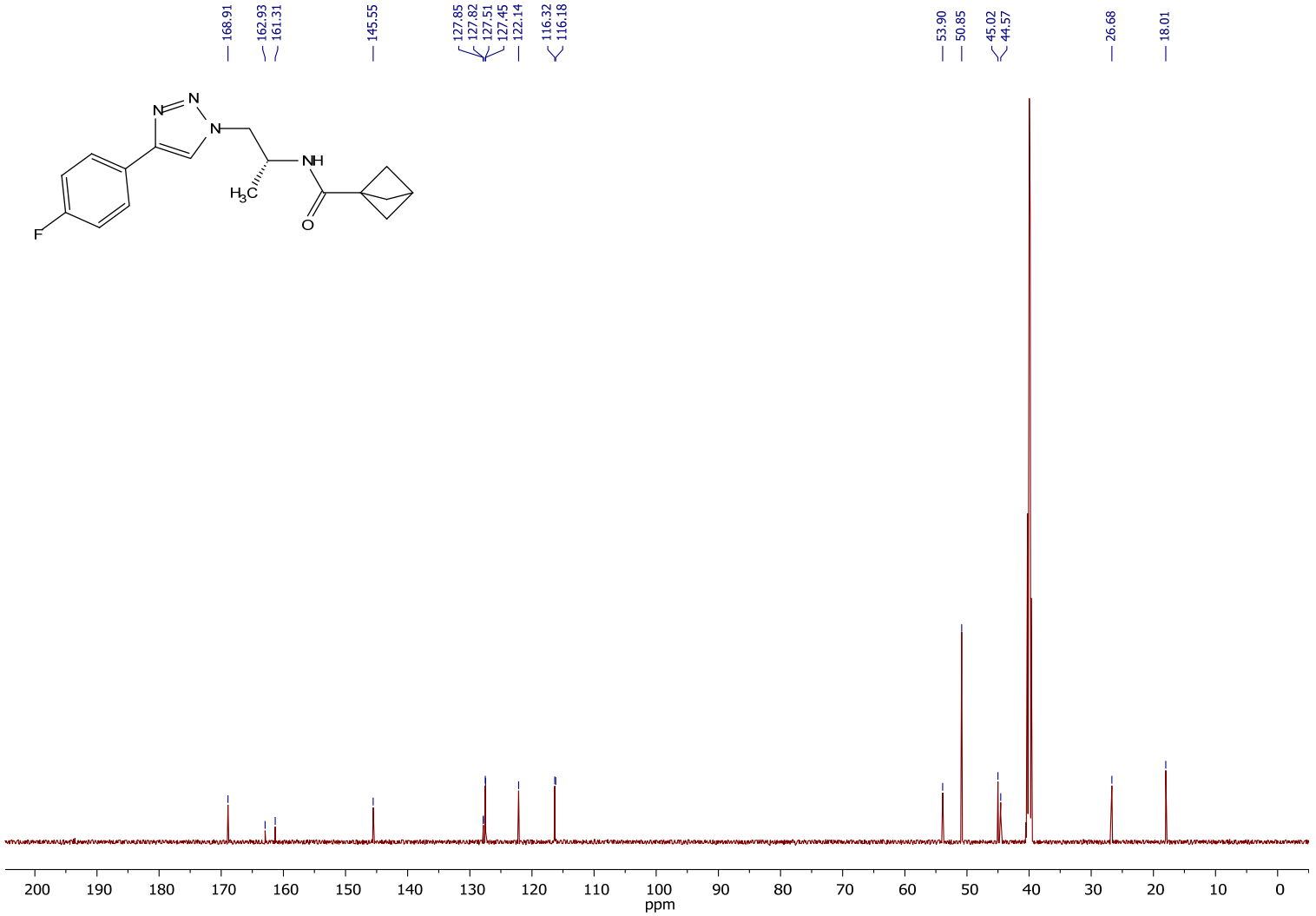

(*S*)-3-Cyclopropyl-*N*-(1-(4-(2-methylpyridin-3-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)propanamide (**15**{*6*,*27*,*27*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



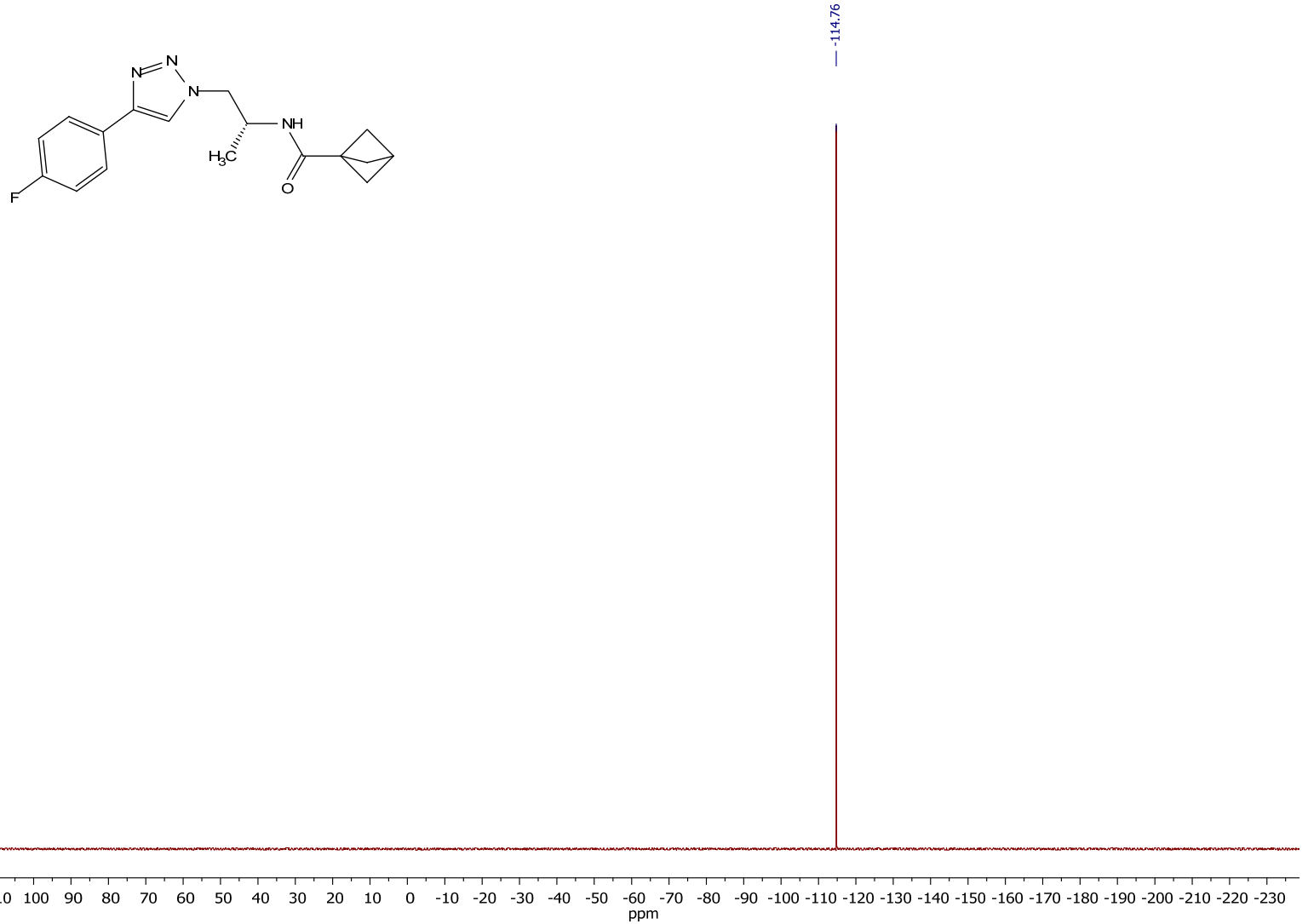

(*S*)-3-Cyclopropyl-*N*-(1-(4-(2-methylpyridin-3-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)propanamide (**15**{*6*,*27*,*27*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



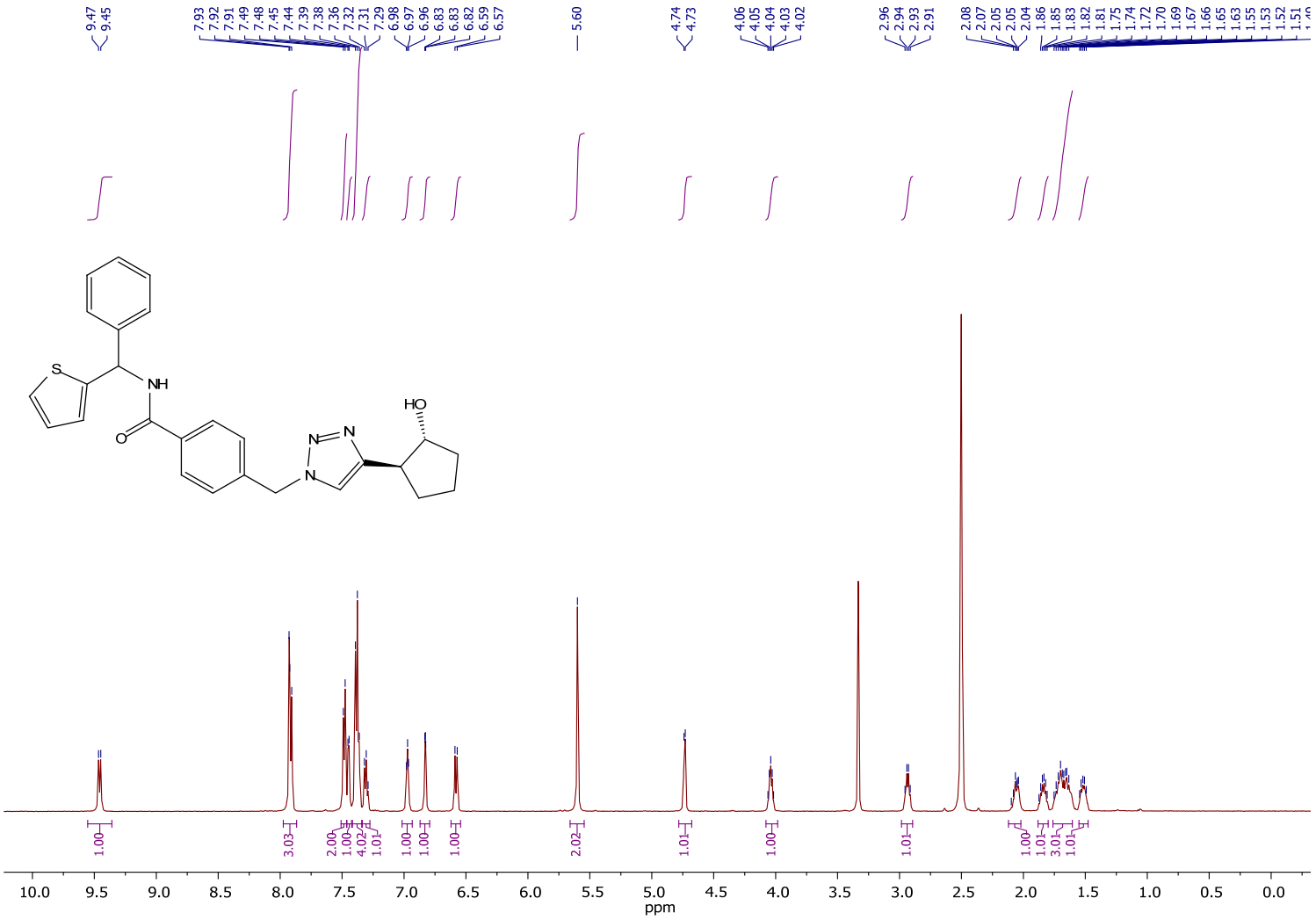

(*R*)-*N*-(1-(4-(4-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)bicyclo[1.1.1]pentane-1-carboxamide (**15**{*2*,*2*,*2*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



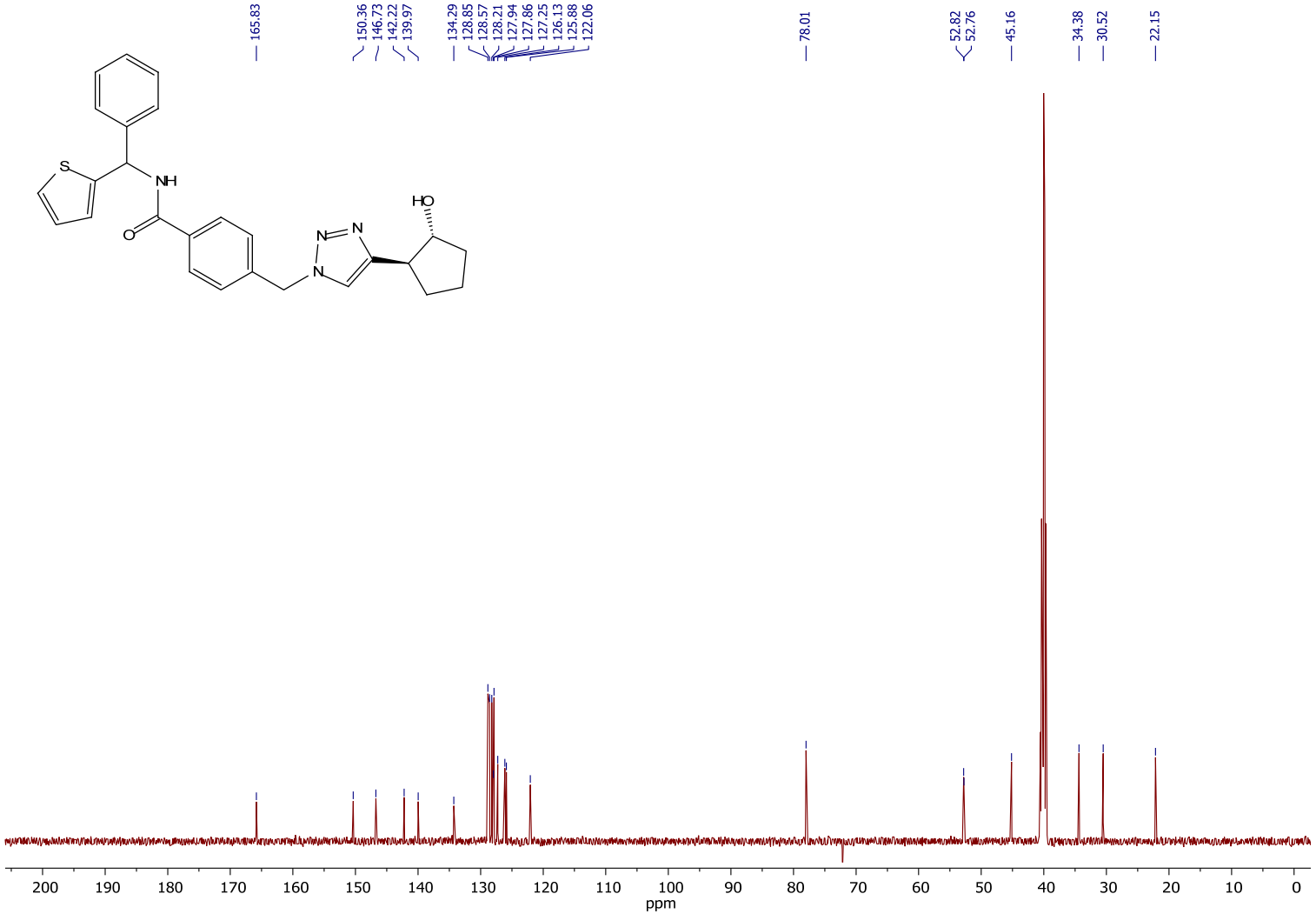

(*R*)-*N*-(1-(4-(4-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)bicyclo[1.1.1]pentane-1-carboxamide (**15**{*2*,*2*,*2*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



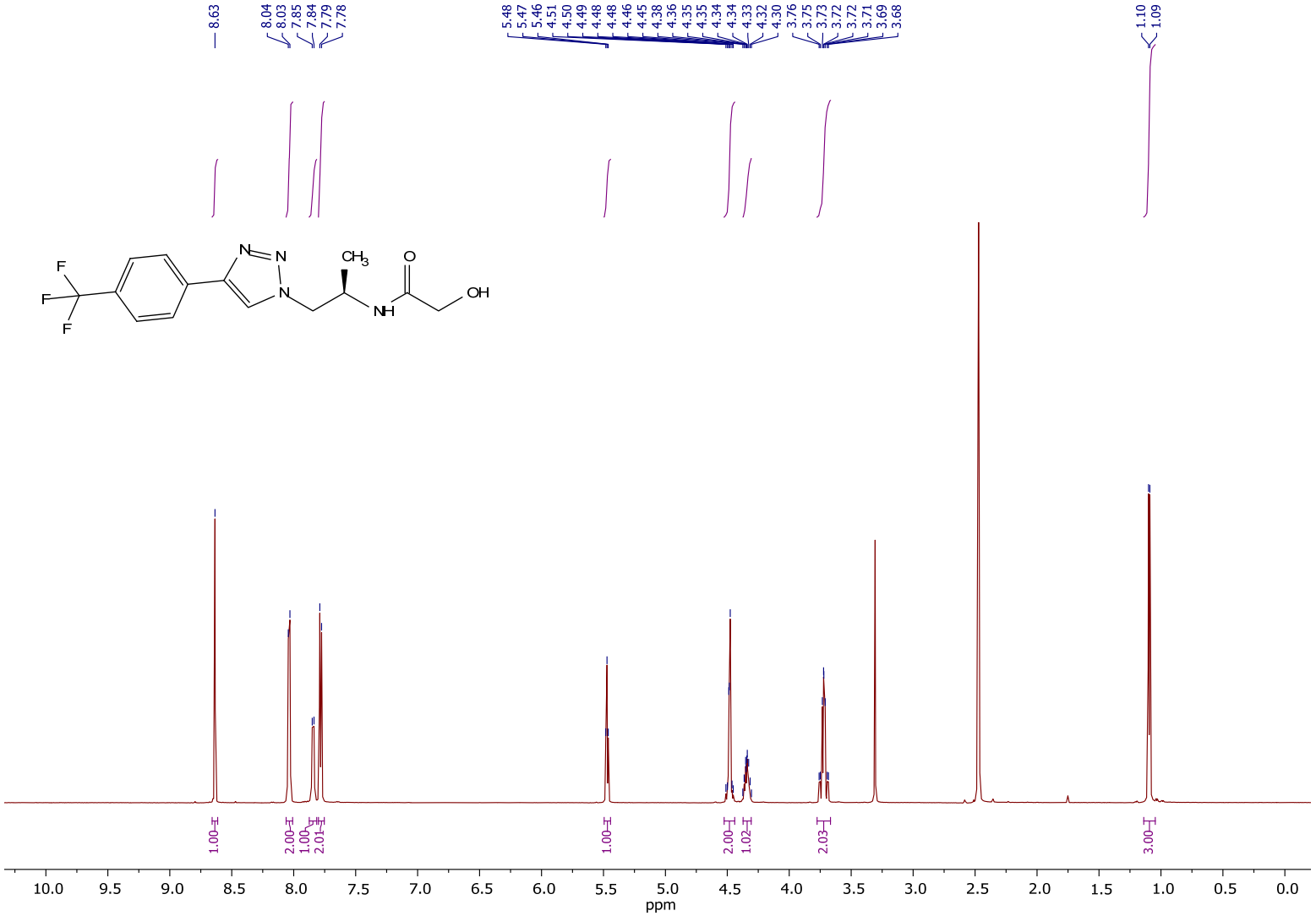

(*R*)-*N*-(1-(4-(4-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)bicyclo[1.1.1]pentane-1-carboxamide (**15**{*2*,*2*,*2*}), $^{19}$F NMR (376 MHz, DMSO)



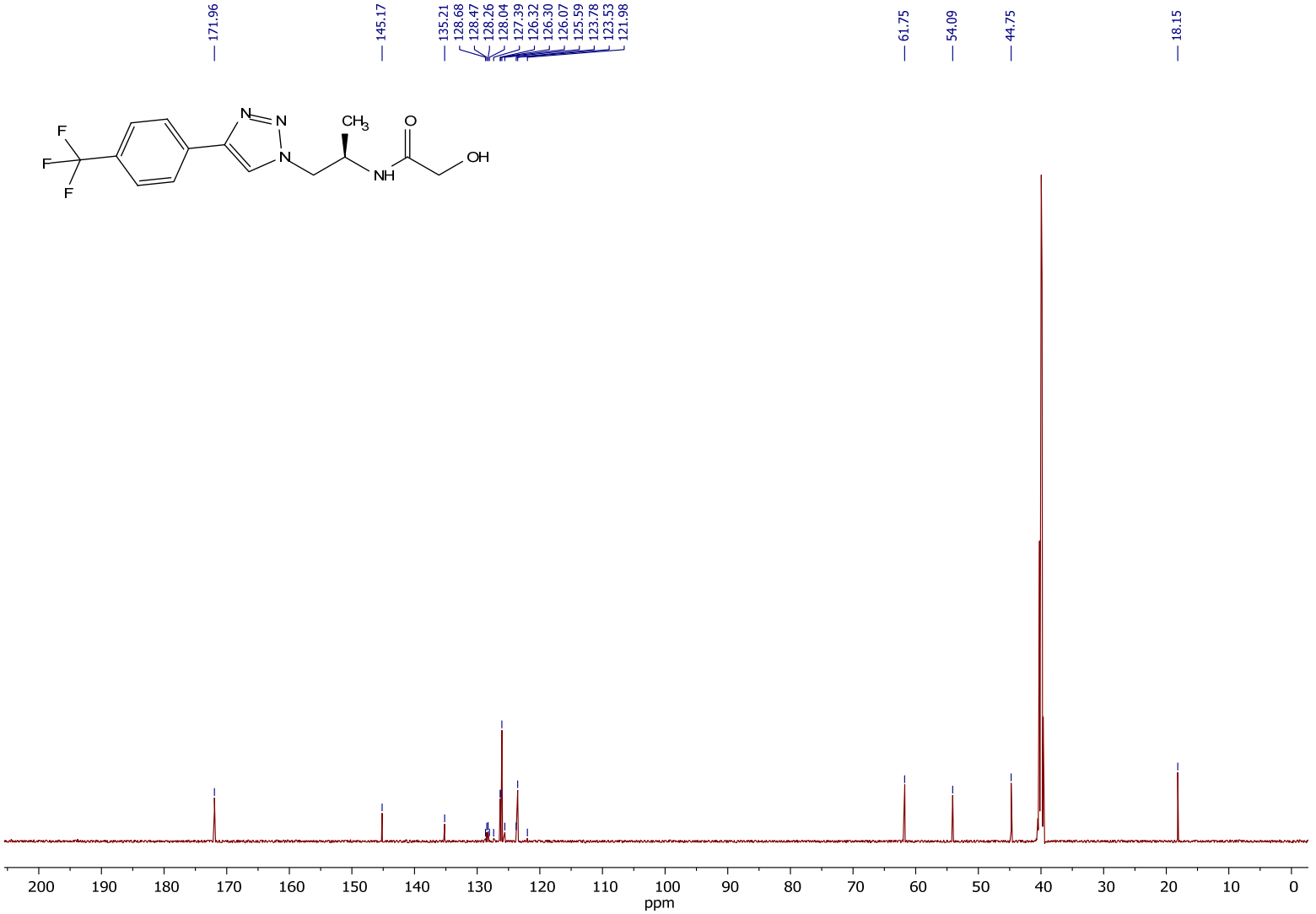

*rac*-4-((4-((1*R*,2*S*)-2-Hydroxycyclopentyl)-1*H*-1,2,3-triazol-1-yl)methyl)-*N*-(phenyl(thiophen-2-yl)methyl)benzamide (**15**{*1*,*2*,*17*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



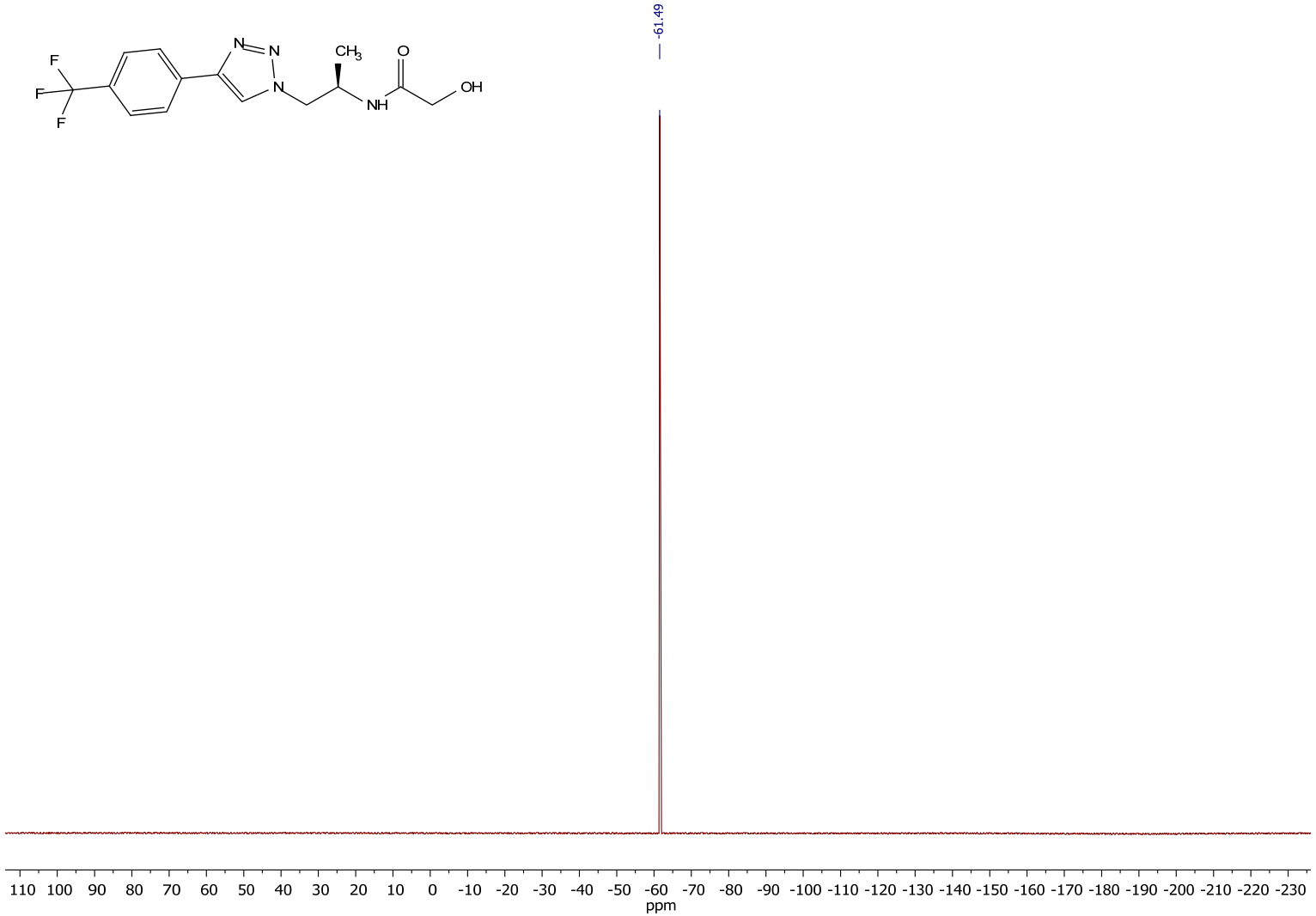

*rac*-4-((4-((1*R*,2*S*)-2-Hydroxycyclopentyl)-1*H*-1,2,3-triazol-1-yl)methyl)-*N*-(phenyl(thiophen-2-yl)methyl)benzamide (**15**{*1*,*2*,*17*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



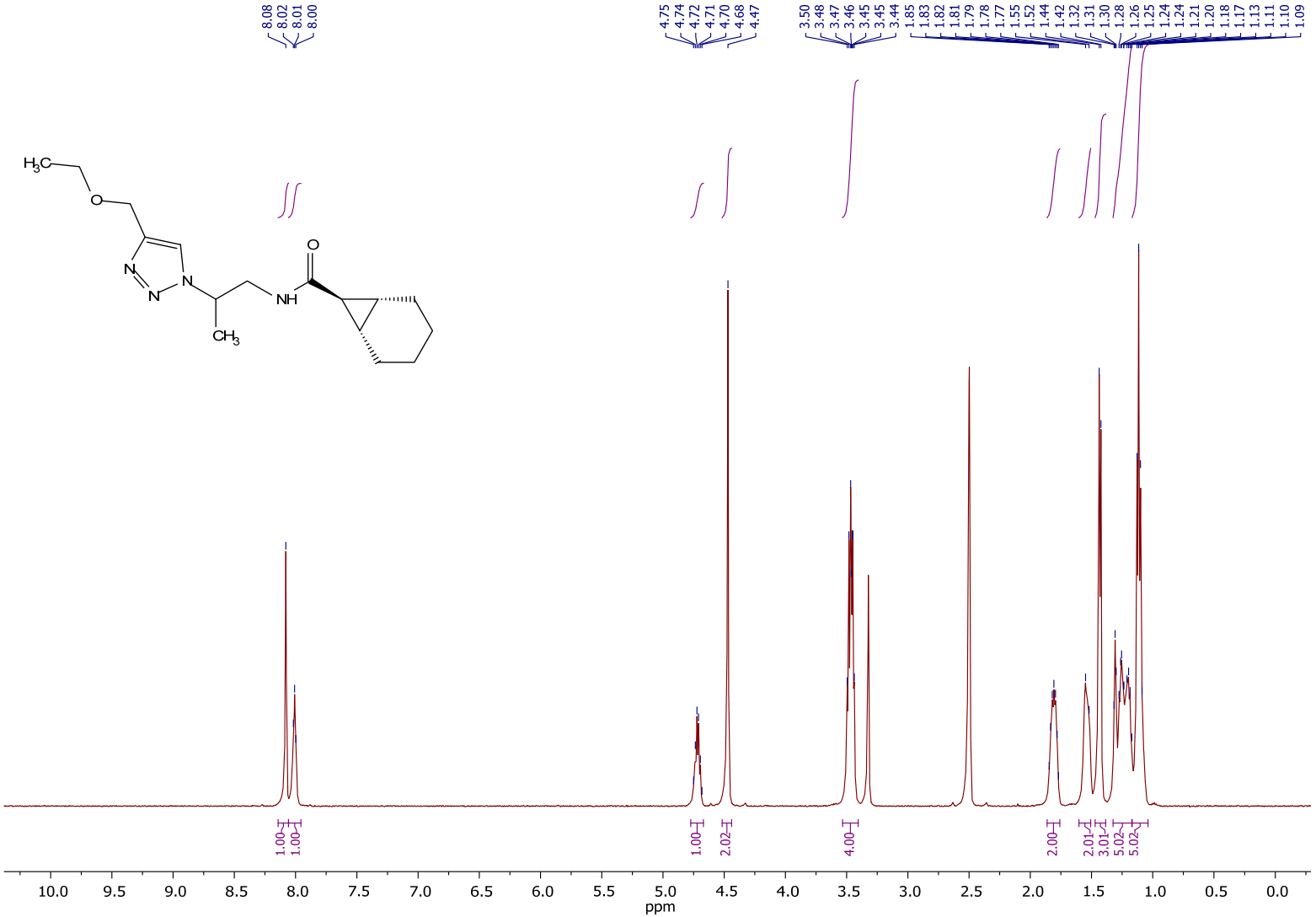

(*R*)-2-Hydroxy-*N*-(1-(4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)acetamide **15**{*2*,*30*,*29*}, $^{1}$H NMR (600 MHz, DMSO-$d_6$)



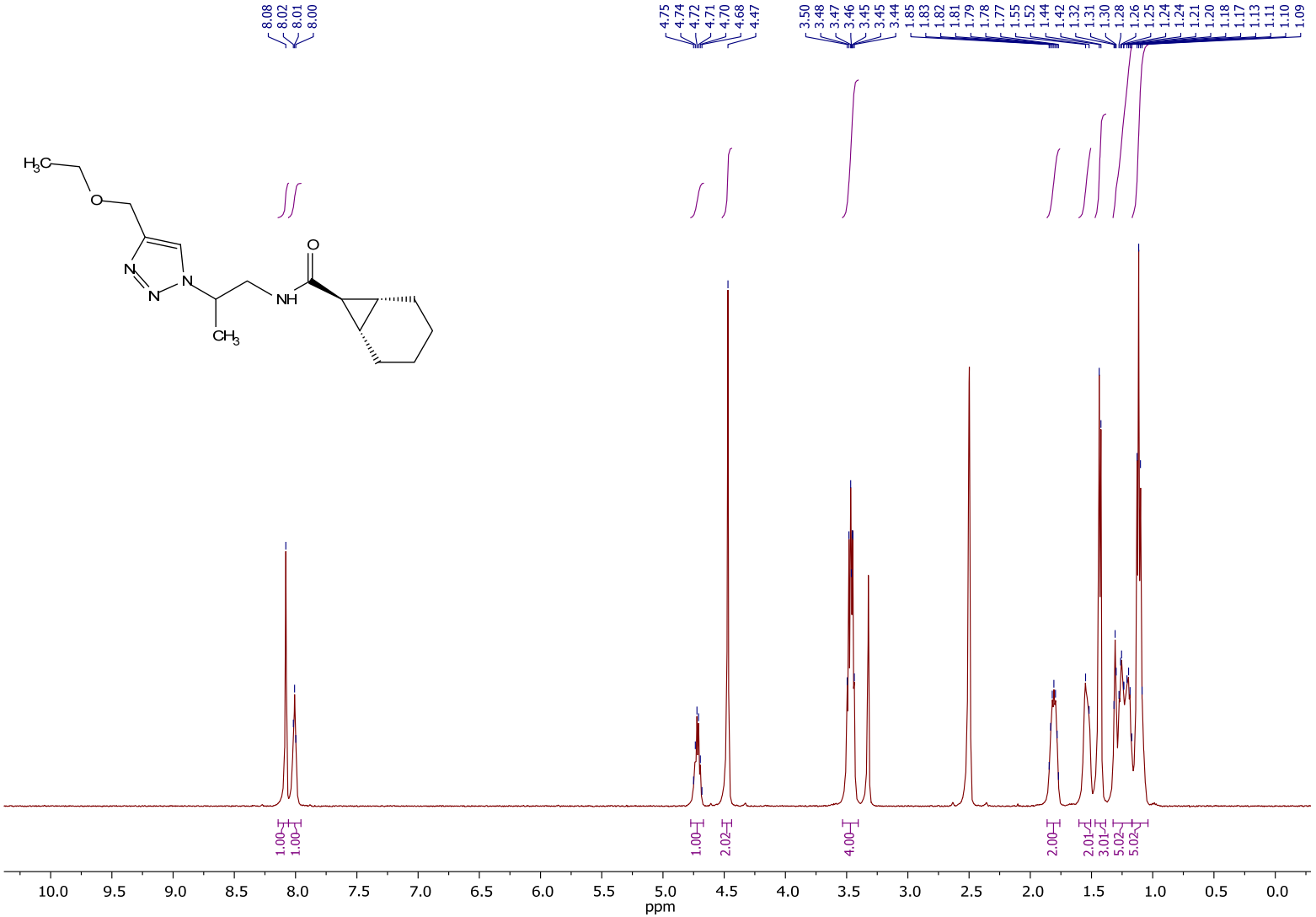

(*R*)-2-Hydroxy-*N*-(1-(4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)acetamide **15**{*2*,*30*,*29*}, $^{13}$C NMR (151 MHz, DMSO-$d_6$)



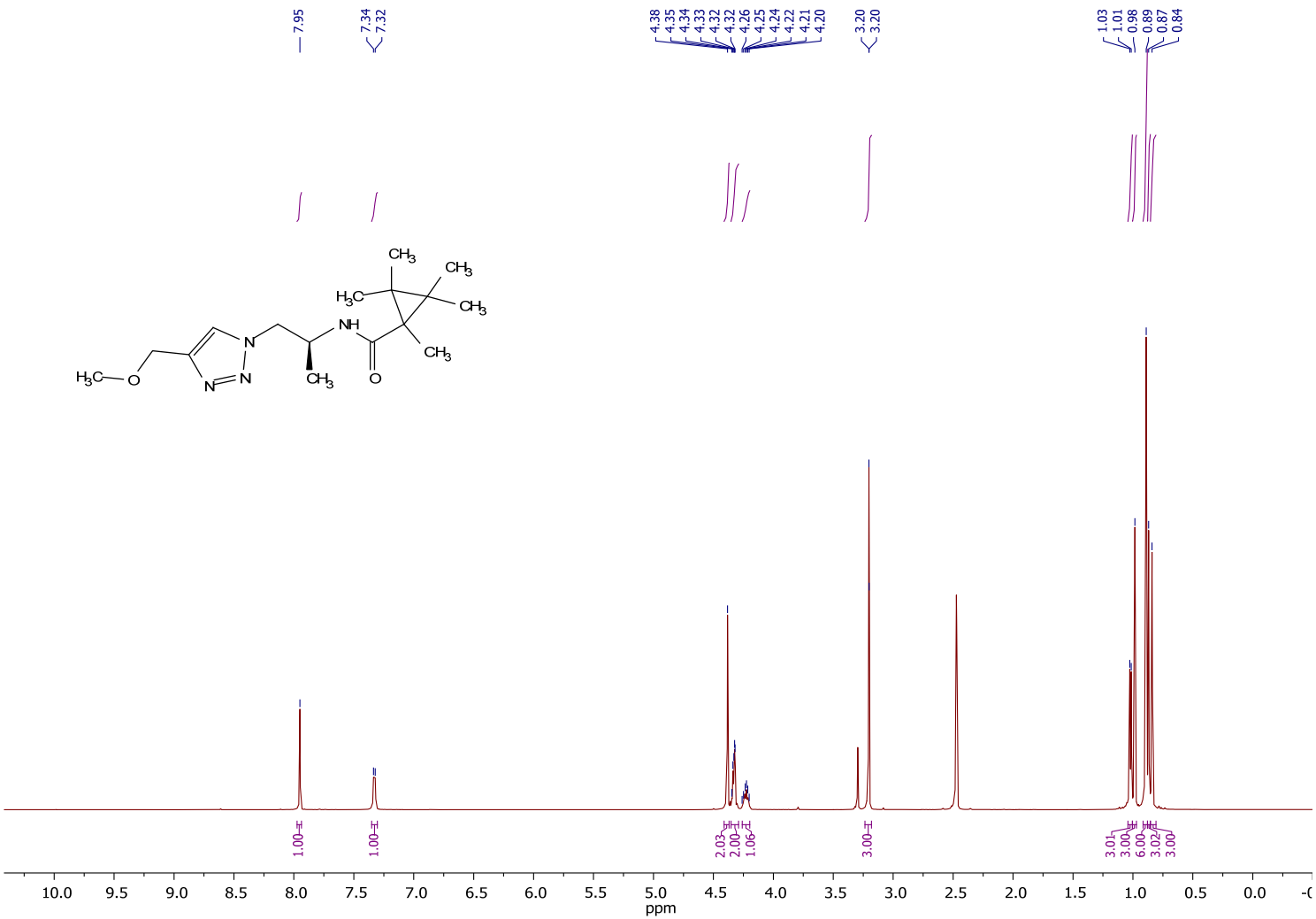

(*R*)-2-Hydroxy-*N*-(1-(4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)acetamide **15**{*2*,*30*,*29*},$^{19}$F NMR (376 MHz, DMSO-$d_6$)



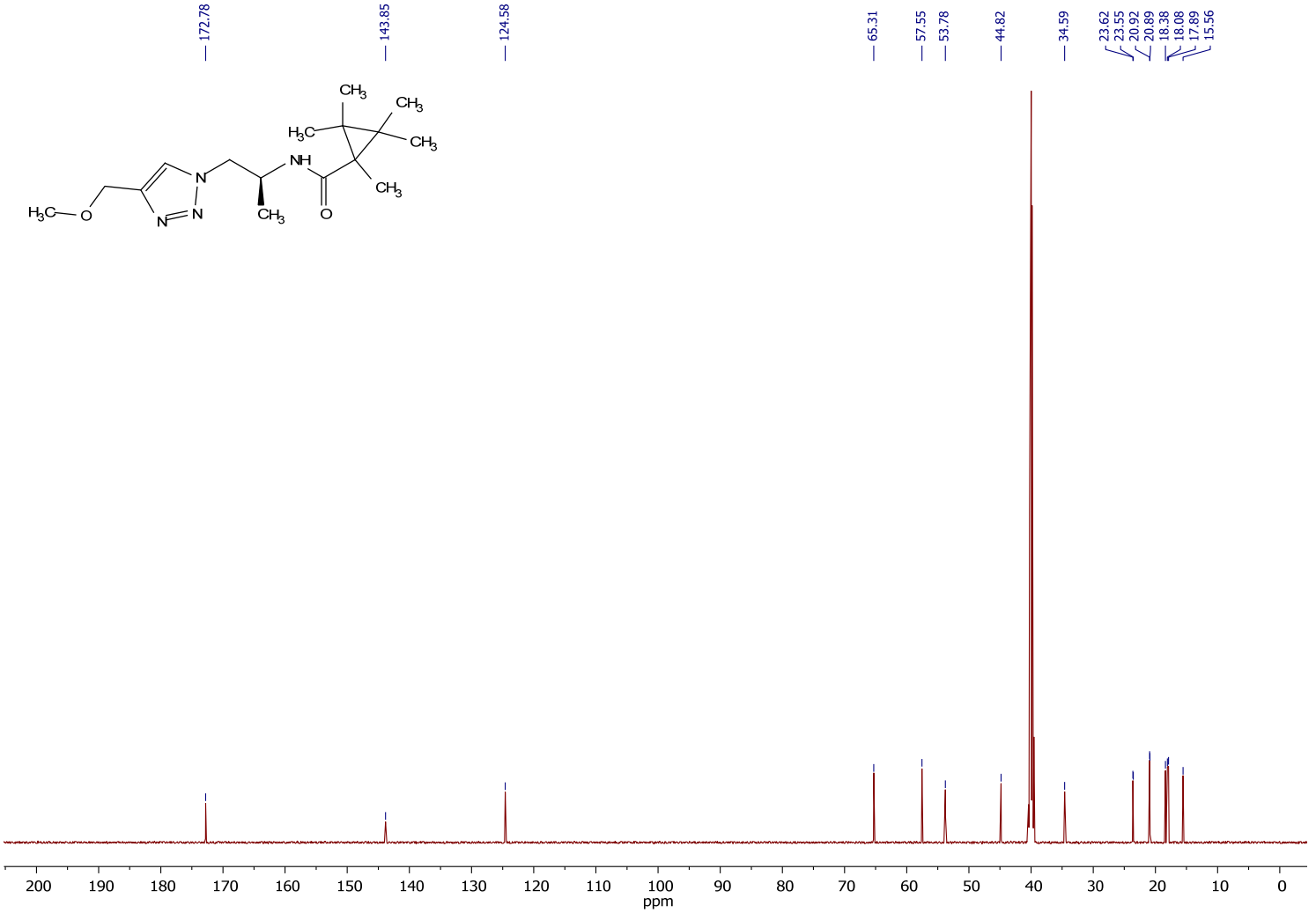

(1*R*,6*S*,7*r*)-*N*-(2-(4-(Ethoxymethyl)-1*H*-1,2,3-triazol-1-yl)propyl)bicyclo[4.1.0]heptane-7-carboxamide (**15**{*4*,*15*,*14*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)



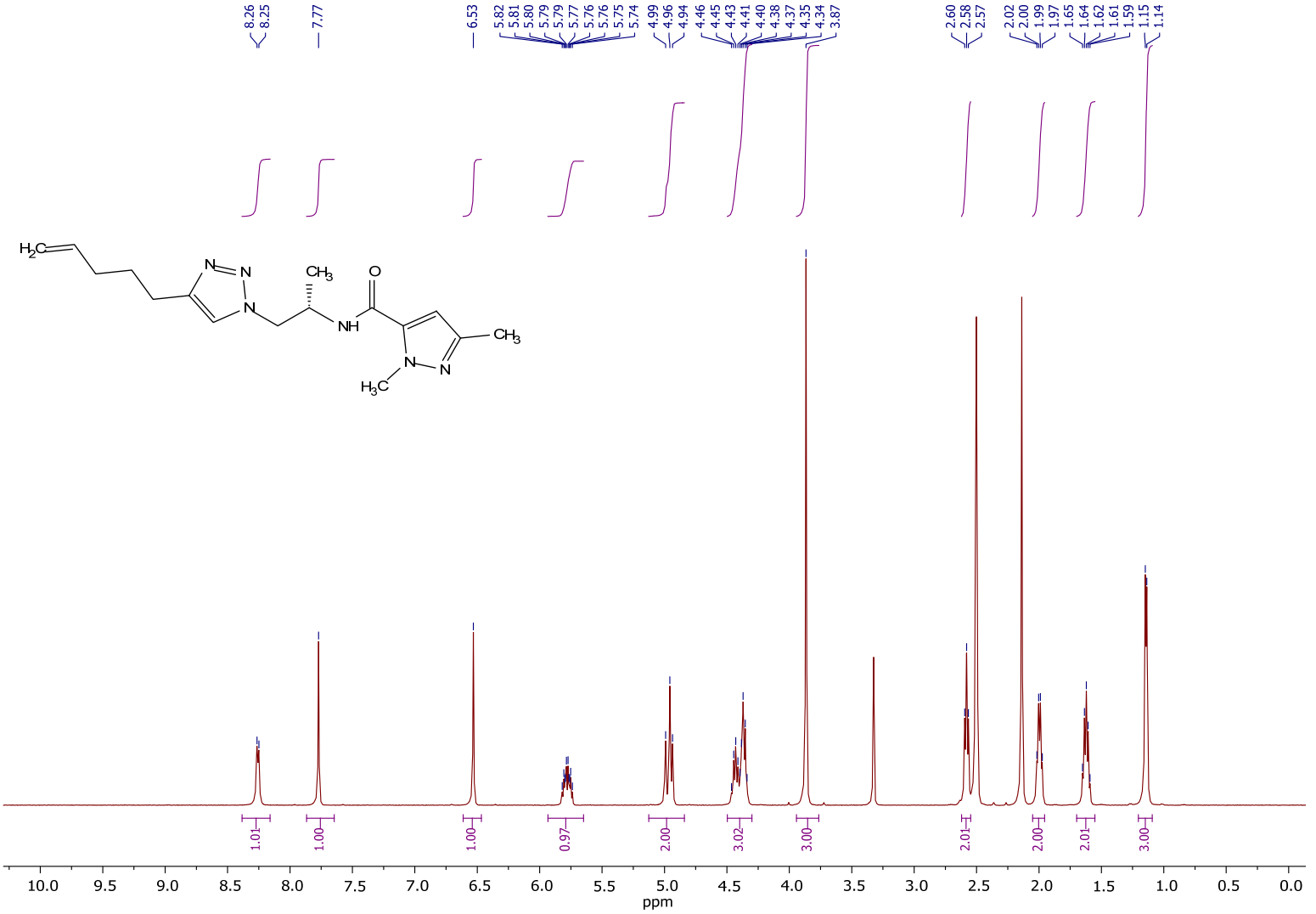

(1*R*,6*S*,7*r*)-*N*-(2-(4-(Ethoxymethyl)-1*H*-1,2,3-triazol-1-yl)propyl)bicyclo[4.1.0]heptane-7-carboxamide (**15**{*4*,*15*,*14*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)



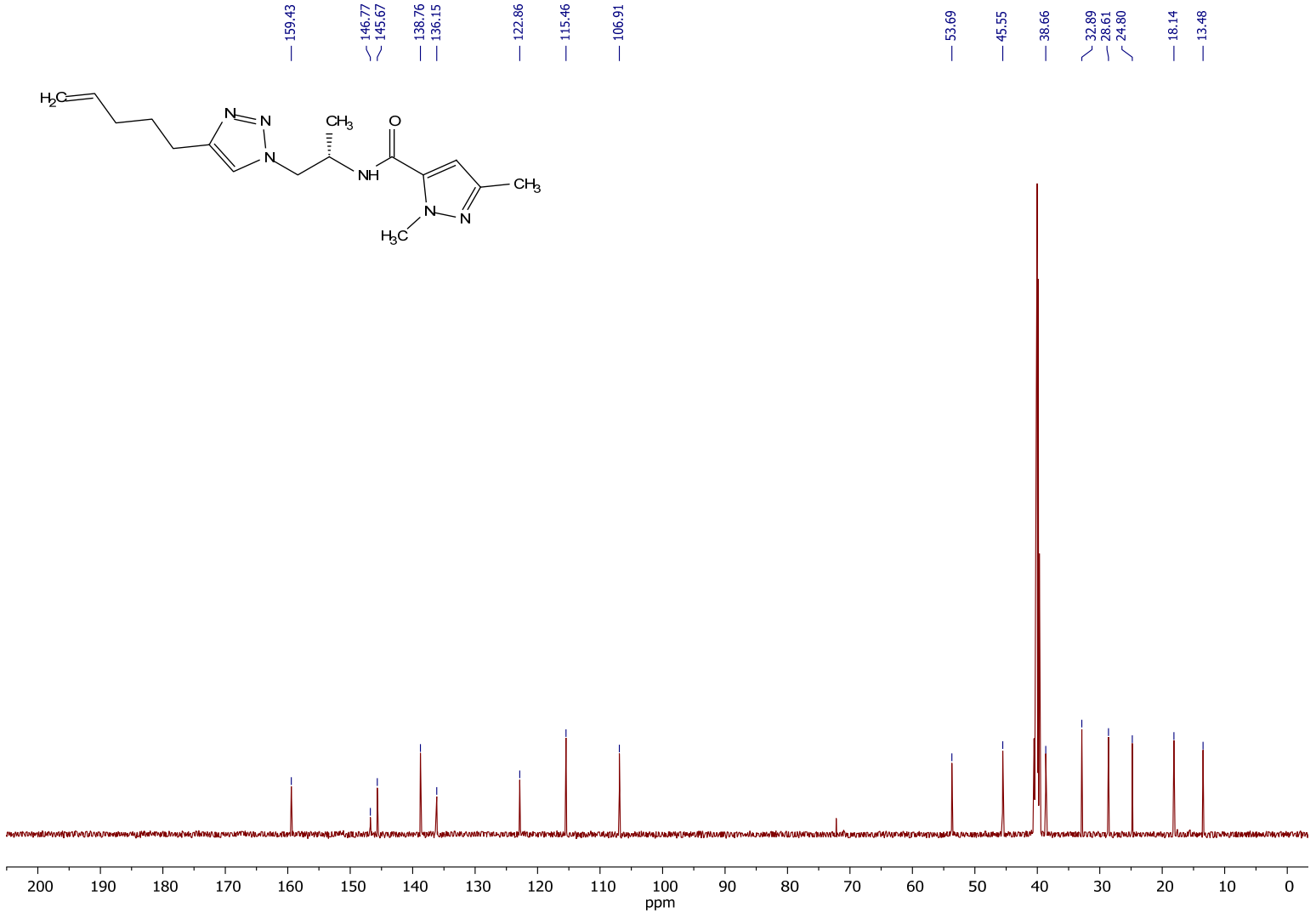

(*S*)-*N*-(1-(4-(Methoxymethyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-1,2,2,3,3-pentamethylcyclopropanecarboxamide (**15**{*6*,*14*,*13*}), $^{1}$H NMR (600 MHz, DMSO-$d_6$)



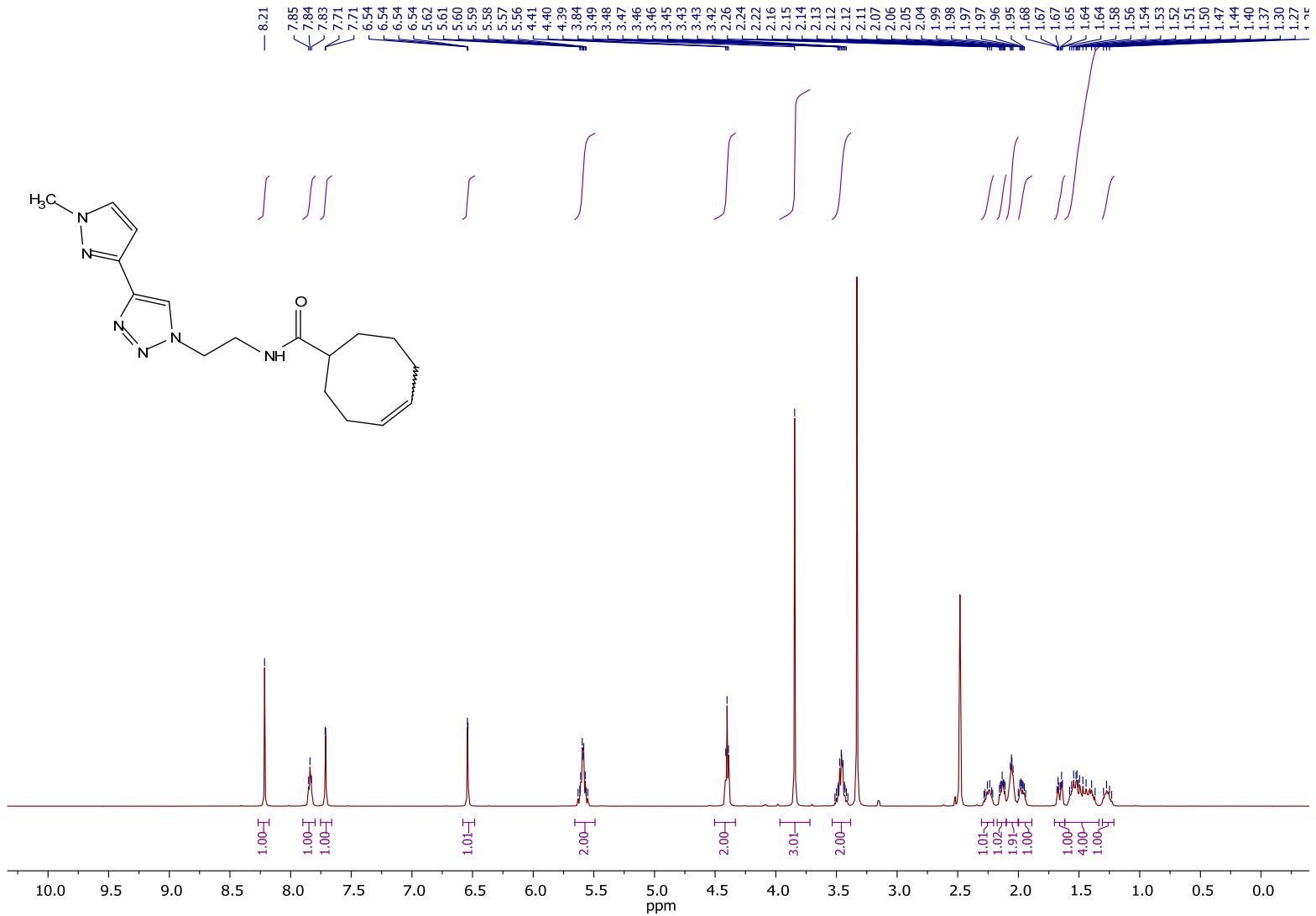

(*S*)-*N*-(1-(4-(Methoxymethyl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-1,2,2,3,3-pentamethylcyclopropanecarboxamide (**15**{*6*,*14*,*13*}), $^{13}$C NMR (151 MHz, DMSO-$d_6$)



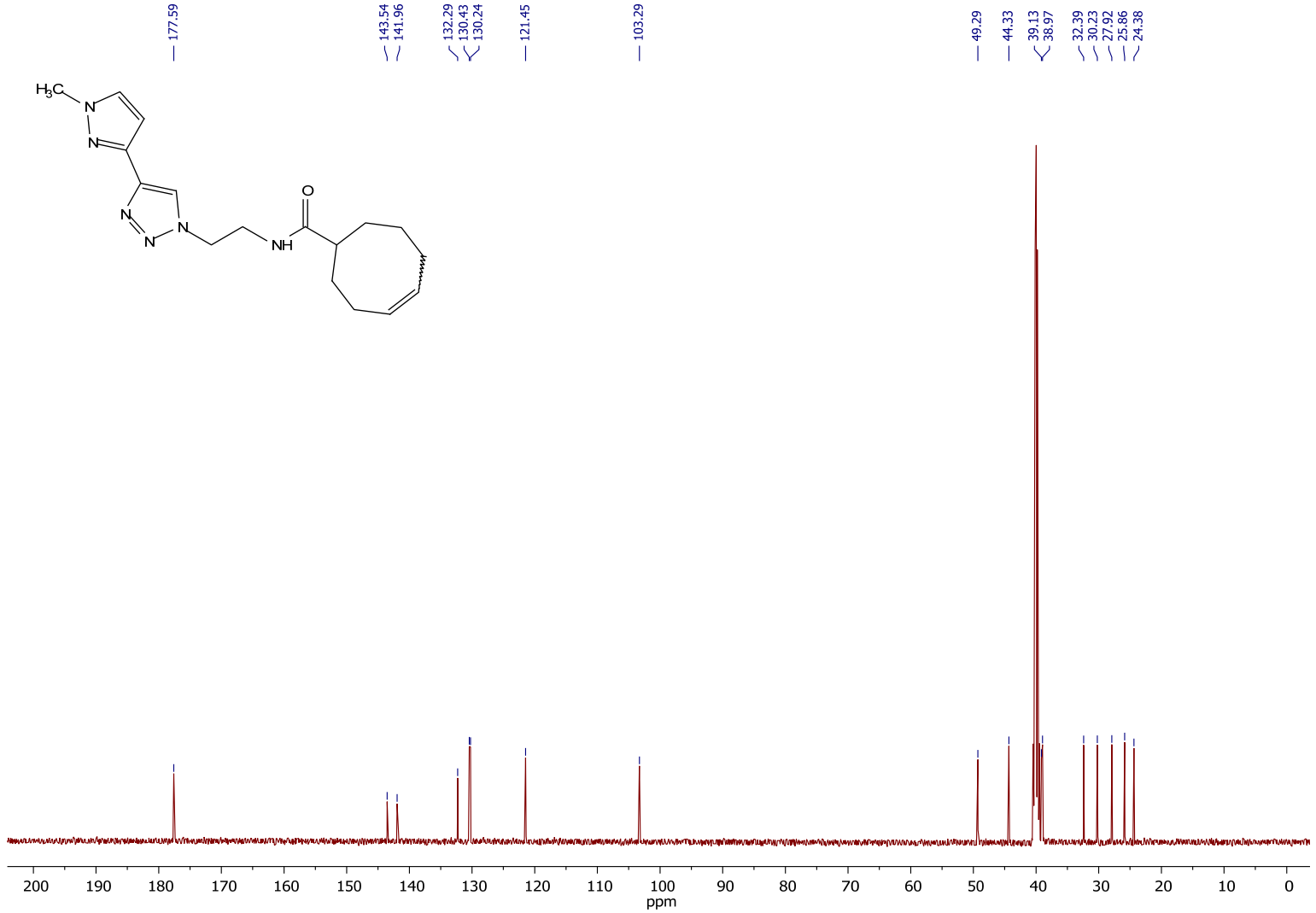

(*S*)-1,3-Dimethyl-*N*-(1-(4-(pent-4-en-1-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-1*H*-pyrazole-5-carboxamide **15**{*6*,*9*,*9*}, $^{1}$H NMR (500 MHz, DMSO-$d_6$)



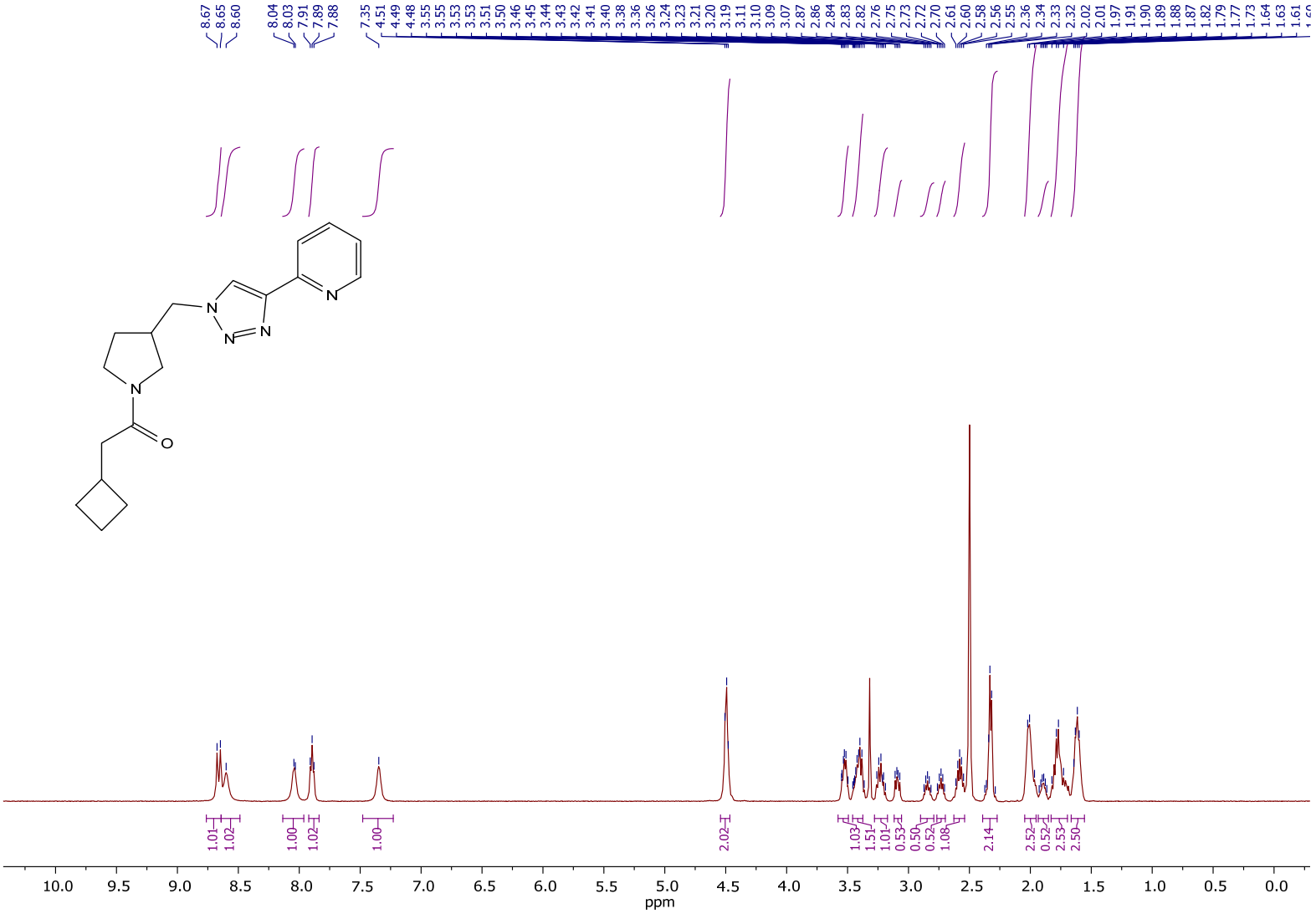

(*S*)-1,3-Dimethyl-*N*-(1-(4-(pent-4-en-1-yl)-1*H*-1,2,3-triazol-1-yl)propan-2-yl)-1*H*-pyrazole-5-carboxamide **15**{*6*,*9*,*9*}, $^{13}$C NMR (126 MHz, DMSO-$d_6$)



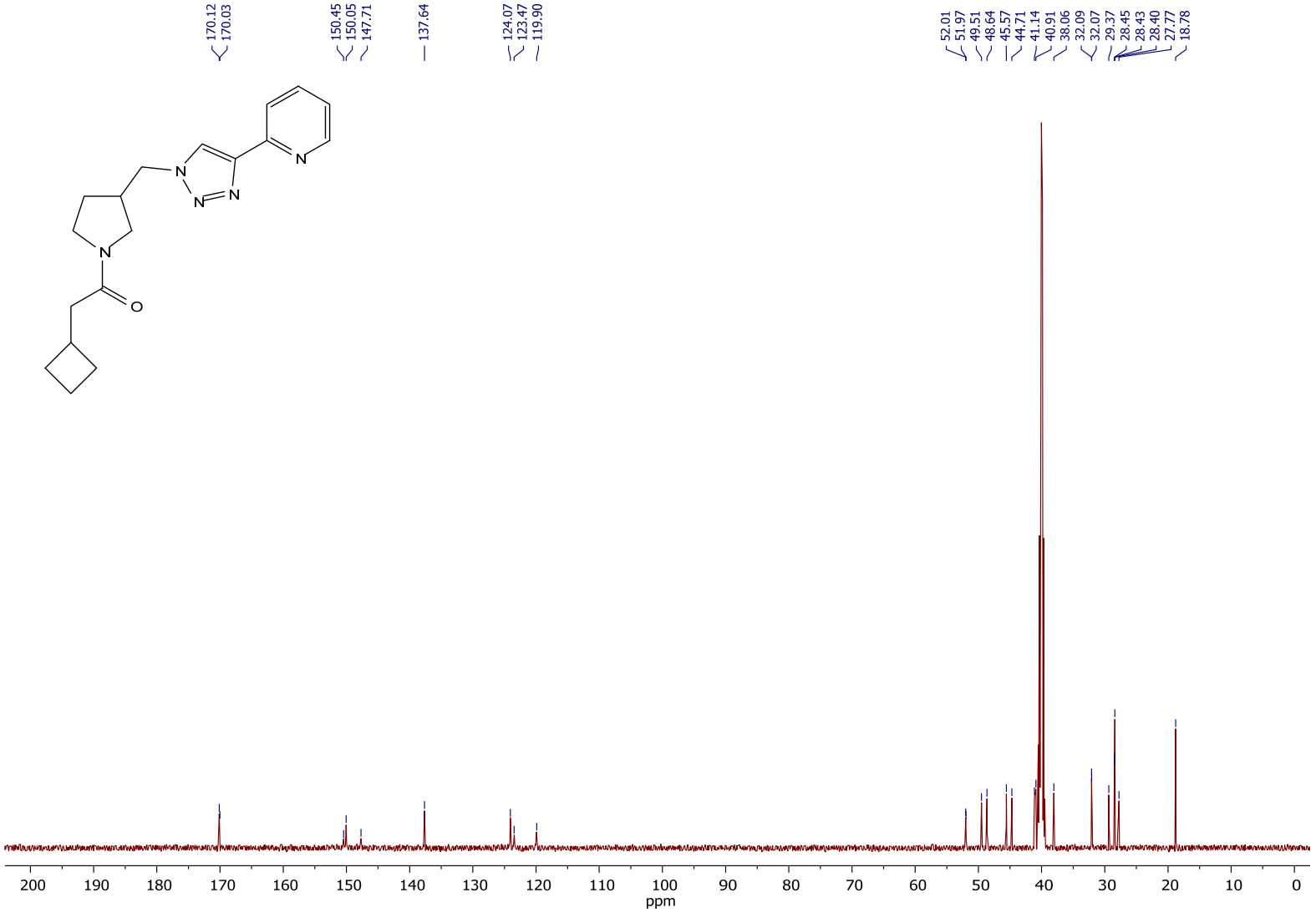

*N*-(2-(4-(1-Methyl-1*H*-pyrazol-3-yl)-1*H*-1,2,3-triazol-1-yl)ethyl)cyclooct-4-enecarboxamide **15**{*3*,*3*,*3*}, $^{1}$H NMR (500 MHz, DMSO-$d_6$)




*N*-(2-(4-(1-Methyl-1*H*-pyrazol-3-yl)-1*H*-1,2,3-triazol-1-yl)ethyl)cyclooct-4-enecarboxamide **15**{*3*,*3*,*3*}, $^{13}$C NMR (126 MHz, DMSO-$d_6$)




2-Cyclobutyl-1-(3-((4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)methyl)pyrrolidin-1-yl)ethanone (**15**{*8*,*10*,*10*}), $^{1}$H NMR (500 MHz, DMSO-$d_6$)




2-Cyclobutyl-1-(3-((4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)methyl)pyrrolidin-1-yl)ethanone (**15**{*8*,*10*,*10*}), $^{13}$C NMR (126 MHz, DMSO-$d_6$)