Supporting Information

Library-to-library synthesis of highly substituted α-aminomethyl tetrazoles via Ugi reaction.

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Table of Contents

Experimental section

1. General methods

Nuclear magnetic resonance spectra (NMR) were recorded on a Bruker Avance 500 spectrometer (^{1}H NMR (500 MHz), ^{13}C NMR (126 MHz)). Chemical shifts for ^{1}H NMR were reported as δ values and coupling constants were in hertz (Hz). The following abbreviations were used for spin multiplicity: s = singlet, d = doublet, t = triplet, dd = double doublet, m = multiplet, bs = broad singlet. Chemical shifts for ^{13}C NMR reported in ppm relative to the solvent peak. Thin layer chromatography was performed on Fluka precoated silica gel plates (0.20 mm thick, particle size 25 μm). Flash chromatography was performed using SiliCycle silica gel type SiliaFlash P60 (230 – 400 mesh) as obtained from Screening Devices or with automated column chromatography using a Reveleris flash purification system purchased from Grace Davison Discovery Sciences. Reveleris pre-fabricated silica cartridges were purchased and used, for automated column chromatography, containing 40 μm silica. Reagents were available from commercial suppliers and used without any purification unless otherwise noted. All isocyanides were made in house by performing the Ugi procedure. Other reagents were purchased from Sigma Aldrich, ABCR, Acros and AK Scientific and were used without further purification. Electrospray ionization mass spectra (ESI-MS) were recorded on a Waters Investigator Semi-prep 15 SFC-MS instrument.

2. General Procedure

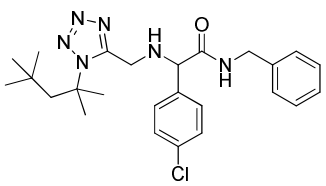
Procedure A (Synthesis of *N*-methyl-2-(((1-methyl-1H-tetrazol-5-yl)methyl)amino) acetamides):

To a stirred solution of α-aminomethyltetrazoles (**A**, 1 equiv.) in methanol (1M) was added aldehyde/ketone (1 equiv.), isocyanide (1 equiv.) and *p*-toluenesulfinic acid (1 equiv.). The reaction was allowed to stir at room temperature for 18 h. The solvents were evaporated under vacuum, the crude mass obtained was purified by flash column chromatography by using Pet-ether/EtOAc as an eluent to give the pure product (**d**).

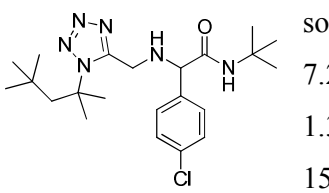
Note: α-aminomethyltetrazoles (**A**) were obtained via Ugi-tetrazole reaction as reported in our previous reports in reference: 1) Patil, P.; de Haan, M.; Kurpiewska, K.; Kalinowska-Tłuścik, J.; Dömling, A., Versatile Protecting-Group Free Tetrazolomethane Amine Synthesis by Ugi Reaction. *ACS Combinatorial Science* **2016,** *18*, 170-175; 2) Zhao, T., Boltjes, A.,

Herdtweck, E., & Doemling, A. (**2013**). Tritylamine as an Ammonia Surrogate in the Ugi Tetrazole Synthesis. Organic Letters, **2013***, 15*, 639-641.

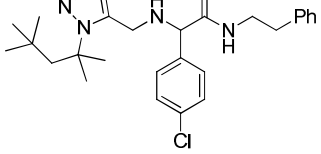
1d: *N*-benzyl-2-(4-chlorophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide: The product was obtained using procedure **A**, 96 % as white solid, M.P. = 138-140 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.6 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.30 – 7.25 (m, 3H), 7.21 – 7.18 (m, 2H), 7.16 (t, *J* = 6.0 Hz, 1H), 4.50 – 4.37 (m, 3H), 4.11 (s, 2H), 1.80 (s, 2H), 1.72 (s, 3H), 1.69 (s, 3H), 0.71 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 152.6, 138.0, 136.5, 134.2, 129.0, 128.9, 128.6, 127.6, 127.4, 65.5, 64.5, 53.1, 43.3, 42.8, 31.4, 30.5, 29.8; SFC-MS (ESI) m/z calcd for $C_{25}H_{33}ClN_6O$ $[M]^+$: 468.24; found $[M-H]^+$:467.30.



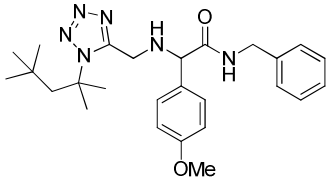
2d: ***N*-(*tert*-butyl)-2-(4-chlorophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:** The product was obtained using procedure **A**, 97 % as white solid, M.P. = 130-132 ^{o}C; ^{1}H NMR (500 MHz, CDCl3) δ 7.34 – 7.29 (m, 4H), 4.24 (s, 1H), 4.12 (s, 2H), 1.88 (s, 2H), 1.76 (s, 6H), 1.31 (s, 9H), 0.74 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 152.7, 136.9, 134.2, 129.0, 128.8, 66.2, 64.6, 53.3, 51.2, 43.0, 31.6, 30.6, 30.0, 29.9, 28.6; SFC-MS (ESI) m/z calcd for $C_{22}H_{35}ClN_6O$ $[M]^+$: 434.26; found $[M-H]^+$:433.22.



3d : 2-(4-chlorophenyl)-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1H-tetrazol-5-yl)methyl)amino)acetamide: The product was obtained using procedure **A**, 98 % as white solid, M.P. = 129-131 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.23 (m, 7H), 7.10 – 7.05 (m, 2H), 6.66 (t, *J* = 5.9 Hz, 1H), 4.32 (s, 1H), 4.05 (s, 2H), 3.54 (q, *J* = 6.7 Hz, 2H), 2.79 (t, *J* = 6.9 Hz, 2H), 1.85 (s, 2H), 1.74 (s, 3H), 1.72 (s, 3H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 152.7, 138.4, 136.5, 134.3, 129.1, 129.0, 128.6, 126.5, 65.6, 64.5, 53.2, 42.8, 40.4, 35.4, 31.6, 30.6, 29.9; SFC-MS (ESI) m/z calcd for $C_{26}H_{35}ClN_6O$ $[M]^+$: 482.26; found $[M-H]^+$: 481.28.

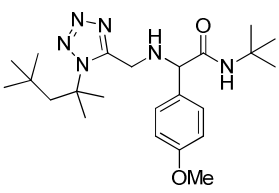


4d: *N*-benzyl-2-(4-methoxyphenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide : The product was obtained using procedure **A**, 97 % as white solid, M.P. = 100-102 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.5 Hz, 2H), 7.33 – 7.26 (m, 4H), 7.23 – 7.20 (m, 2H), 7.10 (t, *J* = 6.0 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.50 – 4.41 (m, 3H), 4.12 (s, 2H), 3.81 (s, 3H), 1.84 (d, *J* = 1.9 Hz, 2H), 1.74 (s, 3H), 1.70 (s, 3H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 159.7, 152.8, 138.1, 129.9,

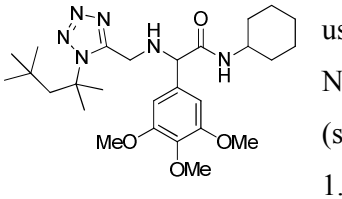


128.8, 128.6, 127.6, 127.4, 114.3, 65.9, 64.5, 55.3, 53.1, 43.3, 42.9, 31.5, 30.5, 29.9, 29.9.SFC-MS (ESI) m/z calcd for $C_{26}H_{36}N_6O_2$ $[M]^+$: 464.29; found $[M-H]^+$: 463.36.

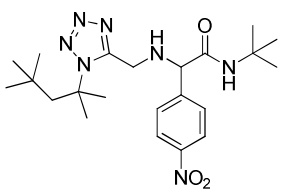
5d: *N*-(*tert*-butyl)-2-(4-methoxyphenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide : The product was obtained using procedure **A**, 97 % as white solid, M.P. = 102-104 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 4.20 (s, 1H), 4.10 (s, 2H), 3.78 (s, 3H), 1.87 (s, 2H), 1.75 (s, 3H), 1.74 (s, 3H), 1.31 (s, 9H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 159.4, 152.8, 130.4, 128.7, 114.2, 66.3, 64.4, 55.2, 53.1, 50.9, 42.9, 31.5, 30.5, 29.9, 29.8, 28.6. SFC-MS (ESI) m/z calcd for $C_{23}H_{38}N_5O_2$ $[M]^+$: 430.31; found $[M-H]^+$: 429.34.



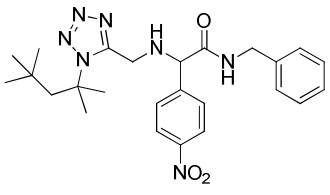
6d: *N*-cyclohexyl-2-(3,4,5-trimethoxyphenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide: The product was obtained using procedure **A**, 99 % as white solid, M.P. = 142-144 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 6.64 (s, 2H), 6.63 – 6.57 (m, 1H), 4.32 (s, 1H), 4.16 (s, 2H), 3.86 (s, 6H), 3.84 (s, 3H), 3.72 – 3.70 (m, 1H), 1.90 (s, 2H), 1.88-1.84 (m, 2H), 1.78 (s, 3H), 1.77 (s, 3H), 1.73 – 1.67 (m, 2H), 1.64 – 1.59 (m, 1H), 1.39 – 1.34 (m, 2H), 1.20 – 1.13 (m, 3H), 0.76 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 153.5, 153.1, 152.8, 133.7, 104.6, 66.6, 64.5, 60.8, 56.1, 55.9, 53.2, 48.0, 43.0, 33.0, 31.6, 30.6, 30.0, 25.4, 24.7; SFC-MS (ESI) m/z calcd for $C_{27}H_{44}N_6O_4$ $[M]^+$: 516.34; found $[M-H]^+$: 515.31.



7d: *N*-(*tert*-butyl)-2-(4-nitrophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide: The product was obtained using procedure **A**, 94 % as white solid, M.P. = 134-136 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 6.74 (s, 1H), 4.40 (s, 1H), 4.17 (s, 2H), 1.89 (s, 2H), 1.79 (s, 6H), 1.32 (s, 9H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 152.5, 147.7, 145.7, 128.4, 123.9, 66.0, 64.7, 53.3, 51.5, 42.9, 31.6, 30.6, 30.0, 29.9, 28.6; SFC-MS (ESI) m/z calcd for $C_{22}H_{35}N_7O_3$ $[M]^+$: 445.28; found $[M-H]^+$: 446.37.

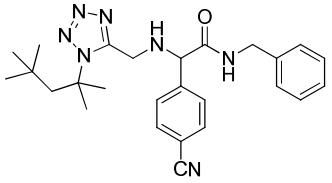


8d: *N*-benzyl-2-(4-nitrophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamid: The product was obtained using procedure **A**, 94 % as white solid, M.P. = 135-137 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.19 (d,

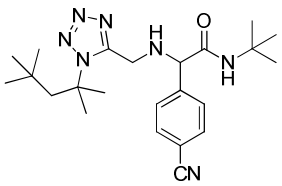


J = 8.7 Hz, 2H), 7.64 (d, *J* = 8.7 Hz, 2H), 7.46 (t, *J* = 6.0 Hz, 1H), 7.30 – 7.26 (m, 3H), 7.22 – 7.18 (m, 2H), 4.61 (s, 1H), 4.49 – 4.37 (m, 2H), 4.16 (s, 2H), 1.85 (s, 2H), 1.74 (s, 3H), 1.72 (s, 3H), 0.71 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 152.5, 147.8, 145.2, 137.8, 65.5, 64.7, 53.2, 43.5, 42.9, 30.5, 29.9; SFC-MS (ESI) m/z calcd for $C_{25}H_{33}N_7O_3$ $[M]^+$: 479.26; found $[M\text{-}H]^+$: 478.32.

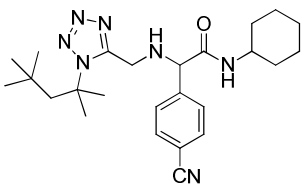
9d: *N*-benzyl-2-(4-cyanophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide: The product was obtained using procedure **A**, 95 % as white solid, M.P. = 106-108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.38 (t, *J* = 6.0 Hz, 1H), 7.32 – 7.29 (m, 3H), 7.22 – 7.19 (m, 2H), 4.56 (s, 1H), 4.51 – 4.38 (m, 2H), 4.15 (s, 2H), 2.94 (s, 1H), 1.86 (s, 2H), 1.75 (s, 3H), 1.73 (s, 3H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 152.5, 143.2, 137.8, 132.5, 128.6, 128.3, 127.6, 127.5, 118.3, 112.2, 65.6, 64.7, 53.1, 43.4, 42.8, 31.5, 30.5, 29.8; SFC-MS (ESI) m/z calcd for $C_{26}H_{33}N_7O$ $[M]^+$: 459.27; found $[M\text{-}H]^+$: 458.33.



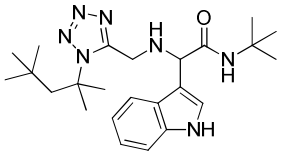
10d: *N*-(*tert*-butyl)-2-(4-cyanophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide: The product was obtained using procedure **A**, 96 % as white solid, M.P. = 130.-132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 6.67 (s, 1H), 4.33 (s, 1H), 4.15 (s, 2H), 2.83 (s, 1H), 1.89 (s, 2H), 1.77 (s, 6H), 1.32 (s, 9H), 0.74 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.2, 152.5, 143.7, 132.5, 128.2, 118.4, 112.0, 66.1, 64.6, 53.2, 51.3, 42.8, 31.5, 30.5, 29.9, 29.8, 28.5; SFC-MS (ESI) m/z calcd for $C_{23}H_{35}N_7O$ $[M]^+$: 425.29; found $[M\text{-}H]^+$: 424.33.



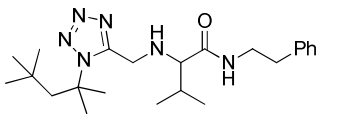
11d: 2-(4-cyanophenyl)-*N*-cyclohexyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:The product was obtained using procedure **A**, 99 % as white solid, M.P. = 124-126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 4.42 (s, 1H), 4.16 (s, 2H), 3.77 – 3.67 (m, 1H), 1.88 (s, 2H), 1.86 – 1.80 (m, 2H), 1.76 (s, 6H), 1.71 – 1.55 (m, 3H), 1.37-1.28 (m, 2H), 1.19-1.05 (m, 3H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 152.5, 143.5, 132.6, 128.3, 118.4, 112.2, 65.8, 64.7, 53.3, 48.3, 43.0, 33.0, 32.8, 31.6, 30.6, 30.0, 29.9, 25.3, 24.7; SFC-MS (ESI) m/z calcd for $C_{25}H_{37}N_7O$ $[M]^+$: 451.31; found $[M+Na]^+$: 474.39.



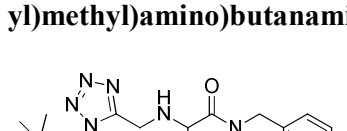
12d: *N*-(*tert*-butyl)-2-(1H-indol-3-yl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide: The product was obtained using procedure **A**, 73 % as white solid, M.P. = 158-160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.15 – 7.10 (m, 1H), 7.07 – 7.03 (m, 1H), 7.00 (d, *J* = 2.5 Hz, 1H), 6.76 (s, 1H), 4.58 (s, 1H), 4.20 – 4.10 (m, 2H), 1.82 (s, 2H), 1.70 (s, 3H), 1.66 (s, 3H), 1.31 (s, 9H), 0.69 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 153.2, 136.7, 125.5, 124.4, 122.2, 119.7, 119.2, 112.1, 111.7, 64.5, 59.8, 53.1, 51.1, 42.7, 31.5, 30.5, 29.9, 29.8, 28.6; SFC-MS (ESI) m/z calcd for $C_{24}H_{37}N_7O$ $[M]^+$: 439.31; found $[M\text{-}H]^+$: 438.24.



13d: 3-methyl-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)butanamide: The product was obtained using procedure **A**, 97 % as white solid, M.P. = 118-120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.25 – 7.19 (m, 3H), 7.02 (t, *J* = 6.0 Hz, 1H), 4.07 (d, *J* = 15.2 Hz, 1H), 3.93 (d, *J* = 15.2 Hz, 1H), 3.68 – 3.61 (m, 1H), 3.60 – 3.52 (m, 1H), 2.92 (d, *J* = 5.4 Hz, 1H), 2.90 – 2.81 (m, 2H), 2.05 – 2.00 (m, 1H), 1.90 (s, 2H), 1.77 (s, 6H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.77 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 152.9, 138.7, 128.6, 128.5, 126.4, 68.2, 64.5, 53.2, 43.7, 40.1, 35.7, 31.5, 30.6, 30.0, 29.9, 19.4, 18.3; SFC-MS (ESI) m/z calcd for $C_{23}H_{38}N_6O$ $[M]^+$: 414.31; found $[M\text{-}H]^+$: 413.35.



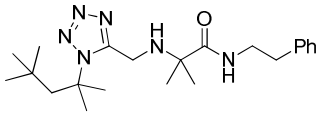
14d: *N*-benzyl-3-methyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)butanamide: The product was obtained using procedure **A**, 97 % as white solid, M.P. = 92-94 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 5H), 4.55 (dd, *J* = 14.6, 6.3 Hz, 1H), 4.44 (dd, *J* = 14.6, 5.7 Hz, 1H), 4.15 (d, *J* = 15.1 Hz, 1H), 4.01 (d, *J* = 15.0 Hz, 1H), 3.04 (d, *J* = 5.3 Hz, 1H), 2.38 (s, 1H), 2.16 – 2.08 (m, 1H), 1.88 (s, 2H), 1.75 (s, 3H), 1.74 (s, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.75 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 152.8, 138.4, 128.6, 127.8, 127.4, 68.4, 64.5, 53.2, 43.9, 43.1, 31.6, 31.5, 30.6, 29.9, 19.4, 18.3; SFC-MS (ESI) m/z calcd for $C_{22}H_{36}N_6O$ $[M]^+$: 400.30; found $[M\text{-}H]^+$: 399.30.



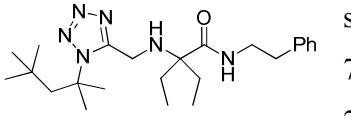
15d: *N*-benzyl-4-methyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)pentanamide: The product was obtained using procedure **A**, 85 % as oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 6.0 Hz, 1H), 7.32 –

7.23 (m, 5H), 4.52 (dd, *J* = 14.7, 6.3 Hz, 1H), 4.41 (dd, *J* = 14.7, 5.8 Hz, 1H), 4.11 (d, *J* = 15.2 Hz, 1H), 4.00 (d, *J* = 15.1 Hz, 1H), 3.27 (dd, *J* = 8.5, 5.4 Hz, 1H), 2.36 (s, 1H), 1.84 (s, 2H), 1.82 – 1.75 (m, 1H), 1.73 (s, 3H), 1.71 (s, 3H), 1.67 – 1.59 (m, 1H), 1.54 – 1.47 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 152.8, 138.4, 128.7, 127.7, 127.4, 64.5, 61.3, 53.2, 43.7, 43.1, 43.0, 31.5, 30.6, 30.0, 29.9, 24.9, 23.0, 22.1.SFC-MS (ESI) m/z calcd for $C_{23}H_{38}N_6O$ $[M]^+$: 414.31; found $[M\text{-}H]^+$: 413.25.

16d: 2-methyl-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)propenamide: The product was obtained using procedure **A**, 90 % as white solid, M.P. = 52-54 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, *J* = 6.1 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.21 – 7.15 (m, 3H), 3.98 (s, 2H), 3.52 (d, *J* = 7.1 Hz, 2H), 2.82 (t, *J* = 7.1 Hz, 2H), 1.89 (s, 2H), 1.76 (s, 6H), 1.39 (s, 6H), 0.77 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.7, 153.5, 138.7, 128.6, 128.4, 126.3, 64.3, 59.0, 53.1, 40.3, 39.6, 35.5, 31.5, 30.6, 29.9, 25.3; SFC-MS (ESI) m/z calcd for $C_{22}H_{36}N_6O$ $[M]^+$: 400.30; found $[M\text{-}H]^+$: 399.34.



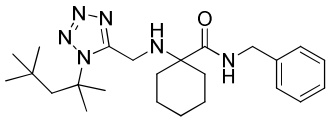
17d: 2-ethyl-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)butanamide: The product was obtained using procedure **A**, 79 % as white solid, M.P. = 102-104 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 1H), 7.27 – 7.23 (m, 2H), 7.19 – 7.15 (m, 3H), 3.90 (s, 2H), 3.55 – 3.49 (m, 2H), 2.80 (t, *J* = 7.2 Hz, 2H), 1.88 (s, 2H), 1.82 – 1.75 (m, 8H), 1.68 (dd, *J* = 14.6, 7.4 Hz, 2H), 0.82 (t, *J* = 7.5 Hz, 6H), 0.75 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 153.2, 138.7, 128.6, 128.5, 126.3, 65.2, 64.2, 53.1, 40.3, 38.4, 35.8, 31.6, 30.6, 30.0, 26.7, 7.8; SFC-MS (ESI) m/z calcd for $C_{24}H_{40}N_6O$ $[M]^+$: 428.33; found $[M\text{-}H]^+$: 427.36.



18d: *N*-phenethyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino) cyclopentanecarboxamide.The product was obtained using procedure **A**, 37 % as white solid, M.P. = 130-132 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 1H), 7.26 – 7.21 (m, 2H), 7.20 – 7.12 (m, 3H), 3.88 (s, 2H), 3.54 – 3.47 (m, 2H), 2.80 (t, *J* = 7.2 Hz, 2H), 2.18 – 2.11 (m, 2H), 1.84 (s, 2H), 1.83 – 1.77 (m, 2H), 1.75 – 1.62 (m, 10H), 0.73 (d, *J* = 0.9 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 153.4, 138.7, 128.6, 128.5, 126.4, 70.3, 64.3, 53.1, 40.5,

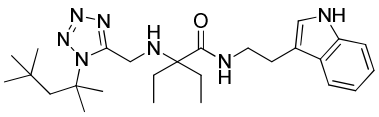
40.4, 36.0, 35.7, 31.6, 30.6, 29.9, 24.3; SFC-MS (ESI) m/z calcd for $C_{24}H_{38}N_6O$ $[M]^+$: 426.31; found $[M\text{-}H]^+$: 425.31.

19d: *N*-benzyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino) cyclohexane-1-carboxamide: The product was obtained using procedure **A**, 87 % as oil; 1H



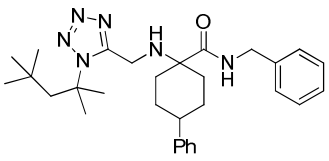
NMR (500 MHz, CDCl3) δ 7.73 (t, J = 6.3 Hz, 1H), 7.26 – 7.23 (m, 2H), 7.22 – 7.18 (m, 3H), 4.39 (d, J = 6.1 Hz, 2H), 3.91 (s, 2H), 2.57 (s, 1H), 2.04 – 1.90 (m, 2H), 1.80 (s, 2H), 1.76 – 1.59 (m, 12H), 1.46 – 1.29 (m, 3H), 0.70 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 153.4, 138.6, 128.6, 127.6, 127.3, 64.2, 61.2, 53.0, 43.2, 38.9, 32.0, 31.5, 30.6, 29.9, 25.1, 21.4.SFC-MS (ESI) m/z calcd for $C_{24}H_{38}N_6O$ $[M]^+$: 426.31; found $[M\text{-}H]^+$: 425.48.

20d: *N*-(2-(1H-indol-3-yl)ethyl)-2-ethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)butanamide: The product was obtained using procedure **A**, 96 % as white



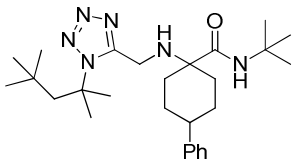
solid, M.P. = 168-170 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.15 (d, *J* = 80.0 Hz, 1H), 7.09 – 7.04 (m, 1H), 7.03 (d, *J* = 2.3 Hz, 1H), 3.85 (s, 2H), 3.59 (q, *J* = 6.6 Hz, 2H), 2.94 (t, *J* = 6.9 Hz, 2H), 1.84 – 1.75 (m, 5H), 1.72 – 1.66 (m, 2H), 1.65 (s, 6H), 0.82 (t, *J* = 7.4 Hz, 6H), 0.70 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 153.3, 136.4, 127.1, 122.1, 122.0, 119.3, 118.6, 112.6, 111.2, 65.1, 64.3, 53.0, 39.0, 38.5, 31.5, 30.6, 29.8, 26.8, 25.6, 7.8; SFC-MS (ESI) m/z calcd for $C_{26}H_{41}N_7O$ $[M]^+$: 467.34; found $[M\text{-}H]^+$: 466.33.

21d: *N*-benzyl-4-phenyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)cyclohexane-1-carboxamide: The product was obtained using procedure **A**, 97 % as



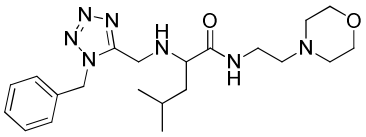
white solid, M.P. = 116-118 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) (major) δ 7.32 – 7.26 (m, 6H), 7.25 – 7.19 (m, 4H), 4.45 (d, *J* = 6.0 Hz, 2H), 4.05 (s, 2H), 2.57 (tt, *J* = 11.8, 3.9 Hz, 1H), 2.44 – 2.38 (m, 2H), 2.01 – 1.96 (m, 2H), 1.91 – 1.88 (m, 2H), 1.84 (s, 2H), 1.70 (s, 6H), 1.55 (td, *J* = 13.1, 4.0 Hz, 2H), 0.74 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) (major) δ 174.2, 153.5, 146.3, 138.7, 128.7, 128.3, 127.8, 127.4, 126.9, 126.1, 64.4, 60.7, 53.0, 43.7, 43.3, 39.0, 36.0, 30.6, 29.9; SFC-MS (ESI) m/z calcd for $C_{30}H_{42}N_6O$ $[M]^+$: 502.34; found $[M\text{-}H]^+$: 501.49.

22d: *N*-(*tert*-butyl)-4-phenyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)



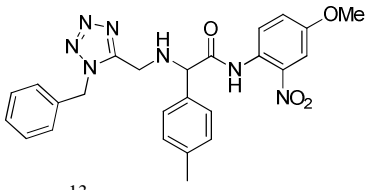
amino)cyclohexane-1-carboxamide: The product was obtained using procedure **A**, 98 % as white solid, M.P. = 142-144 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) (major) δ 7.43 (s, 1H), 7.34 – 7.30 (m, 2H), 7.27 – 7.19 (m, 3H), 4.02 (s, 2H), 2.66 – 2.59 (m, 1H), 2.59 – 2.51 (m, 1H), 2.43 – 2.36 (m, 1H), 2.15 (td, *J* = 14.6, 14.2, 4.0 Hz, 2H), 1.94 (s, 3H), 1.92 – 1.89 (m, 2H), 1.83 (s, 6H), 1.67 – 1.57 (m, 2H), 1.34 (s, 9H), 0.80 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) (major) δ 175.2, 153.5, 146.1, 128.4, 126.7, 126.2, 64.3, 60.9, 53.2, 50.5, 43.1, 39.1, 36.1, 31.5, 30.7, 30.1, 28.8, 28.7; SFC-MS (ESI) m/z calcd for $C_{27}H_{44}N_6O$ $[M]^+$: 468.36; found $[M+H]^+$: 469.49.

23d: 2-(((1-benzyl-1*H*-tetrazol-5-yl)methyl)amino)-4-methyl-*N*-(2-morpholinoethyl) pentanamide: The product was obtained using procedure **A**, 63 % as oil; ^{1}H NMR (500



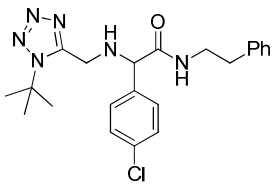
MHz, $CDCl_3$) δ 7.44 – 7.31 (m, 3H), 7.27 – 7.18 (m, 2H), 6.75 (s, 1H), 5.75 – 5.54 (m, 2H), 3.89 (s, 2H), 3.71 – 3.63 (m, 4H), 3.35 (d, *J* = 5.8 Hz, 2H), 2.97 (t, *J* = 7.0 Hz, 1H), 2.60 – 2.32 (m, 6H), 2.02 (s, 1H), 1.67 – 1.54 (m, 1H), 1.41 (ddd, *J* = 31.2, 13.7, 6.9 Hz, 2H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 153.0, 133.2, 129.2, 128.9, 127.6, 66.8, 60.3, 57.0, 53.3, 51.0, 42.9, 40.5, 35.5, 24.7, 22.8, 22.0; SFC-MS (ESI) m/z calcd for $C_{21}H_{33}N_7O$ $[M]^+$: 415.27; found $[M+H]^+$: 416.39.

24d: 2-(((1-benzyl-1*H*-tetrazol-5-yl)methyl)amino)-*N*-(4-methoxy-2-nitrophenyl)-2-(*p*-tolyl)acetamide: The product was obtained using procedure **A**, 78 % as oil; ^{1}H NMR (500



MHz, $CDCl_3$) δ 8.58 (d, *J* = 9.3 Hz, 1H), 7.64 (d, *J* = 3.0 Hz, 1H), 7.33 – 7.25 (m, 6H), 7.23 – 7.15 (m, 3H), 7.15 – 7.07 (m, 2H), 5.58 (s, 2H), 4.36 (s, 1H), 4.03 (d, *J* = 15.0 Hz, 1H), 3.92 (d, *J* = 15.0 Hz, 1H), 3.85 (s, 3H), 2.63 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 155.2, 152.6, 138.9, 137.2, 133.9, 133.2, 129.9, 129.2, 128.9, 127.8, 127.5, 123.7, 123.2, 108.7, 67.2, 55.9, 51.0, 40.3, 21.2; SFC-MS (ESI) m/z calcd for $C_{25}H_{25}N_7O_4$ $[M]^+$: 487.20; found $[M-H]^+$: 486.22.

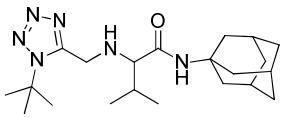
25d: 2-(((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)methyl)amino)-2-(4-chlorophenyl)-*N*-phenethylacetamide: The product was obtained using procedure **A**, 79 % as oil; ^{1}H NMR



(500 MHz, $CDCl_3$) δ 7.35 – 7.15 (m, 7H), 7.06 (d, *J* = 7.1 Hz, 2H), 6.82 (t, *J* = 5.6 Hz, 1H), 4.28 (s, 1H), 4.04 (s, 2H), 3.60 – 3.43 (m, 2H), 2.77 (t, *J* = 6.9 Hz, 2H), 1.64 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 152.3, 138.4, 136.5, 134.1, 128.9, 128.6, 128.5,

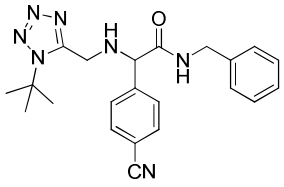
126.4, 65.3, 61.1, 42.4, 40.3, 35.2, 29.5; SFC-MS (ESI) m/z calcd for $C_{22}H_{27}ClN_6O$ $[M]^+$: 426.19; found $[M+H]^+$: 427.29

26d: *N*-((1S,3s)-adamantan-1-yl)-2-(((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)methyl)amino)-3-methylbutanamide: The product was obtained using procedure **A**, 71 % as oil; ^{1}H NMR



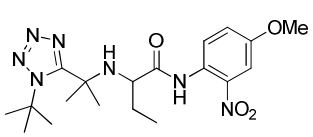
(500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.8 Hz, 1H), 4.18 (d, *J* = 15.0 Hz, 1H), 4.13 – 4.07 (m, 1H), 4.04 (d, *J* = 15.1 Hz, 1H), 2.89 (d, *J* = 5.5 Hz, 1H), 2.34 (s, 1H), 2.09 – 2.00 (m, 1H), 1.96 – 1.90 (m, 1H), 1.89 – 1.78 (m, 9H), 1.71 (s, 11H), 1.67 – 1.59 (m, 2H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 152.6, 68.3, 61.1, 52.8, 43.4, 37.5, 37.1, 37.0, 32.3, 32.2, 32.0, 31.8, 31.6, 29.7, 29.5, 27.1, 27.0, 19.5, 18.3; SFC-MS (ESI) m/z calcd for $C_{21}H_{36}N_6O$ $[M]^+$: 388.30; found $[M+H]^+$: 389.42

27d: *N*-benzyl-2-(((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)methyl)amino)-2-(4-cyanophenyl) acetamide: The product was obtained using procedure **A**, 86 % as oil;



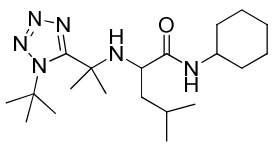
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.32 – 7.25 (m, 3H), 7.20 (d, *J* = 6.4 Hz, 2H), 4.55 – 4.43 (m, 2H), 4.39 (dd, *J* = 14.7, 5.7 Hz, 1H), 4.12 (s, 2H), 2.88 (s, 1H), 1.63 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 152.1, 143.2, 137.8, 132.6, 128.7, 128.3, 127.7, 127.7, 118.4, 112.3, 65.7, 61.2, 43.5, 42.6, 29.5; SFC-MS (ESI) m/z calcd for $C_{21}H_{25}ClN_6O$ $[M]^+$: 403.21; found $[M-H]^+$: 402.12

28d: 2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-*N*-(4-methoxy-2-nitrophenyl)butanamide:The product was obtained using procedure **A**, 52 % as white solid,



M.P. = 120-122 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.45 (s, 1H), 8.65 (d, *J* = 9.3 Hz, 1H), 7.67 (d, *J* = 2.9 Hz, 1H), 7.21 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.84 (s, 3H), 3.12 – 3.08 (m, 1H), 2.84 (d, *J* = 2.5 Hz, 1H), 2.03 – 1.94 (m, 1H), 1.83 – 1.76 (m, 10H), 1.69 (s, 3H), 1.66 (s, 3H), 0.93 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 160.4, 154.9, 137.1, 128.1, 123.6, 123.3, 108.6, 63.0, 60.8, 56.5, 55.9, 31.2, 27.8, 26.1, 9.6; SFC-MS (ESI) m/z calcd for $C19H_{29}N_7O_4$ $[M]^+$: 419.23; found $[M-H]^+$: 418.22

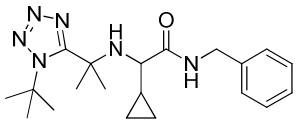
29d: 2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-*N*-cyclohexyl-4-methyl pentanamide: The product was obtained using procedure **A**, 81 % as white solid, M.P. =



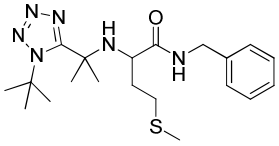
162-164 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.94 (d, *J* = 8.5 Hz, 1H),

3.73 – 3.60 (m, 1H), 2.92 (q, *J* = 6.7 Hz, 1H), 2.32 (d, *J* = 5.9 Hz, 1H), 1.89 – 1.78 (m, 11H), 1.73 – 1.65 (m, 5H), 1.63 (s, 3H), 1.62 – 1.55 (m, 2H), 1.43 – 1.37 (m, 2H), 1.37 – 1.29 (m, 2H), 1.19 – 1.05 (m, 3H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.80 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 159.9, 63.5, 56.4, 55.3, 47.9, 45.0, 33.0, 32.8, 31.2, 30.6, 28.3, 25.5, 24.8, 24.6, 22.9, 22.5, SFC-MS (ESI) m/z calcd for $C_{20}H_{38}N_6O$ $[M]^+$: 378.31; found $[M-H]^+$: 377.23.

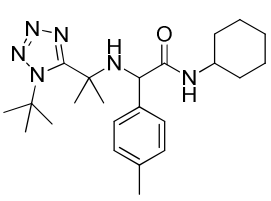
30d: *N*-benzyl-2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-2-cyclopropylacetamide: The product was obtained using procedure **A**, 73 % as white solid, M.P. = 108-110 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.29 – 7.26 (m, 3H), 6.71 – 6.61 (m, 1H), 4.49 – 4.37 (m, 2H), 2.67 (s, 1H), 2.45 (d, *J* = 8.8 Hz, 1H), 1.83 (s, 9H), 1.64 (s, 3H), 1.61 (s, 3H), 1.02 – 0.93 (m, 1H), 0.59 – 0.40 (m, 3H), 0.11 – 0.04 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 159.8, 138.1, 128.7, 127.8, 127.5, 63.5, 61.9, 55.1, 43.4, 31.2, 30.2, 27.9, 16.6, 4.6, 3.5; SFC-MS (ESI) m/z calcd for $C_{20}H_{30}N_6O$ $[M]^+$: 370.25; found $[M-H]^+$: 369.40.



31d: *N*-benzyl-2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-4-(methylthio) butanamide: The product was obtained using procedure **A**, 42 % as white solid, M.P. = 96-98 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.27 (m, 3H), 6.57 (t, *J* = 6.0 Hz, 1H), 4.47 (dd, *J* = 14.5, 6.3 Hz, 1H), 4.31 (dd, *J* = 14.5, 5.3 Hz, 1H), 3.19 (t, *J* = 6.7 Hz, 1H), 2.57 – 2.47 (m, 2H), 2.43 – 2.34 (m, 1H), 1.98 (s, 3H), 1.94 – 1.84 (m, 5H), 1.83 (s, 9H), 1.65 (d, *J* = 3.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 159.7, 137.9, 128.7, 127.9, 127.6, 63.6, 56.2, 55.3, 43.6, 34.2, 33.8, 31.2, 30.8, 30.5, 30.3, 29.7, 28.2, 15.1; SFC-MS (ESI) m/z calcd for $C_{20}H_{32}N_6OS$ $[M]^+$: 404.24; found $[M-H]^+$: 403.27

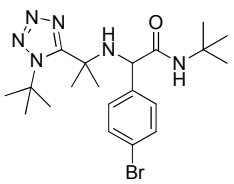


33d: 2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-*N*-cyclohexyl-2-(*p*-tolyl)acetamide: The product was obtained using procedure **A**, 78 % as white solid, M.P. = 163-165 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.8 Hz, 2H), 6.93 (d, *J* = 7.8 Hz, 2H), 5.99 (d, *J* = 8.4 Hz, 1H), 4.01 (d, *J* = 5.0 Hz, 1H), 3.72 – 3.62 (m, 1H), 2.92 (d, *J* = 5.2 Hz, 1H), 2.28 (s, 3H), 1.89 – 1.82 (m, 1H), 1.75 – 1.67 (m, 7H), 1.64 – 1.54 (m, 11H), 1.35 – 1.21 (m, 2H), 1.10 (ddd, *J* = 10.8, 8.8, 5.0 Hz, 2H), 0.98 (dd, *J* = 11.2, 3.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 159.3, 137.8, 137.4, 129.4, 127.3, 63.8, 61.0, 55.0, 48.3, 32.8,

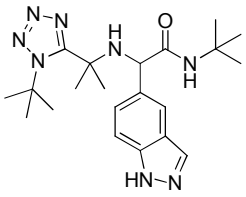


32.6, 30.9, 29.9, 28.9, 25.4, 24.7, 24.6, 21.0; SFC-MS (ESI) m/z calcd for $C_{23}H_{36}N_6O$ $[M]^+$: 412.30; found $[M-H]^+$: 411.26.

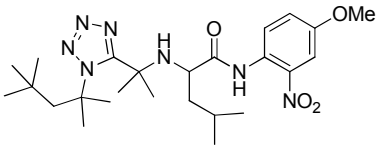
34d: 2-(4-bromophenyl)-*N*-(*tert*-butyl)-2-((2-(1-(tert-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)acetamide: The product was obtained using procedure **A**, 75 % as white solid, M.P. = 199-201 °C; ^{1}H NMR (500 MHz, $CDCl_3$+MeOH-d_4) δ 7.34 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 6.51 (s, 1H), 3.82 (s, 1H), 1.69 (s, 3H), 1.64 (s, 3H), 1.58 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$+MeOH-d_4) δ 172.2, 159.3, 139.7, 131.5, 128.5, 121.3, 64.4, 60.4, 54.9, 51.1, 30.7, 29.9, 28.8, 28.1, 28.1; SFC-MS (ESI) m/z calcd for $C_{20}H_{31}BrN_6O$ $[M]^+$: 450.17; found $[M+H]^+$: 451.21.



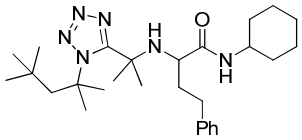
35d: *N*-(*tert*-butyl)-2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-2-(1*H*-indazol-5-yl)acetamide: The product was obtained using procedure **A**, 71 % as white solid, M.P. = 207-209 °C; ^{1}H NMR (500 MHz, $CDCl_3$+MeOD) δ 10.49 (s, 1H), 7.99 (s, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 6.99 (s, 1H), 6.84 (dd, *J* = 8.1, 1.4 Hz, 1H), 5.92 (s, 1H), 4.06 (s, 1H), 1.79 (s, 3H), 1.70 (s, 3H), 1.48 (s, 9H), 1.25 (s, 9H); 13C NMR (126 MHz, $CDCl_3$+MeOD) δ 172.3, 159.2, 139.9, 139.3, 133.8, 122.2, 121.1, 119.9, 108.7, 64.2, 61.4, 54.7, 51.2, 30.7, 29.8, 29.0, 28.3.SFC-MS (ESI) m/z calcd for C21H32N8O $[M]^+$: 412.27; found $[M-H]^+$: 411.26.



37d: *N*-(4-methoxy-2-nitrophenyl)-4-methyl-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)pentanamide: The product was obtained using procedure **A**, 43 % as white solid, M.P. = 112-114 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 9.3, 2.1 Hz, 1H), 7.68 (d, *J* = 3.1 Hz, 1H), 7.21 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.84 (s, 3H), 3.13 (dd, *J* = 8.0, 5.5 Hz, 1H), 2.07 (d, *J* = 15.1 Hz, 1H), 1.96 (s, 3H), 1.84 – 1.79 (m, 4H), 1.76 – 1.70 (m, 1H), 1.69 (s, 3H), 1.67 (s, 3H), 1.64 – 1.56 (m, 2H), 0.87 (d, *J* = 6.0 Hz, 3H), 0.84 (d, *J* = 6.0 Hz, 3H), 0.79 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 161.0, 154.9, 137.1, 128.2, 123.6, 123.3, 108.6, 66.8, 58.5, 57.0, 55.9, 53.2, 44.5, 31.8, 31.6, 30.8, 26.2, 24.7, 23.0, 22.0; SFC-MS (ESI) m/z calcd for $C_{25}H_{41}N_7O_4$ $[M]^+$: 503.32 found $[M-H]^+$: 502.28.

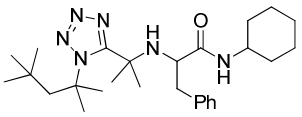


38d: *N*-cyclohexyl-4-phenyl-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl) propan-2-yl)amino)butanamide: The product was obtained using procedure **A**, 61 % as

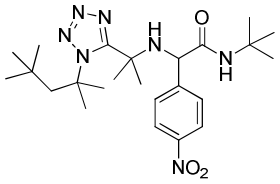


white solid, M.P. = 96-98 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.13 (d, *J* = 7.5 Hz, 2H), 6.04 (d, *J* = 8.4 Hz, 1H), 3.84 – 3.65 (m, 1H), 2.97 (s, 1H), 2.68 – 2.51 (m, 3H), 2.13 (d, *J* = 15.1 Hz, 1H), 2.00 – 1.85 (m, 11H), 1.75 – 1.58 (m, 9H), 1.43 – 1.31 (m, 2H), 1.22 – 1.09 (m, 2H), 0.81 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 160.4, 141.2, 128.4, 128.3, 126.0, 67.3, 57.3, 56.0, 53.6, 48.1, 37.1, 33.1, 33.0, 31.8, 31.6, 31.5, 30.9, 30.8, 28.1, 25.5, 24.9, 24.8; SFC-MS (ESI) m/z calcd for $C_{28}H_{46}N_6O$ $[M]^+$: 482.37; found $[M\text{-}H]^+$: 481.31.

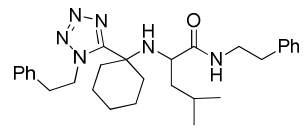
39d: *N*-cyclohexyl-3-phenyl-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)propenamide: The product was obtained using procedure **A**, 54 % as white solid, M.P. = 198-200 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.13 (m, 3H), 7.05 (d, *J* = 8.2 Hz, 2H), 5.66 (d, *J* = 8.6 Hz, 1H), 3.60 – 3.50 (m, 1H), 3.22 – 3.15 (m, 1H), 2.93 – 2.80 (m, 2H), 2.42 (s, 1H), 2.04 (d, *J* = 14.8 Hz, 1H), 1.90 – 1.82 (m, 5H), 1.75 (s, 3H), 1.62 – 1.59 (m, 5H), 1.57 (s, 3H), 1.53 – 1.49 (m, 2H), 1.30 – 1.18 (m, 2H), 1.08 – 0.86 (m, 2H), 0.77 (s, 11H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 160.0, 137.2, 129.3, 128.6, 126.9, 67.2, 59.0, 55.5, 53.6, 47.8, 41.3, 32.7, 31.8, 31.6, 31.2, 30.9, 30.5, 28.5, 25.4, 24.7; SFC-MS (ESI) m/z calcd for $C_{27}H_{44}N_6O$ $[M]^+$: 468.36; found $[M\text{-}H]^+$: 467.34.



40d: *N*-(*tert*-butyl)-2-(4-nitrophenyl)-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)acetamide: The product was obtained using procedure **A**, 17 % as white solid, M.P. = 175-177 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 6.14 (s, 1H), 4.09 (s, 1H), 3.20 (s, 1H), 1.99 (d, *J* = 15.0 Hz, 1H), 1.88 (d, *J* = 15.0 Hz, 1H), 1.79 (s, 3H), 1.74 (s, 3H), 1.71 (s, 6H), 1.28 (s, 9H), 0.75 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 159.4, 148.4, 147.3, 128.1, 123.8, 67.9, 61.1, 55.7, 53.8, 51.7, 31.7, 31.5, 30.8, 30.6, 29.3, 28.4; SFC-MS (ESI) m/z calcd for $C_{24}H_{39}N_7O_3$ $[M]^+$: 473.31; found $[M\text{-}H]^+$: 472.38.

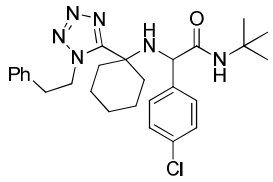


45d: 4-methyl-*N*-phenethyl-2-((1-(1-phenethyl-1*H*-tetrazol-5-yl)cyclohexyl)amino) pentanamide: The product was obtained using procedure **A**, 96 % as oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.4 Hz, 2H), 7.28 – 7.25 (m, 3H), 7.23 – 7.18 (m, 3H), 7.15 (d, *J* = 7.8 Hz, 2H), 4.80 – 4.71 (m, 1H), 4.63 – 4.54 (m, 1H), 3.50 – 3.42 (m, 1H), 3.34 – 3.19 (m, 3H), 2.78 – 2.66 (m, 3H), 2.25 – 2.13 (m, 3H), 1.76 – 1.55 (m, 4H), 1.46 – 1.31 (m, 4H), 1.26 –

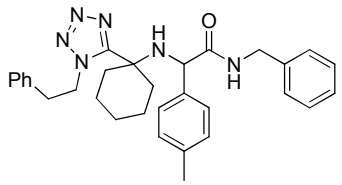


1.16 (m, 3H), 0.73 (d, J = 6.6 Hz, 3H), 0.65 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 157.1, 138.5, 136.8, 128.8, 128.6, 128.5, 127.1, 126.4, 55.6, 54.6, 50.4, 45.0, 40.4, 36.2, 35.8, 35.3, 25.2, 24.3, 22.7, 22.2, 22.1.SFC-MS (ESI) m/z calcd for $C_{29}H_{40}N_6O$ $[M]^+$: 488.33; found $[M-H]^+$: 487.17.

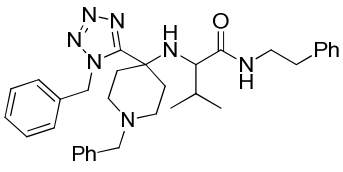
46d: *N*-(*tert*-butyl)-2-(4-chlorophenyl)-2-((1-(1-phenethyl-1*H*-tetrazol-5-yl)cyclohexyl) amino)acetamide: The product was obtained using procedure **A**, 84 % as white solid, M.P. = 124-126 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 3H), 7.25 – 7.22 (m, 1H), 7.22 – 7.18 (m, 2H), 7.01 (d, J = 8.3 Hz, 2H), 6.94 (d, J = 8.3 Hz, 2H), 5.49 (s, 1H), 4.61 – 4.52 (m, 1H), 4.08 – 3.98 (m, 1H), 3.81 (s, 1H), 3.20 – 3.11 (m, 1H), 2.94 – 2.85 (m, 1H), 2.44 – 2.36 (m, 1H), 1.98 – 1.89 (m, 1H), 1.81 – 1.75 (m, 1H), 1.73 – 1.65 (m, 2H), 1.53 (s, 1H), 1.48 – 1.37 (m, 2H), 1.21 (s, 9H), 1.18 – 1.11 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 157.5, 139.6, 136.8, 133.6, 128.9, 128.7, 128.5, 127.0, 59.6, 55.7, 51.7, 50.8, 49.9, 36.7, 35.5, 34.0, 28.4, 25.2, 22.0, 21.7; SFC-MS (ESI) m/z calcd for $C_{27}H_{35}ClN_6O$ $[M]^+$: 494.26; found $[M-H]^+$: 493.34.



47d: *N*-benzyl-2-((1-(1-phenethyl-1*H*-tetrazol-5-yl)cyclohexyl)amino)-2-(*p*-tolyl) acetamide: The product was obtained using procedure **A**, 94 % as oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 6H), 7.09 – 6.97 (m, 6H), 6.83 (d, J = 7.9 Hz, 2H), 5.68 (s, 1H), 4.60 – 4.48 (m, 1H), 4.40 – 4.27 (m, 2H), 4.01 – 3.89 (m, 2H), 3.42 (s, 1H), 3.16 – 3.05 (m, 1H), 2.91 – 2.78 (m, 1H), 2.48 – 2.36 (m, 1H), 2.27 (s, 3H), 2.00 (s, 1H), 1.82 – 1.62 (m, 4H), 1.59 – 1.33 (m, 3H), 1.17 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 157.4, 137.8, 137.7, 137.1, 137.0, 129.5, 128.7, 128.7, 128.6, 127.5, 127.4, 127.3, 126.9, 59.8, 55.3, 49.7, 43.8, 36.8, 35.4, 33.6, 25.2, 21.9, 21.7, 21.0; SFC-MS (ESI) m/z calcd for $C_{31}H_{36}N_6O$ $[M]^+$: 508.30; found $[M-H]^+$: 507.62.

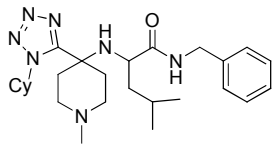


48d: 2-((1-benzyl-4-(1-benzyl-1*H*-tetrazol-5-yl)piperidin-4-yl)amino)-3-methyl-*N*-phenethylbutanamide: The product was obtained using procedure **A**, 61 % as oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 8H), 7.24 – 7.21 (m, 3H), 7.18 (d, J = 7.3 Hz, 2H), 7.12 (d, J = 7.2 Hz, 2H), 5.91 (d, J = 16.4 Hz, 1H), 5.65 (d, J = 16.4 Hz, 1H), 5.33 (s, 1H), 3.55 – 3.44 (m, 1H), 3.35 (s, 2H), 3.29 – 3.20 (m, 1H), 2.74 (t, J = 7.3 Hz, 2H), 2.61 – 2.26 (m, 5H), 2.22 – 1.85 (m, 5H), 1.75 – 1.59 (m, 1H), 0.84 (d, J = 6.7 Hz, 3H),



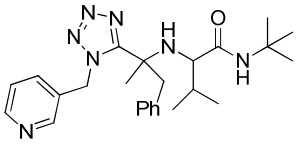
0.75 (d, J = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 157.1, 138.5, 138.3, 134.4, 128.9, 128.6, 128.5, 128.1, 126.9, 126.5, 62.6, 61.5, 53.8, 52.2, 49.5, 49.4, 40.6, 35.4, 32.7, 19.3, 18.8; SFC-MS (ESI) m/z calcd for $C_{33}H_{41}N_7O$ $[M]^+$: 551.34; found $[M-H]^+$: 550.59.

49d: *N*-benzyl-2-((4-(1-cyclohexyl-1*H*-tetrazol-5-yl)-1-methylpiperidin-4-yl)amino)-4-methylpentanamide: The product was obtained using procedure **A**, 71 % as oil; ^{1}H NMR



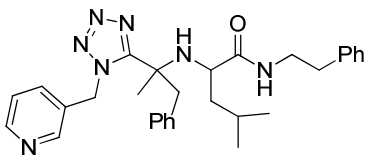
(500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 3H), 7.23 (d, J = 7.6 Hz, 2H), 5.83 (s, 1H), 4.74 (t, J = 11.4 Hz, 1H), 4.36 (dd, J = 14.5, 6.0 Hz, 1H), 4.23 (dd, J = 14.5, 5.1 Hz, 1H), 2.81 – 2.68 (m, 1H), 2.65 – 2.49 (m, 2H), 2.43 – 2.23 (m, 3H), 2.21 (s, 3H), 2.16 – 1.86 (m, 8H), 1.71 (s, 3H), 1.59 – 1.49 (m, 1H), 1.40 (tt, J = 22.2, 9.8 Hz, 3H), 1.30 – 1.18 (m, 1H), 0.79 – 0.74 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 155.8, 137.7, 128.6, 128.0, 127.5, 59.3, 55.1, 54.1, 51.7, 45.8, 45.2, 43.7, 36.4, 35.2, 33.5, 33.3, 25.5, 24.9, 24.4, 22.8, 22.5; SFC-MS (ESI) m/z calcd for $C_{26}H_{41}N_7O$ $[M]^+$: 467.34; found $[M-H]^+$: 466.30.

50d: *N*-(*tert*-butyl)-3-methyl-2-((1-phenyl-2-(1-(pyridin-3-ylmethyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)butanamide: The product was obtained using procedure **A**, 80 % as



oil; ^{1}H NMR (500 MHz, $CDCl_3$) (major) δ 8.57 – 8.53 (m, 2H), 7.59 – 7.53 (m, 1H), 7.27 – 7.24 (m, 1H), 7.22 – 7.15 (m, 3H), 6.93 – 6.88 (m, 2H), 6.81-6.75 (m, 1H), 5.91 (d, J = 16.1 Hz, 1H), 5.80 (d, J = 16.1 Hz, 1H), 5.34 (s, 1H), 3.02 – 2.93 (m, 2H), 2.73 (d, J = 6.3 Hz, 1H), 1.85 – 1.75 (m, 1H), 1.55 (s, 3H), 1.21 (s, 9H), 0.90 – 0.80 (m, 6H); ^{13}C NMR (major) (126 MHz, $CDCl_3$) δ 172.6, 149.8, 148.8, 135.2, 130.3, 128.4, 127.3, 123.7, 62.8, 56.3, 50.1, 46.9, 28.5, 23.5, 19.3, 18.9; SFC-MS (ESI) m/z calcd for $C_{25}H_{35}N_7O$ $[M]^+$: 449.29; found $[M-H]^+$: 448.39.

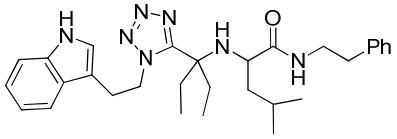
51d: 4-methyl-*N*-phenethyl-2-((1-phenyl-2-(1-(pyridin-3-ylmethyl)-1*H*-tetrazol-5-yl) propan-2-yl)amino)pentanamide: The product was obtained using procedure **A**, 84 % as oil;



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 – 8.49 (m, 2H), 7.34 – 7.09 (m, 9H), 6.89 – 6.81 (m, 2H), 6.27 – 6.17 (m, 1H), 5.86 (d, J = 15.8 Hz, 1H), 5.66 (d, J = 15.8 Hz, 1H), 3.46 – 3.39 (m, 1H), 3.25 (dd, J = 13.1, 6.2 Hz, 1H), 3.03 (s, 2H), 2.75 – 2.65 (m, 2H), 1.94 (d, J = 6.2 Hz, 1H), 1.54 (s, 3H), 1.48 – 1.39 (m, 2H), 1.31 – 1.21 (m, 1H), 0.84 (d, J = 6.3 Hz, 3H), 0.78 (d, J = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 138.5, 135.4, 134.8, 130.1, 128.6,

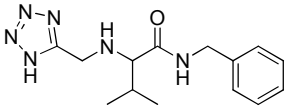
128.5, 128.4, 128.4, 127.3, 126.4, 123.6, 56.9, 55.3, 49.9, 46.7, 44.4, 40.2, 35.2, 24.5, 23.5, 22.5; SFC-MS (ESI) m/z calcd for $C_{30}H_{37}N_7O$ $[M]^+$: 511.31; found $[M+H]^+$: 510.25

52d: 2-((3-(1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-tetrazol-5-yl)pentan-3-yl)amino)-4-methyl-*N*-phenethylpentanamide: The product was obtained using procedure **A**, 80 % as white solid,



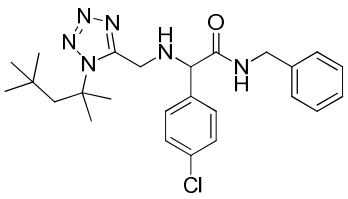
M.P. = 156-158 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.32-7.27 (m, 2H), 7.25-7.20 (m, 2H), 7.19 – 7.12 (m, 3H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.04 (q, *J* = 5.5 Hz, 1H), 4.89 – 4.75 (m, 2H), 3.53 – 3.43 (m, 3H), 3.31 – 3.23 (m, 1H), 2.90-2.85 (m, 1H), 2.78-2.65 (m, 2H), 1.95 – 1.72 (m, 5H), 1.45-1.38 (m, 1H), 1.32-1.26 (m, 1H), 1.14-1.08 (m, 1H), 0.96 (dd, *J* = 8.6, 6.5 Hz, 1H), 0.78 (dd, *J* = 8.0, 6.5 Hz, 6H), 0.57 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 157.4, 138.5, 136.3, 128.5, 126.8, 126.4, 122.7, 122.1, 119.5, 117.9, 111.5, 110.6, 70.6, 59.8, 55.0, 49.8, 45.04, 43.7, 40.2, 35.2, 27.5, 26.9, 25.6, 24.4, 23.4, 22.9, 22.1, 21.3, 7.2; SFC-MS (ESI) m/z calcd for $C_{30}H_{41}N_7O$ $[M]^+$: 515.34; found $[M+H]^+$: 514.38.

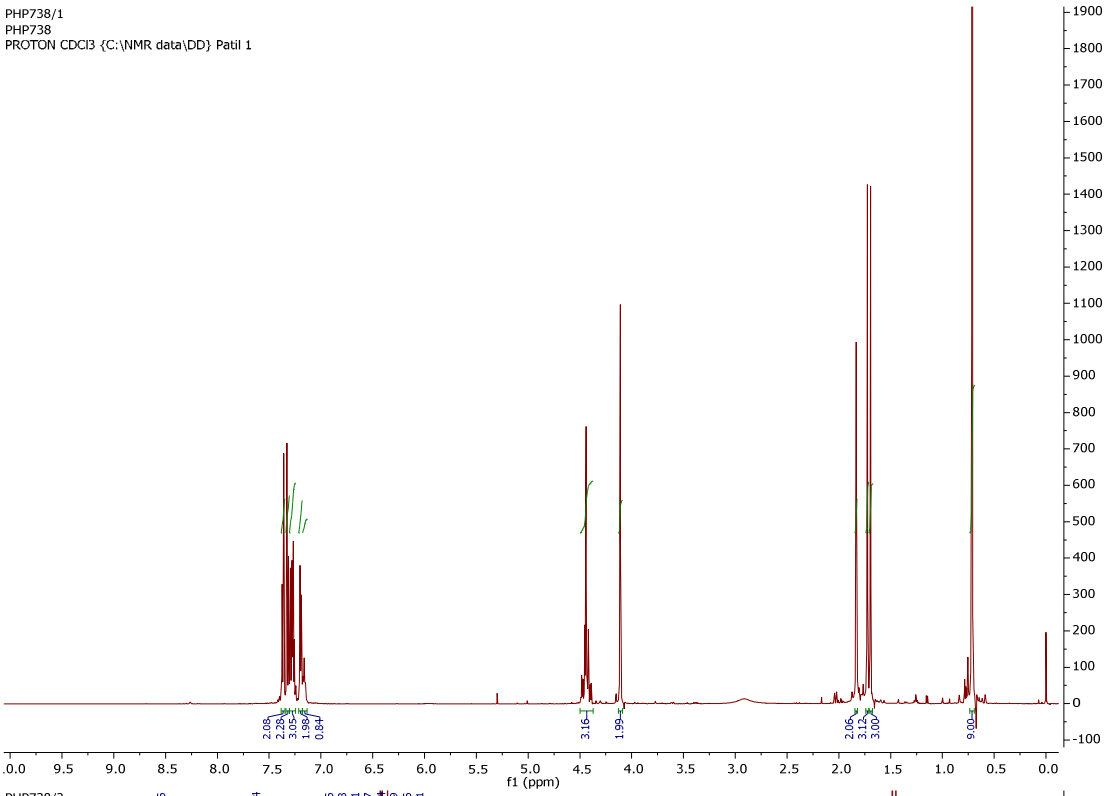
5: 2-(((1*H*-tetrazol-5-yl)methyl)amino)-*N*-benzyl-3-methylbutanamide: The solution of



Ugi product (**14d**, 1 mmol) in 6N hydrochloric acid in water (10 ml) was stirred at 75-80 oC for 48 hrs. Then the reaction was cooled to room temperature, solvent was evaporated under vacuum on rotavapor. The crude mass obtained was washed with diethyl ether (10 ml X 3) to give hydrochloride salt of product **5** in 97 % as white solid, M.P. = 202-204 ^oC; ^1H NMR (500 MHz, MeOD) δ 7.27 – 7.09 (m, 5H), 4.57 – 4.19 (m, 4H), 3.87-3.76 (m, 1H), 2.25-2.10 (m, 1H), 1.00-0.89 (m, 6H); ^{13}C NMR (126 MHz, MeOD) δ 167.2, 155.4, 139.2, 129.8, 129.1, 128.7, 66.7, 44.6, 41.1, 31.3, 30.8, 19.0, 18.2; SFC-MS (ESI) m/z calcd for $C_{14}H_{20}N_6O$ $[M]^+$: 288.17; found $[M-H]^+$: 289.28.

1d: ***N*-benzyl-2-(4-chlorophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:**




PHP738/1
PHP738
PROTON CDCl3 {C:\NMR data\DD} Patil 1
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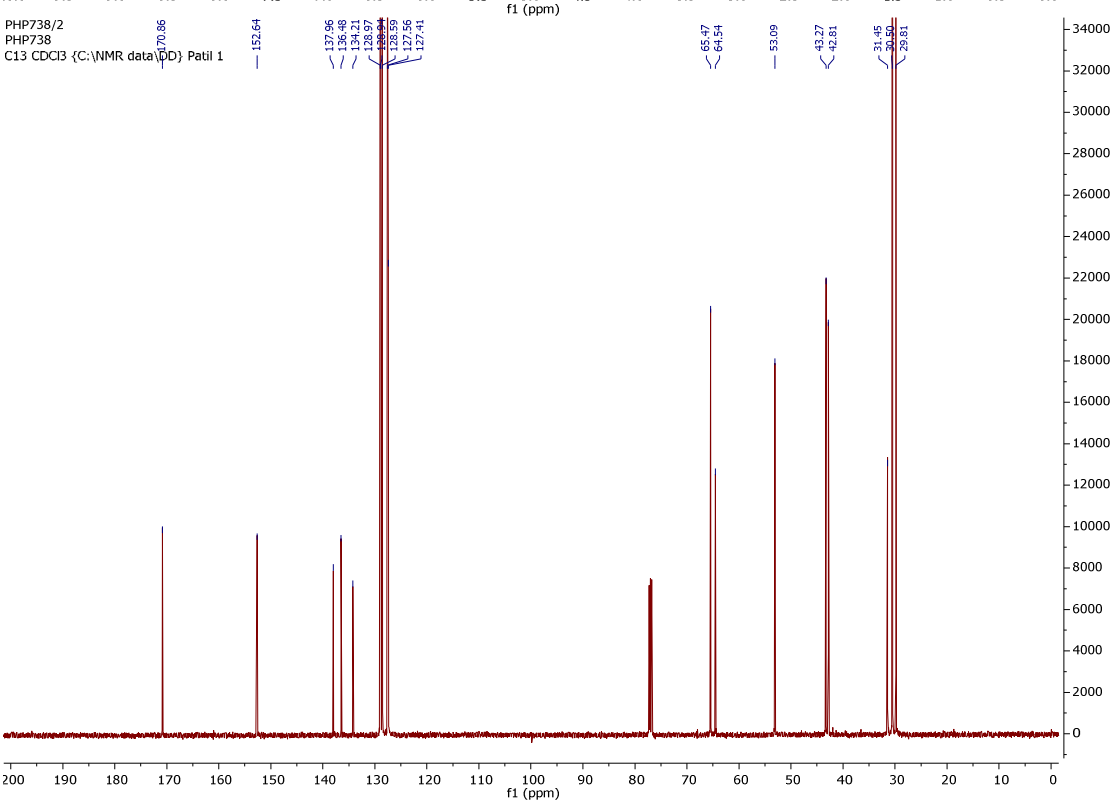
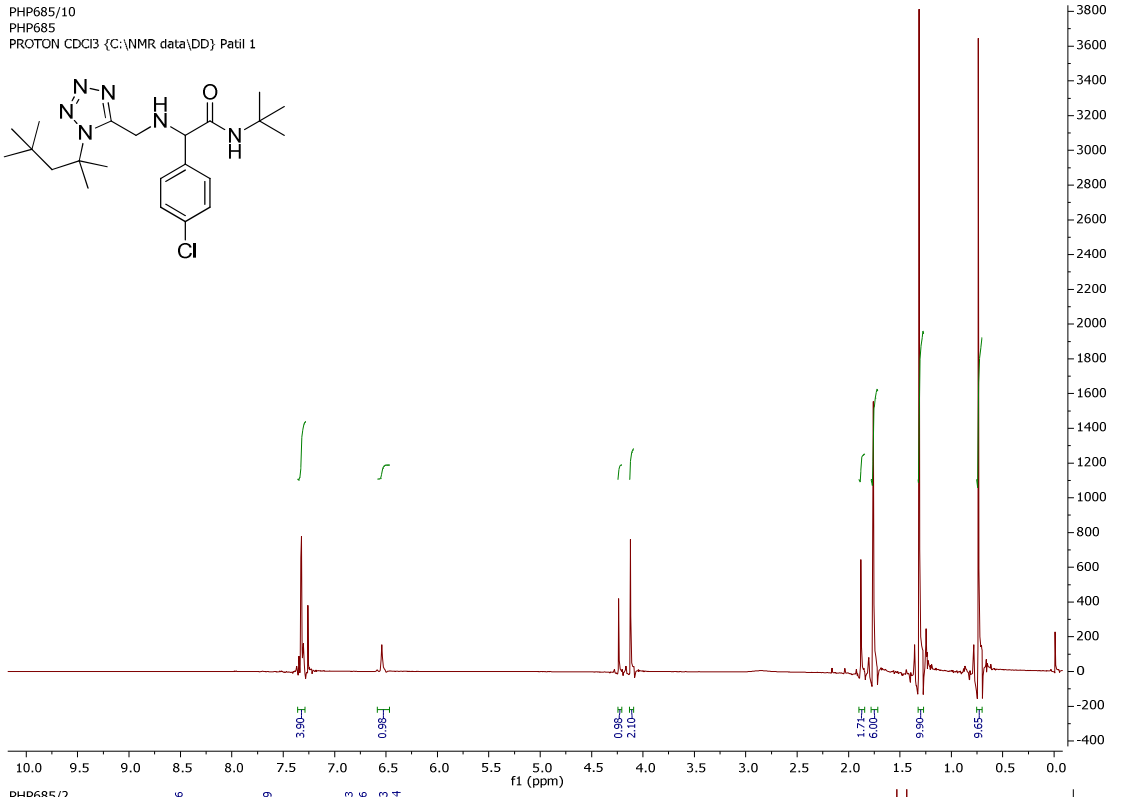
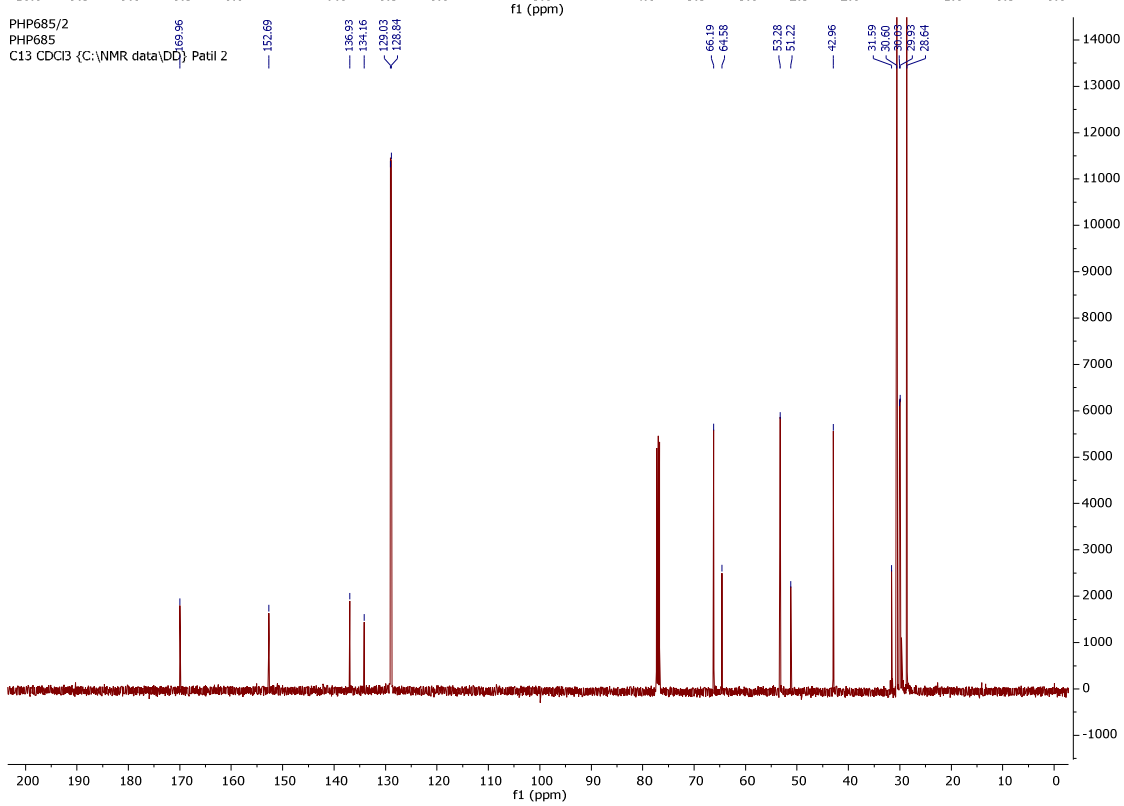
2.28
3.05
1.98
0.84
3.16
1.99
2.06
3.12
3.00
9.00
f1 (ppm)

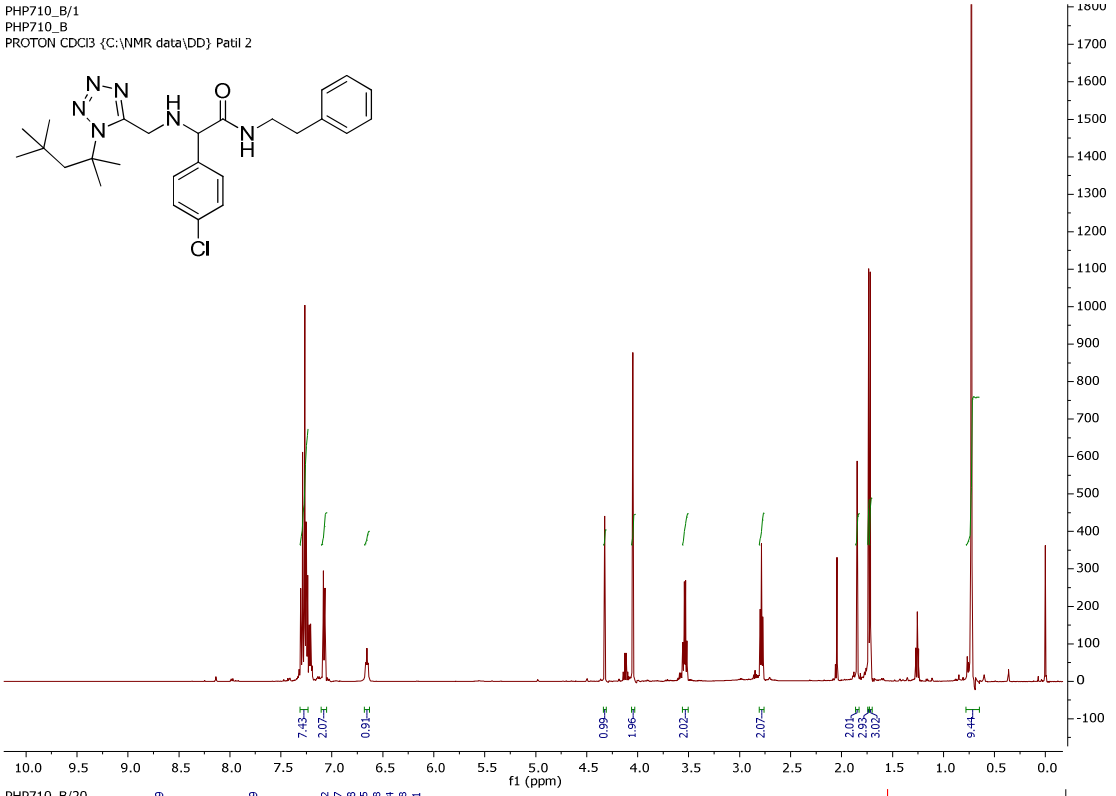

PHP738/2
PHP738
C13 CDCl3 {C:\NMR data\DD} Patil 1
170.86
152.64
137.96
136.48
134.21
128.97
128.94
128.59
127.56
127.41
65.47
64.54
53.09
43.27
42.81
31.45
30.50
29.81
f1 (ppm)

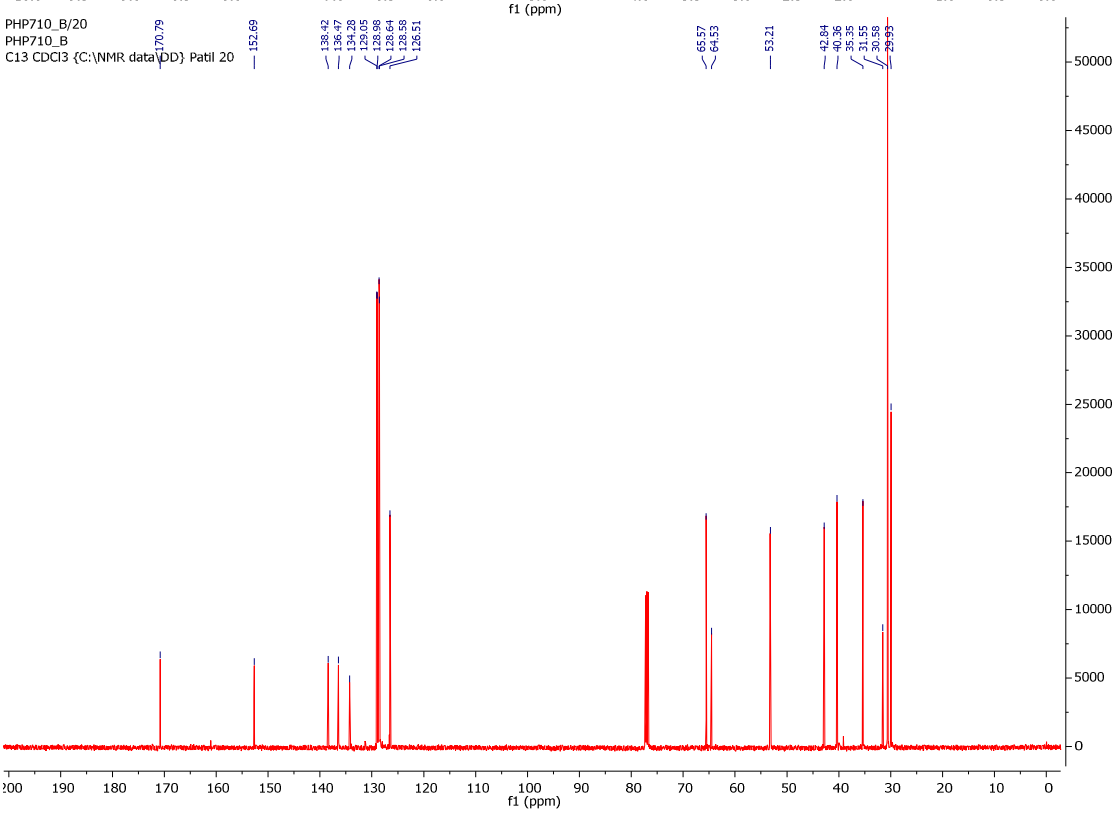
2d: ***N*-(*tert*-butyl)-2-(4-chlorophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:**



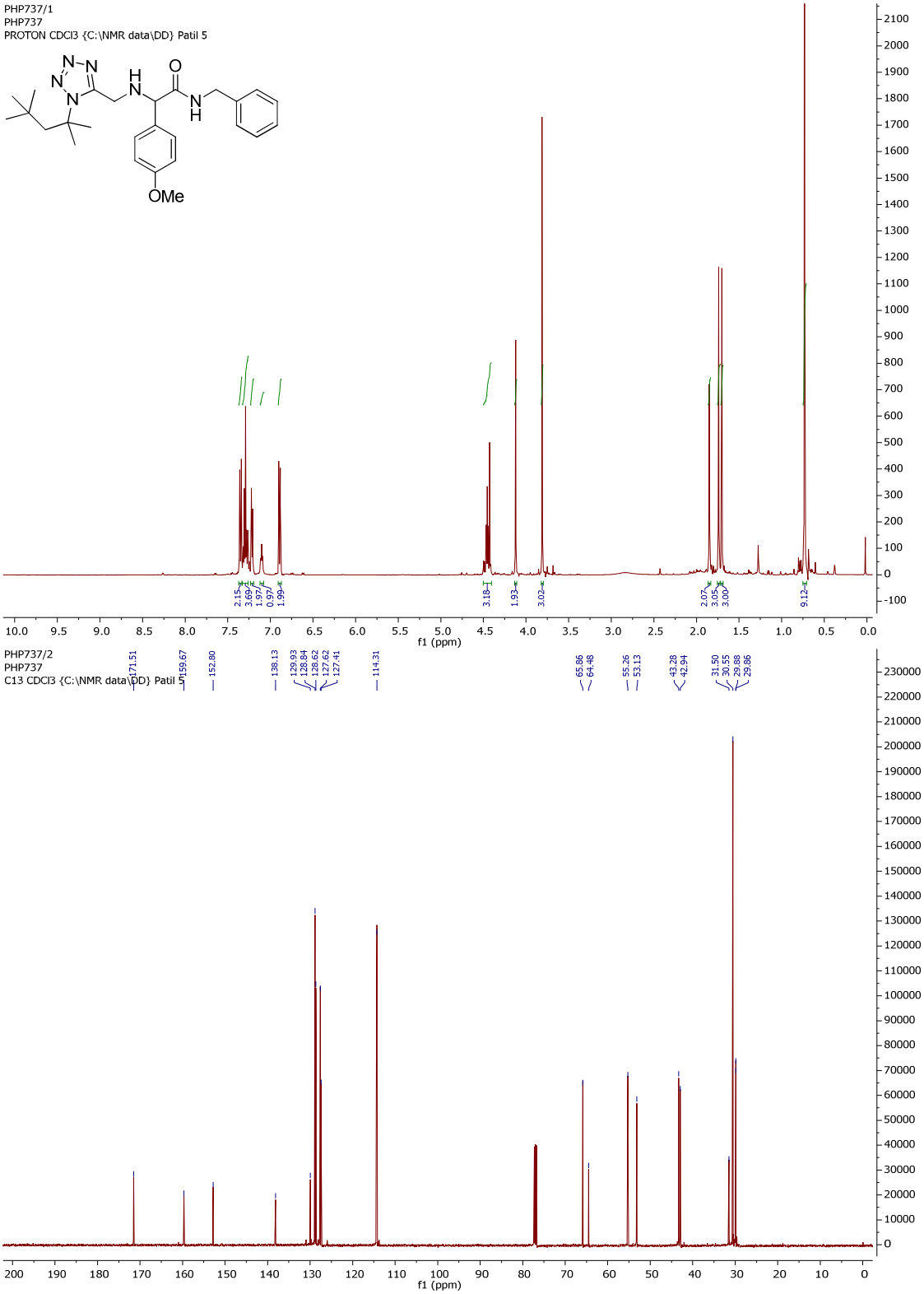


3d: 2-(4-chlorophenyl)-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:

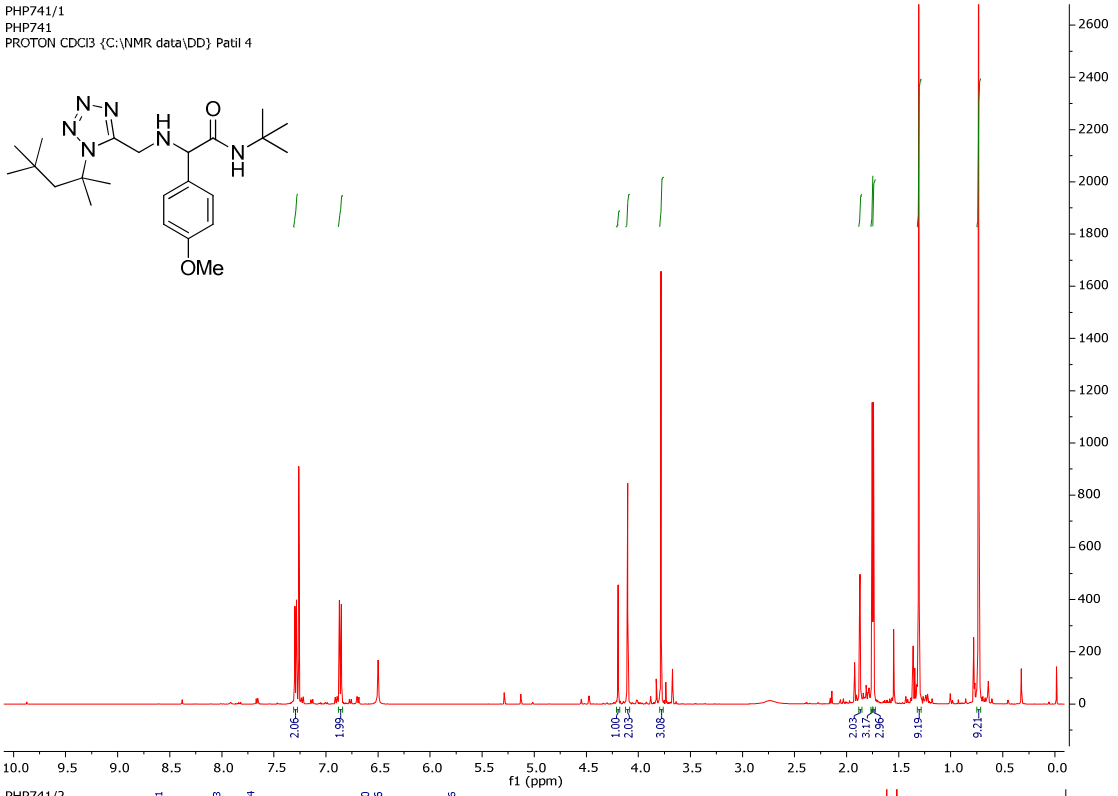


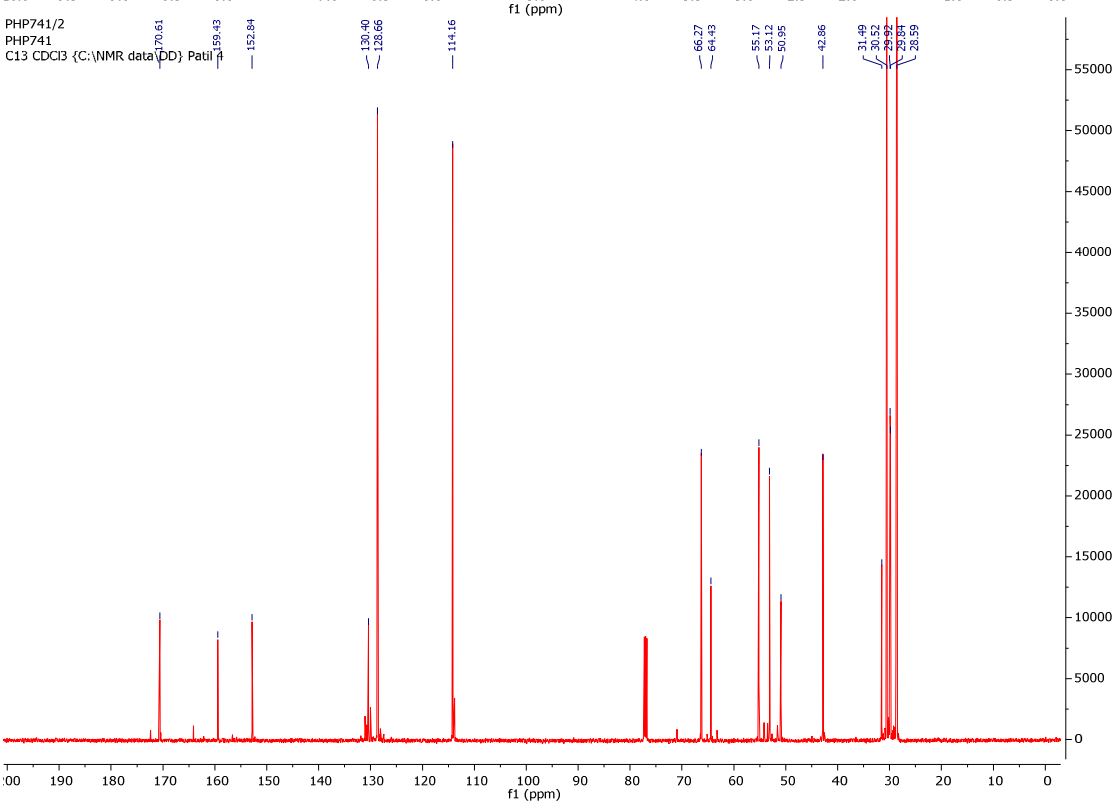


4d: *N*-benzyl-2-(4-methoxyphenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide :

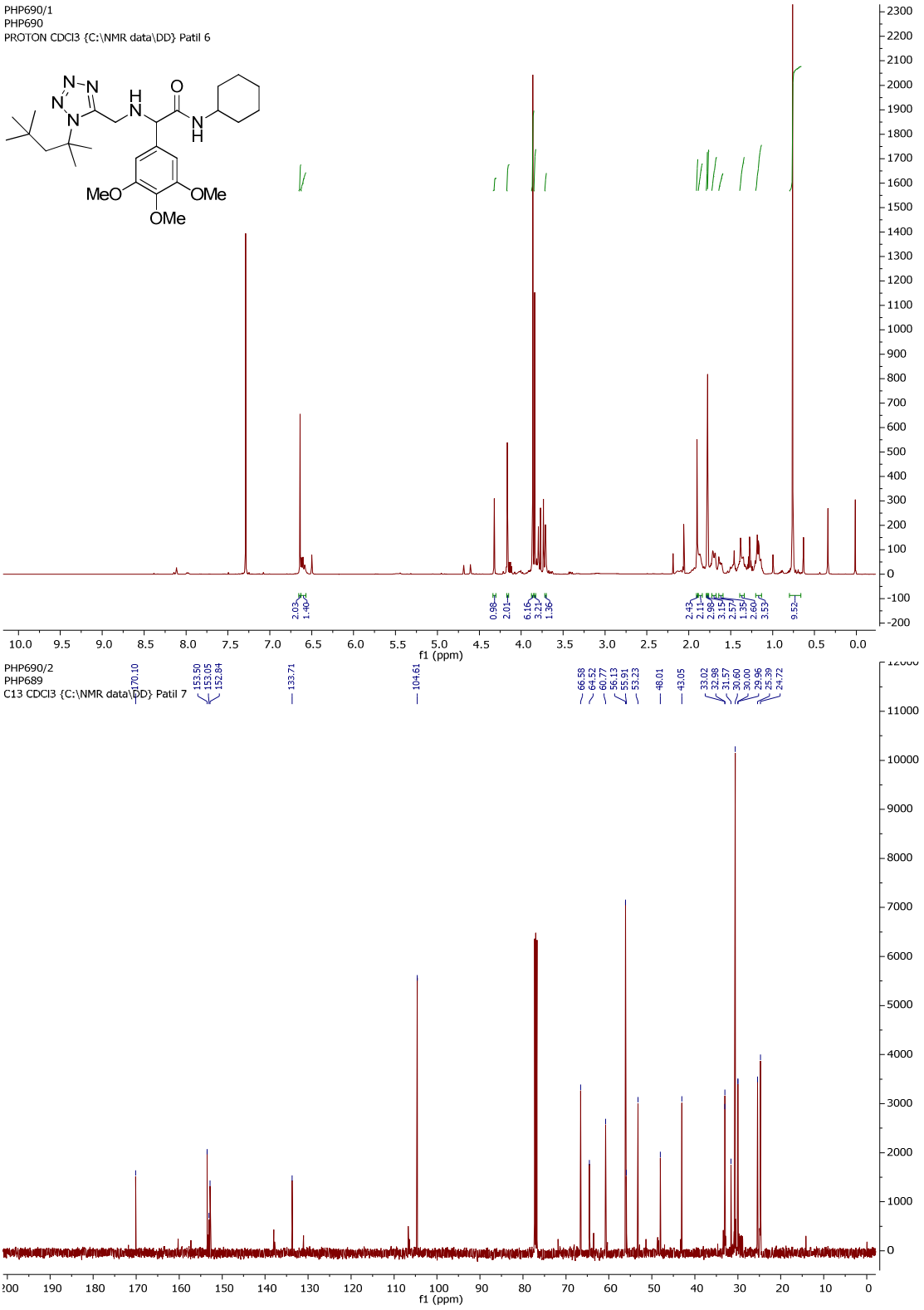


5d: *N*-(*tert*-butyl)-2-(4-methoxyphenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide :

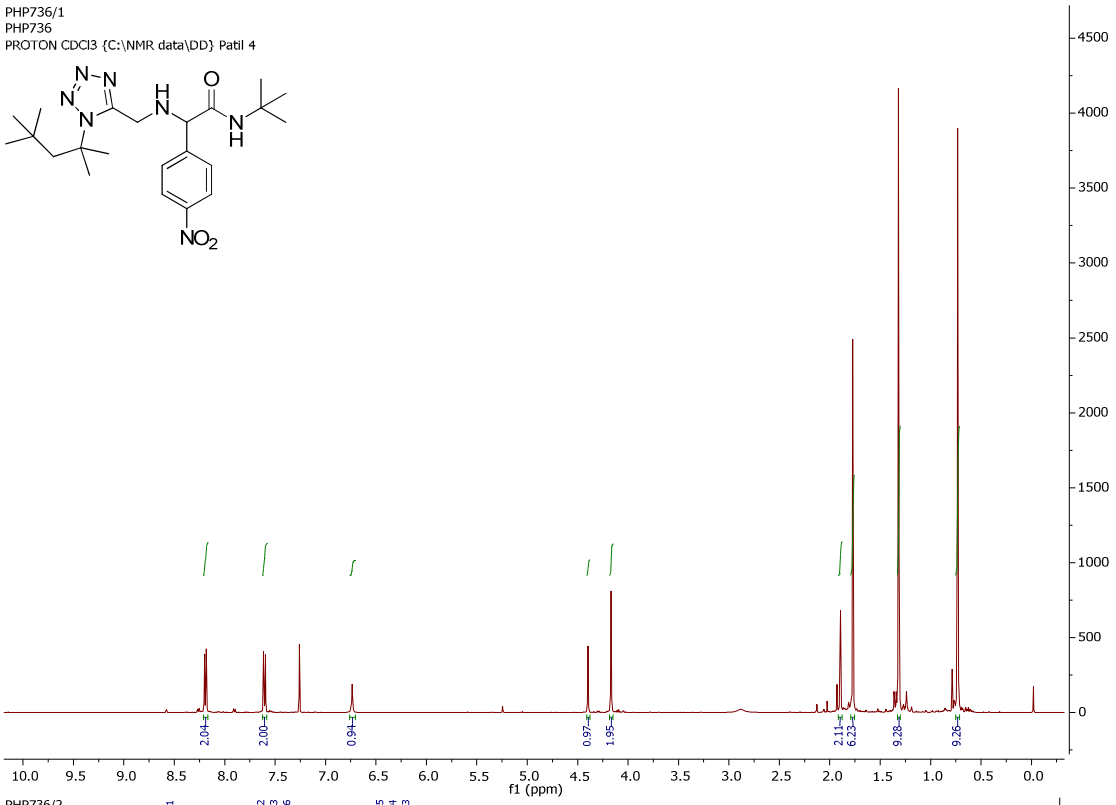


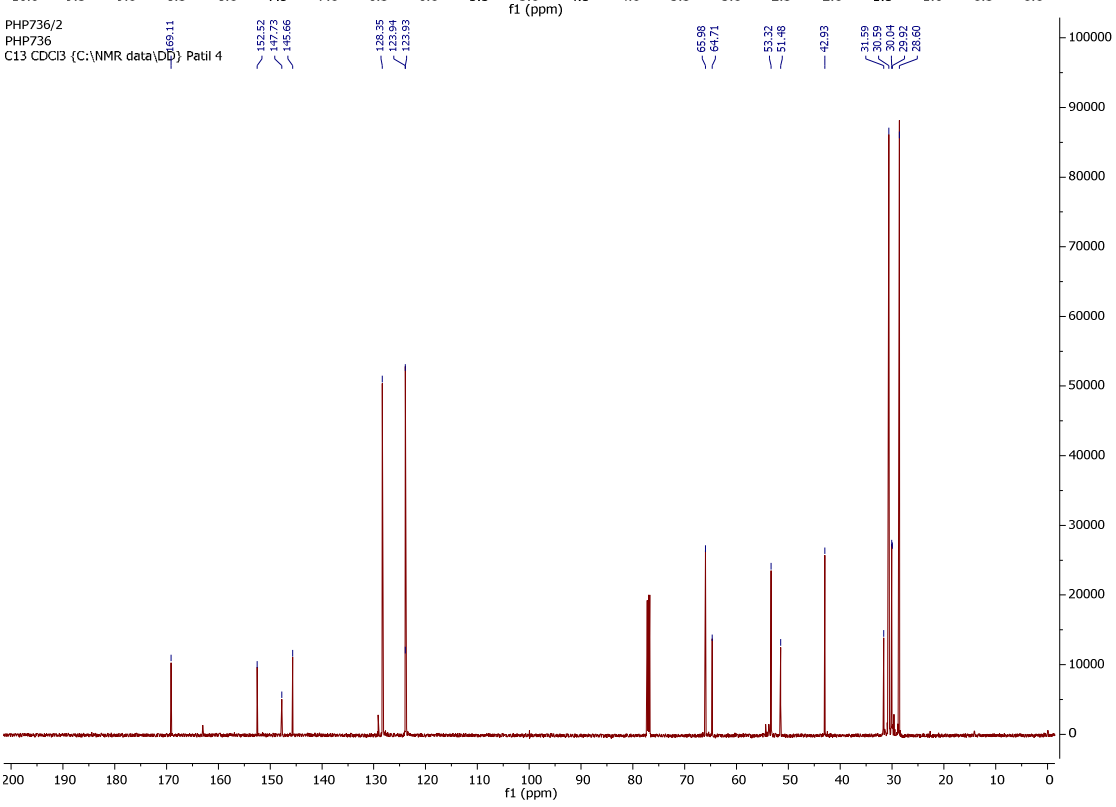


6d: *N*-cyclohexyl-2-(3,4,5-trimethoxyphenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:

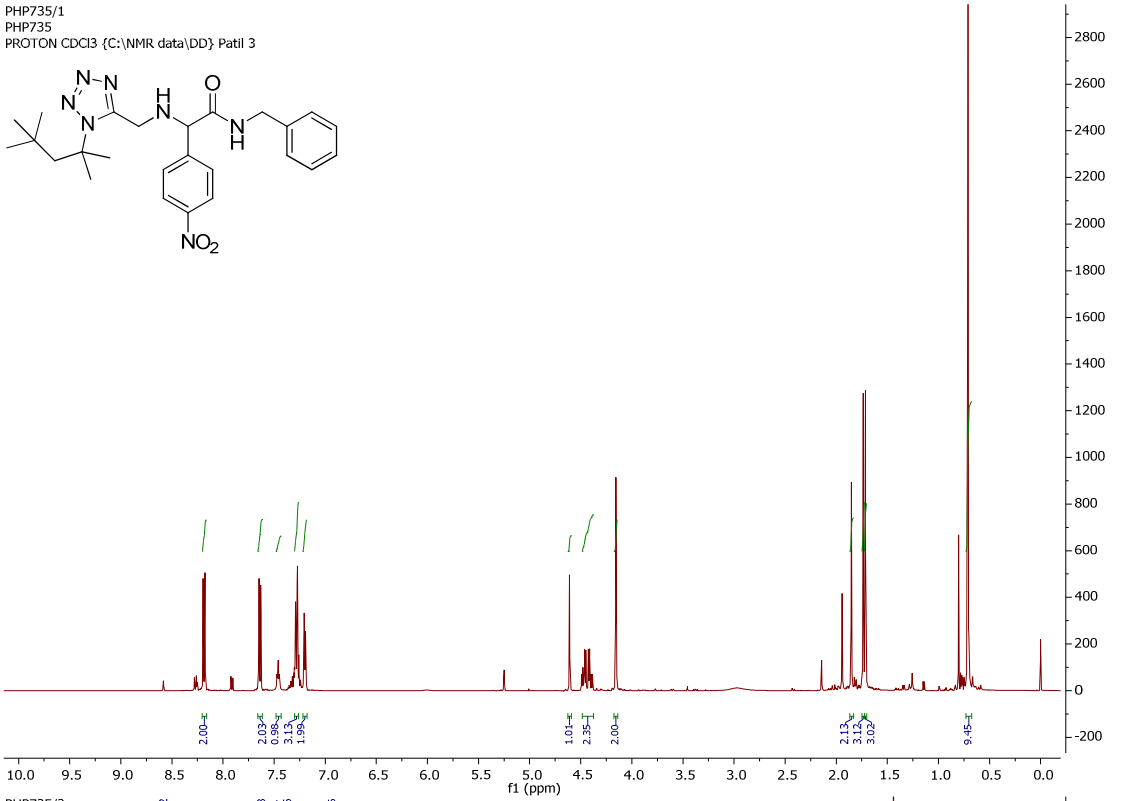


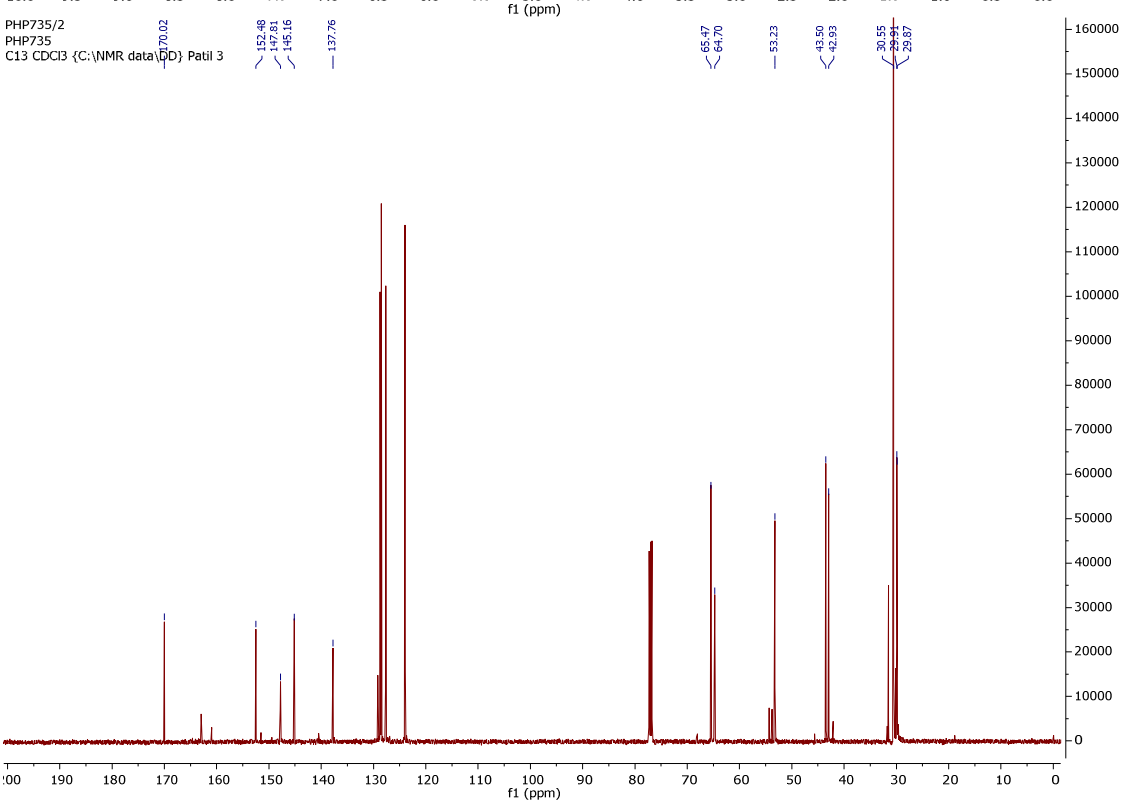
7d: *N*-(*tert*-butyl)-2-(4-nitrophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:



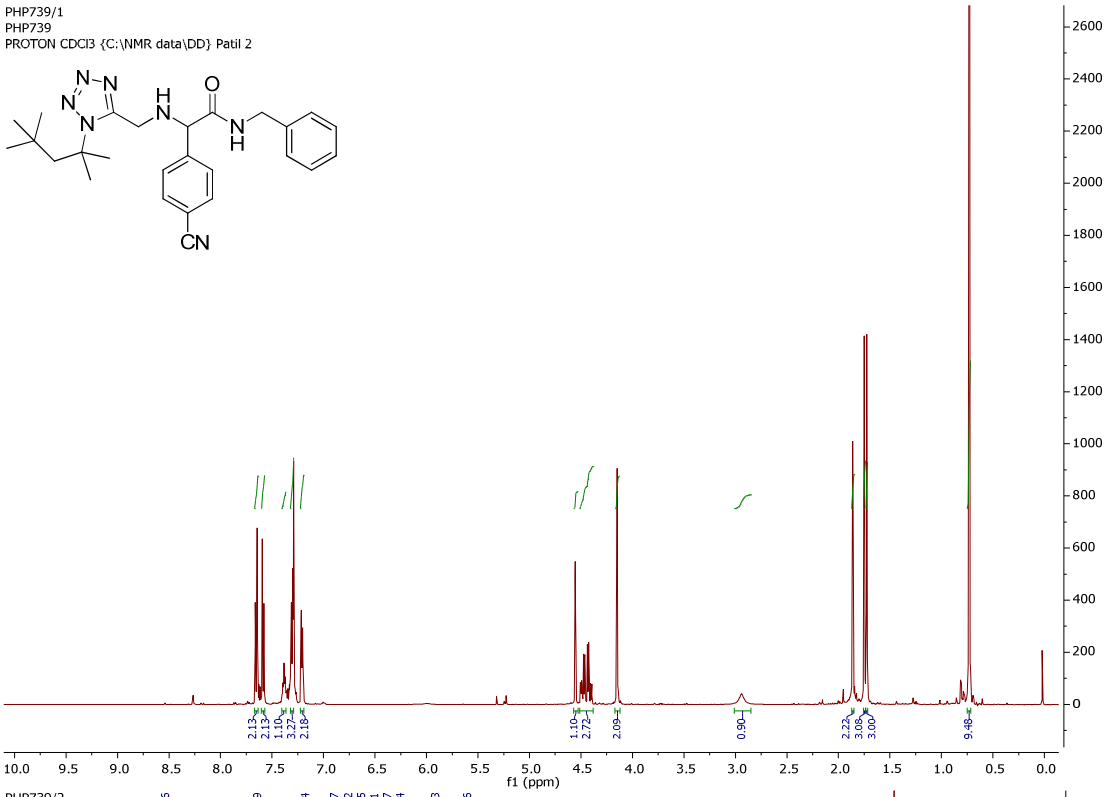


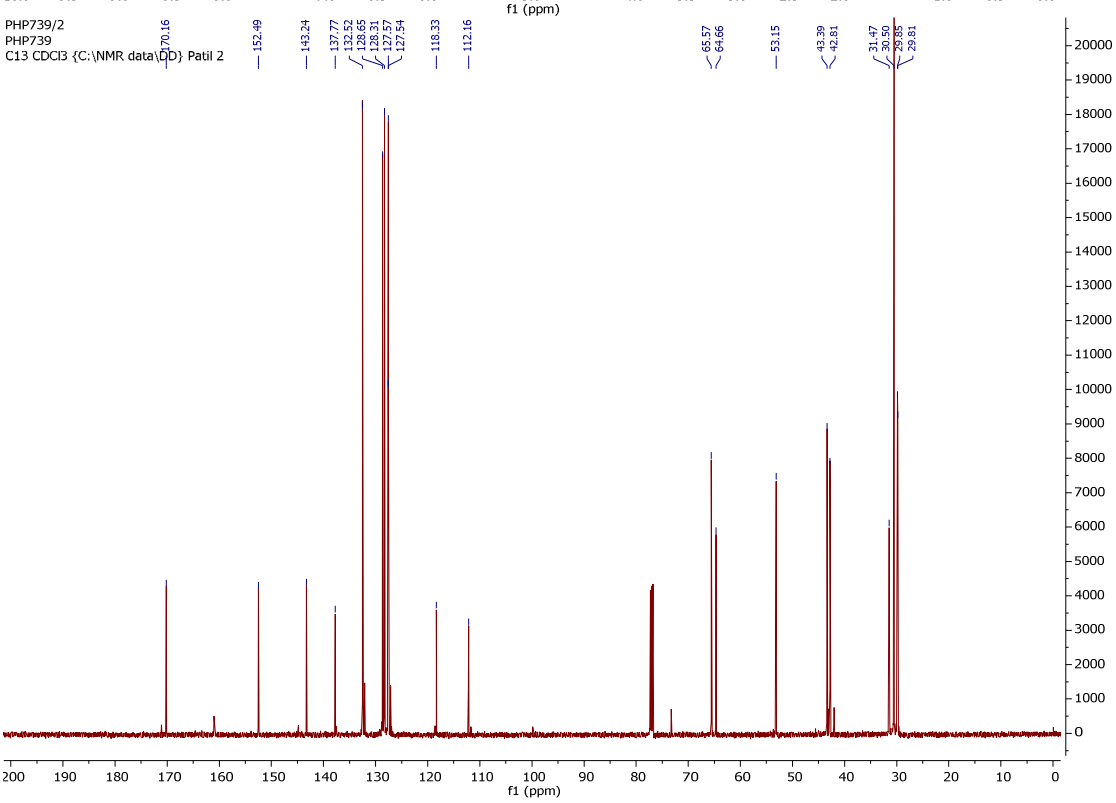
8d: *N*-benzyl-2-(4-nitrophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamid:



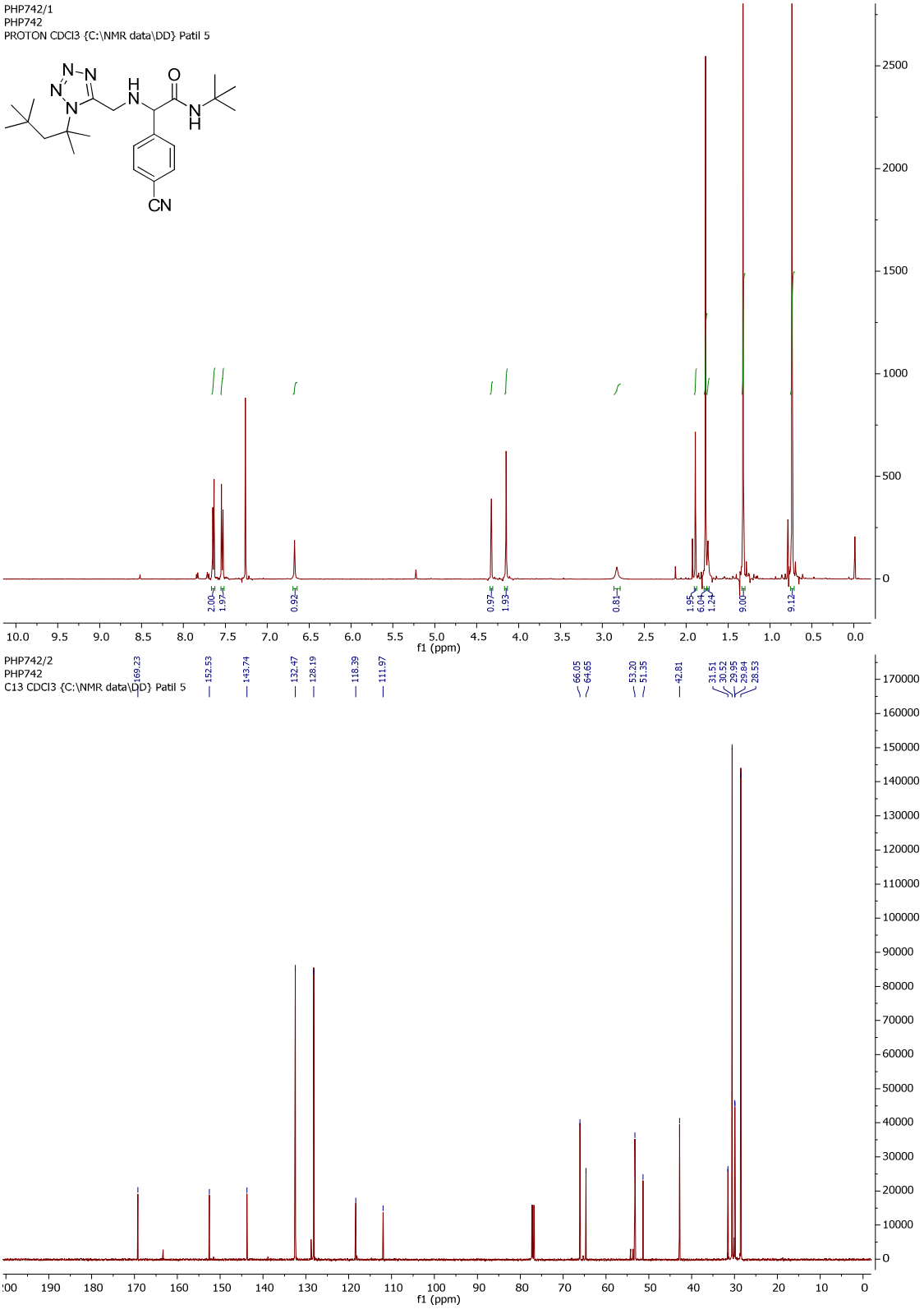


9d: *N*-benzyl-2-(4-cyanophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:

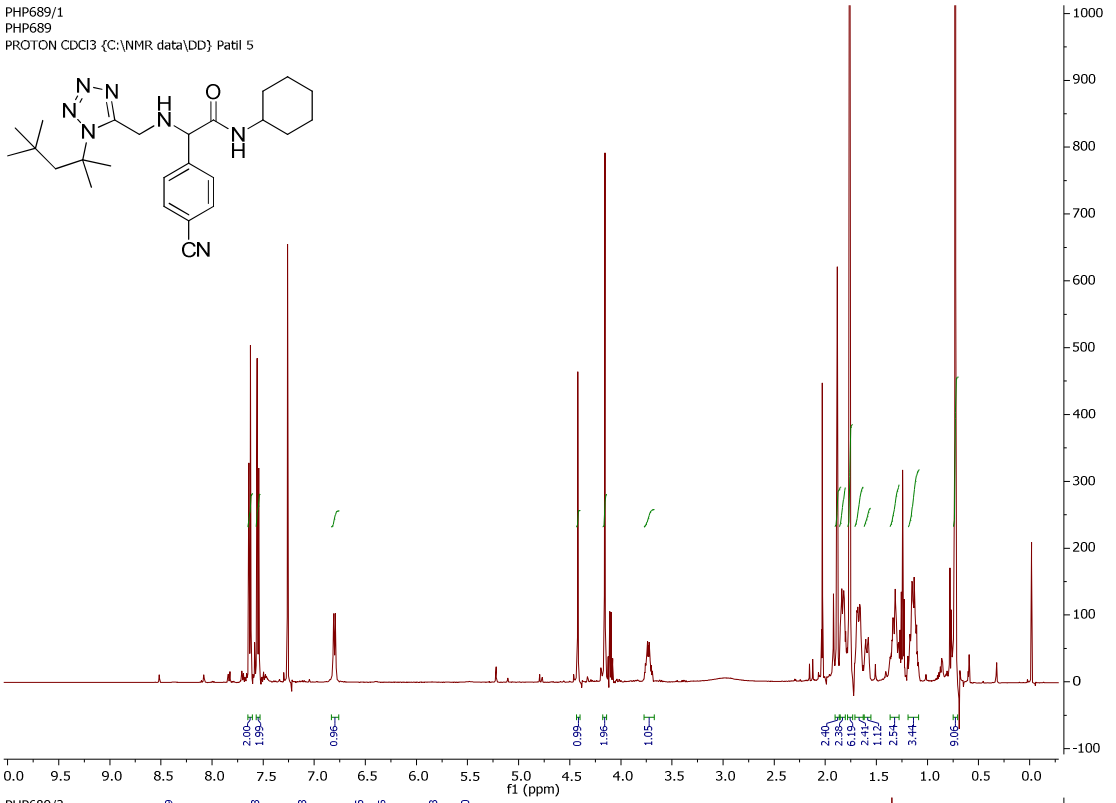


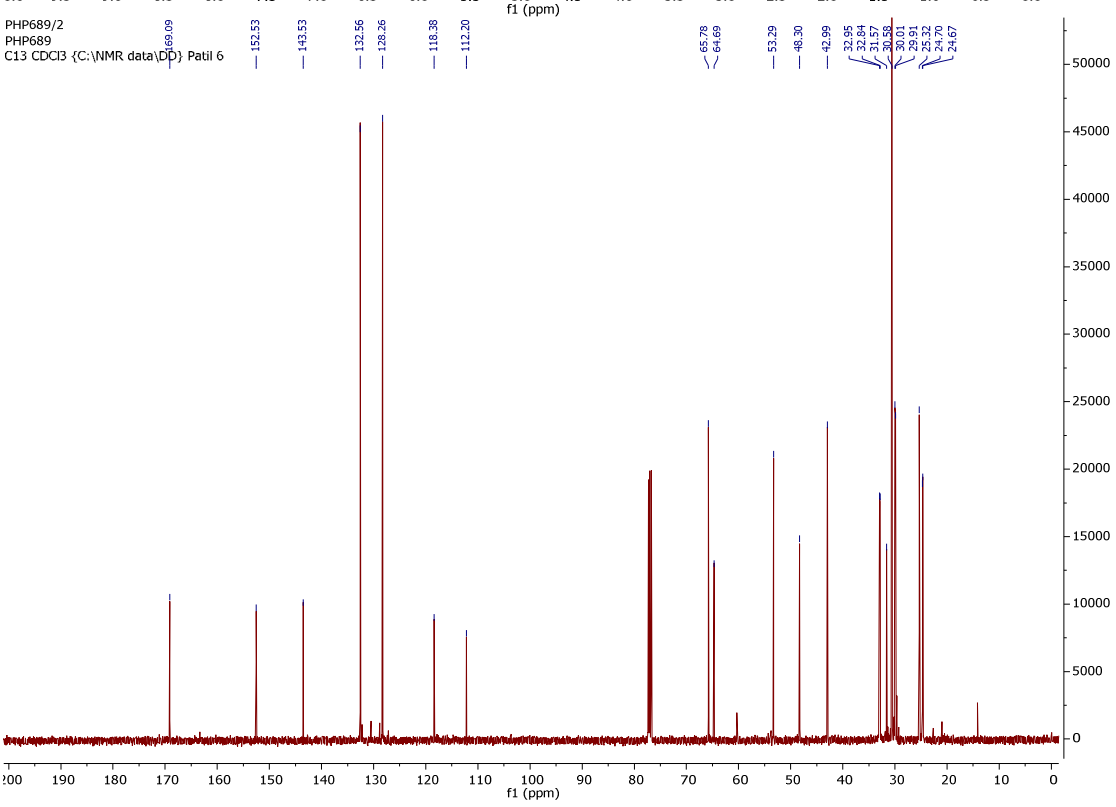


10d: *N*-(*tert*-butyl)-2-(4-cyanophenyl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:

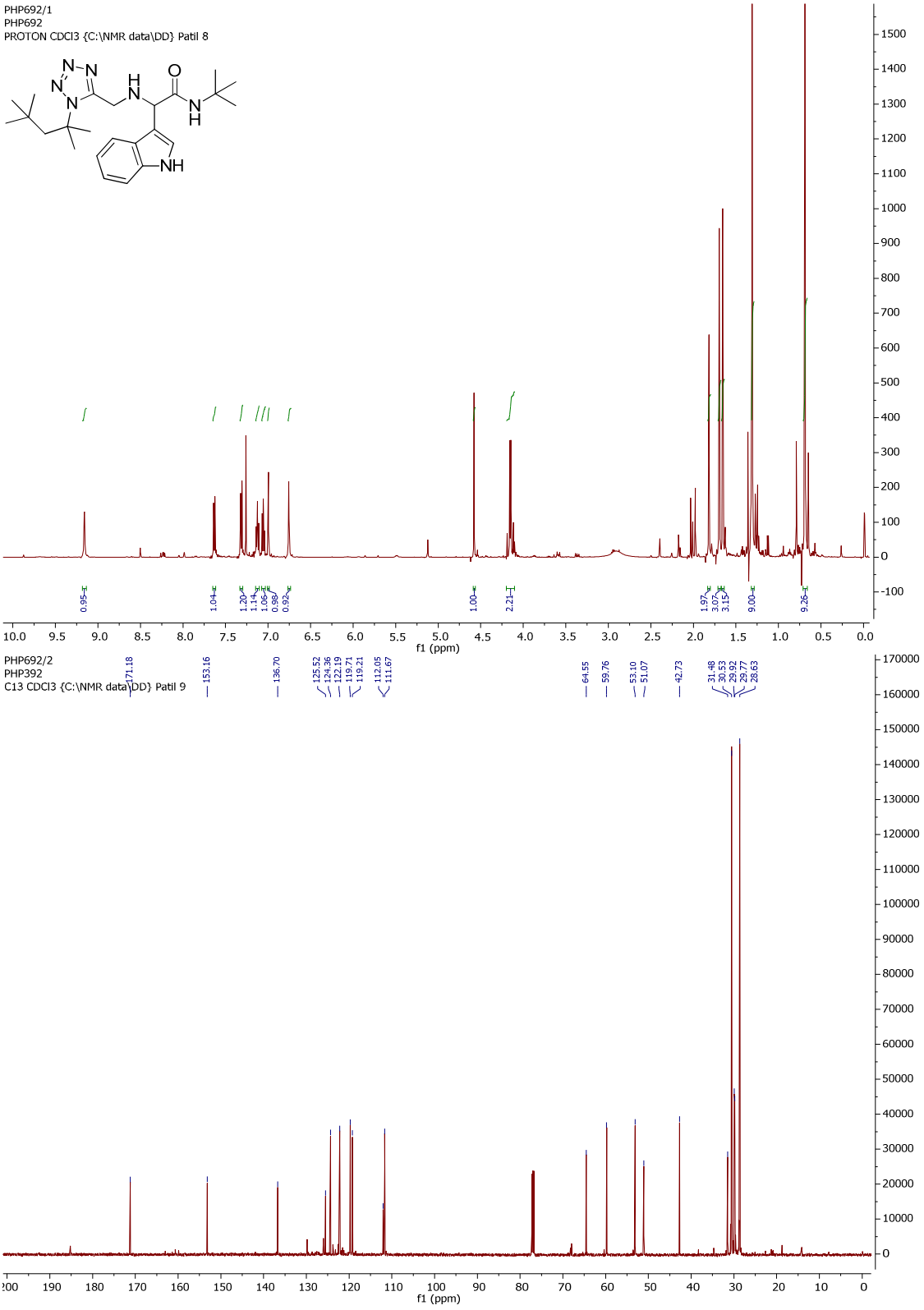


11d: 2-(4-cyanophenyl)-*N*-cyclohexyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:

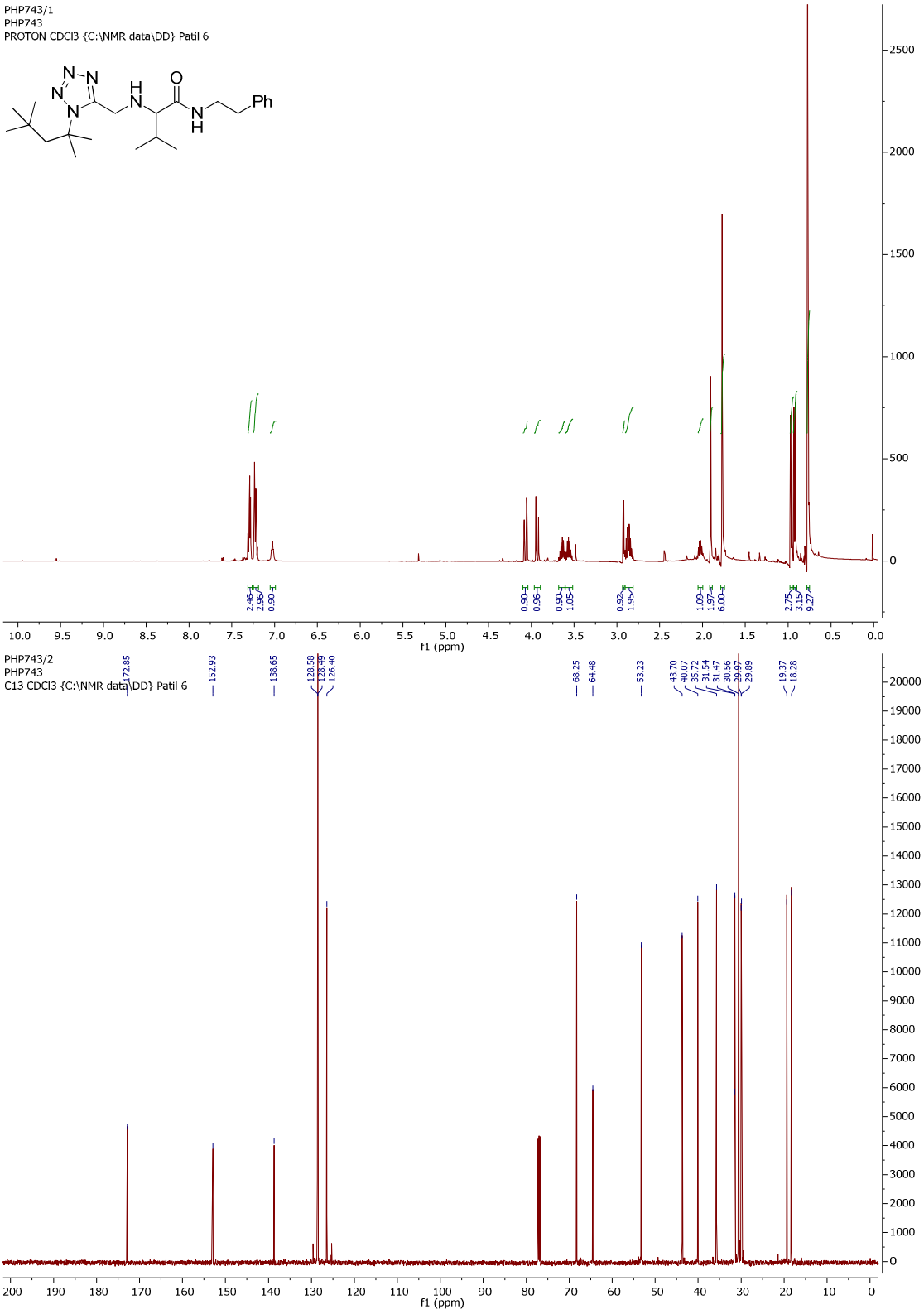




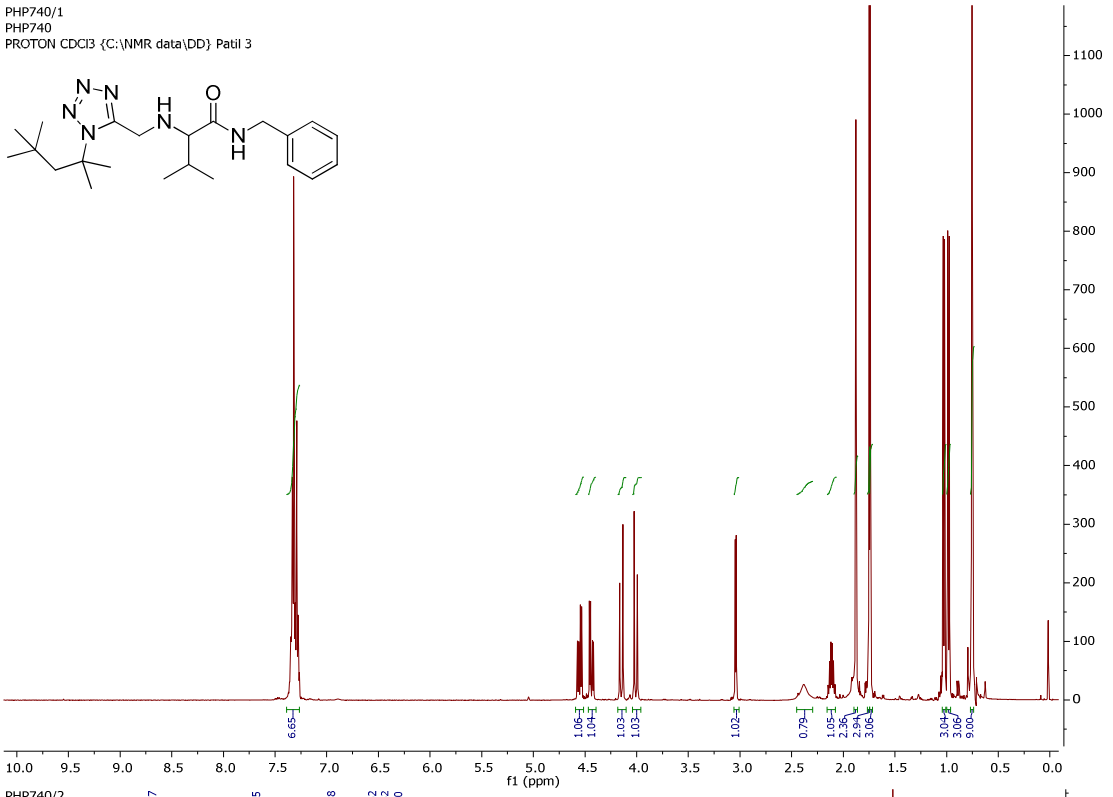
12d: *N*-(*tert*-butyl)-2-(1H-indol-3-yl)-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)acetamide:

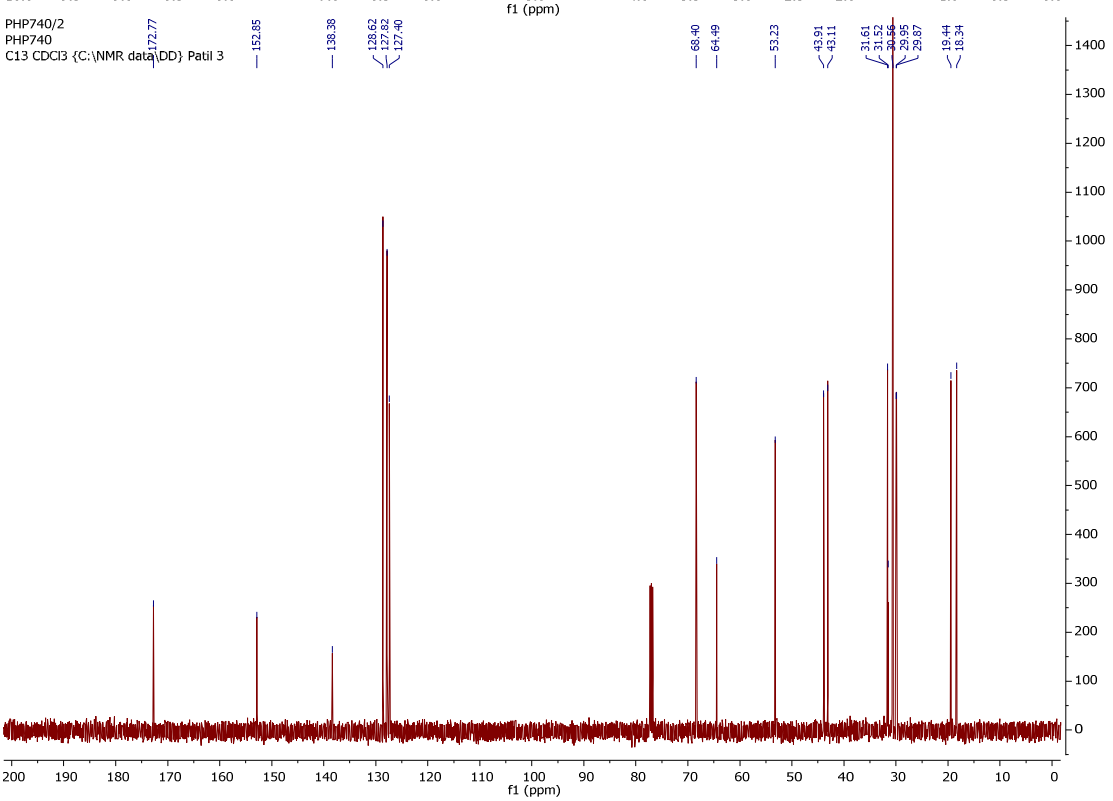


13d: 3-methyl-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)butanamide:

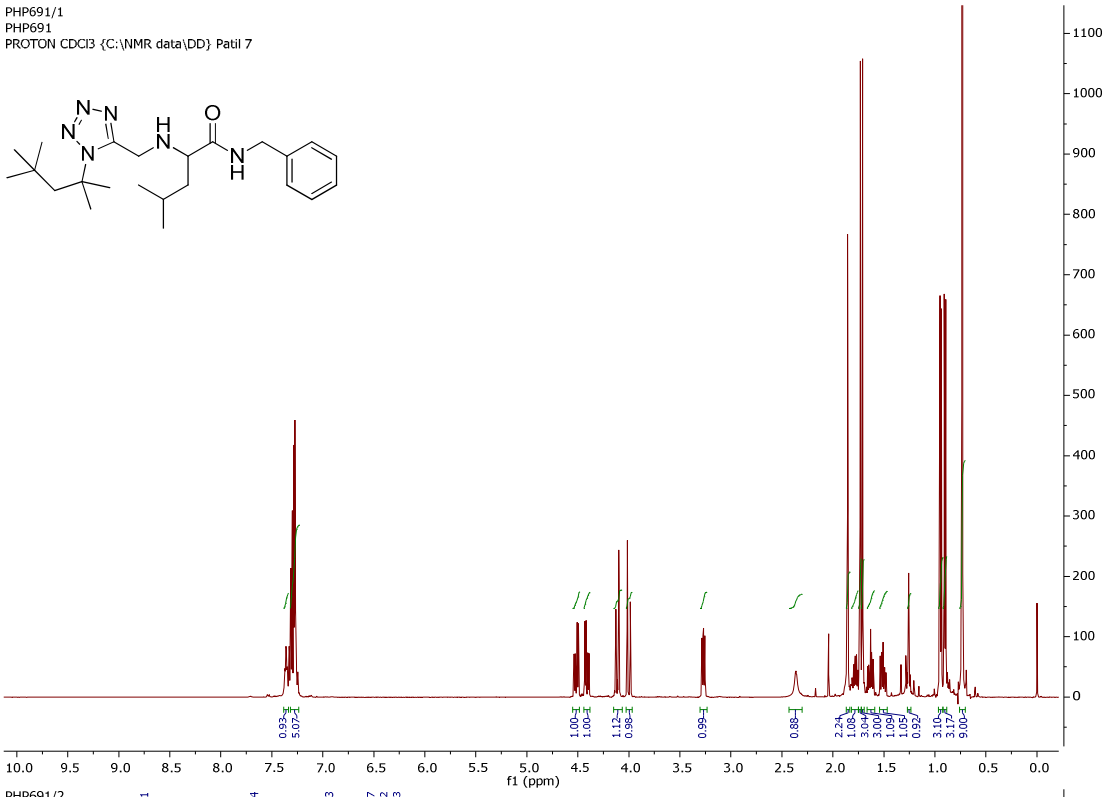


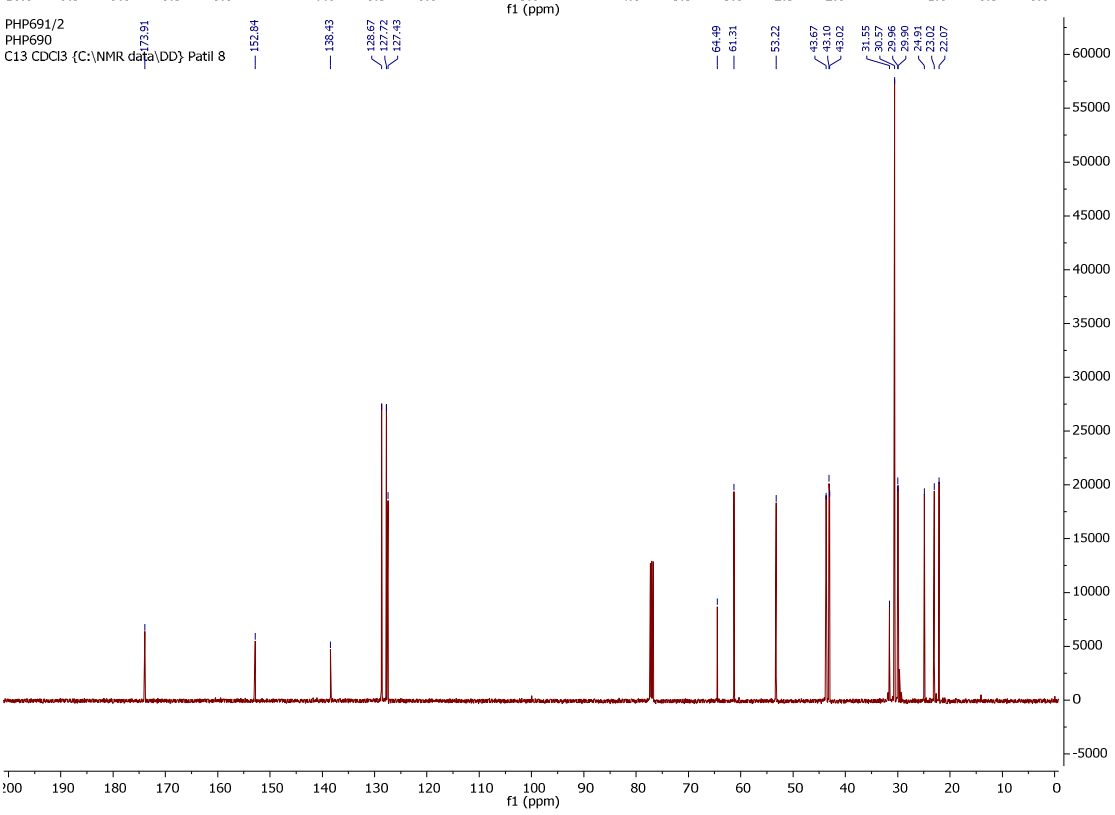
14d: *N*-benzyl-3-methyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)butanamide:



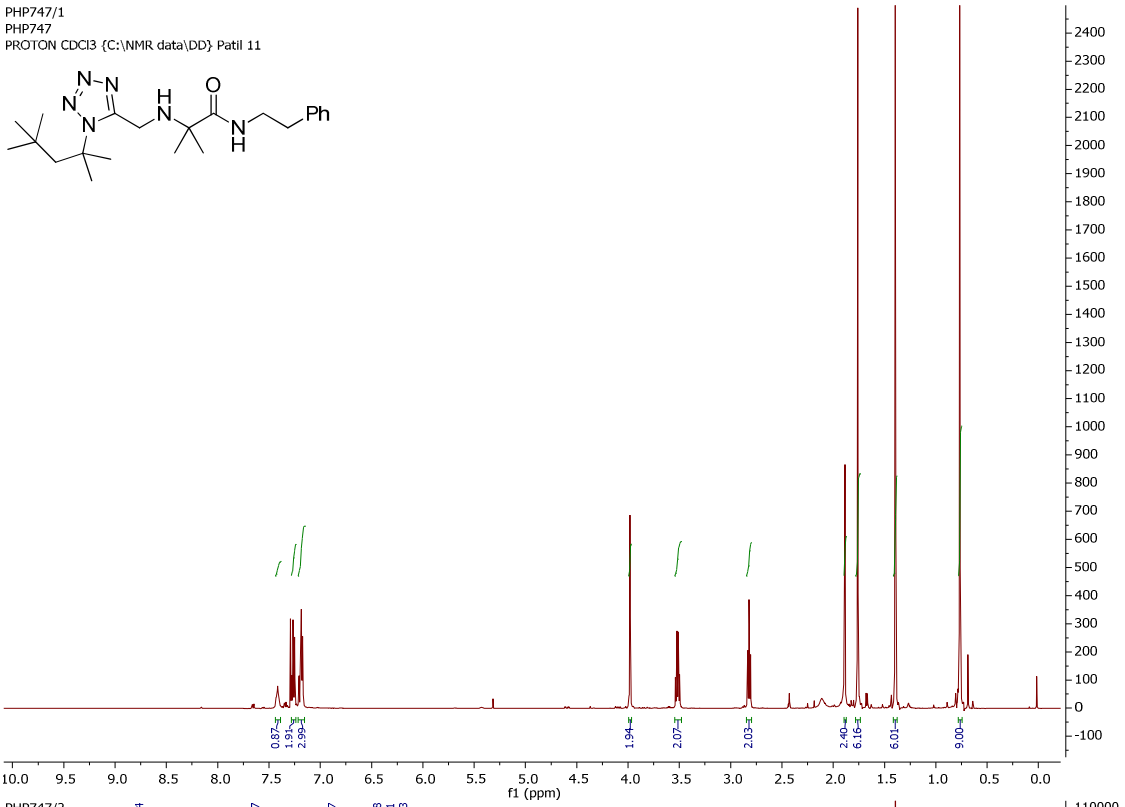


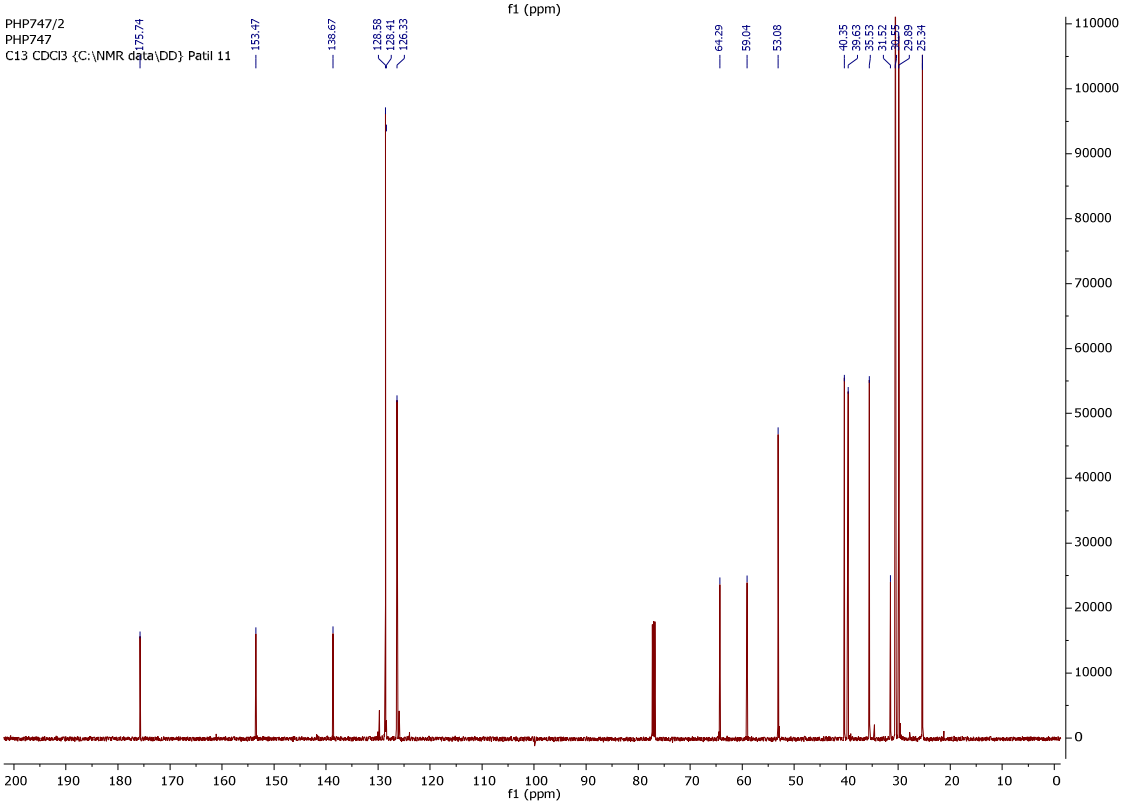
15d: *N*-benzyl-4-methyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)pentanamide:



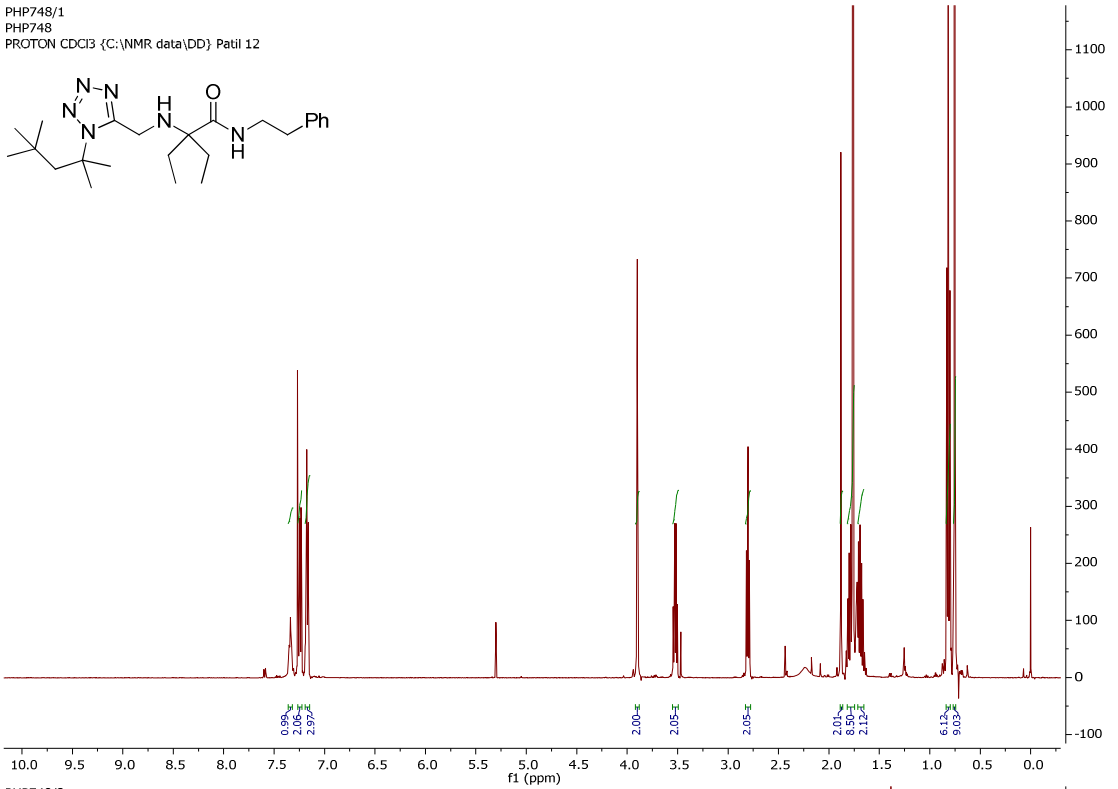


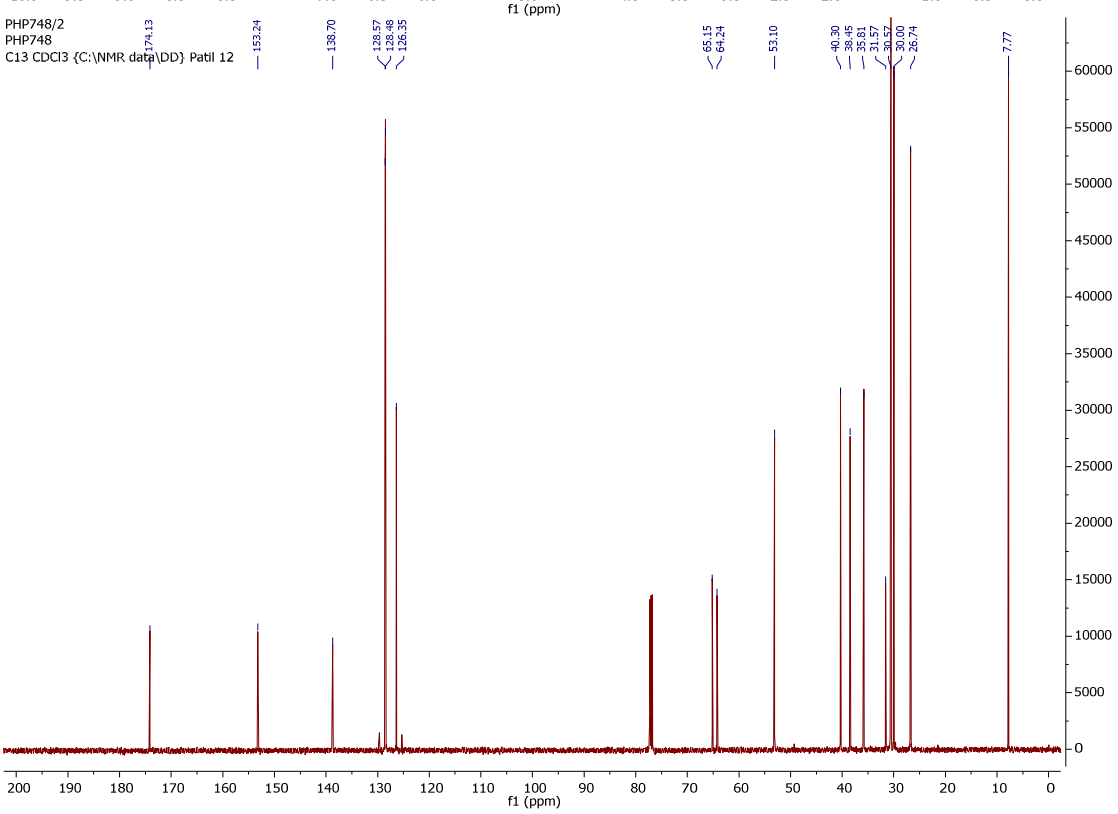
16d: 2-methyl-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)propenamide:



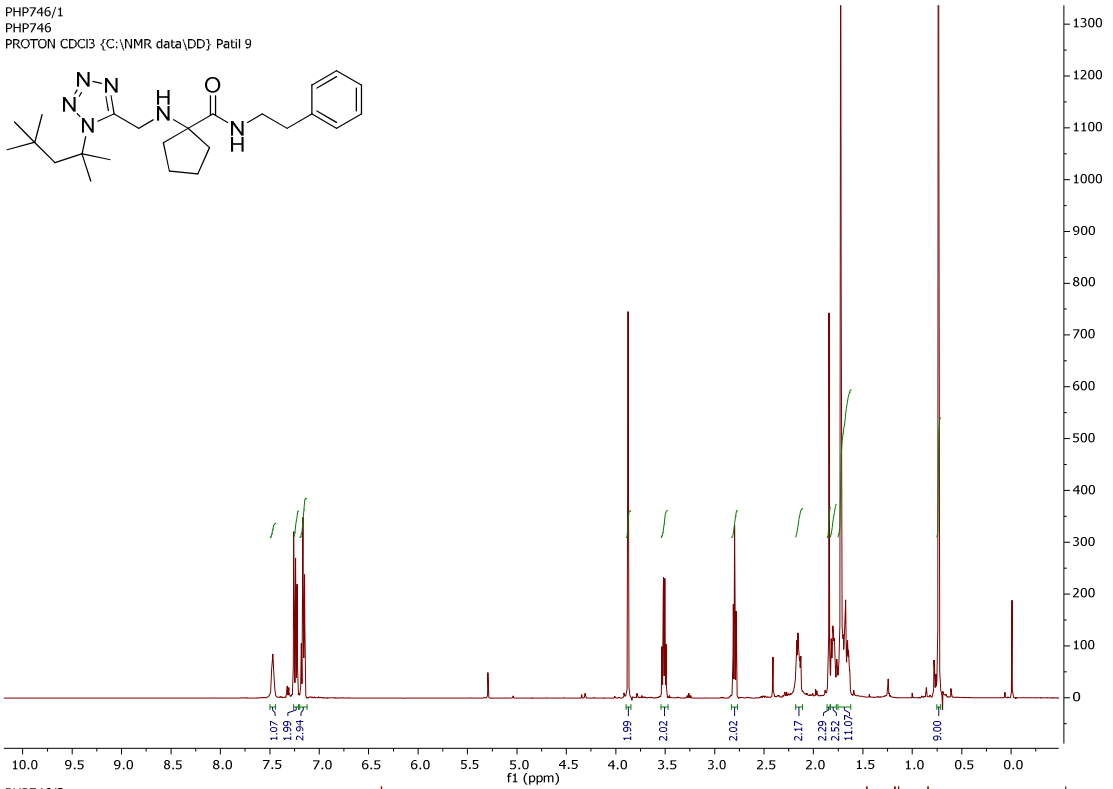


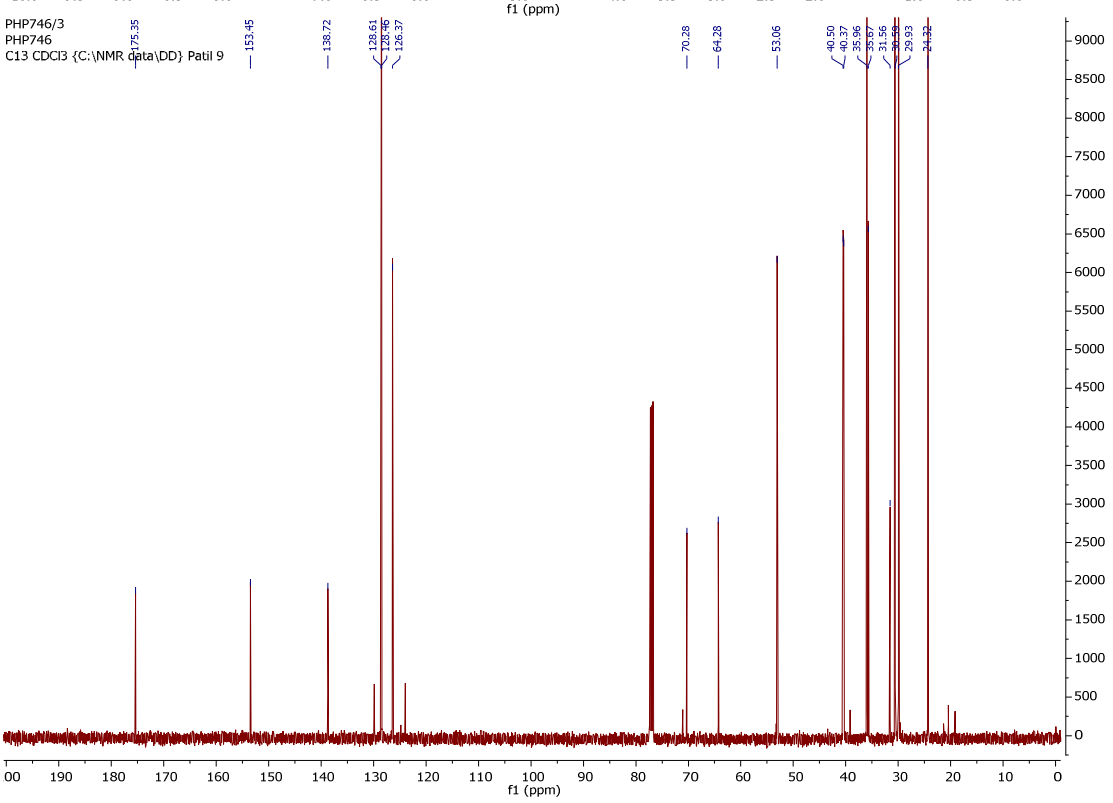
17d: 2-ethyl-*N*-phenethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)butanamide:



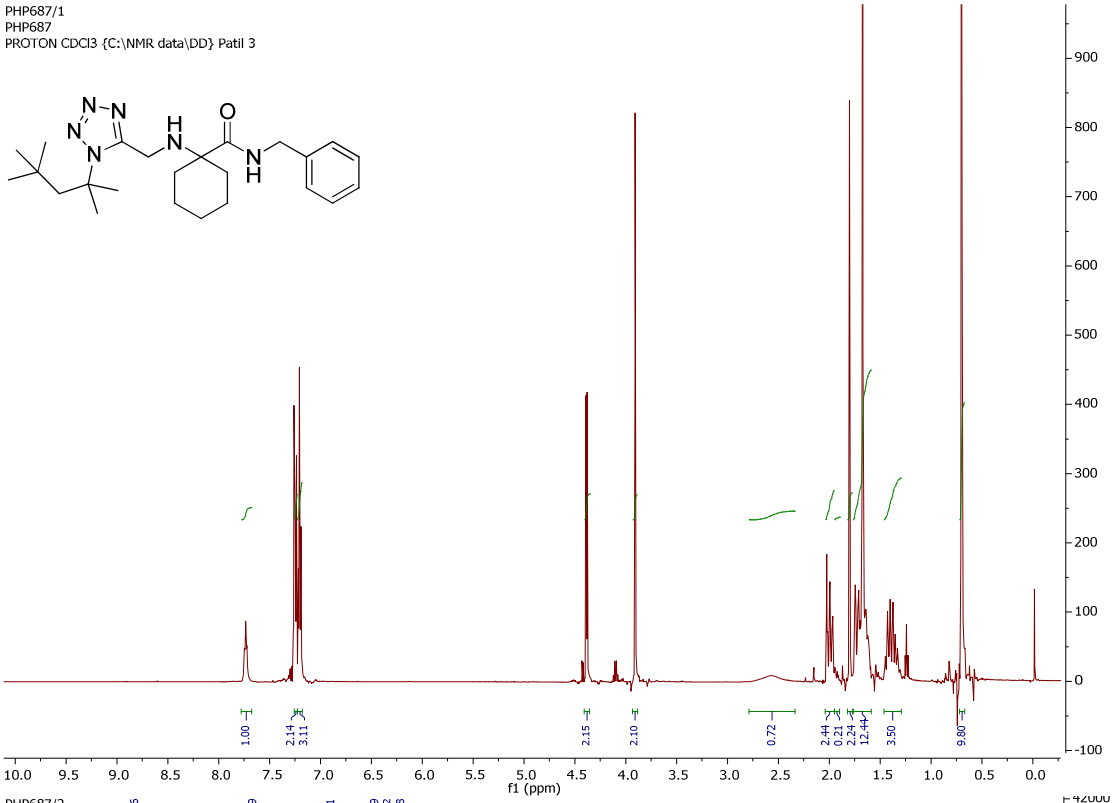


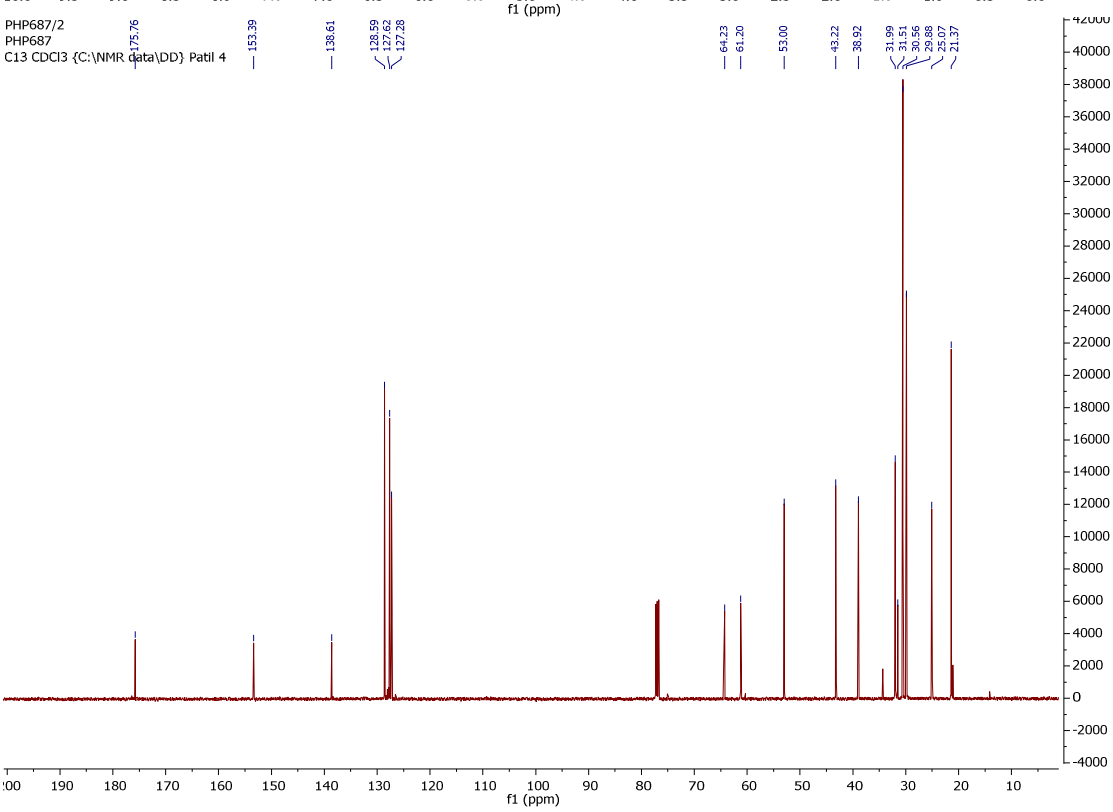
18d: *N*-phenethyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino) cyclopentanecarboxamide.



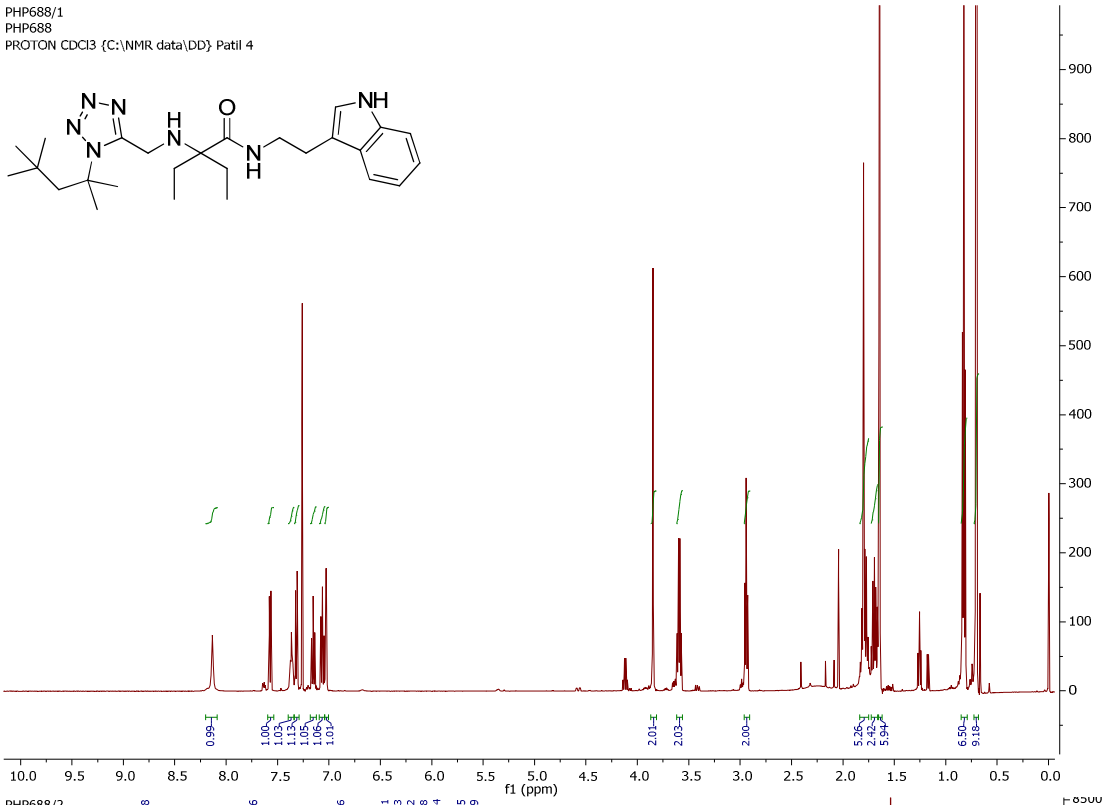


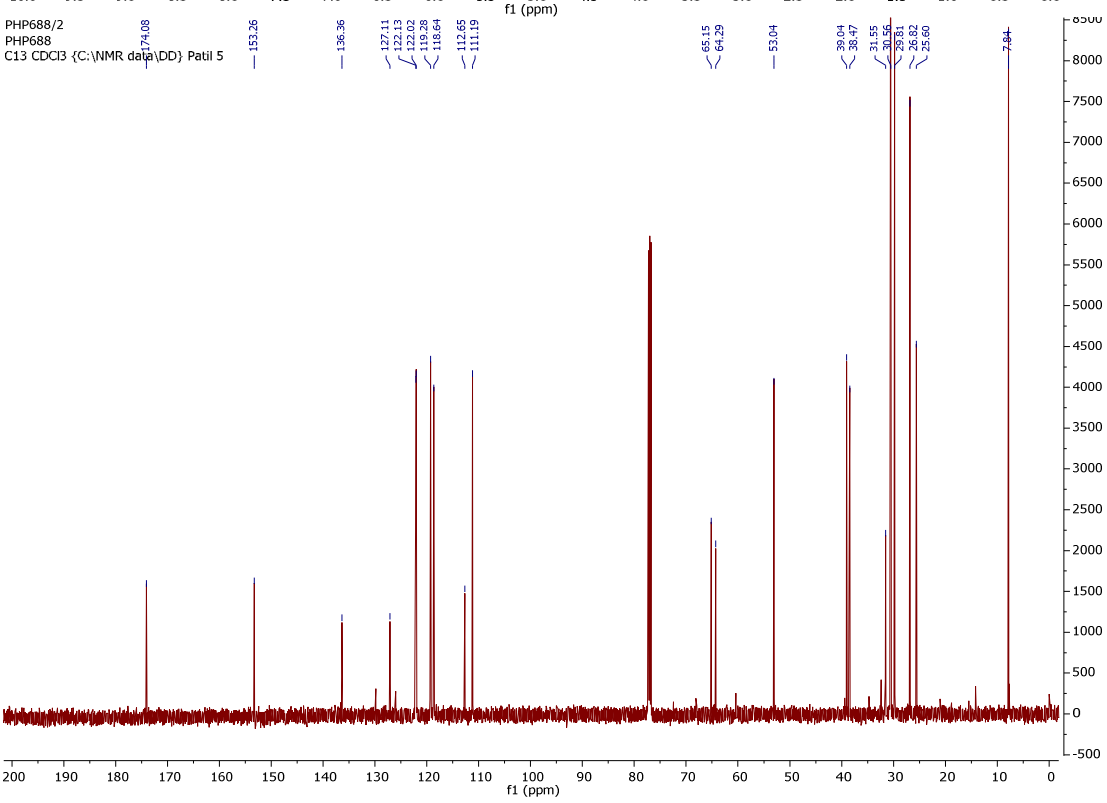
19d: *N*-benzyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino) cyclohexane-1-carboxamide:



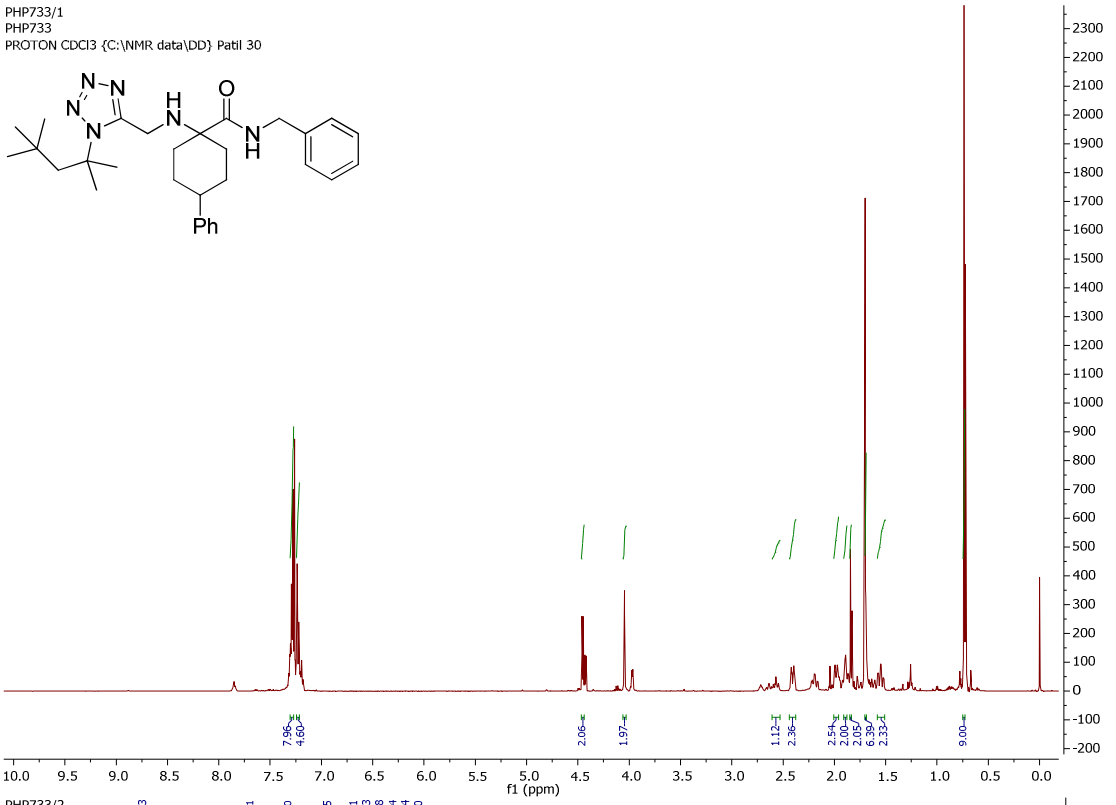


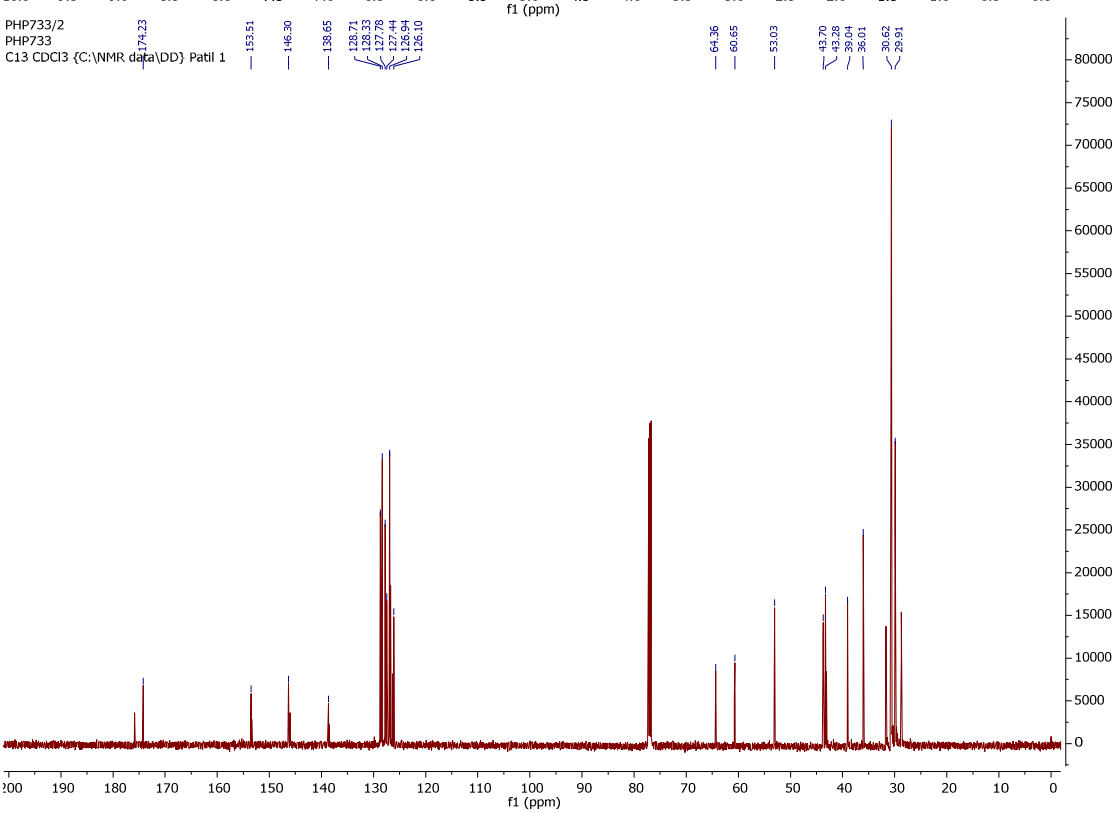
20d: *N*-(2-(1*H*-indol-3-yl)ethyl)-2-ethyl-2-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl)amino)butanamide:



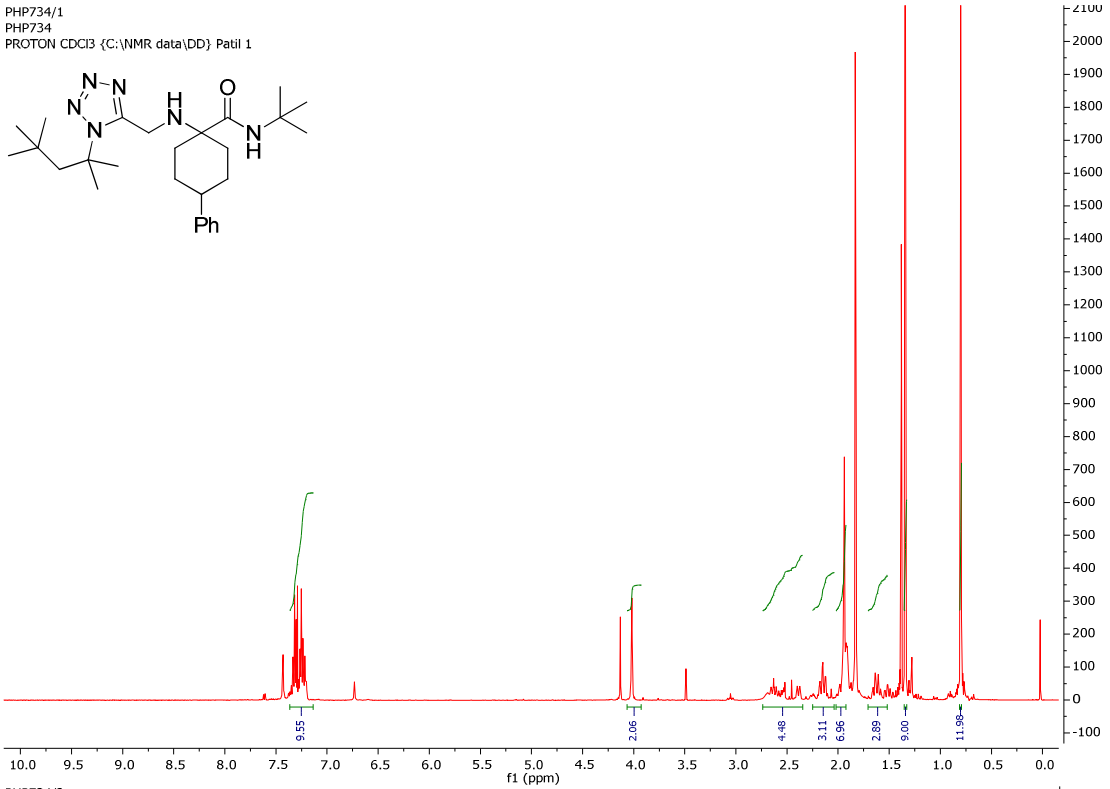


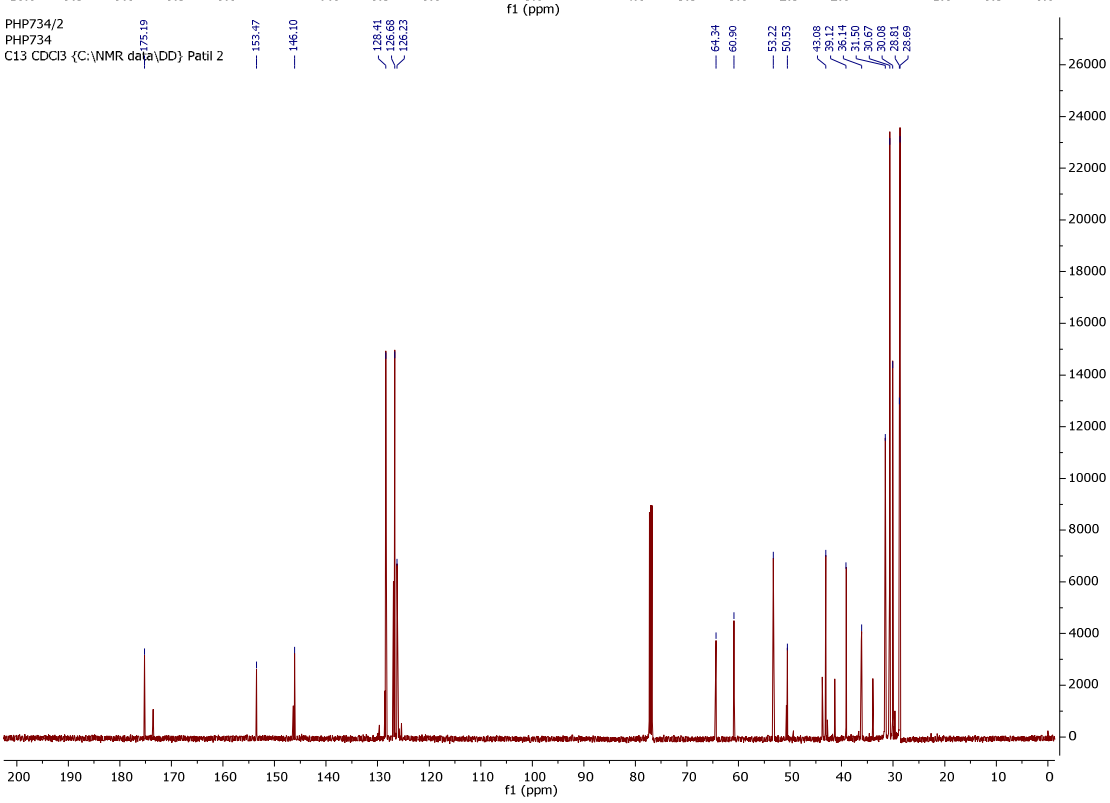
21d: *N*-benzyl-4-phenyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)cyclohexane-1-carboxamide:



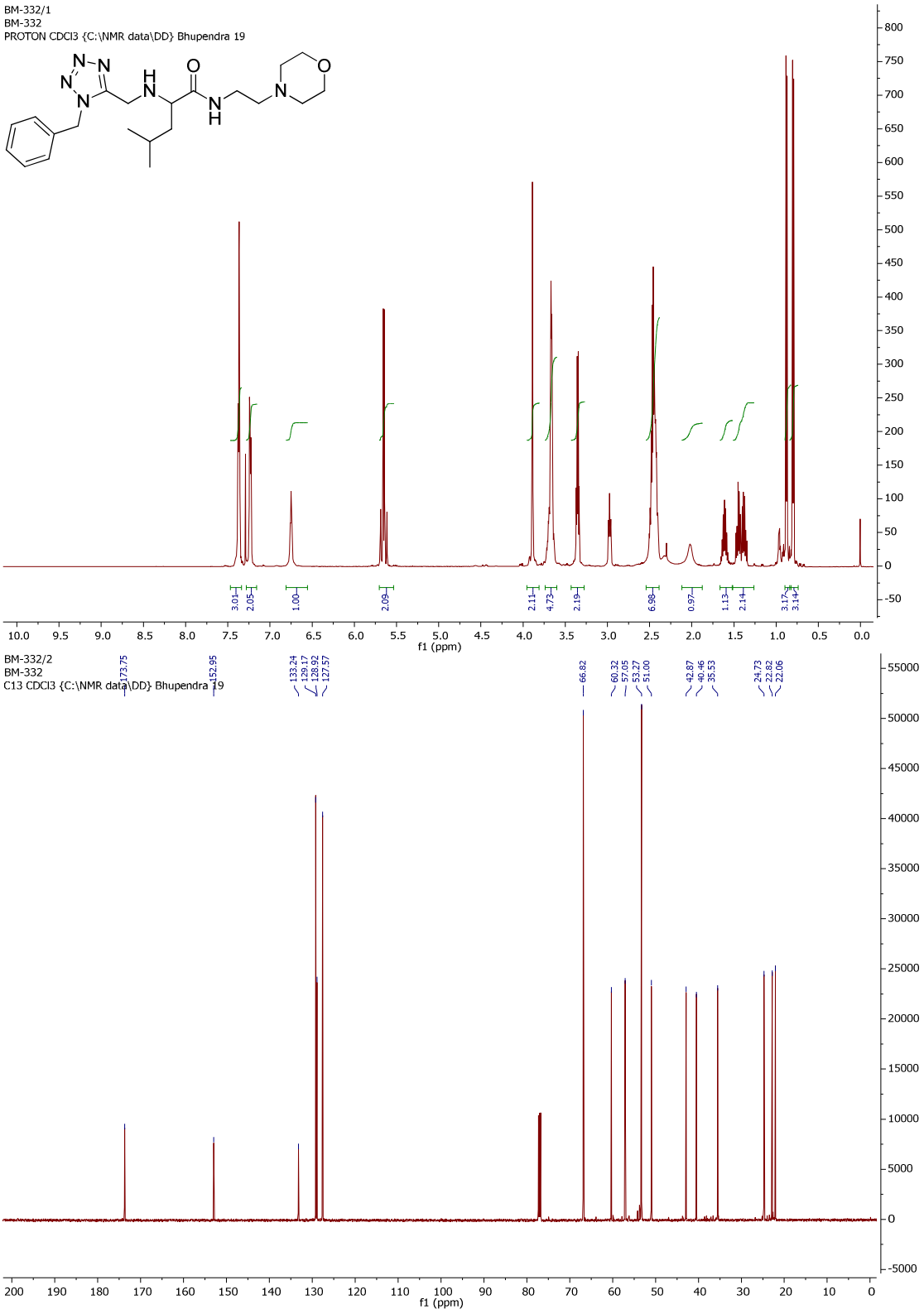


22d: *N*-(*tert*-butyl)-4-phenyl-1-(((1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)methyl) amino)cyclohexane-1-carboxamide:

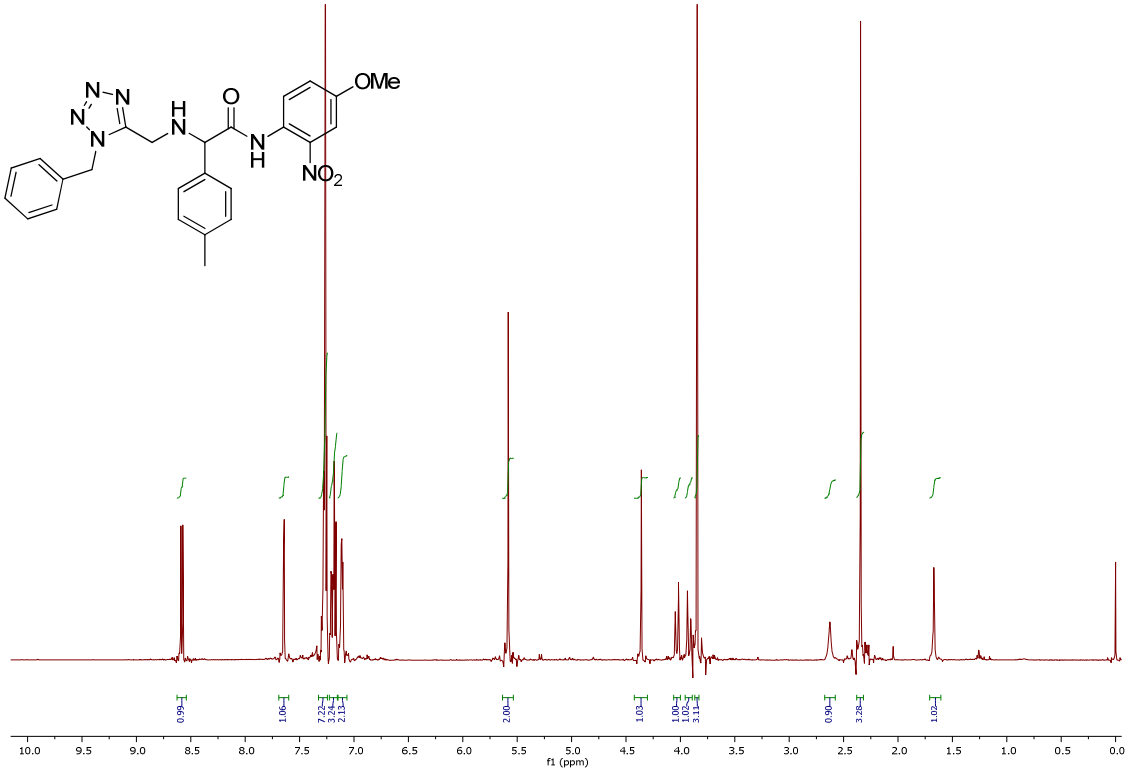


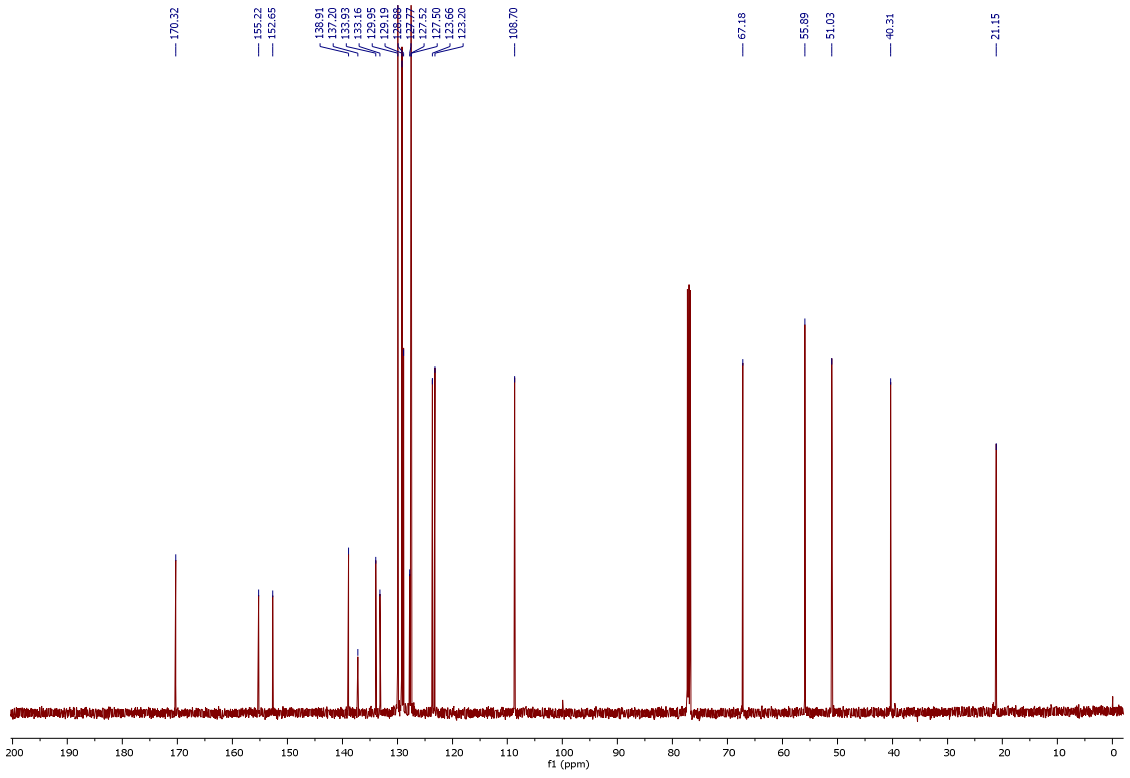


23d: 2-(((1-benzyl-1*H*-tetrazol-5-yl)methyl)amino)-4-methyl-*N*-(2-morpholinoethyl) pentanamide:

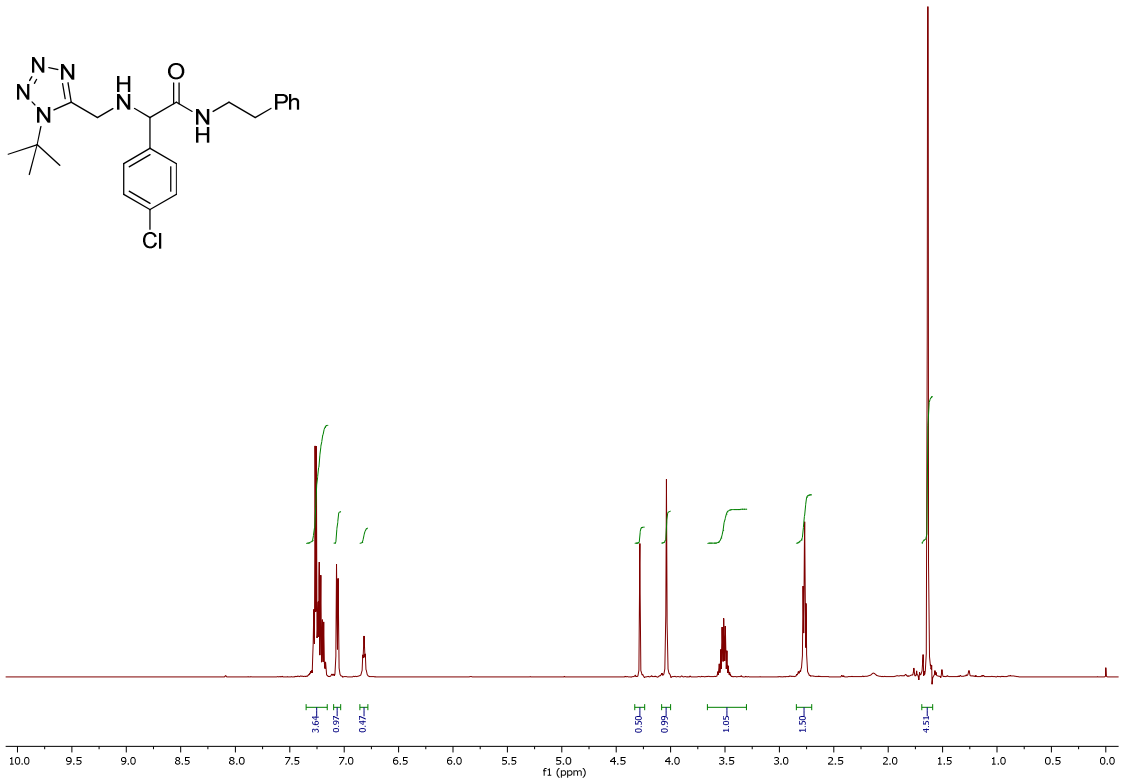


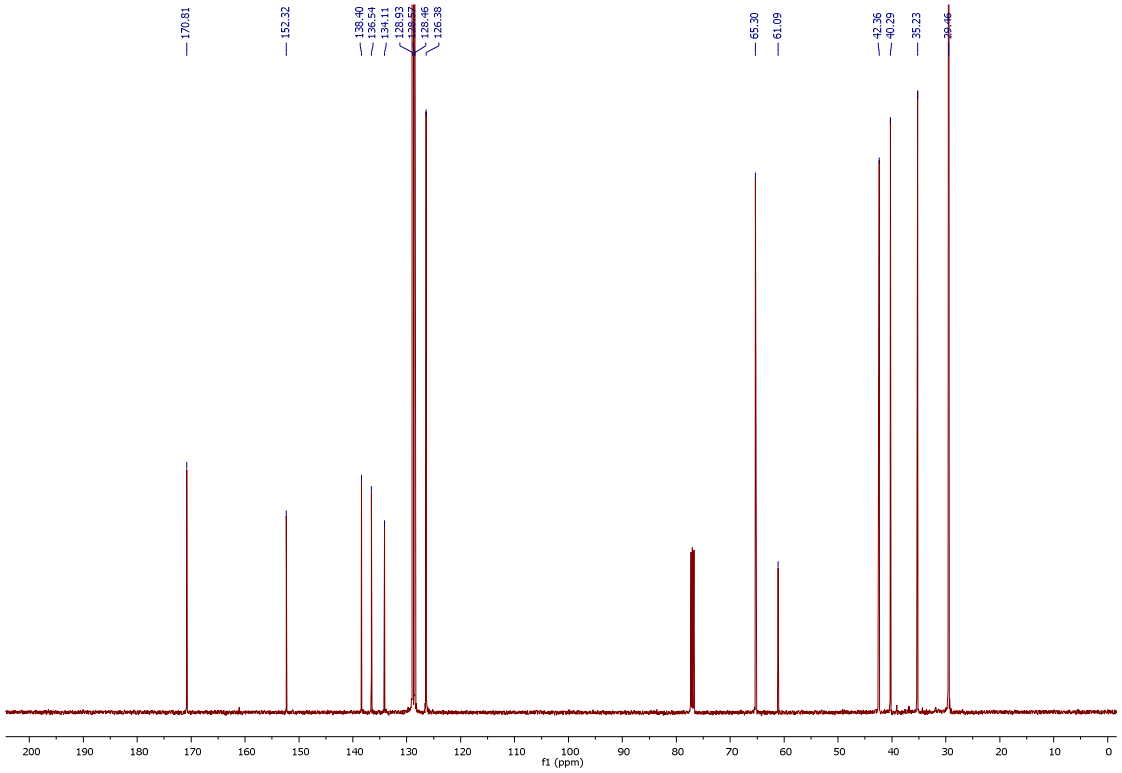
24d: 2-(((1-benzyl-1*H*-tetrazol-5-yl)methyl)amino)-*N*-(4-methoxy-2-nitrophenyl)-2-(*p*-tolyl)acetamide:



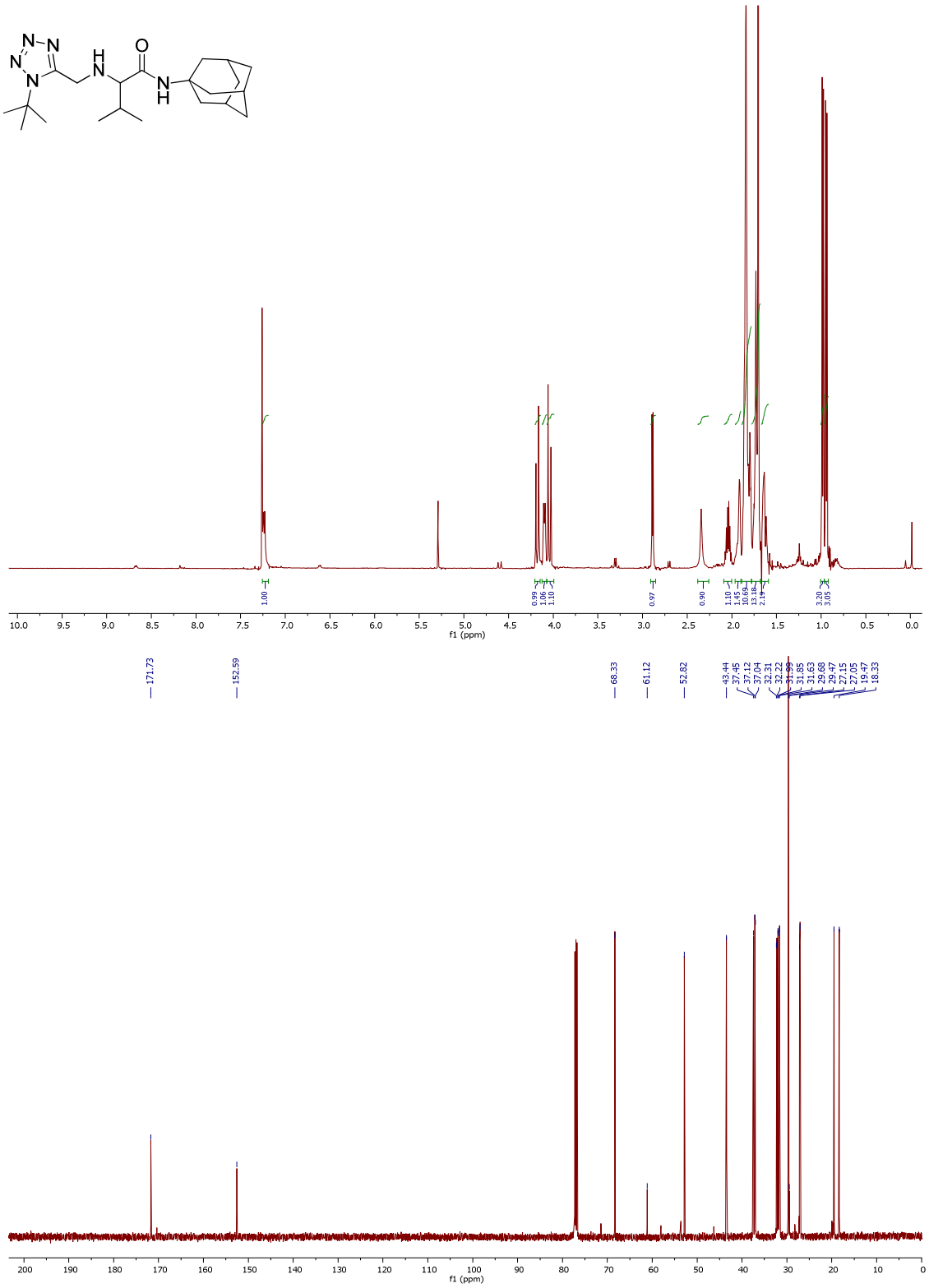


25d: 2-(((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)methyl)amino)-2-(4-chlorophenyl)-*N*-phenethylacetamide:

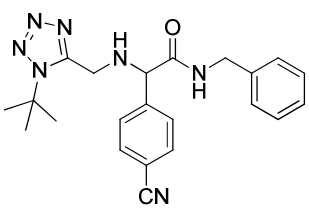


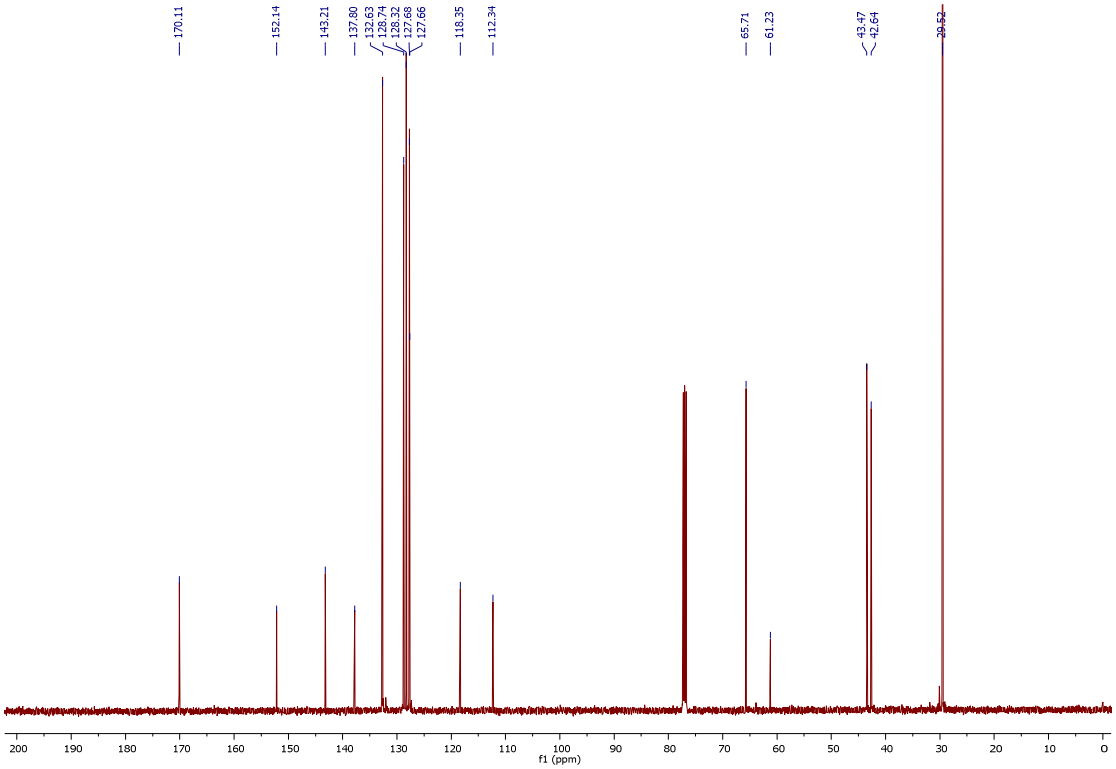


26d: ***N*-((1S,3s)-adamantan-1-yl)-2-(((1-(*tert*-butyl)-1*H*-tetrazol-5-yl)methyl)amino)-3-methylbutanamide:**

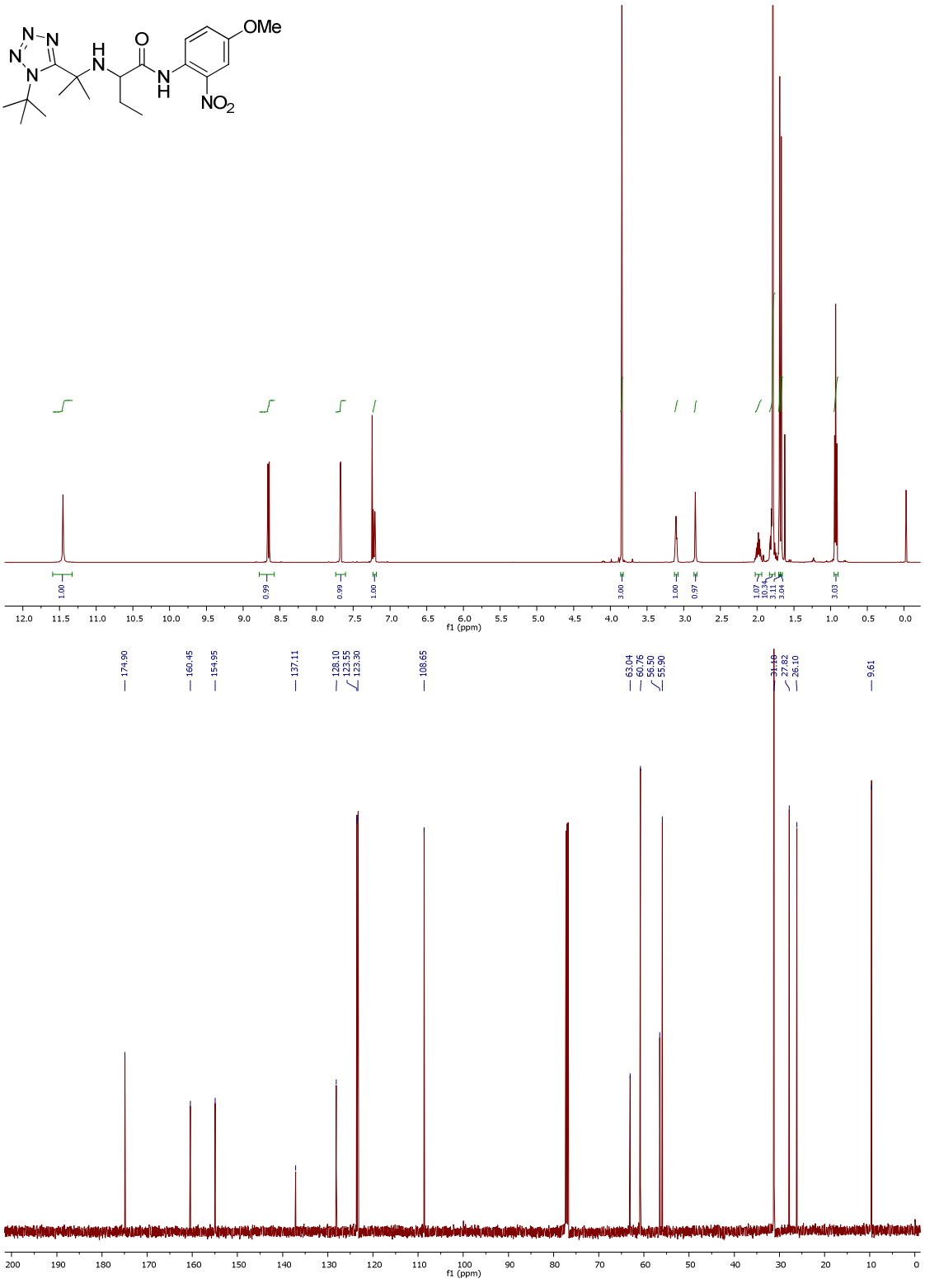


27d: ***N*-benzyl-2-(((1-(tert-butyl)-1*H*-tetrazol-5-yl)methyl)amino)-2-(4-cyanophenyl) acetamide:**

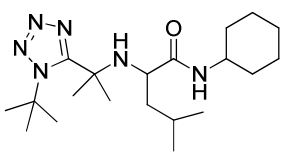


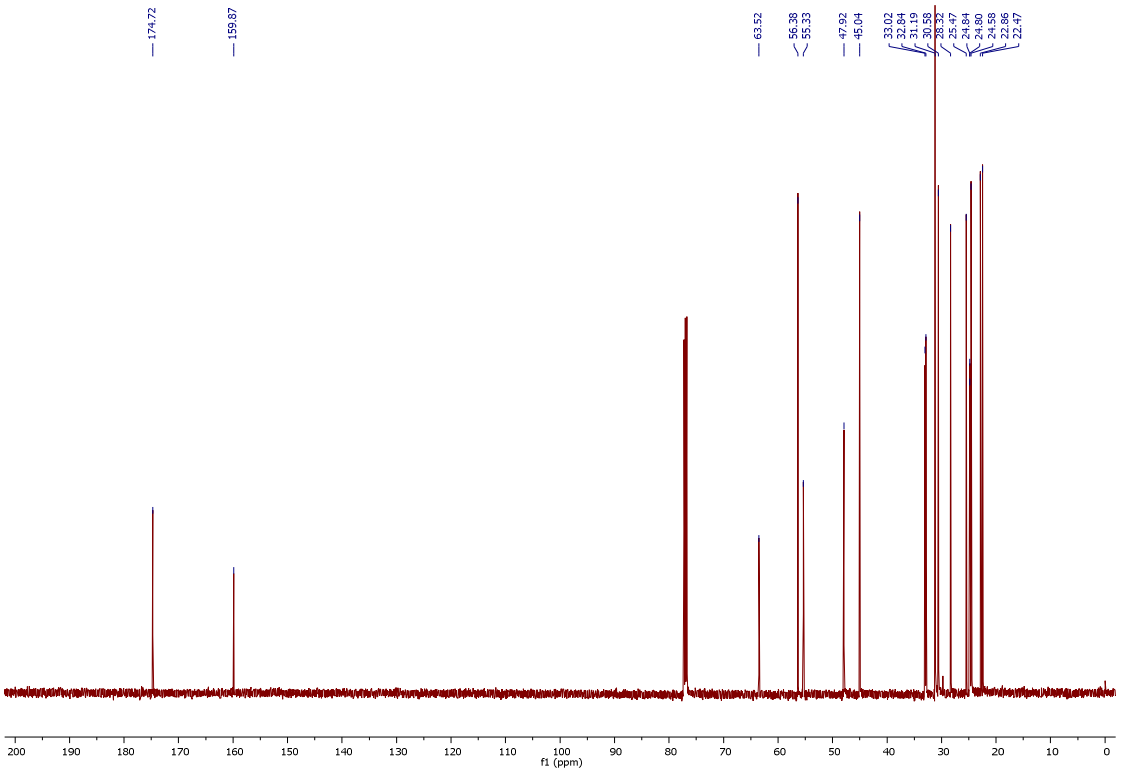


28d: 2-((2-(1-(tert-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-*N*-(4-methoxy-2-nitrophenyl)butanamide:

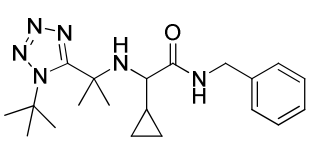


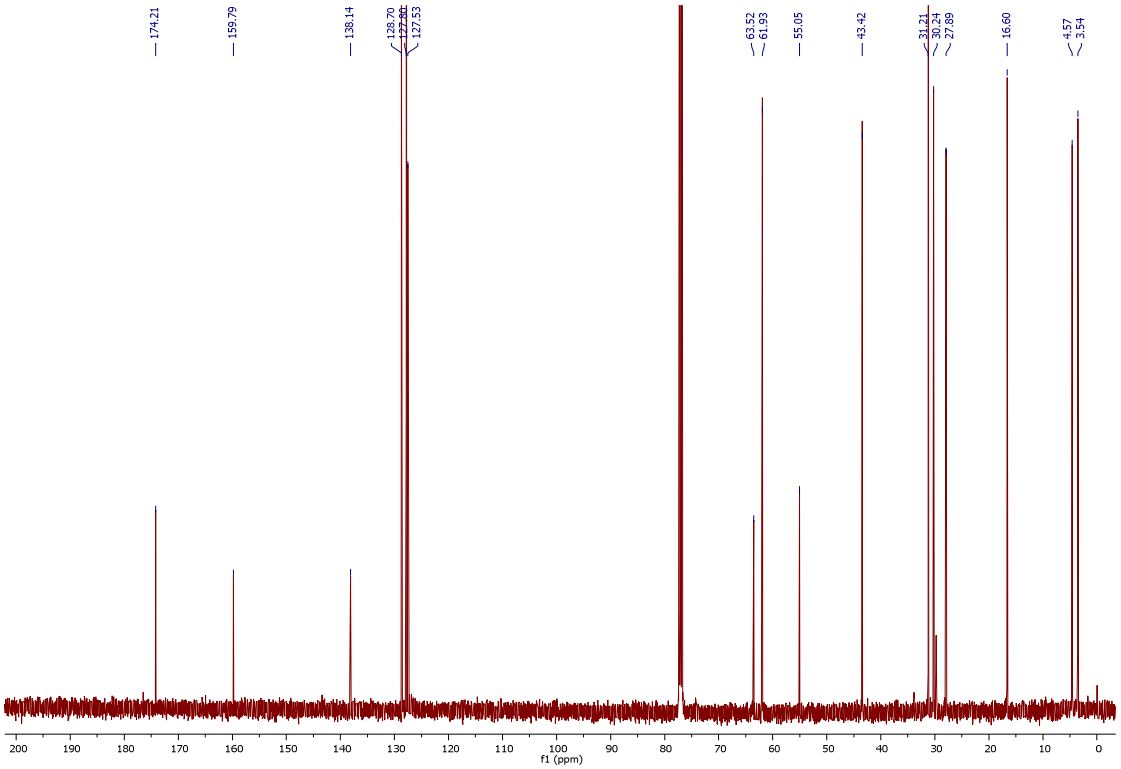
29d: 2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-*N*-cyclohexyl-4-methylpentanamide:



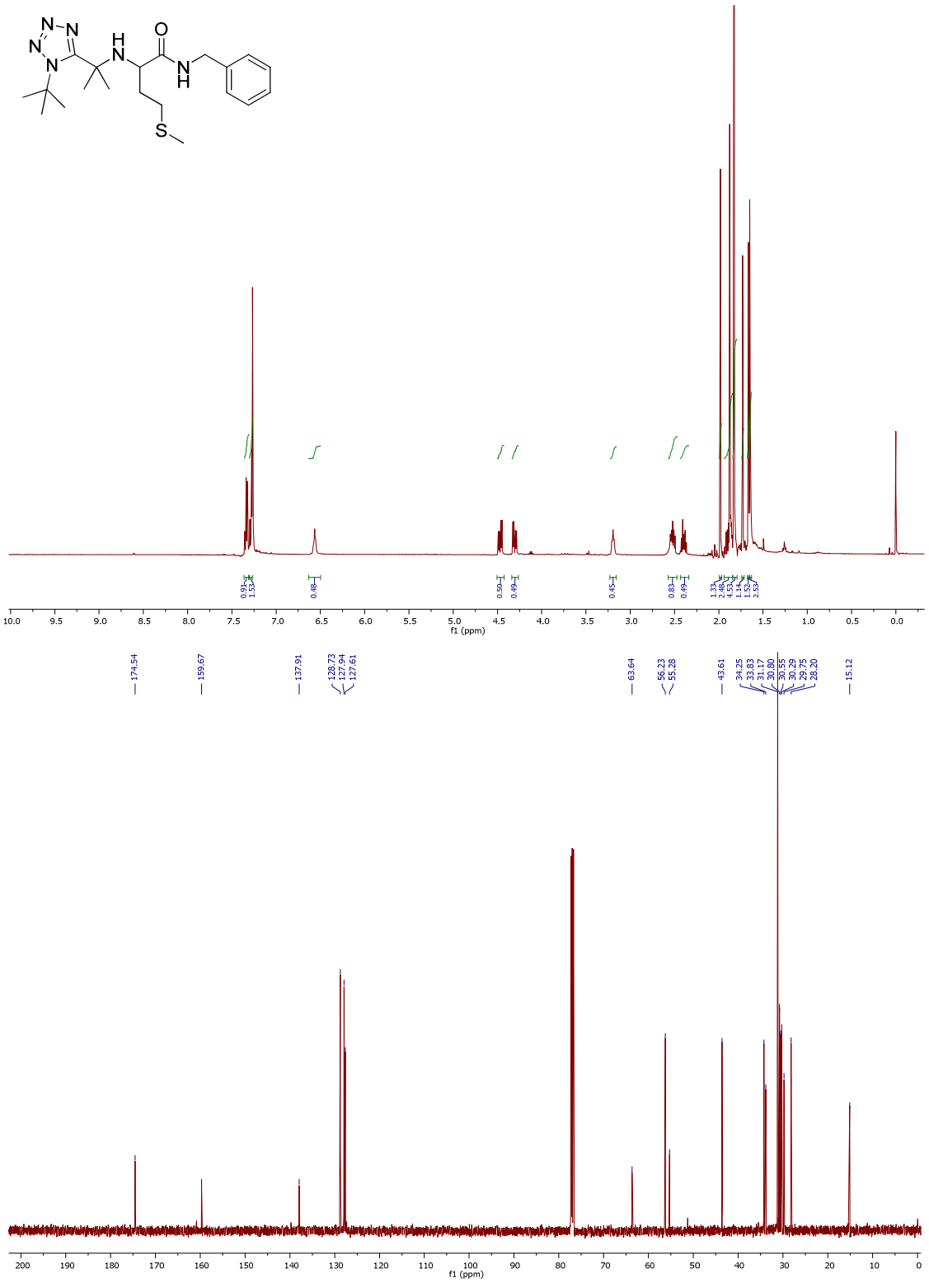


30d: ***N*-benzyl-2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-2-cyclopropylacetamide:**

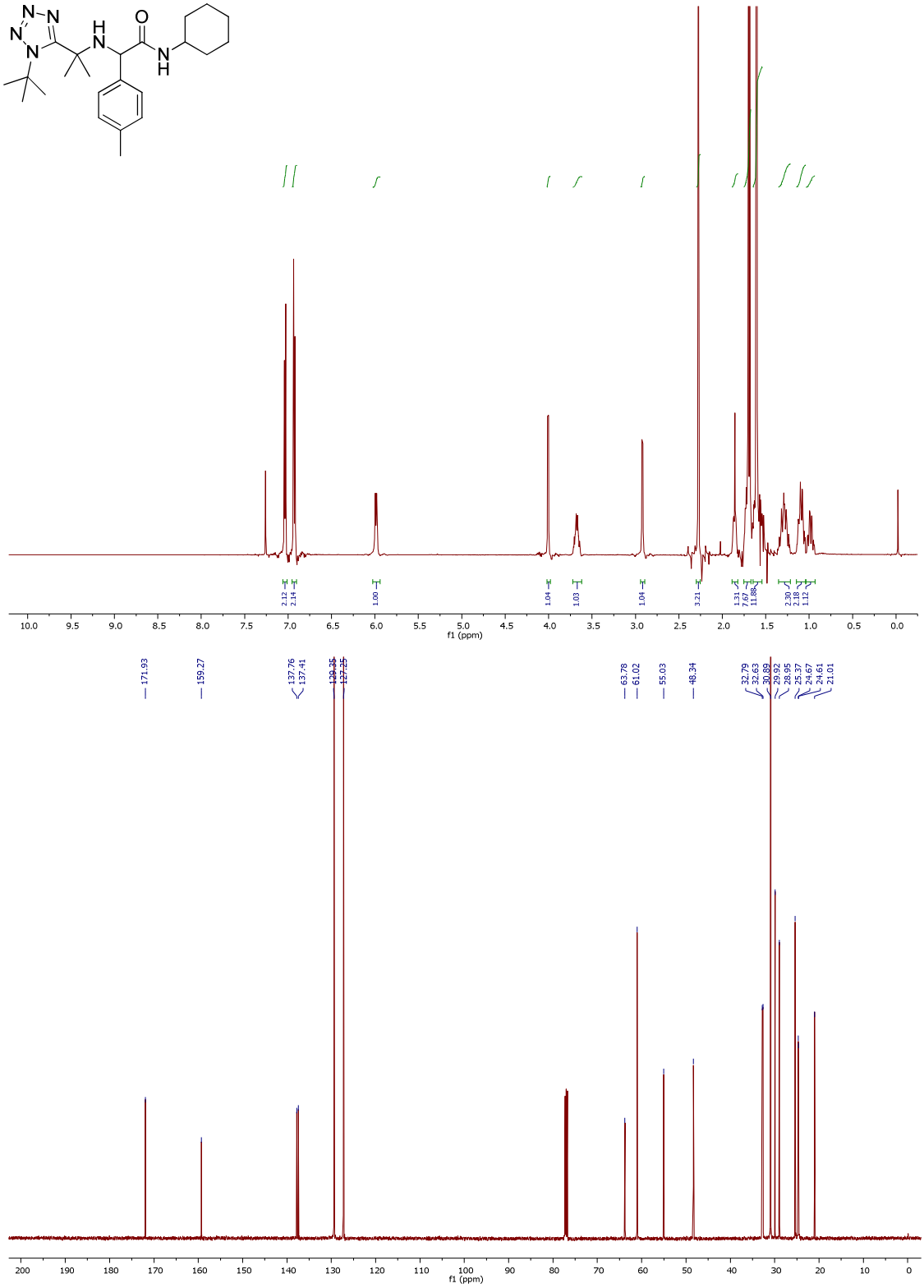




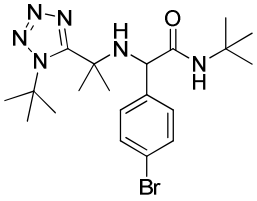
31d: *N*-benzyl-2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-4-(methylthio) butanamide:

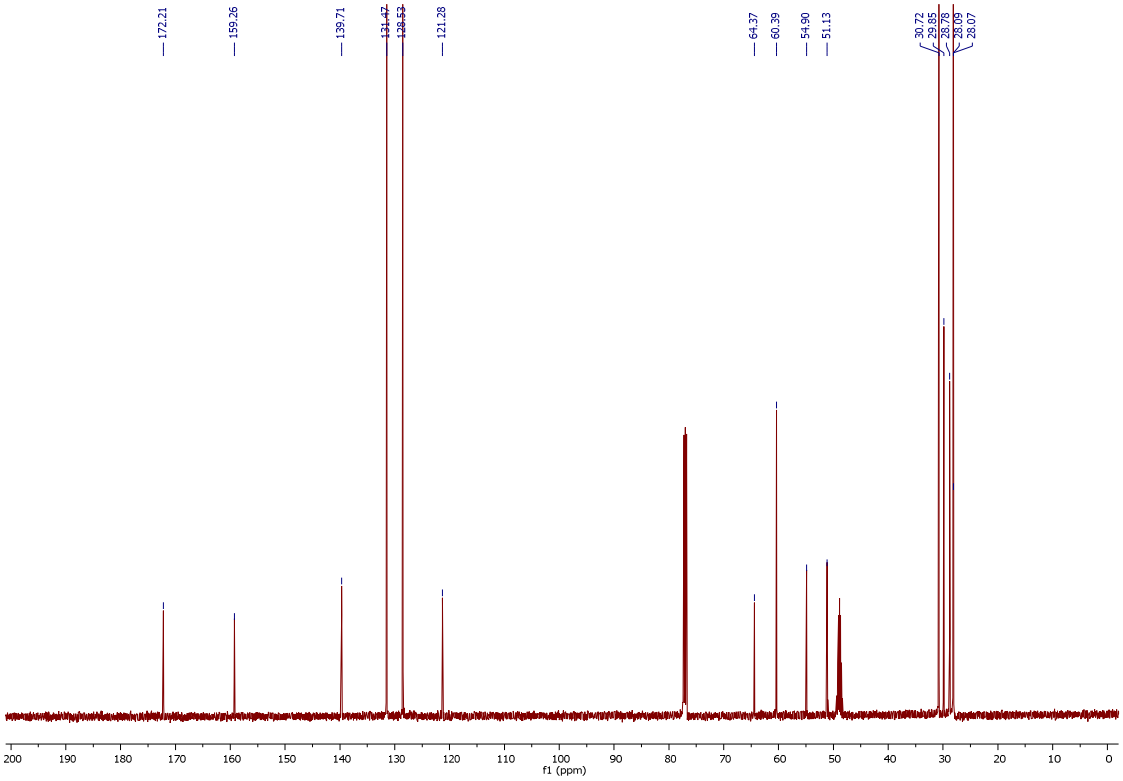


33d: 2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-*N*-cyclohexyl-2-(*p*-tolyl) acetamide:

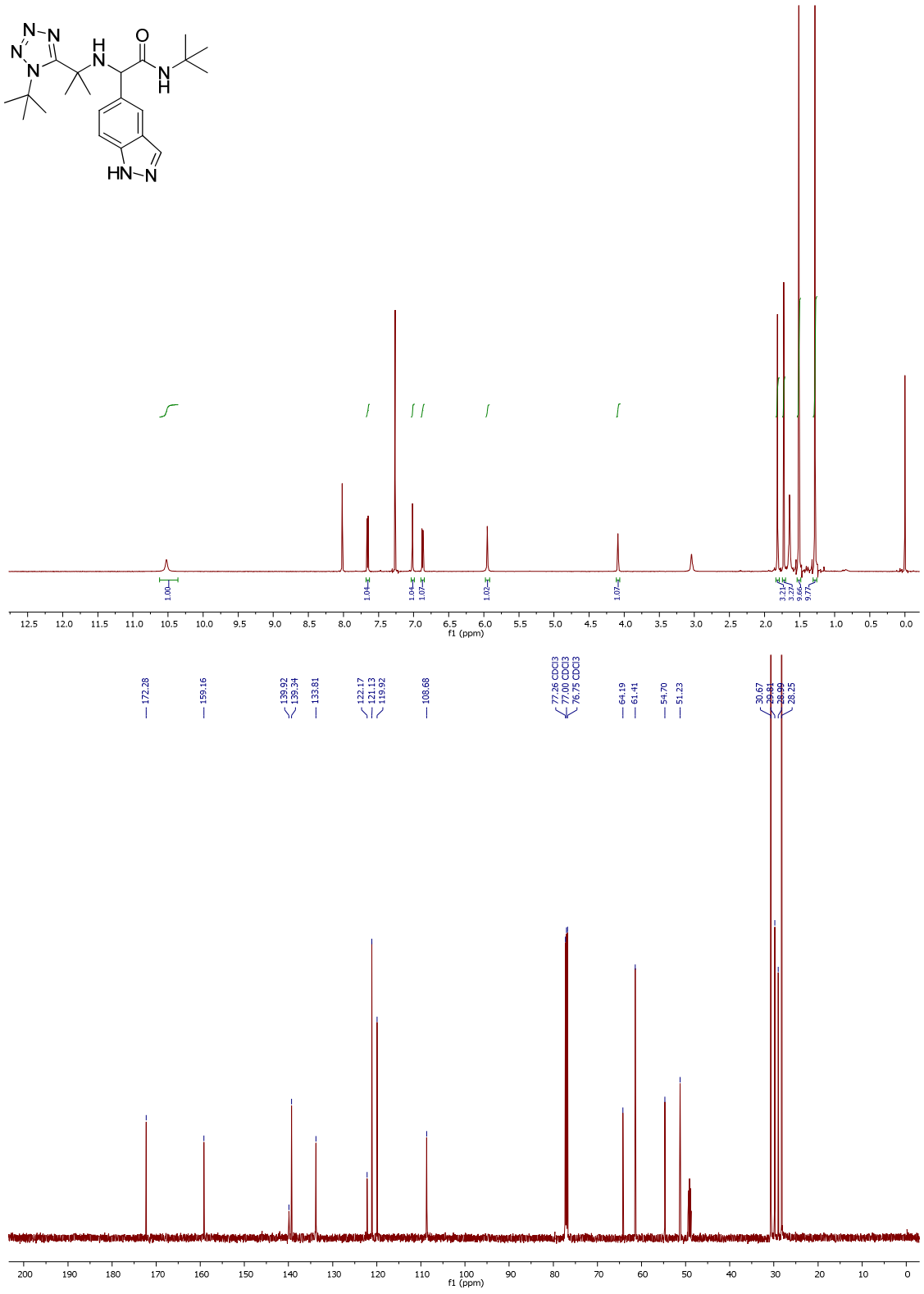


34d: 2-(4-bromophenyl)-*N*-(*tert*-butyl)-2-((2-(1-(tert-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)acetamide:

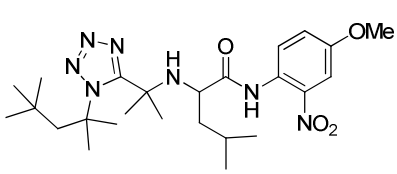


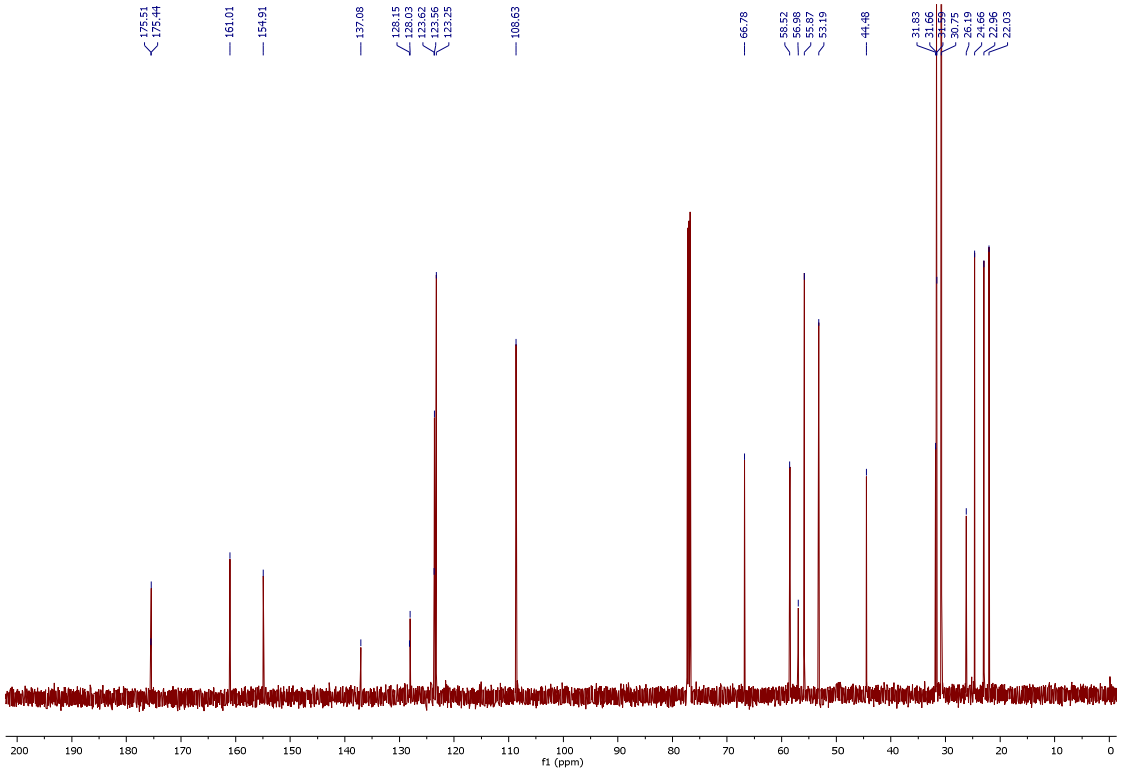


35d: ***N*-(*tert*-butyl)-2-((2-(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)-2-(1*H*-indazol-5-yl)acetamide:**

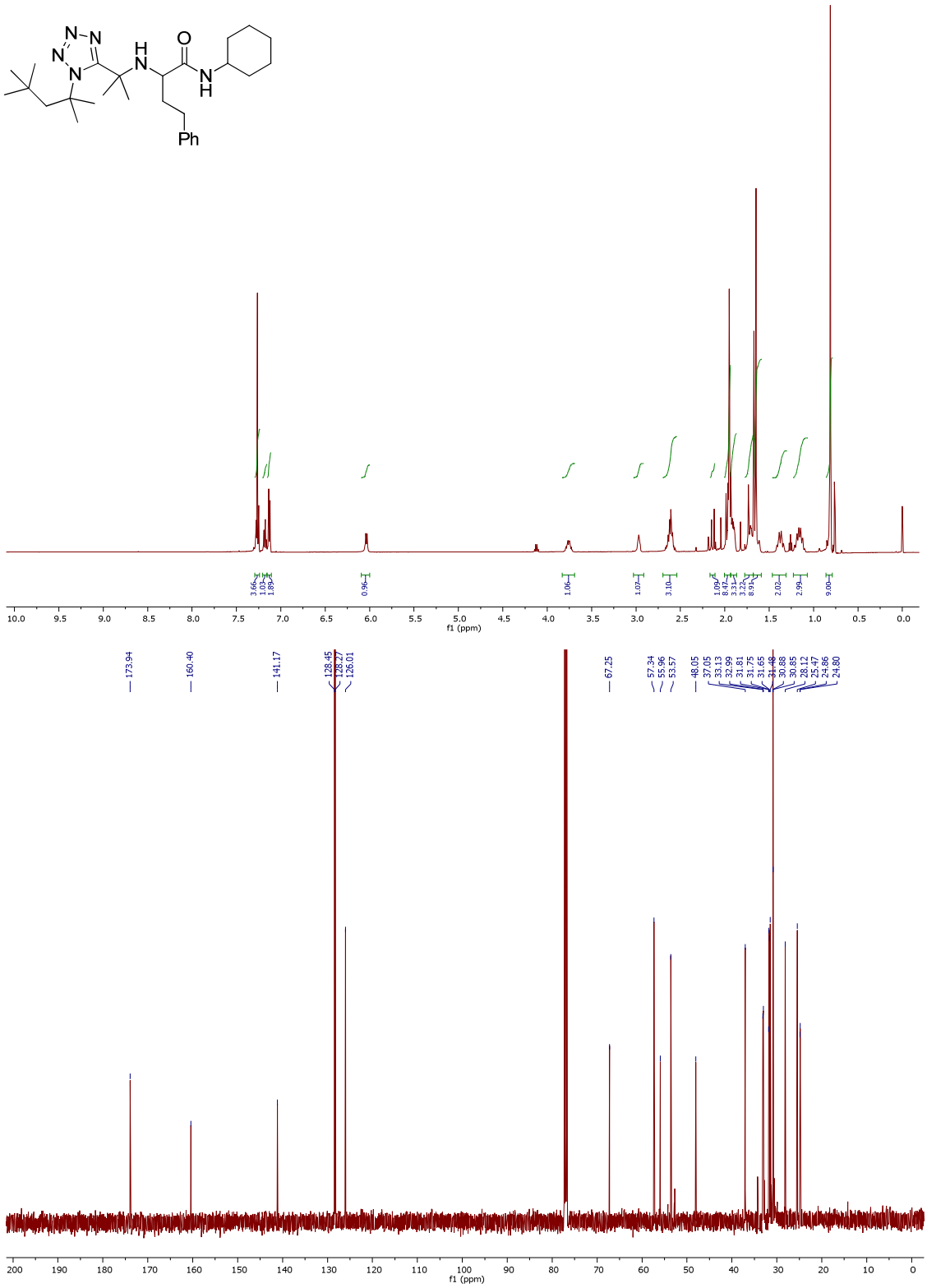


37d: ***N*-(4-methoxy-2-nitrophenyl)-4-methyl-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)pentanamide:**

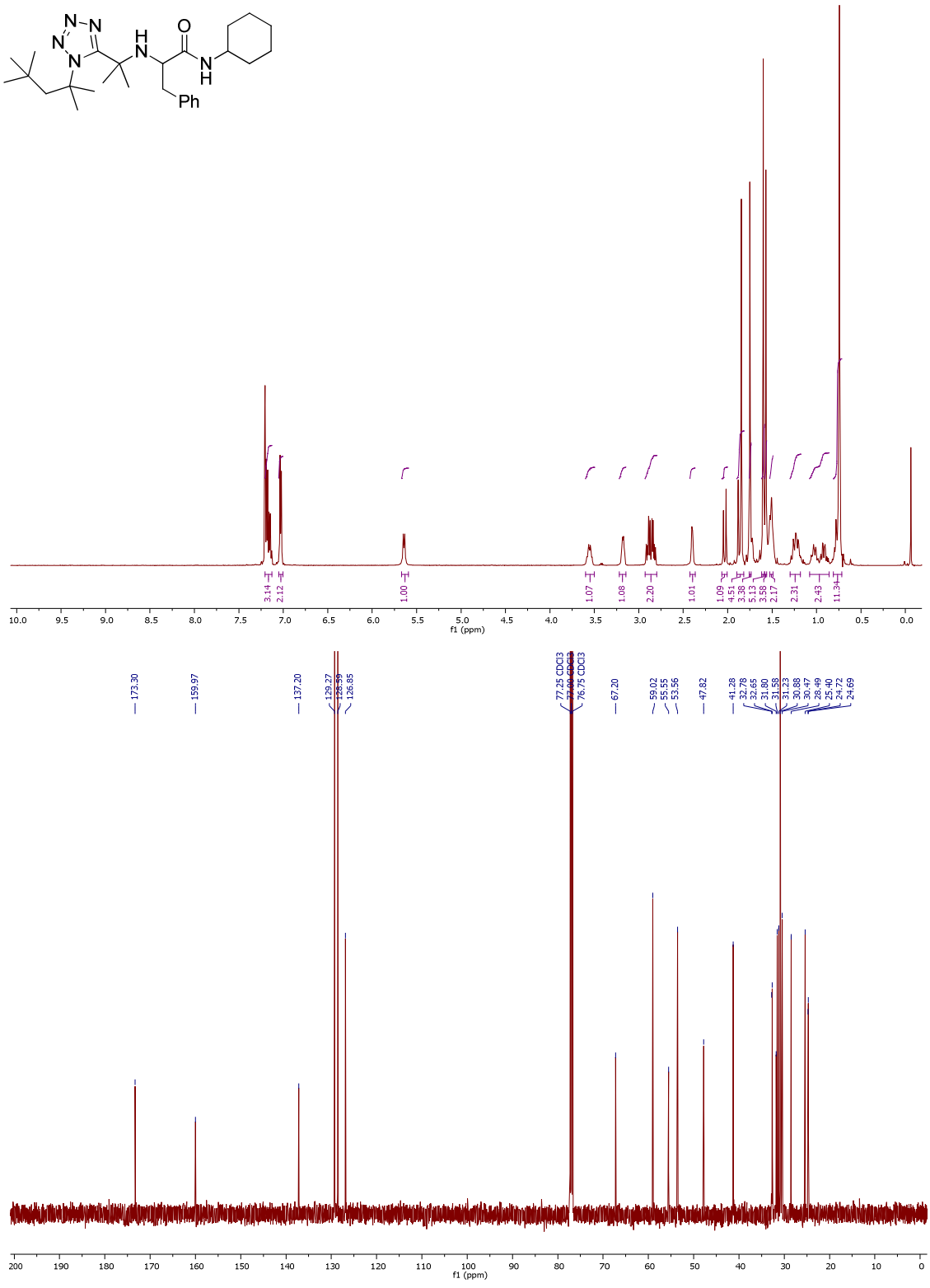




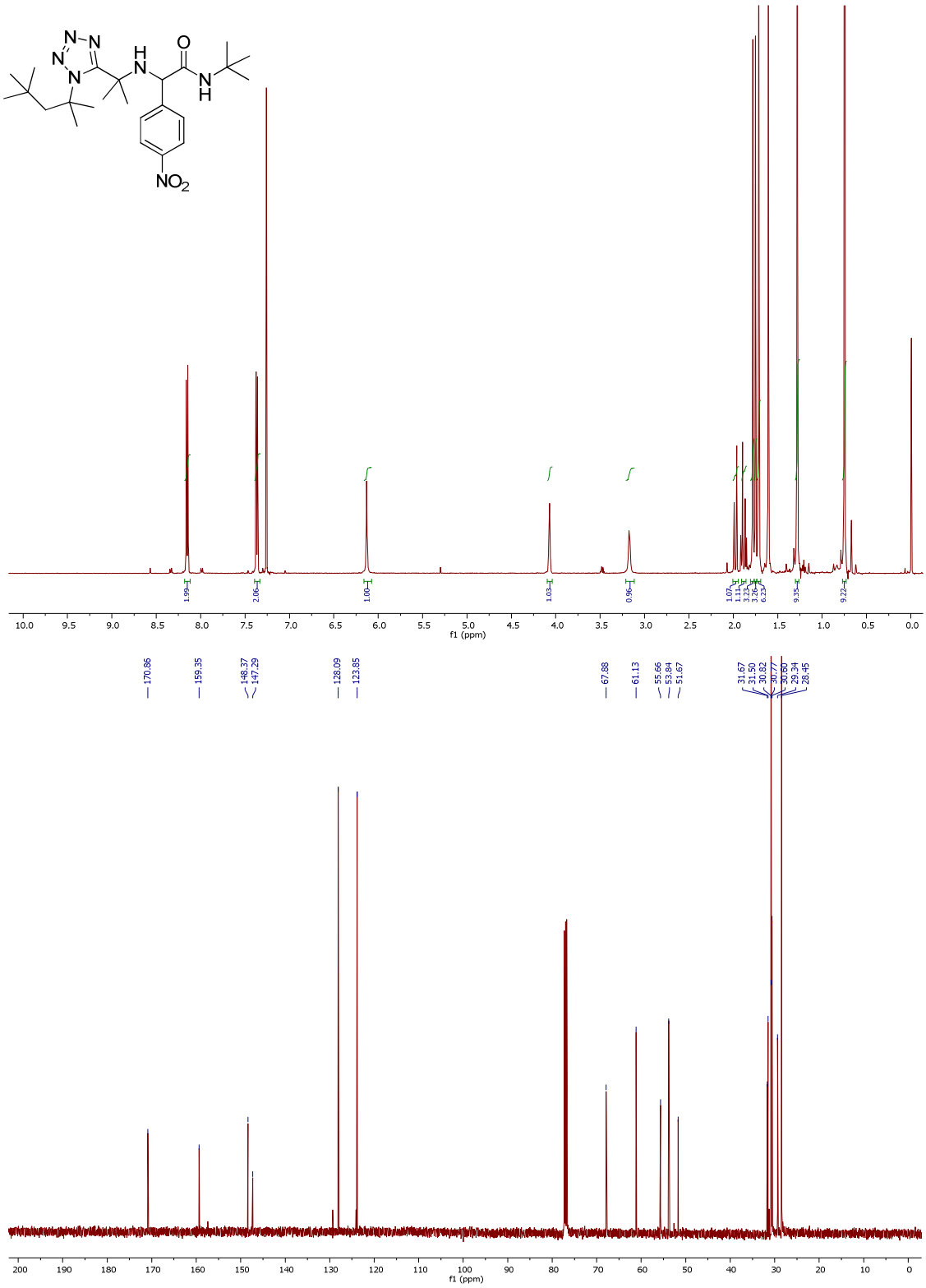
38d: ***N*-cyclohexyl-4-phenyl-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl) propan-2-yl)amino)butanamide:**



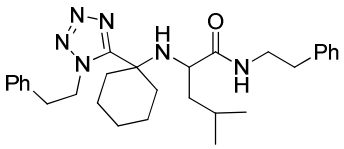
39d: ***N*-cyclohexyl-3-phenyl-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl) propan-2-yl)amino)propenamide:**

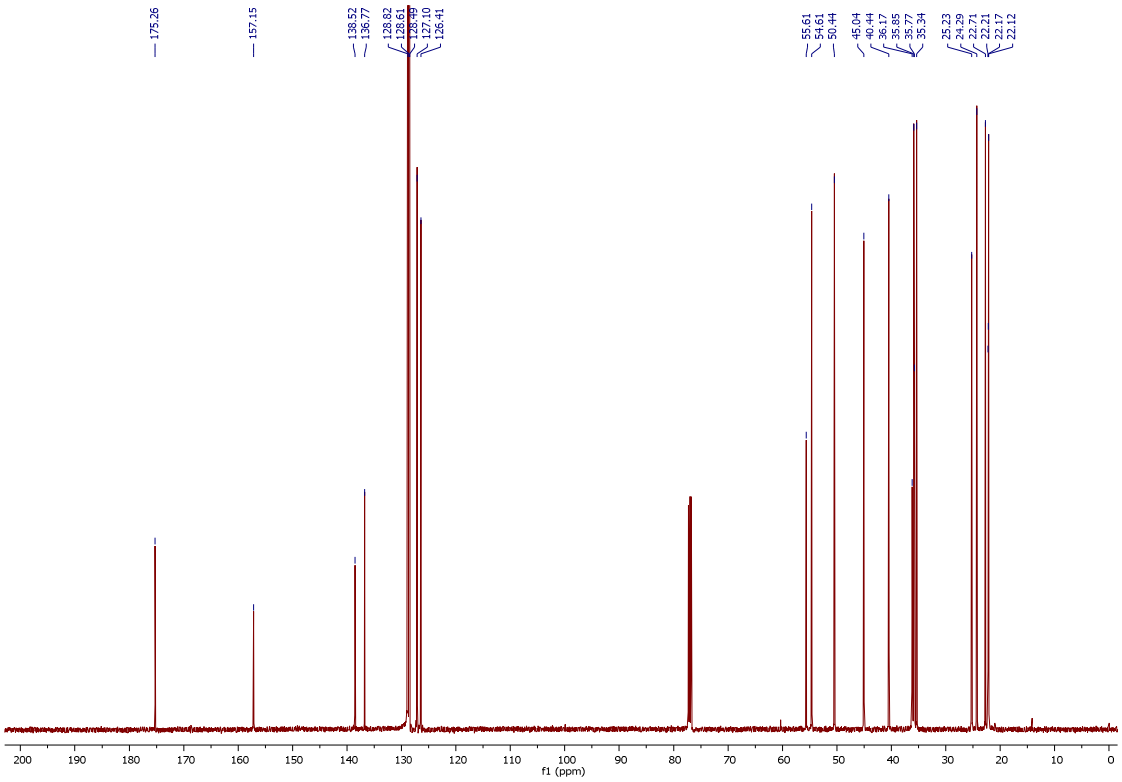


40d: *N*-(*tert*-butyl)-2-(4-nitrophenyl)-2-((2-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)acetamide:

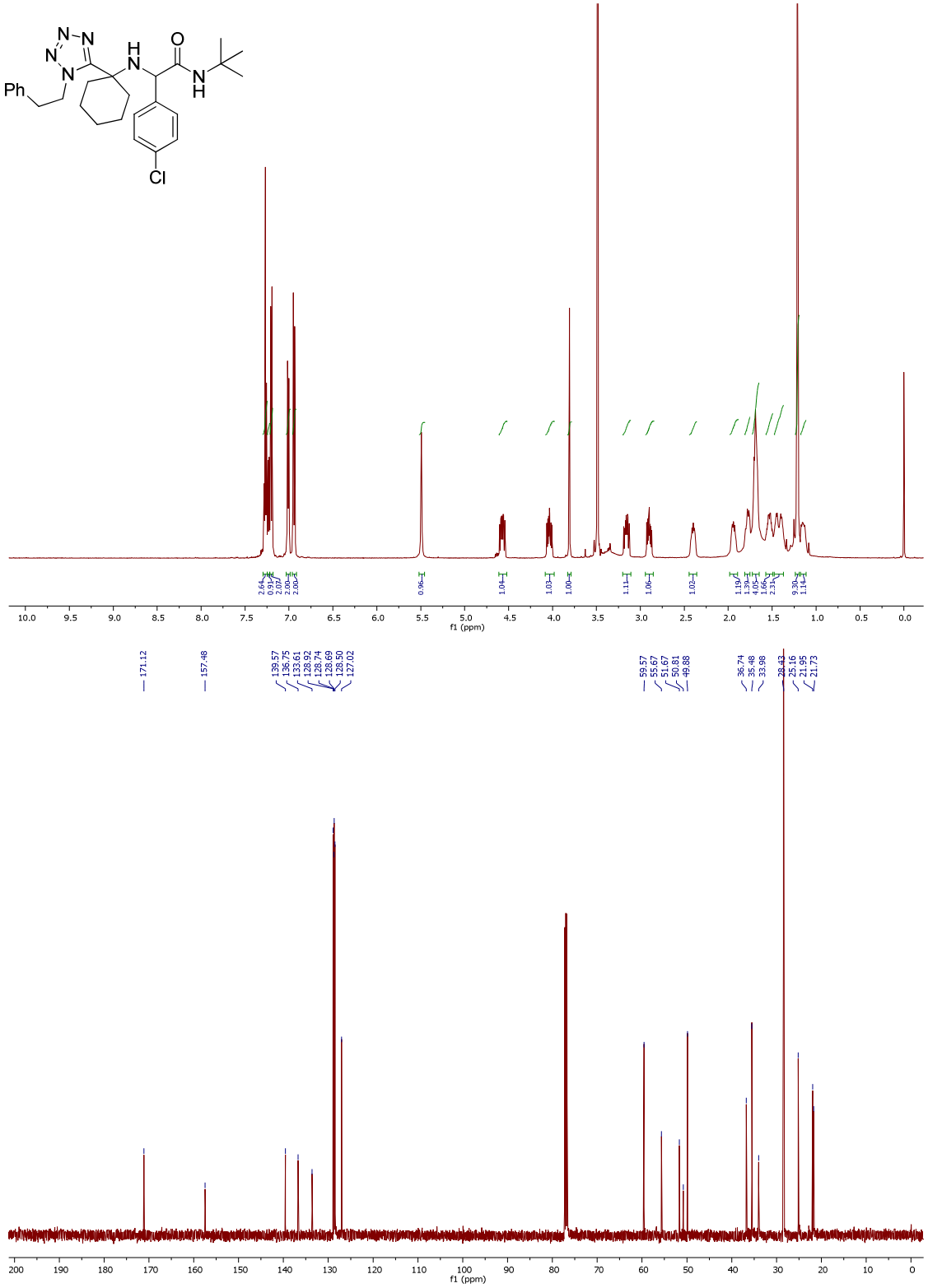


45d: 4-methyl-*N*-phenethyl-2-((1-(1-phenethyl-1*H*-tetrazol-5-yl)cyclohexyl)amino) pentanamide:

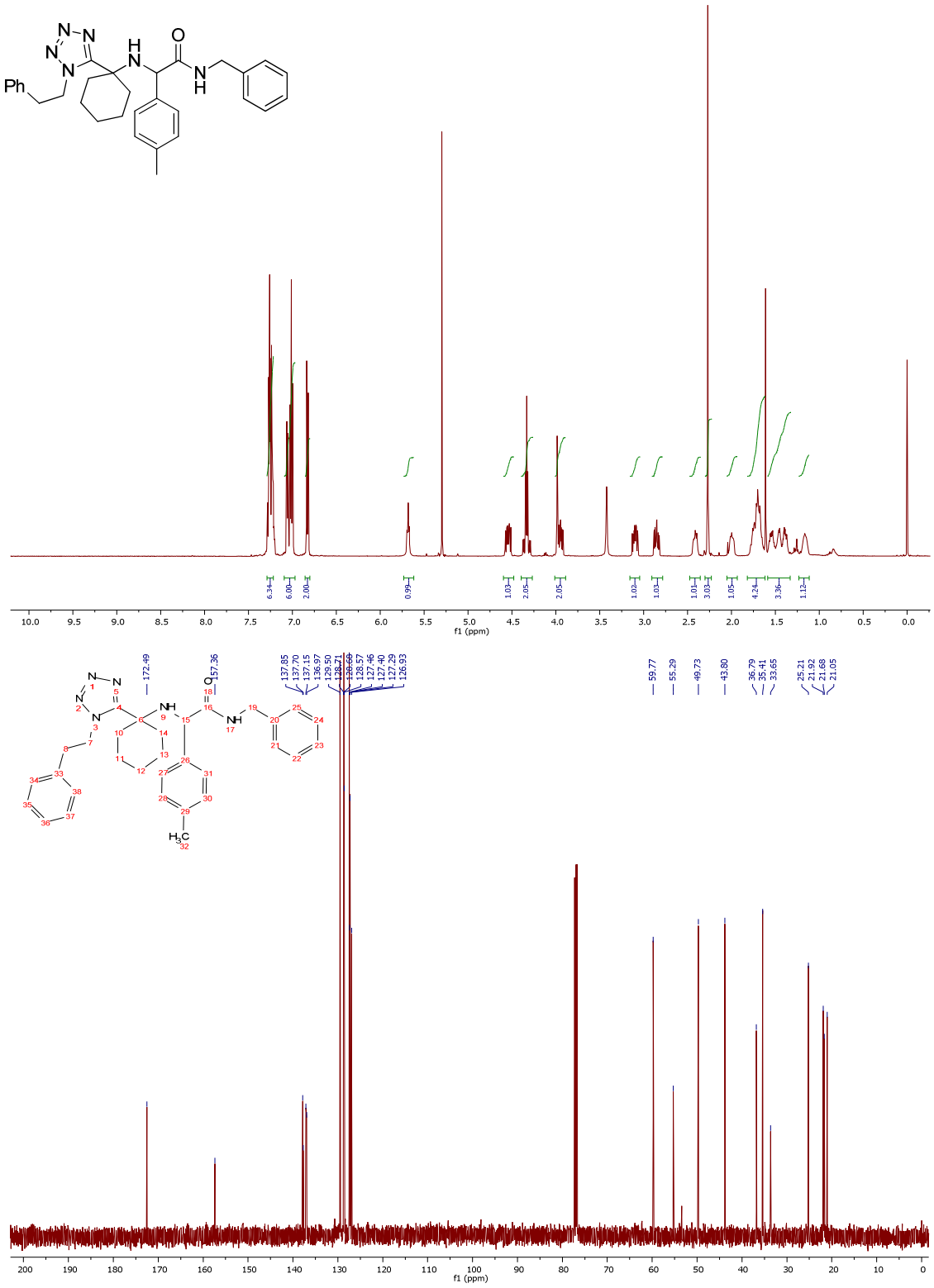




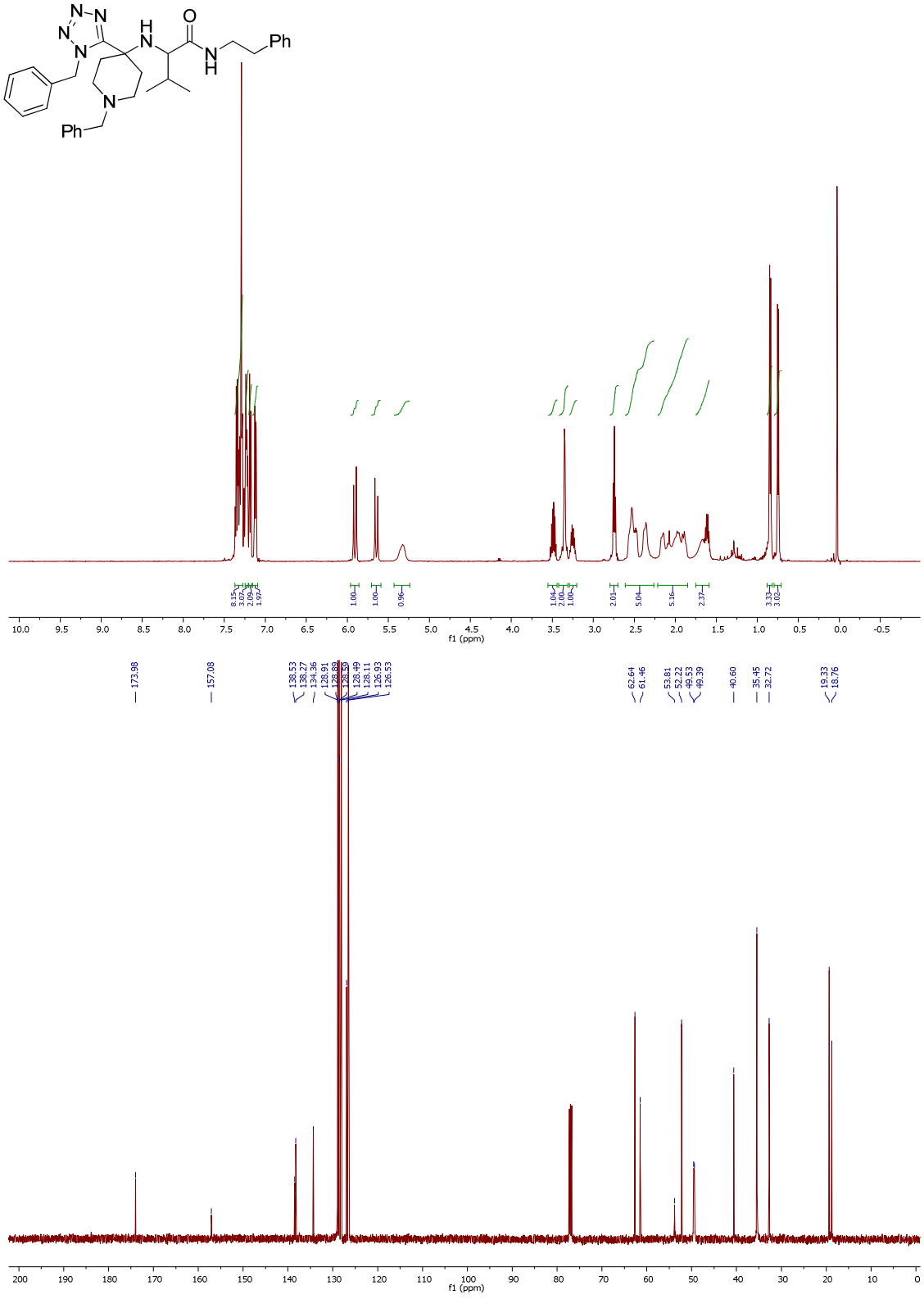
46d: ***N*-(*tert*-butyl)-2-(4-chlorophenyl)-2-((1-(1-phenethyl-1*H*-tetrazol-5-yl)cyclohexyl) amino)acetamide:**



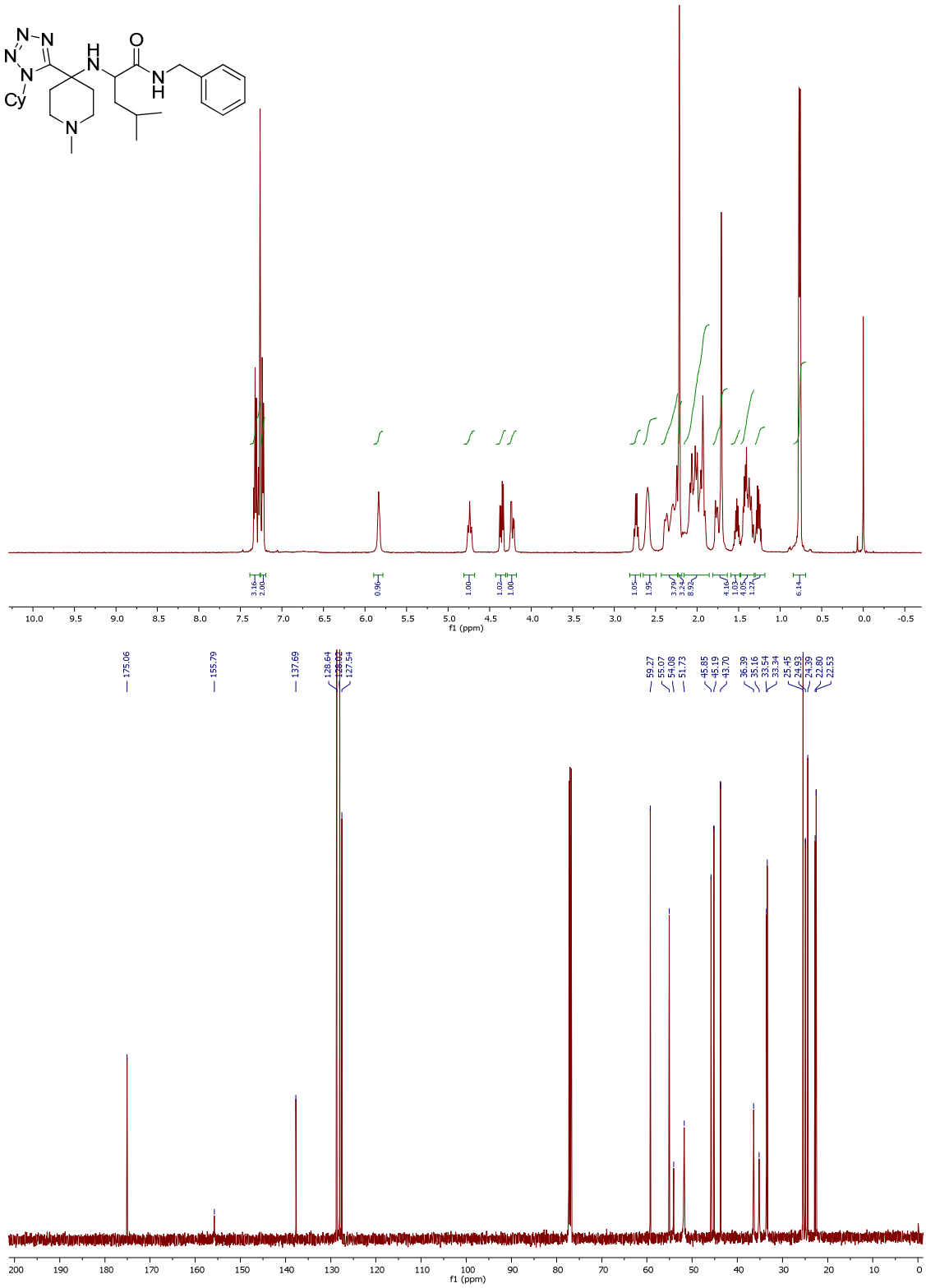
47d: ***N*-benzyl-2-((1-(1-phenethyl-1*H*-tetrazol-5-yl)cyclohexyl)amino)-2-(*p*-tolyl) acetamide:**



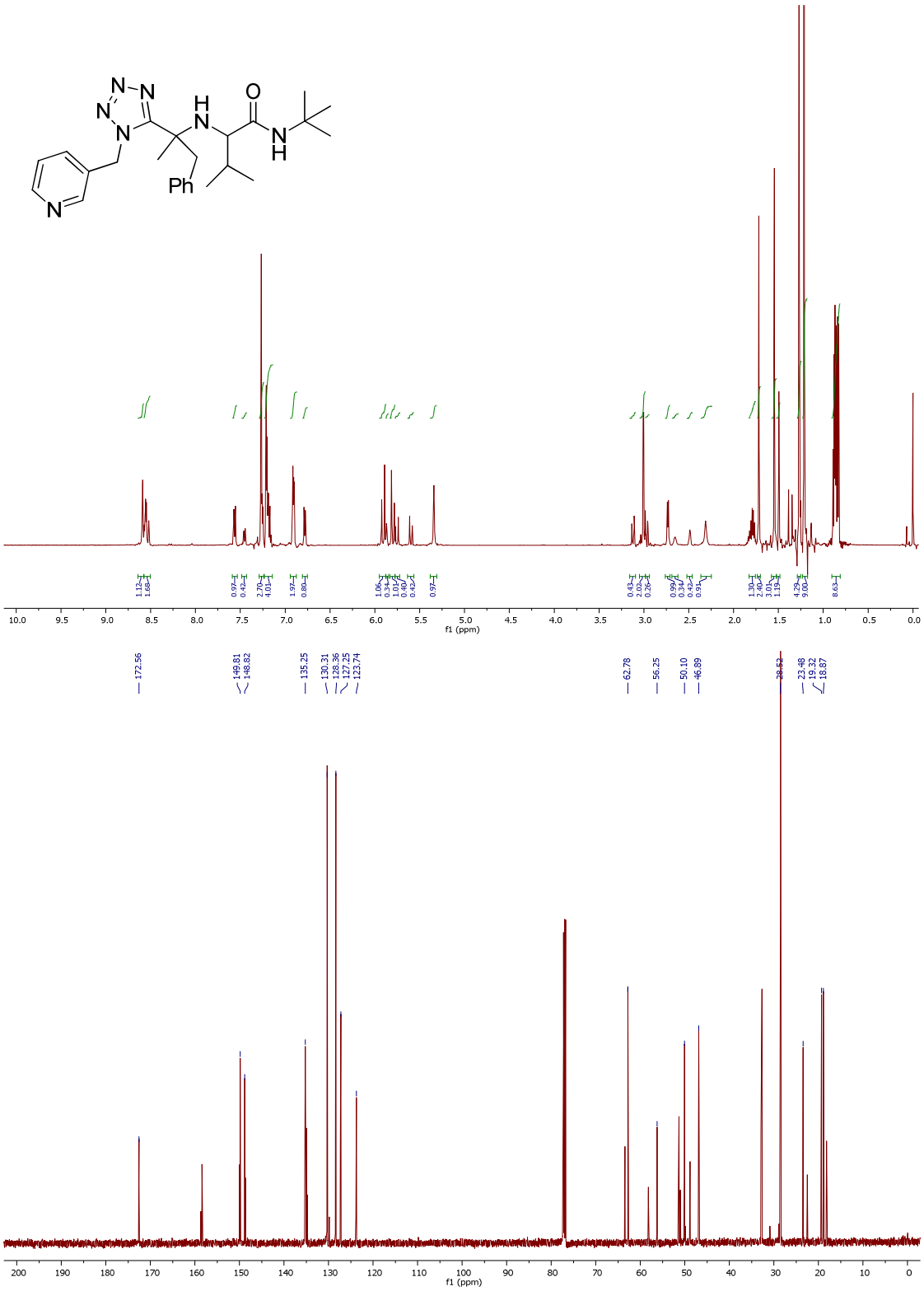
48d: 2-((1-benzyl-4-(1-benzyl-1*H*-tetrazol-5-yl)piperidin-4-yl)amino)-3-methyl-*N*-phenethylbutanamide:



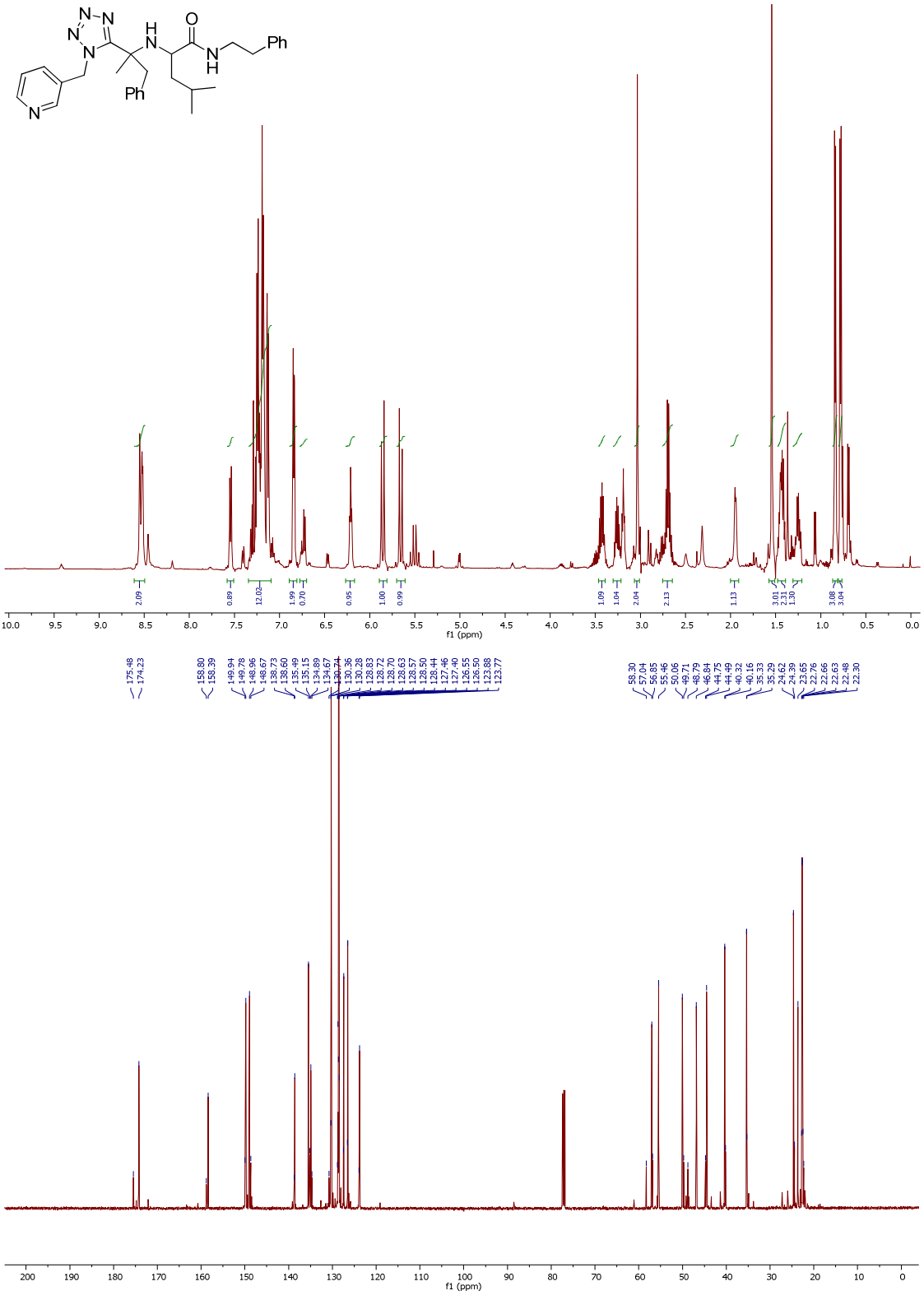
49d: ***N*-benzyl-2-((4-(1-cyclohexyl-1*H*-tetrazol-5-yl)-1-methylpiperidin-4-yl)amino)-4-methylpentanamide:**



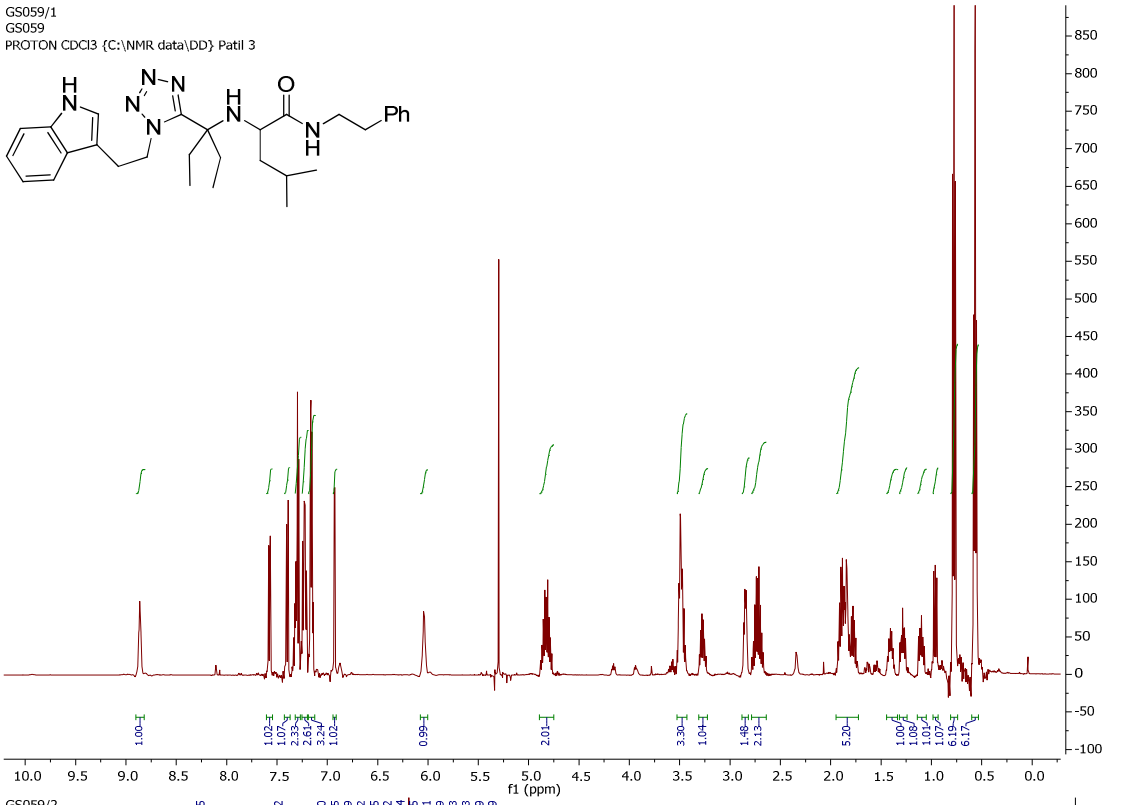
50d: ***N*-(*tert*-butyl)-3-methyl-2-((1-phenyl-2-(1-(pyridin-3-ylmethyl)-1*H*-tetrazol-5-yl) propan-2-yl)amino)butanamide:**

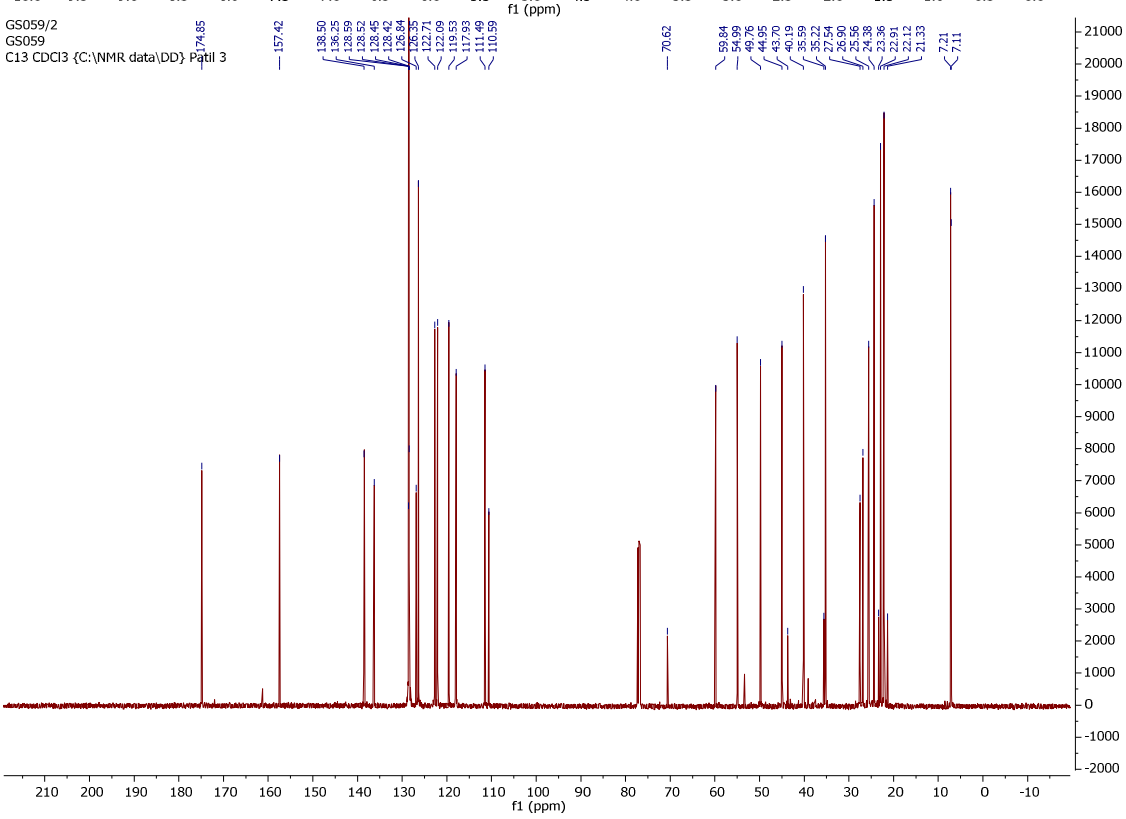


51d: 4-methyl-*N*-phenethyl-2-((1-phenyl-2-(1-(pyridin-3-ylmethyl)-1*H*-tetrazol-5-yl)propan-2-yl)amino)pentanamide.

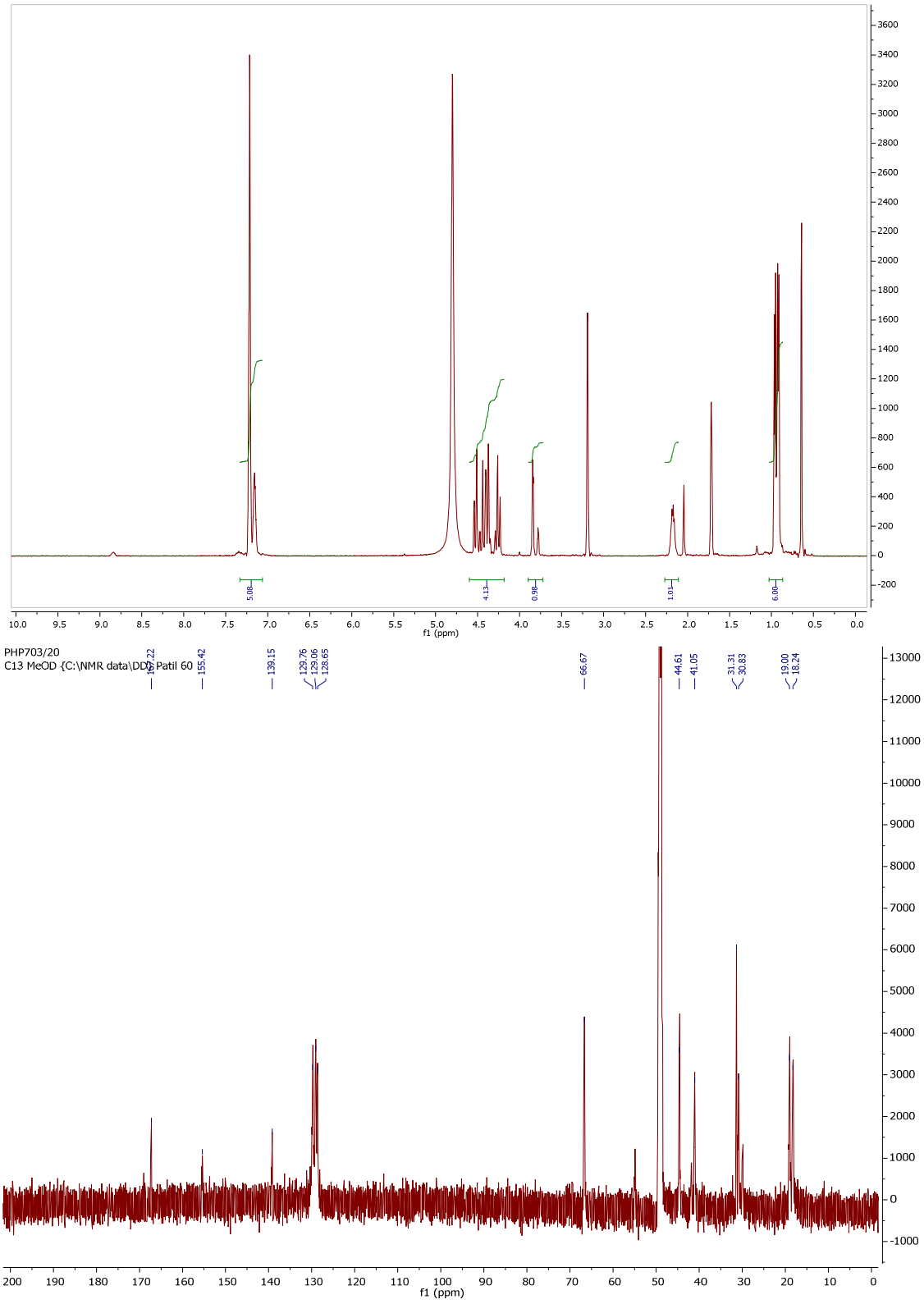


52d: 2-((3-(1-(2-(1*H*-indol-3-yl)ethyl)-1*H*-tetrazol-5-yl)pentan-3-yl)amino)-4-methyl-*N*-phenethylpentanamide:





5: 2-(((1*H*-tetrazol-5-yl)methyl)amino)-*N*-benzyl-3-methylbutanamide:



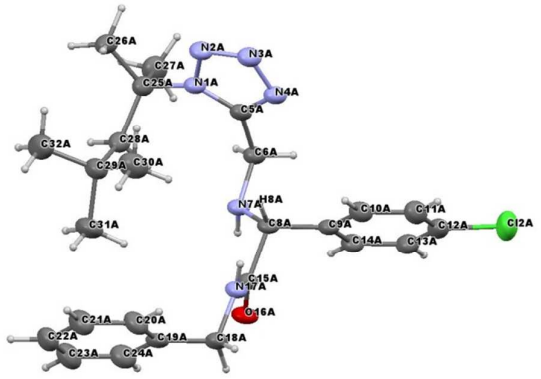
Crystal structure determination

X-ray diffraction data for single crystals of compounds **1d, 2d, 17d, 18d,** and **22d** were collected using SuperNova (Rigaku - Oxford Diffraction) four circle diffractometer with a mirror monochromator and a microfocus CuKα radiation source (λ = 1.5418 Å) for **1d, 2d, 17d, 18d,** and **22d**. Additionally, the diffractometer was equipped with a CryoJet HT cryostat system (Oxford Instruments) allowing low-temperature experiments. Single crystals were mounted on MicroMounts^{TM} and measured at temperature range 114-293 K. The obtained data sets were processed with CrysAlisPro software [S1]. The phase problem was solved by direct methods using SHELXS [S2], SIR2002 [S3] or SUPERFLIP [S4]. Parameters of obtained models were refined by full-matrix least-squares on F^2 using SHELXL-2014/6 [S2]. Calculations were performed using WinGX integrated system (ver. 2013.2) [S5]. Figures were prepared with Mercury 3.5 software [S6].

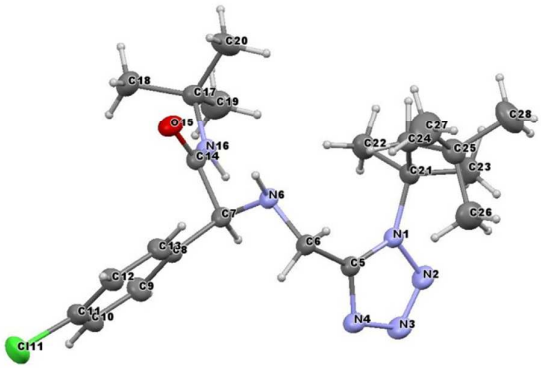
All non-hydrogen atoms in the crystal structures of **1d, 2d, 17d, 18d,** and **22d** were refined anisotropically to ensure the convergence of the refinement process. All hydrogen atoms attached to carbon atoms were positioned with the idealized geometry and refined using the riding model with the isotropic displacement parameter $U_{iso}[H] = 1.2$ (or 1.5) $U_{eq}[C]$. The position of hydrogen atoms linked to the N atoms were found on the difference Fourier map and refined with no restrains on the isotropic displacement parameter. Crystal data and structure refinement results for compounds **1d, 2d, 17d, 18d,** and **22d** are shown in Table S1.

In the crystal structure of compound **18d**, a conformational disorder is observed for the C11 atom of the 5-carbon ring. The two alternative conformations were modeled with 86% and 14% refined occupancies for components A and B, respectively. The partial molecular disorder is also observed in structure **17d** with site occupancy 54% and 46% (Figure S1).

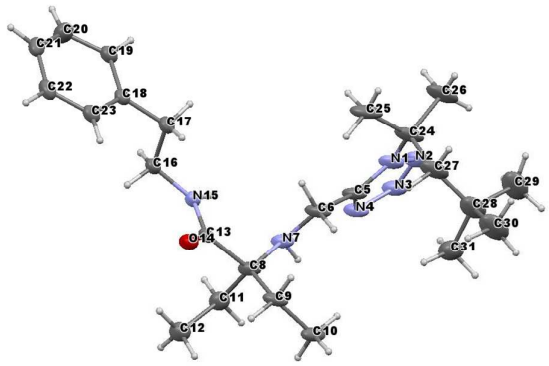
Crystallographic data for structures presented in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. 1484778 (**1d**), CCDC 1484777 (**2d**), CCDC 1484779 (**17d**), CCDC 1485017 (**18d**), CCDC 1485016 (**22d**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).



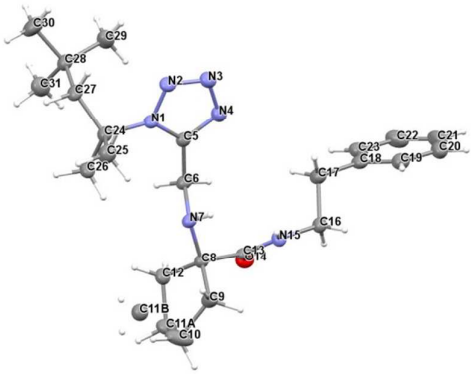
1d



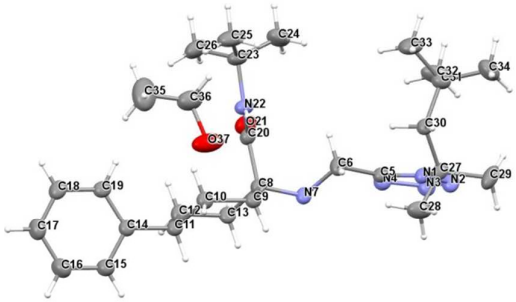
2d



17d



18d



22d

Figure S1. Molecular geometry observed in the crystal structures of compounds **1d, 2d, 17d, 18d,** and **22d**, showing the atom labeling scheme. For structure **1d** is only one molecule of the asymmetric unit is presented for clarity of the figure. For the crystal structure of compound **18d** both conformers of C11 are presented. In case of a partially disordered molecule of compound **17d** only the more abundant conformation is shown. Displacement ellipsoids of non-hydrogen atoms are drawn at the 30% probability level. H atoms are presented as small spheres with an arbitrary radius.

Table S1. Crystal data and structure refinement results for compounds **1d, 2d, 17d, 18d,** and **22d**.

	1d	**2d**	**17d**	**18d**	**22d**
Empirical moiety formula	C_{25} H_{33} Cl N_6 O	C_{22} H_{35} Cl N_6 O	C_{24} H_{40} N_6 O	C_{24} H_{38} N_6 O	C_{27} H_{44} N_6 O, C_2 H_6 O
Formula weight [g/mol]	469.02	435.01	428.62	426.6	514.75
Temperature [K]	130(2)	293(2)	293(2)	129.9(3)	129(2)
Wavelength [Å]	1.5418	1.5418	1.5418	1.5418	1.5418
Crystal system	Monoclinic	Triclinic	Triclinic	Monoclinic	Triclinic
Space group	$P2_1/n$	P-1	P-1	$P2_1/a$	P-1
Unite cell dimensions	a = 12.0024(4) Å b = 27.7074(9) Å c = 15.6066(6) Å α=90° β=105.557(4)° γ=90°	a = 11.2796(6) Å b = 11.5563(6) Å c = 11.7295(8) Å α= 119.416(6)° β=100.098(5)° γ=102.977(4)°	a = 9.8021(5) Å b = 9.8837(5) Å c = 14.5865(8) Å α= 106.946(4)° β=91.423(4)° γ=110.709(5)°	a = 10.1252(2) Å b = 14.3993(3) Å c = 16.6915(4) Å α=90° β=104.023(2)° γ=90°	a = 6.8375(3) Å b = 13.6370(8) Å c = 17.7027(11) Å α= 69.278(6)° β=84.568(4)° γ=77.034(4)°
Volume [$Å^3$]	4999.9(3)	1222.13(14)	1251.47(12)	2361.03(9)	1504.29(16)
Z	8	2	2	4	2
D_{calc} [Mg/m^3]	1.246	1.182	1.137	1.200	1.136
μ [mm^{-1}]	1.576	1.568	0.563	0.597	0.570
F(000)	2000	468	468	928	564
Crystal size [mm^3]	0.4 x 0.15 x 0.05	0.3 x 0.3 x 0.2	0.5 x 0.3 x 0.1	0.5 x 0.2 x 0.1	0.4 x 0.2 x 0.02
Θ range	3.19° to 77.49°	4.60° to 71.16°	4.87° to 71.03°	4.11° to 77.83°	3.53° to 76.65°
Index ranges	-15 ≤ h ≤ 15, -34 ≤ k ≤ 34, -19 ≤ l ≤ 19	-13 ≤ h ≤ 13, -14 ≤ k ≤ 12, -14 ≤ l ≤ 12	-11 ≤ h ≤ 11, -7 ≤ k ≤ 12, -17 ≤ l ≤ 16	-12 ≤ h ≤ 12, -18 ≤ k ≤ 18, -20 ≤ l ≤ 20	-5 ≤ h ≤ 8, -17 ≤ k ≤ 17, -22 ≤ l ≤ 22
Refl. collected	88427	7012	8448	40827	11228
Independent reflections	10530 [R(int)=0.1204]	4393 [R(int) = 0.0626]	4641 [R(int) = 0.0189]	4970 [R(int) = 0.0648]	6347 [R(int) = 0.0513]
Completeness [%] to Θ	100 (Θ 67.68°)	94.4 (Θ 68.0°)	97.8 (Θ 67.7°)	99.8 (Θ 77.8°)	96.7 (Θ 74.3°)
Absorption correction	Multi-scan	Multi-scan	Multi-scan	Multi-scan	Multi-scan
Max. and min. transmission	0.374 and 1.000	1.00 to 1.00	0.718 to 1.000	0.383 to 1.000	0.723 to 1.000

Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/ restraints/parameters	10530 / 0 / 621	4393 / 0 / 285	4641 / 0 / 371	4970 / 0 / 299	6055 / 0 / 356
GooF on F2	1.024	1.037	1.033	1.060	1.047
Final R indices [I>2sigma(I)]	R1= 0.0571, wR2= 0.1403	R1= 0.0611, wR2= 0.1783	R1= 0.0591, wR2= 0.1541	R1= 0.0418, wR2= 0.1113	R1= 0.0604, wR2= 0.1536
R indices (all data)	R1= 0.0948, wR2= 0.1704	R1= 0.0695, wR2= 0.1934	R1= 0.0646, wR2= 0.1608	R1= 0.0479, wR2= 0.1173	R1= 0.0853, wR2= 0.1752
$\Delta\rho_{max}$, $\Delta\rho_{min}$ [e·Å^{-3}]	0.36 and -0.32	0.38 and -0.39	0.33 and -0.24	0.28 and -0.27	0.37 and -0.26

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