'Atypical Ugi' Tetrazoles

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Supporting Information

Contents

| Section                                                                 | Page |
|------------------------------------------------------------------------|------|
| General methods                                                        | S2   |
| General experimental procedures                                        | S2   |
| Analytical data for the cyanoacetamides                                | S3-S5|
| Analytical data for Ugi products                                        | S5-S17|
| ¹H, ¹³C NMR, chromatograms of the novel synthesized compounds           | S18-S56|
| Crystal X-ray structure determination                                  | S57-S68|
| References                                                             | S68  |
Experimental section

General information:

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 $\delta$ 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 on a Teledyne ISCO Combiflash Rf, using RediSep Rf Normal-phase Silica Flash Columns (Silica Gel 60 Å, 230 - 400 mesh). Reagents were available from commercial suppliers and used without any purification unless otherwise noted. All isocyanides were made in house by either performing the Hoffman or Ugi procedure. Other reagents were purchased from Sigma Aldrich, ABCR, Acros and AK Scientific and were used without further purification. Mass spectra were measured on a Waters Investigator Supercritical Fluid Chromatograph with a 3100 MS Detector (ESI) using a solvent system of methanol and CO$_2$ on a Viridis silica gel column (4.6 × 250 mm, 5 µm particle size) and reported as (m/z). High resolution mass spectra (HRMS) were recorded using a LTQ-Orbitrap-XL (Thermo Fisher Scientific; ESI pos. mode) at a resolution of 60000@m/z400. Electrospray ionization mass spectra (ESI-MS) were recorded on a Waters Investigator Semi-prep 15 SFC-MS instrument. Yields given refer to chromatographically purified and spectroscopically pure compounds unless otherwise stated.

General experimental

General procedure and analytical data for synthesis of isocyanoacetamides:

10 mmol of isocyano methyl ester was added to 10 mmol of amine and the mixture was stirred at room temperature overnight. In case of precipitation, it was filtered off, washed with cold diethyl ether, and dried under vacuum. Otherwise, cold diethyl ether was added to the reaction mixture, and the product was allowed to crystallize at -20 °C. In case of no precipitaiton, the product was purified by preparative chromatography using silica gel and ethyl acetate as eluent.
**N-benzyl-2-isocyanoacetamide 3a:**

White solid (1.7g, 98%); $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.43 – 7.38 (m, 2H), 7.38 – 7.31 (m, 3H), 6.73 (s, 1H), 4.54 (d, $J$ = 5.8 Hz, 2H), 4.24 (s, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 178.9, 162.1, 136.8, 128.8, 128.1, 127.9, 45.3, 44.01.

**N-(4-chlorobenzyl-2-cyanoacetamide 3b:**

Cream solid (0.6g, 88%); $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.33 (d, $J$ = 8.3 Hz, 2H), 7.23 (d, $J$ = 8.2 Hz, 2H), 6.77 (s, 1H), 4.46 (d, $J$ = 5.9 Hz, 2H), 4.21 (s, 2H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 172.4, 162.3, 135.4, 129.3, 129.1, 45.3, 43.3.

**N-(3,4-dimethylbenzyl)-2-isocyanoacetamide 3c:**

Yellow Solid (0.5g, 99%); $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 6.86 (d, $J$ = 8.1 Hz, 1H), 6.80 – 6.74 (m, 2H), 6.45 (s, 1H), 4.17 (s, 2H), 3.92 (s, 3H), 3.90 (s, 3H), 3.60 (d, $J$ = 7.0, 5.7 Hz, 2H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 170.2, 162.2, 149.2, 130.4, 120.6, 111.8, 111.6, 56.0, 41.2, 35.0.

**N-benzyl-2-isocyano-3-phenylpropanamide 3d:**

White solid (1.2g, 94%), $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.37 – 7.31 (m, 6H), 7.31 – 7.26 (m, 2H), 7.23 – 7.08 (m, 2H), 6.64 (t, $J$ = 6.0 Hz, 1H), 4.53 – 4.45 (m, 2H), 4.40 (dd, $J$ = 14.7, 5.5 Hz, 1H), 3.32 (dd, $J$ = 13.9, 4.4 Hz, 1H), 3.23 (dd, $J$ = 13.9, 7.2 Hz, 1H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 164.7, 162.4, 136.9, 134.5, 129.7, 128.8, 128.7, 127.9, 127.8, 127.7, 43.9, 38.6.

**3-(1H-indol-3-yl)-2-isocyano-N-phenethylpropanamide 3e:**

White Solid (1.5g, 97%), $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 8.24 (s, 1H), 7.69 (dd, $J$ = 7.9, 1.1 Hz, 1H), 7.48 – 7.36 (m, 1H), 7.34 – 7.14 (m, 7H), 7.02 – 6.89 (m, 2H), 6.17 (t, $J$ = 5.9 Hz, 1H), 4.47 (dd, $J$ = 6.3, 4.6 Hz, 1H), 3.55 – 3.32 (m, 4H), 2.62 (dt, $J$ = 13.6, 6.8 Hz, 1H), 2.51 (dt, J...
\( \delta = 13.9, 7.2 \text{ Hz, 1H}. \) \(^{13}\text{C NMR (126 MHz, Chloroform-d)} \) \( \delta \) 165.3, 161.7, 138.1, 136.1, 128.7, 126.7, 124.0, 123.9, 122.5, 119.9, 119.0, 118.8, 111.3, 108.8, 59.5, 40.9, 35.2, 29.3.

**N-benzyl-2-isocyno-2-methylpropanamide 3f:**

White Solid (0.6g, 90%); \(^1\text{H NMR (500 MHz, Chloroform-d) } \delta \) 7.48 – 7.42 (m, 2H), 7.41 – 7.37 (m, 1H), 7.36 – 7.33 (m, 2H), 6.90 (s, 1H), 4.55 (d, \( J = 5.8 \text{ Hz}, 2H), 1.73 – 1.70 (m, 6H). \) \(^{13}\text{C NMR (126 MHz, Chloroform-d)} \) \( \delta \) 171.8, 168.9, 137.2, 129.0, 127.9, 127.7, 61.4, 44.1, 27.9, 27.7.

**N-(2-chlorobenzyl)-3-isocyanopropanamide 3g:**

Brown Solid (0.8g, 79%); \(^1\text{H NMR (500 MHz, Chloroform-d) } \delta \) 7.32 (m, 2H), 7.24 – 7.13 (m, 2H), 4.47 (m, 1H), 3.87 (m, 2H), 3.70 (d, \( J = 5.3 \text{ Hz}, 2H), 3.64 (m, 2H). \) \(^{13}\text{C NMR (126 MHz, Chloroform-d)} \) \( \delta \) 169.9, 159.5, 140.4, 129.5, 128.9, 128.2, 127.1, 44.5, 36.9, 33.7.

**N-benzyl-3-cyanopropanamide 3h:**

White Solid (0.3g, 85%); \(^1\text{H NMR (500 MHz, Chloroform-d) } \delta \) 7.49 – 7.18 (m, 5H), 5.95 (s, 1H), 4.50 (d, \( J = 5.7 \text{ Hz}, 2H), 3.78 (tt, \( J = 6.9, 1.8 \text{ Hz}, 2H), 2.61 (tt, \( J = 6.8, 2.0 \text{ Hz}, 2H). \) \(^{13}\text{C NMR (126 MHz, Chloroform-d)} \) \( \delta \) 168.1, 158.5, 137.5, 128.9, 127.9, 127.8, 43.9, 39.4, 36.1.

**4-isocyno-N-phenethybutanamide 3i:**

White Solid (0.6g, 50%); \(^1\text{H NMR (500 MHz, Chloroform-d) } \delta \) 7.6 – 7.5 (m, 5H), 5.7 (s, 1H), 4.5 (d, \( J = 5.7 \text{ Hz}, 2H), 3.4 (tt, \( J = 6.3, 1.9 \text{ Hz}, 2H), 2.3 (t, \( J = 7.1 \text{ Hz}, 2H), 1.7 (t, \( J = 8.5, 6.8, 4.1 \text{ Hz}, 2H), 1.7 (t, \( J = 6.5, 2.1 \text{ Hz}, 2H). \) \(^{13}\text{C NMR (126 MHz, Chloroform-d)} \) \( \delta \) 171.3, 155.1, 136.7, 128.8, 127.9, 127.7, 43.7, 41.4, 37.4, 28.6, 22.4.

**N-benzyl-4-isocyanobutanamide 3j:**
White Solid (1.4g, 70%); $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.36 – 7.26 (m, 5H), 6.22 (s, 1H), 4.48 – 4.38 (m, 2H), 3.48 (ddd, J = 8.3, 5.1, 1.9 Hz, 2H), 2.39 (t, J = 7.1 Hz, 2H), 2.07 – 1.97 (m, 2H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 170.9, 156.6, 129.9, 126.5, 43.6, 41.4, 32.2, 24.6.

$N$-benzyl-5-isocyanopentanamide 3k:

$NH\begin{array}{c}O\end{array}$

White Solid (0.7g, 65%); $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.39 – 7.28 (m, 5H), 5.79 (s, 1H), 4.47 (d, J = 5.7 Hz, 2H), 3.44 (tt, J = 6.3, 1.9 Hz, 2H), 2.30 (t, J = 7.1 Hz, 2H), 1.87 – 1.85 (m, 2H), 1.77 – 1.76 (m, 2H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 171.7, 156.2, 138.1, 128.8, 127.9, 127.7, 43.7, 41.4, 35.4, 28.6, 22.4.

$N$-(6-aminohexyl)-3-(1H-indol-3-yl)-2-isocyanopropanamide 3l:

$NH\begin{array}{c}O\end{array}$

Orange oil (2.9g, 95%). $^1$H NMR (500 MHz, Methanol-d4) $\delta$ 7.61 (d, J = 8 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.20 (s, 1H), 7.17 – 7.09 (m, 1H), 7.09 – 6.95 (m, 1H), 4.55 (t, 1H), 3.46 – 3.36 (m, 2H), 3.14 (dt, 1H), 3.08 – 2.95 (m, 1H), 2.61 (t, 1H), 1.46 – 1.34 (m, 2H), 1.34 – 1.18 (m, 4H), 1.11 (m, 2H). $^{13}$C NMR (126 MHz, Methanol-d4) $\delta$ 166.9, 158.0, 136.6, 127.1, 123.9, 121.2, 118.6, 117.9, 111.0, 107.8, 40.9, 39.3, 31.8, 29.8, 29.5, 28.4, 26.7, 26.1.

General procedure and analytical data for the synthesis of Ugi products:

Aldehyde (1 equiv) was added to the appropriate amine (1 equiv) in methanol (1M solution) and it was allowed to stir for an hour to form the Schiff base. Then, isocyanoacetamides (1 equiv) and TMSN$_3$ (1 equiv) were added, and the reaction mixture was stirred overnight. The following day the crude mixture was tested by TLC before being adsorbed onto silica and being purified via column chromatography using ethyl acetate and petroleum ether as the eluent.

$N$-(4-chlorobenzyl)-2-(5-(2-methyl-1-(tritylamino)propyl)-1H-tetrazol-1-yl)acetamide 6a:
White Solid (0.14g, 24%); the rotamers was observed; \(^1\)H NMR (500 MHz, Chloroform-\(d\)) \(\delta\) 7.40 – 7.37 (m, 5H), 7.32 (d, \(J = 8.4\) Hz, 1H), 7.29 – 7.25 (m, 2H), 7.23 – 7.19 (m, 7H), 7.17 – 7.13 (m, 2H), 7.13 – 7.10 (m, 2H), 6.65 (s, 1H), 6.56 (t, \(J = 6.0\) Hz, 1H), 5.33 (d, \(J = 16.0\) Hz, 1H), 5.24 (d, \(J = 16.0\) Hz, 1H), 4.89 (dd, \(J = 6.6, 5.1\) Hz, 1H), 4.58 (d, \(J = 16.8\) Hz, 1H), 4.44 (d, \(J = 5.9\) Hz, 1H), 4.32 (d, \(J = 6.0\) Hz, 2H), 4.25 (d, \(J = 16.8\) Hz, 1H), 3.86 – 3.83 (m, 1H), 3.82 (d, \(J = 5.5\) Hz, 1H), 3.05 (d, \(J = 8.8\) Hz, 1H), 2.47 – 2.37 (m, 1H), 2.33 – 2.30 (m, 1H), 1.05 (d, \(J = 6.7\) Hz, 2H), 0.99 (d, \(J = 6.8\) Hz, 3H), 0.94 (d, \(J = 6.9\) Hz, 3H), 0.62 (d, \(J = 6.9\) Hz, 3H). \(^1\)C NMR (126 MHz, Chloroform-\(d\)) \(\delta\) 163.8, 156.8, 144.9, 135.5, 133.7, 129.2, 128.9, 128.5, 127.9, 126.8, 71.3, 70.8, 62.2, 50.1, 34.1, 31.1, 20.2, 17.8. HRMS calculated for C\(_{33}\)H\(_{33}\)N\(_{6}\)OClNa: 587.22966; found [M+Na]\(^+\): 587.23041.

\(\text{N-}((1-(4-chlorobenzyl)-1H-tetrazol-5-yl)methyl)-3\text{-methyl-2-}(\text{tritylamino})\text{butanamide 7a:}\)

\(\text{White Solid (0.1g, 16%); } \text{\(^1\)H NMR (500 MHz, Chloroform-\(d\)) }\ \text{\(\delta\) 7.33 (dd, } \text{\(J = 8.1, 3.6\) Hz, 7H)}\text{, 7.24 (d, } \text{\(J = 8.3\) Hz, 2H)}, \text{ 7.19 (t, } \text{\(J = 7.5\) Hz, 6H)}, \text{ 7.13 (t, } \text{\(J = 7.2\) Hz, 3H)}, \text{ 7.08 (t, } \text{\(J = 6.2\) Hz, 1H)}, \text{ 5.59 (s, 2H)}, \text{ 4.09 (dd, } \text{\(J = 15.6, 6.1\) Hz, 1H)}, \text{ 3.95 (dd, } \text{\(J = 15.6, 6.2\) Hz, 1H)}, \text{ 3.23 (t, } \text{\(J = 4.1\) Hz, 1H)}, \text{ 2.75 (d, } \text{\(J = 4.6\) Hz, 1H)}, \text{ 1.89 (m, 1H)}, \text{ 0.88 (t, } \text{\(J = 7.3\) Hz, 6H)}. \text{\(^1\)C NMR (126 MHz, Chloroform-\(d\)) }\ \text{\(\delta\) 174.0, 152.1, 145.3, 135.0, 129.4, 129.4, 128.9, 127.9, 126.8, 71.5, 62.2, 50.1, 34.1, 31.1, 20.2, 17.8}. \text{ HRMS calculated for C}\(_{33}\)H\(_{33}\)N\(_{6}\)OClNa: 587.22966; found [M+Na]\(^+\): 587.23029.

\(\text{\(N\)-benzyl-2-}(5-(3\text{-methyl-1-}(\text{tritylamino})\text{butyl)-1H-tetrazol-1-yl})\text{acetamide 6b:}\)

\(\text{White Solid (0.16g, 29%); } \text{\(^1\)H NMR (500 MHz, Chloroform-\(d\)) }\ \text{\(\delta\) 7.36 – 7.32 (m, 7H)}, \text{ 7.32 – 7.29 (m, 2H)}, \text{ 7.22 (dd, } \text{\(J = 8.3, 6.4\) Hz, 6H)}, \text{ 7.18 (dd, } \text{\(J = 7.4, 2.3\) Hz, 5H)}, \text{ 6.28 (t, } \text{\(J = 5.9\) Hz, 1H)}, \text{ 4.45 – 4.33 (m, 2H)}, \text{ 4.22 – 4.12 (m, 2H)}, \text{ 2.80 (d, } \text{\(J = 6.1\) Hz, 1H)}, \text{ 1.81 – 1.74 (m, 1H)}, \text{ 1.62 – 1.57 (m, 1H)}, \text{ 1.05 – 0.99 (m, 2H)}, \text{ 0.75 (d, } \text{\(J = 6.5\) Hz, 3H)}, \text{ 0.70 (d, } \text{\(J = 6.6\) Hz, 3H})\).
\( ^{13} \text{C NMR (126 MHz, Chloroform-d)} \delta \) 164.0, 158.5, 153.7, 144.8, 128.8, 128.5, 128.0, 127.8, 126.9, 71.7, 50.2, 47.4, 47.04, 43.9, 24.5, 23.2, 21.8. HRMS calculated for \( C_{34}H_{36}N_6ONa \): 567.28428; found \([M+Na]^+\): 567.28442.

\( N-((1\text{-benzyl-1H-tetrazol-5-yl}) \text{methyl})-4\text{-methyl-2-(tritylamino)pentanamide 7b} : \)

![Chemical structure of 7b]

White Solid (0.11g, 21%); \( ^1\text{H NMR (500 MHz, Chloroform-d)} \delta \) 7.38 (m, 3H), 7.34 (d, \( J = 7.3 \) Hz, 6H), 7.30 (d, \( J = 2.5 \) Hz, 1H), 7.25 (t, \( J = 7.6 \) Hz, 6H), 7.18 (t, \( J = 7.2 \) Hz, 3H), 7.03 (t, \( J = 6.2 \) Hz, 1H), 5.61 (d, \( J = 3.7 \) Hz, 2H), 4.22 – 4.10 (m, 1H), 3.99 (dd, \( J = 15.8, 6.1 \) Hz, 1H), 3.35 (dd, \( J = 7.9, 5.7 \) Hz, 1H), 2.72 (s, 1H), 1.67 (s, 1H), 1.62 (m, 1H), 1.49 – 1.41 (m, 2H), 0.82 (dd, \( J = 6.5, 4.2 \) Hz, 6H). \( ^{13} \text{C NMR (126 MHz, Chloroform-d)} \delta \) 176.0, 152.0, 145.2, 133.6, 129.2, 129.0, 128.9, 127.9, 127.8, 126.9, 71.6, 56.4, 50.8, 45.5, 31.5, 24.7, 23.4, 22.3. HRMS calculated for \( C_{34}H_{36}N_6ONa \): 567.28428; found \([M+Na]^+\): 567.2851.

\( 2-\text{(5-((1-(4-chlorobenzyl)amino)cyclohexyl-1H-tetrazol-1-yl)}-N-(3,4\text{-dimethoxybenzyl}) \text{acetamide 6c} : \)

Brown oil (0.22 g, 44%); \( ^1\text{H NMR (500 MHz, Chloroform-d)} \delta \) 8.07 (t, \( J = 6.3 \) Hz, 1H), 7.35 – 7.32 (m, 2H), 7.28 – 7.25 (m, 2H), 6.78 (d, \( J = 8.1 \) Hz, 1H), 6.58 (dd, \( J = 8.2, 2.1 \) Hz, 1H), 6.48 (d, \( J = 2.0 \) Hz, 1H), 4.69 (t, \( J = 6.7 \) Hz, 2H), 4.09 (d, \( J = 6.2 \) Hz, 2H), 3.86 (s, 3H), 3.81 (s, 3H), 3.44 (s, 2H), 3.15 (t, \( J = 6.7 \) Hz, 2H), 1.81 (d, \( J = 13.6 \) Hz, 2H), 1.67 (d, \( J = 13.0 \) Hz, 5H), 1.34 – 1.27 (m, 3H). \( ^{13} \text{C NMR (126 MHz, Chloroform-d)} \delta \) 177.3, 153.04, 149.1, 148.2, 137.9, 133.2, 129.5, 128.8, 128.6, 120.8, 111.6, 111.5, 61.1, 55.9, 55.8, 49.1, 46.4, 36.0, 31.7, 31.3, 25.0, 21.3. HRMS calculated for \( C_{26}H_{34}N_6O_3Cl \): 513.23754; found \([M+H]^+\): 513.23834.
1-((4-chlorobenzyl)amino)-N-((1-(3,4-dimethoxybenzyl)-1H-tetrazol-5-yl)methyl)cyclohexanecarboxamide 7c:

Brown oil (0.1 g, 17%); $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.28 (d, $J = 8.4$ Hz, 2H), 7.11 (d, $J = 8.3$ Hz, 2H), 6.78 (d, $J = 8.1$ Hz, 1H), 6.62 – 6.55 (m, 2H), 5.75 (s, 1H), 5.46 (s, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.44 (q, $J = 6.7$ Hz, 2H), 3.31 (s, 2H), 2.68 (t, $J = 6.9$ Hz, 2H), 2.07 (m, 2H), 1.97 (m, 2H), 1.60 (m, 2H), 1.50 (m, 2H), 1.43 (m, 1H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 165.2, 159.1, 149.5, 148.2, 137.9, 133.5, 130.7, 129.6, 129.1, 120.8, 111.7, 56.5, 56.3, 55.9, 51.5, 46.3, 41.4, 35.0, 34.8, 25.3, 21.8. HRMS calculated for C$_{26}$H$_{34}$N$_6$O$_3$Cl: 513.23754; found [M+H]$^+$: 513.23828.

$N$-benzyl-2-(5-(1-(benzylamino)-2-methylpropyl)-1H-tetrazol-1-yl)acetamide 6d:

Orange oil (0.2 g ,53%); $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.34 – 7.30 (m, 7H), 7.26 – 7.14 (m, 3H), 6.35 (s, 1H), 5.35 (d, $J = 16.3$ Hz, 1H), 5.10 (d, $J = 16.4$ Hz, 1H), 4.41 (t, $J = 5.2$ Hz, 1H), 3.93 (d, $J = 8.3$ Hz, 1H), 3.63 (d, $J = 13.3$ Hz, 1H), 3.50 (d, $J = 13.3$ Hz, 1H), 2.13 – 2.08 (m, 1H), 1.66 (s, 1H), 1.05 (d, $J = 6.6$ Hz, 3H), 0.78 (d, $J = 6.7$ Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 164.2, 156.5, 138.7, 136.9, 128.8, 128.6, 128.1, 127.9, 127.8, 127.5, 59.4, 51.8, 50.2, 43.9, 32.2, 19.6. HRMS calculated for C$_{21}$H$_{27}$N$_6$O: 379.22409; found [M+H]$^+$: 379.22440.

$N$-((1-benzyl-1H-tetrazol-5-yl)methyl)-2-(benzylamino)-3-methylbutanamide 7d:

Orange oil (0.07g ,19%), Melting Point: N/A, $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 8.09 (t, $J = 6.4$ Hz, 1H), 7.40 – 7.38 (m, 3H), 7.39 – 7.29 (m, 5H), 7.28 – 7.25 (m, 2H), 5.69 (d, $J = 3.5$ Hz, 2H), 4.64 (dd, $J = 15.8$, 6.6 Hz, 1H), 4.56 (dd, $J = 15.8$, 5.7 Hz, 1H), 3.71 – 3.58 (m, 2H), 3.03 (d, $J = 4.4$ Hz, 1H), 2.13 – 2.10 (m, 1H), 1.71 (s, 1H), 0.95 (d, $J = 6.9$ Hz, 3H), 0.85 (d, $J = 6.9$ Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 174.6, 152.4, 139.1, 133.5, 129.2, 128.9, 128.6, 128.3, 127.8,
127.4, 67.6, 53.7, 50.9, 31.6, 31.4, 19.5, 17.7. HRMS calculated for C_{21}H_{27}N_{6}O: 379.22409; found [M+H]^+: 379.22458.

**N-benzyl-2-(5-(cyclopropyl((3,4,5-trifluorobenzyl)amino)methyl)-1H-tetrazol-1-yl)-3-phenylpropanamide 6e:**

Yellow solid (0.3g, 65%); two diastomers in ratio (1:1); ^1^H NMR (500 MHz, Chloroform-d) δ 7.54 – 7.45 (m, 7H), 7.43 – 7.37 (m, 9H), 7.35 – 7.30 (m, 4H), 7.26 – 7.21 (m, 3H), 7.18 (dt, J = 7.1, 2.3 Hz, 3H), 7.05 (dd, J = 8.1, 6.4 Hz, 2H), 6.98 (dd, J = 8.1, 6.4 Hz, 2H), 6.08 (dd, J = 11.5, 3.9 Hz, 1H), 6.04 (dd, J = 11.1, 4.4 Hz, 1H), 4.76 – 4.70 (m, 3H), 4.65 (dd, J = 14.7, 5.7 Hz, 1H), 4.00 – 3.85 (m, 4H), 3.51 (dd, J = 14.1, 11.5 Hz, 2H), 3.40 (d, J = 8.4 Hz, 2H), 3.37 (t, J = 4.3 Hz, 1H), 3.07 (d, J = 9.6 Hz, 1H), 1.38 – 1.25 (m, 1H), 0.87 – 0.79 (m, 1H), 0.69 – 0.62 (m, 1H), 0.58 – 0.56 (m, 1H), 0.43 – 0.37 (m, 1H), 0.34 – 0.30 (m, 1H), 0.31 – 0.24 (m, 1H), 0.18 – 0.11 (m, 1H), 0.08 – 0.05 (m, 1H), 0.03 – 0.04 (m, 1H). ^1^C NMR (126 MHz, Chloroform-d) δ 166.8, 156.9, 152.1, 150.1, 139.7, 137.7, 137.4, 135.8, 135.1, 129.1, 128.9, 128.8, 128.7, 128.6, 127.7, 127.5, 127.4, 111.8, 111.6, 111.6, 65.0, 58.3, 50.8, 43.7, 38.9, 15.0, 13.7, 5.8, 2.2. HRMS calculated for C_{28}H_{28}N_{6}OF_{3}: 521.22712; found [M+H]^+: 521.22778.

**N-(1-(1-benzyl-1H-tetrazol-5-yl)-2-phenylethyl)-2-cyclopropyl-2-((3,4,5-trifluorobenzyl)amino)acetamide 7e:**

Yellow solid (0.07g, 14%); ^1^H NMR (500 MHz, Chloroform-d) δ 7.39 – 7.28 (m, 4H), 7.25 – 7.12 (m, 5H), 6.97 – 6.94 (m, 2H), 6.92 – 6.83 (m, 1H), 6.79 – 6.74 (m, 1H), 5.61 (s, 1H), 5.50 (s, 1H), 3.47 (d, J = 13.6 Hz, 1H), 5.41 (s, 1H), 3.41 – 3.30 (m, 1H), 3.28 – 3.21 (m, 1H), 3.06 – 3.02 (m, 1H), 2.27 (dd, J = 12.8, 9.1 Hz, 1H), 1.39 – 1.14 (m, 1H), 0.97 – 0.67 (m, 2H), 0.57 – 0.38 (m, 3H), 0.17 – 0.04 (m, 1H). ^1^C NMR (126 MHz, Chloroform-d) δ 173.2, 155.4, 152.2, 150.1, 139.8, 137.8, 135.3, 133.7, 129.3, 128.9, 128.8, 127.7, 127.6, 127.3, 111.9, 111.5, 66.6, 50.9, 44.1, 39.9, 15.2, 3.8, 3.2, 3.1. HRMS calculated for C_{28}H_{28}N_{6}OF_{3}: 521.22712; found [M+H]^+: 521.22797.
**N-benzyl-2-(5-(1-benzyl-4-(cyclopropylamino)piperidin-4-yl)-1H-tetrazol-1-yl)-3-phenylpropanamide 6f:**

White solid (0.2g, 44%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.34 – 7.31 (m, 2H), 7.30 (q, J = 3.2, 2.7 Hz, 2H), 7.28 (q, J = 2.0, 1.5 Hz, 1H), 7.27 – 7.23 (m, 3H), 7.21 – 7.16 (m, 5H), 7.05 – 7.01 (m, 2H), 6.78 (t, J = 5.9 Hz, 1H), 5.87 (dd, J = 11.2, 4.3 Hz, 1H), 4.46 (dd, J = 14.7, 5.9 Hz, 1H), 4.39 (dd, J = 14.7, 5.7 Hz, 1H), 3.72 (dd, J = 14.0, 11.2 Hz, 1H), 3.60 (dd, J = 14.0, 4.3 Hz, 1H), 3.42 (d, J = 13.0 Hz, 1H), 3.31 (d, J = 13.0 Hz, 1H), 2.43 (s, 2H), 2.31 – 2.29 (m, 1H), 2.19 – 2.14 (m, 1H), 2.06 – 2.01 (m, 1H), 1.78 – 1.76 (m, 1H), 1.73 (s, 2H), 1.66 (d, J = 5.8 Hz, 2H), 0.24 – 0.20 (m, 1H), 0.17 – 0.15 (m, 1H), 0.14 – 0.12 (m, 1H), 0.25 – 0.36 (m, 1H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 167.2, 159.7, 138.1, 137.2, 135.5, 129.4, 129.3, 129.1, 128.9, 128.8, 128.2, 127.8, 127.7, 127.5, 127.1, 126.7, 126.5, 126.2, 125.9, 125.8, 125.7, 125.0, 65.4, 62.8, 54.4, 54.0, 51.6, 48.3, 39.4, 34.7, 34.3, 24.6, 6.4, 5.8. HRMS calculated for C$_{32}$H$_{38}$N$_7$O: 536.31324; found [M+H]$^+$: 536.31396.

**1-benzyl-N-(1-(1-benzyl-1H-tetrazol-5-yl)-2-phenylethyl)-4-(cyclopropylamino) piperidine-4-carboxamide 7f:**

Yellow solid (0.1g, 14%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.66 (d, J = 8.4 Hz, 1H), 7.35 – 7.30 (m, 7H), 7.29 – 7.25 (m, 1H), 7.20 – 7.17 (m, 3H), 7.16 – 7.13 (m, 2H), 6.95 (dd, J = 6.5, 2.9 Hz, 2H), 5.58 (d, J = 15.4 Hz, 1H), 5.48 (d, J = 15.4 Hz, 1H), 5.41 (q, J = 8.1 Hz, 1H), 3.48 (s, 2H), 3.21 (dd, J = 13.7, 8.2 Hz, 1H), 3.05 (dd, J = 13.6, 7.8 Hz, 1H), 2.68 – 2.52 (m, 2H), 2.21 (q, J = 10.4 Hz, 2H), 2.06 – 1.90 (m, 2H), 1.90 – 1.79 (m, 1H), 1.67 – 1.53 (m, 2H), 1.28 (s, 1H), 0.34 – 0.27 (m, 1H), 0.26 – 0.16 (m, 2H), 0.12 – 0.05 (m, 1H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 177.4, 155.3, 138.3, 135.5, 133.7, 129.2, 129.1, 128.9, 128.7, 128.2, 127.7, 127.6, 127.2, 127.1, 63.00, 59.4, 50.8, 49.3, 44.3, 39.6, 32.4, 31.9, 29.7, 25.1, 6.1. HRMS calculated for C$_{32}$H$_{38}$N$_7$O: 536.31324; found [M+H]$^+$: 536.31396.
2-(5-(1-(benzylamino)cyclopentyl)-1H-tetrazol-1-yl)-3-(1H-indol-3-yl)-N-phenethyl propanamide 6g:

Yellow solid (0.3g, 62%); $^1$H NMR (500 MHz, Chloroform-d) δ 8.13 – 8.12 (m, 1H), 7.59 – 7.54 (m, 1H), 7.29 (t, J = 4.0 Hz, 1H), 7.30 – 7.28 (m, 1H), 7.26 – 7.25 (m, 1H), 7.25 – 7.23 (m, 2H), 7.23 – 7.22 (m, 1H), 7.21 – 7.20 (m, 1H), 7.19 – 7.17 (m, 1H), 7.14 – 7.12 (m, 1H), 6.99 (dd, J = 7.4, 2.1 Hz, 2H), 6.91 – 6.86 (m, 2H), 6.69 (d, J = 2.4 Hz, 1H), 6.30 (t, J = 5.7 Hz, 1H), 5.94 (dd, J = 10.4, 4.9 Hz, 1H), 3.89 – 3.74 (m, 2H), 3.43 – 3.40 (m, 1H), 3.22 – 3.11 (m, 2H), 3.00 (d, J = 12.6 Hz, 1H), 2.63 – 2.54 (m, 2H), 2.35 – 2.32 (m, 1H), 1.94 – 1.88 (m, 1H), 1.66 – 1.56 (m, 2H), 1.50 – 1.45 (m, 1H), 1.43 – 1.31 (m, 2H), 1.23 – 1.19 (m, 1H), 1.16 – 1.07 (m, 1H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 167.4, 159.5, 138.8, 138.2, 135.9, 128.7, 128.6, 128.5, 127.7, 127.2, 126.8, 126.5, 123.5, 122.4, 119.9, 118.2, 111.3, 109.7, 63.9, 47.9, 40.8, 36.9, 36.3, 34.9, 28.8, 22.9. HRMS calculated for C$_{32}$H$_{36}$N$_7$O: 534.29759; found [M+H]$^+$: 534.29828.

N-(2-(1H-indol-3-yl)-1-(1-phenethyl-1H-tetrazol-5-yl)ethyl)-1-(benzylamino) cyclopentane carboxamide 7g:

Yellow oil (0.1g, 13%); $^1$H NMR (500 MHz, Chloroform-d) δ 8.35 (d, J = 8.3 Hz, 1H), 8.10 (d, J = 2.5 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.31 (s, 1H), 7.30 – 7.25 (m, 3H), 7.24 – 7.12 (m, 5H), 6.81 – 6.69 (m, 3H), 5.36 – 5.31 (m, 1H), 4.28 – 4.06 (m, 2H), 3.50 (dd, J = 14.1, 6.3 Hz, 1H), 3.46 – 3.37 (m, 2H), 3.16 (dd, J = 14.2, 9.3 Hz, 1H), 2.94 – 2.88 (m, 1H), 2.51 – 2.45 (m, 1H), 2.13 – 2.04 (m, 1H), 2.04 – 1.96 (m, 1H), 1.81 – 1.79 (m, 2H), 1.73 – 1.62 (m, 4H), 1.33 – 1.26 (m, 1H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 176.4, 155.8, 139.6, 136.2, 128.7, 128.6, 128.5, 128.1, 127.3, 127.1, 127.0, 126.9, 123.1, 123.0, 122.6, 120.1, 118.5, 118.4, 111.5, 109.7, 69.9, 48.4, 48.2, 43.9, 35.9, 35.8, 35.67, 30.6, 24.3. HRMS calculated for C$_{32}$H$_{36}$N$_7$O: 534.29759; found [M+H]$^+$: 534.29816.
**N-benzyl-2-((4-chlorophenyl)(isopropylamino)methyl)-1H-tetrazol-1-yl)-3-(1H-indol-3-yl)propanamide 6h:**

Orange oil (0.3g, 49%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.57 (d, J = 7.9 Hz, 1H), 7.42 – 7.40 (m, 1H), 7.28 (s, 1H), 7.26 (s, 1H), 7.24 – 7.22 (m, 3H), 7.20 – 7.18 (m, 1H), 7.17 (s, 1H), 7.15 (s, 1H), 6.97 – 6.95 (m, 1H), 6.84 – 6.74 (m, 2H), 6.43 – 6.41 (m, 2H), 5.37 (dd, J = 11.9, 4.1 Hz, 1H), 4.11 (s, 1H), 3.99 – 3.91 (m, 1H), 3.87 – 3.82 (m, 1H), 3.76 – 3.71 (m, 1H), 3.60 – 3.33 (m, 2H), 2.76 – 2.71 (m, 1H), 2.68 – 2.55 (m, 1H), 2.22 – 2.19 (m, 1H), 0.83 (d, J = 6.5 Hz, 3H). 0.63 (d, J = 6.3 Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 165.9, 155.9, 139.1, 136.3, 133.8, 129.0, 128.9, 128.7, 128.6, 126.1, 123.9, 122.4, 119.9, 117.8, 112.0, 108.7, 60.7, 52.4, 44.9, 35.3, 29.3, 27.3, 23.6. HRMS calculated for C$_{30}$H$_{33}$N$_7$OCl: 542.24296; found [M+H]$^+$: 542.24371.

**N-((1-(1-(1H-indol-2-yl)-2-phenylethyl)-1H-tetrazol-5-yl)methyl)-2-(4-chlorophenyl)-2-(isopropylamino)acetamide 7h:**

Yellow solid (0.1g, 17%); $^1$H NMR (500 MHz, Chloroform-d) δ 8.47 (s, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 5.1 Hz, 1H), 7.29 – 7.26 (m, 2H), 7.24 (dt, J = 8.4, 4.2 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H), 7.08 – 6.95 (m, 4H), 6.85 (d, J = 8.4 Hz, 2H), 6.56 (d, J = 2.3 Hz, 1H), 6.03 – 5.93 (m, 1H), 5.29 – 5.25 (m, 1H), 4.71 (d, J = 3.4 Hz, 1H), 3.77 (dd, J = 14.9, 4.4 Hz, 1H), 3.61 – 3.55 (m, 1H), 3.53 – 3.45 (m, 1H), 3.35 – 3.27 (m, 1H), 2.75 – 2.60 (m, 2H), 2.21 (dd, J = 7.5, 5.0 Hz, 1H), 0.76 (d, J = 6.2 Hz, 3H), 0.72 (d, J = 6.2 Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 156.9, 138.2, 136.2, 135.8, 134.4, 129.3, 128.8, 128.7, 128.2, 126.7, 126.3, 123.6, 122.6, 120.1, 117.71, 111.9, 63.1, 53.9, 46.3, 41.1, 35.1, 22.3, 21.9. HRMS calculated for C$_{30}$H$_{33}$N$_7$OCl: 542.24296; found [M+H]$^+$: 542.24377.
**N-benzyl-2-(5-(1-(benzylamino)-2-methylpropyl)-1H-tetrazol-1-yl)-2-methyl propanamide 6i:**

White solid (0.13g, 31%); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.31 – 7.07 (m, 10H), 6.56 (t, $J = 5.9$ Hz, 1H), 4.35 (dd, $J = 14.6$, 6.0 Hz, 1H), 4.24 (dd, $J = 14.6$, 5.6 Hz, 1H), 3.83 (d, $J = 5.5$ Hz, 1H), 3.64 (d, $J = 12.8$ Hz, 1H), 3.46 (d, $J = 12.9$ Hz, 1H), 2.10 (m, 1H), 1.89 (d, $J = 7.0$ Hz, 7H), 0.95 (dt, $J = 6.8$, 1.7 Hz, 6H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 170.11, 157.47, 139.73, 137.24, 128.79, 128.38, 128.07, 127.79, 127.75, 127.14, 65.68, 57.88, 57.81, 50.31, 44.11, 44.07, 44.04, 31.52, 27.23, 27.16, 26.57, 26.49, 20.40, 20.32, 16.88, 16.81. HRMS calculated for C$_{23}$H$_{31}$N$_6$O: 407.25539; found [M+H]$^+$: 407.25586.

**N-(2-(1-benzyl-1H-tetrazol-5-yl)propan-2-yl)-2-(benzylamino)-3-methylbutanamide 7i:**

White solid (0.09 g, 23%); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 8.03 (s, 1H), 7.42 – 7.23 (m, 8H), 7.15 – 7.05 (m, 2H), 5.71 (d, $J = 15.8$ Hz, 1H), 5.64 (d, $J = 15.8$ Hz, 1H), 3.72 (d, $J = 2.0$ Hz, 2H), 2.91 (d, $J = 4.4$ Hz, 1H), 2.17 (m, 1H), 1.75 (s, 3H), 1.64 (s, 3H), 0.98 (d, $J = 7.0$ Hz, 3H), 0.89 (d, $J = 6.9$ Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 173.84, 158.16, 139.34, 134.36, 129.04, 128.72, 128.47, 128.18, 127.54, 127.04, 67.70, 53.88, 51.70, 50.49, 31.23, 27.60, 27.32, 27.30, 19.63, 19.58, 17.65, 17.62. HRMS calculated for C$_{23}$H$_{31}$N$_6$O: 407.25539; found [M+H]$^+$: 407.25601.

**5’-((1H-indol-3-yl)methyl)-7’,8’,9’,10’,11’,12’,13’,14’-octahydrospiro[cyclopentane-1,15’-tetrazolo[5,1-c][1,4,7]triazacyclotridecin]-6’(5’H)-one 6j:**

White solid (0.1 g, 25%); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.38 – 7.32 (m, 3H), 7.13 – 7.08 (m, 1H), 6.63 (s, 1H), 4.22 – 4.06 (m, 1H), 3.69 (s, 1H), 2.59 – 2.52 (m, 2H), 2.04 (q, $J = 7.7$ Hz, 1H), 1.64 (s, 1H), 1.31 (s, 1H), 1.28 (d, $J = 4.2$ Hz, 2H), 0.91 – 0.85 (m, 1H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 176.1, 136.5, 129.2, 128.8, 128.7, 128.7, 127.1, 65.6, 64.4, 62.5, 58.2, 48.9, 39.9, 35.0, 30.7, 29.7, 28.3, 27.9, 19.9, 18.9. HRMS calculated for C$_{23}$H$_{32}$N$_7$O: 422.26629; found [M+H]$^+$: 422.2660.
15'-(1H-indol-3-yl)methyl)-6',7',8',9',10',11',14',15'-octahydro-5'H,13'H-spiro
cyclopentane-12'-tetrazolo[1,5-a][1,4,7]triazacyclotridecin-13'-one 7j:

Yellow oil (0.06 g, 15%); \(^1\)H NMR (500 MHz, Chloroform-d) \(\delta\) 8.10 (s, 1H), 7.84 (d, \(J = 8.7\) Hz, 1H), 7.73 (d, \(J = 7.8\) Hz, 1H), 7.35 (d, \(J = 8.0\) Hz, 1H), 7.24 – 7.18 (m, 1H), 7.18 – 7.13 (m, 1H), 6.98 (d, \(J = 2.3\) Hz, 1H), 5.97 – 5.79 (m, 1H), 4.11 – 4.02 (m, 1H), 3.90 – 3.82 (m, 1H), 3.58 (dd, \(J = 7.3, 4.3\) Hz, 2H), 2.72 – 2.56 (m, 1H), 2.26 – 2.15 (m, 2H), 2.14 – 2.04 (m, 1H), 2.00 – 1.90 (m, 1H), 1.85 – 1.76 (m, 3H), 1.72 – 1.59 (m, 3H), 1.46 – 1.38 (m, 1H), 1.33 – 1.20 (m, 5H), 1.15 – 1.07 (m, 1H), 1.03 – 0.94 (m, 1H). \(^{13}\)C NMR (126 MHz, Chloroform-d) \(\delta\) 176.9, 127.2, 123.3, 122.3, 119.9, 118.6, 111.2, 110.2, 69.4, 49.3, 46.7, 44.3, 30.2, 28.9, 26.6, 24.4, 19.5, 17.5. HRMS calculated for C\(_{23}\)H\(_{32}\)N\(_{7}\)O: 422.26629; found [M+H]\(^+\): 422.26678.

5-((1H-indol-3-yl)methyl)-1-isopropyl-8,9,10,11,12,13,14,15-octahydro-5H-tetrazolo[5,1-c][1,4,7]triazacyclotridecin-6(7H)-one 6k:

White solid (0.18 g, 43%); \(^1\)H NMR (500 MHz, Chloroform-d) \(\delta\) 8.11 – 7.99 (m, 2H), 7.70 (d, \(J = 7.9\) Hz, 1H), 7.40 – 7.33 (m, 1H), 7.26 – 7.20 (m, 1H), 7.20 – 7.14 (m, 1H), 7.07 – 7.00 (m, 1H), 5.94 – 5.82 (m, 1H), 4.02 – 3.94 (m, 1H), 3.89 – 3.81 (m, 1H), 3.67 – 3.60 (m, 1H), 3.58 – 3.49 (m, 1H), 2.90 – 2.78 (m, 2H), 2.51 – 2.42 (m, 1H), 2.17 – 2.09 (m, 1H), 1.60 (s, 3H), 1.37 – 1.17 (m, 5H), 0.98 (d, \(J = 7.0\) Hz, 3H), 0.95 – 0.85 (m, 1H), 0.82 (d, \(J = 6.9\) Hz, 3H). \(^{13}\)C NMR (126 MHz, CDC\(_3\)) \(\delta\) 174.5, 154.7, 127.3, 123.4, 122.4, 119.9, 118.6, 111.2, 110.2, 69.4, 49.3, 46.7, 44.3, 30.2, 28.9, 26.6, 24.4, 19.5, 17.5. HRMS calculated for C\(_{22}\)H\(_{32}\)N\(_{7}\)O: 410.26629; found [M+H]\(^+\): 410.26669.

15-((1H-indol-3-yl)methyl)-12-isopropyl-5,6,7,8,9,10,11,12,14,15-decahydro-13H-tetrazolo[1,5-a][1,4,7]triazacyclotridecin-13-one 7k:

White solid (0.08 g, 19%); \(^1\)H NMR (500 MHz, Chloroform-d) \(\delta\) 7.37 (s, 1H), 7.37 – 7.33 (m, 3H), 7.30 (d, \(J = 6.9\) Hz, 1H), 7.18 (d, \(J = 5.9\) Hz, 1H), 5.56 (t, \(J = 6.4\) Hz, 1H), 4.26 (s, 1H), 3.83 (d, \(J = 5.9\) Hz, 2H), 3.58 (dt, \(J = 14.5, 5.9\) Hz, 2H), 3.32 (q, \(J = 5.3\) Hz, 2H), 3.14 (td, \(J = 9.3, 8.9, 4.4\) Hz, 1H), 3.08 – 2.99 (m, 1H), 2.37 (ddd, \(J = 15.0, 8.1, 2.9\) Hz, 1H), 2.21 (ddd, \(J = 15.1, 9.9, 2.8\) Hz, 1H), 1.88 (d, \(J = 7.3\) Hz, 2H), 1.83 – 1.75 (m, 1H), 1.54 – 1.48 (m, 3H), 1.34 (dq,
J = 11.4, 3.7 Hz, 1H), 1.23 (d, J = 6.0 Hz, 1H), 0.91 (t, J = 6.2 Hz, 8H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 173.2, 151.2, 134.9, 128.9, 128.7, 126.99, 115.0, 109.5, 60.9, 48.9, 41.5, 40.7, 37.5, 35.2, 29.1, 28.6, 24.9, 22.9, 22.1.

HRMS calculated for C$_{22}$H$_{32}$N$_{7}$O: 410.26629; found [M+H]$^+$: 410.26678.

3-(5-(1-(benzylamino)-2-methylpropyl)-1H-tetrazol-1-yl)-N-(2-chlorobenzyl) propanamide 6l:

Yellow solid (0.3g, 66%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.37 – 7.32 (m, 1H), 7.30 – 7.27 (m, 2H), 7.26 – 7.18 (m, 6H), 6.49 (t, J = 6.0 Hz, 1H), 4.63 – 4.52 (m, 2H), 4.47 (d, J = 6.0 Hz, 2H), 3.89 (d, J = 7.7 Hz, 1H), 3.61 (d, J = 3.9 Hz, 1H), 3.49 (d, J = 13.4 Hz, 1H), 2.92 – 2.90 (m, 2H), 2.20 – 2.07 (m, J = 6.7 Hz, 1H), 2.03 (s, 1H), 1.06 (d, J = 6.6 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 168.8, 156.6, 139.4, 135.2, 133.3, 129.5, 128.9, 128.4, 128.1, 127.2, 127.0, 58.4, 51.5, 43.4, 41.5, 35.2, 32.5, 19.3, 19.1. HRMS calculated for C$_{22}$H$_{28}$N$_{6}$OCl: 427.1948; found [M+H]$^+$: 427.1950.

N-(2-chlorobenzyl)-3-(5-((isopropylamino)(phenyl)methyl)-1H-tetrazol-1-yl) propanamide 6m:

Yellow solid (0.2g, 52%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.38 – 7.33 (m, 5H), 7.33 – 7.28 (m, 2H), 7.24 – 7.19 (m, 3H), 6.37 (t, J = 5.9 Hz, 1H), 5.47 (s, 1H), 4.56 – 4.53 (m, 1H), 4.48 – 4.45 (m, 2H), 2.80 – 2.74 (m, 1H), 2.74 – 2.67 (m, 2H), 2.30 (s, 1H), 1.11 (d, J = 2.7 Hz, 3H), 1.09 (d, J = 2.7 Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 168.8, 156.5, 138.2, 135.2, 133.4, 129.5, 128.9, 128.4, 128.1, 127.0, 58.4, 51.5, 43.4, 41.5, 35.2, 32.5, 22.92, 22.5. HRMS calculated for C$_{21}$H$_{26}$N$_{6}$OCl: 413.18511; found [M+H]$^+$: 413.18552.

N-benzyl-5-(3-(methylthio)-1-(tritylamino)propyl)-1H-tetrazole-1-carboxamide 6n:

White solid (0.3g, 46%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.44 – 7.38 (m, 6H), 7.34 – 7.28 (m, 2H), 7.29 – 7.25 (m, 1H), 7.24 – 7.18 (m, 7H), 7.19 – 7.14 (m, 4H), 6.29 (s, 1H), 4.42 – 4.31 (m, 2H), 4.21 – 4.15 (m, 1H), 3.88– 3.86 (m, 1H), 3.05 (d, J = 9.0 Hz, 1H), 2.78 – 2.60 (m, 2H), 2.60 –
2.47 (m, 1H), 2.29 – 2.16 (m, 2H), 2.09 – 2.05 (m, 1H), 2.06 (s, 3H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 168.5, 157.6, 145.2, 137.7, 128.7, 128.53, 127.9, 127.7, 127.6, 126.7, 71.5, 47.1, 43.6, 43.2, 36.6, 34.9, 29.5, 15.3. HRMS calculated for $C_{34}H_{36}N_6OSNa$: 599.25635; found [M+Na]$^+$: 599.25684.

$N$-benzyl-4-(5-(1-(phenethylamino)butyl)-1H-tetrazol-1-yl)butanamide 6o:

Yellow oil (0.36g, 70%); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.35 – 7.29 (m, 3H), 7.26 (dd, $J = 7.0, 5.1$ Hz, 4H), 7.22 – 7.17 (m, 1H), 7.14 – 7.10 (m, 2H), 6.63 (t, $J = 5.9$ Hz, 1H), 4.47 – 4.32 (m, 4H), 4.13 (t, $J = 7.2$ Hz, 1H), 4.03 (m, 1H), 2.78 – 2.69 (m, 3H), 2.69 – 2.60 (m, 1H), 2.28 (t, $J = 7.1$ Hz, 2H), 2.24 – 2.15 (m, 2H), 2.13 (s, 1H), 1.78 (m, 2H), 1.34 – 1.24 (m, 3H), 1.21 – 1.09 (m, 1H), 0.89 (t, $J = 7.3$ Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 171.4, 156.4, 139.5, 138.4, 128.7, 128.6, 128.5, 127.7, 127.4, 126.3, 62.4, 62.4, 53.2, 53.1, 48.4, 46.6, 43.5, 36.2, 36.1, 32.4, 25.4, 19.2, 13.8, 13.9. HRMS calculated for $C_{24}H_{33}N_6O$: 421.27104; found [M+H]$^+$: 421.27148.

$N$-benzyl-4-(5-(1-((4-chlorobenzyl)amino)cyclopentyl)-1H-tetrazol-1-yl)butanamide 6p:

Yellow solid (0.3g, 60%); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.33 – 7.28 (m, 2H), 7.28 – 7.22 (m, 5H), 7.12 (d, $J = 8.2$ Hz, 2H), 6.42 (d, $J = 6.0$ Hz, 1H), 4.67 (t, $J = 6.9$ Hz, 2H), 4.41 (d, $J = 5.8$ Hz, 2H), 3.38 (s, 2H), 2.35 (m, 4H), 2.27 (q, $J = 6.9$ Hz, 2H), 2.18 – 2.10 (m, 2H), 1.87 – 1.76 (m, 4H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 171.3, 158.1, 138.2, 138.0, 132.8, 129.2, 129.1, 128.7, 128.6, 127.8, 127.5, 63.6, 47.6, 47.4, 43.6, 43.6, 37.3, 32.7, 25.4, 23.4. HRMS calculated for $C_{24}H_{30}N_6OCl$: 453.21641; found [M+H]$^+$: 453.21698.

$N$-benzyl-4-(5-(3-methyl-1-(tritylamino)butyl)-1H-tetrazol-1-yl)butanamide 6q:

White Solid (0.4g, 77%); $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.38 – 7.34 (m, 7H), 7.34 – 7.30 (m, 2H), 7.28 (td, $J = 7.6, 7.2, 1.6$ Hz, 4H), 7.19 (dd, $J = 8.4, 6.7$ Hz, 6H), 7.16 – 7.11 (m, 3H), 5.96 (d, $J = 6.5$ Hz, 1H), 4.54 – 4.32 (m, 2H), 2.64 – 2.58 (m, 1H), 2.20 – 2.12 (m, 2H), 1.69 – 1.60 (m, 4H), 1.35 – 1.24 (m, 3H), 0.89 (t, $J = 7.3$ Hz, 3H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 169.5, 157.6, 145.2, 137.7, 128.7, 128.53, 127.9, 127.7, 127.6, 126.7, 71.5, 47.1, 43.6, 43.2, 36.6, 34.9, 29.5, 15.3. HRMS calculated for $C_{34}H_{36}N_6OSNa$: 599.25635; found [M+Na]$^+$: 599.25684.
4.05 (dd, J = 11.7, 5.5 Hz, 2H), 3.90 (m, 1H), 2.75 (d, J = 7.0 Hz, 1H), 2.24 (t, J = 6.9 Hz, 2H), 2.04 (m, 2H), 1.73 (m, 1H), 1.65 (s, 1H), 1.51 (m, 1H), 1.18 – 1.05 (m, 1H), 0.74 (dd, J = 6.6, 1.5 Hz, 6H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 171.0, 157.9, 145.2, 138.1, 128.78, 128.59, 127.93, 127.83, 127.64, 126.74, 71.74, 47.26, 46.99, 46.27, 43.71, 32.68, 25.02, 24.46, 23.27, 22.12. HRMS calculated for C$_{36}$H$_{40}$N$_{6}$ONa: 595.31558; found [M+Na]$^+$: 595.31604.

4-(5-(2-methyl-1-(tritylamino)propyl)-1H-tetrazol-1-yl)-N-phenylbutanamide 6x:

White solid (0.3g, 53%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.41 – 7.36 (m, 6H), 7.33 (dd, J = 8.1, 6.8 Hz, 2H), 7.28 – 7.25 (m, 1H), 7.22 (t, J = 7.5 Hz, 8H), 7.19 – 7.14 (m, 3H), 5.62 (s, 1H), 4.07 – 4.03 (m, 1H), 3.93 – 3.84 (m, 1H), 3.55 (q, J = 6.7 Hz, 2H), 2.84 (t, J = 7.0 Hz, 2H), 2.23 – 2.12 (m, 2H), 2.02 – 1.98 (m, 2H), 1.75 – 1.72 (m, 1H), 1.55 – 1.51 (m, 1H), 1.21 – 1.06 (m, 1H), 0.76 (d, J = 6.6 Hz, 6H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 171.1, 156.4, 139.4, 128.7, 128.6, 128.5, 128.4, 126.6, 126.4, 51.7, 48.6, 46.3, 43.2, 40.6, 36.2, 35.6, 32.5, 25.3, 24.9, 22.6, 22.4. HRMS calculated for C$_{37}$H$_{42}$N$_{6}$ONa: 609.33123; found [M+Na]$^+$: 609.33173.

N-benzyl-4-(5-((tert-butylamino)(4-(trifluoromethyl)phenyl)methyl)-1H-tetrazol-1-yl)butanamide 6y:

Orange solid (0.2 g, 42%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.61 (d, J = 8.1 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.38 – 7.35 (m, 2H), 7.34 – 7.32 (m, 1H), 7.31 (d, J = 1.7 Hz, 2H), 5.84 (s, 1H), 5.59 (s, 1H), 4.47 (d, J = 5.9 Hz, 2H), 2.30 – 2.24 (m, 2H), 2.16 (m, 2H), 2.07 (s, 1H), 1.30 – 1.25 (m, 2H), 1.12 (s, 9H); $^{13}$C NMR (126 MHz, Chloroform-d) δ 170.9, 158.7, 157.1, 144.4, 137.9, 130.3, 128.8, 127.8, 126.1, 52.1, 51.5, 46.5, 43.8, 31.9, 29.7, 29.6, 24.9. HRMS calculated for C$_{24}$H$_{30}$N$_{6}$OF$_{3}$: 475.24277; found [M+H]$^+$: 475.24319.

N-benzyl-5-(5-(3-methyl-1-(tritylamino)butyl)-1H-tetrazol-1-yl)pentanamide 6z:

White solid (0.2g, 35%); $^1$H NMR (500 MHz, Chloroform-d) δ 7.41 – 7.36 (m, 6H), 7.36 – 7.34 (m, 2H), 7.32 – 7.26 (m, 1H), 7.24 (t, J = 7.5 Hz, 8H), 7.19 – 7.14 (m, 3H), 5.62 (s, 1H), 4.07 – 4.03 (m, 1H), 3.93 – 3.84 (m, 1H), 3.55 (q, J = 6.7 Hz, 2H), 2.84 (t, J = 7.0 Hz, 2H), 2.23 – 2.12 (m, 2H), 2.02 – 1.98 (m, 2H), 1.75 – 1.72 (m, 1H), 1.55 – 1.51 (m, 1H), 1.21 – 1.06 (m, 1H), 0.76 (d, J = 6.6 Hz, 6H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 171.1, 156.4, 139.4, 128.7, 128.6, 128.5, 128.4, 126.6, 126.4, 51.7, 48.6, 46.3, 43.2, 40.6, 36.2, 35.6, 32.5, 25.3, 24.9, 22.6, 22.4. HRMS calculated for C$_{36}$H$_{40}$N$_{6}$ONa: 595.31558; found [M+Na]$^+$: 595.31604.
(m, 4H), 7.23 (dd, J = 8.5, 6.6 Hz, 5H), 7.19 – 7.15 (m, 3H), 5.82 (s, 1H), 4.45 (d, J = 5.7 Hz, 2H),
4.03 (m, 1H), 3.87 (m, 1H), 3.82 – 3.67 (m, 1H), 2.78 (d, J = 7.3 Hz, 1H), 2.24 (t, J = 7.2 Hz, 2H),
1.81– 1.77 (m, 2H), 1.72–1.67 (m, 2H), 1.59 –1.54 (m, 1H), 1.28 (s, 1H), 1.16 – 1.07 (m, 1H),
0.77 (d, J = 6.5 Hz, 6H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 171.6, 157.9, 145.2, 138.1, 128.8,
128.6, 127.9, 127.8, 127.6, 126.8, 71.7, 47.4, 46.9, 43.7, 35.6, 28.8, 24.4, 23.3, 22.6, 22.1.
HRMS calculated for C$_{37}$H$_{42}$N$_6$ONa: 609.33123; found [M+H]$^+$: 609.3316.

$^1$H, $^{13}$C NMR, chromatograms of the novel synthesized compounds:

\[ \text{Figure 1. The change of the temperature of the reaction from room temperature to 0°C and -10°C showed a slight increase in the formation of the minor product B.} \]
Compound 6a:
Compound 7a:
Compound 6b:
Compound 7b:
Compound 6c:
Compound 7c:
Compound 6d:
Compound 6e:
Compound 7e:
Compound 6f:
Compound 7f:
Compound 6g:
Compound 7g:
Compound 6h:
Compound 7h:
Compound 6i:
Compound 7i:
Compound 6j:
Compound 7j:
Compound 6k:
Compound 7k:
Compound 6l:
Compound 6m:
Compound 6n:
Compound 6o:
Compound 6p:
Compound 6q:
Compound 6x:
Compound 6y:
Compound 6z:
Crystal structure determination

X-ray diffraction data for single crystals of compounds 6f, 6p, 6l, 6g, 6e, 6h, 7a, 6a, 6b, 7j, and 7k was collected using SuperNova (Rigaku - Oxford Diffraction) four circle diffractometer with a mirror monochromator and a microfocus MoKα radiation source (λ = 0.71073 Å, used for monocrystals of 6f, 6p, 6g, 7a, 6a, 6b, 7j and 7k) and CuKα radiation source (λ = 1.5418 Å used for 6l, 6e and 6h). The diffractometer was equipped with a CryoJet HT cryostat system (Oxford Instruments) allowing low temperature experiments, performed at 130(2)-132(4) K. The obtained data sets were processed with CrysAlisPro software [S1]. The phase problem was solved with direct methods using SIR2004 [S2] or SUPERFLIP [S3]. Parameters of obtained models were refined by full-matrix least-squares on F² using SHELXL-2014/6 [S4]. Calculations were performed using WinGX integrated system (ver. 2014.1) [S5]. Figure was prepared with Mercury 3.7 software [S6].

All non-hydrogen atoms were refined anisotropically. All hydrogen atoms attached to carbon atoms were positioned with the idealised geometry and refined using the riding model with the isotropic displacement parameter U_iso[H] = 1.2 (or 1.5 (methyl groups only)) U_eq[C]. Hydrogen atoms bound to nitrogen atoms were positioned on the difference Fourier map and refined with no restrains on the isotropic displacement parameters. Crystal data and structure refinement results for presented crystal structures are shown in Table S1. The molecular geometry observed in the crystal structures are shown in Figure S1.

In the asymmetric units of 6p, 6l and 6e two independent molecules are observed. Compound 6p crystallised as a solvate, with the chloroform molecule forming several interactions with the main compound atoms and additionally stabilising the crystal lattice. In structures 6l and 6e, a conformational disorder was observed. In the case of 6l one of two molecules of the asymmetric units exhibits disorder within the benzylamine fragment of the molecule. Two alternative conformers were modelled (refined site occupancies: 84.5% and 15.4%, respectively) based on the difference Fourier maps interpretation. To guarantee the reliable geometry of the modelled fragment for the less abundant conformer, several geometrical constraints were applied. In the crystal structure of compound 6e, the two independent molecules of the asymmetric units show different orientations of the aromatic rings. Additionally, a conformational disorder in the cyclopropyl fragment orientation for both
molecules was observed, with the refined site occupancies 55:45 and 60:40, for molecule 1 and 2, respectively. Crystals of 6a were poor quality plates. In the asymmetric unit of 7j there are two independent molecules of the macrocyclic compound (here only one of them is presented) and chloroform molecules. The data processing revealed the twinning phenomena, with two components of 55% and 45% ratio. Data was processed with TWIN option of the CrysAlisPro software [S1]. The obtained model was refined against HKLF4.

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos.: CCDC 1842386 (6f), CCDC 1842385 (6p), CCDC 1844783 (6l), CCDC 1844786 (6g), CCDC 1844784 (6e), CCDC 1844787 (6h), CCDC 1842390 (7a), CCDC 1844788 (6a) and CCDC 1844785 (6b). CCDC 1548702 (7j), CCDC 1548703 (7k), 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).

Acknowledgements

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Figure S1. Molecular geometry observed in the crystal structures of compounds 6f, 6p, 6l, 6g, 6e, 6h, 7a, 6a, 6b, 7j, and 7k showing the atom labelling scheme (here asymmetric units are presented except for 6p, 6l and 6e, for which two independent molecules are observed in the asymmetric unit). Additionally, a partial, conformational disorder was observed in structures 6l and 6e - here only one of alternative conformers are presented. Displacement ellipsoids of non-hydrogen atoms are drawn at the 30% probability level. H atoms are presented as small spheres with an arbitrary radius. In the asymmetric unit of 7j there are two independent molecules of the macrocyclic compound (here only one of them is presented) and chloroform molecules.
| Empirical moiety formula | 6f | 6p | 6l | 6g | 6e |
|--------------------------|----|----|----|----|----|
| C\textsubscript{32} H\textsubscript{37} N\textsubscript{7} O | 2 (C\textsubscript{24} H\textsubscript{29} N\textsubscript{6} Cl, C H Cl\textsubscript{3}) | 2 (C\textsubscript{22} H\textsubscript{27} Cl N\textsubscript{6} O) | C\textsubscript{32} H\textsubscript{35} N\textsubscript{7} O | 2 (C\textsubscript{28} H\textsubscript{27} F\textsubscript{3} N\textsubscript{6} O) |
| **Formula weight [g/mol]** | 535.7 | 1144.7 | 853.89 | 533.67 | 1041.11 |
| **Crystal system** | Triclinic | Triclinic | Triclinic | Monoclinic | Triclinic |
| **Space group** | P\textsubscript{1} | P\textsubscript{1} | P\textsubscript{1} | P\textsubscript{2} \textsubscript{1} | P\textsubscript{1} |
| **Unite cell dimensions** | a = 6.3741(8) Å | a = 10.764(6) Å | a = 10.764(6) Å | a = 10.8092(4) Å | a = 10.8092(4) Å |
| | b = 9.3723(12) Å | b = 14.0058(6) Å | b = 7.9643(4) Å | b = 14.1679(6) Å | b = 14.1679(6) Å |
| | c = 24.838(2) Å | c = 15.9242(8) Å | c = 26.039(2) Å | c = 17.2034(7) Å | c = 17.2034(7) Å |
| | α=83.121(9)° | α=89.704(4)° | α=89.704(4)° | α=78.408(4)° | α=78.408(4)° |
| | β=85.819(9)° | β=78.054(4)° | β=78.054(4)° | β=86.646(3)° | β=86.646(3)° |
| | γ=79.949(10)° | γ=87.542(3)° | γ=67.659(5)° | γ=94.113(6)° | γ=94.113(6)° |
| **Volume [Å\textsuperscript{3}]** | 1448.5(3) | 2759.08(17) | 2165.3(2) | 1404.17(17) | 2572.64(18) |
| **Z** | 2 | 2 | 2 | 2 | 2 |
| **D\textsubscript{calc} [Mg/m\textsuperscript{3}]** | 1.228 | 1.378 | 1.310 | 1.262 | 1.344 |
| **μ [mm\textsuperscript{-1}]** | 0.077 | 0.459 | 1.769 | 0.080 | 0.835 |
| **F(000)** | 572 | 1192 | 904 | 568 | 1088 |
| **Crystal size [mm\textsuperscript{3}]** | 0.2 x 0.15 x 0.10 | 0.2 x 0.2 x 0.15 | 0.6 x 0.4 x 0.1 | 0.4 x 0.4 x 0.02 | 0.4 x 0.3 x 0.1 |
| Θ range          | 3.14° to 28.52° | 2.87° to 28.67° | 3.42° to 71.39° | 3.01° to 28.73° | 3.19° to 71.30° |
|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Index ranges     | -8 ≤ h ≤ 7, -9 ≤ k ≤ 12, -31 ≤ l ≤ 33 | -13 ≤ h ≤ 13, -20 ≤ k ≤ 20, -24 ≤ l ≤ 24 | -13 ≤ h ≤ 12, -16 ≤ k ≤ 17, -19 ≤ l ≤ 16 | -9 ≤ h ≤ 9, -10 ≤ k ≤ 10, -32 ≤ l ≤ 34 | -13 ≤ h ≤ 11, -17 ≤ k ≤ 15, -21 ≤ l ≤ 20 |
| Refl. collected  | 8886 25215 13358 19388 16985 | 6321 12499 7978 6631 9771 |
| Independent reflections | 6321 [R(int) = 0.0327] | 12499 [R(int) = 0.0350] | 7978 [R(int) = 0.0358] | 6631 [R(int) = 0.0681] | 9771 [R(int) = 0.0317] |
| Completeness [%] to Θ | 98.6 (Θ 26.3°) | 99.9 (Θ 26.3°) | 96.4 (Θ 67.7°) | 99.8 (Θ 25.2°) | 99.9 (Θ 67.7°) |
| Absorption correction | Multi-scan | Multi-scan | Multi-scan | Multi-scan | Multi-scan |
| Tmin. and Tmax.  | 0.428 and 1.000 | 0.428 and 1.000 | 0.427 and 1.000 | 0.621 and 1.000 | 0.695 and 1.000 |
| Data/restraints/parameters | 6321 / 0 / 2370 | 12499 / 0 / 661 | 7978 / 10 / 620 | 6631 / 1 / 373 | 9771 / 3 / 739 |
| GooF on F2       | 1.086 | 1.052 | 1.020 | 1.068 | 1.024 |
| Final R indices [I>2σ(I)] | R1= 0.0658, wR2= 0.1458 | R1= 0.0461, wR2= 0.1131 | R1= 0.0511, wR2= 0.1380 | R1= 0.0799, wR2= 0.1706 | R1= 0.0566, wR2= 0.1514 |
| R indices (all data) | R1= 0.0984, wR2= 0.1622 | R1= 0.0659, wR2= 0.1310 | R1= 0.0599, wR2= 0.1493 | R1= 0.1017, wR2= 0.1845 | R1= 0.0764, wR2= 0.1705 |
| Δρ_{max} Δρ_{min} [e·Å^{-3}] | 0.28 and -0.27 | 0.59 and 0.46 | 0.44 and 0.47 | 0.34 and 0.25 | 0.43 and 0.48 |
|               | 6h                        | 7a                        | 6a                        | 6b                        |
|---------------|---------------------------|---------------------------|---------------------------|---------------------------|
| **Empirical moiety formula** | C$_{30}$ H$_{32}$ Cl N$_{7}$ O | C$_{33}$ H$_{33}$ Cl N$_{6}$ O | C$_{33}$ H$_{33}$ Cl N$_{6}$ O | C$_{34}$ H$_{36}$ N$_{6}$ O |
| **Formula weight [g/mol]**      | 542.07                    | 565.1                     | 565.10                    | 544.69                    |
| **Crystal system**               | Monoclinic                | Triclinic                 | Monoclinic                | Triclinic                 |
| **Space group**                  | P2$_1$/n                  | P-1                       | P2$_1$/n                  | p1$_1$                    |
| **Unite cell dimensions**        |                           |                           |                           |                           |
| a = 9.8002(3) Å                  | a = 9.1544(3) Å           | a = 9.0985(3) Å           | a = 11.2953(14) Å         |
| b = 15.1210(5) Å                 | b = 10.8644(4) Å          | b = 10.3538(3) Å          | b = 11.4120(10) Å         |
| c = 18.4804(7) Å                 | c = 15.5035(5) Å          | c = 30.3383(10) Å         | c = 13.0664(13) Å         |
| β=90.374(3)°                    | α= 72.725(3)°             | α= 97.525(3)°             | α=70.404(9)°              |
|                             | β= 84.894(3)°             | β= 97.525(3)°             | β=73.213(10)°             |
|                             | γ= 83.984(3)°             | γ= 83.984(3)°             | γ=70.603(10)°             |
| **Volume [Å$^3$]**               | 2886.72(17)               | 1461.55(9)                | 2833.38(16)               | 1466.5(3)                 |
| **Z**                          | 4                         | 2                         | 4                         | 2                          |
| Property                                      | Value/Range                      |
|----------------------------------------------|----------------------------------|
| D<sub>calc</sub> [Mg/m³]                    | 1.247 - 1.233                    |
| μ [mm⁻¹]                                     | 1.451 - 0.077                    |
| F(000)                                       | 1144 - 580                      |
| Crystal size [mm³]                           | 0.6 x 0.6 x 0.4 - 0.2 x 0.2 x 0.15 | 0.4 x 0.2 x 0.05 - 0.2 x 0.2 x 0.05 |
| Θ range                                      | 3.70° to 71.92° - 2.84° to 28.50° - 3.00° to 30.33° - 3.11° to 30.36° |
| Index ranges                                 | -9 ≤ h ≤ 11, -18 ≤ k ≤ 18, -21 ≤ l ≤ 23 | -11 ≤ h ≤ 11, -14 ≤ k ≤ 13, -20 ≤ l ≤ 19 | -12 ≤ h ≤ 12, -13 ≤ k ≤ 12, -36 ≤ l ≤ 40 | -15 ≤ h ≤ 15, -15 ≤ k ≤ 15, -16 ≤ l ≤ 18 |
| Refl. collected                              | 18364 - 20432 - 27066 - 12639      |
| Independent reflections                      | 5568 [R(int) = 0.0477] - 6744 [R(int) = 0.0295] - 7892 [R(int) = 0.0784] - 7920 [R(int) = 0.0676] |
| Completeness [%] to Θ                        | 100.0 (Θ 67.7°) - 99.8 (Θ 26.3°) - 99.8 (Θ 25.2°) - 99.8 (Θ 25.2°) |
| Absorption correction                        | Multi-scan - Multi-scan - Multi-scan - Multi-scan |
| Tmin. and Tmax.                              | 0.152 and 1.000 - 0.873 and 1.000 - 0.808 and 1.000 - 0.817 and 1.000 |
| Data/restraints/parameters                   | 5568 / 0 / 367 - 6744 / 0 / 376 - 7892 / 1 / 379 - 7920 / 0 / 380 |
| Goof on F2                                   | 1.037 - 1.039 - 1.439 - 1.042 |
| Final R indices [I>2sigma(I)]                | R1 = 0.0444, wR2 = 0.1221 | R1 = 0.0414, wR2 = 0.0886 | R1 = 0.1130, wR2 = 0.3278 | R1 = 0.0717, wR2 = 0.1428 |
| R indices (all data) | R1= 0.0496, wR2= 0.1270 | R1= 0.0586, wR2= 0.0982 | R1= 0.1223, wR2= 0.3461 | R1= 0.1305, wR2= 0.1931 |
|----------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Δρ<sub>max</sub>, Δρ<sub>min</sub> [e·Å<sup>-3</sup>] | 0.29 and -0.49 | 0.29 and -0.26 | 0.68 and -0.53 | 0.32 and -0.32 |
| Empirical moiety formula | 2(C<sub>23</sub>H<sub>31</sub>N<sub>7</sub>O), 3CHCl<sub>3</sub> | C<sub>22</sub>H<sub>31</sub>N<sub>7</sub>O |  |
| Crystal system | Triclinic | Orthorhombic |  |
| Space group | P-1 | Pbca |  |
| Unite cell dimensions | a = 12.9113(4) Å, b = 13.8869(4) Å, c = 16.5533(3) Å, α = 102.178(2)°, β = 91.521(2)°, γ = 97.504(2)° | a = 9.8856(6) Å, b = 10.4180(5) Å, c = 42.5525(16) Å, α = 90.0°, β = 90.0°, γ = 90.0° | |
| Volume [Å<sup>3</sup>] | 2871.85(13) | 4382.4(4) | |
| Z | 2 | 8 | |
| D<sub>calc</sub> | 1.389 | 1.241 | |
|                                      | Value 1      | Value 2      |
|--------------------------------------|--------------|--------------|
| [Mg/m³]                              |              |              |
| μ [mm⁻¹]                             | 0.491        | 0.081        |
| F(000)                               | 1252         | 1760         |
| Crystal size [mm³]                   | 0.4 x 0.4 x 0.2 | 0.6 x 0.1 x 0.4 |
| Θ range                             | 3.05 to 28.67° | 3.00° to 28.57° |
| Index ranges                         | -17 ≤ h ≤ 16, | -12 ≤ h ≤ 9, |
|                                     | -18 ≤ k ≤ 18, | -8 ≤ k ≤ 13, |
|                                     | -21 ≤ l ≤ 20 | -34 ≤ l ≤ 56 |
| Reflected collected                  | 40860        | 13478        |
| Independent reflections             | 13393        | 5024         |
| [R(int) = 0.0474]                    |              | [R(int)=0.1206] |
| Completeness [%] (Θ 25.24°)          | 99.8         | 99.4         |
| Absorption correction               | Multi-scan   | Multi-scan   |
| Max. and min. transmission           | 0.715 and 1.000 | 0.2818 and 1.000 |
| Refinement method                   | Full-matrix least-squares on F² | Full-matrix least-squares on F² |
| Data/restraints/parameters           | 13393 / 0 / 695 | 5024 / 0 / 276 |
| GooF on F2                           | 1.030        | 0.981        |
| Final R indices [I>2sigma(I)] | R1= 0.0662, wR2= 0.1639 | R1= 0.0836, wR2= 0.1581 |
|-----------------------------|---------------------------|---------------------------|
| R indices (all data)        | R1= 0.1015, wR2= 0.1928   | R1= 0.2098, wR2= 0.2206   |
| \(\Delta \rho_{\text{max}}\), \(\Delta \rho_{\text{min}}\) [e\(\cdot\)Å\(^{-3}\)] | 0.79 and -0.70            | 0.39 and -0.38            |

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