Supporting Information

for

Construction of bis-, tris- and tetrahydrazones by addition of azoalkenes to amines and ammonia

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Experimental procedures, characterization data for new compounds, copies of \textsuperscript{1}H and \textsuperscript{13}C NMR spectra

Contents

Experimental part S2
Data for compounds and copies of NMR spectra S5
X-ray data for 2(13b)-2H\textsubscript{2}O\cdot MeOH S51

S1
Experimental part

Reactions were monitored by analytical TLC using silica gel TLC plates with QF-254. Visualization was accomplished with UV light and staining with a solution of ninhydrin in methanol. NMR spectra were acquired on Bruker AM300 and AC200 spectrometers at 297 K with residual solvents peaks as an internal standard. Coupling constants (J) are given in Hz. The ratio of E/Z-fragments is determined by NMR and refers to the ratio of isomers in solution at the moment of spectra acquisition. HRMS spectra were acquired on Bruker MicrOTOF instrument. Elemental analyses were performed at the Analytical center of N.D. Zelinsky Institute of Organic Chemistry. Melting points (uncorrected) were determined on a Kofler hot-stage microscope. Commercial reagents were used without additional purification. Compound 1g was prepared accordingly to a literature procedure.¹

Synthesis of α-chloro hydrazones 1

To a solution of acylhydrazine (10 mmol) in MeOH (20 mL) acetic acid (15 mmol) was added. The solution was cooled on an ice-bath and α-haloketone (15 mmol of chloroacetone, dropwise; 10 mmol of phenacylchloride, in one portion; or 30 mmol of chloroacetaldehyde (50% w/w in water), in one portion) was added. The reaction mixture was kept at same temperature for 0.5–2 h (TLC control of conversion) and further isolation of product was performed as following:

For products 1c–e: The precipitate was filtered, washed with chilled (approx. −20 °C) MeOH (5 mL) and dried on a filter.

For products 1a,g: The reaction mixture was poured in cold water (100 mL), the precipitate was filtered, washed with water and dried on filter.

For product 1b: The reaction mixture was evaporated, the residue triturated with Et₂O (15 mL) and dried in vacuo (0.1 Torr).

For product 1h: The reaction mixture was poured in cold water (100 mL) and extracted with Et₂O (100 ml). After washing with brine (50 ml) and drying with Na₂SO₄, the extract was evaporated (25 °C) and crude 1h was used without additional purification.

NMR and physical data for compounds 1 are in accordance with literature data (1a and 1b,² 1e,³ 1f⁴).

Table 1: Synthesis of α-halogen-substituted hydrazones 1 from α-halocarbonyl compounds and acyl hydrazines or carbazates.

![Diagram](image)

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*aProcedures: A: 1.5 equiv of α-haloketone, 1.0 equiv of hydrazide, 1.5 equiv of AcOH, MeOH, 0 °C; B: 1.0 equiv of α-haloketone, 1.0 equiv of hydrazide, 1.5 equiv of AcOH, MeOH, 0 °C; C: 1.0 equiv of α-haloketone, 1.5 equiv of hydrazide, 0.05 equiv of AcOH, Et₂O, 0 °C [1]; D: 3 equiv of chloroacetaldehyde, 1.0 equiv of hydrazide, 1.5 equiv of AcOH, MeOH, 0 °C. bYield based on hydrazide used. cYield based on α-haloketone. dWas used in further step in crude form due to low stability.

Reaction of α-halogen hydrazones with amines

To a solution of amine or its hydrochloride salt (1.0 mmol) in MeOH (7 mL) K₂CO₃ (1.0 mmol for morpholine and aniline, 2.0 mmol for benzylamine and propargylamine, 3.0 mmol for valine methyl ester hydrochloride and tacd, 4.0 mmol for cyclam, 6.0 mmol for tacn tryhydrochloride) was added and the mixture was stirred for 30 min. Then α-halohydrazones (1.0 mmol for morpholine and aniline, 2.0 mmol for benzylamine, propargylamine and valine methyl ester hydrochloride, 3.1 mmol for tacn and tacd or 4.2 mmol for cyclam) was added in one portion with vigorous stirring. The reaction mixture was stirred for 1 h and evaporated in vacuo. Water (50 mL) was added to the residue and further purification was performed as following:

For products 2a–d, 3–9: The precipitate was filtered off and washed with appropriate solvent (water for 2a–c, MeOH for 7–9, Et₂O for 3–6, acetone for 2d) and dried with air.

For products 2f,g: EtOAc (50 mL) was added, the organic extract was separated, washed with brine (50 mL), dried with Na₂SO₄ and evaporated. The residue was purified by
column chromatography on silica gel (hexane–EtOAc (5:1) → EtOAc) to give products 2f and 2g.

**Reaction of α-halogen hydrazones with ammonia**

Trishydrazones 1a,b,h. To a stirred solution of 1 (5 mmol) in MeOH (10 mL) aqueous ammonia (25–28%, 5 mL) was added. After 15 min water (50 mL) was added and the precipitate was filtered, thoroughly washed with water (11a,h) or water, MeOH and acetone (11b), and dried on filter.

Trishydrazones 1d,f: To a stirred solution of 1 (2 mmol) in MeOH (5 mL) aqueous ammonia (25–28%, 1 mL) was added dropwise with cooling on ice-bath. After 15 min water (15 mL) was added, the precipitate was filtered off and further purification was performed as following:

For products 11d: The precipitate was quickly washed with cooled (0 °C) acetone and dried in vacuo (0.1 Torr, 20 °C).

For products 11f and 12f: The precipitate was purified by column chromatography on silica gel (hexane–EtOAc (5:1) → EtOAc) to give 11f and 12f.

**Reaction of 3 with BnN₃**

To a stirred solution of 3 (99 mg, 0.25 mmol) in MeOH (5 ml) BnN₃ (67 mg, 0.5 mmol) was added, followed by solutions of CuSO₄·5H₂O (3.1 mg, 0.0125 mmol) in water (0.5 mL) and sodium L-ascorbate (7.4 mg, 0.0375 mmol) in water (1 mL). The reaction mixture was stirred for 5 h evaporated and water (25 mL) was added to the residue. The resulting precipitate was filtered, washed with 0.1 M EDTA solution and water, and then dried on filter to give 115 mg of 10 (87%).

**Cyclization of 11b**

To 11b (443 mg, 1 mmol) AcOH (1.5 mL) was added. After ca. 5 min the starting compound dissolved forming a transparent solution. The mixture was diluted with water (30 mL) and K₂CO₃ was added in small portions until neutral pH. The solution was extracted with EtOAc (50 mL), organic extract was washed with brine (20 mL) and dried under Na₂SO₄. The solution was concentrated in vacuo, and the residue was crystallized form pentane–EtOAc, filtered, washed with pentane and dried on filter to give 390 mg of 13b (88%).

For single-crystal X-ray diffraction analysis 13b was recrystallized from MeOH/MTBE to give solvate 13b·H₂O·MeOH (mp 130–138 °C) (CCDC 1501437).
Data for compounds and copies of NMR spectra

Compound 1c


$^1$H NMR (200 MHz, CDCl$_3$): E-1c, $\delta$ = 1.98 (s, 3 H, CH$_3$), 2.21 (s, 3 H, CH$_3$CO), 4.09 (s, 2 H, CH$_2$), 9.63 (s, 1 H, NH); selected signals of Z-1c, $\delta$ = 2.07 (s), 4.17 (s), 8.93 (s).

$^{13}$C NMR (50 MHz, CDCl$_3$): E-1c, $\delta$ = 13.5 (CH$_3$), 20.5 (CH$_3$CO), 49.0 (CH$_2$), 146.7 (C=N), 174.6 (C=O).

HRMS: Calcd for C$_5$H$_9$ClN$_2$ONa [MH$^+$] m/z: 171.0296. Found: 171.0310.
Compound **1d**

White cryst., m.p. 44-42 °C, mixture of *E*- and *Z*-1d in ratio 8:1.

$^1$H NMR (200 MHz, CDCl$_3$): main isomer, $\delta = 0.87$ (m, 3 H, $CH_2$CH$_2$), 1.29 (m, 8 H, $CH_3$(CH$_2$)$_4$), 1.62 (m, 2 H, $CH_3$(CH$_2$)$_3$), 1.99 (s, 3 H, $CH_3$), 2.61 (t, $J = 7.4$, 2 H, $CH_2$(CH$_2$)$_5$), 4.12 (s, 2 H, $CH_2$), 9.34 (s, 1 H, NH); selected signals of minor isomer, $\delta = 2.09$ (s), 2.30 (m), 4.21 (s), 8.47 (s).

$^{13}$C NMR (50 MHz, CDCl$_3$): main isomer, $\delta = 13.3$ and 14.1 ($CH_3$ and $CH_3$CH$_2$), 22.7, 24.6, 29.1, 29.4, 31.8 and 32.6 (($CH_2$)$_6$), 49.0 ($CH_2$), 146.0 ($C=N$), 176.9 ($C=O$).

HRMS: Calcd for $C_{11}H_{21}ClN_2ONa$ [$M+Na^+$] m/z: 255.1235. Found: 255.1259.
White solid, m.p. 204-206 °C, mixture of isomers with ratio of $E$- and $Z$- fragments >20:1.

$^1$H NMR (300 MHz, DMSO-$d_6$): main isomer ($E,E$), $\delta = 1.45$ (s, 18 H, 6 $CH_3$ (tBu)), 1.83 (s, 6 H, 2 $CH_3$), 2.97 (s, 4 H, 2 $CH_2$), 3.46 (s, 2 H, $CH_2$Ph), 7.2-7.4 (m, 5 H, Ph), 9.45 (s, 2 H, 2 NH); selected signals of minor isomers, $\delta = 1.77$ and 1.87 (2 s), 3.21 (s), 3.50 (s).

$^{13}$C NMR (75 MHz, CDCl$_3$): main isomer, $\delta = 14.4$ (2 $CH_3$), 28.1 (6 $CH_3$ (tBu)), 56.9 ($CH_3$), 59.9 (2 $CH_2$), 79.0 (2 $C$ (tBu)), 126.9, 128.1, 129.0 and 138.2 (Ph), 151.6 and 153.1 (2 $C=\text{N}$ and 2 $C=\text{O}$); selected signals of minor isomers, $\delta = 23.5$, 55.7, 58.3, 60.7.

Elemental analysis. For $C_{23}H_{37}N_5O_4$ calcd: C, 61.72%; H, 8.33%; N, 15.65%. Found: C, 61.38%; H, 8.21%; N, 15.11%.
Compound 2b


$^1$H NMR (300 MHz, DMSO-$d_6$): $E,E$-2b, $\delta = 1.22$ (t, $J = 7.1$, 6 H, 2 CH$_3$CH$_2$), 1.84 (s, 6 H, 2 CH$_3$), 3.00 (s, 4 H, 2 CH$_2$), 3.47 (s, 2 H, CH$_2$Ph), 4.11 (q, $J = 7.1$, 4 H, 2 CH$_3$CH$_2$), 7.2-7.4 (m, 5 H, Ph), 9.74 (s, 2 H, 2 NH); selected signals of minor isomers, $\delta = 1.79$ and 1.89 (2 s), 3.04 and 3.22 (2 s), 3.51 (s), 9.81 and 11.03 (2 s).

$^{13}$C NMR (75 MHz, CDCl$_3$): $E,E$-2b, $\delta = 14.4$ and 14.5 (2 CH$_3$ and 2 CH$_3$CH$_2$), 57.0 (CH$_2$Ph), 59.9 and 60.2 (2 CH$_2$ and 2 CH$_3$CH$_2$), 126.9, 128.0, 129.0 and 138.2 (Ph), 152.1 and 154.0 (2 C=N and 2 C=O); selected signals of minor isomers, $\delta = 14.4$, 14.7, 23.2, 55.2, 58.3, 60.3, 60.5, 127.4, 128.3, 129.1, 137.2.

HRMS: Calcd for C$_{19}$H$_{30}$N$_5$O$_4$ [MH$^+$] m/z: 392.2292. Found: 392.2292.
White solid, m.p. 171-173 °C, mixture of isomers with ratio of \(E\) and \(Z\) fragments 1.4:1.

\(^1\)H NMR (300 MHz, DMSO-\(d_6\)): \(E,E-2c\), \(\delta = 1.84\) (s, 6 H, 2 \(CH_3\)), 2.10 (s, 6 H, 2 \(CH_3CO\)), 3.06 (s, 4 H, 2 \(CH_2\)), 3.52 (s, 2 H, \(CH_2Ph\)), 7.2-7.4 (m, 5 H, \(Ph\)), 10.05 (s, 2 H, 2 \(NH\)); selected signals of other isomers, \(\delta = 1.88\) (s), 1.94 (s), 3.03 (s), 3.55 (s).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(E,E-2c\), \(\delta = 14.3\) (2 \(CH_3\)), 20.5 (2 \(CH_3CO\)), 57.5 (\(CH_2Ph\)), 60.3 (2 \(CH_2\)), 126.9, 128.0, 128.9 and 138.2 (\(Ph\)), 150.0 (2 \(C=\)N), 172.2 (2 \(C=\)O); selected signals of other isomers, \(\delta = 14.6, 21.4, 60.2, 128.3, 129.1, 154.1, 165.7\).

HRMS: Calcd for \(C_{17}H_{26}N_5O_2\) [MH\(^+\)] \(m/z\): 332.2081. Found: 332.2079.
Compound 2d

White solid, m.p. 120-124 °C, mixture of isomers with ratio of E- and Z- fragments 2:1.

$^1$H NMR (300 MHz, DMSO-d$_6$): $\delta = 0.86$ (s, 6 H, 2 CH$_3$ (Hept)), 1.26 (s, 16 H, 2 (CH$_2$)$_4$), 1.54 (s, 4 H, 2 CH$_2$(CH$_2$)$_4$), 1.86, 1.88 and 1.84 (3 s, 6 H, 2 CH$_3$), 2.10, 2.22 and 2.48 (3 s, 4 H, CH$_2$CO), 3.08 and 3.24 (2 s, 4 H, 2 CH$_2$), 3.52 and 3.54 (2 s, 2 H, CH$_2$Ph), 7.1-7.4 (m, 5 H, Ph), 10.00 (s, 2 H, 2 NH).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 13.8$ and 14.2 (2 CH$_3$ and 2 CH$_3$ (Hept)), 21.9, 24.0, 24.2, 25.0, 28.3, 28.6, 31.1, 32.1 and 33.8 (2 (CH$_2$)$_6$), 57.3 and 60.2 (2 CH$_2$ and CH$_2$), 126.9, 128.0, 128.3, 128.9, 129.1 and 138.2 (Ph), 149.8 (2 C=N), 174.6 (2 C=O).

HRMS: Calcd for C$_{29}$H$_{50}$N$_5$O$_2$ [MH$^+$] m/z: 500.3959. Found: 500.3964.

S15
Compound 2f

Pale yellow solid, softening at 67 °C, melting at 95 °C, mixture of isomers.

$^1$H NMR (300 MHz, DMSO-d$_6$): $\delta = 1.41, 1.43$ and 1.47 (3 s, 18 H, 6 CH$_3$ (tBu)), 3.42, 3.51, 3.60, 3.66 and 3.76 (5 s, 6 H, 2 CH$_2$ and CH$_3$), 6.8-7.8 (m, 15 H, 2 Ph and Ph), 8.47, 8.72 and 10.56 (3 s, 2 H, 2 NH).

$^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta = 27.8$ and 27.9 (6 CH$_3$ (tBu)), 56.4, 57.5 and 59.1 (2 CH$_2$ and CH$_3$), 79.1 and 79.6 (2 C (tBu)), 126.2, 126.6, 127.0, 127.3, 127.4, 127.6, 128.1, 128.2, 128.5, 128.6, 128.7, 128.9, 129.0, 129.4, 132.0, 132.7, 137.2, 137.5 and 137.7 (2 Ph and Ph), 150.1, 151.1, 151.7 and 152.1 (2 C=N and 2 C=O).

HRMS: Calcd for C$_{33}$H$_{42}$N$_5$O$_4$ [MH$^+$] m/z: 572.3231. Found: 572.3226.
Compound 2g

Pale yellow foam, softening at 79 °C, melting at 98 °C, mixture of isomers with ratio of $E$- and $Z$-fragments 1:7.

$^1$H NMR (300 MHz, DMSO-$d_6$): main isomer (Z,Z), $\delta$ = 1.23 (t, $J = 7.1$, 6 H, 2 CH$_3$CH$_2$), 1.49 (s, 18 H, 6 C$_3$H$_3$(tBu)), 3.49 (s, 2 H, CH$_2$), 3.55 (s, 4 H, 2 CH$_2$), 4.17 (q, 4 H, 2 CH$_2$CH$_3$), 7.2-7.4 (m, 5 H, Ph), 10.79 (s, 2 H, 2 NH); selected signals of minor isomers, $\delta$ = 1.47 (s), 3.70 (s).

$^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ = 13.9 (2 CH$_3$CH$_2$), 27.8 (6 CH$_3$ (tBu)), 49.6, 58.8 and 60.8 (2 CH$_2$, 2 CH$_2$CH$_3$, CH$_2$), 80.7 (2 C (tBu)), 127.6, 128.3, 128.8 and 136.8 (Ph), 138.6, 151.5 and 163.7 (2 C=N and 4 C=O).

HRMS: Calcd for C$_{27}$H$_{41}$N$_5$O$_8$Na [MNa$^+$] m/z: 586.2847. Found: 586.2839.
Compound 3

White solid, m.p. 169-174 °C (with decomposition), E.E- 3.

$^1$H NMR (300 MHz, DMSO-$_d_6$): $\delta = 1.45$ (s, 18 H, $6 \text{CH}_3$ (tBu)), 1.83 (s, 6 H, 2 CH$_2$), 3.08 (s, 4 H, 2 CH$_2$), 3.14 (s, 1 H, CCH), 3.25 (s, 2 H, CH$_2$CC), 9.43 (s, 2 H, 2 NH).

$^{13}$C NMR (75 MHz, DMSO-$_d_6$): $\delta = 14.3$ (2 CH$_3$), 28.0 (6 CH$_3$ (tBu)), 41.8 (CH$_2$CC), 59.3 (2 CH$_2$), 75.7 (CCH), 78.8 (CCH), 79.0 (2 C (tBu)), 151.3 and 153.0 (2 C=N and 2 C=O).

HRMS: Calcd for C$_{19}$H$_{34}$N$_5$O$_4$ [MH$^+$] m/z: 396.2605. Found: 396.2600.
Compound 4

White solid, m.p. 164-166 °C. (s)-E,E-4.

\(^1\)H NMR (300 MHz, DMSO-\(d_6\)): \(\delta = 0.80\) and 0.96 (2 s, 6 H, 2 CH\(_3\) (\(^i\)Pr)), 1.45 (s, 18 H, 6 CH\(_3\) (\(^t\)Bu)), 1.81 (s, 6 H, 2 CH\(_3\)), 2.01 (s br, 1 H, CH (\(^i\)Pr)), 2.76 (m, 1 H, CH), 3.11 (dd, \(J_1 = 9.9\), \(J_2 = 1.32\), 4 H, 2 CH\(_2\)), 3.66 (s, 3 H, CH\(_3\)O), 9.40 (s, 2 H, 2 NH).

\(^{13}\)C NMR (75 MHz, DMSO-\(d_6\)): \(\delta = 14.5\) (2 CH\(_3\)), 19.5 and 19.7 (2 CH\(_3\) (\(^i\)Pr)), 26.9 (CH (\(^i\)Pr)), 28.1 (6 CH\(_3\) (\(^t\)Bu)), 50.7 (CH), 57.3 (2 CH\(_2\)), 68.9 (CH\(_3\)O), 79.0 (2 C (\(^t\)Bu)), 151.4 and 153.0 (2 C=\(\equiv\)N and 2 C=O), 171.4 (C=O).

HRMS: Calcd for C\(_{22}\)H\(_{42}\)N\(_5\)O\(_6\) [MH\(^+\)] m/z: 472.3130. Found: 472.3122.
Compound 5

White solid, m.p. 150-156 °C, mixture of E- and Z-5 in ratio 1:1.

$^{1}$H NMR (300 MHz, DMSO-$d_6$): $\delta$ = 1.45 and 1.47 (2 s, 9 H, 3 CH$_3$(tBu)), 1.75 and 1.81 (2 s, 3 H, CH$_3$), 3.73 and 4.05 (s and d, $J$ = 5.9, 2 H, CH$_2$), 5.89, 6.56, 6.77 and 7.10 (4 m, 5 H, Ph), 9.52 (s, 1 H, NH).

$^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ = 13.7 and 1.9 (CH$_3$), 28.1 (CH$_3$(tBu)), 49.6 and 57.4 (CH$_2$), 78.9 (C(tBu)), 112.1, 112.7, 115.9, 116.4, 128.8 and 128.9 (Ph), 148.5, 148.6 and 153.0 (Ph (C-N), C=N and C=O).

HRMS: Calcd for C$_{14}$H$_{22}$N$_3$O$_2$ [MH$^+$] m/z: 264.1707. Found: 264.1712.
Compound 6

\[ \text{White solid, m.p. 186-189 °C, E-6.} \]

\(^1\)H NMR (300 MHz, DMSO-d\(_6\)): \( \delta = 1.45 \) (s, 9 H, 3 CH\(_3\) (t-Bu)), 1.84 (s, 3H, CH\(_3\)), 2.30 (s, 4 H, (CH\(_2\))\(_2\)N), 2.96 (s, 2 H, CH\(_2\)), 3.98 (s, 4 H, (CH\(_2\))\(_2\)O), 9.48 (s, 1 H, NH).

\(^{13}\)C NMR (75 MHz, DMSO-d\(_6\)): \( \delta = 14.3 \) (CH\(_3\)), 28.0 (3 CH\(_3\) (t-Bu)), 53.1 ((CH\(_2\))\(_2\)N), 64.9 (CH\(_2\)), 66.1 ((CH\(_2\))\(_2\)O), 78.9 (C, (t-Bu)), 151.0 and 153.0 (C=O and C=O).

HRMS: Calcd for C\(_{12}\)H\(_{24}\)N\(_3\)O\(_3\) [MH\(^+\)] m/z: 258.1812. Found: 258.1829.
Compound 7


$^1$H NMR (200 MHz, CDCl$_3$): $\delta = 1.50$ (s, 27 H, $9 CH_3(tBu)$), 1.86 (s, 9 H, 3 CH$_3$), 2.70 (s, 12 H, 3 CH$_2$CH$_2$), 3.20 (s, 6 H, 3 CH$_2$), 7.49 (s, 3 H, 3 NH).

$^{13}$C NMR (50 MHz, CDCl$_3$): $\delta = 13.6$ (3 CH$_3$), 28.4 (9 CH$_3(tBu)$), 55.7 (3 CH$_2$CH$_2$), 65.5 (3 CH$_2$), 81.1 (3 C(tBu)), 151.6 and 152.8 (3 C=N and 3 C=O).

HRMS: Calcd for C$_{30}$H$_{58}$N$_9$O$_6$ [MH$^+$] m/z: 640.4505. Found: 640.4510.
Compound 8

White solid, softening at 180 °C, decomposition at 240-250 °C, \textit{E,E,E}-8

\begin{align*}
\text{\textsuperscript{1}H NMR} \ (200 \text{ MHz, CDCl}_3): \ & \delta = 1.50 \ (s, 27 \text{ H, 9 CH}_3 (tBu)), 1.77 \ (m, 6 \text{ H, 3 CH}_2CH_2CH_2), 1.84 \ (s, 9 \text{ H, 3 CH}_3), 2.43 \ (m, 12 \text{ H, 3 CH}_2CH_2CH_2), 3.08 \ (s, 6 \text{ H, 3 CH}_2), 7.50 \ (s, 3 \text{ H, 3 NH}). \\
\text{\textsuperscript{13}C NMR} \ (50 \text{ MHz, CDCl}_3): \ & \delta = 13.6 \ (3 \text{ CH}_3), 21.3 \ (3 \text{ CH}_2CH_2CH_2), 28.4 \ (9 \text{ CH}_3 (tBu)), 49.4 \ (3 \text{ CH}_2CH_2CH_2), 61.6 \ (3 \text{ CH}_2), 81.2 \ (3 \text{ C (tBu)}), 151.5 \text{ and } 152.8 \ (3 \text{ C=N and 3 C=O}). \\
\text{HRMS: Calcd for C}_{33}H_{64}N_{9}O_{6} [\text{MH}^+] \text{ m/z: 682.4974. Found: 682.4983}}
\end{align*}
Compound 9


$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 1.50 (s, 36 H, 12 CH$_3$ (tBu)), 1.82 (s, 12 H, 4 CH$_3$), 1.86 (m, 4 H, 2 CH$_2$CH$_2$CH$_2$), 2.42 and 2.51 (2 m, 16 H, 2 CH$_3$CH$_2$ and 2 CH$_2$CH$_2$CH$_2$), 3.07 (s, 8 H, 4 CH$_2$), 7.54 (s, 4 H, 4 NH).

$^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 13.3 (4 CH$_3$), 22.7 (2 CH$_2$CH$_2$CH$_2$), 28.4 (12 CH$_3$ (tBu)), 50.4 and 51.5 (2 CH$_2$CH$_2$ and 2 CH$_2$CH$_2$CH$_2$), 61.7 (4 CH$_2$), 81.1 (4 C (tBu)), 151.4 and 152.8 (4 C=N and 4 C=O).

HRMS: Calcd for C$_{42}$H$_{81}$N$_{12}$O$_8$ [MH$^+$] m/z: 881.6295. Found: 881.6302.
Compound 10

White solid, m.p. 140-144 °C, mixture of isomers with ratio of E- and Z-fragments 4.8:1.

$^1$H NMR (300 MHz, DMSO-d$_6$): main isomer, $\delta = 1.44$ (s, 18 H, 6 CH$_3$ (tBu)), 1.80 (s, 6 H, 2 CH$_3$), 2.99 (s, 4 H, 2 CH$_2$), 3.59 (s, 2 H, CH$_2$), 5.60 (s, 2 H, CH$_2$Ph), 7.2-7.4 (m, 5 H, Ph), 8.13 (s, 1 H, Tz), 9.47 (s, 2 H, 2 NH); selected signals of minor isomers, $\delta = 1.89$ (s), 3.05 and 3.17 (2 s), 9.59 and 10.91 (2 s).

$^{13}$C NMR (75 MHz, DMSO-d$_6$): main isomer, $\delta = 14.4$ (2 CH$_3$), 28.1 (6 CH$_3$ (tBu)), 47.6 and 52.8 (CH$_2$ and CH$_3$Ph), 59.7 (2 CH$_2$), 79.0 (2 C (tBu)), 124.3 and 143.3 (Tz), 127.7, 128.0, 128.7 and 136.2 (Ph), 151.6 and 153.1 (2 C=N and 2 C=O); selected signals of minor isomers, $\delta = 14.6$ and 23.4, 47.2, 60.2, 79.1, 124.5, 127.6, 136.0.

HRMS: Calcd for C$_{26}$H$_{41}$N$_8$O$_4$ [MH$^+$] m/z: 529.3245. Found: 529.3238.
Compound 11a


$^1$H NMR (300 MHz, DMSO-$d_6$): main isomer ($E,E,E$-11a), $\delta = 1.45$ (s, 27 H, 9 $CH_3$ ($t$Bu)), 1.82 (s, 9 H, 3 $CH_3$), 2.94 (s, 6 H, 3 $CH_2$), 9.47 (3 NH); selected signals of minor isomers, $\delta = 1.41$ (s), 1.86 (s), 3.02 (s), 3.20 (s), 9.55 (s).

$^{13}$C NMR (75 MHz, DMSO-$d_6$): main isomer ($E,E,E$-11a), $\delta = 14.5$ (3 $CH_3$), 28.1 (9 $CH_3$ ($t$Bu)), 60.0 (3 $CH_2$), 79.0 (3 $C$ ($t$Bu)), 151.4 and 153.0 (3 $C$=N and 3 $C$=O); selected signals of minor isomers, $\delta = 14.8$, 23.5, 27.9, 61.3.

HRMS: Calcd for $C_{24}H_{46}N_7O_6$ [MH$^+$] m/z: 528.3504. Found: 528.3489.

$^1$H NMR (300 MHz, DMSO-$d_6$): main isomer ($E,E,E$-11b), $\delta$ = 1.23 (t, $J = 7.0$, 9 H, 3 CH$_2$CH$_3$), 1.84 (s, 9 H, 3 CH$_3$), 3.00 (s, 6 H, 3 CH$_2$), 4.12 (q, $J = 7.0$, 6 H, 3 CH$_2$CH$_3$), 9.5-9.8 (s br, 3 H, 3 NH); selected signals of minor isomers, $\delta$ = 1.88 (s), 3.07 (s), 3.20 (s).

$^{13}$C NMR (75 MHz, DMSO-$d_6$): main isomer ($E,E,E$-11b), $\delta$ = 14.5 (3 CH$_3$ and 3 CH$_2$CH$_3$), 60.0 and 60.2 (3 CH$_2$ and 3 CH$_2$CH$_3$), 151.8 and 154.1 (3 C=N and 3 C=O); selected signals of minor isomers, $\delta$ = 14.8, 23.3, 55.3, 61.1, 150.7.

Elemental analysis. For C$_{18}$H$_{33}$N$_7$O$_6$ calcd: C, 48.75%; H, 7.50%; N, 22.11%. Found: C, 48.85%; H, 7.63%; N, 21.89%.
Compound 11d

White solid, m.p. 118-124 °C, mixture of isomers with ratio of E- and Z-fragments 1:1.2.

\(^1\)H NMR (200 MHz, DMSO-\text{d}_6): \(\delta = 0.85\) (m, 9 H, 3 CH\textsubscript{3} (Hept)), 1.25 (s, 24 H, 3 (CH\textsubscript{2})\textsubscript{4}), 1.51 (m, 6 H, 3 CH\textsubscript{2}(CH\textsubscript{2})\textsubscript{4}), 1.83 and 1.85 (2 s, 9 H, 3 CH\textsubscript{3}), 2.21 and 2.44 (2 m, 6 H, 3 CH\textsubscript{2}CO), 3.05 and 3.09 (2 s, 6 H, 3 CH\textsubscript{2}), 10.0 (s, 3 H, 2 NH).

\(^{13}\)C NMR (50 MHz, DMSO-\text{d}_6): \(\delta = 13.9\) and 14.4 (3 CH\textsubscript{3} and 3 CH\textsubscript{3} (Hept)), 22.1, 24.3, 25.1, 28.5, 28.7, 31.2 and 32.2 (3 (CH\textsubscript{2})\textsubscript{4}), 60.7 (3 CH\textsubscript{2}), 149.6 (3 C=N), 174.8 (3 C=N).

HRMS: Calcd for C\textsubscript{33}H\textsubscript{64}N\textsubscript{7}O\textsubscript{3} [MH\textsuperscript{+}] m/z: 606.5065. Found: 606.5073.
Compound 11h

White solid, m.p. 169-172 °C (with decomposition), \textit{E,E,E-11h}.

$^1$H NMR (200 MHz, DMSO-d$_6$): $\delta = 1.42$ (s, 27 H, 9 CH$_3$ (tBu)), 3.13 (d, $J = 4.4$, 6 H, 3 CH$_2$), 7.27 (m, 3 H, 3 CH), 10.54 (s, 3 H, 3 NH).

$^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta = 28.1$ (9 CH$_3$ (tBu)), 54.7 (3 CH$_2$), 79.2 (3 C (tBu)), 144.1 (3 C=N), 152.4 (3 C=O).

HRMS: Calcd for C$_{21}$H$_{40}$N$_7$O$_6$ [MH$^+$] m/z: 486.3035. Found: 486.3035.
Compound 11f

Pale yellow foam, softening at 77 °C, melting at 103 °C, mixture of isomers.

$^1$H NMR (200 MHz, DMSO-d$_6$): $\delta = 1.39, 1.44$ and $1.48$ (3 s, 27 H, 9 CH$_3$ (i-Bu)), 3.61, 3.88 and 3.89 (3 s, 6 H, 3 CH$_2$), 7.1-7.8 (m, 15 H, 3 Ph), 8.68, 8.90, 10.0 and 10.1 (4 s, 3 H, 3 NH).

$^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta = 28.0$ (9 CH$_3$ (i-Bu)), 58.9 (3 CH$_2$), 79.2 and 79.8 (3 C (i-Bu)), 126.3, 127.2, 128.0, 128.2, 128.5, 128.9, 129.2, 132.3 and 137.5 (3 Ph), 145.6, 150.6, 152.1 and 152.3 (3 C=N and 3 C=O).

HRMS: Calcd for C$_{39}$H$_{52}$N$_7$O$_6$ [MH$^+$] m/z: 714.3974. Found: 714.3955.
Compound 12f

White foam, softening at 99 °C, melting at 110 °C, E.E-12f.

$^1$H NMR (200 MHz, DMSO-d$_6$): $\delta = 1.39$ (s, 18 H, 6 CH$_3$ (tBu)), 3.49 (s, 4 H, 2 CH$_2$), 6.67, 7.19 and 7.34 (3 m, 10 H, 2 Ph), 8.28 (s, 2 H, 2 NH)

$^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta = 27.9$ (6 CH$_3$ (tBu)), 59.3 (2 CH$_2$), 79.7 (2 C (tBu)), 127.3, 128.6 and 132.7 (2 Ph), 150.7 and 152.1 (2 C=N and 2 C=O).

HRMS: Calcd for C$_{26}$H$_{35}$N$_5$O$_4$ [MNa$^+$] m/z: 504.2581. Found: 504.2569.
Compound 13b

White solid, m.p. 135-138 °C. Mixture of conformers.

$^1$H NMR (200 MHz, DMSO-d$_6$): $\delta$ = 0.82 and 0.99 (2 s, 9 H, 3 CH$_3$), 1.17 (m, 9 H, 3 CH$_2$CH$_3$), 2.67, 2.96 and 3.30 (3 m, 6 H, 3 CH$_2$), 4.04 (m, 6 H, 3 CH$_2$CH$_3$), 7.34, 7.55, 8.21, 8.44 and 8.69 (5 br, 3 H, 3 NH).

$^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta$ = 14.6, 18.3 and 19.5 (6 CH$_3$), 46.2, 53.0, 54.6, 59.9 and 62.2 (6 CH$_2$), 72.9, 73.1 and 73.7 (3 C), 157.0 and 157.7 (3 C=O).

HRMS: Calcd for C$_{18}$H$_{34}$N$_7$O$_6$ [MH$^+$] m/z: 444.2565. Found: 444.2556.
$^1$H NMR of 13b at 330 K

X-ray data for 2(13b)·2H$_2$O·MeOH

Figure S1: General view of 13b in representation of atoms with thermal ellipsoids at 50% probability level; all hydrogen atoms (except for those of the NH groups) are omitted for clarity. The compound crystallizes as a crystallosolvate with two water and one methanol molecule (those are not shown) per two symmetry-independent molecules of the product.

S51
Crystallographic data: Crystals of 13b (C_{37}H_{74}N_{14}O_{15}, M = 955.10) are monoclinic, space group P2_1/n, at 100 K: a = 14.325(2), b = 12.234(2), c = 29.447(5) Å, β = 64.3830(10)*, V = 102.398(4) Å³, Z = 4 (Z' = 2), d_{calc} = 1.259 g·cm⁻³, μ(MoKα) = 0.98 cm⁻¹, F(000) = 2056. Intensities of 61716 reflections were measured with a Bruker APEX2 DUO CCD diffractometer [λ(MoKα) = 0.71072Å, ω-scans, 2θ<58°], and 13409 independent reflections [R_{int} = 0.2198] were used in the further refinement. The structure was solved by direct methods and refined by the full-matrix least-squares technique against F² in the anisotropic–isotropic approximation. The hydrogen atoms of the NH groups and those of water and methanol molecules were found in difference Fourier synthesis; the H(C) atom positions were calculated. All the hydrogen atoms were refined in the isotropic approximation within the riding model. The refinement converged to wR² = 0.2712 and GOF = 1.054 for all the independent reflections (R1 = 0.0896 was calculated against F for 5215 observed reflections with I > 2σ(I)). All calculations were performed using SHELXTL PLUS 5.0.

CCDC 1501437 contains the supplementary crystallographic data for 13b. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge, CB21EZ, UK; or deposit@ccdc.cam.ac.uk).