Microscale Parallel Synthesis of Acylated Aminotriazoles Enabling the Development of Factor XIIa and Thrombin Inhibitors

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Table S1. DMAP-induced decomposition of *N*-acylated aminotriazoles *1* and *13c*\(^a\)

| Additive | 1     | 13c   |
|----------|-------|-------|
| —        | 0%    | 0%    |
| DMAP     | 30%   | 6%    |

\(^a\) - aminotriazoles *1* and *13c* were treated with DMSO-\(d_6\) (no additives), or DMSO-\(d_6\) + DMAP (1.5 eq.) for 48 h at r.t. on air. The % of decomposition was determined by \(^1\)H NMR spectroscopy.
Table S2. Optimization of the parallel microscale amide coupling reactions performed in a 96-well plate

| Entry | Coupling reagent / base (eq. / eq.) | Stirring\(^c\) | Temperature \(^°C\) | Reaction time \([h]\) | Reaction yield \([\%]\) | Average yield \([\%]\) |
|-------|------------------------------------|----------------|-------------------|-----------------|-----------------|-----------------|
|       |                                    |                |                   | 13a  | 13b  | 13c  | 13d  | 13e  |                  |
| 1     | EDCI / DMAP (1.1 / 1.1)             | -              | 50                | 16   | 36   | 6    | 60   | 54   | 34   | 38   |
| 2     | COMU / DIPEA (1.1 / 1.1)            | -              | 50                | 16   | -    | -    | -    | -    | -    | -    |
| 3     | HATU / DIPEA (1.1 / 1.1)            | -              | 50                | 16   | 63   | 39   | 79   | 77   | 54   | 62   |
| 4     | EDCI / DMAP (1.1 / 1.1)             | -              | r.t.              | 16   | 31   | 1    | 73   | 23   | 31   | 32   |
| 5     | EDCI / DMAP (1.1 / 1.1)             | -              | r.t.              | 92   | 23   | 3    | 72   | 22   | 30   | 30   |
| 6     | EDCI / DMAP (1.5 / 1.5)             | -              | r.t.              | 16   | 79   | 58   | 92   | 94   | 67   | 78   |
| 7     | EDCI / DMAP (1.5 / 1.5)             | +              | r.t.              | 16   | 48   | 84   | 88   | 58   | 70   |      |
| 8     | EDCI / DMAP (1.1 / 1.1)             | +              | r.t.              | 16   | 73   | 48   | 84   | 88   | 58   | 70   |      |
| 9     | EDCI / DMAP (1.5 / 1.5)             | +              | r.t.              | 16   | 85   | 71   | 91   | 92   | 56   | 79   |      |
| 10\(^h\) | EDCI / DMAP (1.5 / 1.5)          | +              | r.t.              | 16   | 80   | 46   | 93   | 90   | 61   | 74   |      |
| 11    | EDCI (1.5)                          | +              | r.t.              | 16   | 12   | 30   | 9    | 14   | 29   | 19   |      |
| 12    | EDCI / HOBt (1.5 / 1.5)             | +              | r.t.              | 16   | 6    | 2    | 34   | 64   | 82   | 38   |      |
| 13    | DCC / DMAP (1.5 / 1.5)              | +              | r.t.              | 16   | 46   | 32   | 39   | 60   | 60   | 42   |      |
| 14    | EDCI / DIPEA (1.5 / 3.0)            | +              | r.t.              | 16   | 25   | 27   | 21   | 11   | 10   | 19   |      |
| 15    | COMU / DIPEA (1.5 / 3.0)            | +              | r.t.              | 16   | -    | -    | -    | -    | 5    | 1    |      |
| 16    | HATU / DIPEA (1.5 / 3.0)            | +              | r.t.              | 16   | -    | -    | 6    | -    | 34   | 8    |      |
| 17\(^h\) | EDCI / DMAP (1.5 / 1.5)         | +              | r.t.              | 16   | 88   | 74   | 93   | 96   | 55   | 81   |      |
| 18    | EDCI / DMAP (1.5 / 1.5)             | +              | r.t.              | 6    | 86   | 71   | 84   | 89   | 54   | 77   |      |
| 19    | EDCI / DMAP (1.5 / 1.5)             | +              | r.t.              | 3    | 87   | 72   | 82   | 85   | 53   | 76   |      |
| 20    | CDI (1.5)                           | +              | r.t.              | 16   | 41   | 22   | 21   | 37   | 31   | 30   |      |
| 21\(^h\) | EDCI / DMAP / HOBt (1.5 each)    | +              | r.t.              | 16   | 13   | 7    | 45   | 78   | 73   | 43   |      |

[a] Reaction conditions: in one well of 96-well plate, in DMSO-\(d_6\) (120 \(\mu\)L). 7 (3 mg, 18.6 \(\mu\)mol) reacted with a carboxylic acid (1 eq.) in the presence of indicated coupling reagent and base at the indicated temperature and reaction time.  \([b]\) As measured by \(^1\)H NMR. \([c]\) Micro magnetic stirring bars implemented into each well of the well plate were used; \([d]\) 1.1 eq. of carboxylic acid was used; \([e]\) Reaction was performed under

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X-Ray diffraction: Data sets for compound 33g (33g*) were collected with a Bruker D8 Venture PHOTON III diffractometer. Programs used: data collection: APEX3 V2019.1-01 (Bruker AXS Inc., 2019); cell refinement: SAINT V8.40A (Bruker AXS Inc., 2019); data reduction: SAINT V8.40A (Bruker AXS Inc., 2019); absorption correction, SADABS V2016/2 (Bruker AXS Inc., 2019); structure solution SHELXT-2015² (Sheldrick, G. M. Acta Cryst., 2015, A71, 3-8); structure refinement SHELXL-2015³ (Sheldrick, G. M. Acta Cryst., 2015, C71 (1), 3-8) and graphics, XPD (Version 5.1, Bruker AXS Inc., Madison, Wisconsin, USA, 1998). R-values are given for observed reflections, and wR² values are given for all reflections.

X-ray crystal structure analysis of 33g (dan10075): A colorless prism-like specimen of C₂₂H₁₉N₅O, approximate dimensions 0.060 mm x 0.140 mm x 0.140 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Kappa CCD APEXII Bruker APEXII Diffractometer system equipped with a fine-focus sealed tube Cu sealed tube (CuKa, λ = 1.54178 Å) and a graphite monochromator. A total of 1754 frames were collected. The total exposure time was 22.16 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 27265 reflections to a maximum θ angle of 66.67° (0.84 Å resolution), of which 6386 were independent (average redundancy 4.269, completeness = 99.9%, Rint = 6.83%, Rfree = 5.62%) and 5377 (84.20%) were greater than 2σ(F²). The final cell constants of a = 8.5517(2) Å, b = 16.1109(5) Å, c = 13.2164(4) Å, β = 94.293(2)°, volume = 1815.79(9) Å³, are based upon the refinement of the XYZ-centroids of 4502 reflections above 20 θ with 6.706° < 2θ < 130.3°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.850. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9090 and 0.9590. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P2₁, with Z = 4 for the formula unit, C₂₂H₁₉N₅O. The final anisotropic full-matrix least-squares refinement on F² with 521 variables converged at R1 = 4.32%, for the observed data and wR2 = 10.13% for all data. The goodness-of-fit was 1.069. The largest peak in the final difference electron density synthesis was 0.262 e/Å³ and the largest hole was -0.244 e/Å³ with an RMS deviation of 0.044 e/Å³. On the basis of the final model, the calculated density was 1.351 g/cm³ and F(000), 776 e. The hydrogens at N₄A and N₄B atoms were refined freely, but with N-H distance restraint (DFIX). Flack parameter was refined to: -0.12. CCDC Nr.: 2089066.

X-ray crystal structure analysis of 33g* (dan9995): A colorless plate-like specimen of C₂₂H₁₉N₅O, approximate dimensions 0.026 mm x 0.100 mm x 0.117 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker D8 Venture Bruker D8 Venture Photon III Diffractometer system equipped with a micro focus tube CuKα (CuKα, λ = 1.54178 Å) and a MX mirror monochromator. A total of 1337 frames were collected. The total exposure time was 19.64 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 31525 reflections to a maximum θ angle of 66.99° (0.84 Å resolution), of which 6372 were independent (average redundancy 4.947, completeness = 99.3%, Rint = 36.20%, Rfree = 23.59%) and 2577 (40.44%) were greater than 2σ(F²). The final cell constants of a = 8.5503(5) Å, b = 16.1338(9) Å, c = 13.2124(8) Å, β = 94.245(4)°, volume = 1817.63(18) Å³, are based upon the refinement of the XYZ-centroids of 1590 reflections above 20 θ with 6.708° < 2θ < 96.14°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.827. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9230 and 0.9820. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P2₁, with Z = 4 for the formula unit, C₂₂H₁₉N₅O. The final anisotropic full-matrix least-squares refinement on F² with 522 variables converged at R1 = 8.05%, for the observed data and wR2 = 21.79% for all data. The goodness-of-fit was 0.946. The largest peak in the
final difference electron density synthesis was 0.280 e/Å³ and the largest hole was -0.268 e/Å³ with an RMS deviation of 0.070 e/Å³. On the basis of the final model, the calculated density was 1.350 g/cm³ and F(000), 776 e. The hydrogens at N4A and N4B atoms were refined freely, but with N-H distance restraint (DFIX and U-fixed value). Flack parameter was refined to: -0.1(8). CCDC Nr.: 2089052.

Figure S1: Crystal structure of compound 33g. Two conformers of 33g were found in the asymmetric unit (conformer A and B). Thermal ellipsoids are shown at 15% probability.
SYNTHETIC PROCEDURES

General procedure A
The carboxylic acid ethyl ester (1.0 eq.) and hydrazine monohydrate were refluxed neat or in EtOH for the indicated time. After cooling down to r.t., the mixture was refrigerated at 5 °C overnight. The resulting precipitate was filtered off and washed with EtOH. If necessary, the product was recrystallized from EtOH or EtOH/H₂O, or purified via flash-column chromatography.

General procedure B
Benzhydrazide (1 eq.) and S-methylisothiouronium sulfate (2-5 eq.) were suspended in EtOH/H₂O and heated to reflux for the indicated time (in particular cases, S-methylisothiouronium sulfate was added in portions). Then, KOH was added, and the reaction mixture was heated to reflux for 3-6 h. After cooling down, the mixture was neutralized with HCl (2 M) and extracted with EtOAc (5 ×, equal amounts). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. The residue was recrystallized or purified by flash-column chromatography.

General procedure C
If not explicitly described otherwise, ketone (1.0 eq.) was dissolved in DMF-DMA (2.0 eq.) and heated to reflux (neat) for 16 h. The reaction mixture was cooled to r.t. and was concentrated in vacuo. The resulting solids were filtered off, washed with n-hexane (3 ×), and dried in vacuo.

General procedure D
If not explicitly described otherwise, enaminone (1.0 eq.) and ammonium acetate (8.0 eq.) were dissolved in acetic acid, followed by the addition of β-ketoester (1.2 eq.). The reaction mixture was refluxed for 16 h, cooled to r.t. and poured into H₂O (0 °C). The formed precipitate was filtered off, washed with H₂O and dried in vacuo. If no solid precipitated, the aqueous phase was extracted with EtOAc (3 ×, equal amounts), the combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. The crude product was purified by flash-column chromatography.
(5-Amino-1-(benzoyl-1-prolyl)-1H-1,2,4-triazol-3-yl)pyridine (13e). Triazole amine 15a (100 mg, 621 µmol), benzoyl-L-proline (12, 136 mg, 621 µmol, 1.0 eq.), EDCI-HCl (155 mg, 807 µmol, 1.3 eq.) and DMAP (98.5 mg, 807 µmol, 1.3 eq.) were dissolved in DMF and the reaction mixture was stirred at r.t. overnight. After dilution with H2O, the solution was extracted with ethyl acetate (7 × 50 mL). The organic phase was dried over Na2SO4 and the solvent was removed in vacuo. The residue was purified by column chromatography (DCM/MeOH = 1/0 → 9/1), to obtain 13e as a colorless solid (34.3 mg, 94.7 µmol, 15%). TLC: Rf = 0.54 (DCM/MeOH = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.71 (d, J = 4.7 Hz, 1H, 6-Hpyridyl), 8.04 (d, J = 7.8 Hz, 1H, 3-Hpyridyl), 7.95 (dd, J = 7.5, 2.0 Hz, 1H, 4-Hpyridyl), 7.76 (s, 2H, NH2), 7.60–7.57 (m, 2H, 2-/6-Hpyridyl), 7.53–7.45 (m, 4H, 3-/4-/5-Hphenyl, 5-Hpyridyl), 5.52 (dd, J = 8.5, 5.9 Hz, 1H, 2-Hpyrrolidinyl), 3.68–3.59 (m, 2H, 5-Hpyrrolidinyl), 2.49–2.45 (m, 1H, 3-Hpyrrolidinyl), 2.07 (dq, J = 12.9, 6.4 Hz, 1H, 13-Hpyrrolidinyl), 1.97 (p, J = 6.7 Hz, 2H, 4-Hpyrrolidinyl). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 171.9 (1C, C=Opyridyl), 168.1 (1C, C=Obenzoyl), 159.7 (1C, 3-Ctriazolyl), 149.8 (1C, 6-Cpyridyl), 148.8 (1C, 2-Cpyridyl), 137.1 (1C, 4-Cpyridyl), 135.8 (1C, 1-Cphenyl), 130.3 (1C, 4-Cphenyl), 128.3 (2C, 3-/5-Cphenyl), 127.2 (2C, 2-/6-Cphenyl), 124.8 (1C, 5-Cpyridyl), 122.6 (1C, 3-Cpyridyl).

3-(Pyridin-2-yl)-1H-1,2,4-triazol-5-amine (15a). Picolinic acid (3.00 g, 24.4 mmol, 1.0 eq.) and amino guanidine sulfate (6.00 g, 24.4 mmol, 1.0 eq.) were ground in a mortar to a homogenous powder. Under stirring, the mixture was melted at 190 °C without solvent for 5 h. After cooling to r.t., the solid was suspended in water and the pH of the solution was set to neutral with an aqueous NaOH solution (2 mol). The suspension was filtrated, washed with water and the residue was dried in vacuo to yield 15a as a yellow solid (2.74 g, 17.0 mmol, 70%). M.p. = 210–211 °C. TLC: Rf = 0.33 (DCM/MeOH = 1/1). 1H-NMR (600 MHz, DMSO-d6, 299 K) δ (in ppm) = 13.45* and 12.23 and (two s, 1H, NH), 8.69 (br s, 1H, 1-Hpyridyl), 8.03–7.74 (m, 2H, 3-/5-Hpyridyl), 7.55–7.18 (m, 1H, 5-Hpyridyl), 6.08 and 5.34* (two s, 2H, NH2).

IR (neat): ν [cm⁻¹] = 3345, 3125, 2739, 1639, 1589, 1501, 1408, 1346, 1173, 1111, 1053, 988, 729. HRMS (APCI): m/z = 363.1564 calculated for C₁₉H₁₉N₆O₃⁺ [M+H]⁺, found: 363.1589.

3-(5-Amino-1H-1,2,4-triazol-3-yl)pyridine-1-oxide (15e). Carboxylic acid 14c (1.64 g, 11.8 mmol, 1.0 eq.) and amino guanidine hydrochloride (2.60 g, 23.6 mmol, 2.0 eq.) were ground in a mortar to a homogenous powder. Under stirring, the mixture was melted at 180 °C for 5 h. After cooling down, the solid was dissolved in H₂O (50 mL) and the pH was adjusted to neutral with an aqueous NaOH solution. The solvent was evaporated in vacuo and the residue was suspended in MeOH (20 mL) and stirred at r.t. overnight. The suspension was filtrated, washed with MeOH and dried in vacuo to obtain compound 14c as a yellowish solid (930 mg, 5.25 mmol, 45%). M.p. = 243–244 °C. TLC: Rf = 0.56 (DCM/MeOH = 7/3). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.50 (s, 1H, NH), 8.47 (s, 1H, 2-Hpyrdine-1-oxidy), 8.20 (d, J = 6.5 Hz, 1H, 6-Hpyrydine-1-oxidy), 7.73 (d, J = 8.0 Hz, 1H, 4-Hpyrydine-1-oxidy), 7.46 (dd, J = 8.0, 6.5 Hz, 1H, 5-Hpyrydine-1-oxidy), 6.28 (s, 2H, NH2).

IR (neat): ν [cm⁻¹] = 3294, 3179, 3071, 1636, 1566, 1517, 1267. 861, 729. HRMS (APCI): m/z = 191.0774 calculated for C₁₇H₁₇N₅O₂⁺ [M+H]⁺, found 191.0782.
3-(5-Bromopyridin-3-yl)-1H-1,2,4-triazol-5-amine (15d). 5-Bromonicotinic acid (14d, 956 mg, 4.73 mmol, 1.0 eq.) and aminoguanidine hydrochloride (1.08 g, 9.74 mmol, 2.1 eq.) were ground in a mortar to a homogenous powder. Under stirring, the mixture was melted without solvent at 190 °C for 5 h. After cooling to r.t., the solid was suspended in H₂O and the pH of the solution was set to neutral with an aqueous NaOH solution (2 M). The suspension was filtrated, washed with H₂O and diethyl ether/cyclohexane (1/1). The residue was dried in vacuo to give compound 15d as a yellowish amorphous solid (818 mg, 3.41 mmol, 72%). M.p. = 245–249 °C. TLC: Rf = 0.54 (EtOAc/MeOH, 9:1). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.36 (s, 1H, 1-Htriazolyl), 9.00 (d, J = 1.8 Hz, 1H, 2-Hpyridyl), 8.68 (d, J = 2.4 Hz, 1H, 6-Hpyridyl), 8.30 (t, J = 2.1 Hz, 1H, 4-Hpyridyl), 6.25 (s, 2H, NH₂). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 157.7 (5-Ctriazolyl), 154.9 (3-Ctriazolyl), 149.6 (6-Cpyridyl), 144.9 (2-Cpyridyl), 134.5 (4-Cpyridyl), 129.8 (3-Cpyridyl), 120.3 (5-Cpyridyl). IR (neat): ν [cm⁻¹] = 3310, 3105, 1639, 1593, 1558, 1477, 1096, 883, 690. HRMS (APCI) m/z = 239.9879 calculated for C₈H₇BrN₃⁺ [M+H]⁺, found: 239.9871.

3-(6-Methylpyridin-2-yl)-1H-1,2,4-triazol-5-amine (15e). 6-Methylpicolinic acid (14e, 2.00 g, 14.6 mmol, 1.0 eq.) and aminoguanidine sulfate (3.59 g, 14.6 mmol, 1.0 eq.) were ground in a mortar to a homogenous powder. Under stirring, the mixture was melted without solvent at 180 °C for 5 h. After cooling to r.t., the solid was suspended in H₂O and the pH of the solution was set to neutral with an aqueous NaOH solution (2 M). The suspension was filtrated, washed with H₂O and the residue was dried in vacuo to give compound 15e as a yellow solid (1.08 g, 6.13 mmol, 42%). M.p. = 275–276 °C. TLC: Rf = 0.35 (DCM/MeOH = 7:3). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 13.25 and 12.20 (bs, 1H, NH), 7.76–7.71 (m, 1H, 3-Hpyridyl), 7.71–7.68 (m, 1H, 4-Hpyridyl), 7.22 (s, 1H, 5-Hpyridyl), 6.00 and 5.38 (bs, 2H, NH₂). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 157.6 (1C, 6-Cpyridyl), 137.0 (1C, 3-Cpyridyl), 122.5 (1C, 5-Cpyridyl), 118.0 (1C, 4-Cpyridyl), 24.1 (1C, CH₃), signals for 2-Cpyridyl, 3-Ctriazolyl and 5-Ctriazolyl could not be seen, two tautomers exist in the ratio 15e/15e* = 65/35. IR (neat): ν [cm⁻¹] = 3094; 1667; 1597; 1516; 1327; 1184; 1088; 795; 741; 671. HRMS (APCI): m/z = 176.0931 calculated for C₈H₁₀N₃⁺ [M+H]⁺, found: 176.0933.

3-Cyclohexyl-1H-1,2,4-triazol-5-amine (15f). Aminoguanidine hydrochloride (1.51 g, 13.64 mmol, 2.0 eq.) was ground to a fine powder in a mortar and mixed with cyclohexanecarbonyl chloride (1.00 g, 6.82 mmol, 1.0 eq.) in a round bottom flask. The mixture was heated up to 220 °C upon stirring without any solvent. After 3 h, the mixture was cooled down to r.t. and suspended in H₂O (100 mL). The resulting suspension was neutralized with aqueous NaOH solution and stored at 4 °C overnight. The suspension was filtered, the remaining solid was washed with H₂O and then discarded. The filtrate was extracted with EtOAc (3 ×, equal amounts), the combined organic layers were washed with brine and dried over Na₂SO₄. The desired product was obtained as a colourless powder (359 mg, 2.16 mol; 32%) and used without further purification. M.p. = 195.5 °C. TLC: Rf = 0.43 (DCM/MeOH = 10/1). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.23* and 11.49 (s, 1H, -NH), 5.73 and 5.05* (s, 2H, -NH₂), 2.44 (br, 1H, -CH₂-), 1.84 (m, 2H, -CH₂-), 1.70 (m, 2H, -CH₂-), 1.62 (m, 1H, -CH₂-), 1.39 (m, 2H, -CH₂-), 1.29 (m, 2H, -CH₂-), 1.19 (m, 1H, -CH₂-). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 164.5 (1C, 3/-5-Ctriazolyl), 156.4 (1C, 3/-5-Ctriazolyl), 31.3 (2C, -CH₂-), 25.7 (1C, -CH₂-), 25.5 (2C, -CH₂-). Signal for -CH₂- from 1-Ccyclohexyl could not be seen, two tautomers exist in the ratio 15f/15f* = 2/1, signals of the minor tautomer 15f* are marked with *. IR (neat): ν [cm⁻¹] = 3468, 2931, 2855, 1628, 1574, 1535, 1439, 1061, 822, 756, 679. HRMS (APCI): m/z = 167.1291 calculated for C₈H₁₅N₄⁺, found: 167.1288.
3-Heptyl-1H-1,2,4-triazol-5-amine (15g). Aminoguanidine hydrochloride (1.36 g, 12.30 mmol, 2.0 eq.) was ground to a fine powder in a mortar, added into a round bottom flask and mixed with octanoyl chloride (1.00 g, 6.15 mmol, 1.0 eq.). The mixture was heated up to 220 °C upon stirring. After 3.5 h, the reaction mixture was cooled down to r.t. and suspended in H2O (50 mL). The suspension was neutralized using aqueous NaOH solution and stored at 4 °C overnight. The suspension was extracted with EtOAc (5 ×, equal amounts), the combined organic layers were washed with brine and dried over Na2SO4. The solvent was evaporated, the product was obtained as a yellow solid (324.4 mg, 2.31 mmol, 28%) and used without further purification. M.p. = 132.1 °C. TLC: Rf = 0.46 (DCM/MeOH = 10/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.20* and 11.52 (bs, 1H, -NH-), 5.69 and 5.11* (bs, 2H, -NH2), 2.38 (br, 2H, -CH2-), 1.56 (m, 2H, -CH2-), 1.25 (m, 8H, -(CH2)2-), 0.85 (t, J = 7.04 Hz, 3H, -CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 160.6 (1C, 3'/5'-C-triazolyl), 156.7 (1C, 3'/5'-C-triazolyl), 31.2 (1C, 3'/4/5-C, -CH2-), 28.6 (1C, 3'/4/5-C, -CH2-), 28.5 (1C, 3'/4/5-C, -CH2-), 27.6 (1C, 2-C, -CH2-), 22.1 (1C, 6-C, -CH2-), 14.0 (1C, 7-C, -CH3). Signal from 1-C (-CH2-) could not be seen. *— two tautomers exist in the ratio 15g/15g* = 2.34/1, the signals of the minor tautomer 15g* are marked with *.

IR (neat): ν [cm⁻¹] = 3418, 3325, 2924, 1620, 1535, 1404, 1065, 887, 756, 725, 640. HRMS (APCI): m/z = 183.1604 calculated for C9H18N4+ [M+H]⁺, found: 183.1603.

3-(Tert-butyl)-1H-1,2,4-triazol-5-amine (15h). Aminoguanidine hydrochloride (1.83 g, 16.59 mmol, 2.0 eq.) was ground to a fine powder in a mortar, added into a round bottom flask and mixed with trimethylacetyl chloride (1.00 g, 8.29 mmol, 1.0 eq.). The mixture was heated up to 200 °C upon stirring. After 3 h, the reaction mixture was cooled down to r.t. and the residue was suspended in H2O (50 mL) and stored at 4 °C overnight. The suspension was extracted with EtOAc (5 ×, equal amounts), the combined organic layers were washed with brine and dried over Na2SO4. The solvent was evaporated, the product was obtained as a yellow solid (324.4 mg, 2.31 mmol, 28%) and used without further purification. M.p. = 121.1 °C. TLC: Rf = 0.45 (DCM/MeOH = 10/1). 1H-NMR (400 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.46 (s, 1H, -NH-), 5.52 (s, 2H, -NH2), 1.20 (s, 9H, -(CH3)3). 13C-NMR (101 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.2 (1C, 3/5-C-triazolyl), 158.7 (1C, 3/5-C-triazolyl), 31.9 (1C, -(CH3)3), 29.2 (3C, -(CH3)3). IR (neat): ν [cm⁻¹] = 3476, 3066, 2959, 1639, 1520, 1520, 1412, 1204, 1107, 1030, 768. HRMS (APCI): m/z = 141.1135 calculated for C9H12N4+ [M+H]⁺, found: 141.1147.

3-(Naphthalen-2-yl)-1H-1,2,4-triazol-5-amine (15i). 2-Naphthoyl chloride (1.00g, 5.25 mmol, 1.0 eq.) and aminoguanidine hydrochloride (1.16 g, 10.49 mmol, 2.0 eq.) were ground together to a fine powder in a mortar and transferred into a round bottom flask. The mixture was heated up to 220 °C upon stirring. After 3.5 h the reaction mixture was cooled down to r.t., the residue was suspended in H2O (50 mL). The yellow suspension was neutralized using aqueous NaOH solution followed by extraction with EtOAc (5 ×, equal amounts). The combined organic layers were washed with brine and dried over Na2SO4, the crude product was purified via flash-column chromatography (DCM/MeOH = 10 → 9/1). The product was obtained as a colourless solid (324.1 mg, 1.54 mmol, 29%). M.p. = 214.7 °C. TLC: Rf = 0.38 (DCM/MeOH = 10/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.15 (s, 1H, -NH-), 8.40 (d, J = 1.6 Hz, 1H, 1-H-naphthyl), 8.05 (dd, J = 8.5, 1.7 Hz, 1H, 3-H-naphthyl), 7.99–7.95 (m, 1H, 8-H-naphthyl), 7.94–7.87 (m, 2H, 4-/5-H-naphthyl), 7.55–7.47 (m, 2H, 6-/7-H-naphthyl), 6.11 (s, 2H, -NH2). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 158.4 (1C, 3'-C-triazolyl), 157.4 (1C, 5'-C-triazolyl), 132.9 (1C, 8a-C-naphthyl), 132.9 (1C, 4a-C-naphthyl), 128.9 (1C, 2-C-naphthyl), 128.2 (1C, 8-C-naphthyl), 127.9 (1C, 4-C-naphthyl), 127.6 (1C, 5-C-naphthyl), 126.3 (1C, 6-/7-C-naphthyl), 126.1 (1C, 6-/7-C-naphthyl), 124.1 (1C, 1-C-naphthyl), 123.6 (1C, 3-C-naphthyl). IR (neat): ν [cm⁻¹] = 3410, 3318, 3055, 2750, 1620, 1525, 1504, 1404, 1088, 910, 825, 763. HRMS (APCI): m/z = 211.0978 calculated for C12H11N4+ [M+H]⁺, found: 211.1004.
3-(3,4-Dimethoxyphenyl)-1H-1,2,4-triazol-5-amine (15j). Aminoguanidine hydrochloride (1.21 g, 10.98 mmol, 2.0 eq.) was ground to a fine powder in a mortar, added into a round bottom flask and mixed with 3,2-dimethoxyphenylcarbonyl chloride (1.00 g, 5.49 mmol, 1.0 eq.). The mixture was heated up to 220 °C upon stirring. After 3 h, the reaction mixture was cooled down to r.t. and suspended in H2O (50 mL). The suspension was extracted with EtOAc (5 ×, equal amounts), the combined organic layers were washed with brine and dried over Na2SO4. The solvent was evaporated, and the crude product was purified via flash-column chromatography (DCM/MeOH = 1/0 → 94/6). The product was obtained as a colourless solid (145.3 mg, 0.66 mmol, 12%). M.p. = 209.3 °C. TLC: Rf = 0.36 (DCM/MeOH = 10/1). 1H-NMR (400 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.98* and 11.94 (s, 1H, -NH-), 7.43 (m, 2H, 2-/6-H(6r), 6.98 (m, 1H, 5-H(5r), 5.96 and 5.17* (s, 2H, -NH2), 3.78 (s, 3H, -OCH3), 3.77 (s, 3H, -OCH3). 13C-NMR (101 MHz, DMSO-d6, 299 K): δ (in ppm) = 185.1 (1C, 3-/5-C(triazolyl)), 157.4 (1C, 3-/5-C(triazolyl)), 149.1 (1C, 4-C(phenyl)), 148.6 (1C, 3-C(phenyl)), 125.3 (1C, 1-C(phenyl)), 117.9 (1C, 2-/6-C(phenyl)), 111.0 (1C, 5-C(phenyl)), 108.9 (1C, 2-/6-C(phenyl)), 55.5 (1C, (3-C(OCH3)), 55.3 (1C, (4-C(OCH3)). — Two tautomers exist, signals of the minor tautomer are marked with *. IR (neat): ν [cm⁻¹] = 3422, 3233, 3021, 2804, 1643, 1543, 1512, 1230, 1142, 1018, 860, 760, 625. HRMS (APCI): m/z = 221.1033 calculated for C10H13N2O2 [M+H]+, found: 221.1038.

3-(quinoline-2-yl)-1H-1,2,4-triazol-5-amine (15k). Quinaldic acid (1.00 g, 5.77 mmol, 1.0 eq.) and aminoguanidine hydrochloride (1.28 g, 11.55 mmol, 2.0 eq.) were ground together in a mortar. The resulting powder was transferred into a round bottom flask and heated up to 210 °C under continuous stirring without any solvent. After 3 h, the mixture was cooled down and suspended in H2O (100 mL) via sonication. The resulting suspension was neutralized with aqueous NaOH solution and stored at 4 °C for complete precipitation. The precipitate was filtered off, washed with H2O and EtOAc and dried in vacuo. The product was obtained as a colourless solid (962 mg, 4.55 mmol, 79%). M.p. >265 °C (decomp.). TLC: Rf = 0.45 (DCM/MeOH = 1/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 13.13–11.53 (bs, 1H, -NH), 8.40 (d, J = 8.6 Hz, 1H, 3-/4-H(quinoline), 8.09 (d, J = 8.6 Hz, 1H, 3-/4-H(quinoline), 8.04 (d, J = 8.4 Hz, 1H, 5-/8-H(quinoline), 7.98 (d, J = 7.4 Hz, 1H, 5-/8-H(quinoline), 7.78 (dd, J = 8.4, 6.8 Hz, 1H, 6-/7-H(quinoline), 7.60 (dd, J = 7.4, 6.8 Hz, 1H, 6-/7-H(quinoline), 6.17 (s, 2H, -NH2). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 147.3 (1C, 4a-/8a-C(quinoline), 136.4 (1C, 3-/4-C(quinoline), 129.9 (1C, 6-/7-C(quinoline), 128.9 (1C, 5-/8-C(quinoline), 127.9 (1C, 5-/8-C(quinoline), 127.5 (1C, 4a-/8a-C(quinoline), 126.6 (1C, 6-/7-C(quinoline), 119.2 (1C, 3-/4-C(quinoline); signals for 2-C(quinoline) and 3-/5-C(triazolyl) could not be seen. IR (neat): ν [cm⁻¹] = 3310, 2758, 2326, 1647, 1549, 1489, 1408, 1211, 1177, 1096, 945, 829, 760. HRMS (APCI): m/z = 212.0931 calculated for C11H10N2O2 [M+H]+, found: 212.0934.

3-(4-Fluorophenyl)-1H-1,2,4-triazol-5-amine (15l). Aminoguanidine hydrochloride (1.19 g, 10.75 mmol, 5.0 eq.) and KOH (724 mg, 12.90 mmol, 6.0 eq.) were dissolved in H2O (16 mL) and cooled down to 0 °C. To this, 4-fluorophenylcarbonyl chloride (341 mg, 2.15 mmol, 1.0 eq.) in THF (10 mL) was added dropwise (1 mL/h). The solution was stirred at 0 °C for 1 h. NaHCO3 (542 mg, 6.45 mmol, 3.0 eq.) was added and the reaction mixture was heated up to reflux (110 °C) for 3 h. The reaction mixture was cooled down to r.t. and neutralized with aqueous HCl. The resulting suspension was extracted with EtOAc (5 ×, equal amounts), the combined organic layers were washed with brine and dried over Na2SO4. The solvent was evaporated, the resulting colourless solid was purified via flash-column chromatography (DCM/MeOH = 1/0 → 9/1). The product was obtained as a colourless solid (221 mg, 1.24 mmol, 58%). M.p. 184.8 °C. TLC: Rf = 0.47 (DCM/MeOH = 10/1). 1H-NMR (400 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.06 (s, 1H, -NH-), 7.94–7.86 (m, 2H, 2-/6-H(phenyl), 7.29–7.16 (m, 2H, 3-/5-H(phenyl)), 6.04 (s, 2H, -NH2). 13C-NMR (101 MHz, DMSO-d6, 299 K) δ (in ppm) = 162.2 (d, JCF = 244.5 Hz 1C, 4-C(phenyl)), 157.4 (1C, 3-/5-C(triazolyl), 128.8 (1C, 1-C(phenyl)), 127.3 (d, JCF = 8.39 Hz, 2C, 2-/6-C(phenyl)), 115.3 (d, JCF = 21.36 Hz,
2C, 3/-5-C-phenyl). Second 3/-5-C-triazolyl could not be seen. IR (neat): ν [cm⁻¹] = 3410, 3321, 3017, 2854, 1608, 1539, 1479, 1396, 1223, 1083, 984, 844. HRMS (APCI): m/z = 179.0728 calculated for CsH₈FN₂⁺ [M+H]⁺, found: 179.0726.

3-(4-Nitrophenyl)-IH-1,2,4-triazol-5-amine (15m). Aminoguanidine hydrochloride (1.19 g, 10.8 mmol, 5.0 eq.) and KOH (724 mg, 12.9 mmol, 6.0 eq.) were dissolved in H₂O and cooled down to 0 °C. To this, 4-nitrophenylcarbonyl chloride (399 mg, 2.15 mmol, 1.0 eq.) in THF (2 mL) was added dropwise (1 mL/h). The reaction mixture was stirred at 0 °C for 1 h. NaHCO₃ (542 mg, 6.45 mmol, 3.0 eq.) was added to the solution, the mixture was heated up to reflux for 4.5 h. After cooling down to r.t., the reaction mixture was neutralized with aqueous HCl and extracted with EtOAc (5 ×, equal amounts). The combined organic layers were washed with brine and dried over Na₂SO₄. The solvent was evaporated, the resulting brown crude product was purified by flash-column chromatography (DCM/MeOH = 1/0 → 9/1). The product was obtained as an orange solid (367 mg, 1.79 mmol, 83%). M.p. >265 °C (decomp.). TLC: Rᵣ = 0.47 (DCM/MeOH = 10/1). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.45 (s, 1H, -NH-), 8.27 (td, J = 9.0, 2.1 Hz, 2H, 3/-5-H phenyl), 8.11 (dd, J = 9.0, 2.1 Hz, 2H, 2/-6-H phenyl), 6.24 (s, 2H, -NH2). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 157.8 (1C, 5'-C-triazolyl), 156.8 (1C, 3'-C-triazolyl), 147.0 (1C, 4-C phenyl), 138.4 (1C, 1-C phenyl), 126.1 (2C, 3/-5-C phenyl), 124.0 (2C, 2/-6-C phenyl). IR (neat): ν [cm⁻¹] = 3399, 3163, 1647, 1608, 1512, 1335, 1096, 856, 714, 632. HRMS (APCI): m/z = 206.0673 calculated for CsH₈N₂O₂⁺ [M+H]⁺, found: 206.0692.

3-(4-Methoxyphenyl)-IH-1,2,4-triazol-5-amine (15n). Aminoguanidine hydrochloride (1.19 g, 10.75 mmol, 5.0 eq.) and KOH (724 mg, 12.90 mmol, 6.0 eq.) were dissolved in H₂O (16 mL) and cooled down to 0 °C. To this, 4-methoxynylcarbonyl chloride (367 mg, 2.15 mmol, 1.0 eq.) in THF (1 mL) was added dropwise (1 mL/h). The reaction mixture was stirred at 0 °C for 1 h. NaHCO₃ (542 mg, 6.45 mmol, 3.0 eq.) was added to the solution, the mixture was heated up to reflux for 2 h. The reaction mixture was cooled down to r.t. and neutralized with aqueous HCl solution, followed by extraction using EtOAc (4 ×, equal amounts). The combined organic layers were washed with brine and dried over Na₂SO₄, the crude product was purified via flash-column chromatography (DCM/MeOH = 1/0 → 9/1). The product was obtained as a colourless solid (141 mg, 0.74 mmol, 34%). M.p. = 226 °C. TLC: Rᵣ = 0.47 (DCM/MeOH = 10/1). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.98* and 11.90 (s, 1H, -NH-), 7.83–7.77 (m, 2H, 2/-6-H phenyl), 7.03–6.92 (m, 2H, 3/-5-H phenyl), 5.99 and 5.22* (s, 2H, -NH2), 3.77 (s, 3H, OCH₃). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K) δ (in ppm) = 159.3 (1C, 4-C phenyl), 158.3 (1C, 3'-C triazolyl), 157.2 (1C, 5'-C triazolyl), 126.7 (2C, 2/-6-C phenyl), 125.1 (1C, 1-C phenyl), 113.8 (2C, 3/-5-C phenyl), 55.1 (1C, -OCH3). *—two tautomers exist in the ratio 15n/15n⁺ = 6.7/1, signals of the minor tautomers 15n⁺ are marked with *. IR (neat): ν [cm⁻¹] = 3441, 3329, 3051, 2854, 1612, 1539, 1454, 1392, 1246, 1018, 826, 756, 687. HRMS (APCI): m/z = 191.0927 calculated for CsH₁₁N₂O⁺ [M+H]⁺, found: 191.0944.

3-Benzyl-IH-1,2,4-triazol-5-amine (15o). Aminoguanidine hydrochloride (1.19 g, 10.8 mmol, 5.0 eq.) and KOH (724 mg, 12.9 mmol, 6.0 eq.) were dissolved in H₂O (16 mL) and cooled down to 0 °C. To this, 2-phenylacetyl chloride (332 mg, 2.15 mmol, 1.0 eq.) in THF (1 mL) was added dropwise (1 mL/h). The reaction mixture was stirred for 1 h at 0 °C. NaHCO₃ (542 mg, 6.45 mmol, 3.0 eq.) was added and the reaction mixture was heated up to reflux for 2 h. After cooling down to r.t. the reaction mixture was neutralized using aqueous HCl followed by extraction with EtOAc (5 ×, equal amounts). The combined organic layers were washed with brine and dried over Na₂SO₄, the solvent was evaporated. The crude product was purified via flash-column chromatography (DCM/MeOH = 1/0 → 94/6). The product was obtained as a colourless solid (116 mg, 0.67 mmol, 31%). M.p. = 166.5 °C. TLC: Rᵣ = 0.36 (DCM/MeOH = 10/1). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 11.86 (s, 1H, -NH-), 7.28–7.23 (m, 4H, 2/-3/-5/-6-H benzyl), 7.20–7.16 (m, 1H,
4-H-benzyl), 5.64 (s, 2H, -NH₂), 3.73 (s, 2H, -CH₂-). 13C-NMR (151 MHz, DMSO-d₆, 299 K) δ (in ppm) = 158.4 (1C, 3’/5’-C-triazolyl), 138.8 (1C, 1-C-benzyl), 128.7 (2C, 2-/3-/5/6-C-benzyl), 128.1 (2C, 2-/3-/5/6-C-benzyl), 126.0 (1C, 4-C-benzyl), 34.0 (1C, -CH₂-). Second signal for 3’/5’-C-triazolyl could not be seen. IR (neat): ν [cm⁻¹] = 3429, 3028, 2720, 1628, 1547, 1466, 1385, 1065, 1022, 806, 690. HRMS (APCI): m/z = 175.0978 calculated for C₉H₁₇N₄⁺ [M+H]⁺, found: 175.0991.

3-(Naphthalen-1-yl)-1H-1,2,4-triazol-5-amine (15p). Aminoguanidine hydrochloride (1.19 g, 10.8 mmol, 5.0 eq.) and KOH (724 mg, 12.9 mmol, 6.0 eq.) were dissolved in H₂O (16 mL) and cooled down to 0 °C. To this, 1-naphthyl chloride (410 mg, 2.15 mmol, 1.0 eq.) in THF (1 mL) was added dropwise (1 mL/h). The reaction mixture was stirred at 0 °C for 1 h. NaHCO₃ (542 mg, 6.45 mmol, 3.0 eq.) was added and the reaction mixture was heated up to reflux (110 °C) for 2 h. After cooling down, the reaction mixture was neutralized with aqueous HCl and extracted with EtOAc (5 ×, equal amounts). The combined organic layers were washed with brine and dried over Na₂SO₄. The solvent was evaporated, the residue was purified via flash-column chromatography (DCM/MeOH = 1/0 → 9/1). The product was obtained as a colourless solid (55.2 mg, 0.26 mmol, 12%). M.p. = 229 °C. TLC: Rf = 0.49 (DCM/MeOH = 10/1). ¹H-NMR (400 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.29 (s, 1H, -NH⁻), 9.29–9.13 (m, 1H, 8-H-naphthyl), 8.06 (d, J = 7.2 Hz, 1H, 2-H-naphthyl), 7.98–7.90 (m, 2H, 4-/5-H-naphthyl), 7.59–7.46 (m, 3H, 3-/6-/7-H-naphthyl), 6.08 (s, 1H, -NH₂). 13C-NMR (101 MHz, DMSO-d₆, 299 K): δ (in ppm) = 158.8 (1C, 3’/5’-C-triazolyl), 157.3 (1C, 3’/5’-C-triazolyl), 133.6 (1C, 4a-C-naphthyl), 130.2 (1C, 8a-C-naphthyl), 128.7 (1C, 4-C-naphthyl), 128.2 (1C, 5-C-naphthyl), 126.8 (1C, 8-C-naphthyl), 126.7 (1C, 2-C-naphthyl), 126.2 (1C, 3-/6-/7-C-naphthyl), 125.7 (1C, 3-/6-/7-C-naphthyl), 125.3 (1C, 3-/6-/7-C-naphthyl). IR (neat): ν [cm⁻¹] = 3449, 3310, 3048, 2720, 1631, 1535, 1423, 1369, 1096, 949, 871, 771. HRMS (APCI): m/z = 211.0978 calculated for C₁₂H₁₁N₄⁺ [M+H]⁺, found: 211.0971.

3-(Cyclohexylmethyl)-1H-1,2,4-triazol-5-amine (15q). Aminoguanidine hydrochloride (272 mg, 2.00 mmol, 1.0 eq.) was suspended in pyridine (5 mL) and cooled down to 0 °C. To this, cyclohexylacetyl chloride (321 mg, 2.00 mmol, 1.0 eq.) in THF (1 mL) was added dropwise (2 mL/h) and the reaction mixture was stirred at r.t. overnight. The solvent was removed in vacuo, the residue was suspended in EtOH (12 mL), NaHCO₃ (504 mg, 6.00 mmol, 3.0 eq.) was added and the reaction mixture was heated up to 90 °C for 4 h. The solvent was evaporated, the residue was suspended in H₂O and then neutralized using aqueous HCl. The mixture was extracted with EtOAc (5 ×, equal amounts), the combined organic layers were washed with brine and dried over Na₂SO₄. The solvent was evaporated, the resulting crude product was purified via flash-column chromatography (DCM/MeOH = 1/0 → 9/1). The product was obtained as a colourless solid (35.5 mg, 0.20 mmol, 10%). M.p. = 180 °C. TLC: Rf = 0.36 (DCM/MeOH = 10/1). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.23* and 11.49 (s, 1H, -NH⁻), 5.68 and 5.06* (s, 2H, -NH₂), 1.66 1.55 (m, 7H, -CH-/-(CH₂)₃-), 1.21–1.08 (m, 4H, -((CH₂)₃)), 0.94–0.86 (m, 2H, -CH₂-). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K) δ (in ppm) = 159.5 (1C, 3’/5’-C-triazolyl), 156.4 (1C, 3’/5’-C-triazolyl), 36.5 (1C, -CH₃), 32.6 (2C, -((CH₂)₂)), 26.0 (1C, -CH₂⁻), 25.7 (3C, -((CH₂)₃)). IR (neat): ν [cm⁻¹] = 3414, 3329, 2920, 2846, 1632, 1551, 1466, 1389, 1350, 1091, 1064, 799, 656. HRMS (APCI): m/z = 181.1448 calculated for C₁₂H₁₂N₄⁺ [M+H]⁺, found: 181.1443.

3-Undecyl-1H-1,2,4-triazol-5-amine (15r). Aminoguanidine bicarbonate (350 mg, 2.57 mmol, 1.3 eq.) was suspended in pyridine (5 mL) and cooled down to 0 °C. To this, dodecanoyl chloride (438 mg, 2.00 mmol, 1.0 eq.) in THF (0.5 mL) was added dropwise (5 min). The reaction mixture was stirred at 0 °C for 30 min and at r.t. overnight. The solvent then was evaporated, the residue was suspended in a mixture of H₂O (7 mL) and MeOH (3 mL) and NaHCO₃ (500 mg, 5.95 mmol, 3.0 eq.) was added. The reaction mixture was heated up to 100°C for 4 h upon stirring. After cooling down to 0 °C again, the mixture was neutralized using aqueous HCl and extracted with EtOAc (5 ×,
equal amounts). The combined organic phases were washed with brine and dried over Na₂SO₄, the solvent was evaporated. The crude product was purified via flash-column chromatography (DCM/MeOH = 96/4 → 93/7), the product was obtained as a colourless solid (145 mg, 0.61 mmol, 31%). M.p. = 135.5 °C. TLC: Rf = 0.38 (DCM/MeOH = 10/1). 1H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.20* and 11.49 (s, 1H, -NH-), 5.65 and 5.31* (s, 2H, -NH₂), 1.60–1.51 (m, 2H, -CH₂-), 1.29–1.20 (m, 18H, -(CH₂)₉), 0.85 (t, J = 7.0 Hz, 3H, -CH₃). 13C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 160.5 (3'-/5'-C₃riazolyl), 156.8 (3'-/5'-C₃riazolyl), 31.1 (1C, -CH₂-), 29.9 (1C, -CH₂-), 29.0 (1C, -CH₂-), 28.8 (1C, -CH₂-), 28.7 (1C, -CH₂-), 28.7 (1C, -CH₂-), 27.6 (1C, -CH₂-), 22.1 (1C, -CH₃), 14.0 (1C, -CH₃). One -CH₂- could not be seen, *— two tautomers exist in the ratio 15r/15r* = 2/1, signals of the minor tautomer 15r* are marked with *. IR (neat): ν [cm⁻¹] = 3441, 2920, 2847, 1620, 1582, 1546, 1466, 1400, 1061, 802, 725. HRMS (APCI): m/z = 239.2230 calculated for C₁₃H₁₇N₄⁺ [M+H]⁺, found: 239.2286.

(E)-3-Styryl-1H-1,2,4-triazol-5-amine (15s). Aminoguanidine bicarbonate (544 mg, 4.00 mmol, 2.0 eq.) was suspended in pyridine (6 mL) and cooled down to 0 °C. To this, cinnamoyl chloride (333 mg, 2.00 mmol, 1.0 eq.) in THF (1 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and at r.t. for 48 h. The solvent was evaporated, the residue suspended in a mixture of H₂O and MeOH (1/1, 10 mL) and NaHCO₃ (500 mg, 5.95 mmol, 3.0 eq.) was added. The reaction mixture was heated up to 105 °C for 4 h upon stirring. After cooling down to 0 °C again, the mixture was neutralized using aqueous HCl and extracted with EtOAc (5 ×, equal amounts). The combined organic layers were washed with brine and dried over Na₂SO₄, the solvent was evaporated. The resulting crude product was purified via flash-column chromatography (DCM/MeOH = 1/0% → 95/5). The product was obtained as a colourless solid (102 mg, 0.55 mmol, 28%). M.p. = 207.5 °C. TLC: Rf = 0.38 (DCM/MeOH = 10/1). 1H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.04 (br, 1H, -NH-), 7.57–7.55 (m, 2H, 2-/6-Hₐpyphenyl), 7.37–7.35 (t, J = 7.7 Hz, 2H, 3-/5-Hₐpyphenyl), 7.29–7.25 (m, 2H, 4-Hₐphenyl /1-Ch olephine), 6.90 (d, J = 16.2 Hz, 1H, 2-Ch olephine), 5.91 (s, 1.12H, -NH₂). 13C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 158.0 (1C, 3-/5-C₃riazolyl), 157.4 (1C, 3-/5-C₃riazolyl), 136.5 (1C, 1-Cphenyl), 130.9 (1C, 1'-C olephine), 128.2 (2C, 3-/5-C₃pyphenyl), 127.9 (1C, 4-Cphenyl), 126.6 (2C, 2-/6-Cphenyl), 119.4 (1C, 2'-C olephine), two tautomers exist in the ratio 15s/15s* = 1/4/1, signals of the major tautomer are given. IR (neat): ν [cm⁻¹] = 3410, 3055, 1647, 1528, 1423, 1107, 1069, 960, 821, 756, 682. HRMS (APCI): m/z = 187.0978 calculated for C₁₃H₁₁N₄⁺ [M+H]⁺, found: 187.1010.

3-(Isoquinolin-1-yl)-1H-1,2,4-triazol-5-amine (15u). Compound 18u (521 mg, 2.78 mmol, 1.0 eq.) was suspended in a mixture of EtOH and H₂O (1/2, 15 mL), S-methylisothiouronium sulfate (3.87 g, 13.92 mmol, 5.0 eq.) was added. The reaction mixture was heated up to 105 °C upon stirring. After 24 h, KOH (7 g) was added as a solid and stirring continued at 105 °C for 3 h. The reaction mixture was cooled down to 0 °C and neutralized with aqueous HCl. The suspension was extracted with EtOAc (5 ×, equal amounts), the combined organic layers were washed with brine and dried over Na₂SO₄. The product was obtained as a yellow solid (97 mg, 0.46 mmol, 17%) after recrystallization from MeOH. M.p. >255 °C (decomp.). TLC: Rf = 0.11 (DCM/MeOH = 10/1). 1H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 13.60* and 12.42 (s, 1H, -NH-), 8.60–8.52 (m, 1H, CHisoquinoline), 8.10–8.04 (m, 1H, CHisoquinoline), 8.03–7.98 (m, 1H, CHisoquinoline), 7.94–7.83 (m, 1H, CHisoquinoline), 7.82–7.77 (m, 1H, CHisoquinoline), 7.74–7.65 (m, 1H, CHisoquinoline), 6.15 and 5.50* (s, 1H, -NH₂). 13C-NMR (151 MHz, DMSO-d₆, 299 K) δ (in ppm) = 158.9 (1C, C₃riazolyl), 156.9 (1C, C₃riazolyl), 152.0 (1C, Cisoquinoline), 141.8 (1C, Cisoquinoline), 136.4 (1C, Cisoquinoline), 130.8 (1C, Cisoquinoline), 130.4 (1C, Cisoquinoline), 128.3 (1C, Cisoquinoline), 127.1 (1C, Cisoquinoline), 127.0 (1C, Cisoquinoline), 122.2 (1C, Cisoquinoline). *— two tautomers exist in the ratio 15u/15u* = 1/1, signals of the second tautomer 15u* are marked with *. IR (neat): ν [cm⁻¹] = 3348, 3048, 2742, 1639, 1558, 1423, 1319, 1057, 968, 872, 826, 664. HRMS (APCI): m/z = 212.0936 calculated for C₁₁H₁₀N₄⁺ [M+H]⁺, found: 212.0942.
3-(Benzo[b]thiophene-2-yl)-1H-1,2,4-triazole-5-amine (15v). Benzo[b]thiophene-2-carboxyhydrazide (18v, 500 mg, 2.60 mmol, 1.0 eq.) was dissolved in aqueous EtOH (20%, 20 mL) and S-methylisothiouronium sulfate (362 mg, 1.30 mmol, 0.5 eq.) was added. The suspension was stirred under reflux for 24 h, then a second portion of S-methylisothiouronium sulfate (362 mg, 1.30 mmol, 0.5 eq.) was added. After another 24 h additional S-methylisothiouronium sulfate (362 mg, 1.30 mmol, 0.5 eq.) was added a third time. After heating for 5 days in total the reaction mixture was allowed to cool to r.t. KOH (10 g) was added to the mixture and heated under reflux for 3 h. The mixture was neutralized with H$_2$SO$_4$ (conc.), extracted with EtOAc, dried over Na$_2$SO$_4$, and the solvent was removed in vacuo. The crude product was purified by flash column chromatography (DCM/MeOH = 95/5 → 8/2) to yield product 15v as a colourless solid (134 mg, 0.62 mmol, 24%). M.p. = 253 °C (decomp.). TLC: R$_f$ = 0.65 (DCM/MeOH = 85/15). $^1$H-NMR (400 MHz, DMSO-d$_6$, 299 K): δ (in ppm) = 12.20 (s, 1H, NH), 7.98–7.89 (m, 1H, 7-H$_{\text{benzo}[b]_{\text{thiophenyl}}$), 7.89–7.81 (m, 1H, 4-H$_{\text{benzo}[b]_{\text{thiophenyl}}$), 7.71 (s, 1H, 3-H$_{\text{benzo}[b]_{\text{thiophenyl}}$), 7.43–7.30 (m, 2H, 5-/6-H$_{\text{benzo}[b]_{\text{thiophenyl}}$), 6.20 (s, 2H, NH$_2$). $^{13}$C-NMR (101 MHz, DMSO-d$_6$, 299 K): δ (in ppm) = 157.4 (1C, 5-C$_{\text{triazoly}}$), 154.8 (1C, 3-C$_{\text{triazoly}}$), 139.7 (1C, 7a-C$_{\text{benzo}[b]_{\text{thiophenyl}}$), 138.7 (1C, 3a-C$_{\text{benzo}[b]_{\text{thiophenyl}}$), 135.7 (1C, 2-C$_{\text{benzo}[b]_{\text{thiophenyl}}$), 124.7 (1C, 6-C$_{\text{benzo}[b]_{\text{thiophenyl}}$), 124.5 (1C, 5-C$_{\text{benzo}[b]_{\text{thiophenyl}}$), 123.8 (1C, 4-C$_{\text{benzo}[b]_{\text{thiophenyl}}$), 122.4 (1C, 7-C$_{\text{benzo}[b]_{\text{thiophenyl}}$), 120.6 (1C, 3-C$_{\text{benzo}[b]_{\text{thiophenyl}}$). IR (neat): ν [cm$^{-1}$] = 1392, 1577, 1643, 2981, 3059, 3456. HRMS (APCI): m/z = 217.0542 calculated for C$_7$H$_9$N$_3$S$^+$ [M+H$^+$], found 217.0478.

3-(5-Chlorothiophene-2-yl)-1H-1,2,4-triazole-5-amine (15w). 5-Chlorothiophene-2-carboxyhydrazide (18w, 650 mg, 3.68 mmol, 1.0 eq.) was dissolved in EtOH (20%, 20 mL) and S-methylisothiouronium sulfate (1.02 g, 3.68 mmol, 1.0 eq.) was added. The mixture was stirred under reflux for 24 h, then additional S-methylisothiouronium sulfate (1.02 g, 3.68 mmol, 1.0 eq.) was added. After another 24 h additional S-methylisothiouronium sulfate (1.02 g, 3.68 mmol, 1.0 eq.) was added a third time. After heating for 5 days in total the reaction mixture was allowed to cool to r.t. KOH (12 g) was added and the reaction mixture was heated under reflux for 2 h. The mixture was neutralized with H$_2$SO$_4$ (conc.), extracted with EtOAc, dried over Na$_2$SO$_4$ and the solvent was removed in vacuo. The crude product was purified by flash column chromatography (DCM/MeOH = 95/5 → 8/2) to yield product 15w as a colourless solid (236 mg, 1.17 mmol, 32%). M.p. = 235 °C (decomp.). TLC: R$_f$ = 0.65 (DCM/MeOH = 85/15). $^1$H-NMR (400 MHz, DMSO-d$_6$, 299 K): δ (in ppm) = 12.10 (s, 1H, NH), 7.22 (d, J = 3.9 Hz, 1H, 3-H$_{\text{S-chlorothiophenyl}}$), 7.08 (d, J = 3.9 Hz, 1H, 4-H$_{\text{S-chlorothiophenyl}}$), 6.15 (brs, 1H, NH$_2$). $^{13}$C-NMR (101 MHz, DMSO-d$_6$, 299 K): δ (in ppm) = 157.3 (1C, 5-C$_{\text{triazoly}}$), 153.9 (1C, 3-C$_{\text{triazoly}}$), 134.6 (1C, 5-C$_{\text{S-chlorothiophenyl}}$), 127.5 (1C, 4-C$_{\text{S-chlorothiophenyl}}$), 127.3 (1C, 2-C$_{\text{S-chlorothiophenyl}}$), 123.7 (1C, 3-C$_{\text{S-chlorothiophenyl}}$). IR (neat): ν [cm$^{-1}$] = 1312, 1587, 3397, 3461. HRMS (APCI): m/z = 200.9996 calculated for C$_9$H$_8$ClN$_3$S$^+$ [M+H$^+$], found 200.9996.

Ethyl isoquinoline-1-carboxylate (17u). Isoquinoline-1-carboxylic acid (1.00 g, 5.77 mmol, 1.0 eq.) was suspended in EtOH (12 mL) and thionyl chloride (3.4 mL, 46.82 mmol, 8.1 eq.) was added dropwise at r.t. over 15 min. The reaction mixture was heated up to 90 °C for 8 h. After cooling down to r.t., the excess thionyl chloride and the solvent were distilled off, the residue was neutralized using saturated aqueous NaHCO$_3$ solution. The solution was extracted with EtOAc (5 ×, equal amounts), the combined organic layers were washed with H$_2$O and brine and dried over Na$_2$SO$_4$. The solvent was evaporated, the product was obtained as a yellow oil (777 mg, 3.86 mmol, 67%) and was used without further purification in the next step. TLC: R$_f$ = 0.29 (cyclohexane/EtOAc = 4/1). $^1$H-NMR (600 MHz, DMSO-d$_6$, 299 K): δ (in ppm) = 8.59 (d, J = 5.6 Hz, 1H, 3-H$_{\text{isoquinoline}}$), 8.42 (d, J = 8.5 Hz, 1H, 8-H$_{\text{isoquinoline}}$), 8.09 (d, J = 8.3 Hz, 1H, 5-H$_{\text{isoquinoline}}$), 8.07 (d, J = 5.6 Hz, 1H, 4-H$_{\text{isoquinoline}}$), 7.86 (dd, J = 8.3, 6.8 Hz, 1H, 6-H$_{\text{isoquinoline}}$), 7.78 (dd, J = 8.5, 6.9 Hz, 1H, 7-H$_{\text{isoquinoline}}$), 4.48 (q, J = 7.1 Hz, 2H, -OCH$_2$), 1.39 (t, J = 7.1 Hz, 3H, -
Isoquinoline-1-carbohydrazide (18u). Compound 17u (766 mg, 3.81 mmol, 1.0 eq.) was dissolved in EtOH (3 mL) and hydrazine (3.36 mL, 68.52 mmol, 18.0 eq.) was added. The solution was heated up to 90 °C for 2 h upon stirring. The reaction was cooled down to r.t. and stored at 4 °C overnight to precipitate the product. The product was filtered off and washed with H2O and EtOH to give colourless needles (379 mg). After evaporation of the filtrate and recrystallisation of the residue, additional product was obtained (+152 mg; overall: 531 mg, 2.84 mmol, 75%). M.p. = 133 °C. TLC: Rf = 0.75 (DCM/MeOH = 20/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.91 (s, 1H, -NH), 8.73 (d, J = 8.5 Hz, 1H, 8-Hisoquinoline), 8.51 (d, J = 5.6 Hz, 1H, 3-Hisoquinoline), 8.04 (d, J = 8.3 Hz, 1H, 5-Hisoquinoline), 7.97 (d, J = 5.6 Hz, 1H, 4-Hisoquinoline), 7.82 (dd, J = 8.3, 6.8 Hz, 1H, 6-Hisoquinoline), 7.72 (dd, J = 8.5, 6.8 Hz, 1H, 7-Hisoquinoline), 4.67 (s, 2H, -NH2). 13C-NMR (151 MHz, DMSO-d6, 299 K) δ (in ppm) = 165.3 (1C; C=O), 151.8 (1C, 1-Cisoquinoline), 141.1 (1C, 3-Cisoquinoline), 136.3 (1C, 4a-Cisoquinoline), 130.7 (1C, 6-Cisoquinoline), 128.2 (1C, 7-Cisoquinoline), 127.1 (1C; 5-Cisoquinoline), 126.3 (1C, 8-Cisoquinoline), 125.4 (1C, 8a-Cisoquinoline), 122.8 (1C, 4-Cisoquinoline). IR (neat): ν [cm⁻¹] = 3383, 3043, 1659, 1620, 1582, 1474, 1377, 1292, 1034, 945, 826, 737. HRMS (APCI): m/z = 188.0818 calculated for C10H16N3O [M+H]⁺, found: 188.0828.

Benzo[b]thiophene-2-carbohydrazide (18v). Ethyl benzo[b]thiophene-2-carboxylate (17v, 950 mg, 4.61 mmol, 1.0 eq.) was dissolved in EtOH (dry, 3 mL) and hydrazine monohydrate (3.39 mL, 69.11 mmol, 15 eq.) was added. The mixture was stirred under reflux for 90 min and then cooled to r.t. The precipitate was filtered off and washed with cold H2O (20 mL) and cold EtOH (20 mL). The product 18v was obtained as a colourless solid (775 mg, 4.03 mmol, 87%). M.p. = 187 °C (decomp.). TLC: Rf = 0.69 (DCM/MeOH = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 10.03 (s, 1H, NH), 8.02–8.00 (m, 2H, 3-/7-Hbenzo[b]thiophenyl), 7.93–7.89 (m, 1H, 4-Hbenzo[b]thiophenyl), 7.47–7.41 (m, 2H, 5-/6-Hbenzo[b]thiophenyl), 4.56 (brs, 2H, NH2). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 161.4 (1C, C=O), 139.9 (1C, 7a-Cbenzo[b]thiophenyl), 139.2 (1C, 3a-Cbenzo[b]thiophenyl), 138.5 (1C, 2-Cbenzo[b]thiophenyl), 126.0 (1C, 6-Cbenzo[b]thiophenyl), 125.1 (1C, 4-Cbenzo[b]thiophenyl), 124.9 (1C, 5-Cbenzo[b]thiophenyl), 124.1 (1C, 3-Cbenzo[b]thiophenyl), 122.8 (1C, 7-Cbenzo[b]thiophenyl). IR (neat): ν [cm⁻¹] = 1519, 1616, 3001, 3190, 3302. HRMS (APCI): m/z = 193.0430 calculated for C16H13N3O2 [M+H]⁺, found 193.0433.

3-(Pyridin-2-yl)-N-benzyl-1H-1,2,4-triazol-5-amine (19a). 3-(Pyridine-2-yl)-1H-1,2,4-triazol-5-amine (15a, 150 mg, 930 µmol, 1.0 eq.) was dissolved in THF (dry, 2 mL) and toluene (dry, 10 mL). Benzaldehyde (198 mg, 515 µmol, 2.0 eq.) was added dropwise at r.t.. The mixture was stirred under reflux for 18 h. The solvent was removed in vacuo and the residue was dissolved in DCM (dry, 20 mL), NaBH(OAc)₃ (201 mg, 946 µmol, 5.0 eq.) was added. The mixture was heated to reflux for 18 h. The reaction mixture was poured into H₂O (20 mL), extracted with DCM and the organic solvent was removed in vacuo. The crude product was purified by flash column chromatography (DCM/MeOH = 1/0 → 95/5) to obtain product 19a as a colourless solid (61.0 mg, 244 µmol, 26%). M.p. = 84 °C (decomp.). TLC: Rf = 0.40 (DCM/MeOH = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.70 (d, J = 4.7 Hz, 1H, 6-Hpyridinyl), 8.05 (d, J = 7.8 Hz, 1H, 3-Hpyridinyl), 8.03–7.97 (m, 1H, 4-Hpyridinyl), 7.54 (dd, J = 8.1, 4.4 Hz, 1H, 5-Hpyridinyl), 7.34–7.25 (m, 4H, 2-/3-/5-/6-Hbenzyl), 7.23–7.18 (m, 1H, 4-Hbenzyl), 5.00 (s, 2H, CH₂). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 160.1 (1C, 5-C triazolyl), 153.5 (1C, 3-C triazolyl), 149.6 (1C, 6-C pyridinyl), 145.5 (1C, 2-
C<sub>pyridinyl</sub>), 137.9 (1C, 4-C<sub>pyridinyl</sub>), 137.7 (1C, 1-C<sub>benzyl</sub>), 128.2 (2C, 3-/5-C<sub>benzyl</sub>), 127.3 (2C, 2-/6-C<sub>benzyl</sub>), 126.9 (1C, 4-C<sub>benzyl</sub>), 125.4 (1C, 5-C<sub>pyridinyl</sub>), 121.4 (1C, 3-C<sub>pyridinyl</sub>), 49.6 (1C, CH<sub>3</sub>). IR (neat): δ [cm<sup>-1</sup>] = 1396, 1504, 1593, 1643, 3005, 3089, 3132. HRMS (APCI): m/z = 252.1244 calculated for C<sub>14</sub>H<sub>14</sub>N<sub>5</sub><sup>+</sup> [M+H]<sup>+</sup>, found 252.1152.

3-(Benzo[b]thiophen-2-yl)-N-benzyl-1H-1,2,4-triazol-5-amine (19v). Triazole amine 15v (100 mg, 462 μmol, 1.00 eq.) was dissolved in THF (dry, 2 mL) and toluene (dry, 10 mL). Freshly distilled benzaldehyde (98.2 mg, 515 μmol, 2.00 eq.) was added dropwise at r.t. The mixture was stirred under reflux for 18 h. The solvent was removed in vacuo and the residue was dissolved in DCM (dry, 20 mL), NaBH(OAc)<sub>3</sub> (201 mg, 946 μmol, 5.00 eq.) was added. The mixture was heated to reflux for 2 h and then stirred for 16 h. The reaction mixture was poured into H<sub>2</sub>O (20 mL), extracted with DCM and the solvent was removed in vacuo. The crude product was purified by flash column chromatography (DCM/MeOH = 1/0 → 95/5) to obtain product 19v as a colourless solid (33.0 mg, 108 μmol, 23%). M.p. = 195 °C (decomp.). TLC: R<sub>f</sub> = 0.48 (DCM/MeOH = 95/5). <sup>1</sup>H-NMR (600 MHz, DMSO-d<sub>6</sub>, 299 K): δ (in ppm) = 12.44 (s, 1H, NH), 7.93 (d, J = 7.7 Hz, 1H, 7-H<sub>benzol[b]phenyl</sub>), 7.86 (dd, J = 7.9, 1.6 Hz, 1H, 4-H<sub>benzol[b]phenyl</sub>), 7.74 (s, 1H, 3-H<sub>benzol[b]phenyl</sub>), 7.40–7.28 (m, 7H, 5-/6-H<sub>benzol[b]phenyl</sub>, 2-/3-/5-/6-H<sub>benzyl</sub>, NHCH<sub>2</sub>), 7.28–7.22 (m, 1H, 4-H<sub>benzyl</sub>), 4.43 (d, J = 6.4 Hz, 2H, NHCH<sub>2</sub>). <sup>13</sup>C-NMR (151 MHz, DMSO-d<sub>6</sub>, 299 K): δ (in ppm) = 158.0 (1C, 5-C<sub>triazolyl</sub>), 154.9 (1C, 3-C<sub>triazolyl</sub>), 139.7 (2C, 3a-C<sub>benzol[b]phenyl</sub>, 1-C<sub>benzyl</sub>), 138.8 (1C, 7a-C<sub>benzol[b]phenyl</sub>), 135.4 (1C, 2-C<sub>benzol[b]phenyl</sub>), 128.3 (2C, 3-/5-C<sub>benzyl</sub>), 127.2 (2C, 2-/6-C<sub>benzyl</sub>), 126.9 (1C, 4-C<sub>benzyl</sub>), 124.7 (1C, 6-C<sub>benzol[b]phenyl</sub>), 124.5 (1C, 5-C<sub>benzol[b]phenyl</sub>), 123.9 (1C, 4-C<sub>benzol[b]phenyl</sub>), 122.4 (1C, 7-C<sub>benzol[b]phenyl</sub>), 121.0 (1C, 3-C<sub>benzol[b]phenyl</sub>), 46.1 (2C, CH<sub>2</sub>). IR (neat): δ [cm<sup>-1</sup>] = 1354, 1573, 1624, 3028, 3059. HRMS (APCI): m/z = 307.1012 calculated for C<sub>17</sub>H<sub>15</sub>N<sub>5</sub>S<sup>+</sup> [M+H]<sup>+</sup>, found 307.0927.

Ethyl 3-methylquinoxaline-2-carboxylate (22a). Ethyl acetoacetate (1.00 g, 7.68 mmol, 1.0 eq.) and NBS (1.64 g, 9.22 mmol, 1.2 eq.) were suspended in H<sub>2</sub>O (15 mL) and stirred for 1 h at 70 °C. Then, 1,2-phenylenediamine (830 mg, 7.68 mmol, 1.0 eq.) was added and the reaction mixture was stirred at 70 °C for 3 h. After cooling down to r.t., the reaction mixture was extracted with EtOAc (4 × 10 mL), the combined organic fractions were washed with H<sub>2</sub>O and brine and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed in vacuo. After purification via flash-column chromatography (cyclohexane/EtOAc = 7/3), the product was obtained as a brownish solid (376 mg, 1.74 mmol, 23%). M.p. = 75 °C; TLC: R<sub>f</sub> = 0.51 (cyclohexane/EtOAc = 7/3); <sup>1</sup>H-NMR (400 MHz, DMSO-d<sub>6</sub>, 299 K): δ (in ppm) = 8.14 (dd, J = 8.2, 1.6 Hz, 1H, 5-/8-H<sub>quinoxaline</sub>), 8.07 (dd, J = 8.4, 1.6 Hz, 1H, 5-/8-H<sub>quinoxaline</sub>), 7.94 (dd, J = 8.4, 6.9, 1.6 Hz, 1H, 6-/7-H<sub>quinoxaline</sub>), 7.87 (dd, J = 8.3, 6.9, 1.5 Hz, 1H, 6-/7-H<sub>quinoxaline</sub>), 4.46 (q, J = 7.1 Hz, 2H, -OCH=CH<sub>2</sub>), 2.83 (s, 3H, -CH<sub>3</sub>), 1.39 (t, J = 7.1 Hz, 3H, O-CH<sub>2</sub>-CH<sub>3</sub>). <sup>13</sup>C-NMR (101 MHz, DMSO-d<sub>6</sub>, 299 K): δ (in ppm) = 165.1 (1C, C=O), 152.3 (1C, 2-C<sub>quinoxaline</sub>), 144.5 (1C, 3-C<sub>quinoxaline</sub>), 141.7 (1C, 4a-/8a-C<sub>quinoxaline</sub>), 139.1 (1C, 4a-/8a-C<sub>quinoxaline</sub>), 132.1 (1C, 6-/7-C<sub>quinoxaline</sub>), 130.2 (1C, 6-/7-C<sub>quinoxaline</sub>), 129.2 (1C, 5-/8-C<sub>quinoxaline</sub>), 128.2 (1C, 5-/8-C<sub>quinoxaline</sub>), 61.9 (1C, O-CH=CH<sub>2</sub>), 23.0 (1C, -CH<sub>3</sub>), 14.0 (1C, -OCH<sub>2</sub>-CH<sub>3</sub>). IR (neat): δ [cm<sup>-1</sup>] = 2970, 1716, 1551, 1369, 1269, 1195, 1123, 1076, 1022, 849, 768, 709. HRMS (APCI): m/z = 217.0972 calculated for C<sub>12</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>, found 217.0971.

Ethyl 3-ethylquinoxaline-2-carboxylate (22b). Ethyl 3-oxopentanoate (500 mg, 3.47 mmol, 1.0 eq.) and NBS (741 mg, 4.16 mmol, 1.2 eq.) were suspended in H<sub>2</sub>O (8 mL) and stirred for 3 h at 75 °C. Then, 1,2-phenylenediamine (750 mg, 6.91 mmol, 2.0 eq.) was added into the solution and the reaction mixture was stirred further at 75 °C for 4 h. The resulting dark brown solution was extracted with EtOAc (5 × 25 mL each). The combined organic fractions were washed with H<sub>2</sub>O and brine and dried over Na<sub>2</sub>SO<sub>4</sub>, the solvent was removed in vacuo. The crude product was purified via flash-column chromatography (cyclohexane/EtOAc = 1/0 → 85/15), the product was obtained as a
yellowish solid (347 mg, 1.50 mmol, 43%). M.p. = 66 °C; TLC: Rf = 0.40 (cyclohexane/EtOAc = 5/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.14 (d, J = 8.3 Hz, 1H, 5-/8-Hquinoxaline), 8.10 (d, J = 8.4 Hz, 1H, 5-/8-Hquinoxaline), 7.94 (dd, J = 8.4, 6.9 Hz, 1H, 6-/7-Hquinoxaline), 7.88 (dd, J = 8.3, 6.9 Hz, 1H, 6-/7-Hquinoxaline), 4.47 (q, J = 7.1 Hz, 2H, -O-CH2-CH3), 3.15 (q, J = 7.5 Hz, 2H, -CH2-CH3), 1.38 (t, J = 7.1 Hz, 3H, -OCH2-CH3), 1.33 (t, J = 7.5 Hz, 3H, -CH2-CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.4 (1C, C=O), 156.0 (1C, 2-Cquinoxaline), 144.9 (1C, 3-Cquinoxaline), 141.8 (1C, 4a-/8a-Cquinoxaline), 139.0 (1C, 4a-/8a-Cquinoxaline), 132.0 (6-/7-Cquinoxaline), 130.4 (1C, 6-/7-Cquinoxaline), 129.2 (1C, 5-/8-Cquinoxaline), 128.4 (1C, 5-/8-Cquinoxaline), 62.1 (1C, -O-CH2-CH3), 28.3 (1C, -CH2-CH3), 14.0 (-O-CH2-CH3), 12.7 (1C, -CH2-CH3). IR (neat): ν [cm⁻¹] = 3063, 2974, 1713, 1551, 1447, 1412, 1180, 1138, 1119, 1076, 984, 698. HRMS (APCI): m/z = 231.1128 calculated for C13H15N2O2 [M+H]+, found: 231.1127.

**Ethyl 3-phenylquinoxaline-2-carboxylate (22c).** Ethyl 3-oxo-3-phenylpropanoate (1.12 g, 5.83 mmol, 1.2 eq.) and NBS (1.12 g, 6.80 mmol, 1.4 eq.) were suspended in H2O (15 mL) and stirred at 80 °C for 1 h. Then, 1,2-phenylenediamine (525 mg, 4.86 mmol, 1.0 eq.) was added to the solution. The reaction mixture was stirred at 80 °C for additional 4 h. After cooling down to r.t., the reaction mixture was extracted with EtOAc (5 × 25 mL). The combined organic fractions were washed with H2O and brine and dried over Na2SO4. The solvent was removed in vacuo, the crude product was purified by flash-column chromatography (cyclohexane/EtOAc = 1/0 → 10/1). The product was obtained as a brownish amorphous solid (415 mg, 1.49 mmol, 31%). M.p. = 66 °C; TLC: Rf = 0.54 (cyclohexane/EtOAc = 7/3). 1H-NMR (400 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.24–8.19 (m, 2H, 5-/8-Hquinoxaline), 8.04–7.94 (m, 2H, 6-/7-Hquinoxaline), 7.75–7.70 (m, 2H, Hphenyl), 7.60–7.55 (m, 3H, Hphenyl), 4.29 (q, J = 7.1 Hz, 2H, -O-CH2-CH3), 1.13 (t, J = 7.1 Hz, 3H, -O-CH2-CH3). 13C-NMR (101 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.9 (1C, C=O), 151.3 (1C, 2'-Cquinoxaline), 145.5 (1C, 3'-Cquinoxaline), 141.5 (1C, 4a-/8a-Cquinoxaline), 139.1 (1C, 4a-/8a-Cquinoxaline), 137.1 (1C, 1'-Cphenyl), 132.3 (1C, 6-/7-Cquinoxaline), 131.3 (1C, 6-/7-Cquinoxaline), 129.7 (1C, Cphenyl), 129.1 (1C, 5-/8-Cquinoxaline), 129.0 (1C, 5-/8-Cquinoxaline), 128.7 (2C, Cphenyl), 128.5 (2C, Cphenyl), 62.1 (1C, -O-CH2-CH3), 13.6 (1C, -O-CH2-CH3). IR (neat): ν [cm⁻¹] = 3437, 2345, 1728, 1543, 1477, 1443, 1369, 1323, 1153, 1219, 1130, 760, 698. HRMS (APCI): m/z = 279.1128 calculated for C17H13N2O2 [M+H]+, found: 279.1136.

**Ethyl 3,6,7-trimethylquinoxaline-2-carboxylate (22d).** Ethyl acetooacetate (1.02 g, 7.84 mmol, 1.2 eq.) and NBS (1.63 g, 9.14 mmol, 1.4 eq.) were suspended in H2O (15 mL), heated up to 70 °C and stirred for 1 h. Then, 4,5-dimethyl-1,2-phenylenediamine (890 mg, 6.53 mmol, 1.0 eq.) was added into the solution and the reaction mixture was stirred further at 70 °C for 4 h. The mixture was extracted with EtOAc (5 × 25 mL each). The combined organic fractions were washed with H2O and brine and dried over Na2SO4. The solvent was removed in vacuo. The crude product was purified by flash-column chromatography (cyclohexane/EtOAc = 1/0 → 5/1) to yield 11c (340 mg, 1.39 mmol, 21%) as a brownish amorphous solid. M.p. = 79 °C; TLC: Rf = 0.31 (cyclohexane/EtOAc = 10/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 7.89 (s, 1H, 5-/8-Hquinoxaline), 7.82 (s, 1H, 5-/8-Hquinoxaline), 4.43 (q, J = 7.1 Hz, 2H, -O-CH2-), 2.79 (s, 3H, 3-Cquinoxaline-CH3), 2.47 (s, 3H, 6-/7-Cquinoxaline-CH3), 2.46 (s, 3H, 6-/7-Cquinoxaline-CH3), 1.37 (t, J = 7.1 Hz, 3H, -CH2-CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.4 (1C, C=O), 151.3 (1C, 2-Cquinoxaline), 143.4 (1C, 3-Cquinoxaline), 142.9 (1C, 6-/7-Cquinoxaline), 140.8 (1C, 4a-/8a-Cquinoxaline), 140.7 (1C, 6-/7-Cquinoxaline), 138.1 (1C, 4a-/8a-Cquinoxaline), 127.9 (1C, 5-/8-Cquinoxaline), 127.1 (1C, 5-/8-Cquinoxaline), 61.8 (1C, -CH2-), 23.0 (1C, 3-Cquinoxaline-CH3), 20.0 (6-/7-Cquinoxaline-CH3), 19.8 (6-/7-Cquinoxaline-CH3), 14.1 (1C, -CH2-CH3). IR (neat): ν [cm⁻¹] = 3483, 2981, 2905, 1721, 1547, 1481, 1404, 1319, 1234, 1088, 883, 667. HRMS (APCI): m/z = 245.1285 calculated for C14H17N2O2 [M+H]+, found: 245.1295.
3-Methylquinoxaline-2-carbohydrazide (23a). Synthesized according to general procedure A from 22a (726 mg, 3.36 mmol, 1.0 eq.) and hydrazine monohydrate (2.5 mL) refluxing in EtOH (4.5 mL) for 1.5 h. The product was obtained as colourless needles (505 mg, 2.50 mmol, 74% yield). M.p. = 172 °C; TLC: Rf = 0.24 (DCM/MeOH = 50/1). 1H-NMR (400 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.92 (s, 1H, -NH-NH2), 8.10–8.06 (m, 1H, 6-/9-H_quinoxaline), 8.06–8.03 (m, 1H, 6-/9-H_quinoxaline), 7.91–7.82 (m, 2H, 7-/8-H_quinoxaline), 4.69 (s, 2H, -NH-NH2), 2.79 (s, 3H, -CH3). 13C-NMR (101 MHz, DMSO-d6, 299 K) δ (in ppm) = 164.8 (1C, C=O), 152.1 (1C, 2-/3-C_quinoxaline), 147.7 (1C, 2-/3-C_quinoxaline), 141.5 (1C, 5-/10-C_quinoxaline), 138.9 (1C, 5-/10-C_quinoxaline), 131.1 (1C, 7-/8-C_quinoxaline), 129.9 (1C, 7-/8-C_quinoxaline), 128.9 (1C, 6-/9-C_quinoxaline), 128.2 (1C, 6-/9-C_quinoxaline), 22.5 (1C, -CH3). IR (neat): ν [cm⁻¹] = 3302, 2330, 1647, 1516, 1435, 1331, 1120, 1123, 914, 848, 760, 690. HRMS (APCI): m/z = 203.0927 calculated for C10H11N2O [M+H]+, found: 203.0920.

3-ethylquinoxaline-2-carbohydrazide (23b). Synthesized according to general procedure A from 22b (840 mg, 3.65 mmol, 1.0 eq.) and hydrazine monohydrate (3.0 mL) refluxing in EtOH (3.0 mL) for 2.5 h. The resulting precipitate was recrystallized from H2O/EtOH (95/5). The product was obtained as slightly brownish needles (512 mg, 2.37 mmol, 65%). M.p. = 120 °C; TLC: Rf = 0.20 (DCM/MeOH = 50/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.92 (s, 1H, -NH-), 8.09–8.08 (m, 1H, 5-/8-H_quinoxaline), 8.08–8.06 (m, 1H, 5-/8-H_quinoxaline), 7.89 (dd, J = 8.4, 6.9 Hz, 1H, 6-/7-H_quinoxaline), 7.85 (dd, J = 8.3, 6.9 Hz, 1H, 6-/7-H_quinoxaline), 4.68 (s, 2H, -NH2), 3.12 (q, J = 7.5 Hz, 2H, -CH2-CH3), 1.31 (t, J = 7.5 Hz, 3H, -CH2-CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): 7.43 (in ppm) = 165.0 (1C, C=O), 156.3 (1C, 2-C_quinoxaline), 148.1 (1C, 3-C_quinoxaline), 141.5 (1C, 4a-/8a-C_quinoxaline), 138.9 (1C, 4a-/8a-C_quinoxaline), 131.1 (1C, 6-/7-C_quinoxaline), 129.9 (1C, 6-/7-C_quinoxaline), 128.9 (1C, 5-/8-C_quinoxaline), 128.4 (1C, 5-/8-C_quinoxaline), 28.0 (1C, -CH2-CH3), 12.8 (1C, -CH2-CH3). IR (neat): ν [cm⁻¹] = 3229, 2970, 1678, 1639, 1516, 1435, 1331, 1145, 1116, 935, 791, 706. HRMS (APCI): m/z = 217.1084 calculated for C10H11N2O+ [M+H]+, found: 217.1092.

3-phenylquinoxaline-2-carbohydrazide (23c). Synthesized according to general procedure A from 22c (780 mg, 2.8 mmol, 1.0 eq.) and hydrazine monohydrate (2.5 mL) refluxing in EtOH (4.5 mL) for 3.5 h. The product was obtained as colourless needles (634 mg, 2.4 mmol, 86%). M.p. = 210 °C; TLC: Rf = 0.25 (DCM/MeOH = 50/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.95 (s, 1H, -NH-), 8.20–8.14 (m, 2H, 5-/8-H_quinoxaline), 7.99–7.88 (m, 2H, 6-/7-H_quinoxaline), 7.87–7.81 (m, 2H, Hphenyl), 7.55–7.50 (m, 3H, Hphenyl), 4.60 (s, 2H, -NH2). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.7 (1C, C=O), 151.3 (1C, 2-C_quinoxaline), 148.7 (1C, 3-C_quinoxaline), 141.3 (1C, 4a-/8a-C_quinoxaline), 139.1 (1C, 4a-/8a-C_quinoxaline), 137.2 (1C, 1-Cphenyl), 131.4 (1C, 6-/7-C_quinoxaline), 130.8 (1C, 6-/7-C_quinoxaline), 129.5 (1C, 4-Cphenyl), 129.0 (1C, 5-/8-C_quinoxaline), 128.7 (1C, 5-/8-C_quinoxaline), 128.6 (2C, Cphenyl), 128.4 (2C, Cphenyl). IR (neat): ν [cm⁻¹] = 3321, 3036, 2345, 1643, 1528, 1466, 1443, 1331, 1276, 1130, 922, 718. HRMS (APCI): m/z = 265.1084 calculated for C15H13N4O+ [M+H]+, found: 265.1088.

3,6,7-Trimethylquinoxaline-2-carbohydrazide (23d). Synthesized according to general procedure A from 22d (785 mg, 3.21 mmol, 1.0 eq.) and hydrazine monohydrate (2.5 mL) refluxing in EtOH (2.0 mL) for 5 h. The product was obtained as slightly brownish needles (544 mg, 2.36 mmol, 74%). M.p. = 198 °C; TLC: Rf = 0.40 (DCM/MeOH = 50/1). 1H-NMR (400 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.85 (s, 1H, -NH-), 7.81 (s, 1H, H_quinoxaline), 7.80 (s, 1H, H_quinoxaline), 4.65 (s, 2H, -NH2), 2.75 (s, 3H, 3-C_quinoxaline-CH3), 2.47 (s, 3H, 6-/7-C_quinoxaline-CH3), 2.46 (s, 3H, 6-/7-C_quinoxaline-CH3). 13C-NMR (101 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.0 (1C, C=O), 151.0 (1C, 2-C_quinoxaline), 146.5 (1C, 3-C_quinoxaline), 141.6 (1C, 6-/7-C_quinoxaline), 140.5 (1C, 4a-/8a-C_quinoxaline), 140.1 (1C, 6-/7-C_quinoxaline), 137.8 (1C, 4a-/8a-C_quinoxaline), 127.6 (1C, 5-/8-C_quinoxaline), 127.1 (1C, 5-/8-C_quinoxaline), 22.5 (1C, 3-C_quinoxaline-CH3), 19.9 (1C, 6-/7-C_quinoxaline-CH3), 19.7 (1C, 6-/7-C_quinoxaline-CH3). IR (neat): ν [cm⁻¹] = 3329, 3248, 2963,1670, 1477, 1369, 1211, 1153, 995,
845, 818, 718. HRMS (APCI): $m/z = 231.1240$ calculated for C$_2$H$_{15}$N$_3$O$^+$ [M+H]$^+$, found: 231.1232.

3-(3-Methylquinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (24a). Synthesized according to general procedure B. Compound 23a (448 mg, 2.22 mmol, 1.0 eq.) was refluxed in 20% EtOH (12 mL) with S-methylisothiourea sulphate (3.09 g, 11.1 mmol, 5 eq.), which was added in portions (first 2 eq. and then 1 eq. every 16 h (3 times)). After 72 h, KOH (1.6 g) was added, and the reaction mixture was refluxed for another 3 h. The product was recrystallised from EtOH, and obtained as a rose powder (161 mg, 0.71 mmol, 32%). M.p. = 270 °C (decomp.); TLC: $R_f = 0.56$ (DCM/MeOH = 1/1).

$^1$H-NMR (600 MHz, DMSO-$d_6$, 299 K): $\delta$ (in ppm) = 12.51 (s, 1H, -NH), 8.07–8.03 (m, 1H, 5/-8-H$_{\text{quinoxaline}}$), 8.03–7.99 (m, 1H 5/-8-H$_{\text{quinoxaline}}$), 7.83–7.78 (m, 2H, 6/-7-H$_{\text{quinoxaline}}$), 6.23 (br s, 2H, -NH$_2$), 2.94 (s, 3H, CH$_3$). $^{13}$C-NMR (151 MHz, DMSO-$d_6$, 299 K): $\delta$ (in ppm) = 158.0 (1C, 3-/5-C$_{\text{triazolyl}}$), 157.1 (1C, 3-/5-C$_{\text{triazolyl}}$), 153.0 (1C, 2-C$_{\text{quinoxaline}}$), 145.9 (1C, 3-C$_{\text{quinoxaline}}$), 140.4 (1C, 4a-/8a-C$_{\text{quinoxaline}}$), 140.0 (1C, 4a-/8a-C$_{\text{quinoxaline}}$), 131.0 (1C, 6-/7-C$_{\text{quinoxaline}}$), 129.4 (1C, 6-/7-C$_{\text{quinoxaline}}$), 128.8 (1C, 5/-8-C$_{\text{quinoxaline}}$), 128.0 (1C, 5/-8-C$_{\text{quinoxaline}}$), 24.8 (1C, -CH$_3$). IR (neat): $\nu$ [cm$^{-1}$] = 3306, 3028, 2974, 1636, 1589, 1454, 1354, 1211, 1080, 980, 813, 717. HRMS (APCI): $m/z = 227.1040$ calculated for C$_{11}$H$_{11}$N$_3$O$^+$ [M+H]$^+$, found: 227.1028.

3-(3-Ethylquinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (24b). Synthesized according to general procedure B. Compound 23b (500 mg, 2.31 mmol, 1.0 eq.) was refluxed in 30% EtOH (15 mL) with S-methylisothiourea sulphate (3.22 g, 11.56 mmol, 5 eq.). After 72 h, KOH (7.0 g) was added, and the reaction mixture was refluxed for another 4 h. The product was recrystallised from EtOH to be obtained as a yellowish solid (156 mg, 0.65 mmol, 28%). M.p. = 215 °C (decomp.); TLC: $R_f = 0.40$ (DCM/MeOH = 10/1). $^1$H-NMR (600 MHz, DMSO-$d_6$, 299 K): $\delta$ (in ppm) = 13.67* and 12.45 (s, 0.71H, -NH$_2$), 8.06–8.00 (m, 2H, 5/-8-H$_{\text{quinoxaline}}$), 7.82–7.76 (m, 2H, 6/-7-H$_{\text{quinoxaline}}$), 6.26 and 5.47* (s, 0.23H, -NH$_2$), 1.26 (t, $J = 7.5$ Hz, 3H, -CH$_3$), the signal of CH$_2$- protons overlapped with the H$_2$O protons signal. $^{13}$C-NMR (151 MHz, DMSO-$d_6$, 299 K): $\delta$ (in ppm) = 157.8 (1C, 3-/5-C$_{\text{triazole}}$), 157.1 (1C, 3-/5-C$_{\text{triazole}}$), 156.8 (1C, 2/-3-C$_{\text{quinoxaline}}$), 145.9 (1C, 2/-3-C$_{\text{quinoxaline}}$), 140.6 (1C, 4a-/8a-C$_{\text{quinoxaline}}$), 139.9 (1C, 4a-/8a-C$_{\text{quinoxaline}}$), 130.1 (1C, 6-/7-C$_{\text{quinoxaline}}$), 129.5 (1C, 6-/7-C$_{\text{quinoxaline}}$), 128.8 (1C, 5/-8-C$_{\text{quinoxaline}}$), 128.4 (1C, 5/-8-C$_{\text{quinoxaline}}$), 29.0 (1C, -CH$_2$), 12.7 (1C, -CH$_3$). *— two tautomers exist in the ratio $24b/24b^*$ = 7/1, the signals of the minor tautomer $24b^*$ are marked with *.

IR (neat): $\nu$ [cm$^{-1}$] = 3453, 3098, 2935, 1639, 1589, 1485, 1193, 1123, 972, 763, 691, 667. HRMS (APCI): $m/z = 241.1196$ calculated for C$_{11}$H$_{11}$N$_3$O$^+$ [M+H]$^+$, found: 241.1198.

3-(3-Phenylquinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (24c). Synthesized according to general procedure B. Compound 23c (423 mg, 1.60 mmol, 1.0 eq.) was refluxed in 30% EtOH (15 mL) with S-methylisothiourea sulphate (892 mg, 3.2 mmol, 2 eq.), which was added in portions (first 1 eq. and then 0.5 eq. every 24 h (2 times)). After 72 h, KOH (2.0 g) was added, and the reaction mixture was refluxed for another 6.5 h. The product was washed with H$_2$O and EtOAc to be obtained as a slightly yellowish powder (150 mg, 0.52 mmol, 33%). M.p. = 260 °C (decomp.). TLC: $R_f = 0.62$ (toluene/MeOH = 2/1). $^1$H-NMR (600 MHz, DMSO-$d_6$, 299 K): $\delta$ (in ppm) = 12.26 (s, 1H, -NH$_2$), 8.17–8.13 (m, 2H, 5/-8-H$_{\text{quinoxaline}}$), 7.93–7.88 (m, 2H, 6/-7-H$_{\text{quinoxaline}}$), 7.59–7.54 (m, 2H, 2/-6-H$_{\text{phenyl}}$), 7.41–7.39 (m, 3H, 3/-4/-5-H$_{\text{phenyl}}$), 6.11 (s, 2H, -NH$_2$). $^{13}$C-NMR (151 MHz, DMSO-$d_6$, 299 K): $\delta$ (in ppm) = 158.1 (1C, 3-/5-C$_{\text{triazole}}$), 156.9 (1C, 3-/5-C$_{\text{triazole}}$), 153.2 (1C, 2-C$_{\text{quinoxaline}}$), 146.4 (1C, 3-C$_{\text{quinoxaline}}$), 140.8 (1C, 4a-/8a-C$_{\text{quinoxaline}}$), 139.9 (1C, 4a-/8a-C$_{\text{quinoxaline}}$), 138.7 (1C, 1-C$_{\text{phenyl}}$), 130.9 (1C, 6/-7-C$_{\text{quinoxaline}}$), 130.5 (1C, 6/-7-C$_{\text{quinoxaline}}$), 129.0 (2C, 2/-6-C$_{\text{phenyl}}$), 128.9 (2C, 5/-8-C$_{\text{quinoxaline}}$), 128.8 (1C, 4-C$_{\text{phenyl}}$), 127.9 (2C, 3/-5-C$_{\text{phenyl}}$). IR (neat): $\nu$ [cm$^{-1}$] = 3310, 3070, 1639, 1589, 1485, 1450, 1219, 1088, 764, 694, 667. HRMS (APCI): $m/z = 289.1196$ calculated for C$_{16}$H$_{13}$N$_6$O$^+$ [M+H]$^+$, found: 289.1220.
3-(3,6,7-Trimethylquinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (24d). Compound 23d (500 mg, 2.17 mmol, 1.0 eq.) was refluxed in 30% EtOH (15 mL) with S-methylsulphonium sulphate (3.02 g, 10.9 mmol, 5.0 eq.). After 48 h, KOH (7.0 g) was added, and the reaction mixture was refluxed for another 4 h. The product was recrystallised from EtOH to be obtained a yellow solid (224 mg, 0.88 mmol, 41%). M.p. = 250 °C (decomp.); TLC: Rf = 0.39 (DCM/MeOH = 10/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.43 (s, 1H, -NH-) 7.79 (s, 1H, 5-/8-H_quinoxaline), 7.77 (s, 1H, 5-/8-H_quinoxaline), 2.91 (s, 3H, 3-C_quinoxaline–CH3), 2.46 (s, 6H, 6-/7-H_quinoxaline–CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K) δ (in ppm) = 158.3 (3C, 3-/5-C_triazole), 157.0 (1C, 3-/5-C_triazole), 151.6 (1C, 2-C_quinoxaline), 145.0 (1C, 3-C_quinoxaline), 140.5 (2C, 6-/7-H_quinoxaline), 139.5 (1C, 4a-/8a-C_quinoxaline), 138.9 (1C, 4a-/8a-C_quinoxaline), 127.0 (1C 5-/8-C_quinoxaline), 127.0 (1C 5-/8-C_quinoxaline), 25.3 (1C, 3-C_quinoxaline–CH3), 19.9 (2C, 6-/7-C_quinoxaline–CH3). IR (neat): ν [cm⁻¹] = 3302, 2920, 1627, 1558, 1450, 1373, 1211, 1119, 868, 687, 617. HRMS (APCI): m/z = 255.1353 calculated for C13H15N6 [M+H]⁺, found: 255.1354.

(E)-3-(Dimethylamino)-1-phenylprop-2-en-1-one (26a). Synthesized according to general procedure C. Acetophenone (25a, 2.43 mL, 20.8 mmol, 1.0 eq.) was dissolved in DMF-DMA (5.55 mL, 41.6 mmol, 2.0 eq.) and the reaction mixture was heated to reflux for 16 h yielding enamine 26a (3.14 g, 17.9 mmol, 86%) as an orange solid. M.p. = 92 °C. TLC: Rf = 0.44 (DCM/MeOH = 95/5). 1H-NMR (600 MHz, CDCl3, 299 K): δ (in ppm) = 7.91–7.87 (m, 2H, 2/6-Hphenyl), 7.80 (d, J = 12.4 Hz, 1H, COCHCHN), 7.46–7.43 (m, 1H, 4-Hphenyl), 7.43–7.39 (m, 2H, 3/5-Hphenyl), 5.71 (d, J = 12.4 Hz, 1H, COCHCHN), 3.14 (bs, 3H, CH3), 2.92 (bs, 3H, CH3). 13C-NMR (151 MHz, CDCl3, 299 K): δ (in ppm) = 188.8 (1C, C=O), 154.4 (1C, COCHCHN), 140.7 (1C, 1-Cphenyl), 131.0 (1C, 4-Cphenyl), 128.2 (2C, 3-/5-Cphenyl), 127.6 (2C, 4-/6-Cphenyl), 92.4 (1C, COCHCHN), 45.2 (1C, CH3), 37.4 (1C, CH3). IR (neat): ν [cm⁻¹] = 3022, 2914, 2806, 1631, 1581, 1531, 1483, 1273, 1122, 1053, 898, 738. HRMS (APCI): m/z = 176.1070 calculated for C11H14NO [M+H]⁺, found: 176.1081.

(E)-1-(3,4-dimethoxyphenyl)-3-(dimethylamino)prop-2-en-1-one (26c). Synthesized according to general procedure C. 3,4-Dimethoxycacetophenone (25c, 2.30 g, 12.8 mmol, 1.0 eq.) was suspended in DMF-DMA (3.44 mL, 25.6 mmol, 2.0 eq.) and the reaction mixture was heated to reflux for 16 h yielding enamine 26c (2.88 g, 12.2 mmol, 96%) as a yellow solid. M.p. = 123.5 °C. TLC: Rf = 0.49 (DCM/MeOH = 95/5). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 7.67 (d, J = 12.3 Hz, 1H, COCHCHN), 7.54 (dd, J = 8.4, 2.1 Hz, 1H, 6-Hdimethoxyphenyl), 7.46 (d, J = 2.2 Hz, 1H, 2-Hdimethoxyphenyl), 6.97 (d, J = 8.4 Hz, 1H, 5-Hdimethoxyphenyl), 5.82 (d, J = 12.3 Hz, 1H, COCHCHN), 3.80 (s, 6H, OCH3), 3.12 (bs, 3H, CH3), 2.90 (bs, 3H, CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 184.8 (1C, C=O), 153.6 (1C, COCHCHN), 151.2 (1C, 4-Cdimethoxyphenyl), 148.3 (1C, 3-Cdimethoxyphenyl), 133.0 (1C, 1-Cdimethoxyphenyl), 120.8 (1C, 6-Cdimethoxyphenyl), 110.6 (1C, 5-Cdimethoxyphenyl), 110.4 (1C, 2-Cdimethoxyphenyl), 90.7 (1C, COCHCHN), 55.5 (1C, -OCH3), 55.4 (1C, -OCH3), 44.4 (1C, -CH3), 37.1 (1C, -CH3). IR (neat): ν [cm⁻¹] = 3082, 2997, 2931, 2839, 1633, 1537, 1423, 1286, 1116, 1026, 756. HRMS (APCI): m/z = 236.1281 calculated for C13H18NO3 [M+H]⁺, found: 236.1294.

(E)-3-(Dimethylamino)-1-(4-isobutylphenyl)prop-2-en-1-one (26d). Synthesized according to general procedure C. 4-Isobutylacetophenone (25d, 2.60 mL, 14.2 mmol, 1.0 eq.) was dissolved in DMF-DMA (3.82 mL, 28.4 mmol, 2.0 eq.) and the reaction mixture was heated to reflux for 16 h yielding enamine X (2.39 g, 10.3 mmol, 73%) as yellow solid. M.p. = 76.5 °C. TLC: Rf = 0.50 (DCM/MeOH = 95/5). 1H-NMR (600 MHz, CDCl3, 299 K): δ (in ppm) = 7.81 (m, 2H, 2/6-Hisobutylphenyl), 7.79 (d, J = 12.4 Hz, 1H, COCHCHN), 7.18 (m, 2H, 3/5-Hisobutylphenyl), 5.72 (d, J = 12.4 Hz, 1H, COCHCHN), 3.13 (bs, 3H, NCH3), 2.92 (bs, 3H, NCH3), 2.51 (d, J = 7.2 Hz, 2H, CH2), 1.92–1.84 (m, 1H, CH), 0.91 (s, 3H, (CH)CH3), 0.89 (s, 3H, (CH)CH3). 13C-NMR (151 MHz,
CDCl₃, 299 K): δ (in ppm) = 154.1 (1C, COCHCN), 188.7 (1C, C=O), 145.2 (1C, 4-C₆isothiophenyl), 138.2 (1C, 1-C₆isothiophenyl), 129.0 (1C, 3-/5-C₆isothiophenyl), 127.6 (1C, 2-/6-C₆isothiophenyl), 92.3 (1C, COCHCN), 45.5 (1C, CH₂), 45.1 (1C, NCH₃), 37.4 (1C, NCH₃), 30.3 (1C, CH), 22.5 (2C, (CH)CH₃). IR (neat): ν [cm⁻¹] = 3020, 2949, 2912, 2864, 1637, 1577, 1427, 1276, 1238, 754. HRMS (APCI): m/z = 232.1696 calculated for C₁₃H₂₂NO⁺ [M+H]⁺, found: 232.1705.

(E)-3-(Dimethylamino)-1-(pyridin-3-yl)prop-2-en-1-one (26e). Synthesized according to general procedure C. 3-Acetylpyridine (25e, 2.72 mL, 24.8 mmol, 1.0 eq.) was dissolved in DMF-DMA (6.61 mL, 49.5 mmol, 2.0 eq.) and the reaction mixture was heated to reflux for 16 h yielding enammine 26e (3.69 g, 20.9 mmol, 85%) as brown solid. M.p. = 79.5 °C. TLC: 0.47 (DCM/MeOH = 95/5). ¹H-NMR (600 MHz, CDCl₃, 299 K): δ (in ppm) = 9.07 (d, J = 2.1 Hz, 1H, 2-Hpyridyl), 8.66 (dd, J = 4.9, 1.8 Hz, 1H, 6-Hpyridyl), 8.18 (dt, J = 8.0, 2.0 Hz, 1H, 4-Hpyridyl), 7.84 (d, J = 12.3 Hz, 1H, COCHCN), 7.36-7.32 (m, 1H, 5-Hpyridyl), 5.67 (d, J = 12.3 Hz, 1H, COCHCN), 3.17 (bs, 3H, CH₃), 2.95 (bs, 3H, CH₃). ¹³C-NMR (151 MHz, CDCl₃, 299 K): δ (in ppm) = 186.5 (1C, C=O), 154.8 (1C, COCHCN), 151.6 (1C, 6-C₆pyridyl), 149.1 (1C, 2-C₆pyridyl), 135.8 (1C, 3-C₆pyridyl), 135.2 (1C, 4-C₆pyridyl), 123.4 (1C, 5-C₆pyridyl), 92.0 (1C, COCHCN), 45.3 (1C, CH₃), 37.5 (1C, CH₃). IR (neat): ν [cm⁻¹] = 2914, 2872, 2804, 1633, 1581, 1531, 1438, 1409, 1274, 1124, 1064, 902, 771. HRMS (APCI): m/z = 177.1022 calculated for C₁₀H₁₃N₂O⁺ [M+H]⁺, found: 177.1034.

(E)-3-(Dimethylamino)-1-(thiophen-2-yl)prop-2-en-1-one (26f). Synthesized according to general procedure C. 2-Acetylthiophene (25f, 2.14 mL, 19.8 mmol, 1.0 eq.) was dissolved in DMF-DMA (5.34 mL, 39.6 mmol, 2.0 eq.) and the reaction mixture was heated to reflux for 16 h yielding enammine 26f (3.45 g, 19.3 mmol, 96%) as orange solid. M.p. = 115 °C. TLC: Rᵣ = 0.51 (DCM/MeOH = 95/5). ¹H-NMR (600 MHz, CDCl₃, 299 K): δ (in ppm) = 7.74 (d, J = 12.3 Hz, 1H, COCHCN), 7.60 (dd, J = 3.7/11 Hz, 1H, 3-Hthiophenyl), 7.44 (dd, J = 4.9/11 Hz, 1H, 5-Hthiophenyl), 7.05 (dd, J = 4.9/3.7 Hz, 1H, 4-Hthiophenyl), 5.59 (d, J = 12.3 Hz, 1H, COCHCN), 3.09 (bs, 3H, CH₃), 2.88 (bs, 3H, CH₃). ¹³C-NMR (151 MHz, CDCl₃, 299 K): δ (in ppm) = 180.8 (1C, C=O), 153.6 (1C, COCHCN), 147.5 (1C, 2-C₆thiophenyl), 130.3 (1C, 5-C₆thiophenyl), 128.4 (1C, 3-C₆thiophenyl), 127.6 (1C, 4-C₆thiophenyl), 91.7 (1C, COCHCN), 45.0 (1C, CH₃), 37.3 (1C, CH₃). IR (neat): ν [cm⁻¹] = 3070, 2910, 2804, 1631, 1504, 1431, 1408, 1282, 1112, 761. HRMS (APCI): m/z = 182.0634 calculated for C₇H₇NO⁺ [M+H]⁺, found: 182.0651.

(E)-1-(Dimethylamino)-5-methylhex-1-en-3-one (26g). Synthesized according to general procedure C. Isobutylmethylketone (25g, 2.49 mL, 20.0 mmol, 1.0 eq.) was dissolved in DMF-DMA (5.38 mL, 40.0 mmol, 2.0 eq.) and the reaction mixture was heated to reflux for 24 h. The reaction mixture was cooled to r.t., concentrated in vacuo and purified via flash column chromatography (DCM/MeOH = 1/1 → 9/1) yielding enammine 26g (1.77 g, 11.4 mmol, 57%) as a yellow oil. TLC: Rᵣ = 0.49 (DCM/MeOH = 95/5). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 7.45 (d, J = 12.8 Hz, 1H, COCHCN), 4.94 (d, J = 12.9 Hz, 1H, COCHCN), 3.04 (bs, 3H, NCH₃), 2.73 (bs, 3H, NCH₃), 2.11 (d, J = 7.1 Hz, 2H, CH₂), 2.02–1.95 (m, 1H, CH), 0.85 (s, 3H, (CH)CH₃), 0.84 (s, 3H, (CH)CH₃). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 195.0 (1C, C=O), 152.3 (1C, COCHCN), 96.2 (1C, COCHCN), 44.0 (2C, NCH₃), 36.6 (1C, COCHCN), 25.4 (2C, CH₂), 22.6 (2C, (CH)CH₃). IR (neat): ν [cm⁻¹] = 2953, 2868, 2810, 1651, 1435, 1417, 1278, 1111, 763. HRMS (APCI): m/z = 156.1383 calculated for C₉H₁₈NO⁺ [M+H]⁺, found: 156.1391.

Ethyl-2-methyl-6-phenylnicotinate (27a). Synthesized according to general procedure D. Enaminone 26a (1.50 g, 8.56 mmol, 1.0 eq.), ammonium acetate (5.28 g, 86.5 mmol, 8.0 eq.) and ethyl acetooacetate (1.30 mL, 10.3 mmol, 1.2 eq.) were dissolved in acetic acid (25 mL) and refluxed for 16 h. The crude product was filtered and purified (cyclohexane/EtOAc = 1/0 → 0/1) yielding ester 27a (1.41 g, 5.84 mmol, 68%) as colorless solid. M.p. = 46.0 °C. TLC: Rᵣ = 0.51
Ethyl-6-(2-bromophenyl)-2-methylnicotinate (27b). Intermediate 26b was synthesized according to general procedure C. 2′-Bromoacetophenone (25b, 1.36 g, 10.1 mmol, 1.0 eq.) was dissolved in DMF-DMA (2.71 mL, 20.1 mmol, 2.0 eq.) and the reaction mixture was heated to reflux for 16 h. The reaction mixture was cooled to r.t., concentrated in vacuo and purified via flash column chromatography (DCM/MeOH = 1/0 → 9/1) yielding enaminone 26b (2.48 g, 9.76 mmol, 97%) as orange oil, which was immediately used for the next synthesis step. The second synthesis step was performed according to general procedure D. Enaminone 26b (2.12 g, 8.34 mmol, 1.0 eq.), ammonium acetate (5.14 g, 66.7 mmol, 8.0 eq.) and ethyl acetoacetate (1.25 mL, 10.0 mmol, 1.2 eq.) were dissolved in acetic acid (25 mL) and refluxed for 16 h. The crude product was extracted and purified (cyclohexane/EtOAc = 1/0 → 0/1) yielding ester 27b (2.14 g, 6.68 mmol, 80%) as a colorless oil. TLC: Rf = 0.39 (cyclohexane/EtOAc = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.26 (d, J = 8.0 Hz, 1H, 4-Hpyridyl), 7.76 (dd, J = 7.9, 1.1 Hz, 1H, 3-/6-/Hbromophenyl), 7.59 (dd, J = 8.1, 0.7 Hz, 1H, 5-Hpyridyl), 7.54 (dd, J = 7.6, 1.9 Hz, 1H, 3-/6-/Hbromophenyl), 7.51 (t, J = 7.4, 1.2 Hz, 1H, 4-/(5-Hbromophenyl), 7.40 (ddd, J = 8.1, 7.2, 1.9 Hz, 1H, 4-/5-Hbromophenyl), 4.35 (q, J = 7.1 Hz, 2H, OCH2CH3), 2.76 (s, 3H, CH3), 1.35 (t, J = 7.1 Hz, 3H, OCH2CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.9 (1C, C=O), 159.5 (1C, 6-Cpyridyl), 158.2 (1C, 2-Cpyridyl), 140.1 (1C, 1-Cbromophenyl), 138.3 (1C, 4-Cpyridyl), 133.1 (1C, 3-/6-/Cbromophenyl), 131.4 (1C, 3-/6-/Cbromophenyl), 130.6 (1C, 4-/5-/Cbromophenyl), 127.9 (1C, 4-/5-/Cbromophenyl), 124.1 (1C, 3-Cpyridyl), 122.0 (1C, 5-Cpyridyl), 120.9 (1C, 2-Cbromophenyl), 61.1 (1C, OCH2CH3), 24.3 (1C, CH3), 14.1 (1C, OCH2CH3). IR (neat): v [cm⁻¹] = 2978, 1716, 1581, 1261, 1074, 754. HRMS (APCI): m/z = 320.0281 calculated for C15H14BrNO2⁺ [M+H]⁺, found: 320.0302.

Ethyl-6-(3,4-dimethoxyphenyl)-2-methylnicotinate (27c). Synthesized according to general procedure D. Enaminone 26c (1.50 g, 6.38 mmol, 1.0 eq.), ammonium acetate (3.93 g, 51.0 mmol, 8.0 eq.) and ethyl acetoacetate (986 µL, 7.65 mmol, 1.2 eq.) were dissolved in acetic acid (20 mL) and refluxed for 16 h. The crude product was filtered and purified (cyclohexane/EtOAc = 1/0 → 0/1) yielding ester 27c (1.61 g, 5.34 mmol, 84%) as a colorless solid. M.p. = 103 °C. TLC: Rf = 0.12 (cyclohexane/EtOAc = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.19 (d, J = 8.3 Hz, 1H, 4-Hpyridyl), 7.70 (d, J = 8.3 Hz, 1H, 5-Hpyridyl), 7.75 (d, J = 2.1 Hz, 1H, 2-Hdimethoxyphenyl), 7.74 (dd, J = 8.3, 2.1 Hz, 1H, 6-Hdimethoxyphenyl), 7.08 (d, J = 8.3 Hz, 1H, 5-Hdimethoxyphenyl), 4.32 (q, J = 7.1 Hz, 2H, OCH2CH3), 3.86 (s, 3H, OCH3), 3.83 (s, 3H, OCH3), 2.78 (s, 3H, CH3), 1.34 (t, J = 7.1 Hz, 3H, OCH2CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 169.1 (1C, C=O), 161.6 (1C, 2-Cpyridyl), 160.6 (1C, 6-Cpyridyl), 153.7 (1C, 4-Cdimethoxyphenyl), 152.0 (1C, 3-Cdimethoxyphenyl), 142.2 (1C, 4-Cpyridyl), 133.2 (1C, 1-Cdimethoxyphenyl), 125.8 (1C, 3-Cpyridyl), 123.2 (1C, 6-Cdimethoxyphenyl), 119.9 (1C, 5-Cpyridyl), 114.8 (1C, 5-Cdimethoxyphenyl), 113.3 (1C, 2-Cdimethoxyphenyl), 63.9 (1C, OCH2CH3), 58.68 (1C, OCH3), 58.67 (1C, OCH3), 28.0 (1C, CH3), 17.2 (1C, OCH2CH3). IR (neat): v [cm⁻¹] = 2966, 2926, 2841, 1708, 1581, 1514, 1452, 1265, 1244, 1163, 1072, 1018. HRMS (APCI): m/z = 302.1387 calculated for C17H18NO2⁺ [M+H]⁺, found: 302.1405.
Ethyl-6-(4-isobutylphenyl)-2-methylnicotinate (27d). Synthesized according to general procedure D. Enaminone 26d (1.50 g, 6.48 mmol, 1.0 eq.), ammonium acetate (4.00 g, 51.9 mmol, 8.0 eq.) and ethyl acetoacetate (984 µL, 7.78 mmol, 1.2 eq.) were dissolved in acetic acid (20 mL) and refluxed for 16 h. The crude product was extracted and purified (1. Cyclohexane/EtOAc = 1/0 → 76/24, 2. Cyclohexane/EtOAc = 1/0 → 85/15) yielding ester 27d (1.59 g, 5.35 mmol, 82%) as a colorless oil. TLC: Rf = 0.56 (cyclohexane/EtOAc = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.23 (d, J = 8.2 Hz, 1H, 4-H-pyridyl), 8.08–8.05 (m, 2H, 2-/6-H-isobutylphenyl), 7.90 (d, J = 8.2 Hz, 1H, 6-H-pyridyl), 7.30 (m, 2H, 3-/5-H-isobutylphenyl), 4.33 (q, J = 7.1 Hz, 2H, OCH2CH3), 2.79 (s, 3H, CH3), 2.51 (d, J = 7.3 Hz, 1H, CH2), 1.83–1.92 (m, 1H, CH3), 1.34 (t, J = 7.1 Hz, 3H, OCH2CH3), 0.89 (s, 2H, (CH)CH3), 0.88 (s, 3H, (CH)CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.9 (1C, C=O), 158.5 (1C, 6-C-pyridyl), 157.8 (1C, 2-C-pyridyl), 143.3 (1C, 1-isobutylphenyl), 139.2 (1C, 4-C-pyridyl), 135.1 (1C, 1-isobutylphenyl), 129.4 (2C, 3-/5-C-isobutylphenyl), 126.8 (2C, 2-/6-C-isobutylphenyl), 123.2 (1C, 3-C-pyridyl), 117.1 (1C, 5-C-pyridyl), 60.9 (1C, OCH2CH3), 44.3 (1C, CH3), 29.6 (1C, CH), 24.8 (1C, CH3), 22.1 (2C, (CH)CH3), 14.1 (1C, OCH2CH3). IR (neat): ν [cm⁻¹] = 2954, 1716, 1583, 1261, 1087, 777. HRMS (APCI): m/z = 298.1802 calculated for C19H23NO2⁺ [M+H]⁺, found: 298.1787.

Ethyl-6-methyl-2,3'-bipyridine-5-carboxylate (27e). Synthesized according to general procedure D. Enaminone 26e (2.00 g, 11.4 mmol, 1.0 eq.), ammonium acetate (7.00 g, 90.8 mmol, 8.0 eq.) and ethyl acetoacetate (1.71 mL, 13.6 mmol, 1.2 eq.) were dissolved in acetic acid (25 mL) and refluxed for 16 h. The crude product was filtered and purified via flash column chromatography (cyclohexane/EtOAc = 1/0 → 0/1), yielding ester 27e (1.41 g, 5.84 mmol, 68%) as a beige solid. M.p. = 61 °C. TLC: Rf = 0.11 (cyclohexane/EtOAc = 7/3). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.31 (dd, J = 2.4, 0.9 Hz, 1H, 2'-H-pyridyl), 8.67 (dd, J = 4.8, 1.7 Hz, 1H, 6'-H-pyridyl), 8.48 (dd, J = 8.1, 2.4, 1.7 Hz, 1H, 4'-H-pyridyl), 8.27 (d, J = 8.2 Hz, 1H, 4-H-pyridyl), 8.02 (d, J = 8.2 Hz, 1H, 5-H-pyridyl), 7.54 (dd, J = 8.1, 4.8, 0.9 Hz, 1H, 5'-H-pyridyl), 4.33 (q, J = 7.1 Hz, 2H, OCH2CH3), 2.80 (s, 3H, CH3), 1.34 (t, J = 7.1 Hz, 3H, OCH2CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.8 (1C, C=O), 158.8 (1C, 6-C-pyridyl), 155.5 (1C, 2-C-pyridyl), 150.6 (1C, 6'-C-pyridyl), 148.2 (1C, 2'-C-pyridyl), 139.4 (1C, 4-C-pyridyl), 134.4 (1C, 4'-C-pyridyl), 133.0 (1C, 3'-C-pyridyl), 124.3 (1C, 5'-C-pyridyl), 123.8 (1C, 5'-C-pyridyl), 117.9 (1C, 3-C-pyridyl), 61.1 (1C, OCH2CH3), 24.7 (1C, CH3), 14.1 (1C, OCH2CH3). IR (neat): ν [cm⁻¹] = 2980, 2929, 1708, 1583, 1483, 1417, 1263, 1166, 1012. HRMS (APCI): m/z = 243.1128 calculated for C13H15NO2⁺ [M+H]⁺, found: 243.1140.

Ethyl 2-methyl-6-(thiophen-2-yl)nicotinate (27f). Synthesized according to general procedure D. Enaminone 26f (1.70 g, 9.38 mmol, 1.0 eq.), ammonium acetate (5.78 g, 75.3 mmol, 8.0 eq.) and ethyl acetoacetate (1.42 mL, 11.3 mmol, 1.2 eq.) were dissolved in acetic acid (25 mL) and refluxed for 16 h. The crude product was filtered and purified (cyclohexane/EtOAc = 1/0 → 0/1) yielding ester 27f (1.92 g, 7.76 mmol, 83%) as a colorless solid. M.p. = 59 °C. TLC: Rf = 0.42 (cyclohexane/EtOAc = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.19 (d, J = 8.2 Hz, 1H, 4-H-pyridyl), 7.90 (dd, J = 3.8, 1.2 Hz, 1H, 3-H-thiophenyl), 7.86 (d, J = 8.2 Hz, 1H, 5-H-pyridyl), 7.73 (dd, J = 5.0, 1.1 Hz, 1H, 5-H-thiophenyl), 7.20 (dd, J = 5.0, 3.7 Hz, 1H, 3-H-thiophenyl), 4.31 (q, J = 7.1 Hz, 2H, -OCH2CH3), 2.73 (s, 3H, -CH3), 1.33 (t, J = 7.1 Hz, 3H, -OCH2CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 165.7 (1C, C=O), 158.9 (1C, 2-C-pyridyl), 153.5 (1C, 6-C-pyridyl), 143.4 (1C, 2-C-thiophenyl), 139.2 (1C, 4-C-pyridyl), 130.1 (1C, 5-C-thiophenyl), 128.7 (1C, 4-C-thiophenyl), 127.1 (1C, 3-C-thiophenyl), 123.0 (1C, 3-C-pyridyl), 115.9 (1C, 5-C-pyridyl), 60.9 (1C, -OCH2CH3), 24.6 (1C, -CH3), 14.1 (1C, -OCH2CH3). IR (neat): ν [cm⁻¹] = 2974, 2931, 1708, 1581, 1460, 1423, 1236, 1089, 846. HRMS (APCI): m/z = 248.0740 calculated for C13H13NO2S⁺ [M+H]⁺, found: 248.0737.
Ethyl-6-isobutyl-2-methylnicotinate (27g). Synthesized according to general procedure D. Enaminone 26g (1.77 g, 11.4 mmol, 1.0 eq.), ammonium acetate (7.03 g, 91.2 mmol, 8.0 eq.) and ethyl acetoacetate (1.73 mL, 13.7 mmol, 1.2 eq.) were dissolved in acetic acid (30 mL) and refluxed for 16 h. The crude product was extracted and purified via flash column chromatography (cyclohexane/EtOAc = 1/0 → 68/32) yielding ester 27g (1.70 g, 7.68 mmol, 67%) as a colorless oil. TLC: Rf = 0.40 (cyclohexane/EtOAc = 9/1). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 8.07 (d, J = 8.0 Hz, 1H, 4-Hpyridyl), 7.18 (d, J = 8.0 Hz, 1H, 5-Hpyridyl), 4.29 (q, J = 7.1 Hz, 2H, OCH2CH3), 2.68 (s, 3H, CH3), 2.60 (d, J = 7.2 Hz, 2H, CH2), 2.05 (m, 1H, CH), 1.31 (t, J = 7.1 Hz, 3H, OCH2CH3), 0.87 (s, 3H, (CH)CH3), 0.86 (s, 3H, (CH)CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 166.1 (1C, C=O), 163.8 (1C, 6-Cpyridyl), 158.0 (1C, 2-Cpyridyl), 138.2 (1C, 4-Cpyridyl), 122.5 (1C, 3-Cpyridyl), 120.8 (1C, 5-Cpyridyl), 60.8 (1C, OCH3), 46.6 (1C, CH2), 28.3 (CH), 24.4 (1C, CH), 22.2 (2C, (CH)CH3), 14.1 (1C, OCH3). IR (neat): ν [cm⁻¹] = 2954, 1716, 1589, 1267, 1147, 1076. HRMS (APCI): m/z = 222.1489 calculated for C13H20NO₂⁺ [M+H]⁺, found: 222.1502.

2-Methyly-6-phenylnicotinohydrazone (28a). Synthesized according to general procedure A. Ester 27a (900 mg, 3.73 mmol, 1.0 eq.) was suspended in hydrazine monohydrate (4.0 mL) and refluxed for 3 h. The crude product was purified (DCM/MeOH = 1/0 → 89/11) yielding hydrazone 28a as a colorless solid (705 mg, 3.10 mmol, 83%). M.p. = 146.5 °C. TLC: Rf = 0.32 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.60 (bs, 1H, NH), 8.11–8.09 (m, 2H, 2-/6-Hphenyl), 7.83 (d, J = 8.1, 1H, 5-Hpyridyl), 7.76 (d, J = 8.0 Hz, 1H, 4-Hpyridyl), 7.52–7.48 (m, 2H, 3-/5-Hpyridyl), 7.47–7.43 (m, 1H, 4-Hphenyl), 4.53 (bs, 2H, NH2), 2.60 (s, 3H, CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 167.2 (1C, C=O), 155.8 (1C, 6-Cpyridyl), 155.6 (1C, 2-Cpyridyl), 138.0 (1C, 4-Cphenyl), 136.4 (1C, 4-Cphenyl), 129.3 (1C, 4-Cphenyl), 129.2 (1C, 3-Cpyridyl), 128.8 (2C, 3-/5-Cphenyl), 126.7 (2C, 2-/6-Cphenyl), 117.0 (1C, 5-Cpyridyl), 23.0 (1C, CH3). IR (neat): ν [cm⁻¹] = 3315, 3294, 3192, 1633, 1581, 1450, 1301, 680. HRMS (APCI): m/z = 228.1131 calculated for C13H14N3O⁺ [M+H]⁺, found: 228.1131.

6-(2-Bromophenyl)-2-methylnicotinohydrazone (28b). Synthesized according to general procedure A. Ester 27b (2.13 g, 6.65 mmol, 1.0 eq.) was suspended in hydrazine monohydrate (5.0 mL) and refluxed for 1 h. The crude product was purified (DCM/MeOH = 1/0 → 9/1) yielding hydrazone 28b as a colorless solid (1.43 g, 4.67 mmol, 70%). M.p. = 199 °C. TLC: Rf = 0.14 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.67 (bs, 1H, NH), 7.77 (d, J = 7.8 Hz, 1H, 4-Hpyridyl), 7.76–7.74 (m, 1H, 3-/4-/5-/6-Hbromophenyl), 7.51–7.49 (m, 2H, 3-/4-/5-/6-Hbromophenyl), 7.49 (d, J = 7.9 Hz, 1H, 5-Hpyridyl), 7.40–7.36 (m, 1H, 3-/4-/5-/6-Hbromophenyl), 4.56 (bs, 2H, NH2), 2.57 (s, 3H, CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 167.0 (1C, C=O), 157.5 (1C, 6-Cpyridyl), 155.3 (1C, 2-Cpyridyl), 140.5 (1C, 4-Cphenyl), 135.4 (1C, 4-Cpyridyl), 133.0 (1C, 3-/4-/5-/6-Cbromophenyl), 131.5 (1C, 4-/5-/6-Cbromophenyl), 130.3 (1C, 3-/4-/5-/6-Cbromophenyl), 129.6 (1C, 3-/4-/5-/6-Cbromophenyl), 127.8 (1C, 3-/4-/5-/6-Cbromophenyl), 121.4 (1C, 5-Cpyridyl), 121.0 (1C, 2-Cbromophenyl), 22.7 (1C, CH3). IR (neat): ν [cm⁻¹] = 3315, 3294, 3194, 1643, 1583, 1502, 1454, 1022, 742. HRMS (APCI): m/z = 306.0237 calculated for C13H13BrN3O⁺ [M+H]⁺, found: 306.0245.

6-(3,4-Dimethoxyphenyl)-2-methylnicotinohydrazone (28c). Synthesized according to general procedure A. Ester 27c (1.30 g, 4.31 mmol, 1.0 eq.) was suspended hydrazine monohydrate (5.0 mL) and refluxed for 3 h. The crude product was purified (DCM/MeOH = 1/0 → 88/12) yielding hydrazone 28c as colorless solid (1.08 g, 3.76 mmol, 87%). M.p. = 198.5 °C. TLC: Rf = 0.29 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.57 (bs, 1H, NH), 7.80 (d, J = 8.1 Hz, 1H, 4-Hpyridyl), 7.72 (d, J = 8.1 Hz, 1H, 5-Hpyridyl), 7.70 (d, J = 2.1 Hz, 1H, 2-Hdimethoxyphenyl), 7.68 (dd, J = 8.3, 2.1 Hz, 1H, 6-Hdimethoxyphenyl), 7.06 (d, J = 8.4 Hz, 1H, 5-Hdimethoxyphenyl), 4.51 (bs, 2H, NH2), 3.85 (s, 3H, -OCH3), 3.82 (s, 3H, -OCH3), 2.59 (s, 3H, -CH3).
13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 167.3 (1C, C=O), 155.6 (1C, 6-Cpyridyl), 155.4 (1C, 2-Cpyridyl), 150.1 (1C, 4-Cdimethoxyphenyl), 148.9 (1C, 3-Cdimethoxyphenyl), 136.2 (1C, 5-Cpyridyl), 130.7 (1C, 1-Cdimethoxyphenyl), 128.3 (1C, 3-Cpyridyl), 119.5 (1C, 6-Cdimethoxyphenyl), 116.3 (1C, 4-Cpyridyl), 111.7 (1C, 5-Cdimethoxyphenyl), 109.9 (1C, 2-Cdimethoxyphenyl), 55.6 (2C, -OCH3), 23.1 (1C, -CH3). IR (neat): ν [cm⁻¹] = 3273, 3209, 2841, 1614, 1581, 1417, 1274, 1020. HRMS (APCI): m/z = 288.1343 calculated for C15H18N3O3+ [M+H]+, found: 288.1344.

6-(4-Isobutylphenyl)-2-methylnicotinohydrazide (28d). Synthesized according to general procedure A. Ester 27d (1.20 g, 4.03 mmol, 1.0 eq.) was dissolved in EtOH (abs., 3.0 mL) followed by the addition of hydrazine monohydrate (8.0 mL) and the mixture was refluxed for 9 h. The crude product was purified (DCM/MeOH = 1/0 → 88/12) yielding hydrazide 28d as colorless solid (819 mg, 2.89 mmol, 72%). M.p. = 147 °C. TLC: Rf = 0.40 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.58 (bs, 1H, NH), 8.01 (m, 2H, 2-/6-Hisobutylphenyl), 7.79 (d, J = 8.1 Hz, 1H, 4-Hpyridyl), 7.74 (d, J = 8.1 Hz, 1H, 4-Hpyridyl), 7.29–7.26 (m, 2H, 3-/5-Hisobutylphenyl), 4.51 (bs, 2H, NH2), 2.59 (s, 3H, -CH3), 2.50 (d, J = 7.0 Hz, 2H, -CH2-), 1.87 (m, 1H, -CH-), 0.89 (s, 3H, -CH(CH3)2), 0.88 (s, 3H, -(CH)CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 167.2 (1C, C=O), 155.9 (1C, 6-Cpyridyl), 155.5 (1C, 2-Cpyridyl), 142.6 (1C, 4-Cisobutylphenyl), 136.3 (1C, 4-Cpyridyl), 135.6 (1C, 1-Cisobutylphenyl), 129.4 (2C, 3-/5-Cisobutylphenyl), 128.8 (1C, 3-Cpyridyl), 126.5 (2C, 2-/6-Cisobutylphenyl), 116.7 (1C, 5-Cpyridyl), 44.3 (1C, -CH2-), 29.6 (1C, -CH-), 23.0 (1C, -CH3), 22.2 (2C, -(CH)CH3). IR (neat): ν [cm⁻¹] = 3290, 2949, 1597, 1585, 1519, 1301, 974, 956, 831. HRMS (APCI): m/z = 284.1757 calculated for C17H14N3O2+ [M+H]+, found: 284.1769.

6-Methyl-[2,3′-bipyridine]-5-carboxyhydrazide (28e). Synthesized according to general procedure A. Ester 27e (1.15 g, 4.75 mmol, 1.0 eq.) was suspended in hydrazine monohydrate (5.0 mL) and refluxed for 1 h. The crude product was purified (DCM/MeOH = 1/0 → 9/1) yielding hydrazide 28e as a colorless solid (847 mg, 3.71 mmol, 78%). M.p. = 174 °C. TLC: Rf = 0.17 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.63 (bs, 1H, NH), 9.27 (dd, J = 2.4, 0.9 Hz, 1H, 2′-Hpyridyl), 8.65 (dd, J = 4.7, 1.6 Hz, 1H, 6′-Hpyridyl), 8.45 (dd, J = 8.0, 2.3, 1.7 Hz, 1H, 4′-Hpyridyl), 7.94 (d, J = 8.0 Hz, 1H, 3′-Hpyridyl), 7.81 (d, J = 8.0 Hz, 1H, 4-Hpyridyl), 7.53 (dd, J = 8.0, 4.8, 0.9 Hz, 1H, 5′-Hpyridyl), 4.54 (bs, 2H, -NH2), 2.61 (s, 3H, -CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 167.0 (1C, C=O), 156.0 (1C, 6-Cpyridyl), 153.6 (1C, 2-Cpyridyl), 150.1 (1C, 6′-Cpyridyl), 147.9 (1C, 2′-Cpyridyl), 136.6 (1C, 4-Cpyridyl), 134.1 (1C, 4′-Cpyridyl), 133.5 (1C, 3′-Cpyridyl), 129.8 (1C, 5-Cpyridyl), 123.8 (1C, 5′-Cpyridyl), 117.5 (1C, 3-Cpyridyl), 23.0 (1C, -CH3). IR (neat): ν [cm⁻¹] = 3223, 2980, 1643, 1581, 1421, 1298, 1026, 929, 702. HRMS (APCI): m/z = 293.1328 calculated for C17H15N2O2+ [M+H]+, found: 293.1327.

2-Methyl-6-(thiophen-2-yl)nicotinohydrazide (28f). Synthesized according to general procedure A. Ester 27f (1.20 g, 4.97 mmol, 1.0 eq.) was suspended in hydrazine monohydrate (5.0 mL) and refluxed for 3 h. The crude product was purified (DCM/MeOH = 1/0 → 9/1) yielding hydrazide 28f as a colorless solid (905 mg, 3.98 mmol, 80%). M.p. = 170 °C. TLC: Rf = 0.28 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.57 (bs, 1H, NH), 7.83 (dd, J = 3.7, 1.2 Hz, 1H, 3′-Hthiophenyl), 7.78 (d, J = 8.1 Hz, 1H, 5-Hpyridyl), 7.71 (d, J = 8.1 Hz, 1H, 4-Hpyridyl), 7.66 (dd, J = 5.0, 1.1 Hz, 1H, 5′-Hthiophenyl), 7.17 (dd, J = 5.1, 3.7 Hz, 1H, 4-Hthiophenyl), 4.51 (bs, 2H, -NH2), 2.54 (s, 3H, -CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 167.0 (1C, C=O), 155.7 (1C, 2-Cpyridyl), 151.7 (1C, 6-Cpyridyl), 143.9 (1C, 2′-Cthiophenyl), 136.4 (1C, 4-Cpyridyl), 129.0 (1C, 5-Cthiophenyl), 128.7 (1C, 3-Cpyridyl), 128.5 (1C, 4′-Cthiophenyl), 125.9 (1C, 3-Cthiophenyl), 115.5 (1C, 5-Cpyridyl), 22.8 (1C, -CH3). IR (neat): ν [cm⁻¹] = 3311, 3288, 3190, 3064, 1639, 1585, 1504, 1294, 821. HRMS (APCI): m/z = 234.0696 calculated for C11H12N3OS+ [M+H]+, found: 234.0709.
6-Isobutyl-2-methylnicotinohydrazide (28g). Synthesized according to general procedure A. Ester 27g (1.70 g, 7.68 mmol, 1.0 eq.) was suspended in hydrazine monohydrate (8.0 mL) and refluxed for 5 h. The crude product was purified (DCM/MeOH = 1/0 → 9/1) yielding hydrazide 28g as a colorless solid (1.39 g, 6.71 mmol, 87%). M.p. = 143 °C. TLC: Rf = 0.25 (DCM/MeOH = 93/7).

1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 9.49 (bs, 1H, NH), 7.57 (d, J = 7.9 Hz, 1H, 4-Hpyridyl), 7.07 (d, J = 7.8 Hz, 1H, 5-Hpyridyl), 4.47 (bs, 2H, NH2), 2.56 (d, J = 7.2 Hz, 2H, -CH2-), 2.48 (s, 3H, -CH3), 2.03 (m, 1H, CH), 0.88 (s, 3H, -CH(CH3)2), 0.87 (s, 3H, -CH(CH3)). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 167.5 (1C, C=O), 161.1 (1C, 2-Cpyridyl), 154.9 (1C, 6-Cpyridyl), 135.4 (1C, 4-Cpyridyl), 127.9 (1C, 3-Cpyridyl), 120.1 (1C, 5-Cpyridyl), 46.5 (1C, -CH2-), 28.4 (1C, -CH3), 22.7 (1C, -CH3), 22.2 (2C, -CH(CH3)). IR (neat): ν [cm⁻¹] = 3280, 3261, 3143, 2949, 2866, 1625, 1589, 1529, 1325, 968, 875. HRMS (APCI): m/z = 208.1444 calculated for C11H18N3O+ [M+H]+, found: 208.1440.

3-(2-Methyl-6-phenylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29a). Synthesized according to general procedure B. Hydrazide 28a (722 mg, 3.18 mmol, 1.00 eq.) and S-methylisothiouroium sulfate (443 mg, 1.59 mmol, 0.50 eq.) were suspended in EtOH (50%, 24 mL) and refluxed for 4 d. After 24 h, additional S-methylisothiouroium sulfate (222 mg, 795 μmol, 0.25 eq.) was added to the reaction mixture and refluxing was continued for 3 d. After adding KOH (1.20 g), the mixture was refluxed for an additional 3 h and work-up performed as described above. The crude product was purified (1. DCM/MeOH = 1/0 → 9/1, 2. DCM/MeOH = 1/0 → 9/1) yielding triazole 29a as a colorless solid (379 mg, 1.51 mmol, 47%). M.p. = 195.5 °C. TLC: Rf = 0.38 (DCM/MeOH = 93/7).

1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.24 (bs, 1H, NH), 8.27 (d, J = 8.2 Hz, 1H, 4-Hpyridyl), 8.14–8.10 (m, 2H, 2-/6-Hphenyl), 7.85 (d, J = 8.1 Hz, 1H, 5-Hpyridyl), 7.51–7.47 (m, 2H, 3-/5-Hphenyl), 7.45–7.40 (m, 1H, 4-Hphenyl), 6.14 (bs, 2H, -NH2), 2.87 (s, 3H, -CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 157.6 (1C, 3-Ctriaryl), 156.9 (1C, 5-Ctriaryl), 155.3 (1C, 2-Cpyridyl), 153.9 (1C, 6-Cpyridyl), 138.4 (1C, 1-Cphenyl), 136.9 (1C, 4-Cpyridyl), 128.9 (1C, 4-Cphenyl), 128.7 (2C, 3-/5-Cphenyl), 126.4 (2C, 2-/6-Cphenyl), 125.4 (1C, 3-Cpyridyl), 117.3 (1C, 4-Cphenyl), 25.4 (1C, CH3). IR (neat): ν [cm⁻¹] = 3468, 3315, 3190, 3061, 2698, 1633, 1402, 1056, 850. HRMS (APCI): m/z = 252.1244 calculated for C14H14N3S+ [M+H]+, found: 252.1267.

3-(6-(2-Bromophenyl)-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29b). Synthesized according to general procedure B. Hydrazide 28b (1.32 g, 4.31 mmol, 1.00 eq.) and S-methylisothiouroium sulfate (601 mg, 2.16 mmol, 0.50 eq.) were suspended in EtOH (30%, 36 mL) and refluxed for 4 d. After 24 h, additional S-methylisothiouroium sulfate (300 mg, 1.08 mmol, 0.25 eq.) was added to the reaction mixture and refluxing was continued for 3 d. After adding KOH (1.25 g), the mixture was refluxed for an additional 3 h and work-up was performed as described above. The crude product was purified (1. DCM/MeOH = 1/0 → 88/12, 2. DCM/MeOH = 1/0 → 88/12), yielding triazole 29b as a colorless solid (587 mg, 1.68 mmol, 41%). M.p. = 246 °C. TLC: Rf = 0.22 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.26 (bs, 1H, NH), 8.26 (d, J = 8.0 Hz, 1H, 4-Hpyridyl), 7.74 (dd, J = 8.1, 1.2 Hz, 1H, 3-/6-Hbromophenyl), 7.55 (dd, J = 7.7, 1.8 Hz, 1H, 3-/6-Hbromophenyl), 7.51–7.47 (m, 2H, 4-/5-Hbromophenyl, 5-Hpyridyl), 7.37 (td, J = 7.7, 1.8 Hz, 1H, 4-/5-Hbromophenyl), 6.16 (bs, 2H, NH2), 2.83 (s, 3H, CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 157.5 (1C, 3-Ctriaryl), 156.9 (1C, 5-Ctriaryl), 155.7 (1C, 6-Cpyridyl), 155.2 (1C, 2-Cpyridyl), 140.8 (1C, 1-Cbromophenyl), 135.9 (1C, 4-Cpyridyl), 133.0 (1C, 3-/6-Cbromophenyl), 131.5 (1C, 3-/6-Cbromophenyl), 130.1 (1C, 4-/5-Cbromophenyl), 127.8 (1C, 4-/5-Cbromophenyl), 125.6 (1C, 3-Cpyridyl), 121.6 (1C, 5-Cpyridyl), 121.1 (1C, 2-Cbromophenyl), 25.0 (1C, -CH3). IR (neat): ν [cm⁻¹] = 3458, 3311, 3091, 1651, 1402, 848. HRMS (APCI): m/z = 330.0349 calculated for C14H13BrN3S+ [M+H]+, found: 330.0362.
3-(6-(3,4-Dimethoxyphenyl)-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29c). Synthesized according to general procedure B. Hydrazide 28c (800 mg, 2.78 mmol, 1.00 eq.) and S-methylisothiouroium sulfate (581 mg, 2.09 mmol, 0.75 eq.) were suspended in EtOH (50%, 18 mL) and refluxed for 4 d. After adding KOH (900 mg), the mixture was refluxed for additional 3 h and work-up was performed as described above. The crude product was purified (1. DCM/MeOH = 1/0 → 9/1, 2. DCM/MeOH = 1/0 → 9/1), yielding triazole 29c as colorless a solid (478 mg, 1.78 mmol, 55%). M.p. = 268 °C. TLC: Rf = 0.19 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.21 (bs, 1H, NH), 8.22 (d, J = 8.2 Hz, 1H, 4'-Hpyridyl), 7.81 (d, J = 8.2 Hz, 1H, 5'-Hpyridyl), 7.73 (d, J = 2.1 Hz, 1H, 2-Hdimethoxyphenyl), 7.69 (dd, J = 8.4, 2.1 Hz, 1H, 6-Hdimethoxyphenyl), 7.05 (d, J = 8.5 Hz, 1H, 5-Hdimethoxyphenyl), 6.12 (bs, 2H, NH2), 3.86 (s, 3H, -OCH3), 3.81 (s, 3H, -OCH3), 2.85 (s, 3H, -CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 157.7 (1C, 3-Ctriazolyl), 156.8 (1C, 5-Ctriazolyl), 155.0 (1C, 2-Cpyridyl), 153.7 (1C, 6-Cpyridyl), 149.8 (1C, 4-Cdimethoxyphenyl), 148.9 (1C, 3-Cdimethoxyphenyl), 136.7 (1C, 4-Cpyridyl), 131.1 (1C, 1-Cdimethoxyphenyl), 124.6 (1C, 3-Cpyridyl), 119.2 (1C, 6-Cdimethoxyphenyl), 116.6 (1C, 5-Cpyridyl), 111.7 (1C, 5-Cdimethoxyphenyl), 109.8 (1C, 2-Cdimethoxyphenyl), 55.5 (2C, -OCH3), 25.5 (1C, -CH3). IR (neat): ν [cm⁻¹] = 3429, 3323, 3238, 2839, 1643, 1541, 1271, 1018. HRMS (APCI): m/z = 312.1455 calculated for C16H18N2O2+ [M+H]+, found: 312.1480.

3-(6-(4-Isobutylphenyl)-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29d). Synthesized according to general procedure B. Hydrazide 28d (726 mg, 2.56 mmol, 1.00 eq.) and S-methylisothiouroium sulfate (581 mg, 2.09 mmol, 0.75 eq.) were suspended in EtOH (50%, 18 mL) and refluxed for 4 d. After adding KOH (900 mg), the mixture was refluxed for additional 3 h and work-up was performed as described above. The crude product was purified (1. DCM/MeOH = 1/0 → 91/9, 2. DCM/MeOH = 1/0 → 9/1), yielding triazole 29d as colorless a solid (343 mg, 1.12 mmol, 44%). M.p. = 201 °C. TLC: Rf = 0.01 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.23 (bs, 1H, NH), 8.24 (d, J = 8.2 Hz, 1H, 4'-Hpyridyl), 8.04–8.01 (m, 2H, 2/-6-Hisobutylphenyl), 7.81 (d, J = 8.2 Hz, 1H, 5'-Hpyridyl), 7.28–7.25 (m, 2H, 3/-5-Hisobutylphenyl), 6.13 (bs, 2H, NH2), 2.85 (s, 3H, CH3), 2.50 (d, J = 7.3 Hz, 2H, CH2), 1.91–1.83 (m, 1H, CH), 0.89 (s, 3H, (CH)CH3), 0.88 (s, 3H, (CH)CH3). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 157.7 (1C, 3-Ctriazolyl), 156.8 (1C, 5-Ctriazolyl), 155.2 (1C, 2-Cpyridyl), 154.0 (1C, 6-Cpyridyl), 142.1 (1C, 4-Cisobutylphenyl), 136.8 (1C, 4-Cpyridyl), 135.9 (1C, 1-Cisobutylphenyl), 129.3 (2C, 3/-5-Cisobutylphenyl), 126.3 (2C, 2/-6-Cisobutylphenyl), 125.0 (1C, 3-Cpyridyl), 117.0 (1C, 5-Cpyridyl), 44.3 (1C, CH2), 29.6 (1C, CH), 25.4 (1C, CH3), 22.2 (2C, (CH)CH3). IR (neat): ν [cm⁻¹] = 3468, 3331, 2953, 1645, 1597, 1537, 1392, 1163, 981. HRMS (APCI): m/z = 308.1870 calculated for C18H16N2O2+ [M+H]+, found: 308.1899.

3-(6-Methyl-[2,3'-bipyridin]-5-yl)-1H-1,2,4-triazol-5-amine (29e). Synthesized according to general procedure B. Hydrazide 28e (500 mg, 2.19 mmol, 1.00 eq.) and S-methylisothiouroium sulfate (304 mg, 1.10 mmol, 0.50 eq.) were suspended in H2O (10 mL) and refluxed for 4 d. After 24 h, additional S-methylisothiouroium sulfate (152 mg, 550 μmol, 0.25 eq.) was added to the reaction mixture and refluxing was continued for 3 d. After adding KOH (500 mg), the mixture was refluxed for additional 3 h and work-up was performed as described above. The crude product was purified (DCM/MeOH = 1/0 → 9/1), yielding triazole 29e as colorless a solid (319 mg, 1.26 mmol, 58%). M.p. = 229 °C. TLC: Rf = 0.13 (DCM/MeOH = 93/7). 1H-NMR (600 MHz, DMSO-d6, 299 K): δ (in ppm) = 12.28 (bs, 1H, NH), 9.30–9.28 (m, 1H, 2'-Hpyridyl), 8.62 (dd, J = 4.7, 1.6 Hz, 1H, 6'-Hpyridyl), 8.46 (dt, J = 8.1, 2.0 Hz, 1H, 4'-Hpyridyl), 8.31 (d, J = 8.2 Hz, 1H, 1H, 4'-Hpyridyl), 7.94 (d, J = 8.1 Hz, 1H, 3'-Hpyridyl), 7.52 (ddd, J = 8.0, 4.7, 0.9 Hz, 1H, 5'-Hpyridyl), 2.88 (s, 3H, CH3), 6.17 (bs, 2H, NH2). 13C-NMR (151 MHz, DMSO-d6, 299 K): δ (in ppm) = 157.4 (1C, 3-Ctriazolyl), 156.9 (1C, 5-Ctriazolyl), 155.7 (1C, 4-Cpyridyl), 151.7 (1C, 2-Cpyridyl), 149.8 (1C, 6'-Cpyridyl), 147.8 (1C, 2'-Cpyridyl), 137.0 (1C, 4-Cpyridyl), 133.8 (1C, 4'-Cpyridyl), 133.7 (1C, 3'-Cpyridyl),
123.8 (1C, 5'-C-pyridyl), 117.8 (1C, 3-C-pyridyl), 25.4 (1C, CH3). IR (neat): ν [cm⁻¹] = 3305, 3107, 2787, 1566, 1415, 1379, 1056, 767. HRMS (APCI): m/z = 253.1196 calculated for C13H13N6⁻ [M+H]⁻, found: 253.1216.

3-(2-Methyl-6-(thiophen-2-yl)pyridin-3-yl)-1H-1,2,4-triazol-5-amine (29f). Synthesized according to general procedure B. Hydrazide 28f (850 mg, 3.64 mmol, 1.00 eq.) and S-methylisothiouroum sulfate (507 mg, 1.82 mmol, 0.50 eq.) were suspended in EtOH (50%, 24 mL) and refluxed for 4 d. After 24 h, additional S-methylisothiouroum sulfate (254 mg, 910 μmol, 0.25 eq.) was added to the reaction mixture and refluxing was continued for 3 d. After adding KOH (1.20 g), the mixture was refluxed for additional 3 h and work-up was performed as described above. The crude product was purified (1. DCM/MeOH = 1/0 → 9/1, 2. DCM/MeOH = 1/0 → 9/1), yielding triazole 29f as a colorless solid (433 mg, 1.68 mmol, 46%). M.p. = 230.5 °C. TLC: Rf = 0.40 (DCM/MeOH = 93/7). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.24 (bs, 1H, NH), 8.21 (d, J = 8.2 Hz, 1H, 4-H(pyrindyl), 7.79–7.76 (m, 2H, 3-H thiophenyl, 5-H(pyrindyl)), 7.62 (dd, J = 5.1, 1.1 Hz, 1H, 5-H(thiophenyl)), 7.16 (dd, J = 5.0, 3.7 Hz, 1H, 4-H(thiophenyl)), 6.13 (bs, 2H, NH2), 2.80 (s, 3H, CH3). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 157.5 (1C, 3-C(3-thiophenyl)), 156.8 (1C, 5-C(3-thiophenyl)), 155.3 (1C, 2-C(pyrinyl)), 150.0 (1C, 6-C(pyrinyl)), 144.4 (1C, 2-C(thiophenyl)), 136.7 (1C, 4-C(pyrindyl)), 128.3 (1C, 4-/5-C(thiophenyl)), 128.1 (1C, 4-/5-C(thiophenyl)), 125.1 (1C, 3-C(thiophenyl)), 125.0 (1C, 3-C(pyridyl)), 115.9 (1C, 5-C(pyridyl)), 25.1 (1C, CH3). IR (neat): ν [cm⁻¹] = 3462, 3311, 3086, 2698, 1631, 1583, 1415, 1056, 769. HRMS (APCI): m/z = 258.0808 calculated for C₁₂H₁₂N₅S⁻ [M+H]⁻, found: 258.0805.

3-(6-Isobutyl-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29g). Synthesized according to general procedure B. Hydrazide 28g (1.00 g, 4.82 mmol, 1.00 eq.) and S-methylisothiouroum sulfate (1.01 g, 3.62 mmol, 0.75 eq.) were suspended in EtOH (50%, 32 mL) and refluxed for 4 d. After adding KOH (1.60 g), the mixture was refluxed for additional 3 h and work-up was performed as described above. The crude product was purified (1. DCM/MeOH = 1/0 → 9/1, 2. DCM/MeOH = 1/0 → 9/1), yielding triazole 29g as a colorless solid (224 mg, 968 μmol, 20%). M.p. = 223.6 °C. TLC: Rf = 0.12 (DCM/MeOH = 93/7). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.14 (bs, 1H, NH), 8.04 (d, J = 7.9 Hz, 1H, 4-H(pyrindyl)), 7.07 (d, J = 8.0 Hz, 1H, 5-H(pyrindyl)), 6.08 (bs, 2H, NH2), 2.56 (d, J = 7.2 Hz, 2H, CH2), 2.72 (s, 3H, CH3), 2.08–2.01 (m, 1H, CH), 0.88 (s, 3H, (CH)CH3), 0.89 (s, 3H, (CH)CH3). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 159.2 (1C, 2-C(pyridyl)), 157.9 (1C, 3-C(3-thiophenyl)), 156.8 (1C, 5-C(3-thiophenyl)), 154.7 (1C, 6-C(pyridyl)), 136.0 (1C, 4-C(pyridyl)), 124.1 (1C, 3-C(pyridyl)), 120.4 (1C, 5-C(pyridyl)), 46.5 (1C, CH3), 28.4 (1C, CH), 25.0 (1C, CH3), 22.3 (2C, (CH)CH3). IR (neat): ν [cm⁻¹] = 3238, 3101, 2954, 1587, 1381, 1309, 1149, 848. HRMS (APCI): m/z = 253.1557 calculated for C₁₂H₁₈N₅S⁻ [M+H]⁻, found: 232.1560.

(1S,2R,3S)-1-(quinoxalin-2-yl)butane-1,2,3,4-tetraol (35). 1,2-Phenylenediamine (3.30 g, 30.51 mmol) was suspended in AcOH solution (aq., 10%, 20 mL) and d-fructose was added (6.32 g, 35.08 mmol, 1.2 eq.). The reaction mixture was heated up to 80 °C and stirred for 18 h. After cooling down to r.t., the suspension was cooled down to 4 °C for 4 h. The formed precipitate was filtered off and washed vigorously with H₂O. The brown solid was dried at 60 °C for 24 h and used without further purification (3.03 g, 12.12 mmol, 40%). M.p. = 180 °C (decomp.). TLC: Rf = 0.18 (DCM/MeOH = 9/1). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 9.09 (s, 1H, 3-H(quinoxaline), 8.10–8.07 (m, 1H, 5-H(quinoxaline), 8.06–8.03 (m, 1H, 8-H(quinoxaline), 7.86–7.82 (m, 1H, 7-H(quinoxaline), 7.82–7.79 (m, 1H, 6-H(quinoxaline), 5.60 (d, J = 6.2 Hz, 1H, 1'-OH(butyl)), 5.15 (dd, J = 6.1, 1.2 Hz, 1H, 1'-CH(butyl)), 4.71–4.70 (m, 1H, 2'-OH(butyl)), 4.63–4.61 (m, 1H, 3'-OH(butyl)), 4.39 (t, J = 5.6 Hz, 1H, 4'-OH(butyl)), 3.69–3.63 (m, 3H, 2'/3'-4'-CH(butyl), 3.49–3.43 (m, 1H, 4'-CH(butyl)). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 159.5 (1C, 2'-C(quinoxaline) 145.2 (1C,
3-C-quinualine), 141.0 (4a-C-quinualine), 140.8 (1C, 8a-C-quinualine), 130.0 (1C, 7-C-quinualine), 129.3 (1C, 6-C-quinualine), 128.9 (1C, 5-C-quinualine), 128.6 (1C, 8-C-quinualine), 74.3 (1C, 3-C-buty1), 72.5 (1C, 1-C-buty1) 71.2 (1C, 2-C-buty1), 63.5 (1C, 4-C-buty1). IR (neat): \(\tilde{\nu}\) [cm\(^{-1}\)] = 3659, 3401, 3327, 3163, 2980, 2884, 1495, 1447, 1371, 1256, 1153, 1107, 1091, 1043, 957, 901, 874, 810. HRMS (APCI): \(m/z = 251.1027\) calculated for \(\text{C}_{12}\text{H}_{15}\text{N}_{2}\text{O}_{4}^{+} [\text{M+H}]^{+}\), found: 251.1026.

**Quinaline-2-carboxylic acid (36).** Compound 35 (7.00 g, 27.97 mmol) was suspended in NaOH-solution (aq., 10%, 150 mL) at 40 °C. To this suspension, the first portion of \(\text{H}_2\text{O}\) (30%, 12 mL) was added dropwise under continuous stirring at 40 °C. After complete addition, the reaction mixture was heated up to 60 °C and stirred for 3 h. The second portion \(\text{H}_2\text{O}\) (30%, 12 mL) was added dropwise at 60 °C, the reaction mixture was continued stirring at 60 °C. After 30 min, the reaction mixture was heated up to reflux for another 30 min. The solution was let cool down to 80 °C and was decanted from a black, tar-like solid. The solution was acidified with HCl (conc.) and stored at 4 °C for 18 h. The formed precipitate was filtered off and washed with \(\text{H}_2\text{O}\). After drying in vacuo, the product was obtained as an off-white solid (2.86 g, 16.42 mmol, 59%), no further purification was necessary. M.p. = 196 °C (decomp.). TLC: 0.34 (DCM/MeOH = 4/1). \(^1\)H-NMR (600 MHz, DMSO-d\(_6\), 299 K): \(\delta\) (in ppm) = 13.95 (s, 1H, -OH), 9.43 (s, 1H, 3-H-quinualine), 8.26–8.21 (m, 1H, 8-H-quinualine), 8.20–8.17 (m, 1H, 5-H-quinualine), 8.03–7.99 (m, 1H, 7-H-quinualine), 7.99–7.95 (m, 1H, 6-H-quinualine). \(^13\)C-NMR (151 MHz, DMSO-d\(_6\), 299 K): \(\delta\) (in ppm) = 165.2 (1C, C=O), 145.2 (1C, 3-C-quinualine), 143.6 (1C, 2-C-quinualine), 142.7 (1C, 4a-C-quinualine), 140.8 (1C, 8a-C-quinualine), 132.4 (1C, 6-C-quinualine), 131.2 (1C, 7-C-quinualine), 130.0 (1C, 8-C-quinualine), 129.0 (1C, 5-C-quinualine). IR (neat): \(\tilde{\nu}\) [cm\(^{-1}\)] = 3440, 3040, 1690, 1570, 1490 1300, 1100. HRMS (APCI): \(m/z = 175.0502\) calculated for \(\text{C}_9\text{H}_7\text{N}_2\text{O}_2^{+} [\text{M+H}]^{+}\), found: 175.0526.

**Ethyl quinaline-2-carboxylate (37).** Compound 36 (2.00 g, 11.5 mmol, 1.0 eq.) was suspended in EtOH (30 mL, abs.) and cooled down to 0 °C under nitrogen atmosphere. SOC\(_2\)l (7.00 mL, 96.5 mmol, 8.4 eq.) were added dropwise into the cold solution upon stirring. After complete addition, the reaction mixture was heated up to reflux for 3 h. The excess SOC\(_2\)l was distilled off, the residue was suspended in \(\text{H}_2\text{O}\), neutralized using Na\(_2\)CO\(_3\)-solution (aq., sat.) and extracted with EtOAc (4×, equal amount). The combined organic layers were dried over Na\(_2\)SO\(_4\). After purification with flash chromatography (cyclohexane/EtOAc = 1/0 → 75/25) the product was obtained as a reddish solid (2.11 g, 10.45 mmol, 91%). M.p. = 80–84 °C. TLC: 0.37 (cyclohexane/EtOAc = 4/1). \(^1\)H-NMR (600 MHz, DMSO-d\(_6\), 299 K): \(\delta\) (in ppm) = 9.43 (s, 1H, 3-H-quinualine), 8.29–8.23 (m, 1H, 5/H-quinualine), 8.21–8.18 (m, 1H, 5-8/H-quinualine), 8.05–7.95 (m, 2H, 6/-7/H-quinualine), 4.47 (q, \(J = 7.1\) Hz, 2H, -CH\(_2\)-), 1.40 (t, \(J = 7.1\) Hz, 3H, -CH\(_3\)). \(^13\)C-NMR (151 MHz, DMSO-d\(_6\), 299 K): \(\delta\) (in ppm) = 163.6 (1C, C=O), 144.9 (1C, 3-C-quinualine), 142.8 (1C, 2-C-quinualine), 142.7 (1C, 4a-C-quinualine), 140.7 (1C, 8a-C-quinualine), 132.6 (1C, 6-C-quinualine), 131.4 (1C, 7-C-quinualine), 130.0 (1C, 8-C-quinualine), 129.0 (1C, 5-C-quinualine), 61.4 (1C, -OCH\(_2\)-), 14.5 (1C, -CH\(_3\)). IR (neat): \(\tilde{\nu}\) [cm\(^{-1}\)] = 2980, 2889, 1708, 1466, 1366, 1315, 1232, 1204, 1155, 1128, 1018, 978, 970. HRMS (APCI): \(m/z = 203.0815\) calculated for \(\text{C}_{11}\text{H}_{15}\text{N}_{2}\text{O}_{2}^{+} [\text{M+H}]^{+}\), found: 203.0835.

3-(Quinalin-2-yl)-1H-1,2,4-triazol-5-amine (38). Potassium hydroxide (373 mg, 6.65 mmol, 5.0 eq.) was dissolved in EtOH (5 mL, dry). Aminoguanidine hydrochloride (735 mg, 6.65 mmol, 5.0 eq.) were added, the resulting suspension was stirred at r.t. for 3 h under nitrogen atmosphere. The precipitate was filtered off, washed with EtOH (10 mL, dry) and the filtrate was concentrated to give an orange oil. To this oil, compound 37 (269 mg, 1.33 mmol, 1.0 eq.) dissolved in EtOH (3 mL, dry) was added. The reaction mixture was heated up to 80 °C stirred for 24 h under nitrogen atmosphere. The resulting suspension was let cool down to r.t. and neutralized using HCl (1M, 1 mL). The formed precipitate was filtered off and washed with \(\text{H}_2\text{O}\) and Et\(_2\)O and dried in vacuo to give a mixture of the desired product and an open-chain intermediate (N-carbamohydrazonoyl

S29
amide). This mixture was redissolved in H₂O/EtOH (10 mL, 1/1) with NaOH (400 mg, 7.16 mmol, 5.4 eq.) and heated up to reflux for 3 h. The mixture was let cool down to r.t. and was neutralized with HCl (2M). The resulting precipitate was filtered off, washed with H₂O and Et₂O and dried in vacuo to give the desired product as a pale red solid (152 mg, 0.72 mmol, 54%). M.p. = 295 °C (decomp.). TLC: Rf = 0.41 (DCM/MeOH = 85/15). ¹H-NMR (600 MHz, DMSO-d₆, 299 K): δ (in ppm) = 12.62 (s, 1H, -NH-), 9.44 (s, 1H, 3-H_quinoxaline), 8.11–8.05 (m, 2H, 5-/8-H_quinoxaline), 7.88–7.78 (m, 2H, 6-/7-H_quinoxaline), 6.32 (s, 2H, -NH₂). ¹³C-NMR (151 MHz, DMSO-d₆, 299 K): δ (in ppm) = 157.9 (1C, 3-/5-C_triazolyl), 157.1 (1C, 3-/5-C_quinoxaline), 145.6 (1C, 2-C_quinoxaline), 144.0 (1C, 3-C_quinoxaline), 141.4 (4a-/8a-C_quinoxaline), 141.3 (1C, 4a-/8a-C_quinoxaline), 130.5 (1C, 6-/7-C_quinoxaline), 129.9 (1C, 6-/7-C_quinoxaline), 129.2 (1C, 5-/8-C_quinoxaline), 128.9 (1C, 5-/8-C_quinoxaline). IR (neat): $\tilde{\nu}$ [cm⁻¹] = 3354, 3204, 1643, 1556, 1502, 1209, 1175, 1136, 1062, 955, 926. HRMS (APCI): $m/z = 316.1193$ calculated for C₁₀H₉N₆⁺ [M+H]⁺, found: 316.1192.
**NMR spectral data**

2-(5-Amino-1-(benzoyl-L-prolyl)-1H-1,2,4-triazol-3-yl)pyridine (13e)

**$^1$H-NMR (600 MHz, DMSO-$d_6$)**

**$^{13}$C-NMR (151 MHz, DMSO-$d_6$)**

S31
3-(Pyridin-2-yl)-1H-1,2,4-triazol-5-amine (15a)

$\text{H-NMR} (600 \text{ MHz, DMSO-}d_6)$

$\text{C-NMR} (151 \text{ MHz, DMSO-}d_6)$
3-(5-Amino-1H-1,2,4-triazol-3-yl)pyridine 1-oxide (15c)

$^{1}H$-NMR (600 MHz, DMSO-$d_6$)

$^{13}C$-NMR (151 MHz, DMSO-$d_6$)
3-(5-Bromopyridin-3-yl)-1H-1,2,4-triazol-5-amine (15d)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(6-Methylpyridin-2-yl)-1H-1,2,4 triazol-5-amine (15e)

$^{1}$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-cyclohexyl-1H-1,2,4-triazol-5-amine (15f)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-Heptyl-1H-1,2,4-triazol-5-amine (15g)

\[ \text{1H-NMR (600 MHz, DMSO-}d_6\text{)} \]

\[ \text{13C-NMR (151 MHz, DMSO-}d_6\text{)} \]

S37
3-(Tert-butyl)-1H-1,2,4-triazol-5-amine (15h)

$^1$H-NMR (400 MHz, DMSO-$d_6$)

$^{13}$C-NMR (101 MHz, DMSO-$d_6$)
3-(Naphthalen-2-yl)-1H-1,2,4-triazol-5-amine (15i)

$\text{H-NMR (600 MHz, DMSO-d}_6$)

$\text{C-NMR (151 MHz, DMSO-d}_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(3,4-Dimethoxyphenyl)-1H-1,2,4-triazol-5-amine (15j)

\[ \text{MeO} \quad \text{OMe} \]

\[ \begin{array}{c}
\text{N} - \text{NH} - \text{NH}_2 \\
\end{array} \]

\[ \text{G (m, 5.56)} \]
\[ \text{F (m, 11.96)} \]
\[ \text{E (m, 7.43)} \]
\[ \text{C (m, 5.96)} \]
\[ \text{B (m, 5.17)} \]
\[ \text{A (b, 7.8)} \]

$^1$H-NMR (400 MHz, DMSO-\(d_6\))

$^{13}$C-NMR (101 MHz, DMSO-\(d_6\))

S40
3-(Quinolin-2-yl)-1H-1,2,4-triazol-5-amine (15k)

\[
\begin{align*}
\text{\textsuperscript{1}H-NMR (600 MHz, DMSO-\textit{d}_6)} \\
\text{\textsuperscript{13}C-NMR (151 MHz, DMSO-\textit{d}_6)}
\end{align*}
\]
3-(4-Fluorophenyl)-IH-1,2,4-triazol-5-amine (15l)

1H-NMR (400 MHz, DMSO-\(d_6\))

\[
\begin{array}{c}
\text{D} \ (\delta) \\
12.06 \\
\end{array}
\]

\[
\begin{array}{c}
\text{C} \ (\text{ppm}) \\
7.90 \\
7.22 \\
6.94 \\
\end{array}
\]

13C-NMR (101 MHz, DMSO-\(d_6\))

\[
\begin{array}{c}
163.4 \\
160.9 \\
157.4 \\
137.4 \\
127.3 \\
115.4 \\
114.2 \\
\end{array}
\]
3-(4-nitrophenyl)-1H-1,2,4-triazol-5-amine (15m)

$\text{O}_2\text{N}$

$\text{N}-\text{NH}$

$\text{N}^{}-\text{NH}_2$

$^1\text{H-NMR} (600 \text{ MHz, DMSO-$d_6$})$

$\begin{array}{c}
\text{D (ex)} \\
\text{12.45}
\end{array}$

$\begin{array}{c}
\text{C (ex)} \\
\text{2.96}
\end{array}$

$\begin{array}{c}
\text{A (ex)} \\
\text{8.24}
\end{array}$

$\begin{array}{c}
\text{0.85} \\
\text{1.96} \\
\text{2.59} \\
\text{8.96}
\end{array}$

$^1\text{C-NMR} (151 \text{ MHz, DMSO-$d_6$})$

$\begin{array}{c}
\text{150.4} \\
\text{147.0} \\
\text{138.4} \\
\text{126.1} \\
\text{124.0}
\end{array}$
3-(4-Methoxyphenyl)-1H-1,2,4-triazol-5-amine (15n)

$\text{H-NMR (600 MHz, DMSO-$d_6$)}$

$\text{C NMR (151 MHz, DMSO-$d_6$)}$
3-benzyl-1H-1,2,4-triazol-5-amine (15o)

$\text{H-NMR (600 MHz, DMSO-}$d$_6$)$

$\text{13C-NMR (151 MHz, DMSO-}$d$_6$)$
3-(Naphthalen-1-yl)-1H-1,2,4-triazol-5-amine (15p)

$\text{H-NMR (400 MHz, DMSO-}d_6)$

$\text{C-NMR (101 MHz, DMSO-}d_6)$
3-(Cyclohexylmethyl)-1H-1,2,4-triazol-5-amine (15q)

$\text{H-NMR (600 MHz, DMSO-$d_6$)}$

$\text{C-NMR (151 MHz, DMSO-$d_6$)}$

S47
3-Undecyl-1H-1,2,4-triazol-5-amine (15r)

$\begin{align*}
\text{N} & & \text{N} \\
\text{NH} & & \text{NH}_2
\end{align*}$

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^1$C-NMR (151 MHz, DMSO-$d_6$)
(E)-3-Styryl-1H-1,2,4-triazol-5-amine (15s)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(Isoquinolin-1-yl)-1H-1,2,4-triazol-5-amine (15u)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(Benzo[b]thiophene-2-yl)-1H-1,2,4-triazole-5-amine (15v).

$^1$H-NMR (400 MHz, DMSO-$d_6$)

$^{13}$C-NMR (101 MHz, DMSO-$d_6$)
3-(5-Chlorothiophene-2-yl)-1H-1,2,4-triazole-5-amine (15w)

$\text{H-NMR (400 MHz, DMSO-}$d$_6$\text{)}

$\text{C-NMR (101 MHz, DMSO-}$d$_6$\text{)}
Ethyl isoquinoline-1-carboxylate (17u)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
Isoquinoline-1-carbohydrazide (18u)

$\text{H-NMR (600 MHz, DMSO-}d_6\text{)}$

$\text{C-NMR (151 MHz, DMSO-}d_6\text{)}$
Benzo[b]thiophene-2-carbohydrazide (18v).

\[
\text{\text{H}}\text{-NMR (600 MHz, DMSO-}d_6\text{)}
\]

\[
\text{\text{C}}\text{-NMR (151 MHz, DMSO-}d_6\text{)}
\]
3-(Pyridin-2-yl)-N-benzyl-1H-1,2,4-triazol-5-amine (19a).

$^{1}$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(Benzo[b]thiophen-2-yl)-N-benzyl-1H-1,2,4-triazol-5-amine (19v).

$\text{H-NMR (600 MHz, DMSO-$d_6$)}$

$\text{C-NMR (151 MHz, DMSO-$d_6$)}$
3-Methylquinoxaline-2-carboxylate (22a)

$^1$H-NMR (400 MHz, DMSO-d$_6$)

$^{13}$C-NMR (101 MHz, DMSO-d$_6$)
Ethyl 3-phenylquinoxaline-2-carboxylate (22b)

$\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2$ (22b)

$^1\text{H}-\text{NMR (400 MHz, DMSO-}d_6)$

$^1\text{C}-\text{NMR (101 MHz, DMSO-}d_6)$
$3,6,7$-Trimethylquinoxaline-2-carboxylate (22c)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-ethylquinoxaline-2-carboxylate (22d)

\[ \text{H-NMR (600 MHz, DMSO-}d_6\text{)} \]

\[ \text{C-NMR (151 MHz, DMSO-}d_6\text{)} \]
3-Methylquinoxaline-2-carbohydrazide (23a)

$^1$H-NMR (400 MHz, DMSO-$d_6$)

$^{13}$C-NMR (101 MHz, DMSO-$d_6$)
3-Phenylquinoxaline-2-carbohydrazide (23b)

\[
\text{R} \quad \text{O} \\
\text{NH}_2
\]

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3,6,7-Trimethylquinoxaline-2-carbohydrazide (23c)

$^1$H-NMR (400 MHz, DMSO-$d_6$)

$^{13}$C-NMR (101 MHz, DMSO-$d_6$)
3-Ethylquinoxaline-2-carbohydrazide (23d)

\[
\begin{align*}
\text{1H-NMR (600 MHz, DMSO-}d_6) \\
\text{13C-NMR (151 MHz, DMSO-}d_6)
\end{align*}
\]
3-(3-Methylquinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (24a)

\[
\text{N=C=N} \quad \text{N=NH} \quad \text{NH}_2
\]

$^{1}$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)

S66
3-(3-Ethylquinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (24b)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)

S67
3-(3-Phenylquinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (24c)

$^{1}$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(3,6,7-Trimethylquinoxalin-2-yl)-1H-1,2,4-triazole-5-amine (24d)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)

S69
(E)-3-(Dimethylamino)-1-phenylpropan-2-en-1-one (26a)

$^1$H-NMR (600 MHz, CDCl$_3$)

$^{13}$C-NMR (151 MHz, CDCl$_3$)

S70
(E)-1-(3,4-Dimethoxyphenyl)-3-(dimethylamino)prop-2-en-1-one (26c)

$^1$H-NMR (600 MHz, DMSO-$_d^6$)

$^{13}$C-NMR (151 MHz, DMSO-$_d^6$)
(E)-3-(Dimethylamino)-1-(4-isobutylphenyl)prop-2-en-1-one (26d)

$^1$H-NMR (600 MHz, CDCl$_3$)

$^{13}$C-NMR (151 MHz, CDCl$_3$)
(E)-3-((Dimethylamino)-1-(pyridin-3-yl)prop-2-en-1-one (26e)

$^1$H-NMR (600 MHz, CDCl$_3$)

$^{13}$C-NMR (151 MHz, CDCl$_3$)

S73
(E)-3-(Dimethylamino)-1-(thiophen-2-yl)prop-2-en-1-one (26f)

$^1$H-NMR (600 MHz, CDCl$_3$)

$^{13}$C-NMR (151 MHz, CDCl$_3$)
(E)-1-(Dimethylamino)-5-methylhex-1-en-3-one (26g)

**1H-NMR (600 MHz, DMSO-d$_6$)**

- H at 7.45 ppm
- H at 4.94 ppm
- C at 3.04 ppm
- F at 0.84 ppm

**13C-NMR (151 MHz, DMSO-d$_6$)**

- C at 194.98 ppm
- C at 152.29 ppm
- C at 46.19 ppm
- C at 36.61 ppm
- C at 35.41 ppm
Ethyl-2-methyl-6-phenylnicotinate (27a)

$^{1}$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
**Ethyl-6-(2-bromophenyl)-2-methylnicotinate (27b)**

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
Ethyl-6-(3,4-dimethoxyphenyl)-2-methylnicotinate (27c)

$^1$H NMR (600 MHz, DMSO-$d_6$)

$^{13}$C NMR (151 MHz, DMSO-$d_6$)
Ethyl-6-(4-isobutylphenyl)-2-methylnicotinate (27d)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)

$^1$H-NMR (600 MHz, DMSO-$d_6$)
Ethyl-6-methyl-[2,3'-bipyridine]-5-carboxylate (27e)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
Ethyl-2-methyl-6-(thiophen-2-yl)nicotinate (27f)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
Ethyl-6-isobutyl-2-methylnicotinate (27g)

$^{1}H$-NMR (600 MHz, DMSO-$d_{6}$)

$^{13}C$-NMR (151 MHz, DMSO-$d_{6}$)
2-Methyl-6-phenylnicotinohydrazide (28a)

\[
\text{\includegraphics{structure.png}}
\]

\[ ^{1}H\text{-NMR (600 MHz, DMSO-}d_6\text{)} \]

\[ ^{13}C\text{-NMR (151 MHz, DMSO-}d_6\text{)} \]
6-(2-Bromophenyl)-2-methylnicotinohydrazide (28b)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
6-(3,4-Dimethoxyphenyl)-2-methylnicotinohydrazide (28c)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)

S85
6-(4-Isobutylphenyl)-2-methylnicotinohydrazide (28d)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)

S86
6-Methyl-[2,3'-bipyridine]-5-carbohydrazide (28e)

**1H-NMR (600 MHz, DMSO-d$_6$)**

**13C-NMR (151 MHz, DMSO-d$_6$)**
2-Methyl-6-(thiophen-2-yl)nicotinohydrazide (28f)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
6-Isobutyl-2-methylnicotinohydrazide (28g)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(2-Methyl-6-phenylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29a)

\[ \text{N} = \text{NH} \]

\[ 8 (s) \quad 12.24 \]
\[ 2 (m) \quad 8.83 \]
\[ 2 (m) \quad 7.43 \]
\[ 4 (s) \quad 6.14 \]
\[ A (6) \quad 2.87 \]

\(^1H\)-NMR (600 MHz, DMSO-\(d_6\))

\[^{13}C\]-NMR (151 MHz, DMSO-\(d_6\))
3-(6-(2-Bromophenyl)-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29b)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-((6-(3,4-Dimethoxyphenyl)-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29c)

\[
\begin{align*}
\text{H-NMR (600 MHz, DMSO-}d_6\text{)}
\end{align*}
\]

\[
\begin{align*}
\text{C-NMR (151 MHz, DMSO-}d_6\text{)}
\end{align*}
\]
3-(6-(4-Isobutylphenyl)-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29d)

$\text{F (m) 12.21}$

$\text{C (m) 1.80}$

$\text{D (m) 8.03}$

$\text{A (m) 6.11}$

$\text{K (m) 2.90}$

$\text{H (m) 0.84}$

$\text{E (d) 8.24}$

$\text{1H-NMR (600 MHz, DMSO-d$_6$)}$

$\text{13C-NMR (151 MHz, DMSO-d$_6$)}$

S93
3-(6-Methyl-[2,3'-bipyridin]-5-yl)-1H-1,2,4-triazol-5-amine (29e)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-(2-Methyl-6-(thiophen-2-yl)pyridin-3-yl)-1H-1,2,4-triazol-5-amine (29f)

$\text{H-NMR (600 MHz, DMSO-d}_6)$

$\text{C-NMR (151 MHz, DMSO-d}_6)$
3-(6-Isobutyl-2-methylpyridin-3-yl)-1H-1,2,4-triazol-5-amine (29g)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
$1-(5\text{-Amino-3-(pyridin-2-yl)}\text{-IH-1,2,4-triazol-1-yl}}\text{-2-(2-iodophenyl)}\text{ethan-1-one (32a)}$

$^1\text{H-NMR (600 MHz, DMSO-}d_6\text{)}$

$^1\text{C-NMR (151 MHz, DMSO-}d_6\text{)}$
$1^\text{H}-\text{NMR} \ (600 \text{ MHz, DMSO-$d_6$})$

$1^\text{C}-\text{NMR} \ (151 \text{ MHz, DMSO-$d_6$})$
$1\text{-}(5\text{-Amino}-3\text{-}(pyrazin-2\text{-yl})\text{-}1\text{-}H\text{-}1,2,4\text{-triazol-1-yl})\text{-}2\text{-}(2\text{-iodophenyl})\text{ethan-1-one (32c)}$

$^1\text{H-NMR (600 MHz, DMSO-}d_6\text{)}$

$^{13}\text{C-NMR (151 MHz, DMSO-}d_6\text{)}$
1-(5-Amino-3-(2-methyl-6-(thiophen-2-yl)pyridin-3-yl)-1H-1,2,4-triazol-1-yl)-2-(2-iodophenyl)-ethan-1-one (32d)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)

S100
$^{1}H$-NMR (600 MHz, DMSO-$d_6$)

$^{13}C$-NMR (151 MHz, DMSO-$d_6$)
(S)-(5-Amino-3-(pyridin-2-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydro-naphthalen-2-yl)-methanone (33a).

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(S)-(5-Amino-3-(6-methylpyridin-2-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)-methanone (33b)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(S)-(5-Amino-3-(pyrazin-2-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)methanone (33c)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(S)-(5-Amino-3-(2-methyl-6-(thiophen-2-yl)pyridin-3-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)methanone (33d)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(S)-(5-Amino-3-(tert-butyl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)methanone (33e)

\[ \text{1}^\text{H-NMR (600 MHz, DMSO-}d_6\text{)} \]

\[ \text{1}^\text{3C-NMR (151 MHz, DMSO-}d_6\text{)} \]
(S)-(5-Amino-3-(4-fluorophenyl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)-methanone (33f)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(S)-(5-Amino-3-(quinolin-2-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)methanone (33g)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(S)-(5-amino-3-(3-methylquinoxalin-2-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)-methanone (33h)

$^1$H-NMR (600 MHz, DMSO-d$_6$)

$^{13}$C-NMR (151 MHz, DMSO-d$_6$)
(S)-(5-amino-3-(isoquinolin-1-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl) methanone (33i)

$^{1}H$-NMR (600 MHz, DMSO-$d_6$)

$^{13}C$-NMR (151 MHz, DMSO-$d_6$)
(S)-(2-(5-Amino-1-(1,2,3,4-tetrahydronaphthalene-1-carbonyl)-1H-1,2,4-triazol-3-yl)phenyl)-(piperidin-1-yl)methanone (33j)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(1S,2R,3S)-1-(Quinoxalin-2-yl)butane-1,2,3,4-tetraol (35)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
Quinoxaline-2-carboxylic acid (36)

\[
\begin{array}{c}
\text{OH} \\
\end{array}
\]

\(^1\text{H-NMR (600 MHz, DMSO-}d_6)\)

\[^{13}\text{C-NMR (151 MHz, DMSO-}d_6)\)
Ethyl quinoxaline-2-carboxylate (37)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
3-((Quinoxalin-2-yl)-1H-1,2,4-triazol-5-amine (38))

\[
\text{H-NMR (600 MHz, DMSO-d}_6)\]

\[
\text{C-NMR (151 MHz, DMSO-d}_6)\]
(S)-(5-Amino-3-(quinoxalin-2-yl)-1H-1,2,4-triazol-1-yl)(1,2,3,4-tetrahydronaphthalen-1-yl)-methanone (39a)

$^{1}H$-NMR (600 MHz, DMSO-$d_6$)

$^{13}C$-NMR (151 MHz, DMSO-$d_6$)
(5-Amino-3-(quinoxalin-2-yl)-1H-1,2,4-triazol-1-yl)(naphthalen-1-yl)methanone (39b)

**1H-NMR (600 MHz, DMSO-d<sub>6</sub>)**

**13C-NMR (151 MHz, DMSO-d<sub>6</sub>)**
(5-Amino-3-(quinolin-2-yl)-1H-1,2,4-triazol-1-yl)(phenyl)methanone (40a)

$^1$H-NMR (600 MHz, DMSO-$d_6$)

$^{13}$C-NMR (151 MHz, DMSO-$d_6$)
(5-Amino-3-(quinolin-2-yl)-1H-1,2,4-triazol-1-yl)(naphthalen-1-yl)methanone (40b)

\[\text{Structure Image}\]

$^1\text{H-NMR (600 MHz, DMSO-}d_6\text{)}$

$^{13}\text{C-NMR (151 MHz, DMSO-}d_6\text{)}$
(5-Amino-3-(isoquinolin-1-yl)-1H-1,2,4-triazol-1-yl)(phenyl)methanone (41a)

$\text{H-NMR (400 MHz, DMSO-$d_6$)}$

$\text{C-NMR (101 MHz, DMSO-$d_6$)}$
(5-Amino-3-(isoquinolin-1-yl)-1H-1,2,4-triazol-1-yl)(naphthalen-2-yl)methanone (41c)

$\text{H-NMR (600 MHz, DMSO-$d_6$)}$

$\text{C-NMR (151 MHz, DMSO-$d_6$)}$
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