Supporting Information

Synthesis of new pyrazolo[1,2,3]triazines by cyclative cleavage of pyrazolo-triazenes

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# 1 General remarks

NMR spectra of dissolved samples were recorded on a Bruker Ascend 400 at 21 °C. Chemical shifts (*δ*) are expressed in parts per million (ppm) downfield from tetramethylsilane (TMS). References for 1H NMR and 13C NMR were the residual solvent peaks of chloroform-*d1* (1H: *δ* = 7.26 ppm; 13C: *δ* = 77.0 ppm) if not stated otherwise. All coupling constants (*J*) are absolute values and are expressed in Hertz (Hz). The description of signals includes: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets and ddd = double doublet of doublets and so forth. The spectra were analyzed according to first order. The assignments of the signal structure in 1H NMR were made by the detected multiplicity and for 13C NMR by DEPT 90- and DEPT 135-spectra (DEPT = Distortionless Enhancement by Polarization Transfer) and are described as follows: + = primary or tertiary C‑atom (positive DEPT-signal), – = secondary C-atom (negative signal) and Cq = quaternary C-atom (no signal). Furthermore, 2D experiments such as COSY (Correlated Spectroscopy) and HSQC (Heteronuclear Single Quantum Coherence) were performed.

IR spectra were recorded on a Bruker Alpha ATR spectrometer. The compounds were measured as pure substances by the ATR (ATR = attenuated total reflection) technique. The position of the absorption band is given in wave numbers *ṽ* in cm-1. The intensities of the bands were characterized as follows: vs = very strong (0–20% T), s = strong (21–40 % T), m = medium (41–60% T), w = weak (61–80% T), vw = very weak (81–100% T).

Mass spectra were measured by EI-MS (electron impact mass spectrometry) and were recorded on a Finnigan MAT 95. The peaks are given as mass-to-charge-ratio (*m/z*). The molecule peak is given as [M]+ and characteristic fragment peaks are given as [M–fragment]+ or [fragment]+. The signal intensities are given in percent, relatively to the intensity of the base signal (100%). For the high resolution mass, the following abbreviations were used: Calcd = calculated data, Found = measured data. The software of FAB and EI adds the mass of one electron.

Analytical thin layer chromatography (TLC) was carried out on Merck silica gel coated aluminum plates (silica gel 60, F254), detected under UV-light at 254 nm or stained with “Seebach staining solution” (mixture of molybdato phosphoric acid, cerium(IV)-sulfate tetrahydrate, sulfuric acid and water) or basic potassium permanganate solution. Solvent mixtures are understood as volume/volume.

All solvents, reagents and chemicals were used as purchased unless stated otherwise.

Air- or moisture-sensitive reactions were carried out under argon atmosphere in oven-dried and previously evacuated glass ware. Liquids were transferred with plastic syringes and steel cannula. Silica gel 60 (0.040 × 0.063 mm, Geduran®, Merck) was used as stationary phase and solvents of *p.a.* quality were used as mobile phase.

InChI Strings were generated with InChI Version (1.04), Smiles with the SMILES Version of Daylight.

# 2 Synthesis and Characterization

## 5-[(~{E})-[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile (15)



**15**: 5-[(~{E})-[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile; Formula: C10H16N6; Exact Mass: 220.1436; Smiles: CC(N(C(C)C)/N=N/c1n[nH]cc1C#N)C; InChIKey: UCPMQTTXXMXIFF-CCEZHUSRSA-N.

To a mixture of 5-amino-1H-pyrazole-4-carbonitrile (2.00 g, 19 mmol, 1.00 equiv) in 6 mL of water, conc. hydrochloric acid (6.17 mL, 74 mmol, 4.00 equiv) was added. The mixture was cooled to 0 °C and a solution of sodium;nitrite (1.91 g, 28 mmol, 1.50 equiv) in 20 mL of water was added. Additional 10 mL of water were added to get a stirrable slurry. After stirring for 30 min at 0 °C, a mixture of diisopropylamine (2.43 g, 3.37 mL, 24 mmol, 1.30 equiv) and dipotassium carbonate (5.11 g, 37 mmol, 2.00 equiv) in 50 mL of water were added. The reaction mixture was stirred at 21 C until TLC showed that all diazonium salt had disappeared. The reaction mixture was extracted with 3 × 150 mL of DCM. Some precipitate was formed between the layers which had to be filtered off (clogged the frit). The combined organic phases were washed with 3 × 60 mL of water, dried over sodium sulfate and the solvent was evaporated under reduced pressure to give the desired product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 2:1 to give the target compound in 45% yield (1.85 g, 8.4 mmol).

*Rf* = 0.08 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 9.04 (bs, 1H), 7.76 (s, 1H), 5.27 (hept, *J* = 6.80 Hz, 1H), 4.08 (hept, *J* = 6.7 Hz, 1H), 1.44 (d, *J* = 6.6 Hz, 6H), 1.28 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 158.4, 141.3, 115.4 (+, CH), 79.7, 50.8 (+, CH), 47.6 (+, CH), 23.4 (+, 2C, CH3), 19.2 (+, 2C, CH3); EI (*m/z*, 70 eV, 80 °C): 220 (100) [M]+, 135 (23), 134 (11), 120 (35), 109 (16), 108 (37), 100 (32), 86 (87), 84 (38), 70 (15), 69 (13), 65 (23), 58 (74), 52 (21); HRMS (C10H16N6): Calcd 220.1436, Found 220.1438; IR (ATR, ṽ) = 611, 629, 643, 713, 722, 751, 771, 816, 839, 861, 880, 899, 928, 948, 1031, 1067, 1077, 1096, 1130, 1163, 1194, 1217, 1231, 1262, 1295, 1306, 1319, 1339, 1364, 1378, 1392, 1412, 1451, 1466, 1492, 1543, 1572, 1720, 1792, 2183, 2227, 2873, 2934, 2973, 3053, 3095, 3143, 3231 cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-UCPMQTTXXM-UHFFFADPSC-NUHFF-NRHPV-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/UCPMQTTXXMXIFF-CCEZHUSRSA-N.1>

## (E)-1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (12a), (E)-1-benzyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (13a)



(E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-4-carbonitrile-1H-pyrazole (**15**, 76.5 mg, 347 μmol, 1.00 equiv) was dissolved in 10 mL of DMSO. Cesium carbonate (133 mg, 409 μmol, 1.18 equiv) was added and the solution was cooled to 0 °C. Bromomethylbenzene (117 mg, 80.9 μL, 681 μmol, 1.96 equiv) was added and the vial was closed and slowly warmed to 21 °C. The reaction mixture was stirred at 21 °C for 48 hours. The reaction was quenched by addition of ice and was extracted with EtOAc (3 × 15 mL). The obtained organic layers were co-evaporated with Celite(R) to give the Celite-immobilized crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 4:1, giving (E)-1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12a**, 58.2 mg, 188 μmol, 54% yield) as a light-orange solid and (E)-1-benzyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**13a**, 38.7 mg, 125 μmol, 36% yield) as a light-orange solid.

**12a**: (E)-1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C17H22N6; Exact Mass: 310.1906; Smiles: N#Cc1cn(nc1/N=N/N(C(C)C)C(C)C)Cc1ccccc1; InChIKey: AONLLYWWGOIMLR-XUTLUUPISA-N

*Rf* = 0.23 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.53 (s, 1H), 7.30–7.15 (m, 5H), 5.32 (hept, *J* = 6.8 Hz, 1H), 5.13 (s, 2H), 3.93 (hept, *J* = 6.6 Hz, 1H), 1.35 (d, *J* = 6.6 Hz, 6H), 1.15 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 162.9, 135.7 (+, CH), 134.8, 129.1 (+, 2C, CH), 128.8 (+, CH), 128.3 (+, 2C, CH), 115.3, 81.5, 56.9 (–, CH2), 49.9 (+, CH), 46.5 (+, CH), 23.3 (+, 2C, CH3), 19.3 (+, 2C, CH3); EI (m/z, 70 eV, 80 °C): 310 (39) [M]+, 210 (60), 181 (13), 131 (17), 100 (48), 92 (11), 91 (100), 86 (10), 84 (14), 77 (22), 71 (12), 70 (10), 69 (35), 58 (54), 57 (23), 55 (15). HRMS (C17H22N6): Calcd 310.1906, Found 310.1905; IR (ATR, ṽ) = 3122 (w), 3058 (vw), 3031 (vw), 2979 (w), 2934 (w), 2868 (vw), 2223 (m), 1816 (vw), 1700 (vw), 1604 (vw), 1537 (s), 1497 (w), 1456 (m), 1412 (vs), 1368 (vs), 1353 (s), 1326 (w), 1313 (w), 1261 (vs), 1239 (m), 1227 (vs), 1184 (w), 1149 (vs), 1132 (m), 1095 (m), 1081 (w), 1028 (s), 1001 (m), 970 (w), 909 (w), 881 (w), 851 (m), 843 (m), 819 (w), 799 (w), 752 (w), 741 (s), 721 (m), 711 (vs), 694 (s), 649 (m), 632 (w) cm–1.

**13a**: (E)-1-benzyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C17H22N6; Exact Mass: 310.1906; Smiles: CC(N(C(C)C)/N=N/c1n(ncc1C#N)Cc1ccccc1)C; InChIKey: AQYSAXXLCHFEGV-QZQOTICOSA-N

*Rf* = 0.30 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.65 (s, 1H), 7.35–7.21 (m, 5H), 5.36 (s, 2H), 5.16 (hept, *J* = 6.9 Hz, 1H), 4.08 (hept, *J* = 6.6 Hz, 1H), 1.44 (d, *J* = 6.6 Hz, 6H), 1.26 (d, *J* = 6.8 Hz, 6H). 13C NMR (100 MHz, CDCl3, ppm) δ = 154.8, 142.5 (+, CH), 136.5, 128.8 (+, 2C, CH), 128.0 (+, CH), 127.9 (+, 2C, CH), 116.0, 77.9, 52.3 (–, CH2), 51.4 (+, CH), 48.1 (+, CH), 23.3 (+, 2C, CH3), 19.0 (+, 2C, CH3); EI (m/z, 70 eV, 70 °C): 311 (10) [M+H]+, 310 (55) [M]+, 210 (26), 181 (20), 131 (30), 119 (12), 100 (42), 91 (78), 69 (100), 58 (21). HRMS (C17H22N6): Calcd 310.1906, Found 310.1905; IR (ATR, ṽ) = 3111 (w), 3089 (vw), 3067 (vw), 3031 (w), 2987 (w), 2975 (w), 2935 (w), 2871 (w), 2220 (s), 1761 (vw), 1606 (vw), 1533 (m), 1494 (w), 1466 (w), 1455 (m), 1441 (w), 1419 (vs), 1391 (s), 1375 (vs), 1363 (vs), 1313 (m), 1272 (s), 1238 (vs), 1211 (vs), 1164 (s), 1132 (s), 1103 (vs), 1078 (m), 1026 (vs), 946 (w), 936 (w), 909 (m), 884 (s), 850 (w), 815 (w), 785 (m), 722 (vs), 710 (s), 691 (vs), 666 (m), 630 (m), 615 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-KRKANRSFKB-UHFFFADPSC-NUHFF-NVGOA-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/AONLLYWWGOIMLR-XUTLUUPISA-N.1>

<https://doi.org/10.14272/AQYSAXXLCHFEGV-QZQOTICOSA-N.1>

## (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile (12b), (E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile (13b)



In a vial, 5-(E)-[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile (**15**, 563 mg, 2.55 mmol, 1.00 equiv) was dissolved in 20 mL of DMSO. The solution was cooled to 0 °C. Cesium carbonate (1.00 g, 3.07 mmol, 1.20 equiv) and 1-(bromomethyl)-4-methylbenzene (700 mg, 3.78 mmol, 1.48 equiv) were added. The mixture was stirred first at 21 °C for 2 hours, then at 50 °C for 12 hours. The reaction was quenched with ice and extracted with EtOAc (3 × 20 mL). The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 4:1, giving 3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile (**12b**, 485 mg, 1.50 mmol, 59% yield) as a colorless solidand 5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile (**13b**, 329 mg, 1.01 mmol, 40% yield) as a colorless solid.

**12b**: (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile; Formula: C18H24N6; Exact Mass: 324.2062; Smiles: N#Cc1cn(nc1/N=N/N(C(C)C)C(C)C)Cc1ccc(cc1)C; InChIKey: GJXVYPGROXVEAZ-LSDHQDQOSA-N

*Rf* = 0.34 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.58 (s, 1H), 7.21–7.10 (m, 4H), 5.39 (hept, *J* = 7.1 Hz, 1H), 5.16 (s, 2H), 4.01 (hept, *J* = 6.6 Hz, 1H), 2.33 (s, 3H), 1.43 (d, *J* = 6.7 Hz, 6H), 1.23 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 162.8, 138.6, 135.5 (+, CH), 131.7, 129.8 (+, CH, 2C), 128.4 (+, CH, 2C), 115.3, 81.3, 56.6 (–, CH2), 49.8 (+, CH), 46.4 (+, CH), 23.3 (+, CH3, 2C), 21.2 (+, CH3), 19.3 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 326 (22) [M+2H]+, 325 (100) [M+H]+, 324 (20) [M]+, 224 (20), 154 (10), 105 (45), 100 (11), 95 (10). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C18H25N6 325.2141; Found 325.2139; IR (ATR, ṽ) = 3132 (vw), 2978 (w), 2931 (w), 2873 (vw), 2218 (vs), 1615 (vw), 1540 (s), 1513 (w), 1468 (w), 1456 (m), 1439 (w), 1414 (vs), 1405 (vs), 1384 (s), 1370 (vs), 1353 (s), 1310 (w), 1264 (vs), 1232 (s), 1203 (w), 1157 (vs), 1132 (m), 1115 (w), 1099 (m), 1031 (m), 1021 (w), 1001 (w), 932 (vw), 912 (w), 843 (w), 820 (s), 782 (s), 752 (s), 717 (vs), 693 (m), 640 (w), 630 (m) cm–1.

**13b**: (E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile; Formula: C18H24N6; Exact Mass: 324.2062; Smiles: N#Cc1cnn(c1/N=N/N(C(C)C)C(C)C)Cc1ccc(cc1)C; InChIKey: RAZAPXAZBSDVNH-QURGRASLSA-N

*Rf* = 0.43 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.64 (s, 1H), 7.22–7.07 (m, 4H), 5.32 (s, 2H), 5.19 (hept, *J* = 6.8 Hz, 1H), 4.10 (hept, *J* = 6.6 Hz, 1H), 2.31 (s, 3H), 1.45 (d, *J* = 6.6 Hz, 6H), 1.28 (d, *J* = 6.8 Hz, 6H). 13C NMR (100 MHz, CDCl3, ppm) δ = 154.7, 142.4 (+, CH), 137.8, 133.5, 129.4 (+, CH, 2C), 128.0 (+, CH, 2C), 116.0, 77.8, 52.0 (–, CH2), 51.4 (+, CH), 48.1 (+, CH), 23.2 (+, CH3, 2C), 21.2 (+, CH3), 19.0 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 326 (22) [M+2H]+, 325 (100) [M+H]+, 324 (29) [M]+, 105 (49), 100 (11). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C18H25N6 325.2141; Found 325.2140; IR (ATR, ṽ) = 3121 (vw), 2972 (w), 2945 (w), 2873 (w), 2221 (vs), 1741 (vw), 1615 (vw), 1537 (m), 1514 (w), 1489 (w), 1466 (w), 1422 (vs), 1394 (vs), 1378 (vs), 1366 (vs), 1322 (w), 1279 (m), 1266 (s), 1238 (vs), 1208 (s), 1173 (w), 1162 (m), 1133 (m), 1102 (vs), 1026 (vs), 990 (w), 945 (w), 925 (w), 909 (w), 881 (w), 873 (m), 851 (w), 839 (w), 817 (m), 810 (w), 762 (s), 754 (vs), 728 (w), 707 (m), 659 (w), 642 (vw), 618 (m), cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-UZTCZZRTCD-UHFFFADPSC-NUHFF-NPQQK-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/GJXVYPGROXVEAZ-LSDHQDQOSA-N.1>

<https://doi.org/10.14272/RAZAPXAZBSDVNH-QURGRASLSA-N.1>

## (E)-1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (12c), (E)-1-(3,5-difluorobenzyl)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (13c)



In a vial, 5-[(E)-(diisopropylamino)azo]-1~{H}-pyrazole-4-carbonitrile (**15**, 75.0 mg, 340 μmol, 1.00 equiv) was dissolved in 5 mL of DMSO. Cesium carbonate (133 mg, 409 μmol, 1.20 equiv) was added and the solution was cooled to 0 °C. 1-(Bromomethyl)-3,5-difluorobenzene (141 mg, 88.1 μL, 681 μmol, 2.00 equiv) was added and the vial was closed and slowly warmed to 21 °C. The reaction mixture was stirred at 21 °C for 48 hours. The reaction was quenched by addition of ice and was extracted with EtOAc (3 × 15 mL). The obtained organic layers were co-evaporated with Celite(R) to give the Celite-immobilized crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 4:1, giving (E)-1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12c**, 57.0 mg, 165 μmol, 48% yield) as a colorless solid and (E)-1-(3,5-difluorobenzyl)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**13c**, 49.2 mg, 142 μmol, 42% yield) as a colorless solid.

**12c**: (E)-1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C17H20F2N6; Exact Mass: 346.1718; Smiles: N#Cc1cn(nc1/N=N/N(C(C)C)C(C)C)Cc1cc(F)cc(c1)F; InChIKey: WSQPCVJPBSUDNZ-XTQSDGFTSA-N

*Rf* = 0.21 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.74 (s, 1H), 6.83–6.68 (m, 3H), 5.39 (hept, *J* = 6.8 Hz, 1H), 5.19 (s, 2H), 4.03 (hept, *J* = 6.5 Hz, 1H), 1.43 (d, *J* = 6.6 Hz, 6H), 1.23 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 163.3 (dd, *J* = 250.3 Hz, *J* = 12.6 Hz; 2C), 163.2, 138.9 (t, *J* = 9.0 Hz), 136.2 (+, CH), 115.0, 111.7 (dd, *J* = 18.8 Hz, *J* = 7.3 Hz; +, CH, 2C), 104.1 (t, *J* = 25.2 Hz; +, CH), 82.1, 55.7 (t, *J* = 2.3 Hz; –, CH2), 50.0 (+, CH), 46.7 (+, CH), 23.3 (+, CH3, 2C), 19.2 (+, CH3, 2C); 19F NMR (376 MHz, CDCl3, ppm) δ = -108.33 (2F); EI (m/z, 70 eV, 80 °C): 346 (9) [M]+, 253 (24), 252 (16), 246 (11), 127 (100), 101 (11), 100 (12), 83 (11), 77 (10), 71 (13), 69 (24), 58 (27), 57 (29), 55 (15). HRMS (C17H20N6F2): Calcd 346.1718, Found 346.1716; IR (ATR, ṽ) = 3125 (vw), 3098 (vw), 3055 (vw), 2989 (w), 2976 (w), 2962 (w), 2932 (w), 2873 (w), 2221 (s), 1625 (s), 1598 (m), 1540 (s), 1460 (s), 1439 (m), 1411 (vs), 1368 (vs), 1356 (vs), 1329 (w), 1317 (vs), 1262 (vs), 1230 (s), 1188 (w), 1156 (vs), 1143 (s), 1119 (vs), 1099 (s), 1031 (s), 1014 (s), 997 (s), 976 (w), 948 (w), 909 (w), 892 (w), 873 (m), 849 (vs), 839 (vs), 796 (s), 734 (s), 718 (vs), 690 (m), 654 (s), 633 (m), 612 (w), 601 (w) cm–1.

**13c**: (E)-1-(3,5-difluorobenzyl)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C17H20F2N6; Exact Mass: 346.1718; Smiles: CC(N(C(C)C)/N=N/c1n(ncc1C#N)Cc1cc(F)cc(c1)F)C; InChIKey: ZFEWCQZPKGQXCJ-GHVJWSGMSA-N

*Rf* = 0.30 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.65 (s, 1H), 6.89–6.73 (m, 2H), 6.72–6.64 (m, 1H), 5.31 (s, 2H), 5.14 (hept, *J* = 6.8 Hz, 1H), 4.10 (hept, *J* = 6.6 Hz, 1H), 1.44 (d, *J* = 6.7 Hz, 6H), 1.25 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 163.1 (dd, *J* = 249.4 Hz, *J* = 12.7 Hz, 2C), 154.9, 142.6 (+, CH), 140.2 (t, *J* = 9.1 Hz), 115.6, 110.8 (dd, *J* = 18.6 Hz, *J* = 7.0 Hz, CH, 2C), 103.4 (t, *J* = 25.2 Hz; +, CH), 79.4, 51.5 (+, CH), 51.3 (t, *J* = 2.3 Hz, –, CH2), 48.2 (+, CH), 23.1 (+, CH3, 2C), 18.8 (+, CH3, 2C); 19F NMR (376 MHz, CDCl3, ppm) δ = -109.1; EI (m/z, 70 eV, 80 °C): 347 (10) [M+H]+, 346 (52) [M]+, 246 (29), 181 (19), 131 (29), 127 (51), 119 (10), 100 (33), 69 (100), 58 (22). HRMS (C17H20N6F2): Calcd 346.1718, Found 346.1716; IR (ATR, ṽ) = 3129 (vw), 3074 (vw), 3055 (vw), 2985 (w), 2948 (w), 2878 (vw), 2218 (s), 1822 (vw), 1737 (vw), 1711 (vw), 1660 (vw), 1625 (m), 1599 (s), 1536 (m), 1493 (w), 1466 (m), 1446 (m), 1424 (vs), 1392 (w), 1366 (vs), 1349 (vs), 1315 (s), 1293 (w), 1271 (s), 1242 (s), 1221 (vs), 1205 (s), 1174 (m), 1164 (m), 1136 (m), 1122 (vs), 1101 (vs), 1043 (w), 1028 (vs), 990 (s), 935 (s), 911 (m), 884 (w), 873 (m), 858 (vs), 847 (vs), 773 (s), 734 (w), 713 (s), 697 (m), 663 (m), 632 (s), 606 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-RPEOLKMCSJ-UHFFFADPSC-NUHFF-NJTWA-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/WSQPCVJPBSUDNZ-XTQSDGFTSA-N.1>

<https://doi.org/10.14272/ZFEWCQZPKGQXCJ-GHVJWSGMSA-N.1>

## (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazole-4-carbonitrile (12d), (E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazole-4-carbonitrile (13d)



To a solution of 5-[(~{E})-[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile (**15**, 301 mg, 1.36 mmol, 1.00 equiv) in 8 mL of anhydrous *N,N*-dimethylformamide, potassium carbonate (226 mg, 1.63 mmol, 1.20 equiv) was added at 0 °C and the resulting mixture was stirred at 0 °C for 45 minutes. Iodoethane (255 mg, 131 μL, 1.63 mmol, 1.20 equiv) was slowly added over 15 minutes and the reaction mixture was heated to 90 °C for 14 hours. The resulting mixture was cooled, poured over ice and the aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over Na2SO4, filtered and the solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 2:1, giving (E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazole-4-carbonitrile (**12d**, 194 mg, 780 μmol, 57% yield) as a slightly grey solid and (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazole-4-carbonitrile (**13d**, 117 mg, 470 μmol, 34% yield) as a slightly grey solid.

**12d**: (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazole-4-carbonitrile; Formula: C12H20N6; Exact Mass: 248.1749; Smiles: N#Cc1cn(nc1/N=N/N(C(C)C)C(C)C)CC; InChIKey: IOAQHBXBXAUXJG-JQIJEIRASA-N

*Rf* = 0.49 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.66 (s, 1H), 5.38 (hept, *J* = 6.8 Hz, 1H), 4.09 (q, *J* = 7.3 Hz, 2H), 4.00 (hept, *J* = 6.7 Hz, 1H), 1.48 (t, *J* = 7.3 Hz, 3H), 1.42 (d, *J* = 6.6 Hz, 6H), 1.21 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 162.8, 134.9 (+, CH), 115.4, 80.6, 49.8 (+, CH), 47.9 (–, CH2), 46.4 (+, CH), 23.3 (+, CH3, 2C), 19.2 (+, CH3, 2C), 15.1 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 250 (17) [M+2H]+, 249 (100) [M+H]+, 248 (15) [M]+, 148 (53), 147 (23), 137 (12), 136 (10), 123 (11), 111 (20), 109 (22), 100 (28), 99 (10), 97 (39), 95 (32), 93 (10), 85 (25). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C12H21N6, 249.1822; Found 249.1823; IR (ATR, ṽ) = 3125 (vw), 3061 (vw), 2975 (m), 2935 (w), 2873 (w), 2220 (m), 2169 (vw), 1650 (vw), 1537 (s), 1455 (m), 1412 (vs), 1377 (s), 1366 (vs), 1349 (s), 1322 (w), 1261 (vs), 1225 (vs), 1186 (w), 1153 (vs), 1132 (m), 1102 (s), 1082 (w), 1033 (s), 1013 (w), 958 (w), 908 (w), 884 (w), 839 (m), 819 (m), 802 (w), 771 (vw), 718 (m), 690 (w), 629 (m) cm–1.

**13d**: (E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazole-4-carbonitrile; Formula: C12H20N6; Exact Mass: 248.1749; Smiles: N#Cc1cnn(c1/N=N/N(C(C)C)C(C)C)CC; InChIKey: ZTYVCHQAFNRURB-FOCLMDBBSA-N

*Rf* = 0.71 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.61 (s, 1H), 5.18 (hept, *J* = 6.9 Hz, 1H), 4.23 (q, *J* = 7.3 Hz, 2H), 4.09 (hept, *J* = 6.6 Hz, 1H), 1.45 (d, *J* = 6.6 Hz, 6H), 1.41 (t, *J* = 7.3 Hz, 3H), 1.30 (d, *J* = 6.9 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 154.2, 142.0 (+, CH), 116.1, 77.7, 51.3 (+, CH), 47.9 (+, CH), 43.7 (–, CH2), 23.2 (+, CH3, 2C), 19.0 (+, CH3, 2C), 15.0 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 250 (15) [M+2H]+, 249 (100) [M+H]+, 248 (45) [M]+, 148 (13). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C12H21N6 249.1822; Found 249.1825; IR (ATR, ṽ) = 3111 (vw), 2978 (w), 2938 (w), 2874 (w), 2221 (s), 2172 (vw), 1758 (vw), 1536 (w), 1497 (w), 1470 (w), 1462 (w), 1422 (vs), 1392 (vs), 1378 (vs), 1367 (vs), 1319 (m), 1272 (s), 1251 (m), 1220 (s), 1196 (m), 1179 (m), 1162 (m), 1135 (m), 1109 (s), 1098 (s), 1086 (m), 1028 (w), 1010 (s), 958 (m), 909 (w), 882 (s), 846 (w), 793 (vw), 735 (vw), 722 (w), 711 (m), 674 (vw), 652 (w), 623 (vw), 606 (w), 577 (w), 550 (w), 531 (m), 518 (w), 431 (vw), 408 (vw), 384 (vw) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-PTHGCHFVSV-UHFFFADPSC-NUHFF-NXOJS-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/IOAQHBXBXAUXJG-JQIJEIRASA-N.1>

<https://doi.org/10.14272/ZTYVCHQAFNRURB-FOCLMDBBSA-N.1>

## (E)-1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (12e), (E)-1-cyclopentyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (13e)



To a solution of 5-[[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile (**15**, 306 mg, 1.39 mmol, 1.00 equiv) in 15 mL of anhydrous *N,N*-dimethylformamide, potassium carbonate (231 mg, 1.67 mmol, 1.20 equiv) was added at 0 °C and the resulting mixture was stirred at 0 °C for 45 minutes. Bromocyclopentane (249 mg, 179 μL, 1.67 mmol, 1.20 equiv) was slowly added over 15 minutes and the reaction mixture was heated to 90 °C for 14 hours. The resulting mixture was cooled, poured over ice and the aqueous phase was extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na2SO4, filtered and the solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 4:1, giving 1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12e**, 157 mg, 544 μmol, 39% yield) as a colorless solid and 1-cyclopentyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**13e**, 207 mg, 718 μmol, 52% yield) as a colorless solid.

**12e**: (E)-1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C15H24N6; Exact Mass: 288.2062; Smiles: CC(N(C(C)C)/N=N/c1nn(cc1C#N)C1CCCC1)C; InChIKey: VHDGMVPZVVGIBB-HTXNQAPBSA-N

*Rf* = 0.18 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.69 (s, 1H), 5.46 (hept, *J* = 6.5 Hz, 1H), 4.54 (p, *J* = 7.1 Hz, 1H), 4.00 (hept, *J* = 6.7 Hz, 1H), 2.20–1.98 (m, 4H), 1.94–1.77 (m, 2H), 1.77–1.60 (m, 2H), 1.44 (d, *J* = 6.6 Hz, 6H), 1.22 (d, *J* = 6.9 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 162.8, 134.3 (+, CH), 115.7, 80.3, 64.0 (+, CH), 49.7 (+, CH), 46.2 (+, CH), 32.7 (–, CH2, 2C), 24.2 (–, CH2, 2C), 23.4 (+, CH3, 2C), 19.4 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 290 (20) [M+2H]+, 289 (100) [M+H]+, 288 (14) [M]+, 287 (12) [M-H]+, 221 (12), 188 (65), 147 (32), 136 (11), 123 (10), 120 (19), 111 (14), 109 (21), 107 (10), 100 (52), 97 (28), 95 (25), 86 (10), 85 (35). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C15H25N6, 289.2135; Found 289.2133; IR (ATR, ṽ) = 3128 (vw), 2975 (m), 2938 (w), 2873 (w), 2224 (s), 2169 (vw), 1541 (m), 1459 (w), 1451 (w), 1402 (vs), 1381 (vs), 1366 (vs), 1315 (w), 1258 (vs), 1227 (vs), 1187 (w), 1157 (vs), 1129 (s), 1101 (s), 1028 (m), 1000 (w), 942 (vw), 909 (w), 882 (w), 823 (m), 720 (m), 690 (vw), 637 (w) cm–1.

**13e**: (E)-1-cyclopentyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C15H24N6; Exact Mass: 288.2062; Smiles: CC(N(C(C)C)/N=N/c1n(ncc1C#N)C1CCCC1)C; InChIKey: OPJIUORDWAXUPI-VHEBQXMUSA-N

*Rf* = 0.33 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.61 (s, 1H), 5.19 (hept, *J* = 6.8 Hz, 1H), 5.01 (p, *J* = 7.6 Hz, 1H), 4.08 (hept, *J* = 6.8 Hz, 1H), 2.11–1.98 (m, 4H), 1.98–1.83 (m, 2H), 1.73–1.58 (m, 2H), 1.45 (d, *J* = 6.7 Hz, 6H), 1.29 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 154.4, 141.8 (+, CH), 116.3, 77.6, 58.6 (+, CH), 51.2 (+, CH), 47.8 (+, CH), 32.4 (–, CH2, 2C), 24.9 (–, CH2, 2C), 23.2 (+, CH3, 2C), 19.1 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 290 (20) [M+2H]+, 289 (100) [M+H]+, 288 (43) [M]+, 188 (10), 154 (13), 136 (10), 120 (10), 100 (11). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C15H25N6, 289.2135; Found 289.2133; IR (ATR, ṽ) = 3101 (vw), 2970 (w), 2935 (w), 2870 (w), 2218 (s), 2166 (vw), 1747 (vw), 1531 (m), 1480 (w), 1470 (m), 1445 (w), 1418 (s), 1394 (vs), 1378 (s), 1358 (vs), 1322 (w), 1269 (vs), 1222 (s), 1197 (m), 1171 (m), 1160 (m), 1130 (m), 1098 (s), 1031 (w), 1013 (s), 931 (w), 907 (w), 875 (m), 846 (w), 734 (vw), 711 (w), 652 (w), 608 (vw) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-CCXXYIBWZN-UHFFFADPSC-NUHFF-NCWUQ-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/VHDGMVPZVVGIBB-HTXNQAPBSA-N.1>

<https://doi.org/10.14272/OPJIUORDWAXUPI-VHEBQXMUSA-N.1>

## (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile (12f), (E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile (13f)



To a stirred suspension of 5-[(~{E})-[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile (**15**, 507 mg, 2.30 mmol, 1.00 equiv) and potassium carbonate (314 mg, 2.27 mmol, 0.986 equiv) in 5 mL of *N,N*-dimethylformamide, 1-bromo-2-methylpropane (366 mg, 291 μL, 2.67 mmol, 1.16 equiv) was added dropwise within 10 min at 21 °C. The reaction mixture was stirred at 21 °C for 14 hours. The reaction was quenched in ice-cold water and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and concentrated in vacuo to give the crude product.

The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 20:1 to 4:1, giving 3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile (**12f**, 177 mg, 640 μmol, 28% yield) as a light-yellow solid and 5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile (**13f**, 299 mg, 1.08 mmol, 47% yield) as a transparent yellow solid.

**12f**: (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile; Formula: C14H24N6; Exact Mass: 276.2062; Smiles: N#Cc1cn(nc1/N=N/N(C(C)C)C(C)C)CC(C)C; InChIKey: GSWCLGSPFBAJHR-FBMGVBCBSA-N

*Rf* = 0.34 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.62 (s, 1H), 5.40 (hept, *J* = 6.6 Hz, 1H), 4.01 (hept, *J* = 6.8 Hz, 1H), 3.81 (d, *J* = 7.3 Hz, 2H), 2.27 (hept, *J* = 6.9 Hz, 1H), 1.43 (d, *J* = 6.6 Hz, 6H), 1.22 (d, *J* = 6.8 Hz, 6H), 0.91 (d, *J* = 6.7 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 162.9, 136.0 (+, CH), 115.5, 80.4, 60.6 (–, CH2), 49.8 (+, CH), 46.4 (+, CH), 29.1 (+, CH), 23.3 (+, CH3, 2C), 19.9 (+, CH3, 2C), 19.3 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 278 (18) [M+2H]+, 277 (100) [M+H]+, 276 (17) [M]+, 176 (50), 109 (15), 107 (11), 100 (31), 97 (15), 95 (25), 93 (16), 91 (14). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C14H25N6 277.2141; Found 277.2139; IR (ATR, ṽ) = 3123 (vw), 3064 (vw), 2972 (w), 2956 (w), 2934 (w), 2871 (w), 2225 (s), 1544 (s), 1460 (m), 1445 (w), 1405 (vs), 1387 (vs), 1370 (vs), 1357 (vs), 1296 (w), 1258 (vs), 1227 (s), 1215 (m), 1157 (vs), 1130 (m), 1115 (w), 1101 (s), 1031 (m), 1009 (m), 948 (w), 926 (w), 909 (w), 894 (w), 881 (w), 858 (m), 844 (w), 819 (w), 796 (w), 724 (m), 711 (w), 630 (m) cm–1.

**13f**: (E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile; Formula: C14H24N6; Exact Mass: 276.2062; Smiles: N#Cc1cnn(c1/N=N/N(C(C)C)C(C)C)CC(C)C; InChIKey: MWOHIDYQOPZPNH-ISLYRVAYSA-N

*Rf* = 0.62 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.62 (s, 1H), 5.12 (hept, *J* = 6.8 Hz, 1H), 4.09 (hept, *J* = 6.6 Hz, 1H), 3.98 (d, *J* = 7.2 Hz, 2H), 2.22 (hept, *J* = 6.8 Hz, 1H), 1.45 (d, *J* = 6.6 Hz, 6H), 1.29 (d, *J* = 6.8 Hz, 6H), 0.90 (d, *J* = 6.7 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 154.9, 141.9 (+, CH), 116.1, 77.4, 55.6 (–, CH2), 51.4 (+, CH), 48.1 (+, CH), 29.3 (+, CH), 23.2 (+, CH3, 2C), 20.1 (+, CH3, 2C), 19.0 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 278 (17) [M+2H]+, 277 (100) [M+H]+, 276 (29) [M]+, 176 (16), 100 (12), 95 (12). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C14H25N6, 277.2141; Found 277.2142; IR (ATR, ṽ) = 3112 (vw), 2968 (m), 2955 (m), 2946 (m), 2925 (m), 2868 (w), 2853 (w), 2217 (s), 2163 (vw), 1738 (vw), 1690 (vw), 1533 (s), 1490 (w), 1468 (m), 1446 (w), 1435 (m), 1417 (vs), 1397 (vs), 1383 (vs), 1357 (vs), 1322 (m), 1271 (vs), 1241 (vs), 1220 (vs), 1173 (s), 1162 (s), 1130 (s), 1111 (s), 1098 (s), 1034 (m), 1014 (vs), 946 (m), 926 (w), 908 (m), 892 (w), 882 (w), 873 (m), 847 (m), 823 (w), 775 (m), 727 (w), 708 (m), 654 (w), 628 (w), 620 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-NZDLOEMQHU-UHFFFADPSC-NUHFF-NXEFH-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/GSWCLGSPFBAJHR-FBMGVBCBSA-N.1>

<https://doi.org/10.14272/MWOHIDYQOPZPNH-ISLYRVAYSA-N.1>

## Ethyl (E)-2-(4-cyano-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)acetate (12g), ethyl (E)-2-(4-cyano-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)acetate (13g)



To a stirred suspension of 5-[(~{E})-[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile (**15**, 529 mg, 2.40 mmol, 1.00 equiv) and potassium carbonate (314 mg, 2.27 mmol, 0.946 equiv) in 10 mL of *N,N*-dimethylformamide, ethyl 2-bromoacetate (447 mg, 297 μL, 2.67 mmol, 1.11 equiv) was added dropwise within 10 min at 21 °C. The reaction mixture was stirred at 21 °C for 14 hours. The reaction was quenched in ice-cold water and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over sodium sulfate and concentrated under vacuo to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:0 to 4:1, giving ethyl 2-(4-cyano-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)acetate (**12g**, 397 mg, 1.30 mmol, 54% yield) as a colorless solid and ethyl 2-(4-cyano-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)acetate (**13g**, 109 mg, 356 μmol, 15% yield) as a colorless solid.

**12g**: ethyl (E)-2-(4-cyano-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)acetate; Formula: C14H22N6O2; Exact Mass: 306.1804; Smiles: CCOC(=O)Cn1nc(c(c1)C#N)/N=N/N(C(C)C)C(C)C; InChIKey: GMSYXQOQYOUAHU-FBMGVBCBSA-N

*Rf* = 0.16 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.80 (s, 1H), 5.37 (hept, *J* = 6.8 Hz, 1H), 4.82 (s, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.03 (hept, *J* = 6.6 Hz, 1H), 1.44 (d, *J* = 6.6 Hz, 6H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 6H). 13C NMR (100 MHz, CDCl3, ppm) δ = 166.8, 163.0, 137.5 (+, CH), 115.0, 82.5, 62.4 (–, CH2), 53.6 (–, CH2), 50.0 (+, CH), 46.7 (+, CH), 23.3 (+, CH3, 2C), 19.3 (+, CH3, 2C), 14.2 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 308 (17) [M+2H]+, 307 (100) [M+H]+, 306 (10) [M]+, 305 (11), 207 (13), 206 (76), 154 (14), 147 (12), 136 (20), 135 (11), 133 (10), 131 (11), 123 (19), 121 (33), 119 (16), 117 (11), 111 (23), 109 (38), 107 (26), 106 (17), 105 (24), 100 (42), 97 (43), 95 (70), 94 (10), 93 (34), 91 (40), 86 (10). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C14H23O2N6, 307.1882; Found 307.1882; IR (ATR, ṽ) = 3132 (vw), 3071 (vw), 2976 (w), 2936 (w), 2874 (vw), 2227 (m), 1748 (vs), 1544 (s), 1465 (m), 1409 (vs), 1368 (vs), 1356 (vs), 1299 (w), 1261 (vs), 1208 (vs), 1157 (vs), 1130 (s), 1099 (s), 1031 (s), 1006 (s), 970 (w), 909 (m), 874 (m), 843 (m), 805 (w), 718 (s), 697 (m), 639 (m), 620 (w) cm–1.

**13g**: ethyl (E)-2-(4-cyano-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)acetate; Formula: C14H22N6O2; Exact Mass: 306.1804; Smiles: CCOC(=O)Cn1ncc(c1/N=N/N(C(C)C)C(C)C)C#N; InChIKey: UVXRQPKXJULFTR-ISLYRVAYSA-N

*Rf* = 0.26 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.67 (s, 1H), 5.10 (hept, *J* = 6.8 Hz, 1H), 4.94 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.10 (hept, *J* = 6.6 Hz, 1H), 1.45 (d, *J* = 6.6 Hz, 6H), 1.30–1.21 (m, 9H); 13C NMR (100 MHz, CDCl3, ppm) δ = 167.5, 155.4, 142.6 (+, CH), 115.6, 78.1, 61.9 (–, CH2), 51.7 (+, CH), 50.0 (–, CH2), 48.3 (+, CH), 23.2 (+, CH3, 2C), 18.9 (+, CH3, 2C), 14.3 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 308 (18) [M+2H]+, 307 (100) [M+H]+, 306 (23) [M]+, 206 (10). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C14H23O2N6, 307.1882; Found 307.1881; IR (ATR, ṽ) = 2982 (w), 2941 (w), 2878 (vw), 2220 (s), 1735 (vs), 1538 (m), 1502 (w), 1473 (w), 1465 (w), 1426 (vs), 1418 (vs), 1391 (vs), 1375 (s), 1363 (vs), 1341 (s), 1313 (w), 1293 (m), 1278 (vs), 1255 (vs), 1242 (vs), 1211 (vs), 1191 (m), 1177 (w), 1163 (s), 1142 (m), 1135 (m), 1102 (vs), 1051 (m), 1030 (vs), 1021 (vs), 945 (w), 911 (m), 884 (w), 867 (w), 858 (m), 850 (m), 805 (w), 779 (m), 730 (w), 711 (m), 646 (m), 626 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-HLSFJQKZZG-UHFFFADPSC-NUHFF-NQFOL-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/GMSYXQOQYOUAHU-FBMGVBCBSA-N.1>

<https://doi.org/10.14272/UVXRQPKXJULFTR-ISLYRVAYSA-N.1>

## (E)-1-(4-bromobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (12h), (E)-1-(4-bromobenzyl)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (13h)

## 



In a vial, 5-(E)-[di(propan-2-yl)amino]diazenyl]-1~{H}-pyrazole-4-carbonitrile (**15**, 307 mg, 1.39 mmol, 1.00 equiv) was dissolved in 12 mL of DMSO. Cesium carbonate (532 mg, 1.63 mmol, 1.17 equiv) was added and the solution was cooled to 0 °C. 1-Bromo-4-(bromomethyl)benzene (681 mg, 2.72 mmol, 1.96 equiv) was added and the vial was closed and slowly warmed to 21 °C. The reaction mixture was stirred at 40 °C for 2 days. The reaction was quenched by addition of ice and was extracted with EtOAc (3 × 15 mL). The obtained organic layers were co-evaporated with Celite(R) to give the Celite-immobilized crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 41:, giving (E)-1-(4-bromobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12h**, 278 mg, 713 μmol) 51% yield and (E)-1-(4-bromobenzyl)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**13h**, 227 mg, 582 μmol) in 42% yield.

**12h**: (E)-1-(4-bromobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C17H21BrN6; Exact Mass: 388.1011; Smiles: N#Cc1cn(nc1/N=N/N(C(C)C)C(C)C)Cc1ccc(cc1)Br; InChIKey: JVCZUZVUVDDSML-LSDHQDQOSA-N

R*f* = 0.2 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.67 (s, 1H), 7.48–7.38 (m, 2H), 7.17–7.09 (m, 2H), 5.42–5.28 (m, 1H), 5.14 (d, *J* = 3.1 Hz, 2H), 4.06–3.93 (m, 1H), 1.41 (dd, *J* = 6.7 Hz, *J* = 3.0 Hz, 6H), 1.20 (dd, *J* = 7.0 Hz, J = 3.5 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 163.0, 135.8 (+, CH), 134.0, 132.1 (+, CH, 2C), 129.8 (+, CH, 2C), 122.7, 115.1, 81.6, 56.0 (–, CH2), 49.8 (+, CH), 46.5 (+, CH), 23.2 (+, CH3, 2C), 19.2 (+, CH3, 2C); MS (EI, 70 eV, 90 °C): m/z (%) = 490/388 (20/22) [M]+, 297/295 (21/18), 290/288 (11/11), 208 (11), 181 (24), 171/169 (92/100), 149 (11), 131 (24), 116 (19), 100 (58), 97 (15), 91/89 (15/27), 90 (29), 85 (14), 84 (15), 83 (15), 71 (21), 70 (11), 69 (53), 58 (51), 57 (33), 55 (16). HRMS (EI, C17H21N679Br): Calcd 388.1011; Found 388.1010.

**13h**: (E)-1-(4-bromobenzyl)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile; Formula: C17H21BrN6; Exact Mass: 388.1011; Smiles: N#Cc1cnn(c1/N=N/N(C(C)C)C(C)C)Cc1ccc(cc1)Br;

InChIKey: HUNPOMLAEFCWSA-QURGRASLSA-N

R*f* = 0.31 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.64 (s, 1H), 7.46–7.37 (m, 2H), 7.16–7.08 (m, 2H), 5.30 (s, 2H), 5.14 (sept, *J* = 6.8 Hz, 1H), 4.09 (sept, *J* = 6.6 Hz, 1H), 1.44 (d, *J* = 6.6 Hz, 6H), 1.26 (d, *J* = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 154.7, 142.4 (+, CH), 135.4, 131.8 (+, CH, 2C), 129.6 (+, CH, 2C), 121.9, 115.7, 77.9, 51.5 (–, CH2), 51.4 (+, CH), 48.2 (+, CH), 23.1 (+, CH3, 2C), 18.9 (+, CH3, 2C); MS (EI, 70 eV, 80 °C): m/z (%) = 390/388 (32/31) [M]+, 338 (12), 290/288 (11/11), 231/229 (23/22), 187/185 (53/58), 181 (20), 172/170 (11/12), 171/169 (95/100), 131 (26), 100 (74), 91/89 (24/31), 90 (44), 84 (14), 78 (17), 77 (32), 71 (11), 69 (52), 58 (67), 57 (18), 55 (12). HRMS (EI, C17H21N679Br): Calcd 388.1011; Found 388.1010.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-CYZFVCDWYP-UHFFFADPSC-NUHFF-NPQQK-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/JVCZUZVUVDDSML-LSDHQDQOSA-N.1>

<https://doi.org/10.14272/HUNPOMLAEFCWSA-QURGRASLSA-N.1>

## (E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (9a)



Step 1: (E)-1-Benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12a**, 120 mg, 388 μmol, 1.00 equiv) was dissolved in 65 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (44.1 mg, 1.16 mL, 1.16 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (70 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 × 70 mL). The combined organic layers were washed with brine (200 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (E)-(1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: The crude (E)-(1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine was dissolved in 65 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before acetic anhydride (59.3 mg, 55.0 μL, 581 μmol, 1.50 equiv) was added dropwise. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (70 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 70 mL). The combined organic layers were washed with brine (200 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using methylene chloride/methanol 50:1 to 30:1. It was further purified *via* HPLC using MeCN/H₂O 10:1, to give (E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (**9a**, 32.0 mg, 89.8 μmol, 23% yield) as a brown oil.

**9a**: (E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide; Formula: C19H28N6O; Exact Mass: 356.2325; Smiles: CC(=O)NCc1cn(nc1/N=N/N(C(C)C)C(C)C)Cc1ccccc1; InChIKey: VXSAZKPHEZACHZ-XTQSDGFTSA-N

*Rf* = 0.06 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.40–7.31 (m, 5H), 7.20 (s, 1H), 5.91 (br.t, *J* = 5.5 Hz, 1H), 5.41 (br.s, 1H), 5.16 (s, 2H), 4.29 (d, *J* = 5.3 Hz, 2H), 3.98 (br.s, 1H), 1.88 (s, 3H), 1.32 (br.s, 6H), 1.20 (br.s, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.3, 158.0, 136.4, 130.2 (+, CH), 128.8 (+, CH, 2C), 128.1 (+, CH, 3C), 107.5, 56.2 (–, CH2), 48.3 (+, CH), 45.3 (+, CH), 34.4 (–, CH2), 23.7 (+, CH3, 2C), 23.5 (+, CH3), 19.4 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 358 (22) [M+2H]+, 357 (100) [M+H]+, 356 (21) [M]+, 355 (13) [M-H]+, 298 (31), 257 (12), 256 (79), 100 (13), 91 (60). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C19H29ON6, 357.2403; Found 357.2402; IR (ATR, ṽ) = 3285 (w), 3080 (vw), 3065 (vw), 3033 (vw), 2973 (w), 2931 (w), 2871 (vw), 2230 (vw), 1650 (s), 1543 (m), 1497 (w), 1465 (m), 1455 (s), 1419 (vs), 1402 (vs), 1364 (vs), 1341 (s), 1244 (vs), 1224 (vs), 1150 (vs), 1128 (s), 1096 (m), 1033 (s), 1011 (m), 969 (w), 909 (m), 851 (w), 841 (w), 813 (w), 727 (vs), 704 (vs), 643 (m), 630 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-VXSAZKPHEZ-UHFFFADPSC-NUHFF-NQYKM-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/VXSAZKPHEZACHZ-XTQSDGFTSA-N.1>

## (E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide (9b)



Step 1: 1-Benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12a**, 202 mg, 650 μmol, 1.00 equiv) was dissolved in 100 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (74.0 mg, 1.95 mL, 1.95 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (100 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 100 mL). The combined organic layers were washed with brine (300 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: The crude (1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine was dissolved in 100 mL of dry THF under nitrogen atmosphere. Triethylamine (197 mg, 272 μL, 1.95 mmol, 3.00 equiv) was added and the solution was cooled to 0 °C before benzoyl chloride (137 mg, 113 μL, 975 μmol, 1.50 equiv) was slowly added. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (100 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 100 mL). The combined organic layers were washed with brine (300 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 4:1, giving *N*-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide (**9b**, 111 mg, 266 μmol, 41% yield) as a brown oil.

**9b**: (E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide; Formula: C24H30N6O; Exact Mass: 418.2481; Smiles: CC(N(C(C)C)/N=N/c1nn(cc1CNC(=O)c1ccccc1)Cc1ccccc1)C; InChIKey: CYCAXLGFKDSWNS-BYCLXTJYSA-N

*Rf* = 0.38 (cyclohexane/ethyl acetate 1:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.73–7.66 (m, 2H), 7.49–7.27 (m, 9H), 6.50 (br.t, *J* = 5.5 Hz, 1H), 5.42 (br.s, 1H), 5.21 (s, 2H), 4.53 (d, *J* = 5.3 Hz, 2H), 3.97 (br.s, 1H), 1.33–1.17 (m, 12H); 13C NMR (100 MHz, CDCl3, ppm) δ = 167.2, 158.1, 136.4, 135.0, 131.4 (+, CH, 2C), 130.5 (+, CH), 128.9 (+, CH, 2C), 128.6 (+, CH, 2C), 128.2 (+, CH, 2C), 127.0 (+, CH, 2C), 107.5, 56.3 (–, CH2), 48.6 (+, CH), 45.5 (+, CH), 35.0 (–, CH2), 23.7 (+, CH3, 2C), 19.5 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 419 (27) [M+H]+, 318 (36) [M]+, 298 (22), 154 (12), 136 (12), 109 (11), 107 (14), 105 (75), 102 (16), 100 (10), 97 (12), 95 (23), 93 (16), 91 (100). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C24H31ON6 419.2559; Found 419.2559; IR (ATR, ṽ) = 3312 (w), 3064 (w), 3031 (vw), 2972 (w), 2928 (w), 2868 (w), 1730 (vw), 1642 (s), 1602 (w), 1578 (w), 1530 (s), 1487 (m), 1465 (m), 1455 (s), 1417 (vs), 1404 (vs), 1380 (m), 1363 (s), 1346 (s), 1293 (m), 1244 (vs), 1224 (vs), 1150 (vs), 1128 (s), 1098 (m), 1075 (w), 1031 (s), 1010 (w), 1001 (w), 986 (w), 925 (w), 911 (w), 890 (vw), 850 (vw), 802 (w), 755 (w), 694 (vs), 647 (m), 605 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-CYCAXLGFKD-UHFFFADPSC-NUHFF-NULGB-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/CYCAXLGFKDSWNS-BYCLXTJYSA-N.1>

## (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methyl)-3-methylbutanamide (9c)



Step 1: (E)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile (**12b**, 293 mg, 903 μmol, 1.00 equiv) was dissolved in 150 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (103 mg, 2.71 mL, 2.71 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (150 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 150 mL). The combined organic layers were washed with brine (400 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (E)-(3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: The crude (E)-(3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methanamine was dissolved in 150 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before 3-methylbutanoyl 3-methylbutanoate (252 mg, 271 μL, 1.35 mmol, 1.50 equiv) was slowly added. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (150 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 150 mL). The combined organic layers were washed with brine (400 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 1:1, giving (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methyl)-3-methylbutanamide (**9c**, 227 mg, 551 μmol, 61% yield) as a light-brown oil.

**9c**: (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methyl)-3-methylbutanamide; Formula: C23H36N6O; Exact Mass: 412.2951; Smiles: CC(CC(=O)NCc1cn(nc1/N=N/N(C(C)C)C(C)C)Cc1ccc(cc1)C)C; InChIKey: MORMFGNFEXIKDM-IMVLJIQESA-N

*Rf* = 0.05 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.21–7.08 (m, 5H), 5.82 (br.t, *J* = 5.5 Hz, 1H), 5.42 (br.s, 1H), 5.14 (s, 2H), 4.31 (d, *J* = 5.5 Hz, 2H), 4.00 (br.s, 1H), 2.32 (s, 3H), 2.13–1.99 (m, 1H), 1.94 (d, *J* = 7.1 Hz, 2H), 1.34 (br.s, 6H), 1.22 (br.s, 6H), 0.88 (d, *J* = 6.6 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 171.8, 157.9, 137.9, 133.3, 130.1 (+, CH), 129.5 (+, CH, 2C), 128.2 (+, CH, 2C), 107.8, 56.0, 48.4, 46.5 (–, CH2), 45.4 (–, CH2), 34.1 (–, CH2), 26.2 (+, CH), 23.8 (+, CH3, 2C), 22.5 (+, CH3, 2C), 21.2 (+, CH3), 19.4 (+, CH3, 2C). MS (FAB, Matrix: 3-NBA): *m/z* (%) = 414 (13) [M+2H]+, 413 (54) [M+H]+, 412 (14) [M]+, 411 (15), 313 (24), 312 (100), 105 (78). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C23H37ON6, 413.3029; Found 413.3030; IR (ATR, ṽ) = 3432 (vw), 3292 (w), 3078 (vw), 3055 (vw), 2956 (m), 2928 (w), 2868 (w), 1643 (vs), 1536 (m), 1516 (m), 1465 (s), 1421 (vs), 1402 (vs), 1380 (m), 1364 (vs), 1307 (w), 1242 (vs), 1224 (vs), 1181 (m), 1149 (vs), 1126 (vs), 1099 (m), 1033 (s), 1010 (m), 962 (w), 922 (w), 911 (w), 885 (w), 843 (w), 823 (w), 796 (s), 752 (m), 727 (m), 698 (w), 677 (w), 640 (w), 629 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-MORMFGNFEX-UHFFFADPSC-NUHFF-NIWVK-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/MORMFGNFEXIKDM-IMVLJIQESA-N.1>

## (E)-N-((1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (9d)



Step 1: 1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12c**, 261 mg, 754 μmol, 1.00 equiv) was dissolved in 75 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (85.9 mg, 2.26 mL, 2.26 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (75 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 75 mL). The combined organic layers were washed with brine (150 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: The crude (1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine was dissolved in 75 mL of dry THF under nitrogen atmosphere. Triethylamine (229 mg, 315 μL, 2.26 mmol, 3.00 equiv) was added and the solution was cooled to 0 °C before acetyl chloride (88.8 mg, 80.4 μL, 1.13 mmol, 1.50 equiv) was added dropwise. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (75 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 75 mL). The combined organic layers were washed with brine (150 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using methylene chloride/methanol 50:1 to 30:1. It was further purified *via* HPLC using MeCN/H₂O 10:1, to give (E)-N-((1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (**9d**, 15.0 mg, 38.2 μmol, 5% yield) as a colorless oil.

**9d**: (E)-N-((1-(3,5-difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide; Formula: C19H26F2N6O; Exact Mass: 392.2136; Smiles: CC(=O)NCc1cn(nc1/N=N/N(C(C)C)C(C)C)Cc1cc(F)cc(c1)F; InChIKey: NQVQLXTURKHERM-WJTDDFOZSA-N

*Rf* = 0.47 (cyclohexane/ethyl acetate 1:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.30 (s, 1H), 6.80–6.65 (m, 3H), 5.91 (br.t, *J* = 5.6 Hz, 1H), 5.43 (br.s, 1H), 5.15 (s,2H), 4.34 (d, *J* = 5.5 Hz, 2H), 4.02 (br.s, 1H), 1.93 (s, 3H), 1.36 (d, *J* = 6.6 Hz, 6H), 1.22 (d, *J* = 6.8 Hz, 6H); 19F NMR (375 MHz, ppm) δ = -109.05; 13C NMR (100 MHz, CDCl3, ppm) δ = 169.5, 163.3 (2C; dd, *J* = 249.5 Hz, *J* = 12.6 Hz), 158.5, 140.6 (t, *J* = 8.9 Hz), 130.7 (+, CH), 110.6 (+, CH, 2C; dd, *J* = 18.6 Hz, *J* = 7.2 Hz), 108.2, 103.5 (+, CH; t, *J* = 25.3 Hz), 55.2 (–, CH2; t, *J* = 2.3 Hz), 48.4 (+, CH), 45.5 (+, CH), 34.3 (–, CH2), 23.8 (+, CH3, 2C), 23.6 (+, CH3), 19.5 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 394 (20) [M+2H]+, 393 (100) [M+H]+, 392 (14) [M]+, 375 (11), 334 (17), 292 (52), 154 (30), 138 (12), 137 (19), 136 (24), 127 (32), 100 (21). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C19H27ON6F2, 393.2214; Found 393.2212; IR (ATR, ṽ) = 3288 (w), 3081 (vw), 2975 (w), 2931 (w), 2870 (vw), 1650 (s), 1626 (vs), 1596 (s), 1543 (m), 1460 (s), 1418 (vs), 1364 (vs), 1340 (s), 1317 (s), 1245 (vs), 1224 (vs), 1153 (vs), 1118 (vs), 1098 (m), 1034 (m), 1001 (m), 846 (s), 728 (vs), 670 (m), 645 (w), 526 (m), 510 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-NQVQLXTURK-UHFFFADPSC-NUHFF-NCVEK-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/NQVQLXTURKHERM-WJTDDFOZSA-N.1>

## (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazol-4-yl)methyl)acetamide (9e)



Step 1: (E)-3-(3,3-Diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazole-4-carbonitrile (**12d**, 88.7 mg, 357 μmol, 1.00 equiv) was dissolved in 60 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (40.7 mg, 1.07 mL, 1.07 mmol, 1.00M, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (60 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 60 mL). The combined organic layers were washed with brine (150 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (E)-(3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: The crude (E)-(3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazol-4-yl)methanamine was dissolved in 60 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before acetic anhydride (54.7 mg, 50.6 μL, 536 μmol, 1.50 equiv) was slowly added. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (60 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 60 mL). The combined organic layers were washed with brine (150 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 2:1 to 1:1 to pure ethyl acetate, to give (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazol-4-yl)methyl)acetamide (**9e**, 62.1 mg, 211 μmol, 59% yield) as a light-brown oil.

**9e**: (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazol-4-yl)methyl)acetamide; Formula: C14H26N6O; Exact Mass: 294.2168; Smiles: CCn1cc(c(n1)/N=N/N(C(C)C)C(C)C)CNC(=O)C; InChIKey: SSTDOKZYUWDQQQ-FBMGVBCBSA-N

*Rf* = 0.15 (pure ethyl acetate). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.24 (s, 1H), 5.94 (t, *J* = 5.3 Hz, 1H), 5.41 (br.s, 1H), 4.30 (d, *J* = 5.4 Hz, 2H), 4.11–3.89 (m, 3H), 1.90 (s, 3H), 1.44 (t, *J* = 7.3 Hz, 3H), 1.32 (br.s, 6H), 1.19 (br.s, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.4, 157.8, 129.5 (+, CH), 106.6, 48.2 (+, CH), 47.1 (–, CH2), 45.3 (+, CH), 34.3 (–, CH2), 23.7 (+, CH3, 2C), 23.5 (+, CH3), 19.4 (+, CH3, 2C), 15.5 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 296 (17) [M+2H]+, 295 (99) [M+H]+, 294 (13) [M]+, 293 (26) [M-H]+, 237 (10), 236 (69), 195 (13), 194 (100), 154 (12), 150 (14), 139 (12), 133 (41), 125 (34), 124 (15), 109 (13), 107 (12), 100 (14), 95 (16), 93 (12), 91 (19). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C14H27ON6, 295.2241; Found 295.2243; IR (ATR, ṽ) = 3360 (w), 3262 (w), 3210 (w), 3077 (w), 2976 (w), 2932 (w), 2873 (w), 2225 (vw), 1650 (vs), 1571 (s), 1462 (w), 1407 (vs), 1380 (s), 1364 (vs), 1344 (vs), 1334 (s), 1302 (m), 1254 (vs), 1238 (vs), 1224 (vs), 1181 (s), 1166 (s), 1153 (vs), 1129 (s), 1096 (s), 1034 (s), 1018 (m), 992 (w), 953 (w), 926 (w), 912 (w), 882 (w), 849 (w), 829 (m), 792 (w), 724 (m), 713 (s), 701 (m), 639 (m), 606 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-SSTDOKZYUW-UHFFFADPSC-NUHFF-NUVCO-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/SSTDOKZYUWDQQQ-FBMGVBCBSA-N.1>

## (E)-N-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (9f)



Step 1: 1-Cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12e**, 132 mg, 459 μmol, 1.00 equiv) was dissolved in 75 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (52.2 mg, 1.38 mL, 1.38 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (75 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 75 mL). The combined organic layers were washed with brine (200 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: The crude (1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine was dissolved in 75 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before acetic anhydride (70.3 mg, 65.0 μL, 688 μmol, 1.50 equiv) was slowly added. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (75 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 75 mL). The combined organic layers were washed with brine (200 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 2:1 to 1:1 to pure ethyl acetate, to give *N*-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (**9f**, 114 mg, 340 μmol, 74% yield) as a light-brown oil.

**9f**: (E)-N-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide; Formula: C17H30N6O; Exact Mass: 334.2481; Smiles: CC(=O)NCc1cn(nc1/N=N/N(C(C)C)C(C)C)C1CCCC1; InChIKey: GZXDXORFZUUVGU-XUTLUUPISA-N

*Rf* = 0.03 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.28 (s, 1H), 5.91 (t, *J* = 5.5 Hz, 1H), 5.49 (br.s, 1H), 4.50 (p, *J* = 7.4 Hz, 1H), 4.30 (d, *J* = 5.4 Hz, 2H), 3.97 (br.s, 1H), 2.16–1.96 (m, 4H), 1.91 (s, 3H), 1.88–1.77 (m, 2H), 1.71–1.58 (m, 2H), 1.32 (s, 6H), 1.19 (s, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.3, 157.7, 128.8 (+, CH), 106.2, 63.2 (+, CH), 48.0 (+, CH), 45.0 (+, CH), 34.4 (–, CH2), 32.8 (–, CH2, 2C), 24.1 (–, CH2, 2C), 23.7 (+, CH3, 2C), 23.6 (+, CH3), 19.5 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 235 (14) [M+2H]+, 234 (100) [M+H]+, 233 (6) [M]+, 232 (10) [M-H]+, 192 (10), 155 (15), 154 (48), 139 (10), 138 (20), 137 (30), 136 (34), 109 (11), 107 (13), 97 (11), 95 (15), 91 (13); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 336 (20) [M+2H]+, 335 (100) [M+H]+, 334 (17) [M]+, 333 (17) [M-H]+, 276 (43), 235 (12), 234 (85), 100 (23), 97 (31), 96 (17), 95 (15), 85 (10). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C17H31ON6, 355.2554; Found 335.2555; IR (ATR, ṽ) = 3288 (w), 3274 (w), 3080 (vw), 3070 (vw), 2969 (m), 2938 (w), 2871 (w), 2230 (vw), 1650 (vs), 1543 (s), 1465 (m), 1421 (vs), 1402 (vs), 1363 (vs), 1340 (m), 1319 (w), 1239 (vs), 1224 (vs), 1152 (vs), 1128 (s), 1095 (m), 1033 (s), 1011 (w), 911 (w), 885 (vw), 847 (vw), 806 (w), 728 (m), 643 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-GZXDXORFZU-UHFFFADPSC-NUHFF-NHIGY-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/GZXDXORFZUUVGU-XUTLUUPISA-N.1>

## (E)-N-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide (9g)



Step 1: (E)-1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**12e**, 327 mg, 1.14 mmol, 1.00 equiv) was dissolved in 180 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (129 mg, 3.41 mL, 3.41 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (150 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 150 mL). The combined organic layers were washed with brine (400 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (E)-(1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: The crude (E)-(1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine was dissolved in 150 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before benzoyl benzoate (385 mg, 1.70 mmol, 1.50 equiv) was slowly added. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (150 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 150 mL). The combined organic layers were washed with brine (400 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 1:1, to give (E)-N-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide (**9g**, 285 mg, 719 μmol, 63% yield) as a colorless solid.

**9g**: (E)-N-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide; Formula: C22H32N6O; Exact Mass: 396.2638; Smiles: CC(N(C(C)C)/N=N/c1nn(cc1CNC(=O)c1ccccc1)C1CCCC1)C; InChIKey: SMDRKVWNQXOQTQ-SHHOIMCASA-N

*Rf* = 0.50 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.75–7.67 (m, 2H), 7.50–7.42 (m, 1H), 7.42–7.34 (m, 3H), 6.47 (br.t, *J* = 5.4 Hz, 1H), 5.51 (br.s, 1H), 4.60–4.46 (m, 3H), 3.95 (br.s, 1H), 2.18–2.00 (m, 4H), 1.92–1.79 (m, 2H), 1.73–1.60 (m, 2H), 1.27–1.14 (m, 12H). 13C NMR (100 MHz, CDCl3, ppm) δ = 167.1, 157.8, 135.0, 131.4 (+, CH), 129.1 (+, CH), 128.6 (+, CH, 2C), 127.0 (+, CH, 2C), 106.1, 63.2 (+, CH), 48.2 (+, CH), 45.1 (+, CH), 35.0 (–, CH2), 32.8 (–, CH2, 2C), 24.1 (–, CH2, 2C), 23.7 (+, CH3, 2C), 19.5 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 397 (39) [M+H]+, 396 (13) [M]+, 395 (20) [M-H]+, 297 (20), 296 (100), 277 (11), 276 (59), 269 (14), 165 (14), 133 (74), 106 (10), 105 (93), 100 (12), 99 (11), 97 (54), 96 (14). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C22H33ON6, 397.2710; Found 397.2710. IR (ATR, ṽ) = 3360 (w), 3061 (vw), 2973 (m), 2867 (w), 1738 (vw), 1656 (s), 1636 (s), 1599 (w), 1575 (w), 1560 (w), 1534 (vs), 1489 (s), 1463 (m), 1441 (s), 1421 (vs), 1398 (vs), 1361 (vs), 1341 (m), 1327 (m), 1299 (s), 1239 (vs), 1224 (vs), 1190 (w), 1179 (m), 1153 (vs), 1129 (vs), 1098 (m), 1078 (m), 1033 (s), 1011 (m), 1003 (m), 980 (w), 942 (w), 912 (m), 880 (w), 849 (w), 822 (w), 812 (w), 802 (w), 793 (w), 725 (vs), 696 (vs), 670 (w), 632 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-SMDRKVWNQX-UHFFFADPSC-NUHFF-NSKKF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/SMDRKVWNQXOQTQ-SHHOIMCASA-N.1>

## (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)acetamide (9h)



Step 1: (*E*)-3-(3,3-Diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile (**12f**, 186 mg, 672 μmol, 1.00 equiv) was dissolved in 27 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (76.5 mg, 2.02 mL, 2.02 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (30 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 30 mL). The combined organic layers were washed with brine (100 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (*E*)-(3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methanamine, which was used for the next step without further purification.

Step 2: Crude (E)-(3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methanamine was dissolved in 27 mL of dry THF under nitrogen atmosphere. Triethylamine (204 mg, 280 μL, 2.02 mmol, 3.00 equiv) was added and the solution was cooled to 0 °C before acetic anhydride (103 mg, 95.3 μL, 1.01 mmol, 1.50 equiv) was added dropwise. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (30 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 30 mL). The combined organic layers were washed with brine (100 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using methylene chloride/methanol 50:1 to 30:1, giving (*E*)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)acetamide (**9h**, 114 mg, 353 μmol, 52% yield) as a colorless oil.

**9h**: (E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)acetamide; Formula: C16H30N6O; Exact Mass: 322.2481; Smiles: CC(=O)NCc1cn(nc1/N=N/N(C(C)C)C(C)C)CC(C)C; InChIKey: RZSNDUJLUYXXQT-CZIZESTLSA-N

*Rf* = 0.06 (cyclohexane/ethyl acetate 1:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.20 (s, 1H), 5.92 (s, 1H), 5.43 (br.s, 1H), 4.30 (d, *J* = 5.4 Hz, 2H), 3.98 (br.s, 1H), 3.75 (d, *J* = 7.3 Hz, 2H), 2.22 (hept, *J* = 6.8 Hz, 1H), 1.90 (s, 3H), 1.32 (br.s, 6H), 1.19 (br.s, 6H), 0.88 (d, *J* = 6.7 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.3, 157.8, 130.7 (+, CH), 106.3, 59.9 (–, CH2), 48.1 (+, CH), 45.2 (+, CH), 34.3 (–, CH2), 29.4 (+, CH), 23.7 (+, 2C, CH3), 23.6 (+, 2C, CH3), 20.1 (+, CH3), 19.4 (+, 2C, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 324 (11) [M+2H]+, 323 (58) [M+H]+, 322 (7) [M]+, 321 (13) [M-H]+, 265 (11), 264 (65), 223 (13), 222 (100), 178 (14), 153 (19), 152 (11), 109 (14), 100 (21), 99 (10), 97 (21), 96 (15), 95 (20), 93 (13). HRMS–FAB *(m/z)*: [M+H]+ Calcd for C16H31ON6, 323.2559; Found 323.2561; IR (ATR, ṽ) = 2968 (m), 2931 (m), 2871 (w), 1650 (vs), 1541 (s), 1465 (s), 1421 (vs), 1402 (vs), 1364 (vs), 1341 (s), 1244 (vs), 1220 (vs), 1153 (vs), 1126 (vs), 1095 (s), 1034 (vs), 1014 (s), 946 (m), 924 (s), 911 (s), 851 (m), 841 (m), 819 (m), 806 (m), 730 (vs), 643 (m), 628 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-RZSNDUJLUY-UHFFFADPSC-NUHFF-NJAII-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/RZSNDUJLUYXXQT-CZIZESTLSA-N.1>

## (E)-2-(4-(acetamidomethyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)ethyl acetate (9i)



Step 1: Ethyl (E)-2-(4-cyano-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)acetate (**12g**, 277 mg, 904 μmol, 1.00 equiv) was dissolved in 150 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (103 mg, 2.71 mL, 2.71 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (150 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 x 150 mL). The combined organic layers were washed with brine (400 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (E)-2-(4-(aminomethyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)ethan-1-ol, which was used for the next step without further purification.

Step 2: The crude (E)-2-(4-(aminomethyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)ethan-1-ol was dissolved in 150 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before acetic anhydride (369 mg, 342 μL, 3.61 mmol, 4.00 equiv) was slowly added. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (150 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 150 mL). The combined organic layers were washed with brine (400 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 2:1 to 1:1 to pure ethyl acetate, giving (E)-2-(4-(acetamidomethyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)ethyl acetate (**9i**, 229 mg, 650 μmol, 72% yield) as a light-brown oil.

**9i**: (E)-2-(4-(acetamidomethyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)ethyl acetate; Formula: C16H28N6O3; Exact Mass: 352.2223; Smiles: CC(=O)NCc1cn(nc1/N=N/N(C(C)C)C(C)C)CCOC(=O)C; InChIKey: BBXJSLXPCZXILR-CZIZESTLSA-N

*Rf* = 0.14 (pure ethyl acetate). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.20 (s, 1H), 6.06 (t, *J* = 5.5 Hz, 1H), 5.31 (s, 1H), 4.32 (t, *J* = 5.4 Hz, 2H), 4.24 (d, *J* = 5.5 Hz, 2H), 4.14 (t, *J* = 5.4 Hz, 2H), 3.92 (s, 1H), 1.93 (s, 3H), 1.84 (s, 3H), 1.25 (s, 6H), 1.13 (s, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 170.5, 169.3, 158.1, 130.8 (+, CH), 107.2, 62.6 (–, CH2), 50.8 (–, CH2), 48.2 (+, CH), 45.2 (+, CH), 34.2 (–, CH2), 23.4 (+, CH3, 2C), 23.2 (+, CH3), 20.7 (+, CH3), 19.2 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 354 (13) [M+2H]+, 353 (62) [M+H]+, 352 (10) [M]+, 351 (11) [M-H]+, 295 (10), 294 (50), 253 (15), 252 (100), 208 (18), 182 (16); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C16H29O3N6, 353.2296; Found 353.2297; IR (ATR, ṽ) = 3284 (w), 3082 (vw), 2973 (w), 2932 (w), 2873 (vw), 1738 (s), 1652 (s), 1541 (m), 1419 (vs), 1364 (vs), 1227 (vs), 1153 (vs), 1128 (s), 1096 (m), 1034 (vs), 952 (w), 932 (m), 909 (m), 885 (w), 849 (w), 813 (m), 790 (m), 769 (w), 730 (m), 714 (m), 701 (m), 667 (m), 630 (m), 602 (s) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-BBXJSLXPCZ-UHFFFADPSC-NUHFF-NJAII-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/BBXJSLXPCZXILR-CZIZESTLSA-N.1>

## 1-(6-Benzyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (5a)



(E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (**9a**, 32.0 mg, 89.8 μmol, 1.00 equiv) was dissolved in 5 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (30.7 mg, 20.6 μL, 269 μmol, 3.00 equiv) was added and the mixture was stirred at 21 °C for 14 hours. The reaction was diluted with 10 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 10 mL of methylene chloride. The combined organic layers were washed with 20 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 2:1, giving 1-(6-benzyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (**5a**, 13.5 mg, 52.9 μmol, 59% yield) as a colorless solid.

**5a**: 1-(6-benzyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one; Formula: C13H13N5O; Exact Mass: 255.1120; Smiles: CC(=O)N1N=Nc2c(C1)cn(n2)Cc1ccccc1; InChIKey: PGERMRZARQFUFX-UHFFFAOYSA-N

*Rf* = 0.25 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.40–7.26 (m, 5H), 7.15 (s, 1H), 5.32 (s, 2H), 4.84 (s, 2H), 2.56 (s, 3H); 13C NMR (100 MHz, CDCl3, ppm) δ = 174.3, 147.1, 135.2, 129.2 (+, CH, 2C), 128.8 (+, CH), 128.2 (+, CH, 2C), 126.1 (+, CH), 99.9, 57.1 (–, CH2), 39.0 (–, CH2), 22.3 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 257 (17) [M+2H]+, 256 (82) [M+H]+, 214 (17), 212 (12), 165 (12), 155 (19), 154 (50), 136 (46); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C13H14ON5, 256.1198; Found 256.1197; IR (ATR, ṽ) = 3383 (vw), 3129 (w), 3091 (vw), 3064 (vw), 3037 (vw), 3007 (vw), 2949 (vw), 2925 (vw), 2167 (vw), 1701 (vs), 1659 (vw), 1635 (vw), 1595 (vw), 1497 (vw), 1469 (s), 1456 (w), 1441 (w), 1424 (w), 1402 (w), 1368 (s), 1317 (vs), 1293 (w), 1268 (w), 1207 (m), 1160 (w), 1142 (w), 1111 (vs), 1054 (w), 1037 (w), 1004 (m), 955 (s), 878 (vs), 815 (m), 764 (w), 724 (w), 697 (vs), 680 (s), 637 (w), 618 (s), 591 (w), 577 (s), 564 (s), 518 (w), 466 (w), 458 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-PGERMRZARQ-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ.1>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/PGERMRZARQFUFX-UHFFFAOYSA-N.2>

## (6-Benzyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)(phenyl)methanone (5b)



(E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide (**9b**, 41.5 mg, 99.2 μmol, 1.00 equiv) was dissolved in 5 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (33.9 mg, 22.8 μL, 297 μmol, 3.00 equiv) was added and the mixture was stirred at 21 °C for 14 hours. The reaction was diluted with 10 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 10 mL of methylene chloride. The combined organic layers were washed with 20 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 2:1, giving (6-benzyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)(phenyl)methanone (**5b**, 13.6 mg, 42.9 μmol, 43% yield) as a colorless solid.

**5b**: (6-benzyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)(phenyl)methanone; Formula: C18H15N5O; Exact Mass: 317.1277; Smiles: O=C(N1N=Nc2c(C1)cn(n2)Cc1ccccc1)c1ccccc1; InChIKey: WJOQJVSLWFMJNK-UHFFFAOYSA-N

*Rf* = 0.31 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.79–7.70 (m, 2H), 7.55–7.47 (m, 1H), 7.47–7.28 (m, 7H), 7.21 (s, 1H), 5.34 (s, 2H), 5.01 (s, 2H); 13C NMR (100 MHz, CDCl3, ppm) δ = 172.6, 147.2, 135.2, 133.7, 131.6 (+, CH), 130.3 (+, CH, 2C), 129.2 (+, CH, 2C), 128.8 (+, CH), 128.2 (+, CH, 2C), 128.0 (+, CH, 2C), 126.0 (+, CH), 100.3, 57.2 (–, CH2), 39.6 (–, CH2); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 319 (11) [M+2H]+, 318 (48) [M+H]+, 307 (29), 292 (15), 290 (10), 289 (15), 155 (31), 154 (100), 152 (10), 139 (17), 138 (36), 137 (62), 136 (71), 124 (10), 120 (12), 107 (23), 105 (40), 97 (10), 95 (14), 91 (45), 90 (12), 89 (16); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C18H16ON5, 318.1355; Found 318.1356; IR (ATR, ṽ) = 3119 (w), 3030 (w), 2924 (w), 1645 (m), 1598 (w), 1575 (w), 1531 (w), 1479 (m), 1453 (m), 1448 (m), 1408 (w), 1347 (vs), 1324 (m), 1307 (m), 1289 (m), 1213 (m), 1186 (w), 1174 (w), 1157 (m), 1061 (s), 1028 (w), 1001 (m), 950 (w), 912 (s), 870 (vs), 822 (w), 792 (m), 758 (w), 698 (vs), 635 (vs), 618 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-WJOQJVSLWF-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/WJOQJVSLWFMJNK-UHFFFAOYSA-N.1>

## 3-Methyl-1-(6-(4-methylbenzyl)-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)butan-1-one (5c)



(E)-N-((3-(3,3-Diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methyl)-3-methylbutanamide (**9c**, 61.7 mg, 150 μmol, 1.00 equiv) was dissolved in 40 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (34.1 mg, 22.9 μL, 299 μmol, 2.00 equiv) was added and the mixture was stirred at 21 °C for 16 hours. The reaction was diluted with 40 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 40 mL of methylene chloride. The combined organic layers were washed with 40 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product.

The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 1:1, giving 3-methyl-1-(6-(4-methylbenzyl)-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)butan-1-one (**5c**, 14.1 mg, 45.3 μmol, 30% yield) as an off-colorless solid.

**5c**: 3-methyl-1-(6-(4-methylbenzyl)-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)butan-1-one; Formula: C17H21N5O; Exact Mass: 311.1746; Smiles: CC(CC(=O)N1N=Nc2c(C1)cn(n2)Cc1ccc(cc1)C)C; InChIKey: KEQOQOHNHBUGFW-UHFFFAOYSA-N

*Rf* = 0.30 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.23–7.15 (m, 4H), 7.12 (s, 1H), 5.27 (s, 2H), 4.82 (s, 2H), 2.86 (d, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 2.25 (thept, *J* = 13.5 Hz, *J* = 6.8 Hz, 1H), 0.99 (d, *J* = 6.6 Hz, 6H); 13C NMR (100MHz, CDCl3, ppm) δ = 176.2, 147.1, 138.8, 132.2, 129.9 (+, CH, 2C), 128.3 (+, CH, 2C), 125.9 (+, CH), 100.0, 56.9 (–, CH2), 43.0 (–, CH2), 38.9 (–, CH2), 25.7 (+, CH), 22.8 (+, CH3, 2C), 21.3 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 313 (19) [M+2H]+, 312 (88) [M+H]+, 311 (6) [M]+, 228 (22), 226 (10), 155 (13), 154 (42), 139 (11), 138 (20), 137 (29), 136 (39), 121 (10), 120 (10), 109 (14), 107 (17), 106 (14), 105 (100), 97 (17), 95 (22), 93 (10), 91 (22), 89 (12); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C17H22ON5, 312.1819; Found 312.1821.IR (ATR, ṽ) = 3125 (w), 3031 (w), 3012 (w), 2956 (w), 2925 (w), 2867 (w), 2730 (vw), 1672 (vs), 1618 (vw), 1596 (w), 1514 (w), 1476 (vs), 1463 (m), 1438 (w), 1431 (w), 1405 (m), 1391 (m), 1377 (vs), 1361 (vs), 1346 (m), 1337 (m), 1317 (vs), 1312 (vs), 1288 (w), 1261 (w), 1228 (w), 1207 (s), 1167 (m), 1128 (w), 1116 (w), 1061 (vs), 1010 (vs), 946 (m), 902 (w), 875 (vs), 867 (vs), 833 (vs), 806 (s), 768 (w), 749 (vs), 725 (m), 717 (m), 680 (s), 645 (m), 637 (m), 619 (vs), 575 (vs), 564 (m), 535 (vs), 509 (w), 470 (s), 433 (w), 414 (w), 402 (w), 394 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-KEQOQOHNHB-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/KEQOQOHNHBUGFW-UHFFFAOYSA-N.1>

## 1-(6-(3,5-Difluorobenzyl)-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (5d)



(E)-N-((1-(3,5-Difluorobenzyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (**9d**, 12.9 mg, 32.9 μmol, 1.00 equiv) was dissolved in 5 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (7.87 mg, 5.29 μL, 69.0 μmol, 2.10 equiv) was added and the mixture was stirred at 21 °C for 14 hours. The reaction was diluted with 10 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 10 mL of methylene chloride. The combined organic layers were washed with 20 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product.

The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 2:1, giving 1-(6-(3,5-difluorobenzyl)-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (**5d**, 1.40 mg, 4.81 μmol, 15% yield) as a colorless solid.

**5d**: 1-(6-(3,5-difluorobenzyl)-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one; Formula: C13H11F2N5O; Exact Mass: 291.0932; Smiles: Fc1cc(cc(c1)F)Cn1cc2c(n1)N=NN(C2)C(=O)C; InChIKey: CEFFSZUXPZAWPN-UHFFFAOYSA-N

*Rf* = 0.27 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.22 (s, 1H), 6.84–6.71 (m, 3H), 5.30 (s, 2H), 4.88 (s, 2H), 2.59 (s, 3H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.5, 163.3 (2C; dd, *J* = 249.5 Hz, *J* = 12.6 Hz), 158.5, 140.6 (t, *J* = 8.9 Hz), 130.7 (+, CH), 110.6 (+, CH, 2C; dd, *J* = 18.6 Hz, *J* = 7.2 Hz), 108.2, 103.5 (+, CH; t, *J* = 25.3 Hz), 55.2 (–, CH2; t, *J* = 2.3 Hz), 48.4 (+, CH), 45.5 (+, CH), 34.3 (–, CH2), 23.8 (+, CH3, 2C), 23.6 (+, CH3), 19.5 (+, CH3, 2C); 19F NMR (375 MHz, CDCl3, ppm) δ = –108.08; MS (FAB, Matrix: 3-NBA): *m/z* (%) = 293 (7) [M+2H]+, 292 (37) [M+H]+, 191 (11) [M]+, 163 (10), 159 (12), 155 (21), 154 (43), 137 (30), 136 (40), 125 (20), 123 (36), 111 (48); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C13H12ON5F2, 292.1010; Found 292.1012; IR (ATR, ṽ) = 3125 (w), 3102 (vw), 3041 (w), 2951 (w), 2922 (w), 2870 (w), 2853 (w), 1701 (vs), 1666 (w), 1622 (m), 1596 (vs), 1538 (vw), 1519 (vw), 1468 (vs), 1446 (s), 1443 (s), 1424 (m), 1402 (w), 1368 (s), 1344 (m), 1315 (vs), 1275 (w), 1258 (w), 1241 (w), 1205 (s), 1159 (w), 1143 (w), 1109 (vs), 1055 (m), 1038 (m), 1004 (vs), 976 (w), 955 (vs), 941 (m), 875 (vs), 856 (vs), 829 (m), 819 (s), 793 (w), 752 (w), 737 (vs), 722 (s), 671 (w), 647 (m), 619 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-CEFFSZUXPZ-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/CEFFSZUXPZAWPN-UHFFFAOYSA-N.1>

## 1-(6-Ethyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (5e)



(E)-N-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-ethyl-1H-pyrazol-4-yl)methyl)acetamide (**9e**, 57.7 mg, 196 μmol, 1.00 equiv) was dissolved in 20 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (67.0 mg, 45.0 μL, 588 μmol, 3.00 equiv) was added and the mixture was stirred at 21 °C for 16 hours. The reaction was diluted with 20 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 20 mL of methylene chloride. The combined organic layers were washed with 20 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 2:1, giving 1-(6-ethyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (**5e**, 16.9 mg, 87.5 μmol, 45% yield) as colorless solid.

**5e**: 1-(6-ethyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one; Formula: C8H11N5O; Exact Mass: 193.0964; Smiles: CCn1nc2c(c1)CN(N=N2)C(=O)C; InChIKey: AHUQBMJJIBAFGD-UHFFFAOYSA-N

*Rf* = 0.05 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.21 (s, 1H), 4.86 (s, 2H), 4.19 (q, *J* = 7.3 Hz, 2H), 2.55 (s, 3H), 1.51 (t, *J* = 7.3 Hz, 3H); 13C NMR (100 MHz, CDCl3, ppm) δ = 174.2, 147.0, 125.4 (+, CH), 99.1, 48.1 (–, CH2), 39.0 (–, CH2), 22.3 (+, CH3), 15.5 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 195 (13) [M+2H]+, 194 (100) [M+H]+, 193 (6) [M]+, 192 (11) [M-H]+, 154 (8), 152 (26), 150 (18), 136 (12), 133 (33), 124 (24), 123 (10), 109 (14), 107 (11), 97 (11), 96 (10), 95 (16), 93 (10), 91 (16); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C8H12ON5, 194.1036; Found 194.1036; IR (ATR, ṽ) = 3417 (w), 3363 (w), 3125 (w), 2990 (w), 2955 (w), 2915 (w), 2884 (w), 2854 (w), 2766 (w), 1687 (vs), 1628 (w), 1589 (w), 1574 (w), 1537 (w), 1475 (vs), 1421 (m), 1377 (vs), 1350 (s), 1327 (vs), 1255 (w), 1201 (s), 1173 (s), 1103 (vs), 1050 (s), 1034 (m), 1013 (s), 973 (m), 955 (vs), 875 (vs), 833 (vs), 788 (m), 754 (m), 725 (s), 652 (w), 618 (s) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-AHUQBMJJIB-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/AHUQBMJJIBAFGD-UHFFFAOYSA-N.1>

## 1-(6-Cyclopentyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (5f)



(E)-N-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (**9f**, 116 mg, 347 μmol, 1.00 equiv) was dissolved in 35 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (119 mg, 79.7 μL, 1.04 mmol, 3.00 equiv) was added and the mixture was stirred at 21 °C for 16 hours. The reaction was diluted with 35 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 35 mL of methylene chloride. The combined organic layers were washed with 35 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 2:1, giving 1-(6-cyclopentyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (**5f**, 29.2 mg, 125 μmol, 36% yield) as a light-brown solid.

**5f**: 1-(6-cyclopentyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one; Formula: C11H15N5O; Exact Mass: 233.1277; Smiles: CC(=O)N1N=Nc2c(C1)cn(n2)C1CCCC1; InChIKey: QFPQAGCPTOKOBM-UHFFFAOYSA-N

*Rf* = 0.21 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.23 (s, 1H), 4.84 (s, 2H), 4.63 (p, *J* = 7.0 Hz, 1H), 2.54 (s, 3H), 2.22–2.10 (m, 2H), 2.09–1.97 (m, 2H), 1.97–1.80 (m, 2H), 1.77–1.63 (m, 2H); 13C NMR (100 MHz, CDCl3, ppm) δ = 174.2, 146.8, 124.8 (+, CH), 98.8, 64.2 (+, CH), 39.0 (–, CH2), 33.2 (–, CH2, 2C), 24.3 (–, CH2, 2C), 22.3 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 235 (14) [M+2H]+, 234 (100) [M+H]+, 233 (6) [M]+, 232 (10) [M-H]+, 192 (10), 155 (15), 154 (48), 139 (10), 138 (20), 137 (30), 136 (34), 109 (11), 107 (13), 97 (11), 95 (15), 91 (13); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C11H16ON5, 234.1349; Found 234.1350; IR (ATR, ṽ) = 3370 (vw), 3129 (w), 2970 (w), 2944 (w), 2921 (w), 2873 (w), 1693 (vs), 1656 (w), 1632 (w), 1591 (w), 1538 (vw), 1503 (vw), 1475 (vs), 1456 (w), 1448 (m), 1418 (w), 1374 (vs), 1357 (s), 1332 (vs), 1286 (m), 1248 (w), 1204 (s), 1176 (w), 1159 (w), 1109 (vs), 1052 (m), 1034 (m), 1004 (vs), 953 (vs), 912 (w), 877 (vs), 827 (vs), 741 (m), 722 (s), 623 (m), 594 (w), 578 (vs), 562 (vs), 537 (m), 496 (m), 470 (w), 436 (w), 418 (w), 394 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-QFPQAGCPTO-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/QFPQAGCPTOKOBM-UHFFFAOYSA-N.1>

## (6-Cyclopentyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)(phenyl)methanone (5g)



(E)-N-((1-cyclopentyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)benzamide (**9g**, 250 mg, 631 μmol, 1.00 equiv) was dissolved in 50 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (216 mg, 145 μL, 1.89 mmol, 3.00 equiv) was added and the mixture was stirred at 21 °C for 16 hours. The reaction was diluted with 50 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 50 mL of methylene chloride. The combined organic layers were washed with 100 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 1:1, to give (6-cyclopentyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)(phenyl)methanone (**5g**, 55.4 mg, 188 μmol, 30% yield). Comment: the reaction was stopped after 16 h, remaining starting material (136 mg) was re-isolated. Based on the consumed starting material, the yield of the reaction is 65%.

**5g**: (6-cyclopentyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)(phenyl)methanone; Formula: C16H17N5O; Exact Mass: 295.1433; Smiles: O=C(c1ccccc1)N1N=Nc2c(C1)cn(n2)C1CCCC1; InChIKey: JUJUWEBLNYJZJO-UHFFFAOYSA-N

*Rf* = 0.47 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, Chloroform-d [7.27 ppm], ppm) δ = 7.75–7.73 (m, 2H), 7.53–7.48 (m, 1H), 7.45–7.41 (m, 2H), 7.29 (s, 1H), 5.03 (s, 2H), 4.67 (t, *J* = 7.1 Hz, 1H), 2.22–2.15 (m, 2H), 2.11–2.03 (m, 2H), 1.94–1.86 (m, 2H), 1.77–1.70 (m, 2H); 13C NMR (100 MHz, Chloroform-d [77.0 ppm], ppm) δ = 172.5, 146.9, 133.8, 131.4 (+, CH), 130.2 (+, CH, 2C), 127.9 (+, CH, 2C), 124.6 (+, CH), 99.2, 64.1 (+, CH), 39.5 (–, CH2), 33.2 (–, CH2, 2C), 24.2 (–, CH2, 2C); MS (EI, 70 eV), m/z (%): 296 (61), 270 (67), 154 (62), 149 (33), 137 (43), 136 (58), 105 (100), 95 (38). IR (ATR, ṽ) = 3114 (w), 2953 (w), 2876 (w), 1677 (s), 1663 (vs), 1448 (m), 1341 (vs), 1315 (s), 1207 (m), 1068 (vs), 904 (s), 871 (vs), 826 (vs), 783 (m), 714 (vs), 700 (vs), 693 (vs), 636 (s), 601 (vs) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-JUJUWEBLNY-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/JUJUWEBLNYJZJO-UHFFFAOYSA-N.1>

## 1-(6-Isobutyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (5h)



*N*-((3-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)acetamide (**9h**, 95.4 mg, 296 μmol, 1.00 equiv) was dissolved in 10 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (101 mg, 68.0 μL, 888 μmol, 3.00 equiv) was added and the mixture was stirred at 21 °C for 14 hours. The reaction was diluted with 10 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 10 mL of methylene chloride. The combined organic layers were washed with 20 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 2:1, giving 1-(6-isobutyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one (**5h**, 45.1 mg, 204 μmol, 69% yield) as a colorless solid.

**5h**: 1-(6-isobutyl-4,6-dihydro-3H-pyrazolo[3,4-d][1,2,3]triazin-3-yl)ethan-1-one; Formula: C10H15N5O; Exact Mass: 221.1277; Smiles: CC(Cn1cc2c(n1)N=NN(C2)C(=O)C)C; InChIKey: WDXQCIDOHPSJHM-UHFFFAOYSA-N

*Rf* = 0.17 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.16 (s, 1H), 4.86 (s, 2H), 3.91 (d, *J* = 7.3 Hz, 2H), 2.55 (s, 3H), 2.23 (hept, *J* = 7.3 Hz, *J* = 6.8 Hz, 1H), 0.91 (d, *J* = 6.7 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 174.2, 147.0, 126.5 (+, CH), 98.9, 60.6 (–, CH2), 39.0 (–, CH2), 29.7 (+, CH), 22.3 (+, CH3), 19.9 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 222 (42) [M+H]+, 196 (82), 194 (72), 192 (22), 178 (26), 167 (34), 166 (24), 165 (26), 153 (25), 152 (57), 151 (38), 150 (22), 137 (100), 136 (35), 135 (24), 133 (59), 121 (25), 109 (23), 108 (22), 107 (24), 97 (23), 96 (36), 95 (34), 93 (24), 91 (29); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C10H16ON5, 222.1355; Found 222.1353; IR (ATR, ṽ) = 3265 (w), 3057 (w), 2961 (m), 2934 (w), 2873 (w), 1655 (vs), 1541 (vs), 1466 (vs), 1434 (vs), 1405 (s), 1390 (vs), 1370 (vs), 1271 (vs), 1221 (s), 1162 (vs), 1115 (s), 1091 (s), 1020 (s), 992 (s), 946 (m), 926 (m), 894 (m), 849 (s), 819 (s), 769 (s), 732 (vs), 700 (vs), 662 (s), 619 (s), 594 (vs), 540 (s), 489 (s), 435 (m), 409 (m), 398 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-WDXQCIDOHP-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/WDXQCIDOHPSJHM-UHFFFAOYSA-N.1>

## 2-(3-Acetyl-3,4-dihydro-6H-pyrazolo[3,4-d][1,2,3]triazin-6-yl)ethyl acetate (5i)



(E)-2-(4-(Acetamidomethyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-1-yl)ethyl acetate (**9i**, 136 mg, 385 μmol, 1.00 equiv) was dissolved in 40 mL of dry methylene chloride under nitrogen atmosphere. 2,2,2-Trifluoroacetic acid (132 mg, 88.5 μL, 1.16 mmol, 3.00 equiv) was added and the mixture was stirred at 21 °C for 16 hours. The reaction was diluted with 40 mL of saturated K2CO3-solution and the aqueous phase was extracted with 3 × 40 mL of methylene chloride. The combined organic layers were washed with 40 mL of brine and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 4:1 to 1:1, giving 2-(3-acetyl-3,4-dihydro-6H-pyrazolo[3,4-d][1,2,3]triazin-6-yl)ethyl acetate (**5i**, 49.5 mg, 197 μmol, 51% yield) as a colorless solid.

**5i**: 2-(3-acetyl-3,4-dihydro-6H-pyrazolo[3,4-d][1,2,3]triazin-6-yl)ethyl acetate; Formula: C10H13N5O3; Exact Mass: 251.1018; Smiles: CC(=O)OCCn1nc2c(c1)CN(N=N2)C(=O)C; InChIKey: KPRSIIAWIWZXCG-UHFFFAOYSA-N

*Rf* = 0.17 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.25 (s, 1H), 4.86 (s, 2H), 4.45 (t, *J* = 5.2 Hz, 2H), 4.37 (t, *J* = 5.4 Hz, 2H), 2.55 (s, 3H), 2.03 (s, 3H); 13C NMR (100 MHz, CDCl3, ppm) δ = 174.2, 170.5, 147.4, 126.9 (+, CH), 99.5, 62.5 (–, CH2), 51.9 (–, CH2), 38.9 (–, CH2), 22.2 (+, CH3), 20.8 (+, CH3); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 253 (13) [M+2H]+, 252 (100) [M+H]+, 251 (5) [M]+, 155 (16), 154 (52), 138 (20), 137 (35), 136 (38), 107 (13), 89 (10); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C10H14O3N5, 252.1091; Found 252.1093; IR (ATR, ṽ) = 3459 (vw), 3376 (vw), 3122 (w), 2992 (vw), 2968 (vw), 2953 (vw), 2925 (vw), 2887 (vw), 2851 (vw), 1871 (vw), 1745 (s), 1734 (vs), 1697 (vs), 1657 (w), 1589 (vw), 1574 (vw), 1476 (s), 1460 (w), 1436 (w), 1422 (w), 1409 (w), 1371 (vs), 1368 (vs), 1347 (w), 1327 (vs), 1313 (s), 1276 (w), 1254 (w), 1234 (vs), 1204 (s), 1188 (m), 1162 (m), 1128 (w), 1102 (vs), 1050 (s), 1038 (vs), 1013 (s), 996 (w), 972 (w), 956 (vs), 936 (s), 868 (vs), 827 (s), 738 (w), 725 (w), 659 (m), 635 (w), 611 (vs) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-KPRSIIAWIW-UHFFFADPSC-NUHFF-NUHFF-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/KPRSIIAWIWZXCG-UHFFFAOYSA-N.1>

# 3. Amidation of triazenes 13

Table S1: Synthesis of amides 10 *via* reduction of nitriles 13 to pyrazolo-ortho-methylamines 17 and subsequent conversion with aliphatic anhydrides or chlorides 11.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | |
| **Entrya** | **13** | **R1** | **17** | **11** | **10** | **R2** | **Yield**  **10 (%)** |
| 1 | **13a** | Bn | **17a** | **11d** | **10a** | Me | 40 (from 13) |
| 2 | **13b** | -CH2tolyl | **17b** | **11a** | **10c** | Me | 77 (from 17) |
| 3 | **13f** | *i*Bu | **17c** | **11a** | **10h** | Me | 88 (from 17) |
| 4 | **13f** | *i*Bu | **17c** | **11b** | **10i** | Ph | 88 (from 17) |

**11a** = Acetic anhydride, **11b** = Benzoyl anhydride, **11d** = Acetyl chloride

## (E)-N-((1-benzyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (10a)



Step1: (E)-1-benzyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazole-4-carbonitrile (**13a**, 120 mg, 385 μmol, 1.00 equiv) was dissolved in 40 mL of dry THF under nitrogen atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (43.9 mg, 1.16 mL, 1.16 mmol, 3.00 equiv) was slowly added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The solution was cooled to 21 °C and the reaction was quenched with a saturated K/Na-tartrate solution (40 mL). The organic solvent was removed under reduced pressure and the remaining aqueous phase was extracted with methylene chloride (3 × 40 mL). The combined organic layers were washed with brine (100 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude (E)-(1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine (**17a**), which was used for the next step without further purification.

Step 2: The crude (E)-(1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methanamine (**17a**) was dissolved in 40 mL of dry THF under nitrogen atmosphere. Triethylamine (117 mg, 161 μL, 1.16 mmol, 3.00 equiv) was added and the solution was cooled to 0 °C before acetyl chloride (45.4 mg, 41.1 μL, 578 μmol, 1.50 equiv) was added dropwise. The cooling was removed and the solution was stirred for 14 hours at 21 °C. The reaction was quenched with a saturated K2CO3-solution (40 mL) and the organic solvent was removed under reduced pressure. The remaining aqueous phase was extracted with methylene chloride (3 × 40 mL). The combined organic layers were washed with brine (100 mL) and dried over Na2SO4. The solvent was removed under reduced pressure to give the crude product. The obtained crude product was purified *via* flash-chromatography on silica gel using methylene chloride/methanol 50:1 to 30:1, giving (E)-N-((1-benzyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide (**10a**, 55.2 mg, 155 μmol, 40% yield) as a brown oil.

**10a**: (E)-N-((1-benzyl-5-(3,3-diisopropyltriaz-1-en-1-yl)-1H-pyrazol-4-yl)methyl)acetamide; Formula: C19H28N6O; Exact Mass: 356.2325; Smiles: CC(=O)NCc1cnn(c1/N=N/N(C(C)C)C(C)C)Cc1ccccc1

InChIKey: MPRWSIYLAUTZRJ-GHVJWSGMSA-N

*Rf* = 0.06 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.33–7.23 (m, 5H), 7.20 (s, 1H), 5.96 (t, *J* = 5.4 Hz, 1H), 5.40 (s, 1H), 5.16 (s, 2H), 4.29 (d, *J* = 5.3 Hz, 2H), 3.99 (s, 1H), 1.89 (s, 3H), 1.32 (s, 6H), 1.20 (s, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.4, 157.9, 136.3, 130.2 (+, CH), 128.8 (+, CH, 2C), 128.1 (+, CH), 128.1 (+, CH, 2C), 107.5, 56.2 (–, CH2), 48.3 (+, CH3), 45.3 (+, CH3), 34.4 (–, CH2), 23.6 (+, CH3, 2C), 23.5 (+, CH3), 19.4 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): m/z (%) = 358 (22) [M+2H]+, 357 (100) [M+H]+, 356 (21) [M]+, 355 (13) [M-H]+, 298 (31), 257 (12), 256 (79), 100 (13), 91 (60); HRMS–FAB (m/z): [M+H]+ Calcd for C19H29ON6, 357.2403; Found 357.2402; IR (ATR, ṽ) = 3285 (w), 3080 (vw), 3065 (vw), 3033 (vw), 2973 (w), 2931 (w), 2871 (vw), 2228 (vw), 1650 (s), 1543 (m), 1497 (w), 1465 (m), 1455 (s), 1419 (vs), 1402 (vs), 1364 (vs), 1341 (s), 1244 (vs), 1224 (vs), 1150 (vs), 1128 (s), 1096 (m), 1033 (s), 1011 (m), 969 (w), 909 (m), 851 (w), 841 (w), 813 (w), 727 (vs), 704 (vs), 643 (m), 630 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-MPRWSIYLAU-UHFFFADPSC-NUHFF-NOHLW-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/MPRWSIYLAUTZRJ-GHVJWSGMSA-N.1>

## (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methanamine (17b)



(E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazole-4-carbonitrile (**13b**, 177 mg, 545 μmol, 1.00 equiv) was dissolved in dry THF under nitrogen-atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (70.2 mg, 1.85 mL, 1.85 mmol, 3.39 equiv) was added. The cooling was removed and the solution was stirred at 21 °C for 14 hours. The reaction was quenched with K/Na-tartrate-solution and the aqueous layer was extracted with DCM. The organic solvent was removed in vacuo and (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methanamine (**17b**, 113 mg, 345 μmol, 63% yield) was obtained.

**17b**: (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methanamine; Formula: C18H28N6; Exact Mass: 328.2375; Smiles: NCc1cnn(c1/N=N/N(C(C)C)C(C)C)Cc1ccc(cc1)C

InChIKey: KQBXWZPQDCVAGS-QURGRASLSA-N

13C NMR (100 MHz, CDCl3, ppm) δ = 157.6, 137.8, 133.6, 129.5 (+, CH, 2C), 128.7 (+, CH), 128.2 (+, CH, 2C), 113.4, 55.9 (–, CH2), 48.4 (+, CH), 45.1 (+, CH), 37.2 (–, CH2), 23.7 (+, CH3, 2C), 21.2 (+, CH3), 19.5 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 329 (10) [M+H]+, 328 (4) [M]+, 313 (19), 312 (91), 228 (25), 105 (100); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C18H29N6, 329.2454; Found 329.2453; IR (ATR, ṽ) = 2972 (m), 2928 (m), 2867 (w), 1558 (w), 1516 (w), 1465 (m), 1421 (vs), 1402 (vs), 1380 (m), 1363 (vs), 1237 (vs), 1180 (m), 1150 (vs), 1126 (s), 1098 (m), 1033 (s), 1009 (m), 925 (w), 908 (w), 878 (w), 824 (m), 816 (m), 792 (m), 752 (m), 738 (m), 720 (w), 558 (w), 523 (w), 475 (w) cm–1

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-KQBXWZPQDC-UHFFFADPSC-NUHFF-NBDJD-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/KQBXWZPQDCVAGS-QURGRASLSA-N.1>

## (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methyl)acetamide (10c)



To a solution of (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methanamine (**17b**, 90.5 mg, 276 μmol, 1.00 equiv) in THF (2.8 mL), acetic anhydride (56.3 mg, 52.1 μL, 551 μmol, 2.00 equiv) were added at 21 °C. The mixture was stirred at room temperature. After 14 hours, 2 mL of a 2M NaOH-solution were added and the organic solvent was removed under reduced pressure. The remaining aqueous layer was extracted with methylene chloride. The combined organic layers were washed with a saturated NaHCO3-solution and brine, dried over MgSO4 and the solvent was removed under reduced pressure. The obtained crude product was purified *via* flash-chromatography on silica gel using methylene chloride/methanol 50:1 to 30:1, to give (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methyl)acetamide (**10c**, 78.8 mg, 213 μmol, 77% yield) as a colorless oil.

**10c**: (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-(4-methylbenzyl)-1H-pyrazol-4-yl)methyl)acetamide; Formula: C20H30N6O; Exact Mass: 370.2481; Smiles: CC(=O)NCc1cnn(c1/N=N/N(C(C)C)C(C)C)Cc1ccc(cc1)C

InChIKey: AATCYLWHXDDRIG-WCWDXBQESA-N

*Rf* = 0.06 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.20–7.03 (m, 5H), 5.95 (br.t, *J* = 5.4 Hz, 1H), 5.40 (br.s, 1H), 5.10 (s, 2H), 4.27 (d, *J* = 5.4 Hz, 2H), 3.97 (br.s, 1H), 2.29 (s, 3H), 1.87 (s, 3H), 1.31 (br.s, 6H), 1.20 (br.s, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.2, 157.8, 137.8, 133.2, 129.9 (+, CH), 129.4 (+, CH, 2C), 128.1 (+, CH, 2C), 107.4, 55.9 (–, CH2), 48.2 (+, CH), 45.2 (+, CH), 34.3 (–, CH2), 23.6 (+, CH3, 2C), 23.4 (+, CH3), 21.1 (+, CH3), 19.3 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 372 (13) [M+2H]+, 371 (53) [M+H]+, 370 (9) [M]+, 312 (21), 270 (48), 106 (11), 105 (100), 100 (13), 95 (10); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C20H31ON6, 371.2559; Found 371.2558; IR (ATR, ṽ) = 3284 (w), 3085 (vw), 3053 (vw), 2973 (m), 2929 (w), 2870 (w), 1650 (vs), 1541 (m), 1516 (m), 1421 (vs), 1364 (vs), 1244 (vs), 1225 (vs), 1150 (vs), 1128 (s), 1096 (m), 1033 (s), 1010 (m), 921 (w), 911 (m), 796 (s), 751 (w), 728 (vs), 643 (w), 594 (w), 558 (w), 524 (w), 469 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-AATCYLWHXD-UHFFFADPSC-NUHFF-NWIMK-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/AATCYLWHXDDRIG-WCWDXBQESA-N.1>

## (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methanamine (17c)



(E)-5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazole-4-carbonitrile (**13f**, 245 mg, 885 μmol, 1.00 equiv) was dissolved in 26 mL of dry THF under nitrogen-atmosphere. The solution was cooled to 0 °C before lithium aluminum hydride (101 mg, 2.65 mL, 2.65 mmol, 3.00 equiv) was added. The cooling was removed and the solution was stirred at 21 °C for 14 hours, then additional 5 hours at 50 °C. The reaction was quenched with K/Na-tartrate-solution, THF was removed under reduced pressure and the remaining aqueous layer was extracted with CH2Cl2 (3 × 25 mL). The combined organic layers were washed with brine and dried over MgSO4. The solvent was removed under reduced pressure to give (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methanamine (**17c**, 243 mg, 866 μmol, 98% yield) as crude product which was used without further purification.

**17c**: (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methanamine; Formula: C14H28N6; Exact Mass: 280.2375; Smiles: NCc1cnn(c1/N=N/N(C(C)C)C(C)C)CC(C)C

InChIKey: SGMNZUYLCBPNEE-ISLYRVAYSA-N

1H NMR (400 MHz, CDCl3, ppm) δ = 7.30 (s, 1H), 5.08 (br.s, 1H), 4.11–3.91 (m, 3H), 3.70 (s, 2H), 2.20 (hept, *J* = 6.7 Hz, 1H), 1.64 (br.s, 2H), 1.35 (br.s, 6H), 1.26 (br.s, 6H), 0.88 (d, *J* = 6.7 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 146.9, 137.7 (+, CH), 109.9, 55.7 (–, CH2), 49.5 (+, CH), 46.6 (+, CH), 37.4 (–, CH2), 29.7 (+, CH), 23.6 (+, CH3, 2C), 20.3 (+, CH3, 2C), 19.2 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 282 (13) [M+2H]+, 281 (69) [M+H]+, 280 (6) [M]+, 265 (17), 264 (100), 115 (13), 109 (18), 107 (13), 105 (11), 97 (20), 96 (17), 95 (32), 93 (17), 91 (21); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C14H29N6, 281.2454; Found 281.2453; IR (ATR, ṽ) = 3370 (vw), 2966 (m), 2931 (m), 2870 (w), 1632 (w), 1585 (w), 1550 (w), 1465 (s), 1411 (vs), 1363 (vs), 1315 (m), 1298 (m), 1259 (s), 1238 (vs), 1225 (vs), 1159 (vs), 1125 (s), 1096 (s), 1060 (m), 1018 (vs), 945 (m), 924 (m), 907 (s), 892 (s), 877 (s), 846 (s), 820 (m), 785 (m), 735 (m), 717 (m), 694 (m), 656 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-SGMNZUYLCB-UHFFFADPSC-NUHFF-NBSLK-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/SGMNZUYLCBPNEE-ISLYRVAYSA-N.1>

## (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)acetamide (10h)



To a solution of (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methanamine (**17c**, 117 mg, 418 μmol, 1.00 equiv) in 4.45 mL of THF, acetic anhydride (85.3 mg, 79.0 μL, 836 μmol, 2.00 equiv) was added at 21 °C. The mixture was stirred at 21 °C. After 14 hours, 2 mL of a 2 M NaOH-solution were added and the organic solvent was removed under reduced pressure. The remaining aqueous layer was extracted with methylene chloride (3 x 10 mL). The combined organic layers were washed with a saturated NaHCO3-solution and brine, dried over MgSO4 and the solvent was removed under reduced pressure. The obtained crude product was purified *via* flash-chromatography on silica gel using methylene chloride/methanol 50:1 to 20:1, giving (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)acetamide (**10h**, 119 mg, 369 μmol, 88% yield).

**10h**: (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)acetamide; Formula: C16H30N6O; Exact Mass: 322.2481; Smiles: CC(Cn1ncc(c1/N=N/N(C(C)C)C(C)C)CNC(=O)C)C

InChIKey: NFQAOFXQAVIJOU-FMQUCBEESA-N

*Rf* = 0.16 (cyclohexane/ethyl acetate 2:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.35 (s, 1H), 5.68 (br.s, 1H), 5.18–4.99 (m, 1H), 4.33 (d, *J* = 5.0 Hz, 2H), 4.07–4.03 (m, 1H), 4.01 (d, *J* = 7.3 Hz, 2H), 2.22 (sept, *J* = 6.9 Hz, 1H), 1.95 (s, 3H), 1.35 (br.d, *J* = 6.6 Hz, 6H), 1.27 (br.d, *J* = 6.8 Hz, 6H), 0.90 (d, *J* = 6.7 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 169.3, 147.8, 138.7 (+, CH), 103.3, 55.8 (–, CH2), 49.7 (+, CH), 46.9 (+, CH), 35.0 (–, CH2), 29.7 (+, CH), 23.6 (+, CH3), 23.5 (+, CH3, 2C), 20.3 (+, CH3, 2C), 19.2 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 324 (18) [M+2H]+, 323 (100) [M+H]+, 322 (12) [M]+, 265 (10), 264 (54), 222 (20), 209 (19), 167 (13), 100 (13), 97 (10), 96 (12), 95 (11), 91 (11); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C16H31ON6, 323.2559; Found 323.2559; IR (ATR, ṽ) = 3272 (w), 3078 (vw), 2969 (m), 2931 (w), 2871 (w), 1649 (s), 1541 (s), 1466 (s), 1409 (vs), 1381 (s), 1363 (vs), 1313 (m), 1259 (s), 1239 (vs), 1222 (vs), 1159 (vs), 1119 (s), 1096 (s), 1021 (vs), 945 (m), 925 (m), 911 (m), 891 (m), 846 (m), 820 (w), 789 (m), 731 (m), 694 (m), 670 (m), 647 (m), 588 (m), 557 (s), 534 (m), 469 (m), 452 (w), 426 (m), 394 (w), 387 (w) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-NFQAOFXQAV-UHFFFADPSC-NUHFF-NGHTP-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/NFQAOFXQAVIJOU-FMQUCBEESA-N.1>

## (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)benzamide (10i)



To a solution of (E)-(5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methanamine (**17c**, 106 mg, 377 μmol, 1.00 equiv) in 5 mL of THF, benzoyl benzoate (170 mg, 142 μL, 753 μmol, 2.00 equiv) was added at 21 °C. The mixture was stirred at 21 °C. After 14 hours, 2 mL of a 2 M NaOH-solution were added and the organic solvent was removed under reduced pressure. The remaining aqueous layer was extracted with methylene chloride (3 × 10 mL). The combined organic layers were washed with a saturated NaHCO3-solution and brine. It was then dried over MgSO4 and the solvent was removed under reduced pressure. The obtained crude product was purified *via* flash-chromatography on silica gel using cyclohexane/ethyl acetate 10:1 to 2:1, giving (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)benzamide (**10i**, 128 mg, 332 μmol, 88% yield) as pale-yellow fluffy crystals.

**10i**: (E)-N-((5-(3,3-diisopropyltriaz-1-en-1-yl)-1-isobutyl-1H-pyrazol-4-yl)methyl)benzamide; Formula: C21H32N6O; Exact Mass: 384.2638; Smiles: CC(Cn1ncc(c1/N=N/N(C(C)C)C(C)C)CNC(=O)c1ccccc1)C

InChIKey: MPFTVRYGHBGKIC-OCOZRVBESA-N

*Rf* = 0.19 (cyclohexane/ethyl acetate 4:1). 1H NMR (400 MHz, CDCl3, ppm) δ = 7.76–7.68 (m, 2H), 7.51–7.33 (m, 4H), 6.28 (br.s, 1H), 5.15–4.96 (m, 1H), 4.54 (d, *J* = 4.8 Hz, 2H), 4.06–3.93 (m, 3H), 2.25 (sept, *J* = 13.8 Hz, *J* = 7.0 Hz, 1H), 1.28 (br.d, *J* = 6.7 Hz, 12H), 0.91 (d, *J* = 6.7 Hz, 6H); 13C NMR (100 MHz, CDCl3, ppm) δ = 167.1, 147.9, 138.9 (+, CH), 135.1, 131.3 (+, CH), 128.6 (+, CH, 2C), 127.0 (+, CH, 2C), 103.2, 55.8 (–, CH2), 50.0 (+, CH), 46.9 (+, CH), 35.5 (–, CH2), 29.7 (+, CH), 23.4 (+, CH3, 2C), 20.3 (+, CH3, 2C), 19.2 (+, CH3, 2C); MS (FAB, Matrix: 3-NBA): *m/z* (%) = 386 (26) [M+2H]+, 385 (100) [M+H]+, 384 (12) [M]+, 383 (11), 284 (26), 271 (29), 265 (12), 264 (65), 105 (51), 97 (10), 95 (11); HRMS–FAB *(m/z)*: [M+H]+ Calcd for C21H33ON6, 385.2716; Found 385.2715; IR (ATR, ṽ) = 3315 (w), 3071 (vw), 3053 (vw), 2968 (w), 2928 (w), 2868 (w), 1635 (vs), 1601 (w), 1577 (w), 1543 (vs), 1492 (m), 1466 (m), 1446 (w), 1418 (vs), 1405 (vs), 1380 (s), 1363 (vs), 1324 (m), 1299 (vs), 1252 (vs), 1238 (vs), 1224 (vs), 1193 (w), 1153 (s), 1125 (s), 1109 (s), 1095 (m), 1081 (w), 1052 (w), 1017 (vs), 1001 (m), 980 (m), 945 (w), 928 (w), 912 (w), 892 (w), 882 (w), 853 (w), 822 (w), 809 (m), 781 (s), 739 (w), 715 (s), 697 (vs), 669 (m), 646 (s), 616 (m) cm–1.

Additional information on the chemical synthesis is available *via* Chemotion repository:

<https://doi.org/10.14272/reaction/SA-FUHFF-UHFFFADPSC-MPFTVRYGHB-UHFFFADPSC-NUHFF-NWMXW-NUHFF-ZZZ>

Additional information on the analysis of the target compound is available *via* Chemotion repository:

<https://doi.org/10.14272/MPFTVRYGHBGKIC-OCOZRVBESA-N.1>

# 4. Crystal Structure Determinations of compounds 12h and 13c

The single-crystal X-ray diffraction studies were carried out on a Bruker D8 Venture diffractometer with PhotonII detector at 123(2) K using Cu-K radiation ( = 1.54178 Å). Dual space methods (SHELXT) [G. M. Sheldrick, *Acta Crystallogr.* 2015, **A71**, 3-8] were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on *F2*) [G. M. Sheldrick, *Acta Crystallogr.* 2015, **C71**, 3-8]. Hydrogen atoms were localized by difference electron density determination and refined using a riding model. Semi-empirical absorption corrections were applied. For **12h** an extinction correction was applied.

**12h**: colourless crystals, C17H21BrN6, *M*r = 389.31, crystal size 0.18 × 0.108× 0.04 mm, monoclinic, space group *P*21/c (No. 14), *a* = 13.0525(10) Å, *b* = 14.3306(11) Å, *c* = 10.0264(8) Å, *β* = 97.128(2)°, *V* = 1860.9(3) Å3, *Z* = 4, *ρ* = 1.390 Mg/m-3, *µ*(Cu-Kα) = 3.09 mm-1, *F*(000) = 800, *2θ*max = 144.4°, 33389 reflections, of which 3665 were independent (*R*int = 0.024), 218 parameters, *R*1 = 0.022 (for 3621 I > 2σ(I)), w*R*2 = 0.056 (all data), *S* = 1.03, largest diff. peak / hole = 0.30 / -0.28 e Å-3.

**13c**: colourless crystals, C17H20F2N6, *M*r = 346.39, crystal size 0.20 × 0.16 × 0.08 mm, monoclinic, space group *P*21/c (No. 14), *a* = 9.7201(3) Å, *b* = 11.9699(4) Å, *c* = 15.3002(5) Å, *β* = 100.614(1)°, *V* = 1749.70(10) Å3, *Z* = 4, *ρ* = 1.315 Mg/m-3, *µ*(Cu-Kα) = 0.82 mm-1, *F*(000) = 728, *2θ*max = 144.6°, 19144 reflections, of which 3428 were independent (*R*int = 0.023), 226 parameters, *R*1 = 0.037 (for 3330 I > 2σ(I)), w*R*2 = 0.095 (all data), *S* = 1.05, largest diff. peak / hole = 0.53 / -0.24 e Å-3.

CCDC 2054633 (**12h**), and 2054634 (**13c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* [www.ccdc.cam.ac.uk/data\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).



**Fig. S1**. Molecular structure of **12h** (displacement parameters are drawn at 50 % probability level).



**Fig. S2**. Molecular structure of **13c** (displacement parameters are drawn at 50 % probability level).

# 5. Biological Assays

Biological assays were carried out under sterile conditions using the sterile benches LaminAir® HB2448 (Heraeus GmbH), Laminar-Flow Werkbank (BDK Luft- und Reinraumtechnik GmbH) or Clean Air Technik (Clean Air). Cells were incubated at 37 °C, 5% CO2, and 85% humidity using a Binder Ex-Demo Units Incubator.

**Cell culture**

Human epithelial cervix carcinoma (HeLa) cells were cultivated in *Dulbecco ́s Modified Eagle Medium-high glucose* (DMEM, GibcoTM) supplemented with 10% fetal calf serum (FCS) and 1% penicillin/streptomycin (P/S). At 80% confluency, the medium was removed, the cells were washed with *Dulbecco’s Phosphate Buffered Saline* (DPBS, GibcoTM) and treated with trypsin / EDTA (GibcoTM) to passage the cells. The detachment process was stopped with culture medium (DMEM + 10% FBS + 1% P/S) and the cells were seeded according to the desired cell number / area.

**MTT-assay[1]**

In a 96-well plate (Corning® Costar® 3596 96-Well Cell Culture Cluster), 1.0 × 104 HeLa-cells per well of a 96 well plate were cultivated for 16 h. Stock solutions of the single compounds in dimethylsulfoxide were diluted to 0.50 µm, 1.00 µm, 5.00 µm, 10.0 µm, 25.0 µm, and 50.0 µm with cell culture medium (DMEM + 10% FBS + 1% P/S) to ensure a final concentration of DMSO below 0.5%. 100 µL of the prepared DMEM-diluted compounds were added to each well and the cells were incubated for 72 h. All experiments were performed in triplicates. Cells that were solely treated with the culture medium containing 0.5% of DMSO served as a negative control. After incubation, the positive control (cells in DMEM plus 0.5% DMSO) was treated with 1% Triton-X. To determine the viability of the cells 20 µL of a freshly prepared solution of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT, 2.73 mg/mL, Sigma-Aldrich®) in culture medium were added to each well and incubated at 37 °C for 4 h. The reaction was stopped using 100 µL of *Solubilization Solution / Stop Mix* (CellTiter 96® Non-Radioactive Cell Proliferation Assay, Promega). After 72 h, the absorption (A) of every well at 595 nm was monitored using a 96-well plate reader (Ultra Microplate Reader ELx808, Biotech Instruments Inc.).

**Table S1:** Graphical representation of the MTT assays conducted for selected compounds and their respective calculated IC50 values.

|  |  |  |
| --- | --- | --- |
| Compound | IC50 [µm] | Graph |
| **5a** | >50 |  |
| **5d** | >50 |  |
| **5e** | >50 |  |
| **5f** | >50 |  |
| **5h** | >50 |  |
| **9a** | >50 |  |
| **9b** | 17 |  |
| **9c** | >50 |  |
| **9d** | >50 |  |
| **9e** | >50 |  |
| **9f** | >50 |  |
| **9g** | >50 |  |
| **9h** | >50 |  |
| **9i** | >50 |  |
| **10h** | >50 |  |
| **12a** | >50 |  |
| **12b** | 41 |  |
| **12c** | 49 |  |
| **12d** | >50 |  |
| **12e** | >50 |  |
| **12f** | >50 |  |
| **12g** | >50 |  |
| **12h** | >50 |  |
| **13a** | 47 |  |
| **13b** | 45 |  |
| **13c** | >50 |  |
| **13d** | 20 |  |
| **13e** | >50 |  |
| **13f** | 46 |  |
| **13g** | 21 |  |
| **13h** | 29 |  |
| **16f** | >50 |  |

# 6. References

1. Mosmann, T. *J. Immunol. Methods* **1983**,*65*, 55-63.