

Supporting Information

Development of ^{18}F -Labeled Radiotracers for PET Imaging of the Adenosine $\text{A}_{2\text{A}}$ Receptor: Synthesis, Radiolabeling and Preliminary Biological Evaluation

Thu Hang Lai ^{1,2,*}, Susann Schröder ², Magali Toussaint ¹, Sladjana Dukić-Stefanović ¹, Mathias Kranz ^{1,3,4}, Friedrich-Alexander Ludwig ¹, Steffen Fischer ¹, Jörg Steinbach ^{1,2}, Winnie Deuther-Conrad ¹, Peter Brust ¹, Rareș-Petru Moldovan ^{1,*}

¹ Helmholtz-Zentrum Dresden-Rossendorf (HZDR), Department of Neuroradiopharmaceuticals, Institute of Radiopharmaceutical Cancer Research, Research site Leipzig, 04318 Leipzig, Germany; m.toussaint@hzdr.de (M.T.); s.dukic-stefanovic@hzdr.de (S.D.-S.); mathias.kranz@uit.no (M.K.); f.ludwig@hzdr.de (F.-A.L.); s.fischer@hzdr.de (S.F.); steinbach-joerg@web.de (J.S.); w.deuther-conrad@hzdr.de (W.D.-C.); p.brust@hzdr.de (P.B.)

² Department of Research and Development, ROTOP Pharmaka Ltd., Dresden 01328, Germany; s.schroeder@hzdr.de

³ PET Imaging Center, University Hospital of North Norway (UNN), 9009 Tromsø, Norway

⁴ Nuclear Medicine and Radiation Biology Research Group, The Arctic University of Norway, 9009 Tromsø, Norway

* Correspondence: t.lai@hzdr.de (T.H.L.); r.moldovan@hzdr.de (R.-P.M.); Tel.: +49-341-234-179-4635 (T.H.L.); +49-341-234-179-4634 (R.-P.M.)

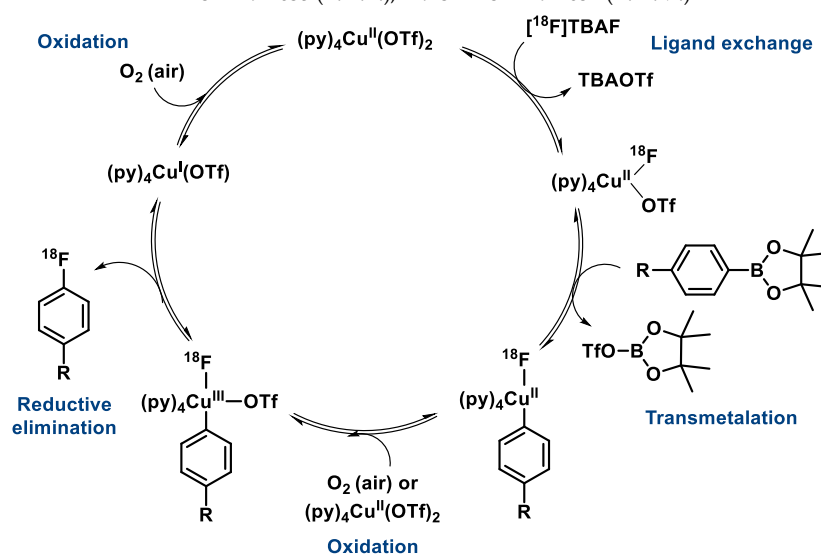


Figure S1: Proposed reaction mechanism based on the Chan-Evans-Lam coupling for the copper-mediated radiofluorination of an aryl boronic pinacol ester acid precursor.

1-(4-Fluorobenzyl)-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-amine (PPY1)

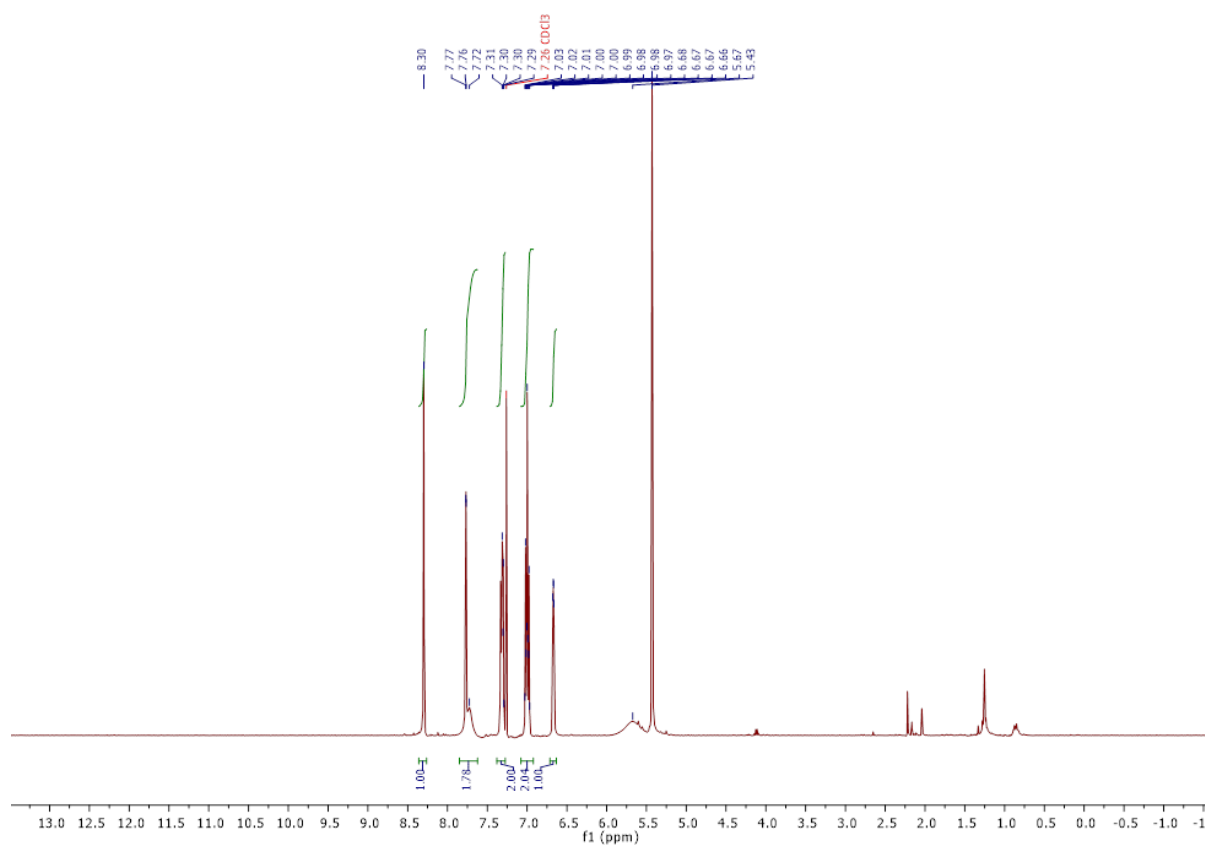


Figure S2: ¹H-NMR of PPY1.

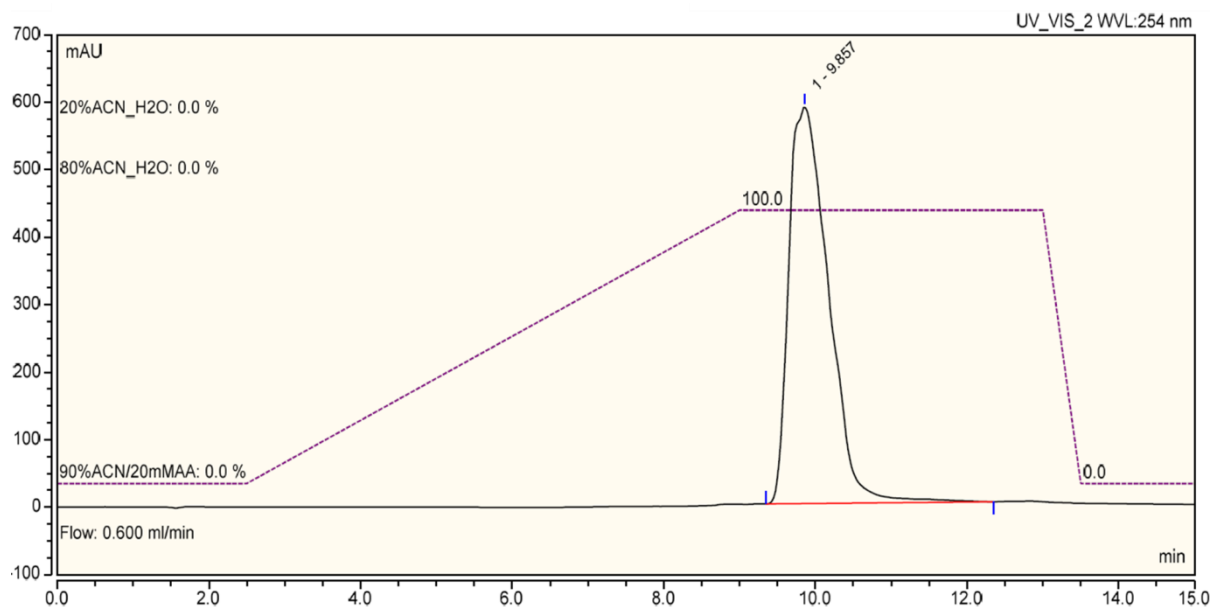


Figure S3: LC-MS chromatogram of PPY1.

1-(2-Fluorobenzyl)-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-amine (PPY2)

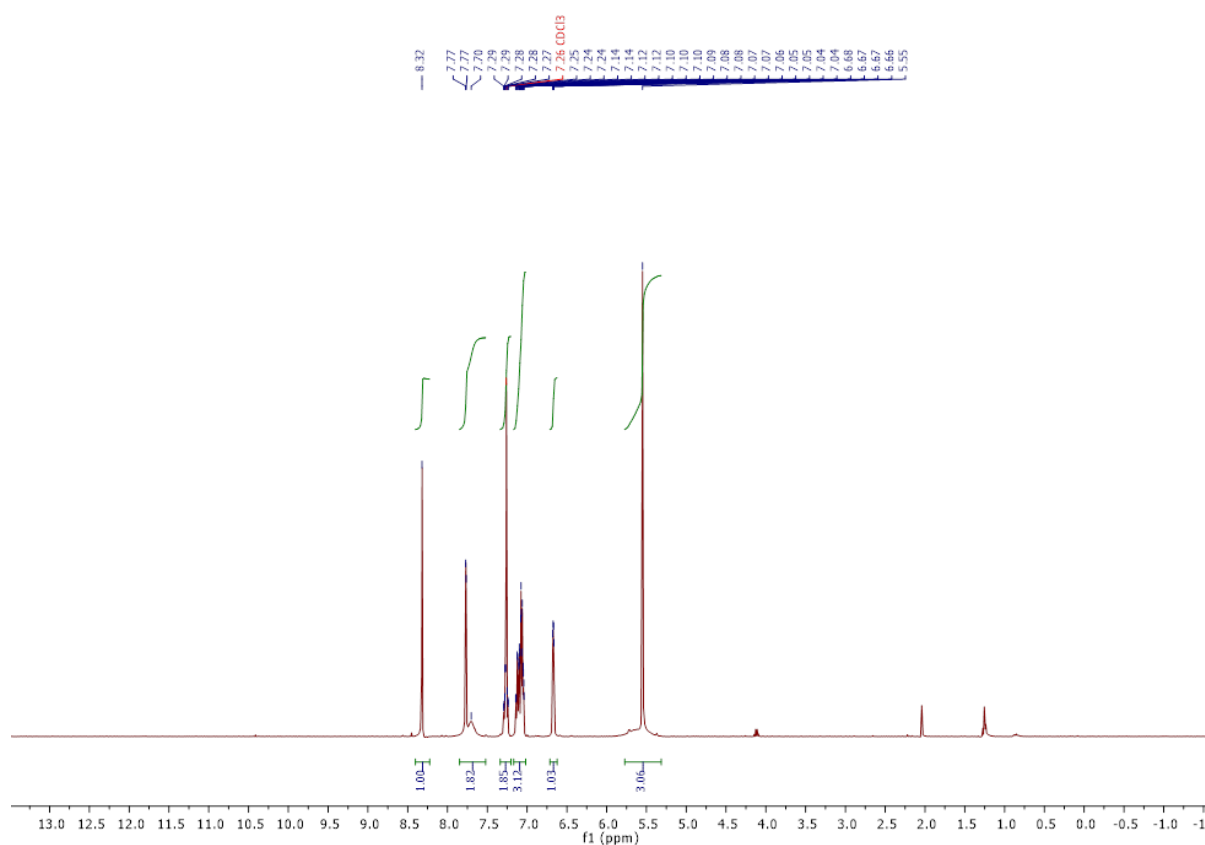


Figure S4: ¹H-NMR of PPY2.

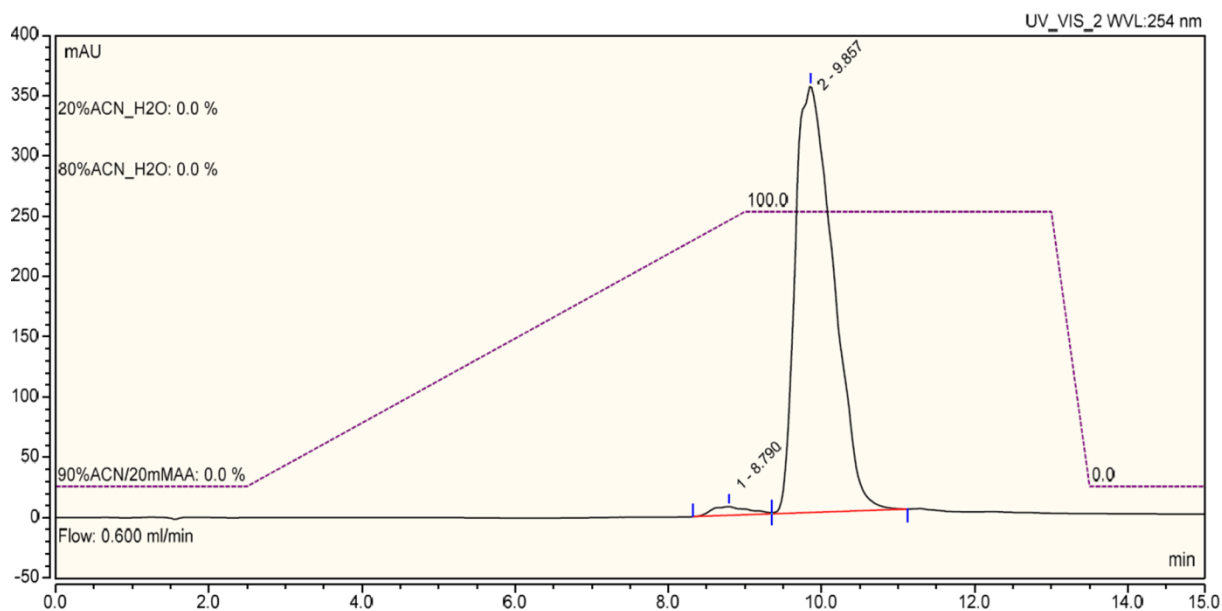


Figure S5: LC-MS chromatogram of PPY2.

Chromatogram showing two peaks at retention times 8.790 and 9.893 minutes. The x-axis represents time in minutes (0.0 to 15.0), and the y-axis represents mAU (-50 to 400). The gradient is indicated by a purple dashed line, starting at 90% ACN/20mMAA (0.0 %) and transitioning to 20% ACN/H₂O (0.0 %). A red line at 0 mAU is also shown. The flow rate is 0.600 ml/min. The UV-VIS wavelength is 254 nm.

S4

1-((2-Fluoropyridin-3-yl)methyl)-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-amine (PPY4)

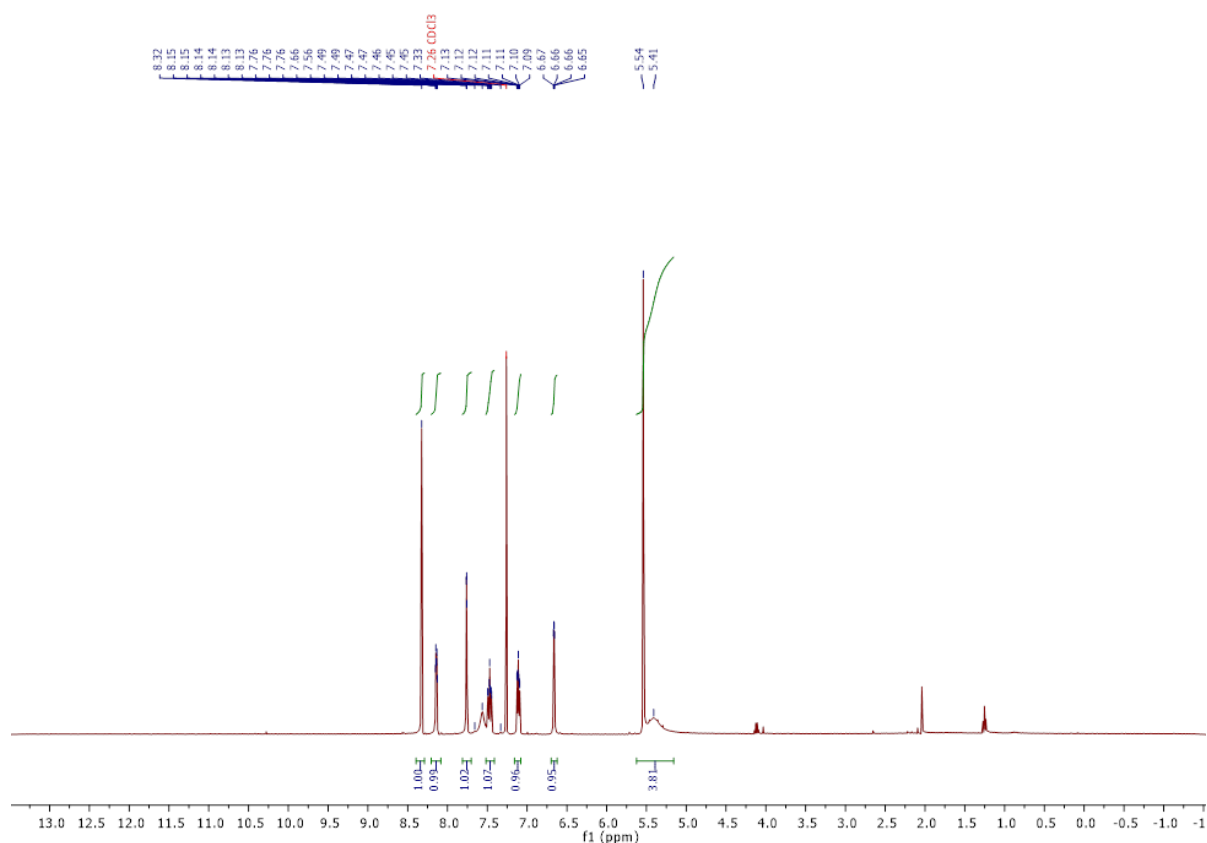


Figure S8: ¹H-NMR of PPY4.

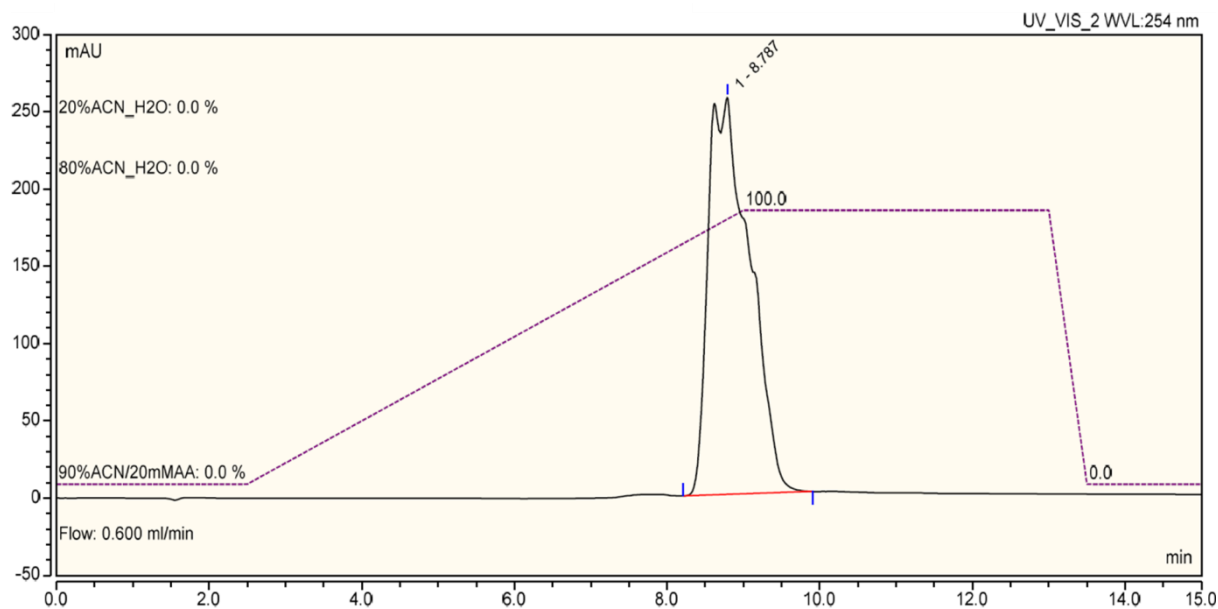


Figure S9: LC-MS chromatogram of PPY4.

UV_VIS_2 WVL: 254 nm

mAU

20%ACN_H2O: 0.0 %

80%ACN_H2O: 0.0 %

90%ACN/20mMAA: 0.0 %

Flow: 0.600 ml/min

8.840

100.0

0.0

min

S6

¹H NMR spectrum (CDCl₃) of compound 1. The x-axis represents chemical shift in ppm, ranging from 13.0 to -1.0. The spectrum shows several peaks in the aromatic region (6.5-8.5 ppm) and aliphatic region (1.0-2.5 ppm). Integration values are provided below the peaks: 2.00, 2.71, 1.03, 1.00, and 2.17. A solvent peak for CDCl₃ is marked at 7.26 ppm. Two peaks are labeled 'EA' at approximately 1.2 ppm and 2.1 ppm. A list of peak chemical shifts is provided at the top: 8.30, 8.29, 8.22, 7.82, 7.80, 7.78, 7.77, 7.70, 7.26 (CDCl₃), 6.90, 6.89, 6.88, 6.87, 6.86, 6.85, 6.67, 5.46.

UV_VIS_2 WVL: 254 nm

mAU

20%ACN_H2O: 0.0 %

80%ACN_H2O: 0.0 %

90%ACN/20mMAA: 0.0 %

Flow: 0.600 ml/min

min

1 8.720

100.0

0.0

S7

1-((2-Fluoropyridin-4-yl)methyl)-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-amine (PPY7)

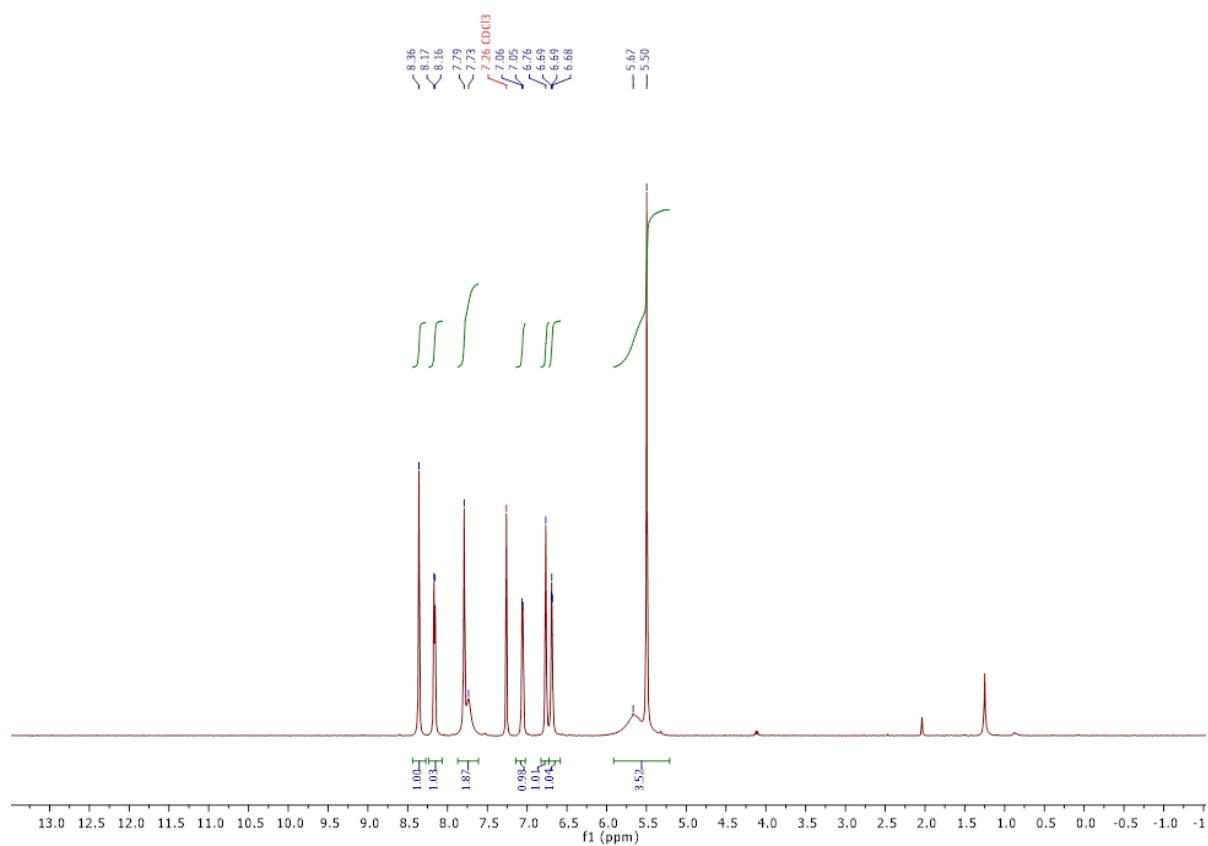


Figure S14: ¹H-NMR of PPY7.

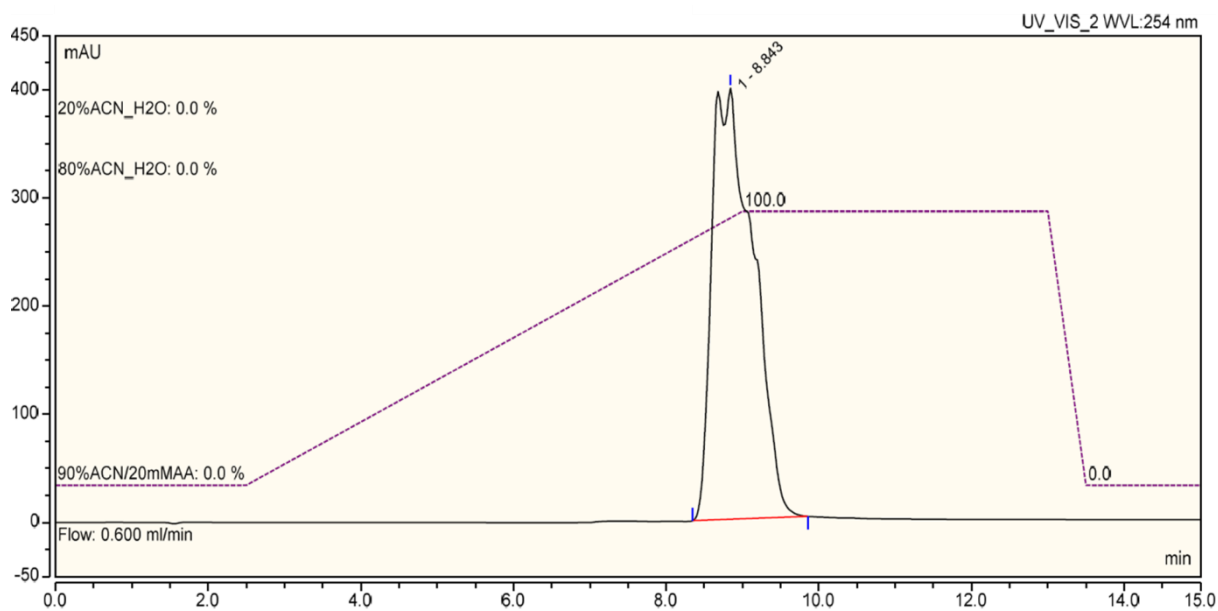


Figure S15: LC-MS chromatogram of PPY7.

1-(4-Bromo-2-fluorobenzyl)-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-amine (PPY8)

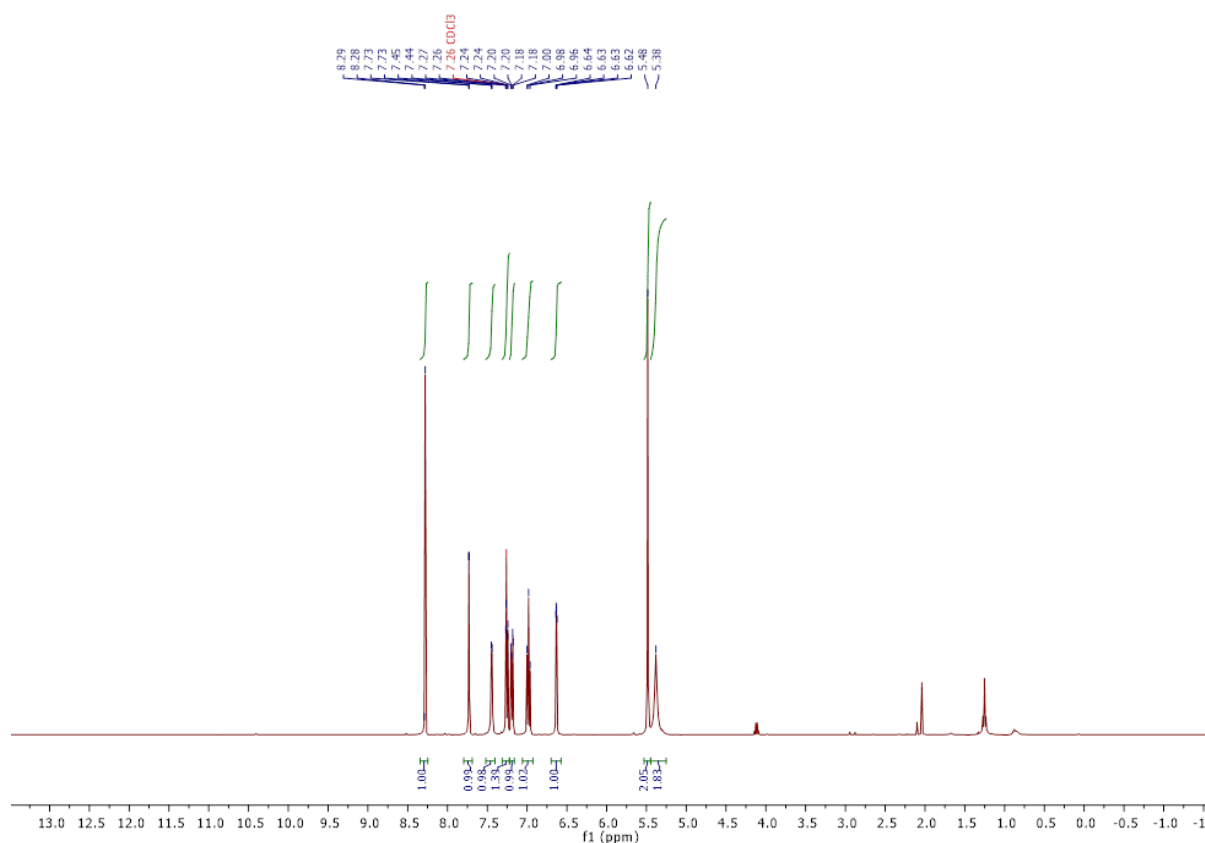


Figure S16: ¹H-NMR of PPY8.

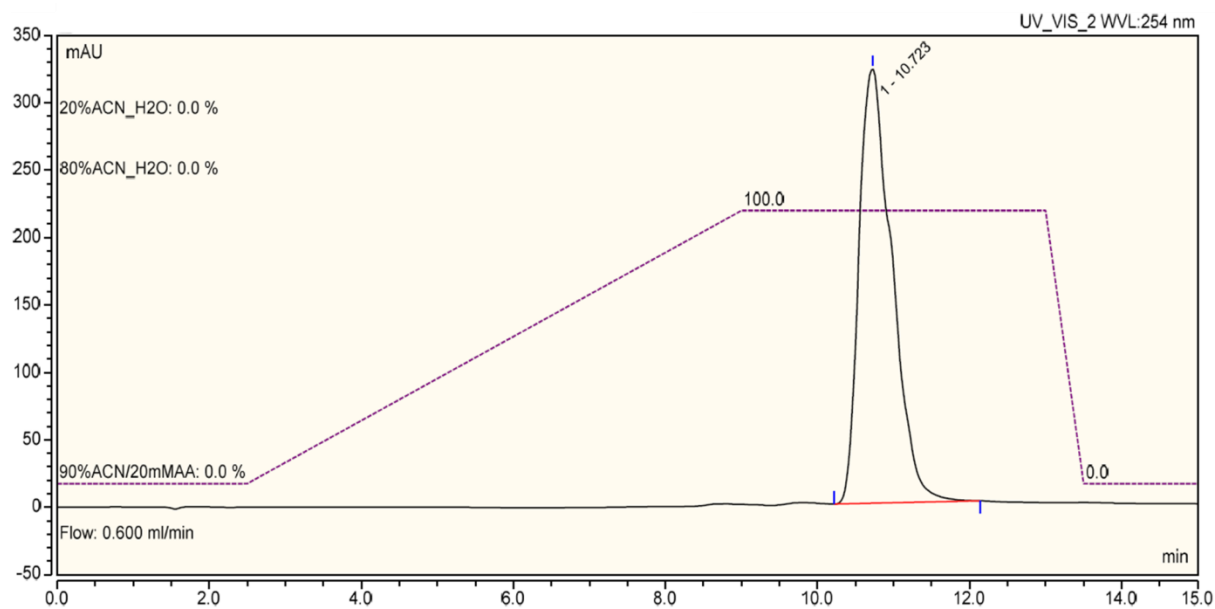


Figure S17: LC-MS chromatogram of PPY8.

1-(2-Bromo-4-fluorobenzyl)-4-(furan-2-yl)-1H-pyrazolo[3,4-d]pyrimidin-6-amine (PPY9)

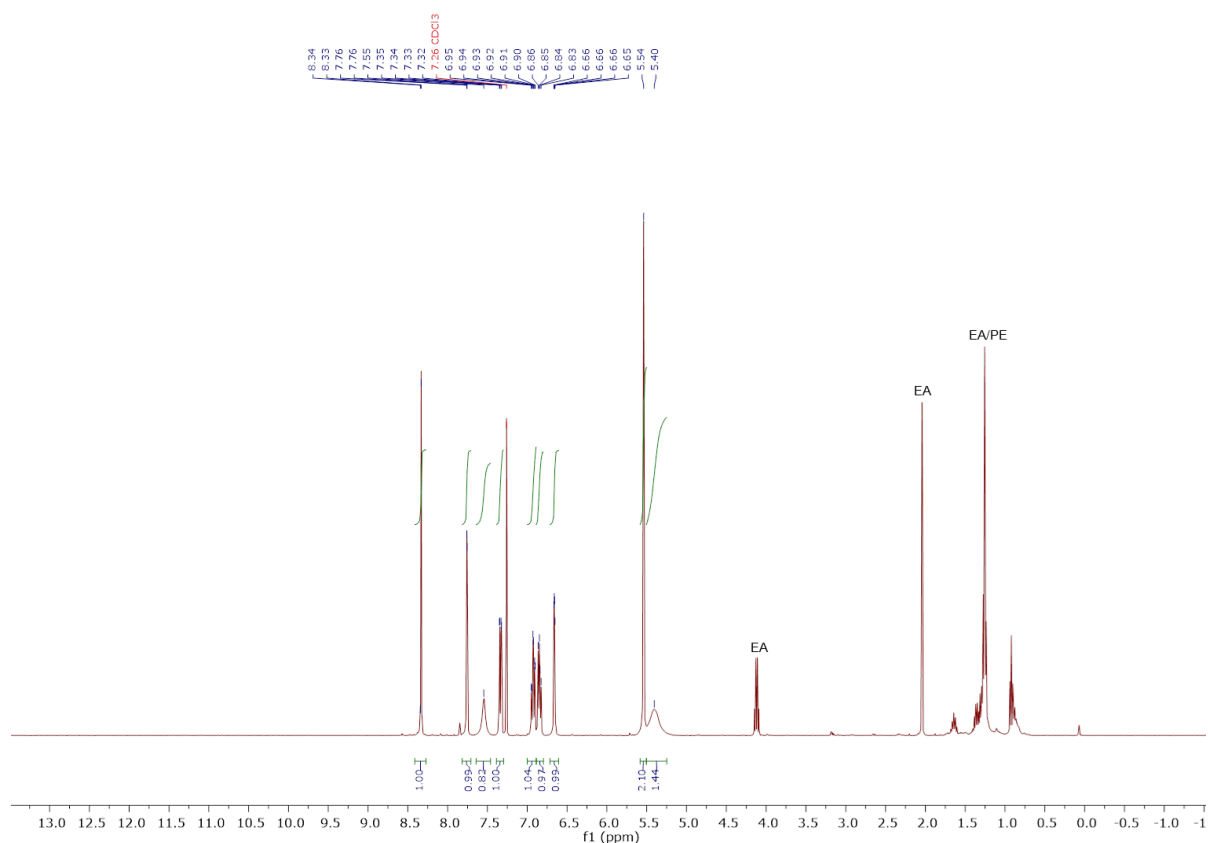


Figure S18: ¹H-NMR of PPY9.

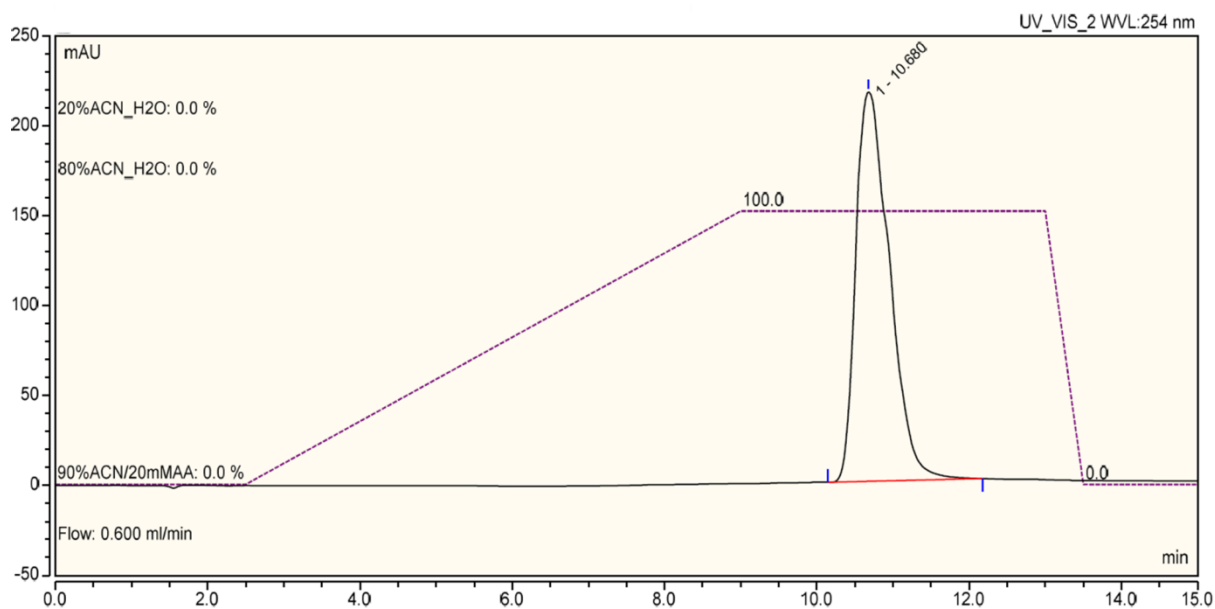


Figure S19: LC-MS chromatogram of PPY9.

1-(3-Bromo-5-fluorobenzyl)-4-(furan-2-yl)-1H-pyrazolo[3,4-d]pyrimidin-6-amine (PPY10)

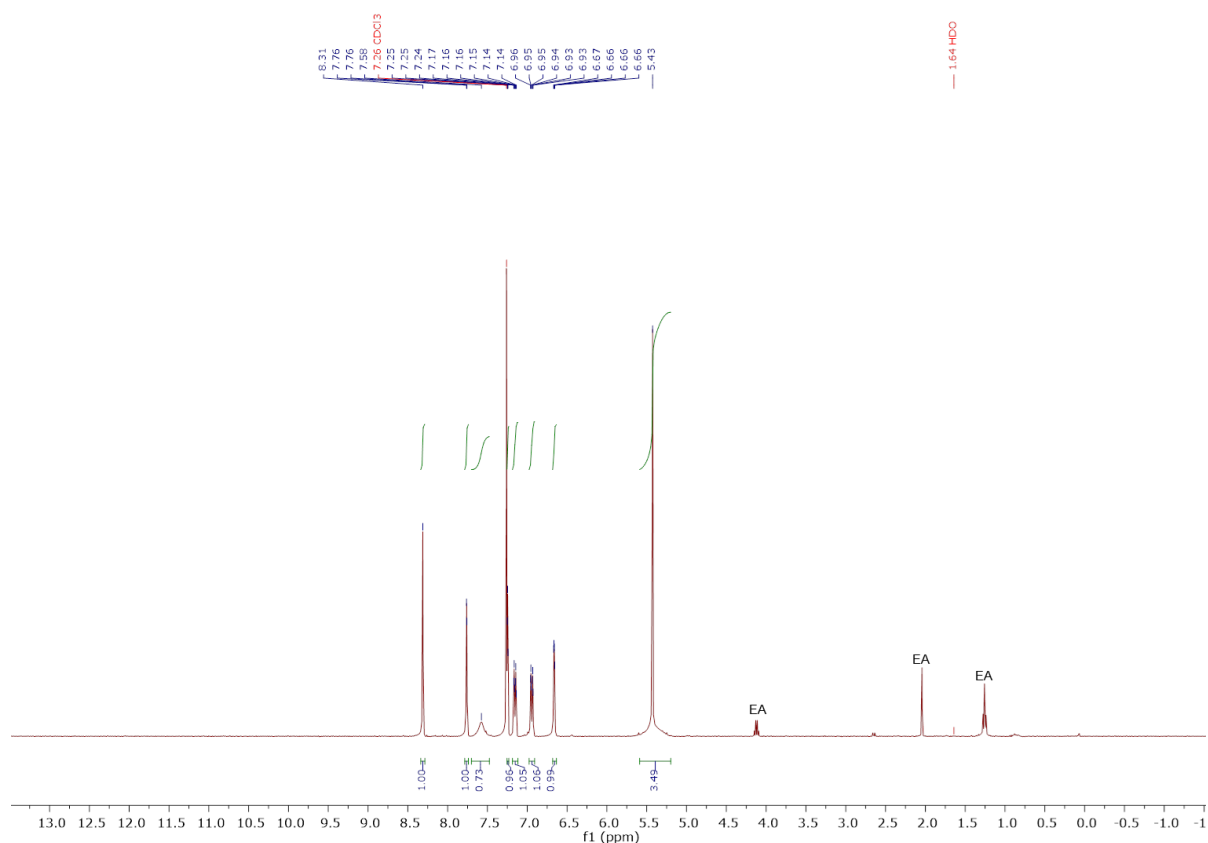


Figure S20: ¹H-NMR of PPY10.

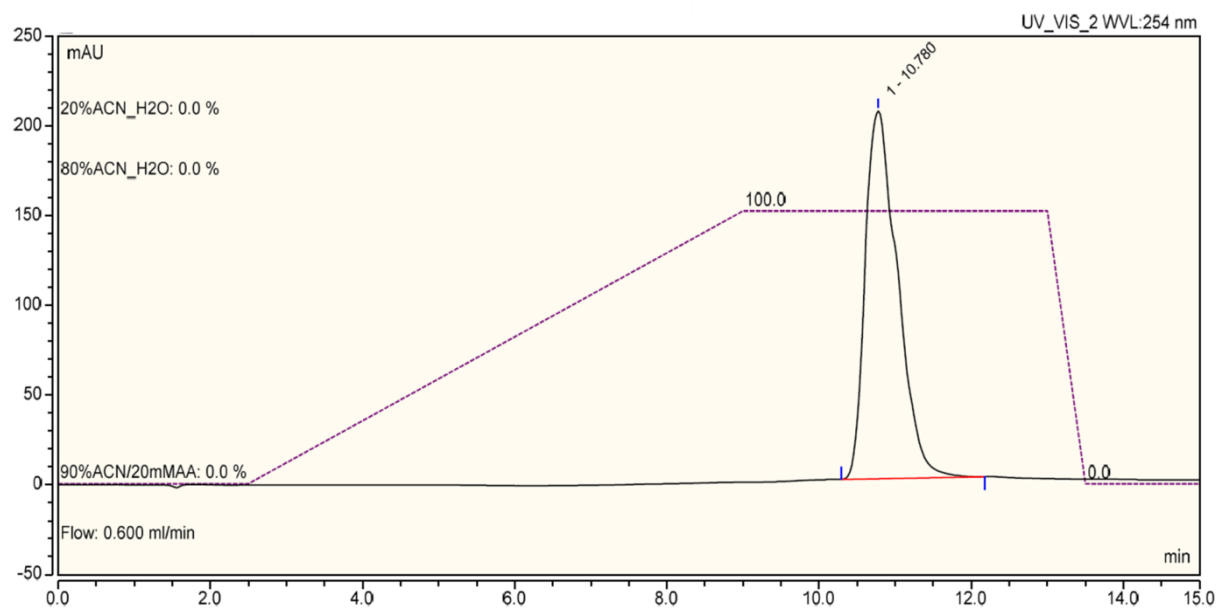


Figure S21: LC-MS chromatogram of PPY10.

1-(2-Bromo-6-fluorobenzyl)-4-(furan-2-yl)-1H-pyrazolo[3,4-d]pyrimidin-6-amin (PPY11)

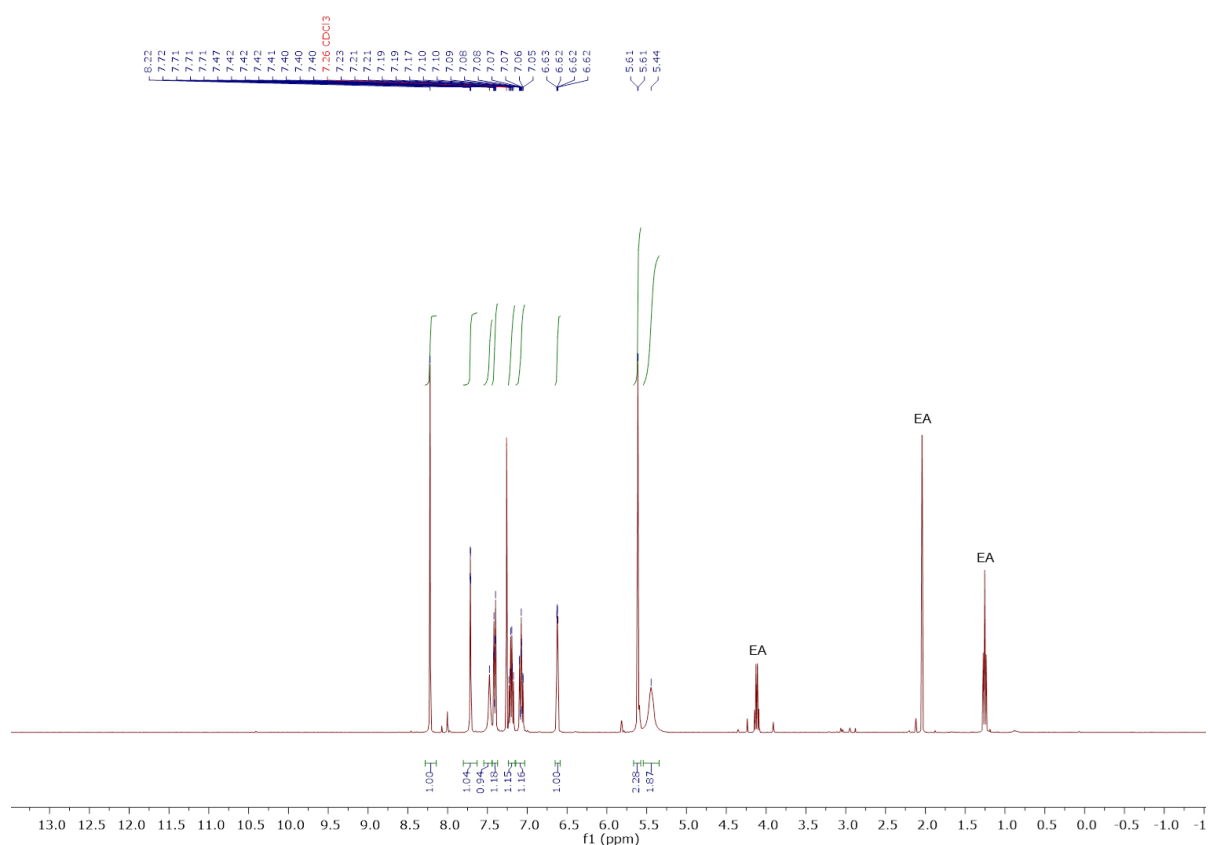


Figure S22: ¹H-NMR of PPY11.

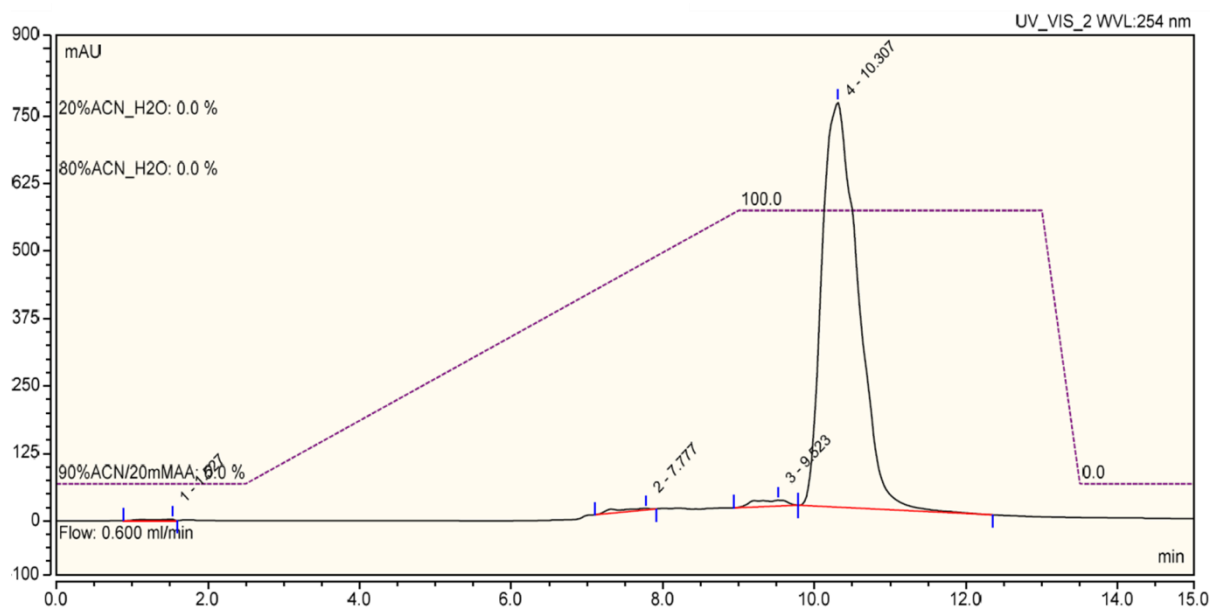


Figure S23: LC-MS chromatogram of PPY11.

2-((6-Amino-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)-5-fluoro-benzonitrile (PPY12)

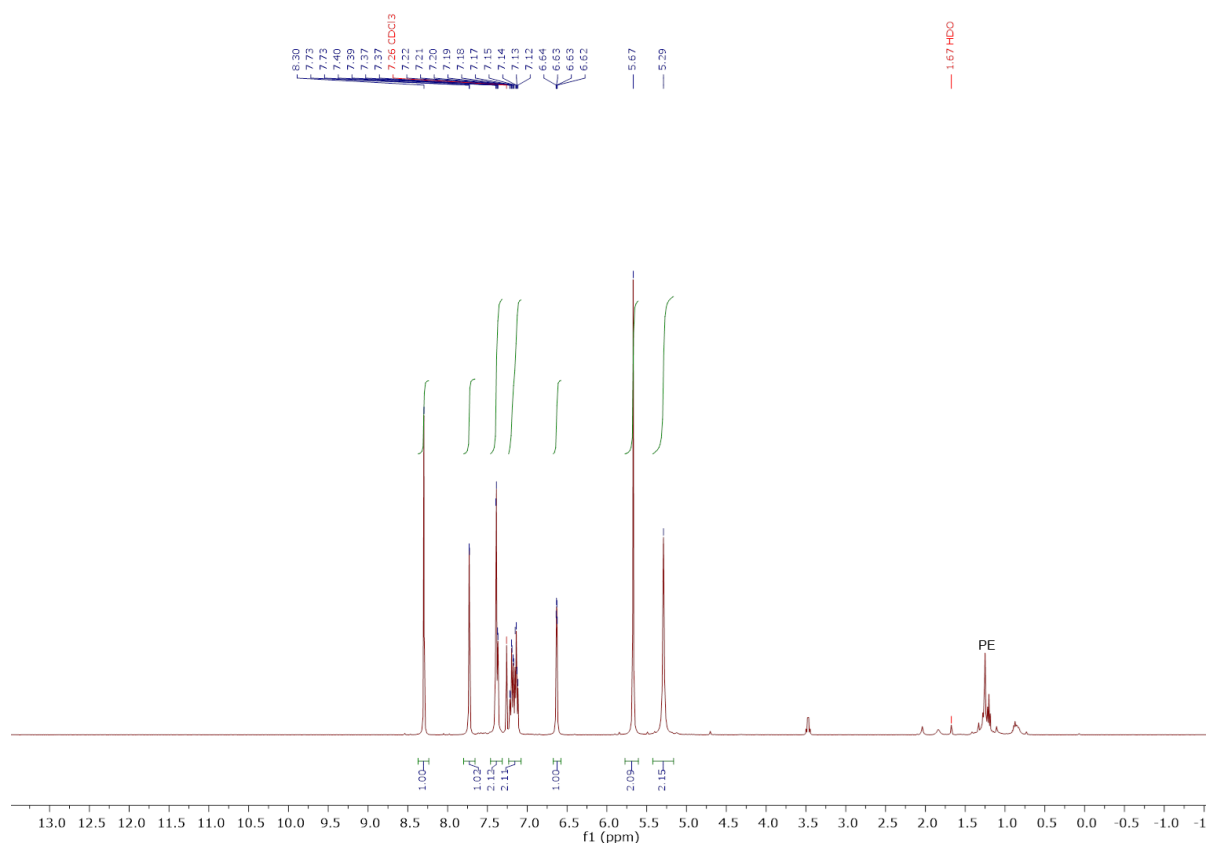


Figure S24: ¹H-NMR of PPY12.

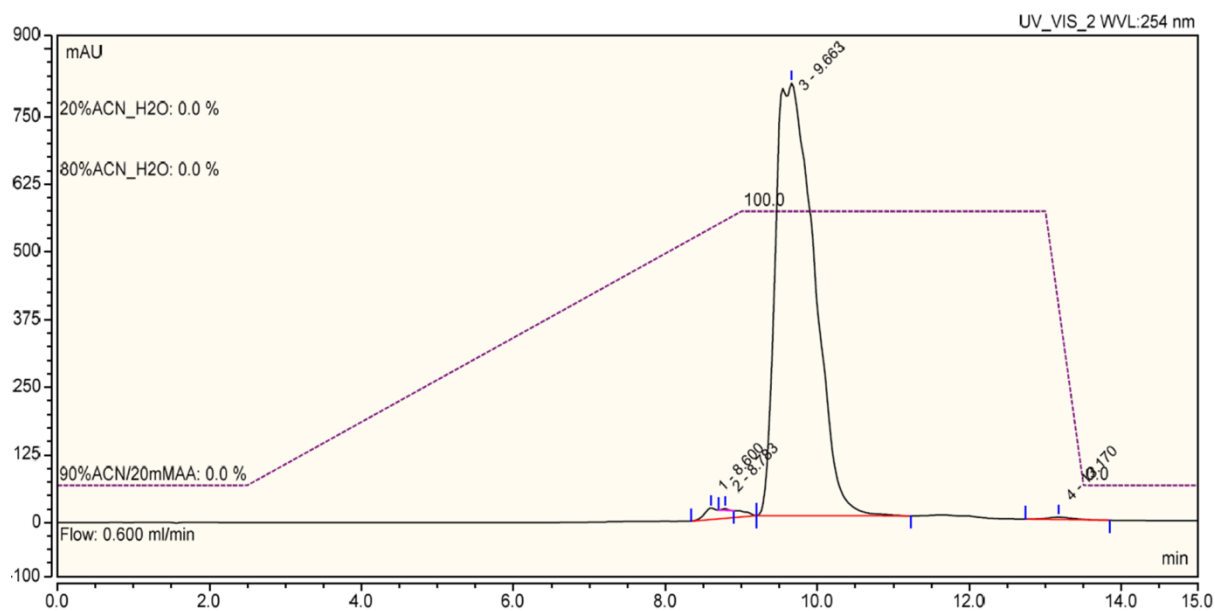


Figure S25: LC-MS chromatogram of PPY12.

4-((6-Amino-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)-3-fluoro-benzonitrile (PPY13)

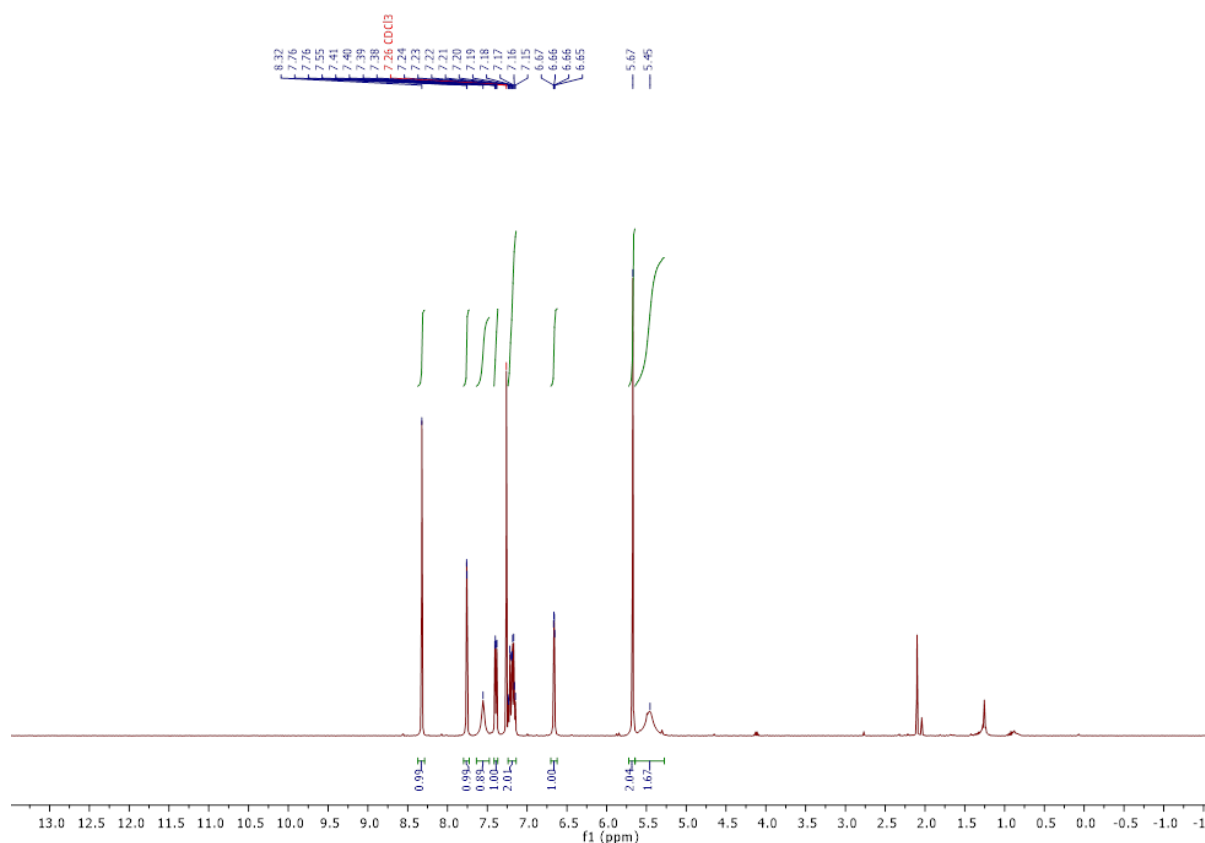


Figure S26: ¹H-NMR of PPY13.

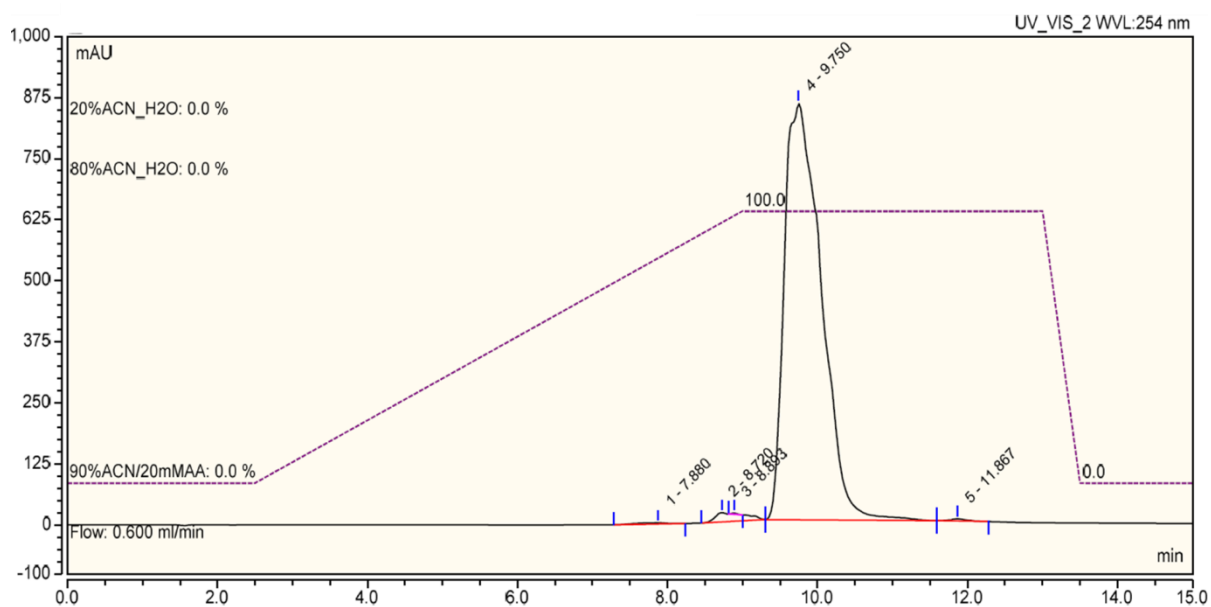


Figure S27: LC-MS chromatogram of PPY13.

3-((6-Amino-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)-5-fluoro-benzonitrile (PPY14)

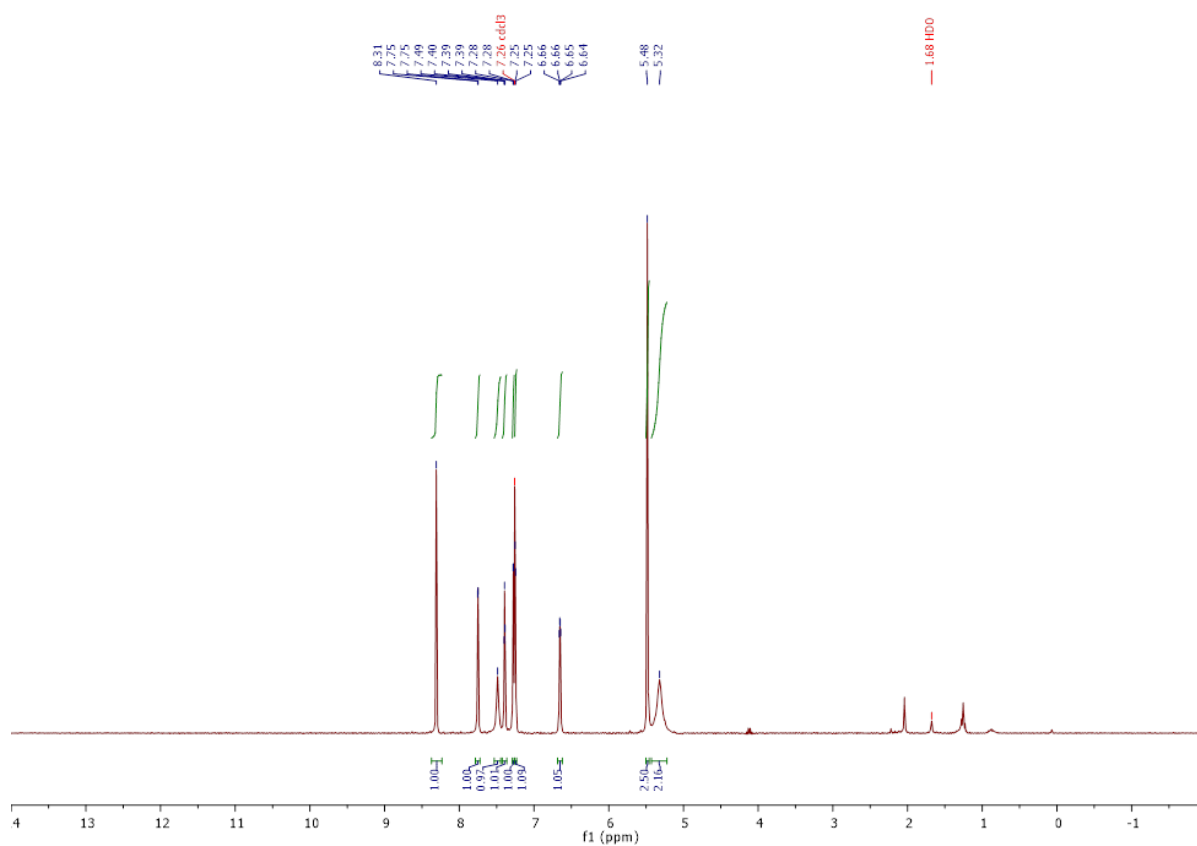


Figure S28: ¹H-NMR of PPY14.

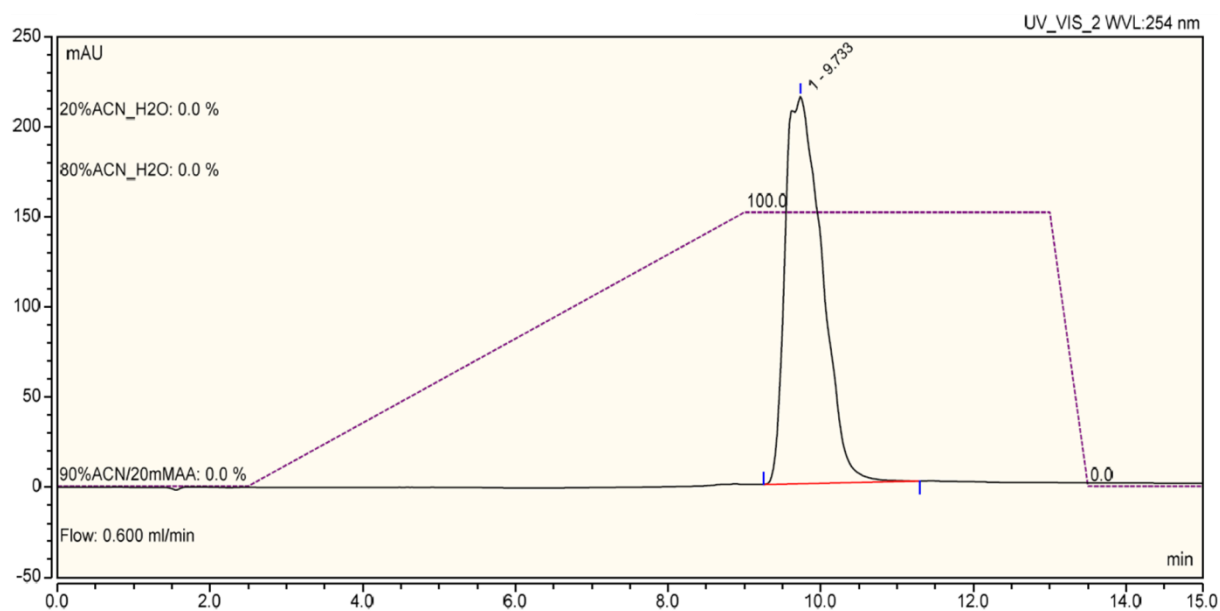


Figure S29: LC-MS chromatogram of PPY14.

2-((6-Amino-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)-3-fluoro-benzonitrile (PPY15)

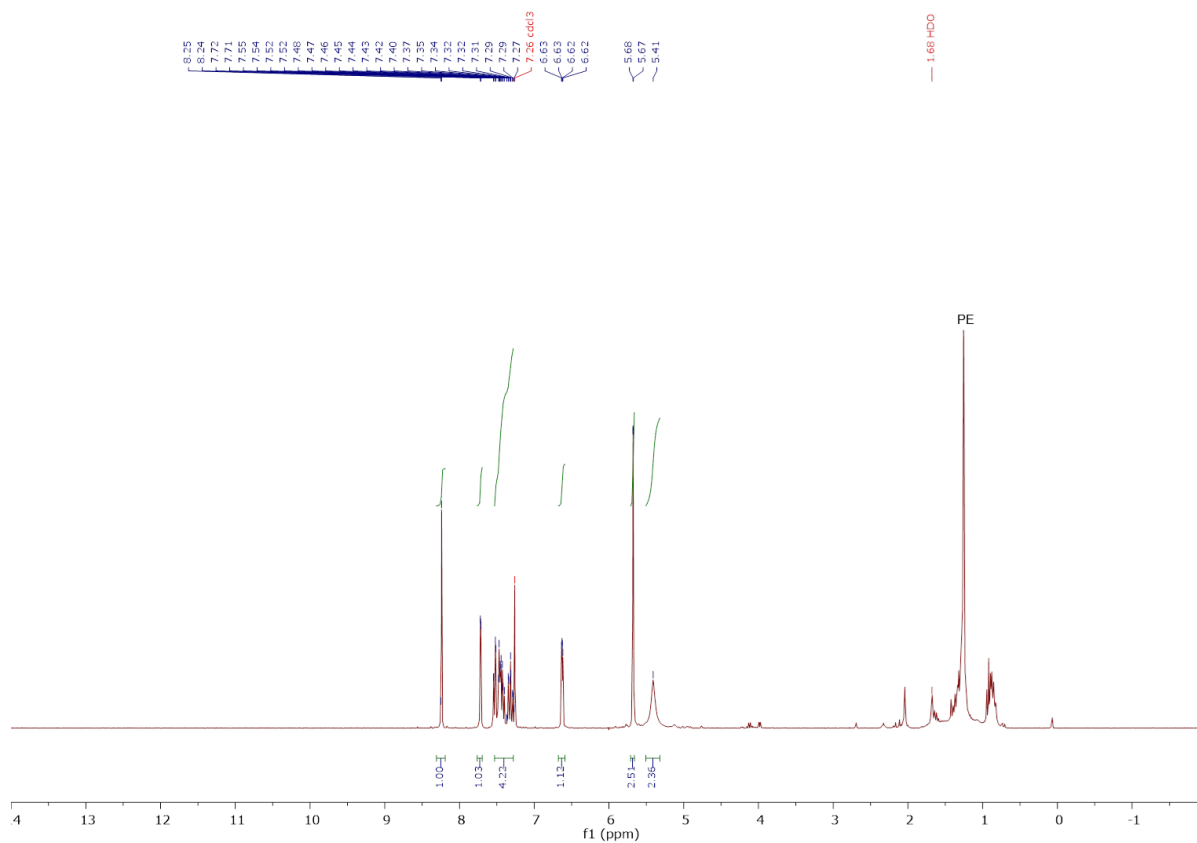


Figure S30: ¹H-NMR of PPY15.

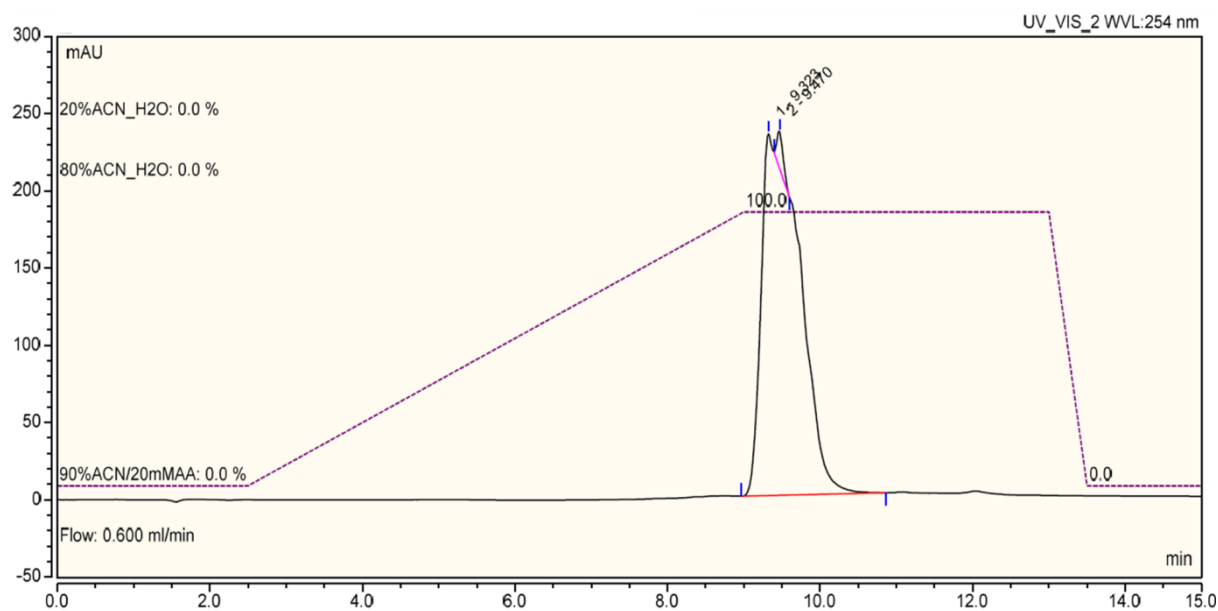


Figure S31: LC-MS chromatogram of PPY15.

1-(3-(2-Fluoroethyl)benzyl)-4-(furan-2-yl)-1*H*-yrazolo[3,4-*d*]pyrimidin-6-amine (PPY16)

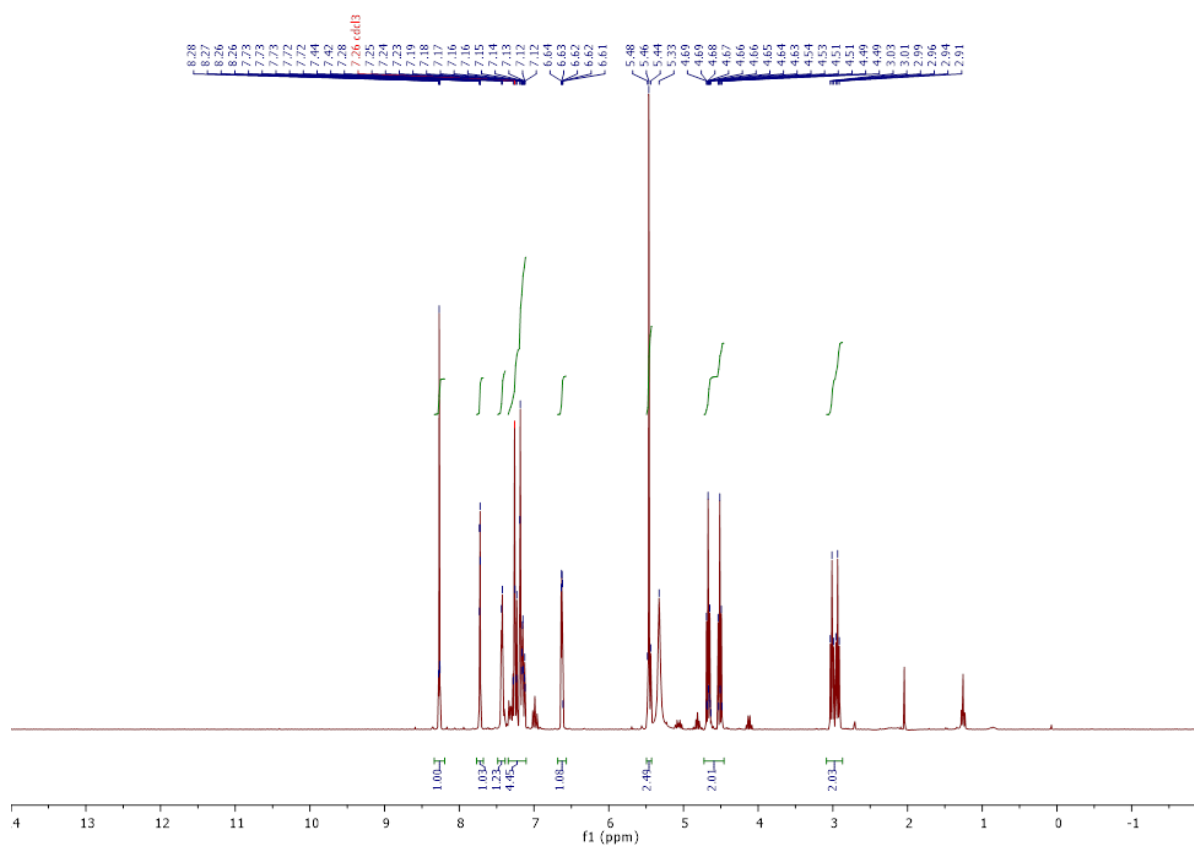


Figure S32: ^1H -NMR of PPY16.

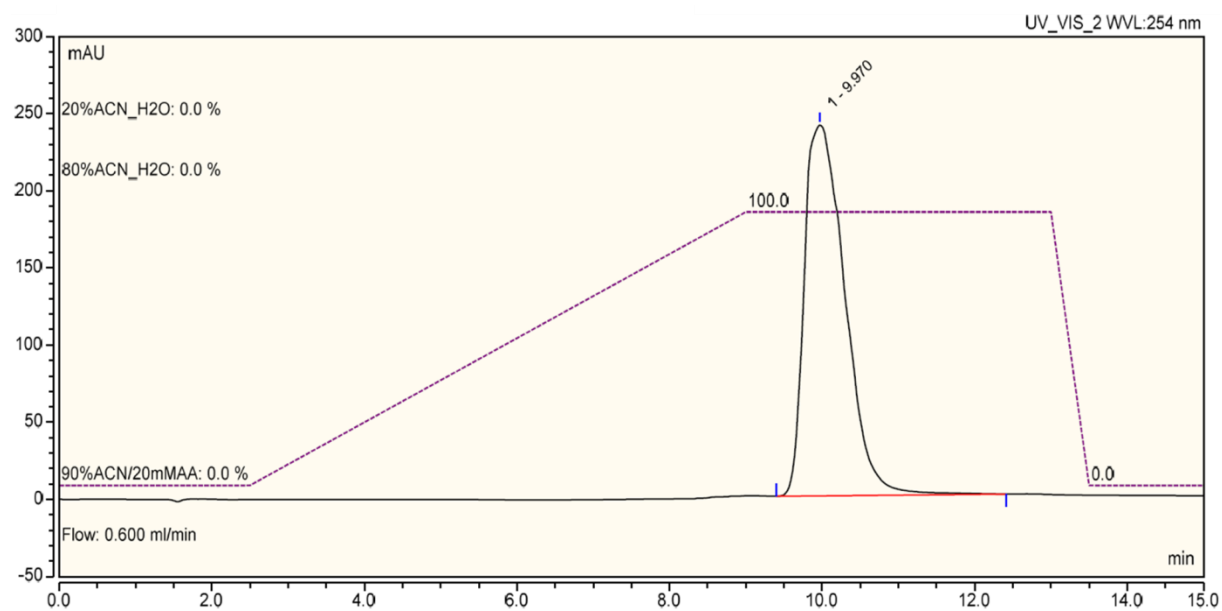


Figure S33: LC-MS chromatogram of PPY16.

1-(3-(2-Fluoroethoxy)benzyl)-4-(furan-2-yl)-1H-pyrazolo[3,4-d]pyrimidin-6-amine (PPY17)

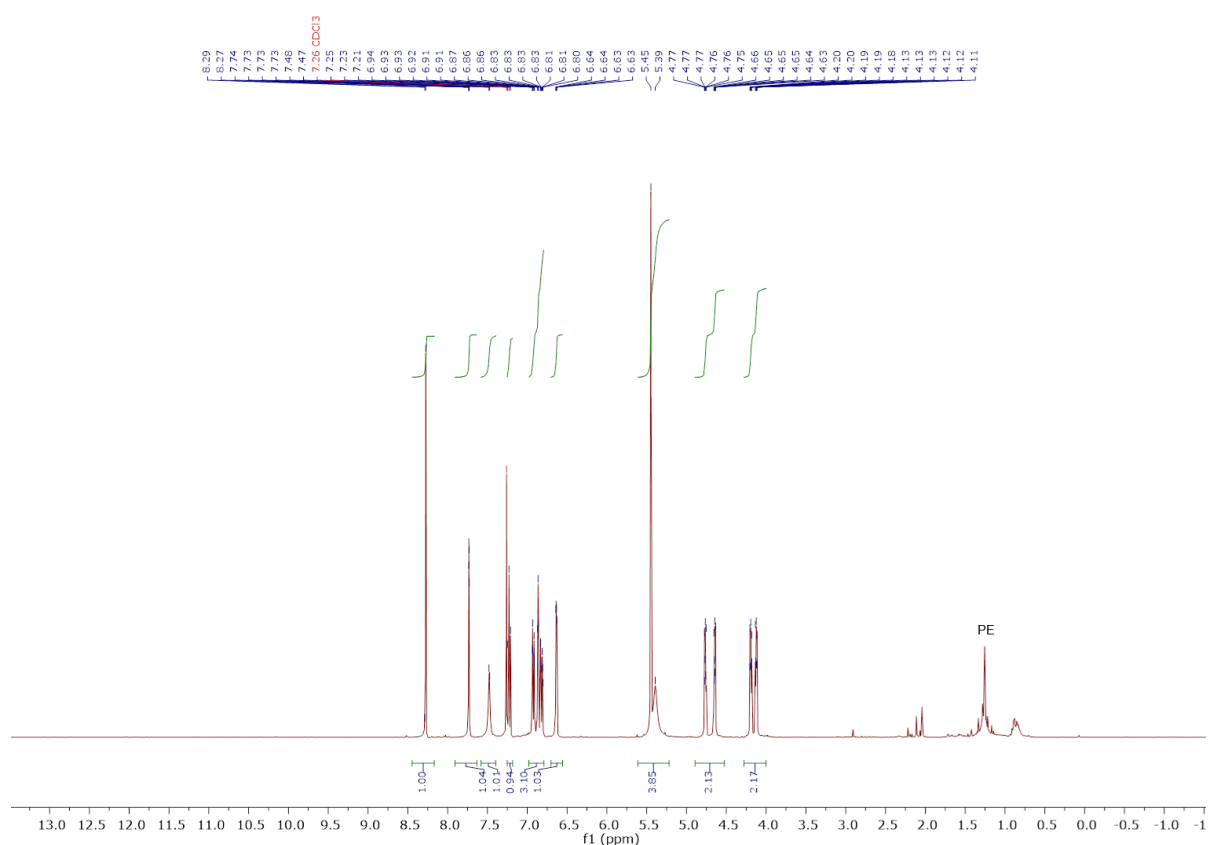


Figure S34: ¹H-NMR of PPY17.

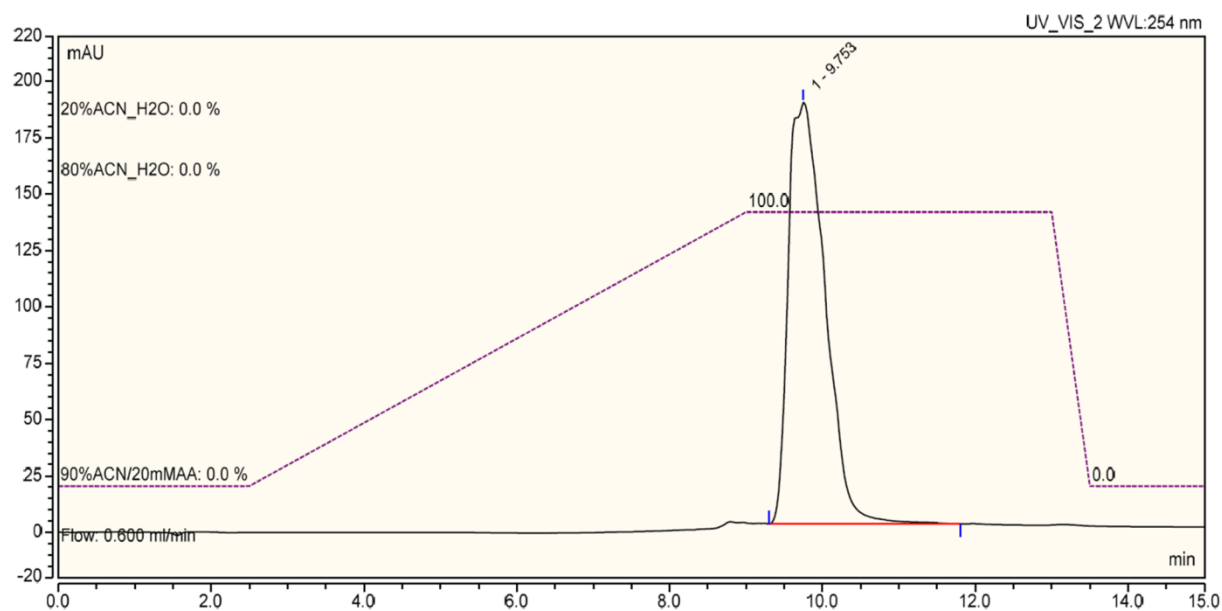


Figure S35: LC-MS chromatogram of PPY17.

1-(3-(3-Fluoropropoxy)benzyl)-4-(furan-2-yl)-1H-pyrazolo[3,4-d]pyrimidin-6-amine (PPY18)

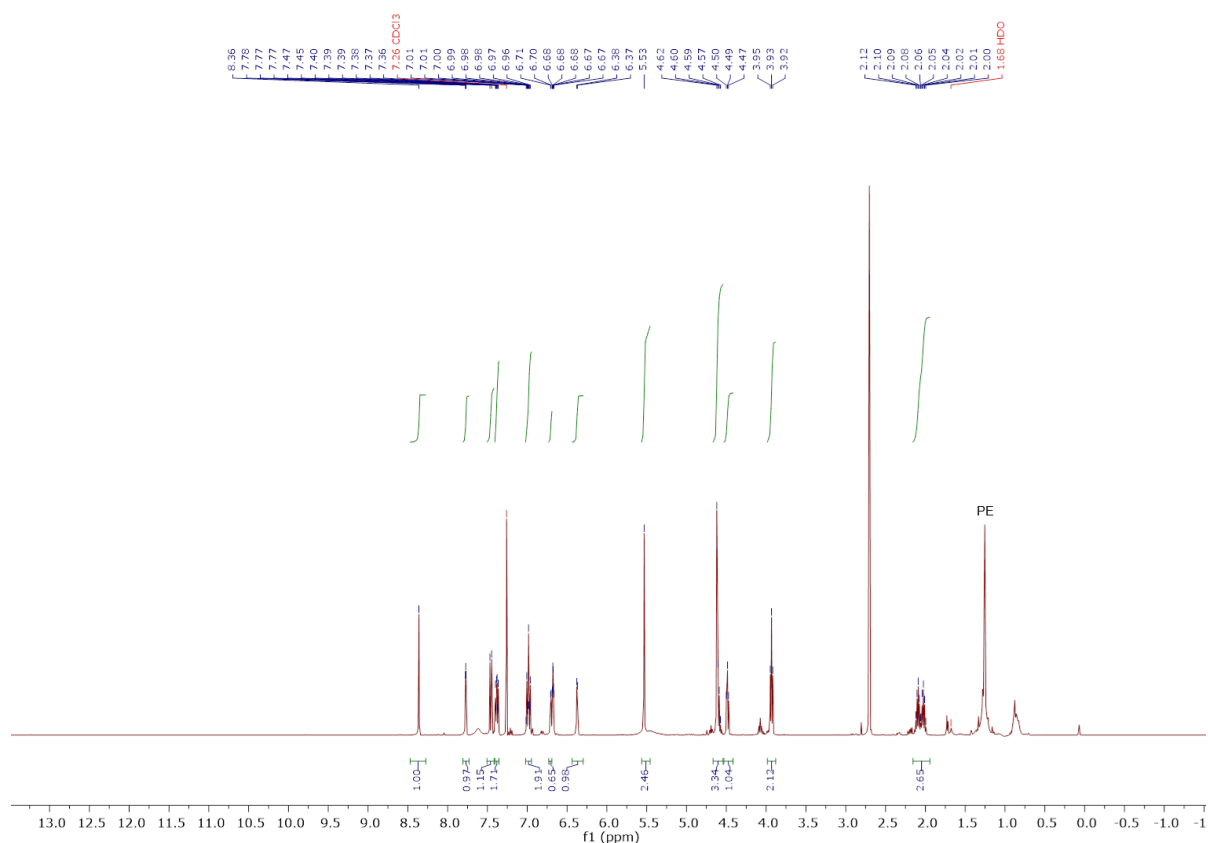


Figure S36: ¹H-NMR of PPY18.

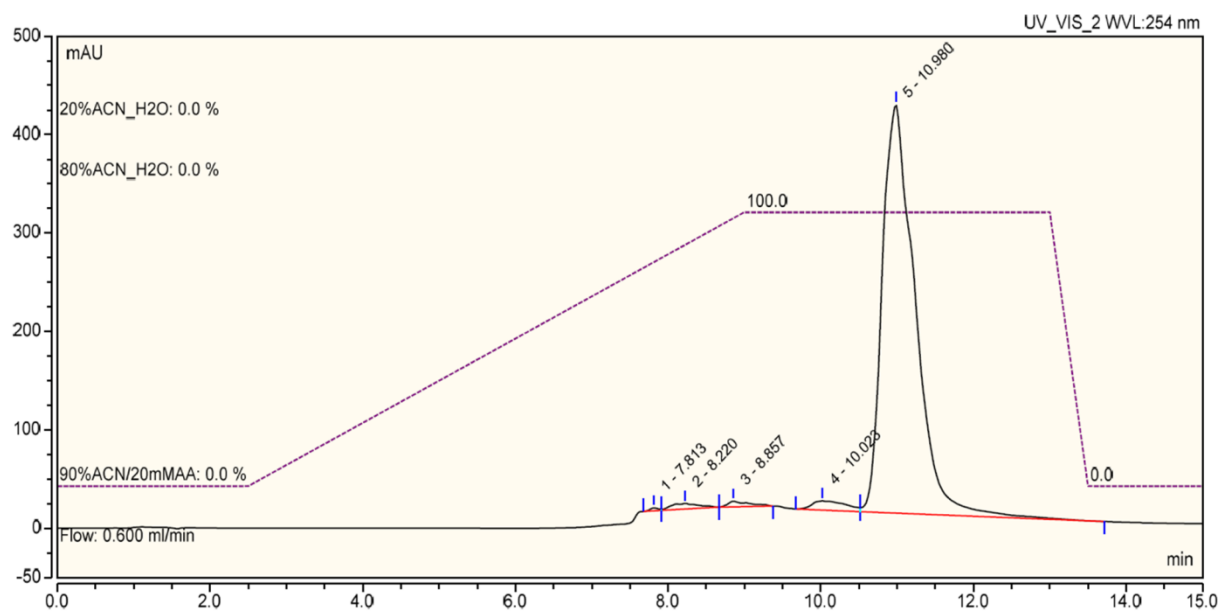


Figure S37: LC-MS chromatogram of PPY18.

1-(2-Fluorophenethyl)-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-amine (PPY19)

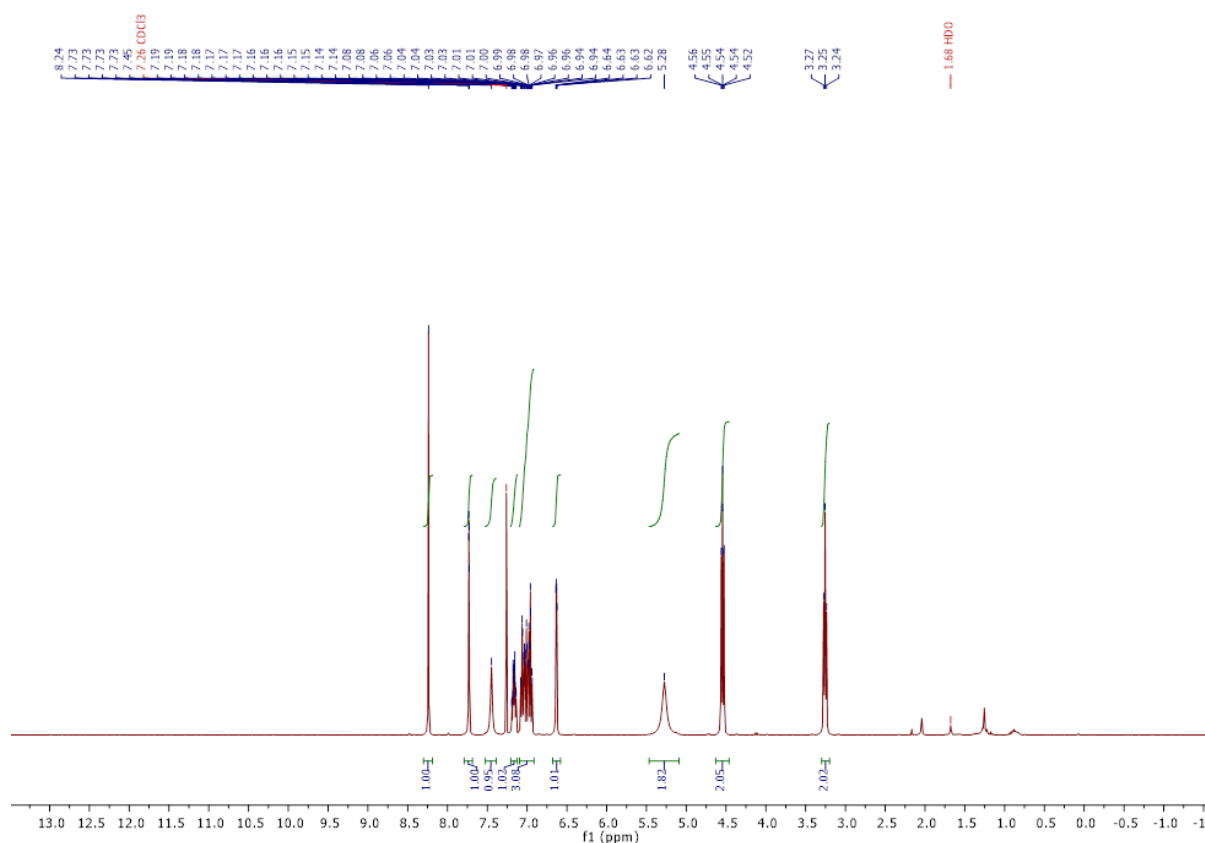


Figure S38: ¹H-NMR of PPY19.

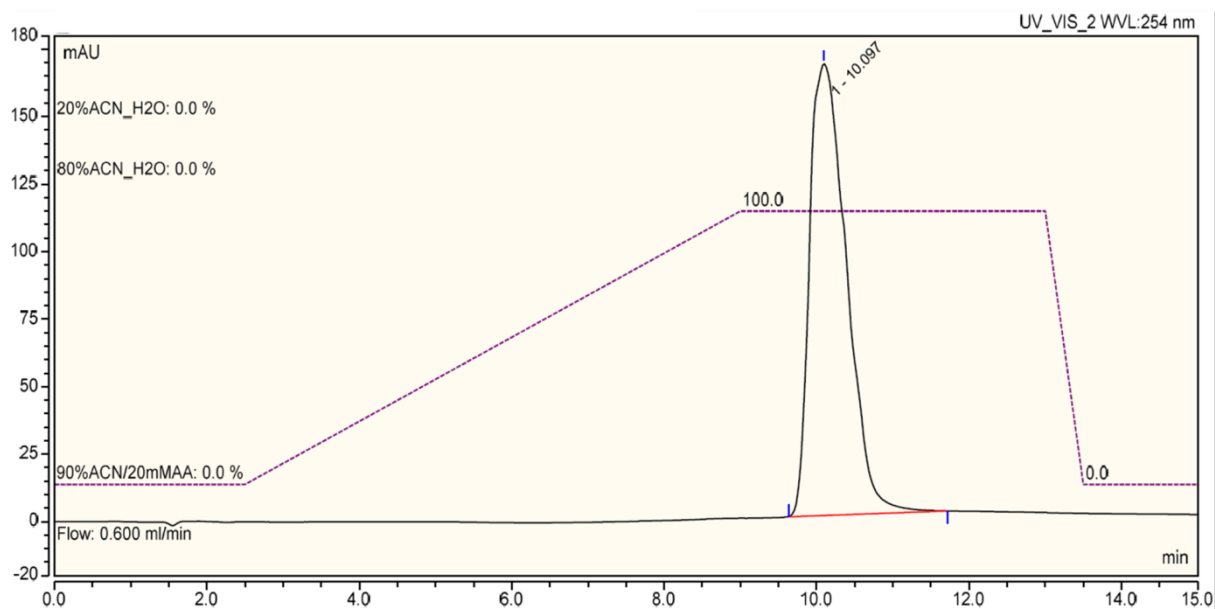


Figure S39: LC-MS chromatogram of PPY19.

(6-Amino-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)(2-fluorophenyl)-methanone (PPY20)

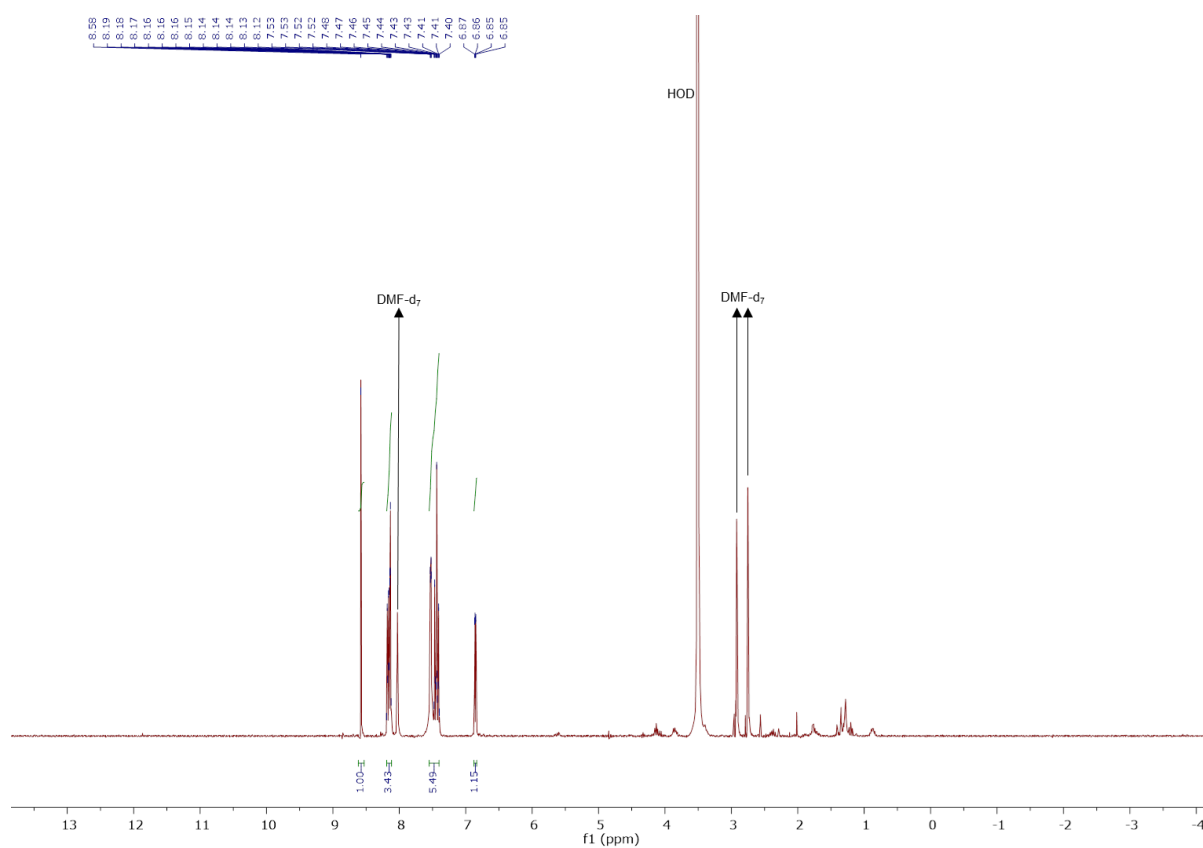


Figure S40: ¹H-NMR of PPY20.

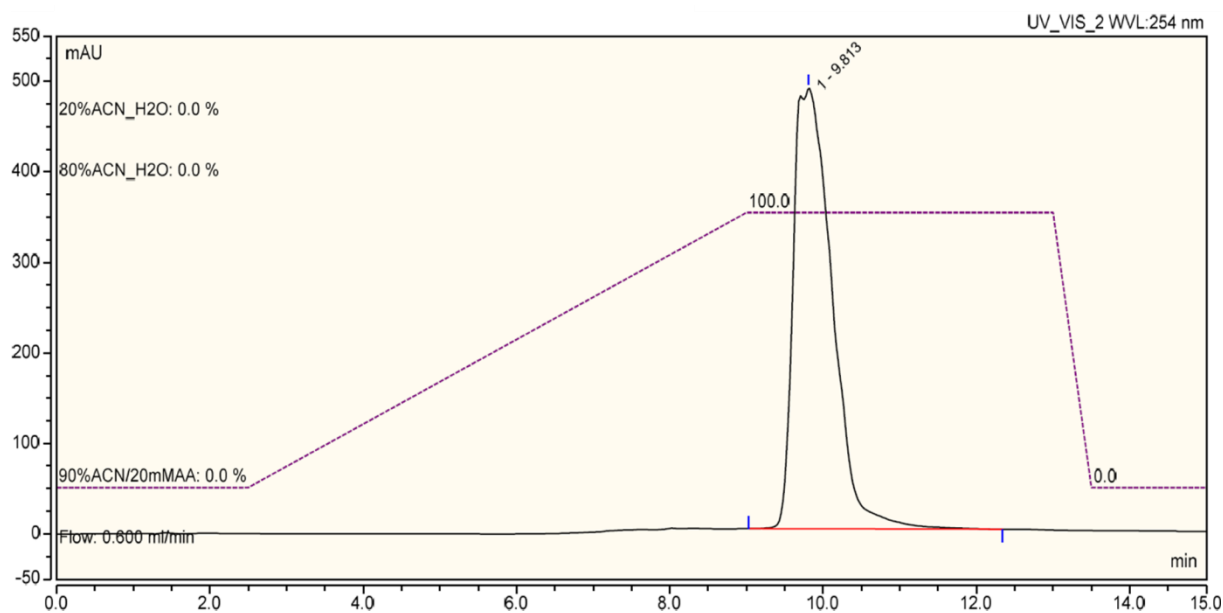


Figure S41: LC-MS chromatogram of PPY20.

(6-Amino-4-(furan-2-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)(2-fluorophenyl)-methanone (PPY21)

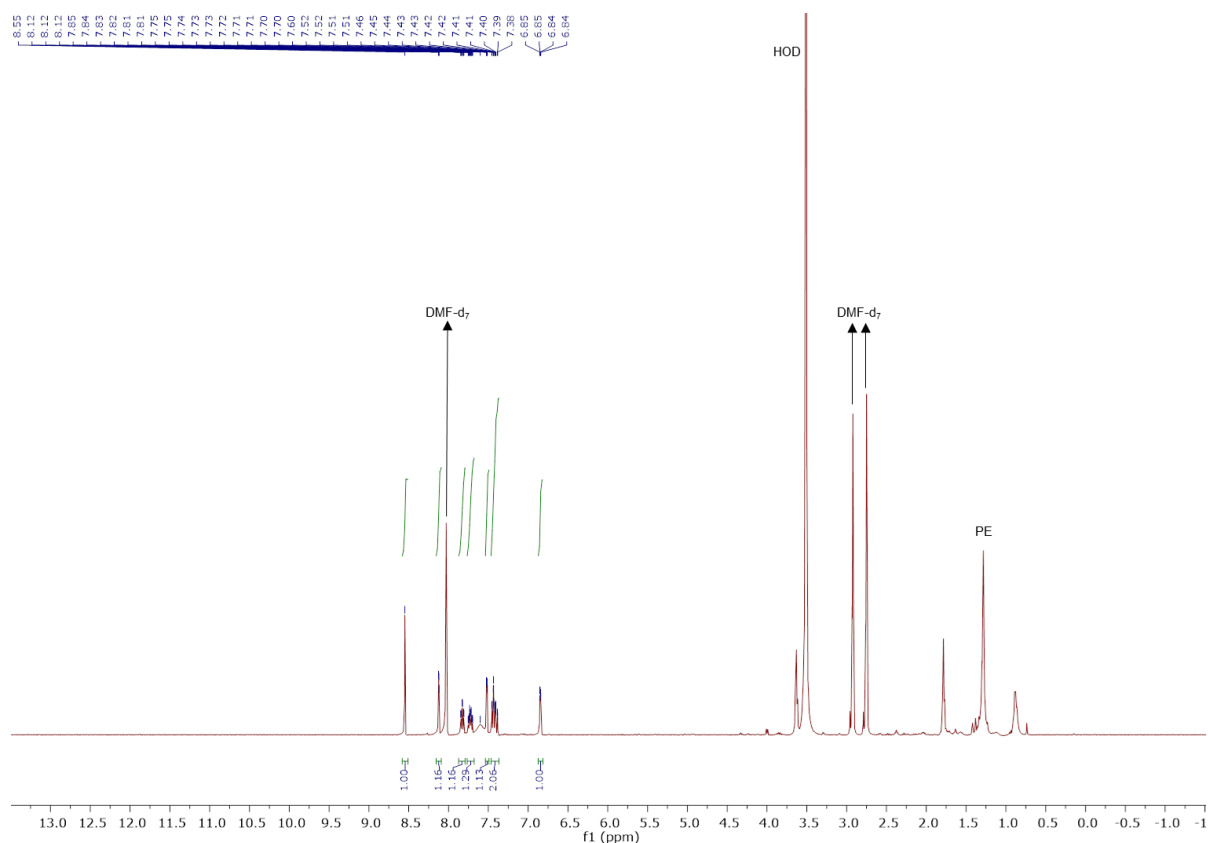


Figure S42: ¹H-NMR of PPY21.

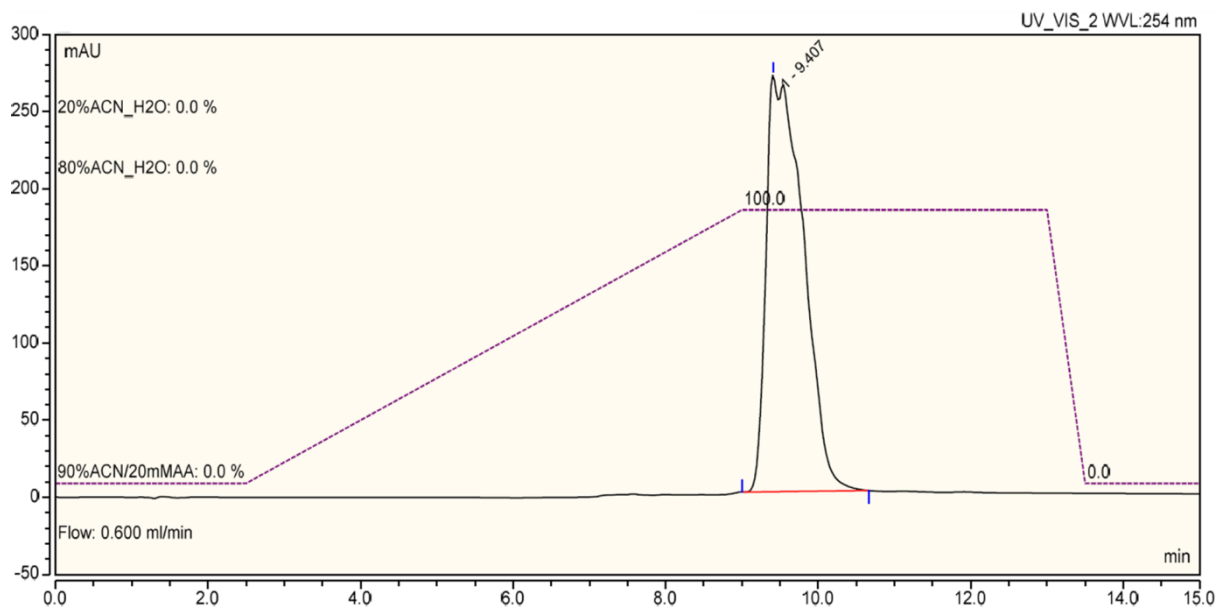


Figure S43: LC-MS chromatogram of PPY21.

1-Benzyl-4-(furan-2-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-amine (PPY22)

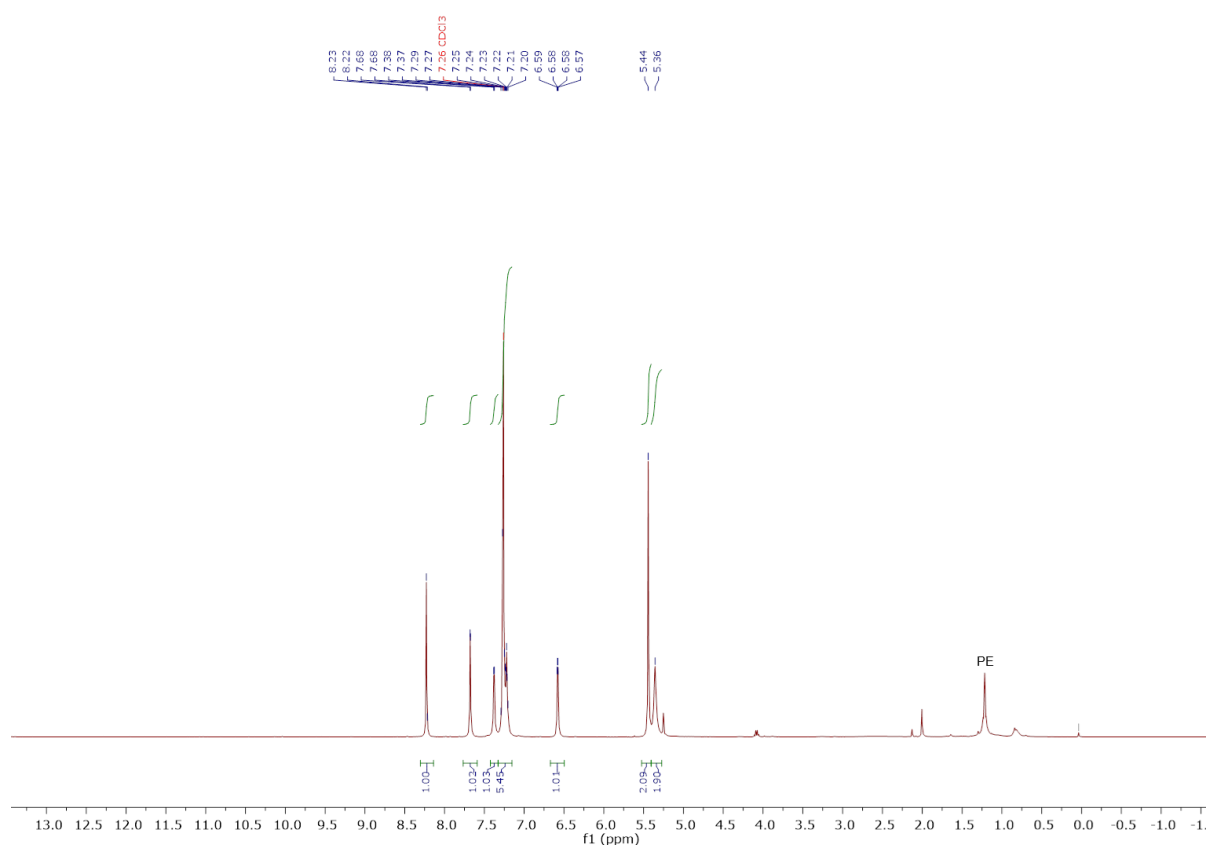


Figure S44: ¹H-NMR of PPY22.

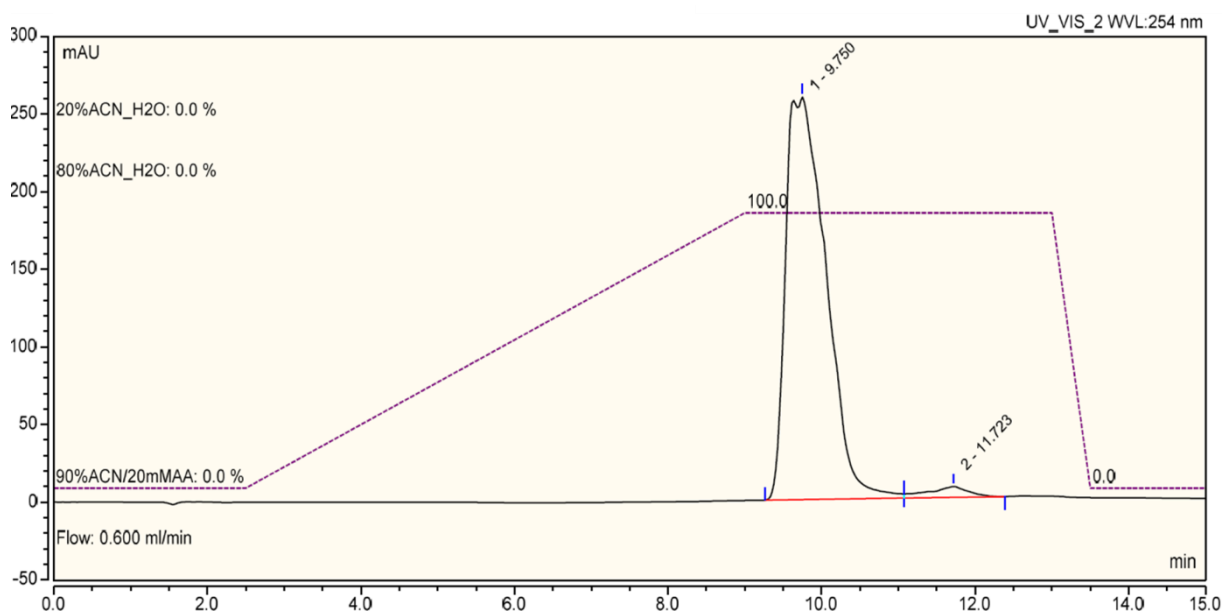


Figure S45: LC-MS chromatogram of PPY22.