

Scope and limitation of propylene carbonate as a sustainable solvent in Suzuki–Miyaura reaction

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Experimental section

General procedures

3,6-dichloropyridazine, 57% aq. HI, phenylboronic acid and 4-biphenylboronic acid were purchased from Alfa Aesar. 2-naphthaleneboronic acid and 4-fluorobenzeneboronic acid were purchased from Lancaster. 2-iodopyridine and 4-iodopyridine were purchased from TCI, while the propylene carbonate was purchased from Sigma-Aldrich and tetrakis-(triphenylphosphine)palladium (0) from FluoroChem.

Thin-layer chromatography (TLC) was performed on aluminium sheets precoated with Merck 5735 Kieselgel 60F254. Column chromatography was carried out either with Merck 5735 Kieselgel 60F (0.040-0.063 nm mesh). All other chemicals and solvents were purchased from different commercial sources and used as received without further purification.

Freeze-drying was performed one night in a LYPH-Lock 1L lyophilizer LabConco (Kansas City, Missouri) with high vacuum pump, at 10 mmHg and -50 °C. Melting points were measured on a Büchi M-550 apparatus (Büchi Labortechnik AG, Switzerland) and are not corrected.

Method A

Suzuki cross-coupling reaction of iodopyridine isomers (Figure 3 and Figure 5)

In a two necked round bottom flask, covered by tinfoil and under argon was measured 2-, or 4-iodopyridine (1.00 mmol, $d = 1.93 \text{ g/mL}$, 0.11 mL or 205 mg), the corresponding aromatic boronic acid: **5**, **6**, **7** or **8** (1.25 mmol), 0.5M Na_2CO_3 (1 mL), tetrakis(triphenylphosphine)palladium (0) (0.05 mmol, 58 mg) and propylene carbonate (5 mL). The reaction mixture was heated by oil-bath at max. 130 °C, refluxed for different time (**Table 1**) and monitored by TLC. After completion of the reaction, the suspension was cooled down and water (25 mL) was added. The aqueous layer was extracted with dichloromethane (2x25 mL), followed by neutralization with few drops of 5% H_2SO_4 and again extracted with dichloromethane (2x25 mL). The collected organic phase was washed with 10% CuSO_4 solution (2x15 mL) and evaporated, after drying over Na_2SO_4 and filtration. The crude product was lyophilized overnight at 10 mmHg and -50°C and weighted the mass of raw product. In all new reactions the product was purified by column chromatography and the pure products: **9**, **10**, **12**, **13**, **14**, **15**, **16** and **17** were characterized by ^1H -, ^{13}C -NMR-spectroscopy and determined the max. absorbance by HPLC-UV method. For the HPLC-MS-analysis we take off sample from the raw product after freeze-drying and from the purified one too.

Suzuki cross-coupling reaction of 6-iodopyridazin-3(2H)-one (Figure 4 and Figure 6)

In a two necked round bottom flask, under argon was measured 6-iodopyridazin-3(2H)-one (2.00 mmol, 444 mg), the corresponding aromatic boronic acid: **5**, **6**, **7** or **8** (2.50 mmol), 0.5M Na_2CO_3 (2 mL), tetrakis(triphenylphosphine)palladium (0) (0.10 mmol, 116 mg) and propylene carbonate (5 mL). The reaction mixture was heated by oil-bath at max. 130 °C, refluxed for different time (**Table 1**) and monitored by TLC. After completion of the reaction, the suspension was cooled down and water (50 mL) was added. The aqueous layer was extracted with chloroform (3x25 mL), followed by neutralization with few drops of 5% H_2SO_4 and again extracted with chloroform (3x25 mL). The collected organic phase was washed with 10% CuSO_4 solution (3x15 mL) and evaporated, after drying over Na_2SO_4 and filtration. The crude product was lyophilized overnight at 10 mmHg and -50°C and weighted

the mass of raw product. In the new reactions the products: **11a** and **11b**, **18a** and **18b**, **19a** and **19b**, **20a** and **20b** were separated by column chromatography (silica gel, 0.040–0.063 mesh size). The separated pure products were characterized by ^1H -, ^{13}C -NMR-spectroscopy and determined the max. absorbance by HPLC-UV method. For the HPLC-MS-analysis we take off sample from the raw product after freeze-drying and from the purified too.

Method B: Reactions under MW conditions

MW assisted experiments were carried out in a monomode CEM-Discover MW reactor, using the standard configuration as delivered, including proprietary software. The experiments were executed in 80 mL MW process vials, dynamic method with control of the temperature by infrared detection. Conditions: 5 min. ramp time, 130 °C temperature, 60 min. hold time, max. 200 Psi pressure and 300 W power. After completion of the reaction, the vial was cooled to 50 °C by air jet cooling, followed by usual work-up. In the Suzuki reaction of 2- and 4-iodopyridine the work-up is described in Method A, and in the case of 6-iodopyridazin-3(2*H*)-on was similar, but two products were prepared. Sample were taken of for NMR-spectroscopy, as well as for HPLC-MS-measurements.

NMR measurements

^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded at room temperature on Varian Mercury Plus spectrometer. Amounts of 10-15 mg of compounds were dissolved in 0.6 ml CDCl_3 or $\text{DMSO}-d_6$ and transferred to 5 mm NMR sample tubes. Chemical shifts are given on the δ -scale and referenced to the solvent (CDCl_3 : $\delta_{\text{C}}=77.00$ ppm and $\delta_{\text{H}}=7.27$ ppm or $\text{DMSO}-d_6$: $\delta_{\text{C}}=39.50$ ppm and $\delta_{\text{H}}=2.50$ ppm). For ^1H NMR measurement 24 K data points, 2.0 s acquisition time and 6400 Hz sweep width were used. ^{13}C spectra were recorded with 62 K data points and 24000 Hz sweep width. For 2D measurements, in case of the gHSQC spectrum the sweep width in F2 was 3000 Hz; data points ($t_2 \times t_1$) were acquired with 1 K x 128, in case of the gHMBC spectrum the sweep width in F2 was 3000 Hz; data points ($t_2 \times t_1$) were acquired with 1 K x 256, respectively.

HPLC-UV method for measuring max. absorbance of the compounds

The analysis was carried out with an Agilent LC MSD 1100 High Performance Liquid Chromatograph (Agilent Technologies Inc. Palo Alto, CA, USA) with HP Chemstation software Rev. A10.02 (Agilent, Waldbronn, Germany). The system consisted of a binary pump, on-line degasser, autosampler, column heater and diode array detector (DAD). An Agilent Zorbax Eclipse Plus C18, 3 mm×150 mm, 3.5 μm column (Agilent Technologies, Waldbronn, Germany) was used for the separation. Column temperature was 40°C. The concentration of the sample was 1 mg/mL and the solvent was acetonitrile. This concentrated solution was diluted with water to: 0.1 mg/mL. Sample injection volume was 10 μL , the flow rate was 1.0 mL min $^{-1}$ and the run time was 10 min. Gradient elution was applied, eluent A contained water with 0.05 % formic acid, eluent B contained acetonitrile with 0.05 % formic acid. The used gradient can be seen in **Table S1**. Detections were in 210–400 nm wavelength range and the maximum wavelength (λ_{max}) of the products was summarized in **Table S2**.

TEM measurements

Samples were dissolved in methanol and dried on Formvar coated 200 mesh copper grids and examined in a JEOL JEM 1011 transmission electron microscope operating at 80 kV. Images were taken with an Olympus Morada 11 megapixel camera and iTEM software (Olympus).

Table S1. Gradient elution in HPLC-UV method

Time (min.)	A(%)	B(%)
0.0	95.0	5.0
8.0	0.0	100.0

A. water with 0.05% formic acid, B. acetonitrile with 0.05% formic acid.

Table S2: Measured maximum absorbance by HPLC-UV method.

λ max. (nm)	2 (270, 218)	3 (262)	4 (228)
5 (228)	9 (308, 246)	10 (316, 274)	11a, 11b (254)
6 (268, 218)	12 (294, 242)	13 (288)	18a, 18b (250)
7 (260)	14 (300)	15 (322, 236)	19a, 19b (278)
8 (262, 214)	16 (294, 242)	17 (292)	20a, 20b (250)

HPLC-MS method for the characterization of products purity

The HPLC-MS system consists of a Shimadzu LC-20AD parallel pumps, with Shimadzu DG-20As Degasser, Shimadzu SIL-20A HT Autosampler, CTO-20A thermostat at 40 °C, and LCMS-2020 mass spectrometer, equipped with ESI ionisator (Drying gas 15L/min, Nebulizing gas 1.5 L/min; the DL temp is 250 °C, ESI 10 000 V). The HPLC column was a Supelco C-18 5 μ m, 50 x 4.6 mm. The eluent A was 0.1% TFA in water (from Merck); eluent B was 0.1% TFA in acetonitrile (from Merck). The gradient was set by a linear program, where eluent B was increased from 0% to 100%, within 10 min (**Table S3**). The flow rate was 1 ml/min. The obtained retention times measured on 254 nm are summarized in **Table S4**.

Table S3. Gradient elution in HPLC-MS method

Time (min.)	A(%)	B(%)
0.0	95.0	5.0
10.0	0.0	100.0

A. water with 0.1% TFA, B. acetonitrile with 0.1% TFA.

Table S4: Retention time measured on 254 nm.

Product rt (min.)	5	6	7	8
2	9 (6.8)	12 (5.3)	14 (7.4)	16 (5.6)
3	10 (6.9)	13 (5.7)	15 (7.5)	17 (5.9)

4	11a (7.8)	18a (6.6)	19a (8.4)	20a (6.8)
	11b (8.1)	18b (7.1)	19b (8.7)	20b (7.3)

The substrate **4** (**Figure 1**) was prepared according to literature procedures:

3,6-diiodopyridazine: A mixture of 6.00 g (40.27 mmol) 3,6-dichloropyridazine and 90 mL 57% (in water) HI (d = 1.7 g/mL, 51.3 mL, 681 mmol) was refluxed 5h at max. 120-130 °C (oil temperature). After cooling down, the reaction mixture was poured on ice, neutralized with 4M NaOH and filtered. The solid was washed with 2x50 mL water, 2x50 mL sat. solution of sodium thiosulfate. The crude product was recrystallized from 100 mL EtOAc¹. Yield: 9.40 g yellow solid (70%), Mp: 164.1-166.3 °C², HPLC (254 nm): 100%, rt = 6.8 min., C₄H₂I₂N₂: 331.88, m/z = 333, ¹H NMR (400 MHz, CDCl₃) δ 7.50 (s, 2H, CH), ¹³C NMR (100 MHz, CDCl₃) δ 137.9, 124.7.

6-iodopyridazine-3(2H)-one (**4**): A mixture of 9.36 g (28.19 mmol) 3,6-diiodopyridazine and 58 mL 8% (in water) NaOH (4.60 g, 115 mmol) was refluxed 2h at max. 110-120 °C (oil temperature). After cooling down, the reaction mixture was poured on ice, neutralized with 50% AcOH and filtered. The solid was washed with 2x30 mL water and the crude product was recrystallized from 70 mL EtOAc. Yield: 4.90 g white solid (78%), Mp: 170.5-172.3 °C³, HPLC (254 nm): 100%, rt = 2.0 min., C₄H₃IN₂O: 221.98, m/z = ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.31 (brs, 1H, NH), 7.62 (d, *J*=9.7 Hz, 1H, OCCH), 6.65 (d, *J*=9.7 Hz, 1H, ICCH), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 159.6, 142.1, 131.3, 102.1.

2-(naphthalen-2-yl)pyridine (**9**):

Reagents refluxed 5h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with net dichloromethane as eluent. Yield: 188 mg yellow solid (92%), Mp: 68.7-70.5 °C^{4, 5}, HPLC (254 nm): 100%, rt = 6.8 min., C₁₅H₁₁N: 205.25, m/z = 206, ¹H NMR (400 MHz, CDCl₃) δ 8.76 (d, *J*= 4.3 Hz, 1H, NCH), 8.49 (s, 1H, CCHC), 8.14 (dd, *J*=8.6, 1.7 Hz, 1H, pyr-CCHCHC), 8.00-7.92 (m, 2H, CCHCCHCH), 7.92-7.84 (m, 2H, NCCH, CCHCHCCH), 7.80 (td, *J*=7.6, 1.7 Hz, 1H, NCCHCH), 7.55-7.48 (m, 2H, pyr-CCHCHC, CCHCHCCHCH), 7.27 (m, 1H, NCHCH), ¹³C NMR (100 MHz, CDCl₃) δ 157.3, 149.8, 136.8, 136.6, 133.6, 133.5, 128.7, 128.4, 127.6, 126.5, 126.3, 126.3, 124.5, 122.2, 120.8.

Repetition of Method A: 210 mg crude product, HPLC (254 nm): 86.53%, estimated yield: 182 mg (89%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with net dichloromethane as eluent. Yield: 190 mg yellow solid (93%), HPLC (254 nm): 100%, rt = 6.8 min., C₁₅H₁₁N: 205.25, m/z = 206.

Repetition of Method B: 220 mg crude product, HPLC (254 nm): 82.26%, estimated yield: 181 mg (88%).

4-(naphthalen-2-yl)pyridine (**10**):

Reagents refluxed 3h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 5:1, respectively 1:1. Yield: 174 mg yellow solid (85%), Mp: 103.8-105.6 °C⁶⁻⁸, HPLC (254 nm): 100%, rt = 6.9 min.,

C₁₅H₁₁N: 205.25, m/z = 206, ¹H NMR (400 MHz, CDCl₃) δ 8.72 (brs, 2H, NCH), 8.12 (s, 1H, CCHC), 8.01-7.54 (m, 3H, CCHCHCCH, CCHCCH,), 7.75 (dd, *J*=8.5, 1.7 Hz, 1H, CCHCHC), 7.72-7.60 (m, 2H, NCHCH), 7.60-7.51 (m, 2H, CCHCCHCHCH), ¹³C NMR (100 MHz, CDCl₃) δ 149.8, 148.6, 135.2, 133.4, 133.4, 129.0, 128.4, 127.7, 126.9, 126.7, 126.5, 124.5, 122.0.

Repetition of Method A: 200 mg crude product, HPLC (254 nm): 83.79%, estimated yield: 168 mg (82%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 5:1, respectively 1:1. Yield: 175 mg yellow solid (85%), HPLC (254 nm): 100%, rt = 6.9 min., C₁₅H₁₁N: 205.25, m/z = 206.

Repetition of Method B: 200 mg crude product, HPLC (254 nm): 88.02%, estimated yield: 176 mg (86%).

6-(naphthalen-2-yl)pyridazin-3(2*H*)-one (**11a**) and 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2*H*)-one (**11b**):

Reagents refluxed 4h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net chloroform, followed by chloroform : ethyl acetate 10:1, respectively 5:1.

Product **11a**: 85 mg white solid (19%), Mp: 249.7-252.1 °C^{9, 10}, HPLC (254 nm): 100%, rt = 7.8 min., C₁₄H₁₀N₂O: 222.24, m/z = 223, ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.29 (brs, 1H, NH), 8.45 (s, 1H, pyr-CCHC), 8.23 (d, *J*=9.9 Hz, 1H, NCCCH), 8.09-7.89 (m, 4H, pyr-CCHCHCCH, pyr-CCHCCH), 7.60-7.54 (m, 2H, pyr-CCHCCHCHCH), 7.06 (d, *J*=9.9 Hz, 1H, NHCOCH), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 160.3, 143.6, 133.0, 132.9, 132.0, 131.5, 130.2, 128.6, 128.5, 127.6, 127.0, 126.7, 125.2, 123.0.

Product **11b**: 110 mg light yellow solid (20%), Mp: 116.5-118.1 °C, HPLC (254 nm): 96.68%, rt = 8.1 min., C₁₇H₁₆N₂O₂: 280.32, m/z = 281, ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.46 (s, 1H, pyr-CCHC), 8.22 (d, *J*=9.7 Hz, 1H, NCOCHCH), 8.07 (dd, *J*=8.6, 1.6 Hz, 1H, pyr-CCHCH), 8.05-7.99 (m, 3H, pyr-CCHCHCCH, pyr-CCHCCH), 7.61-7.53 (m, 2H, pyr-CCHCCHCHCH), 7.10 (d, *J*=9.7 Hz, 1H, NCOCH), 4.90 (d, *J*=4.9 Hz, 1H, OH), 4.27-4.12 (m, 2H, NCH₂CH), 4.11-3.97 (m, 1H, NCH₂CH), 1.15 (d, *J*=5.6 Hz, 3H, CH₃), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 159.3, 143.0, 133.1, 132.9, 131.9, 130.5, 129.7, 128.6, 128.5, 127.6, 127.0, 126.8, 125.3, 123.2, 64.1, 58.3, 21.1.

Repetition of Method A: Product **11a**: 95 mg white solid (21%), Mp: 246.5-250.0 °C^{9, 10}, HPLC (254 nm): 97.11%, rt = 7.8 min., C₁₄H₁₀N₂O: 222.24, m/z = 223. Product **11b**: 117 mg light yellow solid (19%), Mp: 121.7-128.9 °C, HPLC (254 nm): 82.14%, rt = 8.1 min., C₁₇H₁₆N₂O₂: 280.32, m/z = 281.

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net chloroform, followed by chloroform : ethyl acetate 10:1, respectively 5:1. Product **11a**: 158 mg white solid (36%), HPLC (254 nm): 94.58%, rt = 7.8 min., C₁₄H₁₀N₂O: 222.24, m/z = 223. Product **11b**: 292 mg light yellow solid (52%), HPLC (254 nm): 96.65%, rt = 8.1 min., C₁₇H₁₆N₂O₂: 280.32, m/z = 281.

Repetition of Method B: 500 mg crude product, HPLC (254 nm): 42.58% **11a** and 55.67% **11b**, estimated yield: 215 mg (48%) **11a** and 280 mg (50%) **11b**.

2-phenylpyridine (12):

Reagents refluxed 7h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net chloroform, followed by chloroform : ethyl acetate 10:1, respectively 5:1. Yield: 200 mg yellow solid (65%), Mp: 75.1–76.8 °C^{11–13}, HPLC (254 nm): 89.97%, rt = 5.2 min., C₁₁H₉N: 155.20, m/z = 156, ¹H NMR (400 MHz, CDCl₃) δ 8.71 (d, *J*=4.3 Hz, 1H, NCH), 8.00 (d, *J*=7.3 Hz, 2H, orto-phenyl H), 7.81–7.68 (m, 2H, NCCCH), 7.53–7.37 (m, 3H, meta-, para-phenyl H), 7.31–7.20 (m, 1H, NCHCH), ¹³C NMR (100 MHz, CDCl₃) δ 157.5, 149.7, 139.4, 136.7, 128.9, 128.7, 126.9, 122.1, 120.6.

Repetition of Method A: 150 mg crude product, HPLC (254 nm): 66.16%, estimated yield: 99 mg (64%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with net chloroform, followed by chloroform : ethyl acetate 10:1, respectively 5:1. Yield: 100 mg yellow solid (65%), HPLC (254 nm): 97.53%, rt = 5.3 min., C₁₁H₉N: 155.20, m/z = 156.

Repetition of Method B: 120 mg crude product, HPLC (254 nm): 86.45%, estimated yield: 104 mg (67%).

4-phenylpyridine (13):

Reagents refluxed 3h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net chloroform, followed by chloroform : ethyl acetate 10:1, respectively 5:1. Yield: 73 mg yellow solid (47%), Mp: 68.3–69.4 °C^{14–16}, HPLC (254 nm): 100%, rt = 5.5 min., C₁₁H₉N: 155.20, m/z = 156, ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J*=4.4 Hz, 2H, NCH), 7.66 (d, *J*=7.4 Hz, 2H, orto-phenyl H), 7.56–7.41 (m, 5H, NCHCH, meta-, para-phenyl H), ¹³C NMR (100 MHz, CDCl₃) δ 150.2, 148.4, 138.1, 129.1, 129.1, 127.0, 121.7.

Repetition of Method A: 200 mg crude product, HPLC (254 nm): 36.77%, estimated yield: 73 mg (47%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net chloroform, followed by chloroform : ethyl acetate 10:1, respectively 5:1. Yield: 115 mg yellow solid (74%), HPLC (254 nm): 97.60%, rt = 5.8 min., C₁₁H₉N: 155.20, m/z = 156.

Repetition of Method B: 250 mg crude product, HPLC (254 nm): 42.58%, estimated yield: 106 mg (69%).

2-(biphenyl-4-yl)pyridine (14):

Reagents refluxed 3h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with dichloromethane as eluent. Yield: 220 mg yellow solid (95%), Mp: 136.3–138.4 °C^{17, 18}, HPLC (254 nm): 100%, rt = 7.4 min., C₁₇H₁₃N: 231.29, m/z = 232, ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.69 (d, *J*=4.3 Hz, 1H, NCH), 8.20 (d, *J*=8.3 Hz, 2H, NCCCH), 8.03 (d, *J*=8.0 Hz, 1H, NCCCH), 7.90 (tm, *J*=8.0 Hz, 1H, NCCCHCH), 7.81 (d, *J*=8.3 Hz, 2H, NCCCHCH), 7.75 (d, *J*=7.4 Hz, 2H, orto-phenyl H), 7.50 (t, *J*=7.4 Hz, 2H, meta-phenyl H), 7.44–7.33 (m, 2H, NCHCH, para-phenyl H), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 155.5, 149.6, 140.6, 139.5, 137.7, 137.3, 129.0, 127.7, 127.1, 127.0, 126.7, 122.7, 120.2.

Repetition of Method A: 255 mg crude product, HPLC (254 nm): 80.59%, estimated yield: 205 mg (89%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with dichloromethane as eluent. Yield: 225 mg yellow solid (97%) HPLC (254 nm): 100%, *rt* = 7.4 min., C₁₇H₁₃N: 231.29, *m/z* = 232.

Repetition of Method B: 270 mg crude product, HPLC (254 nm): 78.96%, estimated yield: 213 mg (92%).

4-(biphenyl-4-yl)pyridine (15):

Reagents refluxed 2h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Yield: 212 mg light yellow solid (92%), *Mp*: 201.7–203.9 °C^{19, 20}, HPLC (236 nm): 92.41%, *rt* = 7.5 min., C₁₇H₁₃N: 231.29, *m/z* = 232, ¹H NMR (400 MHz, CDCl₃) δ 8.78 (brs, 2H, NCH), 7.78–7.70 (m, 4H, pyr-CCHCHC), 7.70–7.54 (m, 4H, NCHCH, orto-phenyl H), 7.48 (t, *J*=7.4 Hz, 2H, meta-phenyl H), 7.43–7.36 (m, 1H, para-phenyl H), ¹³C NMR (100 MHz, CDCl₃) δ 149.8, 148.0, 142.2, 142.1, 141.6, 140.2, 136.7, 134.2, 128.9, 128.7, 127.8, 127.8, 127.4, 127.2, 127.1, 126.4, 121.9.

Repetition of Method A: 350 mg crude product, HPLC (254 nm): 57.51%, estimated yield: 201 mg (87%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Yield: 210 mg yellow solid (91%), HPLC (236 nm): 92.41%, *rt* = 7.5 min., C₁₇H₁₃N: 231.29, *m/z* = 232.

Repetition of Method B: 350 mg crude product, HPLC (254 nm): 55.17%, estimated yield: 194 mg (84%).

2-(4-fluorophenyl)pyridine (16):

Reagents refluxed 3h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Yield: 74 mg yellow oil (43%)^{21–23}, HPLC (254 nm): 100%, *rt* = 5.6 min., C₁₁H₈FN: 173.19, *m/z* = 174, ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J*=4.1 Hz, 1H, NCH), 8.06–7.91 (m, 2H, FCCHCH), 7.76 (tm, *J*=7.7 Hz, 1H, NCCHCH), 7.69 (d, *J*=7.7 Hz, 1H, NCCH), 7.24 (m, 1H, NCHCH), 7.21–7.08 (m, 2H, FCCH), ¹³C NMR (100 MHz, CDCl₃) δ 163.5 (d, *J*=248.6 Hz), 156.4, 149.7, 136.8, 135.5 (d, *J*=3.1 Hz), 128.7 (d, *J*=8.3 Hz), 122.1, 120.3, 115.7 (d, *J*=21.7 Hz).

Repetition of Method A: 120 mg crude product, HPLC (254 nm): 84.08%, estimated yield: 101 mg (58%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Yield: 86 mg yellow oil (50%), HPLC (254 nm): 100%, *rt* = 5.6 min., C₁₁H₈FN: 173.19, *m/z* = 174.

Repetition of Method B: 120 mg crude product, HPLC (254 nm): 91.23%, estimated yield: 109 mg (63%).

4-(4-fluorophenyl)pyridine (17):

Reagents refluxed 1h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Yield: 123 mg yellow oil (71%)²⁴⁻²⁶, HPLC (254 nm): 100%, *rt* = 5.9 min., $C_{11}H_8FN$: 173.19, *m/z* = 174, 1H NMR (400 MHz, $CDCl_3$) δ 8.86 (brs, 2H, *NCH*), 7.74-7.39 (m, 4H, *NCHCH*, *FCCHCH*), 7.24-7.10 (m, 2H, *FCCH*), ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (d, *J*=249.3 Hz), 150.0, 147.1, 134.3 (d, *J*=3.1 Hz), 132.1, 128.7 (d, *J*=8.3 Hz), 116.2 (d, *J*=21.9 Hz). Repetition of Method A: 150 mg crude product, HPLC (254 nm): 90.54%, estimated yield: 136 mg (79%).

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Yield: 138 mg yellow oil (80%), HPLC (254 nm): 100%, *rt* = 5.9 min., $C_{11}H_8FN$: 173.19, *m/z* = 174.

Repetition of Method B: 150 mg crude product, HPLC (254 nm): 97.20%, estimated yield: 146 mg (84%).

6-phenylpyridazin-3(2*H*)-one (18a) and 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2*H*)-one (18b):

Reagents refluxed 6h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 5:1, respectively 1:1.

Product **18a**: 160 mg light yellow solid (47%), *Mp*: 195.5-197.8 °C^{9, 27, 28}, HPLC (254 nm): 96.73%, *rt* = 6.6 min., $C_{10}H_8N_2O$: 172.18, *m/z* = 173, 1H NMR (400 MHz, $CDCl_3$) δ 11.84 (brs, 1H, *NH*), 7.84-7.74 (m, 3H, *NCCCH*, *orto*-phenyl H), 7.54-7.39 (m, 3H, *meta*-, *para*-phenyl H), 7.09 (d, *J*=9.9 Hz, 1H, *COCH*), ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 145.6, 134.4, 131.7, 130.4, 129.6, 129.0, 125.9.

Product **18b**: 240 mg yellow solid (52%), *Mp*: 95.7-97.1 °C^{29, 30}, HPLC (254 nm): 100%, *rt* = 7.1 min., $C_{13}H_{14}N_2O_2$: 230.26, *m/z* = 231, 1H NMR (400 MHz, $CDCl_3$) δ 7.81-7.74 (m, 2H, *orto*-phenyl H), 7.73 (d, *J*=9.7 Hz, 1H, *NCCCH*), 7.53-7.41 (m, 3H, *meta*-, *para*-phenyl H), 7.08 (d, *J*=9.7 Hz, 1H, *COCH*), 4.43-4.25 (m, 3H, *OH*, *NCH₂CH*), 3.67-3.58 (m, 1H, *NCH₂CH*), 1.32 (d, *J*=6.0 Hz, 3H, *CH₃*), ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 145.2, 134.4, 130.6, 130.3, 129.7, 129.1, 126.0, 67.6, 59.8, 21.0.

Repetition of Method A: 400 mg crude product, HPLC (254 nm): 34.52% **18a** and 65.48% **18b**, estimated yield: 138 mg (40%) **18a** and 262 mg (57%) **18b**.

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 5:1, respectively 1:1. Product **18a**: 155 mg light yellow solid (45%), HPLC (254 nm): 97.92%, *rt* = 5.8 min., $C_{10}H_8N_2O$: 172.18, *m/z* = 173. Product **18b**: 207 mg yellow solid (45%), HPLC (254 nm): 96.59%, *rt* = 6.4 min., $C_{13}H_{14}N_2O_2$: 230.26, *m/z* = 231.

Repetition of Method B: 400 mg crude product, HPLC (254 nm): 44.18% **18a** and 55.05% **18b**, estimated yield: 177 mg (51%) **18a** and 220 mg (48%) **18b**.

6-(biphenyl-4-yl)pyridazin-3(2*H*)-one (**19a**) and 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)-pyridazin-3(2*H*)-one (**19b**):

Reagents refluxed 3h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Product **19a**: 160 mg light yellow solid (32%), Mp: 234.1–236.2 °C³¹, HPLC (254 nm): 100%, rt = 8.4 min., C₁₆H₁₂N₂O: 248.28, m/z = 249, ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.24 (brs, 1H, NH), 8.10 (d, *J*=9.9 Hz, 1H, NCCCH), 7.96 (d, *J*=8.5 Hz, 2H, NCCCHCH), 7.79 (d, *J*=8.5 Hz, 2H, NCCCH), 7.73 (d, *J*=7.4 Hz, 2H, orto-phenyl H), 7.49 (t, *J*=7.4 Hz, 2H, meta-phenyl H), 7.39 (t, *J*=7.4 Hz, 1H, para-phenyl H), 7.01 (d, *J*=9.9 Hz, 1H, COCH), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 160.2, 143.4, 140.7, 139.2, 133.6, 131.4, 130.2, 129.0, 127.8, 127.1, 126.7, 126.2.

Product **19b**: 355 mg white solid (58%), Mp: 130.8–132.7 °C, HPLC (254 nm): 100%, rt = 8.7 min., C₁₉H₁₈N₂O₂: 306.36, m/z = 307, ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.09 (d, *J*=9.7 Hz, 1H, NCCCH), 7.99 (d, *J*=8.5 Hz, 2H, NCCCHCH), 7.80 (d, *J*=8.5 Hz, 2H, NCCCH), 7.74 (d, *J*=7.3 Hz, 2H, orto-phenyl H), 7.50 (t, *J*=7.3 Hz, 2H, meta-phenyl H), 7.40 (t, *J*=7.3 Hz, 1H, para-phenyl H), 7.06 (d, *J*=9.7 Hz, 1H, COCH), 4.89 (d, *J*=4.9 Hz, 1H, OH), 4.23–4.09 (m, 2H, NCH₂CH), 4.06–3.95 (m, 1H, NCH₂CH), 1.13 (d, *J*=5.8 Hz, 3H, CH₃), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 159.3, 142.8, 140.8, 139.3, 133.5, 130.4, 129.6, 129.1, 127.9, 127.1, 126.7, 126.4, 64.1, 58.3, 21.0.

Repetition of Method A: 680 mg crude product, HPLC (254 nm): 15.61% **19a** and 68.45% **19b**, estimated yield: 106 mg (21%) **19a** and 465 mg (76%) **19b**.

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 10:1, 5:1, respectively 1:1. Product **19a**: 130 mg light yellow solid (26%), HPLC (254 nm): 84.24%, rt = 8.4 min., C₁₈H₁₂N₂O: 248.28, m/z = 249. Product **19b**: 302 mg white solid (49%), HPLC (254 nm): 95.63%, rt = 8.7 min., C₁₉H₁₈N₂O₂: 306.36, m/z = 307.

Repetition of Method B: 600 mg crude product, HPLC (254 nm): 24.34% **19a** and 52.18% **19b**, estimated yield: 146 mg (29%) **19a** and 313 mg (51%) **19b**.

6-(4-fluorophenyl)pyridazin-3(2*H*)-one (**20a**) and 6-(4-fluorophenyl)-2-(2-hydroxypropyl)pyridazin-3(2*H*)-one (**20b**):

Reagents refluxed 3h according to Method A. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net chloroform, followed by chloroform : ethyl acetate 10:1, 5:1, respectively 1:1.

Product **20a**: 126 mg white solid (33%), Mp: 266.7–268.9 °C^{32–34}, HPLC (254 nm): 100%, rt = 6.8 min., C₁₀H₇FN₂O: 190.17, m/z = 191, ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.21 (brs, 1H, NH), 8.04 (d, *J*=9.9 Hz, 1H, NCCCH), 7.97–7.84 (m, 2H, FCCHCH), 7.39–7.23 (m, 2H, FCCH), 7.00 (d, *J*=9.9 Hz, 1H, COCH), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.8 (d, *J*=246.7 Hz), 160.2, 143.0, 131.4, 131.2 (d, *J*=3.0 Hz), 130.2, 127.9 (d, *J*=8.6 Hz), 115.8 (d, *J*=21.8 Hz).

Product **20b**: 280 mg yellow solid (56%), Mp: 136.3–138.8 °C, HPLC (254 nm): 96.19%, rt = 7.3 min., C₁₃H₁₃FN₂O₂: 248.25, m/z = 249, ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.03 (d, *J*=9.7 Hz, 1H, COCHCH), 7.98–7.88 (m, 2H, FCCHCH), 7.39–7.27 (m, 2H, FCCH), 7.04 (d, *J*=9.7 Hz, 1H, COCH), 4.86 (d, *J*=4.5 Hz, 1H, OH), 4.19–4.06 (m, 2H, NCH₂CH), 4.04–3.92 (m, 1H, NCH₂CH), 1.11 (d, *J*=5.7 Hz, 3H, CH₃), ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.8 (d,

$J=246.0$ Hz), 159.1, 142.3, 131.1 (d, $J=2.9$ Hz), 130.4, 129.7, 128.1 (d, $J=8.6$ Hz), 115.8 (d, $J=21.8$ Hz), 64.0, 58.2, 21.0.

Repetition of Method A: 430 mg crude product, HPLC (254 nm): 37.70% **20a** and 62.30% **20b**, estimated yield: 162 mg (43%) **20a** and 268 mg (54%) **20b**.

Reagents refluxed 1h according to Method B. Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net chloroform, followed by chloroform : ethyl acetate 10:1, 5:1, respectively 1:1. Product **20a**: 168 mg white solid (44%), HPLC (254 nm): 100%, $rt = 6.8$ min., $C_{10}H_7FN_2O$: 190.17, $m/z = 191$. Product **20b**: 250 mg yellow solid (50%), HPLC (254 nm): 94.44%, $rt = 7.3$ min., $C_{13}H_{13}FN_2O_2$: 248.25, $m/z = 249$.

Repetition of Method B: 420 mg crude product, HPLC (254 nm): 39.73% **20a** and 60.27% **20b**, estimated yield: 167 mg (44%) **20a** and 253 mg (51%) **20b**.

2-(2-hydroxypropyl)-6-iodopyridazin-3(2H)-one (**23**) obtained without and with catalyst:

In an 80 mL vial was measured 6-iodopyridazin-3(2H)-one (0.80 mmol, 178 mg), 0.5M Na_2CO_3 (1.6 mL) and propylene carbonate (4 mL). In another experiment, to the before mentioned reagents was added tetrakis(triphenylphosphine)palladium (0) (0.04 mmol, 46 mg). The suspensions were reacted separated according to Method B. After 1h reaction time, the suspensions were cooled down and water (25 mL) was added. The aqueous layer was extracted with chloroform (3x10 mL), followed by neutralization with few drops of 5% H_2SO_4 and again extracted with chloroform (2x10 mL). The collected organic phase was washed with 10% $CuSO_4$ solution (2x10 mL) and evaporated, after drying over Na_2SO_4 and filtration. The crude product was lyophilized overnight at 10 mmHg and $-50^\circ C$ and weighted the mass of raw product.

Without catalyst: 180 mg yellow solid (80%), Mp: 119.1-122.0 $^\circ C$, HPLC (254 nm): 91.26%, $rt = 5.7$ min., $C_7H_9IN_2O_2$: 280.06, $m/z = 281$.

Crude product purified by column chromatography (silica gel, 0.040–0.063 mesh size) with gradient elution: net dichloromethane, followed by dichloromethane : ethyl acetate 5:1, respectively 1:1.

With catalyst: 175 mg yellow solid (78%), Mp: 120.2-122.0 $^\circ C$, HPLC (254 nm): 95.23%, $rt = 5.7$ min., $C_7H_9IN_2O_2$: 280.06, $m/z = 281$.

1H NMR (400 MHz, $CDCl_3-d_6$) δ 7.42 (d, $J=9.6$ Hz, 1H, ICCH), 6.67 (d, $J=9.6$ Hz, 1H, OCCH), 4.31-4.09 (m 3H, CH_2CHOH), 1.27 (d, $J=9.6$ Hz, 3H, $CHCH_3$) ^{13}C NMR (100 MHz, $CDCl_3-d_6$) δ 160.3, 141.6, 131.0, 99.4, 67.3, 59.6, 21.0.

2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2H)-one (**11b**) from 6-(naphthalen-2-yl)pyridazin-3(2H)-one (**11a**):

In an 80 mL vial was measured 6-naphthalen-2-yl)pyridazin-3(2H)-one (**11a**, 0.50 mmol, 111 mg), 0.5M Na_2CO_3 (1.00 mL) and propylene carbonate (2.5 mL). The reaction mixture was reacted according to Method B. After 1h reaction time, the suspension was cooled down and water (20 mL) was added. The aqueous layer was extracted with chloroform (2x10 mL), followed by neutralization with few drops of 5% H_2SO_4 and again extracted with chloroform (2x10 mL). The collected organic phase was washed with 10% $CuSO_4$ solution (2x10 mL) and evaporated, after drying over Na_2SO_4 and filtration. The crude product was lyophilized overnight at 10 mmHg and $-50^\circ C$ and weighted the mass of raw product: 94 mg yellow solid (67%), Mp: 116.5-118.2 $^\circ C$, HPLC (254 nm): 95.83%, $rt = 8.1$ min., $C_{17}H_{16}N_2O_2$: 280.32, m/z

= 281, ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.46 (s, 1H, pyr-CCHC), 8.22 (d, $J=9.7$ Hz, 1H, NCOCHCH), 8.07 (dd, $J=8.6, 1.6$ Hz, 1H, pyr-CCHCH), 8.05-7.99 (m, 3H, pyr-CCHCHCCH, pyr-CCHCCH), 7.61-7.53 (m, 2H, pyr-CCHCCHCHCH), 7.10 (d, $J=9.7$ Hz, 1H, NCOCH), 4.90 (d, $J=4.9$ Hz, 1H, OH), 4.27-4.12 (m, 2H, NCH_2CH), 4.11-3.97 (m, 1H, NCH_2CH), 1.15 (d, $J=5.6$ Hz, 3H, CH_3), ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 159.3, 143.0, 133.1, 132.9, 131.9, 130.5, 129.7, 128.6, 128.5, 127.6, 127.0, 126.8, 125.3, 123.2, 64.1, 58.3, 21.1.

Fig. S1: UV spectrum of 2-iodopyridine (2)

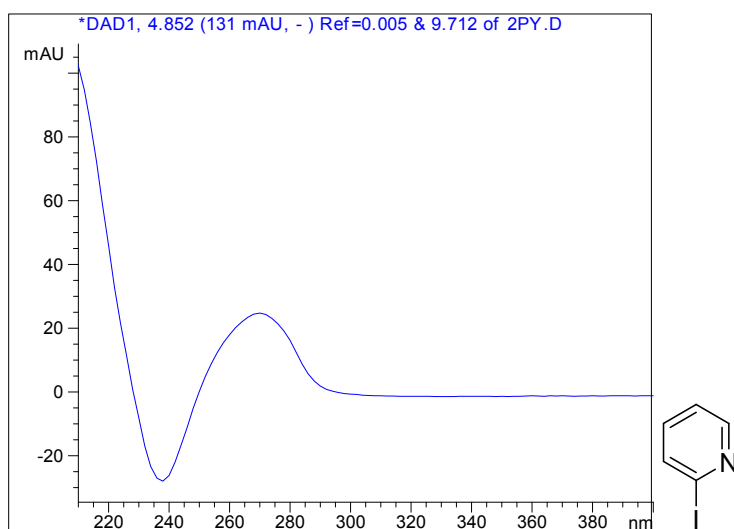


Fig. S2: UV spectrum of 4-iodopyridine (3)

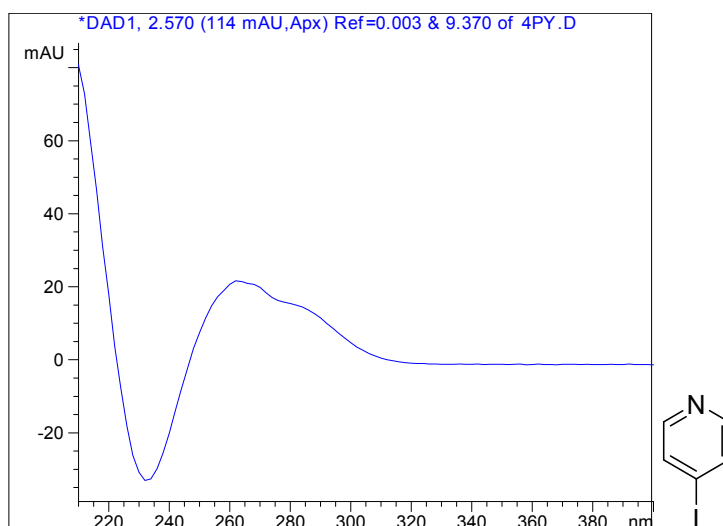


Fig. S3: UV spectrum of 6-iodopyridazin-3(2H)-one (4)

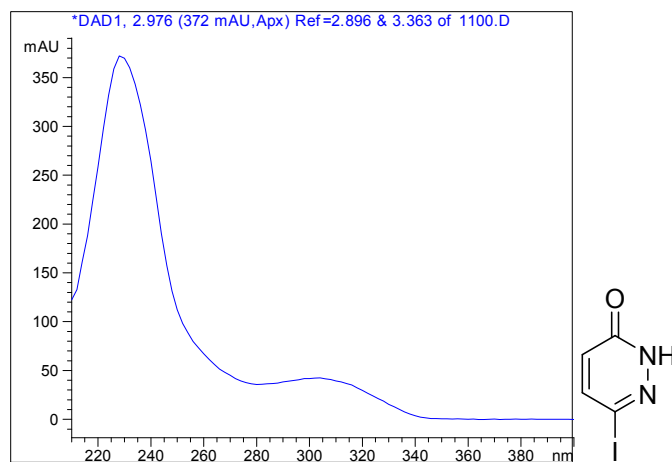


Fig. S4: UV spectrum of 2-naphthaleneboronic acid (5)

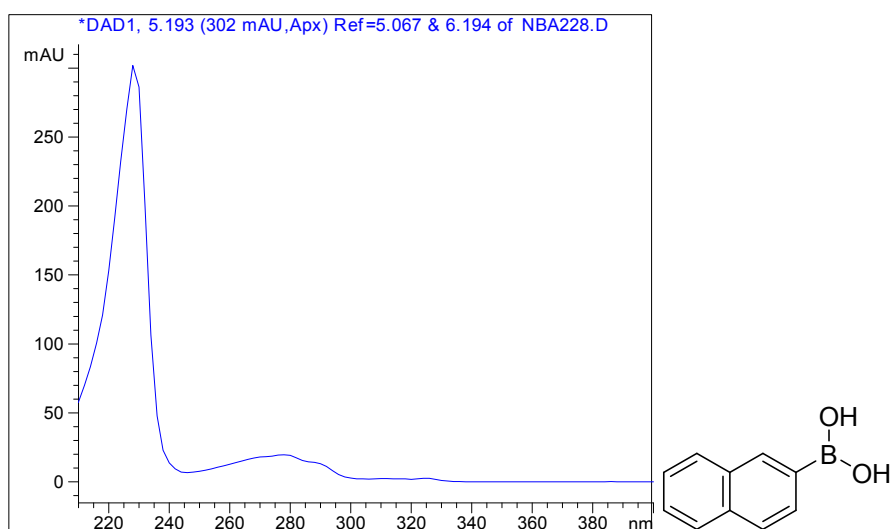


Fig. S5: UV spectrum of phenylboronic acid (6)

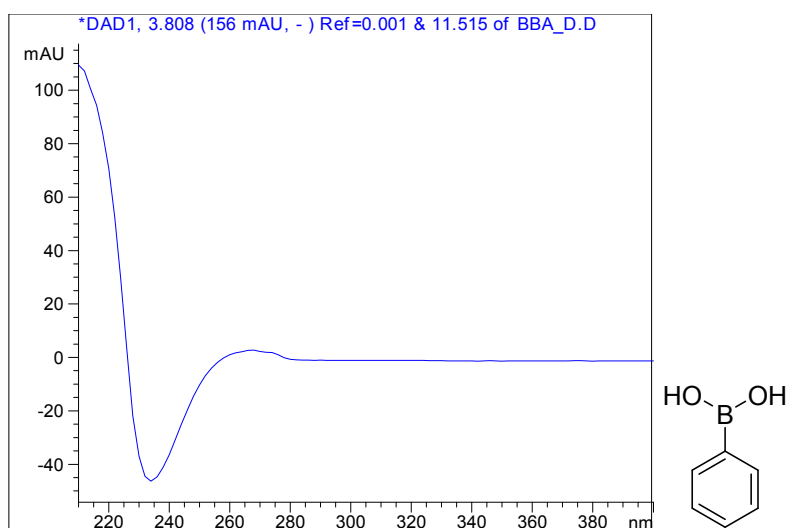


Fig. S6: UV spectrum of 4-biphenylboronic acid (7)

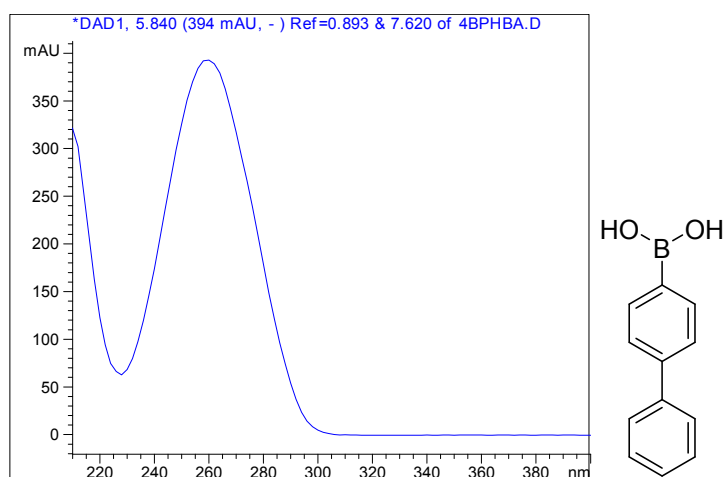


Fig. S7: UV spectrum of 4-fluorophenylboronic acid (8)

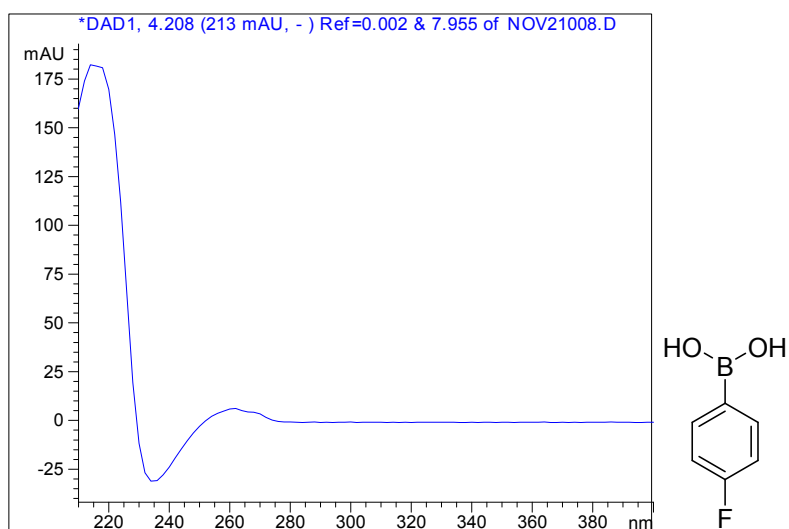


Fig. S8: UV spectrum of 2-(naphthalen-2-yl)pyridine (9)

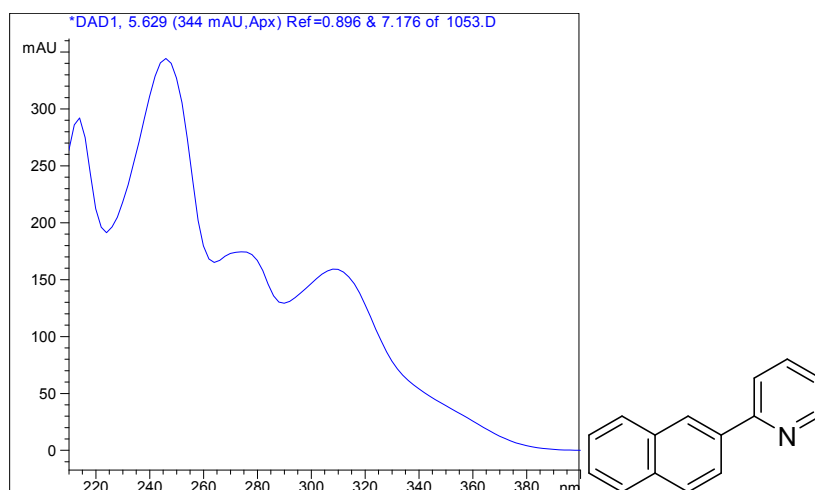


Fig. S9: UV spectrum of 4-(naphthalen-2-yl)pyridine (10)

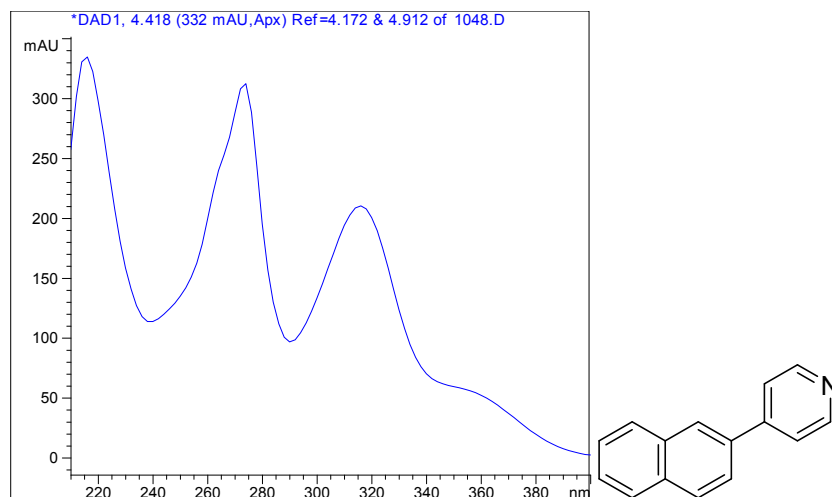


Fig. S10: UV spectrum of 6-(naphthalen-2-yl)pyridazin-3(2H)-one (11a)

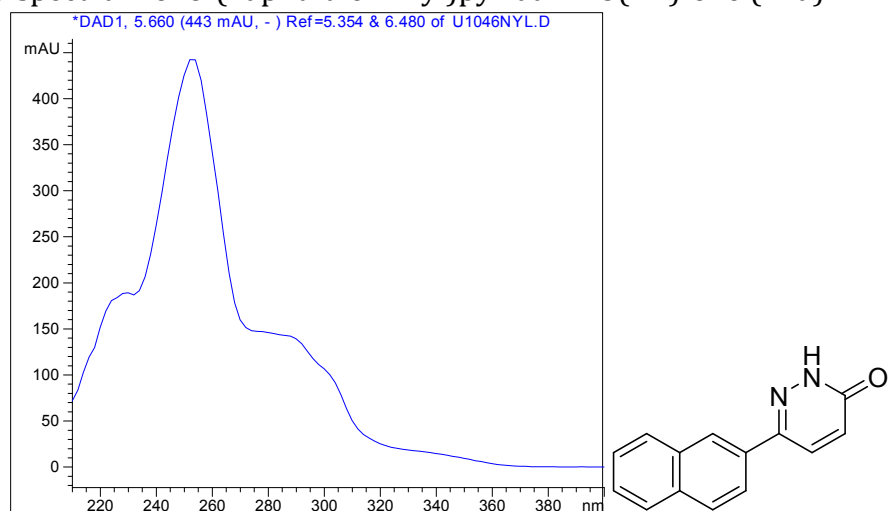


Fig. S11: UV spectrum of 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2H)-one (11b)

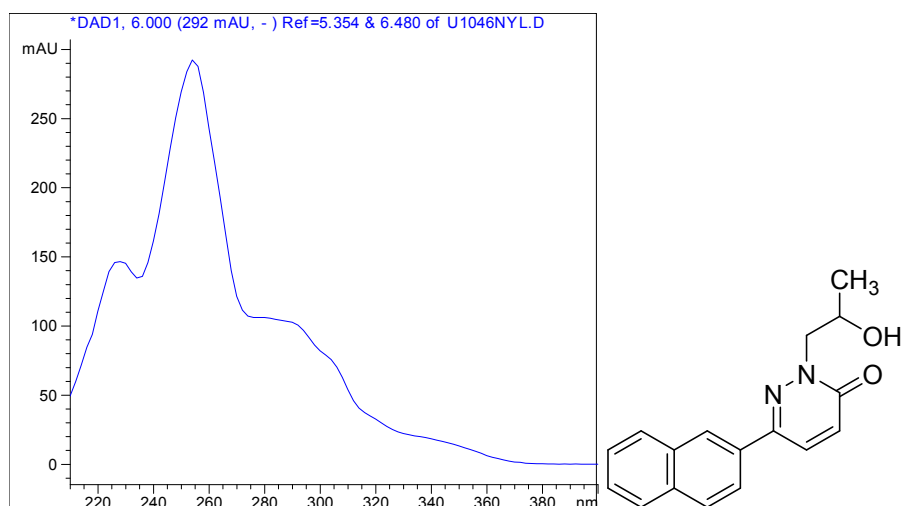


Fig. S12: UV spectrum of 2-phenylpyridine (12)

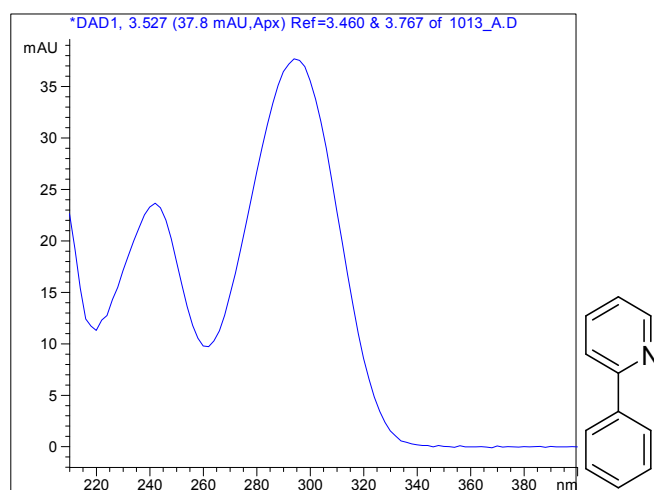


Fig. S13: UV spectrum of 4-phenylpyridine (13)

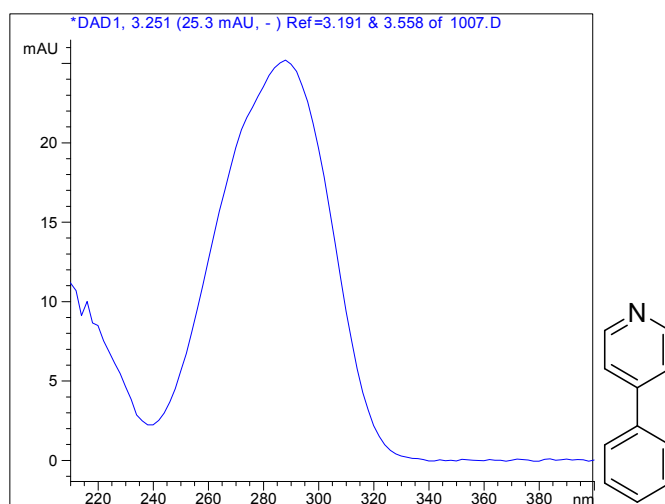


Fig. S14: UV spectrum of 2-(biphenyl-4-yl)pyridine (14)

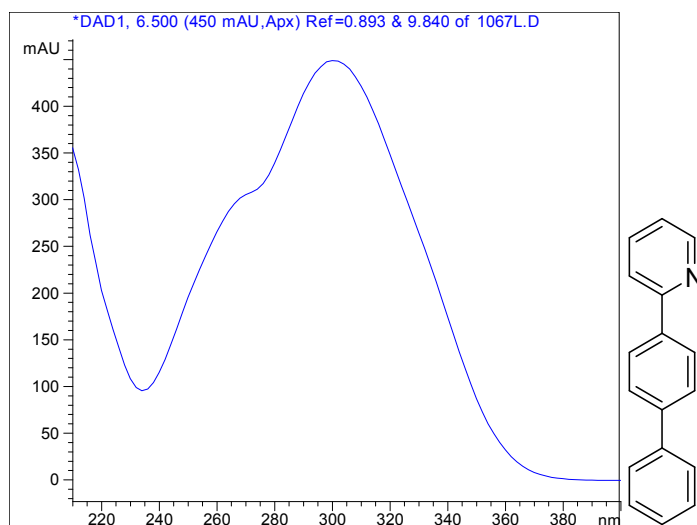


Fig. S15: UV spectrum of 4-(biphenyl-4-yl)pyridine (15)

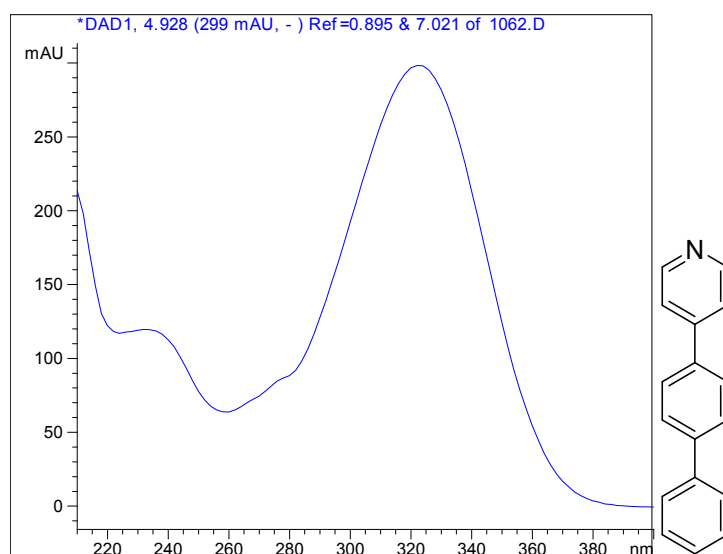


Fig. S16: UV spectrum of 2-(4-fluorophenyl)pyridine (16)

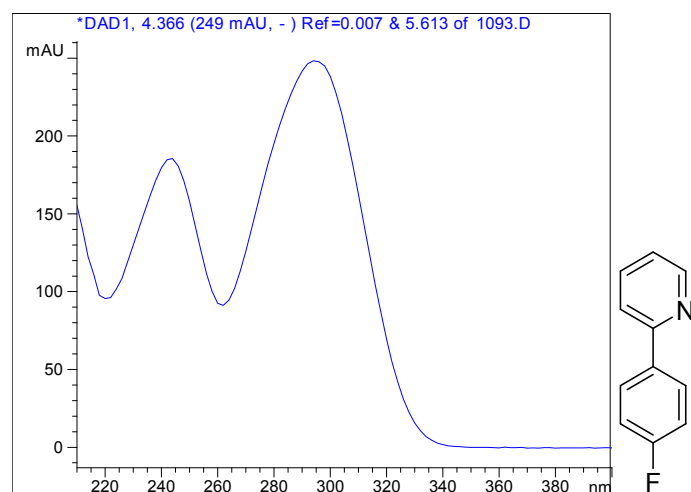


Fig. S17: UV spectrum of 4-(4-fluorophenyl)pyridine (17)

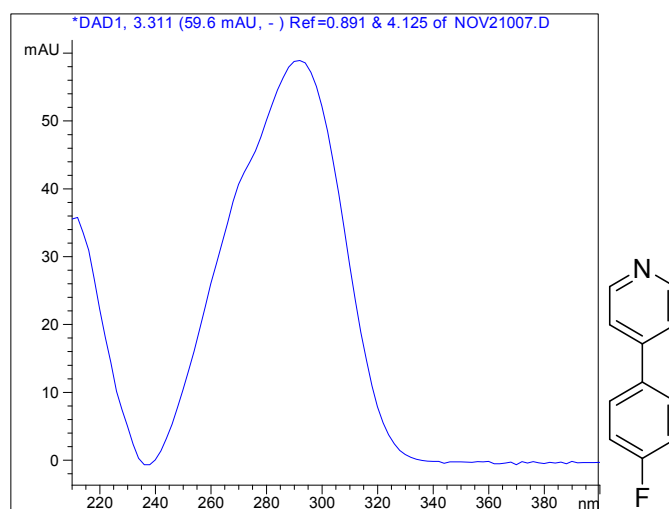


Fig. S18: UV spectrum of 6-phenylpyridazin-3(2H)-one (18a)

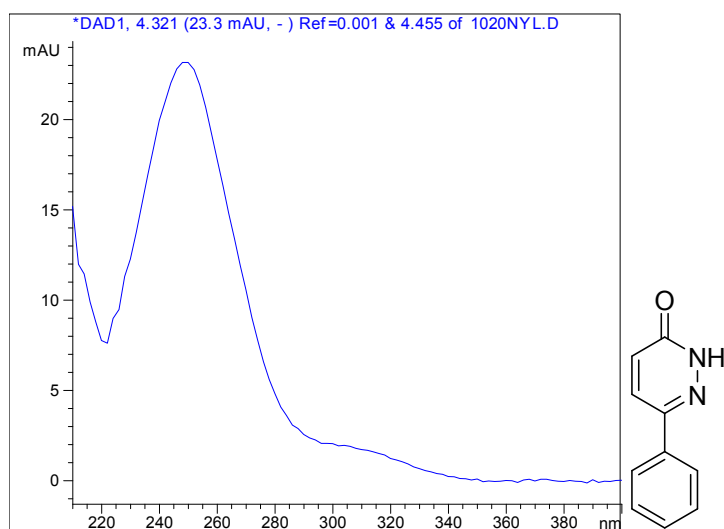


Fig. S19: UV spectrum of 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2H)-one (18b)

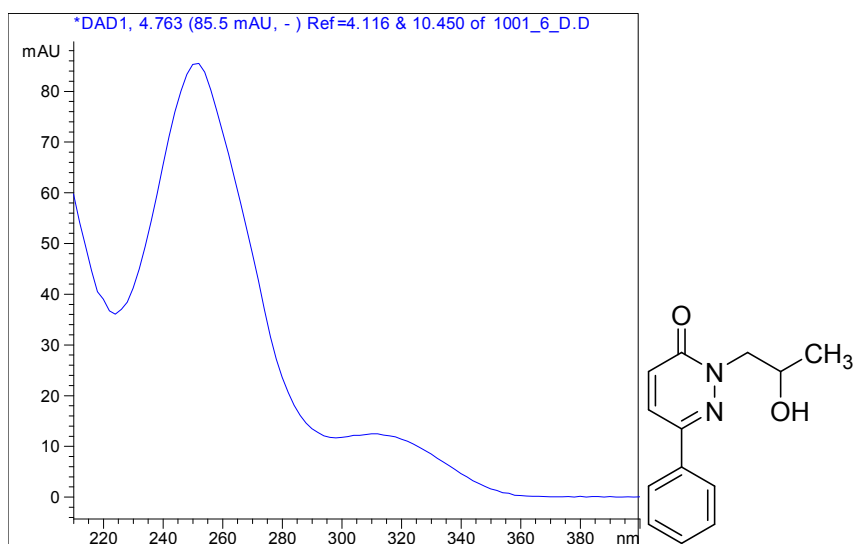


Fig. S20: UV spectrum of 6-(biphenyl-4-yl)pyridazin-3(2H)-one (19a)

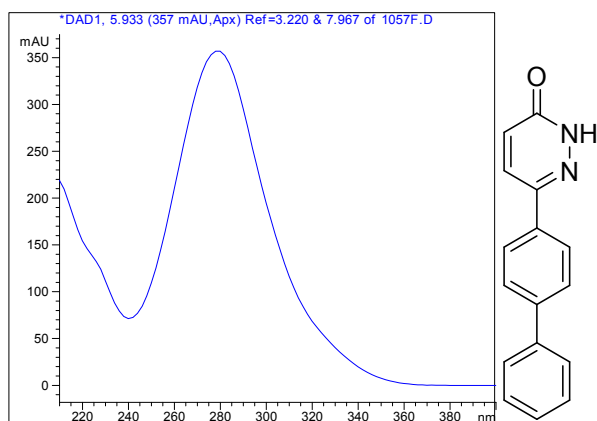


Fig. S21: UV spectrum of 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)-pyridazin-3(2H)-one (19b)

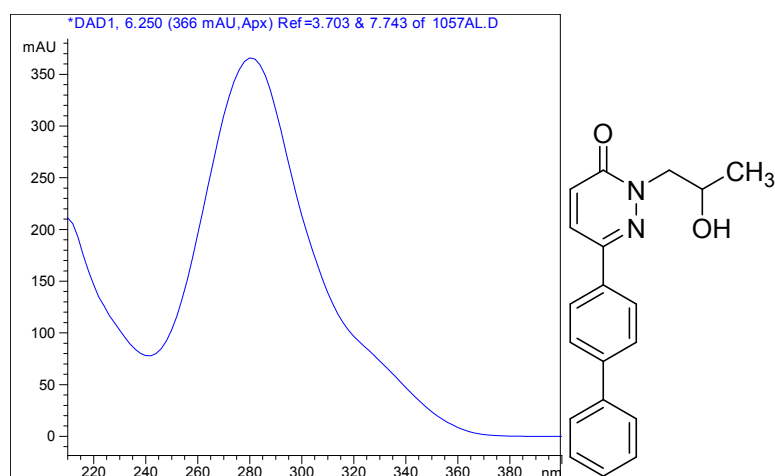


Fig. S22: UV spectrum of 6-(4-fluorophenyl)pyridazin-3(2H)-one (20a)

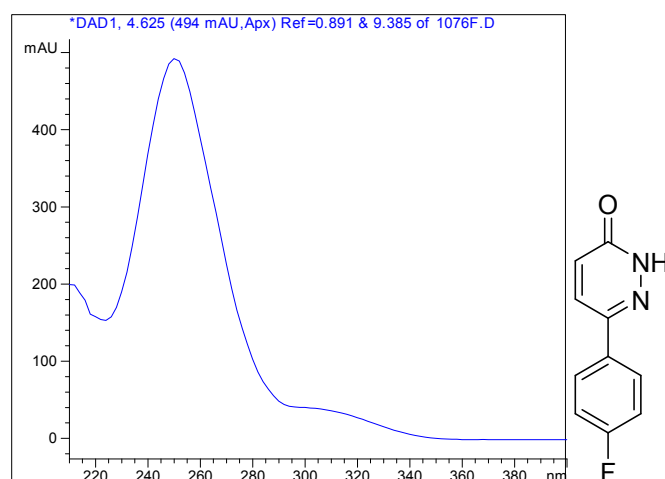


Fig. S23: 6-(4-fluorophenyl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one (20b)

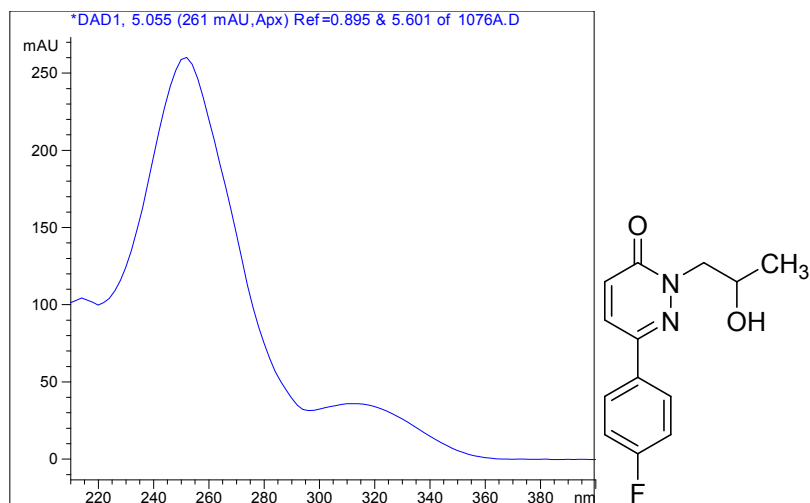


Fig. S24: 2-(2-hydroxypropyl)-6-iodopyridazin-3(2H)-one (23)

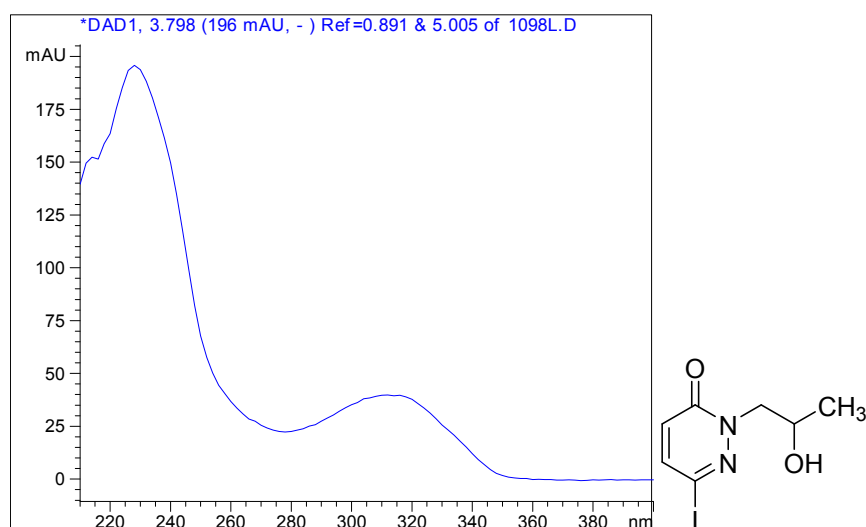


Fig. S25. HPLC-MS data for 3,6-diiodopyridazine:

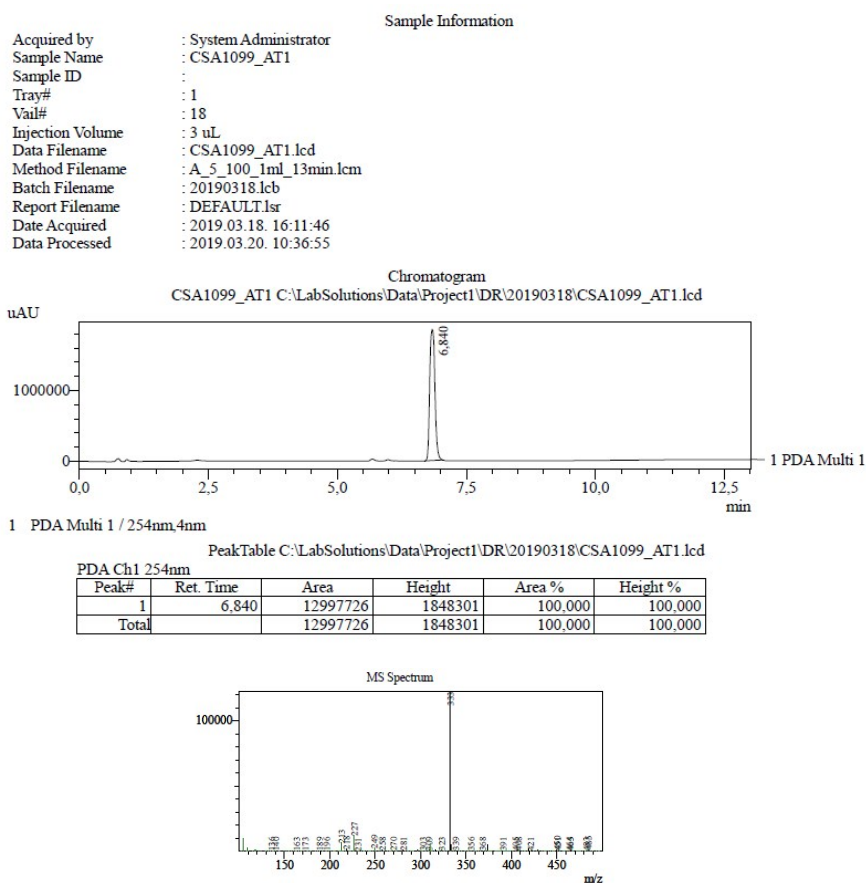


Fig. S26. HPLC-MS data for 6-iodopyridazine-3(2H)-one (4):

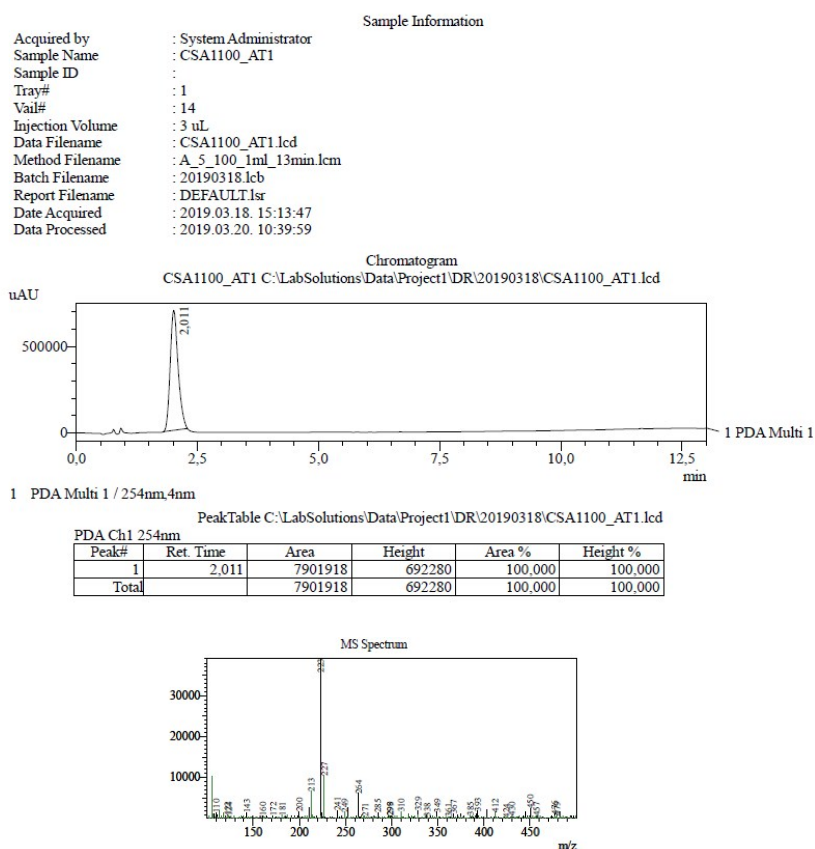


Fig. S27. HPLC-MS data for purified 2-(naphthalen-2-yl)pyridine (9):

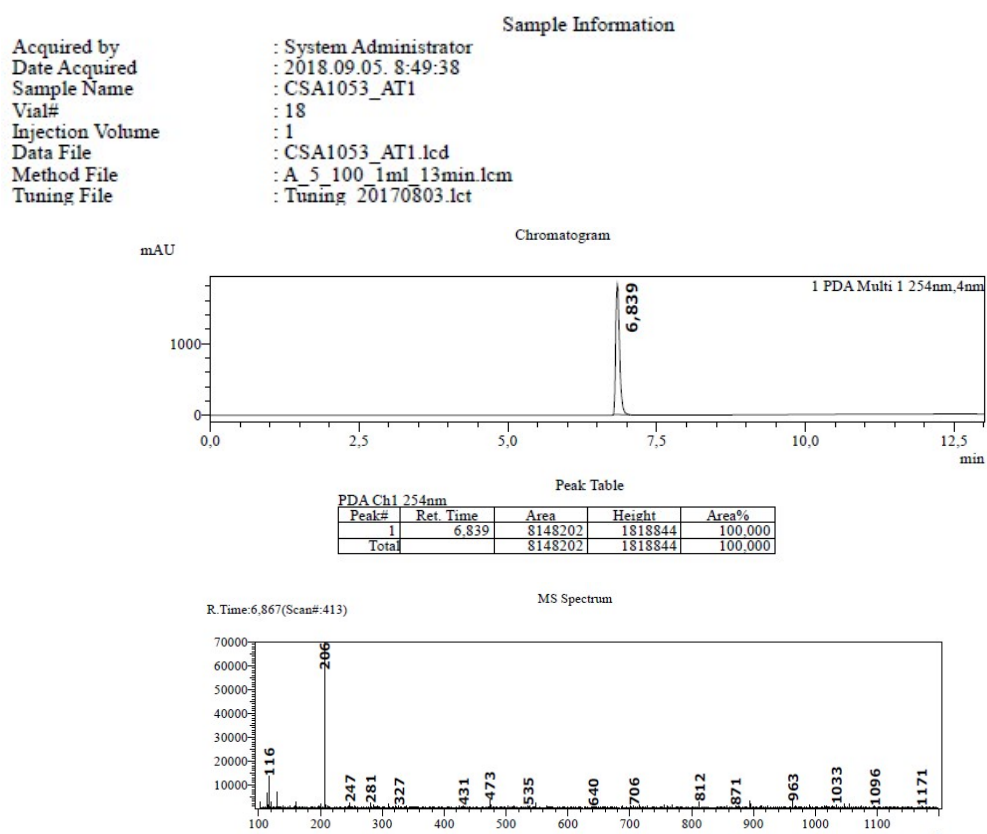


Fig S28. HPLC-MS data for 2-(naphthalen-2-yl)pyridine (9) by Method A:

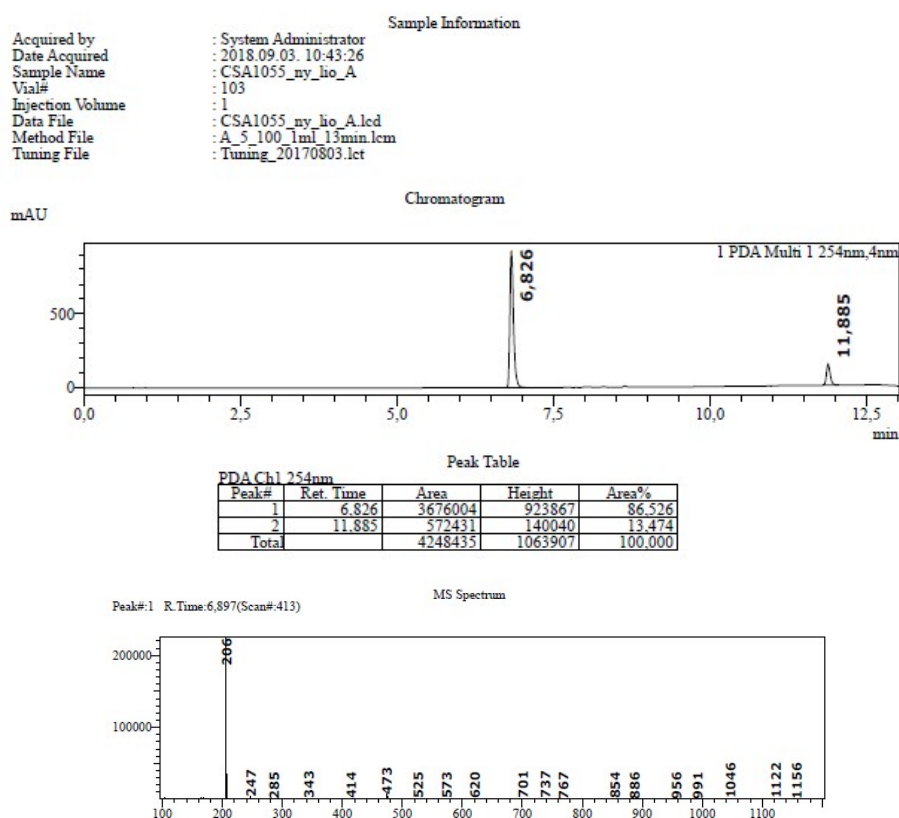


Fig. S29. HPLC-MS data for 2-(naphthalen-2-yl)pyridine (9) by Method B:

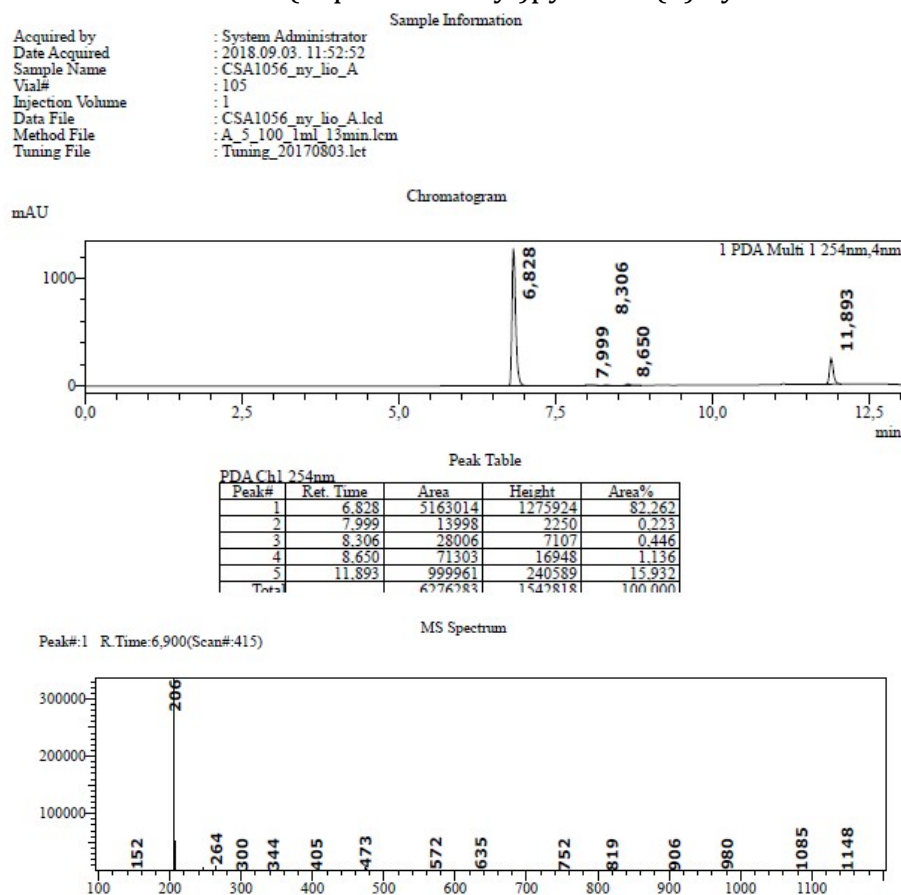


Fig. S30. HPLC-MS data for purified 4-(naphthalen-2-yl)pyridine (10):

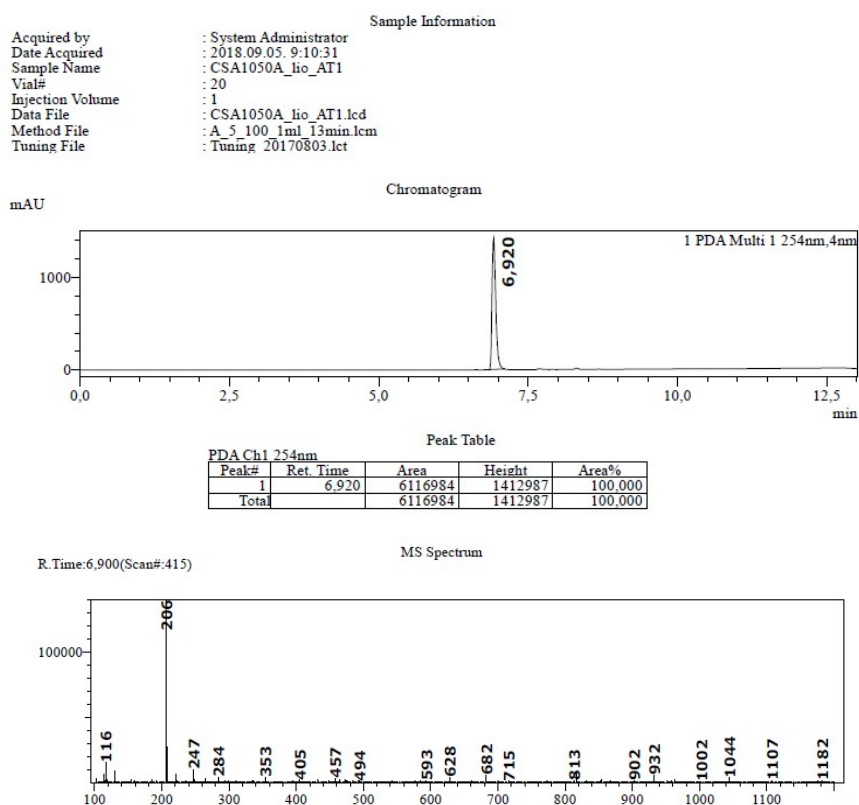


Fig. S31. HPLC-MS data for 4-(naphthalen-2-yl)pyridine (10) by Method A:

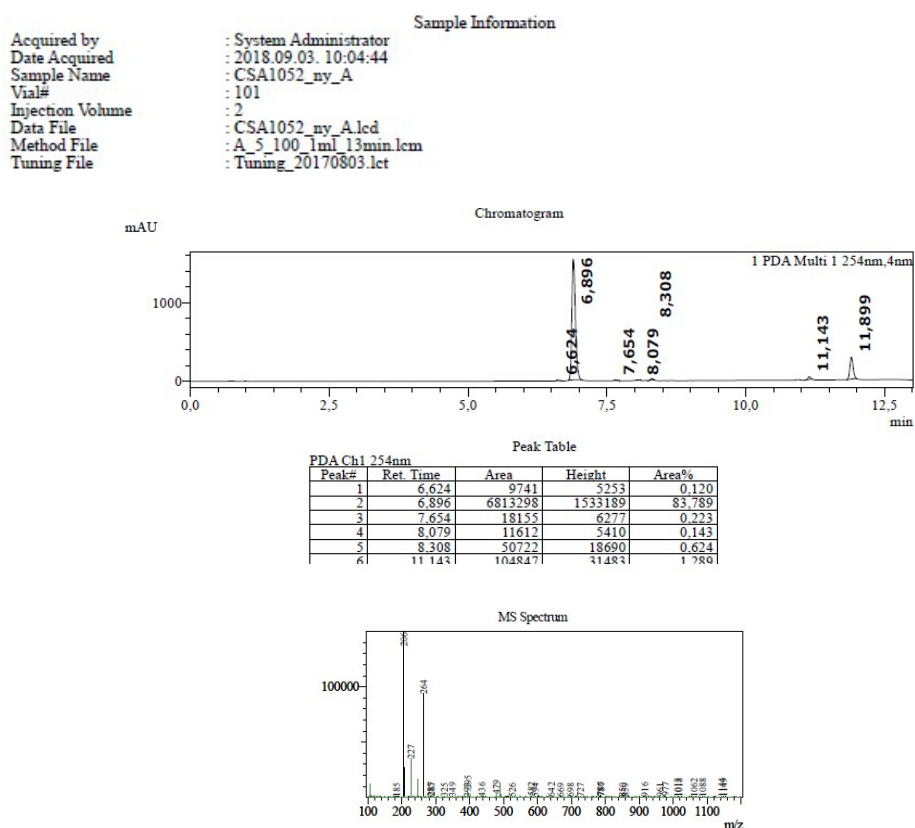


Fig. S32. HPLC-MS data for 4-(naphthalen-2-yl)pyridine (10) by Method B:

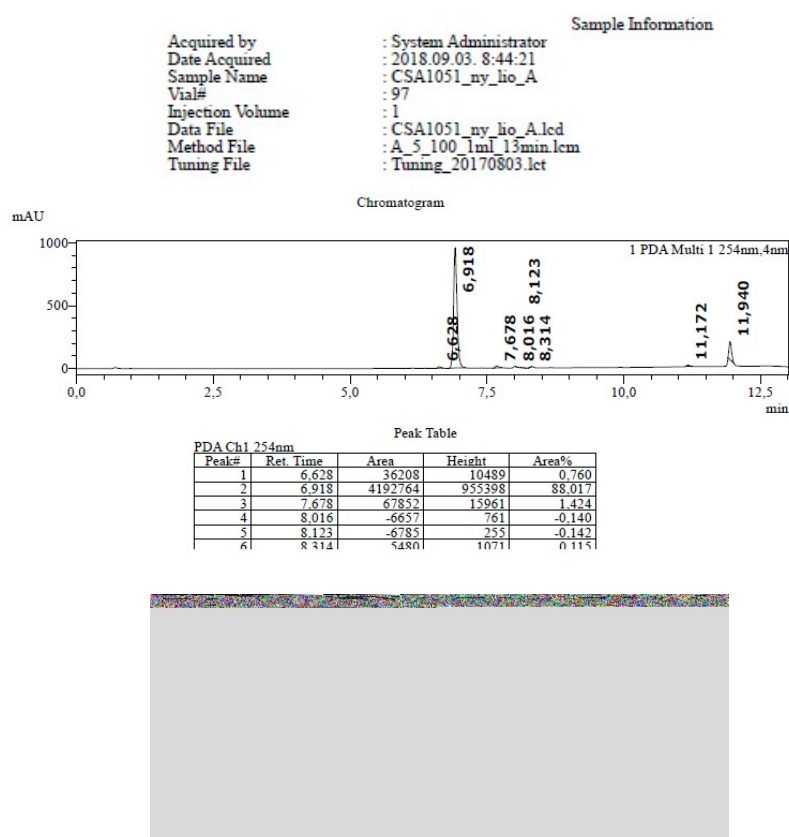


Fig. S33. HPLC-MS data for purified 6-(naphthalen-2-yl)pyridazin-3(2H)-one (11a):

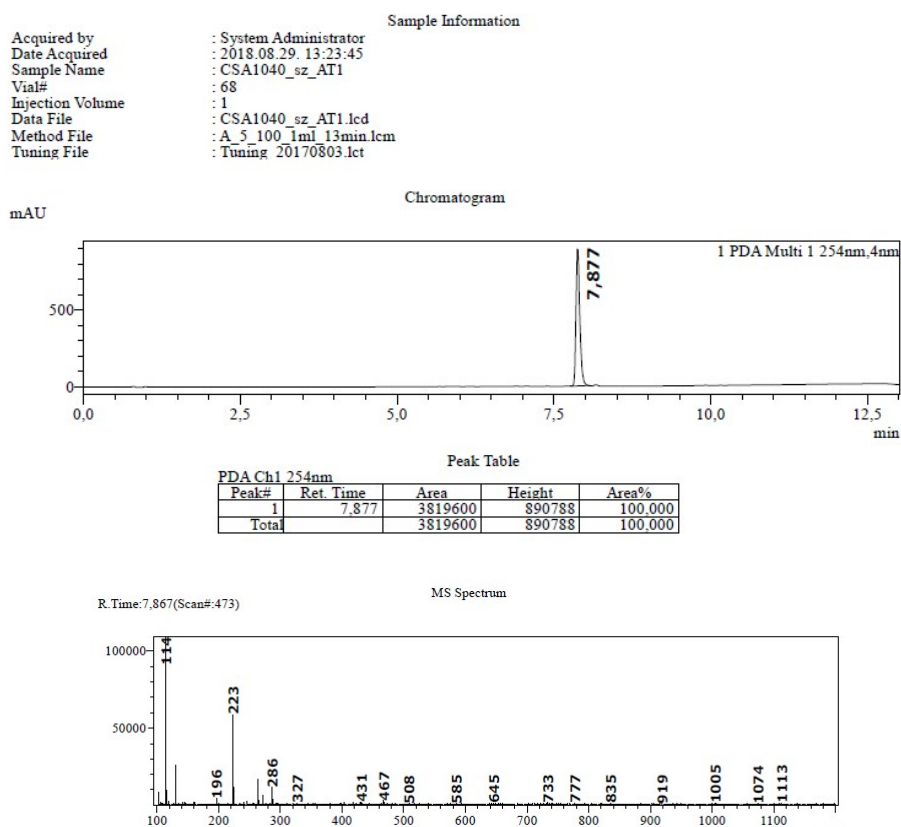


Fig. S34. HPLC-MS data for 6-(naphthalen-2-yl)pyridazin-3(2*H*)-one (11a)
by Method A:

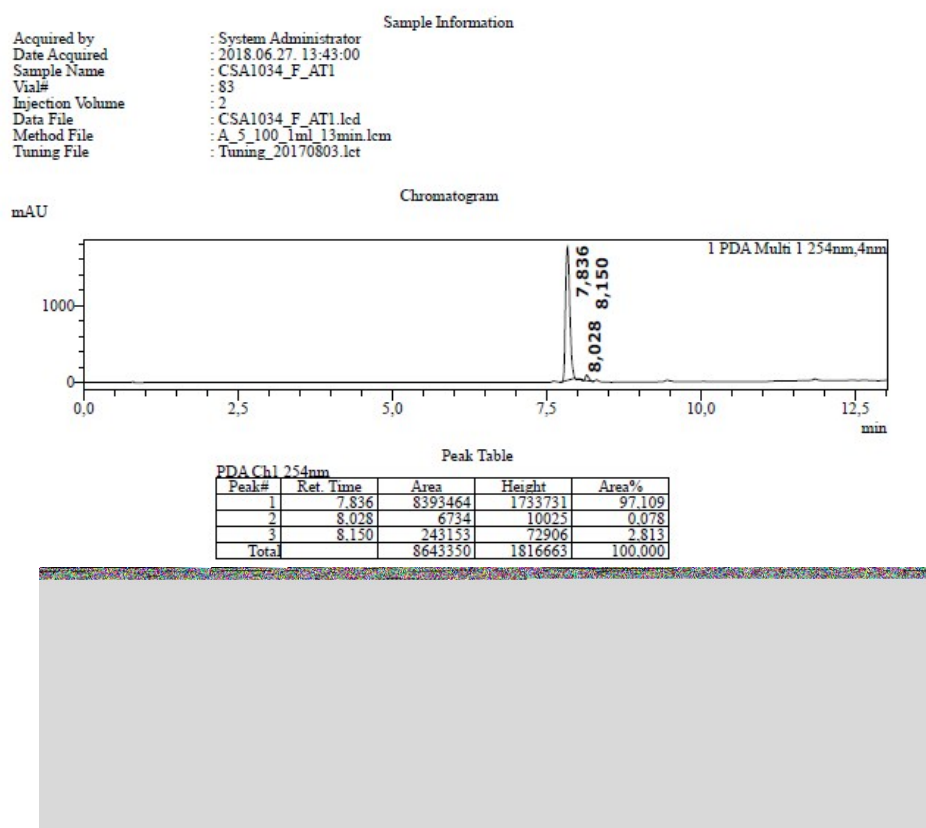


Fig. S35. HPLC-MS data for 6-(naphthalen-2-yl)pyridazin-3(2*H*)-one (11a) by Method B:

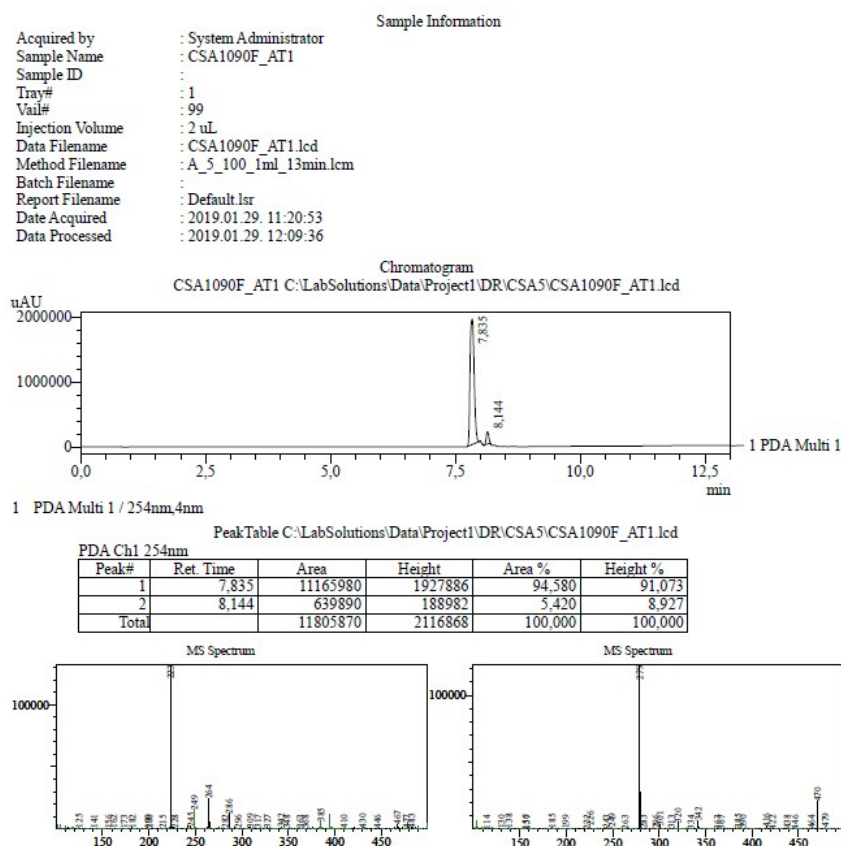


Fig. S36. HPLC-MS data for purified 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2*H*)-one (11b):

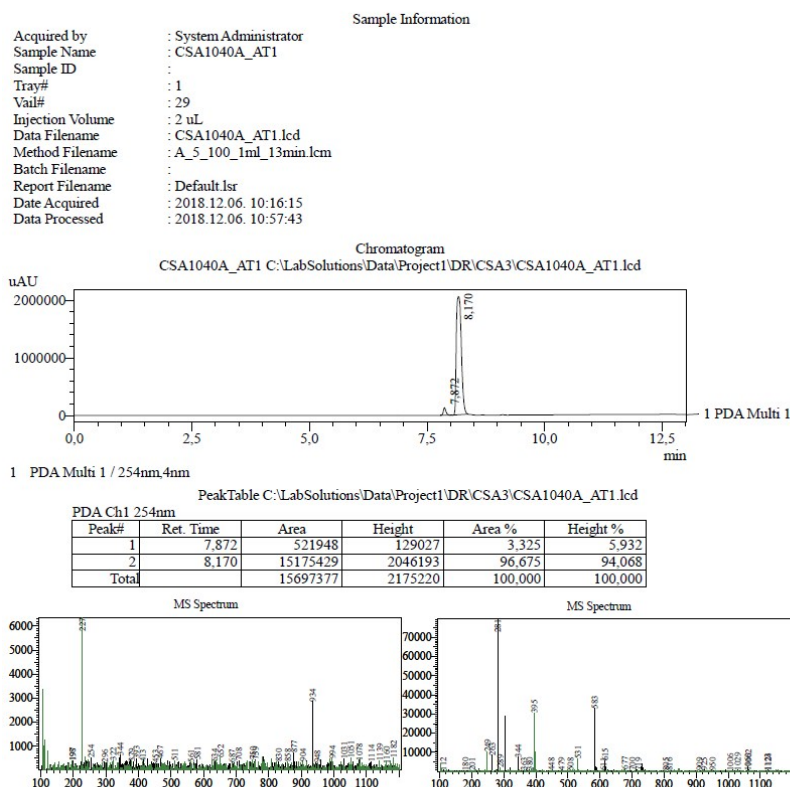


Fig. S37. HPLC-MS data for 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2H)-one (11b) by Method A:

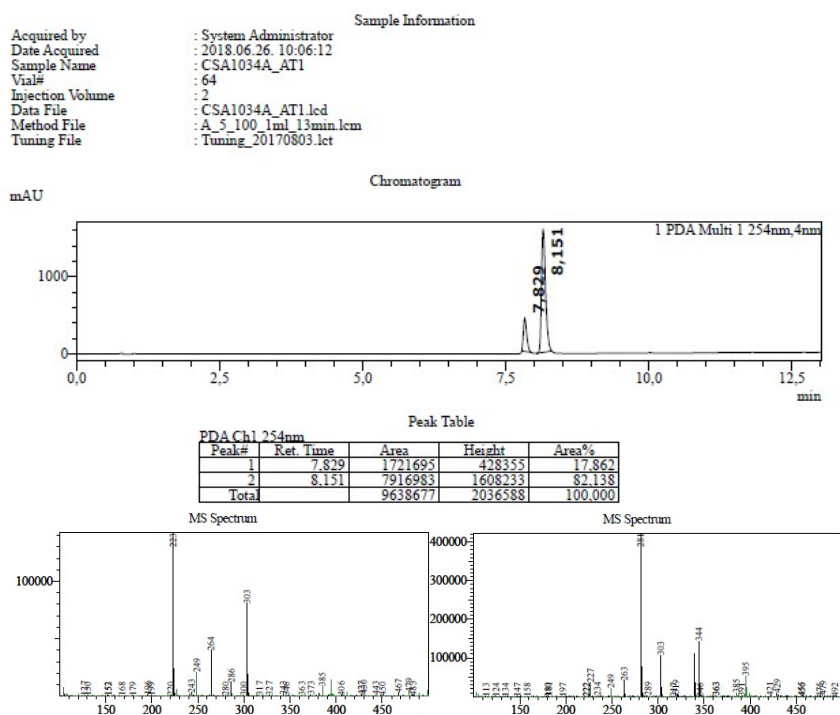


Fig. S38. HPLC-MS data for 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2H)-one (11b) by Method B:

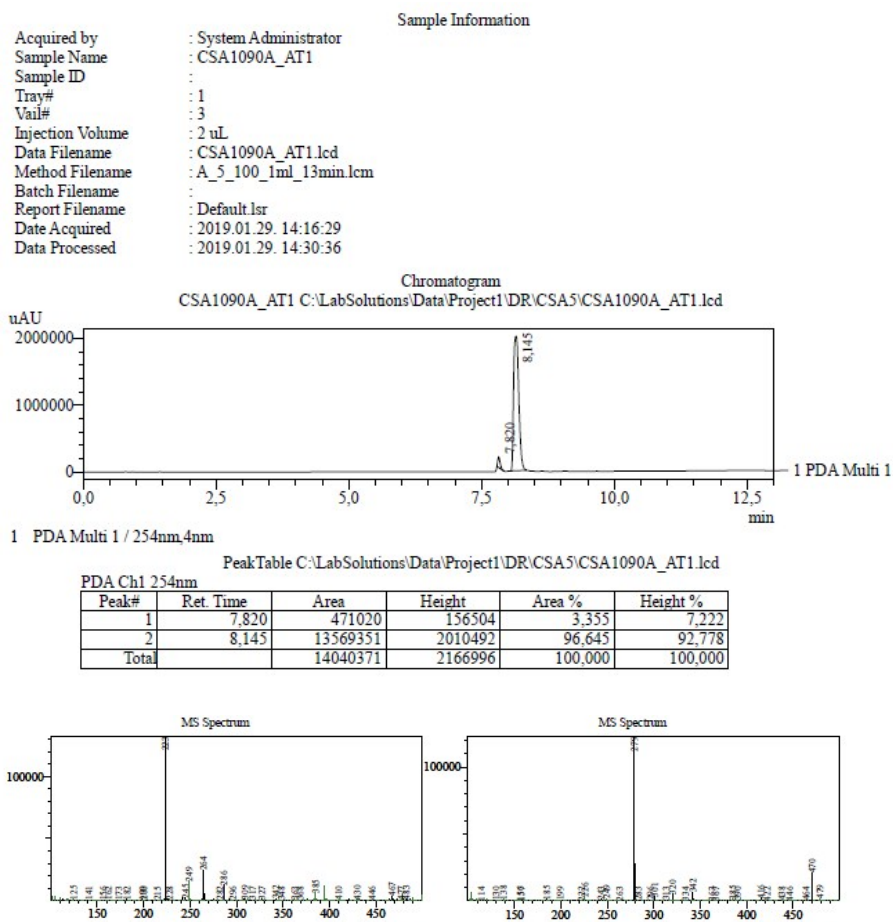


Fig. S39. HPLC-MS data for 6-(naphthalen-2-yl)pyridazin-3(2*H*)-one (11a) and 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2*H*)-one (11b) by Method B:

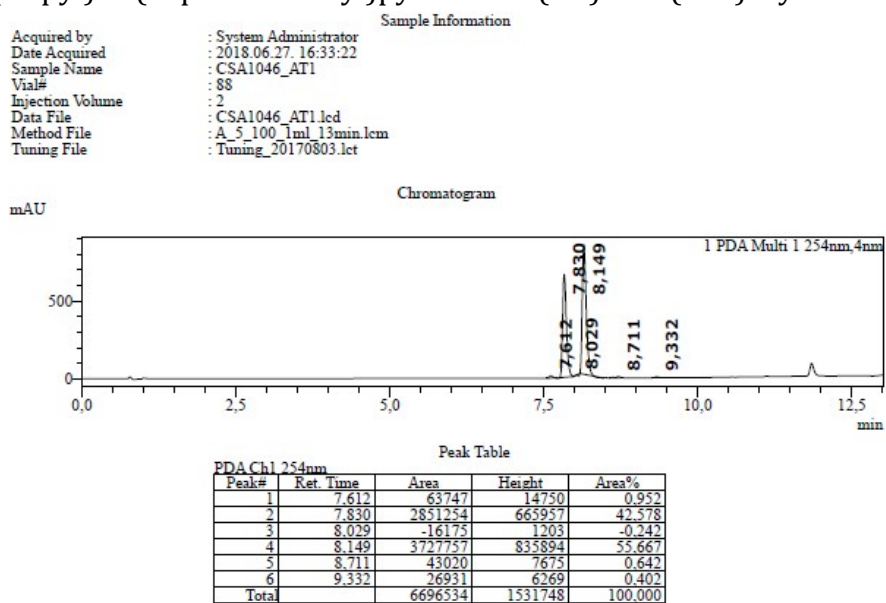


Fig. S40. HPLC-MS data for purified 2-phenylpyridine (12):

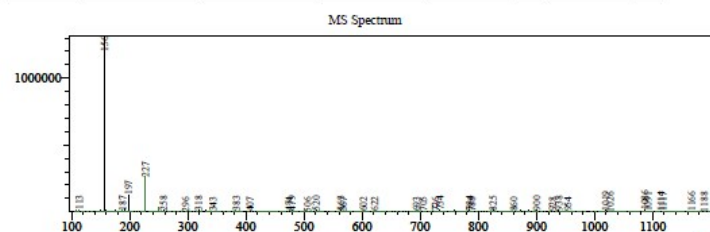
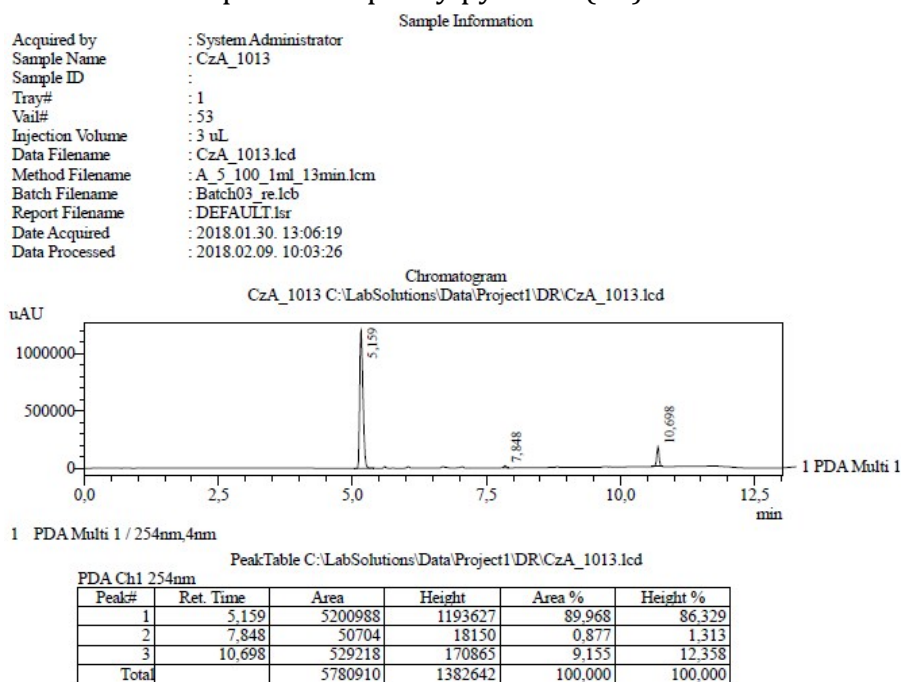


Fig. S41. HPLC-MS data for 2-phenylpyridine (12) by Method A:

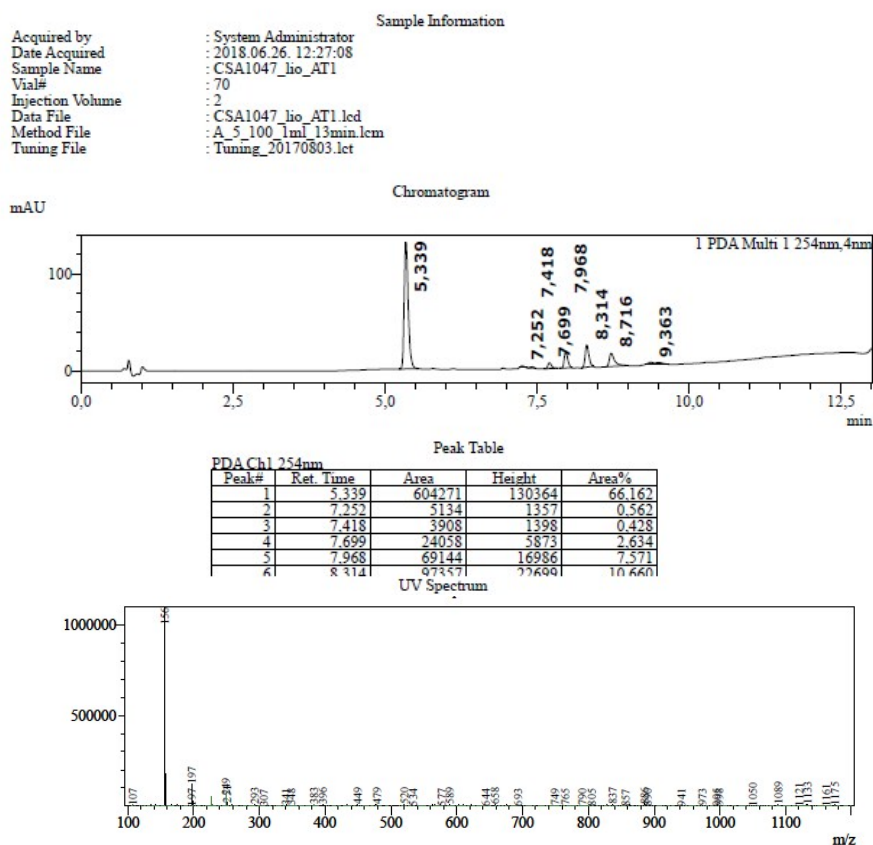


Fig. S42. HPLC-MS data for purified 2-phenylpyridine (12):

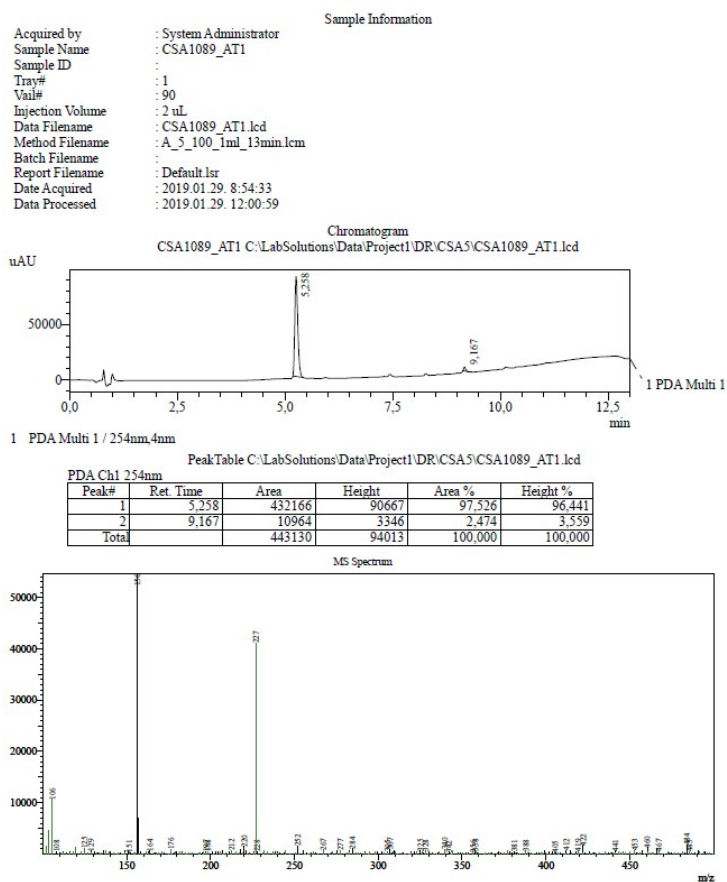


Fig. S43. HPLC-MS data for 2-phenylpyridine (12) by Method B:

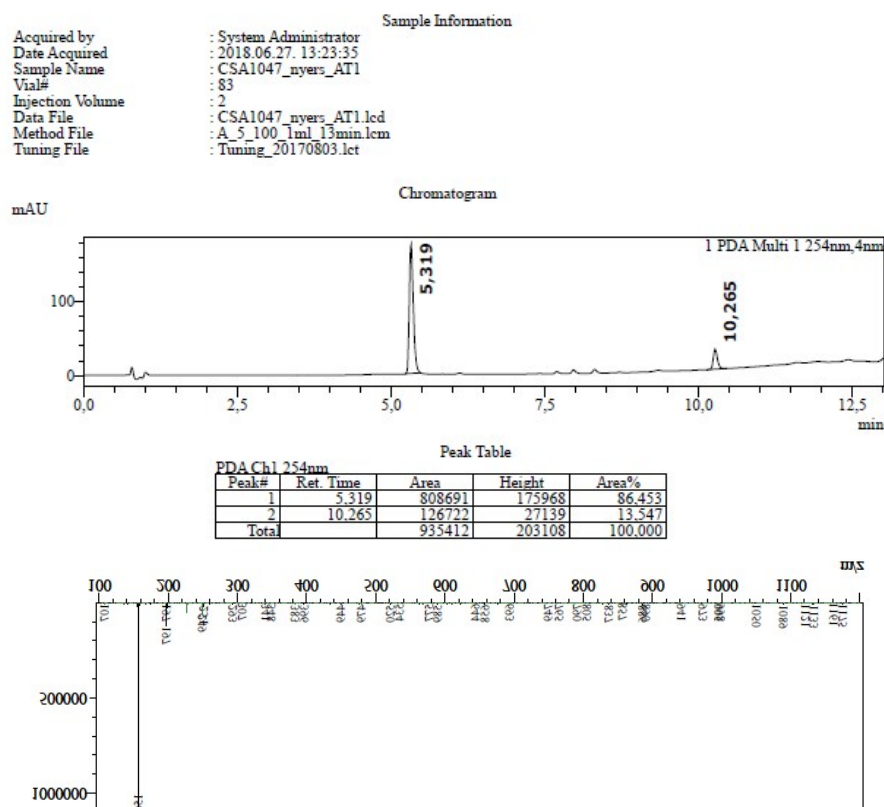


Fig. S44. HPLC-MS data for purified 4-phenylpyridine (13):

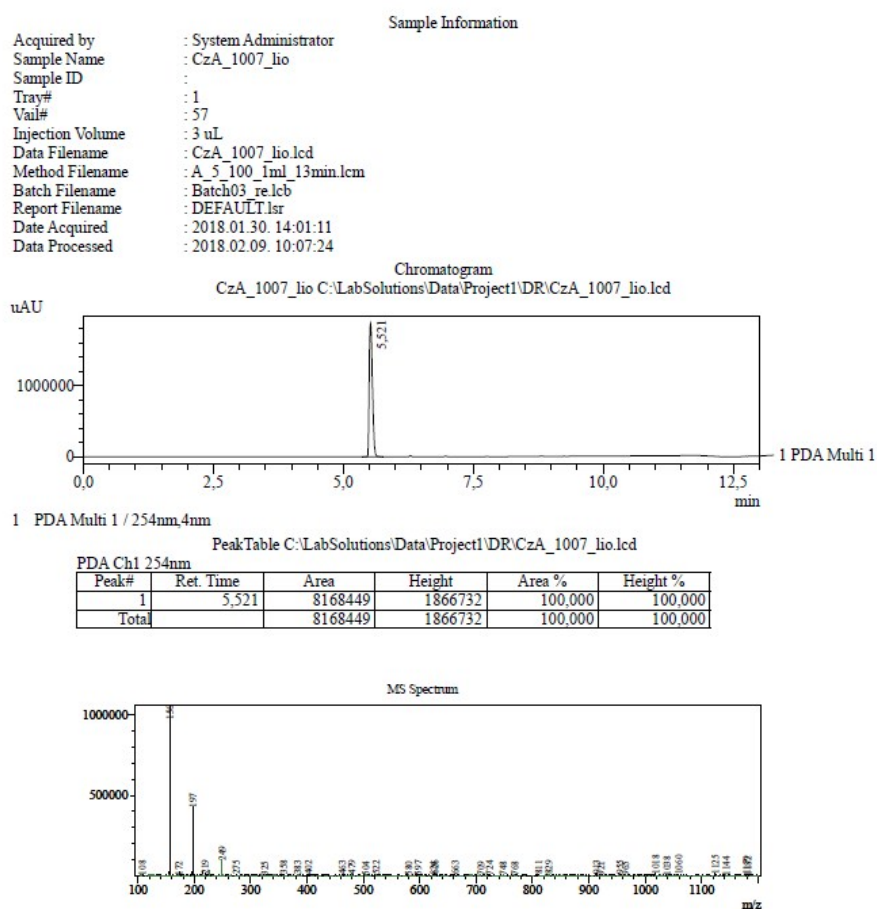


Fig. S45. HPLC-MS data for 4-phenylpyridine (13) by Method A:

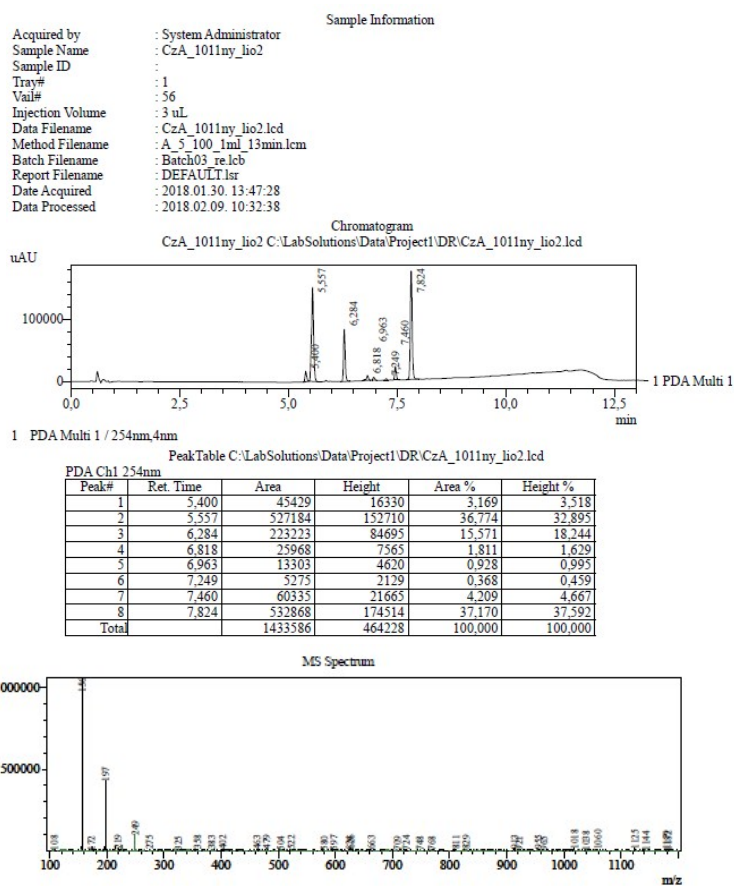


Fig. S46. HPLC-MS data for 4-phenylpyridine (13) by Method B:

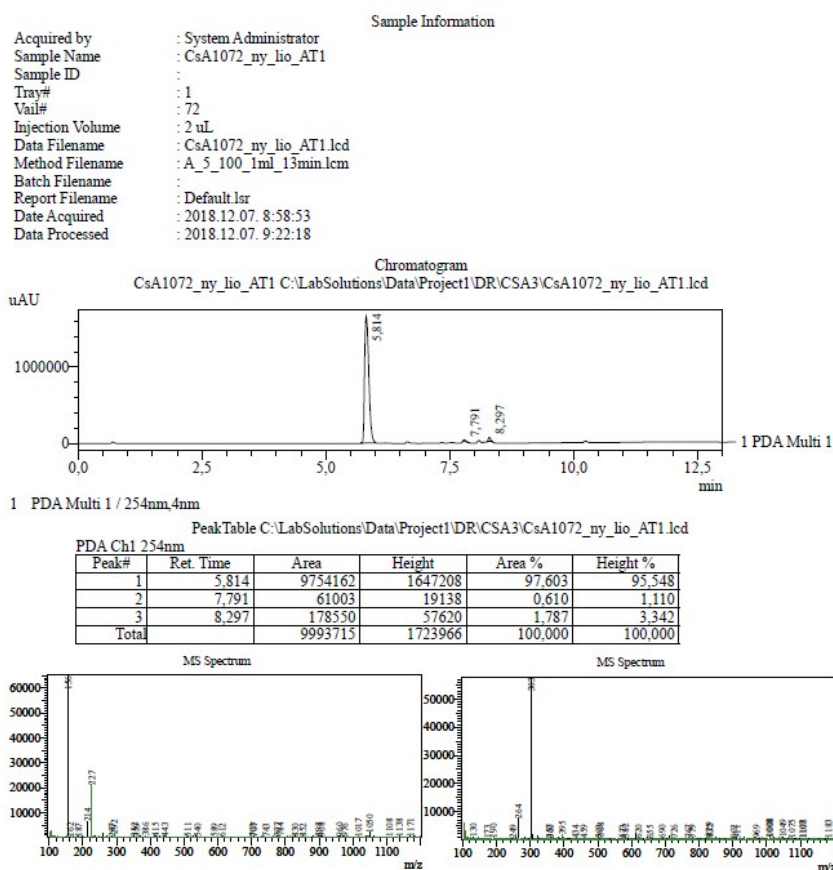


Fig. S47. HPLC-MS data for 4-phenylpyridine (13) by Method B:

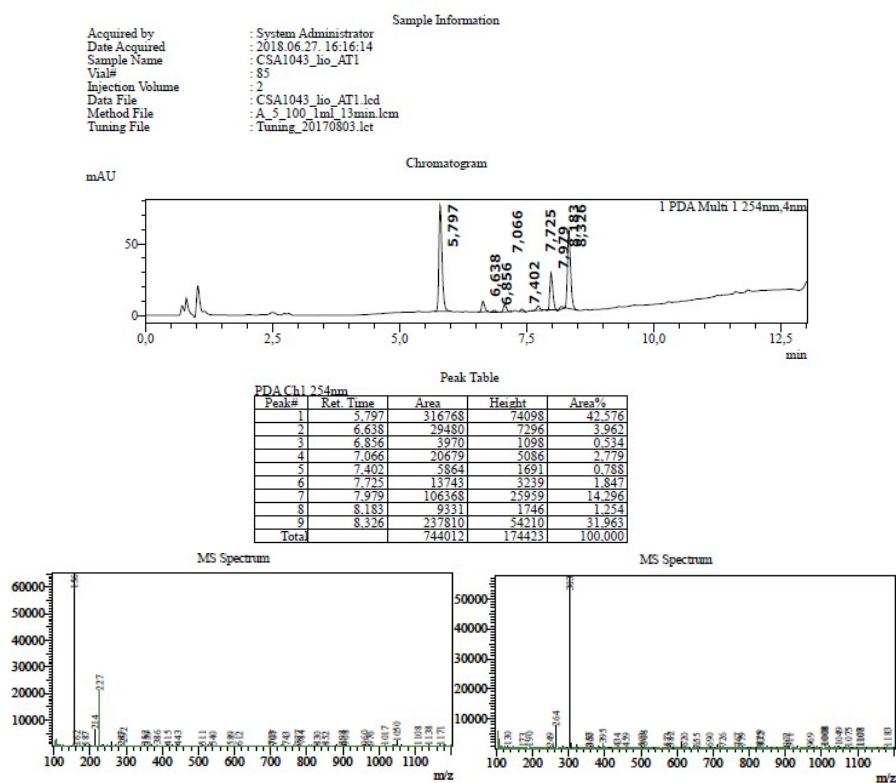


Fig. S48. HPLC-MS data for purified 2-(biphenyl-4-yl)pyridine (14):

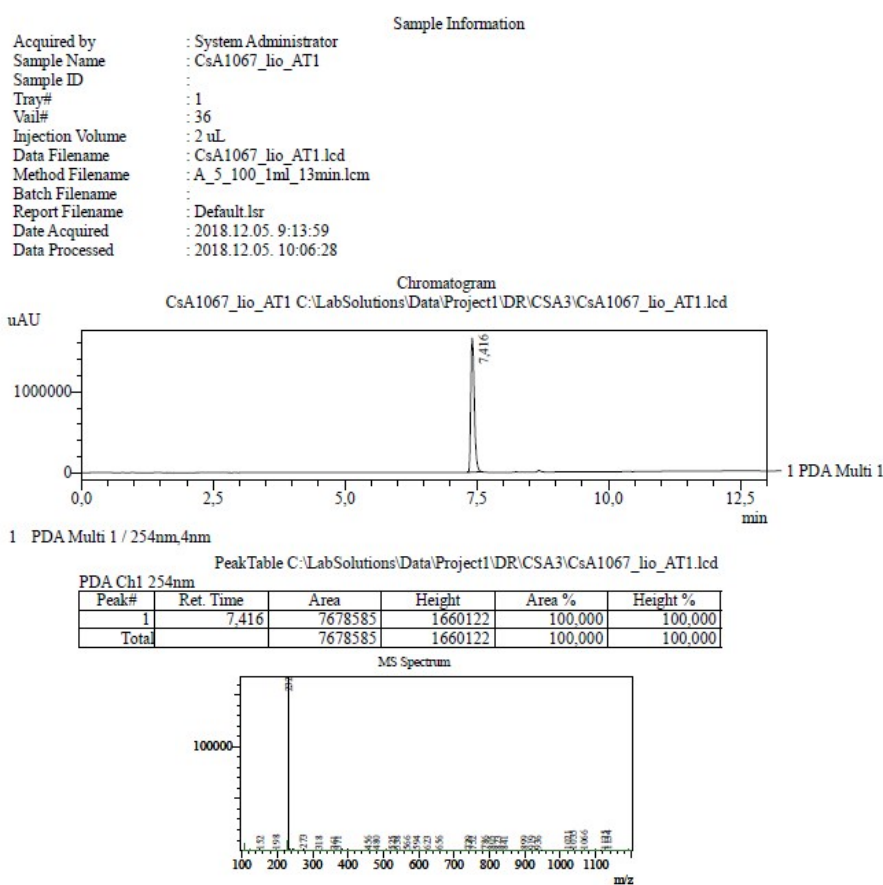
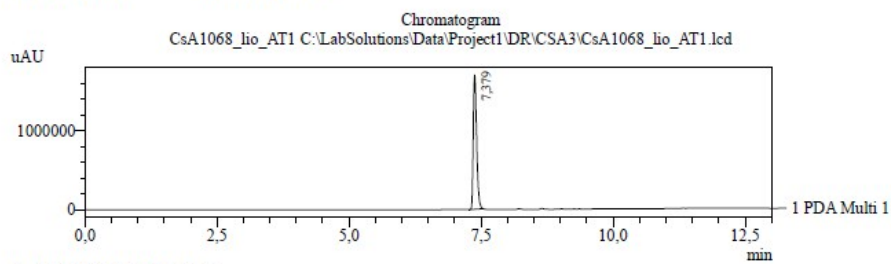


Fig. S50. HPLC-MS data for 2-(biphenyl-4-yl)pyridine (14) by Method B:

	Sample Information
Acquired by	: System Administrator
Sample Name	: CsA1068_lfo_AT1
Sample ID	:
Tray#	: 1
Vial#	: 6
Injection Volume	: 1 uL
Data Filename	: CsA1068_lfo_AT1.lcd
Method Filename	: A_5_100_1ml_13min.lcm
Batch Filename	:
Report Filename	: Default.lsr
Date Acquired	: 2018.11.26. 15:24:41
Data Processed	: 2018.12.05. 10:24:43



1 PDA Multi 1 / 254nm,4nm

PeakTable C:\LabSolutions\Data\Project1\DR\CSA3\CSA1068_hio_AT1.lcd

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.379	7534703	1697133	100.000	100.000
Total		7534703	1697133	100.000	100.000

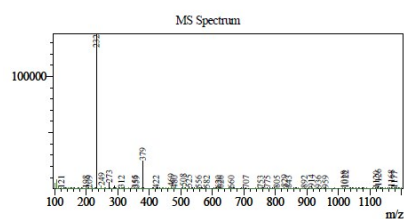


Fig. S51. HPLC-MS data for 2-(biphenyl-4-yl)pyridine (14) by Method B:

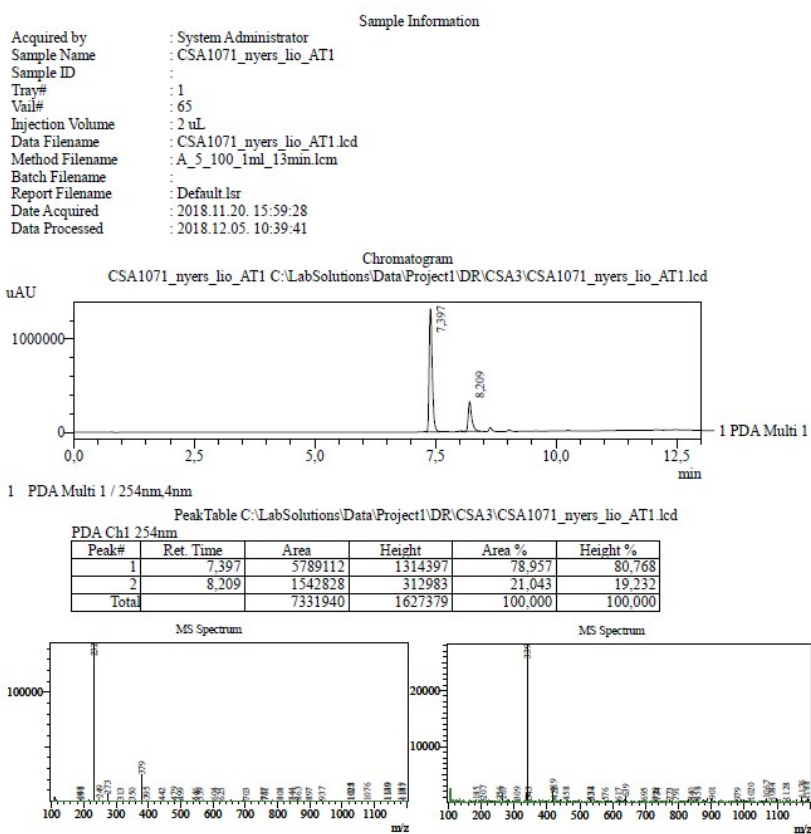


Fig. S52. HPLC-MS data for purified 4-(biphenyl-4-yl)pyridine (15):

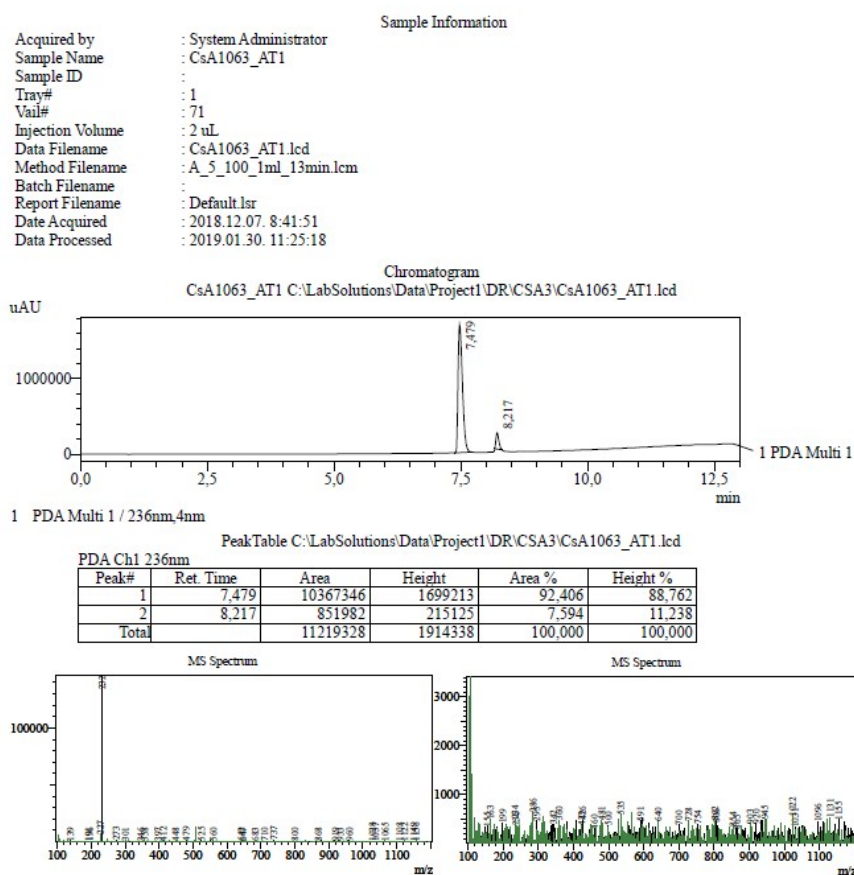


Fig. S53. HPLC-MS data for 4-(biphenyl-4-yl)pyridine (15) by Method A:

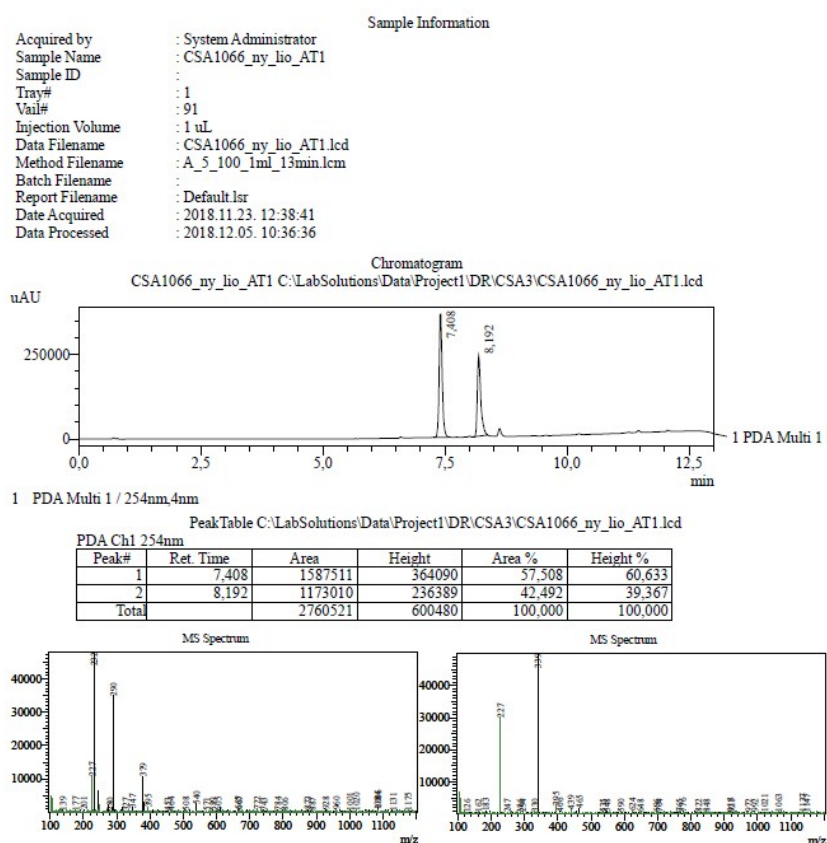


Fig. S54. HPLC-MS data for 4-(biphenyl-4-yl)pyridine (15) by Method B:

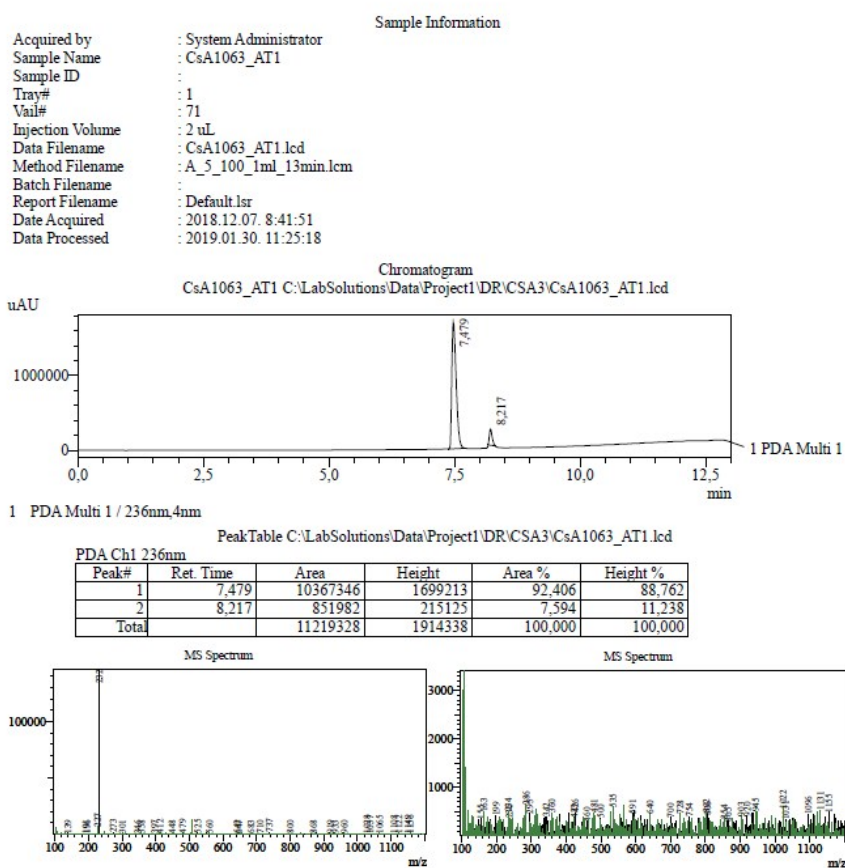


Fig. S55. HPLC-MS data for 4-(biphenyl-4-yl)pyridine (15) by Method B:

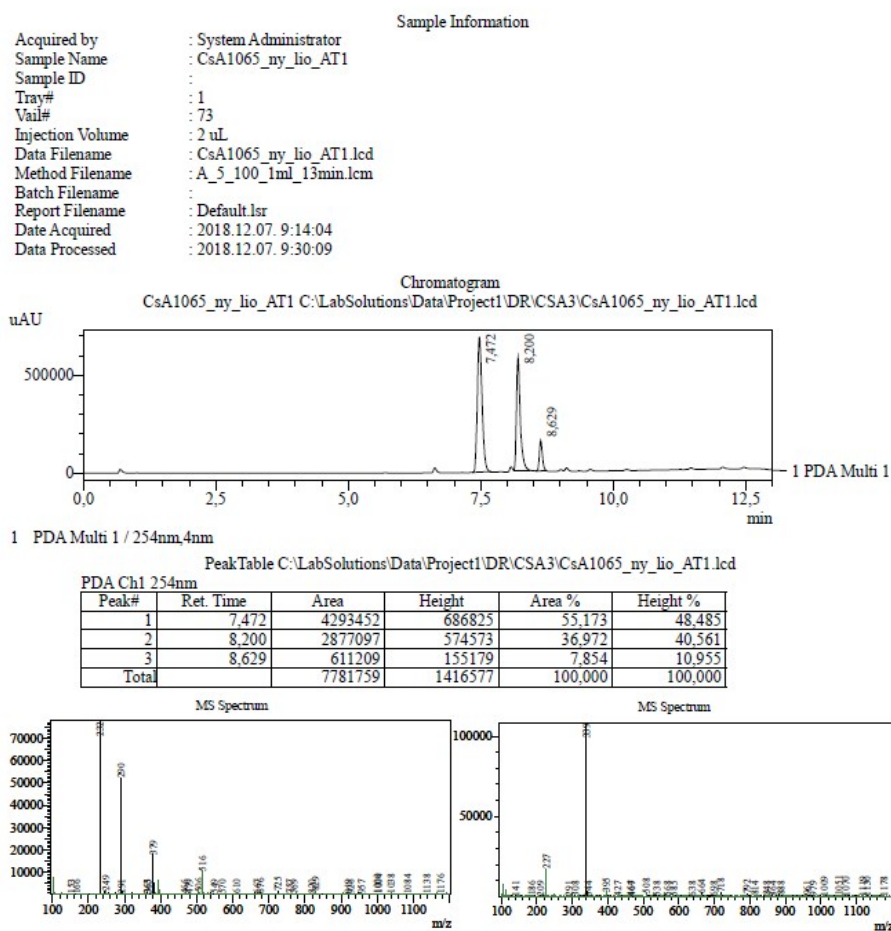


Fig. S56. HPLC-MS data for purified 2-(4-fluorophenyl)pyridine (16):

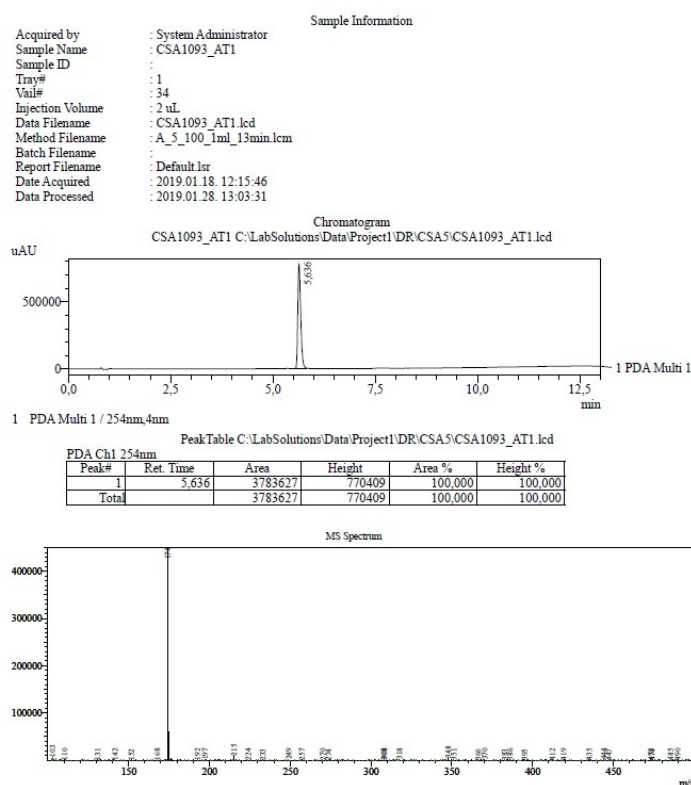


Fig. S57. HPLC-MS data for 2-(4-fluorophenyl)pyridine (16) by Method A:

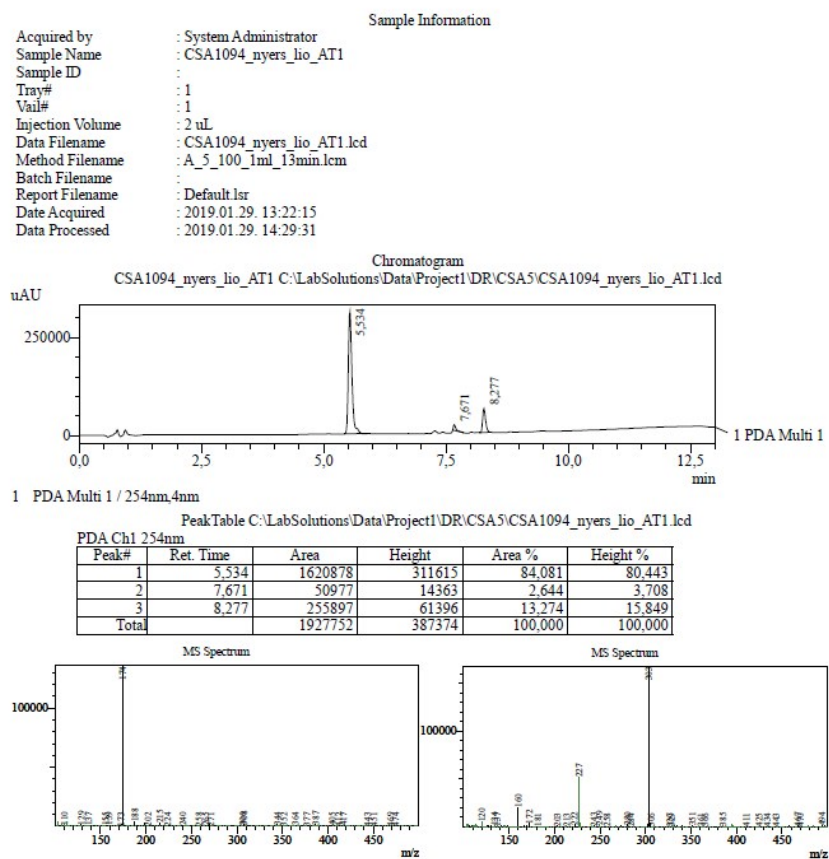


Fig. S58. HPLC-MS data for 2-(4-fluorophenyl)pyridine (16) by Method B:

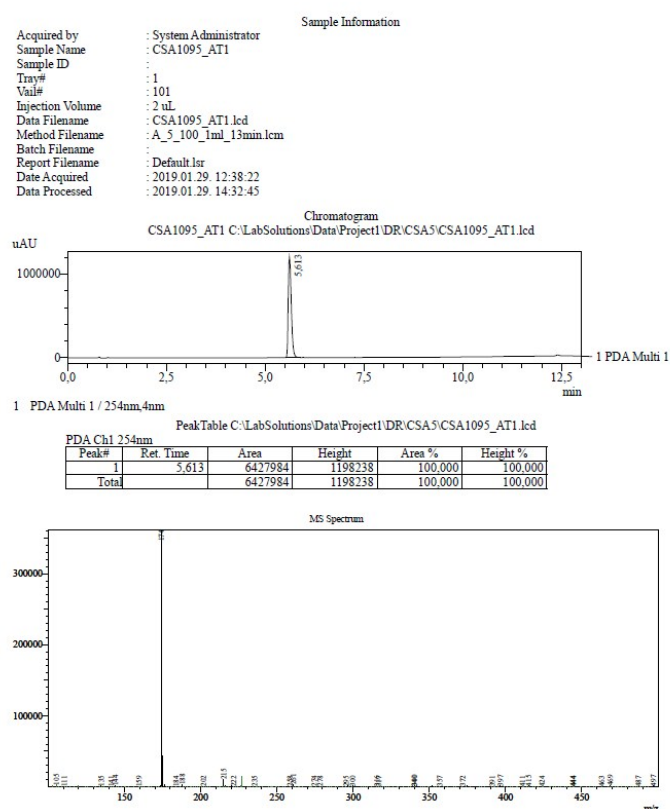


Fig. S59. HPLC-MS data for 2-(4-fluorophenyl)pyridine (16) by Method B:

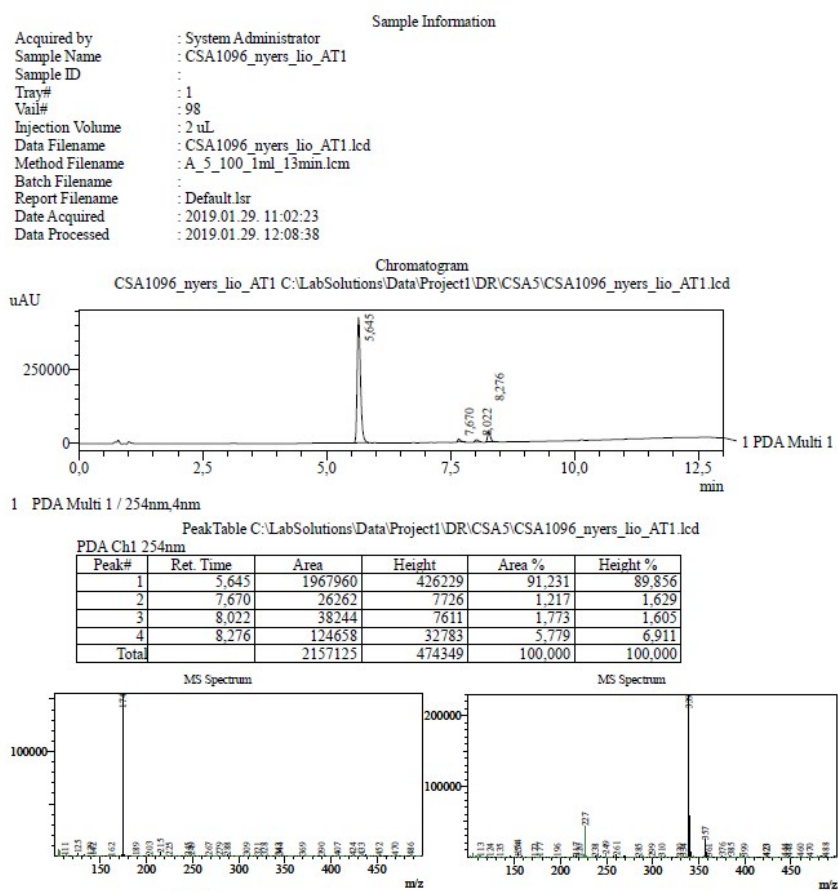


Fig. S60. HPLC-MS data for purified 4-(4-fluorophenyl)pyridine (17):

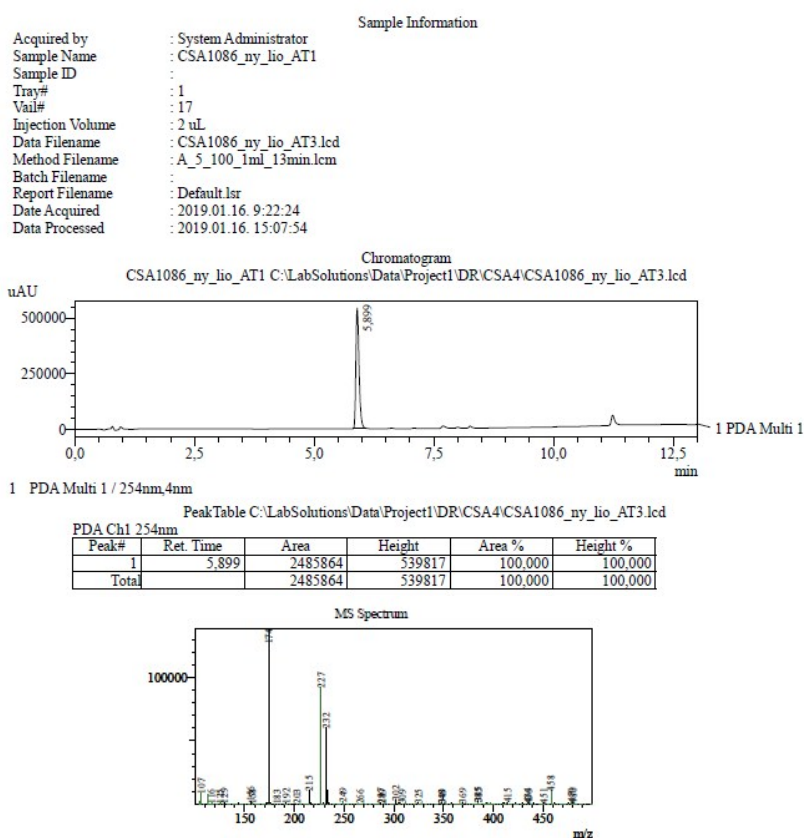


Fig. S61. HPLC-MS data for 4-(4-fluorophenyl)pyridine (17) by Method A:

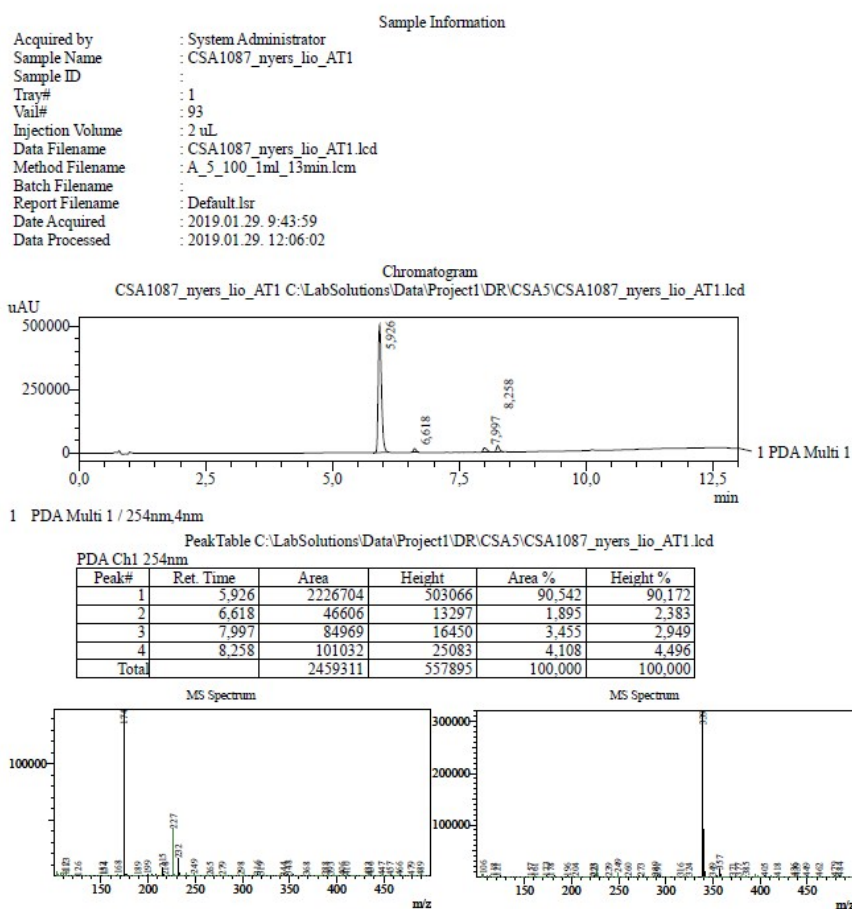


Fig. S62. HPLC-MS data for 4-(4-fluorophenyl)pyridine (17) by Method B:

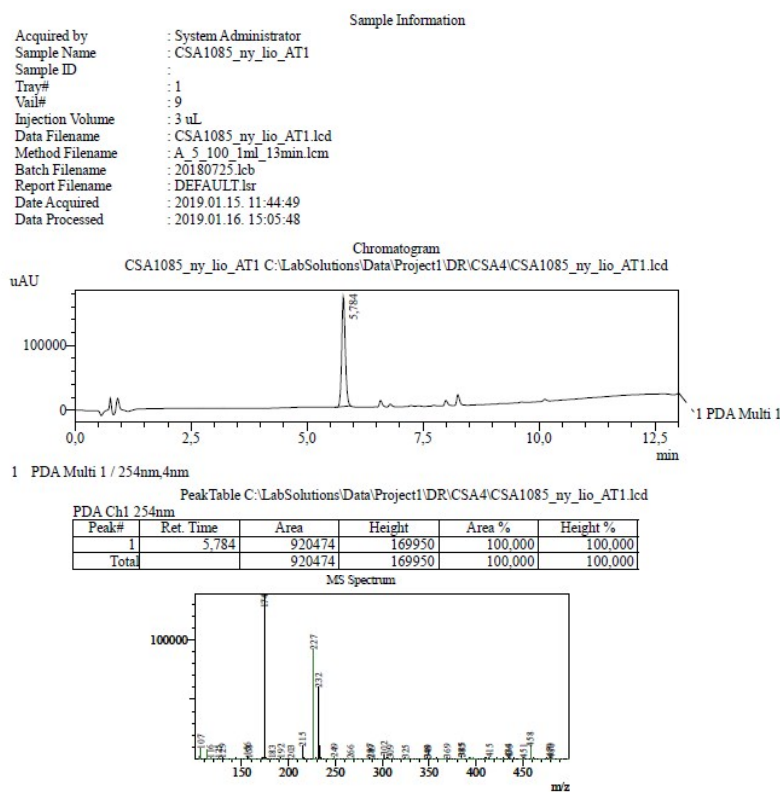


Fig. S63. HPLC-MS data for 4-(4-fluorophenyl)pyridine (17) by Method B:

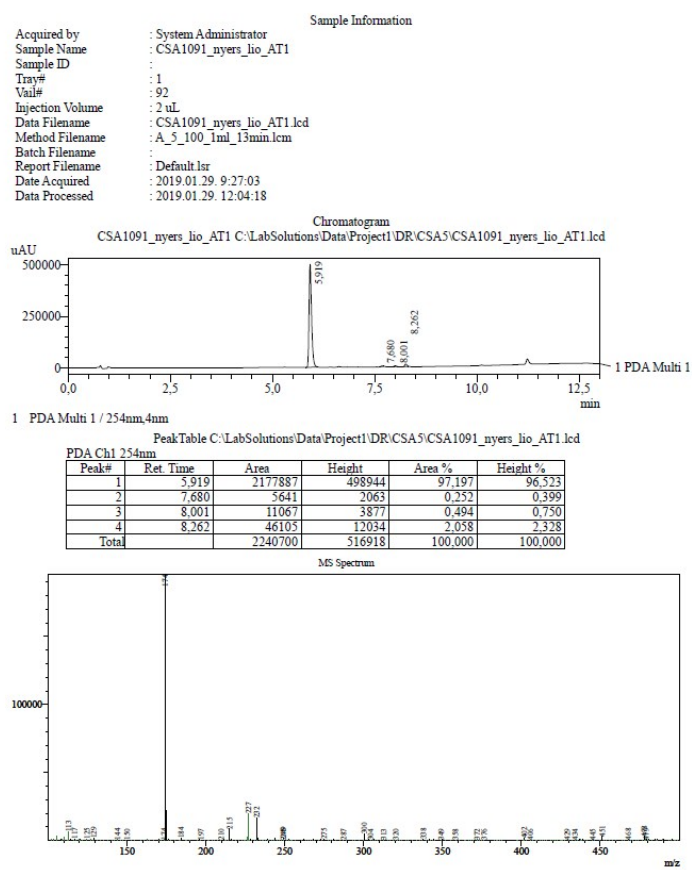


Fig. S64. HPLC-MS data for purified 6-phenylpyridazin-3(2*H*)-one (18a):

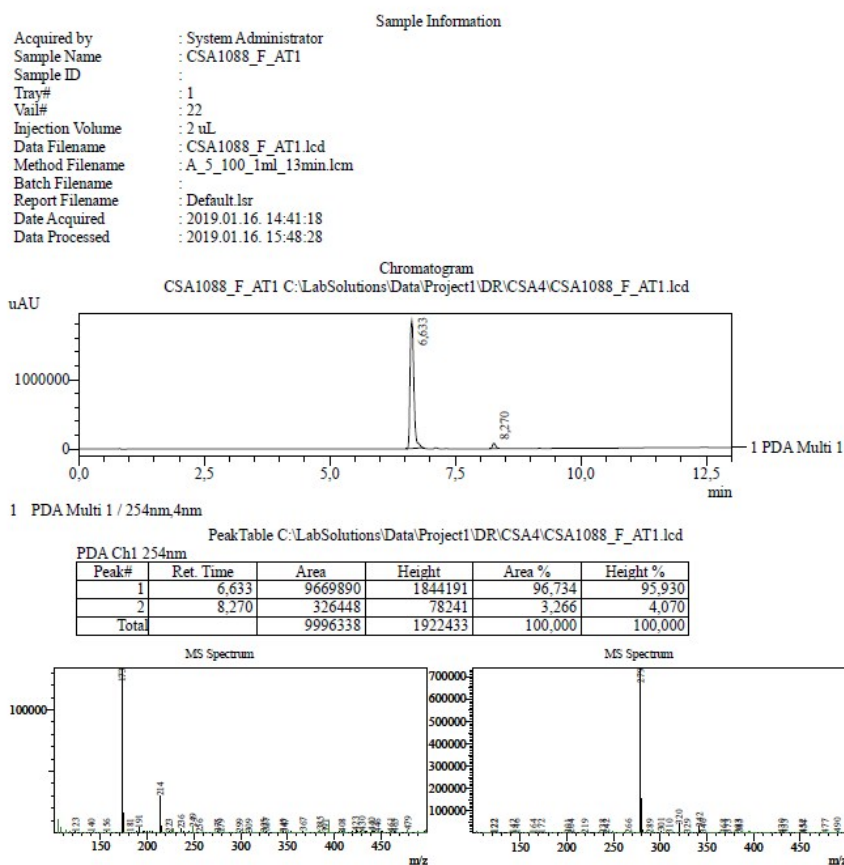


Fig. S65. HPLC-MS data for 6-phenylpyridazin-3(2*H*)-one (18a) by Method A

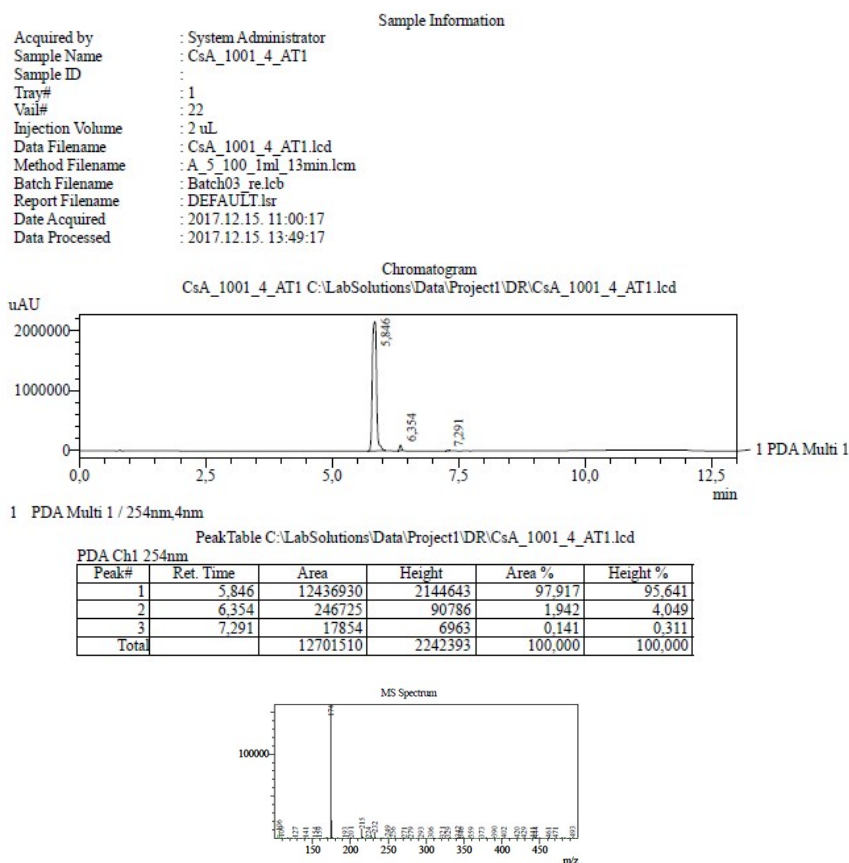


Fig. S66. HPLC-MS data for 6-phenylpyridazin-3(2*H*)-one (18a) and 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2*H*)-one (18b) by Method A:

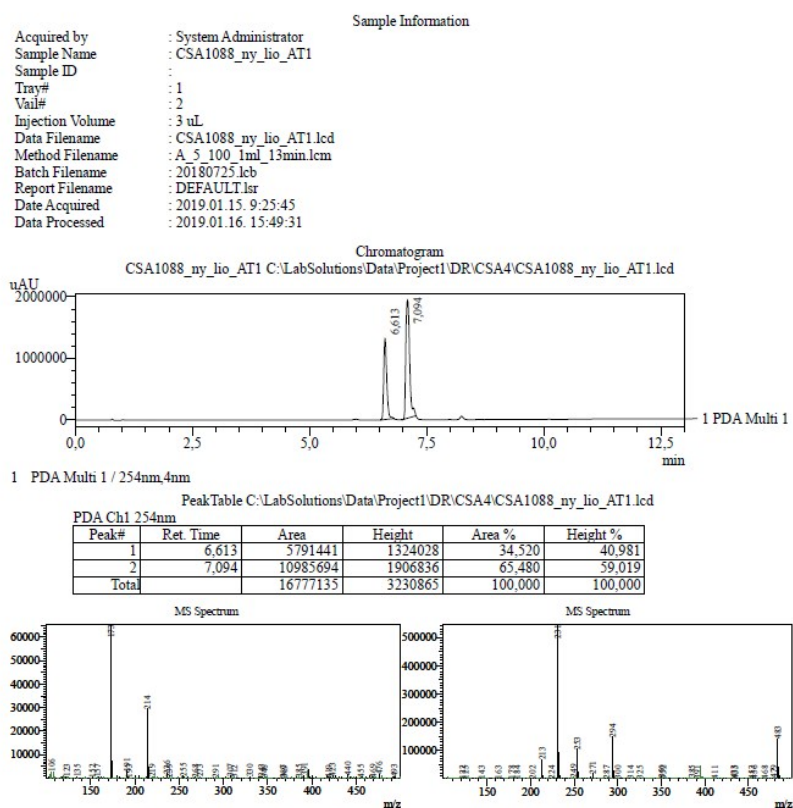


Fig. S67. HPLC-MS data for purified 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2H)-one (18b):

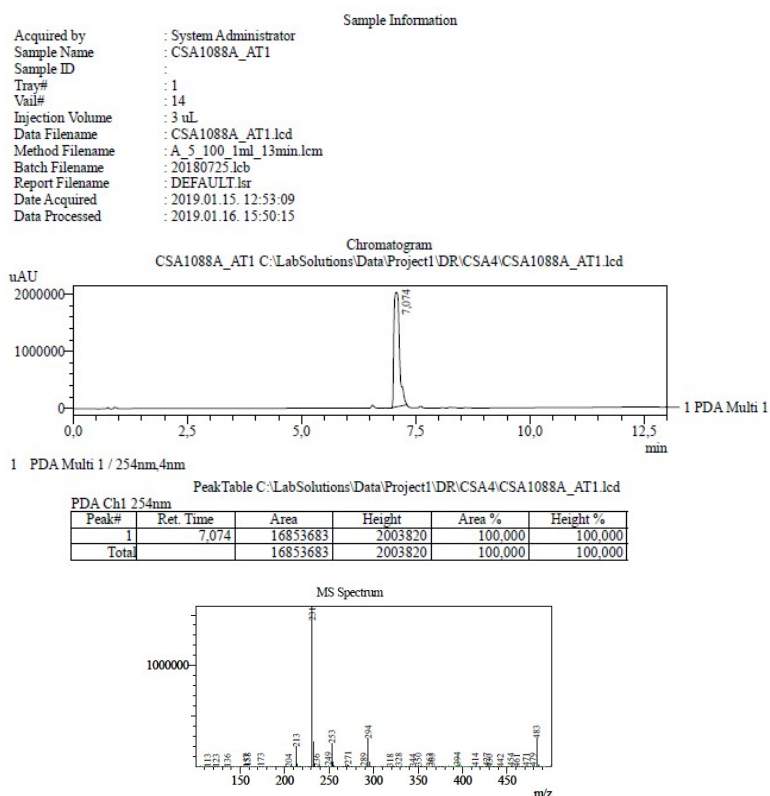


Fig. S68. HPLC-MS data for 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2H)-one (18b) by Method B:

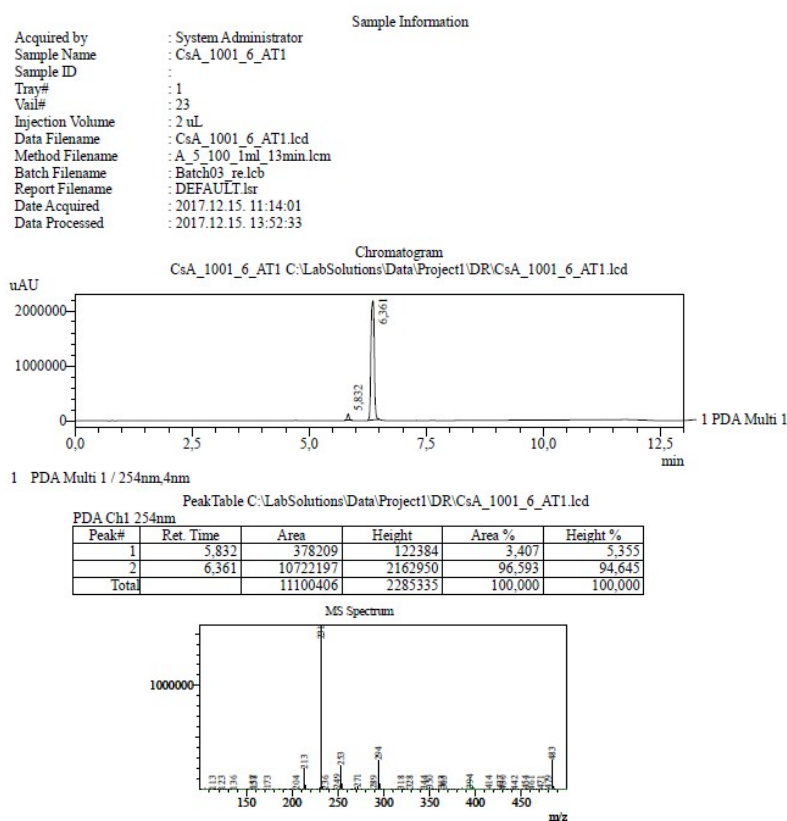


Fig. S69. HPLC-MS data for 6-phenylpyridazin-3(2H)-one (18a) and 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2H)-one (18b) by Method B:

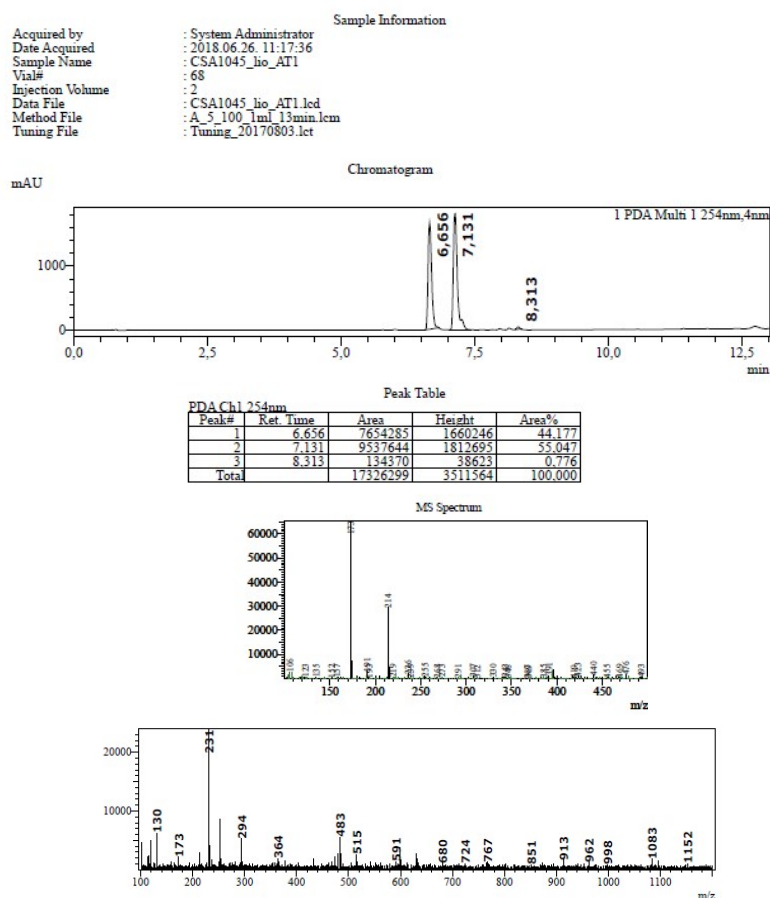


Fig. S70. HPLC-MS data for purified 6-(biphenyl-4-yl)pyridazin-3(2*H*)-one (19a):

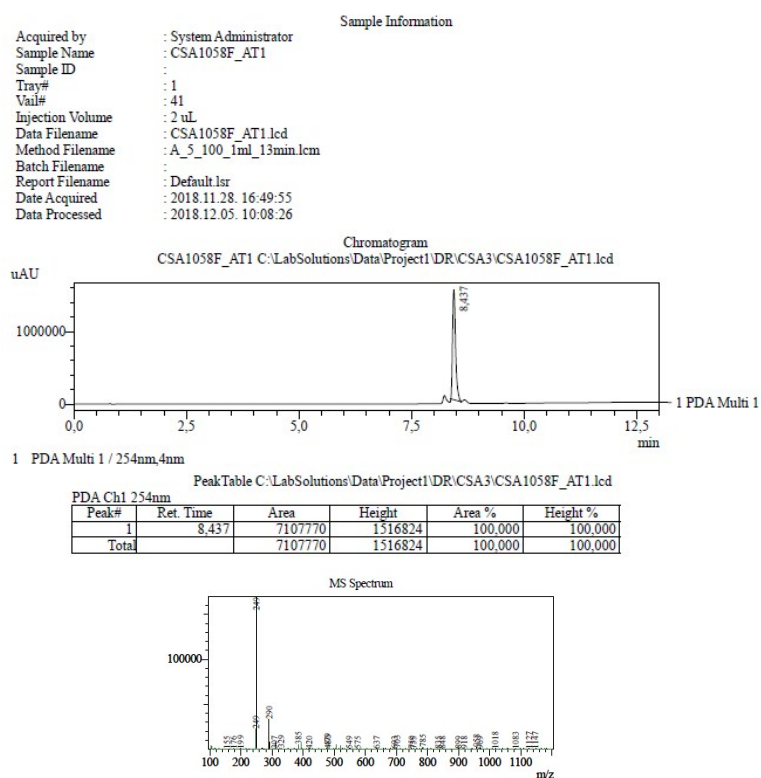


Fig. S71. HPLC-MS data for 6-(biphenyl-4-yl)pyridazin-3(2*H*)-one (19a) by Method A:

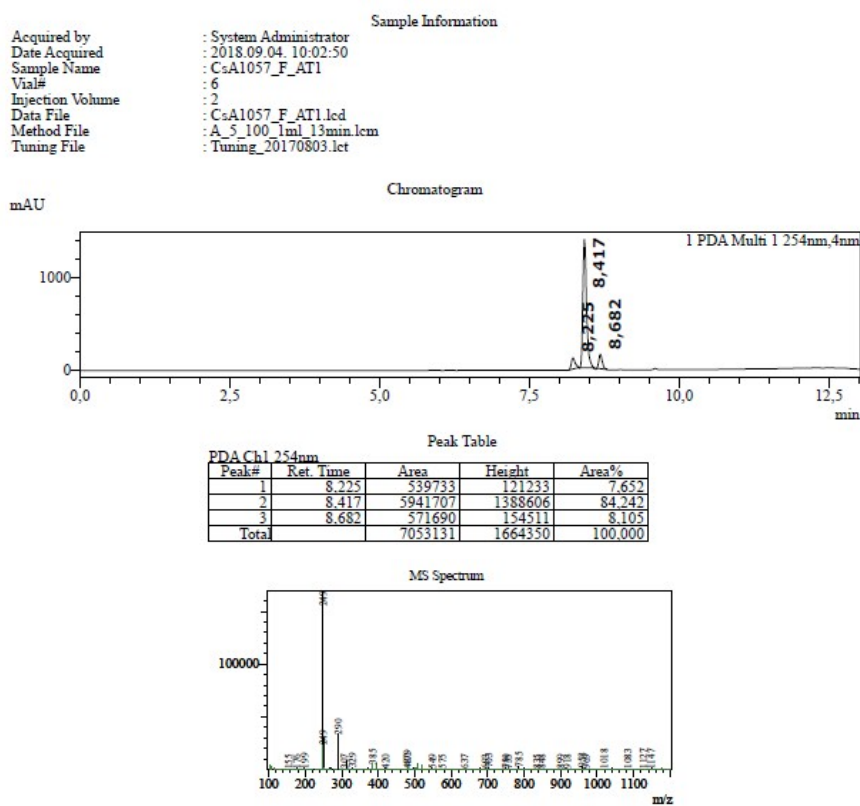


Fig. S72. HPLC-MS data for 6-(biphenyl-4-yl)pyridazin-3(2*H*)-one (19a) and 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)-pyridazin-3(2*H*)-one (19b) by Method A:

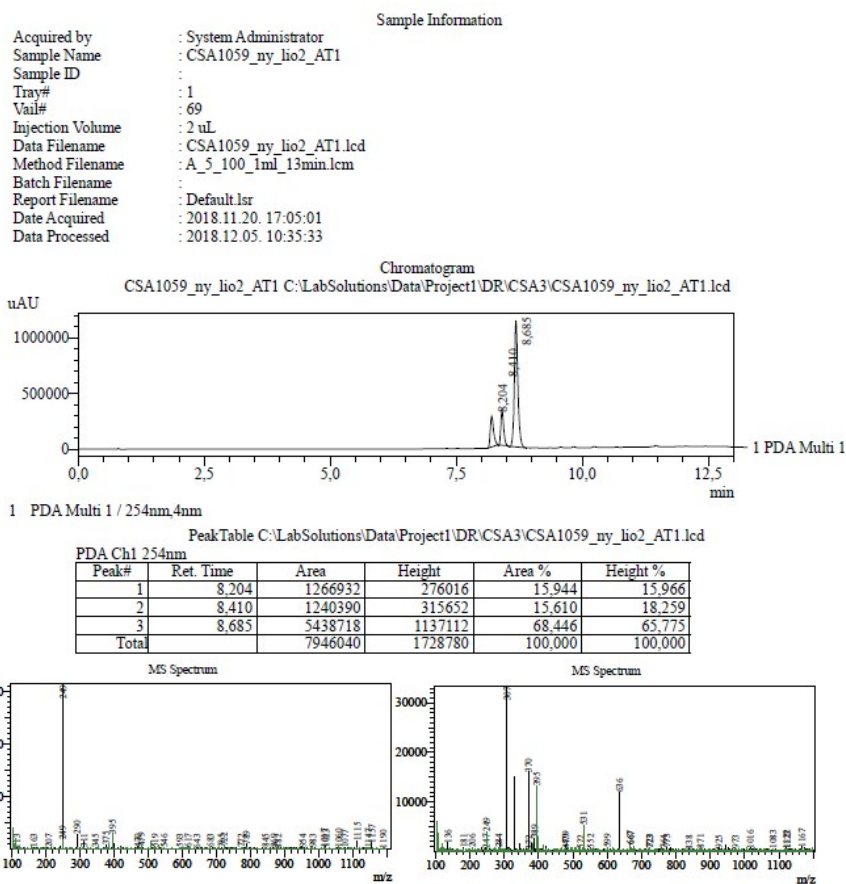


Fig. S73. HPLC-MS data for purified 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one (19b):

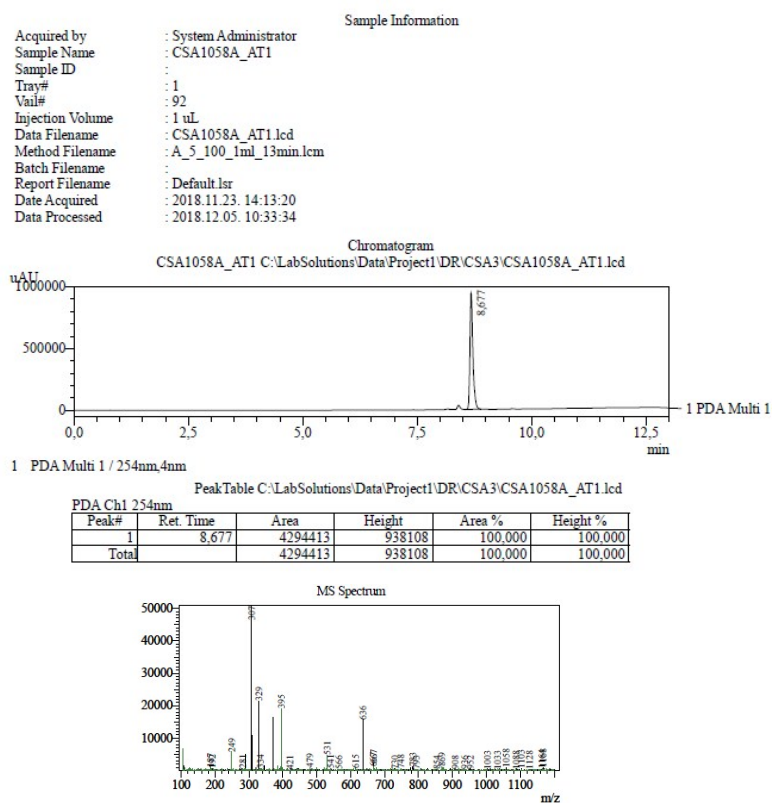


Fig. S74. HPLC-MS data for 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one (19b) by Method B:

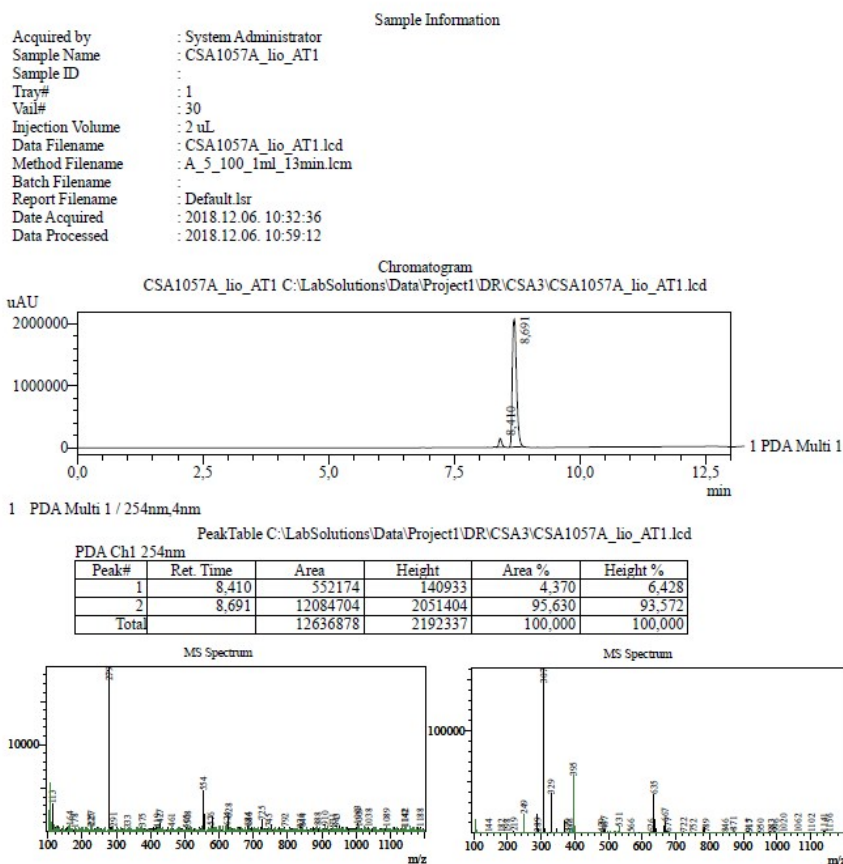


Fig. S75. HPLC-MS data for 6-(biphenyl-4-yl)pyridazin-3(2*H*)-one (19a) and 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)-pyridazin-3(2*H*)-one (19b) by Method B:

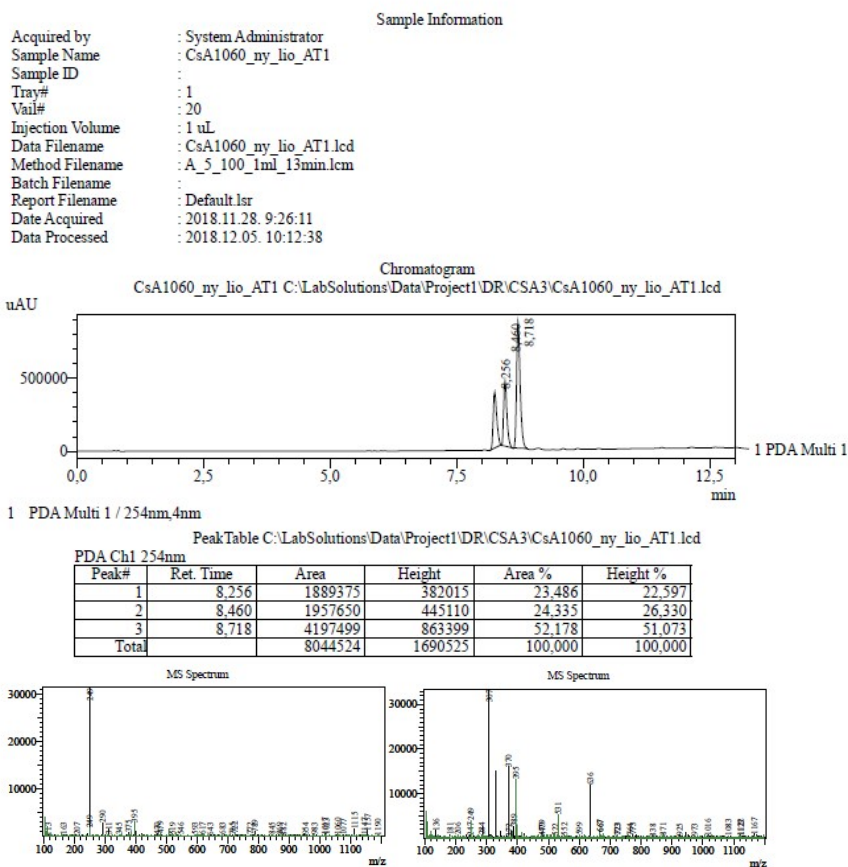


Fig. S76. HPLC-MS data for purified 6-(4-fluorophenyl)pyridazin-3(2H)-one (20a):

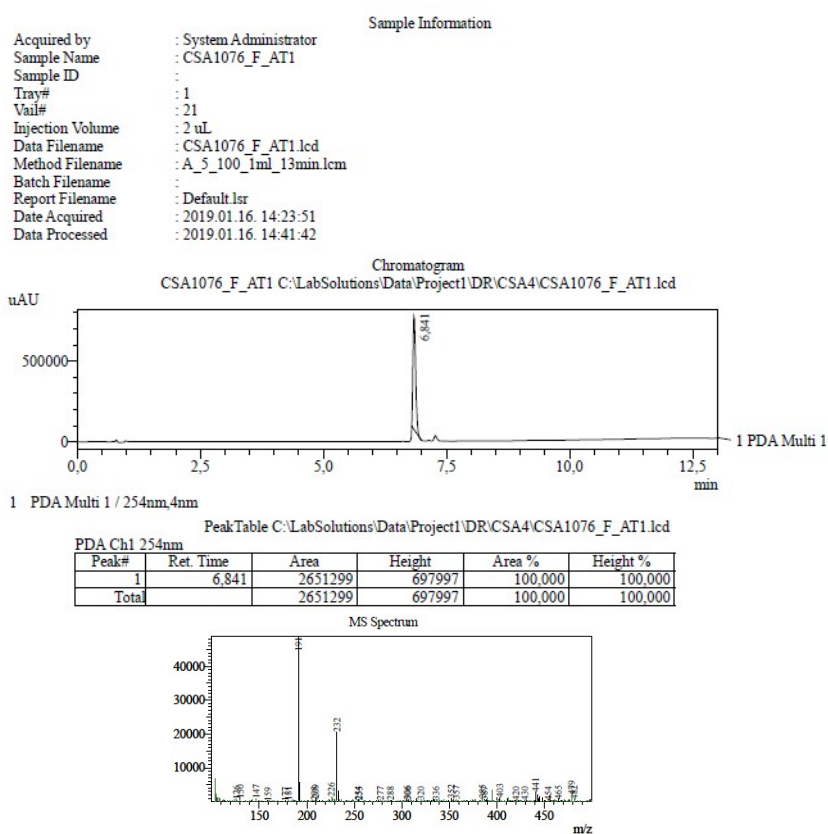


Fig. S77. HPLC-MS data for purified 6-(4-fluorophenyl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one (20b):

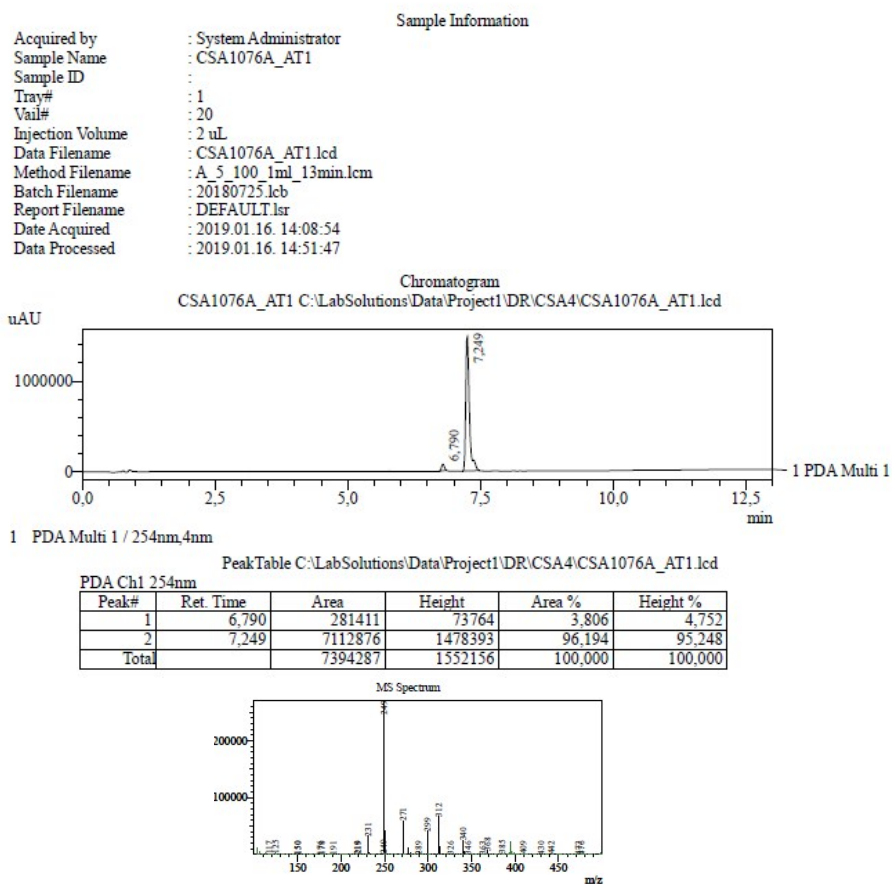


Fig. S78. HPLC-MS data for 6-(4-fluorophenyl)pyridazin-3(2*H*)-one (20a) and 6-(4-fluorophenyl)-2-(2-hydroxyprop-yl)pyridazin-3(2*H*)-one (20b) by Method A:

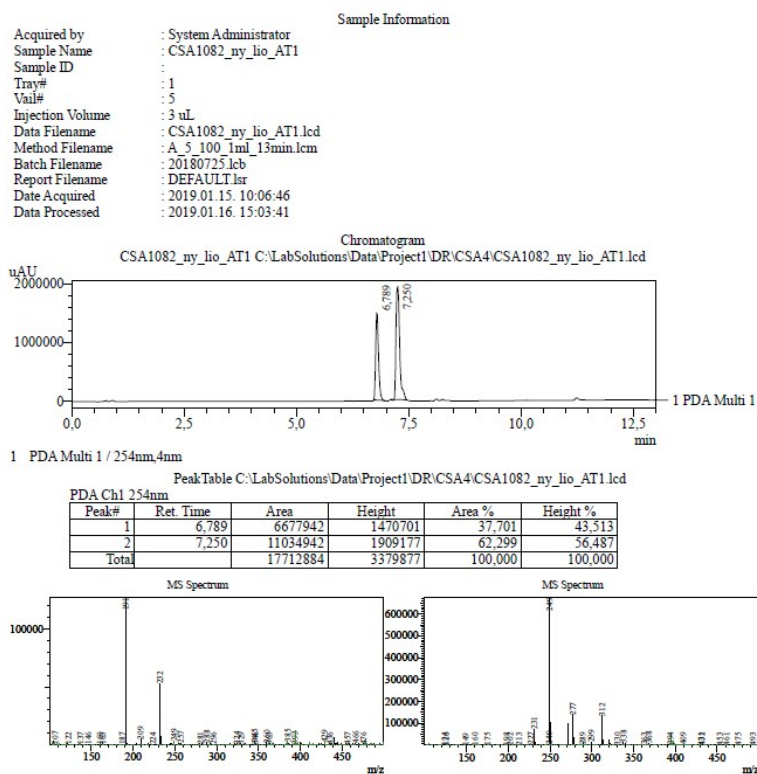


Fig. S79. HPLC-MS data for 6-(4-fluorophenyl)-2-(2-hydroxypropyl)pyridazin-3(2*H*)-one (20b) by Method B:

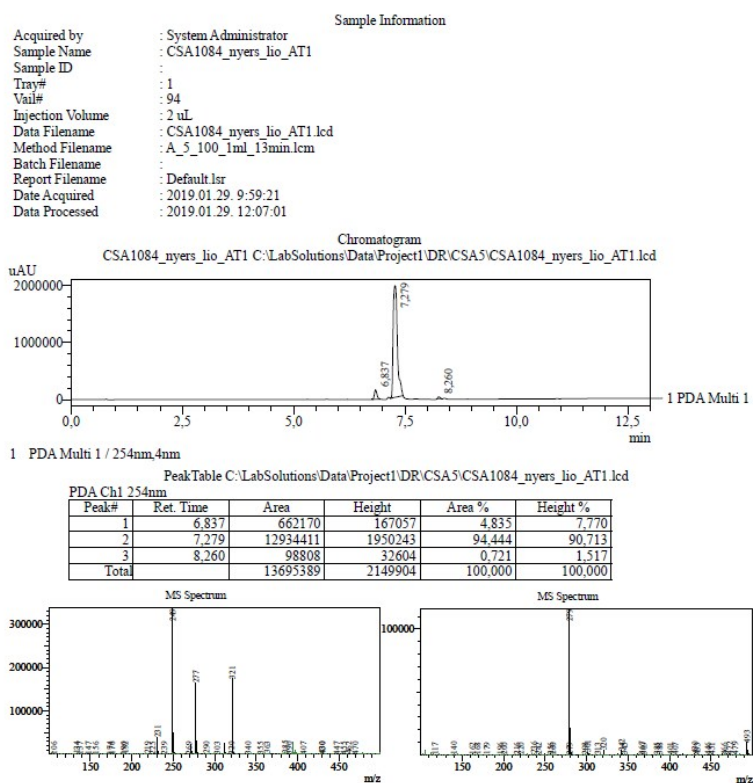


Fig. S80. HPLC-MS data for 6-(4-fluorophenyl)pyridazin-3(2*H*)-one (20a) and 6-(4-fluorophenyl)-2-(2-hydroxypropyl)pyridazin-3(2*H*)-one (20b) by Method B:

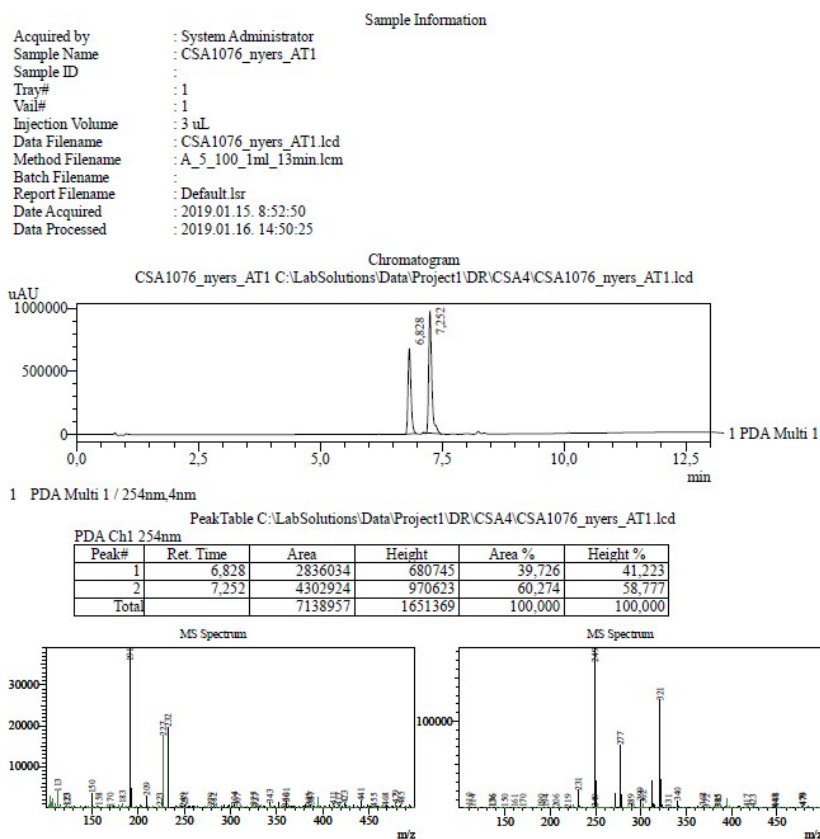


Fig. S81. HPLC-MS data for purified 2-(2-hydroxypropyl)-6-iodopyridazin-3(2*H*)-one (23):

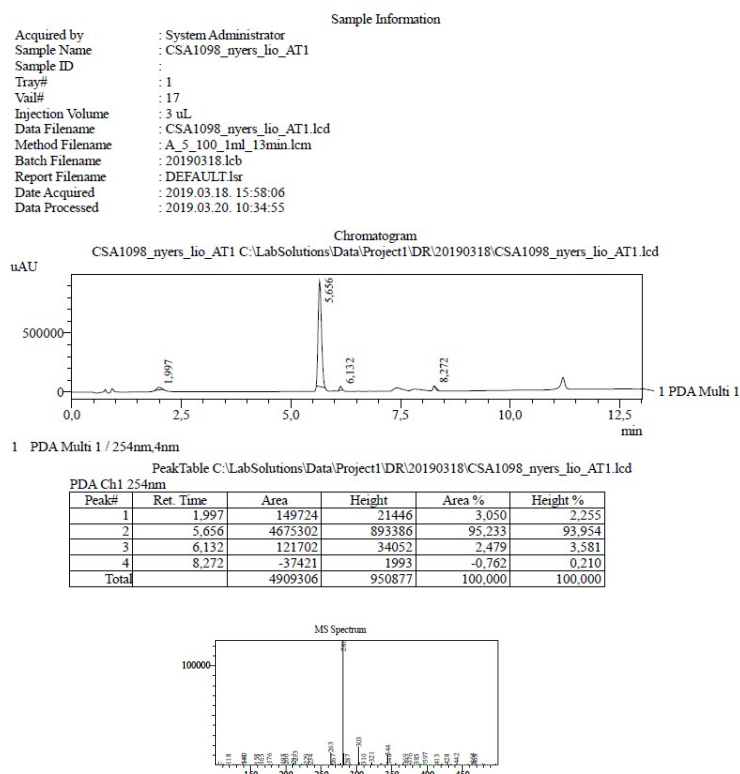


Fig. S82. HPLC-MS data for purified 2-(2-hydroxypropyl)-6-(naphthalene-2-yl)pyridazin-3(2*H*)-one (11b) obtained from 6-(naphthalene-2-yl)pyridazin-3(2*H*)-one (11a):

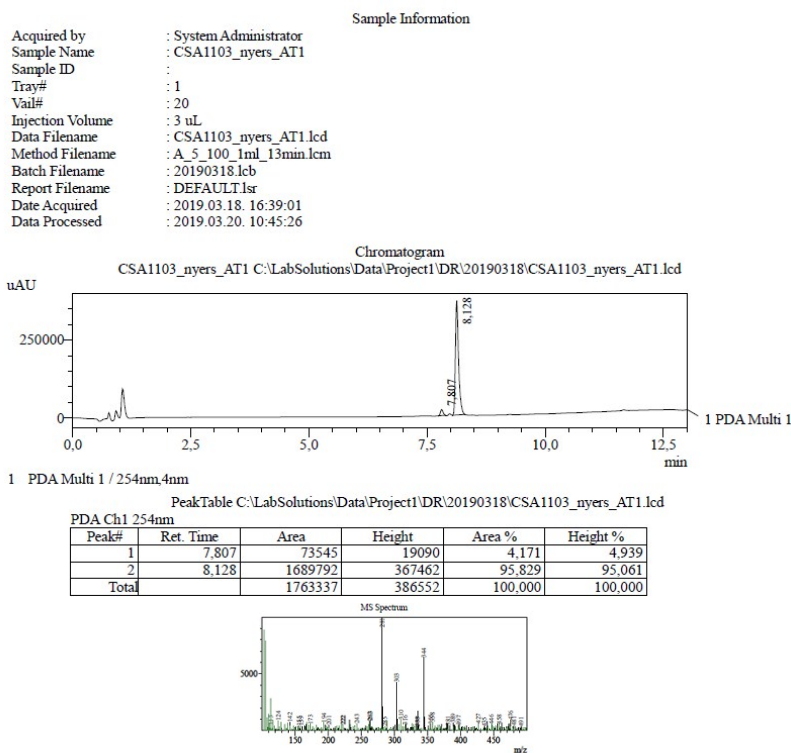


Fig. S83. ^1H NMR spectrum of 3,6-diiodopyridazine:

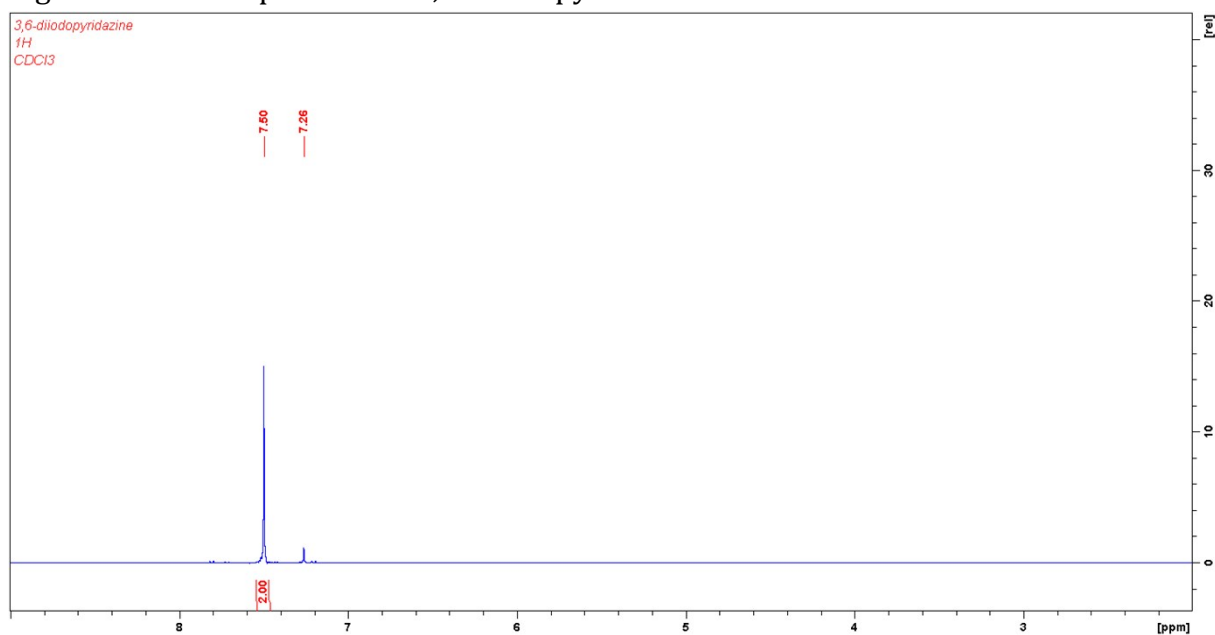


Fig. S84. ^{13}C NMR spectrum of 3,6-diiodopyridazine:

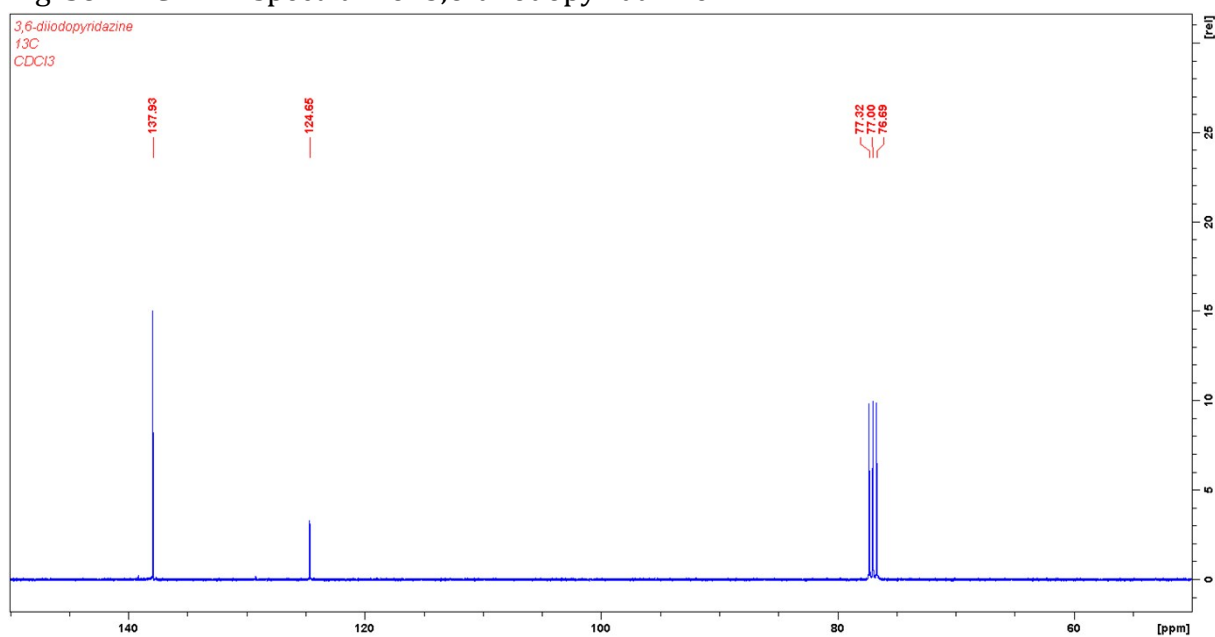


Fig. S85. ^1H NMR spectrum of (4): 6-iodopyridazin-3(2H)-one

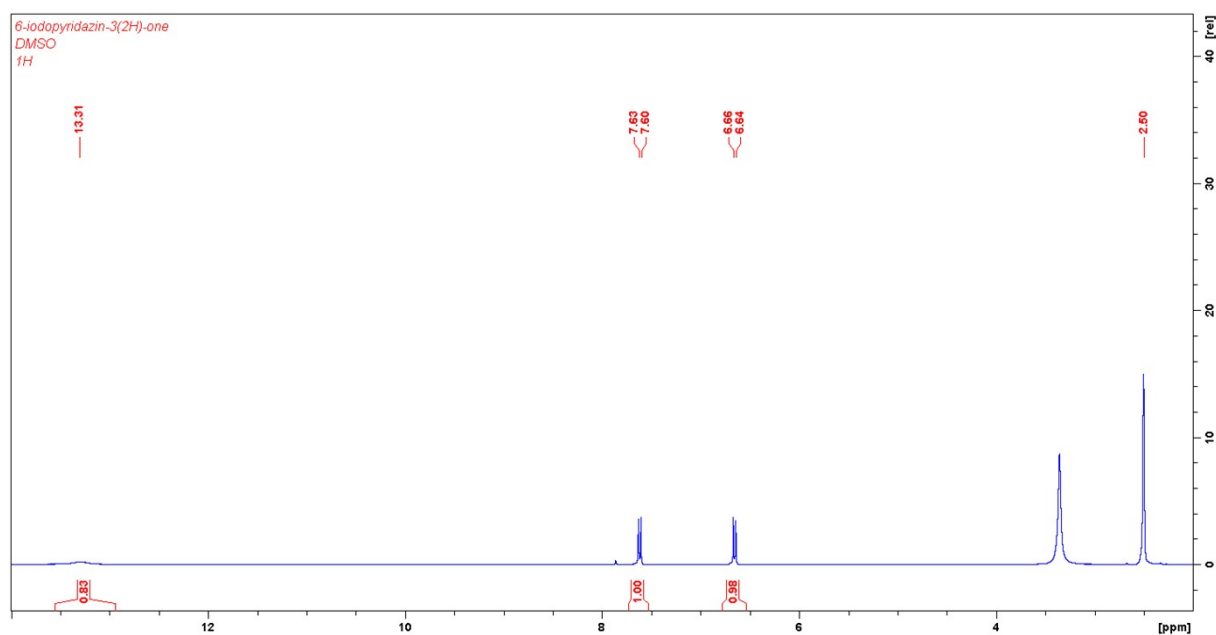


Fig. S86. ^{13}C NMR spectrum of (4): 6-iodopyridazin-3(2H)-one

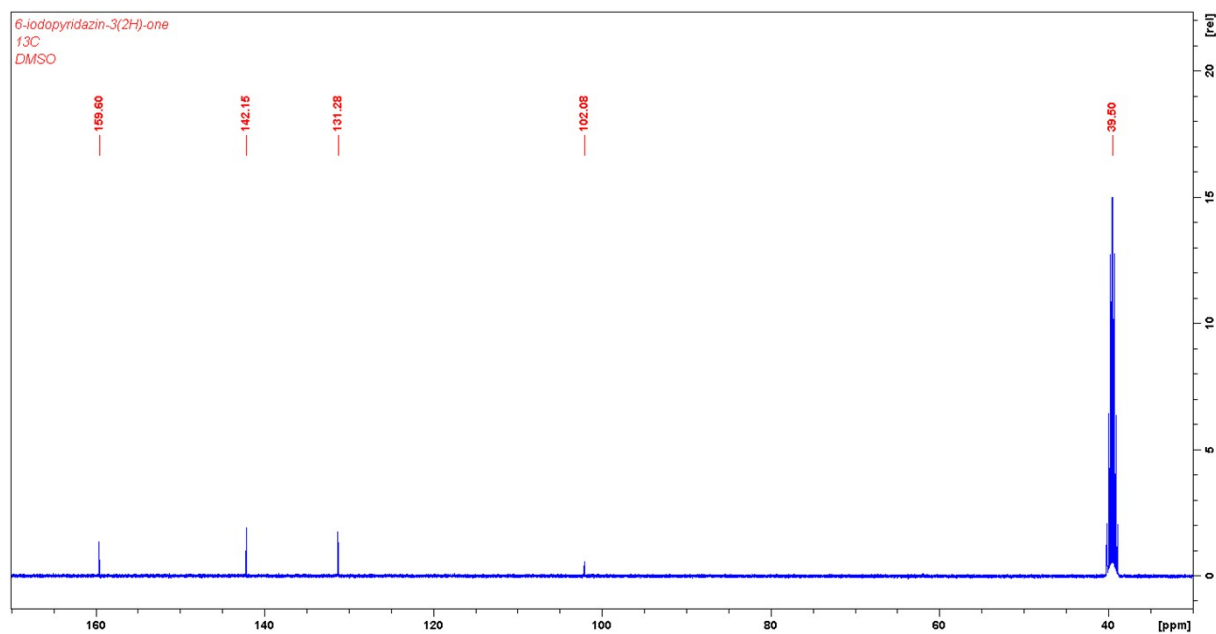


Fig. S87. ^1H NMR spectrum of (9): 2-(naphthalen-2-yl)pyridine

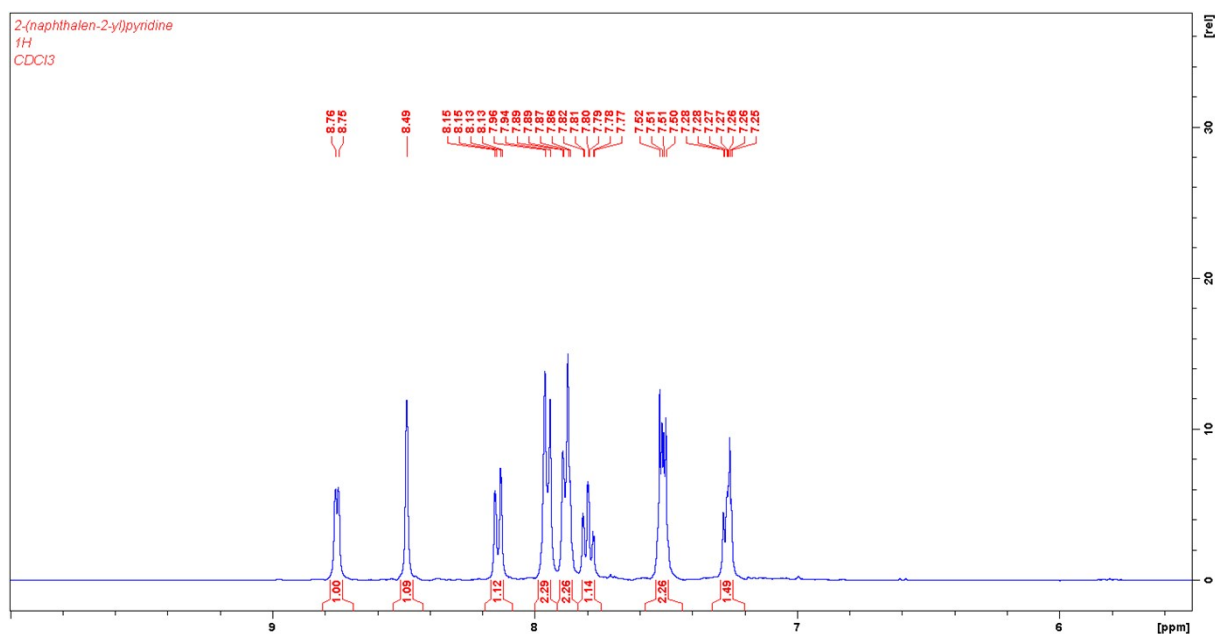
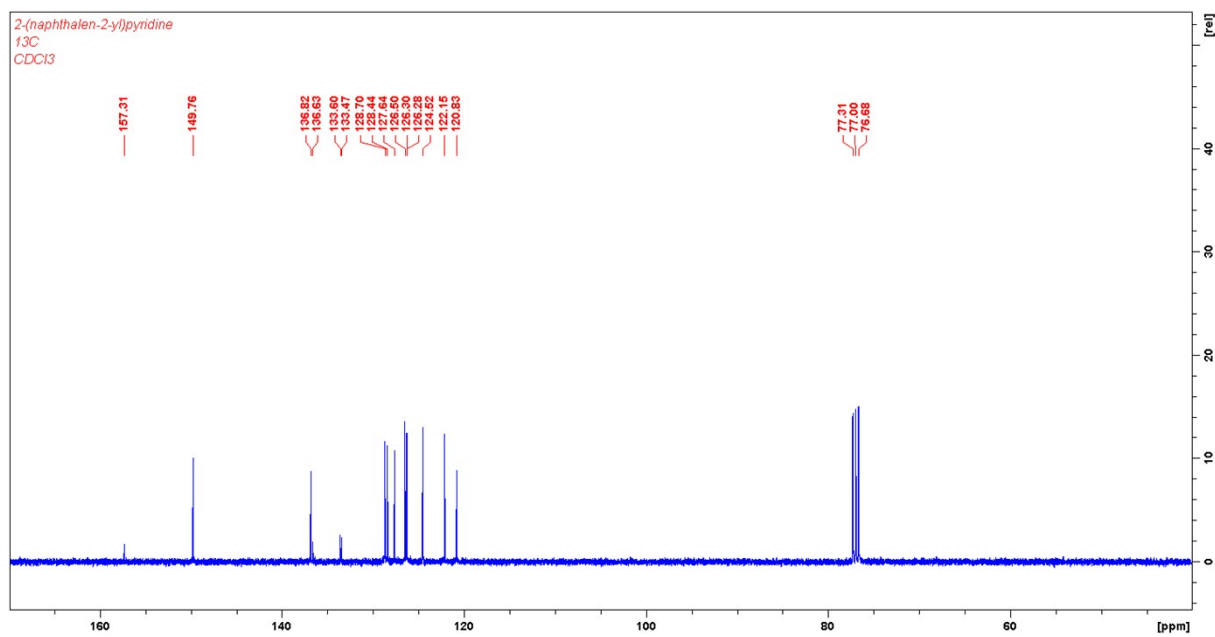


Fig. S88. ^{13}C NMR spectrum of (9): 2-(naphthalen-2-yl)pyridine



4-(naphthalen-2-yl)pyridine
1H
CDC13

8.72, 8.12, 7.98, 7.95, 7.95, 7.94, 7.92, 7.89, 7.88, 7.76, 7.74, 7.74, 7.67, 7.65, 7.65, 7.65, 7.54, 7.26

1.85, 1.00, 3.09, 1.14, 2.66, 2.28

[ppm]

4-(naphthalen-2-yl)pyridine
¹³C
 CDCl₃

149.81
 148.63
 136.18
 133.42
 133.40
 128.89
 127.44
 127.71
 126.90
 126.73
 126.49
 124.46
 122.02
 77.32
 77.00
 76.68

[ppm]

Fig. S91. ^1H NMR spectrum of (11a): 6-(naphthalen-2-yl)pyridazin-3(2*H*)-one

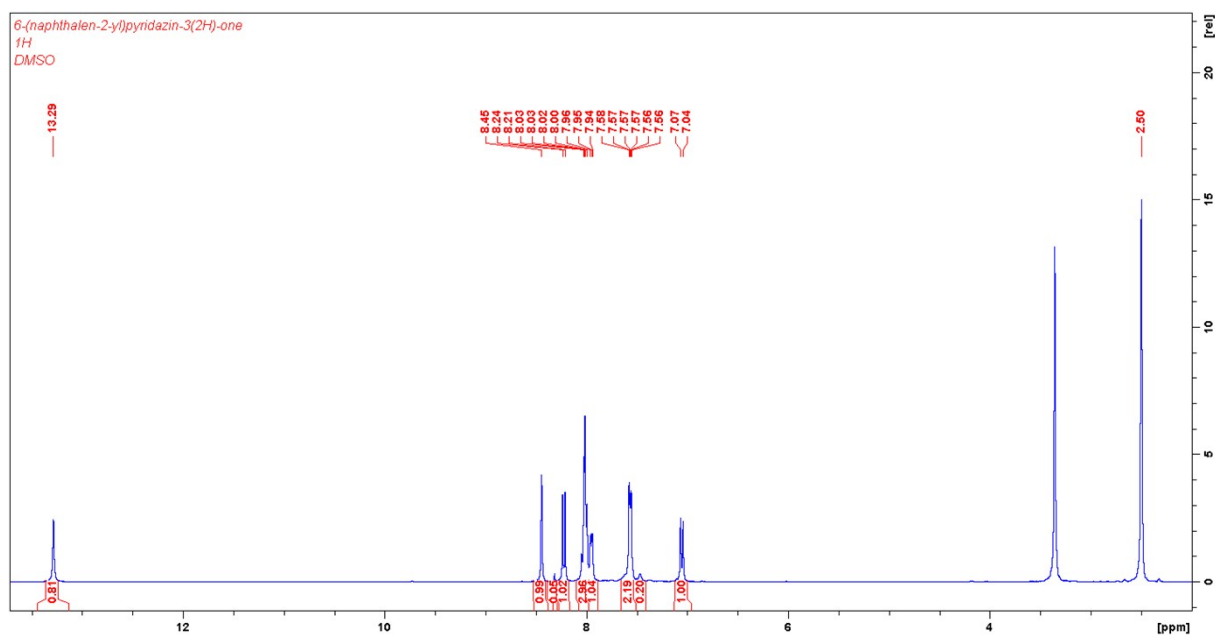


Fig. S92. ^{13}C NMR spectrum of (11a): 6-(naphthalen-2-yl)pyridazin-3(2*H*)-one

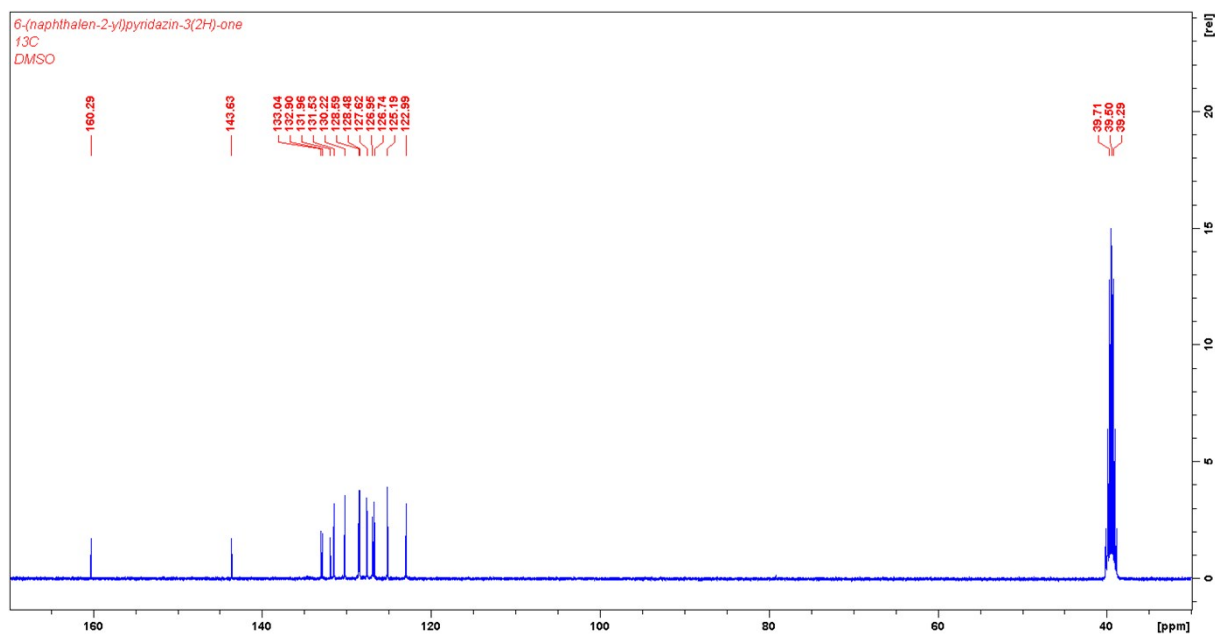


Fig. S93. ^1H NMR spectrum of (11b): 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2H)-one

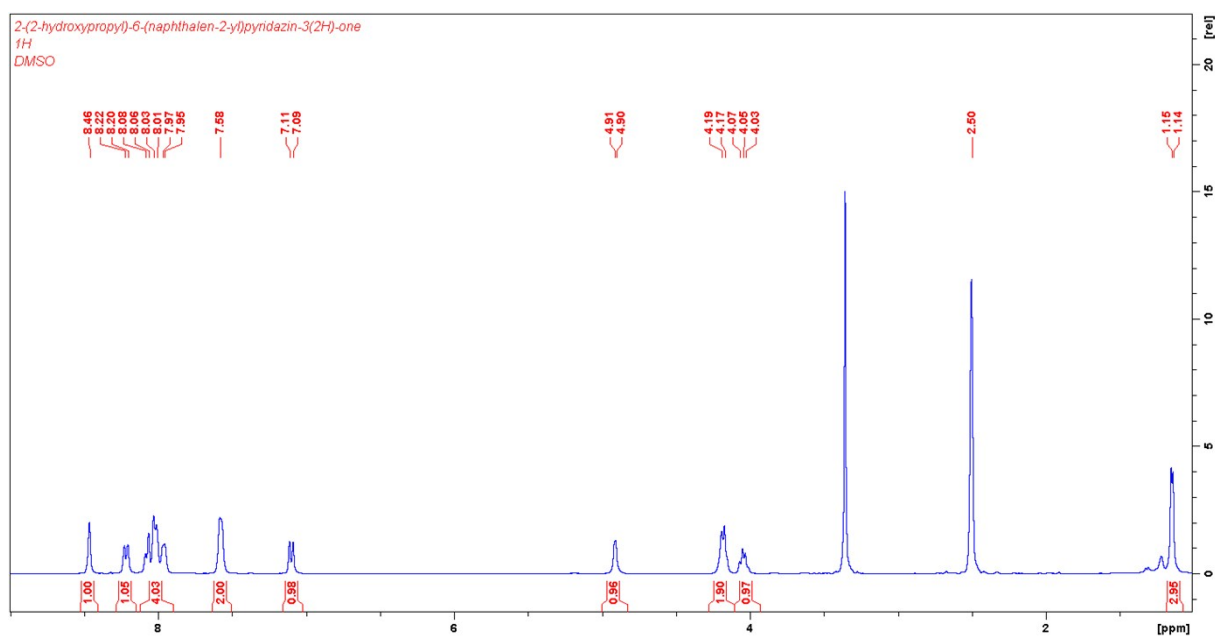


Fig. S94. ^{13}C NMR spectrum of (11b): 2-(2-hydroxypropyl)-6-(naphthalen-2-yl)pyridazin-3(2H)-one

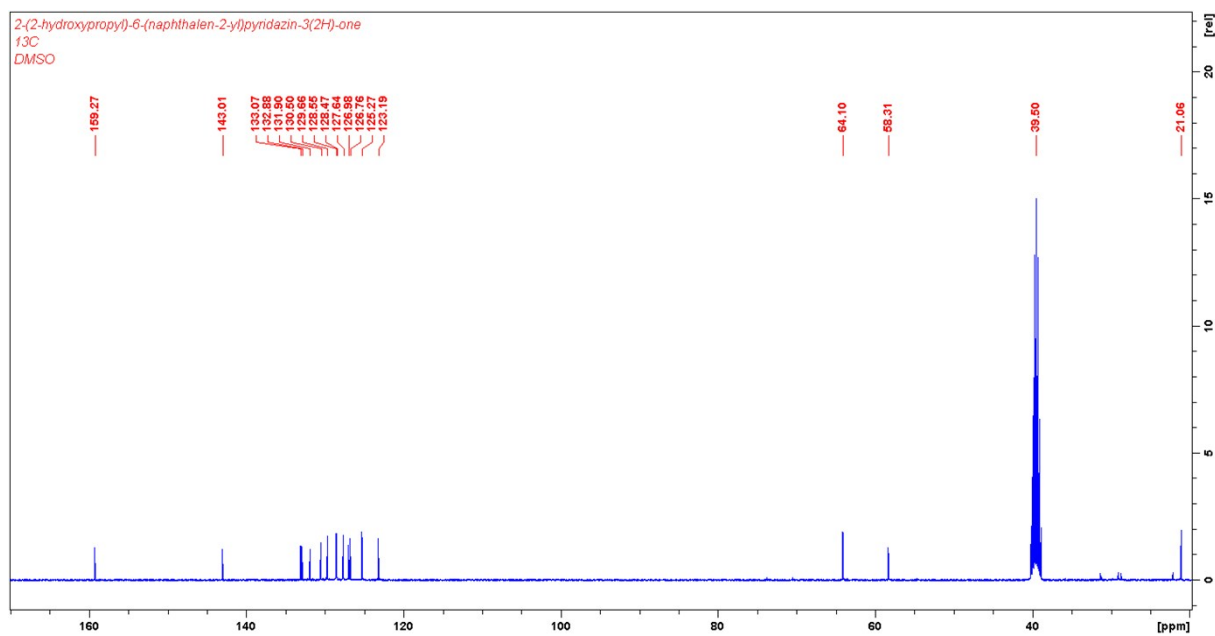


Fig. S95. ^1H NMR spectrum of (12): 2-phenylpyridine

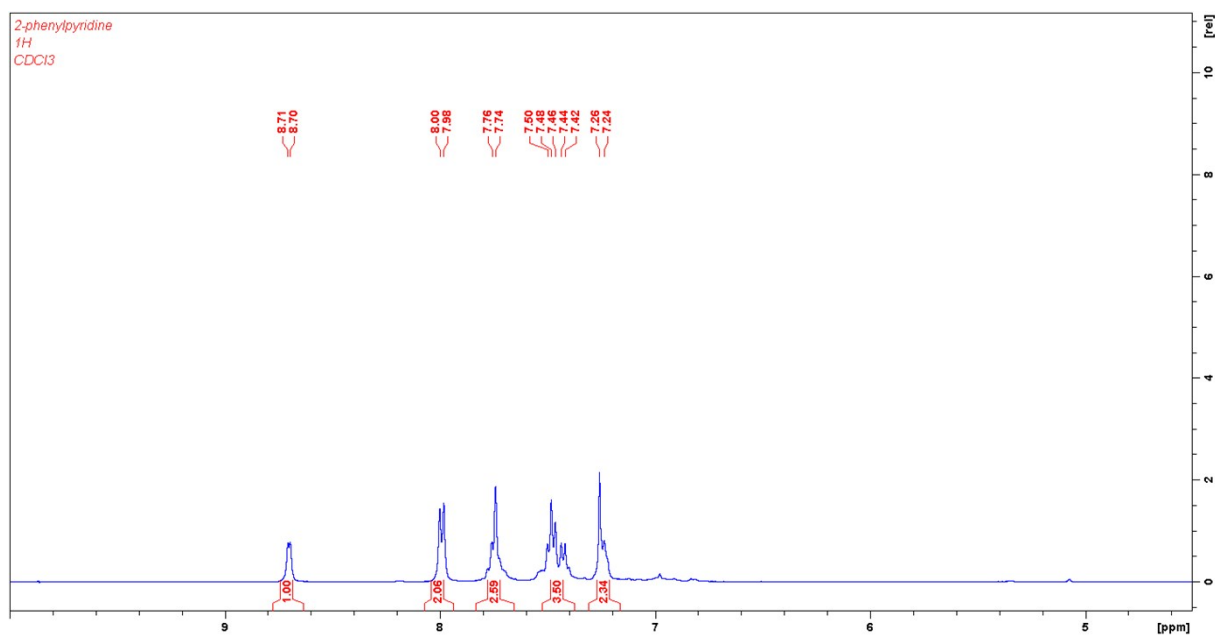


Fig. S96. ^{13}C NMR spectrum of (12): 2-phenylpyridine

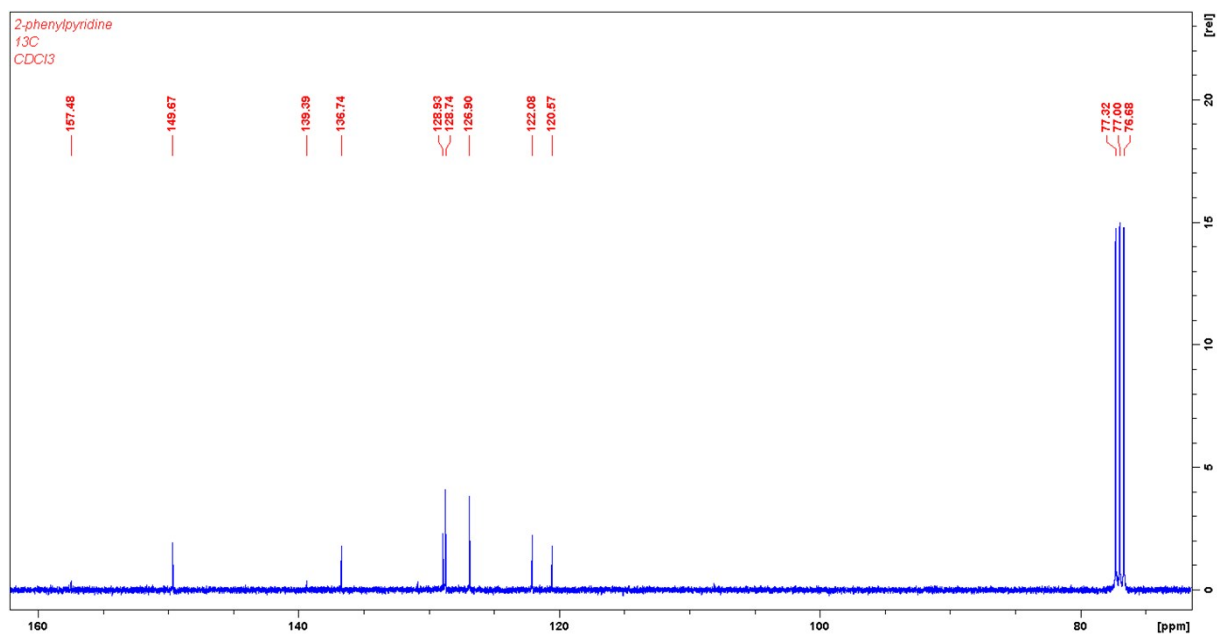


Fig. S97. ^1H NMR spectrum of (13): 4-phenylpyridine

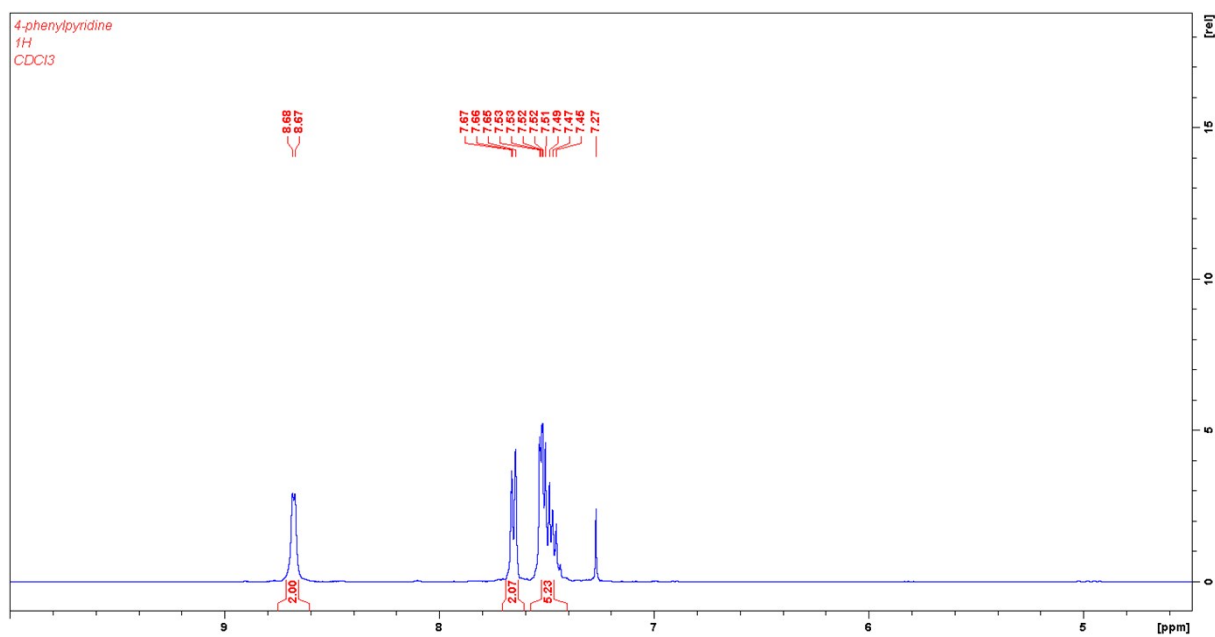


Fig. S98. ^{13}C NMR spectrum of (13): 4-phenylpyridine

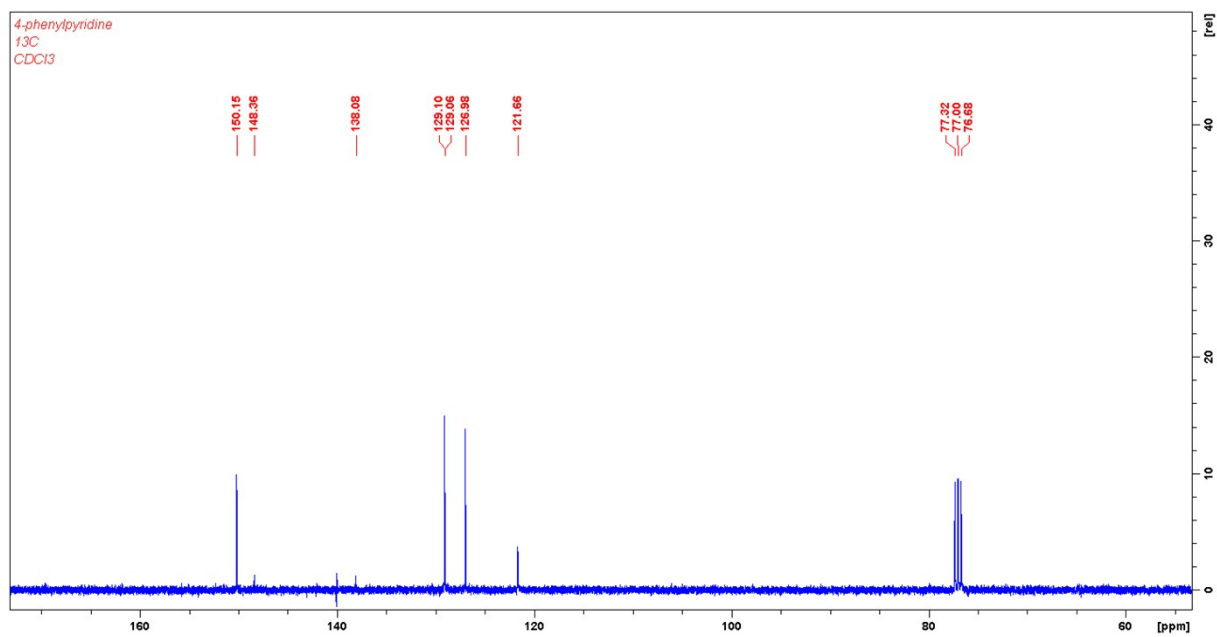


Fig. S99. ^1H NMR spectrum of (14): 2-(biphenyl-4-yl)pyridine

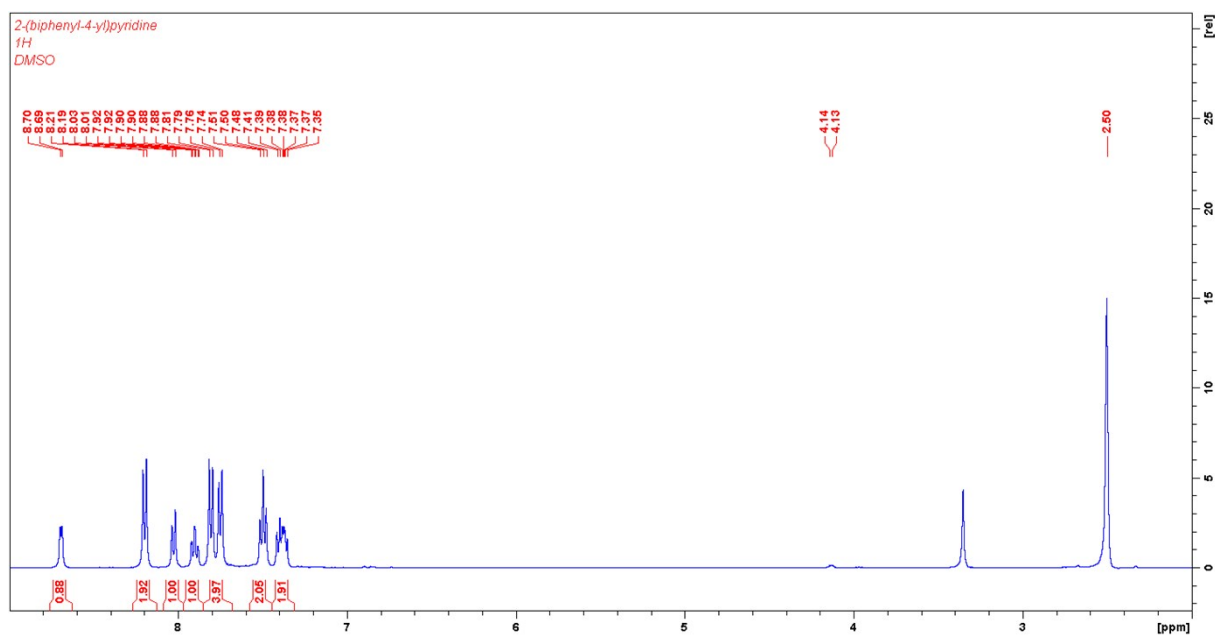


Fig. S100. ^{13}C NMR spectrum of (14): 2-(biphenyl-4-yl)pyridine

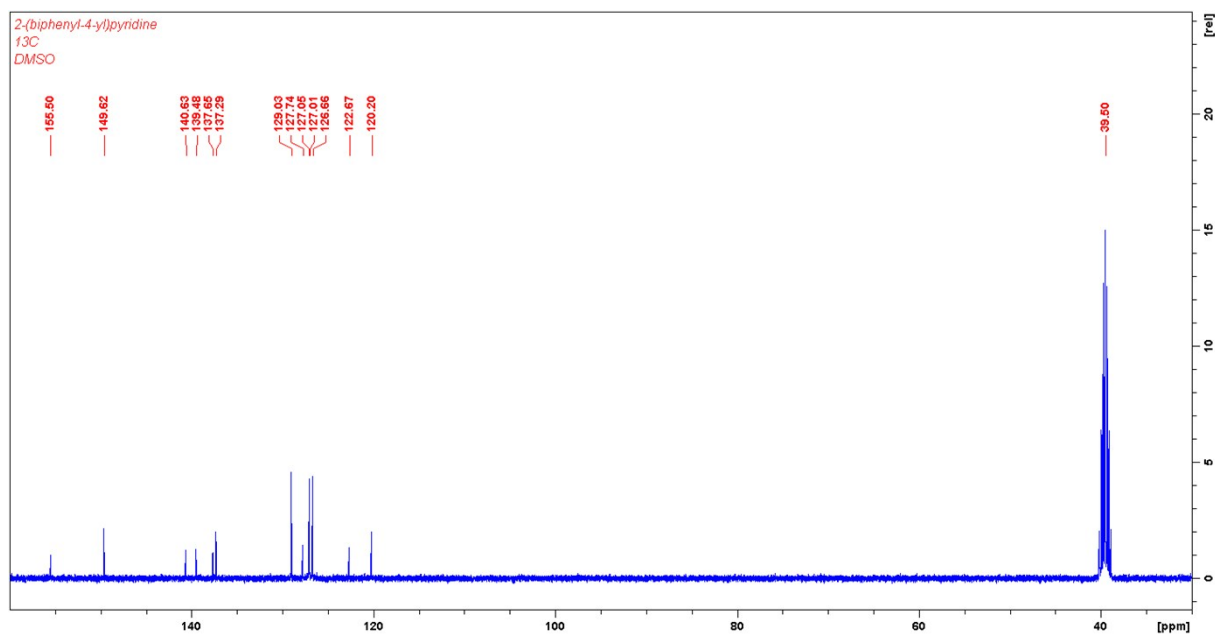


Fig. S101. ^1H NMR spectrum of (15): 4-(biphenyl-4-yl)pyridine

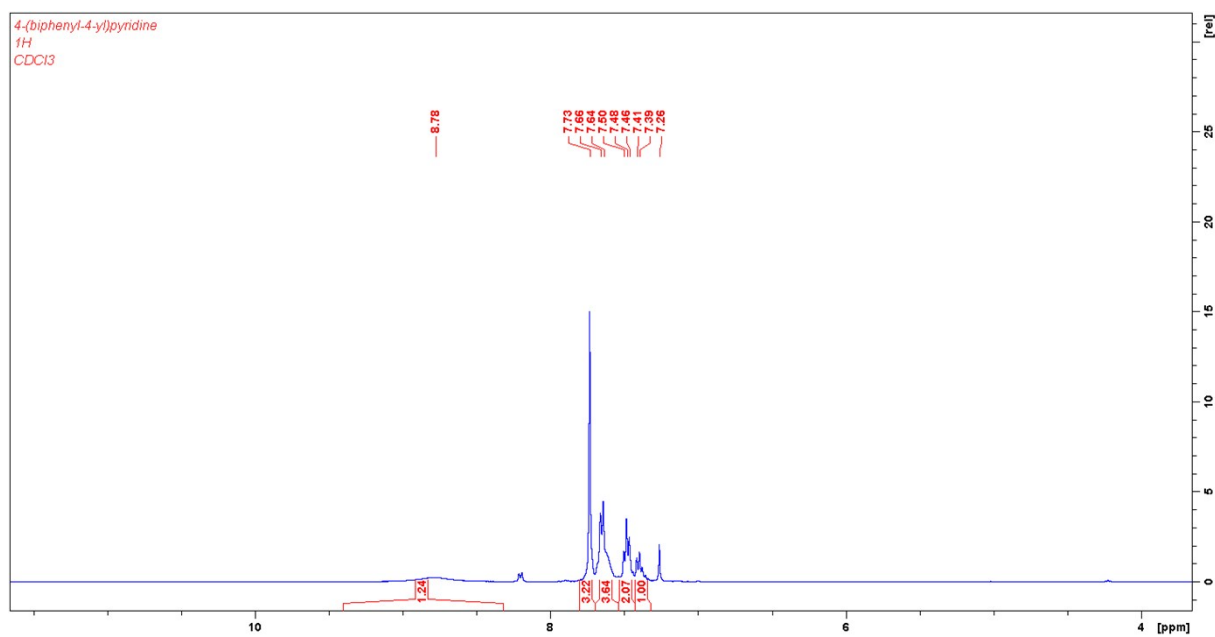


Fig. S102. ^{13}C NMR spectrum of (15): 4-(biphenyl-4-yl)pyridine

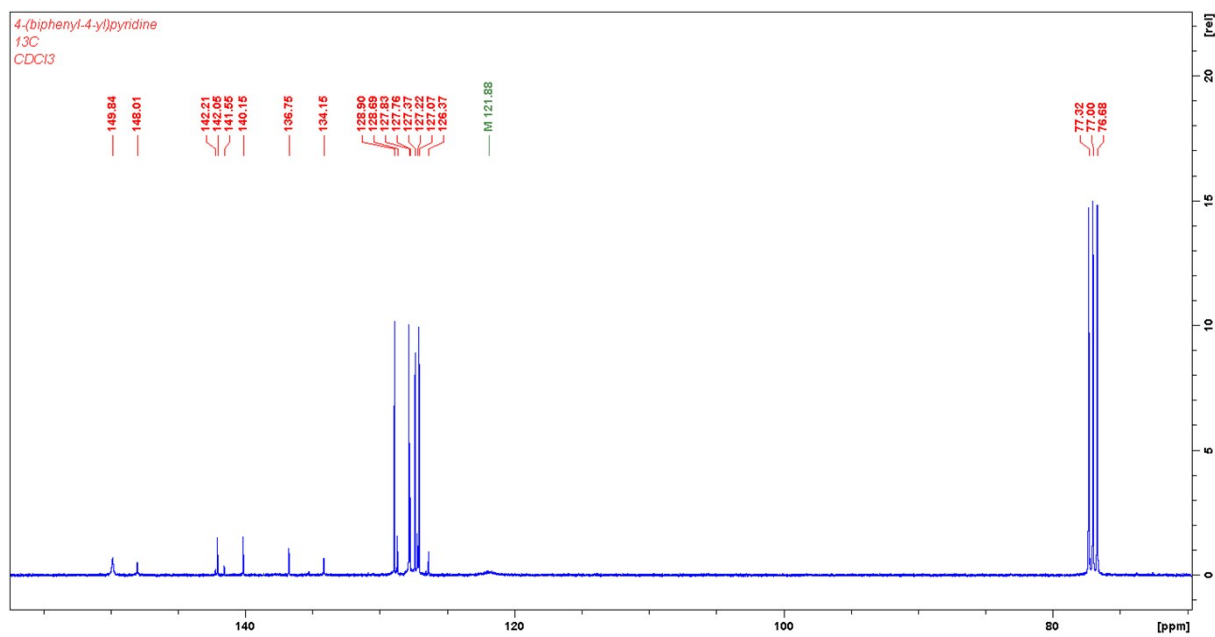


Fig. S103. ^1H NMR spectrum of (16): 2-(4-fluorophenyl)pyridine

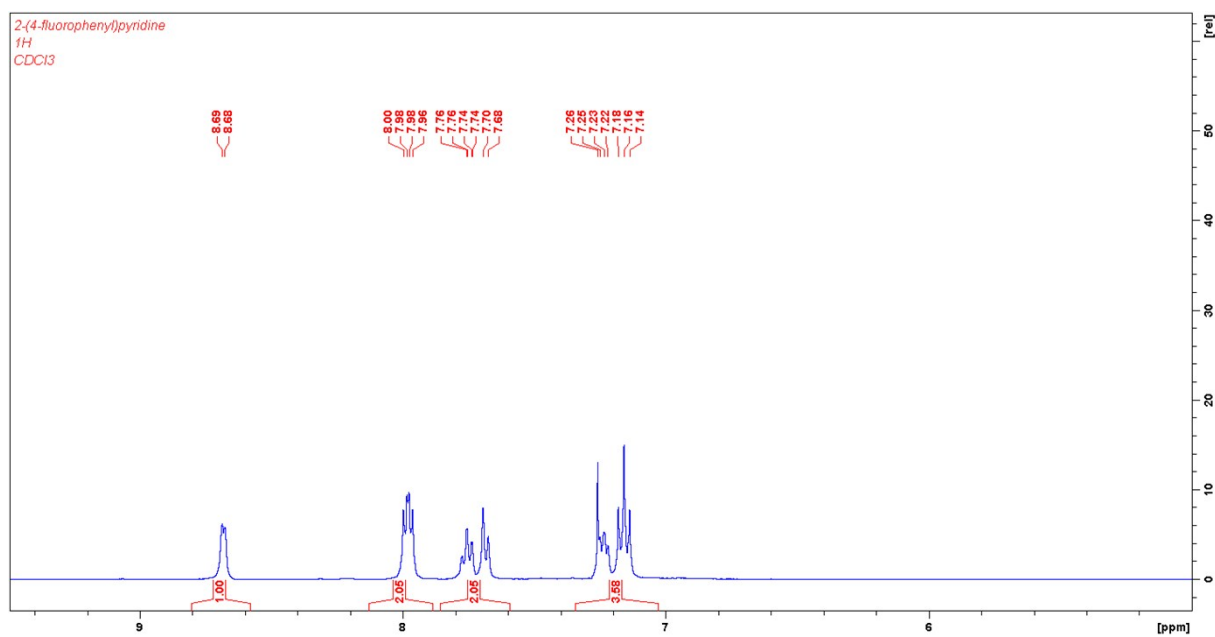


Fig. S104. ^{13}C NMR spectrum of (16): 2-(4-fluorophenyl)pyridine

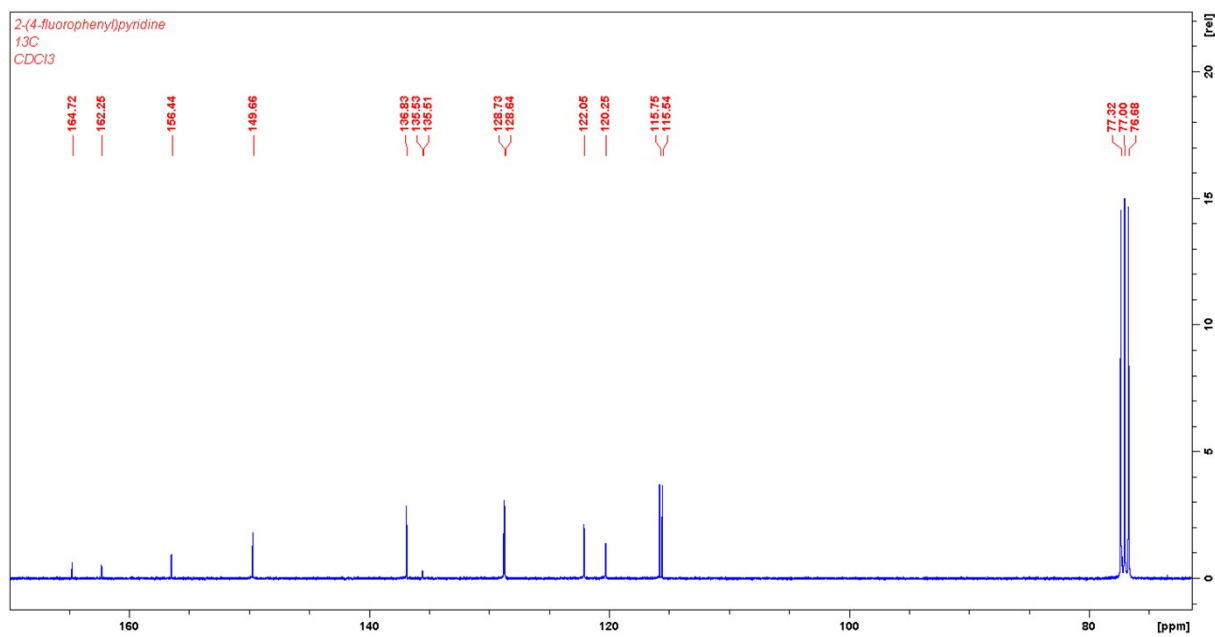


Fig. S105. ^1H NMR spectrum of (17): 4-(4-fluorophenyl)pyridine

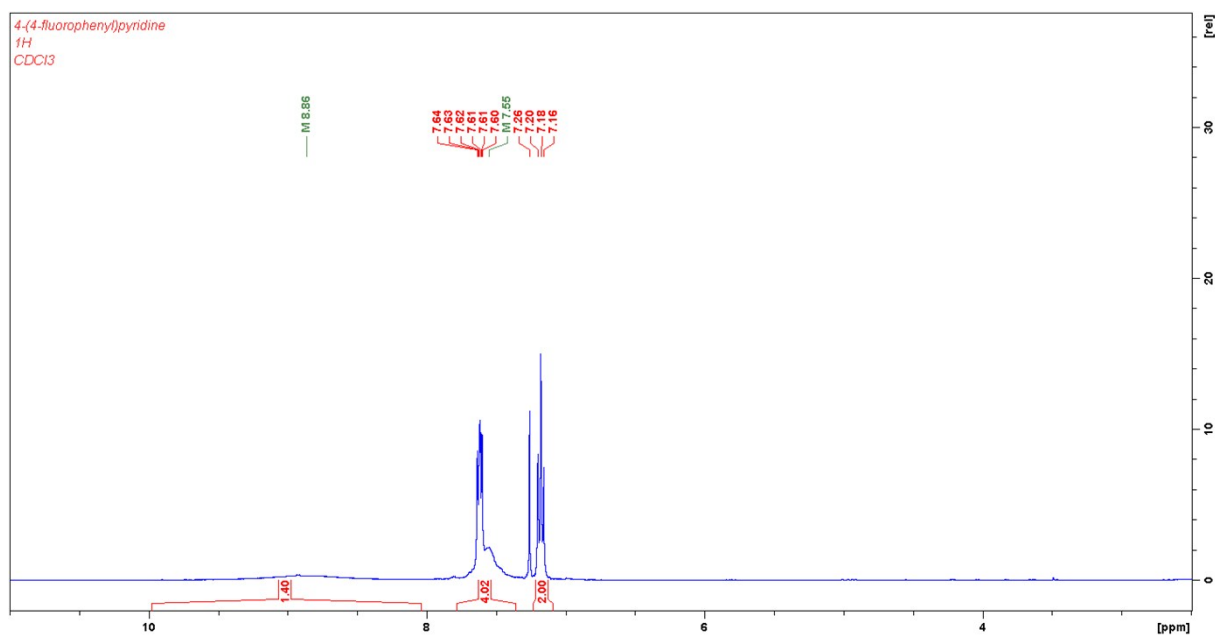


Fig. S106. ^{13}C NMR spectrum of (17): 4-(4-fluorophenyl)pyridine

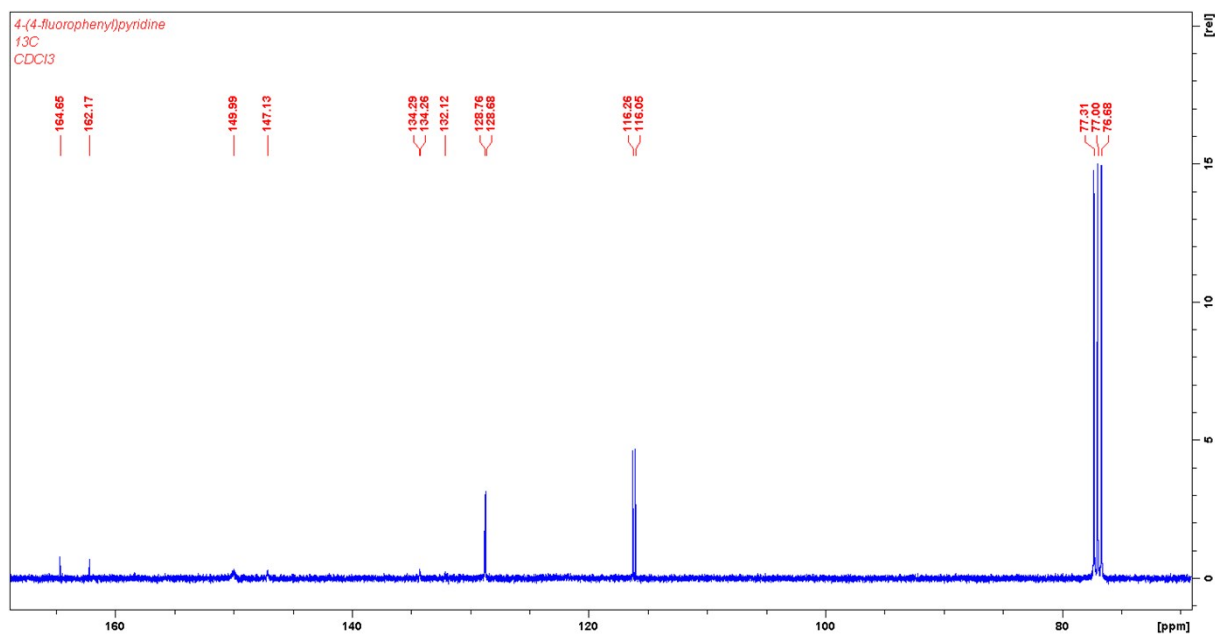


Fig. S107. ^1H NMR spectrum of (18a): 6-phenylpyridazin-3(2H)-one

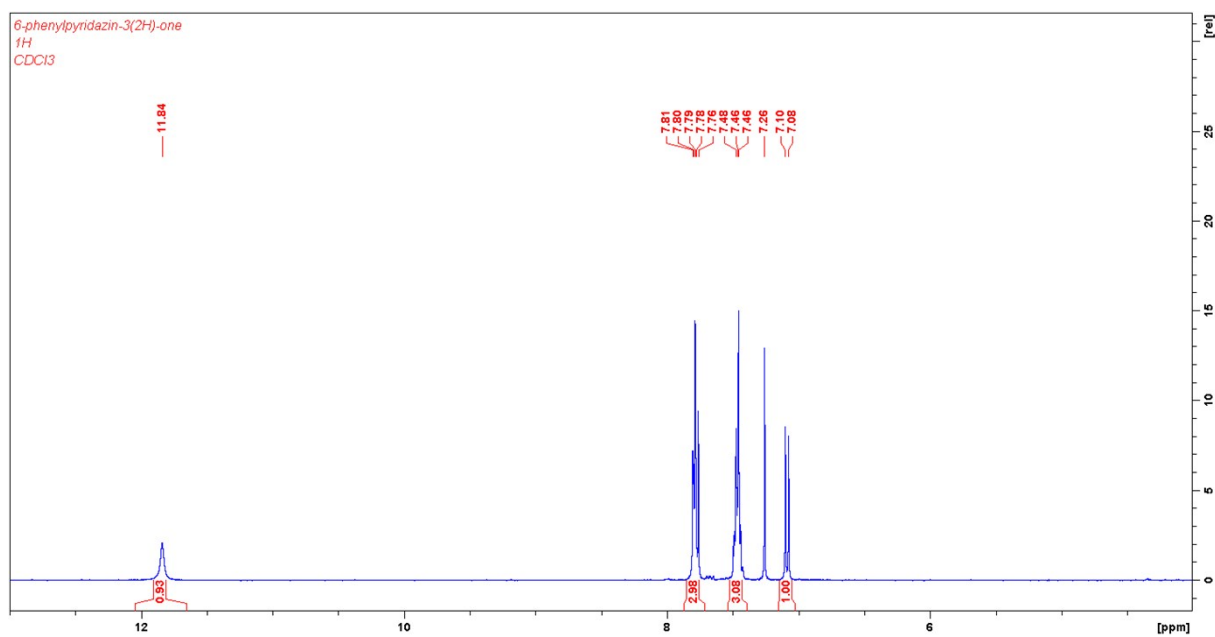


Fig. S108. ^{13}C NMR spectrum of (18a): 6-phenylpyridazin-3(2H)-one

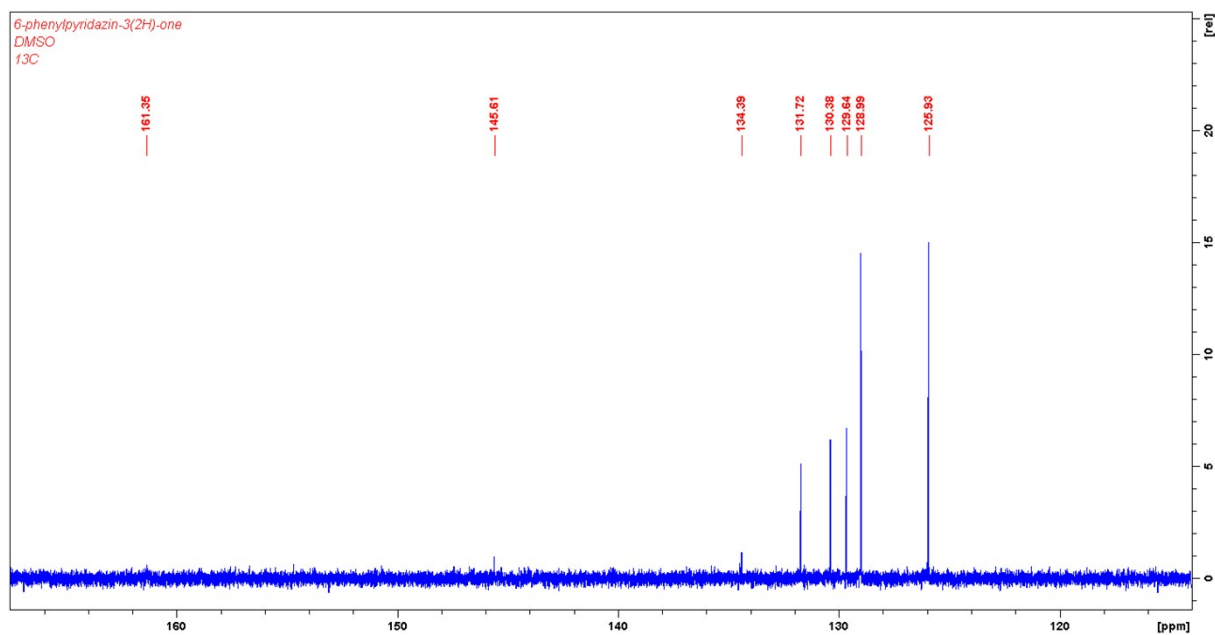


Fig. S109. ^1H NMR spectrum of (18b): 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2H)-one

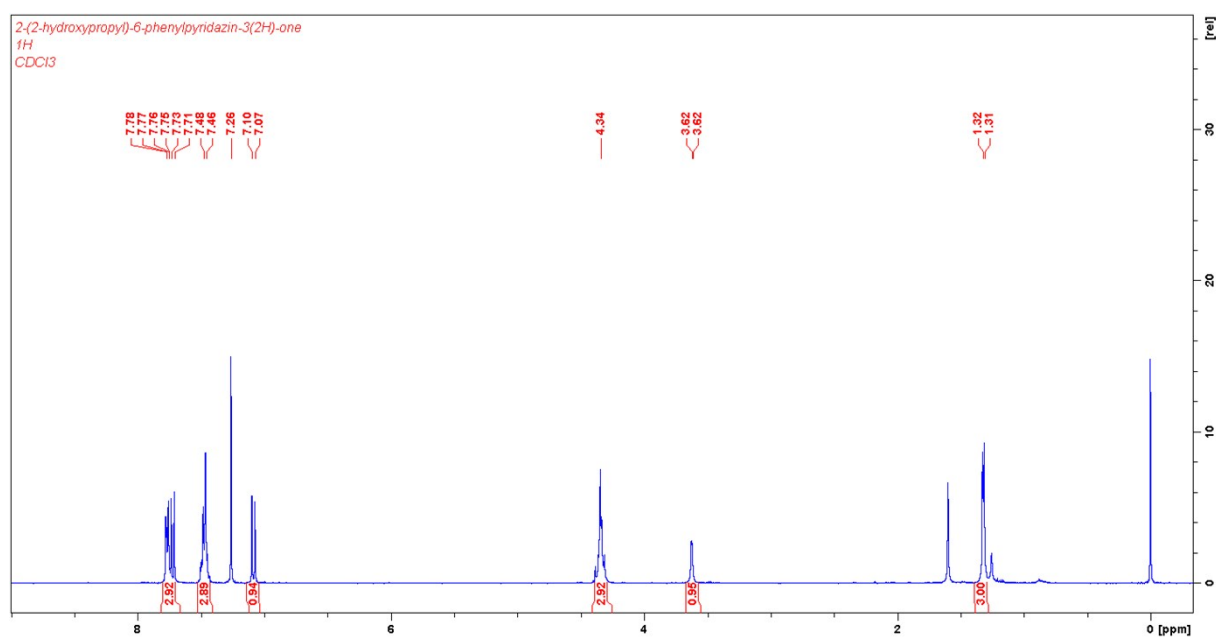


Fig. S110. ^{13}C NMR spectrum of (18b): 2-(2-hydroxypropyl)-6-phenylpyridazin-3(2H)-one

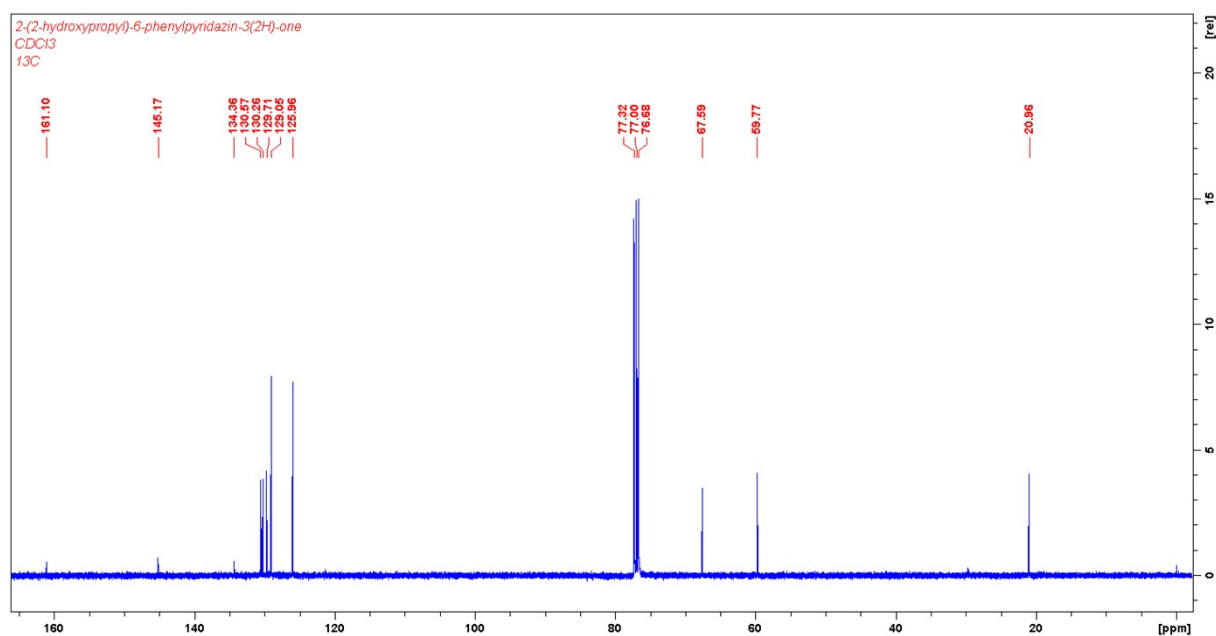


Fig. S111. ^1H NMR spectrum of (19a): 6-(biphenyl-4-yl)pyridazin-3(2H)-one

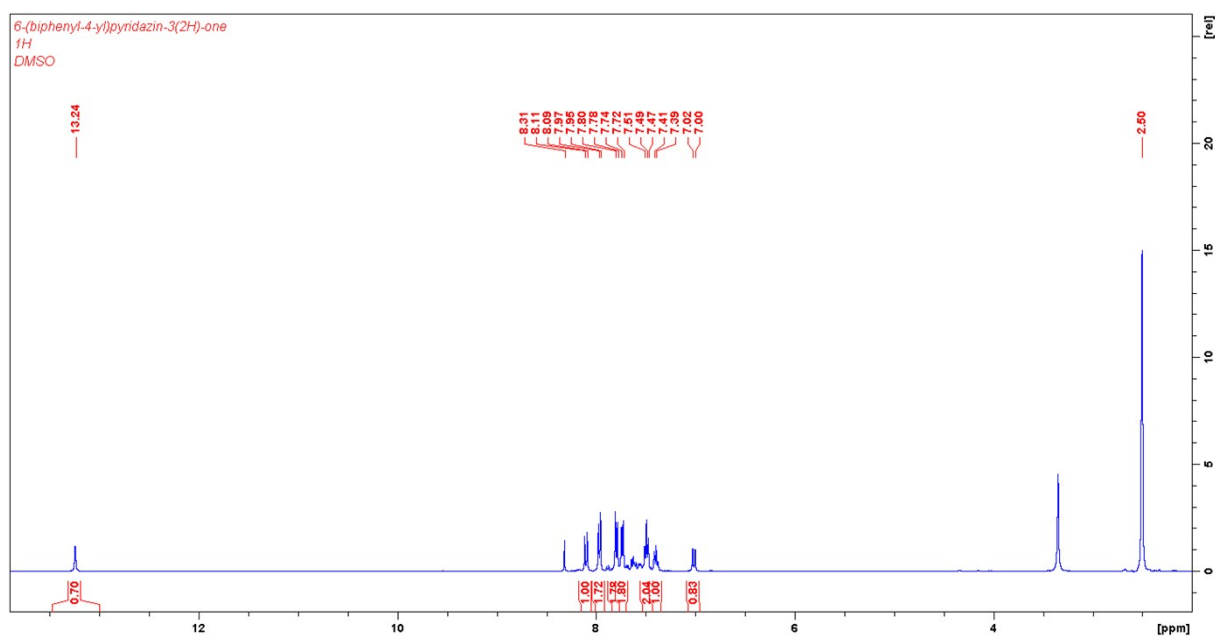


Fig. S112. ^{13}C NMR spectrum of (19a): 6-(biphenyl-4-yl)pyridazin-3(2H)-one

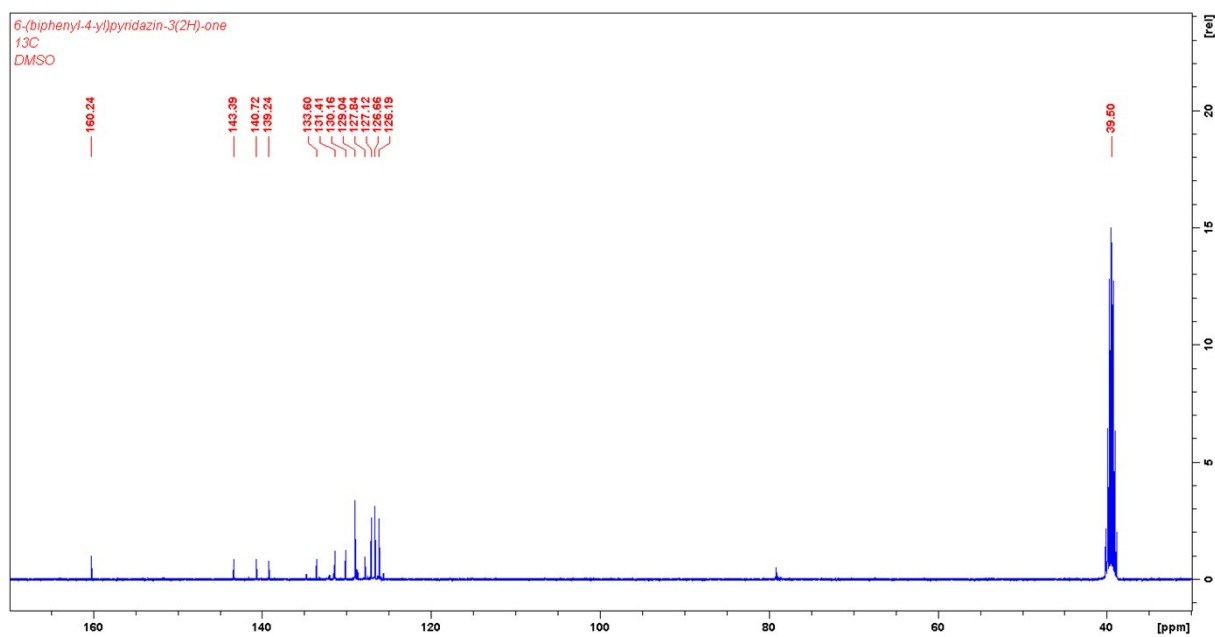


Fig. S113. ^1H NMR spectrum of (19b): 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one

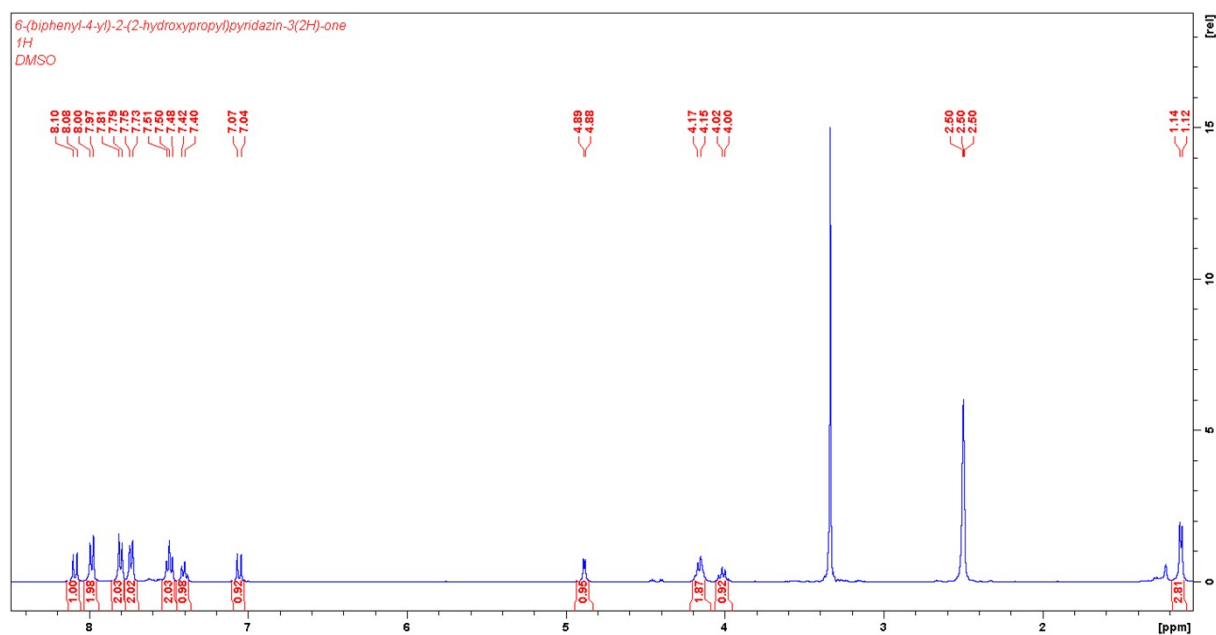


Fig. S114. ^{13}C NMR spectrum of (19b): 6-(biphenyl-4-yl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one

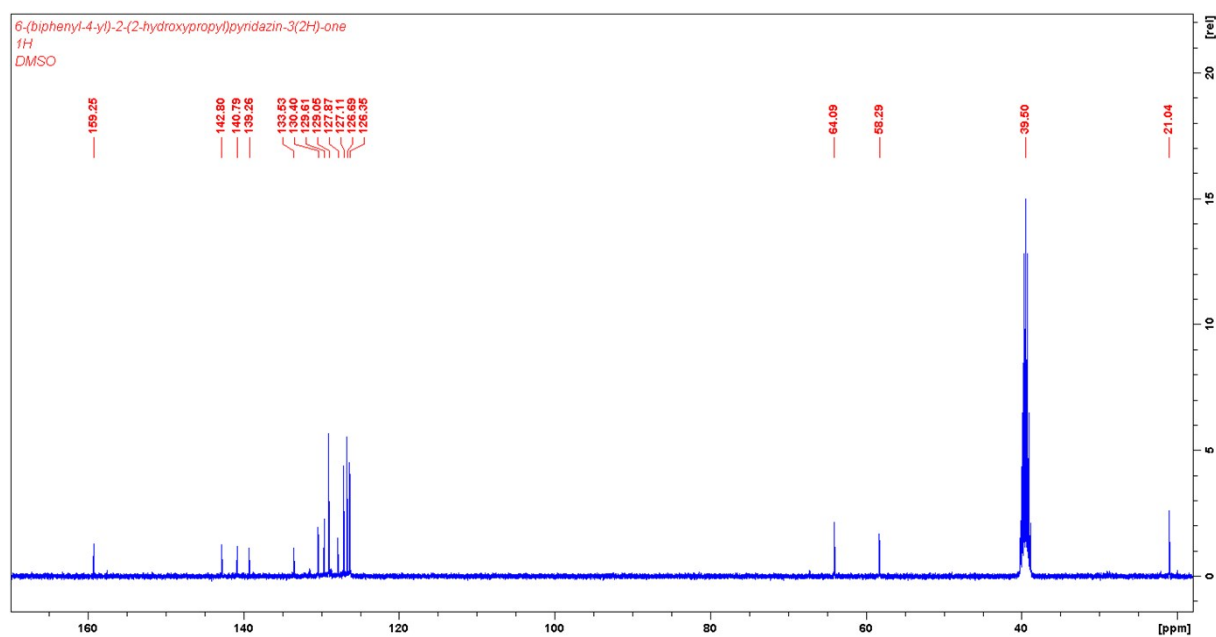


Fig. S115. ^1H NMR spectrum of (20a): 6-(4-fluorophenyl)pyridazin-3(2H)-one

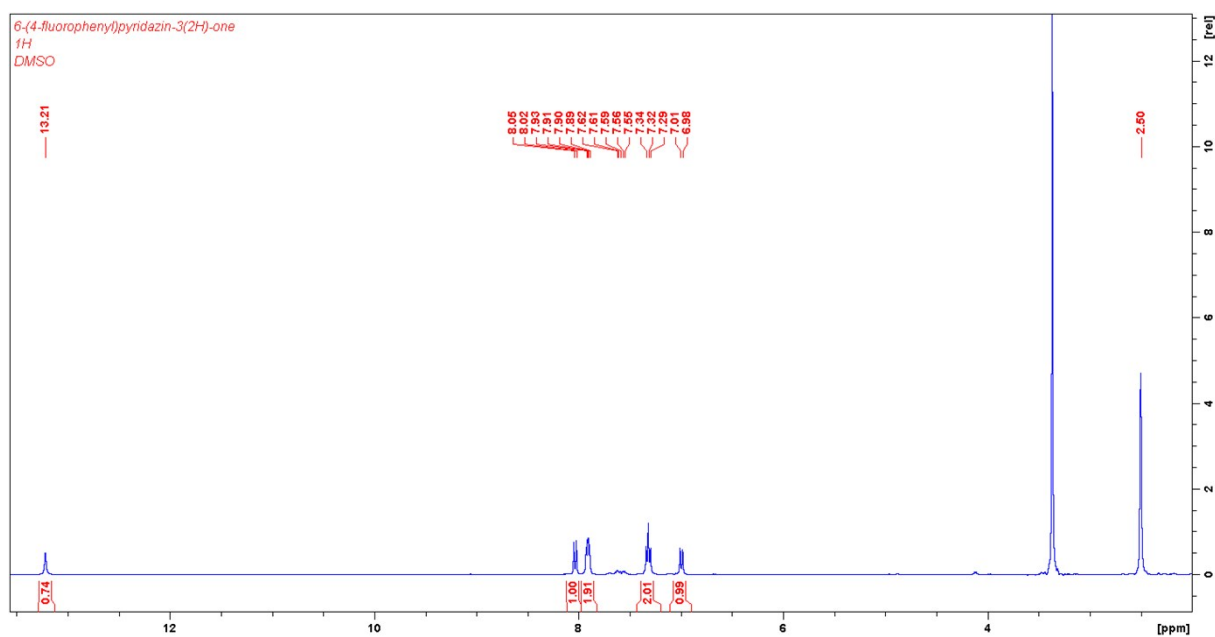


Fig. S116. ^{13}C NMR spectrum of (20a): 6-(4-fluorophenyl)pyridazin-3(2H)-one

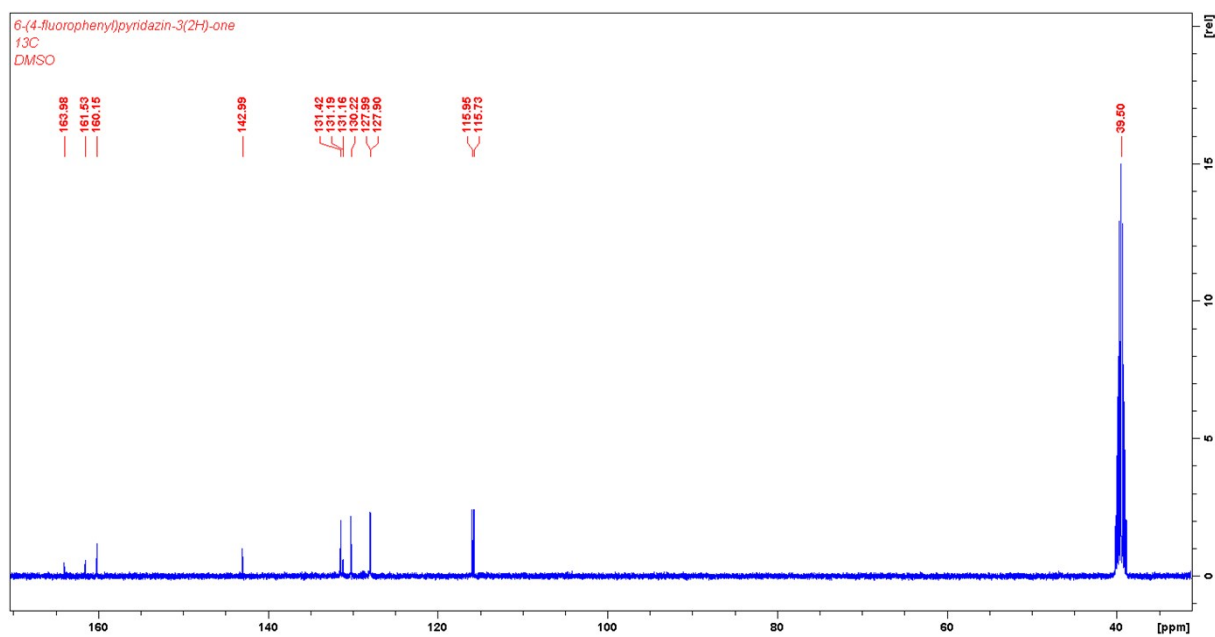


Fig. S117. ^1H NMR spectrum of (20b): 6-(4-fluorophenyl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one

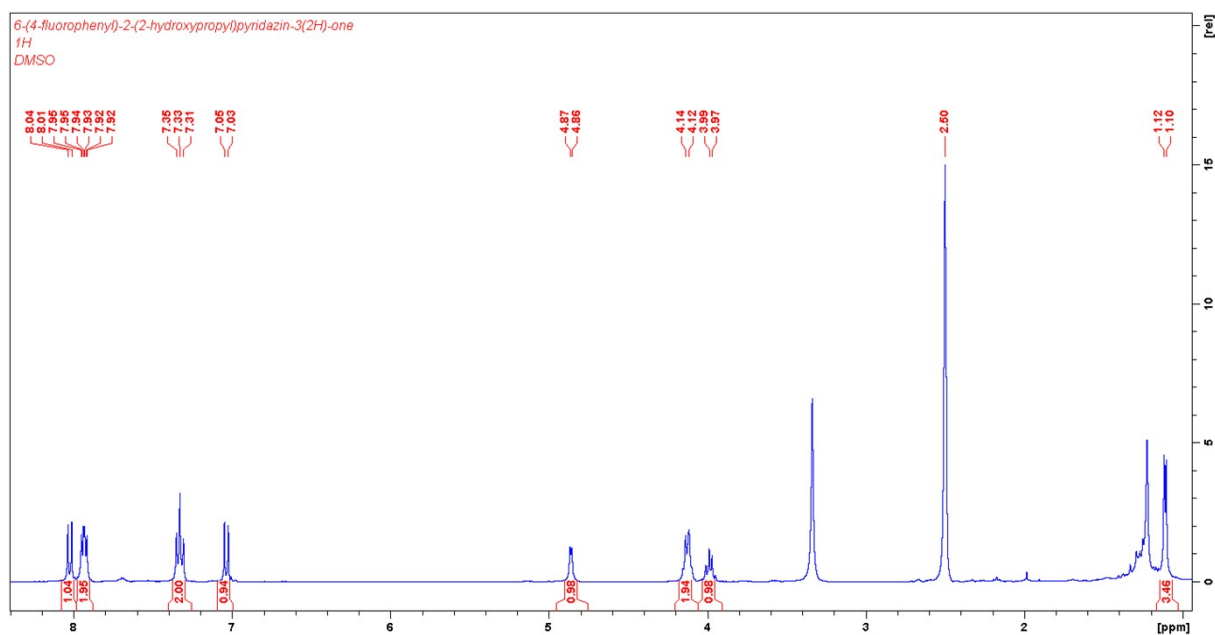


Fig. S118. ^{13}C NMR spectrum of (20b): 6-(4-fluorophenyl)-2-(2-hydroxypropyl)pyridazin-3(2H)-one

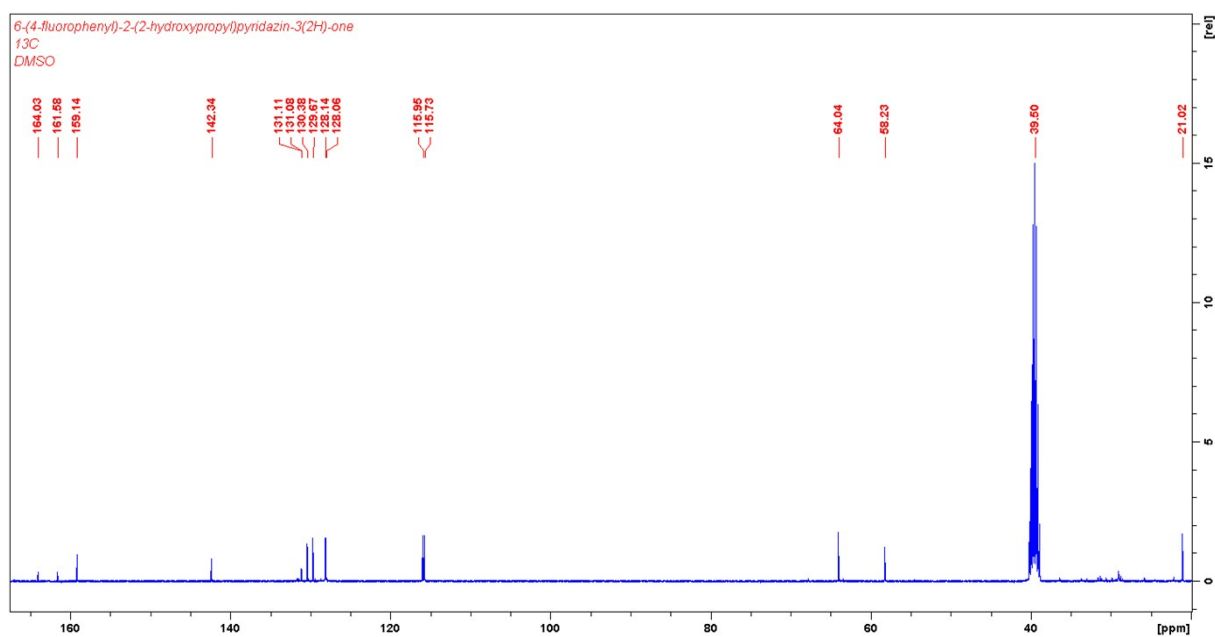


Fig. S119. ^1H NMR spectrum of (23): 2-(2-hydroxypropyl)-6-iodopyridazin-3(2H)-one

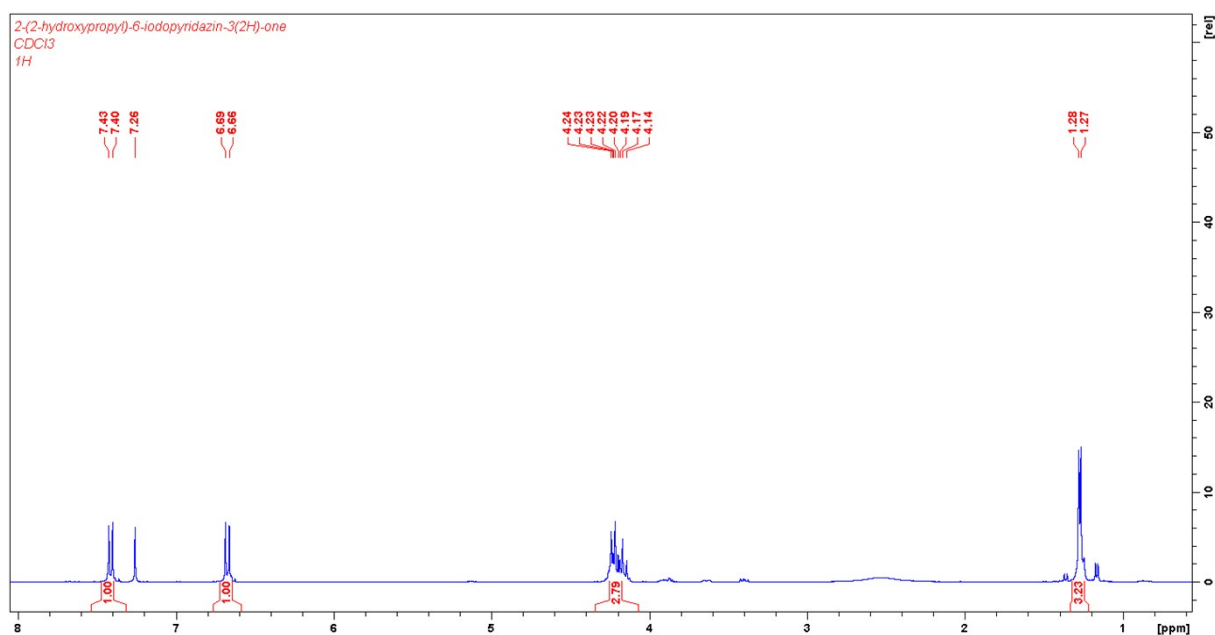
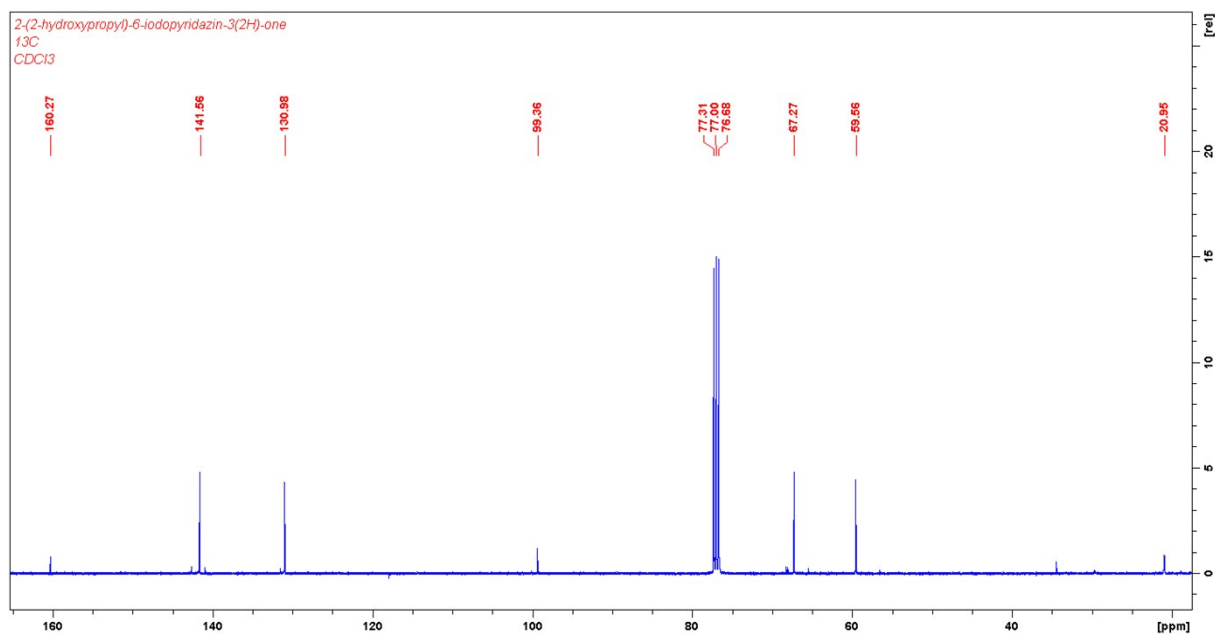


Fig. S120. ^{13}C NMR spectrum of (23): 2-(2-hydroxypropyl)-6-iodopyridazin-3(2H)-one



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