Supporting Information

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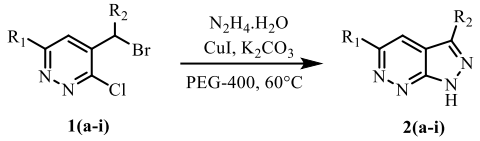
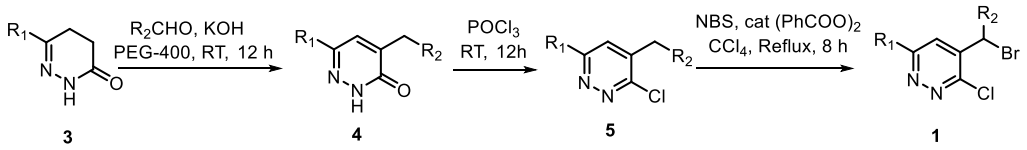
S1: General Information

The NMR experiments were performed with 300 MHz spectrometer, and chemical shifts are expressed in ppm (δ) with TMS as an internal reference. *J* values are given in Hertz. The ^{1}H and ^{13}C NMR spectrum are referenced to the residual solvent signals (7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C in $CDCl_3$, 2.50 ppm for ^{1}H and 39.9 ppm for ^{13}C in DMSO-d_6). IR spectra were recorded by using KBr pellets or neat. The product was visualized by UV light (254 nm), PMA and DNP strain in TLC. Commercially available reagents and solvents were used without further purification and were purchased. Melting points were determined using open capillary tubes and are uncorrected.



1(a-i) 2(a-i)

Scheme-1. Cascade synthesis of pyrazolo[3,4-*c*]pyridazine



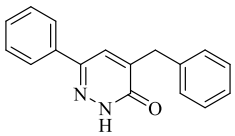
3 4 5 1

Scheme 1. Synthesis of starting substrate 1

*S2: General procedure for the synthesis of 4-benzyl-6-phenyl-pyridazin-3(2H)one **(4)***

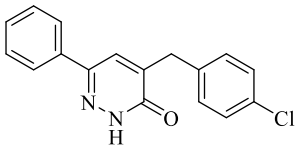
In 25 mL round bottom flask, dihydropyridazin-3(*2H*)one **3** (5.74 mmol) and benzaldehyde (6.31 mmol) in ethanol (10 mL) were stirred for 30 min. The solution of KOH (57.4 mmol) in water (1 mL) was added to the reaction mixture in portionwise at room temperature. Allow the reaction mixture stirred for 12 h at room temperature. The progress of the reaction was checked by TLC (acetone:petroleum ether::2:8). After the completion of reaction, it was poured into crused ice. The solid product was separated and filtered. The crude product was used in further step.

*4-Benzyl -6phenyl-pyridazin-3(3H)-one (**4a**):*



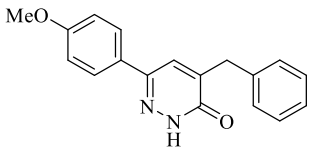
Yield: 89 %; IR (ν cm^{-1}) : 3385, 2770, 1686, 1600, 1520, 1415; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.55 (s, 1H), 7.84-7.47 (m, 11H), 4.09 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 162.7, 155.2, 142.7, 141.0, 137.5, 133.2, 131.1, 129.2, 129.1, 128.9, 128.7, 125.8, 43.7; Anal.Calcd. for $C_{17}H_{14}N_2O$ (262.11): C, 77.84; H, 5.38; N, 10.68; found: C, 77.80; H, 5.40; N, 10.66.

*4-(4-Chlorobenzyl)-6-phenyl-pyridazin-3(2H)-one (**4b**):*



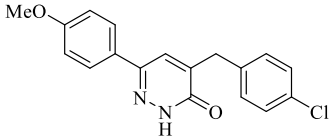
Yield: 91%; IR (ν cm^{-1}) : 3385, 2980, 1668, 1600, 1520, 1415; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.55 (s, 1H), 7.71 (d, J = 8.0, 2H), 7.69-7.28 (m, 8H), 3.98 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 162.7, 155.2, 142.7, 141.0, 135.6, 133.2, 131.3, 130.5, 129.2, 128.9, 128.8, 43.7; Anal. Calcd. for $C_{17}H_{13}N_2OCl$ (296.07): C, 68.81; H, 4.42; N, 9.44; found: C, C, 68.75; H, 4.36; N, 9.37%.

*4-Benzyl-6-(4-methoxyphenyl)-pyridazin-3(2H)-one (**4c**):*



Yield: 86%; IR (ν cm^{-1}): 3300, 086, 2980, 1651, 1604, 1514, 1460, 142; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.58 (s, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.34-7.26 (m, 6H), 6.90 (d, J = 7.8 Hz, 2H), 3.96 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 161.5, 160.3, 144.9, 143.1, 137.0, 129.2, 128.6, 127.7, 127.5, 127.1, 126.6, 113.7, 55.0, 35.3; Anal. Calcd. for $C_{18}H_{16}N_2O_2$ (292.12): C, 73.95; H, 5.52; N, 9.58; found: C, 73.91; H, 5.48; N, 9.51.

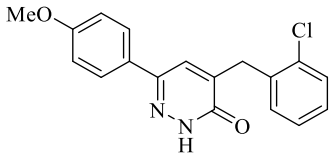
*4-(4-Chlorobenzyl)-6-(4-methoxyphenyl)-pyridazin-3(2H)-one (**4d**):*



Yield: 88%; IR (ν cm^{-1}): 3300, 3070, 2970, 1655, 1600, 1515, 1450, 1420; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.61 (s, 1H), 7.68 (d, J = 8.4 Hz, 2H), 7.38-7.21 (m, 5H), 6.94 (d, J = 8.7 Hz, 2H), 3.96 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 160.5, 159.8, 143.8, 141.8, 136.5, 131.3, 130.4, 128.1,

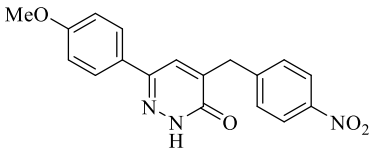
127.6, 127.1, 126.7, 113.8, 54.9, 34.5; Anal. Calcd. for $C_{18}H_{15}N_2O_2Cl$ (326.08): C, 66.16; H, 4.63; N, 8.57; found: C, 66.21; H, 4.70; N, 8.1%.

*4-(2-Chlorobenzyl)-6-(4-methoxyphenyl)-pyridazin-3(2H)-one (**4e**):*



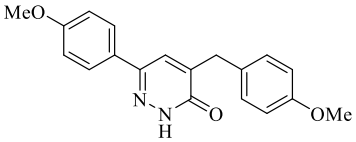
Yield: 85%; IR (ν cm^{-1}): 3470, 2983, 1658, 1600, 1510, 1485, 1400; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.59 (s, 1H), 7.75 (dd, J = 1.8 Hz, J = 8.1 Hz, 1H), 7.65 (m, 6H), 6.90 (d, J = 8.0 Hz, 2H), 3.95 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 163.0, 162.7, 155.2, 142.7, 141.0, 137.4, 134.4, 130.5, 130.2, 128.8, 127.2, 126.8, 125.5, 114.4, 55.9, 34.6; Anal. Calcd. for $C_{18}H_{15}N_2O_2Cl$ (326.08): C, 66.16; H, 4.63; N, 8.57; found: C, 66.16; H, 4.63; N, 8.57 %.

*4-(4-Nitrobenzyl)-6-(4-methoxyphenyl)-pyridazin-3(2H)-one (**4f**):*



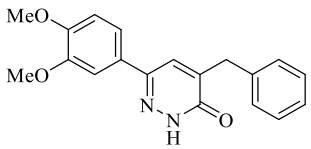
Yield: 77%; IR (ν cm^{-1}): 3332, 2982, 1665, 1600, 1580, 1550, 1490, 1401; ^{1}H NMR (300 MHz, $CHCl_3$): δ 12.55 (s, 1H), 8.07 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.25 (s, 1H), 7.01 (d, J = 8.5 Hz, 2H), 3.96 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 163.0, 162.7, 155.2, 145.4, 143.6, 142.7, 141.0, 130.2, 130.0, 125.5, 121.0, 114.4, 55.9, 43.7; Anal. Calcd. for $C_{18}H_{15}N_3O_4$ (337.10): C, 64.09; H, 4.48; N, 12.46; found: C, 64.14; H, 4.55; N, 12.56 %.

*4-(4-Methoxybenzyl)-6-(4-Methoxyphenyl)-pyridazin-3(2H)-one (**4g**):*



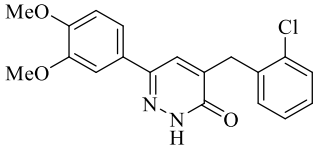
Yield: 70%; IR (ν cm^{-1}): 3385, 3013, 2984, 1668, 1600, 1559, 1400; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.50 (s, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.29-7.15 (m, 3H), 6.98 (dd, J_1 = 8.0 Hz, J_2 = 7.9 Hz, 4H), 4.05 (s, 2H), 4.05 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 163.0, 162.7, 157.7, 155.2, 142.7, 141.0, 130.2, 130.1, 129.8, 125.5, 114.4, 114.2, 55.9, 43.7, 43.5; Anal. Calcd. for $C_{19}H_{18}N_2O_3$ (322.13): C, 70.79; H, 5.63; N, 8.69; found: C, 70.73; H, 5.60; N, 8.63 %.

*4-(4-Benzyl)-6-(3,4-dimethoxyphenyl)-pyridazin-3(2H)-one (4**h**):*



Yield: 93%; IR (ν cm^{-1}) : 3315, 3070, 2975, 1658, 1600, 1518, 1470, 1420; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.50 (s, 1H), 7.42-7.22 (m, 7H), 7.05 (s, 1H), 6.98 (d, J = 8.1 Hz, 1H), 4.05 (s, 2H), 3.85 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): 162.7, 155.2, 152.1, 149.9, 142.7, 141.0, 137.5, 129.1, 129.1, 128.7, 126.5, 125.8, 122.5, 115.4, 114.4, 56.2, 43.7; Anal. Calcd. for $C_{19}H_{18}N_2O_3$ (322.13): C, 70.79; H, 5.63; N, 8.69; found: C, 70.73; H, 5.60; N, 8.63 %.

4-*(2-Chlorobenzyl)-6-(3,4-dimethoxyphenyl)-pyridazin-3(2H)-one (**4i**):*

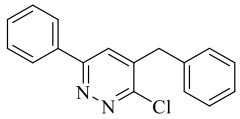


Yield: 88%; IR (ν cm^{-1}) : 3304, 3080, 2969, 1655, 1600, 1515, 1470, 1422; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.50 (s, 1H), 7.78 (d, J = 1.9 Hz, 1H), 7.39-7.21 (m, 6H), 7.01 (d, J = 8.1 Hz, 1H), 3.98 (s, 2H), 3.85 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): 162.7, 155.2, 152.1, 149.9, 142.7, 141.0, 137.4, 134.4, 130.5, 128.8, 127.2, 126.8, 126.5, 122.5, 115.4, 114.4, 56.2, 34.6 ; Anal. Calcd. for $C_{19}H_{17}N_2O_3Cl$ (356.09): C, 63.96; H, 4.80; N, 7.85; found: C, 63.91; H, 4.79; N, 7.81 %.

S3: *General procedure for the synthesis of substrate (**5**)*

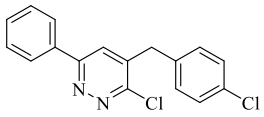
In 50 mL round bottom flask, substituted pyridazin-3(*2H*)one (3.80 mmol) (4) was stirred in $POCl_3$ (20 mL) for 24 h at room temperature. The progress of the reaction was checked by TLC (acetone:petroleum ether::2:8). After the completion of reaction, it was poured into crushed ice. The solid product was separated and filtered. The crude product was used in further step.

*3-Phenyl-5-benzyl-6-chloro-pyridazine (**5a**):*



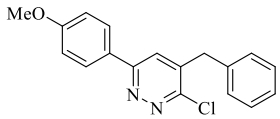
Yield: 80%; IR (ν cm^{-1}) : 3045, 2996, 1600, 1571, 1440; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.84 (dd, J_1 = 8.0 Hz, J_2 = 2.4 Hz, 2H), 7.76-7.47 (m, 9H), 3.98 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 145.6, 137.4, 136.3, 133.1, 129.3, 129.1, 128.8, 128.7, 127.5, 125.9, 125.8, 37.0; Anal. Calcd. for $C_{17}H_{13}N_2Cl$ (280.07): C, 72.73; H, 4.67; N, 9.98; found: C, 72.70; H, 4.61; N, 9.92 %.

*3-Phenyl-5-(4-chlorobenzyl)-6-chloro-pyridazine (**5b**)*:



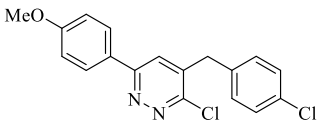
Yield: 84%; IR (ν cm^{-1}) : 3045, 2996, 1600, 1558, 1440; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.10 (d, J = 8.0, 2H), 7.94 (d, J = 8.1 Hz, 2H), 7.70-7.47 (m, 6H), 3.98 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 145.6, 137.4, 133.3, 134.4, 133.1, 131.3, 130.5, 129.3, 128.8, 127.5, 125.9, 37.0; Anal. Calcd. for $C_{17}H_{12}N_2Cl_2$ (314.03): C, 64.78; H, 3.84; N, 8.89; found: C, 64.80; H, 3.89; N, 8.81 %.

3-(4-methoxyphenyl)-5-benzyl-6-chloro-pyridazine (5c):



Yield: 74%; IR (ν cm^{-1}) : 3061, 2958, 1606, 1577, 1516, 1452; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.89 (d, J =8.7 Hz, 2H), 7.40-7.25 (m, 4H), 7.22 (d, J = 7.2 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H), 4.10 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 160.7, 159.2, 145.6, 137.4, 136.3, 129.1, 128.7, 128.5, 125.9, 125.8, 125.4, 114.8, 55.9, 37.0; Anal. Calcd. for $C_{18}H_{15}N_2OCl$ (310.08): C, 69.57; H, 4.87; N, 9.01; found: C, 69.65; H, 4.98; N, 9.13 %.

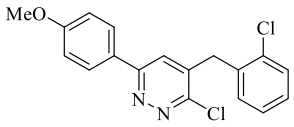
*3-(4-Methoxyphenyl)-5-(4-chlorobenzyl)- 6-chloro-pyridazine (**5d**):*



Yield: 76%; IR (ν cm^{-1}) : 3065, 2950, 1609, 1570, 1515, 1420; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, J = 9 Hz, 2H), 7.40 (s, 1H), 7.36 (d, J = 8.7 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 9 Hz, 2H), 4.09 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):160.7, 159.2, 145.6, 137.4, 134.4, 131.3, 130.5, 128.8,

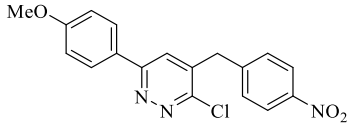
128.5, 125.9, 125.4, 114.8, 55.9, 37.0; Anal. Calcd. for $C_{18}H_{14}N_2OCl_2$ (344.04): C, 62.63; H, 4.09; N, 8.11; found: C, 62.60; H, 4.00; N, 4.10 %.

*3-(4-Methoxyphenyl)-5-(2-chlorobenzyl)- 6-chloro-pyridazine (**5e**):*



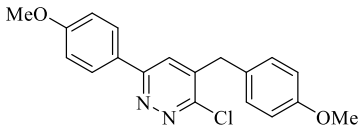
Yield: 78%; IR (ν cm^{-1}) : 2983, 1600, 1573, 1481, 1405; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.70 (d, *J* = 1.8 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.42 (s, 1H), 7.40-7.23 (m, 3H), 7.01 (d, *J* = 8.1 Hz, 2H), 3.99 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 160.7, 159.2, 145.6, 138.1, 137.4, 134.4, 130.5, 128.8, 128.5, 127.2, 126.8, 125.9, 125.4, 114.8, 55.9, 27.9; Anal. Calcd. for $C_{18}H_{14}N_2OCl_2$ (344.04): C, 62.63; H, 4.09; N, 8.11; found: C, 62.60; H, 4.00; N, 8.05 %.

*3-(4-methoxyphenyl)-5-(4-nitrobenzyl)- 6-chloro-pyridazine (**5f**):*



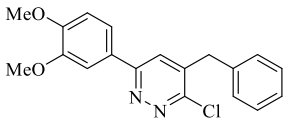
Yield: 69%; IR (ν cm^{-1}) : 2983, 1600, 1550, 1490, 1410; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H), 7.40 (s, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.01 (d, *J* = 8.6 Hz, 2H), 3.96 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.7, 159.2, 145.6, 145.4, 142.4, 137.4, 130.0, 128.5, 125.9, 125.4, 121.0, 114.8, 55.9, 37.0; Anal. Calcd. for $C_{18}H_{14}N_3O_3Cl$ (355.07): C, 60.77; H, 3.97; N, 11.81; found: C, 60.71; H, 3.93; N, 11.81 %.

*3-(4-Methoxyphenyl)-5-(4-chlorobenzyl)- 6-chloro-pyridazine (**5g**):*



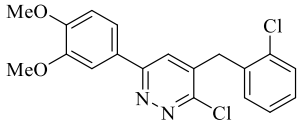
Yield: 78%; IR (ν cm^{-1}) :3085, 2980, 1600, 1559, 1409; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.41 (s, 1H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 3.99 (s, 2H), 3.85 (s, 3H), 3.83 (s, 3H), ^{13}C NMR (100 MHz, $CDCl_3$): 160.7, 159.2, 157.7, 145.6, 137.4, 130.1, 128.6, 128.5, 126.3, 125.9, 125.4, 114.8, 114.2, 55.9, 37.0; Anal. Calcd. for $C_{19}H_{17}N_2O_2Cl$ (340.09): C, 66.96; H, 5.03; N, 8.22; found: C, 66.96; H, 5.03; N, 8.22 %.

*3-(3,4-Dimethoxyphenyl)-5-benzyl-6-chloro-pyridazine (**5h**):*



Yield: 71%; IR (ν cm^{-1}) : 2929, 1600, 1515, 1490, 1410, ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.45-7.25 (m, 8H), 7.01 (d, J = 8.3 Hz, 1H), 4.05 (s, 2H), 3.95 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 150.3, 149.8, 145.6, 137.4, 136.3, 135.3, 129.1, 128.7, 126.8, 126.4, 125.9, 125.8, 120.8, 115.8, 112.3, 56.2, 37.0; Anal. Calcd. for $C_{19}H_{17}N_2O_2Cl$ (340.09): C, 66.96; H, 5.03; N, 8.22; found: C, 66.99; H, 5.10; N, 8.29 %.

*3-(3.4-Dimethoxyphenyl)-5-benzyl-6-chloro-pyridazine (**5i**):*

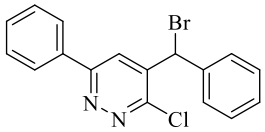


Yield: 77%; IR (ν cm^{-1}) : 3050, 2963, 1600, 1550, 1405; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.71-7.54 (m, 2H), 7.47-7.21 (m, 5H), 6.90 (d, J = 8.1 Hz, 1H), 4.22 (s, 2H), 3.96 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 150.3, 149.8, 145.6, 138.1, 137.4, 134.4, 130.5, 128.8, 127.2, 126.8, 126.4, 125.9, 120.8, 115.8, 112.3, 56.2, 27.9; Anal. Calcd. for $C_{19}H_{16}N_2O_2Cl_2$ (374.05): C, 60.82; H, 4.30; N, 7.47; found: C, 60.89; H, 4.38; N, 7.56 %.

S4:*General Procedure for the Synthesis of Starting Substrate **1***

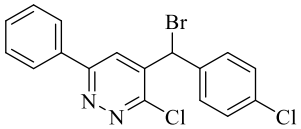
In 100 mL round bottom flask, *N*-bromo succinamide (2.13 mmol) and catalytic amount of benzoylperoxide were dissolved in CCl_4 (30 mL). The substrate **5** (1.42 mmol) was added to the reaction mixture and reflux for 8-12 h. The progress of the reaction was checked by TLC (ethyl acetate:petroleum ether::5:5). The solvent was concentrated under vaccuu. The crude product was purified by column chromatography.

*Substrate **1a**:*



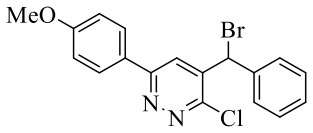
Yield: 62%; IR (ν cm^{-1}): 3045, 2972, 1600, 1592, 1450; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.10 (s, 1H), 7.55-7.10 (m, 10H), 6.39 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 145.6, 137.4, 134.0, 133.1, 129.3, 129.3, 129.1, 129.0, 128.8, 127.5, 125.9, 50.9; Anal. Calcd. for $C_{17}H_{12}N_2ClBr$ (357.98): C, 56.77; H, 3.36; N, 7.79; found: C, 56.77; H, 3.36; N, 7.79 %.

*Substrate **1b***:



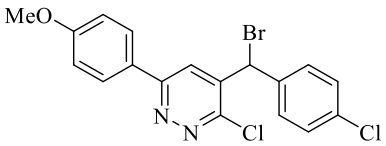
Yield: 62%; IR (ν cm^{-1}): 3040, 2986, 1600, 1410; ^{1}H NMR (300 MHz,DMSO-d_6): δ 8.17 (d, J = 8.0, 2H), 7.95 (d, J = 8.1 Hz, 2H), 7.71-7.47 (m, 6H), 6.35 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 145.6, 137.4, 134.5, 133.1, 132.1, 130.5, 129.3, 129.2, 128.8, 127.5, 125.9, 50.9; Anal. Calcd. for $C_{17}H_{11}N_2Cl_2Br$ (391.94): C, 51.81; H, 2.81; N, 7.11; found: C, 51.83; H, 2.83; N, 7.15 %.

*Substrate **1c***:



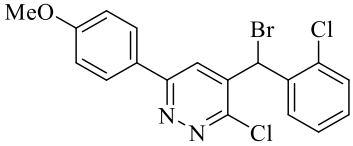
Yield 77%; IR (ν cm^{-1}): 2986, 1600, 1570, 1445; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.18 (s, 1H), 8.05 (d, 8.1 Hz, 2H), 7.45-7.32 (m, 5H), 7.04 (d, J = 8.5 Hz, 2H), 6.43 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 160.7, 159.2, 145.6, 137.4, 134.0, 129.1, 129.0, 128.5, 125.9, 125.4, 114.8, 55.9, 50.9; Anal. Calcd. for $C_{18}H_{14}N_2OClBr$ (387.99): C, 55.48; H, 3.62; N, 7.19; found: C, 55.42; H, 3.60; N, 7.16 %.

*Substrate **1d**:*



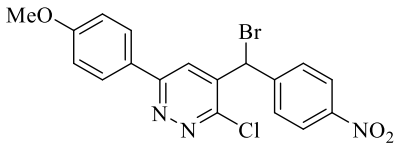
Molecular formula:; Yield: 356 mg (72.4%); IR (ν cm^{-1}): 2945, 1600, 1530, 1440; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 8.12 (d, J = 8.7 Hz, 2H), 8.04 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 6.39 (s, 1H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.8, 141.0, 139.0, 135.9, 135.1, 129.8, 129.7, 129.3, 128.6, 126.9, 125.4, 114.5, 55.4, 47.6; Anal. Calcd. for $C_{18}H_{13}N_2OCl_2Br$ (421.95): C, 50.98; H, 3.09; N, 6.61; found: C, 50.98; H, 3.09; N, 6.61 %.

*Substrate **1e***:



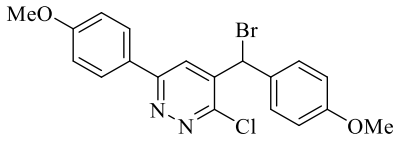
Yield: 64%; IR (ν cm^{-1}): 2993, 1600, 1573, 1485, 1405; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.15 (s, 1H), 7.70 (d, J = 1.8 Hz, 1H), 7.53 - 7.15 (m, 5H), 7.01 (d, J = 8.1 Hz, 2H), 6.39 (s, 1H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 160.7, 159.2, 145.6, 137.4, 132.8, 130.5, 130.4, 129.2, 128.5, 128.5, 127.2, 125.9, 125.4, 114.8, 55.9, 41.8; Anal. Calcd. for $C_{18}H_{13}N_2OCl_2Br$ (421.95): C, 50.98; H, 3.09; N, 6.61; found: C, 50.98; H, 3.09; N, 6.61 %.

*Substrate **1f***:



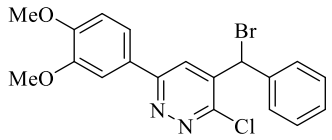
Yield: 64%; IR (ν cm^{-1}): 2983, 1600, 1550, 1492, 1411; ^{1}H NMR (300 MHz, $CDCl_3$): δ δ 8.18 (s, 1H), 8.08 (d, J = 8.1 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.40 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.7, 159.2, 148.6, 145.6, 140.1, 137.4, 130.0, 128.5, 125.9, 125.4, 121.4, 114.8, 55.9, 50.9; Anal. Calcd. for $C_{18}H_{13}N_3O_3ClBr$ (432.98): C, 49.74; H, 3.01; N, 9.67; found: C, 49.71; H, 3.00; N, 9.63 18.35%.

*Substrate **1g***:



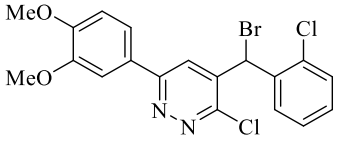
Yield: 64%; IR (ν cm^{-1}): 3030, 2970, 1600, 1560, 1410; ^{1}H NMR (300 MHz, $CDCl_3$): δ δ 7.94 (s, 1H), 7.48 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.2 Hz, 2H), 6.45 (s, 1H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.9, 160.7, 159.2, 145.6, 137.4, 130.1, 128.5, 126.3, 125.9, 125.4, 114.8, 114.6, 55.9, 50.9; Anal. Calcd. for $C_{19}H_{16}N_2O_2ClBr$ (418.00): C, 54.37; H, 3.84; N, 6.67; found: C, 54.31; H, 3.79; N, 6.61 %.

*Substrate **1h***:



Yield: 72%; IR (ν cm^{-1}): 2903, 1600, 1540, 1405; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.12 (s, 1H), δ 7.40-7.25 (m, 7H), 7.01 (s, 1H), 6.42 (s, 2H), 3.95 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 150.3, 149.8, 145.6, 137.4, 136.3, 129.1, 128.7, 126.4, 125.9, 125.8, 120.8, 115.8, 112.3, 56.2, 37.0; Anal. Calcd. for $C_{19}H_{16}N_2O_2ClBr$ (418.00): C, 54.37; H, 3.84; N, 6.67; found: C, 54.31; H, 3.78; N, 6.58 %.

*Substrate **1i**:*



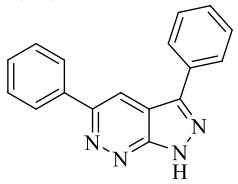
Yield: 71%; IR (ν cm^{-1}): 2983, 1600, 1515, 1489, 1402; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.11 (s, 1H), 7.75 (d, J = 1.5 Hz, 1H), 7.48 (s, 1H), 7.45-7.20 (m, 4H), 6.43 (s, 2H), 3.96 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 159.2, 150.3, 149.8, 145.6, 137.4, 134.4, 132.8, 130.5, 130.4, 129.2, 127.2, 126.4, 125.9, 120.8, 115.8, 112.3, 56.2, 41.8; Anal. Calcd. for $C_{19}H_{15}N_2O_2Cl_2Br$ (451.96): C, 50.25; H, 3.33; N, 6.17; found: C, 50.25; H, 3.33; N, 6.17 %.

S5: *General experimental procedure for the synthesis of pyrazolopyridazine* **2**:

A mixture of substrate **1** (0.55 mmol), potassium carbonate (0.825 mmol) and copper iodide (0.05 mmol) in PEG-400 was stirred at room temperature for 30 min. Placed the reaction mixture in preheated oil bath at 60 ºC. Hydrazine hydrate (1.1 mmol) was added portionwise to reaction mixture. The progress of the reaction was monitored by tlc. The reaction mixture was poured in ice cold water followed by a few

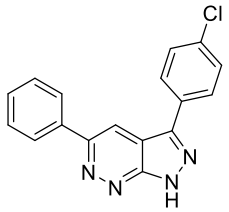
drops of acetic acid. The mixture was extracted by ethyl acetate (3 times) then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude product was purified by column chromatography on silica gel using n-hexane/EtOAc as eluent. The PEG-aqueous solutions was concentrated under reduced pressure until the water was removed and the result PEG recovered was dried in high vacuum pump and further used for cascade reaction and run a new reaction in the solvent recycled.

*3,5-diphenyl-1H-pyrazolo[3,4-c]pyridazine (**2a**):*



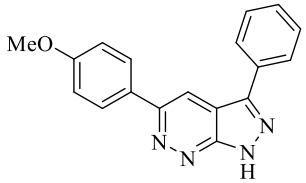
Yield: 82%; mp 221-225 °C; IR (ν cm^{-1}): 3345, 3044, 2994, 1600, 1567, 1415; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.32 (s, 1H), 8.39 (s, 1H), 8.10 (d, J = 7.2 Hz, 2H), 8.00 (d, J = 6.9 Hz, 2H), 7.39-7.91 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): 161.2, 156.1, 145.3, 133.1, 129.1, 129.3, 129.2, 128.5, 128.3, 127.5, 127.1, 125.3, 113.7; Anal. Calcd. for $C_{17}H_{12}N_4$ (272.10): C, 74.98; H, 4.44; N, 20.58; found: C, 74.93; H, 4.41; N, 20.52%.

3-(4-chlorophenyl)-5-phenyl-1H-pyrazolo[3,4-c]pyridazine (2b):



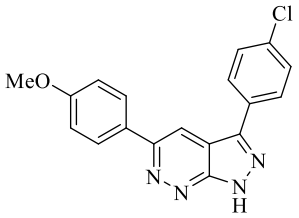
Yield: 84%; mp 185-189 °C; IR (*v* cm^{-1}): 3386, 3040, 2986, 1600, 1585, 1410; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.34 (s, 1H), 8.37 (s, 1H), 8.09 (d, *J* = 8.0, 2H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.69-7.47 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6): 161.2, 156.1, 145.3, 134.3, 133.1, 131.2, 129.4, 129.3, 128.9, 128.8, 127.5, 125.3, 113.7; Anal. Calcd. for $C_{17}H_{11}N_4Cl$ (306.06): C, 66.56; H, 3.61; N, 18.26; found: C, 66.51; H, 3.68; N, 18.21 %.

*5-(4-methoxyphenyl)-3-phenyl-1H-pyrazolo[3,4-c]pyridazine (**2c**):*



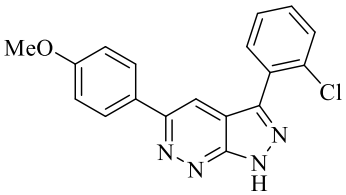
Yield: 81%; mp 208-210 °C; IR (*v* cm^{-1}): 2980, 1600, 1563, 1420; ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.34 (s, 1H), 8.38 (s, 1H), 8.01 (dd, J_1 = 8.7 Hz, J_2 = 7.2 Hz, 4H), 7.59-7.48 (m, 3H), 7.08 (d, *J* = 8.4 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.2, 160.7, 156.1, 145.3, 133.1, 129.3, 128.8, 128.5, 127.5, 125.4, 125.3, 114.8, 113.7, 55.9; Anal. Calcd. for $C_{18}H_{14}N_4O$ (302.11): C, 71.51; H, 4.67; N, 18.53; found: C, 71.57; H, 4.69; N, 18.55 %.

*3-(4-Chlorophenyl)-5-(4-methoxyphenyl)-1H-pyrazolo[3,4-c]pyridazine (**2d**):*



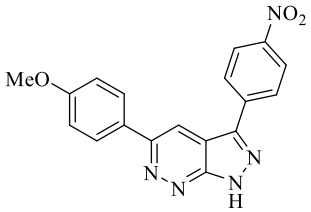
Yield: 85%; mp 198-200 °C; IR (ν cm^{-1}): 2945, 1600, 1540, 1443; ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.35 (s, 1H), 8.31 (s, 1H), 8.06 (d, J = 8.4 Hz, 2H), 7.95 (d, J = 6.9 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.07 (d, J = 7.5 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 159.7, 155.4, 151.3, 141.9, 133.6, 130.4, 129.3, 128.5, 127.8, 127.5, 126.4, 114.3, 113.7, 28.9; Anal. Calcd. for $C_{18}H_{13}N_4OCl$ (336.07): C, 64.20; H, 3.89; N, 16.64; found: C, 64.26; H, 3.89; N, 16.68 %.

*3-(2-chlorophenyl)-5-(4-methoxyphenyl)-1H-pyrazolo[3,4-c]pyridazine (**2e**):*



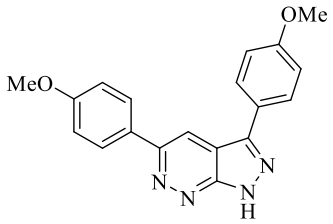
Yield: 76%; mp 188-190 °C; IR (ν cm^{-1}): 3332, 2984, 1600, 1572, 1410; ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.33 (s, 1H), 8.31 (s, 1H), 7.72 (dd, J_1 = 1.8 Hz, J_2 = 8.2 Hz, 1H) 7.56-7.16 (m, 5H), 7.07 (d, J = 7.5 Hz, 2H), 3.90 (s, 3H); NMR (100 MHz, $CDCl_3$): 161.2, 160.7, 156.1, 145.3, 132.3, 130.2, 129.4, 128.6, 128.5, 128.3, 127.4, 125.4, 125.3, 114.8, 113.7, 55.9; Anal. Calcd. for $C_{18}H_{13}N_4OCl$ (336.07): C, 64.20; H, 3.89; N, 16.64; found: C, 64.25; H, 3.90; N, 16.66 %.

*5-(4-methoxyphenyl)-3-(4-nitrophenyl)-1H-pyrazolo[3,4-c]pyridazine (**2f**):*



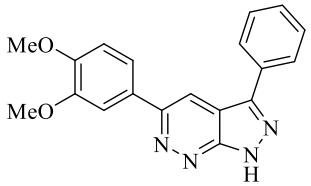
Yield: 69%; mp 225-230 °C; IR (ν cm^{-1}): 3445, 1600, 1550, 1485, 1411; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.32 (s, 1H), 8.31 (s, 1H), 8.08 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 161.2, 160.7, 156.1, 148.4, 145.3, 139.2, 128.5, 125.4, 125.3, 121.6, 114.8, 113.7, 55.9; Anal. Calcd. for $C_{18}H_{13}N_5O_3$ (347.10): C, 62.24; H, 3.77; N, 20.16; found: C, 62.20; H, 3.75; N, 20.13%.

*3,5-bis(4-methoxyphenyl)-1H-pyrazolo[3,4-c]pyridazine (**2g**):*



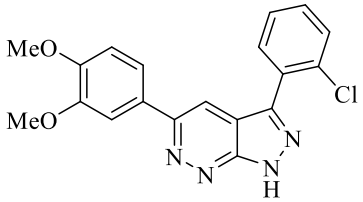
Yield: 78%; mp 180-185 ˚C; IR (ν cm^{-1}): 3389, 3030, 2985, 1600, 1567, 1408; ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.31 (s, 1H), 8.31 (s, 1H), 7.48 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.03 (dd, J_1 = 8.1 Hz, J_2 = 8.2 Hz, 4H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.2, 160.7, 156.1, 145.3, 128.5, 125.3, 114.8, 113.7, 55.9; Anal. Calcd. for $C_{19}H_{16}N_4O_2$ (332.12): C, 68.66; H, 4.85; N, 16.86; found: C, 68.66; H, 4.85; N, 16.86%.

*5-(3,4-dimethoxyphenyl)-3-phenyl-1H-pyrazolo[3,4-c]pyridazine (**2h**):*



Yield: 77%; mp 180-181 ˚C; IR (ν cm^{-1}): 3400, 2983, 1610, 1550, 1490; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.35 (s, 1H), 8.35 (s, 1H), 7.45-7.29 (m, 7H), 7.01 (d, J = 8.3 Hz, 1H), 3.95(s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): 161.2, 156.1, 150.3, 149.8, 145.3, 133.3, 133.1, 129.3, 128.8, 127.5, 126.5, 126.4, 125.3, 120.8, 115.8, 113.7, 112.3, 56.2; Anal. Calcd. for $C_{19}H_{16}N_4O_2$ (332.12): C, 68.66; H, 4.85; N, 16.86; found: C, 68.60; H, 4.80; N, 16.81%.

*3-(2-chlorophenyl)-5-(3,4-dimethoxyphenyl)-1H-pyrazolo[3,4-c]pyridazine (**2i**):*



Yield: 80%; mp 191-196 ˚C; IR (ν cm^{-1}): 3410, 2890, 1600, 1510, 1448, 1418; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.36 (s, 1H), 8.31 (s, 1H), 8.06-7.93 (m, 3H), 7.54-7.42 (m, 3H), 7.07 (d, J = 8.1 Hz, 1H), 3.90 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): 161.2, 156.1, 150.3, 149.8, 145.3, 132.3, 130.1, 130.0, 129.4, 128.9, 127.4, 126.4, 125.3, 120.8, 115.8, 113.7, 112.3, 56.2; Anal. Calcd. for $C_{19}H_{15}N_4O_2Cl$ (366.08): C, 62.22; H, 4.12; N, 15.27; found: C, 62.26; H, 4.17; N, 15.28 %.

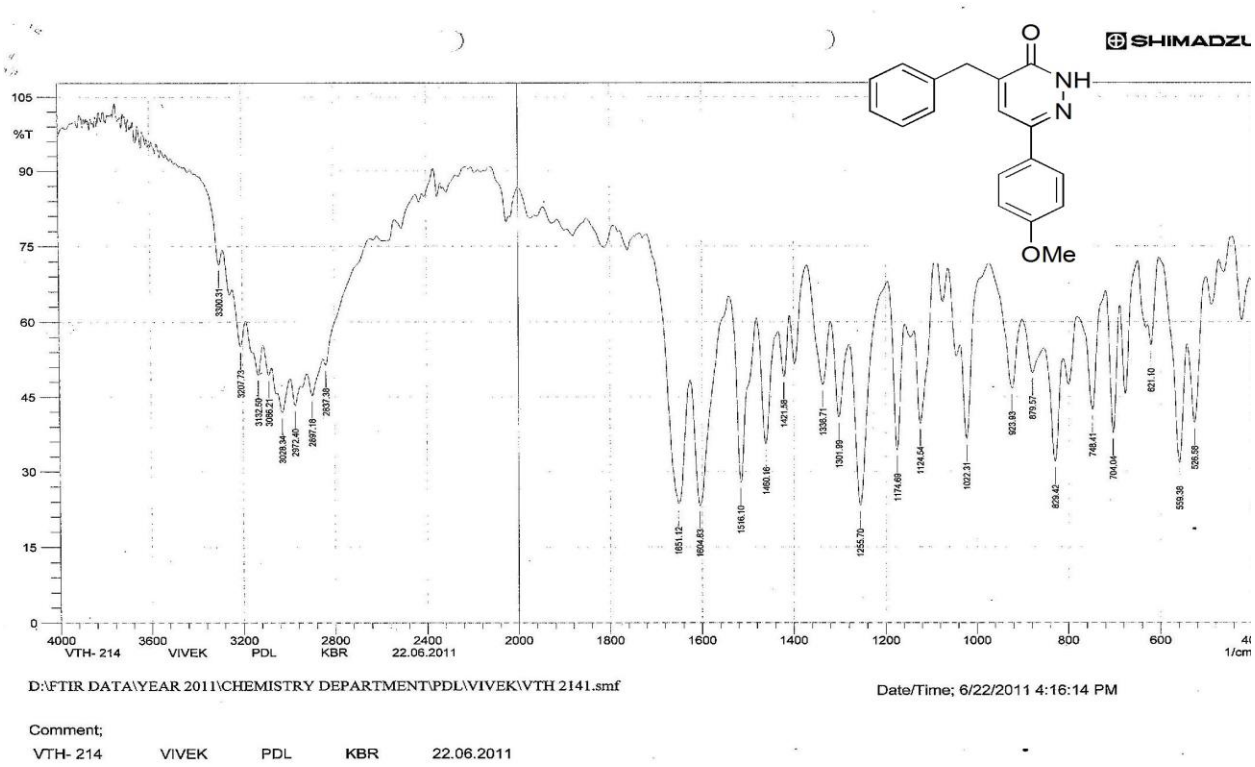


Figure S1: IR of 4-Benzyl-6-(4-methoxyphenyl)-pyridazin-3(*2H*)-one (**4c**)

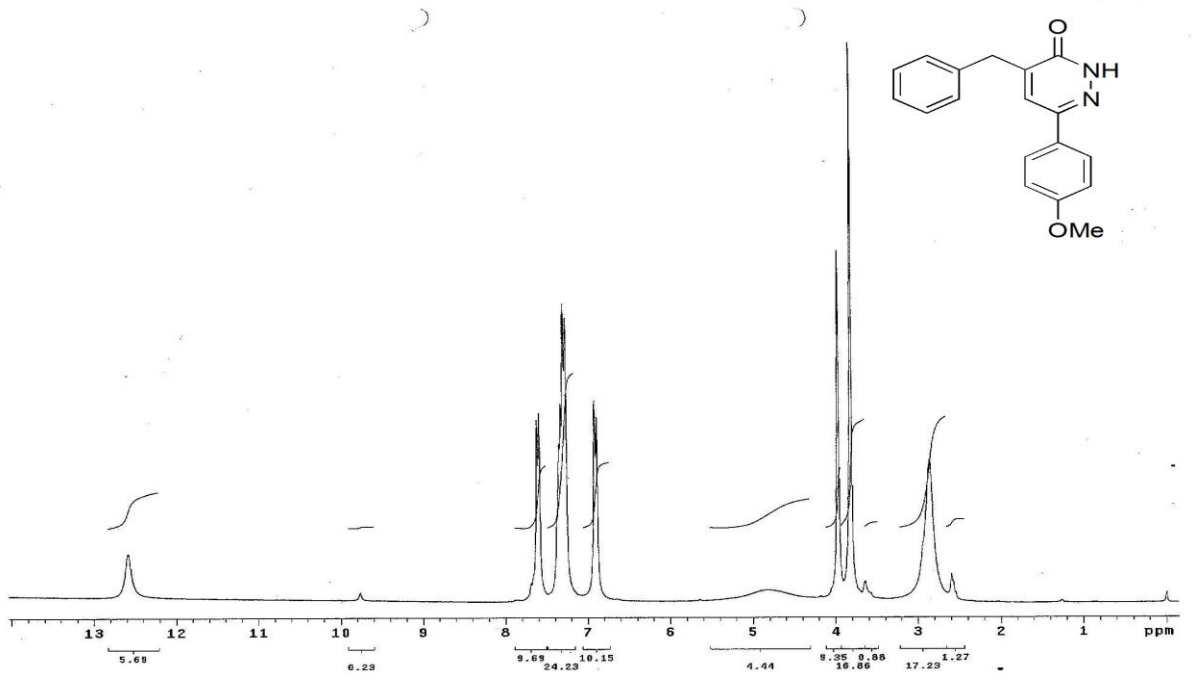


Figure S2: [1]H NMR of 4-Benzyl-6-(4-methoxyphenyl)-pyridazin-3(*2H*)-one (**4c**)

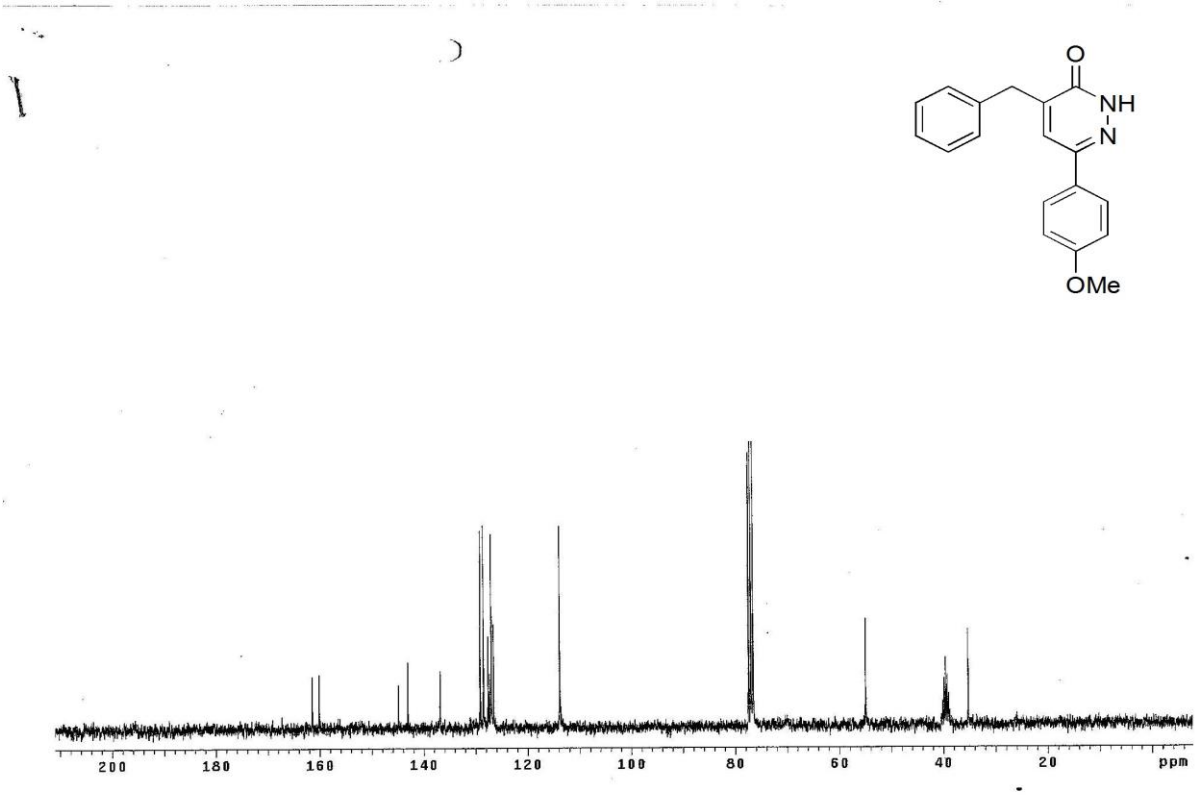


Figure S3: [13]C NMR of 4-Benzyl-6-(4-methoxyphenyl)-pyridazin-3(*2H*)-one (**4c**)

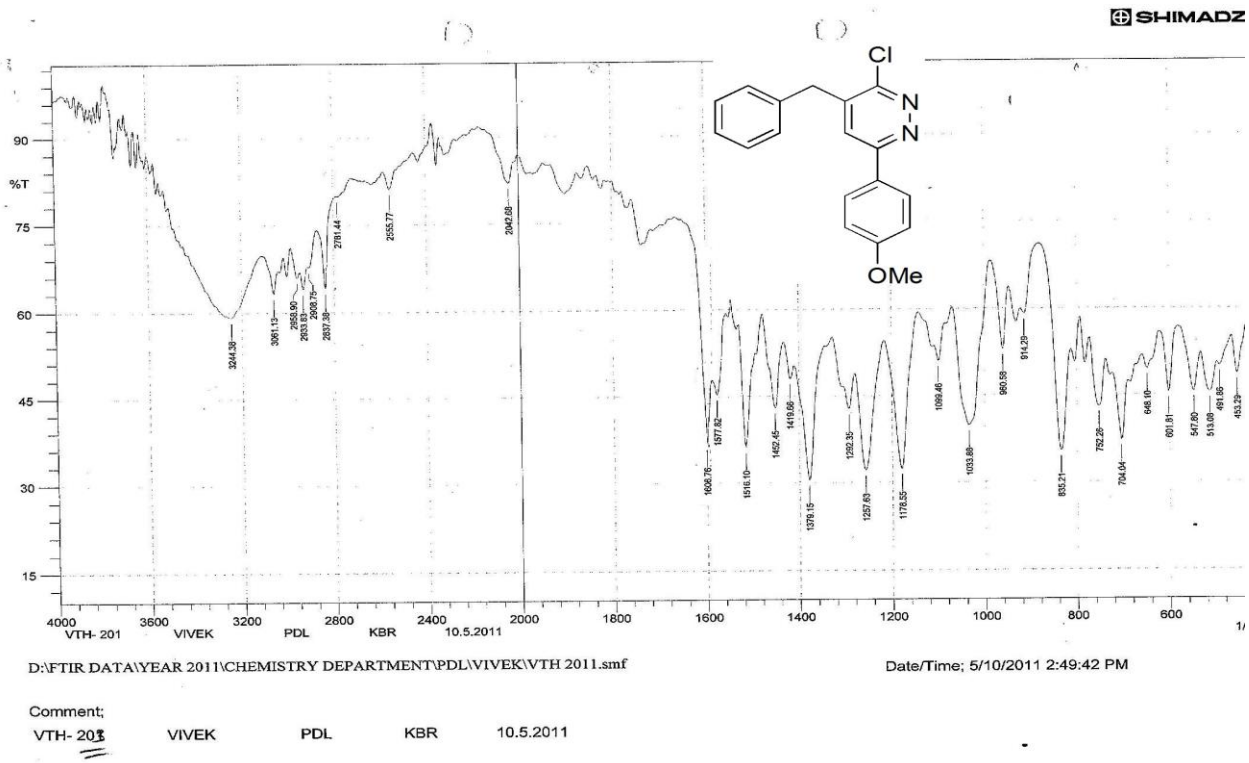


Figure S4: IR of 3-(4-methoxyphenyl)-5-benzyl-6-chloro-pyridazine (**5c**)

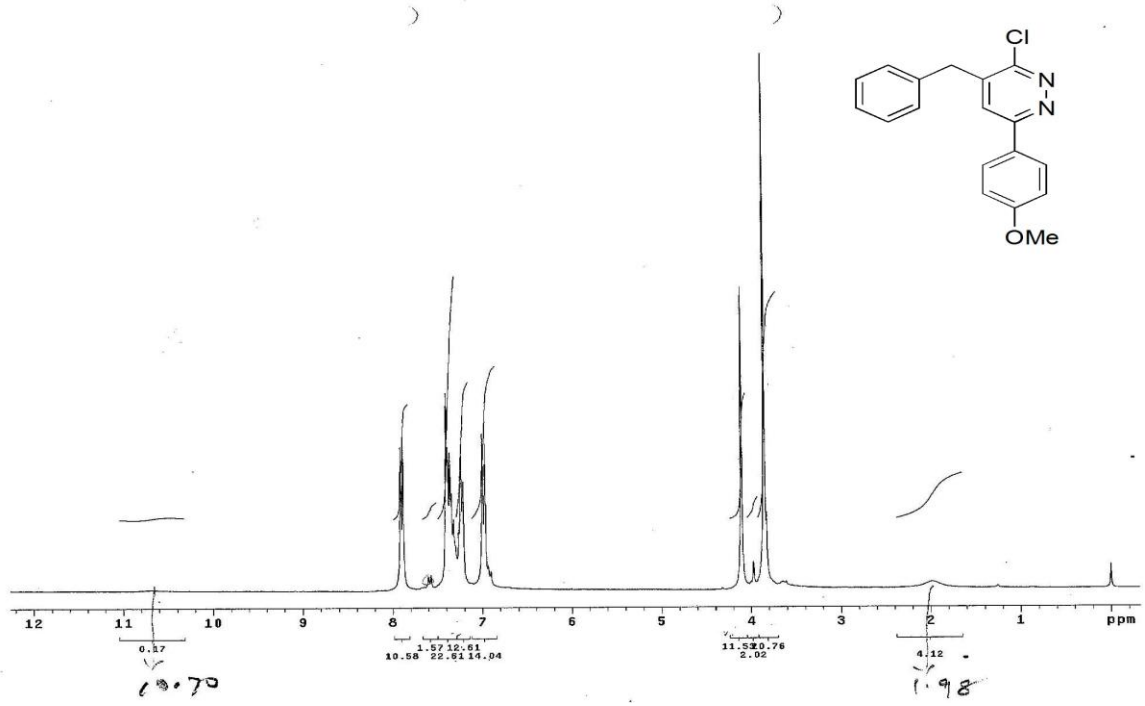


Figure S5: ^{1}H NMR of 3-(4-methoxyphenyl)-5-benzyl-6-chloro-pyridazine (**5c**)

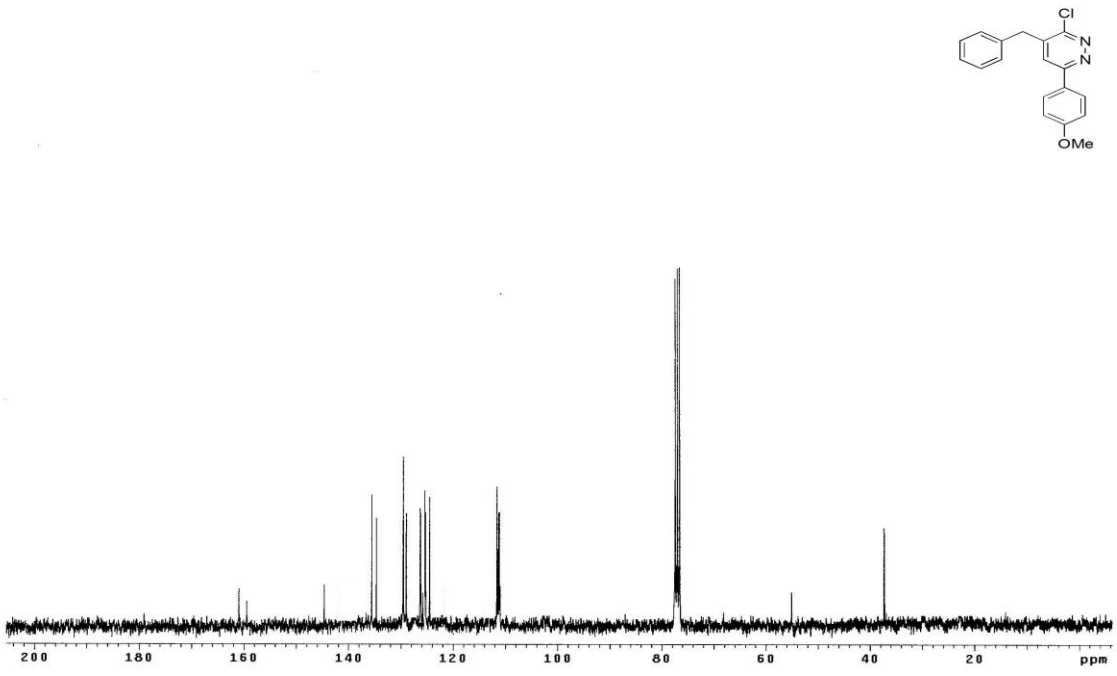


Figure S6: ^{13}C NMR of 3-(4-methoxyphenyl)-5-benzyl-6-chloro-pyridazine (**5c**)

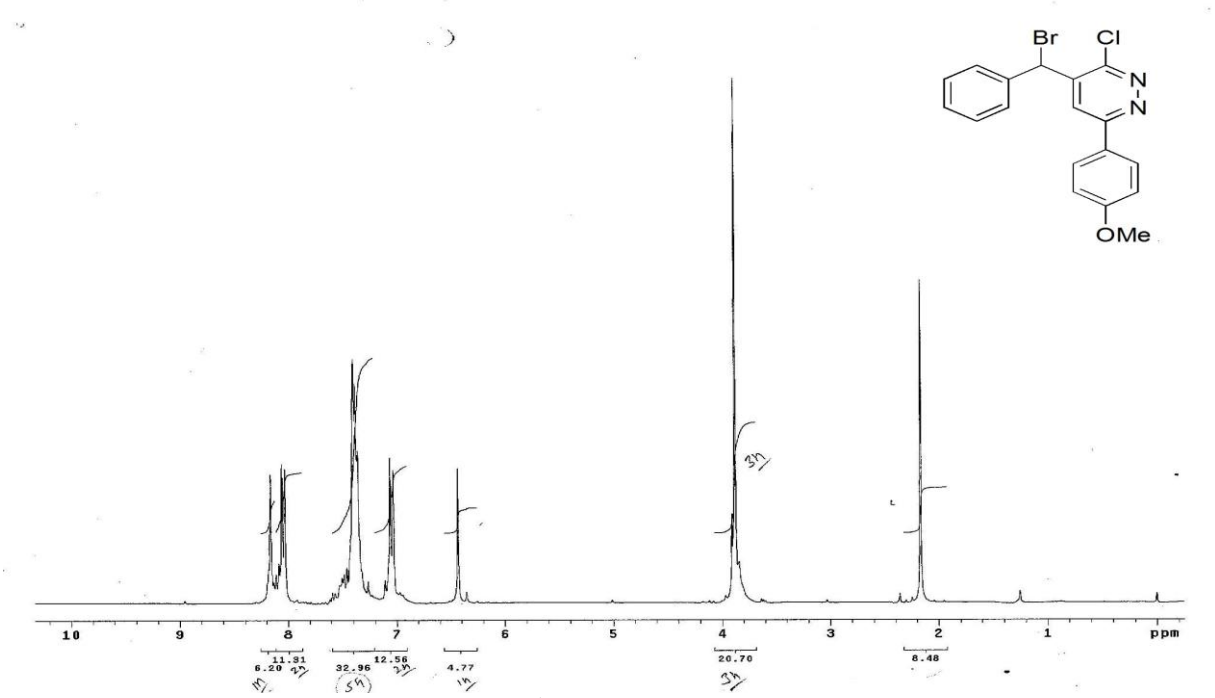


Figure S7: ^{1}H NMR of Substrate **1c**

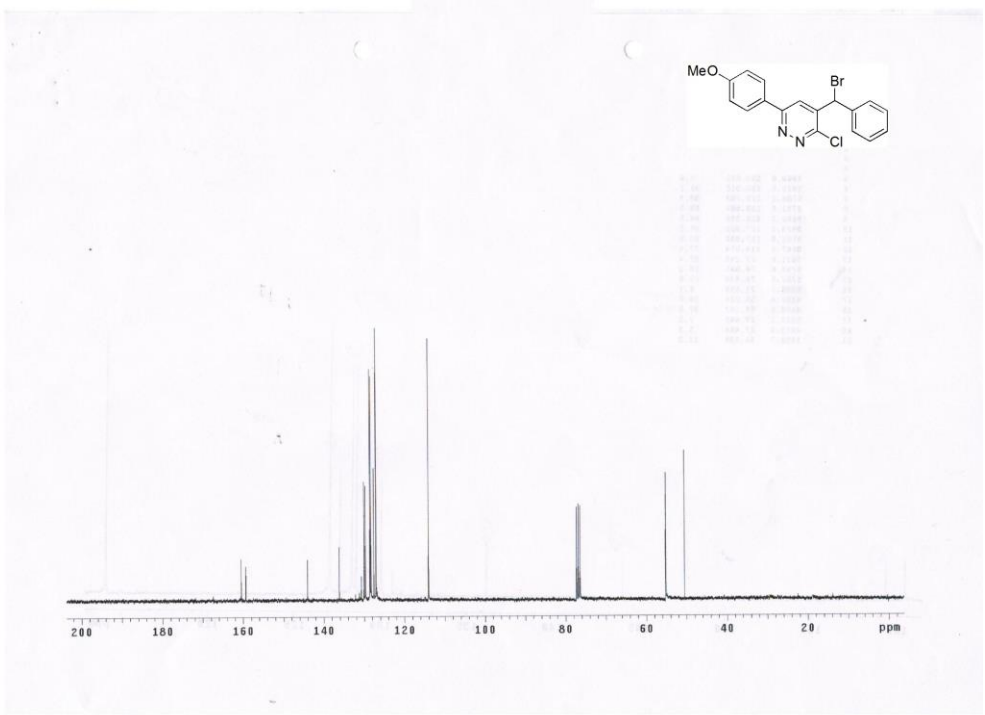


Figure S8: ^{13}C NMR of Substrate **1c**

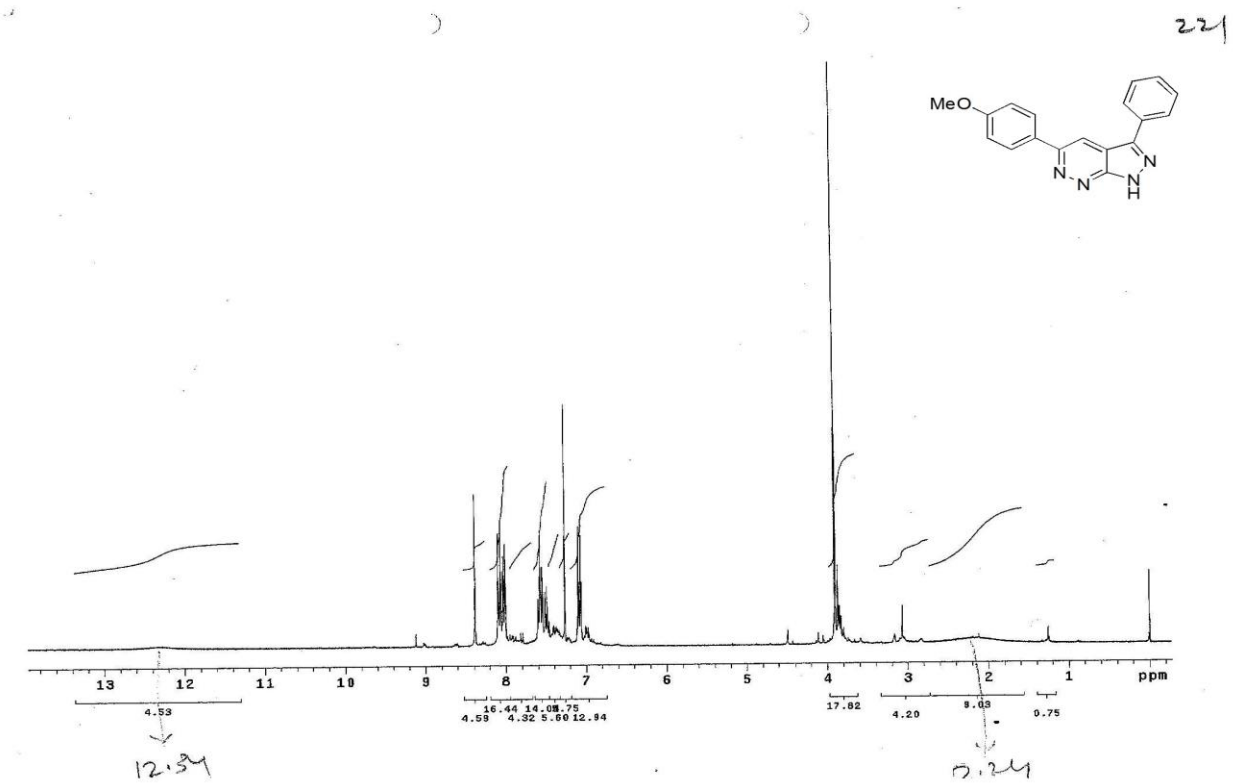


Figure S9: ^{1}H NMR of (4-methoxyphenyl)-3-phenyl-1*H*-pyrazolo[3,4-*c*]pyridazine (**2c**)

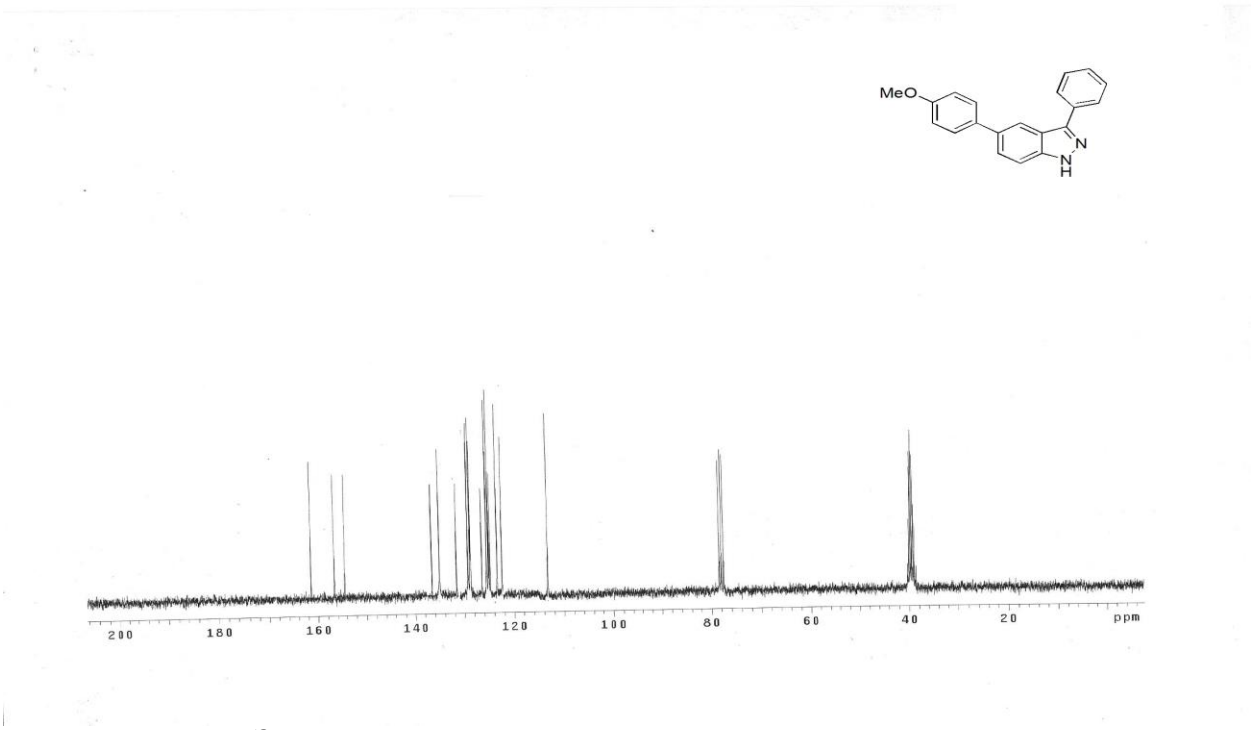


Figure S10: ^{13}C NMR of (4-methoxyphenyl)-3-phenyl-1*H*-pyrazolo[3,4-*c*]pyridazine (**2c**)

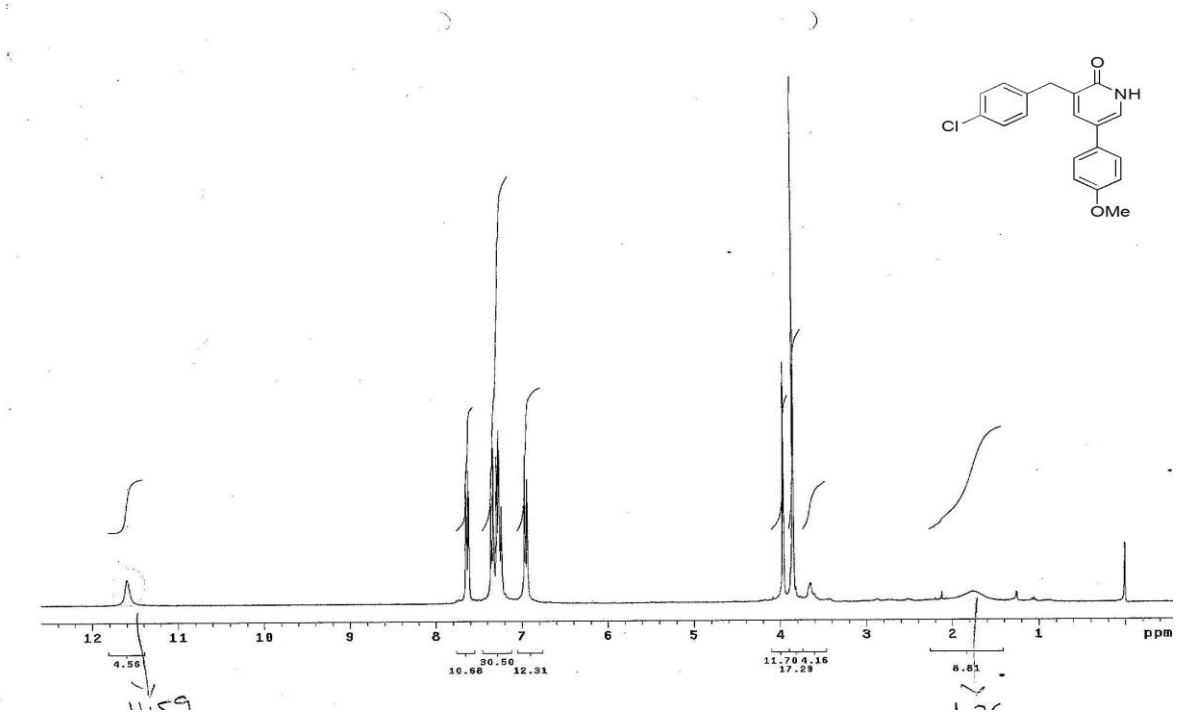


Figure S11: ^{1}H NMR of 4-(4-Chlorobenzyl)-6-(4-methoxyphenyl)-pyridazin-3(*2H*)-one (**4d**)

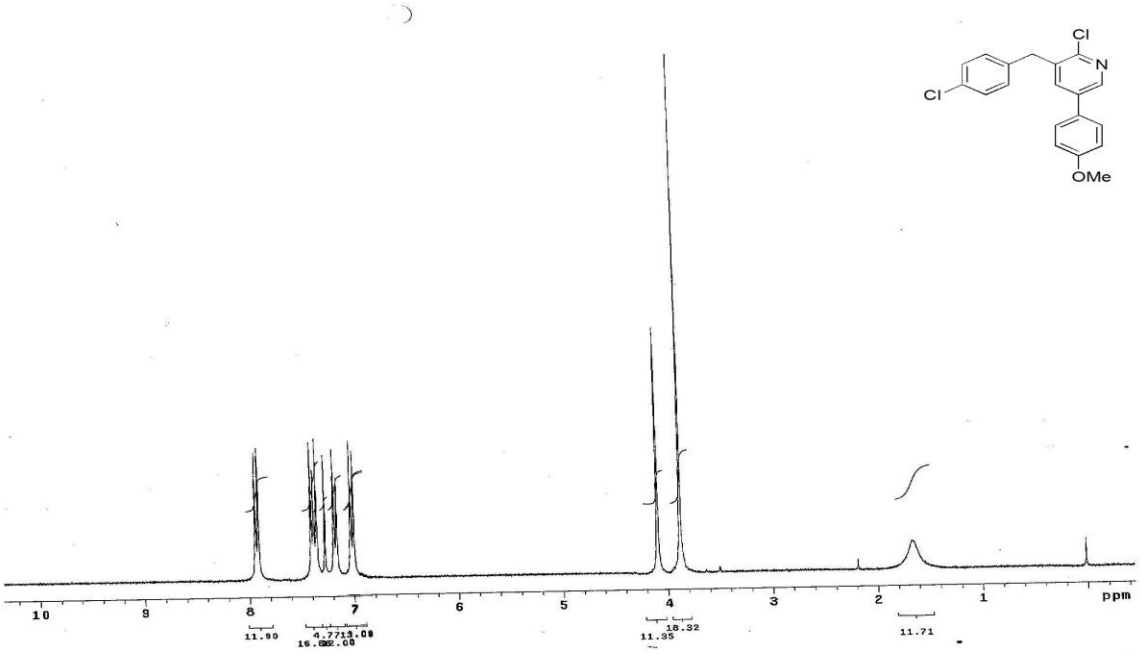


Figure S12: ^{1}H NMR of 3-(4-Methoxyphenyl)-5-(4-chlorobenzyl)- 6-chloro-pyridazine (**5d**)

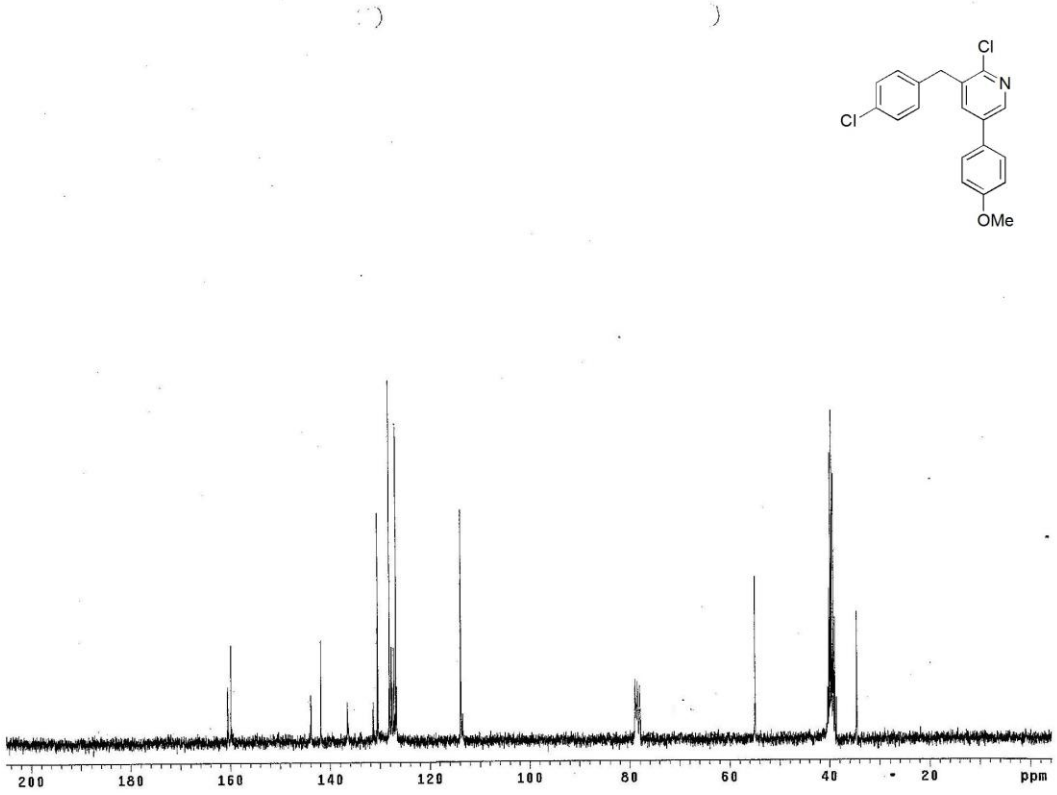


Figure S13: ^{13}C NMR of 3-(4-Methoxyphenyl)-5-(4-chlorobenzyl)- 6-chloro-pyridazine (**5d**)

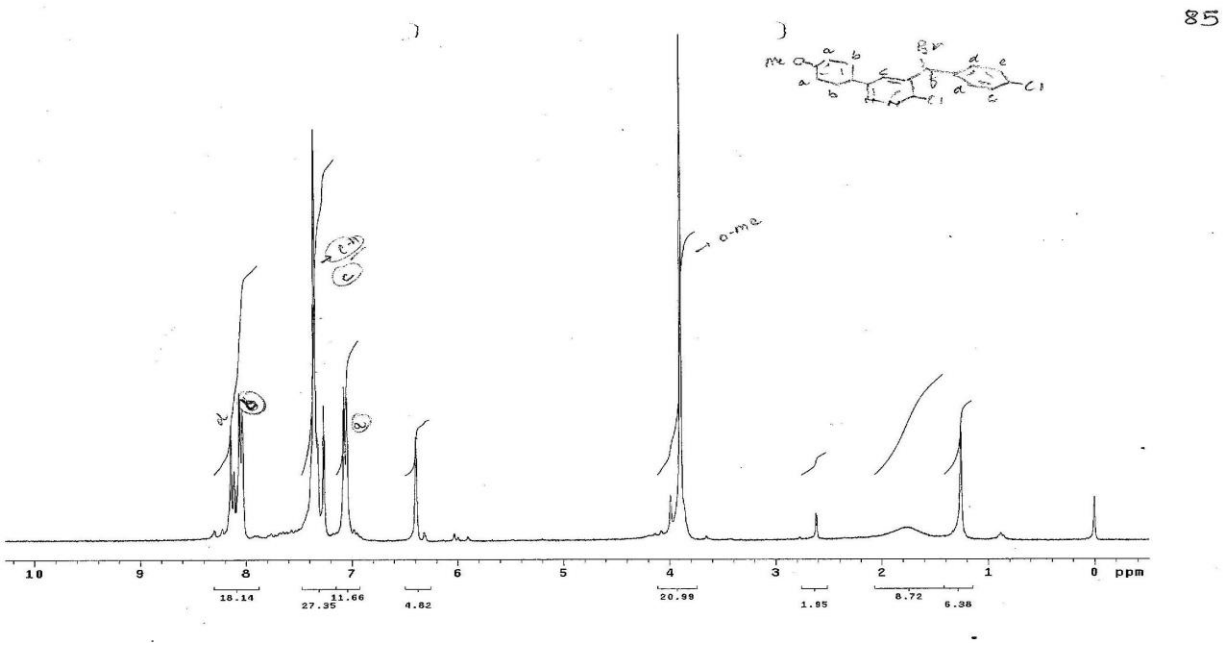


Figure S14: ^{1}H NMR of Substrate **1d**

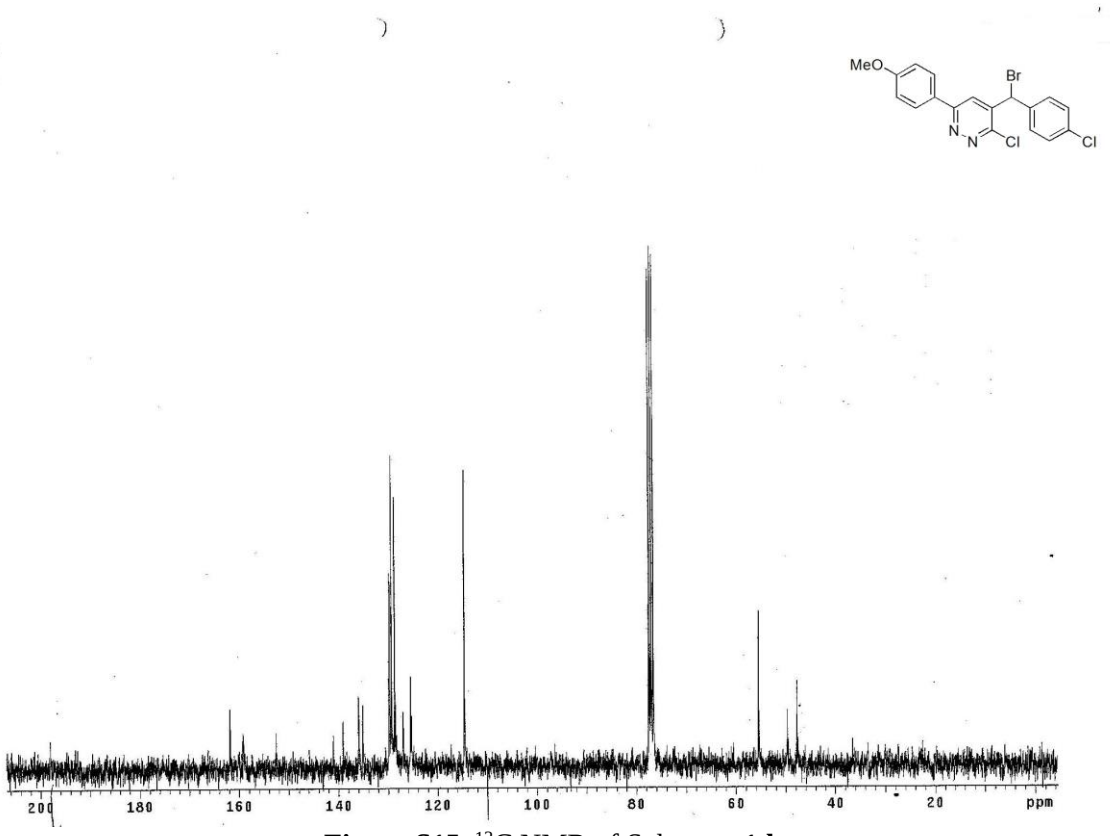


Figure S15: ^{13}C NMR of Substrate **1d**

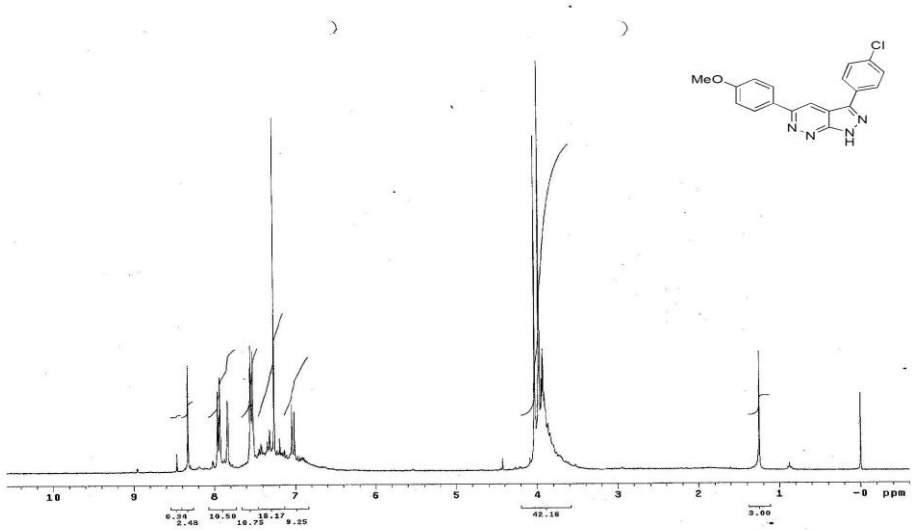


Figure S16: ^{1}H NMR of 3-(4-Chlorophenyl)-5-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*c*]pyridazine (**2d**)

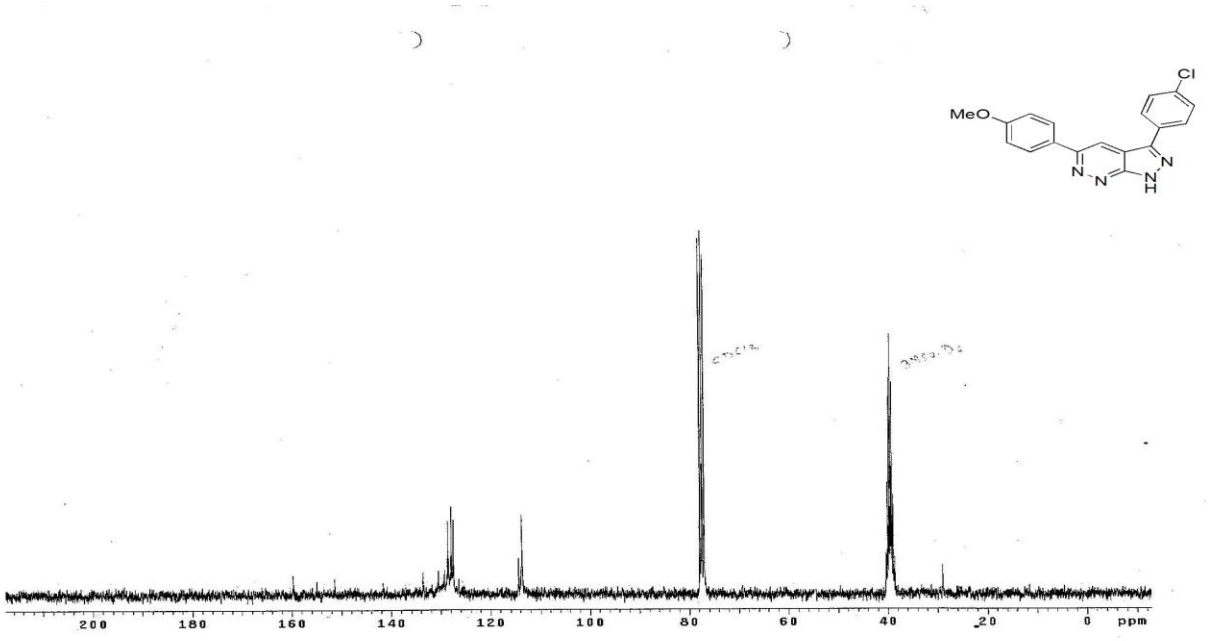


Figure S17: ^{13}C NMR of 3-(4-Chlorophenyl)-5-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*c*]pyridazine (**2d**)

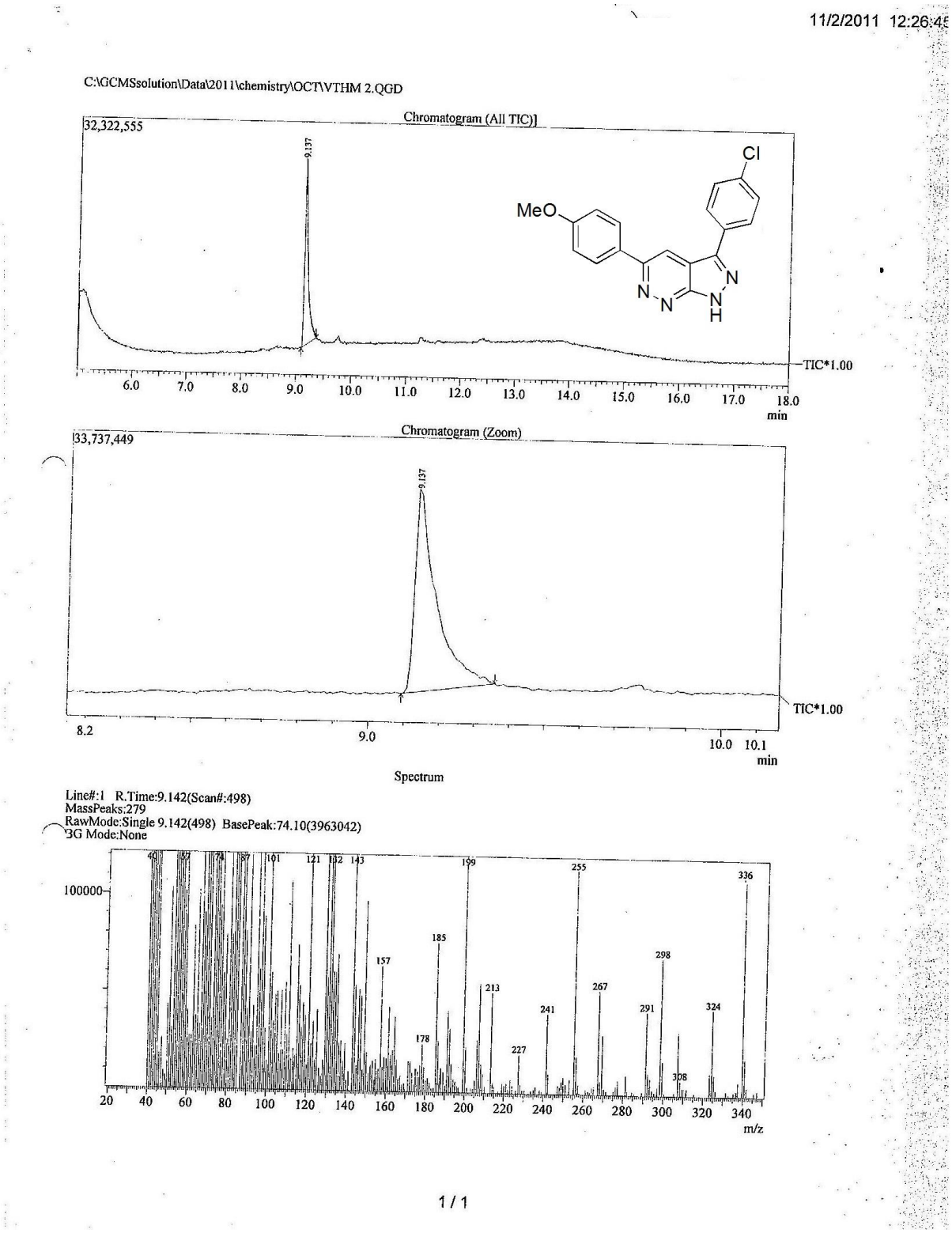


Figure S18: Mass of 3-(4-Chlorophenyl)-5-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*c*]pyridazine (**2d**)