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Palladium N-heterocyclic carbene catalyzed expected and unexpected C–C and C–N functionalization reactions of 1-aryl-3-methyl-1H-pyrazol-5(4H)-ones

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Supplementary information

1. Experimental section

1.1 Materials and Instrumentation

All the chemicals were purchased from Sigma Aldrich and used without further purification. All organic solvents used were of analytical grade and used as received. The progress of all the reactions were monitored by thin-layer chromatography performed on fluorescent coated plates (aluminium plates coated with silica gel 60 F_{254}, 0.25 mm thickness, Merck) and detection of the components was made by exposure to UV light. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on Bruker Avance 400 MHz and 100 MHz spectrometer respectively. The chemical shifts are reported in δ parts per million. IKA RV 10 control rotary evaporator was used to remove the solvents under vacuum. The IR spectra were recorded on a FTIR PerkinElmer Spectrum 100 spectrometer in KBr pellets with absorption in cm^{-1}. Elemental analyses were performed on PerkinElmer 2400 series-II elemental analyzer (PerkinElmer, USA) and all results are found within $\pm$ 0.4% of the theoretical compositions.

1.2 General procedure for the synthesis of compounds 5aa-ac/5ba-bc

To a stirred solution of 1-aryl-3-methyl-1H-pyrazol-5(4H)-one **1a-b** (1 mmol), Ag_2O (0.5 mmol) and Pd(NHC)Cl_2 complex (5 mol %) in AcOH (2 mL) was added aryl iodides **2a-c**. The mixture was magnetically stirred at 100 °C for 5 h and monitored by TLC. After completion, the solvents were removed under vacuum and the resulting crude product so obtained was purified by chromatography on silica gel column with hexane/ethyl acetate (20:10, v/v) as the eluent to afford the desired products **5aa-ac/5ba-bc** with excellent yields.

1.3 General procedure for the synthesis of compounds 6aa-ad/7aa-ad

A mixture of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **1a** (1 mmol), benzylic alcohol **3a-d** (1.0 mmol), TBHP (1.5 mmol, ~5.5 M in decane) and Pd(NHC)Cl_2 complex (5 mol %) in 2 mL AcOH was magnetically stirred at 90 °C for 6 h and then cooled down to room temperature. The volatiles were removed under vacuum and the resulting residues were purified by column chromatography on a silica gel column with hexane/ethyl acetate (20:8, v/v) as the eluent to obtain the desired products **6aa-ad** and **7aa-ad**.

1.4 General procedure for the synthesis of compounds 8a-b

To a stirred solution of 1-aryl-3-methyl-1H-pyrazol-5(4H)-one **1a-b** (1 mmol), $K_2S_2O_8$ (0.5 mmol) and Pd(NHC)Cl_2 complex (5 mol %) in DCE (2 mL) was added MeOH or EtOH (2 mL). The mixture was magnetically stirred at 55 °C for 5 h and monitored by TLC. Upon completion, the solvents were removed under vacuum and the crude product so obtained was then purified by chromatography on silica gel column with hexane/ethyl acetate (20:1, v/v) as the eluent to afford the corresponding products **8a-b** in good yields.

1.5 Spectral data of all compounds

3-Methyl-1-(4'-methyl-[1,1'-biphenyl]-2-yl)-1H-pyrazol-5(4H)-one (5aa)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.21 (s, 6H), 3.44 (s, 2H), 7.32-7.39 (m, 4H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 17.1, 21.1, 41.0, 127.4, 127.6, 127.8, 128.5, 130.4, 133.8, 136.1, 136.5, 139.7, 156.3, 171.1; FTIR (KBr): 3109, 2815, 1626, 1582, 1480, 1315, 1218, 1031, 968 cm^{-1}. Anal. calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60%. Found: C, 77.20; H, 6.06; N, 10.53%.

1-(4'-methoxy-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (5ab)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.21 (s, 3H), 3.43 (s, 2H), 3.79 (s, 3H), 6.69-6.72 (m, 2H), 7.32-7.39 (m, 2H), 7.41-7.45 (m, 1H), 7.50-7.7.52 (m, 1H), 7.57 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 17.1, 41.4, 55.3, 116.3, 127.5, 128.8, 129.8, 130.5, 131.8, 134.8, 138.2, 143.1, 156.5, 171.2; FTIR (KBr): 3105, 2812, 1621, 1586, 1488, 1315, 1214, 1031, 965 cm^{-1}. Anal. calcd. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99%. Found: C, 72.79; H, 5.70; N, 9.94%.

3-Methyl-1-(4'-cyano-[1,1'-biphenyl]-2-yl)-1H-pyrazol-5(4H)-one (5ac)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.22 (s, 3H), 3.44 (s, 2H), 7.32-7.39 (m, 2H), 7.42-7.45 (m, 1H), 7.51 (t, 1H), 7.55 (dd, *J* = 4.0 Hz, *J* = 8.0 Hz, 2H), 7.65 (dd, *J* = 4.0 Hz, *J* = 8.0 Hz, 2H), FTIR (KBr): 3101, 2822, 2222, 1626, 1580, 1484, 1315, 1220, 1030, 968 cm^{-1}.Anal. calcd. for $C_{17}H_{13}N_3O$: C, 74.17; H, 4.76; N, 15.26%. Found: C, 74.09; H, 4.70; N, 15.21%.

1-(4-chloro-4'-methyl-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (5ba)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.21 (s, 6H), 3.43 (s, 2H), 7.31 (dd, J = 2.8 Hz, J = 8.4 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.45 (t, 2H), 7.53 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 17.1, 21.1, 41.4, 116.4, 128.6, 129.7, 129.9, 131.3, 132.9, 135.4, 138.1, 144.3, 157.0, 170.9; FTIR (KBr): 3104, 2812, 1630, 1581, 1483, 1308, 1215, 1032, 967 cm^{-1}. Anal. calcd. for $C_{17}H_{15}ClN_2O$: C, 68.34; H, 5.06; N, 9.38%. Found: C, 68.31; H, 5.01; N, 9.36%.

1-(4-chloro-4'-methoxy-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (5bb)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.21 (s, 3H), 3.43 (s, 2H), 3.79 (s, 3H), 6.69-6.72 (m, 2H), 7.31 (dd, *J* = 2.4 Hz, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 17.4, 41.4, 55.6, 116.4, 128.8, 129.7, 130.1, 131.4, 132.9, 138.2, 140.1, 144.5, 157.0, 168.6; FTIR (KBr): 3110, 2815, 1632, 1585, 1482, 1311, 1215, 1022, 962 cm^{-1}. Anal. calcd. for $C_{17}H_{15}ClN_2O_2$: C, 64.87; H, 4.80; N, 8.90%. Found: C, 64.86; H, 4.75; N, 8.87%.

1-(4-chloro-4'-cyano -[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (5bc)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.21 (s, 3H), 3.44 (s, 2H), 7.30 (dd, J = 8.8 Hz, J = 8.4 Hz, 1H), 7.45 (d, 2H), 7.55 (dd, *J* = 4.0 Hz, *J* = 8.0 Hz, 2H), 7.66 (dd, *J* = 4.0 Hz, *J* = 8.0 Hz, 2H), FTIR (KBr): 3104, 2223, 2810, 1630, 1581, 1486, 1310, 1210, 1032, 969 cm^{-1}.Anal. calcd. for $C_{17}H_{12}ClN_3O$: C, 65.92; H, 3.91; N, 13.57%. Found: C, 65.88; H, 3.87; N, 13.51%.

(E)-4-benzylidine-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (6aa)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.36 (s, 3H), 7.21(t, 1H), 7.45 (dd, *J* = 6.8 Hz and *J* = 14.4 Hz, 2H), 7.53-7.59 (m, 2H), 7.64 (t, 1H), 7.84 (s, 1H), 7.91(d, *J* = 8.4 Hz, 2H), 8.60 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 13.6, 118.4, 118.8, 122.5, 125.1, 127.2, 129.3, 131.4, 133.9, 138.6, 148.8, 152.3, 161.9; FTIR (KBr): 3420, 3088, 2915, 1620, 1593, 1489, 1410, 1322, 1018, 738, 699 cm^{-1}. Anal. calcd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68%. Found: C, 77.81; H, 5.33; N, 10.61%.

(E)-3-methyl-4-(4-methylbenzylidene)-1-phenyl-1H-pyrazol-5(4H)-one (6ab)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.34 (s, 3H), 2.42 (s, 3H), 7.20 (t, 1H), 7.38-7.46 (m, 4H), 7.78 (s, 1H), 7.91(d, *J* = 7.6 Hz, 2H), 8.54 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 13.6, 21.9, 118.8, 125.0, 126.2, 129.3, 129.8, 130.9, 134.4, 138.7, 144.7, 148.8, 152.2, 162.0; FTIR (KBr): 3089, 1638, 1596, 1491, 1419, 1290, 1025, 741, 687 cm^{-1}. Anal. calcd. for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14%. Found: C, 78.14; H, 5.81; N, 10.08%.

(E)-4-(4-methoxybenzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (6ac)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.33 (s, 3H), 3.87 (s, 3H), 7.10-7.21 (m, 3H), 7.43 (t, 2H), 7.74 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 8.71 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 13.6, 56.2, 114.8, 118.8, 124.2, 124.9, 126.6, 129.2, 137.3, 138.8, 148.5, 152.3, 162.3, 164.1; FTIR (KBr): 3078, 1638, 1588, 1492, 1430, 1289, 1025, 759, 699 cm^{-1}. Anal. calcd. for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58%. Found: C, 73.90; H, 5.43; N, 9.53%.

(E)-3-methyl-4-(4-nitrobenzylidene)-1-phenyl-1H-pyrazol-5(4H)-one (6ad)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.40 (s, 3H), 7.28 (s, 1H), 7.42-7.46 (m, 3H), 7.94 (t, 2H), 8.33 (d, *J* = 6.8 Hz, 2H), 8.60 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.2, 119.1, 123.6, 125.3, 126.3, 128.9, 131.6, 133.8, 138.1, 142.7, 152.3, 164.1; FTIR (KBr): 3095, 2924, 1629, 1580, 1496, 1413, 1345, 744, 687 cm^{-1}. Anal. calcd. for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67%. Found: C, 66.39; H, 4.21; N, 13.63%.

4-((5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)(phenyl)methyl)-5-methyl-2-phenyl-1H-pyrazol-3(2H)-one (7aa)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.32 (s, 6H), 4.96 (s, 1H), 7.18 (t, 1H), 7.23-7.28 (m, 6H), 7.43 (t, 4H), 7.71(d, *J* = 8.0 Hz, 4H), 12.47 (s, 1H), 14.00 (s, 1H); ^{13}C NMR (100 MHz,

DMSO-d_6): δ (ppm) 12.3, 33.6, 121.0, 126.0, 126.3, 127.6, 128.6, 129.4, 138.3, 142.7, 146.7, 156.8, 176.1; FTIR (KBr): 3085, 2910, 1629, 1595, 1494, 1413, 1320, 1020, 735, 690 cm^{-1}. Anal. calcd. for $C_{27}H_{24}N_4O_2$: C, 74.29; H, 5.54; N, 12.84%. Found: C, 74.22; H, 5.50; N, 12.79%.

4-((5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)(p-tolyl)methyl)-5-methyl-2-phenyl-1H-pyrazol-3(2H)-one (7ab)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.25 (s, 3H), 2.31 (s, 6H), 4.91 (s, 1H), 7.07 (d, J = 8.0 Hz, 4H), 7.14 (d, J = 8.0 Hz, 2H), 7.23-7.26 (m, 4H), 7.44 (t, 4H), 12.42 (s, 1H), 13.92 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 20.9, 33.2, 120.9, 126.0, 127.5, 129.1, 129.4, 135.2, 139.6, 146.7, 156.2, 164.2; FTIR (KBr): 3442, 3328, 3078, 1632, 1592, 1498, 1418, 1294, 1025, 744, 689 cm^{-1}. Anal. calcd. for $C_{28}H_{26}N_4O_2$: C, 74.65; H, 5.82; N, 12.44%. Found: C, 74.61; H, 5.76; N, 12.41%.

4-((5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)(4-methoxyphenyl)methyl)-5-methyl-2-phenyl-1H-pyrazol-3(2H)-one (7ac)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.31 (s, 6H), 3.70 (s, 3H), 4.90 (s, 1H), 6.84 (d, J = 8.8 Hz, 2H), 7.14 (d, J = 8.8 Hz, 2H), 7.24 (t, 2H), 7.44 (t, 4H), 7.71 (d, J = 8.0 Hz, 4H), 12.43 (s, 1H), 13.94 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 19.0, 32.8, 55.4, 114.0, 120.9, 125.9, 128.6, 129.3, 134.5, 146.6, 158.0, 173.1; FTIR (KBr): 3440, 3330, 3072, 1630, 1588, 1490, 1428, 1291, 1028, 759, 695 cm^{-1}. Anal. calcd. for $C_{28}H_{26}N_4O_3$: C, 72.09; H, 5.62; N, 12.01%. Found: C, 72.01; H, 5.49; N, 11.94%.

4-((5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)(4-nitrophenyl)methyl)-5-methyl-2-phenyl-1H-pyrazol-3(2H)-one (7ad)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.12 (s, 6H), 4.81 (s, 1H), 7.15 (t, 2H), 7.28-7.37 (m, 6H), 7.60 (d, J = 8.4 Hz, 4H), 8.09 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 19.3, 34.4, 119.0, 122.1, 123.6, 128.2, 129.0, 138.1, 145.1, 151.8, 156.1, 171.0; FTIR (KBr): 3441, 3330, 3090, 2920, 1629, 1583, 1492, 1412, 1340, 742, 685 cm^{-1}. Anal. calcd. for $C_{27}H_{23}N_5O_4$: C, 67.35; H, 4.81; N, 14.54%. Found: C, 67.29; H, 4.77; N, 14.47%.

3-methyl-5,6-dihydro-1H-pyrazolo[1,2-a]cinnolin-1-one (8a)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.30 (s, 3H), 3.83 (t, 2H), 4.33 (t, 2H), 5.53 (s, 1H), 7.30 (t, 1H), 7.42-7.46 (m, 2H), 7.84 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 17.1, 41.2, 71.4, 86.4, 121.1, 122.0, 129.3, 129.4, 132.1, 148.1, 158.6, 168.9; FTIR (KBr): 3089, 2981, 1638, 1582, 1483, 1308, 1215, 1038, 967 cm^{-1}. Anal. calcd. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99%. Found: C, 71.95; H, 6.01; N, 13.95%.

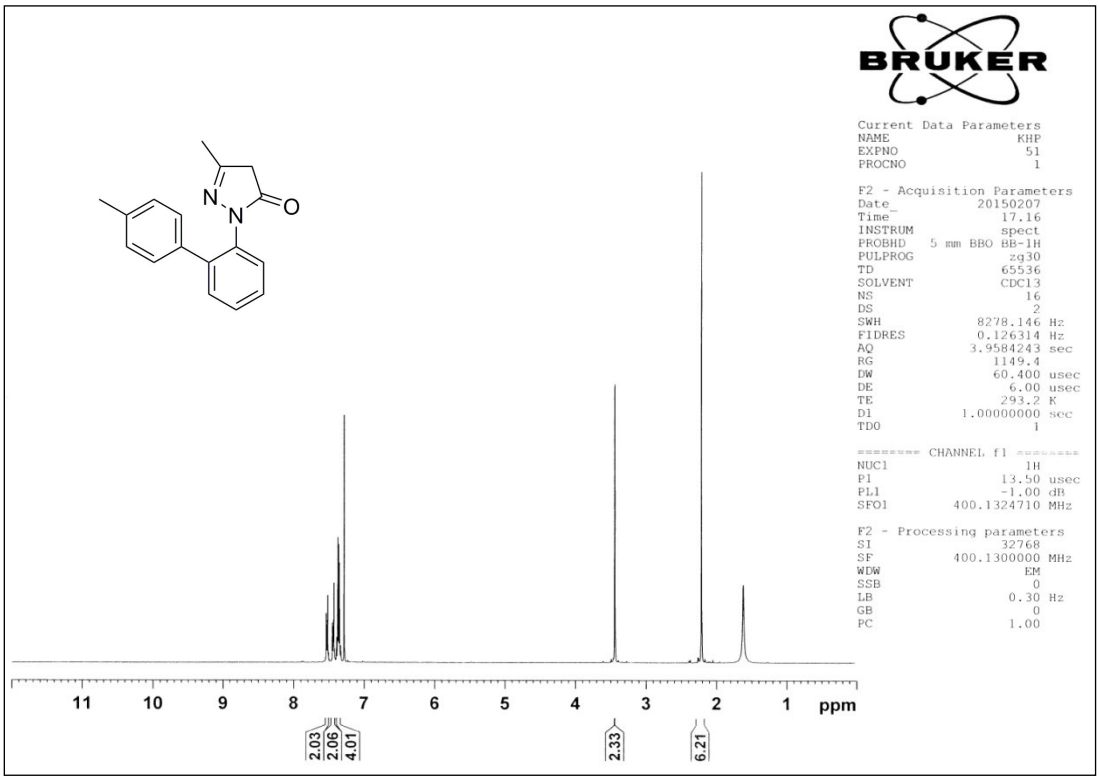
9-chloro-3-methyl-5,6-dihydro-1H-pyrazolo[1,2-a]cinnolin-1-one (8b)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.29 (s, 3H), 3.71 (t, 2H), 4.27 (t, 2H), 5.51 (s, 1H), 7.33-7.37 (m, 1H), 7.42-7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 17.1, 41.2, 71.5, 86.3, 128.6, 129.7, 129.9, 131.3, 132.1, 148.2, 157.3, 170.9; FTIR (KBr): 3085, 2984, 1635, 1580, 1488, 1308, 1217, 1038, 966 cm^{-1}. Anal. calcd. for $C_{12}H_{11}ClN_2O$: C, 61.42; H, 4.72; N, 11.94%. Found: C, 61.37; H, 4.66; N, 11.89%.

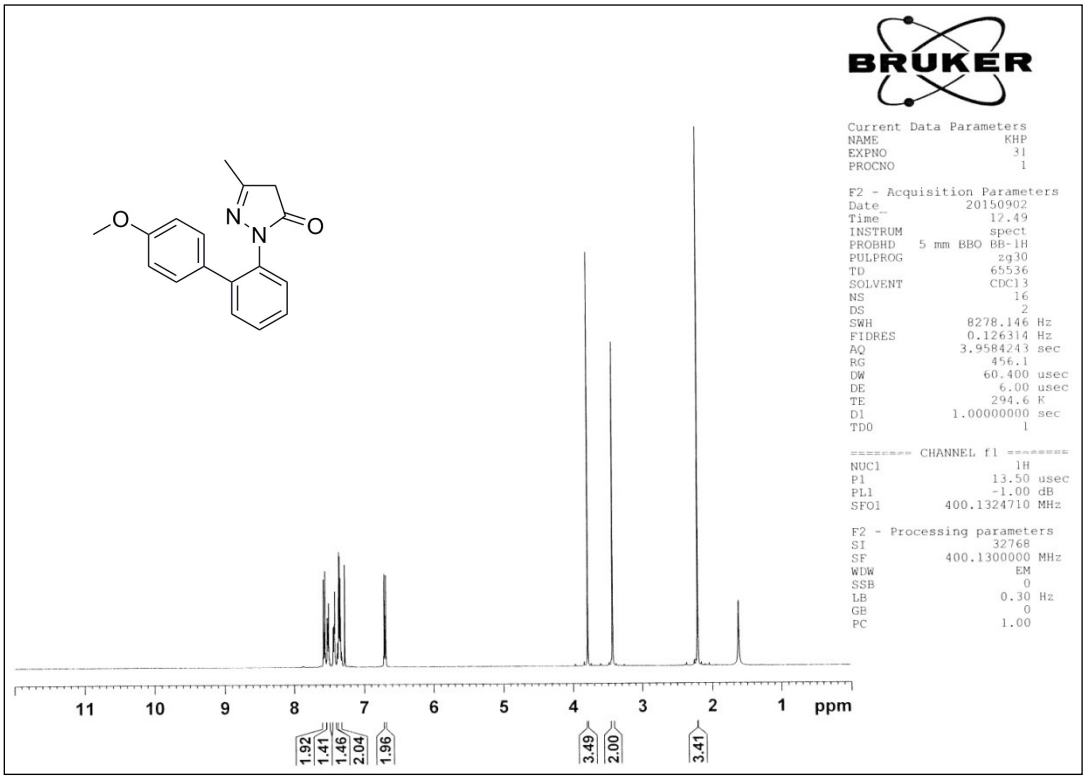
3,3'-dimethyl-1,1'-diphenyl-1H,1'H-[4,4'-bipyrazole]-5,5'-diol (11a)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.09 (s, 6H), 7.16-7.22 (m, 2H), 7.41 (d, J = 7.6 Hz, 2H), 7.65-7.78 (m, 2H), 7.87 (d, J = 7.6 Hz, 2H), 11.30-12.10 (brs, 2H), FTIR (KBr): 3330, 2925, 1585, 1492, 1330, 1310, 1218, 1160, 1128, 1015, 828 cm^{-1}. Anal. calcd. for $C_{20}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.17%. Found: C, 69.29; H, 5.20; N, 16.16%. ESI-MS: m/z: 346.30 $[M]^+$

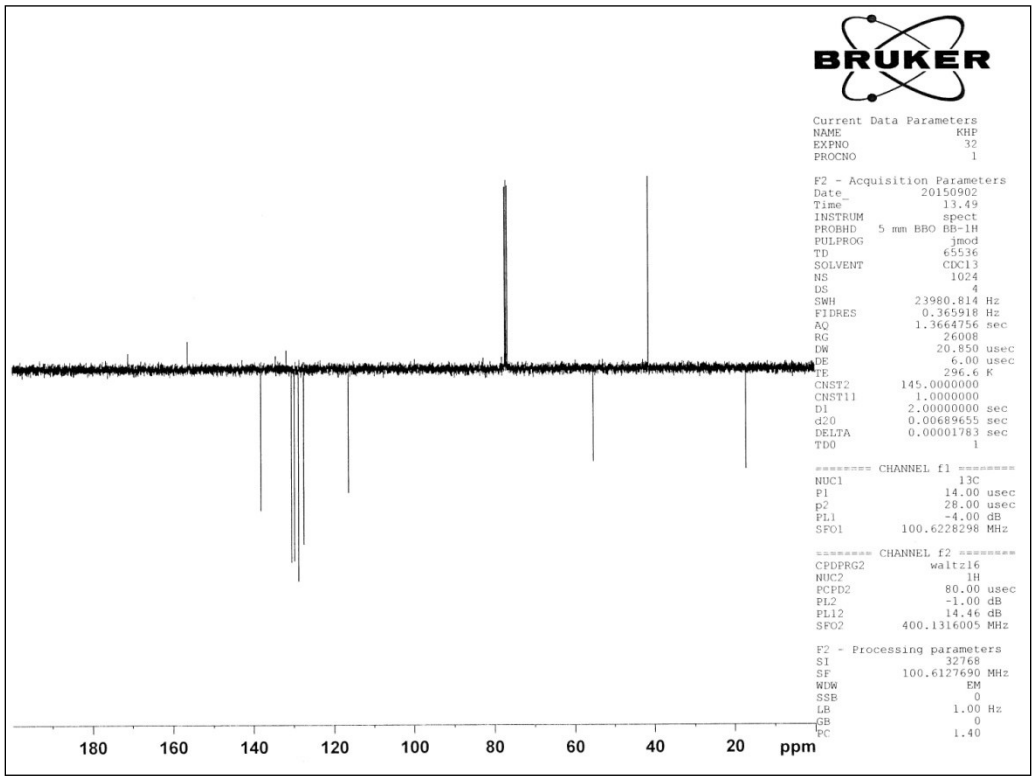
^{1}H NMR spectrum of compound **5aa**



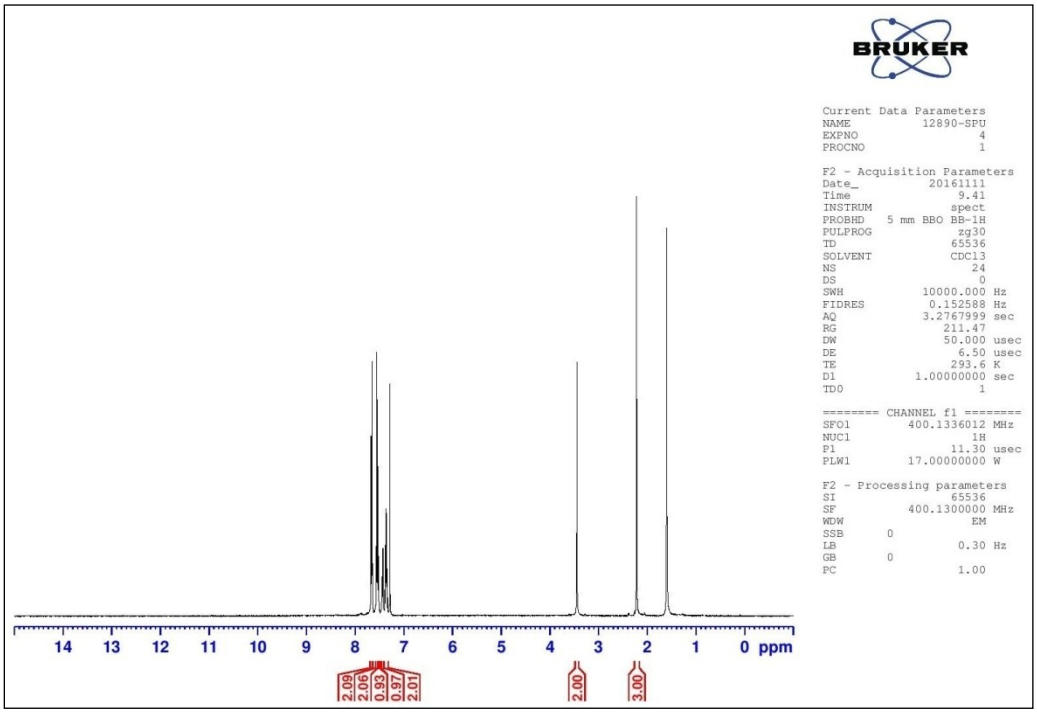
^{1}H NMR spectrum of compound **5ab**



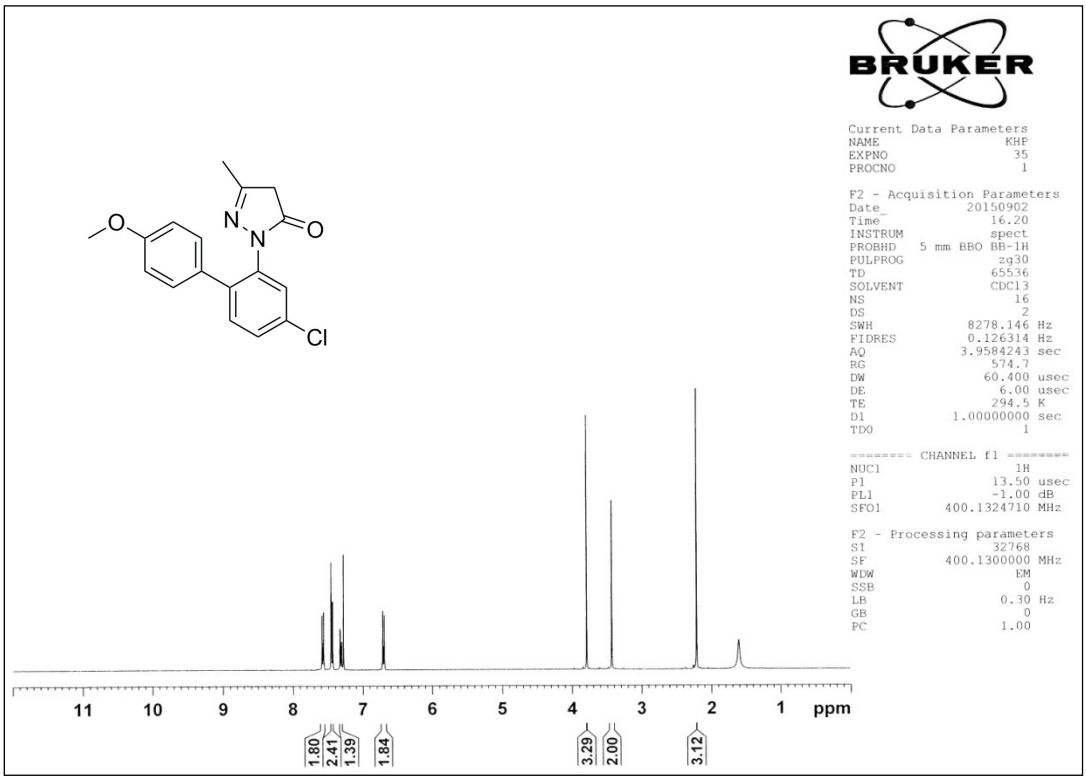
^{13}C APT (Attached Proton Test) spectrum of compound **5ab**



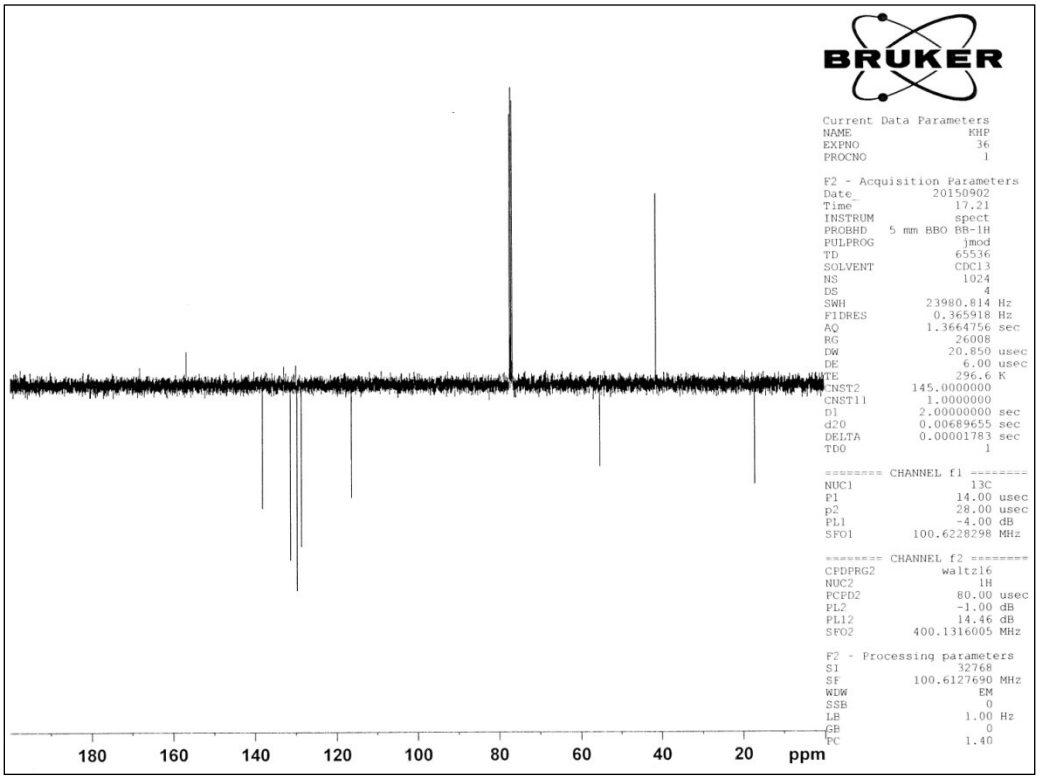
^{1}H NMR spectrum of compound **5ac**



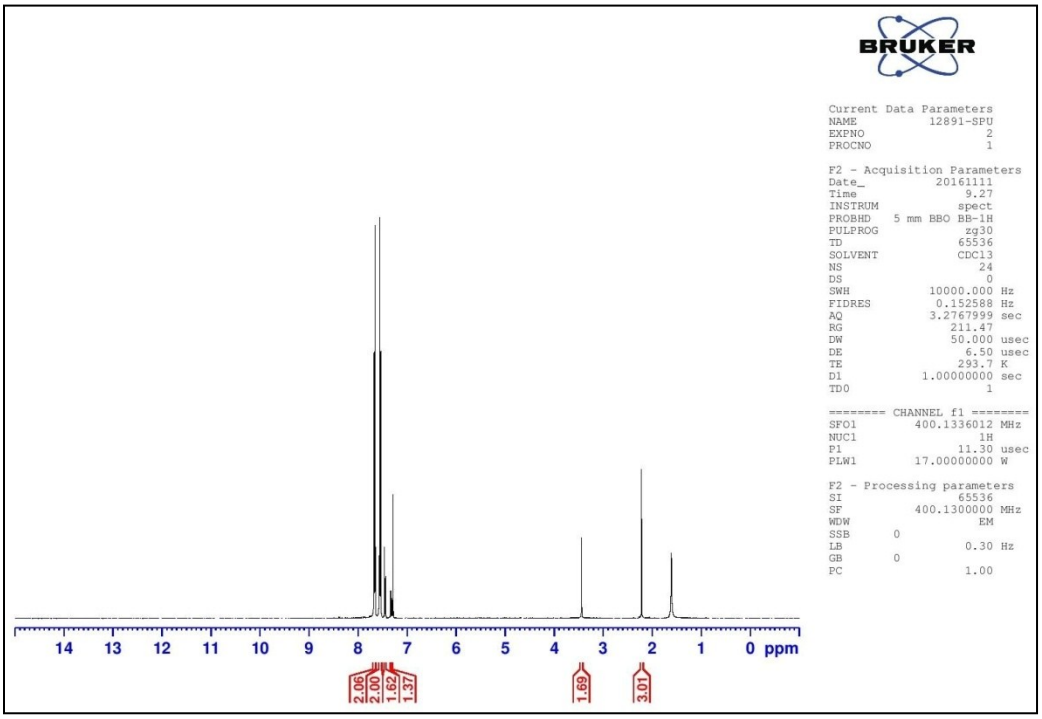
^{1}H NMR spectrum of compound **5bb**



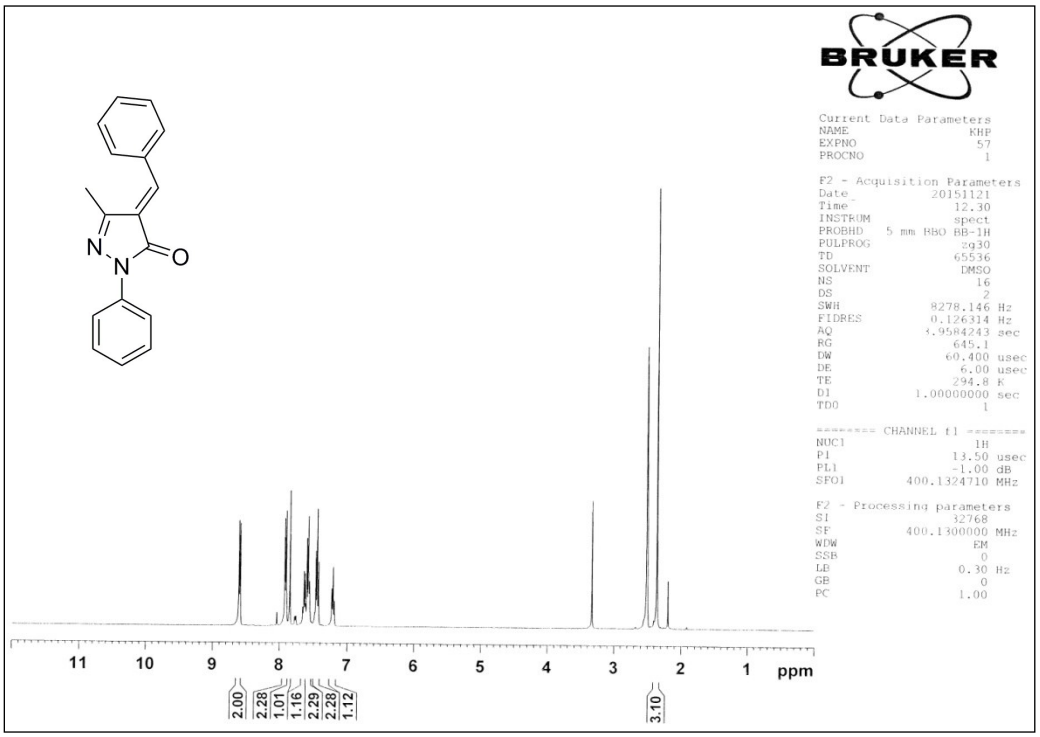
^{13}C APT (Attached Proton Test) spectrum of compound **5bb**



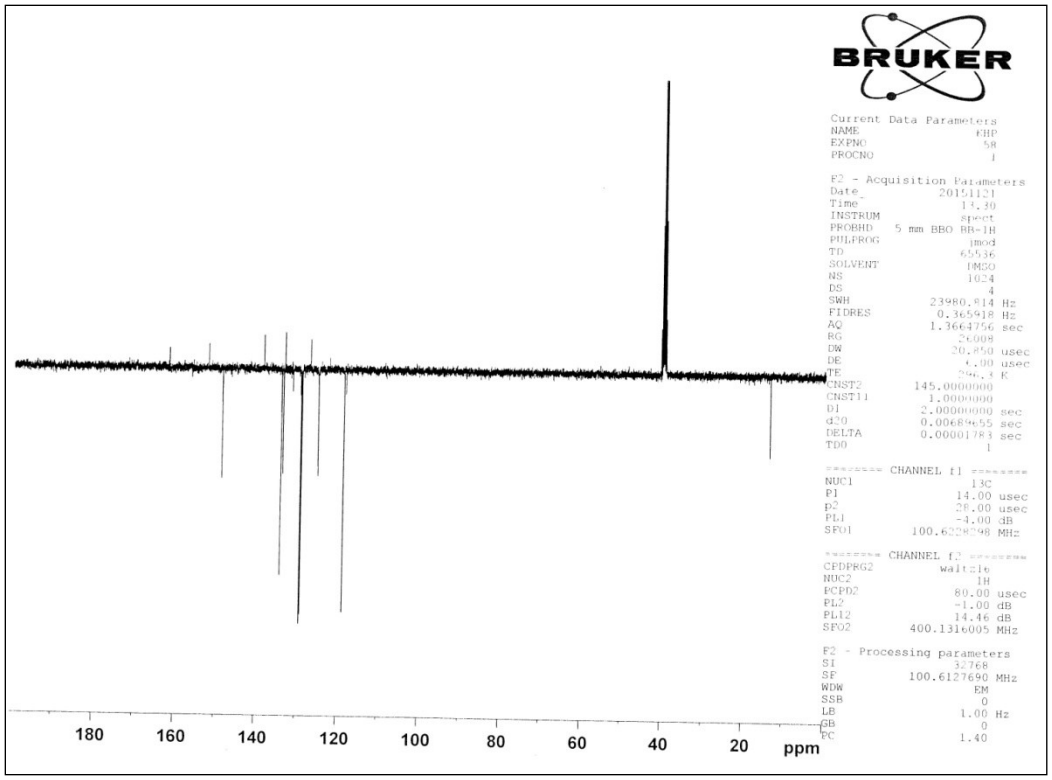
^{1}H NMR spectrum of compound **5bc**



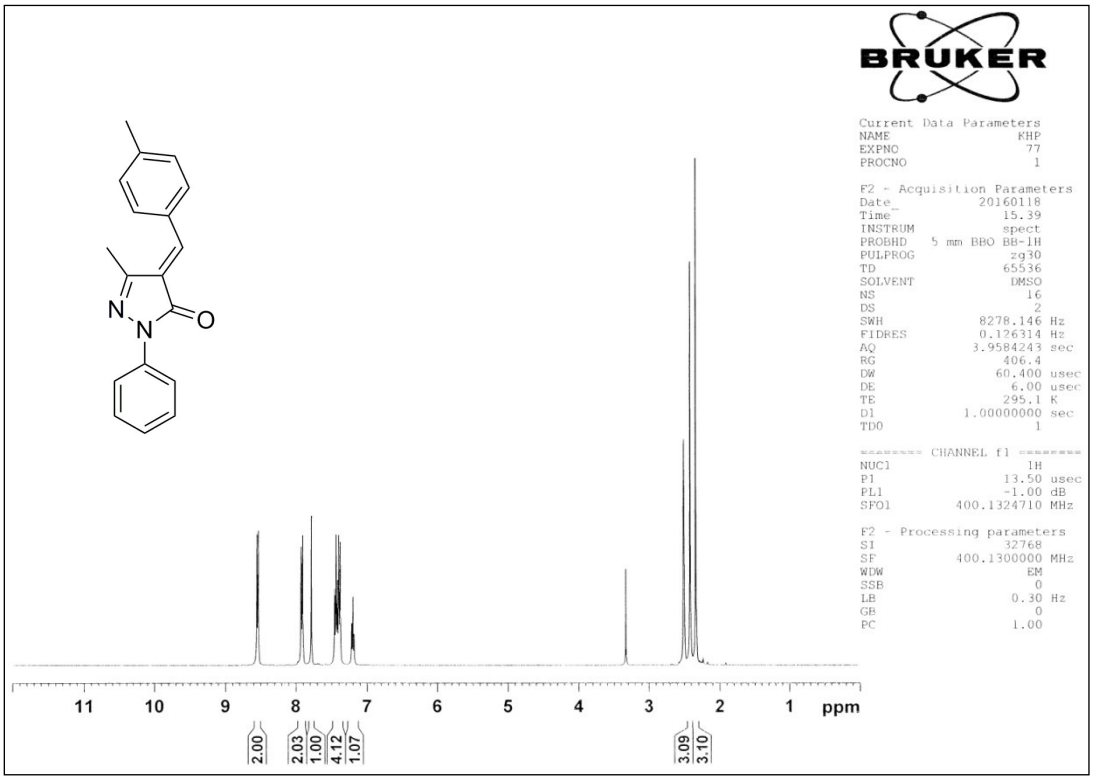
^{1}H NMR spectrum of compound **6aa**



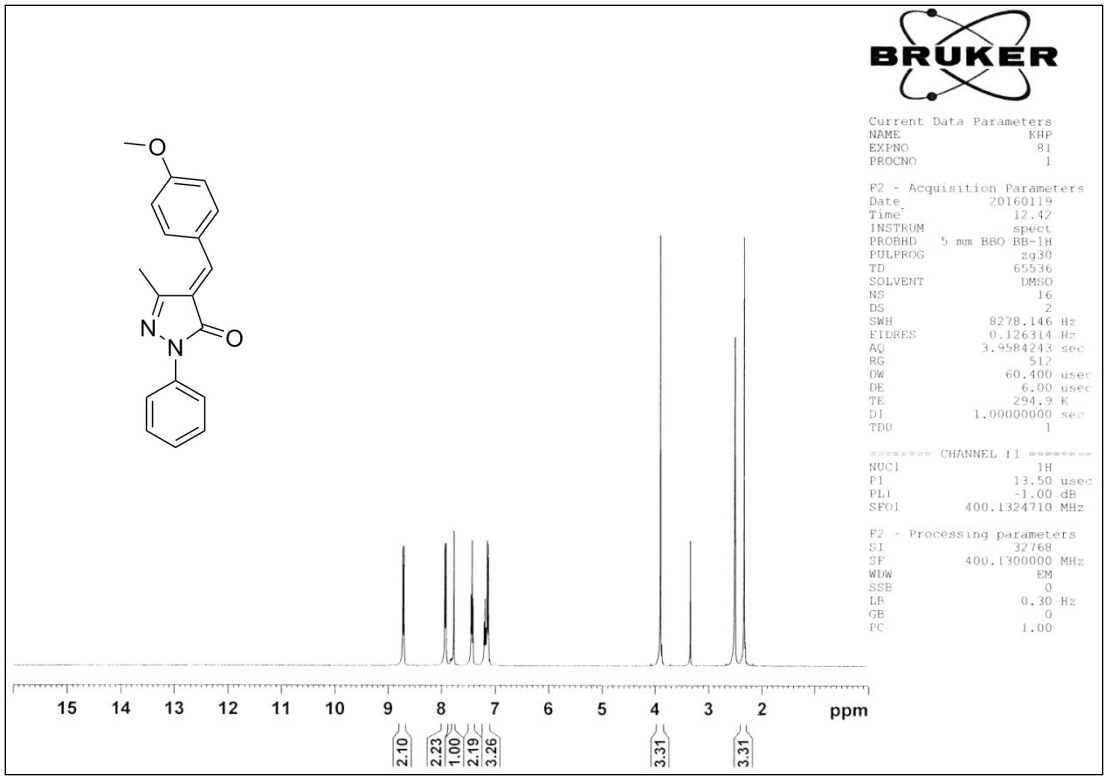
^{13}C APT (Attached Proton Test) spectrum of compound **6aa**



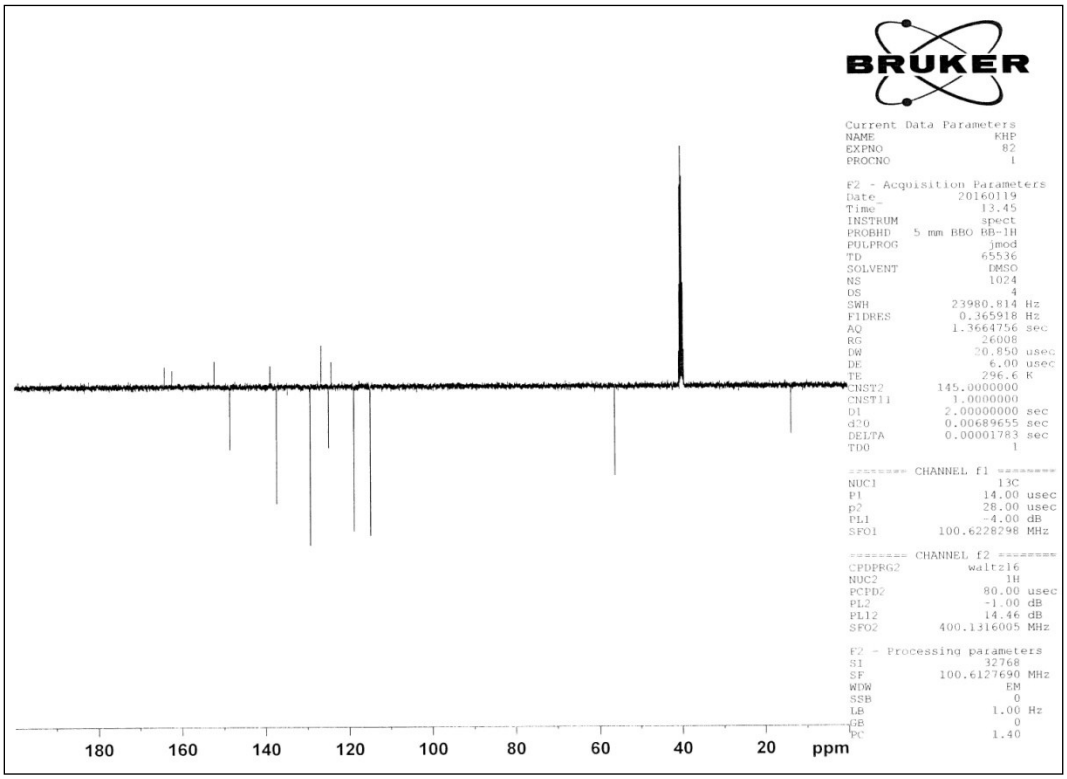
^{1}H NMR spectrum of compound **6ab**



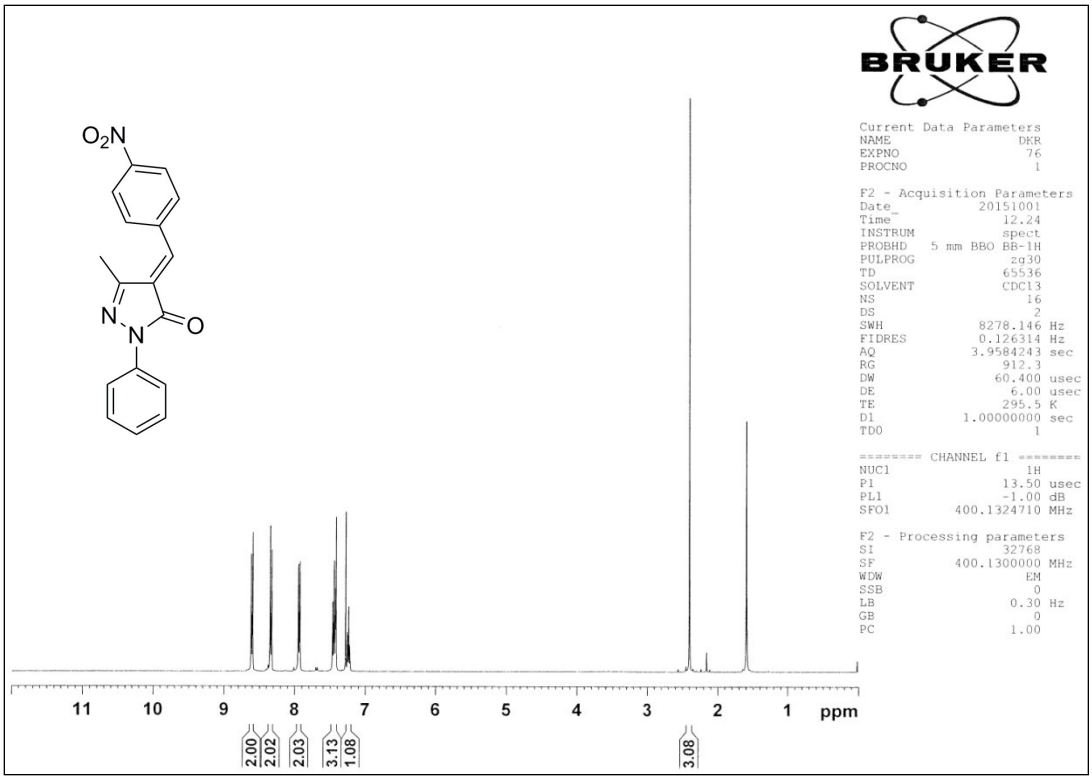
^{1}H NMR spectrum of compound **6ac**



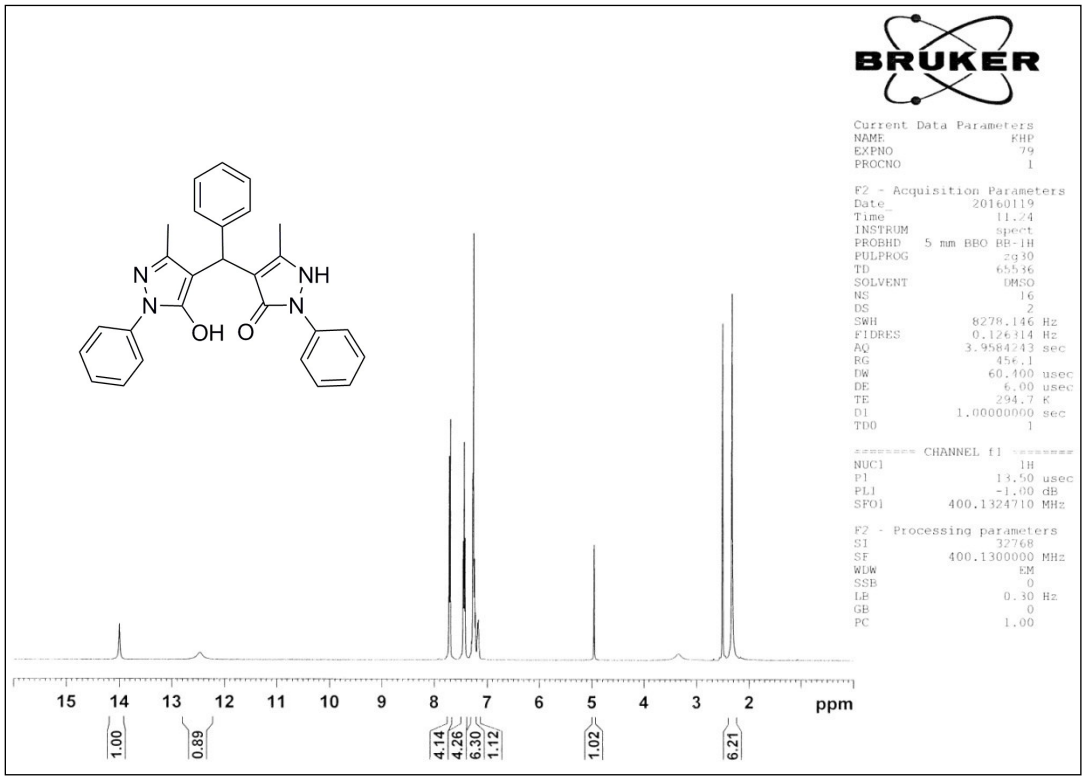
^{13}C APT (Attached Proton Test) spectrum of compound **6ac**



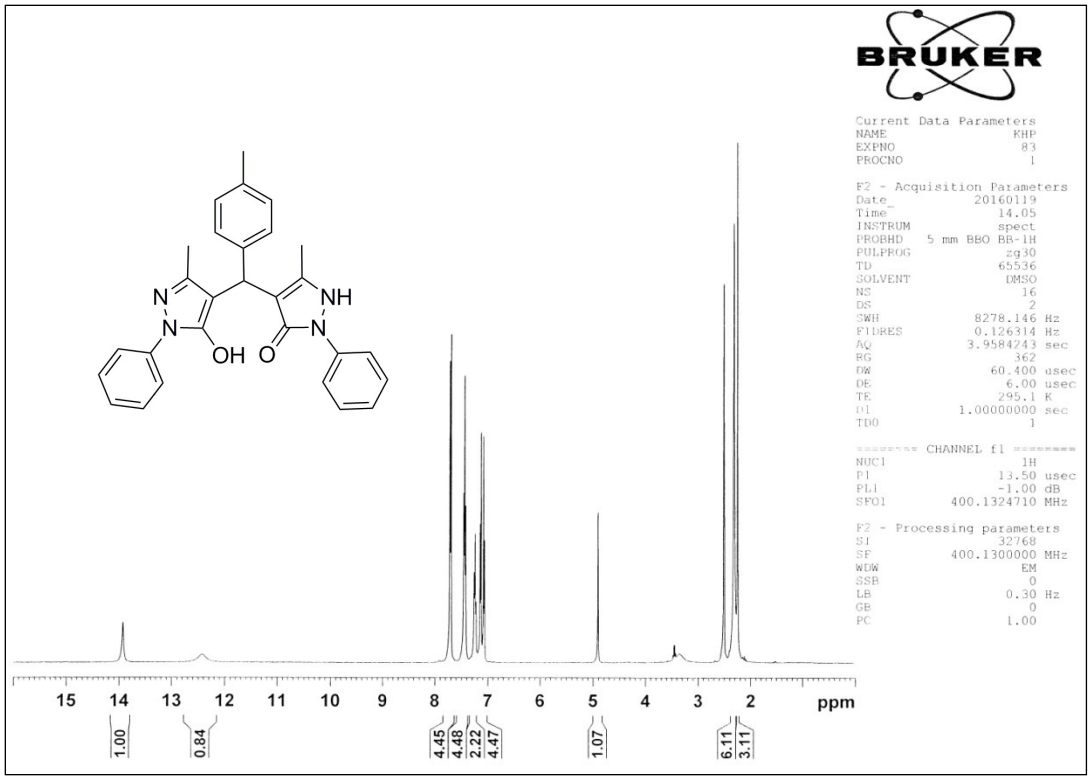
^{1}H NMR spectrum of compound **6ad**



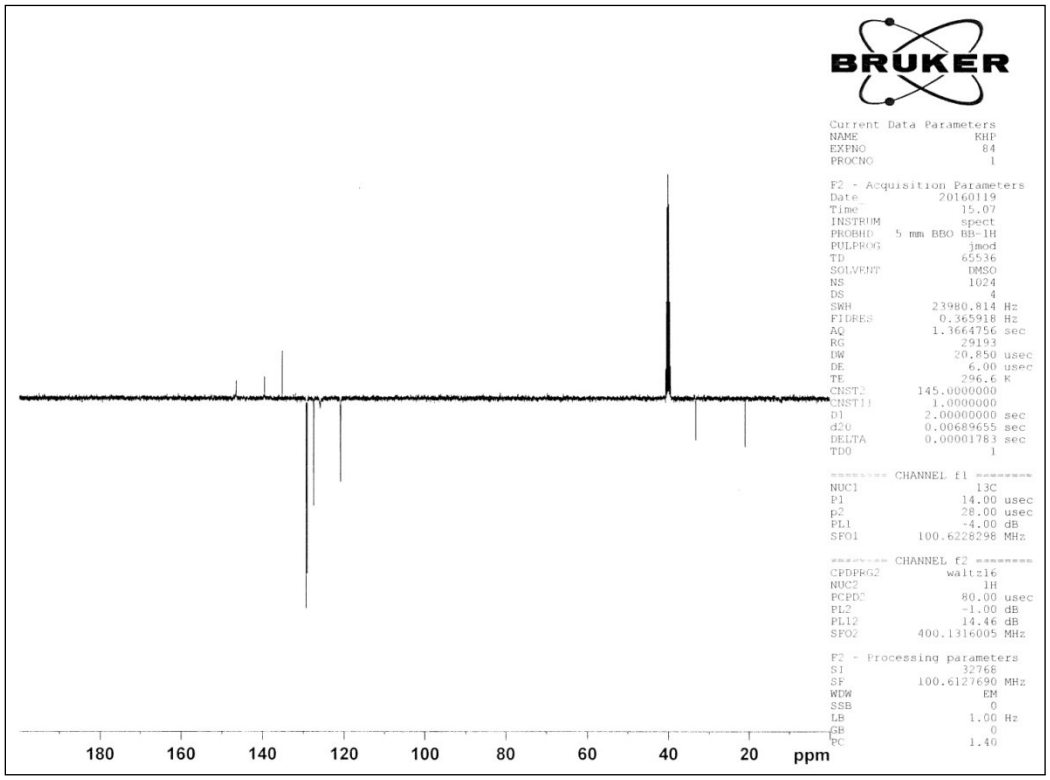
^{1}H NMR spectrum of compound **7aa**



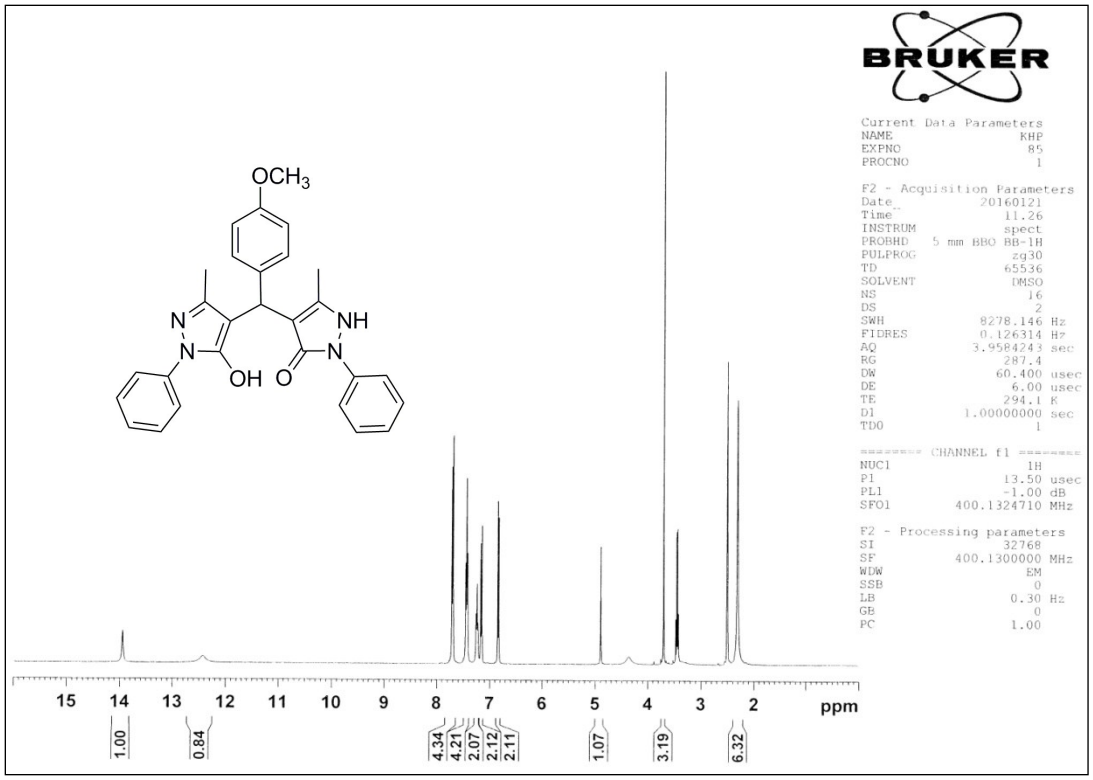
^{1}H NMR spectrum of compound **7ab**



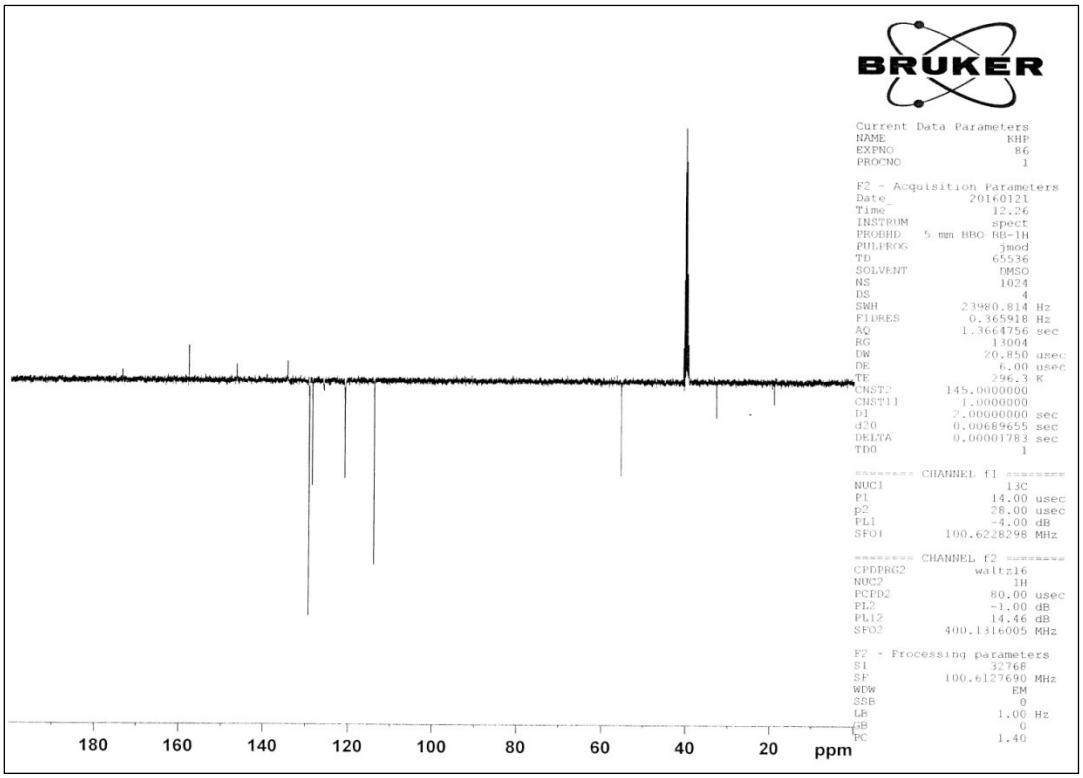
^{13}C APT (Attached Proton Test) spectrum of compound **7ab**



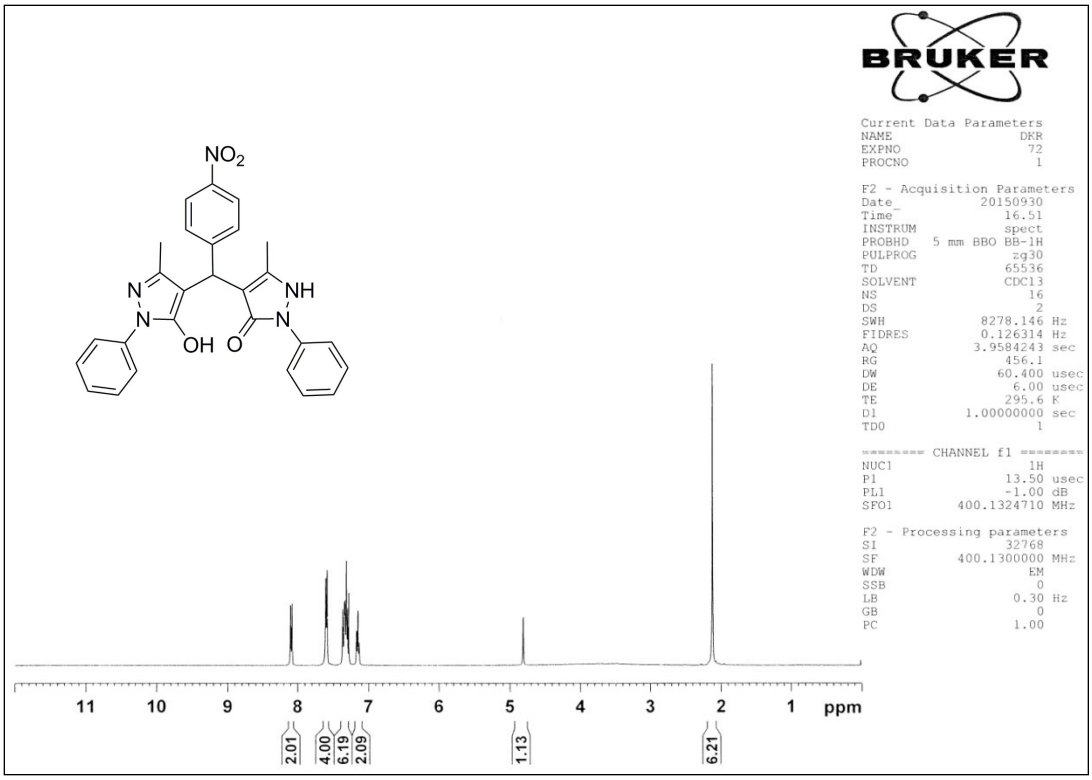
^{1}H NMR spectrum of compound **7ac**



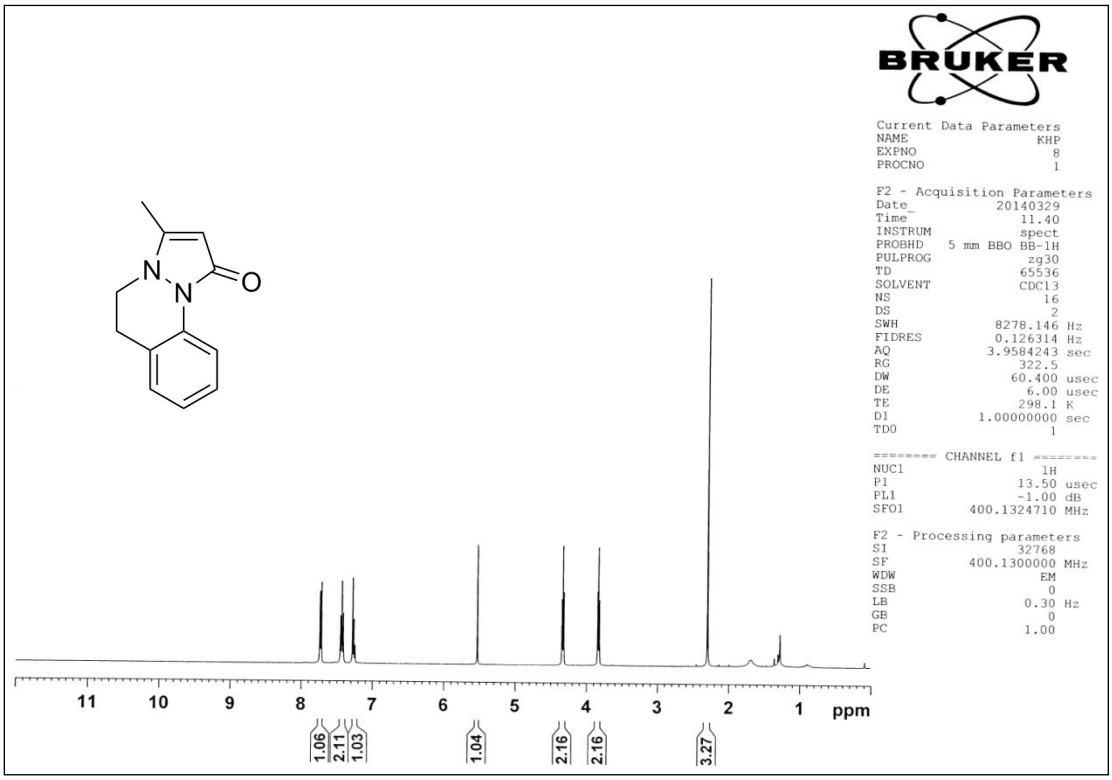
^{13}C APT (Attached Proton Test) spectrum of compound **7ac**



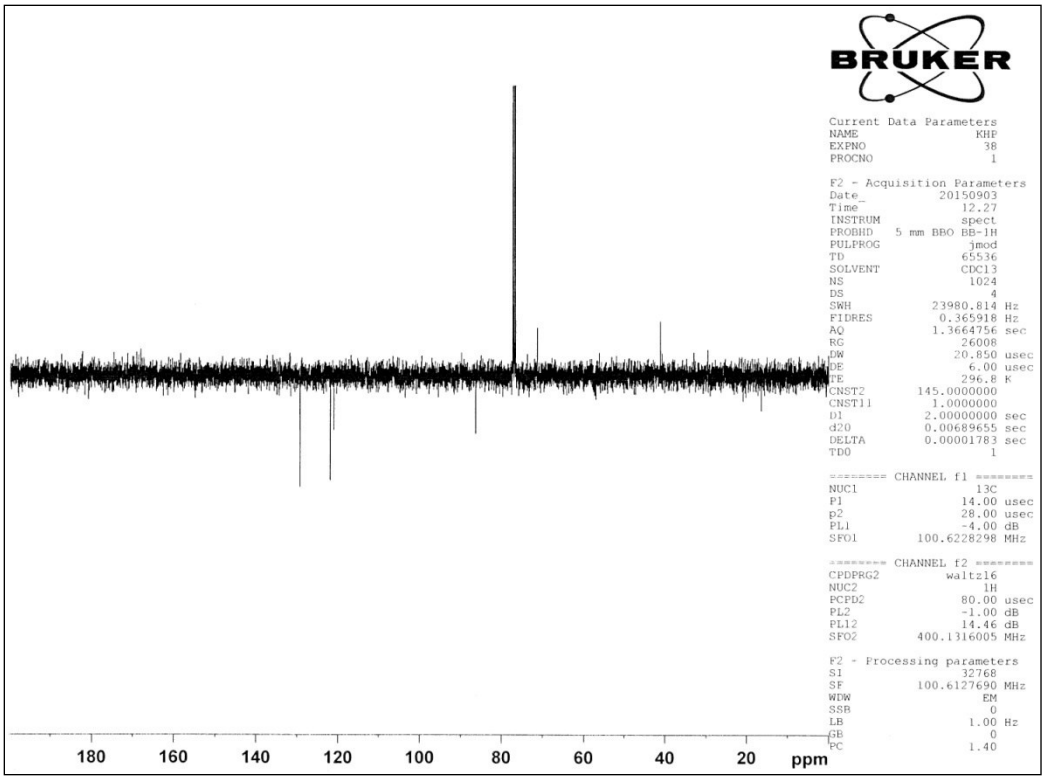
^{1}H NMR spectrum of compound **7ad**



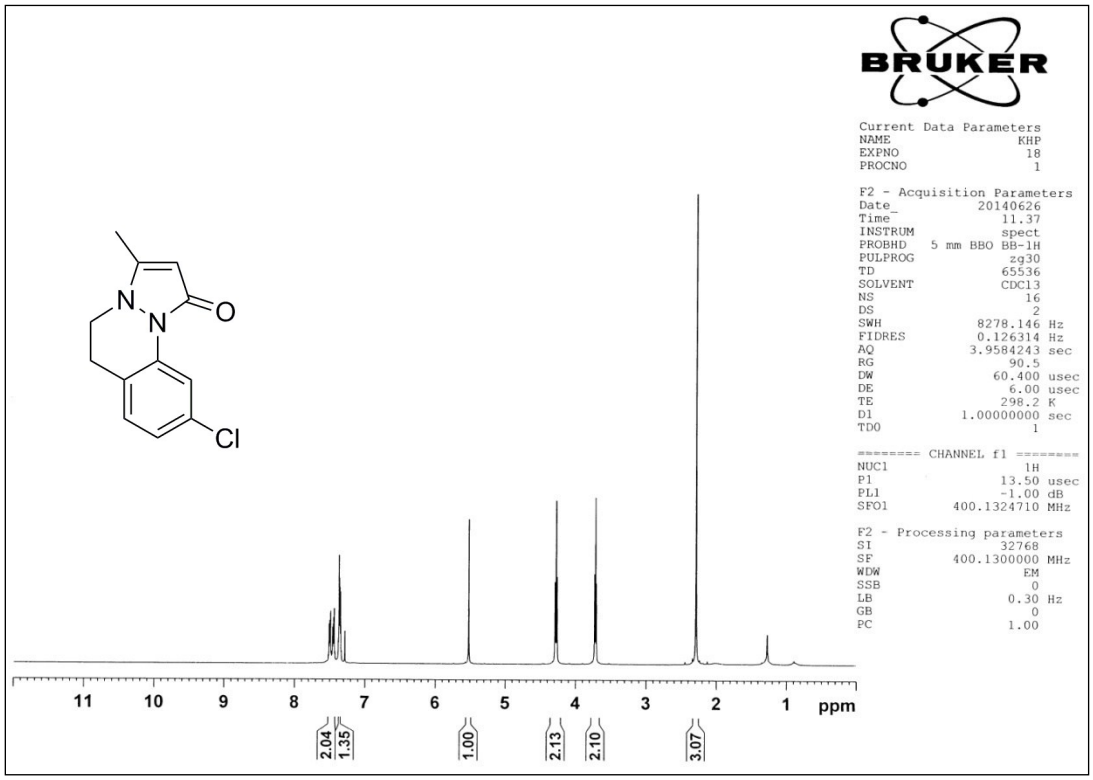
^{1}H NMR spectrum of compound **8a**



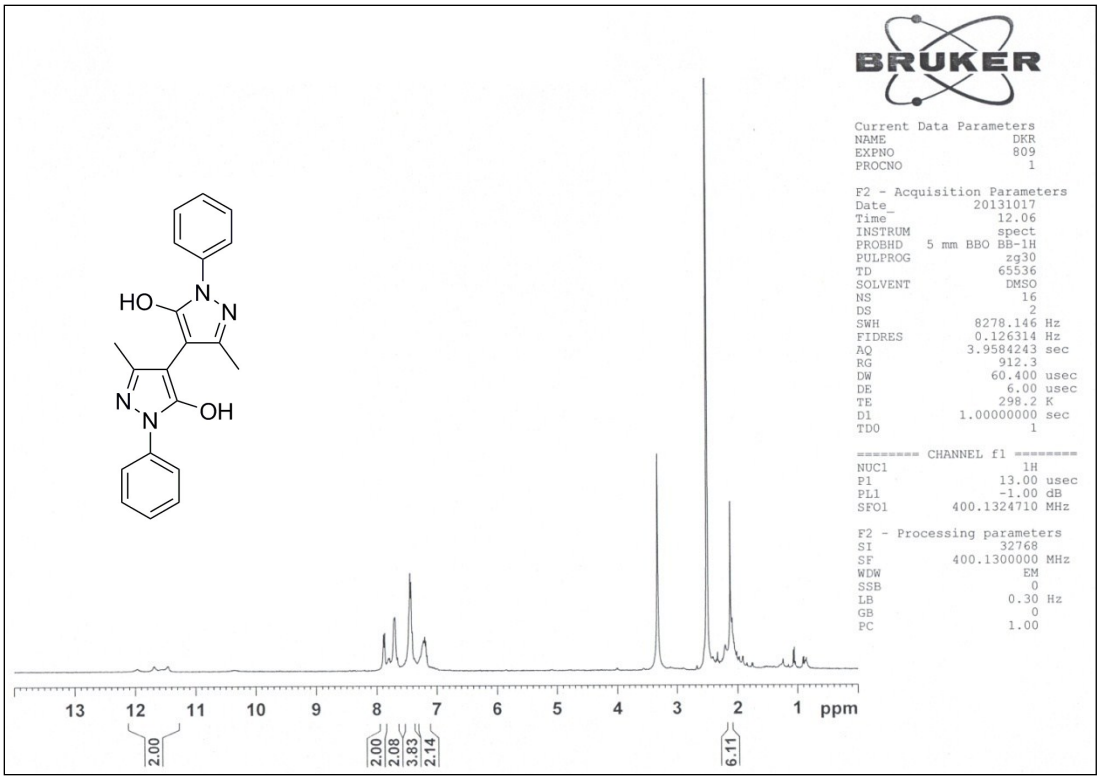
^{13}C APT (Attached Proton Test) spectrum of compound **8a**



^{1}H NMR spectrum of compound **8b**



^{1}H NMR spectrum of compound **11a**



ESI-MS spectrum of compound **11a**