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Synthesis of Fully Functionalised Spiropyran Pyrazolone Skeletons *via* formal [4+2] Cascade Process Using β-Nitro Styrene Derived MBH-Alcohols

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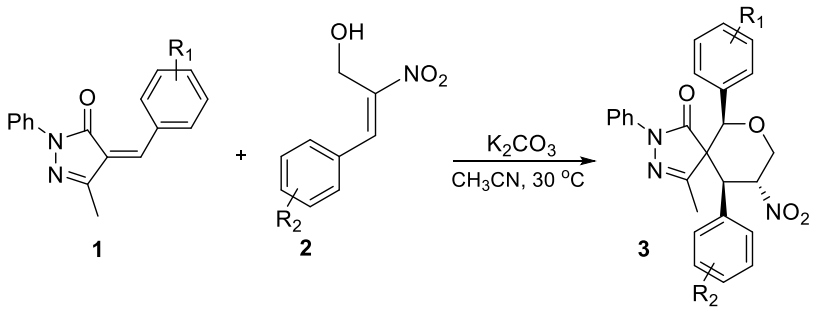
Supporting Information

Experimental Section

General

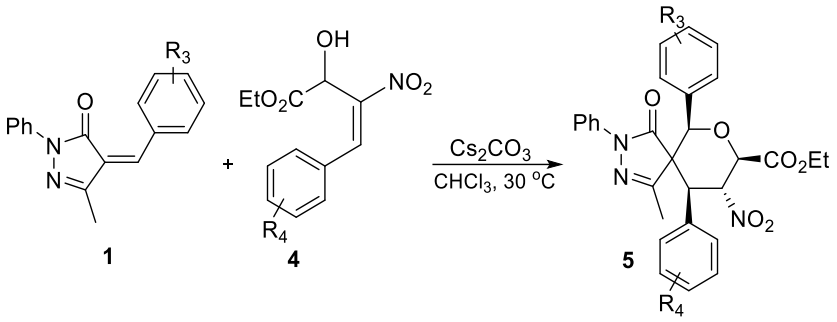
All reactions were carried out with dry, freshly distilled solvents in anhydrous conditions. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was performed on silica gel (230–400 mesh). NMR (400 MHz for ^{1}H NMR, and ^{13}C NMR) spectra were recorded in $CDCl_3$ with TMS as the internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; dd, doublet of doublet; t, triplet; q, quartet; m, multiplet, coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High-resolution mass spectra (HRMS) were recorded on micro mass ESI-TOF MS. Melting points were determined in a Hanon auto melting point system (MP 450). IR was recorded on FTIR Bruker Technologies. HPLC chromatogram was recorded on Shimadzu LC-20AT using chiral cell OD-H column.

General procedure for the synthesis spiropyrazolone teterhydropyran using primary alcohol 3:



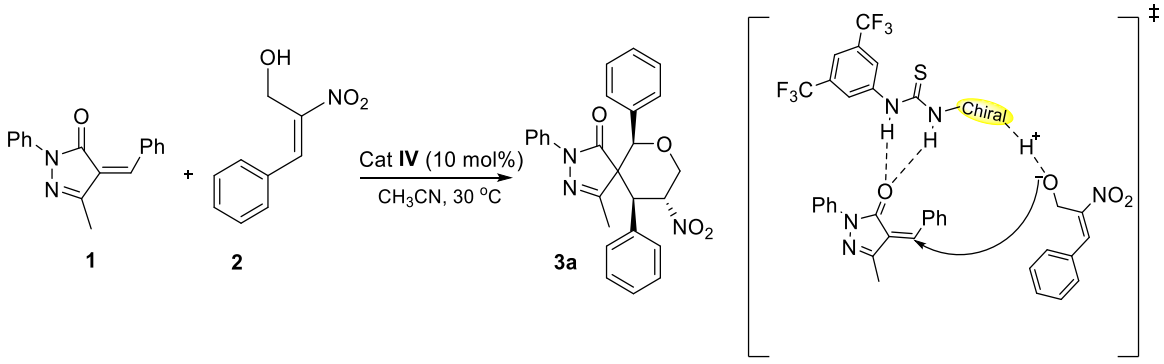
To a solution of arylidene pyrazolone **1** (100 mg, 0.381 mmol, 1.0 equiv.) was added nitro allylic primary alcohol **2** (102 mg, 0.572 mmol, 1.5 equiv.) and K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL). The reaction mixture was stirred at room temperature till the completion reaction. After the completion of the reaction, the organic layer was extracted with ethyl acetate, washed with brine solution and dried over Na_2SO_4, and concentrated under reduced pressure. The resulted crude was subjected to flash column chromatography on silica gel (200-400) by eluting ethyl acetate in hexane (4:96) to afford the desired products **3a**.

General procedure for the synthesis of spiropyrazolone teterhydropyran using secondary alcohol 5:



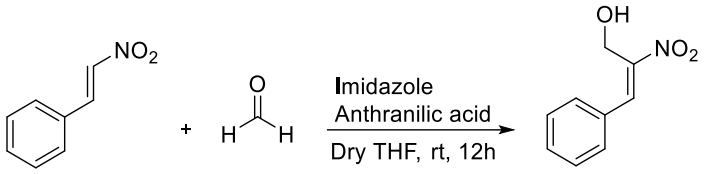
To a solution of arylidene pyrazolone **1** (100 mg, 0.38 mmol, 1.0 equiv.) was added nitro allylic secondary alcohol **4** (143 mg, 0.57 mmol, 1.5 equiv.) and Cs_2CO_3 (310 mg, 0.95 mmol, 2.5 equiv.) in $CHCl_3$ (2 mL). The reaction mixture was stirred at room temperature till the completion reaction. After the completion of the reaction, the organic layer was extracted with ethyl acetate, washed with brine solution and dried over Na_2SO_4, and concentrated under reduced pressure. The resulted crude was subjected to flash column chromatography on silica gel (200-400) by eluting ethyl acetate in hexane (4:96) to afford the desired products **5**.

General procedure for the synthesis of chiral tetrahydrochromene 3a using thiourea catalyst:



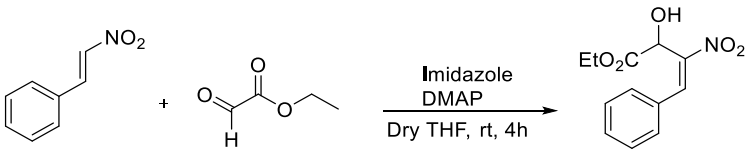
To a solution of arylidene pyrazolone **1** (50 mg, 0.190 mmol, 1.0 equiv.) was added nitro allylic primary alcohol **2** (51 mg, 0.286 mmol, 1.5 equiv.) and 10 mol% of quinine derived thiourea catalyst in CH_3CN (1.5 mL). The reaction mixture was stirred at room temperature till the completion reaction. After the completion of the reaction, the organic layer was extracted with ethyl acetate, washed with brine solution and dried over Na_2SO_4, and concentrated under reduced pressure. The resulted crude was subjected to flash column chromatography on silica gel (200-400) by eluting ethyl acetate in hexane (4:96) to afford the desired products **3a**. We have performed HPLC chromatogram by using chiral cel OD-H column to furnished **3a** as 94% of enantiomeric excess using IPA:Hex (20:80).

General procedure for the synthesis of nitro styrene derived MBH-primary alcohol[1]:



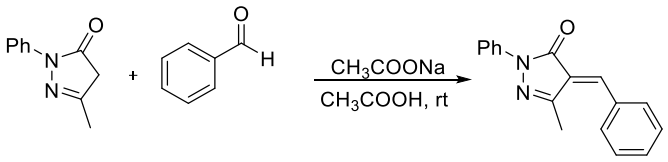
To a stirred solution of nitrostyrene in dry THF as a solvent, imidazole and anthranilic acid was added to the rection mixture at room temperature. The reaction was allowed to stir at room temperature for 15 min. Then add drop wise addition of formalehyde to the reaction mixture was allowed to stir at rt for 12h. After the completion of the reaction, the organic layer was extracted with ethyl acetate, washed with brine solution and dried over Na_2SO_4, and concentrated under reduced pressure. The formation of crude was seapearared by column chromatography by the combination of (6:94%) ethyl acetate and hexane.

General procedure for the synthesis of nitro styrene derived MBH-secondary alcohol[2]:



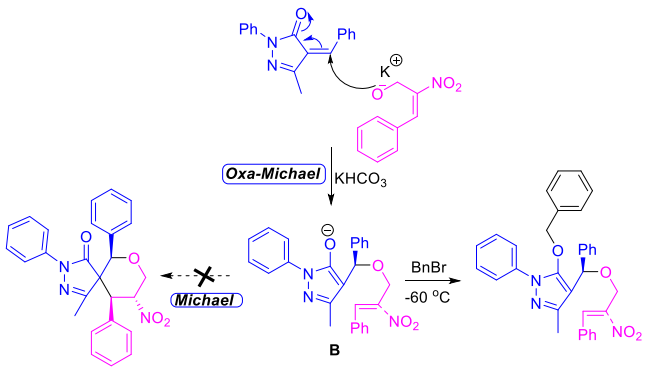
To a stirred solution of Nitrostyrene in dry THF as a solvent, imidazole and DMAP was added to the rection mixture at room temperature. The reaction was allowed to stir at room temperature for 15min. Then add drop wise addition of ethlglyoxylate to the reaction mixture was allowed to stir at rt for 4h. After the completion of the reaction, the organic layer was extracted with ethyl acetate, washed with brine solution and dried over Na_2SO_4, and concentrated under reduced pressure. The formation of crude was seapearared by column chromatography by the combination of (7:93%) ethyl acetate and hexane.

General procedure for the synthesis of unsaturated arylidene pyrazolone[3]:



To a stirred solution of pyrazolone in acetic acid as a solvent, sodium acetate and benzaldehyde was added to the rection mixture at room temperature. The reaction was allowed to stir at room temperature for 3 h. After the completion of the reaction, the organic layer was extracted with ethyl acetate, washed with brine solution and dried over Na_2SO_4, and concentrated under reduced pressure. The formation of crude was seapearared by column chromatography by the combination of (4:96%) ethyl acetate and hexane.

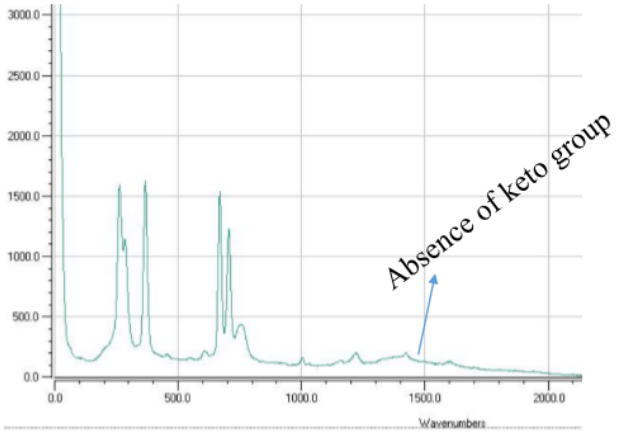
In-situ Raman spectroscopy analysis for reaction mechanisim:



To a solution of arylidene pyrazolone **1** (30 mg, 0.09 mmol, 1.0 equiv.) was added nitro allylic primary alcohol **2** (17 mg, 0.09 mmol, 1.0 equiv.) and K_2CO_3 (30 mg, 0.09 mmol, 1.0 equiv.) in CH_3CN (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 5 min and cooled to -60 ^oC. to the cooled rection mixture benzyl bromide (21 µl, 0.18 mmol, 2.0 equiv.) the reaction mixture was allowed stirr at the same temperature until the disappearance of keto group (monitered by Raman spectroscopy).

Before addition of benzyl bromide (C=O)

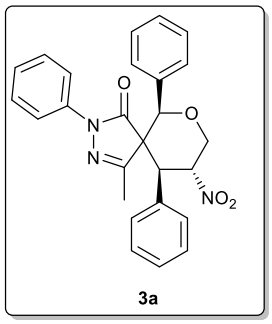
Aftter adition of benzyl bromide (C=O missing)



Compounds Characterisation

4-methyl-9-nitro-2,6,10-triphenyl-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3a):

Compound **3a** was synthesized according to the general procedure by taking **1a** (100 mg, 0.381 mmol, 1.0 equiv.), **2a** (102 mg, 0.572 mmol, 1.5 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3a

Yellow gummy solid: 93% (157.0 mg).

IR (neat, cm^{-1}) 3019, 2956, 1699, 1526, 1096, 779.

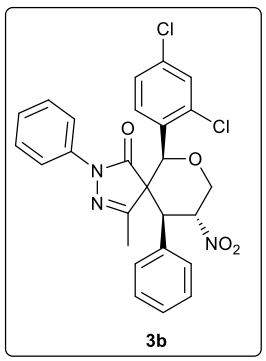
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 3H), 7.28-7.18 (m, 11H), 7.14-7.10 (m, 1H), 5.76-5.69 (m, 1H), 5.12 (s, 1H), 5.09-5.06(m, 1H), 4.91-4.87(m, 1H), 4.44 (d, *J* = 12.4 Hz, 2H), 4.26 (t, *J* = 10.8 Hz, 1H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 157.5, 136.5, 134.5, 128.7, 128.5, 128.2, 125.8, 125.2, 124.2, 120.1, 114.3, 83.4, 81.3, 71.1, 66.7, 55.6, 19.1.

HRMS calcd. $C_{26}H_{24}N_3O_4$, 442.17668; found 442.17651 [M + H]

6-(2,4-dichlorophenyl)-4-methyl-9-nitro-2,10-diphenyl-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3b):

Compound **3b** was synthesized according to the general procedure by taking **1b** (100 mg, 0.302 mmol, 1.0 equiv.), **2a** (102 mg, 0.572 mmol, 1.5 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3b

Yellow gummy solid; Yield: 71% (110.0 mg).

IR (neat, cm^{-1}) 2923, 2896, 1701, 1524, 1096, 715, 821.

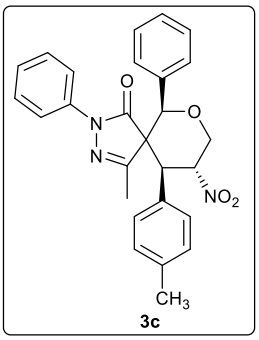
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.34 (m, 1H), 7.33-7.30 (m, 1H), 7.28-7.16 (m, 10H), 7.13-7.06 (m, 1H), 5.79-5.75 (m, 1H), 5.54 (s, 1H), 4.48 (dd, *J* = 28.0, 8.0 Hz, 1H), 4.86 (d, *J* = 12.8 Hz, 1H), 4.29 (t, *J* = 10.8 Hz, 1H), 2.60 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 156.7, 136.4, 135.8, 134.5, 131.8, 131.0, 129.9, 129.0, 128.7, 128.5, 127.6, 127.1, 125.9, 119.6, 80.3, 70.6, 63.9, 50.0, 24.6, 19.9.

HRMS calcd. $C_{26}H_{22}Cl_2N_3O_4$, 510.09874; found 510.09812 [M + H]

4-methyl-9-nitro-2,6-diphenyl-10-(p-tolyl)-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3c):

Compound **3c** was synthesized according to the general procedure by taking **1** (100 mg, 0.381 mmol, 1.0 equiv.), **2c** (110 mg, 0.57 mmol, 1.5 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3c

Yellow gummy solid; Yield: 57% (98.0 mg).

IR (neat, cm^{-1}) 3021, 2923, 1696, 1548, 1093, 827.

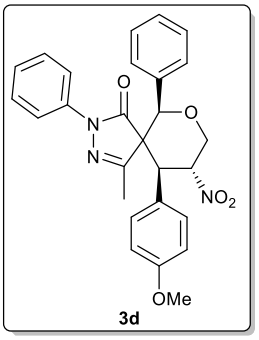
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.22 (m, 6H), 7.21-7.15 (m, 3H), 7.13-7.10 (m, 3H), 7.02 (d, *J* = 8.0 Hz, 2H), 5.74-5.66 (m, 1H), 5.07 (s, 1H), 4.87 (dd, *J* = 4.8, 10.8 Hz, 1H), 4.40 (d, *J* = 12.4 Hz, 1H), 4.24 (t, *J* = 10.8 Hz, 1H), 2.20 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 157.5, 138.6, 136.5, 134.8, 129.6, 129.1, 128.6, 128.2, 127.3, 125.8, 125.2, 120.0, 83.5, 81.0, 70.1, 65.5, 20.9, 19.1.

HRMS calcd. $C_{27}H_{26}N_3O_4$, 456.19233; found 457.19231 [M + H]

10-(4-methoxyphenyl)-4-methyl-9-nitro-2,6-diphenyl-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3d):

Compound **3d** was synthesized according to the general procedure by taking **1** (100 mg, 0.381 mmol, 1.0 equiv.), **2d** (119 mg, 0.572 mmol, 1.0 equiv K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3d

Yellow gummy solid; Yield: 61% (106.0 mg).

IR (neat, cm^{-1}) 2885, 2811, 1699, 1597, 1114, 831, 711.

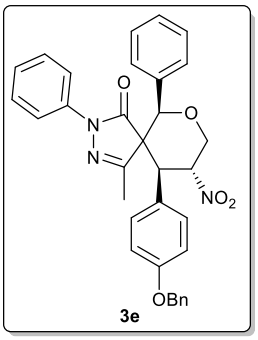
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.25 (m, 5H), 7.22-7.20 (m, 4H), 7.17 (d, *J* = 8.8 Hz, 2H), 7.14-7.10 (m, 1H), 6.74 (d, *J* = 8.8 Hz, 2H), 5.70-5.63 (m, 1H), 5.10 (s, 1H), 4.86 (dd, *J* = 5.2, 11.2, Hz, 1H), 4.38 (d, *J* = 12.8 Hz, 1H), 4.24 (t, *J* = 10.8 Hz, 1H), 3.68 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 159.6, 157.5, 136.5, 134.9, 128.7, 128.6, 128.2, 125.9, 125.2, 124.0, 120.1, 114.3, 83.5, 70.1, 65.6, 55.1, 49.0, 19.1.

HRMS calcd. $C_{27}H_{26}N_3O_5$, 472.18725; found 472.18712

10-(4-(benzyloxy)phenyl)-4-methyl-9-nitro-2,6-diphenyl-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3e):

Compound **3e** was synthesized according to the general procedure by taking **1** (100 mg, 0.381 mmol, 1.0 equiv.), **2e** (163 mg, 0.572 mmol, 1.5 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3e

Yellow gummy solid: 57% (98.0 mg)

IR (neat, cm^{-1}) 3052, 2921, 1701, 1523, 1126, 812.

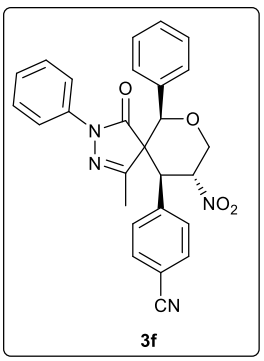
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.37 (m, 4H), 7.34-7.10 (m, 13H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.70-5.63 (m, 1H), 5.10 (s, 1H), 4.92 (s, 2H), 4.86 (dd, *J* = 4.8, 10.8, Hz, 1H), 4.38 (d, *J* = 12.4 Hz, 1H), 4.24 (t, *J* = 10.8 Hz, 1H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 158.9, 157.5, 136.5, 136.4, 134.9, 128.7, 128.6, 128.5, 128.2, 127.9, 127.4, 125.9, 125.2, 124.4, 120.1, 115.2, 83.5, 81.2, 70.1, 65.6, 49.0, 29.6, 19.1.

HRMS calcd. $C_{33}H_{29}N_3O_5$, 547.21072; found 547.21071 [M + H]

4-1-methyl-9-nitro-4-oxo-3,6-diphenyl-7-oxa-2,3-diazaspiro[4.5]dec-1-en-10-yl)benzonitrile (3f):

Compound **3f** was synthesized according to the general procedure by taking **1** (100 mg, 0.381 mmol, 1.0 equiv.), **2f** (116 mg, 0.572 mmol, 1.0 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3f

Yellow gummy solid; Yield: 71% (110.0 mg).

IR (neat, cm^{-1}) 3064, 2924, 1707, 1594, 1097, 821.

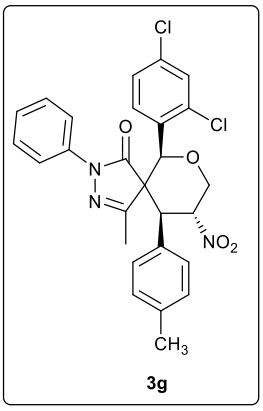
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 6.0 Hz, 1H), 7.36-7.21 (m, 10H), 7.19-7.10 (m, 3H), 5.43-5.37 (m, 1H), 5.20-5.18 (m, 2H), 4.87 (dd, *J* = 11.2, 4.8 Hz, 1H), 4.33 (t, *J* = 10.8 Hz, 1H), 2.53 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 156.3, 136.4, 135.3, 134.5, 130.7, 128.9, 128.7, 128.3, 128.2, 127.3, 125.8, 125.3, 119.6, 83.4, 82.2, 69.9, 64.4, 29.6, 20.0.

HRMS calcd. $C_{27}H_{23}N_4O_4$, 467.17193; found 468.17165 [M + H]

6-(2,4-dichlorophenyl)-4-methyl-9-nitro-2-phenyl-10-(p-tolyl)-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3g):

Compound **3g** was synthesized according to the general procedure by taking **1b** (100 mg, 0.302 mmol, 1.0 equiv.), **2c** (120 mg, 0.453 mmol, 1.5 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3g

Yellow gummy solid; Yield: 55% (95.0 mg).

IR (neat, cm^{-1}) 2923, 2854, 1709, 1499, 1091, 818, 663,

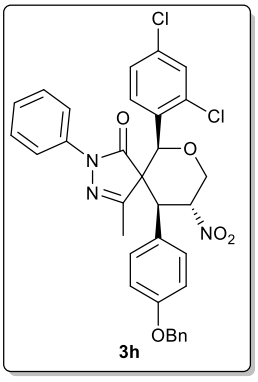
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 2.0 Hz, 1H), 7.30-7.26 (m, 3H), 7.25-7.22 (m, 2H), 7.19-7.09 (m, 4H), 7.02 (d, *J* = 8.4 Hz, 2H), 5.78-5.71 (m, 1H), 5.53 (s, 1H), 4.81 (dd, *J* = 10.8, 5.2 Hz, 1H), 4.45 (d, *J* = 12.8 Hz, 1H), 4.28 (t, *J* = 10.8 Hz, 1H), 2.59 (s, 3H), 2.21 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 156.8, 138.8, 136.5, 135.7, 134.4, 131.0, 129.9, 129.9, 129.7, 128.8, 128.7, 128.5, 127.4, 127.0, 125.8, 119.6, 80.9, 70.6, 64.0, 49.6, 29.6, 20.9, 19.9.

HRMS calcd. $C_{27}H_{24}Cl_2N_3O_4$, 524.11439; found 524.11412 [M + H]

10-(4-(benzyloxy)phenyl)-6-(2,4-dichlorophenyl)-4-methyl-9-nitro-2-phenyl-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3h):

Compound **3h** was synthesized according to the general procedure by taking **1b** (100 mg, 0.302 mmol, 1.0 equiv.), **2e** (129 mg, 0.453 mmol, 1.0 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3h

Yellow gummy solid: 77% (121.0 mg).

IR (neat, cm^{-1}) 3025, 2952, 1705, 1569, 1145, 668, 812.

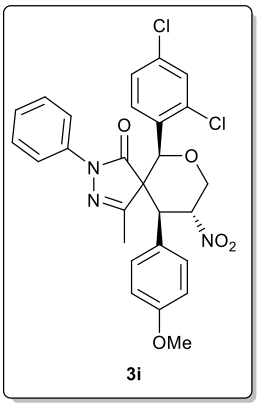
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.43-7.30 (m, 10H), 7.24 (d, *J* = 8.8 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.12-7.09 (m, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.31-6.24 (m, 1H), 5.47 (s, 1H), 4.94 (s, 2H), 4.80 (dd, *J* = 11.2, 5.2, Hz, 1H), 4.15 (t, *J* = 10.8 Hz, 1H), 3.95 (d, *J* = 11.6 Hz, 1H), 2.27 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 159.2, 156.6, 136.6, 136.4, 135.9, 133.1, 131.0, 130.6, 129.5, 129.2, 128.8, 128.5, 128.0, 127.5, 127.4, 126.0, 124.4, 119.8, 115.3, 80.9, 70.5, 69.9, 63.0, 48.9, 29.6, 22.6.

HRMS calcd. $C_{33}H_{26}Cl_2N_3O_5$, 614.12495; found 614.12517 [M - H]

6-(2,4-dichlorophenyl)-10-(4-methoxyphenyl)-4-methyl-9-nitro-2-phenyl-7-oxa-2,3-diazaspiro[4.5]dec-3-en-1-one (3i):

Compound **3i** was synthesized according to the general procedure by taking **1b** (100 mg, 0.302 mmol, 1.0 equiv.), **2d** (127 mg, 0.453 mmol, 1.5 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3i

Yellow gummy solid: 68% (106.0 mg).

IR (neat, cm^{-1}) 2921, 2854, 1698, 1547, 1097, 820, 661,

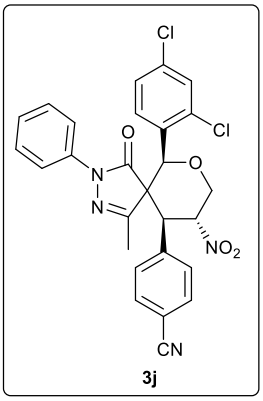
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 1H), 7.41-7.39 (m, 2H), 7.33-7.29 (m, 3H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.10 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 2H), 6.30-6.23 (m, 1H), 5.46 (s, 1H), 4.80-4.76 (m, 1H), 4.15 (t, *J* = 10.8 Hz, 1H), 3.94, (d, *J* = 11.6 Hz, 1H), 3.70 (s, 3H), 2.26 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 159.6, 136.6, 135.9, 128.7, 128.6, 127.5, 125.9, 125.3, 123.0, 120.1, 114.3, 83.5, 81.3, 71.1, 64.6, 55.1, 49.1, 19.1.

HRMS calcd. $C_{27}H_{24}Cl_2N_3O_5$, 540.10930; found 540.10912 [M + H].

6-(2,4-dichlorophenyl)-1-methyl-9-nitro-4-oxo-3-phenyl-7-oxa-2,3-diazaspiro[4.5]dec-1-en-10-yl)benzonitrile (3j):

Compound **3j** was synthesized according to the general procedure by taking **1b** (100 mg, 0.302 mmol, 1.0 equiv.), **2f** (92 mg, 0.453 mmol, 1.5 equiv.), K_2CO_3 (131 mg, 0.952 mmol, 2.5 equiv.) in CH_3CN (2 mL).



3j

Yellow gummy liquid; Yield: 76% (119.0 mg).

IR (neat, cm^{-1}) 2923, 2853, 1727, 1545, 1102, 689, 784.

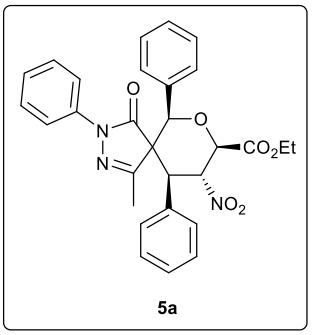
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.52(m, 2H), 7.47-7.41 (m, 2H), 7.39- 7.33(m, 5H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.12-7.08 (m, 2H), 6.28-6.21 (m, 1H), 5.54 (s, 1H), 4.78 (m, 2H), 4.23 (t, *J* = 10.8 Hz, 1H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 156.8, 136.4, 136.1, 135.6, 135.2, 133.3, 130.6, 130.5, 130.3, 129.4, 128.9, 128.2, 127.6, 126.2, 119.5, 118.4, 80.5, 70.3, 62.6, 43.8, 29.6, 15.7.

HRMS calcd. $C_{27}H_{21}Cl_2N_4O_4$, 535.09399; found 535.09312.

Ethyl-1-methyl-9-nitro-4-oxo-3,6,10-triphenyl-7-oxa-2,3-diazaspiro[4.5]dec-1-ene-8-carboxylate (5a):

Compound **5a** was synthesized according to the general procedure by taking **1** (100 mg, 0.38 mmol, 1.0 equiv.), **4a** (143 mg, 0.57 mmol, 1.5 equiv.), Cs_2CO_3 (310 mg, 0.95 mmol, 2.5 equiv.) in $CHCl_3$ (2 mL).



5a

Yellow gummy liquid; Yield: 78% (153.0 mg).

IR (neat, cm^{-1}) 3024, 2931, 1704, 1541, 1078, 812.

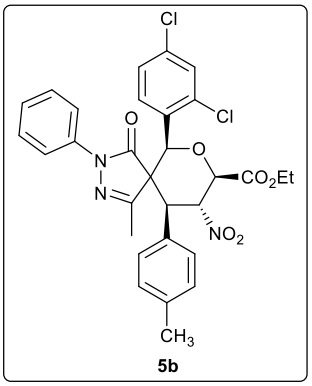
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.26 (m, 6H), 7.22-7.16 (m, 3H), 7.12-7.10 (m, 3H), 7.08 (d, *J* = 6.8 Hz, 1H), 6.8 (d, *J* = 9.2 Hz, 2H), 6.30-6.24 (m, 1H), 5.47 (s, 1H), 4.80-4.76 (m, 1H), 4.51 (t, *J* = 13.6 Hz, 3H), 4.39 (d, *J* = 29.2 Hz, 1H), 4.30 (q, *J* = 8.0 Hz, 2H), 2.27 (s, 1H), 1.27 (t, *J* = 3.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ.169.2, 159.7, 156.6, 136.4, 135.6, 133.1, 131.6, 131.0, 128.9, 128.8, 128.7, 128.5, 127.6, 127.1, 125.9, 119.6, 80.6, 80.3, 70.6, 63.9, 50.1, 24.4, 19.9, 14.1.

HRMS calcd. $C_{30}H_{28}N_3O_6$, 514.19781; found 514.19692 [M + H]

Ethyl 6-(2,4-dichlorophenyl)-1-methyl-9-nitro-4-oxo-3-phenyl-10-(p-tolyl)-7-oxa-2,3-diazaspiro[4.5]dec-1-ene-8-carboxylate (5b):

Compound **5b** was synthesized according to the general procedure by taking **1** (100 mg, 0.302 mmol, 1.0 equiv.), **4b** (120 mg, 0.453 mmol, 1.5 equiv.), Cs_2CO_3 (310 mg, 0.95 mmol, 2.5 equiv.) in $CHCl_3$ (2 mL).



5b

Yellow gummy liquid; Yield: 60% (108.0 mg).

IR (neat, cm^{-1}) 3021, 2986, 1699, 1521, 1156, 714, 779.

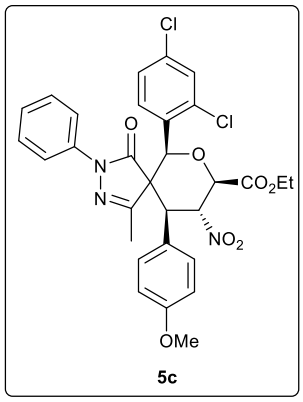
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.0 Hz, 2H), 7.38-7.28 (m, 3H), 7.23-7.09 (m, 5H), 7.03 (d, *J* = 7.6 Hz, 2H), 5.72-5.65 (m, 1H), 5.59 (s, 1H), 4.95 (d, *J* = 10.0 Hz, 1H), 4.44 (d, *J* = 12.4 Hz, 1H), 4.31 (q, *J* = 8.4 Hz, 2H), 2.66 (s, 3H), 2.21 (s, 3H), 1.27 (t, *J* = 3.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 156.6, 139.4, 139.1, 136.4, 13.6.1, 136.0, 134.5, 133.0, 130.8, 130.4, 129.7, 129.2, 128.7, 128.4, 128.1, 127.7, 127.2, 126.0, 125.8, 82.7, 79.5, 62.8, 62.6, 50.7, 22.6, 21.0, 14.1.

HRMS calcd. $C_{30}H_{28}Cl_2N_3O_6$, 596.13552; found 596.13492 [M + H]

Ethyl-1-methyl-9-nitro-4-oxo-3,6,10-triphenyl-7-oxa-2,3-diazaspiro[4.5]dec-1-ene-8-carboxylate (5c):

Compound **5c** was synthesized according to the general procedure by taking **1** (100 mg, 0.302 mmol, 1.0 equiv.), **4c** (127 mg, 0.453 mmol, 1.0 equiv.), Cs_2CO_3 (310 mg, 0.95 mmol, 2.5 equiv.) in $CHCl_3$ (2 mL).



5c

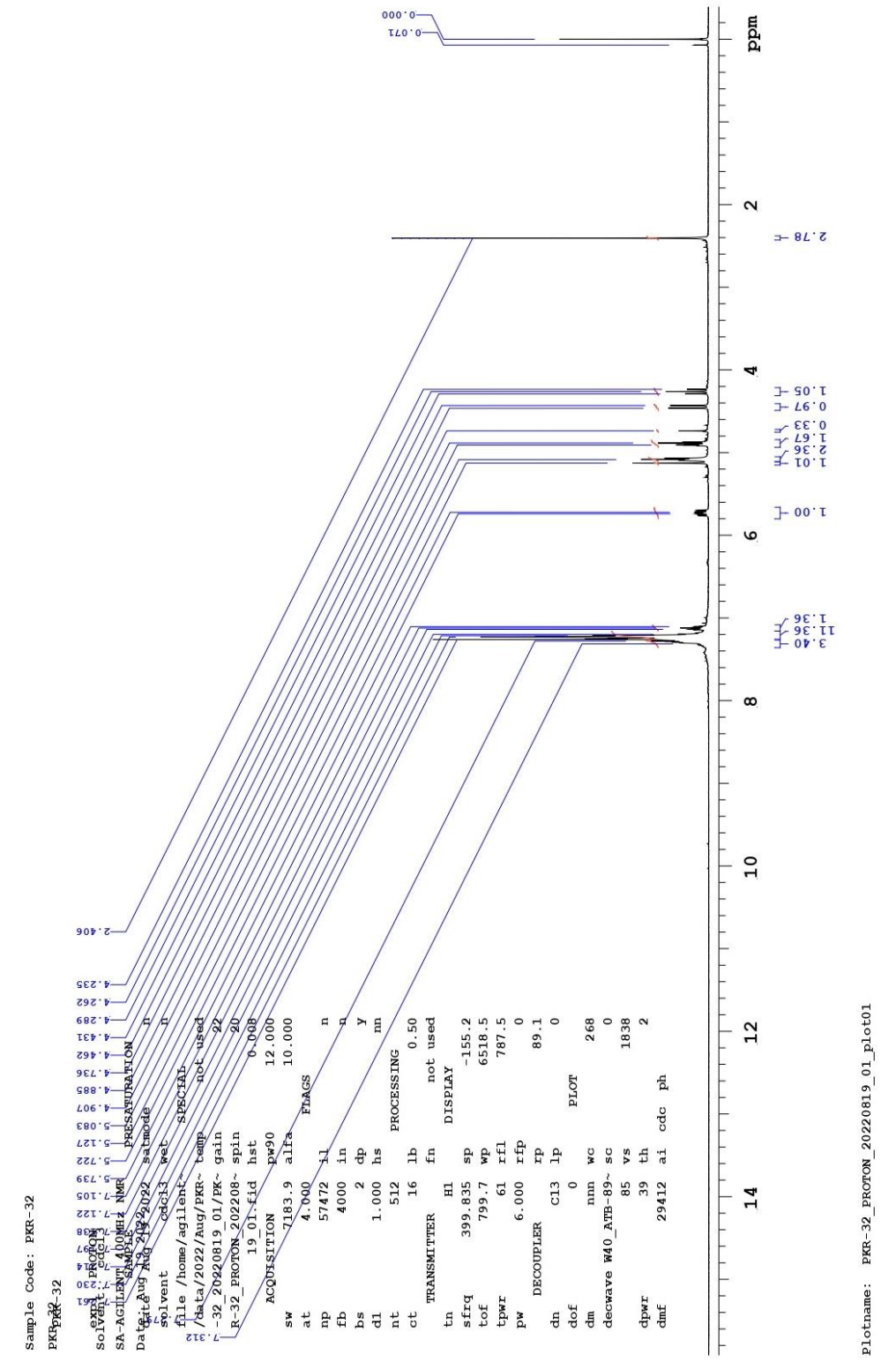
Yellow gummy liquid; Yield: 56% (105.0 mg).

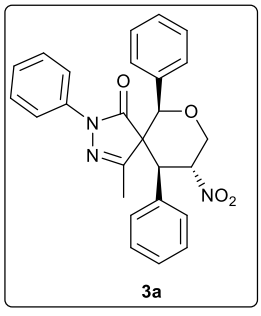
IR (neat, cm^{-1}) 3024, 2652, 1702, 1521, 1067, 667, 812.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.42-7.37 (m, 4H), 7.34-7.28 (m, 3H), 7.18-7.16 (m, 2H), 6.64-5.62 (m, 1H), 5.31 (d, *J* = 6.4 Hz, 2H), 5.19-5.07 (m, 1H), 4.28 (q, *J* = 6.8 Hz, 2H), 3.91 (s, 3H), 2.12 (s, 3H), 1.26 (t, *J* = 3.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 158.0, 156.8, 138.8, 136.6, 135.7, 134.4, 131.1, 129.9, 129.6, 128.8, 128.6, 128.4, 127.4, 127.0, 125.8, 119.6, 80.9, 80.3, 70.6, 64.0, 55.0, 49.6, 29.6, 20.9, 19.9, 14.9.

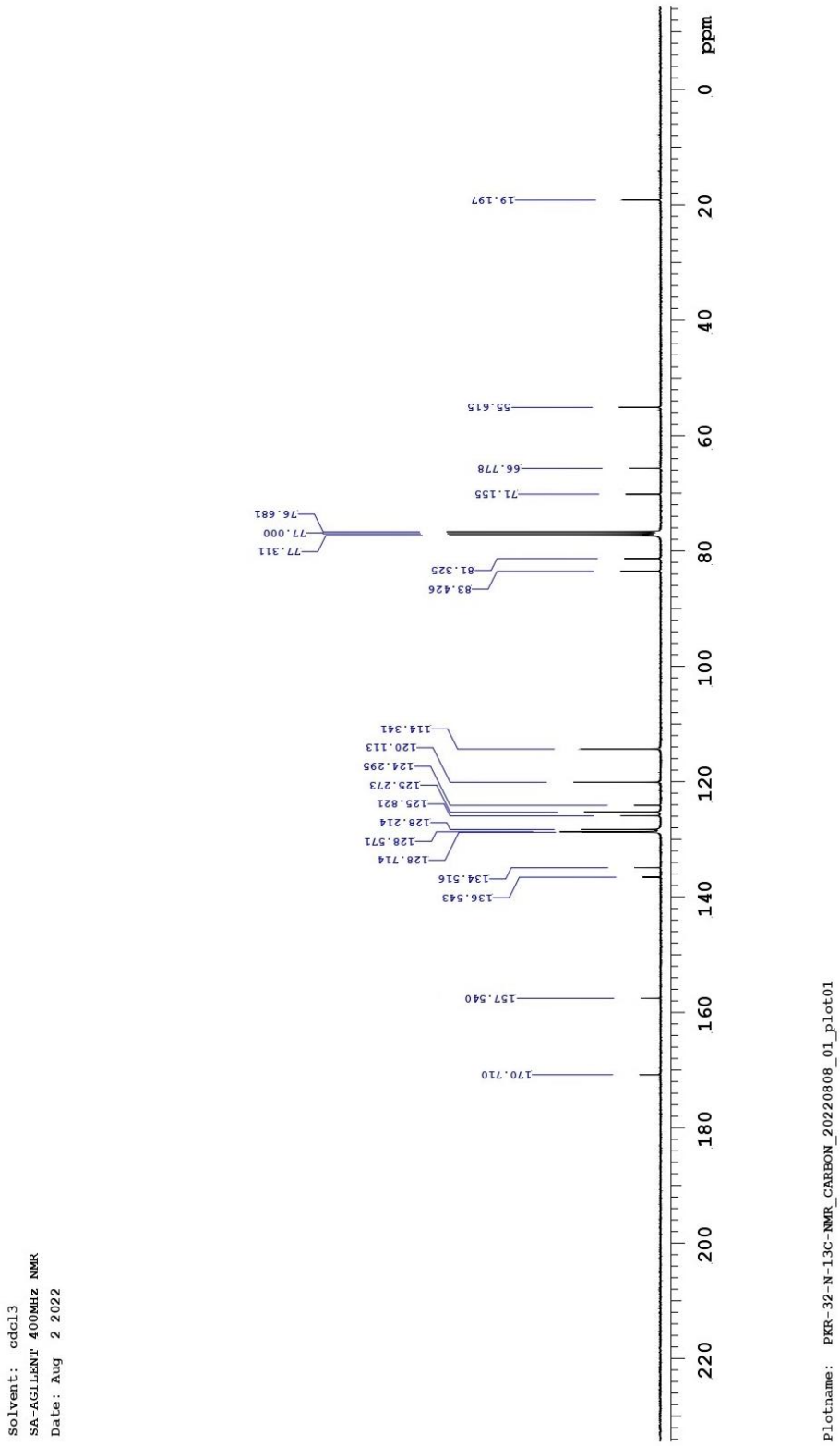
HRMS calcd. $C_{30}H_{28}Cl_2N_3O_7$, 612.13043; found 612.13026 [M + H]

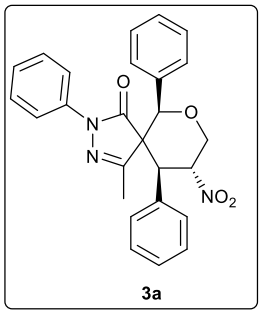




3a

^{1}H NMR Spectrum of compound **3a**





3a

^{13}C NMR Spectrum of compound **3a**

HPLC chromatogram for racemic compound of **3a**

==== Shimadzu LCsolution Analysis Report ====

D:\YPKREDDY\313 res10% ipa-hex OD-H pyrazole1.lcd

Acquired by	: Admin
Sample Name	: 313 res10% ipa-hex OD-H pyrazole
Sample ID	: 313 res10% ipa-hex OD-H pyrazo
Vail #	: 0
Injection Volume	: 20 uL
Data File Name	: 313 res10% ipa-hex OD-H pyrazole1.lcd
Method File Name	: pyrazole313.lcm
Batch File Name	: SingleRun120020101004312.lcb
Report File Name	: Default.lcr
Data Acquired	: 1/1/2002 12:44:32 AM
Data Processed	: 1/1/2002 3:07:38 AM

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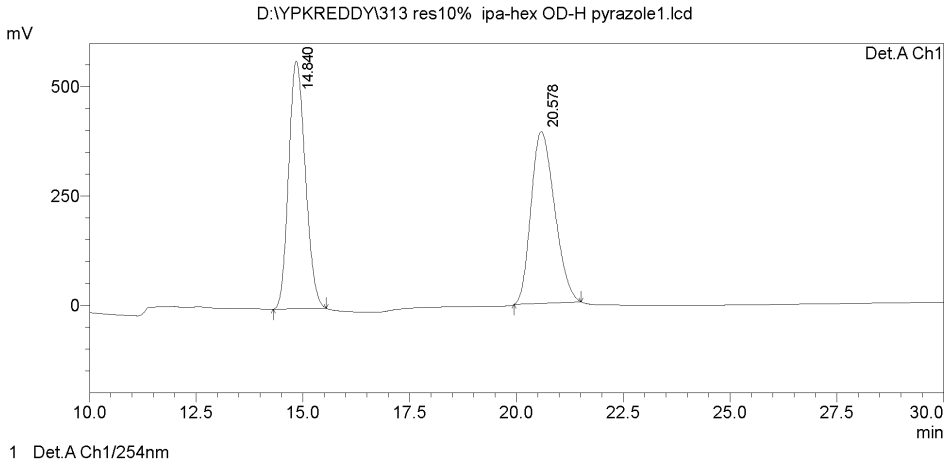

1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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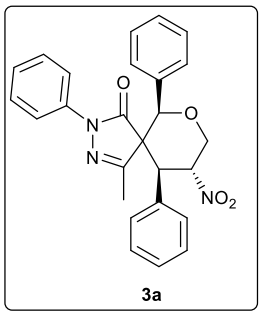
2	20.578	15118573	393197	49.530	40.965
Total		30523806	959835	100.000	100.000



3a

HPLC chromatogram for chiral compound of **3a**

==== Shimadzu LCsolution Analysis Report ====

D:\YPKREDDY\3rd paper data\313 chiral ipahex 14.9.2022 od1.lcd

Acquired by	: Admin
Sample Name	: 313 chiral ipahex 14.9.2022 od
Sample ID	: 313 chiral ipahex 14.9.2022 od
Vail #	: 0
Injection Volume	: 20 uL
Data File Name	: 313 chiral ipahex 14.9.2022 od1.lcd
Method File Name	: 14.9.2022 chiral with ncs.lcm
Batch File Name	: SingleRun120020102000725.lcb
Report File Name	: Default.lcr
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Data Processed	: 1/2/2002 1:16:00 AM

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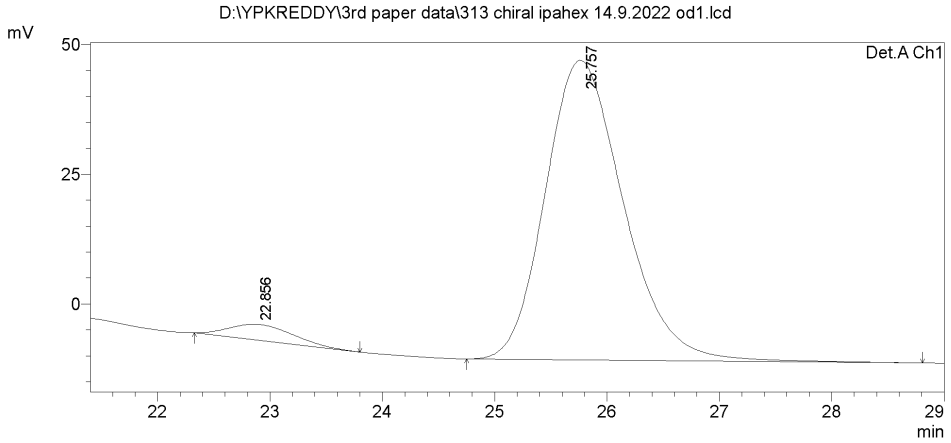
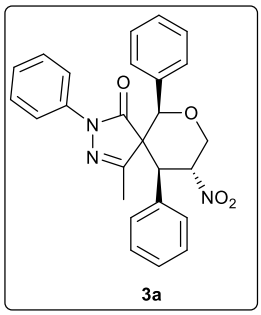


1 Det.A Ch1/254nm

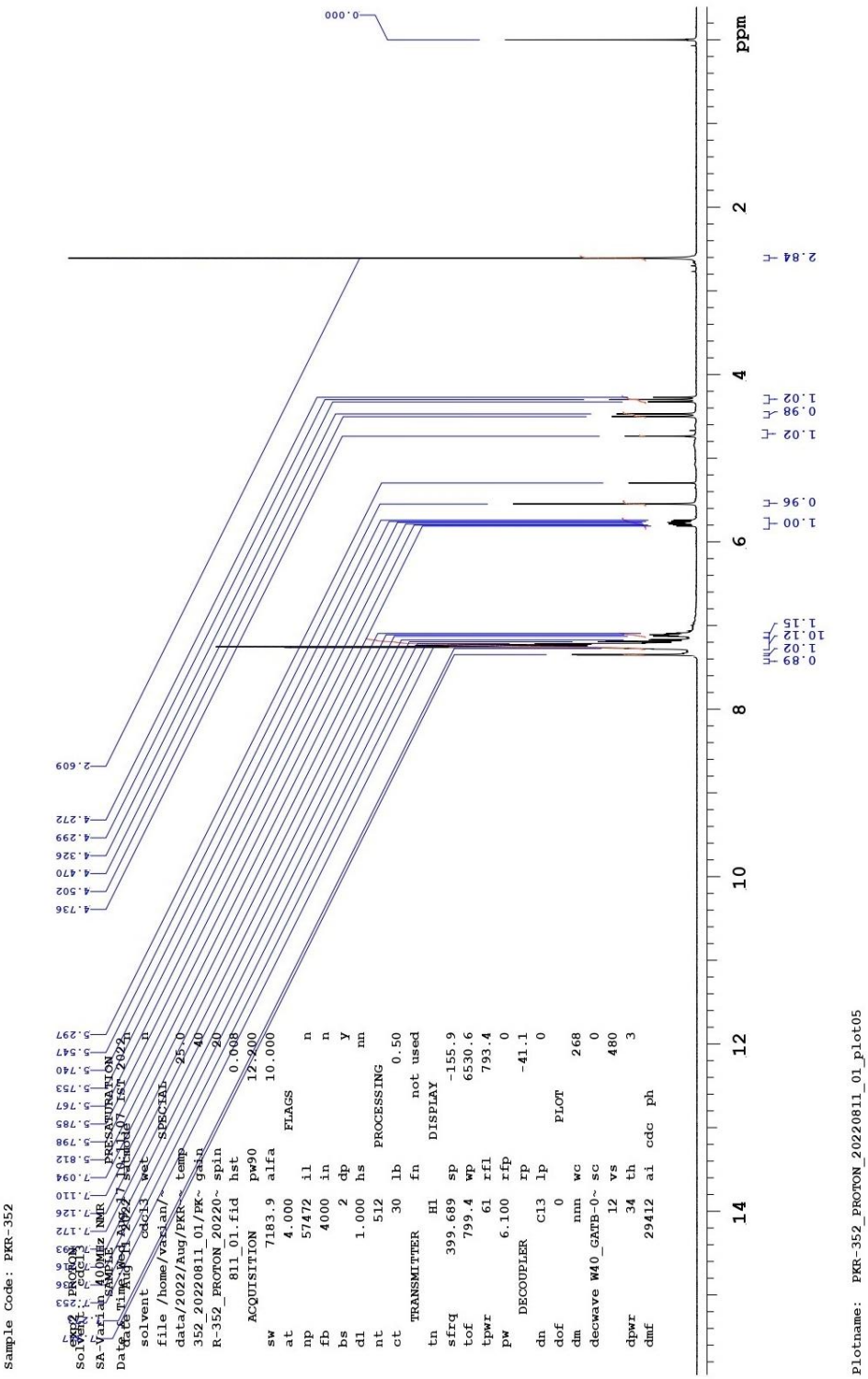
PeakTable

Detector A Ch1 254nm

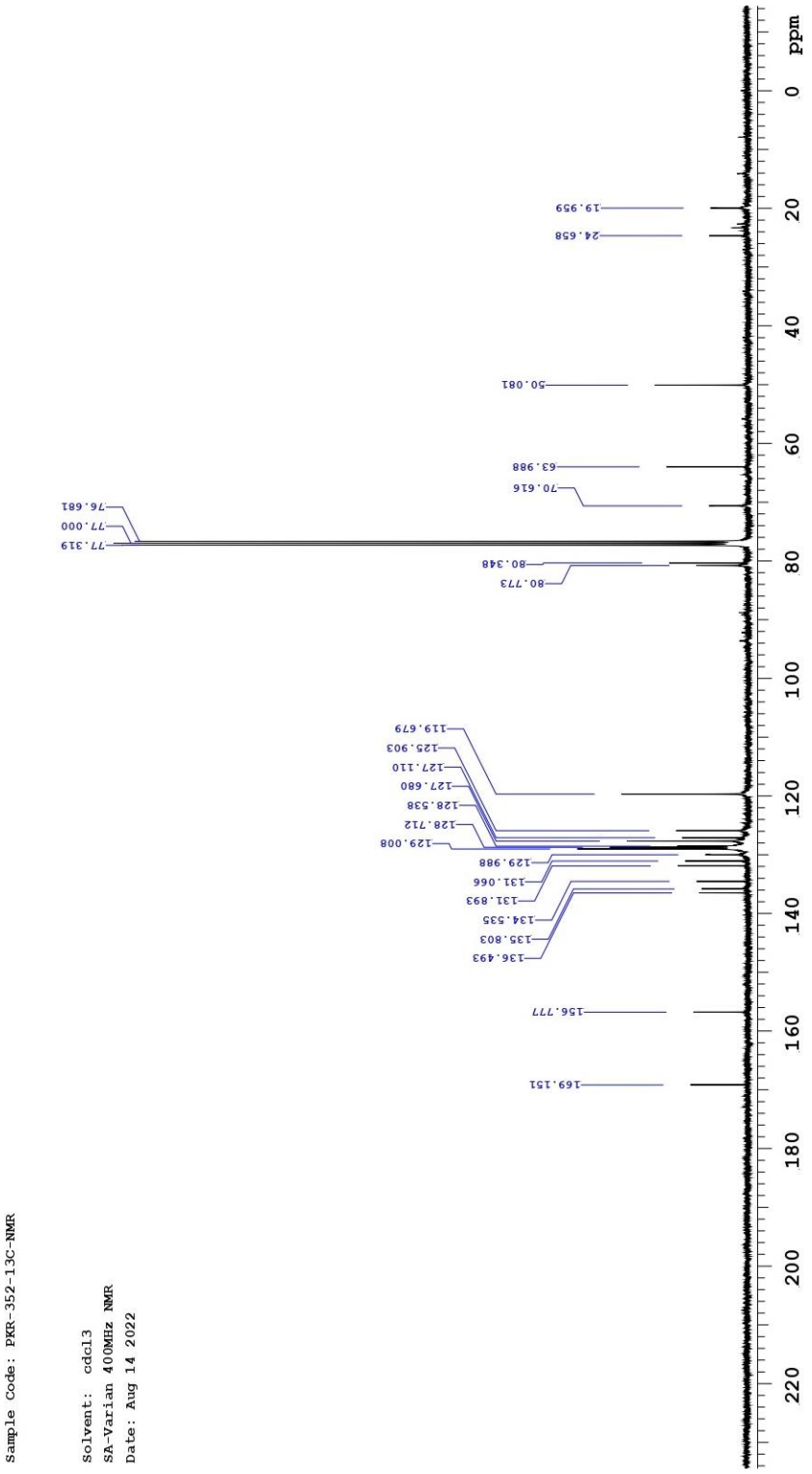
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.856	121293	2997	4.153	4.935
2	25.757	2799151	57738	95.847	95.065
Total		2920443	60735	100.000	100.000

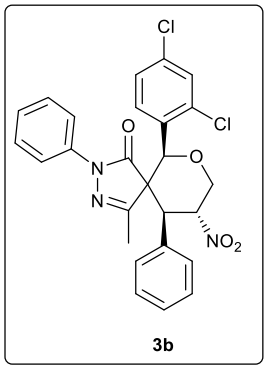


3a

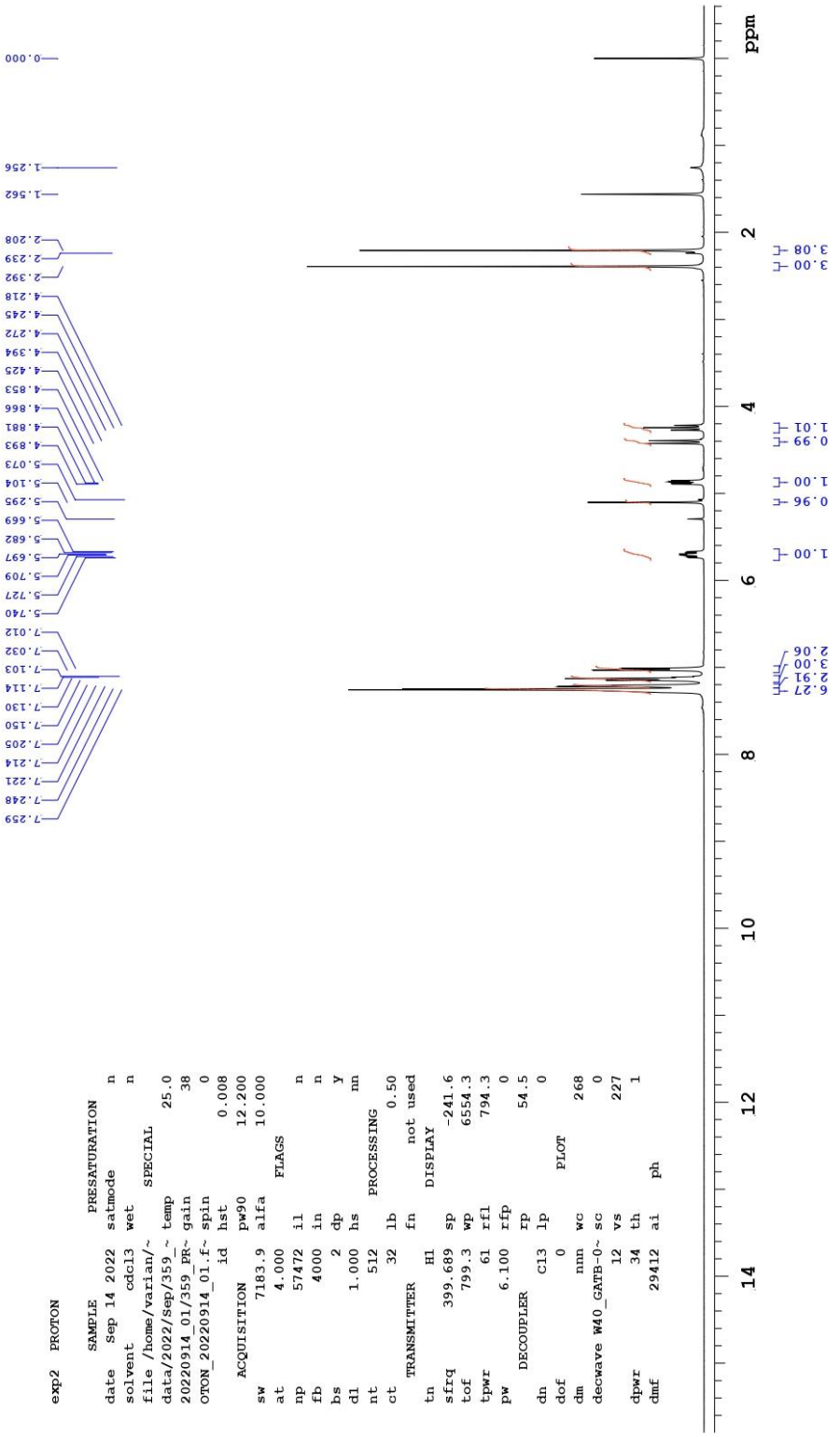


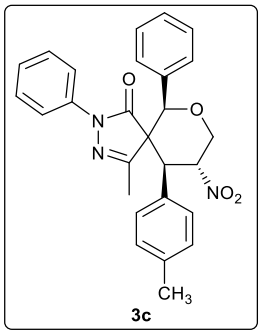
^{1}H NMR Spectrum of compound **3b**





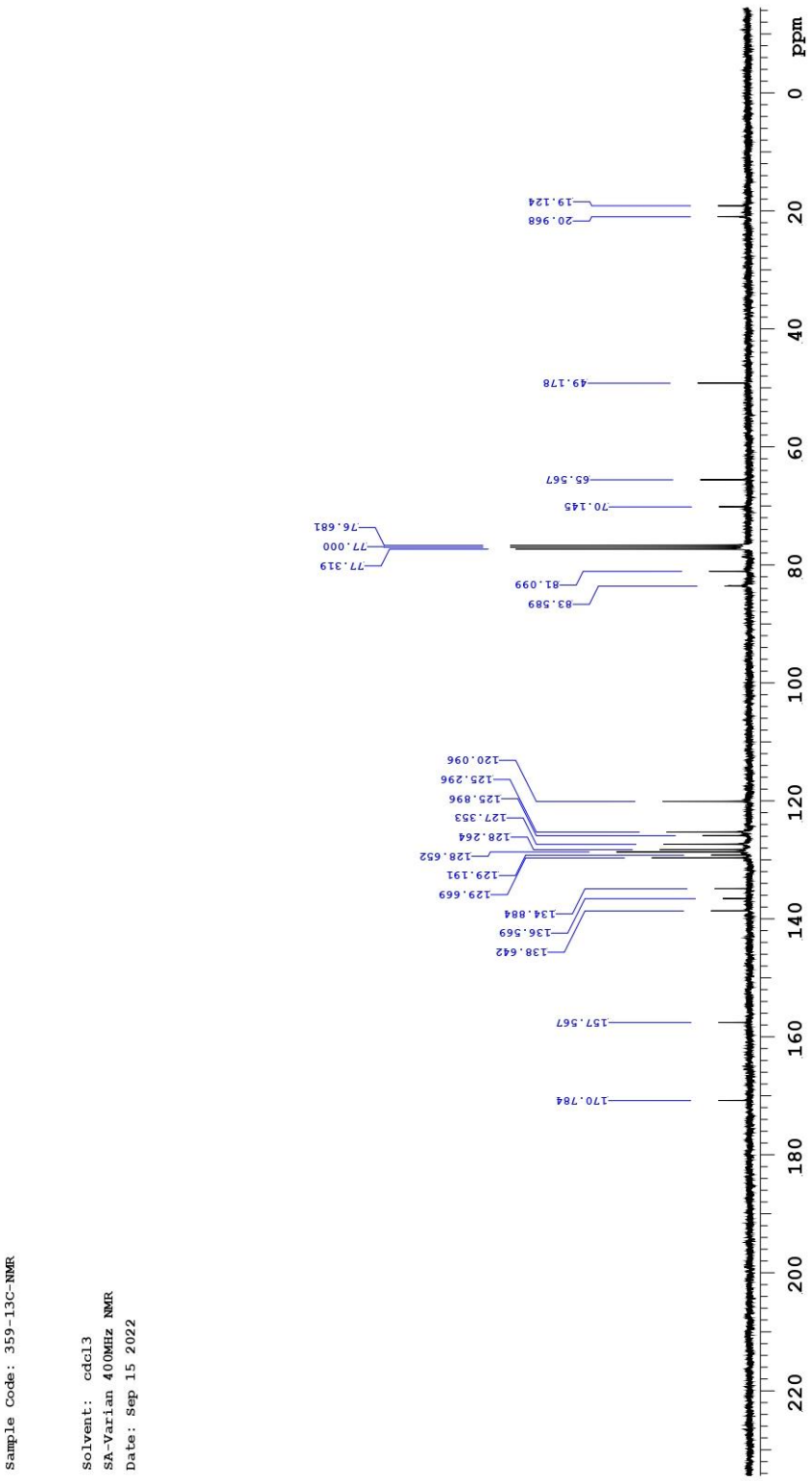
^{13}C NMR Spectrum of compound **3b**

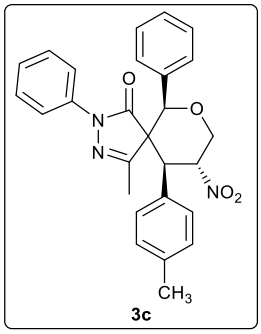




3c

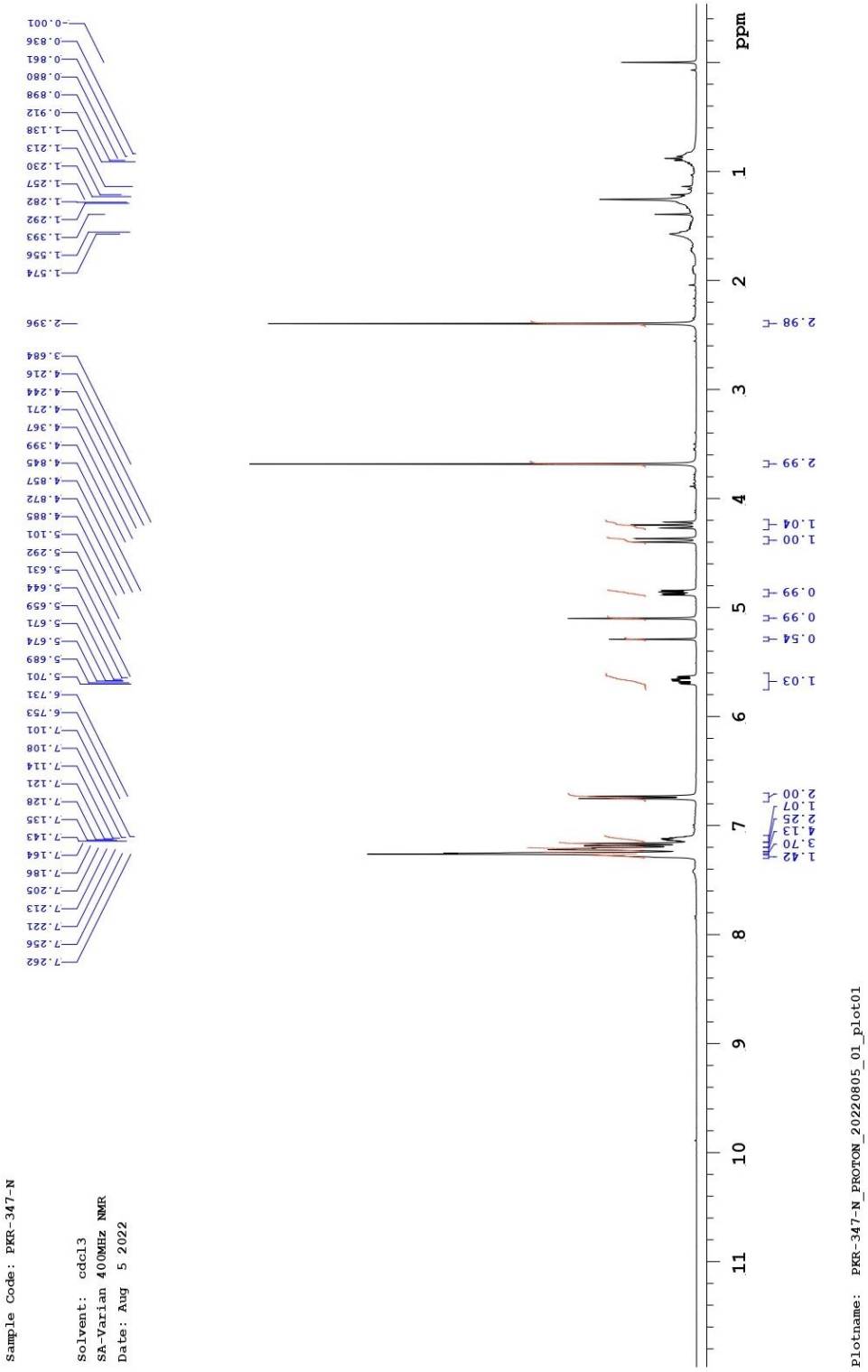
^{1}H NMR Spectrum of compound **3c**

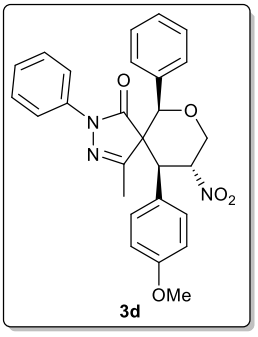




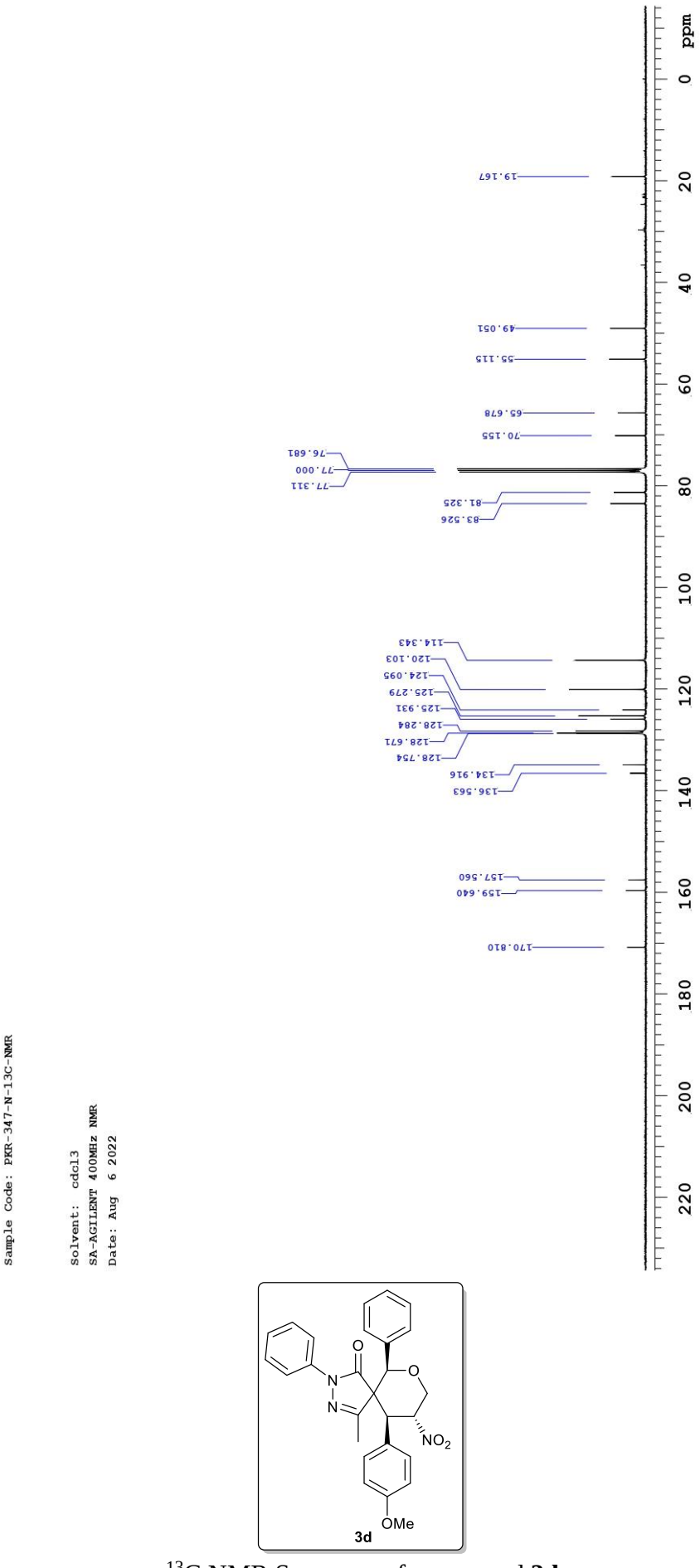
3c

^{13}C NMR Spectrum of compound **3c**

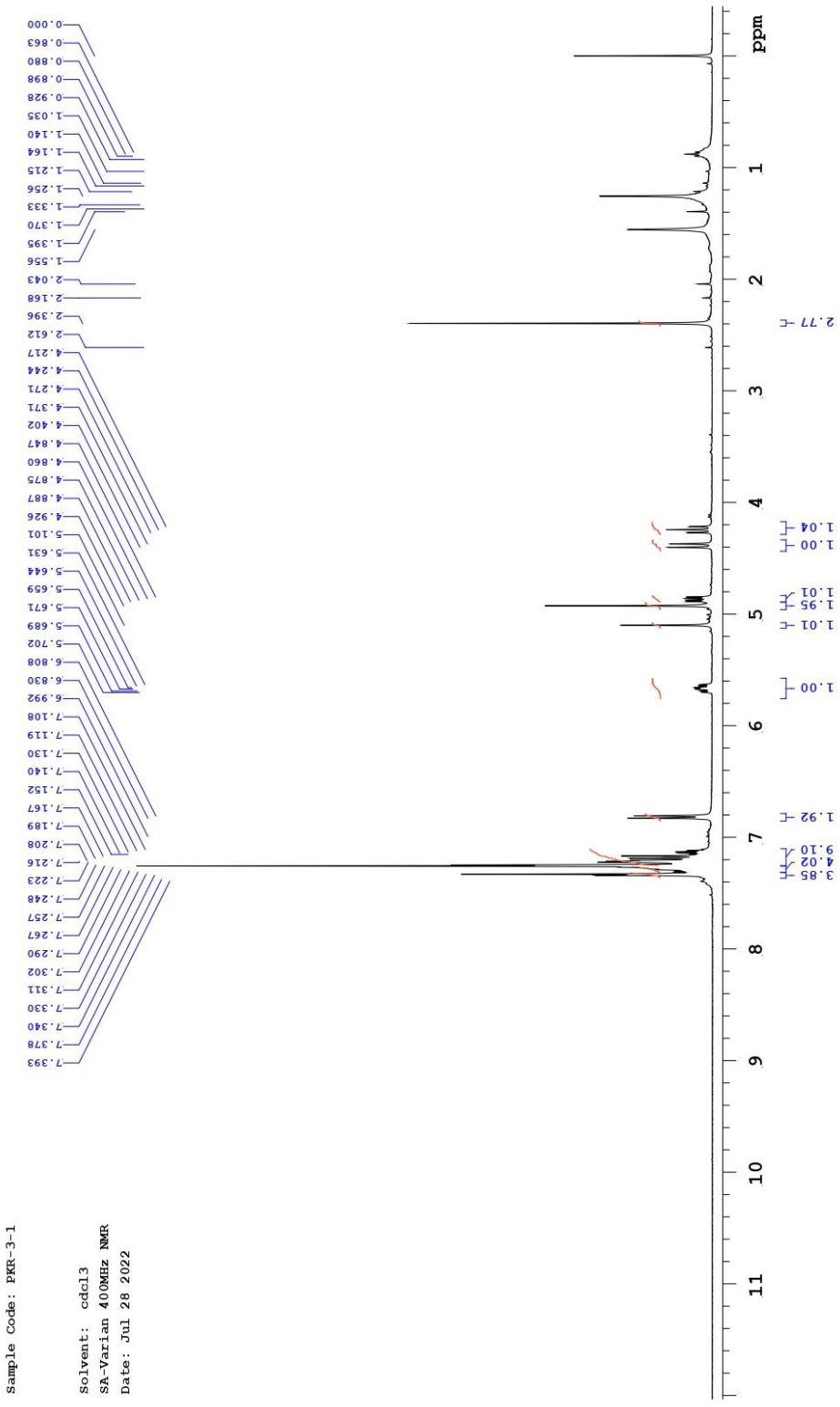


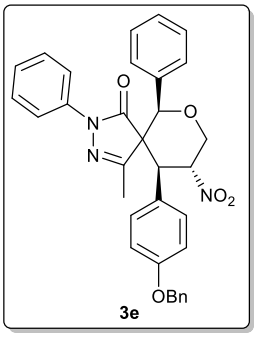


^{1}H NMR Spectrum of compound **3d**

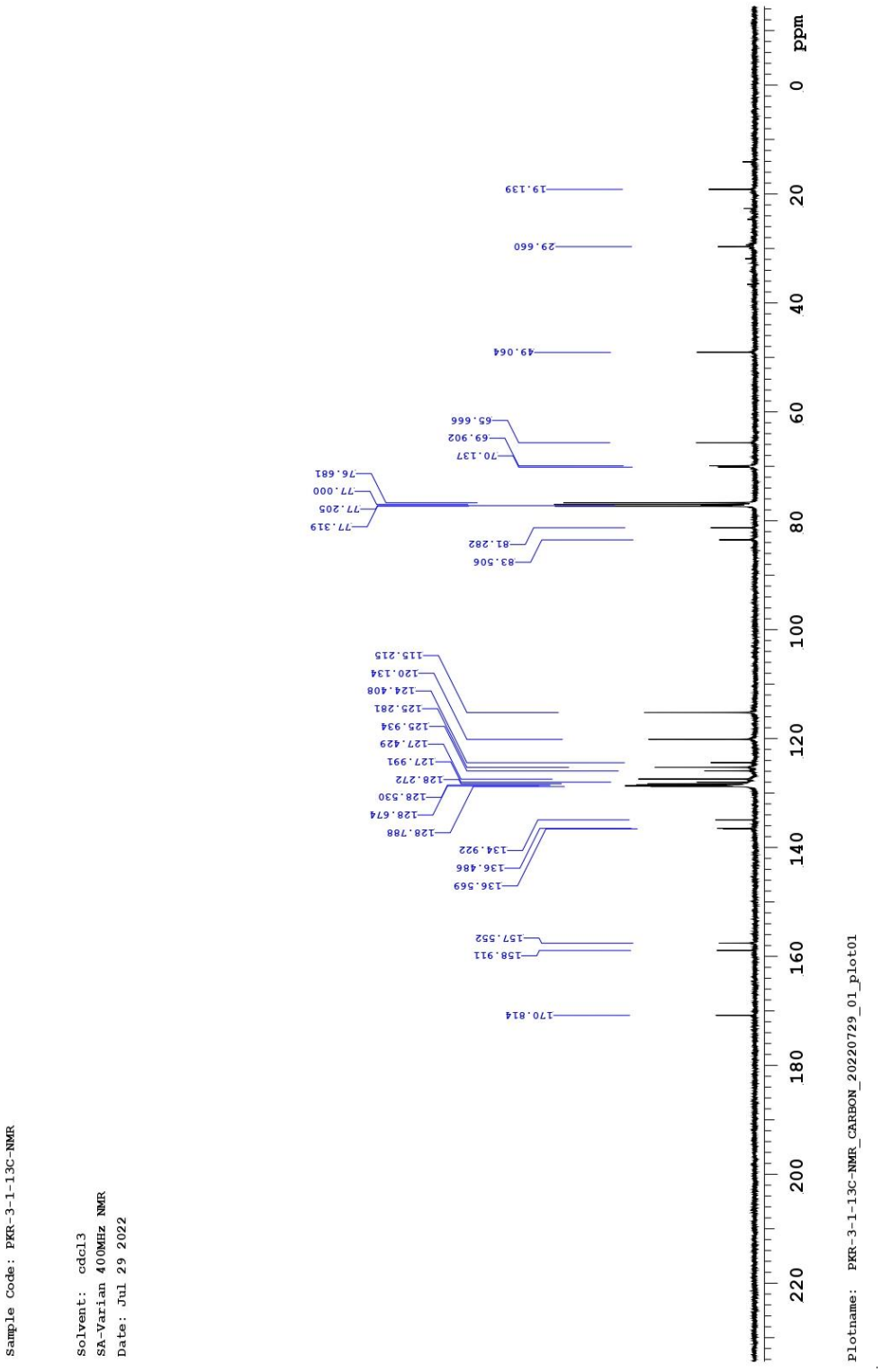


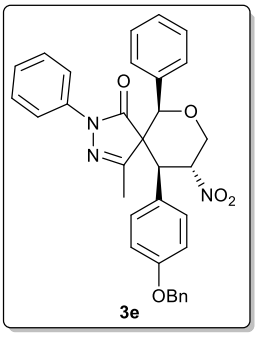
^{13}C NMR Spectrum of compound **3d**



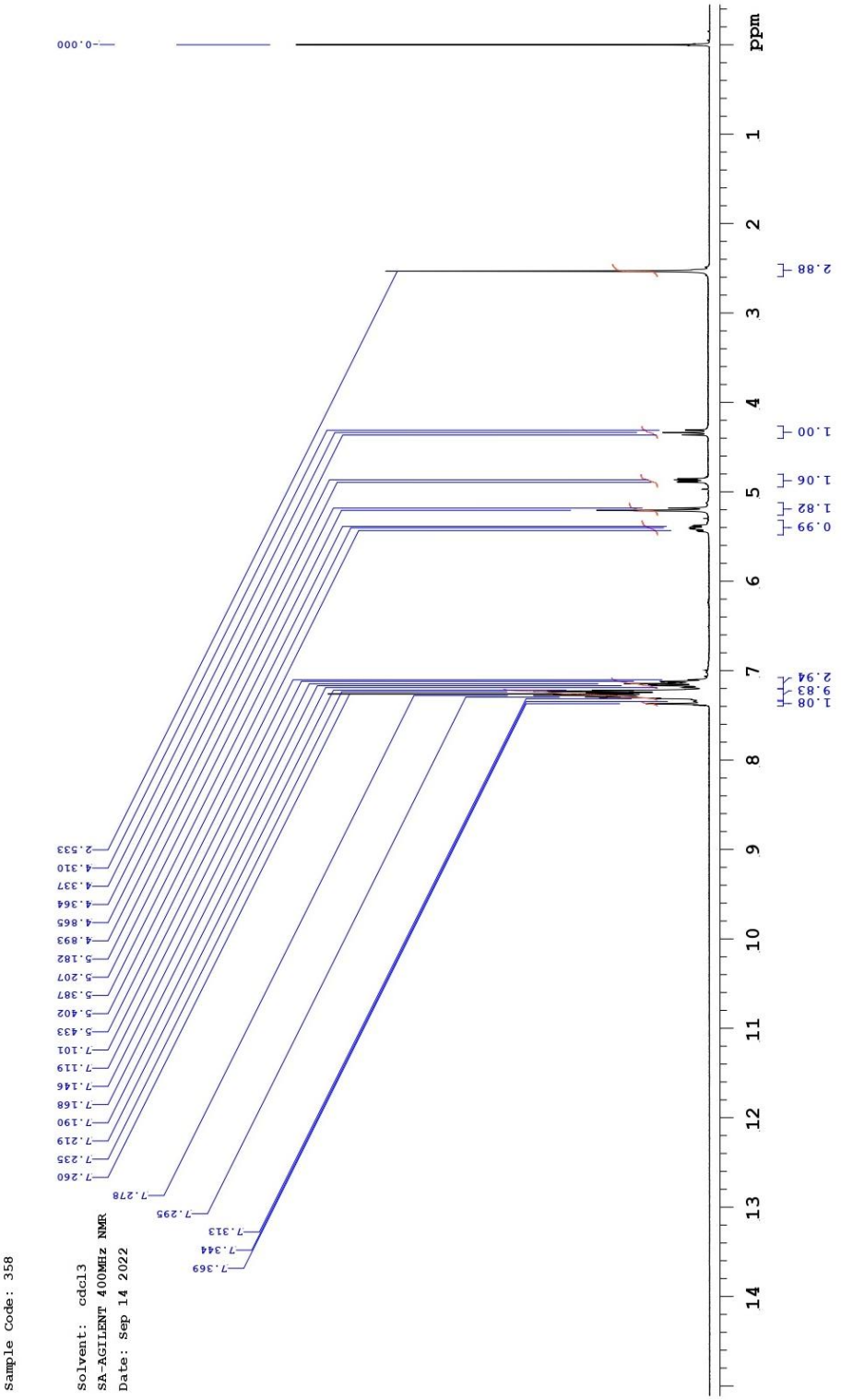


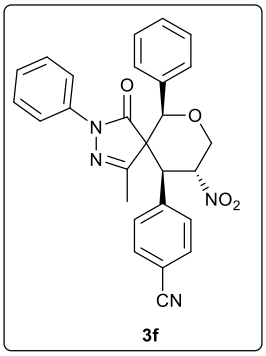
^{1}H NMR Spectrum of compound **3e**





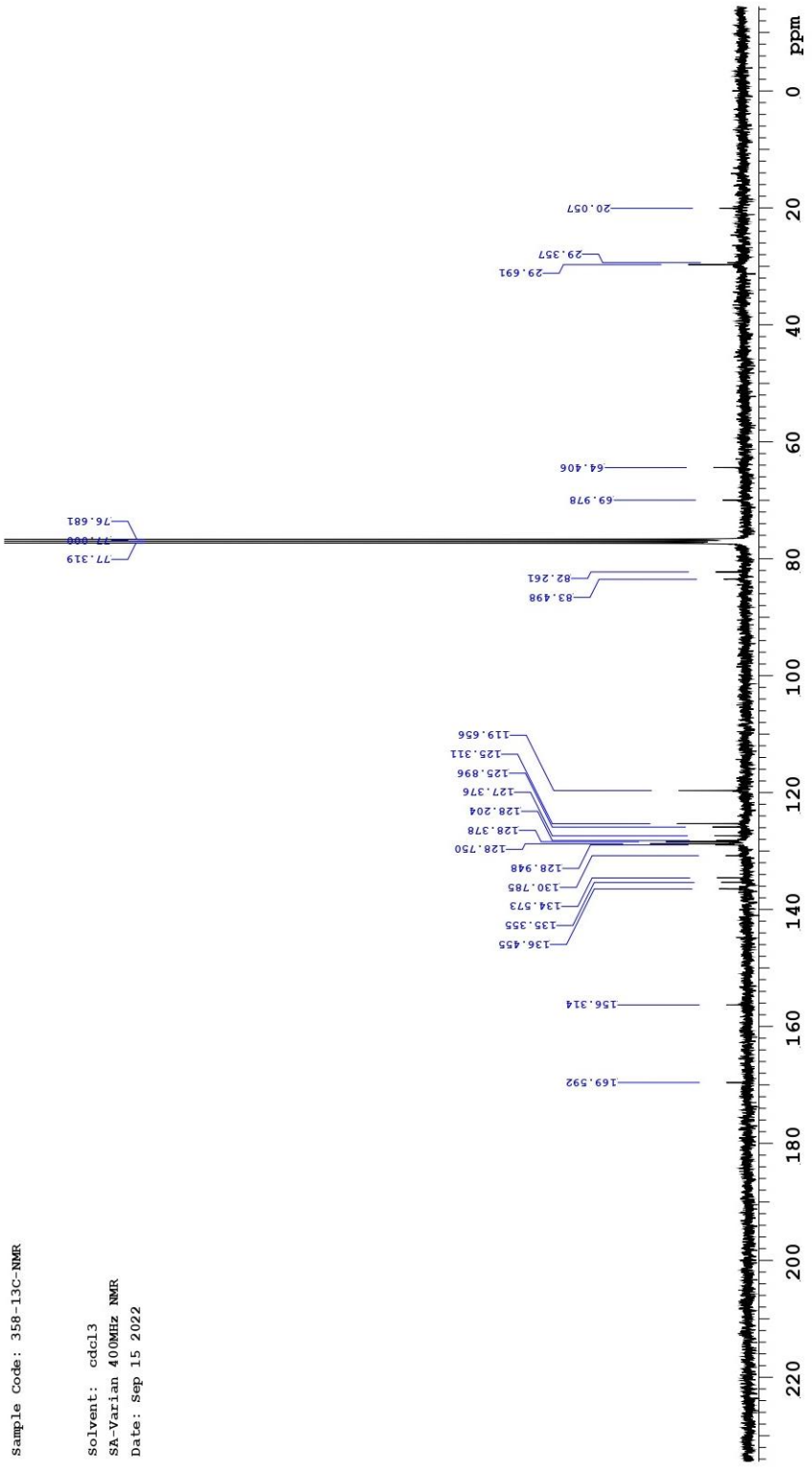
^{13}C NMR Spectrum of compound **3e**

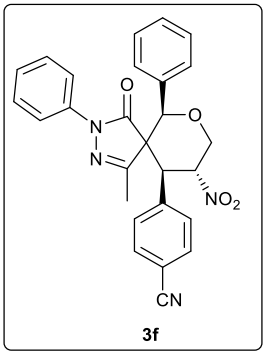




3f

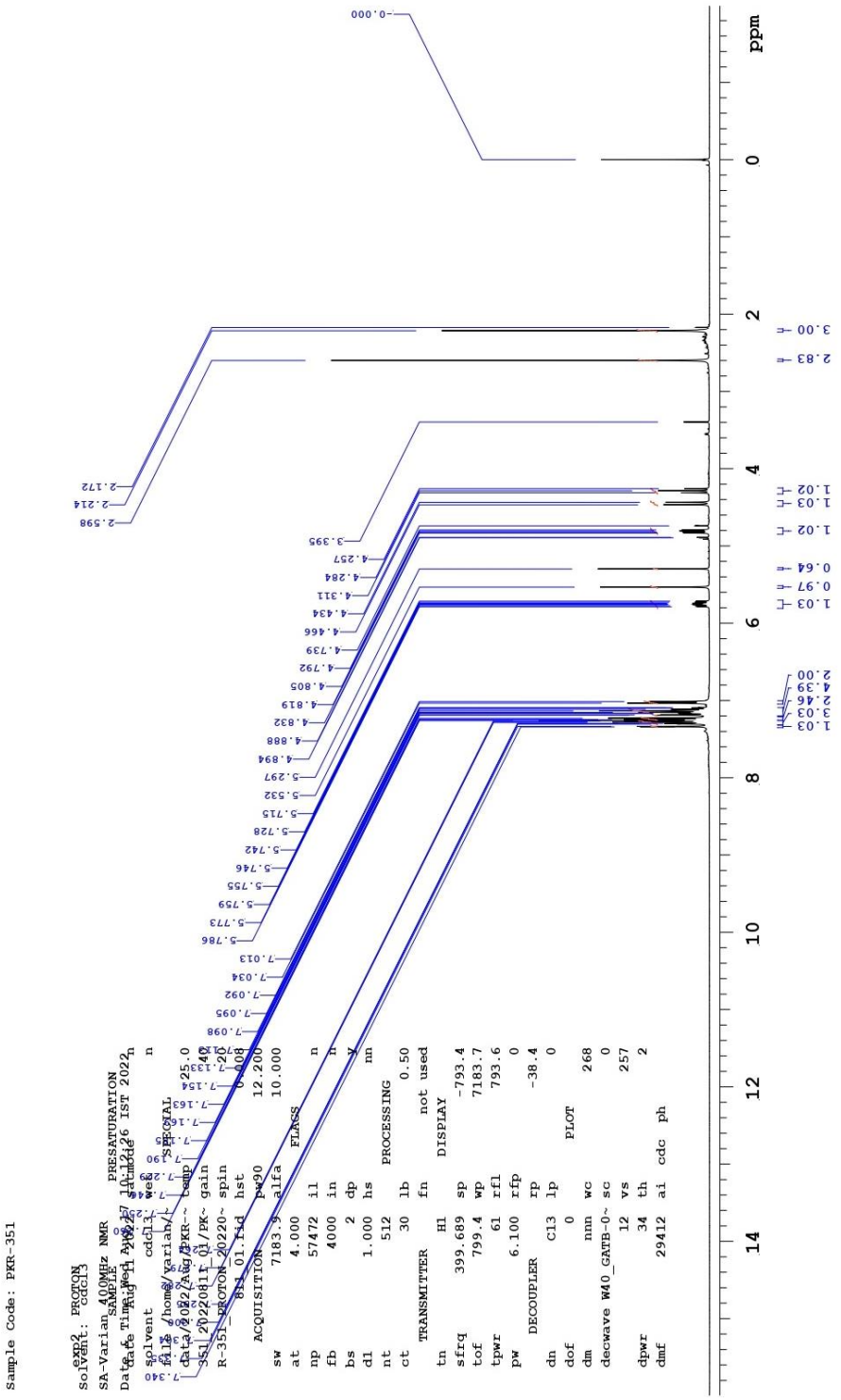
^{1}H NMR Spectrum of compound **3f**

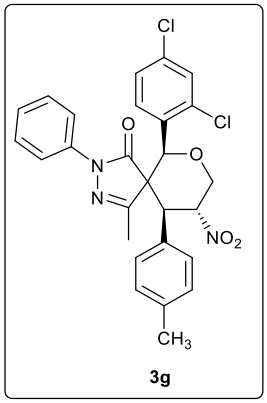




3f

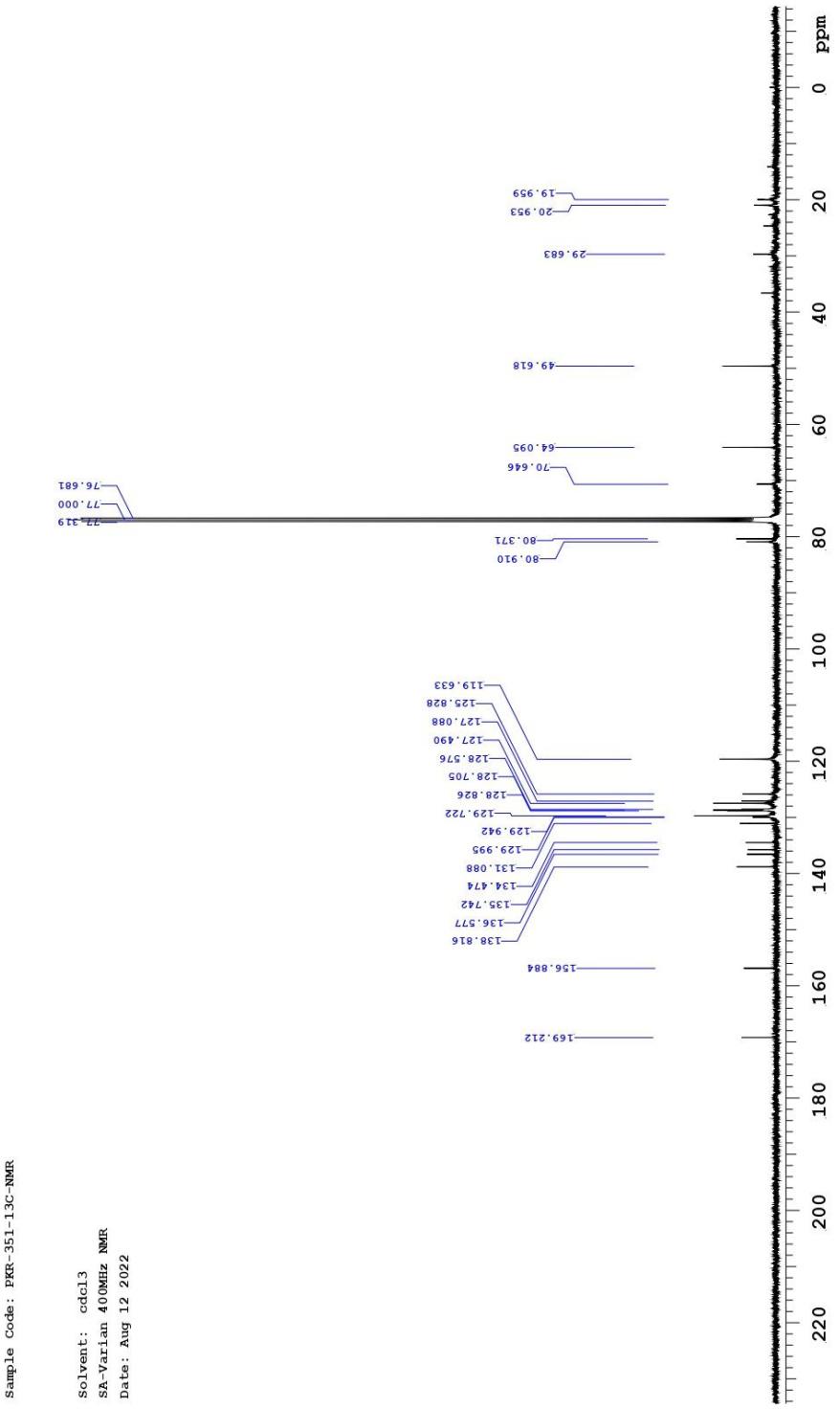
^{13}C NMR Spectrum of compound **3f**

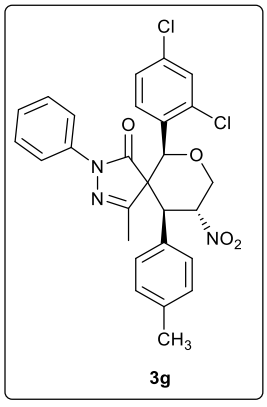




3g

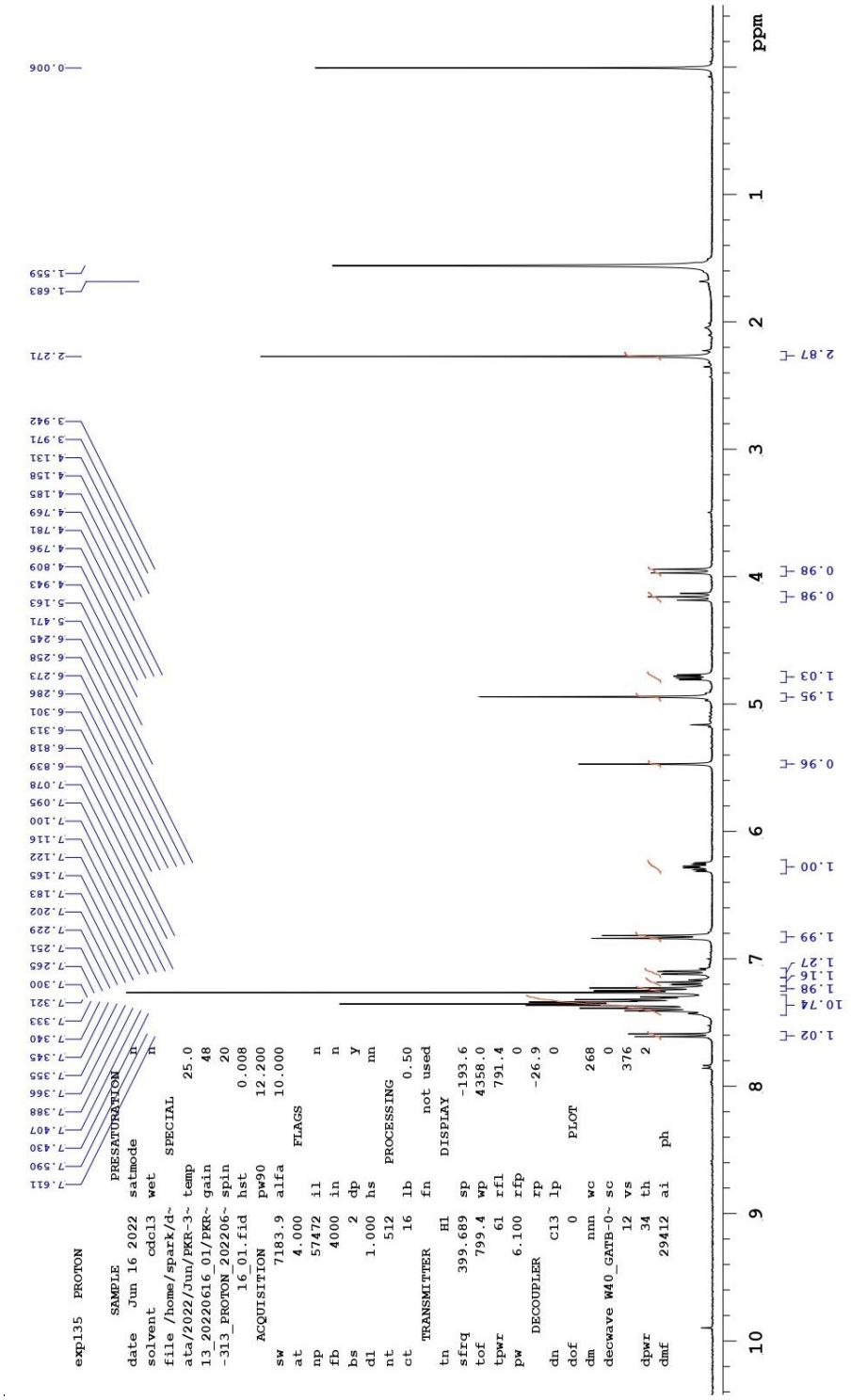
^{1}H NMR Spectrum of compound **3g**



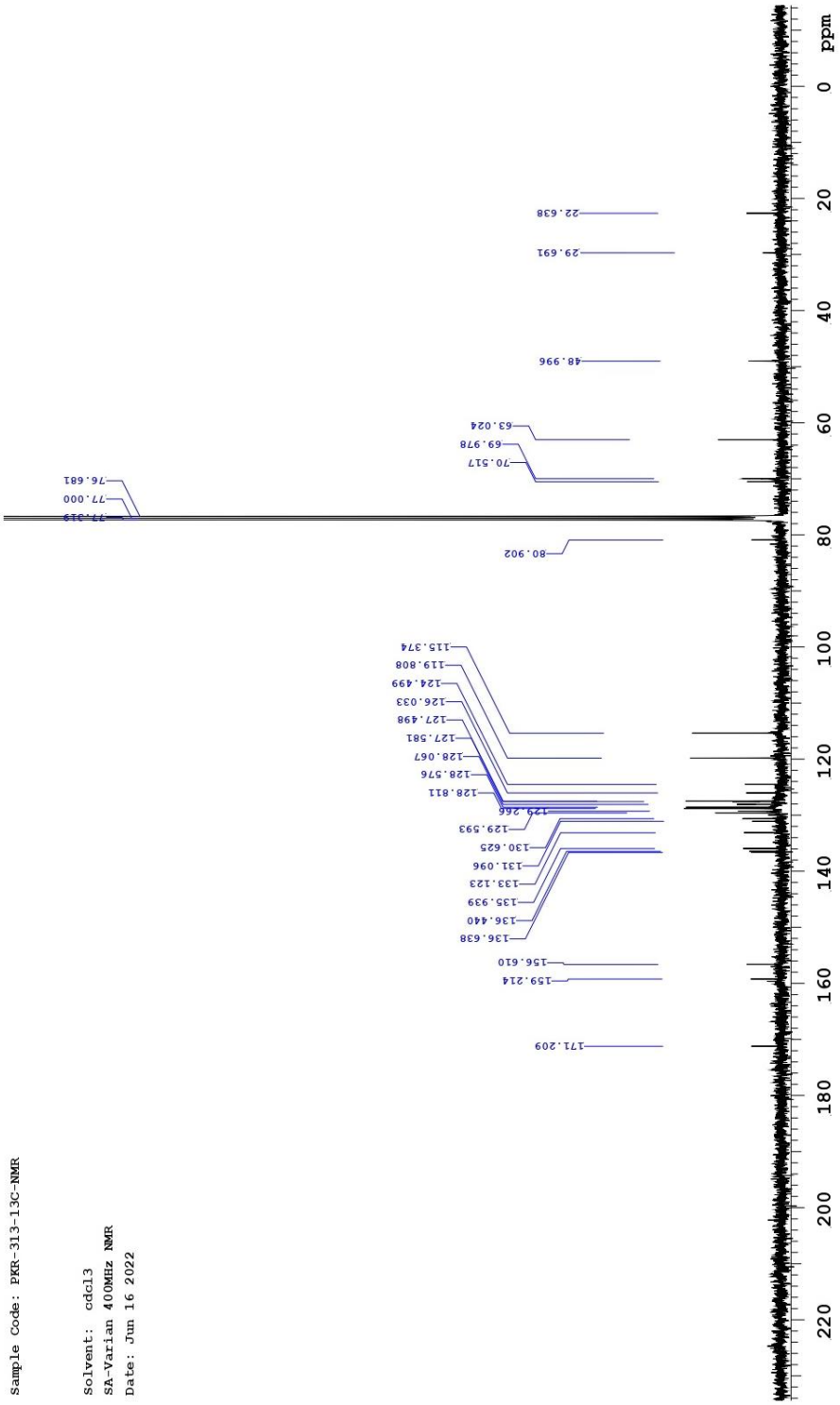


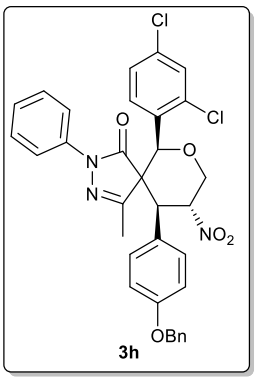
3g

^{13}C NMR Spectrum of compound **3g**

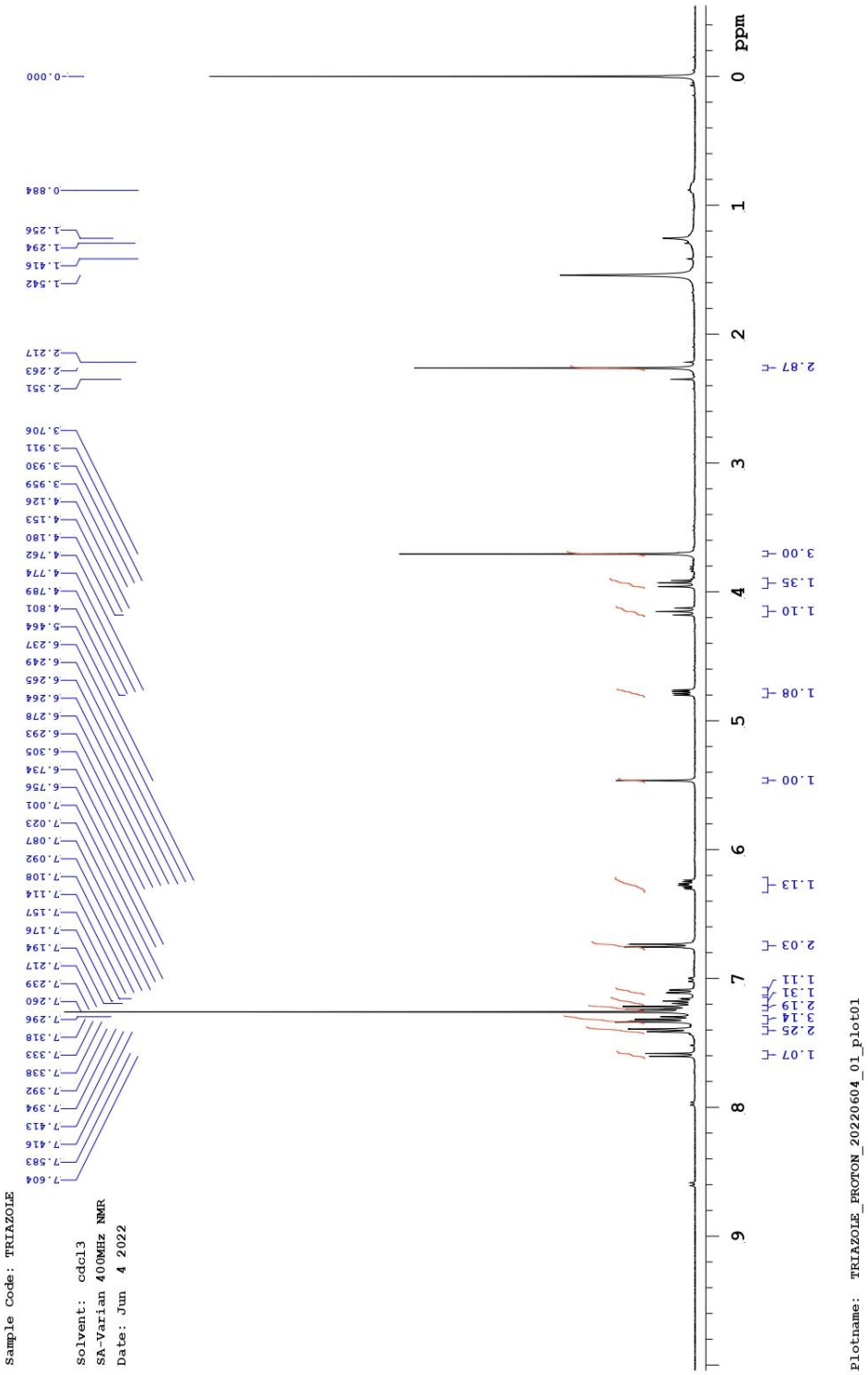


^{1}H NMR Spectrum of compound **3h**

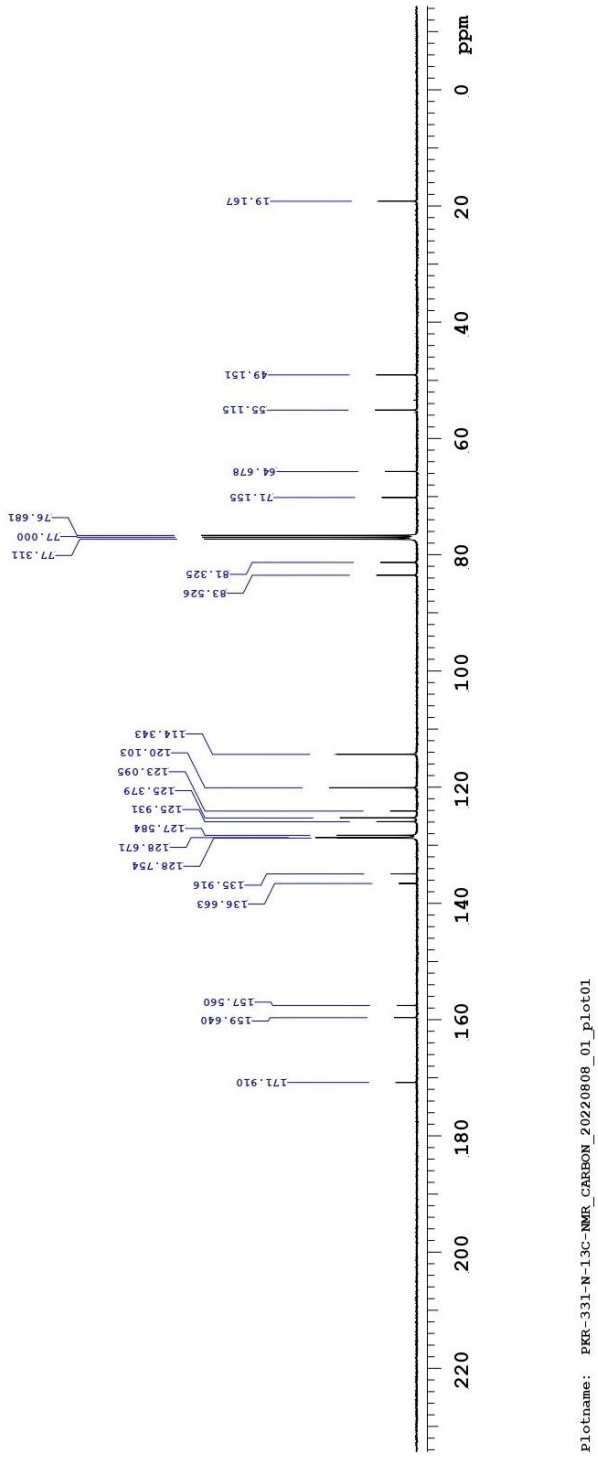


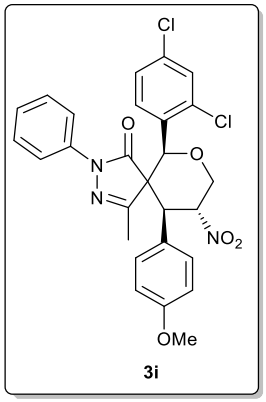


^{13}C NMR Spectrum of compound **3h**

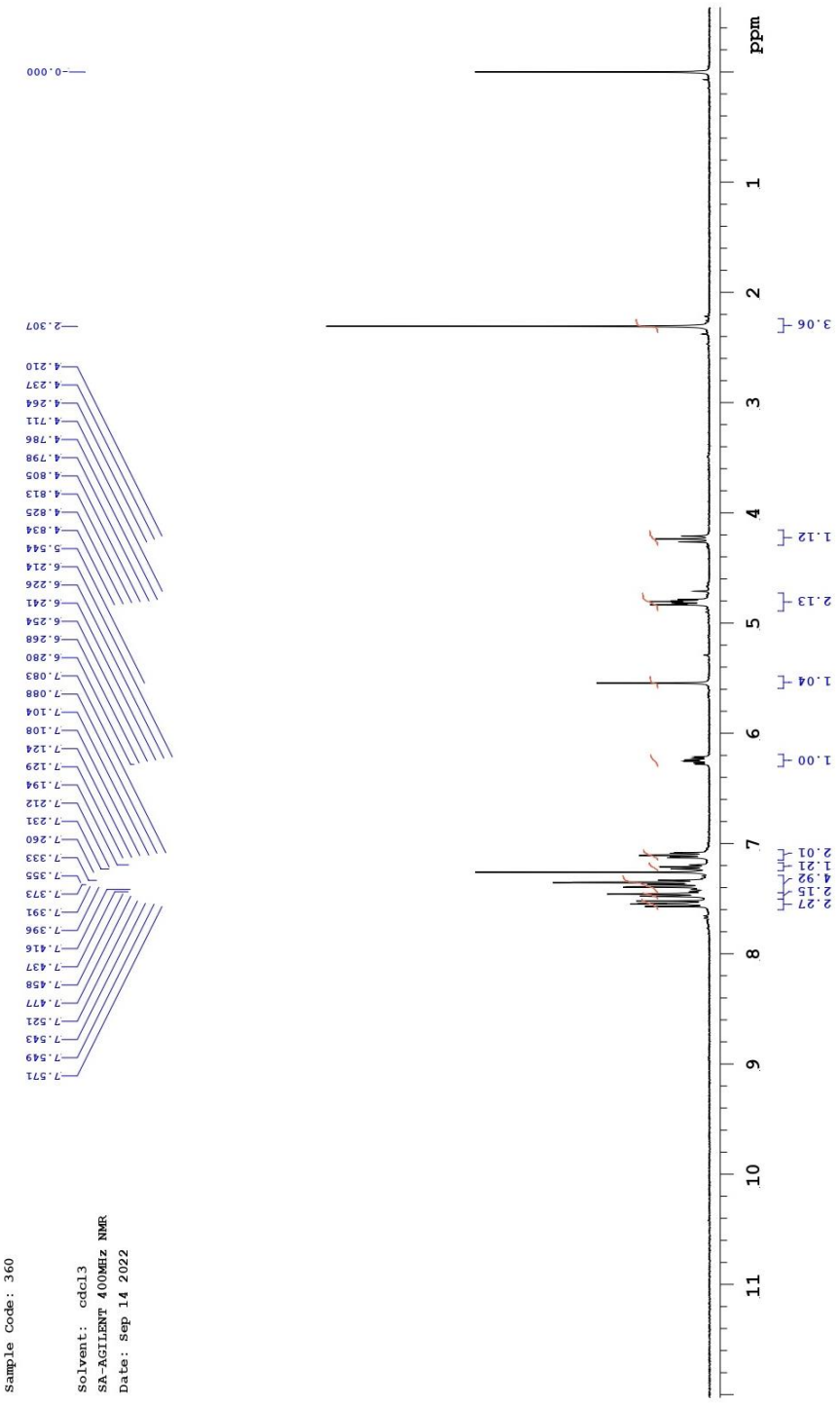


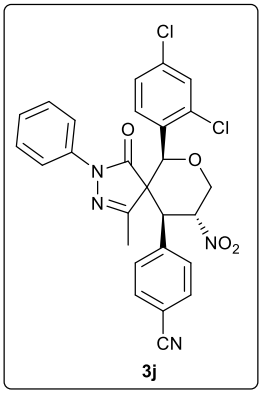
^{1}H NMR Spectrum of compound **3i**





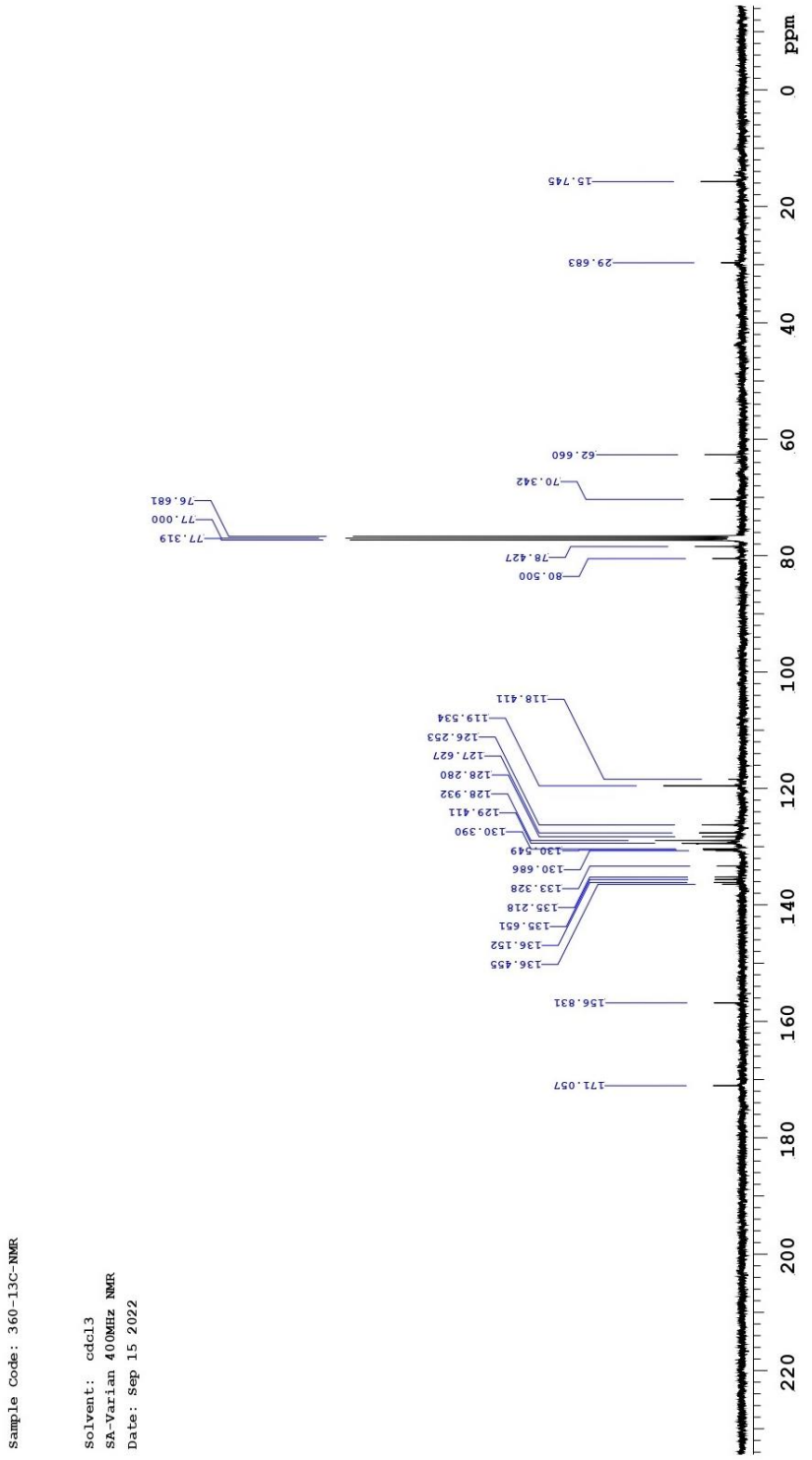
^{13}C NMR Spectrum of compound **3i**

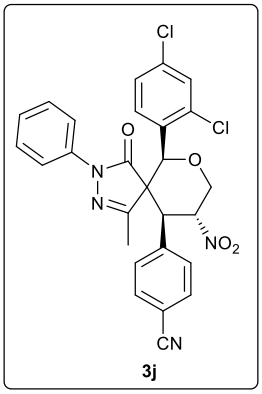




3j

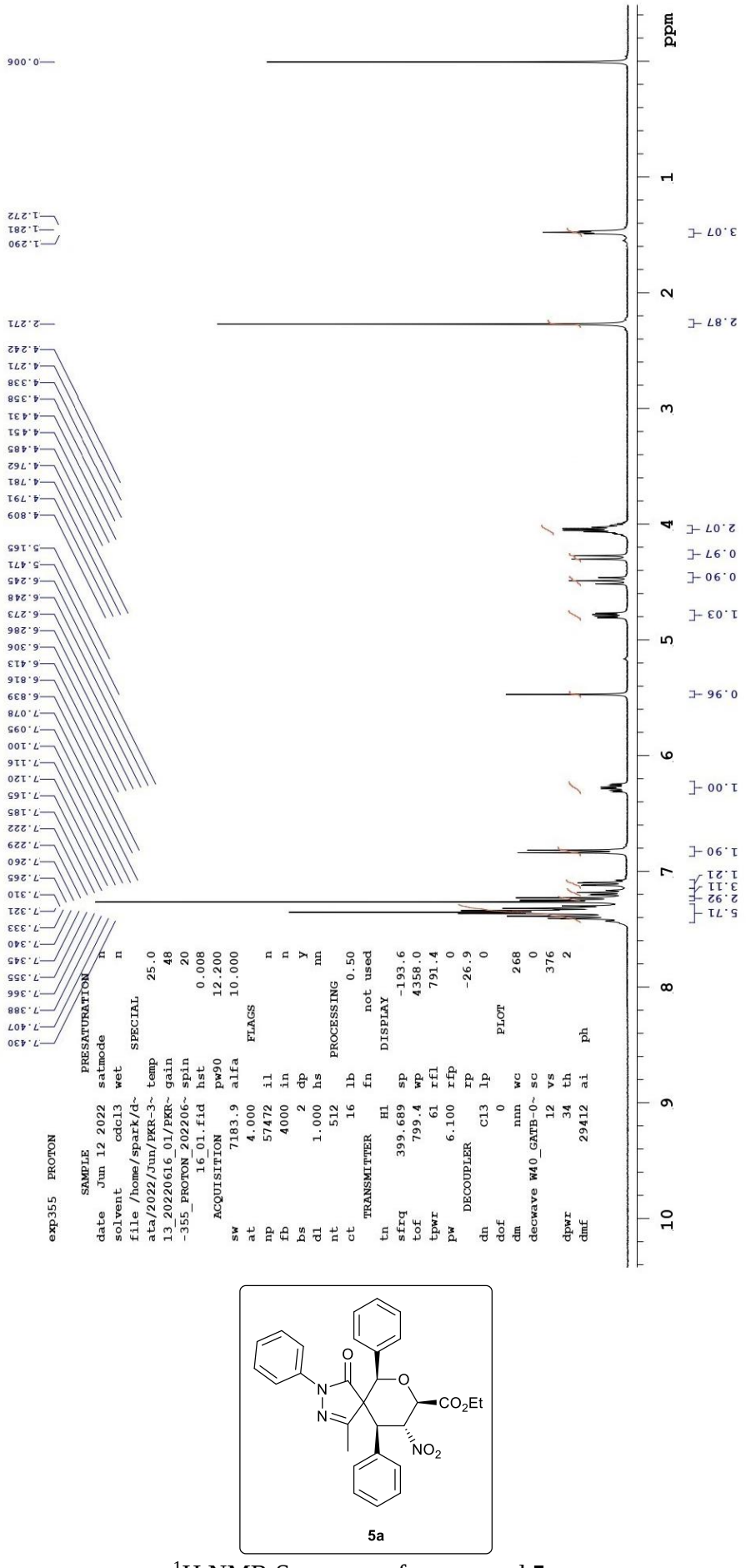
^{1}H NMR Spectrum of compound **3j**



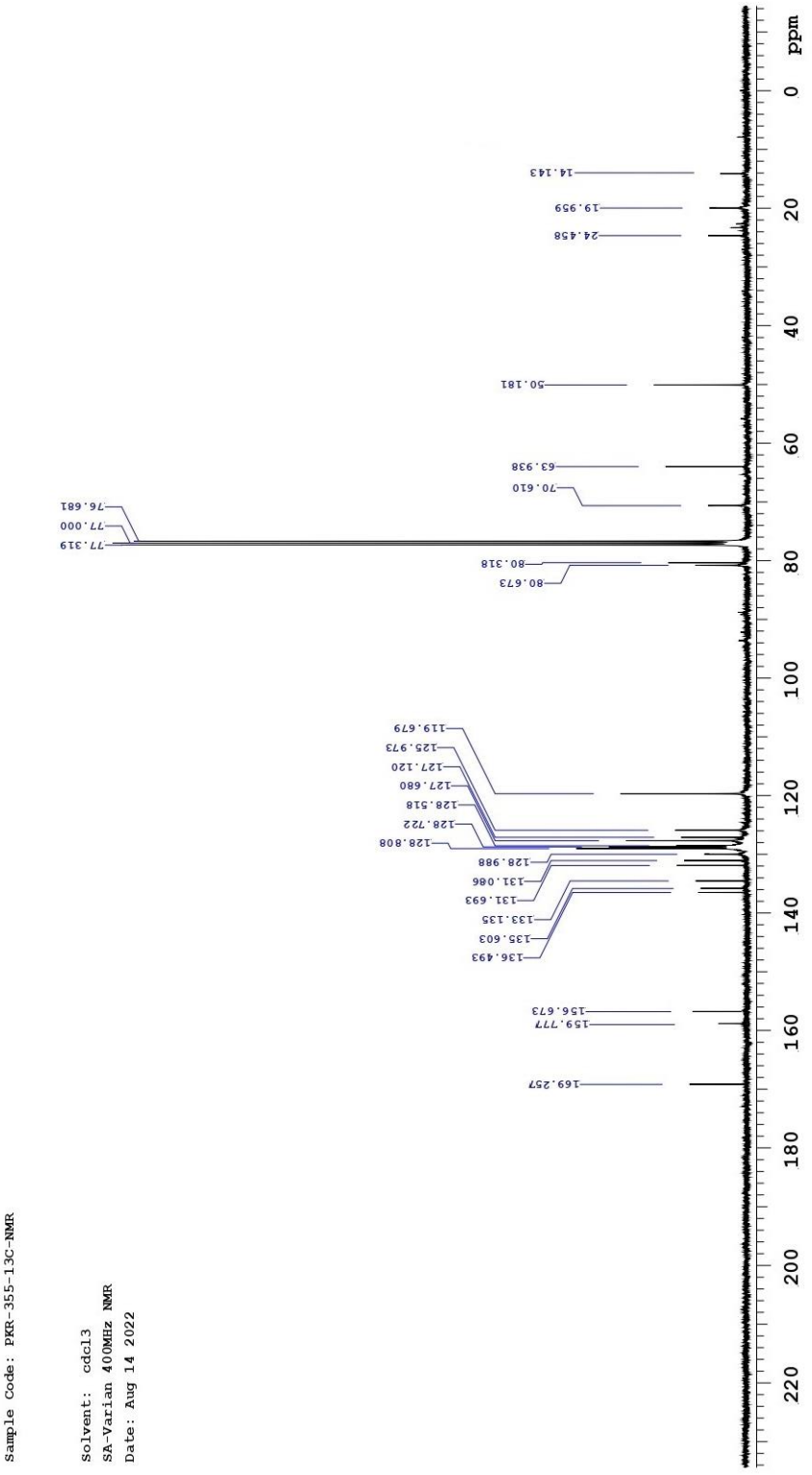


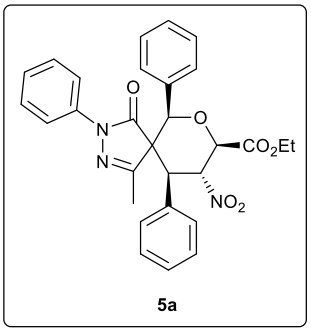
3j

^{13}C NMR Spectrum of compound **3j**



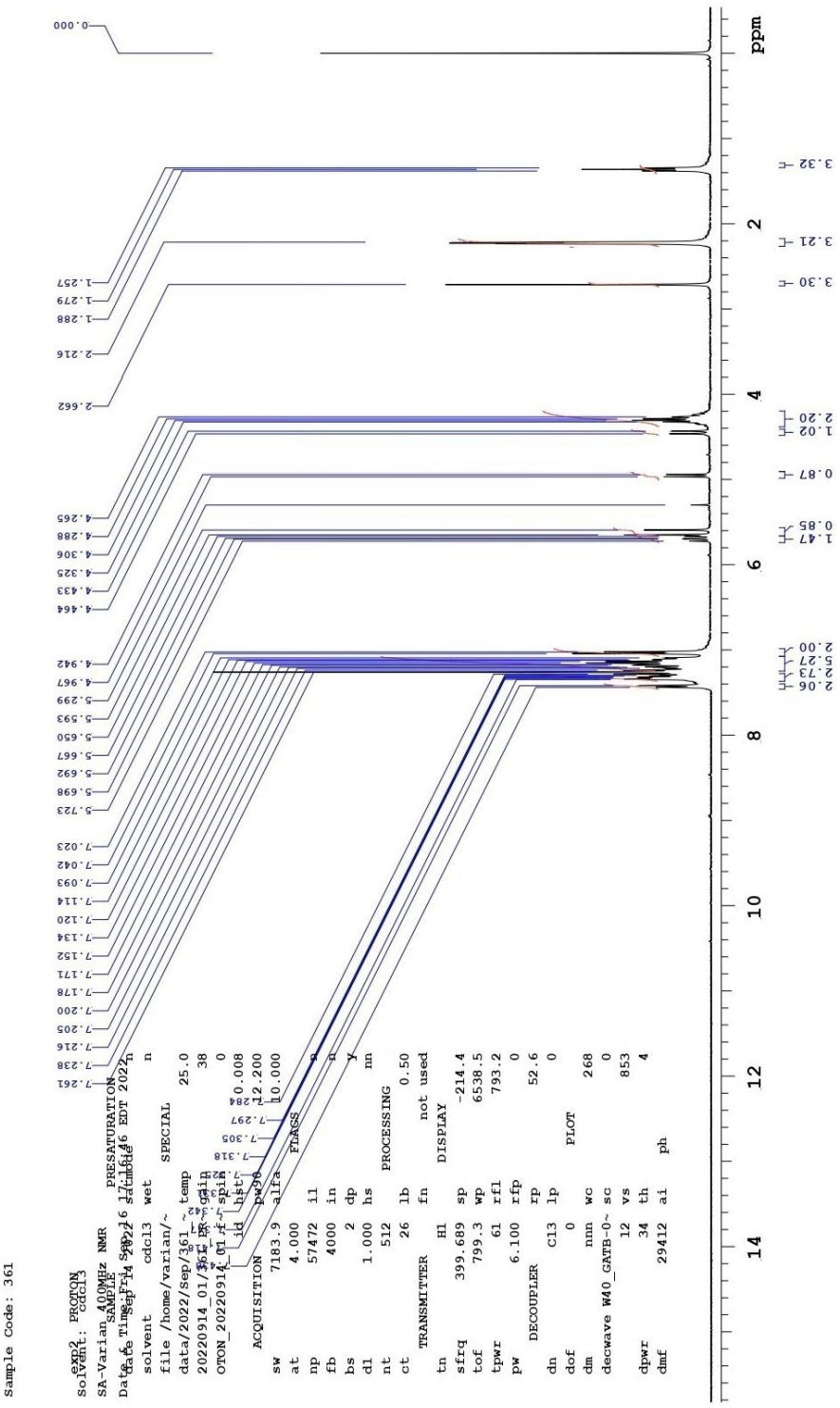
^{1}H NMR Spectrum of compound **5a**



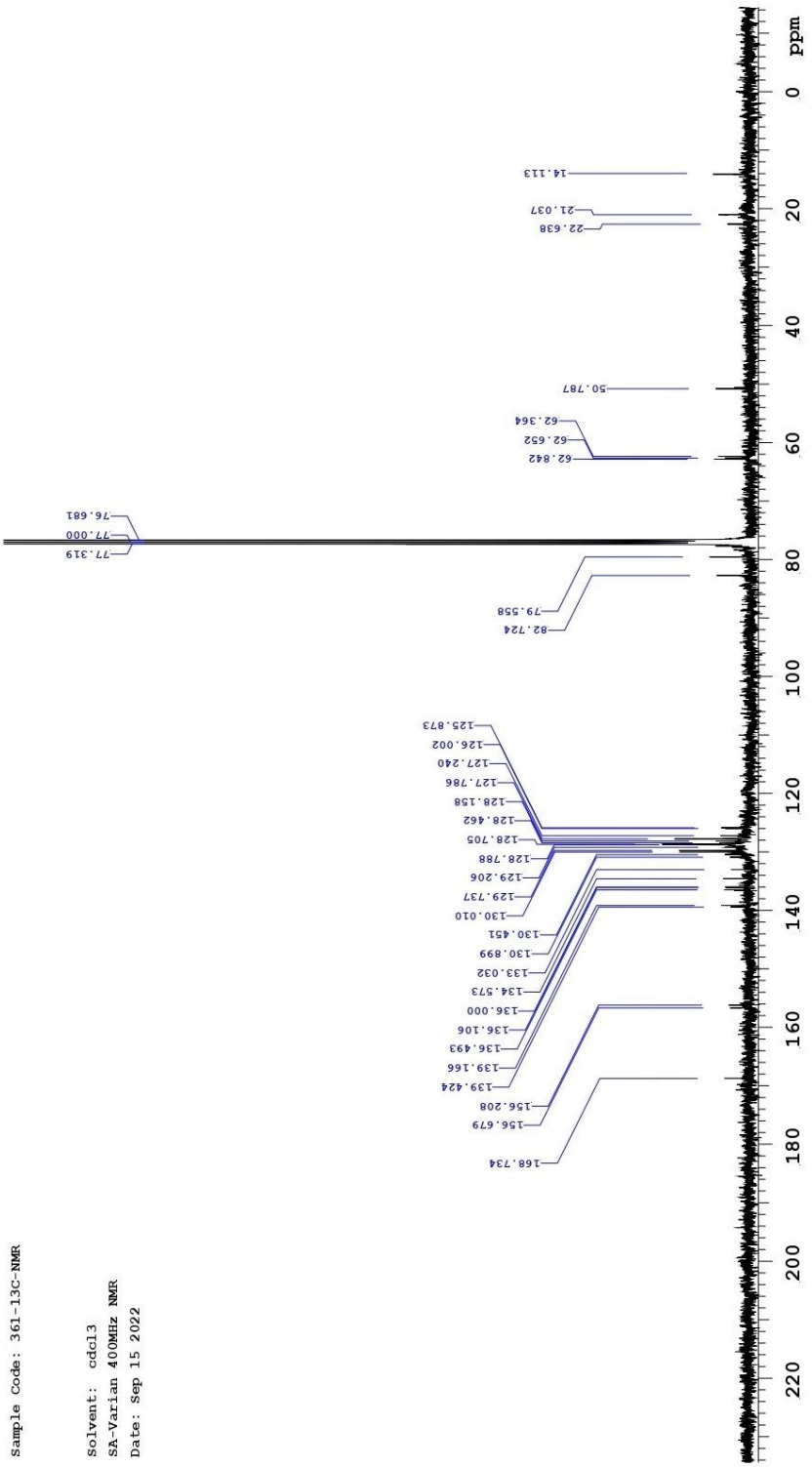


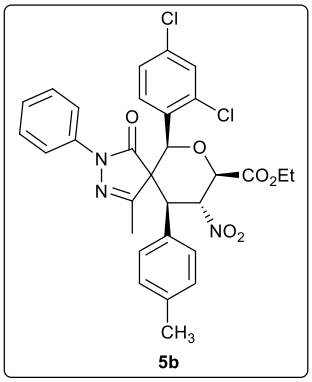
5a

^{13}C NMR Spectrum of compound **5a**

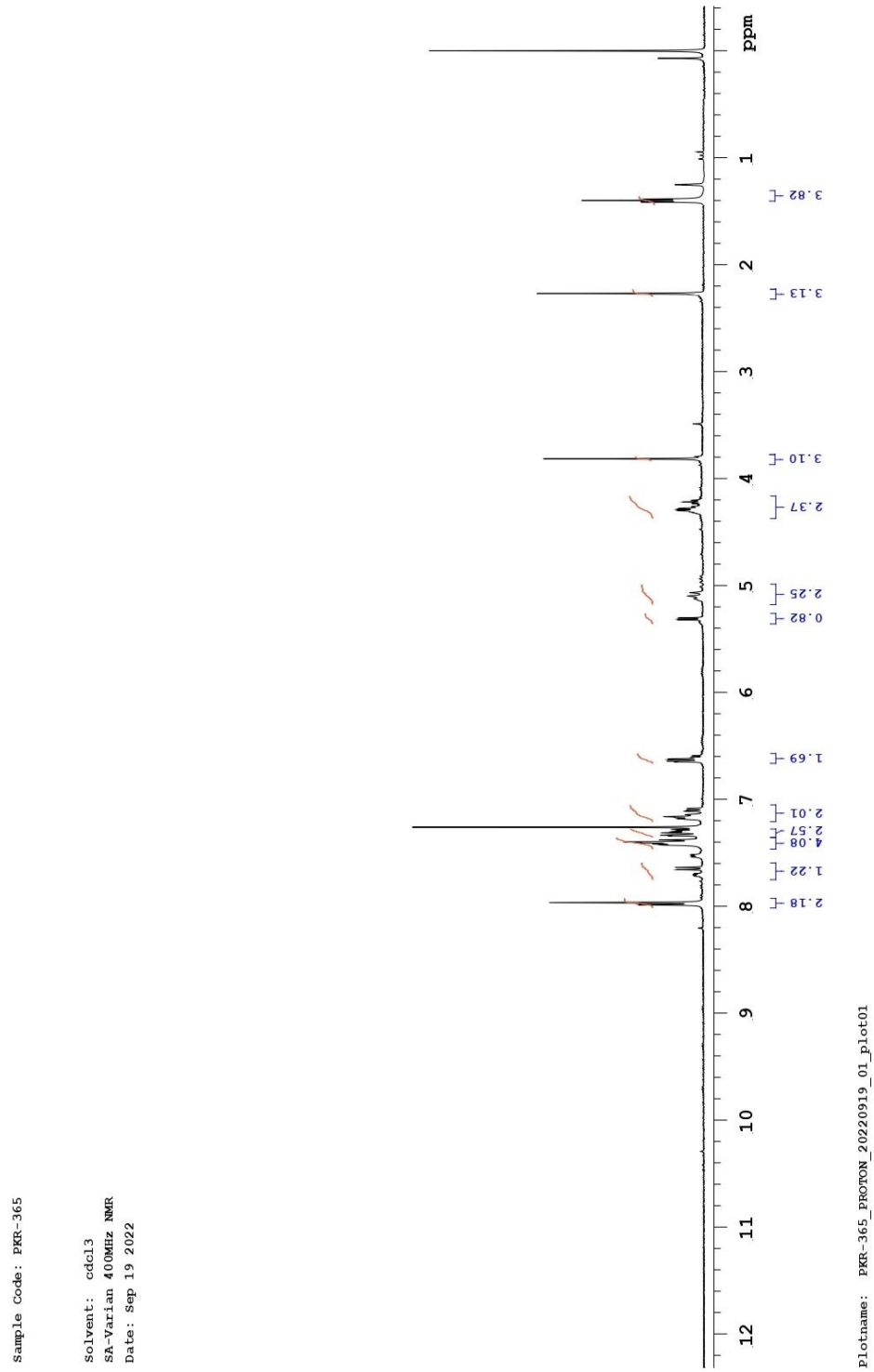


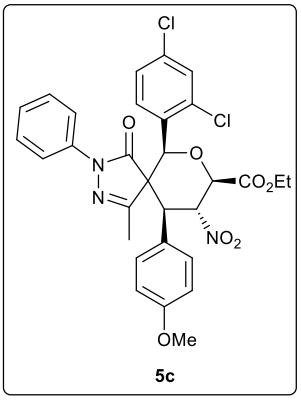
^{1}H NMR Spectrum of compound **5b**





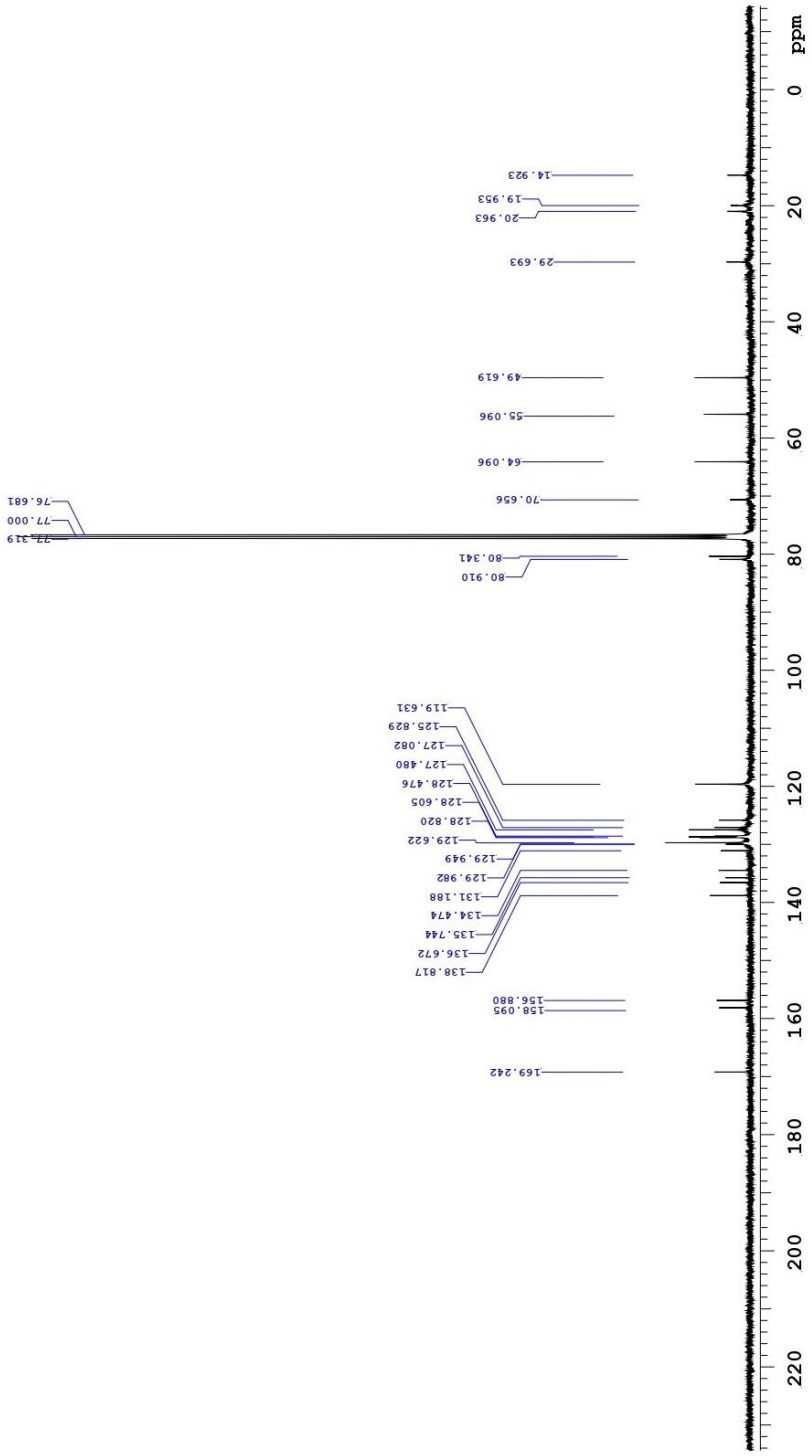
^{13}C NMR Spectrum of compound **5b**

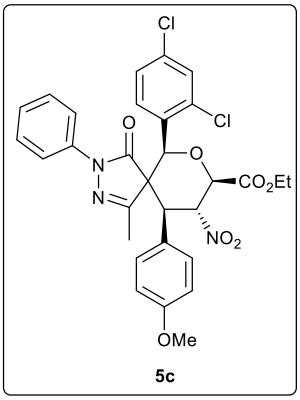




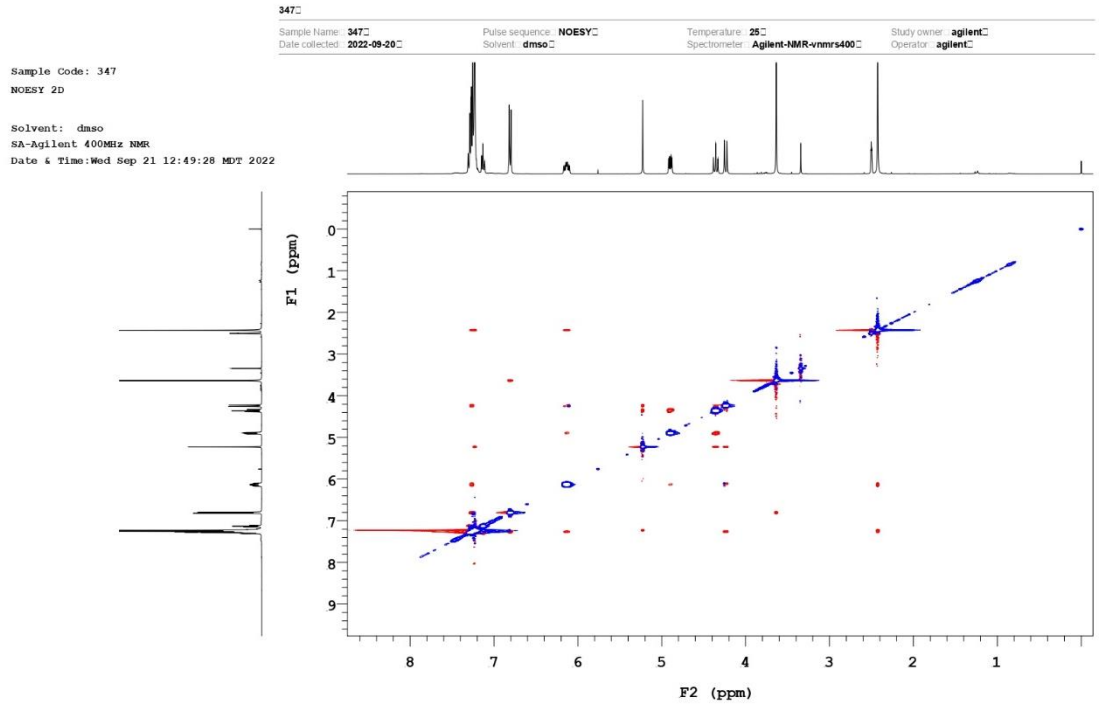
5c

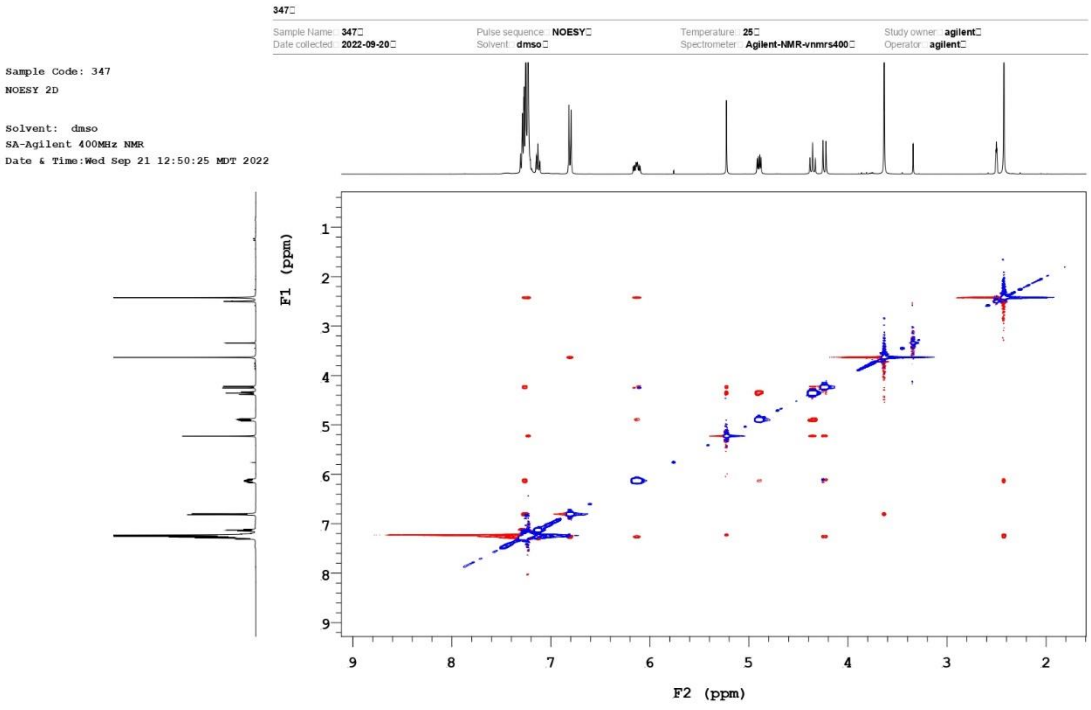
^{1}H NMR Spectrum of compound **5c**

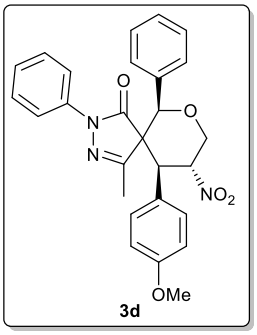




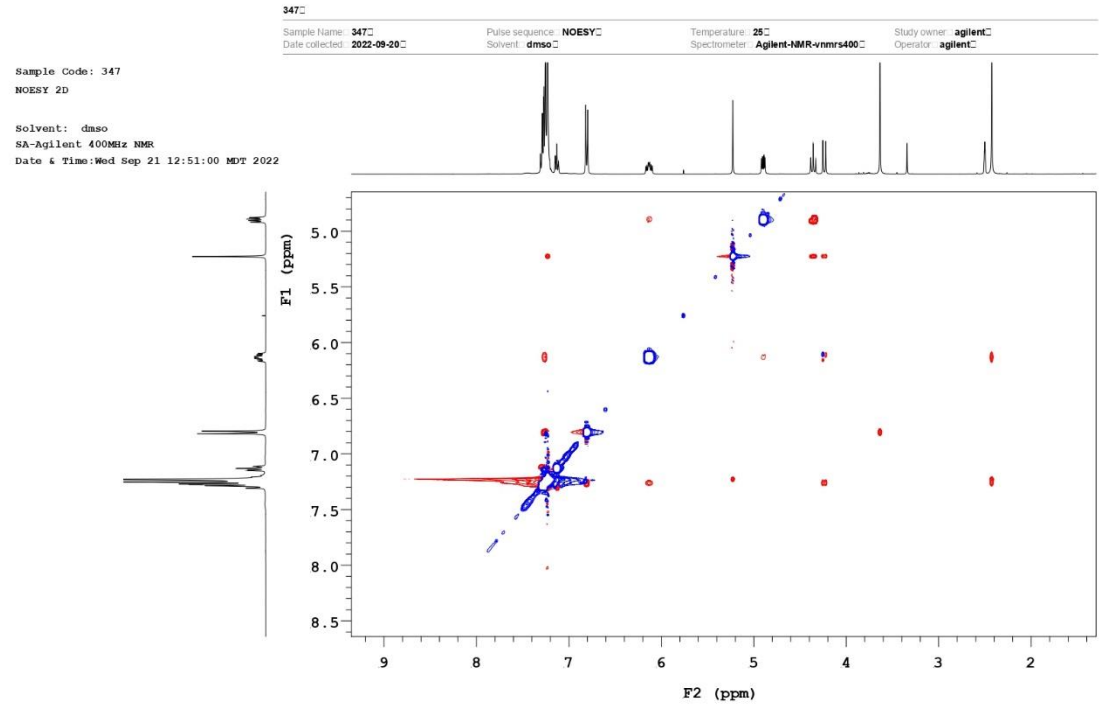
^{13}C NMR Spectrum of compound **5c**

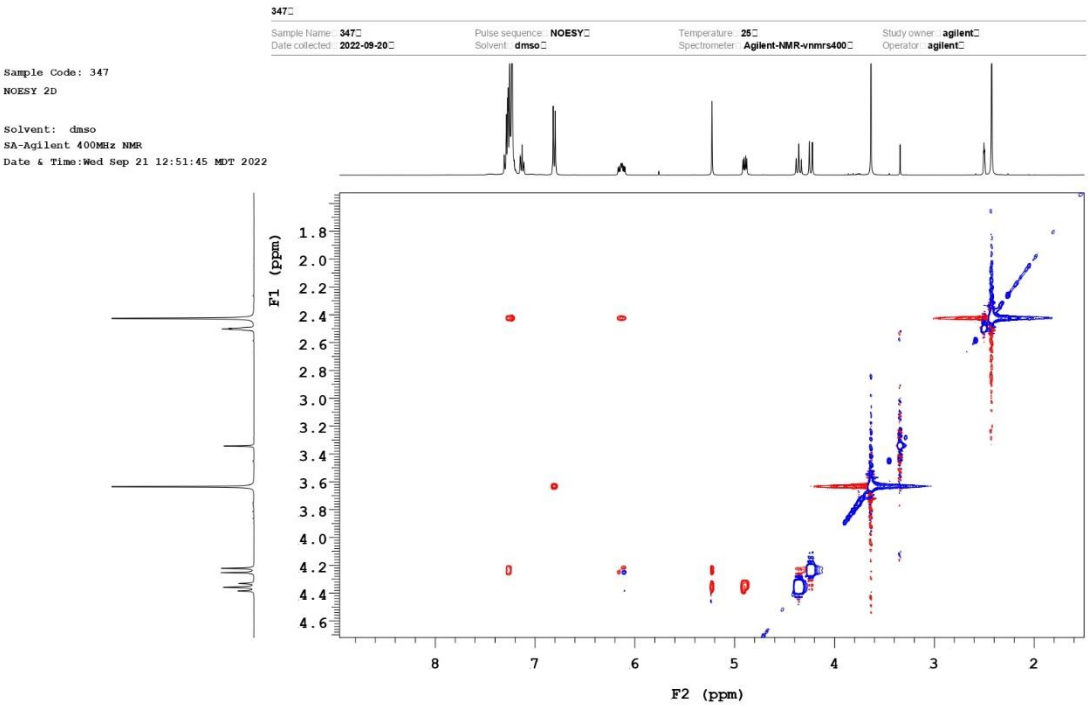


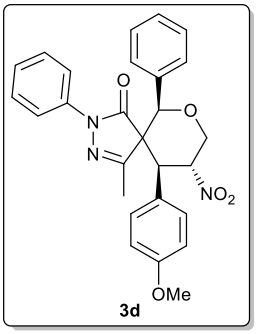




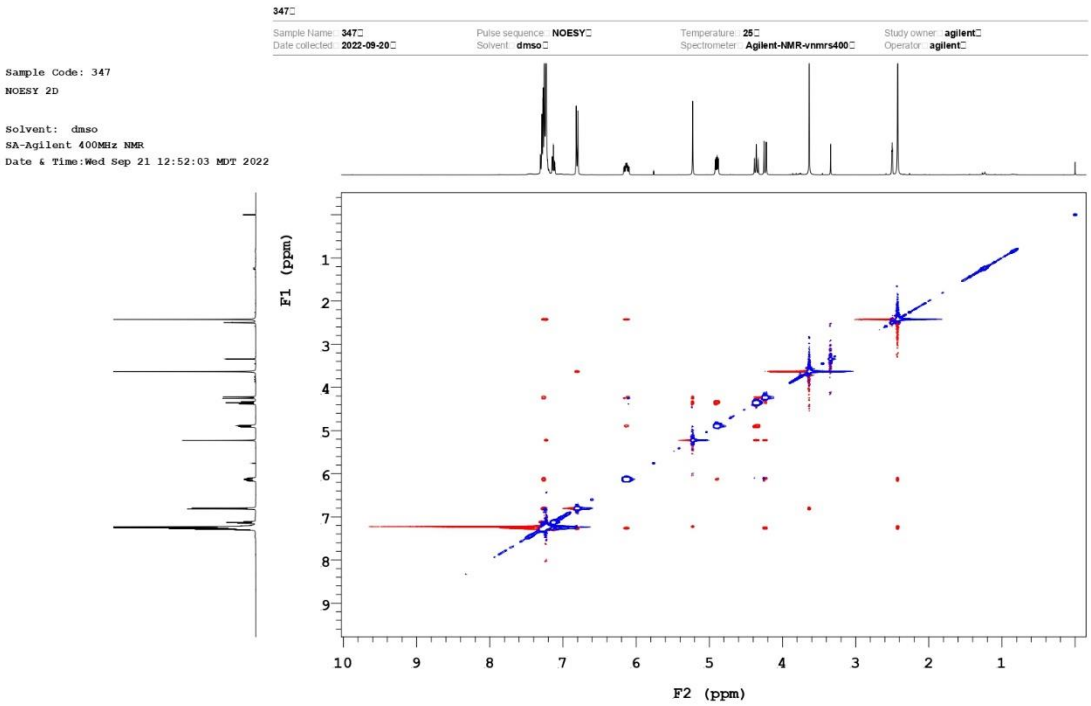
NOESY Spectrum of compound **3d**

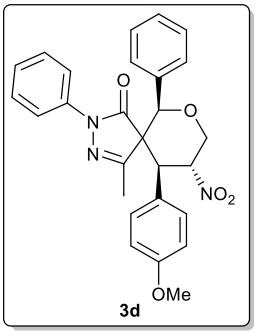






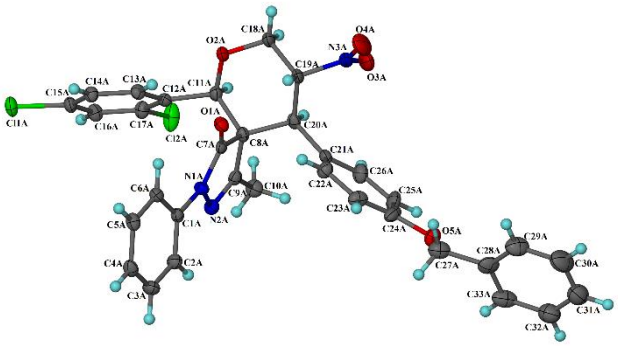
NOESY Spectrum of compound **3d**





NOESY Spectrum of compound **3d**

Crystallographic data of 3a



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) KB665_0m

This report is for guidance only. if used as part of a review procedure for publication, it should not replace the expertise of an experienced crystallographic referee.

No syntax errors found. CIF dictionary Interpreting this report
Datablock: KB665_0m
Bond precision: C-C = 0.0036 A Wavelength=0.71073
Cell: a=24.734(2) b=9.6942(8) c=26.455(3) alpha=90 beta=109.097(3) gamma=90
Temperature: 293 K
Calculated Reported Volume 5994.2(10) 5994.2(9) Space group P 21/c P 21/c Hall group -P 2ybc -P 2ybc
Moiety formula
C66 H54 Cl4 N6 O10, 2(C33 H27 Cl2 N3 O5), 2(O0.67), 1.018(O)
4(C33 H27 Cl2 N3 O5), 2.36(O)
Sum formula C132 H108 Cl8 N12 O22.36 C132 H108 Cl8 N12 O22.36 Mr 2503.73 2503.67
Dx,g cm-3 1.387 1.387 Z 2 2 Mu (mm-1) 0.266 0.266 F000 2597.8 2598.0 F000’ 2601.32
h,k,lmax 29,11,31 29,11,31 Nref 10576 10566 Tmin,Tmax 0.914,0.943 0.632,0.746 Tmin’ 0.914
Correction method= # Reported T Limits: Tmin=0.632 Tmax=0.746 AbsCorr = MULTI-SCAN
Data completeness= 0.999 Theta(max)= 24.998
R(reflections)= 0.0474(9266)
wR2(reflections)= 0.1135(10566)
S = 1.125 Npar= 910
The following ALERTS were generated. Each ALERT has the format test-name_ALERT_alert-type_alert-level. Click on the hyperlinks for more details of the test.
Alert level C PLAT042_ALERT_1_C Calc. and Reported MoietyFormula Strings Differ Please Check PLAT094_ALERT_2_C Ratio of Maximum / Minimum Residual Density .... 2.12 Report PLAT214_ALERT_2_C Atom O1W (Anion/Solvent) ADP max/min Ratio 4.1 prolat PLAT220_ALERT_2_C NonSolvent Resd 1 C Ueq(max)/Ueq(min) Range 3.3

Ratio PLAT242_ALERT_2_C Low 'MainMol' Ueq as Compared to Neighbors of N3B Check PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 3.666 Check PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.595 8 Report

Alert level G PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ... 28 Report PLAT068_ALERT_1_G Reported F000 Differs from Calcd (or Missing)... Please Check PLAT083_ALERT_2_G SHELXL Second Parameter in WGHT Unusually Large 9.52 Why ? PLAT177_ALERT_4_G The CIF-Embedded .res File Contains DELU Records 3 Report PLAT178_ALERT_4_G The CIF-Embedded .res File Contains SIMU Records 3 Report PLAT199_ALERT_1_G Reported _cell_measurement_temperature ..... (K) 293 Check PLAT200_ALERT_1_G Reported _diffrn_ambient_temperature ..... (K) 293 Check PLAT301_ALERT_3_G Main Residue Disorder .....(Resd 1) 19% Note PLAT302_ALERT_4_G Anion/Solvent/Minor-Residue Disorder (Resd 2) 14% Note PLAT302_ALERT_4_G Anion/Solvent/Minor-Residue Disorder (Resd 3) 100% Note PLAT302_ALERT_4_G Anion/Solvent/Minor-Residue Disorder (Resd 4) 100% Note PLAT304_ALERT_4_G Non-Integer Number of Atoms in ..... (Resd 3) 0.67 Check PLAT304_ALERT_4_G Non-Integer Number of Atoms in ..... (Resd 4) 0.51 Check PLAT311_ALERT_2_G Isolated Disordered Oxygen Atom (No H's ?) ..... O1D Check PLAT311_ALERT_2_G Isolated Disordered Oxygen Atom (No H's ?) ..... O1W Check PLAT410_ALERT_2_G Short Intra H...H Contact H23A ..H27D . 2.05 Ang. x,y,z = 1_555 Check PLAT767_ALERT_4_G INS Embedded LIST 6 Instruction Should be LIST 4 Please Check PLAT773_ALERT_2_G Check long C-C Bond in CIF: C32D -- C33D 1.99 Ang. PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle(s) in CIF ... 34.90 Deg. C32D -C32D -H32D 3_665 1_555 1_555 ..... # 164 Check PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle(s) in CIF ... 28.30 Deg. C33D -C32D -H32D 3_665 1_555 1_555 ..... # 166 Check PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd. # 2 Note C33 H27 Cl2 N3 O5 PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd. # 3 Note O0.67 PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd. # 4 Note O PLAT793_ALERT_4_G Model has Chirality at C8A (Centro SPGR) S Verify PLAT793_ALERT_4_G Model has Chirality at C8B (Centro SPGR) S Verify PLAT793_ALERT_4_G Model has Chirality at C11A (Centro SPGR) R Verify PLAT793_ALERT_4_G Model has Chirality at C11B (Centro SPGR) R Verify PLAT793_ALERT_4_G Model has Chirality at C19A (Centro SPGR) R Verify PLAT793_ALERT_4_G Model has Chirality at C19B (Centro SPGR) R Verify

PLAT793_ALERT_4_G Model has Chirality at C20A (Centro SPGR) S Verify PLAT793_ALERT_4_G Model has Chirality at C20B (Centro SPGR) S Verify PLAT860_ALERT_3_G Number of Least-Squares Restraints ..... 385 Note PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary . Please Do ! PLAT909_ALERT_3_G Percentage of I>2sig(I) Data at Theta(Max) Still 76% Note PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min). 3 Note PLAT913_ALERT_3_G Missing # of Very Strong Reflections in FCF .... 1 Note PLAT933_ALERT_2_G Number of HKL-OMIT Records in Embedded .res File 10 Note

PLAT965_ALERT_2_G The SHELXL WEIGHT Optimisation has not Converged Please Check

PLAT967_ALERT_5_G Note: Two-Theta Cutoff Value in Embedded .res .. 50.0 Degree
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 7 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by 2 Check
0 ALERT level A = Most likely a serious problem - resolve or explain
0 ALERT level B = A potentially serious problem, consider carefully
7 ALERT level C = Check. Ensure it is not caused by an omission or oversight
41 ALERT level G = General information/check it is not something unexpected
5 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
13 ALERT type 2 Indicator that the structure model may be wrong or deficient
7 ALERT type 3 Indicator that the structure quality may be low
21 ALERT type 4 Improvement, methodology, query or suggestion
2 ALERT type 5 Informative message, check

References

1. N. Rastogi, I.N.N. Namboothiri, M. Cojocaru, *Tetrahedron Letters*, 2004, **45**, 4745-4748.
2. I. Deb, M. Dadwal, M. Mobin and I. N. N. Namboothiri, *Org. Lett.*2006, **8**, 1201–1204.
3. R. Maity, C. Gharui, A. Sil, S. Pan, *Org. Lett.*, 2017, **19**, 662–665.