

A Triple Cascade Approach Towards Diastereoselective Synthesis of Spiro *trans*-Decalinol Scaffolds.

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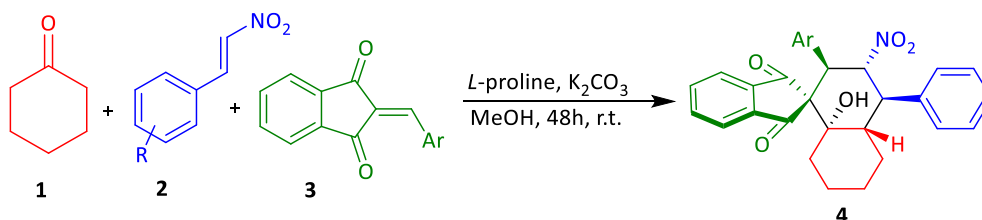
Experimental section

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 ^1H 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 ^1H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublet), 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 with diamond Brucker Technologies.

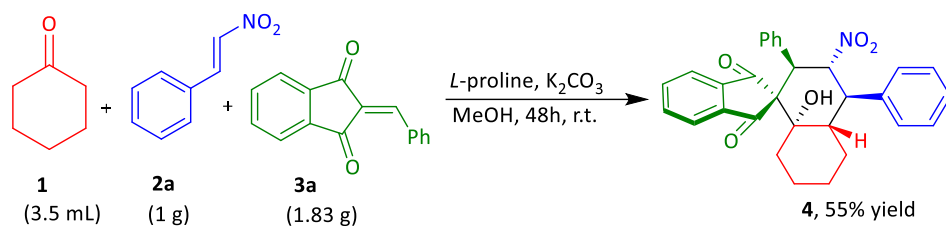
General procedure for the synthesis of spiro *trans*-decalinol derivatives (4):

To a solution of cyclohexanone **1** (0.5 mL, 5.10 mmol) and nitrostyrene **2** (1.02 mmol) with arylidene 1,3-indione **3** (1.12 mmol) and potassium carbonate (209mg, 1.51mmol) and *L*-proline (58mg, 0.5mmol) in methanol (2 mL) at room temperature. The reaction mixture was stirred at room temperature for 48 hours. The reaction was monitored by using TLC till the completion of starting materials. After the completion of the reaction, the organic layer was extracted with dichloromethane, washed with brine solution and dried over Na_2SO_4 , and concentrated under reduced pressure crude was subjected to flash column chromatography on silica gel by eluting ethyl acetate in hexane (2-3 %) to afford the desired products **4a**.



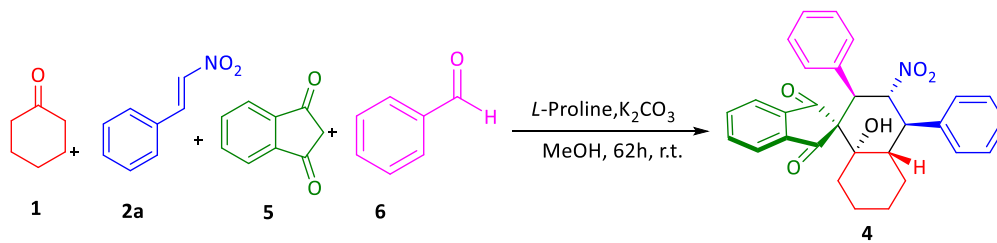
Gram scale preparation:

To a solution of cyclohexanone **1** (3.5mL, 35.7 mmol) and nitrostyrene **2a** (1g, 7.14 mmol) with benzylidene 1,3-indione **3a** (1.83g, 7.85 mmol) and potassium carbonate (1.47g, 1.5 mmol) and *L*-proline (410mg, 3.57mmol, 0.5 equiv.) in methanol (10 mL) at room temperature. The reaction mixture was stirred at room temperature for 48 hours. The reaction was monitored by using TLC till the completion of starting materials. After the completion of reaction, organic layer was extracted with dichloromethane, washed with brine solution and dried over Na_2SO_4 and concentrated under reduced pressure. Crude was subjected to flash column chromatography on silica gel by eluting ethyl acetate in hexane (2-3 %) to afford the desired products **4a**. (i.e. 1.785 g, 55% yield).



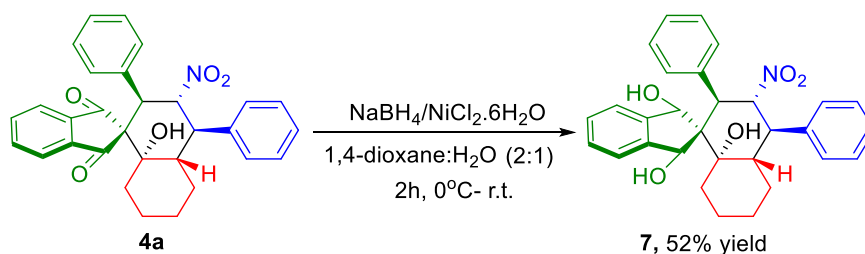
Quadruple cascade approach for the synthesis of spiro *trans*-decalinol **4**:

To a solution of cyclohexanone **1** (50 μL , 0.51 mmol) and nitrostyrene **2** (38mg, 0.25 mmol) with benzylidene **5** (10.6 μL , 0.11 mmol) 1,3-inedione **6** (14.6mg, 0.1 mmol) and potassium carbonate (21mg, 1.5 mmol) and *L*-proline (3.5mg, 0.5eq) in methanol (200 μL) at room temperature. The reaction mixture was stirred at room temperature for 62 hours. The reaction was monitored by using TLC till the completion of starting materials. After the completion of the reaction, the organic layer was extracted with dichloromethane, washed with brine solution and dried over Na_2SO_4 , and concentrated under reduced pressure crude was subjected to flash column chromatography on silica gel by eluting ethyl acetate in hexane (2-3 %) to afford the desired products **4**.



Synthetic Transformation for the product **4a** to **7**.

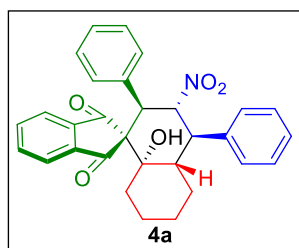
To a solution of **4a** (30mg, 0.06 mmol) with NaBH_4 (10mg, 0.24mmol) and $\text{NiCl}_2 \cdot \text{H}_2\text{O}$ (23mg, 0.18 mmol) in 1,4-dioxane and water (2:1) at 0°C to room temperature for 2 hours. The reaction was monitored by using TLC till the completion of starting materials. After the completion of the reaction, the organic layer was extracted with dichloromethane, washed with brine solution and dried over Na_2SO_4 , and concentrated under reduced pressure crude was subjected to flash column chromatography on silica gel by eluting ethyl acetate in hexane (12-15 %) to afford the desired product **7**.



Compounds characterisation

(2'R,3'R,4'R,8a'S)-8a'-hydroxy-3'-nitro-2',4'-diphenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4a)

White solid; Yield: 75% (0.75mmol, 365 mg); mp 170-172 °C



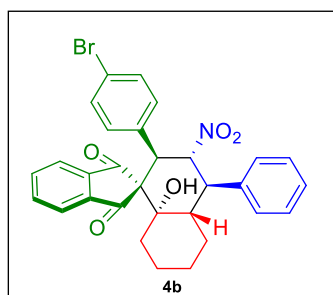
IR (neat, cm^{-1}) 3508, 2931, 1731, 1691, 1587, 1549, 1256, 1159, 774.

^1H NMR (400 MHz, CDCl_3); δ 7.88 (d, $J = 7.2$ Hz, 1H), 7.75 (d, $J = 6$ Hz, 2H), 7.68 (s, 2H), 7.49 (s, 1H), 7.07 (d, $J = 6$ Hz, 3H), 6.94 (d, $J = 7.6$ Hz, 4H), 6.03 (t, $J = 11.6$ Hz, 1H), 4.61 (d, $J = 12.4$ Hz, 1H), 3.72-3.64 (m, 2H), 2.63 (t, $J = 11.6$ Hz, 1H), 2.63 (t, $J = 11.6$ Hz, 1H), 1.65 (t, $J = 13.2$ Hz, 1H), 1.44 (dd, $J = 13.6, 11.6$ Hz, 1H), 1.33-1.15 (m, 3H), 1.08-1.01 (m, 3H).

^{13}C NMR (100MHz, CDCl_3); δ 204.8, 201.9, 143.4, 142.0, 138.7, 136.5, 136.1, 133.4, 131.0, 129.3, 128.7, 128.5, 128.3, 127.8, 125.5, 122.9, 122.8, 91.4, 74.6, 65.0, 49.0, 47.3, 43.0, 36.6, 25.3, 25.2, 20.9.

HRMS calcd. $\text{C}_{30}\text{H}_{26}\text{O}_5\text{N}$, 480.1811; found 480.1815 [M - H]

(2'R,3'R,4'R,8a'S)-2'-(4-bromophenyl)-8a'-hydroxy-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4b)



white solid; Yield: 70% (0.69mmol, 390 mg); mp 160-162 °C

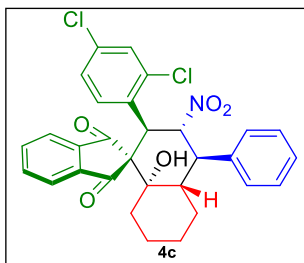
IR (neat, cm^{-1}) 3517, 2925, 1725, 1686, 1589, 1548, 1489, 1368, 1350, 1271, 1250, 1141, 771, 756, 700.

^1H NMR (400 MHz, CDCl_3); δ 7.91 (d, $J = 7.2$ Hz, 1H), 7.82-7.71 (m, 4H), 7.5-7.47 (m, 1H), 7.32-7.26 (m, 2H), 7.11-7.05 (m, 3H), 6.93 (d, $J = 8.4$ Hz, 2H), 5.91 (t, $J = 11.6$ Hz, 1H), 4.59 (d, $J = 12$ Hz, 1H), 3.64 (t, $J = 11.6$ Hz, 1H), 3.57 (s, 1H), 2.61-2.58 (m, 1H), 1.70-1.60 (m, 1H), 1.54-1.48 (m, 1H), 1.44-1.19 (m, 3H), 1.09-0.95 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.4, 201.7, 143.3, 141.9, 138.5, 136.8, 136.5, 132.7, 131.8, 131.0, 129.4, 129.0, 128.7, 128.3, 127.9, 125.5, 123.1, 123.0, 122.5, 91.3, 77.4, 74.7, 65.0, 48.9, 46.7, 43.0, 36.8, 25.2, 20.9.

HRMS calcd. $\text{C}_{30}\text{H}_{24}\text{O}_5\text{NBr}$, 558.0916; found 558.0910 [M - H]

2'-(2,4-dichlorophenyl)-8a'-hydroxy-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4c):



White solid; Yield: 60% (0.61mmol, 338 mg); mp 220-222 °C

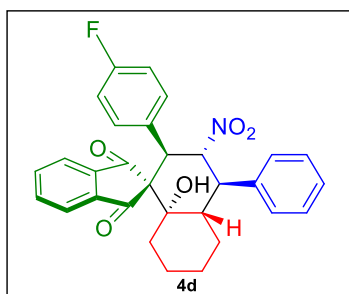
IR (neat, cm^{-1}) 3525, 2937, 1941, 1730, 1589, 1549, 1495, 1475, 1271, 1197, 1137, 1107, 1057, 941, 832, 762, 700, 692, 664, 619.

^1H NMR (400 MHz, CDCl_3); δ 7.98 (d, $J = 7.2$ Hz, 1H), 7.85-7.71 (m, 4H), 7.52-7.48 (m, 1H), 7.30-7.28 (m, 1H), 7.17 (d, $J = 2.4$ Hz, 1H), 7.10-7.06 (m, 2H), 6.80 (dd, $J = 2, 2.4$ Hz, 1H), 5.88 (t, $J = 11.6$ Hz, 1H), 5.47 (d, $J = 12$ Hz, 1H), 3.76-3.66 (m, 2H), 2.64-2.59 (m, 1H), 1.70-1.60 (m, 1H), 1.53-1.41 (m, 2H), 1.34-1.22 (m, 3H), 1.08-0.98 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 202.7, 202.4, 143.4, 141.9, 138.4, 136.8, 136.7, 136.2, 134.7, 131.0, 130.6, 130.3, 129.4, 129.1, 128.8, 127.9, 127.2, 125.4, 123.3, 123.1, 91.9, 77.4, 75.0, 64.3, 49.1, 43.2, 41.6, 36.3, 25.3, 25.2, 20.9

HRMS calcd. $\text{C}_{30}\text{H}_{24}\text{O}_5\text{NCl}_2$, 548.1032; found 548.1036 [M - H]

2'-(4-fluorophenyl)-8a'-hydroxy-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4d):



White solid; Yield: 38% (0.37mmol, 193 mg); mp 124-126 °C

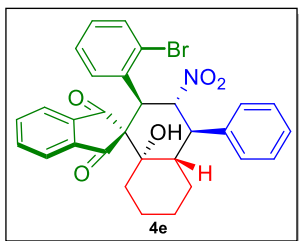
IR (neat, cm^{-1}) 3618, 2954, 1693, 1547, 1508, 1491, 1448, 1349, 1062, 765, 640.

^1H NMR (400 MHz, CDCl_3); δ 7.90 (d, $J = 7.6$ Hz, 1H), 7.80-7.71 (m, 2H), 7.49 (t, $J = 7.6$ Hz, 1H), 7.34-7.02 (m, 6H), 6.66 (t, $J = 8.4$ Hz, 1H), 5.99 (t, $J = 11.6$ Hz, 1H), 4.94 (dd, $J = 4.8, 4.4$ Hz, 1H), 4.66-4.58 (m, 1H), 3.79-3.62 (m, 2H), 2.71-2.35 (m, 3H), 2.11-2.05 (m, 1H), 1.80-1.60 (m, 3H), 1.55-0.88 (m, 2H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.6, 201.8, 138.6, 137.8, 136.7, 136.4, 131.0, 129.4, 129.0, 128.3, 127.9, 123.0, 122.9, 115.7, 115.5, 91.5, 79.0, 74.6, 65.1, 52.6, 48.9, 46.2, 44.0, 43.0, 42.8, 36.7, 33.3, 28.6, 25.1, 20.9.

HRMS calcd. $\text{C}_{30}\text{H}_{24}\text{O}_5\text{NF}$, 498.1717; found 498.1711 [M - H]

2'-(4-bromophenyl)-8a'-hydroxy-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4e):



White solid; Yield: 31% (0.30mmol, 180 mg); mp 162-164 °C

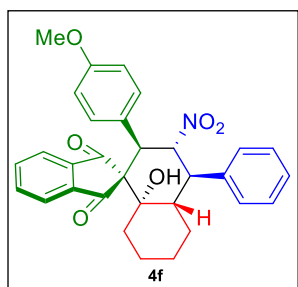
IR (neat, cm^{-1}) 3546, 2938, 2854, 1727, 1693, 1550, 1262, 1035, 711, 630.

^1H NMR (400 MHz, CDCl_3); δ 7.95-7.93 (m, 1H) 7.82-7.71 (m, 4H), 7.50 (t, $J = 7.2$ Hz, 1H), 7.30-7.24 (m, 2H), 7.06 (d, $J = 6.8$ Hz, 1H), 6.84 (d, $J = 5.2$ Hz, 1H), 6.73 (d, $J = 2.8$ Hz, 1H), 6.58-6.56 (m, 1H), 5.92 (t, $J = 11.6$ Hz, 1H), 4.92 (d, $J = 12$ Hz, 1H), 3.66-3.58 (m, 2H), 1.67-1.60 (m, 1H), 1.47-1.37 (m, 1H), 1.31 (d, $J = 13.2$ Hz, 1H), 1.24 (d, $J = 13.2$ Hz, 2H), 1.07-0.98 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.6, 201.7, 143.7, 142.1, 138.5, 136.6, 136.2, 135.6, 131.0, 129.4, 128.7, 128.1, 127.8, 126.6, 125.5, 123.1, 123.0, 93.0, 74.6, 65.3, 49.1, 42.9, 42.8, 36.9, 25.2, 20.9,

HRMS calcd. $\text{C}_{30}\text{H}_{24}\text{O}_5\text{NBr}$, 558.0916; found 558.0911 [M-H]

8a'-hydroxy-2'-(4-methoxyphenyl)-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4f):



White solid; Yield: 30% (0.36mmol, 160 mg); mp 200-202 °C

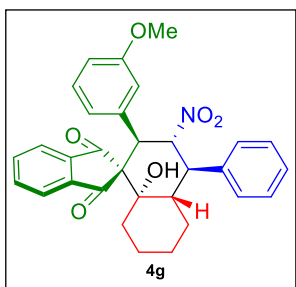
IR (neat, cm^{-1}) 3620, 3060, 1725, 1680, 1580, 1456, 1195, 1260, 780, 630

^1H NMR (400 MHz, CDCl_3); δ 7.90 (d, $J = 7.2$ Hz, 1H) 7.75-7.71 (m, 5H), 7.49 (s, 1H), 7.07-6.94 (m, 3H), 6.48 (d, $J = 7.6$ Hz, 2H), 5.98 (t, $J = 11.6$ Hz, 1H), 4.55 (d, $J = 12$ Hz, 1H), 3.67-3.62 (m, 2H), 3.56 (s, 3H), 2.60 (t, $J = 11.2$ Hz, 1H), 1.67-1.64 (m, 1H), 1.48-1.38 (m, 4H), 1.05-0.95 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3); δ 205.0, 202.1, 159.2, 143.5, 142.1, 138.8, 136.5, 136.2, 131.0, 129.3, 128.7, 127.7, 125.5, 125.4, 123.0, 122.9, 113.9, 91.8, 77.4, 74.6, 65.3, 55.1, 49.0, 46.6, 43.0, 36.7, 29.8, 26.8, 25.3, 25.2, 20.9.

HRMS calcd. $\text{C}_{31}\text{H}_{28}\text{O}_6\text{N}$, 510.1917; found 510.1912[M-H]

8a'-hydroxy-2'-(3-methoxyphenyl)-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4g):



white solid; Yield: 60% (0.56mmol, 295 mg); mp 198-200 °C

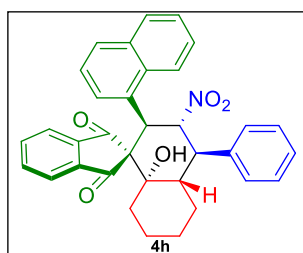
IR (neat, cm^{-1}) 3621, 3059, 2935, 1726, 1689, 1546, 1491, 1264, 1047, 988, 780, 701, 630.

^1H NMR (400 MHz, CDCl_3); δ 7.89 (d, $J = 8$ Hz, 1H), 7.77-7.66 (m, 4H), 7.49 (t, $J = 6.8$ Hz, 1H), 7.30-7.22 (m, 2H), 7.07 (d, $J = 6.8$ Hz, 1H), 6.85 (t, $J = 8$ Hz, 1H), 6.60 (d, $J = 7.2$ Hz, 1H), 6.45 (dd, $J = 2, 2$ Hz, 1H), 6.00 (t, $J = 11.6$ Hz, 1H), 4.58 (d, $J = 12$ Hz, 1H), 3.73-3.46 (m, 5H), 2.66-2.60 (m, 1H), 1.69-1.61 (m, 1H), 1.54-1.27 (m, 4H), 1.07-0.97 (m, 3H), 0.94-0.85 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.8, 201.9, 159.3, 143.5, 142.0, 138.7, 136.5, 136.1, 134.9, 131.0, 129.6, 129.3, 128.7, 127.8, 125.6, 122.9, 114.2, 91.4, 77.4, 74.6, 64.9, 55.2, 49.1, 47.4, 43.0, 36.6, 31.7, 25.3, 25.2, 22.7, 20.9, 14.2.

HRMS calcd. $\text{C}_{31}\text{H}_{28}\text{O}_6\text{N}$, 510.1917; found 510.1911[M-H]

8a'-hydroxy-2'-(naphthalen-1-yl)-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4h):



yellow solid; Yield; 51% (0.54mmol, 272 mg); mp 200-202°C

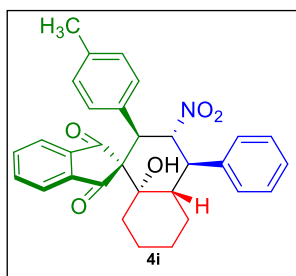
IR (neat, cm^{-1}) 3485, 2931, 2855, 1725, 1690, 1549, 1352, 1266, 1060, 982, 777, 702, 637.

^1H NMR (400 MHz, CDCl_3); δ 8.31 (d, $J = 8.8$ Hz, 1H), 7.92 (d, $J = 8.0$ Hz, 1H), 7.81 (d, $J = 6.8$ Hz, 1H), 7.71 (t, $J = 6.8$ Hz, 1H), 7.61-7.49 (m, 4H), 7.43-7.28 (m, 4H), 7.00 (t, $J = 8$ Hz, 2H), 6.14 (t, $J = 11.6$ Hz, 1H), 5.30 (s, 1H), 3.91 (s, 1H), 3.79 (t, $J = 11.6$ Hz, 1H), 2.77 (t, $J = 11.6$ Hz, 1H), 1.73-1.69 (m, 1H), 1.61-1.47 (m, 1H), 1.35-1.24 (m, 4H), 1.14-1.05 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.4, 202.5, 143.7, 141.8, 138.8, 136.4, 136.0, 135.3, 134.0, 131.7, 131.0, 130.0, 129.4, 129.0, 128.7, 128.4, 127.8, 126.7, 126.5, 125.9, 125.8, 125.6, 125.3, 124.5, 123.7, 123.0, 122.8, 122.8, 92.6, 75.2, 64.9, 49.7, 43.2, 40.1, 36.3, 25.4, 25.3, 21.0.

HRMS calcd. $\text{C}_{34}\text{H}_{28}\text{NO}_5$, 530.1968; found 530.1962 [M-H]

8a'-hydroxy-3'-nitro-4'-phenyl-2'-(p-tolyl)-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4i):



White solid; Yield: 50% (0.59mmol, 254 mg); mp 218-220 °C

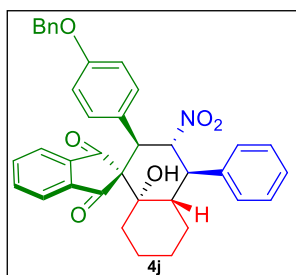
IR (neat, cm^{-1}) 3517, 2950, 2851, 1729, 1692, 1593, 1549, 1256, 1139, 1041, 990, 754, 705, 628.

^1H NMR (400 MHz, CDCl_3); δ 7.89 (d, $J = 7.2$ Hz, 1H), 7.7-7.6 (m, 4H), 7.52-7.47 (m, 1H), 7.29-7.22 (m, 2H), 7.06 (d, $J = 6.8$ Hz, 1H), 6.90 (d, $J = 8.4$ Hz, 2H), 6.74 (d, $J = 8$ Hz, 2H), 6.00 (t, $J = 11.6$ Hz, 1H), 4.56 (d, $J = 12$ Hz, 1H), 3.70-3.62 (m, 2H), 2.64-2.58 (m, 1H), 2.02 (s, 3H), 1.69-1.61 (m, 1H), 1.57-1.20 (m, 4H), 1.07-0.99 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.9, 202.0, 143.5, 142.1, 138.8, 137.9, 136.5, 136.1, 131.0, 130.3, 129.3, 129.2, 128.7, 127.7, 125.6, 122.9, 122.9, 91.6, 77.4, 74.6, 65.1, 49.0, 47.0, 43.1, 36.7, 25.3, 25.2, 20.9, 20.9.

HRMS calcd. $\text{C}_{31}\text{H}_{27}\text{NO}_5$, 494.1968; found 494.1962 [M-H]

2'-(4-(benzyloxy)phenyl)-8a'-hydroxy-3'-nitro-4'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4j):



Yellow solid; Yield: 27% (0.27mmol, 160 mg); mp 192-194 °C

IR (neat, cm^{-1}) 3531, 2920, 2871, 1730, 1693, 1545, 1356, 1251, 1166, 1142, 1031, 765, 631.

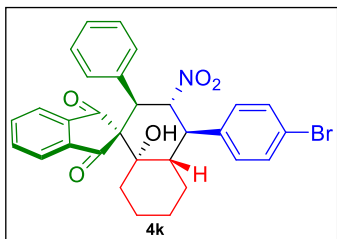
^1H NMR (400 MHz, CDCl_3); δ 7.89 (d, $J = 7.6$ Hz, 1H), 7.78-7.69 (m, 4H), 7.52-7.47 (m, 1H), 7.35-7.26 (m, 8H), 7.08 (d, $J = 8.4$ Hz, 1H), 6.95 (d, $J = 8.4$ Hz, 2H), 5.99 (t, $J = 11.6$ Hz, 1H), 4.79 (s, 2H), 4.55 (d, $J = 12$ Hz, 1H), 3.68-3.62 (m, 2H), 2.64-2.58 (m, 1H), 1.68 (m, 1H), 1.48-1.38 (m, 2H), 1.32-1.20 (m, 3H), 1.07-0.99 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 205.0, 202.1, 158.5, 143.5, 142.1, 138.8, 136.6, 136.5, 136.1, 131.0, 129.3, 128.7, 128.6, 128.0, 127.7, 127.5, 125.7, 125.5, 123.0, 122.9, 114.9, 91.7, 74.6, 69.8, 65.3, 49.0, 46.7, 43.0, 36.7, 25.3, 25.2, 20.9

HRMS calcd. $\text{C}_{37}\text{H}_{33}\text{NO}_6$, 605.2414; found 605.2637 [M + H_2O]

**4'--(4-bromophenyl)-8a'-hydroxy-3'-nitro-2'-phenyl
3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-
1,3-dione (4k)**

White solid; Yield: 72% (0.73mmol, 410 mg); mp 190-192 °C



IR (neat, cm^{-1}) 3501, 2937, 2851, 1731, 1691, 1547, 1250, 1072, 989, 771, 699, 633.

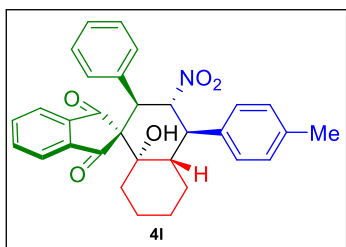
^1H NMR (400 MHz, CDCl_3); δ 7.88 (d, $J = 7.6$ Hz, 1H), 7.76-7.62 (m, 5H), 7.38 (d, $J = 8$ Hz, 1H), 7.0-6.94 (m, 5H), 5.99 (t, $J = 11.6$ Hz, 1H), 4.58 (d, $J = 12$ Hz, 1H), 3.71-3.62 (m, 2H), 2.61-2.55 (m, 1H), 1.71-1.54 (m, 2H), 1.48-1.22 (m, 3H), 1.11-0.97 (m, 3H).

^{13}C NMR (100MHz, CDCl_3); δ 204.6, 201.1, 143.4, 142.0, 137.8, 136.6, 136.2, 133.2, 132.6, 131.8, 138.6, 138.4, 137.4, 133.0, 122.9, 121.7, 91.1, 74.5, 64.9, 48.5, 47.3, 43.0, 36.6, 29.8, 25.2, 25.2, 20.9

HRMS calcd. $\text{C}_{30}\text{H}_{24}\text{NBrO}_5$, 558.0916; found 558.0910 [M -H]

**8a'-hydroxy-3'-nitro-2'-phenyl-4'-(p-tolyl)-3',4',4a',5',6',7',8',8a'-
octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4l)**

White solid; Yield; 57% (0.58mmol, 290 mg); mp 190-192 °C



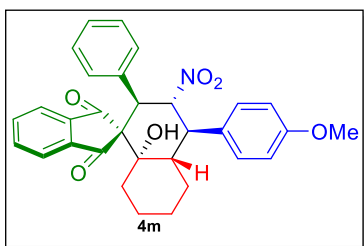
IR (neat, cm^{-1}) 3609, 2933, 2857, 1730, 1693, 1549, 1367, 1351, 1256, 990, 817, 763, 699, 632, 615.

^1H NMR (400 MHz, CDCl_3); δ 7.88 (d, $J = 7.2$ Hz, 1H), 7.76-7.61 (m, 4H), 7.31-7.29 (m, 1H), 7.05-6.91 (m, 7H), 6.02 (t, $J = 11.6$ Hz, 1H), 4.59 (d, $J = 12$ Hz, 1H), 3.71-3.59 (m, 2H), 2.60 (m, 1H), 2.33-2.31 (m, 3H), 1.68-1.65 (m, 1H), 1.44-1.40 (m, 1H), 1.32-1.21 (m, 3H), 1.10-1.00 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.9, 201.9, 143.4, 142.0, 137.3, 136.5, 136.1, 136.6, 132.2, 129.3, 128.5, 128.3, 125.3, 122.9, 122.8, 91.5, 74.7, 65.1, 48.6, 47.4, 43.1, 36.1, 25.3, 25.2, 21.3, 21.0

HRMS calcd. $\text{C}_{31}\text{H}_{27}\text{NO}_5$, 494.1968; found 494.1962 [M -H]

8a'-hydroxy-4'-(4-methoxyphenyl)-3'-nitro-2'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4m):



white solid; Yield; 47% (0.47mmol, 245 mg);-mp 198-200°C

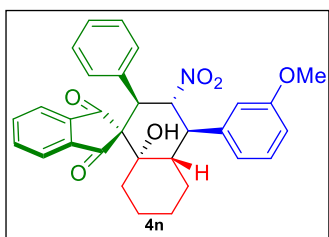
IR (neat, cm^{-1}) 3516, 2931, 2849, 1734, 1693, 1545, 1511, 1454, 1250, 1181, 988, 765, 696.

^1H NMR (400 MHz, CDCl_3); δ 7.88 (d, $J = 7.6$ Hz, 1H), 7.76-7.63 (m, 3H), 7.05-6.89 (m, 7H), 6.76 (d, $J = 8$ Hz, 1H), 6.99 (t, $J = 11.2$ Hz, 1H), 4.59 (d, $J = 12$ Hz, 1H), 3.82-3.76 (m, 3H), 3.70 (d, $J = 1.6$ Hz, 1H), 3.63 (t, $J = 11.6$ Hz, 1H), 2.59 (t, $J = 11.4$ Hz, 1H), 1.69-1.64 (m, 1H), 1.44-1.37 (m, 1H), 1.33-1.21 (m, 4H), 1.11-1.01 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.9, 201.9, 159.1, 143.4, 142.0, 136.5, 136.1, 133.5, 131.9, 130.6, 128.5, 128.3, 126.5, 122.9, 122.8, 115.5, 113.2, 91.5, 80.3, 74.7, 65.1, 55.3, 48.2, 47.4, 43.2, 36.6, 31.7, 25.3, 25.2, 22.8, 21.0, 14.2.

HRMS calcd. $\text{C}_{31}\text{H}_{29}\text{NO}_6$, 510.1917; found 510.1917 [M - H]

8a'-hydroxy-4'-(3-methoxyphenyl)-3'-nitro-2'-phenyl-3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione (4n):



White solid; Yield; 35% (0.35mmol, 180 mg);-mp 192-194 °C

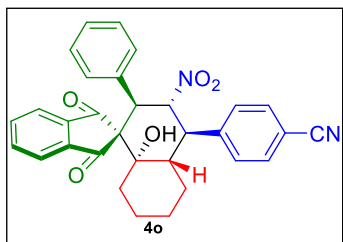
IR (neat, cm^{-1}) 3690, 2937, 2857, 1730, 1693, 1548, 1352, 1253, 1044, 988, 701, 634.

^1H NMR (400 MHz, CDCl_3); δ 7.88 (d, $J = 7.2$ Hz, 1H), 7.76-7.64 (m, 3H), 7.33 (m, $J = 7.6$, 1H), 7.01-6.79 (m, 6H), 6.68 (d, $J = 7.2$, 1H), 6.02 (dd, $J = 12, 11.6$ Hz, 1H), 4.59 (d, $J = 12$ Hz, 1H), 3.92 (s, 1H), 3.79-3.58 (m, 4H), 2.62 (t, $J = 11.6$ Hz, 1H), 1.72-1.62 (m, 1H), 1.49-1.40 (m, 1H), 1.33-1.21 (m, 3H), 1.12-1.00 (m, 3H), 0.88 (t, $J = 6.4$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3); δ 204.8, 201.8, 160.4, 159.9, 143.4, 142.0, 140.4, 136.5, 136.1, 133.4, 130.3, 129.6, 128.5, 128.3, 123.6, 122.9, 122.8, 117.7, 117.0, 113.0, 112.6, 111.4, 91.3, 91.2, 74.6, 65.0, 65.4, 65.2, 53.5, 49.3, 48.8, 47.4, 43.1, 36.6, 31.7, 35.3, 25.2, 20.9, 14.2

HRMS calcd. $\text{C}_{31}\text{H}_{29}\text{NO}_6$, 510.1917; found 510.1917 [M - H]

4-(8a'-hydroxy-3'-nitro-1,3-dioxo-2'-phenyl-1,3,3',4',4a',5',6',7',8',8a'-decahydro-2'H-spiro[indene-2,1'-naphthalen]-4'-yl) benzonitrile(4o):



white solid; Yield; 31% (0.31mmol, 160 mg); mp 210-212 °C

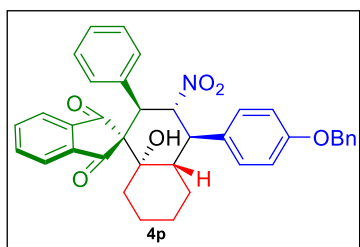
IR (neat, cm^{-1}) 3499, 2950, 2853, 2228, 1735, 1693, 1548, 1253, 1141, 990, 836, 772, 700, 632, 614.

$^1\text{H NMR}$ (400 MHz, CDCl_3); δ 7.89 (d, $J = 7.6$ Hz, 1H), 7.80-7.72 (m, 2H), 7.70-7.66 (m, 2H), 7.56 (d, $J = 7.2$ Hz, 1H), 7.20 (d, $J = 7.6$ Hz, 1H), 7.00-6.94 (m, 5H), 6.02 (t, $J = 11.6$ Hz, 1H), 4.60 (d, $J = 12.4$ Hz, 1H), 3.79-3.73 (m, 2H), 6.65 (t, $J = 11.6$ Hz, 1H), 1.69-1.61 (m, 1H), 1.52-1.41 (m, 1H), 1.35-1.25 (m, 4H), 1.07-0.95 (m, 3H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3); δ 204.4, 201.9, 144.5, 143.3, 142.0, 136.6, 136.3, 133.1, 132.9, 132.7, 131.7, 128.7, 128.7, 126.7, 123.0, 123.0, 118.7, 111.9, 90.8, 74.4, 64.8, 49.2, 47.2, 42.9, 36.5, 25.2, 25.1, 20.8

HRMS calcd. $\text{C}_{31}\text{H}_{26}\text{N}_2\text{O}_6$, 505.1764; found 505.1766 [M -H]

4'-(4-(benzyloxy)phenyl)-8a'-hydroxy-3'-nitro-2'-phenyl 3',4',4a',5',6',7',8',8a'-octahydro-2'H-spiro[indene-2,1'-naphthalene]-1,3-dione(4p):



White solid; Yield: 27% (0.40mmol, 160 mg); mp 188-190 °C

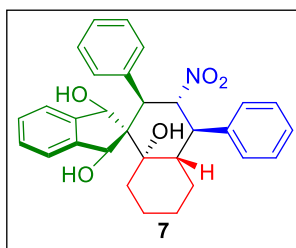
IR (neat, cm^{-1}) 3505, 2930, 2851, 1731, 1694, 1549, 1376, 1252, 1176, 1143, 1032, 767, 632.

$^1\text{H NMR}$ (400 MHz, CDCl_3); δ 7.89 (d, $J = 7.6$ Hz, 1H), 7.77-7.70 (m, 4H), 7.49 (t, $J = 6.8$ Hz, 1H), 7.33-7.24 (m, 5H), 7.07 (d, $J = 6.4$ Hz, 1H), 6.99-6.94 (m, 2H), 6.55 (t, $J = 8.4$ Hz, 2H), 5.99 (t, $J = 11.6$ Hz, 1H), 4.79 (s, 2H), 4.55 (d, $J = 12$ Hz, 1H), 3.68-3.62 (m, 1H), 2.62 (t, $J = 11.6$ Hz, 1H), 1.68-1.61 (m, 1H), 1.48-1.20 (m, 4H), 1.07-0.85 (m, 4H).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3); δ 205.0, 202.1, 158.5, 143.5, 142.1, 138.8, 136.6, 136.5, 136.1, 131.0, 129.3, 128.7, 128.6, 128.0, 127.7, 127.5, 125.7, 125.5, 123.0, 122.9, 114.9, 91.7, 74.6, 69.8, 65.3, 49.0, 46.7, 43.0, 36.7, 25.3, 25.2, 20.9

HRMS calcd. $\text{C}_{37}\text{H}_{33}\text{NO}_6$, 605.2414; found 605.2637 [M + H_2O]

3'-nitro-2',4'-diphenyl-1,2',3,3',4',4a',5',6',7',8'-decahydro-8a'H-spiro[indene-2,1'-naphthalene]-1,3,8a'-triol (7):



Yellow solid; Yield; 52% (0.03mmol, 17 mg); mp 168-170 °C

IR (neat, cm^{-1}) 3398, 3278, 2924, 2852, 1729, 1691, 1256, 1118, 871, 699, 612.

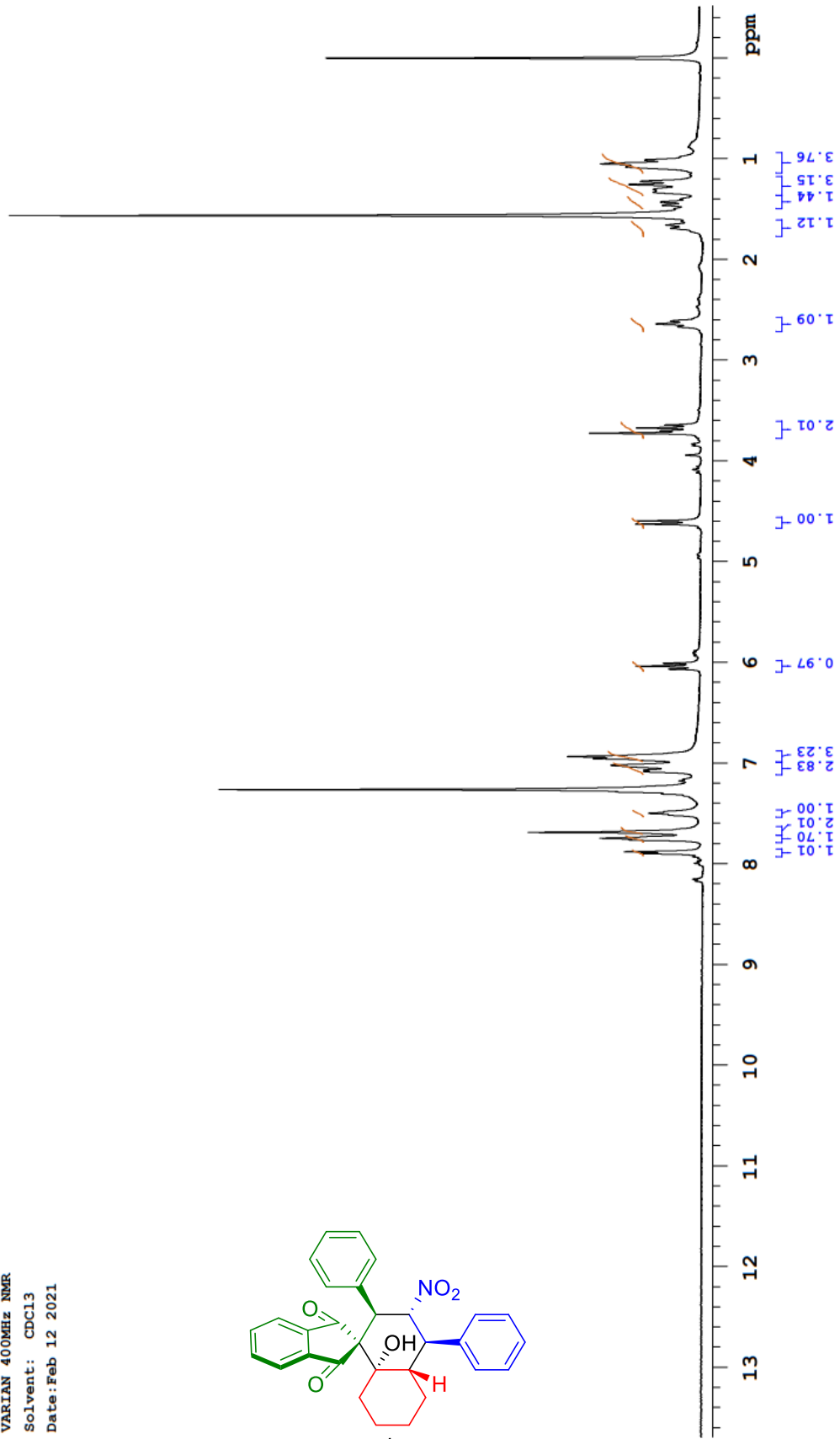
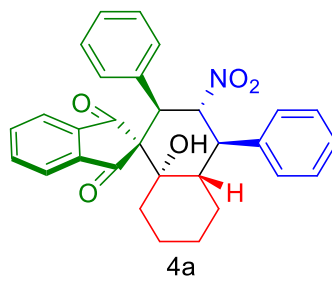
^1H NMR (400 MHz, CDCl_3); δ 16.95 (s, 1H), 7.51 (t, $J = 7.2$, 1H), 7.44-7.40 (m, 1H), 7.33-7.29 (m, 2H), 7.18-7.15 (m, 7H), 7.10-7.08 (m, 2H), 4.93 (d, $J = 8.8$, Hz, 1H), 4.10 (s, 1H), 3.76 (d, $J = 9.6$, 1H), 3.48 (d, $J = 5.2$ Hz, 1H), 3.18-3.14 (m, 1H), 2.36-2.32 (m, 1H), 2.19 (s, 1H), 1.90 (s, 1H), 1.76 (d, $J = 14$, Hz, 1H), 1.50 (s, 1H), 1.41-1.29 (m, 1H), 1.25-1.12 (m, 2H), 1.05-0.91 (m, 1H).

^{13}C NMR (CDCl_3 , 100 MHz); δ 157.68, 138.7, 134.8, 129.8, 129.0, 128.9, 128.5, 127.4, 127.2, 118.3, 109.5, 78.0, 49.8, 37.4, 30.7, 23.2, 23.0, 22.7

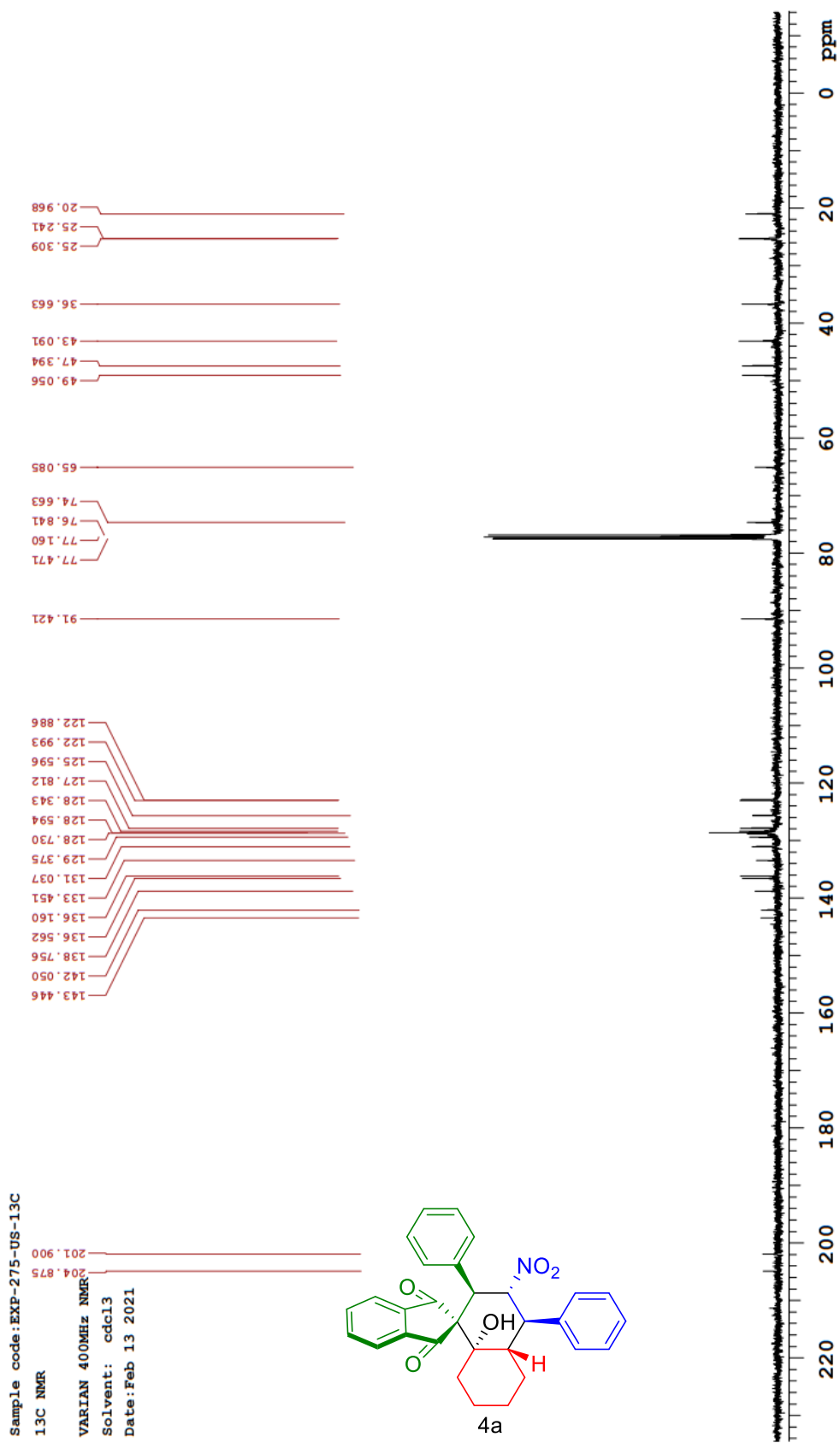
HRMS calcd. $\text{C}_{24}\text{H}_{16}\text{O}_4\text{Na}$, 484.2124; found 484.1663 [M-H]

Sample code: EXP-275-US

VARIAN 400MHz NMR
Solvent: CDCl3
Date: Feb 12 2021



¹H NMR of Compound 4a



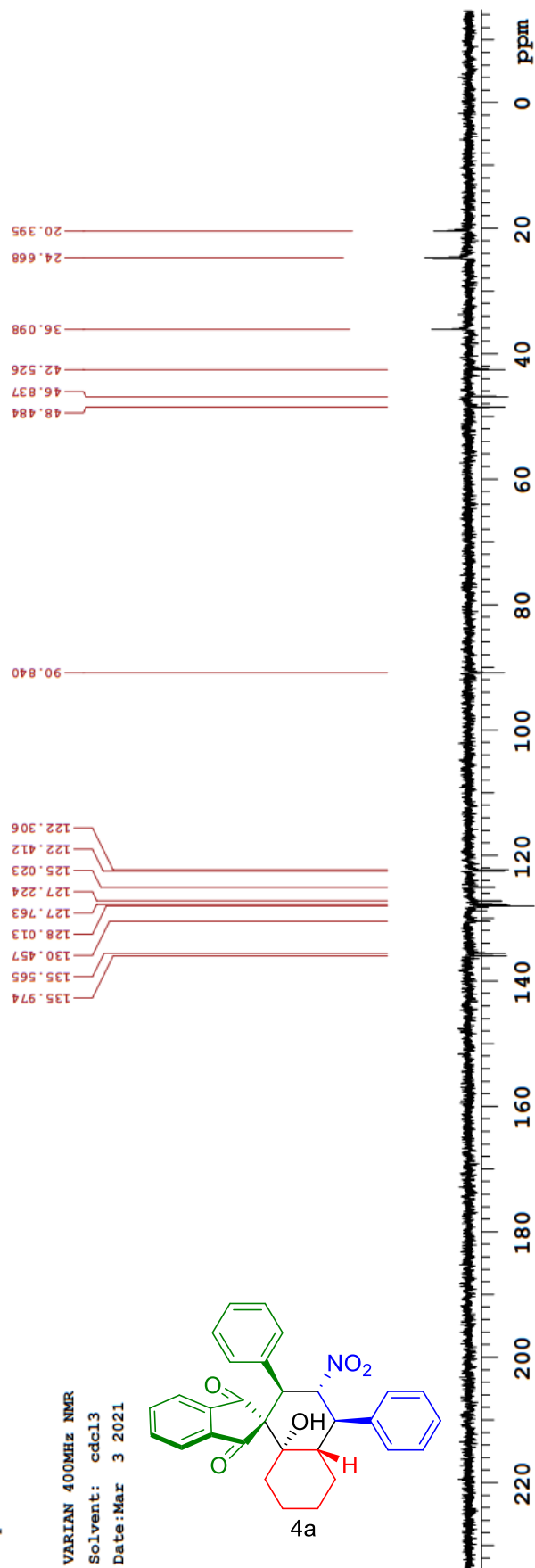
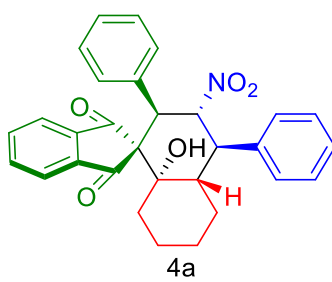
¹³C NMR of Compound 4a

Sample code: 275-US-DEPT135

VARIAN 400MHz NMR

Solvent: cdcl3

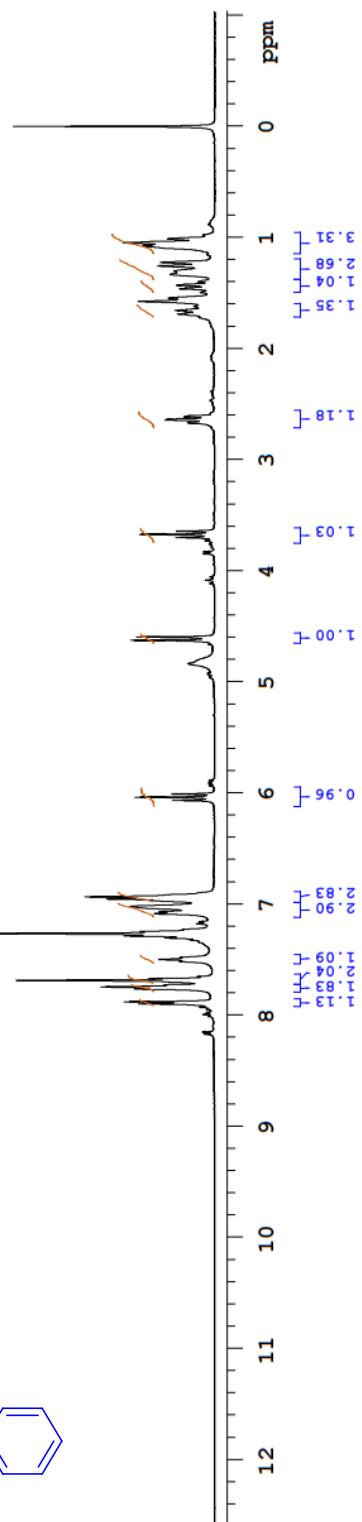
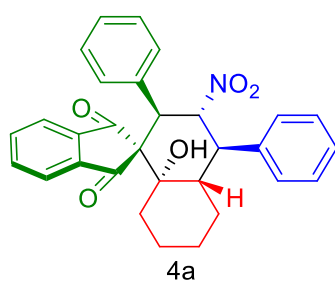
Date: Mar 3 2021



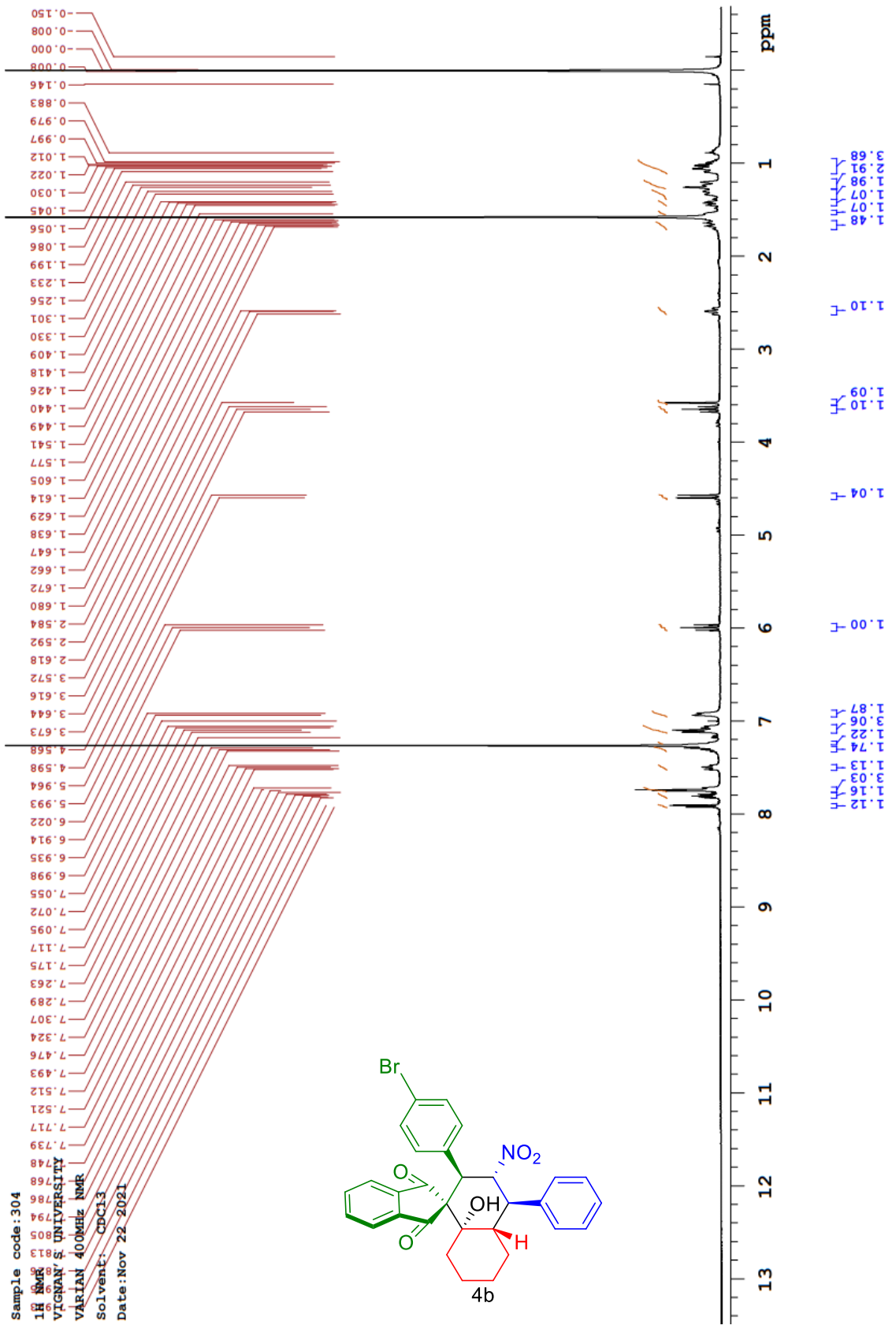
DEPT-135 NMR of Compound 4a

Sample code: EXP-P-275-US-D2O_Exch

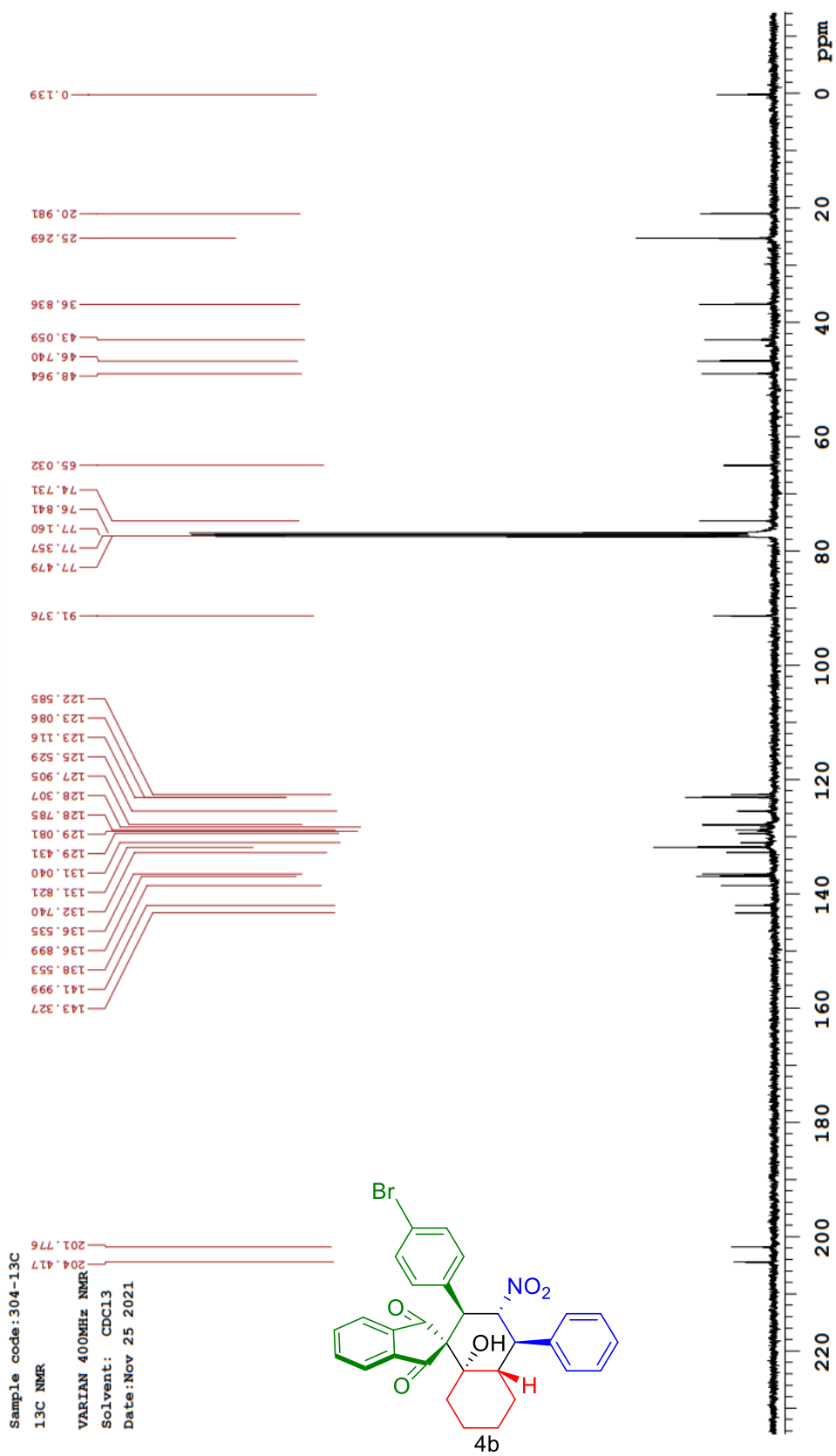
VARIAN 400MHz NMR
Solvent: CDCl3
Date: Feb 13 2021



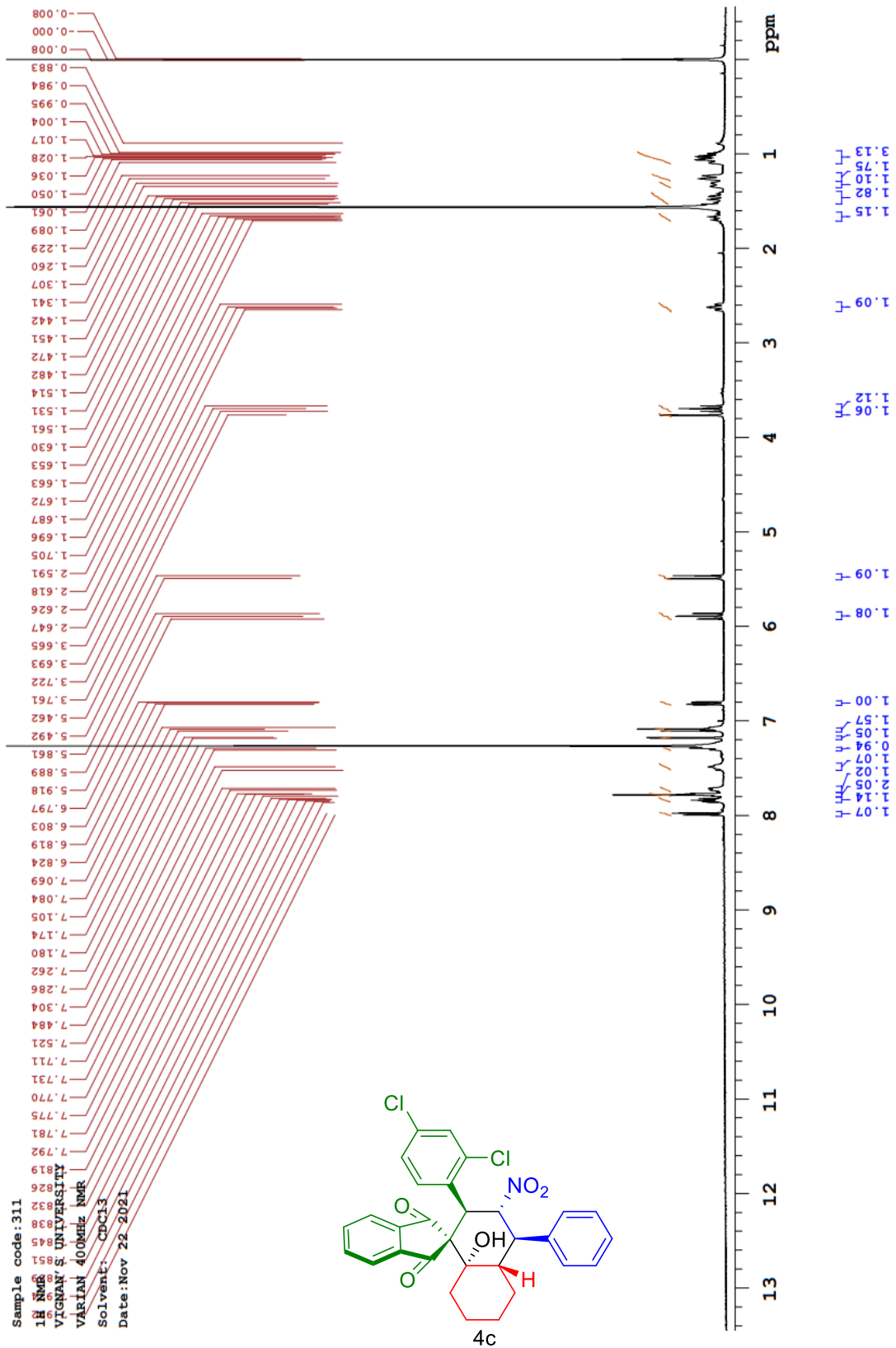
D₂O Exchange of compound **4a**



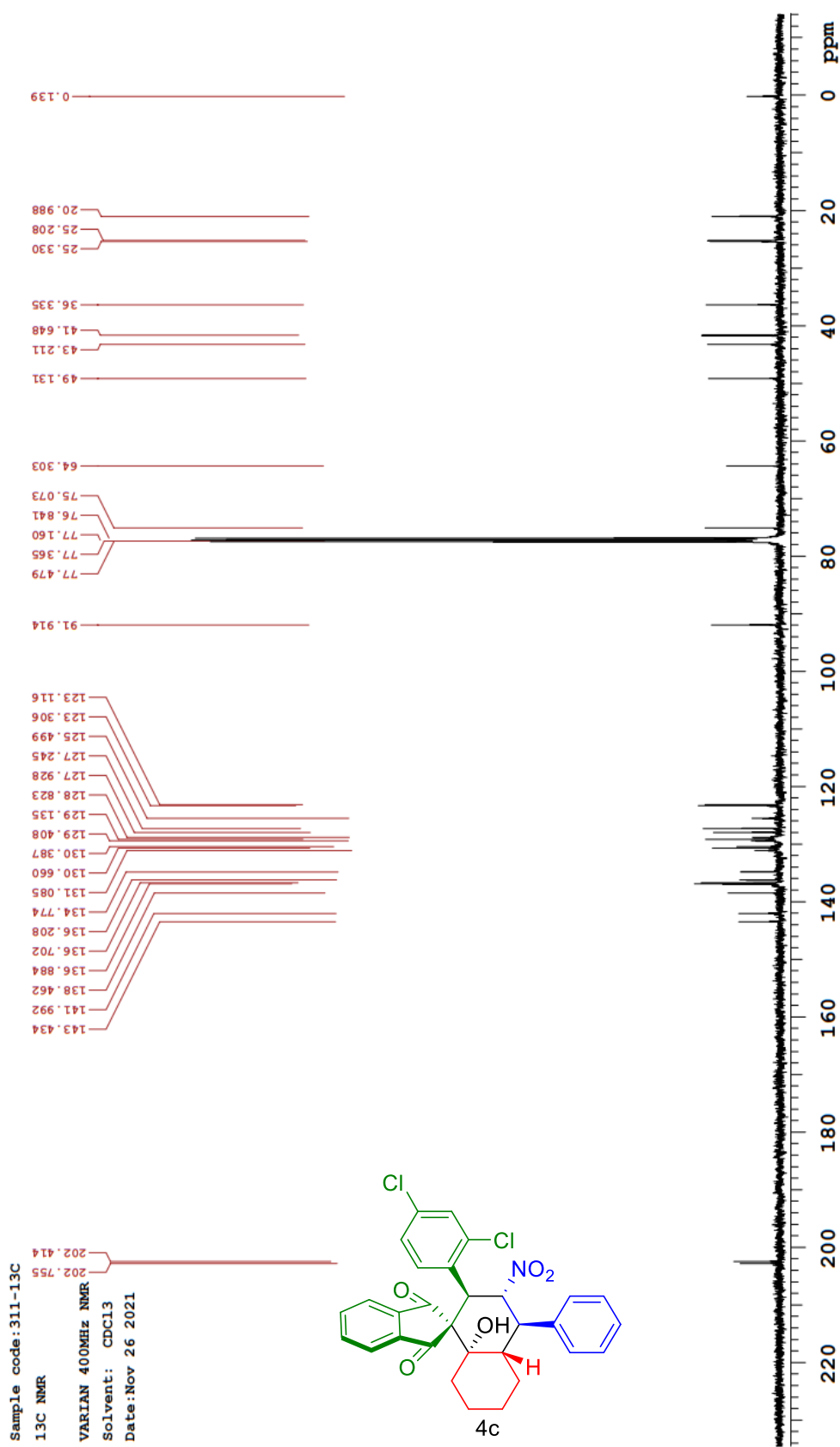
¹H NMR of Compound **4b**



^{13}C NMR of Compound **4b**



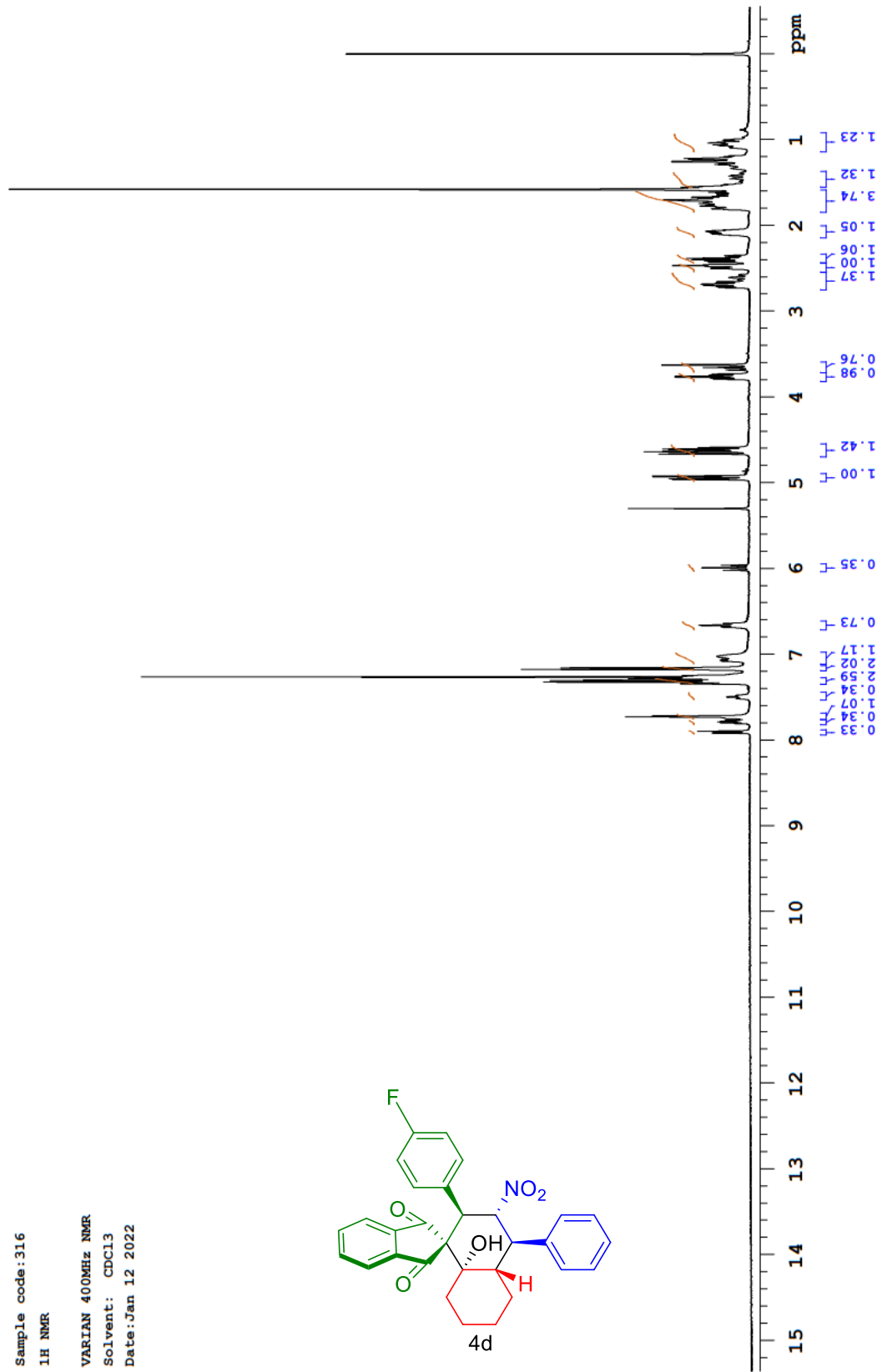
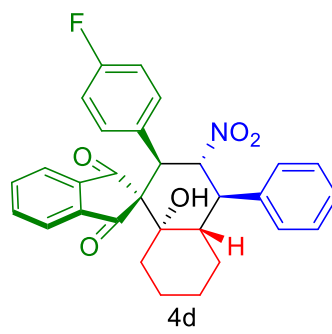
¹H NMR of Compound 4c



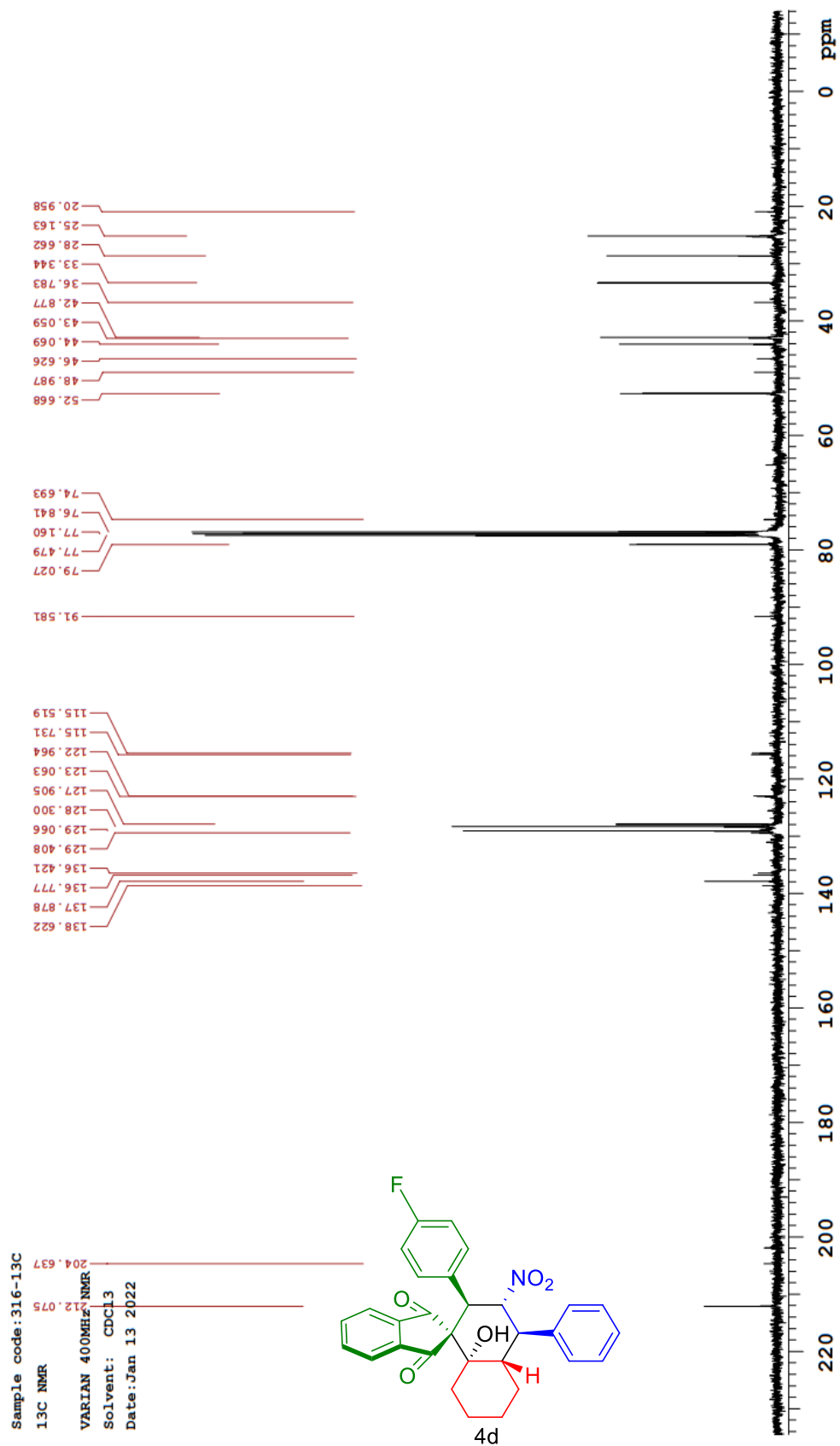
¹³C NMR of Compound 4c

Sample code:316
1H NMR

VARIAN 400MHz NMR
Solvent: CDCl3
Date:Jan 12 2022



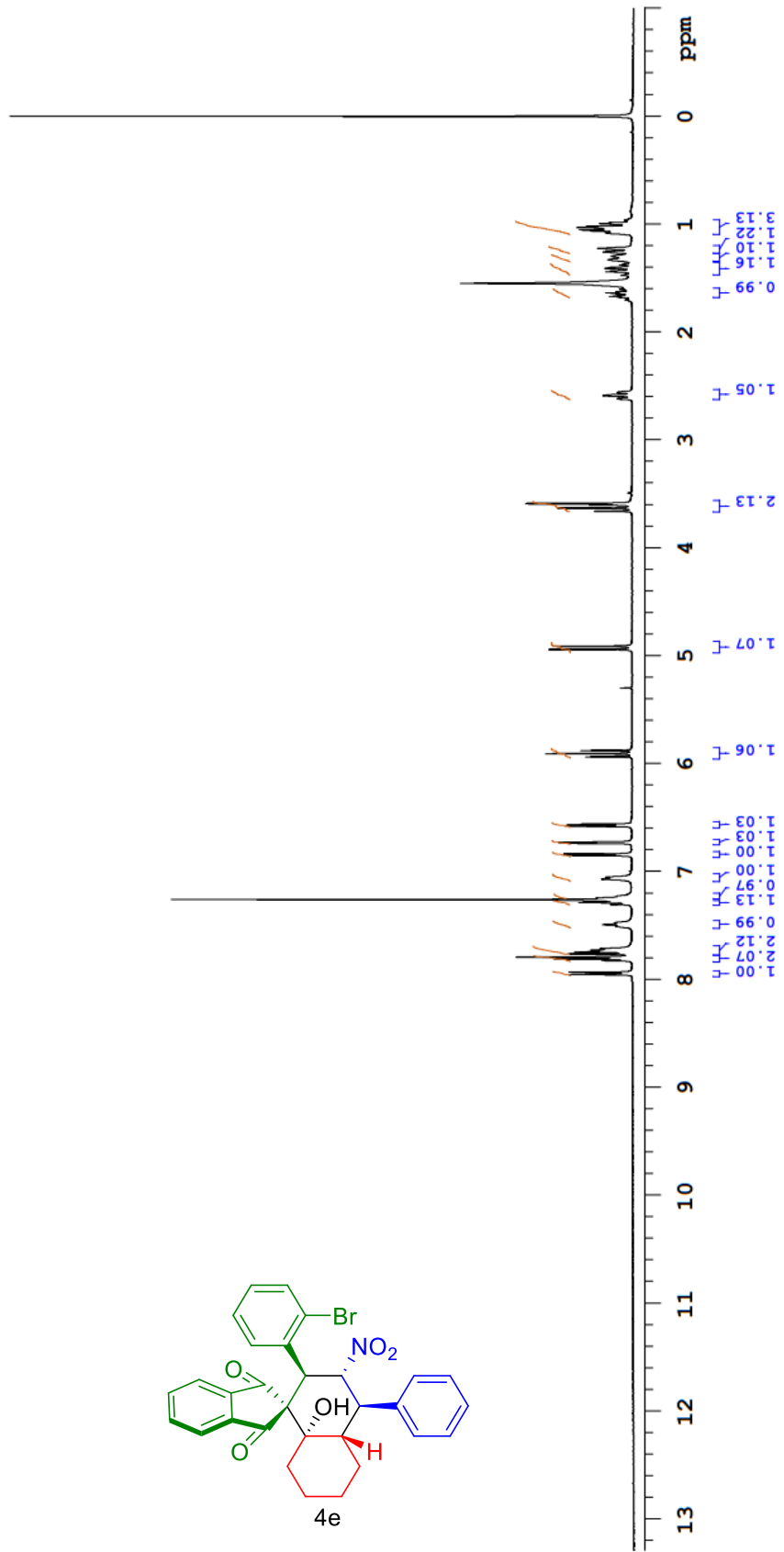
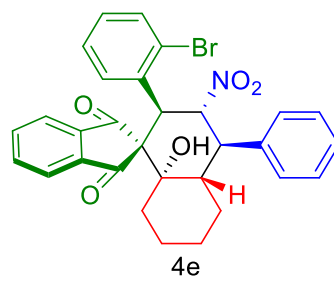
¹H NMR of Compound 4d



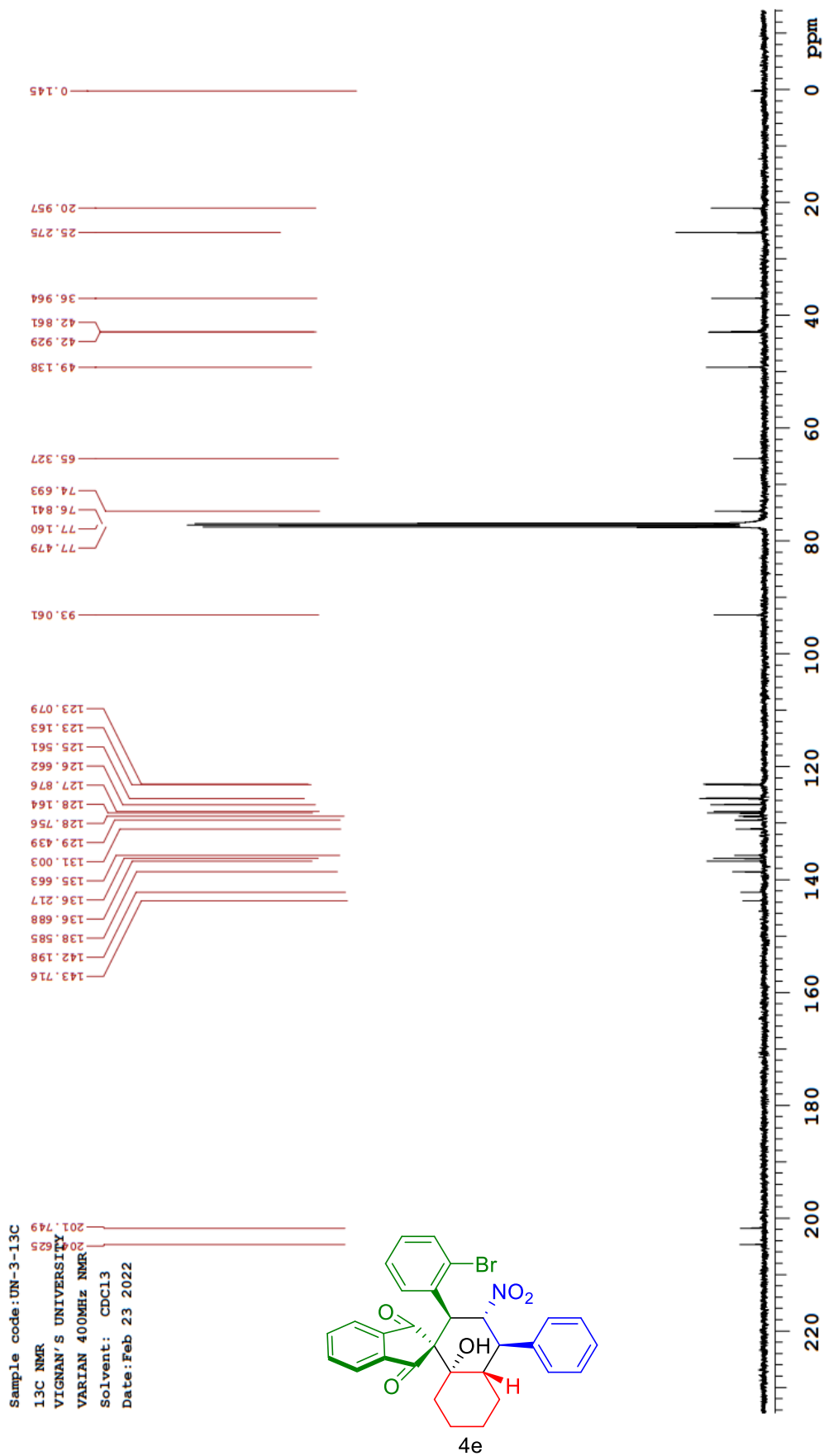
^{13}C NMR of Compound **4d**

Sample code: UN-3

VARIAN 400MHz NMR
Solvent: CDCl3
Date: Feb 8 2022

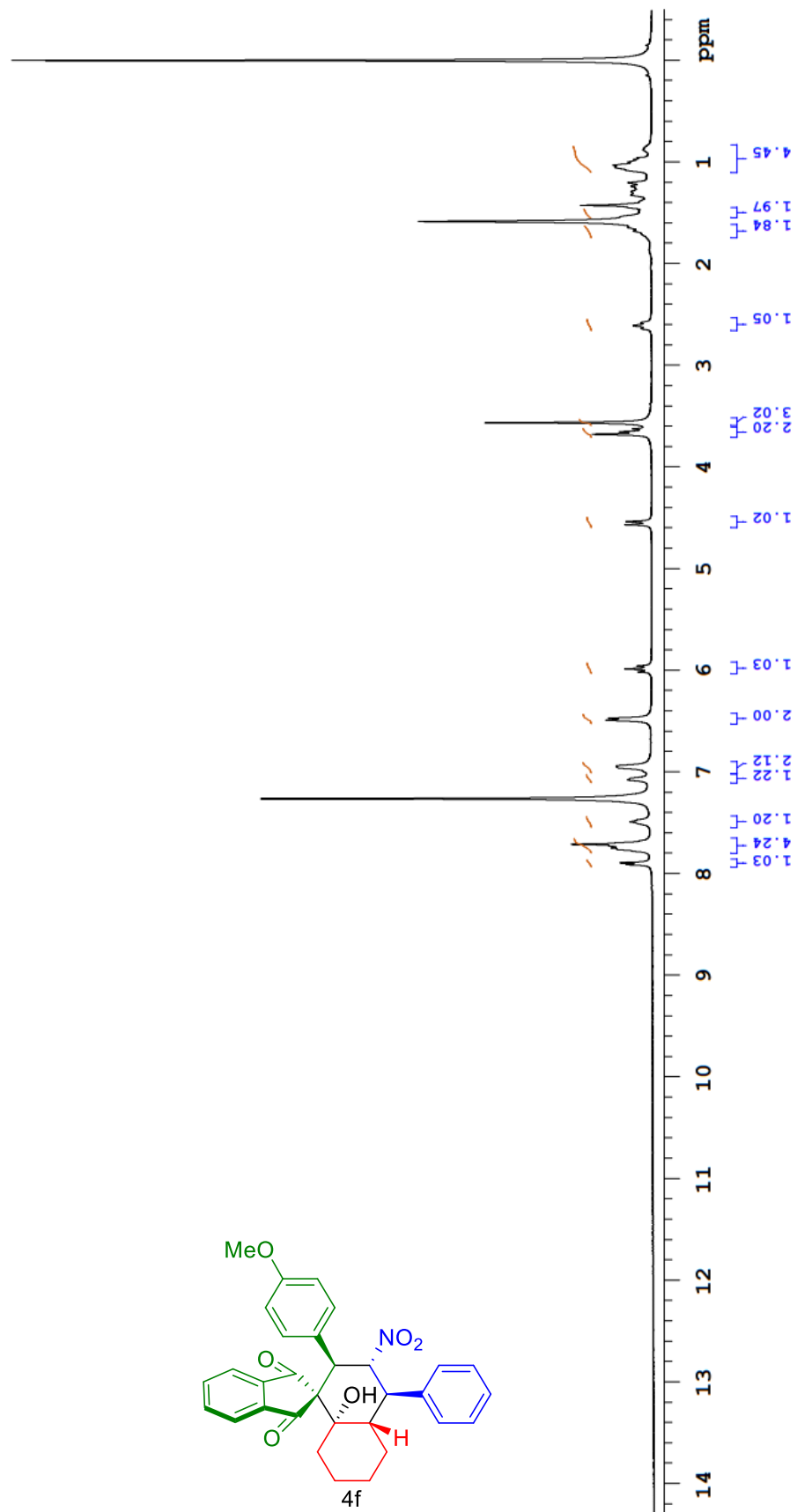
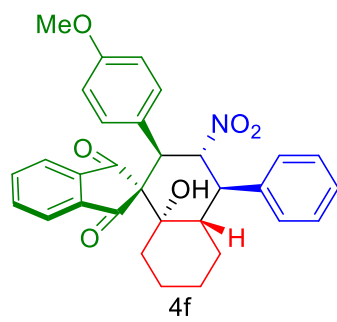


¹H NMR of Compound 4e

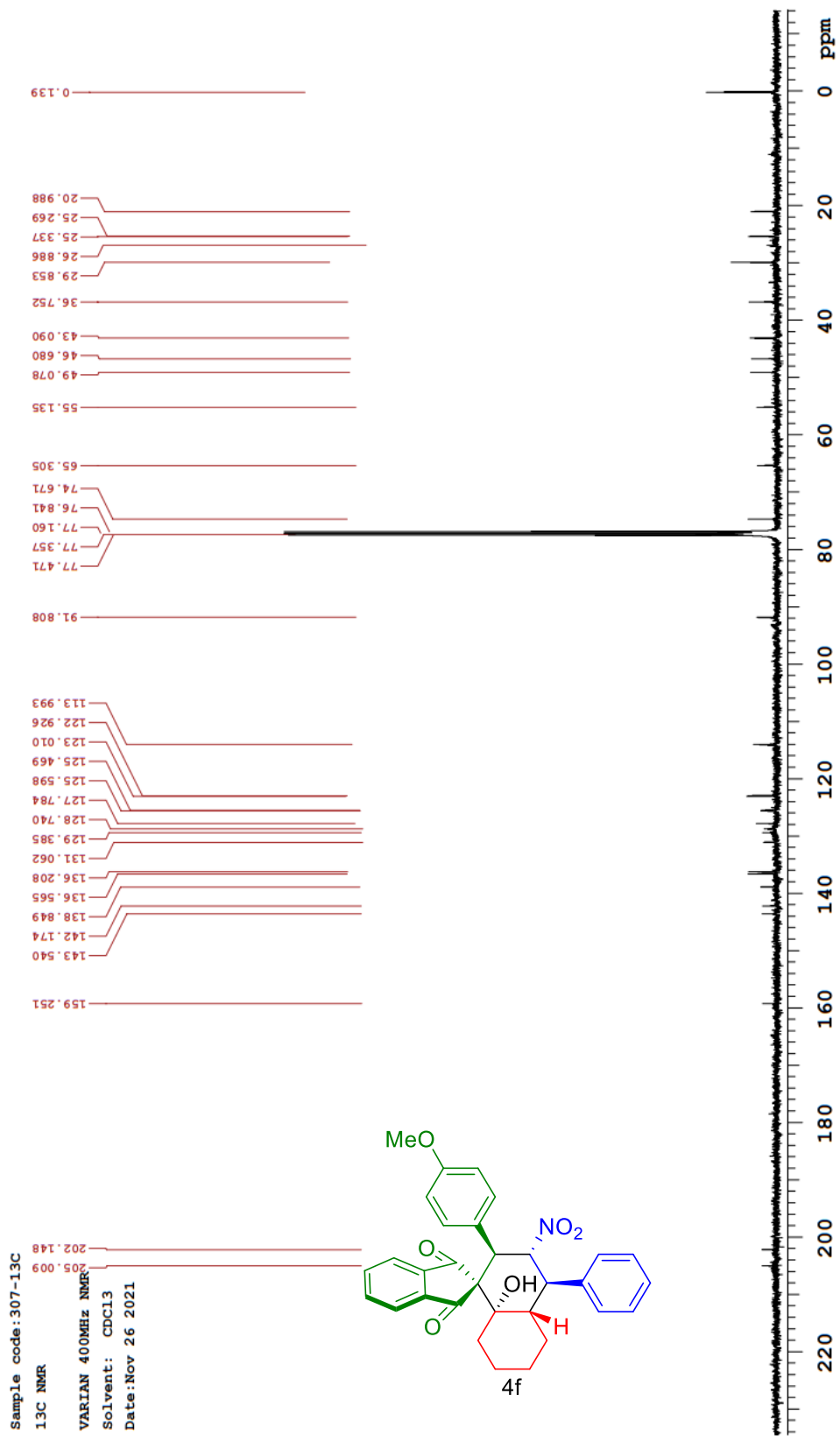


^{13}C NMR of Compound 4e

Sample code:307
1H NMR
VIGGIAN'S UNIVERSITY
VARIAN 400MHz NMR
Solvent: CDCl3
Date:Nov 22 2021

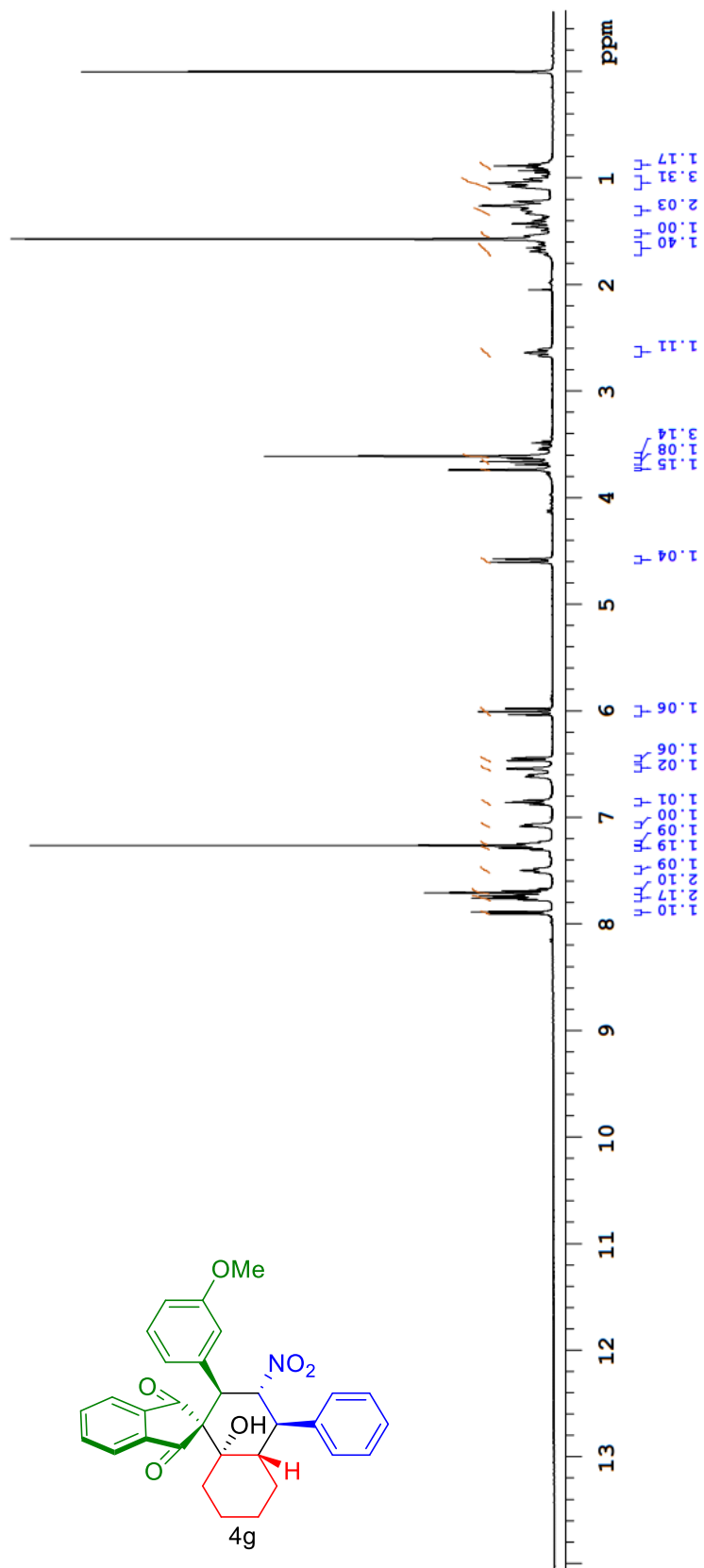


¹H NMR of Compound 4f

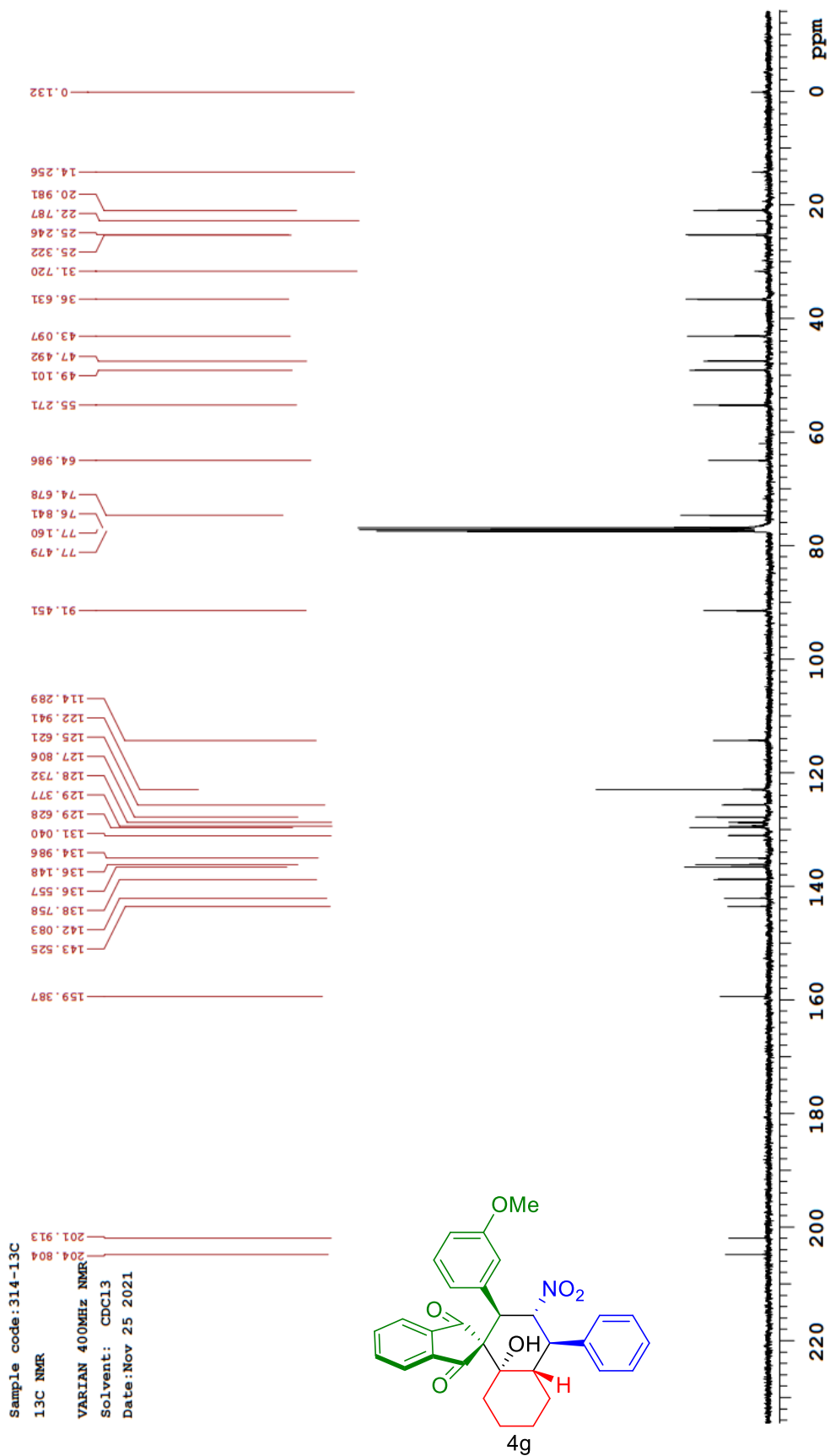


¹³C NMR of Compound **4f**

Sample code: 314
1H NMR
VIGNAN'S UNIVERSITY
VARIAN 400MHz NMR
Solvent: CDCl3
Date: Nov 22 2021



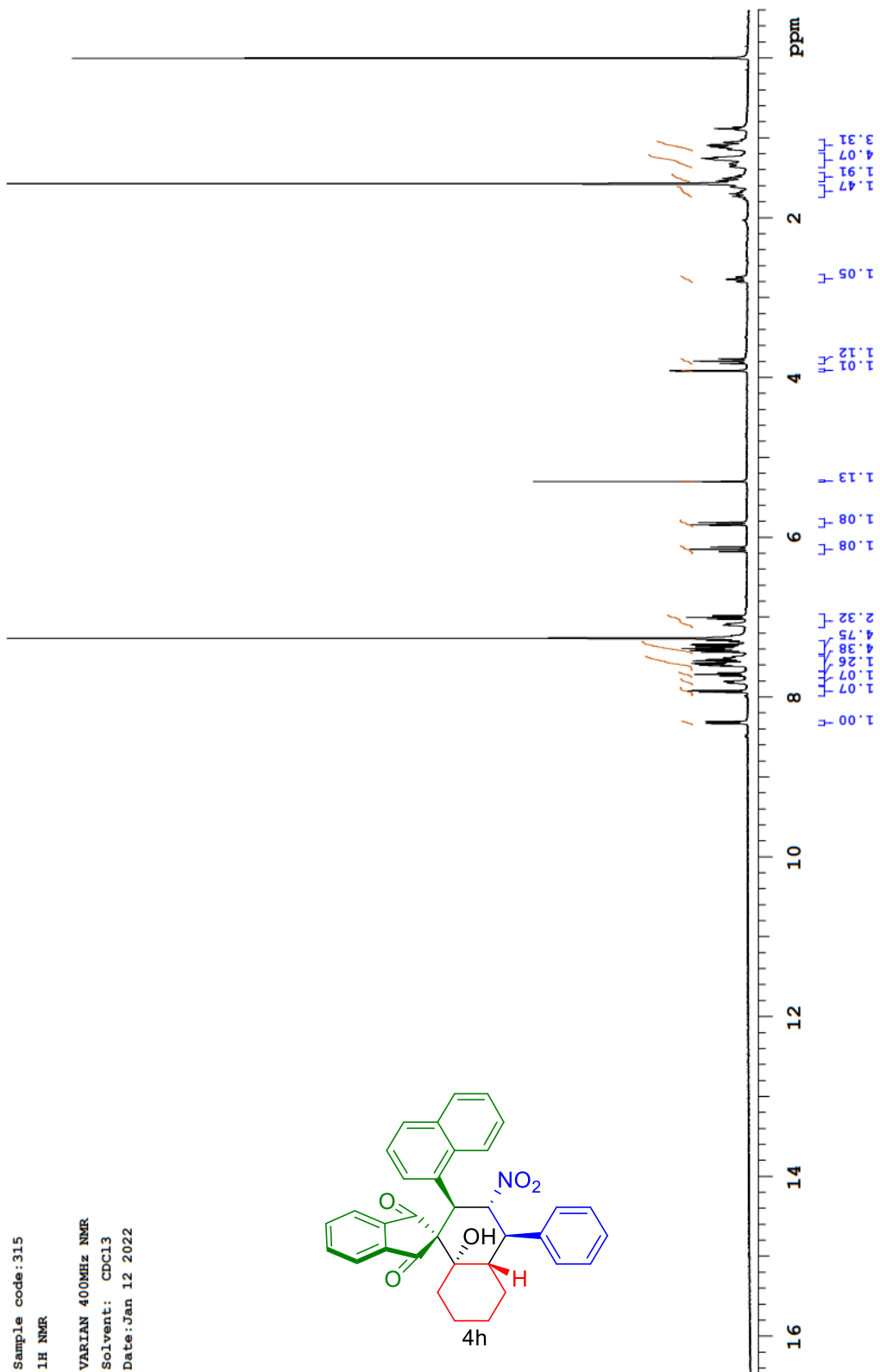
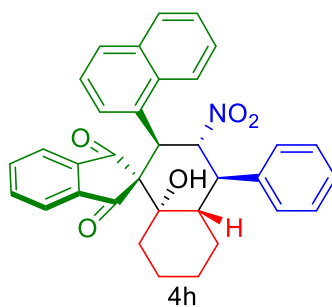
¹H NMR of Compound 4g



¹³C NMR of Compound **4g**

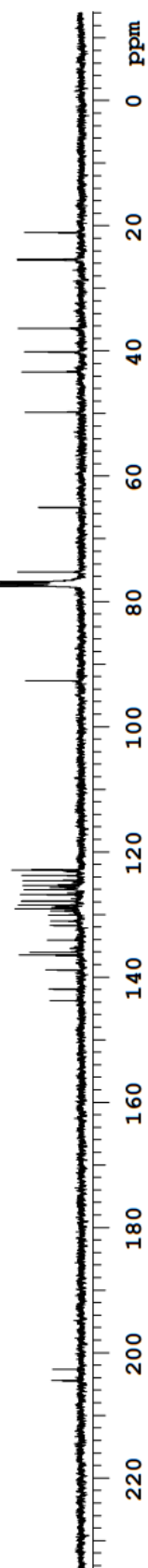
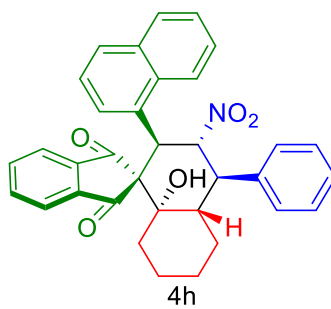
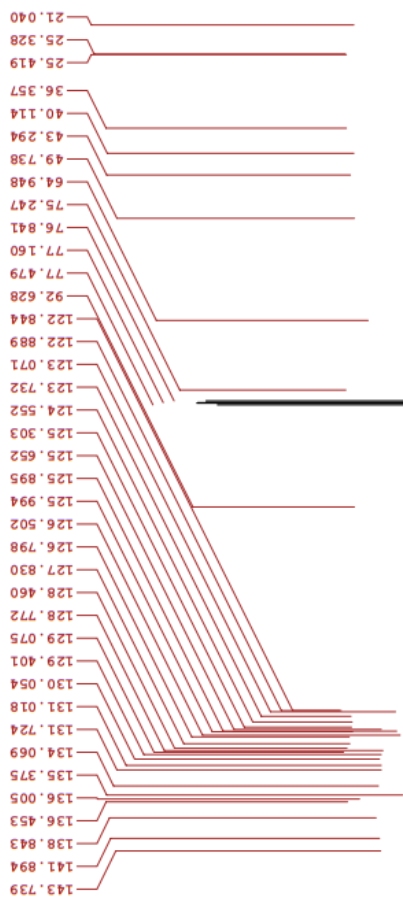
Sample code:315
1H NMR

VARIAN 400MHz NMR
Solvent: CDCl3
Date:Jan 12 2022

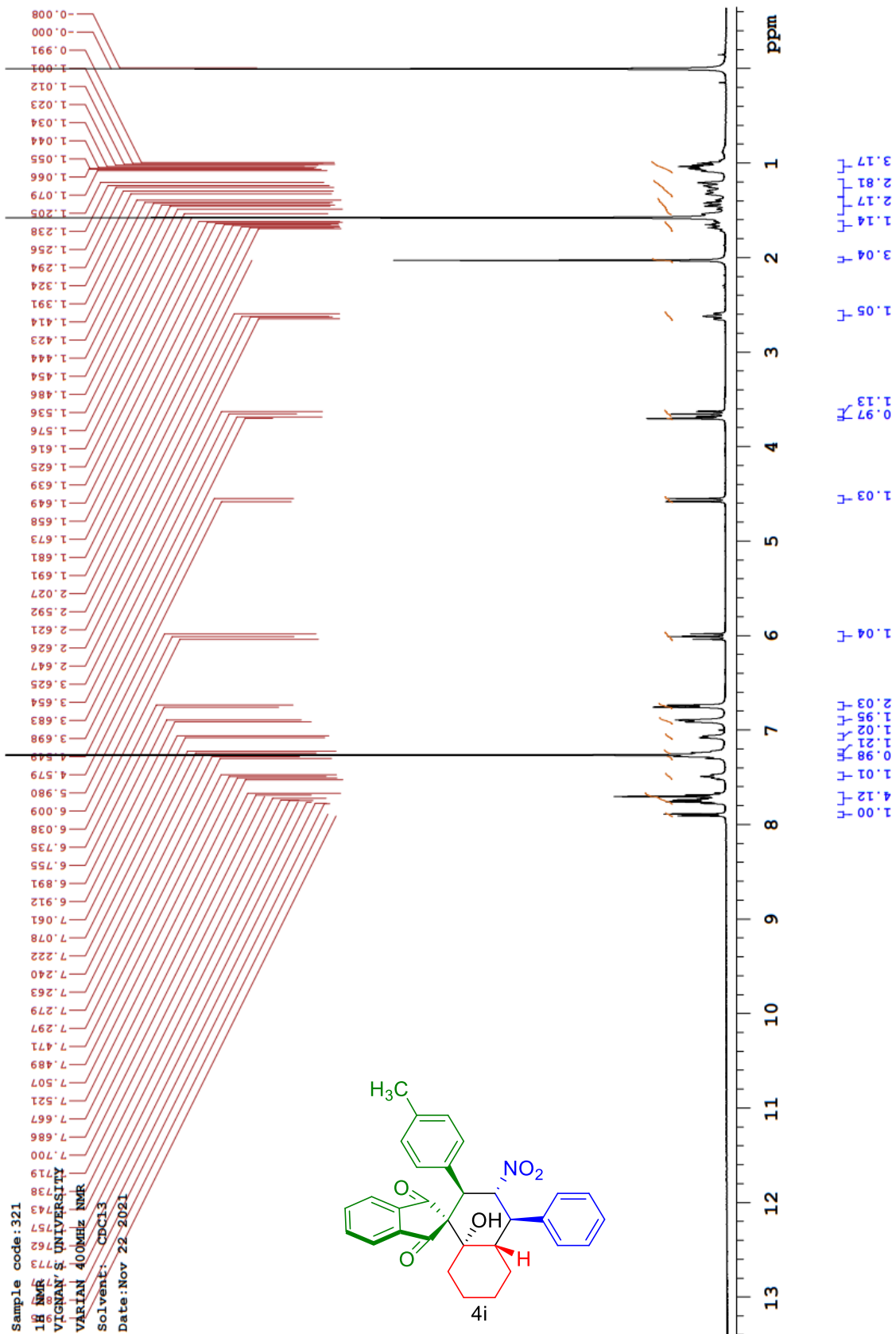


¹H NMR of Compound 4h

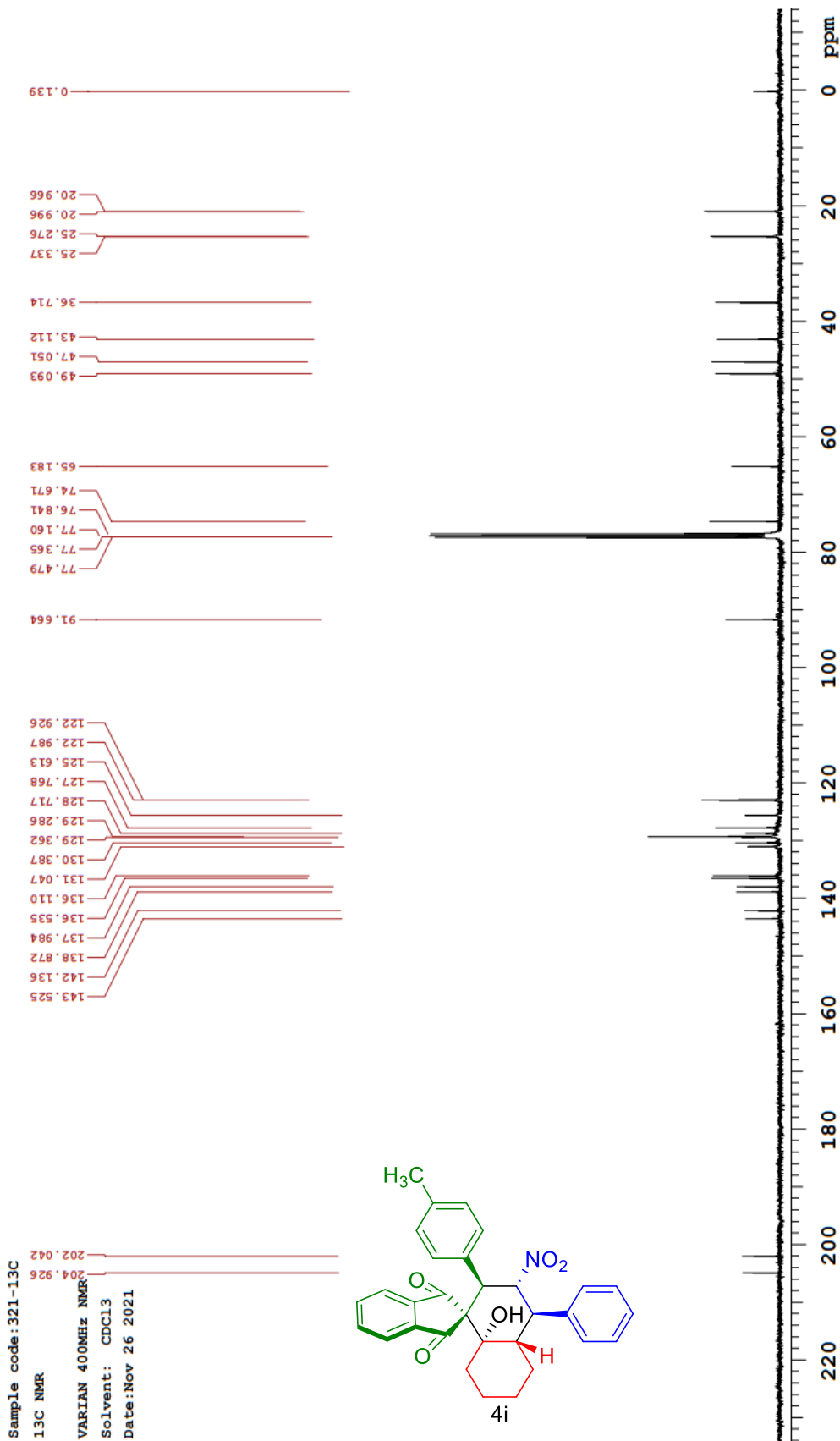
Sample code: 315-13C
13C NMR
VIGNAN'S UNIVERSITY
VARIAN 400MHz NMR
Solvent: CDCl3
Date: Feb 23 2022



¹³C NMR of Compound 4h

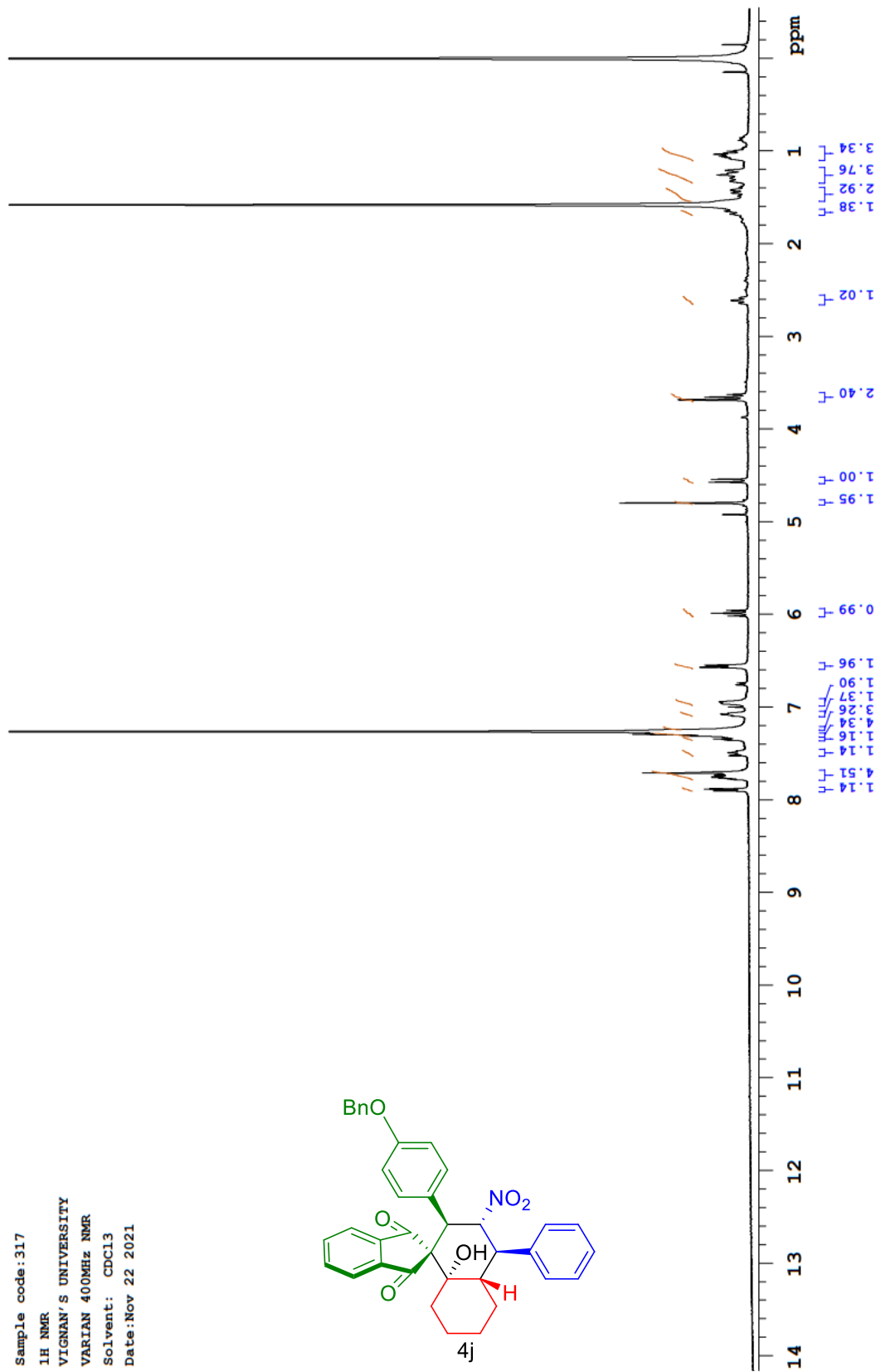
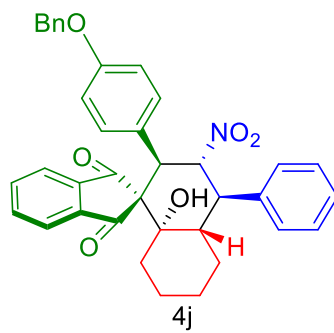


¹H NMR of Compound **4i**

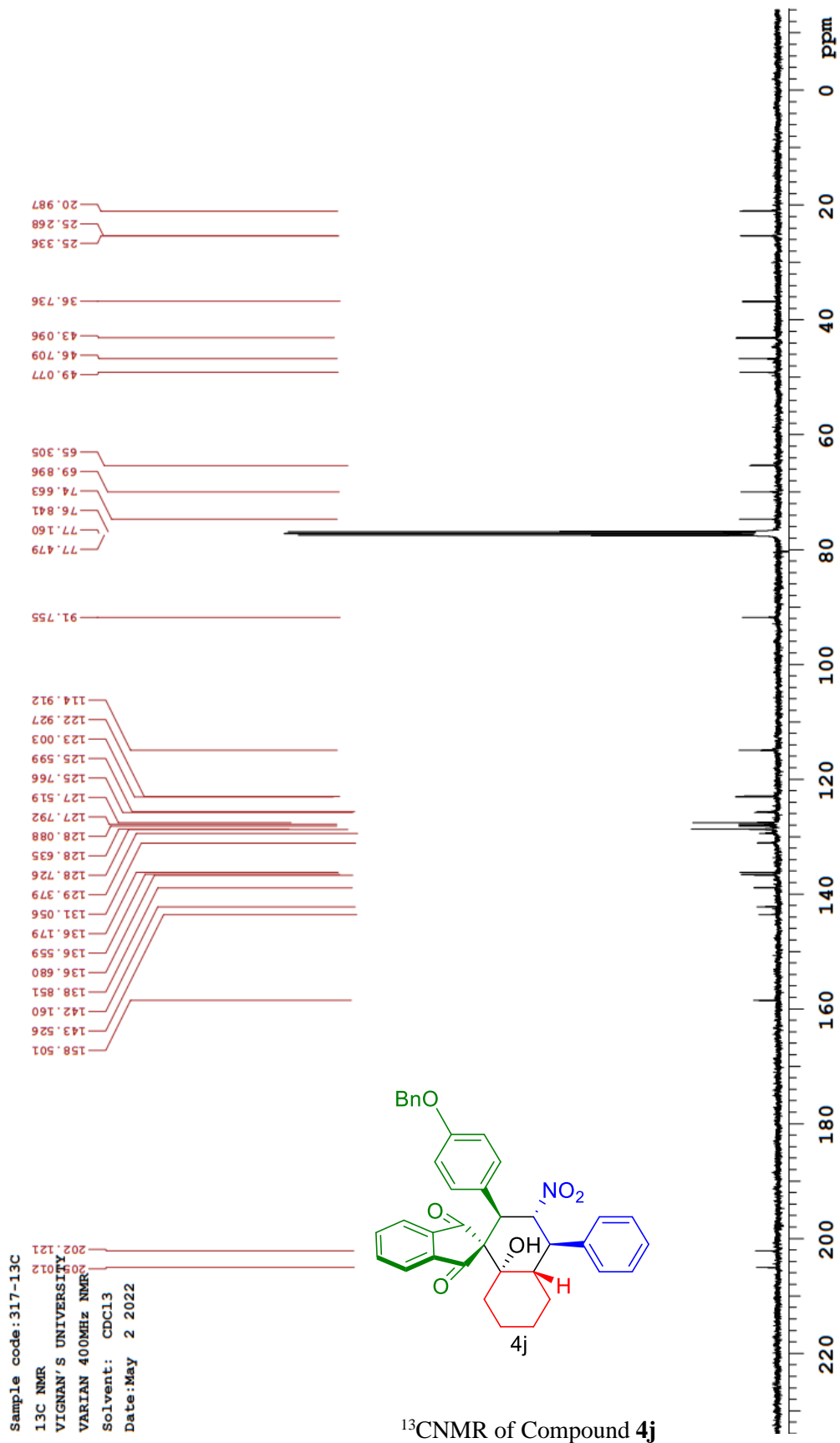


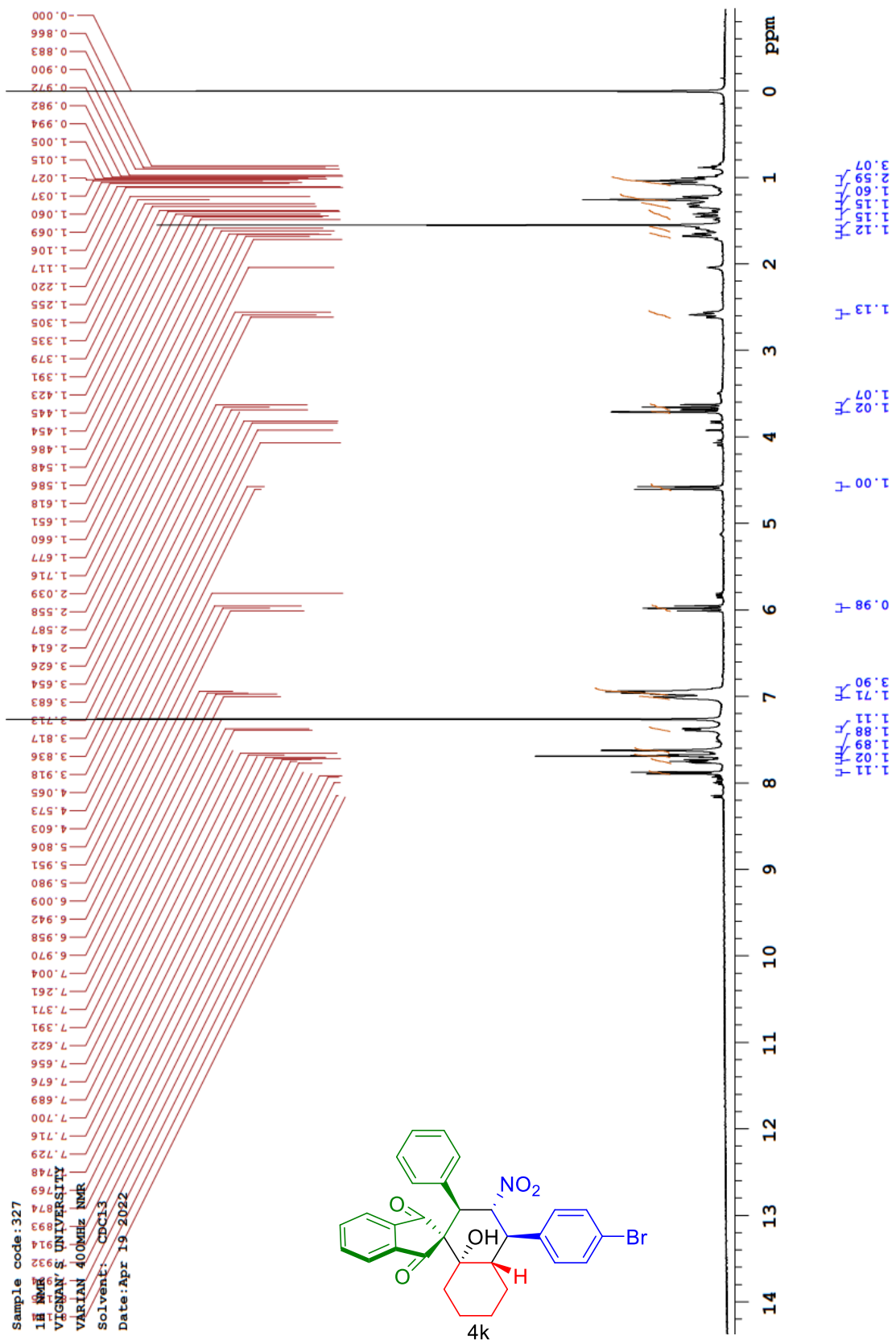
¹³C NMR of Compound **4i**

Sample code: 317
1H NMR
VIGNAN'S UNIVERSITY
VARIAN 400MHz NMR
Solvent: CDCl3
Date: Nov 22 2021

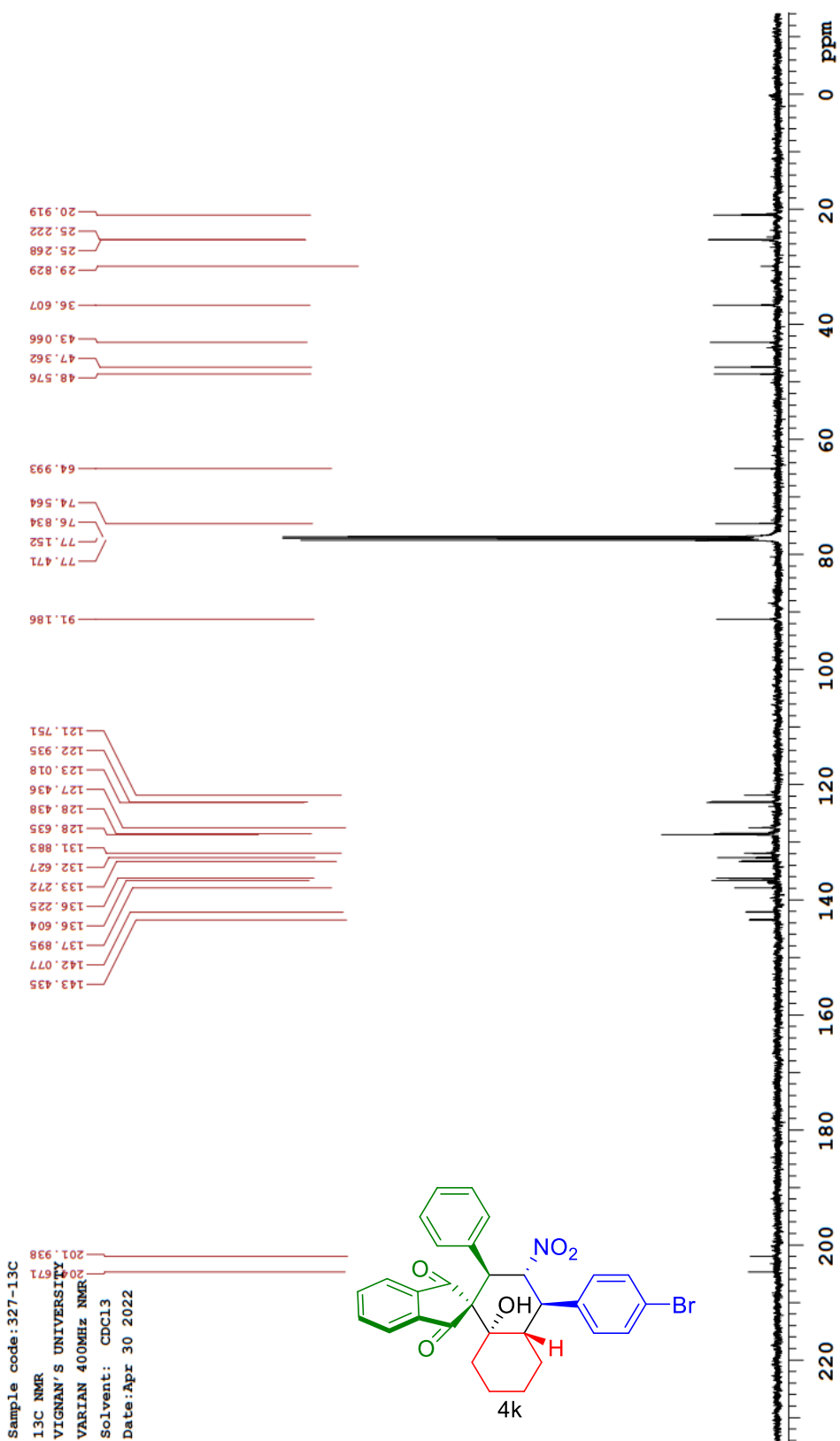


¹H NMR of Compound 4j



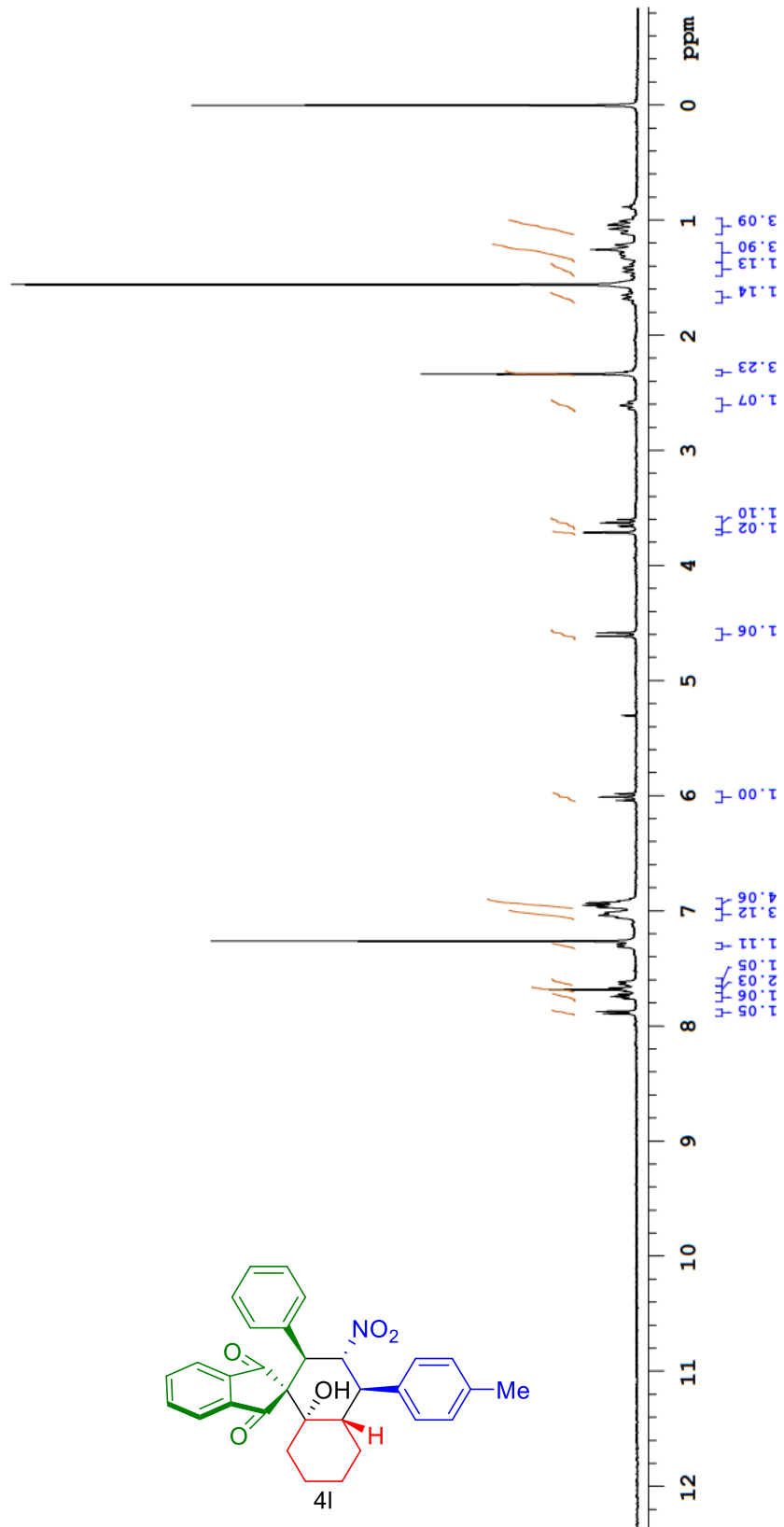
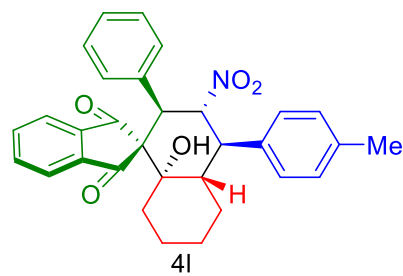


¹H NMR of Compound 4k



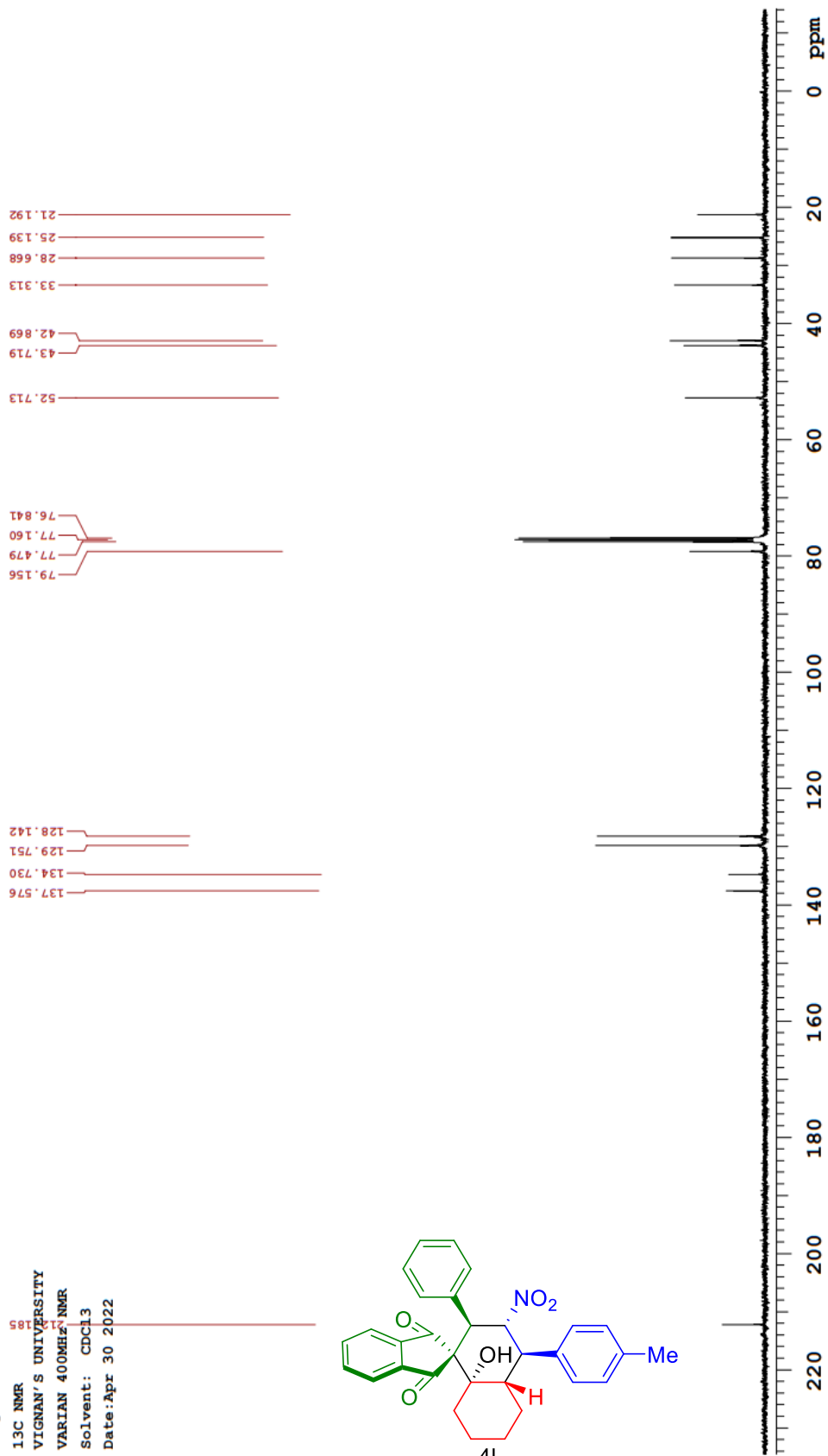
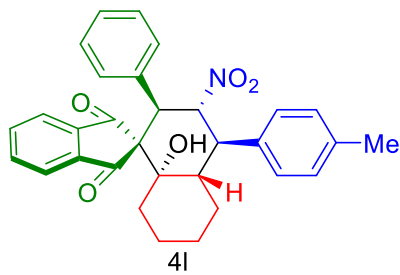
¹³C NMR of Compound **4k**

Sample code: 325
1H NMR
VIGNAN'S UNIVERSITY
VARIAN 400MHz NMR
Solvent: CDCl3
Date: Feb 23 2022

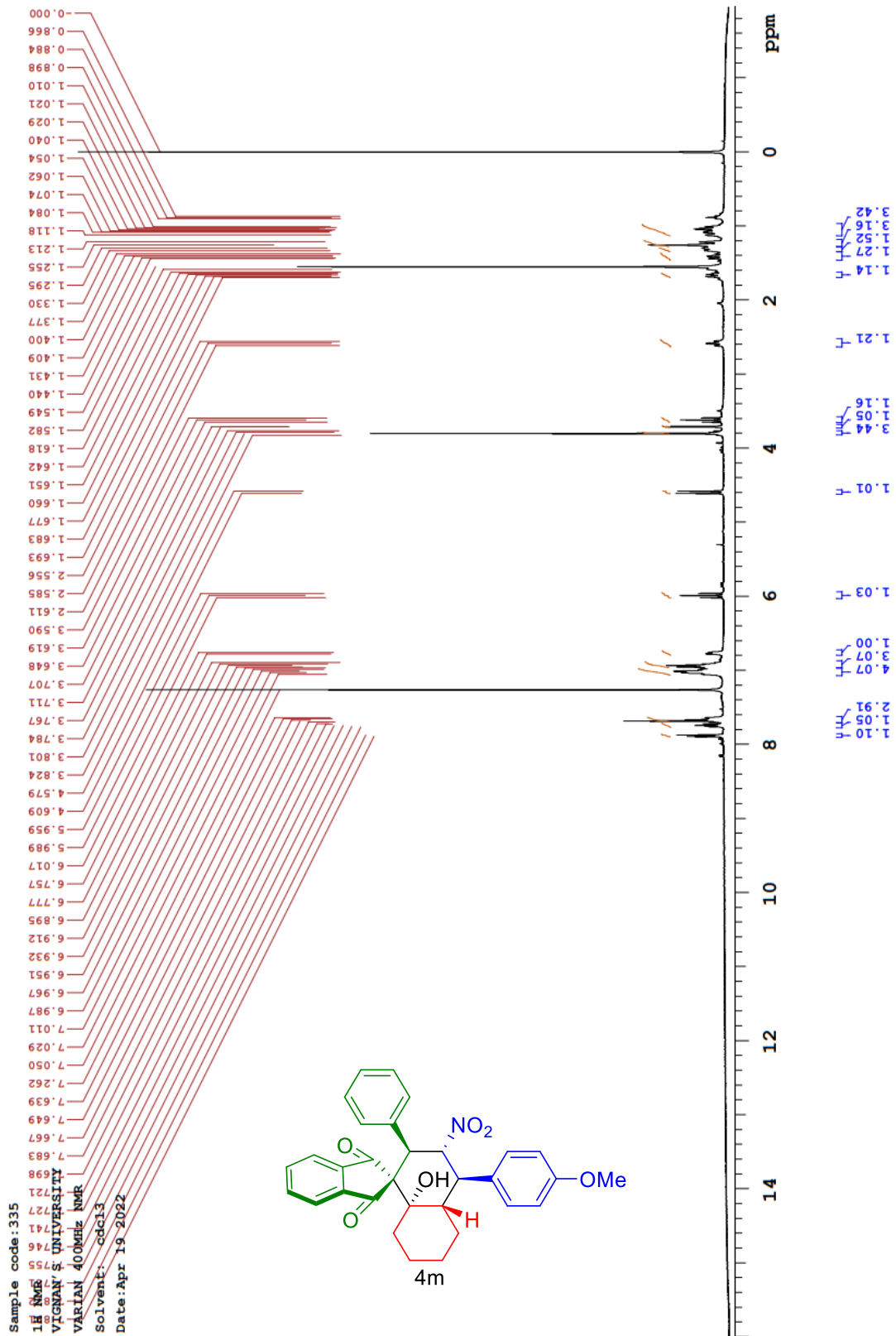


¹H NMR of Compound 4I

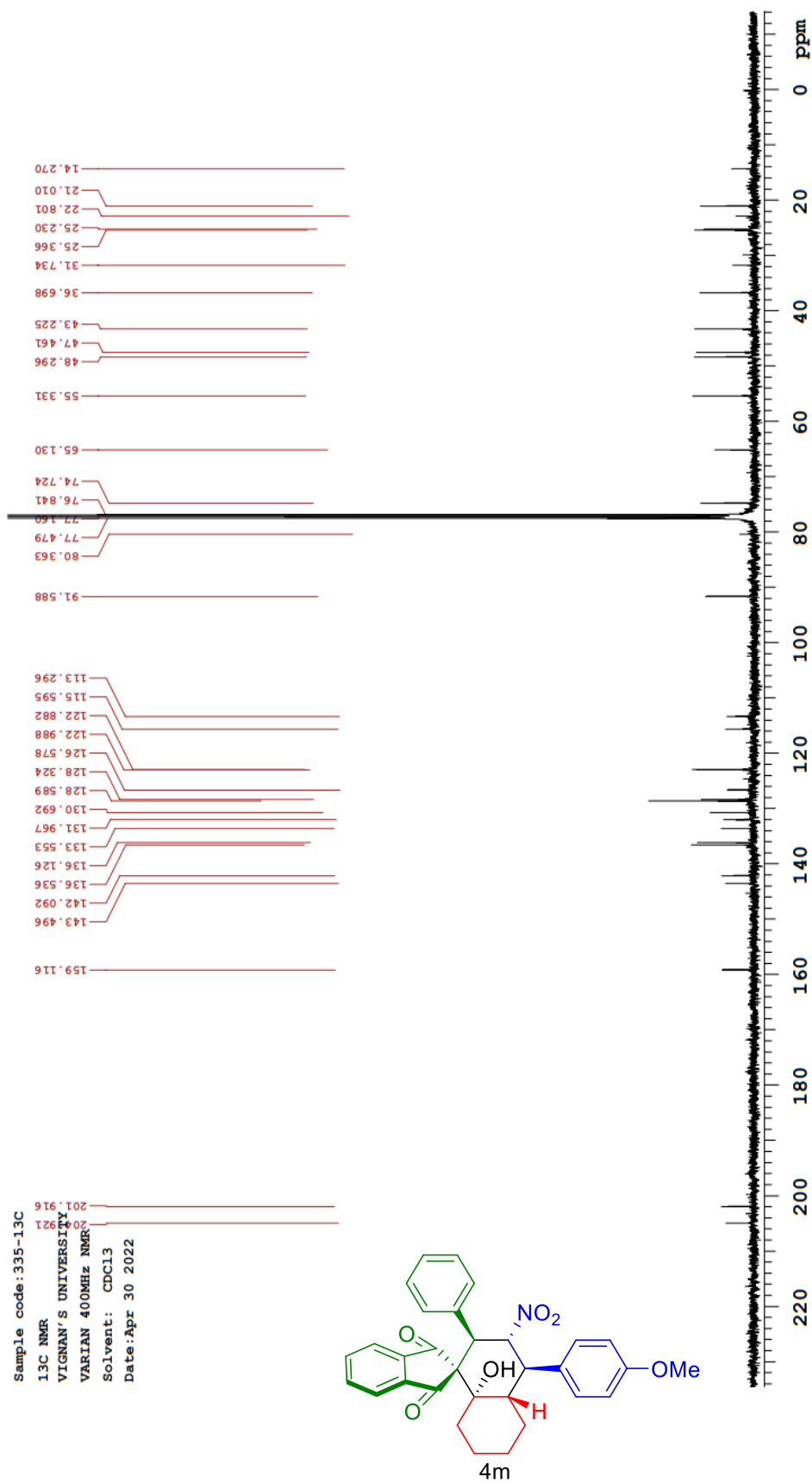
Sample code: 325-13C
13C NMR
VIGNAN'S UNIVERSITY
VARIAN 400MHZ NMR
Solvent: CDCl3
Date: Apr 30 2022



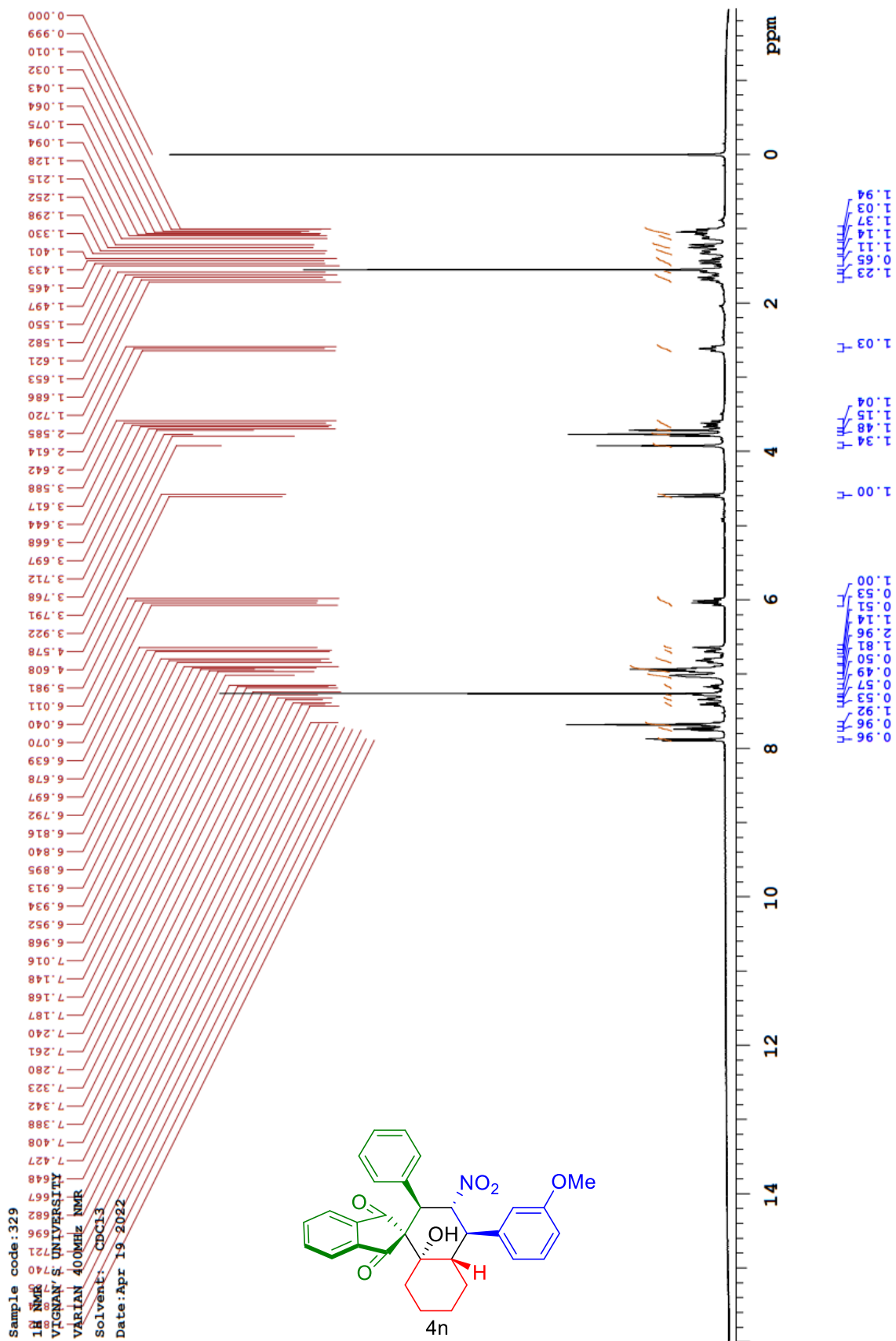
¹³C NMR of Compound 41



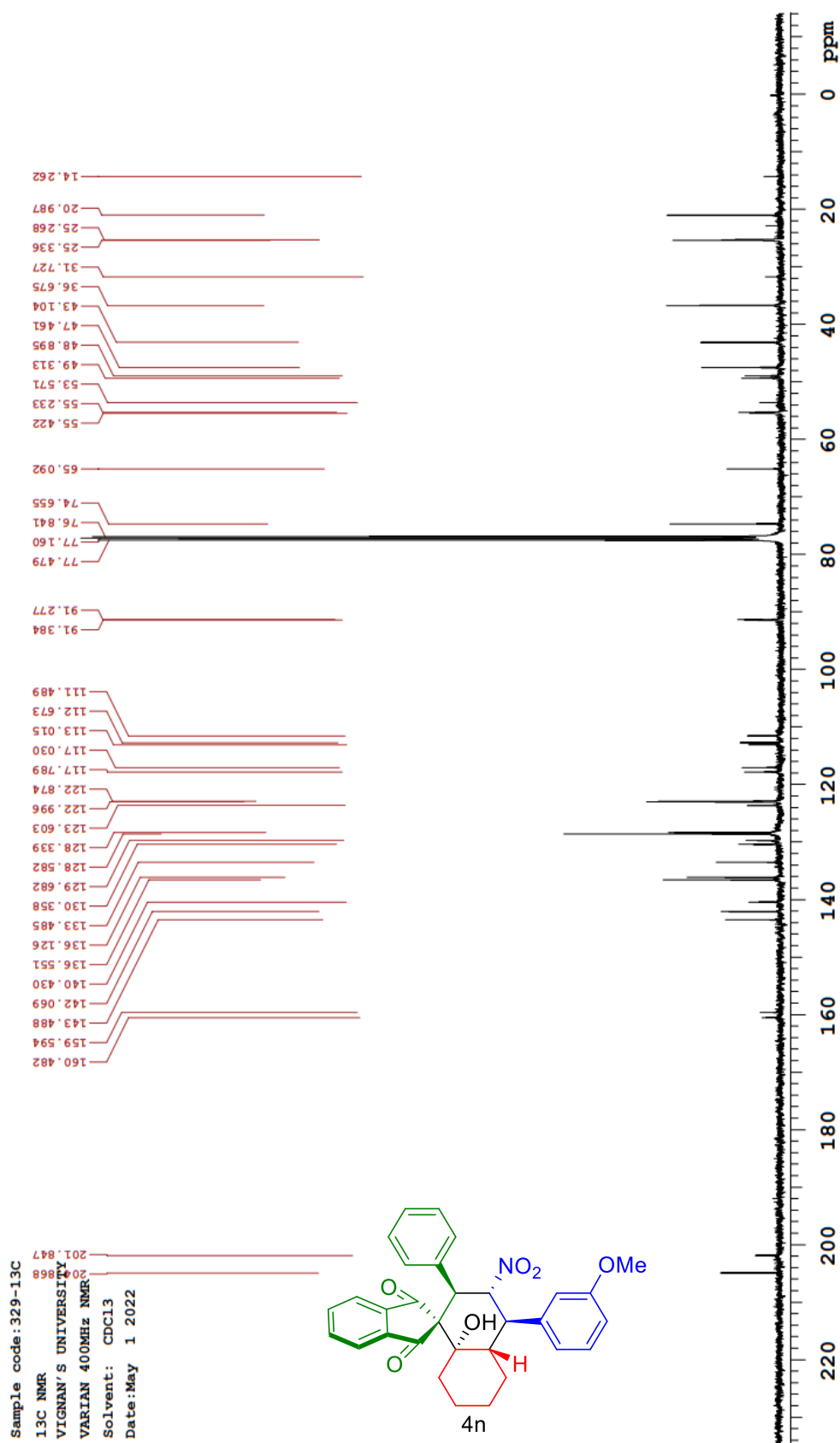
¹³C NMR of Compound **4m**



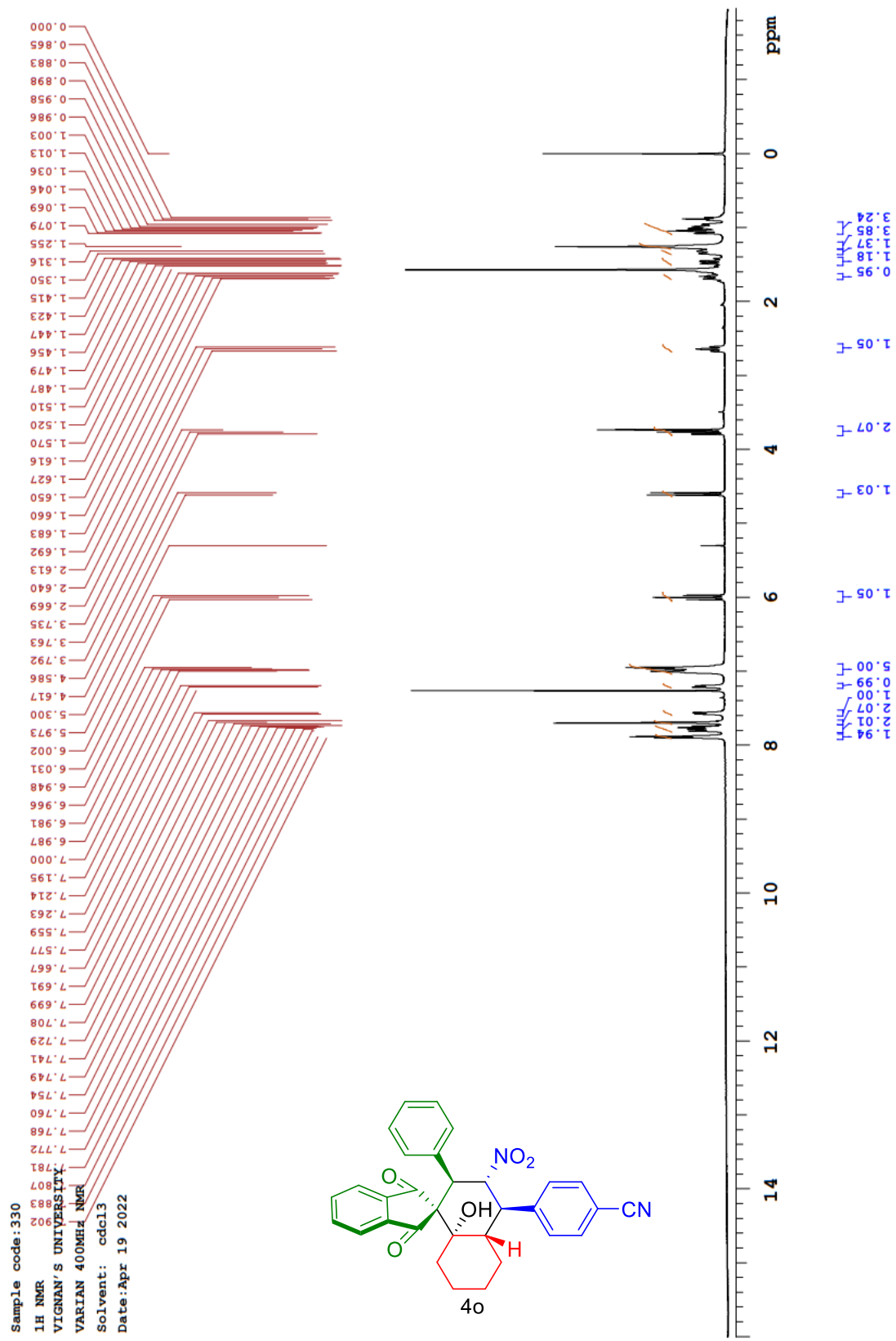
¹³C NMR of Compound **4m**



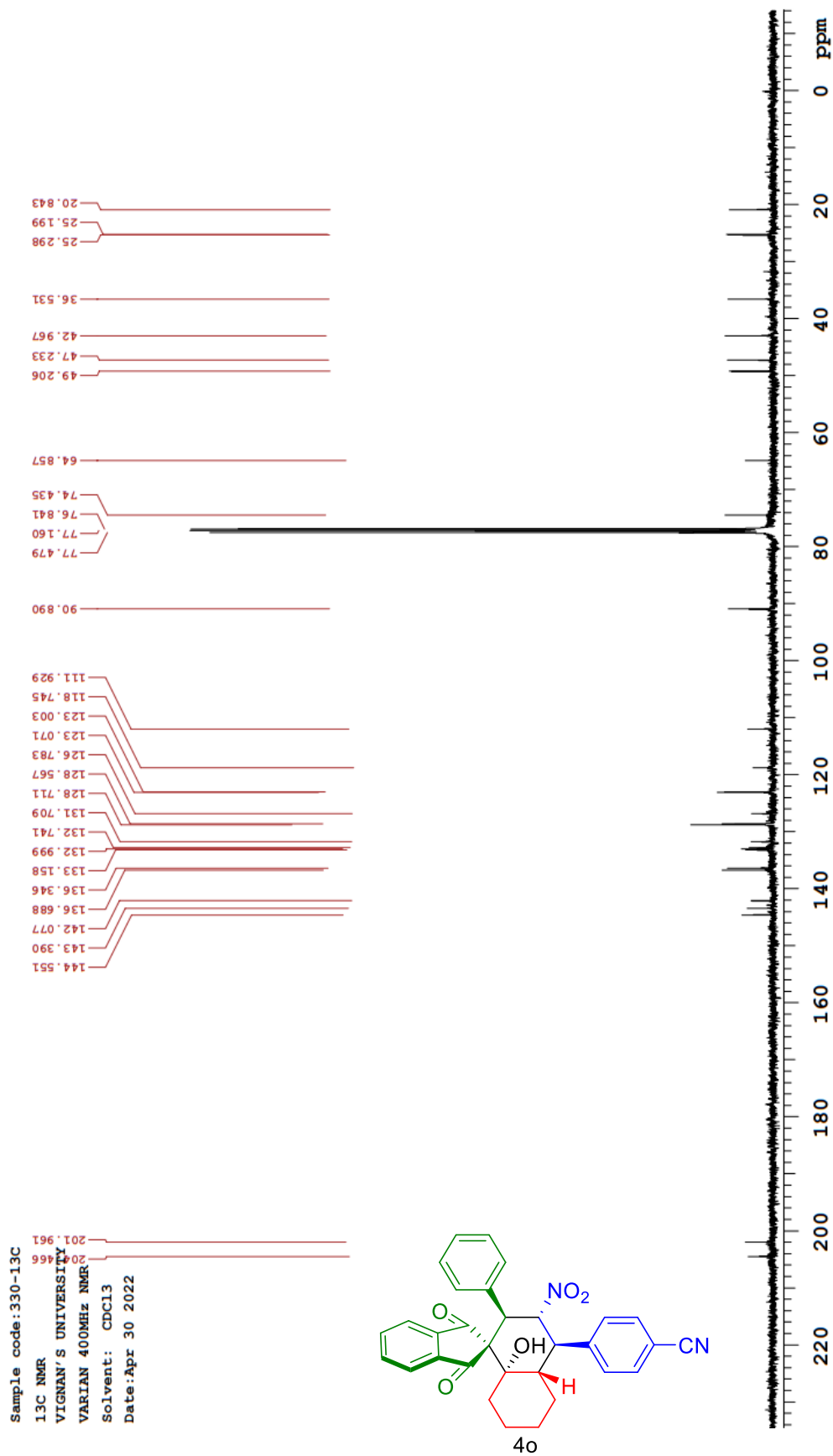
¹H NMR of Compound 4n



¹³C NMR of Compound **4n**

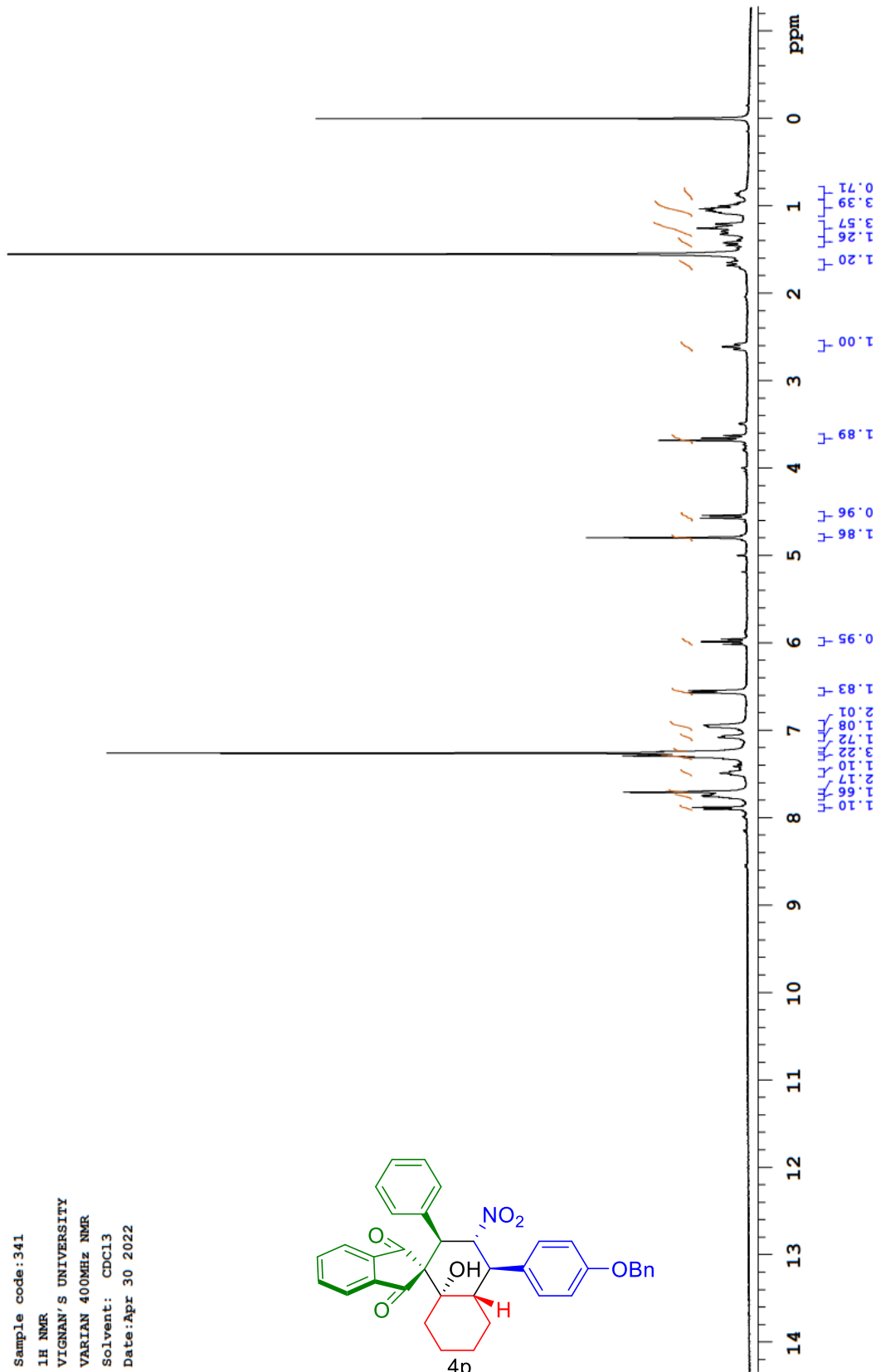
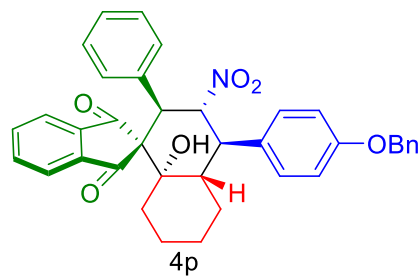


¹H NMR of Compound **4o**

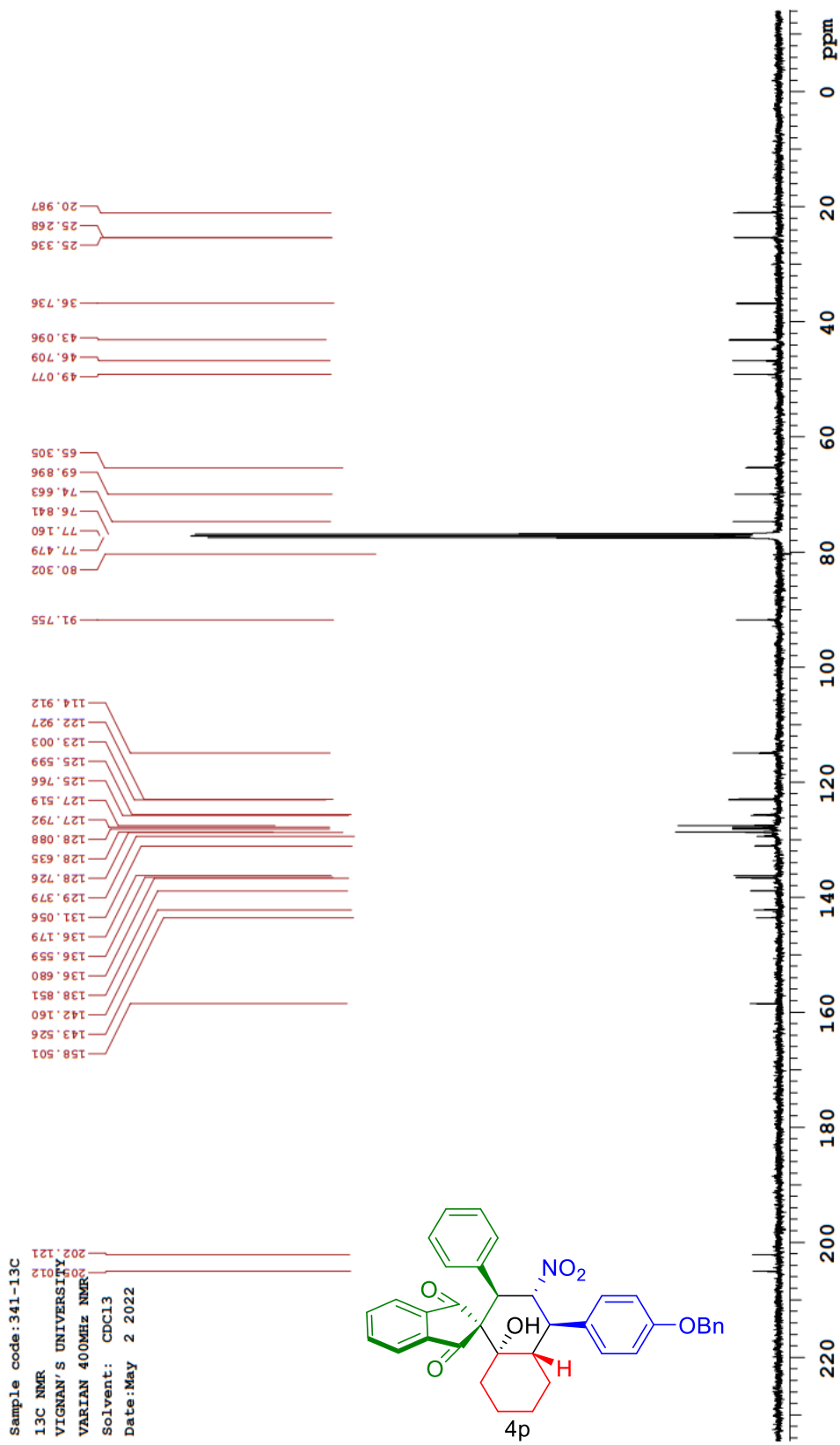


¹³C NMR of Compound 4o

Sample code:341
1H NMR
VIGAN'S UNIVERSITY
VARIAN 400MHz NMR
Solvent: CDCl3
Date:Apr 30 2022

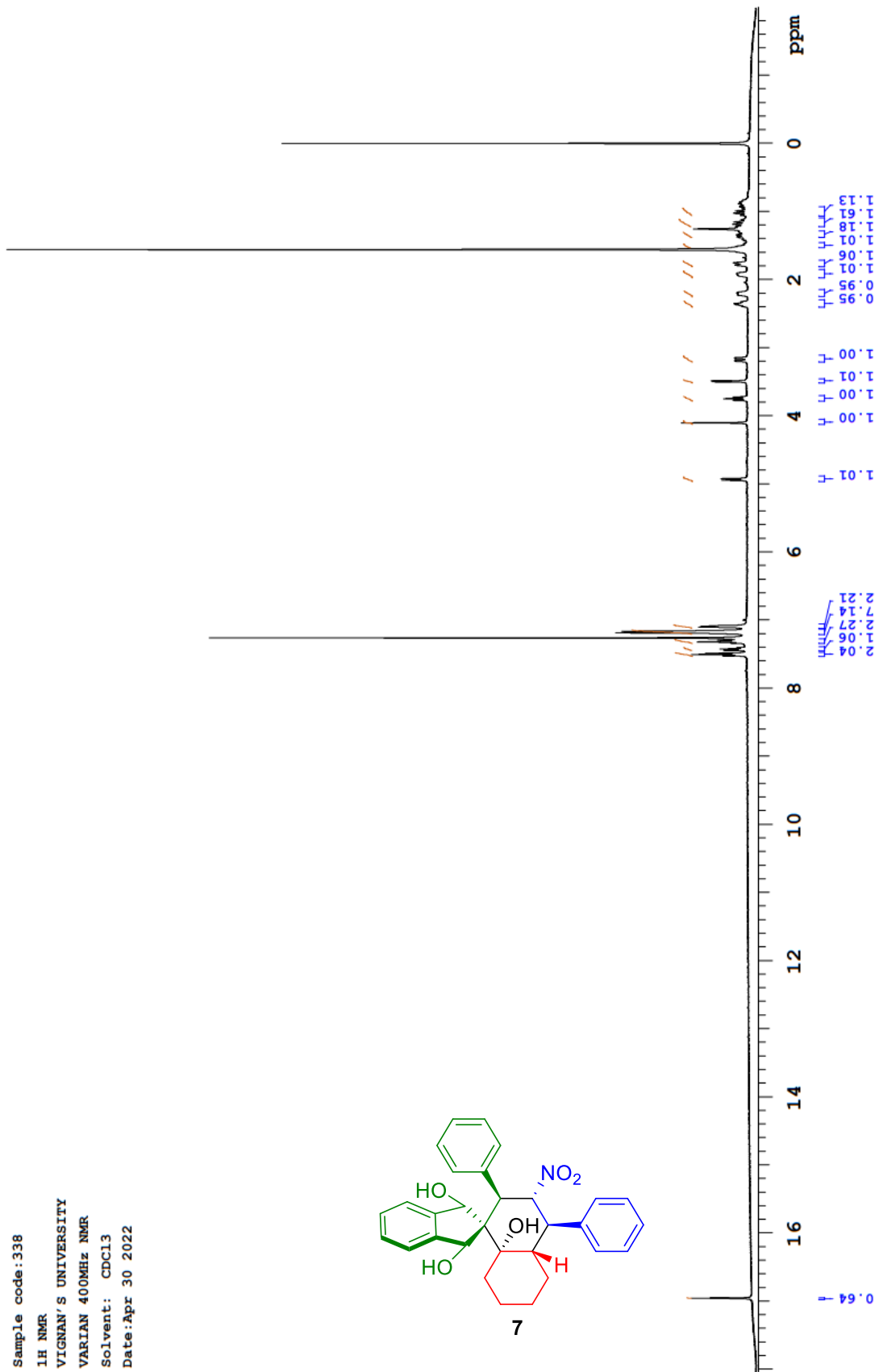
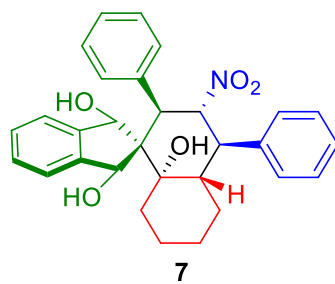


¹H NMR of Compound 4p

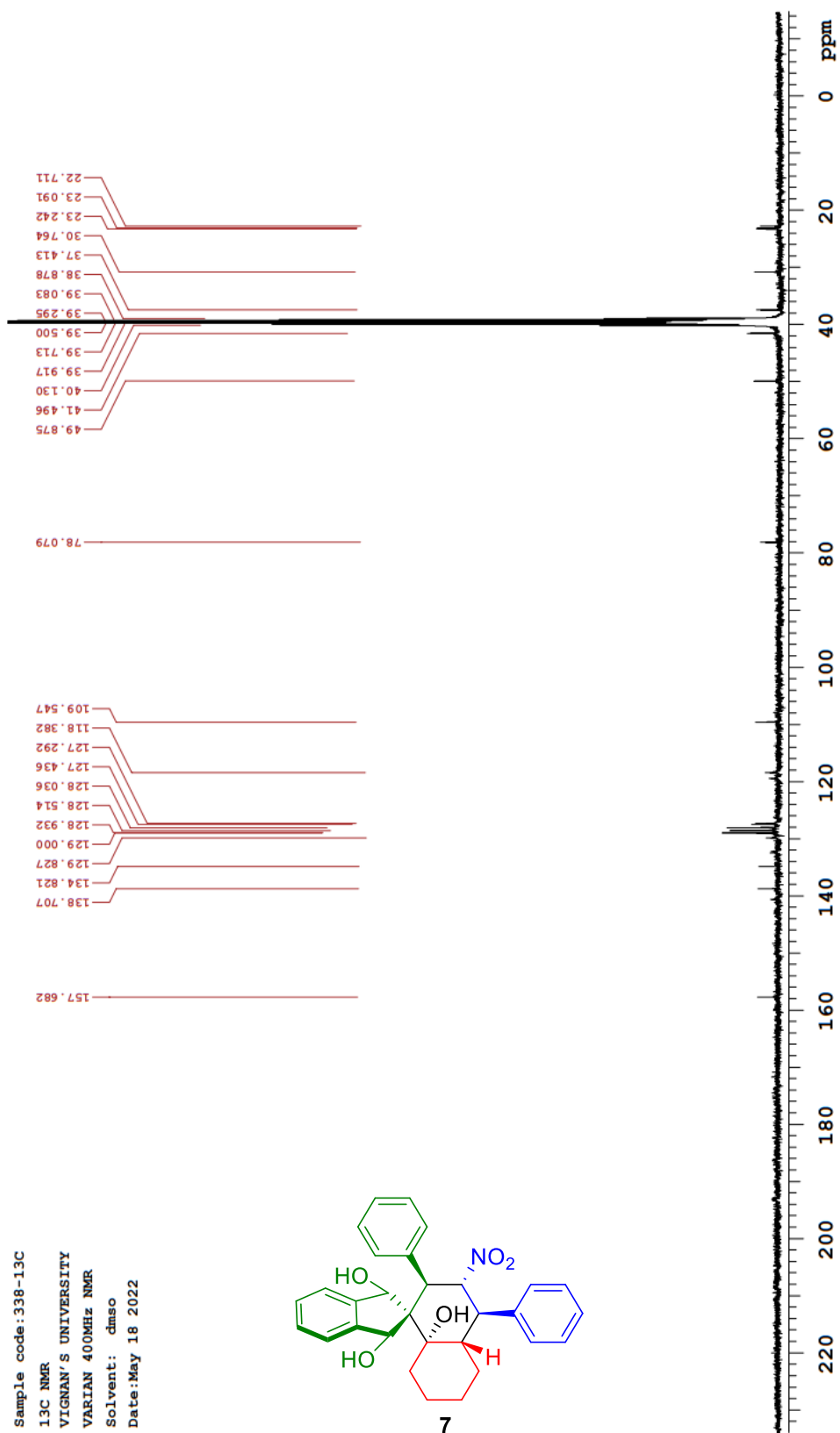


¹³C NMR of Compound 4p

Sample code:338
1H NMR
VIGNAN'S UNIVERSITY
VARIAN 400MHz NMR
Solvent: CDCl3
Date:Apr 30 2022



¹H NMR of the compound 7



¹³C NMR of the compound 7

Crystallographic data (4a)

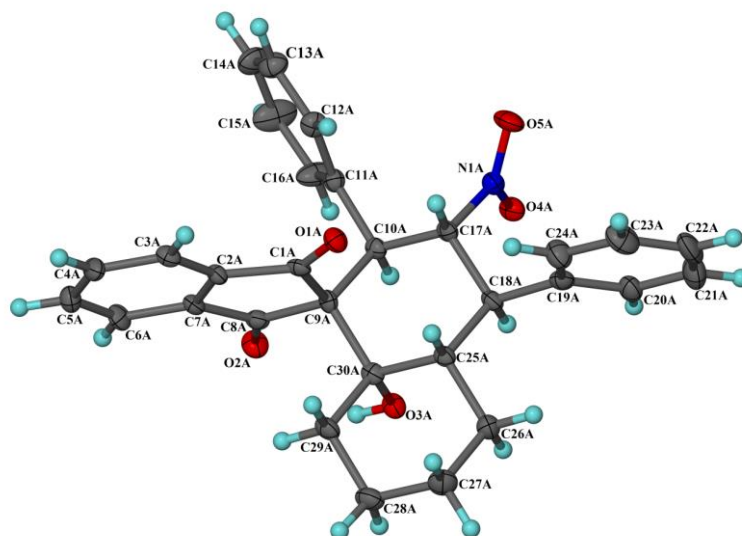


Figure caption: ORTEP diagram of **4a** compound with the atom-numbering. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radius. The asymmetric unit contains two molecules of **4a** compound; however, only one is shown in the ORTEP picture for clarity purpose. CCDC contains (i.e., 2131336) the supplementary crystallographic data for this paper which can be obtained free of charge at <https://www.ccdc.cam.ac.uk/structures/>

Crystal data for 4a: C₃₀H₂₇N₁O₅, *M* = 481.52, Orthorhombic, space group *P*2₁2₁2₁ (No.19), *a* = 12.039(2)Å, *b* = 18.483(3)Å, *c* = 22.273(4)Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, *V* = 4956.2(15)Å³, *Z* = 8, *D*_c = 1.291 g/cm³, *F*₀₀₀ = 2032, Bruker D8 QUEST PHOTON-100, Mo-K α radiation, $\lambda = 0.71073$ Å, *T* = 100(2)K, $2\theta_{\max} = 52^\circ$, $\mu = 0.088$ mm⁻¹, 54146 reflections collected, 9740 unique (*R*_{int} = 0.1113), 655 parameters, *R*1 = 0.0543, *wR*2 = 0.0983, *R* indices based on 7146 reflections with *I* > 2 σ (*I*) (refinement on *F*²), Final *Goof* = 1.005, largest difference hole and peak = -0.261 and 0.214 e.Å⁻³.

Data collection and Structure solution details: Single crystal X-ray data for **4a** compound were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer, Photon 100 detector and an I μ s microfocus Mo source ($\lambda = 0.71073$ Å) from a multi-mirror monochromatic incident beam. Oxford cryostat was used for the low temperature data collection. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 7963 reflections. Integration and scaling of

intensity data were accomplished using SAINT program.¹ The structures were solved by Direct Methods using SHELXS97² and refinement was carried out by full-matrix least-squares technique using SHELXL-2018/3.²⁻³ Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ or $1.5U_{\text{eq}}$ for methyl atoms. The O bound H atoms have been located from the difference Fourier map and their positions were refined. CCDC deposition number (i.e., 2131336) contains the supplementary crystallographic data for this paper which can be obtained free of charge at <https://www.ccdc.cam.ac.uk/structures/>

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL Version 2014/7, <http://shelx.uni-ac.gwdg.de/SHELX/index.php>
3. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.
4. A. L. Spek, Acta Cryst. 2009, D65, 148-155.