

Supporting Information

Synthesis and Cytotoxicity on Human Lung Cancer Cell Lines of 2- Arylidene and Related Analogs of Malabaricol

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Table of Contents:

Serial No.	Description	Page No.
1.1	General Information	S2
1.2	General Experimental Procedure for Synthesis of Derivatives (1-22)	S3-S14
1.3	¹ H NMR and ¹³ C NMR Spectra	S15-S36

General Information

Malabaricol plant resin was collected from Karnataka state, India. Solvents and chemicals were purchased from local vendors, and used as received. Reactions were monitored using thin-layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates (60 F254) and visualization was accomplished with either UV light, iodine adsorbed on silica gel or immersion in an ethanolic solution of *p*-anisaldehyde stain followed by heating. The column chromatography was carried out on silica gel (60-120 mesh). All ^1H NMR spectra were recorded on Bruker at 400 or 500 MHz and All ^{13}C NMR spectra recorded on Bruker at 100 or 125 MHz, respectively. Chemical shifts (δ) were reported in parts per million (ppm) and calibrated to the residual proton and carbon resonance of the CDCl_3 ($\delta_{\text{H}} = 7.26$ and $\delta_{\text{C}} = 77.0$ ppm). The coupling constants (J) were given in Hz. High-Resolution mass spectrometry (HRMS) was recorded using electrospray ionization (ESI)-Time-off light techniques. FTIR spectra were recorded with a Bruker Alpha spectrophotometer and were reported in cm^{-1} . Cellular viability in the presence of test compounds was determined by MTT-microcultured tetrazolium assay. The cells seeded to flat bottom 96 (10000 cells/100 μL) well plates cultured in the medium containing 10% serum and allowed to attach and recover for 24 hours in a humid chamber containing 5% CO_2 . MTT (3-(4, 5-dimethylthiazol-2yl)-2,5diphenyl tetrazolium bromide) was dissolved in PBS at 5mg/ml and filtered to sterilize and remove a small amount of insoluble residue present MTT. Different concentrations of compounds were added to the cells. After 48 hours, stock MTT solution (10 μL) was added to the culture plate. Cells were again kept in CO_2 incubator for 2 hours. After incubation 100 μL of DMSO was added and mixed. The absorbance was read at 562 nm in a plate reader. The results were represented as percentage of cytotoxicity/viability. All the experiments were carried out in duplicates. From the percentage of cytotoxicity the IC_{50} value calculated.

General Experimental Methods:

Synthesis of 2- arylidene derivatives

To the stirred solution of malabaricol **1** (100 mg, 218 μmol) in ethanol (3 ml) was added KOH (73.3 mg, 1.30 mmol) at room temperature. After half an hour benzaldehyde (67 μL , 654 μmol) was added to reaction mixture. The resulting mixture was stirred at room temperature for 12 h. The solvent was removed and extracted with diethyl ether (3 x 50 mL), washed with brine and dried over Na_2SO_4 . The obtained residue was purified by column chromatography (9/91, EtOAc/hexane) to get desired product **2a** (79.8 mg, 67%) as a light green viscous liquid. Yield: IR (Neat) ν_{max} 2962, 2874, 1673, 1449, 1028, 904, 665 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 7.54 (s, 1H), 7.46 – 7.38 (m, 4H), 7.33 (m, 1H), 5.12 (t, J = 7.1 Hz, 1H), 3.70 (t, J = 7.0 Hz, 1H), 2.94 (d, J = 15.8 Hz, 1H), 2.31 (d, J = 15.8 Hz, 1H), 2.17-1.31 (m, 25 H), 1.25 (s, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 1.15 (s, 3H), 0.96 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 207.7, 137.6, 135.9, 133.8, 131.5, 130.3, 128.4, 128.3, 124.5, 85.6, 82.1, 72.7, 59.6, 57.1, 53.1, 45.1, 44.9, 43.9, 38.1, 37.6, 36.3, 36.0, 29.6, 29.5, 26.0, 25.6, 25.1, 24.3, 23.8, 22.3, 22.2, 21.5, 21.4, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{37}\text{H}_{54}\text{O}_3 - \text{H}]^+$: 545.3995, Found: 545.4008.

Compound 2b

The compound **2b** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 4- methoxybenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield: 84.7 mg (67.4%); IR (Neat) ν_{max} 2959, 2873, 1669, 1458, 1032, 907, 665 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ =

7.52 (s, 1H), 7.42 (d, $J = 8.8$ Hz, 2H), 6.94 (d, $J = 8.8$ Hz, 2H), 5.12 (t, $J = 7.0$ Hz, 1H), 3.84 (s, 3H), 3.71 (t, $J = 6.9$ Hz, 1H), 2.92 (d, $J = 15.5$ Hz, 1H), 2.30 (d, $J = 15.5$ Hz, 1H), 2.18-1.30 (m, 25H), 1.25 (s, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 1.13 (s, 3H), 0.96 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 207.6, 159.8, 137.5, 132.1, 131.6, 131.5, 128.5, 124.5, 113.9, 85.6, 82.1, 72.7, 59.9, 57.2, 55.2, 52.9, 45.1, 44.9, 43.9, 38.0, 37.5, 36.3, 35.9, 29.7$ (2C), 26.0, 25.6, 25.1, 24.3, 23.8, 22.2, 22.1, 21.6, 21.4, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{38}\text{H}_{56}\text{O}_4 + \text{H}]^+$: 577.4251, Found: 577.4267.

Compound 2c

The compound **2c** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 1-naphthaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 83.6 mg (64.3%); IR (Neat) ν_{max} 2958, 2853, 1676, 1459, 1078, 907, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): $\delta = 7.90$ (s, 1H), 7.88-7.80 (m, 3H), 7.71 (s, 1H), 7.54 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.52-7.47 (m, 1H), 5.12 (t, $J = 6.9$ Hz, 1H), 3.71 (t, $J = 6.8$ Hz, 1H), 3.05 (d, $J = 16.2$ Hz, 1H), 2.42 (d, $J = 16.1$ Hz, 1H), 2.20-1.31 (m, 26H), 1.26 (s, 3H), 1.22 (s, 3H), 1.19 (s, 6H), 0.96 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 207.6, 137.7, 134.1, 133.4, 133.0, 132.9, 131.5, 130.2, 128.4, 127.8, 127.5, 127.5, 126.7, 126.3, 124.5, 85.6, 82.1, 72.7, 59.7, 57.1, 53.1, 45.2, 45.0, 43.9, 38.1, 37.6, 36.4, 36.1, 29.6, 29.5, 26.0, 25.6, 25.1, 24.3, 23.8, 22.3, 22.2, 21.5, 21.3, 17.6, 15.6$; HRMS (ESI+) calculated for $[\text{C}_{41}\text{H}_{56}\text{O}_3 + \text{H}]^+$: 597.4302, Found: 597.4301.

Compound 2d

The compound **2d** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 4-nitrobenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 70.4 mg (54.6%);

IR (Neat) ν_{max} 2961, 2872, 1678, 1454, 1074, 906, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 8.26 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.6 Hz, 2H), 7.53 (s, 1H), 5.11 (t, J = 7.0 Hz, 1H), 3.71 (t, J = 7.0 Hz, 1H), 2.87 (d, J = 16.3 Hz, 1H), 2.38-1.33 (m, 26H), 1.25 (s, 3H), 1.21 (s, 3H), 1.18 (s, 3H), 1.17 (s, 3H), 0.97 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz): 207.3, 147.8, 142.3, 137.4, 131.5, 130.6, 124.5, 123.6, 85.5, 82.1, 72.8, 59.5, 57.0, 53.1, 45.3, 44.8, 43.9, 38.0, 37.6, 36.2, 36.1, 29.6, 29.3, 25.9, 25.6, 25.1, 24.3, 23.8, 22.3, 22.1, 21.5, 21.3, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{37}\text{H}_{53}\text{NO}_5 - \text{H}]^+$: 590.3840, Found: 590.3856.

Compound 2e

The compound **2e** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 3-nitrobenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 77.0 mg (59.7%); IR (Neat) ν_{max} 2961, 2871, 1678, 1455, 1074, 905, 665 cm^{-1} ; ^1H NMR δ 8.28 (s, 1H), 8.18 (dd, J = 1.8, 7.3 Hz, 1H), 7.72 (d, J = 7.7 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.52 (s, 1H), 5.11 (t, J = 6.9 Hz, 1H), 3.71 (t, J = 6.7 Hz, 1H), 2.89 (d, J = 15.5 Hz, 1H), 2.35 (d, J = 15.5 Hz, 1H), 2.18-1.29 (m, 19H), 1.68 (s, 3H), 1.62 (s, 3H), 1.25 (s, 3H), 1.21 (s, 3H), 1.18 (s, 3H), 1.17 (s, 3H), 0.97 (s, 3H), 0.84 (s, 3H). ^{13}C NMR (100 MHz): δ 207.1, 148.1, 137.4, 136.5, 135.6, 134.4, 131.3, 129.3, 124.5, 124.3, 122.8, 85.4, 82.0, 72.6, 56.9, 53.0, 45.2, 44.6, 43.8, 37.9, 37.6, 36.0, 29.3, 25.9, 25.5, 25.0, 24.1, 22.1, 22.1, 21.4, 21.2, 17.5, 15.6. HRMS (ESI+) calculated for $[\text{C}_{37}\text{H}_{53}\text{NO}_5 - \text{OH}]^+$: 575.3975, Found: 575.3960.

Compound 2f

The compound **2f** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 2-nitrobenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 68.3 mg (53%); IR

(Neat) ν_{max} 2962, 2871, 1679, 1455, 1075, 903, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 8.12 (dd, J = 8.1, 1.2 Hz, 1H), 7.64 (ddd, J = 15.0, 7.4, 1.2 Hz, 2H), 7.50 (ddd, J = 15.6, 8.0, 0.8 Hz, 1H), 7.30 (d, J = 7.7 Hz, 1H), 5.10 (t, J = 7.0 Hz, 1H), 3.68 (t, J = 7.3 Hz, 1H), 2.53 (d, J = 15.2 Hz, 1H), 2.09-1.95 (m, 2H), 1.85-1.24 (m, 24H), 1.21 (s, 6H), 1.18 (s, 3H), 1.15 (s, 3H), 0.98 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 207.1, 148.1, 135.8, 134.1, 133.1, 132.2, 131.5, 130.9, 128.7, 124.8, 124.5, 85.5, 82.1, 72.7, 59.4, 56.9, 53.7, 45.9, 44.0, 43.6, 38.0, 37.5, 36.5, 29.6, 29.3, 28.6, 25.9, 25.6, 25.2, 24.3, 22.6, 22.3, 22.1, 21.2, 21.1, 17.5, 15.5. HRMS (ESI+) calculated for $[\text{C}_{37}\text{H}_{53}\text{NO}_5 + \text{NH}_4]^+$: 609.4262, Found: 609.4261.

Compound 2g

The compound **2g** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 4-methylbenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 76.1 mg (62.3%); IR (Neat) ν_{max} 2962, 2874, 1671, 1452, 1073, 906, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 7.53 (s, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 5.12 (t, J = 6.9 Hz, 1H), 3.71 (t, J = 6.9 Hz, 1H), 2.93 (d, J = 16.2 Hz, 1H), 2.38 (s, 3H), 2.34-2.27 (m, 1H), 2.14-1.30 (m, 25H), 1.25 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 0.96 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 207.7, 138.6, 137.7, 133.0, 132.9, 131.5, 130.4, 129.1, 124.5, 85.6, 82.1, 72.7, 59.8, 57.1, 53.0, 45.0, 45.0, 43.9, 38.0, 37.6, 36.3, 35.9, 29.6, 26.0, 25.6, 25.1, 24.3, 23.8, 22.2, 22.1, 21.5, 21.3, 21.3, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{38}\text{H}_{56}\text{O}_3 + \text{H}]^+$: 561.4302, Found: 561.4308.

Compound 2h

The compound **2h** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 4-*tert*-butylbenzaldehyde and purified by column

chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 83.0 mg (63.2%); IR (Neat) ν_{max} 2957, 2852, 1672, 1461, 1078, 908, 665 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 7.52 (s, 1H), 7.46-7.38 (m, 4 H), 5.12 (t, J = 7.1 Hz, 1H), 3.71 (t, J = 6.8 Hz, 1H), 2.96 (d, J = 16.0 Hz, 1H), 2.33 (d, J = 16.0 Hz, 1H), 2.17-1.39 (m, 25H), 1.34 (s, 9H), 1.25 (s, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 1.13 (s, 3H), 0.96 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 207.8, 151.8, 137.5, 133.0, 133.0, 131.5, 130.3, 125.4, 124.5, 85.6, 82.1, 72.7, 57.1, 53.0, 45.1, 45.0, 43.9, 38.1, 37.6, 35.9, 34.7, 31.1, 29.8, 25.6, 25.1, 24.3, 22.2, 22.2, 21.6, 21.4, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{41}\text{H}_{62}\text{O}_3 + \text{H}]^+$: 603.4772, Found: 603.4776.

Compound 2i

The compound **2i** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 2,4-dichlorobenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 86.2 mg (64.3%); IR (Neat) ν_{max} 2960, 2872, 1678, 1466, 1054, 904, 665 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 7.56 (d, J = 1.9 Hz, 1H), 7.44 (d, J = 2.0 Hz, 1H), 7.28-7.19 (m, 2H), 5.11 (t, J = 7.2 Hz, 1H), 3.69 (t, J = 7.2 Hz, 1H), 2.68 (d, J = 15.8 Hz, 1H), 2.18-1.29 (m, 26H), 1.22 (s, 3H), 1.19 (s, 3H), 1.18 (s, 3H), 1.15 (s, 3H), 0.95 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): 207.1, 136.2, 135.5, 134.4, 133.3, 132.8, 131.5, 130.8, 129.5, 126.6, 124.5, 85.5, 82.1, 72.7, 59.7, 57.1, 53.5, 45.6, 44.0, 38.0, 37.5, 36.3, 29.6, 29.3, 28.9, 25.9, 25.6, 25.2, 24.3, 23.8, 22.6, 22.3, 22.1, 21.3, 21.2, 17.6, 15.5; HRMS (ESI+) calculated for $[\text{C}_{37}\text{H}_{52}\text{Cl}_2\text{O}_3 - \text{H}]^+$: 613.3216, Found: 613.3210.

Compound 2j

The compound **2j** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 4-chlorobenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 72.1 mg (57%); IR

(Neat) ν_{max} 2958, 2853, 1678, 1462, 1078, 908, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 7.48 (d, J = 1.4 Hz, 1H), 7.39 - 7.32 (m, 4H), 5.12 (t, J = 7.0 Hz, 1H), 3.71 (t, J = 7.0 Hz, 1H), 2.87 (d, J = 16.2 Hz, 1H), 2.31-2.20 (m, 2H), 2.18-1.31 (m, 22H), 1.26 (s, 3H), 1.25 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 1.15 (s, 3H), 0.96 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ = 207.5, 136.2, 134.3, 131.5, 131.4, 128.6, 124.5, 85.6, 82.1, 72.7, 59.7, 57.2, 53.0, 45.1, 44.8, 43.9, 38.0, 37.6, 36.0, 29.6, 29.6, 29.5, 29.3, 25.9, 25.6, 25.1, 24.3, 23.8, 22.6, 22.2, 22.1, 21.5, 21.3, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{37}\text{H}_{53}\text{O}_3\text{Cl} - \text{OH}]^+$: 563.3656, Found: 563.3642.

Compound 2k

The compound **2k** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 4-bromobenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 75.4 mg (55.4%); IR (Neat) ν_{max} 2963, 2874, 1674, 1453, 1073, 906, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 7.53 (d, J = 8.4 Hz, 2H), 7.45 (s, 1H), 7.31-7.25 (m, 2H), 5.12 (t, J = 7.0 Hz, 1H), 3.71 (t, J = 6.9 Hz, 1H), 2.86 (d, J = 16.5 Hz, 1H), 2.38 (s, 1H), 2.26 (d, J = 16.5 Hz, 1H), 2.18-1.29 (m, 24H), 1.25 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 0.96 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 207.5, 136.2, 134.7, 134.5, 131.6, 131.5, 131.5, 124.5, 122.6, 85.5, 82.1, 72.7, 59.6, 57.1, 53.0, 45.1, 44.8, 43.9, 38.0, 37.6, 36.0, 29.4, 25.9, 25.6, 25.1, 24.3, 23.8, 22.2, 22.1, 21.5, 21.3, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{37}\text{H}_{53}\text{BrO}_3 - \text{H}]^+$: 623.3100, Found: 623.3139.

Compound 2l

The compound **2l** was prepared according to the general procedure described above by the reaction between malabaricol **1** with phthalaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 109.3mg (49.4%); IR (Neat) ν_{max}

2968, 2879, 1678, 1452, 1025, 908, 668 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 7.54 (d, J = 1.0 Hz, 1H), 7.48 (s, 2H), 5.12 (t, J = 7.0 Hz, 1H), 3.71 (t, J = 6.7 Hz, 1H), 2.95 (d, J = 16.4 Hz, 1H), 2.34 (d, J = 16.4 Hz, 1H), 2.16-1.31 (m, 20H), 1.69 (s, 3H), 1.62 (s, 3H), 1.26 (s, 3H), 1.21 (s, 3H), 1.18 (s, 3H), 1.15 (s, 3H), 0.97 (s, 3H), 0.82 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ = 207.4, 136.7, 135.9, 134.4, 131.3, 130.3, 124.5, 85.5, 82.0, 72.6, 57.0, 52.9, 45.0, 44.9, 43.8, 38.0, 37.6, 36.2, 35.9, 29.5, 25.9, 25.6, 25.1, 24.2, 22.2, 22.1, 21.5, 21.3, 17.5, 15.6. HRMS (ESI+) calculated for $[\text{C}_{68}\text{H}_{102}\text{O}_6 + \text{Na}]^+$: 1037.7569 Found: 1037.7578.

Compound 2m

The compound **2m** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 3-pyridinebenzaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 79.8 mg (67%); IR (Neat) ν_{max} 2965, 2875, 1678, 1454, 1021, 906, 665 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 8.69 (d, J = 1.6 Hz, 1H), 8.55 (dd, J = 4.8, 1.5 Hz, 1H), 7.73 (m, 1H), 7.47 (s, 1H), 7.38-7.33 (m, 1H), 5.11 (t, J = 7.0 Hz, 1H), 3.71 (t, J = 6.8 Hz, 1H), 2.87 (d, J = 16.3 Hz, 1H), 2.40-2.27 (m, 1H), 2.15-1.30 (m, 25H), 1.24 (s, 3H), 1.21 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 0.96 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 207.7, 137.6, 135.9, 133.8, 131.5, 130.3, 128.4, 128.3, 124.5, 85.6, 82.1, 72.7, 59.9, 57.2, 53.1, 45.1, 44.9, 43.9, 38.1, 37.6, 36.4, 36.0, 29.6, 29.5, 26.0, 25.6, 25.1, 24.3, 23.8, 22.3, 22.2, 21.5, 21.4, 17.6, 15.6; HRMS (ESI+) calculated for $[\text{C}_{36}\text{H}_{53}\text{NO}_3 + \text{H}]^+$: 548.4098, Found: 548.4110.

Compound 2n

The compound **2n** was prepared according to the general procedure described above by the reaction between malabaricol **1** with 2-pyridinecarboxaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 82.7 mg (69.3%);

IR (Neat) ν_{max} 2958, 2852, 1679, 1457, 1076, 906, 665 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 8.69 (dd, J = 4.7, 0.9 Hz, 1H), 7.69 (td, J = 7.7, 1.8 Hz, 1H), 7.42 (dd, J = 2.7, 1.5 Hz, 1H), 7.38 (d, J = 7.9, Hz 1H), 7.18 (dddd, J = 12.3, 7.4, 4.8, 0.7 Hz, 1H), 5.11 (t, J = 7.0 Hz, 1H), 3.70 (t, J = 6.8 Hz, 1H), 3.41 (d, J = 17.3 Hz, 1H), 2.48 (d, J = 17.3, Hz, 1H), 2.14-1.97 (m, 3H), 1.79-1.31 (m, 22H), 1.24 (s, 3H), 1.20 (s, 3H), 1.18 (s, 3H), 1.14 (s, 3H), 0.96 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 208.5, 155.5, 149.4, 138.2, 136.0, 134.5, 131.4, 126.6, 124.5, 122.2, 85.6, 82.0, 72.7, 59.9, 56.8, 53.0, 45.2, 43.8, 38.0, 37.5, 36.2, 35.8, 29.6, 29.4, 26.0, 25.6, 25.1, 24.3, 23.8, 22.1, 21.5, 21.3, 17.6, 15.8; HRMS (ESI+) calculated for $[\text{C}_{36}\text{H}_{53}\text{NO}_3 + \text{H}]^+$: 548.4098, Found: 548.4111.

Compound 2o

The compound **2o** was prepared according to the general procedure described above by the reaction between malabaricol **1** with furan-2-carbaldehyde and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 78.0 mg (66.7%); IR (Neat) ν_{max} 2959, 2872, 1671, 1455, 1074, 907, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 7.55 (d, J = 1.5 Hz, 1H), 7.34 - 7.31 (m, 1H), 6.59 (d, J = 3.4 Hz, 1H), 6.50 (dd, J = 3.3, 1.7 Hz, 1H), 5.12 (t, J = 7.0 Hz, 1H), 3.70 (t, J = 7.2 Hz, 1H), 3.02 (d, J = 17.3 Hz, 1H), 2.27 (d, J = 17.4 Hz, 1H), 2.18-1.89 (m, 2H), 1.89-1.32 (m, 17H), 1.68 (d, J = 0.6 Hz, 1H), 1.62 (s, 3H), 1.26 (s, 3H), 1.25 (s, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 1.10 (s, 3H), 0.98 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 207.2, 152.5, 144.3, 131.5, 130.9, 124.5, 124.3, 115.3, 112.1, 85.6, 82.1, 72.7, 57.1, 52.8, 45.1, 44.8, 43.9, 38.1, 37.6, 35.5, 29.7, 29.6, 25.6, 25.0, 24.3, 22.2, 22.1, 21.6, 21.4, 17.6, 16.0; HRMS (ESI+) calculated for $[\text{C}_{35}\text{H}_{52}\text{O}_4 + \text{H}]^+$: 537.3938, Found: 537.3930.

Compound 3

To a stirred solution of malabaricol **1** (100 mg, 218 μmol) and ethylformate (88 μL , 1.09 mmol) in THF at 0° C was added potassium *tert*-butoxide (98 mg, 872 mmol) and stirring was continued for 4 h. The reaction mixture was quenched with saturated NH_4Cl (5 mL) at 0° C followed by concentration of solvent. The reaction mixture was extracted with ethyl acetate (3 x 30 mL), washed with brine, dried over Na_2SO_4 and concentrated. The obtained residue was purified by column chromatography (12/88, EtOAc/hexane) to give **3** (75.5 mg, 71.2%) as a light greenish viscous liquid. (IR (Neat) ν_{max} 2965, 2873, 1711, 1453, 1029, 905, 666 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 14.9 (d, J = 3.2 Hz, 1H), 8.56 (d, J = 2.8, Hz, 1H), 5.11 (t, J = 7.0 Hz, 1H), 3.69 (t, J = 7.0 Hz, 1H), 2.21 (d, J = 14.3, Hz, 1H), 2.15-1.24 (m, 29H), 1.20 (s, 6H), 1.11 (s, 3H), 0.96 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): 191.0, 188.1, 131.5, 124.5, 105.8, 85.6, 82.2, 72.7, 59.4, 57.1, 52.4, 44.0, 40.0, 38.1, 37.6, 36.5, 36.0, 28.4, 25.9, 25.6, 25.3, 24.3, 23.9, 22.1, 21.1, 20.5, 17.6, 15.0; HRMS (ESI+) calculated for $[\text{C}_{31}\text{H}_{50}\text{O}_4 + \text{H}]^+$: 487.3782, Found: 487.3770.

Compound 4

To a stirred solution of malabaricol **1** (100 mg, 218 μmol) and hydroxylamine hydrochloride (75.8 mg, 1.09 mmol) in ethanol at room temperature was added acetic acid (100 μL), the reaction mixture was refluxed for 4 h. The reaction mixture was concentrated, extracted with ethyl acetate (3 x 30 mL), washed with brine, dried over Na_2SO_4 and concentrated. The obtained residue was purified by column chromatography (1/9, EtOAc/hexane) to give **4** (47.9 mg, 46.4%) as a light greenish viscous liquid. IR (Neat) ν_{max} 2964, 2873, 1452, 1072, 930, 665 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 9.19 -8.81 (brs, 1H), 5.11 (t, J = 7.0 Hz, 1H), 3.67 (t, J = 6.9 Hz, 1H), 3.12-3.02 (m, 1H), 2.27-2.16 (m, 1H), 2.15-1.24 (m, 21H), 1.68 (d, J = 0.7 Hz, 3H), 1.61 (s, 3H), 1.18 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 1.06 (s, 3H), 0.95 (s, 6H); ^{13}C NMR (100

MHz, CDCl₃): δ = 166.7, 131.4, 124.6, 85.6, 82.1, 72.7, 58.4, 56.1, 44.0, 40.2, 39.0, 38.1, 37.5, 36.9, 36.8, 27.3, 26.0, 25.9, 25.6, 24.3, 23.8, 22.9, 22.1, 21.0, 20.0, 17.5, 17.0, 15.4; HRMS (ESI+) calculated for [C₃₀H₅₁NO₃ + H]⁺: 474.3942, Found: 474.3952.

Compound 5

To a stirred solution of malabaricol **1** (100 mg, 218 μ mol) and 2,4- dinitrophenylhydrazine (130 mg, 654 μ mol) in ethanol at room temperature was added acetic acid (100 μ L), the reaction mixture was refluxed for 4 h. The reaction mixture was concentrated, extracted with ethyl acetate (3 x 30 mL), washed with brine, dried over Na₂SO₄ and concentrated. The obtained residue was purified by column chromatography (1/9, EtOAc/hexane) to give **5** (93.6 mg, 67.2%) as an orange red solid. M.Pt. 109-111 °C IR (Neat) ν_{max} 2966, 2872, 1451, 1071, 921, 666 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 11.7 (s, 1H), 9.12 (d, J = 2.5 Hz, 1H), 8.29 (dd, J = 2.4, 9.4 Hz, 1H), 7.95 (d, J = 9.6 Hz, 1H), 5.10 (t, J = 7.0 Hz, 1H), 3.68 (t, J = 6.8 Hz, 1H), 2.64 (d, J = 15.5 Hz, 1H), 2.55-2.44 (m, 1H), 2.15-1.96 (m, 3H), 1.96-1.24 (m, 18H), 1.68 (s, 3H), 1.61 (s, 3H), 1.31 (s, 3H), 1.20 (s, 3H), 1.19 (s, 3H), 1.17 (s, 3H), 0.98 (s, 3H), 0.96 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 166.8, 145.5, 137.4, 131.5, 128.9, 124.5, 123.5, 116.4, 85.5, 82.2, 72.7, 58.2, 55.7, 44.1, 42.1, 38.6, 38.1, 37.5, 36.5, 28.8, 25.7, 25.6, 24.3, 23.8, 22.1, 21.0, 20.6, 20.5, 17.5, 15.2; HRMS (ESI+) calculated for [C₃₆H₅₄N₄O₆ + H]⁺: 639.4116, Found: 639.4103.

Compound 6a

To a stirred solution of malabaricol **1** (100 mg, 218 μ mol) and phenylhydrazine hydrochloride (95 mg, 654 μ mol) in ethanol at room temperature was added acetic acid (100 μ L), the reaction mixture was refluxed for 4h. The reaction mixture was concentrated, extracted with ethyl acetate (3 x 30 mL), washed with brine, dried over Na₂SO₄ and concentrated. The obtained residue was purified by column chromatography (1/9, EtOAc/hexane) to give indole **6a** (70.9 mg, 61.2%) as

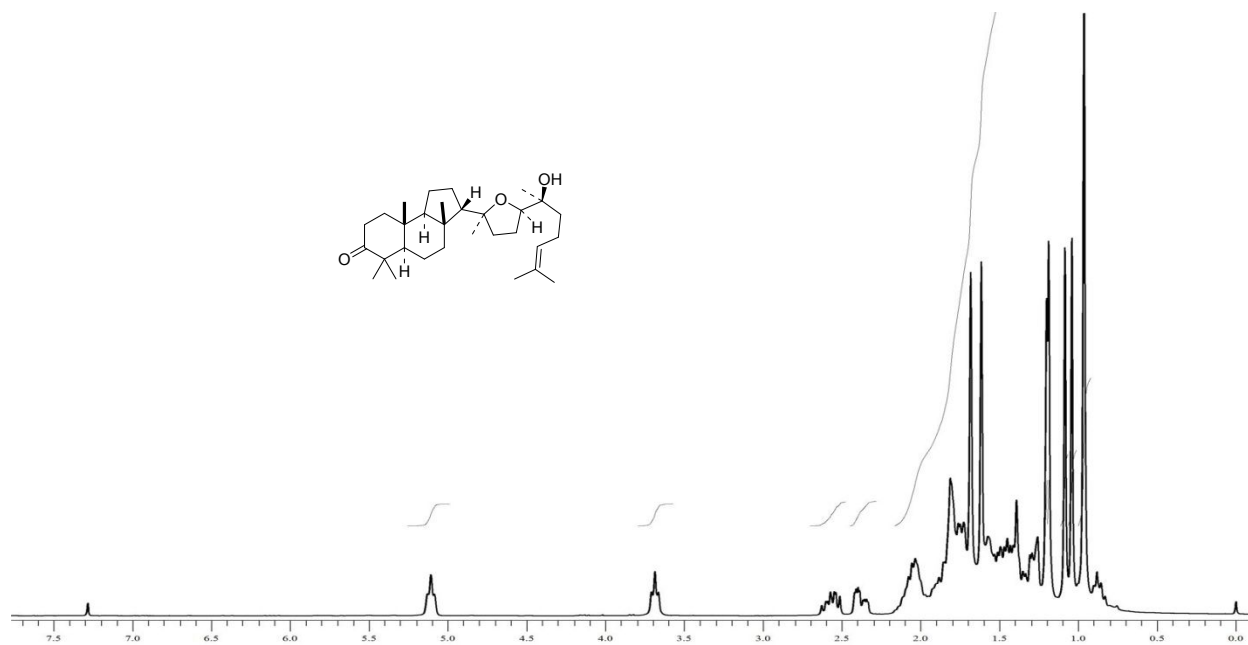
a light greenish viscous liquid. IR (Neat) ν_{max} 2963, 2876, 1459, 1074, 901, 666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 7.75 (s, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.11 (td, J = 1.2, 7.1 Hz, 1H), 7.05 (td, J = 1.2, 7.7 Hz, 1H), 5.11 (t, J = 7.0 Hz, 1H), 3.70 (t, J = 6.8 Hz, 1H), 2.69 (d, J = 15.1 Hz, 1H), 2.25 (d, J = 15.1 Hz, 1H), 2.15-1.22 (m, 20H), 1.68 (s, 3H), 1.61 (s, 3H), 1.31 (s, 3H), 1.24 (s, 3H), 1.22 (s, 3H), 1.20 (s, 3H), 1.00 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 141.0, 136.0, 131.4, 128.2, 124.6, 120.9, 118.8, 118.0, 110.2, 107.0, 85.8, 82.1, 72.8, 57.8, 53.6, 44.2, 38.1, 37.7, 37.5, 33.9, 31.0, 26.9, 25.6, 25.4, 24.3, 22.9, 22.6, 22.2, 21.3, 20.3, 17.6, 16.2, 14.1; HRMS (ESI+) calculated for $[\text{C}_{36}\text{H}_{53}\text{NO}_2 + \text{H}]^+$: 532.4149, Found: 532.4156.

Compound 6b

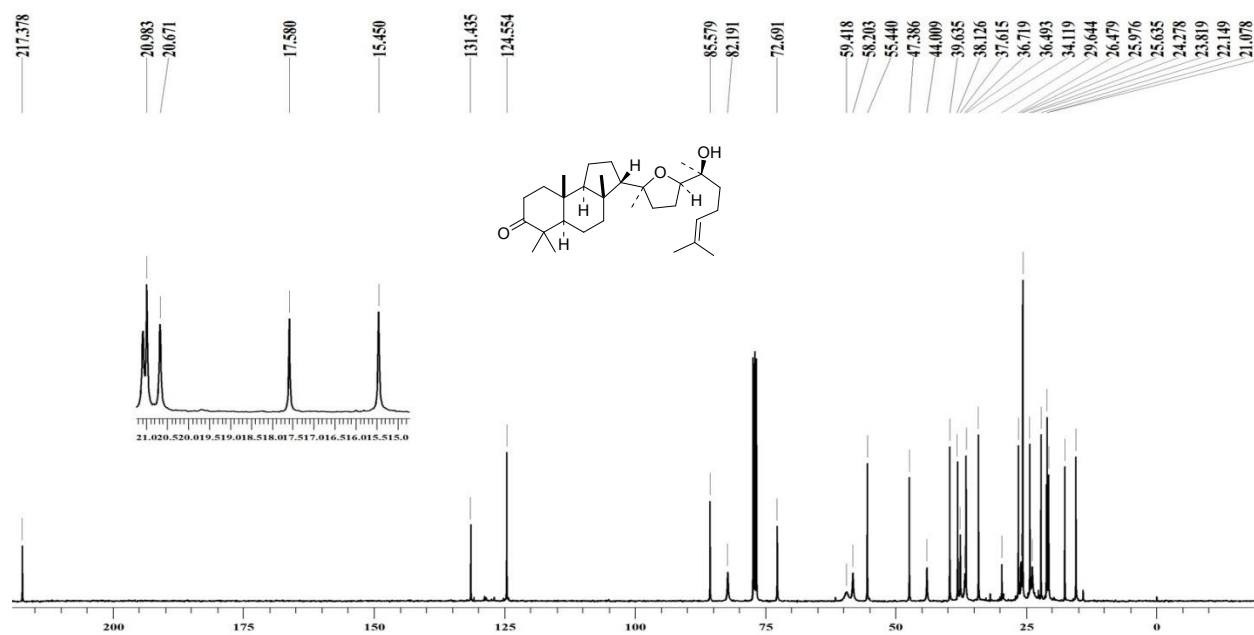
The compound **6b** was prepared according to the procedure **6a** described above by the reaction between malabaricol **1** with 4-bromophenylhydrazine hydrochloride and purified by column chromatography (9/91, EtOAc/hexane) as a light green viscous liquid. Yield 84.7 mg (63.7%); IR (Neat) ν_{max} 2962, 2876, 1458, 1076, 901, 665 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 7.79 (s, 1H), 7.55 (d, J = 1.5 Hz, 1H), 7.20-7.13 (m, 2H), 5.11 (t, J = 6.9 Hz, 1H), 3.70 (t, J = 6.8 Hz, 1H), 2.63 (d, J = 14.9 Hz, 1H), 2.21 (d, J = 14.9 Hz, 1H), 2.25-1.16 (m, 19H), 1.68 (s, 3H), 1.61 (s, 3H), 1.30 (s, 3H), 1.25 (s, 3H), 1.21 (s, 3H), 1.20 (s, 3H), 0.99 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 142.9, 134.5, 131.5, 130.0, 124.5, 123.5, 120.7, 112.0, 111.6, 106.9, 85.7, 82.0, 72.7, 57.6, 53.5, 44.1, 38.1, 37.7, 37.5, 37.3, 34.0, 31.9, 30.9, 29.6, 25.6, 25.4, 24.3, 22.9, 22.6, 22.1, 21.2, 20.2, 17.6, 16.1; HRMS (ESI+) calculated for $[\text{C}_{36}\text{H}_{52}\text{BrNO}_2 + \text{H}]^+$: 610.3254, Found: 610.3258.

Compound 7

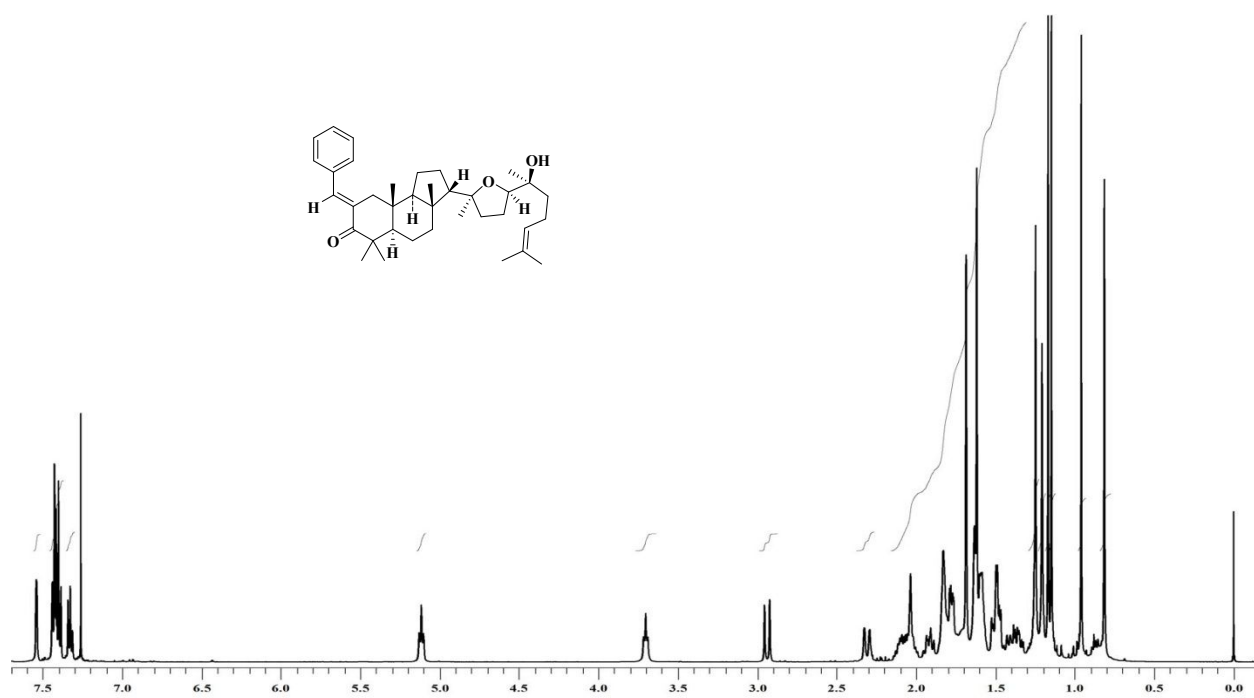
To a stirred solution of malabaricol **1** (100 mg, 218 μmol) ethylenediamine (78 μL , 1.09 mmol) in morpholine at room temperature sulphur (41.8 mg, 1.3mmol) was added and then the reaction mixture was refluxed for 4 h. The reaction mixture was concentrated, the obtained residue was directly purified by column chromatography (1/9, EtOAc/hexane) to give **7** (73.4 mg, 68.1%) as a light greenish viscous liquid. IR (Neat) ν_{max} 2962, 2874, 1452, 1075, 903 665 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ = 8.41 (dd, J = 0.7, 2.3 Hz, 1H), 8.27 (d, J = 2.5 Hz, 1H), 5.11 (t, J = 7.1 Hz, 1H), 3.71 (t, J = 7.1 Hz, 1H), 2.91 (d, J = 16.5 Hz, 1H), 2.57 (d, J = 16.5 Hz, 1H), 2.16-1.40 (m, 18H), 1.68 (s, 3H), 1.61 (s, 3H), 1.41-1.28 (m, 1H), 1.32 (s, 3H), 1.30 (s, 3H), 1.24 (s, 3H), 1.20 (s, 3H), 1.00 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ = 159.8, 150.7, 142.2, 141.4, 131.4, 124.5, 85.6, 82.1, 72.7, 57.2, 53.4, 49.1, 44.0, 39.3, 38.1, 37.6, 36.5, 36.2, 31.6, 26.0, 25.6, 25.2, 24.2, 23.8, 22.1, 21.1, 17.5, 16.0; HRMS (ESI+) calculated for $[\text{C}_{32}\text{H}_{50}\text{N}_2\text{O}_2 + \text{H}]^+$: 495.3945, Found: 495.3932.



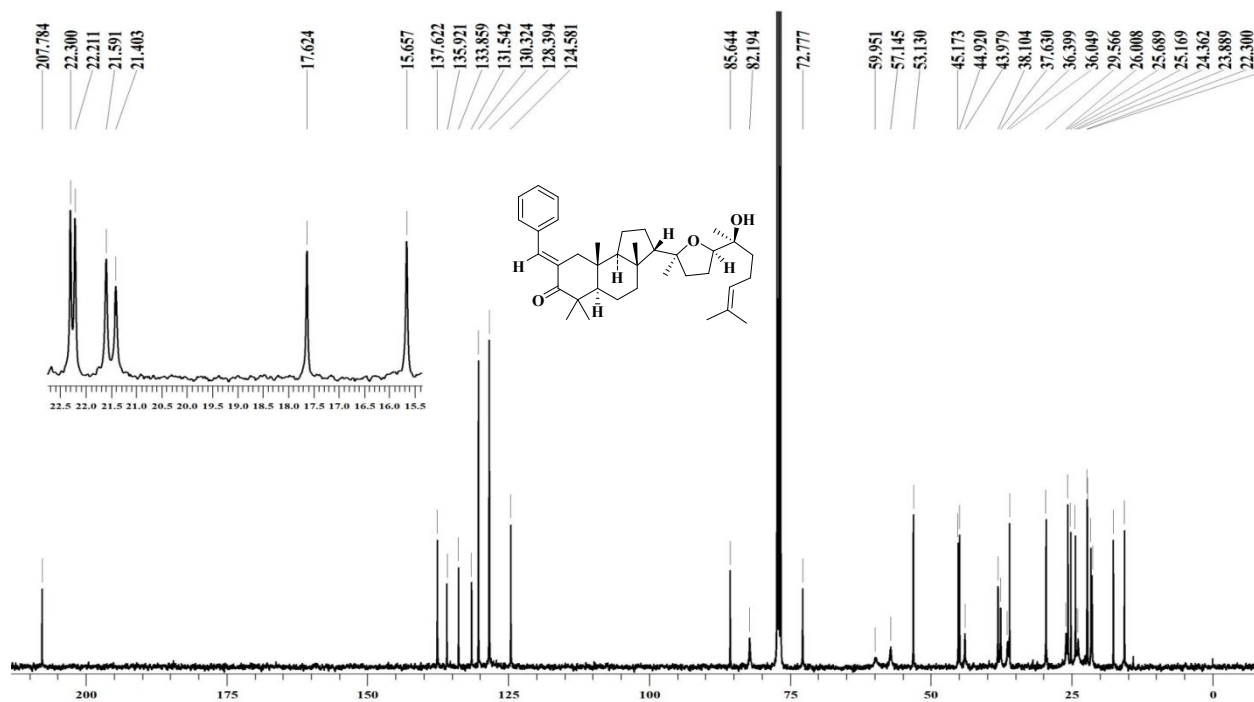
¹H NMR spectrum of compound 1 in CDCl₃



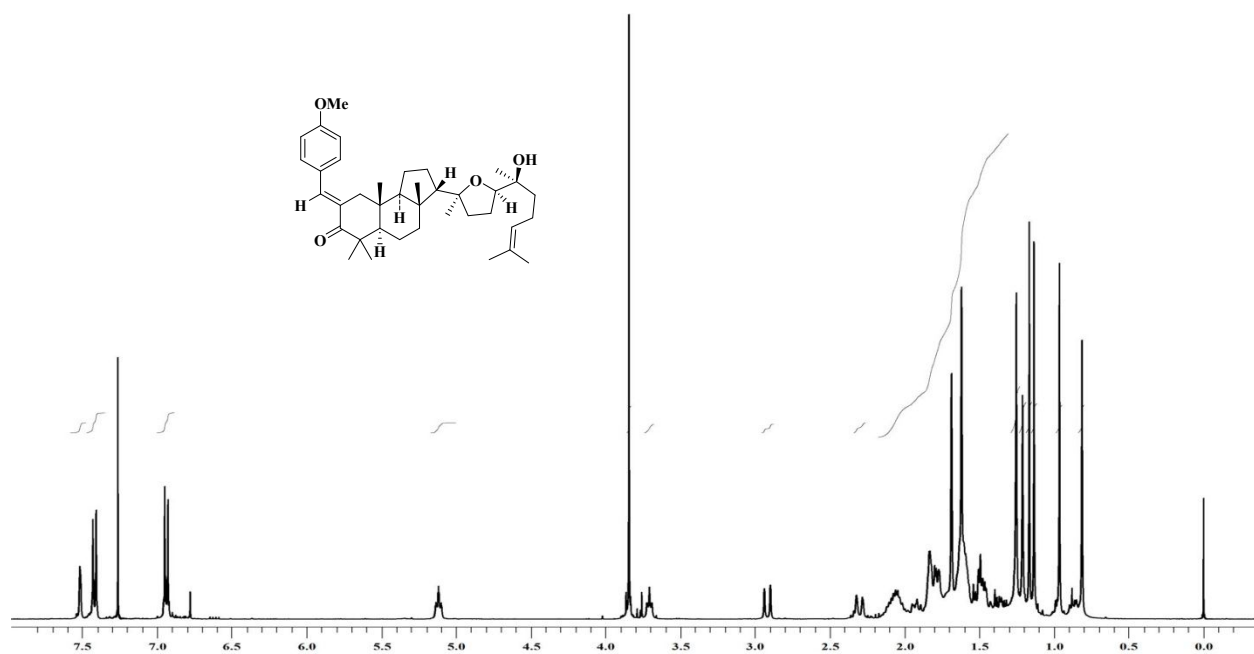
¹³C NMR spectrum of compound 1 in CDCl₃



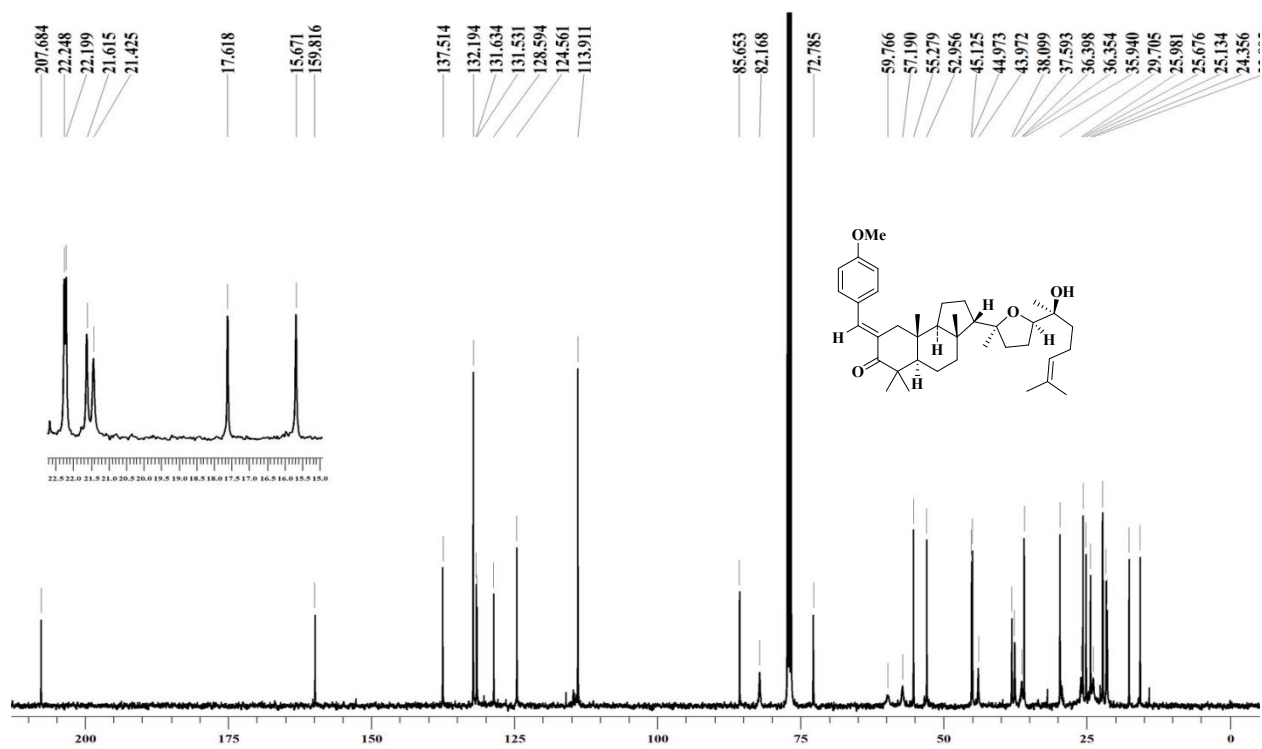
¹H NMR spectrum of compound 2a in CDCl₃



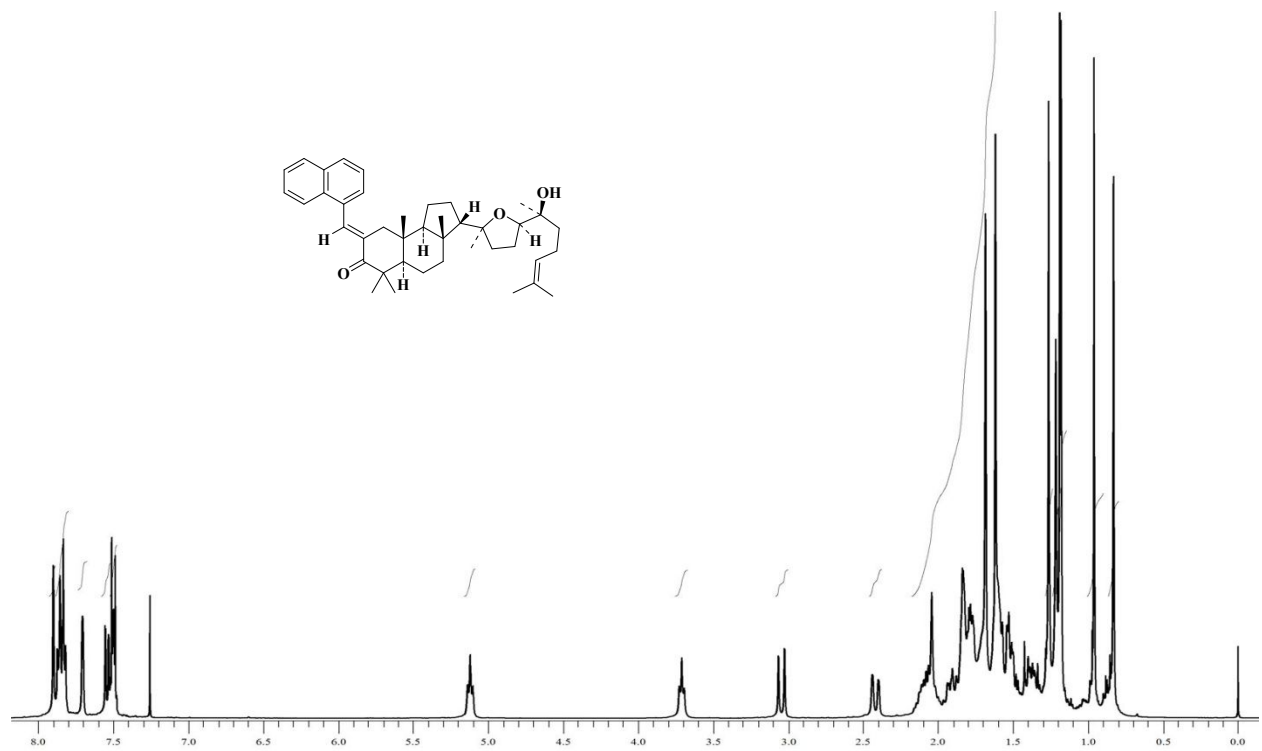
¹³C NMR spectrum of compound 2a in CDCl₃



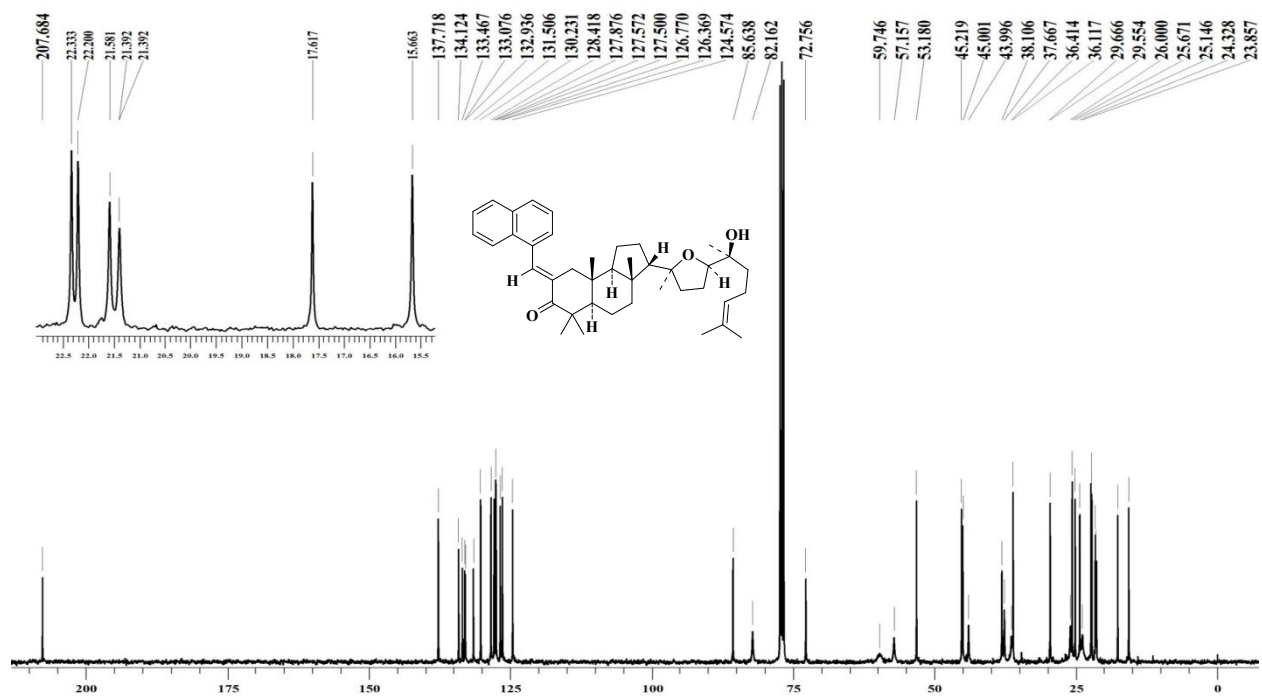
¹H NMR spectrum of compound 2b in CDCl₃



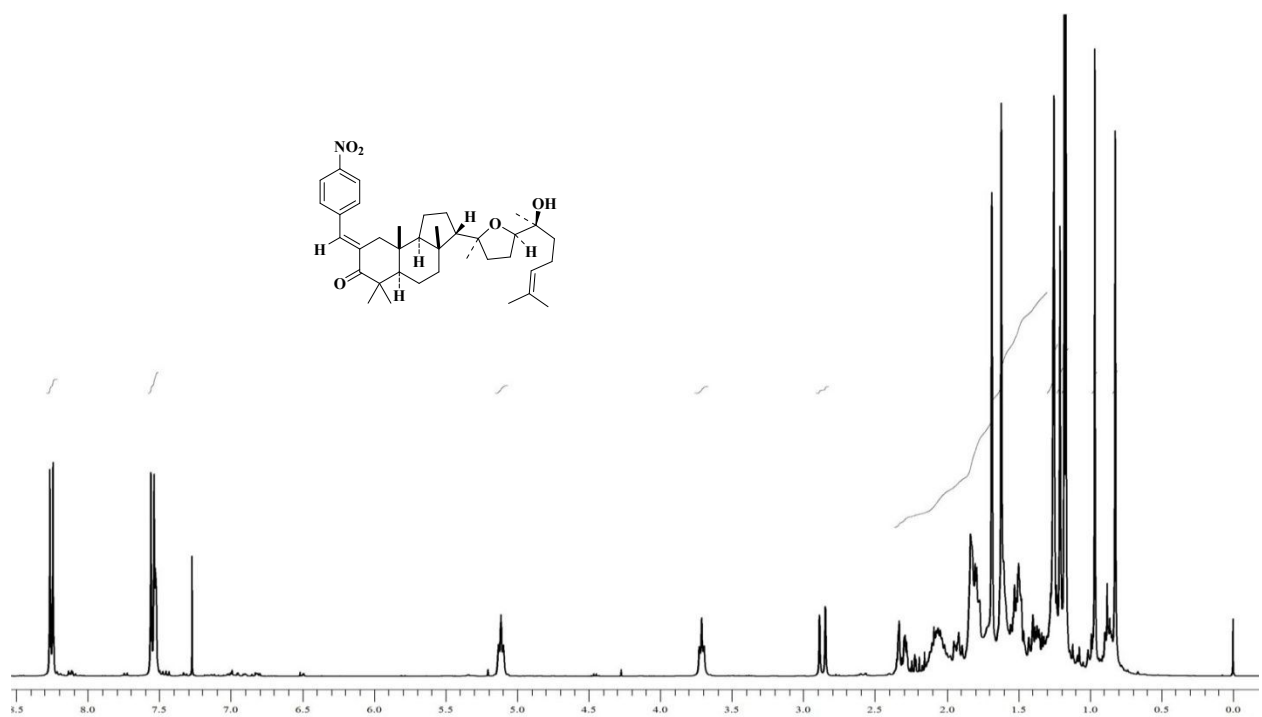
¹³C NMR spectrum of compound 2b in CDCl₃



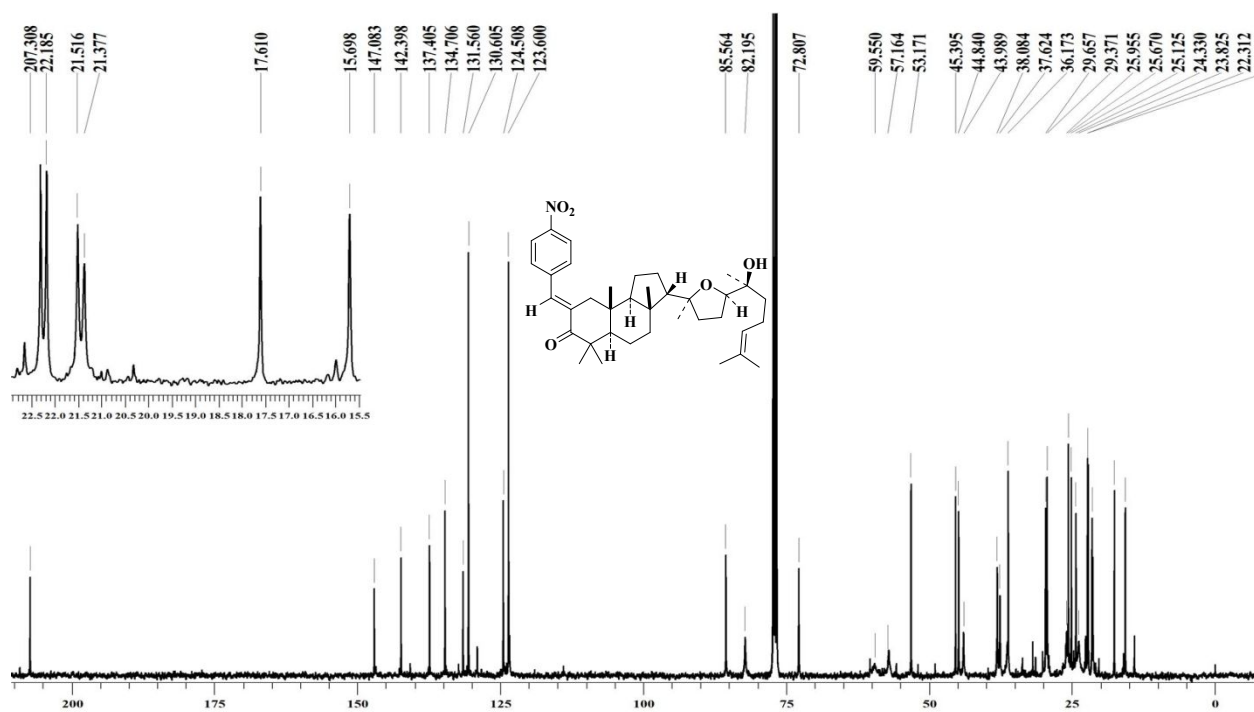
¹H NMR spectrum of compound 2c in CDCl₃



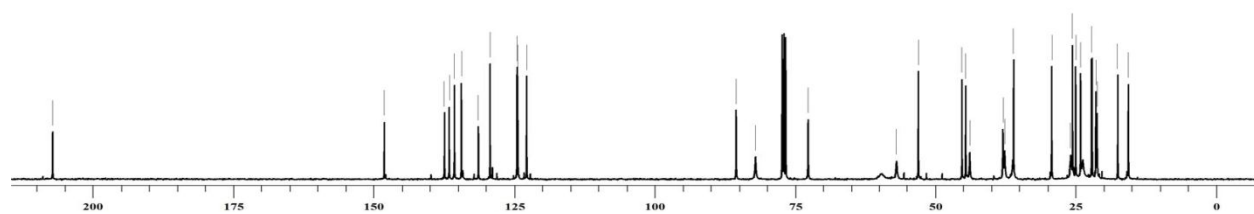
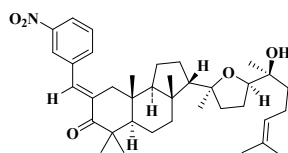
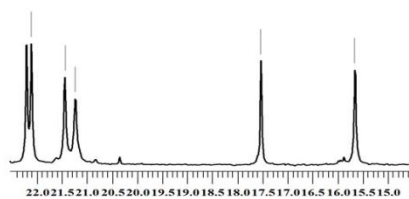
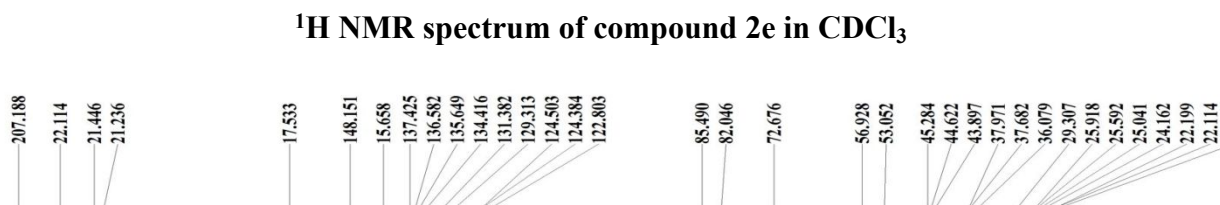
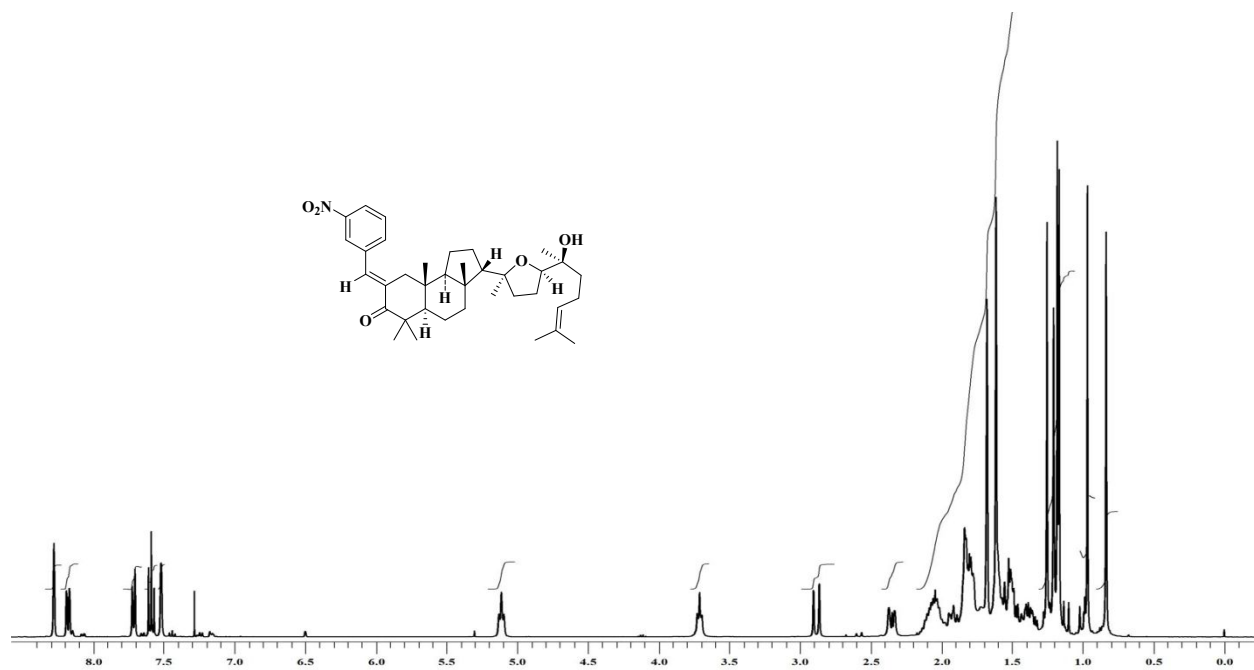
¹³C NMR spectrum of compound 2c in CDCl₃



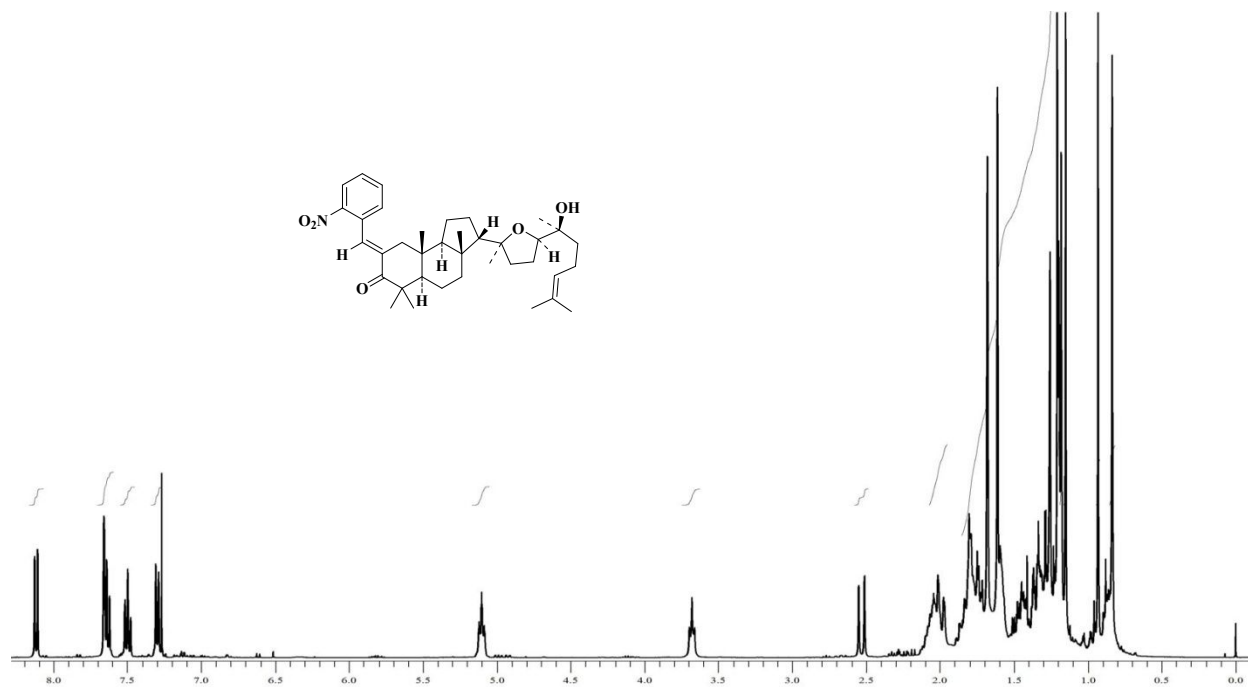
^1H NMR spectrum of compound 2d in CDCl_3



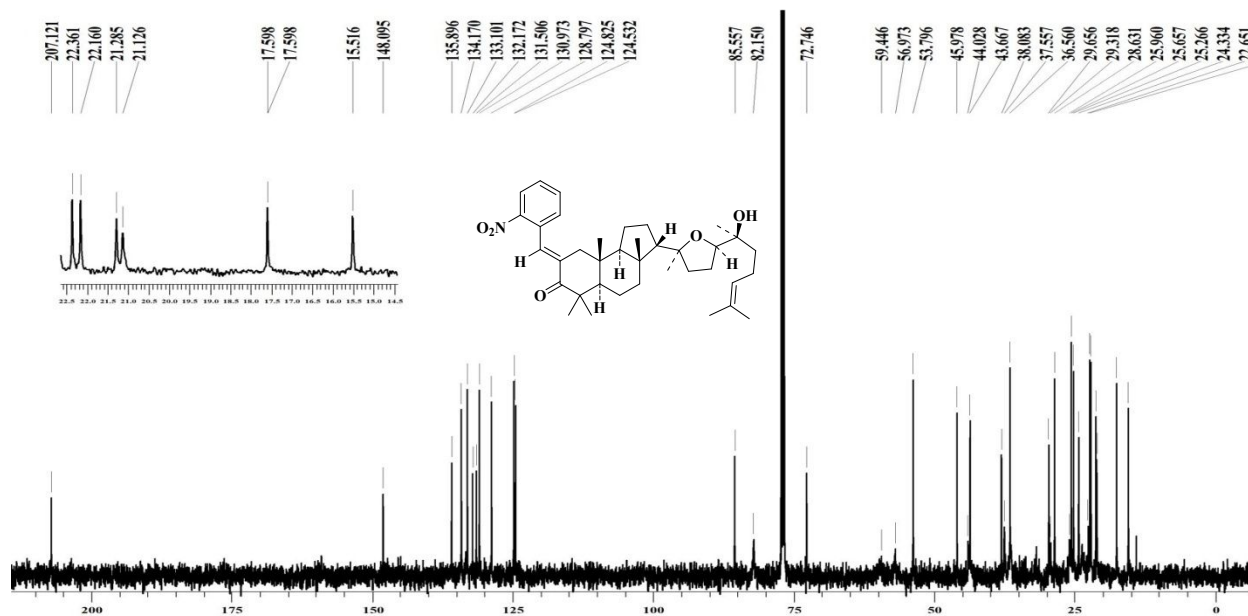
^{13}C NMR spectrum of compound 2d in CDCl_3



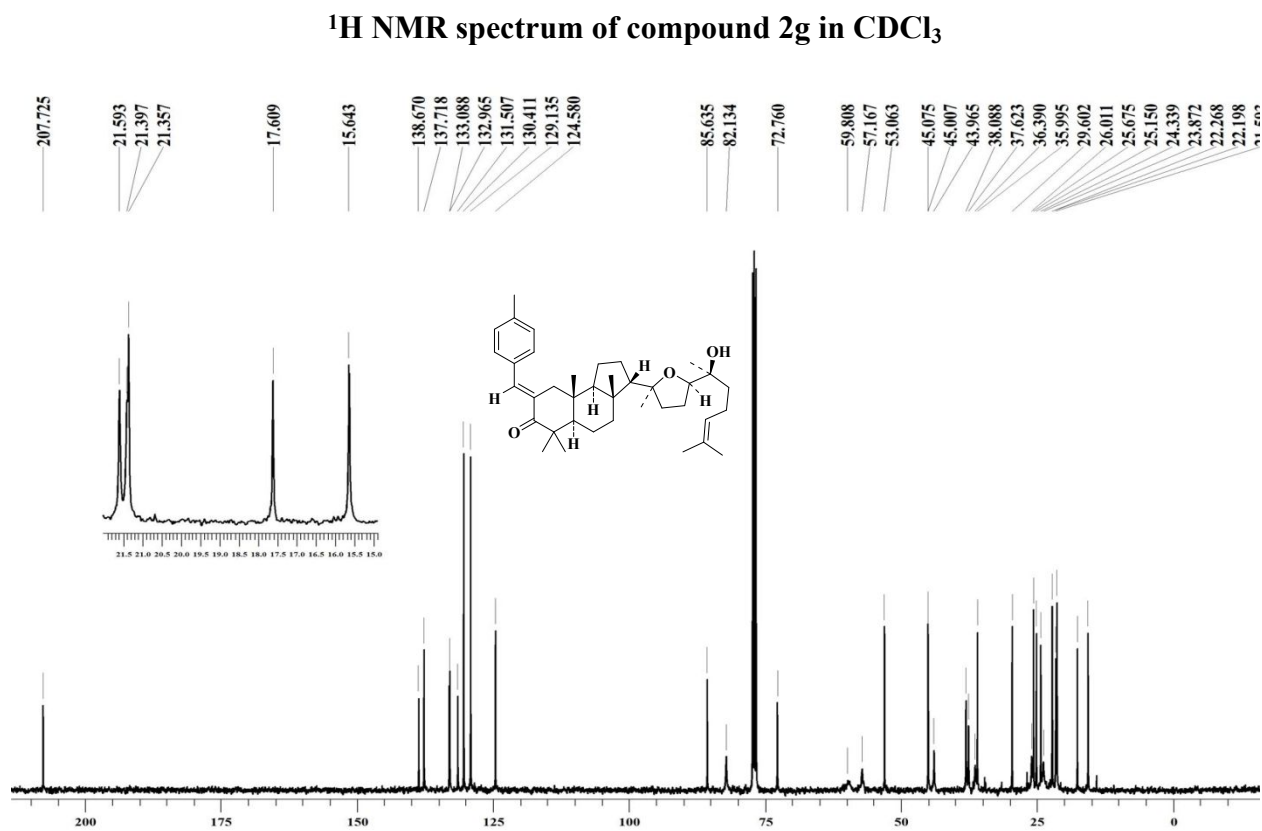
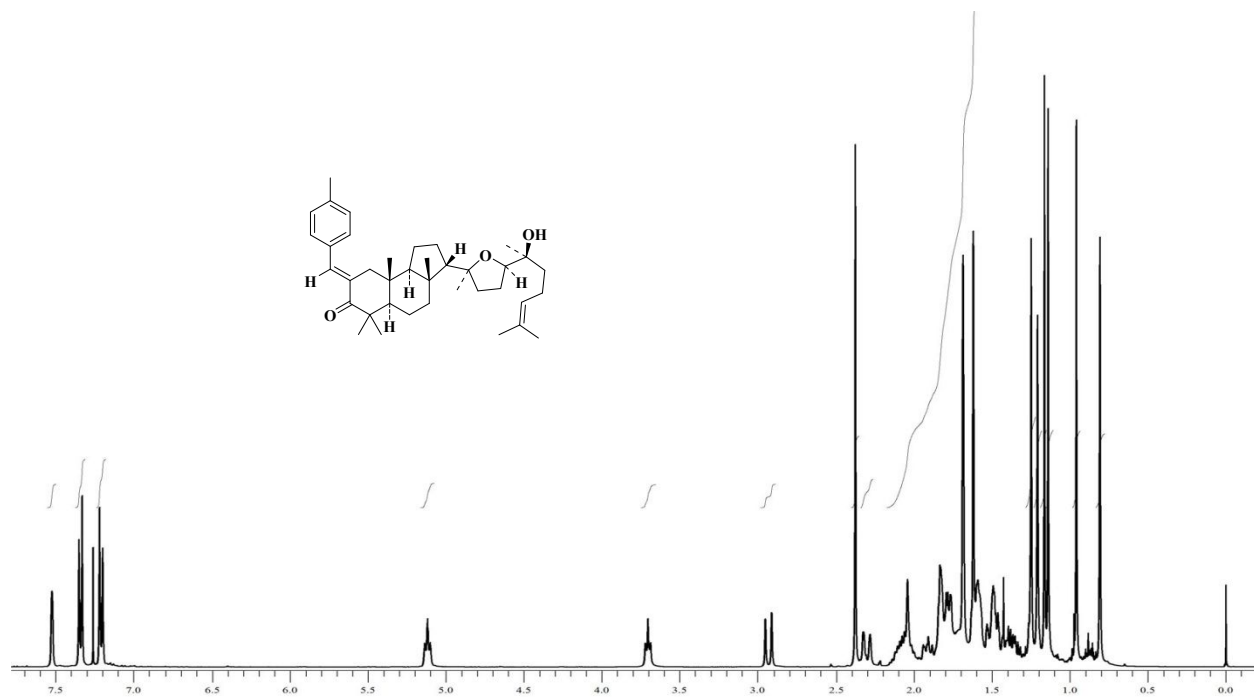
¹³C NMR spectrum of compound 2e in CDCl₃

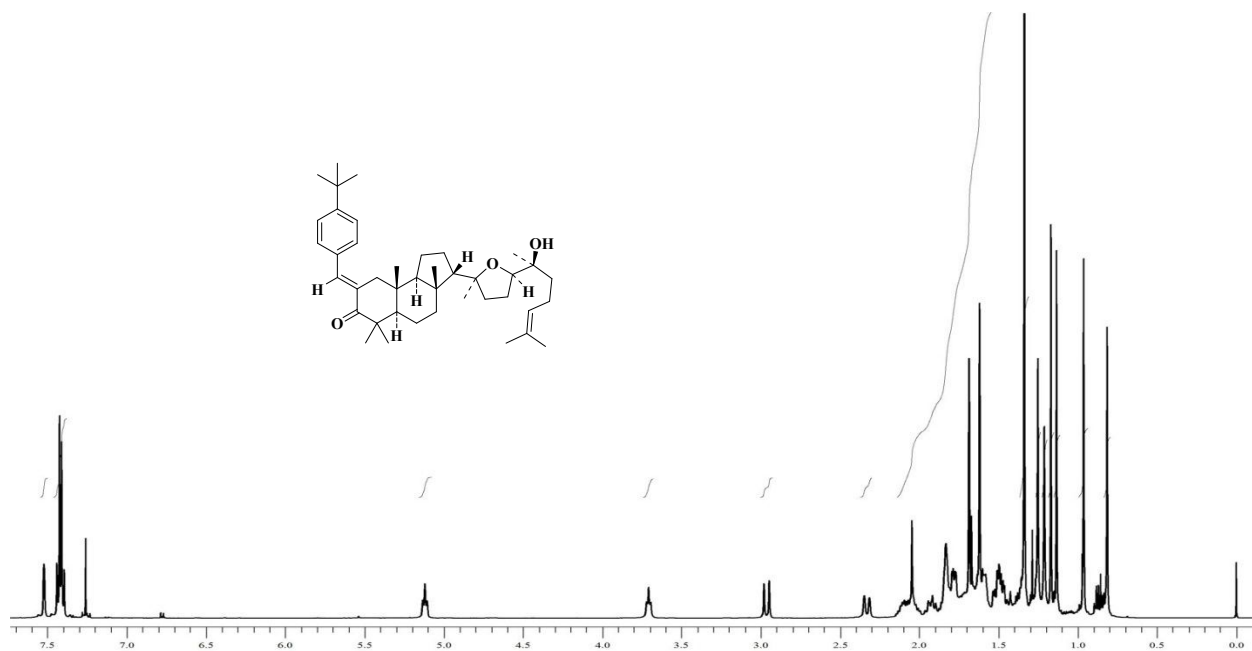


¹H NMR spectrum of compound 2f in CDCl₃

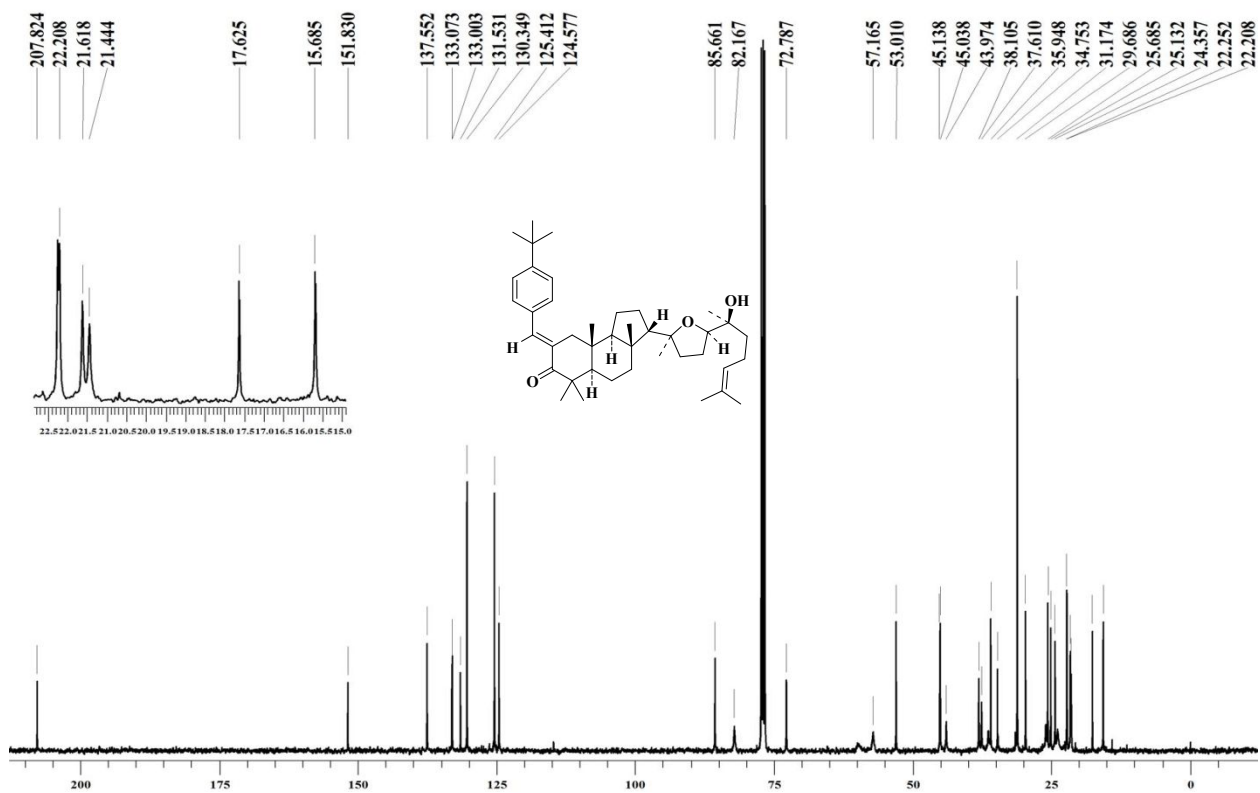


¹³C NMR spectrum of compound 2f in CDCl₃

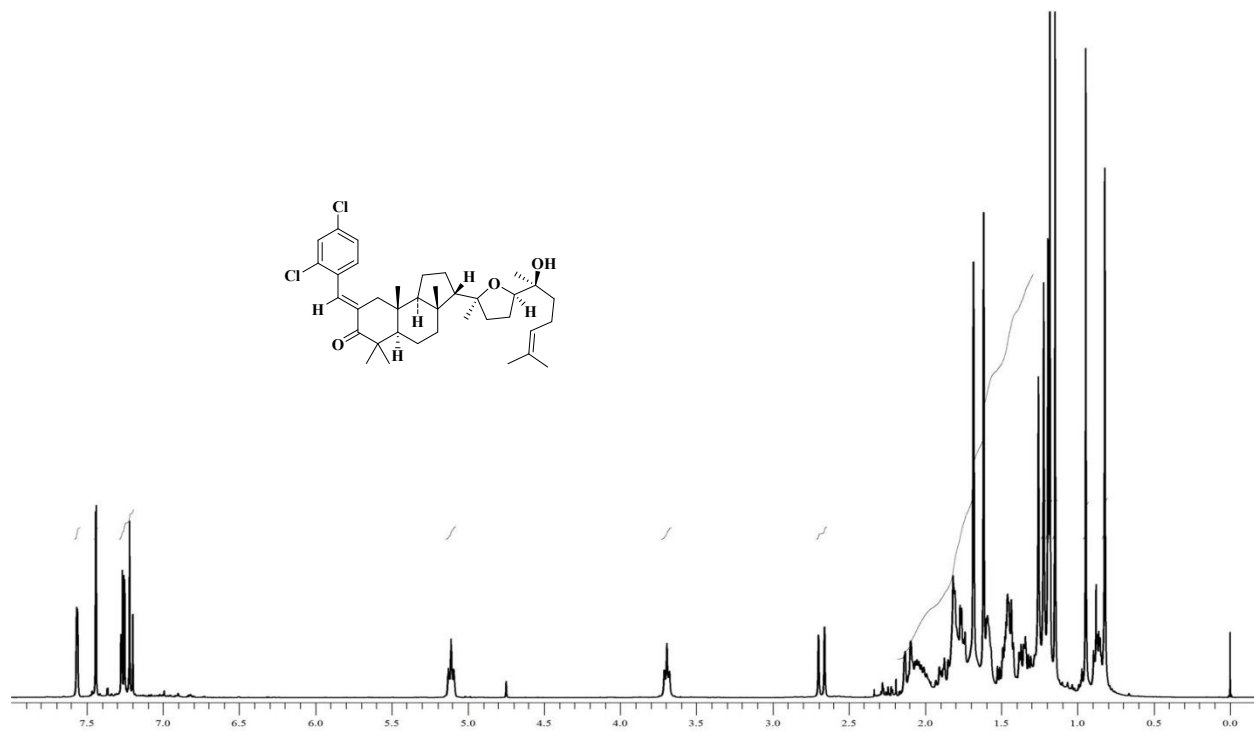




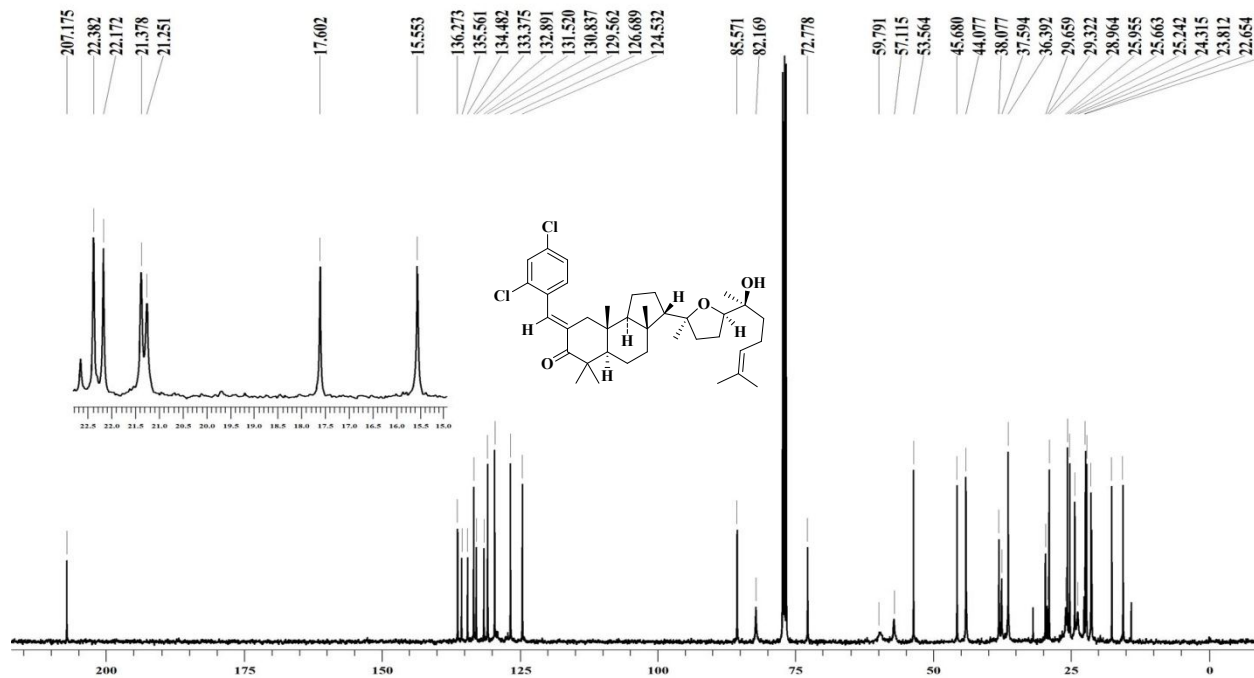
¹H NMR spectrum of compound 2h in CDCl₃



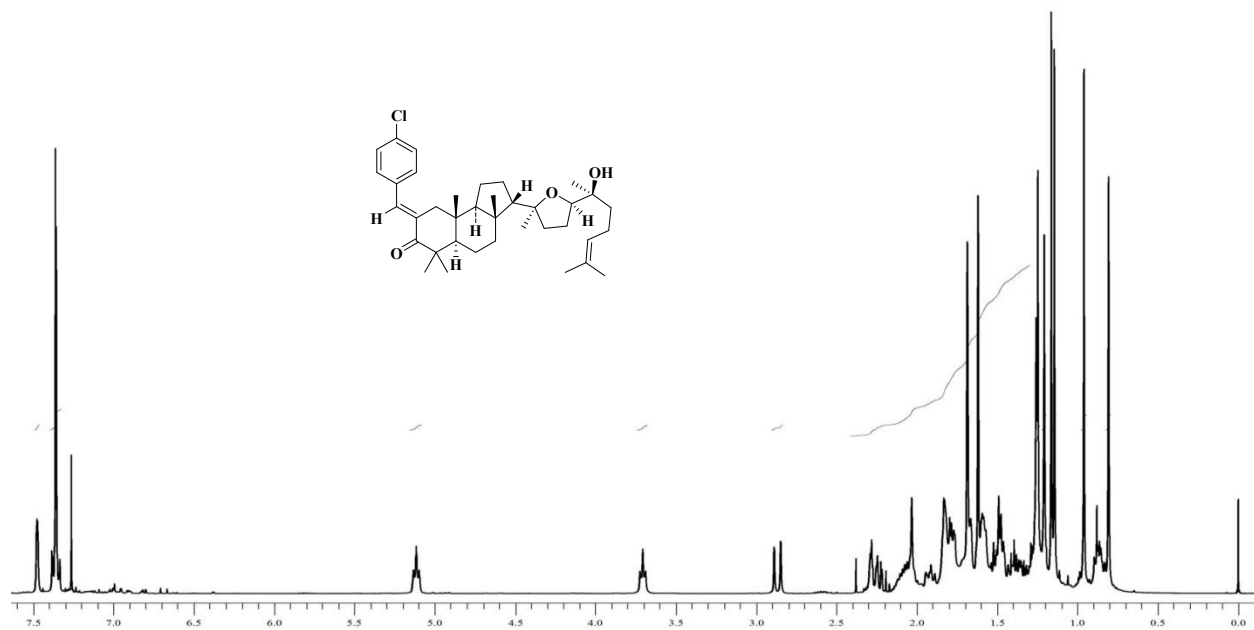
¹³C NMR spectrum of compound 2h in CDCl₃



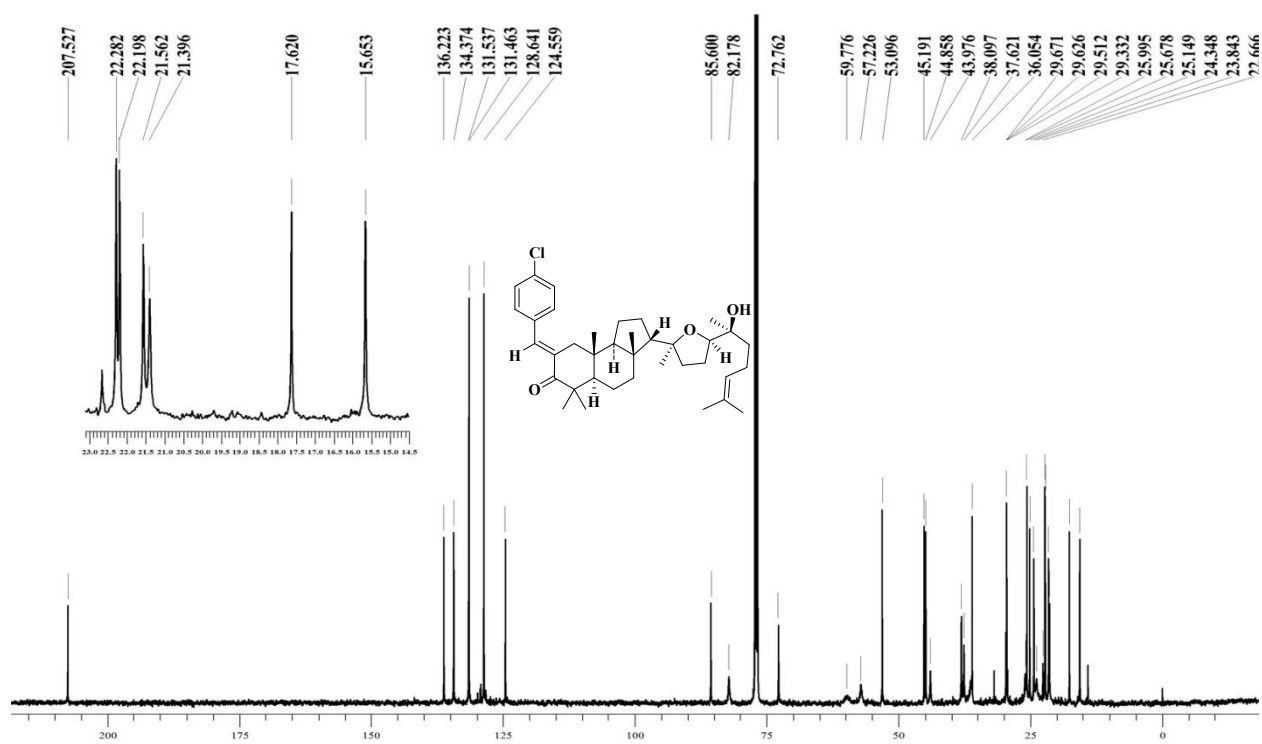
¹H NMR spectrum of compound 2i in CDCl₃



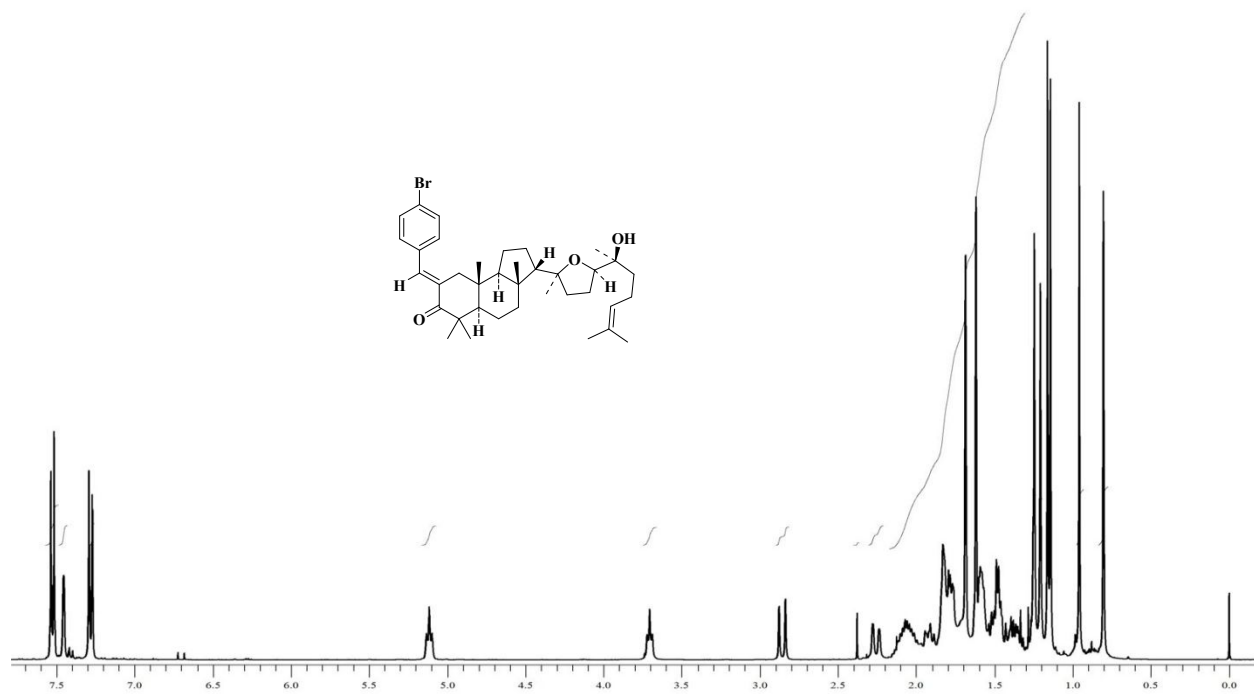
¹³C NMR spectrum of compound 2i in CDCl₃



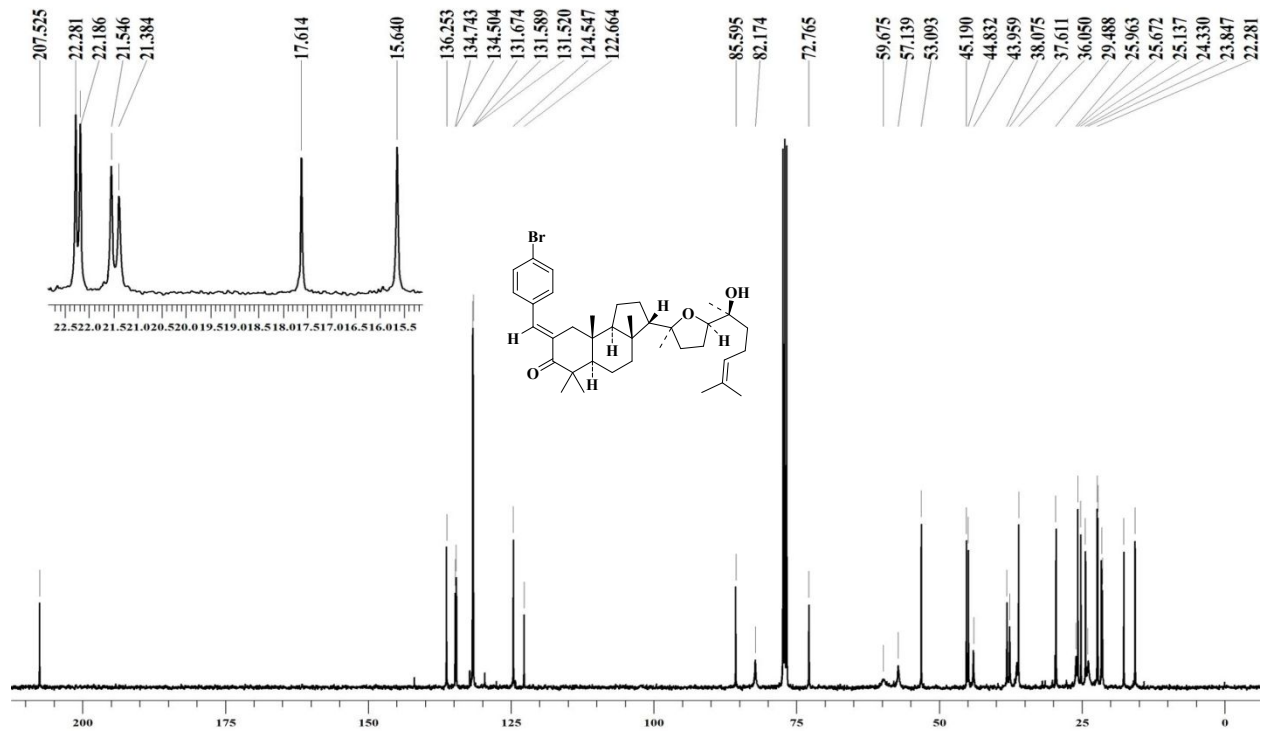
¹H NMR spectrum of compound 2j in CDCl₃



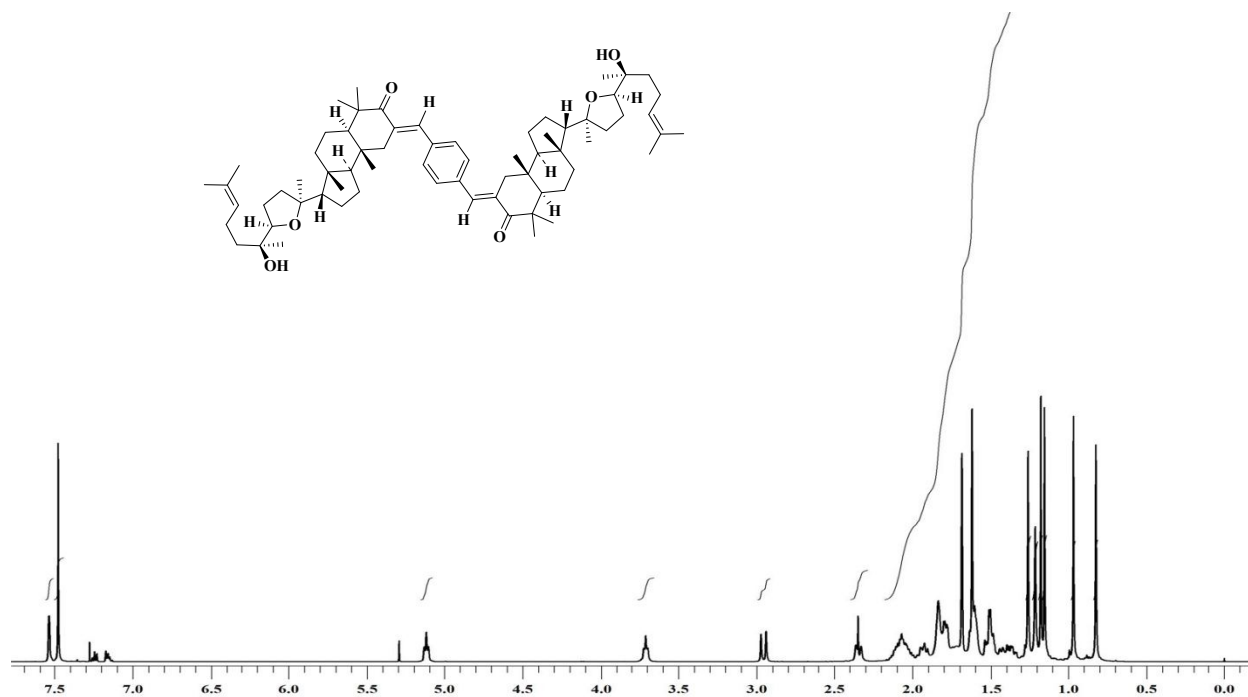
¹³C NMR spectrum of compound 2j in CDCl₃



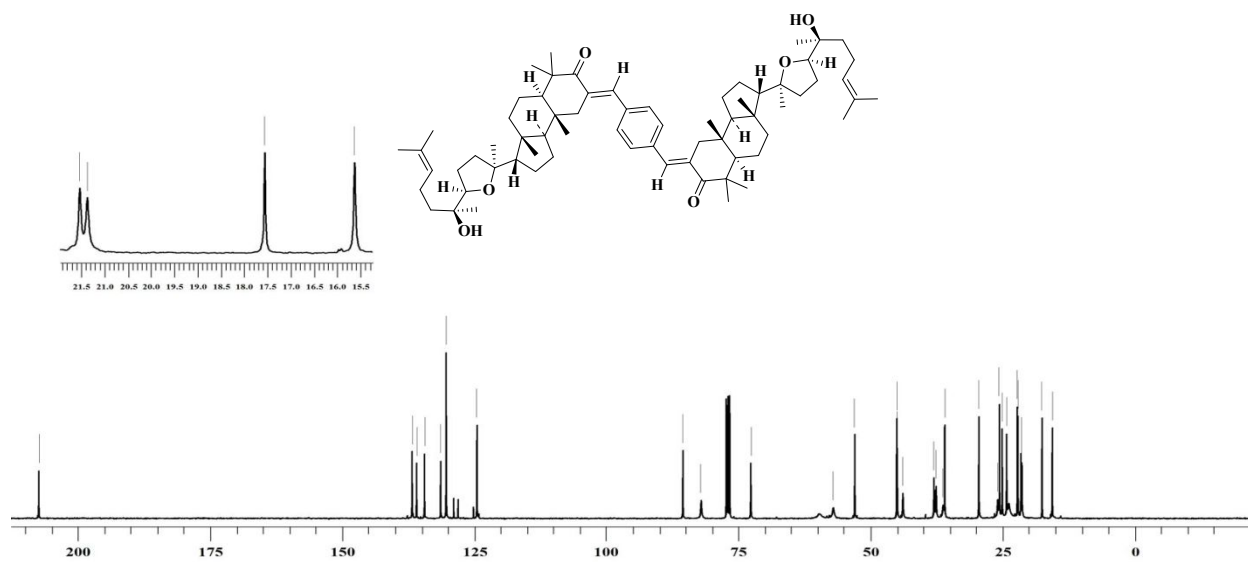
¹H NMR spectrum of compound 2k in CDCl₃



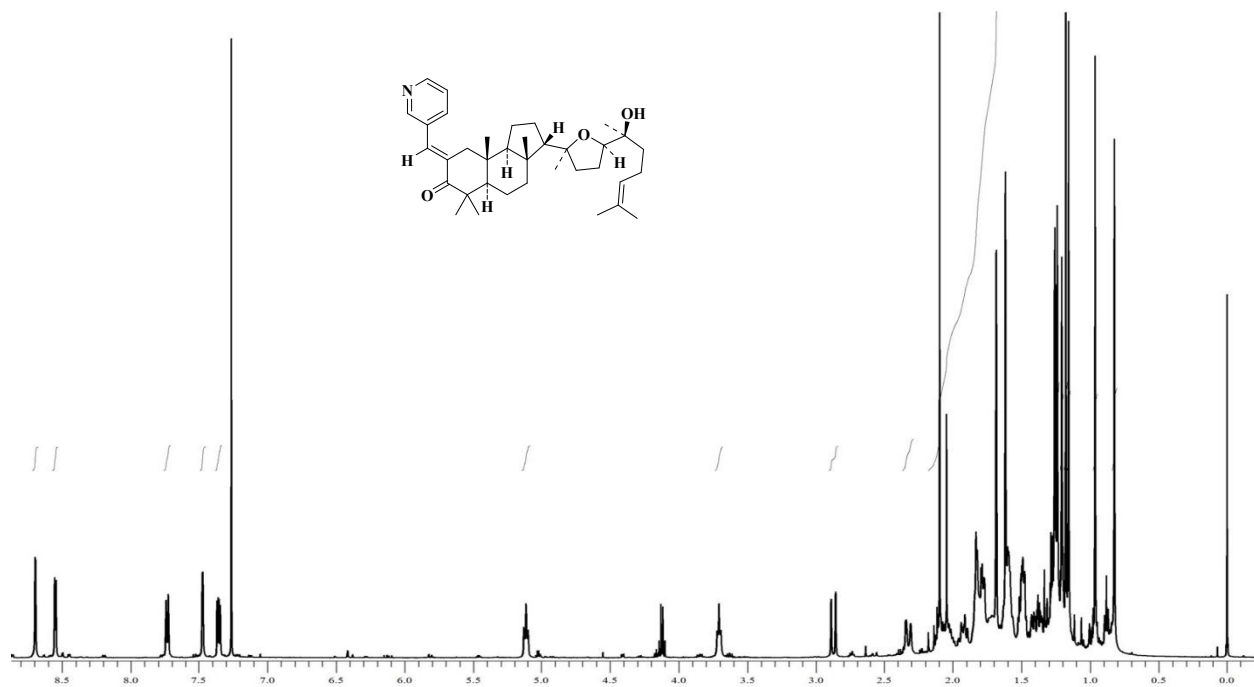
¹³C NMR spectrum of compound 2k in CDCl₃



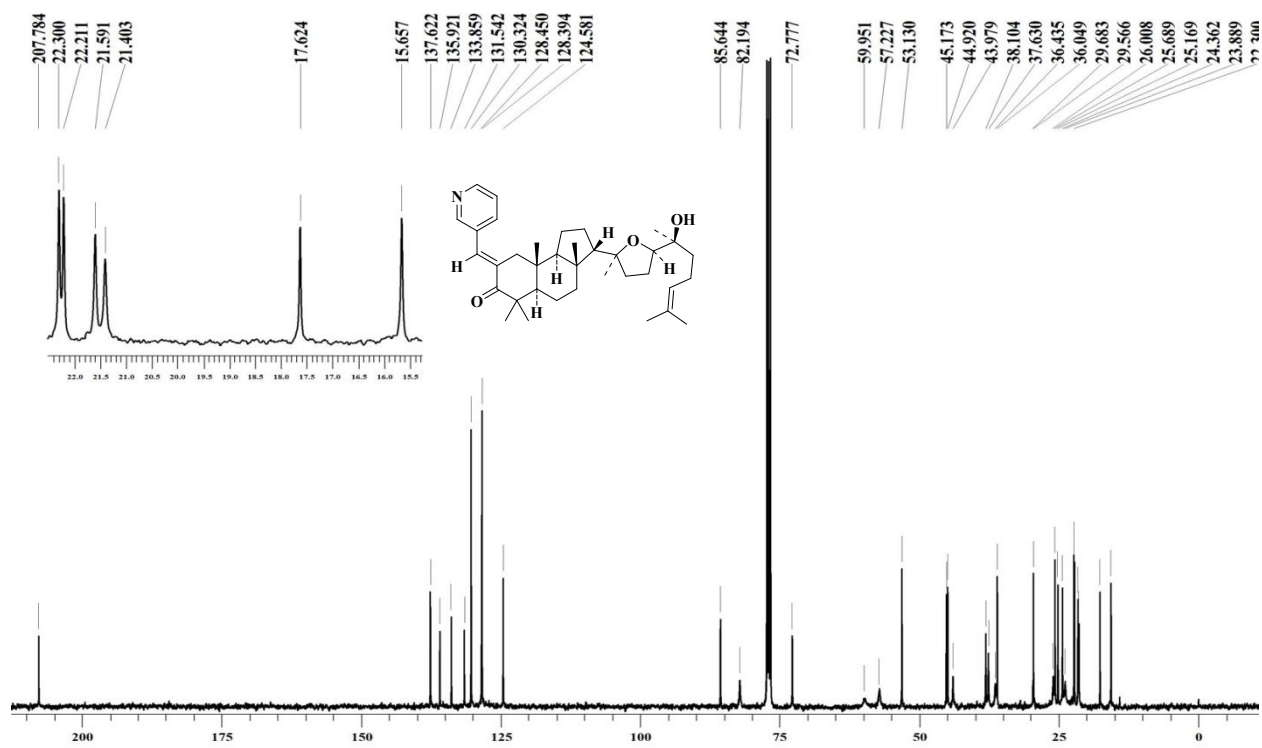
¹H NMR spectrum of compound 2l in CDCl₃



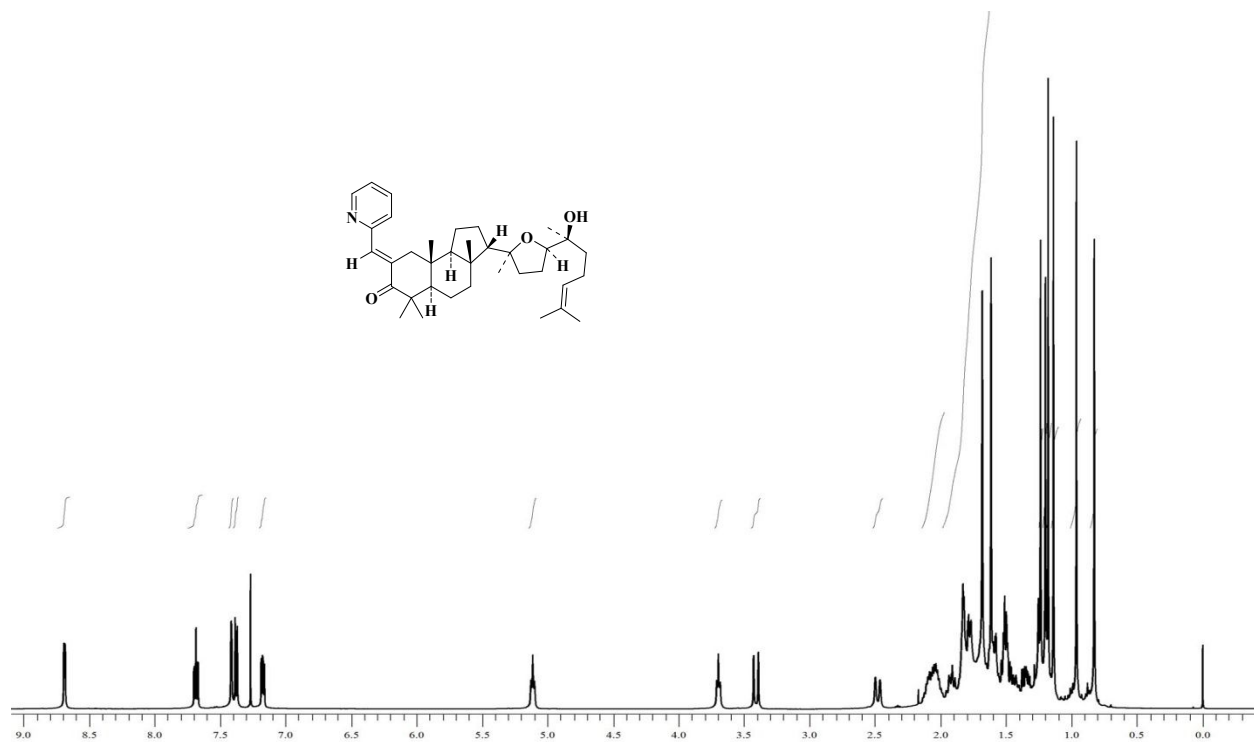
¹³C NMR spectrum of compound 2l in CDCl₃



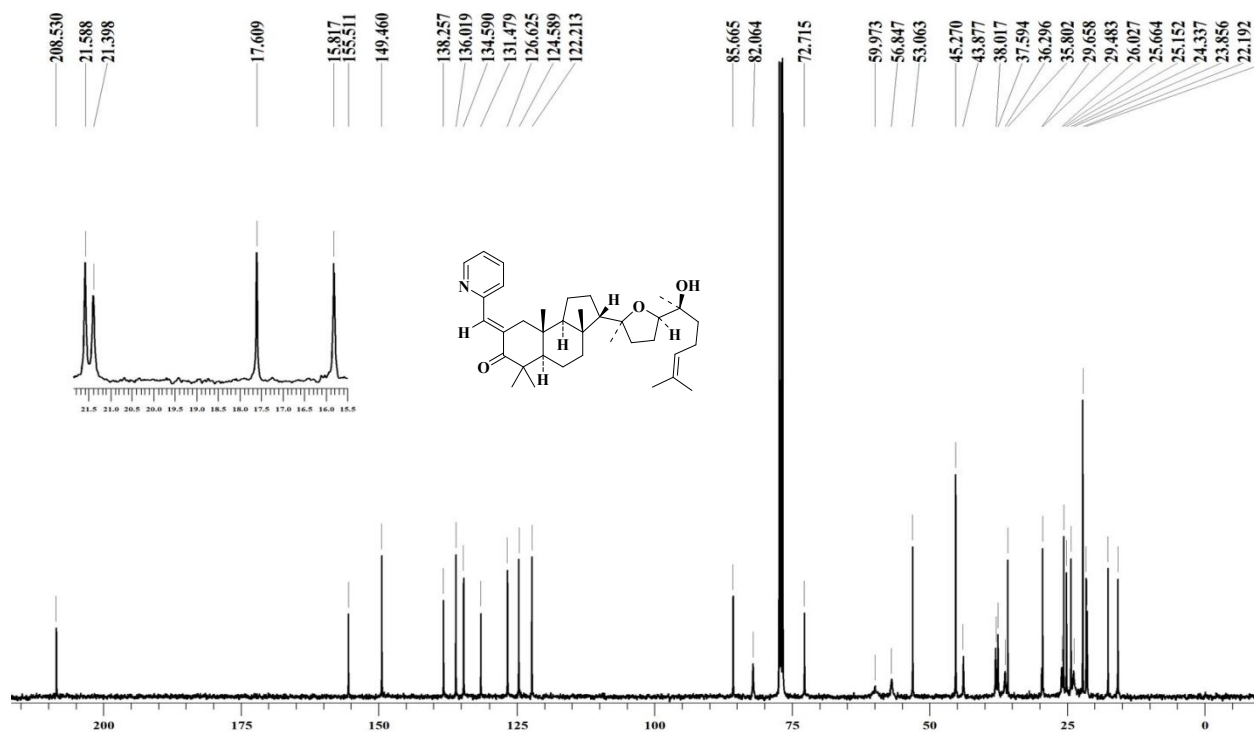
¹H NMR spectrum of compound 2m in CDCl₃



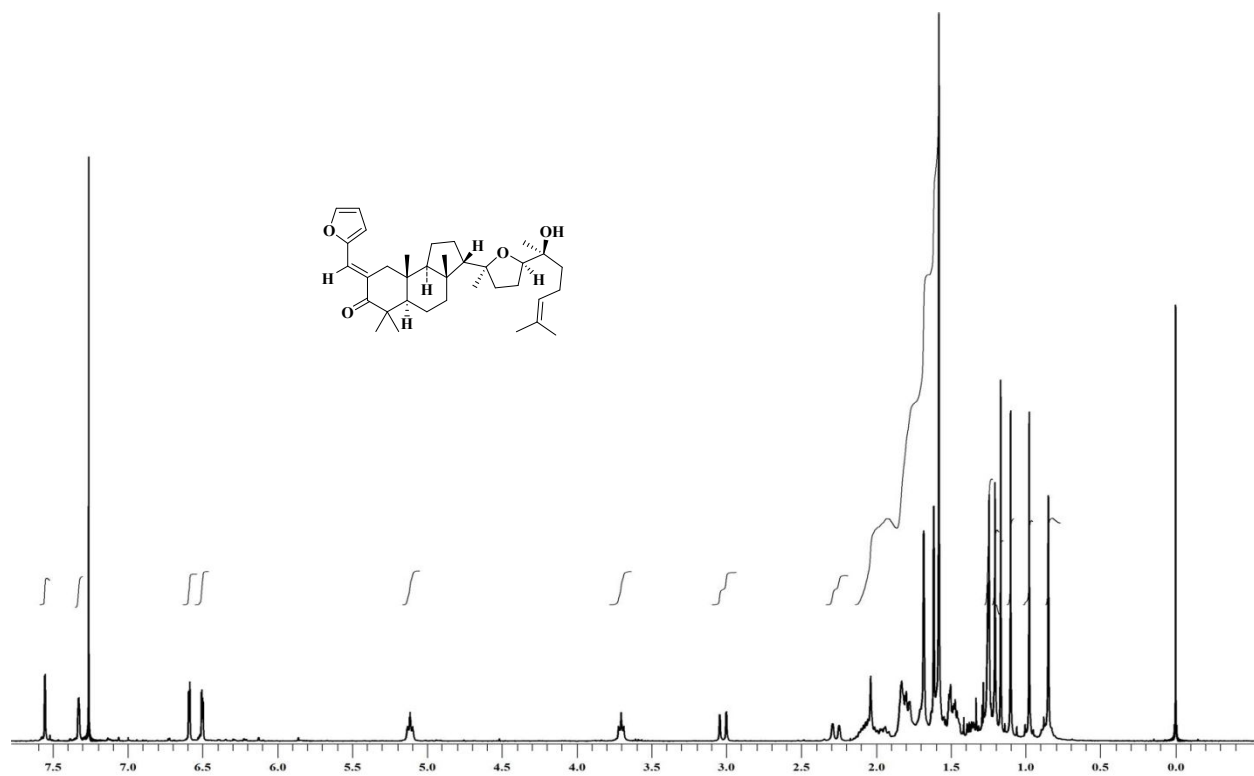
¹³C NMR spectrum of compound 2m in CDCl₃



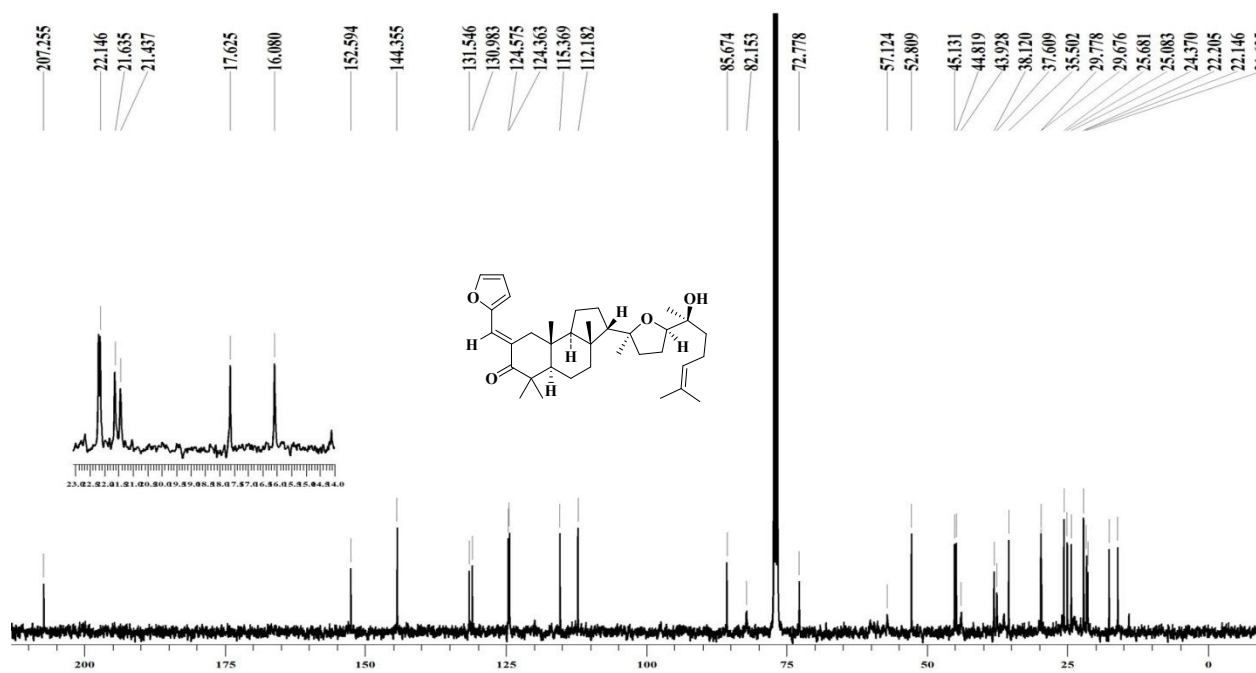
¹H NMR spectrum of compound 2n in CDCl₃



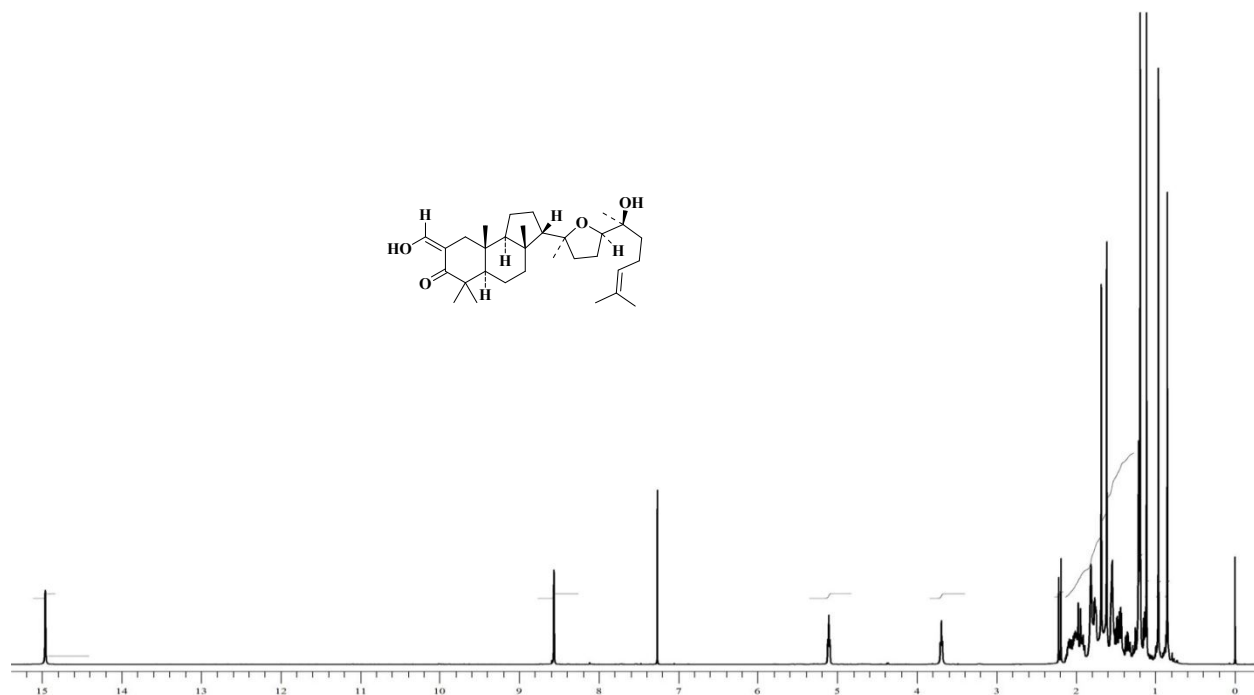
¹³C NMR spectrum of compound 2n in CDCl₃



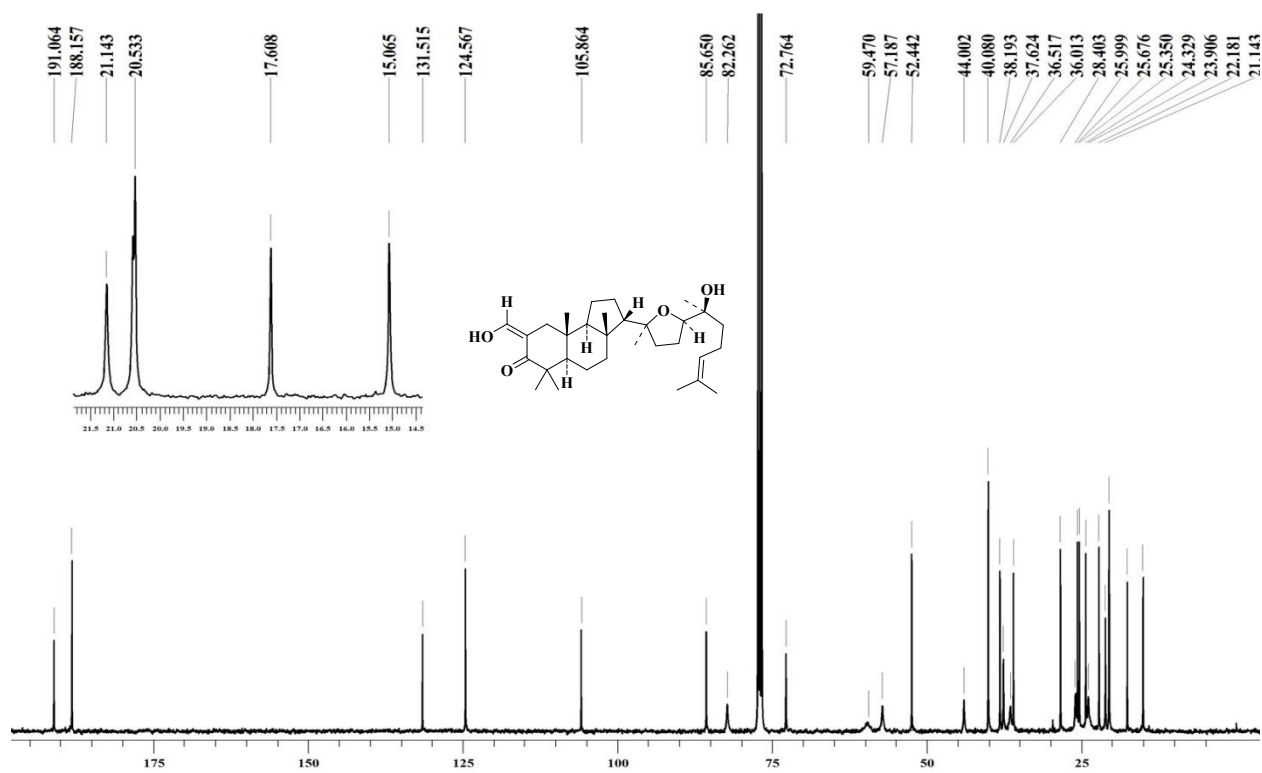
¹H NMR spectrum of compound 2o in CDCl₃



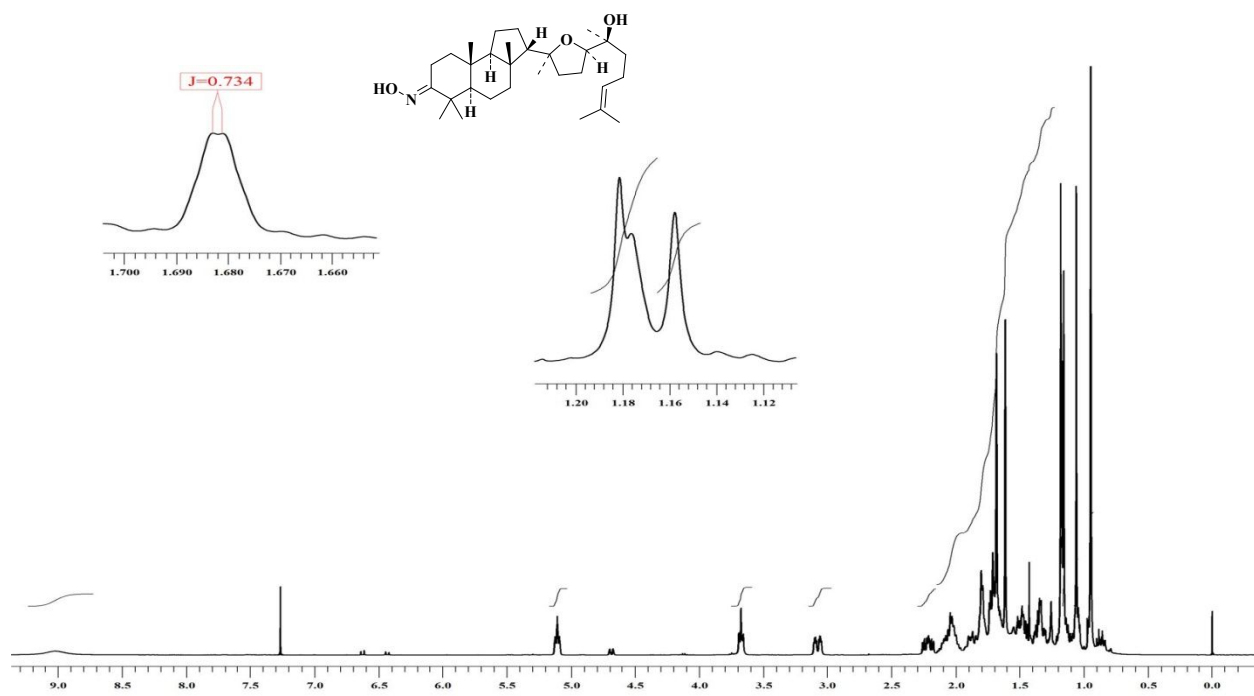
¹³C NMR spectrum of compound 2o in CDCl₃



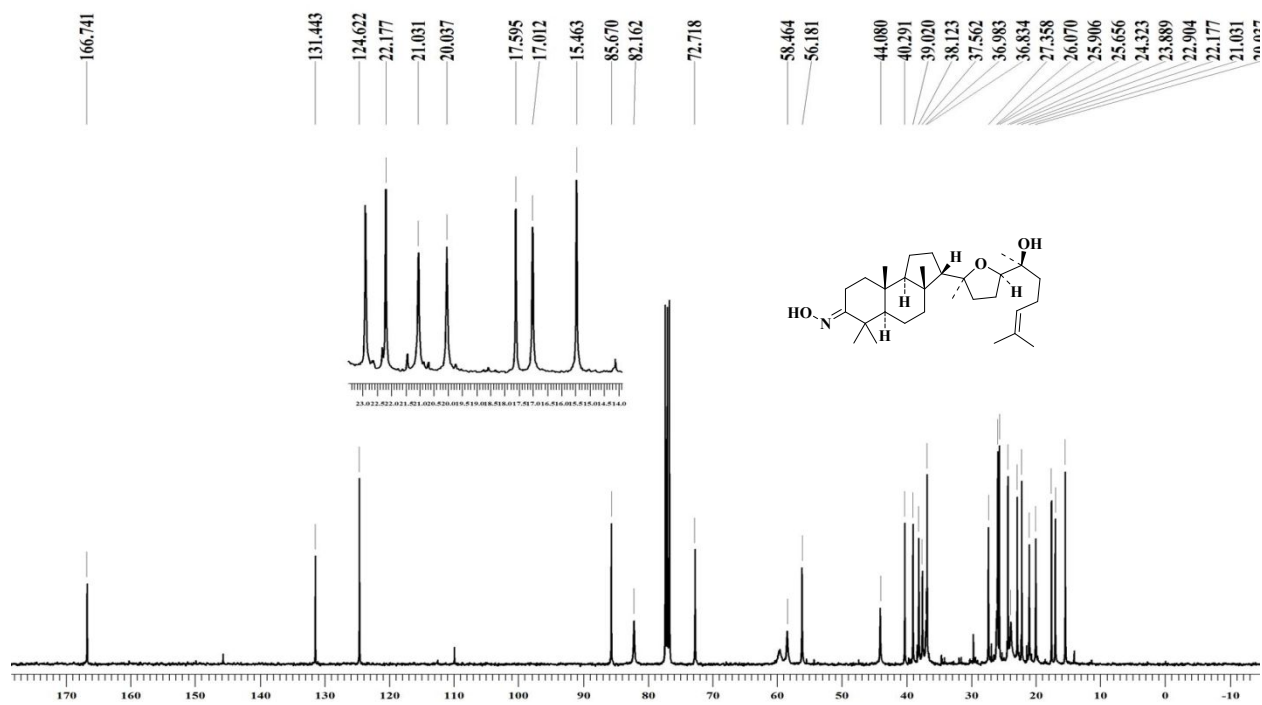
^1H NMR spectrum of compound 3 in CDCl_3



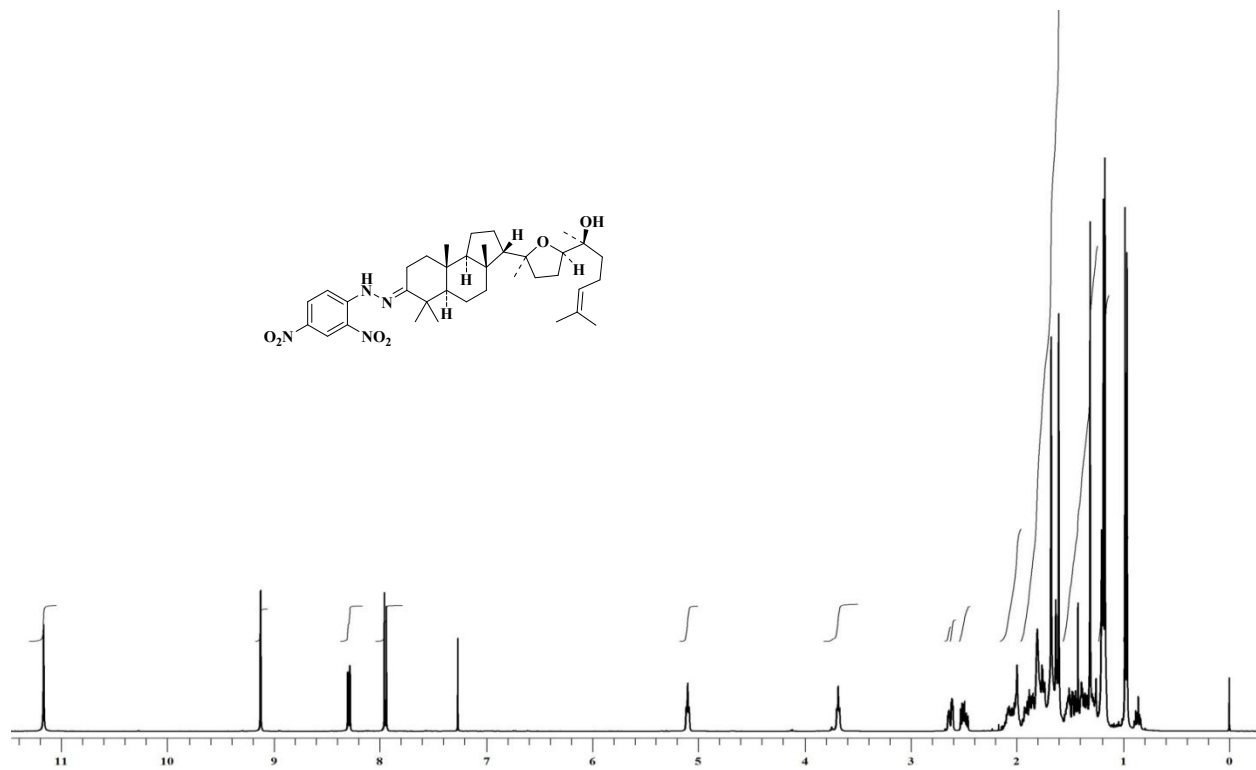
^{13}C NMR spectrum of compound 3 in CDCl_3



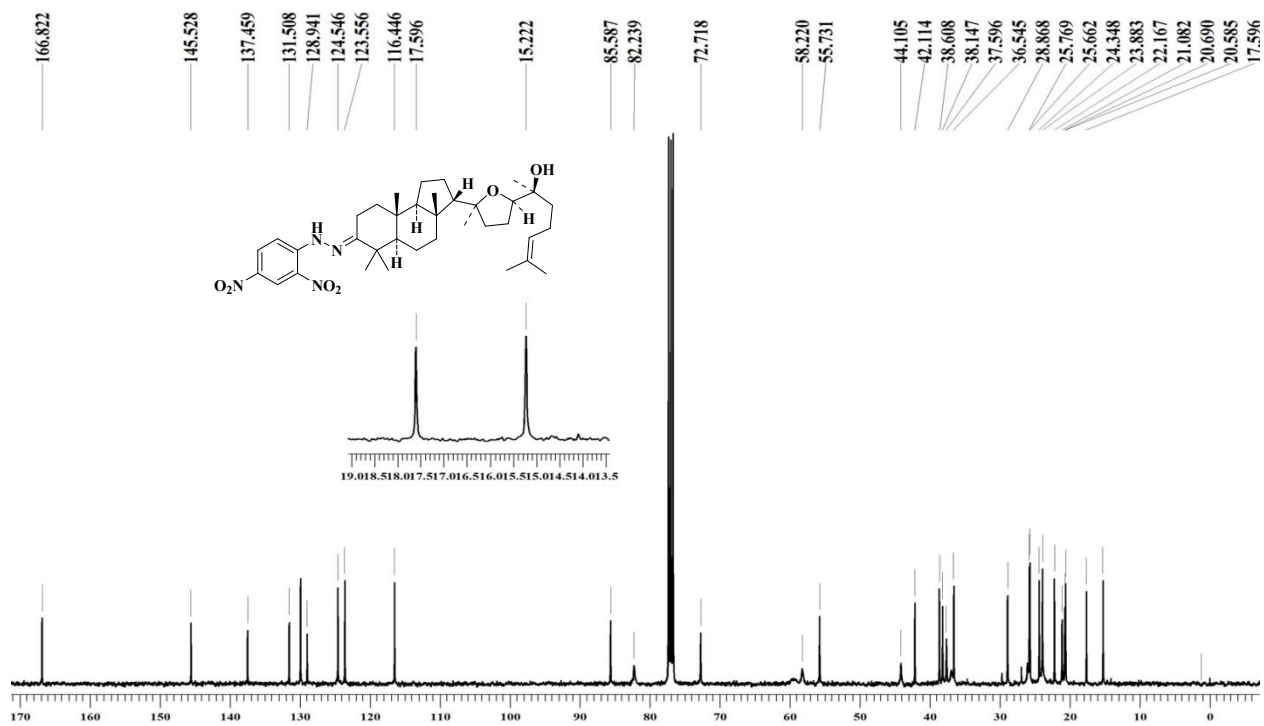
^1H NMR spectrum of compound 4 in CDCl_3



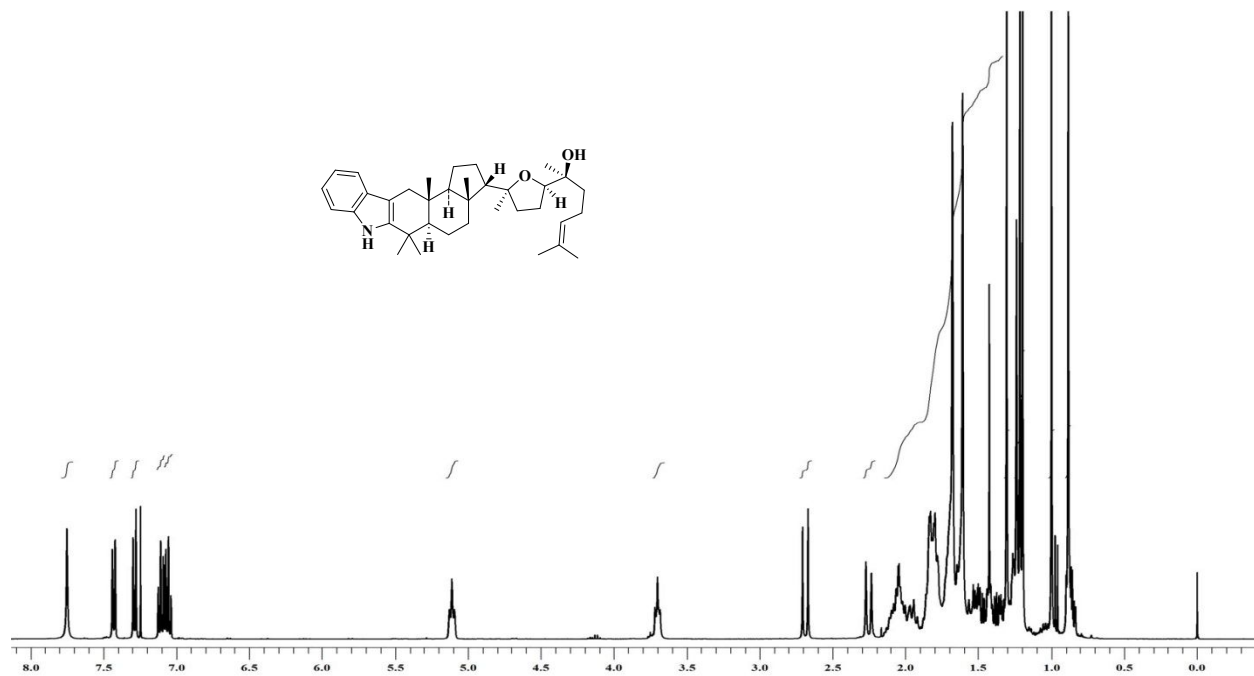
^{13}C NMR spectrum of compound 4 in CDCl_3



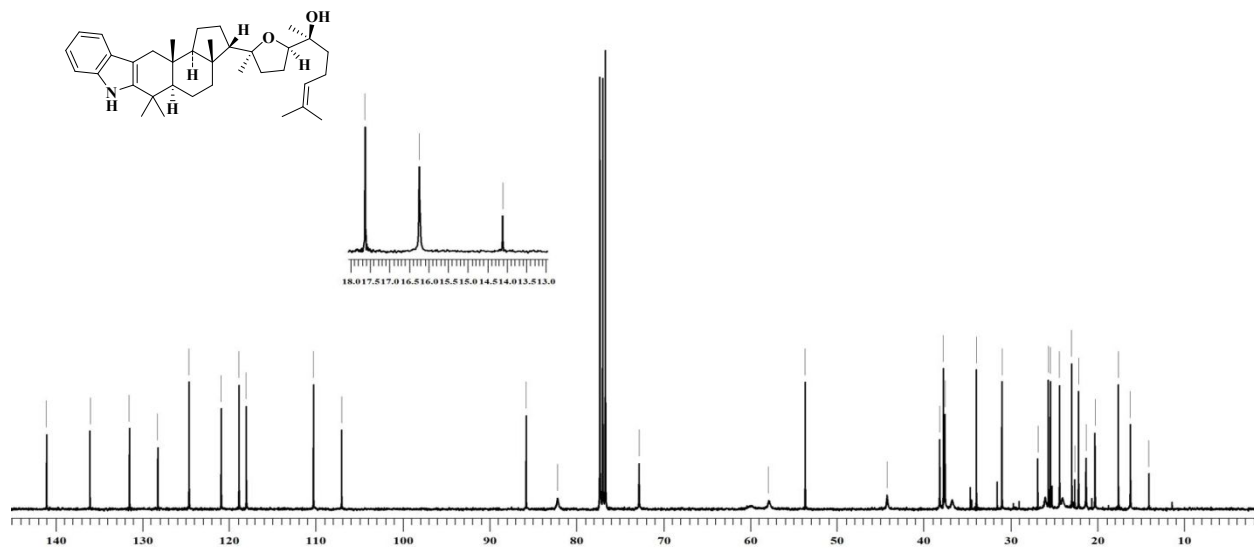
¹H NMR spectrum of compound 5 in CDCl₃



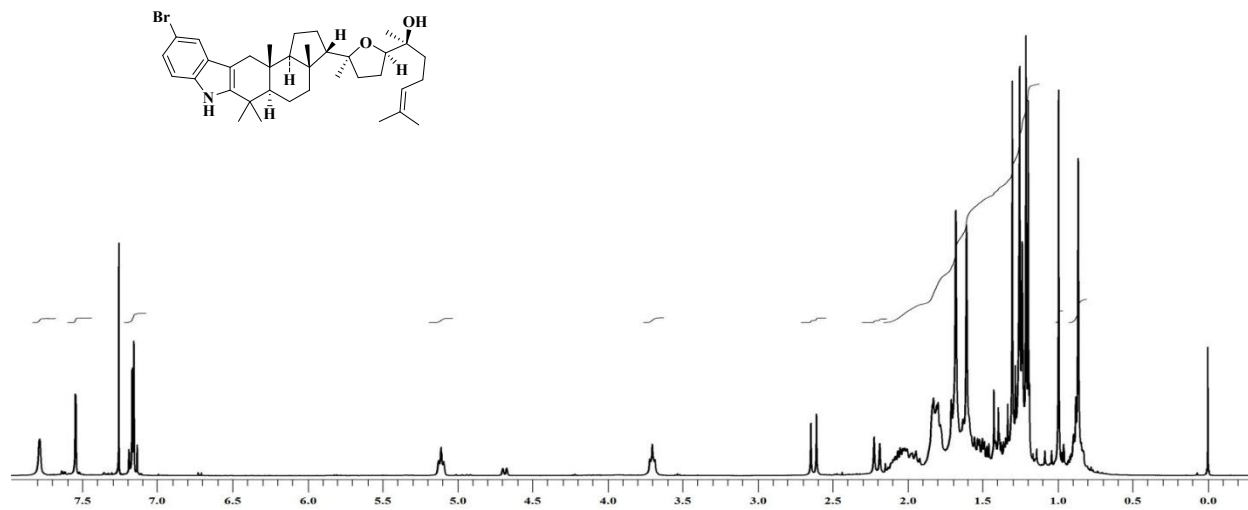
¹³C NMR spectrum of compound 5 in CDCl₃



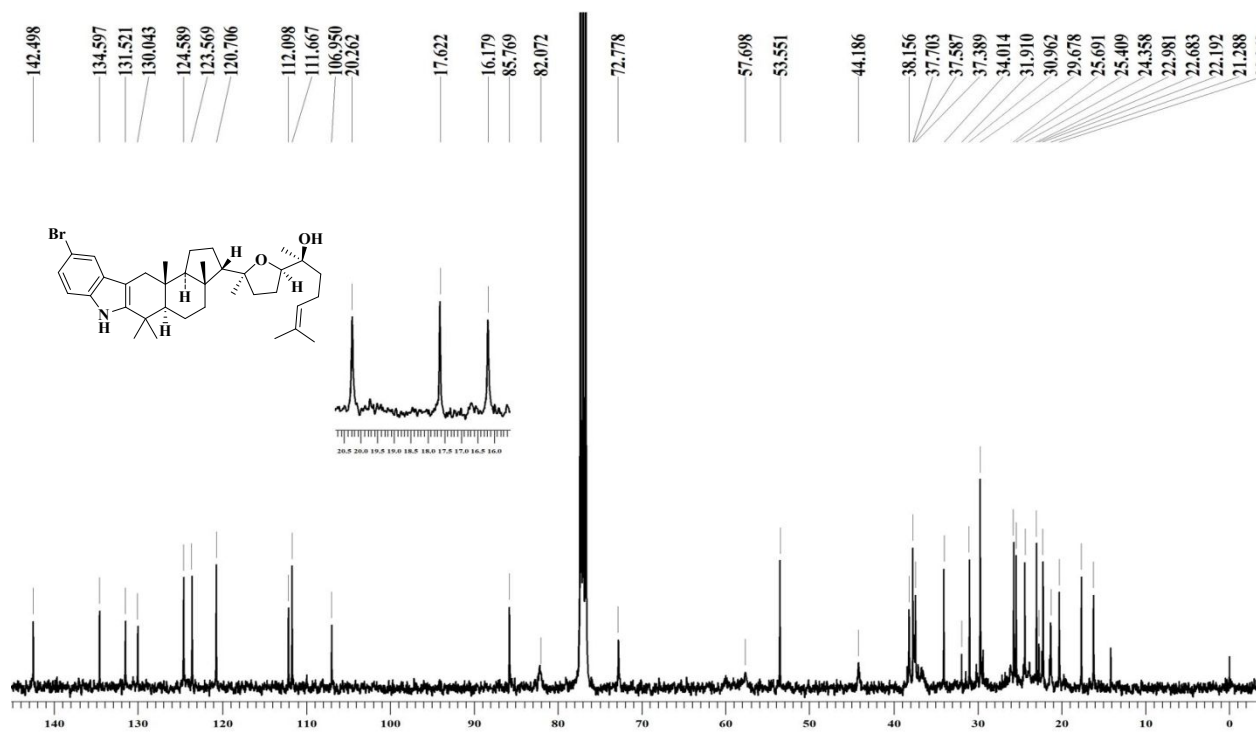
¹H NMR spectrum of compound 6a in CDCl₃



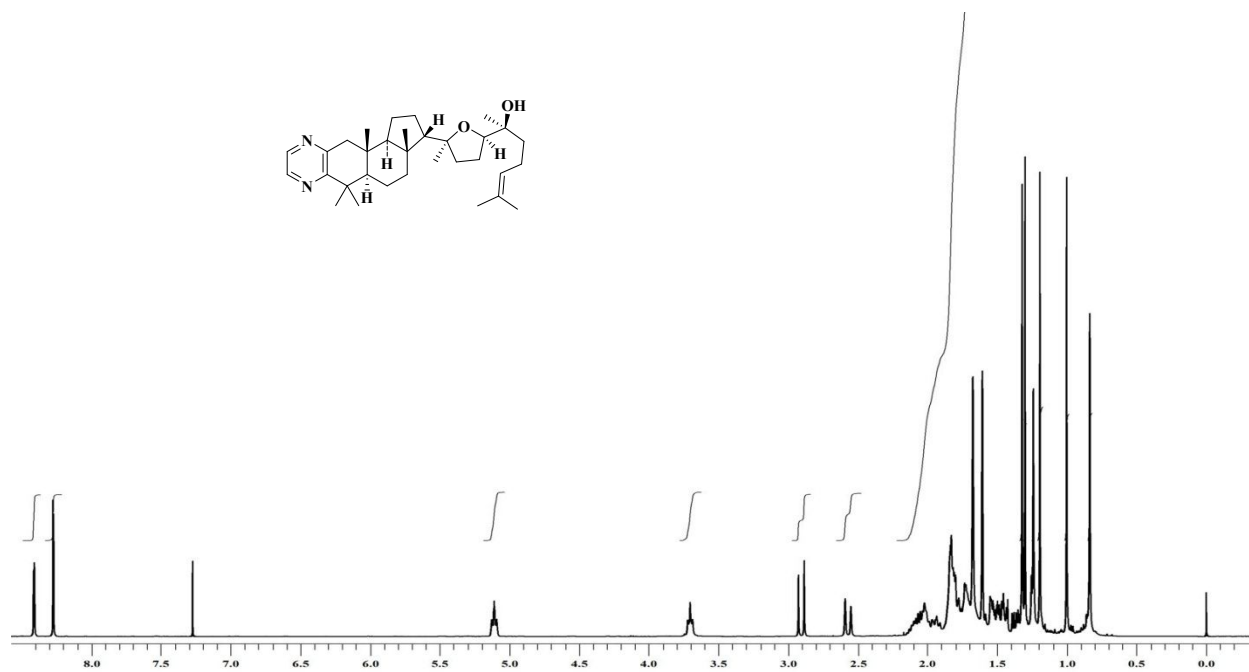
¹³C NMR spectrum of compound 6a in CDCl₃



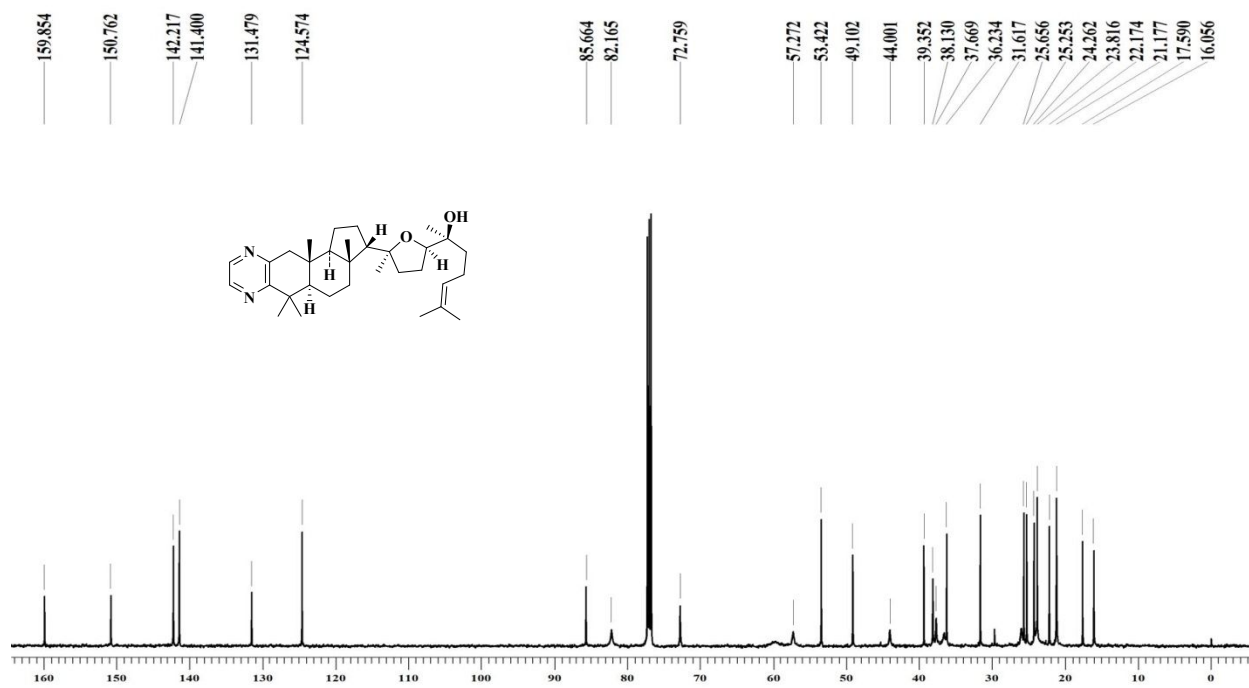
^1H NMR spectrum of compound 6b in CDCl_3



^{13}C NMR spectrum of compound 6b in CDCl_3



¹H NMR spectrum of compound 7 in CDCl₃



¹³C NMR spectrum of compound 7 in CDCl₃