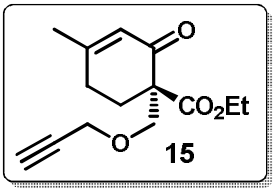
General methods: ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or CDCl3 and CCl_4 as solvent on 300 MHz or 500 MHz spectrometer at ambient temperature. The coupling constant *J* is given in Hz. The chemical shifts are reported in ppm on scale downfield from TMS as internal standard and signal patterns are indicated as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, q = quartet, qd = quartet of doublet, m = multiplet, br = broad. FTIR spectra were recorded on KBr pellets $CHCl_3$/neat (as mentioned) and reported in wave number (cm^{-1}). For low (MS) and High (HRMS) resolution, *m/z* ratios are reported as values in atomic mass units. Mass analysis was done in ESI mode. All reagents were reagent grade and used without further purification unless specified otherwise. Solvents for reactions were distilled prior to use: THF, toluene and diethyl ether were distilled from Na and benzophenone ketyl; MeOH from Mg and I_2; CH_2Cl_2 from CaH_2. All air- or moisture-sensitive reactions were conducted under a nitrogen or argon atmosphere in flame-dried or oven-dried glassware with magnetic stirring. Reactions were monitored by thin-layer chromatography carried out on silica plates (silica gel 60 F254, Merck) using UV-light, iodine and anisaldehyde for visualization. Column chromatography was carried out using silica gel (60-120 mesh or 100- 200 mesh) packed in glass columns. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. All the compounds reported here are in racemic form.

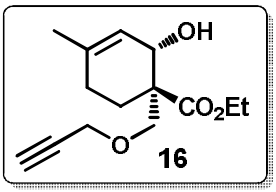
Experimental Section:

Ethyl-4-methyl-2-oxo-1-((prop-2-yn-1-yloxy)methyl)cyclohex-3-enecarboxylate (15):



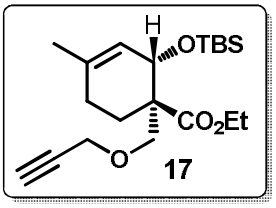
To a stirred solution of β-hydroxy ester **14** (1 g, 5.49 mmol) in dry THF (15 mL) at -10 ^{o}C was added HMPA (3 mL) and NaH (330 mg, 8.24 mmol, 60% in mineral oil) to this 3-(chloromethoxy)prop-1-yne (689 mg, 6.59 mmol) in dry THF (5 mL) was added dropwise and stirred for 3 h. After completion of the reaction monitored by TLC, the reaction mixture was quenched with sat. aq. NH_4Cl (3 mL) and extracted with EtOAc (3 x 25 mL). The combined organic extracts were washed with brine (30 mL) and dried over Na_2SO_4, volatiles were removed to obtain crude compound which was purified by silica gel column chromatography to give **15** as yellow oil (1.02 g, 74%). R_f = 0.5 (4:1 hexane:ethyl acetate); IR (KBr): 3317, 2977, 2873, 2058, 1656, 1610, 1438, 988 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.87 (s, 1H), 4.22-4.10 (m, 4H), 3.93 (d, *J* = 9.1 Hz, 1H), 3.80 (d, *J* = 9.1 Hz, 1H), 2.61-2.44 (m, 2H), 2.37 (t, *J* = 2.5 Hz, 1H), 2.33-2.12 (m, 2H), 1.96 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.7, 169.8, 162.9, 125.8, 79.4, 74.6, 71.2, 61.4, 58.8, 56.9, 28.5, 27.9, 24.3, 14.1; MS (ESI) *m/z* 273 $(M + Na)^{+}$. HRMS (ESI) *m/z* calcd $C_{14}H_{18}O_4$ $(M + Na)^{+}$ = 273.1103, found 275.1113.

Ethyl 2-hydroxy-4-methyl-1-((prop-2-yn-1-yloxy)methyl)cyclohex-3-enecarboxylate (16):



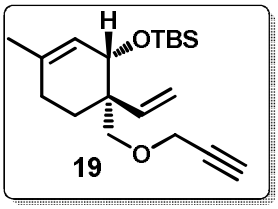
The propargyl enone **15** (950 mg, 3.80 mmol) was dissolved in MeOH (15 mL) and cooled to -10 ^{o}C, to this $CeCl_3.7H_2O$ (1.37 g, 4.18 mmol) was added and stirred for 5 min after which $NaBH_4$ (159 mg, 4.18 mmol) was added and stirred for 15 min. After completion of the reaction monitored by TLC, the reaction mixture was quenched with sat. aq. NH_4Cl (3 mL) and extracted with EtOAc (4 x 25 mL). The combined organic layer washed with brine (40 mL), dried over Na_2SO_4, evaporated to afford crude compound which was purified by column chromatography to obtain pure allylic alcohol **16** as pale oil (785 mg, 82%); R_f = 0.4 (4:1 hexane:ethyl acetate). IR (KBr): 3453, 3300, 2921, 2116, 1732, 1545, 1345, 1274, 1165, 772 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.54 (s, 1H), 4.55 (s, 1H), 4.19 (q, J = 7.2 Hz, 2H), 4.14 (m, 2H), 3.85 (d, J = 8.9 Hz, 1H), 3.71 (d, J = 8.9 Hz, 1H), 2.43 (t, J = 2.5 Hz, 1H), 1.97-1.94 (m, 2H), 1.86-1.79 (m, 2H), 1.69 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.5, 137.6, 122.4, 79.5, 74.6, 71.5, 66.7, 60.7, 58.5, 50.1, 27.2, 23.7, 23.1, 14.1; MS (ESI) *m/z* 275 $(M + Na)^+$; HRMS (ESI) *m/z* calcd $C_{14}H_{20}O_4$ $(M + Na)^+$ = 275.1259, found 275.1264.

Ethyl-2-((tert-butyldimethylsilyl)oxy)-4-methyl-1-((prop-2-yn-1-yloxy)methyl)cyclohex-3-enecarboxylate (17):



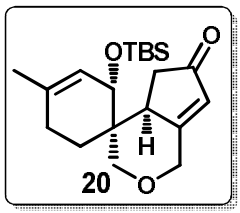
To a stirring solution of allylic alcohol **16** (750 mg, 2.98 mmol) in dry CH_2Cl_2 (15 mL) at 0 ^{o}C were added imidazole (304 mg, 4.46 mmol) and TBSCl (536 mg, 3.57 mmol) and stirred for 8 h. After completion of the reaction monitored by TLC, the reaction mixture was quenched with sat aq. NH_4Cl (4 mL) and diluted with water and extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layer washed with brine and dried over Na_2SO_4. Volatiles were removed to give crude oil which was purified by silica gel column chromatography to afford TBS ether **17** as yellow liquid (914 mg, 84 %); R_f = 0.6 (9:1 hexane:ethyl acetate). IR (KBr): 3310, 2955, 2929, 2857, 2118, 1672, 1254, 1098, 835 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.34-5.33 (m, 1H), 4.44 (d, J = 3.8 Hz, 1H), 4.16-3.98 (m, 4H), 3.76 (d, J = 8.3 Hz, 1H), 3.54 (d, J = 8.3 Hz, 1H), 2.32 (t, J = 2.3 Hz, 1H), 1.99-1.89 (m, 2H), 1.83-1.78 (m, 2H), 1.60 (s, 3H), 1.19 (t, J = 7.6 Hz, 3H), 0.82 (s, 9H), -0.00 (s, 3H), -0.01(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.2, 136.8, 123.5, 79.8, 74.1, 71.5, 67.6, 60.4, 58.5, 51.1, 27.4, 25.8 (3C), 23.5, 23.2, 18.0, 14.1, -4.0, -5.0; MS (ESI) *m/z* 389 $(M + Na)^+$.

tert-Butyldimethyl((-3-methyl-6-((prop-2-yn-1-yloxy)methyl)-6-vinylcyclohex-2-en-1-yl)oxy)silane (19):



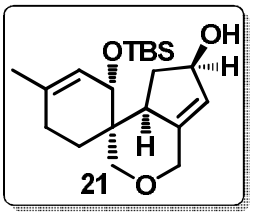
Propargyl ester **17** (900 mg, 2.46 mmol) was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 ^oC, to this DIBAL-H (3.84 mL, 20% *w/v* in toluene) was added dropwise and stirred for 1 h. After completion of the reaction monitored by TLC, the reaction mixture was quenched with saturated solution of sodium potassium tartarate (15 mL) and diluted with CH_2Cl_2 (30 mL) and stirred for 4 h at rt, layers were separated and organic layer washed with brine (20 mL) and dried over Na_2SO_4 and evaporated to give crude alcohol **as** pale yellow oil (740 mg, 93%). R_f = 0.3 (4:1 hexane:ethyl acetate). The crude alcohol (740 mg, 2.29 mmol) was dissolved in THF (10 mL) and added to a pre dissolved solution of IBX (960 mg, 3.43 mmol) in DMSO (4 mL) and stirred for 2 h at rt. After completion of the reaction solids were filtered with the aid of diethyl ether (50 mL). The ethereal layer was washed with sat. aq. $NaHCO_3$ (2 x 20 mL), cold water (2 x 20 mL), brine (20 mL) dried over Na_2SO_4 and evaporated to give crude aldehyde **18** (662 mg, 90%). R_f = 0.7 (4:1 hexane:ethyl acetate). The crude aldehyde **18** was directly used for next reaction (Wittig) without further purification. The crude aldehyde **18** (662 mg, 2.05 mmol) was dissolved in dry THF (10 mL) and the solution was added to a solution of methyl triphenylphosphoniumiodide (2.49 g, 6.12 mmol) and t-BuOK (460 mg, 4.10 mmol) in THF (30 mL) at 0 ^oC under inert atmosphere. The reaction mixture was stirred for 15 min at room temperature. After completion of the reaction (by TLC), quenched with sat.NH_4Cl (5 mL) and extracted with diethyl ether (3 x 30 mL), washed with brine (20 mL). The combined organic extracts were dried over Na_2SO_4. Volatiles were removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel to give enyne **19** as pale yellow oil (453 mg, 69%); R_f =0.5 (95:5 hexane/ethyl acetate); IR (KBr): 2930, 1730, 1465, 1249, 1172, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.88 (dd, J = 17.4, 12.1 Hz, 1H), 5.28 (t, J = 1.5 Hz, 1H), 5.12-5.06 (m, 2H), 4.17 (dd, J = 15.9, 2.3 Hz, 1H), 4.06 (dd, J = 15.9, 2.3 Hz, 1H), 4.03 (s, 1H), 3.57 (d, J = 18.1 Hz, 1H), 3.54 (d, J = 18.1 Hz, 1H), 2.37 (t, J = 2.3 Hz, 1H), 2.02-1.79 (m, 3H), 1.65 (s, 3H), 1.48-1.39 (m, 1H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.6, 136.7, 123.8, 113.5, 80.1, 74.0, 71.8, 72.0, 58.5, 43.9, 27.1, 25.9 (3C), 25.2, 23.1, 18.1, -4.8, -3.9; MS (ESI) *m/z* 343 $(M + Na)^+$; HRMS (ESI) *m/z* calcd for $C_{19}H_{32}O_2SiNa$ $(M + Na)^+$ = 343.2069, found 343.2082.

2-((tert-Butyldimethylsilyl)oxy)-4-methyl-4a',5'-dihydro-1'H-spiro[cyclohex[3]ene-1,4'-cyclopenta[c]pyran]-6'(3'H)-one (20):



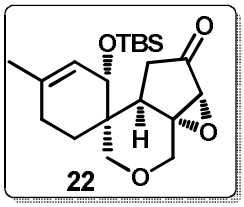
To a solution of the enyne **19** (50 mg, 0.156 mmol) in dry CH_2Cl_2 (8 mL), which was prebubbled with nitrogen for 15 min, was added cobalt octacarbonyl (63 mg, 0.187 mmol). The mixture was stirred for 1 h at room temperature and then cooled to -10 ^oC and added NMO (94 mg, 1.248 mmol) and allowed to stirr at room temperature for 3 h . After completion of the reaction (by TLC), the reaction mixture was filtered through a pad of celite and washed with ethyl acetate (3 x 5 mL) and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the tricyclic enone **20** (40 mg, 75%) as white solid, which was recrystallized in benzene and hexane to result crystalline enone **20**. R_f = 0.4 (3:1hexane/ethyl acetate); mp 96-98 °C; IR (KBr): 2930, 2857, 1713, 1632, 1442, 1381, 1253, 1172, 1081, 838, 774 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.90 (s, 1H), 5.09 (s, 1H), 4.59 (d, J = 13.6 Hz, 1H), 4.09 (d, J = 13.2 Hz, 1H), 4.07 (s, 1H), 3.85 (d, J = 12.3 Hz, 1H), 3.55 (d, J = 12.3 Hz, 1H), 3.35 (br s, 1H), 2.26-2.21 (m, 2H), 2.08 -1.98 (m, 1H), 1.85 (dd, J = 18.1, 5.3 Hz, 1H), 1.66 (s, 3H), 1.66-1.60 (m, 1H), 1.34-1.20 (m, 1H), 0.92 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.0, 175.3, 135.8, 127.6, 124.6, 71.7, 68.3, 67.3, 44.4, 43.0, 35.0, 26.7, 26.0 (3C), 23.0, 21.1, 18.2, -4.8, -3.8; MS (ESI) *m/z* 371 $(M + Na)^+$; HRMS (ESI) *m/z* calcd for $C_{20}H_{32}O_3SiNa$ $(M + Na)^+$ = 371.2018, found 371.2010.

2-((tert-Butyldimethylsilyl)oxy)-4-methyl-3',4a',5',6'-tetrahydro-1'H-spiro[cyclohex[3]ene-1,4'-cyclopenta[c]pyran]-6'-ol (21):



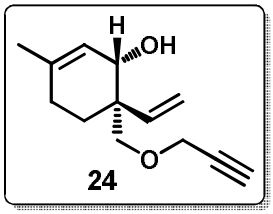
To a stirred solution of tricyclic enone **20** (30 mg, 0.086 mmol) in MeOH (3 mL) at -78 ^oC were added cerium (III) chloride heptahydrate (31 mg, 0.095 mmol) and $NaBH_4$ (4 mg, 0.095 mmol) and stirred for 15 min (gradually warmed to rt). The reaction mixture was quenched with sat. aq. NH_4Cl (0.5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, evaporated volatiles to obtain crude compound which was purified by silica gel column chromatography to afford alcohol **21** as viscous liquid (23.5 mg, 78%). R_f = 0.3 (3:1hexane/ethyl acetate); IR (KBr): 3380, 2922, 2853, 1463, 1252, 1079, 1045, 835, 761 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.50 (s, 1H), 5.12 (s, 1H), 4.82 (br s, 1H), 4.38 (d, J = 13.0 Hz, 1H), 4.04 (s, 1H), 3.90 (d, J = 13.0 Hz, 1H), 3.83 (d, J = 12.0 Hz, 1H), 3.44 (d, J = 12.0 Hz, 1H), 3.03 (t, J = 7.0 Hz, 1H), 2.29 (dt, J = 16.0, 8.0 Hz, 1H), 2.07-2.00 (m, 1H), 1.87 (dd, J = 18.0, 6.0 Hz, 1H), 1.70 (dd, J = 14.0, 6.0 Hz, 1H), 1.70-1.65 (m, 1H), 1.65 (s, 3H), 1.41 (dt, J = 14.0, 6.0 Hz, 1H), 0.91 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.7, 135.6, 125.8, 124.7, 76.6, 71.4, 68.2, 67.1, 46.9, 40.6, 33.2, 26.9, 25.9 (3C), 22.9, 22.4, 18.0, -4.0, -5.1; MS (ESI) *m/z* 373 $(M + Na)^+$.

2-((tert-Butyldimethylsilyl)oxy)-4-methyl-3',3a',5',7'-tetrahydrospiro[cyclohex[3]ene-1,4'-oxireno[2',3':1,5]cyclopenta[1,2-c]pyran]-2'(1a'H)-one (22):



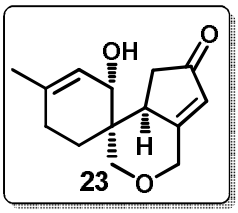
To a stirred solution of enone **20** (25 mg) in MeOH (2.5 mL) at 0 ^{o}C were added H_2O_2 (28 µL, 30% w/v in H_2O) and 6N NaOH (48 µL). After stirring at rt for 2 h, the reaction was diluted with EtOAc (6 mL) and washed with brine containing sodium thiosulfate (5 mL). The aqueous layer was further extracted with EtOAc (3 x 5 mL), the combined oranic layers washed with brine (5 mL), dried over Na_2SO_4, evaporated to obtain crude compound which was purified by silica gel column chromatography to afford epoxyketone **22** as viscous liquid (21 mg, 78%); R_f = 0.5 (4:1hexane/ethyl acetate); IR (KBr): 2925, 2854, 1753, 1463, 1253, 1086, 1046, 843, 774 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.12 (s, 1H), 4.01 (br s, 1H), 3.89 (d, *J* = 11.6 Hz, 1H), 3.87 (d, *J* = 12.5 Hz, 1H), 3.72 (d, *J* = 12.5 Hz, 1H), 3.48 (d, *J* = 12.5 Hz, 1H), 3.35 (s, 1H), 2.93 (d, *J* = 8.0 Hz, 1H), 2.42 (dd, *J* = 17.8, 9.0 Hz, 1H), 1.99 (d, *J* = 17.8 Hz, 2H), 1.84 (dd, *J* = 17.8, 5.4 Hz, 1H), 1.74 (dd, *J* = 13.4, 4.5 Hz, 1H), 1.64 (s, 3H), 1.26-1.19 (m, 1H), 0.92 (s, 9H), 0.07 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.2, 135.5, 124.3, 70.1, 68.1, 66.9, 65.5, 61.2, 42.1, 38.3, 33.7, 26.2, 25.9 (3C), 22.8, 22.0, 18.0, -4.2, -5.1; MS (ESI) *m/z* 387 $(M + Na)^+$.

3-Methyl-6-((prop-2-yn-1-yloxy)methyl)-6-vinylcyclohex-2-enol (24):



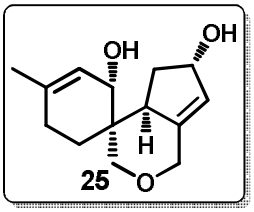
TBS enyne **19** (150 mg, 0.43 mmol) was dissolved in THF (5 mL) and cooled to 0 ^{o}C to this TBAF (0.55 mL, 1M solution in THF) was added dropwise and stirred for 12 h at rt. The reaction mixture was quenched with sat. aq. NH_4Cl (2 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, evaporated to obtain crude oil which was purified by silica gel chromatography to afford alcohol **24** as pale yellow oil (89 mg, 92%). R_f = 0.4 (4:1hexane/ethyl acetate); IR (KBr): 3436, 2918, 1441, 1090, 990, 912 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.78 (dd, *J* = 18.3, 11.0 Hz, 1H), 5.53 (br s, 1H), 5.17-5.13 (m, 2H), 4.15 (qd, *J* = 15.9, 2.4 Hz, 2H), 4.11 (s, 1H), 3.69 (d, *J* = 8.5 Hz, 1H), 3.48 (d, *J* = 8.5 Hz, 1H), 2.40 (t, *J* = 2.4 Hz, 1H), 2.24 (d, *J* = 3.7 Hz, 1H), 1.92 (t, *J* = 6.1 Hz, 1H), 1.72 (dd, *J* = 13.4, 7.3 Hz, 1H), 1.68 (s, 3H), 1.40 (dt, *J* = 13.4, 6.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.0, 138.0, 122.4, 114.3, 79.7, 74.6, 74.3, 69.4, 58.6, 43.4, 27.0, 25.4, 23.2; MS (ESI) *m/z* 229 $(M + Na)^+$; HRMS (ESI) *m/z* calcd for $C_{13}H_{18}O_2Na$ $(M + Na)^+$ = 229.11990, found 229.11994.

2-Hydroxy-4-methyl-4a',5'-dihydro-1'H-spiro[cyclohex[3]ene-1,4'-cyclopenta[c]pyran]-6'(3'H)-one (23):



To a solution of the enyne **24** (50 mg, 0.243 mmol) in dry CH_2Cl_2 (10 mL), which was degassed by bubbling with nitrogen for 15 min, was added cobalt octacarbonyl (107 mg, 0.315 mmol). The mixture was stirred for 1 h at room temperature and then cooled to -10 ^oC and added NMO (227 mg, 1.94 mmol) and allowed to stirr at room temperature for 6 h . After completion of the reaction (by TLC), the reaction mixture was filtered through a pad of celite and washed with ethyl acetate (4 x 5 mL) and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (4:1 hexane/ethylacetate) to afford the tricyclic enone **23** (44 mg, 79%) as a viscous liquid. R_f = 0.4 (2:1hexane/ethyl acetate); IR (KBr): 3431, 2924, 1705, 1628, 1078 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.95 (s, 1H), 5.24 (s, 1H), 4.64 (d, J = 13.6 Hz, 1H), 4.18 (d, J = 13.6 Hz, 1H), 4.12 (s, 1H), 3.88 (d, J = 12.1 Hz, 1H), 3.65 (d, J = 12.1 Hz, 1H), 3.56 (d, J = 6.0 Hz, 1H), 2.38 (dd, J = 18.0, 6.8 Hz, 1H), 2.24 (dd, J = 18.0, 3.0 Hz, 1H), 2.04-2.00 (m, 1H), 1.89 (dd, J = 18.0, 6.0 Hz, 1H), 1.68 (s. 3H), 1.68-1.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.3, 175.7, 137.3, 127.6, 123.6, 71.0, 67.9, 67.3, 44.2, 42.4, 35.0, 26.6, 22.7, 21.0; MS (ESI) *m/z* 257 $(M + Na)^+$; HRMS (ESI) *m/z* calcd for $C_{14}H_{19}O_3$ $(M + H)^+$ = 235.13287, found 235.13323.

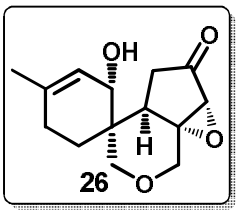
4-Methyl-3',4a',5',6'-tetrahydro-1'H-spiro[cyclohex[3]ene-1,4'-cyclopenta[c]pyran]-2,6'-diol (25):



To a stirred solution of hydroxy-enone **23** (24 mg, 0.103 mmol) in MeOH (2 mL) at -78 ^oC were added cerium (III) chloride heptahydrate (37 mg, 0.113 mmol) and $NaBH_4$ (4.3 mg, 0.113 mmol) and stirred for 15 min (gradually allowed to rt). The reaction mixture was quenched with sat. aq. NH_4Cl (2 mL) and extracted with EtOAc (4 x 5 mL). The combined organic layers washed with brine (5 mL), dried over Na_2SO_4, evaporated volatiles to obtain crude compound which was purified by silica gel column chromatography to afford diol **25** as viscous liquid (17.9 mg, 74%). R_f = 0.25 (2:1hexane/ethyl acetate); IR (KBr): 3374, 2925, 2857, 1442, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.52 (d, J = 1.7 Hz, 1H), 5.22 (s, 1H), 4.84 (s, 1H), 4.40 (d, J = 13.2 Hz, 1H), 4.06 (s, 1H), 3.95 (d, J = 13.0 Hz, 1H), 3.83 (d, J = 11.9 Hz, 1H), 3.45 (d, J = 11.7 Hz, 1H), 3.14 (t, J = 7.2 Hz, 1H), 2.37 (dt, J = 14.0, 8.3 Hz, 1H), 2.05-2.01 (m, 1H), 1.90

(dd, *J* = 18.0, 5.5 Hz, 1H), 1.72 (dd, *J* = 13.4, 5.1 Hz, 1H),1.68 (s, 3H), 1.46-1.36 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.2, 137.4, 126.2, 123.8, 76.6, 71.1, 67.7, 67.1, 46.8, 40.1, 33.1, 27.0, 22.8, 22.4; MS (ESI) *m/z* 259 $(M + Na)^+$; HRMS (ESI) *m/z* calcd for $C_{14}H_{20}O_3Na$ $(M + Na)^+$ = 259.13047, found 259.13058.

2-Hydroxy-4-methyl-3',3a',5',7'-tetrahydrospiro[cyclohex[3]ene-1,4'-oxireno[2',3':1,5]cyclopenta[1,2-c]pyran]-2'(1a'H)-one (26):



To a stirred solution of hydroxy-enone **23** (25 mg) in MeOH (2 mL) at 0 ^oC were added H_2O_2 (28 µL, 30% w/v in H_2O) and 6N NaOH (55 µL). After stirring at rt for 2 h, the reaction was diluted with EtOAc (6 mL) and washed with brine containing sodium thiosulfate (5 mL). The aqueous layer was further extracted with EtOAc (3 x 5 mL), the combined oranic layers washed with brine (5 mL), dried over Na_2SO_4, evaporated to obtain crude compound which was purified by silica gel column chromatography to afford epoxyketone **14** as viscous liquid (20.8 mg, 78%). R_f = 0.3 (3:1hexane/ethyl acetate); IR (KBr): 3455, 2922, 1745, 1443, 1168, 1090, 1019, 935, 863, 756cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.22 (s, 1H), 4.04 (br s, 1H), 3.93 (d, *J* = 12.1 Hz, 1H), 3.86 (d, *J* = 12.1 Hz, 1H), 3.72 (d, *J* = 12.1 Hz, 1H), 3.52 (d, *J* = 12.1 Hz, 1H), 3.34 (s, 1H), 3.09 (d, *J* = 8.5 Hz, 1H), 2.48 (dd, *J* = 18.0, 8.5 Hz, 1H), 2.01 (d, *J* = 18.0 Hz, 1H), 1.86 (dd, *J* = 18.0, 5.7 Hz, 1H), 1.76 (dd, *J* = 13.4, 5.3 Hz, 1H), 1.67 (s, 3H), 1.52 (m, 1H), 1.27-1.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.4, 137.1, 123.5, 69.7, 67.6, 67.0, 65.4, 60.9, 41.6, 38.2, 33.8, 26.3, 22.7, 21.9; MS (ESI) *m/z* 273 $(M + Na)^+$; HRMS (ESI) *m/z* calcd for $C_{14}H_{18}O_4Na$ $(M + Na)^+$ = 273.10973, found 273.11001.

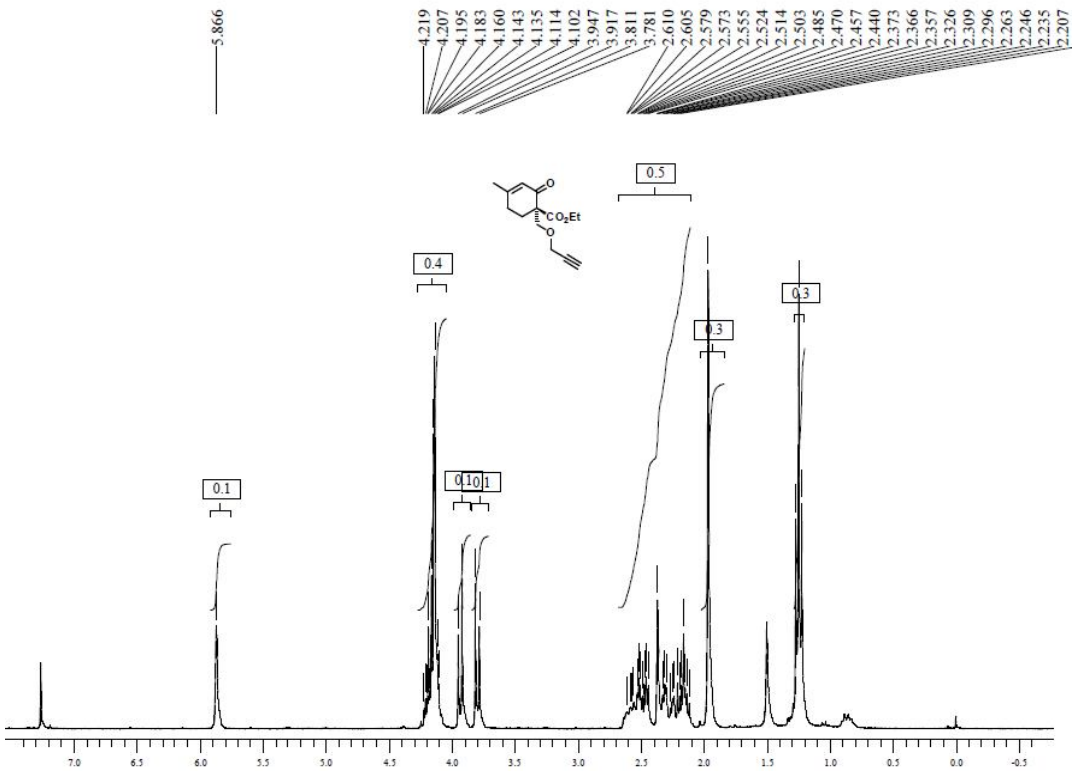
Biological evaluation of compounds **20, 21, 22, 23, 25, 26**

Mouse Neuroblastoma cells (Neuro2a cells) were obtained from the American Type Culture Collection (ATCC) and were grown in Eagle's Minimum Essential Medium (EMEM) supplemented with 10% fetal bovine serum, 1% of 100X antibiotic pencillinstreptomycin (Sigma) at 37°C in 5% CO2/95% air. Neuro2a cells were seeded at 9000 cells/cm2 in 96 well plate, after 24 h the medium was changed in to the serum free medium in the presence and absence of compounds at different concentrations. The pure compounds were diluted in DMSO to different concentrations. The final DMSO concentration in each sample was 0.1% and this concentration did not affect cell growth or death. After being incubated about 48 hours, the cells were fixed with 4% paraformaldehyde/PBS for bright field images. The neurite outgrowths affected by the samples were analyzed under microscope. Three to five random areas (covering 30% of total area) were recorded using an Olympus IX70 (Olympus America, Melville, NY) inverted microscope and the images were captured with an Optronics MagnaFire (Goleta,

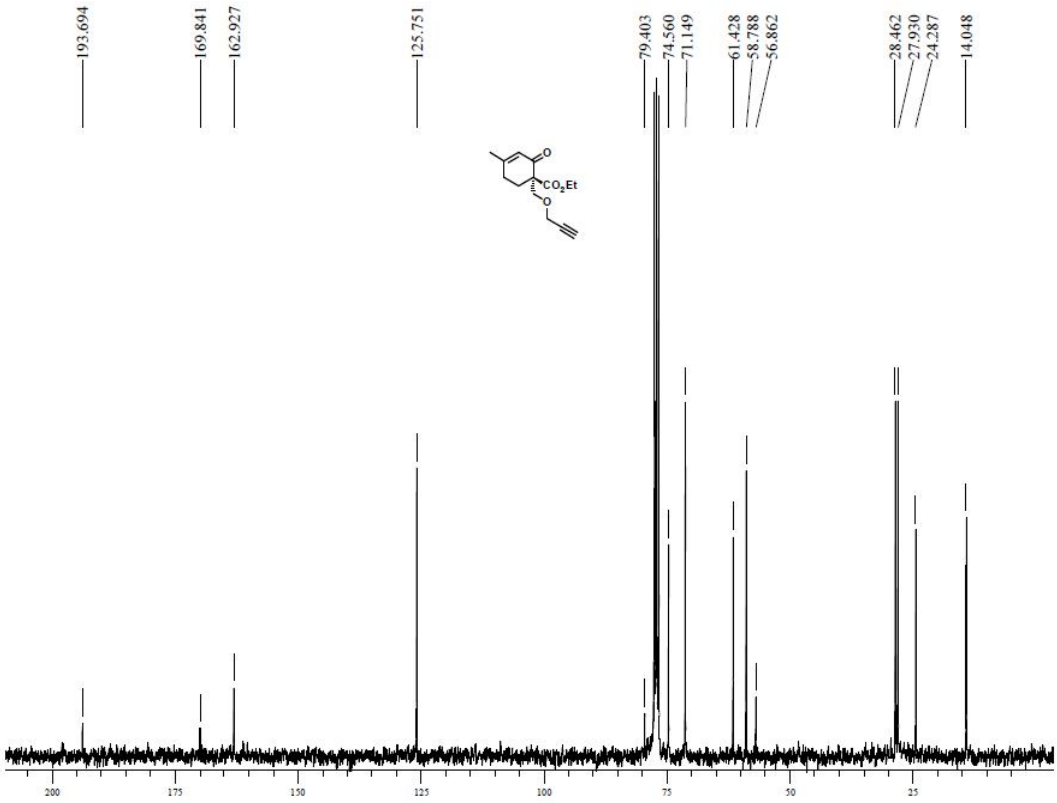
CA) digital color camera. Acquired images were further analyzed by using ImageJ software to generate bar graphs.

Immunostaining

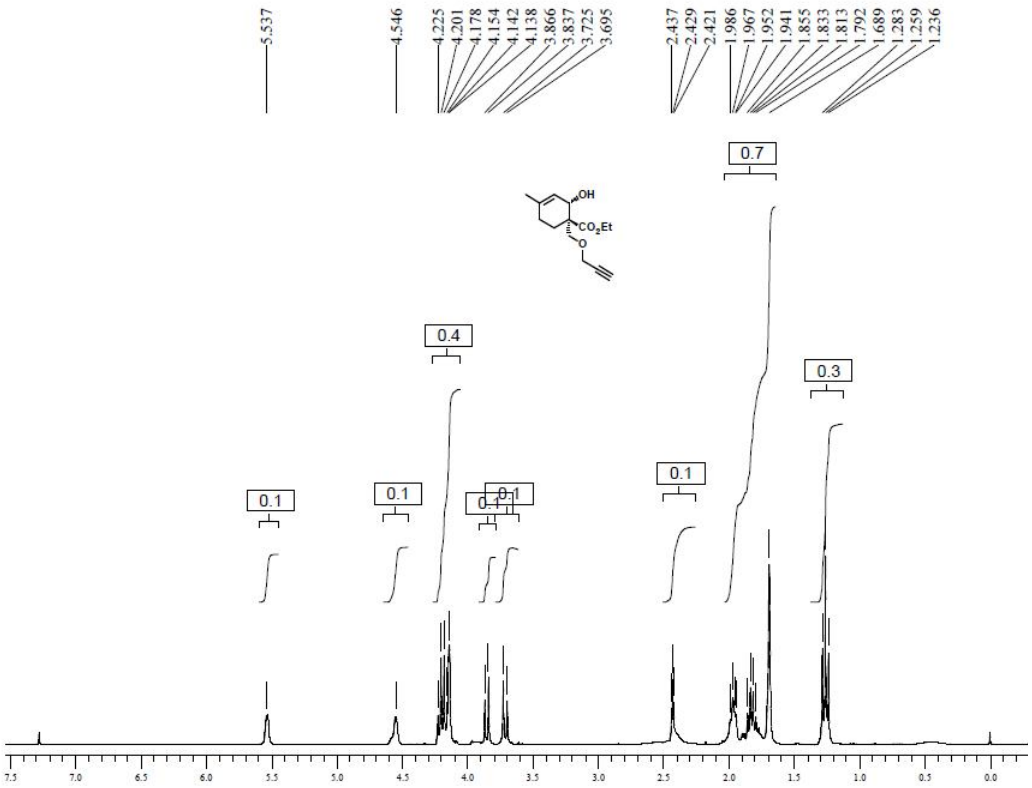
After 48 hours in culture with treatment cells were processed for immunostaning as described earlier. Briefly, cells were fixed with 4%paraformaldehyde at room temperature for 15 minutes, and incubated in blocking buffer (2% bovine serum albumin + 0.3% Triton X-100 in PBS) for 2 hours at room temperature. Primary antibody against betaIII tubulin (1:300, Millipore) was used to visualize neurons. Samples were incubated with primary antibody in blocking buffer overnight at 4°C. Samples were washed with PBST (PBS with 0.1%Tween20) and incubated with goat anti-mouse IgG conjugated to AlexaFlour 488 (1:400, Molecular Probs). Images were captured using an Olympus IX70 (Olympus America, Melville, NY) inverted microscope and with an Optronics MagnaFire (Goleta, CA) digital color camera. Appropriate composite figures were produced using Adobe Photoshop.



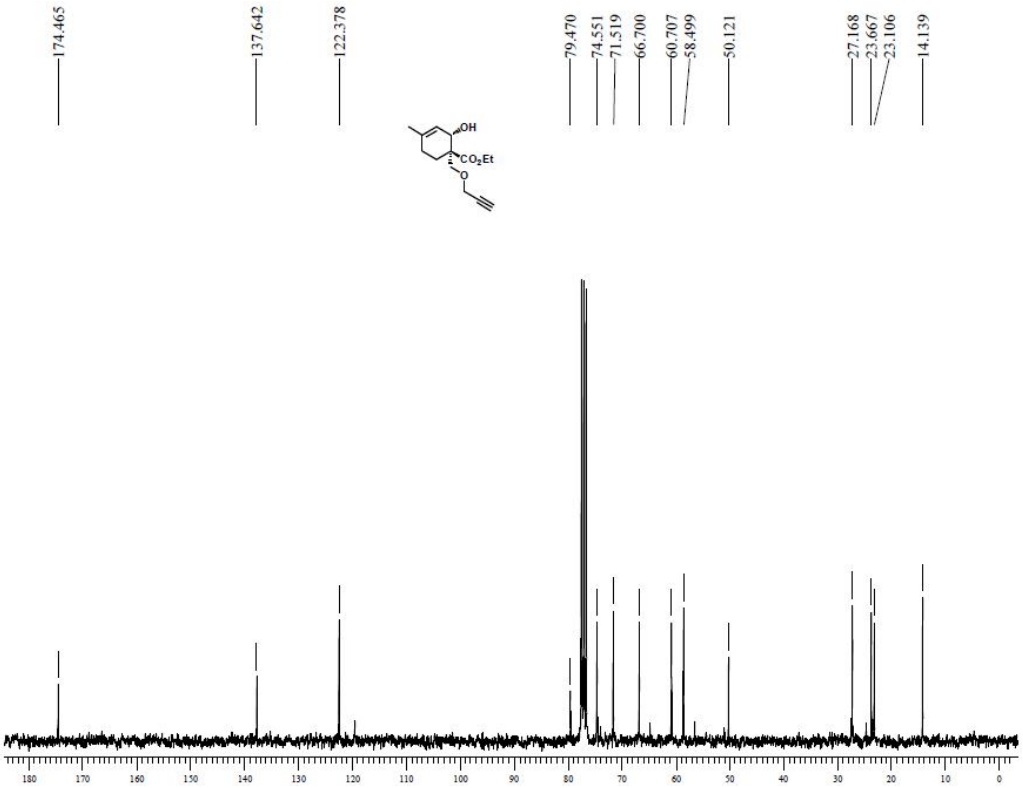
^{1}H NMR spectrum of propargyl enone-**15**



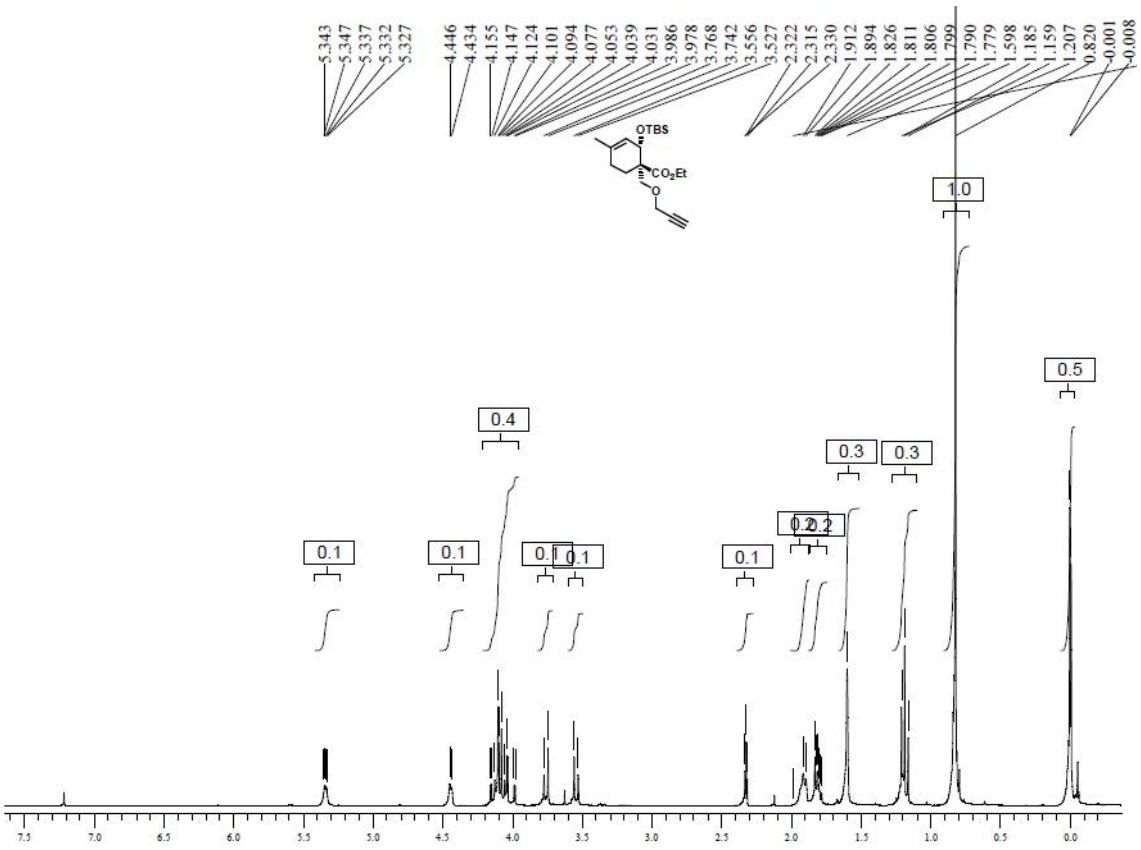
^{13}C NMR spectrum of propargyl enone-**15**



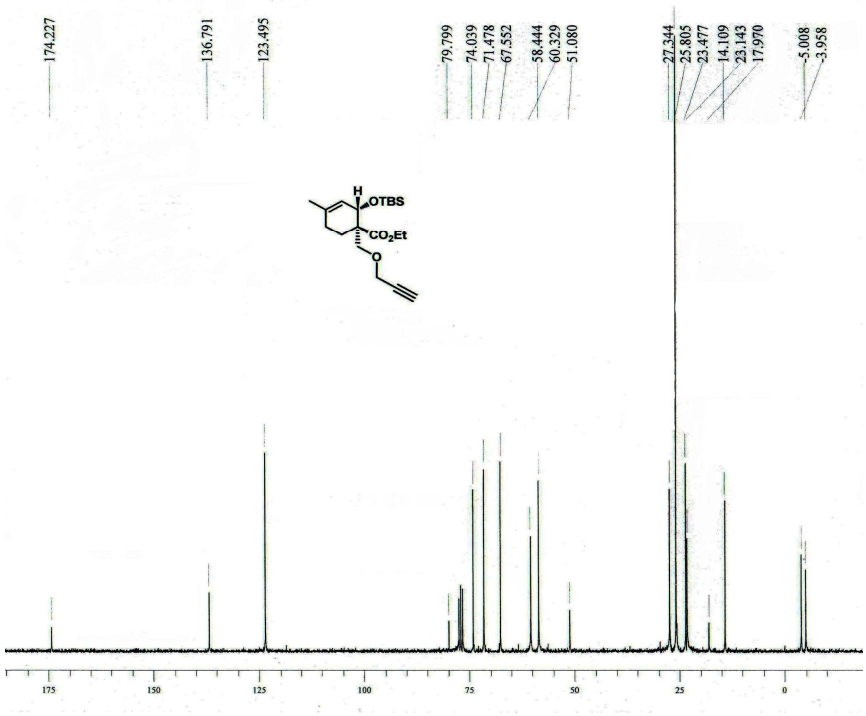
^{1}H NMR spectrum of allyl alcohol-**16**



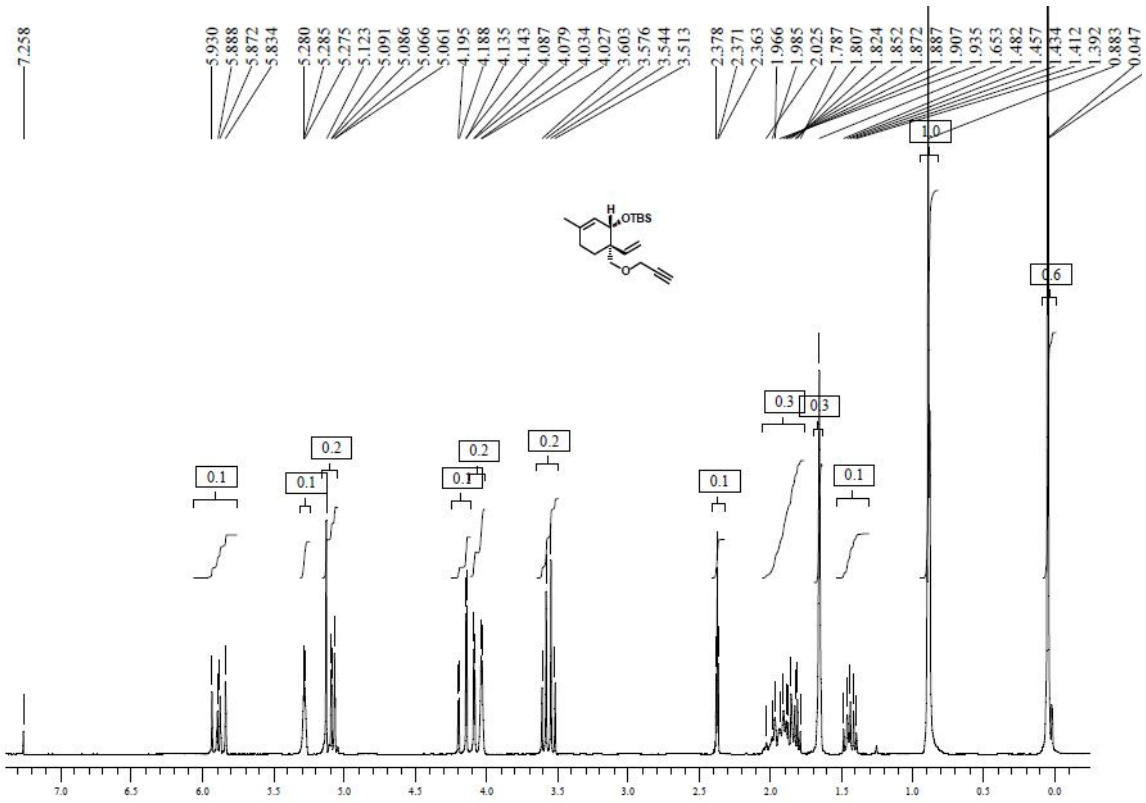
^{13}C NMR spectrum of propargyl enone-**16**



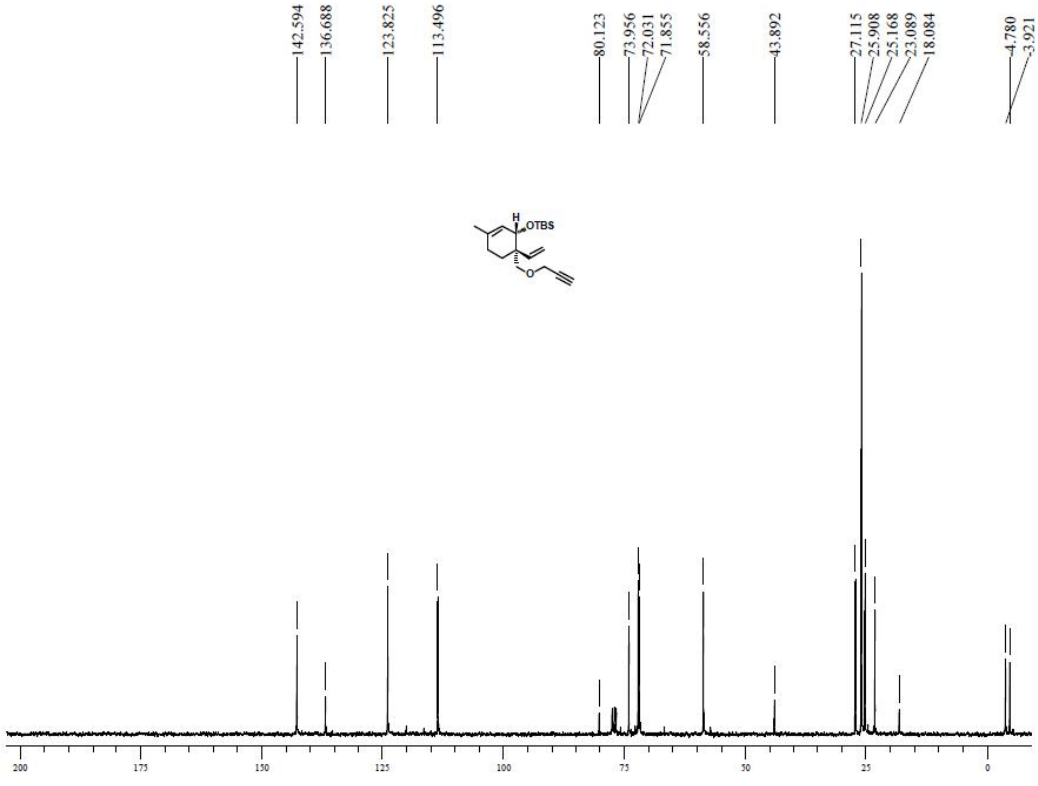
^{1}H NMR spectrum of TBS ester-**17**



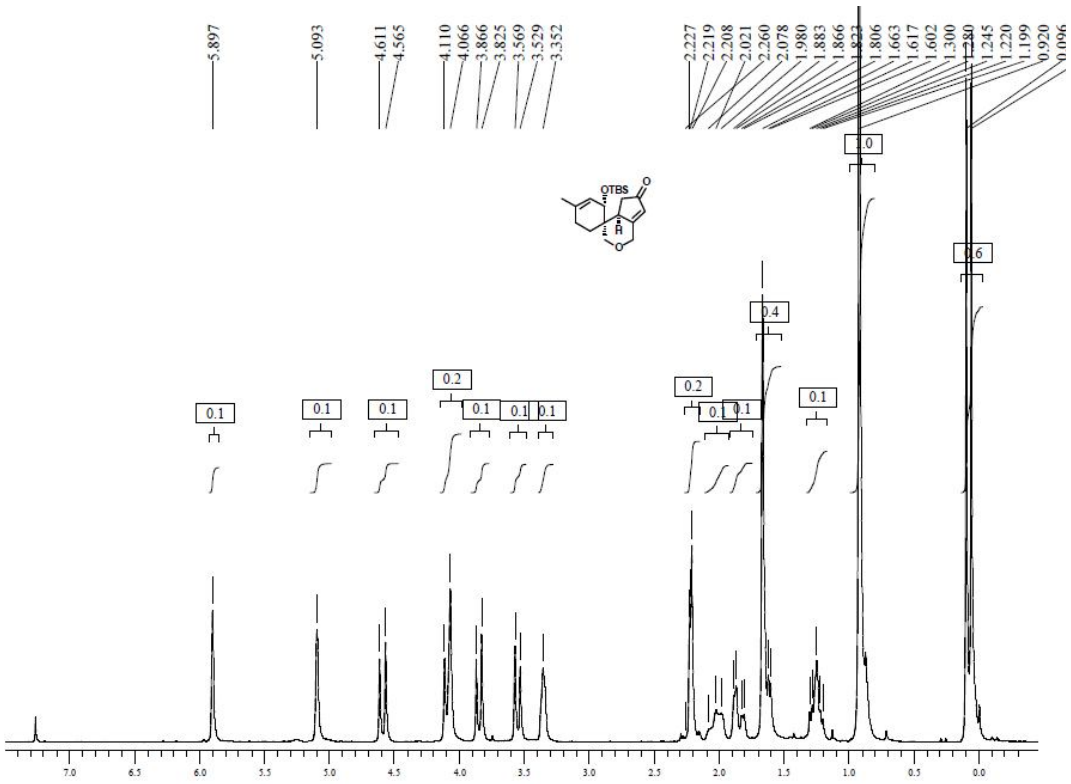
^{13}C NMR spectrum of TBS ester-**17**



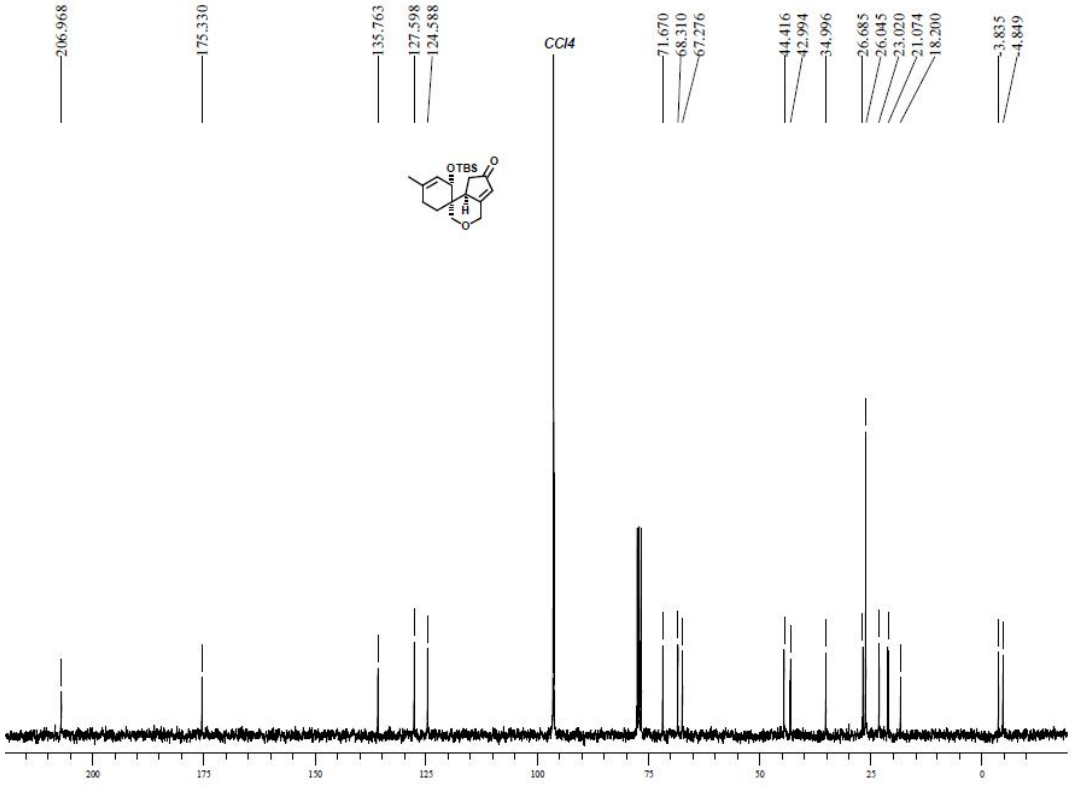
^{1}H NMR spectrum of TBS enyne-**19**



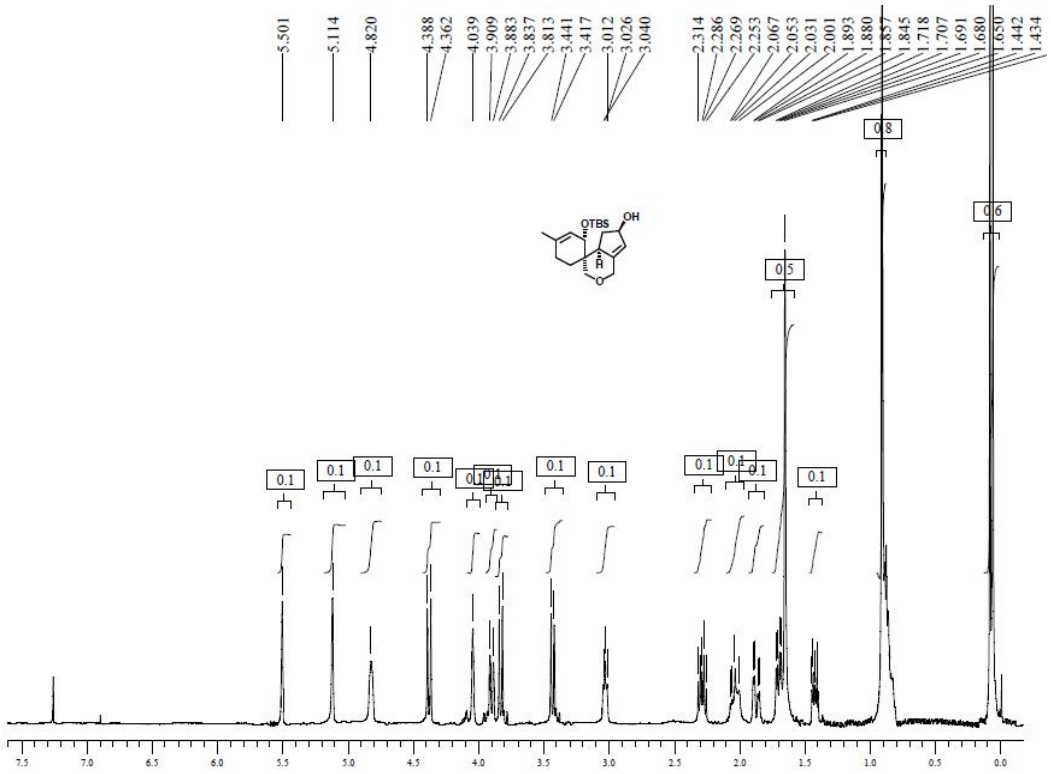
^{13}C NMR spectrum of TBS enyne-**19**



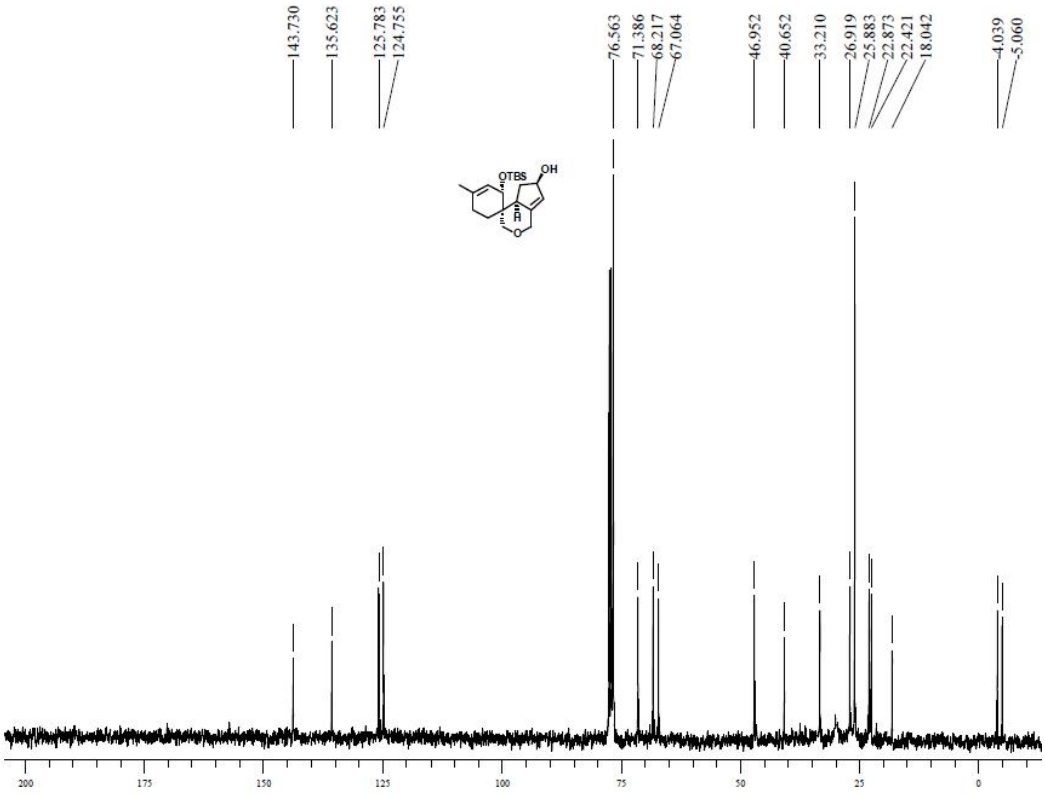
^{1}H NMR spectrum of tricyclicenone-**20**



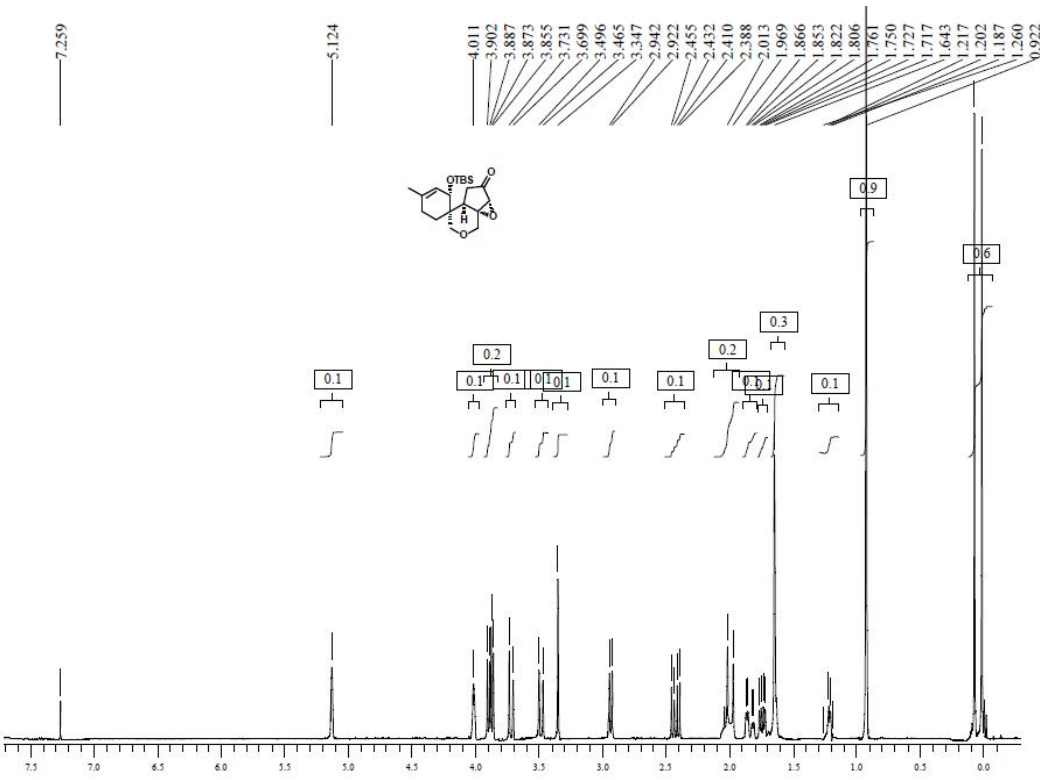
^{13}C NMR spectrum of tricyclicenone-**20**



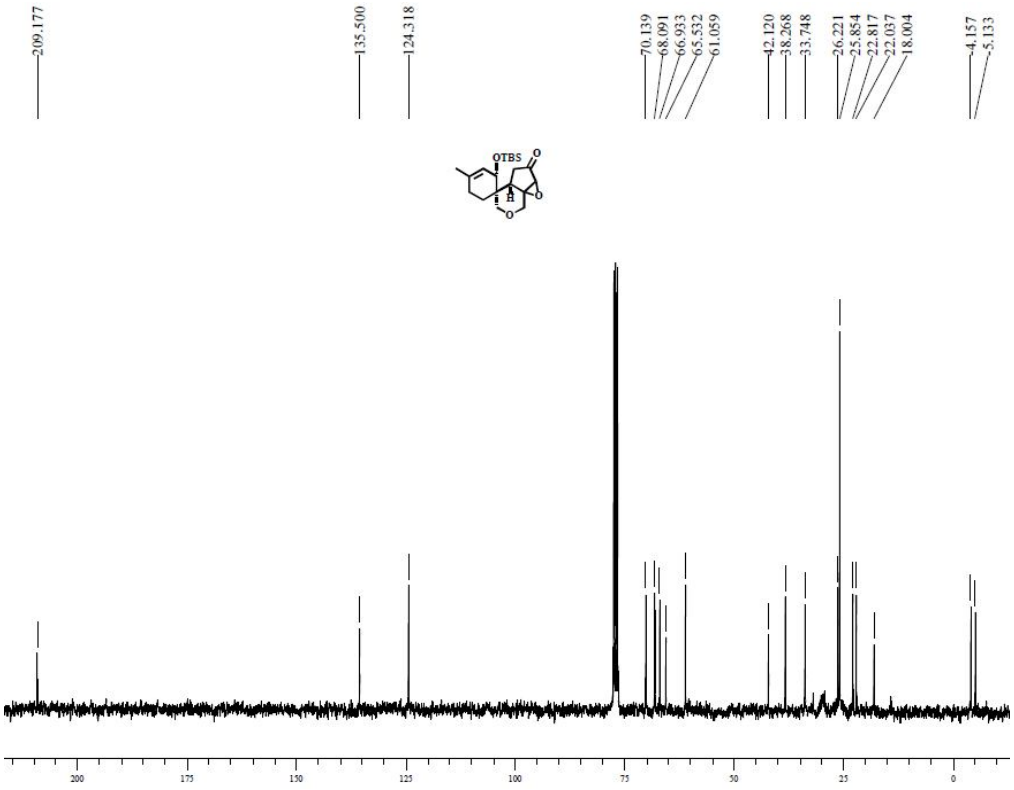
^{1}H NMR spectrum of hydroxy compound-**21**



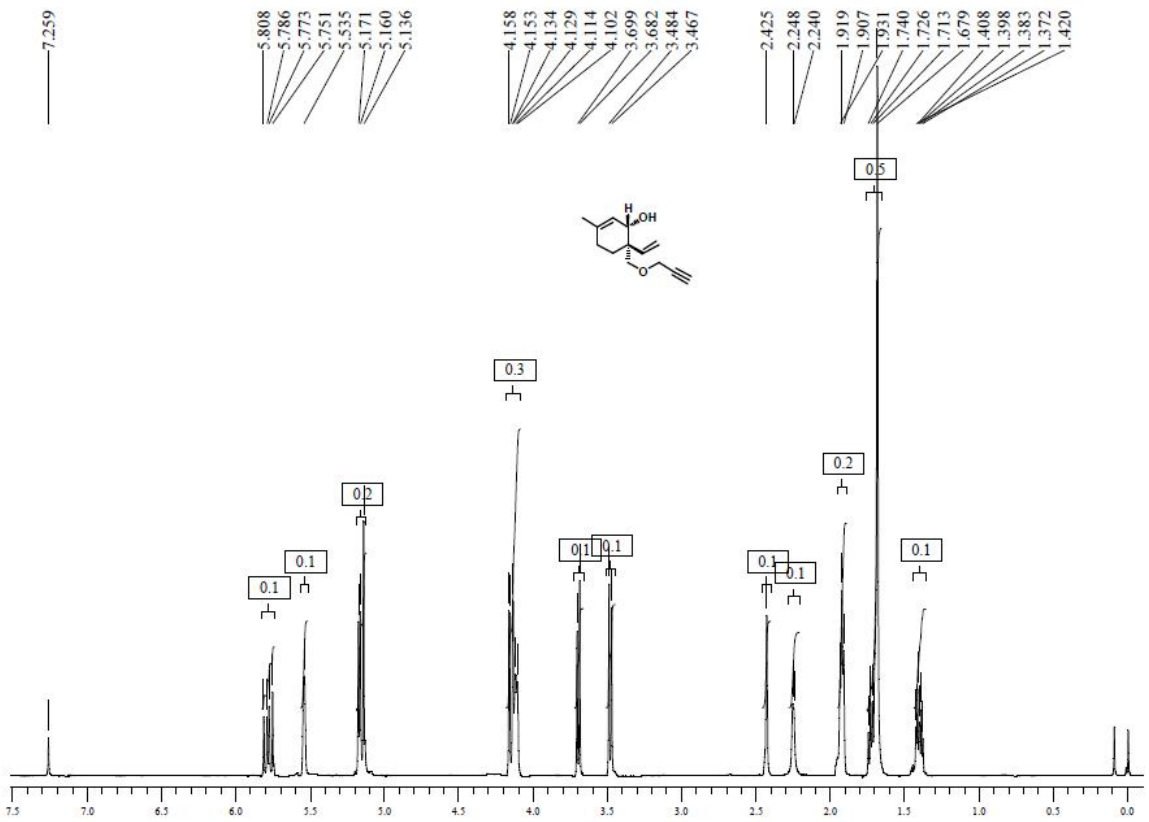
^{13}C NMR spectrum of hydroxy compound-**21**



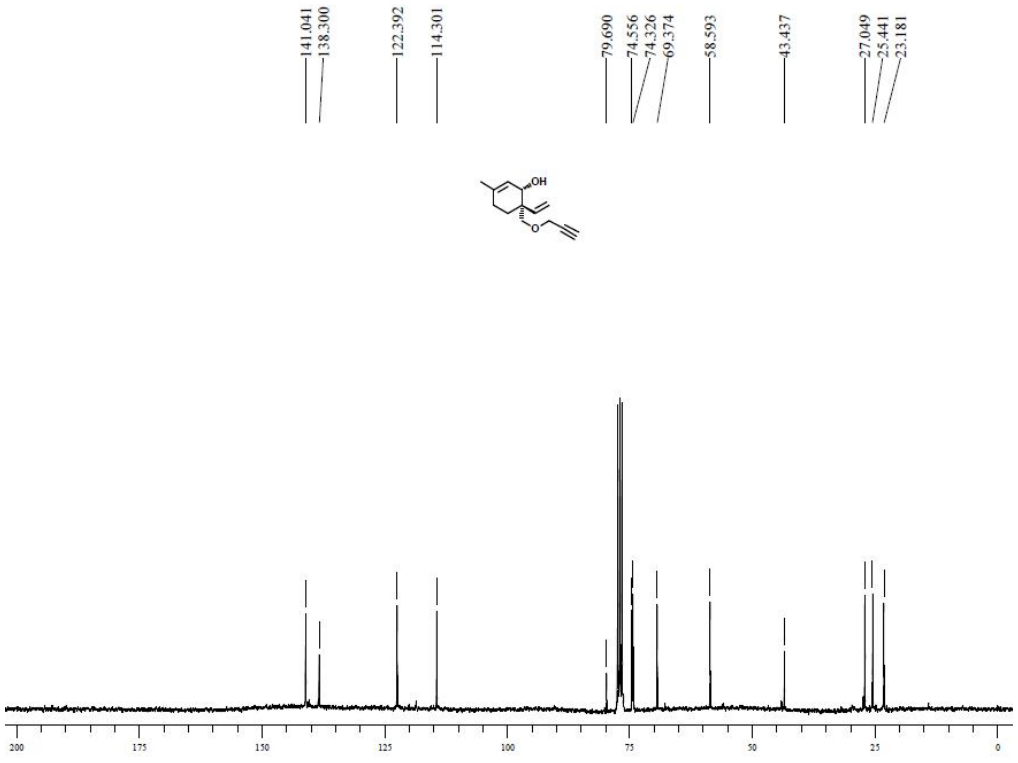
^{1}H NMR spectrum of TBS-epoxide-**22**



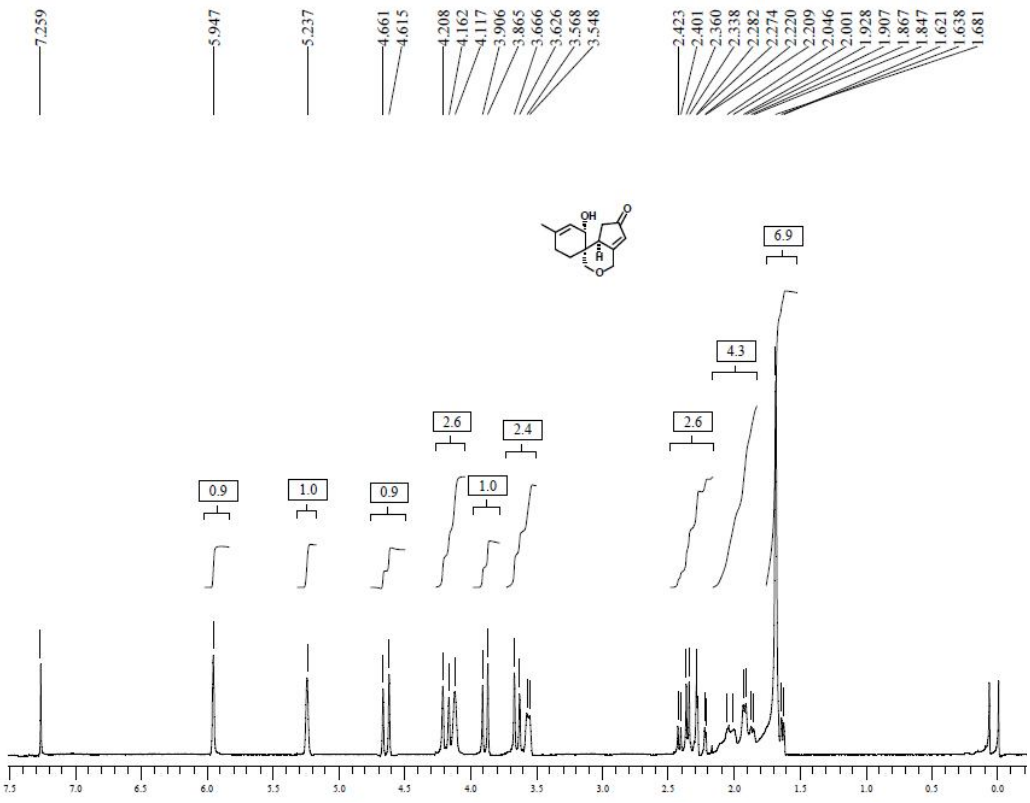
^{13}C NMR spectrum of TBS-epoxide-**22**



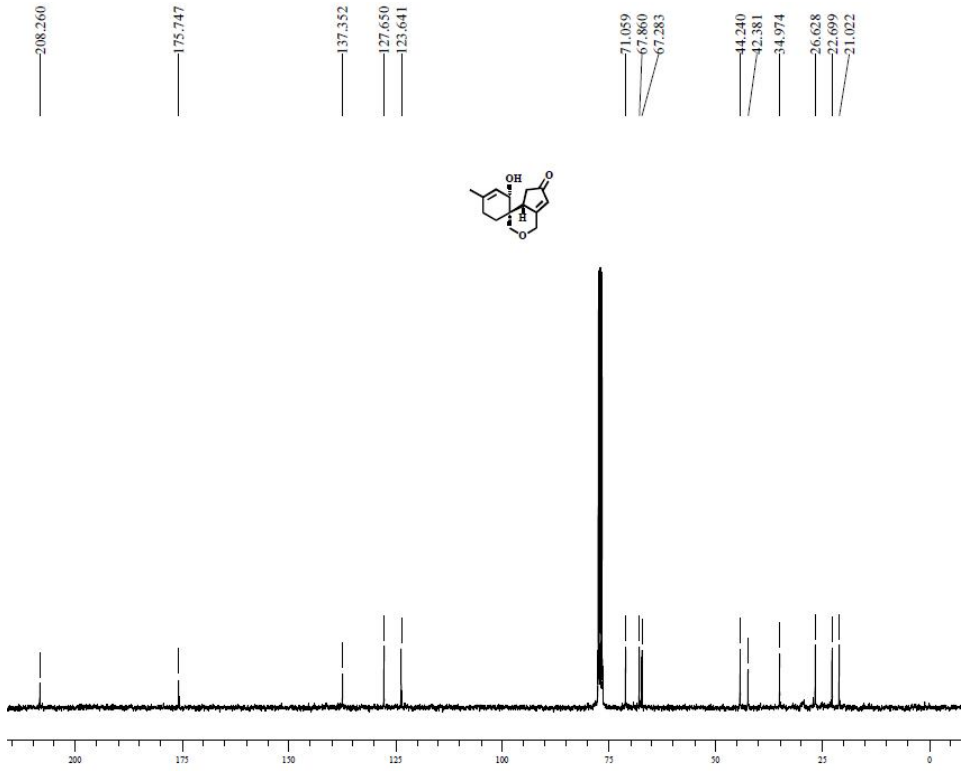
^{1}H NMR spectrum of OH-enyne-**24**



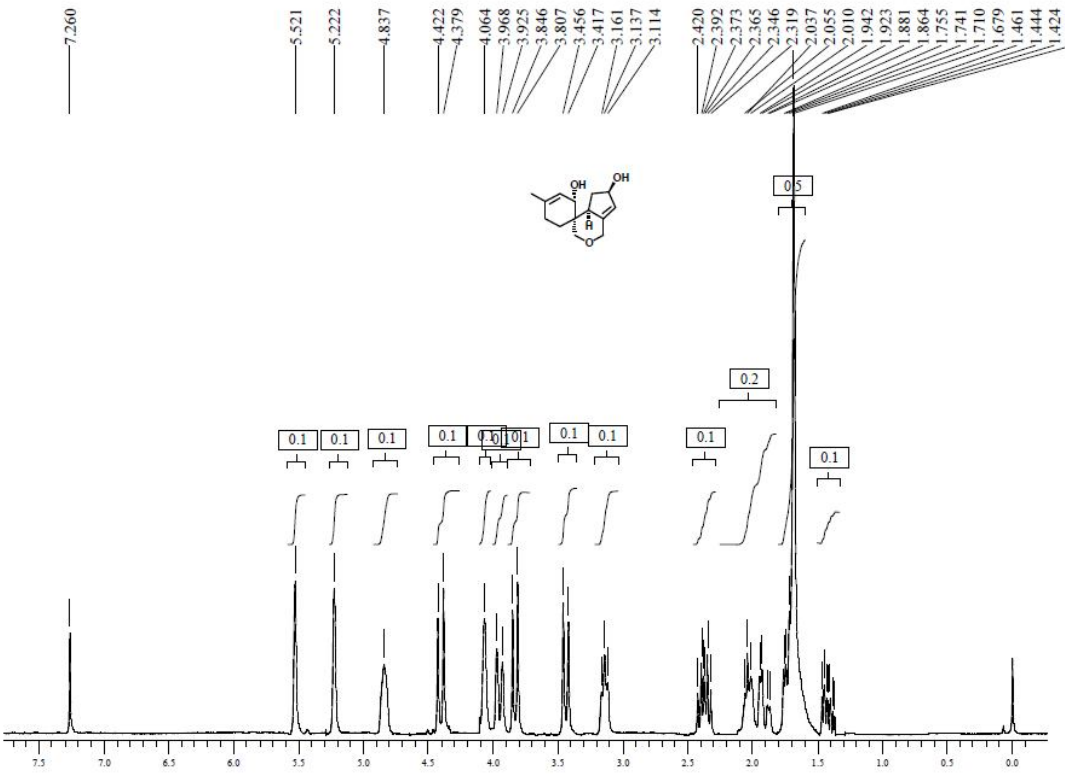
^{13}C NMR spectrum of OH-enyne-**24**



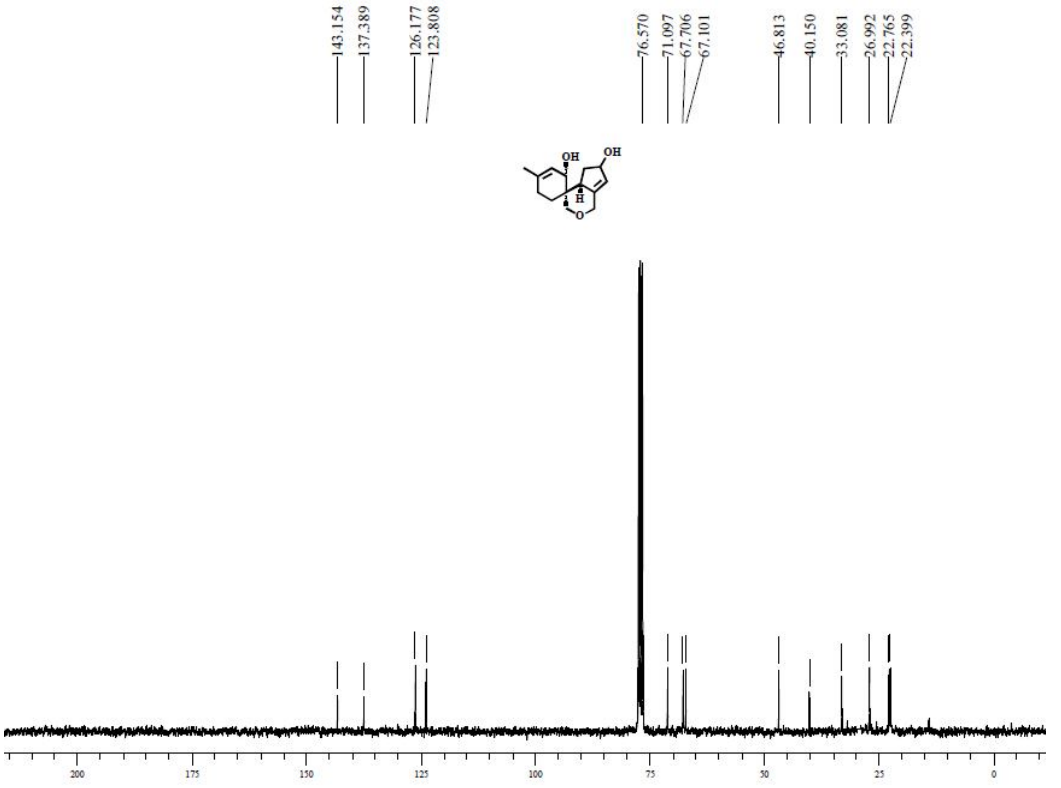
^{1}H NMR spectrum of OH-tricyclicenone-**23**



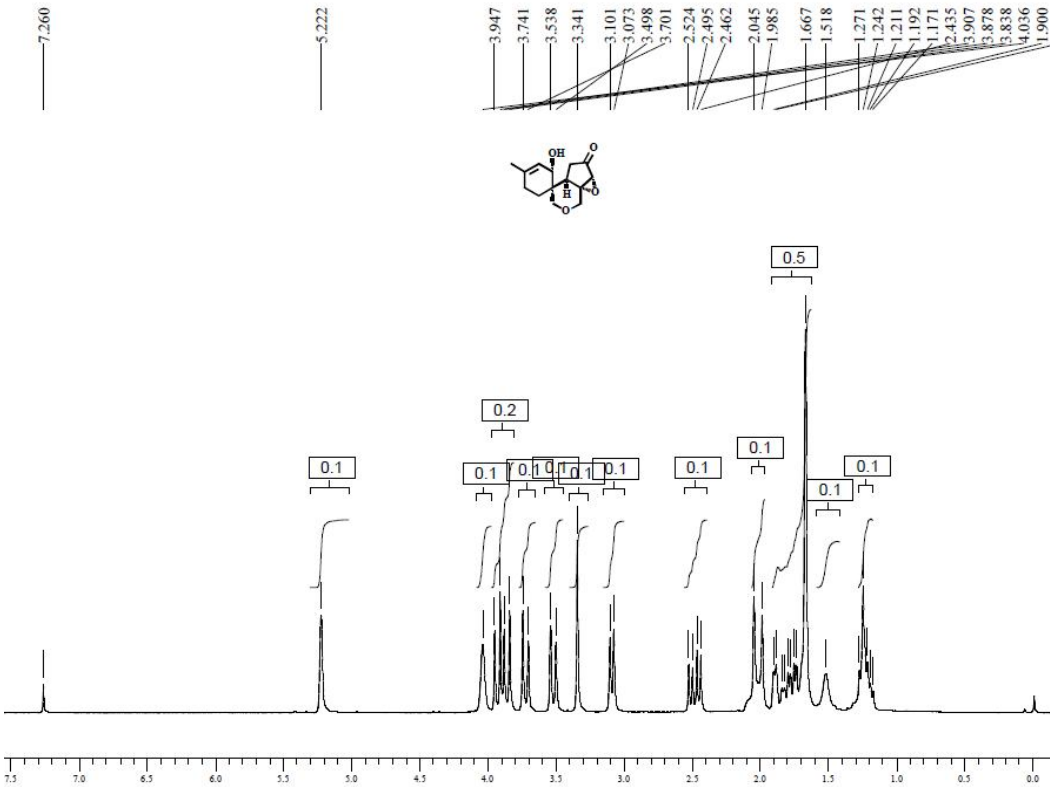
^{13}C NMR spectrum of OH-tricyclicenone-**23**



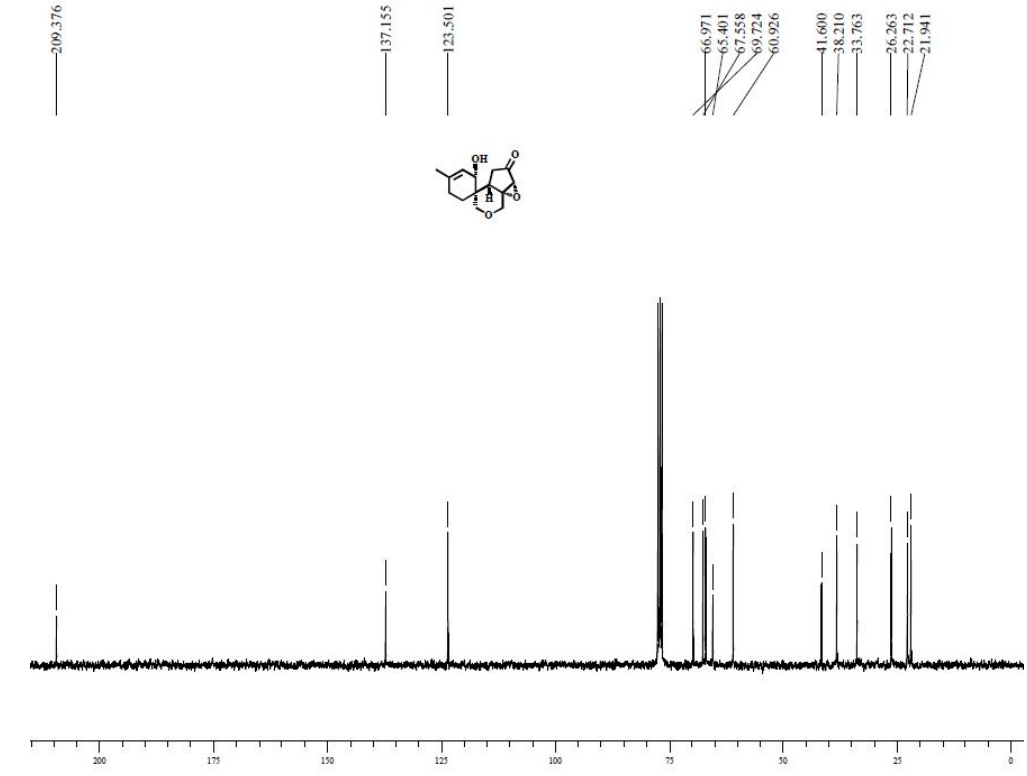
^{1}H NMR spectrum of diol-**25**



^{13}C NMR spectrum of diol-**25**



^{1}H NMR spectrum of OH-epoxide-**26**



^{13}C NMR spectrum of OH-epoxide-**26**