Electronic Supplementary Information

Iridium-catalysed highly selective reduction-elimination of steroidal 4-en-3-ones to 3,5-dienes in water

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Contents

1. General Information

Except for specially stated, all the chemicals were used directly as commercially received. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer, in trichloromethane-*d* with tetramethylsilane as internal standard, and the chemical shifts were recorded in part(s) per million (ppm). Petroleum ether (PE, 60-90 ℃ fraction) and ethyl acetate (EA) were used as the eluent of the column chromatography on silica gel.

Li's catalysts (***LCs***) and Tang's catalysts (***TCs***) were synthesized according to Li's and co-workers' publications[1] and our previous publications,[2] respectively. The catalyst solution was prepared according to our previous publication.[2a]

2. Optimization of reaction conditions

2.1 Optimization of catalyst type in entries 1-11, Table 1

A 5-mL reaction tube was charged with testosterone (**3a**, 29 mg, 0.1 mmol), 0.2 mL of HFIP (hexafluoroisopropanol) and 0.2 mL of catalyst solution (0.0025 mol/L, ***TC-1*** to ***TC-8*** or ***LC-1*** to ***LC-3***) in deionized water. The mixture was stirred for 10 minutes at 80 °C, and then formic acid (92 μL, 2.4 mmol) was added. After stirring for 2 h, the reaction mixture was cooled to room temperature, and then 4-iodonitrobenzene (12.5 mg, 0.05 mmol) was added. The mixture was diluted with water (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure and the crude residue was submitted to ^{1}H NMR yield determination.

2.2 Optimization of solvent in entries 12-21, Table 1

A 5-mL reaction tube was charged with testosterone (29 mg, 0.1 mmol), 0.2 mL of the co-solvent (HFIP, ethanol, isopropanol, tert-butanol, trifluoroethanol, *N*,*N*-dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, acetonitrile or deionized

water) and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deionized water. The mixture was stirred for 10 minutes at 80 °C, and then formic acid (46 μL, 1.2 mmol) was added. After stirring for 2 h, the reaction mixture was cooled to room temperature, and then 4-iodonitrobenzene (12.5 mg, 0.05 mmol) was added. The mixture was diluted with water (2 mL) and extracted with ethyl acetate (2 mL × 3). The solvent was evaporated under reduced pressure and the crude residue was submitted to ^{1}H NMR yield determination.

2.3 Optimization of catalyst loading in entries 22-24, Table 1

A 5-mL reaction tube was charged with testosterone (29 mg, 0.1 mmol), 0.2 mL of acetonitrile and 0.2 mL of catalyst ***TC-4*** solution (0.005 mol/L, 0.001 mol/L, or 0.0005 mol/L) in deionized water. The mixture was stirred for 10 minutes at 80 ℃, and then formic acid (46 μL, 1.2 mmol) was added. After stirring for another 2 h, the reaction mixture was cooled to room temperature, and then 4-iodonitrobenzene (12.5 mg, 0.05 mmol) was added. The mixture was diluted with water (2 mL) and extracted with ethyl acetate (2 mL × 3). The solvent was evaporated under reduced pressure, and the crude residue was submitted to ^{1}H NMR yield determination.

2.4 Optimization of equivalents of formic acid in entries 25-27, Table 1

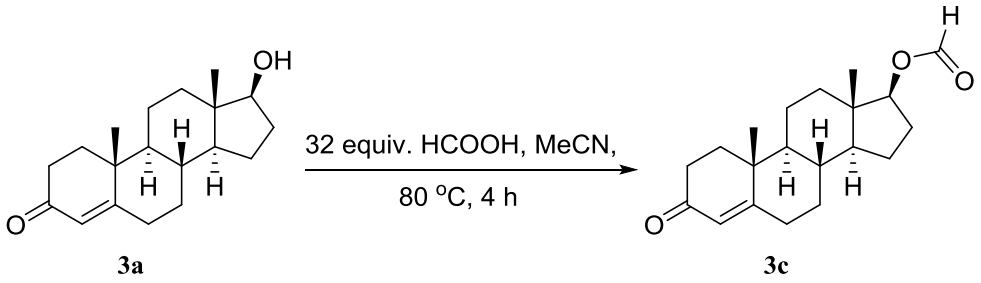
A 5-mL reaction tube was charged with testosterone (29 mg, 0.1 mmol), 0.2 ml of acetonitrile and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deionized water. The mixture was stirred for 10 minutes at 80 °C, and then formic acid (31 μL, 0.8 mmol; 61 μL, 1.6 mmol; or 92 μL, 2.4 mmol) was added. After stirring for another 2 h, the reaction mixture was cooled to room temperature, diluted with water (2 mL), and extracted with ethyl acetate (2 mL × 3). Then 4-iodonitrobenzene (12.5 mg, 0.05 mmol) was added to the combined organic phase. The solvent was evaporated under reduced pressure, and the crude residue was submitted to ^{1}H NMR yield determination.

2.5 Optimization of reaction time in entries 28, Table 1.

A 5-mL reaction tube was charged with testosterone (29 mg, 0.1 mmol), 0.2 ml of acetonitrile and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deionized water. The mixture was stirred for 10 minutes at 80 °C, and then formic acid (61 μL, 1.6 mmol) was added. After stirring for another 4 h, the reaction mixture was cooled to room temperature, diluted with water (2 mL), and extracted with ethyl acetate (2 mL × 3). Then 4-iodonitrobenzene (12.5 mg, 0.05 mmol) was added to the combined organic phase. The solvent was evaporated under reduced pressure, and the crude residue was submitted to ^{1}H NMR yield determination.

3. Preparation of starting materials 3 and 4

3.1 Preparation of testosterone 17-formate (**3c**)

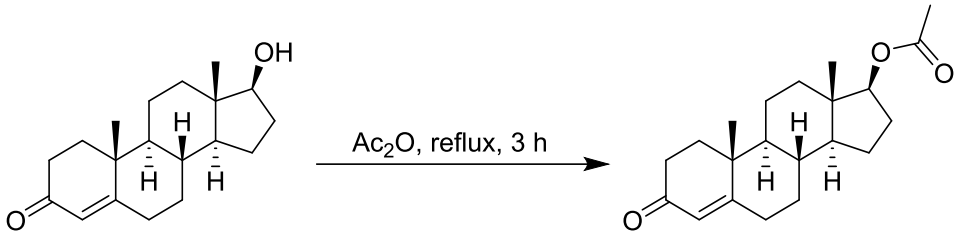


3a **3c**

A 25-mL round bottom flask was sequentially added testosterone (288 mg, 1.0 mmol), 5 mL of acetonitrile, and formic acid (1.2 mL, 32 mmol). The mixture was stirred for 4 h at 80 ℃, and then quenched by saturated solution of sodium bicarbonate, extracted with dichloromethane, dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, 7:1, *v/v*) to give **3c** (200 mg, 63%) as a white solid. R_f = 0.6 (PE/EA, 2:1, *v/v*); m.p.: 123-125 ℃ (reported 127-129 ℃);[3] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.08 (s, 1H), 5.73 (s, 1H), 4.71 (t, *J* = 8.6 Hz, 1H), 2.48 – 2.16 (m, 5H), 2.03 (ddd, *J* = 13.6, 5.2, 3.2 Hz, 1H), 1.91 – 1.77 (m, 2H), 1.77 – 1.64 (m, 2H), 1.64 – 1.51 (m, 3H), 1.49 – 1.32 (m, 2H), 1.24 – 1.15 (m, 1H), 1.20 (s, 3H), 1.14 – 1.01 (m, 2H), 1.01 – 0.91 (m, 1H), 0.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 199.3, 170.7, 161.1, 123.9, 82.3,

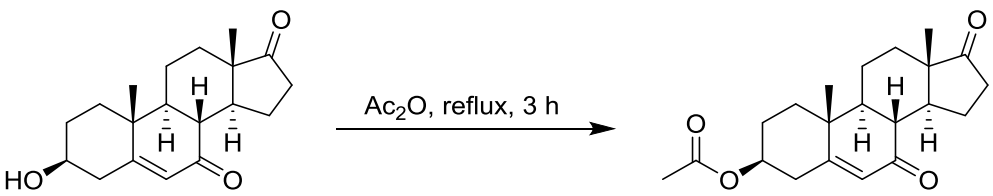
53.6, 50.2, 42.5, 38.6, 36.5, 35.7, 35.3, 33.9, 32.7, 31.4, 27.4, 23.4, 20.5, 17.4, 12.0.

3.2 Preparation of testosterone 17-acetate (**3d**) and 3β-acetoxy-5-androsten-7,17-dione (**3u**)[4]



3a **3d**

A solution of testosterone (144 mg, 0.5 mmol) in 2 mL of acetic anhydride was refluxed for 3 h, and then 1 mL of acetic acid and 2 mL of water were added. After cooling to room temperature, the reaction mixture was neutralized by saturated solution of sodium bicarbonate, extracted with dichloromethane, dried with sodium sulfate, and concentrated under vacuum condition. The crude product was purified by flash column chromatography (PE/EA = 8:1, *v/v*) to give **3d** (138 mg, 84%) as a colorless crystal. R_f = 0.3 (PE/EA = 5:1, *v/v*); m.p. 141-142 ℃ (reported 140-142 ℃);[5] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.73 (s, 1H), 4.60 (t, *J* = 8.6 Hz, 1H), 2.48 – 2.34 (m, 3H), 2.34 – 2.25 (m, 1H), 2.26 – 2.11 (m, 1H), 2.07 – 1.99 (m, 1H), 2.05 (s, 3H), 1.90 – 1.76 (m, 2H), 1.76 – 1.62 (m, 2H), 1.62 – 1.44 (m, 3H), 1.44 – 1.28 (m, 2H), 1.23 – 1.14 (m, 1H), 1.19 (s, 3H), 1.11 – 1.00 (m, 2H), 1.00 – 0.90 (m, 1H), 0.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 199.3, 171.0, 170.9, 123.9, 82.4, 53.6, 50.2, 42.4, 38.5, 36.5, 35.6, 35.3, 33.9, 32.7, 31.4, 27.4, 23.4, 21.1, 20.5, 17.3, 12.0.

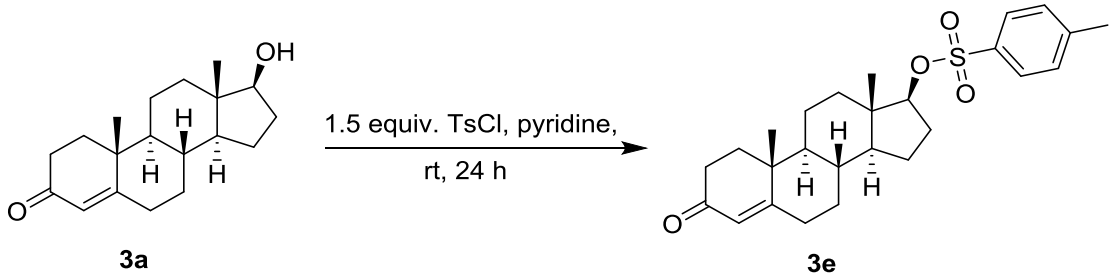


3t **3u**

A solution of 7-keto-dehydroepiandrosterone (**3t**, 600 mg, 1.98 mmol) in 2 mL of acetic anhydride was refluxed for 3 h, and then 2 mL of acetic acid and 4 mL of water were added. After cooling to room temperature, the reaction mixture was neutralized by saturated solution of sodium bicarbonate, extracted with dichloromethane, dried with sodium sulfate, and concentrated under vacuum condition. The crude product was purified by flash column chromatography (PE/EA = 5:1, *v/v*) to give **3u** (583 mg, 85%) as a white solid. R_f = 0.5 (PE/EA = 2:1, *v/v*); m.p. 185-186 ℃, (reported 184.5-187.5 ℃);[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.76 (s, 1H), 4.80 – 4.66 (m, 1H), 2.90 – 2.76 (m, 1H), 2.65 – 2.55 (m, 1H), 2.56 – 2.36 (m, 3H), 2.21 – 1.94 (m, 3H), 2.06 (s, 3H), 1.91 – 1.52 (m, 7H), 1.36 – 1.19 (m, 2H), 1.25 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 220.1, 200.6, 170.1, 164.7, 126.4, 71.9, 49.9, 47.7, 45.6, 44.3, 38.4, 37.7, 35.9, 35.5, 30.6, 27.2, 24.1, 21.2, 20.5, 17.3, 13.7.

3.3 Preparation of testosterone *p*-toluenesulfonate (**3e**) [7]

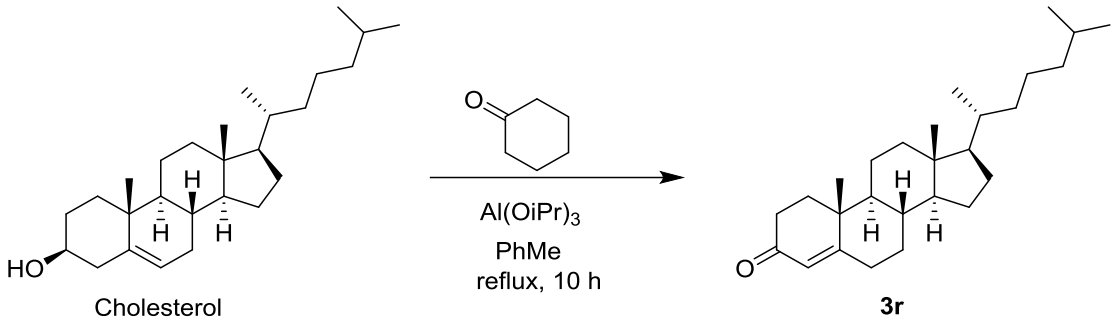


3a **3e**

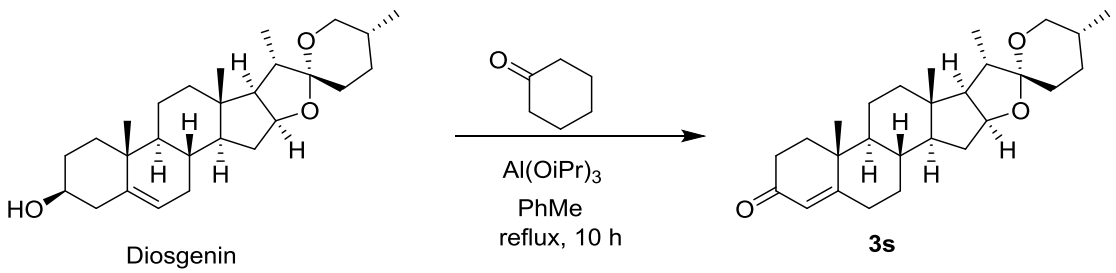
A solution of testosterone (0.5 g) and 4-toluene sulfonyl chloride (0.5 g) in 2 mL of dry pyridine was stirred for 24 h at room temperature, and was then poured into ice water. The reaction mixture was washed with hydrochloric acid (1 mol/L) and water, extracted with dichloromethane, dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 8:1) to give **3e** (299 mg, 39%) as a white solid. R_f = 0.4 (PE/EA, *v/v*, 2:1); m.p.: 170-172 ℃, (reported 171-172 ℃);[8] ^{1}H NMR (400 MHz, CDCl3): 7.78 (d, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 7.6 Hz, 1H), 5.71 (s, 1H), 4.25 (t, *J* = 8.6 Hz, 1H), 2.45 (s, 3H), 2.42 – 2.21 (m, 4H), 2.05 – 1.86 (m, 2H), 1.86 – 1.75 (m, 1H), 1.75 – 1.47 (m,

6H), 1.43 – 1.26 (m, 2H), 1.16 (s, 3H), 1.03 – 0.86 (m, 4H), 0.84 (s, 3H); ^{13}C (101 MHz, $CDCl_3$) δ (ppm): 199.3, 170.5, 144.4, 134.1, 129.6, 127.7, 123.9, 89.4, 53.5, 49.4, 42.8, 38.5, 35.7, 35.6, 35.2, 33.8, 32.5, 31.2, 27.5, 23.2, 21.6, 20.3, 17.3, 11.6.

3.4 Preparation of 4-cholesten-3-one (**3r**) and Diosgenone (**3s**)

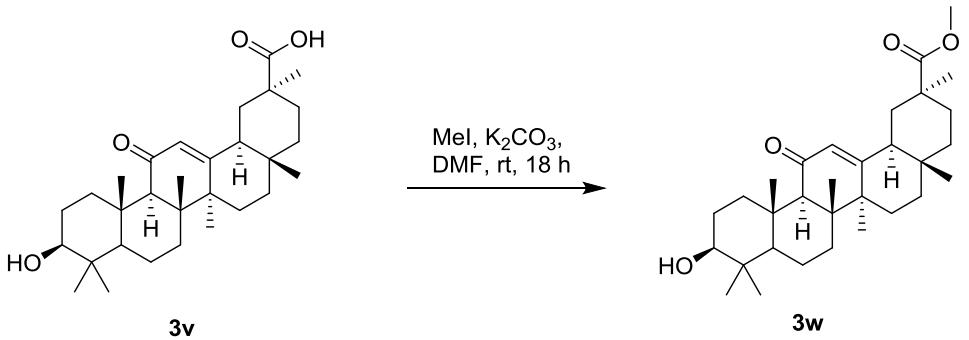


4-Cholesten-3-one (3r) was synthesized from cholesterol (780 mg, 2.02 mmol) according to the method reported by Yuichi Hashimoto,[9] and purified by flash column chromatography (PE/EA, 50:1) to give **3r** (505 mg, 65%) as colorless crystals. R_f = 0.6 (PE/EA, *v/v*, 5:1); m.p.:83-84 ℃, (reported 84-85 ℃);[10] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.72 (s, 1H), 2.48 – 2.21 (m, 4H), 2.09 – 1.96 (m, 2H), 1.90 – 1.78 (m, 2H), 1.75 – 1.46 (m, 6H), 1.46 – 1.21 (m, 5H), 1.18 (s, 3H), 1.17 – 0.93 (m, 9H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 1.6 Hz, 3H), 0.86 (d, *J* = 1.2 Hz, 3H), 0.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 199.6, 171.7, 123.7, 56.1, 55.9, 53.8, 42.4, 39.6, 39.5, 38.6, 36.1, 35.7, 35.6, 34.0, 32.9, 32.0, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.0, 18.6, 17.4, 11.9.



Diosgenone (3s) was prepared according to the method reported by Yuichi Hashimoto :[9] To a 25 mL flame-dried round bottom flask was added diosgenin (828 mg, 2.0 mmol), aluminium isopropoxide (1224 mg, 6.0 mmol), cyclohexanone (1.5 mL) and dry toluene (5 mL). The reaction mixture was refluxed for 10 h. Upon cooling down to room temperature, water (20 mL) and ethyl acetate (20 mL) were added to the solution. After filtering through Celite, the organic layer was separated, washed with water and brine, dried over sodium sulfate, and concentrated in vacuum. The crude compound was purified by flash column chromatography (PE/EA, *v/v*, 20:1) to give **3s** (513 mg, 62%) as a white solid. R_f = 0.3 (PE/EA, *v/v*, 5:1); m.p.: 186-187 ℃, (reported 185-186 ℃);[11] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.73 (s, 1H), 4.41 (q, *J* = 7.6 Hz, 1H), 3.47 (ddd, *J* = 10.8, 4.0, 1.6 Hz, 1H), 3.37 (dd, *J* = 10,8, 10.8 Hz, 1H), 2.48 – 2.24 (m, 4H), 2.06 – 1.98 (m, 2H), 1.92 – 1.82 (m, 2H), 1.81 – 1.37 (m, 11H), 1.36 – 1.23 (m, 2H), 1.20 (s, 3H), 1.18 – 1.10 (m, 1H), 1.10 – 1.01 (m, 1H), 0.97 (d, *J* = 7.2 Hz, 3H), 0.95 – 0.85 (m, 1H), 0.82 (s, 3H), 0.79 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 199.5, 171.1, 123.9, 109.3, 80.6, 66.9, 62.0, 55.6, 53.7, 41.6, 40.4, 39.6, 38.6, 35.7, 35.2, 33.9, 32.8, 32.1, 31.7, 31.4, 30.3, 28.8, 20.8, 17.4, 17.1, 16.3, 14.5.

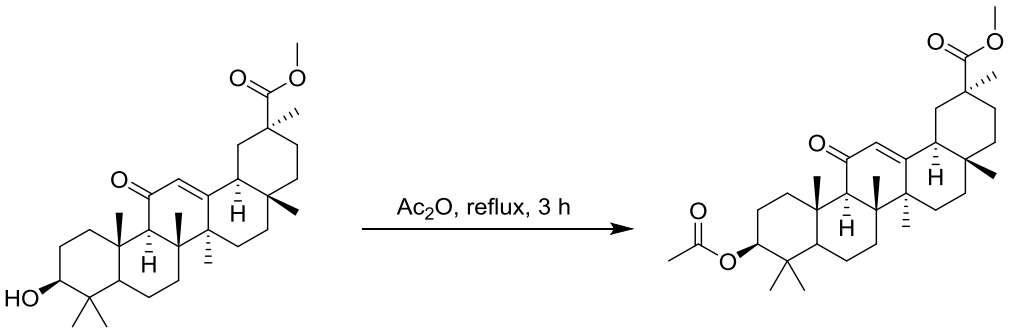
3.5 Preparation of Methyl 3β-hydroxyl-glycyrrhetinate (**3w**) and Methyl 3β-acetoxy-glycyrrhetinate (**3x**)



3v **3w**

Methyl 3β-hydroxyl-glycyrrhetinate (3w) was synthesized from 18β-glycyrrhetinic acid (**3v**, 1.0 g, 2.15 mmol) according to the method reported by Thomas Lectka,[4] and the crude product was purified by flash column chromatography

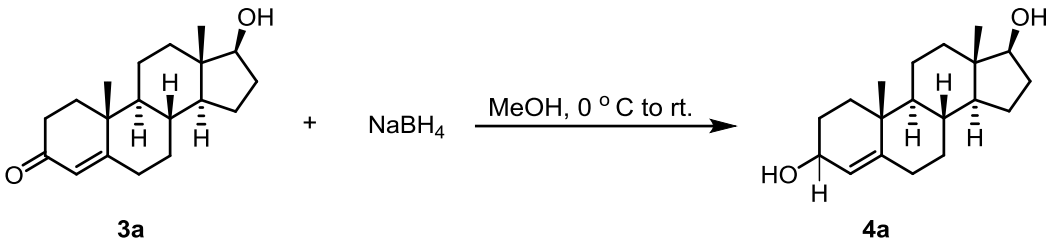
(PE/EA, 2:1) to give **3w** (863 mg, 84%) as a white solid. R_f = 0.6 (PE/EA, *v/v*, 2:1); m.p.: 250-251 ℃, (reported 255-258 ℃);[12] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.66 (s, 1H), 3.69 (s, 3H), 3.23 (dd, *J* = 10.8, 5.2 Hz, 1H), 2.79 (dt, *J* = 13.2, 3.6 Hz, 1H), 2.34 (s, 1H), 2.12 – 1.97 (m, 3H), 1.92 (ddd, *J* = 13.2, 4.0, 2.8 Hz, 1H), 1.83 (td, *J* = 13.6, 4.8 Hz, 1H), 1.72 – 1.56 (m, 5H), 1.51 – 1.38 (m, 4H), 1.37 (s, 3H), 1.35 – 1.28 (m, 2H), 1.23 – 1.17 (m, 1H), 1.15 (s, 3H), 1.14 (s, 3H), 1.13 (s, 3H), 1.06 – 0.93 (m, 2H), 1.01 (s, 3H), 0.81 (s, 6H), 0.74 – 0.66 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 200.2, 176.9, 169.2, 128.5, 78.8, 61.8, 54.9, 51.8, 48.4, 45.4, 44.0, 43.2, 41.1, 39.1, 37.7, 37.1, 32.7, 31.8, 31.1, 28.5, 28.3, 28.1, 27.3, 26.5, 26.4, 23.4, 18.7, 17.5, 16.4, 15.6.



3w **3x**

3β-Acetoxy-glycyrrhetinate (3x) was synthesized from methyl 3β-hydroxyl-glycyrrhetinate (**3w**, 373 mg, 0.77 mmol)) according to the method reported by Thomas Lectka,[4] and **3x** (356 mg, 88 %) was obtained as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): 5.67 (s, 1H), 4.52 (dd, *J* = 11.6, 4.8 Hz, 1H), 3.69 (s, 3H), 2.80 (dt, *J* = 13.7, 3.6 Hz, 1H), 2.36 (s, 1H), 2.12 – 2.06 (m, 1H), 2.05 (s, 3H), 2.05 – 1.97 (m, 2H), 1.97 – 1.88 (m, 1H),1.88 – 1.74 (m, 1H), 1.74 – 1.55 (m, 5H), 1.52 – 1.38 (m, 3H), 1.36 (s, 3H), 1.35 – 1.26 (m, 2H), 1.22 – 1.17 (m, 1H), 1.16 (s, 3H), 1.15 (s, 3H), 1.13 (s, 3H), 1.10 – 0.97 (m, 2H), 0.88 (s, 6H), 0.83 – 0.77 (m, 1H), 0.81 (s, 3H); ^{13}C (101 MHz, $CDCl_3$) δ (ppm): 200.1, 176.9, 171.0, 169.2, 128.5, 80.6, 61.7, 55.0, 51.8, 48.4, 45.4, 44.0, 43.2, 41.1, 38.8, 38.0, 37.7, 36.9, 32.7, 31.8, 31.1, 28.5, 28.3, 28.0, 26.5, 26.4, 23.6, 23.3, 21.3, 18.7, 17.4, 16.7, 16.4.

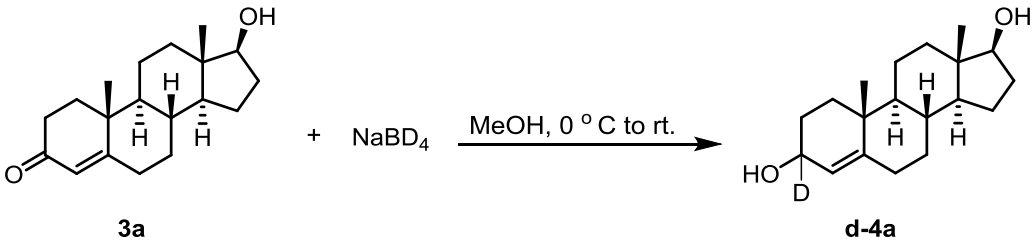
3.6 Preparation of (17β)-Androst-4-ene-3,17-diol (**4a**)



3a **4a**

A solution of testosterone (144 mg, 0.5 mmol) in MeOH (15 mL) was added $NaBH_4$ (113 mg, 3.0 mmol) in one portion at 0 ℃, and then stirred for 3 h at room temperature. The reaction mixture was quenched with water, extracted with dichloromethane, dried over sodium sulfate, and concentrated in vacuo. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 2:1) to give **4a** (93 mg, 64%) as a white solid. R_f : 0.3 (PE/EA, *v/v*, 2:1); m.p.: 84-85 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.28 (s, 1H), 4.20 – 4.08 (m, 1H), 3.61 (t, *J* = 8.6 Hz, 1H), 2.26 – 2.13 (m, 1H), 2.10 – 1.98 (m, 2H), 1.98 – 1.89 (m, 1H), 1.86 – 1.64 (m, 5H), 1.64 – 1.37 (m, 5H), 1.37 – 1.18 (m, 3H), 1.08 – 0.97 (m, 1H), 1.06 (s, 3H), 0.97 – 0.79 (m, 2H), 0.78 – 0.69 (m, 1H), 0.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 147.2, 123.5, 81.7, 67.8, 54.5, 50.7, 42.8, 37.3, 36.6, 35.9, 35.4, 32.6, 32.0, 30.4, 29.4, 23.3, 20.6, 18.9, 11.0.

3.7 Preparation of (17β)-Androst-4-ene-3-d-3,17-diol (***d*-4a**)

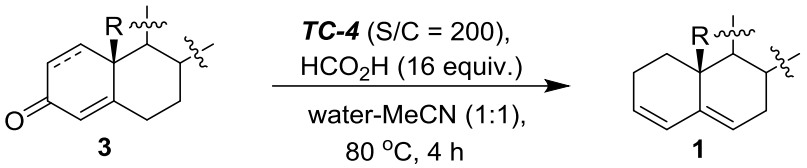


3a **d-4a**

A solution of testosterone (144 mg, 0.5 mmol) in MeOH (15 mL) was added $NaBD_4$ (126 mg, 3.0 mmol) in one portion at 0 ℃, and then stirred for 3 h at room temperature. The reaction mixture was quenched with water, extracted with dichloromethane, dried over sodium sulfate, and concentrated in vacuo. The crude

product was purified by flash column chromatography (PE/EA, *v/v*, 2:1) to give **d-4a** (112 mg, 77%) as a white solid. R_f = 0.3 (PE/EA, *v/v*, 2:1); m.p.: 176-177 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.28 (s, 1H), 3.62 (t, *J* = 8.6 Hz, 1H), 2.20 (tdd, *J* = 13.6, 4.8, 1.6 Hz, 1H), 2.11 – 1.98 (m, 2H), 1.98 – 1.90 (m, 1H), 1.81 (dt, *J* = 12.5, 3.4 Hz, 1H), 1.78 – 1.65 (m, 2H), 1.65 – 1.49 (m, 3H), 1.49 – 1.37 (m, 4H), 1.37 – 1.19 (m, 3H), 1.06 (s, 3H), 1.05 – 0.97 (m, 1H), 0.97 – 0.79 (m, 2H), 0.76 (s, 3H), 0.75 – 0.70 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 147.5, 123.4, 81.8, 67.9, 67.4 (t, $J_{D\text{-}C}$ = 22.5 Hz), 54.5, 50.7, 42.9, 37.4, 36.6, 36.0, 35.4, 32.6, 32.1, 30.5, 29.4, 23.4, 20.6, 18.9, 11.0.

4. General procedure for the preparation of the steroidal 3,5-dienes



A 5-mL reaction tube was charged with 4-en-3-ones **3** (0.1 mmol), 0.2 mL of acetonitrile, and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deionized water. The mixture was stirred for 10 minutes at 80 °C, and then formic acid (61 μL, 1.6 mmol, 16 equiv.) was added. After stirring for another 4 h, the reaction mixture was neutralized by saturated solution of sodium bicarbonate (15 mL), extracted with dichloromethane (10 mL × 3), dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography to give 3,5-dienes **1**.

In some cases, the reaction conditions were slightly adjusted. For details, please see the Table notes in the full text and Characterization data of products (Section 8) in Electronic Supplementary Information.

5. Gram scale preparation

A 100-mL round-bottom flask was charged with testosterone (2.0 g, 6.9 mmol)

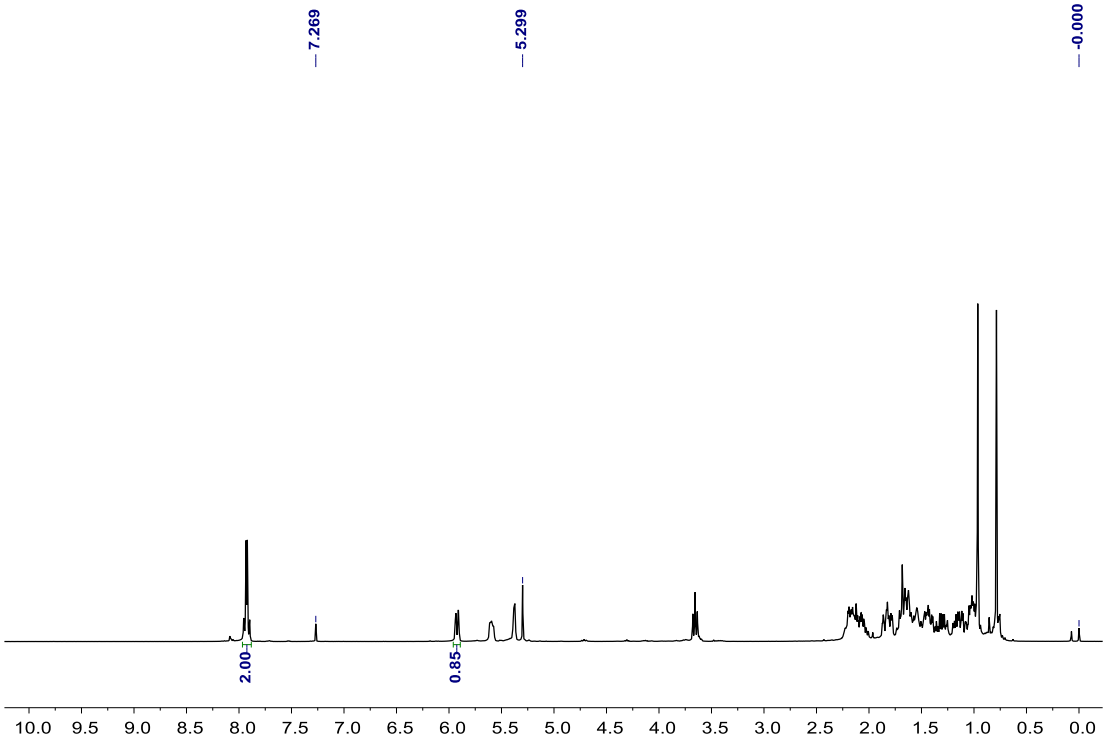
and acetonitrile (14 mL), ***TC-4*** catalyst (19.6 mg, 0.035 mmol), and deionized water (14 mL). The mixture was stirred for 10 minutes at 80 ℃, and then formic acid (8.4 mL, 0.22 mol) was added. The mixture was stirred for 4 h, and a white solid gradually precipitated. Then formic acid (8.4 mL, 0.22 mol) and acetonitrile (14 ml) was added, and the mixture was stirred for another 4 h. A third portion of formic acid (8.4 mL, 0.22 mol) was added, and the reaction mixture was stirred for 4 h. After the reaction mixture was cooled to room temperature, sodium carbonate was added to neutralize excess acid, and then water was added. The mixture was extracted with dichloromethane, and the organic phase was separated and dried with sodium sulfate, and concentrated under reduced pressure to obtain a white solid.

The white solid was refluxed in 50 mL of methanol with sodium carbonate (1.5 g, 14 mmol, 2 equiv.) for half an hour. The methanol was removed under reduced pressure and water was added. The mixture was extracted with dichloromethane, dried over sodium sulfate, filtered through Celite, concentrated under reduced pressure, and recrystallized from EA to give **1a** as a white solid (1.47 g, 78%).

6. Experimental Procedures for Mechanistic studies

6.1 The reaction of **4a** without catalyst

A 5 mL reaction tube was charged with **4a** (29 mg, 0.1 mmol), 0.2 mL of acetonitrile, and 0.2 mL of deionized water. The mixture was stirred for 10 minutes at 80 °C, and then formic acid (61 μL, 1.6 mmol) was added. After stirring for another 2 h, the reaction mixture was cooled to room temperature, and then 4-iodonitrobenzene (12.5 mg, 0.05 mmol) was added. The mixture was diluted with water and extracted with dichloromethane. The solvent was evaporated under reduced pressure and the ^{1}H NMR yield was measured (85%).



6.2 The reaction of **d-4a** without catalyst

A 5-mL reaction tube was charged with **d-4a** (29 mg, 0.1 mmol), 0.2 mL of acetonitrile and 0.2 mL of deionized water. The mixture was stirred for 10 minutes at 80 °C, and then formic acid (61 μL, 1.6 mmol) was added. After stirring for another 4 h, the reaction mixture was neutralized by saturated solution of sodium bicarbonate (15 mL), extracted with dichloromethane (10 mL × 3), dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 15:1) to give **d-1a** (16 mg, 59%) as a white solid and its formate (5 mg, 17%); m.p.: 159-160 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (s, 1H), 5.64 – 5.57 (m, 0.11H), 5.42 – 5.35 (m, 1H), 3.66 (td, J = 8.6, 4.4 Hz, 1H), 2.25 – 2.02 (m, 4H), 1.89 – 1.77 (m, 2H), 1.75 – 1.57 (m, 4H), 1.52 – 1.36 (m, 3H), 1.36 – 1.24 (m, 1H), 1.22 – 1.06 (m, 2H), 1.06 – 0.98 (m, 2H). 0.97 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.5, 128.8, 125.1, 124.8 (t, $J_{D\text{-}C}$ = 24.2 Hz), 122.7, 81.9, 51.5, 48.5, 42.9, 36.6, 35.3, 33.8, 31.9, 31.3, 30.5, 23.4, 22.9, 20.6, 18.8, 11.1.

6.3 Deuteration test

Conditions A: A 5-mL reaction tube was added testosterone (29 mg, 0.1 mmol), 0.2 mL of acetonitrile, and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deionized water. The mixture was stirred for 10 minutes at 80 ℃, and then DCOOD (99% D, 95% in D_2O, 61 μL, 1.6 mmol) was added. After stirring for another 2 h, the reaction mixture was neutralized by saturated solution of sodium bicarbonate (15 mL), extracted with dichloromethane (10 mL×3), dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 10:1) to give a mixture of **1a** and **d-1a** (20 mg, 73%) as a white solid and their formate (3 mg, 10%); M.p.:154-155 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.95 – 5.89 (m, 1H), 5.64 – 5.55 (m, 0.33H), 5.41 – 5.34 (m, 1H), 3.66 (t, *J* = 8.4 Hz, 1H), 2.25 – 2.01 (m, 4H), 1.89 – 1.76 (m, 2H), 1.73 – 1.57 (m, 4H), 1.52 – 1.37 (m, 3H), 1.37 – 1.24 (m, 1H), 1.23 – 1.05 (m, 2H), 1.08 – 0.96 (m, 2H), 0.97 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.51, 141.49, 128.9, 128.8, 125.1, 122.7, 122.7, 81.9, 51.5, 48.5, 42.9, 36.6, 35.2, 33.8, 33.8, 31.9, 31.3, 30.5, 23.4, 23.0, 22.9, 20.6, 18.8, 11.1. (The carbon signal of *C*D did not appear.)

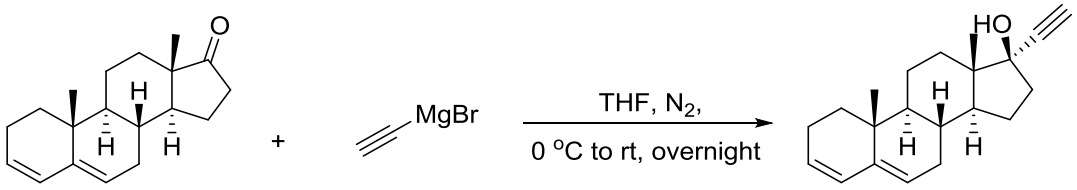
Conditions B: A 5-mL reaction tube was charged with testosterone (29 mg, 0.1 mmol), 0.2 mL of acetonitrile and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deuterium oxide. The mixture was stirred for 10 minutes at 80 ℃, and then formic acid (61 μL, 1.6 mmol) was added. After stirring for another 2 h, the reaction mixture was neutralized by saturated solution of sodium bicarbonate (15 mL), extracted with dichloromethane (10 mL×3), dried with sodium sulfate and concentrated under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 10:1) to give a mixture of **1a** and **d-1a** (20 mg, 73%) as a white solid and their formate (2 mg, 7%). M.p.:156-157 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (d, *J* = 8.4 Hz, 1H), 5.64 – 5.56 (m, 0.86H), 5.41 – 5.36 (m, 1H), 3.66 (t, *J* = 8.6 Hz, 1H), 2.26 – 2.02 (m, 4H), 1.89 – 1.77 (m, 2H), 1.75 – 1.57 (m, 4H), 1.52 – 1.36 (m, 3H), 1.36 – 1.25 (m, 1H), 1.22 – 1.06 (m, 2H), 1.07 – 0.98 (m, 2H), 0.97 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.5, 128.9, 128.8, 125.1, 122.7, 122.7, 81.9, 51.5, 48.5, 42.9,

36.6, 35.2, 33.8, 33.8, 31.9, 31.3, 30.5, 23.4, 23.0, 22.9, 20.6, 18.8, 11.1. (The carbon signal of *C*D did not appear.)

Conditions C: A 5 mL reaction tube was charged with testosterone (29 mg, 0.1 mmol), 0.2 mL of acetonitrile and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deuterium oxide. The mixture was stirred for 10 minutes at 80 ℃, and then DCOOD (99% D, 95% in D_2O, 61 μL, 1.6 mmol) was added. After stirring for another 2 h, the reaction mixture was neutralized by saturated solution of sodium bicarbonate (15 mL), extracted with dichloromethane (10 mL×3), dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 10:1) to give a mixture of **d-1a** (17 mg, 62%) as a white solid and its formate (4 mg, 16%); m.p.: 147-149 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (s, 1H), 5.41 – 5.36 (m, 1H), 3.66 (t, *J* = 8.4 Hz, 1H), 2.25 – 2.01 (m, 4H), 1.89 – 1.76 (m, 2H), 1.74 – 1.56 (m, 4H), 1.51 – 1.35 (m, 3H), 1.35 – 1.23 (m, 1H), 1.21 – 1.07 (m, 2H), 1.07 – 0.98 (m, 2H), 0.97 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.5, 128.8, 124.8, 122.7, 81.9, 51.5, 48.5, 42.9, 36.6, 35.3, 33.8, 31.9, 31.3, 30.5, 23.4, 22.9, 20.6, 18.8, 11.1. (The carbon signal of *C*D did not appear.)

7. Synthetic applications of steroidal 3,5-dienes

7.1 Preparation of Pregna-3,5-dien-20-yn-17β-ol (**10**)



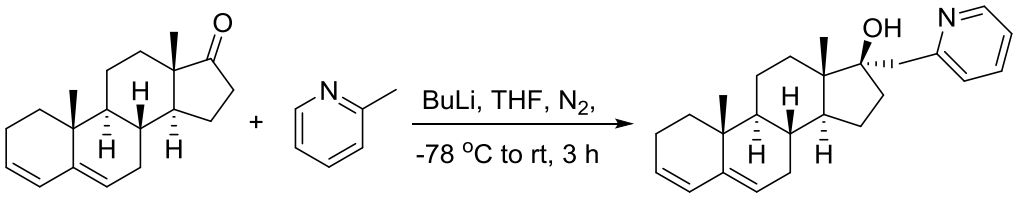
1h **10**

To a 50-mL flame-dry flask was added androsta-3,5-dien-17-one (**1h**, 135 mg, 0.5 mmol) and 10 mL of dry THF under nitrogen atmosphere. The solution was stirred for 5 minutes at 0 ℃, and then a solution of ethynylmagnesium bromide (3 mL,

0.5 M in THF) was added dropwise. The solution was stirred at 0 ℃ for another 5 min, then the flask was warmed to rt, and stirred for overnight. The reaction mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, dried with sodium sulfate, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 40:1) to give product **10** (87 mg, 59%) as a white solid; R_f = 0.3 (PE/EA, 10:1); m.p.: 169-170 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (d, *J* = 10.0 Hz, 1H), 5.65 – 5.55 (m, 1H), 5.41 – 5.35 (m, 1H), 2.57 (s, 1H), 2.35 – 2.26 (m, 1H), 2.26 – 2.06 (m, 3H), 2.06 – 1.95 (m, 1H), 1.87 (s, 1H), 1.85 – 1.60 (m, 7H), 1.58 – 1.48 (m, 1H), 1.48 – 1.29 (m, 2H), 1.18 (td, *J* = 12.1, 5.9 Hz, 1H), 1.11 – 1.02 (m, 1H), 0.97 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.5, 128.9, 125.1, 122.6, 87.5, 79.9, 74.0, 50.9, 48.0, 46.8, 39.0, 35.2, 33.8, 32.6, 32.4, 31.3, 23.1, 23.0, 20.6, 18.8, 12.7.

7.2 Preparation of 17-(2-pyridinylmethyl)androsta-3,5-dien-17β-ol (**11**)

Preparation of **11** referred to the methods reported by Gaši[13] and Yang[14].



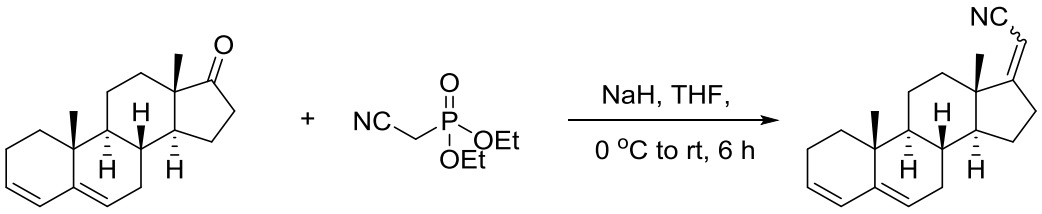
1h **11**

To a 100-mL flame-dry flask was added 2-methylpyridine (150 uL, 1.5 mmol) and 30 mL of dry THF under nitrogen atmosphere. The solution was cooled to -78 ℃, and then *n*-butyllithium (1.2 mL, 1.6 M in hexane) was added dropwise. The mixture was stirred for 1.5 h at -78 ℃, and then a solution of androsta-3,5-dien-17-one (**1h**, 270 mg, 1.0 mmol) in THF (10 mL) was added dropwise. The mixture was stirred for another 0.5 h at -78 ℃, and then warmed to rt, and stirred for 3 h. The reaction was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, dried with sodium sulfate, and concentrated under reduced pressure. The crude product was

purified by flash column chromatography (PE/EA, *v/v*, 40:1) to give **11** (334 mg, 92%) as a colorless crystal; R_f : 0.3 (PE/EA, *v/v*, 5:1); m.p.: 121-122 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.45 (d, *J* = 4.1 Hz, 1H), 7.67 – 7.58 (m, 1H), 7.15 (m, 2H), 6.58 (s, 1H), 5.94 (d, *J* = 9.7 Hz, 1H), 5.63 – 5.56 (m, 1H), 5.40 (m, 1H), 3.08 (d, *J* = 14.5 Hz, 1H), 2.82 (d, *J* = 14.5 Hz, 1H), 2.27 – 2.05 (m, 3H), 1.86 – 1.53 (m, 8H), 1.53 – 1.41 (m, 1H), 1.41 – 1.23 (m, 3H), 1.17 (td, *J* = 12.2, 5.8 Hz, 1H), 1.07 – 1.00 (m, 1H), 0.99 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 160.9, 148.0, 141.5, 136.7, 128.9, 125.1, 124.7, 122.8, 121.3, 83.4, 51.3, 48.5, 46.5, 43.2, 36.0, 35.3, 33.8, 32.6, 32.2, 31.7, 23.9, 23.0, 20.7, 18.8, 14.2.

7.3 Preparation of **13**

2-((8*S*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-1,2,7,8,9,10,11,12,13,14,15,16-dodecahydro-17*H*-cyclopenta[a]phenanthren-17-ylidene)acetonitrile (13) was synthesized according to the method reported by Zanardi.[15]

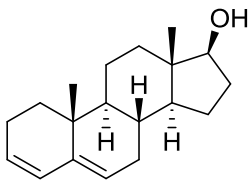


1h **13**

To a 50-mL dry flask was added diethyl cyanomethylphosphonate (200 μL , 1.2 mmol, 1.2 equiv) and dry THF (5 mL). After stirring for 5 minutes at 0 ℃, NaH (60% in mineral oil, 52 mg, 1.3 mmol) was added in one portion, then a solution of androsta-3,5-dien-17-one (**1h**, 270 mg, 1.0 mmol) in THF (8 mL) was added. The reaction mixture was warmed to rt. After stirring for 3 h, TLC indicated that the starting material was not completely consumed. Diethyl cyanomethylphosphonate (200 uL, 1.2 mmol) was added, and NaH (60% in mineral oil, 52 mg, 1.3 mmol) was added in one portion at 0 ℃. After stirring for another 3 h, the mixture was quenched with water, extracted with ethyl acetate, dried with sodium sulfate, and concentrated

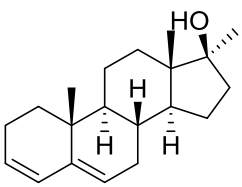
under reduced pressure. The crude product was purified by flash column chromatography (PE/EA, *v/v*, 50:1) to give **13** (150 mg, 51%, *Z/E* = 47:53) as a yellow liquid. R_f = 0.3 (PE/EA, 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (d, *J* = 10.0 Hz, 1H), 5.65 – 5.56 (m, 1H), 5.41 – 5.35 (m, 1H), 5.12 (t, *J* = 2.0 Hz, 0.47H), 5.02 (t, *J* = 2.6 Hz, 0.53H), 1.00 (s, 1.4H), 0.97 (s, 3H), 0.89 (s, 1.6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 180.7, 179.0, 141.5, 141.4, 128.7, 128.7, 125.3, 125.2, 122.2, 122.1, 117.4, 116.6, 87.9, 87.8, 55.4, 54.3, 48.2, 48.0, 46.6, 46.1, 35.2, 35.1, 34.6, 34.5, 33.6, 33.6, 32.4, 31.5, 31.4, 31.3, 31.3, 30.2, 23.7, 23.7, 22.9, 22.9, 20.7, 20.6, 18.7, 18.7, 17.9, 16.7; HRMS (ESI): m/z calculated for $C_{21}H_{28}N^+$ $[M+H]^+$: 294.2216; found: 294.2213.

8. Characterization data of products



(17β)-Androsta-3,5-dien-17-ol (**1a)** *CAS* No. 2602-86-0: synthesized from testosterone (**3a**, 29 mg, 0.1 mmol) according to General Procedure in Section 4, and purified by flash column chromatography (PE/EA, *v/v*, 10:1) to give **1a** (19 mg, 69%) as a white solid and its formate **1c** (5 mg, 16%) as a white solid; **1a**: R_f = 0.6 (PE/EA, *v/v*, 2:1); m.p.: 154-155 ℃ (reported 148-164 °C);[16]

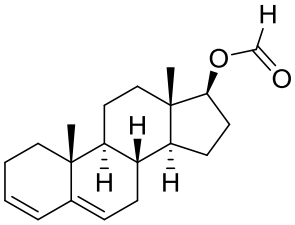
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (d, *J* = 9.6 Hz, 1H), 5.64 – 5.56 (m, 1H), 5.41 – 5.35 (m, 1H), 3.66 (t, *J* = 8.6 Hz, 1H), 2.26 – 2.02 (m, 4H), 1.90 – 1.76 (m, 2H), 1.73 – 1.57 (m, 4H), 1.53 – 1.37 (m, 3H), 1.36 – 1.24 (m, 1H), 1.22 – 1.07 (m, 2H), 1.06 – 0.99 (m, 2H). 0.97 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.5, 128.9, 125.1, 122.7, 81.9, 51.5, 48.5, 42.9, 36.6, 35.2, 33.8, 31.8, 31.3, 30.5, 23.4, 23.0, 20.6, 18.8, 11.1.



Androsta-3,5-dien-17β-ol, 17-methyl-(6CI,7CI,8CI) (**1b)** *CAS* No. 1035-61-6: **Condition 1:** synthesized from 17-methyltestosterone (**3b**, 30 mg, 0.1mmol) according to General Procedure in Section 4, only stirred for 2 h, and purified

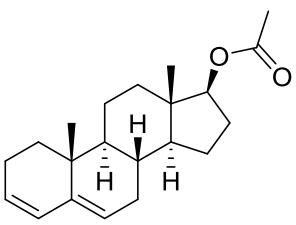
by flash column chromatography (PE/EA, 10:1) to give **1b** (18 mg, 63%) as a yellow crystal; **Condition 2:** synthesized from metandienone (**3g**, 45 mg, 0.15 mmol) according to General Procedure in Section 4, HCOOH (183 μL, 32 equiv.), purified by flash chromatography (PE/EA, 20:1) to give product **1b** (15 mg, 35%); R_f = 0.5 (PE/EA, *v/v*, 5:1); m.p.: 142-144 ℃ (reported 147-148 ºC);[17]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (d, *J* = 9.6 Hz, 1H), 5.64 – 5.55 (m, 1H), 5.41 – 5.36 (m, 1H), 2.26 – 2.05 (m, 3H), 1.88 – 1.72 (m, 3H), 1.72 – 1.58 (m, 4H), 1.54 (dt, *J* = 11.7, 3.2 Hz, 1H), 1.50 – 1.24 (m, 5H), 1.23 (s, 3H), 1.17 (td, *J* = 12.0, 5.8 Hz, 1H), 1.05 – 0.94 (m, 1H), 0.98 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.5, 128.9, 125.1, 122.7, 81.7, 51.3, 48.4, 45.4, 39.0, 35.3, 33.8, 32.7, 31.5, 25.8, 23.3, 23.0, 20.6, 18.8, 13.9.



(17β)-Androsta-3,5-dien-17-yl formate (1c): synthesized from testosterone 17-formate (**3c**, 31 mg, 0.1 mmol) according to General Procedure in Section 4, HCOOH (122 μL, 32 equiv.), and purified by flash column chromatography (PE/EA, *v/v*, 10:1) to give **1c** (9 mg, 31%) and **1a** (12 mg, 45%);

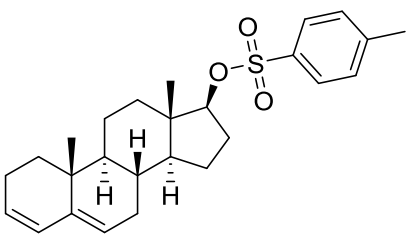
1c: R_f : 0.6 (PE/EA, 10:1); m.p.: 100-101 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.09 (s, 1H), 5.93 (d, *J* = 9.6 Hz, 1H), 5.65 – 5.55 (m, 1H), 5.42 – 5.35 (m, 1H), 4.72 (t, *J* = 8.6 Hz, 1H), 2.28 – 2.05 (m, 4H), 1.87 – 1.76 (m, 2H), 1.76 – 1.60 (m, 4H), 1.60 – 1.52 (m, 1H), 1.48 – 1.32 (m, 2H), 1.28 – 1.10 (m, 3H), 1.09 – 1.00 (m, 1H), 0.96 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 161.2, 141.5, 128.8, 125.2, 122.5, 82.7, 51.2, 48.3, 42.6, 36.7, 35.2, 33.7, 31.6, 31.3, 27.6, 23.5, 23.0, 20.4, 18.8, 12.1; HRMS (ESI): m/z calcd for $C_{20}H_{29}O_2^+$ $[M+H]^+$: 301.2162 found: 301.2161.



17β-Acetoxyandrosta-3,5-diene (1d) *CAS* No. 3214-78-6: synthesized from testosterone 17-acetate (**3d**, 33 mg, 0.1 mmol)

according to General Procedure in Section 4, HCOOH (122 μL, 32 equiv.), and purified by flash column chromatography (PE/EA, *v/v*, 10:1) to give **1d** (19 mg, 62%) as a colorless crystal; R_f : 0.7 (PE/EA, *v/v*, 5:1); m.p.: 123-124 ℃ (reported 122-123 ℃);[18]

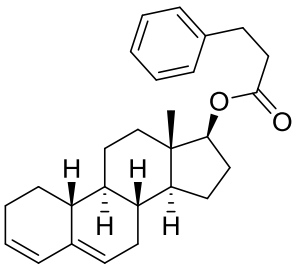
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.92 (d, *J* = 10.0 Hz, 1H), 5.64 – 5.55 (m, 1H), 5.42 – 5.35 (m, 1H), 4.61 (dd, *J* = 9.2, 8.0 Hz, 1H), 2.27 – 2.08 (m, 4H), 2.04 (s, 3H), 1.84 – 1.74 (m, 2H), 1.75 – 1.58 (m, 4H), 1.57 – 1.46 (m, 1H), 1.45 – 1.28 (m, 2H), 1.26 – 0.99 (m, 4H), 0.96 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 171.2, 141.5, 128.9, 125.1, 122.6, 82.7, 51.2, 48.3, 42.5, 36.8, 35.2, 33.7, 31.6, 31.3, 27.5, 23.5, 23.0, 21.2, 20.4, 18.8, 12.0.



(17β)-Androsta-3,5-dien-17-yl *p*-toluenesulfonate (1e): synthesized from testosterone *p*-toluenesulfonate (**3e**, 44 mg, 0.1 mmol) according to General Procedure in Section 4, TFE (0.2 mL) as solvent, HCOOH (122 μL, 32 equiv.), and purified by flash column chromatography (PE/EA, *v/v*, 50:1) to give **1e** (32 mg, 75%) as a white solid; R_f : 0.7 (PE/EA, *v/v*, 10:1); m.p.: 131-133 ℃;

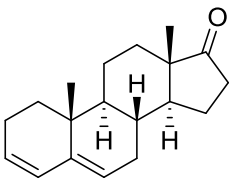
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.79 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 5.90 (d, *J* = 9.2 Hz, 1H), 5.64 – 5.54 (m, 1H), 5.38 – 5.31 (m, 1H), 4.27 (dd, *J* = 8.8, 8.0 Hz, 1H), 2.45 (s, 3H), 2.23 – 2.02 (m, 3H), 2.02 – 1.87 (m, 1H), 1.82 – 1.56 (m, 5H), 1.62 – 1.52 (m, 2H), 1.42 – 1.25 (m, 2H), 1.13 (td, *J* = 12.0, 6.0 Hz, 1H), 1.03 – 0.93 (m, 3H), 0.93 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 144.4, 141.5, 134.3, 129.6, 128.8, 127.8, 125.2, 122.3, 89.9, 50.5, 48.2, 42.9, 36.0, 35.2, 33.7, 31.6, 31.1, 27.7, 23.3, 23.0, 21.6, 20.2, 18.7, 11.7; HRMS (ESI): m/z calcd for $C_{26}H_{35}O_3S^+$ $[M+H]^+$: 427.2301, found: 427.2294.

(17β)-Estra-3,5-dien-17-yl phenylpropanoate (1f): synthesized from nandrolone



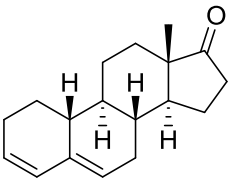
phenylpropionate (**3f**, 41 mg, 0.1 mmol) according to General Procedure in Section 4, and purified by flash column chromatography (PE/EA, *v/v*, 50:1) to give **1f (**10 mg, 25%) as a white solid and **3f** (21 mg) was recovered; R_f = 0.8 (PE/EA, 5:1); m.p.: 138-140 ℃;

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 – 7.24 (m, 2H), 7.24 – 7.16 (m, 3H), 5.99 (d, *J* = 10.0 Hz, 1H), 5.72 – 5.62 (m, 1H), 5.49 – 5.42 (m, 1H), 4.63 (dd, *J* = 9.2, 8.0 Hz, 1H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.64 (t, *J* = 7.8 Hz, 2H), 2.22 – 2.02 (m, 5H), 1.96 – 1.84 (m, 2H), 1.77 – 1.57 (m, 3H), 1.53 – 1.38 (m, 2H), 1.38 – 1.27 (m, 1H), 1.24 – 1.03 (m, 4H), 1.00 – 0.82 (m, 1H), 0.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 173.0, 140.5, 136.8, 129.5, 128.4, 128.3, 127.0, 126.2, 122.8, 82.9, 50.4, 43.9, 42.7, 41.5, 36.6, 36.1, 31.1, 30.8, 27.5, 27.4, 26.2, 26.1, 23.3, 11.9; HRMS (ESI): m/z calcd for $C_{27}H_{35}O_2^+$ $[M+H]^+$: 391.2632, found: 391.2623.

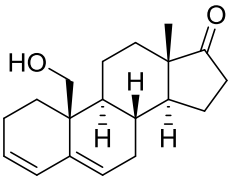


Androsta-3,5-dien-17-one (**1h)** *CAS* No. 1912-63-6: **Condition 1:** synthesized from androst-4-ene-3,17-dione (**3h**, 29 mg, 0.1 mmol) according to General Procedure in Section 4, only stirred for 2 h, and purified by flash column chromatography (PE/EA, 50:1) to give **1h (**21 mg, 78%) as a white solid; **Condition 2:** was synthesized from androst-4-ene-3,17-dione (**3h**, 286 mg, 1 mmol) according to General Procedure in Section 4, and purified by flash column chromatography (PE/EA, 50:1) to give **1h (**215 mg, 80%); R_f : 0.7 (PE/EA, 5:1); m.p.: 90-92 ℃ (reported 88-90 ℃);[19]

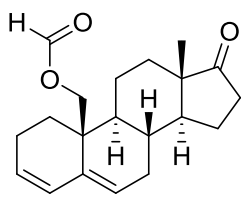
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.94 (d, *J* = 10.0 Hz, 1H), 5.66 – 5.57 (m, 1H), 5.45 – 5.38 (m, 1H), 2.47 (dd, *J* = 19.2, 9.0 Hz, 1H), 2.36 – 2.24 (m, 1H), 2.22 – 2.03 (m, 3H), 1.97 (m, 1H), 1.91 – 1.70 (m, 5H), 1.64 – 1.51 (m, 1H), 1.45 (qd, *J* = 12.8, 4.0 Hz, 1H), 1.39 – 1.24 (m, 2H), 1.18 (td, *J* = 12.0, 6.0 Hz, 1H), 1.08 (td, *J* = 11.2, 4.8 Hz, 1H), 0.98 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 221.1, 141.6, 128.7, 125.3, 122.1, 51.9, 48.5, 47.7, 35.8, 35.3, 33.7, 31.4, 31.4, 30.6, 23.0, 21.8, 20.2, 18.8, 13.7.



Estra-3,5-dien-17-one (**1i):** *CAS* No. 60397-28-6: synthesized from 19-norandrost-4-ene-3,17-dione (**3i**, 41 mg, 0.15 mmol) according to General Procedure in Section 4, and purified by flash column chromatography (PE/EA, *v/v*, 50:3) to give **1i (**19 mg, 49%) as a colorless crystal; R_f = 0.8 (PE/EA, 5:1); m.p.: 110-115 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.01 (d, *J* = 10.0 Hz, 1H), 5.74 – 5.66 (m, 1H), 5.53 – 5.45 (m, 1H), 2.47 (dd, *J* = 19.2, 8.8 Hz, 1H), 2.25 (dt, *J* = 18.0, 5.2 Hz, 1H), 2.21 – 2.14 (m, 2H), 2.14 – 2.09 (m, 1H), 2.08 – 2.00 (m, 2H), 2.00 – 1.89 (m, 2H), 1.88 – 1.75 (m, 2H), 1.67 – 1.49 (m, 2H), 1.41 – 1.30 (m, 2H), 1.30 – 1.20 (m, 1H), 1.20 – 1.05 (m, 1H), 1.05 – 0.93 (m, 1H), 0.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 221.1, 136.9, 129.4, 127.2, 122.3, 51.1, 47.8, 44.1, 41.4, 36.4, 35.8, 31.4, 30.1, 27.3, 26.1, 25.8, 21.7, 13.6.

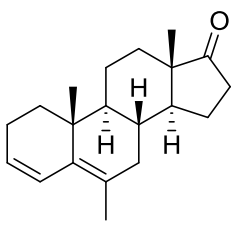


19-Hydroxyandrosta-3,5-dien-17-one (**1j)** *CAS* No. 21899-70-7: synthesized from 19-hydroxyandrost-4-ene-3,17-dione (**3j**, 60 mg, 0.2 mmol) according to General Procedure in Section 4, and purified by flash column chromatography (PE/EA, 10:1) to give **1j** (31 mg, 55%) as a white solid and its formate **1j'**(10 mg, 16%) as a yellow liquid; R_f = 0.4 (PE/EA, *v/v*, 5:1); m.p.: 93-95 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.00 (d, *J* = 10.0 Hz, 1H), 5.74 – 5.69 (m, 1H), 5.68 – 5.61 (m, 1H), 3.72 (d, *J* = 11.2 Hz, 1H), 3.64 (dd, *J* = 12.0, 5.2 Hz, 1H), 2.47 (dd, *J* = 19.2, 8.8 Hz, 1H), 2.39 – 2.18 (m, 2H), 2.18 – 1.99 (m, 4H), 1.99 – 1.86 (m, 2H), 1.85 – 1.76 (m, 2H), 1.75 – 1.64 (m, 1H), 1.63 – 1.50 (m, 1H), 1.34 – 1.20 (m, 4H), 1.09 (td, *J* = 11.6, 4.4 Hz, 1H), 0.96 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 221.1, 136.3, 128.6, 126.4, 125.9, 63.7, 52.6, 48.8, 47.9, 40.3, 35.8, 32.3, 31.7, 30.2, 30.1, 23.2, 21.6, 20.9, 13.9.

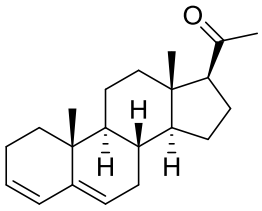


Androsta-3,5-dien-17-on-19-yl formate (**1j'**): R_f = 0.6 (PE/EA, *v/v*, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.08 (s, 1H), 5.97 (d, *J* = 10.0 Hz, 1H), 5.70 – 5.63 (m, 1H), 5.63 – 5.59 (m, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 2.48 (dd, *J* = 19.2, 9.2 Hz, 1H), 2.35 (dt, *J* = 18.8, 5.2 Hz, 1H), 2.23 (m, 1H), 2.19 – 2.11 (m, 2H), 2.11 – 1.92 (m, 3H), 1.92 – 1.75 (m, 3H), 1.66 – 1.46 (m, 2H), 1.38 – 1.22 (m, 3H), 1.22

– 1.12 (m, 1H), 0.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 220.6, 161.0, 136.0, 128.4, 125.9, 125.8, 64.3, 52.3, 48.4, 47.7, 38.6, 35.7, 31.9, 31.7, 30.2, 29.7, 22.9, 21.7, 21.1, 13.8; HRMS (ESI): m/z calcd for $C_{20}H_{27}O_3^+$ $[M+H]^+$: 315.1955 found: 315.1955.

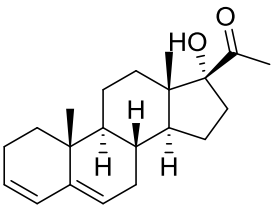


6-Methylandrosta-3,5-dien-17-one (**1k):** synthesized from 6-methyleneandrost-4-ene-3,17-dione (**3k**, 30 mg, 0.1 mmol) according to General Procedure in Section 4, HCOOH (122 μL, 32 equiv.), stirred for 8 h, and purified by flash column chromatography (PE/EA, *v/v*, 50:3) to give **1k (**22 mg, 77%) as a colorless crystal; R_f : 0.5 (PE/EA, *v/v*, 10:1); m.p.: 80-81 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.34 (d, *J* = 10.0 Hz, 1H), 5.70 – 5.61 (m, 1H), 2.47 (dd, *J* = 19.2, 8.8 Hz, 1H), 2.23 – 2.04 (m, 4H), 2.04 – 1.95 (m, 1H), 1.92 – 1.74 (m, 5H), 1.71 (s, 3H), 1.63 – 1.50 (m, 1H), 1.43 (qd, *J* = 13.2, 4.0 Hz, 1H), 1.37 – 1.24 (m, 2H), 1.17 (td, *J* = 12.0, 6.4 Hz, 1H), 1.03 (td, *J* = 11.2, 4.8 Hz, 1H), 0.94 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 221.1, 133.9, 126.3, 125.4, 124.1, 52.0, 48.7, 47.6, 37.7, 35.9, 35.5, 33.9, 31.5, 31.2, 22.9, 21.8, 20.3, 18.6, 18.6, 13.7; HRMS (ESI): m/z calcd for $C_{20}H_{29}O^+$ $[M+H]^+$: 285.2213 found: 285.2217.

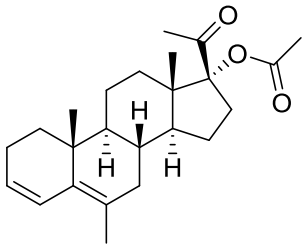


Pregna-3,5-dien-20-one (**1l)** *CAS* No. 1093-87-4: synthesized from progesterone (**3l**, 31 mg, 0.1 mmol) according to General Procedure in Section 4, stirred for 2 h, and purified by flash column chromatography (PE/EA, 15:1) to give **1l (**23 mg, 77%) as a white solid; R_f = 0.8 (PE/EA, *v/v*, 5:1) m.p.: 145-147 ℃; (reported 139-142 ℃);[20]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (d, *J* = 10.0 Hz, 1H), 5.65 – 5.55 (m, 1H), 5.41 – 5.35 (m, 1H), 2.55 (t, *J* = 8.8 Hz, 1H), 2.26 – 2.11 (m, 4H), 2.13 (s, 3H), 2.10 – 2.02 (m, 1H), 1.80 (dd, *J* = 12.4, 4.8 Hz, 1H), 1.76 – 1.61 (m, 5H), 1.53 – 1.37 (m, 2H), 1.36 – 1.12 (m, 3H), 1.12 – 1.02 (m, 1H), 0.95 (s, 3H), 0.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 209.5, 141.4, 128.8, 125.1, 122.7, 63.7, 57.1, 48.3, 44.1, 38.9, 35.2, 33.8, 31.8, 31.6, 31.5, 24.4, 23.0, 22.8, 21.0, 18.7, 13.3.

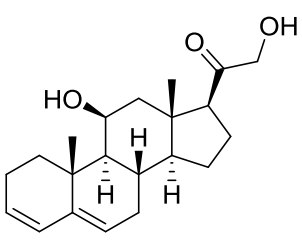


17α-Hydroxypregna-3,5-dien-20-one (**1m)** *CAS* No. 1096-63-5: synthesized from 17alpha-hydroxyprogesterone (**3m**, 33 mg, 0.1 mmol) according to General Procedure in Section 4, HCOOH (122 μL, 32 equiv.), stirred for 8 h, and purified by flash column chromatography (PE/EA, 10:1) to give **1m (**22 mg, 70%) as a colorless crystal; R_f = 0.7 (PE/EA, *v/v*, 2:1); m.p.: 178-180 ℃ (reported 180-190 ℃);[21] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (d, *J* = 9.6 Hz, 1H), 5.63 – 5.57 (m, 1H), 5.42 – 5.36 (m, 1H), 2.74 (s, 1H), 2.69 (ddd, *J* = 14.6, 11.3, 2.9 Hz, 1H), 2.28 (s, 3H), 2.26 – 2.06 (m, 3H), 1.89 – 1.66 (m, 7H), 1.66 – 1.58 (m, 1H), 1.47 – 1.32 (m, 3H), 1.18 (td, *J* = 12.0, 6.0 Hz, 1H), 1.13 – 1.01 (m, 1H), 0.96 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 211.7, 141.4, 128.9, 125.1, 122.7, 90.0, 51.0, 48.4, 47.9, 35.2, 33.8, 33.6, 31.8, 31.7, 30.1, 27.9, 24.1, 23.0, 20.4, 18.8, 15.5.



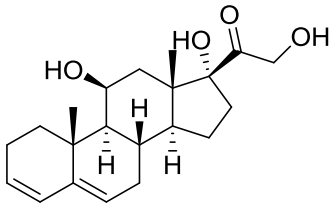
17α-Acetylox-6-methylpregna-3,5-dien-20-one (**1n)** *CAS* No. 2205-79-0: synthesized from medroxyprogesterone 17-acetate (**3n**, 39 mg, 0.1 mmol) according to General Procedure in Section 4, HFIP (0.2 mL) as solvent, and purified by flash column chromatography (PE/EA, *v/v*, 10:1) to give **1n (**23 mg, 62%) as a colorless crystal; R_f = 0.6 (PE/EA, 5:1); m.p.: 109-110 ℃ (reported 128-130 ℃);[22]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.34 (d, *J* = 10.0 Hz, 1H), 5.70 – 5.61 (m, 1H), 3.02 – 2.88 (m, 1H), 2.25 – 1.94 (m, 4H), 2.11 (s, 3H), 2.05 (s, 3H), 1.85 – 1.67 (m, 7H), 1.69 (s, 3H), 1.61 – 1.53 (m, 1H), 1.39 (dq, *J* = 13.2, 4.4 Hz, 1H), 1.35 – 1.23 (m, 1H), 1.18 (td, *J* = 12.0, 6.0 Hz, 1H), 1.11 – 0.99 (m, 1H), 0.92 (s, 3H), 0.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 204.2, 170.8, 133.6, 126.7, 125.2, 124.2, 97.0, 52.1, 48.0, 46.8, 38.7, 35.3, 34.0, 31.7, 31.2, 30.5, 26.4, 23.9, 22.9, 21.3, 20.6, 18.6, 18.5, 14.4.



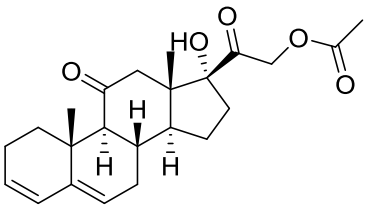
11β,21-Dihydroxypregna-3,5-diene-20-one **(1o)**: synthesized from corticosterone (**3o**, 35 mg, 0.1 mmol) according to General Procedure in Section 4, HCOOH (122

μL, 32 equiv.), and purified by flash column chromatography (PE/EA, 3:1) to give **1o (**12 mg, 36%) as a white solid; m.p.: 140-142 ℃; R_f : 0.5 (PE/EA, *v/v*, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.90 (d, *J* = 10.0 Hz, 1H), 5.68 – 5.61 (m, 1H), 5.32 – 5.26 (m, 1H), 4.50 – 4.43 (m, 1H), 4.24 (dd, *J* = 18.9, 4.8 Hz, 1H), 4.16 (dd, *J* = 18.9, 4.4 Hz, 1H), 3.27 (t, *J* = 4.6 Hz, 1H), 2.46 – 2.33 (m, 2H), 2.33 – 2.21 (m, 1H), 2.20 – 2.05 (m, 3H), 1.93 (dd, *J* = 12.4, 5.2 Hz, 1H), 1.87 – 1.71 (m, 3H), 1.62 (dd, *J* = 13.6, 3.6 Hz, 1H), 1.50 – 1.38 (m, 1H), 1.35 – 1.09 (m, 5H), 1.18 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 210.0, 142.3, 128.1, 125.4, 121.8, 69.3, 68.0, 59.5, 58.8, 52.0, 47.5, 43.9, 35.4, 33.1, 31.6, 28.1, 24.4, 22.6, 22.4, 21.8, 15.9; HRMS (ESI): m/z calcd for $C_{21}H_{31}O_3^+$ $[M+H]^+$: 331.2268 found: 331.2272.



11β,17α,21-Trihydroxypregna-3,5-diene-20-one (1p): synthesized from hydrocortisone (**3p**, 36 mg, 0.1 mmol) according to General Procedure in Section 4, and purified by flash column chromatography (PE/EA, *v/v*, 3:1) to give **1p (**21 mg, 61%) as a white solid; R_f = 0.4 (PE/EA, 2:1) m.p.: 129-130 ℃;

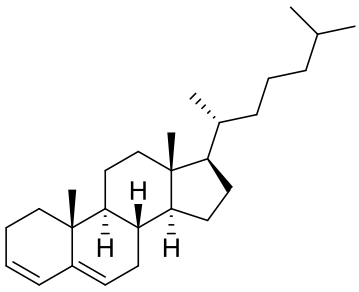
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.90 (dd, *J* = 9.6, 2.6 Hz, 1H), 5.69 – 5.60 (m, 1H), 5.30 (t, *J* = 4.0 Hz, 1H), 4.66 (dd, *J* = 20.0, 5.0 Hz, 1H), 4.56 – 4.50 (m, 1H), 4.31 (dd, *J* = 20.0, 4.6 Hz, 1H), 3.14 (t, *J* = 4.8 Hz, 1H), 2.78 – 2.67 (m, 1H), 2.46 – 2.35 (m, 1H), 2.32 – 2.10 (m, 3H), 2.23 (s, 1H), 2.01 (dd, *J* = 13.6, 3.6 Hz, 1H), 1.96 – 1.72 (m, 4H), 1.62 – 1.44 (m, 3H), 1.30 (td, *J* = 12.0, 5.6 Hz, 1H), 1.18 (s, 3H), 1.14 (dd, *J* = 13.6, 3.6 Hz, 2H), 1.21 – 1.09 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 212.1, 142.3, 128.1, 125.3, 121.8, 88.9, 68.2, 67.4, 53.0, 51.7, 48.0, 39.3, 35.4, 34.2, 33.1, 31.7, 28.2, 23.7, 22.6, 21.8, 17.5; HRMS (ESI): m/z calcd for $C_{21}H_{31}O_4^+$ $[M+H]^+$: 347.2217 found: 347.2213.



21-Acetoxy-17α-hydroxypregna-3,5-diene-11,20-dione, (1q) *CAS* No. 96709-08-9: synthesized from cortisone acetate (**3q**, 40 mg, 0.1 mmol) according to General

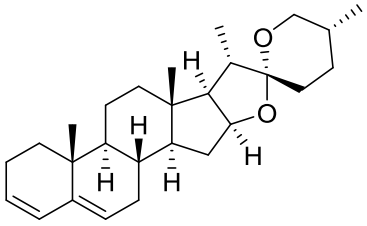
Procedure in Section 4, HCOOH (122 μL, 32 equiv.), stirred for 8 h, and purified by flash column chromatography (PE/EA, *v/v*, 4:1) to give **1q (**31 mg, 81%) as a white solid; R_f : 0.7 (PE/EA, *v/v*, 2:1); m.p.: 171-172 ℃;

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.89 (d, *J* = 9.6 Hz, 1H), 5.70 – 5.61 (m, 1H), 5.38 – 5.32 (m, 1H), 5.16 (d, *J* = 17.2 Hz, 1H), 4.66 (d, *J* = 17.6 Hz, 1H), 2.95 (s, 1H), 2.90 (d, *J* = 12.8 Hz, 1H), 2.79 (ddd, *J* = 15.0, 11.6, 3.2 Hz, 1H), 2.56 (dd, *J* = 12.4, 4.4 Hz, 1H), 2.48 – 2.37 (m, 1H), 2.36 – 2.21 (m, 3H), 2.17 (s, 3H), 2.12 – 1.91 (m, 5H), 1.67 (ddd, *J* = 15.3, 9.2, 6.0 Hz, 1H), 1.47 (qd, *J* = 12.4, 6.0 Hz, 1H),1.17 – 1.06 (m, 1H) 1.14 (s, 3H), 0.65 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 210.6, 204.8, 170.7, 141.9, 128.1, 126.6, 120.8, 89.1, 67.6, 58.7, 51.0, 50.4, 50.0, 35.3, 35.2, 32.9, 32.8, 32.6, 23.4, 22.9, 20.5, 18.3, 15.5.



Cholesta-3,5-diene (**1r)** *CAS* No. 747-90-0: synthesized from 4-cholesten-3-one (**3r**, 38 mg, 0.1 mmol) according to General Procedure in Section 4, HFIP (0.2 mL) as solvent, HCOOH (122 μL, 32 equiv.), and purified by flash column chromatography (PE) to give **1r (**15 mg, 41%) as a colorless crystal; R_f = 0.9 (PE); m.p.: 91-93 ℃, (reported 80-81 ℃);[23]

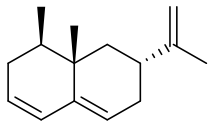
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.92 (d, *J* = 10.0 Hz, 1H), 5.62 – 5.56 (m, 1H), 5.42 – 5.36 (m, 1H), 2.24 – 0.97 (m, 26H), 0.95 (s, 3H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 1.8 Hz, 3H), 0.86 (d, *J* = 1.8 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.5, 129.0, 125.0, 123.2, 57.0, 56.2, 48.4, 42.5, 39.8, 39.5, 36.2, 35.8, 35.2, 33.8, 31.8, 28.3, 28.0, 24.2, 23.8, 23.1, 22.8, 22.6, 21.0, 18.8, 18.7, 12.0.



Spirosta-3,5-diene (**1s)** *CAS* No. 1672-65-7: synthesized from diosgenone (**3s**, 41 mg, 0.1 mmol) according to General Procedure in Section 4, HFIP (0.2 mL) as solvent, HCOOH (122 μL, 32 equiv.), and

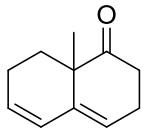
purified by flash column chromatography (PE) to give **1s (**23 mg, 58%) as a colorless crystal; R_f = 0.8 (PE/EA, 10:1) m.p.: 138-140 ℃, (reported 130-140 ℃);[24]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.92 (d, *J* = 9.6 Hz, 1H), 5.64 – 5.54 (m, 1H), 5.42 – 5.34 (m, 1H), 4.42 (q, *J* = 7.6 Hz, 1H), 3.47 (ddd, *J* = 10.8, 4.4, 2.0 Hz, 1H), 3.38 (dd, *J* = 10.8, 10.8 Hz, 1H), 2.26 – 2.05 (m, 3H), 2.00 (ddd, *J* = 12.3, 7.5, 5.4 Hz, 1H), 1.93 – 1.81 (m, 1H), 1.84 – 1.68 (m, 3H), 1.71 – 1.53 (m, 7H), 1.53 – 1.36 (m, 2H), 1.36 – 1.25 (m, 1H), 1.24 – 1.10 (m, 3H), 1.07 – 0.99 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.97 (s, 3H), 0.82 (s, 3H), 0.79 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 141.4, 128.9, 125.0, 122.8, 109.3, 80.8, 66.8, 62.1, 56.7, 48.3, 41.6, 40.4, 39.8, 35.3, 33.7, 31.9, 31.8, 31.4, 31.3, 30.3, 28.8, 23.0, 20.8, 18.8, 17.1, 16.4, 14.5.



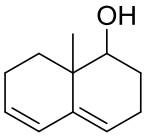
Nootka-3,5-diene (**8a)** *CAS* No. 5090-61-9: synthesized from (+)-nootkatone (**7a**, 70 mg, 0.1 mmol) according to General Procedure in Section 4, HCOOH (0.36 mL, 32 equiv.), and purified by flash column chromatography (PE) to give **8a (**36 mg, 56%) as a colorless liquid; R_f = 0.9 (PE);

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.95 (d, *J* = 9.6 Hz, 1H), 5.63 – 5.54 (m, 1H), 5.45 – 5.40 (m, 1H), 4.77 – 4.72 (m, 2H), 2.49 – 2.37 (m, 1H), 2.23 (dt, *J* = 18.4, 5.4 Hz, 1H), 2.10 – 1.87 (m, 3H), 1.76 (s, 3H), 1.78 – 1.68 (m, 1H), 1.61 – 1.47 (m, 1H), 1.19 (t, *J* = 12.6 Hz, 1H), 0.91 (s, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 150.3, 142.0, 128.7, 125.8, 122.7, 108.6, 40.2, 38.9, 37.3, 36.2, 32.3, 31.1, 20.7, 17.3, 14.8.



3,7,8,8a-Tetrahydro-8a-methyl-1(2*H*)-naphthalenone (**8b)** *CAS* No. 104174-48-3: synthesized from (±)-Wieland-Miescher ketone (**7b**) (58 mg, 0.3 mmol) according to General Procedure in Section 4, HCOOH (0.36 mL, 32 equiv.), and purified by flash column chromatography (PE/EA, 20:1) to give **8b (**18 mg, 34%) as a brown liquid and **9b (**12 mg, 22%) as a colorless liquid; **8b**: R_f = 0.7 (PE/EA, *v/v*, 5:1);

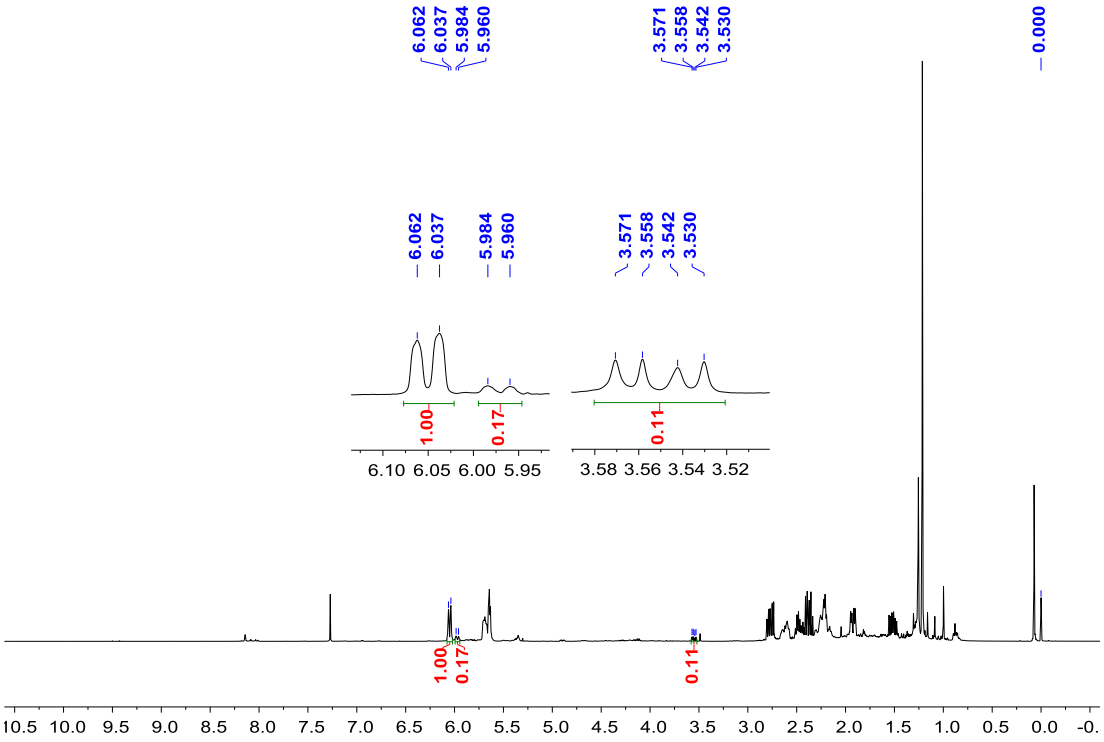
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.05 (d, *J* = 10.0 Hz, 1H), 5.73-5.66 (m, 1H), 5.64 (t, *J* = 4.4 Hz, 1H), 2.82 – 2.72 (m, 1H), 2.68 – 2.57 (m, 1H), 2.53-2.33 (m, 2H), 2.32-2.13 (m, 2H), 1.92 (dd, *J* = 13.4, 5.0 Hz, 1H), 1.52 (td, *J* = 12.6, 6.4 Hz, 1H), 1.21 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 215.3, 139.6, 127.4, 126.8, 122.1, 45.3, 35.5, 28.6, 24.1, 22.5, 22.2.



8a-Methyl-1,2,3,7,8,8a-hexahydronaphthalen-1-ol (9b) *CAS* No. 100056-85-7: R_f = 0.4 (PE/EA, *v/v*, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.97 (d, *J* = 9.6 Hz, 1H), 5.67-5.60 (m, 1H), 5.35 (t, *J* = 3.6 Hz, 1H), 3.55 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.30-2.10 (m, 5H), 1.95 (dd, *J* = 12.8, 5.2 Hz, 1H), 1.89-1.77 (m, 2H), 1.28 (m, 1H), 1.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 139.4, 128.2, 125.8, 122.5, 76.0, 37.4, 32.6, 26.7, 24.8, 22.6, 16.5.

9. Reduction of 8b

A 5-mL flask was charged with 3,7,8,8a-tetrahydro-8a-methyl-1(2*H*)-naphthalenone (**8b**) (16 mg, 0.1 mmol), 0.2 mL of acetonitrile, and 0.2 mL of catalyst ***TC-4*** solution (0.0025 mol/L) in deionized water. The mixture was stirred for 10 minutes at 80 ℃, and then formic acid (122 μL, 3.2 mmol) was added. After stirring for another 4 h, the reaction mixture was neutralized by saturated solution of sodium bicarbonate (15 mL), extracted with dichloromethane (10 mL × 3), dried over sodium sulfate, and concentrated under reduced pressure. The crude residue was directly submitted to the ^{1}H NMR analysis to determine the yield.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6.037
5.984
5.960
3.571
3.558
3.542
3.530
0.000
1.00
0.17
0.11
6.10 6.05 6.00 5.95
3.58 3.56 3.54 3.52
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.

10. Reference

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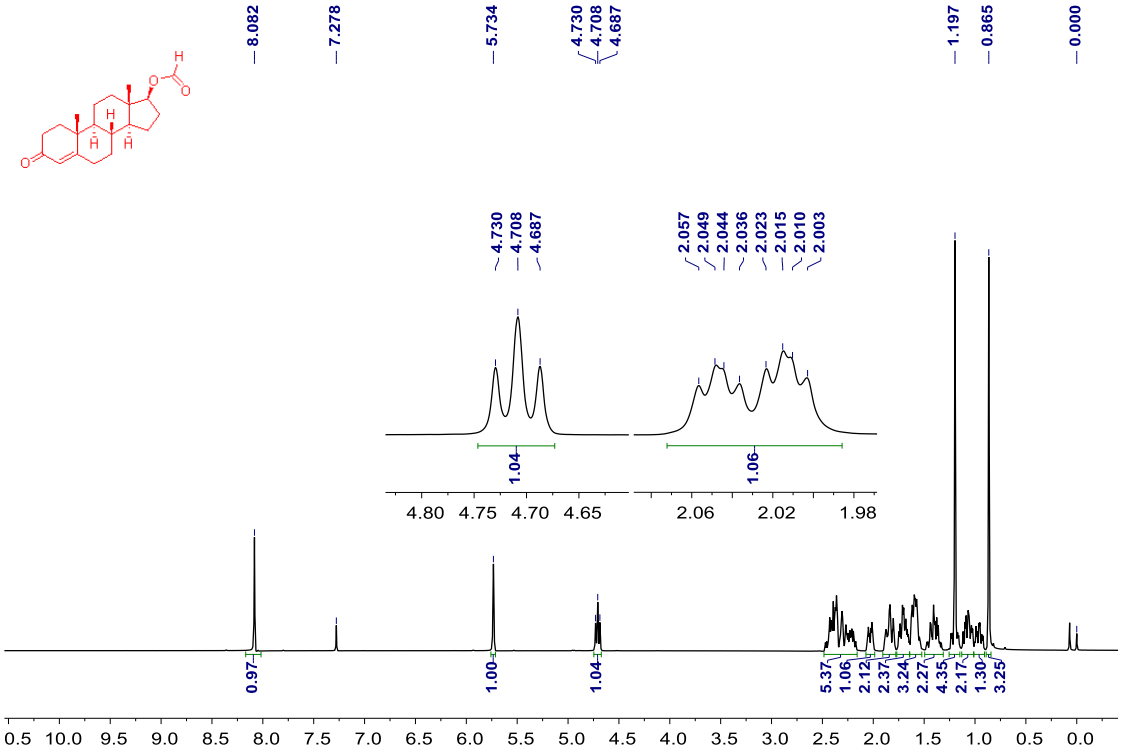
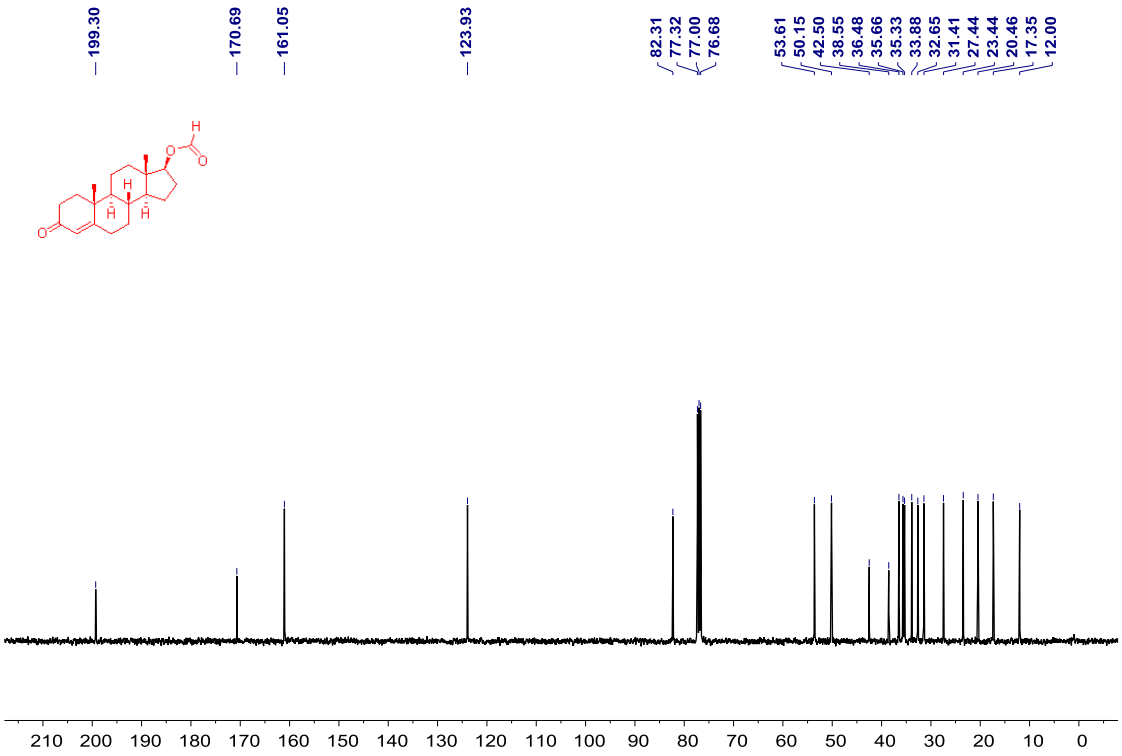
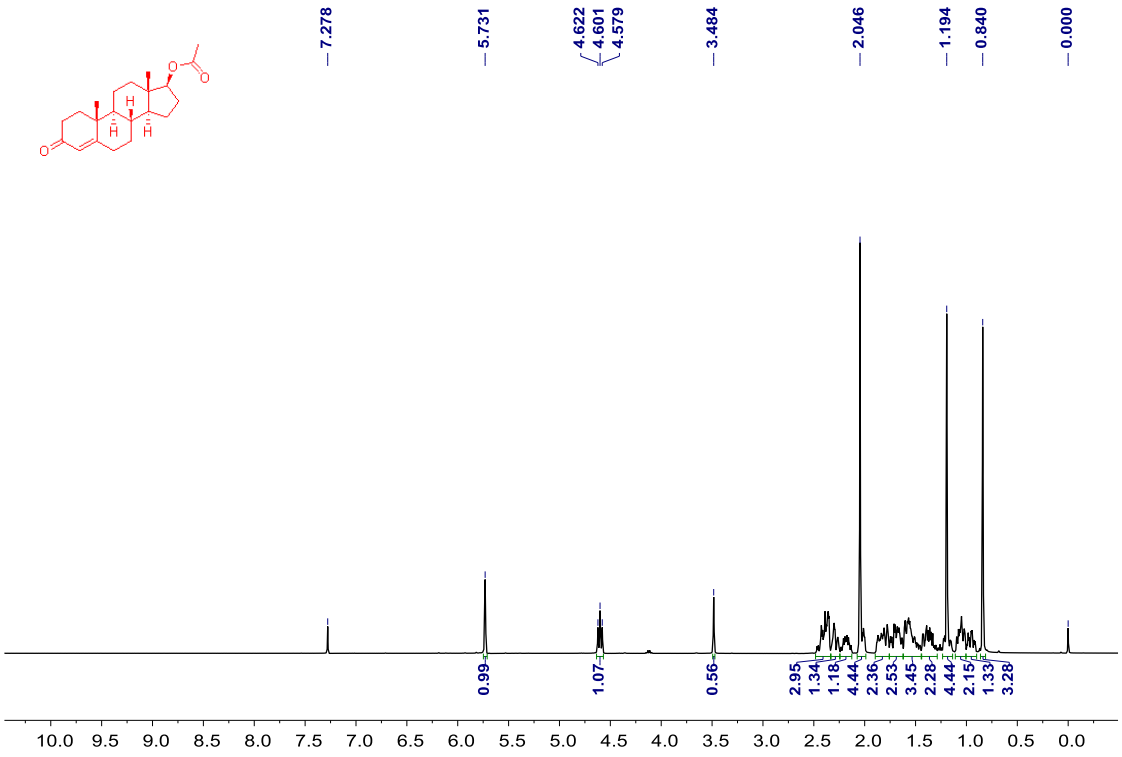
11. Copies of ^{1}H and ^{13}C NMR spectra of starting materials 3 and 4

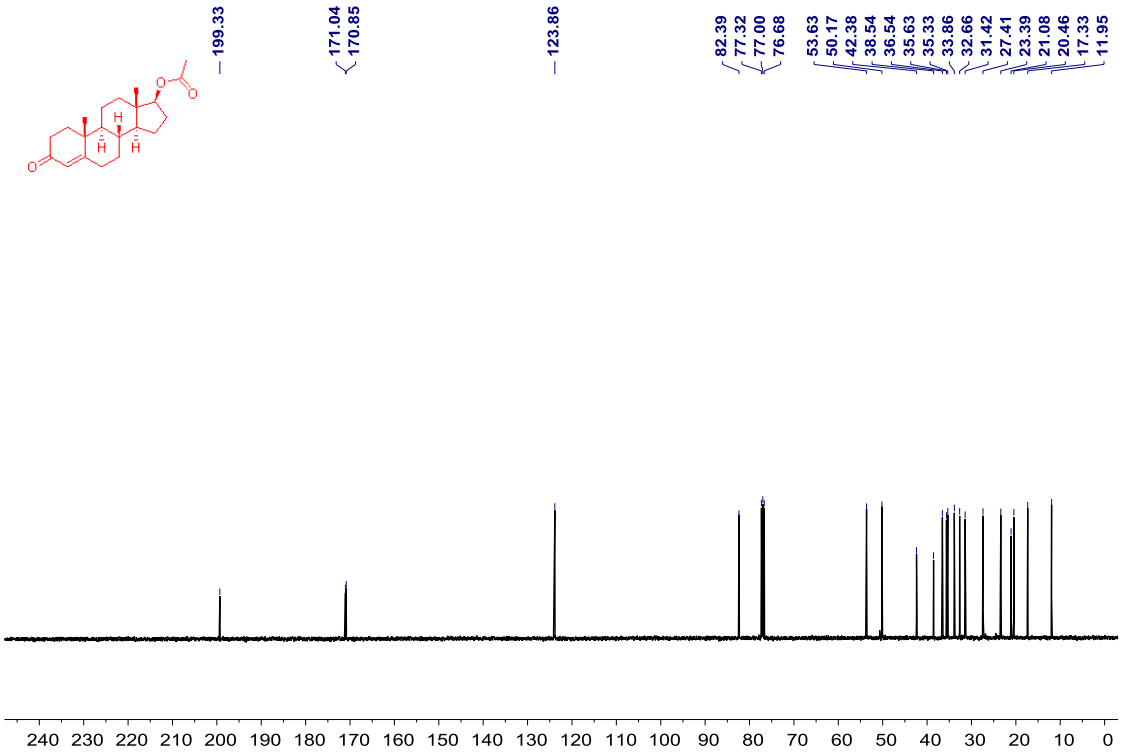
^{1}H and ^{13}C NMR spectra of **3c**



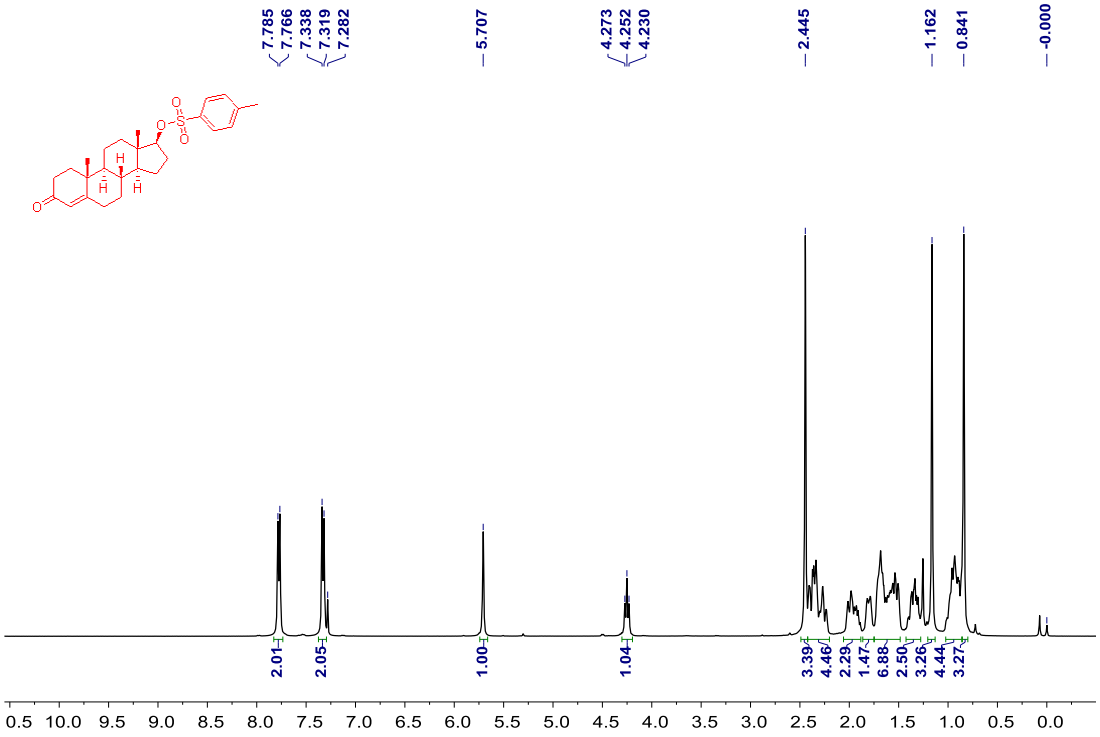


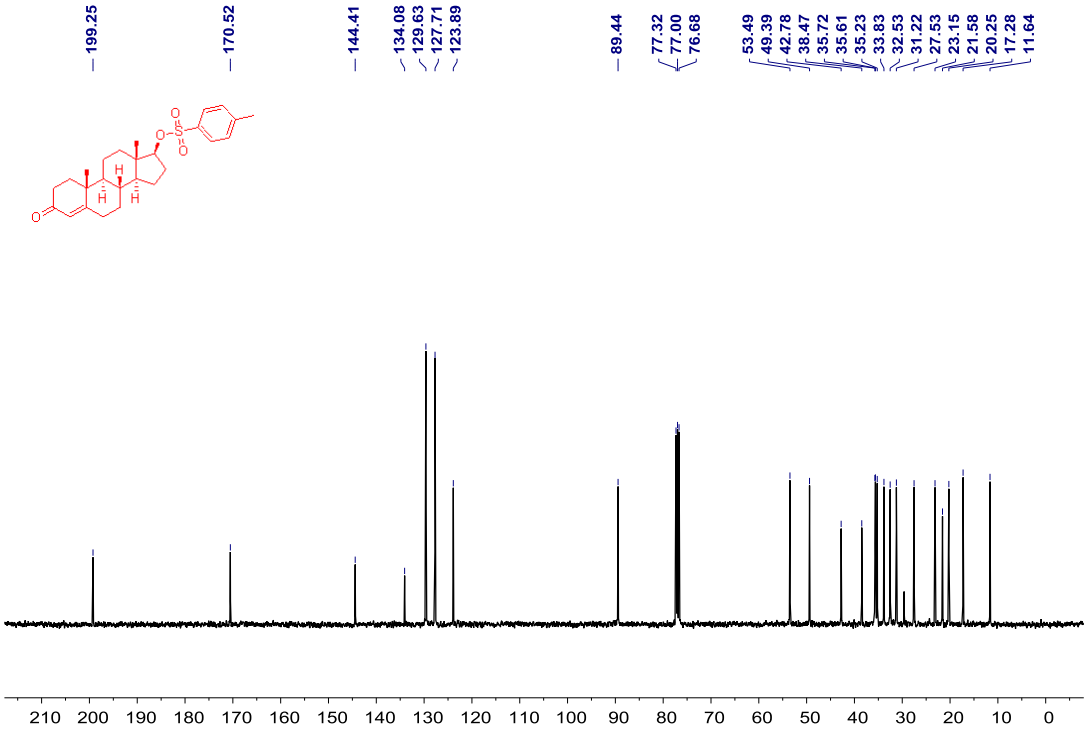
^{1}H and ^{13}C NMR spectra of 3d



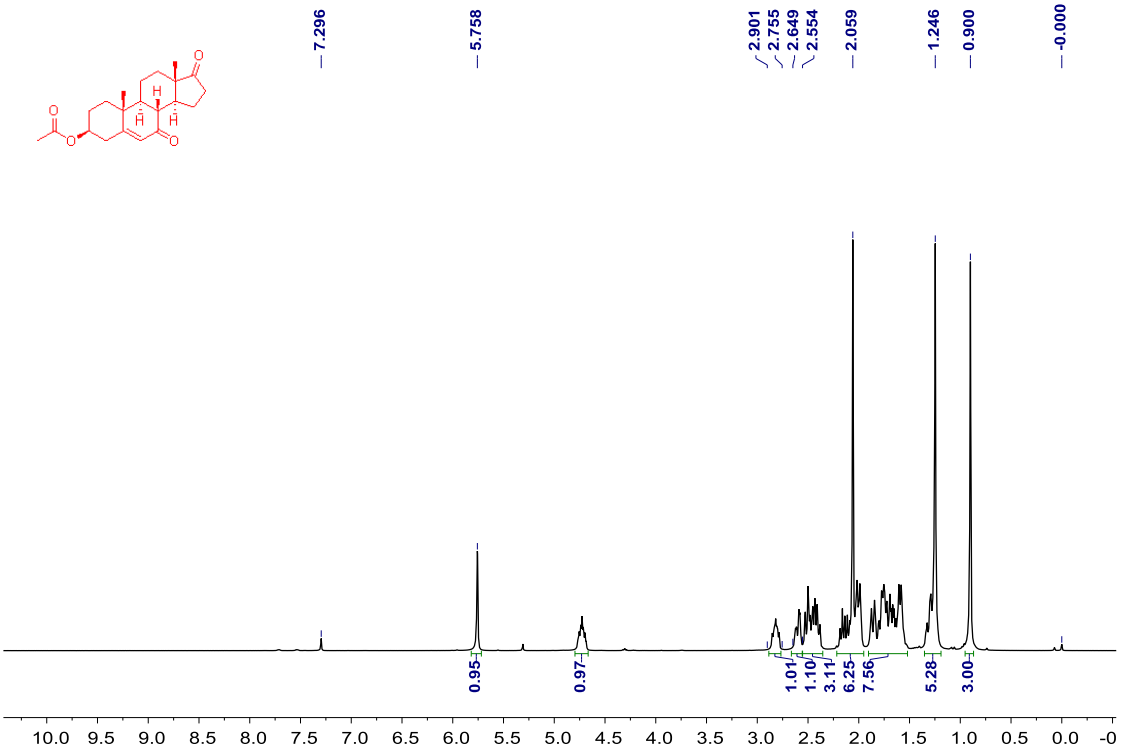


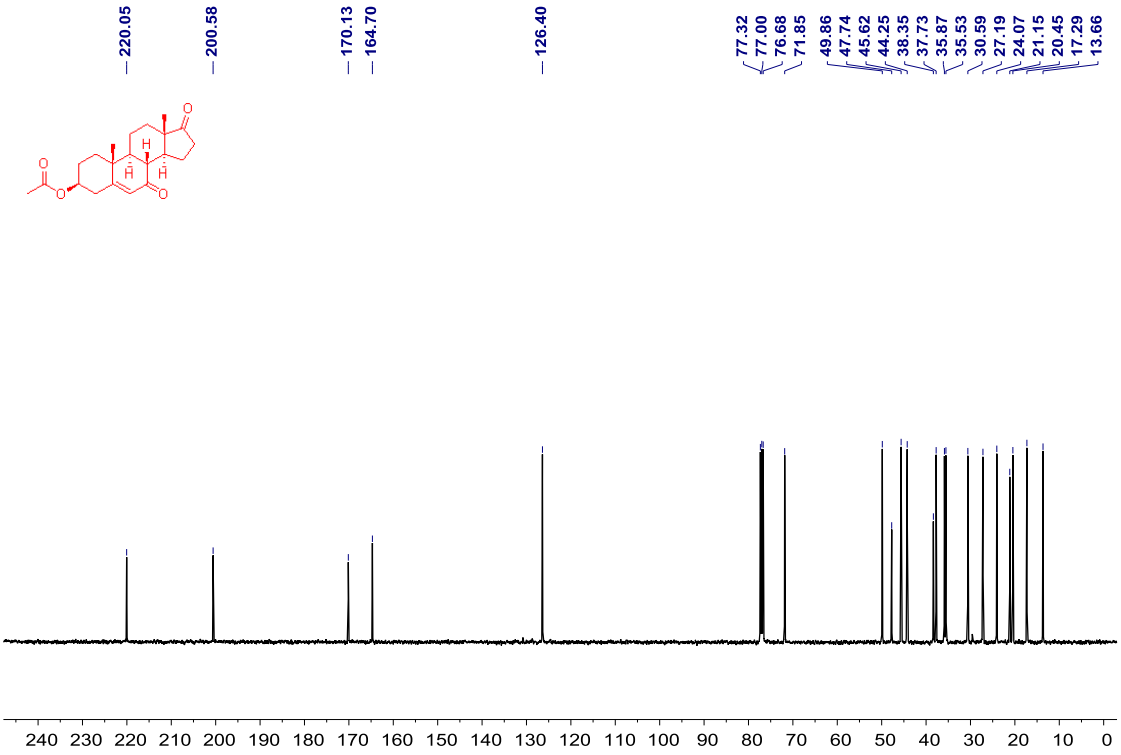
^{1}H and ^{13}C NMR spectra of 3e



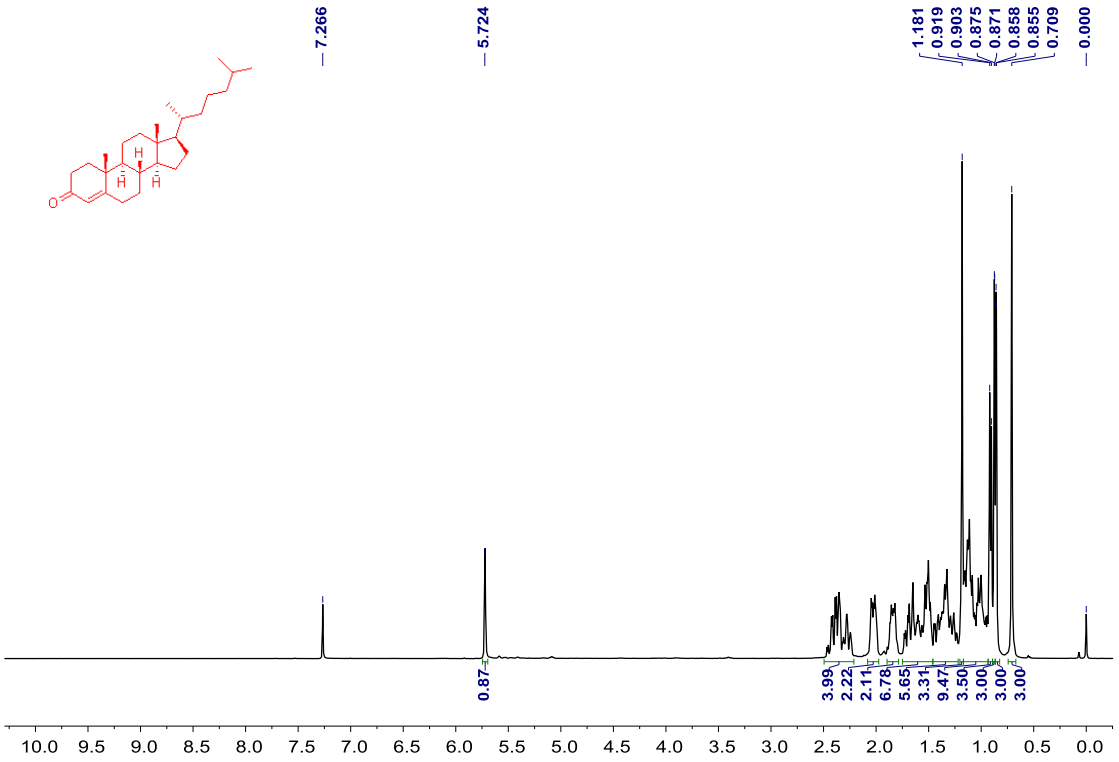


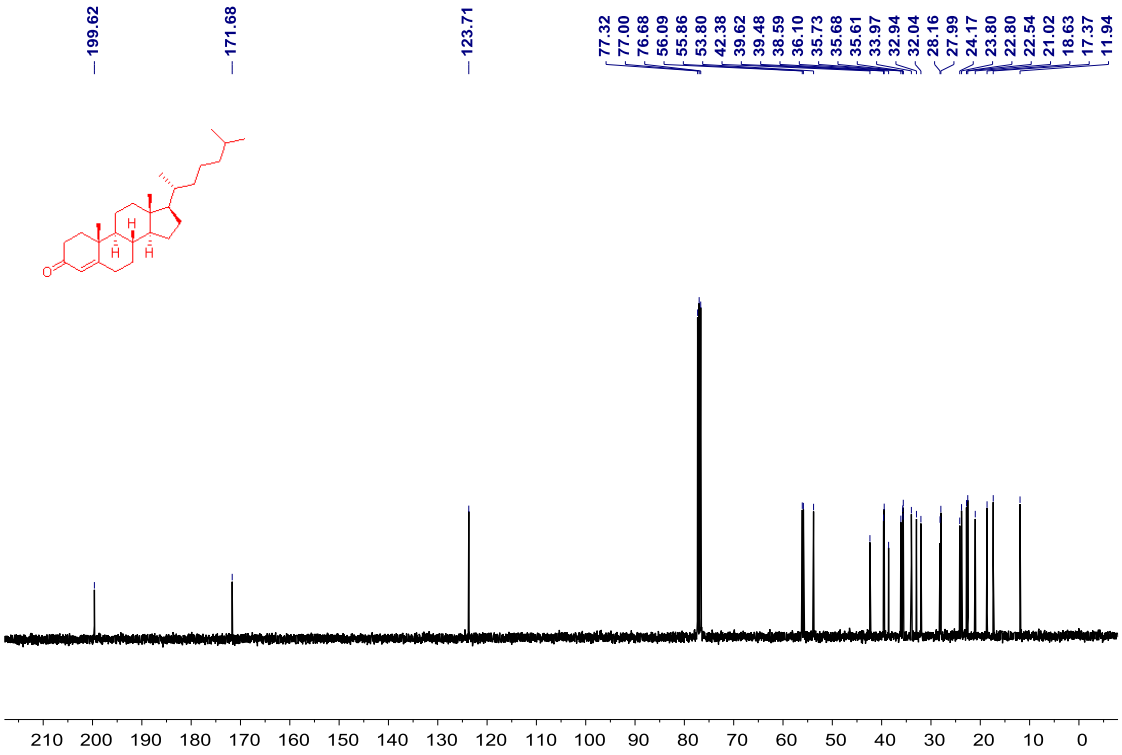
^{1}H and ^{13}C NMR spectra of 3u



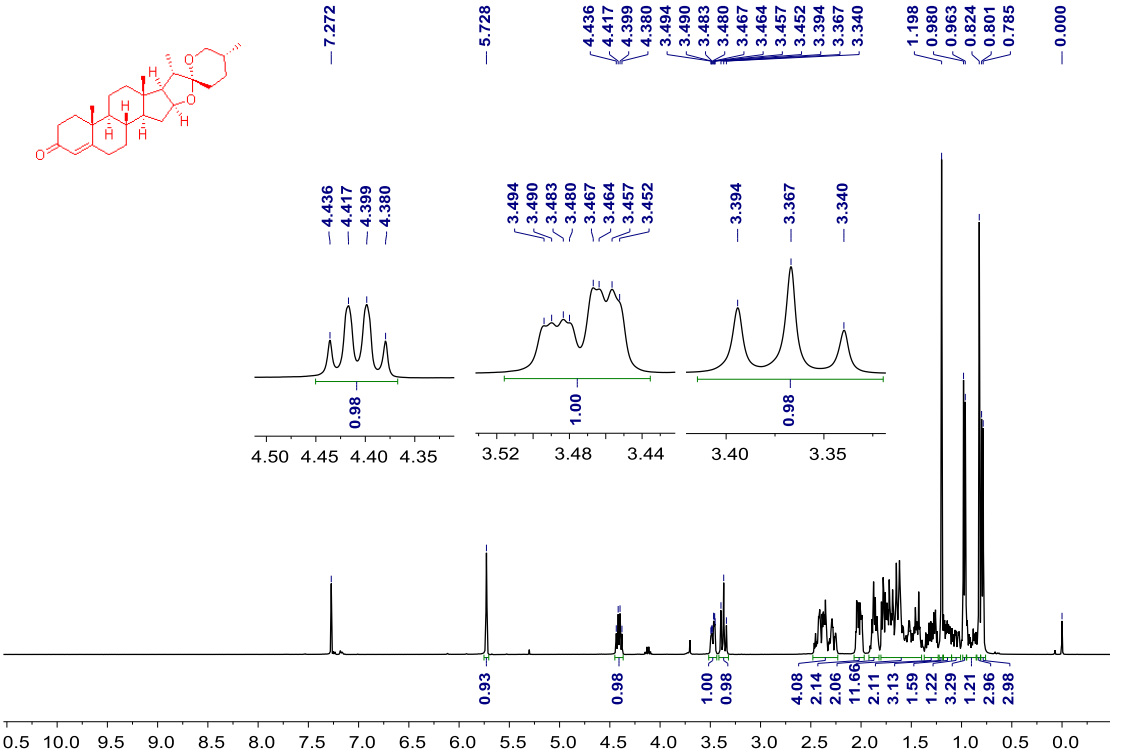


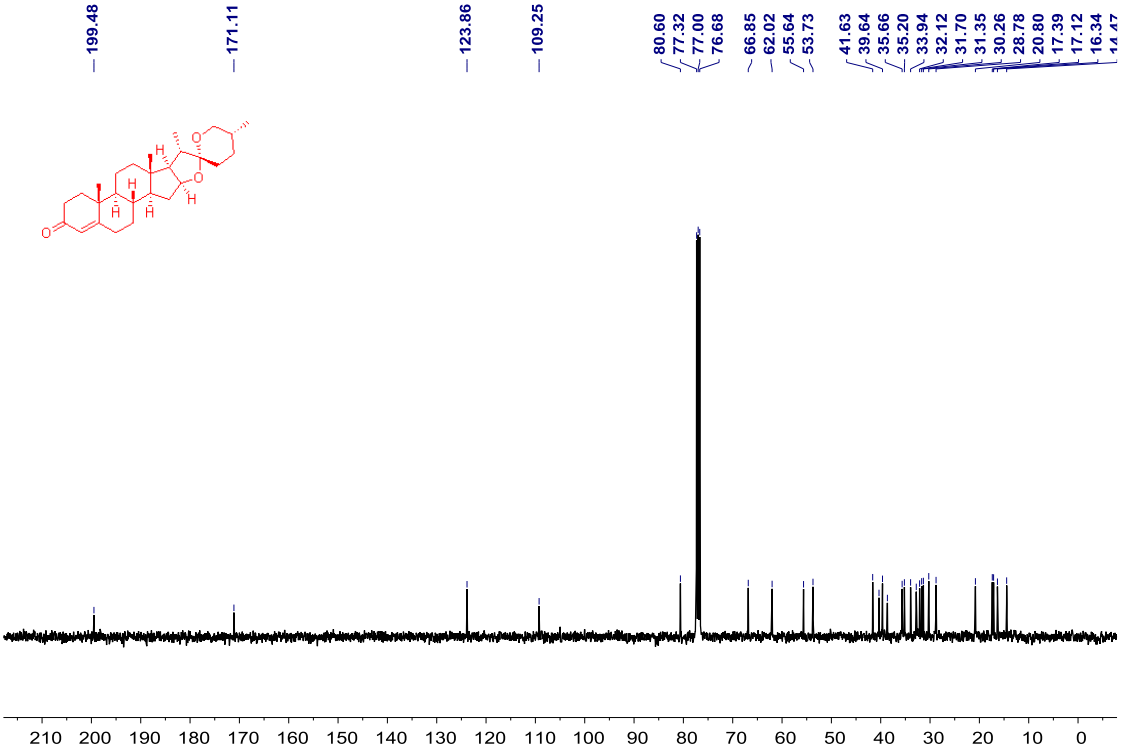
^{1}H and ^{13}C NMR spectra of 3r



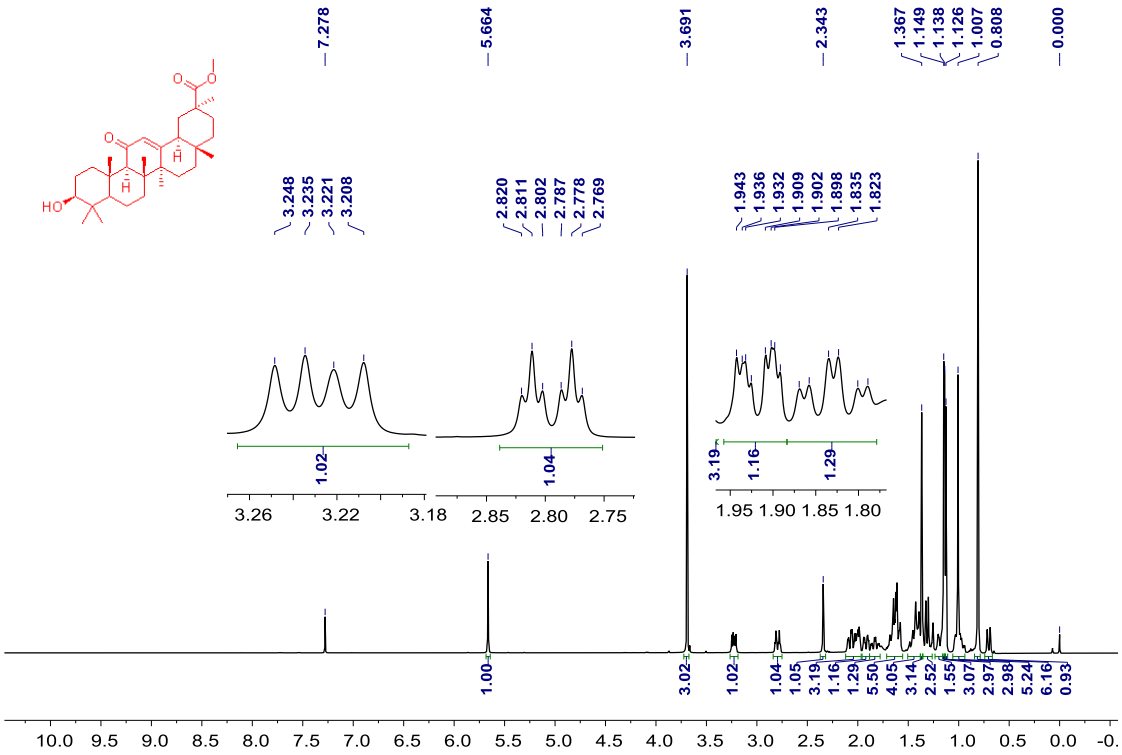


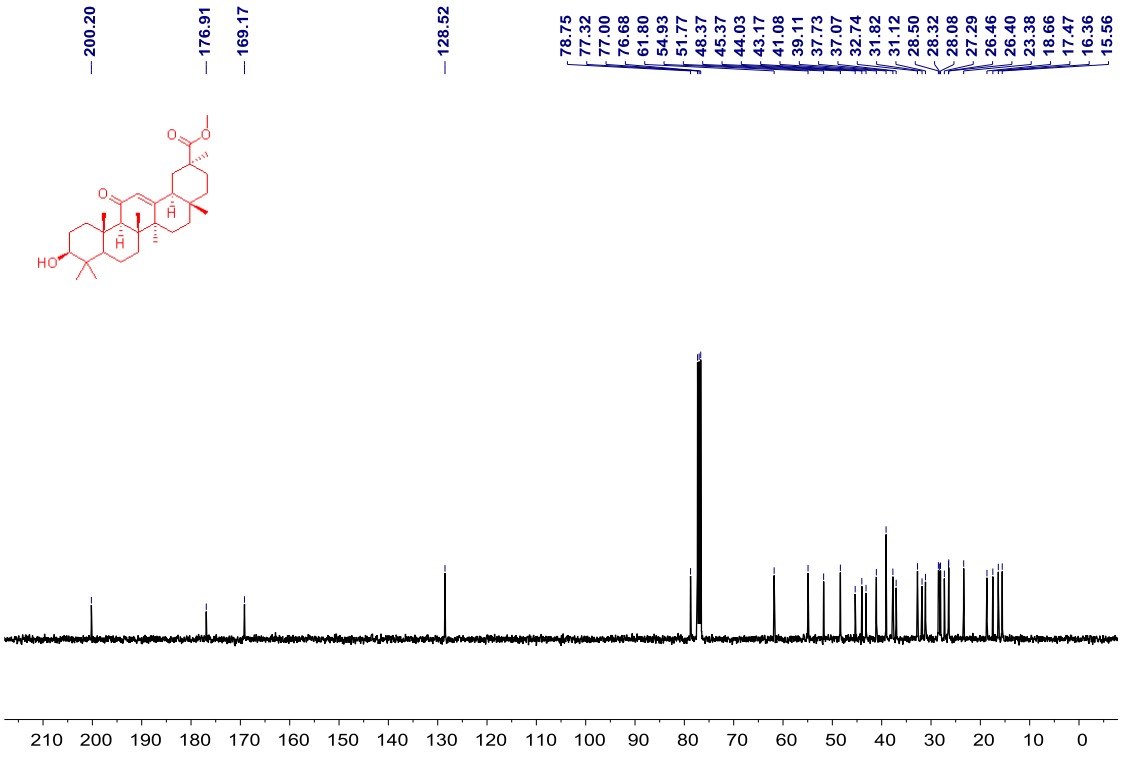
^{1}H and ^{13}C NMR spectra of 3s



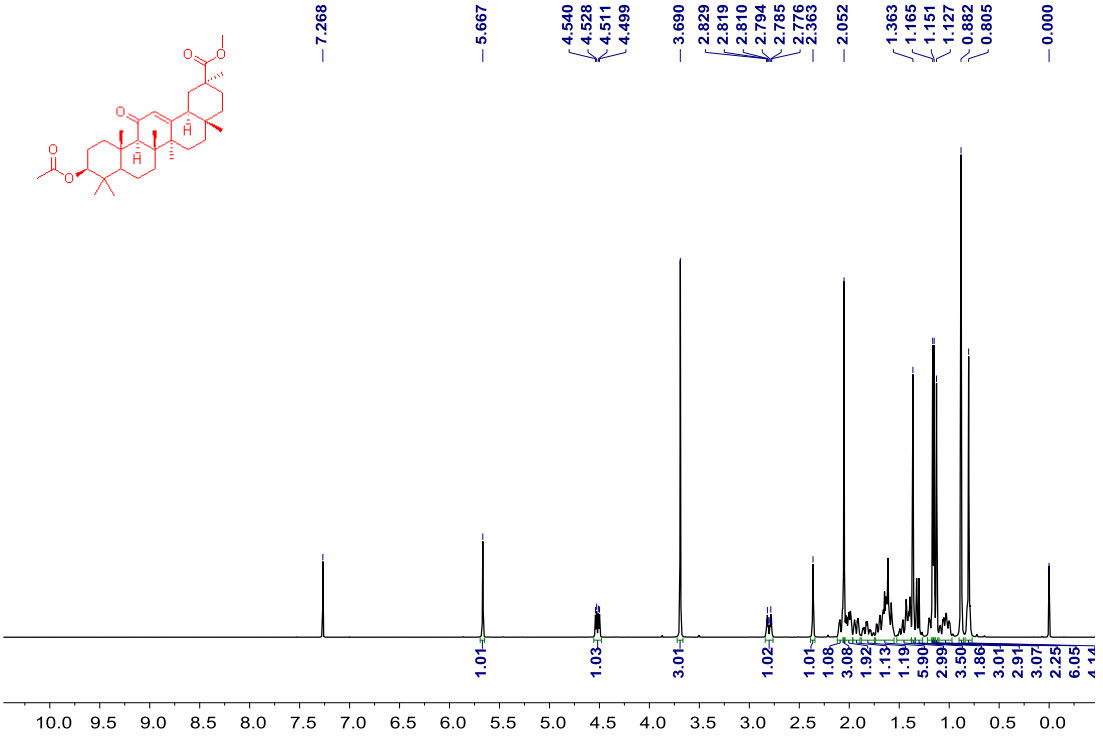


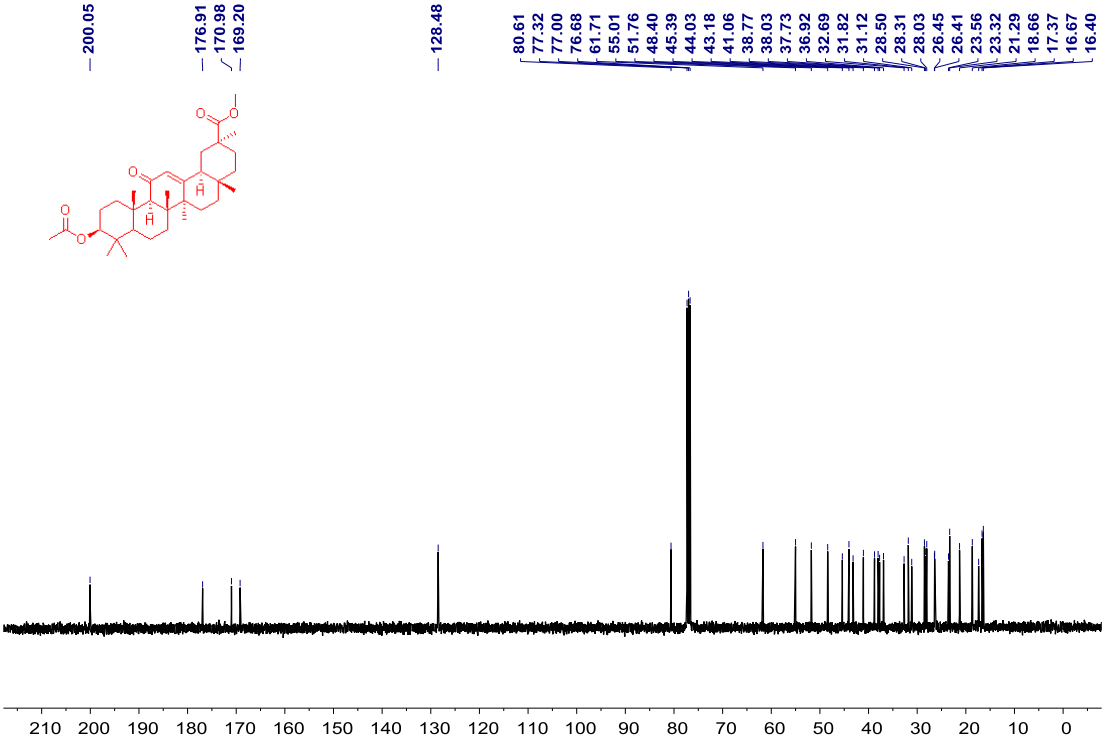
^{1}H and ^{13}C NMR spectra of 3w



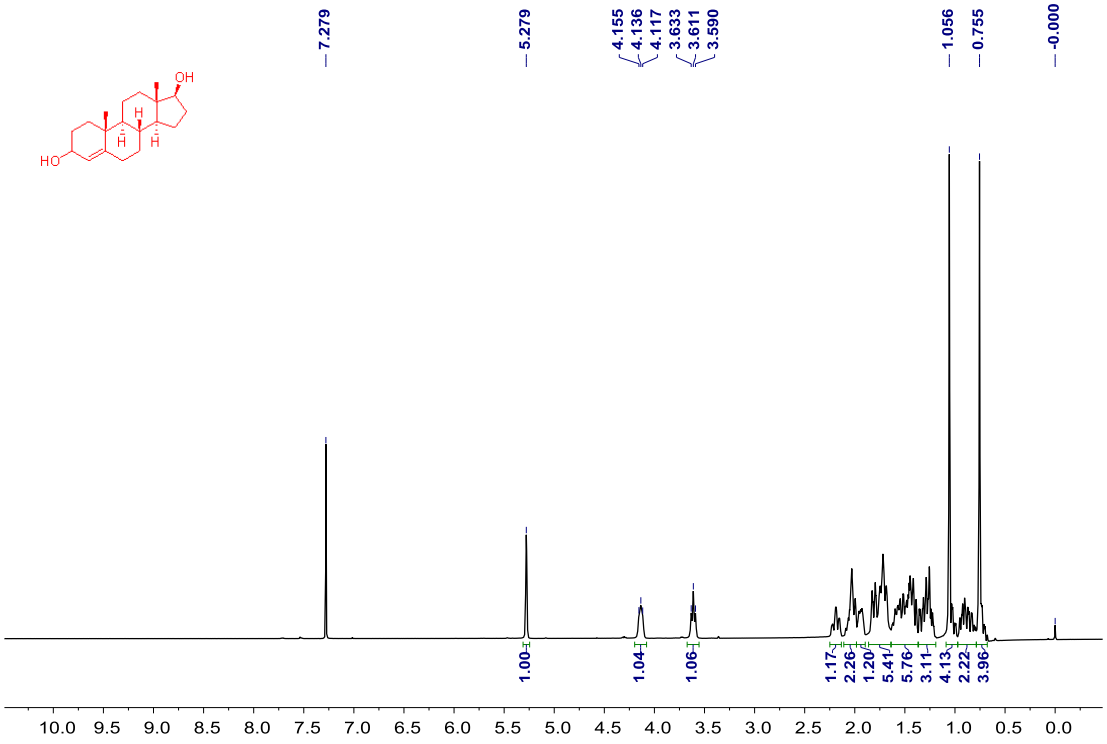


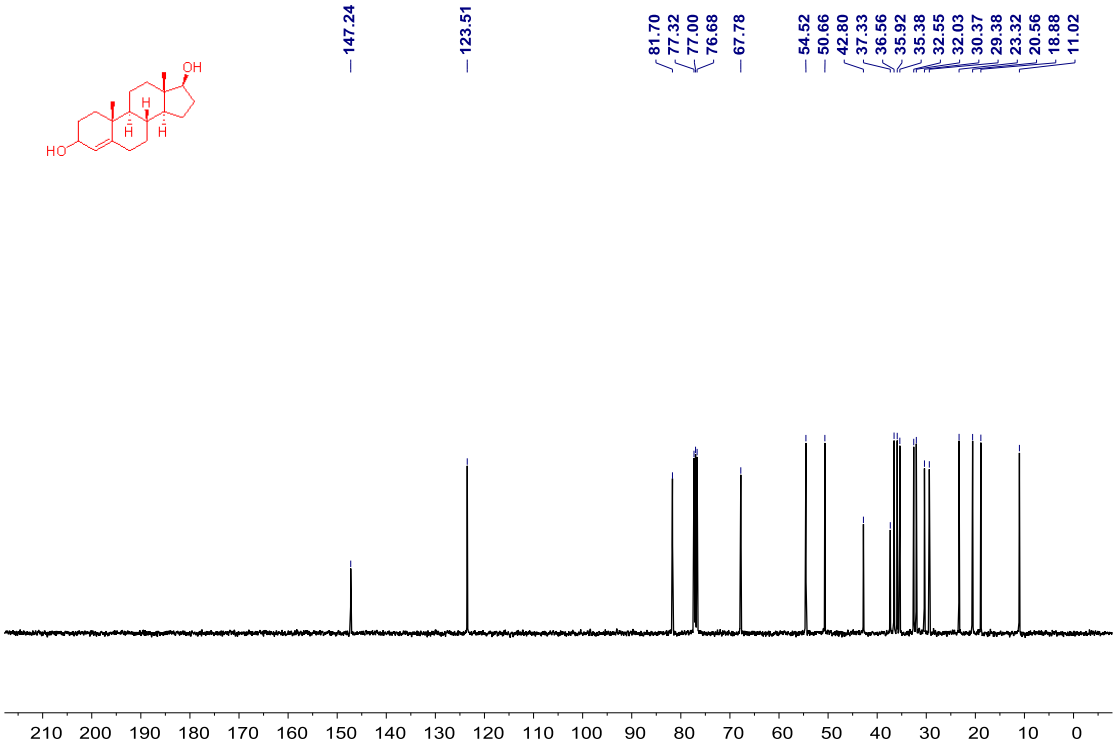
^{1}H and ^{13}C NMR spectra of 3x





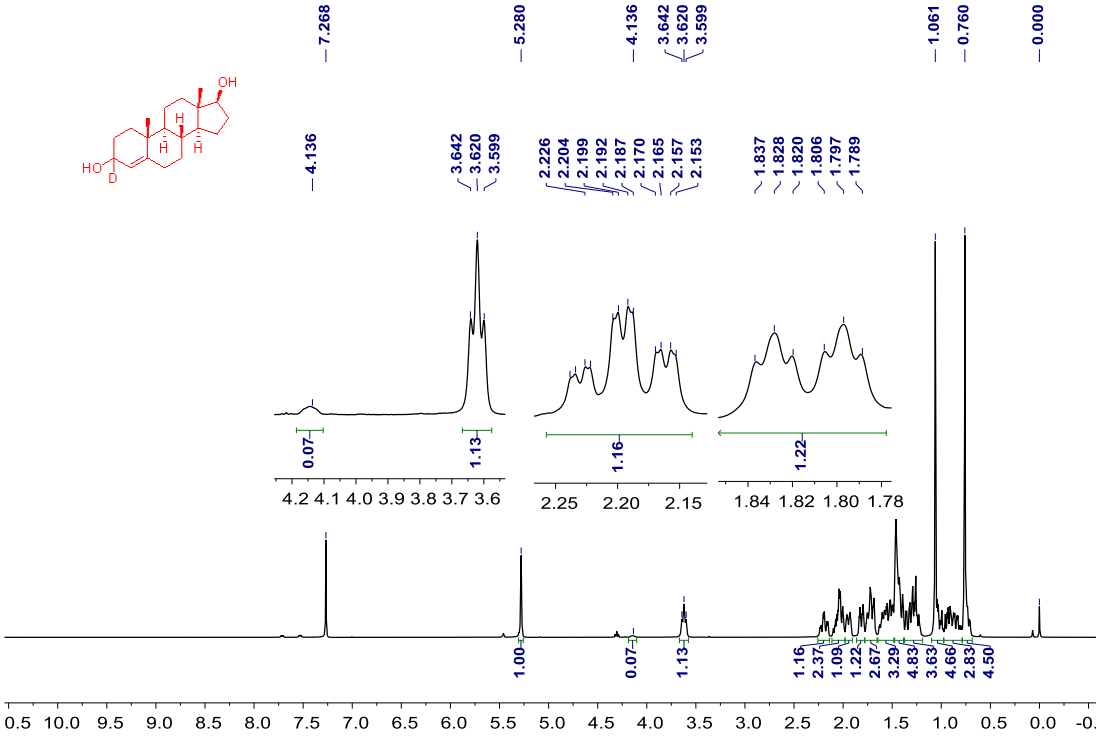
^{1}H and ^{13}C NMR spectra of 4a

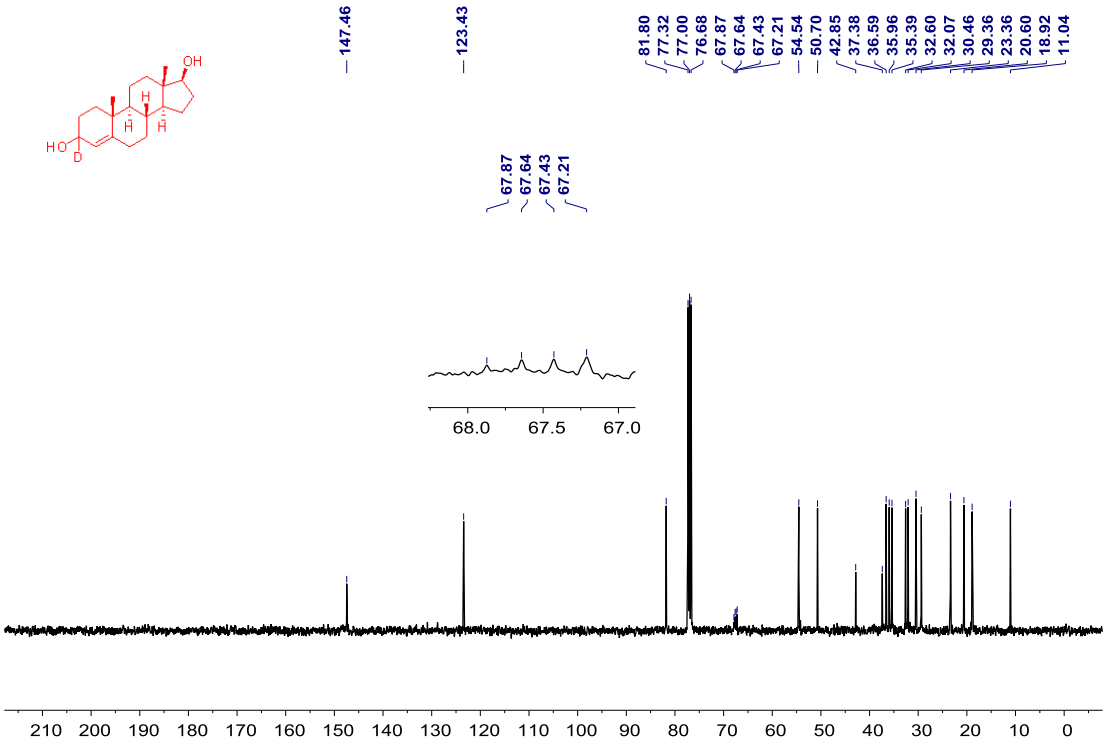




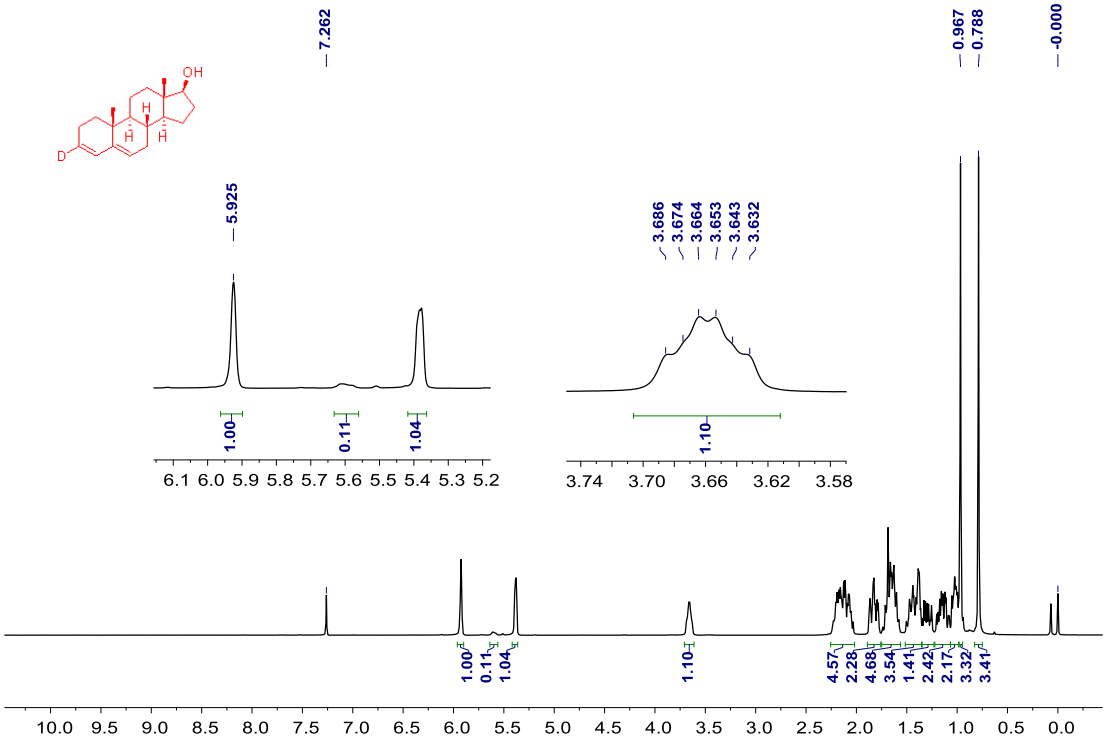
12. Copies of ^{1}H and ^{13}C NMR spectra in mechanistic studies

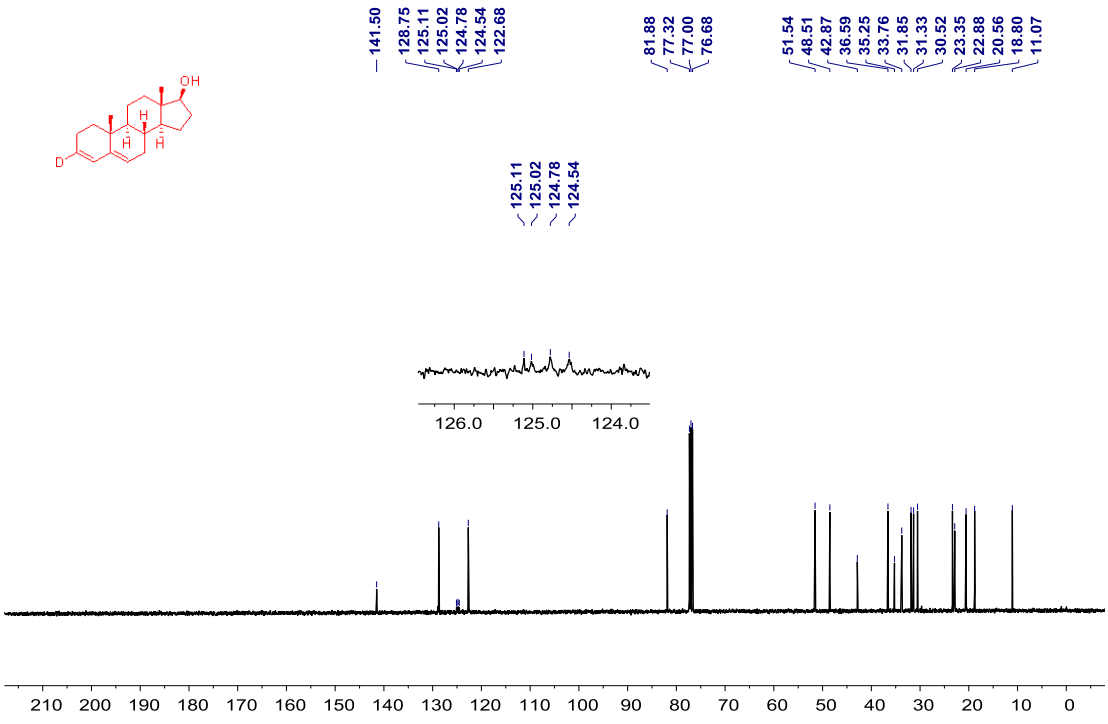
^{1}H and ^{13}C NMR spectra of **d-4a**



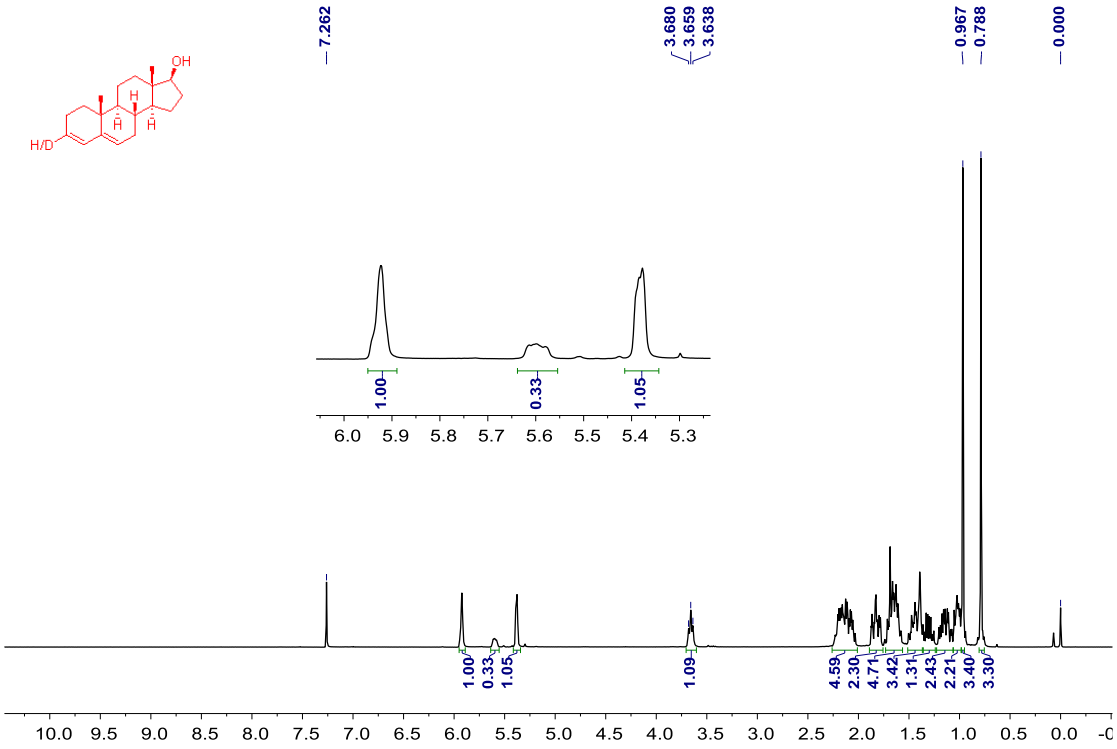


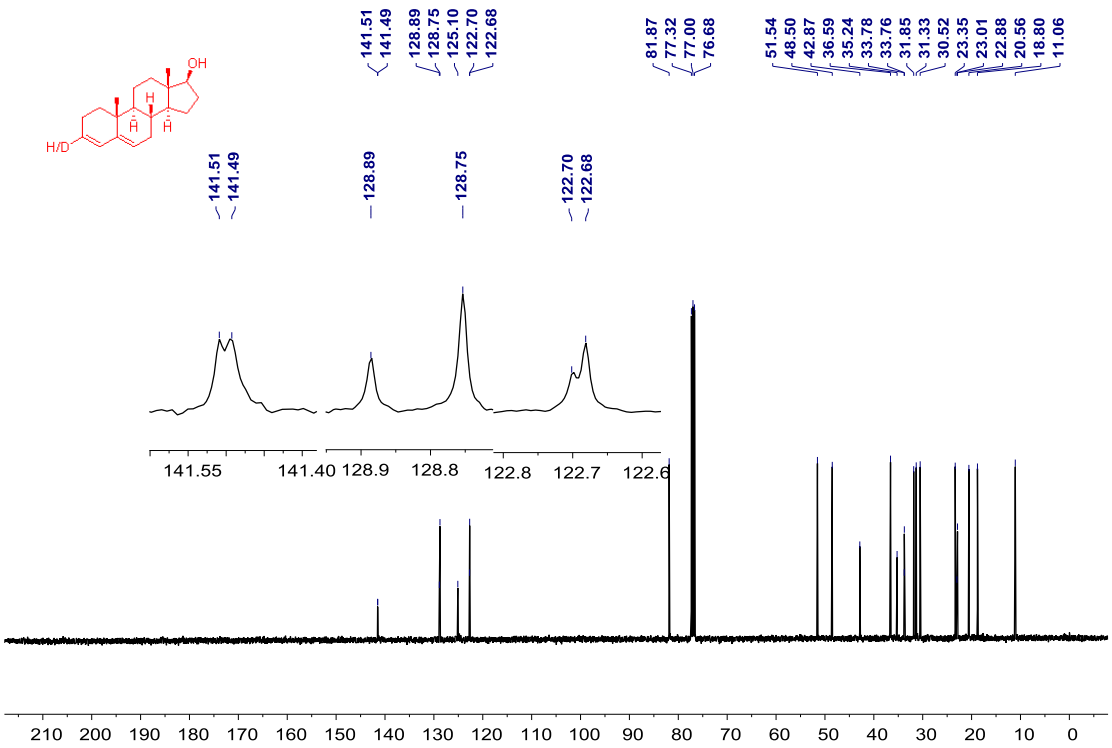
^{1}H and ^{13}C NMR spectra of d-**1a**



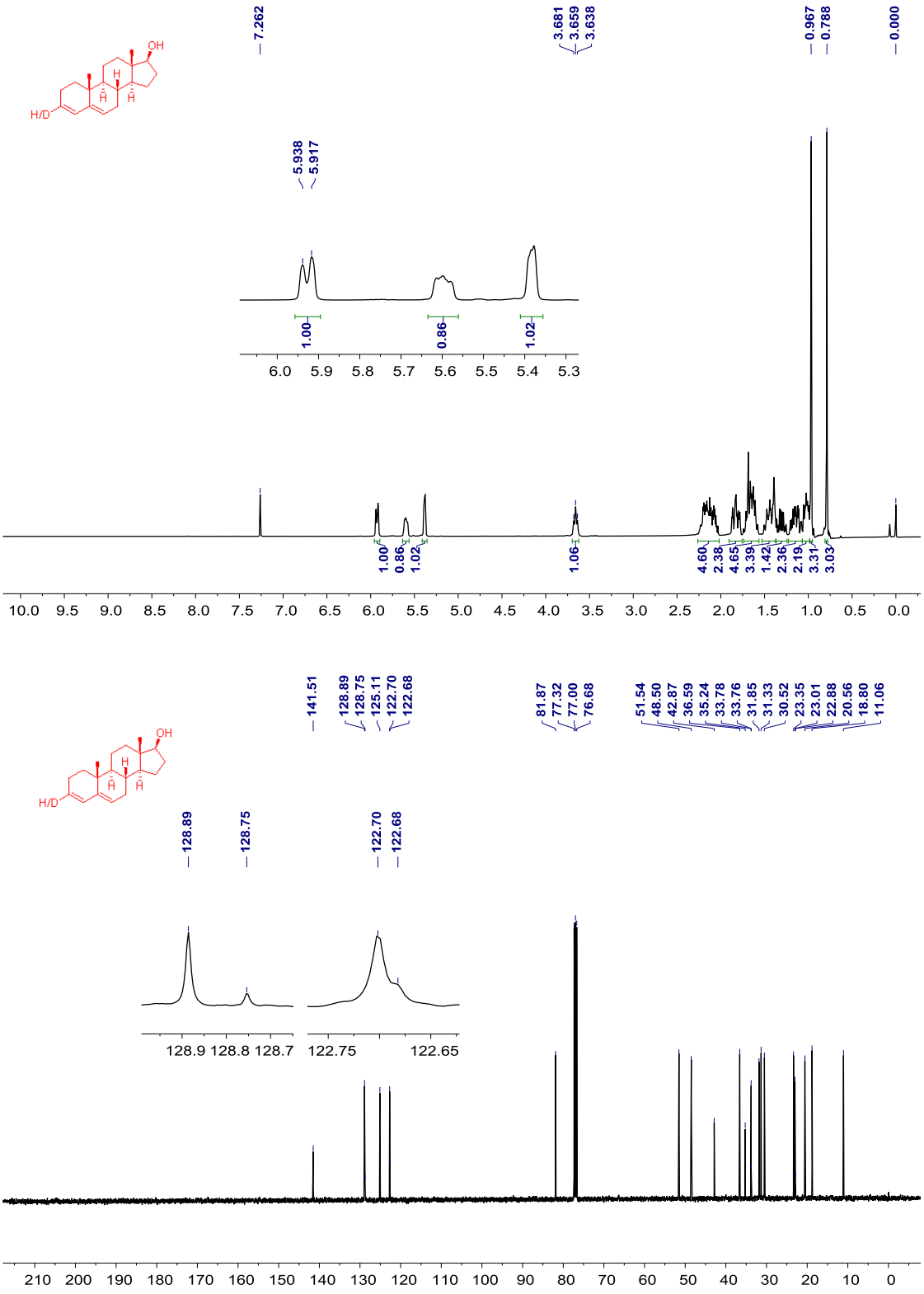


^{1}H and ^{13}C NMR spectra of d-1a Conditions A

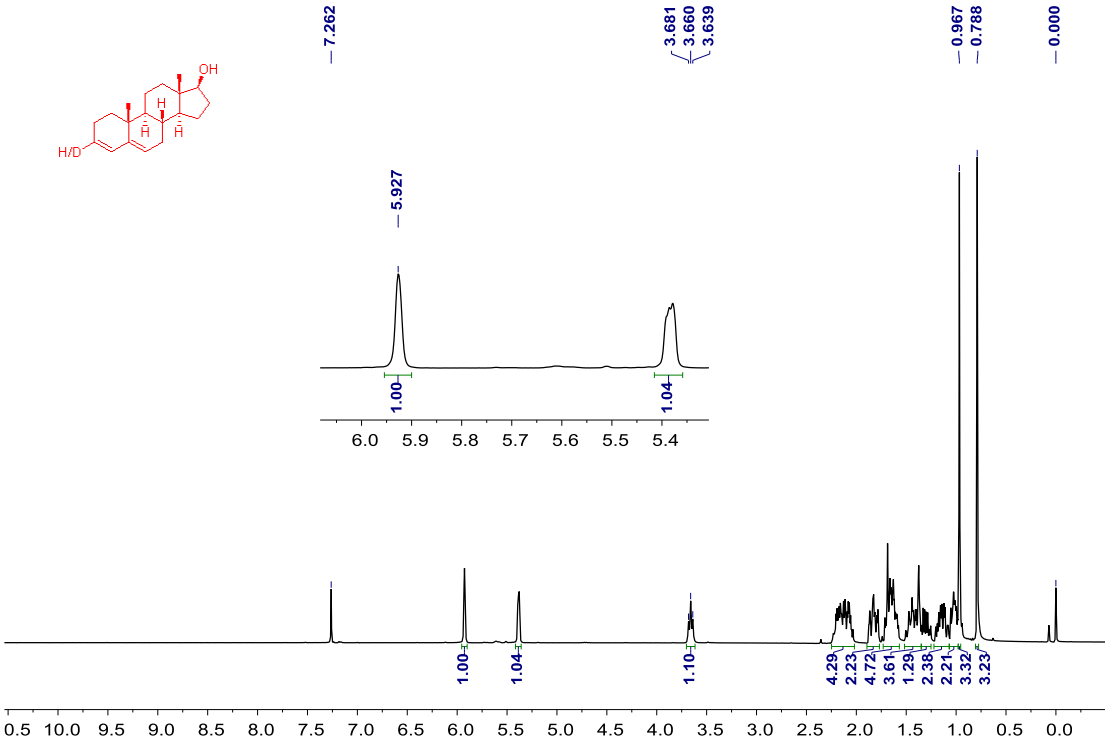


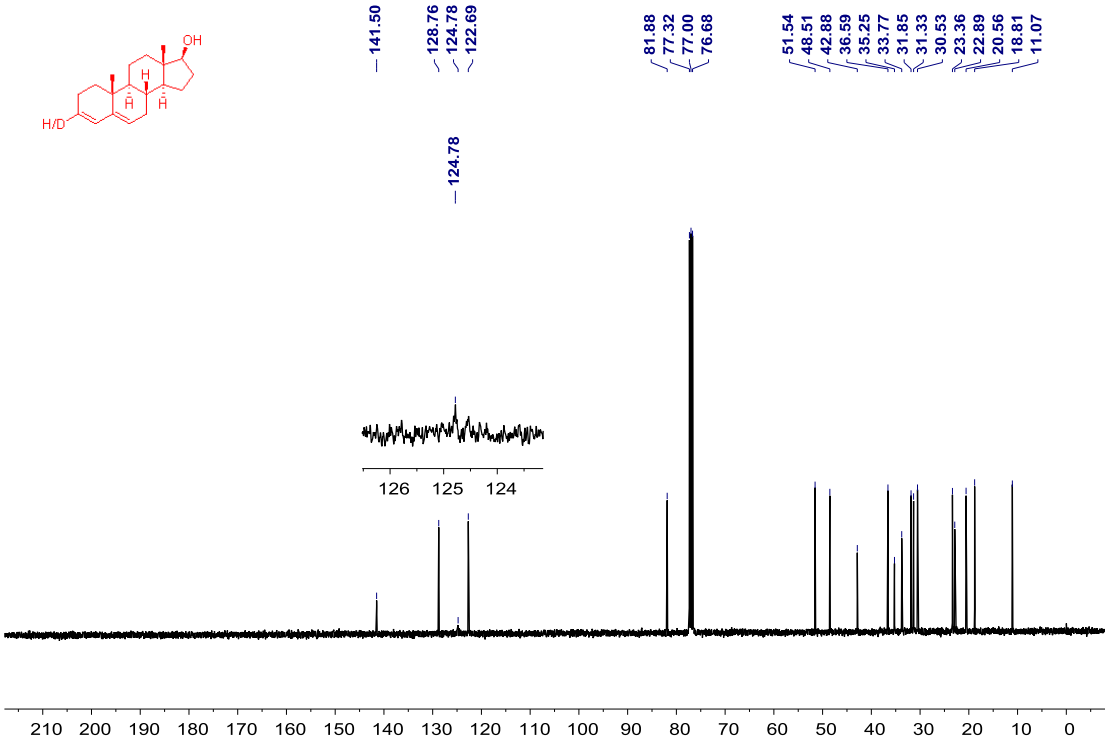


^{1}H and ^{13}C NMR spectra of d-1a Conditions B



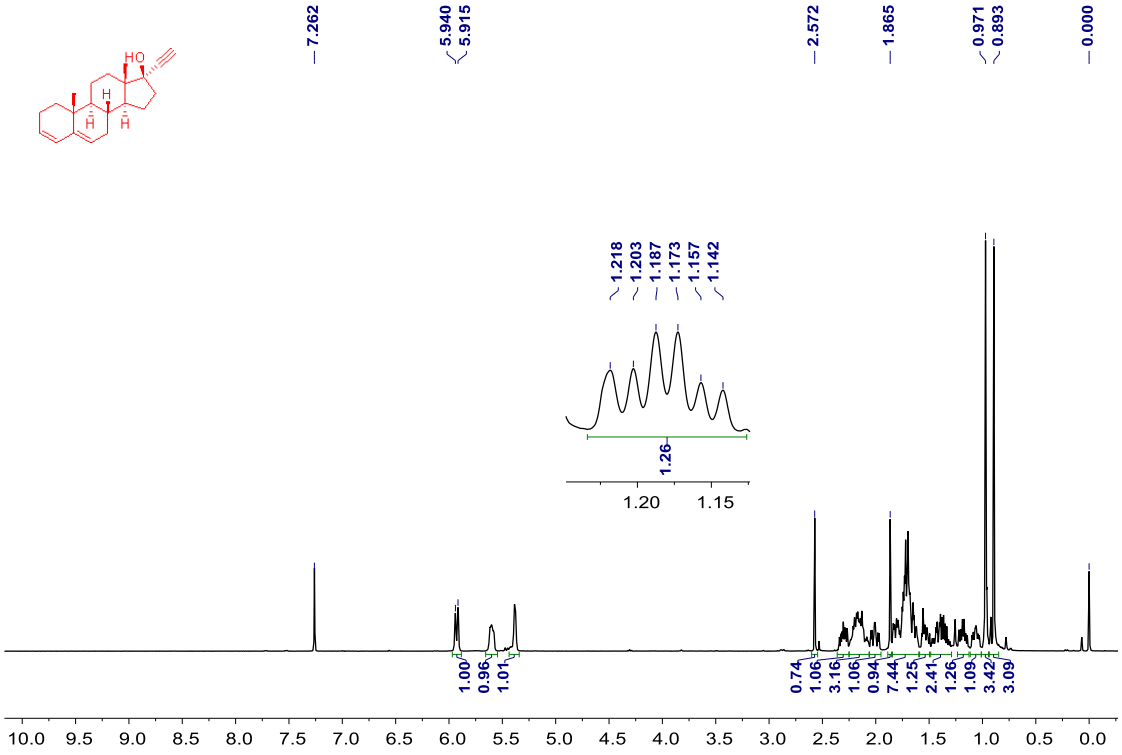
^{1}H and ^{13}C NMR spectra of d-1a Conditions C

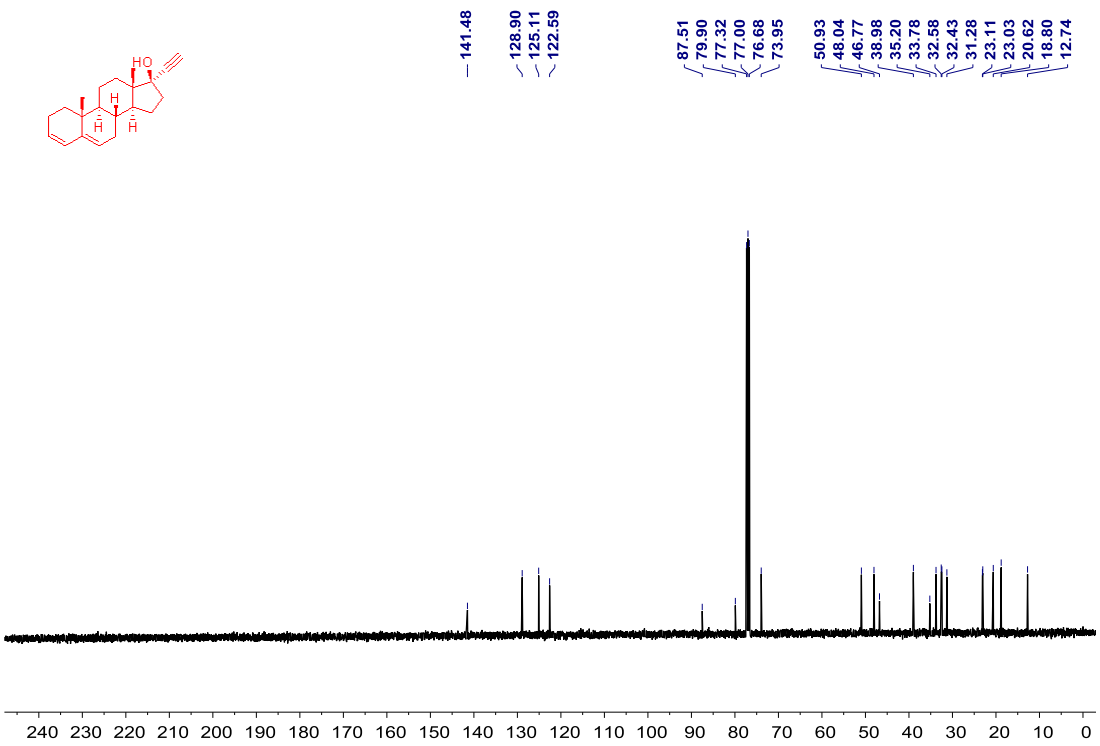




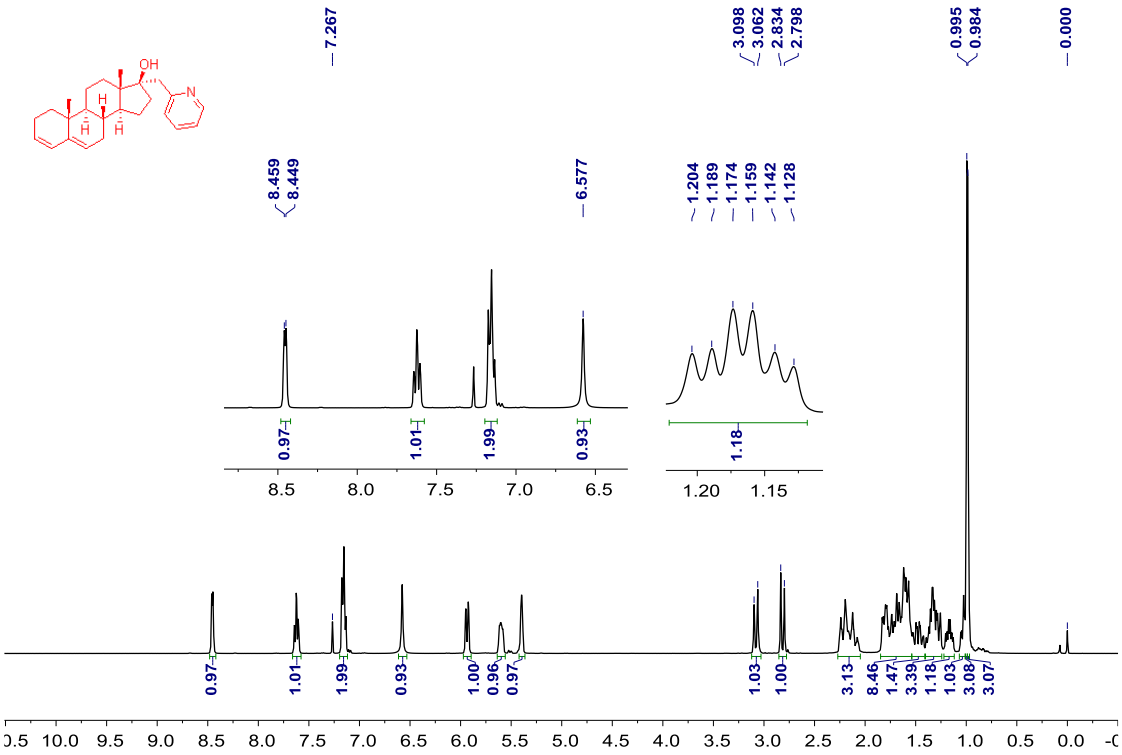
13. Copies of ^{1}H and ^{13}C NMR spectra in synthetic applications of 3,5-dienes

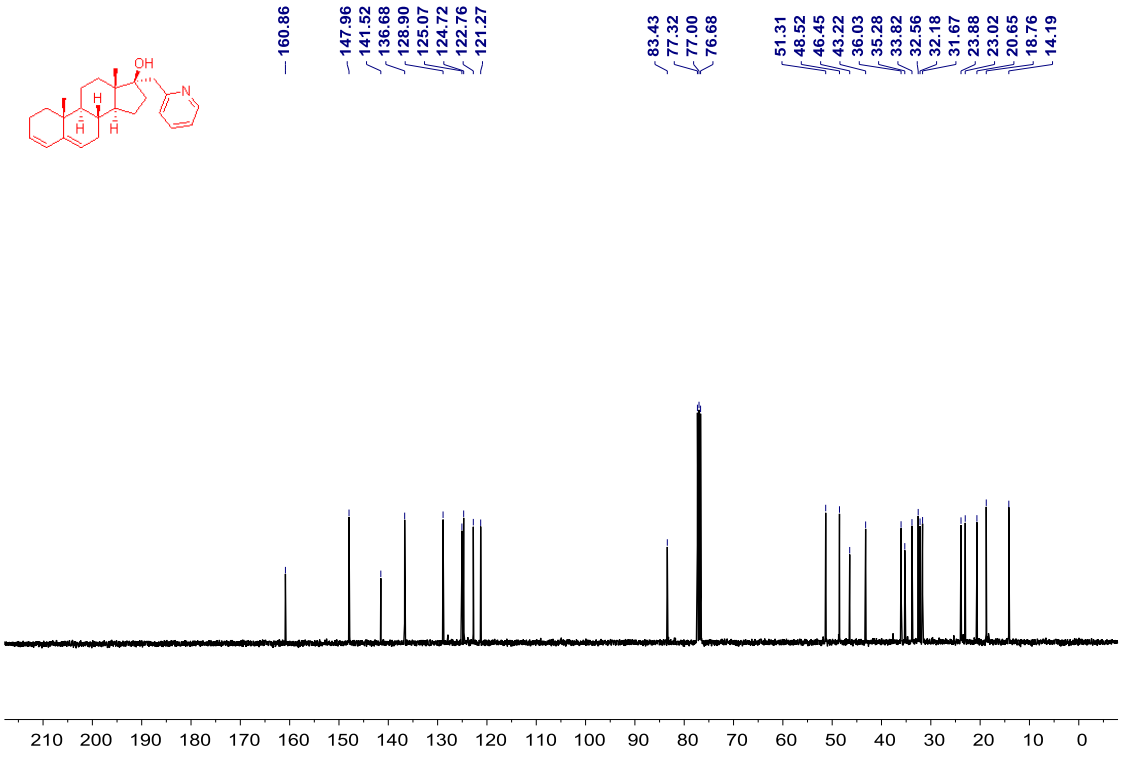
^{1}H and ^{13}C NMR spectra of 10



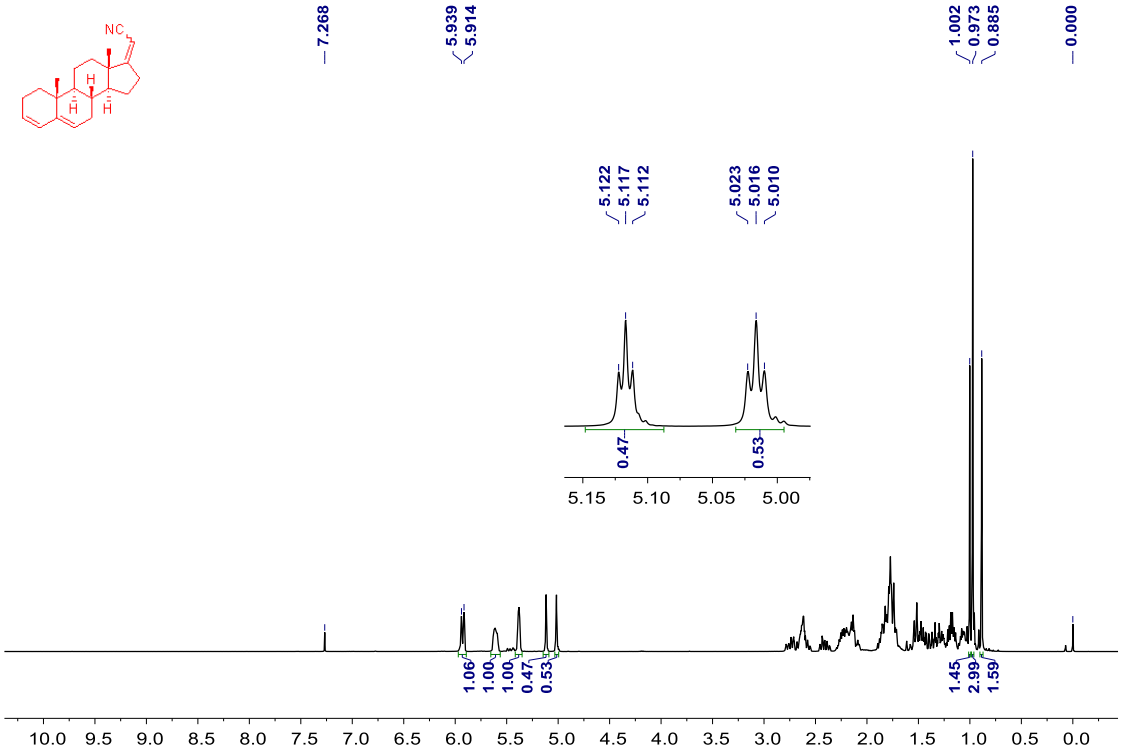


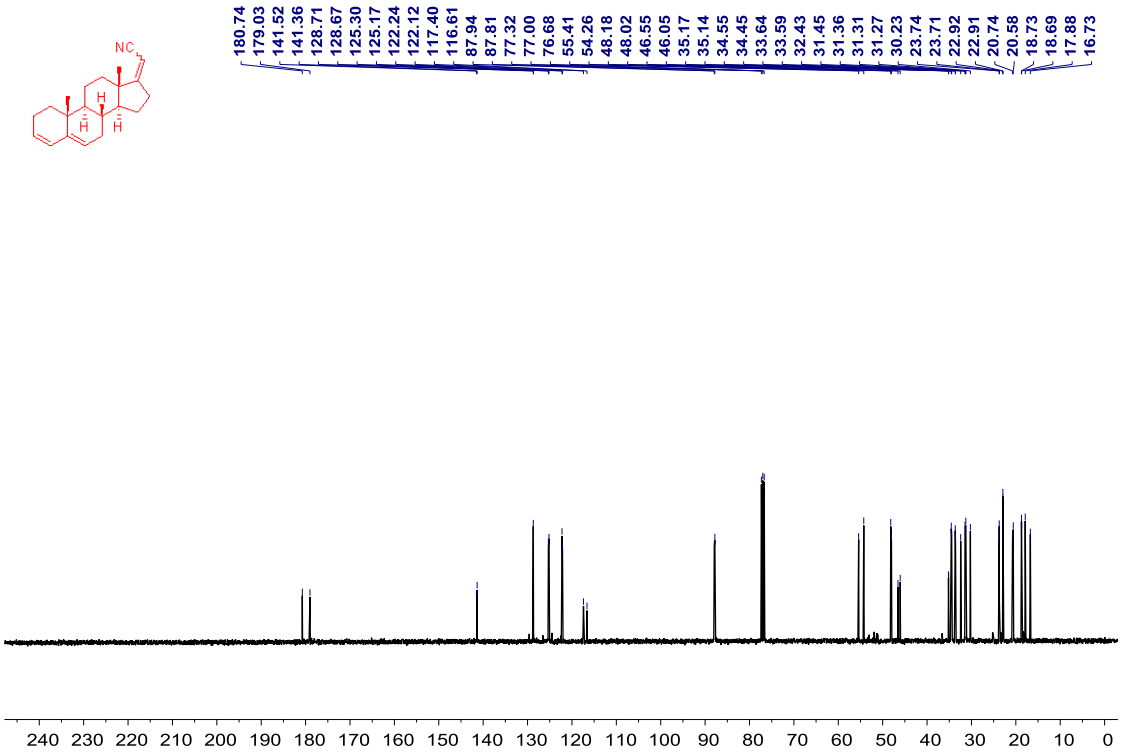
^{1}H and ^{13}C NMR spectra of 11





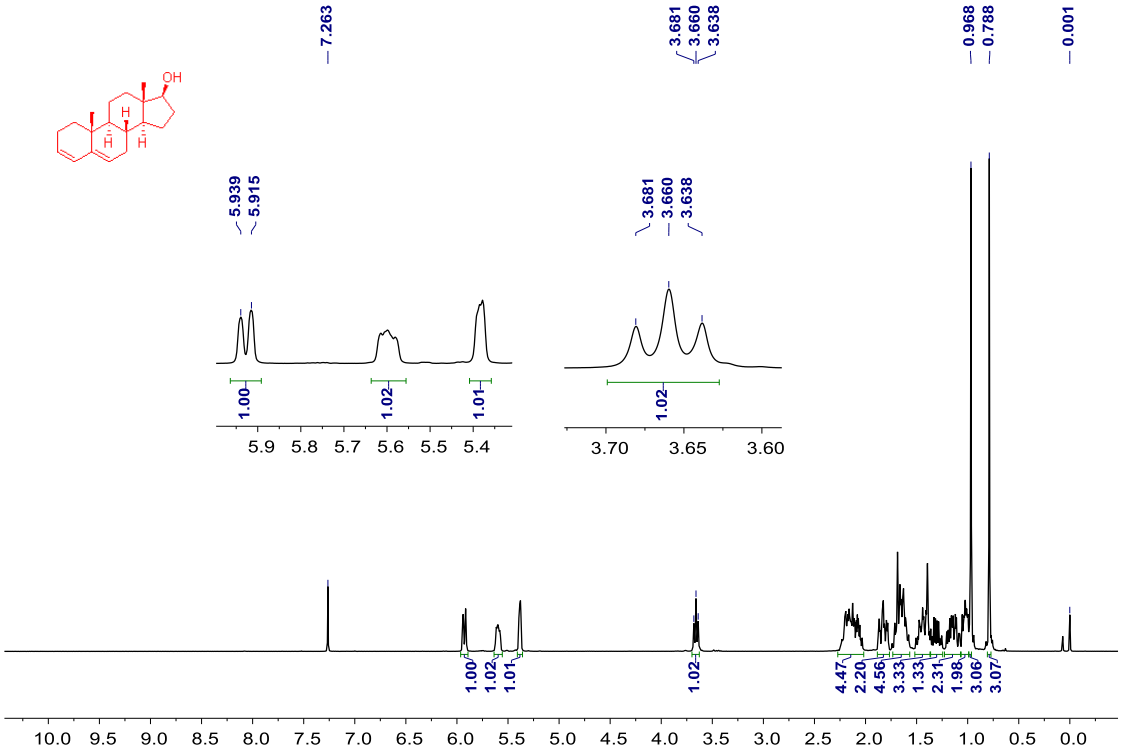
^{1}H and ^{13}C NMR spectra of 13

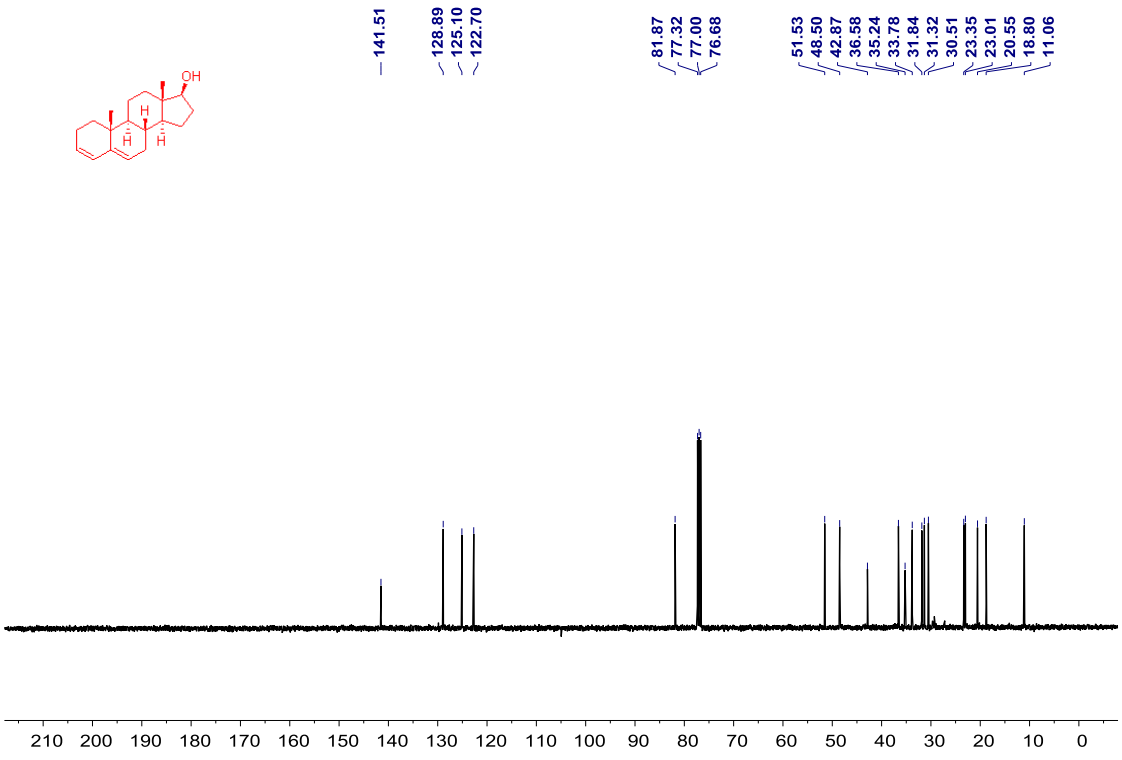




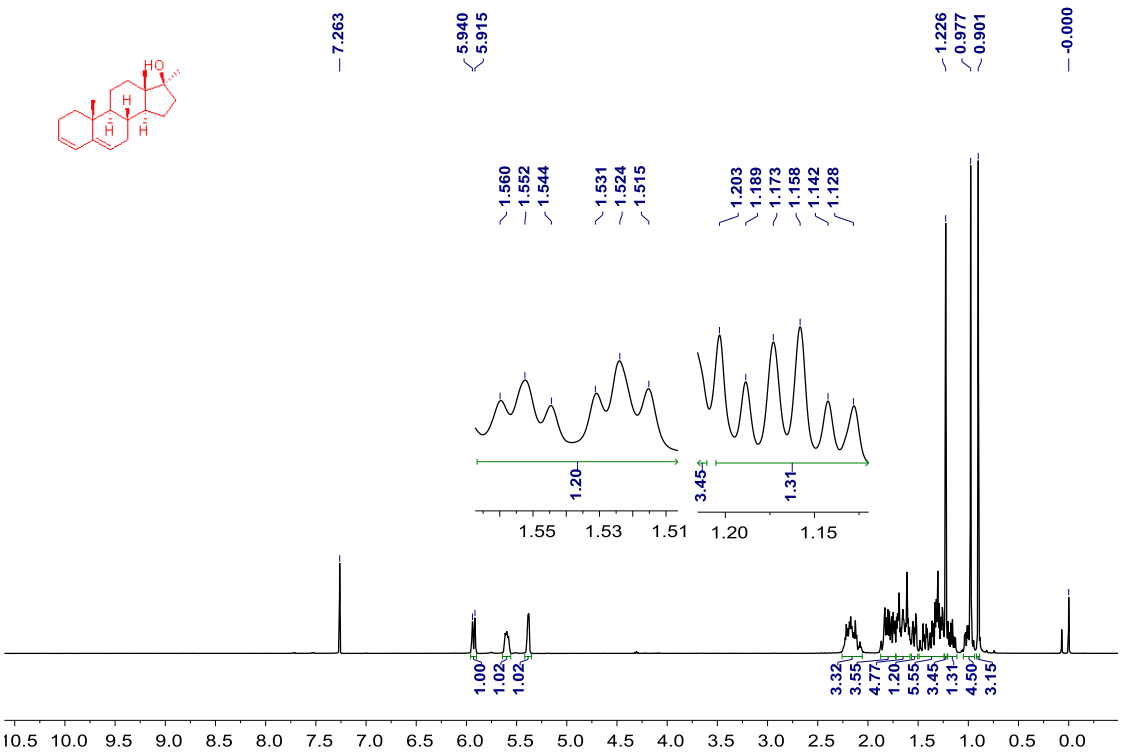
14. Copies of ^{1}H and ^{13}C NMR spectra of products

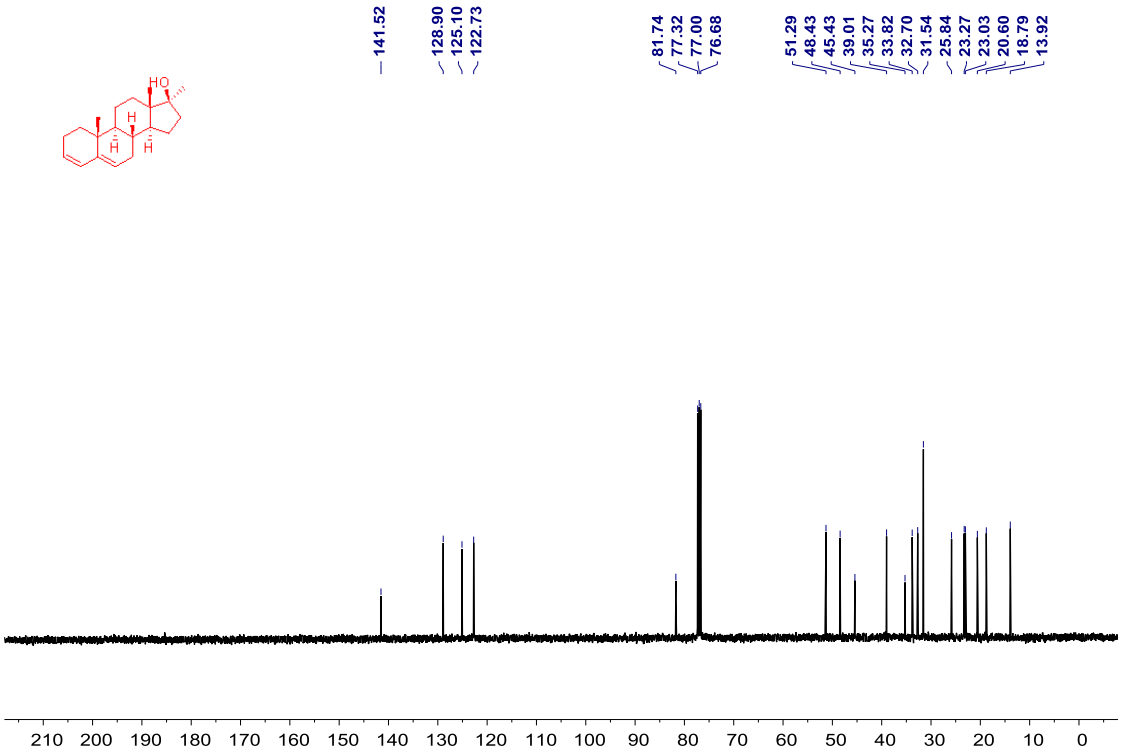
^{1}H and ^{13}C NMR spectra of **1a**



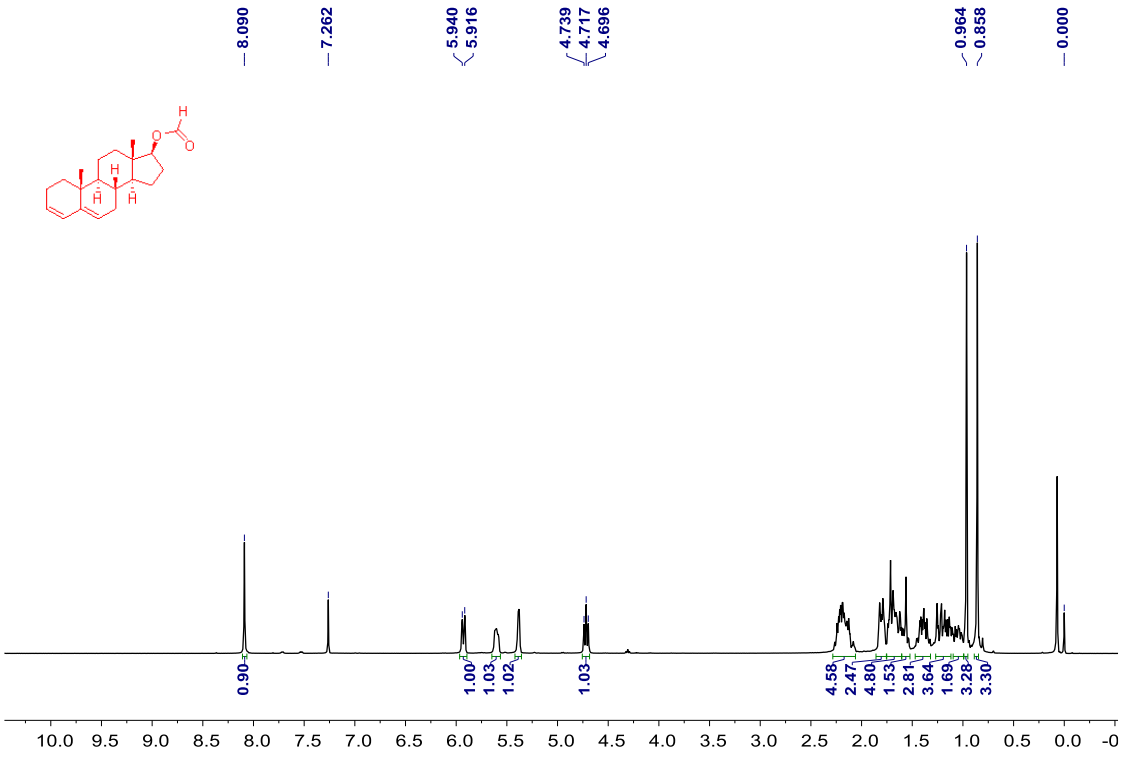


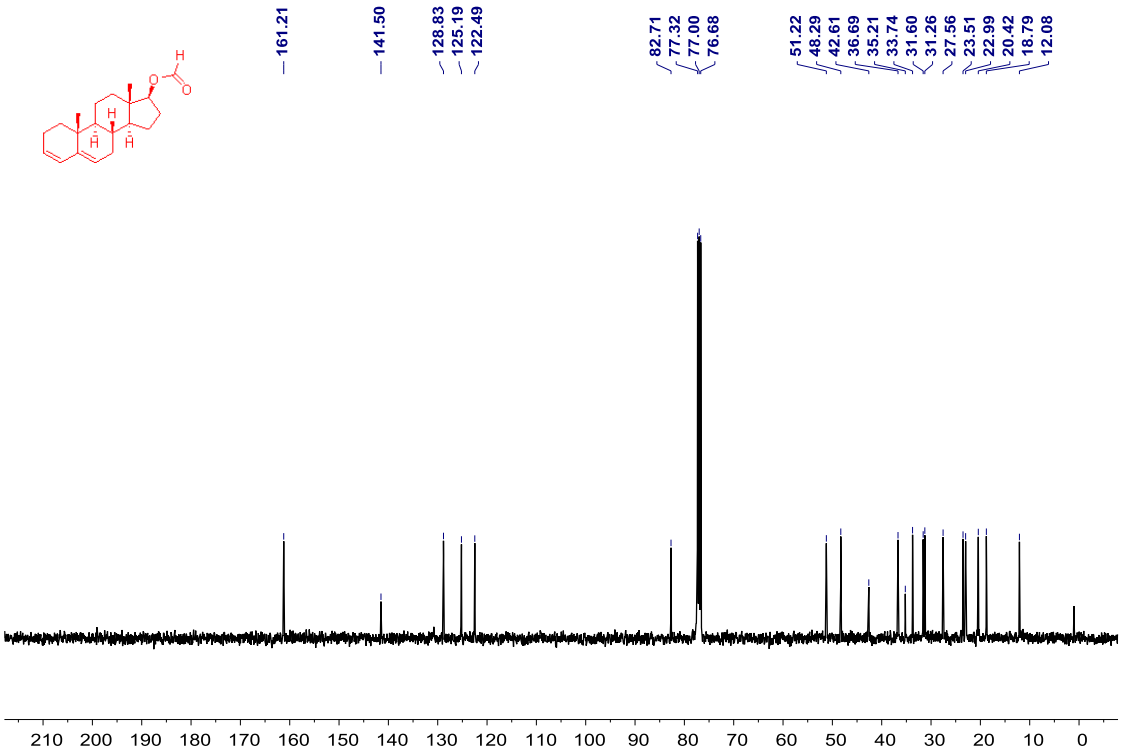
^{1}H and ^{13}C NMR spectra of 1b



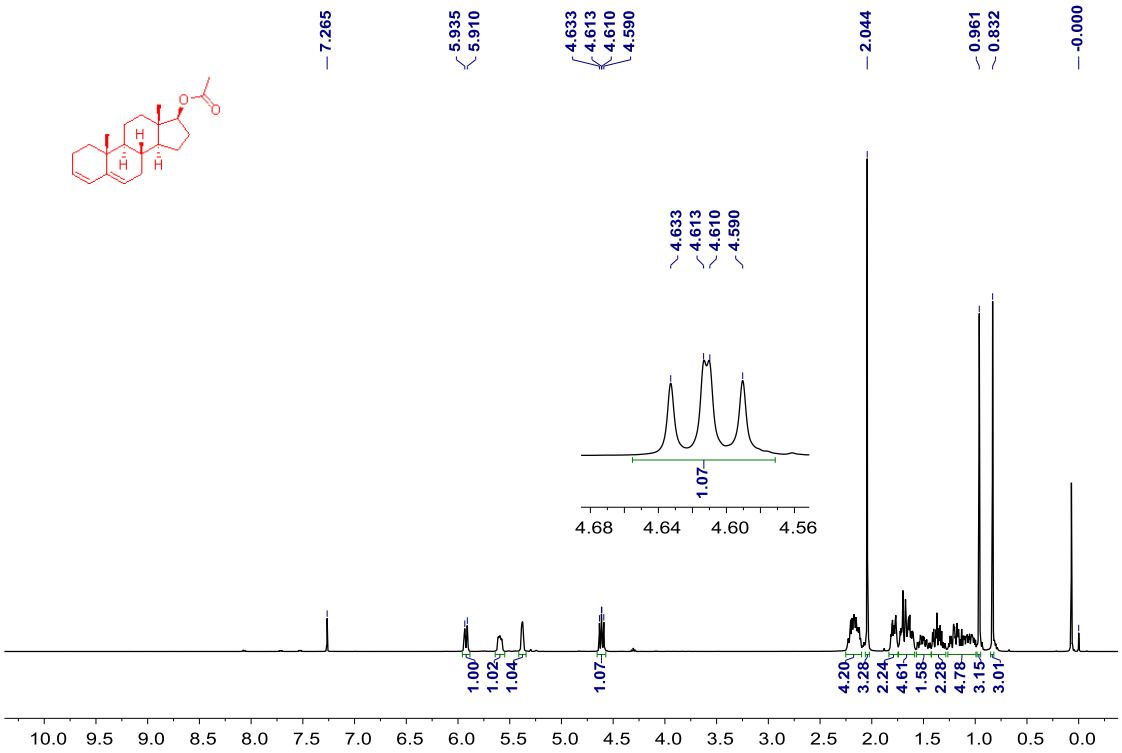


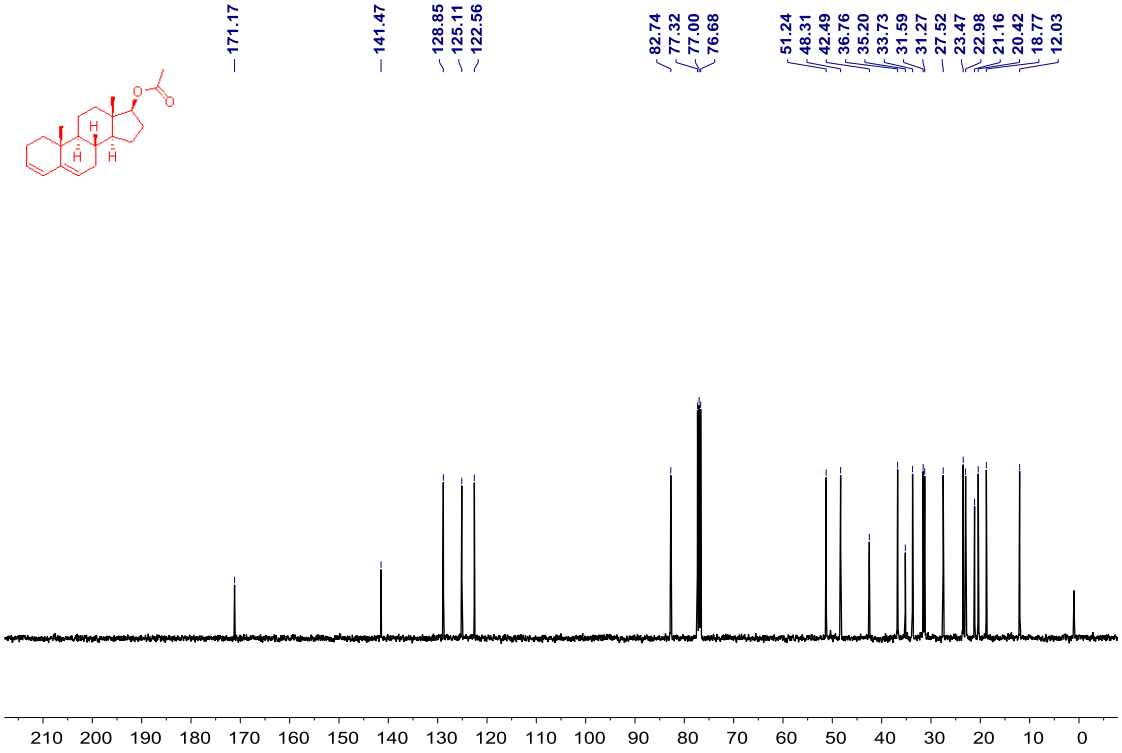
^{1}H and ^{13}C NMR spectra of 1c



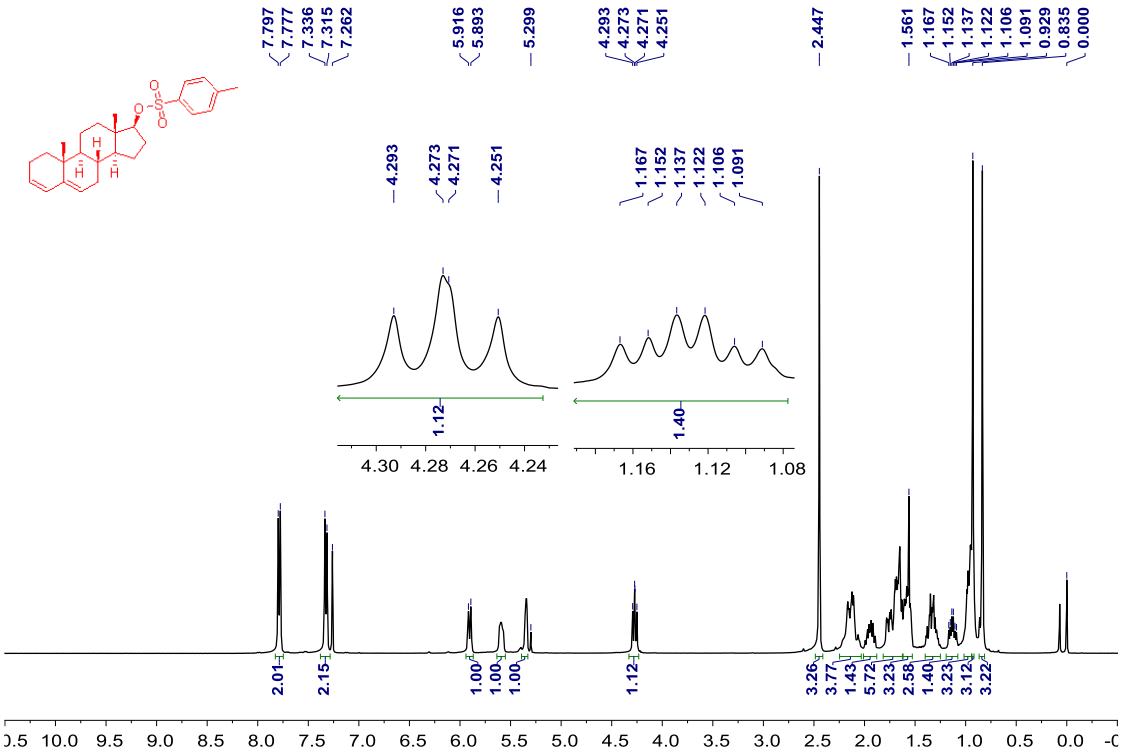


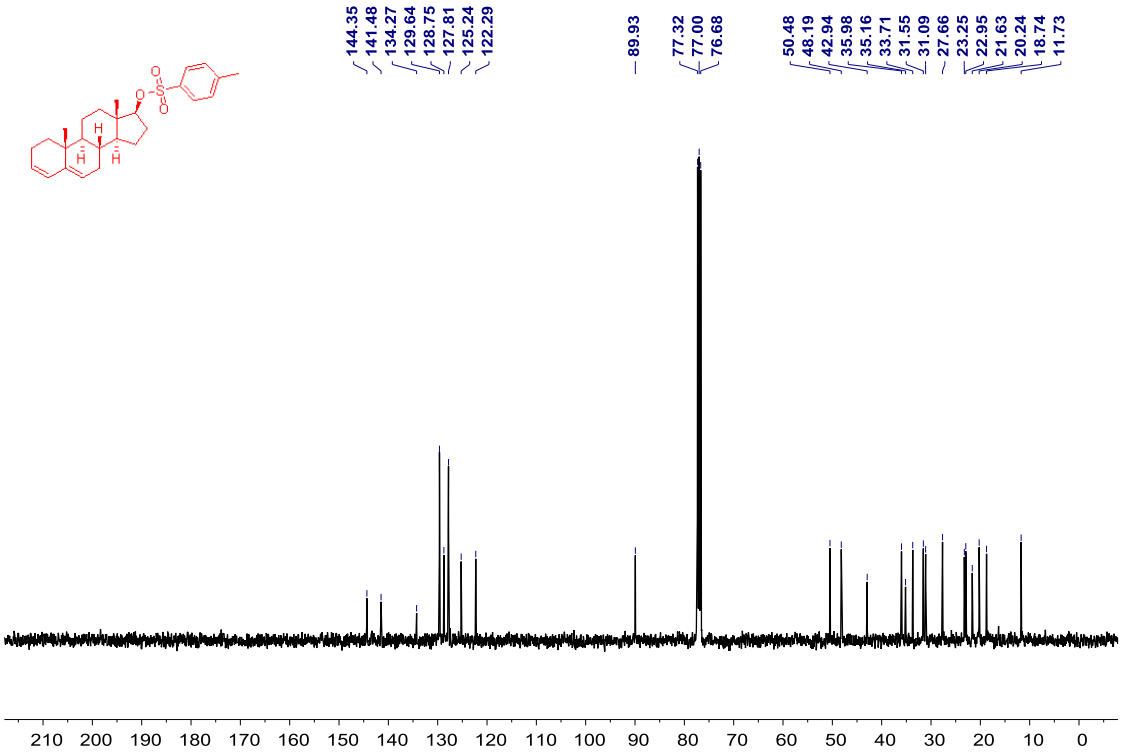
^{1}H and ^{13}C NMR spectra of 1d



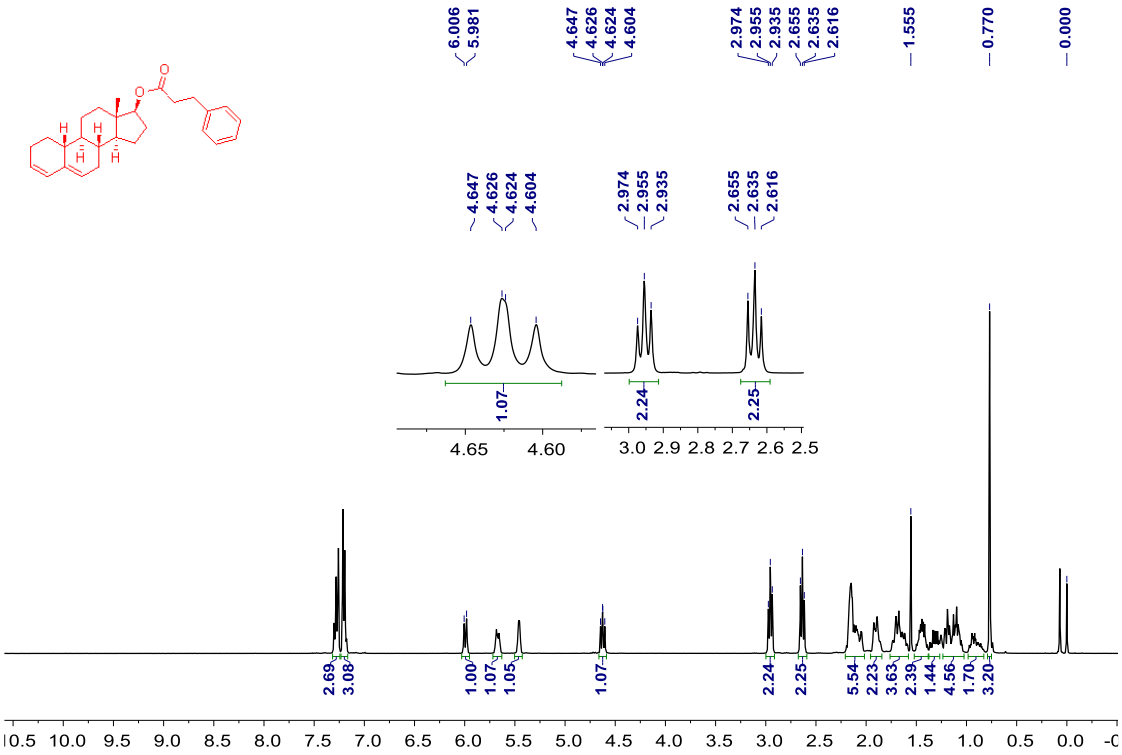


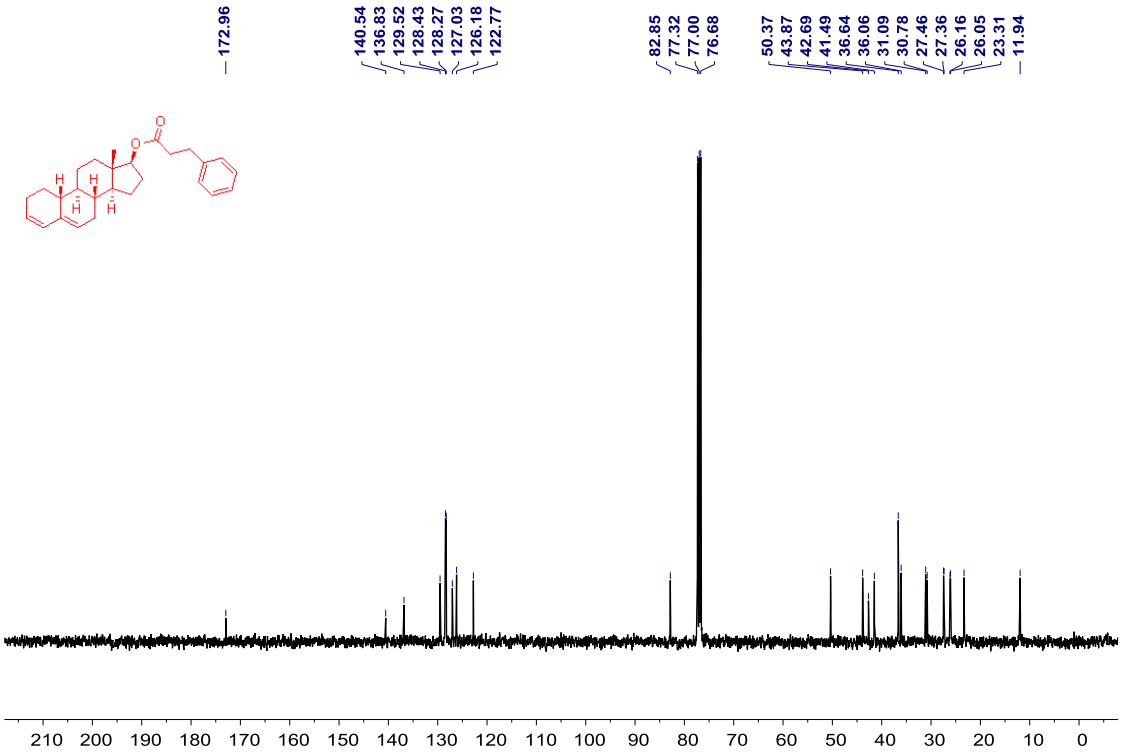
^{1}H and ^{13}C NMR spectra of 1e



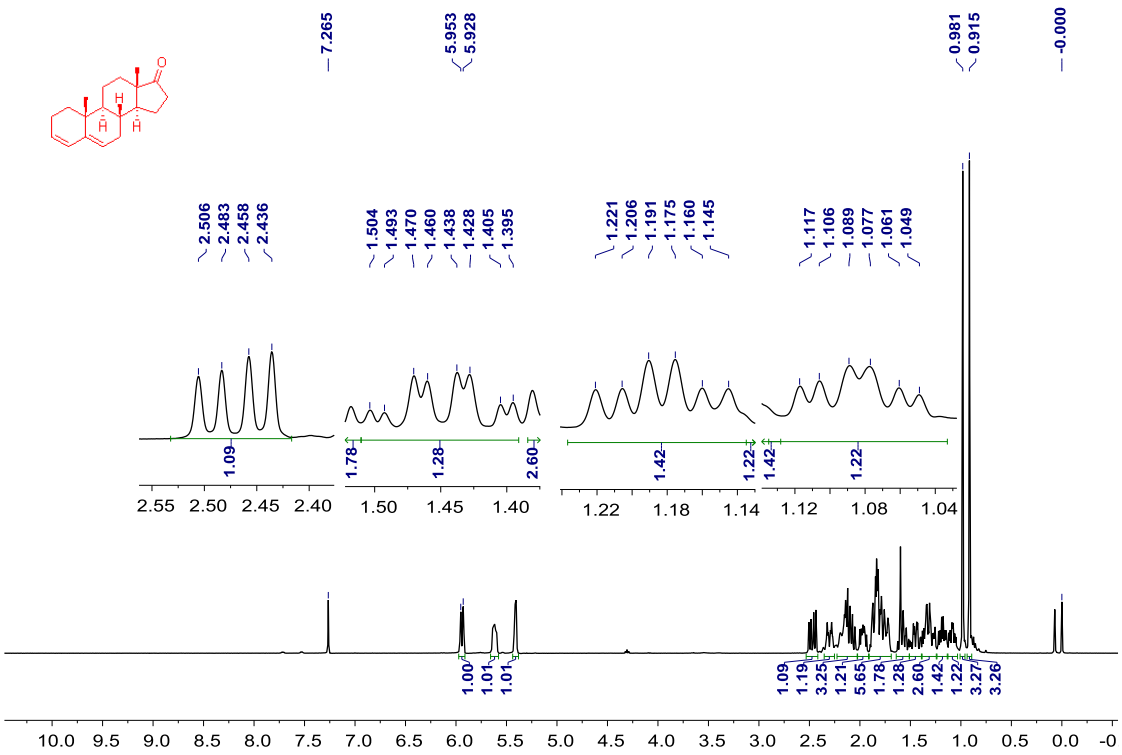


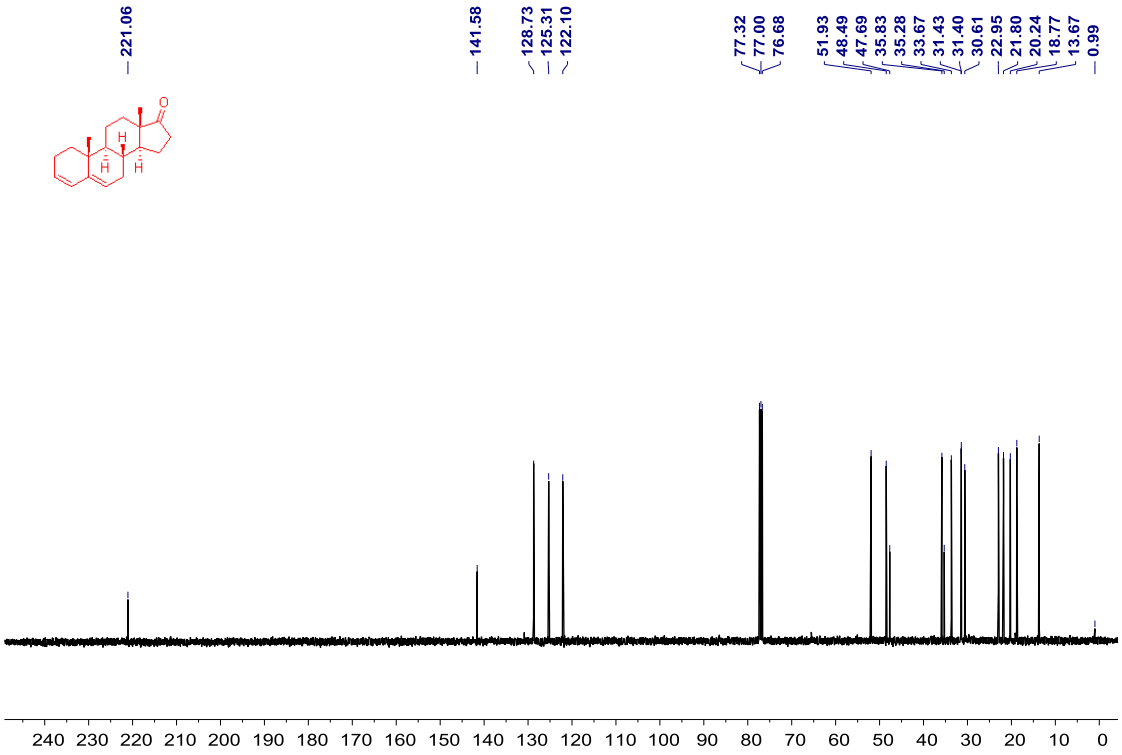
^{1}H and ^{13}C NMR spectra of 1f



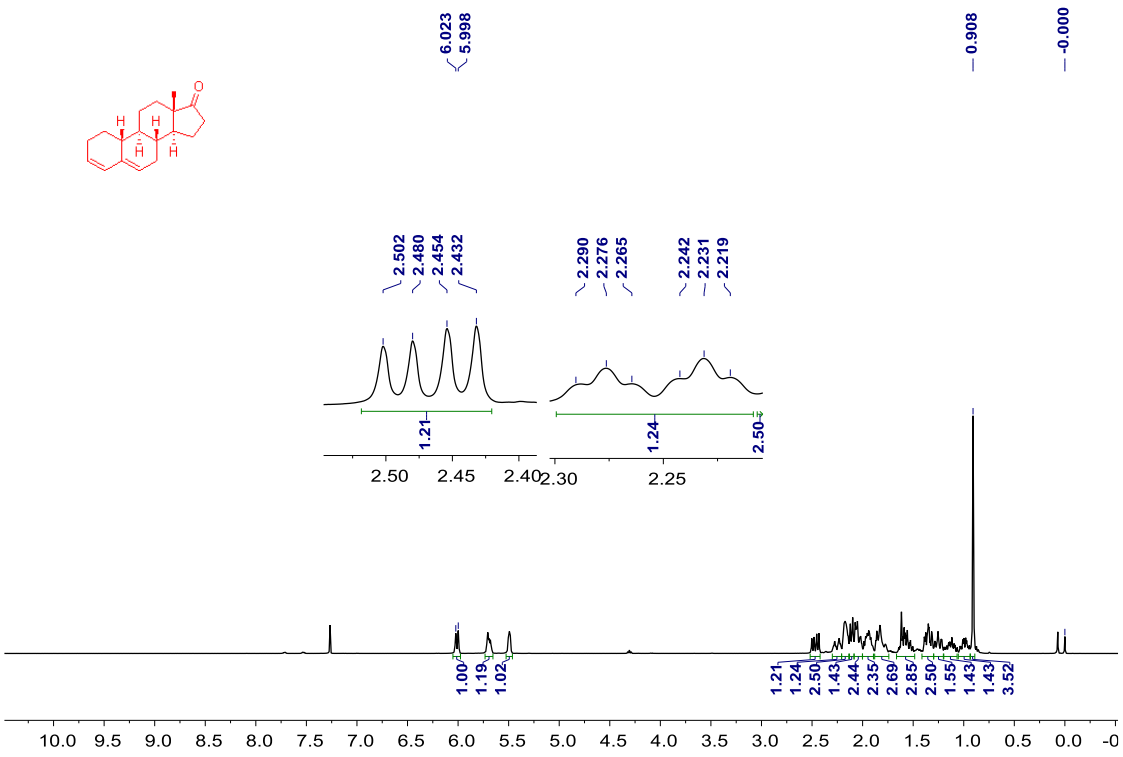


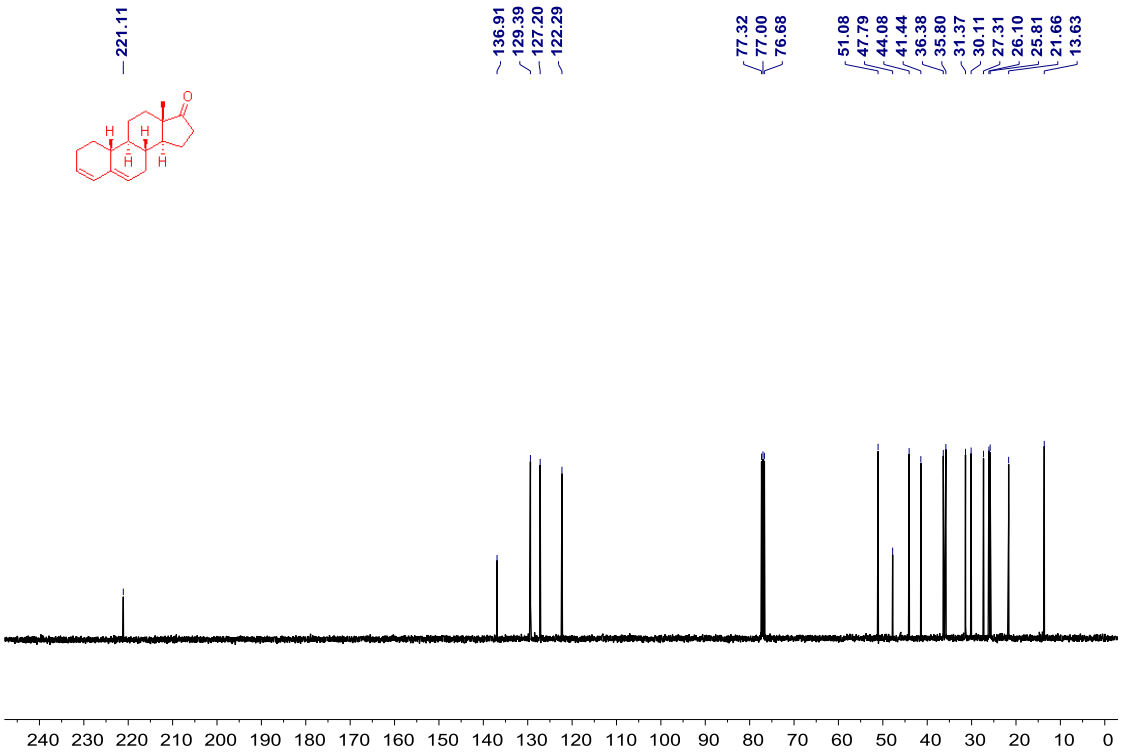
^{1}H and ^{13}C NMR spectra of 1h



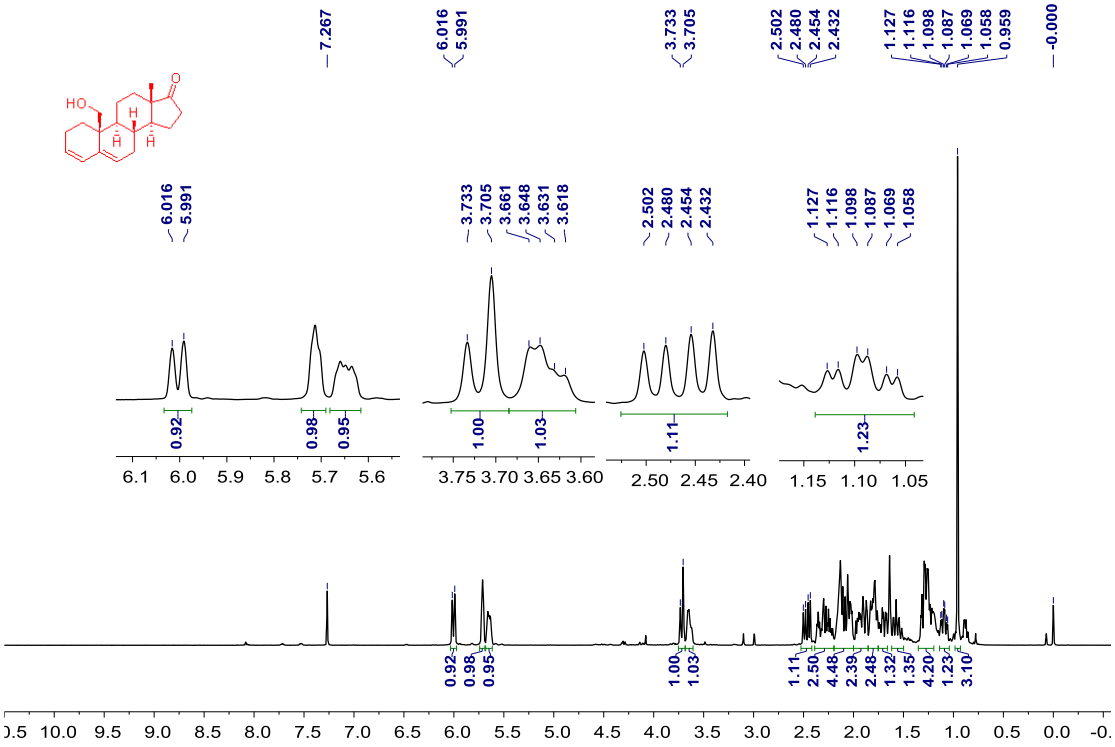


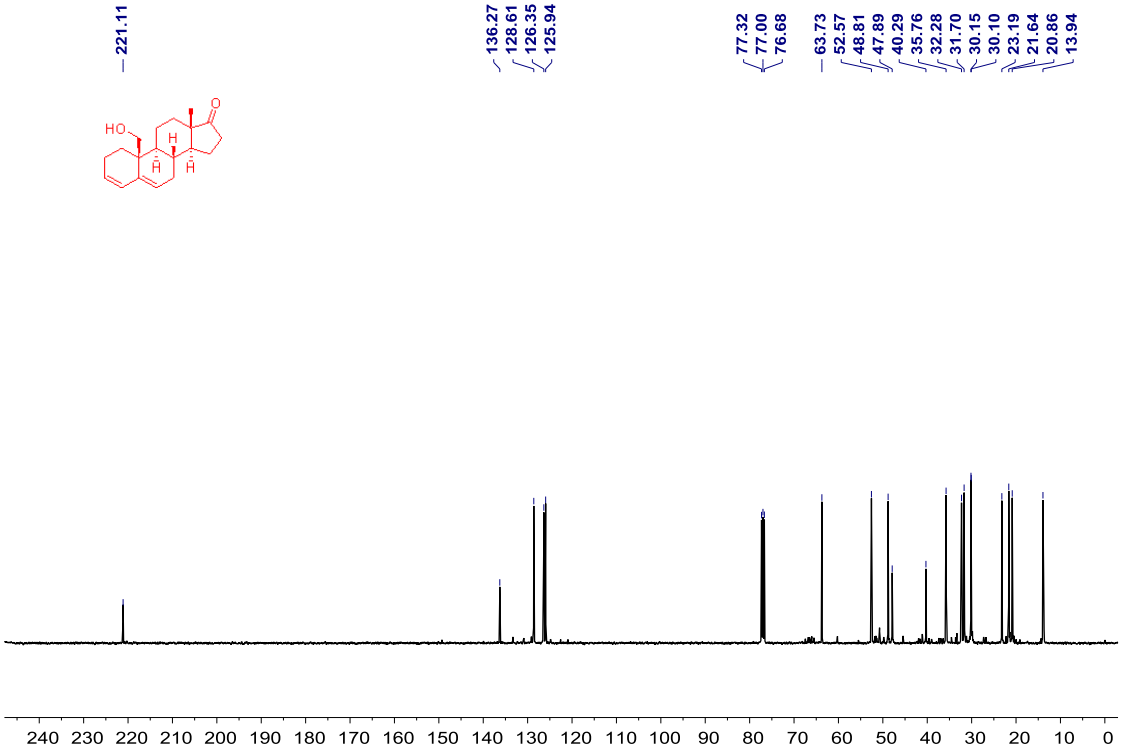
^{1}H and ^{13}C NMR spectra of 1i



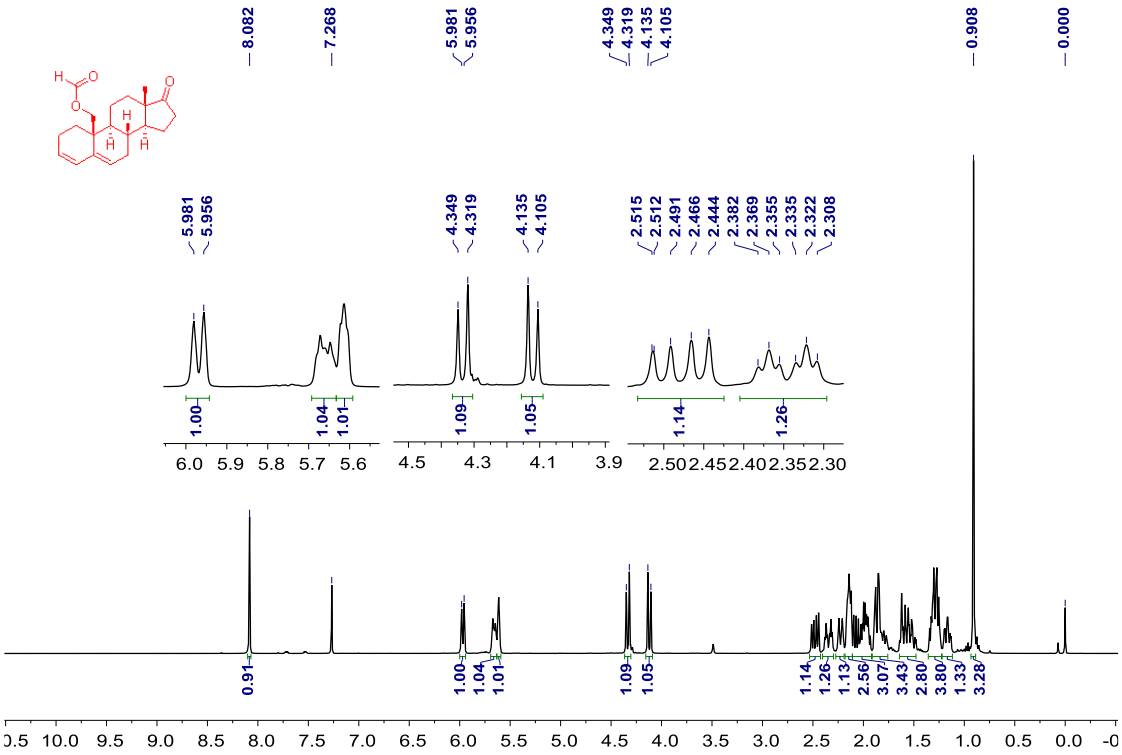


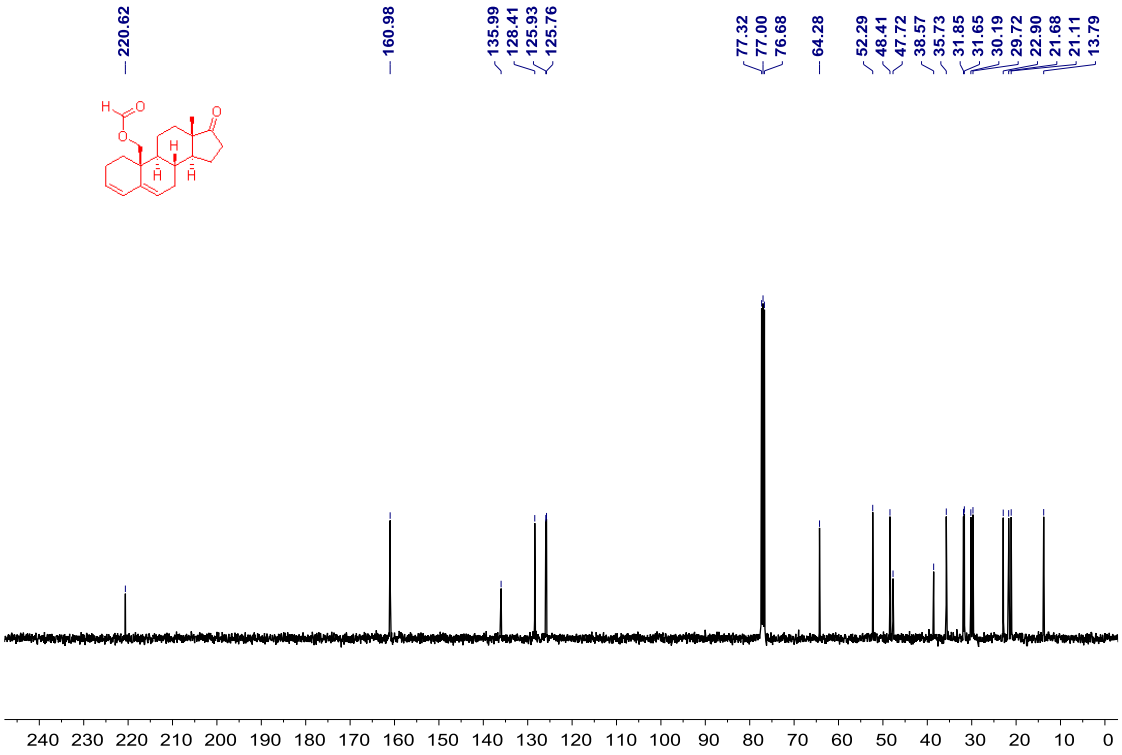
^{1}H and ^{13}C NMR spectra of 1j



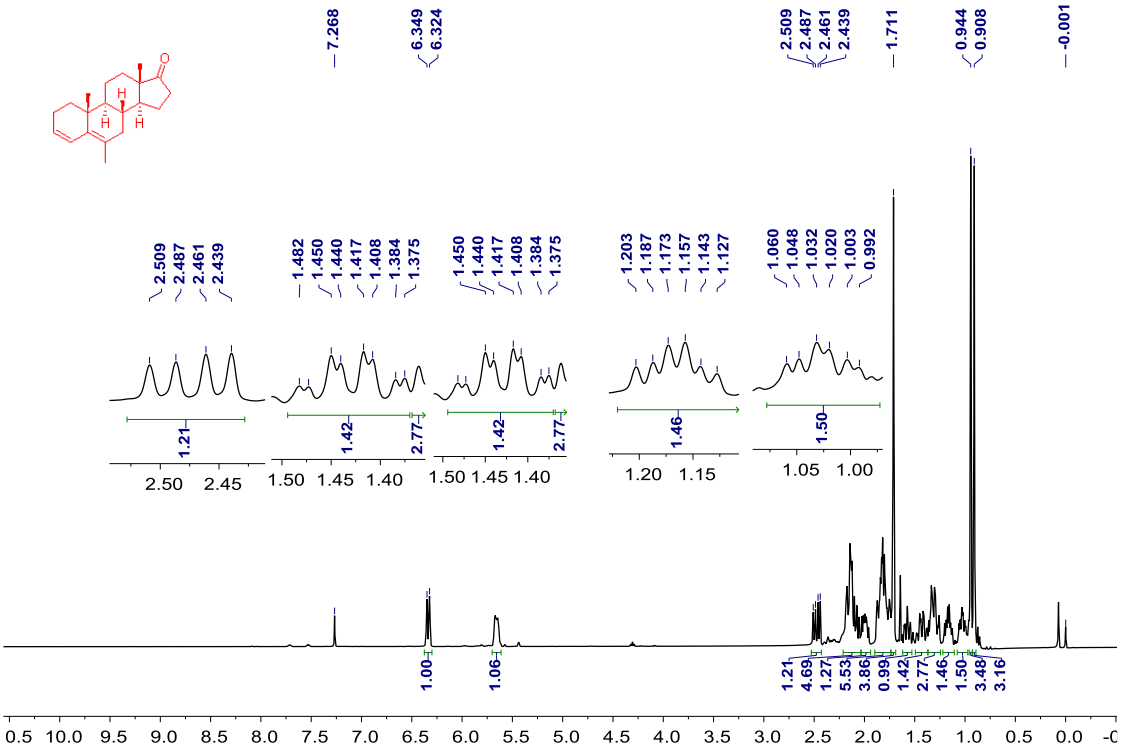


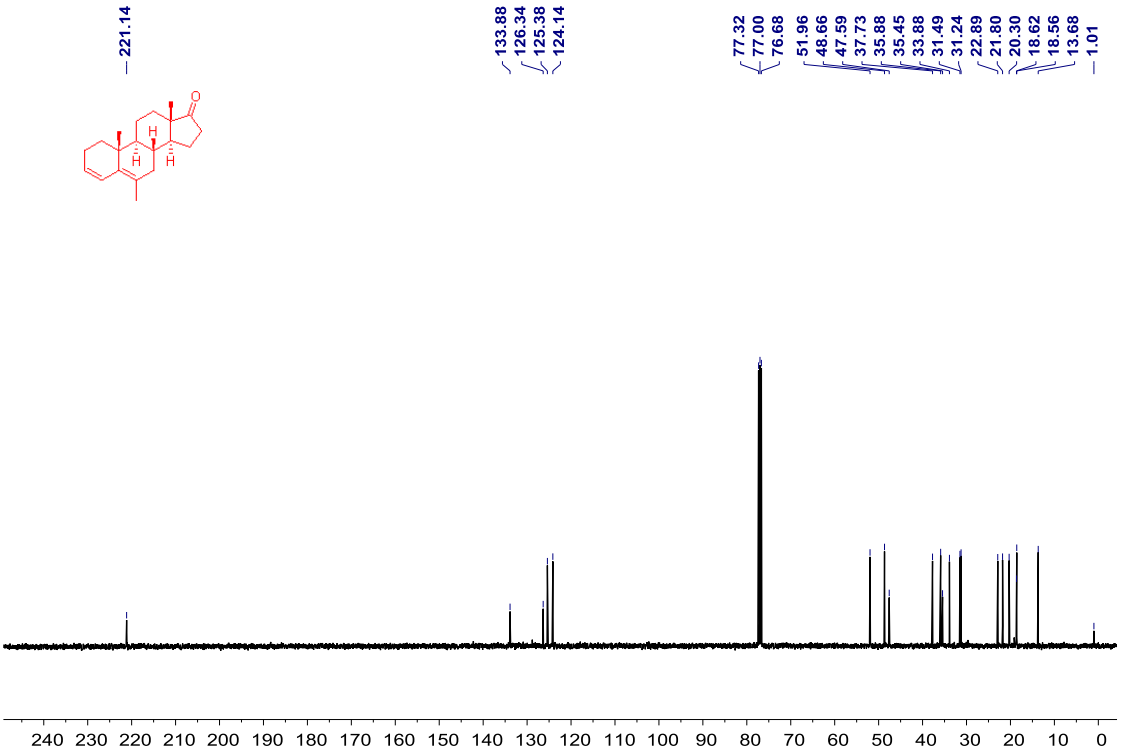
^{1}H and ^{13}C NMR spectra of 1j'



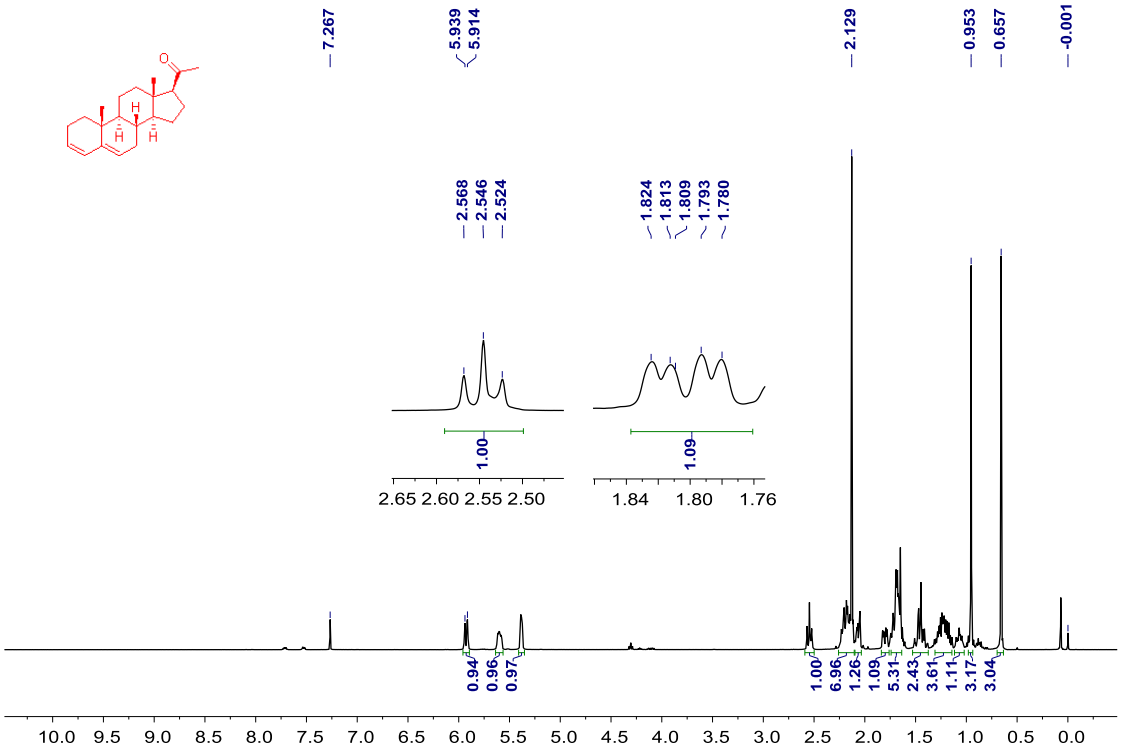


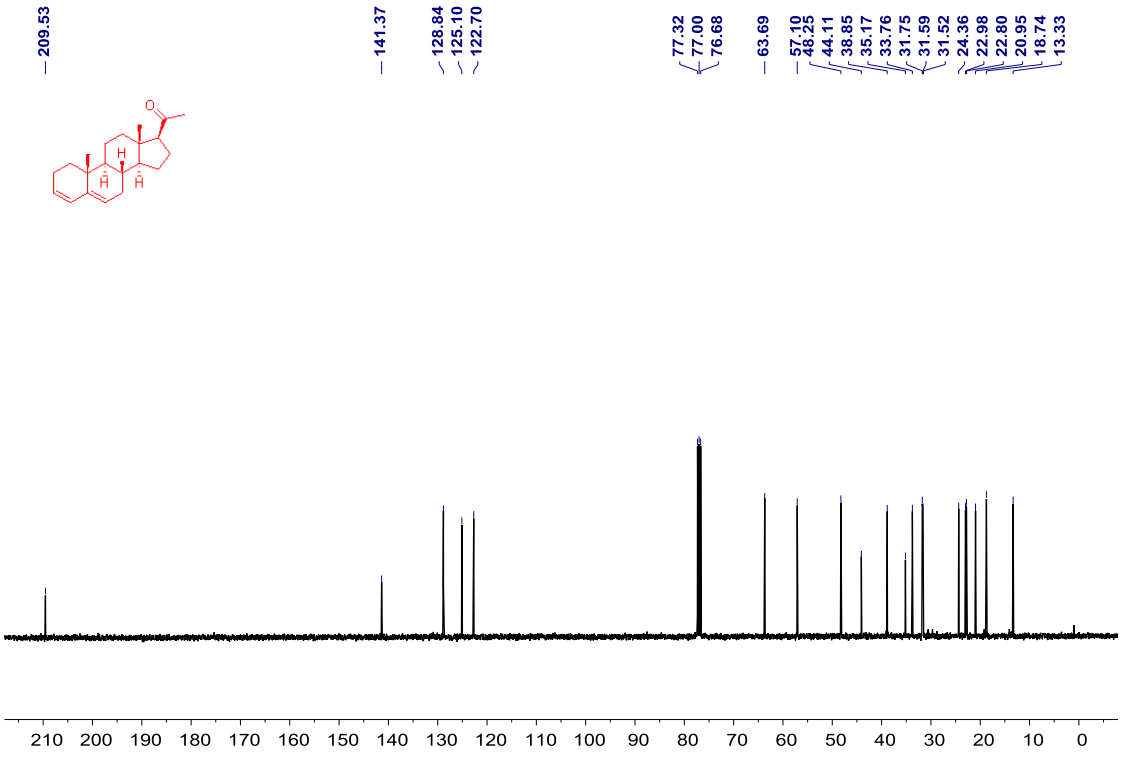
^{1}H and ^{13}C NMR spectra of 1k



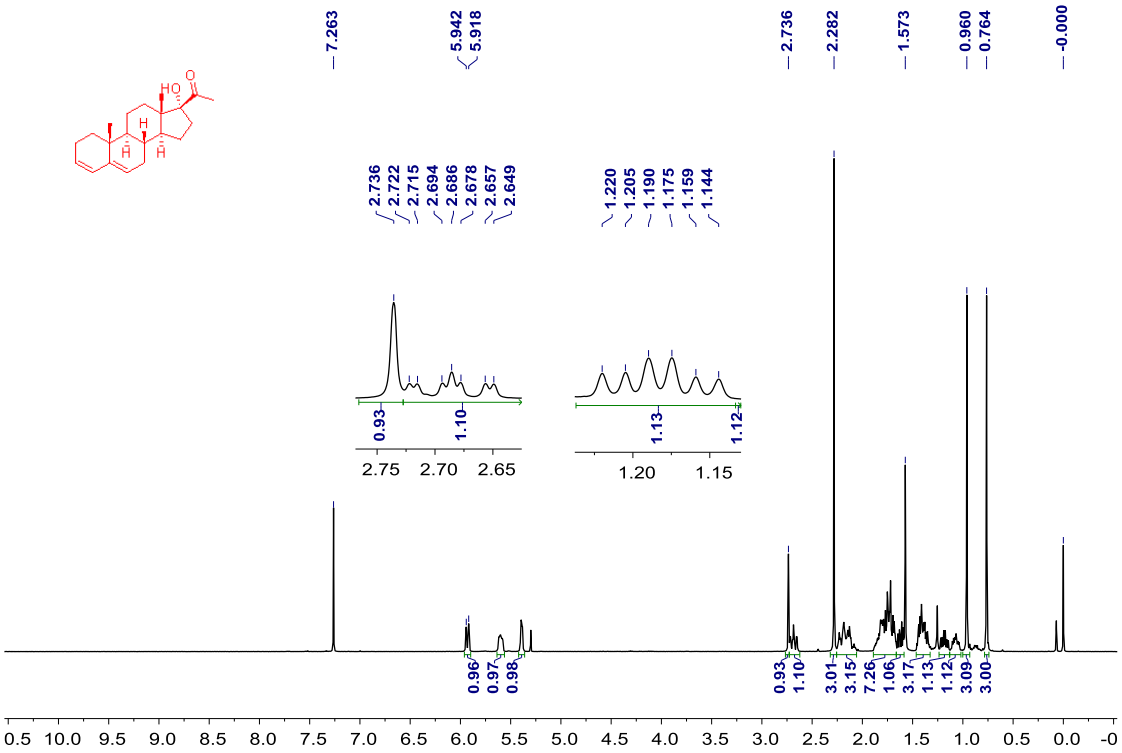


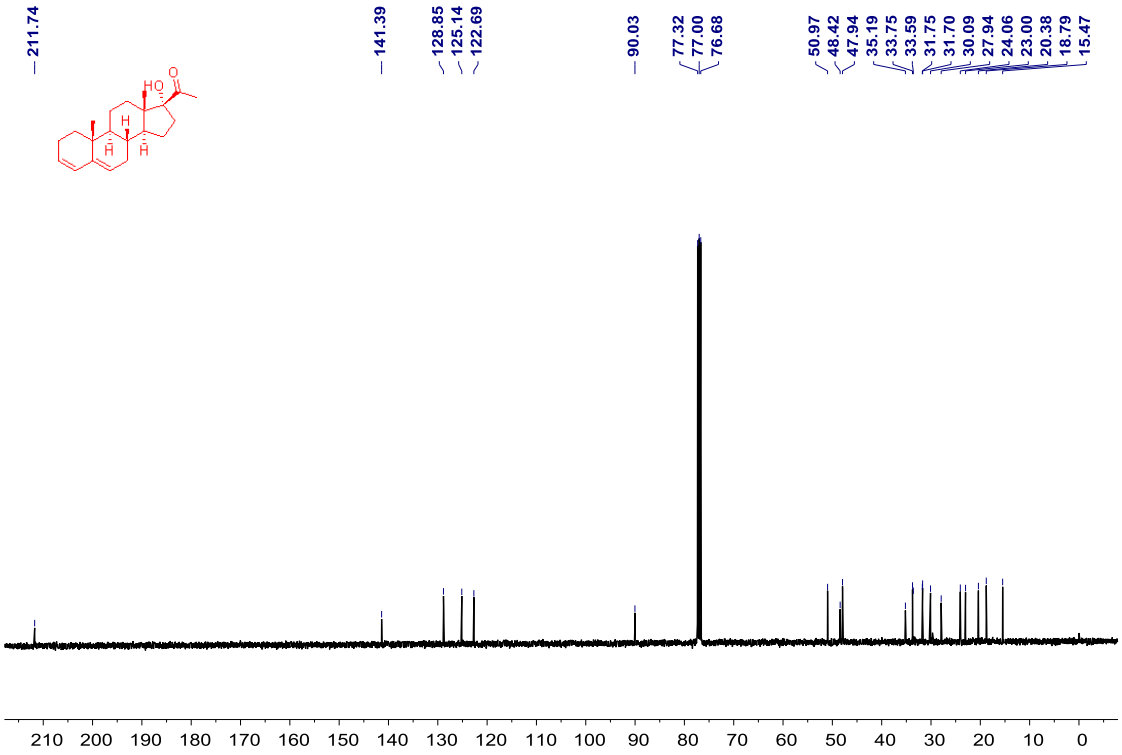
^{1}H and ^{13}C NMR spectra of 1l



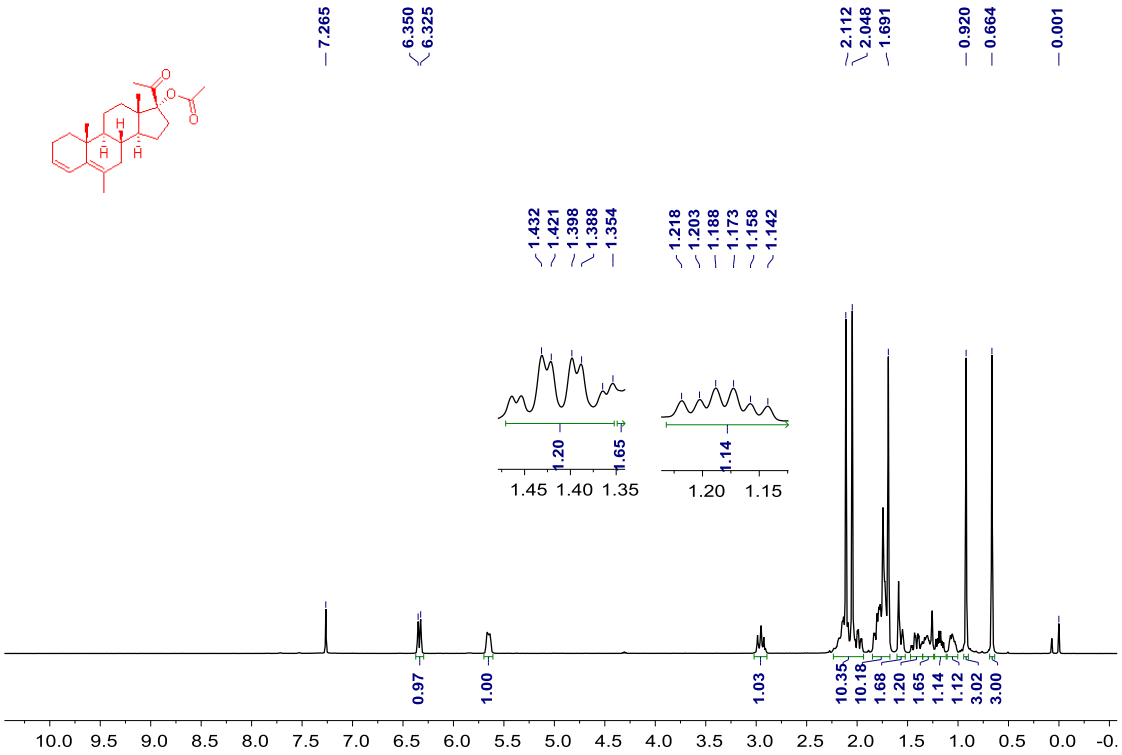


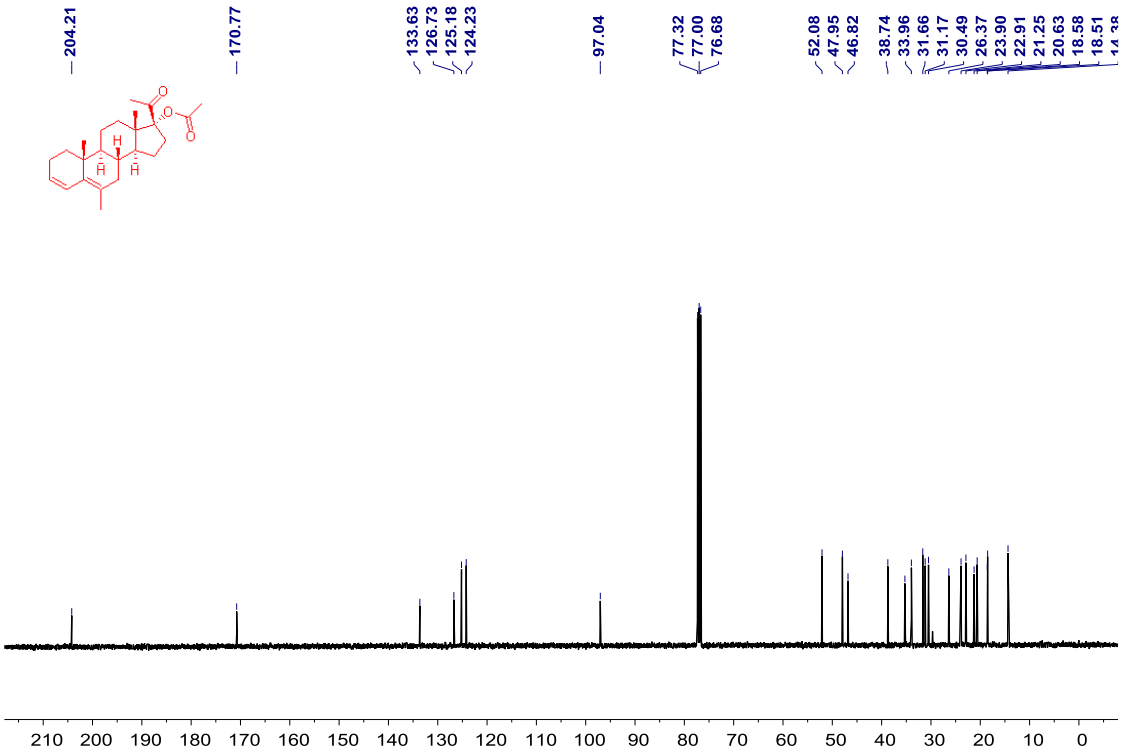
^{1}H and ^{13}C NMR spectra of 1m



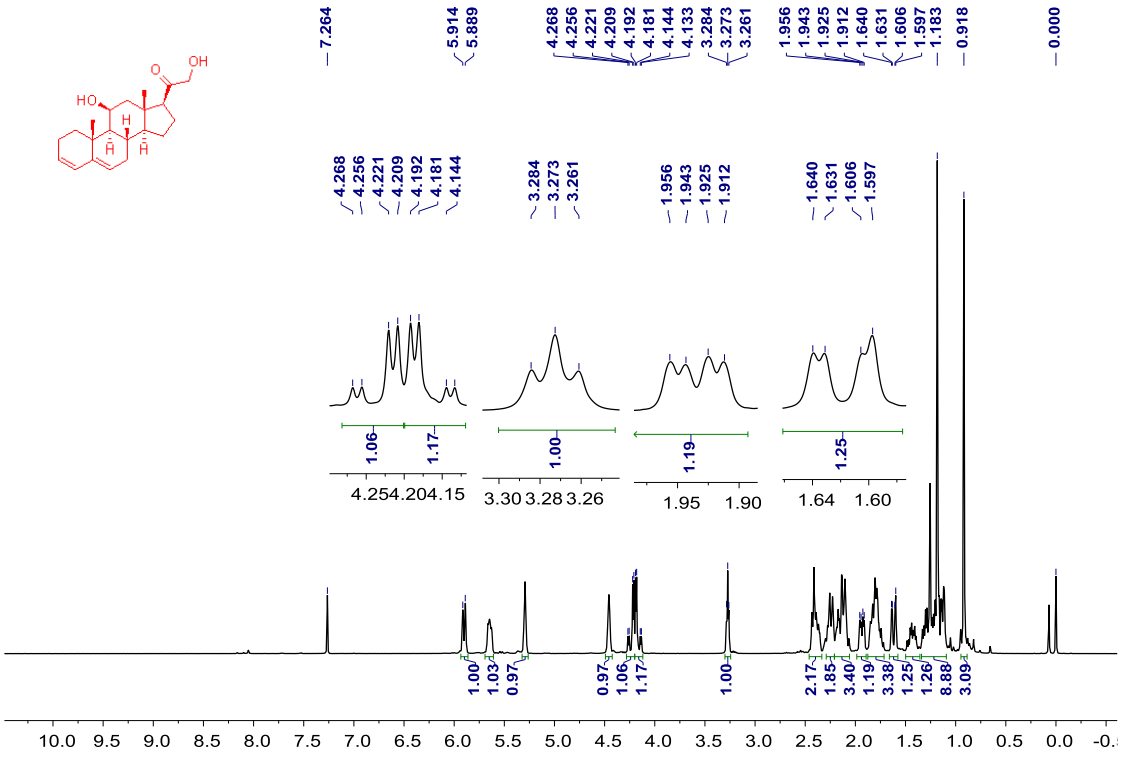


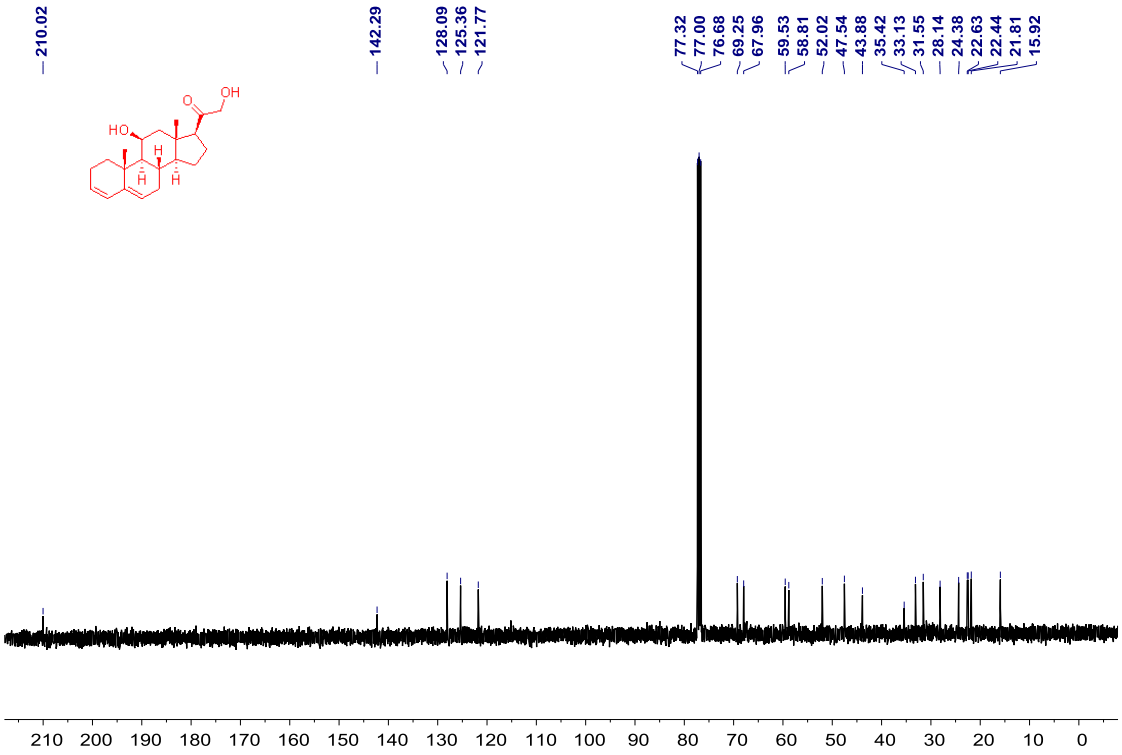
^{1}H and ^{13}C NMR spectra of 1n



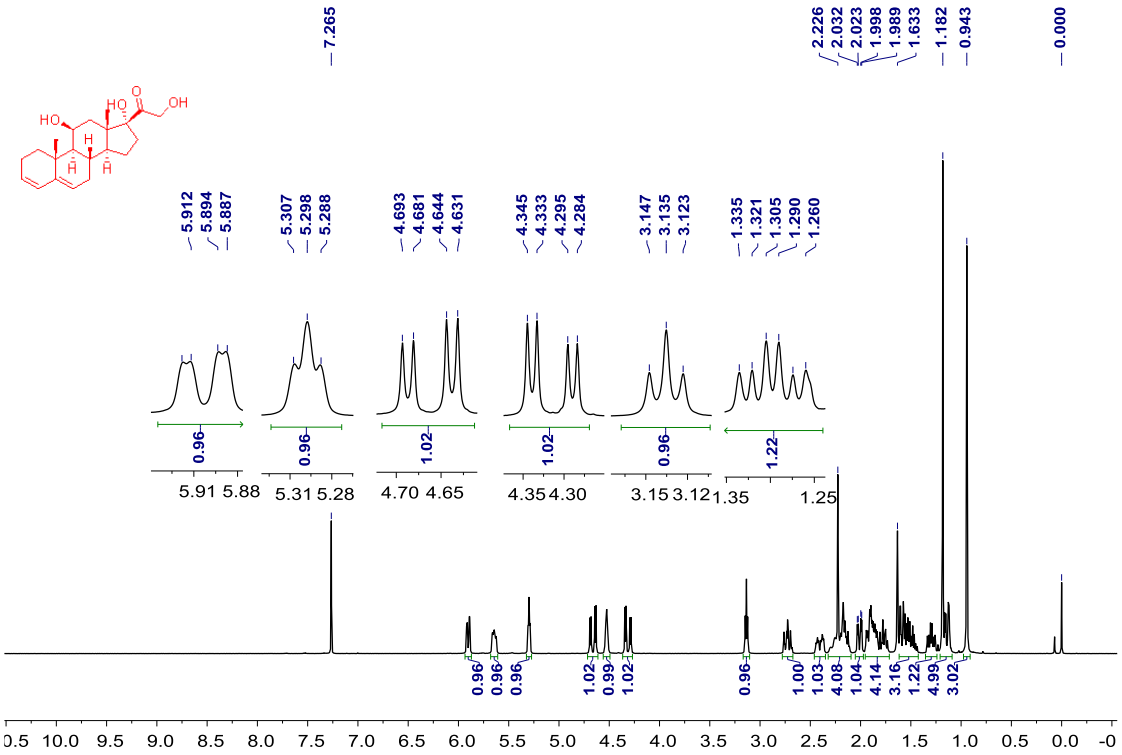


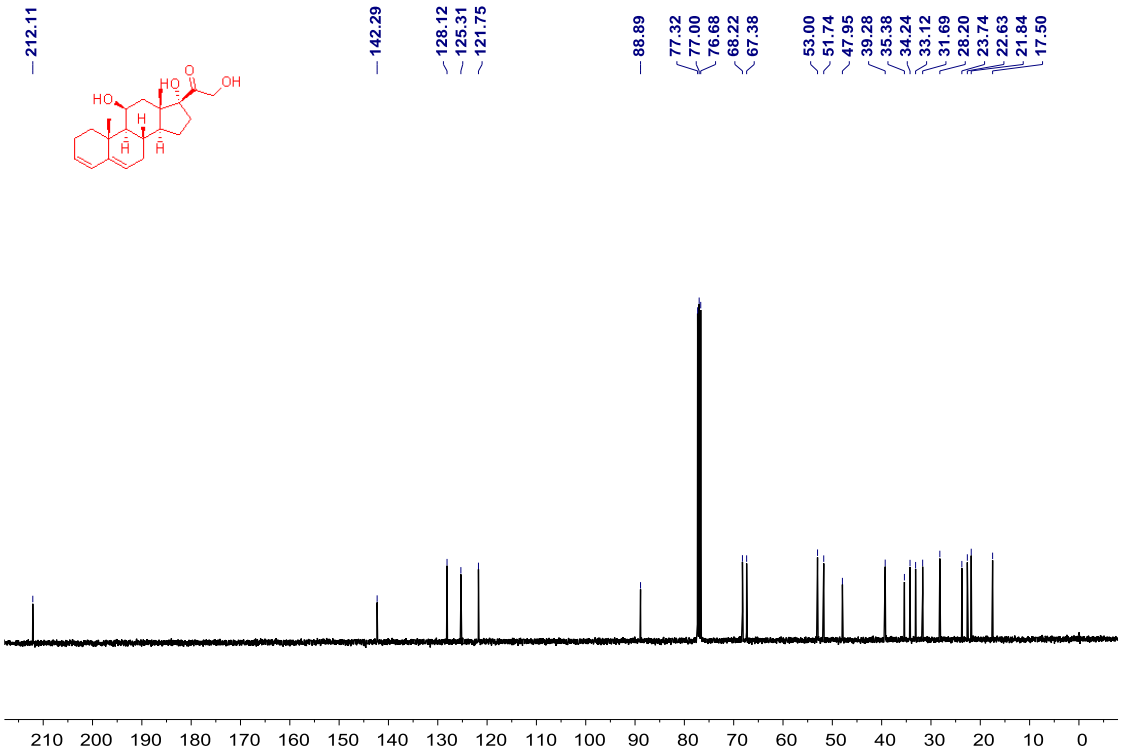
^{1}H and ^{13}C NMR spectra of 1o



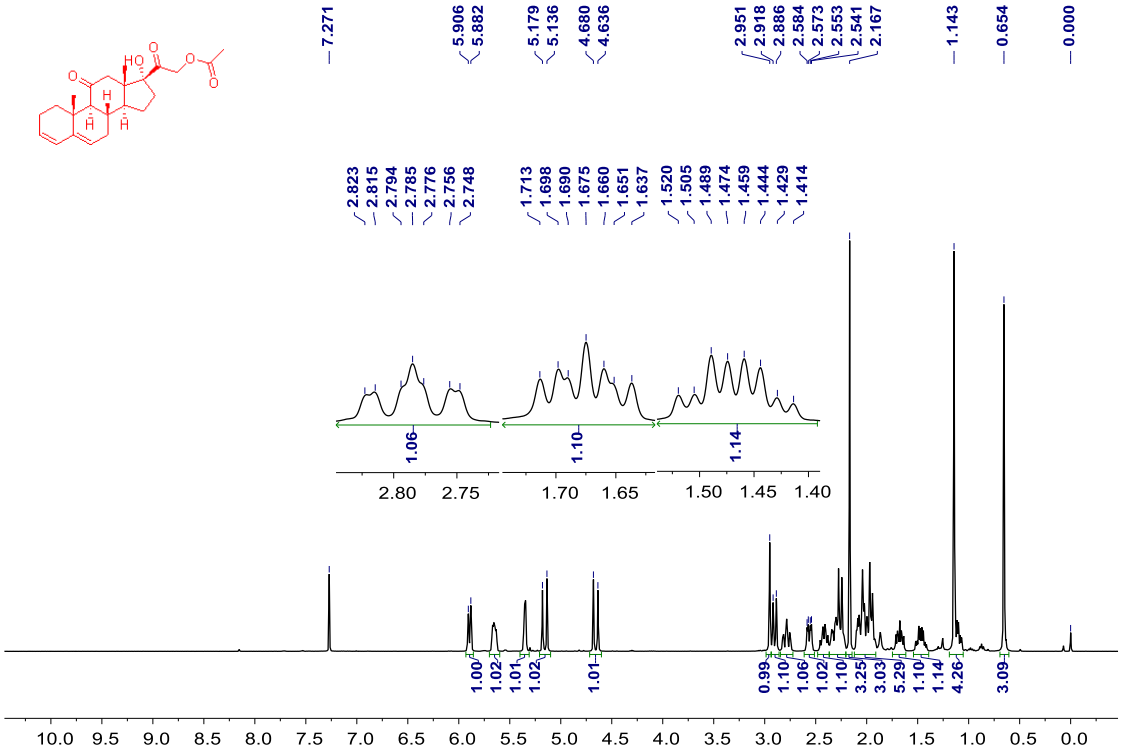


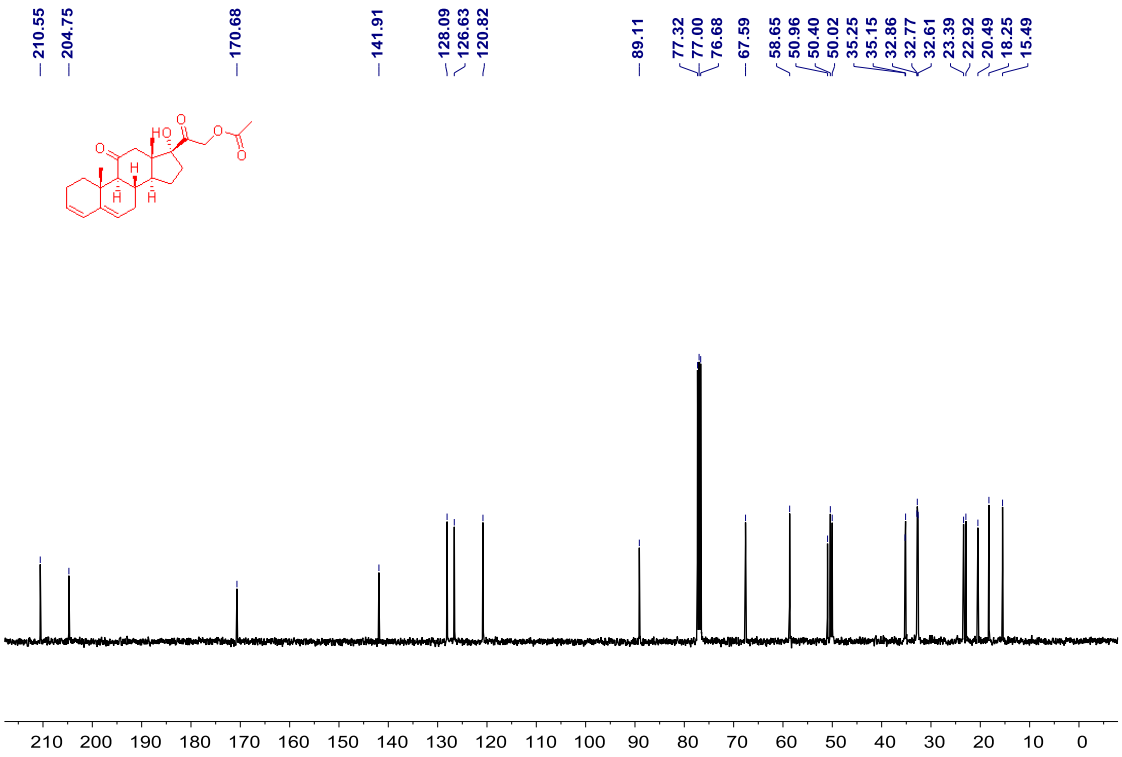
^{1}H and ^{13}C NMR spectra of 1p



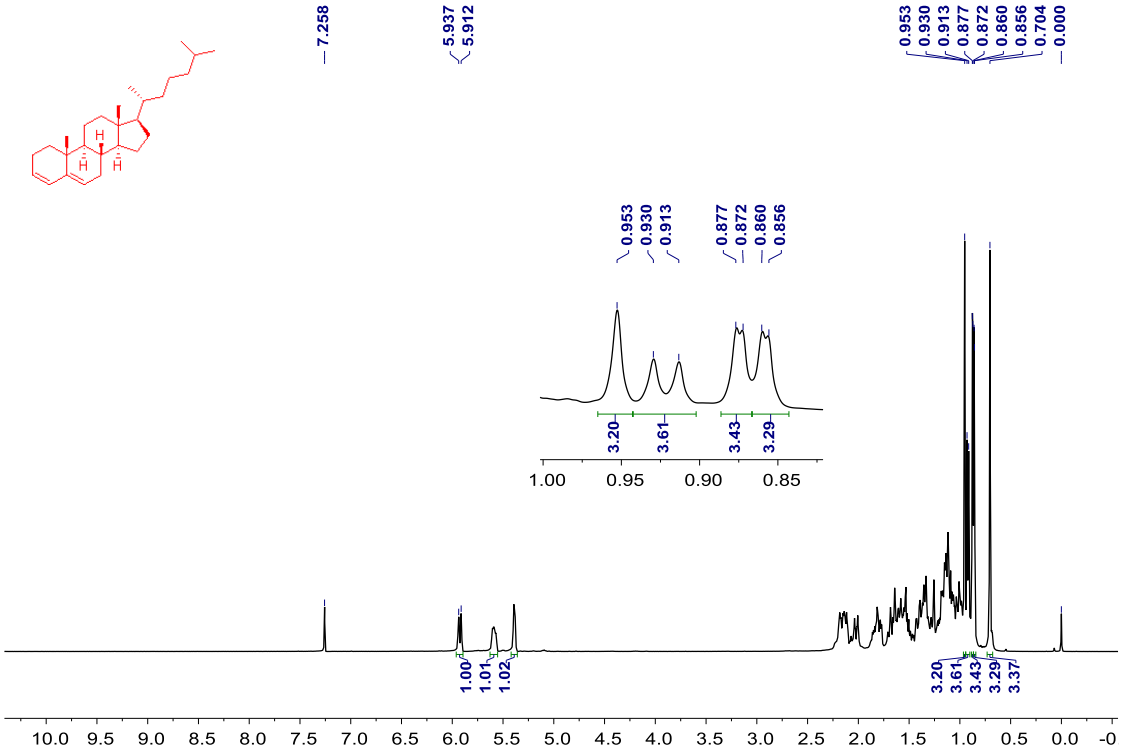


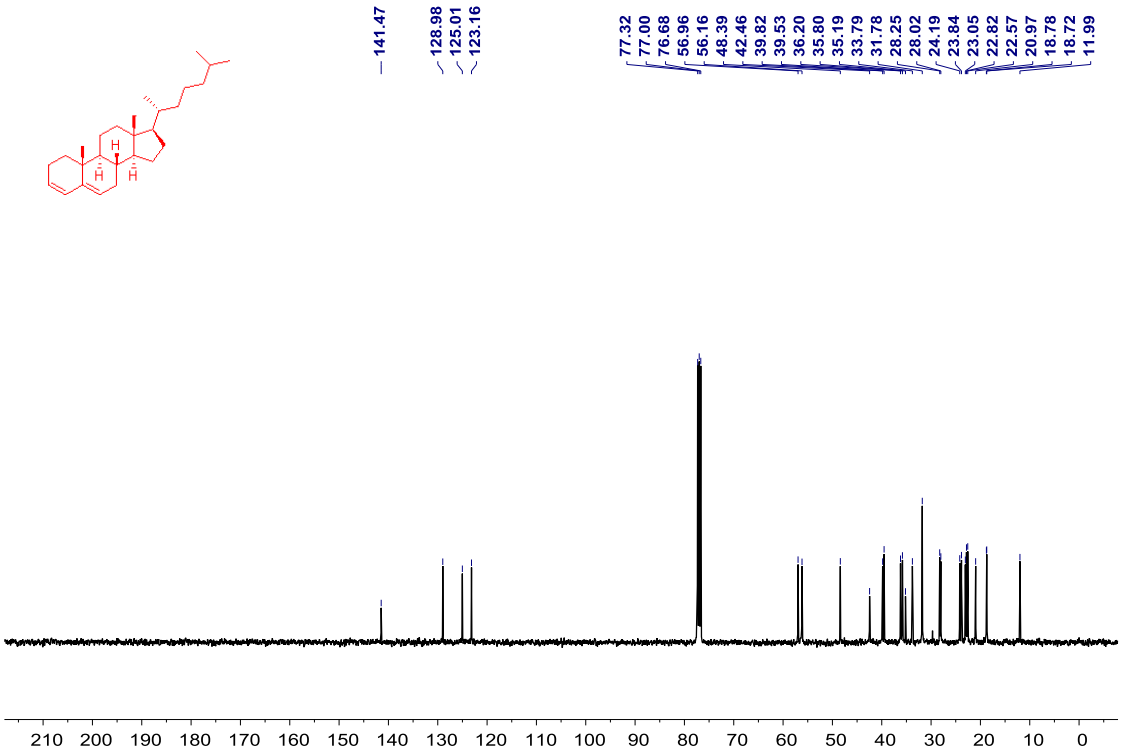
^{1}H and ^{13}C NMR spectra of 1q



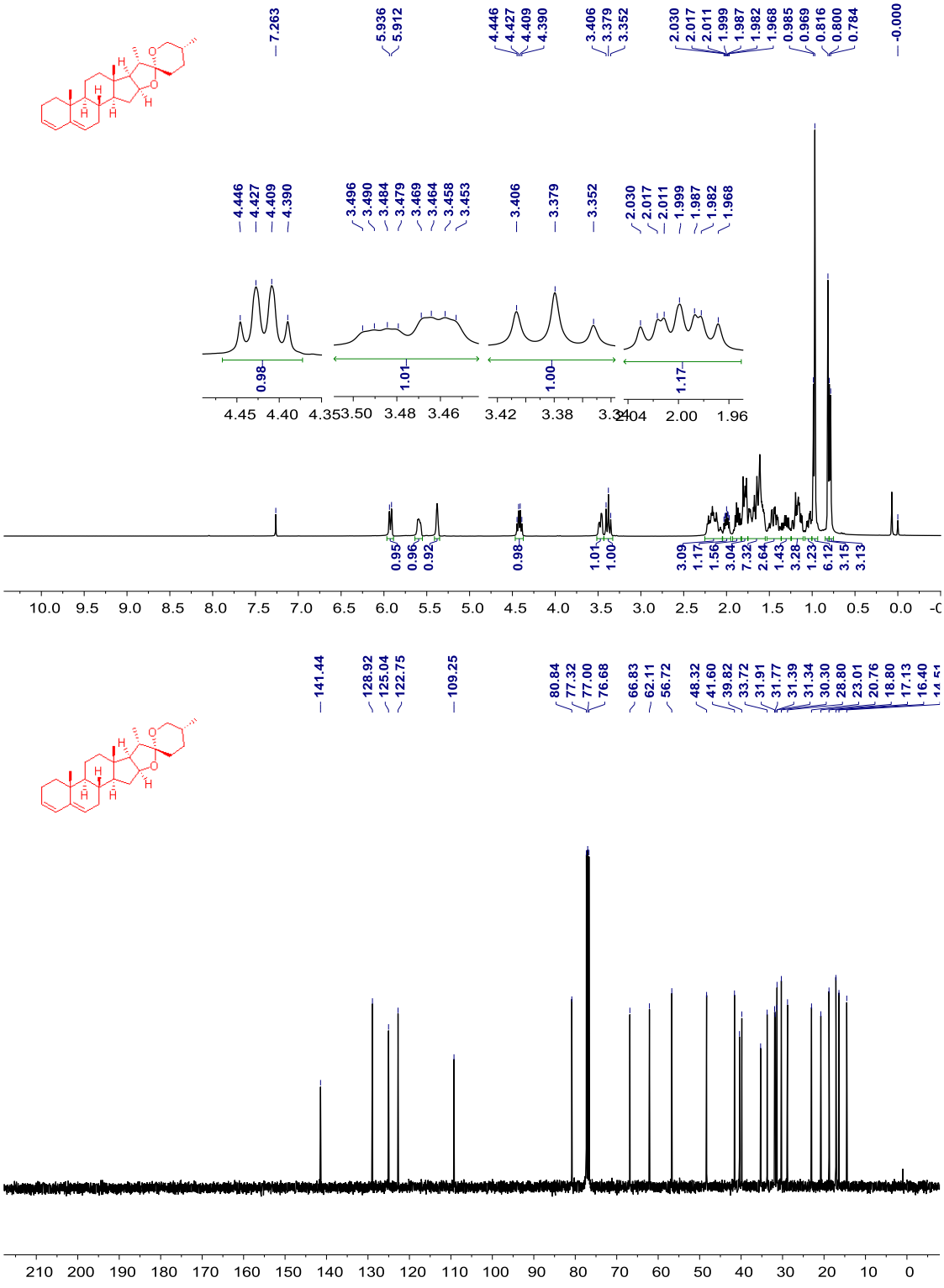


^{1}H and ^{13}C NMR spectra of 1r

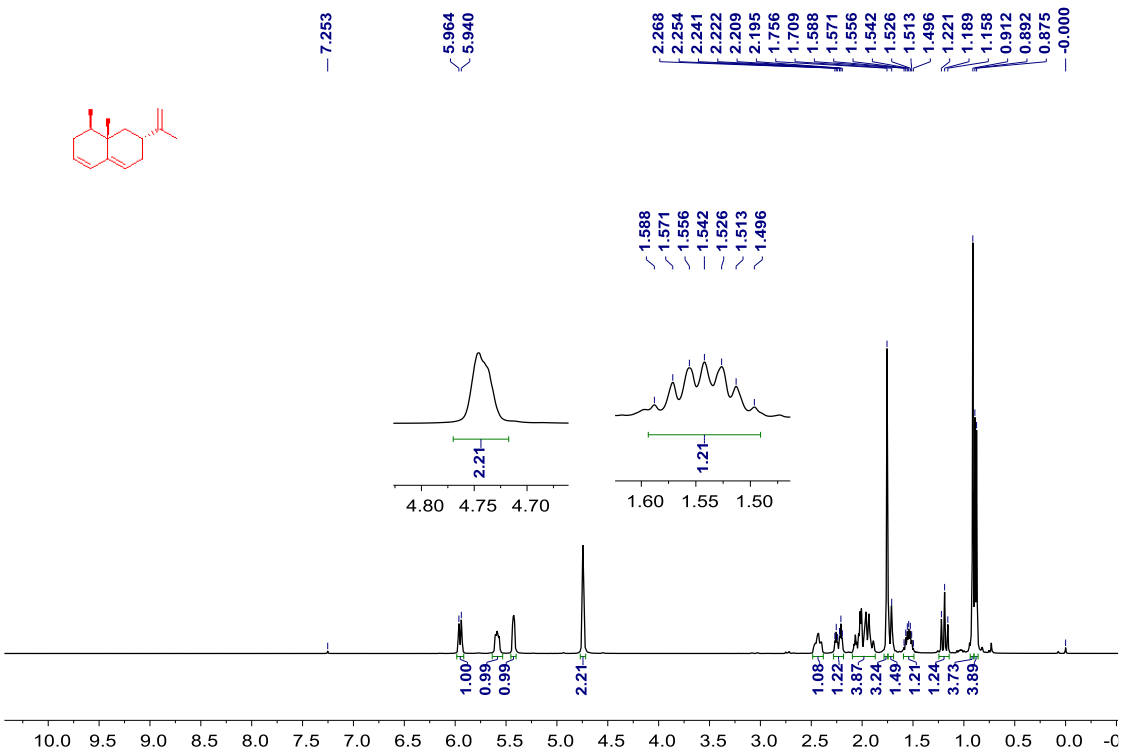


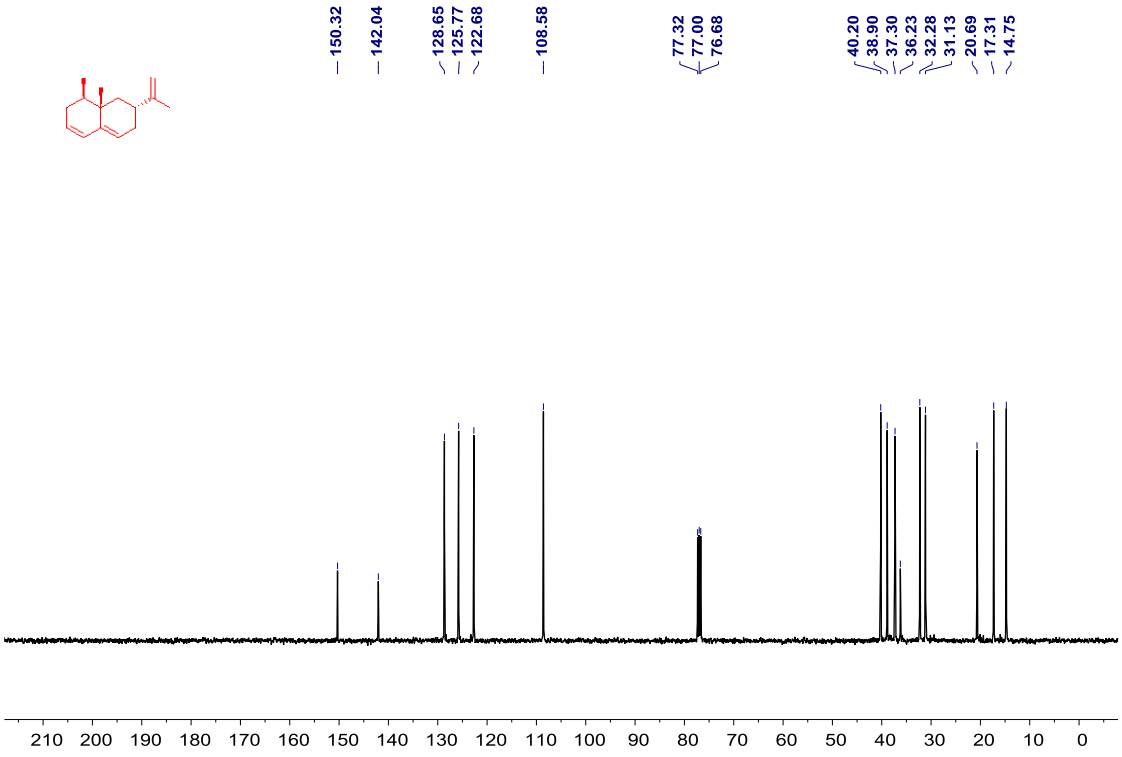


^{1}H and ^{13}C NMR spectra of 1s

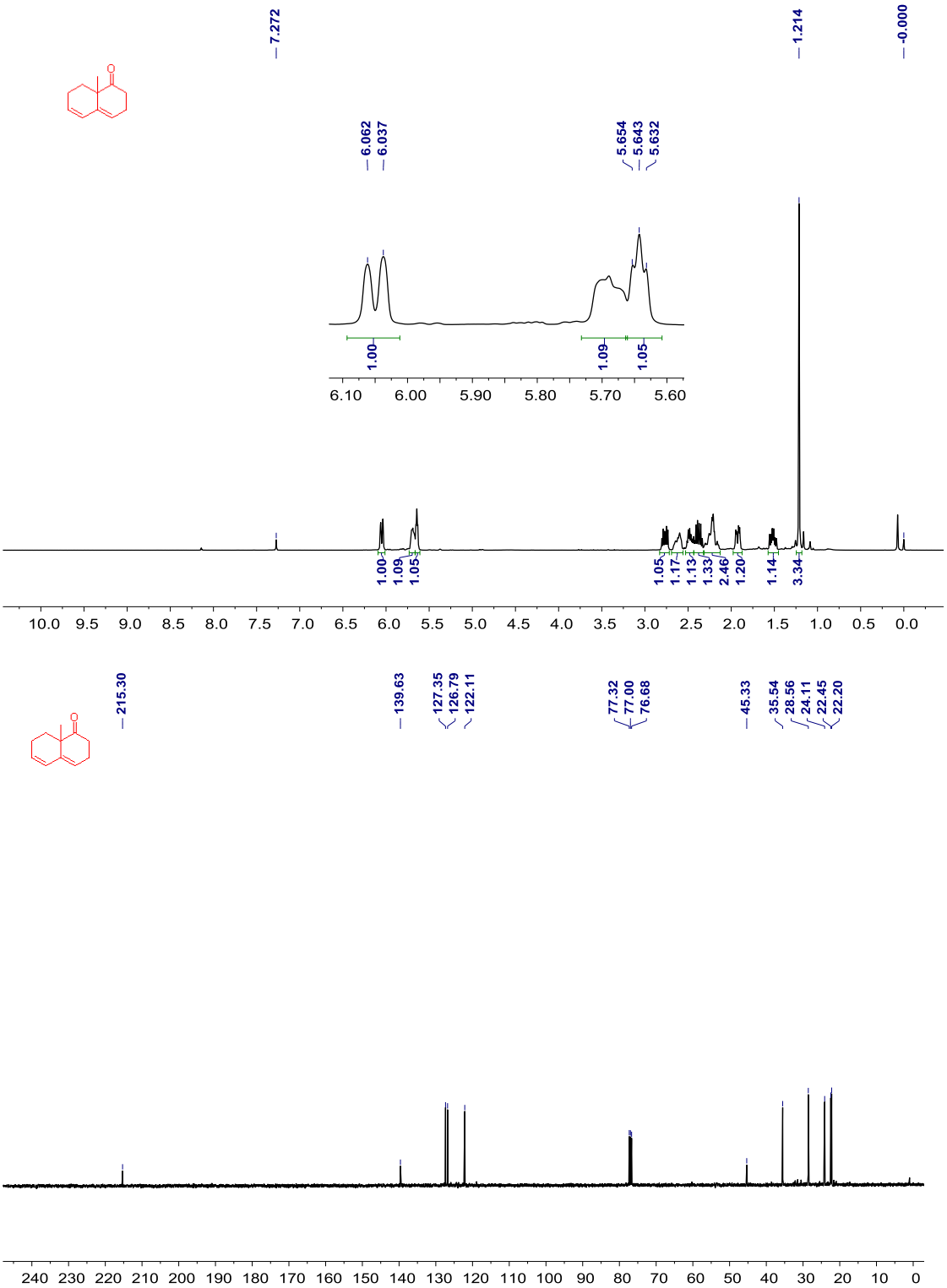


^{1}H and ^{13}C NMR spectra of 8a

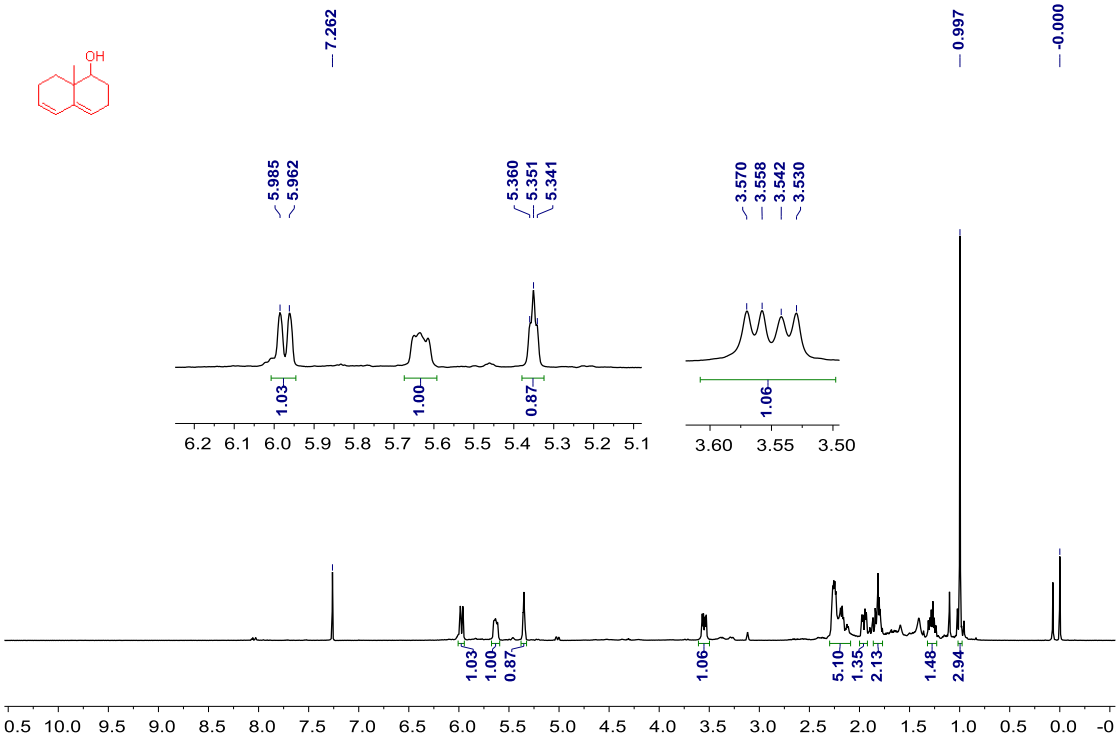


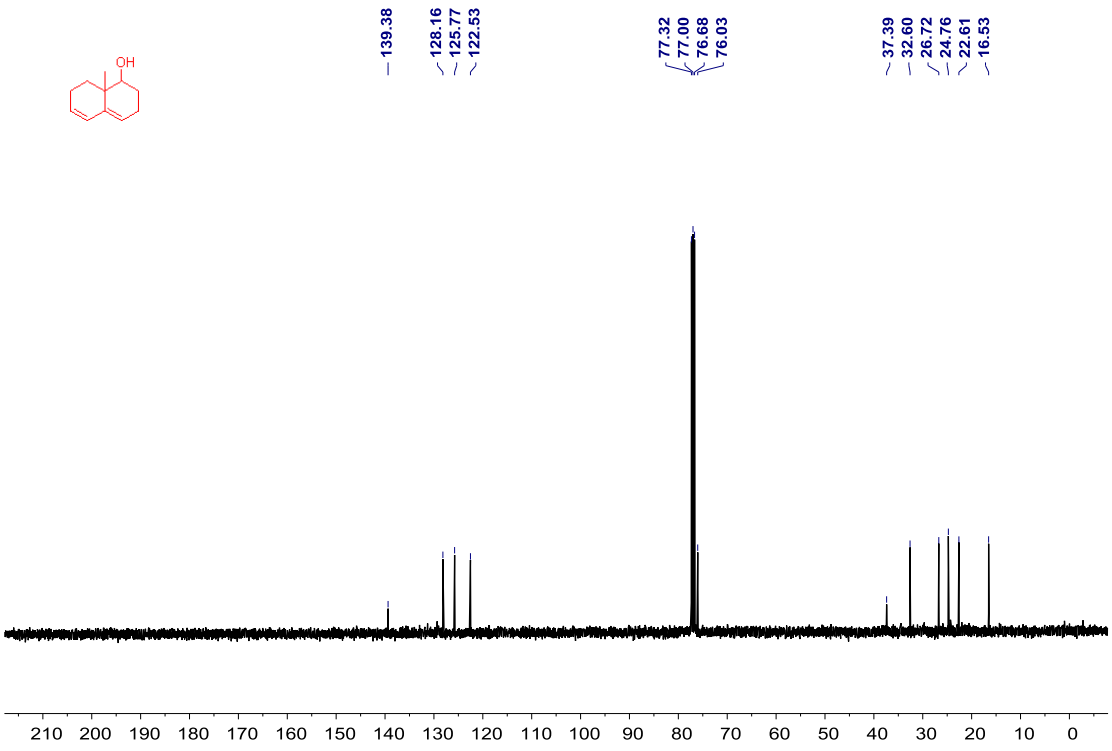


^{1}H and ^{13}C NMR spectra of 8b



^{1}H and ^{13}C NMR spectra of 9b

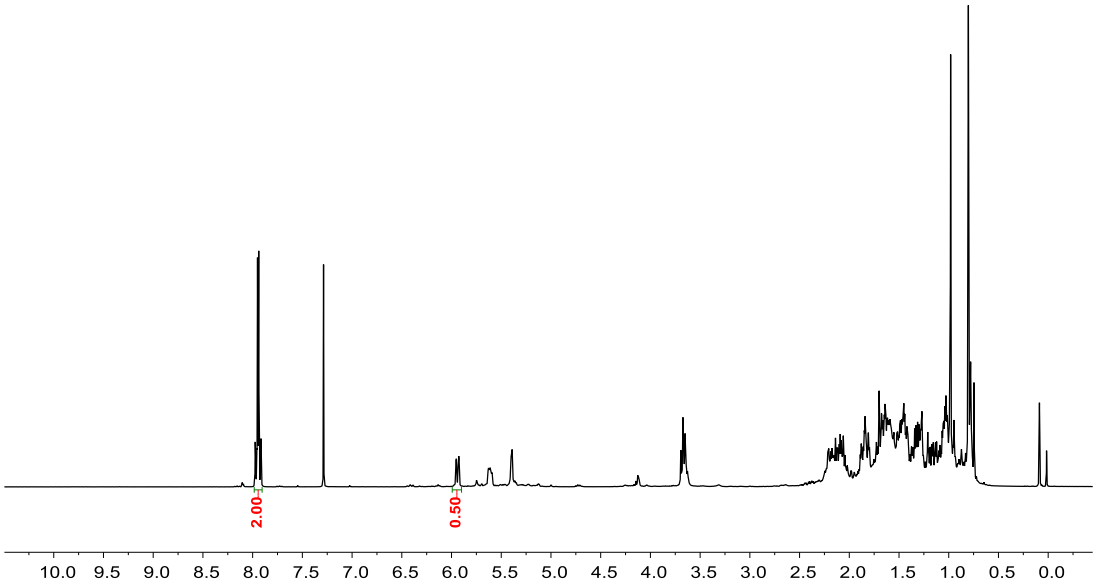




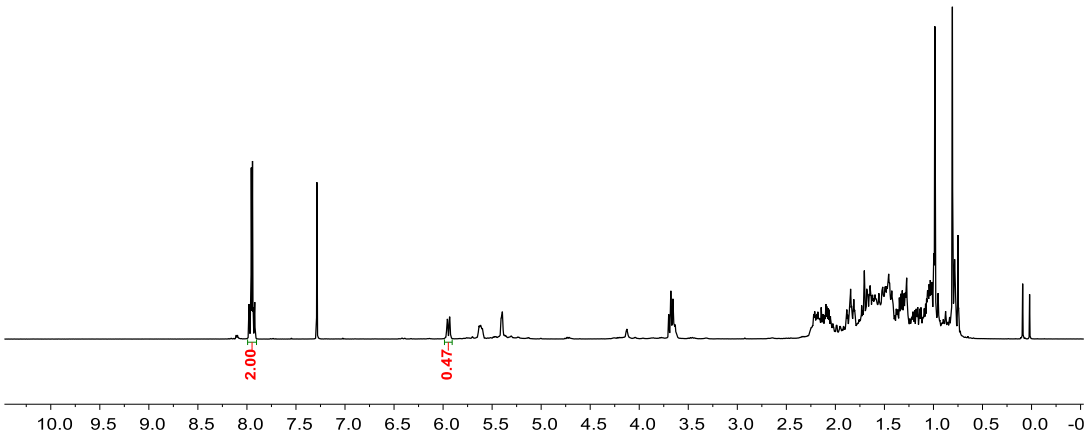
15. Copies of ^{1}H NMR spectra of crude mixtures in optimization of reaction conditions

^{1}H NMR spectra of optimization of catalyst type

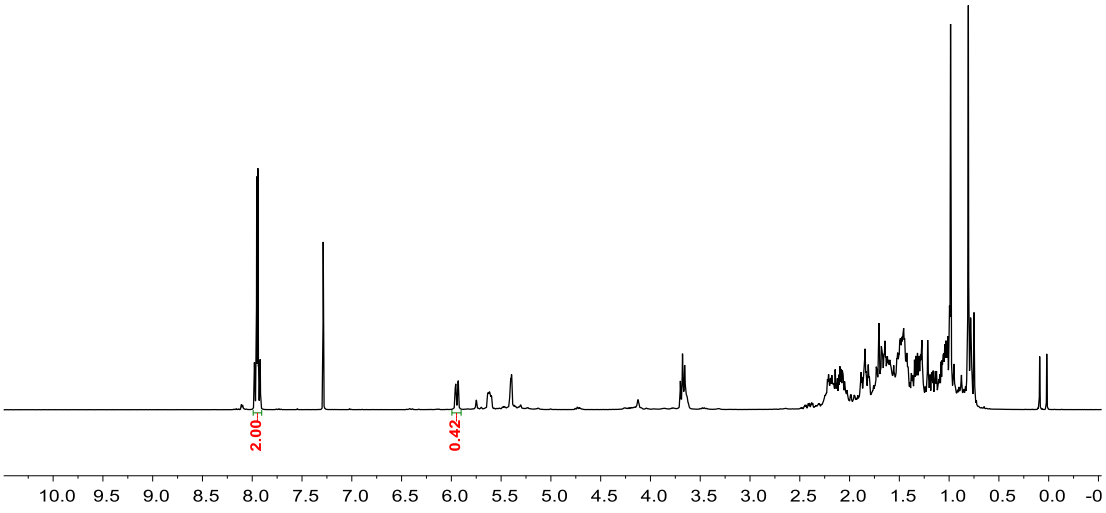
TC−1



TC−2



TC−3


2.00
0.42
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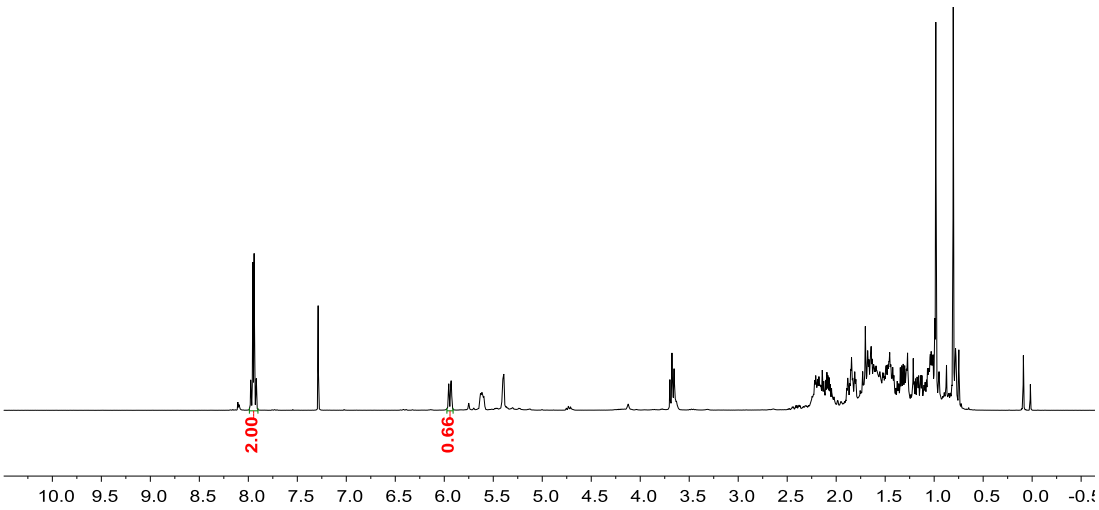
TC−4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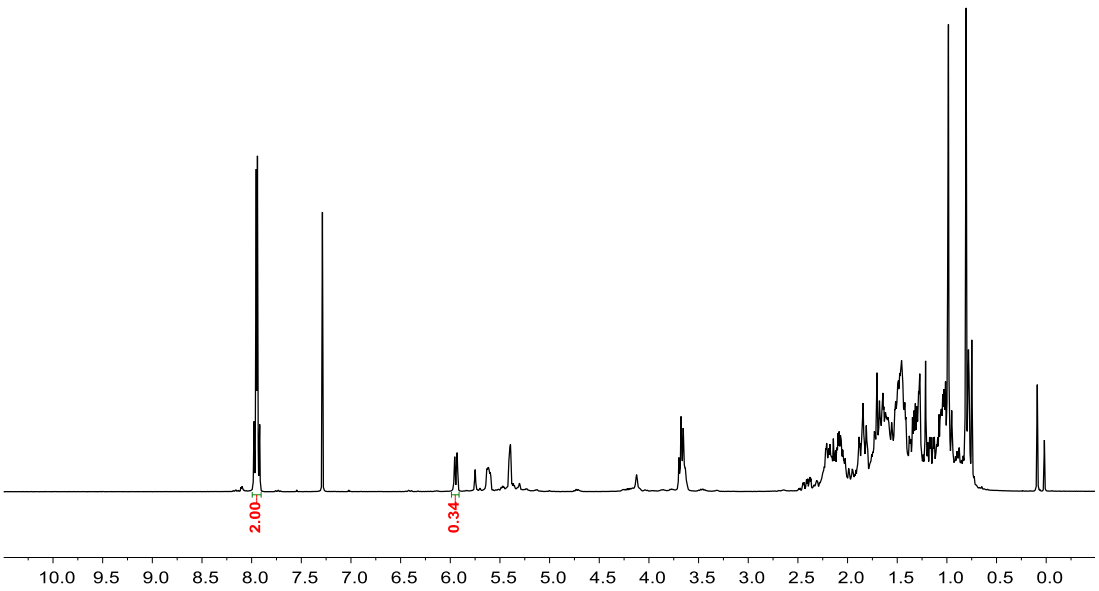
TC−5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0.34
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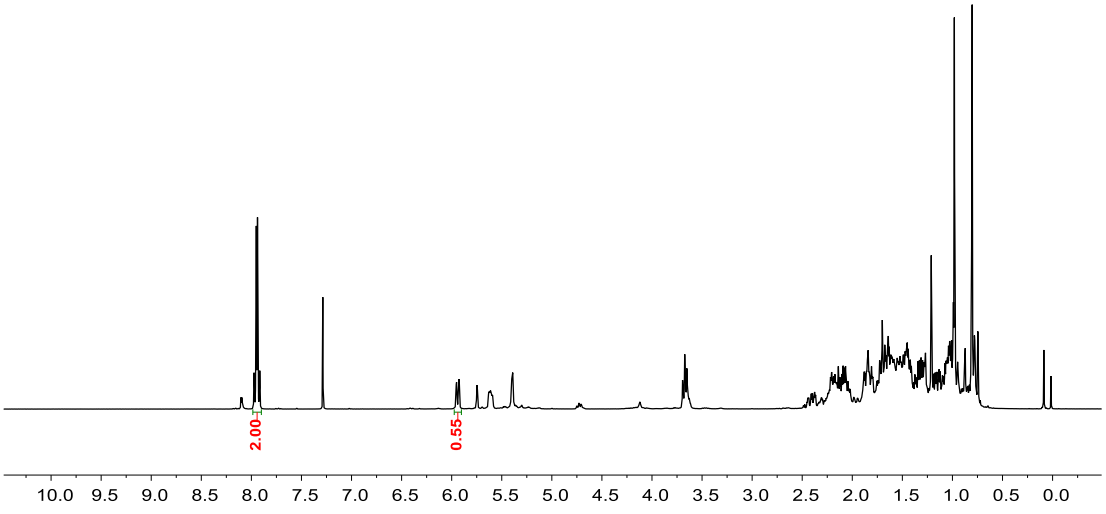
TC−6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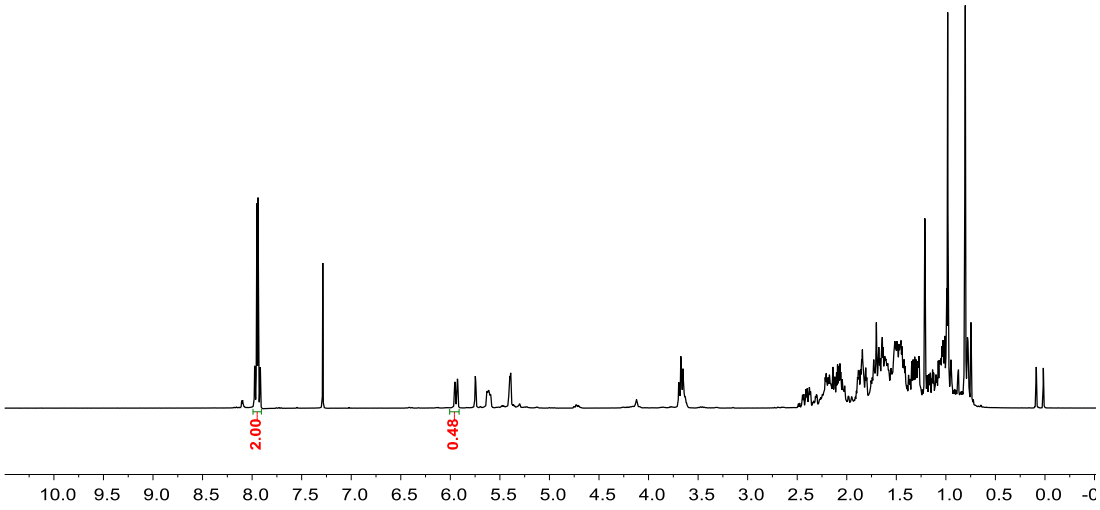
TC−7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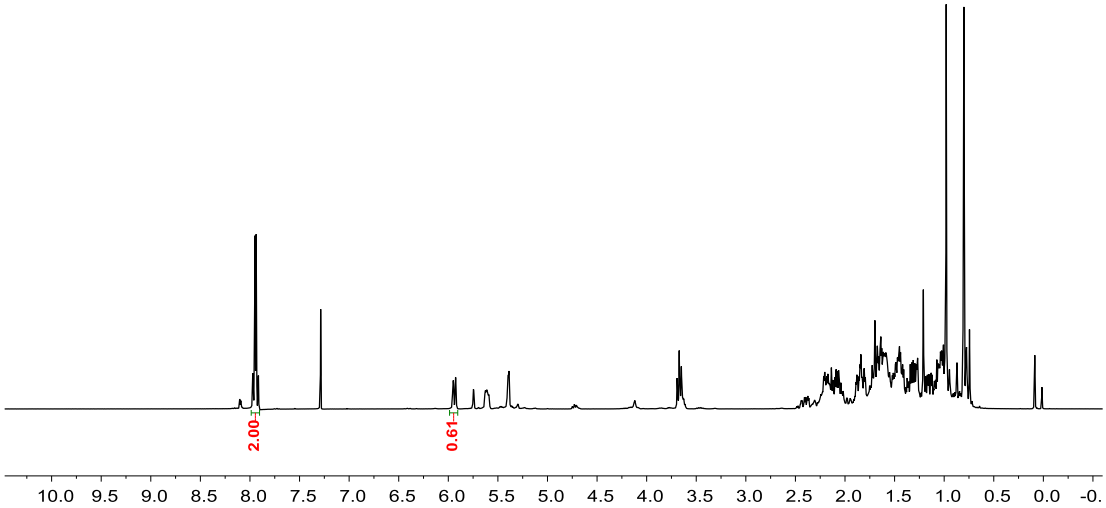
TC−8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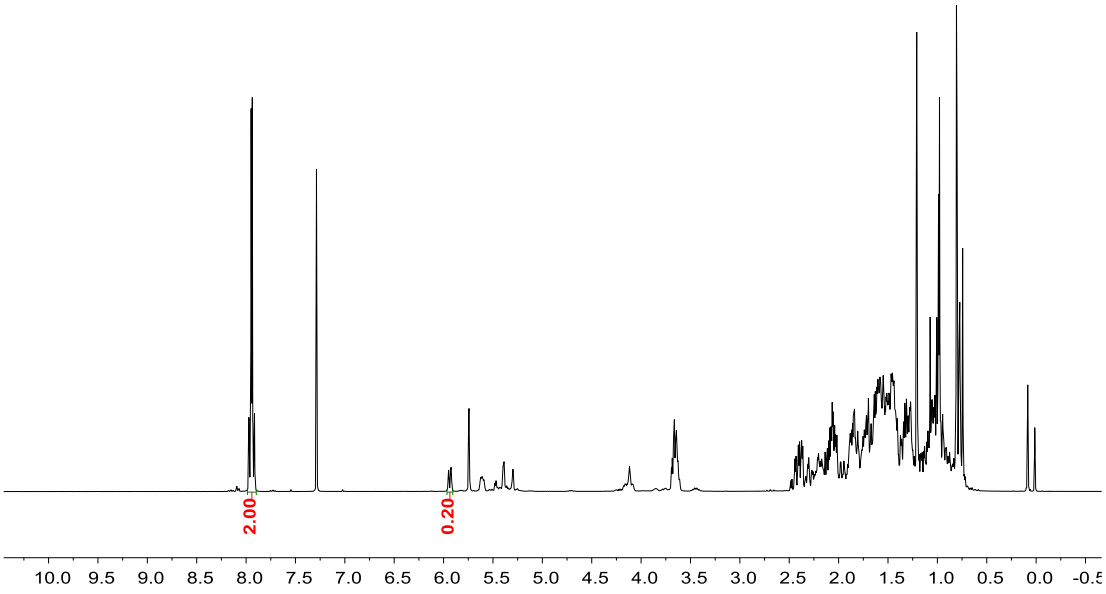
LC−1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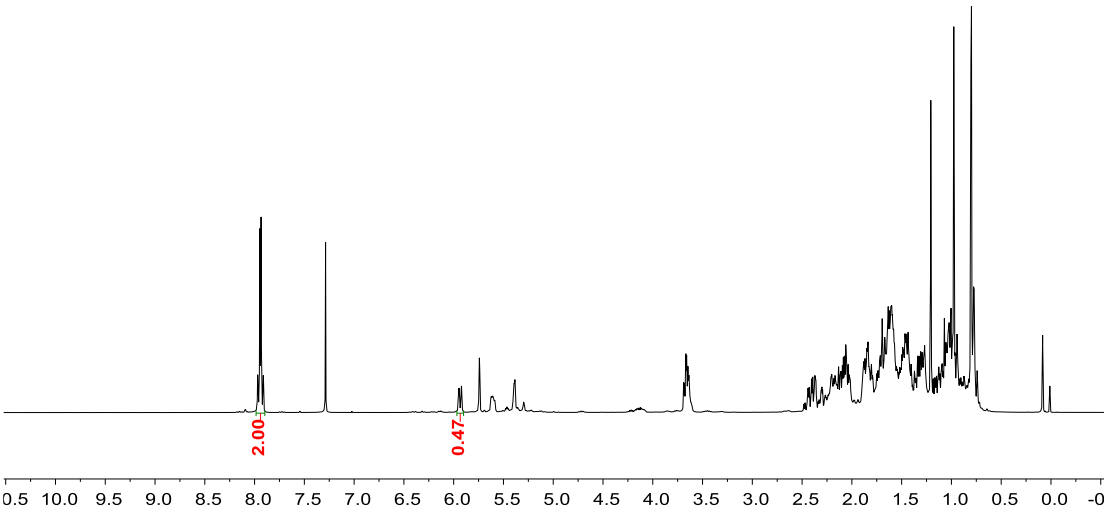
LC−2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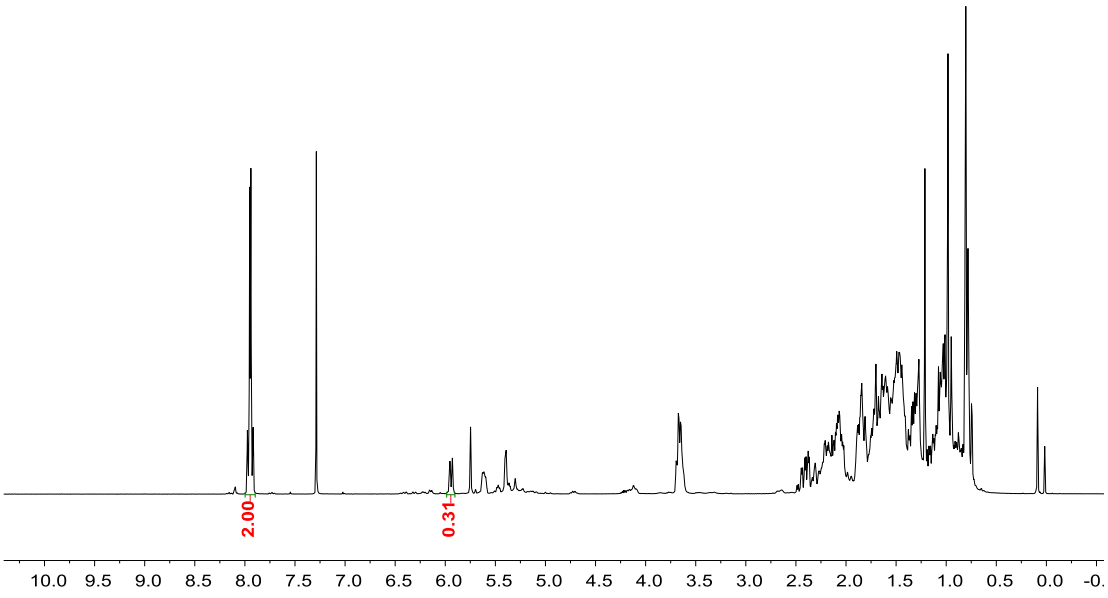
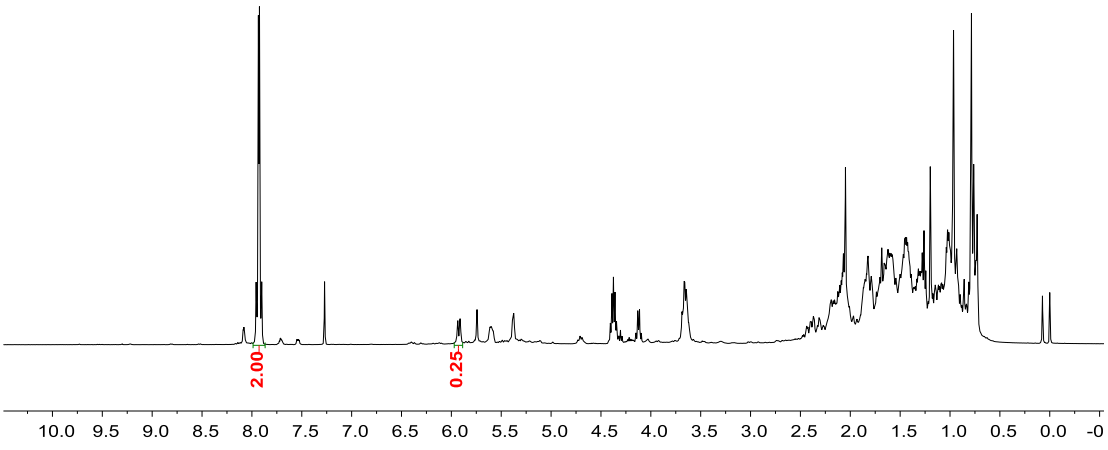
LC−3

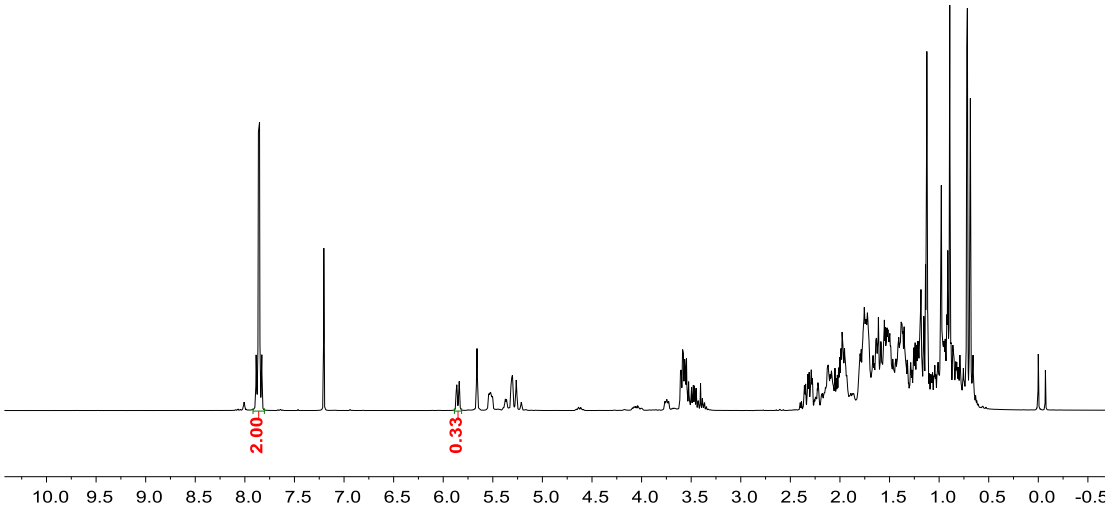


^{1}H NMR spectra of optimization of solvent

HFIP



EtOH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0.33
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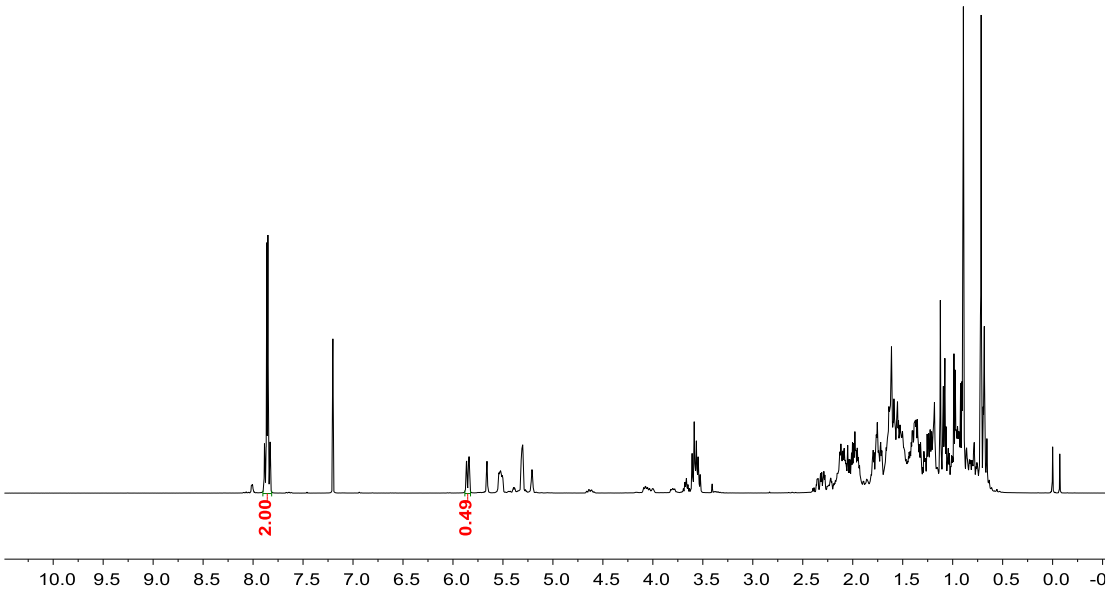
i–PrOH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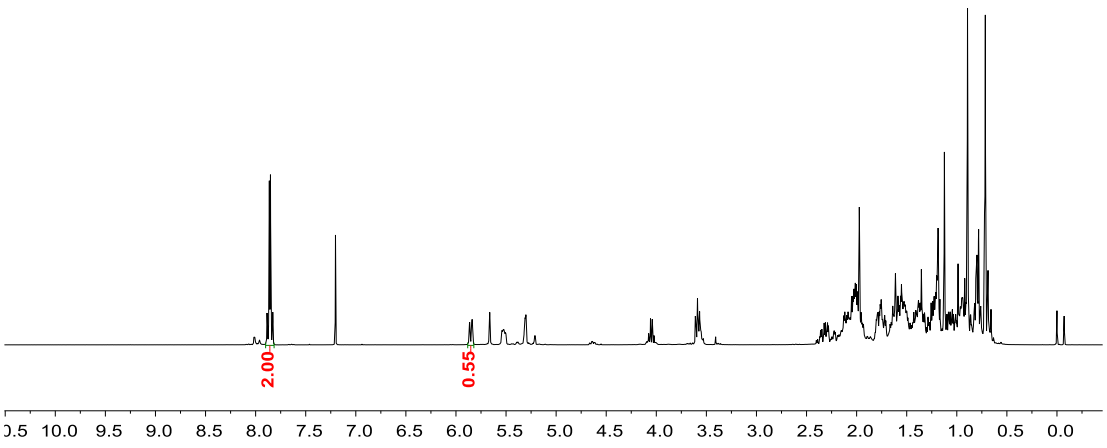
t-BuOH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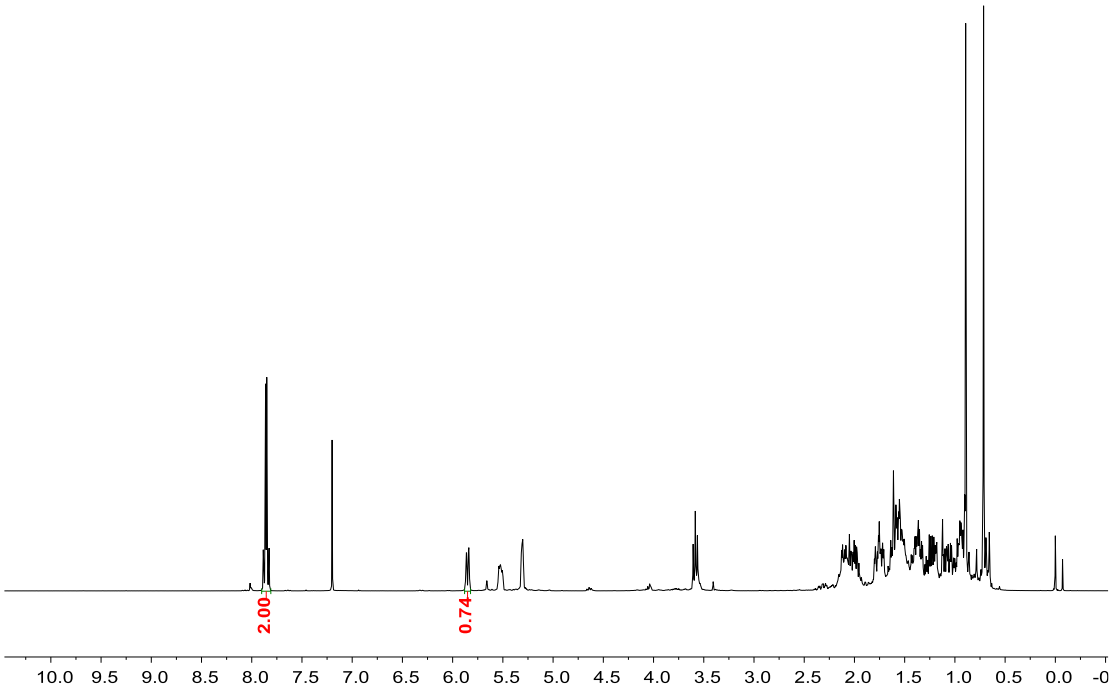
TFE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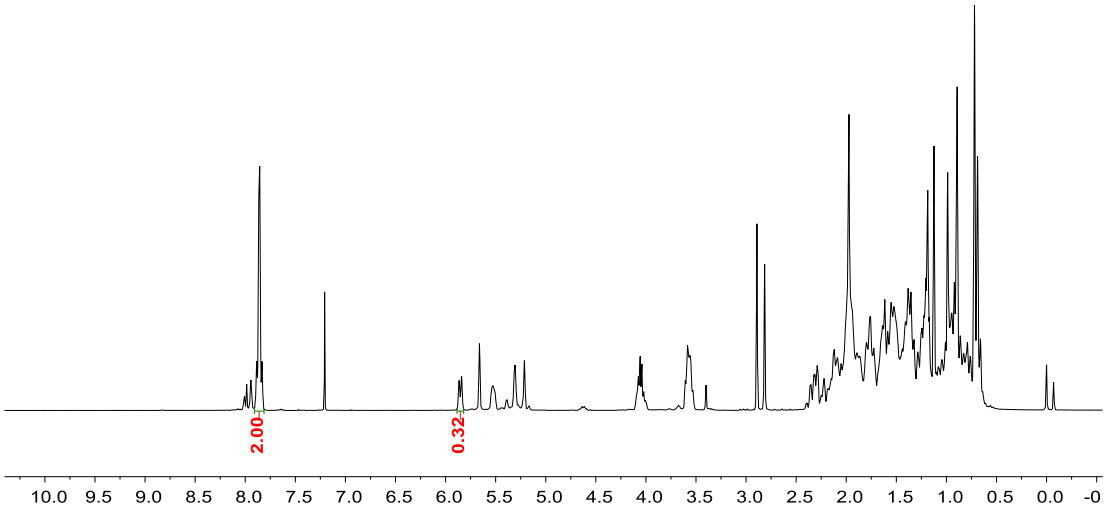
DMF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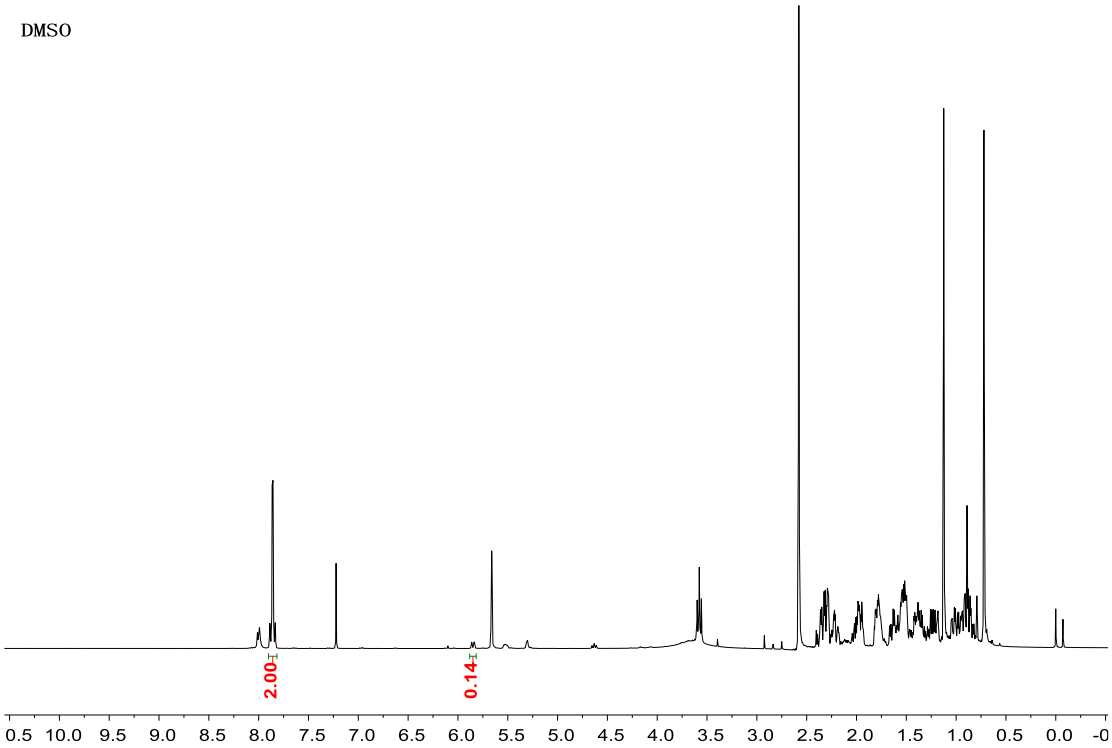
DMSO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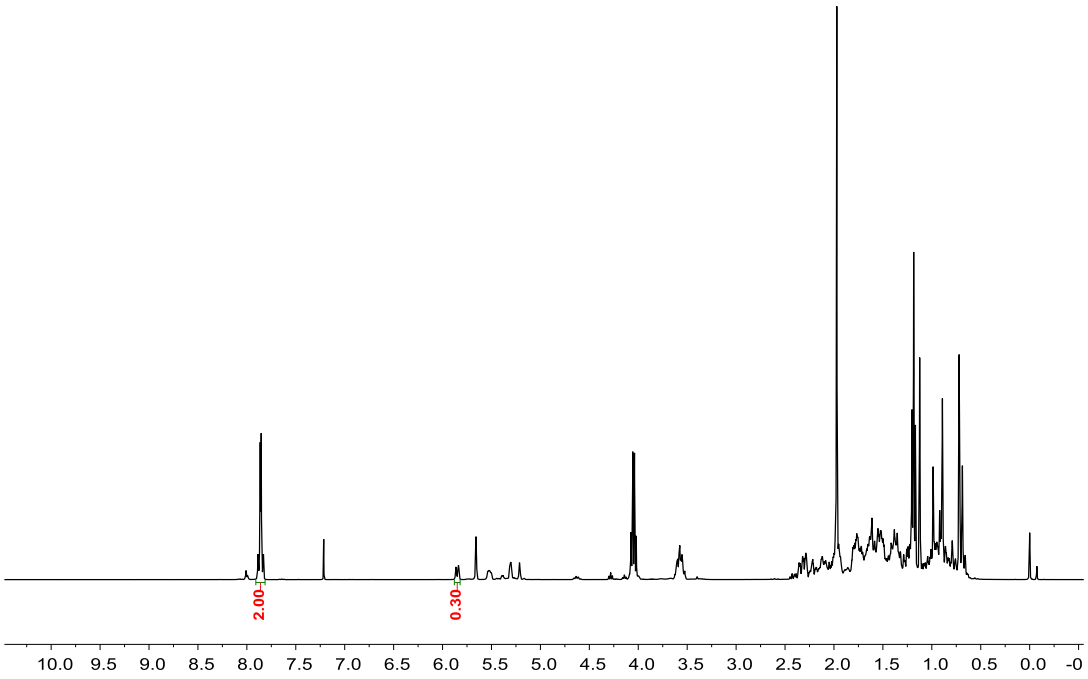
THF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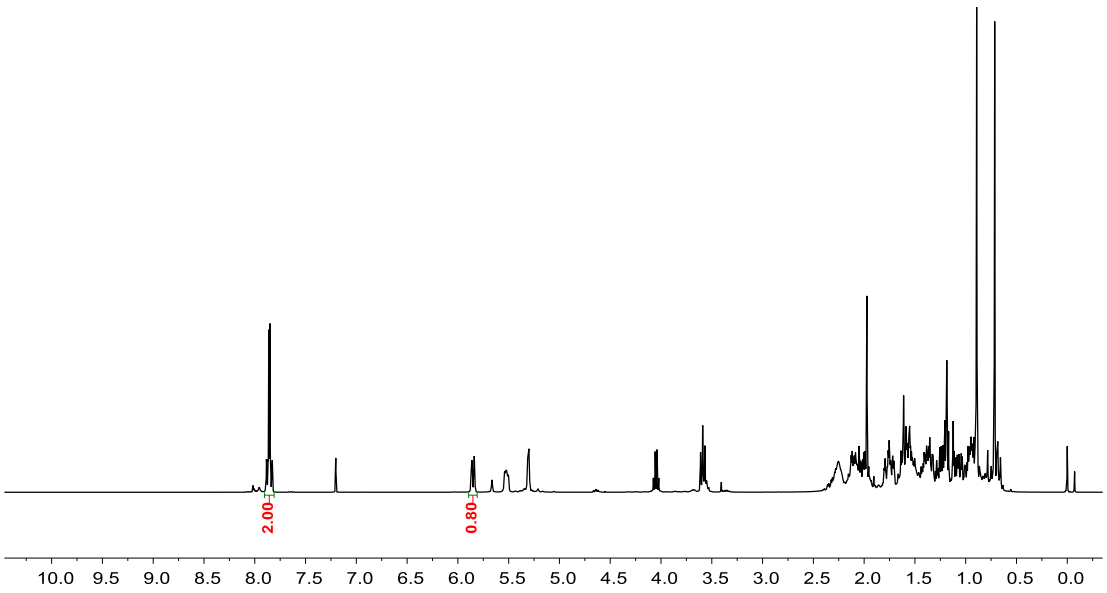
MeCN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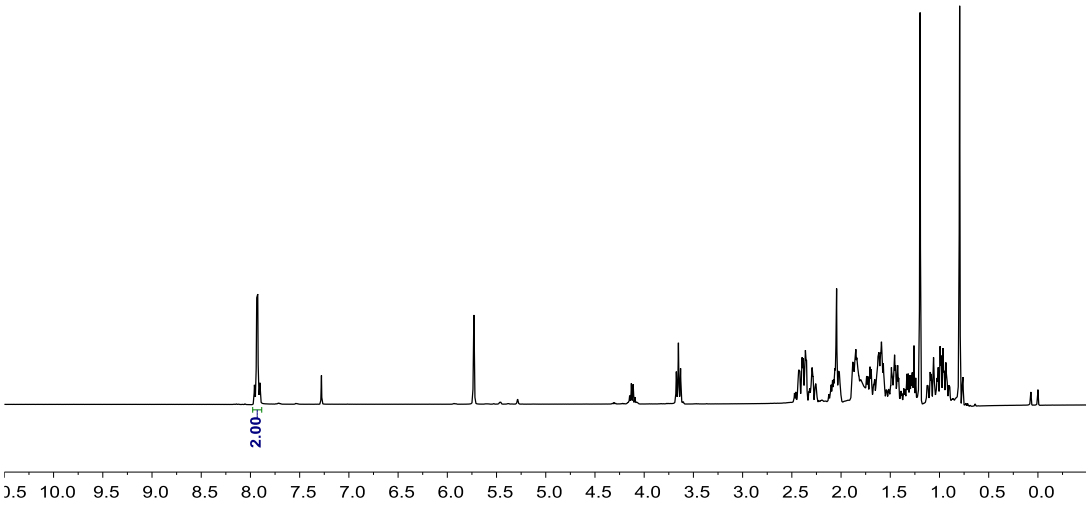
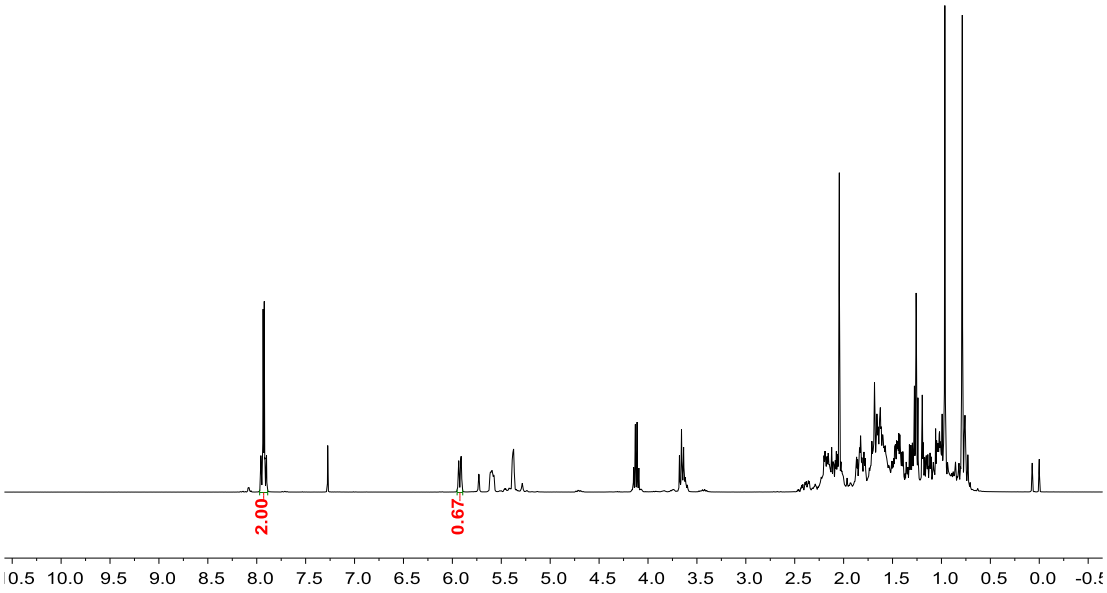
H_2O

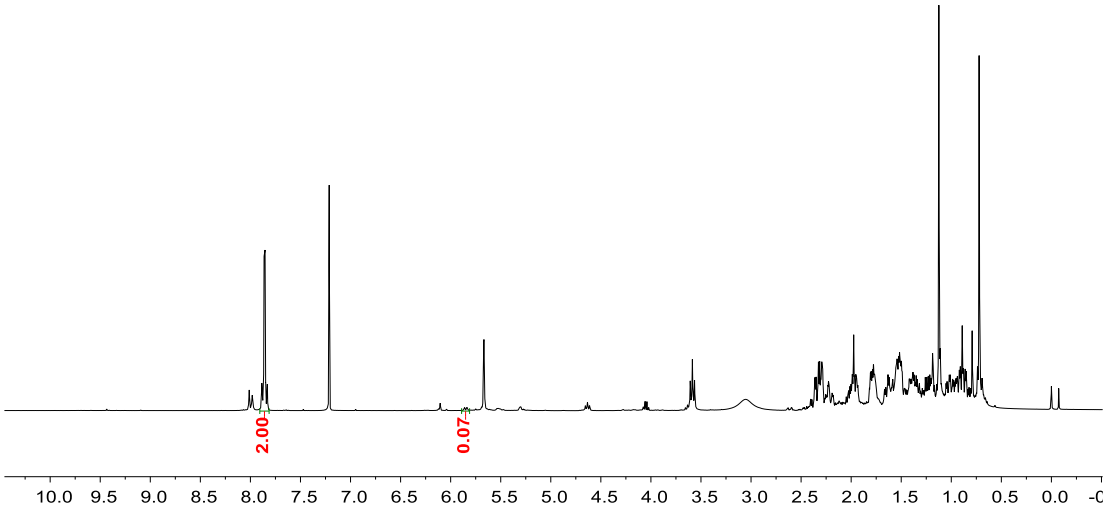


^{1}H NMR spectra of optimization of catalyst loading

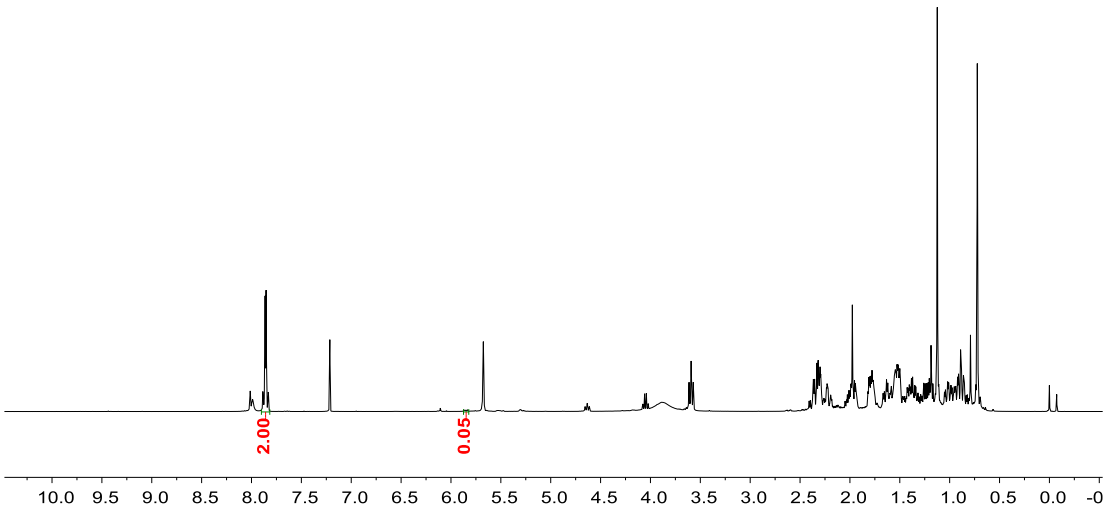
S/C 100



S/C 500

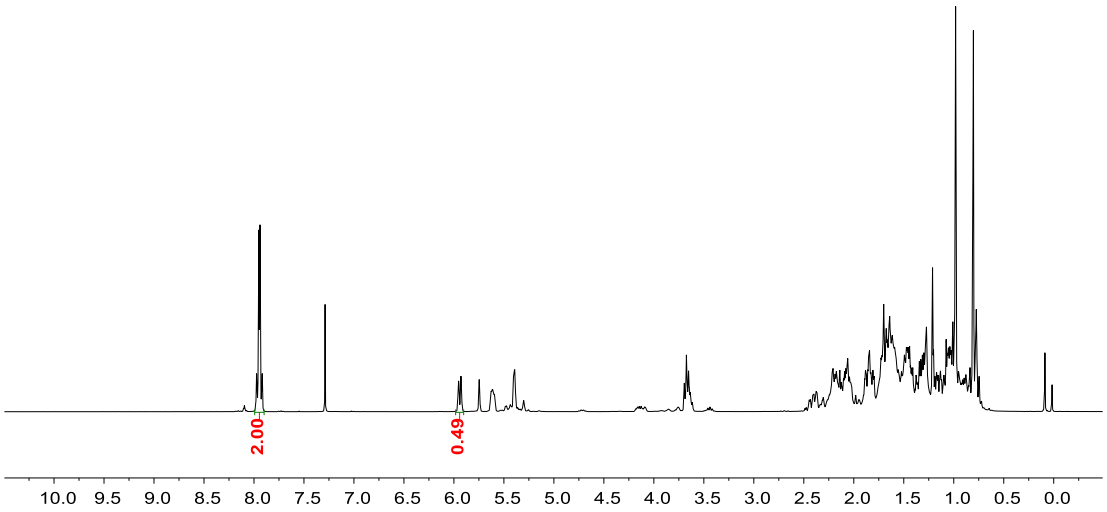


S/C 1000

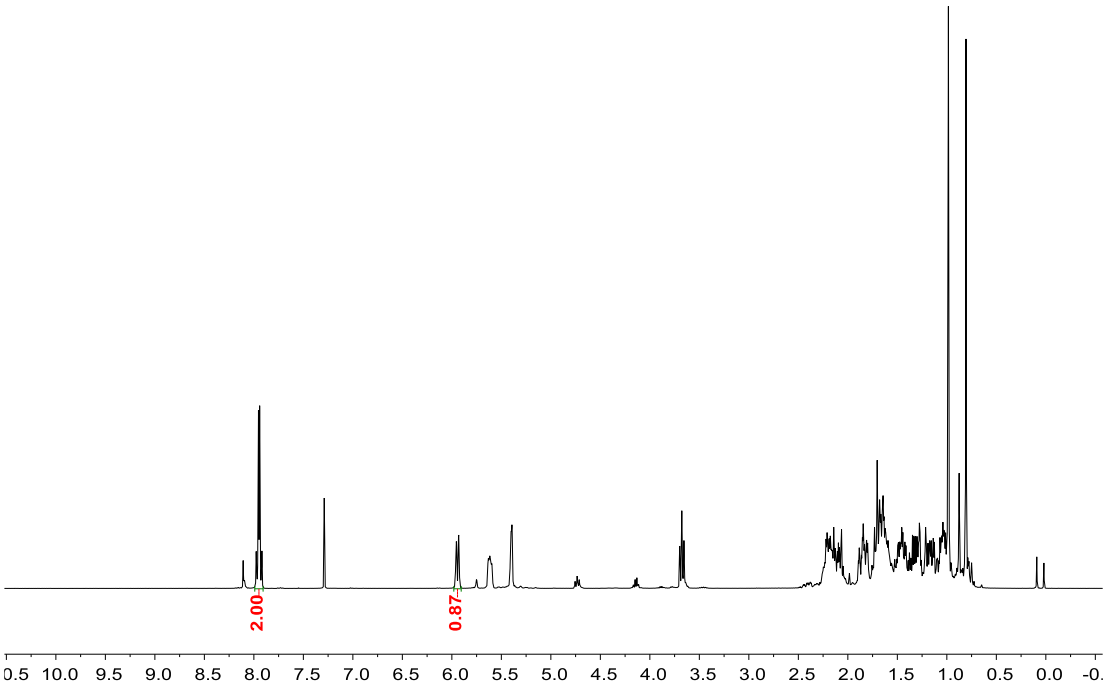


^{1}H NMR spectra of optimization of equivalents of formic acid

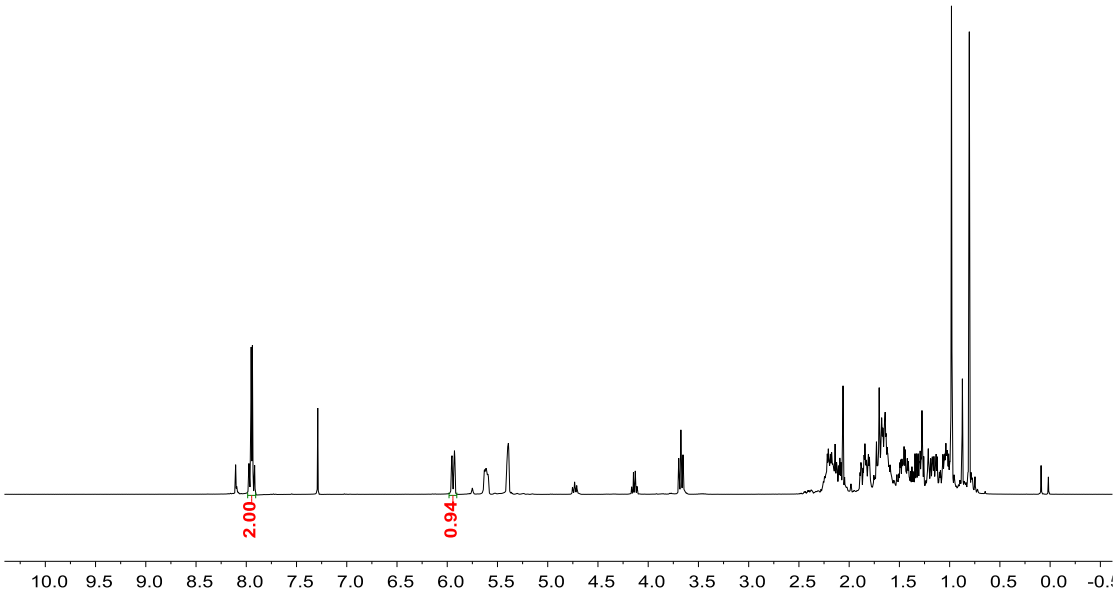
HCOOH 8 equiv.



HCOOH 16 equiv.



HCOOH 24 equiv.



^{1}H NMR spectra of optimization of reaction time

HCOOH 16 equiv., 4 h