Androsterone-based Gels Enable Gelator Reductions and Epoxidations

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Content

^{1}H-NMR data of androsterone-based gelator 1-11

Androsterone derivative **1**: white solid; Mp. 253-254 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 7.2 Hz, 2H), 7.37-7.29 (m, 3H), 5.41 (d, *J* = 5.0 Hz, 1H), 4.24 (s, 1H), 3.60-3.52 (m, 1H), 2.39-2.23 (m, 3H), 2.09 (dd, *J* = 14.1 Hz, 6.8 Hz, 2H), 1.87 (d, *J* = 10.3 Hz, 2H), 1.06 (s, 3H), 0.93 (s, 3H); IR (KBr): *v* 3394, 2936, 2903, 2861, 1746, 1454, 1376, 1058, 998, 751, 698, 616 cm^{-1}.

Androsterone derivative **2**: white solid; Mp. 218-221 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.6 Hz, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 5.39 (d, *J* = 4.8 Hz, 1H), 4.29 (s, 1H), 3.58-3.50 (m, 1H), 2.37-2.22 (m, 3H), 2.14-2.05 (m, 2H), 1.85 (d, *J* = 10.4 Hz, 2H), 1.04 (s, 3H), 0.90 (s, 3H); IR (KBr): *v* 3392, 2934, 2861, 1749, 1604, 1517, 1436, 1350, 1057, 1046, 865, 733 cm^{-1}.

Androsterone derivative **3**: white solid; Mp. 210-212 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.39 (d, *J* = 4.6 Hz, 1H), 4.18 (s, 1H), 3.79 (s, 3H), 3.62-3.48 (m, 1H), 2.33 (dd, *J* = 12.9, 3.3 Hz, 1H), 2.30-2.21 (m, 2H), 2.11-2.02 (m, 2H), 1.85 (d, *J* = 10.7 Hz, 2H), 1.76-1.61 (m, 6H), 1.55-1.33 (m, 3H), 1.11-1.05 (m, 2H), 1.03 (s, 3H), 0.91 (s, 3H); IR (KBr): *v* 3468, 2933, 2861, 1745, 1613, 1515, 1250, 1173, 1035, 921, 733 cm^{-1}.

Androsterone derivative **4**: white solid; Mp. 264-267 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 5.39 (d, *J* = 5.2 Hz, 1H), 4.18 (s, 1H), 3.57-3.51 (m, 1H), 2.33 (ddd, *J* = 13.1, 4.8, 1.8 Hz, 1H), 2.07 (dt, *J* = 14.1, 5.9 Hz, 1H), 1.85 (d, *J* = 9.8 Hz, 1H), 1.03 (s, 3H), 0.90 (s, 3H); IR (KBr): *v* 3478, 2945, 2900, 2861, 2835, 1744, 1492, 1449, 1379, 1093, 1062, 1013, 1000, 921, 866, 789

cm^{-1}.

Androsterone derivative **5**: white solid; Mp. 252-256 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 5.39 (d, *J* = 5.1 Hz, 1H), 4.18 (s, 1H), 3.59-3.50 (m, 1H), 2.33 (dd, *J* = 13.0, 3.2 Hz, 1H), 2.30-2.21 (m, 1H), 2.07 (dd, *J* = 14.2, 7.0 Hz, 1H), 1.85 (d, *J* = 10.1 Hz, 1H), 1.03 (s, 3H), 0.90 (s, 3H); IR (KBr): *v* 3471, 2943, 2898, 2859, 1744, 1489, 1449, 1422, 1140, 1062, 1009, 921, 865, 786, 619, 525 cm^{-1}.

Androsterone derivative **6**: white solid; Mp. 260-262 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.4 Hz, 2H), 7.37-7.27 (m, 8H), 5.38 (d, *J* = 5.0 Hz, 1H), 4.57 (s, 2H), 4.23 (s, 1H), 3.33-3.26 (m, 1H), 2.46 (dd, *J* = 13.2, 2.3 Hz, 1H), 2.29 (t, *J* = 13.5 Hz, 2H), 2.07 (dd, *J* = 14.3, 7.1 Hz, 2H), 1.98 (d, *J* = 12.6 Hz, 1H), 1.04 (s, 3H), 0.91 (s, 3H); IR (KBr): *v* 3033, 2970, 2930, 2906, 2892, 2866, 1744, 1495, 1455, 1370, 1249, 1208, 1108, 1023, 1001, 918, 863, 744, 698 cm^{-1}.

Androsterone derivative **7**: white solid; Mp. 174-176 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (t, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 7.0 Hz, 2H), 5.33 (d, *J* = 5.1 Hz, 1H), 4.16 (s, 1H), 3.54-3.51 (m, 1H), 2.31-2.19 (m, 2H), 1.00 (s, 3H), 0.96 (s, 3H); IR (KBr): *v* 3350, 2929, 2885, 2859, 1747, 1495, 1456, 1409, 1377, 1294, 1148, 1055, 1009, 978, 921, 852, 766, 746, 699 cm^{-1}.

Androsterone derivative **8**: white solid; Mp. 200-201 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39 (d, *J* = 4.7 Hz, 1H), 3.59-3.52 (m, 1H), 3.12 (d, *J* = 6.3 Hz, 1H), 2.97 (d, *J* = 6.3 Hz, 1H), 2.35 (dd, *J* = 12.8, 3.6 Hz, 1H), 2.26 (t, *J* = 12.2 Hz, 1H), 1.94-1.87 (m, 4H), 1.77-1.41 (m, 9H), 1.07 (s, 3H), 1.05 (s, 3H); IR (KBr): *v* 3474, 2925, 2899,

1744, 1463, 1435, 1378, 1066, 1002, 934, 729 cm^{-1}.

Androsterone derivative **9**: white solid; Mp. 237-240 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ 7.44 (d, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 4.21 (s, 1H), 3.63-3.58 (m, 1H), 2.25 (t, *J* = 13.3 Hz, 1H), 2.04 (dd, *J* = 14.2, 6.8 Hz, 1H), 1.81 (d, *J* = 11.7 Hz, 1H), 0.88 (s, 3H), 0.83 (s, 3H); IR (KBr): *v* 3382, 2929, 2857, 1747, 1628, 1450, 1374, 1338, 1155, 1042, 990, 915, 868, 750, 699 cm^{-1}.

Androsterone derivative **10**: white solid; Mp. 193-196 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.15 (s, 1H), 3.79 (s, 3H), 3.64-3.55 (m, 1H), 2.27-2.19 (m, 1H), 2.02 (dd, *J* = 14.2, 7.1 Hz, 1H), 1.81 (d, *J* = 12.5 Hz, 1H), 0.88 (s, 3H), 0.83 (s, 3H); IR (KBr): *v* 3251, 2932, 2858, 1743, 1615, 1515, 1451, 1252, 1173, 1037, 992, 871, 834, 816, 790 cm^{-1}.

Androsterone derivative **11**: white solid; Mp. 201-203 ^oC; ^1H NMR (600 MHz, $CDCl_3$) 7.54 (d, *J* = 7.4 Hz, 2H), 7.42 (dd, *J* = 15.0, 7.7 Hz, 3H), 7.36 (t, *J* = 7.3 Hz, 1H), 5.40 (m, 1H), 3.54 (m, 1H,), 2.89 (m, 1H), 2.45 (m, 1 H), 1.08 (s, 3H), 0.99 (s, 3H); IR (KBr): *v* 3417, 2934, 2858, 1715, 1629, 1448, 1372, 1273, 1132, 1100, 1058, 1010, 978, 841, 770, 694 cm^{-1}.

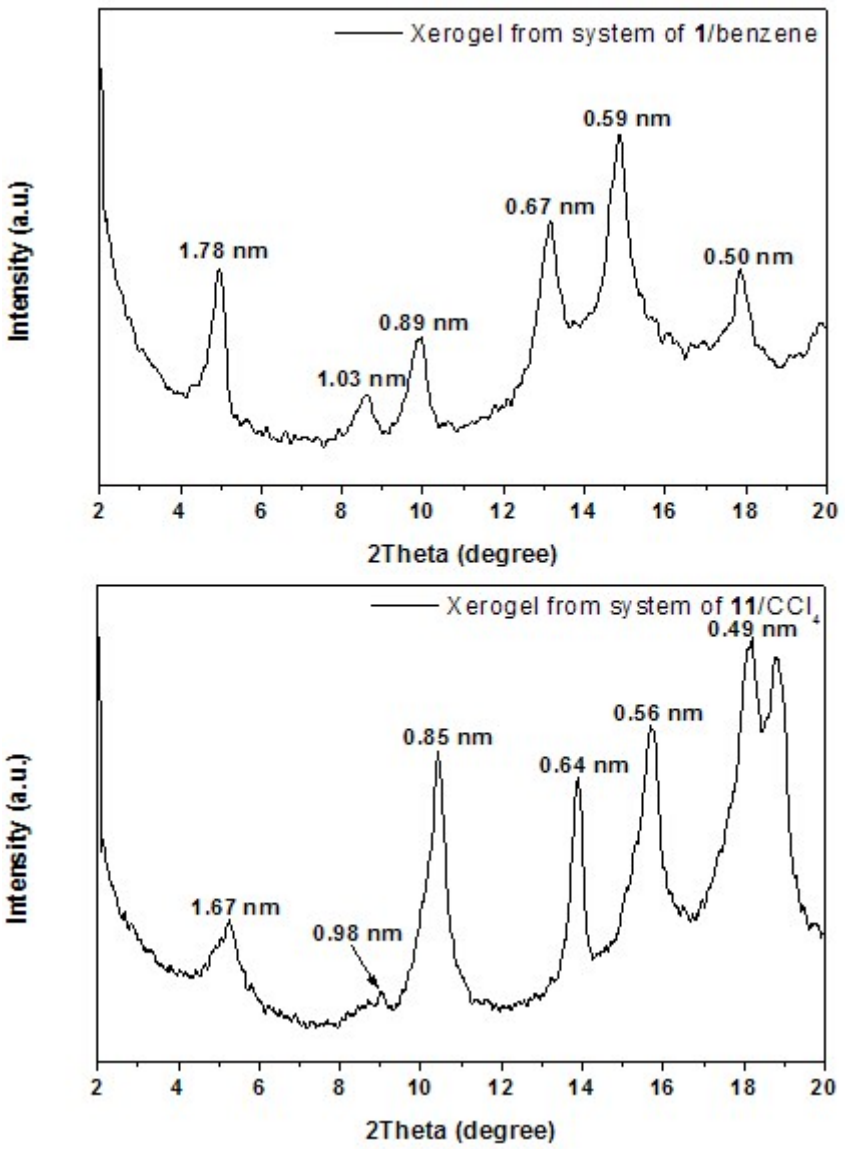


Figure S1. XRD patterns for xerogels (2% w/v) from **1**/benzene and **11**/CCl_4

Control experiment for the reduction of carbonyl group in methanol

$NaBH_4$ (77 mg, 8.0 equiv) was added to a mixture of gelator **1** (100 mg, 1.0 equiv) and methanol (100 mL). The reaction mixture was stirred for 12 h at room temperature. TLC (thin layer chromatography) indicated that the reaction did not take place. Raising the reaction temperature to reflux, after 12 h ^1H NMR indicated that the reaction still did not take place.

Control experiment for the reduction of carbonyl group on water

$NaBH_4$ (77 mg, 8.0 equiv) was added to a mixture of gelator **1** (100 mg, 1.0 equiv) and water (20 mL). The reaction mixture was stirred for 13 h at room temperature. ^1H NMR indicated that the reaction conversion was 26%.

Control experiment for the effects of metal ions (Li^+/Na^+/K^+) on the reduction

Gelator **1** (100 mg, 1.0 equiv) was added to a 50 mL flask, the gelation solvent toluene (2.5 mL) was added to the flask. The mixture was heated until complete dissolution of gelator **1**. The solution was cooled down to room temperature until the gel was formed. The xerogel was prepared by slow evaporation the solvent under reduced pressure. Then LiCl (86 mg, 8.0 equiv), KBH_4 (110 mg, 8.0 equiv) and H_2O (0.20 mL) were added to the prepared xerogel. The reaction mixture was mechanically stirred for 10 h at room temperature, when TLC showed the reaction was complete.

Gelator **1** (100 mg, 1.0 equiv) was added to a 50 mL flask, the gelation solvent toluene (2.5 mL) was added to the flask. The mixture was heated until complete dissolution of gelator **1**. The solution was cooled down to room temperature until the gel was formed. The xerogel was prepared by slow evaporation the solvent under reduced pressure. Then KBH_4 (110 mg, 8.0 equiv) and H_2O (0.12 mL) were added to the prepared xerogel. The reaction mixture was mechanically stirred for 10 h at room temperature. The reaction mixture was extracted with ethyl acetate (5 mL×3) followed by washing with water (10 mL×2). Ethyl acetate was evaporated to give the crude product. ^1H NMR indicated that the reaction conversion was 32%.

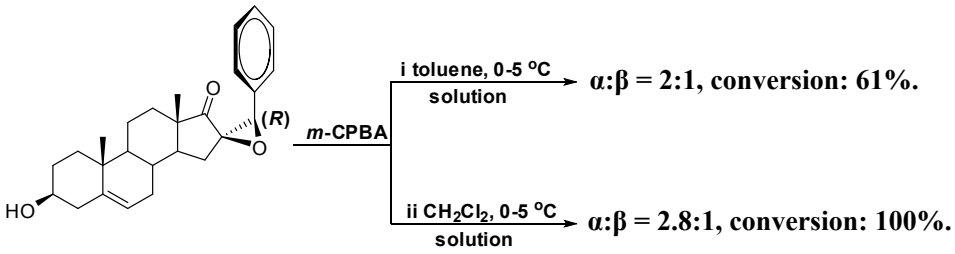
Control experiment for the function of granular PTFE in the reduction: 2

reductions in the absence of granular PTFE

For xerogel: Gelator **1** (100 mg, 1.0 equiv) was added to a 50 mL flask, the gelation solvent toluene (2.5 mL) was added to the flask. The mixture was heated until complete dissolution of gelator **1**. The solution was cooled down to room temperature until the gel was formed. The xerogel was prepared by slow evaporation the solvent under reduced pressure. Then $NaBH_4$ (77 mg, 8.0 equiv) and H_2O (0.12 mL) were added to the prepared xerogel. The reaction mixture was mechanically stirred for 13 h at room temperature. The reaction mixture was extracted with ethyl acetate (5 mL×3) followed by washing with water (10 mL×2). Ethyl acetate was evaporated to give the crude product. ^1H NMR indicated that the reaction conversion was 14%.

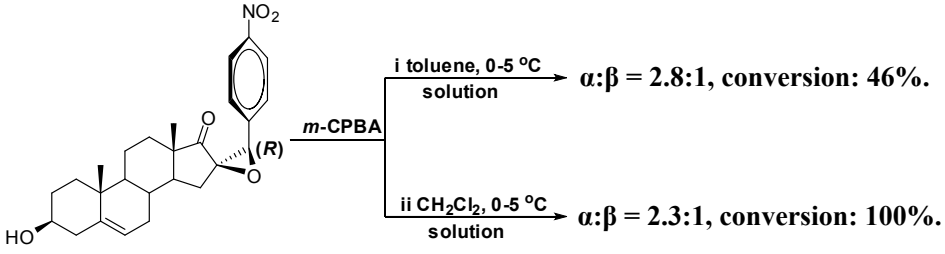
For gel: Gelator **1** (100 mg, 1.0 equiv) was added to a 50 mL flask, the gelation solvent toluene (2.5 mL) was added to the flask. The mixture was heated until complete dissolution of gelator **1**. The solution was cooled down to room temperature until the gel was formed. Then $NaBH_4$ (77 mg, 8.0 equiv) was added to the prepared gel. The reaction mixture was mechanically stirred for 11.5 h at room temperature. The reaction mixture was extracted with ethyl acetate (5 mL×3) followed by washing with water (10 mL×2). Ethyl acetate was evaporated to give the crude product. ^1H NMR indicated that the reaction conversion was 2%.

Control experiments for the epoxidations of double bond in gelation solvent and CH_2Cl_2 solution



(i) 85% *m*-CPBA (62 mg, 1.2 equiv) was added to a mixture of gelator **1** (100 mg, 1.0 equiv) and toluene (100 mL). The reaction mixture was stirred for 12 h at 0-5 °C. Saturated Na_2CO_3 solution (10 mL) was added to the reaction mixture at 0-5 °C followed by stirring for 10 min. Toluene layer was washed by water (50 mL×2) followed by evaporation of toluene to give crude product. ^{1}H NMR indicated that the reaction conversion was 14% and α/β ratio was 2/1.

(ii) 85% *m*-CPBA (62 mg, 1.2 equiv) was added to a mixture of gelator **1** (100 mg, 1.0 equiv) and CH_2Cl_2 (5 mL). The reaction mixture was stirred for 1.5 h at 0-5 °C. TLC indicated that the reaction was complete. Saturated Na_2CO_3 solution (10 mL) and CH_2Cl_2 (20 mL) were added to the reaction mixture at 0-5 °C followed by stirring for 10 min. CH_2Cl_2 layer was washed by water (10 mL×2) followed by evaporation of CH_2Cl_2 to give crude product. ^{1}H NMR indicated that the α/β ratio was 2.8/1.



(i) 85% *m*-CPBA (56 mg, 1.2 equiv) was added to a mixture of gelator **2** (100 mg, 1.0 equiv) and toluene (40 mL). The reaction mixture was stirred for 5.5 h at 0-5 °C. Saturated Na_2CO_3 solution (10 mL) was added to the reaction mixture at 0-5 °C followed by stirring for 10 min. Toluene layer was washed by water (20 mL×2)

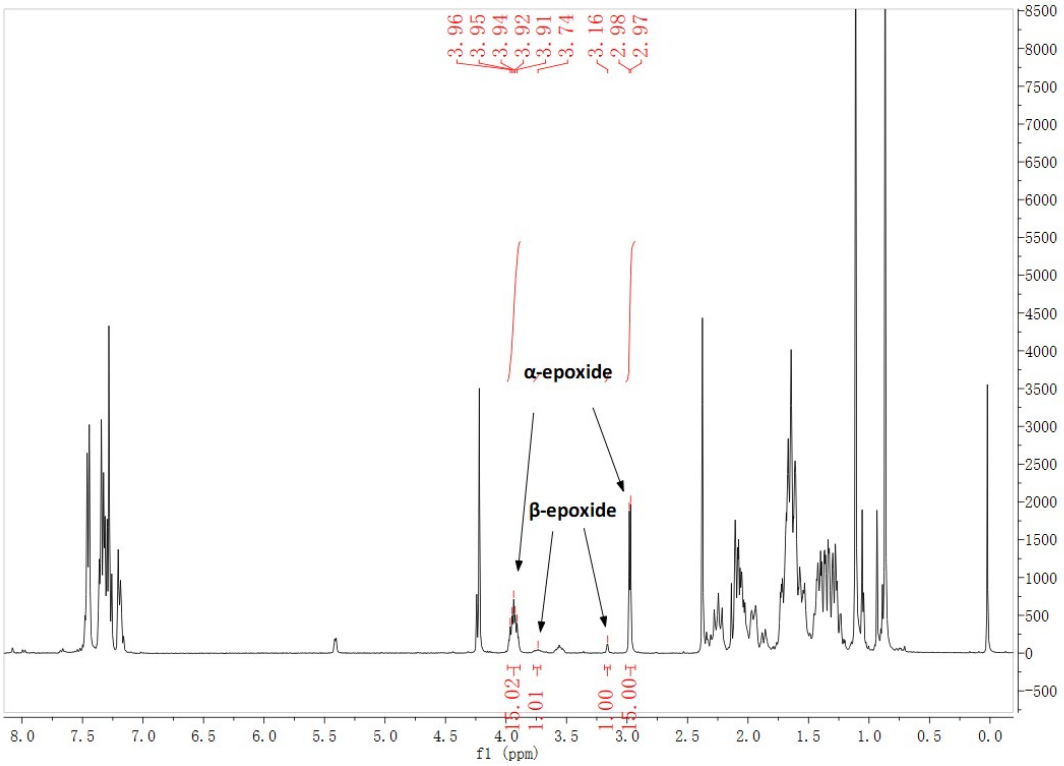
followed by evaporation of toluene to give crude product. ^{1}H NMR indicated that the reaction conversion was 46% and α/β ratio was 2.8/1.

(ii) 85% *m*-CPBA (56 mg, 1.2 equiv) was added to a mixture of gelator **2** (100 mg, 1.0 equiv) and CH_2Cl_2 (10 mL). The reaction mixture was stirred for 3.5 h at 0-5 °C. TLC indicated that the reaction was complete. Saturated Na_2CO_3 solution (10 mL) and CH_2Cl_2 (10 mL) were added to the reaction mixture at 0-5 °C followed by stirring for 10 min. CH_2Cl_2 layer was washed by water (10 mL×2) followed by evaporation of CH_2Cl_2 to give crude product. ^{1}H NMR indicated that the α/β ratio was 2.3/1.

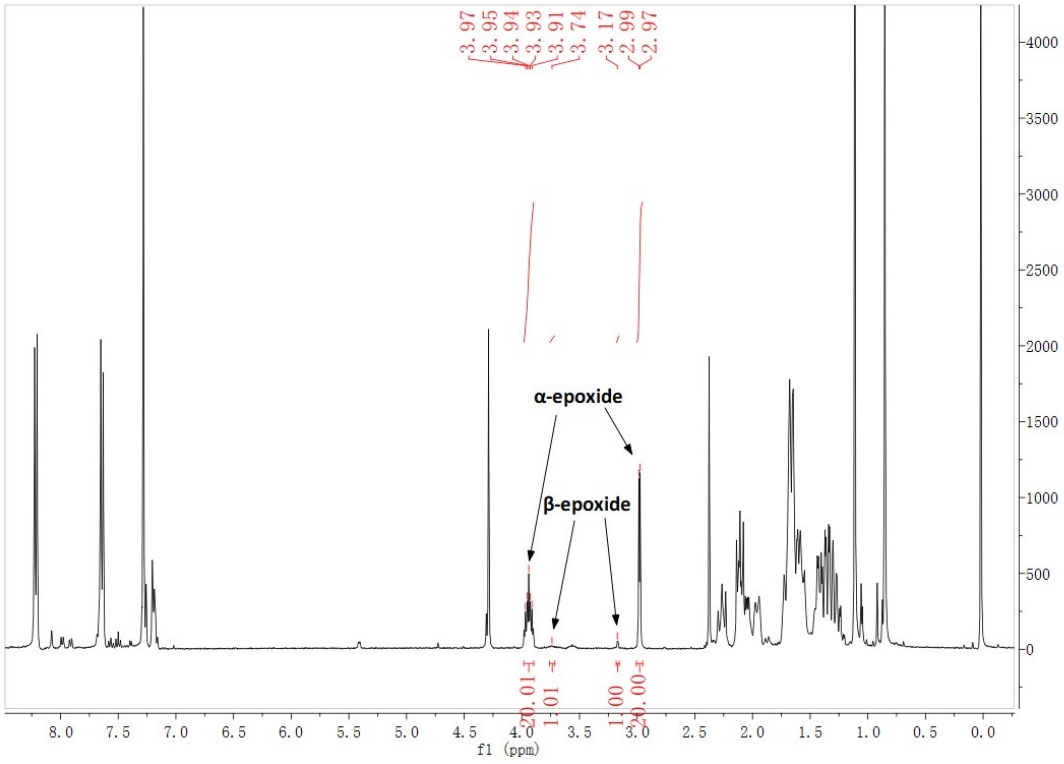
Control experiment for the function of granular PTFE in the epoxidation

Gelator **1** (100 mg, 1.0 equiv) was added to a 50 mL flask, the gelation solvent toluene (2.5 mL) was added to the flask. The mixture was heated until complete dissolution of gelator **1**. The solution was cooled down to room temperature until the gel was formed. 85% *m*-CPBA (62 mg, 1.2 equiv) was added to the prepared gel. The reaction mixture was mechanically stirred for 4 h at 0-5 °C. Saturated Na_2CO_3 solution (10 mL) and ethyl acetate (20 mL) were added to the reaction mixture at 0-5 °C followed by stirring for 10 min. Ethyl acetate layer was washed by water (10 mL×2) followed by evaporation to give crude product. ^{1}H NMR indicated that the reaction conversion was 65% and α/β ratio was 6/1.

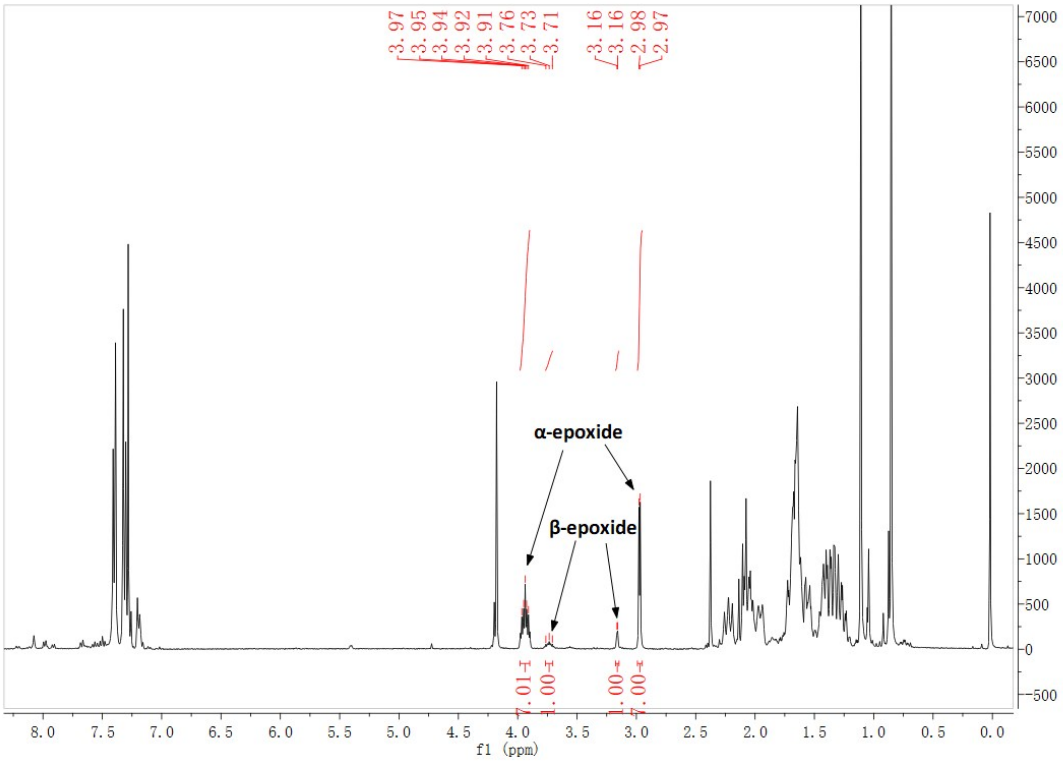
^{1}H NMR spectra for crude epoxidation products of the gels



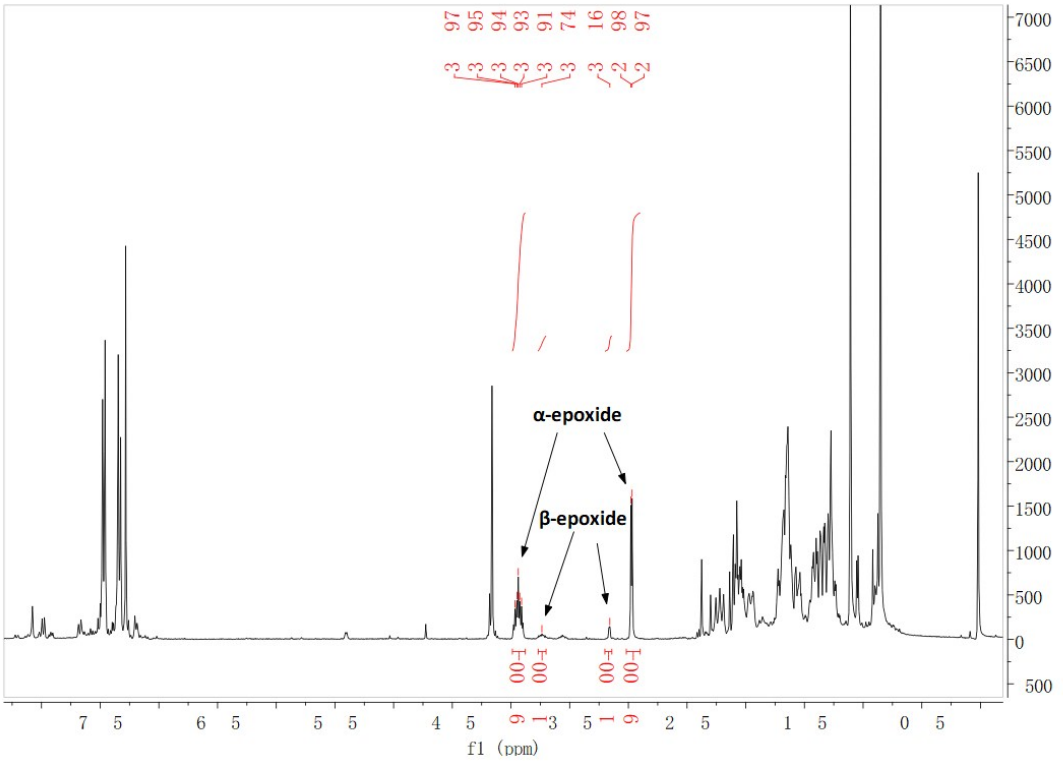
The crude epoxidation product of gelator **1** in gel form



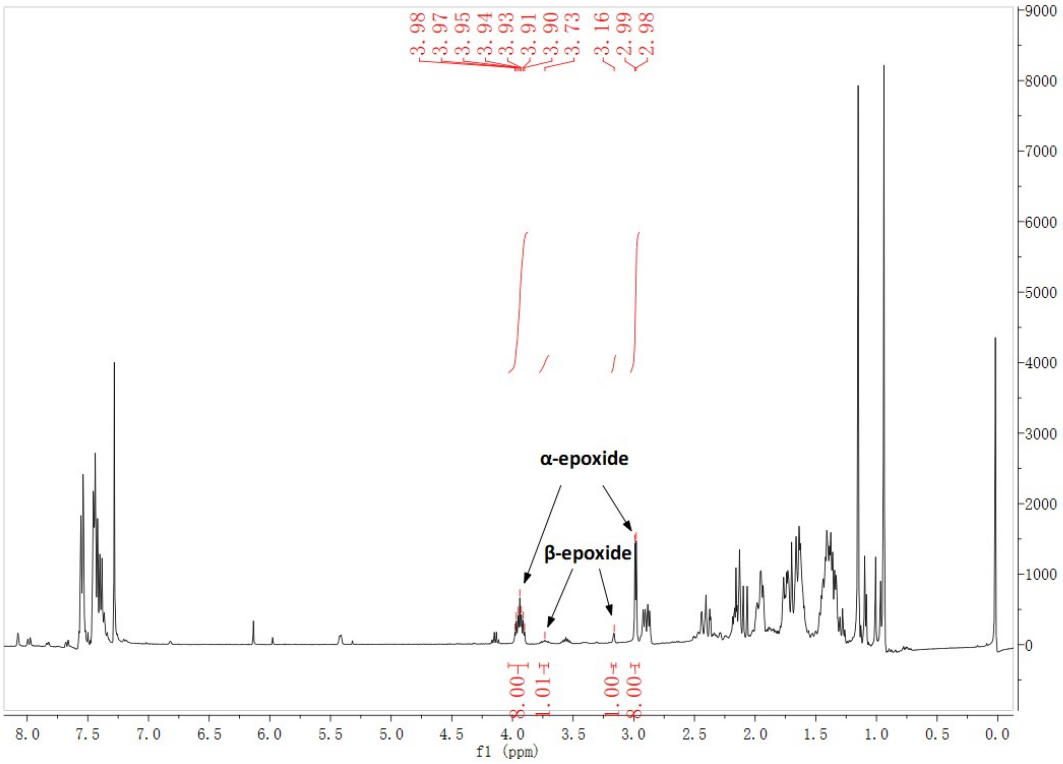
The crude epoxidation product of gelator **2** in gel form



The crude epoxidation product of gelator **4** in gel form

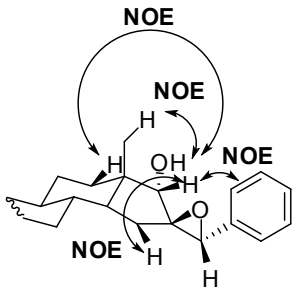


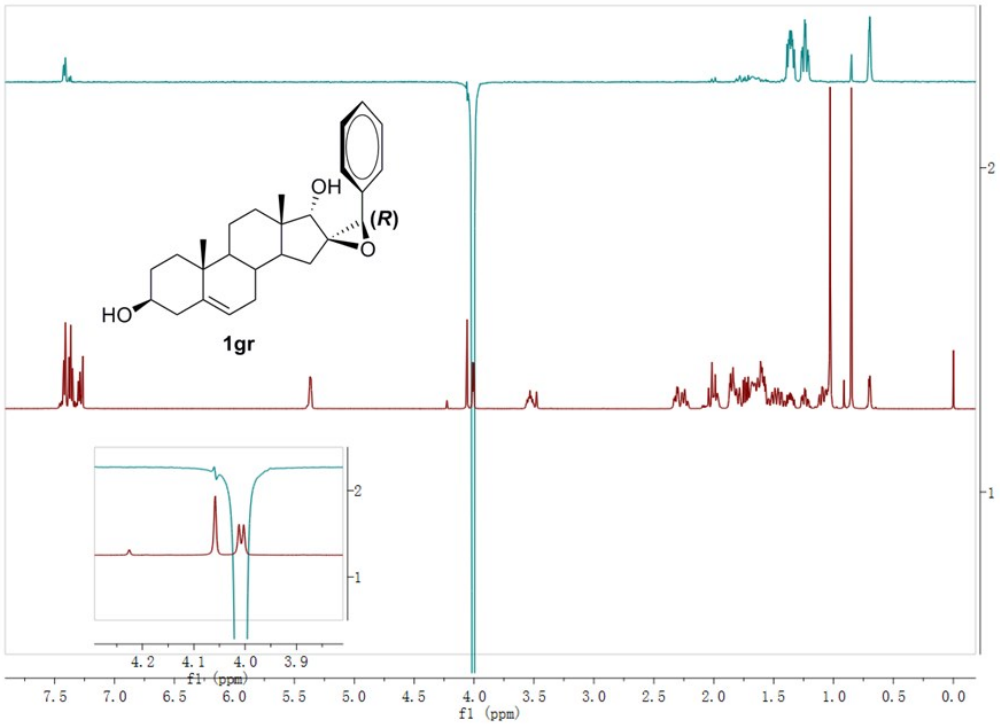
The crude epoxidation product of gelator **5** in gel form



The crude epoxidation product of gelator **11** in gel form

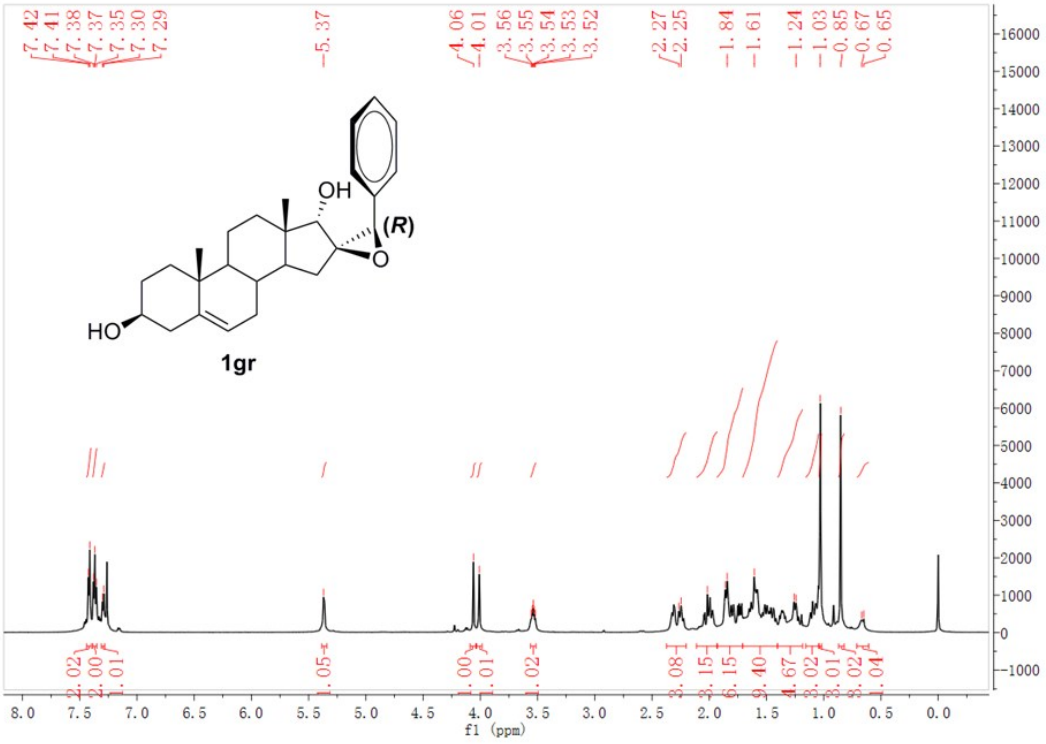
^{1}H NMR, ^{13}C NMR and NOE spectra for new products

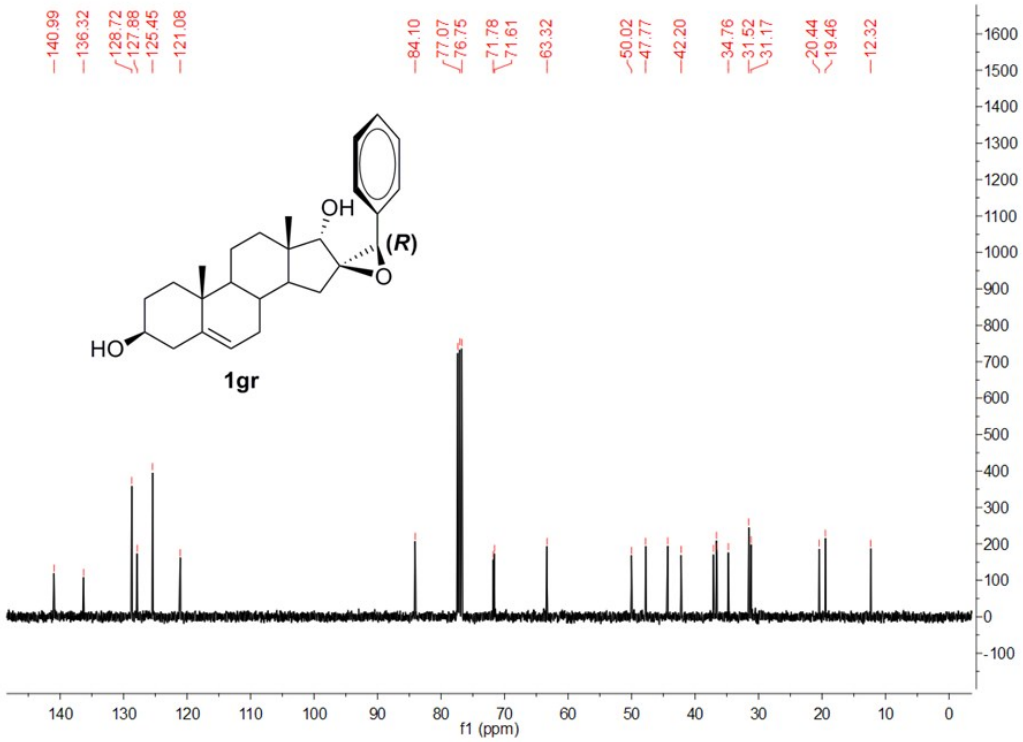




NOE spectra for **1gr** (Irradiation 4.00, 4.01 ppm doublet）

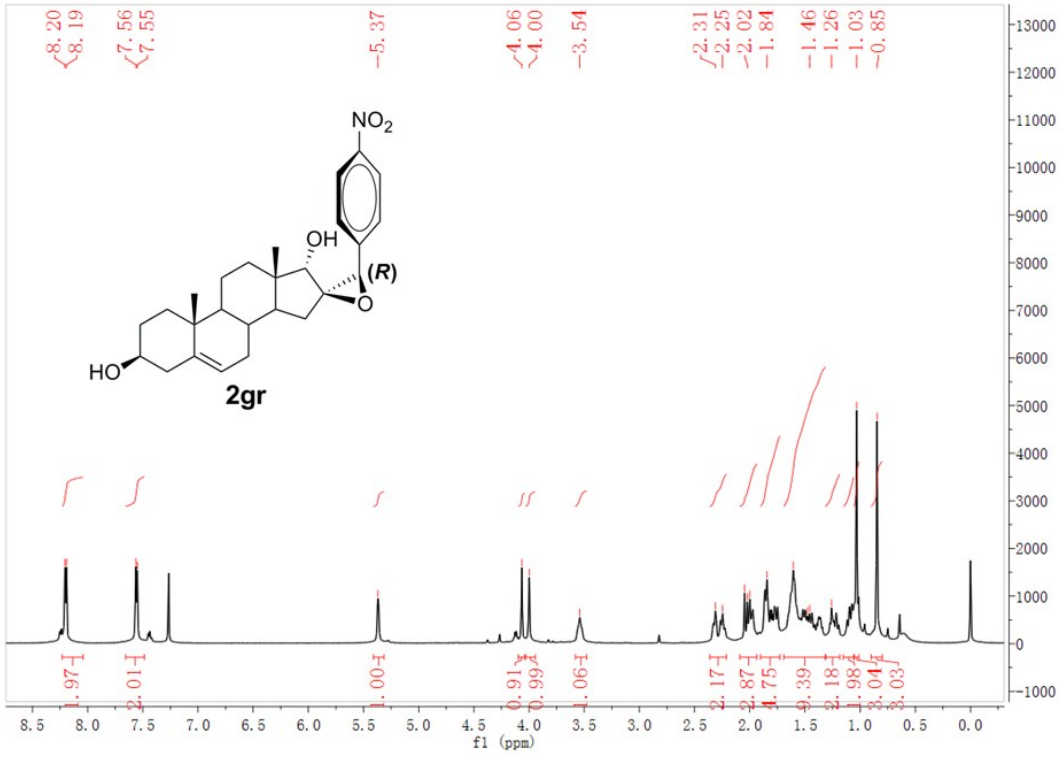
(3′*R*,16*R*)-3β-Hydroxy-3′-phenyl-5-androstene-16-spiro-2′-oxiran-17α-ol (**1gr**) :

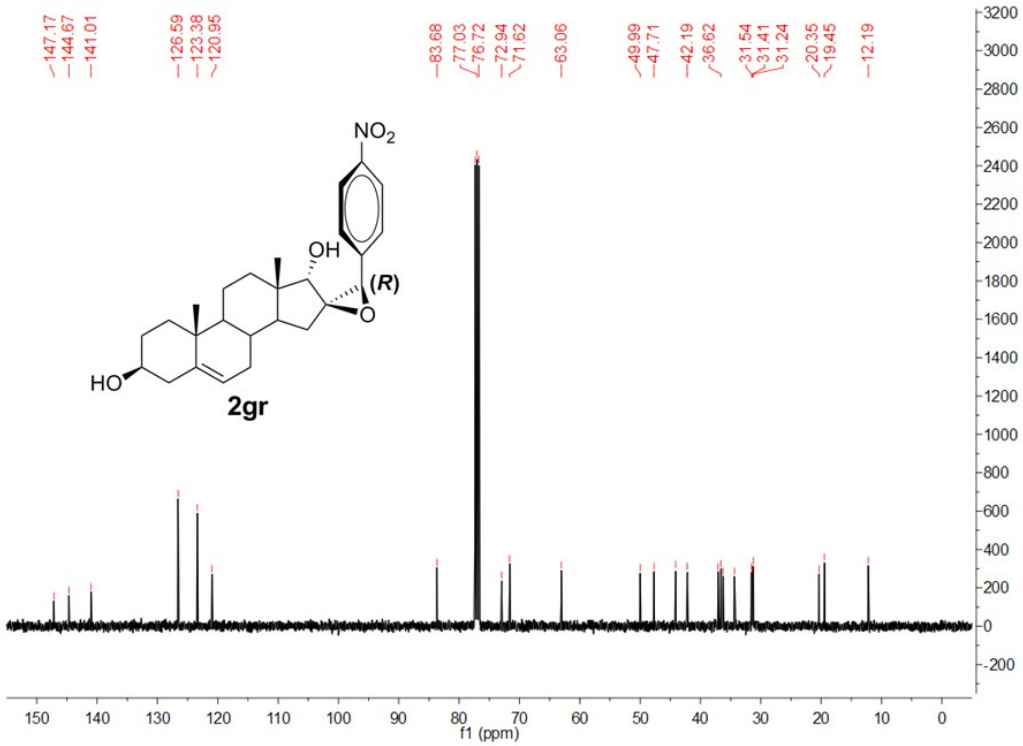




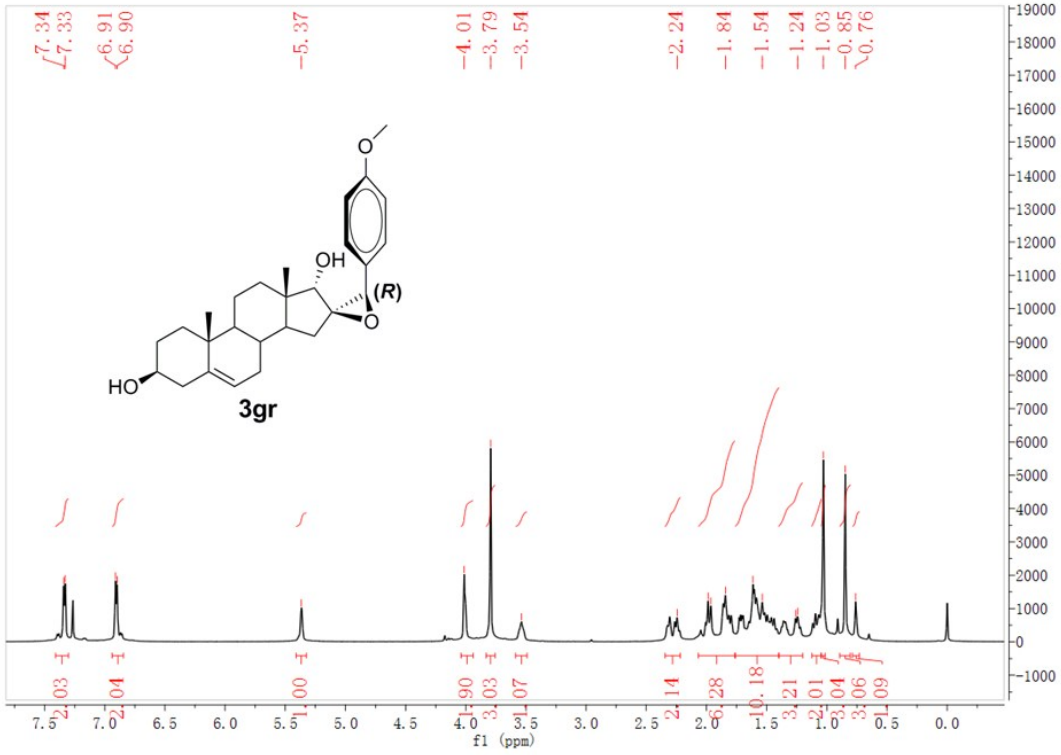
(3′*R*,16*R*)-3β-Hydroxy-3′-(4-nitrophenyl)-5-androstene-16-spiro-2′-oxiran-17α-ol

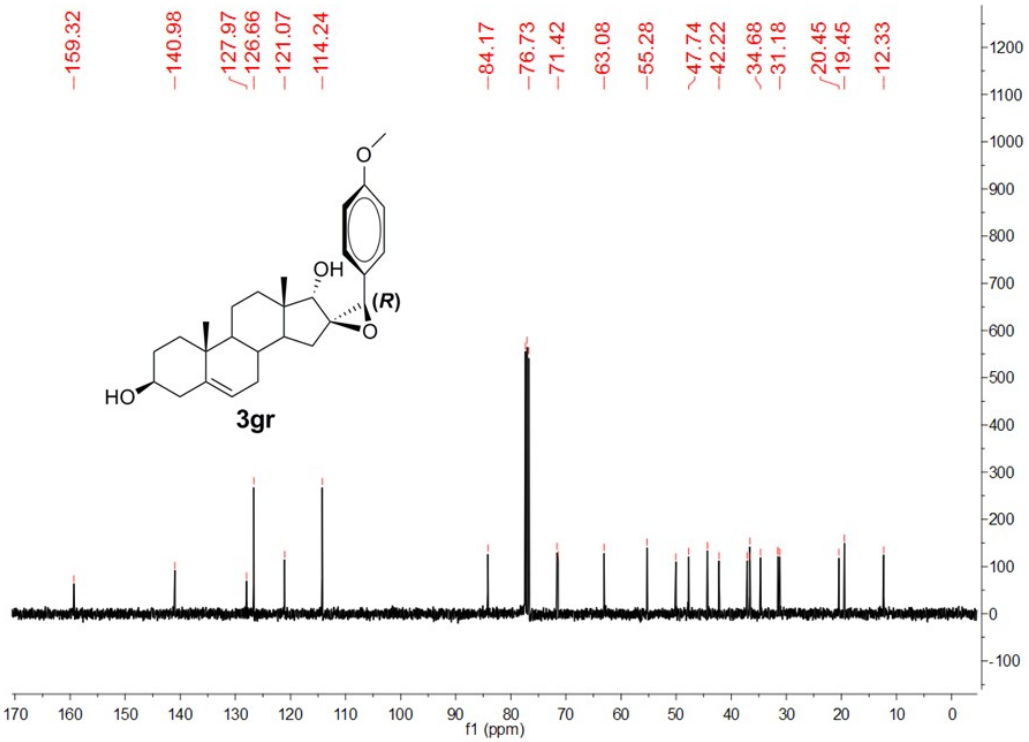
(**2gr**):



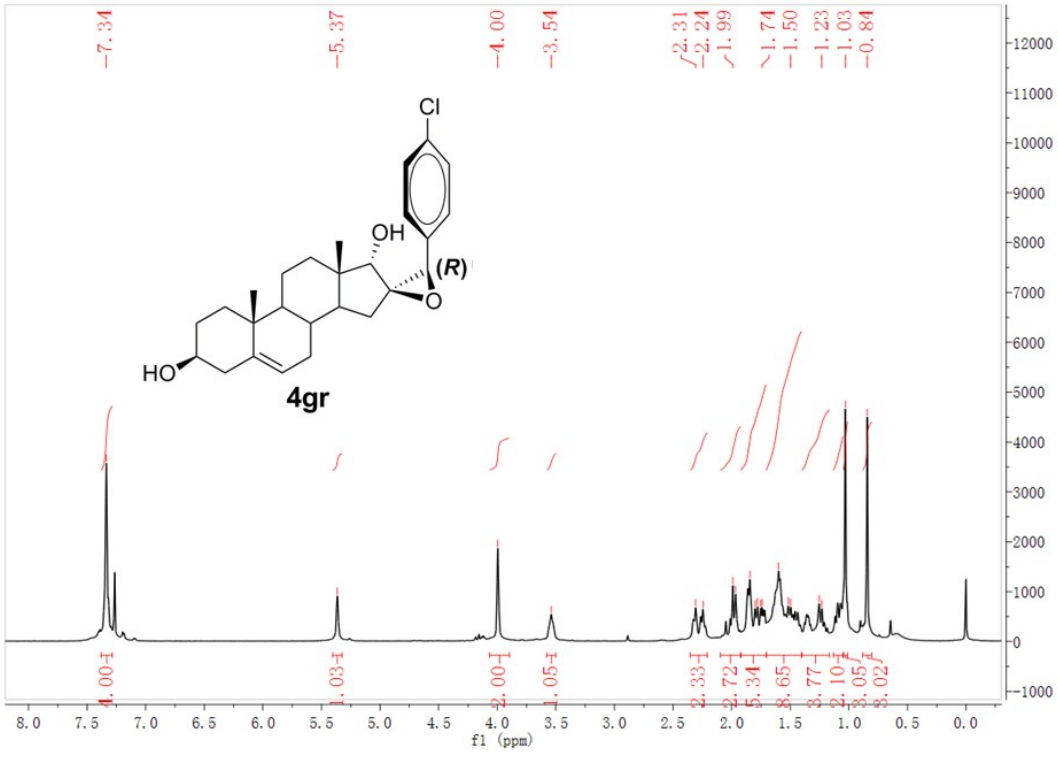


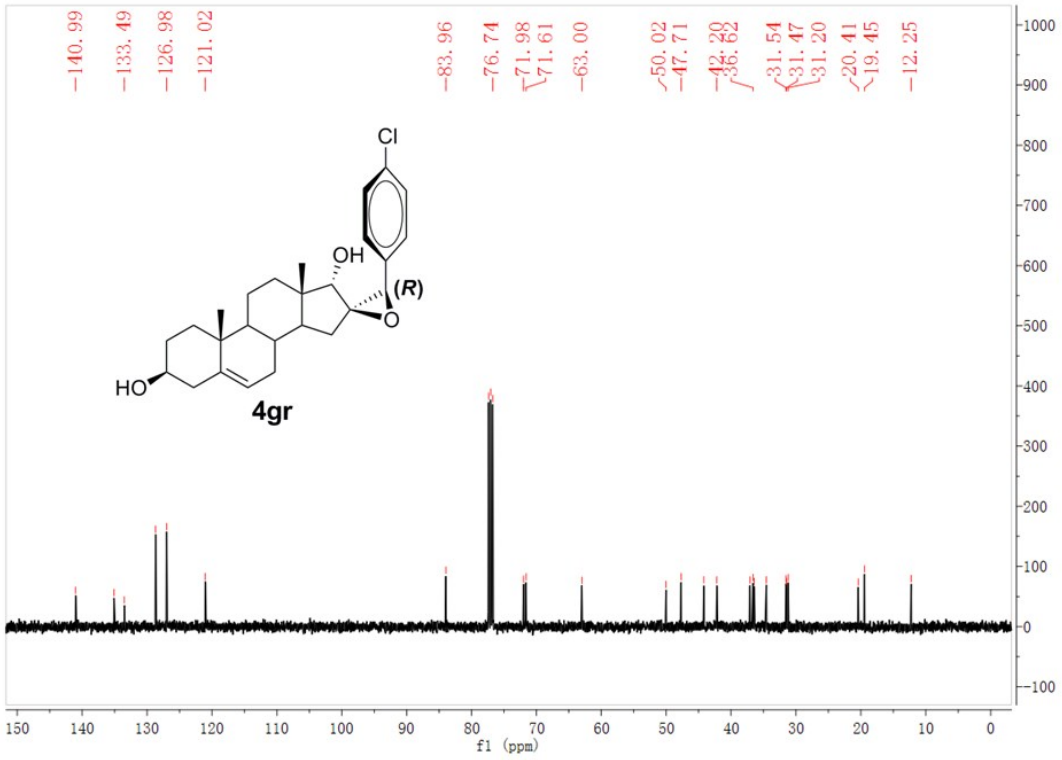
(3′*R*,16*R*)-3β-Hydroxy-3′-(4-methoxyphenyl)-5-androstene-16-spiro-2′-oxiran-17α-ol (**3gr**):





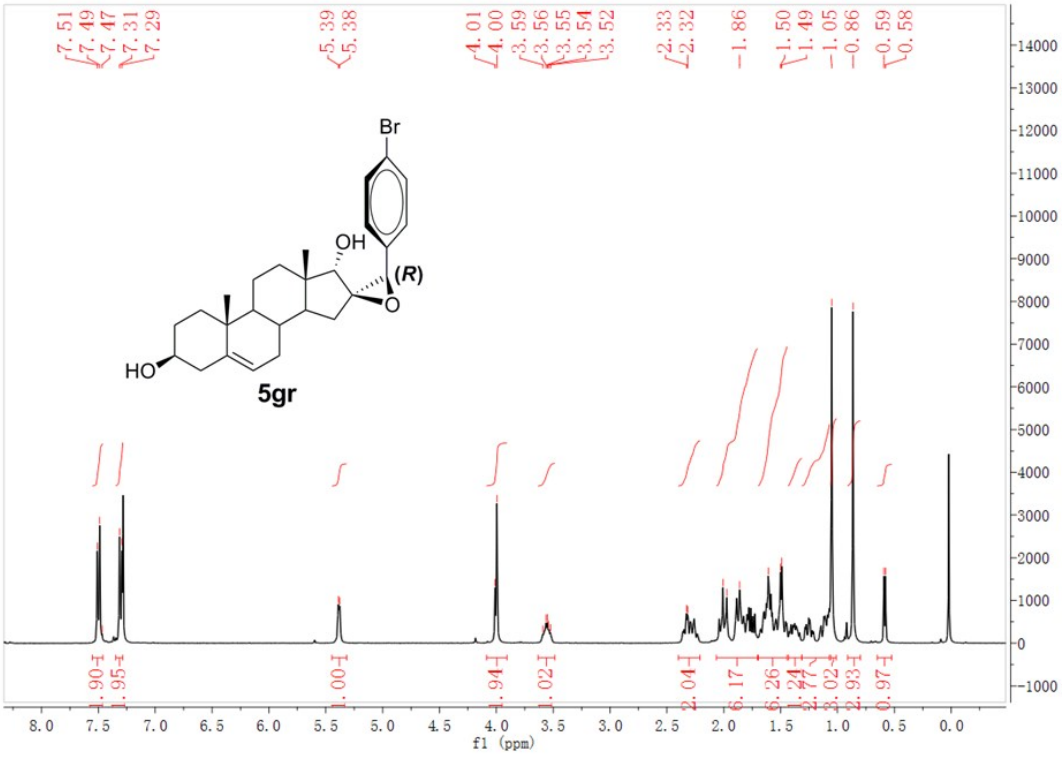
(3′*R*,16*R*)-3β-Hydroxy-3′-(4-chlorophenyl)-5-androstene-16-spiro-2′-oxiran-17α-ol (**4gr**):

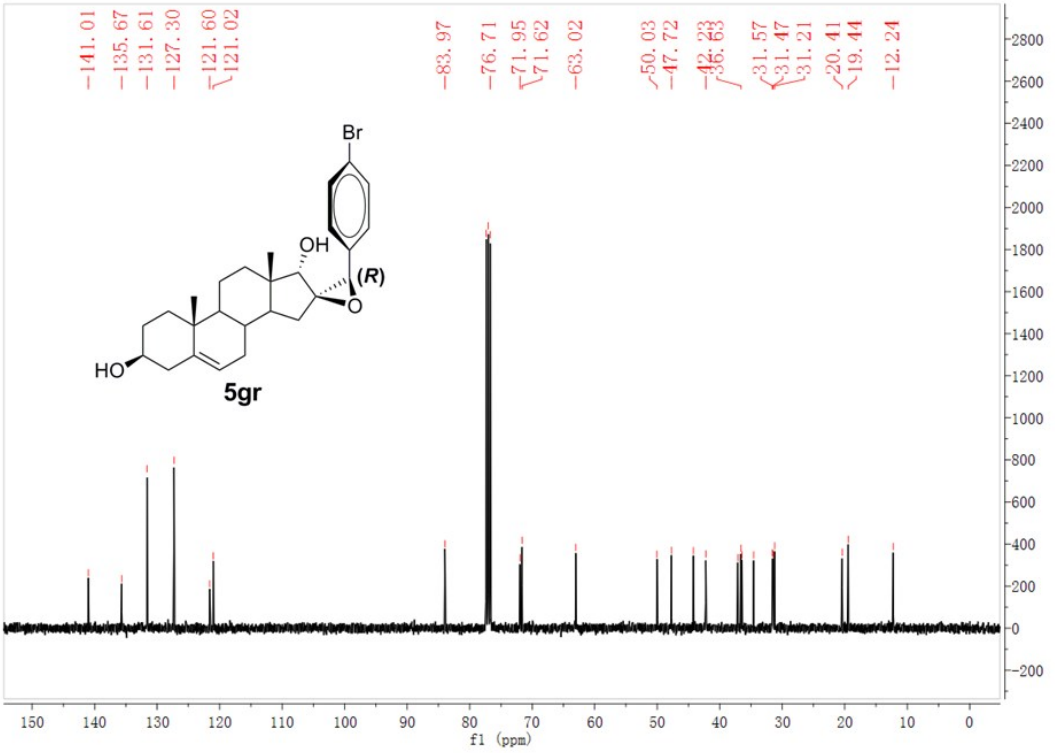




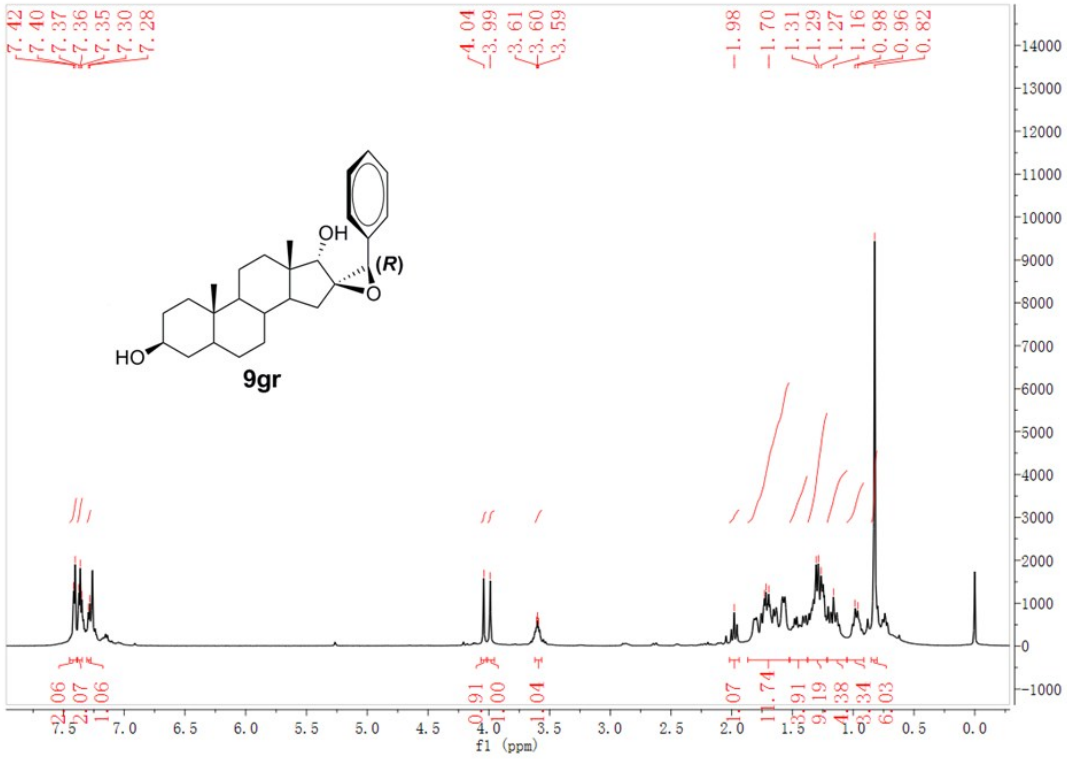
(3′*R*,16*R*)-3β-Hydroxy-3′-(4-bromophenyl)-5-androstene-16-spiro-2′-oxiran-17α-ol

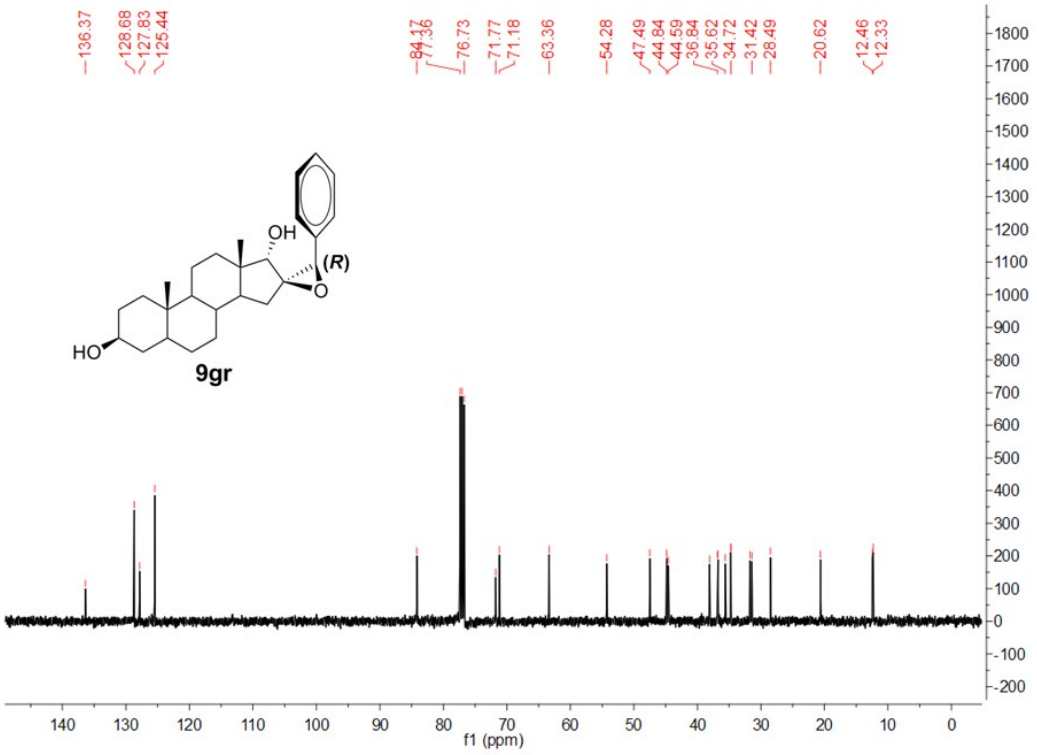
(**5gr**):



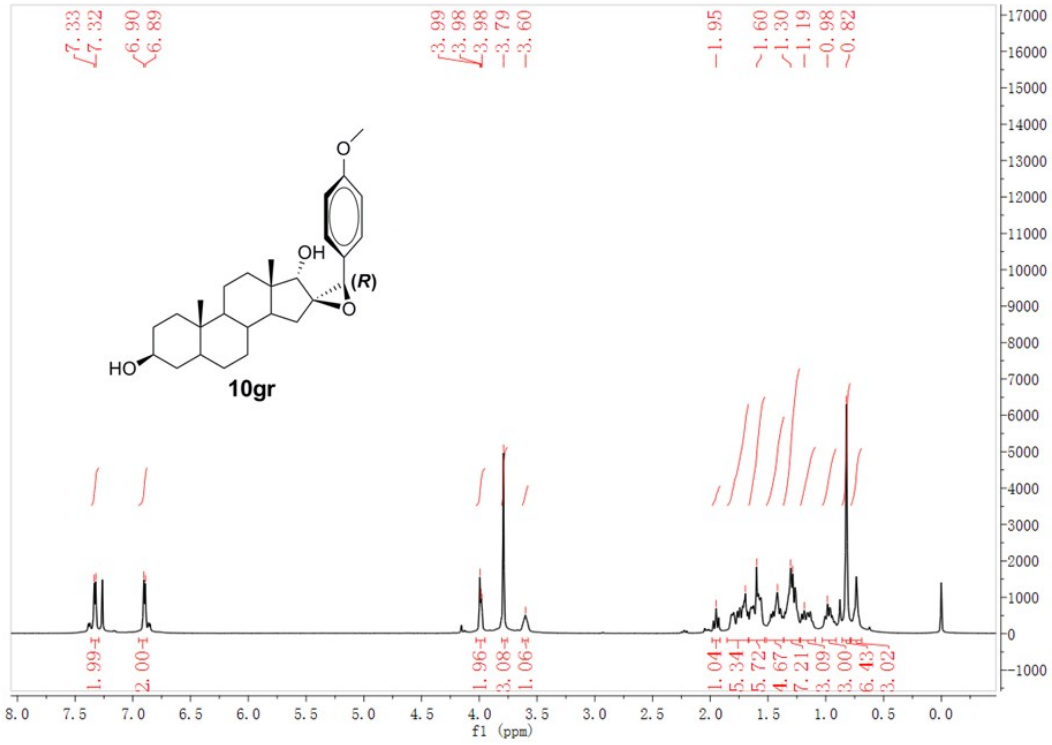


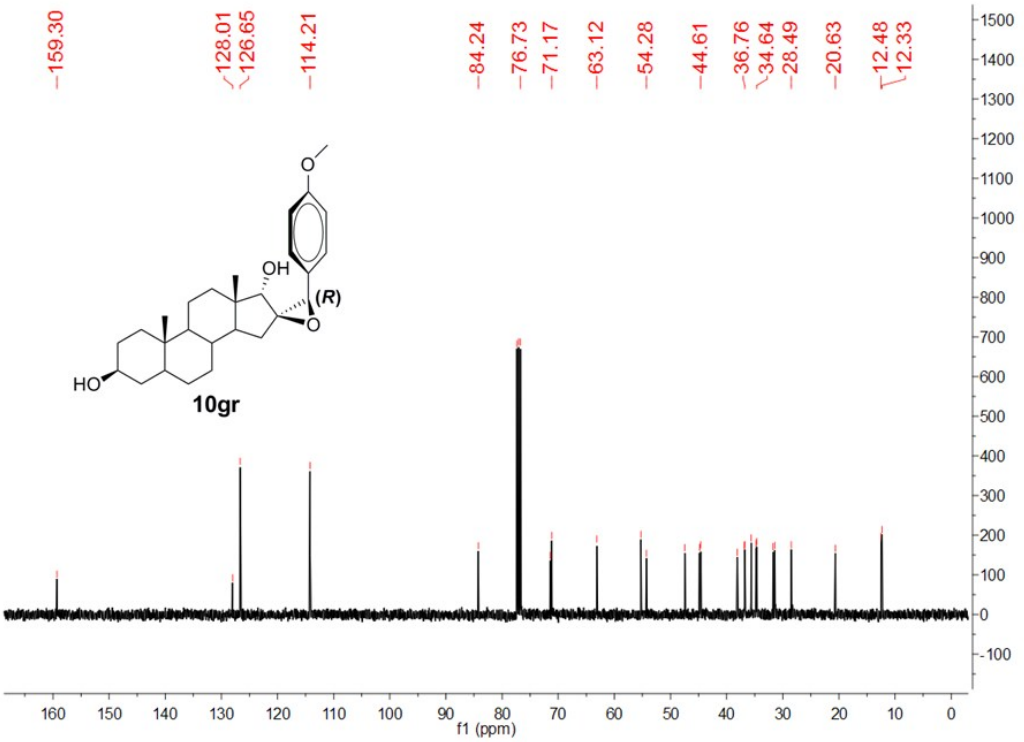
(3′*R*,16*R*)-3β-Hydroxy-3′-phenyl-16-spiro-2′-oxiran-17α-androstanol (**9gr**):



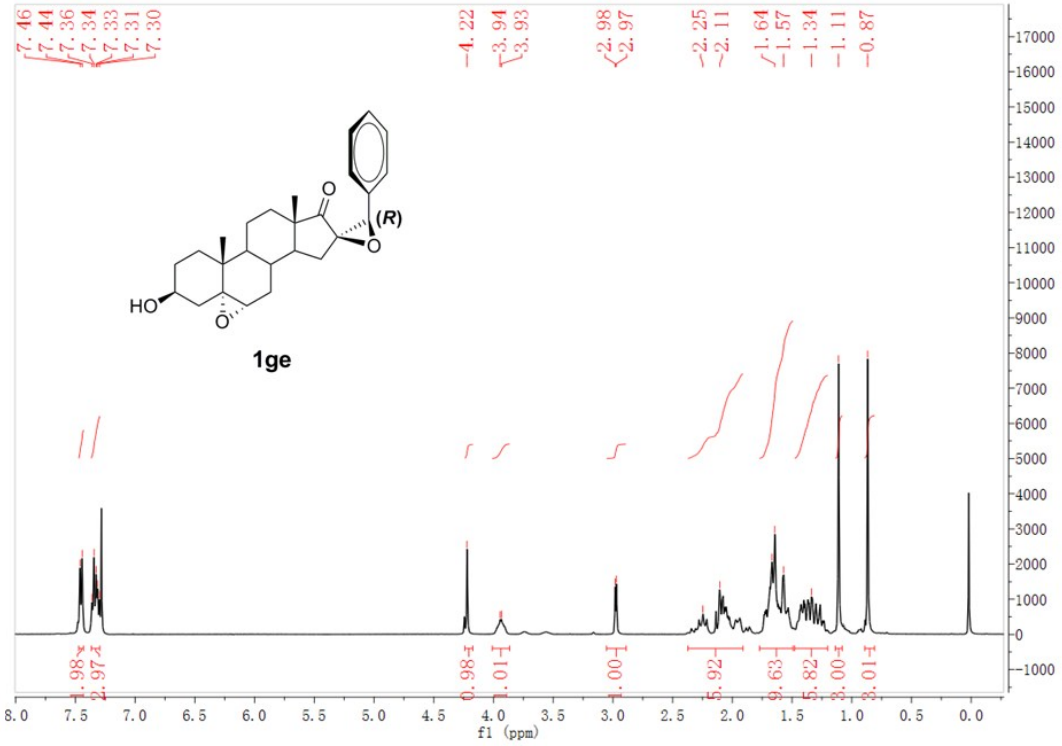


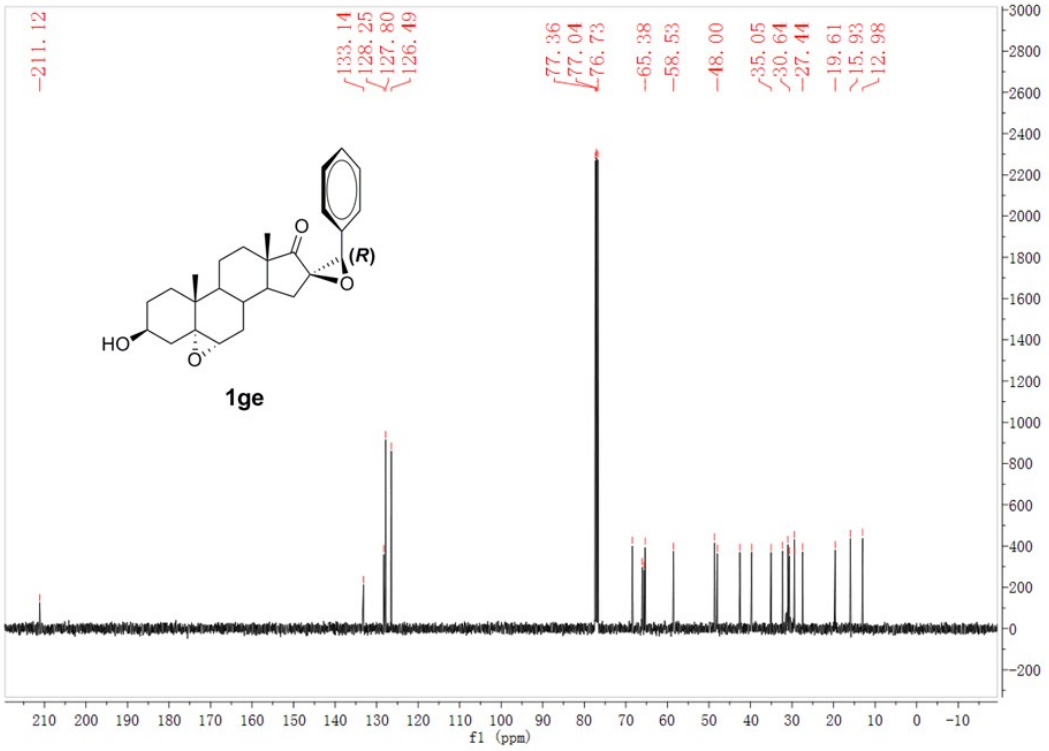
(3′*R*,16*R*)-3β-Hydroxy-3′-(4-methoxyphenyl)-16-spiro-2′-oxiran-17α-androstanol (**10gr**):



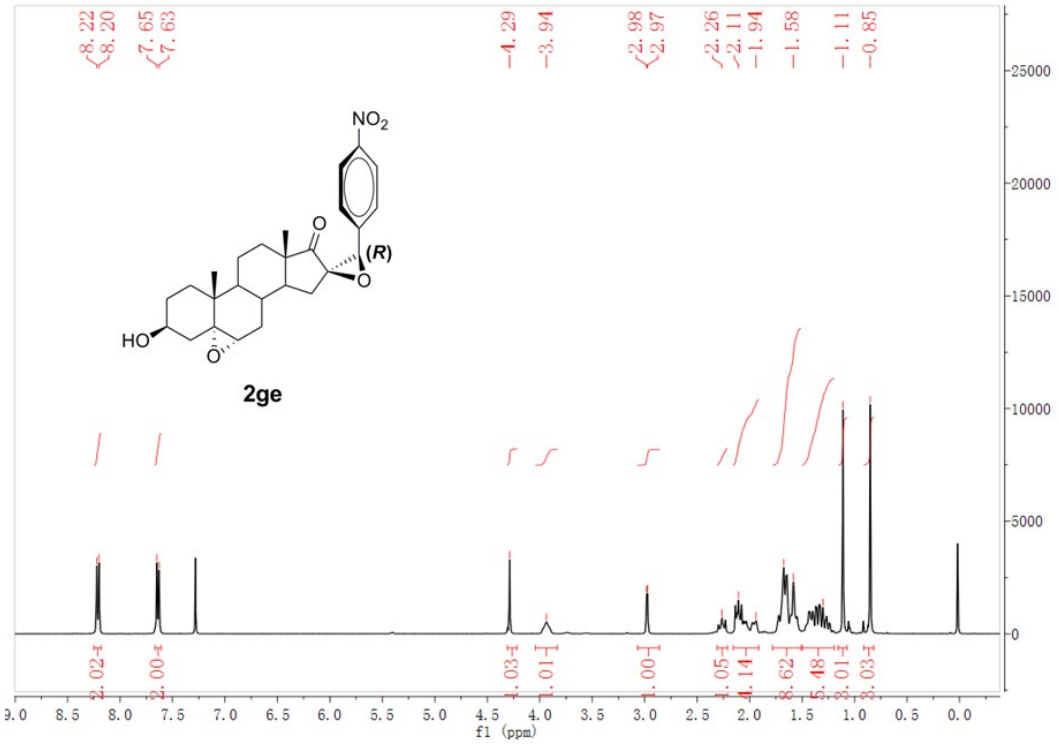


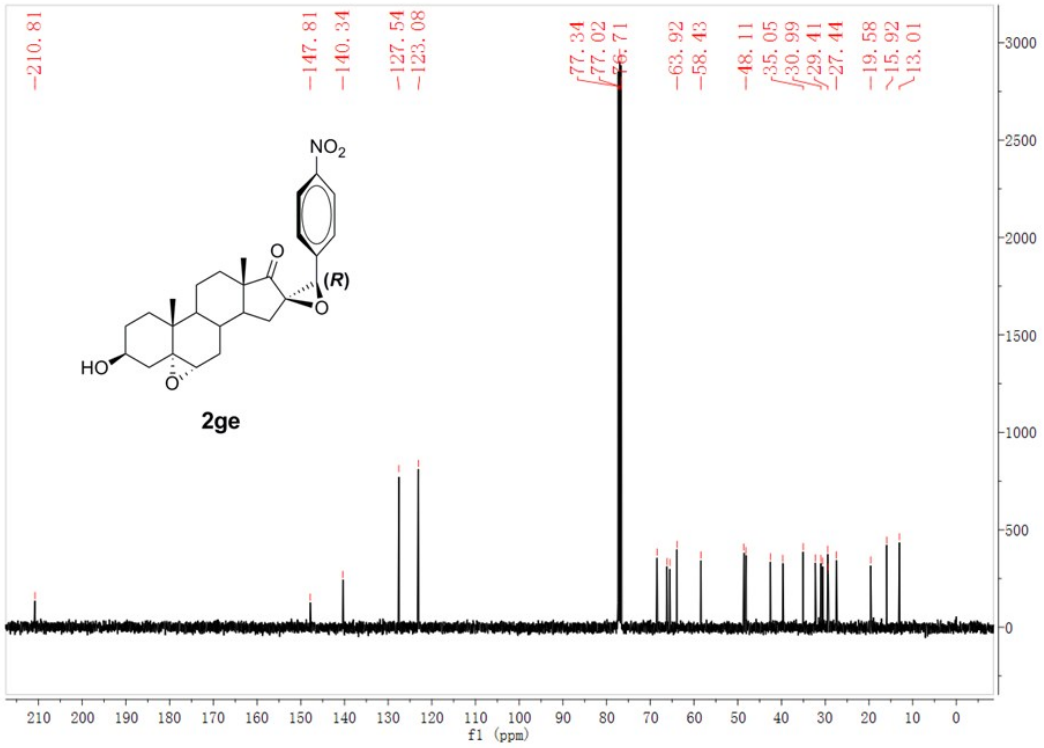
(3′*R*,16*R*)-3β-Hydroxy-5α,6α-epoxy-3′-phenyl-5-androstene-16-spiro-2′-oxiran-17-one (**1ge**):



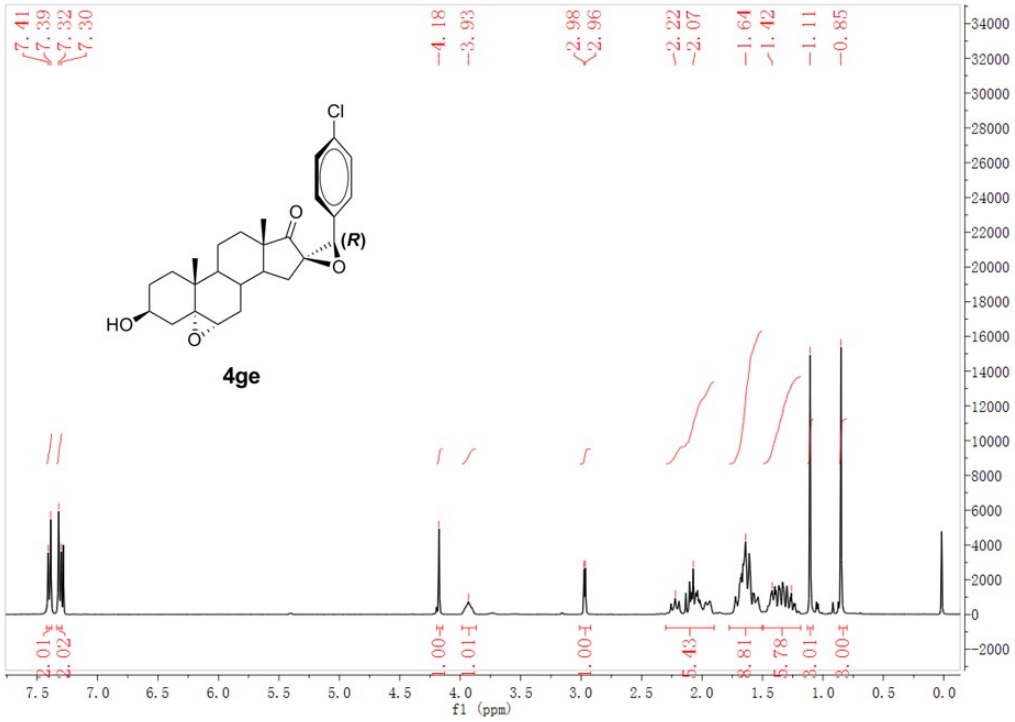


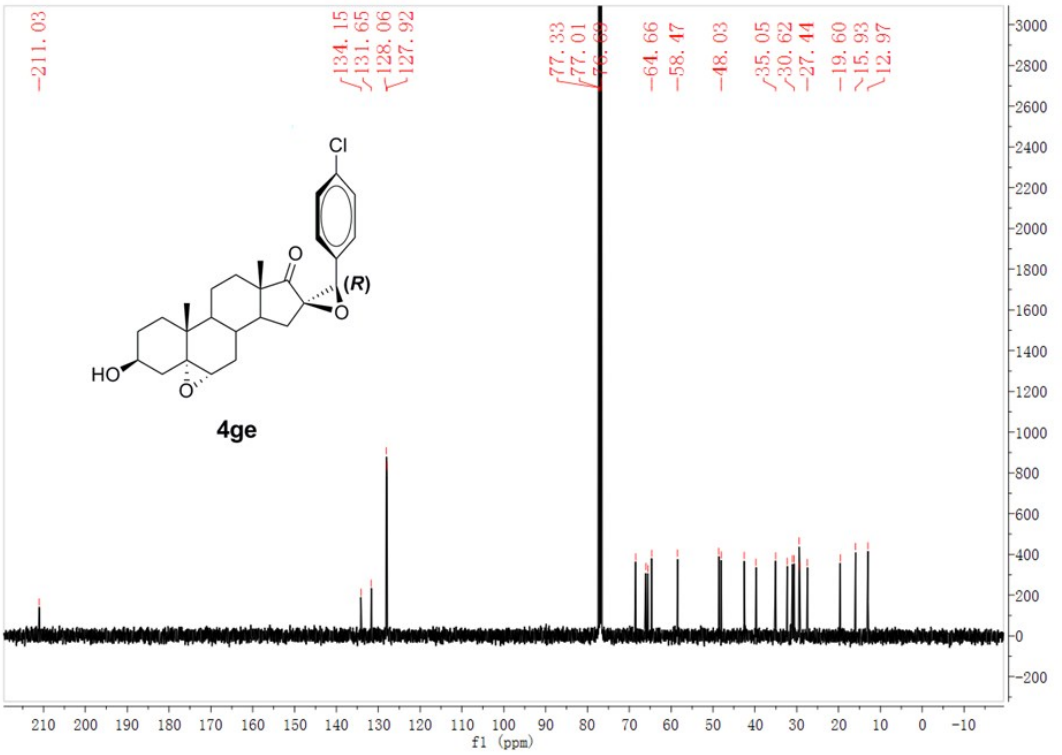
(3′*R*,16*R*)-3β-Hydroxy-5α,6α-epoxy-3′-(4-nitrophenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**2ge**):



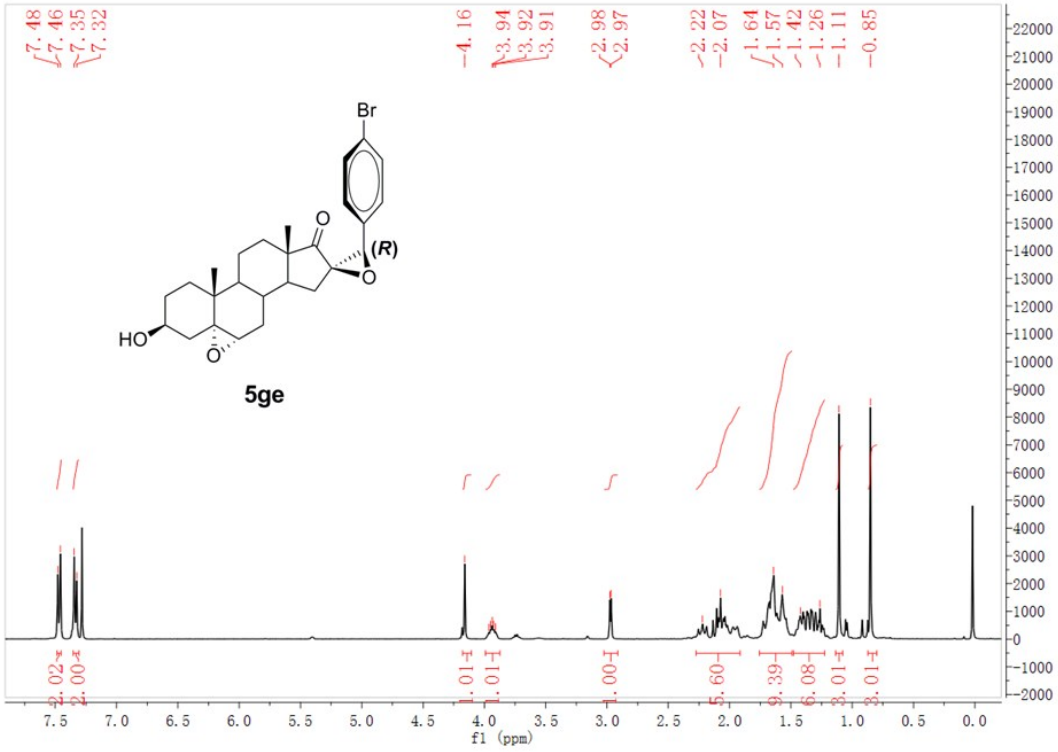


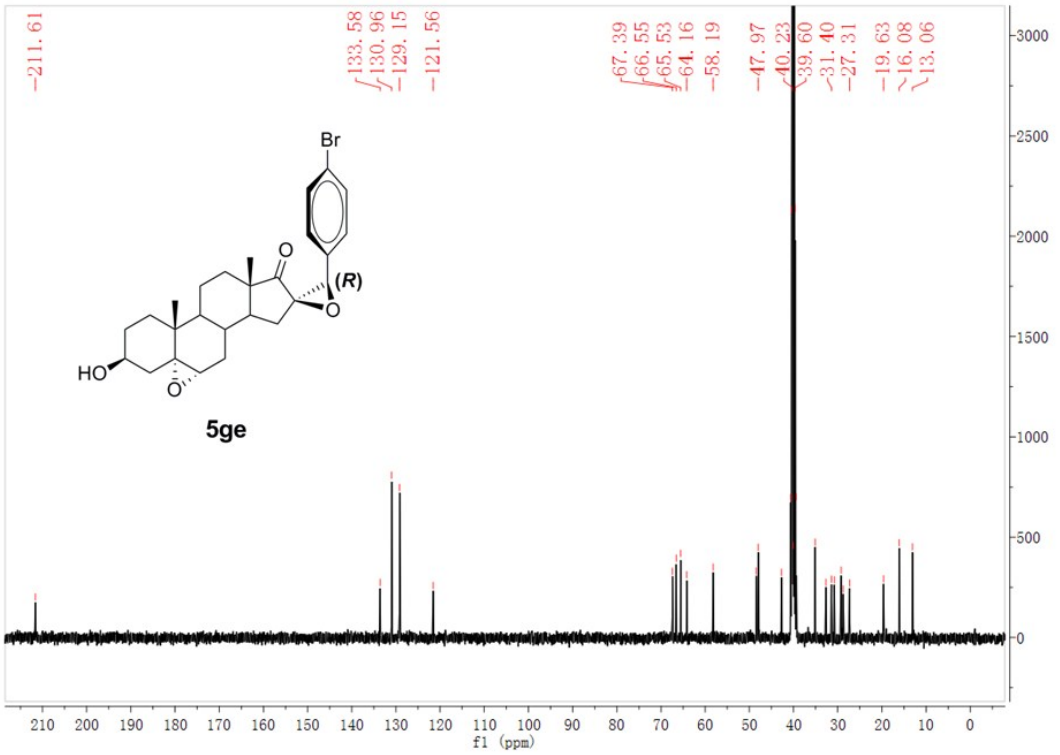
(3′*R*,16*R*)-3β-Hydroxy-5α,6α-epoxy-3′-(4-chlorophenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**4ge**):



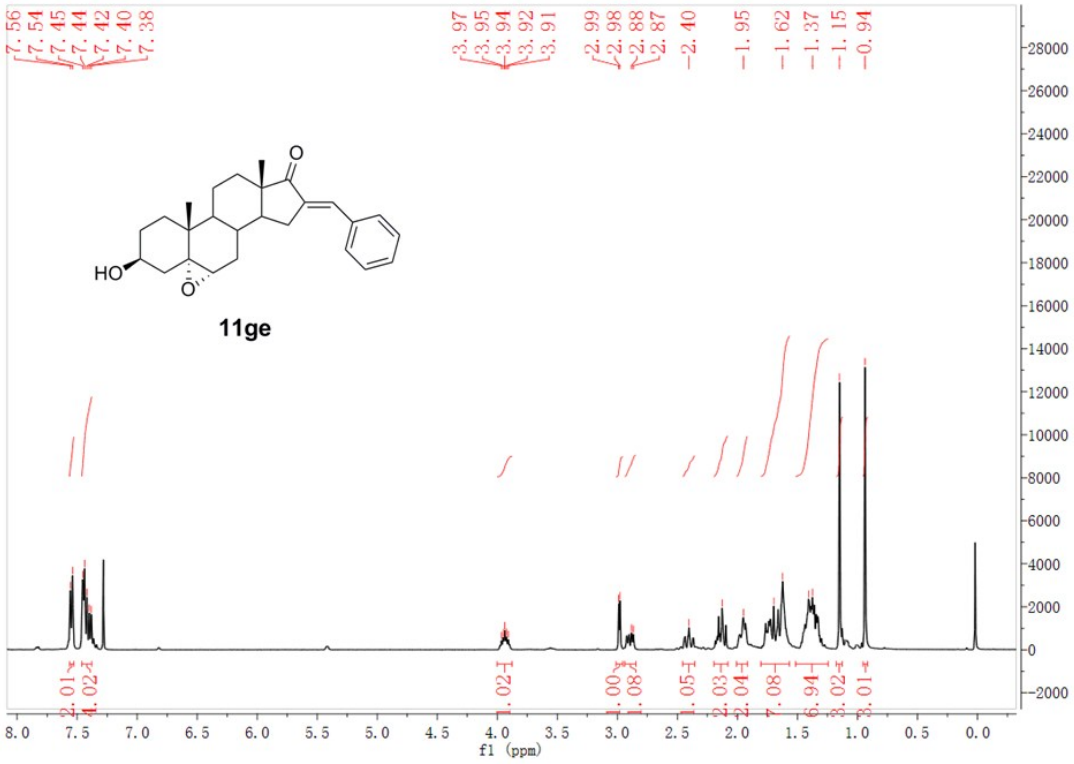


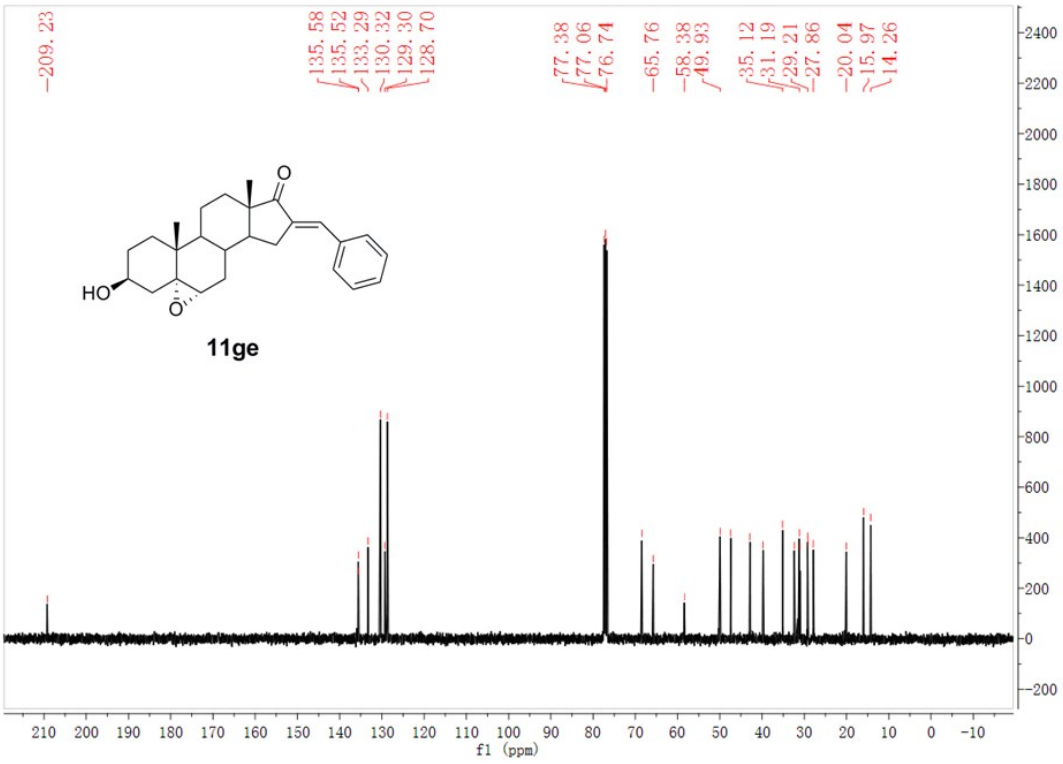
(3′*R*,16*R*)-3β-Hydroxy-5α,6α-epoxy-3′-(4-bromophenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**5ge**):





(16*E*)-Benzylidene-3β-hydroxy-5α,6α-epoxy-androstan-17-one (**11ge**):

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135.52
133.29
130.32
129.30
128.70
77.38
77.06
76.74
65.76
58.38
49.93
35.12
31.19
29.21
27.86
20.04
15.97
14.26
HO
O
O
11ge
f1 (ppm)