

Supplementary Material

Hydroxylation of progesterone and its derivatives by entomopathogenic strain *Isaria farinosa* KCh KW1.1

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17 α -hydroxyprogesterone (**4**): A) one-day transformation; B) three-day transformation; C) seven-day transformation; D) ten-day transformation; E) 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**); F) 12 β ,17 α -dihydroxyprogesterone (**9**); G) 6 β ,17 α -dihydroxyprogesterone (**8**); H) 17 α -hydroxyprogesterone (**4**)

Figure.S41. Thin layer chromatography showing the products of biotransformation

17 α -hydroxyprogesterone (**4**): A) one-day transformation; B) three-day transformation; C) seven-day transformation; D) ten-day transformation; E) 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**); F) 12 β ,17 α -dihydroxyprogesterone (**9**); G) 6 β ,17 α -dihydroxyprogesterone (**8**); H) 17 α -hydroxyprogesterone (**4**)

Figure.S42. Thin layer chromatography showing the products of biotransformation

17 α -hydroxyprogesterone (**4**): A) one-day transformation; B) three-day transformation; C) seven-day transformation; D) ten-day transformation; E) 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**); F) 12 β ,17 α -dihydroxyprogesterone (**9**); G) 6 β ,17 α -dihydroxyprogesterone (**8**); H) 17 α -hydroxyprogesterone (**4**)

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Figure.S44. Thin layer chromatography showing the products of biotransformation

16 α ,17 α -epoxyprogesterone (**5**): A) one-day transformation; B) three-day transformation; C) 16 α ,17 α -epoxyprogesterone (**5**); D) seven-day transformation; E) ten-day transformation

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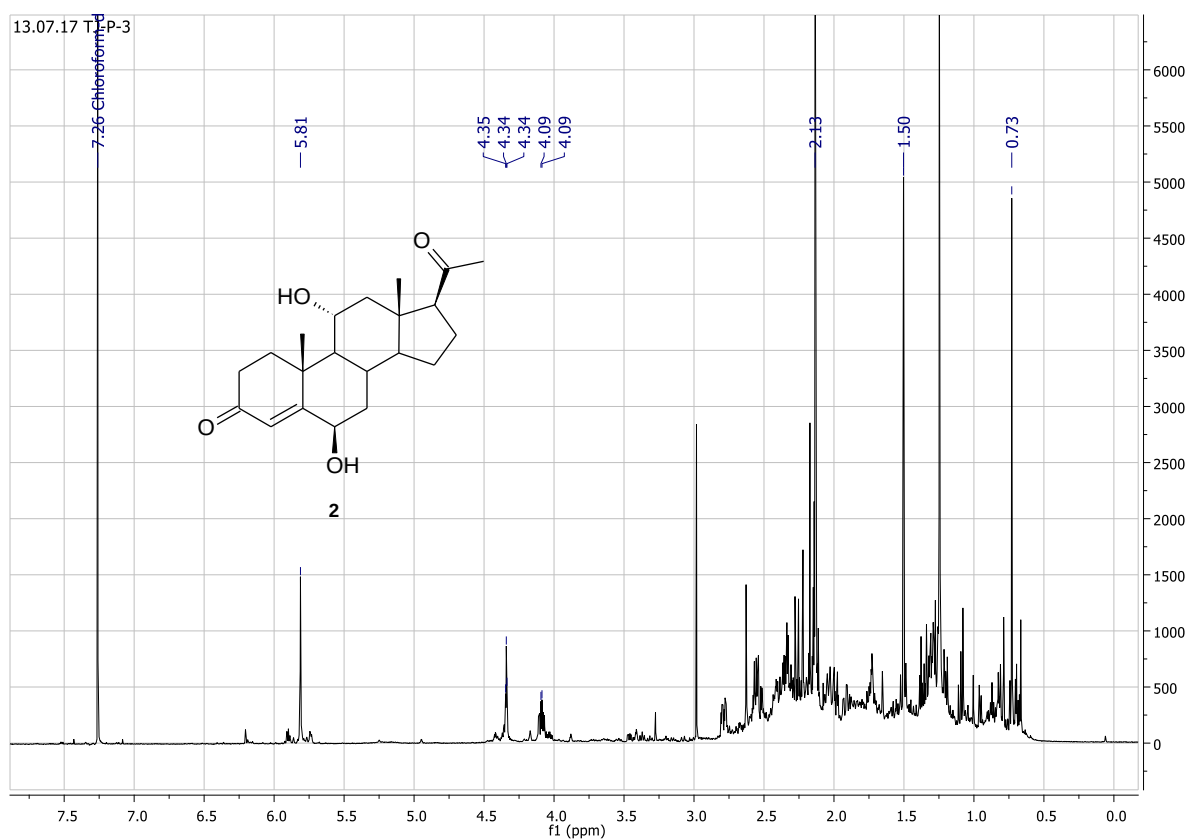


Figure.S1. ¹H NMR spectral of 6β,11α-dihydroxyprogesterone (2) (CDCl₃, 600 MHz)

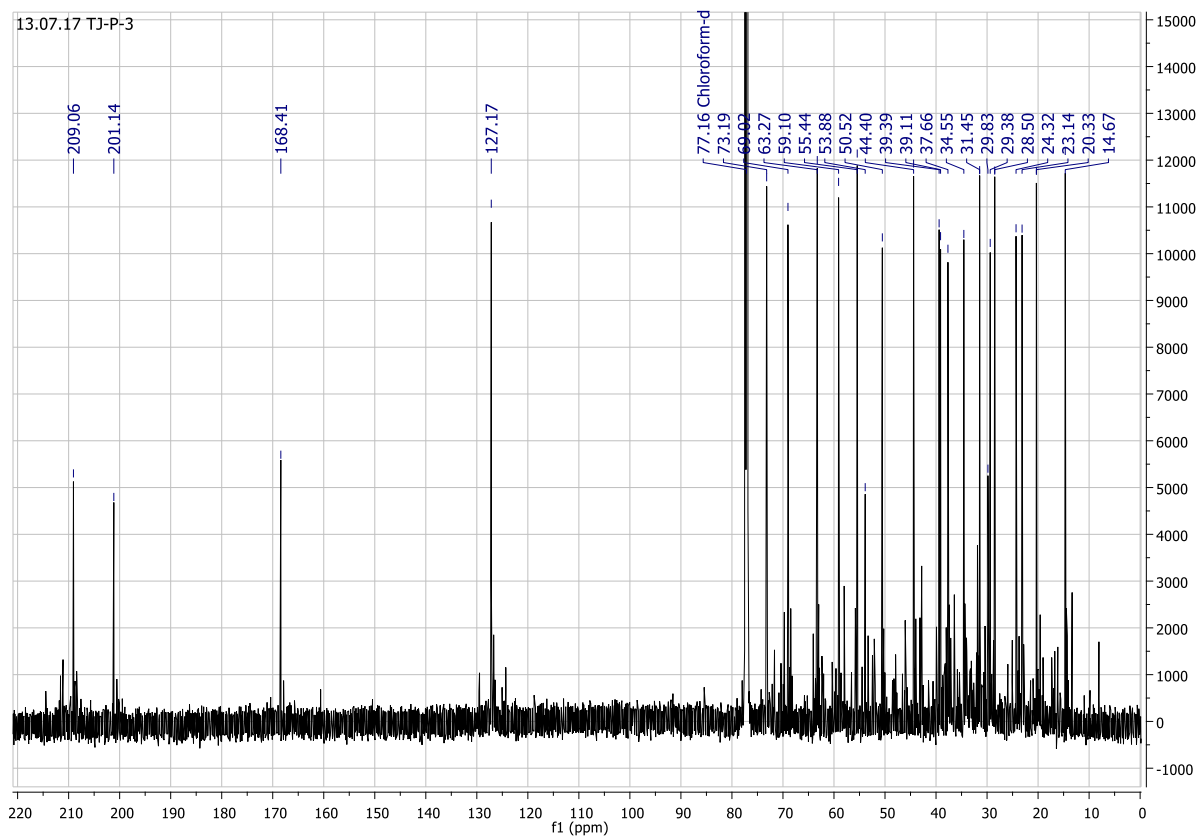


Figure.S2. ¹³C NMR spectral of 6β,11α-dihydroxyprogesterone (2) (CDCl₃, 151 MHz)

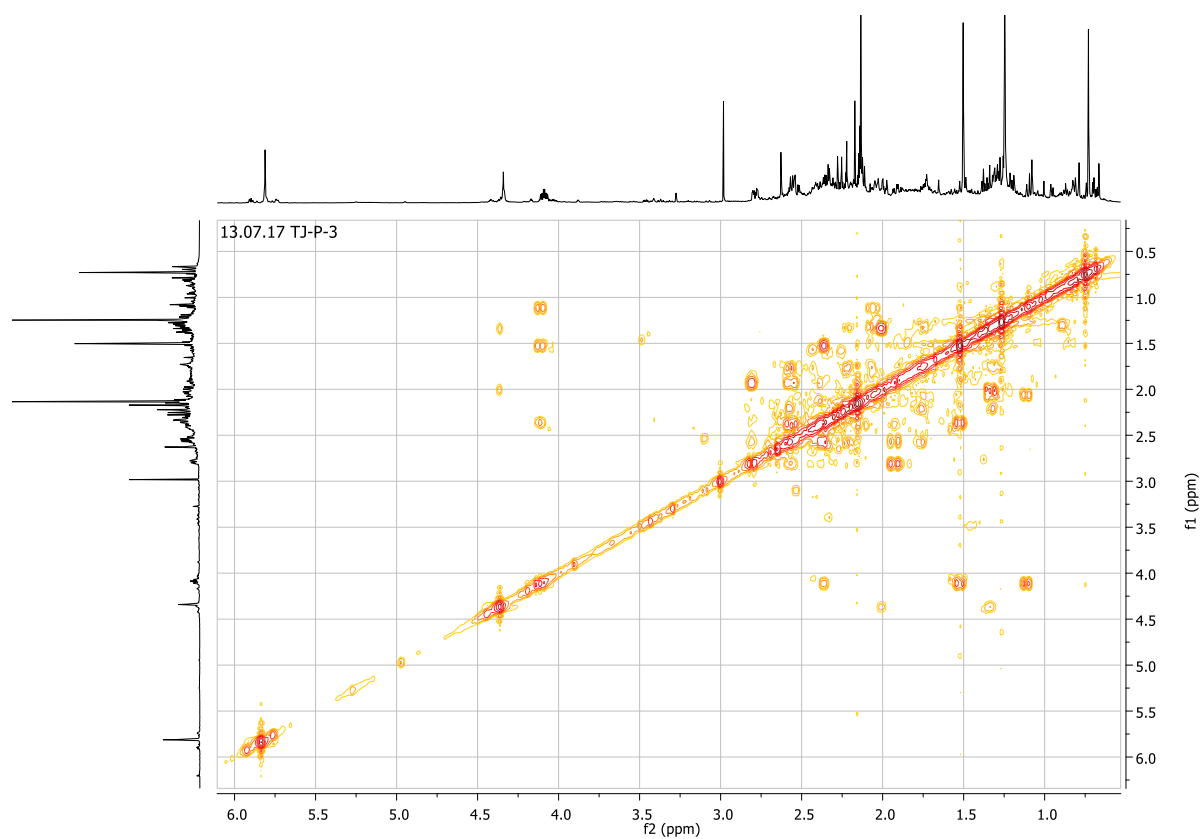


Figure.S3. COSY spectral of 6 β ,11 α -dihydroxyprogesterone (**2**) (CDCl₃, 600 MHz)

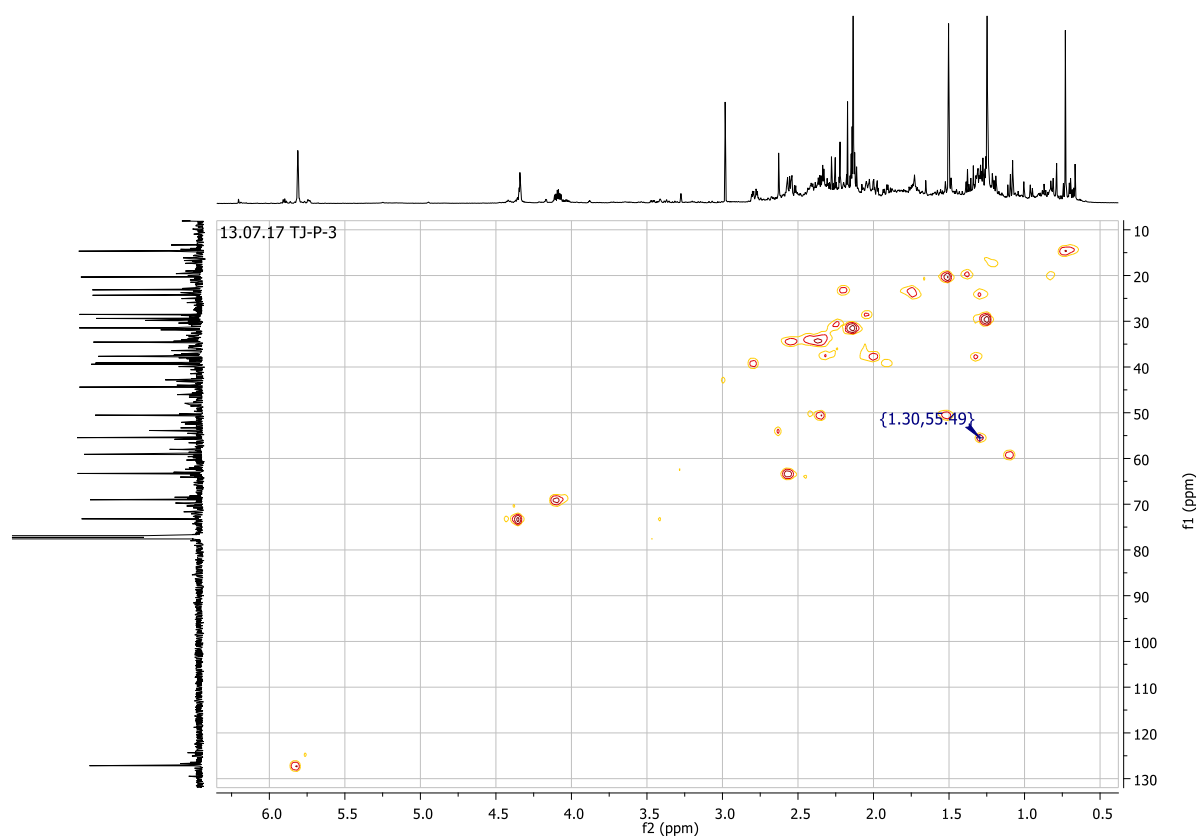


Figure.S4. HSQC spectral of 6 β ,11 α -dihydroxyprogesterone (**2**) (CDCl₃, 151 MHz)

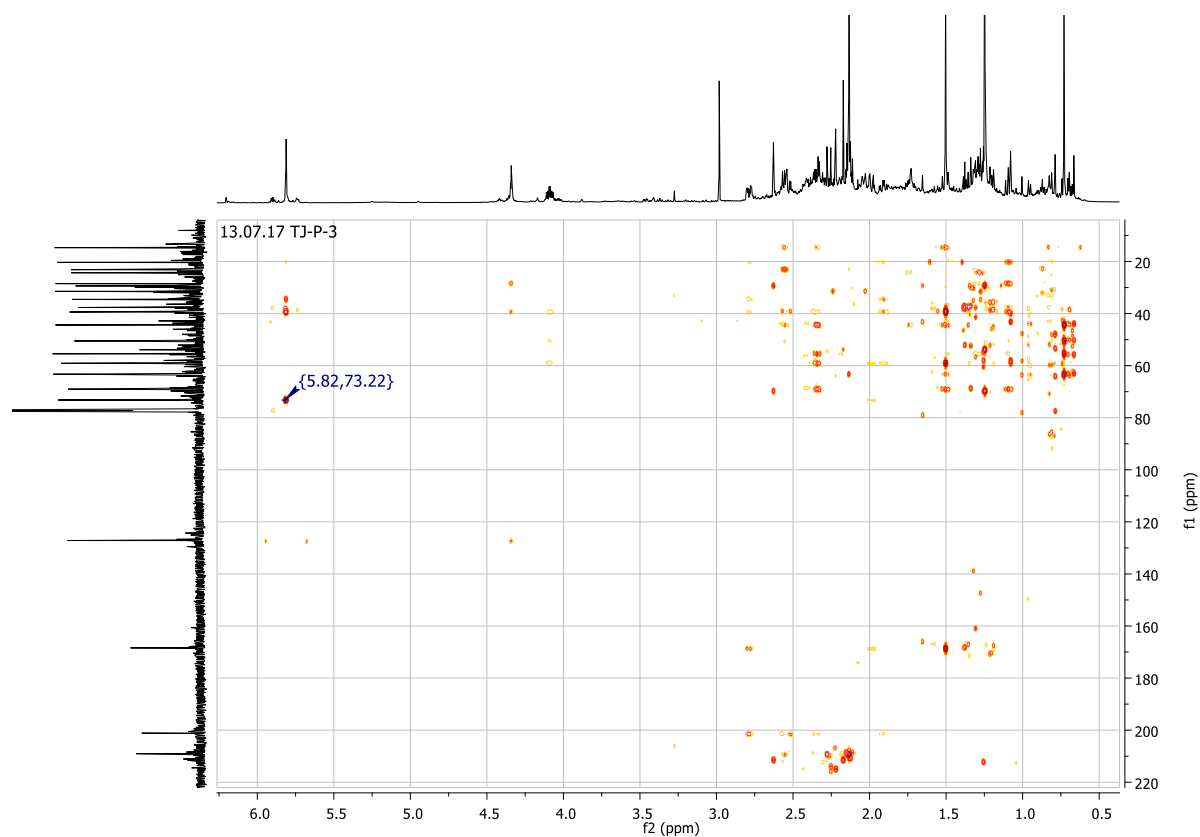


Figure.S5. HMBC spectral of 6 β ,11 α -dihydroxyprogesterone (2) (CDCl₃, 151 MHz)

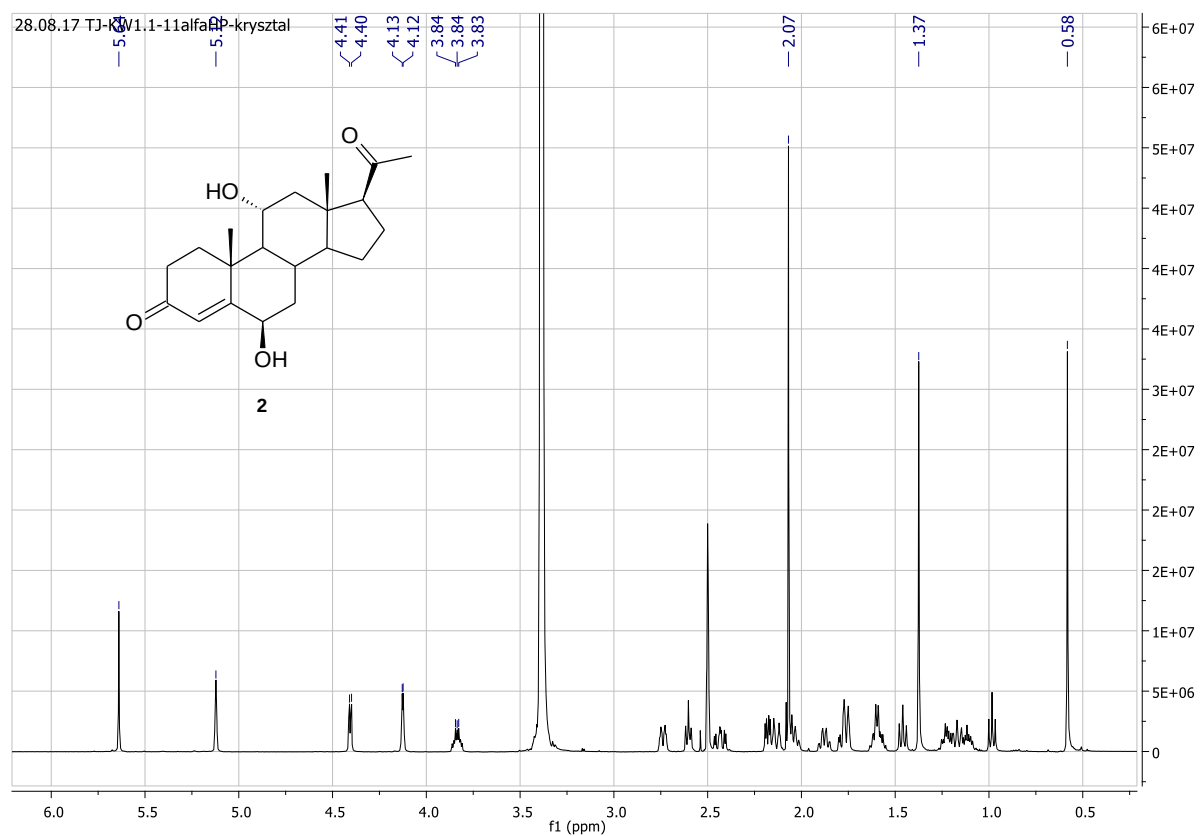


Figure.S6. ¹H NMR spectral of 6 β ,11 α -dihydroxyprogesterone (2) (DMSO-*d*₆, 600 MHz)

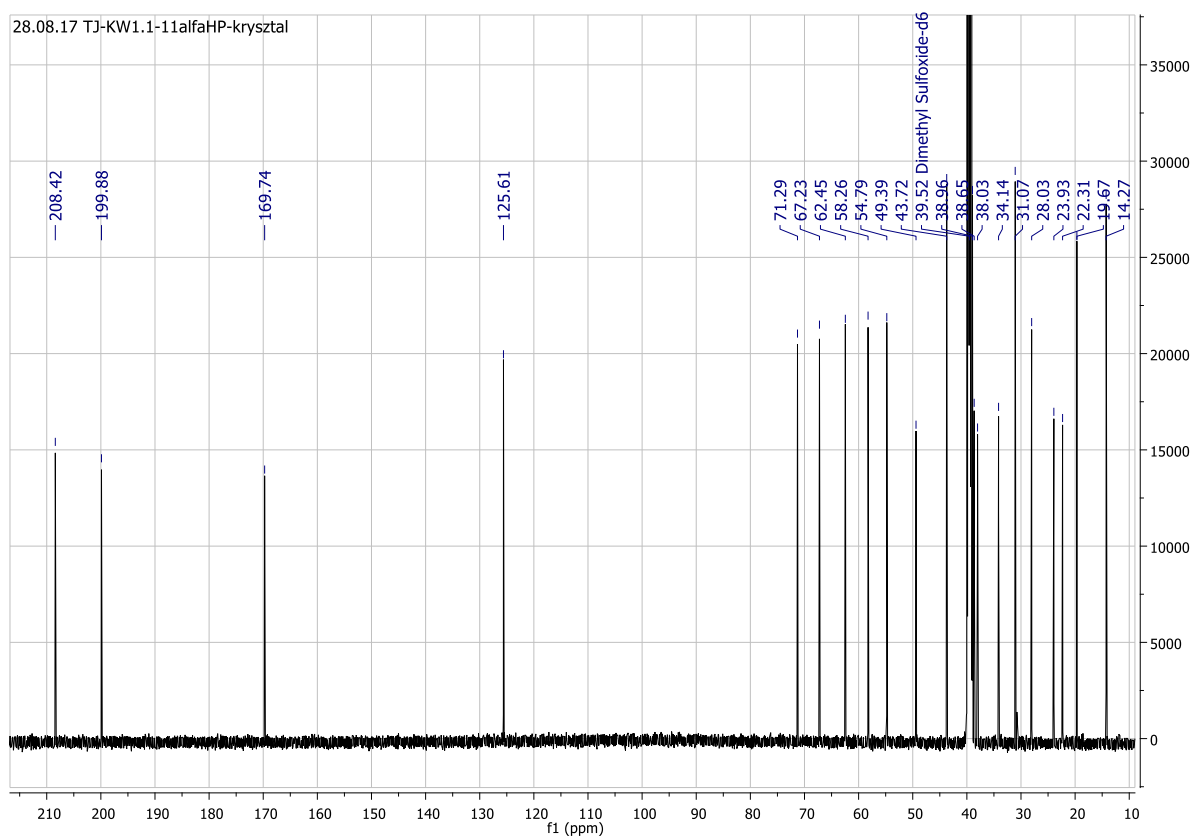


Figure.S7. ^{13}C NMR spectral of $6\beta,11\alpha$ -dihydroxyprogesterone (**2**) ($\text{DMSO}-d_6$, 600 MHz)

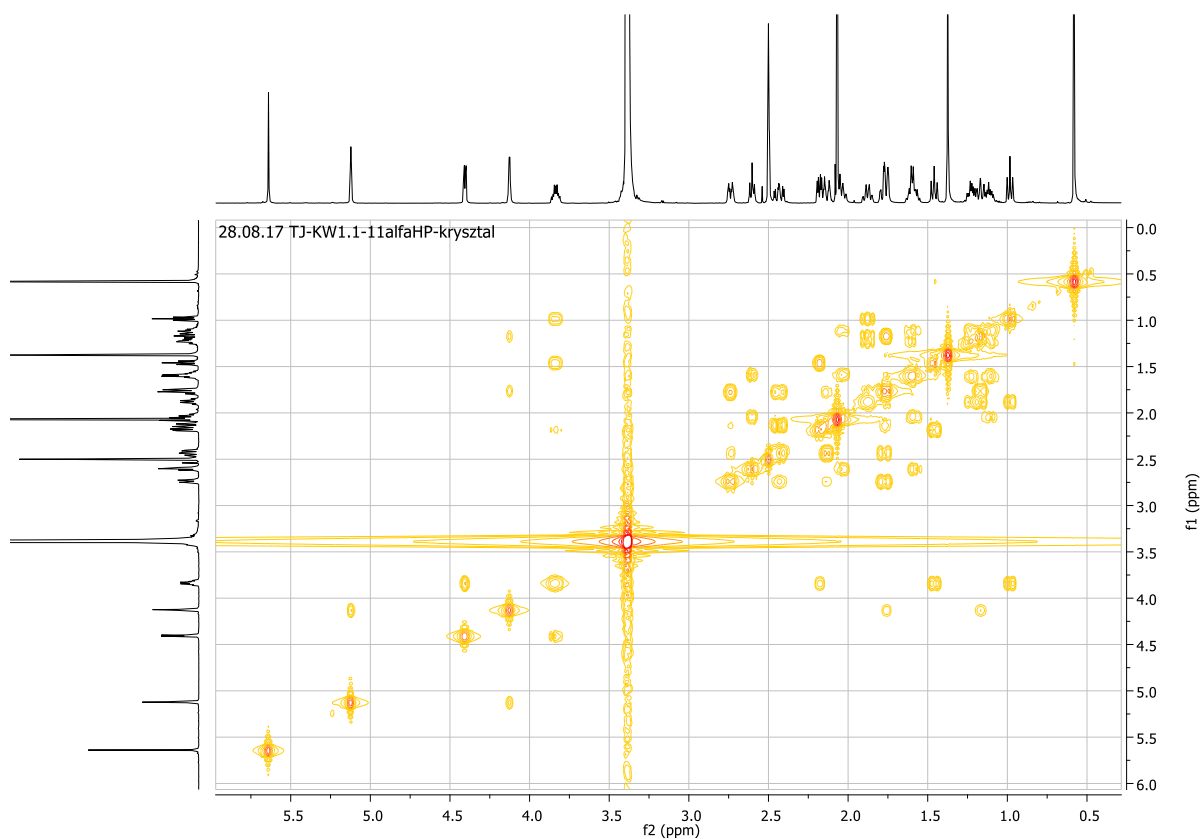


Figure.S8. COSY spectral of $6\beta,11\alpha$ -dihydroxyprogesterone (**2**) ($\text{DMSO}-d_6$, 600 MHz)

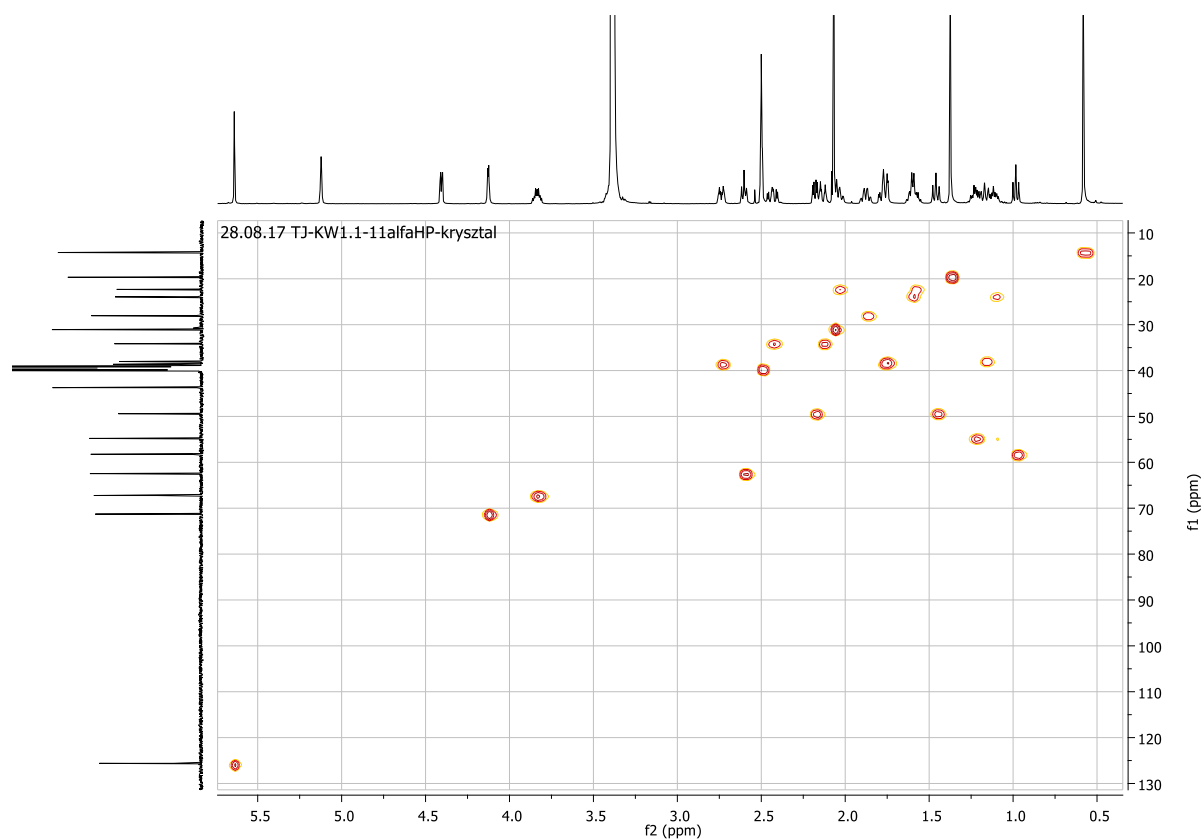


Figure.S9. HSQC spectral of 6 β ,11 α -dihydroxyprogesterone (**2**) (DMSO- d_6 , 600 MHz)

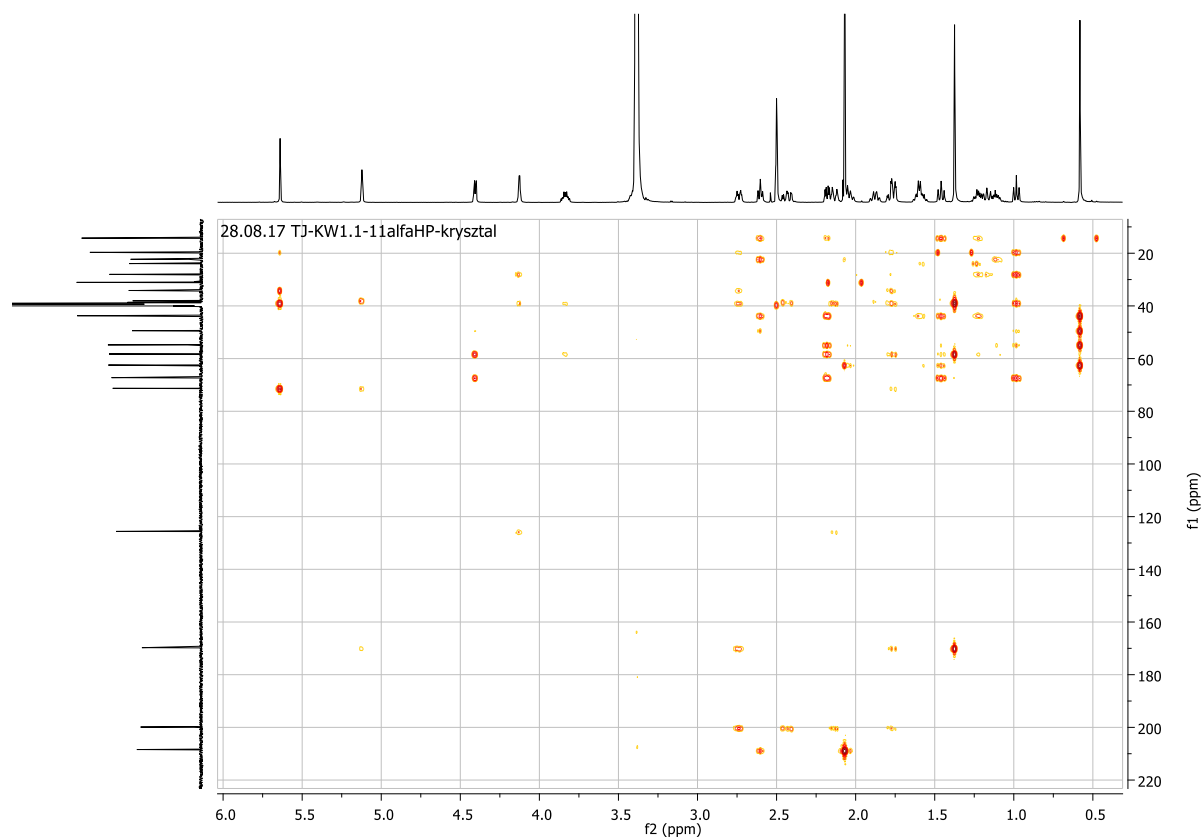


Figure.S10. HMBC spectral of 6 β ,11 α -dihydroxyprogesterone (**2**) (DMSO- d_6 , 600 MHz)

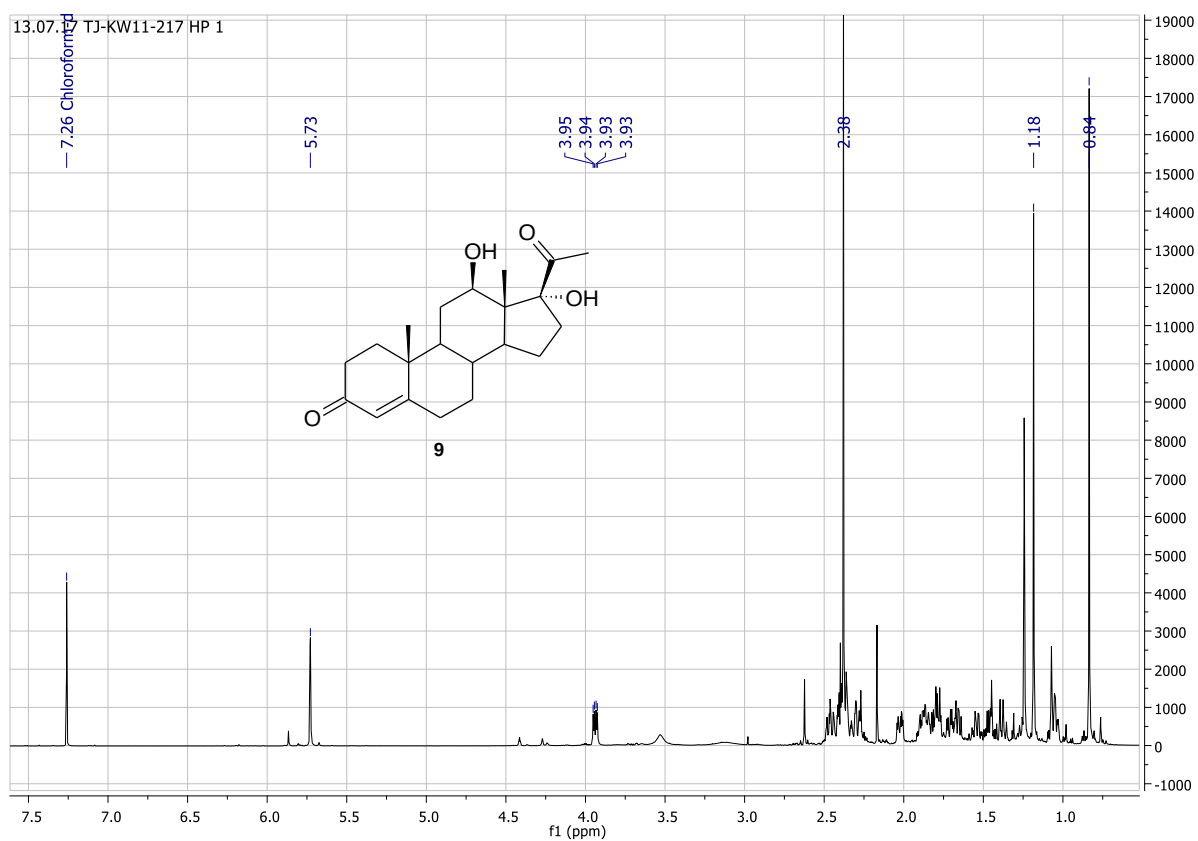


Figure.S11. ^1H NMR spectral of 12 β ,17 α -dihydroxyprogesterone (**9**) (CDCl_3 , 600 MHz)

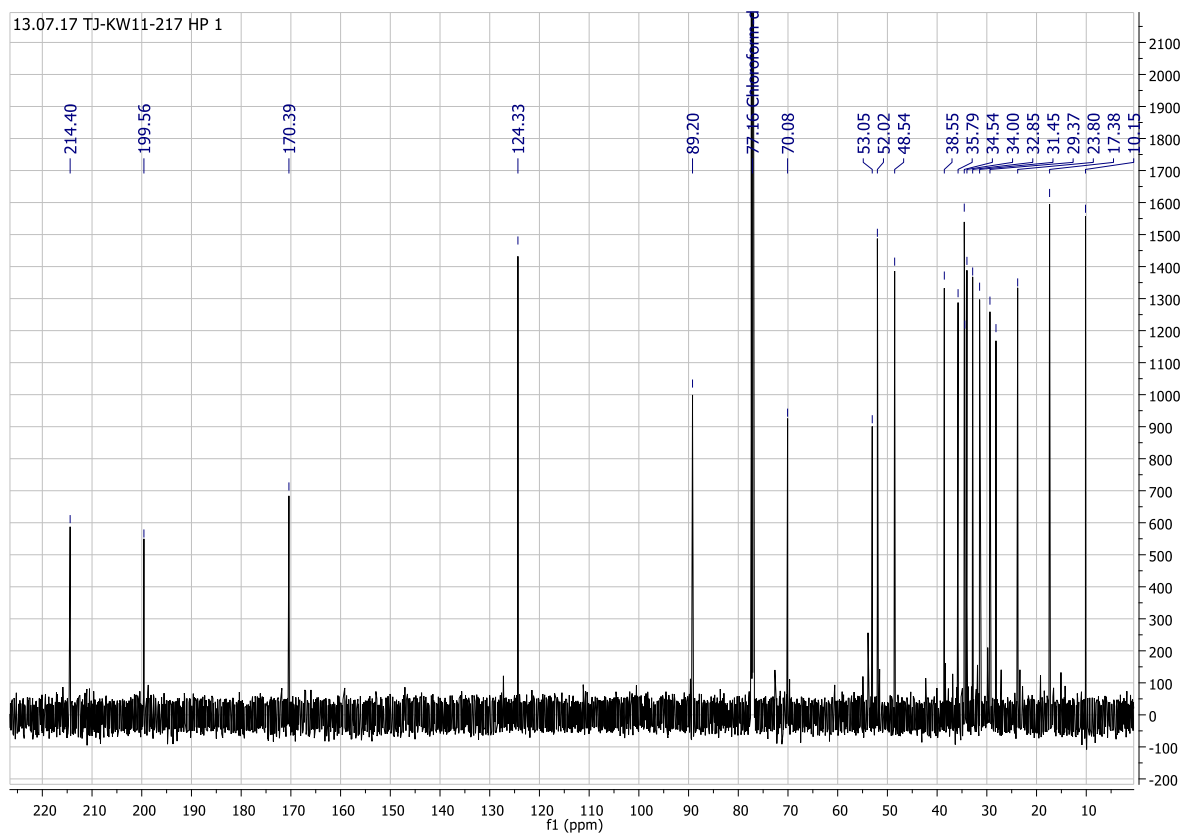


Figure.S12. ^{13}C NMR spectral of 12 β ,17 α -dihydroxyprogesterone (**9**) (CDCl_3 , 151 MHz)

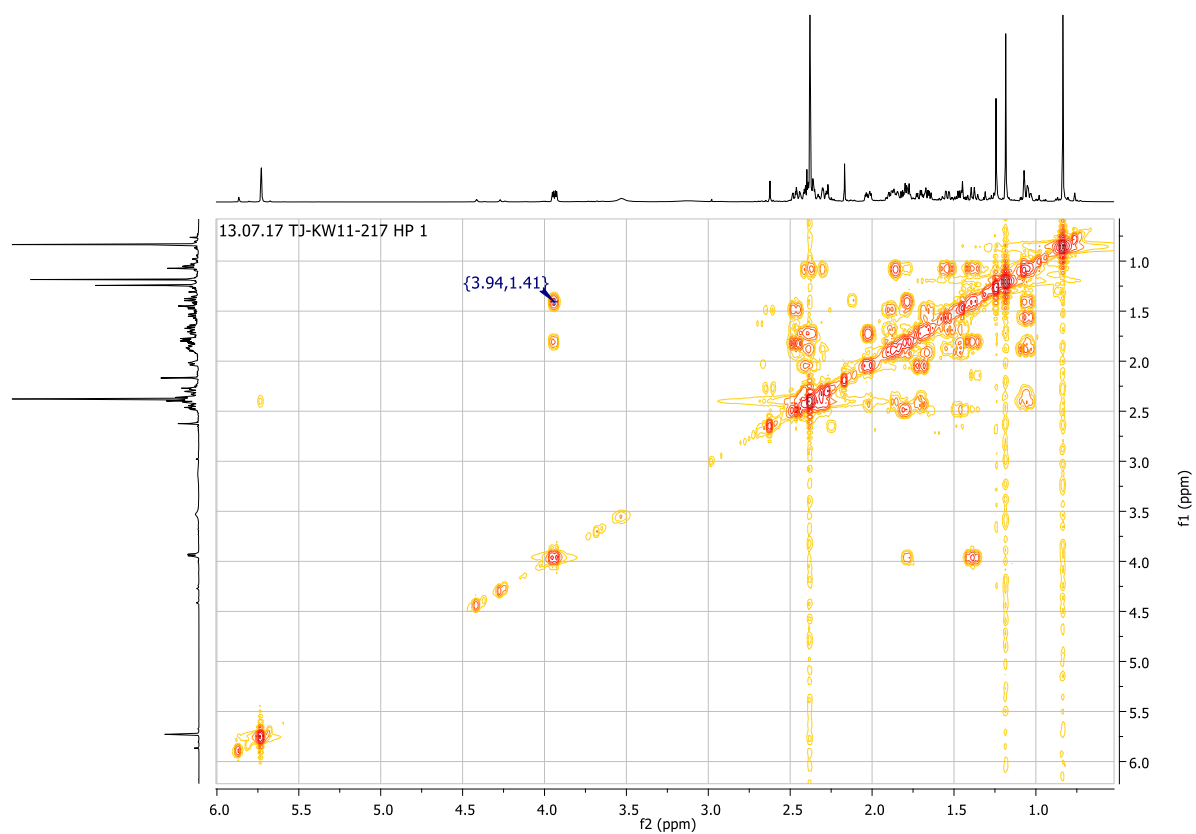


Figure.S13. COSY spectral of 12 β ,17 α -dihydroxyprogesterone (**9**) (CDCl₃, 600 MHz)

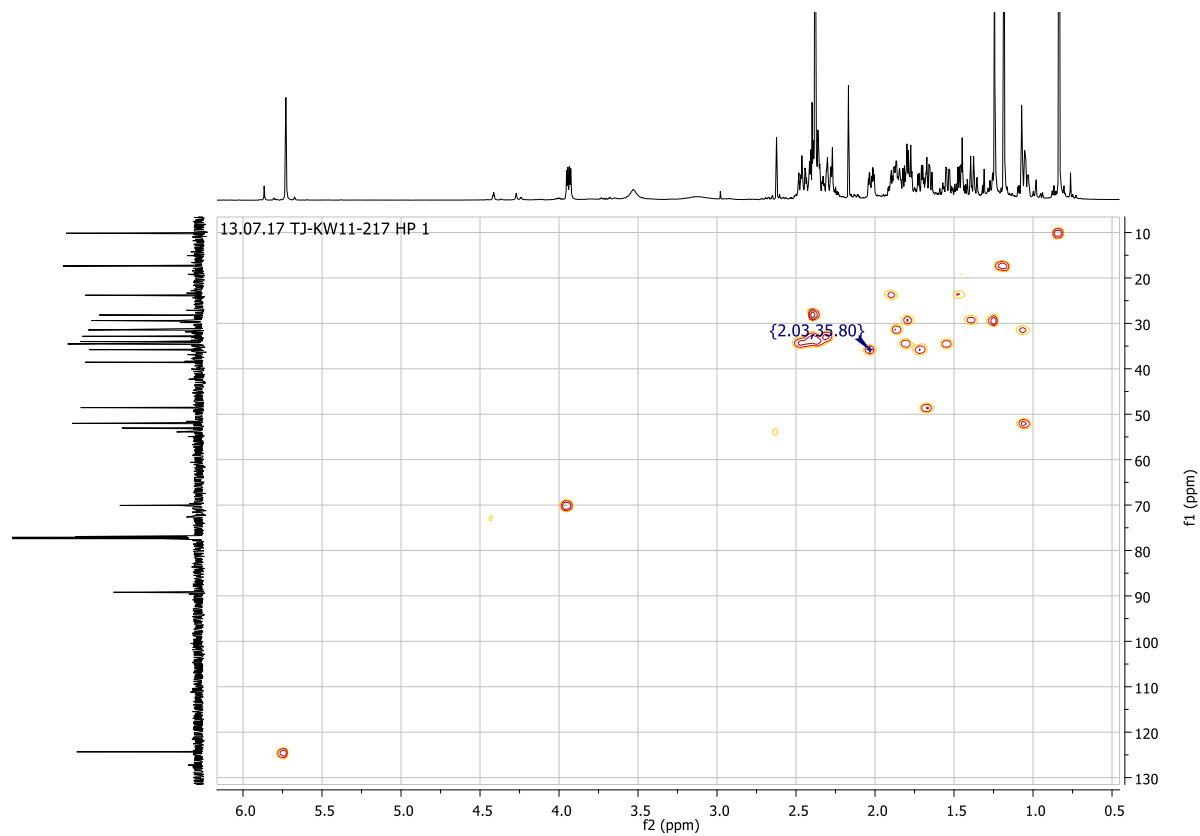


Figure.S14. HSQC spectral of 12 β ,17 α -dihydroxyprogesterone (**9**) (CDCl₃, 151 MHz)

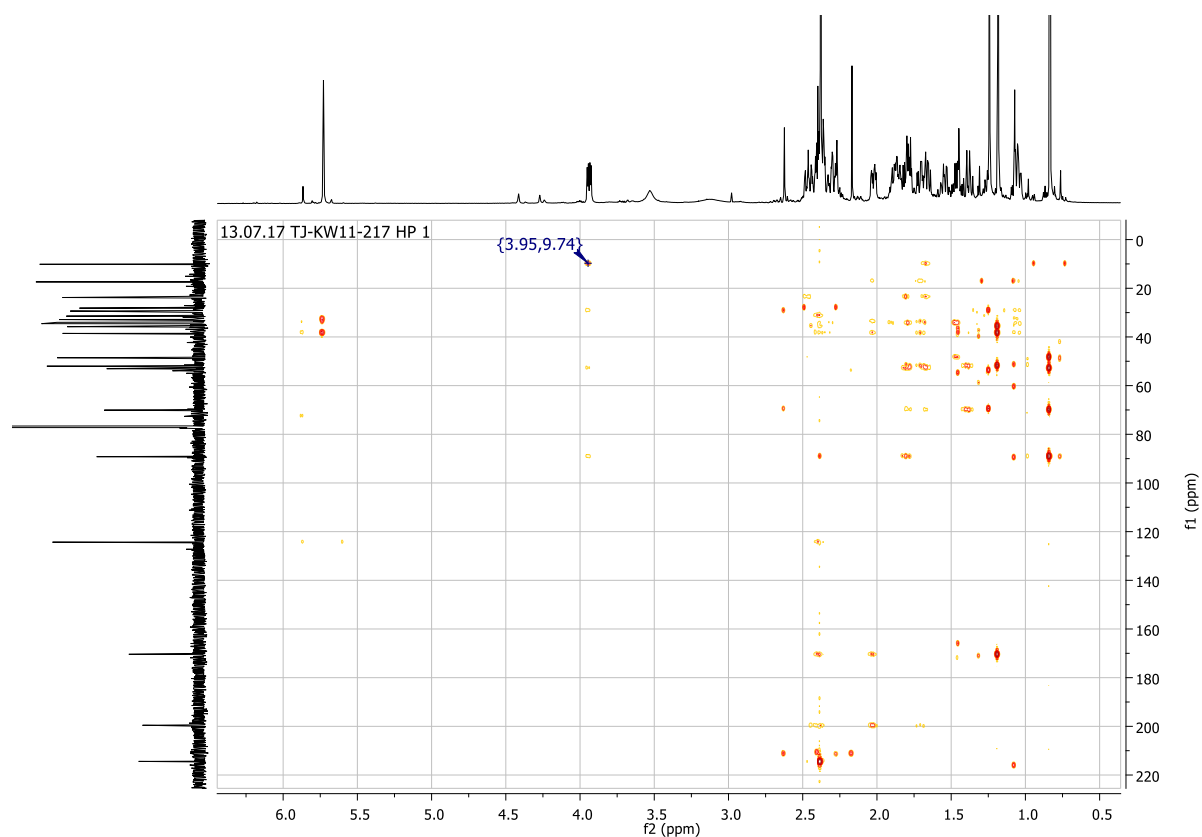


Figure.S15. HMBC spectral of 12 β ,17 α -dihydroxyprogesterone (**9**) (CDCl₃, 151 MHz)

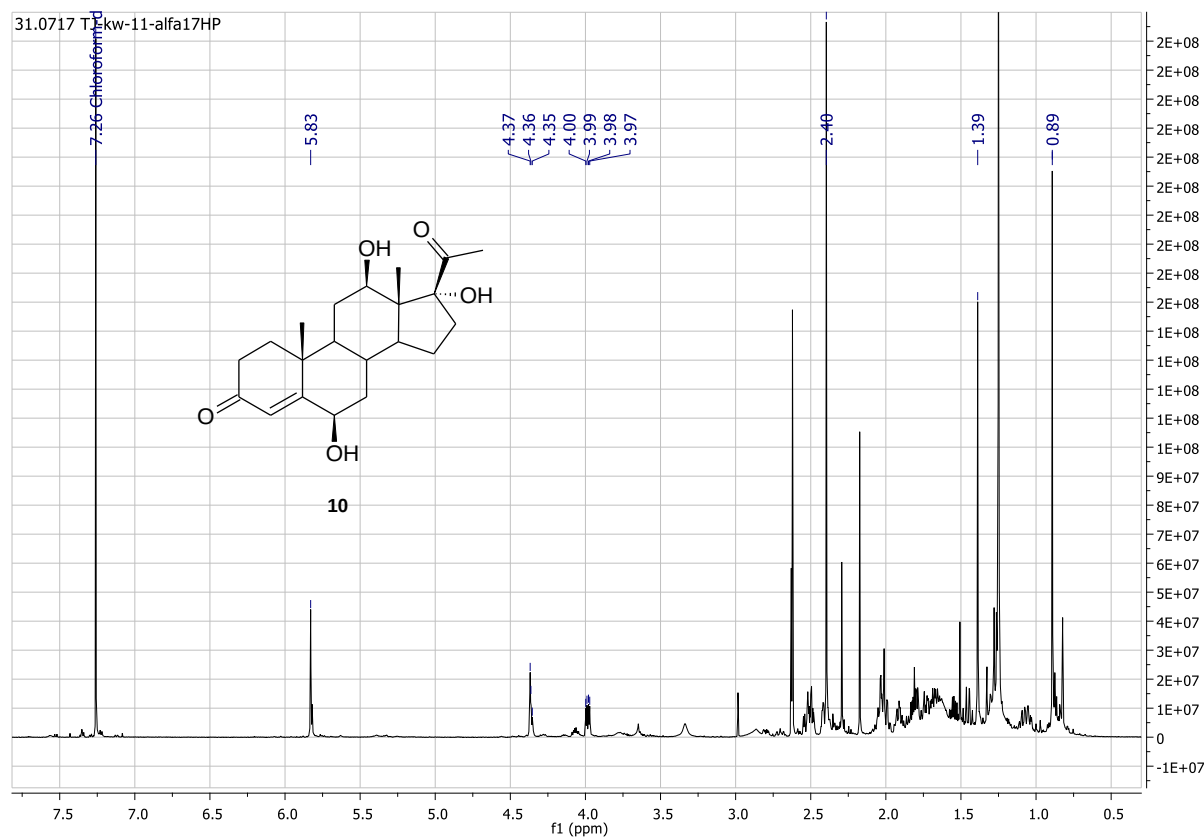


Figure.S16. ¹H NMR spectral of 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**) (CDCl₃, 600 MHz)

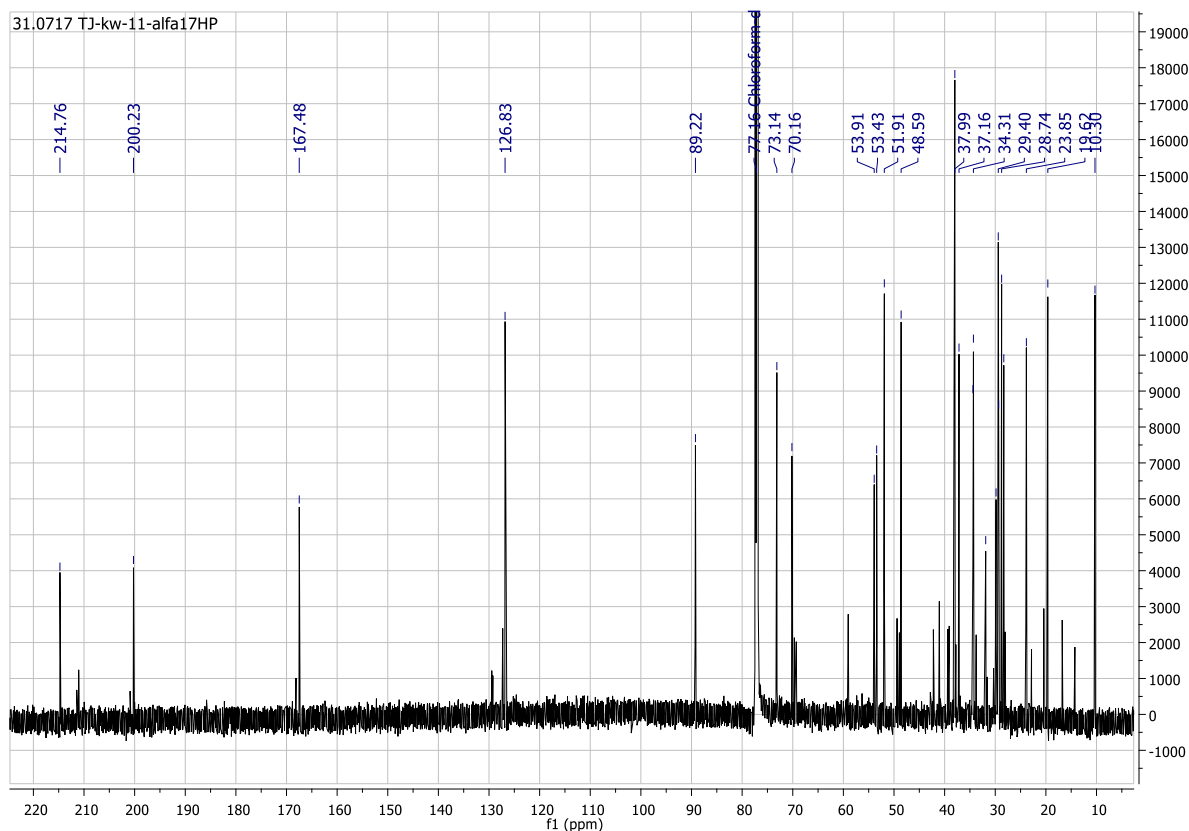


Figure.S17. ¹³C NMR spectral of 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**) (CDCl₃, 151 MHz)

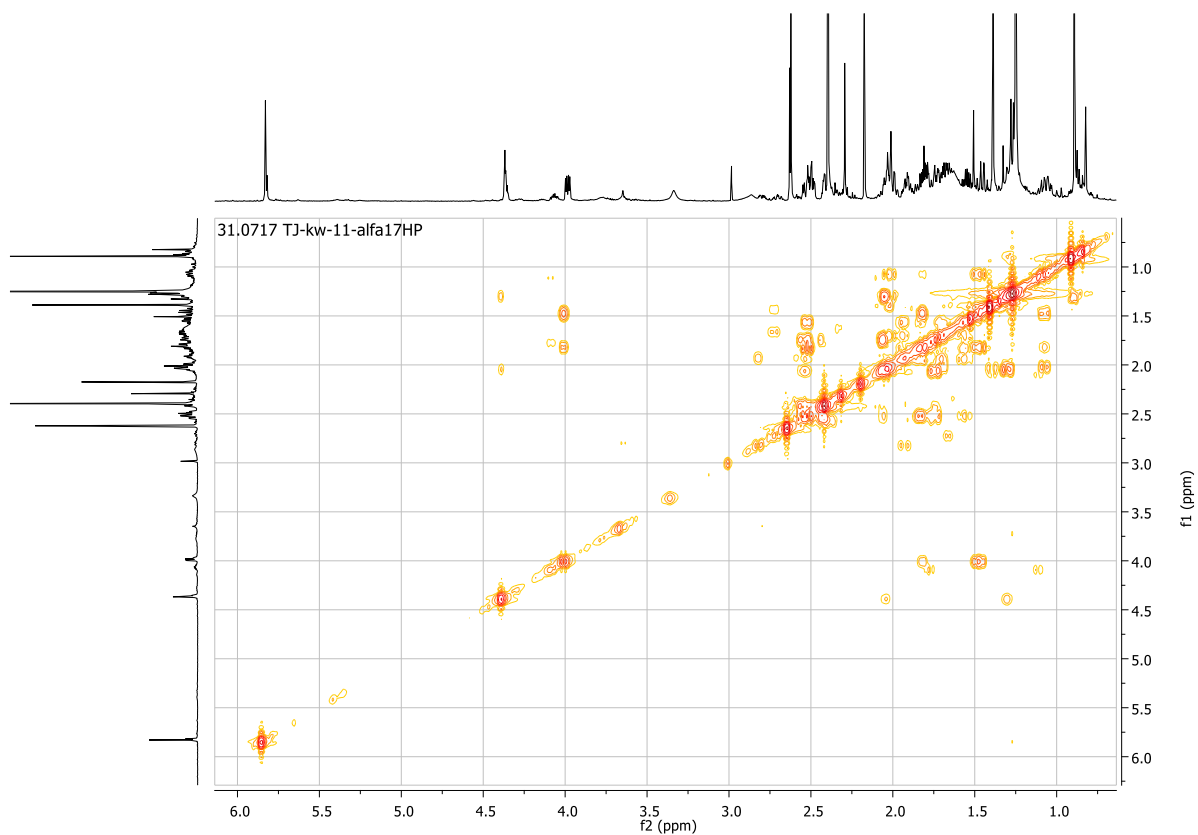


Figure.S18. COSY spectral of 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**) (CDCl₃, 600 MHz)

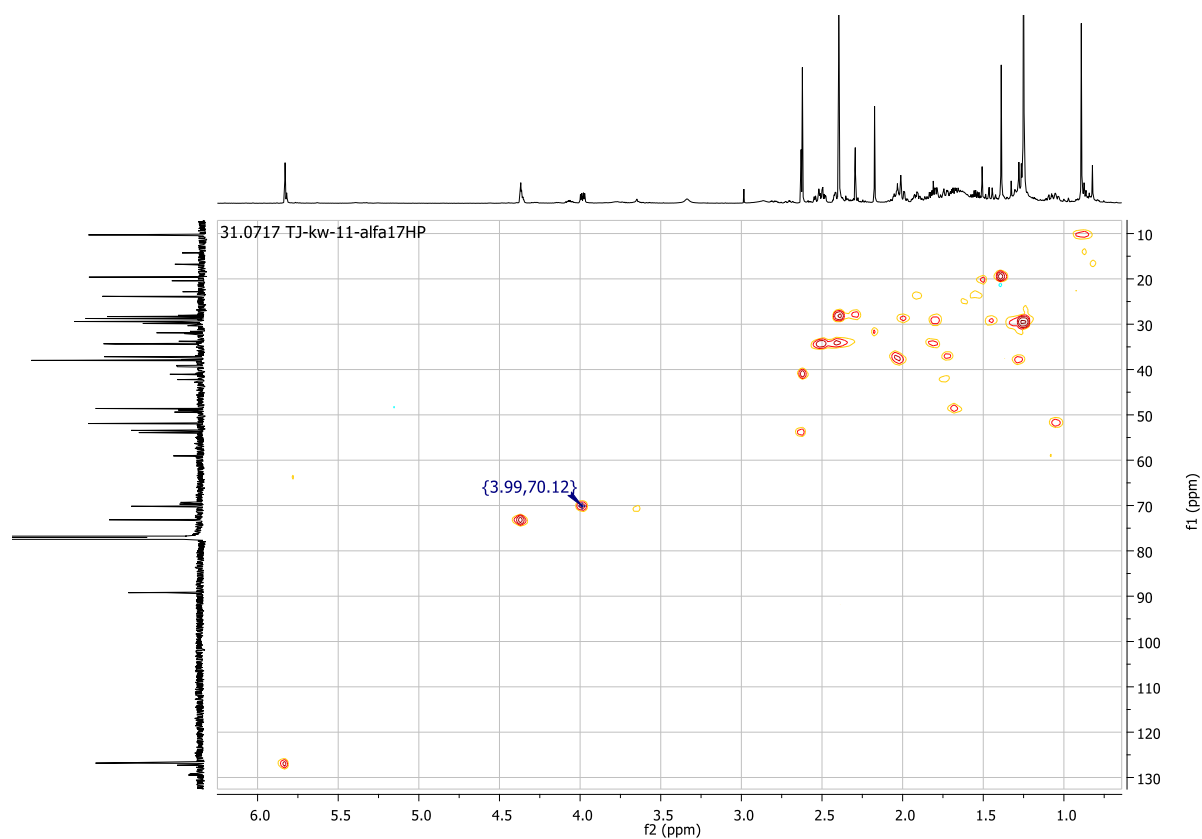


Figure.S19. HSQC spectral of 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**) (CDCl₃, 151 MHz)

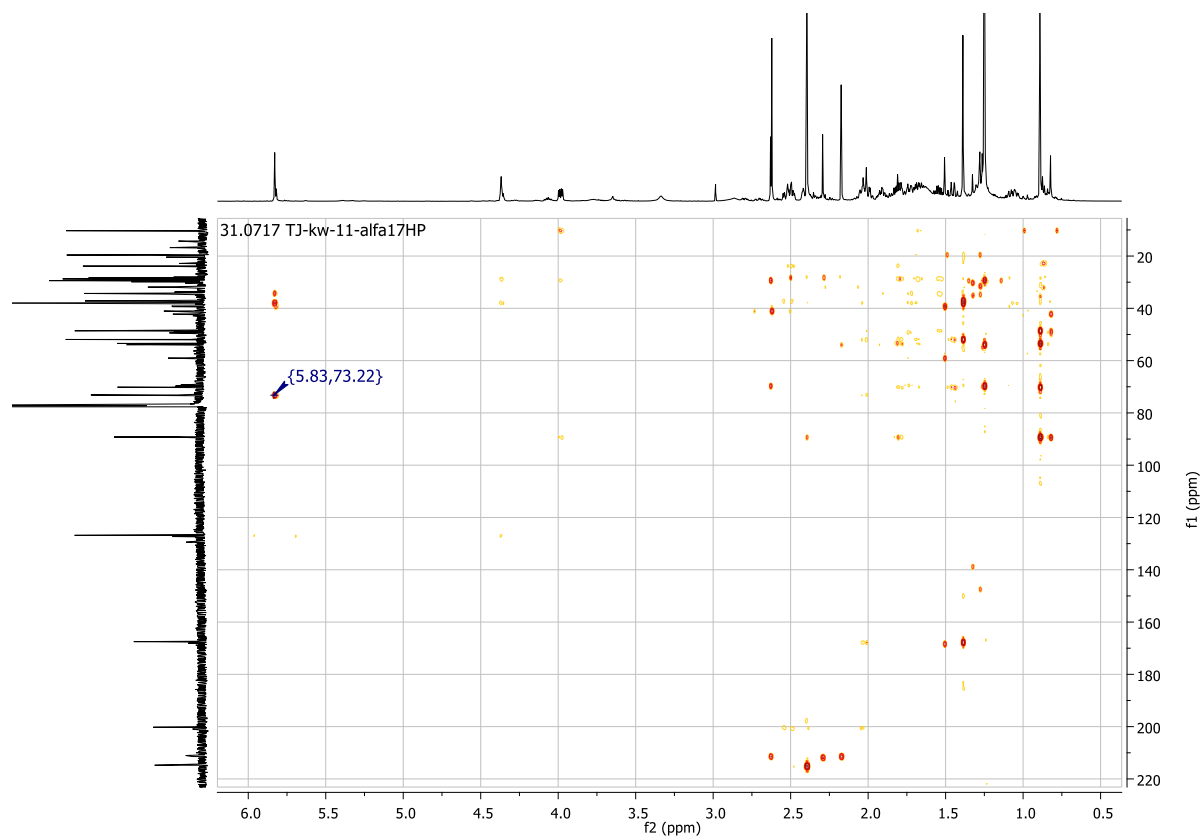


Figure.S20. HMBC spectral of 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**) (CDCl₃, 151 MHz)

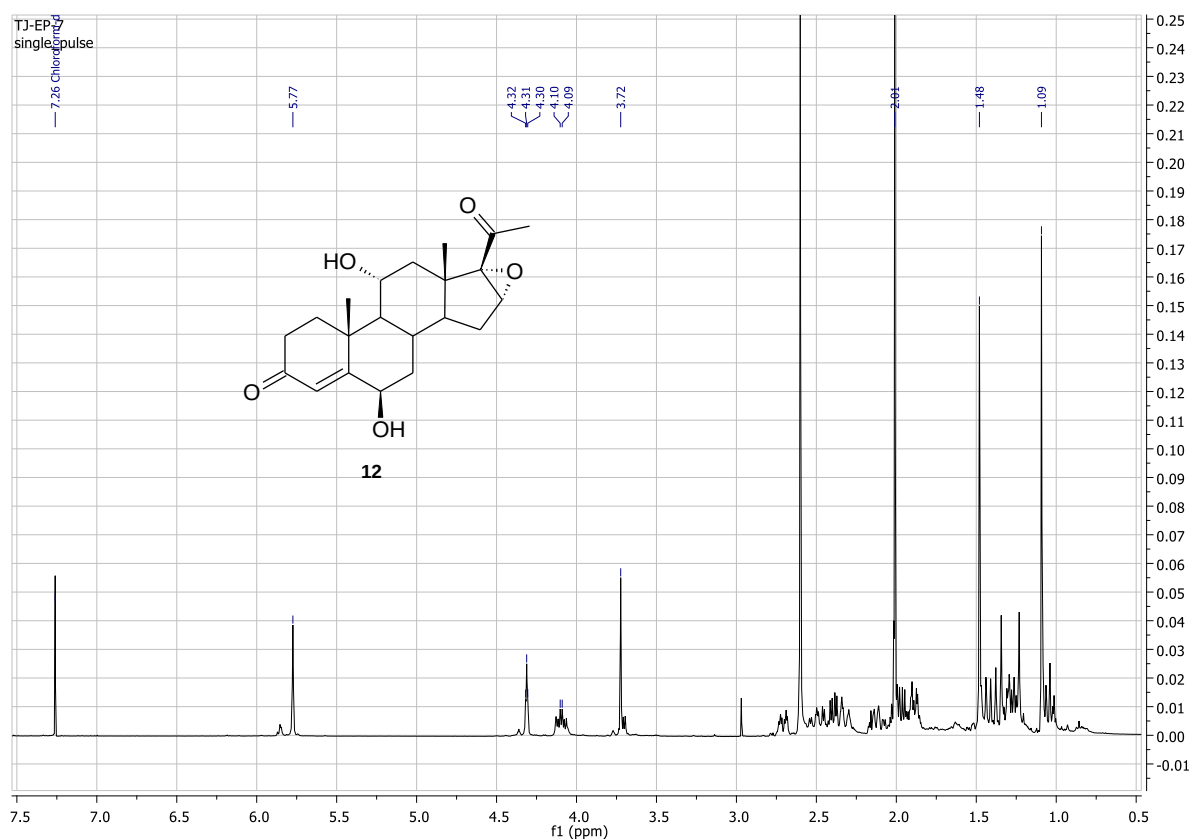


Figure.S21. ^1H NMR spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (**12**) (CDCl_3 , 600 MHz)

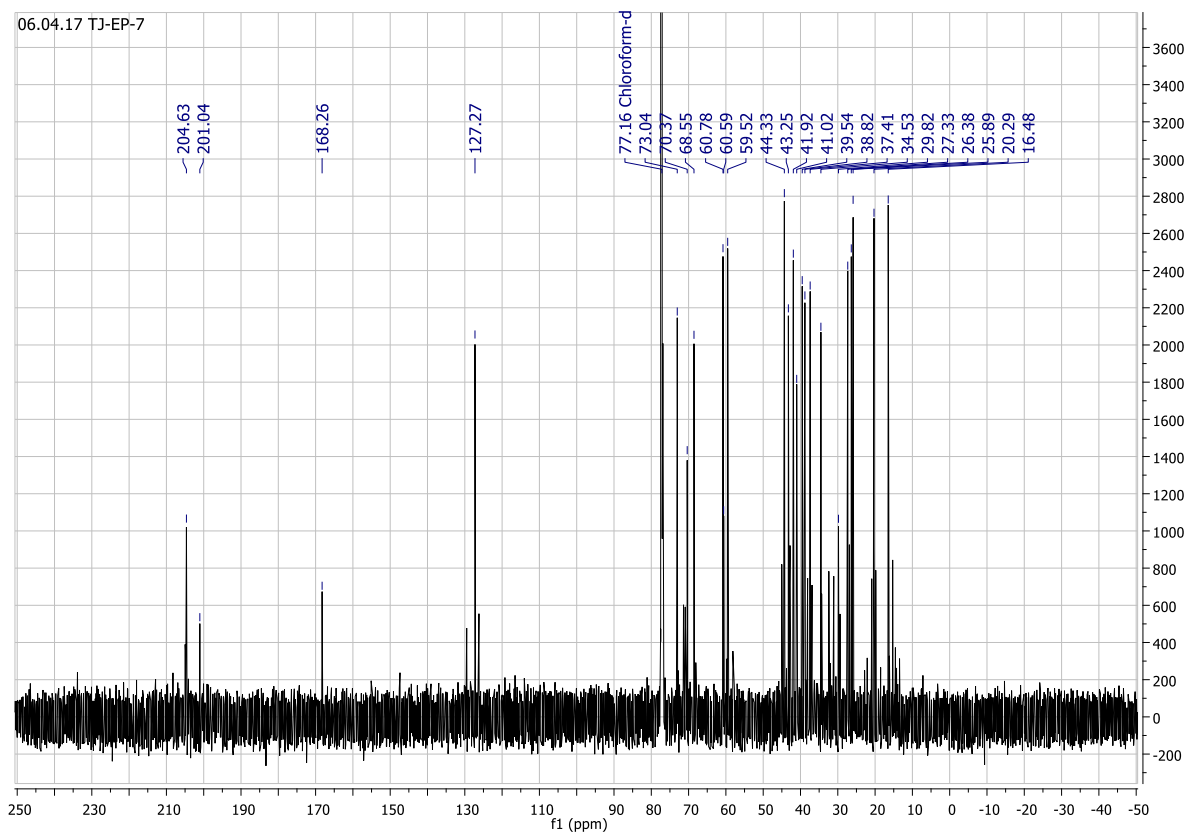


Figure.S22. ^{13}C NMR spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (**12**) (CDCl_3 , 151 MHz)

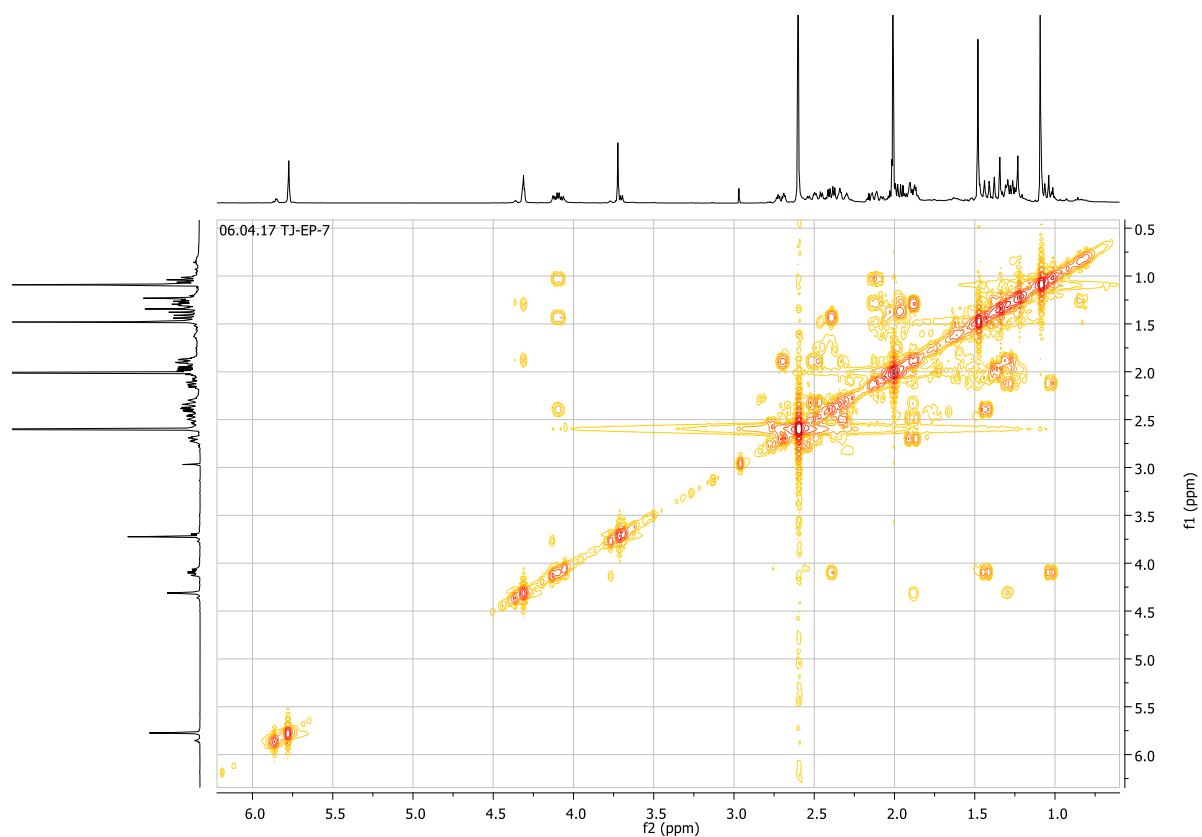


Figure.S23. COSY spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (**12**) (CDCl₃, 600 MHz)

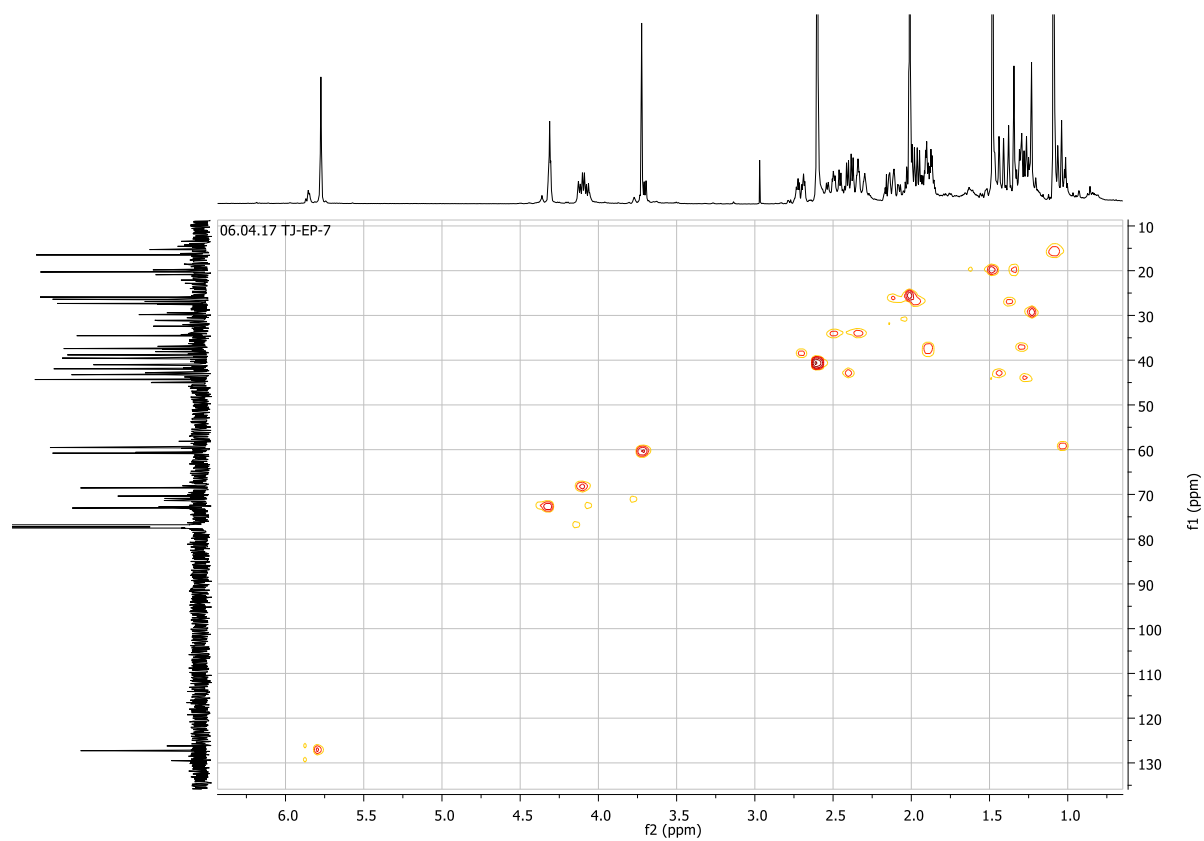


Figure.S24. HSQC spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (**12**) (CDCl₃, 151 MHz)

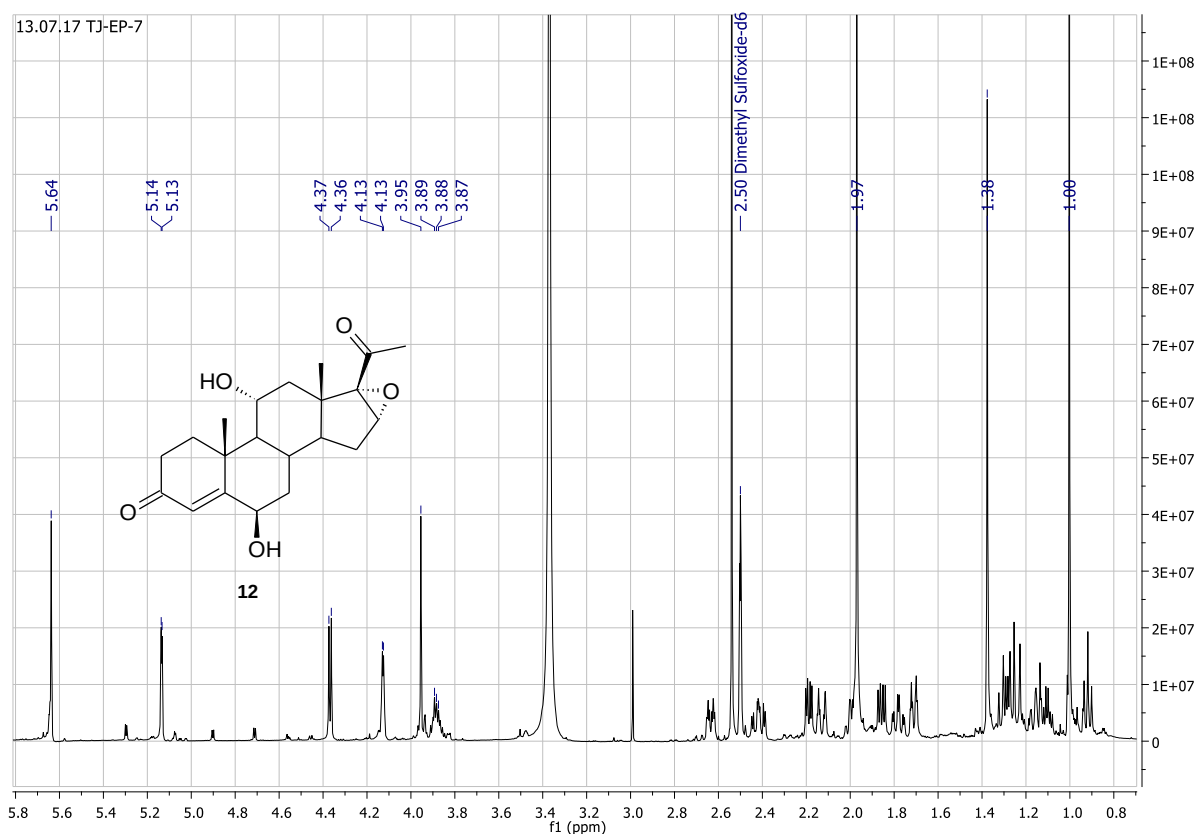


Figure.S25. ^1H NMR spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (12) (DMSO- d_6 , 600 MHz)

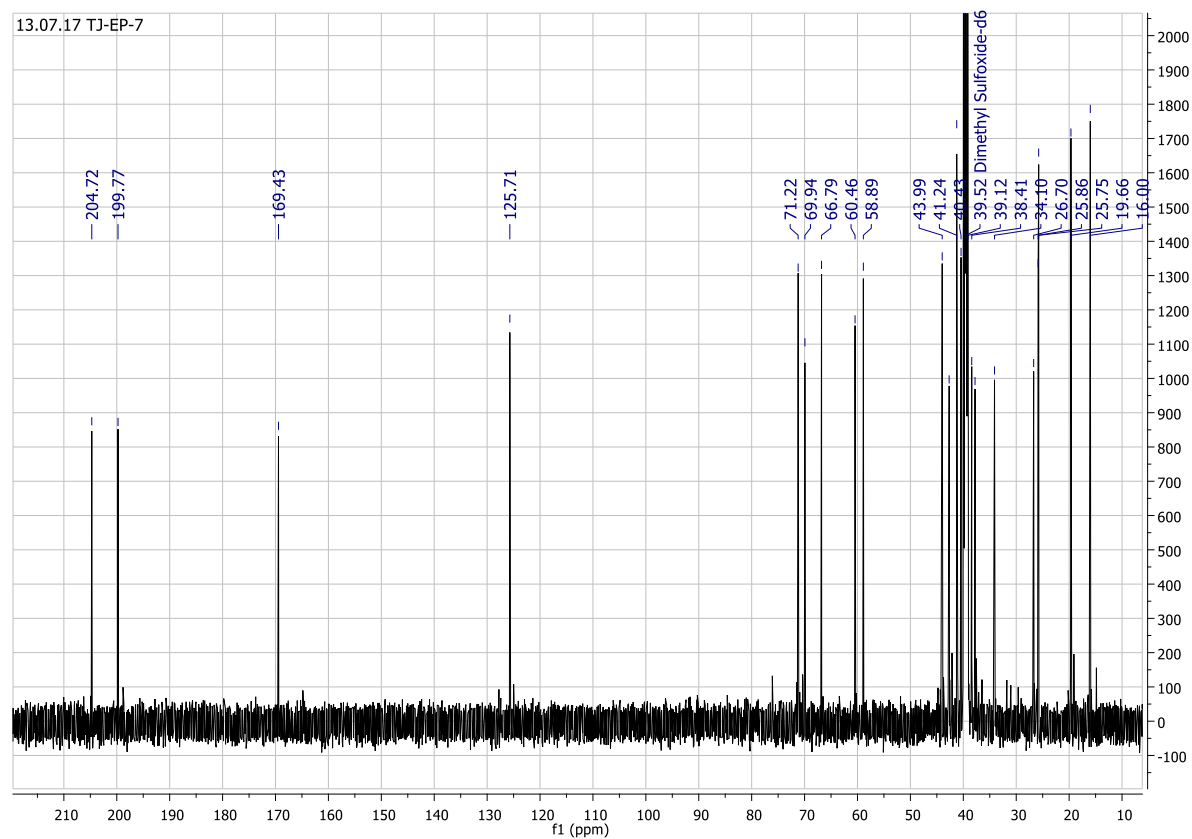


Figure.S26. ^{13}C NMR spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (12) (DMSO- d_6 , 600 MHz)

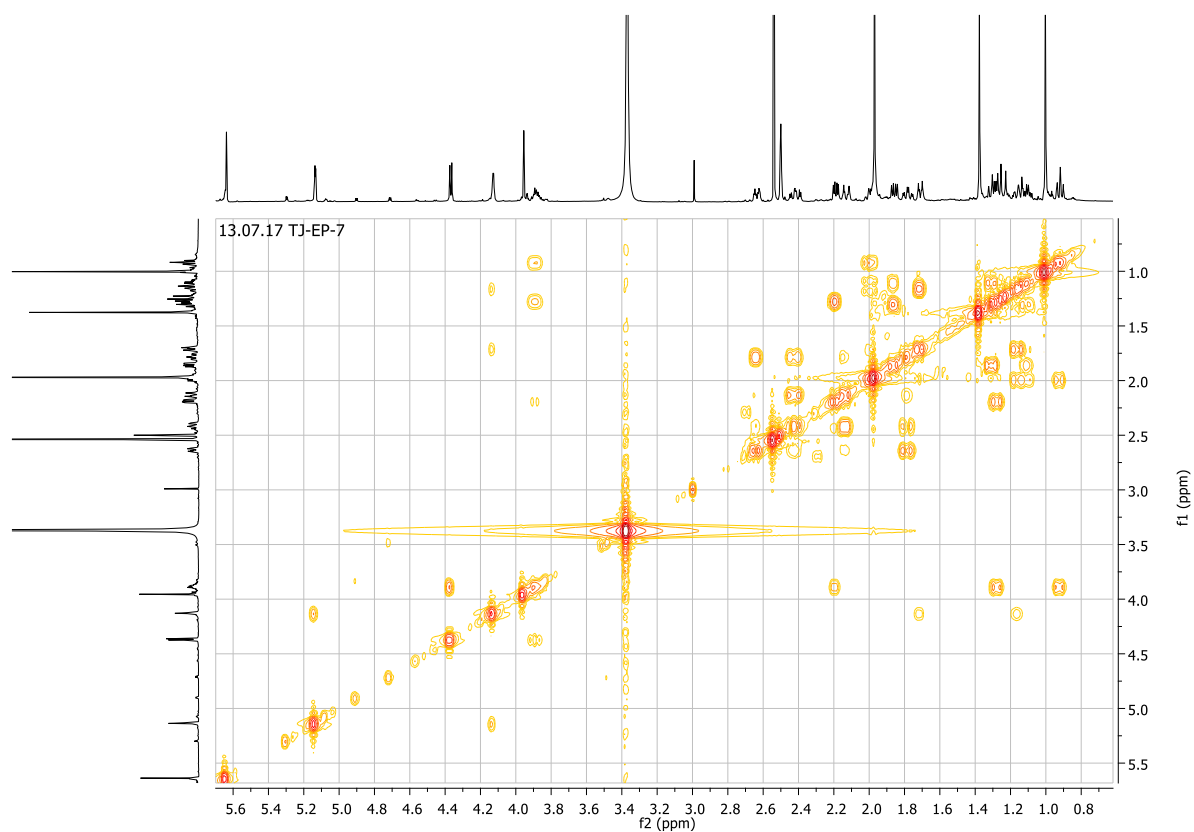


Figure.S27. COSY spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (**12**) (DMSO- d_6 , 600 MHz)

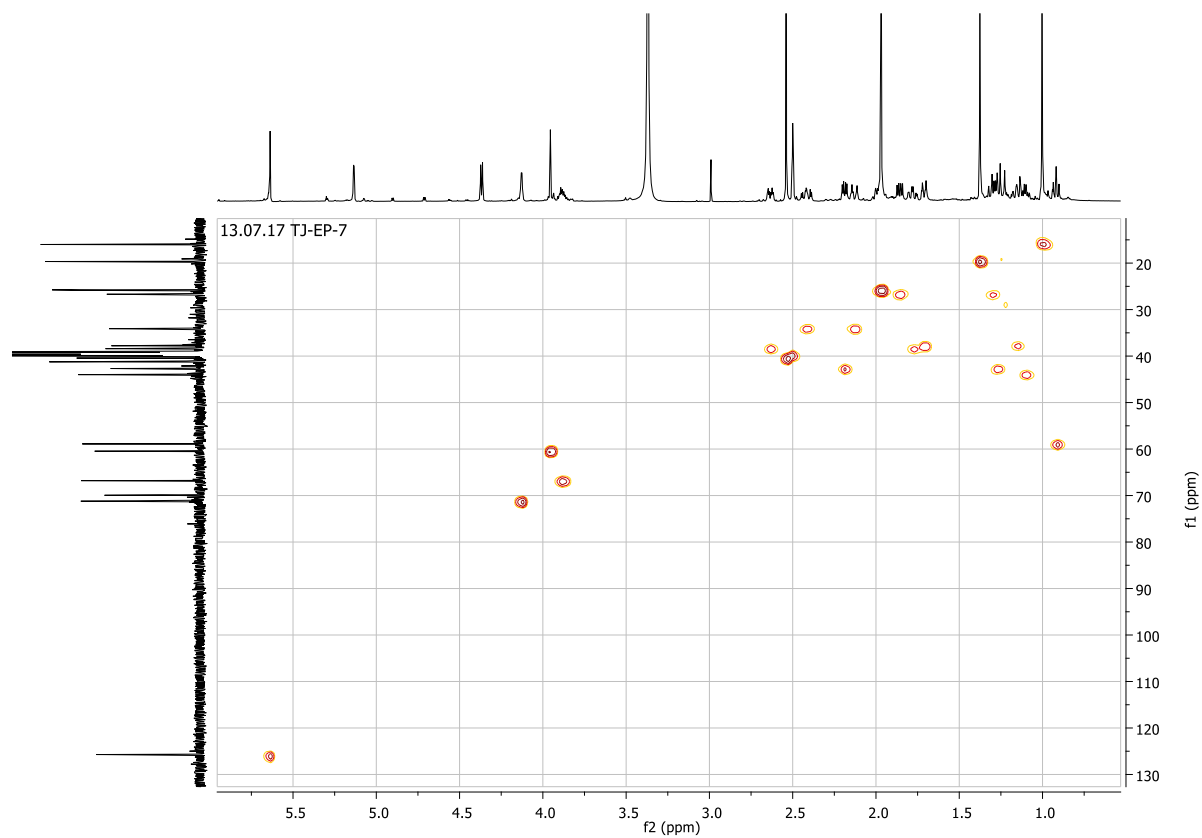


Figure.S28. HSQC spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (**12**) (DMSO- d_6 , 600 MHz)

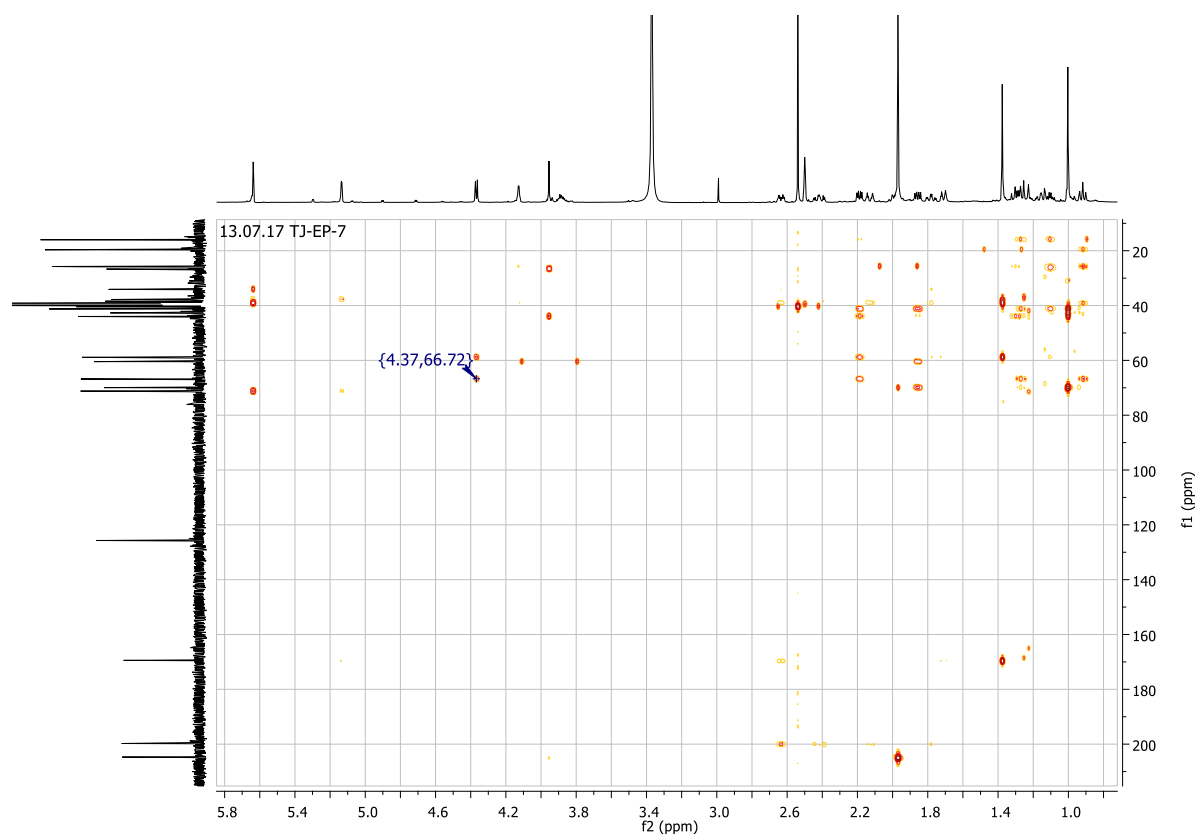


Figure.S29. HMBC spectral of 6 β ,11 α -dihydroxy-16 α ,17 α -epoxyprogesterone (**12**) (DMSO- d_6 , 600 MHz)

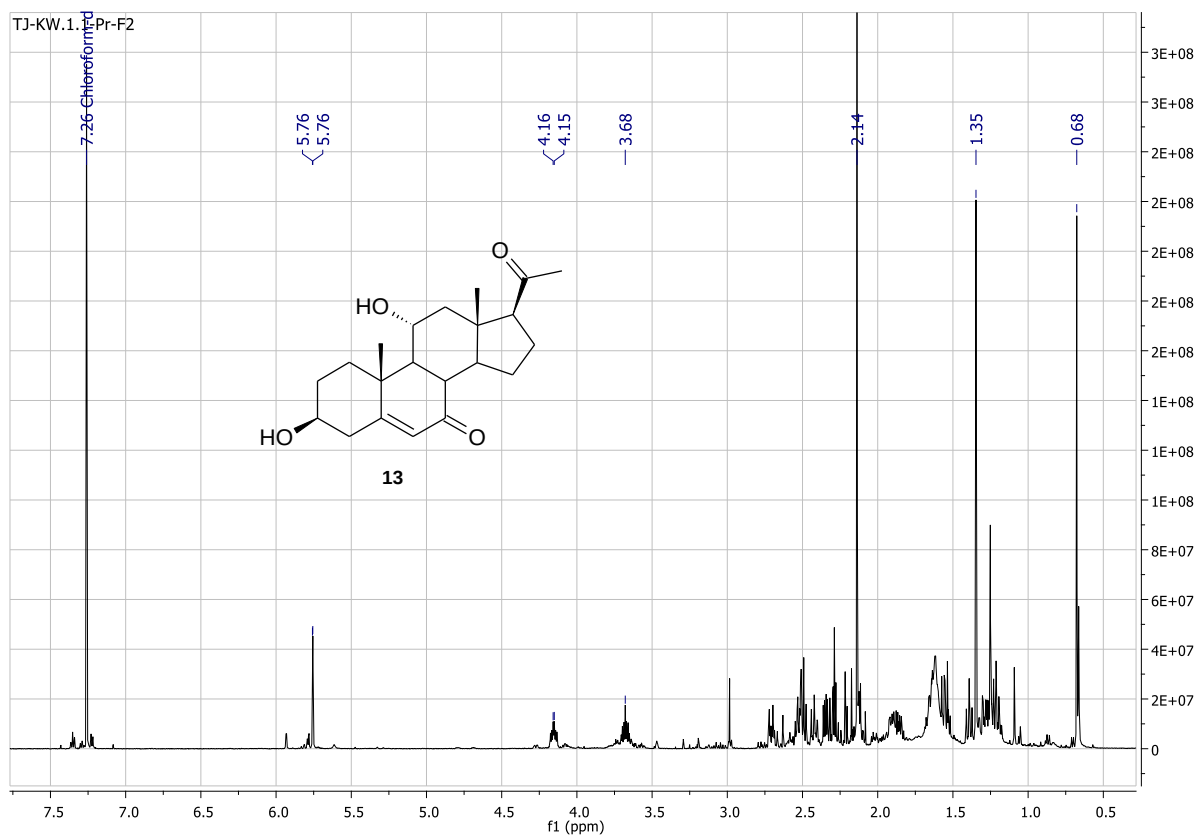


Figure.S30. ^1H NMR spectral of 11 α -hydroxy-7-oxopregnenolone (**13**) (CDCl_3 , 600 MHz)

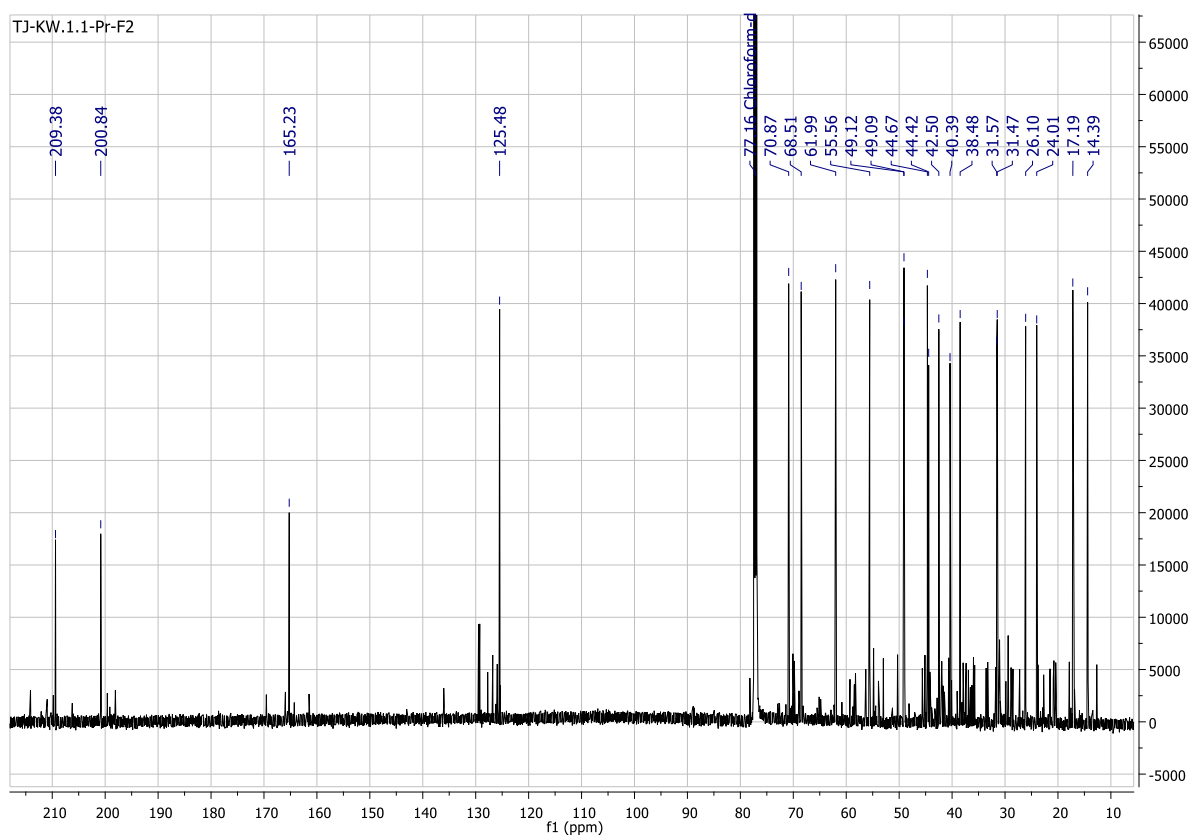


Figure.S31. ^{13}C NMR spectral of 11 α -hydroxy-7-oxopregnenolone (**13**) (CDCl_3 , 151 MHz)

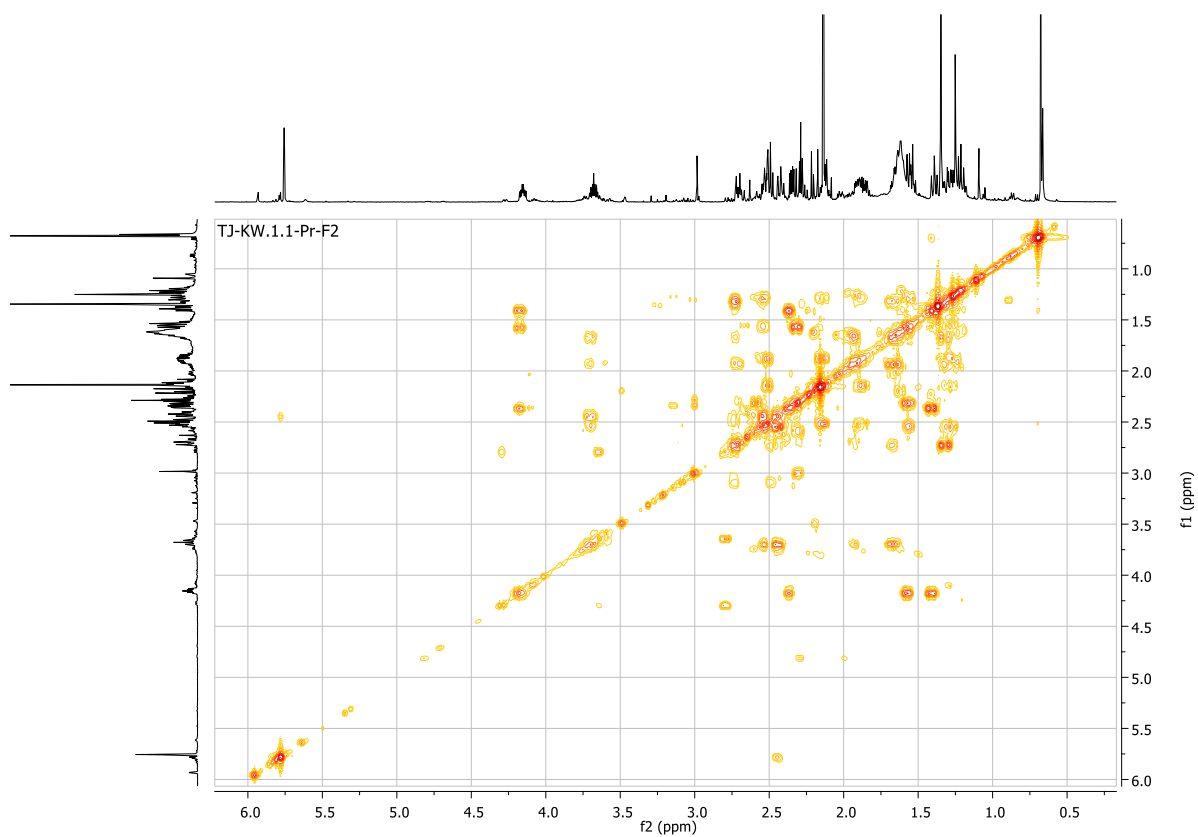


Figure.S32. COSY spectral of 11 α -hydroxy-7-oxopregnenolone (**13**) (CDCl_3 , 600 MHz)

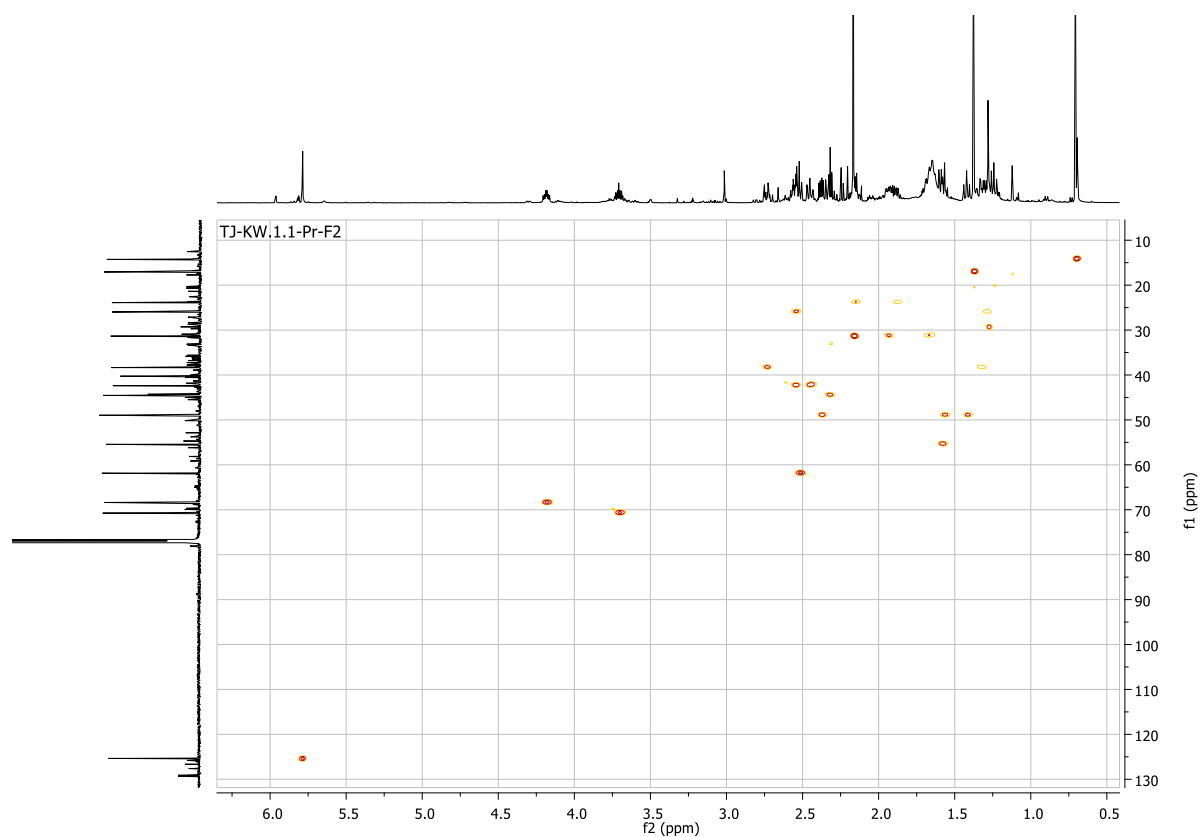


Figure.S33. HSQC spectral of 11 α -hydroxy-7-oxopregnenolone (**13**) (CDCl₃, 151 MHz)

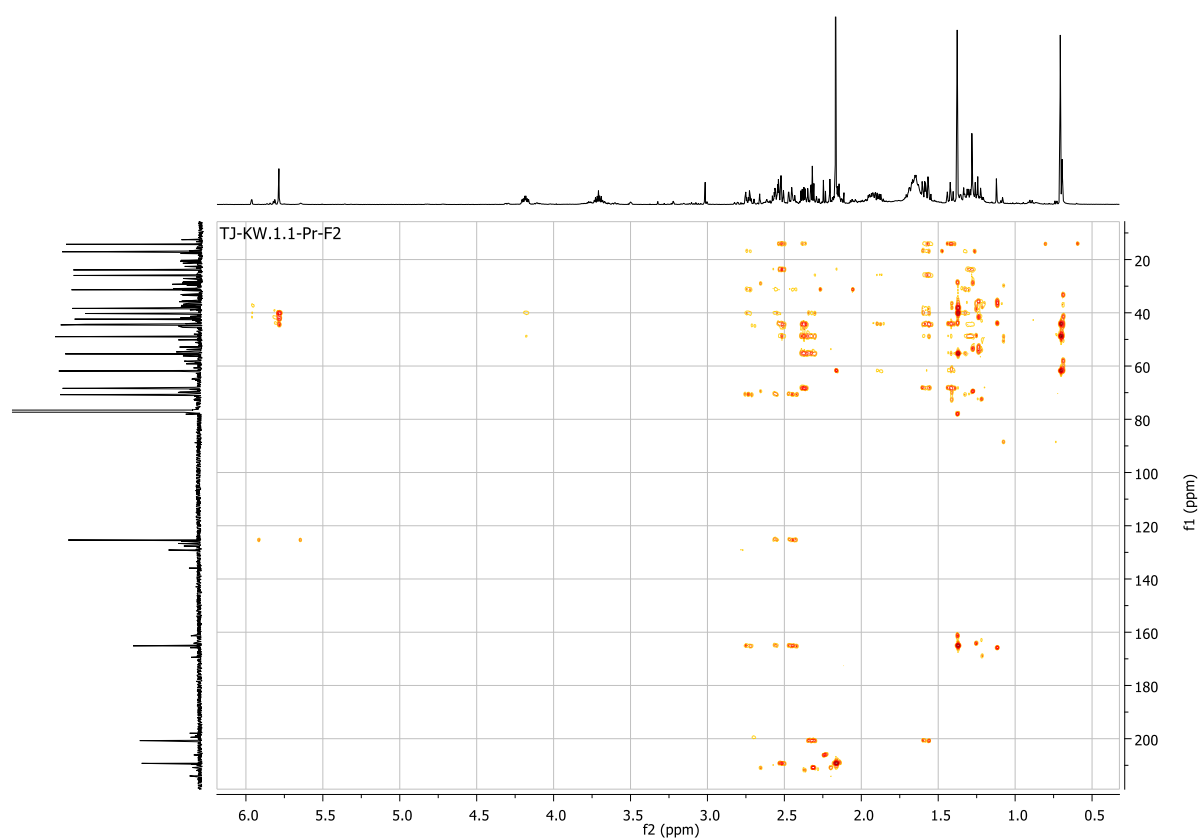


Figure.S34. HMBC spectral of 11 α -hydroxy-7-oxopregnenolone (**13**) (CDCl₃, 151 MHz)

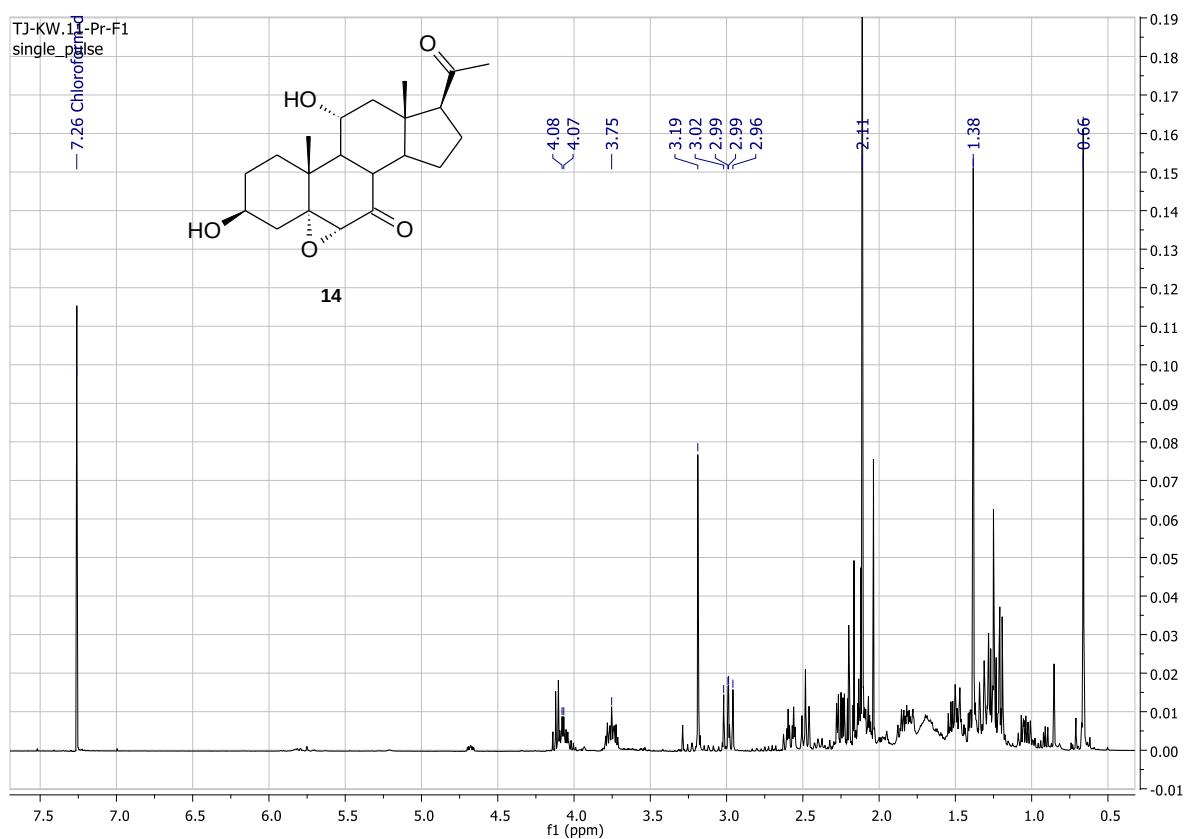


Figure.S35. ^1H NMR spectral of 5 α ,6 α -epoxy-3 β ,11 α -dihydroxypregnan-7,20-dione (**14**) (CDCl_3 , 600 MHz)

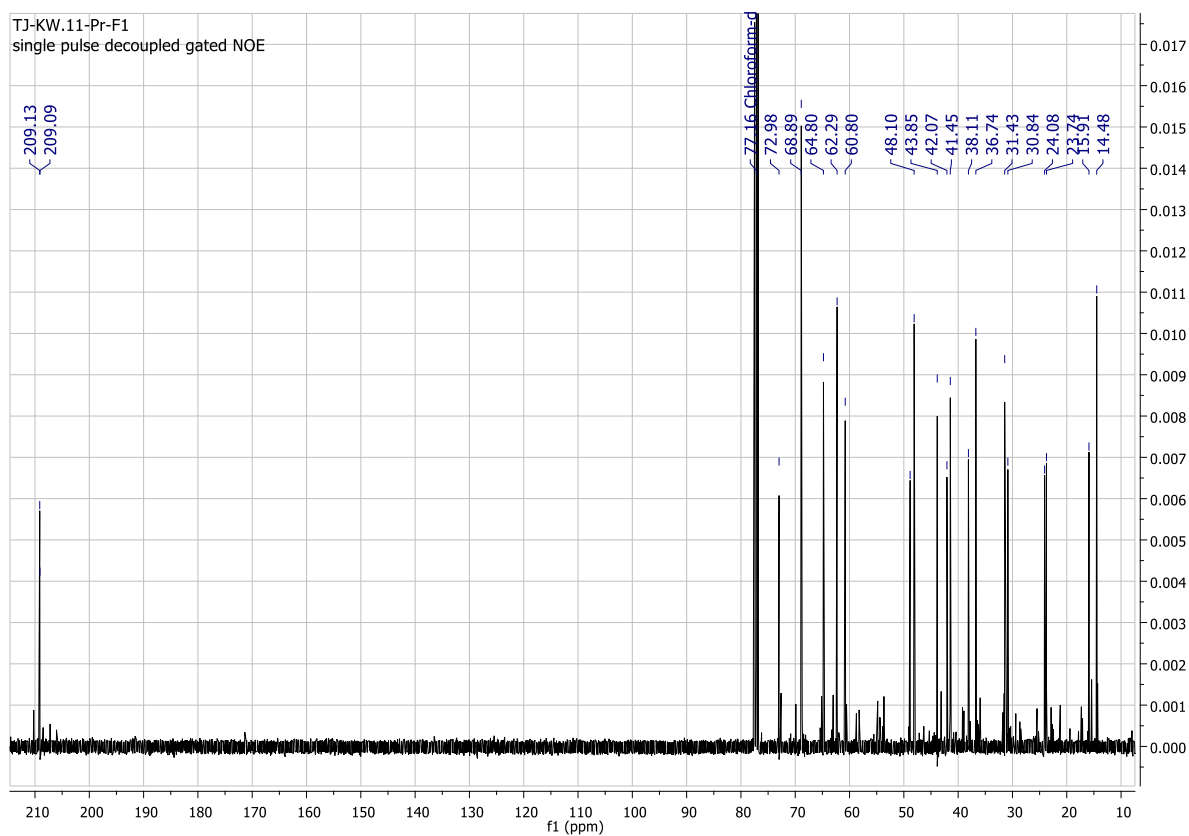


Figure.S36. ^{13}C NMR spectral of 5 α ,6 α -epoxy-3 β ,11 α -dihydroxypregnan-7,20-dione (**14**) (CDCl_3 , 151 MHz)

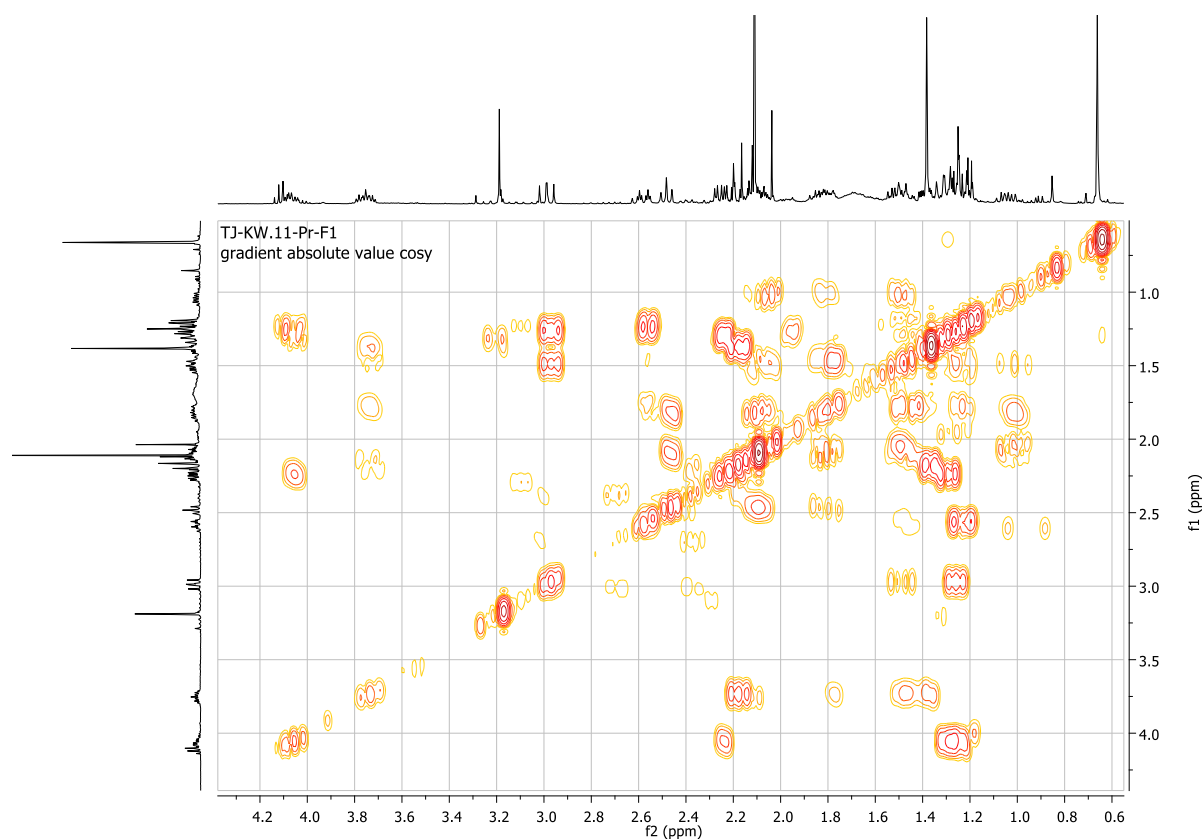


Figure.S37. COSY spectral of 5 α ,6 α -epoxy-3 β ,11 α -dihydroxypregnan-7,20-dione (**14**) (CDCl₃, 600 MHz)

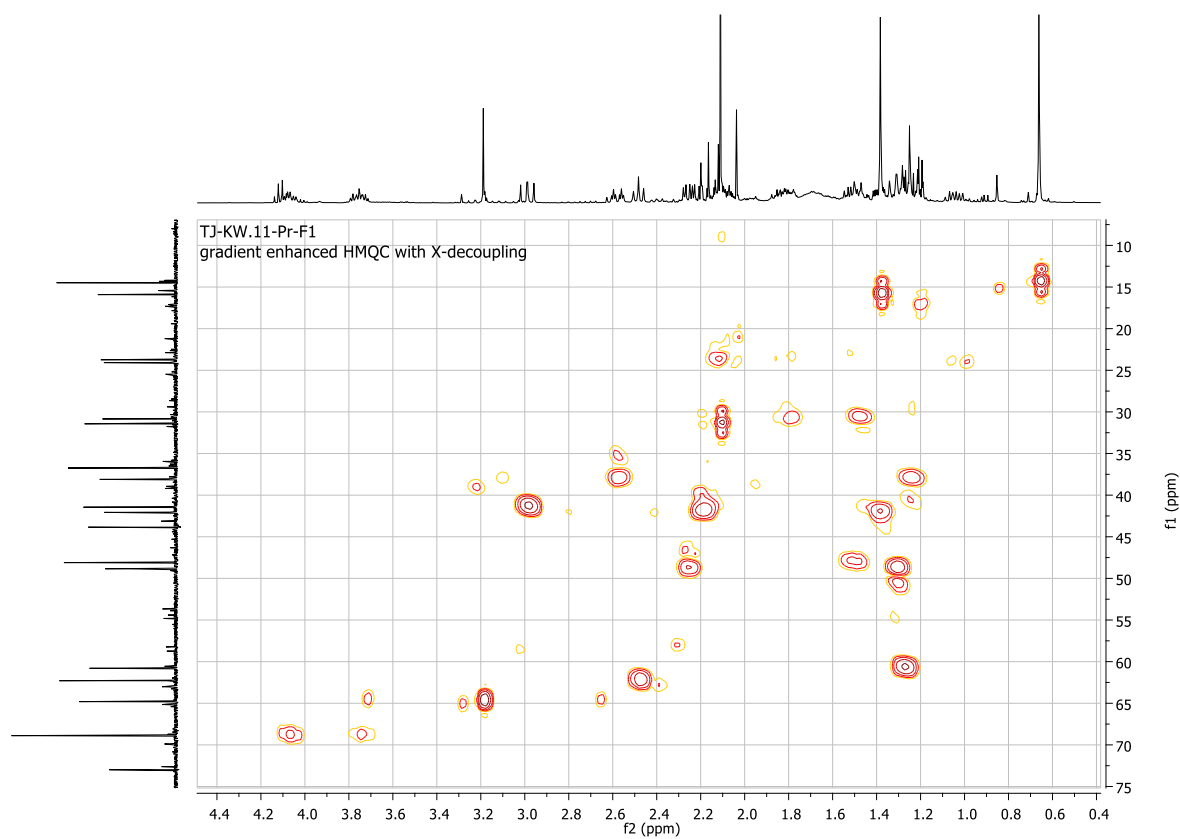


Figure.S38. HSQC spectral of 5 α ,6 α -epoxy-3 β ,11 α -dihydroxypregnan-7,20-dione (**14**) (CDCl₃, 151 MHz)

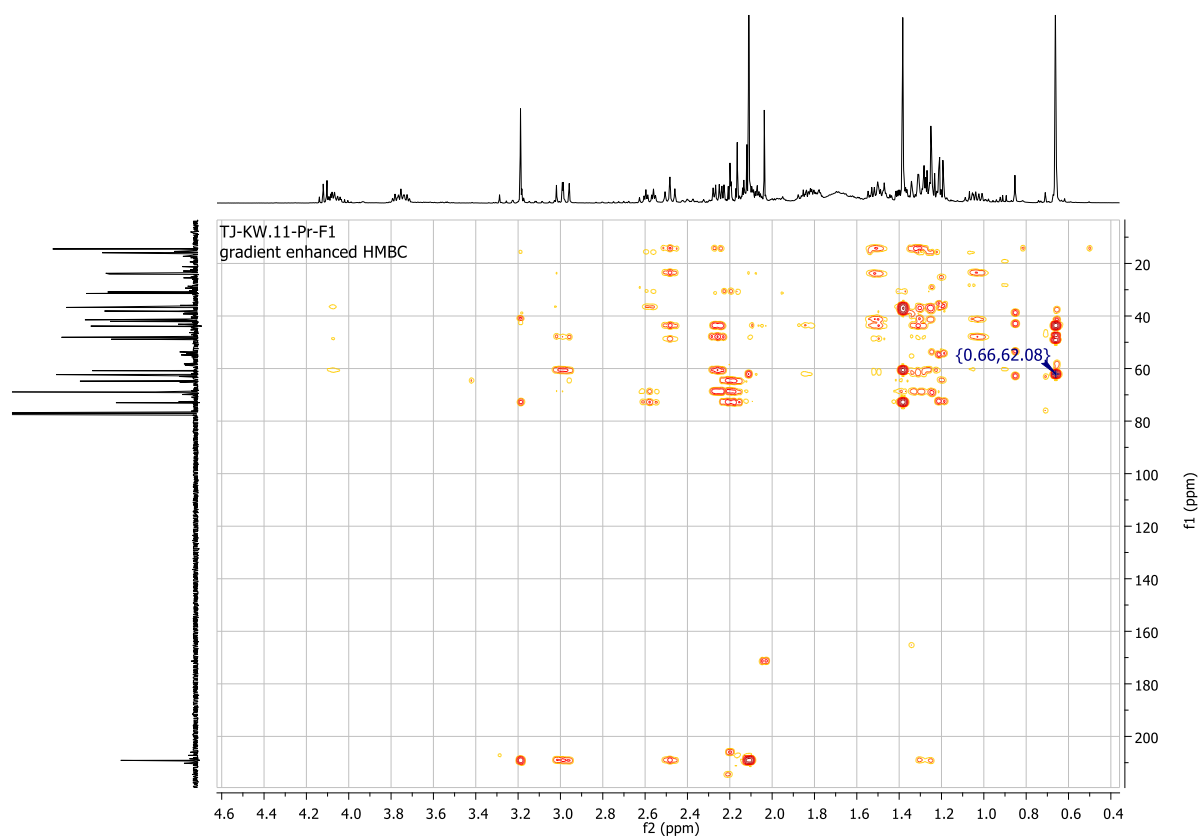


Figure.S39. HMBC spectral of 5 α ,6 α -epoxy-3 β ,11 α -dihydroxypregnan-7,20-dione (**14**) (CDCl_3 , 151 MHz)

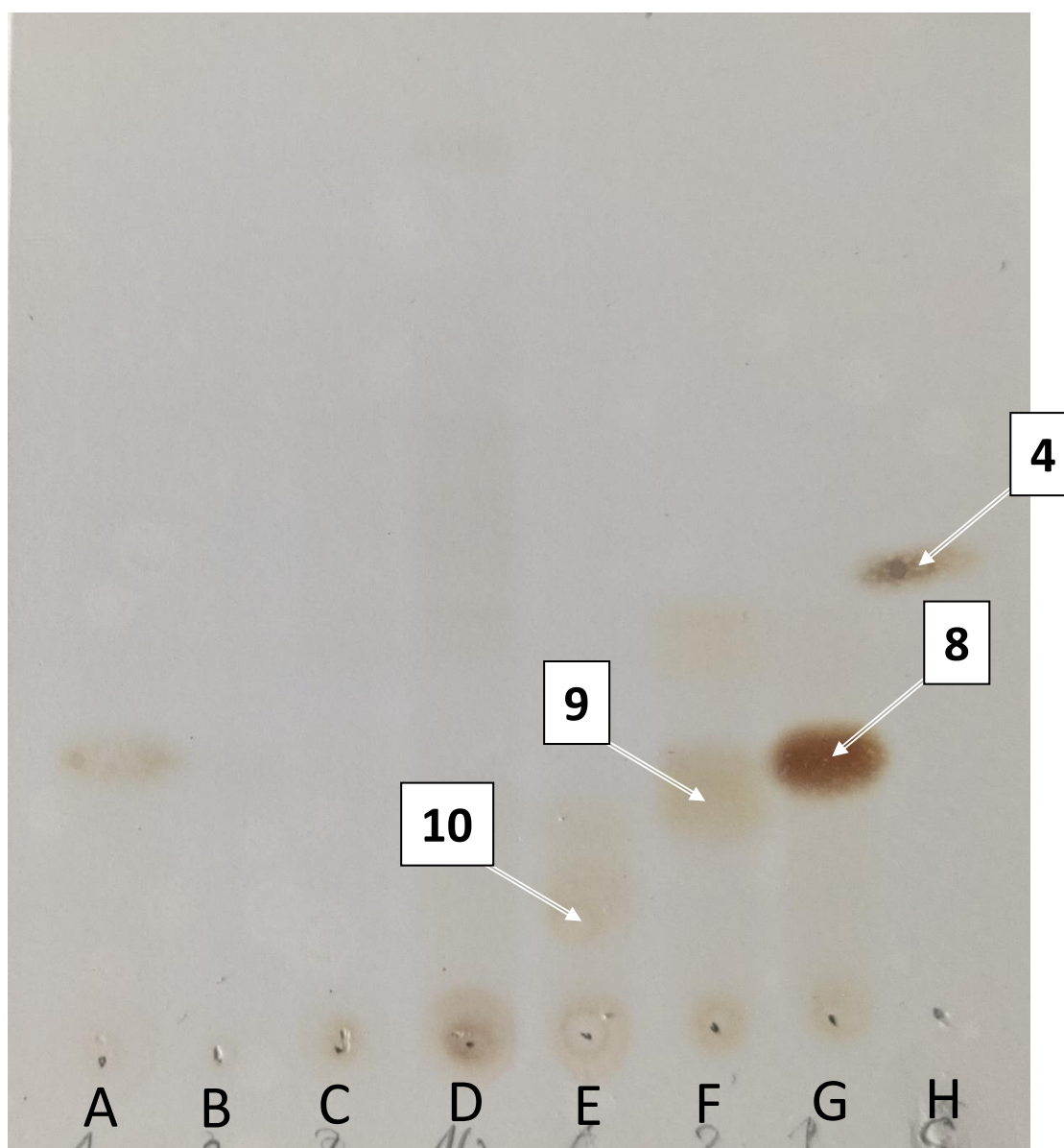


Figure.S40. Thin layer chromatography showing the products of biotransformation 17 α -hydroxyprogesterone(**4**):A)one-day transformation;B) three-day transformation; C) seven-day transformation; D)ten-day transformation;E)6 β ,12 β ,17 α -trihydroxyprogesterone (**10**); F) 1 β ,17 α -dihydroxyprogesterone(**9**); G) 6 β ,17 α -dihydroxyprogesterone(**8**); H)17 α -hydroxyprogesterone(**4**)

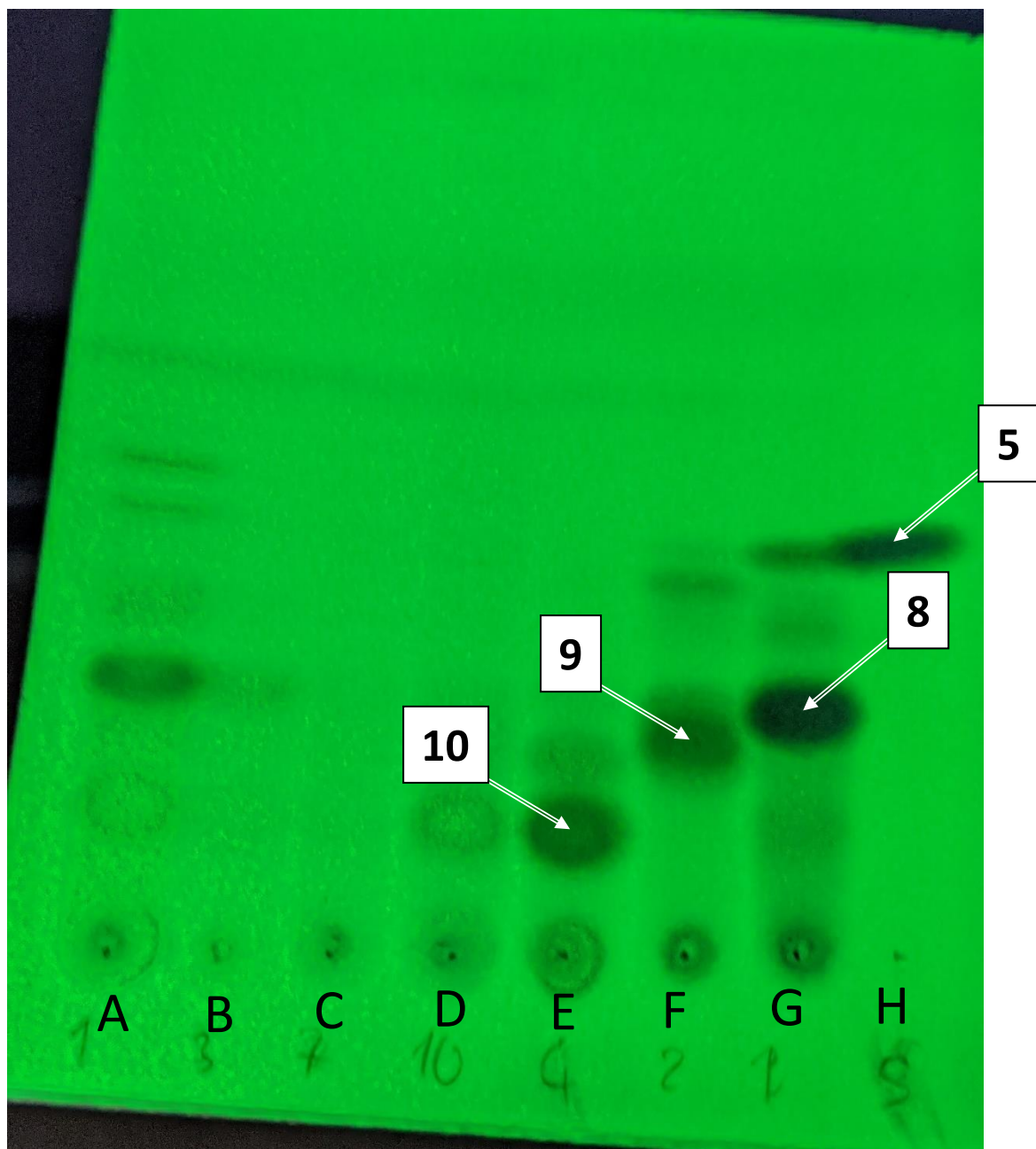


Figure.S41. Thin layer chromatography showing the products of biotransformation of 17 α -hydroxyprogesterone(**4**): A) one-day transformation; B) three-day transformation; C) seven-day transformation; D) ten-day transformation; E) 6 β ,12 β ,17 α -trihydroxyprogesterone (**10**); F) 1 β ,17 α -dihydroxyprogesterone(**9**); G) 6 β ,17 α -dihydroxyprogesterone(**8**); H) 17 α -hydroxyprogesterone(**4**)

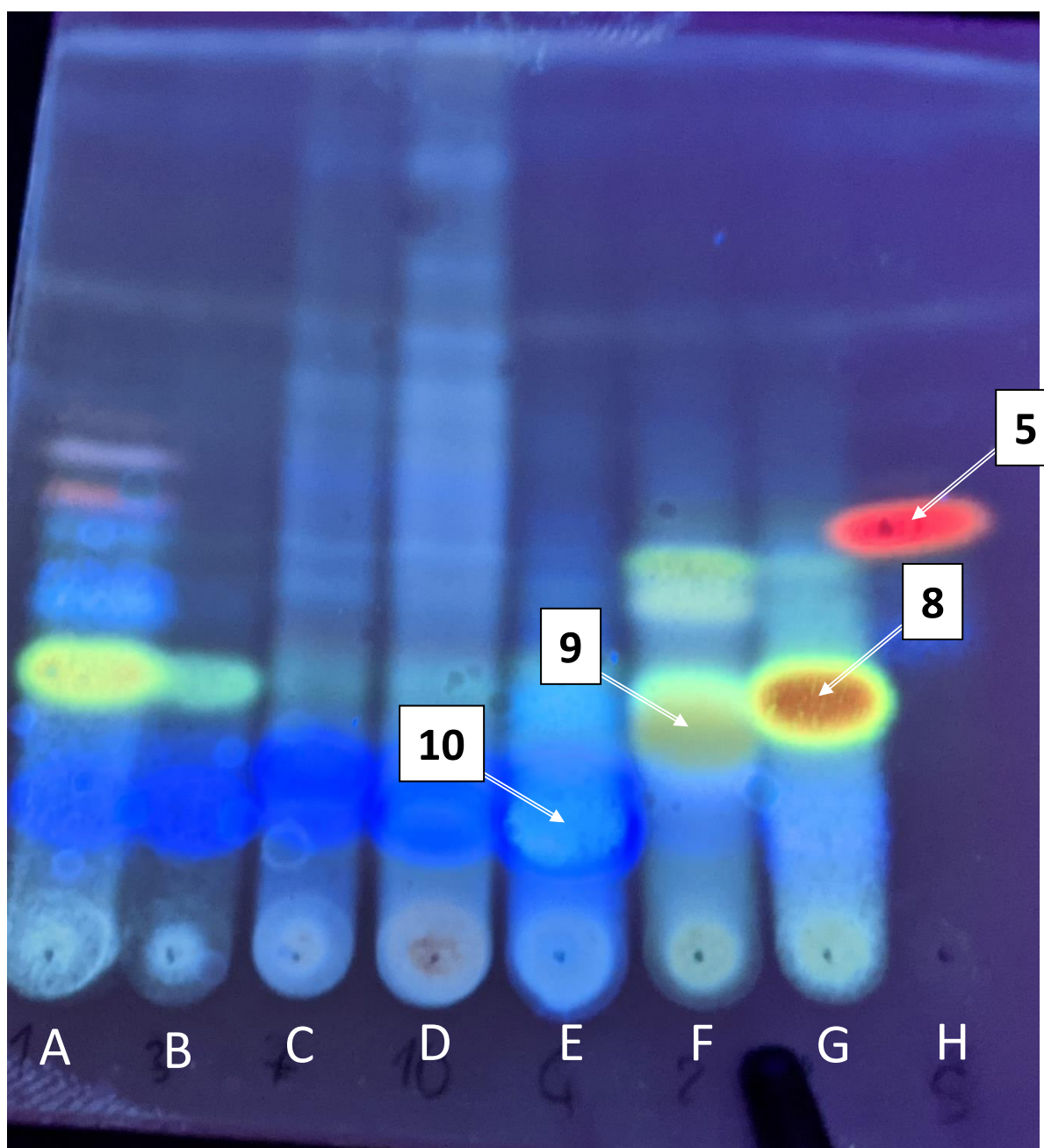


Figure.S42. Thin layer chromatography showing the products of biotransformation of 17 α -hydroxyprogesterone (4): A) one-day transformation; B) three-day transformation; C) seven-day transformation; D) ten-day transformation; E) 6 β ,12 β ,17 α -trihydroxyprogesterone (10); F) 1 β ,17 α -dihydroxyprogesterone (9); G) 6 β ,17 α -dihydroxyprogesterone (8); H) 17 α -hydroxyprogesterone (4)

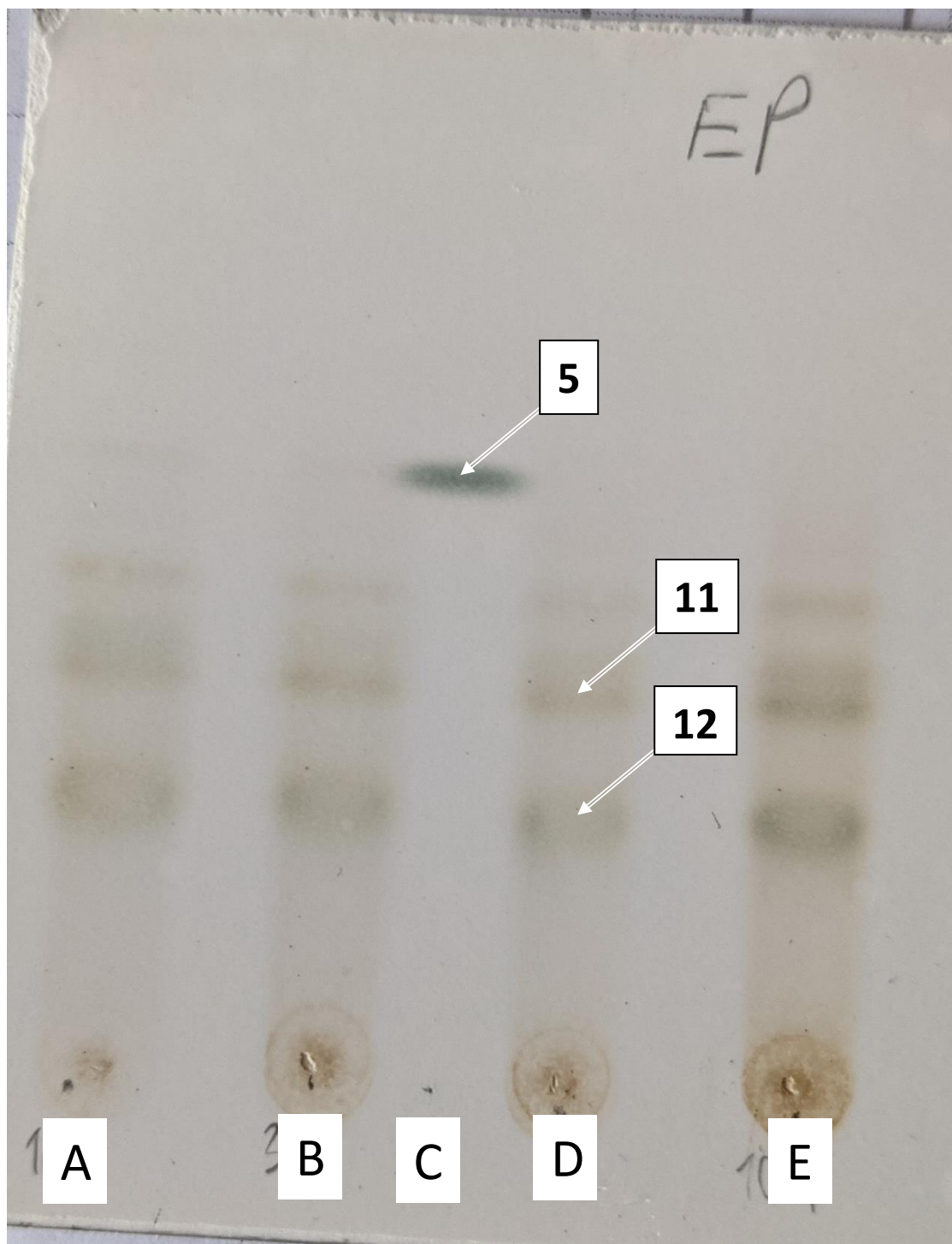


Figure.S43. Thin layer chromatography showing the products of biotransformation of 16 α ,17 α -epoxyprogesterone(**5**): A) one-day transformation; B) three-day transformation; C) 16 α ,17 α -epoxyprogesterone(**5**); D) seven-day transformation; E) ten-day transformation

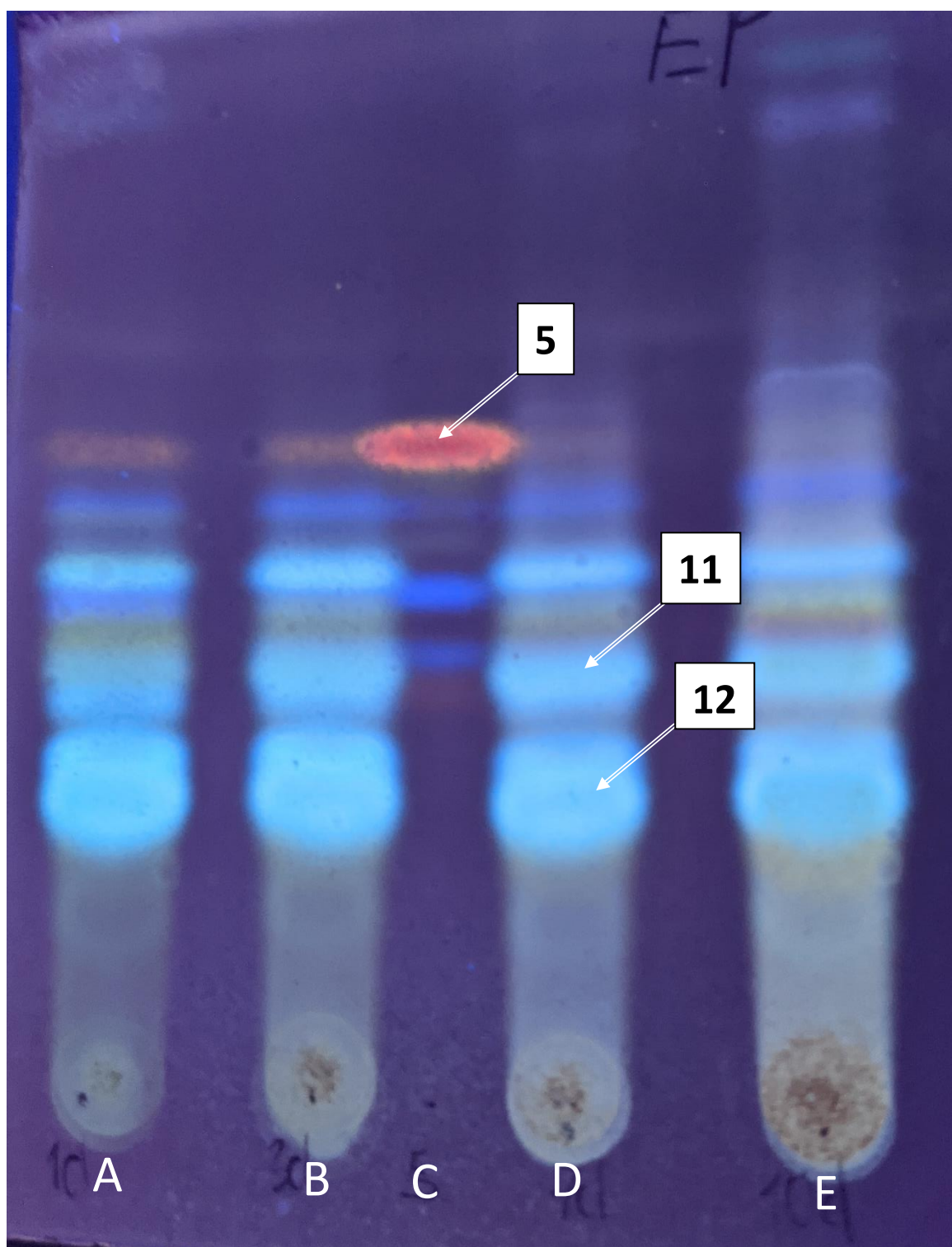
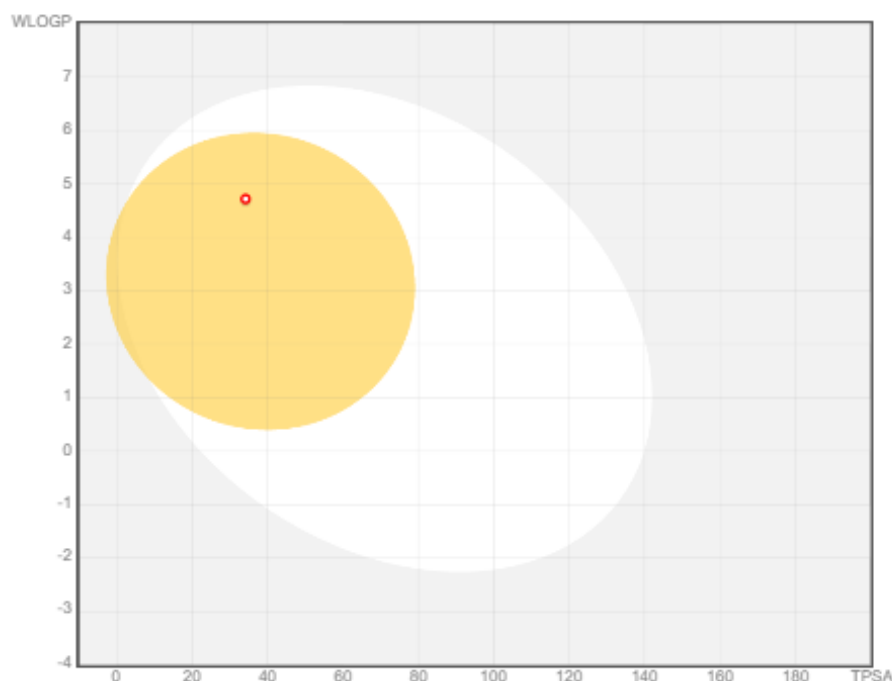


Figure.S44. Thin layer chromatography showing the products of biotransformation 16 α ,17 α -epoxyprogesterone(**5**):A) one-day transformation; B) three-day transformation; C) 16 α ,17 α -epoxyprogesterone(**5**); D) seven-day transformation; E) ten-day transformation

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Actions

☐ Show Molecules Name

Legends

 BBB

 HIA

● PGP+

● PGP-

Remarks

None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)CCC1C2CC[C@]2(C1CC[C@@H]2C(=O)C)C)C

Physicochemical Properties

Formula	C ₂₁ H ₃₀ O ₂
Molecular weight	314.46 g/mol
Num. heavy atoms	23
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	2
Num. H-bond donors	0
Molar Refractivity	94.01
TPSA	34.14 Å ²

Lipophilicity

Log P _{ow} (iLOGP)	3.08
Log P _{ow} (XLOGP3)	3.87
Log P _{ow} (WLOGP)	4.72
Log P _{ow} (MLOGP)	3.95
Log P _{ow} (SILICOS-IT)	4.49
Consensus Log P _{ow}	4.02

Water Solubility

Log S (ESOL)	-4.16
Solubility	2.17e-02 mg/ml ; 6.89e-05 mol/l
Class	Moderately soluble
Log S (Ali)	-4.28
Solubility	1.64e-02 mg/ml ; 5.20e-05 mol/l
Class	Moderately soluble
Log S (SILICOS-IT)	-4.38
Solubility	1.30e-02 mg/ml ; 4.15e-05 mol/l
Class	Moderately soluble

Pharmacokinetics

GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-5.47 cm/s

Druglikeness

Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

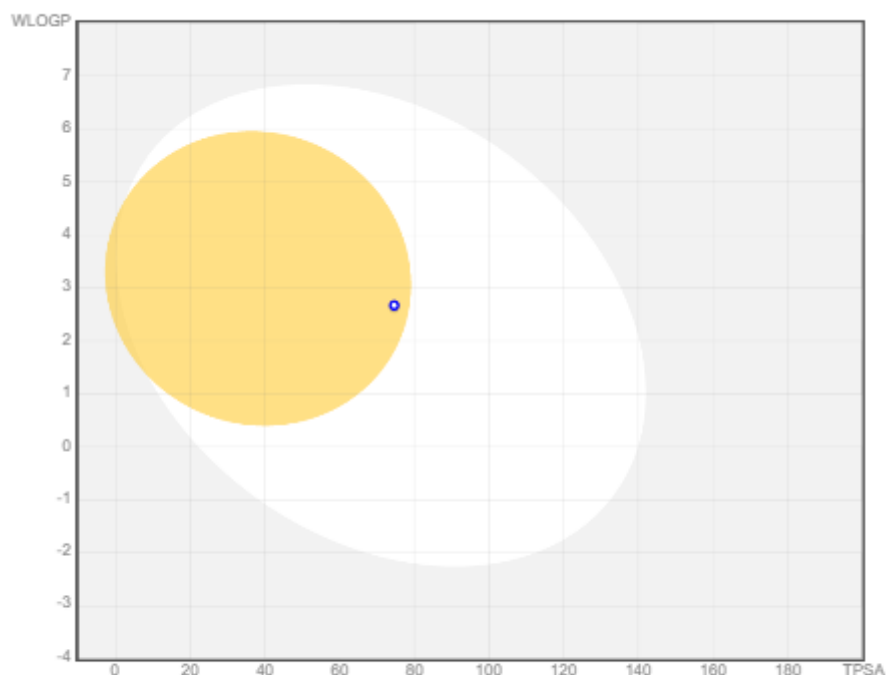
Medicinal Chemistry

PAINS	0 alert
Brenk	0 alert
Leadlikeness	No; 1 violation: XLOGP3>3.5
Synthetic accessibility	4.96

Figure.S45.Progesterone (1) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions

☐ Show Molecules Name

Legends

BBB

HIA

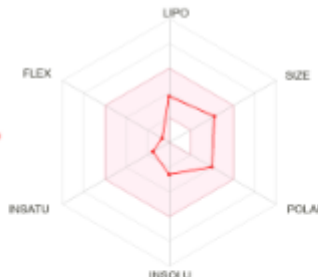
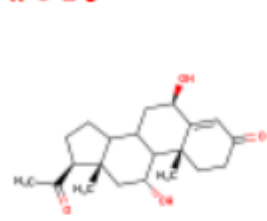
● PGP+

● PGP-

Remarks

None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)[C@H](O)CC1C2[C@H](O)C[C@]2(C1CC[C@H]2C(=O)C)C)C

Physicochemical Properties

Formula	C21H30O4
Molecular weight	346.46 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp3	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	96.33
TPSA	74.60 Å²

Lipophilicity

Log P_{ow} (iLOGP)	2.37
Log P_{ow} (XLOGP3)	1.06
Log P_{ow} (WLOGP)	2.67
Log P_{ow} (MLOGP)	2.22
Log P_{ow} (SILICOS-IT)	2.69
Consensus Log P_{ow}	2.20

Water Solubility

Log S (ESOL)	-2.59
Solubility	8.91e-01 mg/ml ; 2.57e-03 mol/l
Class	Soluble
Log S (Ali)	-2.22
Solubility	2.10e+00 mg/ml ; 6.06e-03 mol/l
Class	Soluble
Log S (SILICOS-IT)	-2.75
Solubility	6.12e-01 mg/ml ; 1.77e-03 mol/l
Class	Soluble

Pharmacokinetics

GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-7.66 cm/s

Druglikeness

Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

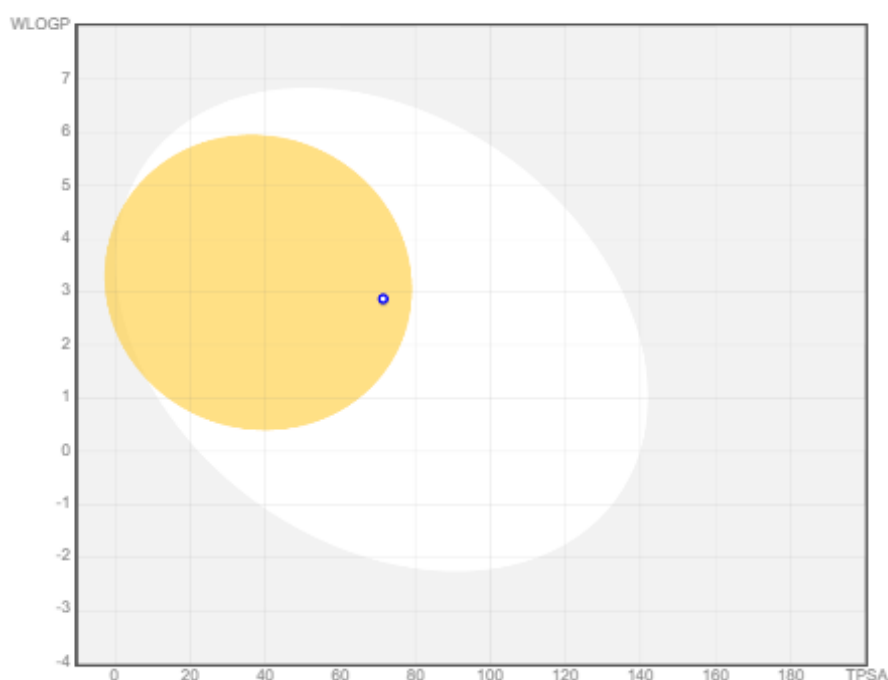
Medicinal Chemistry

PAINS	0 alert
Brenk	0 alert
Leadlikeness	Yes
Synthetic accessibility	5.19

Figure.S46.6β,11α-Dihydroxyprogesterone (2) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions
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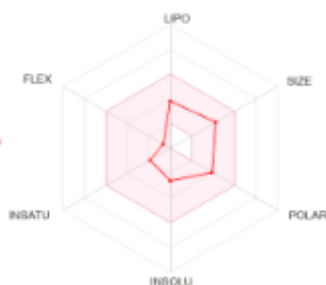
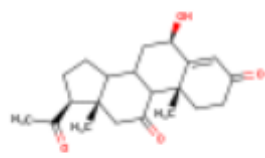
Legends

- BBB
- HIA
- PGP+
- PGP-

Remarks

None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)[C@H](O)CC1C2C(=O)C[C@]2(C1CC[C@@H]2C(=O)C)C)C

Physicochemical Properties

Formula	C ₂₁ H ₂₈ O ₄
Molecular weight	344.44 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp ³	0.76
Num. rotatable bonds	1
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	95.37
TPSA	71.44 Å ²

Lipophilicity

Log P _{ow} (iLOGP)	2.18
Log P _{ow} (XLOGP3)	1.12
Log P _{ow} (WLOGP)	2.87
Log P _{ow} (MLOGP)	2.13
Log P _{ow} (SILICOS-IT)	3.28
Consensus Log P _{ow}	2.32

Water Solubility	
Log S (ESOL)	-2.62
Solubility	8.36e-01 mg/ml ; 2.43e-03 mol/l
Class	Soluble
Log S (Ali)	-2.21
Solubility	2.11e+00 mg/ml ; 6.11e-03 mol/l
Class	Soluble
Log S (SILICOS-IT)	-3.45
Solubility	1.23e-01 mg/ml ; 3.56e-04 mol/l
Class	Soluble

Pharmacokinetics

GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-7.61 cm/s

Druglikeness

Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

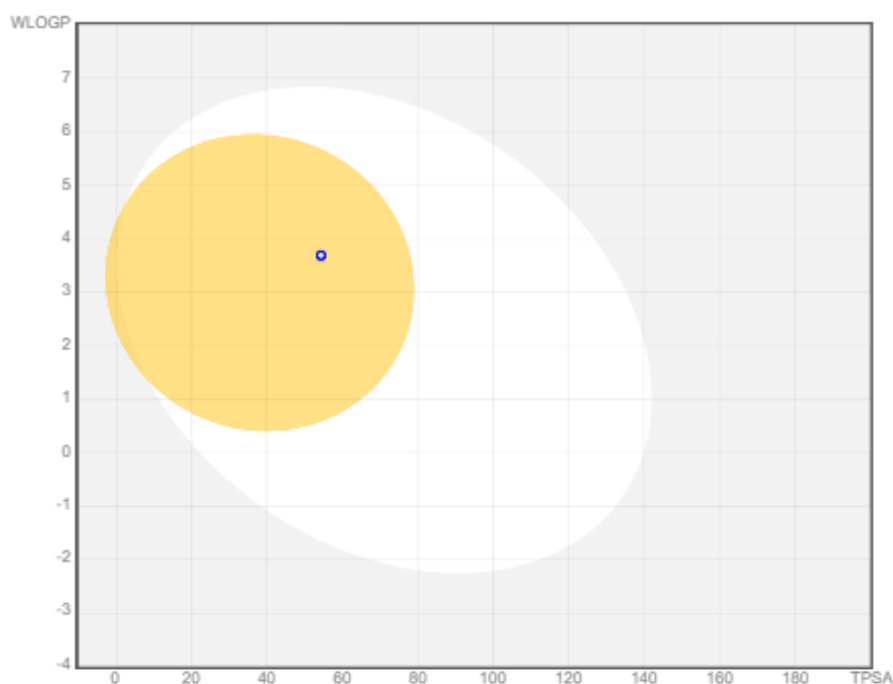
Medicinal Chemistry

PAINS	1 alert: steroid_A
Brenk	0 alert
Leadlikeness	Yes
Synthetic accessibility	5.08

Figure.S47.6β-hydroxy-11-oxo-progesterone (7) physicochemical and ADME parameters prediction using the SwissADME modelling

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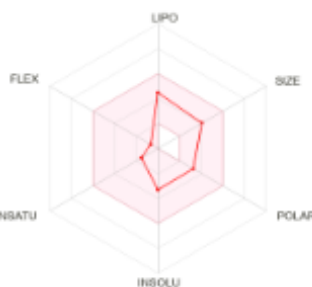
Legends

BBB
 HIA
● PGP+
● PGP-

Remarks

None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)CCC1C2[C@H](O)C[C@]2(C1CC[C@H]2C(=O)C)C)C

Physicochemical Properties

Formula	C ₂₁ H ₃₀ O ₃
Molecular weight	330.48 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	95.17
TPSA	54.37 Å ²

Lipophilicity

Log <i>P</i> _{OW} (iLOGP)	2.75
Log <i>P</i> _{OW} (XLOGP3)	2.36
Log <i>P</i> _{OW} (WLOGP)	3.69
Log <i>P</i> _{OW} (MLOGP)	3.07
Log <i>P</i> _{OW} (SILICOS-IT)	3.59
Consensus Log <i>P</i> _{OW}	3.09

Water Solubility	
Log <i>S</i> (ESOL)	-3.31
Solubility	1.62e-01 mg/ml ; 4.90e-04 mol/l
Class	Soluble
Log <i>S</i> (Ali)	-3.14
Solubility	2.38e-01 mg/ml ; 7.21e-04 mol/l
Class	Soluble
Log <i>S</i> (SILICOS-IT)	-3.57
Solubility	8.94e-02 mg/ml ; 2.70e-04 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log <i>K</i> _p (skin permeation)	-6.64 cm/s

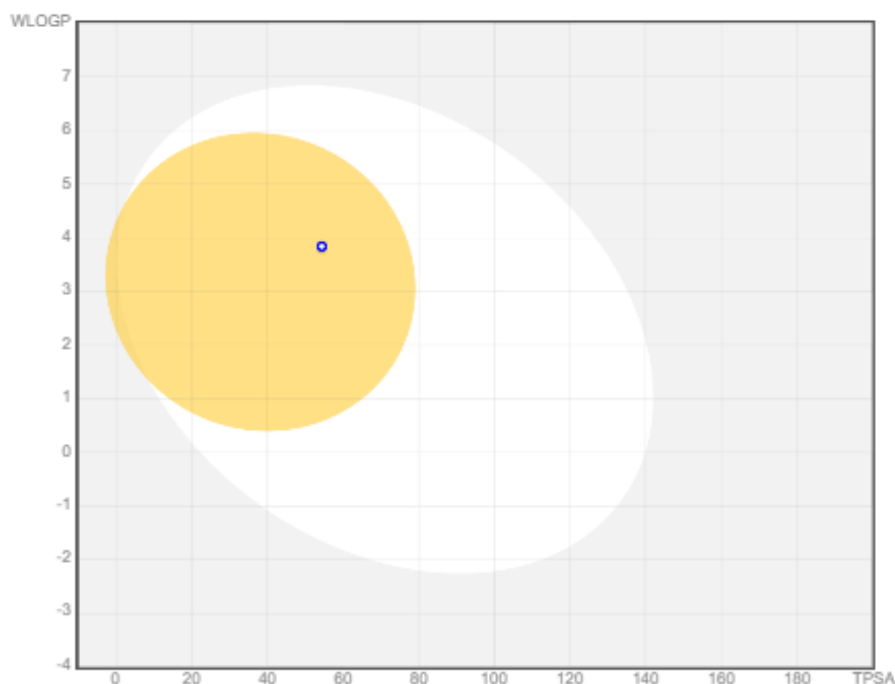
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	0 alert
Leadlikeness	Yes
Synthetic accessibility	4.96

Figure.S48.11 α -Hydroxyprogesterone (**3**) physicochemical and ADME parameters prediction using the SwissADME modelling

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Legends

BBB
 HIA
 PGP+
 PGP-

Remarks

None

Molecule 1



SMILES O=C1CC[C@H]2(C(=C1)CCC1C2CC[C@H]2(C1CC[C@H]2(O)C(=O)C)C)C

Physicochemical Properties

Formula	C ₂₁ H ₃₀ O ₃
Molecular weight	330.46 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	95.21
TPSA	54.37 Å ²

Lipophilicity

Log <i>P</i> _{ow} (iLOGP)	2.80
Log <i>P</i> _{ow} (XLOGP3)	3.17
Log <i>P</i> _{ow} (WLOGP)	3.84
Log <i>P</i> _{ow} (MLOGP)	3.07
Log <i>P</i> _{ow} (SILICOS-IT)	3.98
Consensus Log <i>P</i> _{ow}	3.37

Water Solubility

Log <i>S</i> (ESOL)	-3.82
Solubility	5.00e-02 mg/ml ; 1.51e-04 mol/l
Class	Soluble
Log <i>S</i> (Ali)	-3.98
Solubility	3.44e-02 mg/ml ; 1.04e-04 mol/l
Class	Soluble
Log <i>S</i> (SILICOS-IT)	-4.02
Solubility	3.17e-02 mg/ml ; 9.59e-05 mol/l
Class	Moderately soluble

Pharmacokinetics

GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log <i>K</i> _p (skin permeation)	-6.07 cm/s

Druglikeness

Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

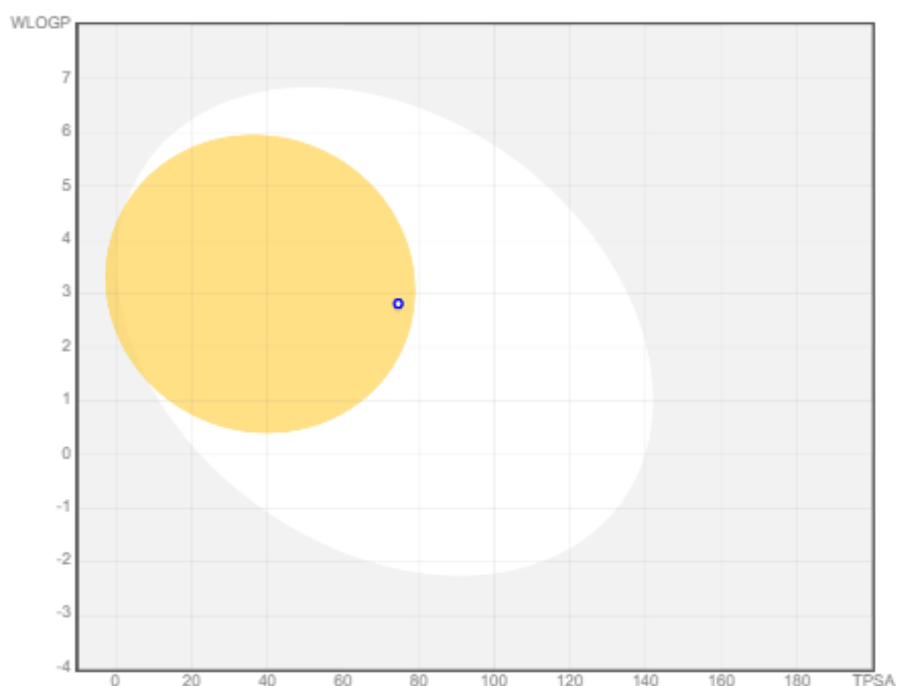
Medicinal Chemistry

PAINS	0 alert
Brenk	0 alert
Leadlikeness	Yes
Synthetic accessibility	4.81

Figure.S49. 17 α -Hydroxyprogesterone (**3**) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions
☐ Show Molecules Name

Legends

- BBB
- HIA
- PGP+
- PGP---

Remarks

None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)[C@H](O)CC1C2CC[C@]2(C1CC[C@]2(O)C(=O)C)C)C

Physicochemical Properties

Formula	C ₂₁ H ₃₀ O ₄
Molecular weight	346.46 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	96.37
TPSA	74.60 Å ²

Lipophilicity

Log P _{ow} (iLOGP)	2.54
Log P _{ow} (XLOGP3)	1.87
Log P _{ow} (WLOGP)	2.81
Log P _{ow} (MLOGP)	2.22
Log P _{ow} (SILICOS-IT)	3.08
Consensus Log P _{ow}	2.50

Water Solubility	
Log S (ESOL)	-3.10
Solubility	2.75e-01 mg/ml ; 7.94e-04 mol/l
Class	Soluble
Log S (Ali)	-3.06
Solubility	3.03e-01 mg/ml ; 8.74e-04 mol/l
Class	Soluble
Log S (SILICOS-IT)	-3.20
Solubility	2.18e-01 mg/ml ; 6.28e-04 mol/l
Class	Soluble

Pharmacokinetics

GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	7.09 cm/s

Druglikeness

Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

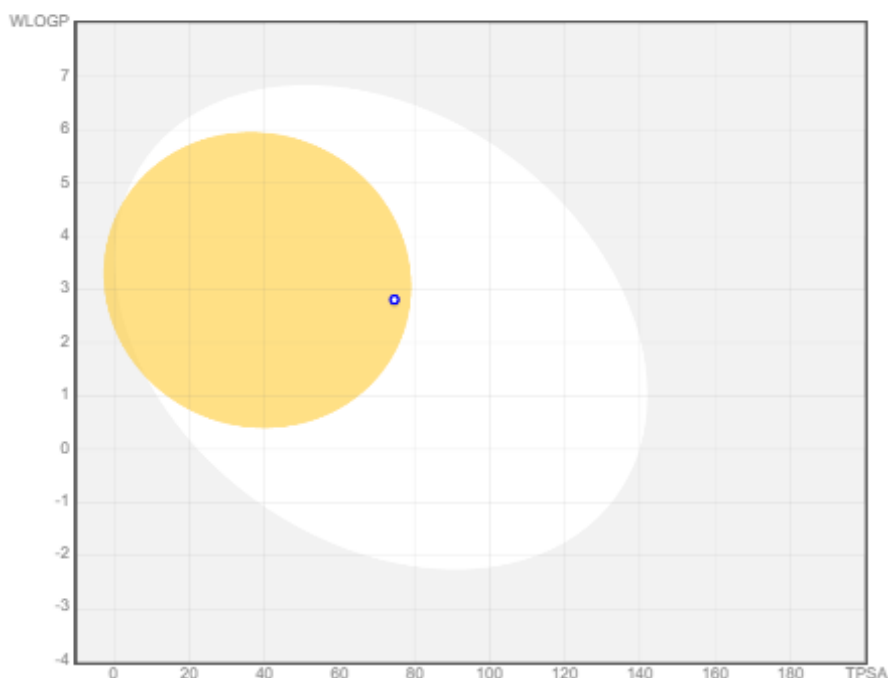
Medicinal Chemistry

PAINS	0 alert
Brenk	0 alert
Leadlikeness	Yes
Synthetic accessibility	5.00

Figure.S50. 6β,17α-dihydroxyprogesterone (8) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions

☐ Show Molecules Name

Legends

 BBB

 HIA

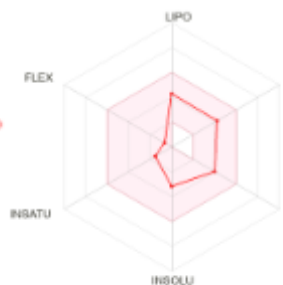
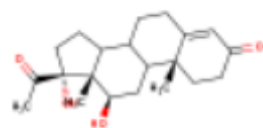
● PGP+

● PGP-

Remarks

 None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)CCC1C2C[C@@H](O)[C@]2(C1CC[C@]2(O)C(=O)C)C)C

Physicochemical Properties

Formula	C ₂₁ H ₃₀ O ₄
Molecular weight	346.46 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	96.37
TPSA	74.60 Å ²

Lipophilicity

Log P _{ow} (iLOGP)	1.60
Log P _{ow} (XLOGP3)	2.01
Log P _{ow} (WLOGP)	2.81
Log P _{ow} (MLOGP)	2.22
Log P _{ow} (SILICOS-IT)	3.08
Consensus Log P _{ow}	2.34

Water Solubility	
Log S (ESOL)	-3.19
Solubility	2.25e-01 mg/ml ; 6.48e-04 mol/l
Class	Soluble
Log S (Ali)	-3.20
Solubility	2.17e-01 mg/ml ; 6.26e-04 mol/l
Class	Soluble
Log S (SILICOS-IT)	-3.20
Solubility	2.18e-01 mg/ml ; 6.26e-04 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-6.99 cm/s

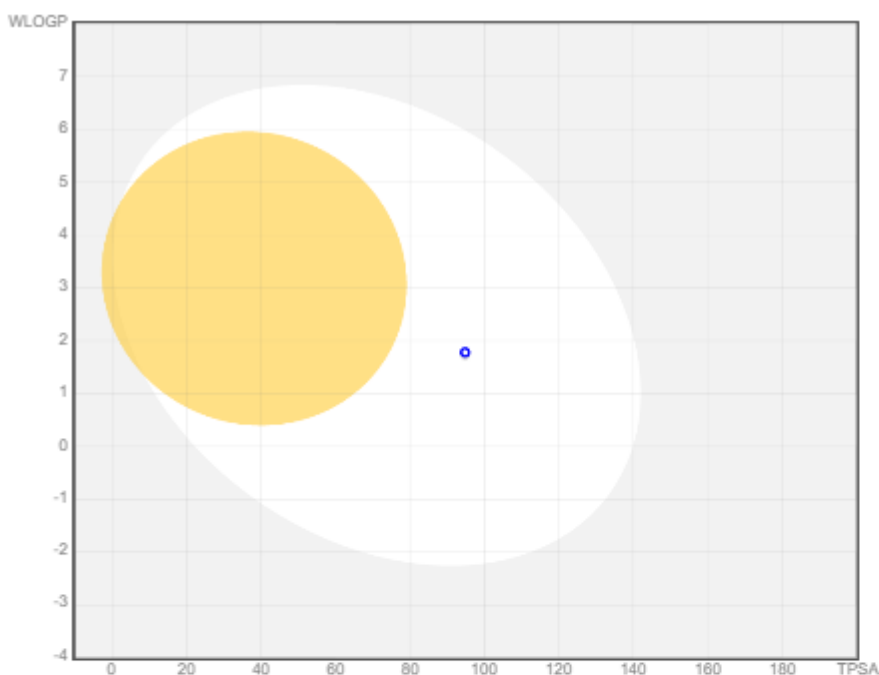
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	0 alert
Leadlikeness	Yes
Synthetic accessibility	5.10

Figure.S51. 12β,17α-dihydroxyprogesterone (8) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions
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Legends

- BBB
- HIA
- PGP+
- PGP---

Remarks

None

Molecule 1

SMILES O=C1CC[C@]2(C(=C1)[C@H](O)CC1C2C[C@H](O)[C@]2(C1CC[C@]2(O)C(=O)C)C

Physicochemical Properties	
Formula	C ₂₁ H ₃₀ O ₅
Molecular weight	362.46 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	5
Num. H-bond donors	3
Molar Refractivity	97.53
TPSA	94.83 Å ²

Lipophilicity	
Log P _{ow} (iLOGP)	2.53
Log P _{ow} (XLOGP3)	0.41
Log P _{ow} (WLOGP)	1.78
Log P _{ow} (MLOGP)	1.39
Log P _{ow} (SILICOS-IT)	2.19
Consensus Log P _{ow}	1.66

Water Solubility	
Log S (ESOL)	-2.28
Solubility	1.90e+00 mg/ml ; 5.25e-03 mol/l
Class	Soluble
Log S (Ali)	-1.97
Solubility	3.90e+00 mg/ml ; 1.08e-02 mol/l
Class	Very soluble
Log S (SILICOS-IT)	-2.39
Solubility	1.49e+00 mg/ml ; 4.11e-03 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-8.22 cm/s

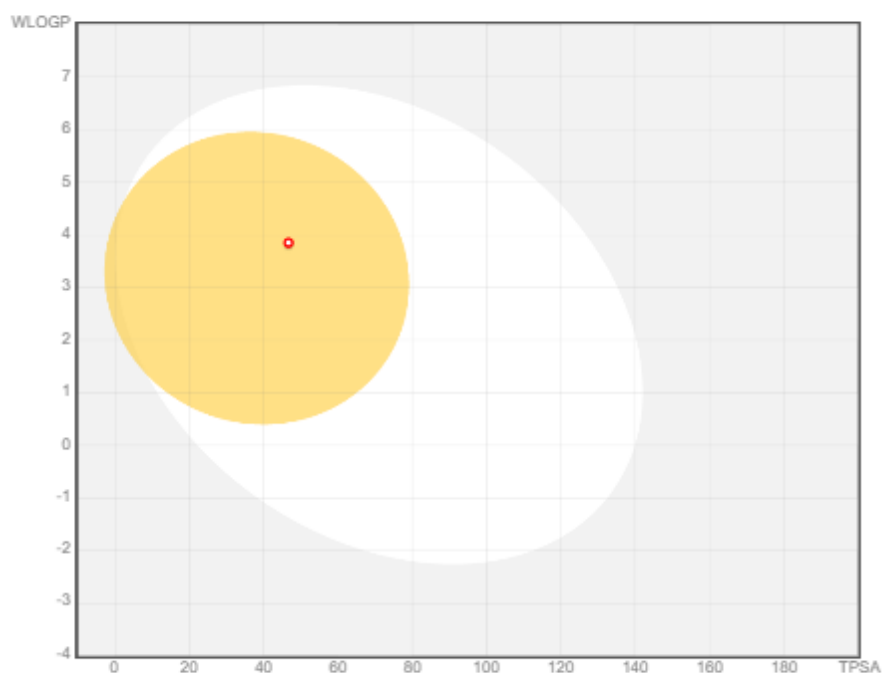
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	0 alert
Leadlikeness	No; 1 violation: MW>350
Synthetic accessibility	5.26

Figure.S52. 6β,12β,17α-trihydroxyprogesterone (**10**) physicochemical and ADME parameters prediction using the SwissADME modelling

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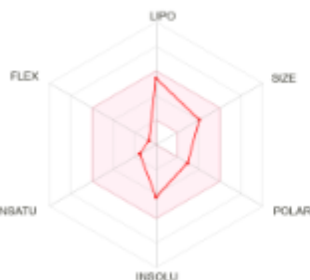
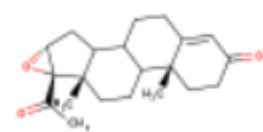
Legends

BBB
HIA
PGP+
PGP—

Remarks

None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)CCC1C2CC[C@]2(C1C[C@@H]1)[C@]2(O1)C(=O)C)C

Physicochemical Properties

Formula	C ₂₁ H ₂₈ O ₃
Molecular weight	328.45 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	3
Num. H-bond donors	0
Molar Refractivity	93.02
TPSA	46.67 Å ²

Lipophilicity

Log P _{ow} (iLOGP)	3.11
Log P _{ow} (XLOGP3)	3.93
Log P _{ow} (WLOGP)	3.85
Log P _{ow} (MLOGP)	3.07
Log P _{ow} (SILICOS-IT)	4.33
Consensus Log P _{ow}	3.66

Water Solubility	
Log S (ESOL)	-4.29
Solubility	1.70e-02 mg/ml ; 5.17e-05 mol/l
Class	Moderately soluble
Log S (Ali)	-4.61
Solubility	8.07e-03 mg/ml ; 2.46e-05 mol/l
Class	Moderately soluble
Log S (SILICOS-IT)	-4.10
Solubility	2.63e-02 mg/ml ; 8.00e-05 mol/l
Class	Moderately soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-5.51 cm/s

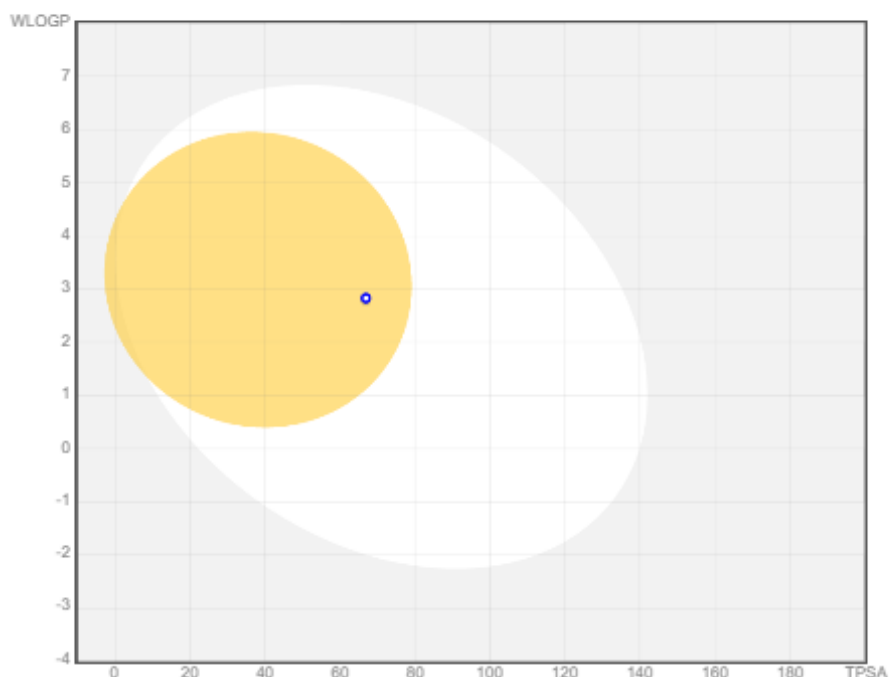
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	1 alert: Three-membered_heterocycle
Leadlikeness	No; 1 violation: XLOGP3>3.5
Synthetic accessibility	4.91

Figure.S53. 16α,17α-epoxyprogesterone (5) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions

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Legends

BBB

HIA

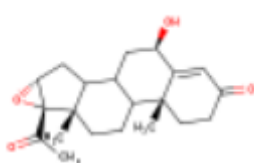
PGP+

PGP---

Remarks

None

Molecule 1



SMILES O=C1CC[C@]2(C(=C1)[C@H](O)CC1C2CC[C@]2(C1C[C@H]1[C@]2(O1)C(=O)C)C

Physicochemical Properties

Formula	C ₂₁ H ₂₈ O ₄
Molecular weight	344.44 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	94.18
TPSA	66.90 Å ²

Lipophilicity

Log P _{ow} (iLOGP)	2.81
Log P _{ow} (XLOGP3)	2.64
Log P _{ow} (WLOGP)	2.83
Log P _{ow} (MLOGP)	2.22
Log P _{ow} (SILICOS-IT)	3.43
Consensus Log P _{ow}	2.78

Water Solubility	
Log S (ESOL)	-3.57
Solubility	9.21e-02 mg/ml ; 2.67e-04 mol/l
Class	Soluble
Log S (Ali)	-3.70
Solubility	6.94e-02 mg/ml ; 2.02e-04 mol/l
Class	Soluble
Log S (SILICOS-IT)	-3.28
Solubility	1.80e-01 mg/ml ; 5.24e-04 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-6.53 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	1 alert: Three-membered_heterocycle
Leadlikeness	Yes
Synthetic accessibility	5.07

Figure.S54. 6β-hydroxy-16α,17α-epoxyprogesterone (**11**) physicochemical and ADME parameters prediction using the SwissADME modelling

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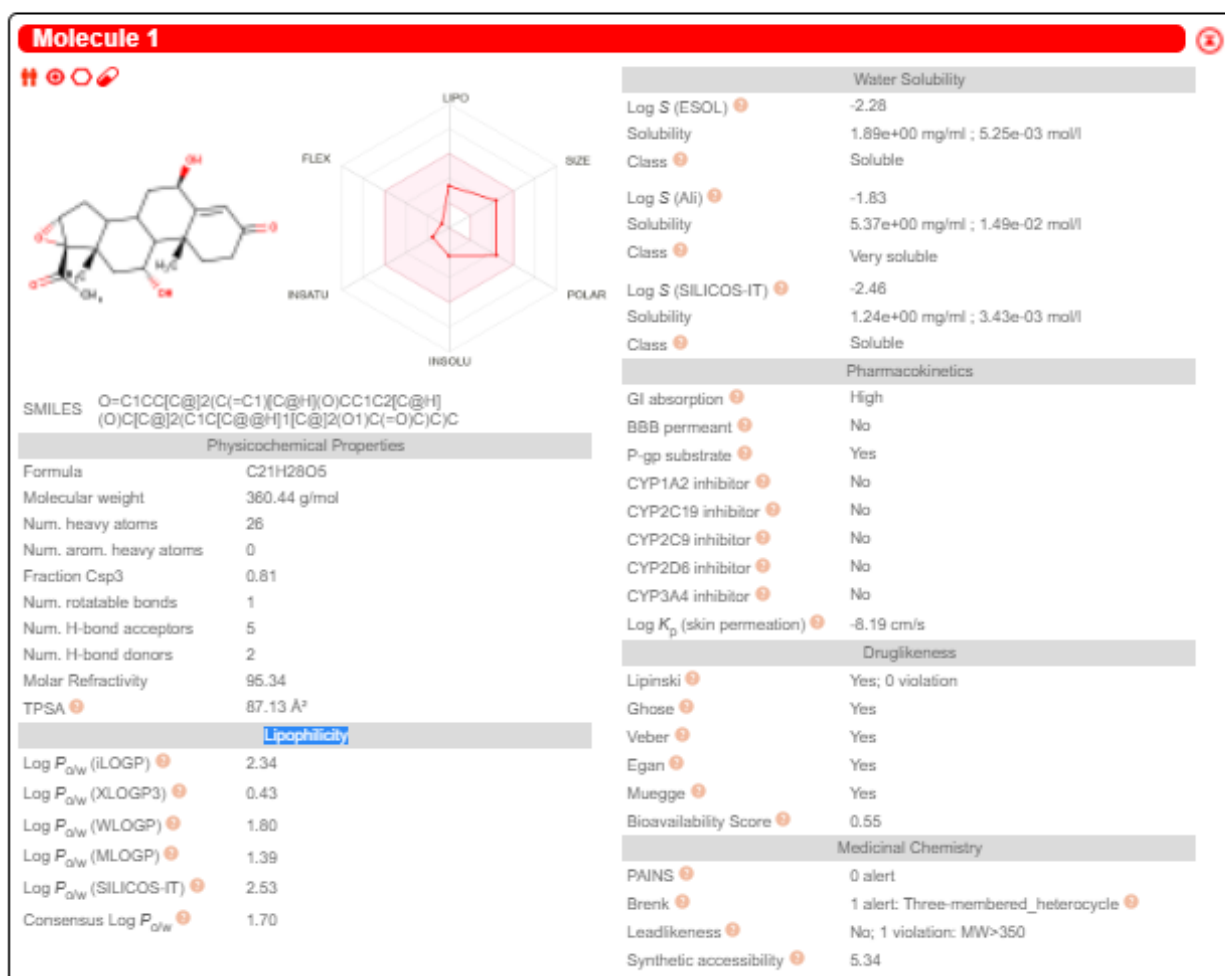
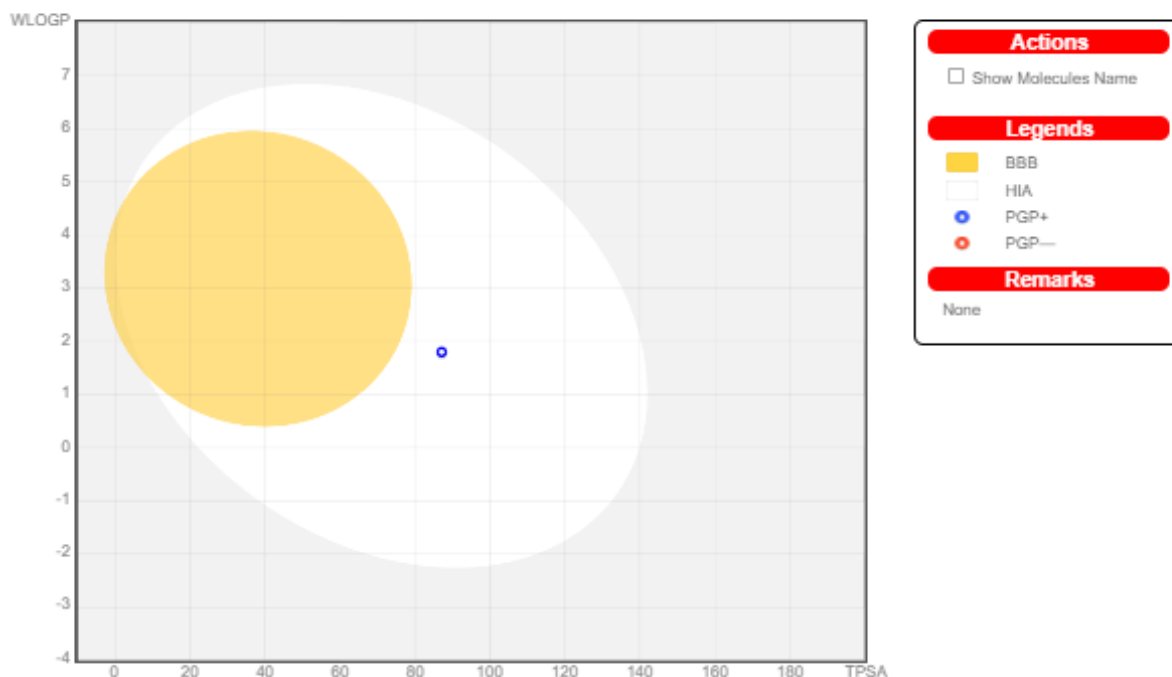


Figure.S55. 6β,11α-dihydroxy-16α,17α-epoxyprogesterone (**12**) physicochemical and ADME parameters prediction using the SwissADME modelling

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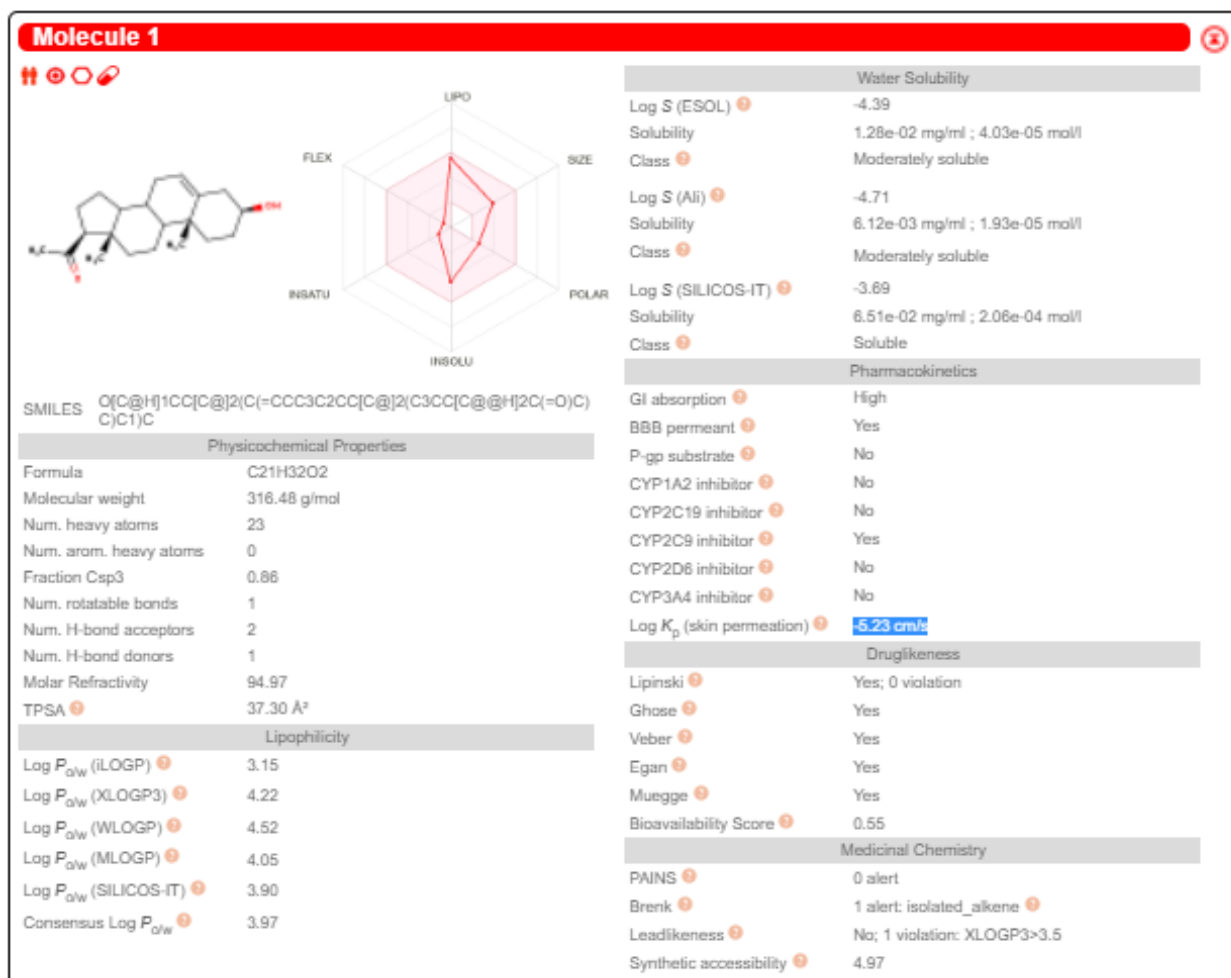
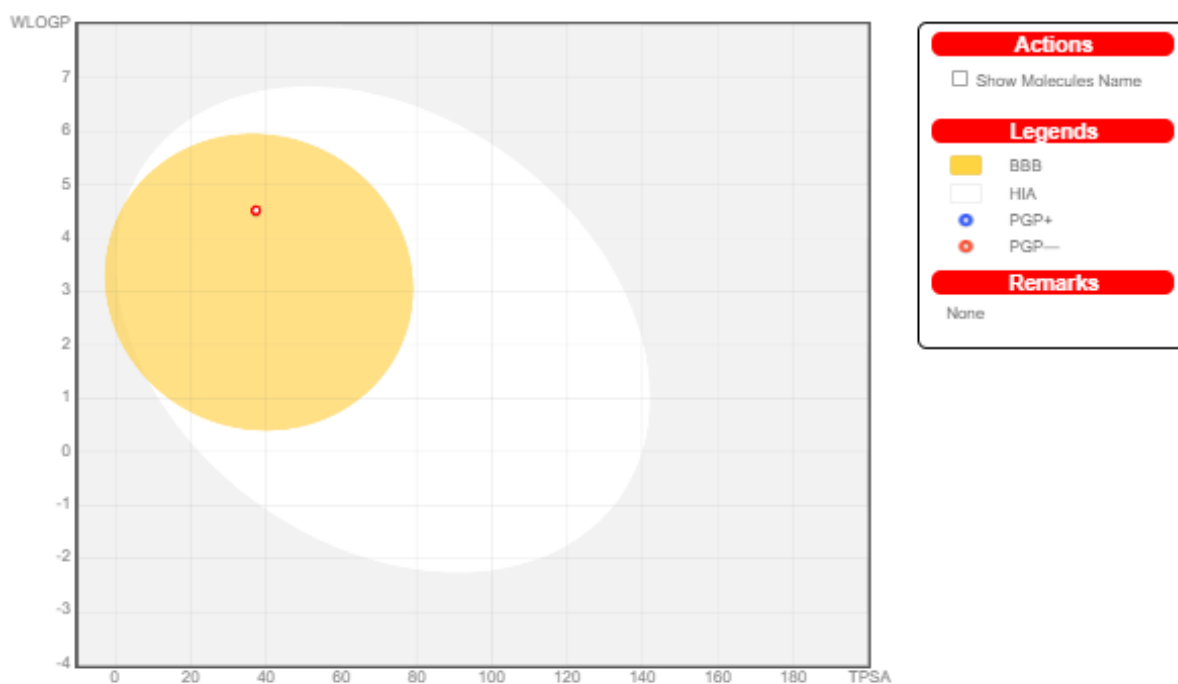
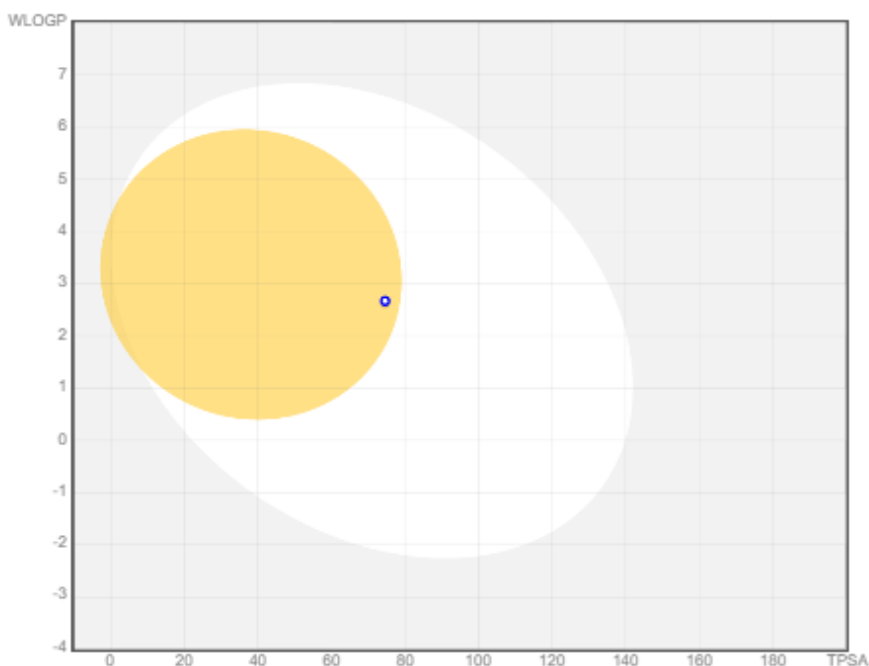


Figure.S56. Pregnenolone (6) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions

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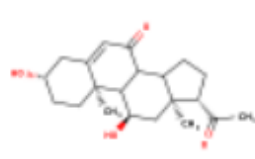
Legends

● BBB
● HIA
● PGP+
● PGP-

Remarks

None

Molecule 1



SMILES: O=C[C@H]1CC[C@]2(C(=O)C3C2[C@H](O)C[C@]3(C)C)C(=O)C1

Physicochemical Properties

Formula	C ₂₁ H ₃₀ O ₄
Molecular weight	346.46 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp ³	0.81
Num. rotatable bonds	1
Num. H-bond acceptors	4
Num. H-bond donors	2
Molar Refractivity	96.33
TPSA	74.60 Å ²

Lipophilicity

Log P _{ow} (iLOGP)	2.45
Log P _{ow} (XLOGP3)	1.63
Log P _{ow} (WLOGP)	2.67
Log P _{ow} (MLOGP)	2.22
Log P _{ow} (SILICOS-IT)	2.69
Consensus Log P _{ow}	2.33

Water Solubility

Log S (ESOL)	-2.95
Solubility	3.90e-01 mg/ml ; 1.12e-03 mol/l
Class	Soluble
Log S (Ali)	-2.81
Solubility	5.38e-01 mg/ml ; 1.55e-03 mol/l
Class	Soluble
Log S (SILICOS-IT)	-2.75
Solubility	6.12e-01 mg/ml ; 1.77e-03 mol/l
Class	Soluble

Pharmacokinetics

GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-7.26 cm ² /s

Druglikeness

Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

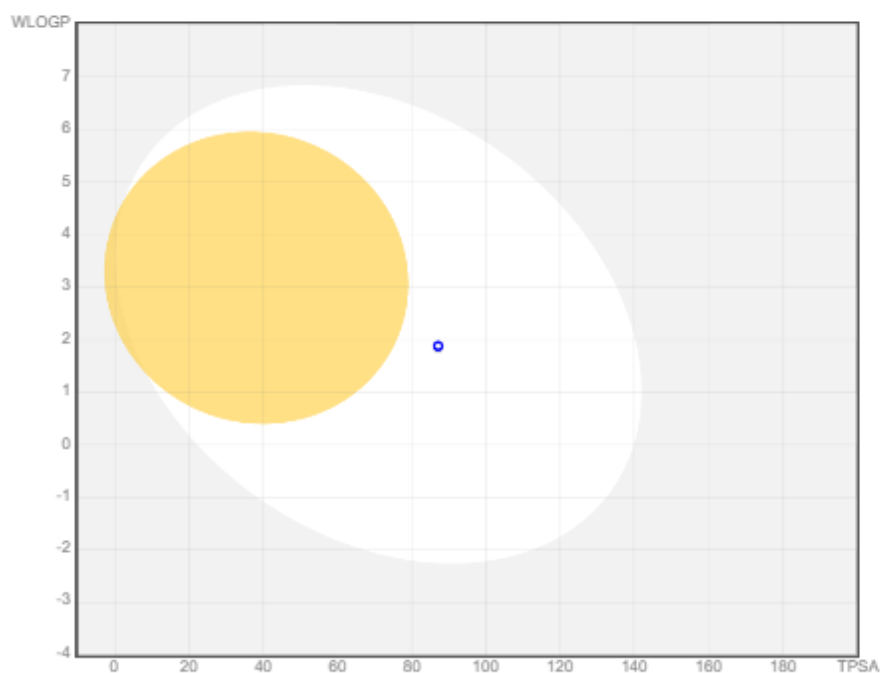
Medicinal Chemistry

PAINS	0 alert
Brenk	0 alert
Leadlikeness	Yes
Synthetic accessibility	5.30

Figure.S57. 11 α -Hydroxy-7-oxopregnenolone (**13**) physicochemical and ADME parameters prediction using the SwissADME modelling

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Actions
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Legends

- BBB
- HIA
- PGP+
- PGP—

Remarks

None

Molecule 1

SMILES: O[C@H]1CC[C@]2([C@@]3(C1)O[C@H]3C(=O)C1C2[C@H](O)[C@]2(C1CC[C@H]2C(=O)C)C

Physicochemical Properties	
Formula	C ₂₁ H ₃₀ O ₅
Molecular weight	362.46 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	0
Fraction Csp ³	0.90
Num. rotatable bonds	1
Num. H-bond acceptors	5
Num. H-bond donors	2
Molar Refractivity	95.82
TPSA	87.13 Å ²

Lipophilicity	
Log P _{ow} (iLOGP)	2.32
Log P _{ow} (XLOGP3)	1.28
Log P _{ow} (WLOGP)	1.88
Log P _{ow} (MLOGP)	1.49
Log P _{ow} (SILICOS-IT)	2.54
Consensus Log P _{ow}	1.90

Water Solubility	
Log S (ESOL)	-2.83
Solubility	5.39e-01 mg/ml ; 1.49e-03 mol/l
Class	Soluble
Log S (Ali)	-2.71
Solubility	7.08e-01 mg/ml ; 1.95e-03 mol/l
Class	Soluble
Log S (SILICOS-IT)	-2.48
Solubility	1.19e+00 mg/ml ; 3.30e-03 mol/l
Class	Soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K _p (skin permeation)	-7.60 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	1 alert: Three-membered_heterocycle
Leadlikeness	No; 1 violation: MW>350
Synthetic accessibility	5.70

Figure.S58. 5α,6α-epoxy-3β,11α-dihydroxypregnan-7,20-dione (14) physicochemical and ADME parameters prediction using the SwissADME modelling