

Supplementary Data

Biotransformation of Δ^1 -progesterone by selected entomopathogenic filamentous fungi and prediction of its products' bioactivity

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Figure S44. HMBC spectrum of $12\beta,17\alpha$ -dihydroxypregn-1,4-diene-3-one (**8**) (DMSO-*d*₆, 600/151 MHz)

Figure S45. Predicted Boiled-Egg plot from swissADME online web tool for $12\beta,17\alpha$ -dihydroxypregn-1,4-diene-3-one (**8**)

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Figure S1. Predicted Boiled-Egg plot from swissADME online web tool for progesterone (**1**)

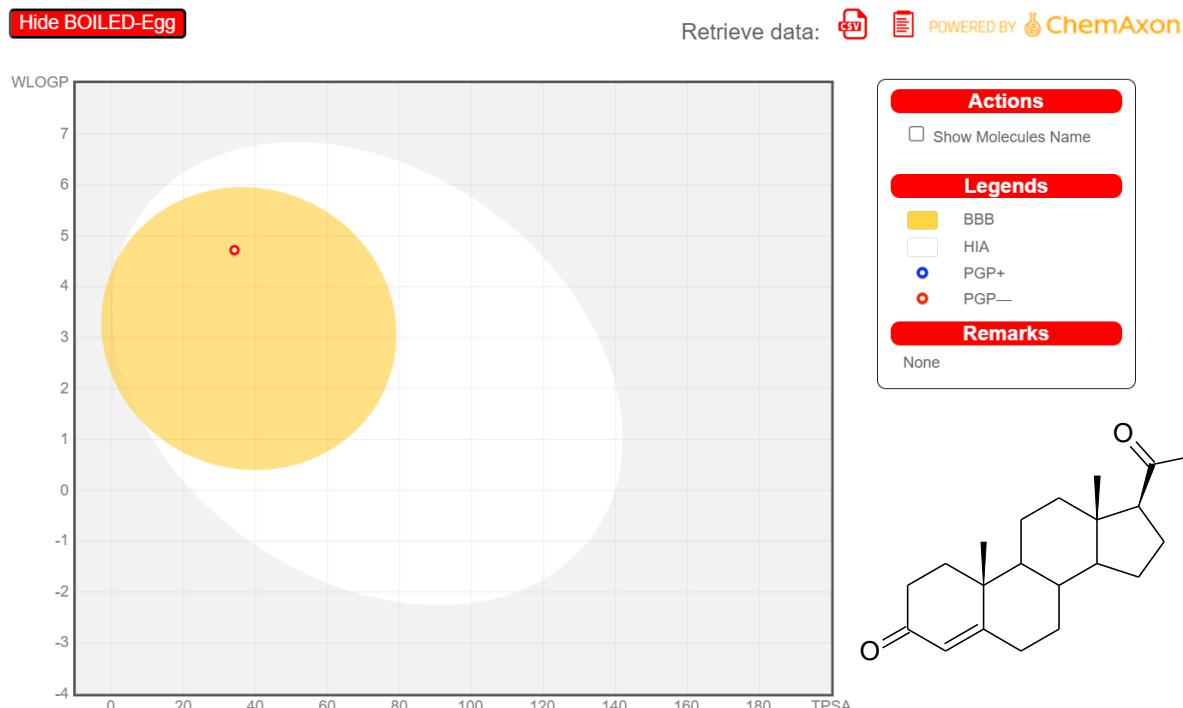


Figure S2. progesterone (**1**) physicochemical and ADME parameters prediction using the SwissADME modelling

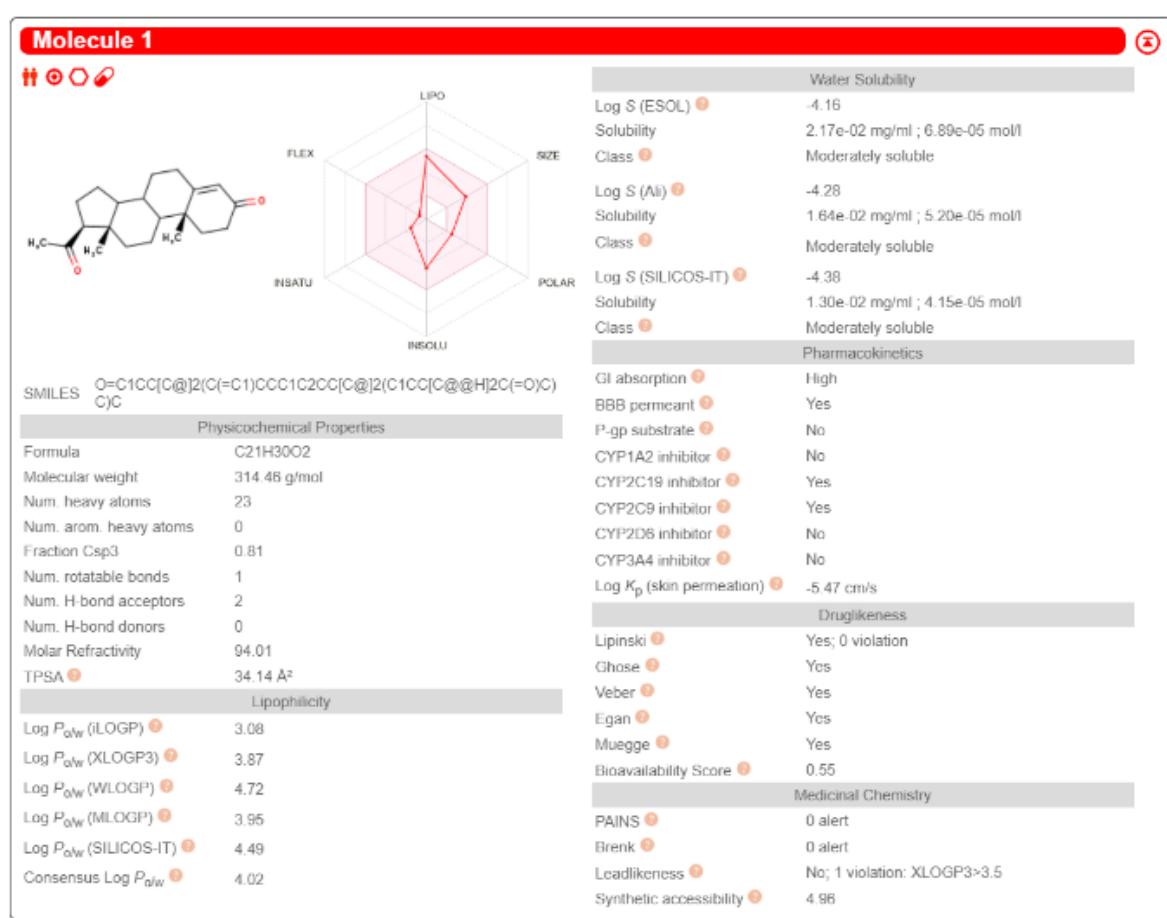


Figure S3. ^1H NMR spectra of pregn-1,4-diene-3,20-dione (Δ^1 -progesterone) (**2**) (CDCl_3 , 600 MHz)

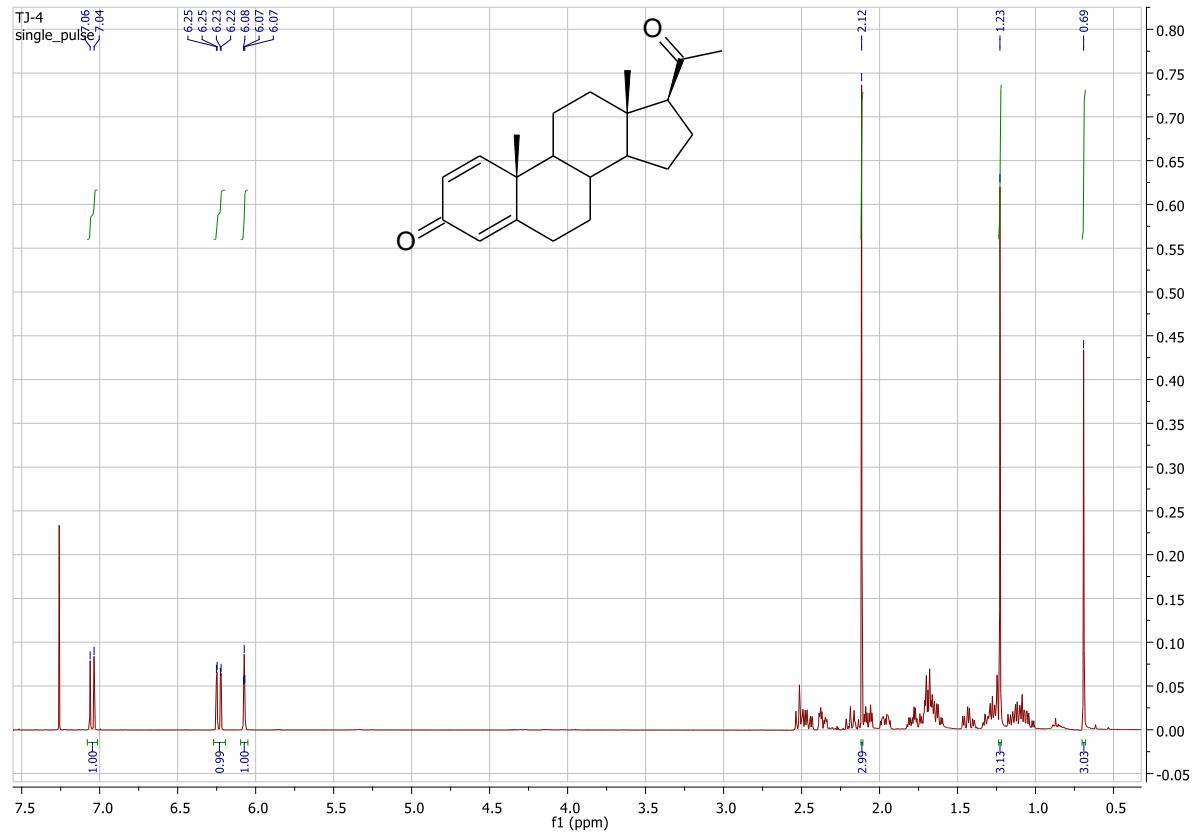


Figure S4. ^{13}C NMR spectra of pregn-1,4-diene-3,20-dione (Δ^1 -progesterone) (**2**) (CDCl_3 , 151 MHz)

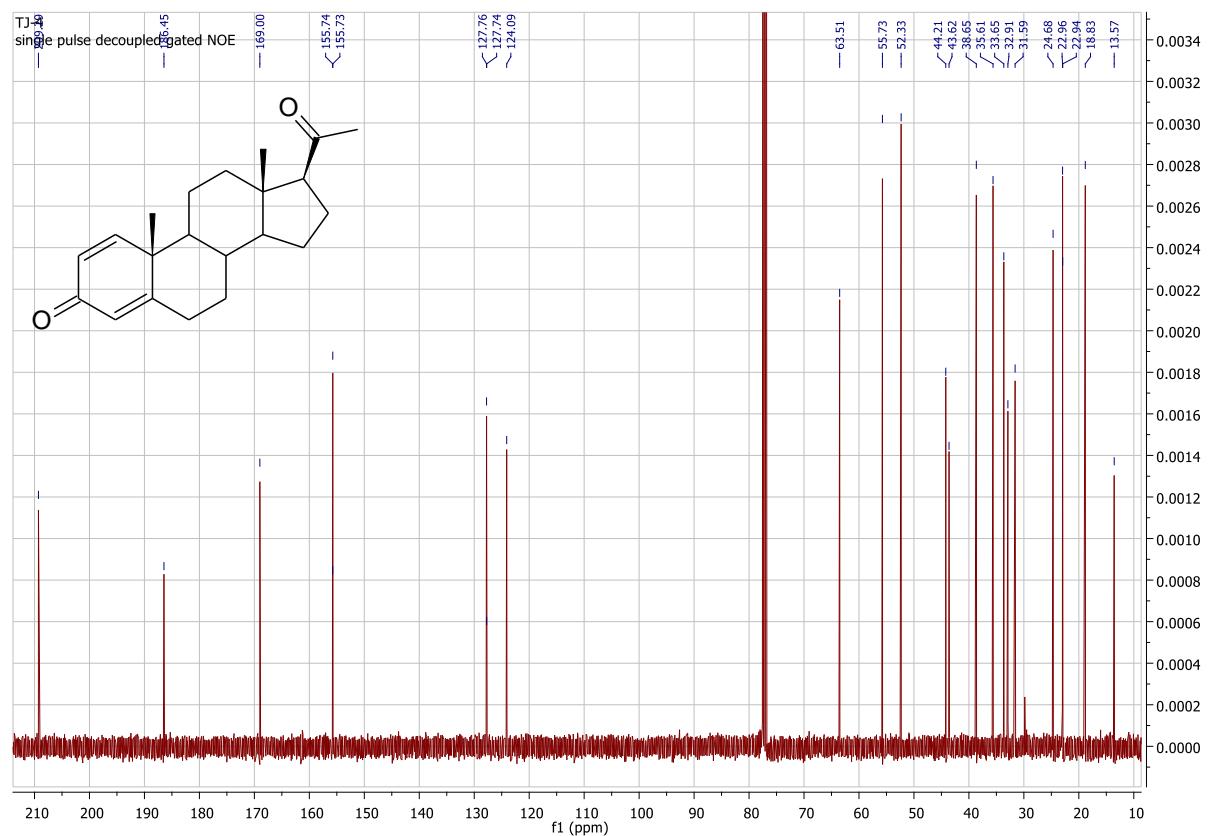


Figure S5. COSY spectrum of pregn-1,4-diene-3,20-dione (Δ^1 -progesterone) (**2**) (CDCl_3 , 600 MHz)

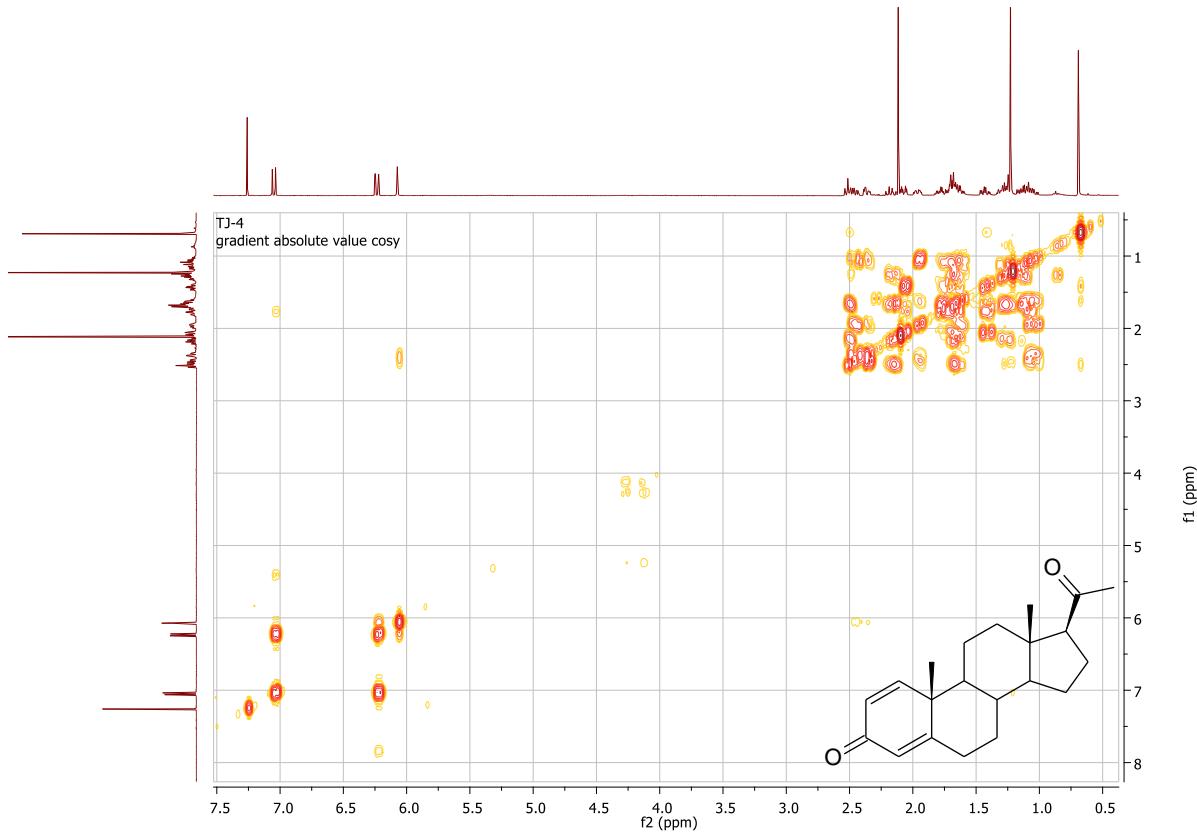


Figure S6. HSQC spectrum of pregn-1,4-diene-3,20-dione (Δ^1 -progesterone) (**2**) (CDCl_3 , 600/151 MHz)

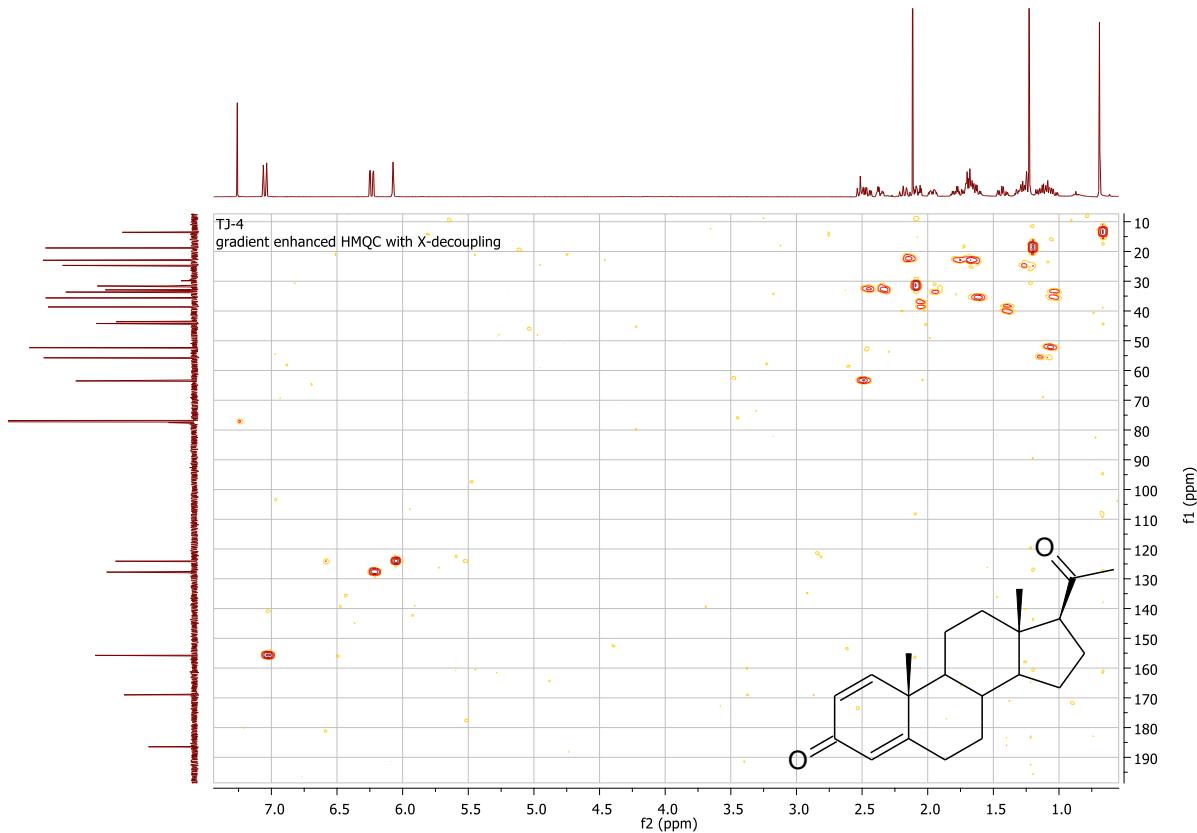


Figure S7. HMBC spectrum of pregn-1,4-diene-3,20-dione (Δ^1 -progesterone) (**2**) (CDCl_3 , 600/151 MHz)

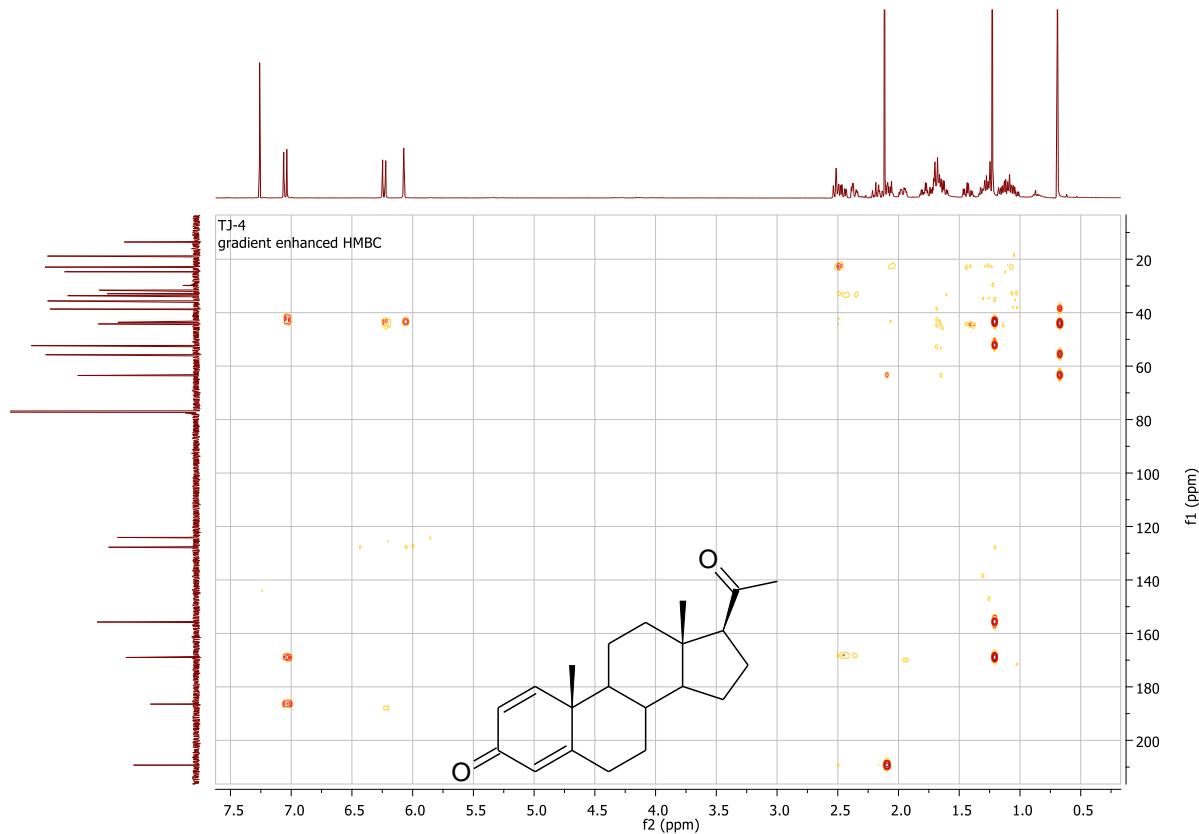


Figure S8. Predicted Boiled-Egg plot from swissADME online web tool for pregn-1,4-diene-3,20-dione (Δ^1 -progesterone) (2)

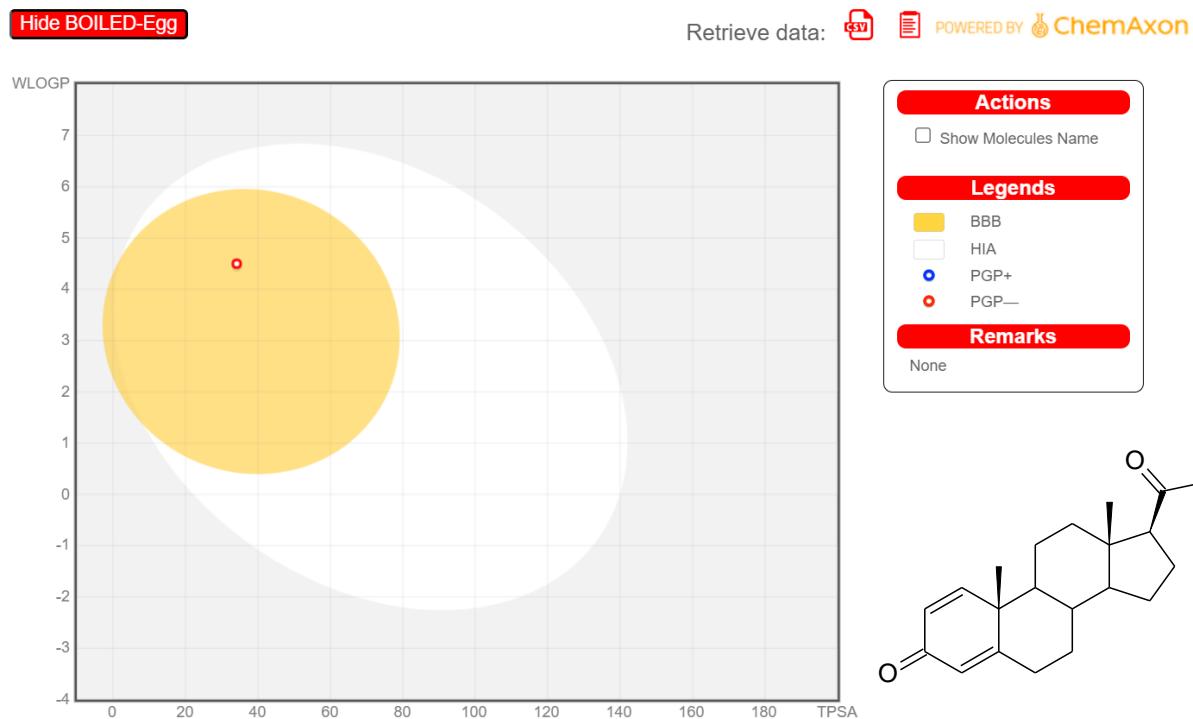


Figure S9. pregn-1,4-diene-3,20-dione (Δ^1 -progesterone) (2) physicochemical and ADME parameters prediction using the SwissADME modelling

Molecule 1

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

Physicochemical Properties

Formula	C ₂₁ H ₂₈ O ₂
Molecular weight	312.45 g/mol
Num. heavy atoms	23
Num. arom. heavy atoms	0
Fraction Csp3	0.71
Num. rotatable bonds	1
Num. H-bond acceptors	2
Num. H-bond donors	0
Molar Refractivity	93.54
TPSA	34.14 Å ²

Lipophilicity

Log P_{ow} (iLOGP)	3.03
Log P_{ow} (XLOGP3)	4.08
Log P_{ow} (WLOGP)	4.50
Log P_{ow} (MLOGP)	3.86
Log P_{ow} (SILICOS-IT)	4.08
Consensus Log P_{ow}	3.91

Water Solubility

Log S (ESOL)	-4.28
Solubility	1.63e-02 mg/ml ; 5.23e-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)	-5.31 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	5.07

Figure S10. ¹H NMR spectra of 11 α -hydroxypregn-1,4-diene-3,20-dione (**3**) (CDCl₃, 600 MHz)

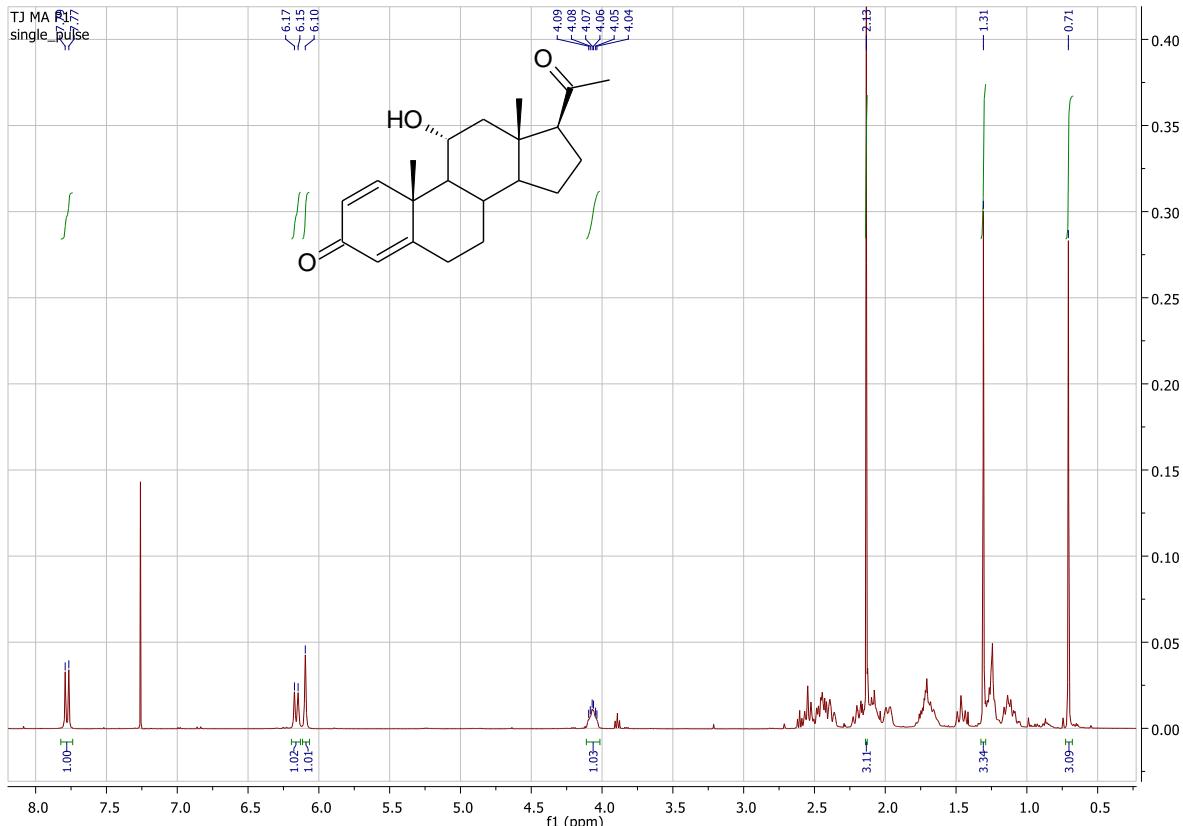


Figure S11. ¹³C NMR spectra of 11 α -hydroxypregn-1,4-diene-3,20-dione (**3**) (CDCl₃, 151 MHz)

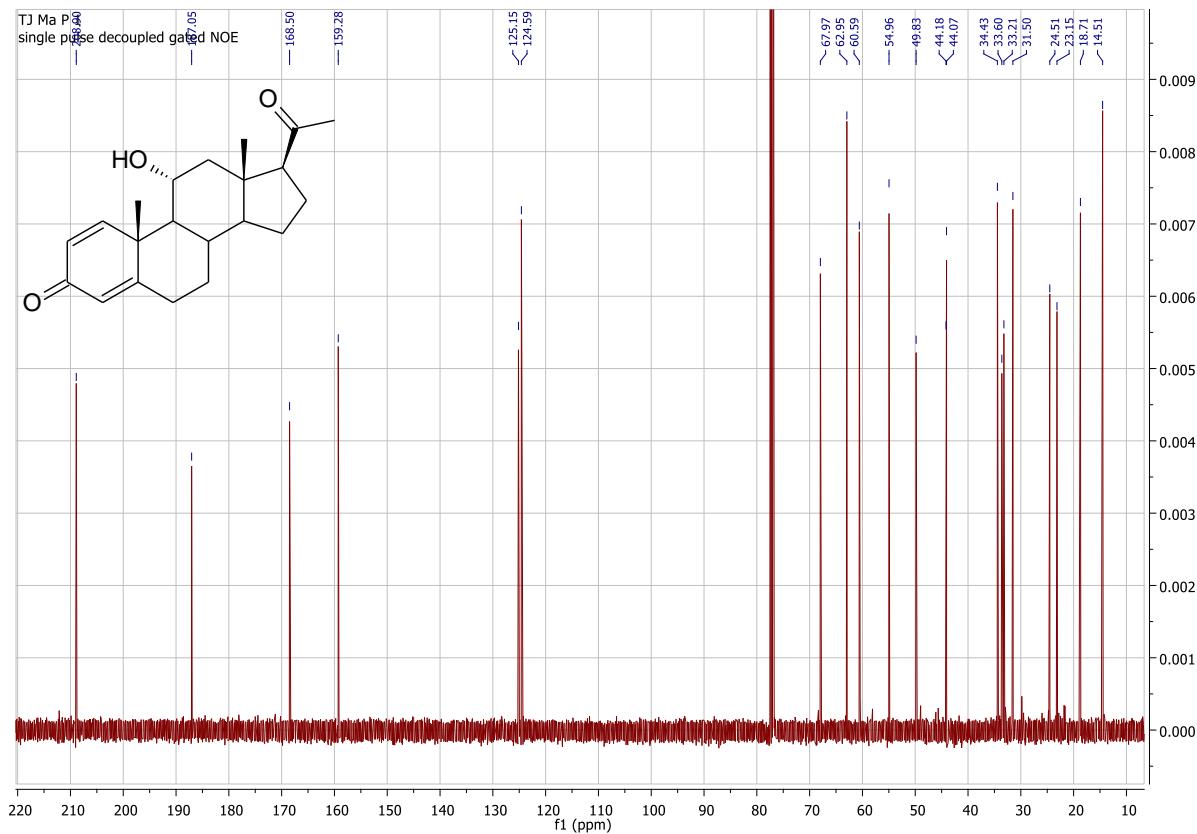


Figure S12. COSY spectrum of 11 α -hydroxypregn-1,4-diene-3,20-dione (**3**) (CDCl_3 , 600 MHz)

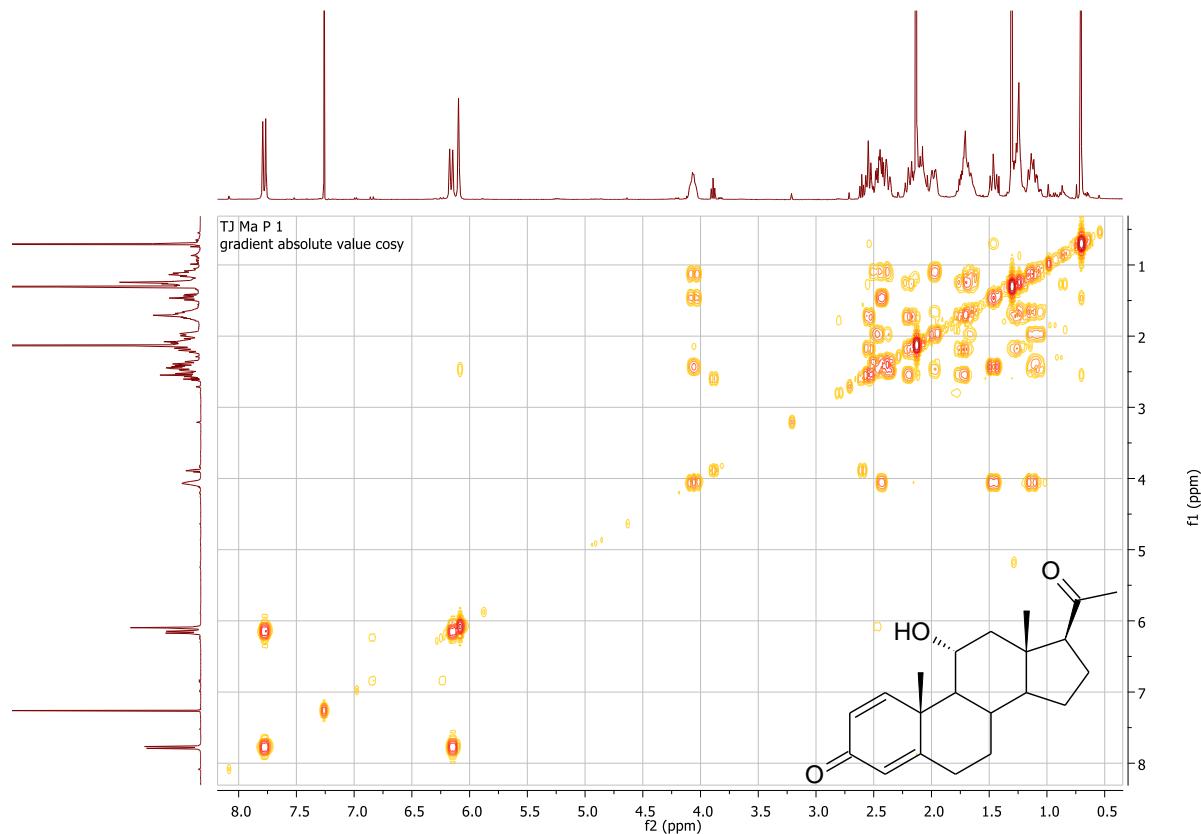


Figure S13. HSQC spectrum of 11 α -hydroxypregn-1,4-diene-3,20-dione (**3**) (CDCl_3 , 600/151 MHz)

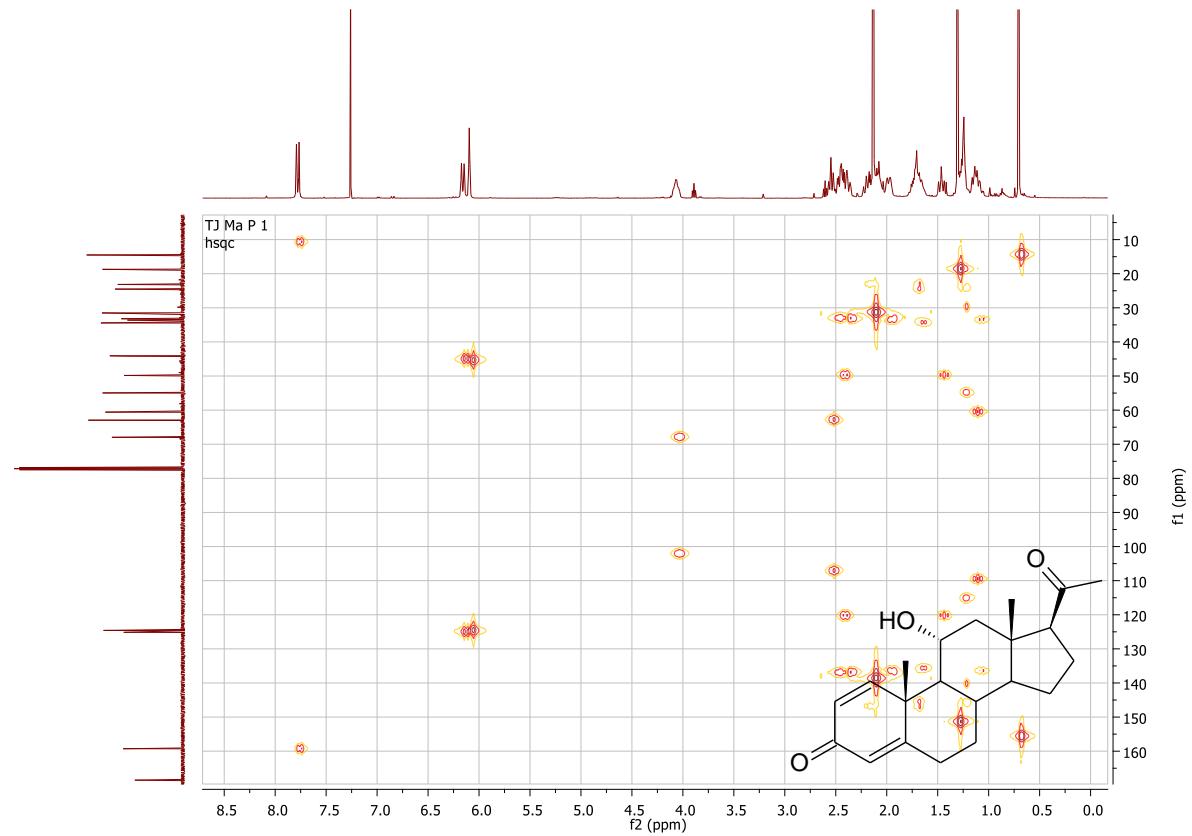


Figure S14. HMBC spectrum of 11 α -hydroxypregn-1,4-diene-3,20-dione (**3**) (CDCl_3 , 600/151 MHz)

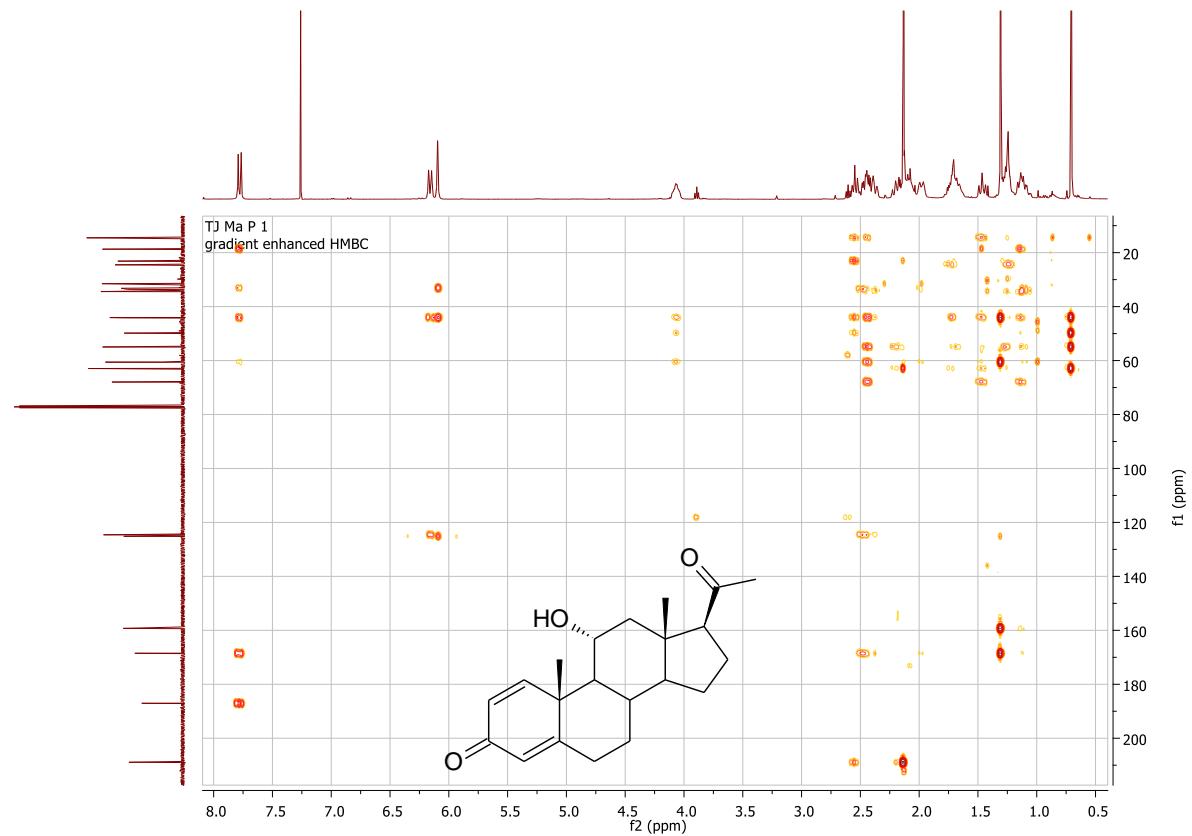


Figure S15. Predicted Boiled-Egg plot from swissADME online web tool for 11 α -hydroxypregn-1,4-diene-3,20-dione (**3**)

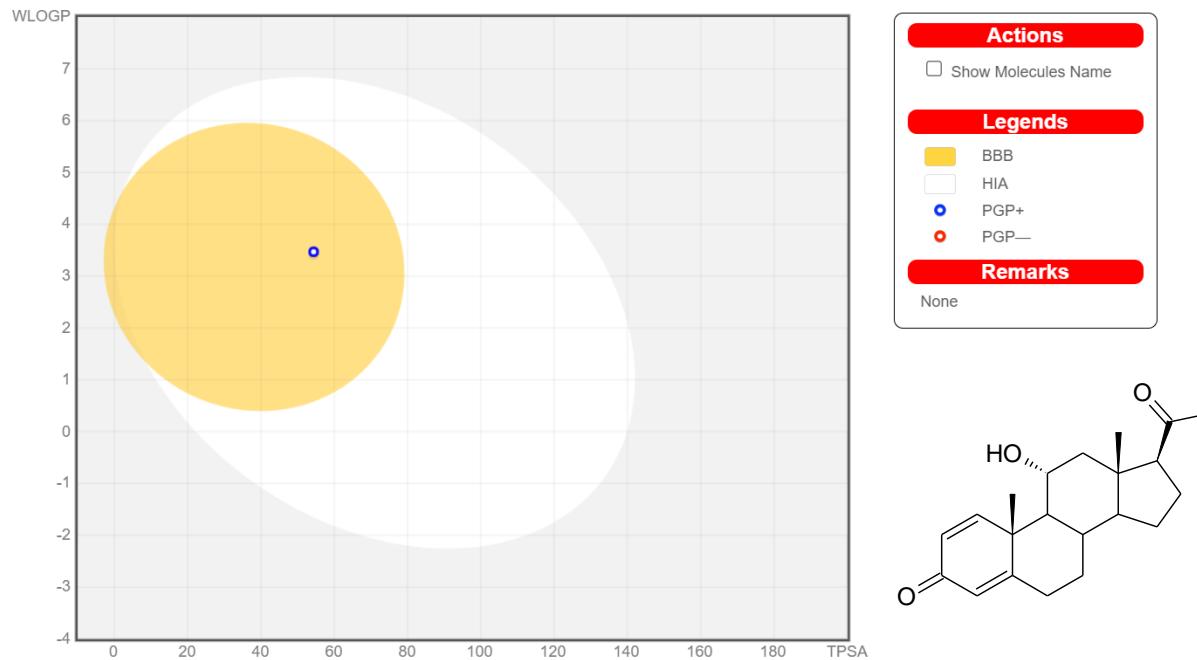
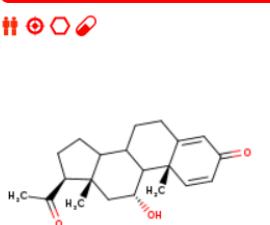
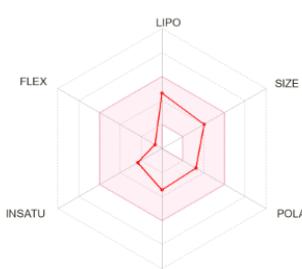
[Hide BOILED-Egg](#)Retrieve data: [CSV](#) [JSON](#) POWERED BY  ChemAxon

Figure S16. 11 α -hydroxypregn-1,4-diene-3,20-dione (**3**) physicochemical and ADME parameters prediction using the SwissADME modelling

Molecule 1





		Water Solubility	
		Log S (ESOL)	-3.43
		Solubility	1.22e-01 mg/ml ; 3.72e-04 mol/l
		Class	Soluble
		Log S (Ali)	-3.36
		Solubility	1.43e-01 mg/ml ; 4.37e-04 mol/l
		Class	Soluble
		Log S (SILICOS-IT)	-3.10
		Solubility	2.60e-01 mg/ml ; 7.93e-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)	-6.48 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	5.05

Figure S17. ^1H NMR spectra of 6 β ,11 α -dihydroxypregn-1,4-diene-3,20-dione (**4**) (DMSO-*d*₆, 600 MHz)

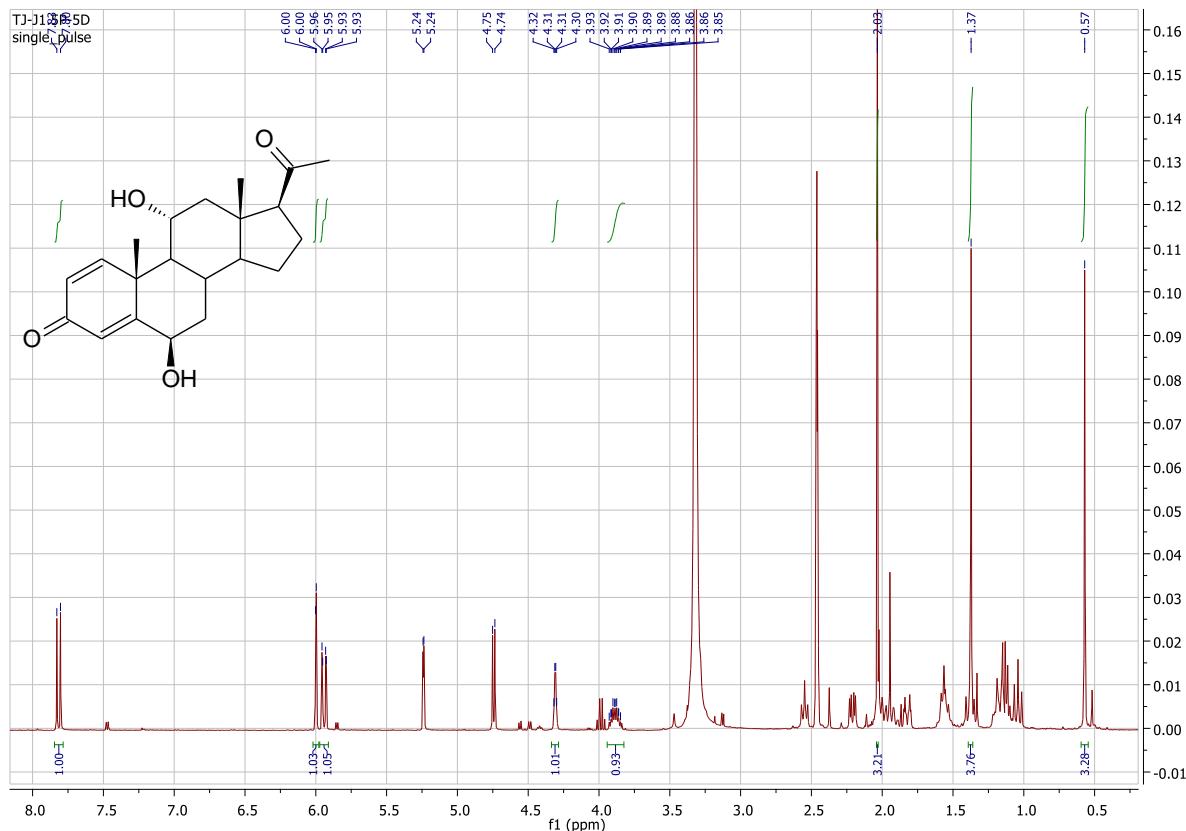


Figure S18. ^{13}C NMR spectra of $6\beta,11\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**4**) (DMSO- d_6 , 151 MHz)

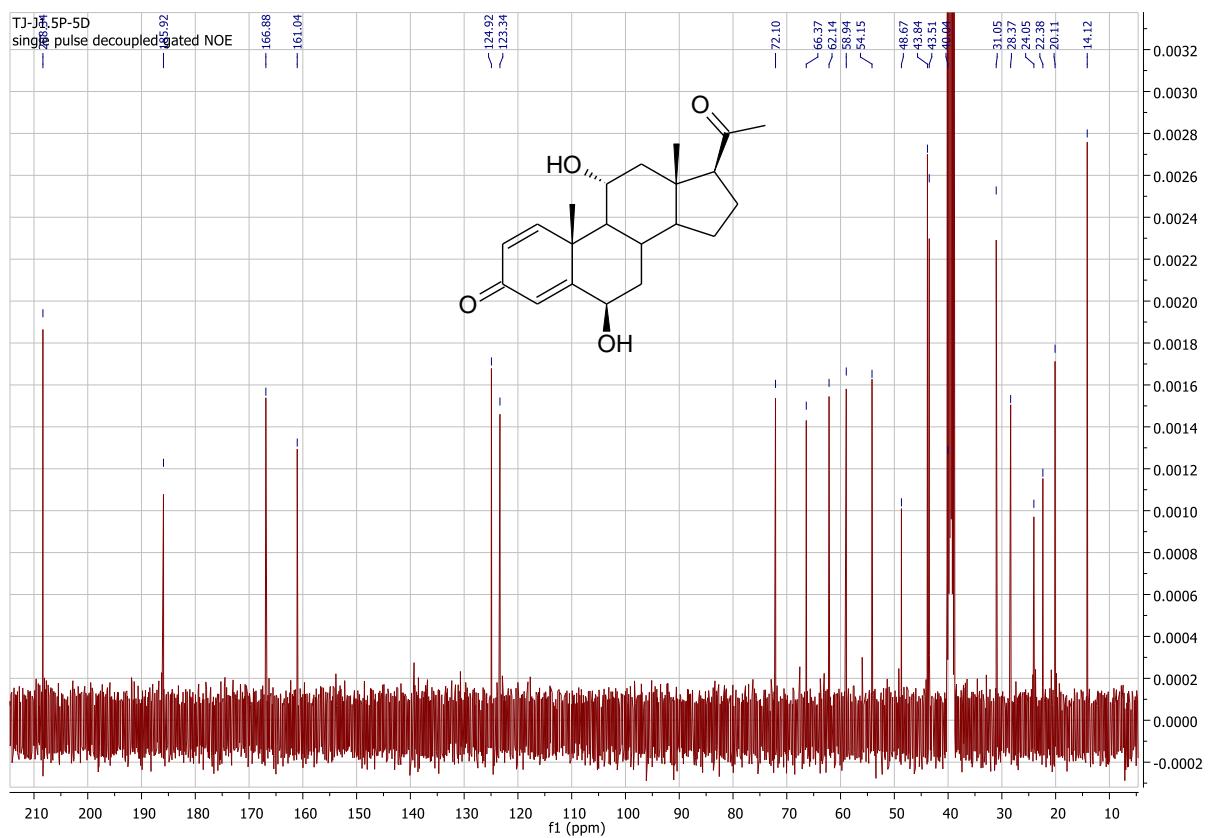


Figure S19. COSY spectrum of $6\beta,11\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**4**) (DMSO- d_6 , 600 MHz)

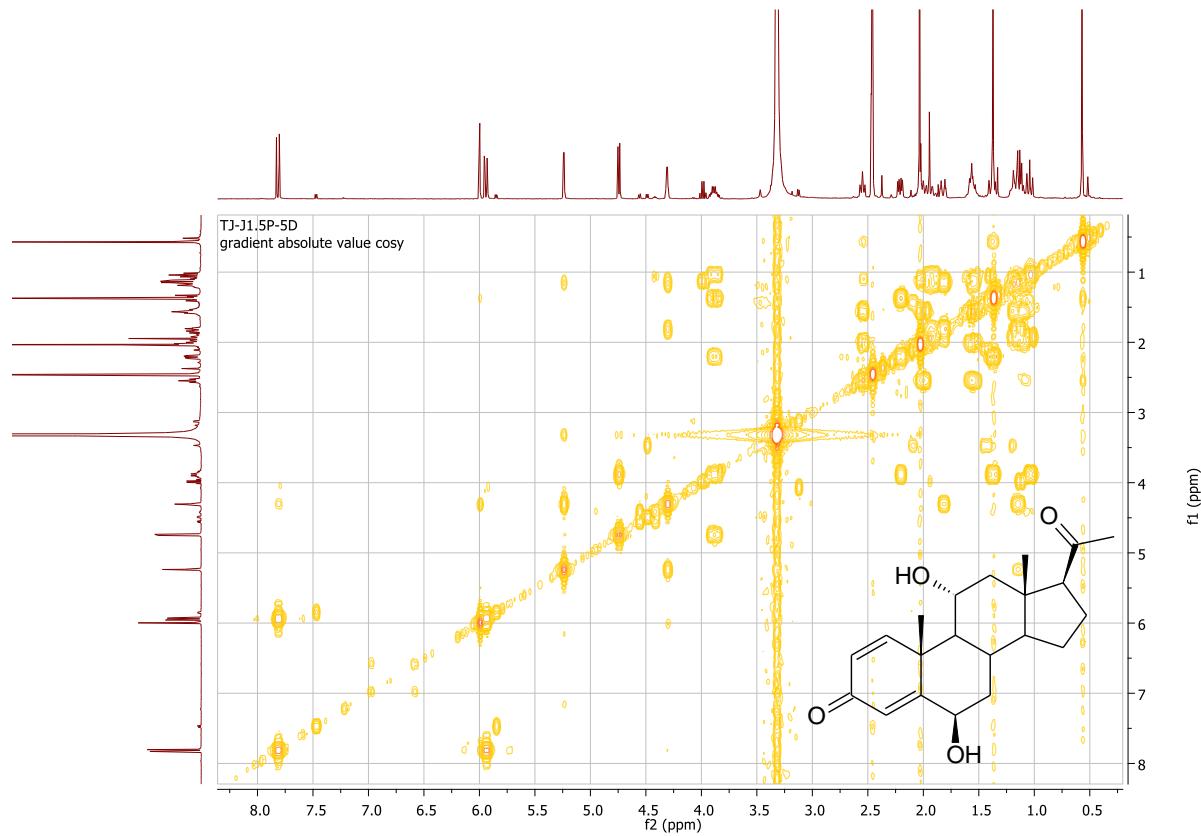


Figure S20. HSQC spectrum of *6 β ,11 α -dihydroxypregn-1,4-diene-3,20-dione* (**4**) (DMSO-*d*₆, 600/151 MHz)

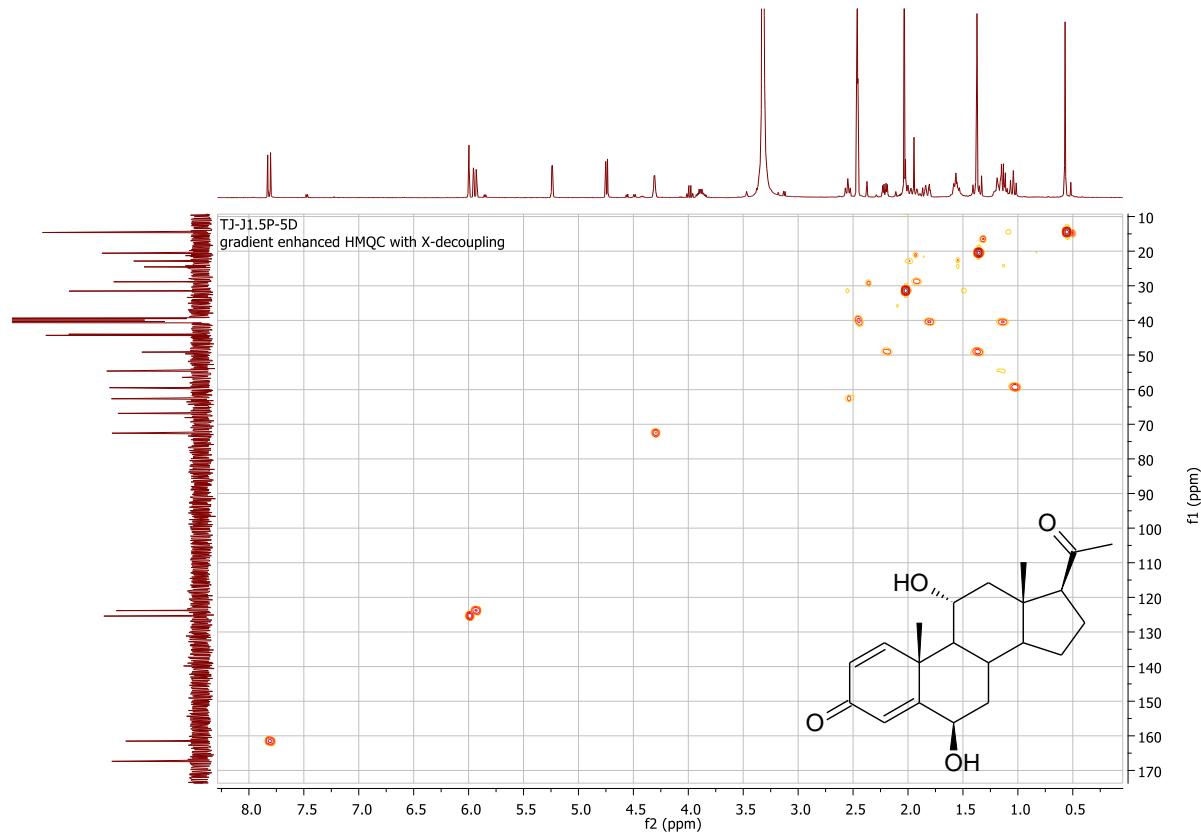


Figure S21. HMBC spectrum of *6 β ,11 α -dihydroxypregn-1,4-diene-3,20-dione* (**4**) (DMSO-*d*₆, 600/151 MHz)

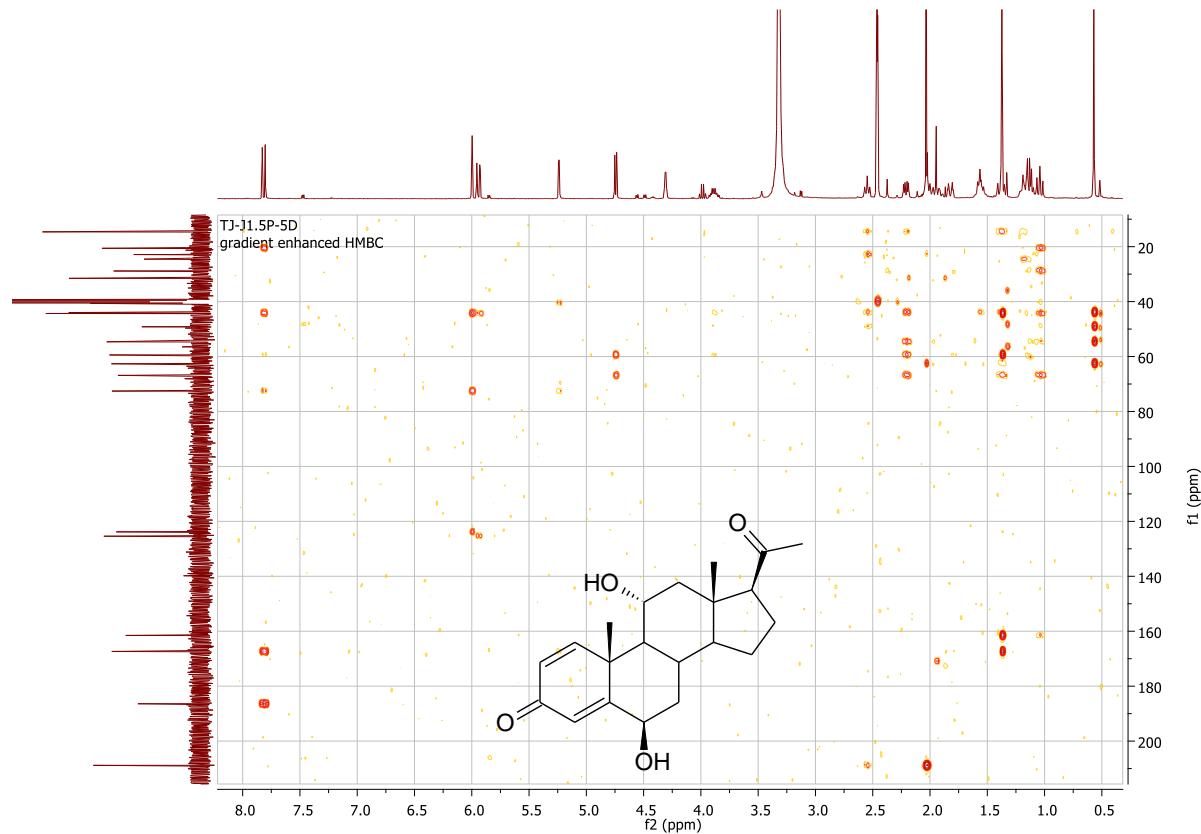


Figure S22. Predicted Boiled-Egg plot from swissADME online web tool for 6 β ,11 α -dihydroxy pregn-1,4-diene-3,20-dione (**4**)

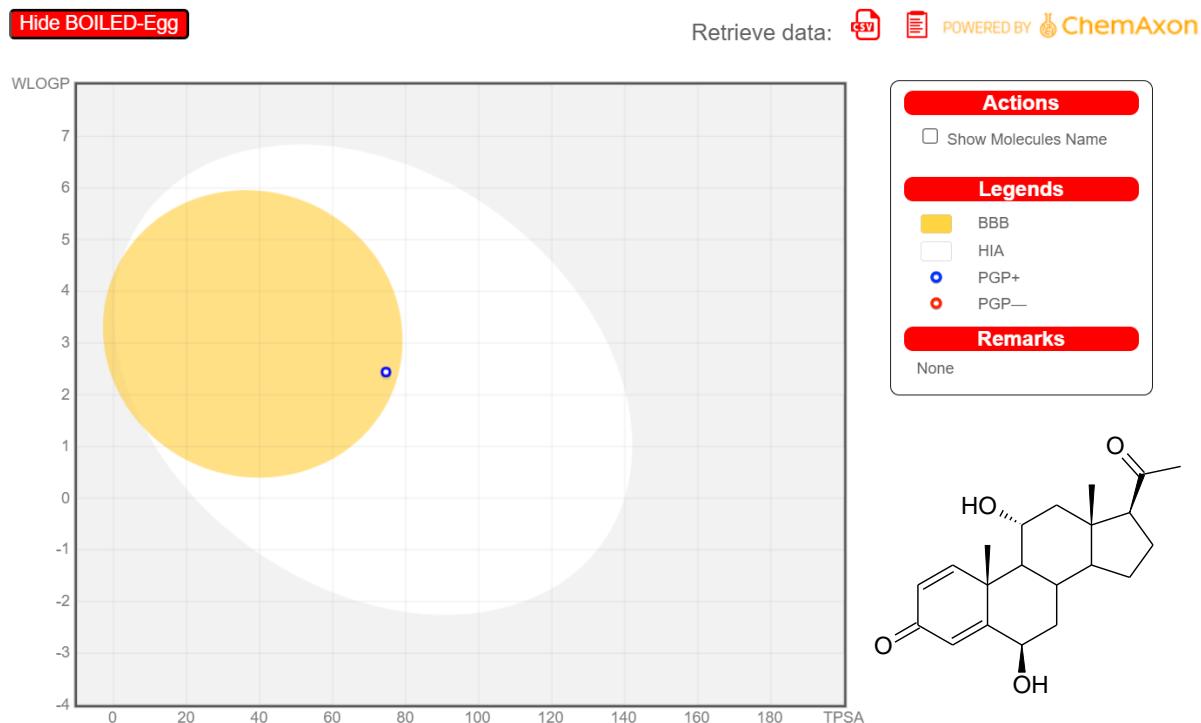


Figure S23. $6\beta,11\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**4**) physicochemical and ADME parameters prediction using the SwissADME modelling

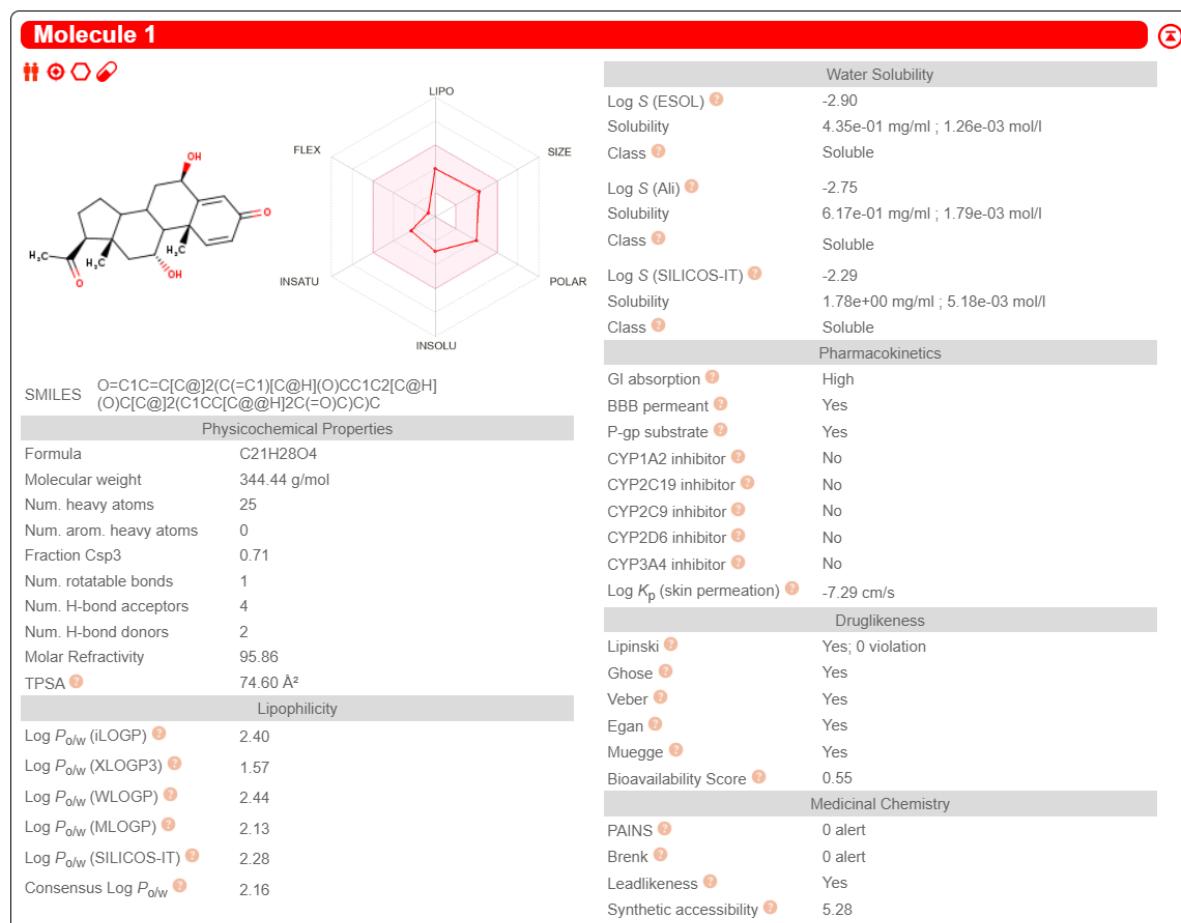


Figure S24. ^1H NMR spectra of 6β -hydroxypregn-1,4-diene-3,11,20-trione (**5**) (CDCl_3 , 600 MHz)

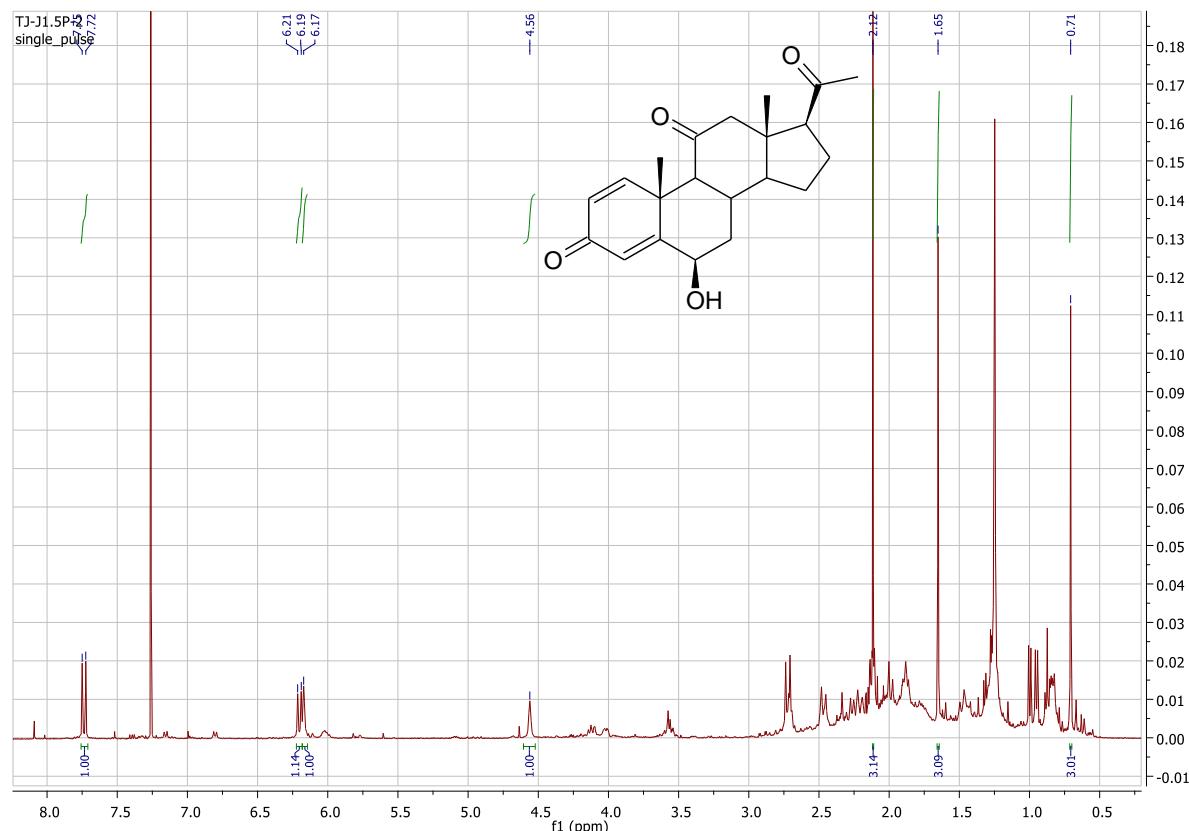


Figure S25. ^{13}C NMR spectra of 6 β -hydroxypregn-1,4-diene-3,11,20-trione (**5**) (CDCl_3 , 151 MHz)

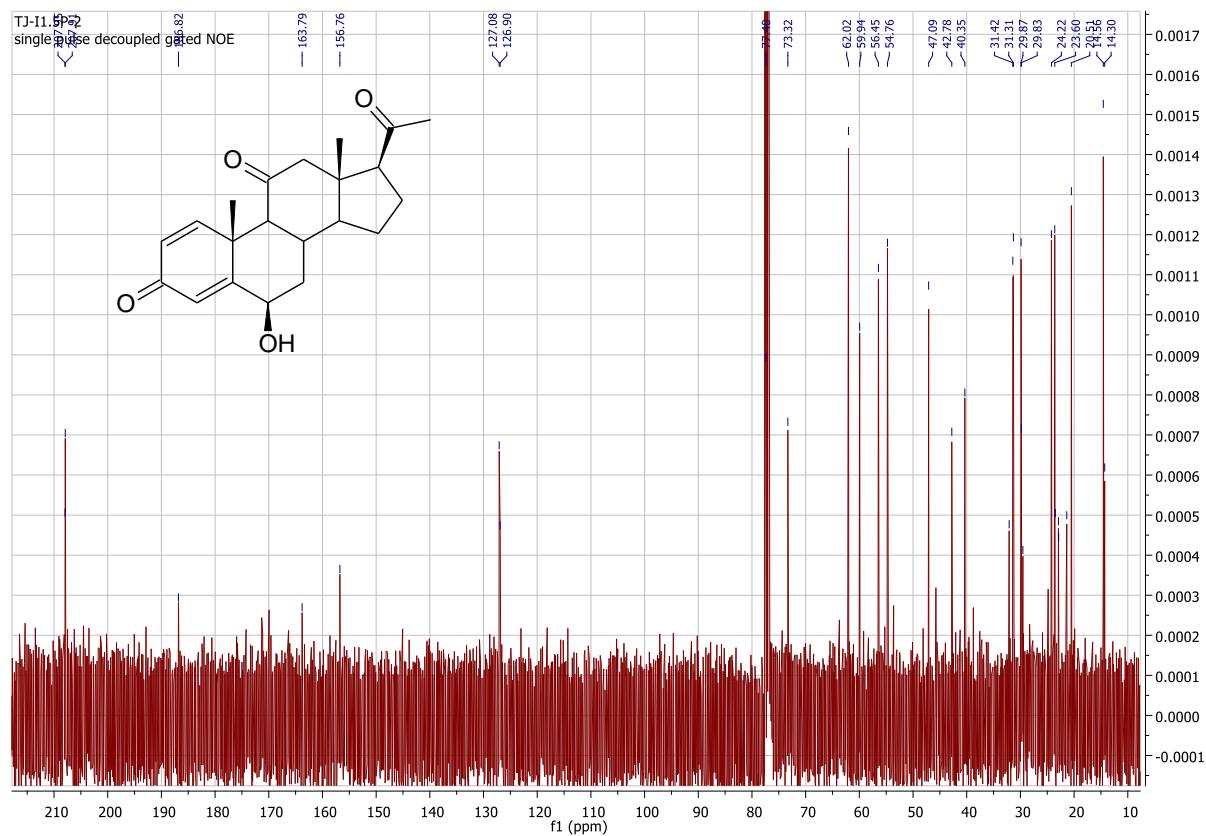


Figure S26. COSY spectrum of 6 β -hydroxypregn-1,4-diene-3,11,20-trione (**5**) (CDCl_3 , 600 MHz)

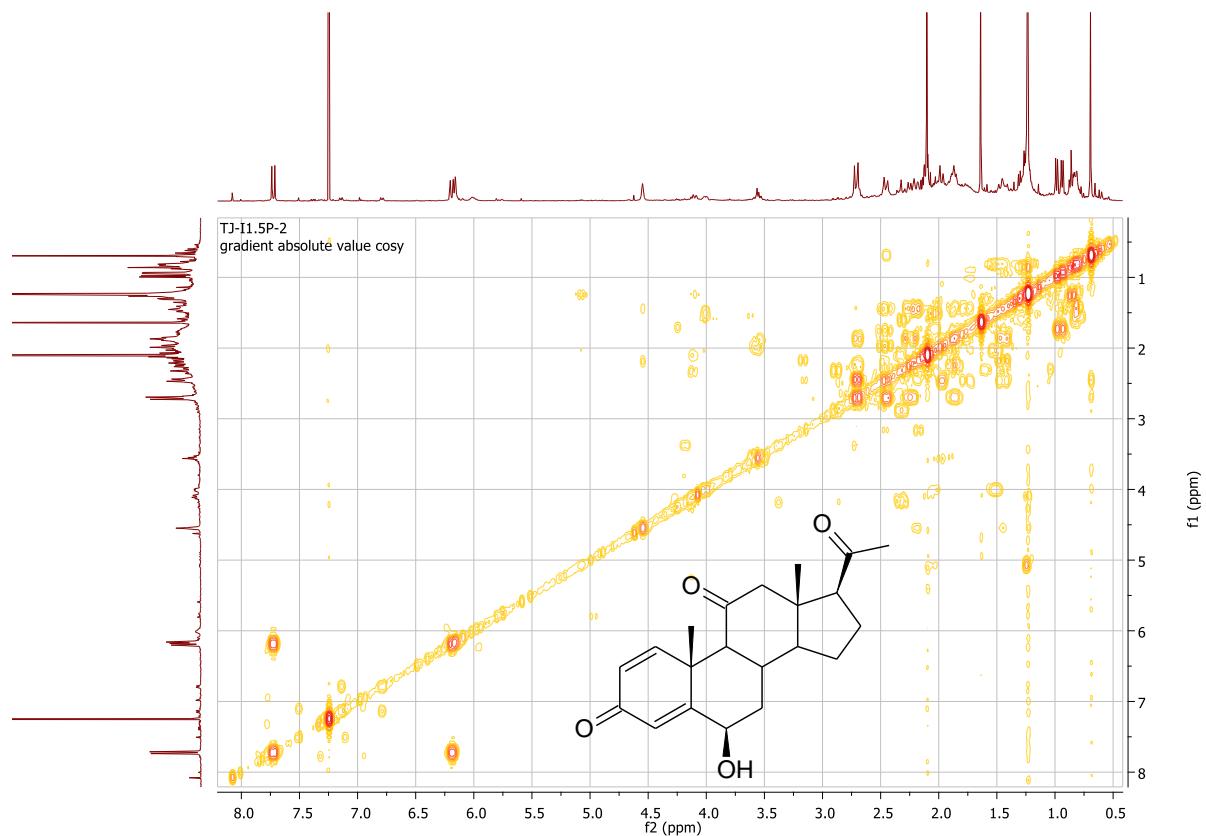


Figure S27. HSQC spectrum of 6β -hydroxypregn-1,4-diene-3,11,20-trione (**5**) (CDCl_3 , 600/151 MHz)

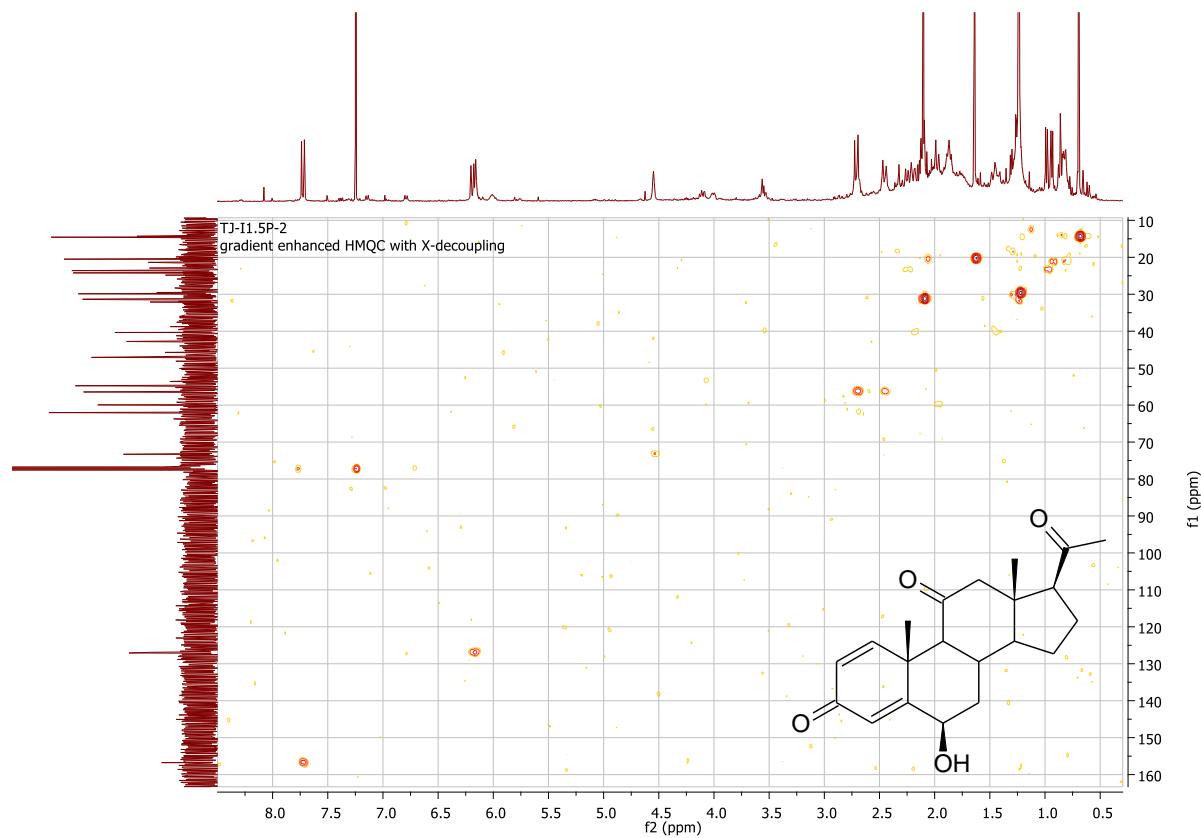


Figure S28. HMBC spectrum of 6β -hydroxypregn-1,4-diene-3,11,20-trione (**5**) (CDCl_3 , 600/151 MHz)

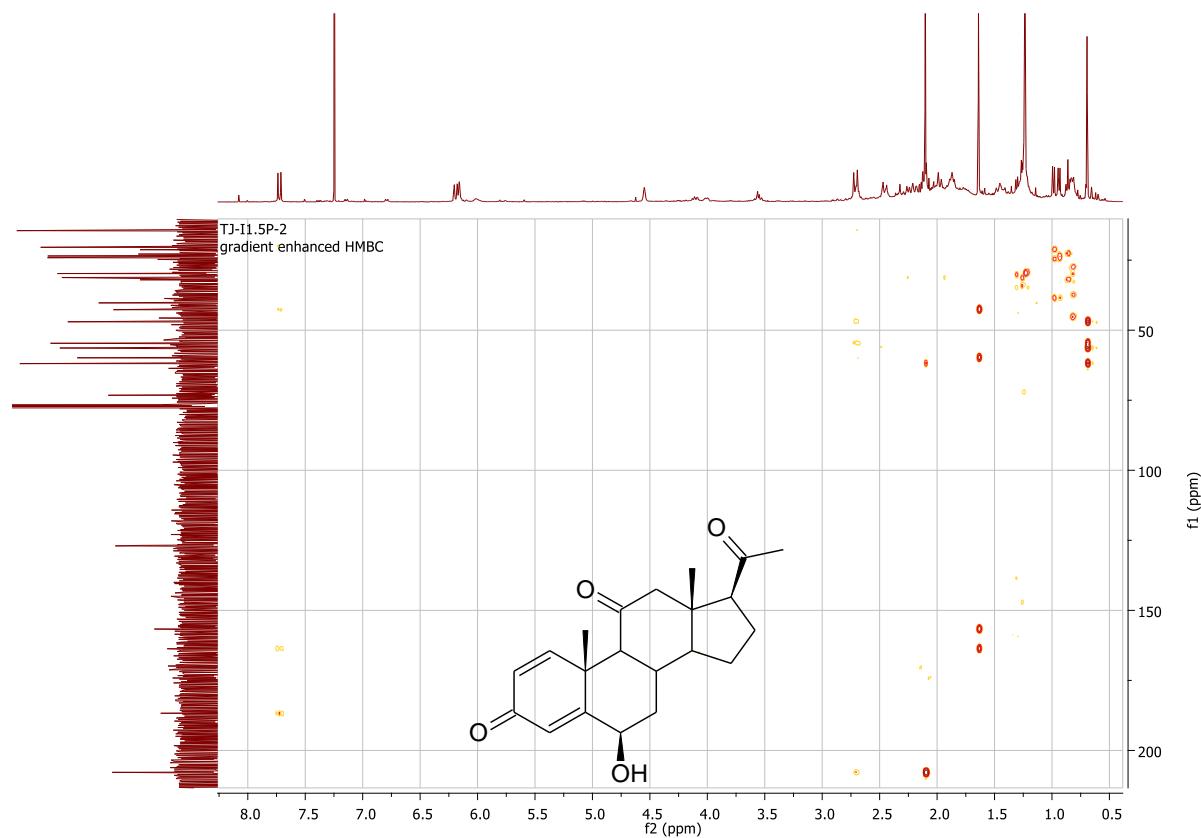


Figure S29. Predicted Boiled-Egg plot from swissADME online web tool for 6β -hydroxypregn-1,4-diene-3,11,20-trione (**5**)

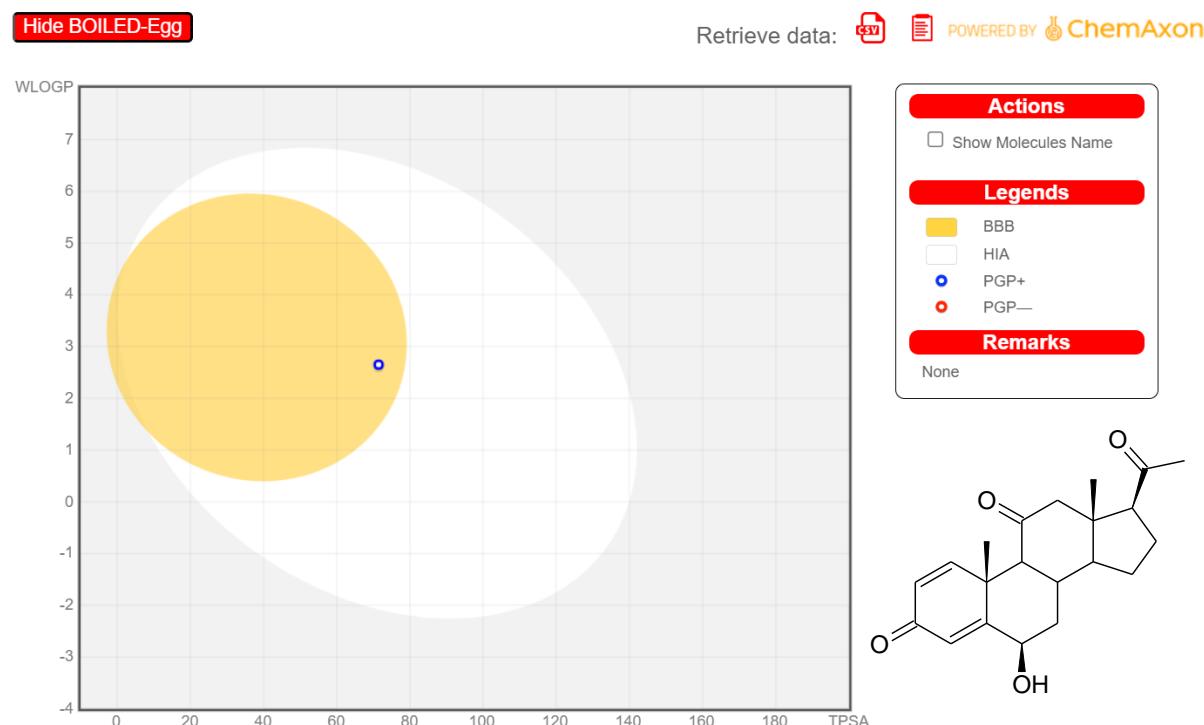


Figure S30. 6β -hydroxypregn-1,4-diene-3,11,20-trione (**5**) physicochemical and ADME parameters prediction using the SwissADME modelling

Molecule 1

Physicochemical Properties

SMILES	<chem>O=C1C=CC[C@]2[C(=C)[C@H](O)C[C@]2(C1)C[C@@H]3[C@H]4[C@H]3[C@H]4C(=O)C5</chem>
Formula	C ₂₁ H ₂₆ O ₄
Molecular weight	342.43 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	0
Fraction Csp3	0.67
Num. rotatable bonds	1
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	94.90
TPSA	71.44 Å ²

Lipophilicity

Log P_{ow} (iLOGP)	2.22
Log P_{ow} (XLOGP3)	1.29
Log P_{ow} (WLOGP)	2.65
Log P_{ow} (MLOGP)	2.04
Log P_{ow} (SILICOS-IT)	2.87
Consensus Log P_{ow}	2.22

Water Solubility

Log S (ESOL)	-2.71
Solubility Class	Soluble
Log S (Ali)	-2.39
Solubility Class	Soluble
Log S (SILICOS-IT)	-2.98
Solubility 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)	-7.47 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	Yes
Synthetic accessibility	5.19

Figure S31. ^1H NMR spectra of $6\beta,17\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**6**) and $6\beta,17\beta$ -dihydroxyandrost-1,4-diene-3-one (**7**) (CDCl_3 , 600 MHz)

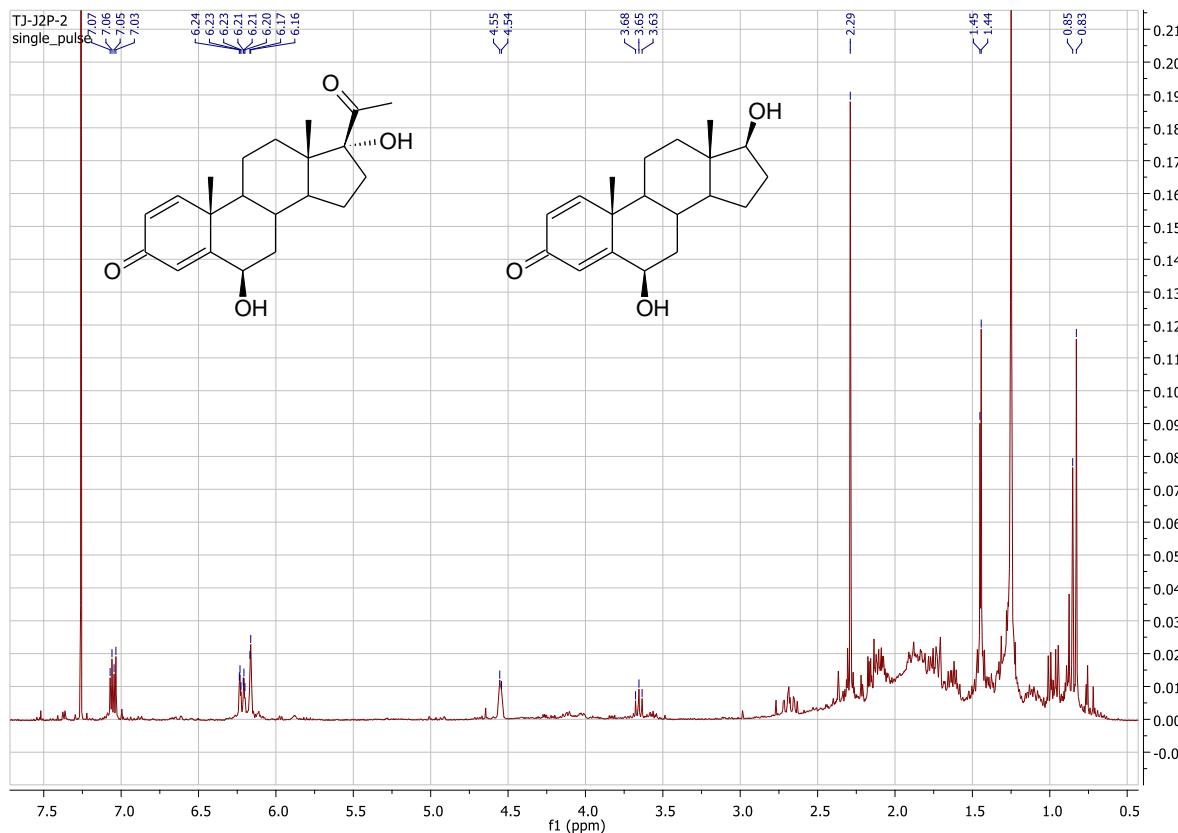


Figure S32. ^{13}C NMR spectra of $6\beta,17\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**6**) and $6\beta,17\beta$ -dihydroxyandrost-1,4-diene-3-one (**7**) (CDCl_3 , 151 MHz)

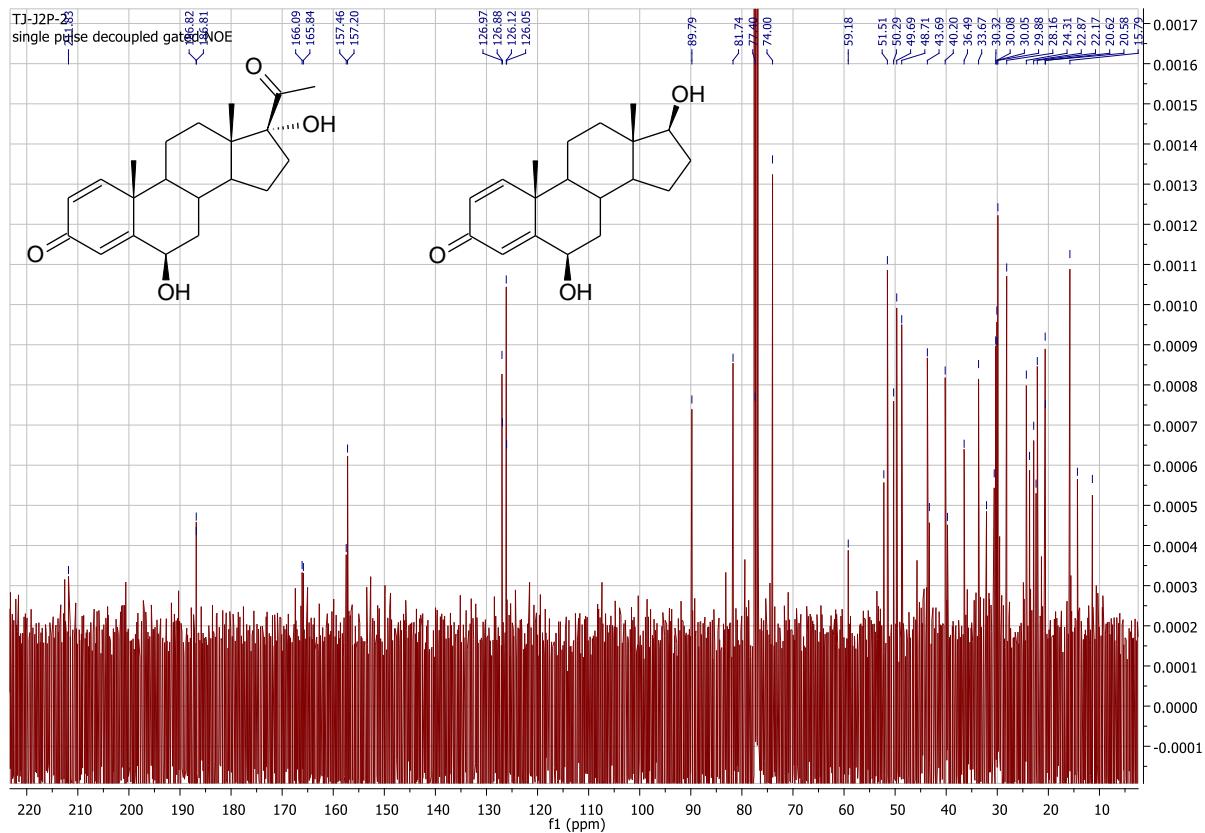


Figure S33. COSY spectrum of $6\beta,17\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**6**) and $6\beta,17\beta$ -dihydroxyandrost-1,4-diene-3-one (**7**) (CDCl_3 , 600 MHz)

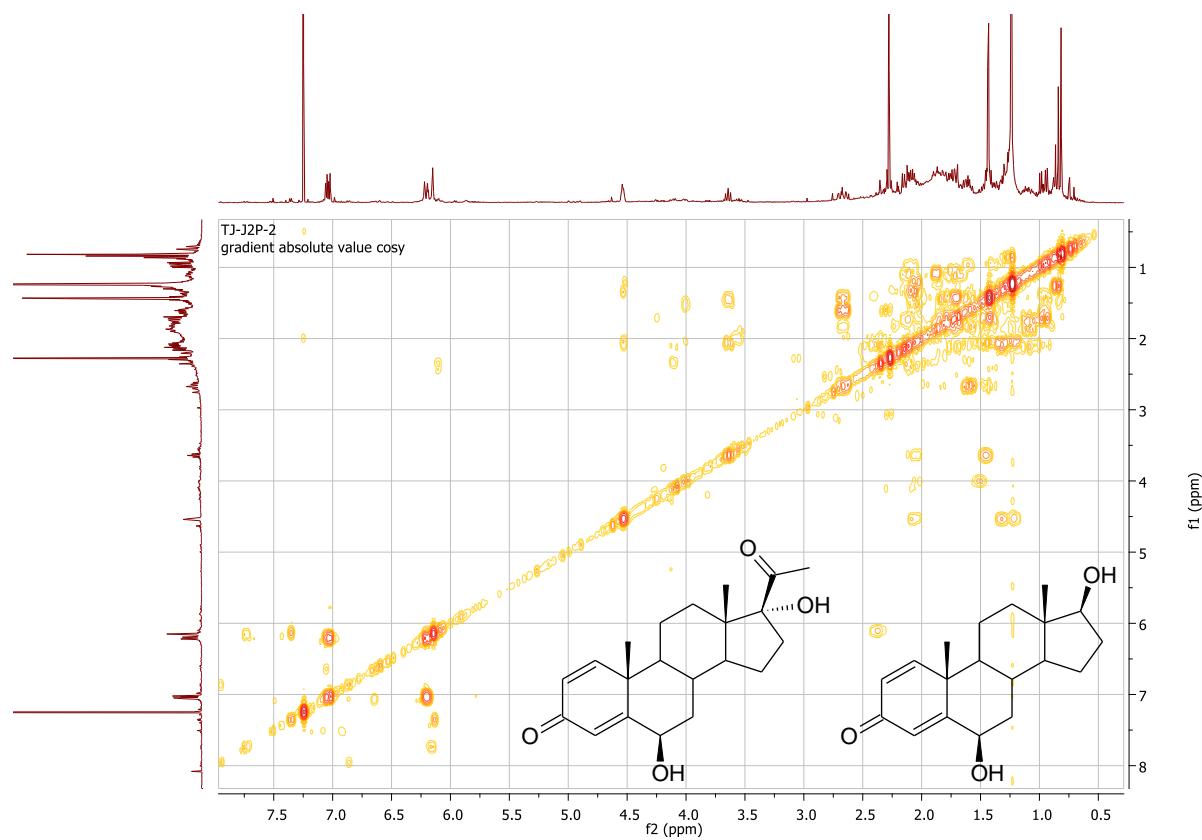


Figure S34. HSQC spectrum of $6\beta,17\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**6**) and $6\beta,17\beta$ -dihydroxyandrost-1,4-diene-3-one (**7**) (CDCl_3 , 600/151 MHz)

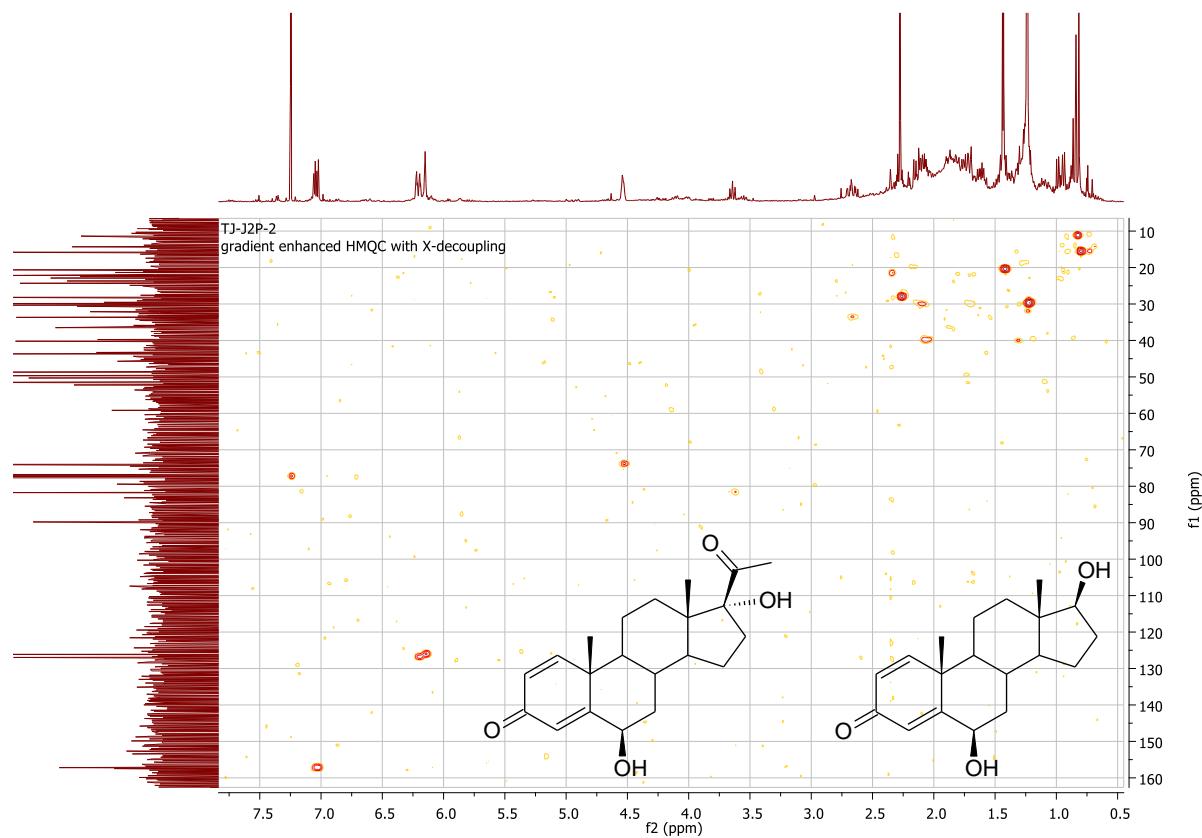


Figure S35. HMBC spectrum of $6\beta,17\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**6**) and $6\beta,17\beta$ -dihydroxyandrost-1,4-diene-3-one (**7**) (CDCl_3 , 600/151 MHz)

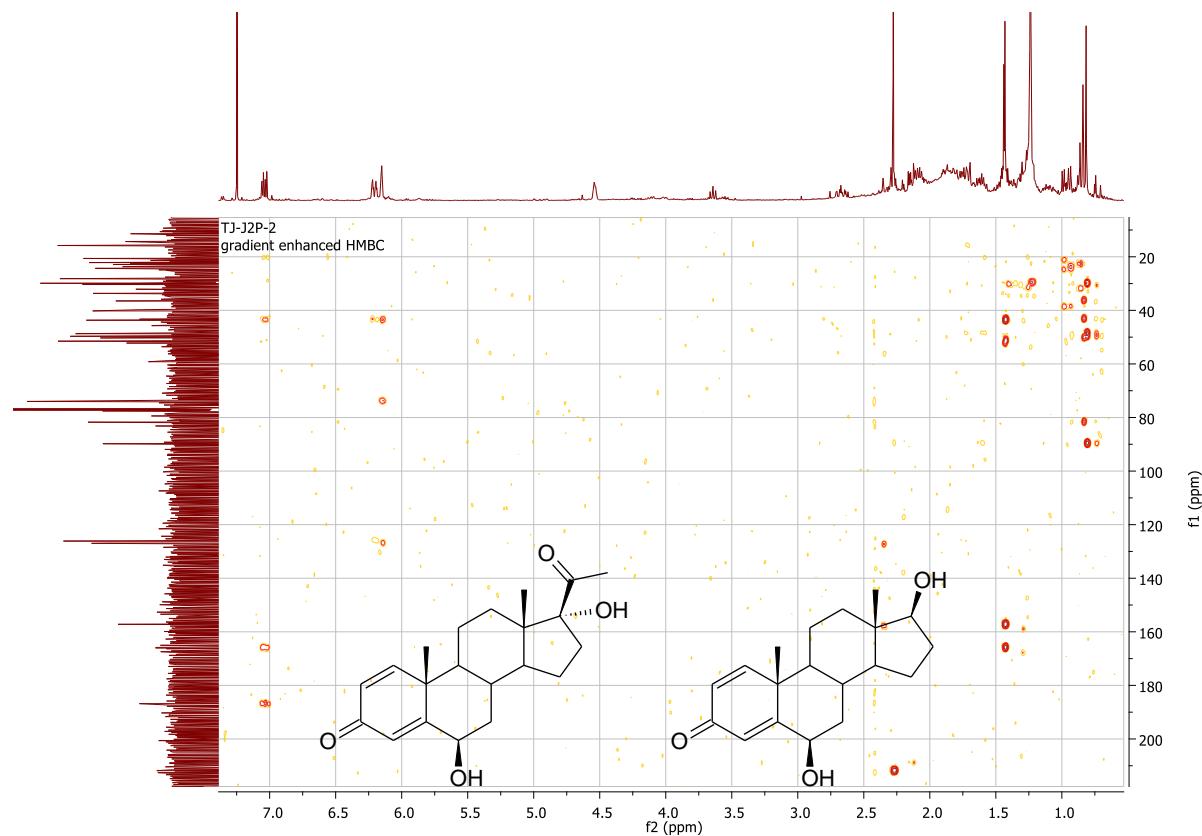


Figure S36. Predicted Boiled-Egg plot from swissADME online web tool for $6\beta,17\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**6**)

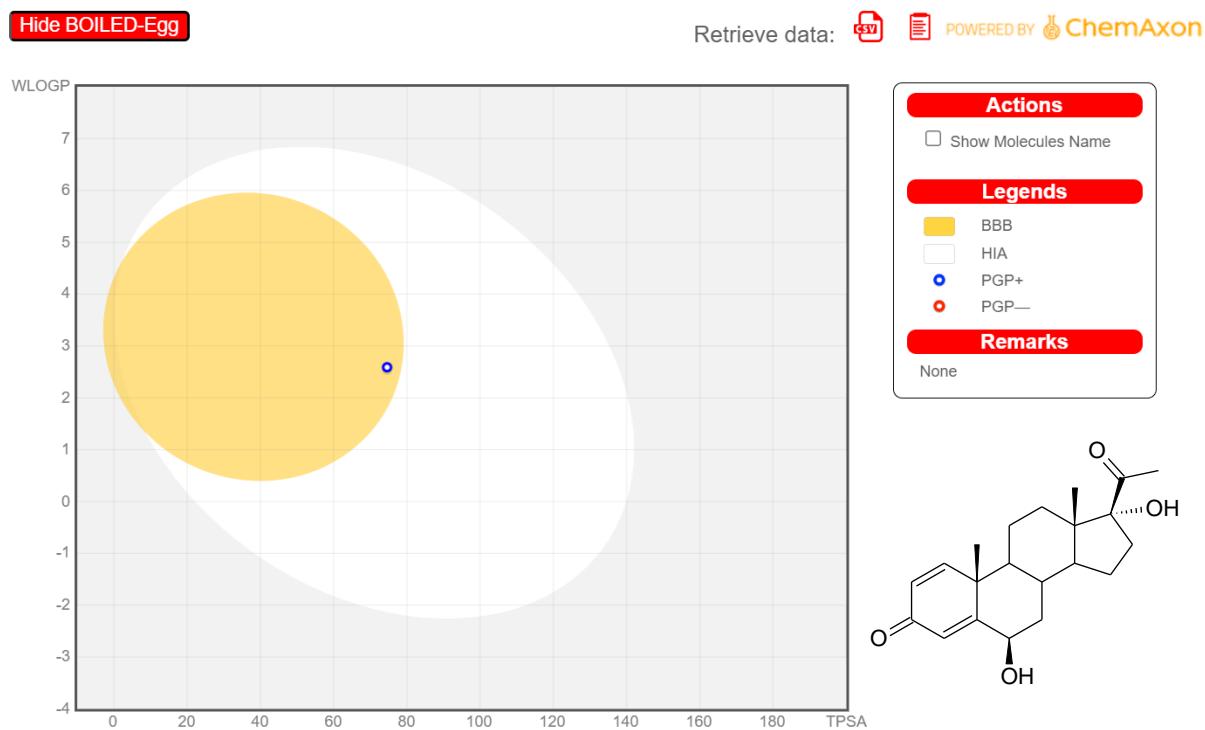


Figure S37. $6\beta,17\alpha$ -dihydroxypregn-1,4-diene-3,20-dione (**6**) physicochemical and ADME parameters prediction using the SwissADME modelling

Molecule 1			
		Water Solubility	
		Log S (ESOL)	-3.01
		Solubility	3.40e-01 mg/ml ; 9.87e-04 mol/l
		Class	Soluble
		Log S (Ali)	-2.92
		Solubility	4.11e-01 mg/ml ; 1.19e-03 mol/l
		Class	Soluble
		Log S (SILICOS-IT)	-2.74
		Solubility	6.33e-01 mg/ml ; 1.84e-03 mol/l
		Class	Soluble
Physicochemical Properties		Pharmacokinetics	
SMILES	O=C1C=C[C@]2(C(=C1)[C@H](O)CC1C2CC[C@]2(C1CC[C@]2(O)C(=O)C)C)C	GI absorption	High
Formula	C ₂₁ H ₂₈ O ₄	BBB permeant	Yes
Molecular weight	344.44 g/mol	P-gp substrate	Yes
Num. heavy atoms	25	CYP1A2 inhibitor	No
Num. arom. heavy atoms	0	CYP2C19 inhibitor	No
Fraction Csp3	0.71	CYP2C9 inhibitor	No
Num. rotatable bonds	1	CYP2D6 inhibitor	No
Num. H-bond acceptors	4	CYP3A4 inhibitor	No
Num. H-bond donors	2	Log K_p (skin permeation)	-7.17 cm/s
Molar Refractivity	95.90	Lipinski	Yes; 0 violation
TPSA	74.60 Å ²	Ghose	Yes
Lipophilicity		Veber	Yes
Log $P_{o/w}$ (iLOGP)	2.52	Egan	Yes
Log $P_{o/w}$ (XLOGP3)	1.74	Muegge	Yes
Log $P_{o/w}$ (WLOGP)	2.59	Bioavailability Score	0.55
Log $P_{o/w}$ (MLOGP)	2.13	PAINS	0 alert
Log $P_{o/w}$ (SILICOS-IT)	2.68	Brenk	0 alert
Consensus Log $P_{o/w}$	2.33	Leadlikeness	Yes
		Synthetic accessibility	5.15
		Medicinal Chemistry	

Figure S38. Predicted Boiled-Egg plot from swissADME online web tool for $6\beta,17\beta$ -dihydroxyandrost-1,4-diene-3-one (**7**)

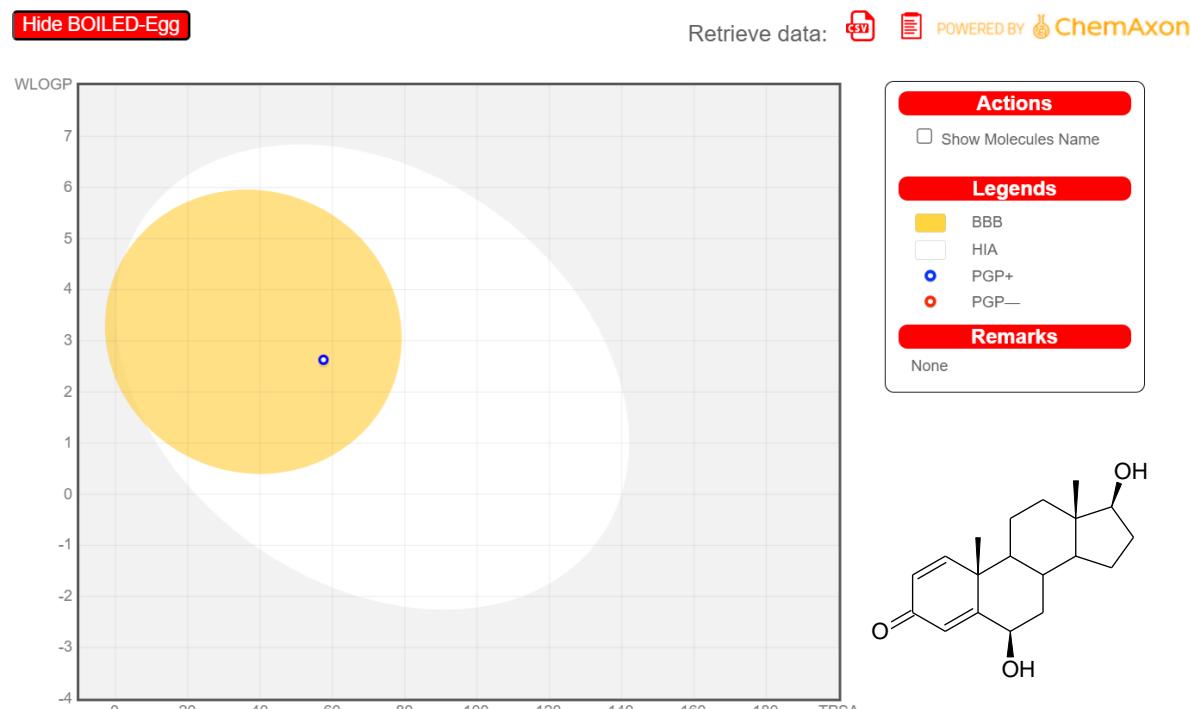


Figure S39. $6\beta,17\beta$ -dihydroxyandrost-1,4-diene-3-one (**7**) physicochemical and ADME parameters prediction using the SwissADME modelling

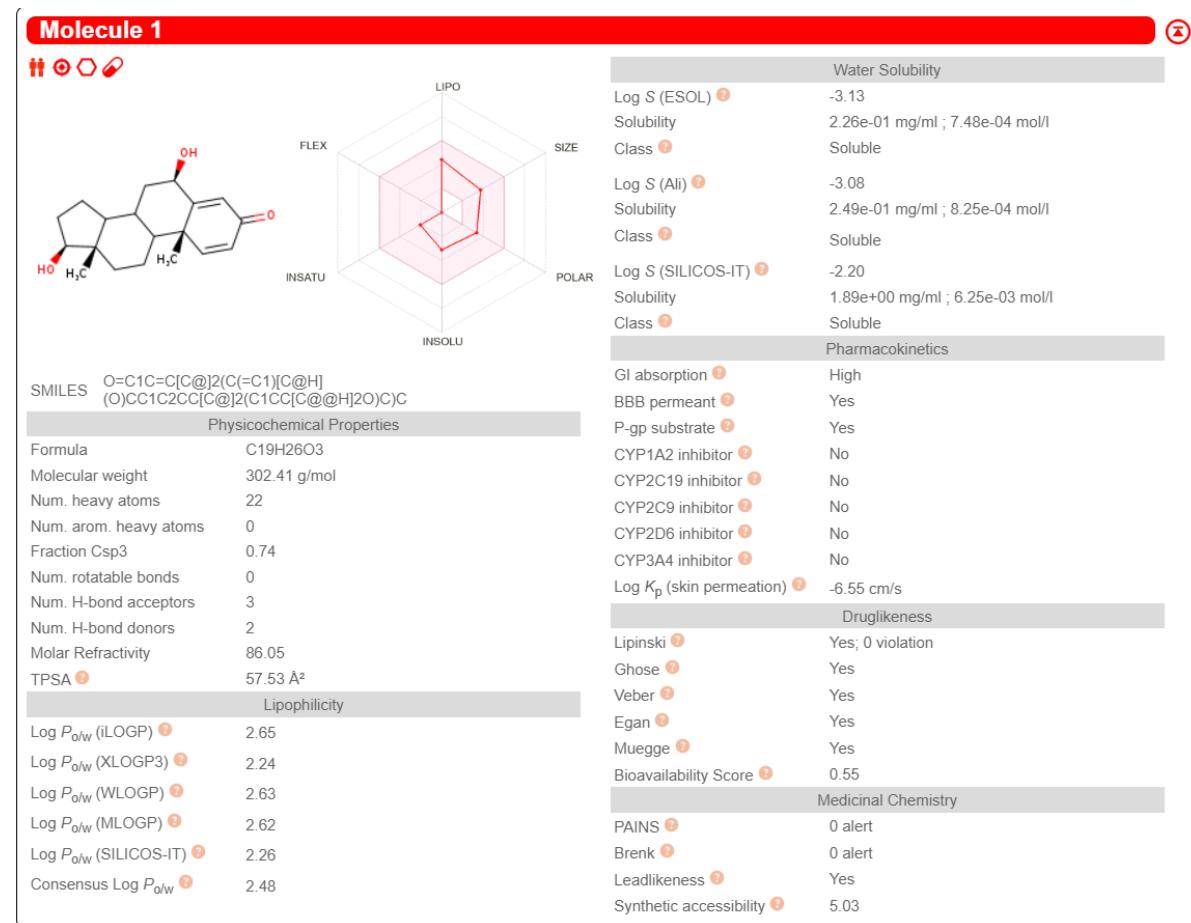


Figure S40. ^1H NMR spectra of $12\beta,17\alpha$ -dihydroxypregn-1,4-diene-3-one (**8**) (DMSO-*d*₆, 600 MHz)

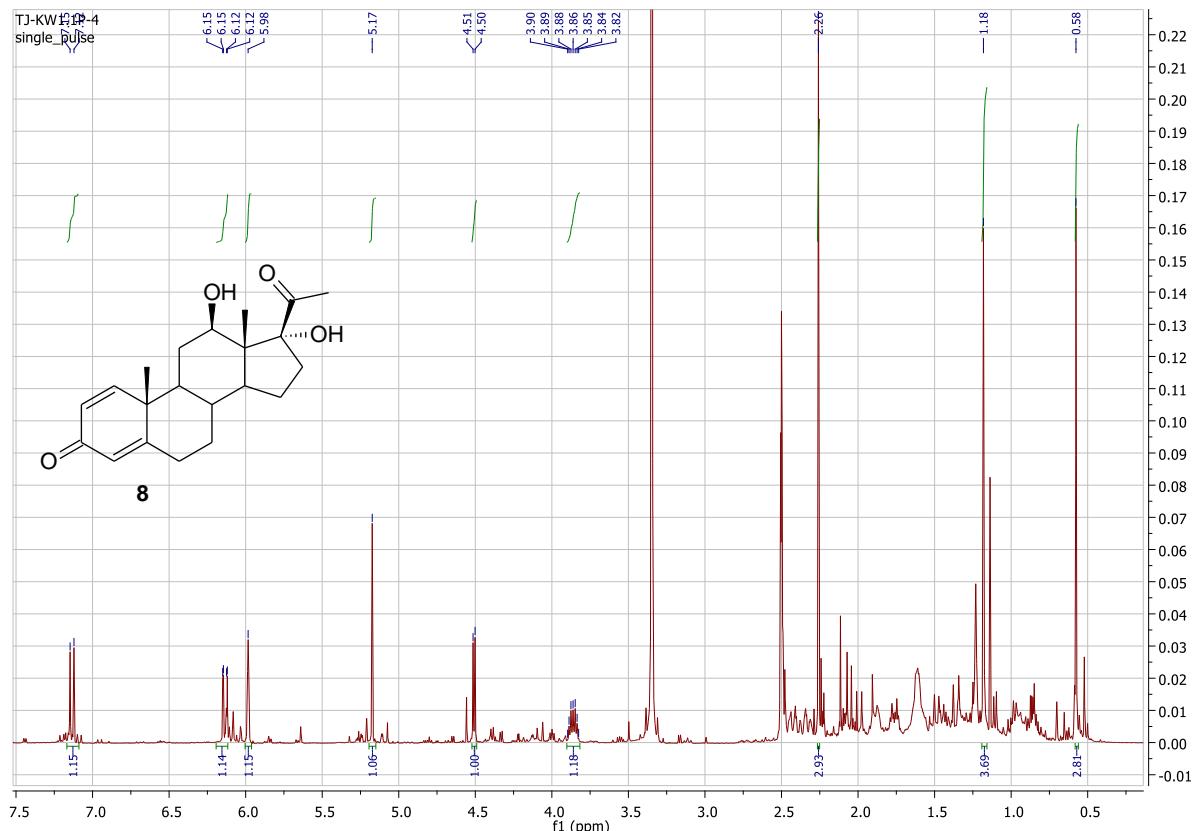


Figure S41. ^{13}C NMR spectra of $12\beta,17\alpha$ -dihydroxypregn-1,4-diene-3-one (**8**) (DMSO- d_6 , 151 MHz)

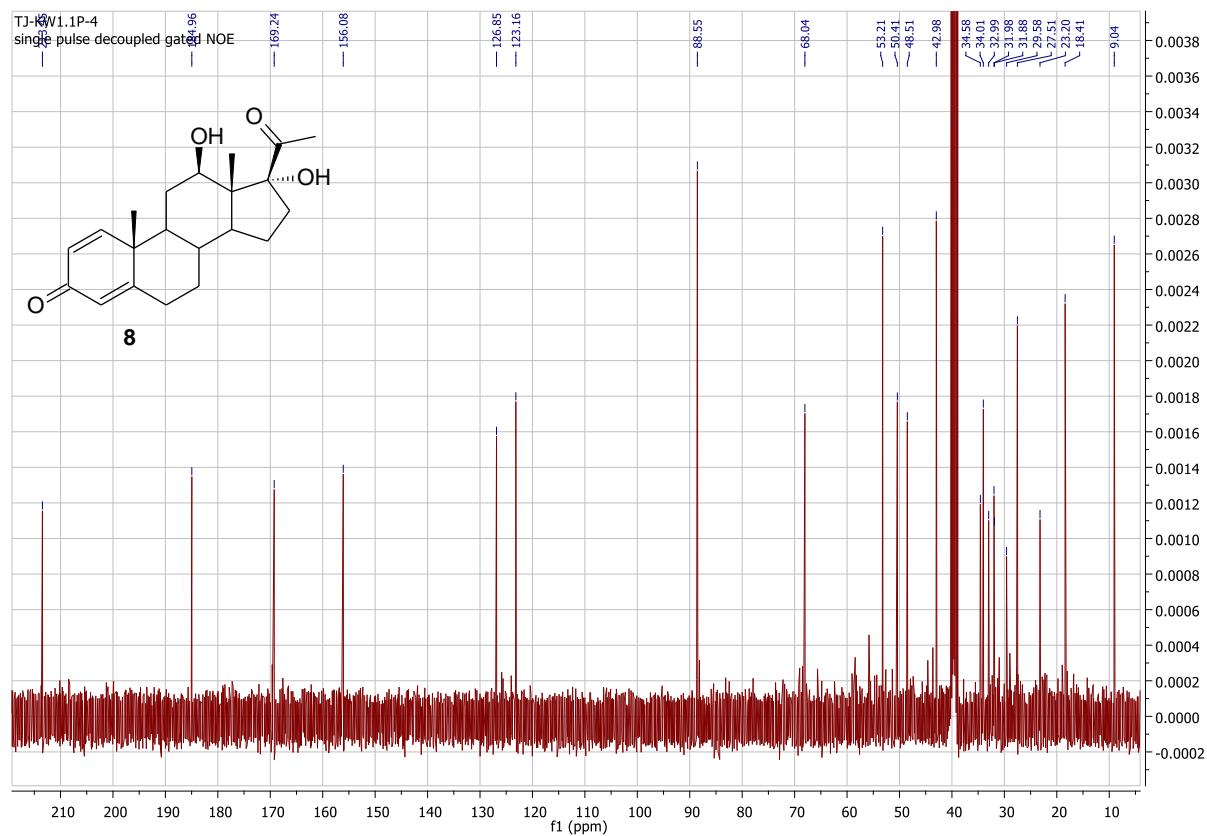


Figure S42. COSY spectrum of $12\beta,17\alpha$ -dihydroxypregn-1,4-diene-3-one (**8**) (DMSO- d_6 , 600 MHz)

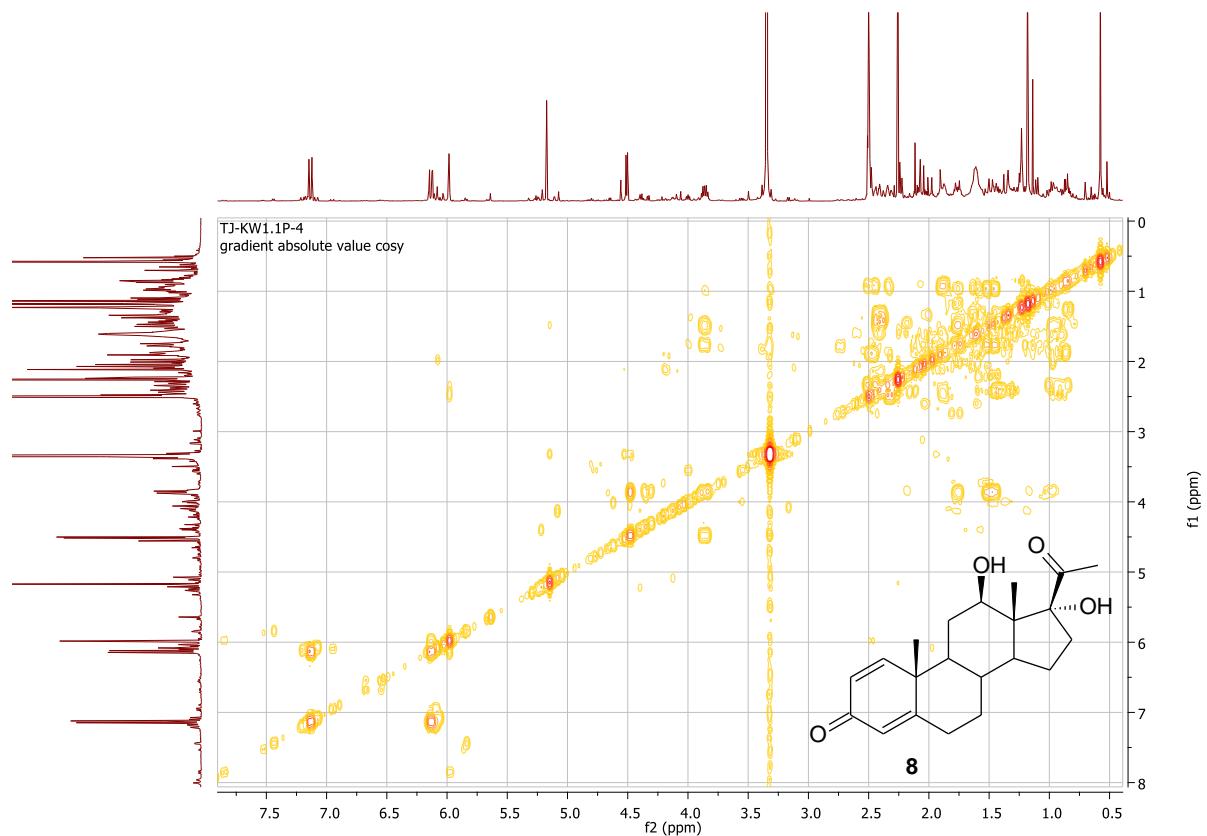


Figure S43. HSQC spectrum of 12 β ,17 α -dihydroxypregn-1,4-diene-3-one (**8**) (DMSO-*d*₆, 600/151 MHz)

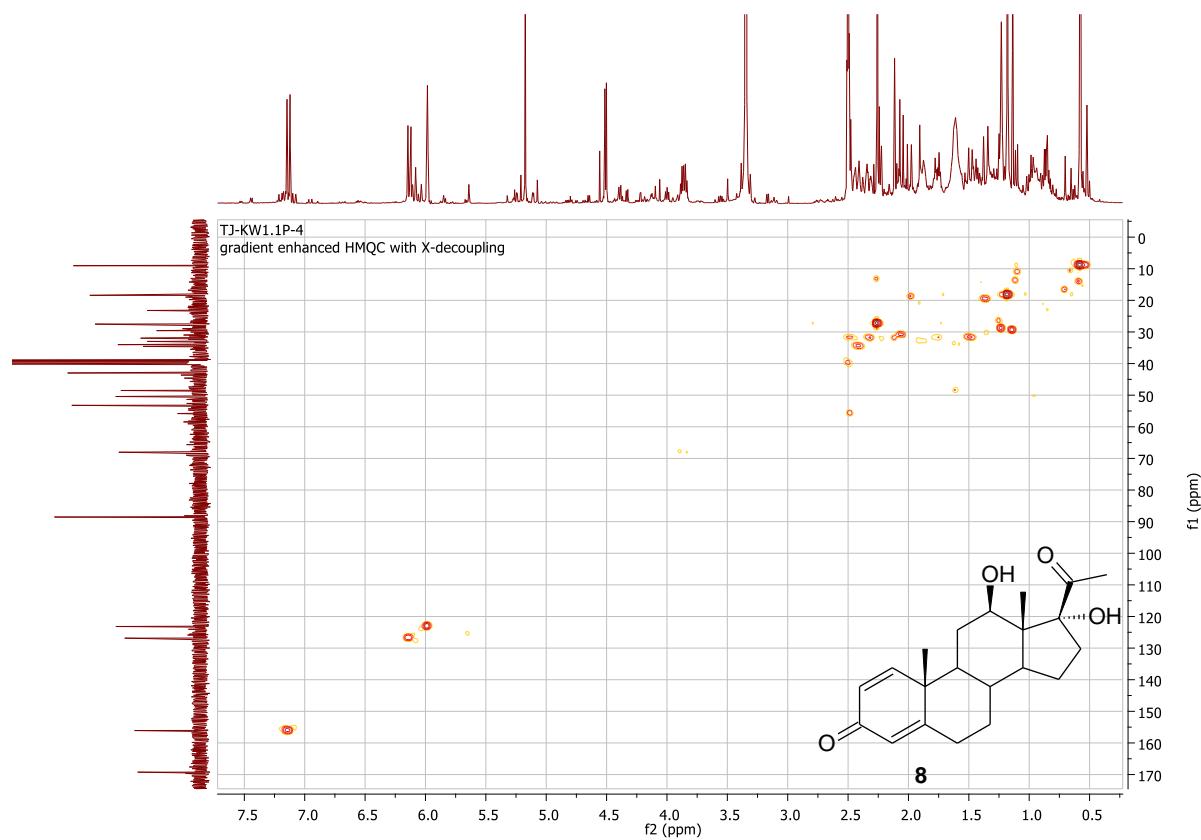


Figure S44. HMBC spectrum of 12 β ,17 α -dihydroxypregn-1,4-diene-3-one (**8**) (DMSO-*d*₆, 600/151 MHz)

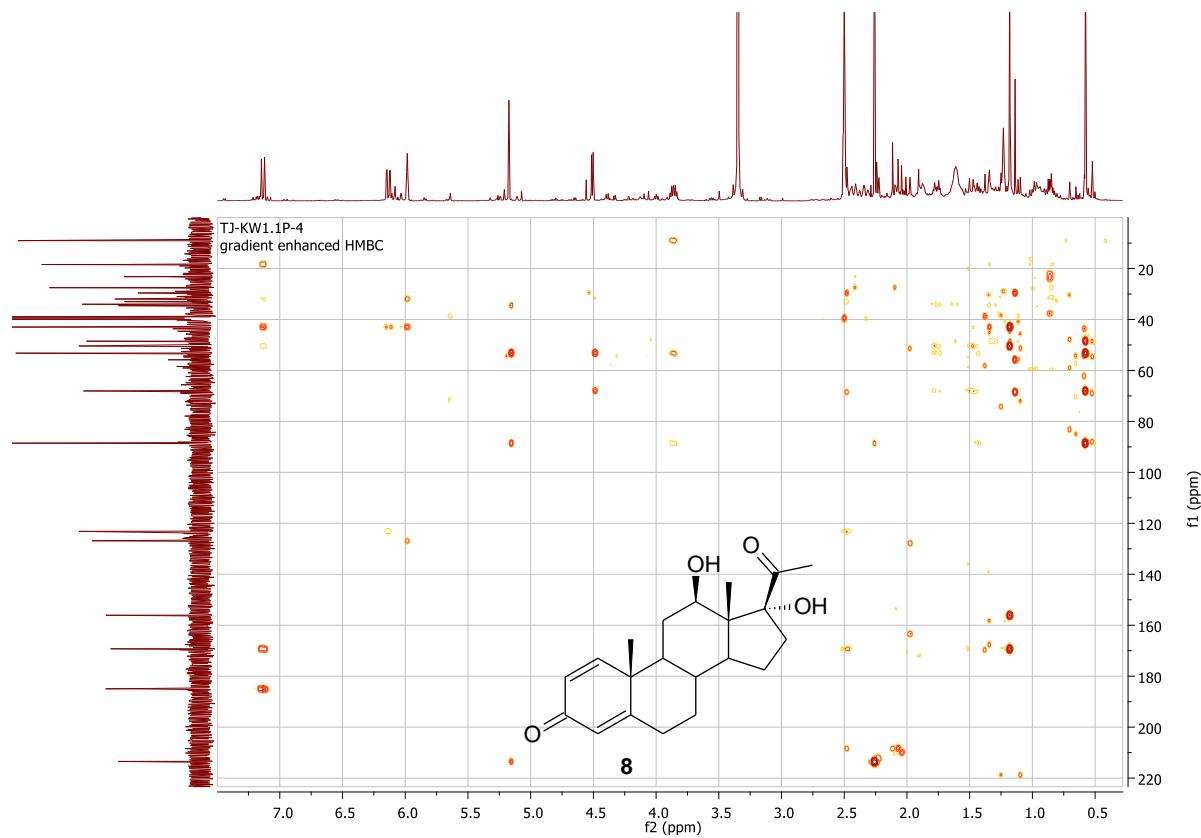


Figure S45. Predicted Boiled-Egg plot from swissADME online web tool for $12\beta,17\alpha$ -dihydroxypregn-1,4-diene-3-one (**8**)

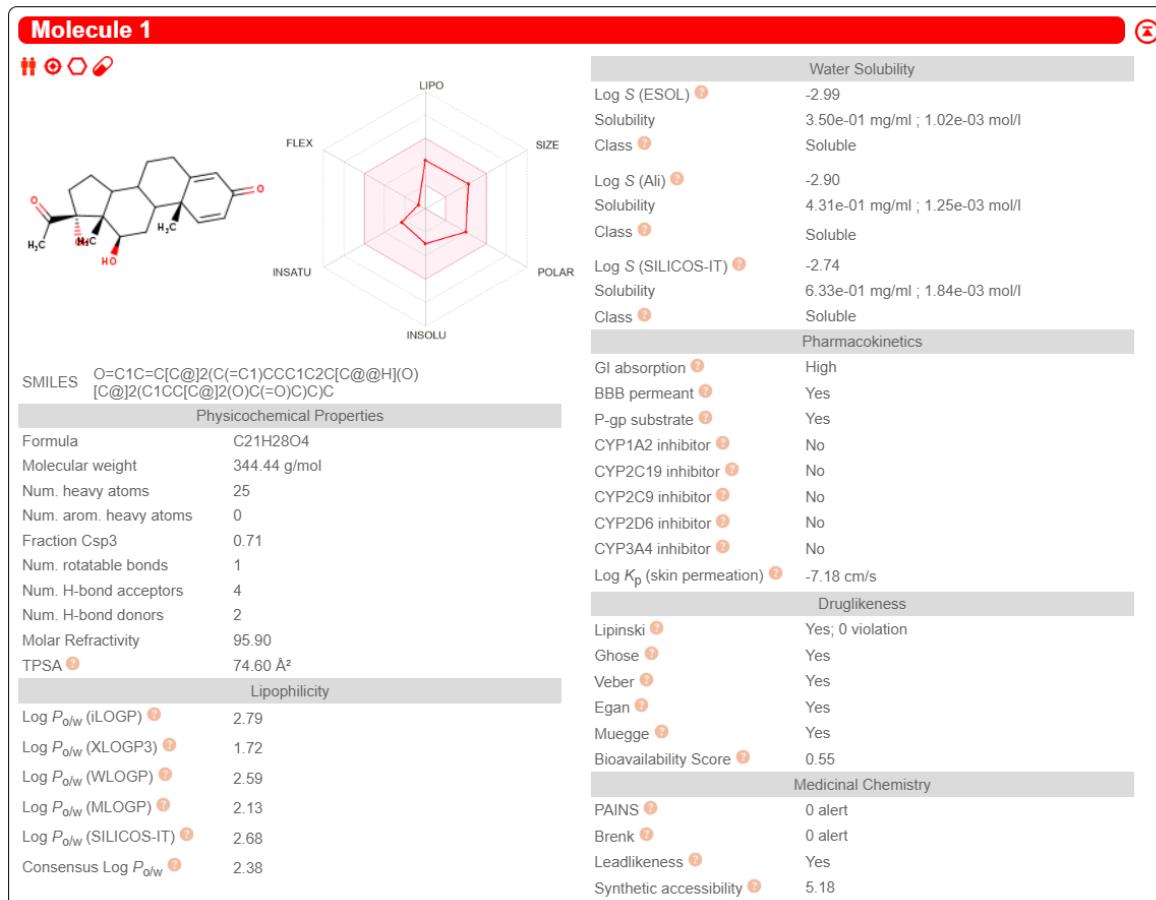


Figure S46. $12\beta,17\alpha$ -dihydroxypregn-1,4-diene-3-one (**8**) physicochemical and ADME parameters prediction using the SwissADME modelling

