

Supporting information

C-Geranylated Flavanones from *Paulownia tomentosa* Fruits as Potential Anti-Inflammatory Compounds Acting via Inhibition of TNF- α Production

Zuzana Hanáková,[†] Jan Hošek,[‡] Petr Babula,[†] Stefano Dall'Acqua,[§] Jiří Václavík,[†] Karel Šmejkal^{‡,†}

[†]Department of Natural Drugs, Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences Brno, Palackého tř. 1/3, 60200 Brno, Czech Republic

[‡]Department of Molecular Biology and Pharmaceutical Biotechnology, Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences Brno, Palackého tř. 1/3, 60200 Brno, Czech Republic

[§]Department of Pharmaceutical and Pharmacological Sciences, University of Padua, Via F. Marzolo 5, 35131 Padua, Italy

Table of contents

Figure S1. ¹ H NMR (400 MHz, MeOD) spectrum of tomentodiplacone J (1)	3
Figure S2. HSQC(400 MHz, MeOD) spectrum of tomentodiplacone J (1)	3
Figure S3. HMBC (400 MHz, MeOD) spectrum of tomentodiplacone J (1)	4
Figure S4. COSY (400 MHz, MeOD) spectrum of tomentodiplacone J (1)	4
Figure S5. NOESY (400 MHz, MeOD) spectrum of tomentodiplacone J (1)	5
Figure S6. ¹ H NMR (400 MHz, MeOD) spectrum of tomentodiplacone K (2)	5
Figure S7. HSQC (400 MHz, MeOD) spectrum of tomentodiplacone K (2)	6
Figure S8. HMBC (400 MHz, MeOD) spectrum of tomentodiplacone K (2)	6
Figure S9. COSY (400 MHz, MeOD) spectrum of tomentodiplacone K (2)	7
Figure S10. NOESY (400 MHz, MeOD) spectrum of tomentodiplacone K (2)	7
Figure S11. ¹ H NMR (400 MHz, MeOD) spectrum of tomentodiplacol B (3)	8
Figure S12. HSQC (400 MHz, MeOD) spectrum of tomentodiplacol B (3)	9
Figure S13. HMBC (400 MHz, MeOD) spectrum of tomentodiplacol B (3)	9
Figure S14. COSY (400 MHz, MeOD) spectrum of tomentodiplacol B (3)	10
Figure S15. NOESY(400 MHz, MeOD) spectrum of tomentodiplacol B (3)	10
Figure S16. ¹ H NMR (400 MHz, MeOD) spectrum of 3',4'- <i>O</i> -dimethyl-5'-hydroxydiplacone (4)	11
Figure S17. HSQC (400 MHz, MeOD) spectrum of 3',4'- <i>O</i> -dimethyl-5'-hydroxydiplacone (4)	11
Figure S18. HMBC (400 MHz, MeOD) spectrum of	

3',4'- <i>O</i> -dimethyl-5'-hydroxydiplacone (4)	12
Figure S19. COSY (400 MHz, MeOD) spectrum of 3',4'- <i>O</i> -dimethyl-5'-hydroxydiplacone (4)	12
Figure S20. NOESY (400 MHz, MeOD) spectrum of 3',4'- <i>O</i> -dimethyl-5'-hydroxydiplacone (4)	13
Figure S21. ¹ H NMR (400 MHz, MeOD) spectrum of mimulone F (5)	13
Figure S22. HSQC (400 MHz, MeOD) spectrum of mimulone F (5)	14
Figure S23. HMBC (400 MHz, MeOD) spectrum of mimulone F (5)	14
Figure S24. COSY (400 MHz, MeOD) spectrum of mimulone F (5)	15
Figure S25. NOESY (400 MHz, MeOD) spectrum of mimulone F (5)	15
Figure S26. ¹ H NMR (400 MHz, MeOD) spectrum of mimulone G (6)	16
Figure S27. HSQC (400 MHz, MeOD) spectrum of mimulone G (6)	16
Figure S28. HMBC (400 MHz, MeOD) spectrum of mimulone G (6)	17
Figure S29. COSY (400 MHz, MeOD) spectrum of mimulone G (6)	17
Figure S30. NOESY (400 MHz, MeOD) spectrum of mimulone G (6)	18
Figure S31. ¹ H NMR (400 MHz, MeOD) spectrum of mimulone H (7)	18
Figure S32. HSQC (400 MHz, MeOD) spectrum of mimulone H (7)	19
Figure S33. HMBC (400 MHz, MeOD) spectrum of mimulone H (7)	19
Figure S34. COSY (400 MHz, MeOD) spectrum of mimulone H (7)	20
Figure S35. NOESY (400 MHz, MeOD) spectrum of mimulone H (7)	20
Figure S36. ¹ H NMR (400 MHz, MeOD) spectrum of paulownione A (8)	21
Figure S37. HSQC (400 MHz, MeOD) spectrum of paulownione A (8)	21
Figure S38. HMBC (400 MHz, MeOD) spectrum of paulownione A (8)	22
Figure S39. COSY (400 MHz, MeOD) spectrum of paulownione A (8)	22
Figure S40. ¹ H NMR (400 MHz, MeOD) spectrum of paulownione B (9)	23
Figure S41. HSQC (400 MHz, MeOD) spectrum of paulownione B (9)	23
Figure S42. HMBC (400 MHz, MeOD) spectrum of paulownione B (9)	24
Figure S43. COSY (400 MHz, MeOD) spectrum of paulownione B (9)	24
Figure S44. NOESY (400 MHz, MeOD) spectrum of paulownione B (9)	25
Figure S45. ¹ H NMR (400 MHz, MeOD) spectrum of tomentodiplacone L (10)	25
Figure S46. HSQC (400 MHz, MeOD) spectrum of tomentodiplacone L (10)	26
Figure S47. HMBC (400 MHz, MeOD) spectrum of tomentodiplacone L (10)	26
Figure S48. COSY (400 MHz, MeOD) spectrum of tomentodiplacone L (10)	27
Figure S49. NOESY (400 MHz, MeOD) spectrum of tomentodiplacone L (10)	27
Figure S50. ¹ H NMR (400 MHz, MeOD) spectrum of tomentone (11)	28
Figure S51. HSQC (400 MHz, MeOD) spectrum of tomentone (11)	28
Figure S52. HMBC (400 MHz, MeOD) spectrum of tomentone (11)	29
Figure S53. COSY (400 MHz, MeOD) spectrum of tomentone (11)	29
Figure S54. NOESY (400 MHz, MeOD) spectrum of tomentone (11)	30
Figure S55. ¹ H NMR (400 MHz, CDCl ₃) spectrum of 3',4',5'-trimethoxyflavanone (12)	30
Figure S56. HSQC (400 MHz, CDCl ₃) spectrum of 3',4',5'-trimethoxyflavanone (12)	31
Figure S57. HMBC (400 MHz, CDCl ₃) spectrum of 3',4',5'-trimethoxyflavanone (12)	31
Figure S58. COSY (400 MHz, CDCl ₃) spectrum of 3',4',5'-trimethoxyflavanone (12)	32
Figure S59. NOESY (400 MHz, CDCl ₃) spectrum of 3',4',5'-trimethoxyflavanone (12)	32
Figure S60. The influence of selected flavanones on the degradation of IκB-α	33
Table S1. IC ₅₀ values of compounds 1–25	34

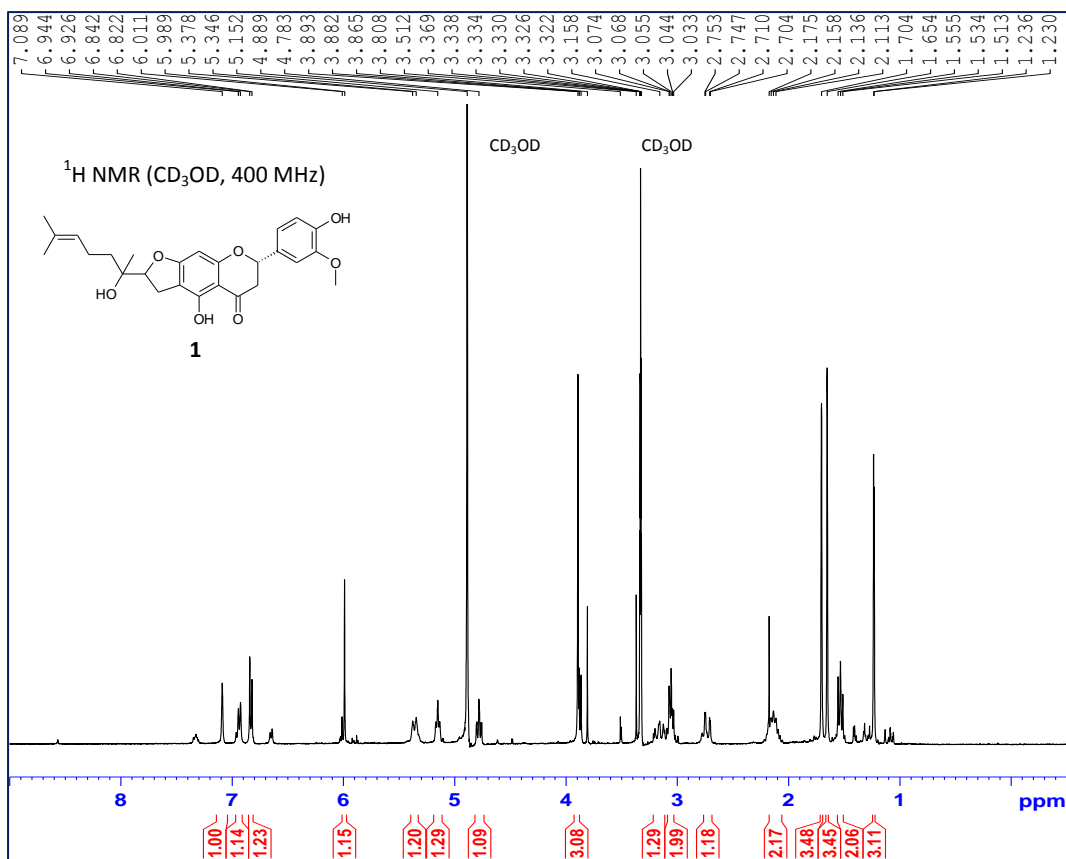


Figure S1. ¹H NMR (400 MHz, MeOD) spectrum of tomentodiplacone J (1)

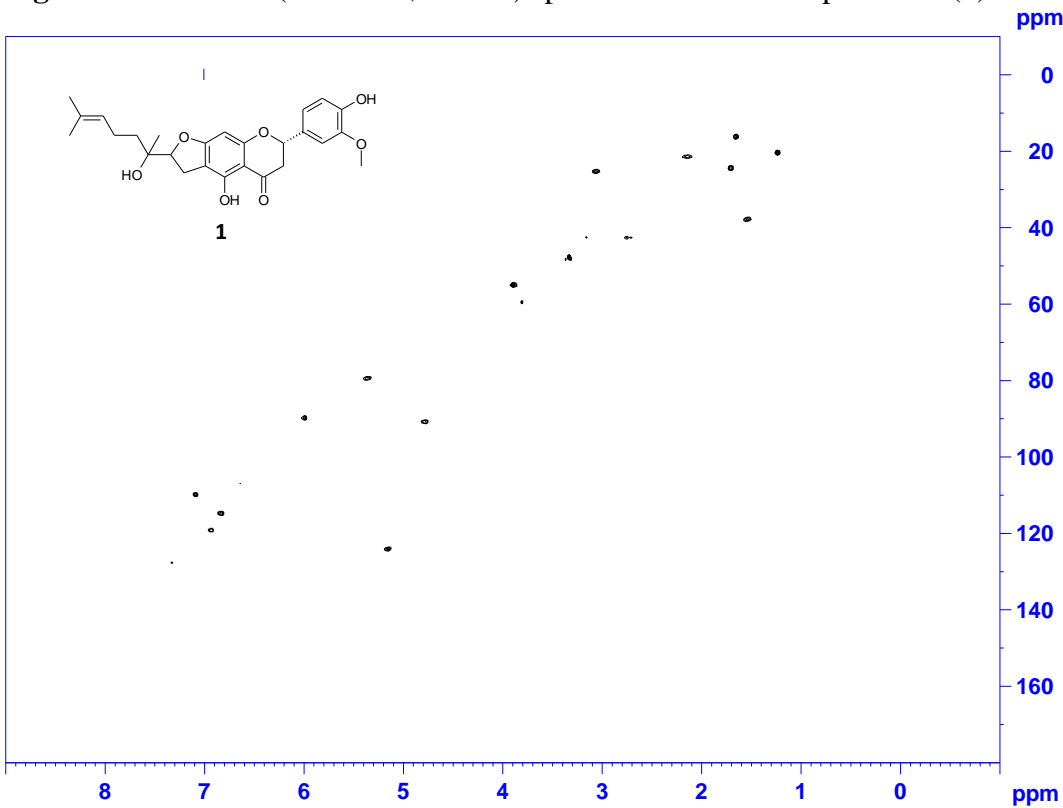


Figure S2. HSQC(400 MHz, MeOD) spectrum of tomentodiplacone J (1)

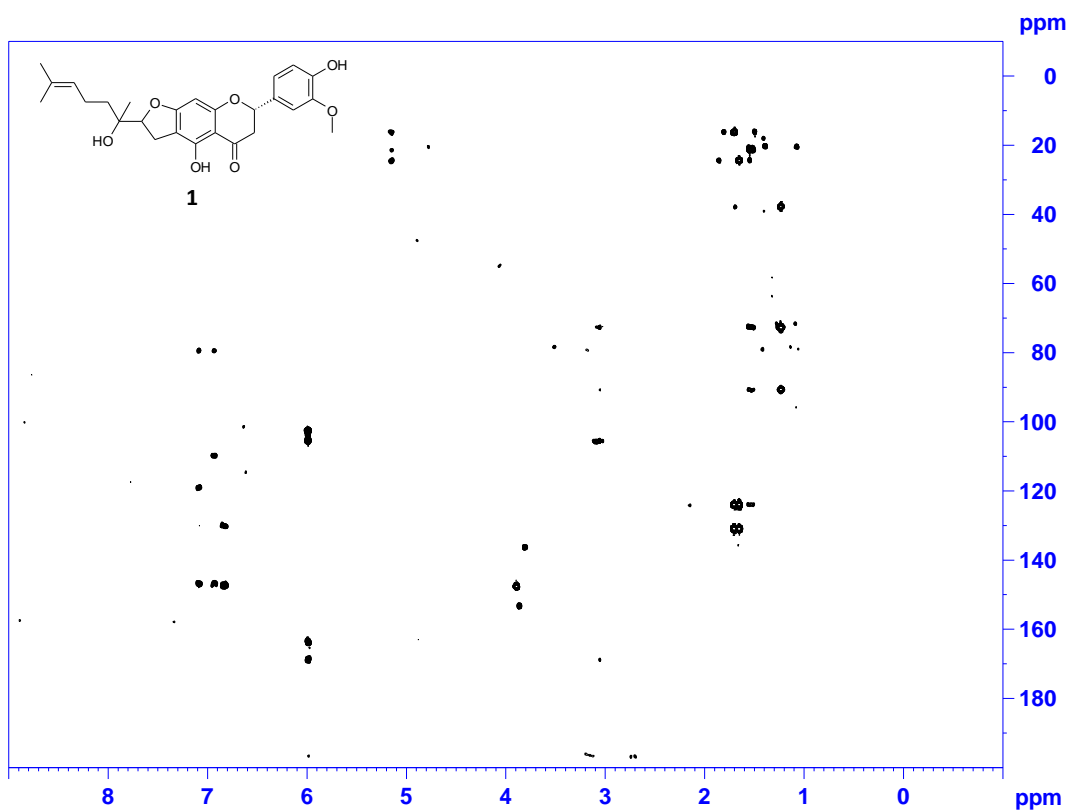


Figure S3. HMBC (400 MHz, MeOD) spectrum of tomentodiplacone J

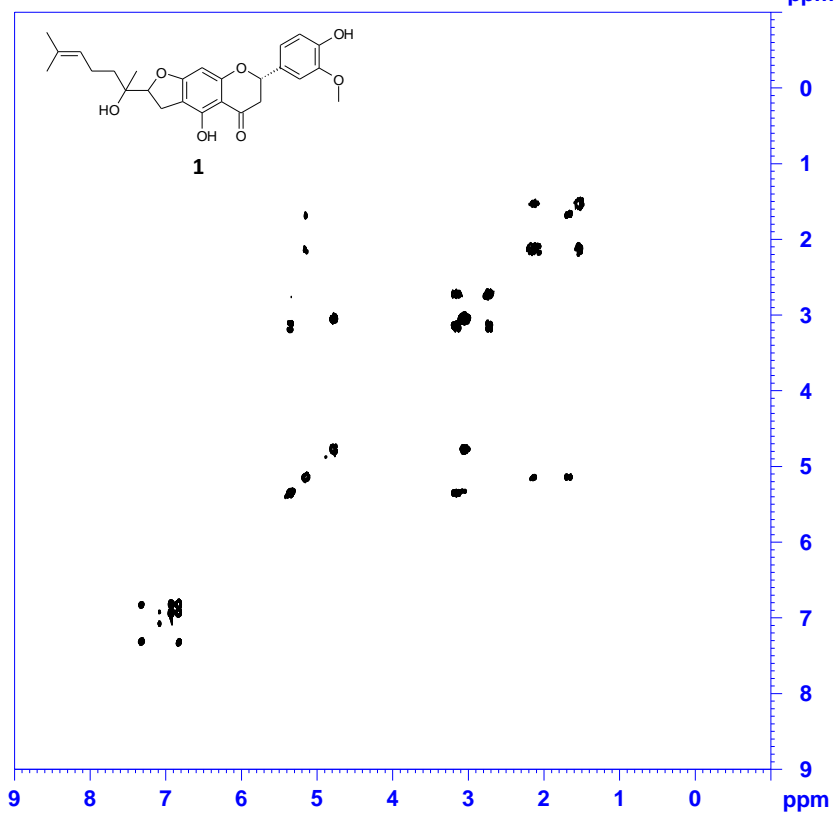


Figure S4. COSY (400 MHz, MeOD) spectrum of tomentodiplacone J (**1**)

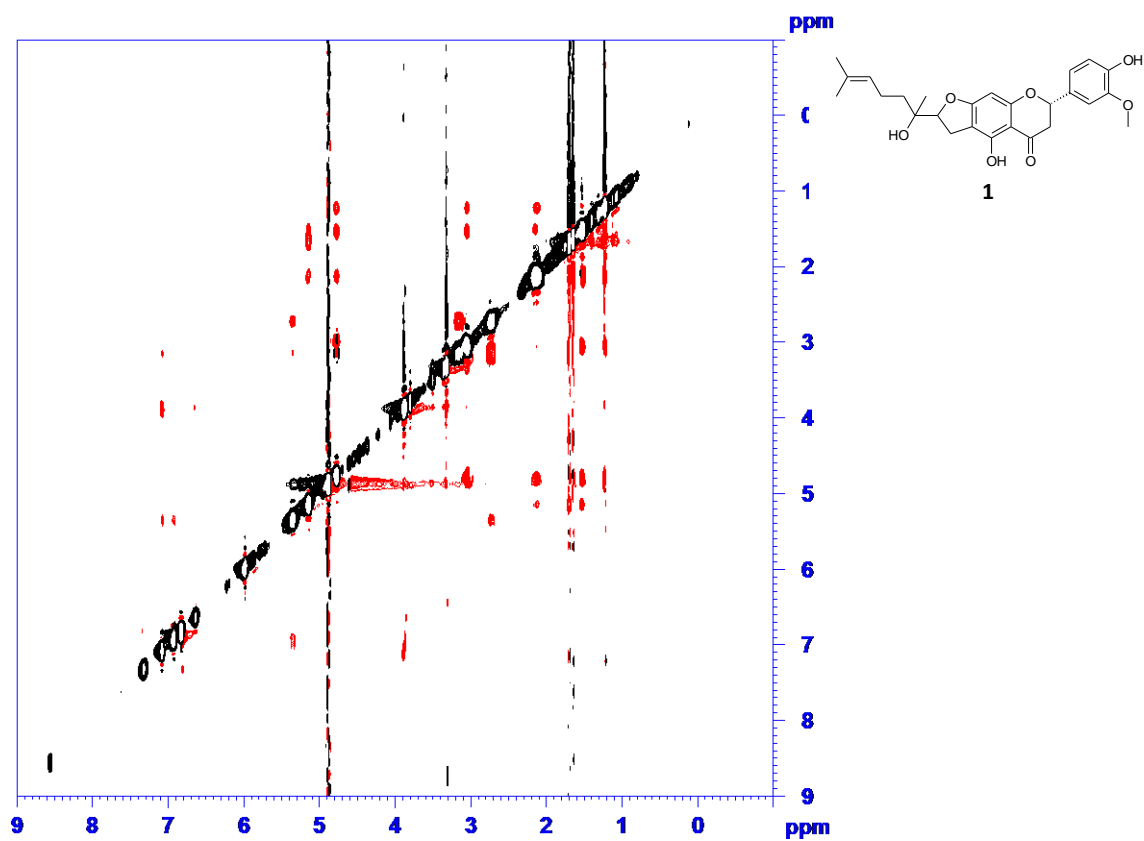


Figure S5. NOESY (400 MHz, MeOD) spectrum of tomentodiplacone J (1)

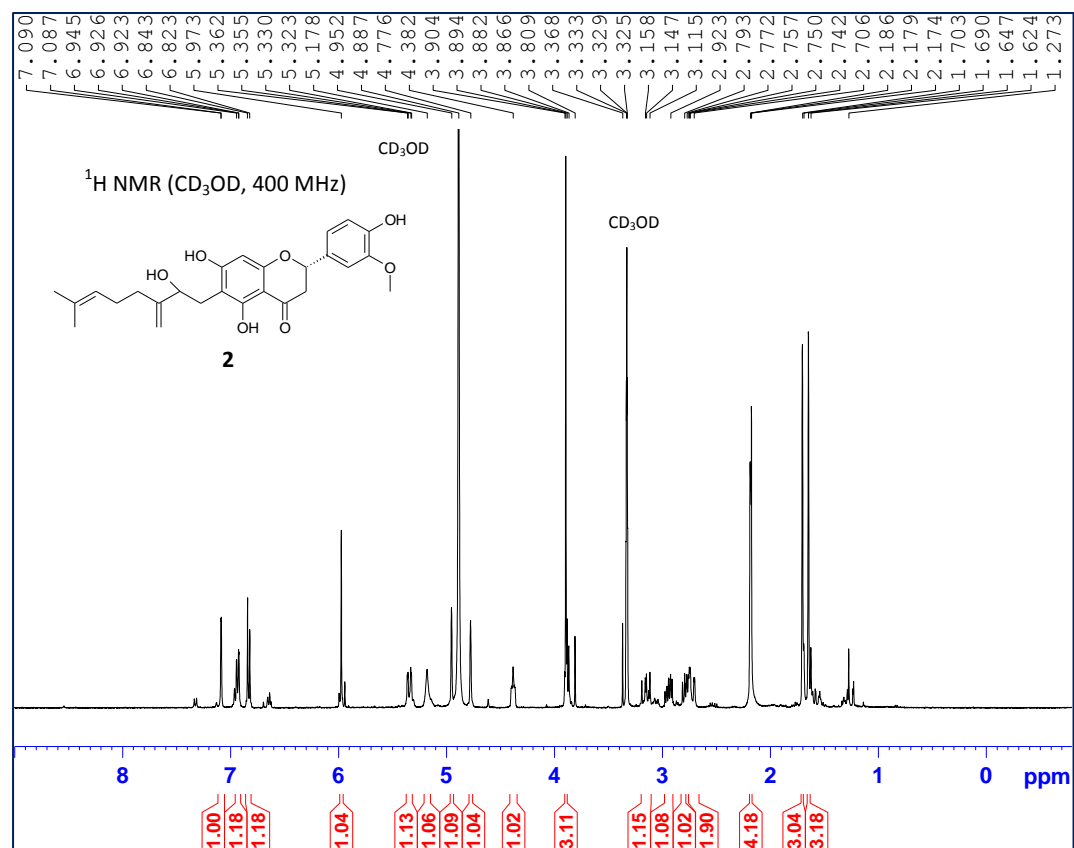


Figure S6. ¹H NMR (400 MHz, MeOD) spectrum of tomentodiplacone K (2)

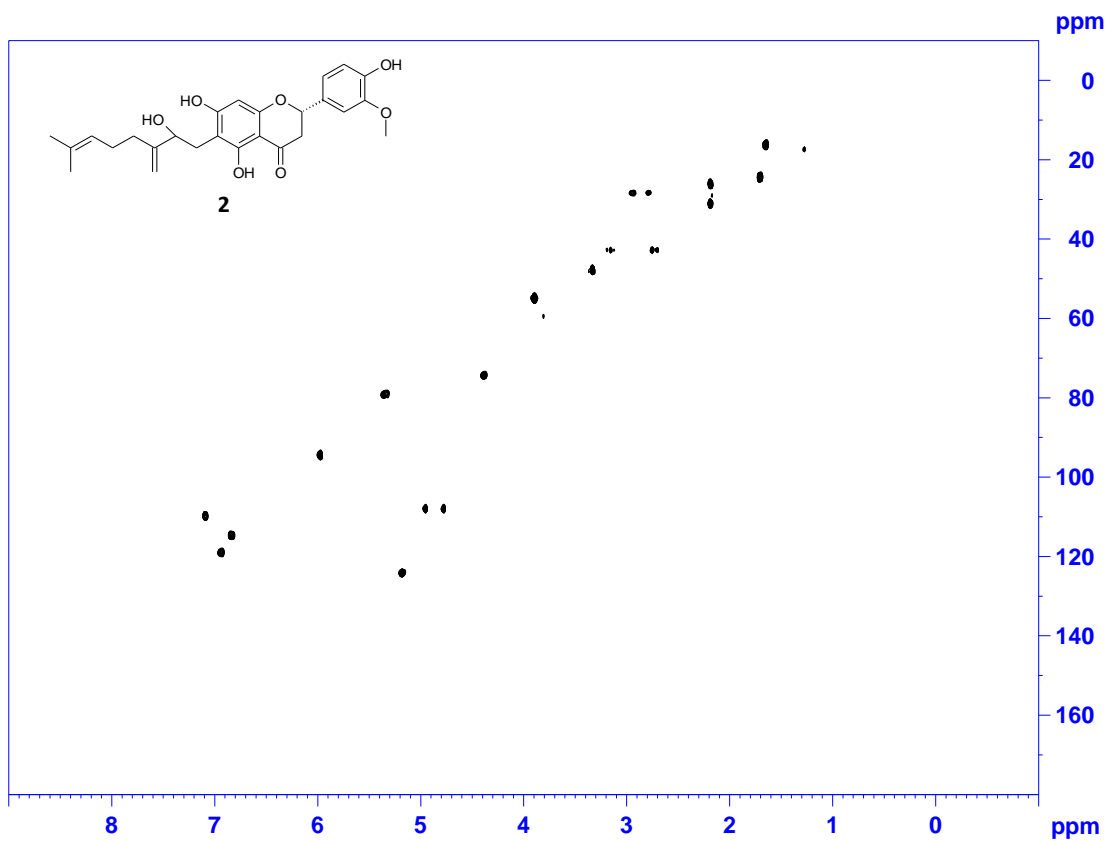


Figure S7. HSQC (400 MHz, MeOD) spectrum of tomentodiplacone K (2)

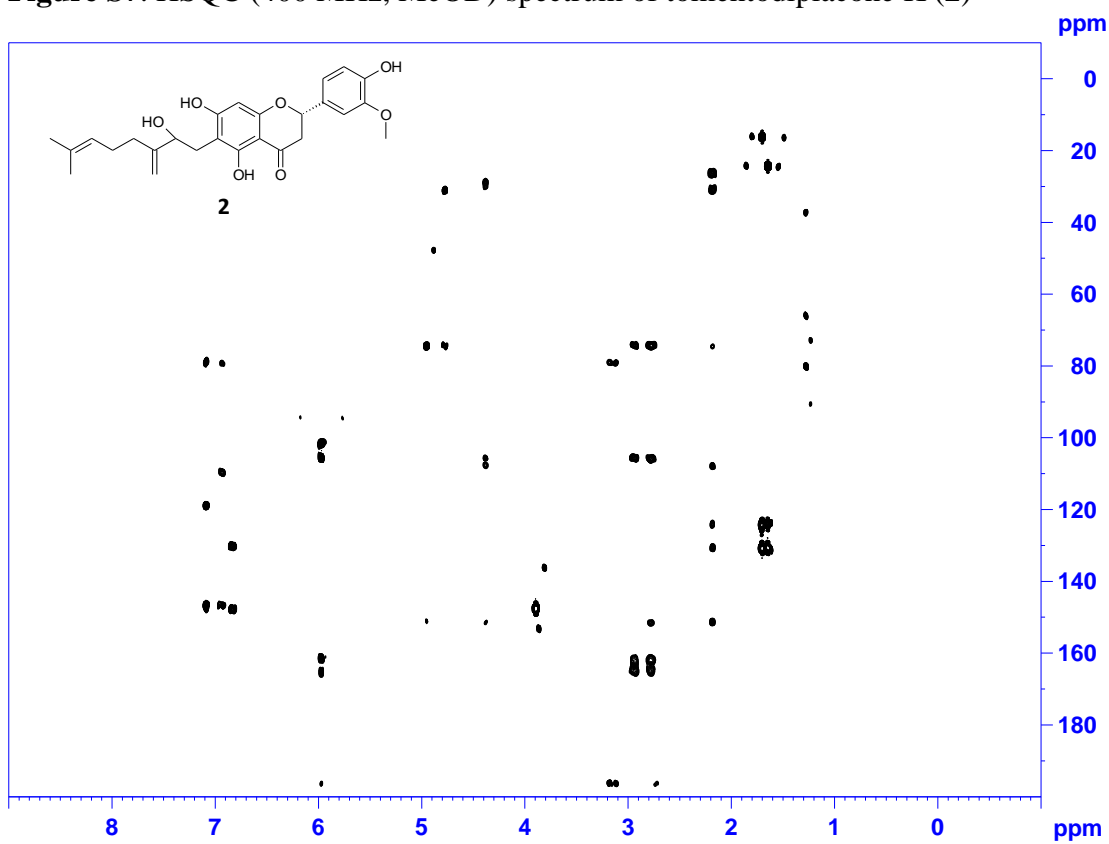
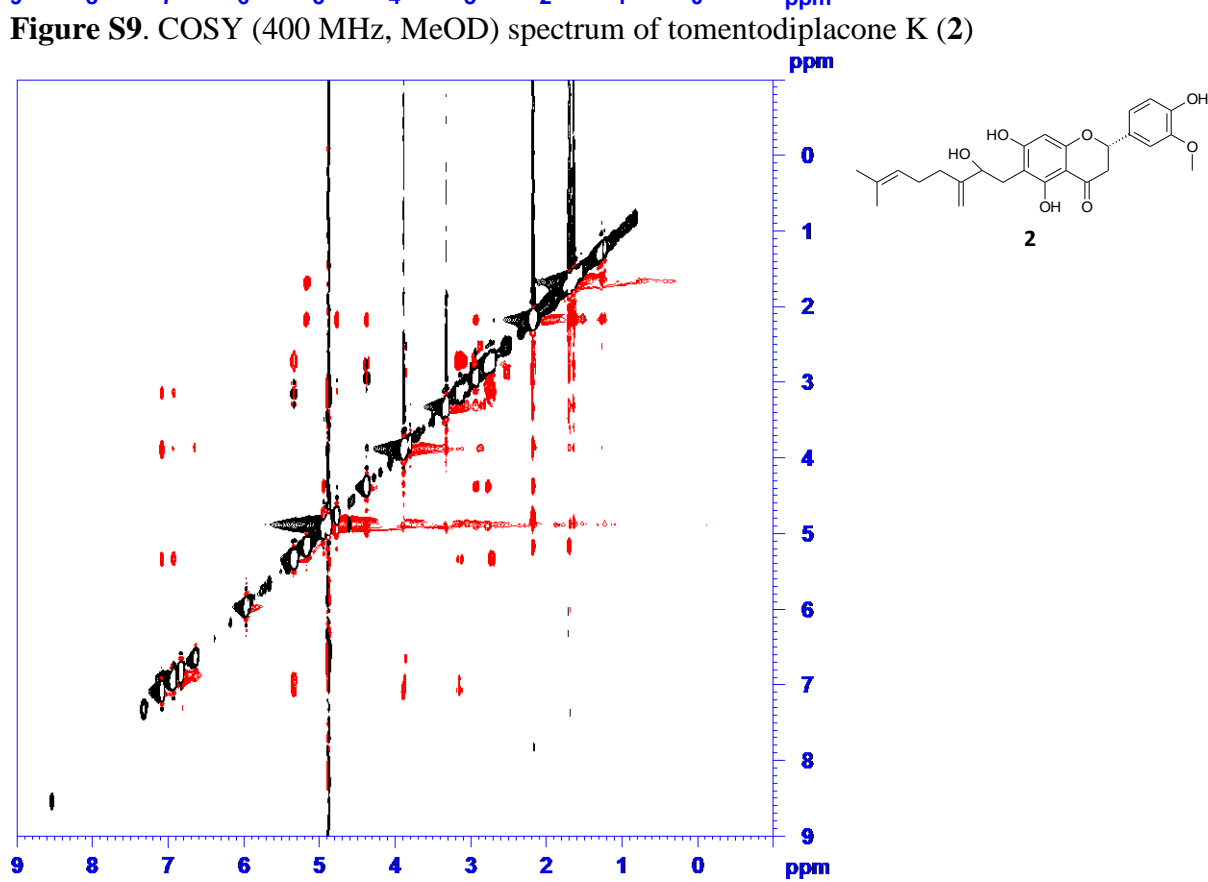
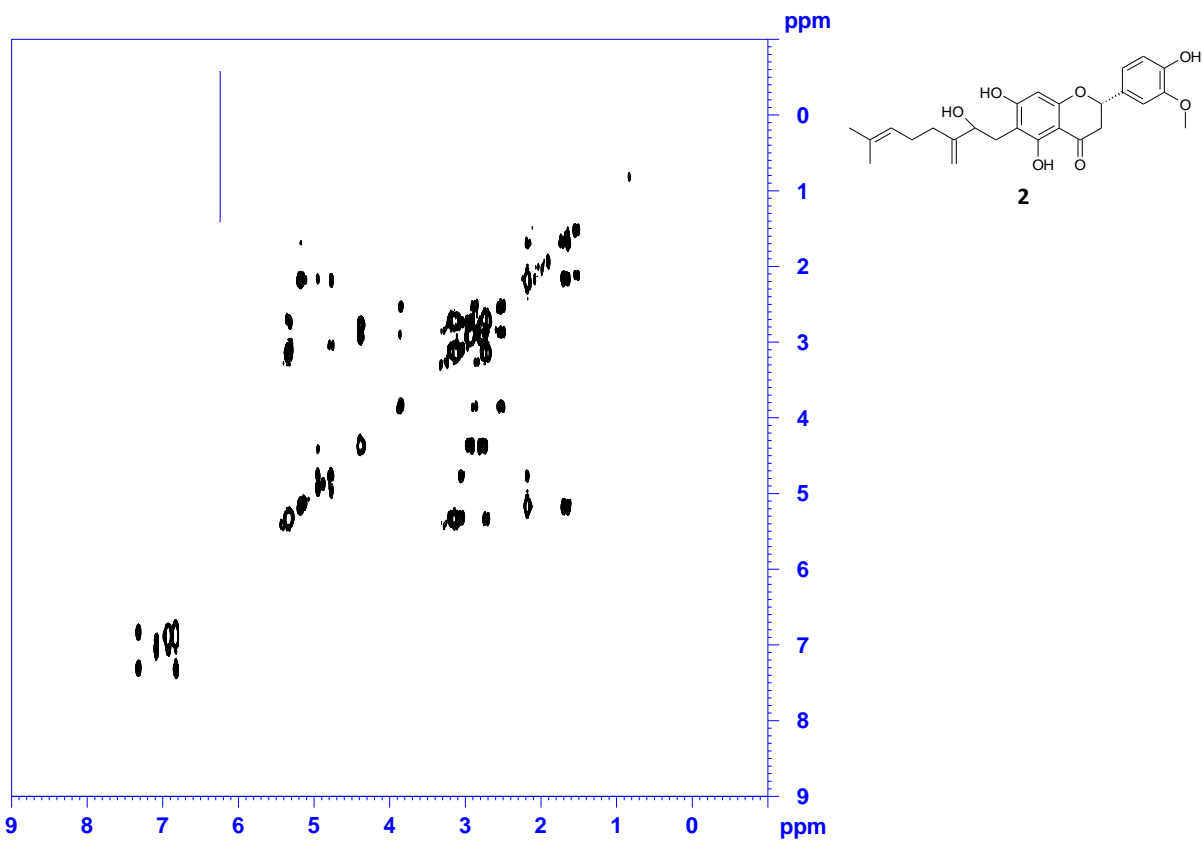


Figure S8. HMBC (400 MHz, MeOD) spectrum of tomentodiplacone K (2)



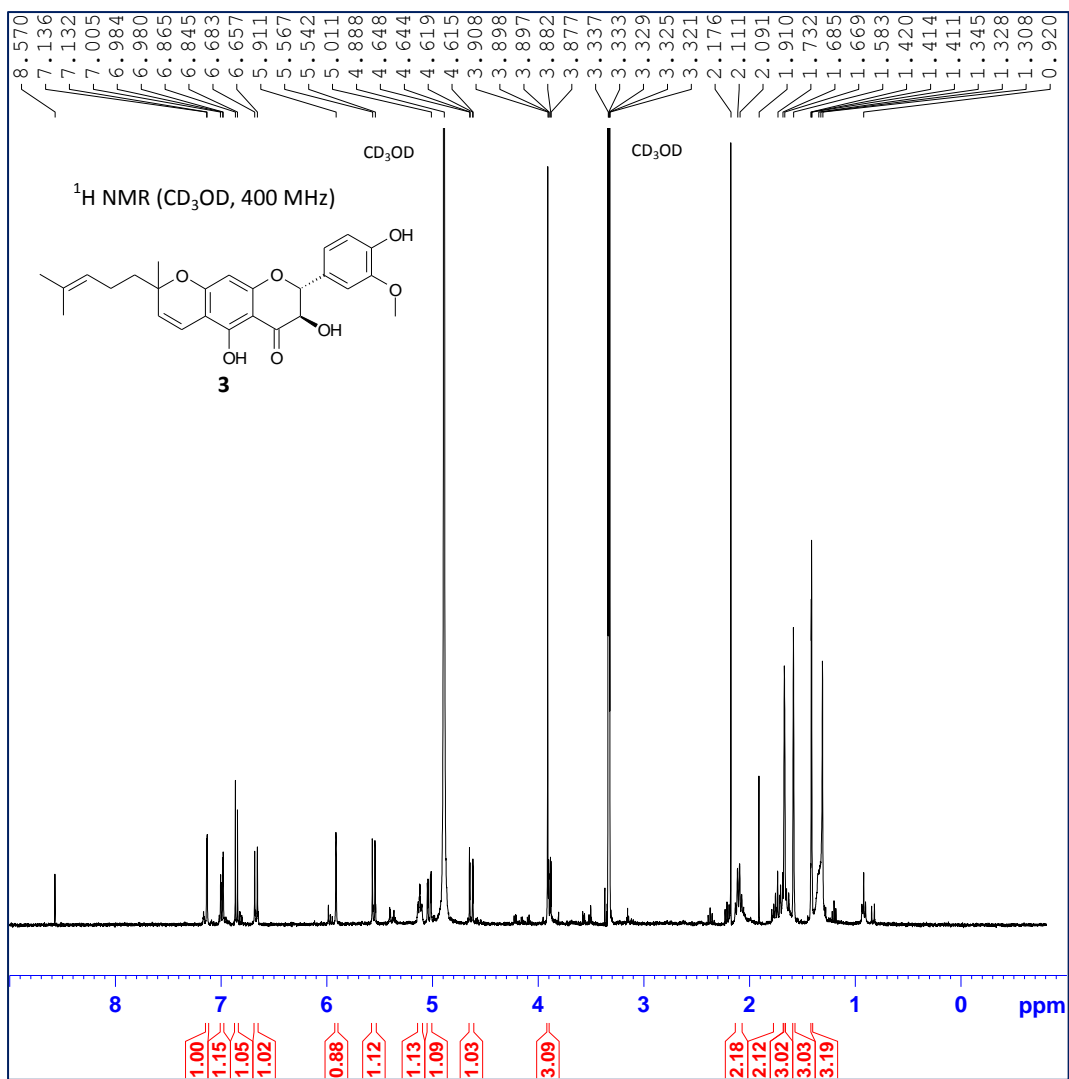


Figure S11. ¹H NMR (400 MHz, MeOD) spectrum of tomentodiplacol B (3)

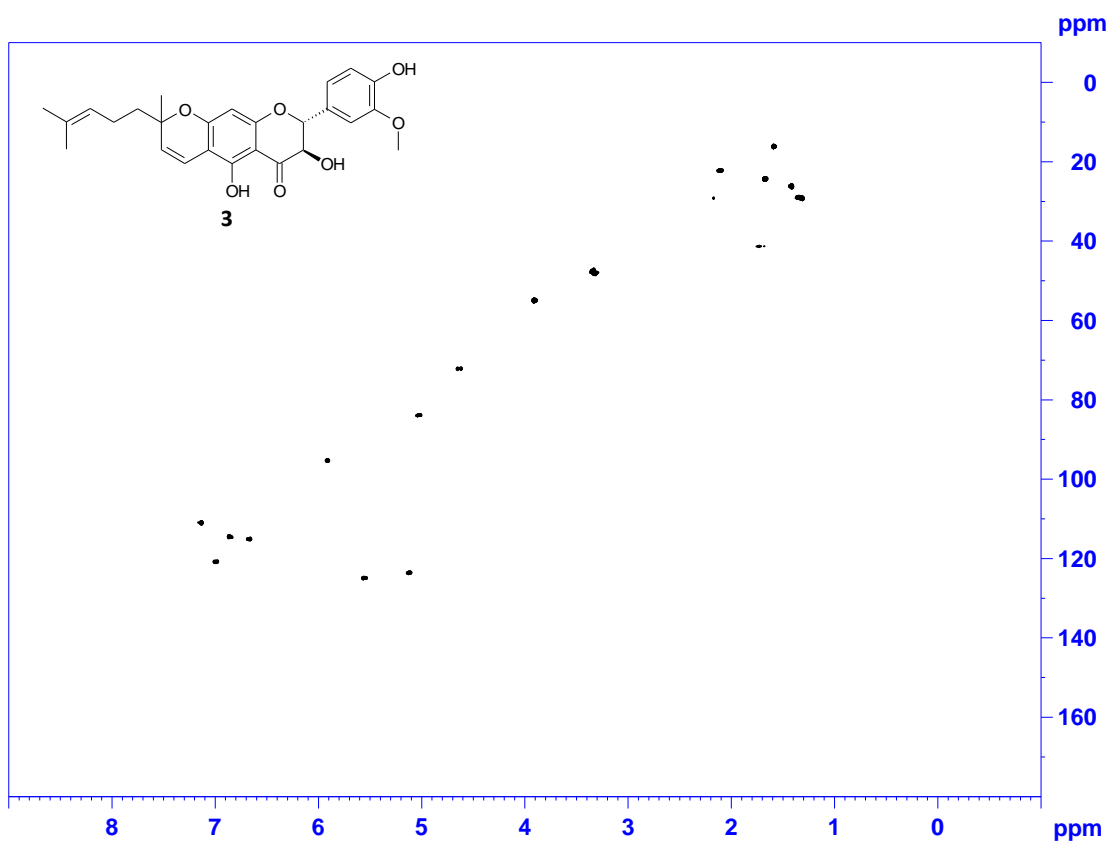


Figure S12. HSQC (400 MHz, MeOD) spectrum of tomentodiplacol B (3)

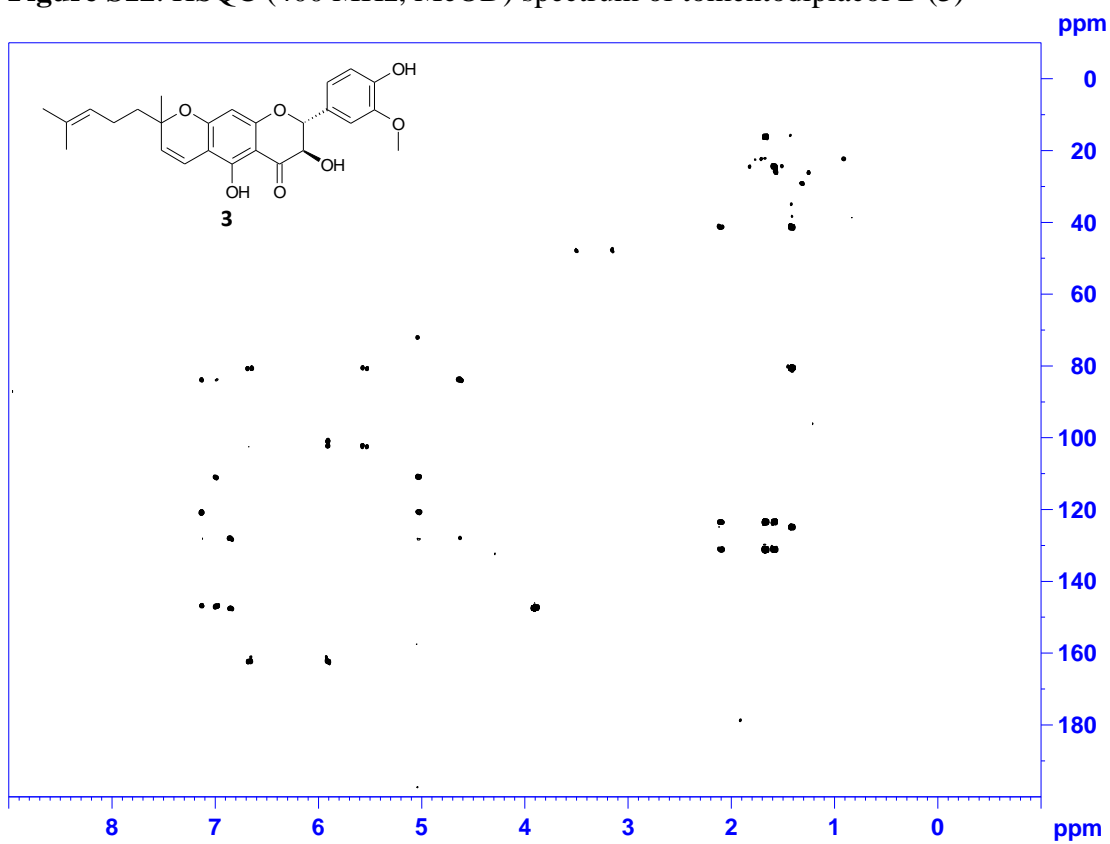


Figure S13. HMBC (400 MHz, MeOD) spectrum of tomentodiplacol B (3)

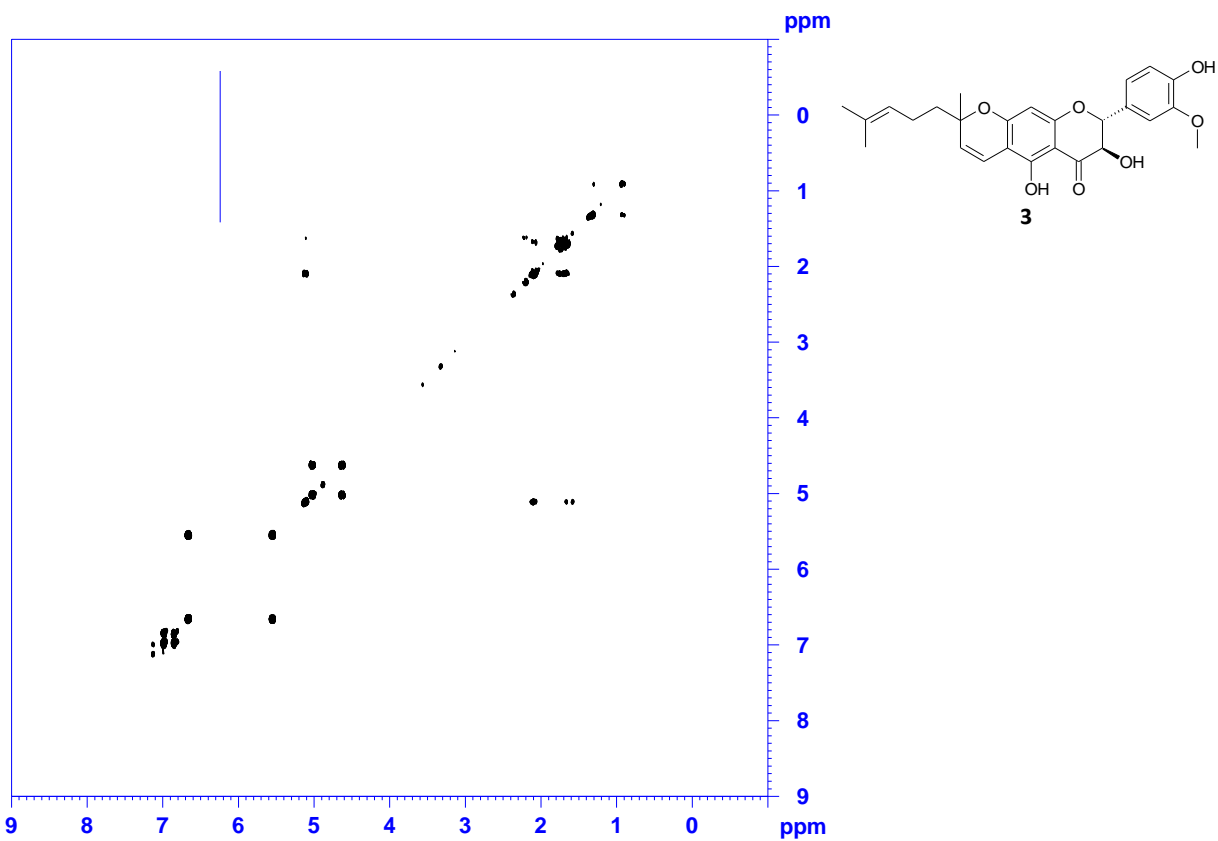


Figure S14. COSY (400 MHz, MeOD) spectrum of tomentodiplacol B (3)

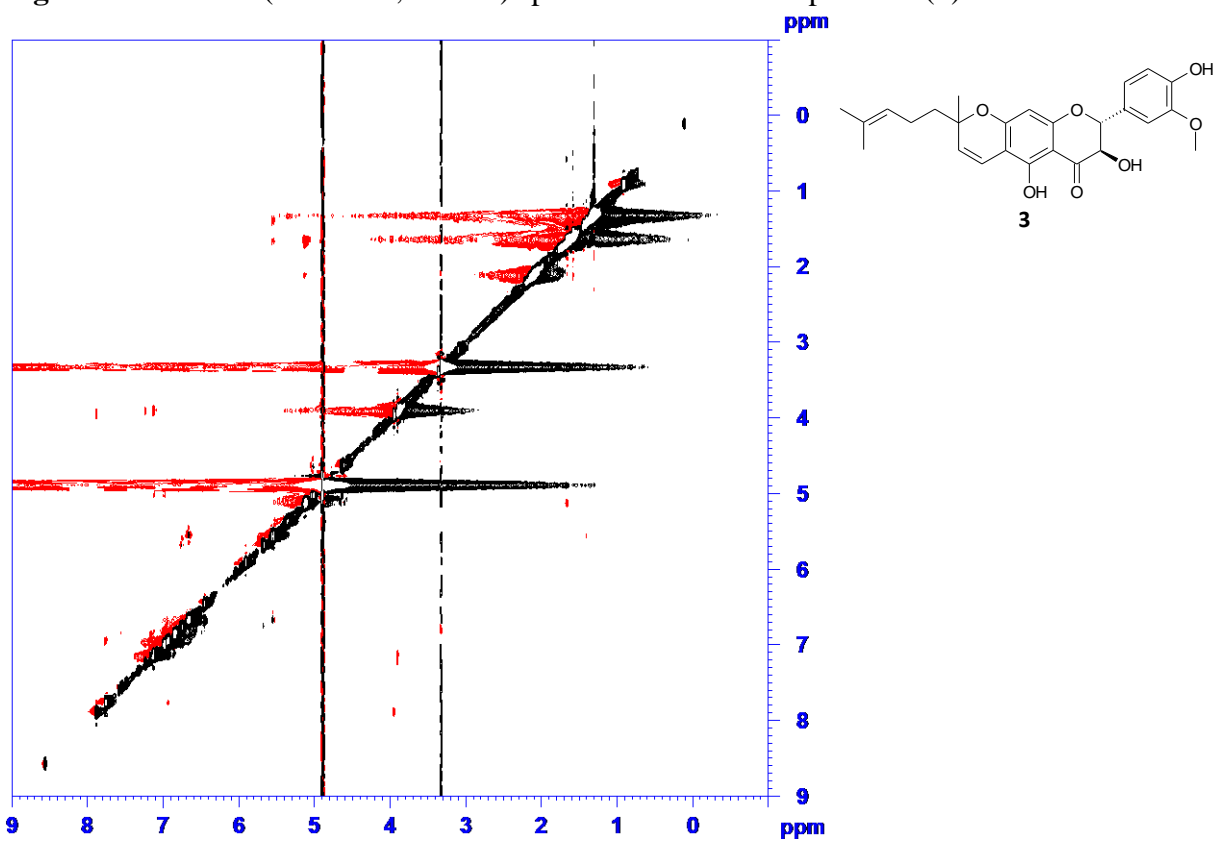


Figure S15. NOESY(400 MHz, MeOD) spectrum of tomentodiplacol B (3)

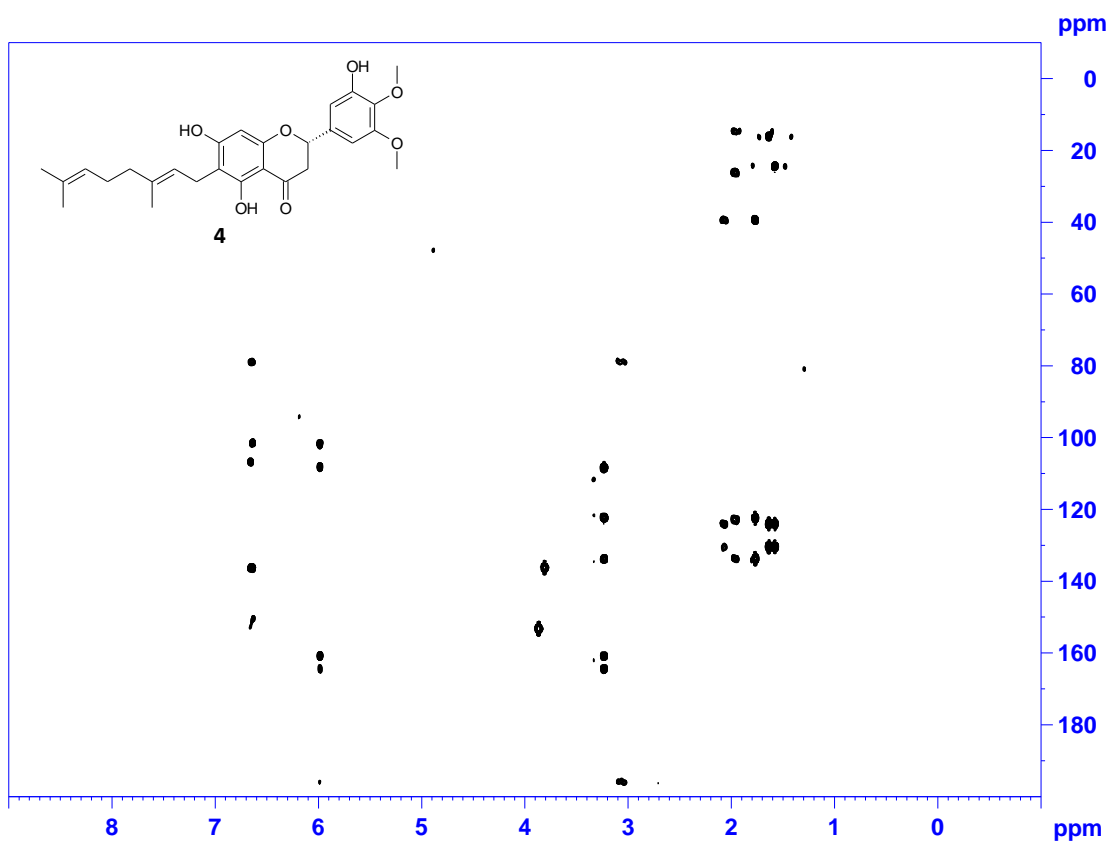


Figure S18. HMBC (400 MHz, MeOD) spectrum of 3',4'-O-dimethyl-5'-OH-diplacone (**4**)

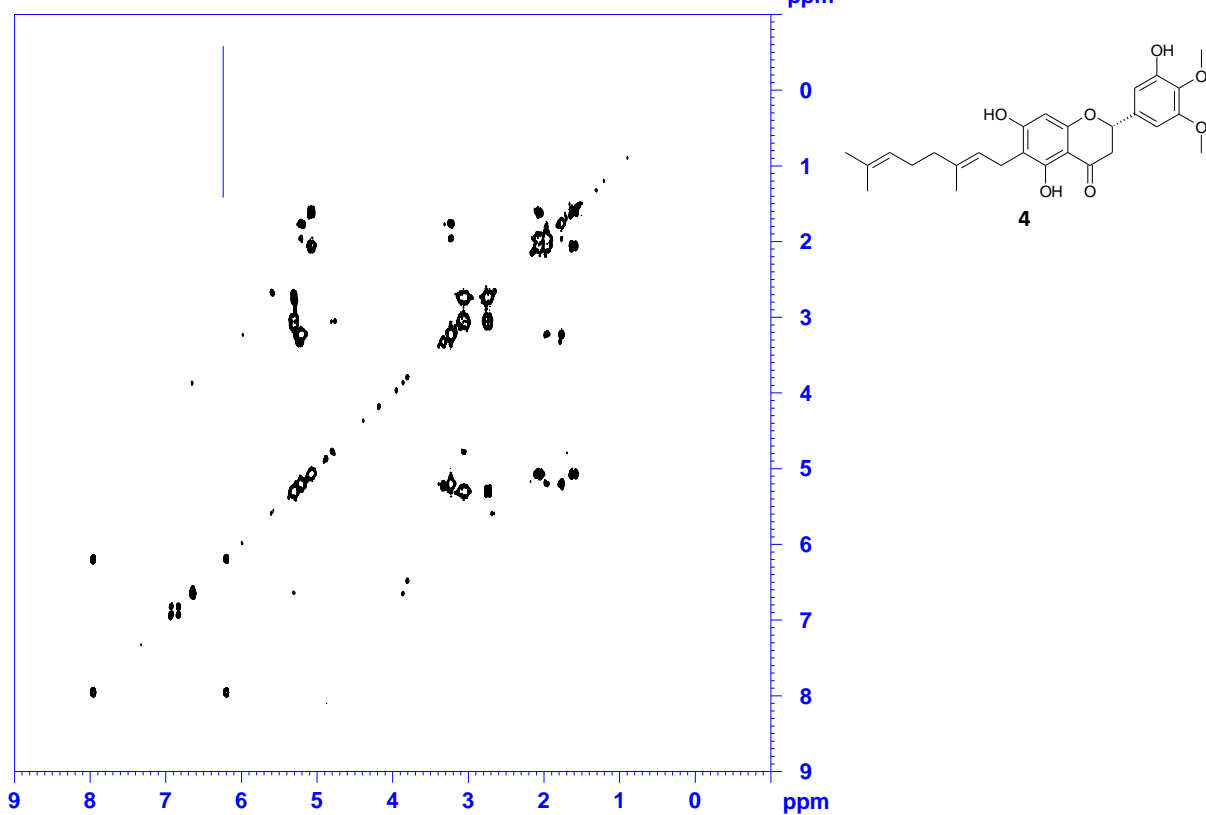


Figure S19. COSY (400 MHz, MeOD) spectrum of 3',4'-O-dimethyl-5'-OH-diplacone (**4**)

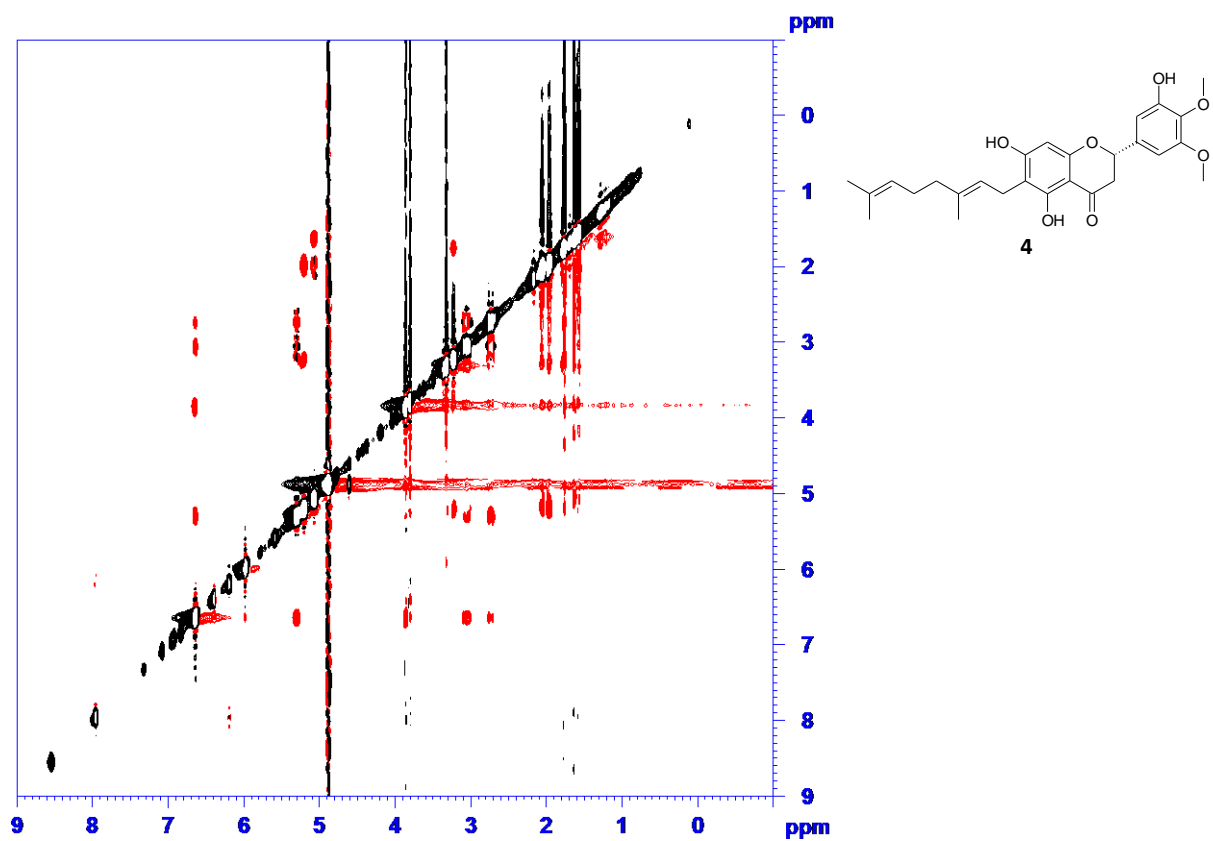


Figure S20. NOESY (400 MHz, MeOD) spectrum of 3',4'-*O*-dimethyl-5'-OH-diplacone (**4**)

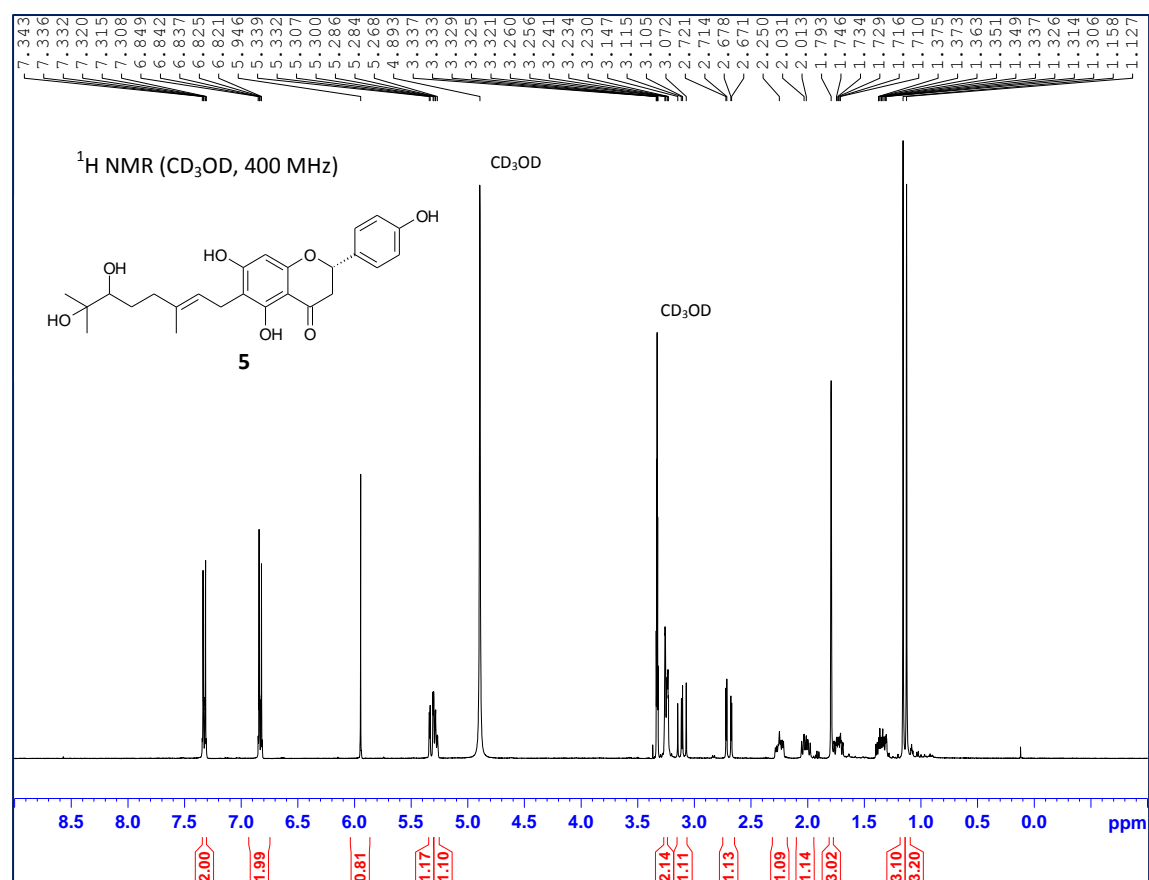
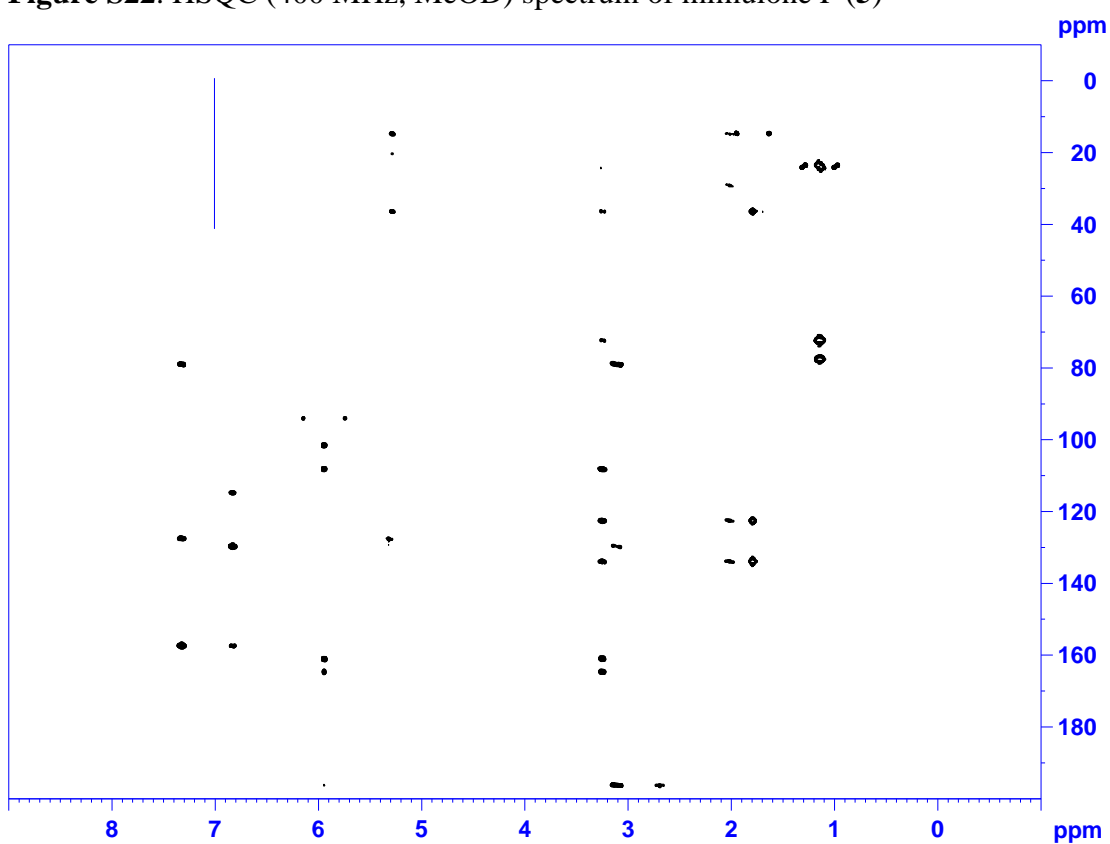
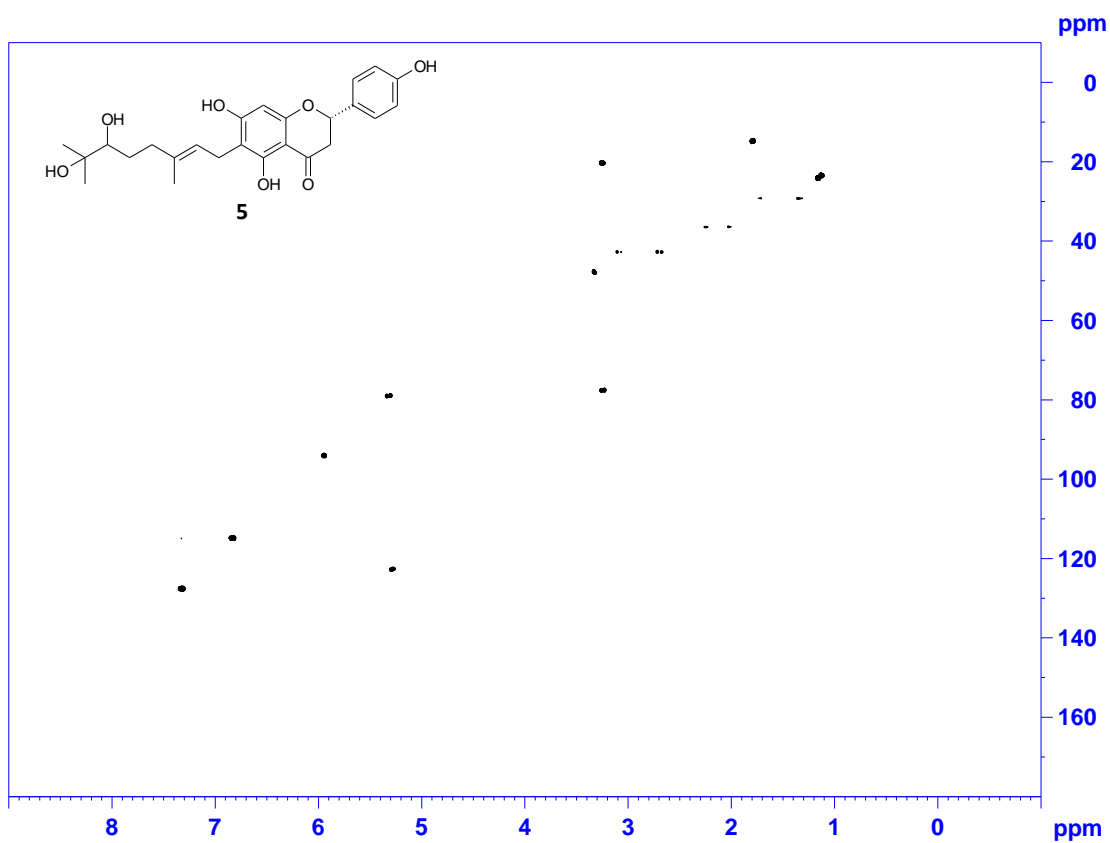


Figure S21. ¹H NMR (400 MHz, MeOD) spectrum of mimulone F (**5**)



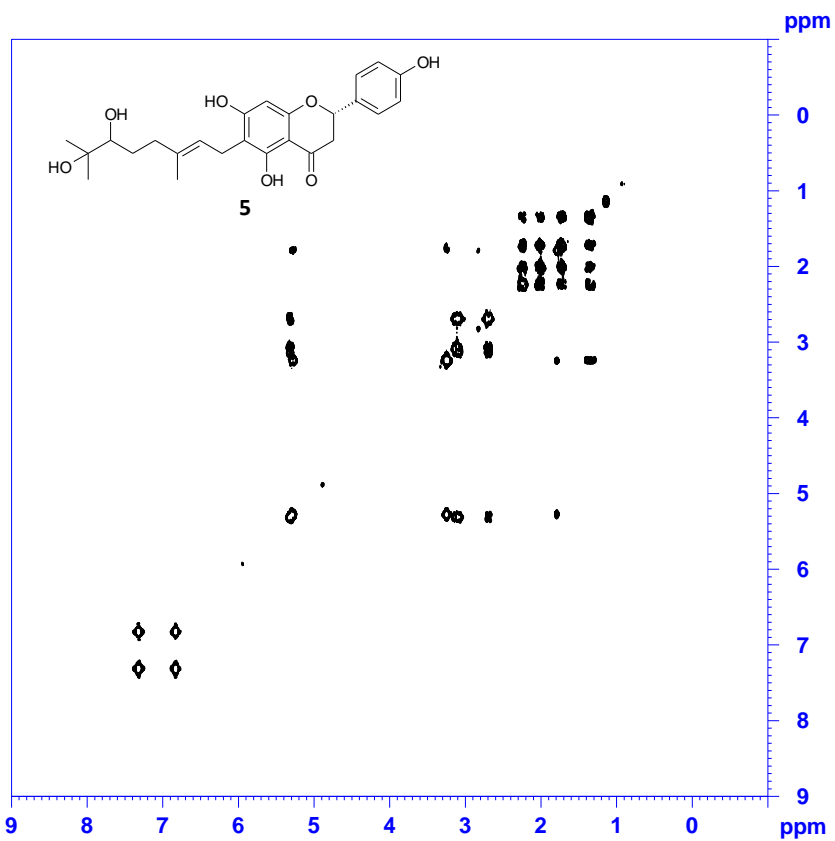


Figure S24. COSY (400 MHz, MeOD) spectrum of mimulone F (**5**)

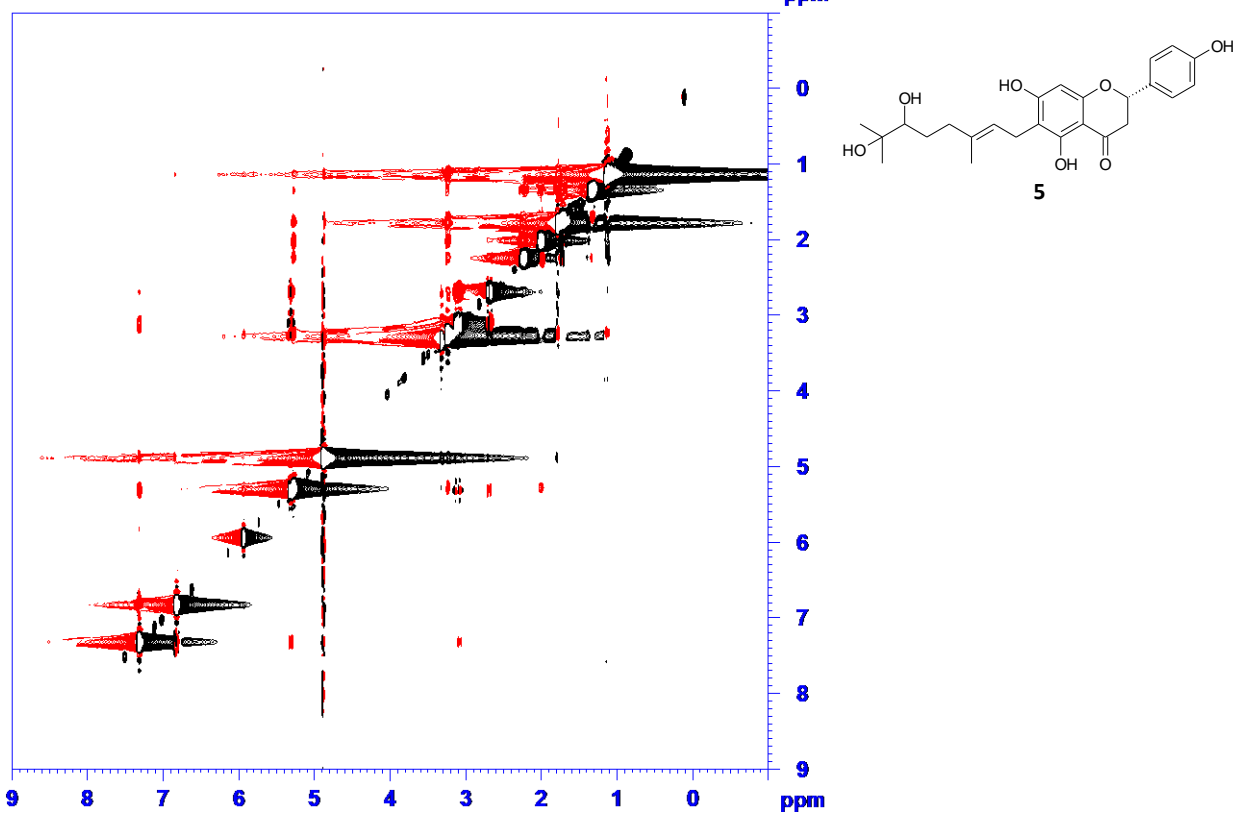


Figure S25. NOESY (400 MHz, MeOD) spectrum of mimulone F (**5**)

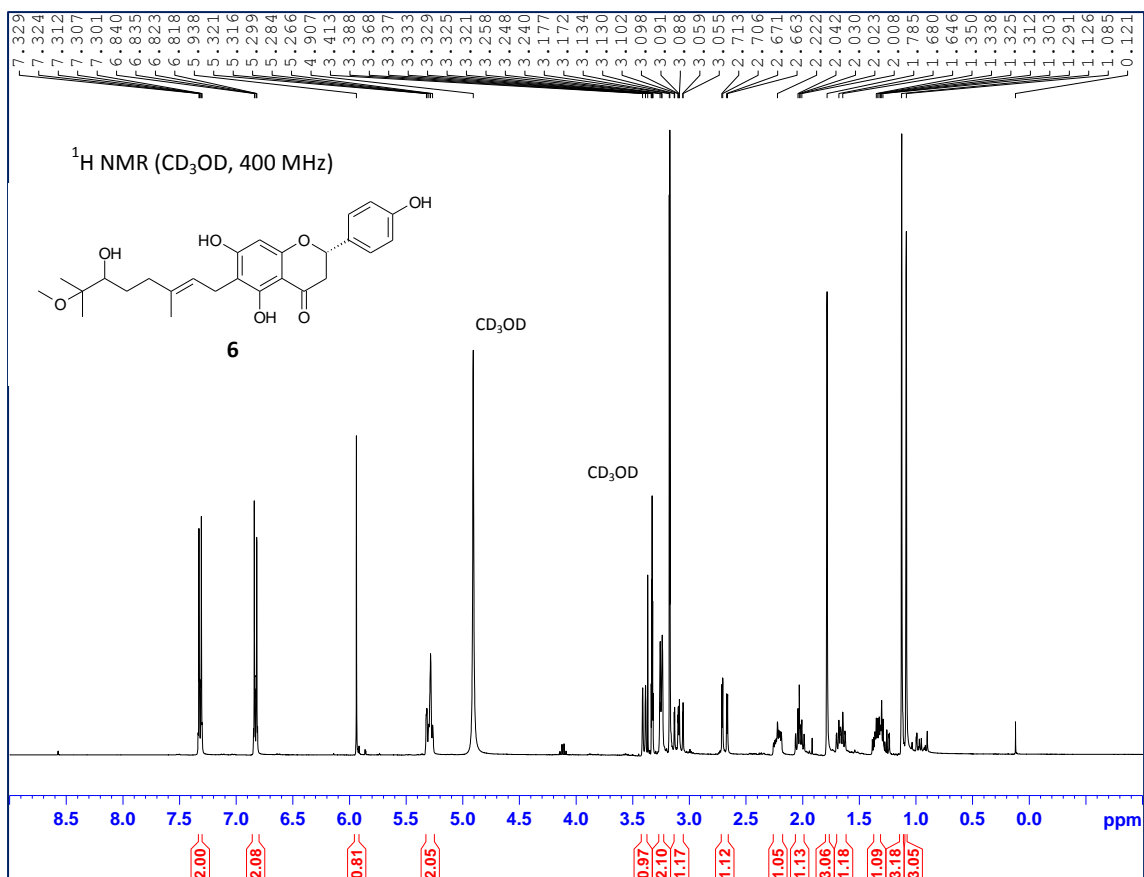


Figure S26. ¹H NMR (400 MHz, MeOD) spectrum of mimulone G (6)

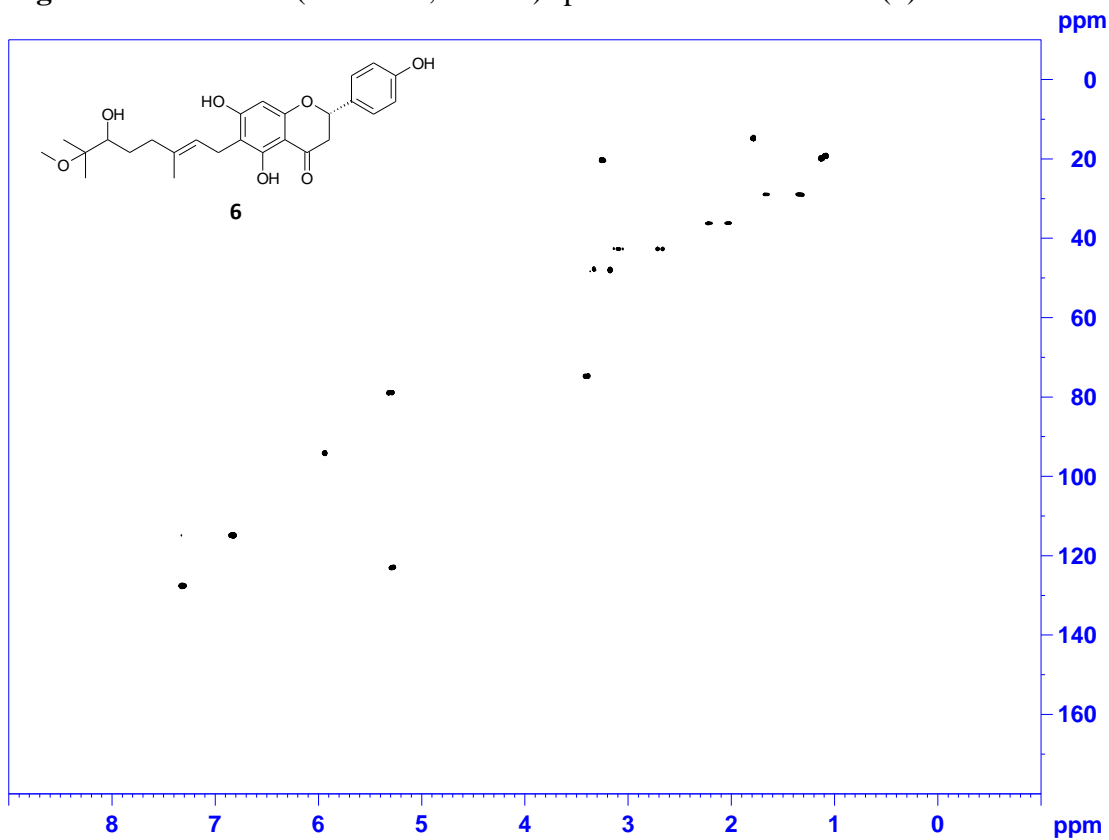


Figure S27. HSQC (400 MHz, MeOD) spectrum of mimulone G (6)

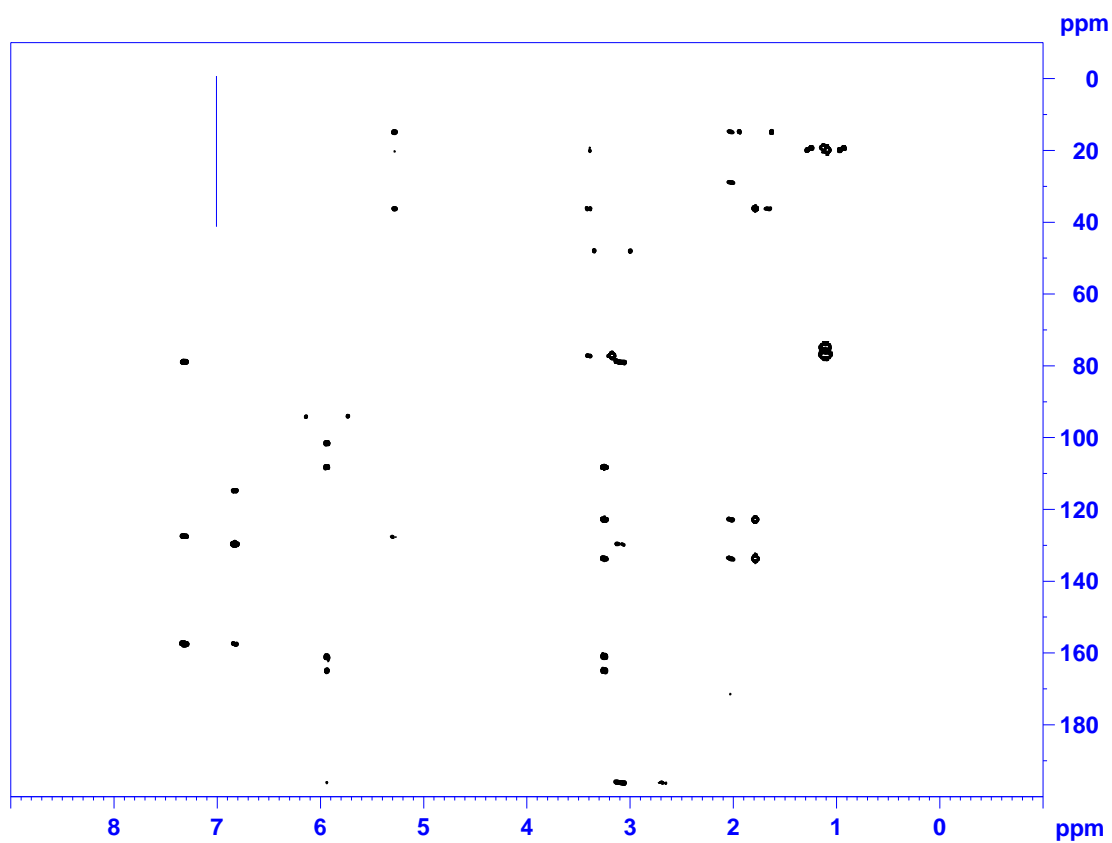


Figure S28. HMBC (400 MHz, MeOD) spectrum of mimulone G (**6**)

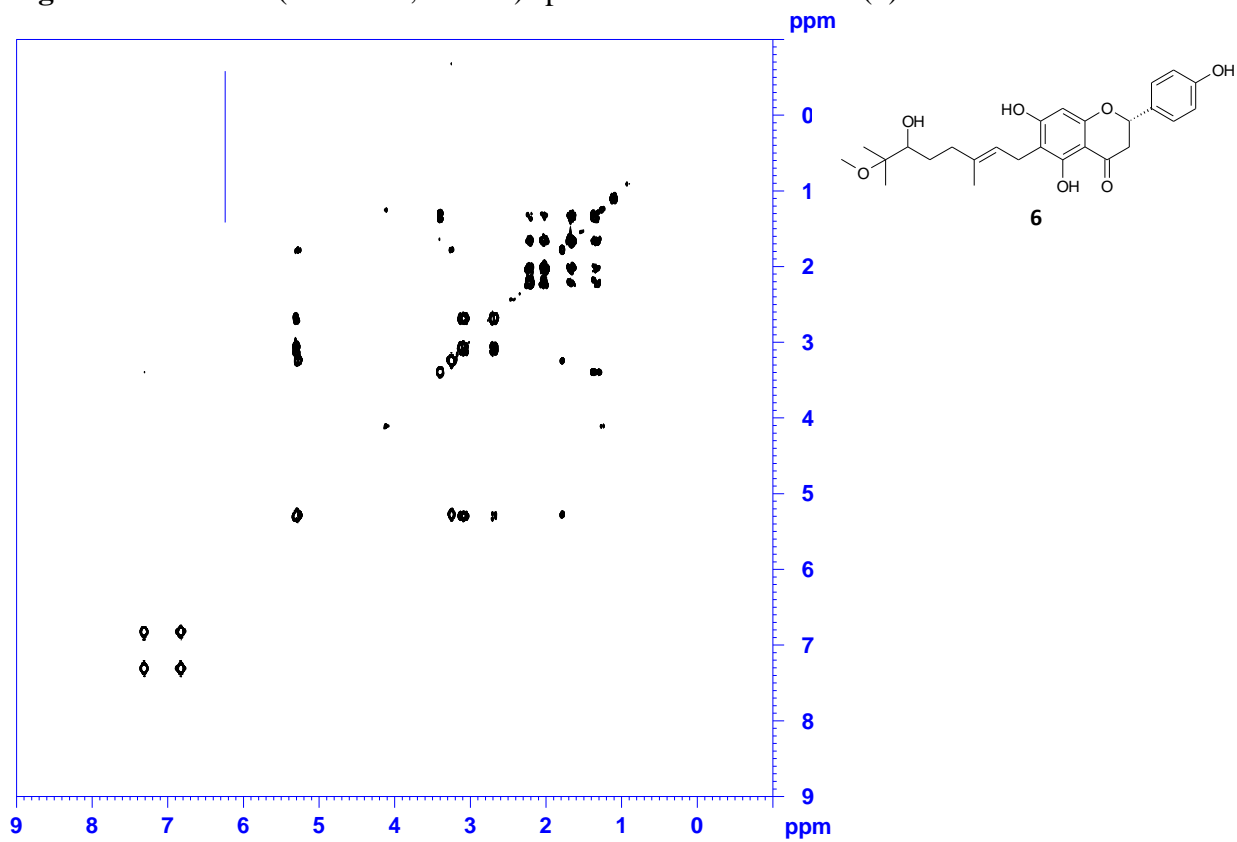


Figure S29. COSY (400 MHz, MeOD) spectrum of mimulone G (**6**)

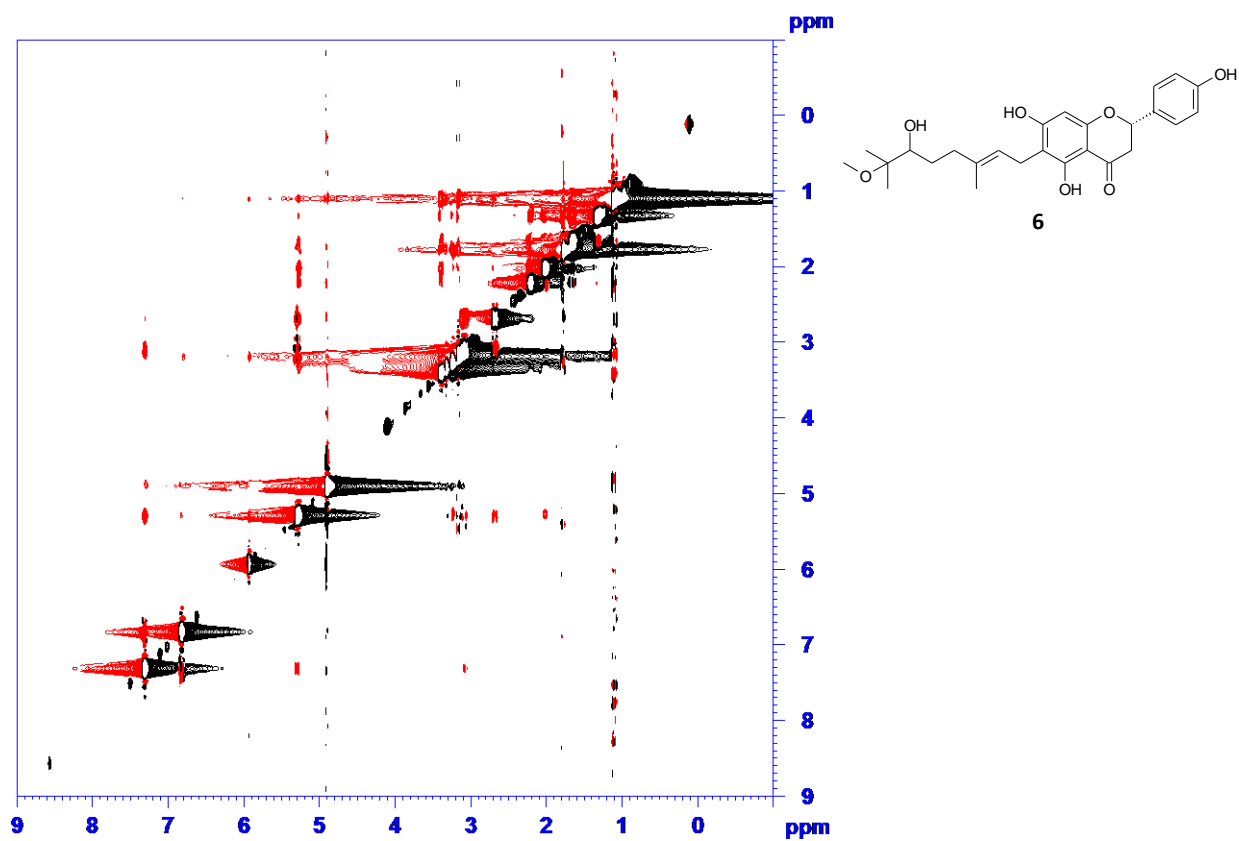


Figure S30. NOESY (400 MHz, MeOD) spectrum of mimulone G (6)

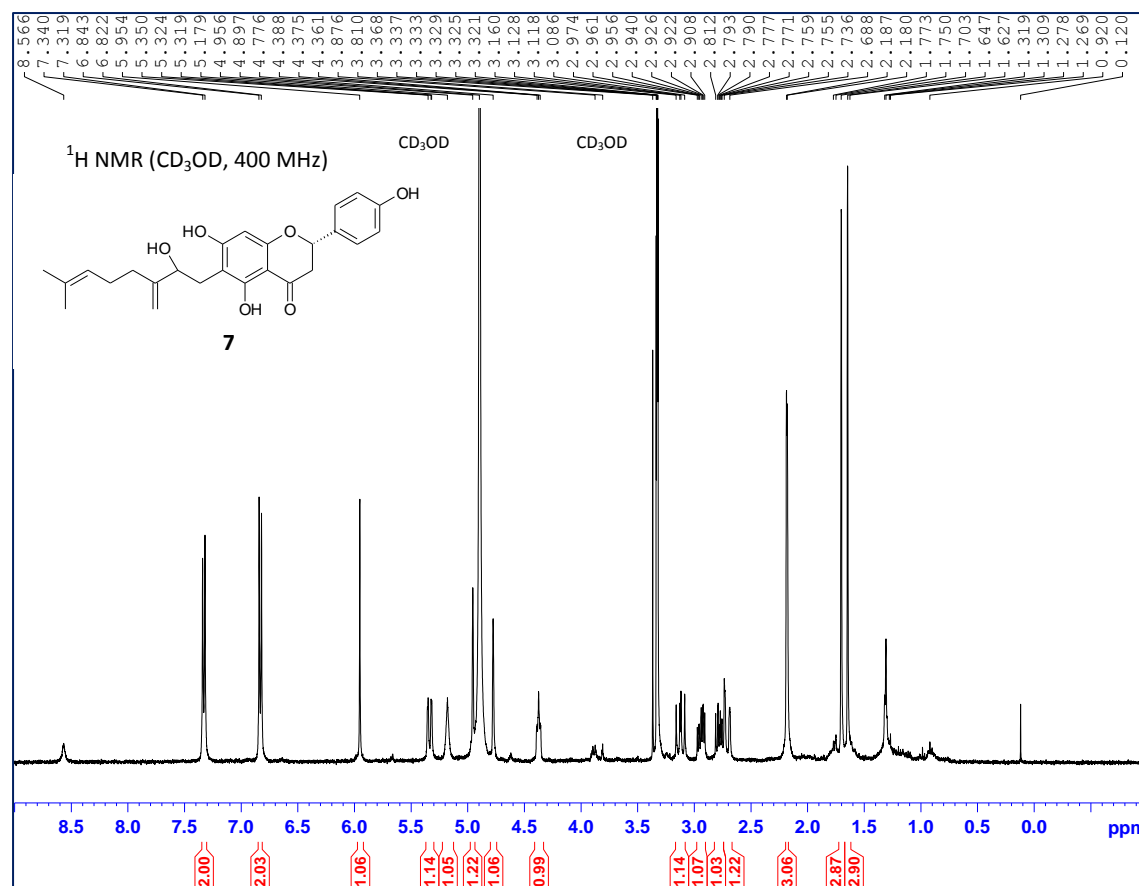


Figure S31. $^1\text{H NMR}$ (400 MHz, MeOD) spectrum of mimulone H (7)

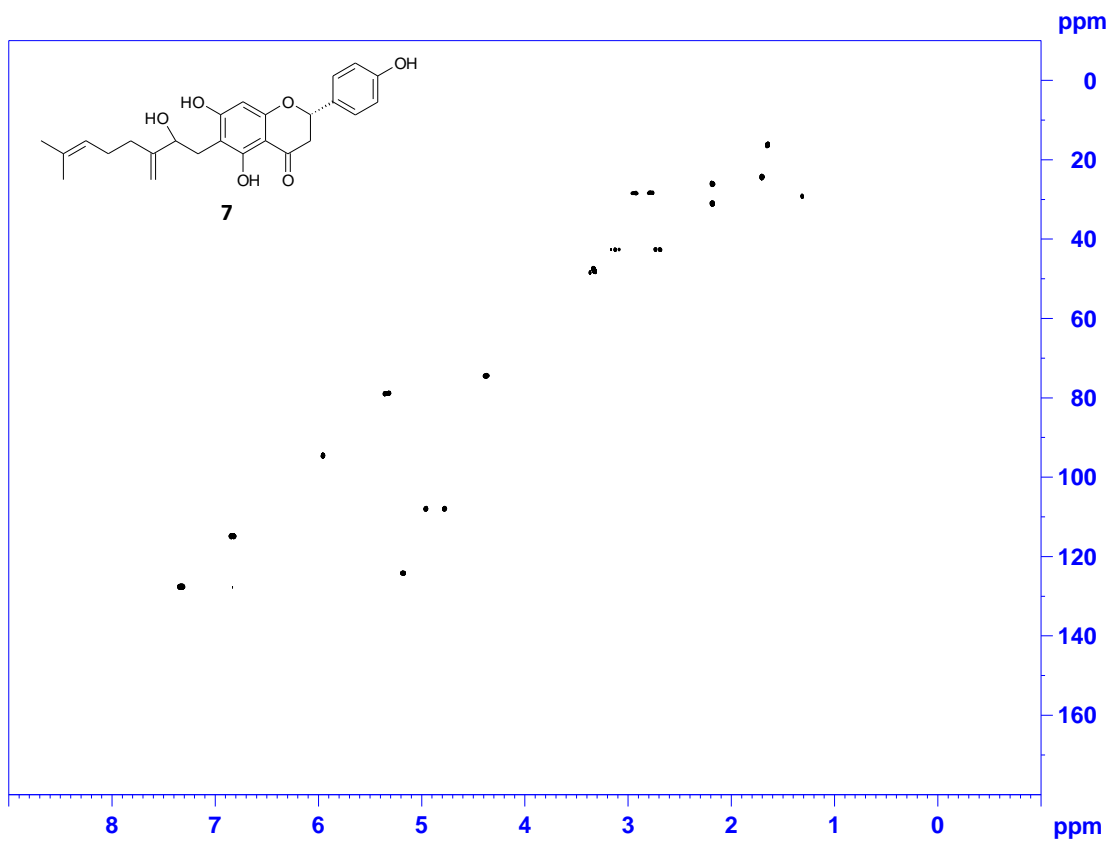


Figure S32. HSQC (400 MHz, MeOD) spectrum of mimulone H (7)

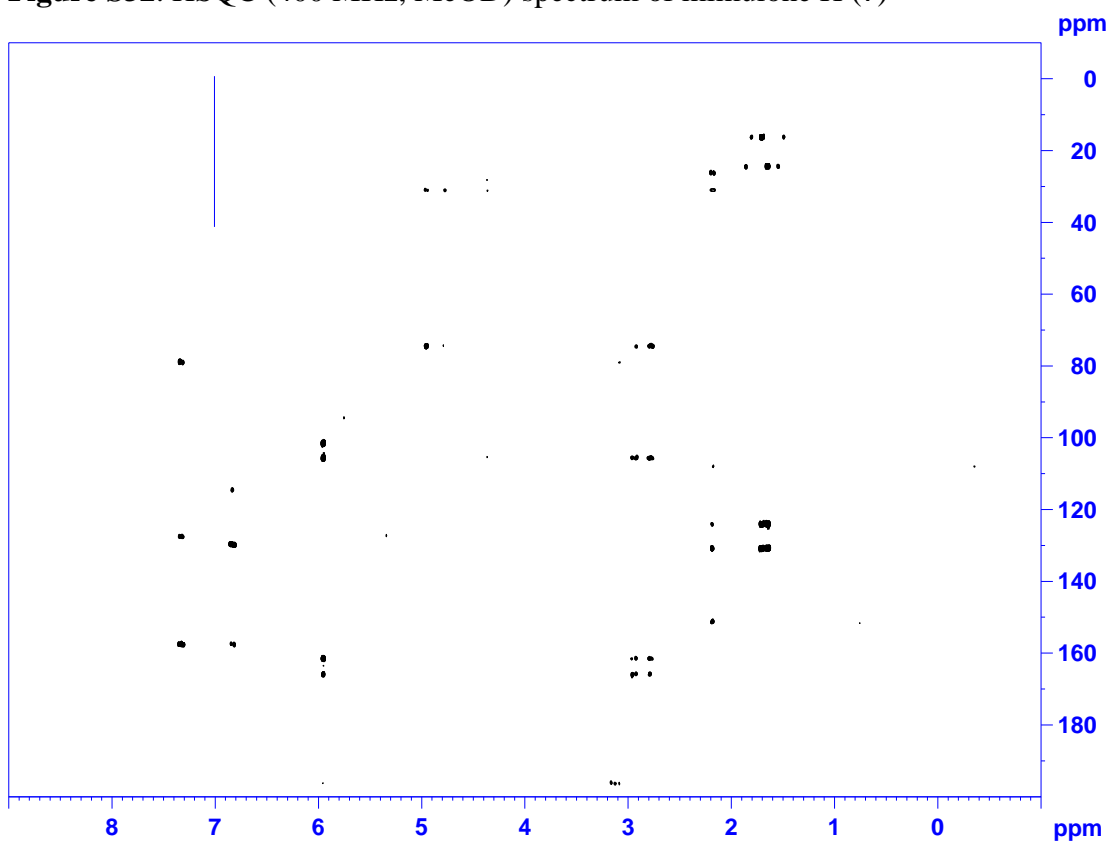


Figure S33. HMBC (400 MHz, MeOD) spectrum of mimulone H (7)

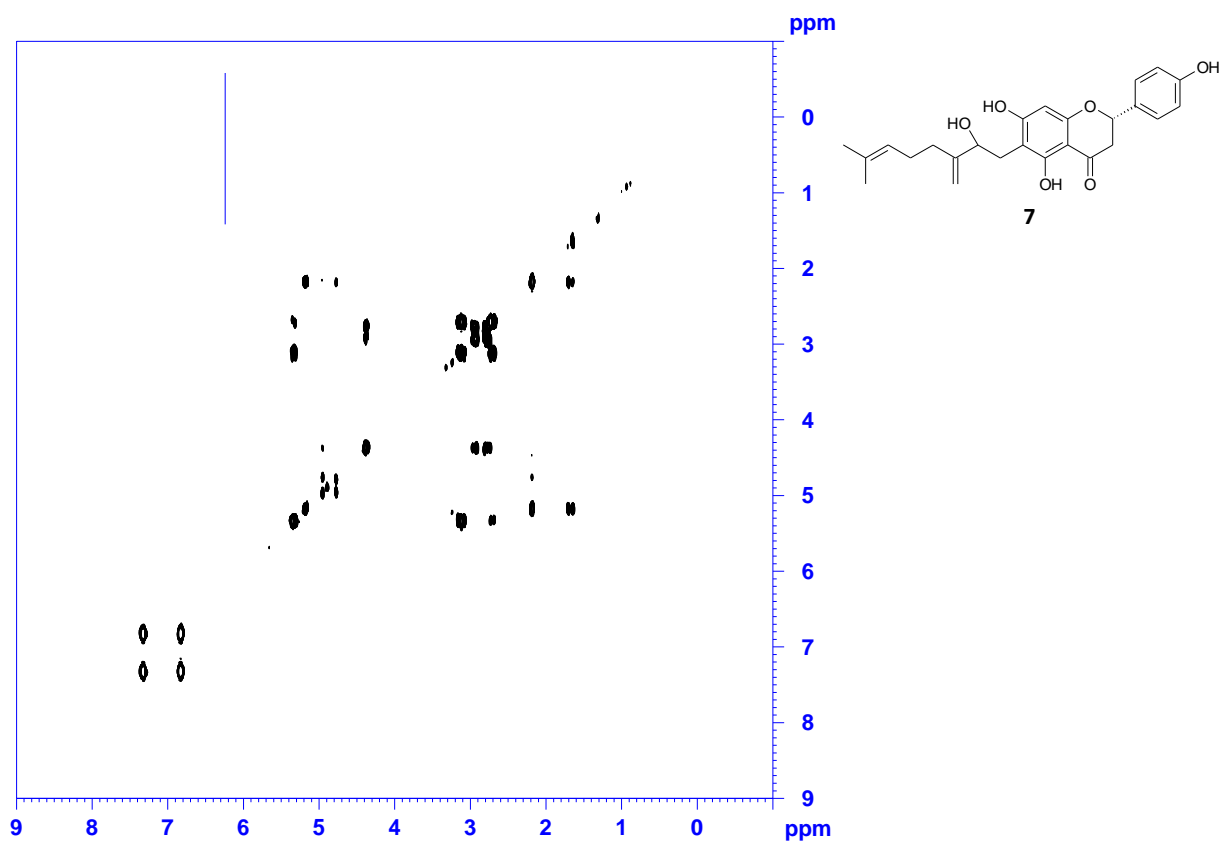


Figure S34. COSY (400 MHz, MeOD) spectrum of mimulone H (7)

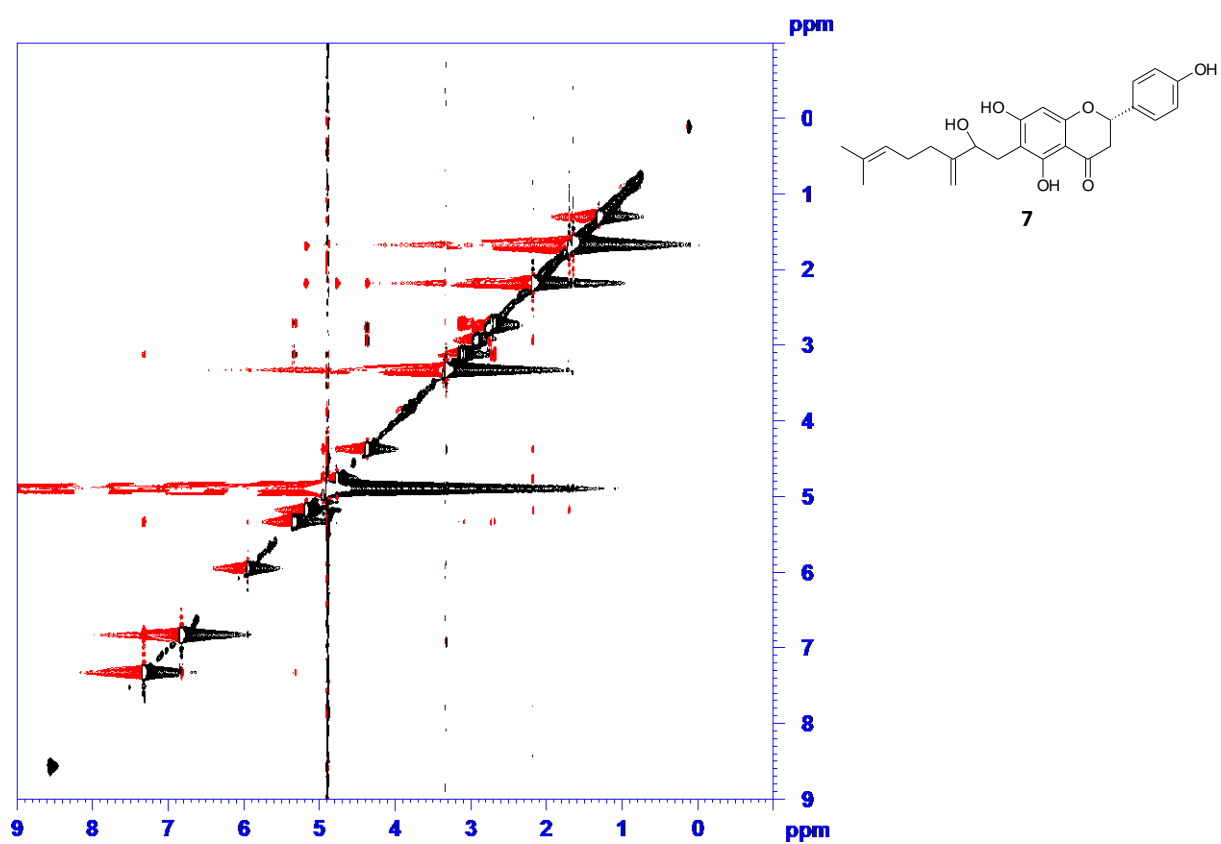


Figure S35. NOESY (400 MHz, MeOD) spectrum of mimulone H (7)

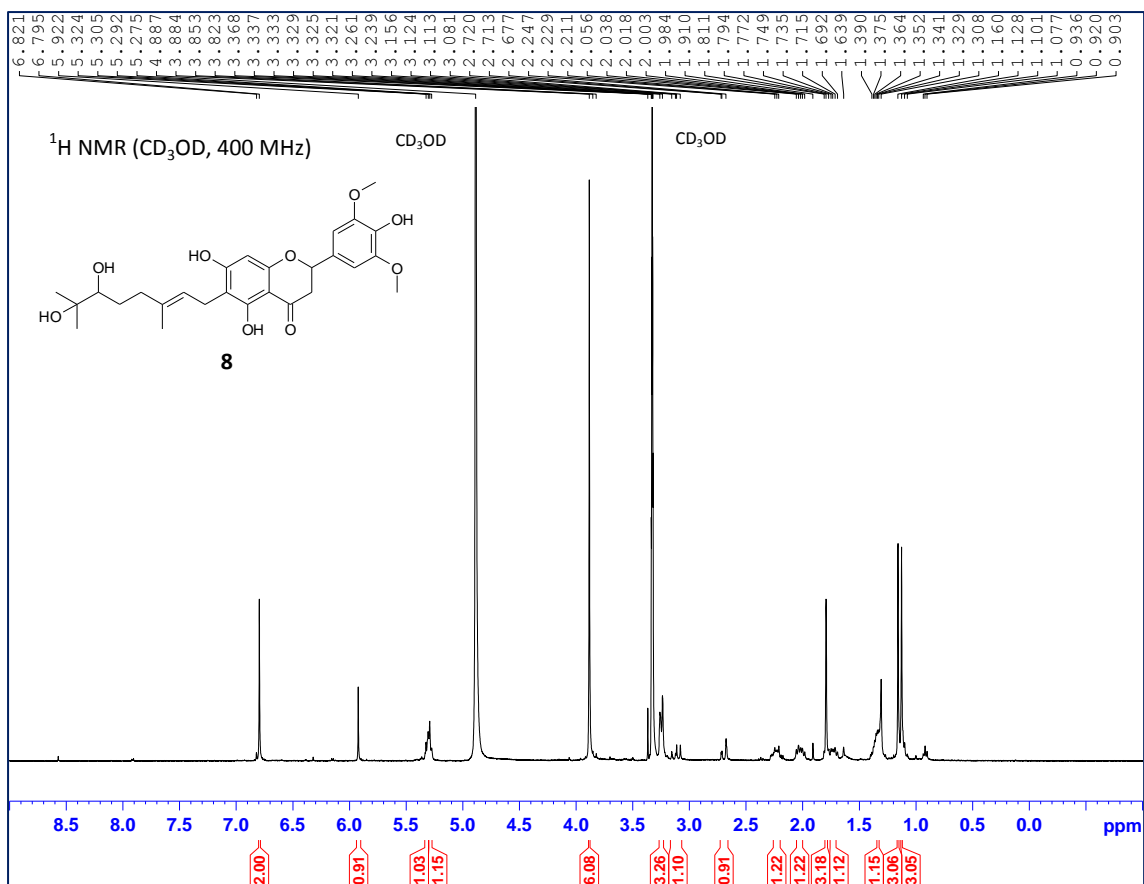


Figure S36. ¹H NMR (400 MHz, MeOD) spectrum of paulownione A (**8**)

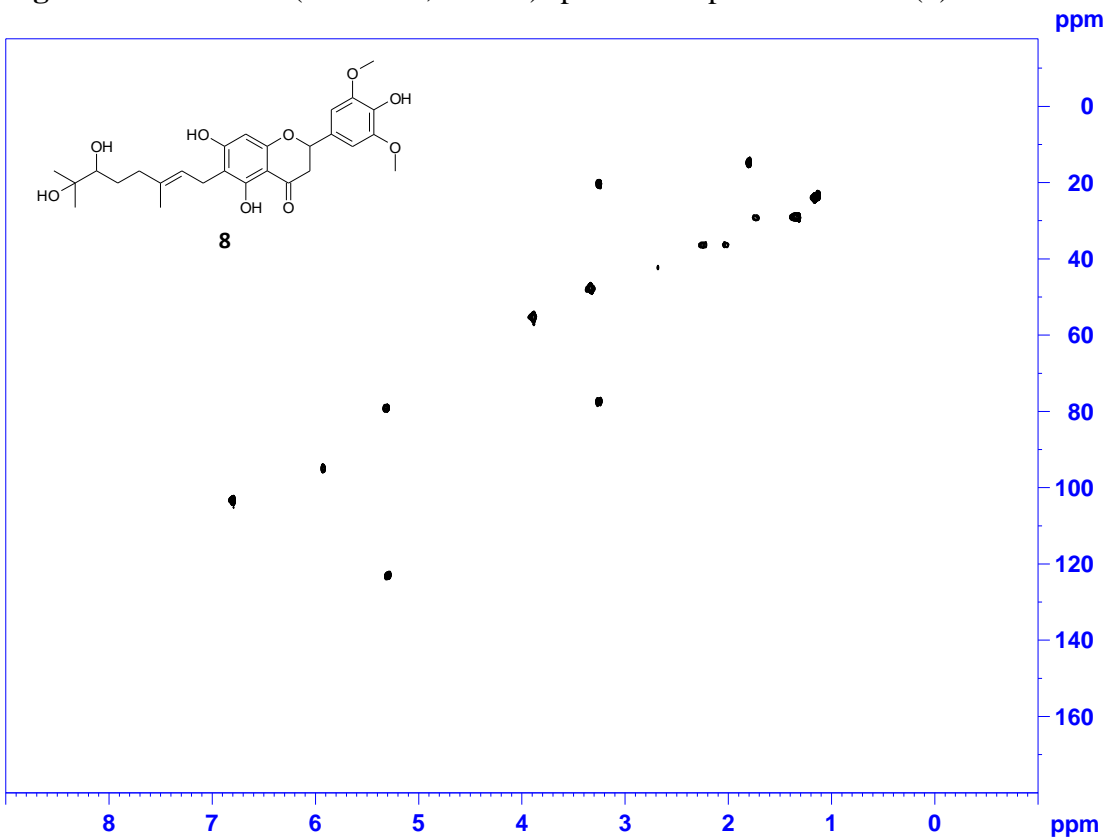


Figure S37. HSQC (400 MHz, MeOD) spectrum of paulownione A (**8**)

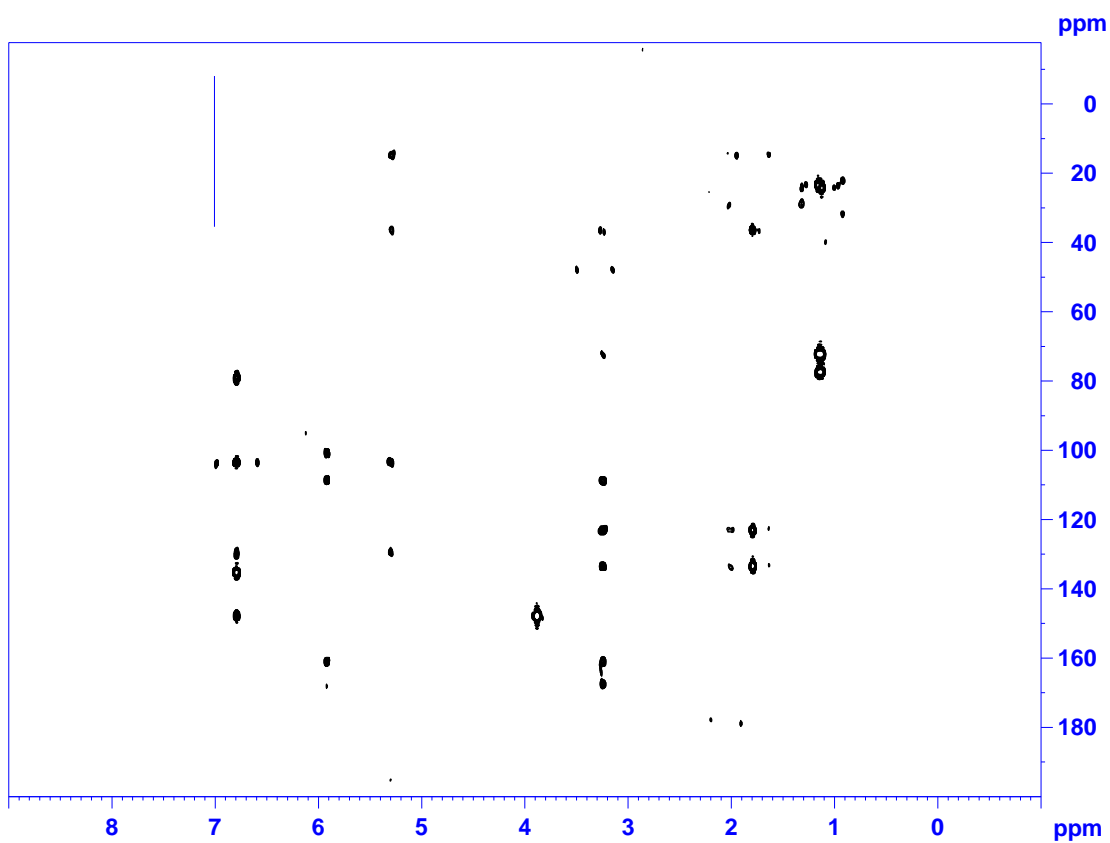


Figure S38. HMBC (400 MHz, MeOD) spectrum of paulownione A (8)

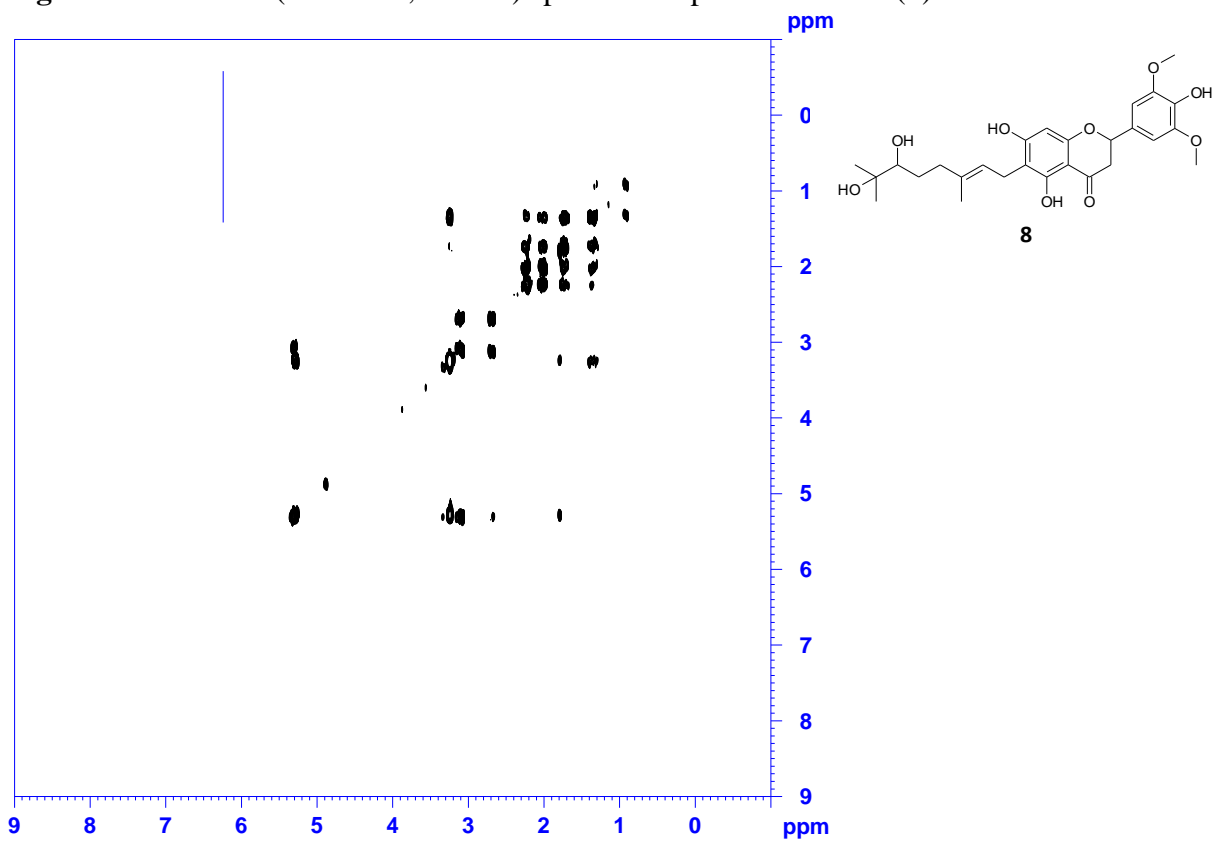


Figure S39. COSY (400 MHz, MeOD) spectrum of paulownione A (8)

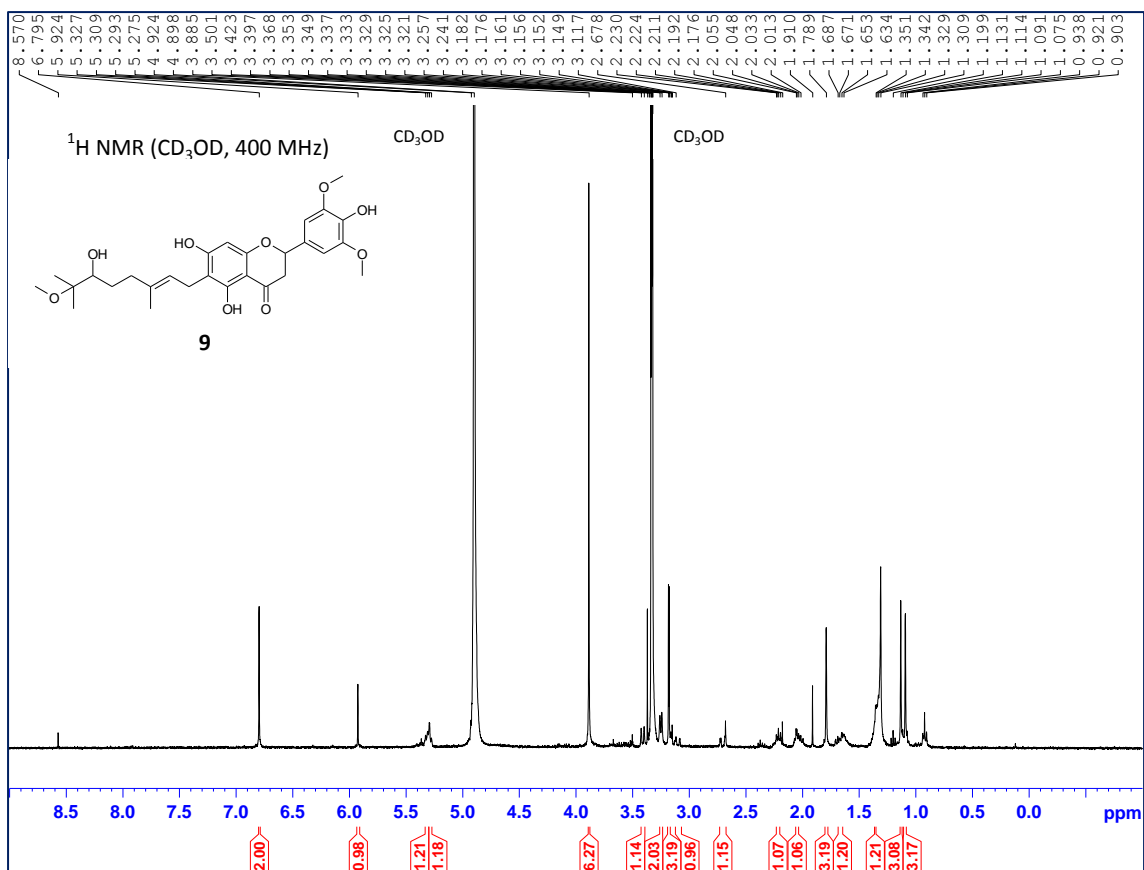


Figure S40. ¹H NMR (400 MHz, MeOD) spectrum of paulownione B (**9**)

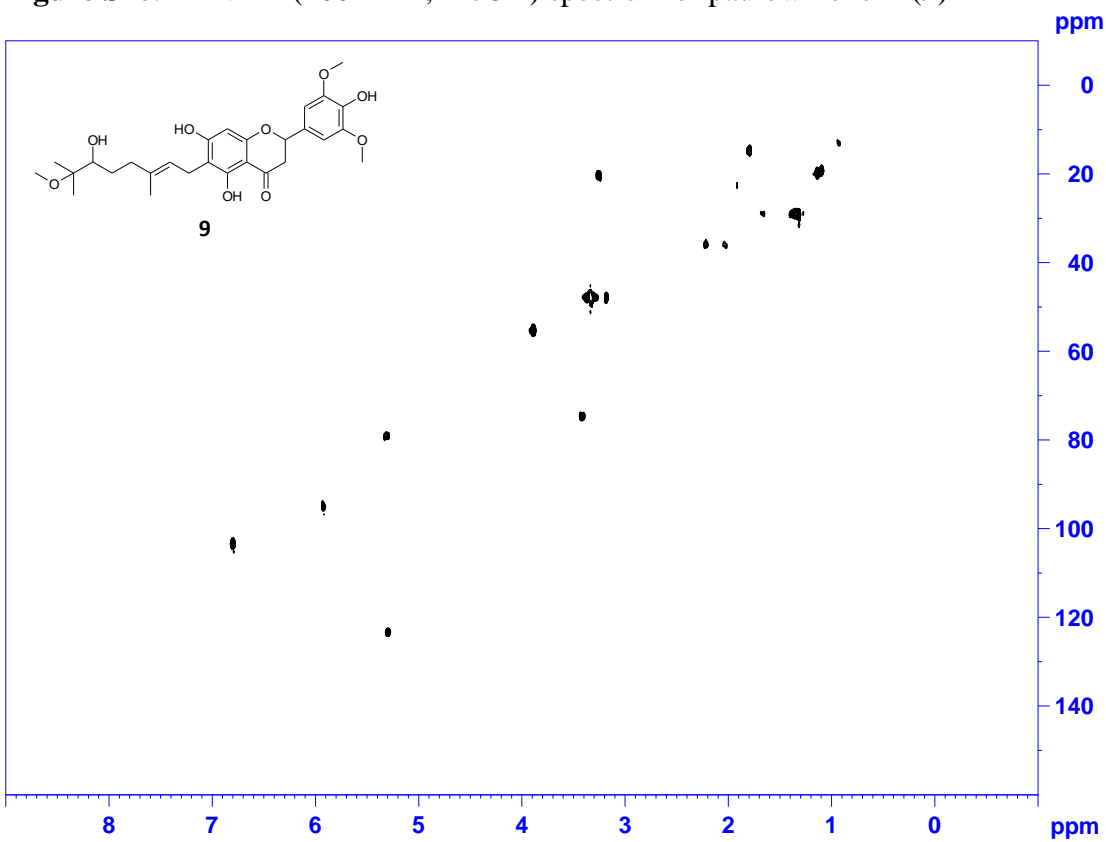


Figure S41. HSQC (400 MHz, MeOD) spectrum of paulownione B (**9**)

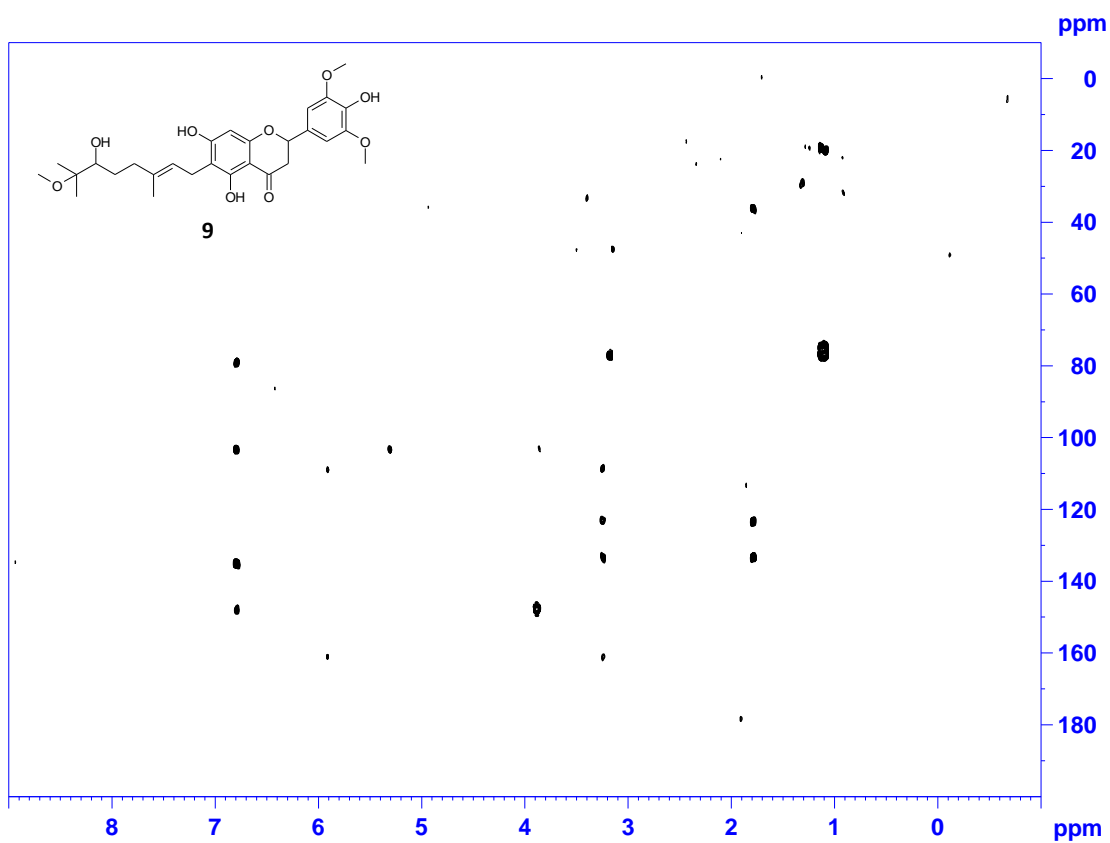


Figure S42. HMBC (400 MHz, MeOD) spectrum of paulownione B (9)

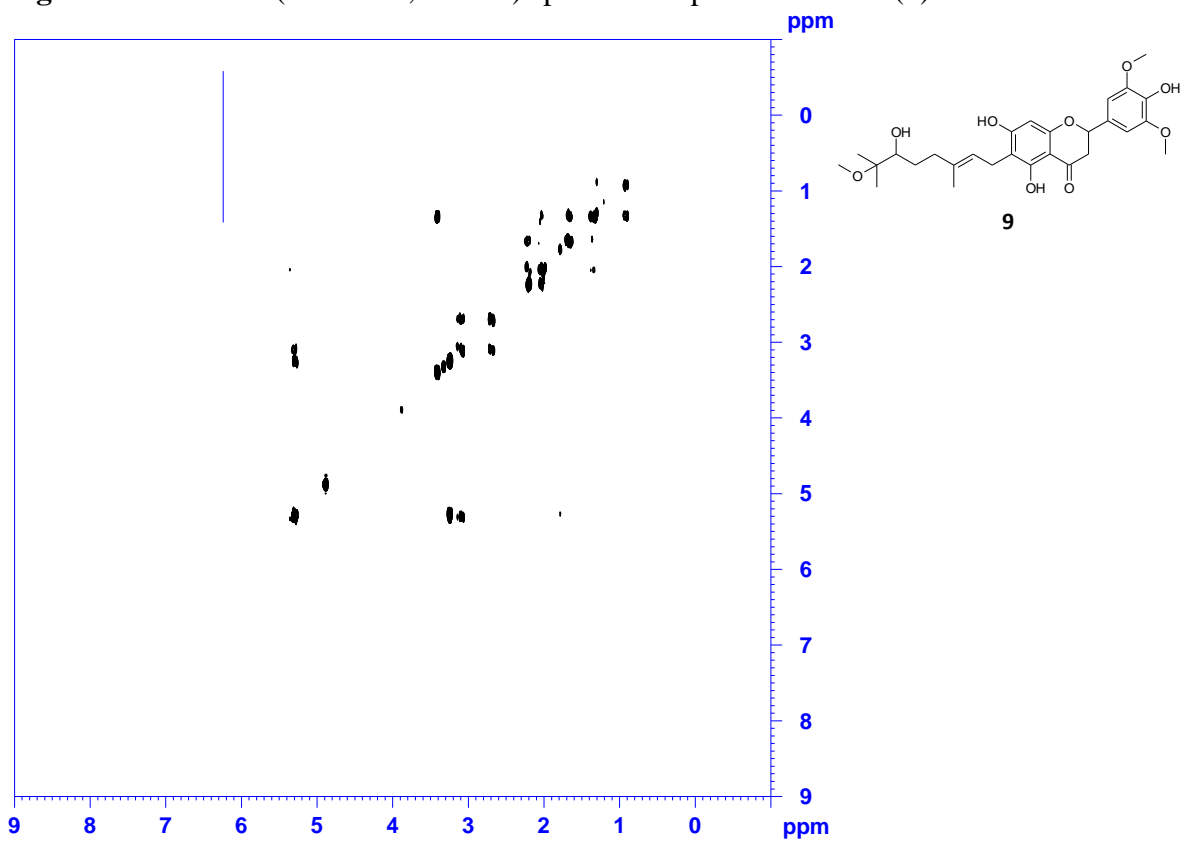


Figure S43. COSY (400 MHz, MeOD) spectrum of paulownione B (9)

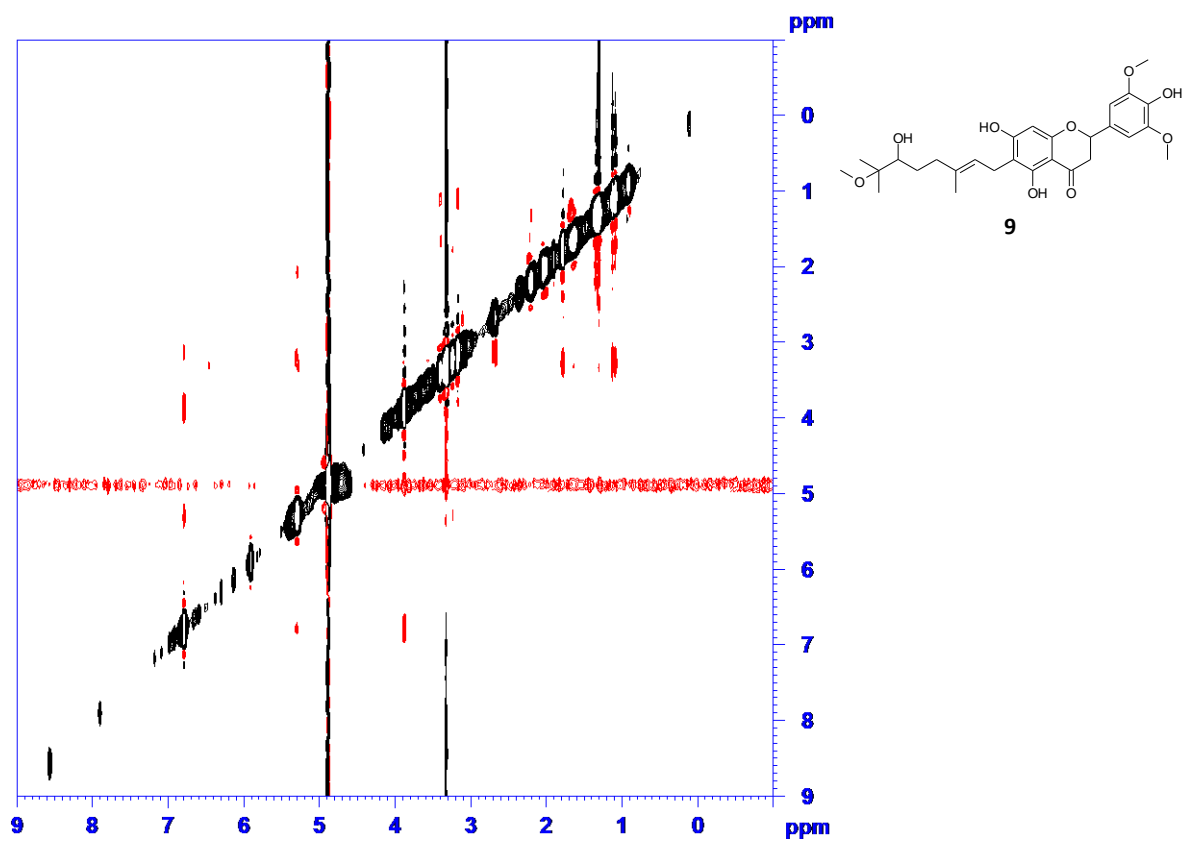


Figure S44. NOESY (400 MHz, MeOD) spectrum of paulownione B (9)

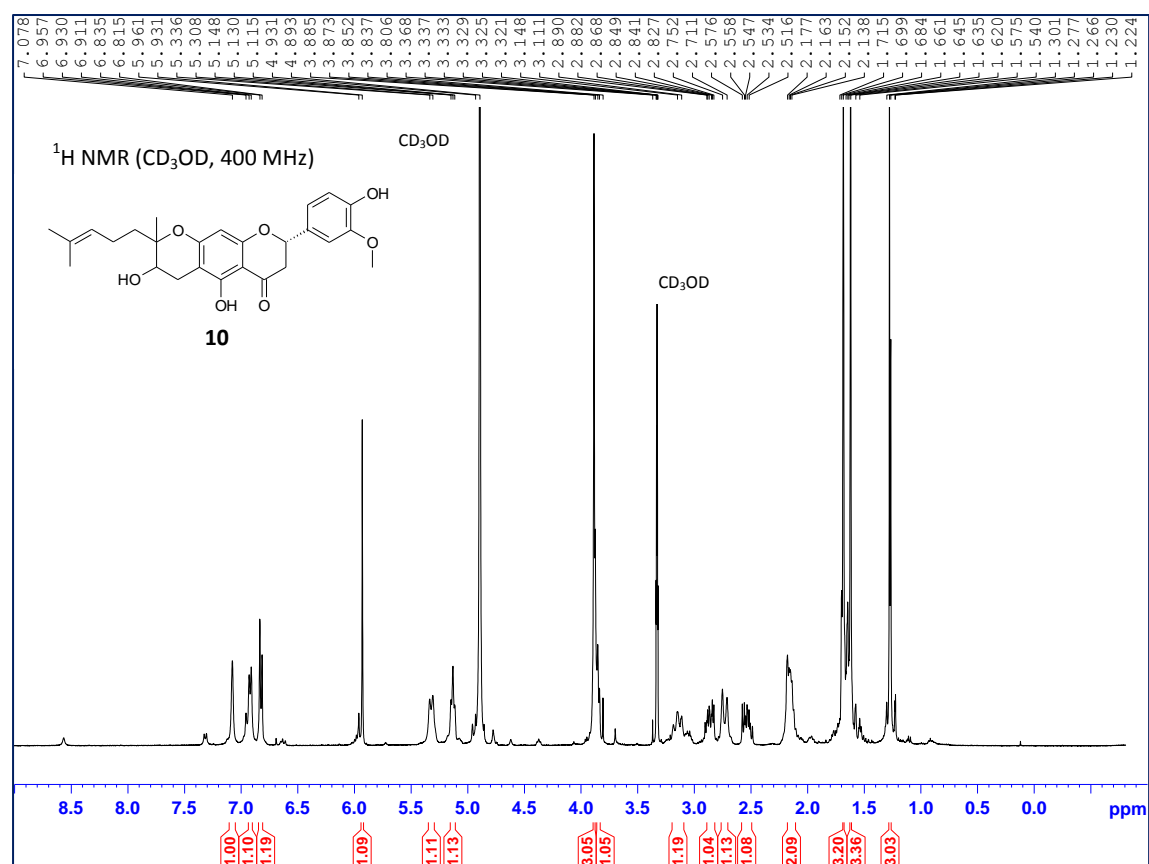


Figure S45. ¹H NMR (400 MHz, MeOD) spectrum of tomentodiplacone L (10)

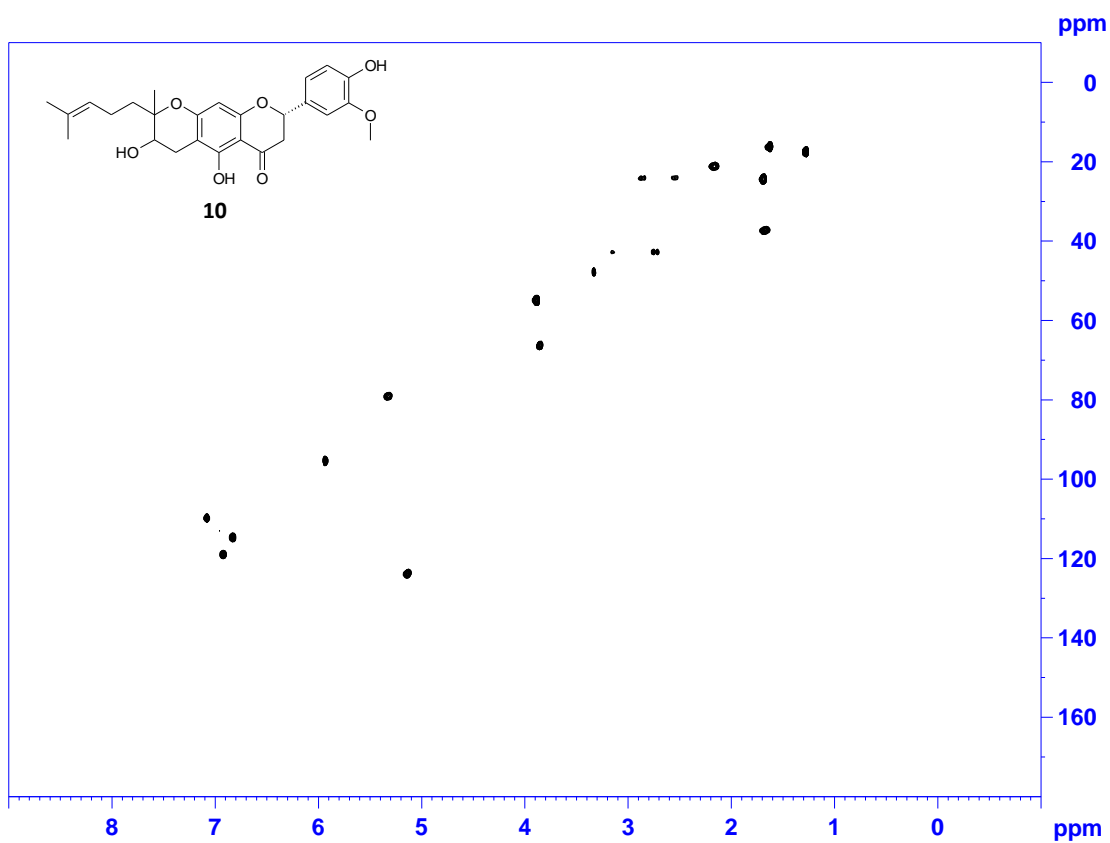


Figure S46. HSQC (400 MHz, MeOD) spectrum of tomentodiplacone L (**10**)

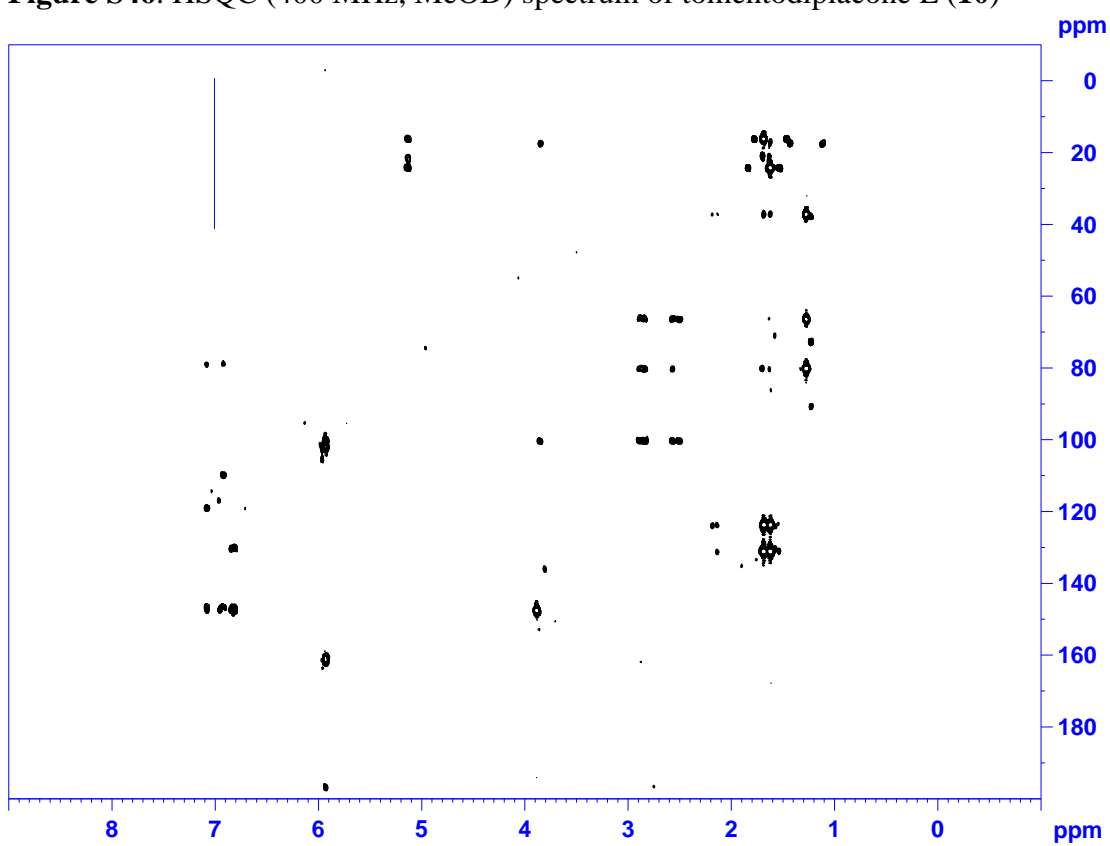


Figure S47. HMBC (400 MHz, MeOD) spectrum of tomentodiplacone L (**10**)

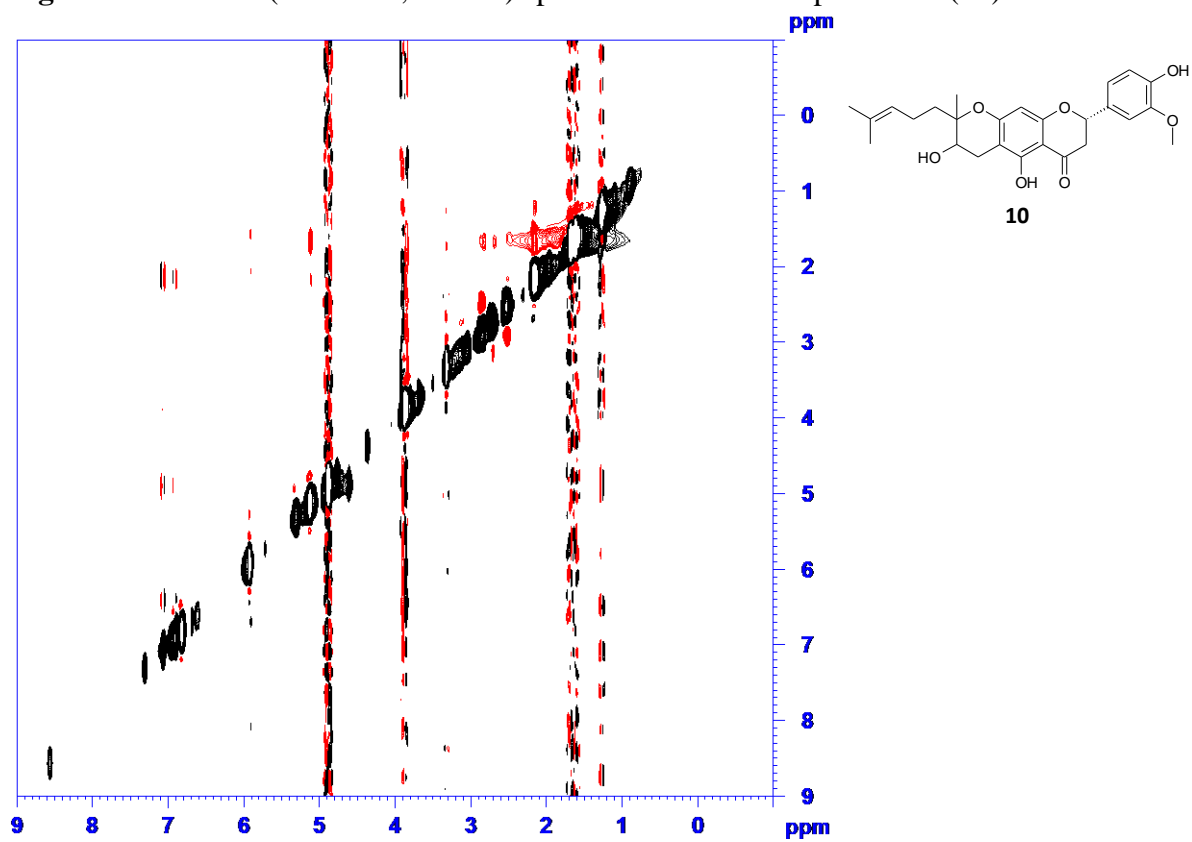
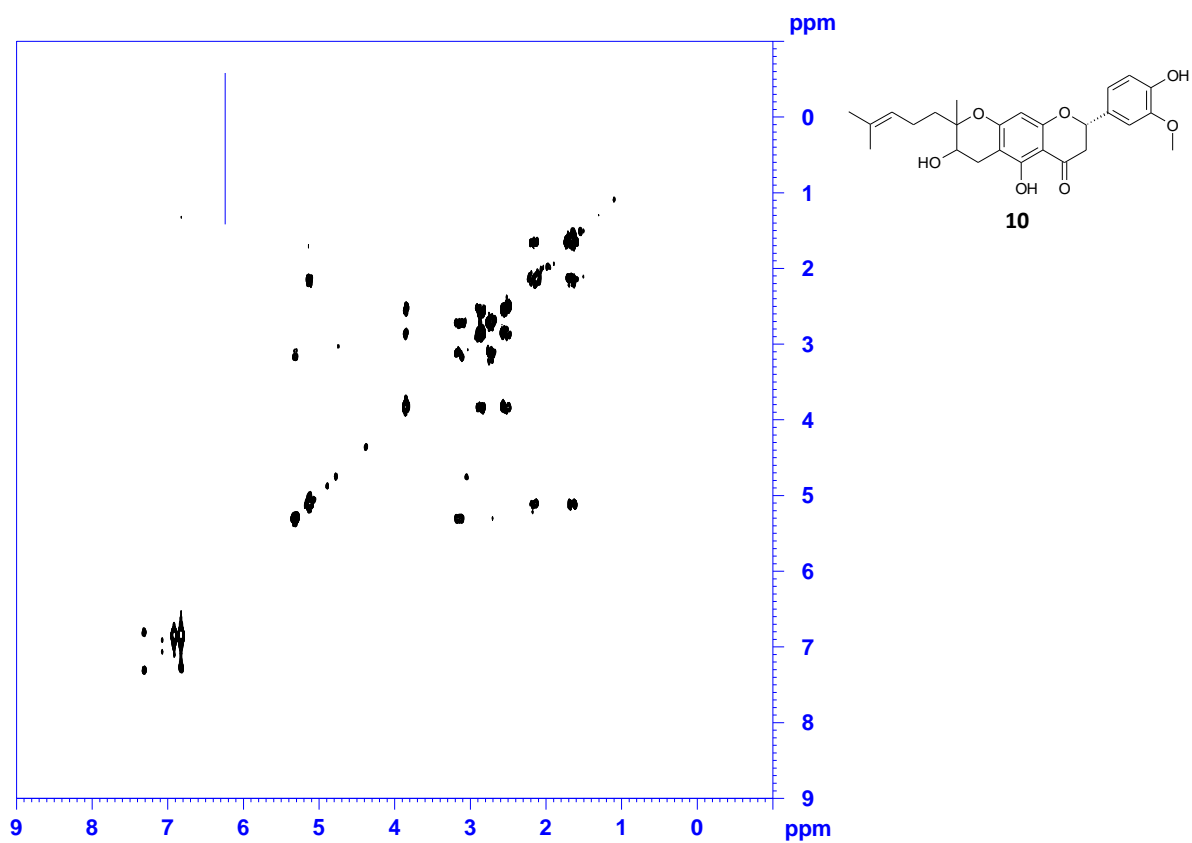


Figure S49. NOESY (400 MHz, MeOD) spectrum of tomentodiplacone L (10)

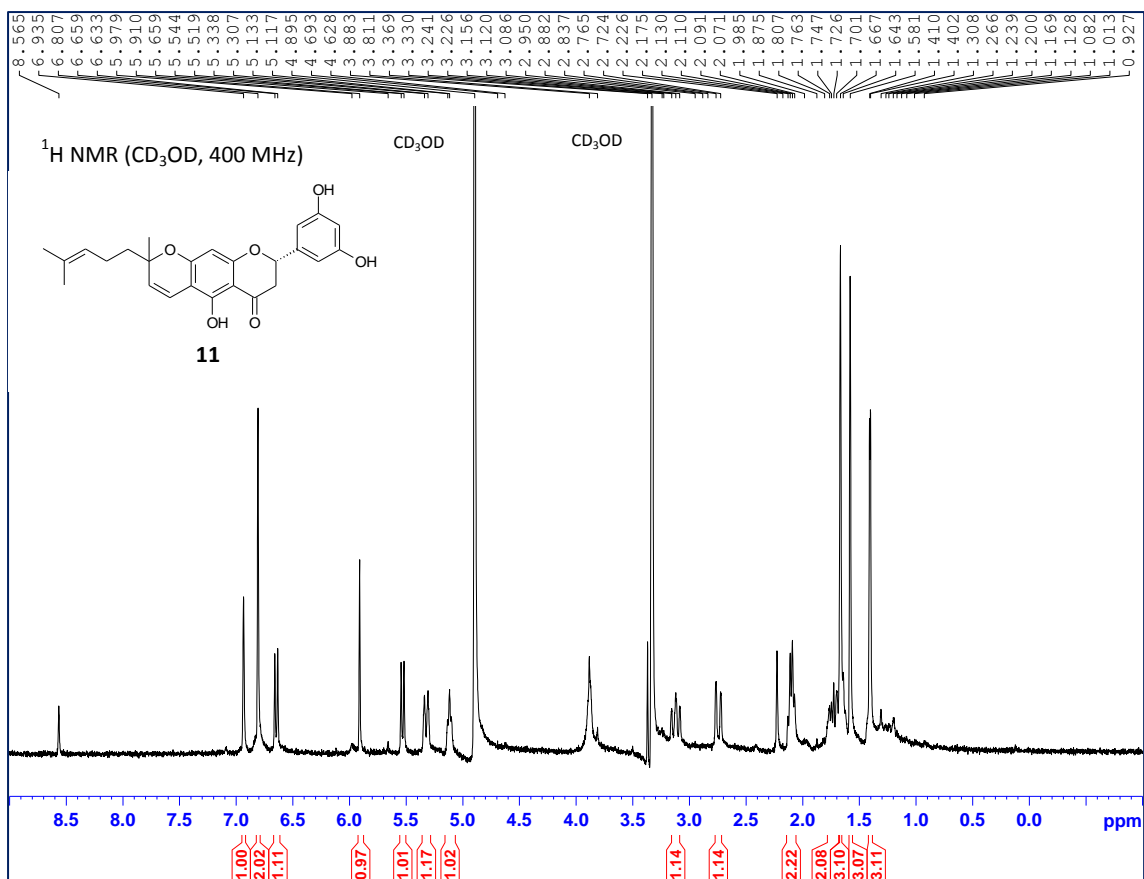


Figure S50. ¹H NMR (400 MHz, MeOD) spectrum of tomentone (**11**)

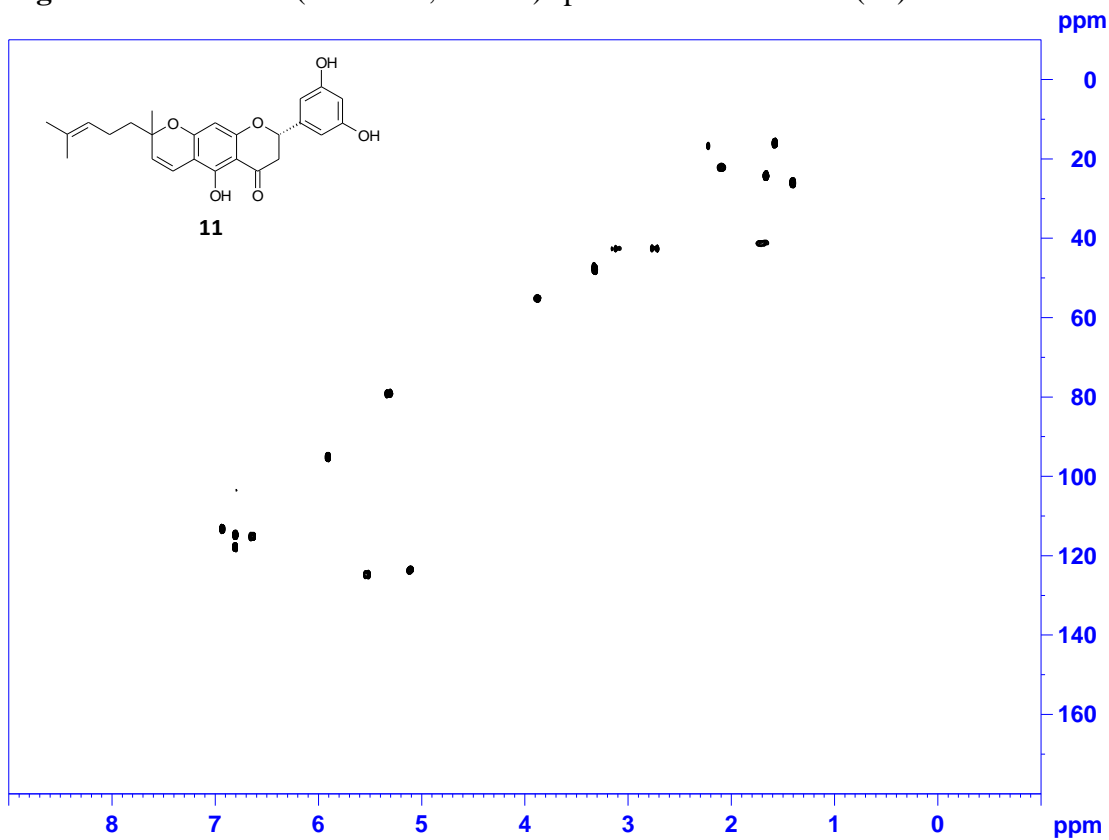


Figure S51. HSQC (400 MHz, MeOD) spectrum of tomentone (**11**)

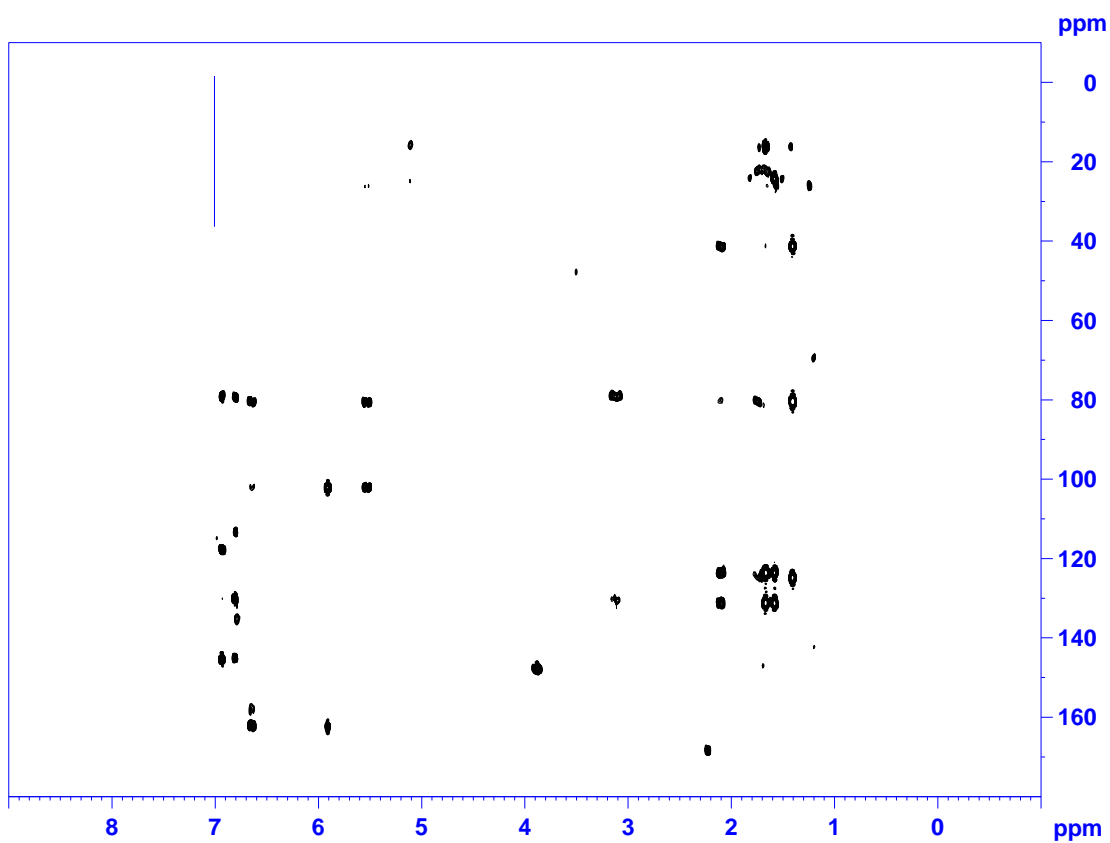


Figure S52. HMBC (400 MHz, MeOD) spectrum of tomentone (**11**)

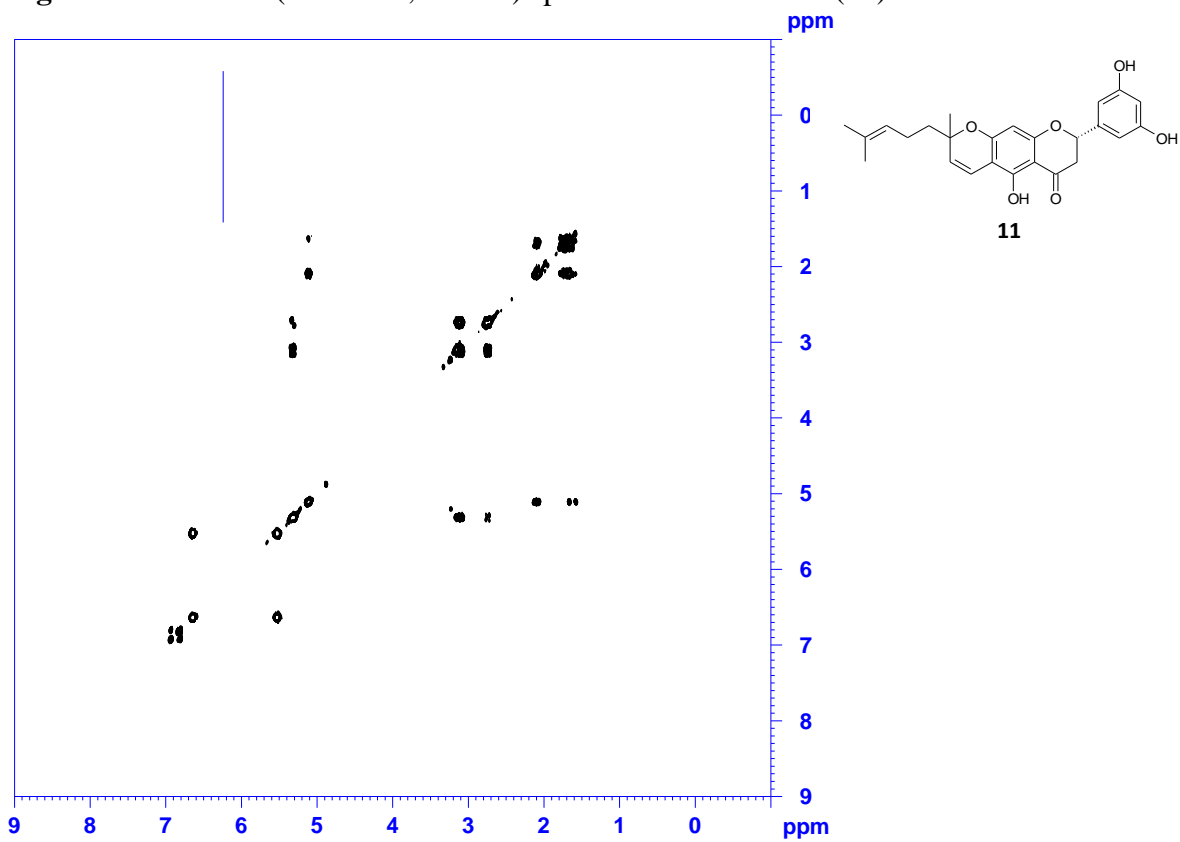


Figure S53. COSY (400 MHz, MeOD) spectrum of tomentone (**11**)

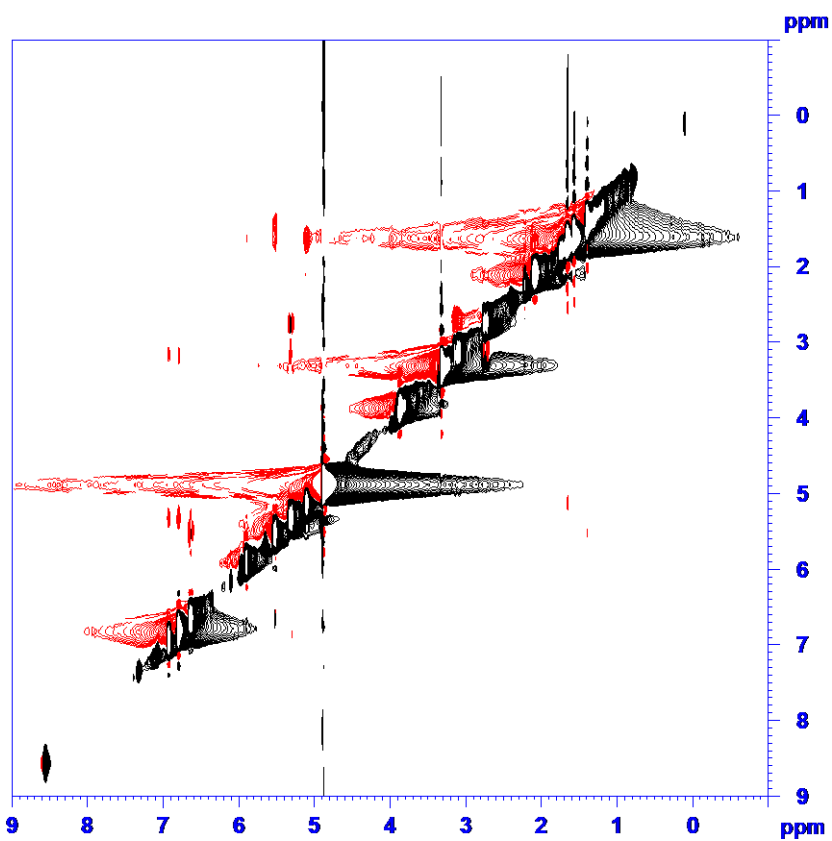


Figure S54. NOESY (400 MHz, MeOD) spectrum of tomentone (**11**)

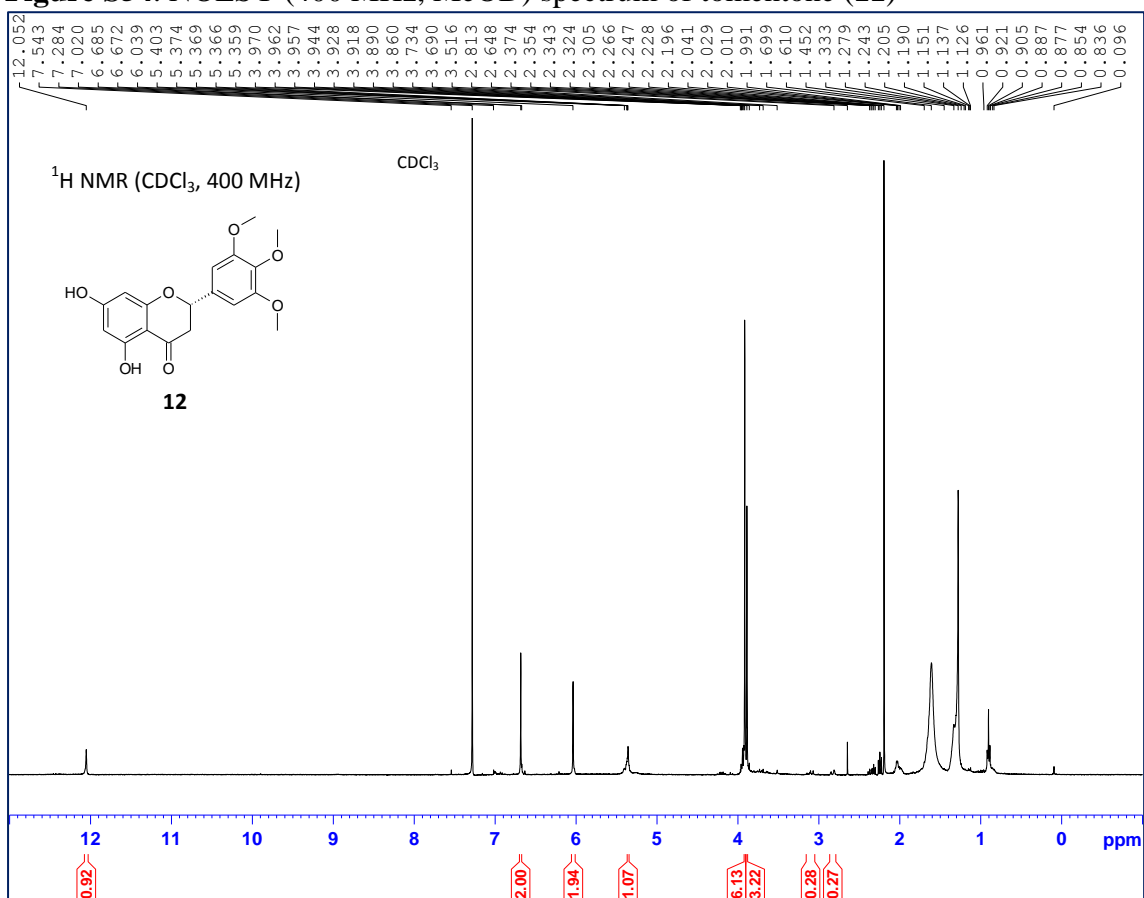
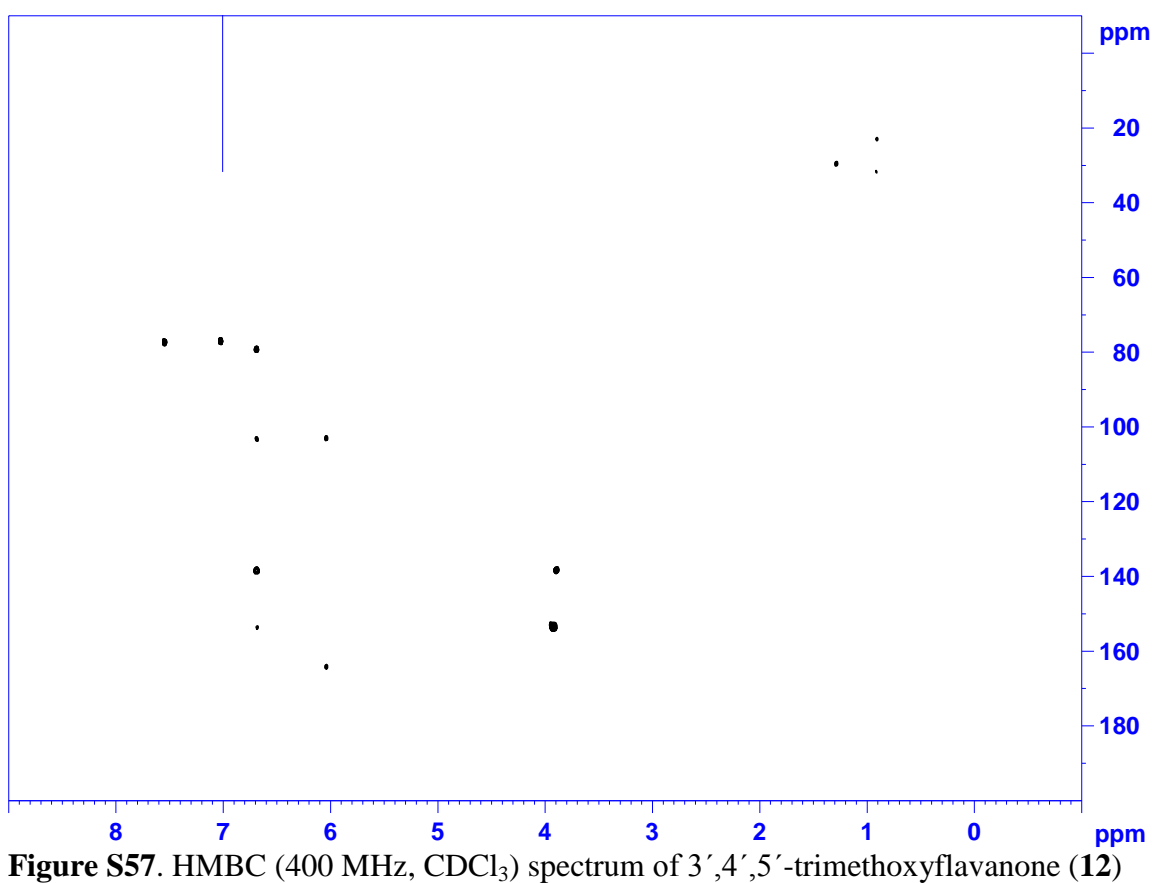
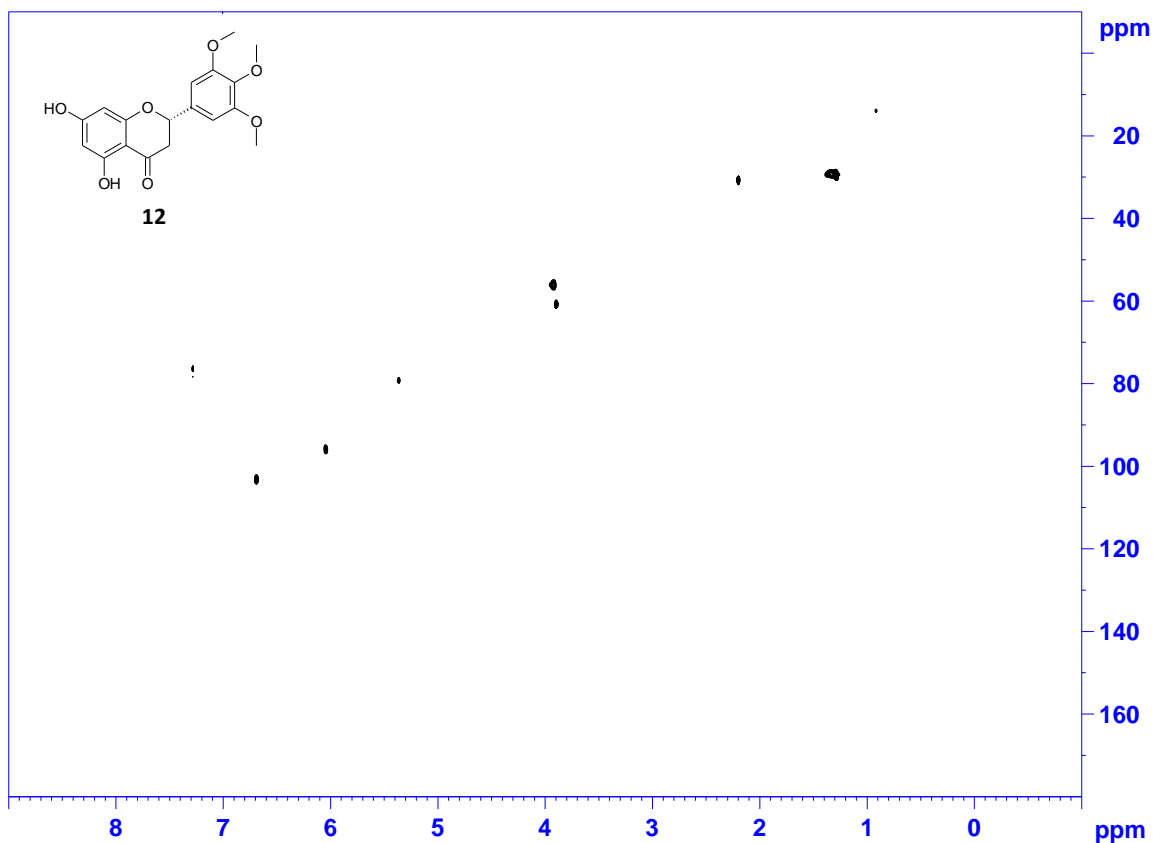


Figure S55. $^1\text{H NMR}$ (400 MHz, CDCl_3) spectrum of 3',4',5'-trimethoxyflavanone (**12**)



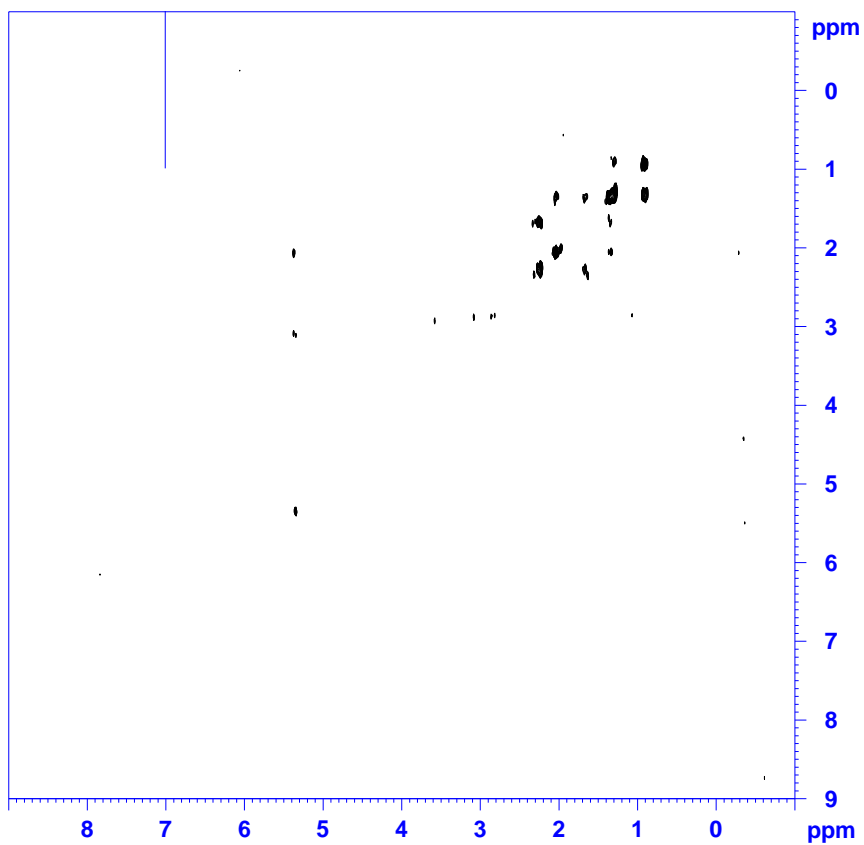


Figure S58. COSY (400 MHz, CDCl_3) spectrum of 3',4',5'-trimethoxyflavanone (**12**)

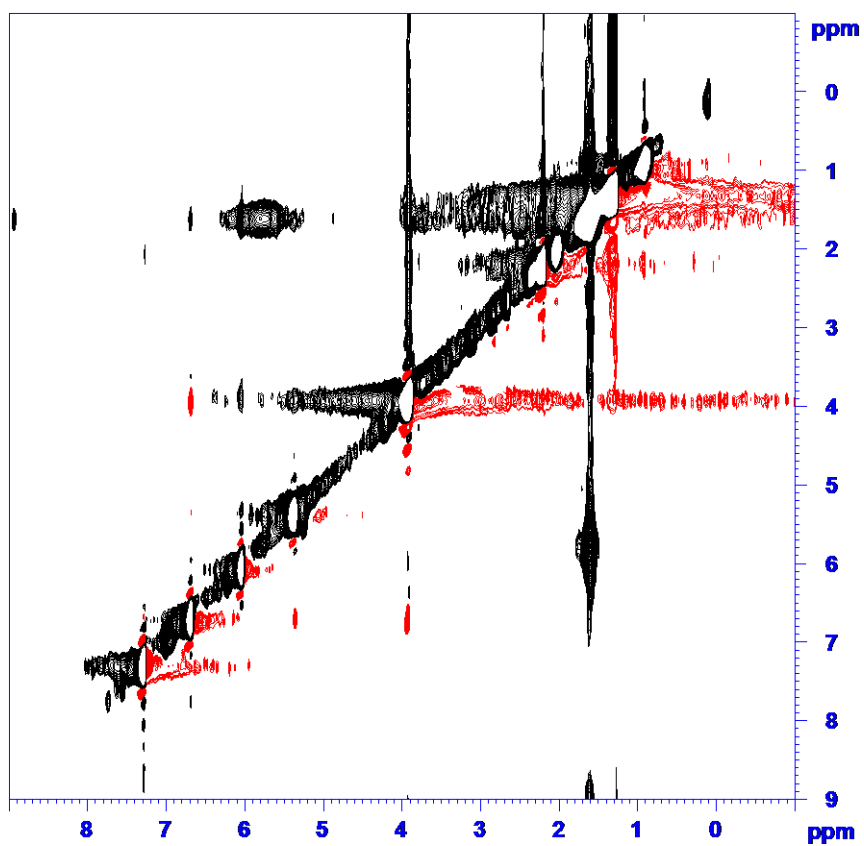


Figure S59. NOESY (400 MHz, CDCl_3) spectrum of 3',4',5'-trimethoxyflavanone (**12**)

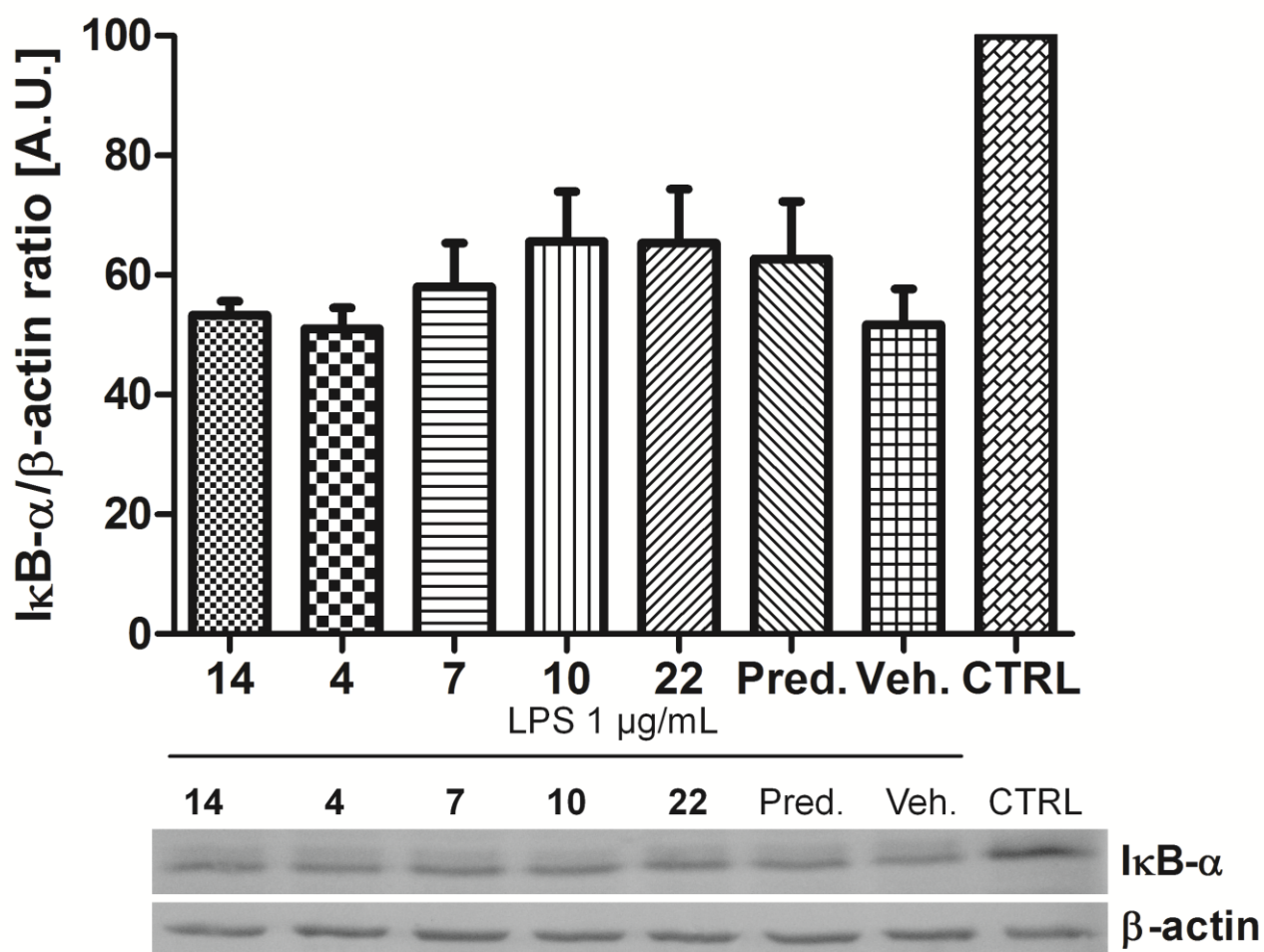


Figure S60. The influence of selected flavanones on the degradation of IκB-α. THP-1 macrophages were pre-treated with compounds **4**, **7**, **10**, **14**, **22**, and prednisone (Pred.) at a concentration of 2 μM or with DMSO only (Veh. and CTRL) for 1 h. Subsequently, LPS (1 μg/mL) was added to trigger the IκB-α degradation. After 30 min, the cells were collected and the amounts of IκB-α and β-actin were detected by Western blot analysis. The intensity of the digested bands was analysed by densitometric analysis. The blots show results representative of three independent experiments. The results are expressed as means ± S.E. for three independent experiments.

Table S1. IC₅₀ values for compounds **1–25**

	IC50
1	6.7 ± 0.1 μM
2	6.5 ± 0.1 μM
3	61% *
4	6.4 ± 0.2 μM
5	26.9 ± 0.8 μM
6	18.0 ± 0.7 μM
7	11.4 ± 0.2 μM
8	84% *
9	87% *
10	6.7 ± 0.1 μM
11	16.0 ± 0.6 μM
12	78% *
13	8.0 ± 0.2 μM
14	7.1 ± 0.1 μM
15	18.6 ± 0.4 μM
16	98% *
17	> 20 μM ^a
18	18.6 ± 0.4 μM
19	6.6 ± 0.6 μM
20	16.4 ± 0.2 μM
21	7.9 ± 0.2 μM
22	> 20 μM ^b
23	7.2 ± 0.5 μM
24	71% *
25	78% *

* viability at 30 μM

^a - DOI: 10.1111/j.1476-5381.2010.01171.x

^b - DOI: 10.1021/np070063w