Supporting Information for

# Stereoselective Glycoconjugation of Steroids with Selenocarbohydrates

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## Summary

## 1. Starting Materials NMR Spectra

### 1.1. Synthesis of acetonide protected carbohydrate diselenides

The carbohydrate diselenides were synthesized according to previously optimized methodologies.[1] Representative compound synthesis and NMR data are described below:


**Scheme S1. Protected D-mannose diselenide synthesis**

To a solution of D-manose (20 mmol, 3.6 g) in acetone (20 mL) and metanol (15 mL) HCl (37%, 0.34 mL) was added. The solution was stirred under reflux for 16 h. After cooling, the mixture was neutralized with pyridine and partitioned in ethyl acetate and an aqueous solution of copper sulfate, yielding the crude *bis*-acetonide, which was then dissolved in acetic acid 60% (50 mL) and stirred for 16 h at room temperature. The solvent was then removed by azeotropic distillation using water/toluene to afford the corresponding diol as a colourless oil in 60% yield.

To a solution of the diol (3 mmol, 0.70 g) in dry dichlorometane (12 mL), pyridine (3.3 mmol) and tosyl chloride (3.3 mmol, 0.63 g) were added at 0ºC, under argon atmosphere. The mixture was stirred at 0 ºC for 16 h. After this time, the reaction was extracted with saturated ammonium chloride solution and dichloromethane. The combined organic layers were dried over $MgSO_4$, filtered and evaporated yielding the crude product. Purification by flash chromatography using hexanes/ethyl acetate (50:50) afforded the tosylate in 50% yield.

To a suspension of selenium (3 mmol, 0.23 g) in ethanol (6 mL), under argon, $NaBH_4$ (2 mmol, 76 mg) was added and the resulting solution refluxed for 1h. After this time, the D-mannose tosylate (2 mmol) was added in a single portion and the mixture refluxed for 24 h. After this time, the reaction was extracted with saturated solution of

[1](a) H. C. Braga, H. A. Stefani, M. W. Paixão, F. W. Santos, D. S. Lüdtke.*Tetrahedron,* 2010, **66**, 3441. (b) H. C. Braga, A. D. Wouters, F. B. Zerillo, D. S. Lüdtke, *Carbohydrate Research,* 2010, **345**, 2328. (c) R. F. Affeldt, H. C. Braga, L. L. Baldassari and D. S. Lüdtke, *Tetrahedron*, 2012, **68**, 10470.

ammonium chloride (20 mL) and dichloromethane (3x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated yielding the crude product. Purification by flash chromatography using hexanes/ethyl acetate afforded the diselenide in 72% yield

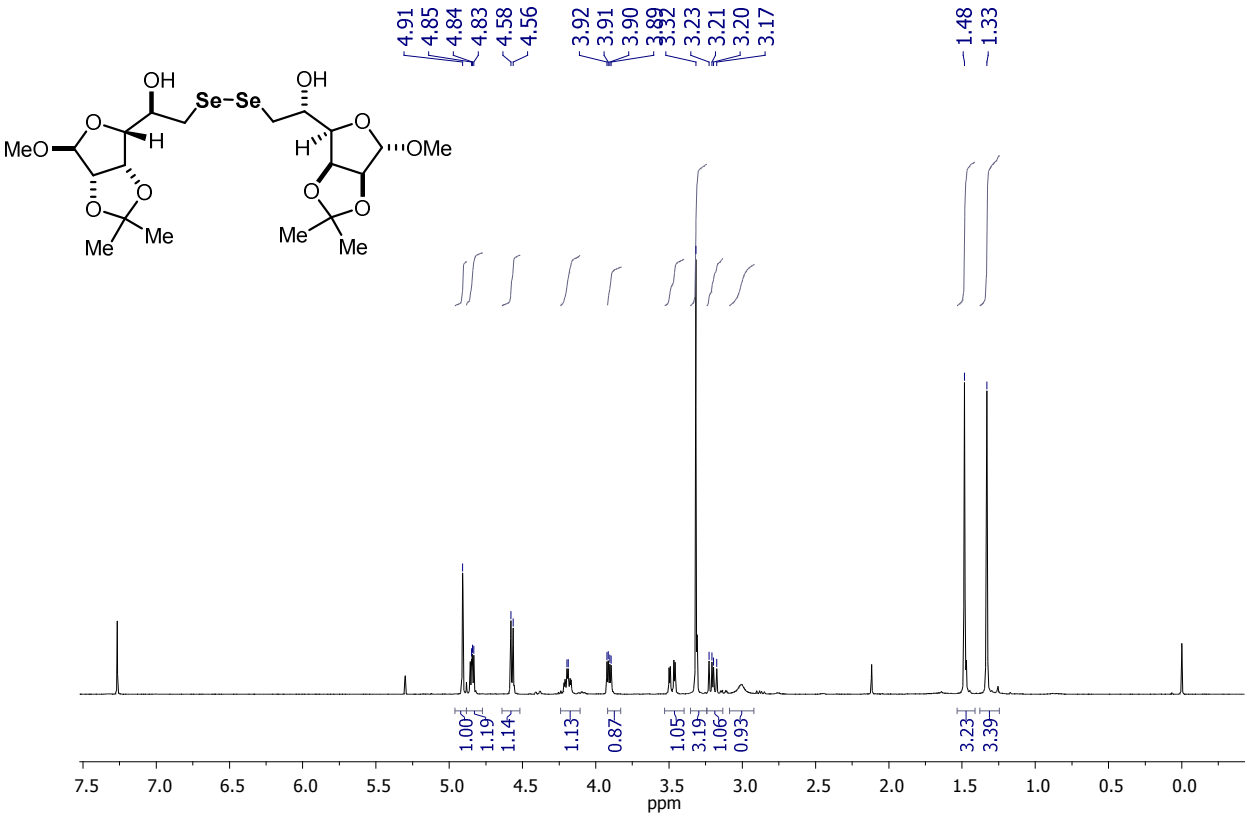


**Figure S1. $^{1}$H NMR (400 MHz, $CDCl_3$) of protected D-mannose diselenide**

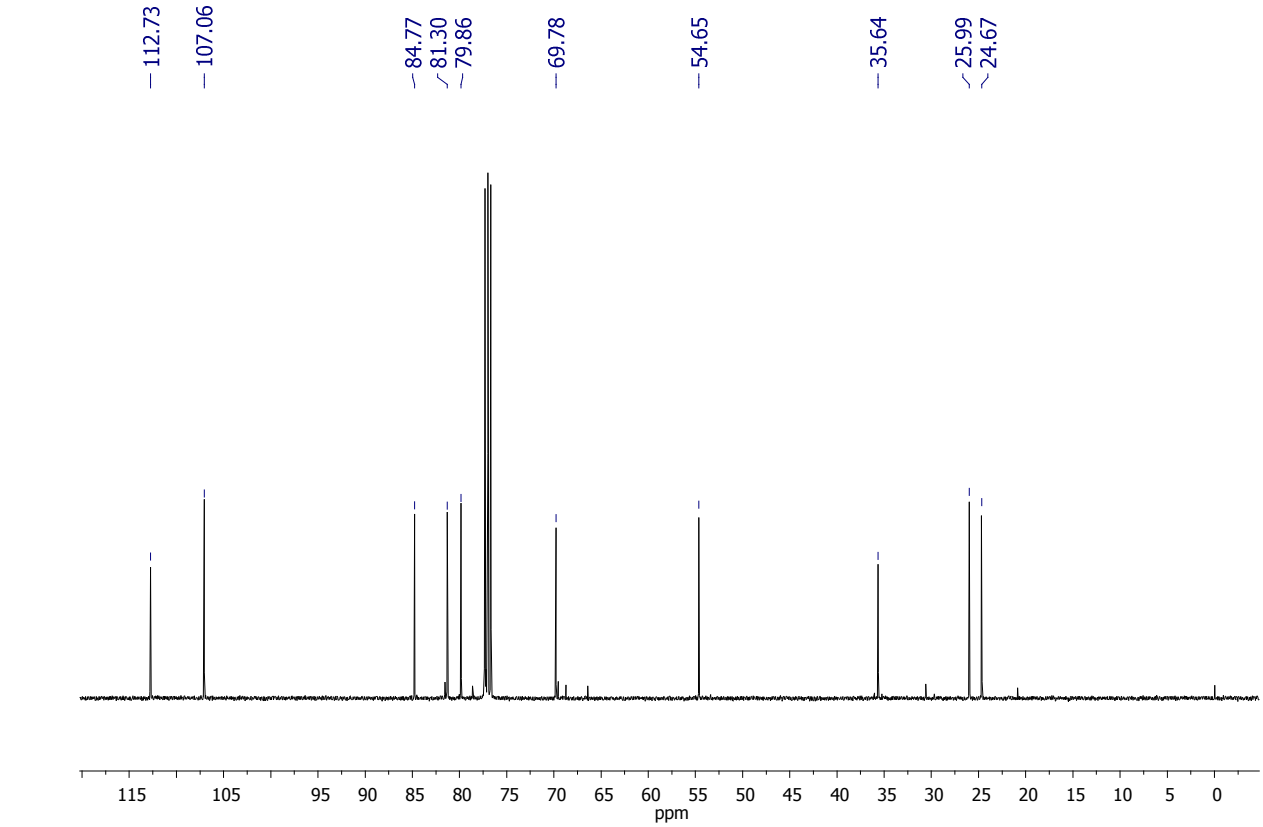


**Figure S2. $^{13}$C NMR (101 MHz, $CDCl_3$) of protected D-mannose diselenide**

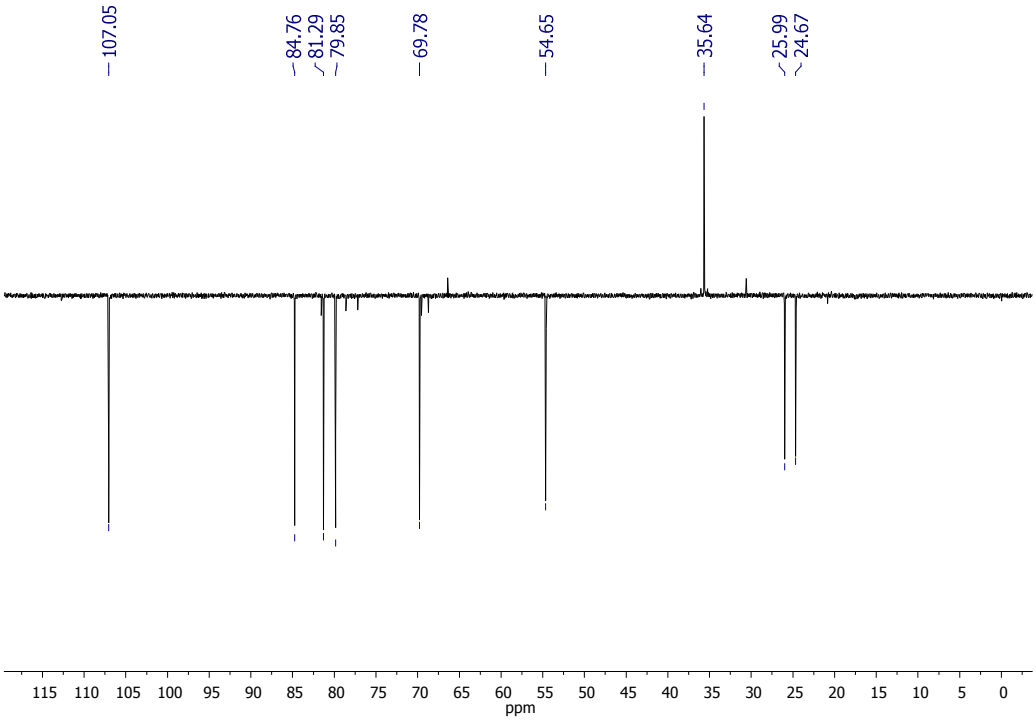


**Figure S3. $^{13}C$ DEPT-135 NMR(101 MHz, $CDCl_3$) of protected D-mannose diselenide**

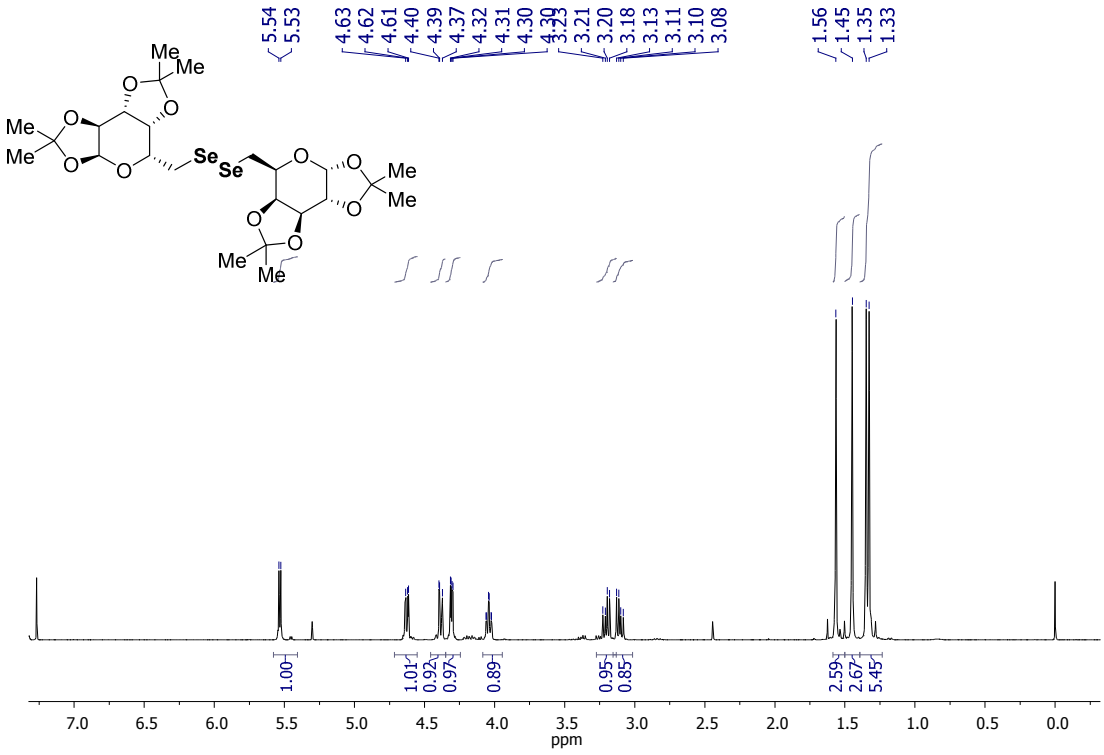


**Figure S4. $^{1}H$ NMR (400 MHz, $CDCl_3$) of protected D-galactose diselenide (5)**

## 1.2. NMR Spectra of steroid starting materials

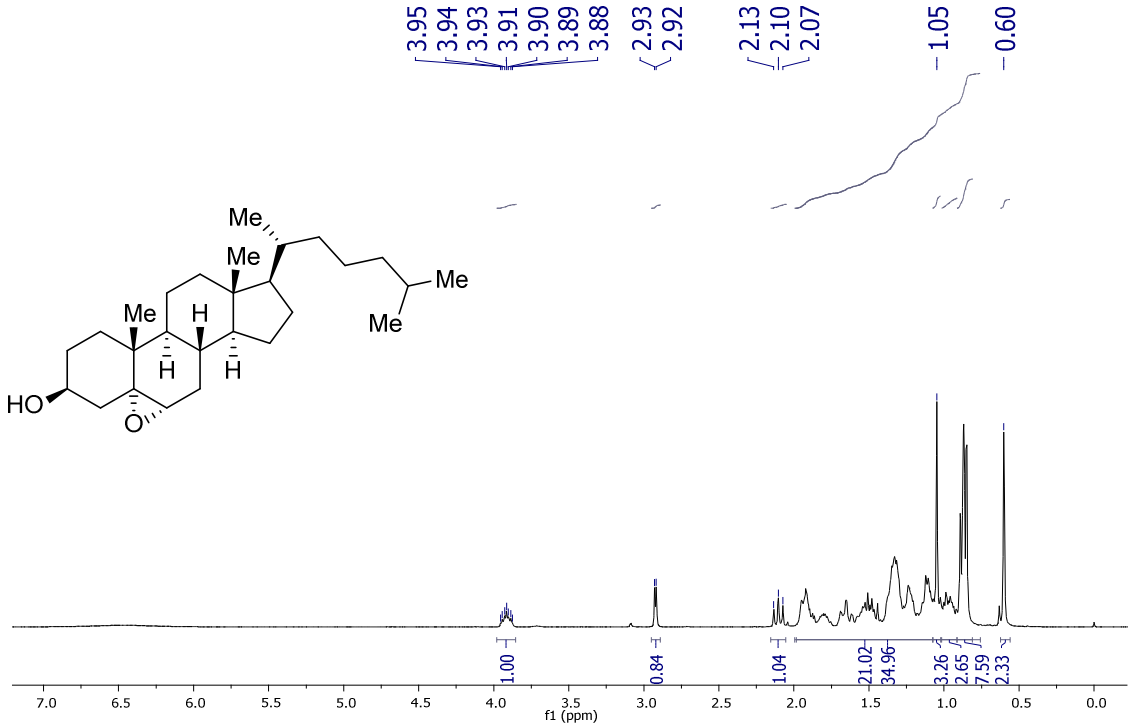


**Figure S5. $^{1}$H NMR (400 MHz, $CDCl_3$) of cholesterol 5,6α-epoxide (1a)**

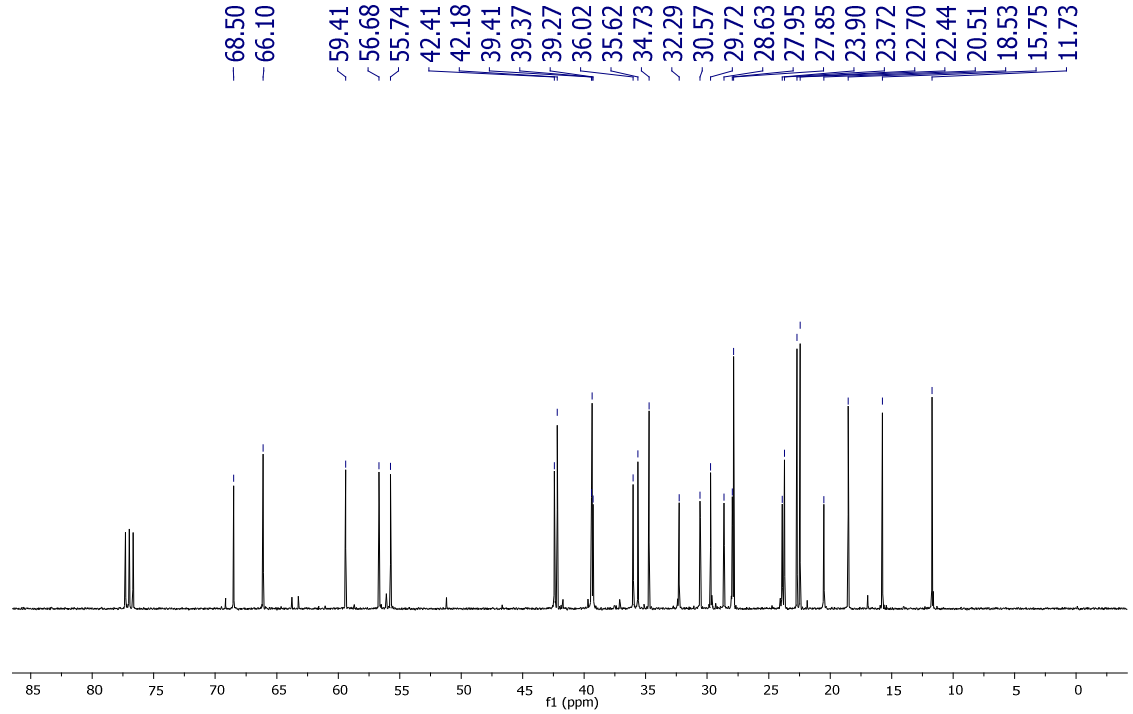


**Figure S6. $^{13}$C NMR (101 MHz, $CDCl_3$) of cholesterol 5,6α-epoxide (1a)**

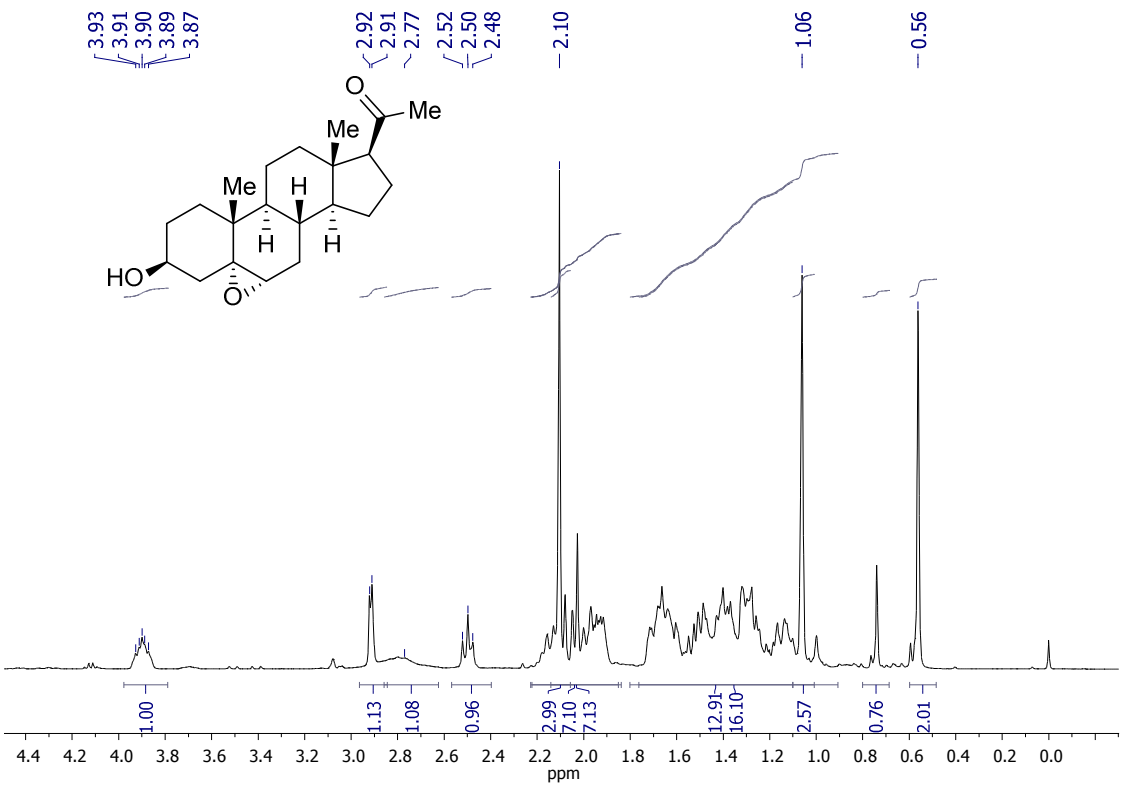


**Figure S7. $^{1}$H NMR (400 MHz, $CDCl_3$) of pregnenolone 5,6α-epoxide (10)**

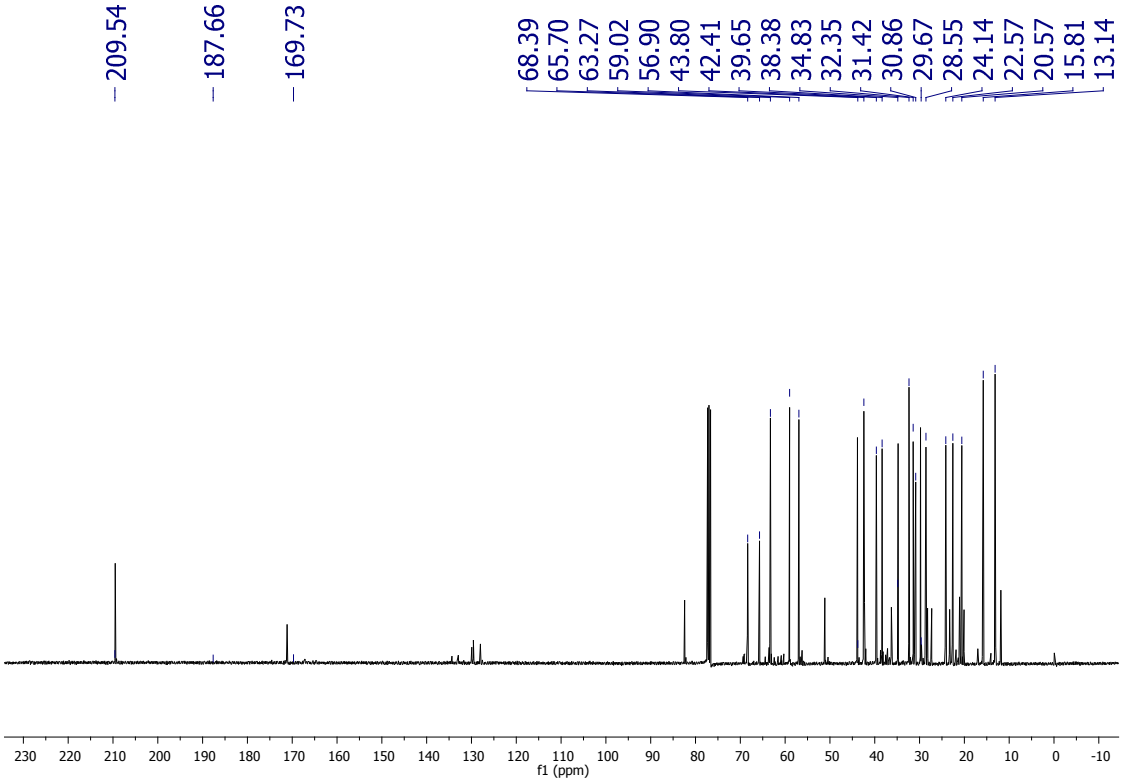


**Figure S8. $^{13}$C NMR (101 MHz, $CDCl_3$) of pregnenolone 5,6α-epoxide (10)**

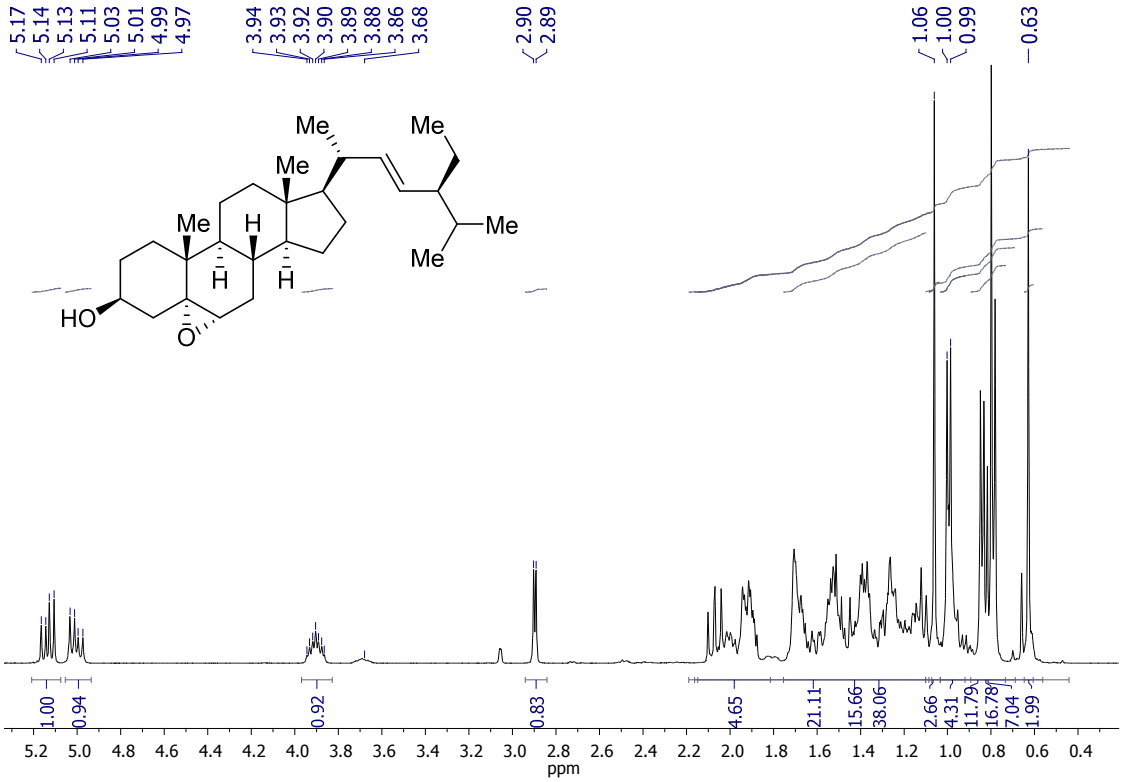


**Figure S9. $^{1}$H NMR (400 MHz, $CDCl_3$) of stigmasterol 5,6α-epoxide (12)**

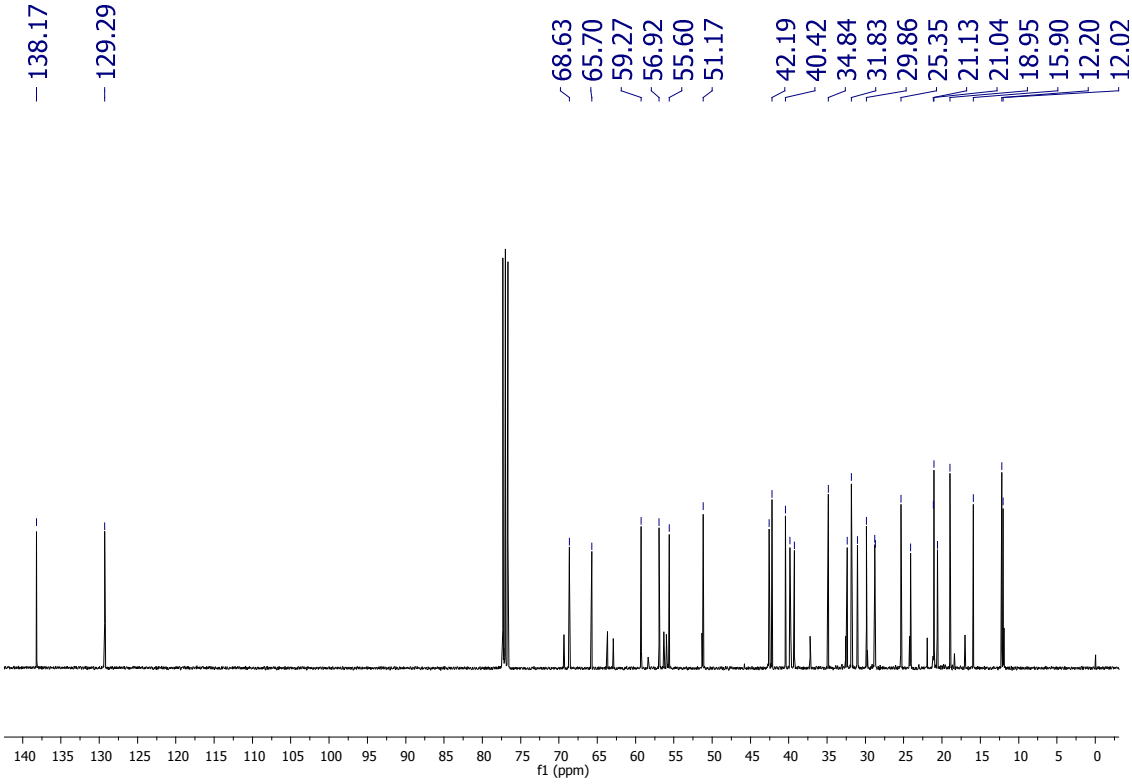


**Figure S9. $^{13}$C NMR (101 MHz, $CDCl_3$) of stigmasterol 5,6α-epoxide (12)**

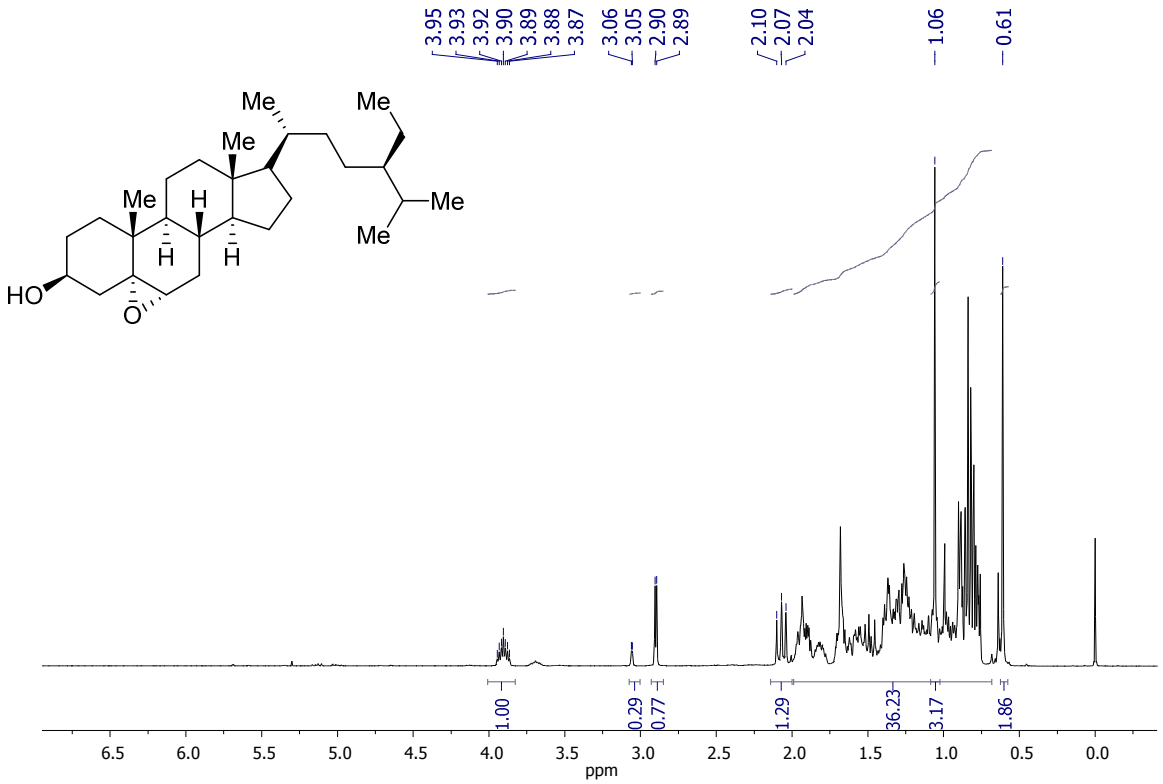


**Figure S10. $^{1}$H NMR (400 MHz, $CDCl_3$) of sitosterol 5,6α-epoxide (13)**

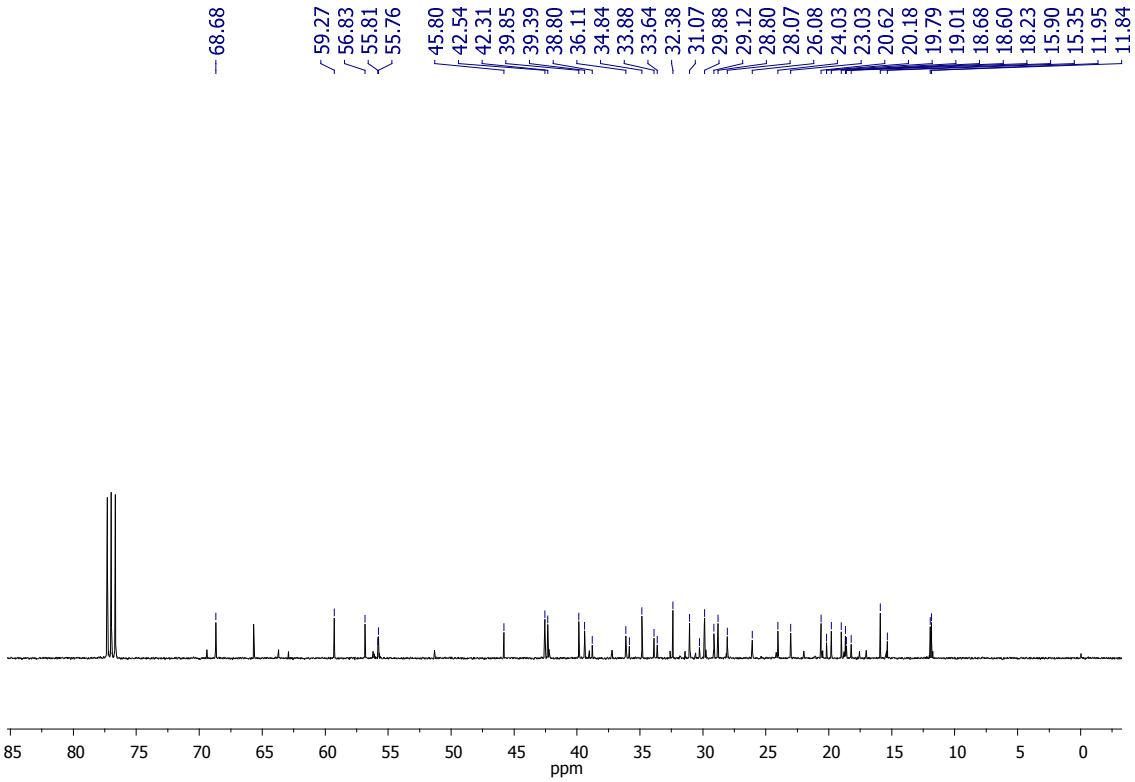


**Figure S11. $^{13}$C NMR (101 MHz, $CDCl_3$) of sitosterol 5,6α-epoxide (13)**

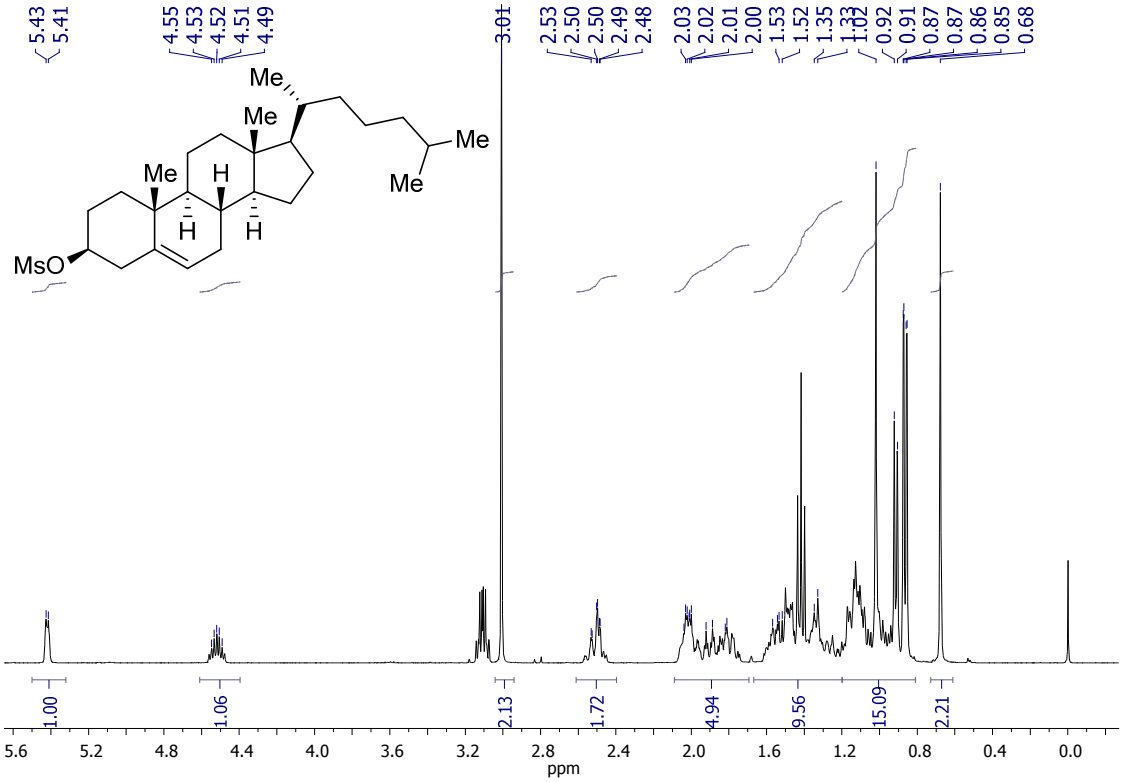


**Figure S12. $^{1}$H NMR (400 MHz, $CDCl_3$) of cholesteryl 3β-mesylate (20)**

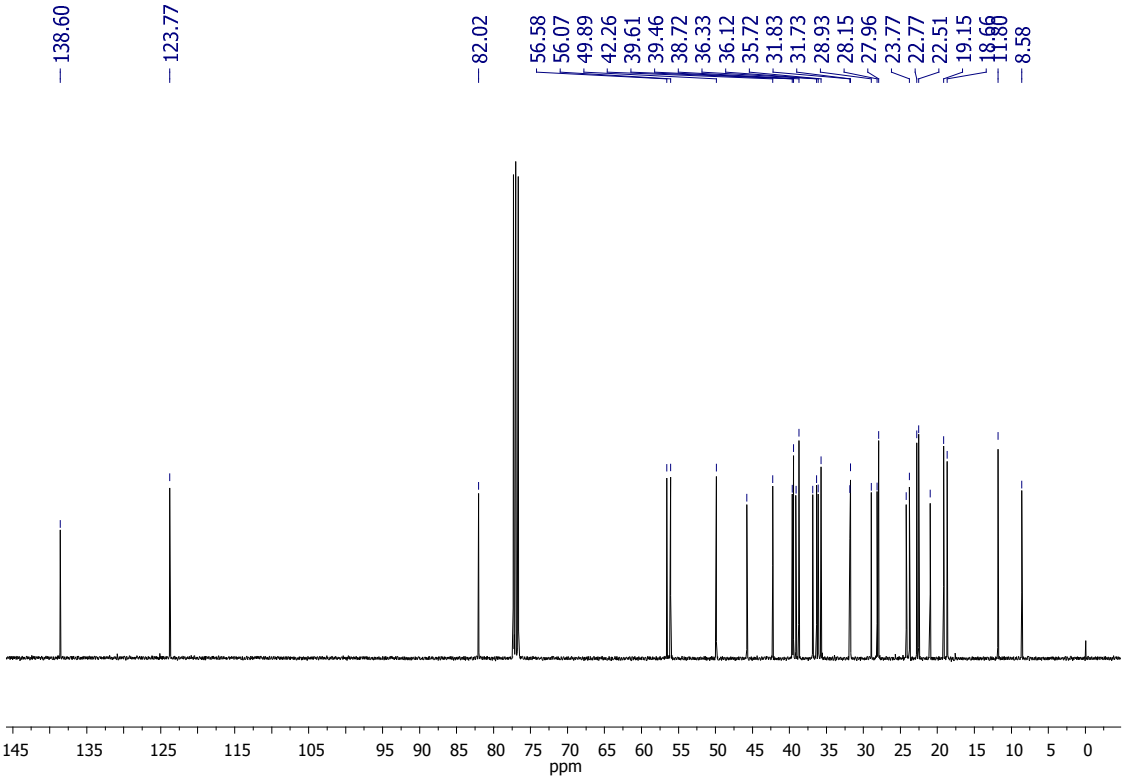


**Figure S13.$^{13}$C NMR (101 MHz, $CDCl_3$) of cholesteryl 3β-mesylate (20)**

## 2. NMR Spectra of Steroidal Selenoglycoconjugates.

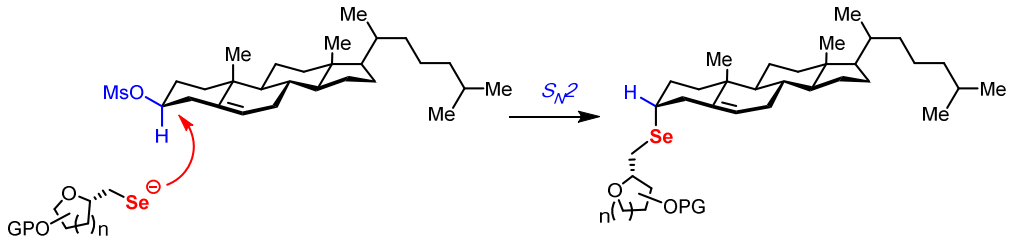


**Figure S14. Nucleophilic substitution at cholesteryl 3β-mesylate (20) with carbohydrate selenolate.**

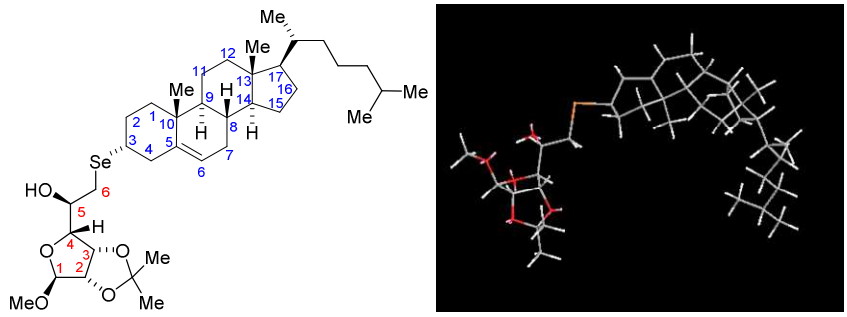


**Figure S15. Product of nucleophilic substitution at cholesteryl 3β-mesylate (20) with D-mannose diselenide derivative (25, atom labeled and 3D structure)**

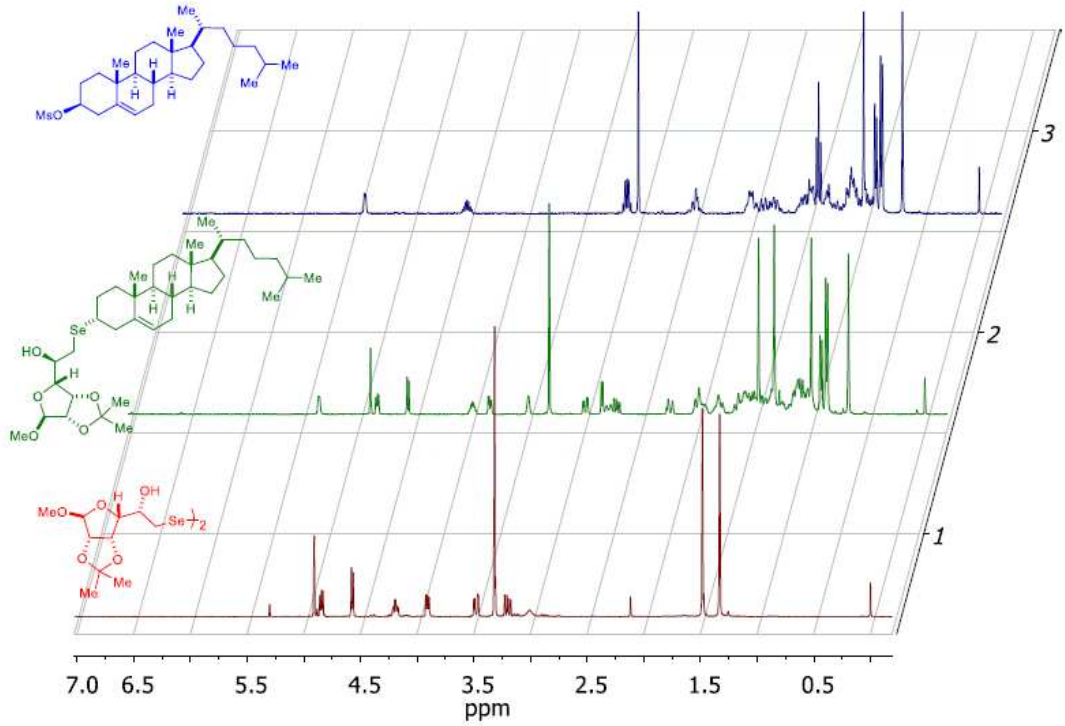


**Figure S16. Overlap of $^{1}H$ NMR (400 MHz, $CDCl_3$) of the glycoconjugated product**

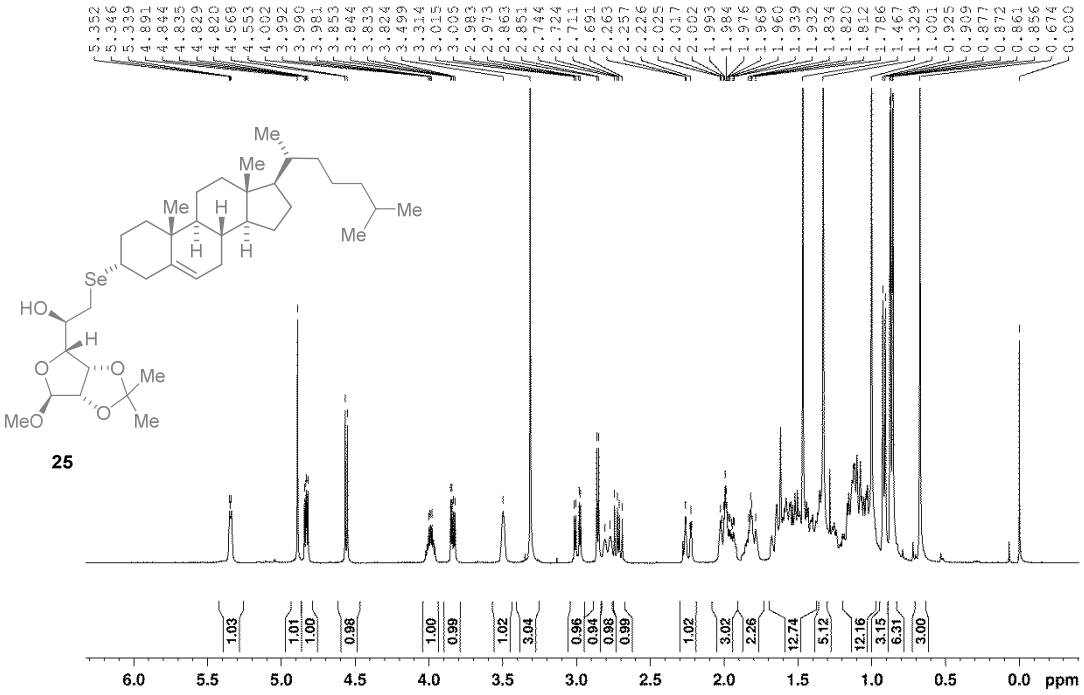


**Figure S17. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 25**

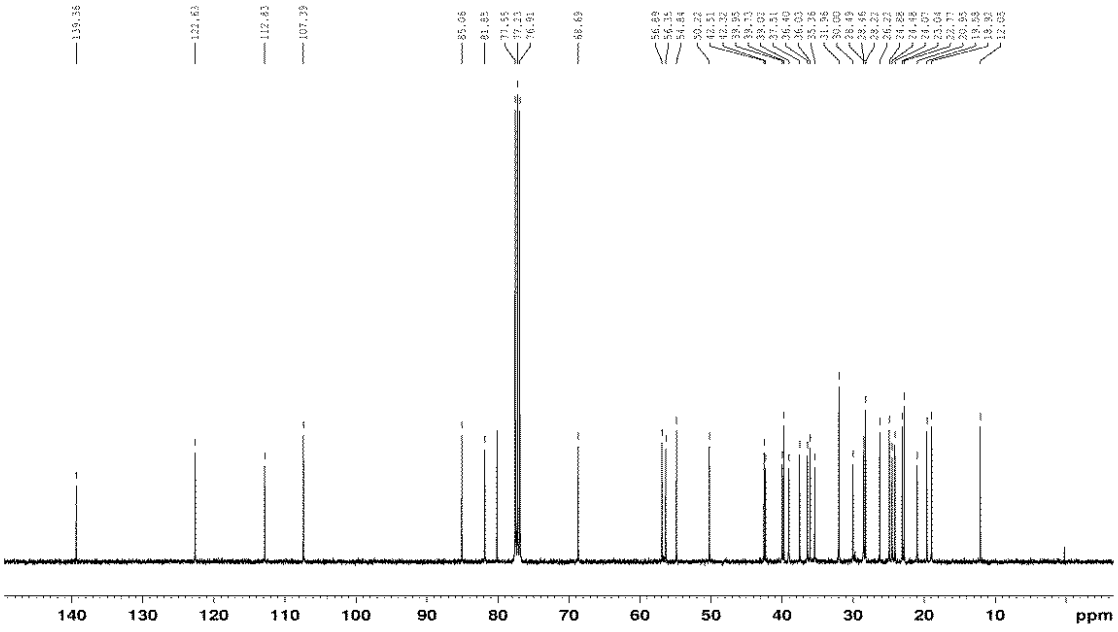


**Figure S18. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 25**

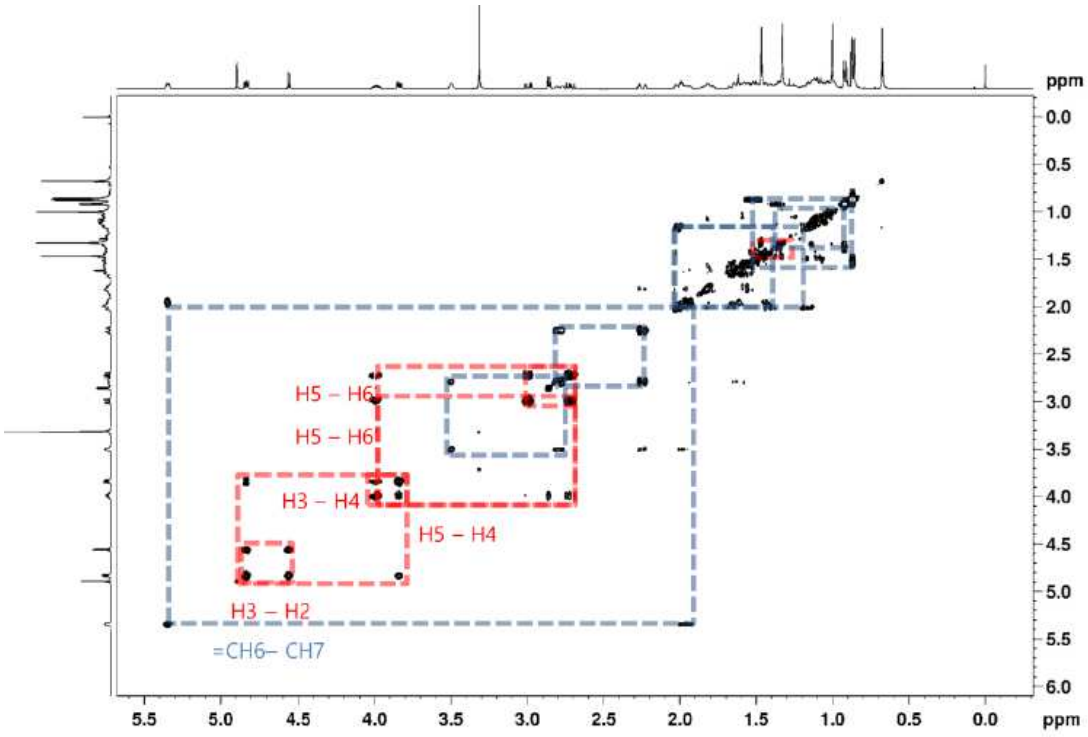


**Figure S19. Contour map of COSY $^{1}$H-$^{1}$H spectra of compound 25. Selected interactions of carbohydrate moiety (red) and steroid moiety hydrogens (blue)**

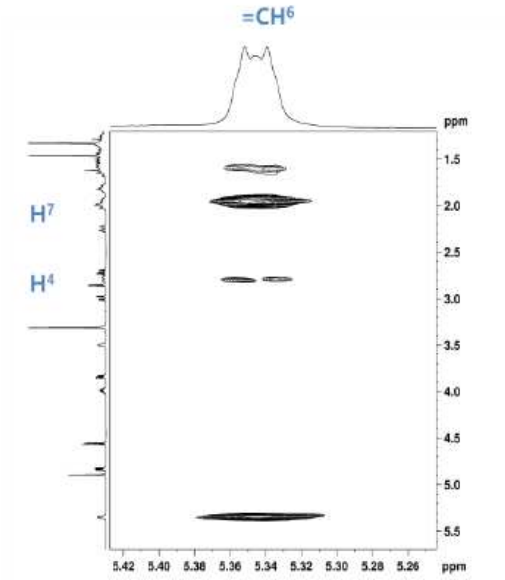


**Figure S20. Expansion of the contour map of COSY $^{1}$H-$^{1}$H spectra of compound 25. Selected interactions of olefin steroid hydrogen H6**

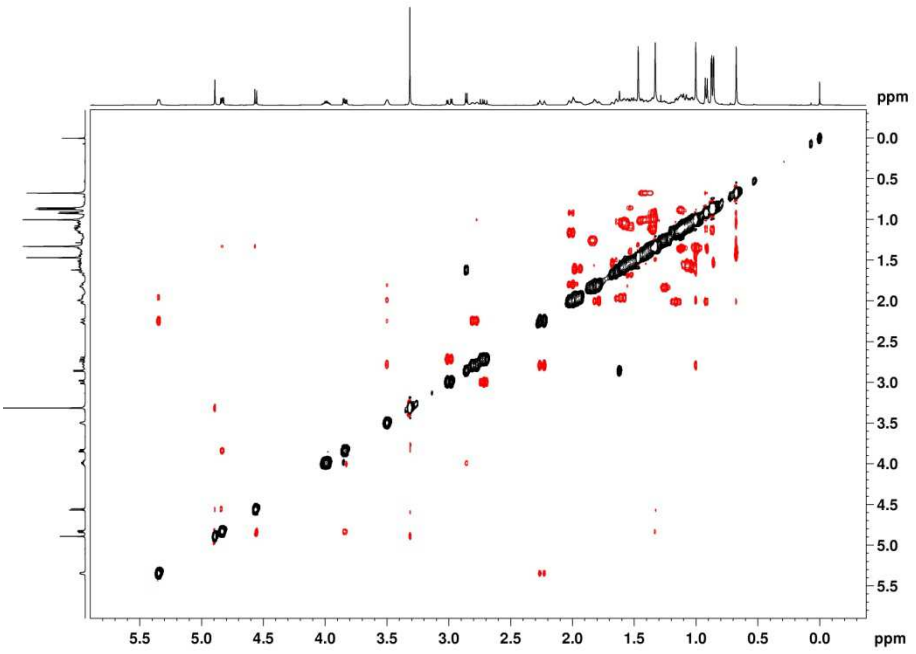


**Figure S21. Contour map of NOESY $^{1}$H-$^{1}$H spectra of compound 25**

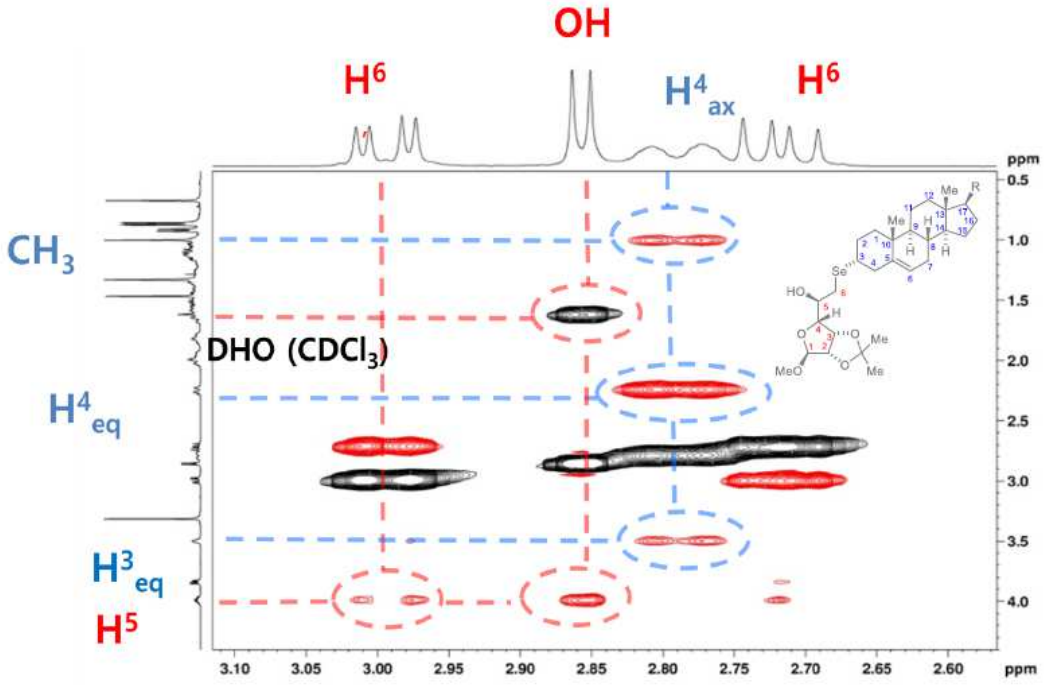


**Figure S22. Expansion of the contour map of NOESY $^{1}$H-$^{1}$H spectra of compound 25. Selected interactions between carbohydrate moiety (red) and steroid moiety hydrogens (blue)**

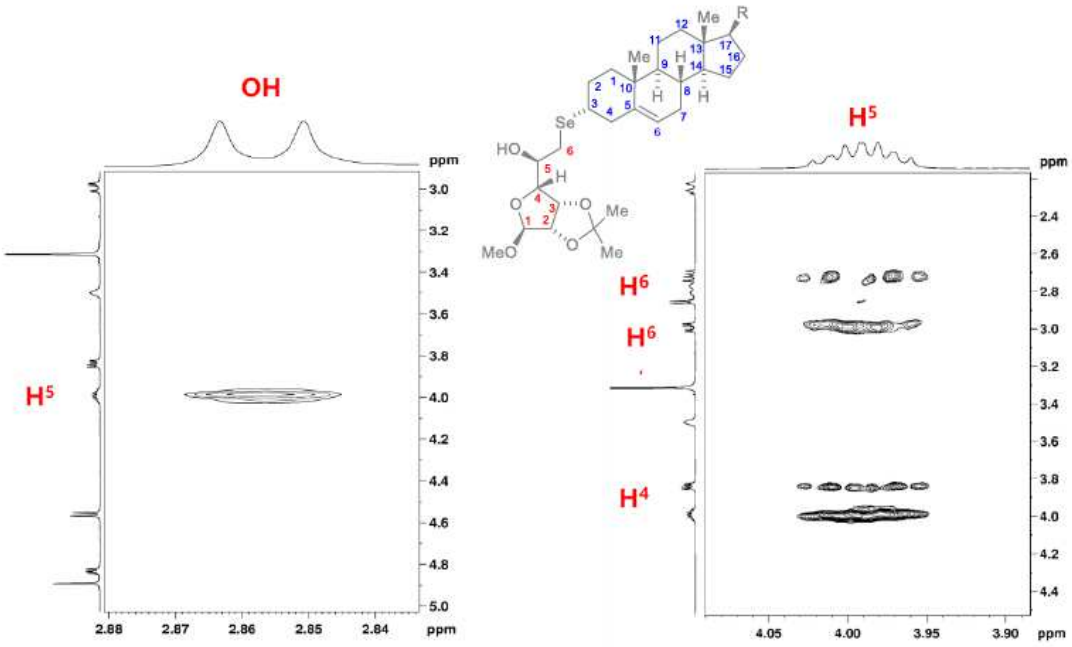


**Figure S23. Expansion of the contour map of NOESY $^{1}$H-$^{1}$H spectra of compound 25. Selected interactions of carbohydrate hydroxyl (left) and H5 (right)**

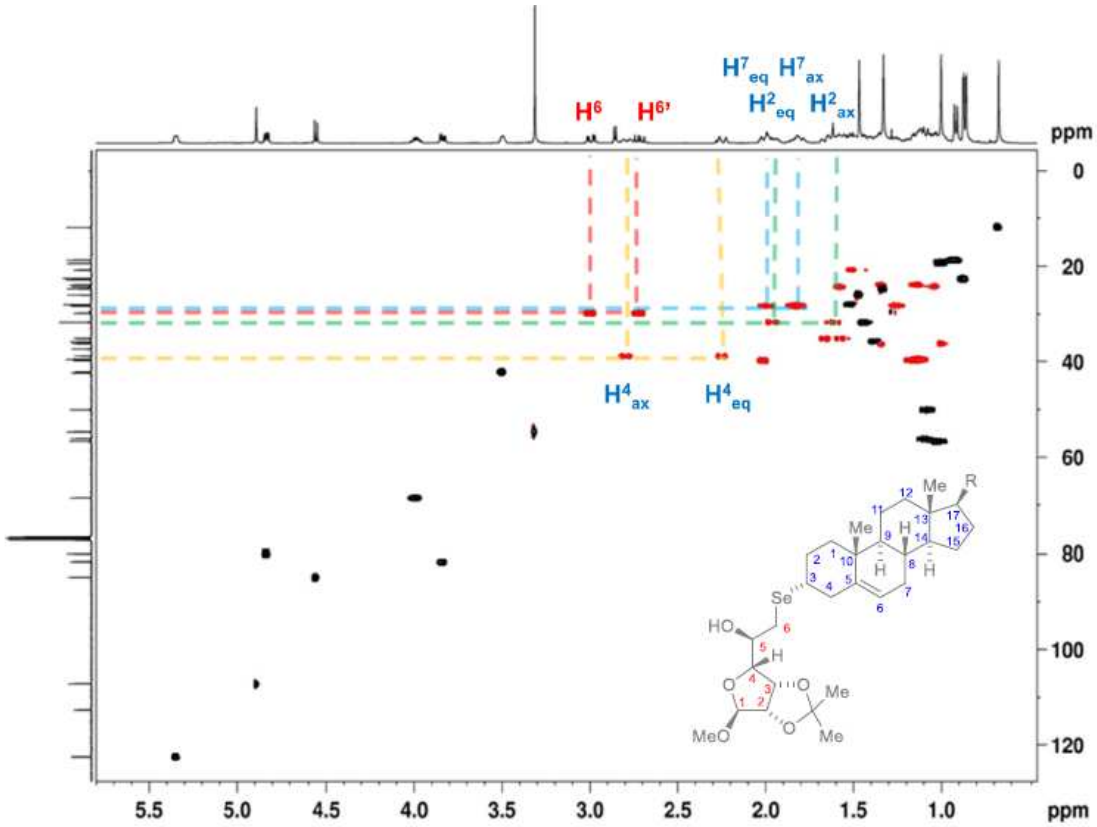


**Figure S24. Contour map of HSQC $^{1}$H-$^{13}$C spectra of compound 25. Selected axial-equatorial hydrogen to carbon attributions**

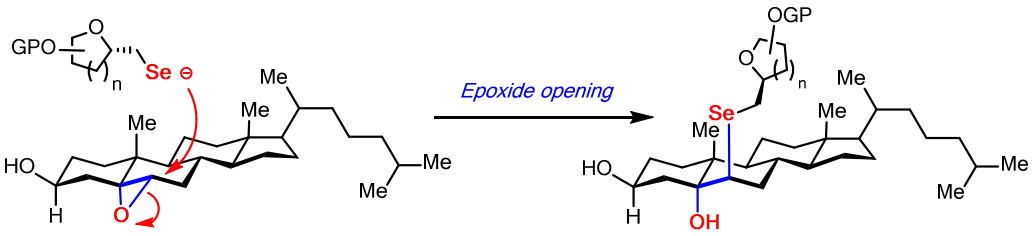


**Figure S25. Nucleophilic *anti*-epoxide opening of cholesterol epoxide (1a) with carbohydrate selenolate.**

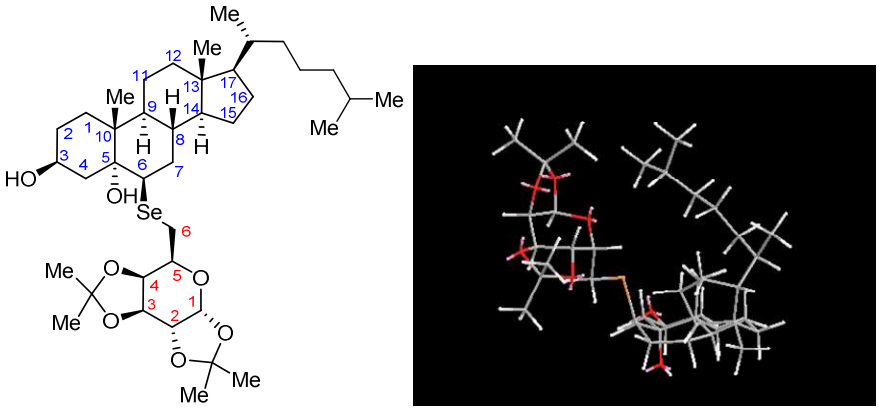


**Figure S26. Product of nucleophilic ring opening of cholesterol epoxide (1a) with D-galactose diselenide derivative (6a, atom labeled and 3D structure)**

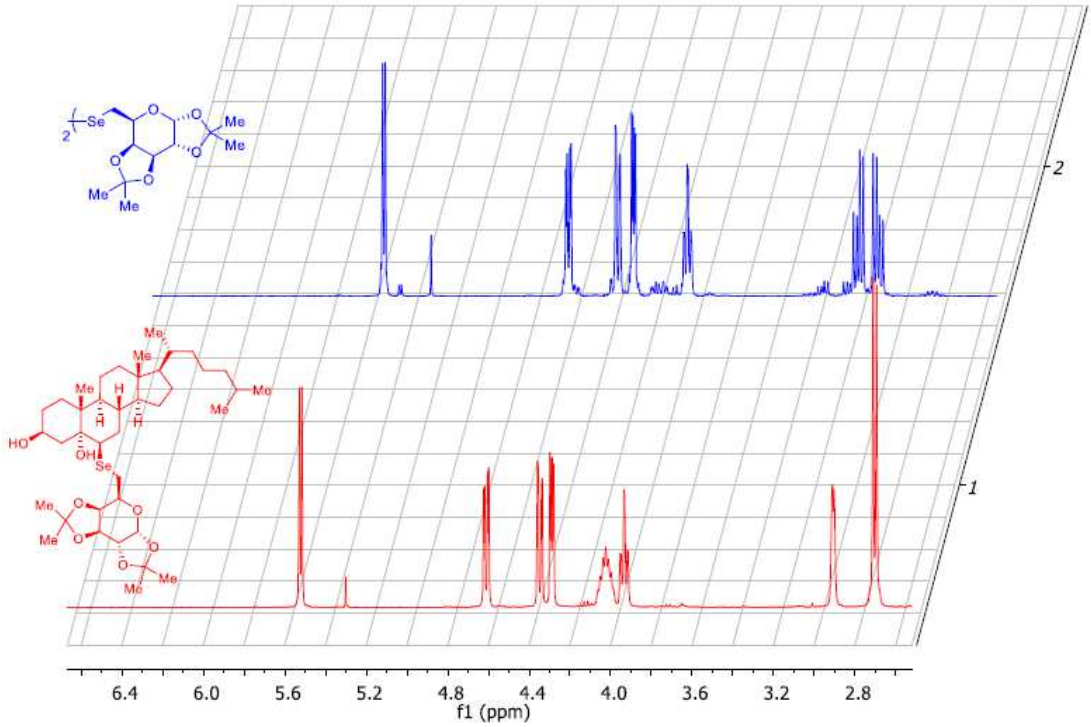


**Figure S27. Overlap of expansion of $^{1}$H NMR (400 MHz, $CDCl_3$) of the glycoconjugated product 6a and diselenide 5.**

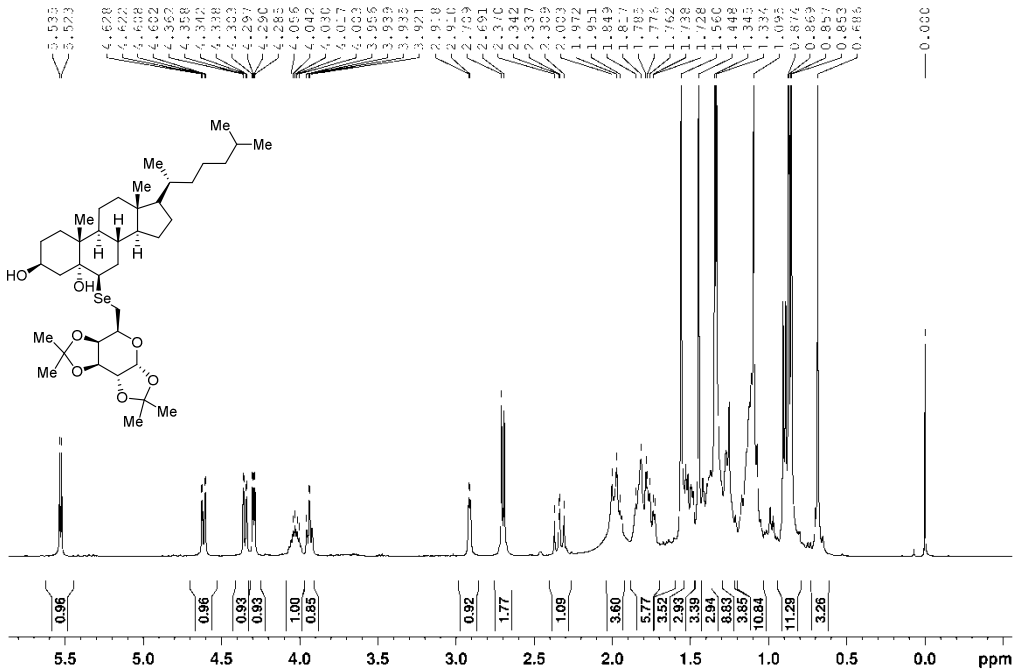


**Figure S28. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 6a**

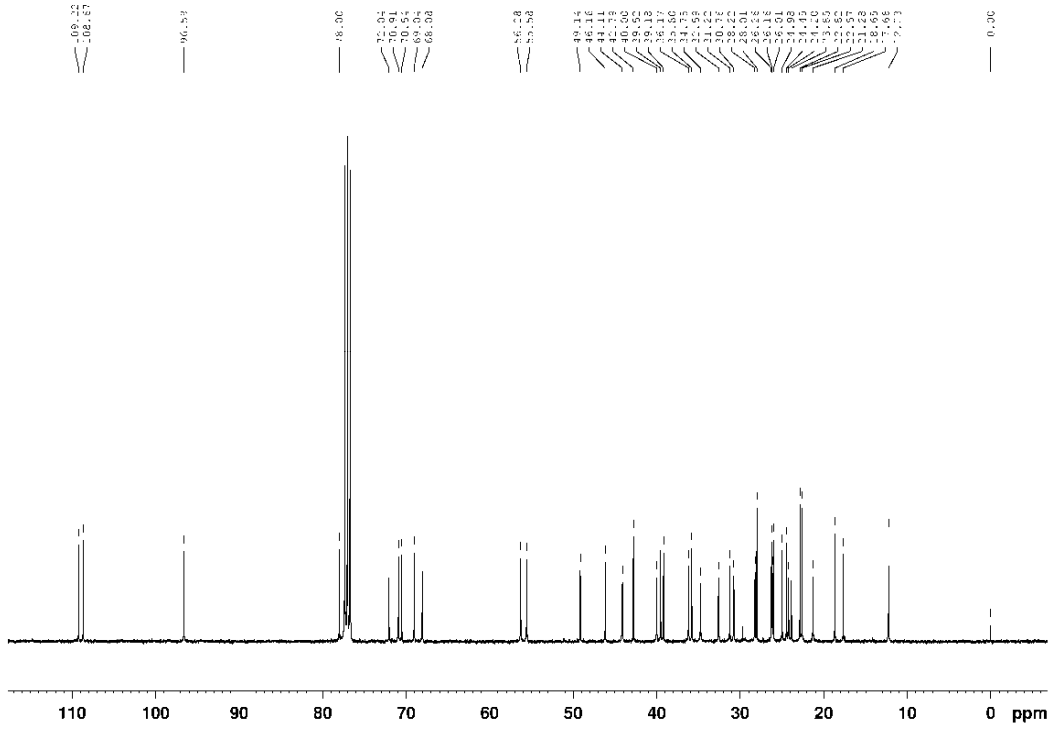


**Figure S29. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 6a**

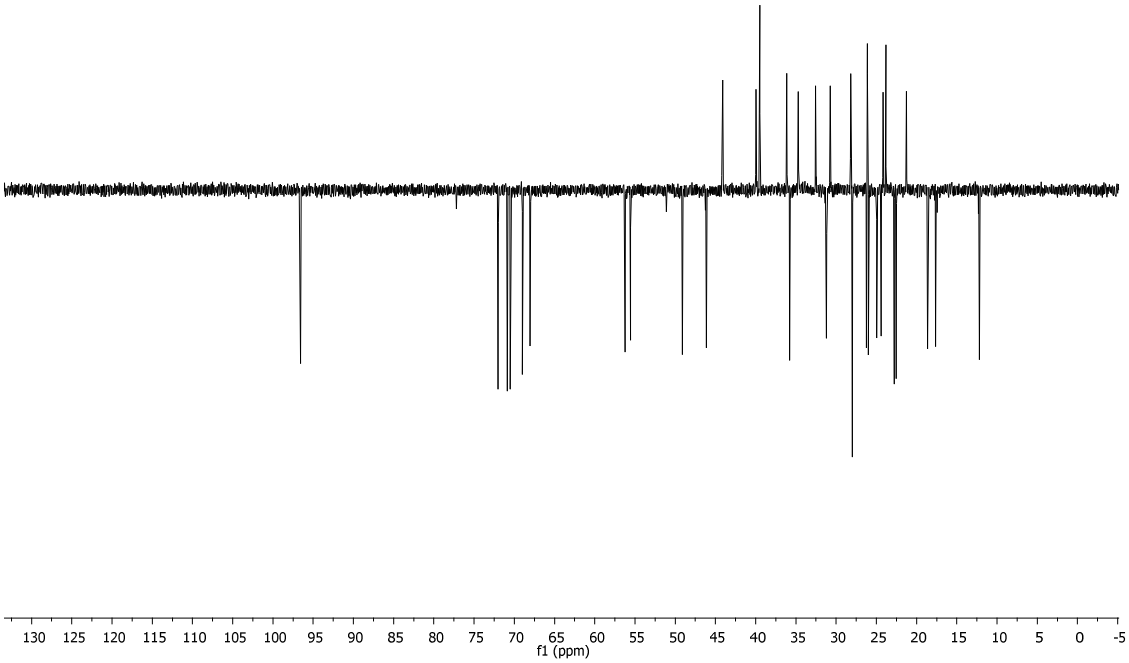


**Figure S30. $^{13}C$ DEPT-135 NMR(101 MHz, $CDCl_3$) of compound 6a**

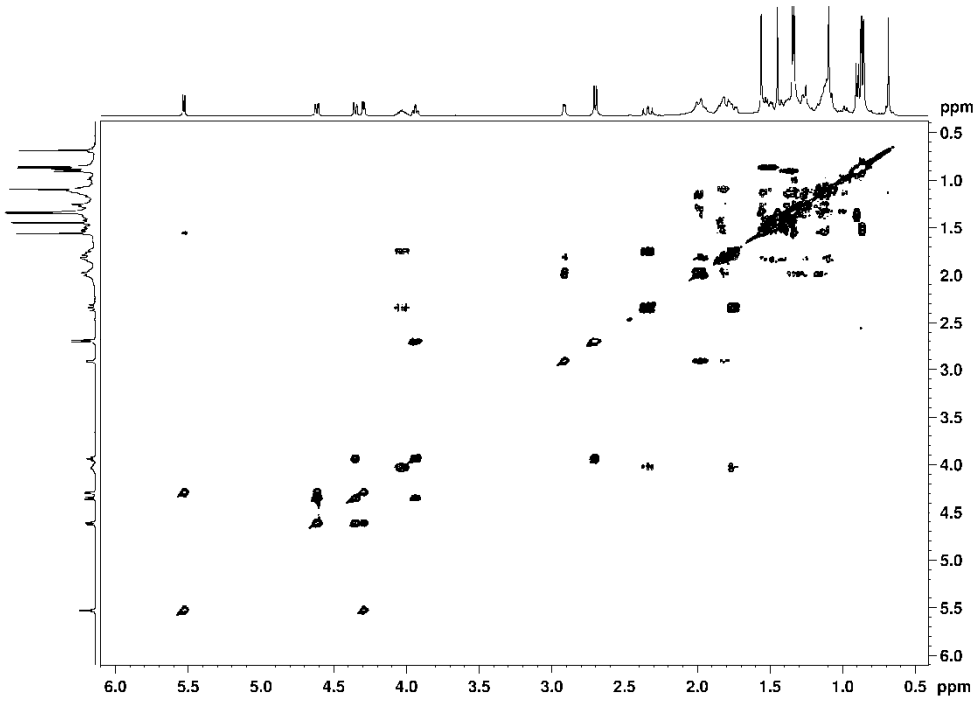


**Figure S31. Contour map of COSY $^{1}H$-$^{1}H$ spectra of compound 6a**

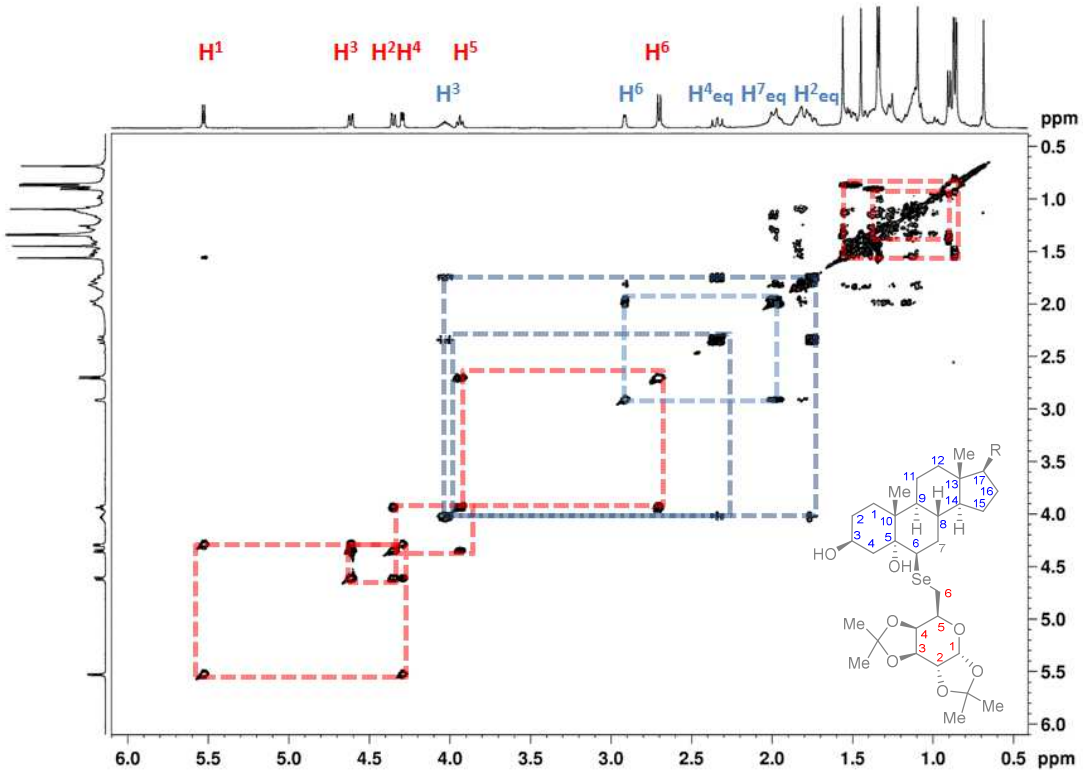


**Figure S32. Contour map of COSY $^{1}$H-$^{1}$H spectra of compound 6a. Selected interactions of carbohydrate moiety (red) and steroid moiety hydrogens (blue)**

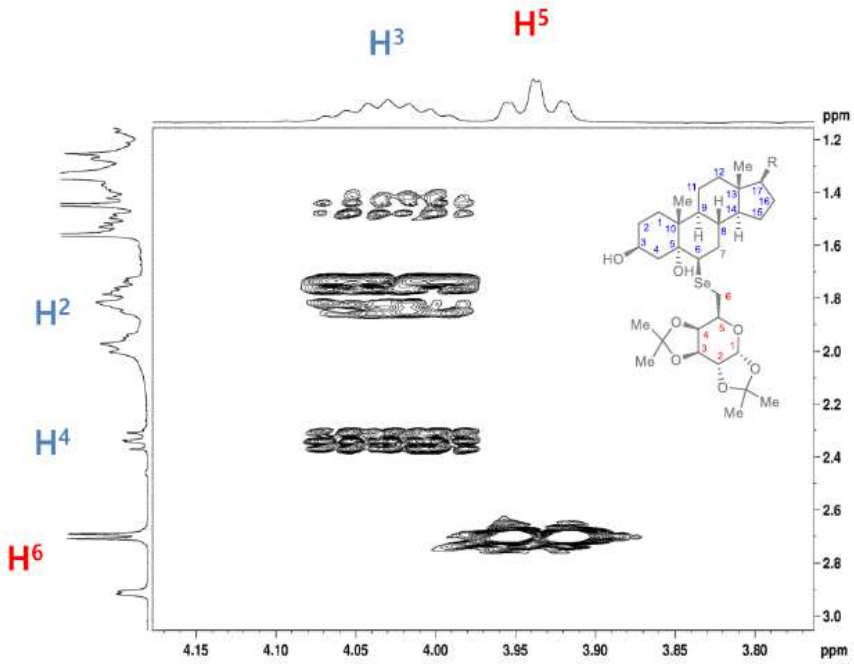


**Figure S33. Expansion of the contour map of COSY $^{1}$H-$^{1}$H spectra of compound 6a. Selected interactions between carbohydrate moiety (red) and steroid hydrogens (blue)**

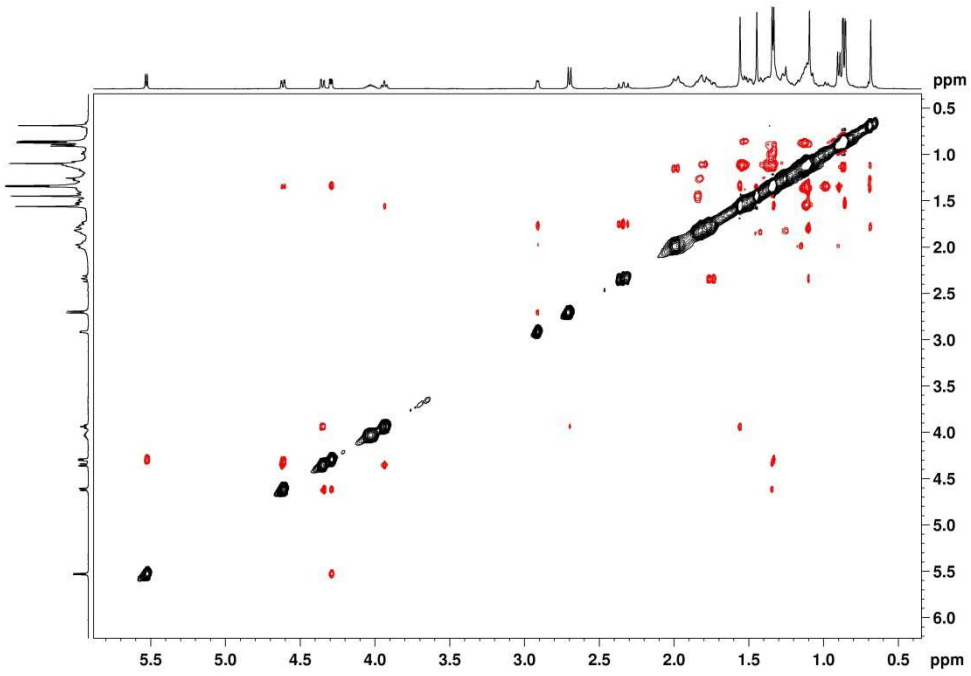


**Figure S34. Contour map of NOESY $^{1}$H-$^{1}$H spectra of compound 6a**

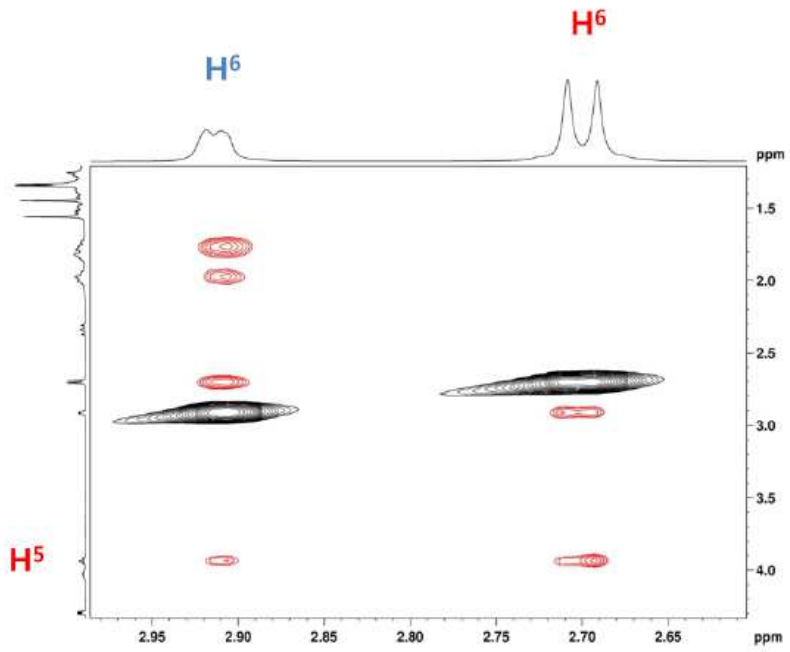


**Figure S35. Expansion of the contour map of NOESY $^{1}$H-$^{1}$H spectra of compound 6a. Selected interactions between carbohydrate moiety (red) and steroid moiety hydrogens (blue)**

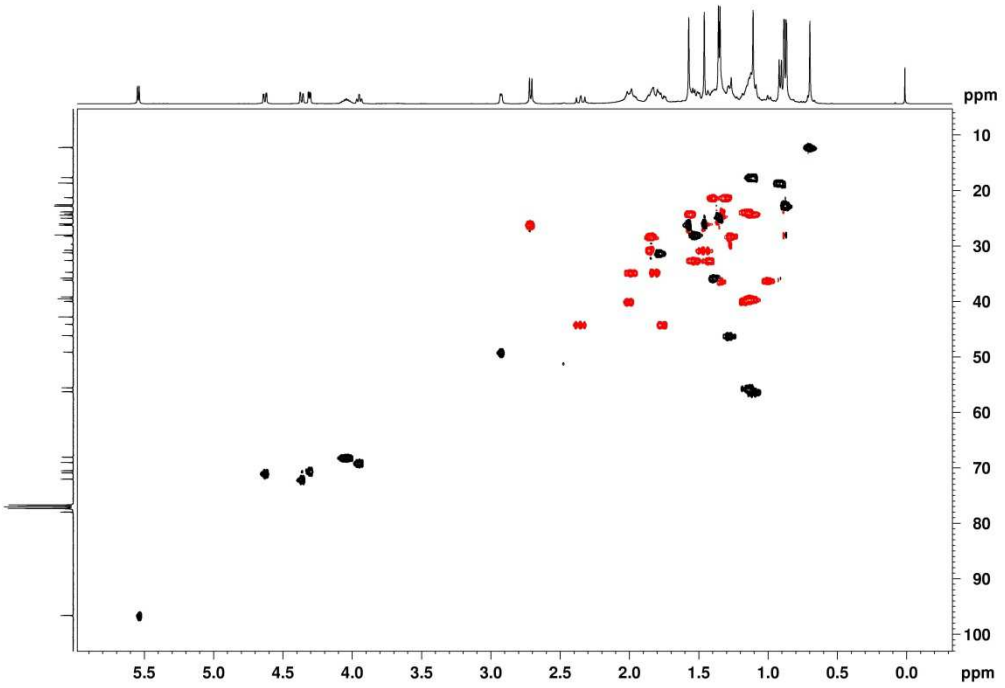


**Figure S36. Contour map of HSQC $^{1}H$-$^{13}C$ spectra of compound 6a**

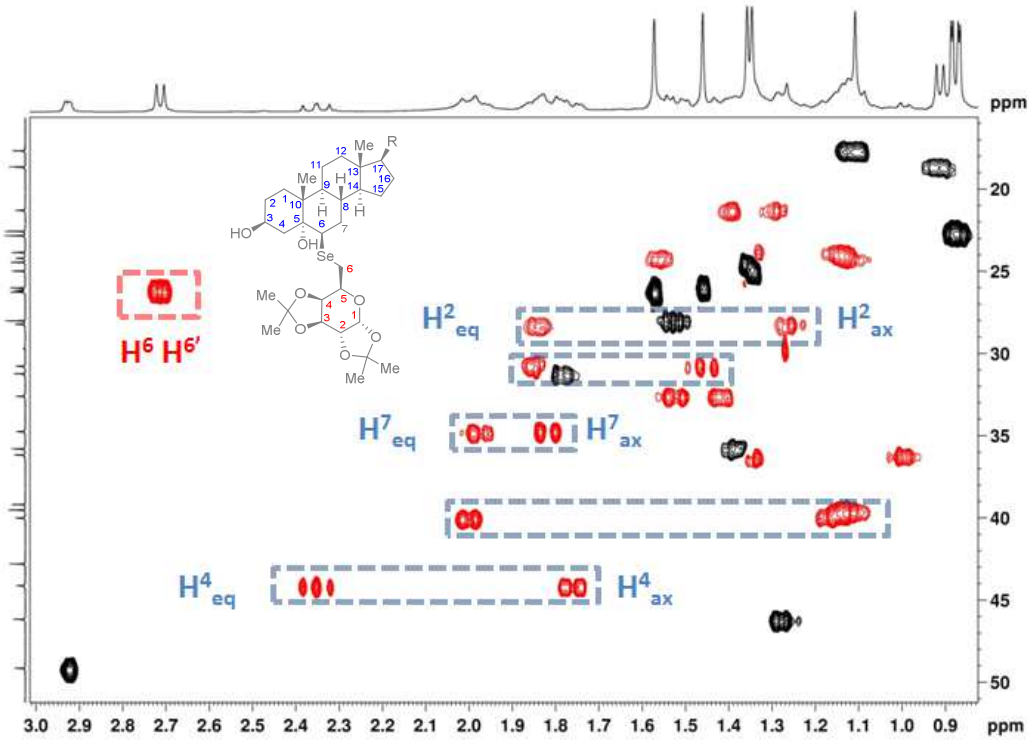


**Figure S37. Expansion of the contour map of HSQC $^{1}H$-$^{13}C$ spectra of compound 6a. Selected axial-equatorial hydrogen to carbon attributions**

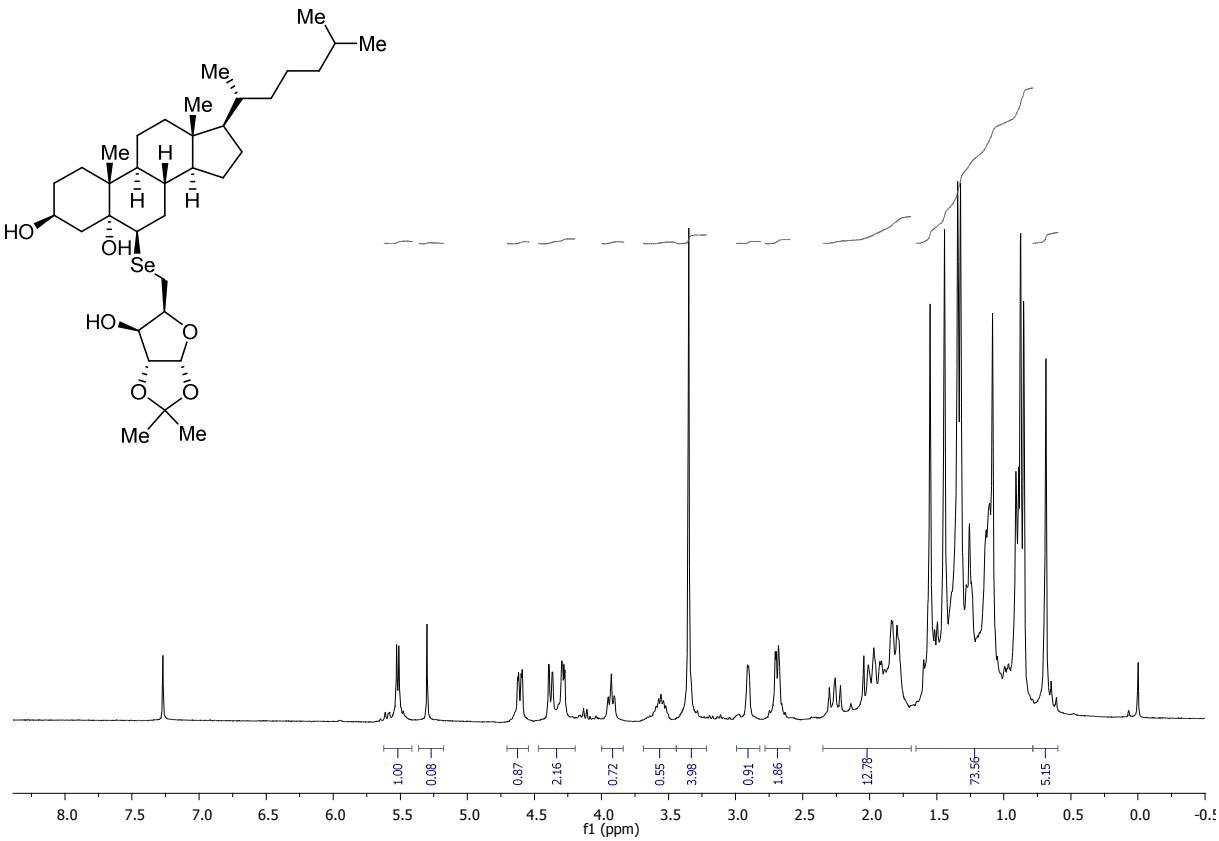


**Figure S38. $^{1}$H NMR (300 MHz, $CDCl_3$) of compound 7a**

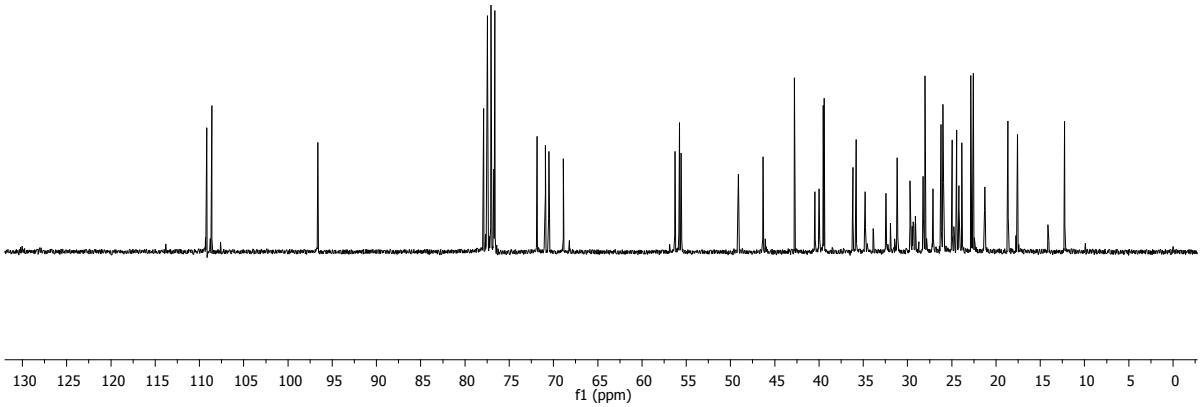


**Figure S39. $^{13}$C NMR (75 MHz, $CDCl_3$) of compound 7a**

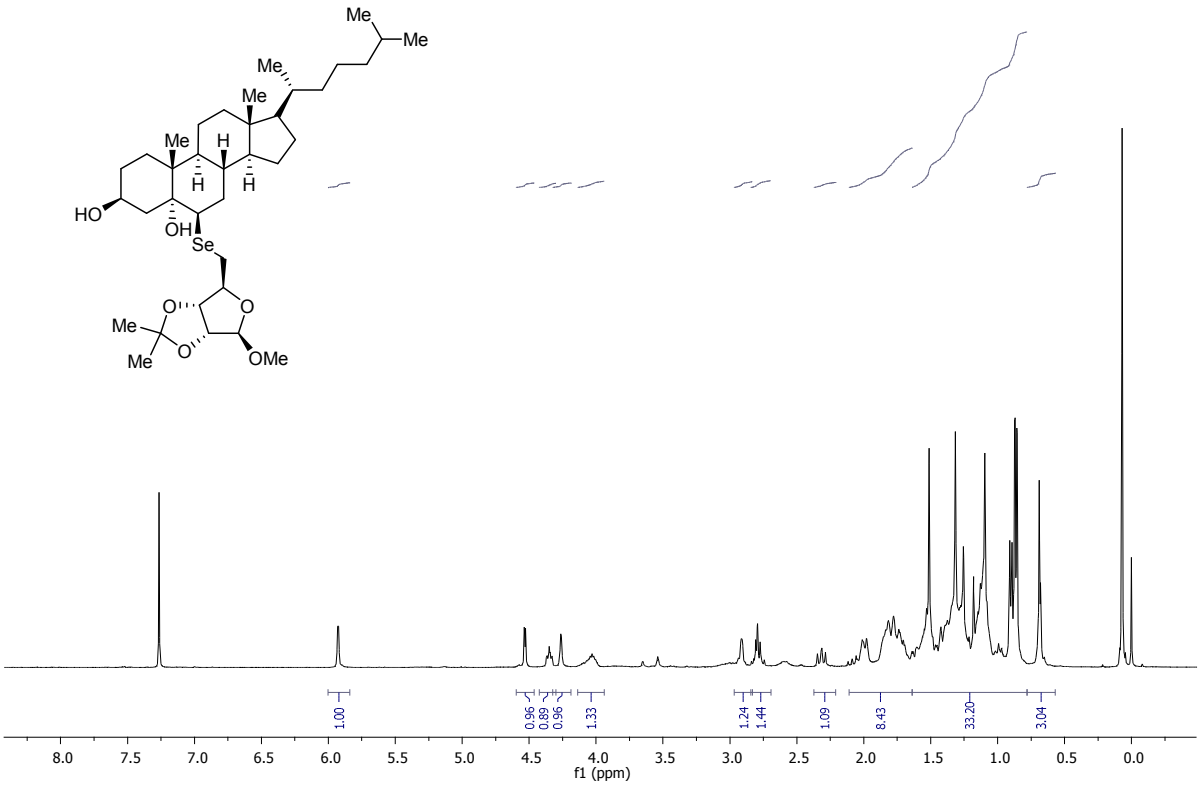


**Figure S40. $^{1}$H NMR (300 MHz, $CDCl_3$) of compound 8a**

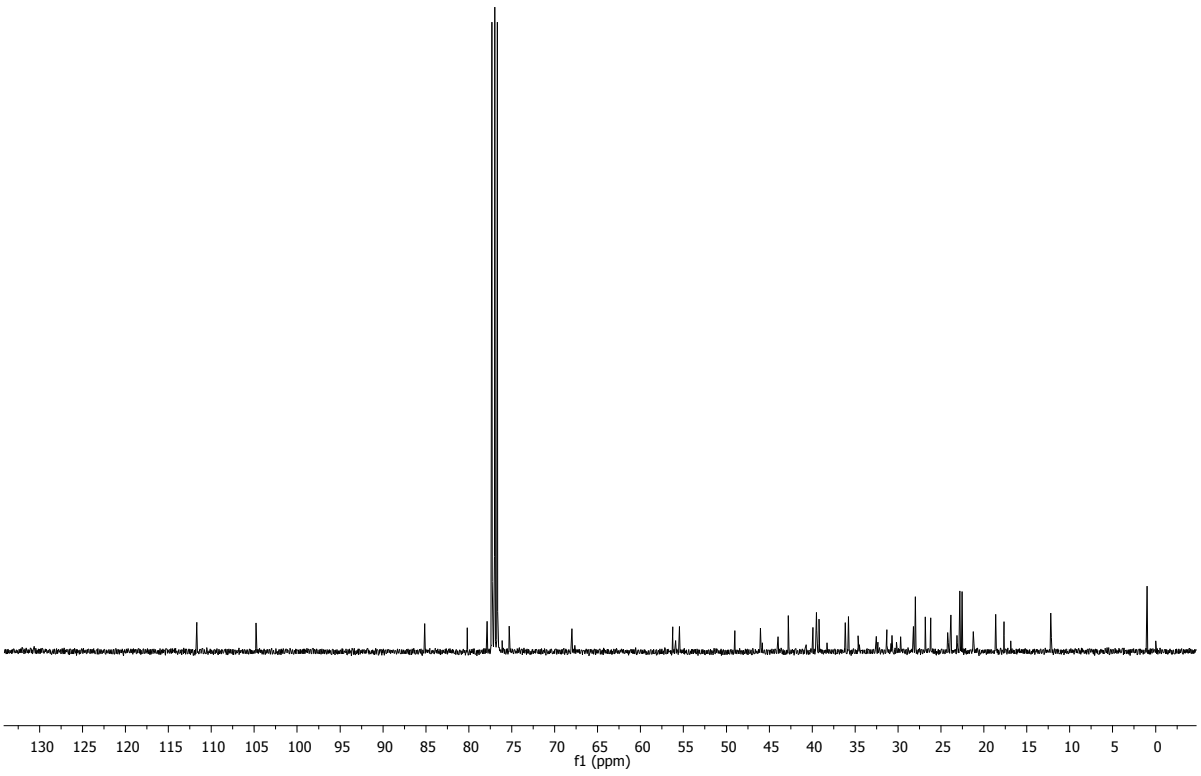


**Figure S41. $^{13}$C NMR (75 MHz, $CDCl_3$) of compound 8a**

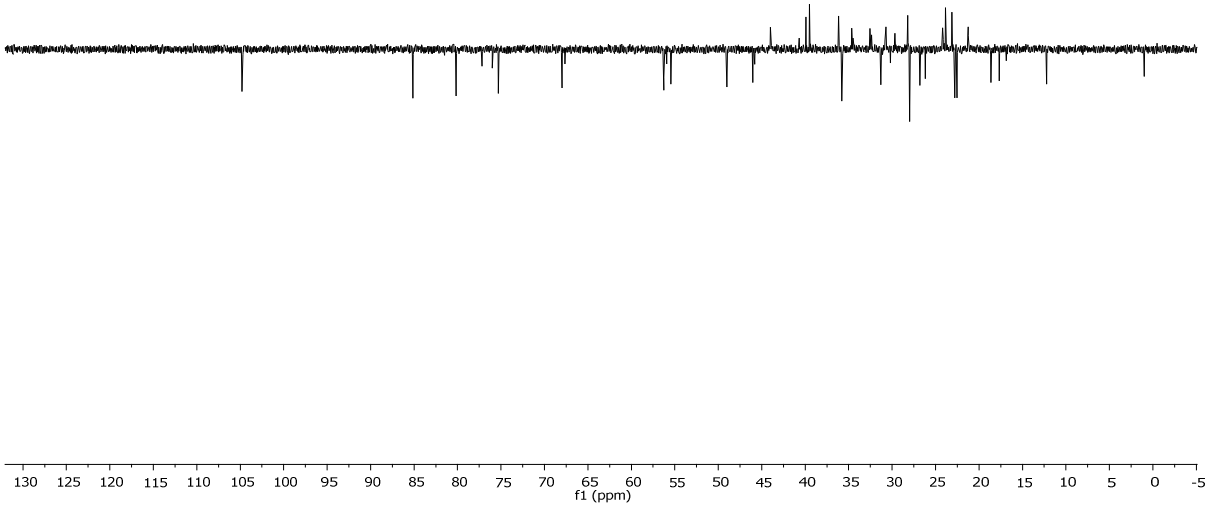


**Figure S42. $^{13}$C DEPT-135 NMR (75 MHz, $CDCl_3$) of compound 8a**

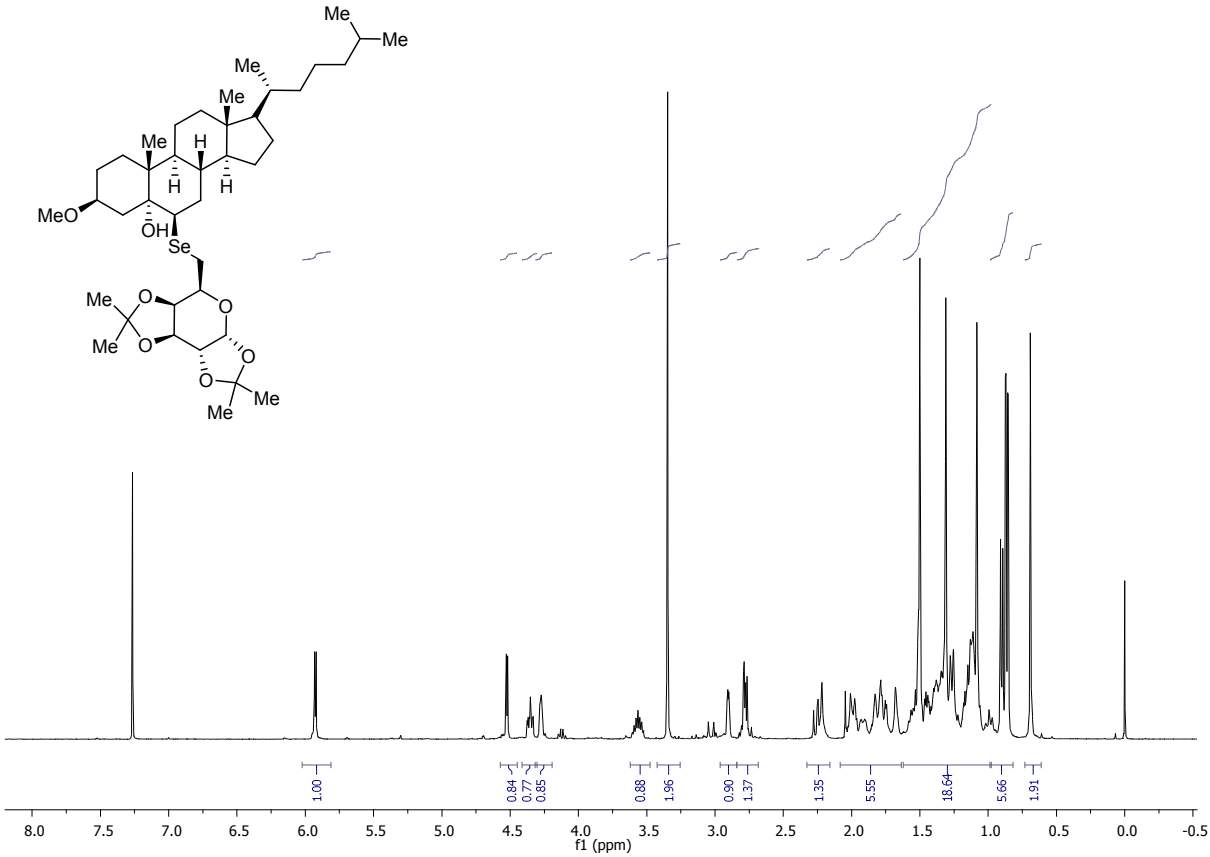


**Figure S43. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 6b**

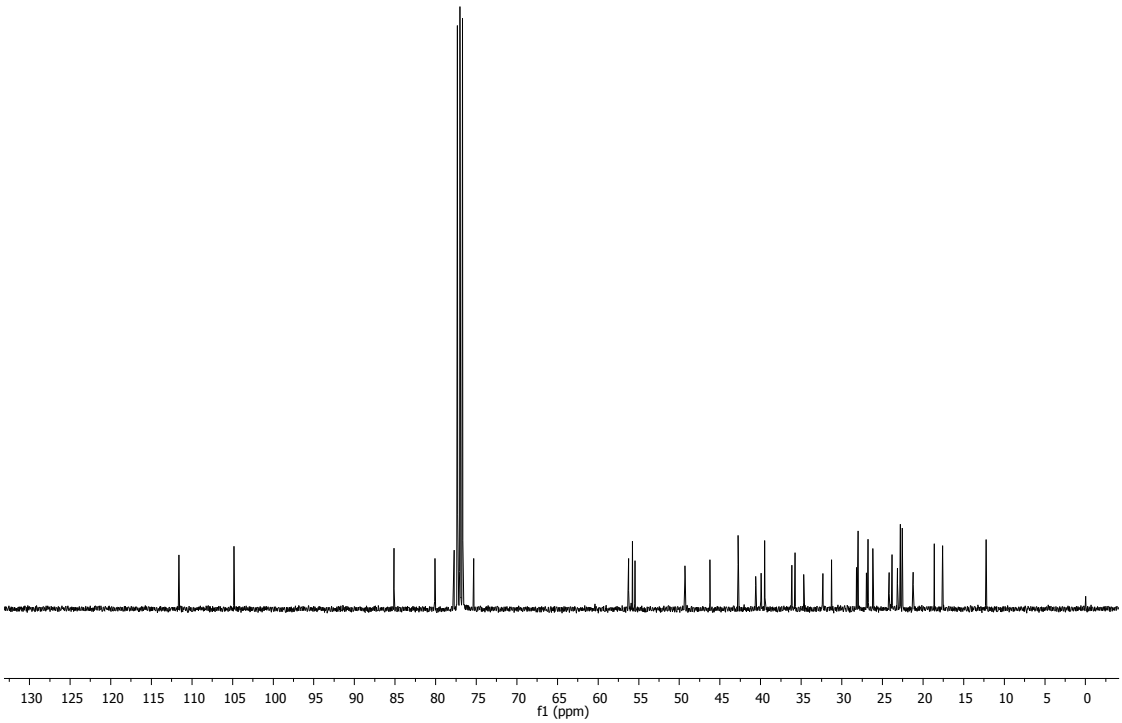


**Figure S44. $^{13}C$ NMR (101 MHz, $CDCl_3$) of compound 6b**

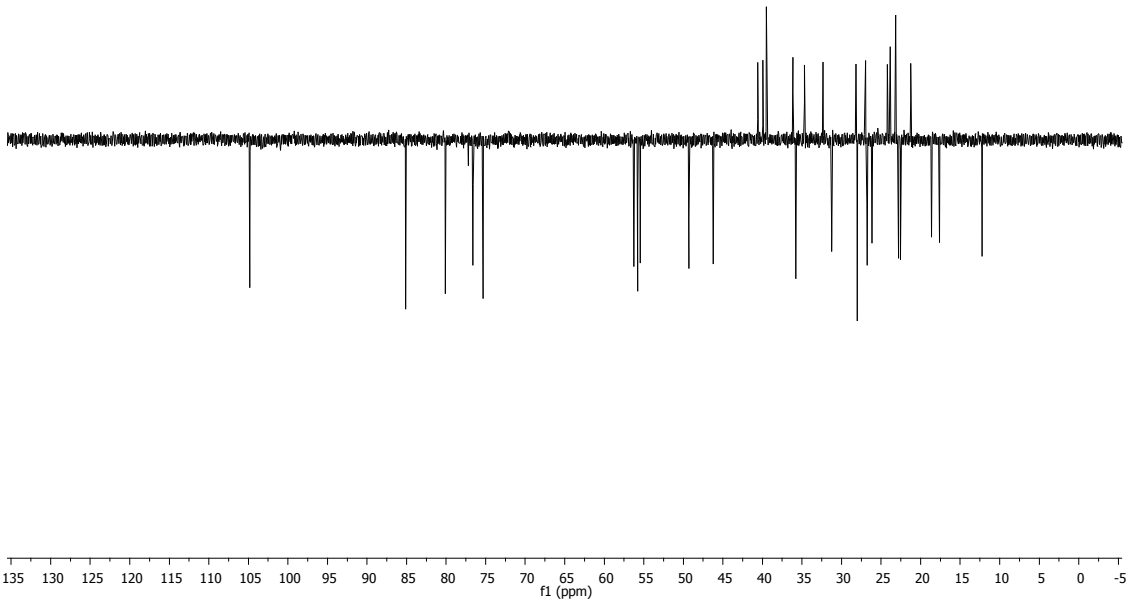


**Figure S45. $^{13}C$ APT NMR (101 MHz, $CDCl_3$) of compound 6b**

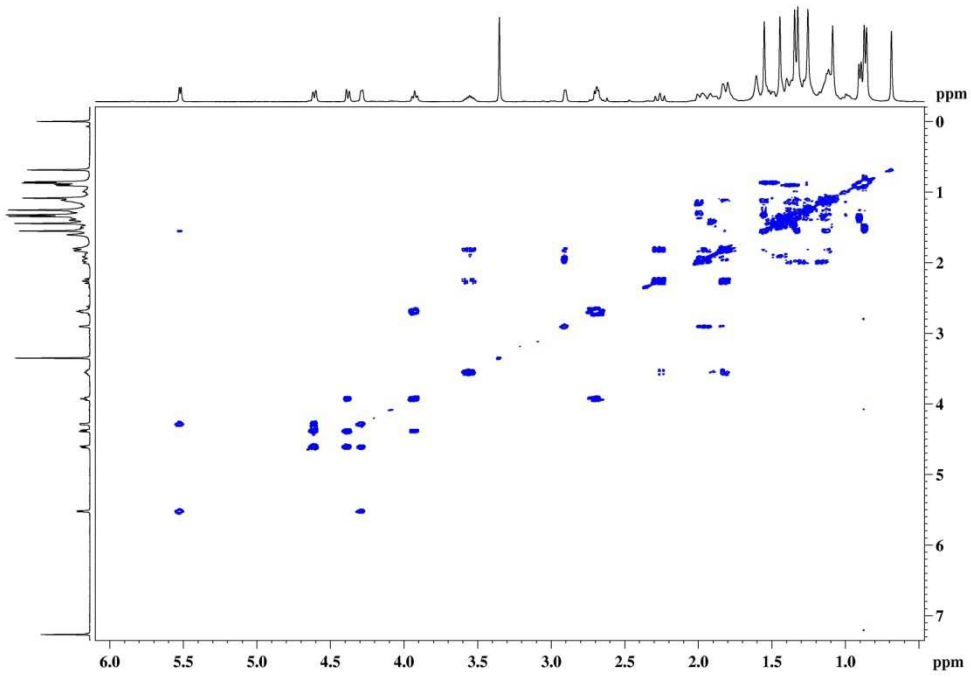


**Figure S46. Contour map of $^{1}$H-$^{1}$H COSY spectra of compound 6b**

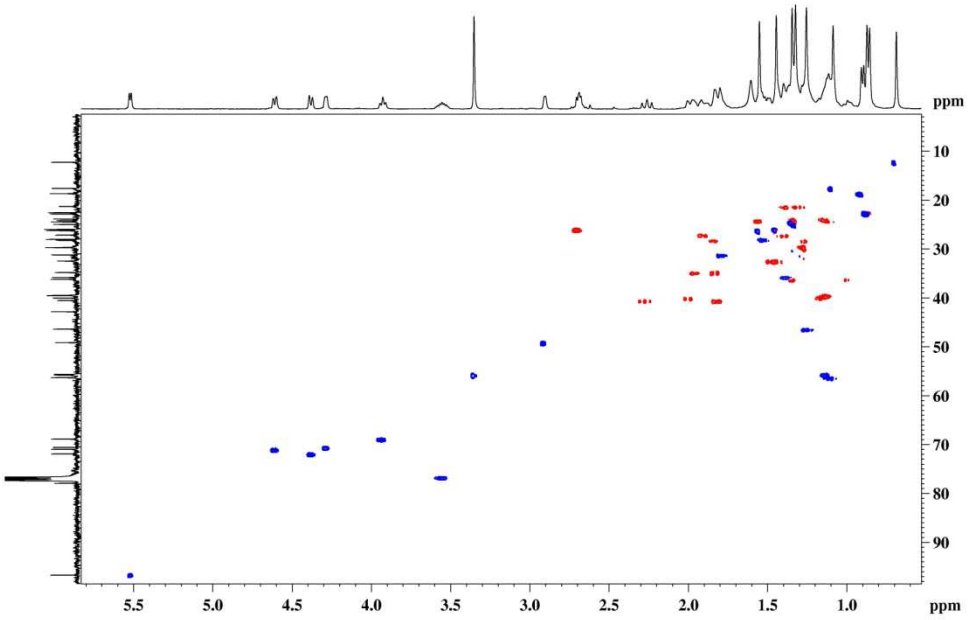


**Figure S47. Contour map of $^{1}$H-$^{13}$C HSQC spectra of compound 6b**

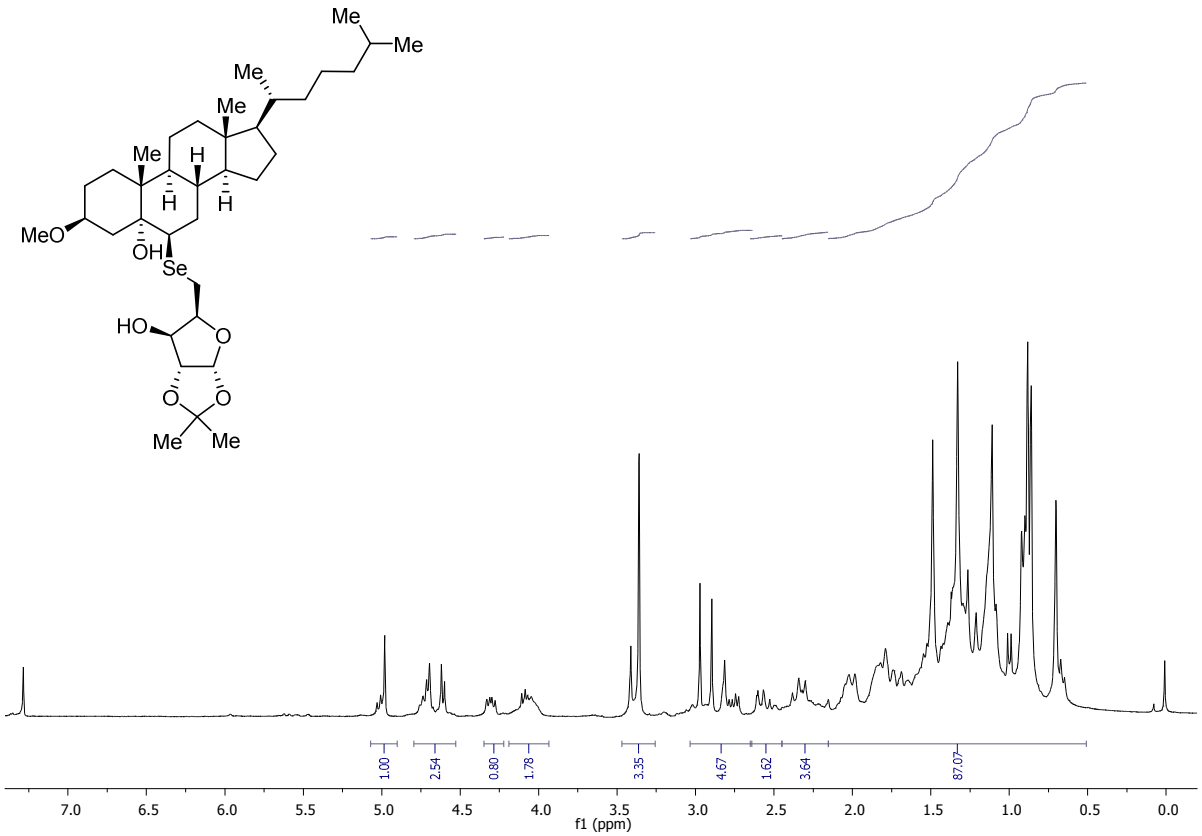


**Figure S48. $^{1}$H NMR (300 MHz, $CDCl_3$) of compound 7b**

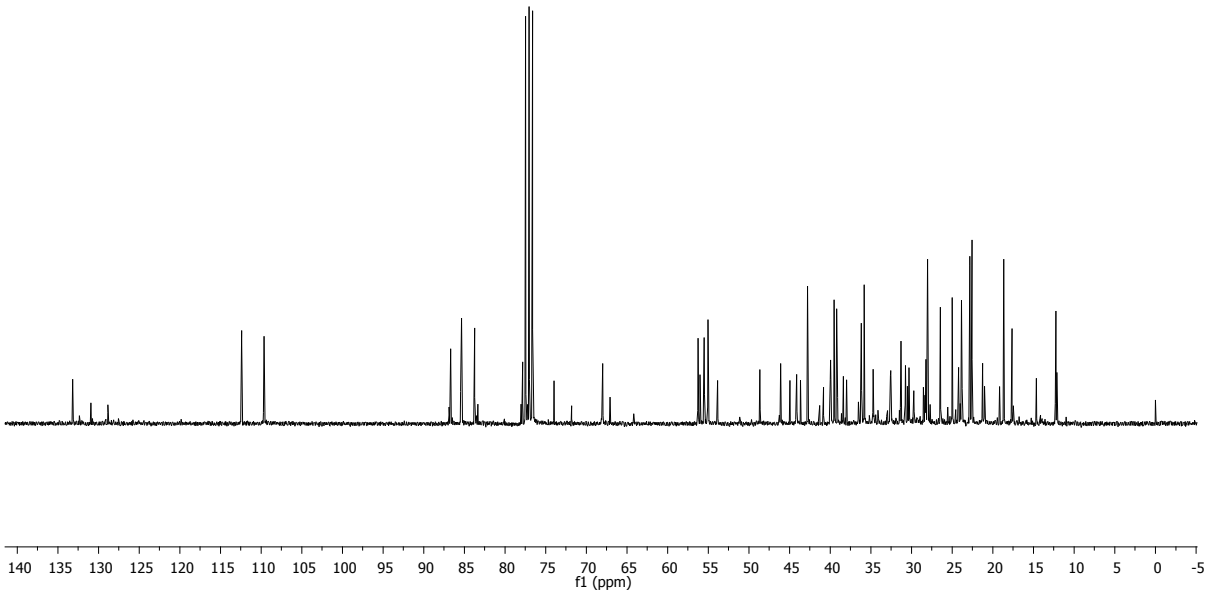


**Figure S48. $^{13}$C NMR (75 MHz, $CDCl_3$) of compound 7b**

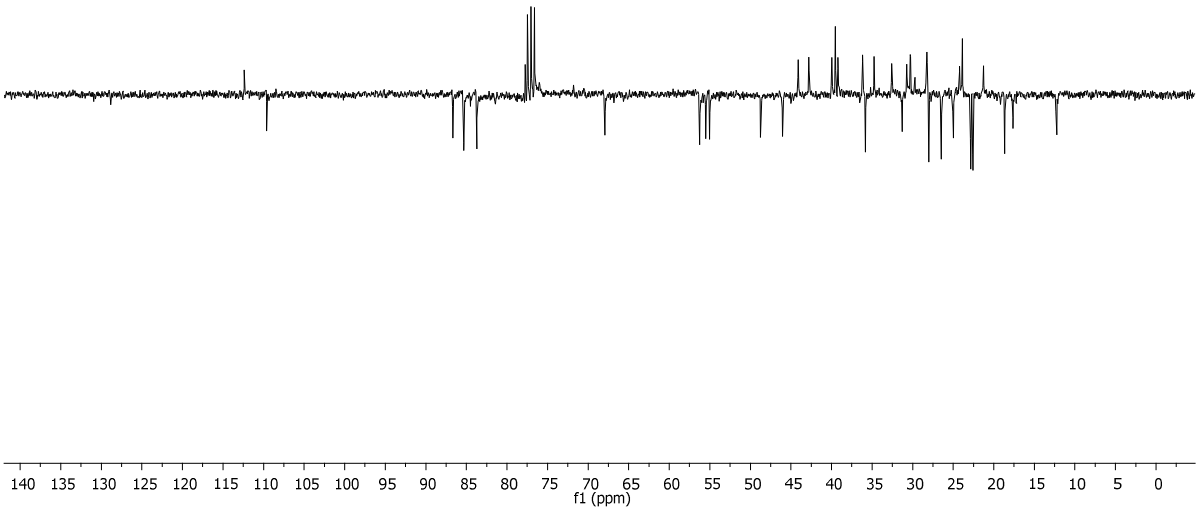


**Figure S49. $^{13}$C APT NMR (75 MHz, $CDCl_3$) of compound 7b**

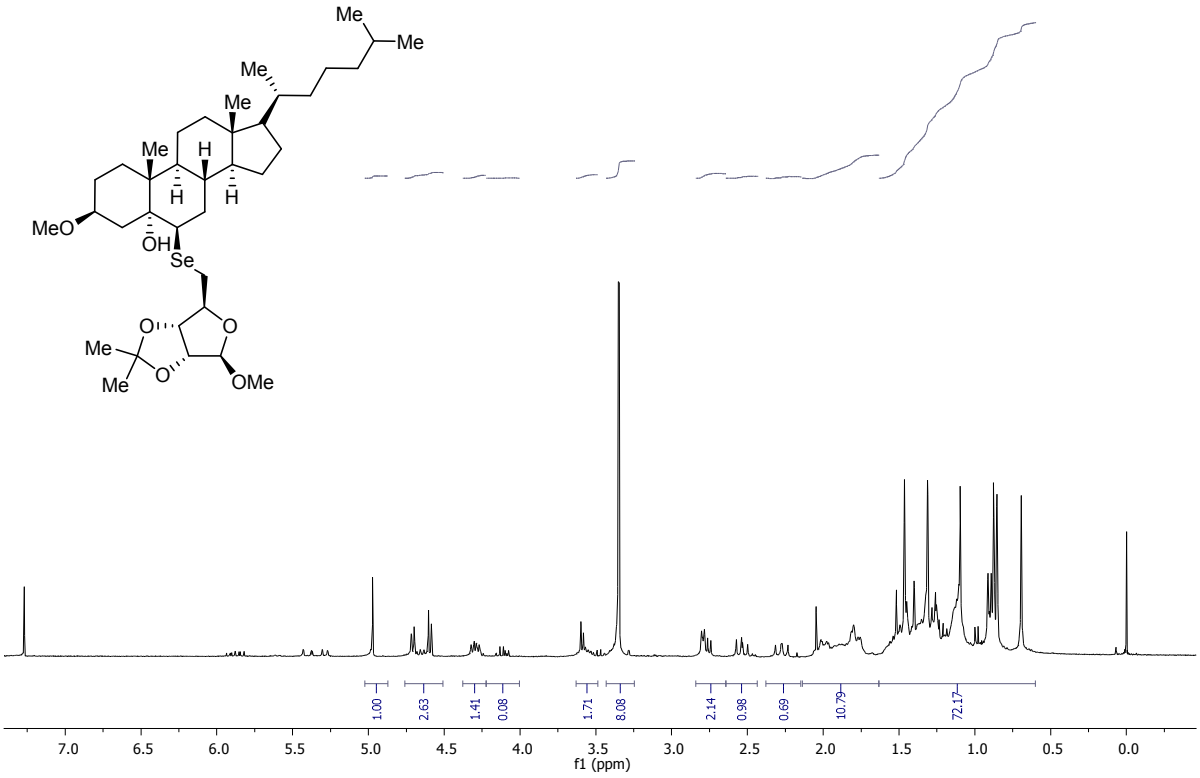


**Figure S50. $^{1}$H NMR (300 MHz, $CDCl_3$) of compound 8b**

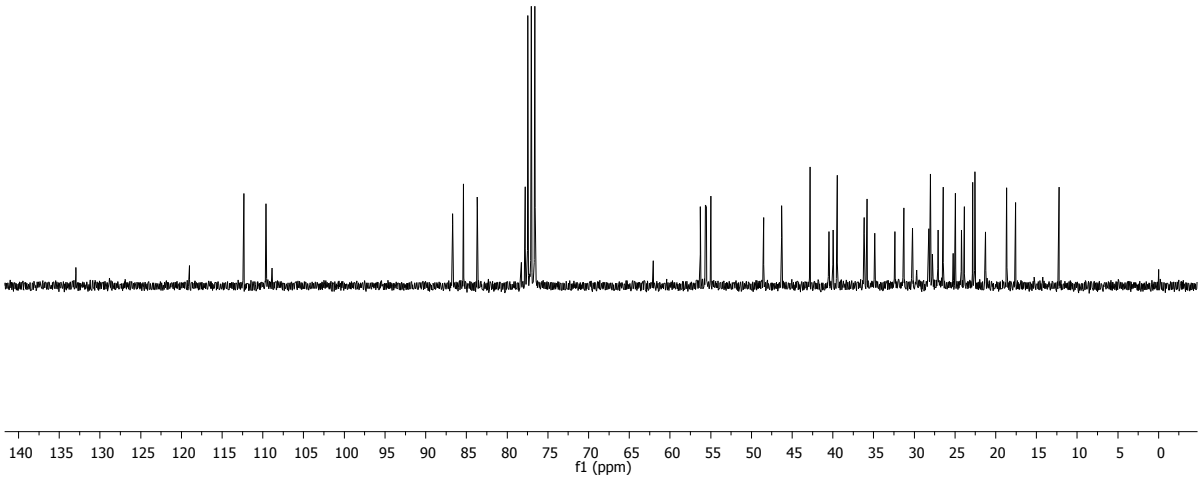


**Figure S51. $^{13}C$ NMR (75 MHz, $CDCl_3$) of compound 8b**

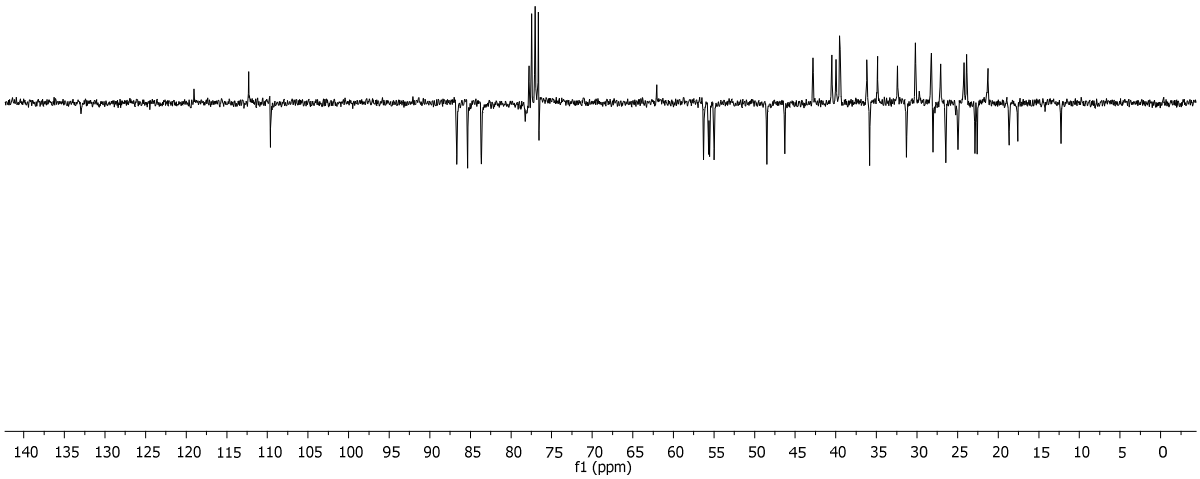


**Figure S52. $^{13}C$ APT NMR (75 MHz, $CDCl_3$) of compound 8b**

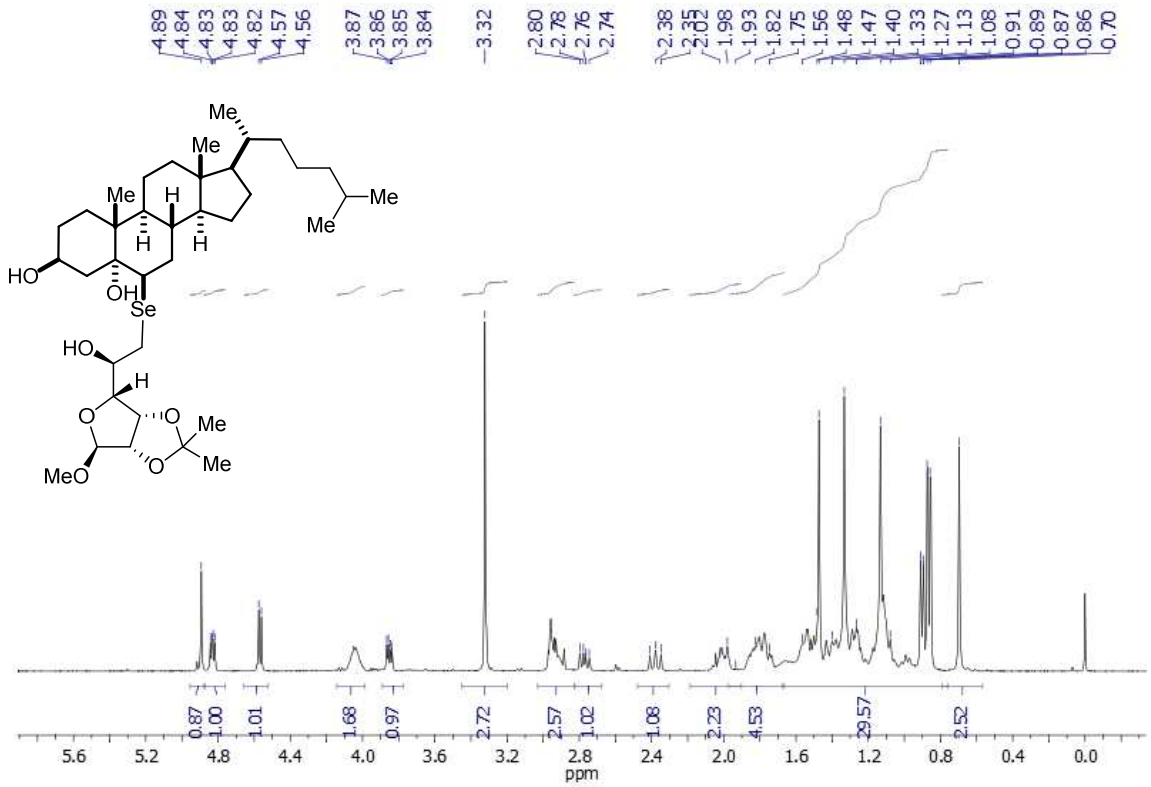


**Figure S53. $^{1}$H NMR (300 MHz, $CDCl_3$) of compound 9a**

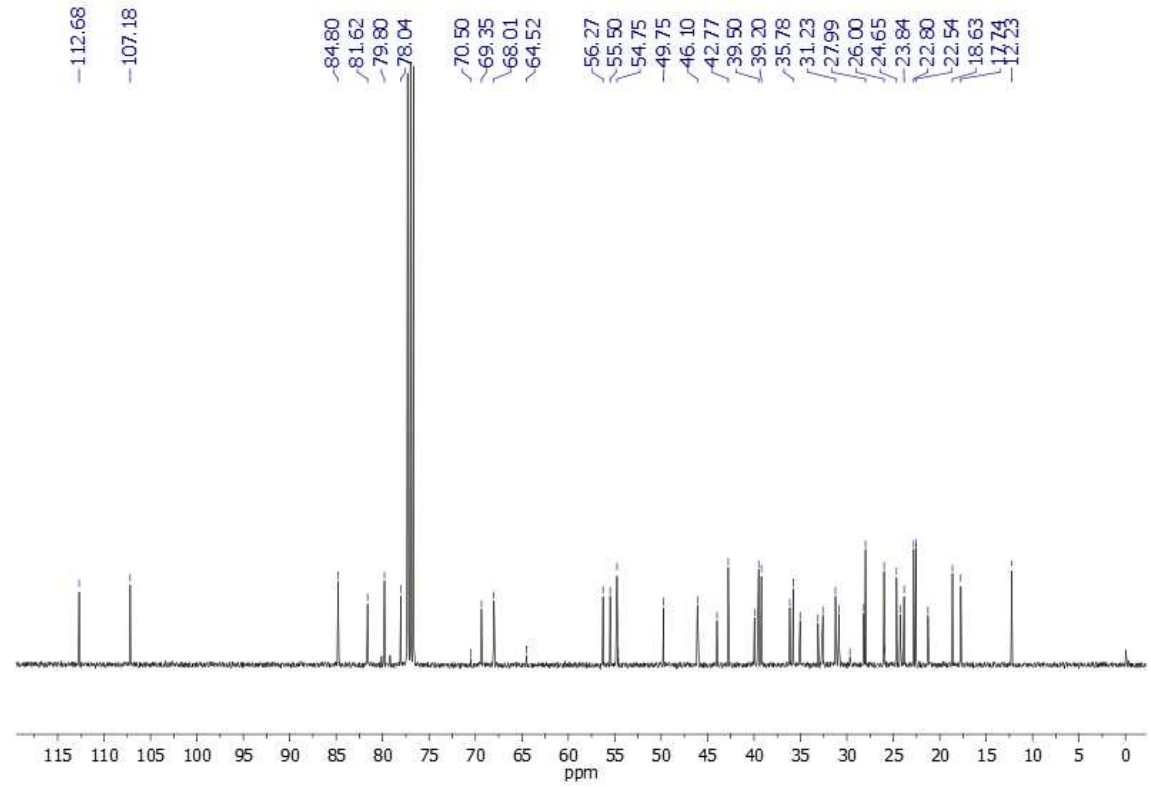


**Figure S54. $^{13}$C NMR (75 MHz, $CDCl_3$) of compound 9a**

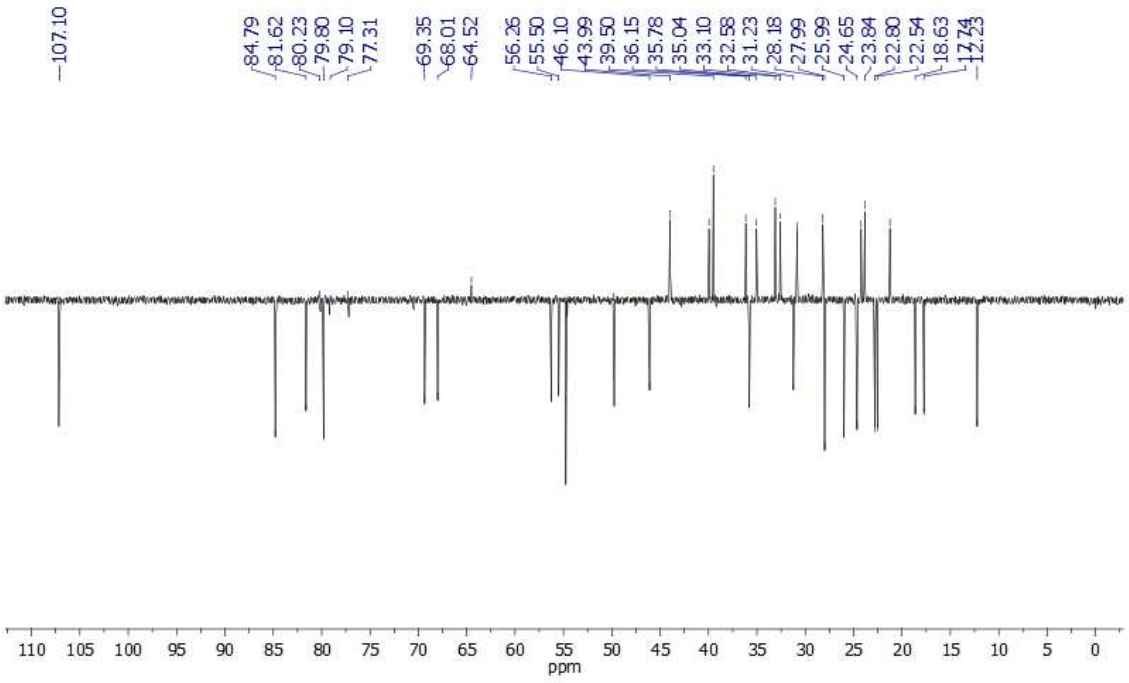


**Figure S55. $^{13}C$ DEPT-135 NMR(75 MHz, $CDCl_3$) of compound 9a**

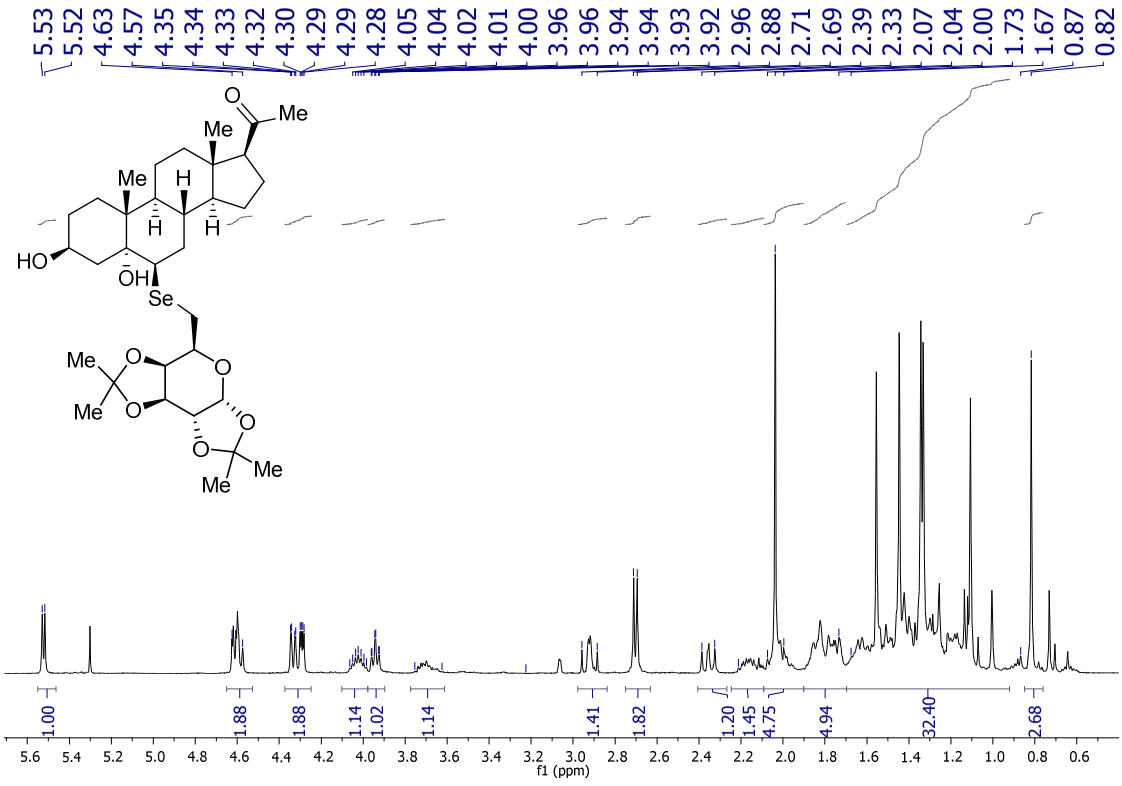


**Figure S56. $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound 11a**

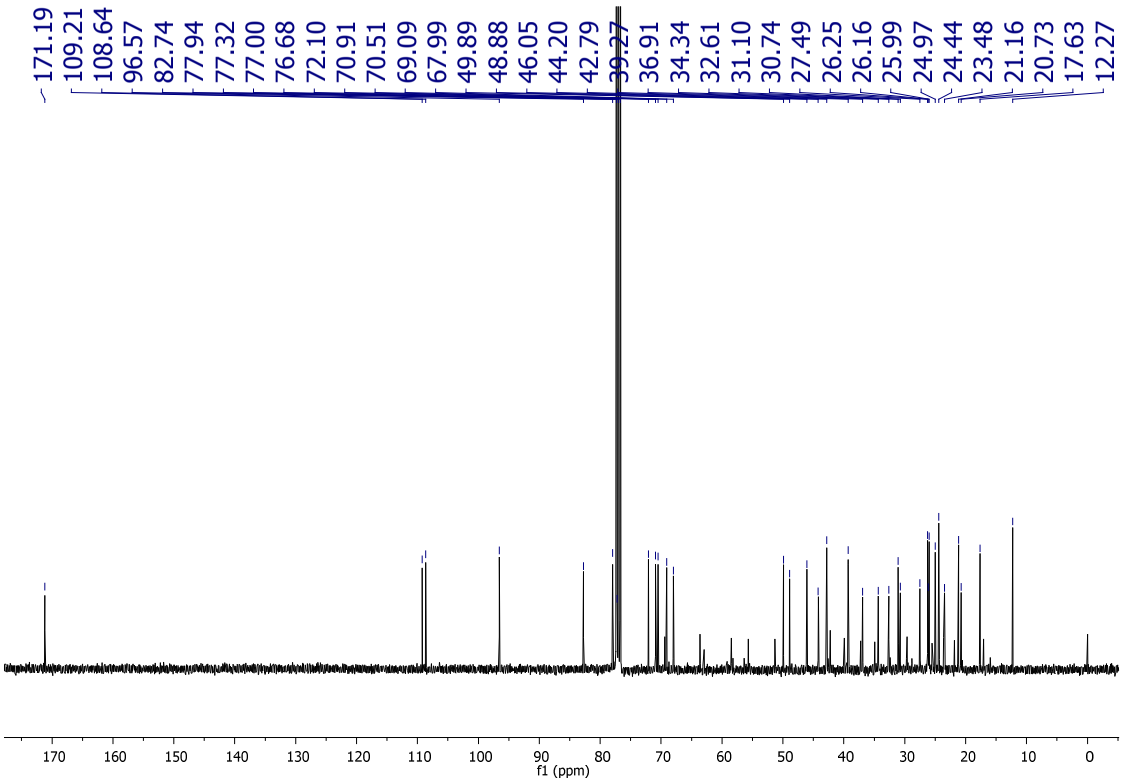


**Figure S57. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 11a**

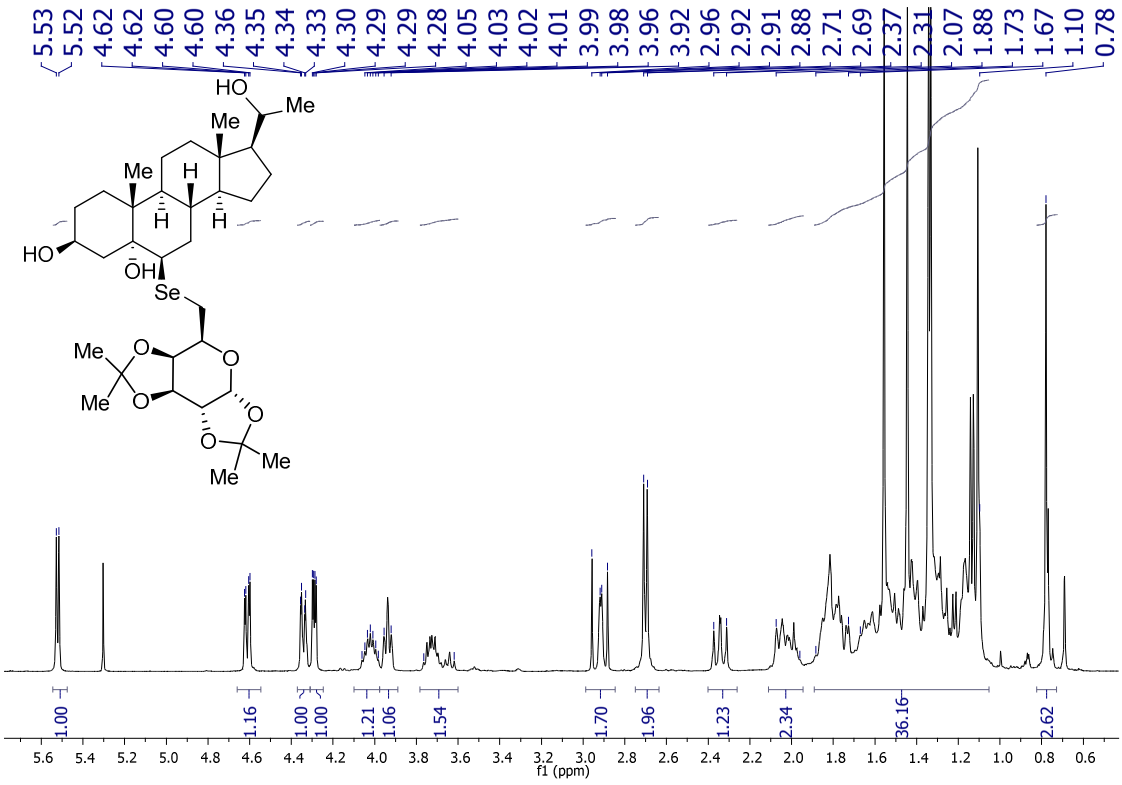


**Figure S58.$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 11b**

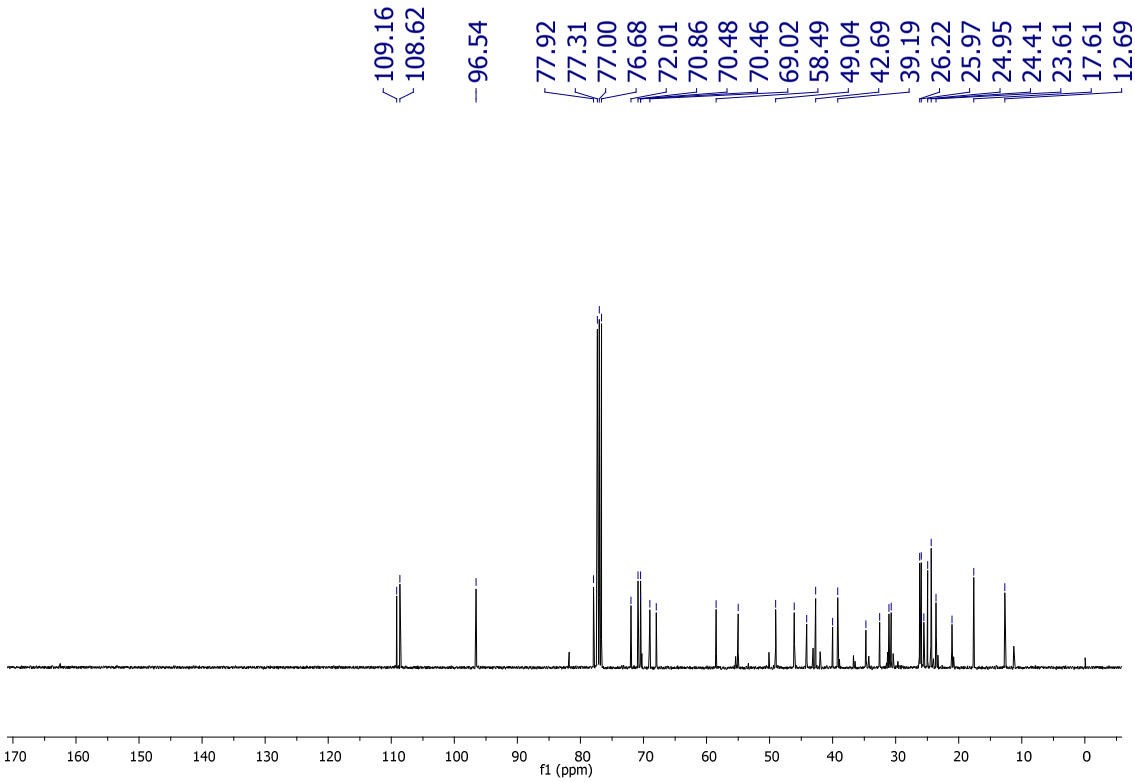


**Figure S59. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 11b**

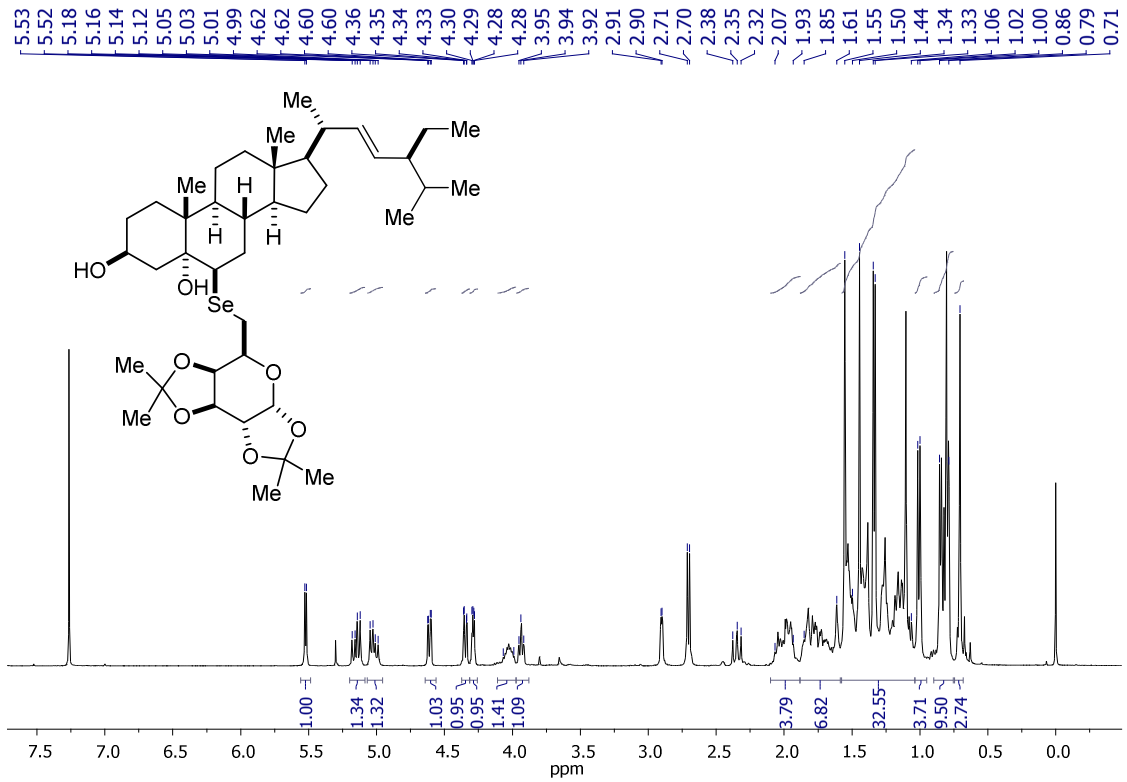


**Figure S60. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 14**

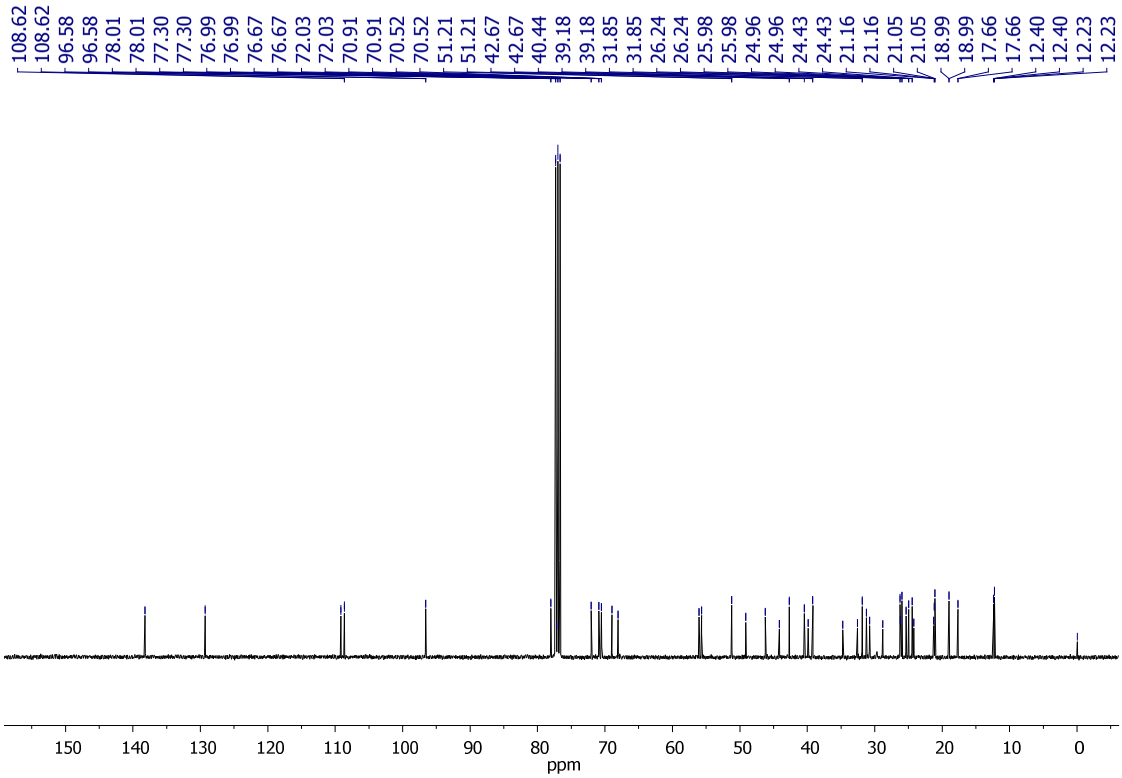


**Figure S61. $^{13}C$ NMR (101 MHz, $CDCl_3$) of compound 14**

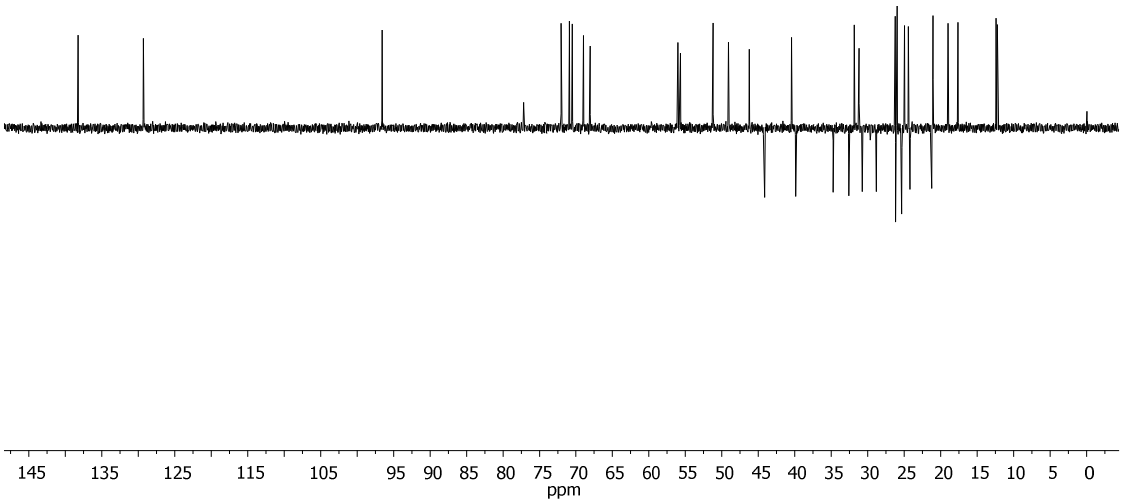


**Figure S62. $^{13}C$ DEPT-135 NMR (101 MHz, $CDCl_3$) of compound 14**

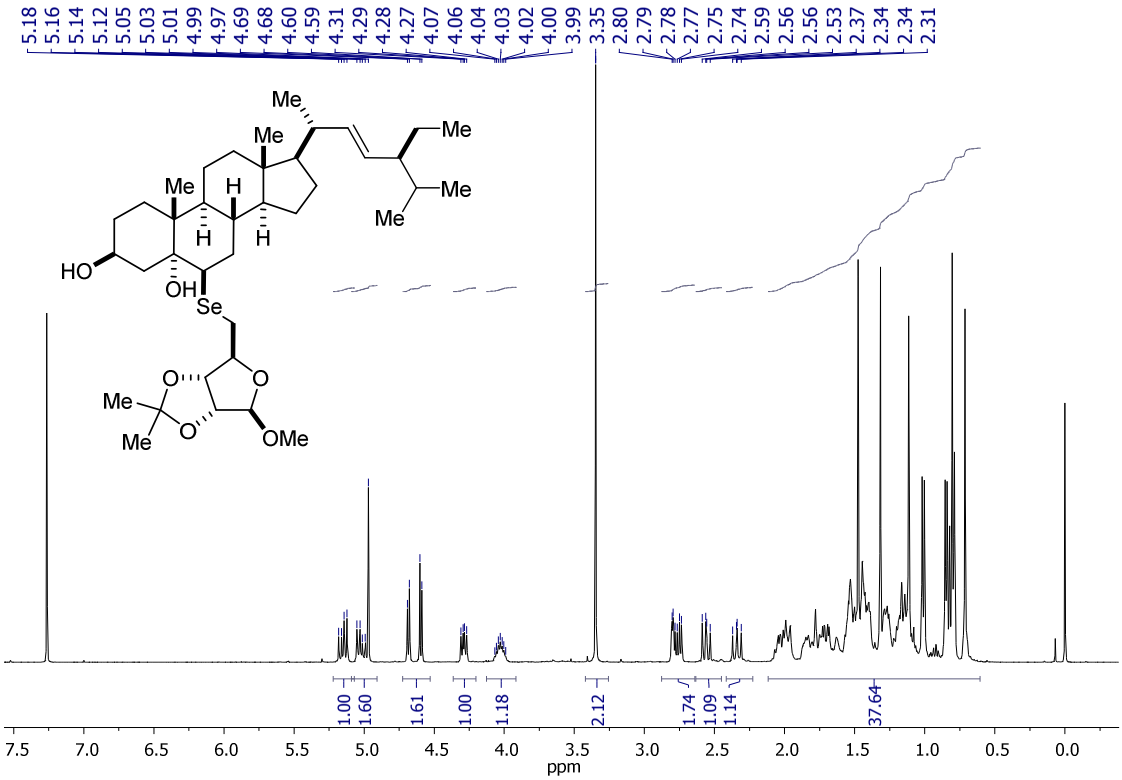


**Figure S63. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 15**

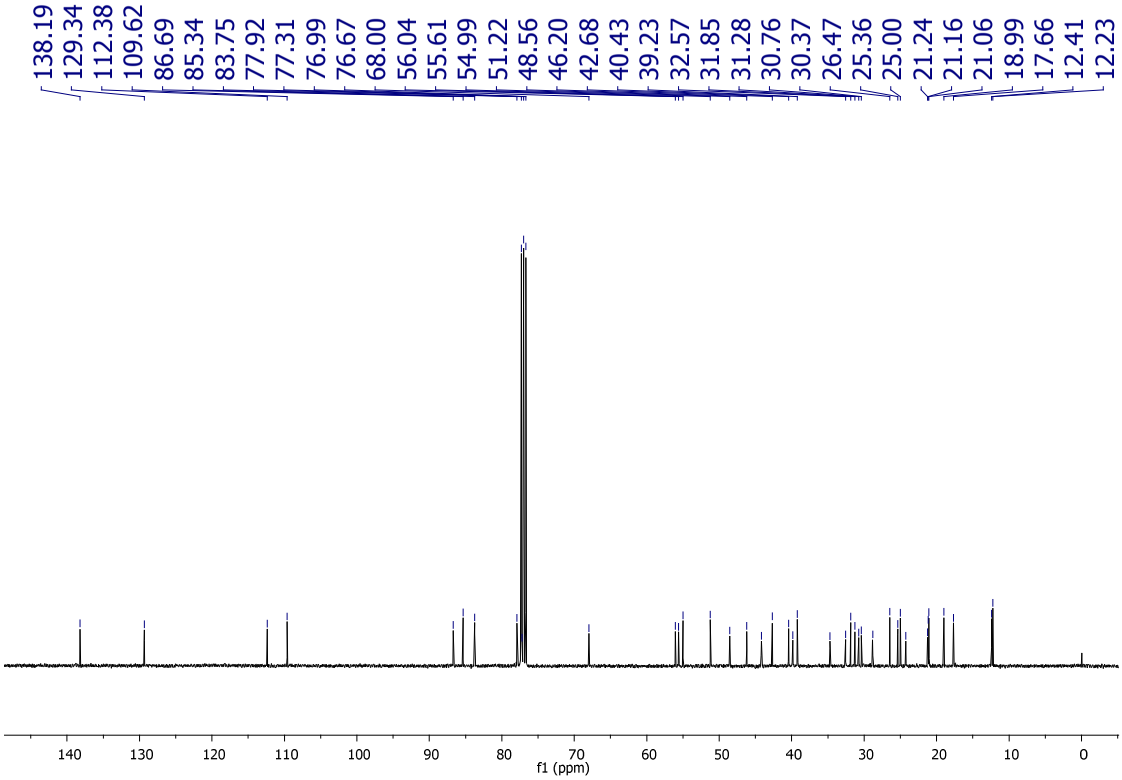


**Figure S64. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 15**

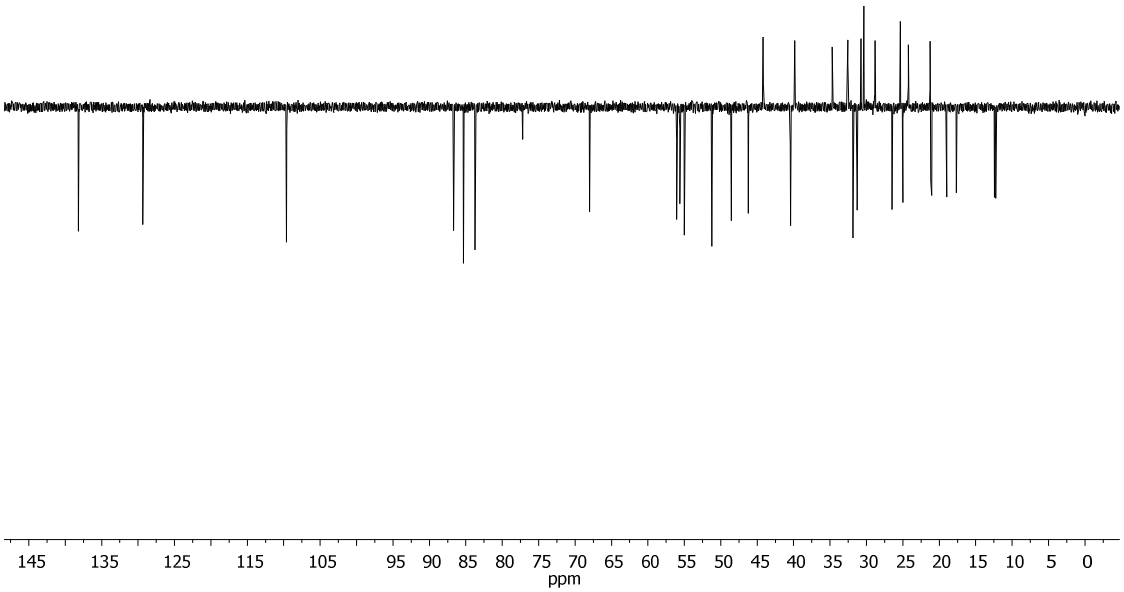


**Figure S65. $^{13}$C DEPT-135 NMR (101 MHz, $CDCl_3$) of compound 15**

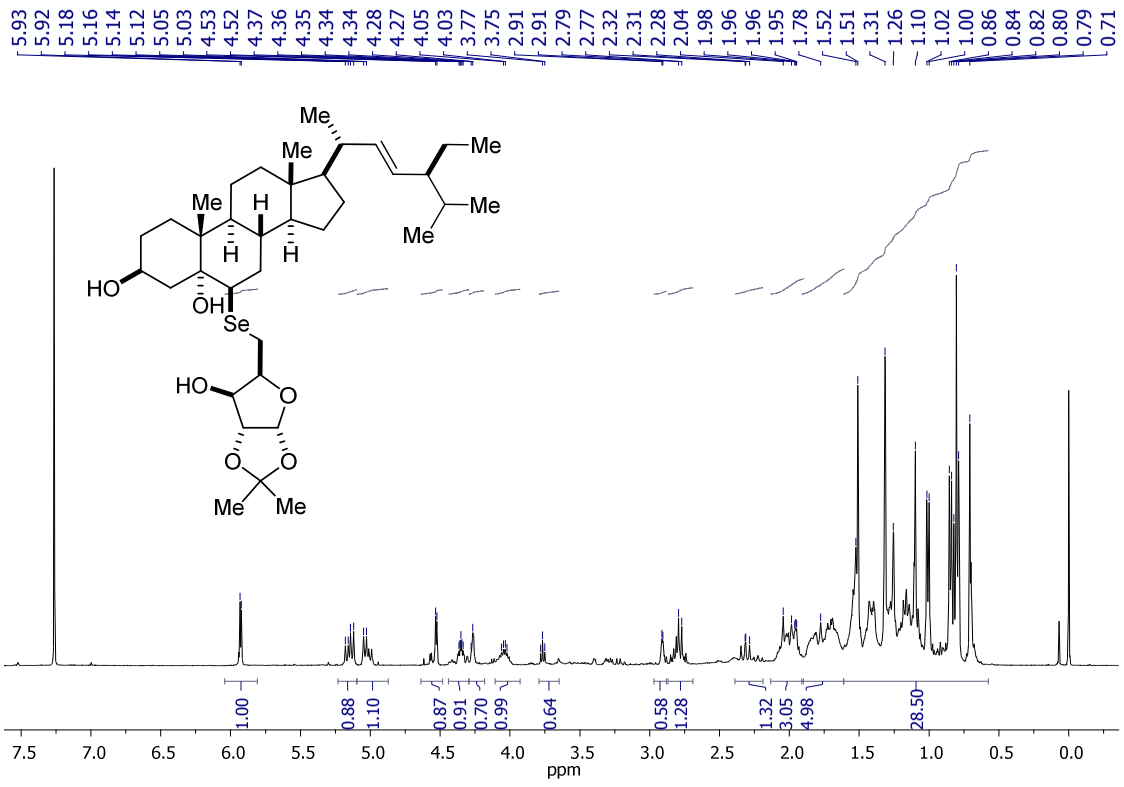


**Figure S66. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 16**

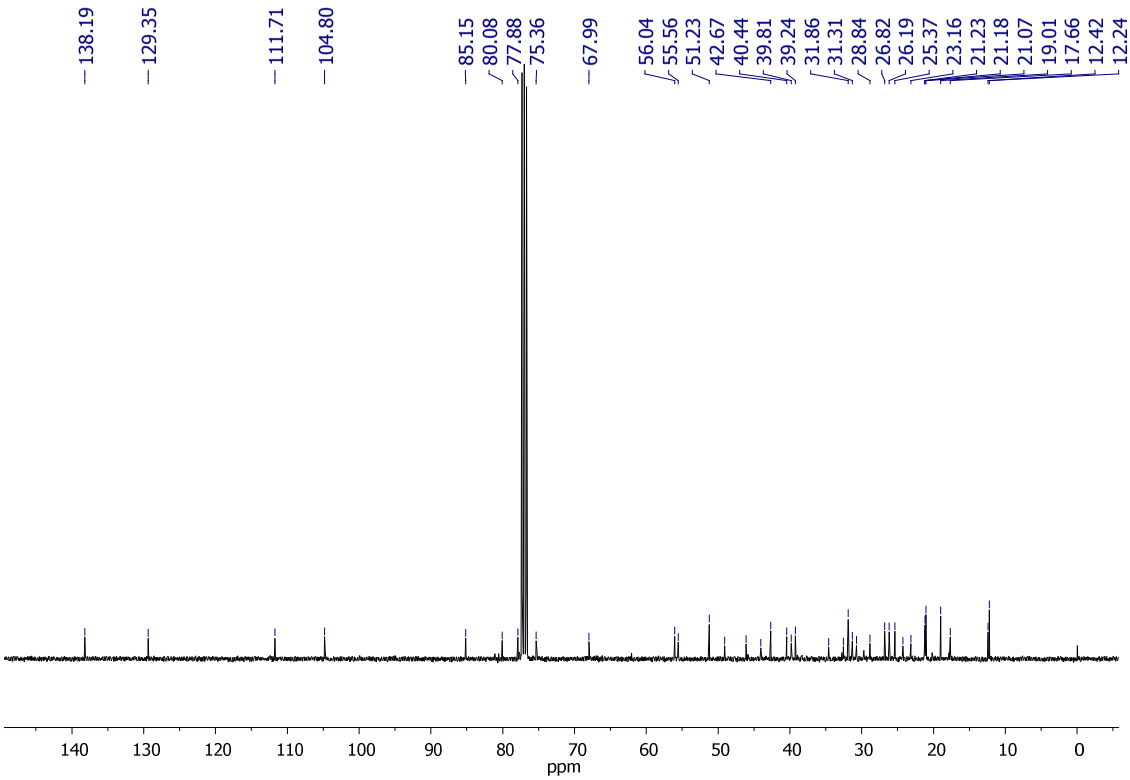


**Figure S67. $^{13}C$ NMR (101 MHz, $CDCl_3$) of compound 16**

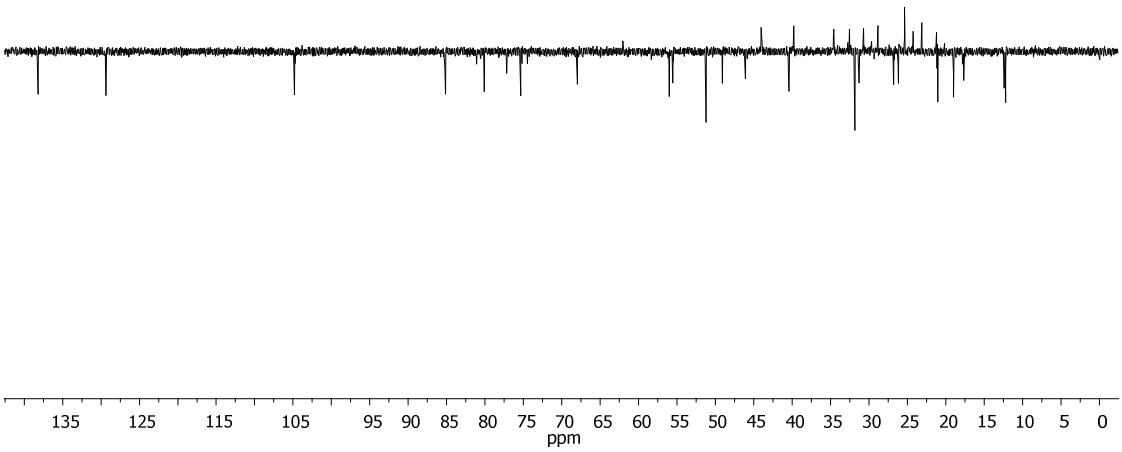


**Figure S68. $^{13}C$ DEPT-135 NMR (101 MHz, $CDCl_3$) of compound 16**

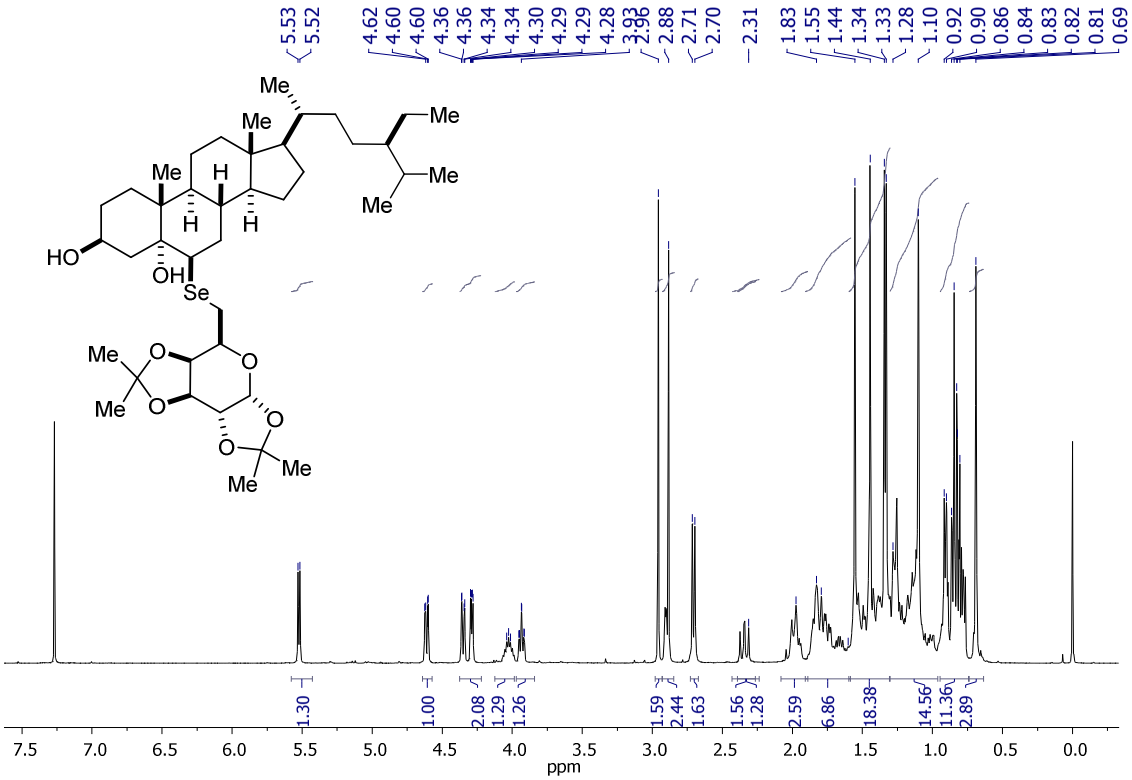


**Figure S69. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 17**

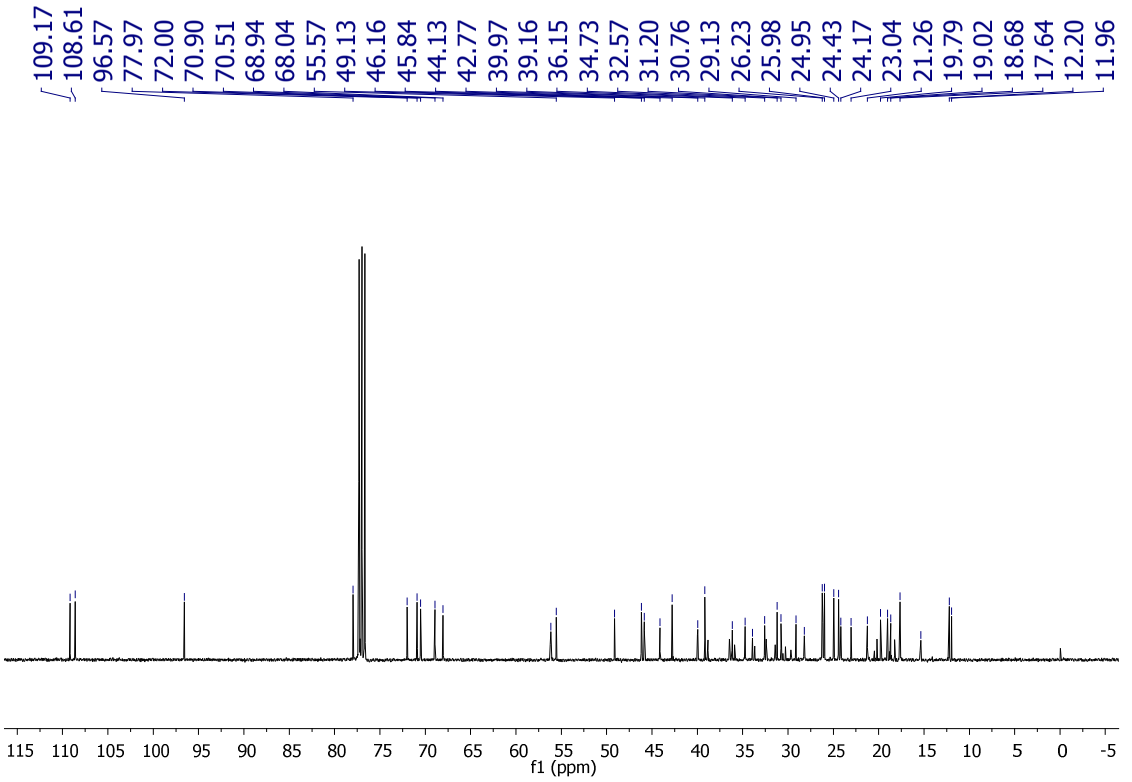


**Figure S70. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 17**

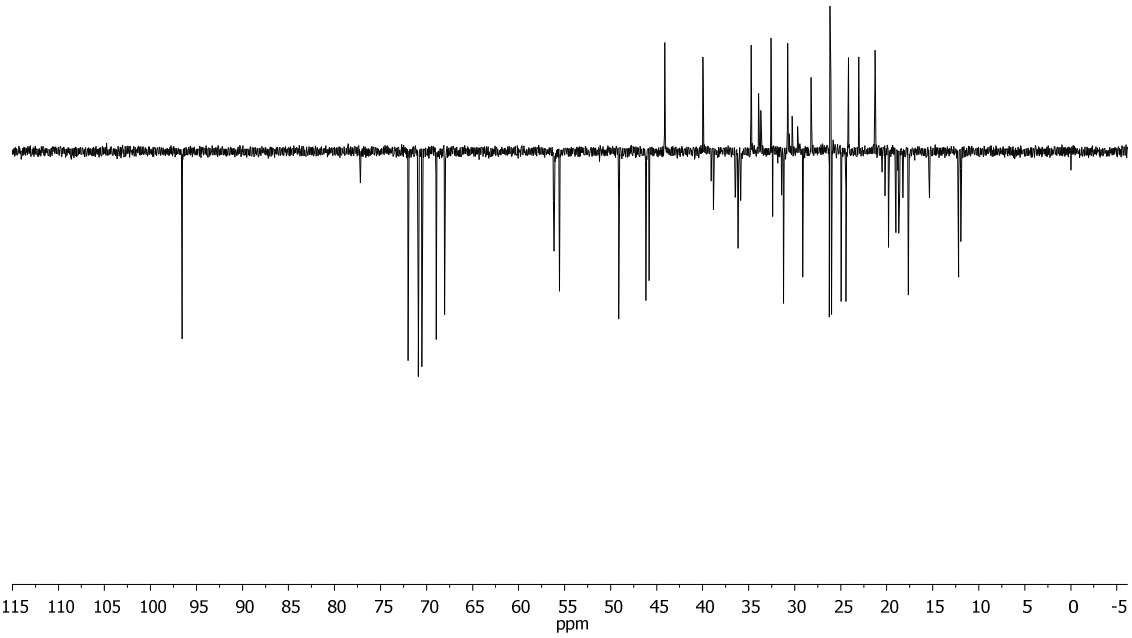


**Figure S71. $^{13}$C DEPT-135 NMR (101 MHz, $CDCl_3$) of compound 17**

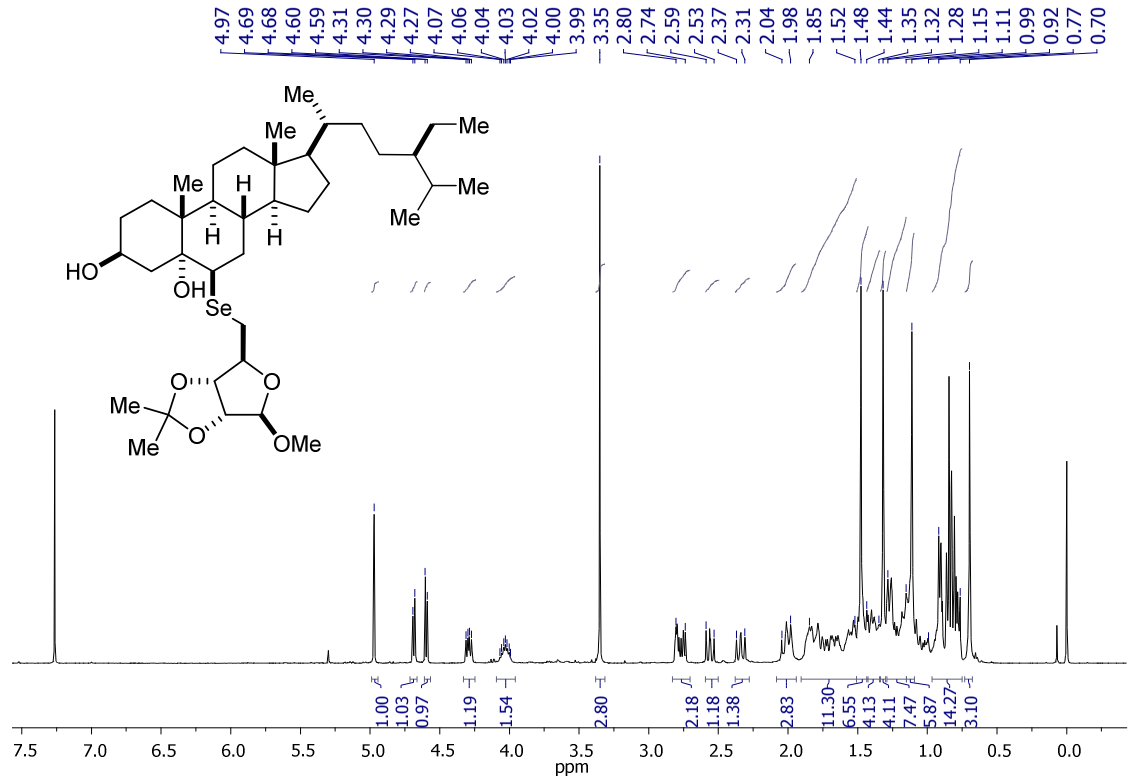


**Figure S72. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 18**

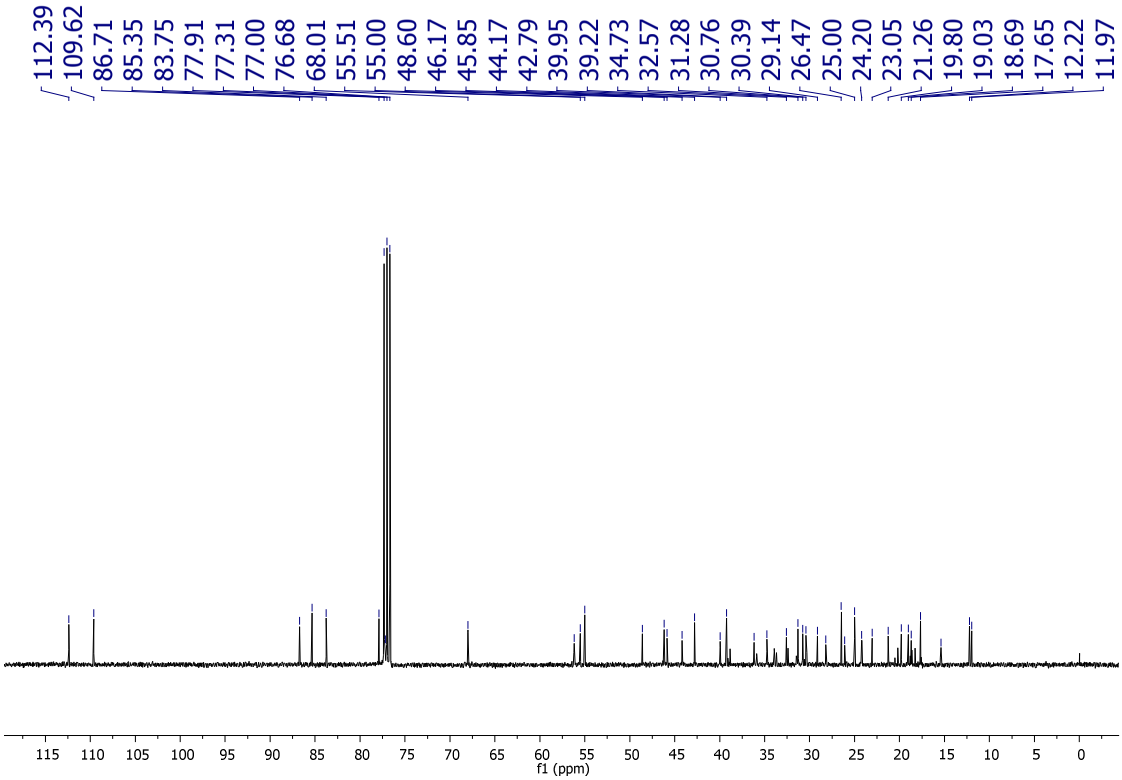


**Figure S73. $^{13}C$ NMR (101 MHz, $CDCl_3$) of compound 18**

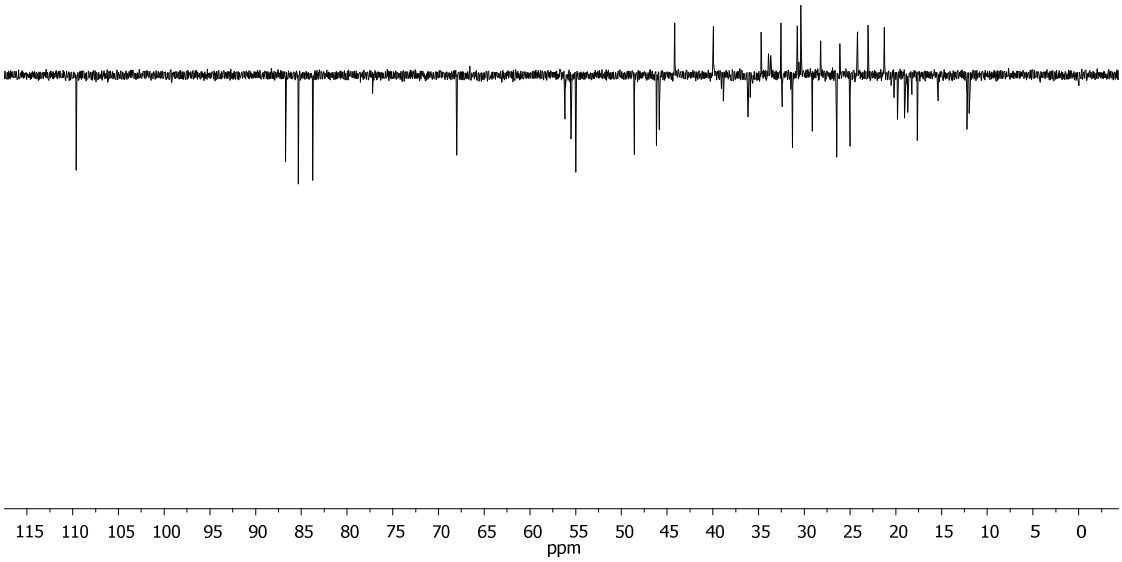


**Figure S74. $^{13}C$ DEPT-135 NMR (101 MHz, $CDCl_3$) of compound 18**

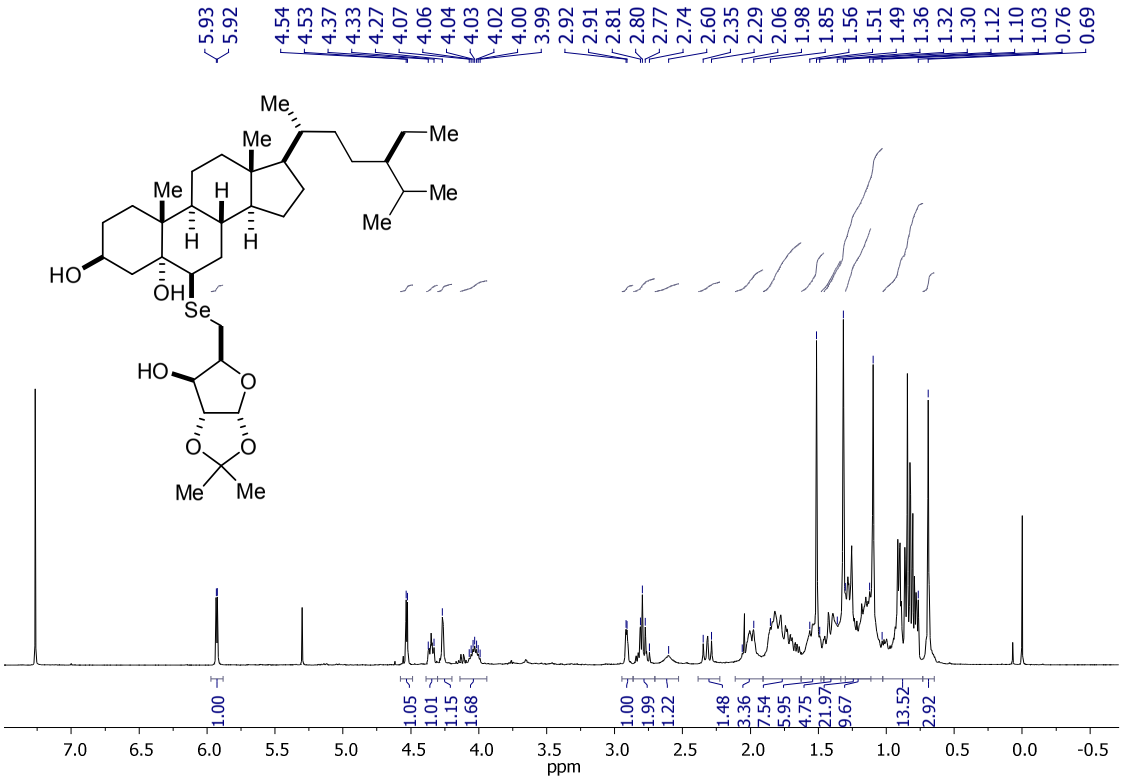


**Figure S75. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 19**

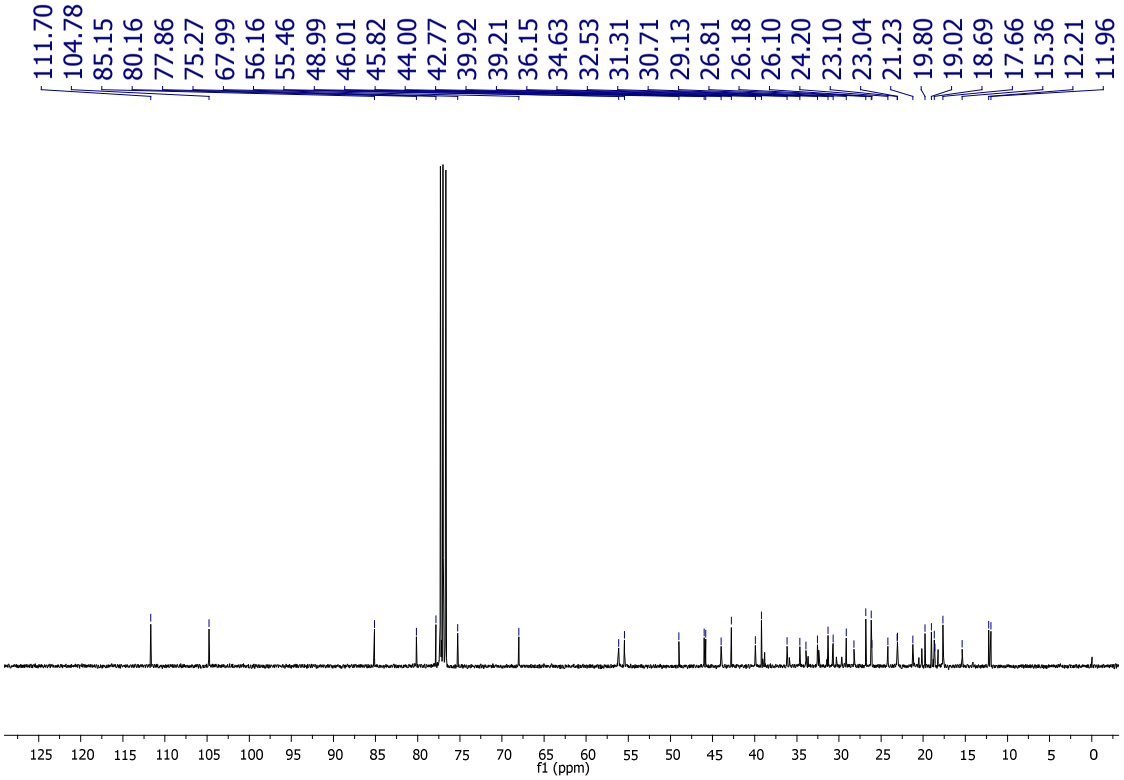


**Figure S76. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 19**

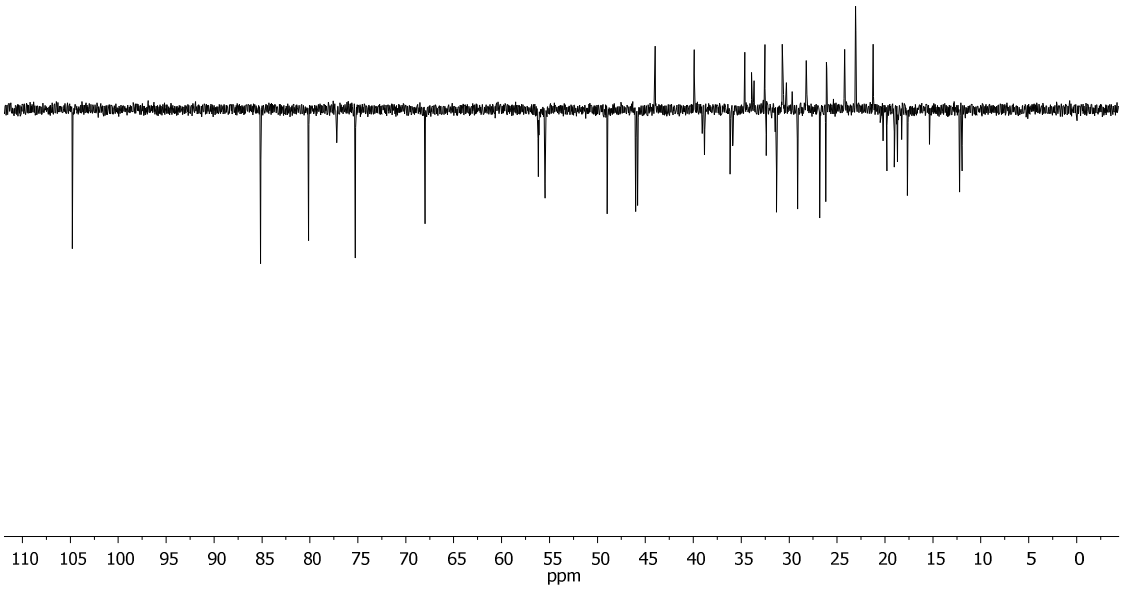


**Figure S77. $^{13}$C DEPT-135 NMR (101 MHz, $CDCl_3$) of compound 19**

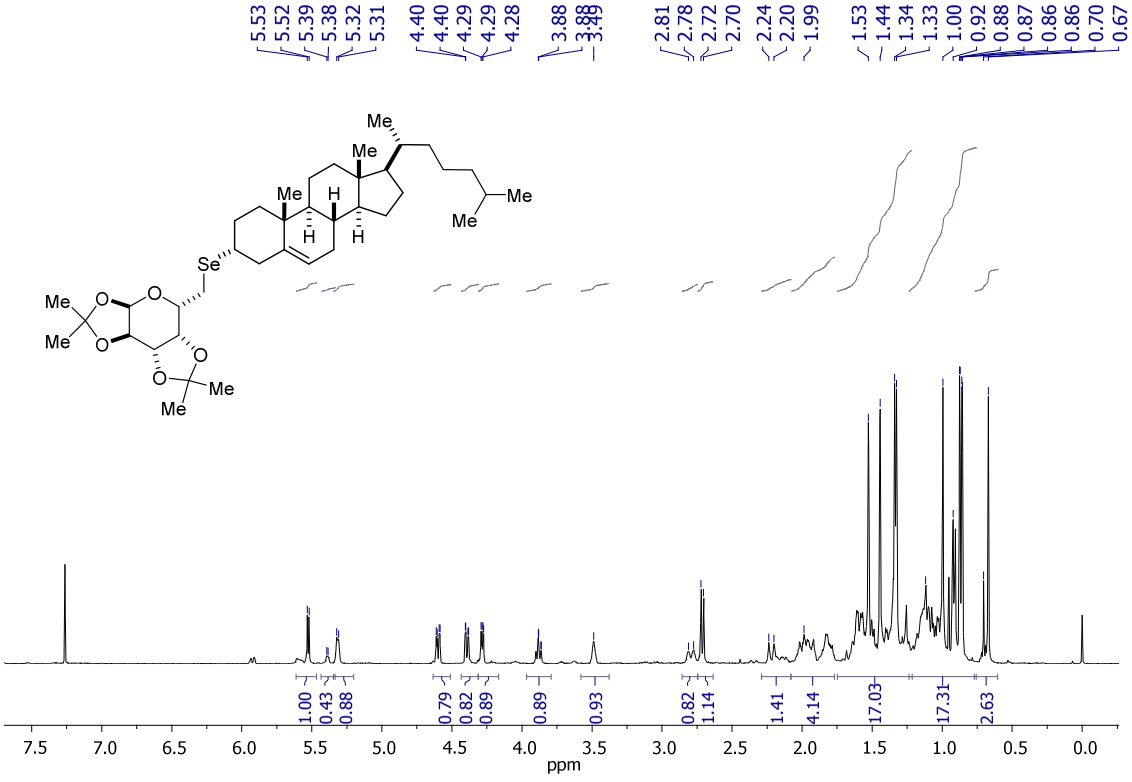


**Figure S78. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 22**

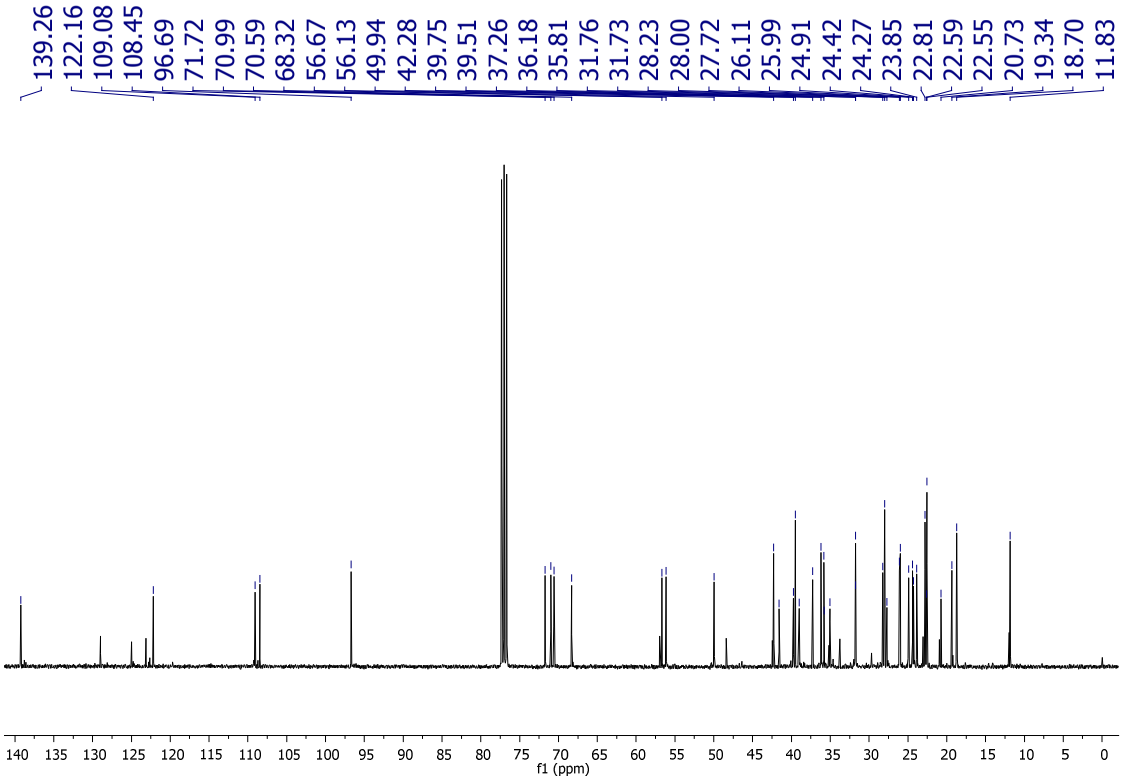


**Figure S79. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 22**

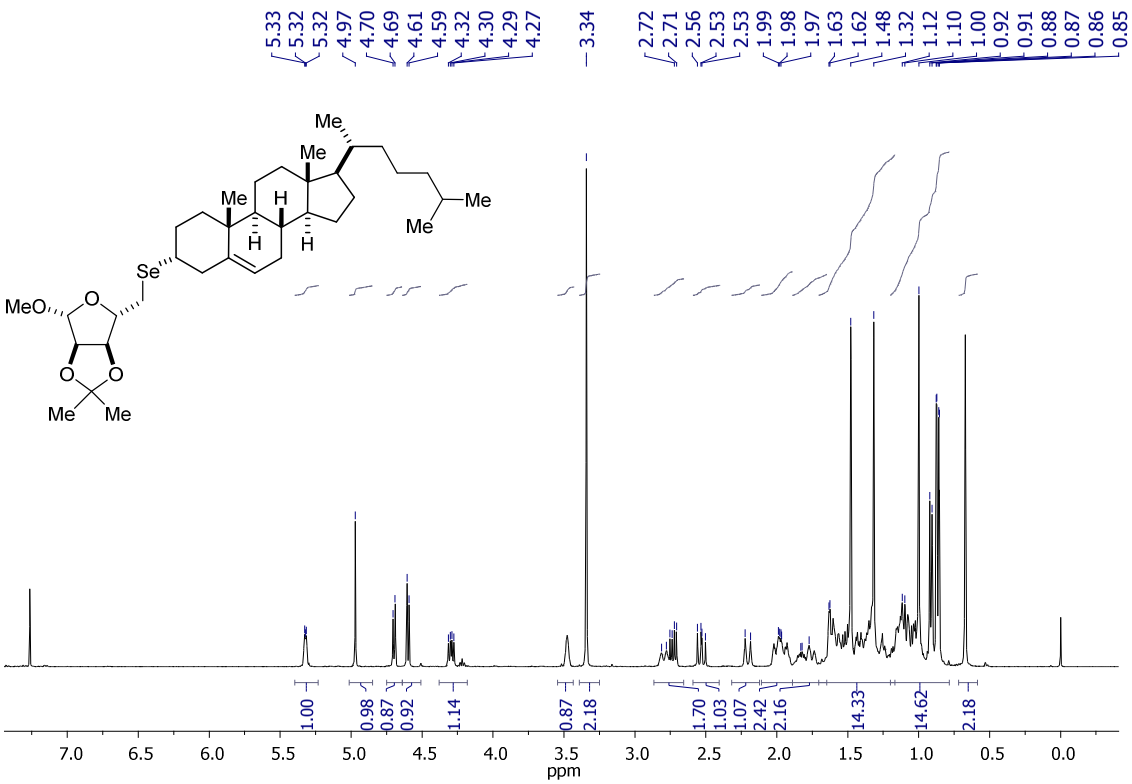


**Figure S80. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 23**

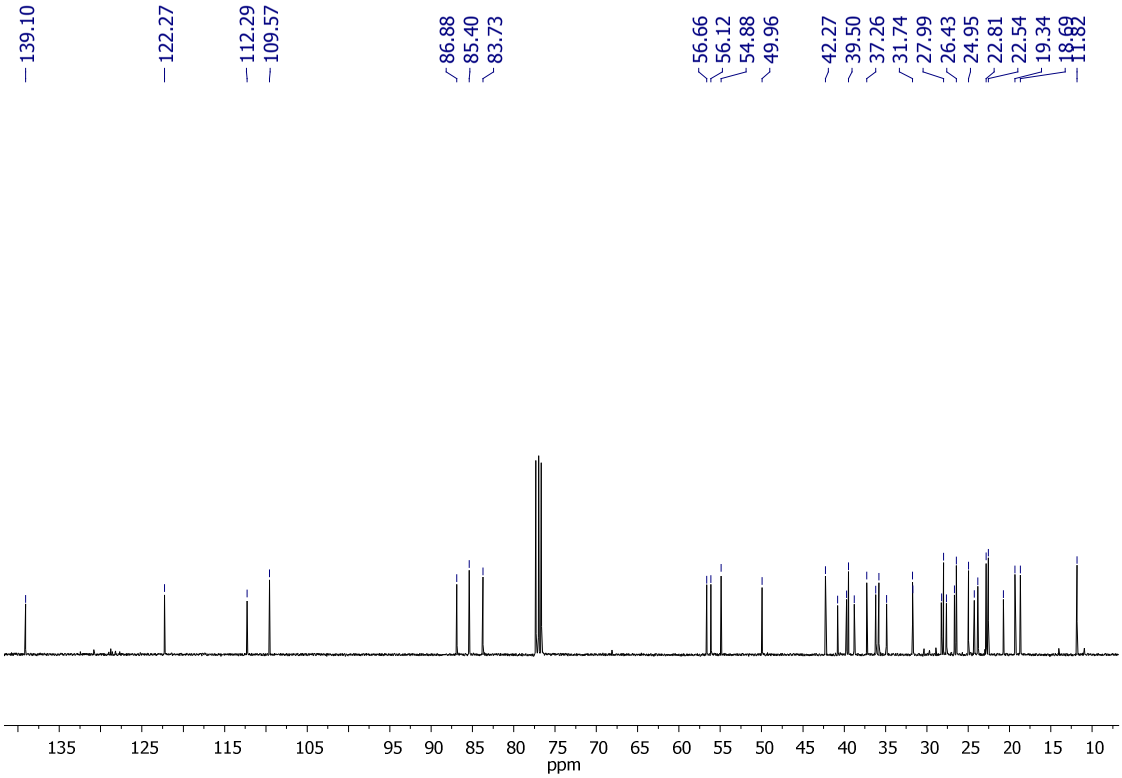


**Figure S81. $^{13}C$ NMR(101 MHz, $CDCl_3$) of compound 23**

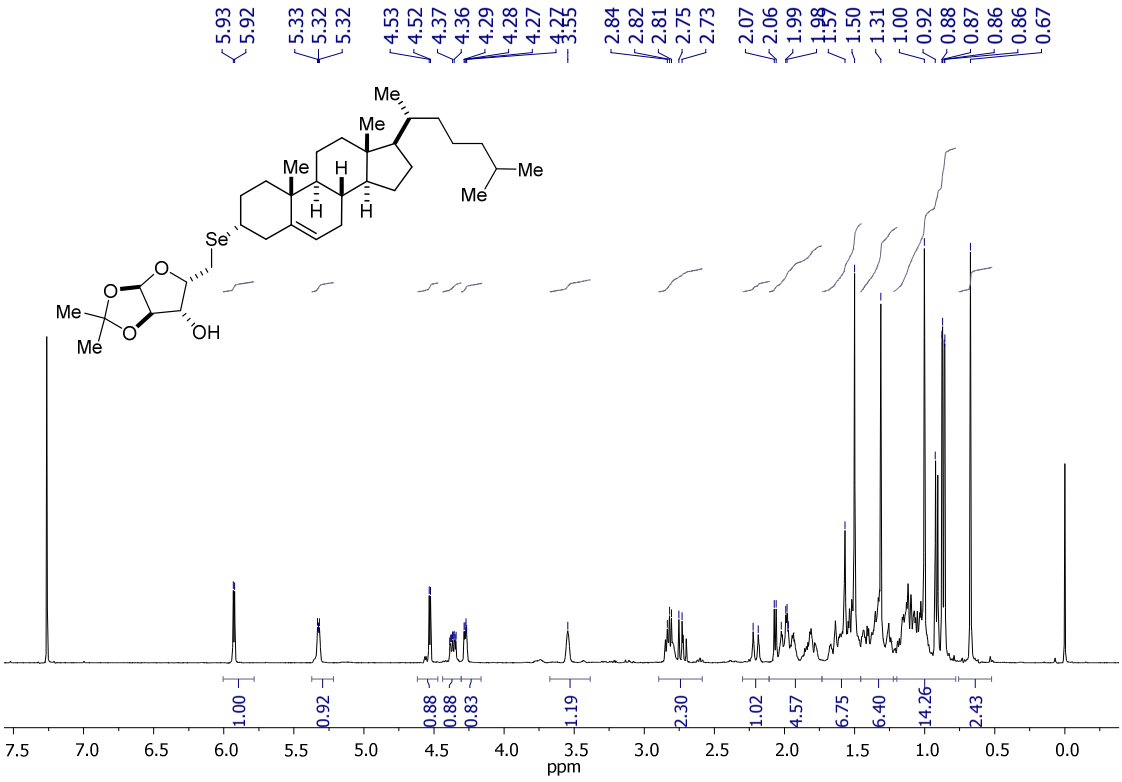


**Figure S82. $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound 24**

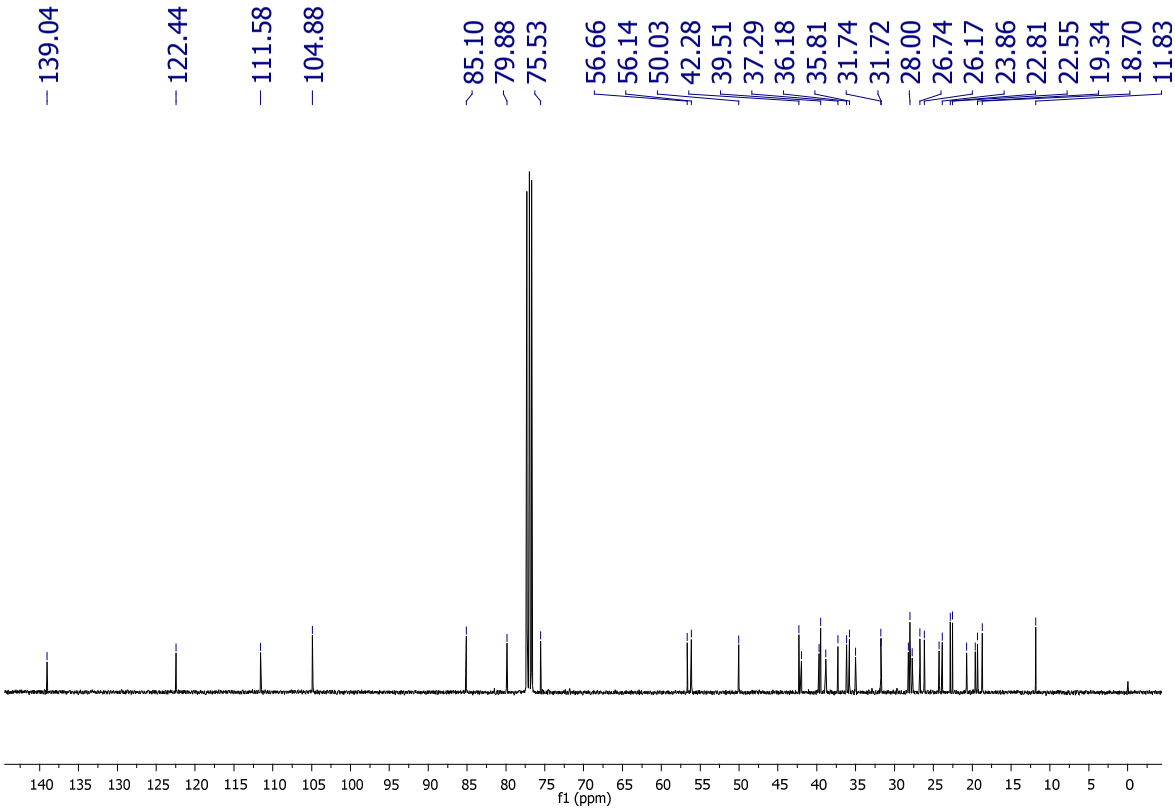


**Figure S83. $^{13}C$ NMR (101 MHz, $CDCl_3$) of compound 24**

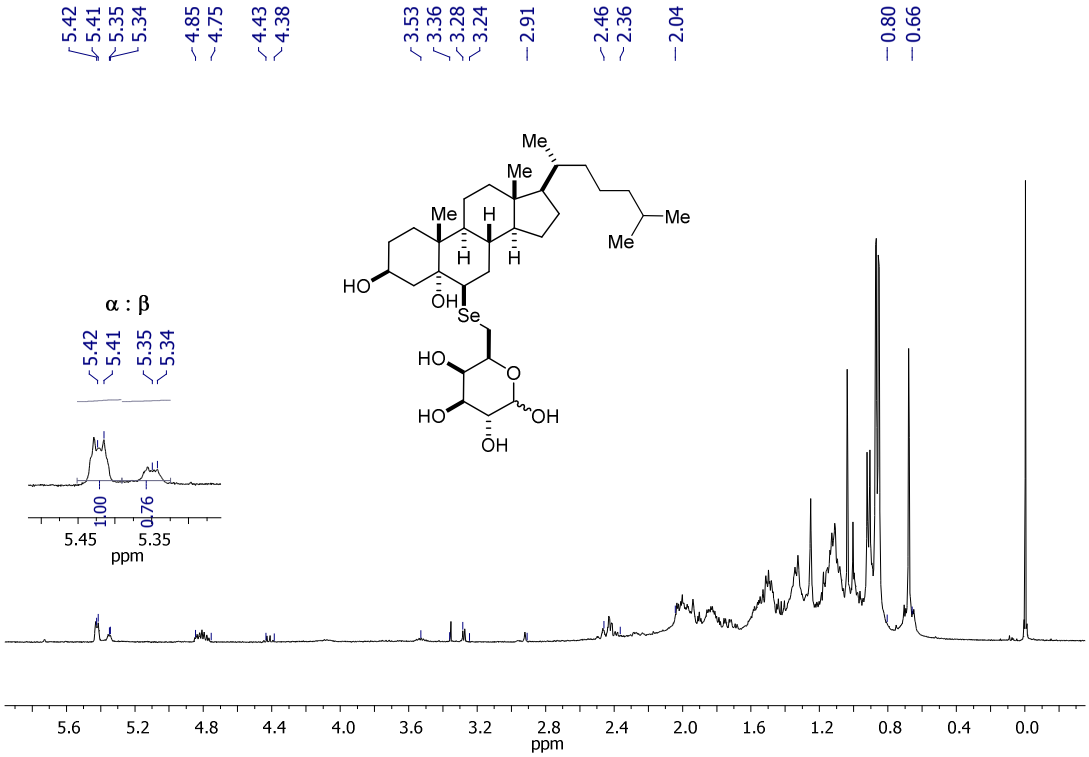


**Figure S84. $^{1}H$ NMR(400 MHz, $CDCl_3$) of compound 26**

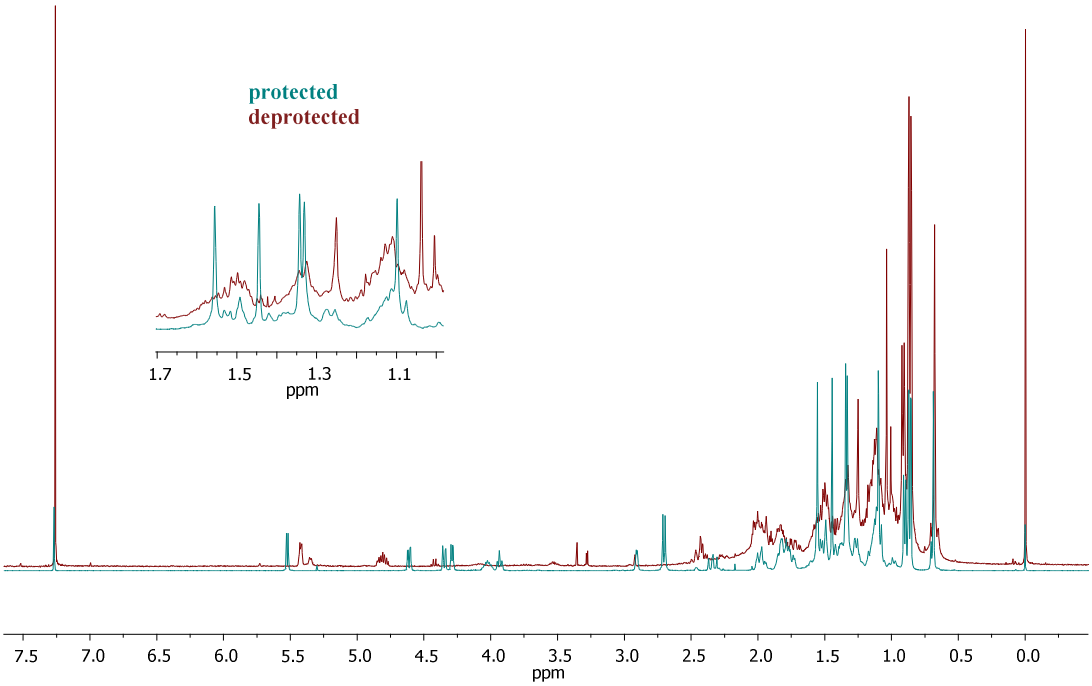


**Figure S85. $^{1}$H NMR (400 MHz, $CDCl_3$) comparison of compounds 6a (protected) and 26 (deprotected)**

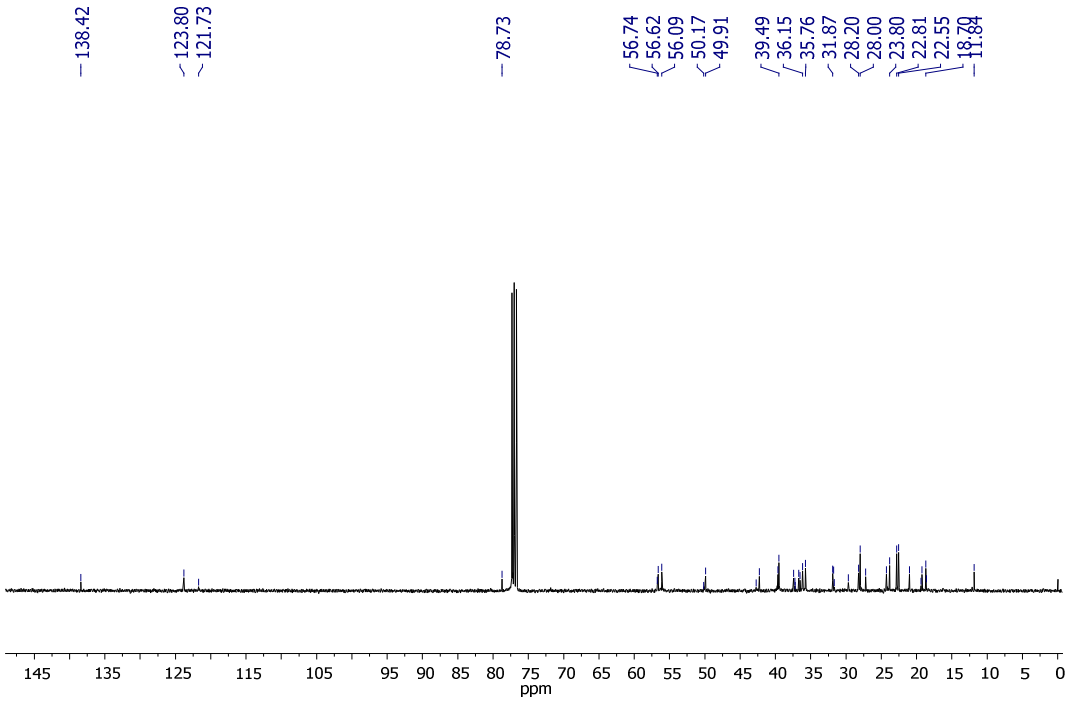


**Figure S86. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 26**

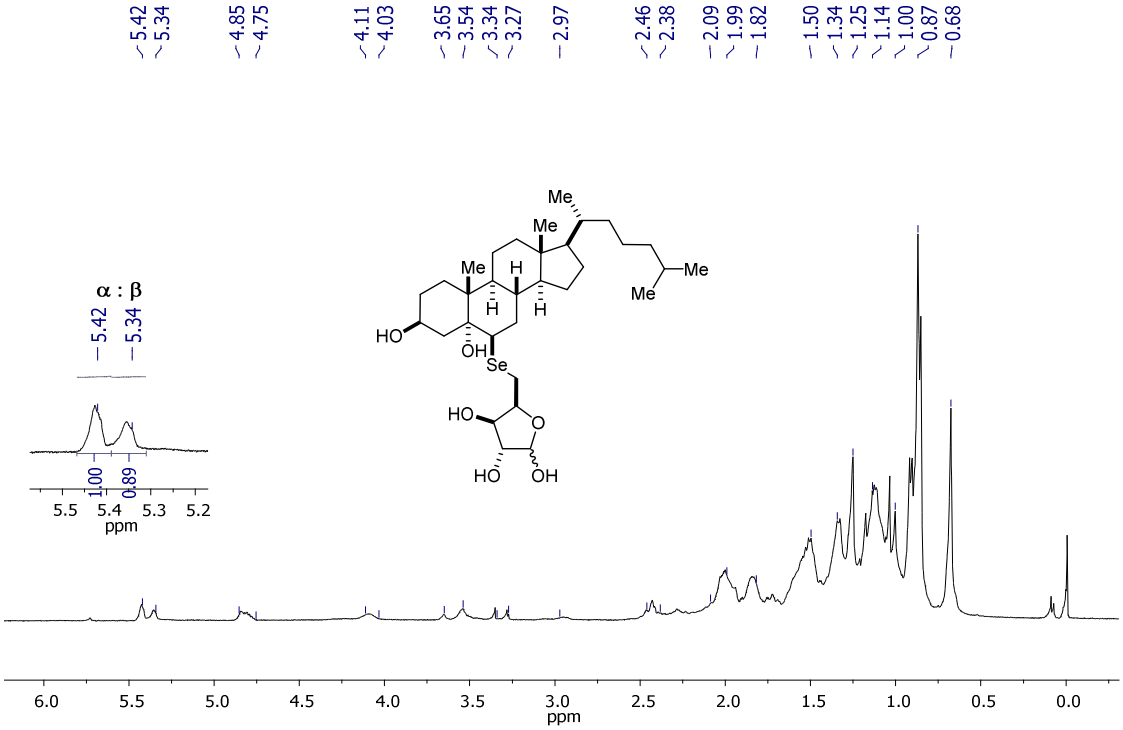


**Figure S87. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 27**

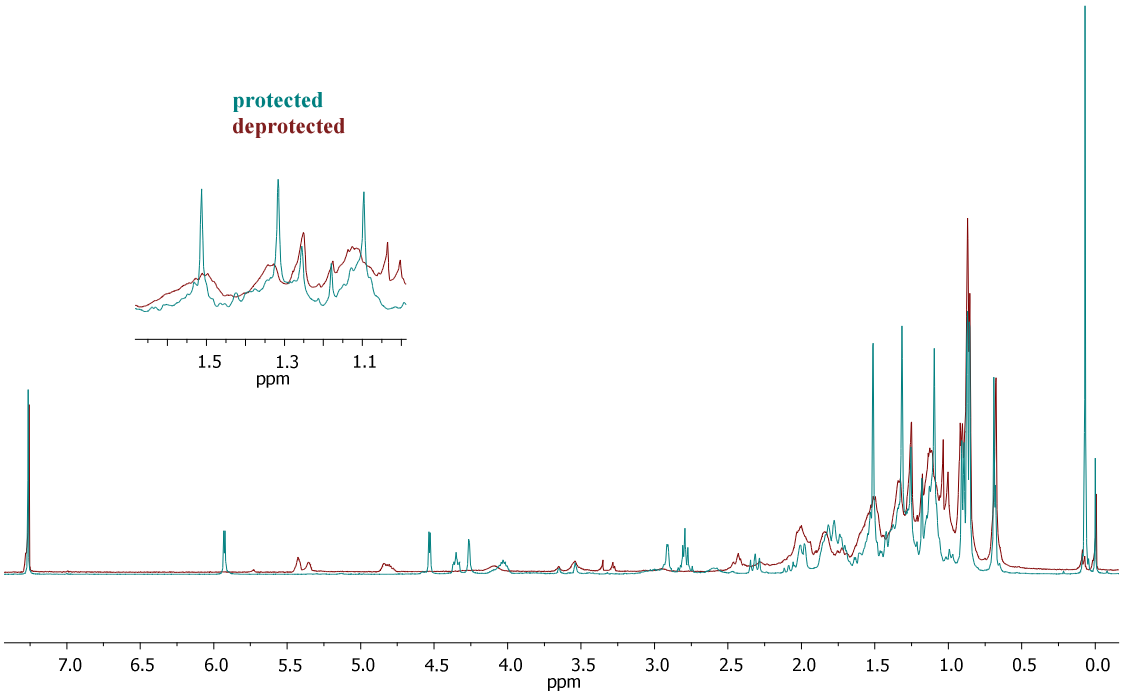


**Figure S88. $^{1}$H NMR (400 MHz, $CDCl_3$) comparison of compounds 7a (protected) and 27 (deprotected)**

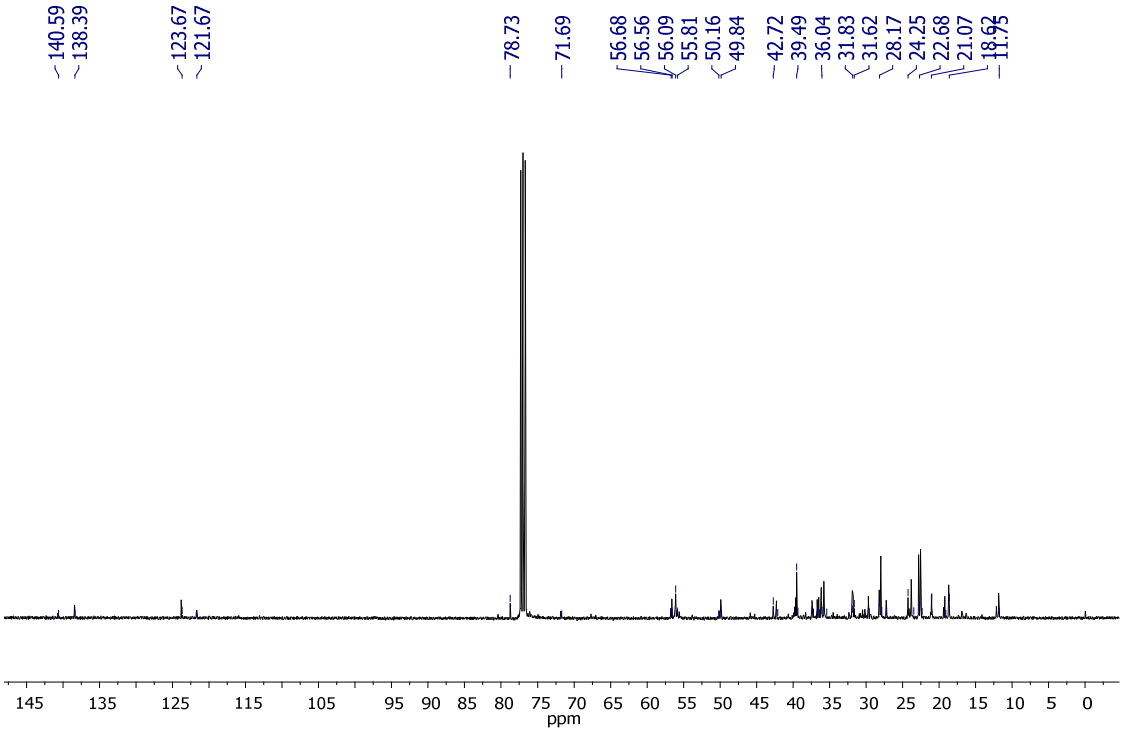


**Figure S89. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 27**

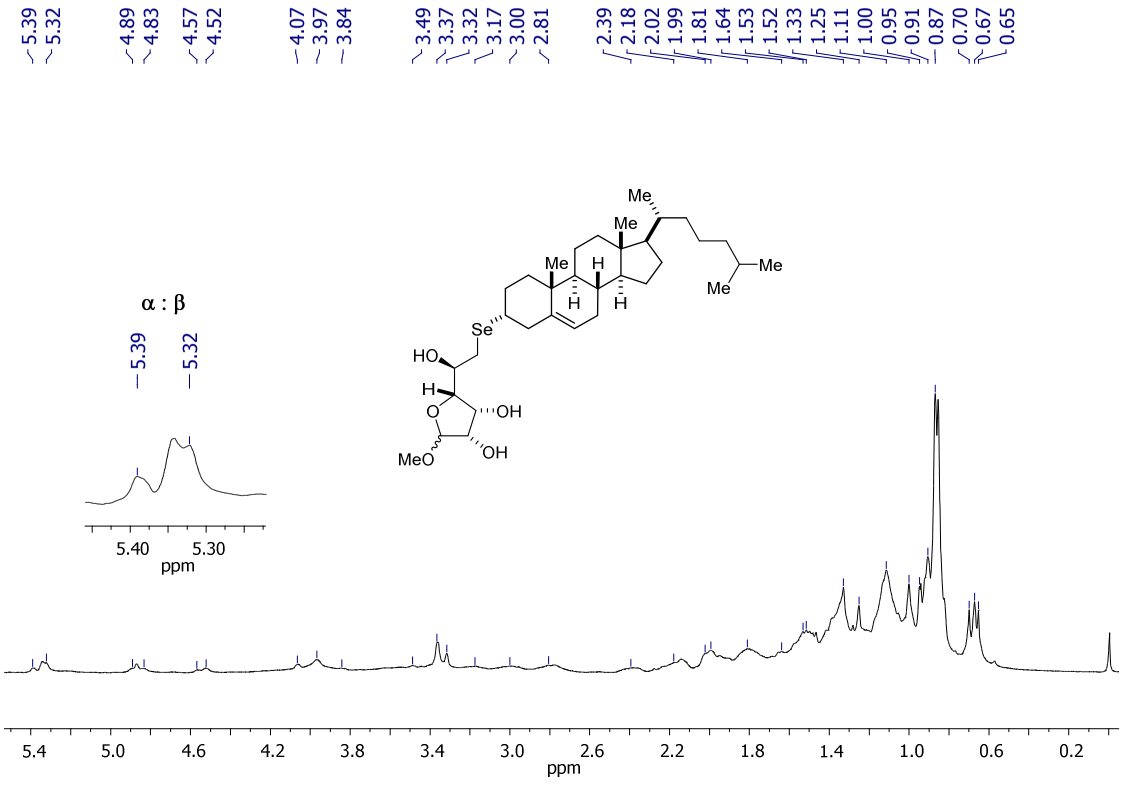


**Figure S90. $^{1}$H NMR (400 MHz, $CDCl_3$) of compound 28**

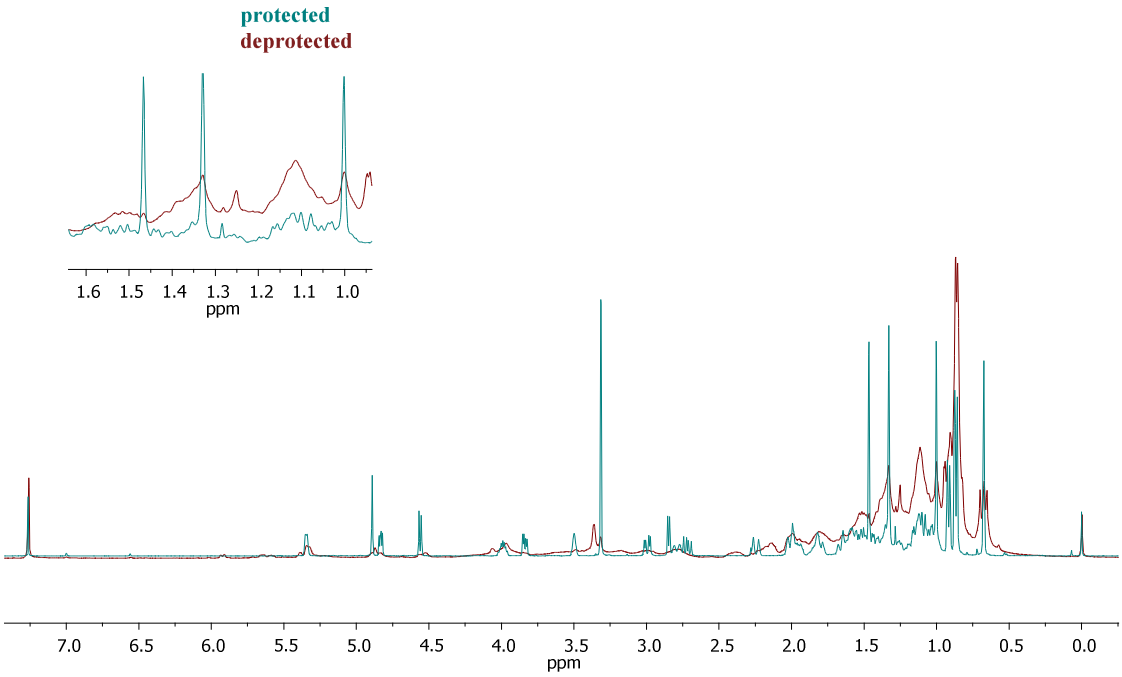


**Figure S91. $^{1}$H NMR (400 MHz, $CDCl_3$) comparison of compounds 25 (protected) and 28 (deprotected)**

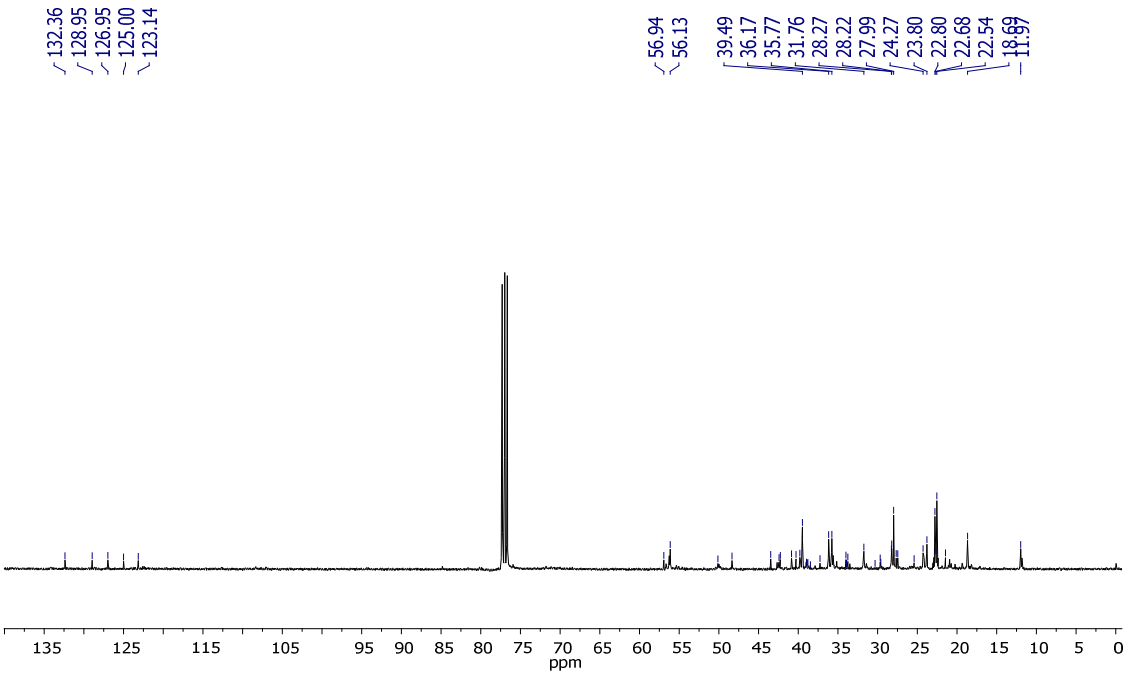


**Figure S92. $^{13}$C NMR (101 MHz, $CDCl_3$) of compound 28**