SUPPORTING INFORMATION

Semisynthesis and biological evaluation of a focused library of unguinol derivatives as next-generation antibiotics

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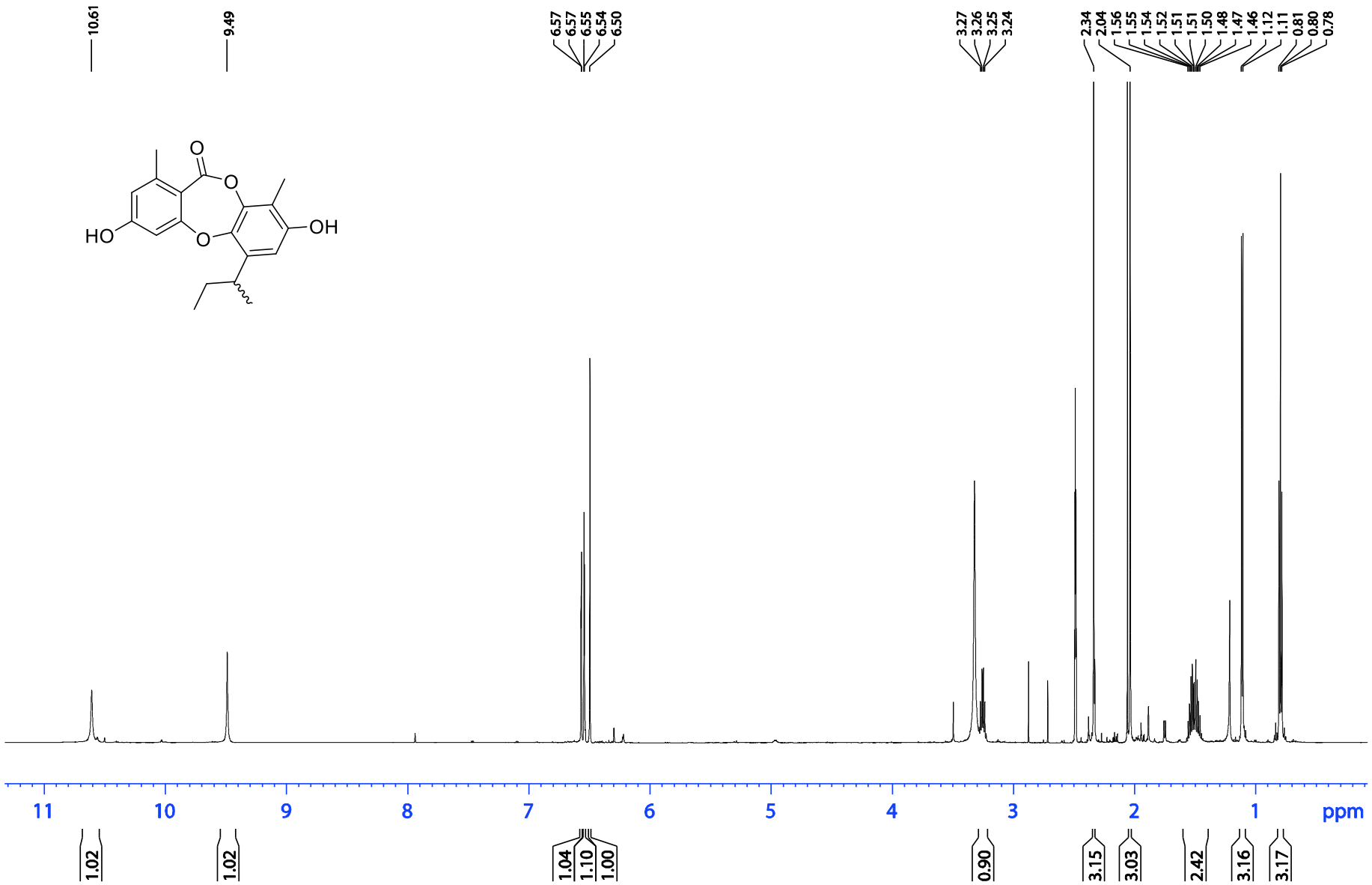

Figure S1. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 1′,2′-dihydrounguinol (**2a**)

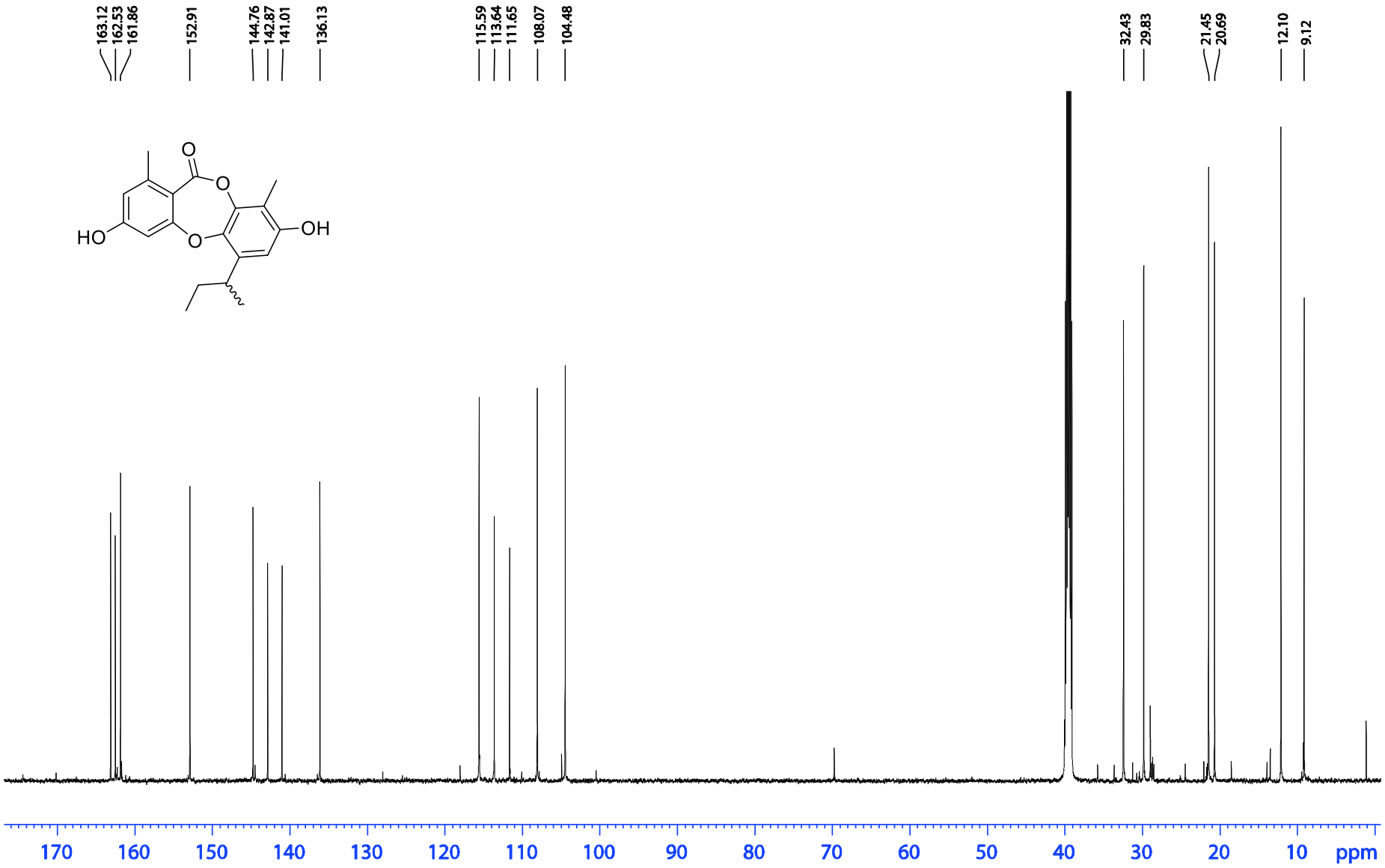

Figure S2. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 1′,2′-dihydrounguinol (**2a**)

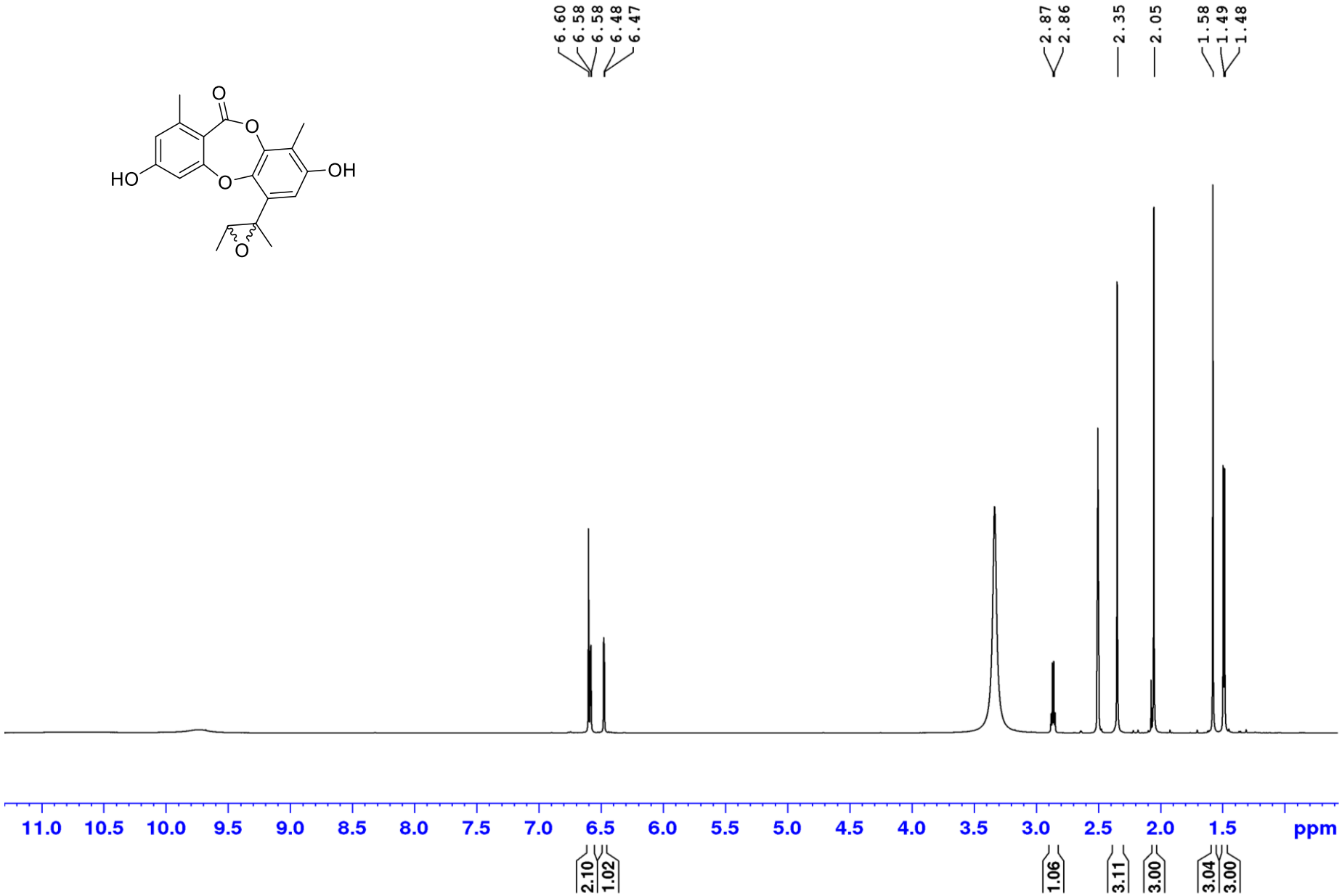

Figure S3. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of *cis*-1′,2′-epoxyunguinol (**2b**)

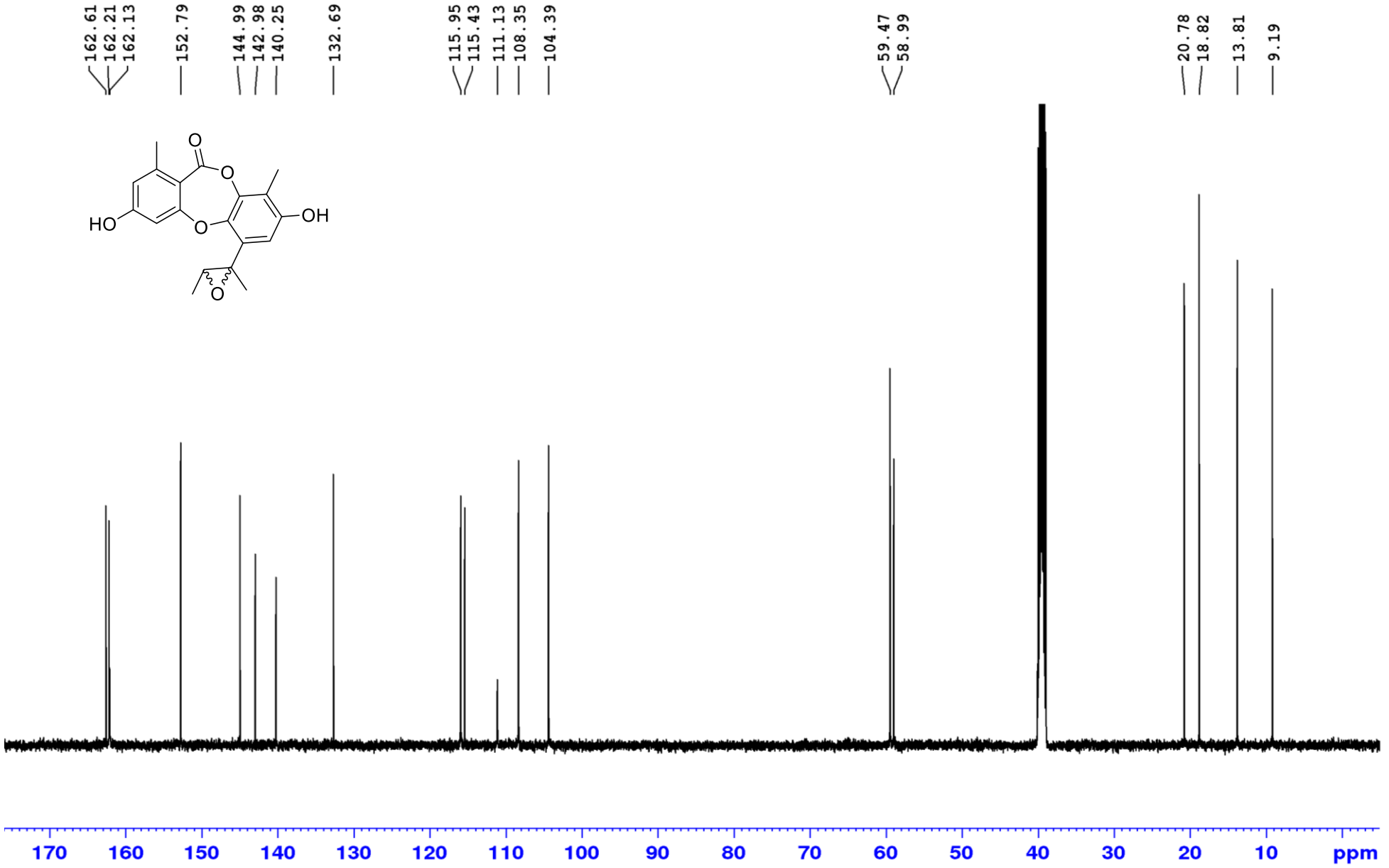

Figure S4. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of *cis*-1′,2′-epoxyunguinol (**2b**)

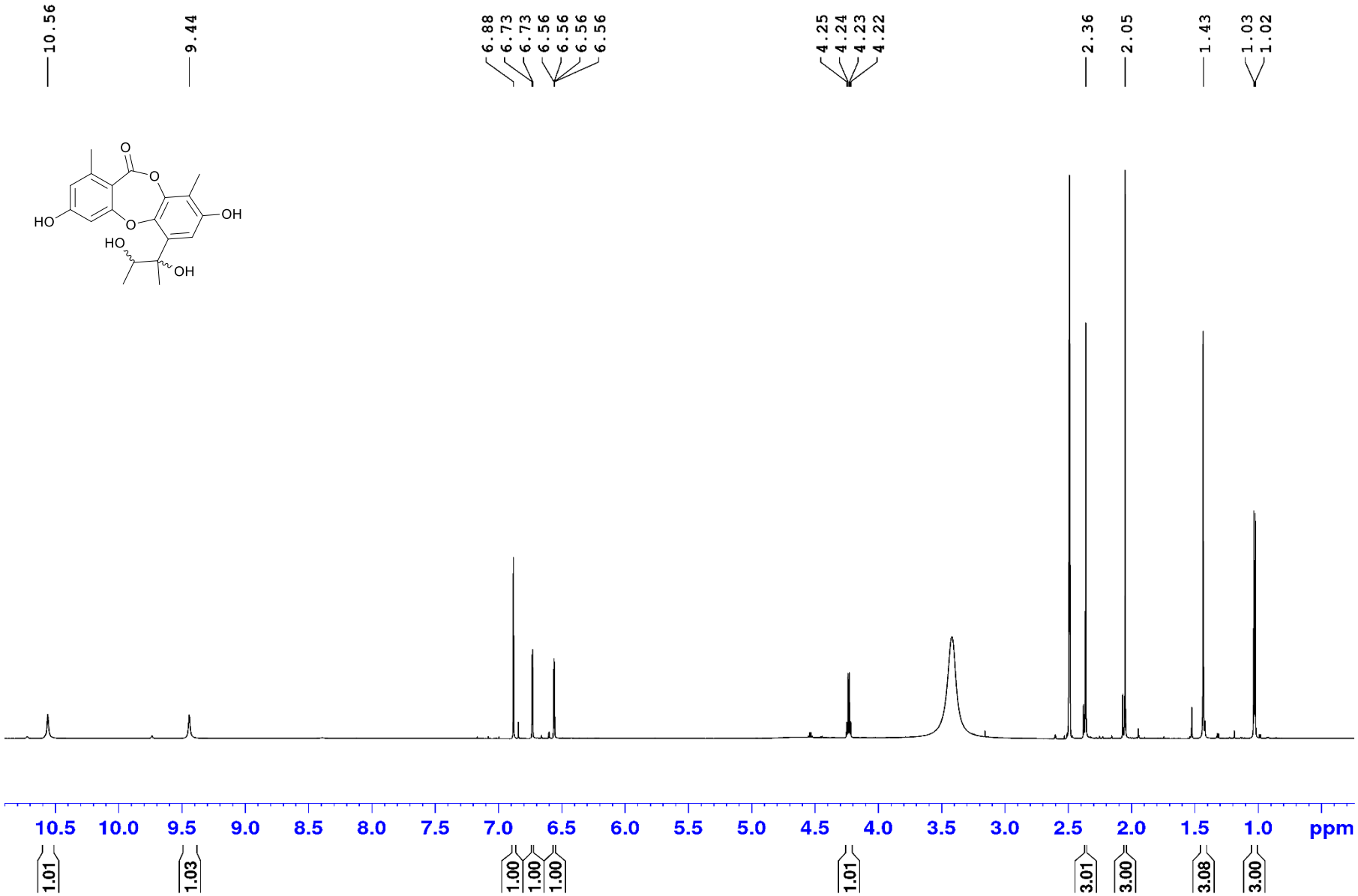

Figure S5. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 1′,2′-dihydroxyunguinol (**2c**)

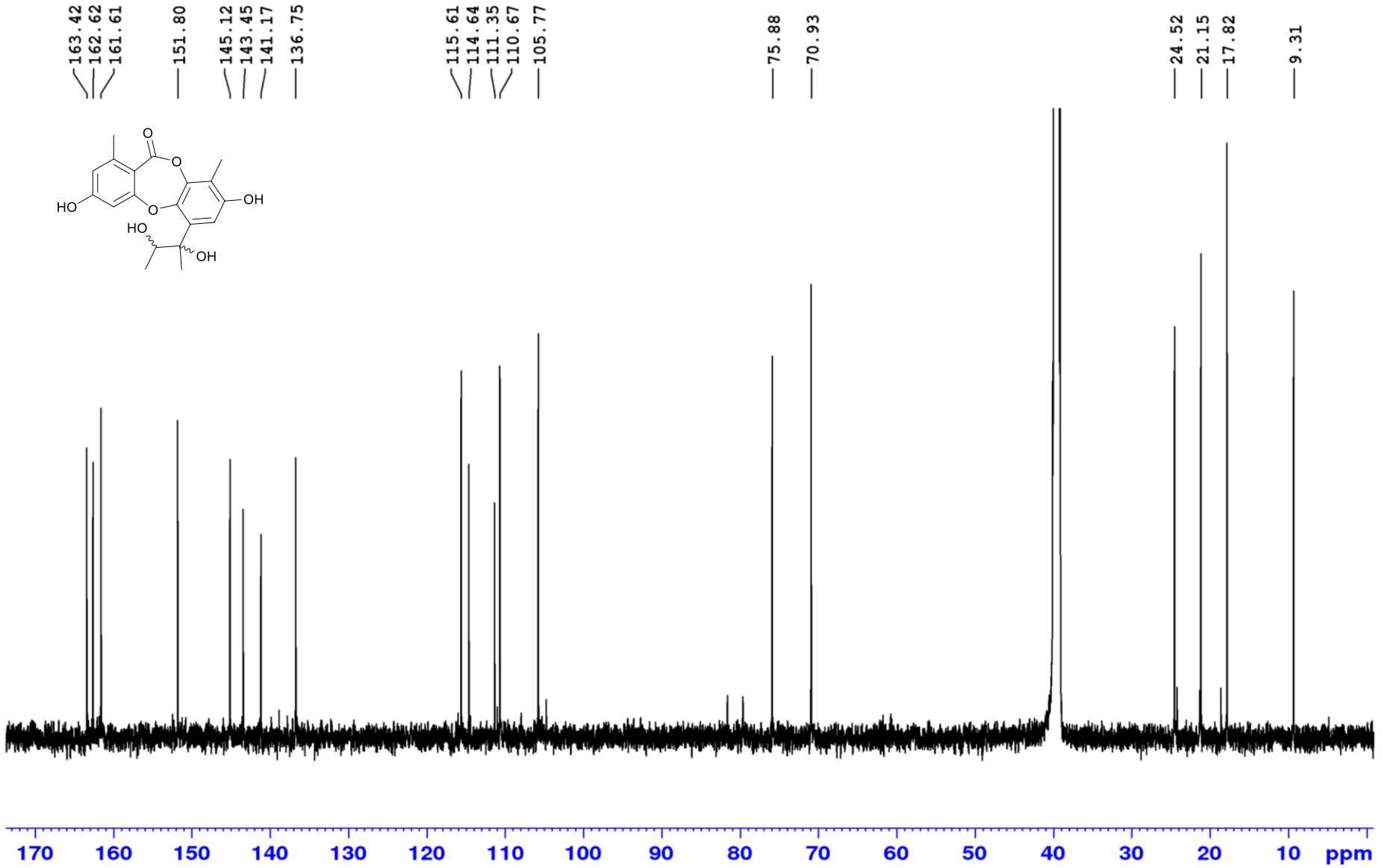

Figure S6. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 1′,2′-dihydroxyunguinol (**2c**)

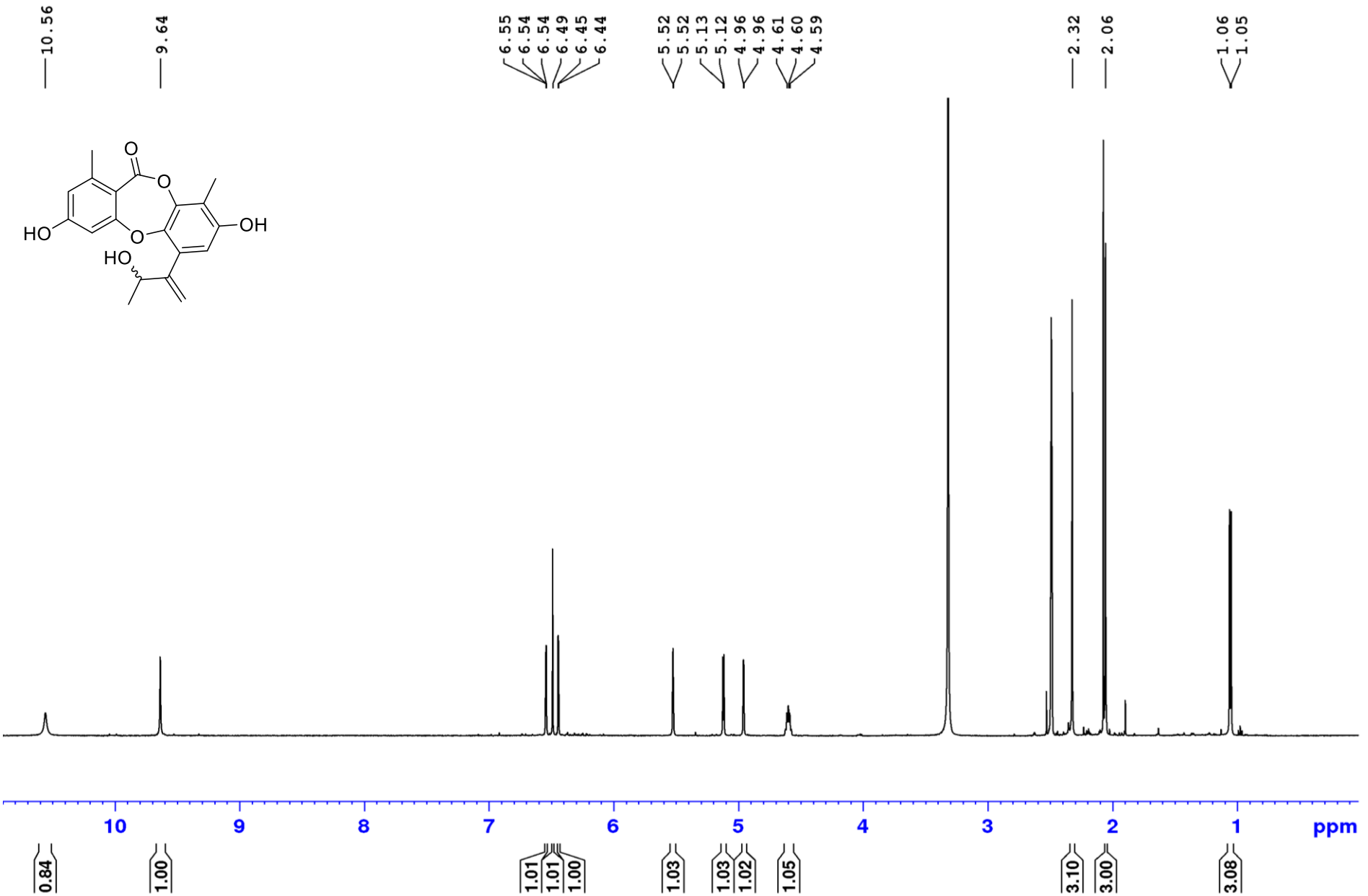

Figure S7. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of 2′-hydroxy-$\Delta^{1',4'}$-unguinol (**2d**)

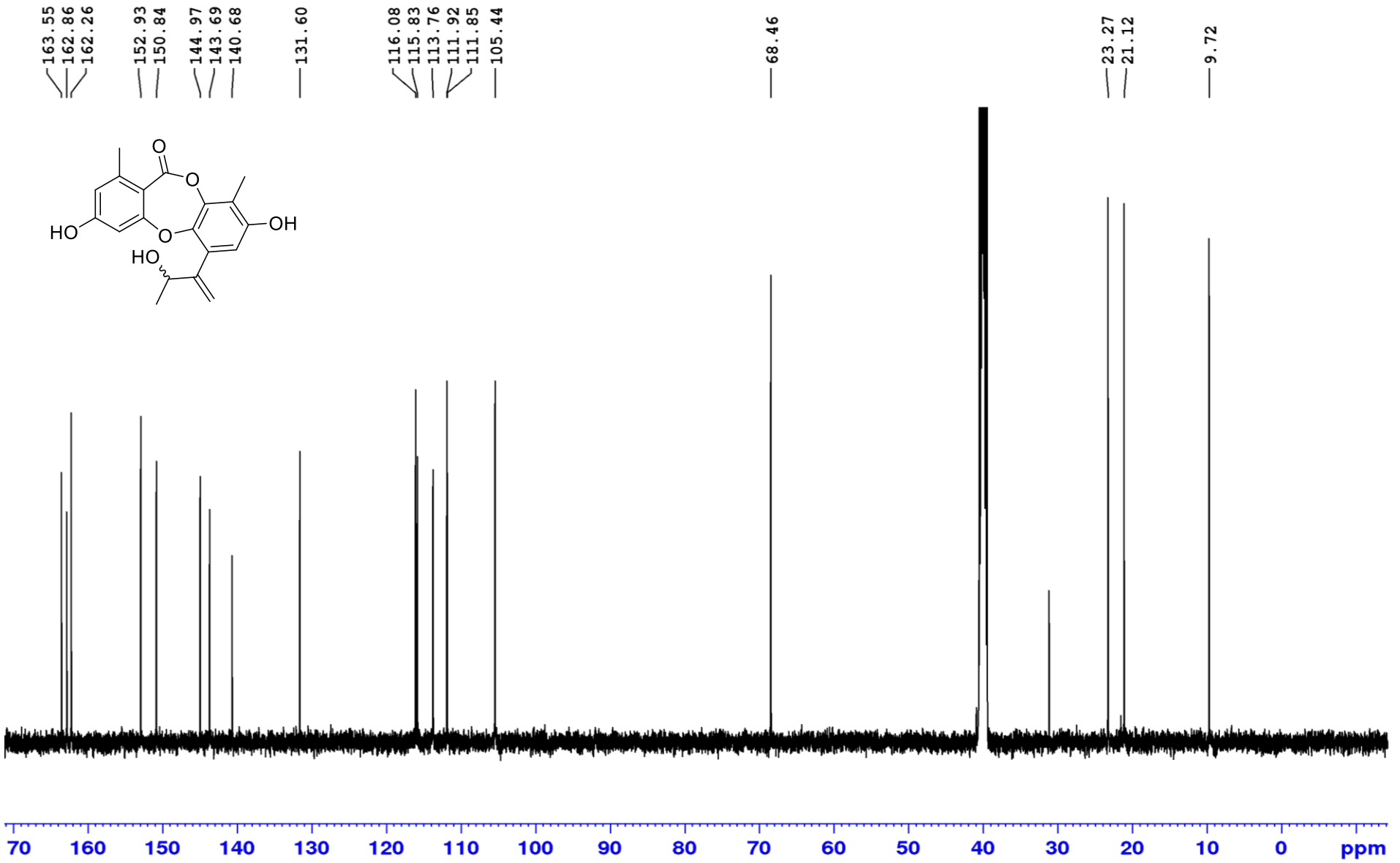

Figure S8. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of 2′-hydroxy-$\Delta^{1',4'}$-unguinol (**2d**)

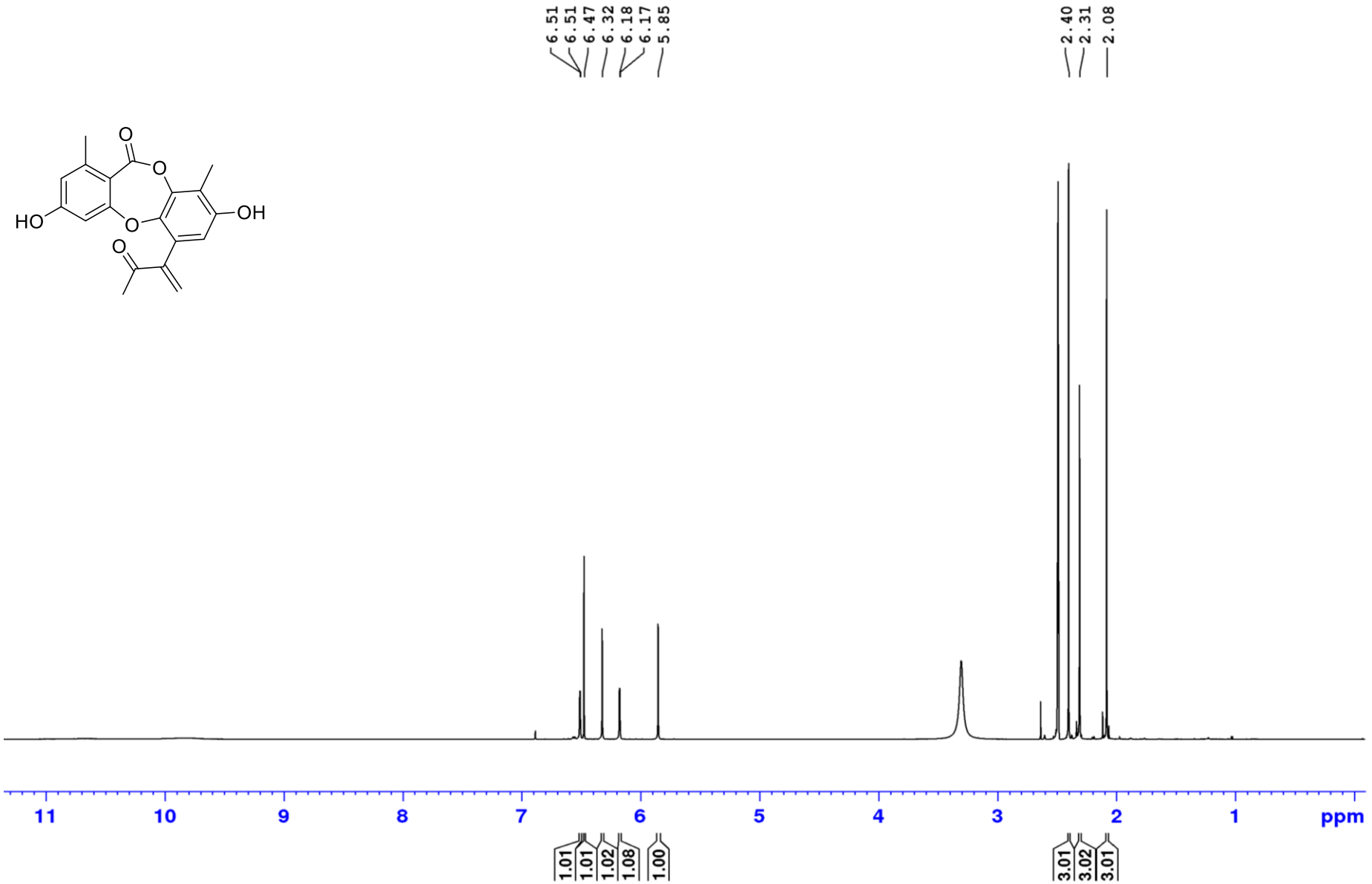

Figure S9. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2′-oxo-$\Delta^{1',4'}$-unguinol (**2e**)

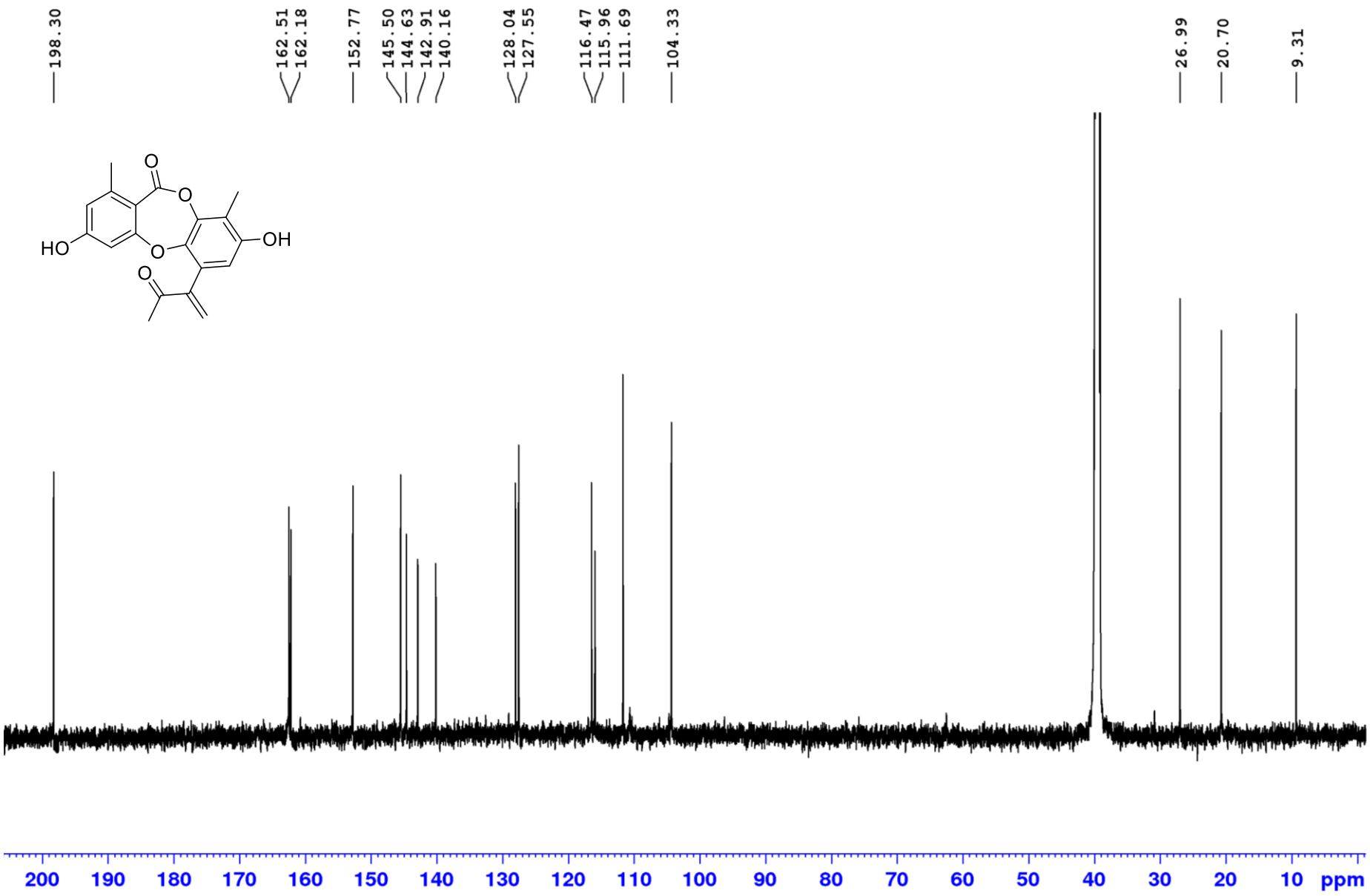

Figure S10. ^{1}H NMR spectrum (150 MHz, DMSO-d_6) of 2′-oxo-$\Delta^{1',4'}$-unguinol (**2e**)

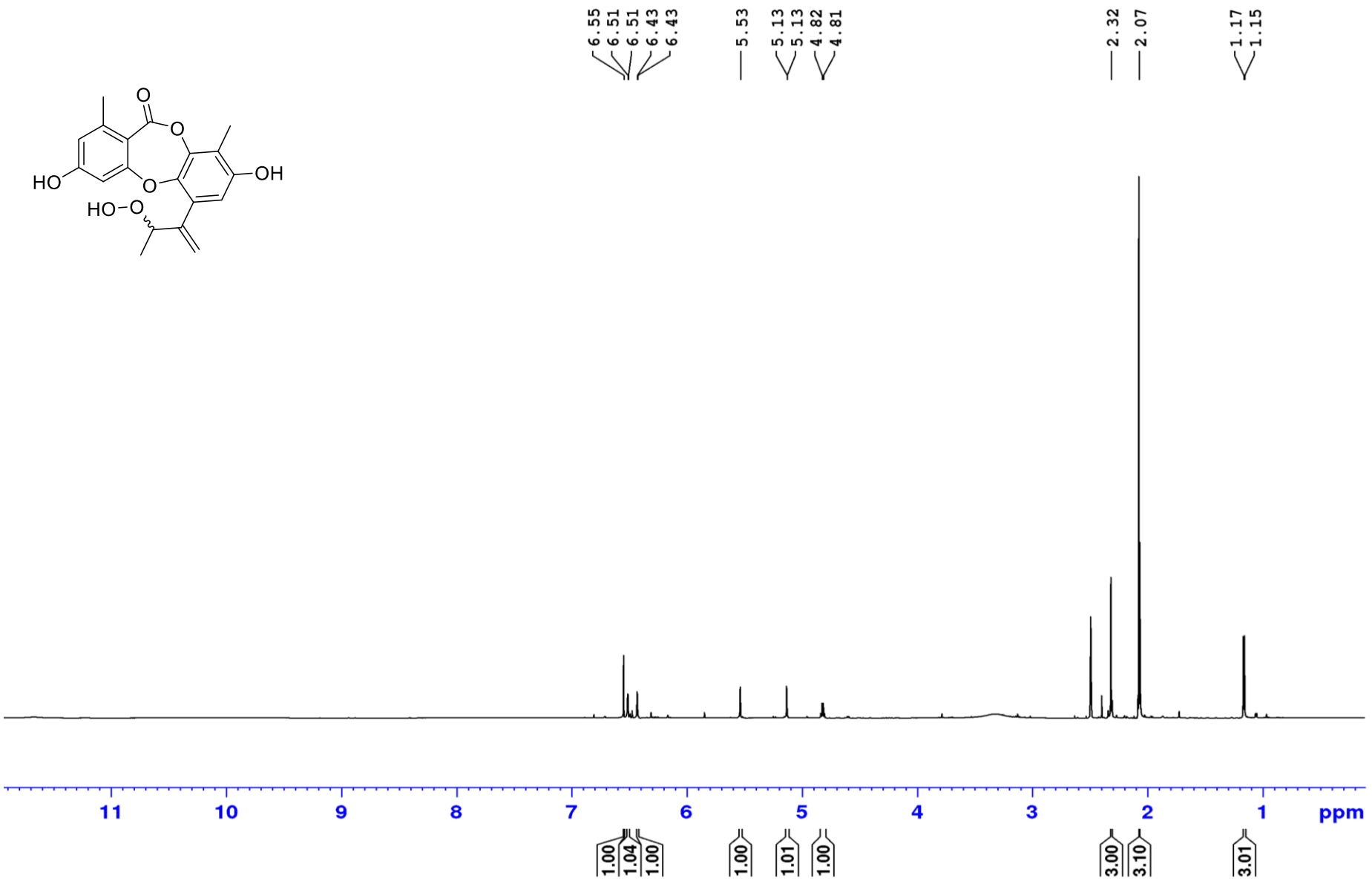

Figure S11. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2′-hydroperoxy-$\Delta^{1',4'}$-unguinol (**2f**)

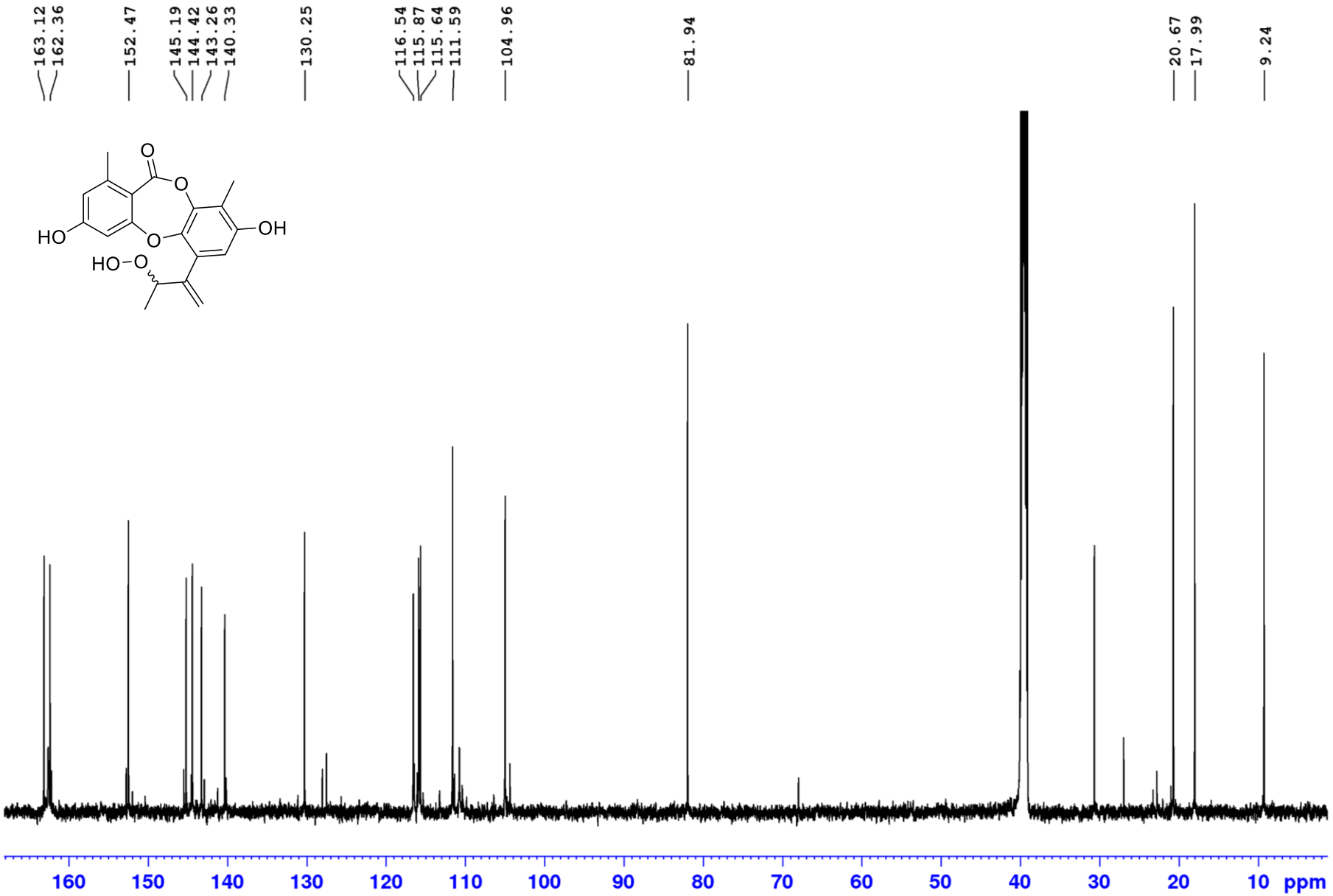

Figure S12. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2′-hydroperoxy-$\Delta^{1',4'}$-unguinol (**2f**)

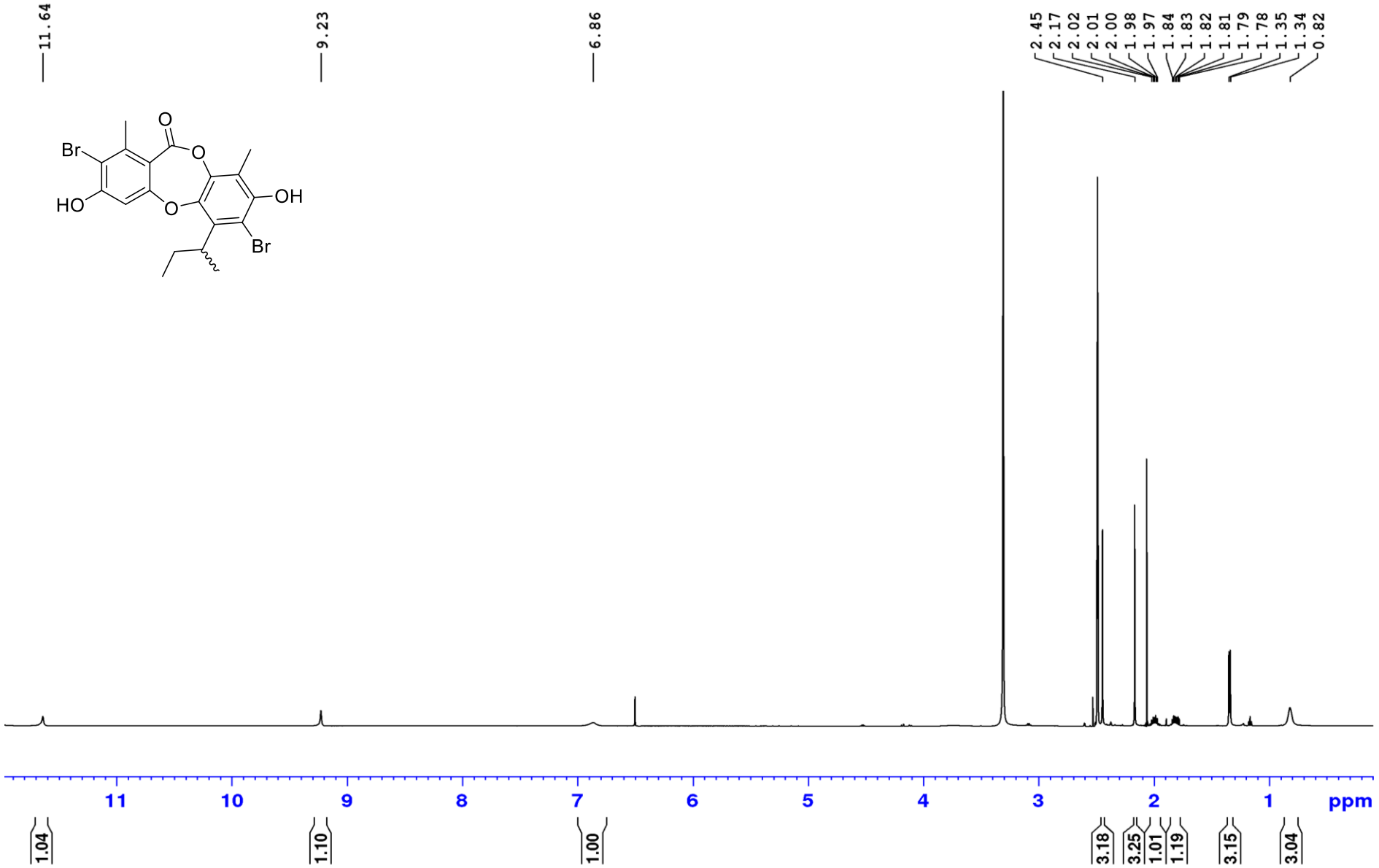

Figure S13. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2,7-dibromo-1′,2′-dihydrounguinol (**3a**)

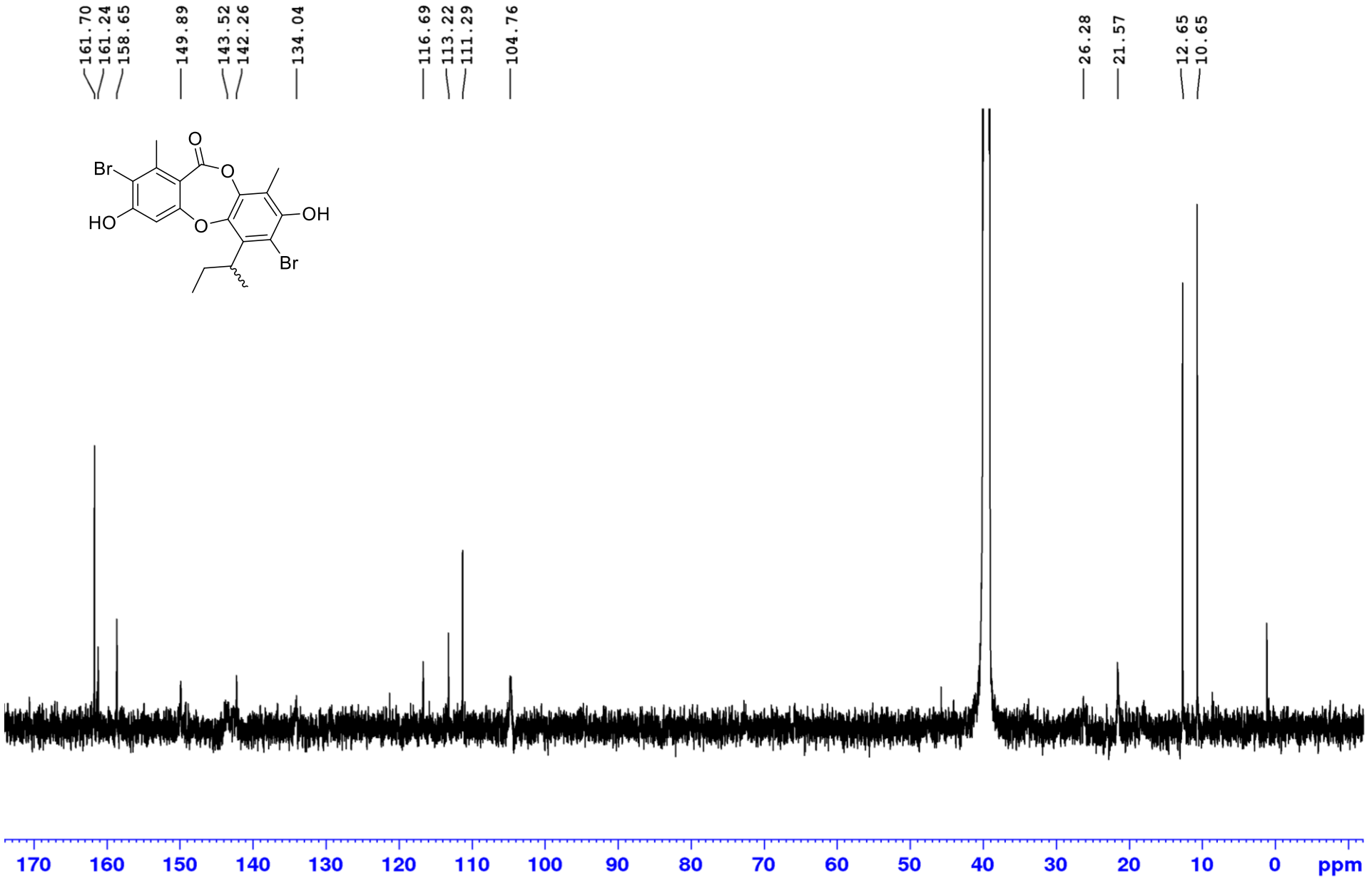

Figure S14. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2,7-dibromo-1′,2′-dihydrounguinol (**3a**)

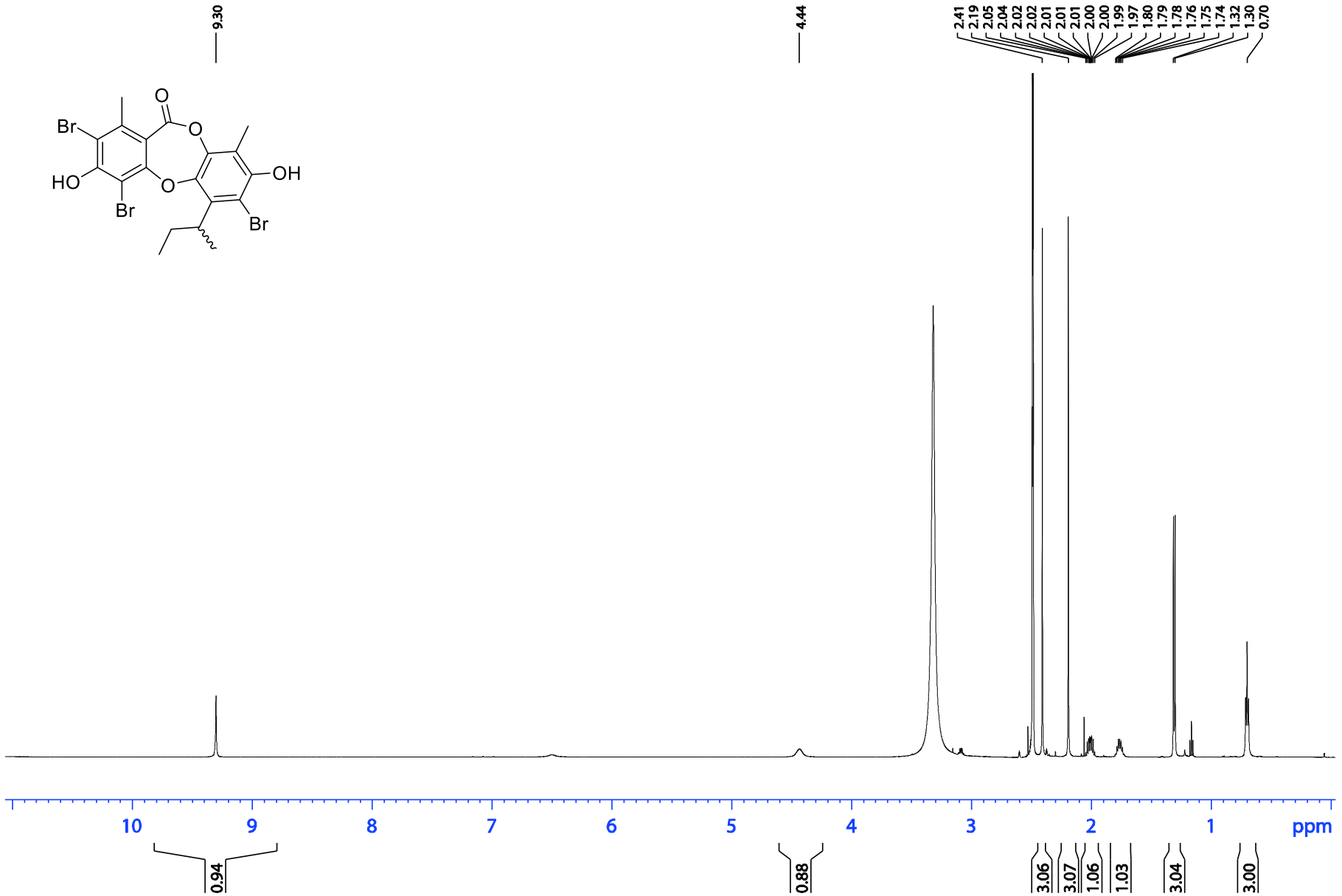

Figure S15. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2,4,7-tribromo-1′,2′-dihydrounguinol (**3b**)

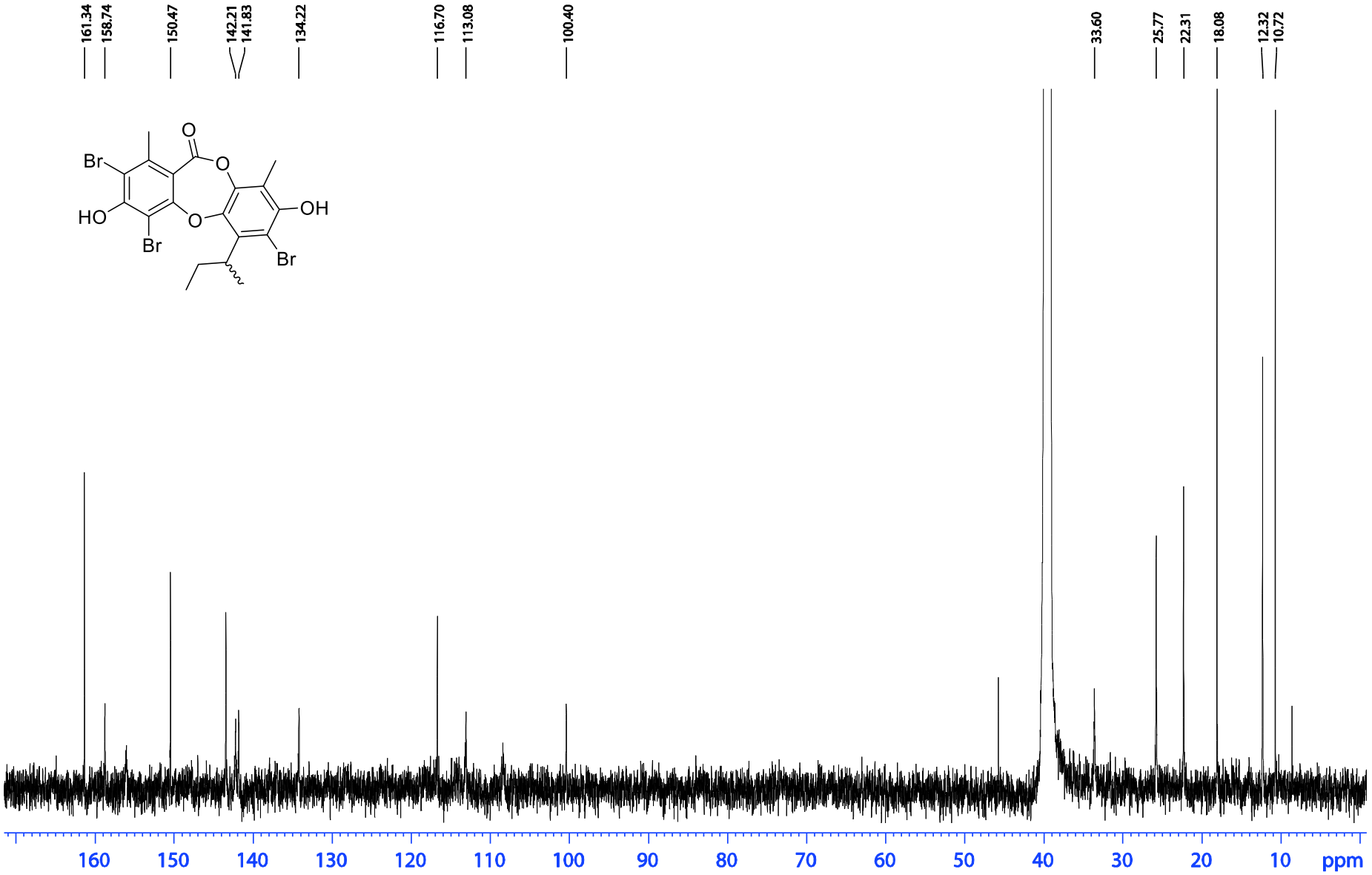

Figure S16. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2,4,7-tribromo-1′,2′-dihydrounguinol (**3b**)

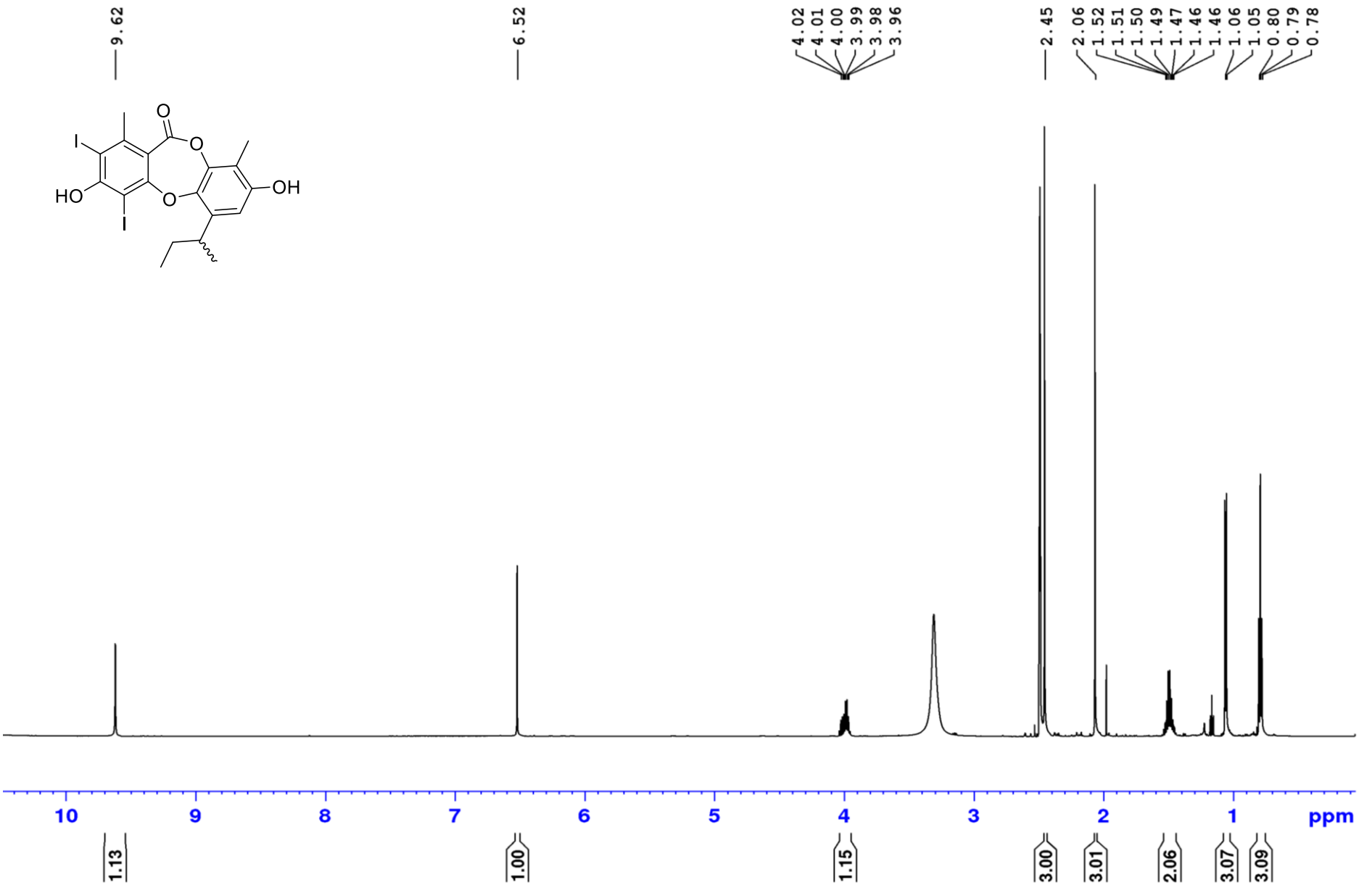

Figure S17. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2,4-diiodo-1′,2′-dihydrounguinol (**3c**)

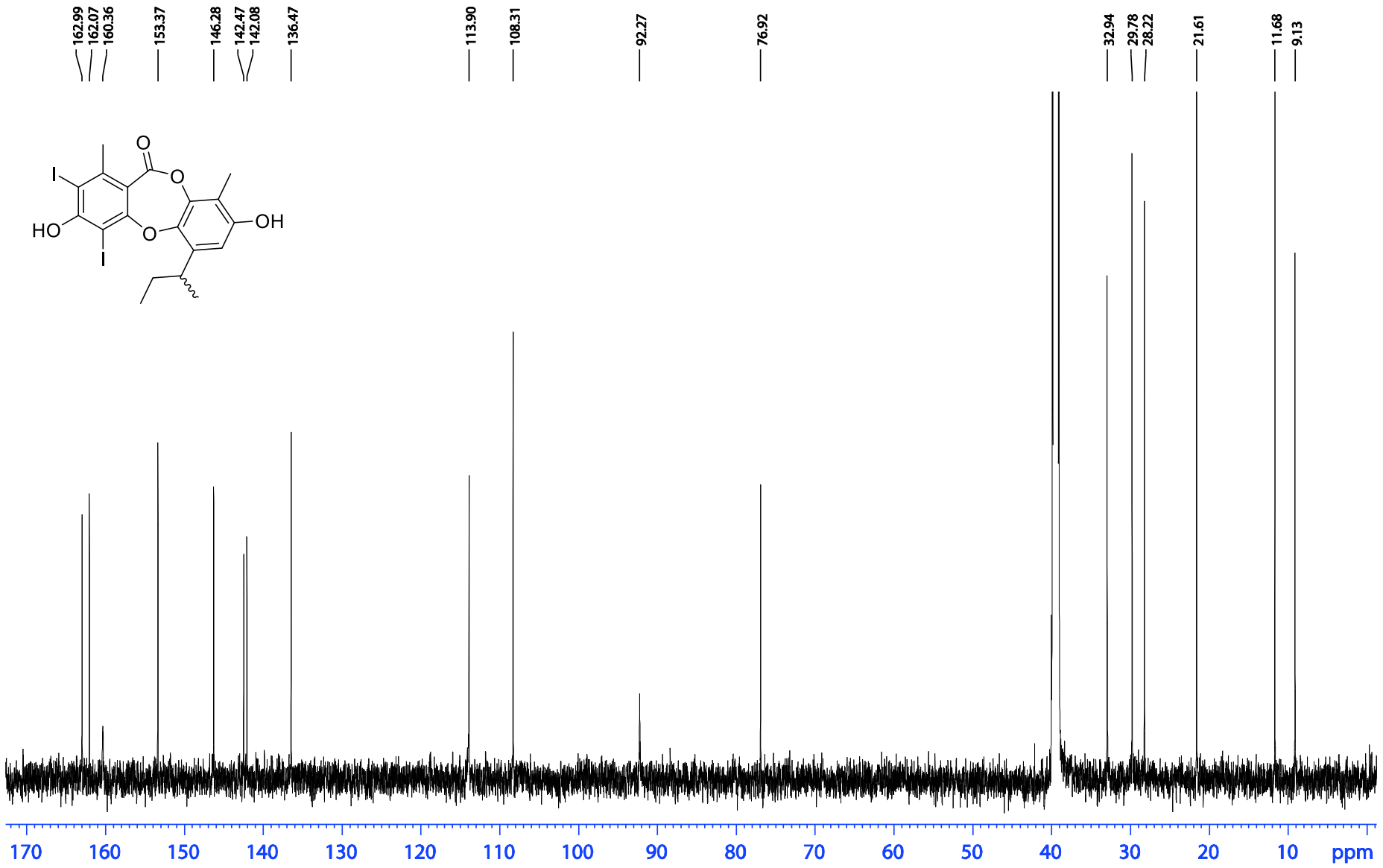

Figure S18. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2,4-diiodo-1′,2′-dihydrounguinol (**3c**)

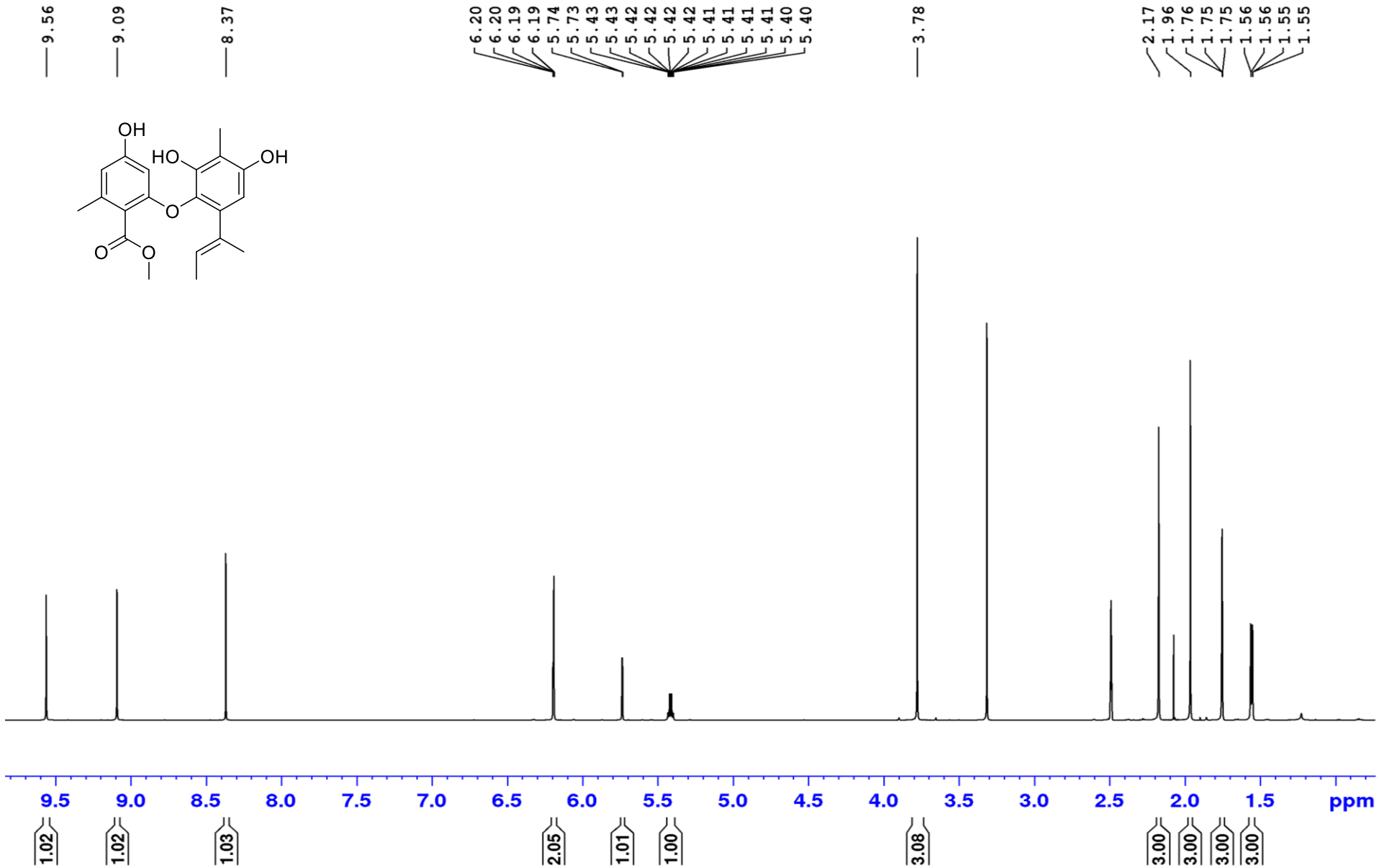

Figure S19. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of methylunguinolate (**4a**)

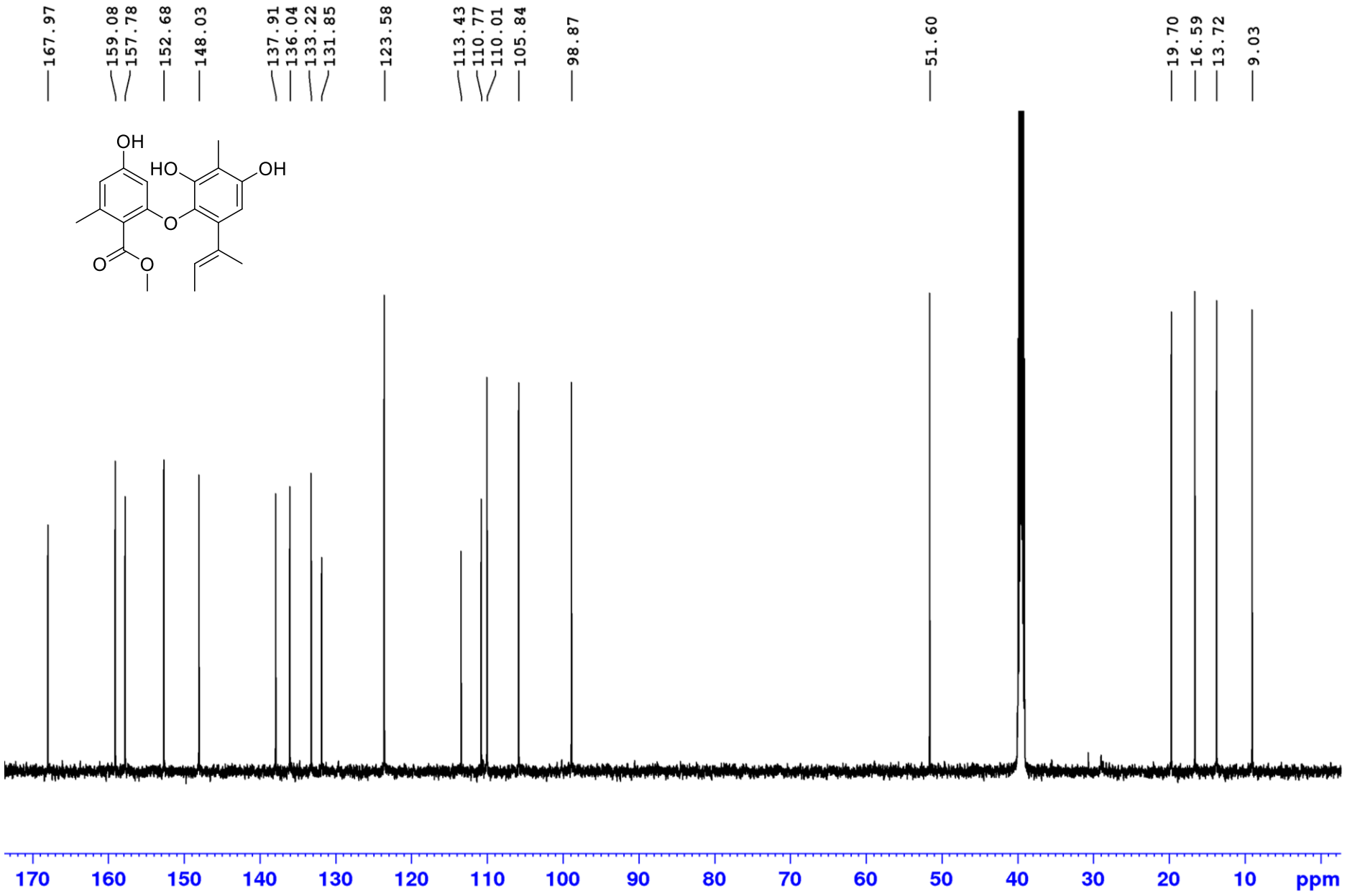

Figure S20. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of methylunguinolate (**4a**)

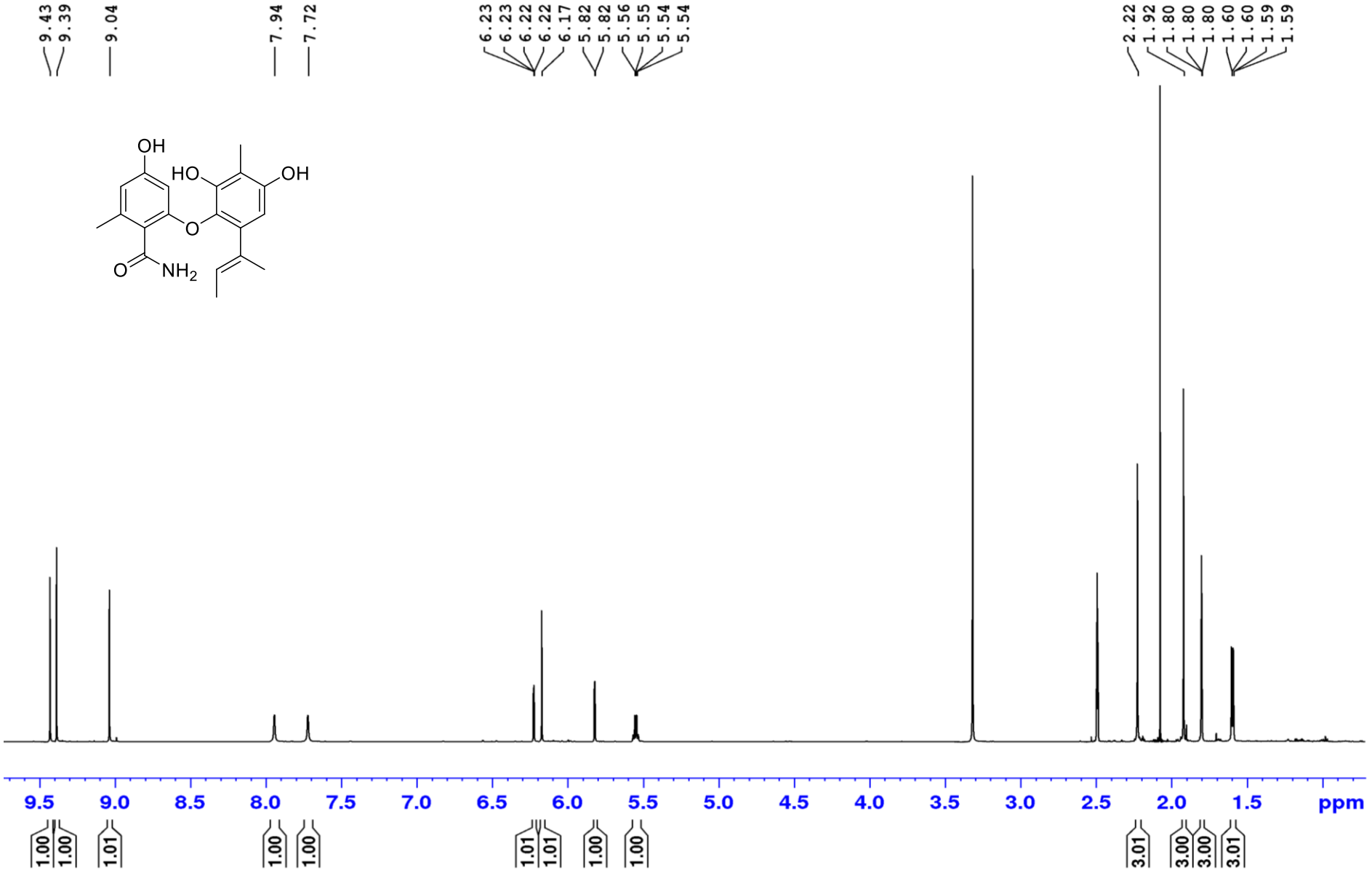

Figure S21. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of unguinolamide (**4b**)

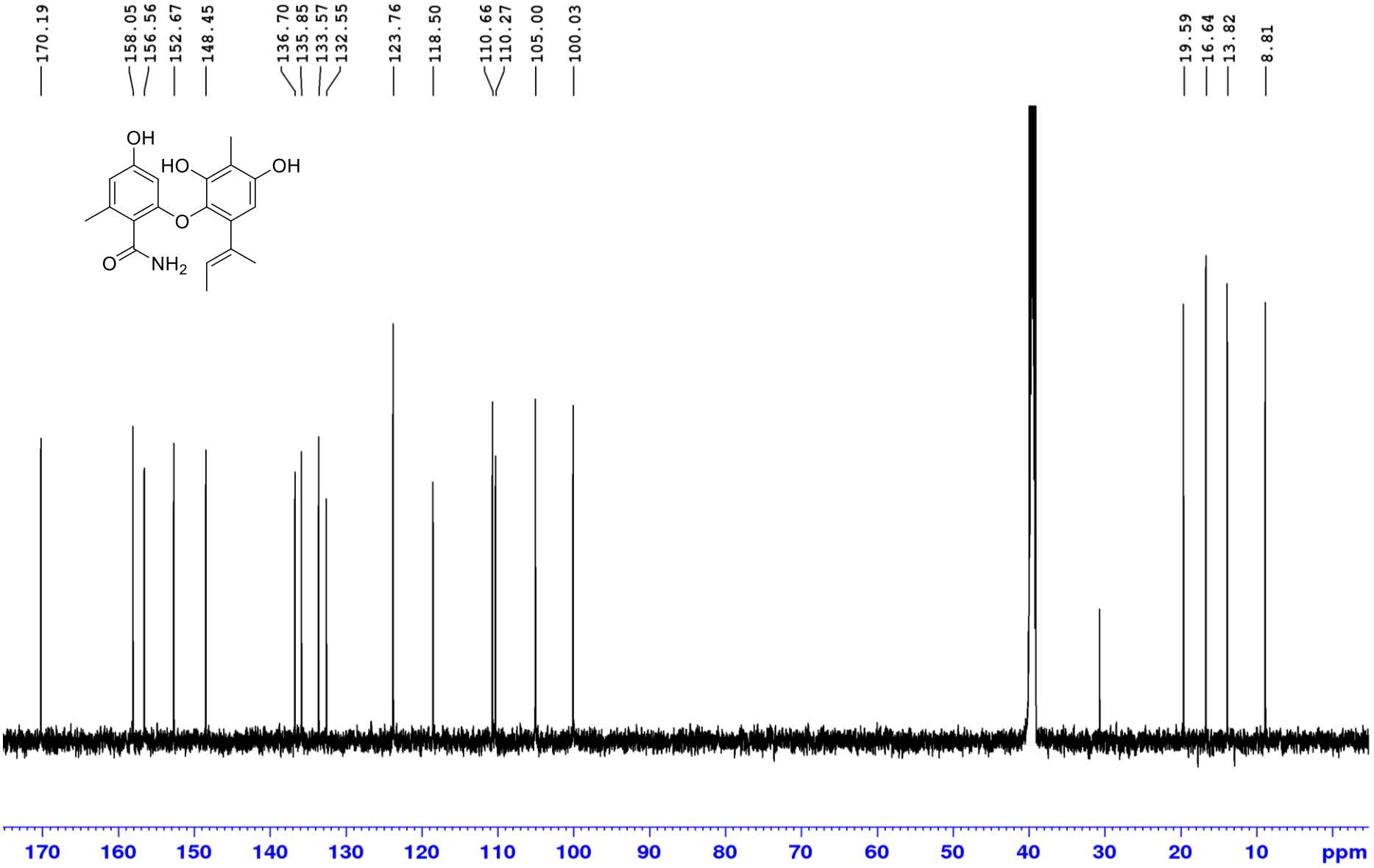

Figure S22. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of unguinolamide (**4b**)

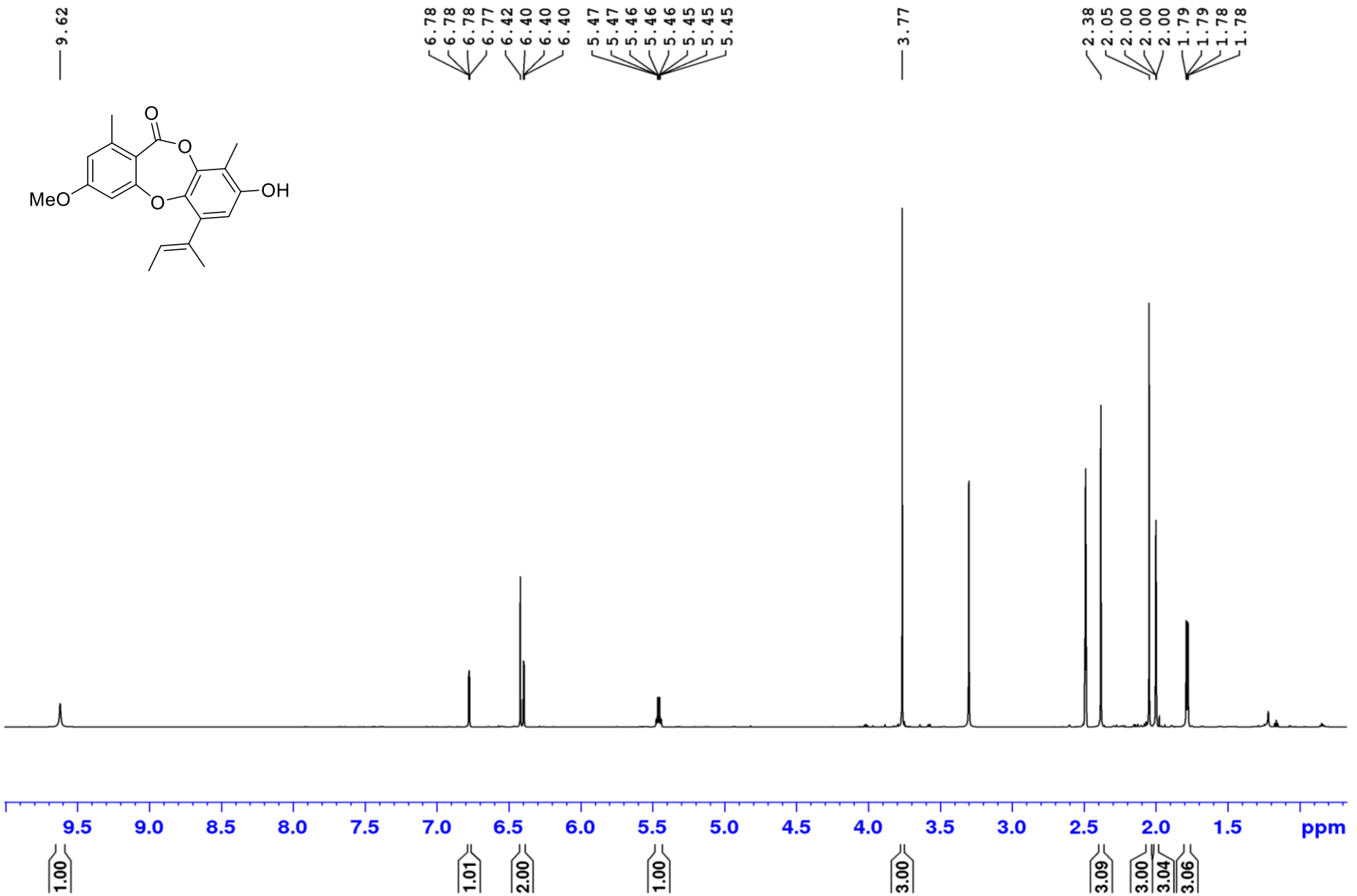

Figure S23. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-methylunguinol (**5a**)

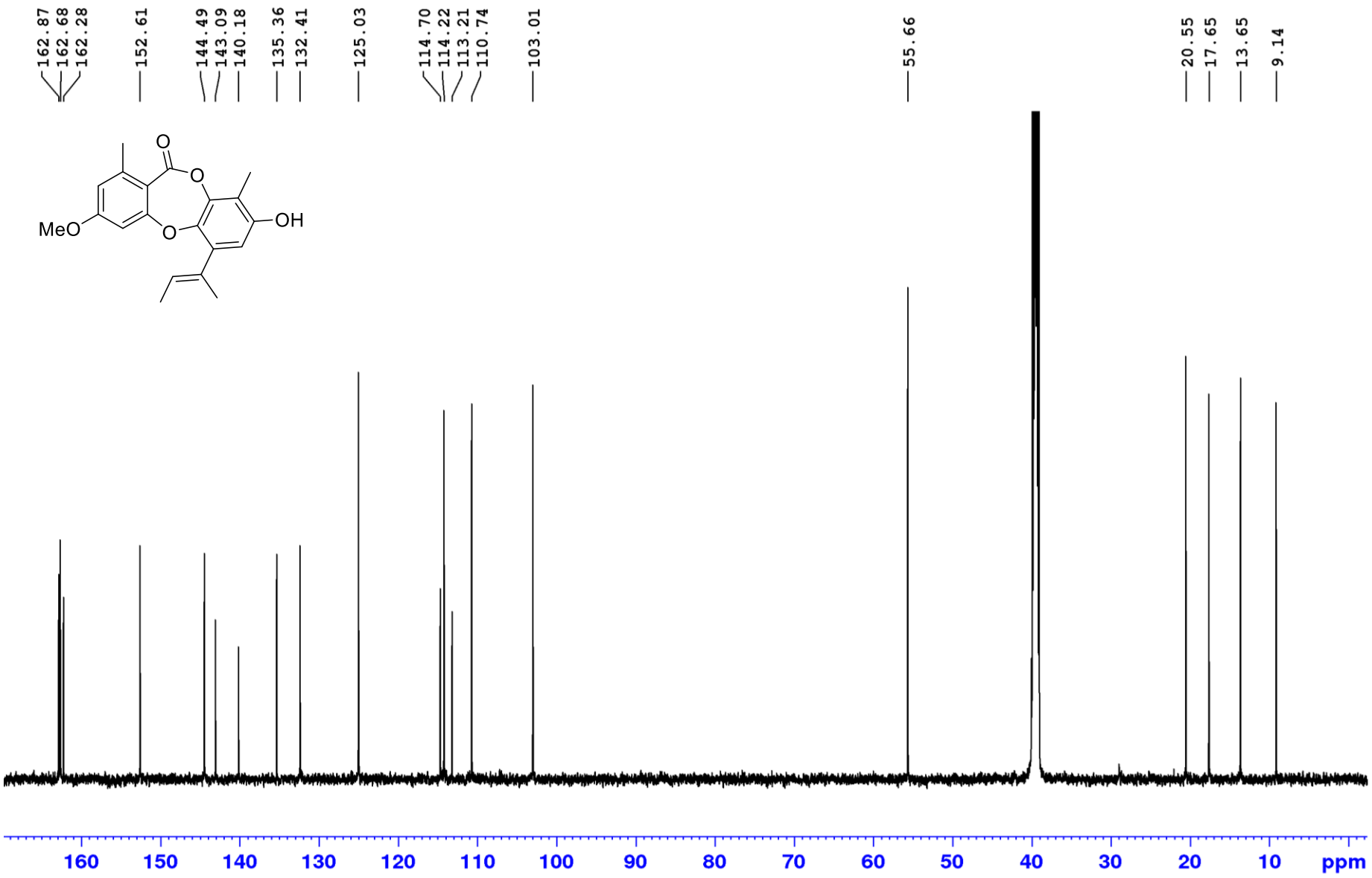

Figure S24. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-methylunguinol (**5a**)

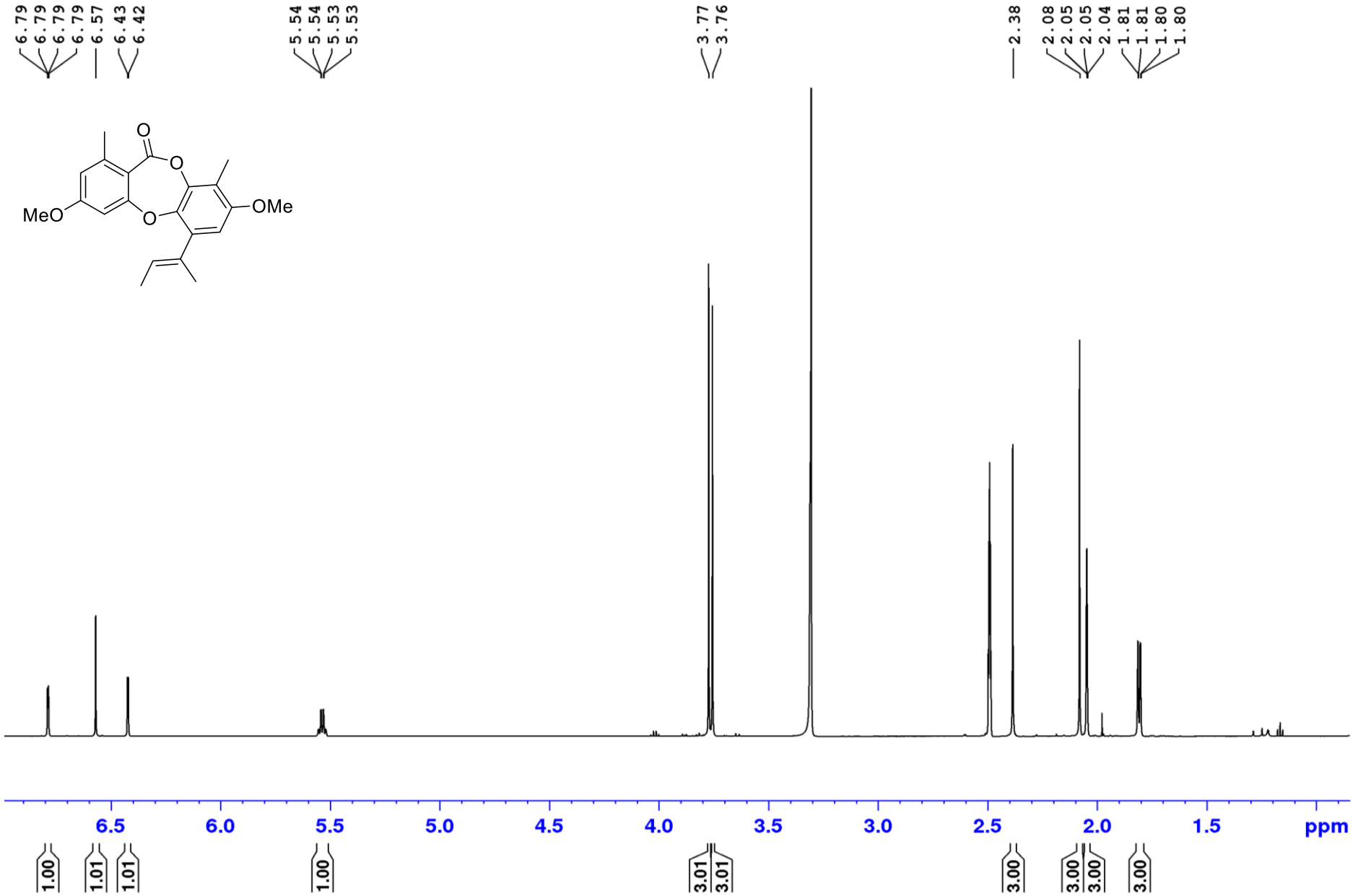

Figure S25. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3,8-di-*O*-methylunguinol (**5b**)

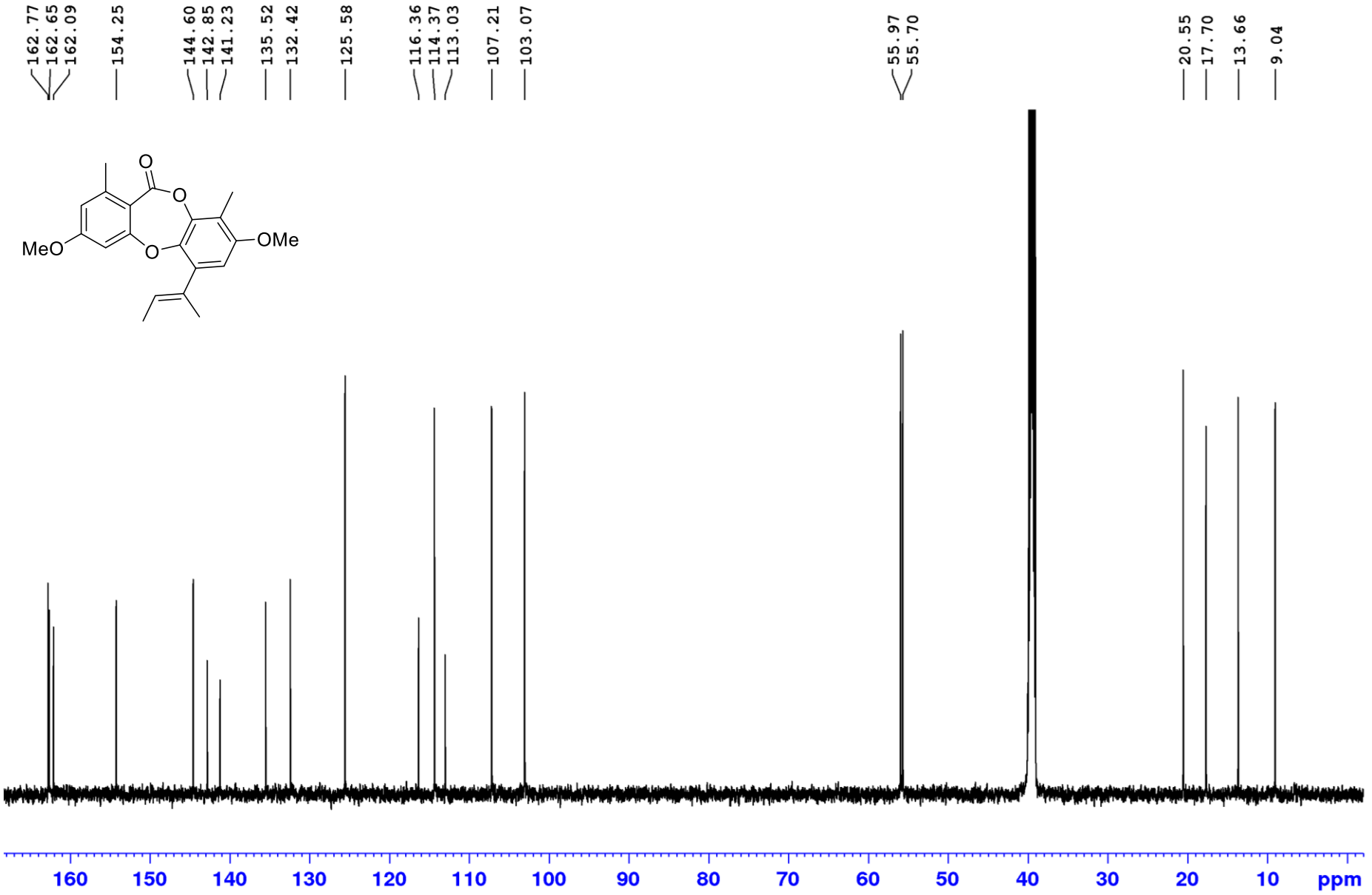

Figure S26. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3,8-di-*O*-methylunguinol (**5b**)

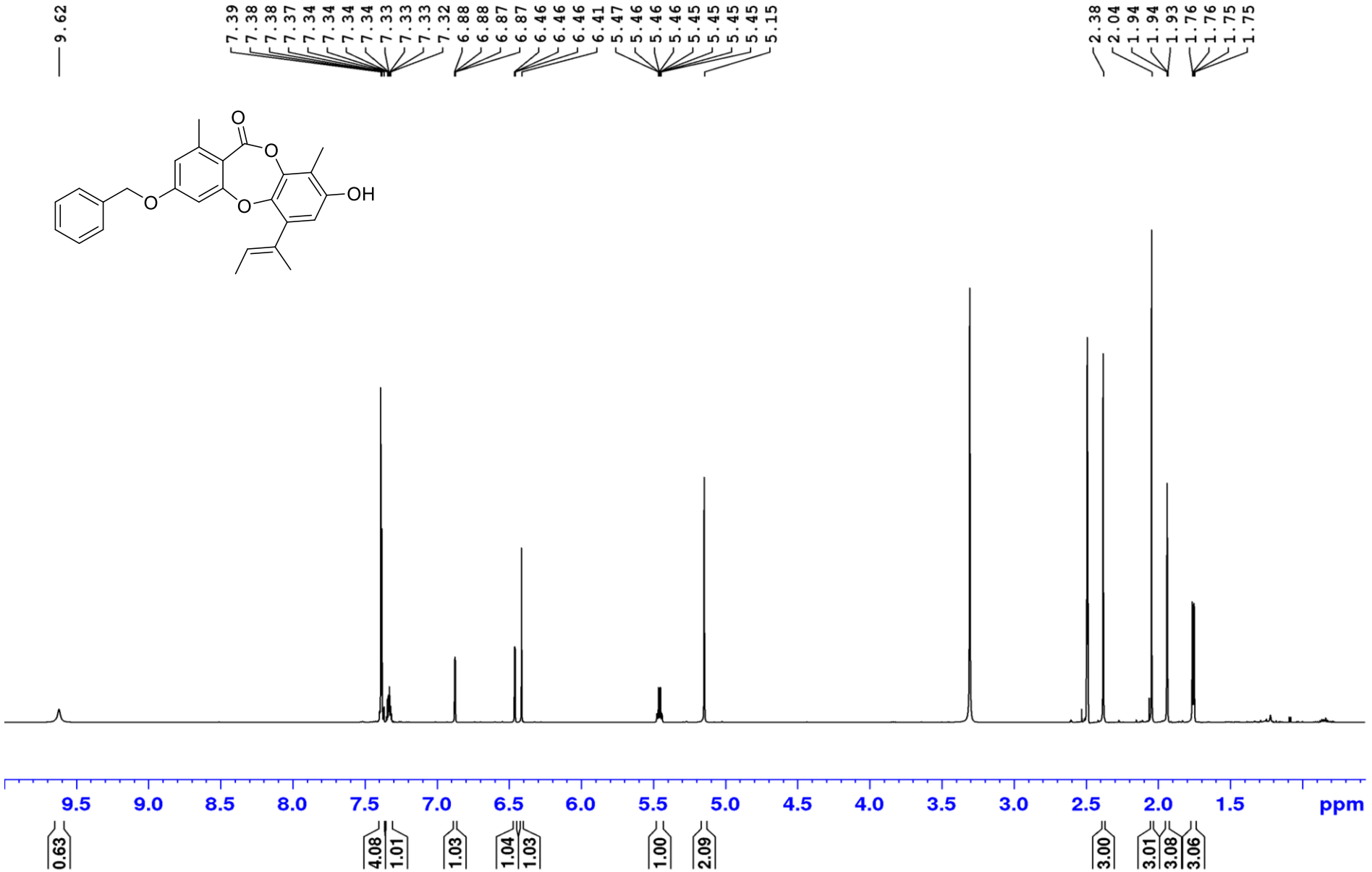

Figure S27. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-benzylunguinol (**6a**)

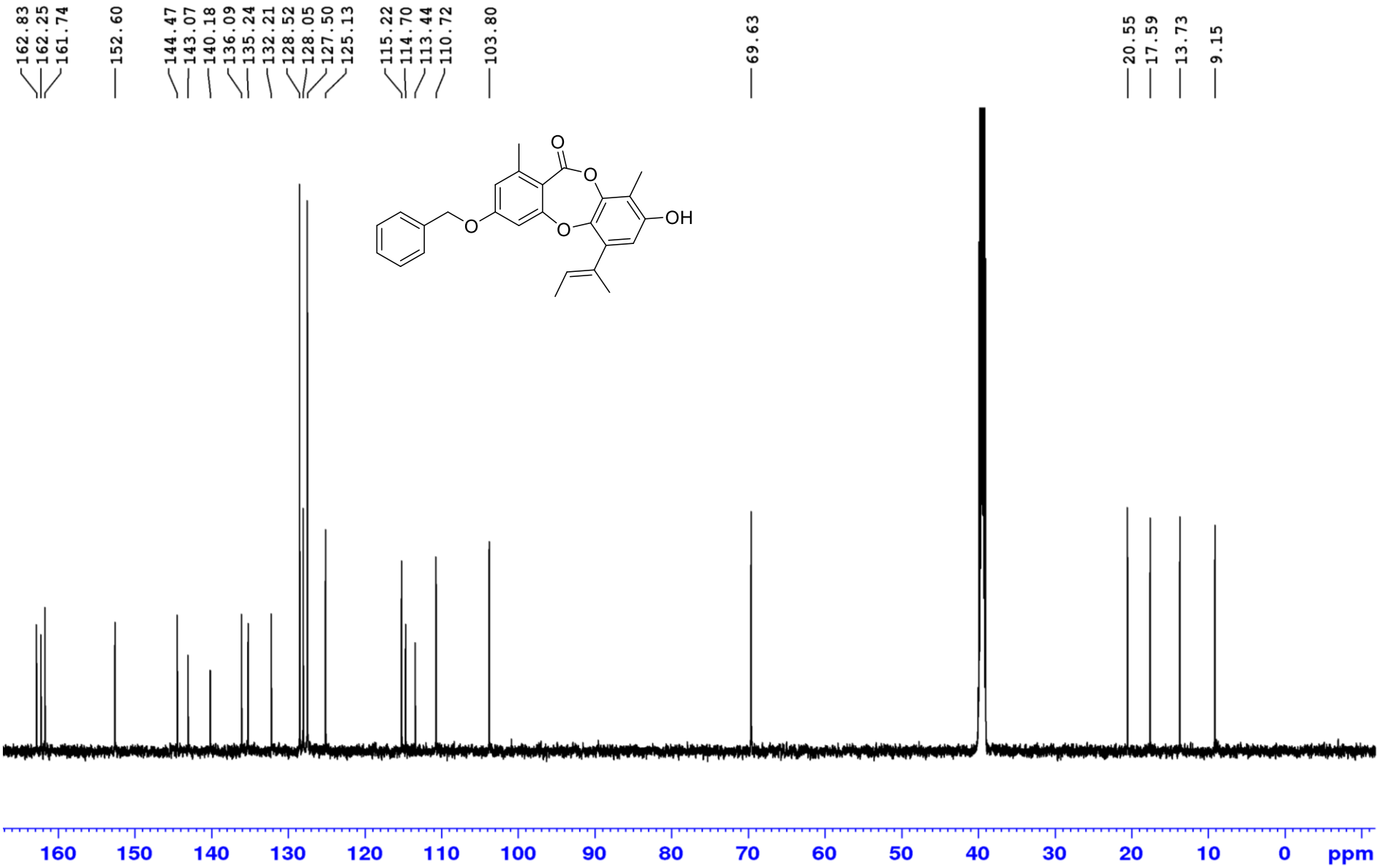

Figure S28. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-benzylunguinol (**6a**)

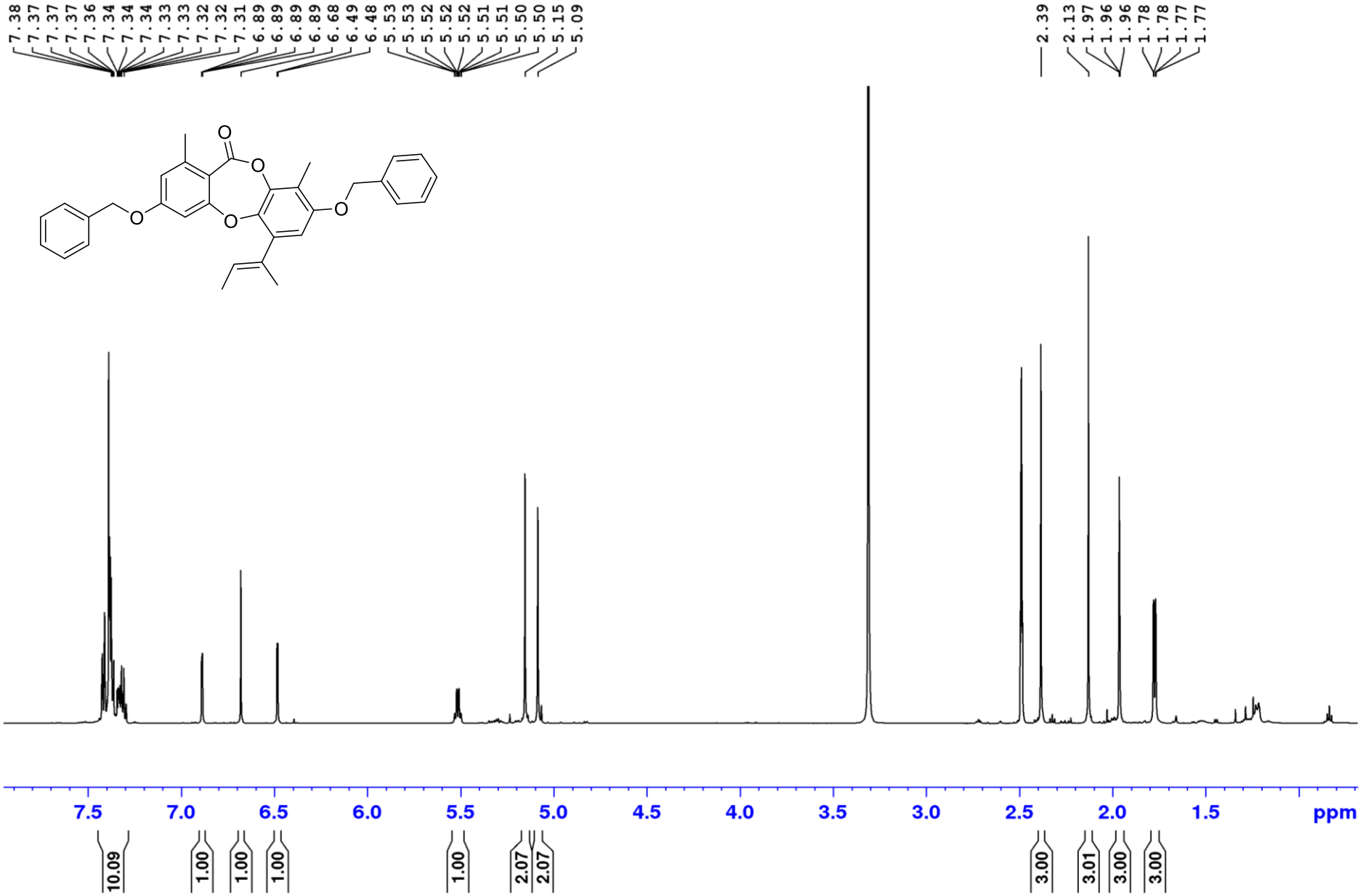

Figure S29. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3,8-*O*-dibenzylunguinol (**6b**)

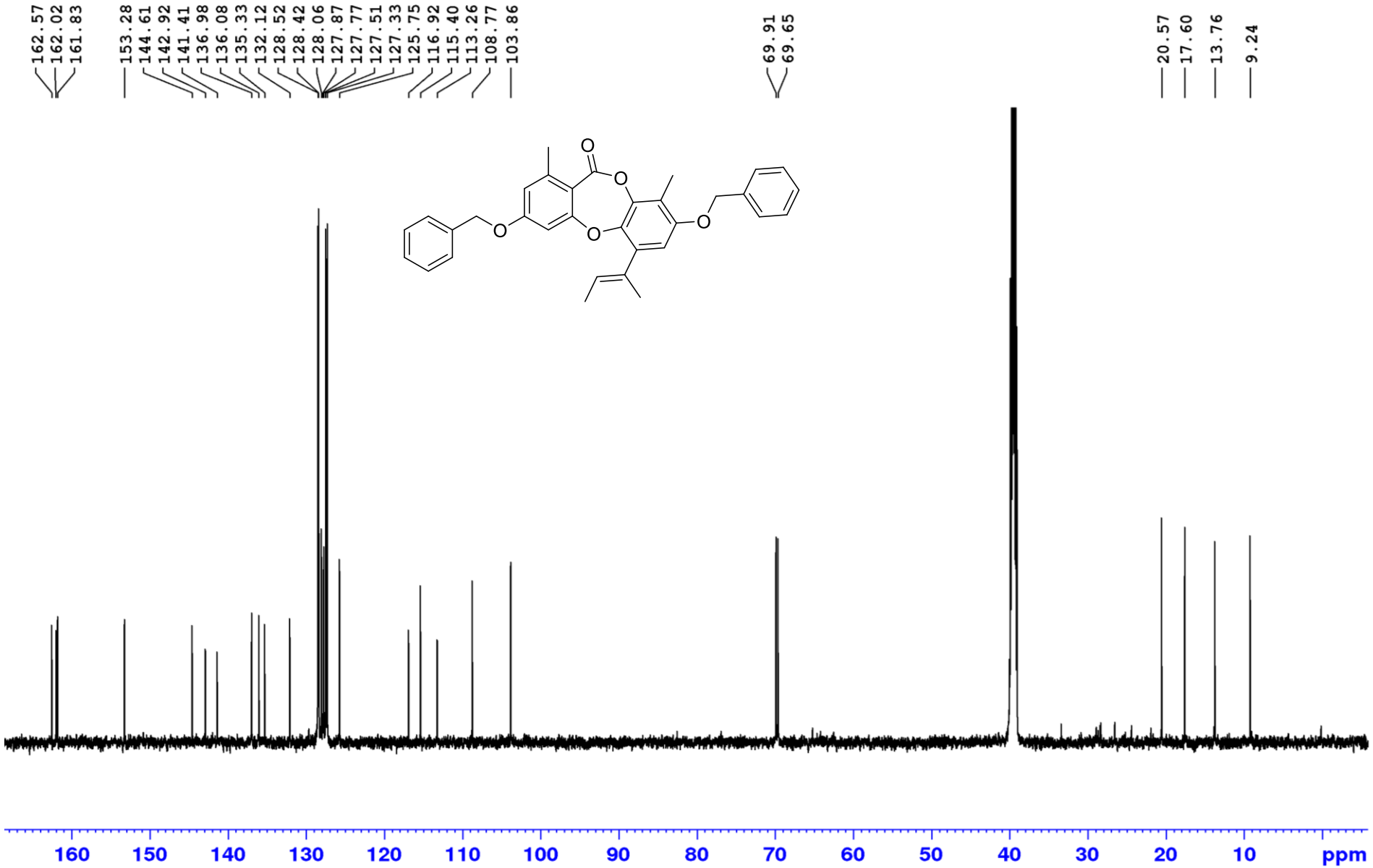

Figure S30. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3,8-*O*-dibenzylunguinol (**6b**)

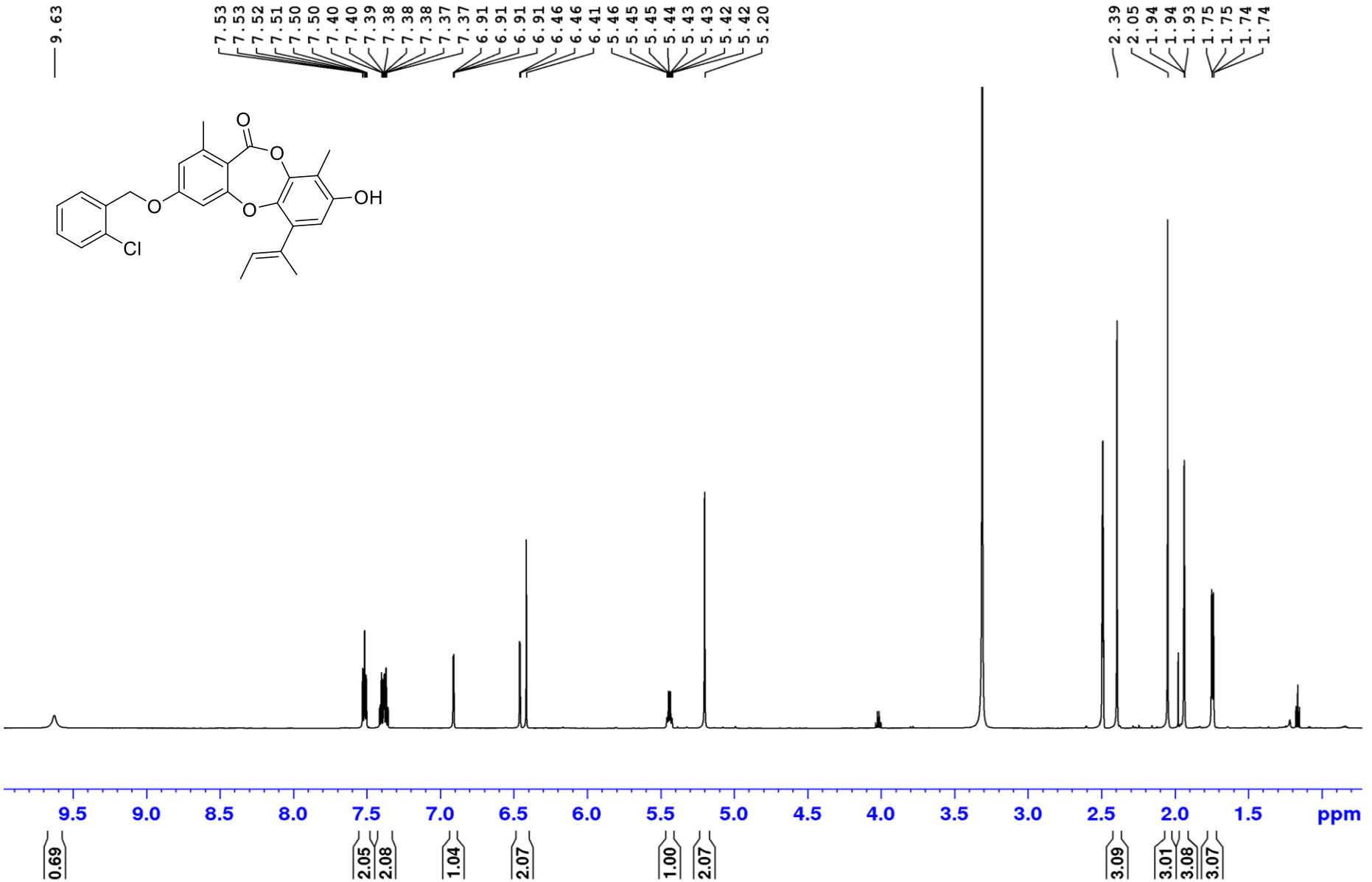

Figure S31. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(2-chlorobenzyl)unguinol (**7a**)

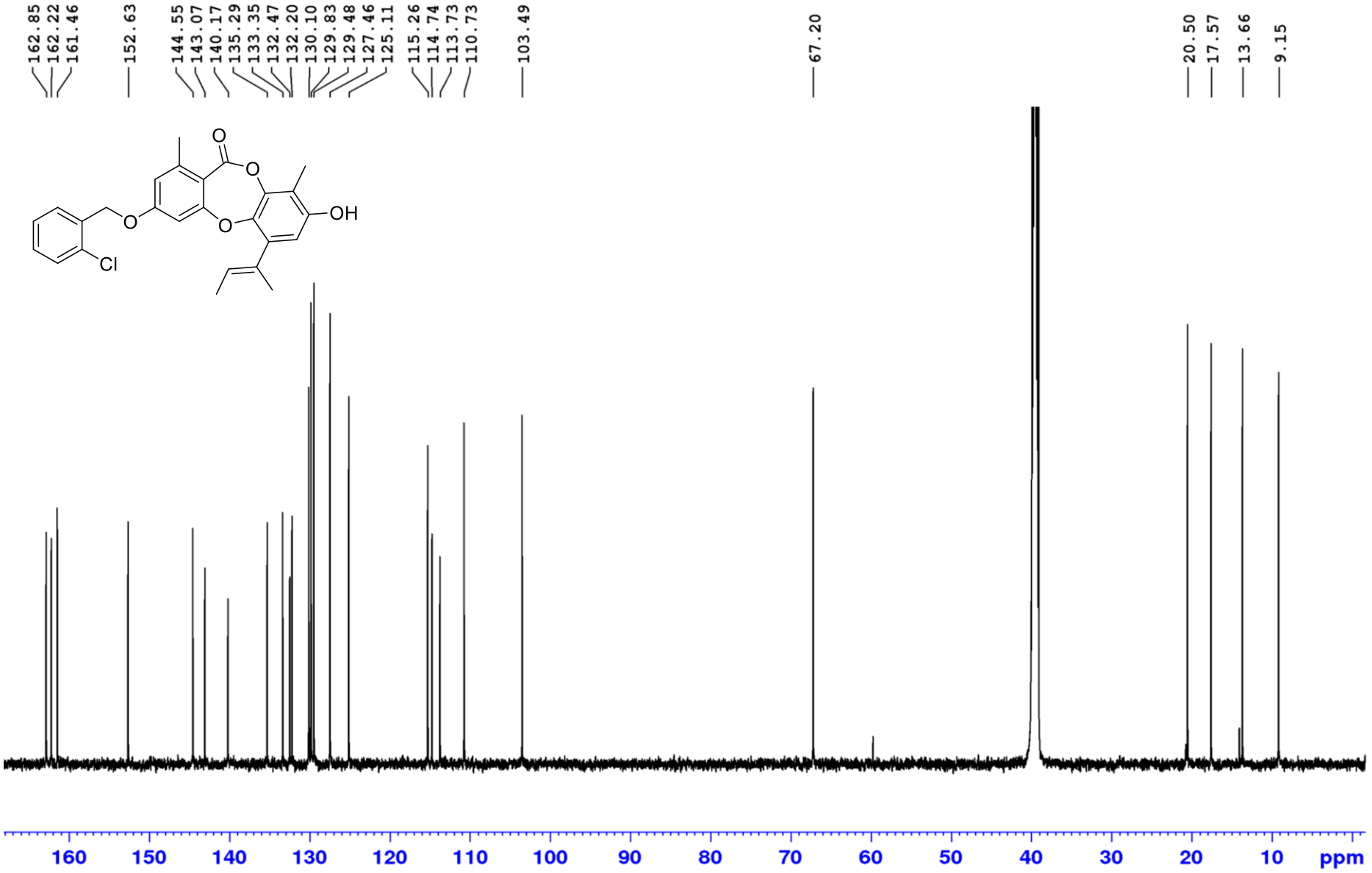

Figure S32. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(2-chlorobenzyl)unguinol (**7a**)

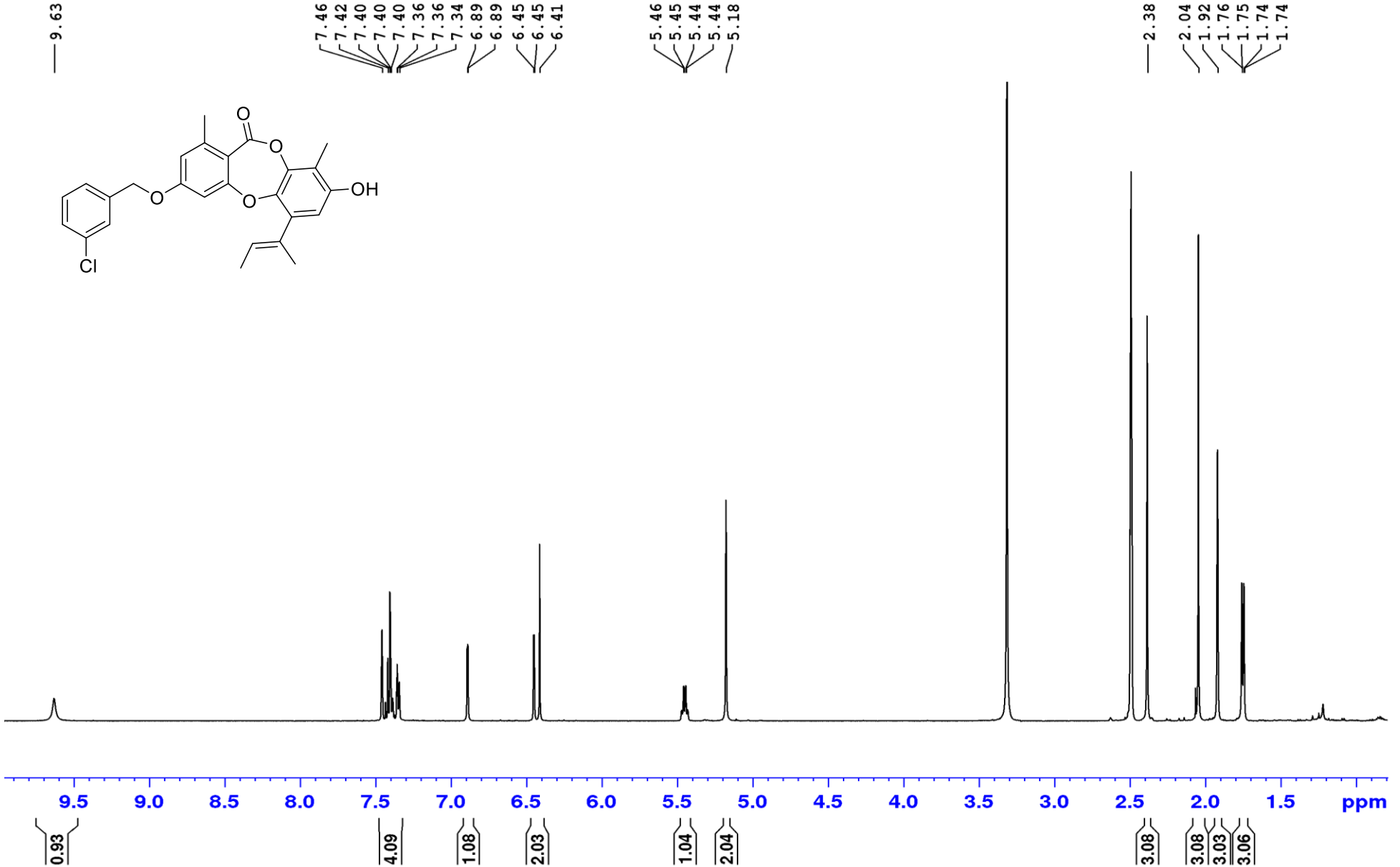

Figure S33. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(3-chlorobenzyl)unguinol (**7b**)

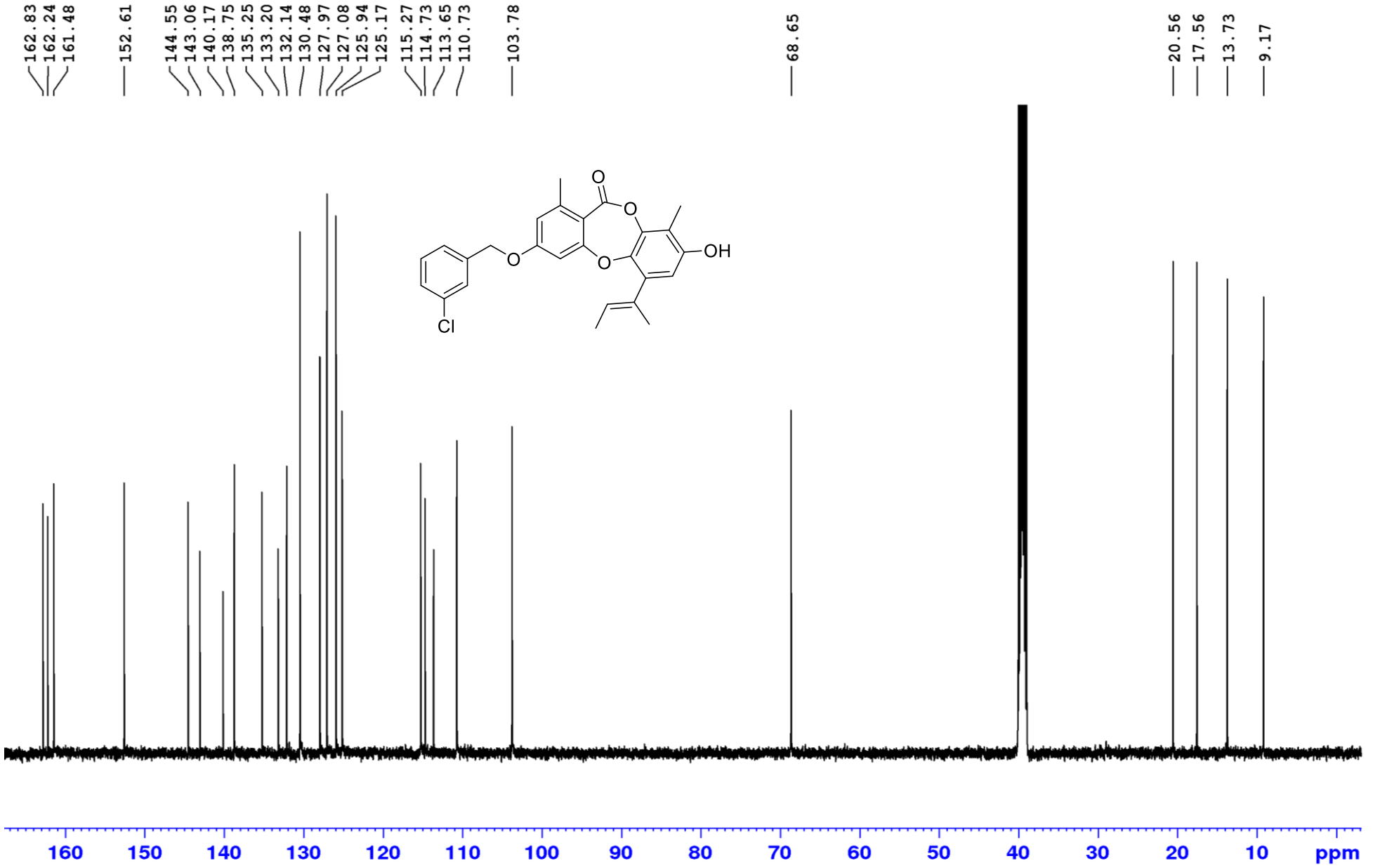

Figure S34. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(3-chlorobenzyl)unguinol (**7b**)

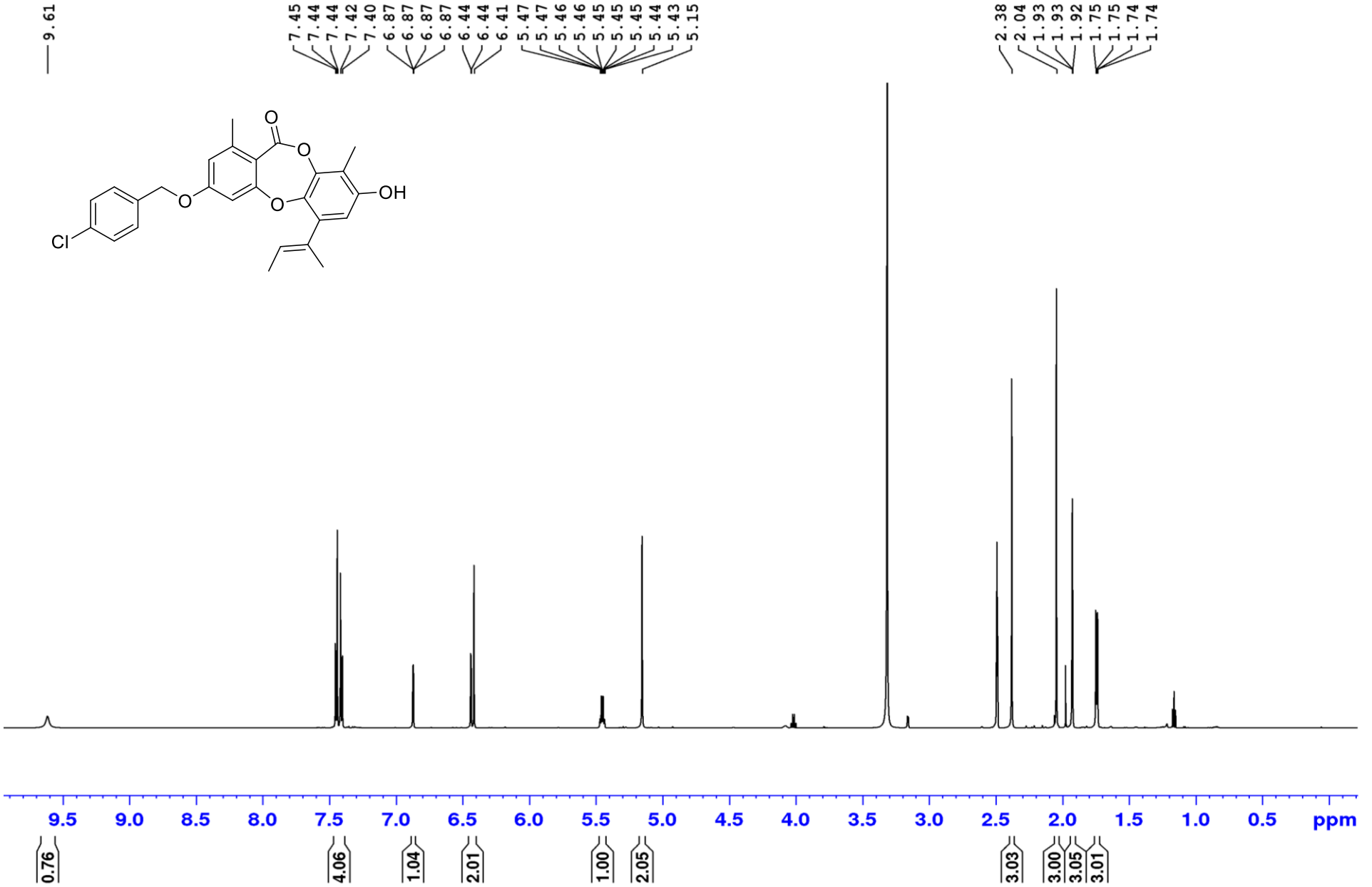

Figure S35. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(4-chlorobenzyl)unguinol (**7c**)

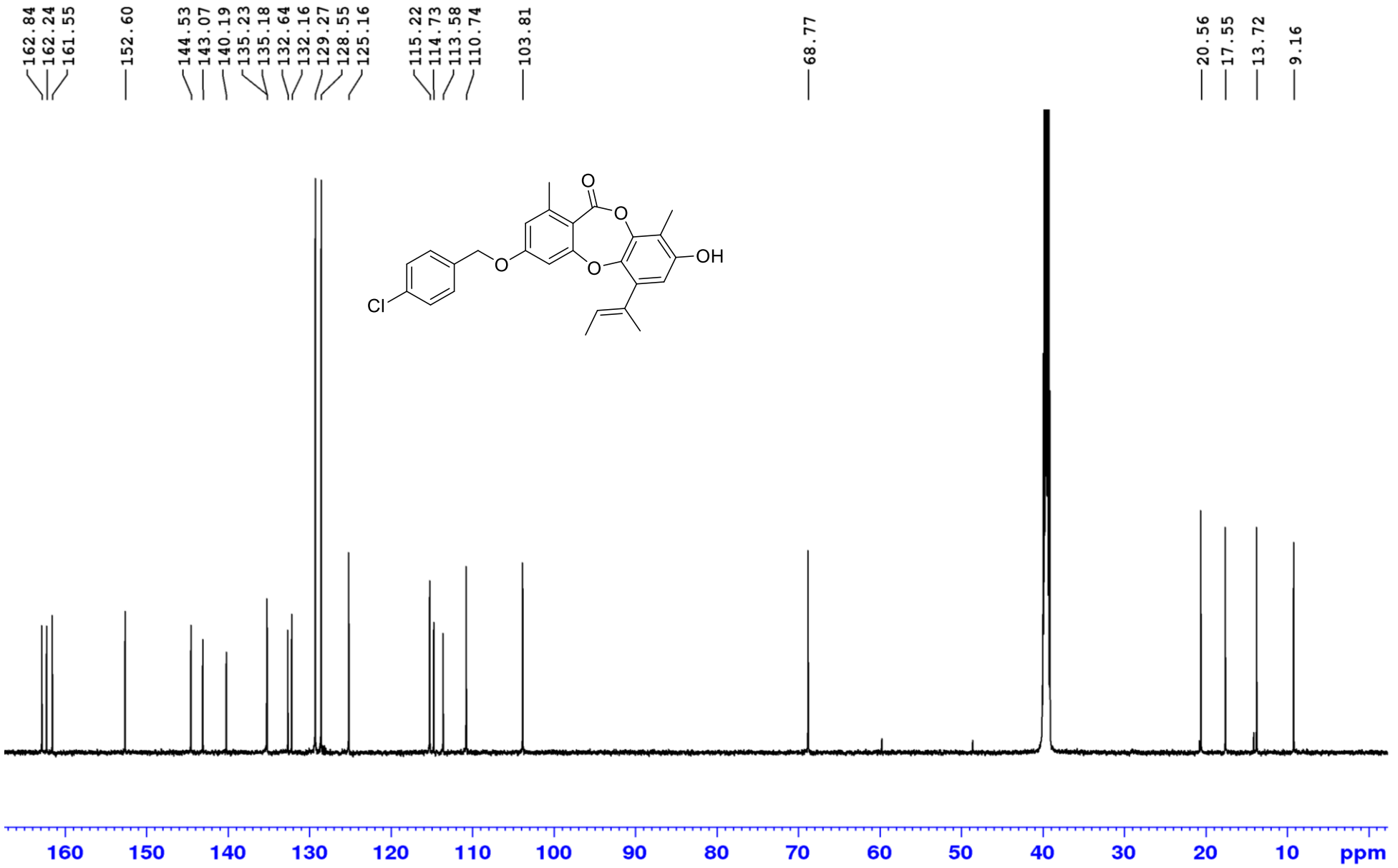

Figure S36. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(4-chlorobenzyl)unguinol (**7c)**

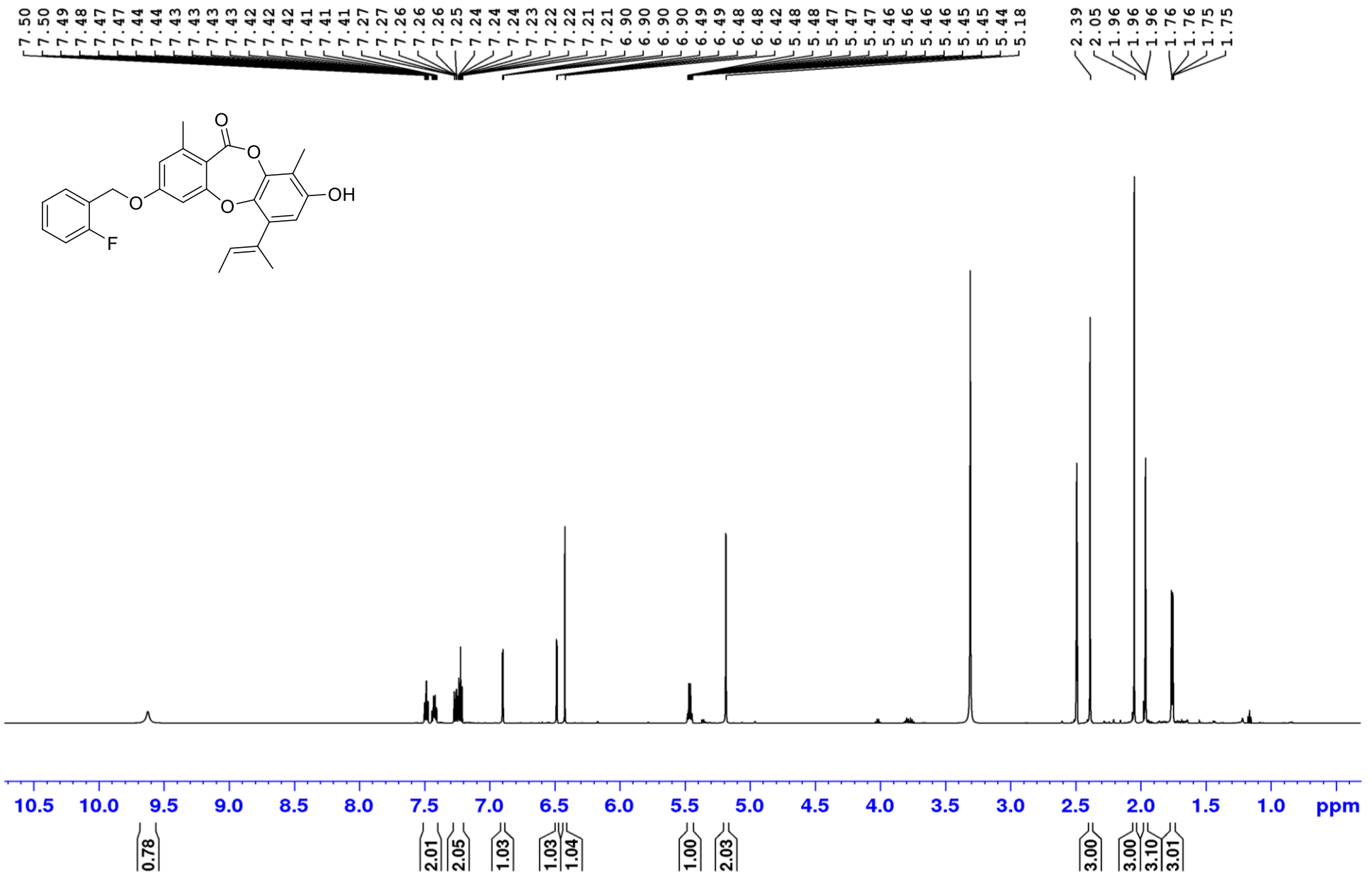

Figure S37. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(2-fluorobenzyl)unguinol (**7d**)

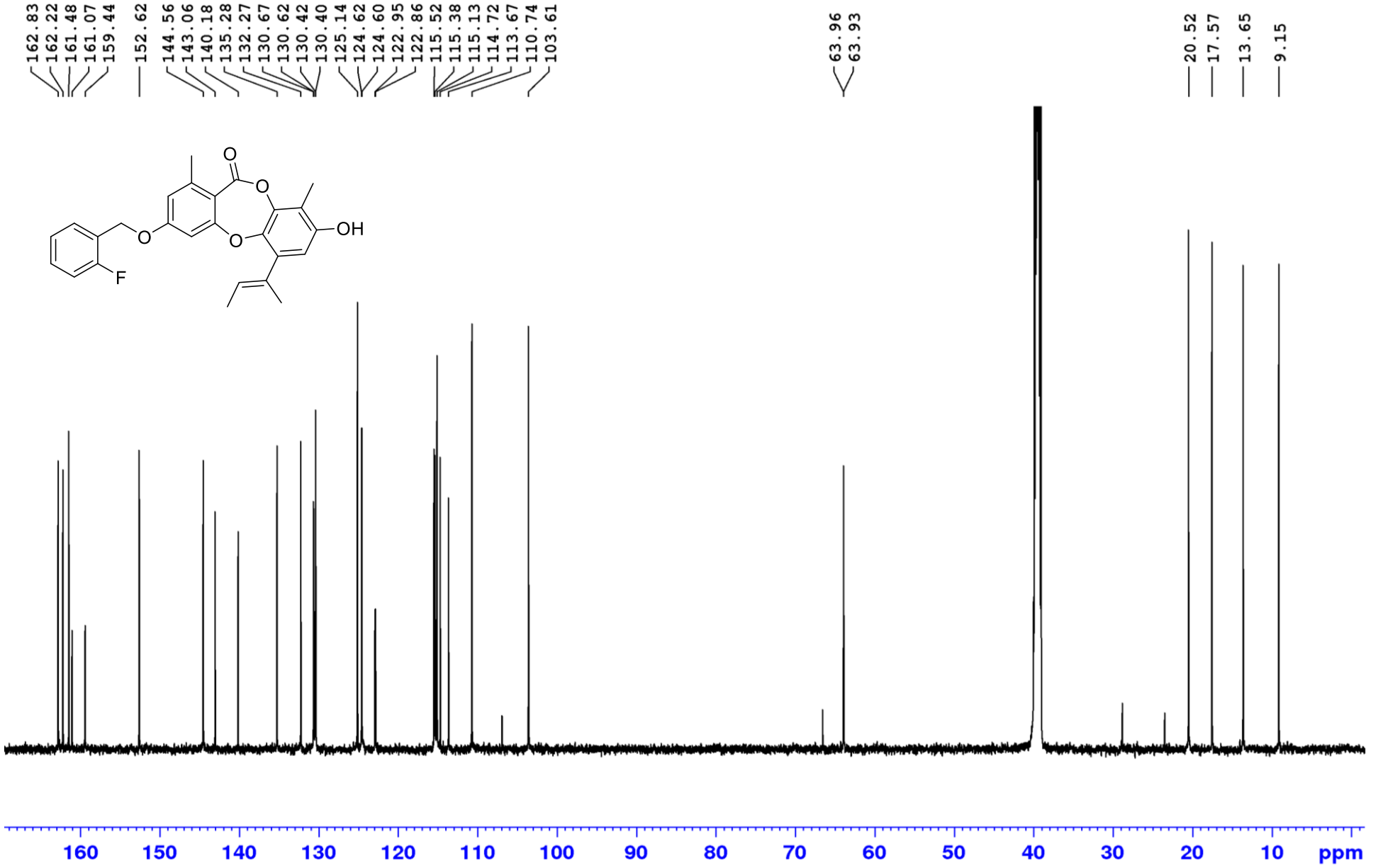

Figure S38. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(2-fluorobenzyl)unguinol (**7d**)

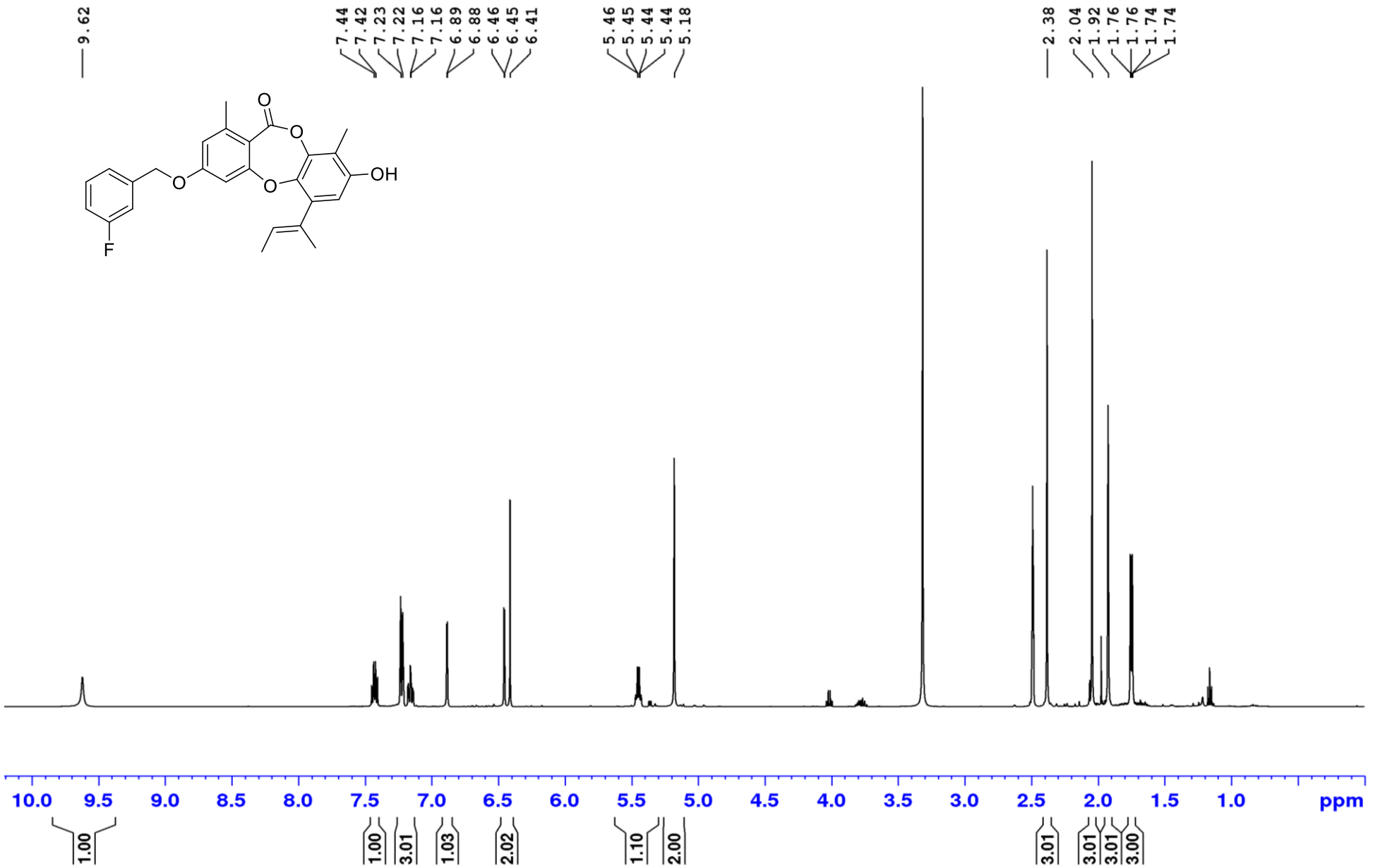

Figure S39. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(3-fluorobenzyl)unguinol (**7e**)

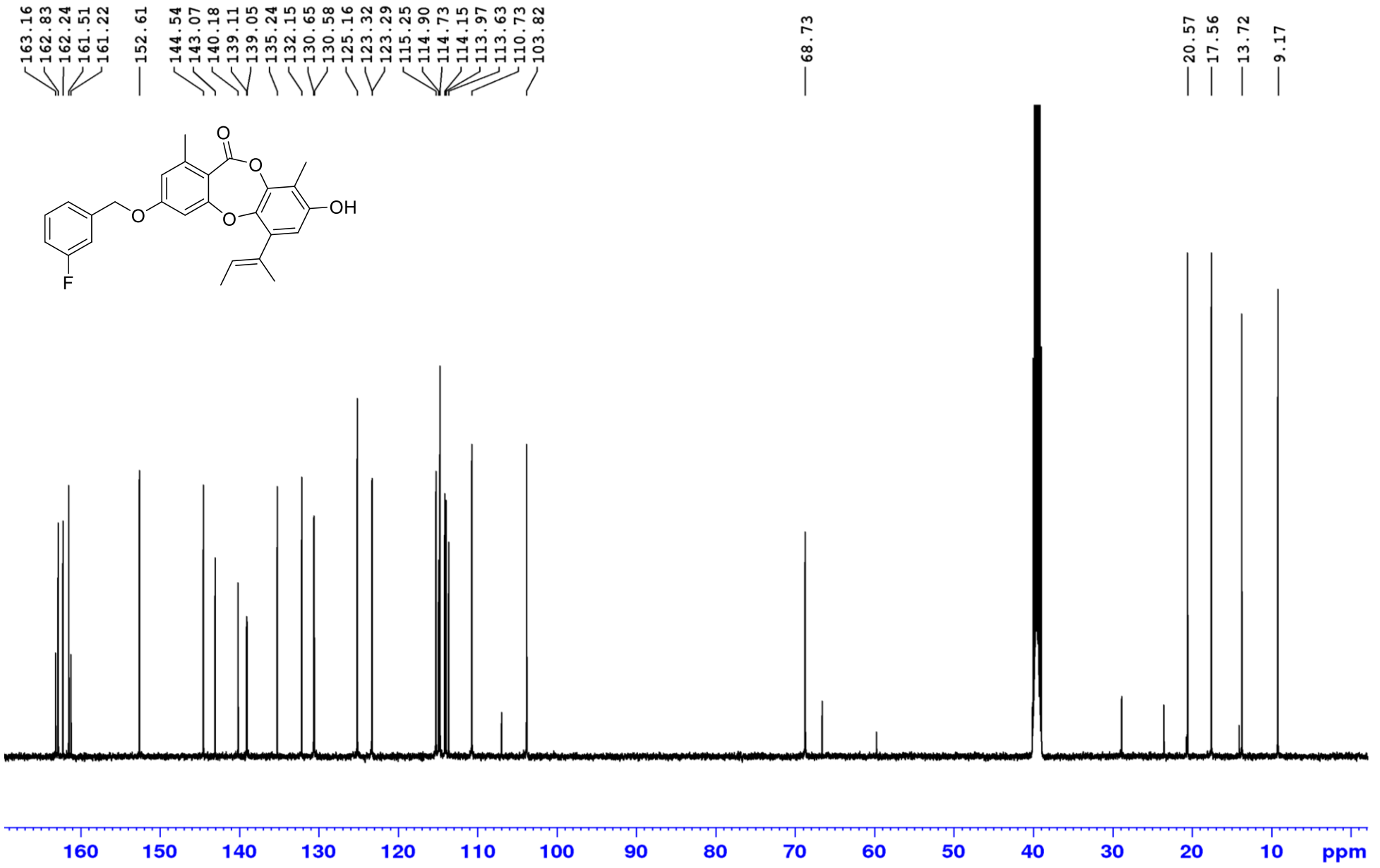

Figure S40. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(3-fluorobenzyl)unguinol (**7e**)

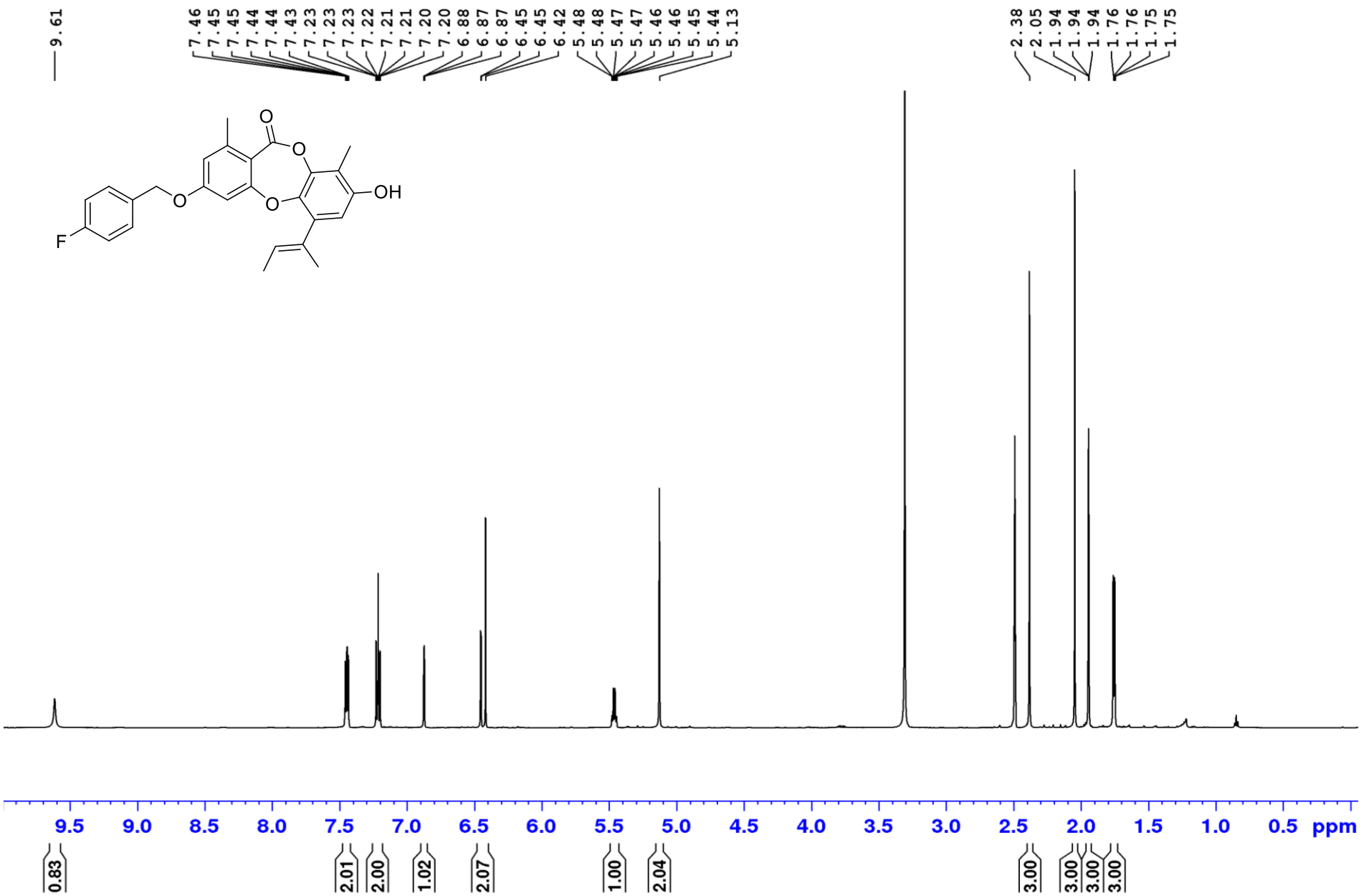

Figure S41. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(4-fluorobenzyl)unguinol (**7f**)

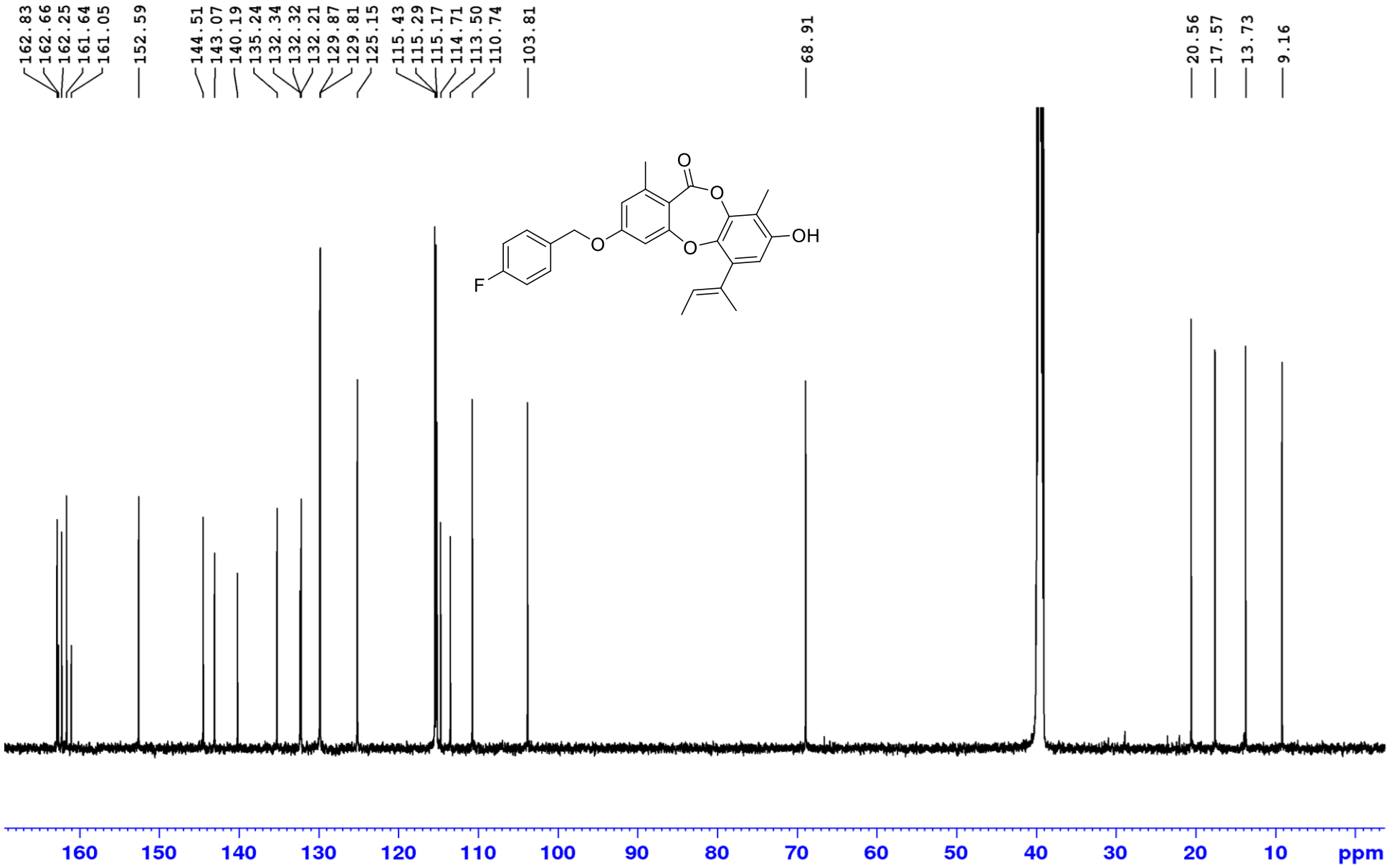

Figure S42. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(4-fluorobenzyl)unguinol (**7f**)

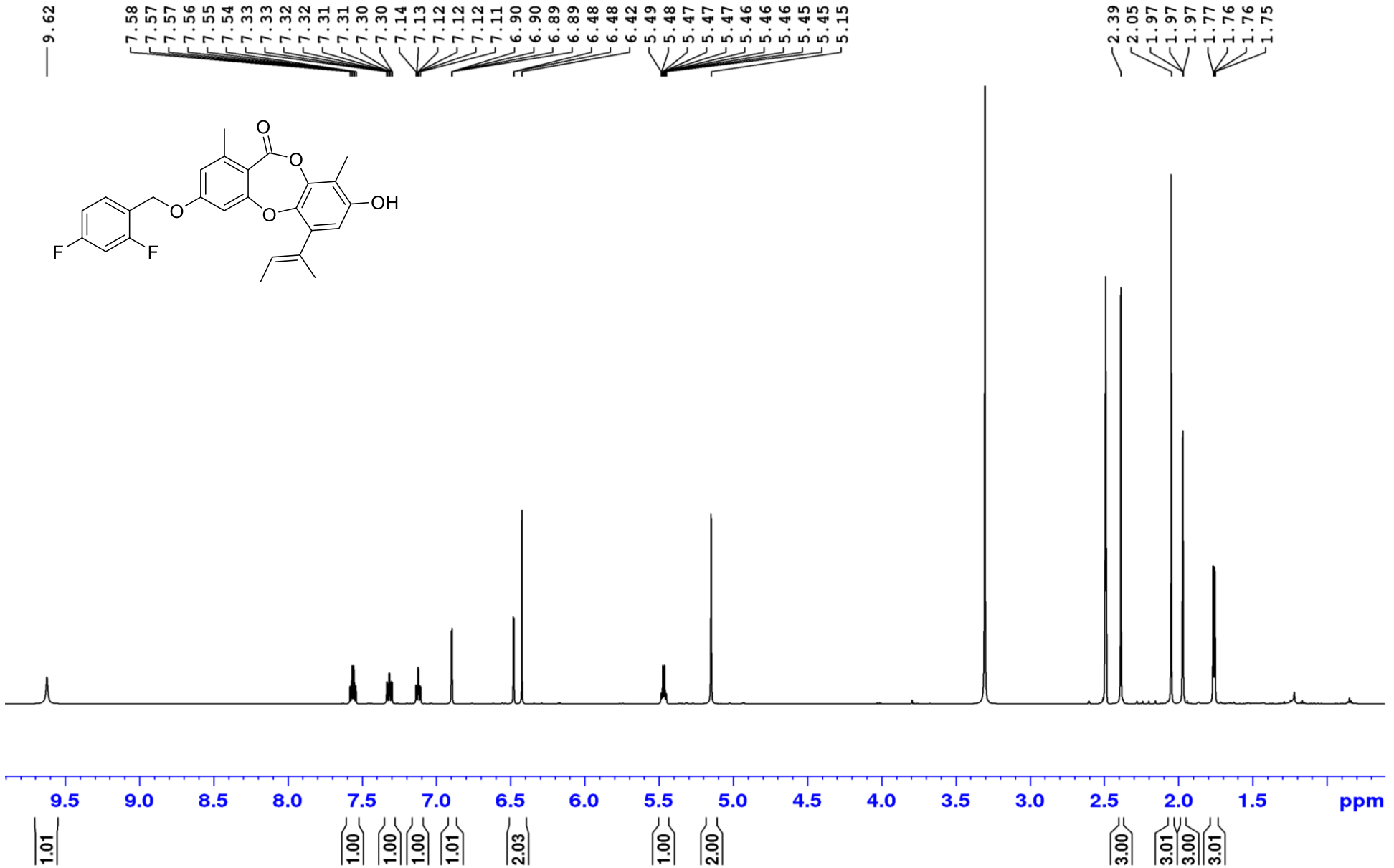

Figure S43. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(2,4-difluorobenzyl)unguinol (**7g**)

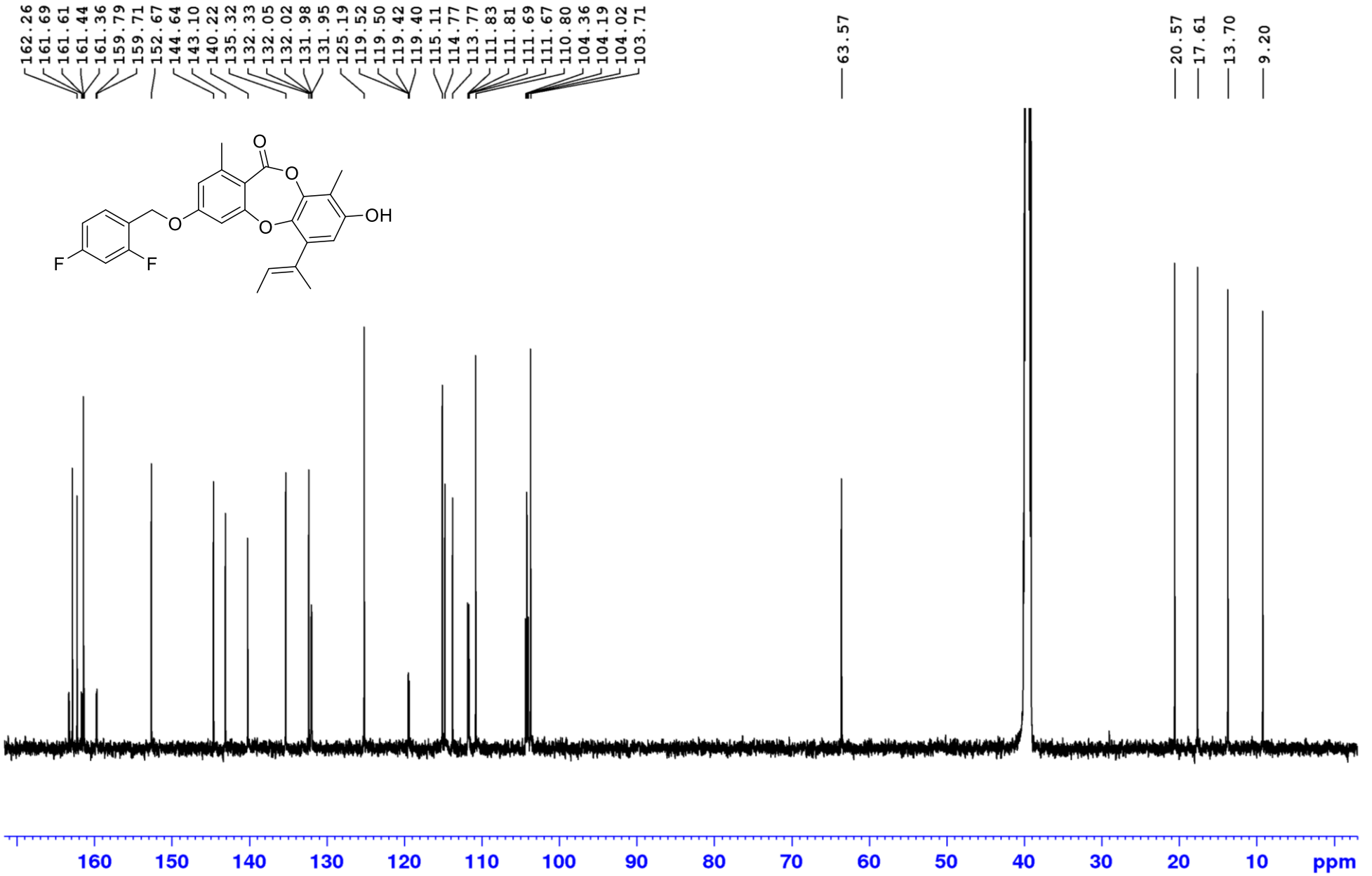

Figure S44. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(2,4-difluorobenzyl)unguinol (**7g**)

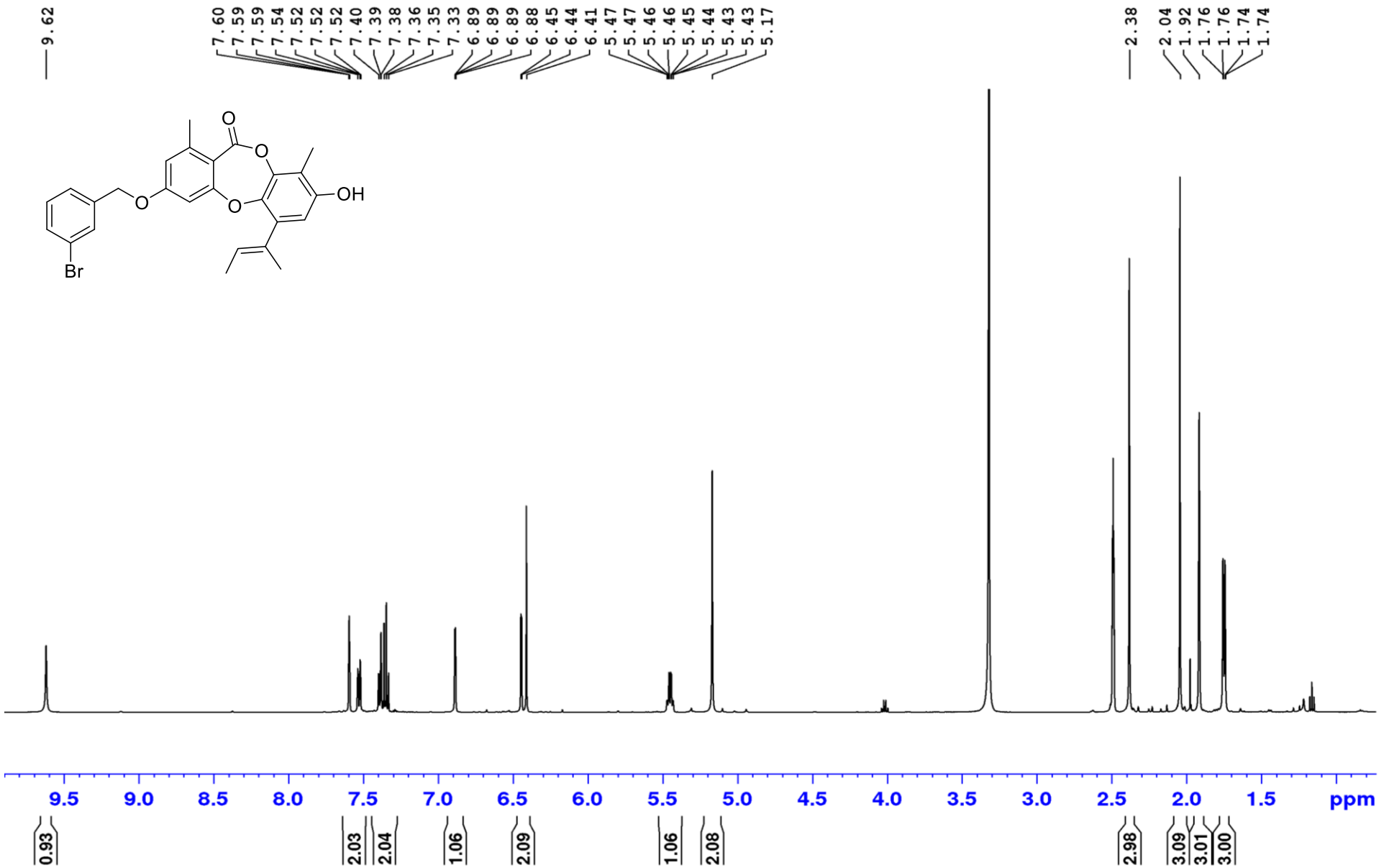

Figure S45. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of 3-*O*-(3-bromobenzyl)unguinol (**7h**)

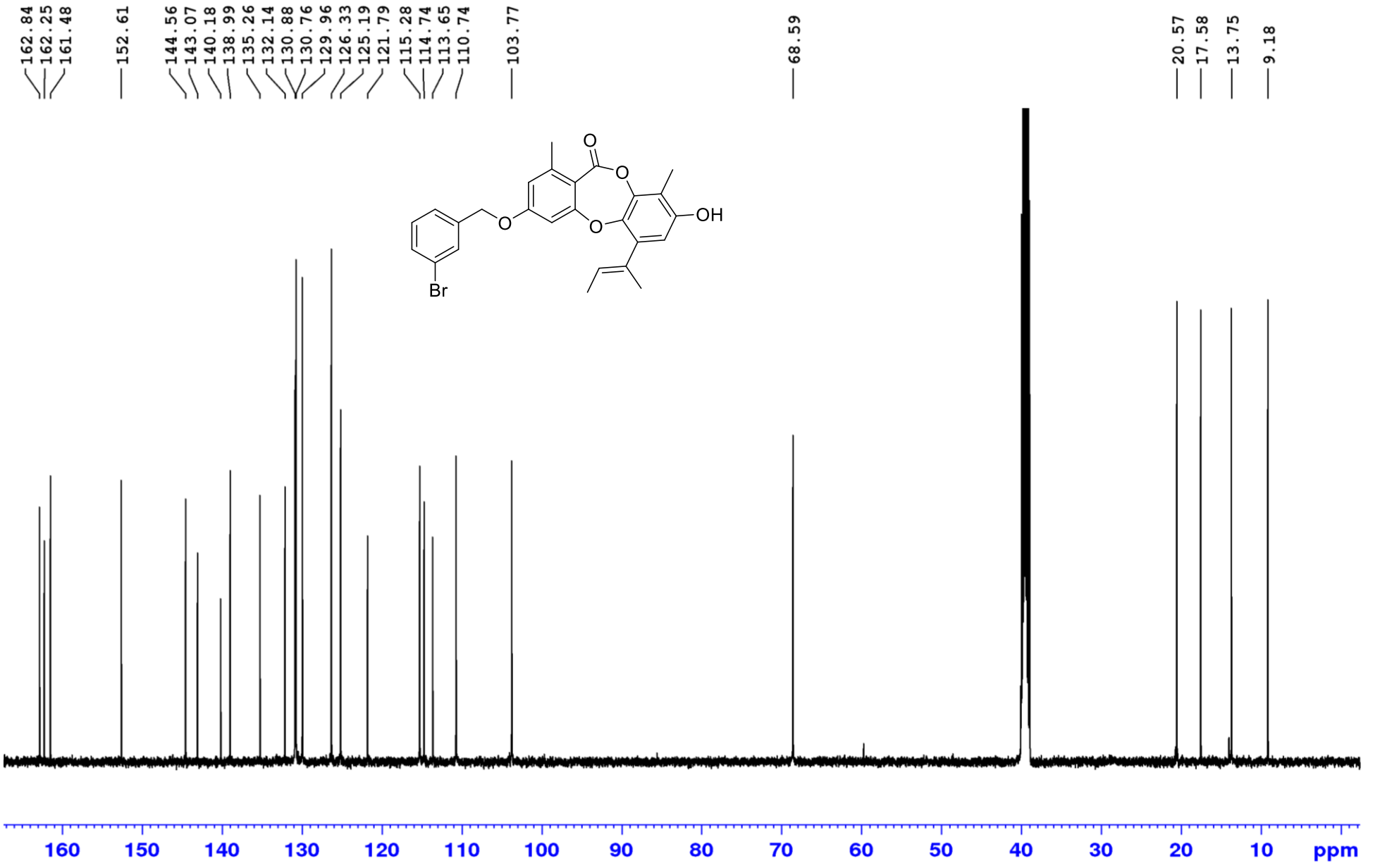

Figure S46. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of 3-*O*-(3-bromobenzyl)unguinol (**7h**)

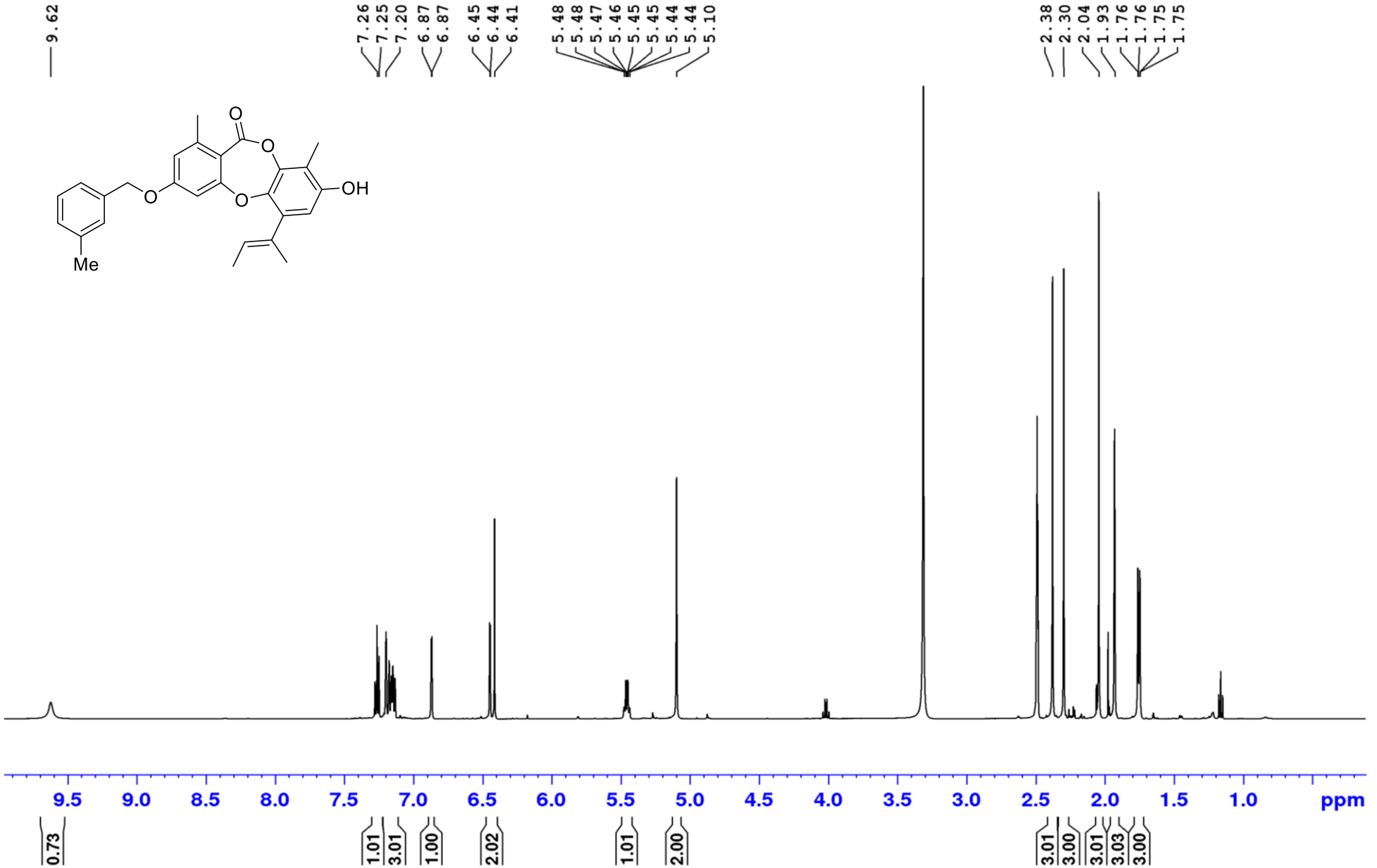

Figure S47. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of 3-*O*-(3-methylbenzyl)unguinol (**7i**)

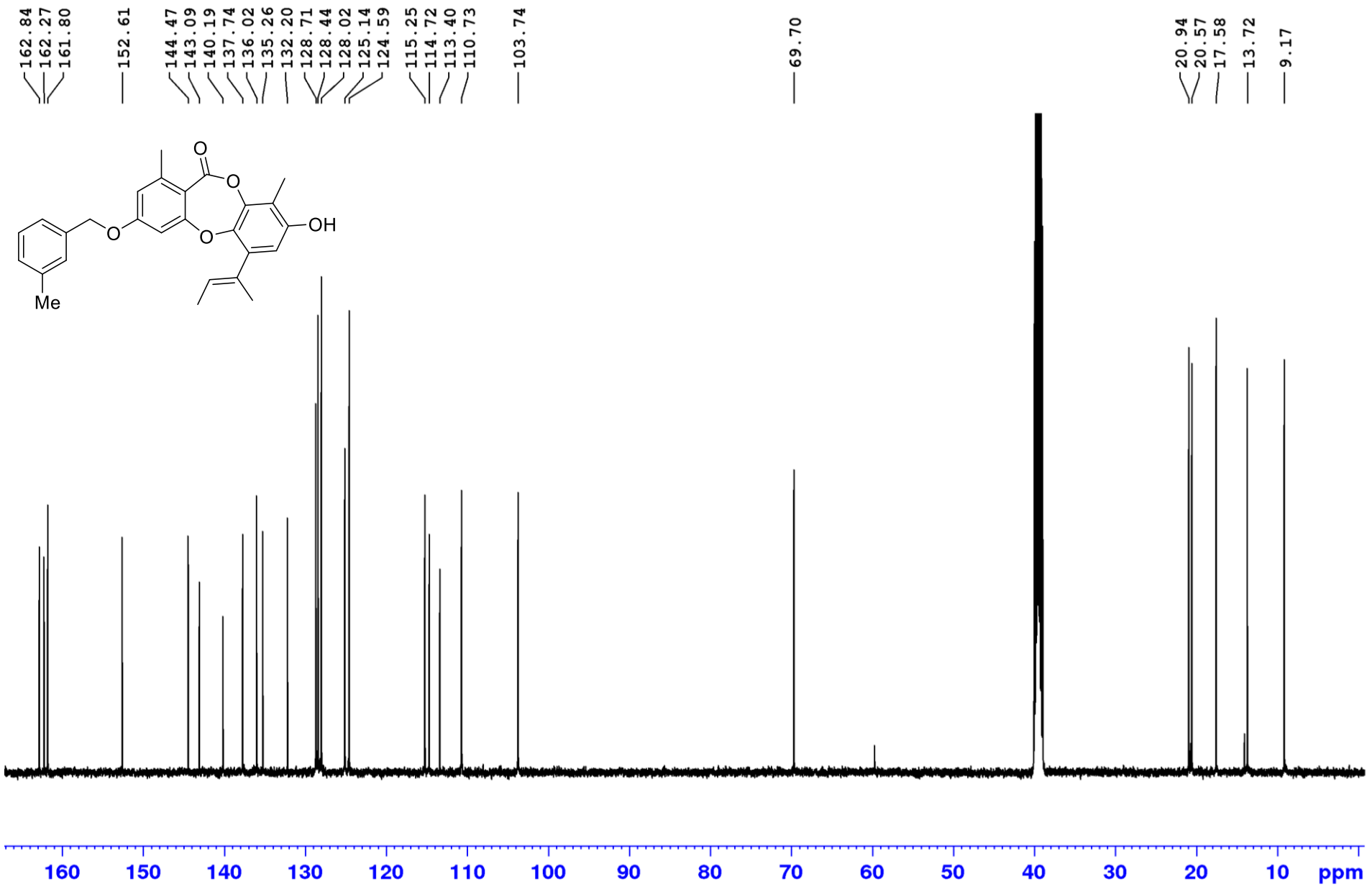

Figure S48. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of 3-*O*-(3-methylbenzyl)unguinol (**7i**)

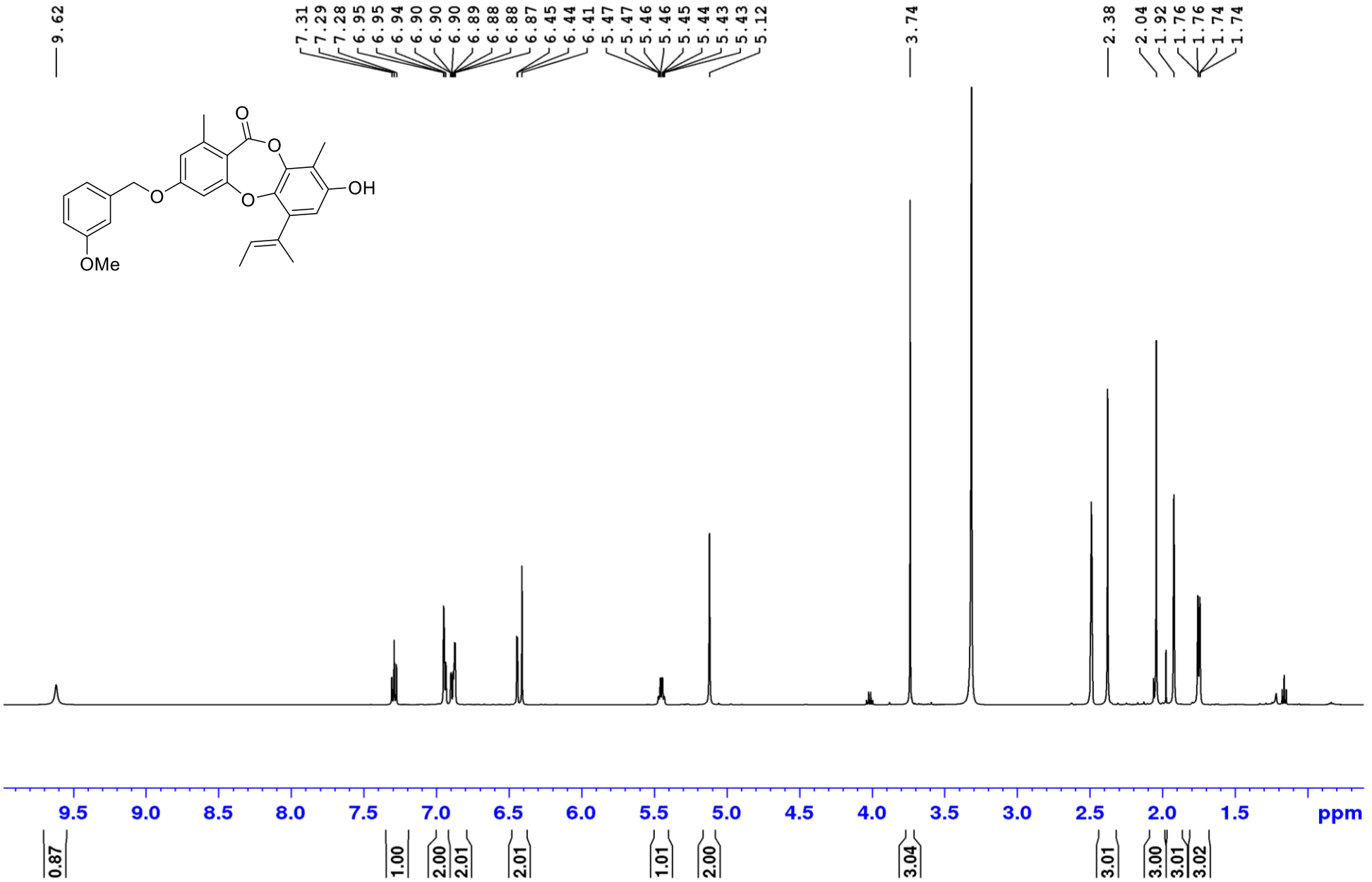

Figure S49. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of 3-*O*-(3-methoxybenzyl)unguinol (**7j**)

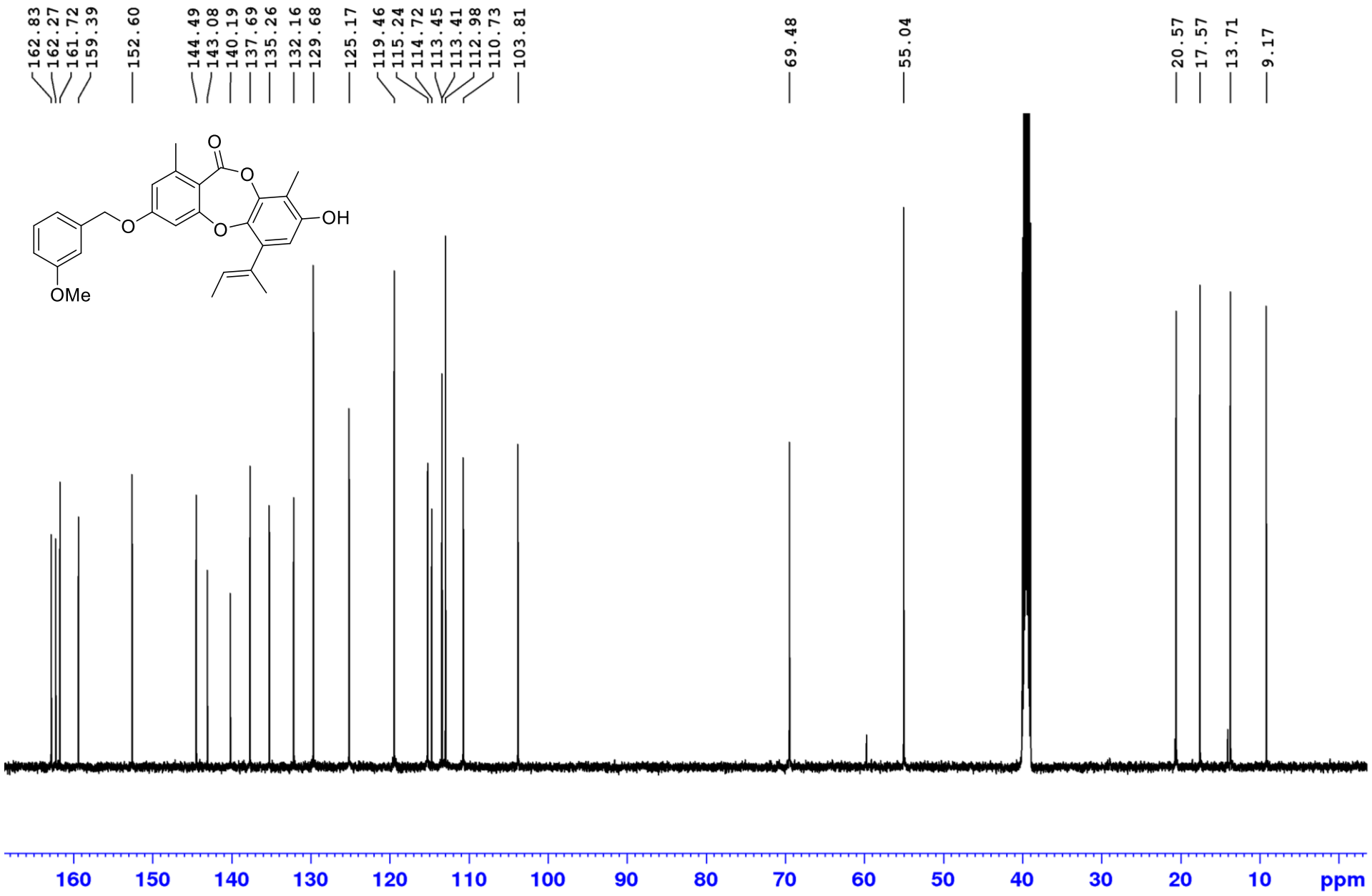

Figure S50. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of 3-*O*-(3-methoxylbenzyl)unguinol (**7j**)

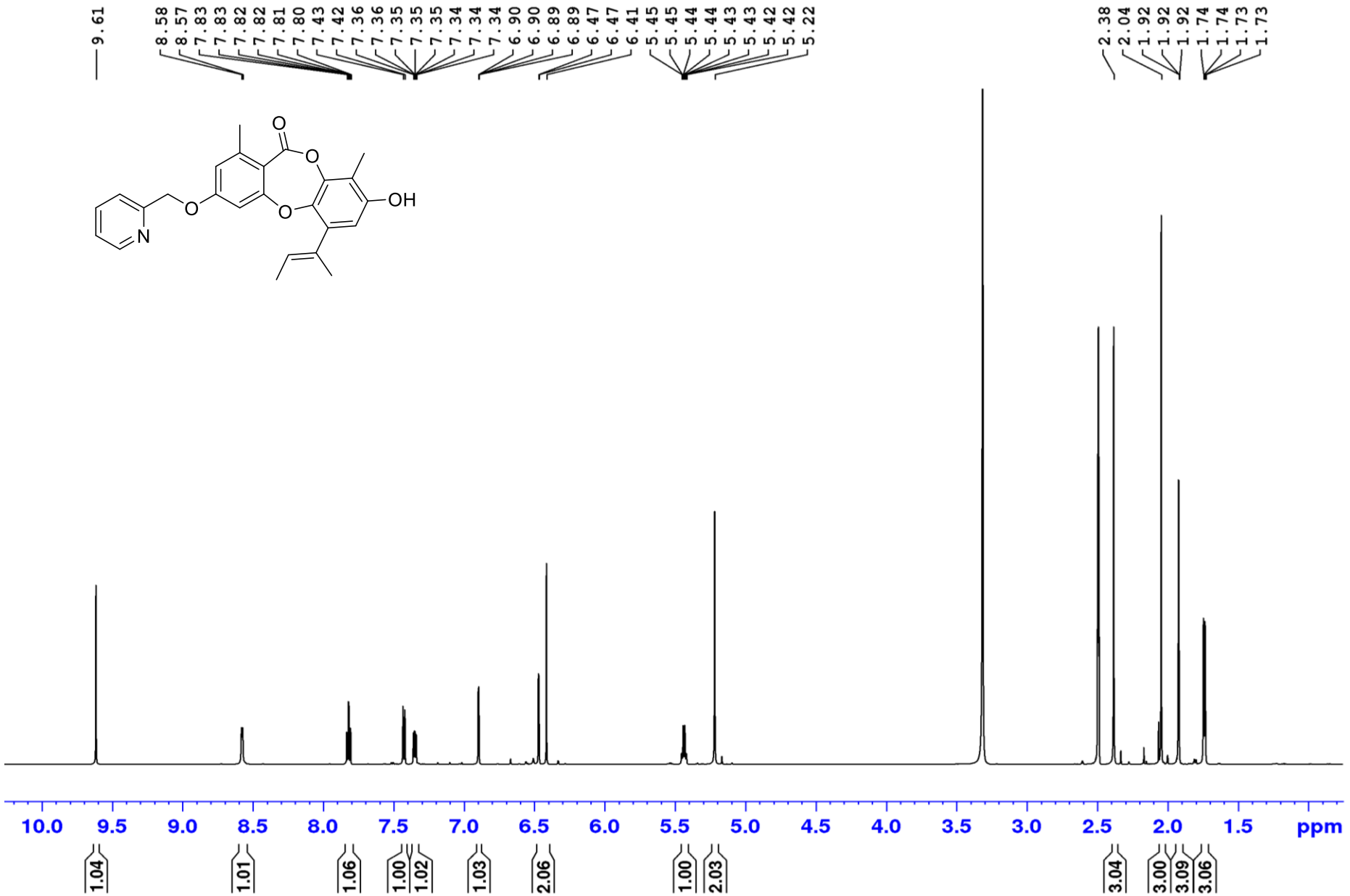

Figure S51. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(2-picolyl)unguinol (**7k**)

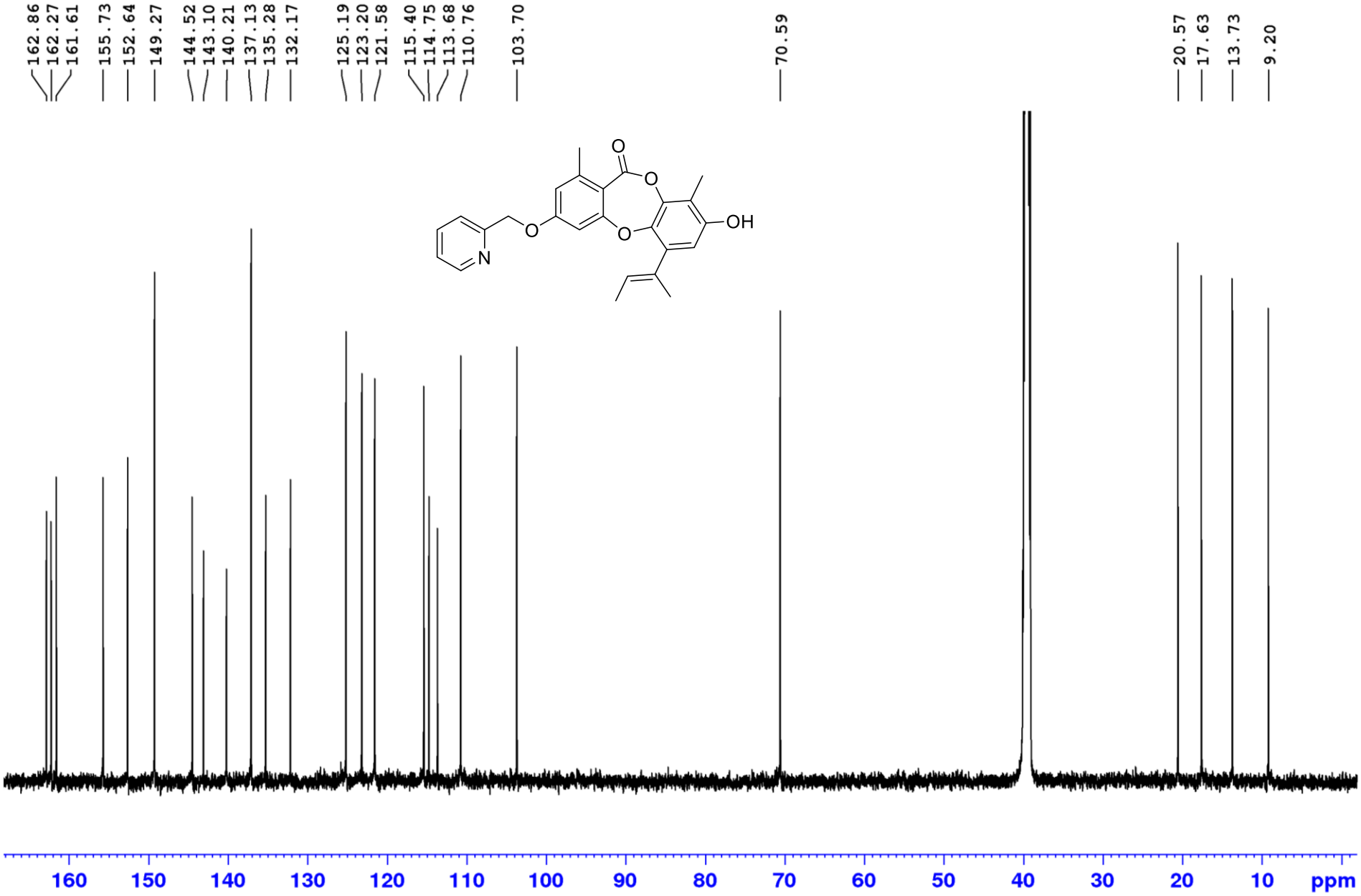

Figure S52. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(2-picolyl)unguinol (**7k**)

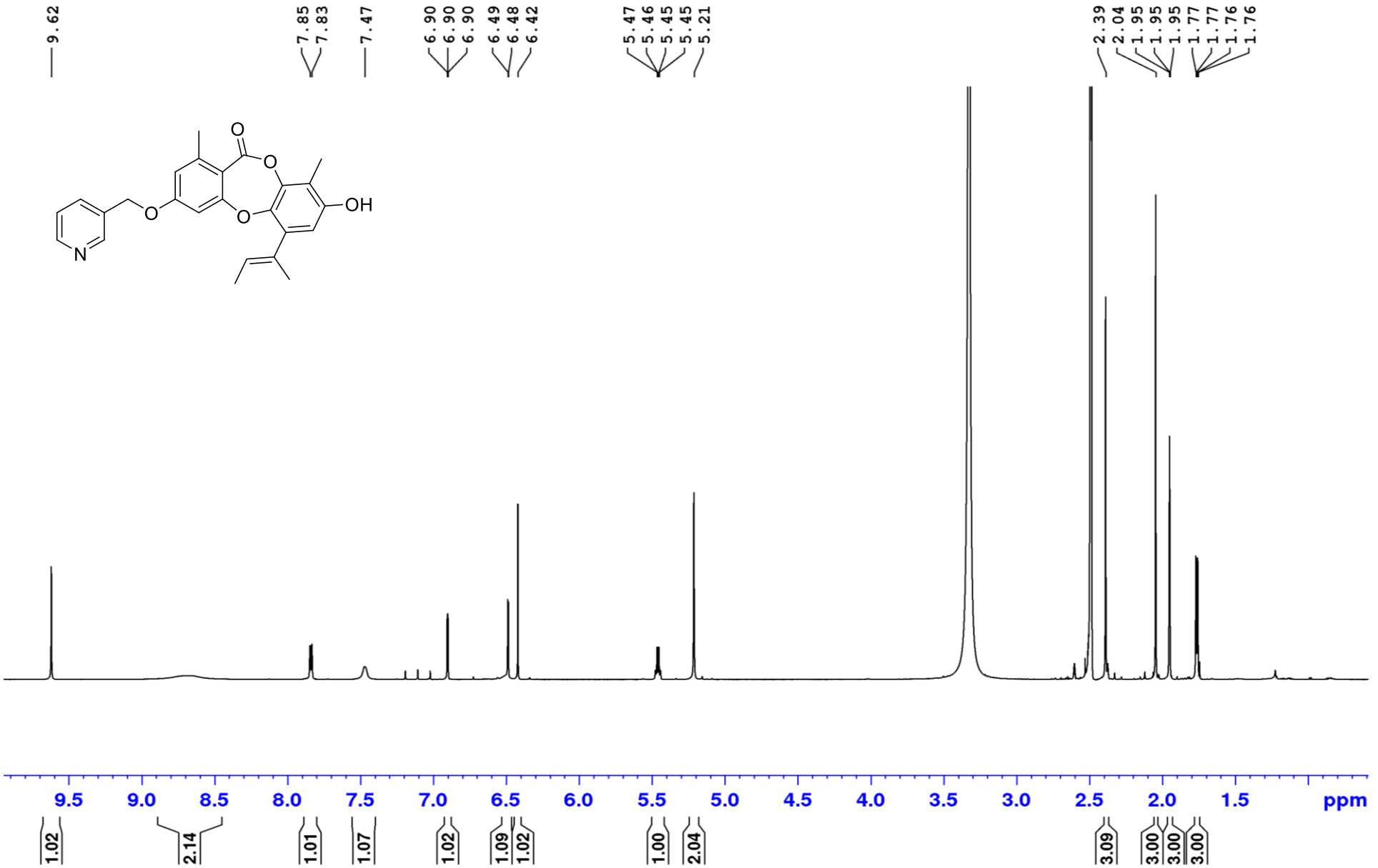

Figure S53. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(3-picolyl)unguinol (**7l**)

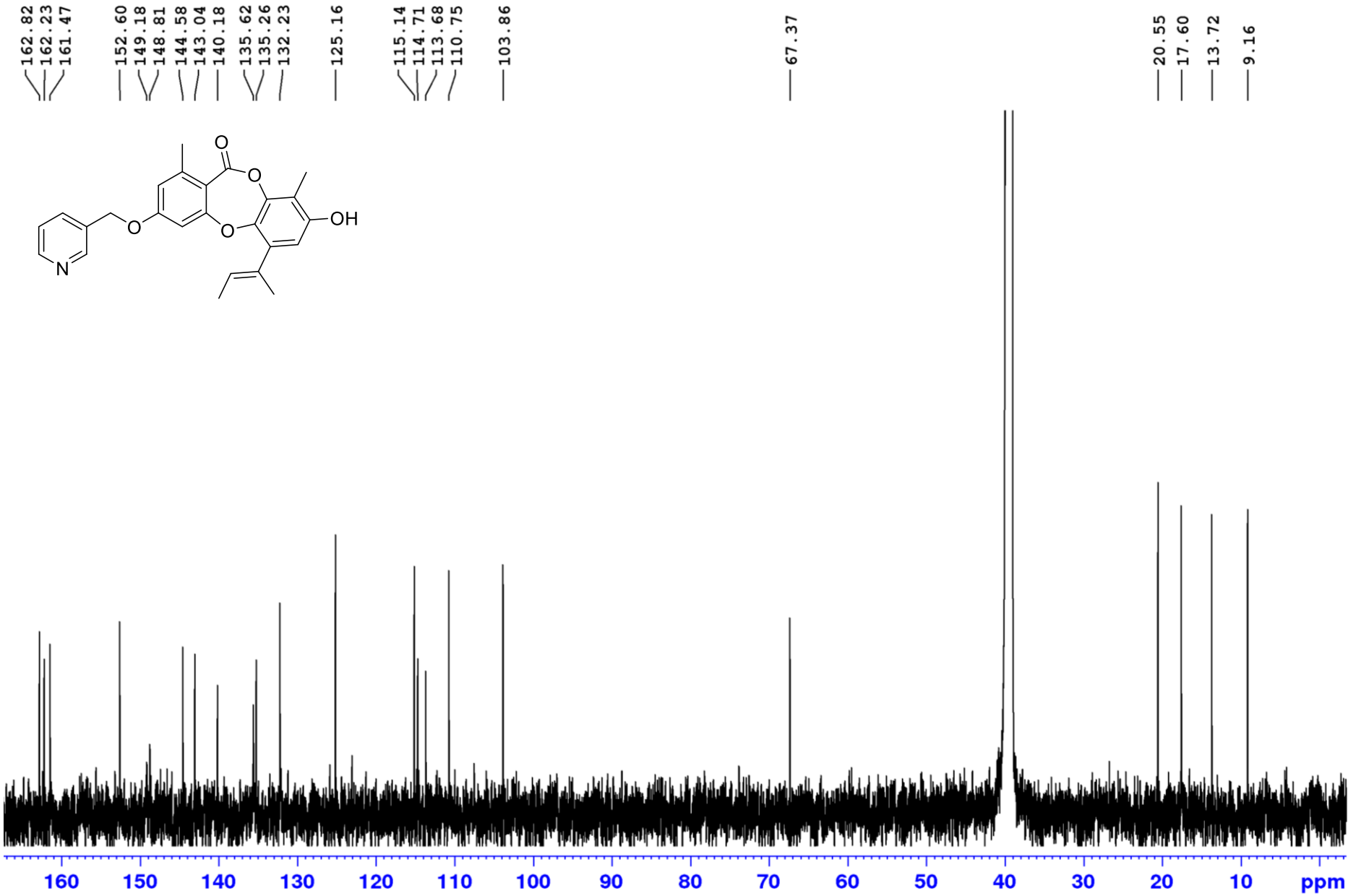

Figure S54. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(3-picolyl)unguinol (**7l**)

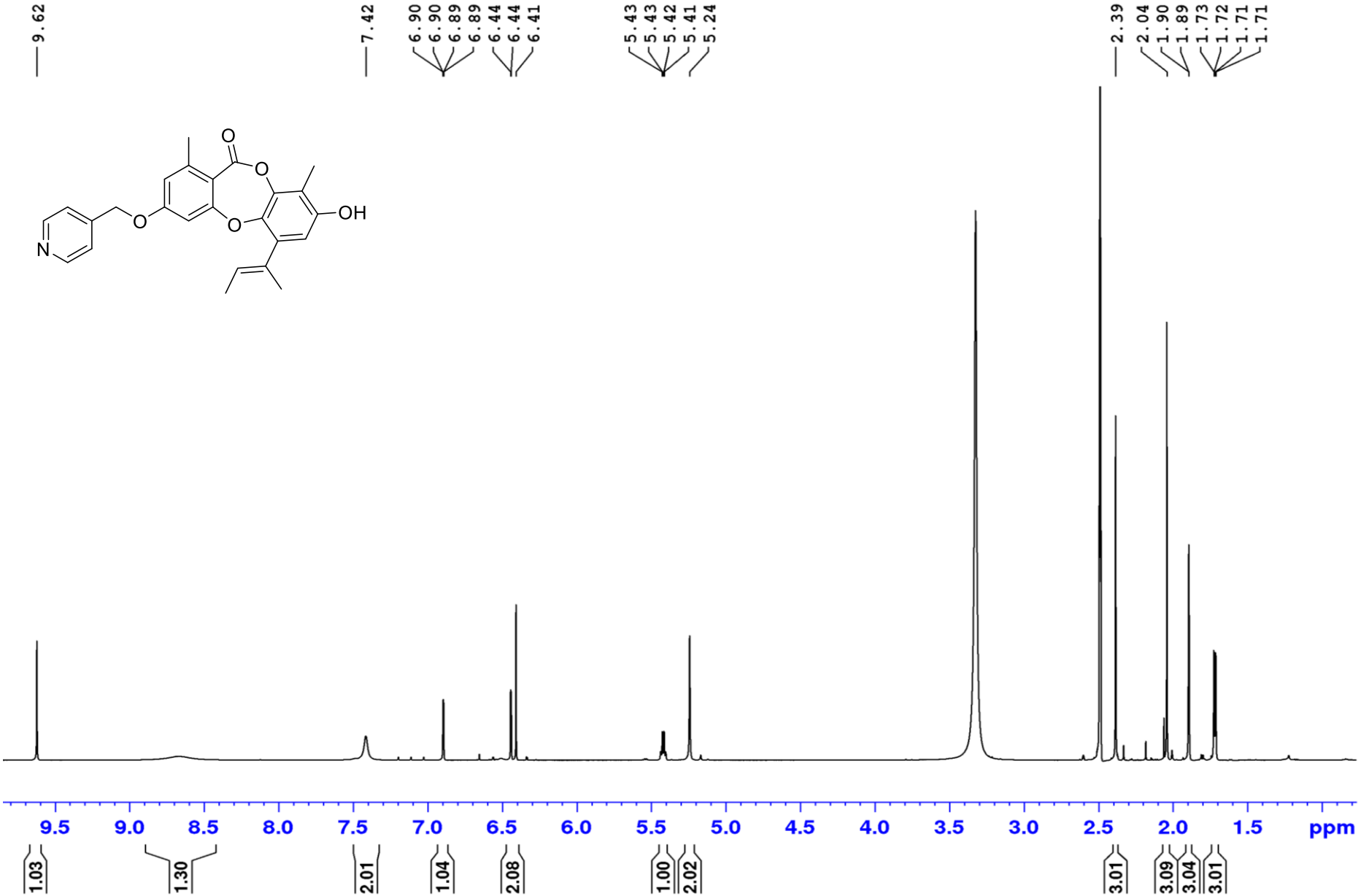

Figure S55. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(4-picolyl)unguinol (**7m**)

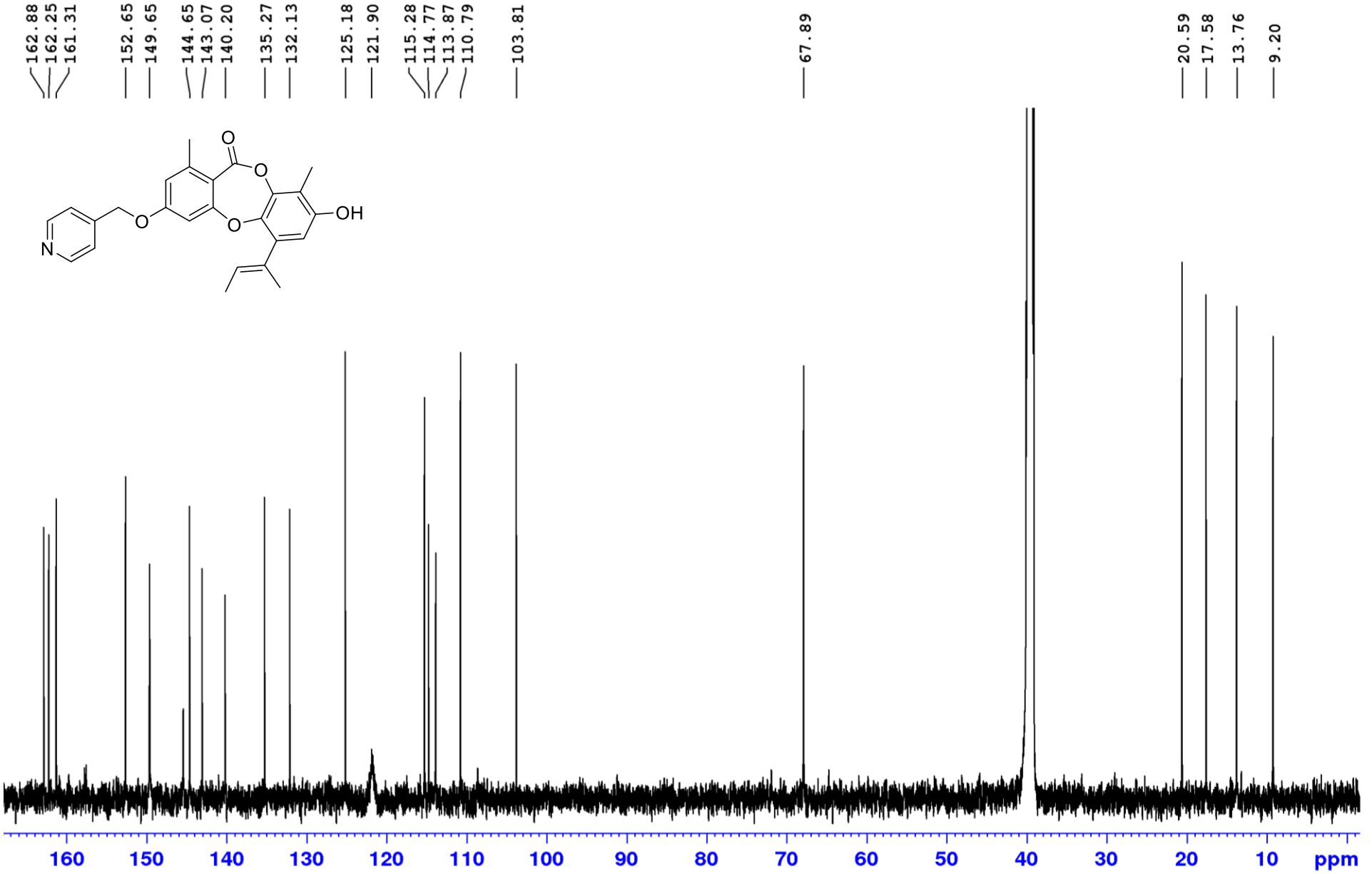

Figure S56. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(4-picolyl)unguinol (**7m**)

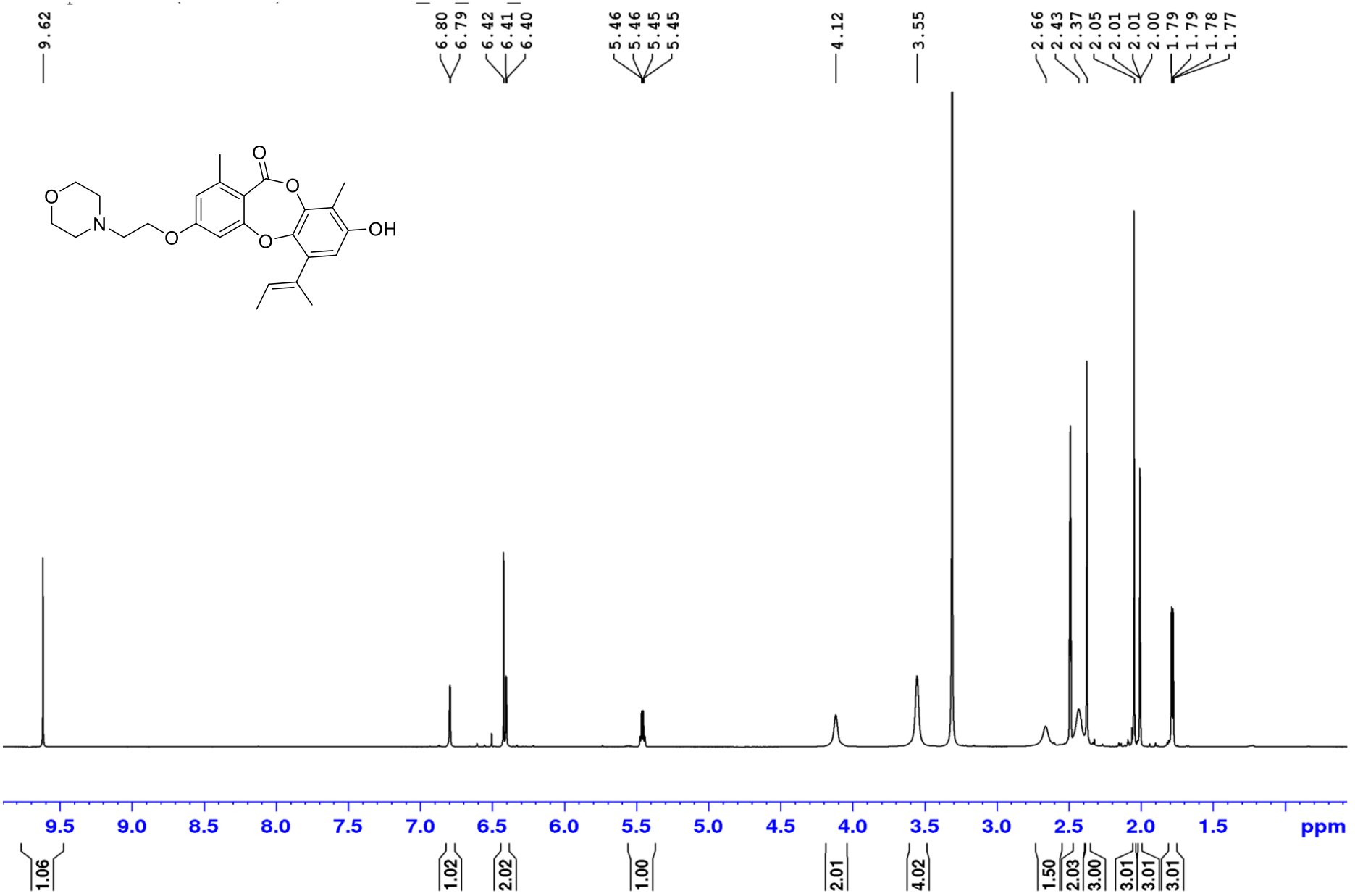

Figure S57. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(4-morpholinoethyl)unguinol (**7n**)

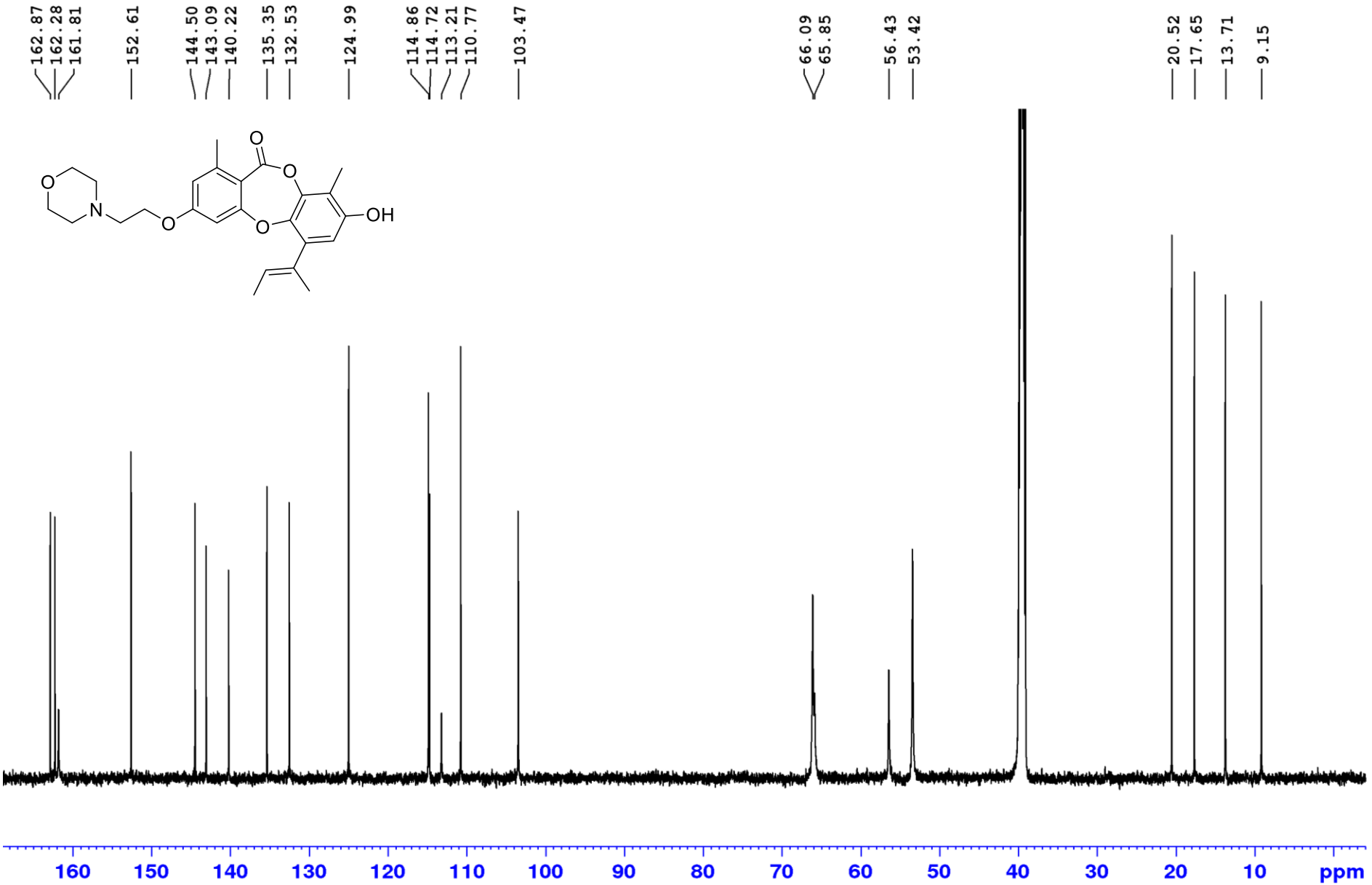

Figure S58. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(4-morpholinoethyl)unguinol (**7n**)

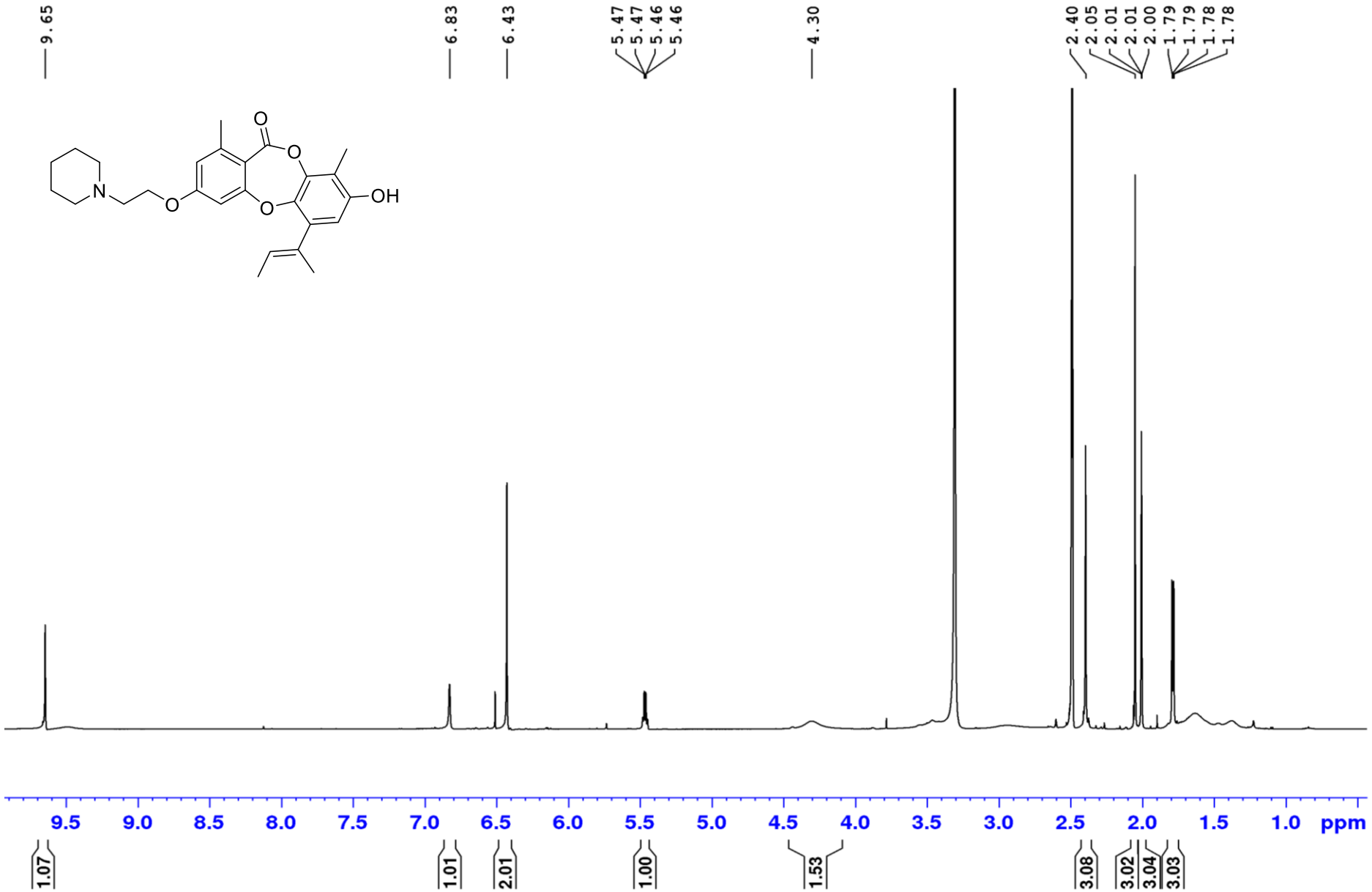

Figure S59. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(1-piperidinylethyl)unguinol (**7o**)

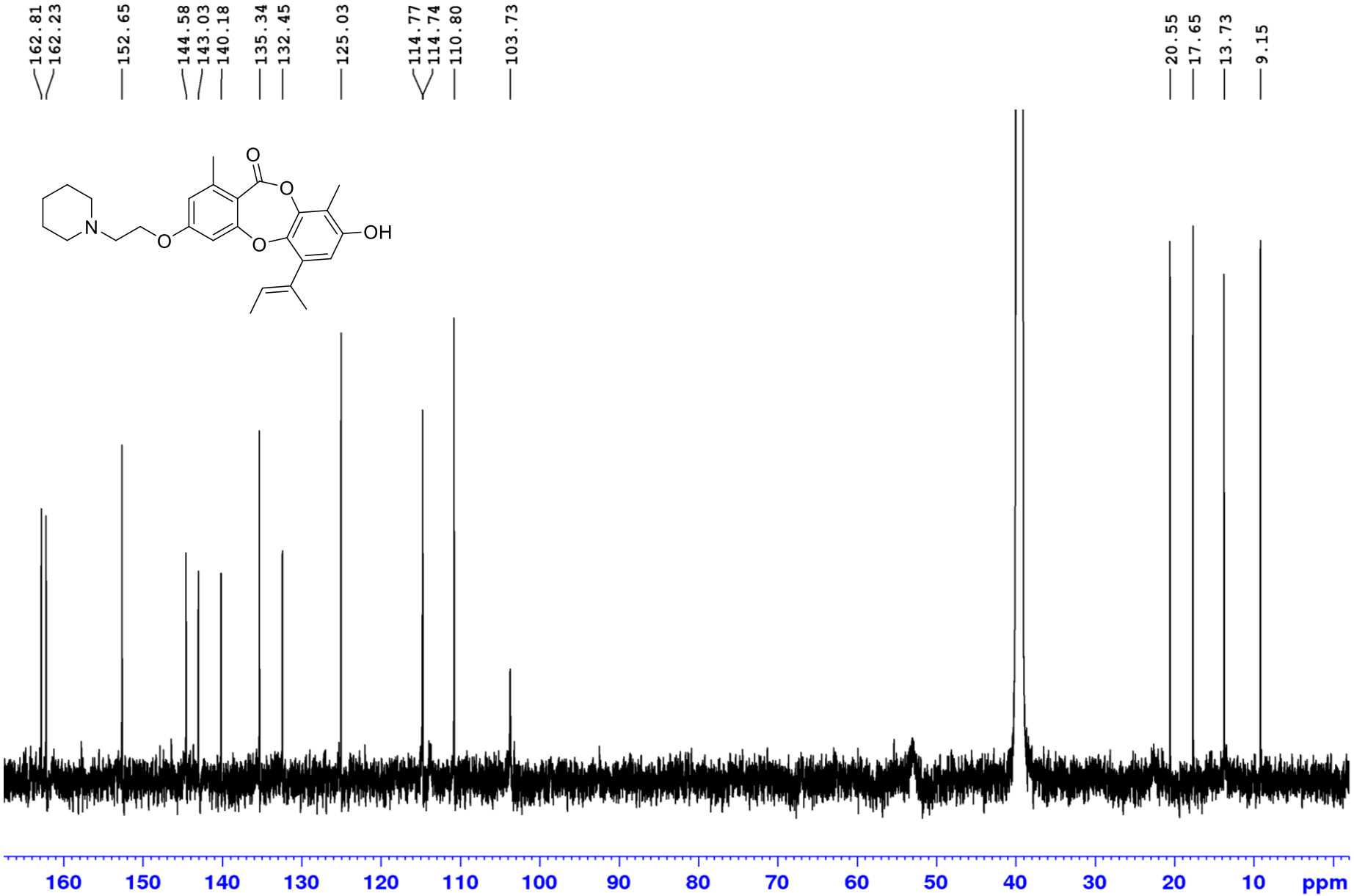

Figure S60. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(1-piperidinylethyl)unguinol (**7o**)

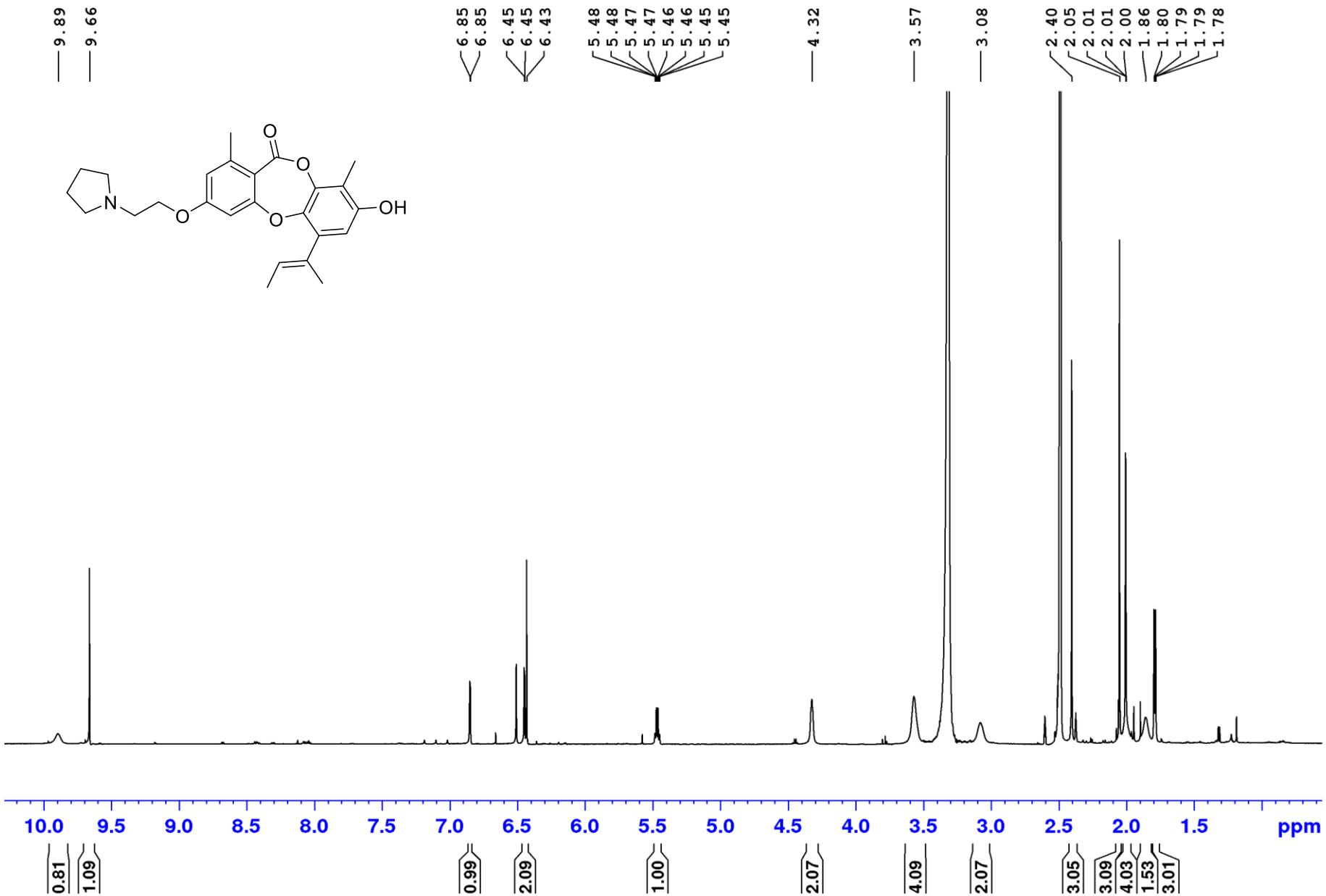

Figure S61. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(1-pyrrolidinylethyl)unguinol (**7p**)

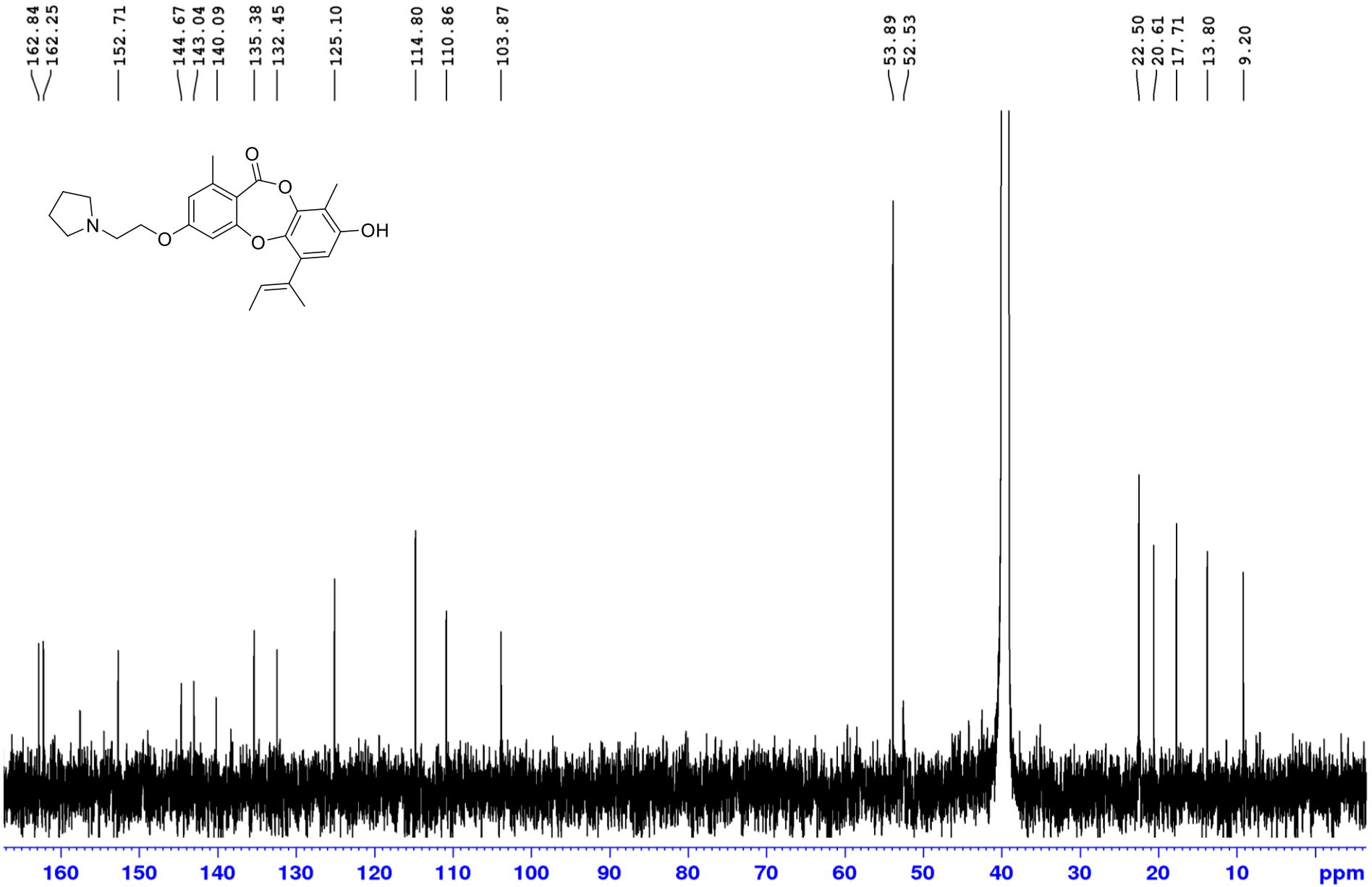

Figure S62. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(1-pyrrolidinylethyl)unguinol (**7p**)

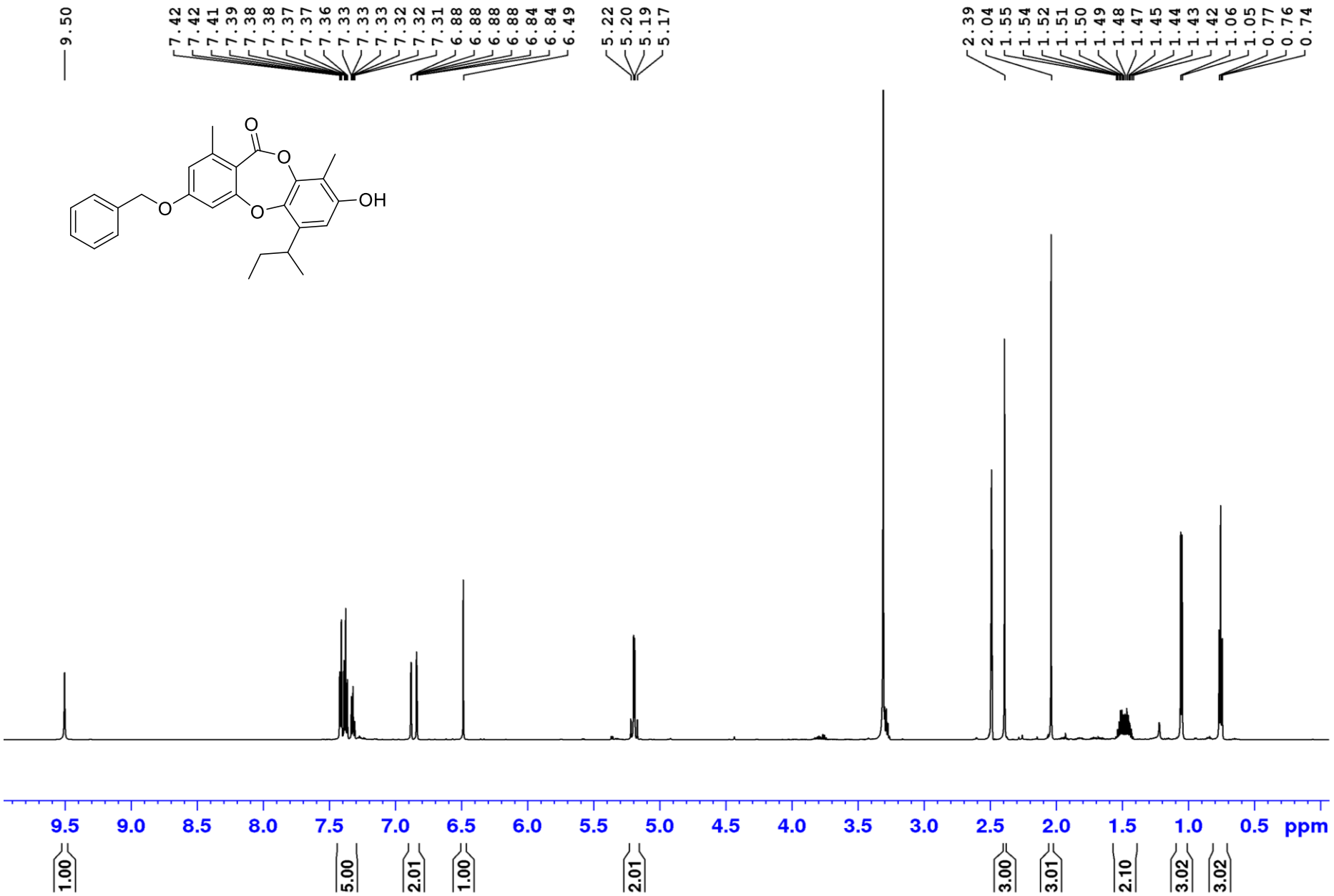

Figure S63. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-benzyl-1′,2′-dihydrounguinol (**8a**)

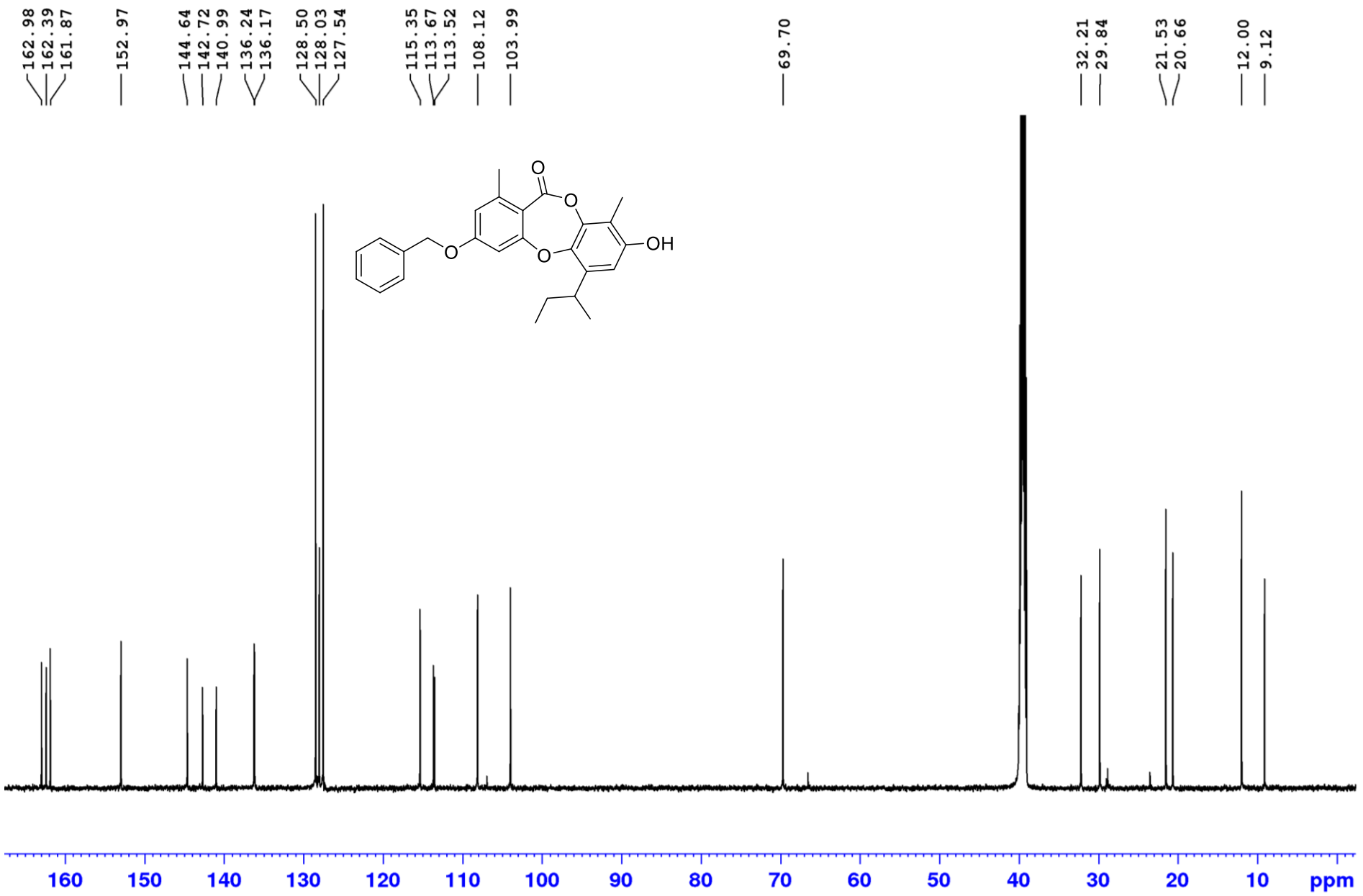

Figure S64. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-benzyl-1′,2′-dihydrounguinol (**8a**)

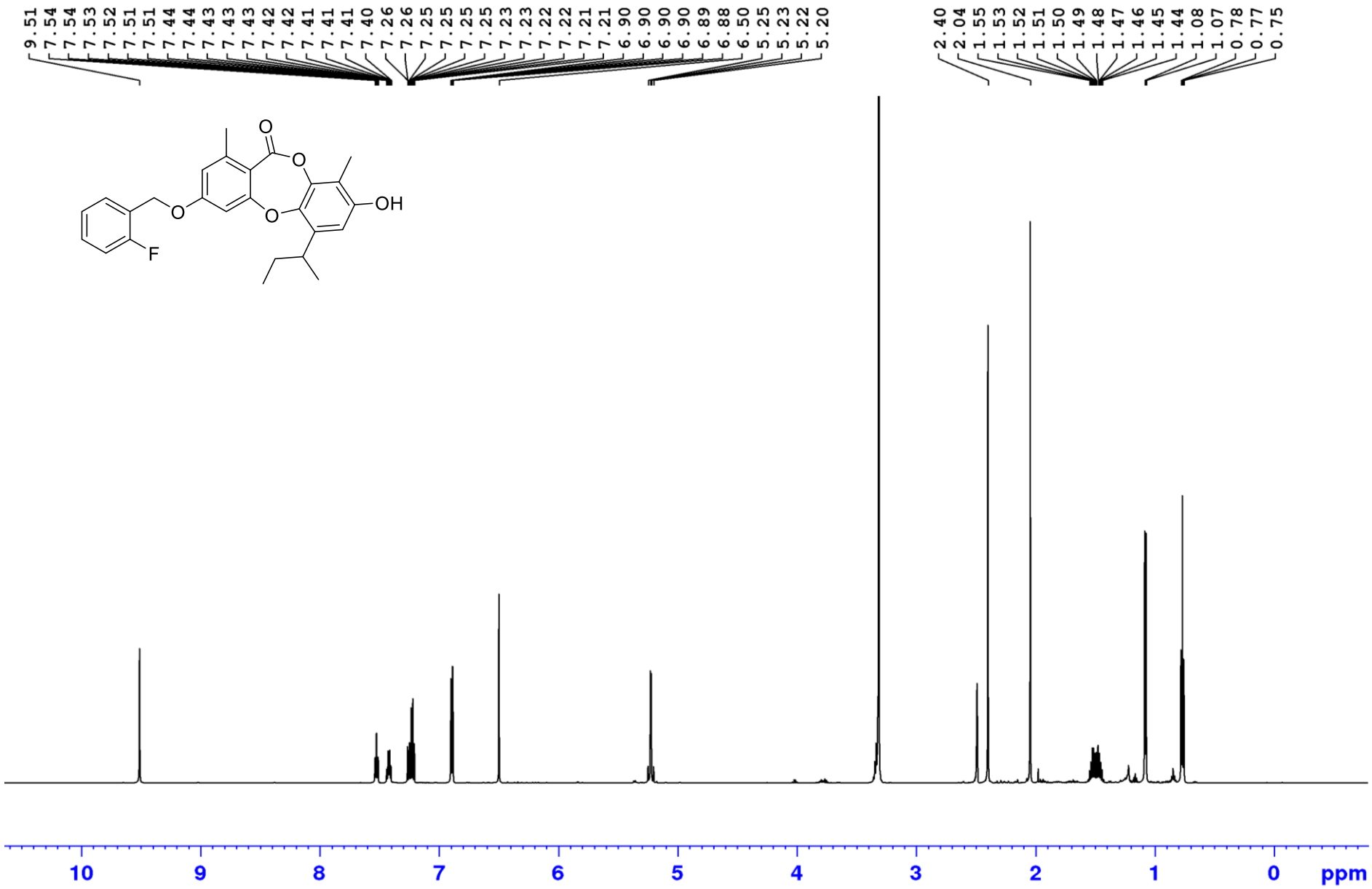

Figure S65. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(2-fluorobenzyl)-1′,2′-dihydrounguinol (**8b**)

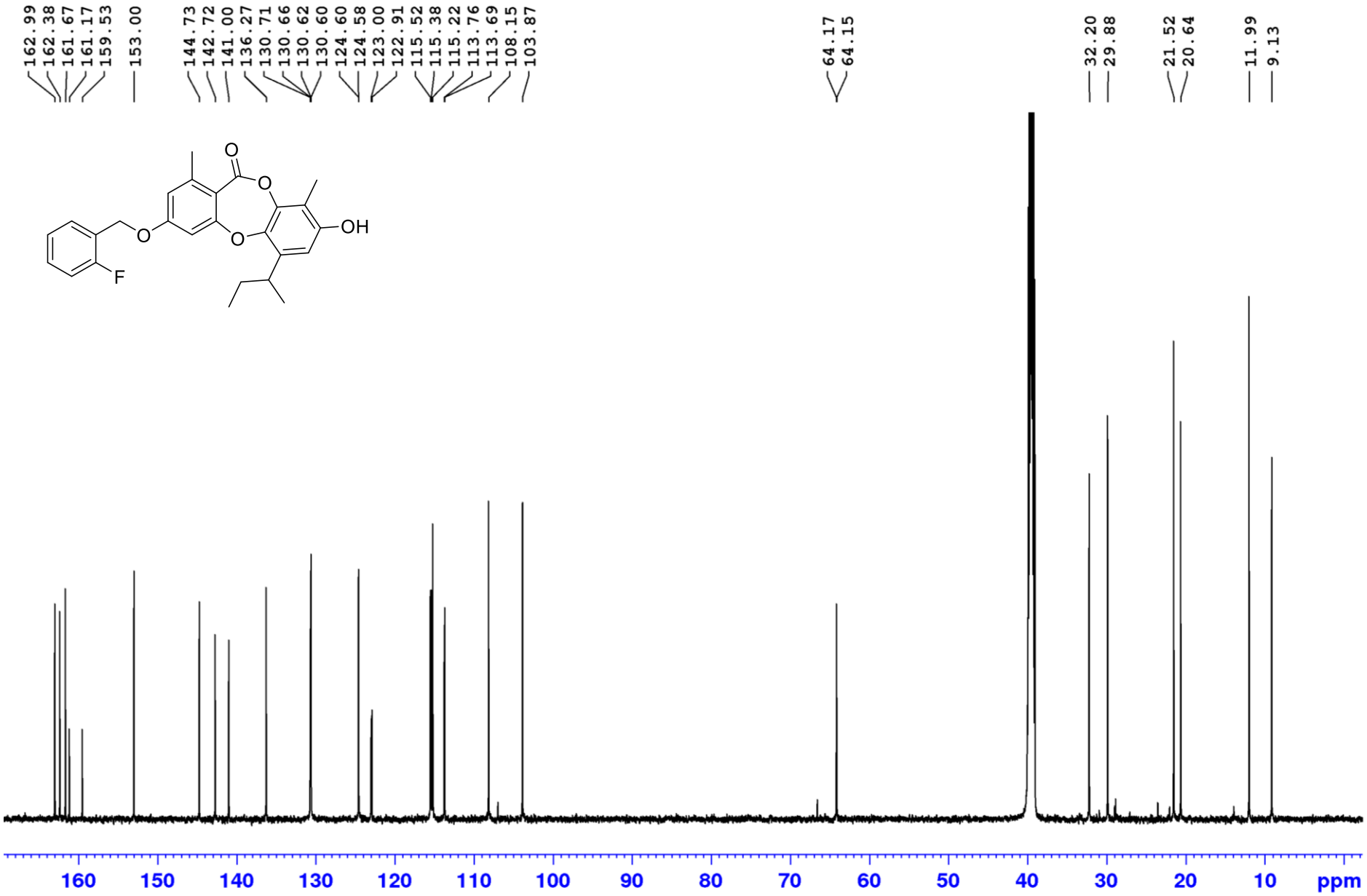

Figure S66. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(2-fluorobenzyl)-1′,2′-dihydrounguinol (**8b**)

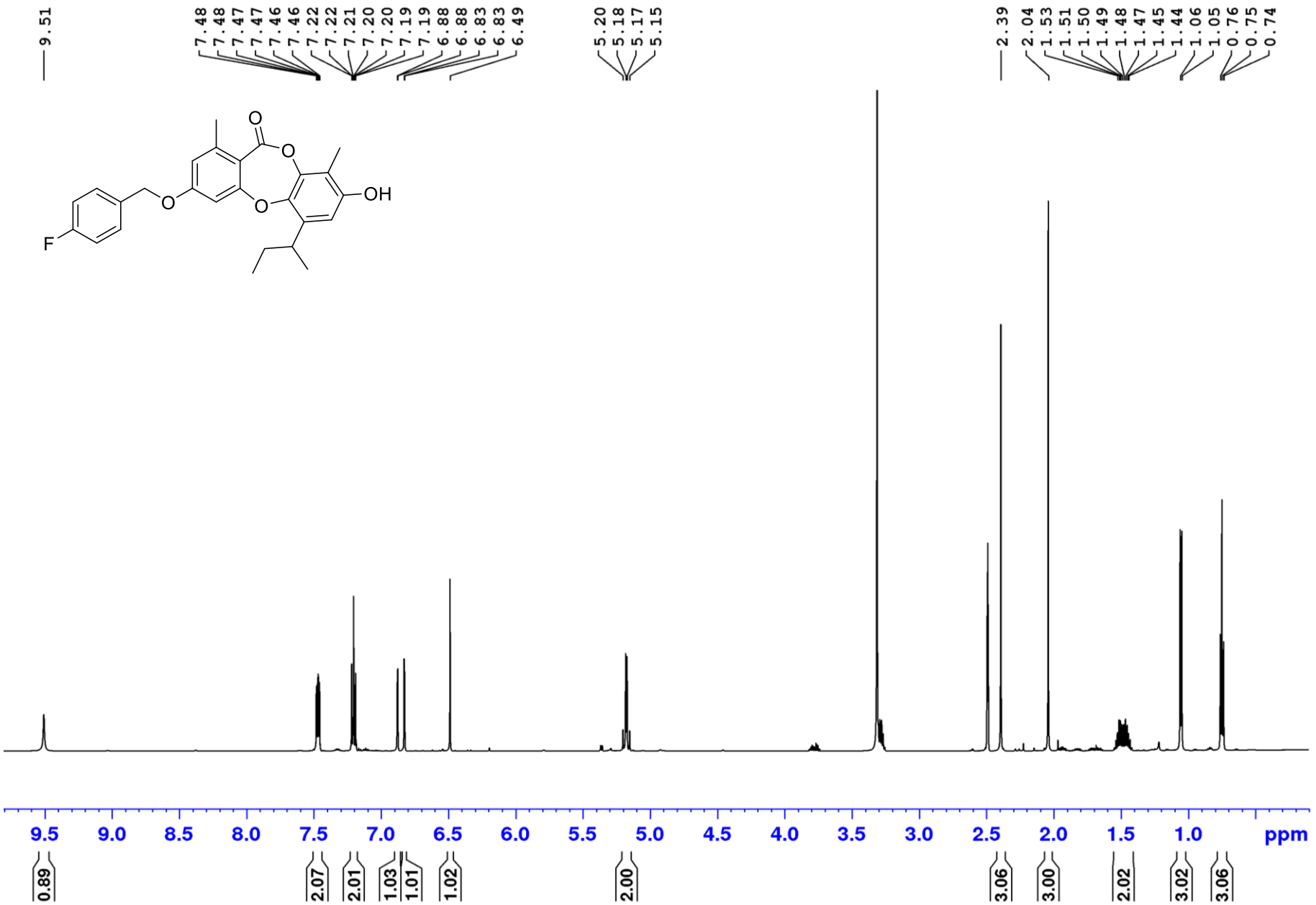

Figure S67. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 3-*O*-(4-fluorobenzyl)-1′,2′-dihydrounguinol (**8c**)

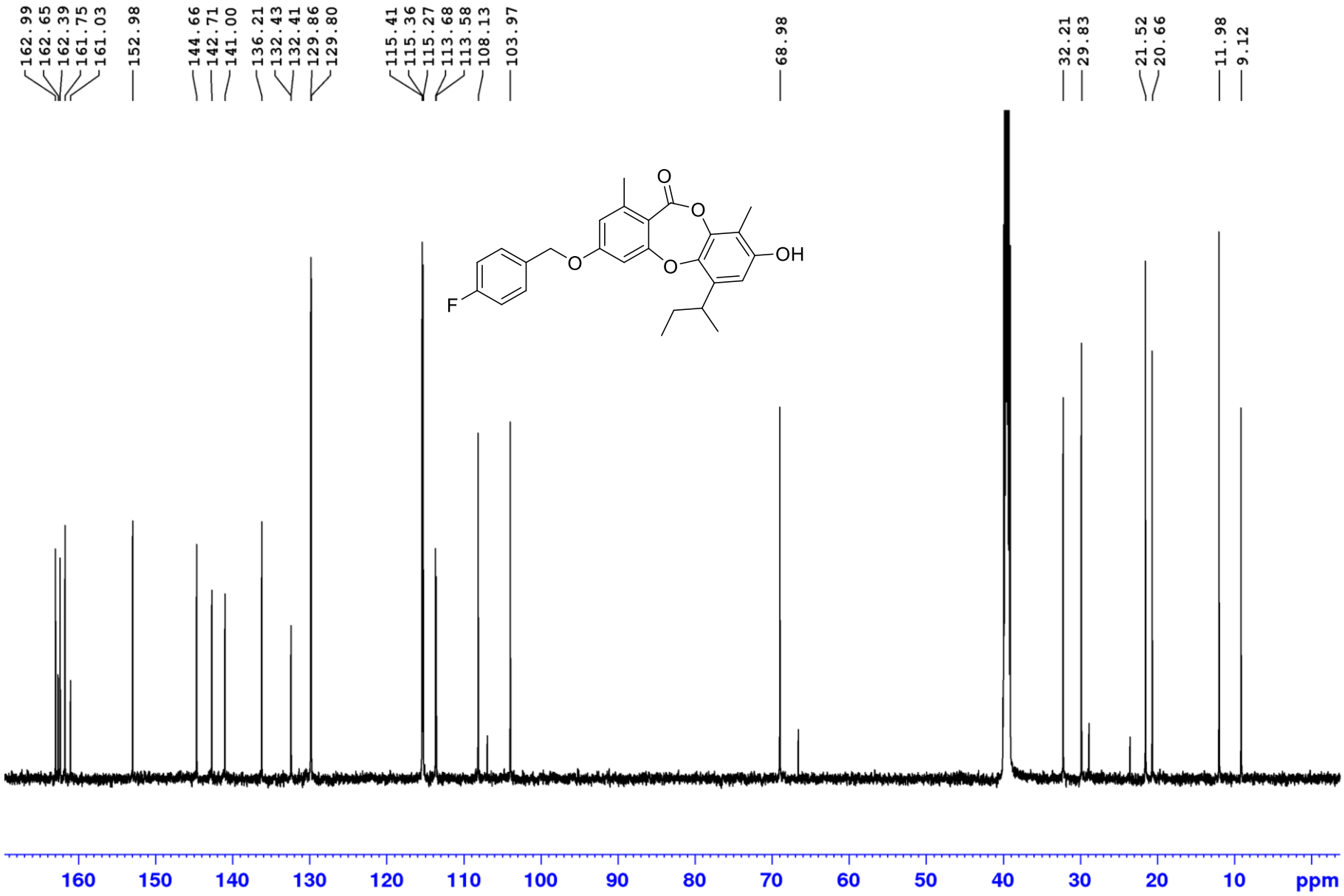

Figure S68. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-*O*-(4-fluorobenzyl)-1′,2′-dihydrounguinol (**8c**)

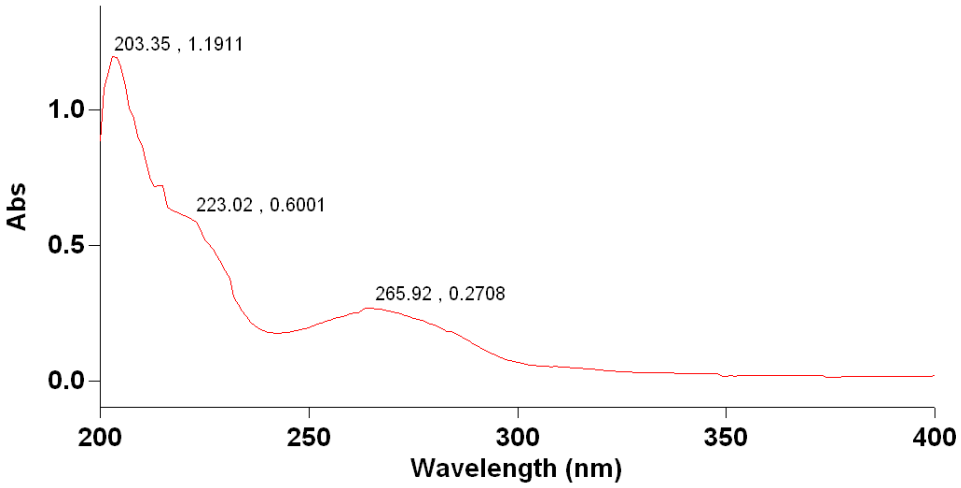

Figure S69. UV-vis spectrum of 1′,2′-dihydrounguinol (**2a**) in MeOH

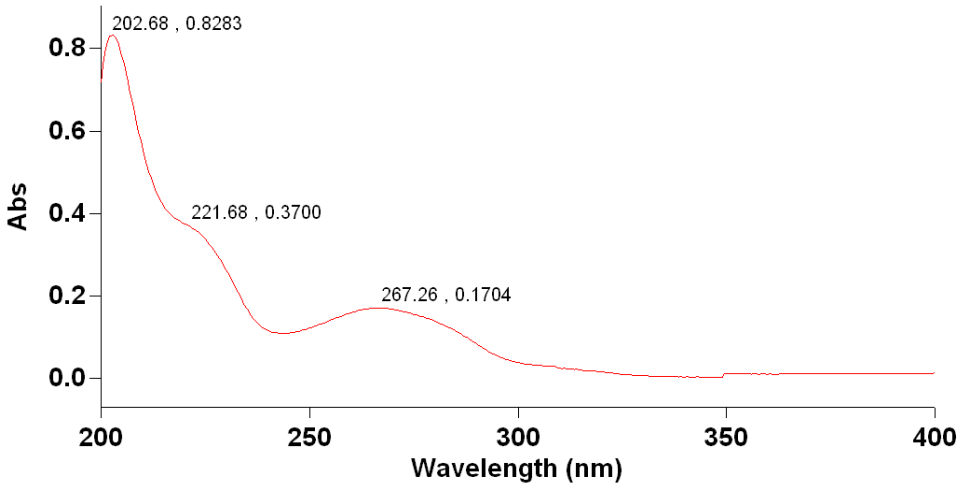

Figure S70. UV-vis spectrum of *cis*-1′,2′-epoxyunguinol (**2b**) in MeOH

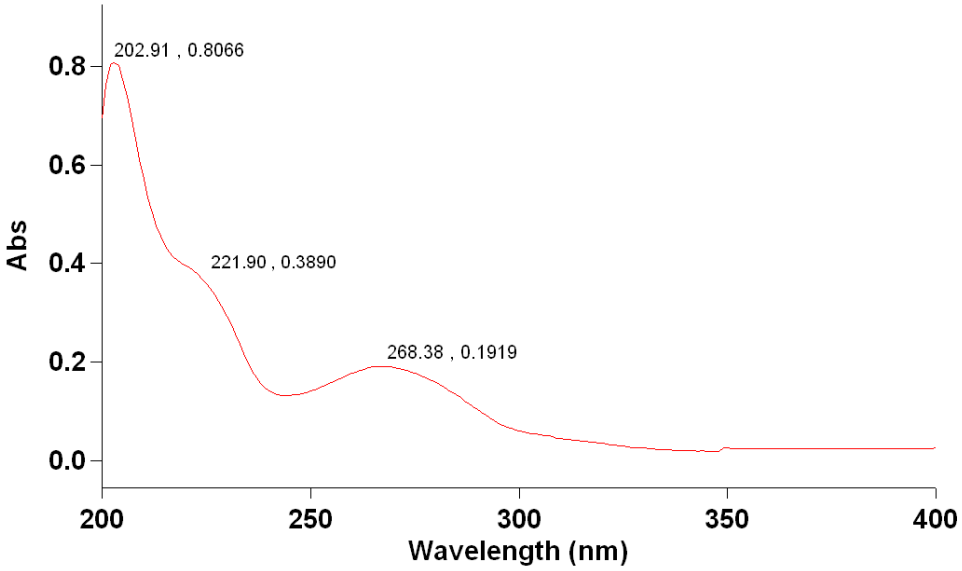

Figure S71. UV-vis spectrum of 1′,2′-dihydroxyunguinol (**2c**) in MeOH

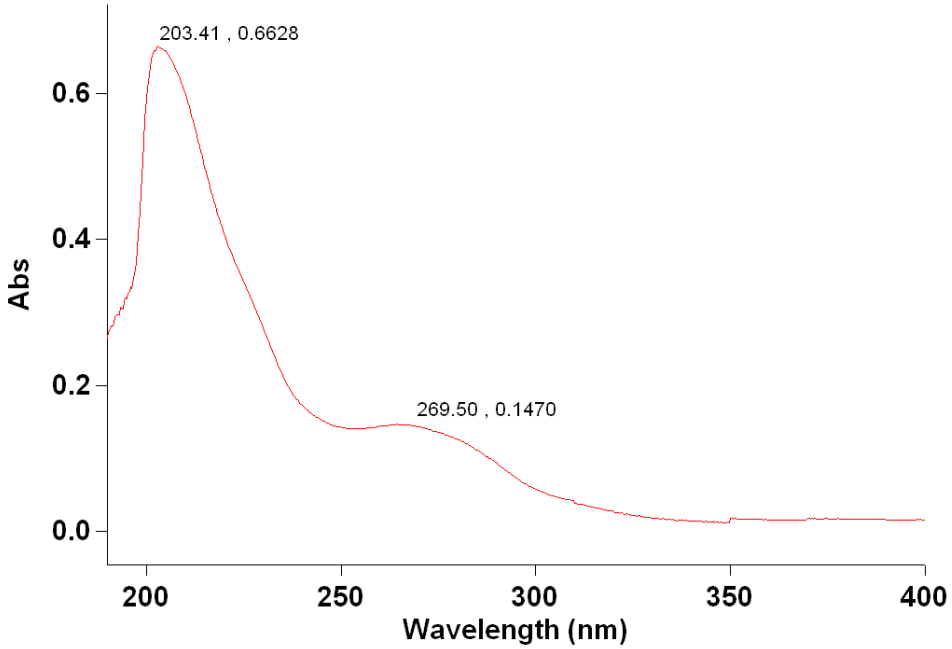

Figure S72. UV-vis spectrum of 2′-hydroxy-$\Delta^{1',4'}$-unguinol (**2d**) in MeOH

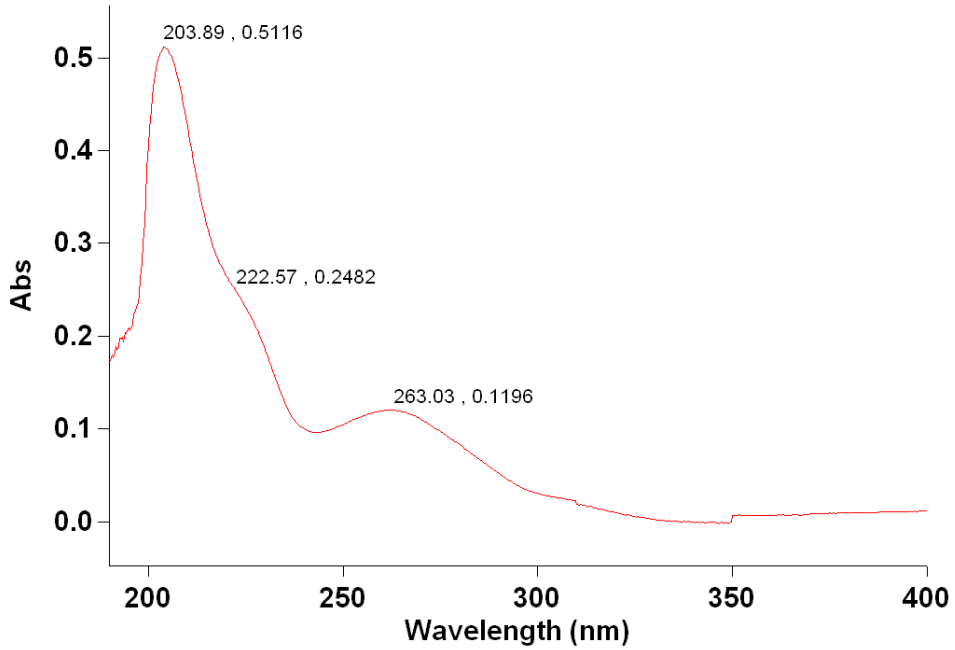

Figure S73. UV-vis spectrum of 2′-oxo-$\Delta^{1',4'}$-unguinol (**2e**) in MeOH

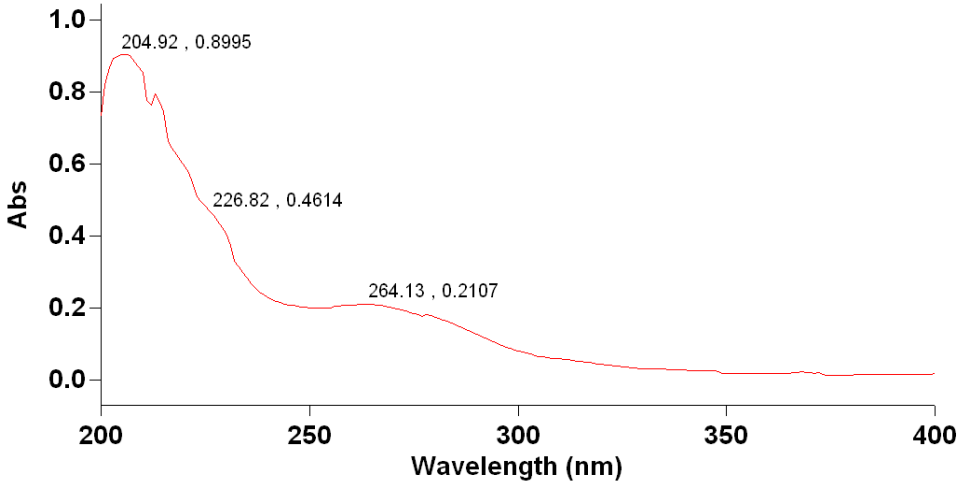

Figure S74. UV-vis spectrum of 2′-hydroperoxy-$\Delta^{1',4'}$-unguinol (**2f**) in MeOH

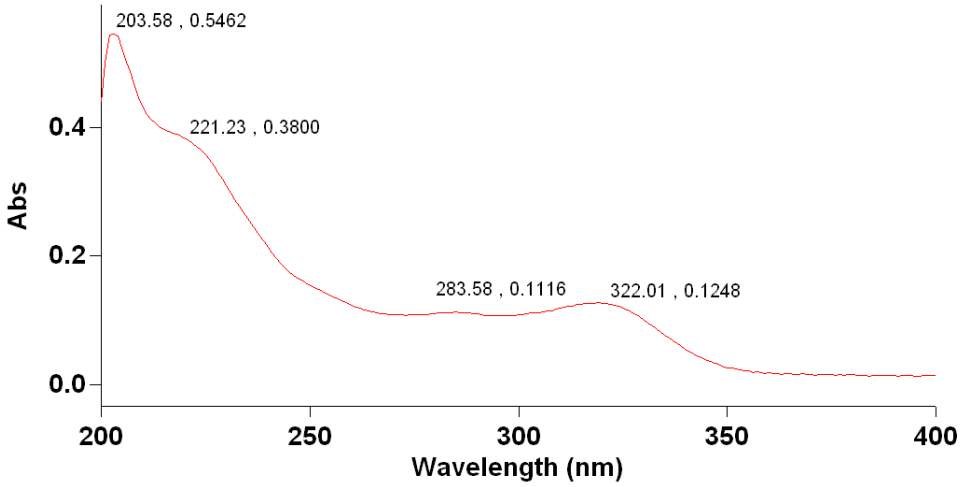

Figure S75. UV-vis spectrum of 2,7-dibromo-1′,2′-dihydrounguinol (**3a**) in MeOH

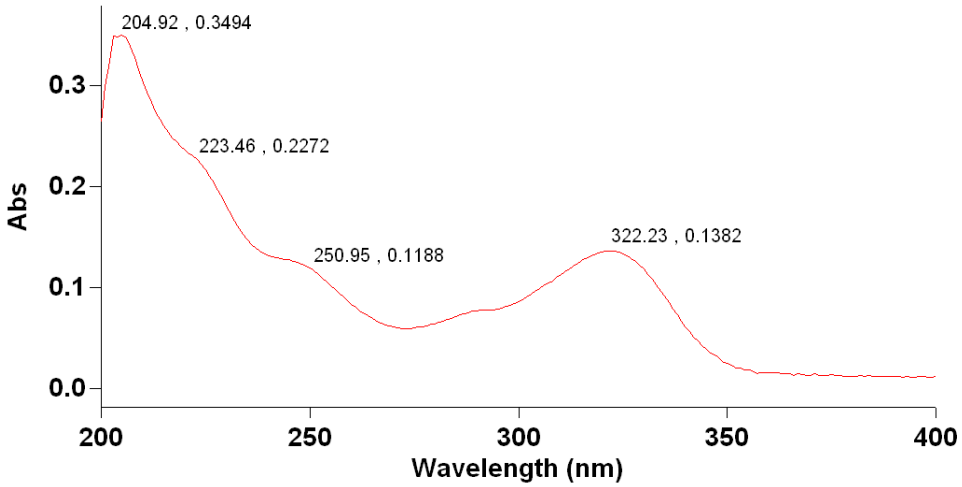

Figure S76. UV-vis spectrum of 2,4,7-tribromo-1′,2′-dihydrounguinol (**3b**) in MeOH

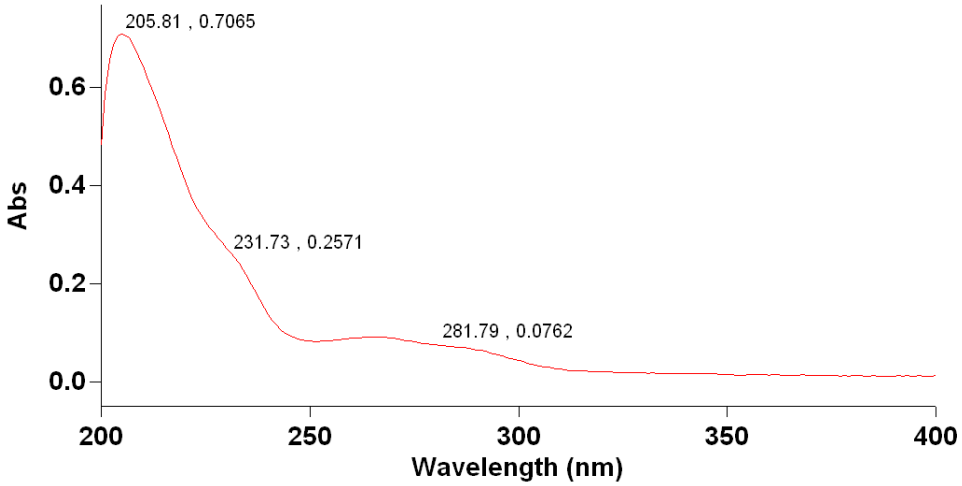

Figure S77. UV-vis spectrum of 2,4-diiodo-1′,2′-dihydrounguinol (**3c**) in MeOH

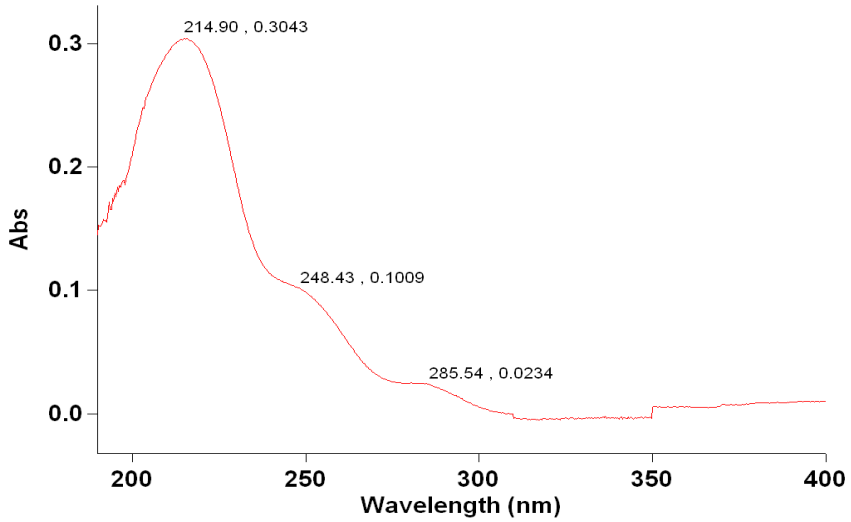

Figure S78. UV-vis spectrum of methylunguinolate (**4a**) in MeOH

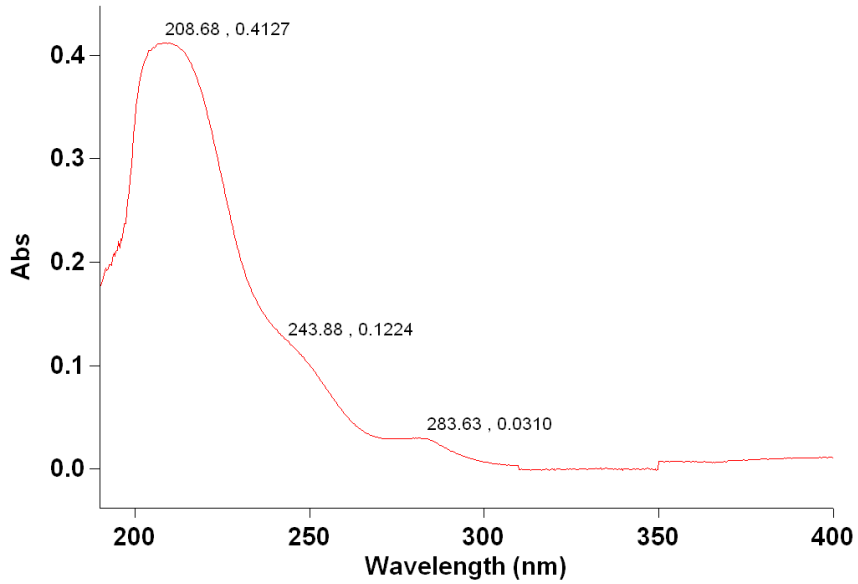

Figure S79. UV-vis spectrum of unguinolamide (**4b**) in MeOH

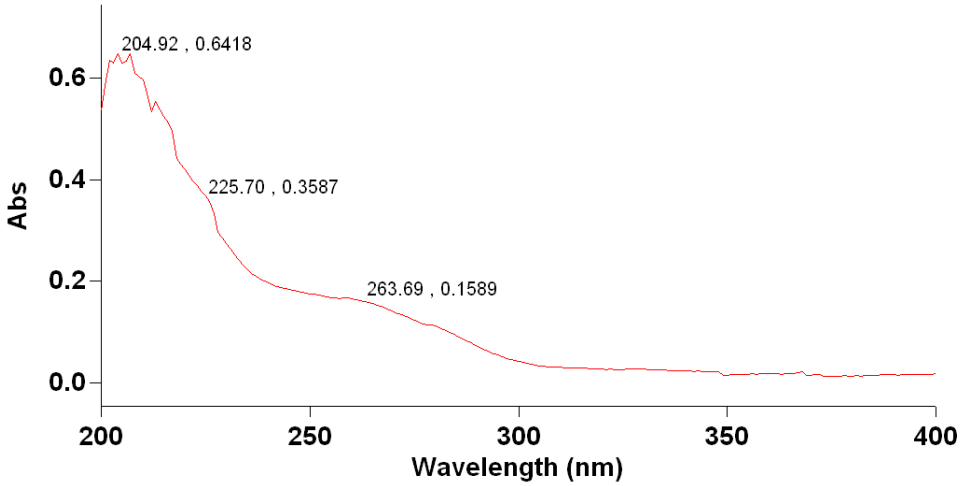

Figure S80. UV-vis spectrum of 3-*O*-methylunguinol (**5a**) in MeOH

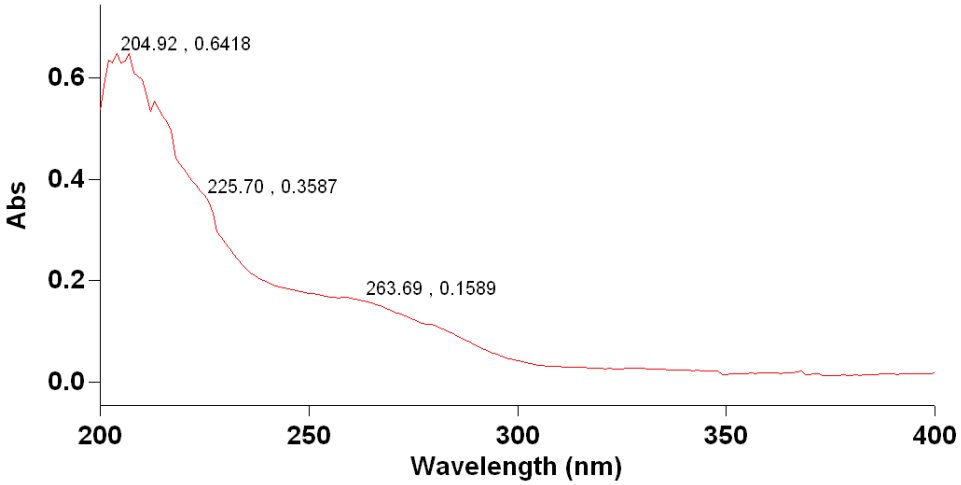

Figure S81. UV-vis spectrum of 3,8-di-*O*-methylunguinol (**5b**) in MeOH

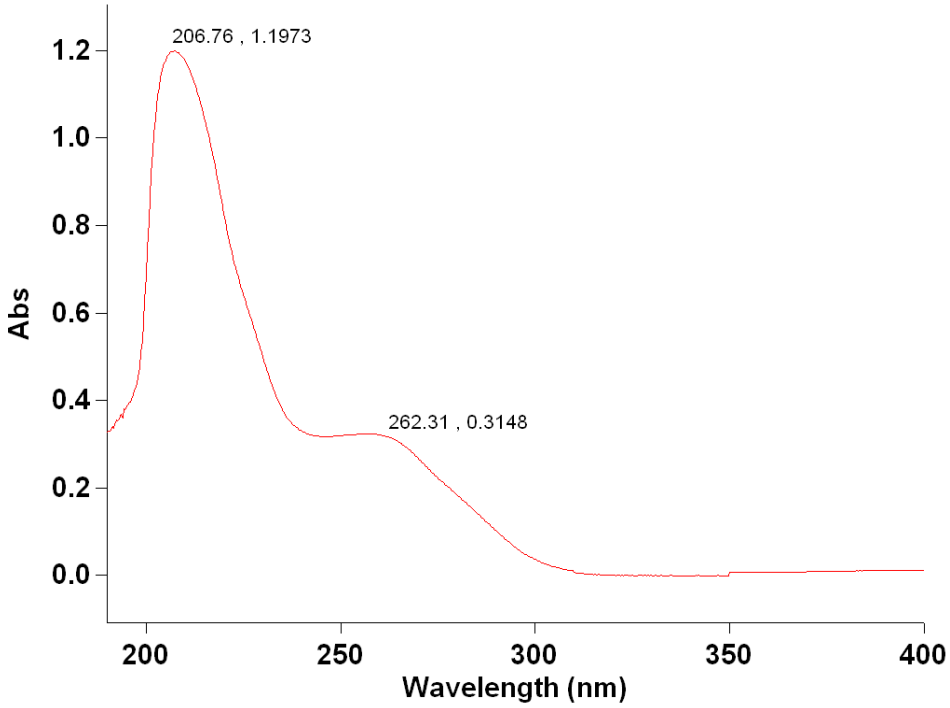

Figure S82. UV-vis spectrum of 3-*O*-benzylunguinol (**6a**) in MeOH

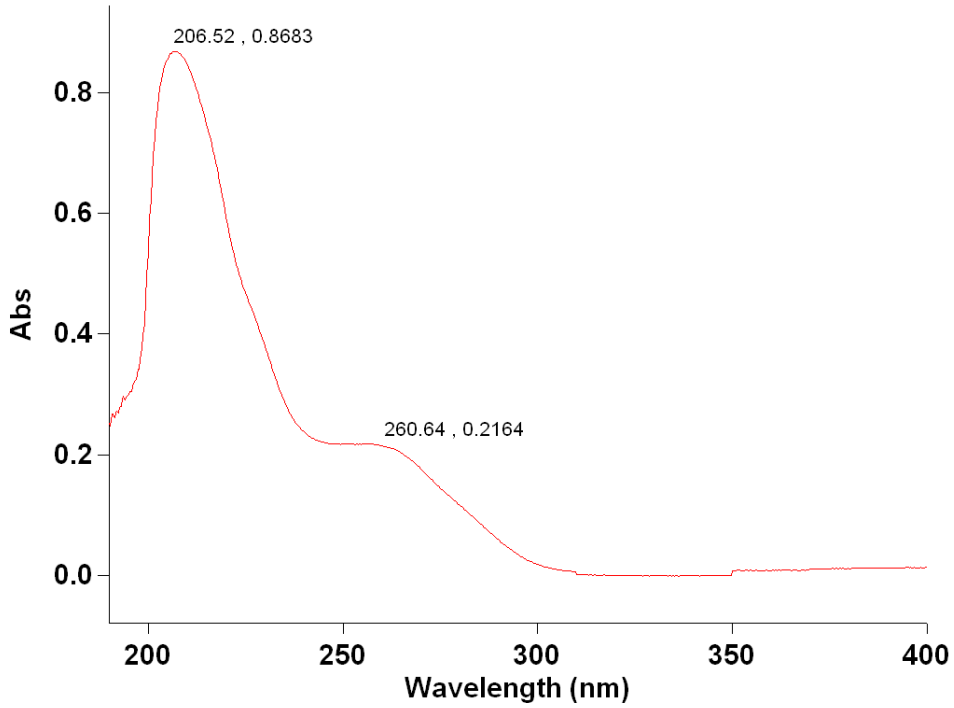

Figure S83. UV-vis spectrum of 3,8-di-*O*-benzylunguinol (**6b**) in MeOH

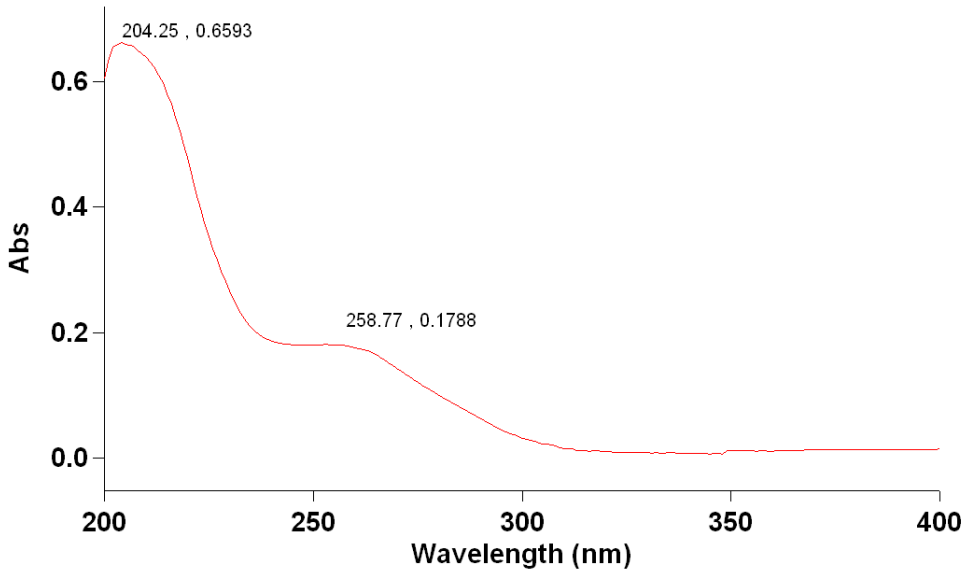

Figure S84. UV-vis spectrum of 3-*O*-(2-chlorobenzyl)unguinol (**7a**) in MeOH

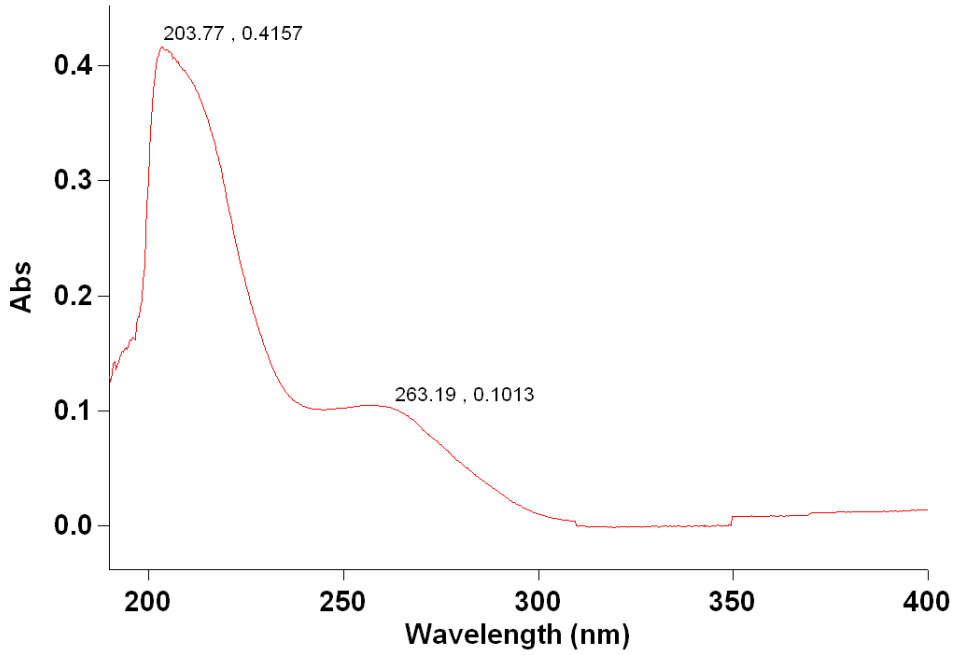

Figure S85. UV-vis spectrum of 3-*O*-(3-chlorobenzyl)unguinol (**7b**) in MeOH

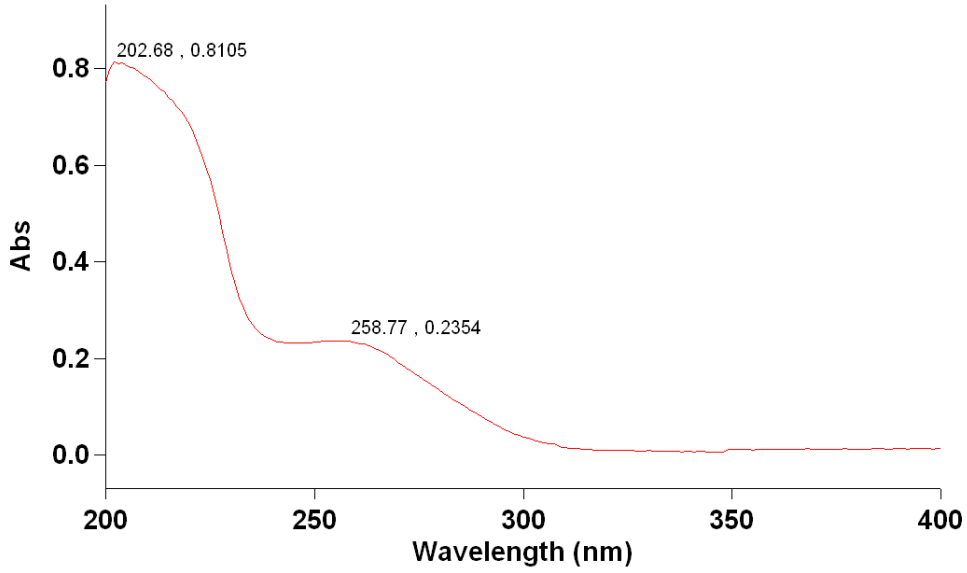

Figure S86. UV-vis spectrum of 3-*O*-(4-chlorobenzyl)unguinol (**7c**) in MeOH

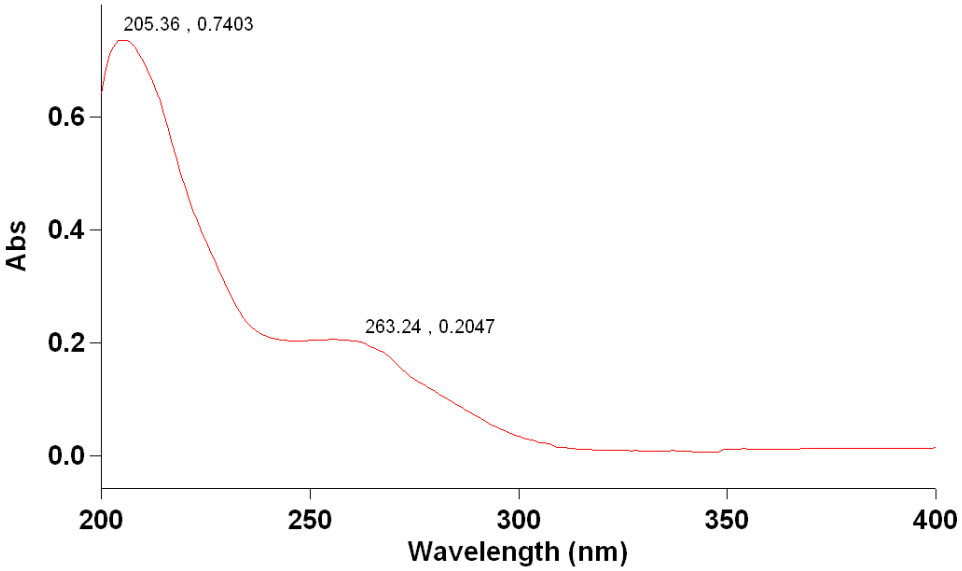

Figure S87. UV-vis spectrum of 3-*O*-(2-fluorobenzyl)unguinol (**7d**) in MeOH

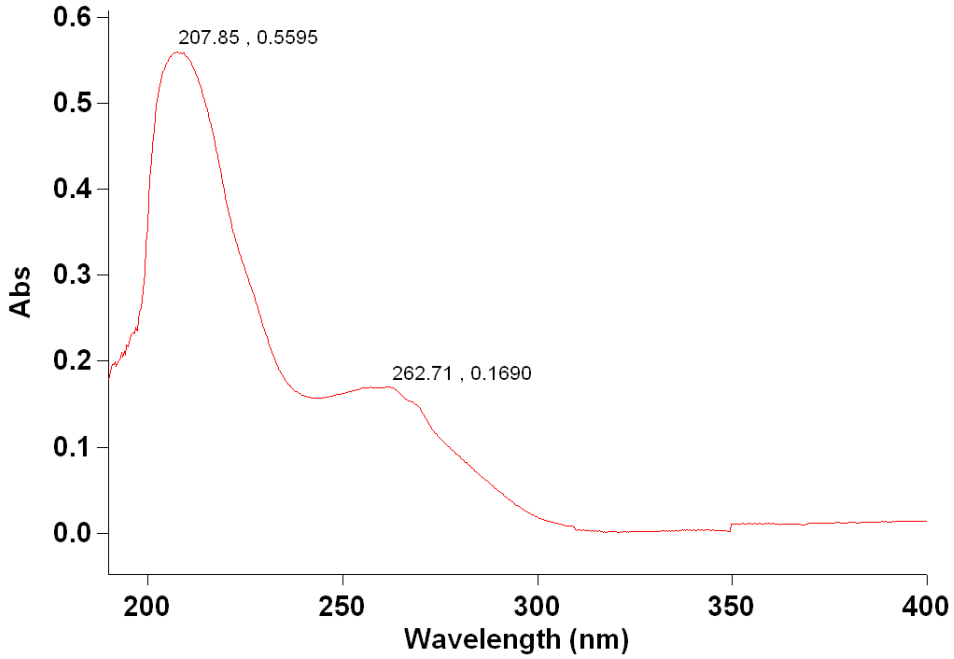

Figure S88. UV-vis spectrum of 3-*O*-(3-fluorobenzyl)unguinol (**7e**) in MeOH

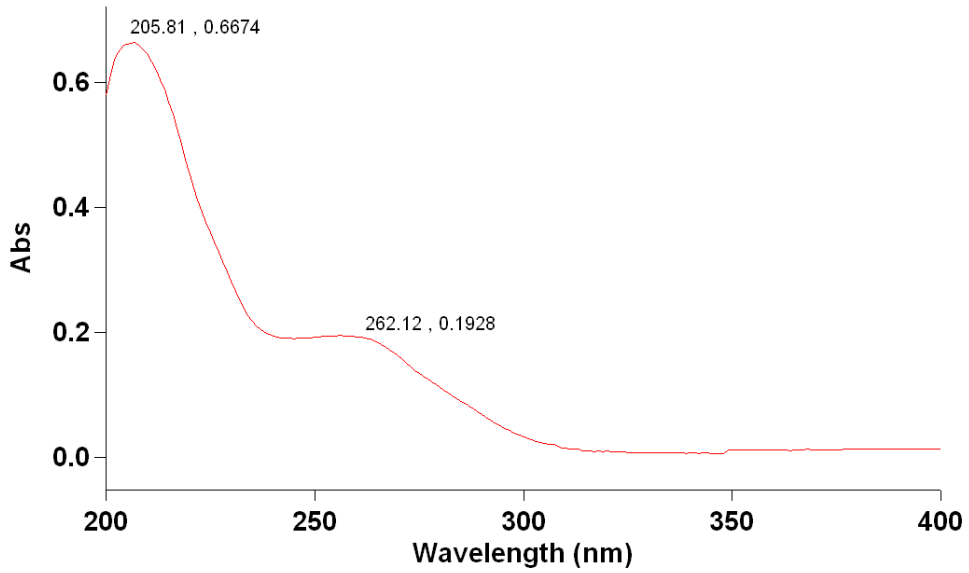

Figure S89. UV-vis spectrum of 3-*O*-(4-fluorobenzyl)unguinol (**7f**) in MeOH

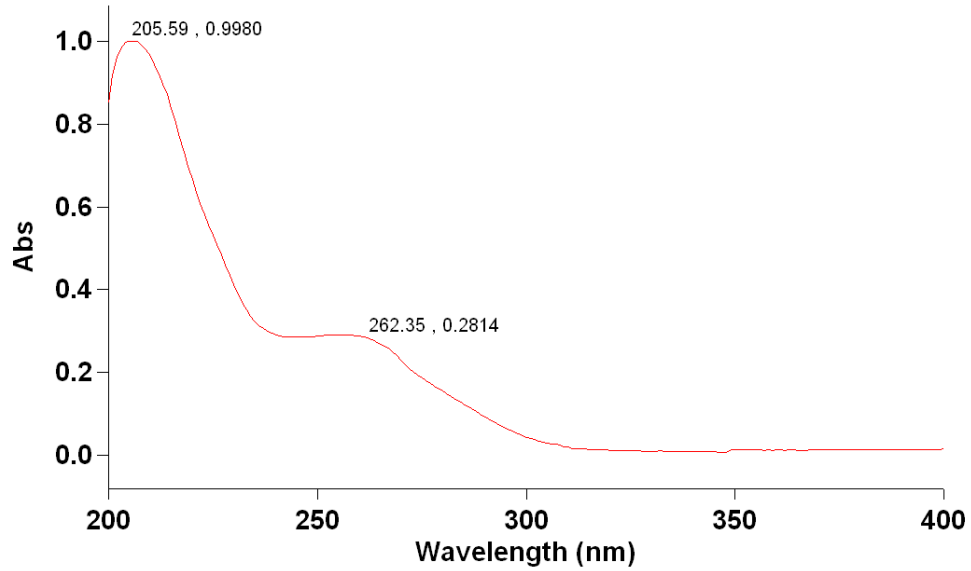

Figure S90. UV-vis spectrum of 3-*O*-(2,4-difluorobenzyl)unguinol (**7g**) in MeOH

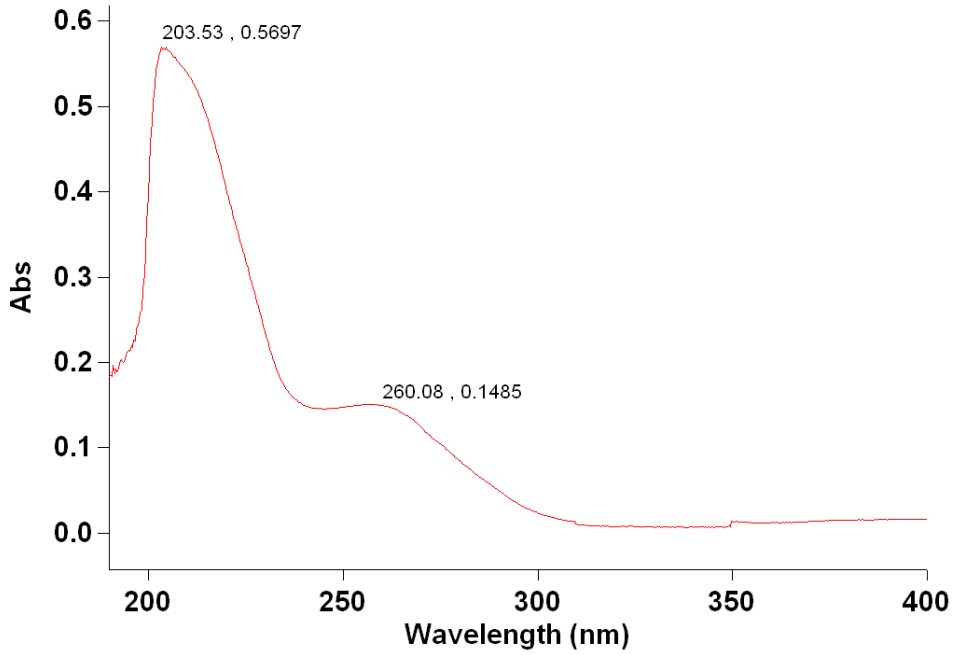

Figure S91. UV-vis spectrum of 3-*O*-(3-bromobenzyl)unguinol (**7h**) in MeOH

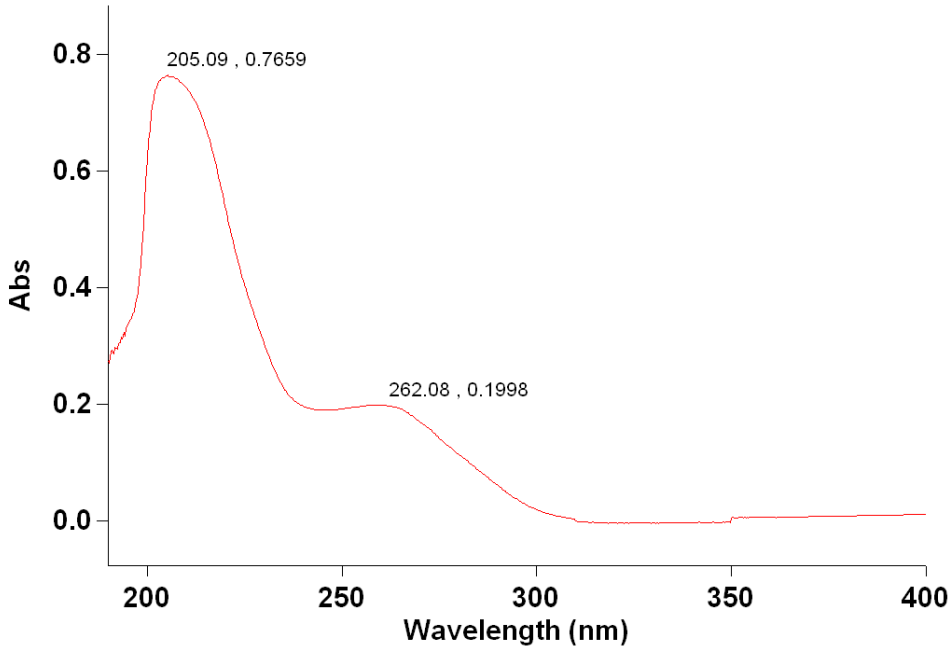

Figure S92. UV-vis spectrum of 3-*O*-(3-methylbenzyl)unguinol (**7i**) in MeOH

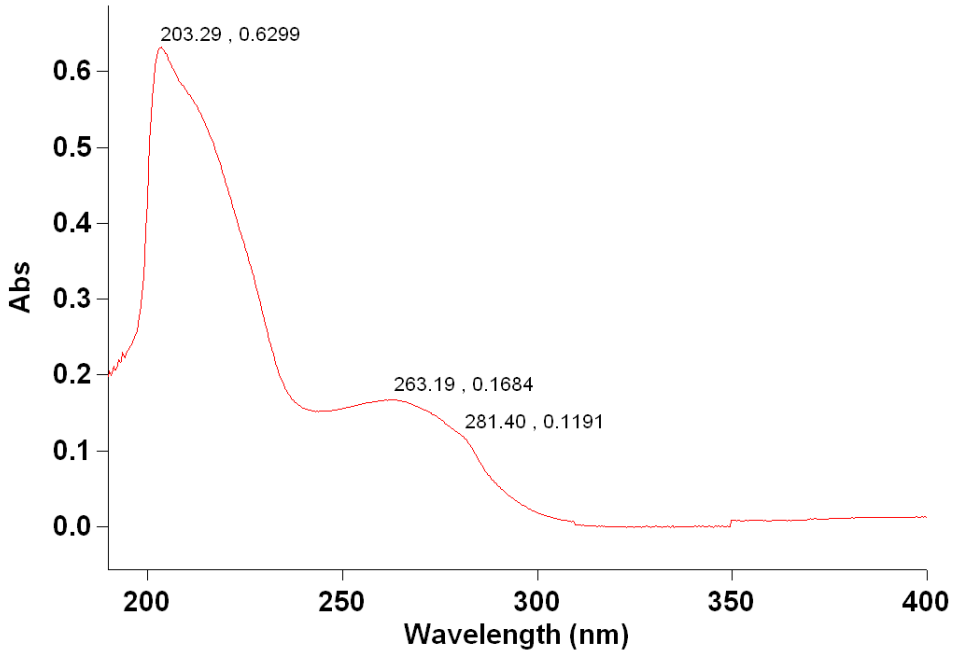

Figure S93. UV-vis spectrum of 3-*O*-(3-methoxybenzyl)unguinol (**7j**) in MeOH

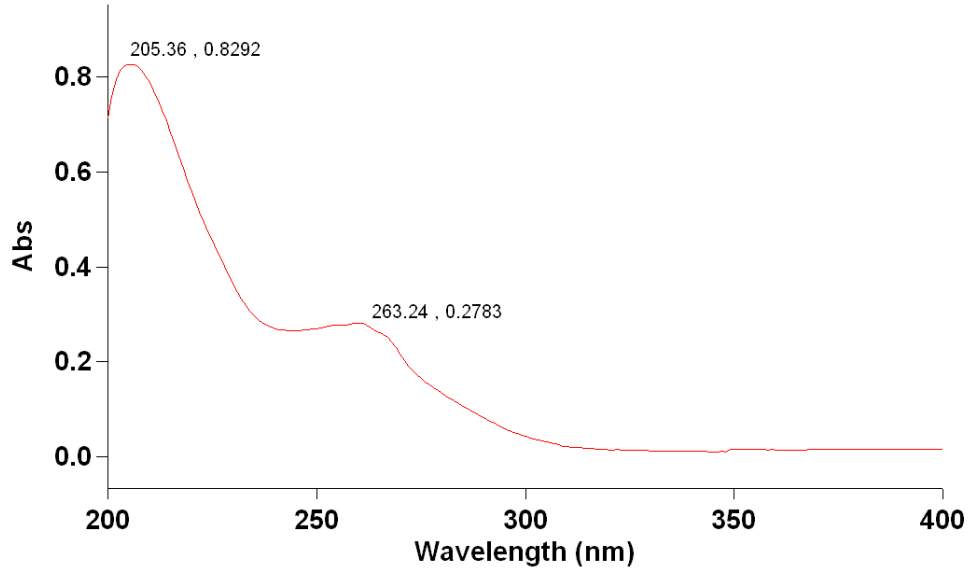

Figure S94. UV-vis spectrum of 3-*O*-(2-picolyl)unguinol (**7k**) in MeOH

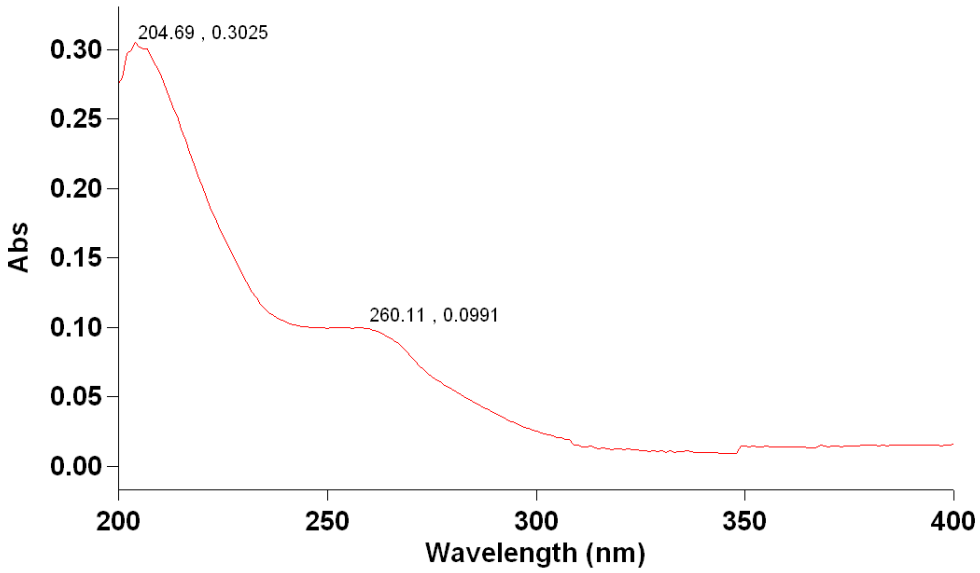

Figure S95. UV-vis spectrum of 3-*O*-(3-picolyl)unguinol (**7l**) in MeOH

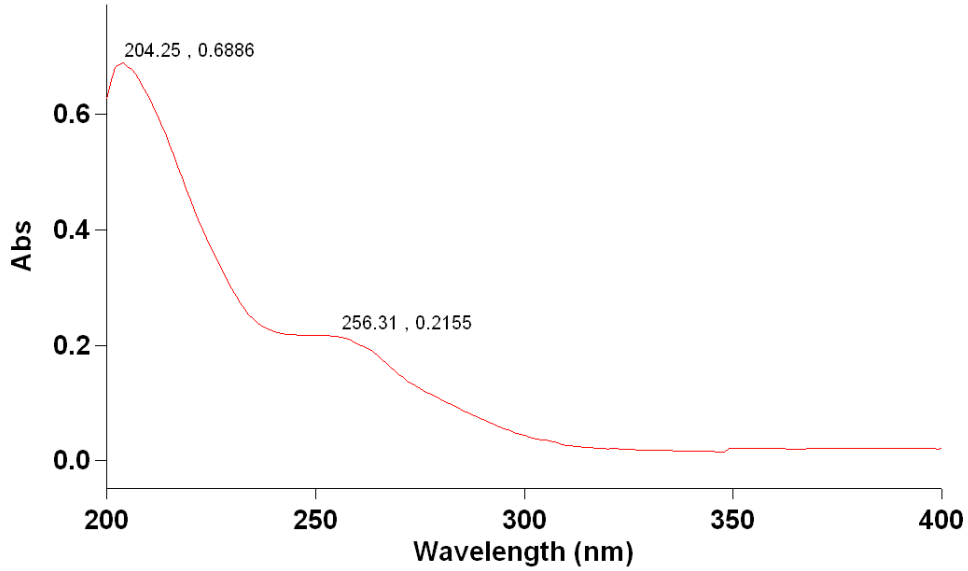

Figure S96. UV-vis spectrum of 3-*O*-(4-picolyl)unguinol (**7m**) in MeOH

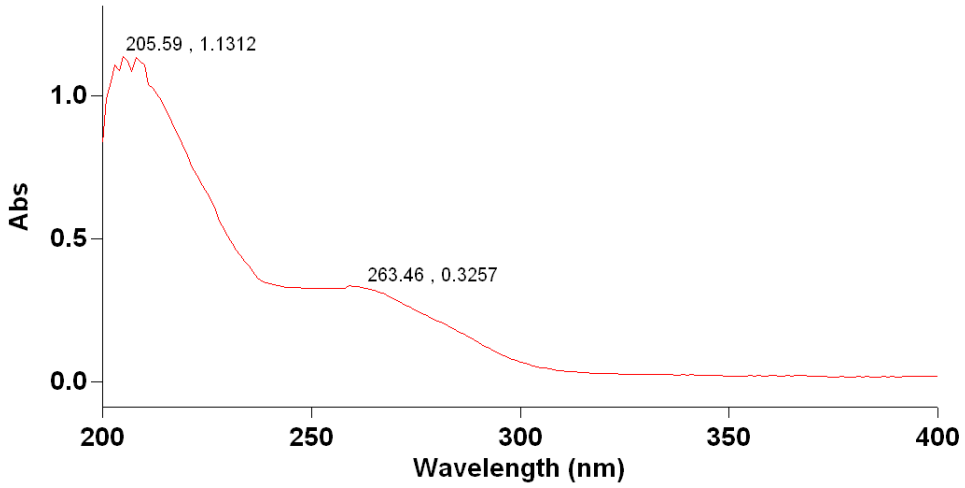

Figure S97. UV-vis spectrum of 3-*O*-(4-morpholinoethyl)unguinol (**7n**) in MeOH

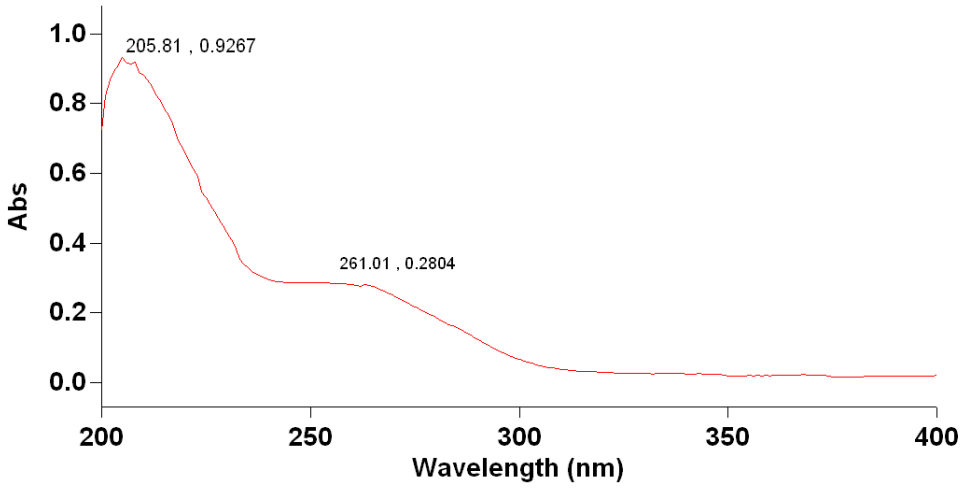

Figure S98. UV-vis spectrum of 3-*O*-(1-piperidinylethyl)unguinol (**7o**) in MeOH

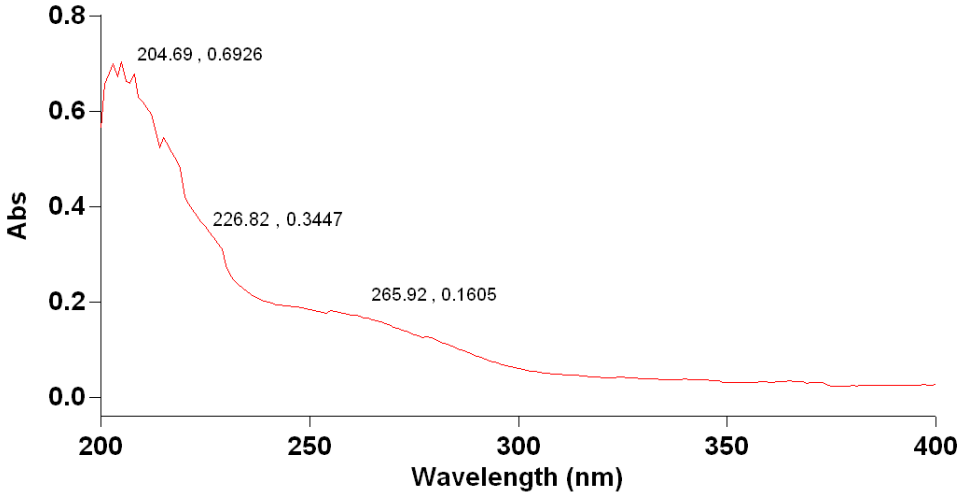

Figure S99. UV-vis spectrum of 3-*O*-(1-pyrrolidinylethyl)unguinol (**7p**) in MeOH

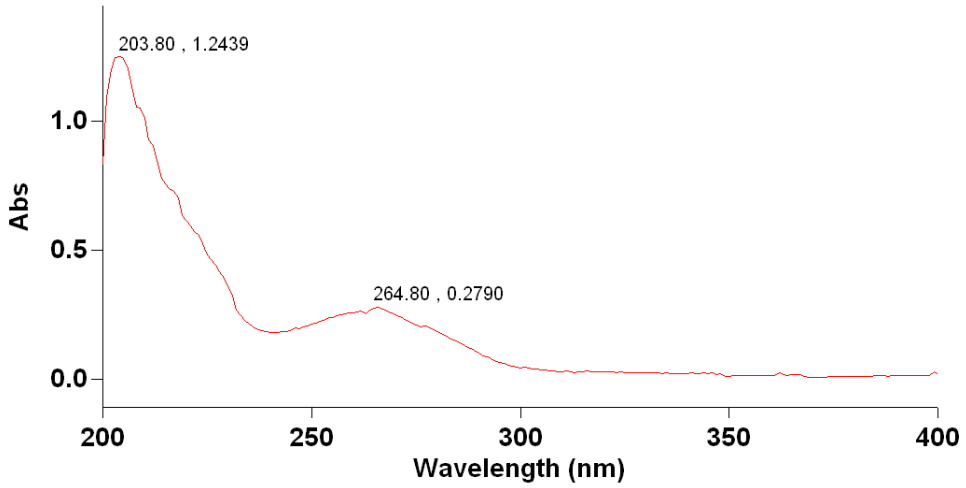

Figure S100. UV-vis spectrum of 3-*O*-1′,2′-dihydrobenzylunguinol (**8a**) in MeOH

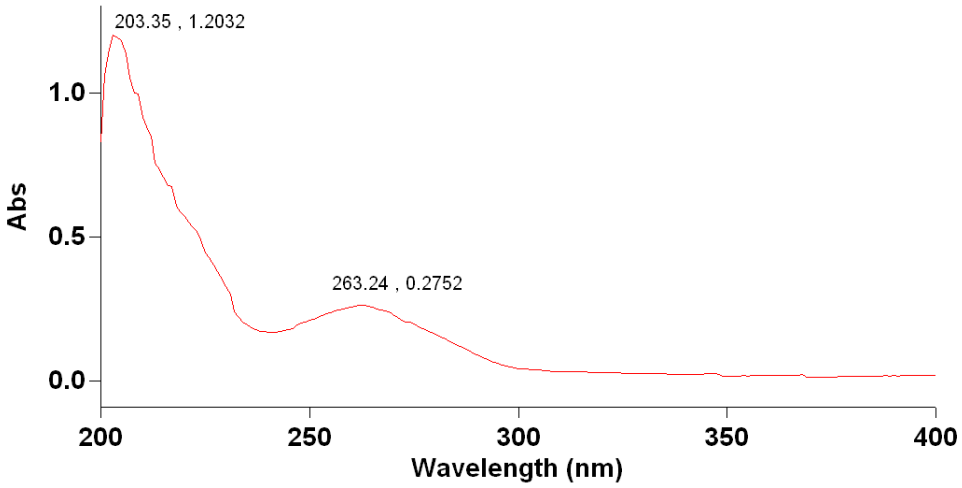

Figure S101. UV-vis spectrum of 3-*O*-(2-fluorobenzyl)-1′,2′-dihydrounguinol (**8b**) in MeOH

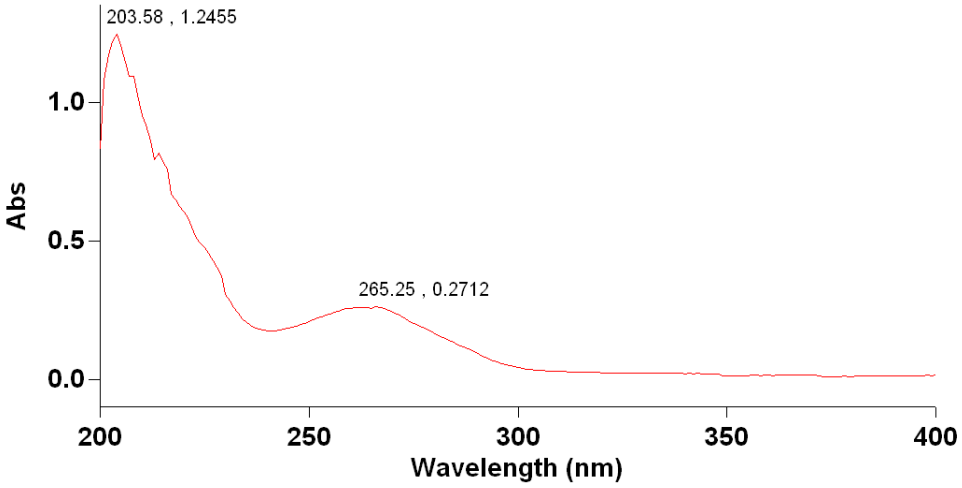

Figure S102. UV-vis spectrum of 3-*O*-(4-fluorobenzyl)-1′,2′-dihydrounguinol (**8c**) in MeOH

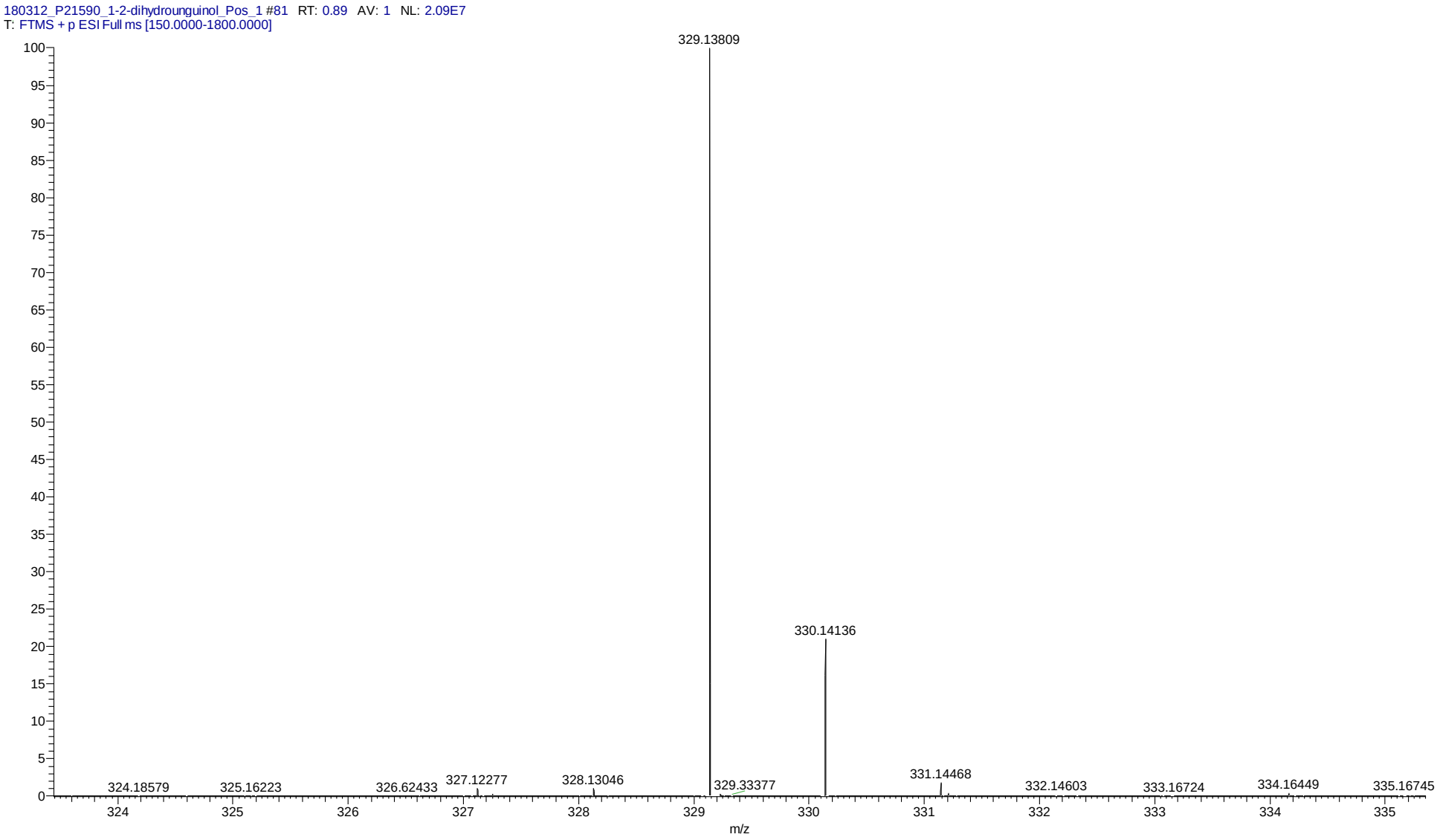

Figure S103. HRESI(+)-MS spectrum of 1′,2′-dihydrounguinol (**2a**)

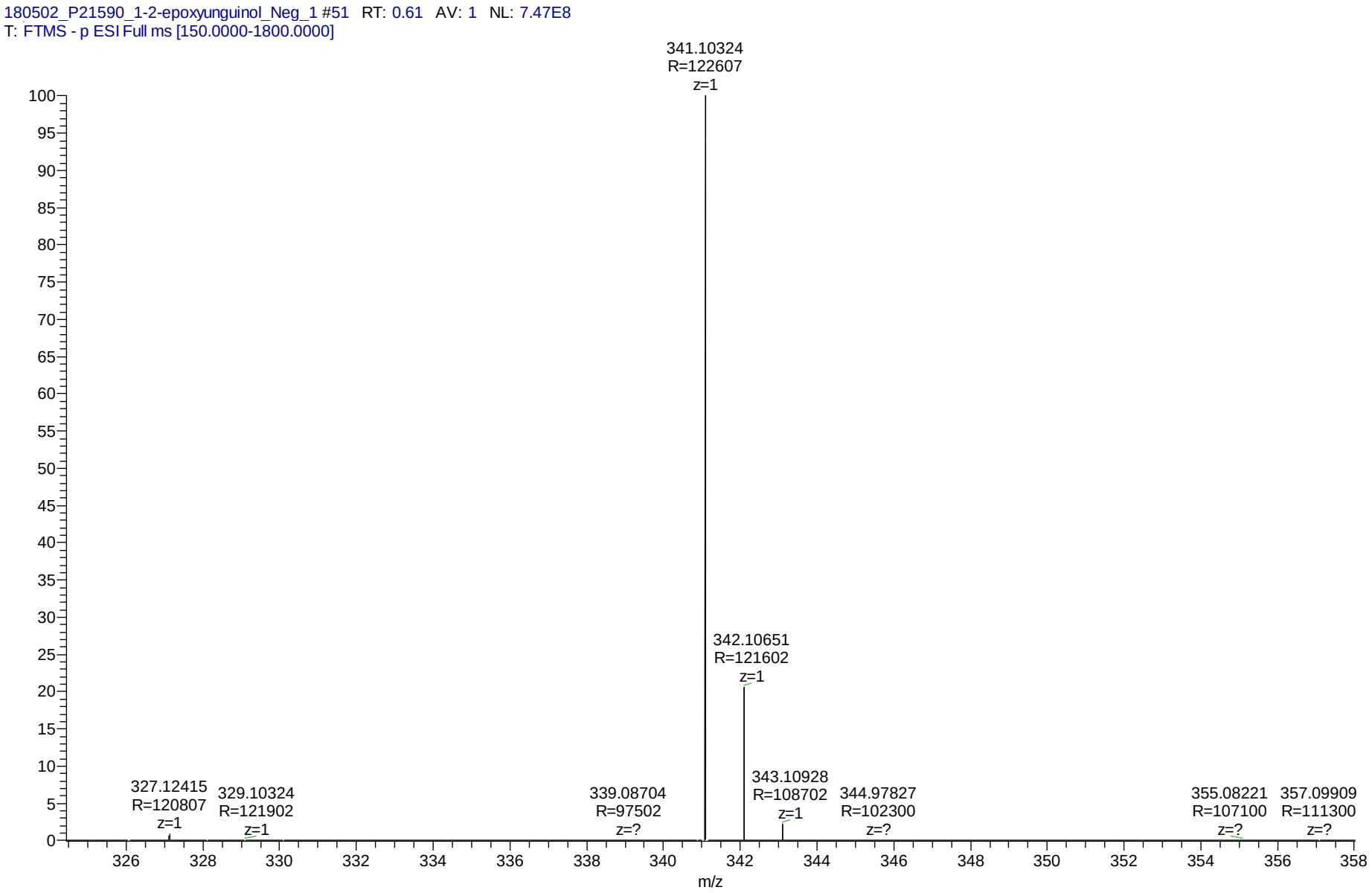

Figure S104. HRESI(–)-MS spectrum of *cis*-1′,2′-epoxyunguinol (**2b**)

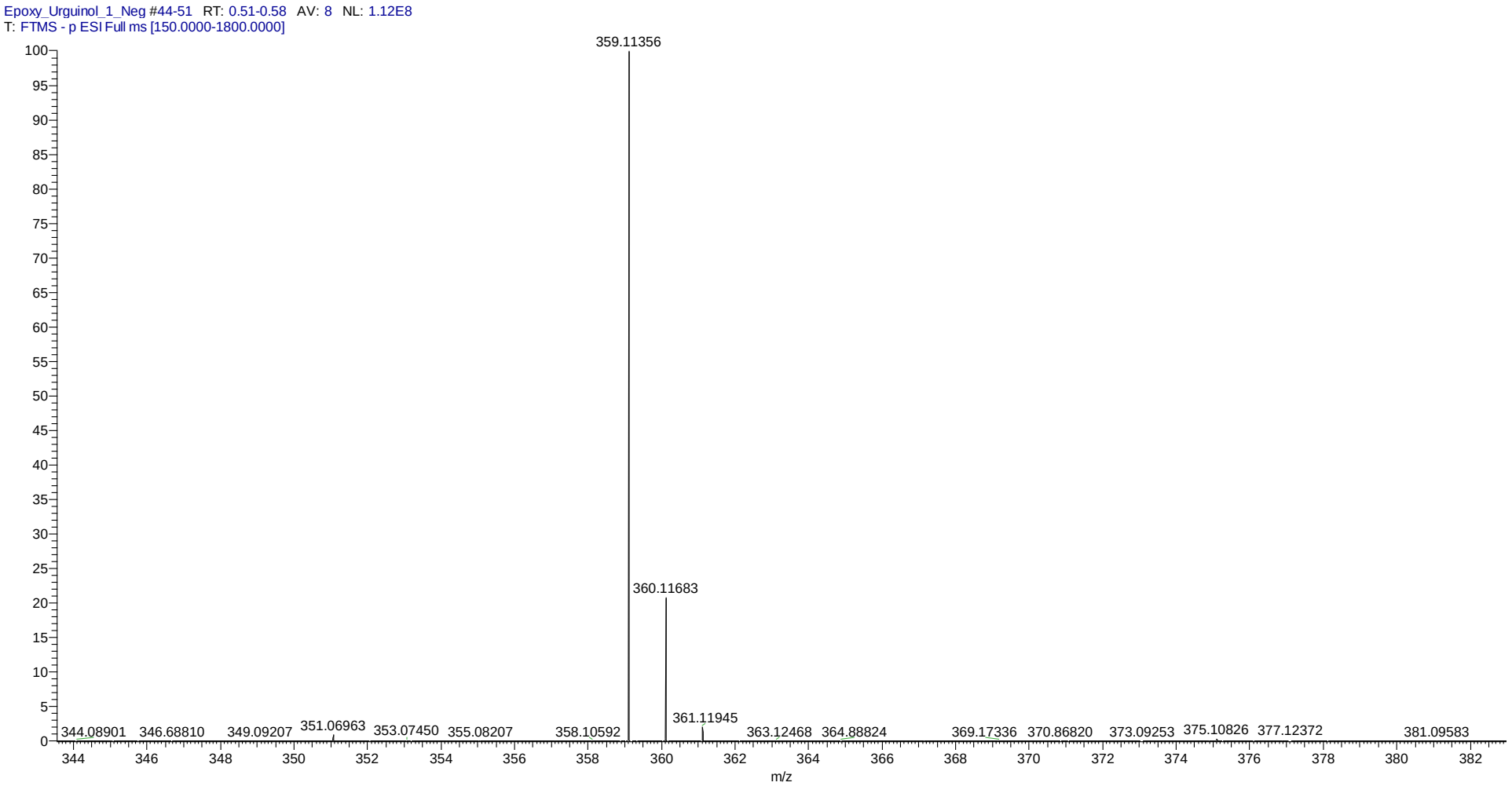

Figure S105. HRESI(–)-MS spectrum of 1′,2′-dihydroxyunguinol (**2c**)

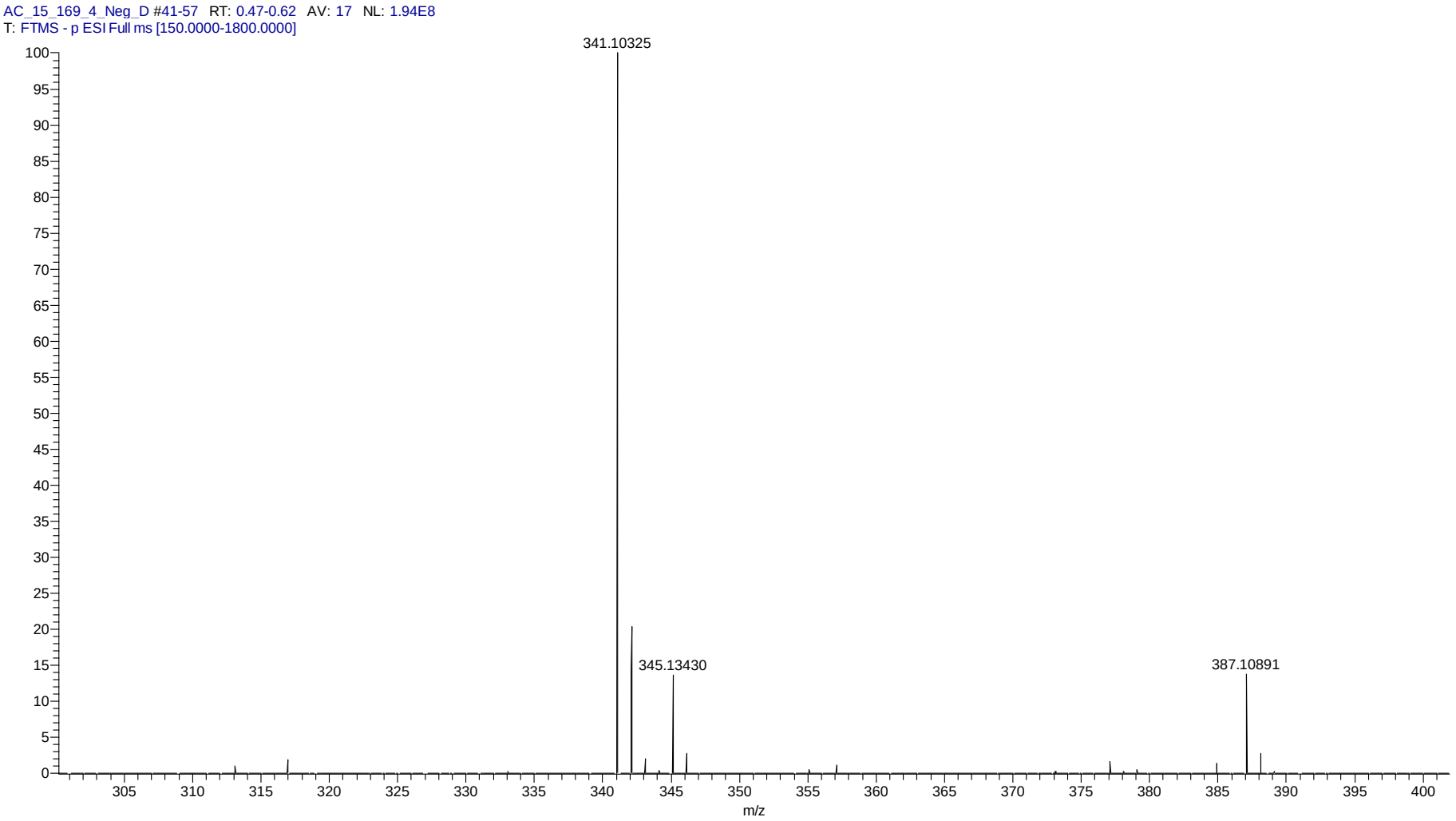

Figure S106. HR-ESI(–)-MS spectrum of 2′-hydroxy-$\Delta^{1',4'}$-unguinol (**2d**)

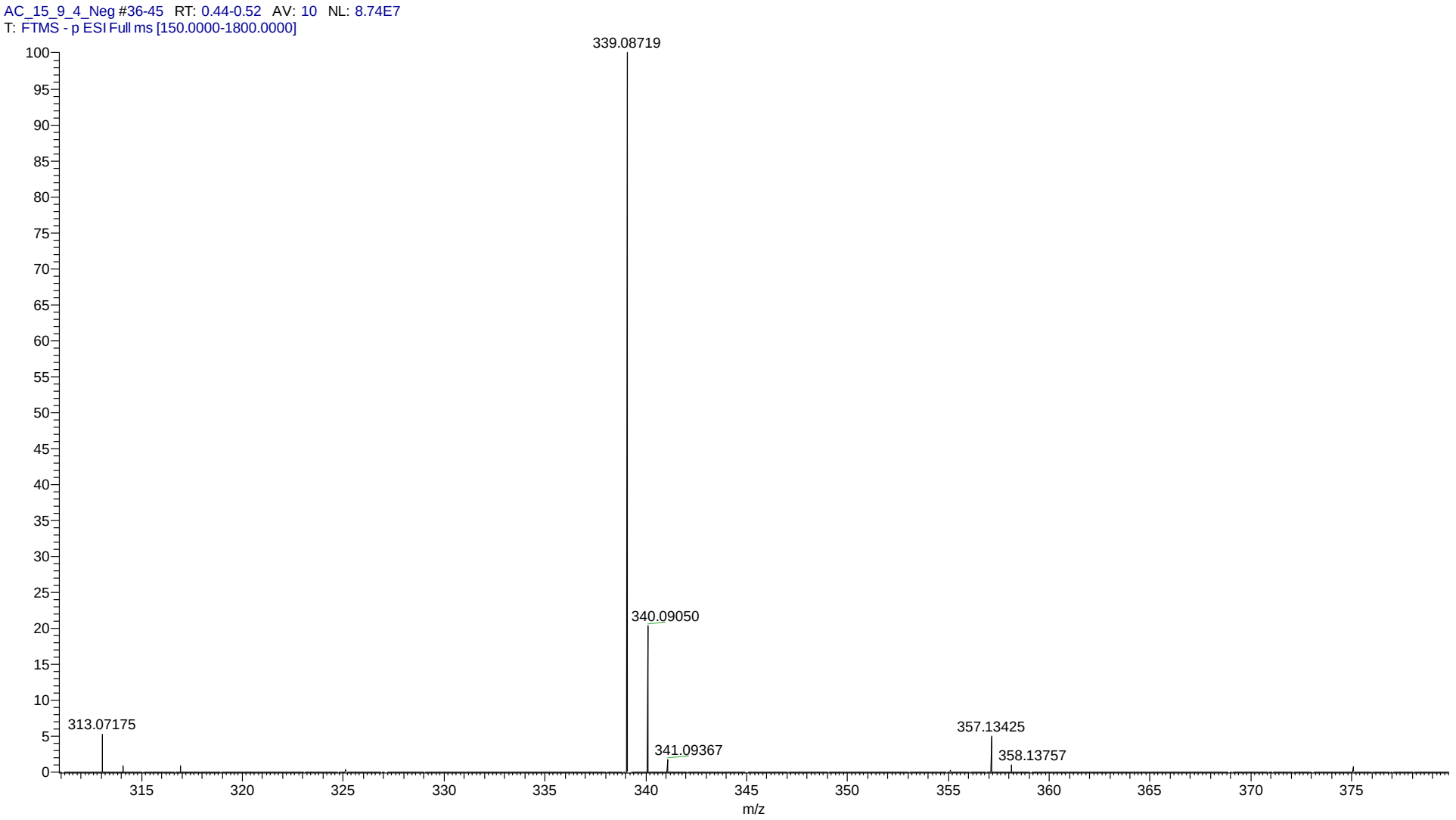

Figure S107. HRESI(–)-MS spectrum of 2′-oxo-$\Delta^{1',4'}$-unguinol (**2e**)

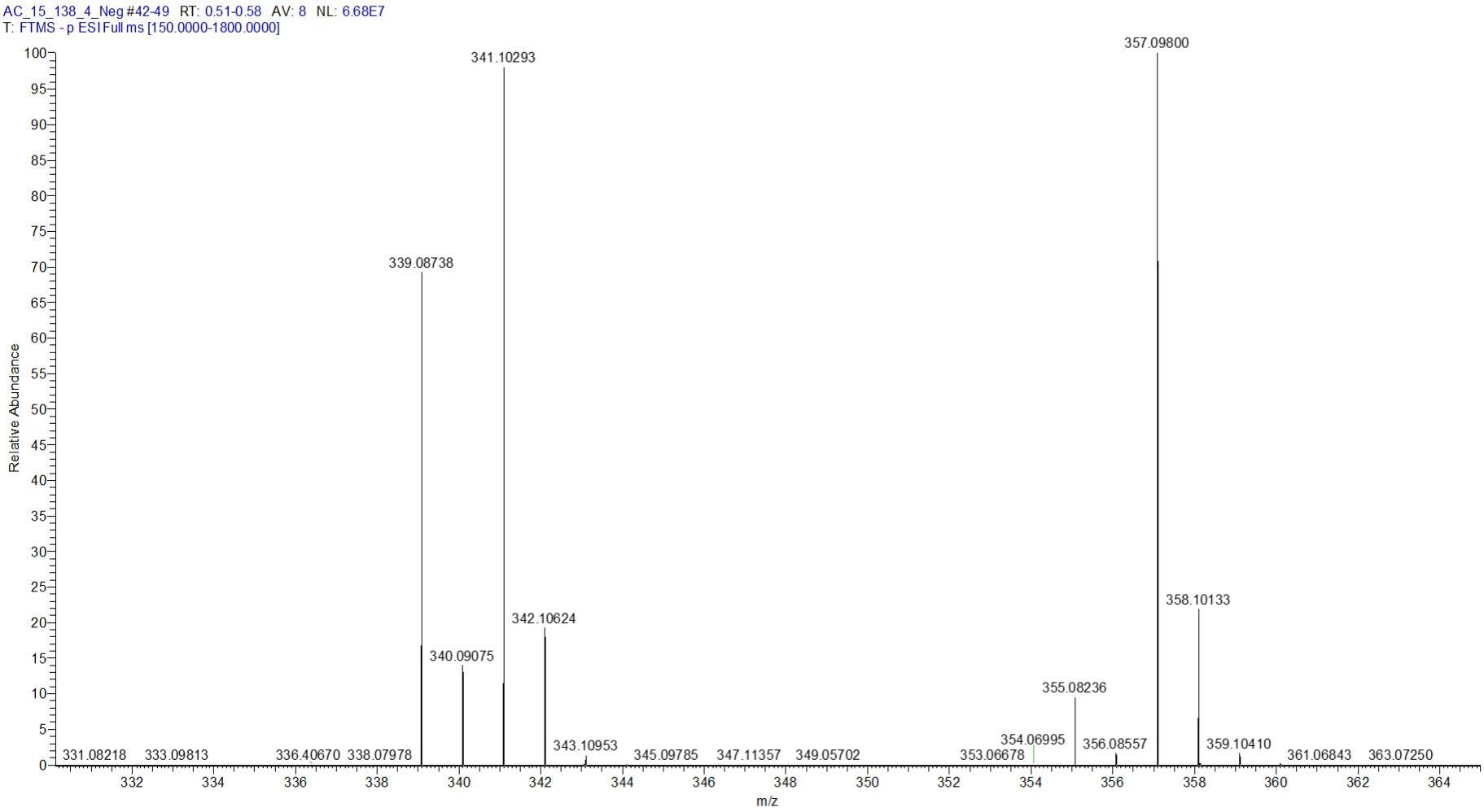

Figure S108. HR-ESI(–)-MS spectrum of 2′-hydroperoxy-$\Delta^{1',4'}$-unguinol (**2f**)

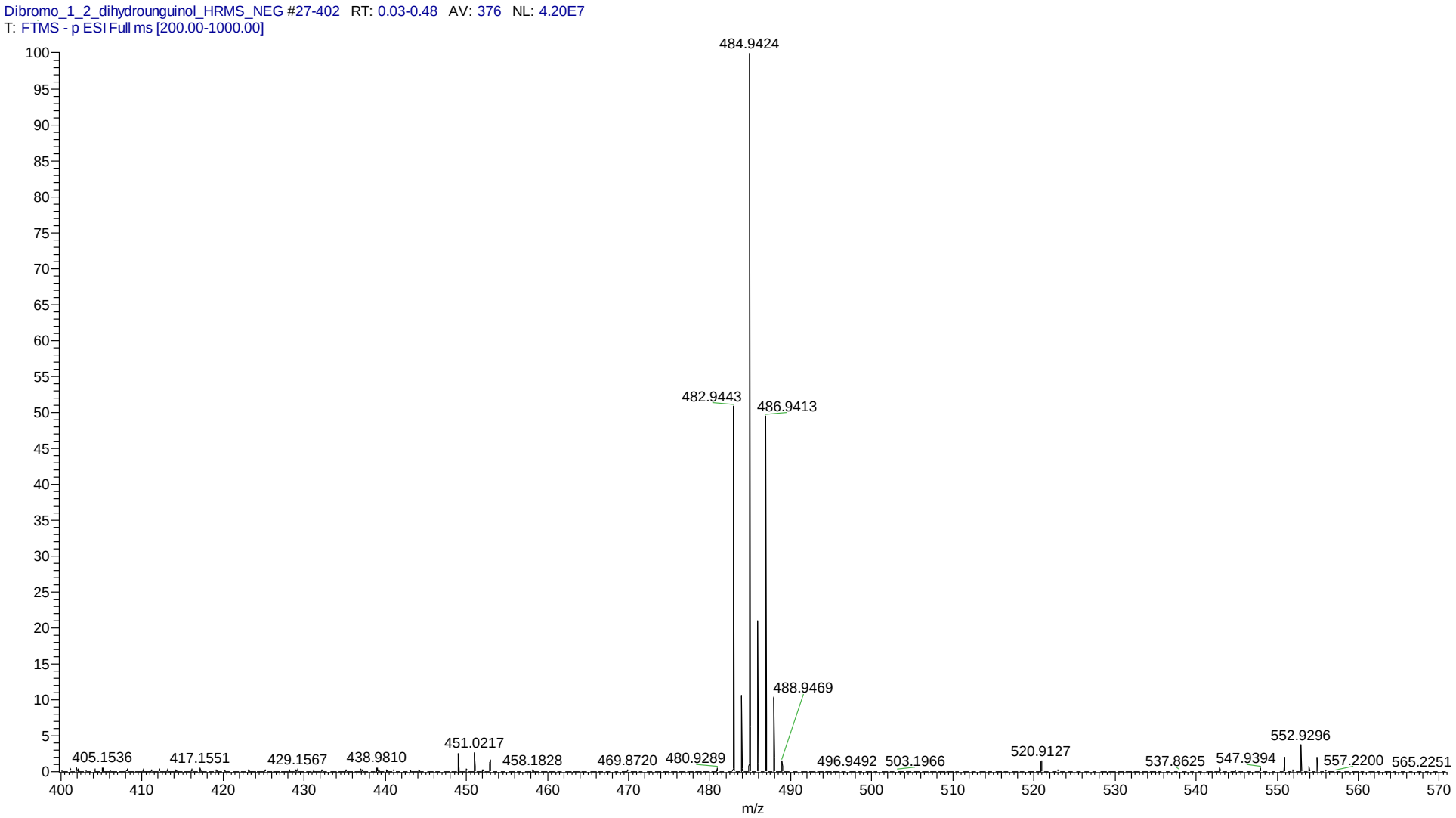

Figure S109. HRESI(–)-MS spectrum of 2,7-dibromo-1′,2′-dihydrounguinol (**3a**)

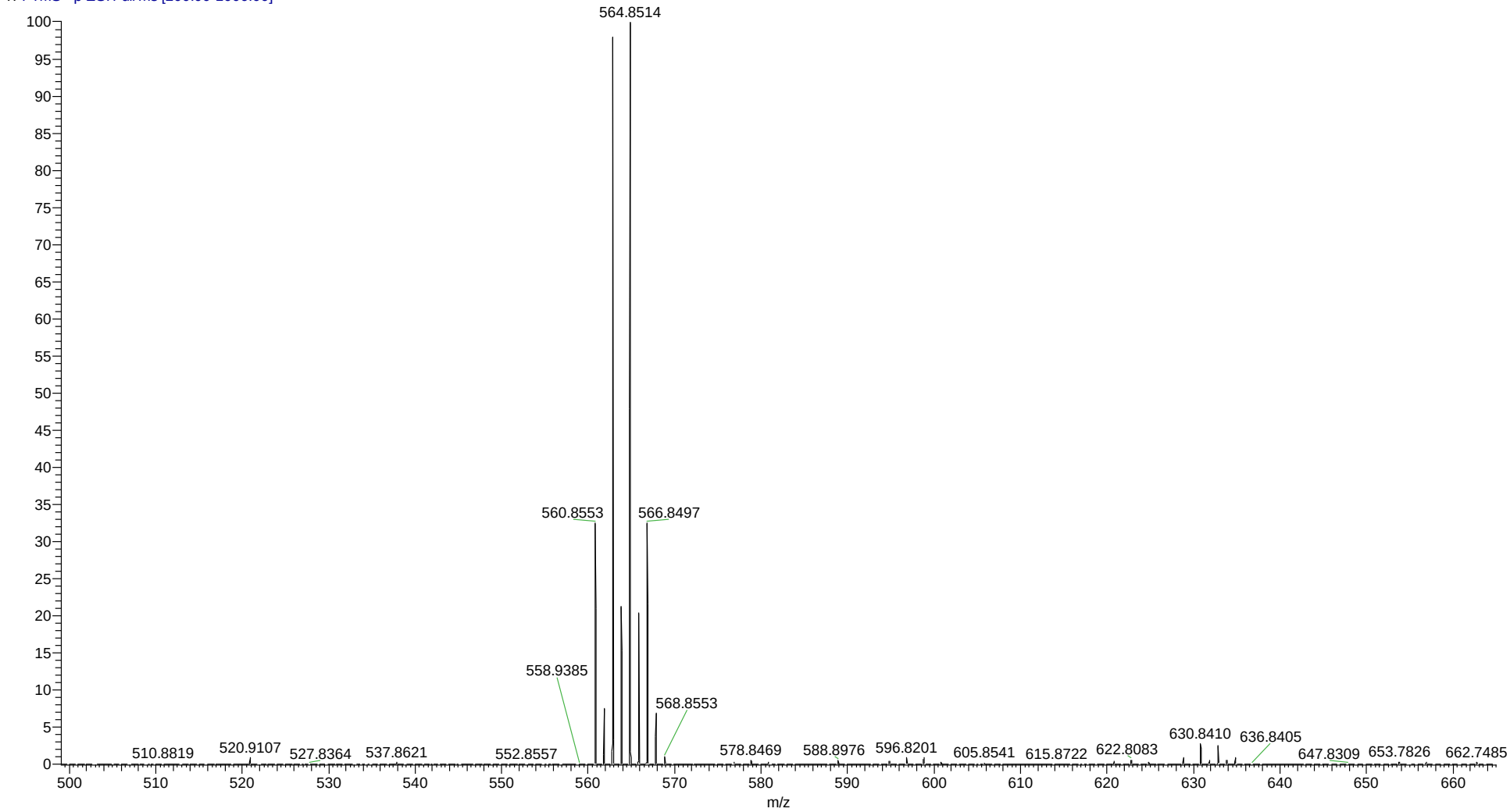

Figure S110. HRESI(–)-MS spectrum of 2,4,7-tribromo-1′,2′-dihydrounguinol (**3b**)

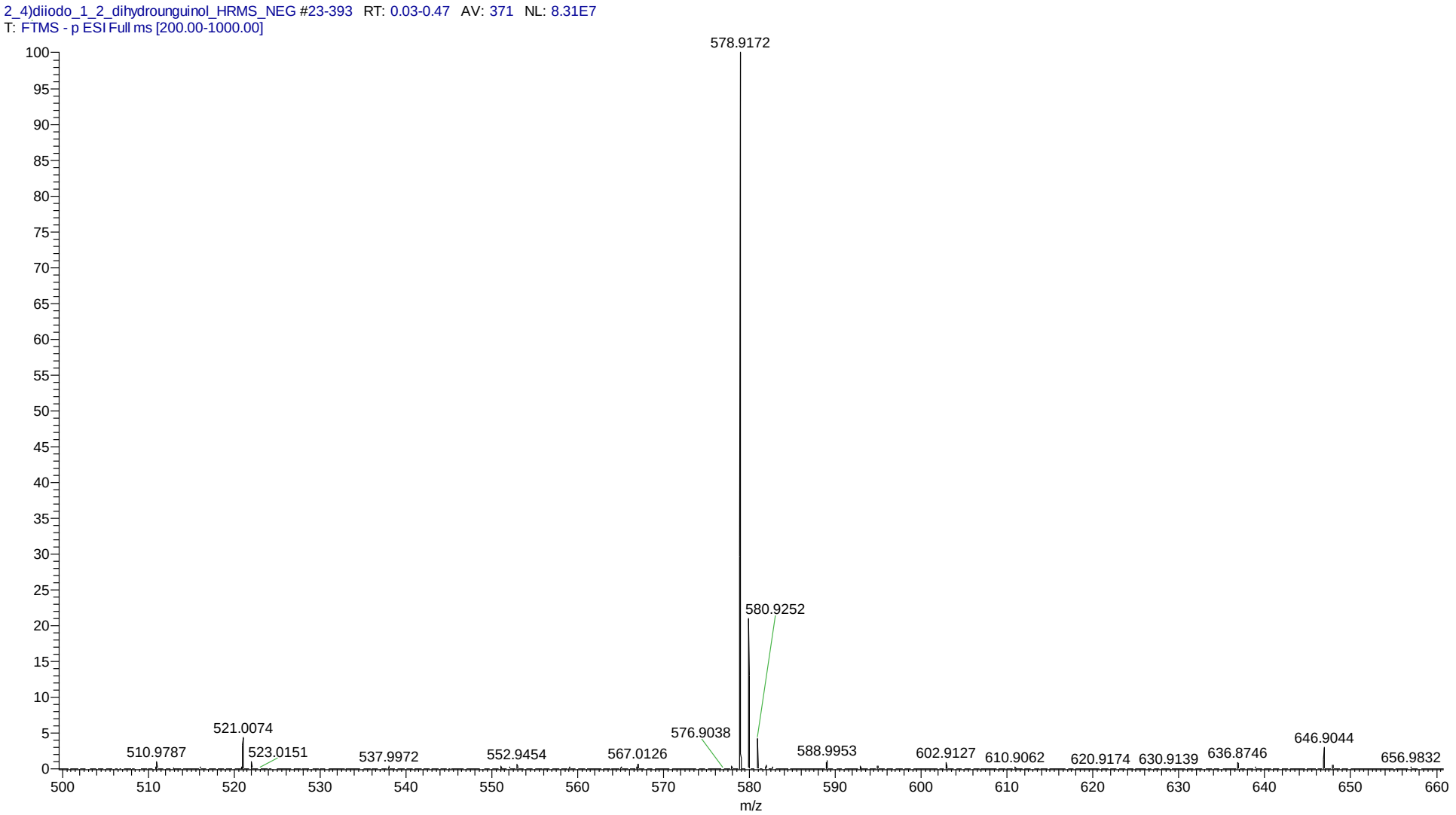

Figure S111. HRESI(–)-MS spectrum of 2,4-diiodo-1′,2′-dihydrounguin (**3c**)

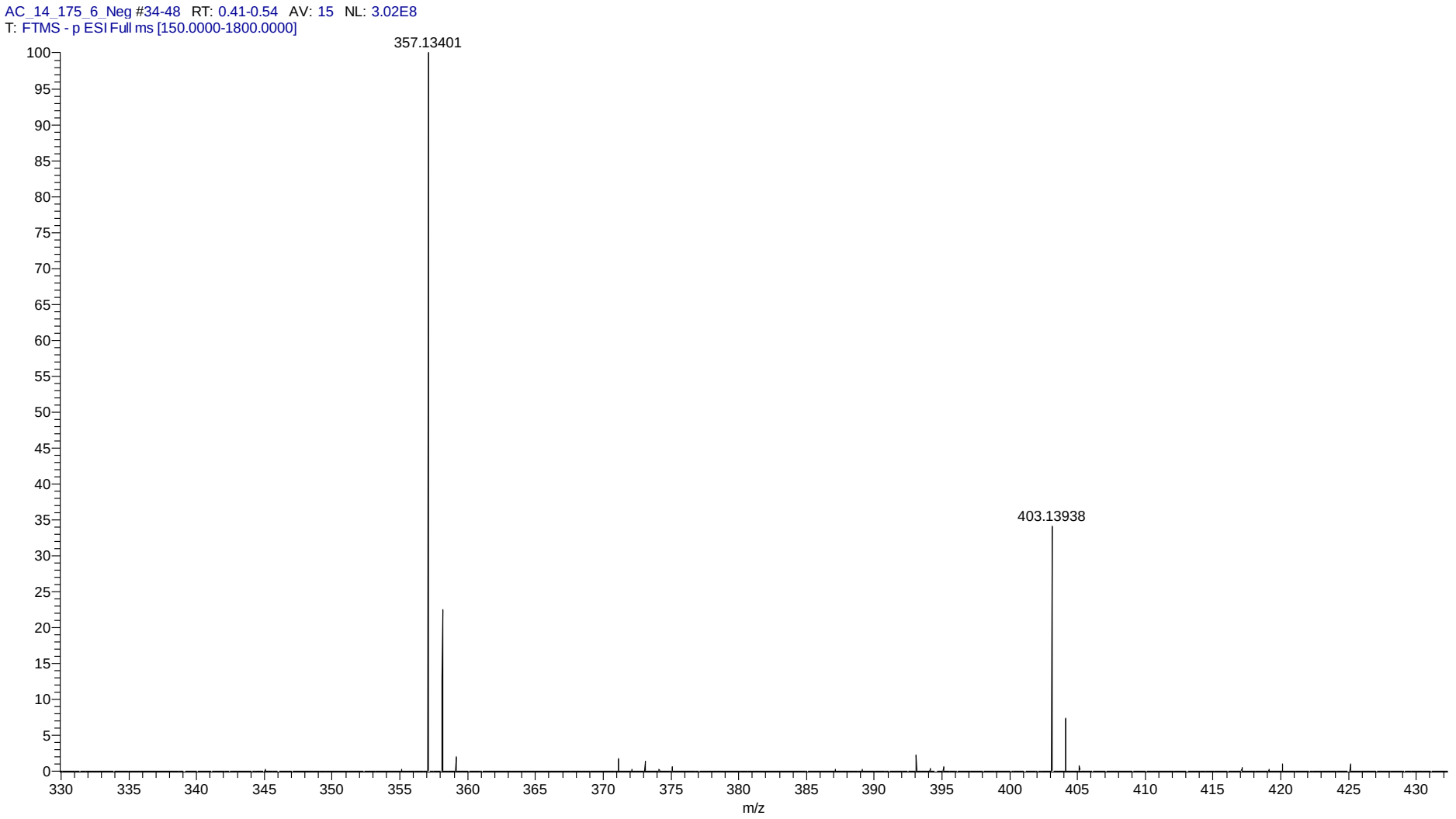

Figure S112. HRESI(–)-MS spectrum of methylunguinolate (**4a**)

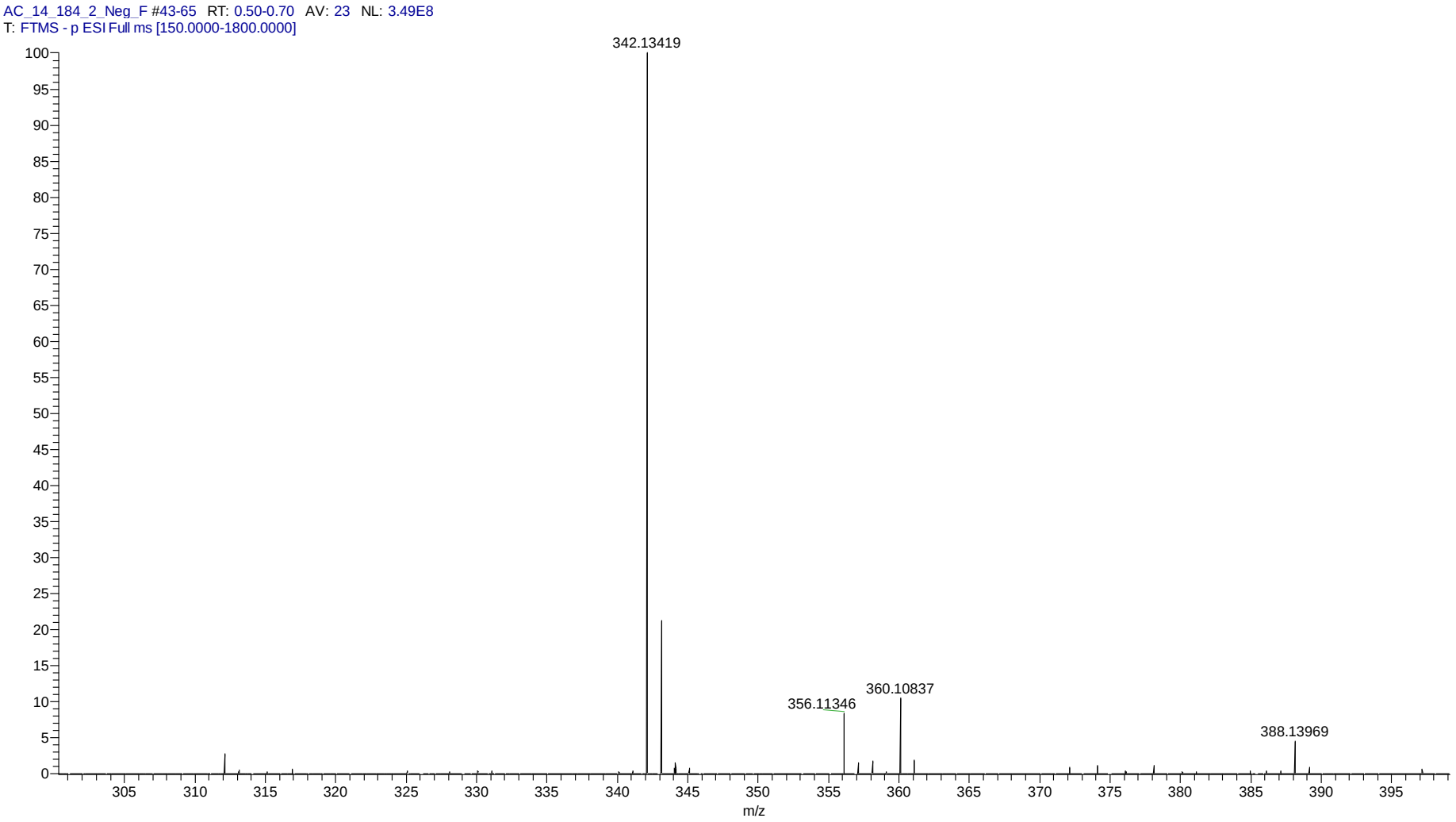

Figure S113. HRESI(–)-MS spectrum of unguinolamide (**4b**)

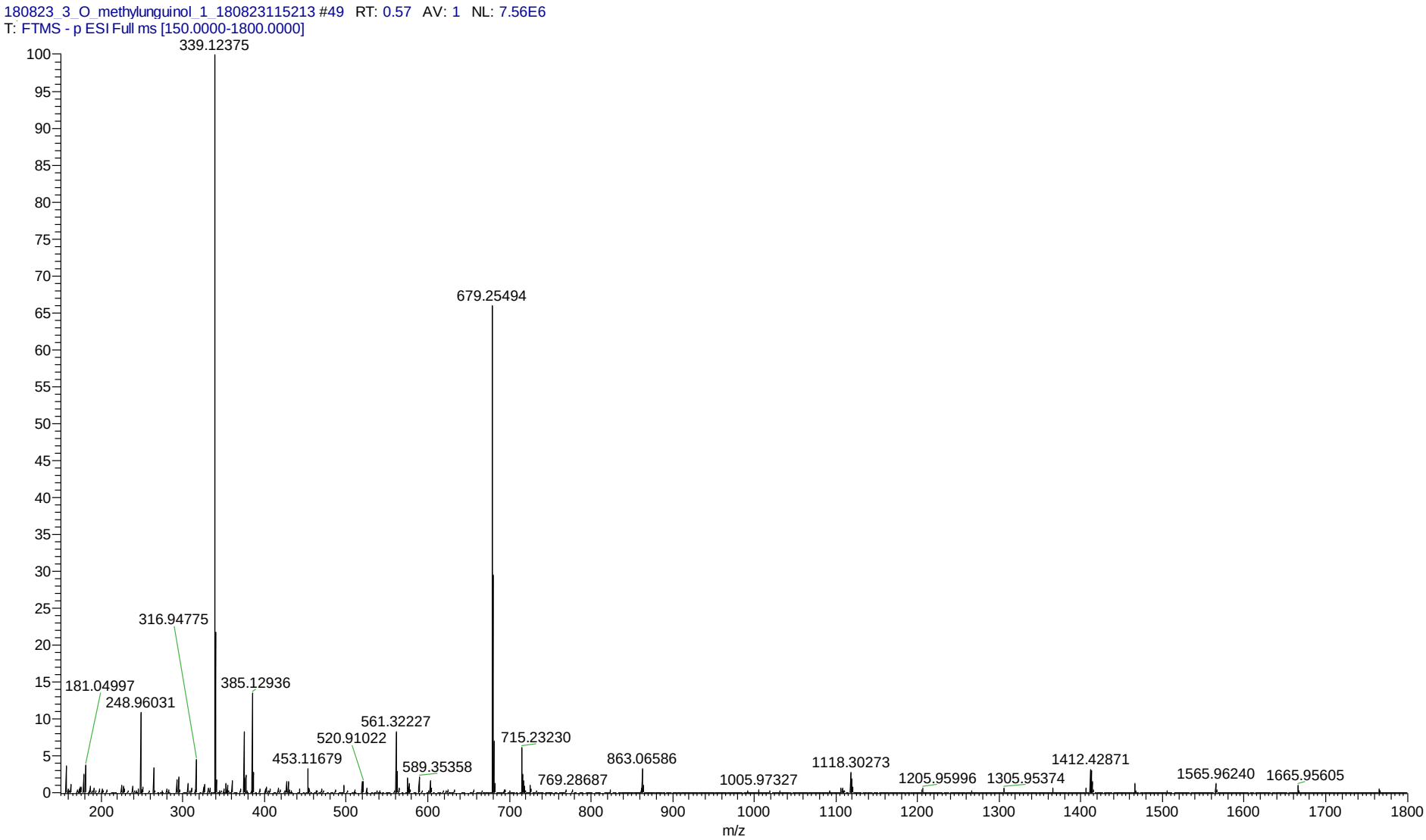

Figure S114. HRESI(–)-MS spectrum of 3-*O*-methylunguinol (**5a**)

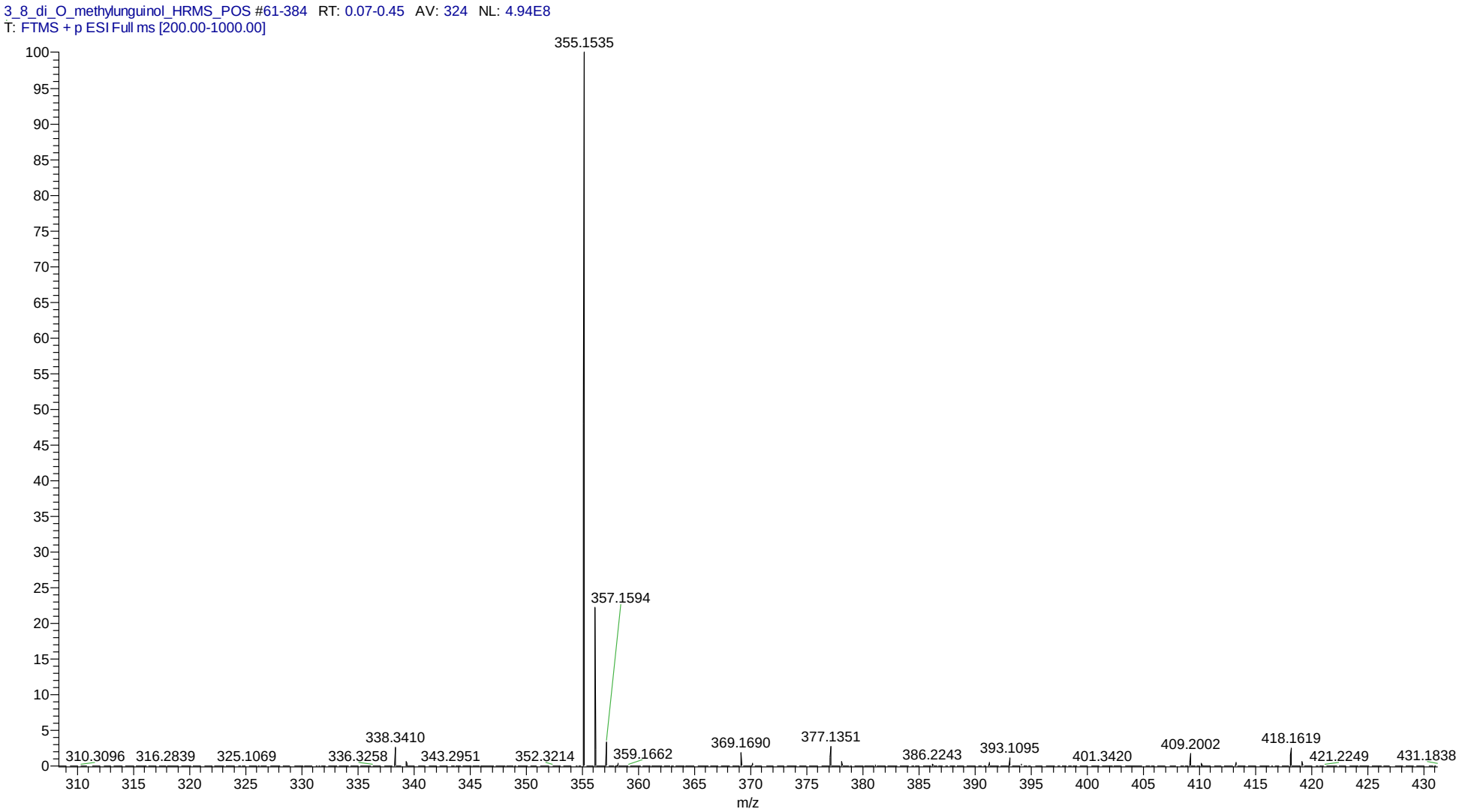

Figure S115. HRESI(+)-MS spectrum of 3,8-di-*O*-methylunguinol (**5b**)

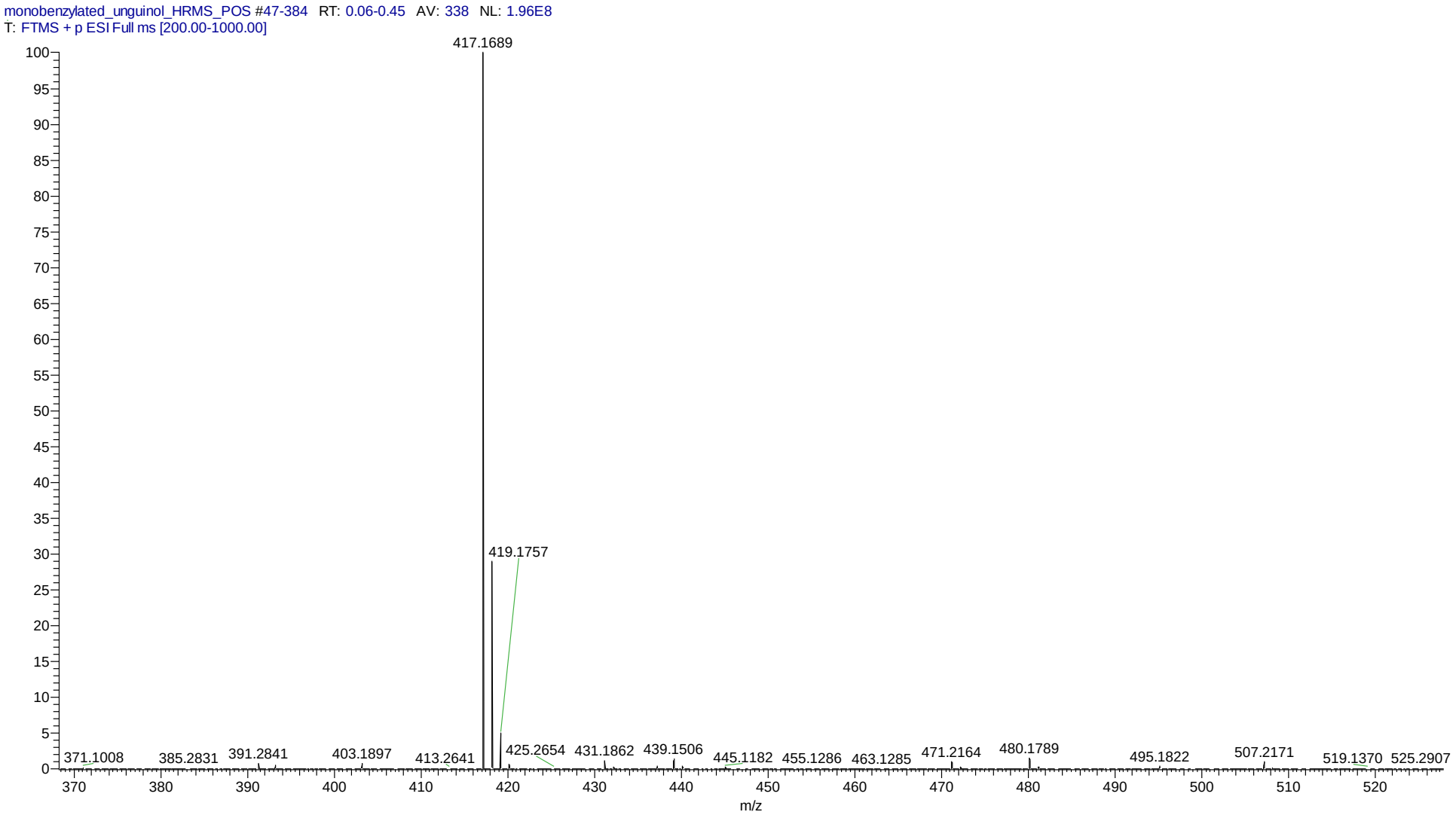

Figure S116. HRESI(+)-MS spectrum of 3-*O*-benzylunguinol (**6a**)

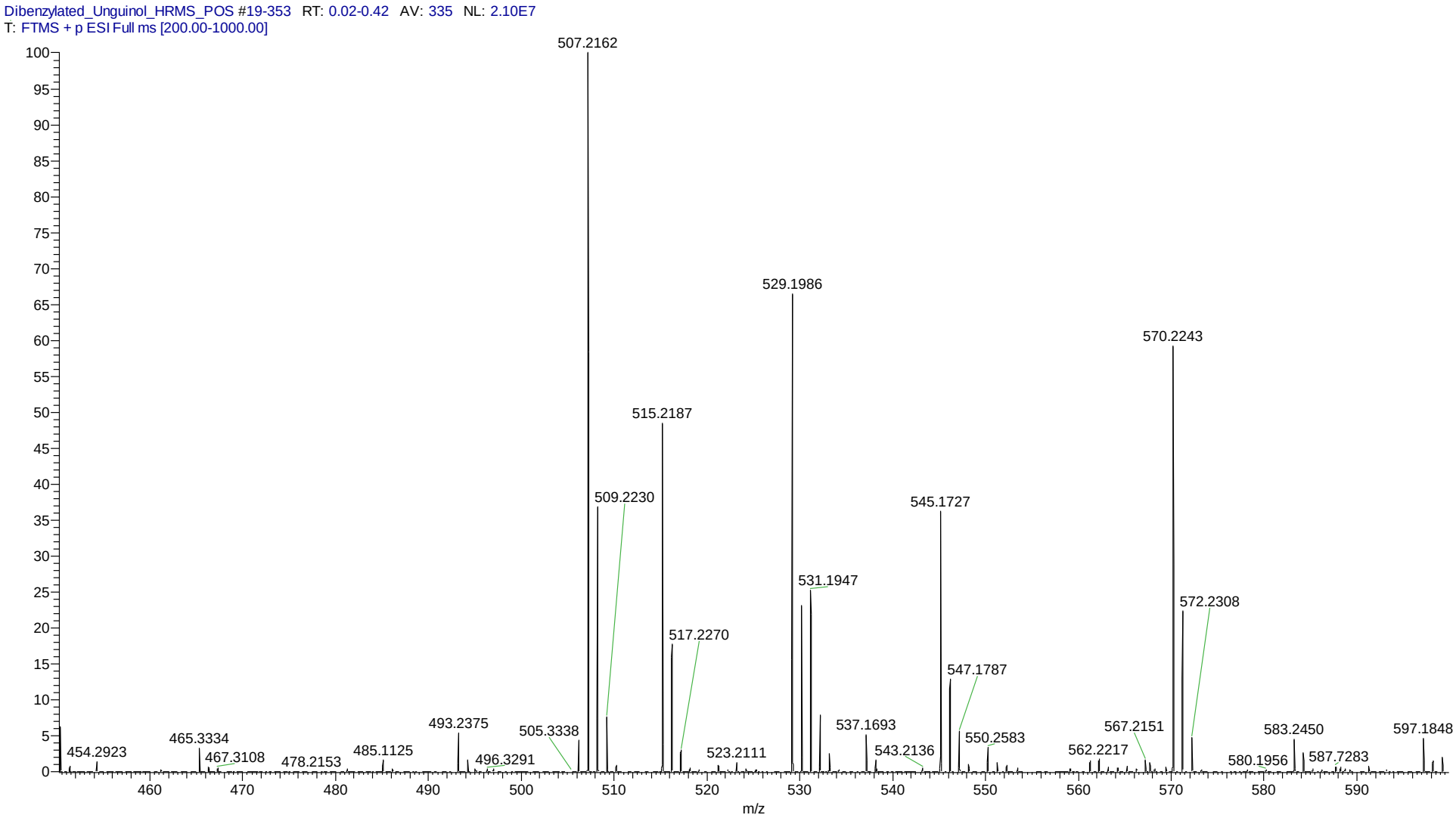

Figure S117. HRESI(+)-MS spectrum of 3,8-di-*O*-benzylunguinol (**6b**)

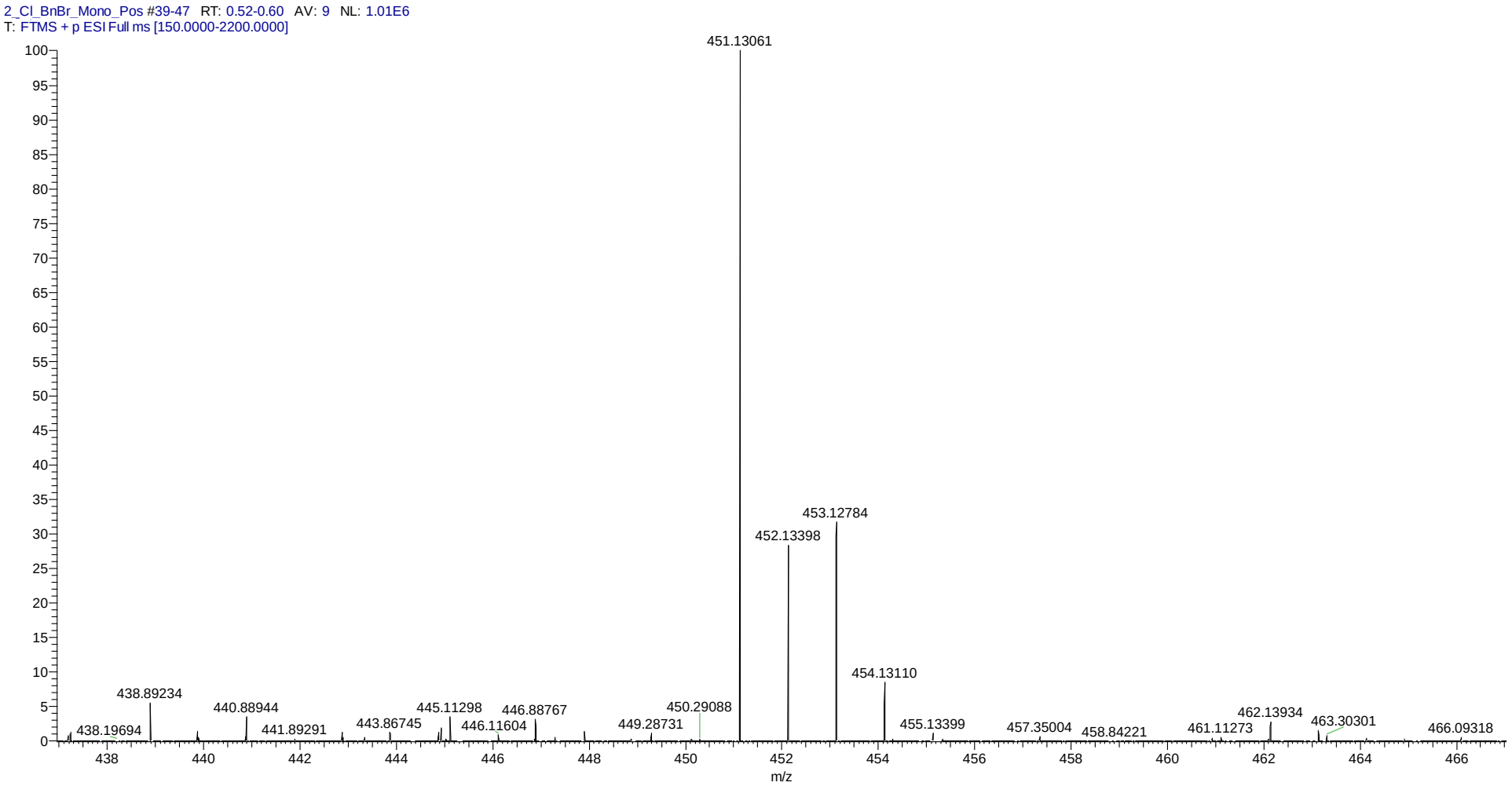

Figure S118. HRESI(+)-MS spectrum of 3-*O*-(2-chlorobenzyl)unguinol (**7a**)

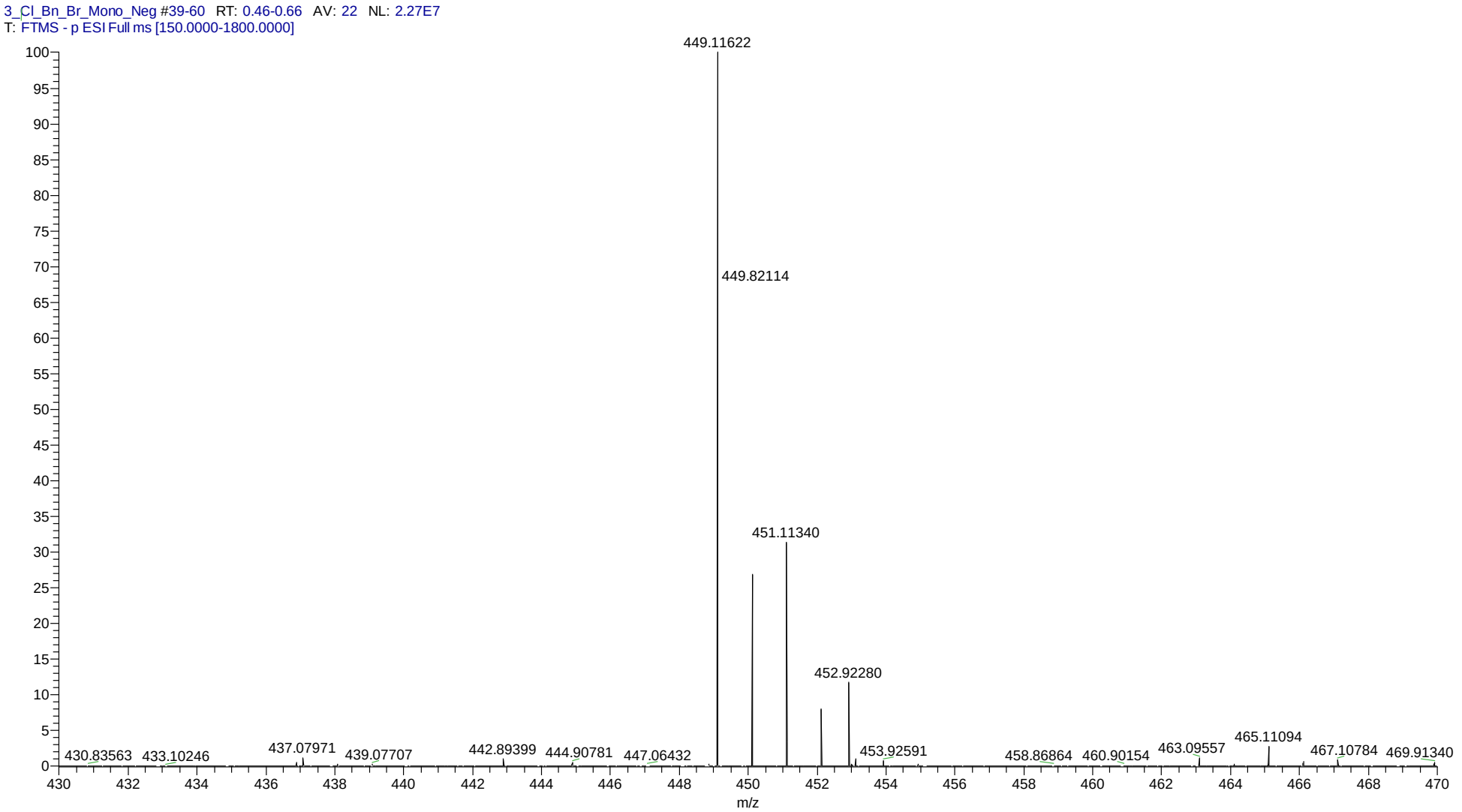

Figure S119. HRESI(–)-MS spectrum of 3-*O*-(3-chlorobenzyl)unguinol (**7b**)

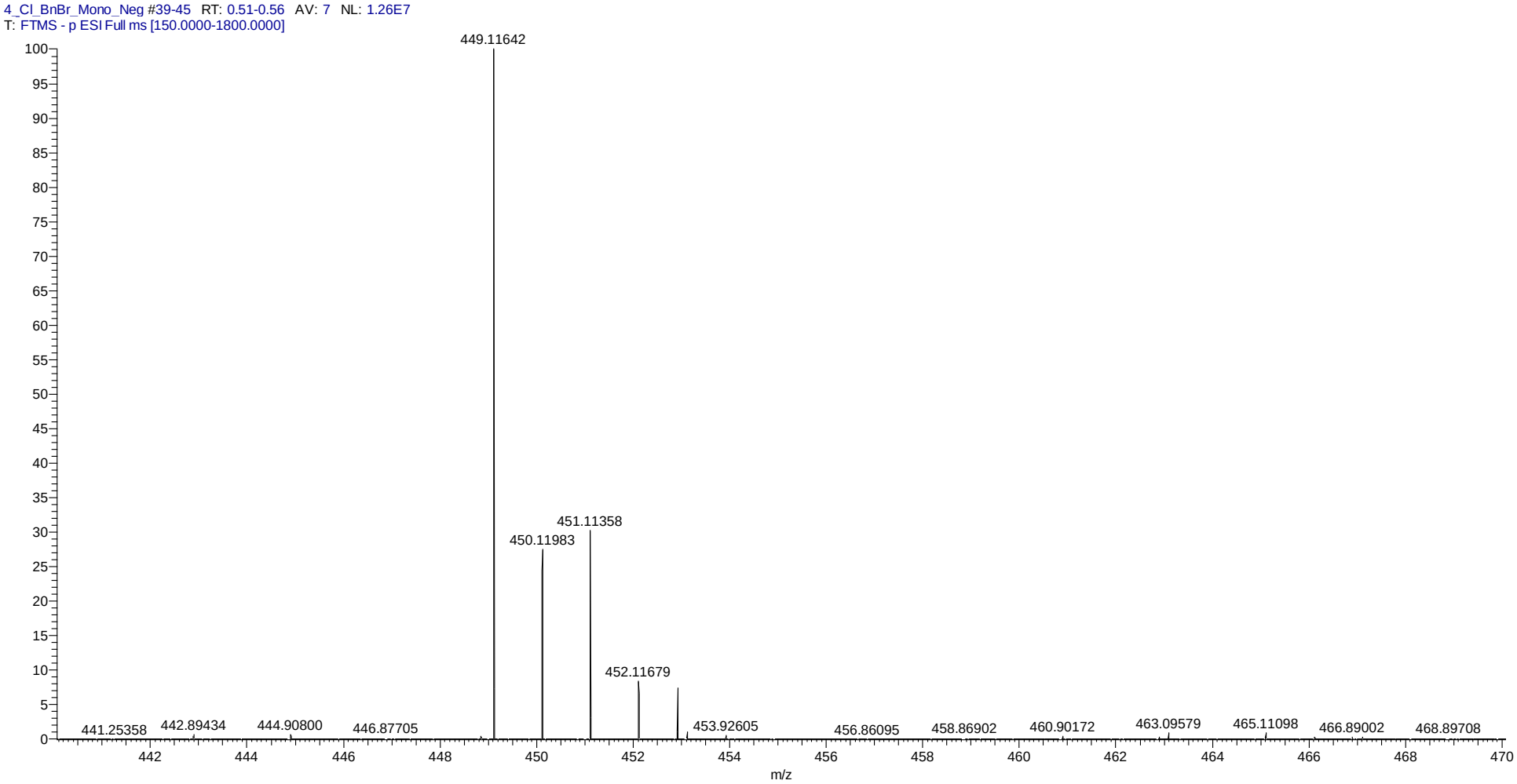

Figure S120. HRESI(–)-MS spectrum of 3-*O*-(4-chlorobenzyl)unguinol (**7c**)

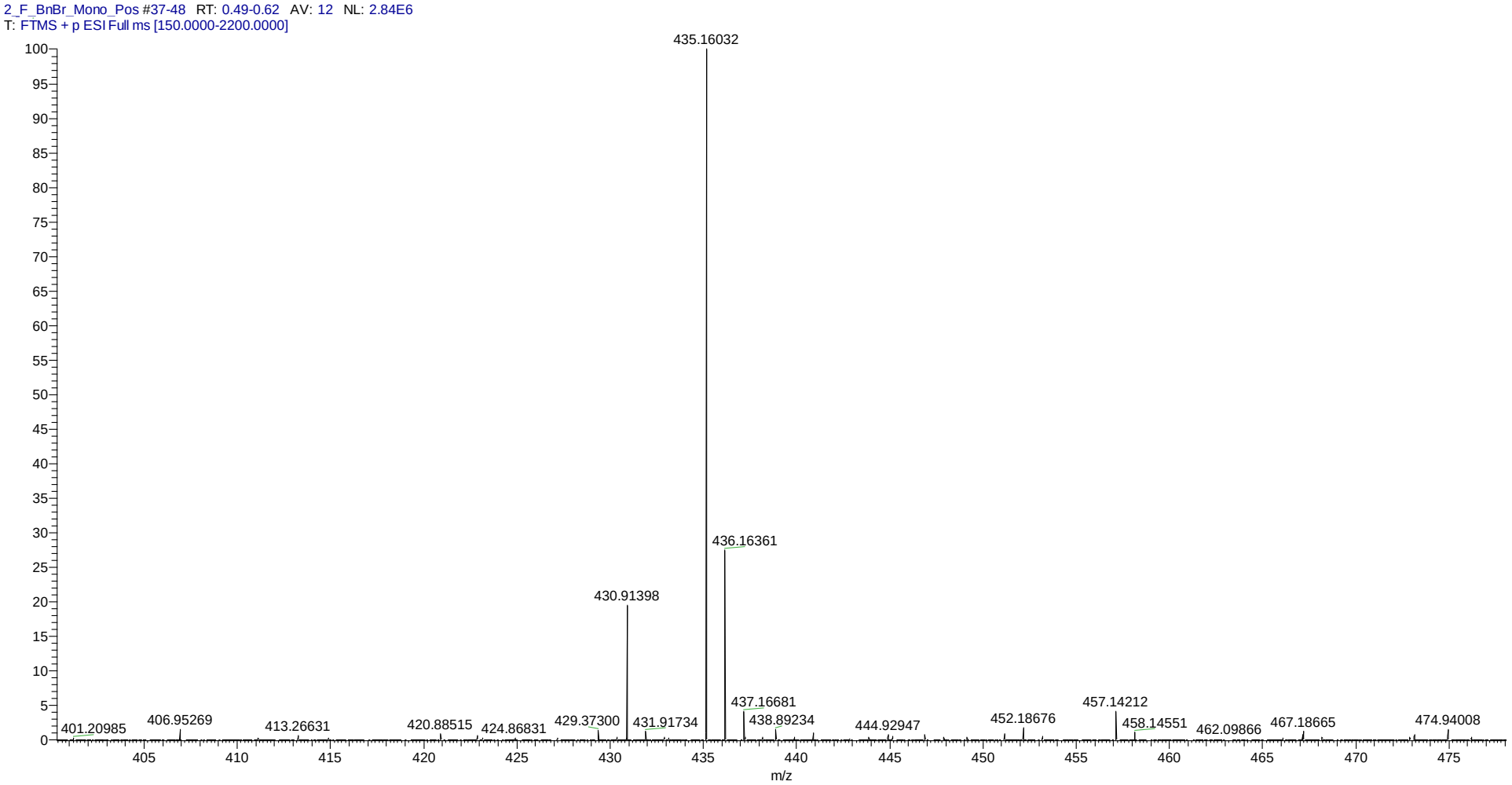

Figure S121. HRESI(+)-MS spectrum of 3-*O*-(2-fluorobenzyl)unguinol (**7d**)

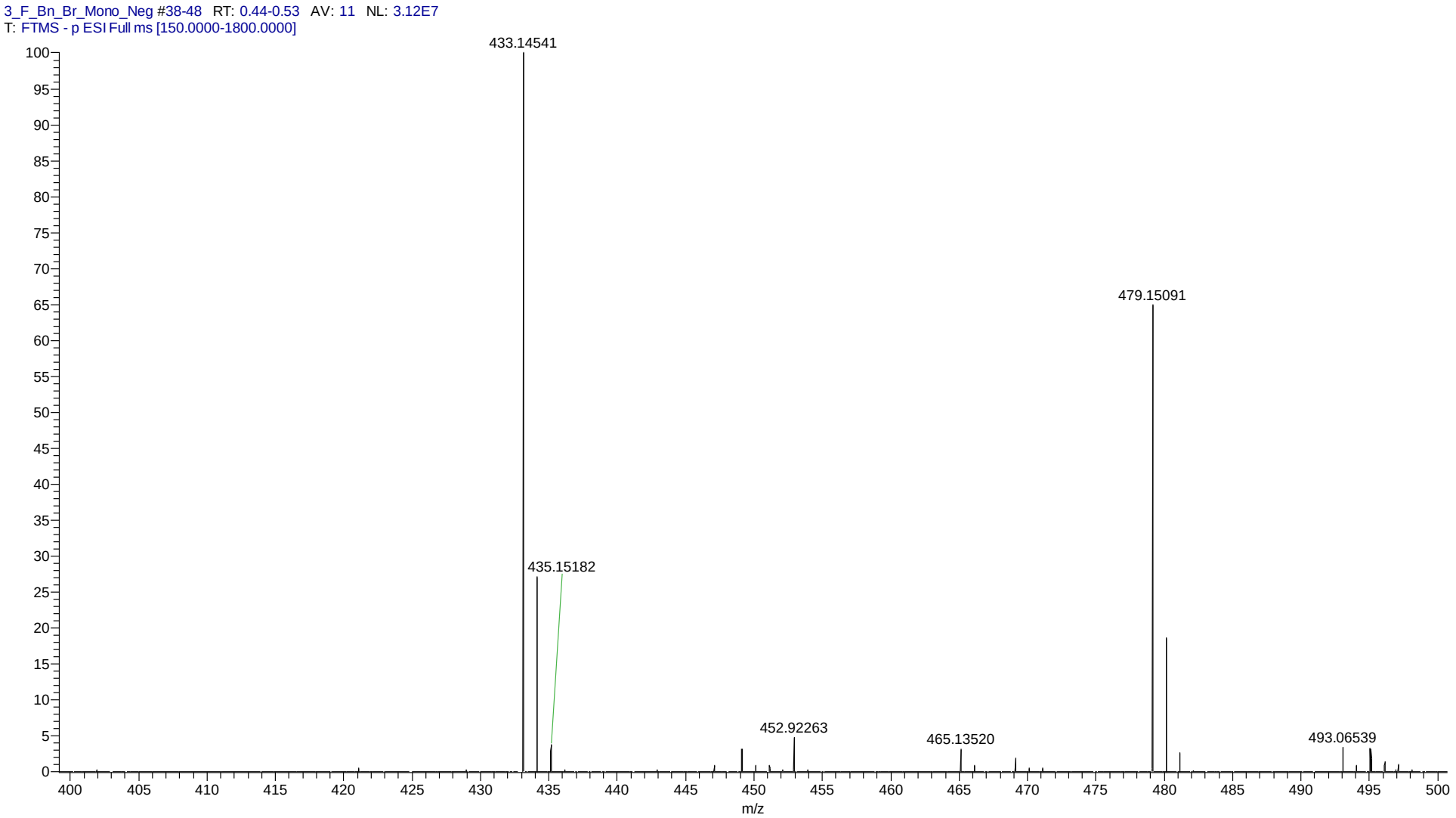

Figure S122. HRESI(–)-MS spectrum of 3-*O*-(3-fluorobenzyl)unguinol (**7e**)

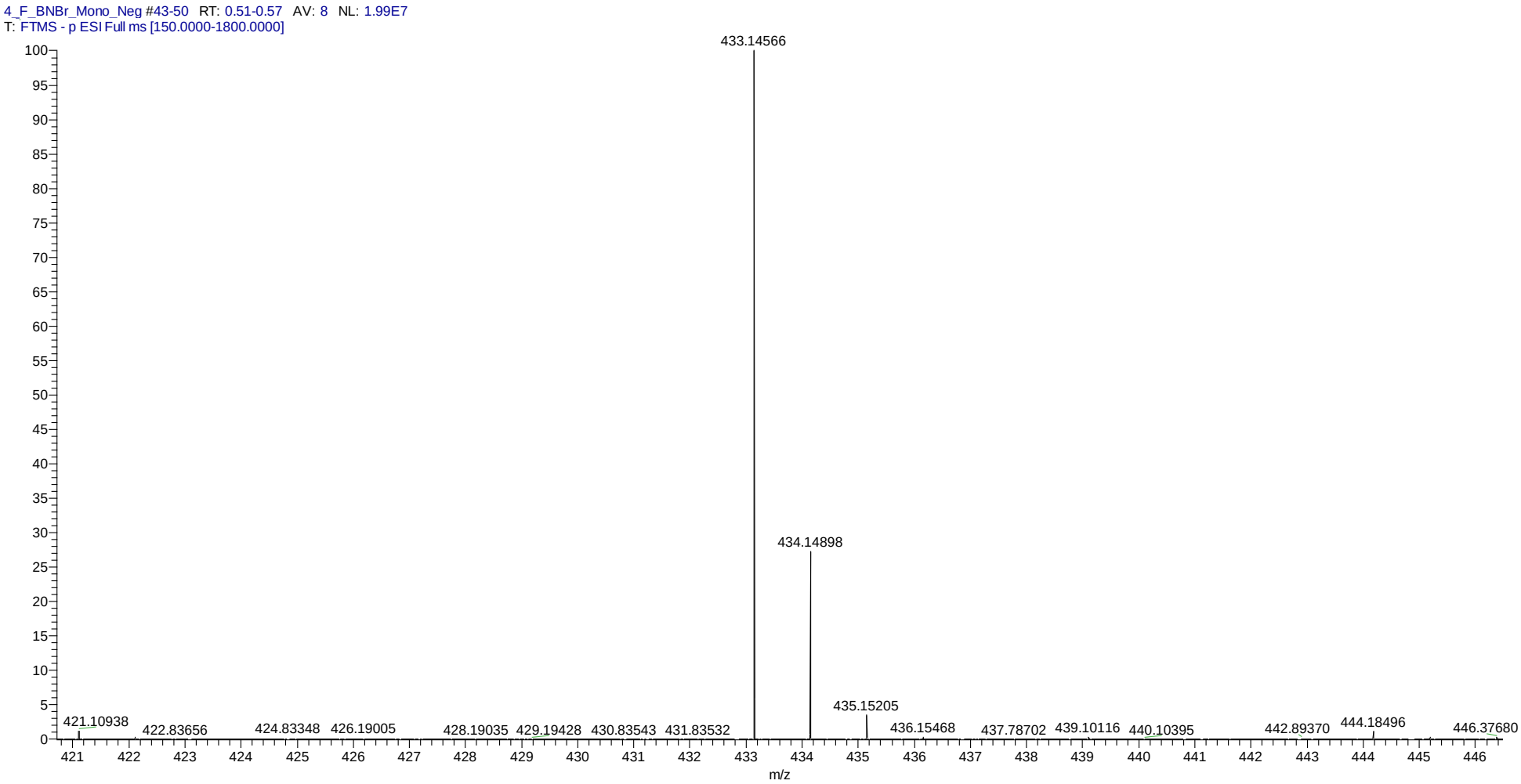

Figure S123. HRESI(–)-MS spectrum of 3-*O*-(4-fluorobenzyl)unguinol (**7f**)

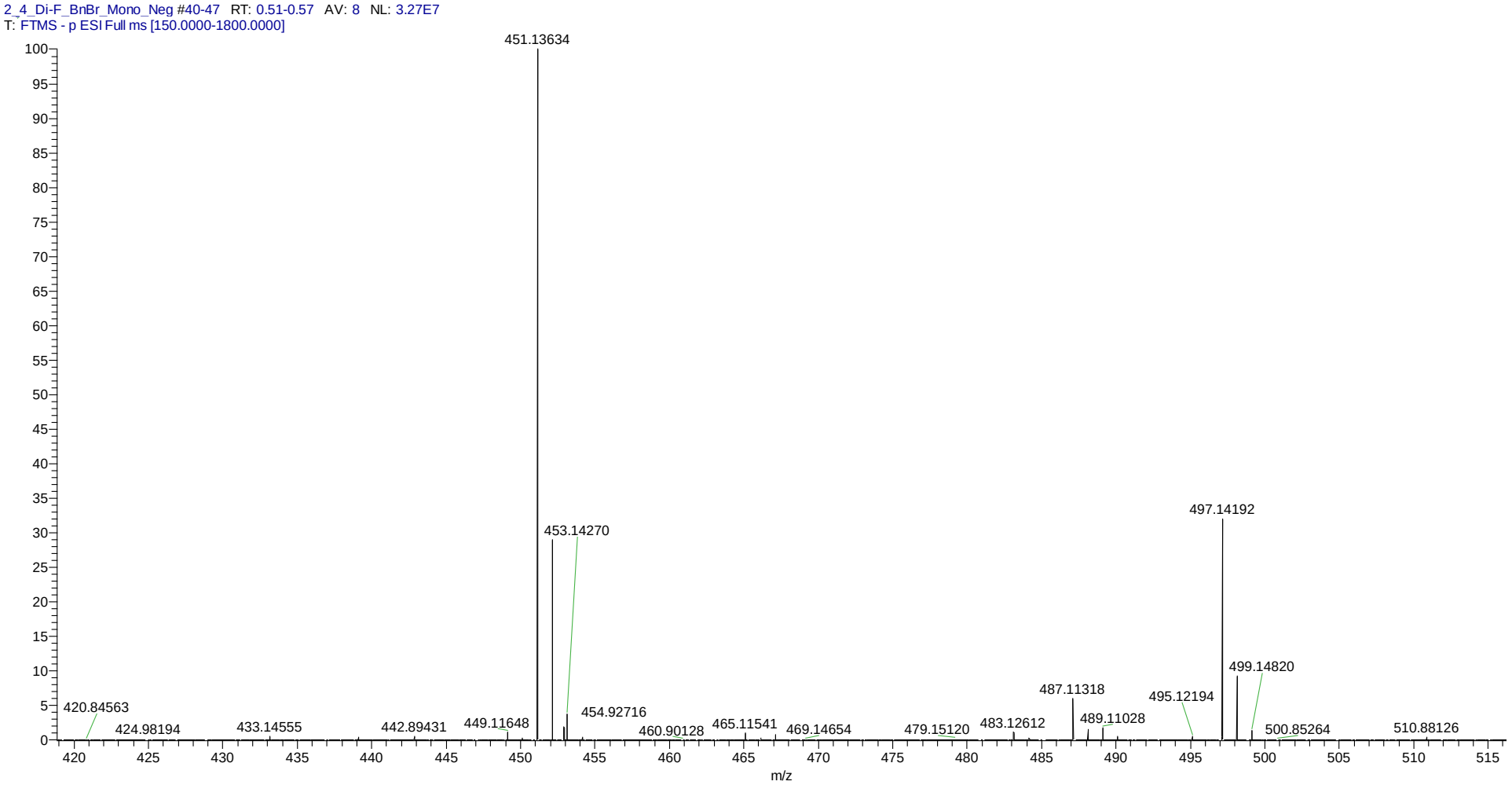

Figure S124. HRESI(–)-MS spectrum of 3-*O*-(2,4-difluorobenzyl)unguinol (**7g**)

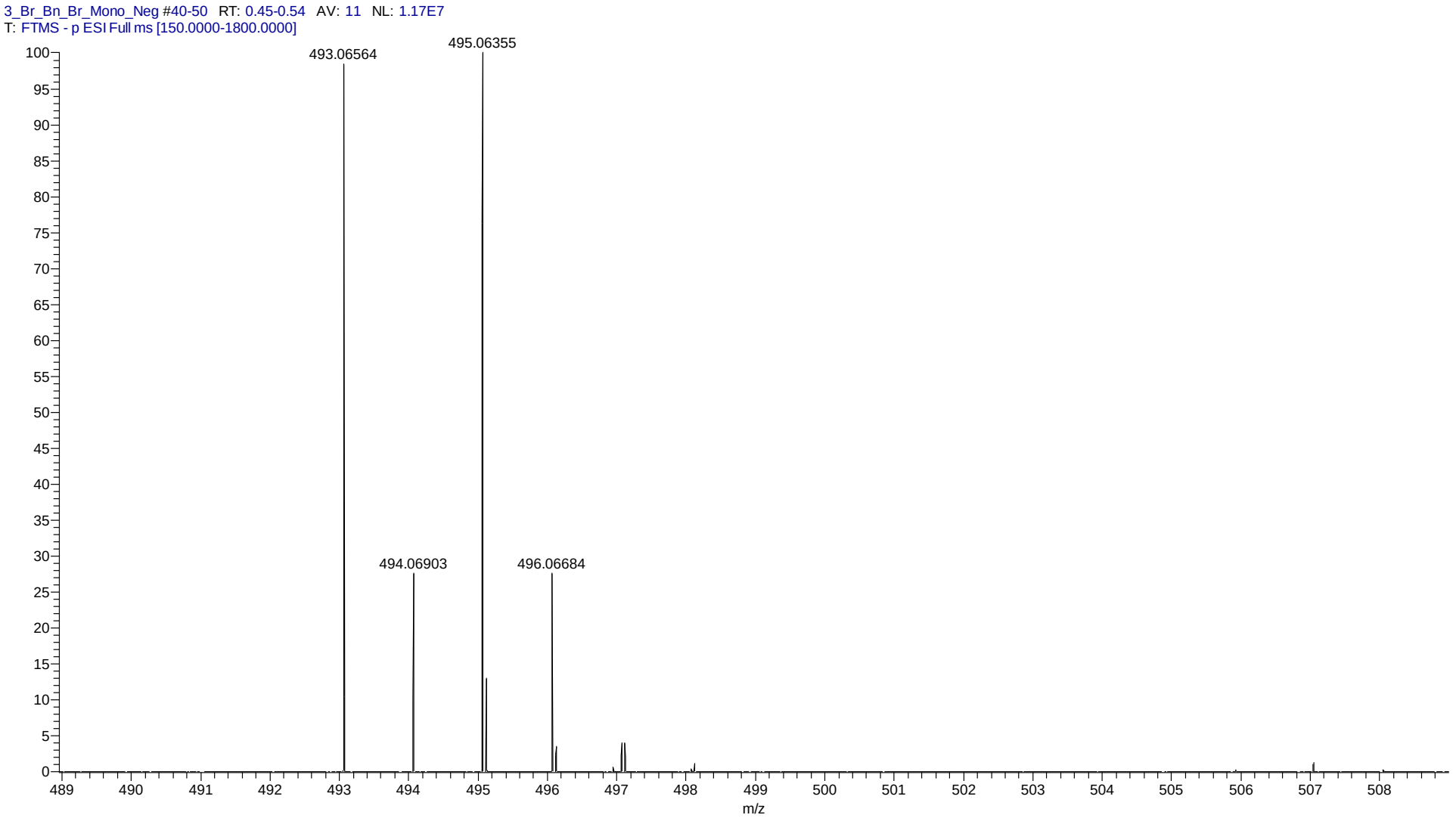

Figure S125. HRESI(–)-MS spectrum of 3-*O*-(3-bromobenzyl)unguinol (**7h**)

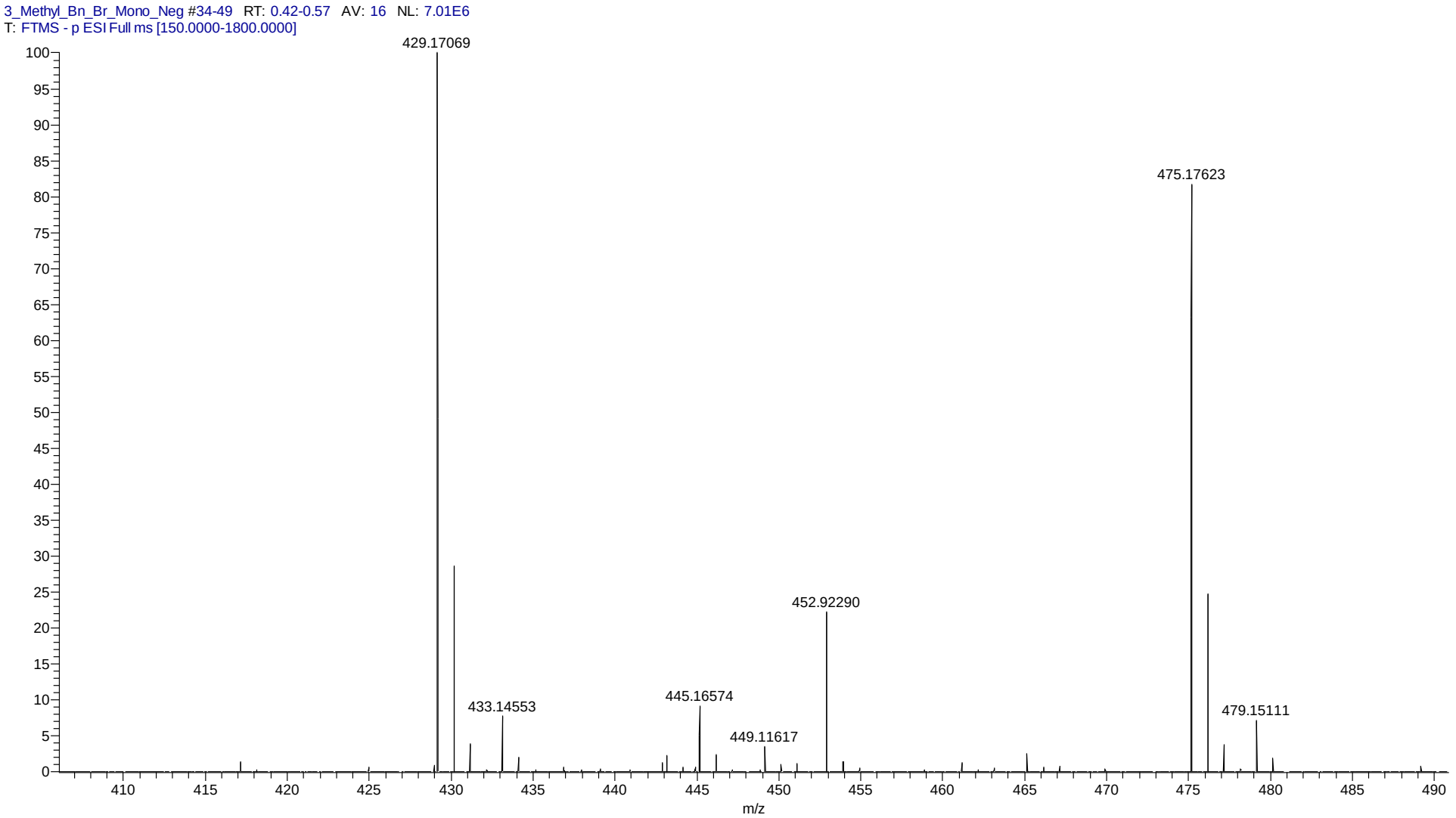

Figure S126. HRESI(–)-MS spectrum of 3-*O*-(3-methylbenzyl)unguinol (**7i**)

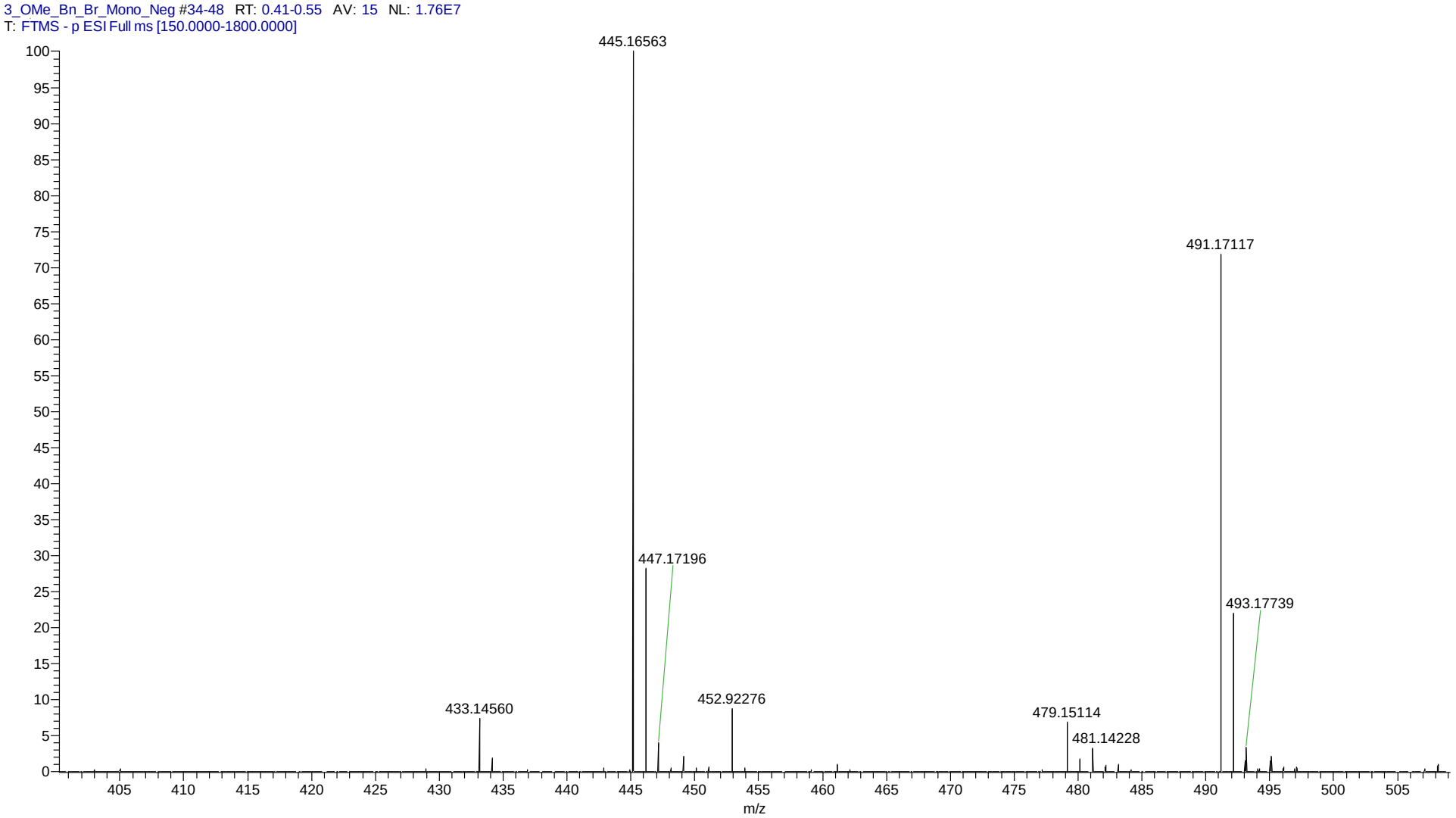

Figure S127. HRESI(–)-MS spectrum of 3-*O*-(3-methoxybenzyl)unguinol (**7j**)

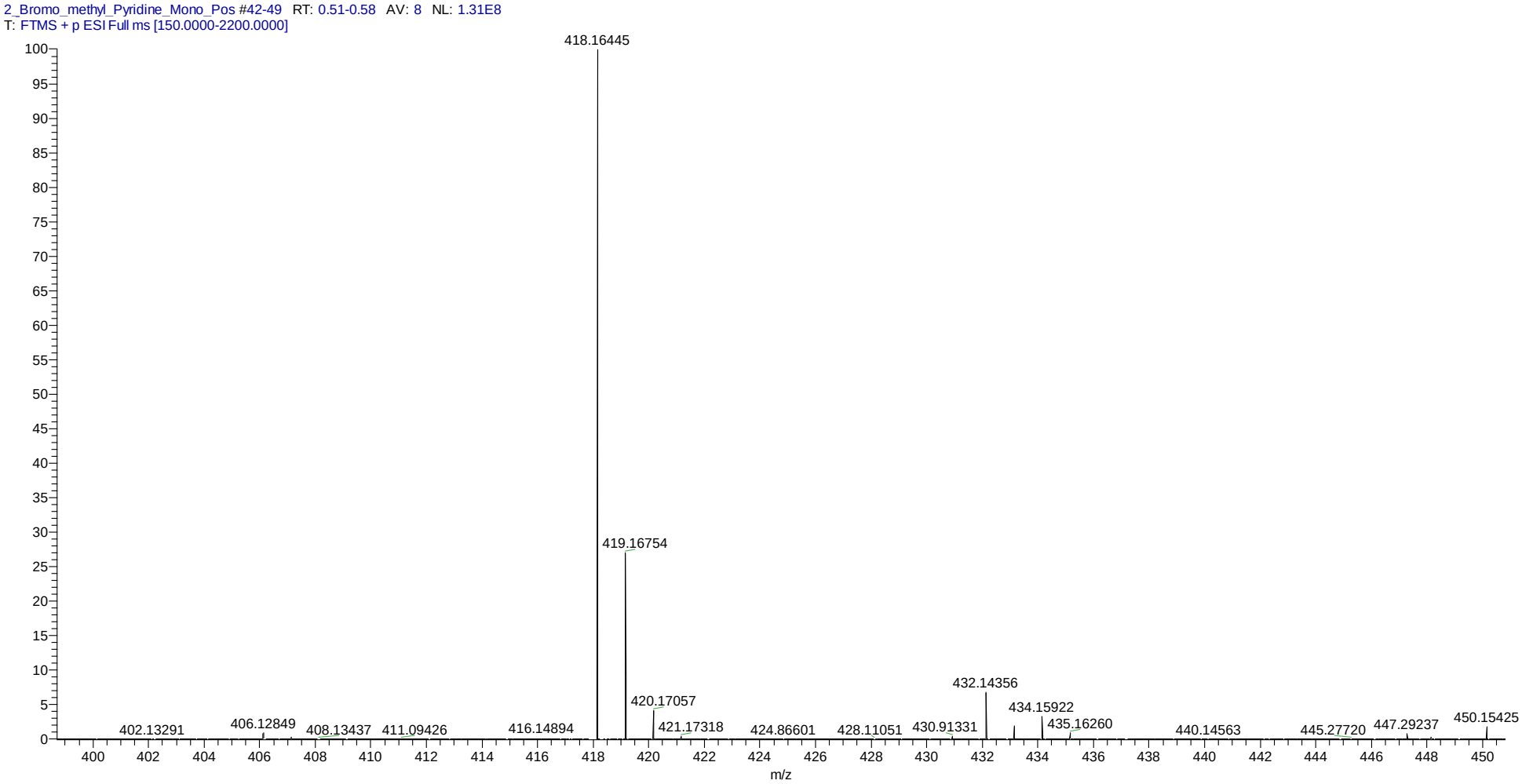

Figure S128. HRESI(+)-MS spectrum of 3-*O*-(2-picolyl)unguinol (**7k**)

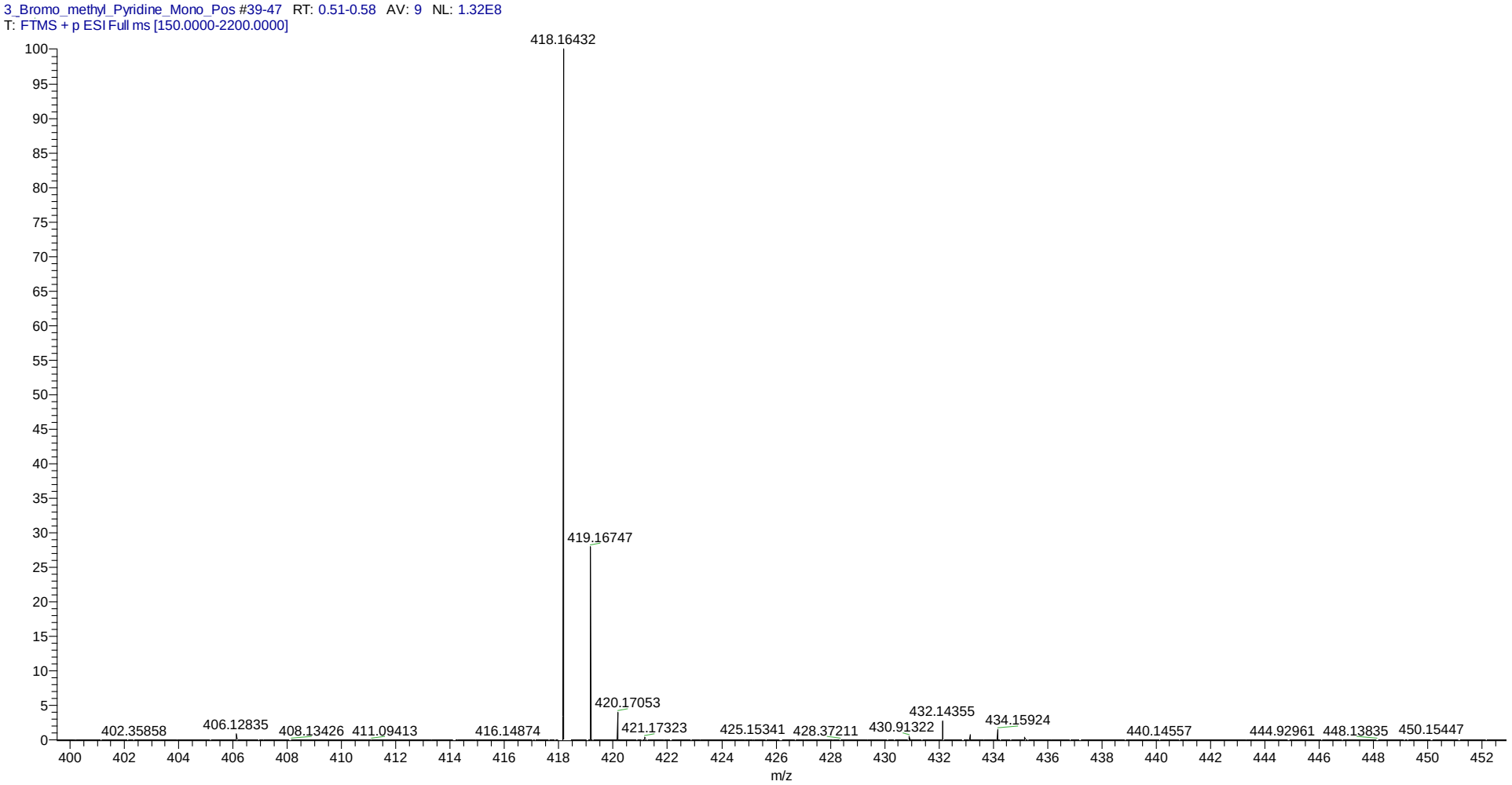

Figure S129. HRESI(+)-MS spectrum of 3-*O*-(3-picolyl)unguinol (**7l**)

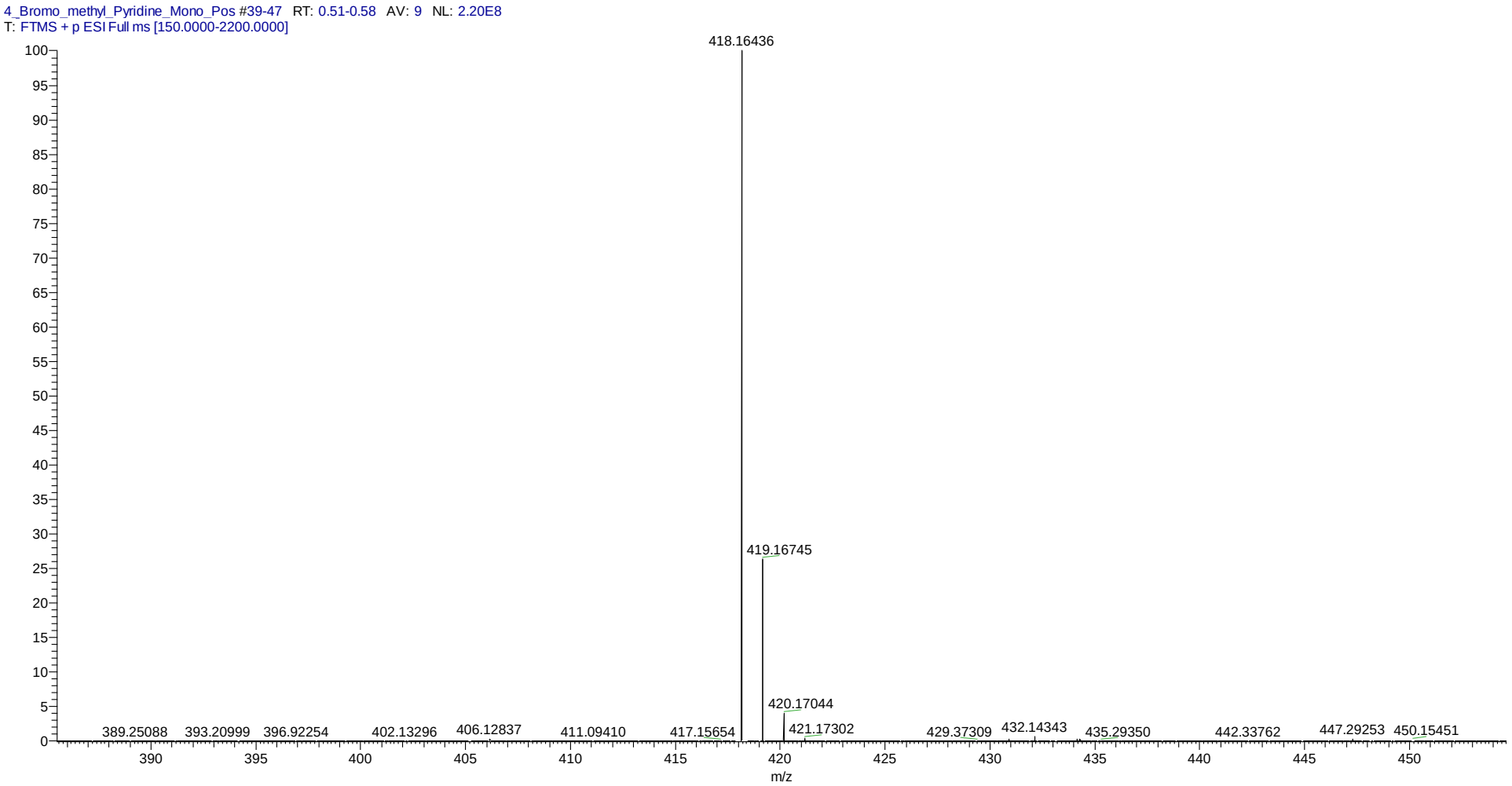

Figure S130. HRESI(+)-MS spectrum of 3-*O*-(4-picolyl)unguinol (**7m**)

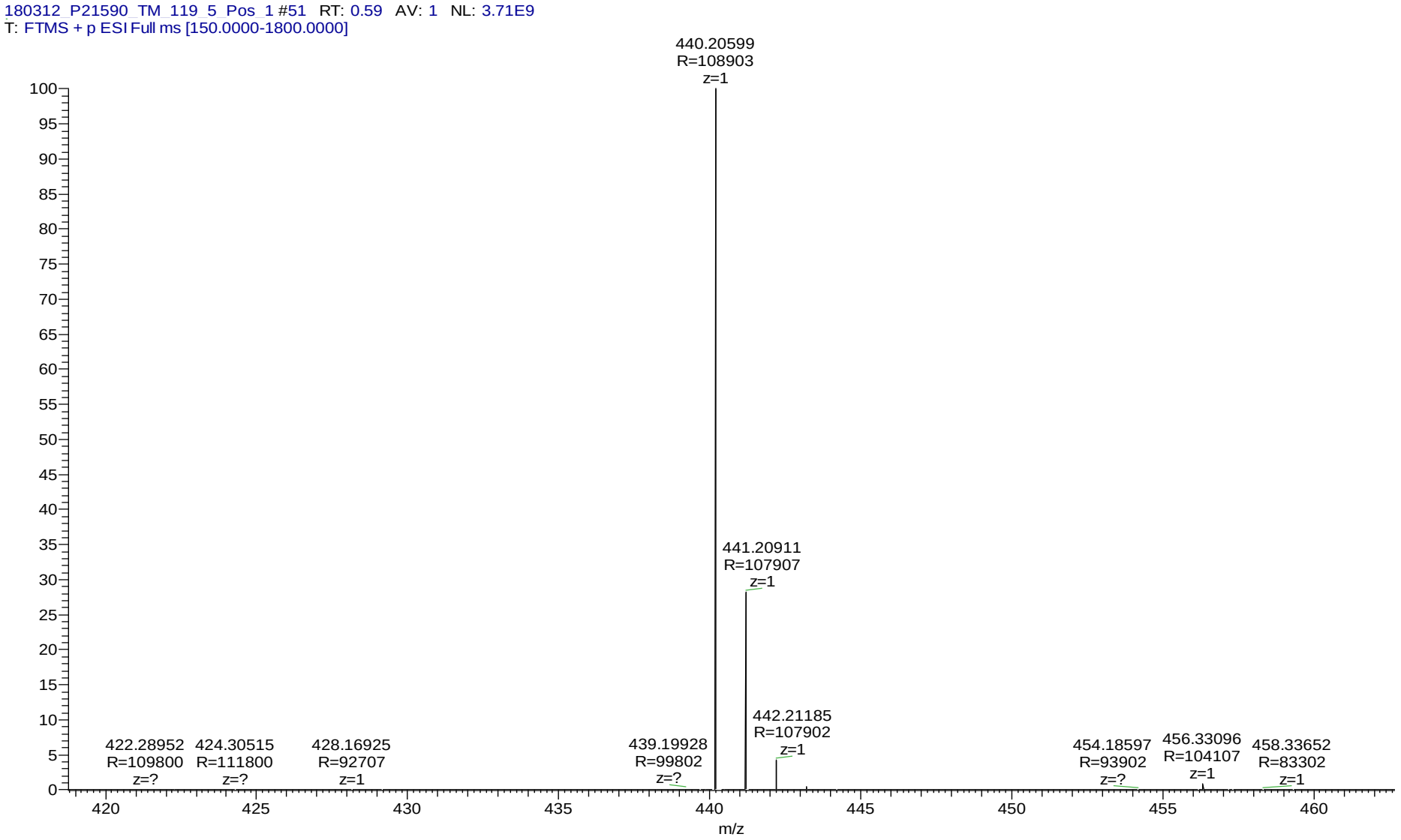

Figure S131. HRESI(+)-MS spectrum of 3-*O*-(4-morpholinoethyl)unguinol (**7n**)

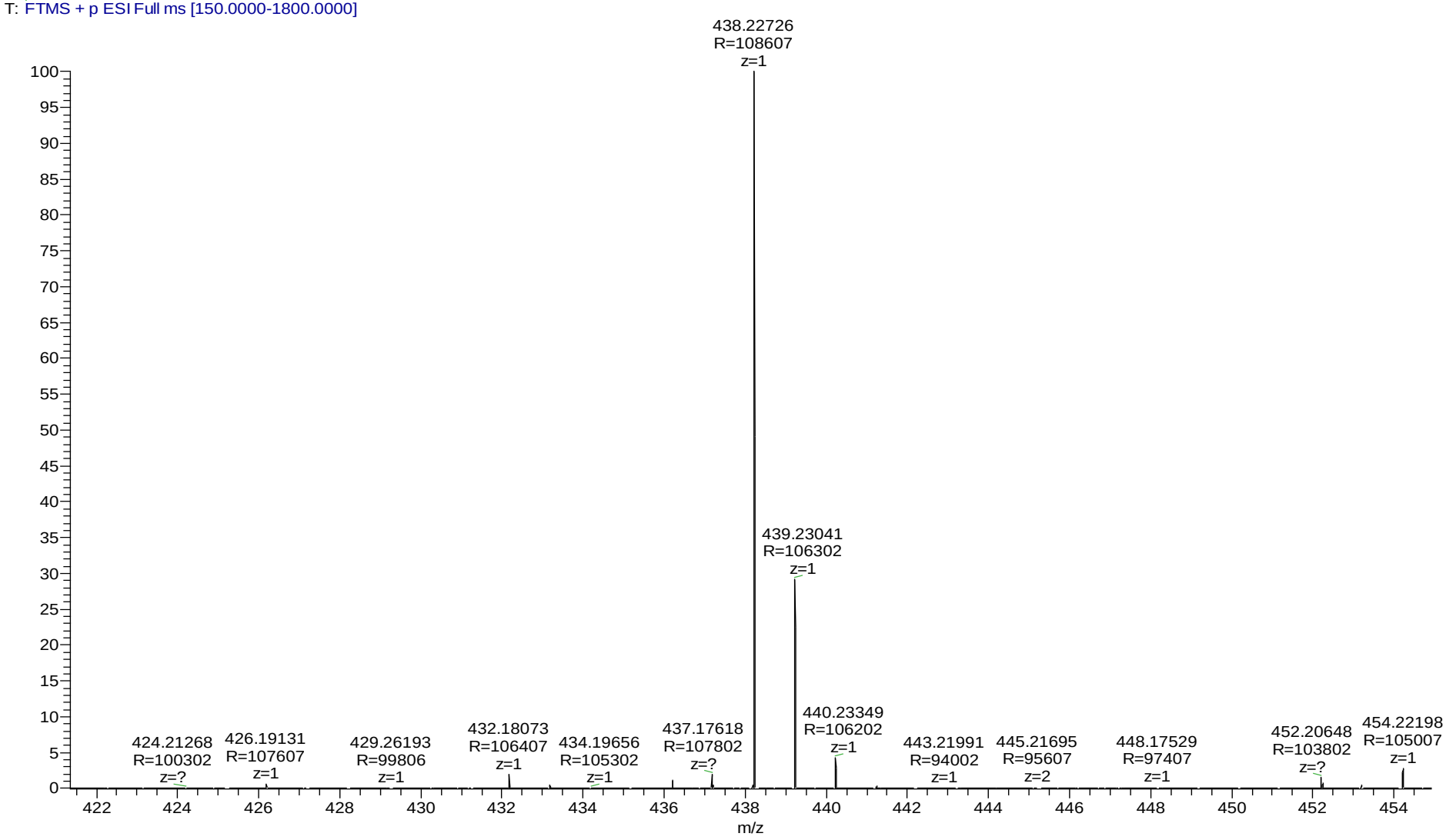

Figure S132. HRESI(+)-MS spectrum of 3-*O*-(1-piperidinylethyl)unguinol (**7o**)

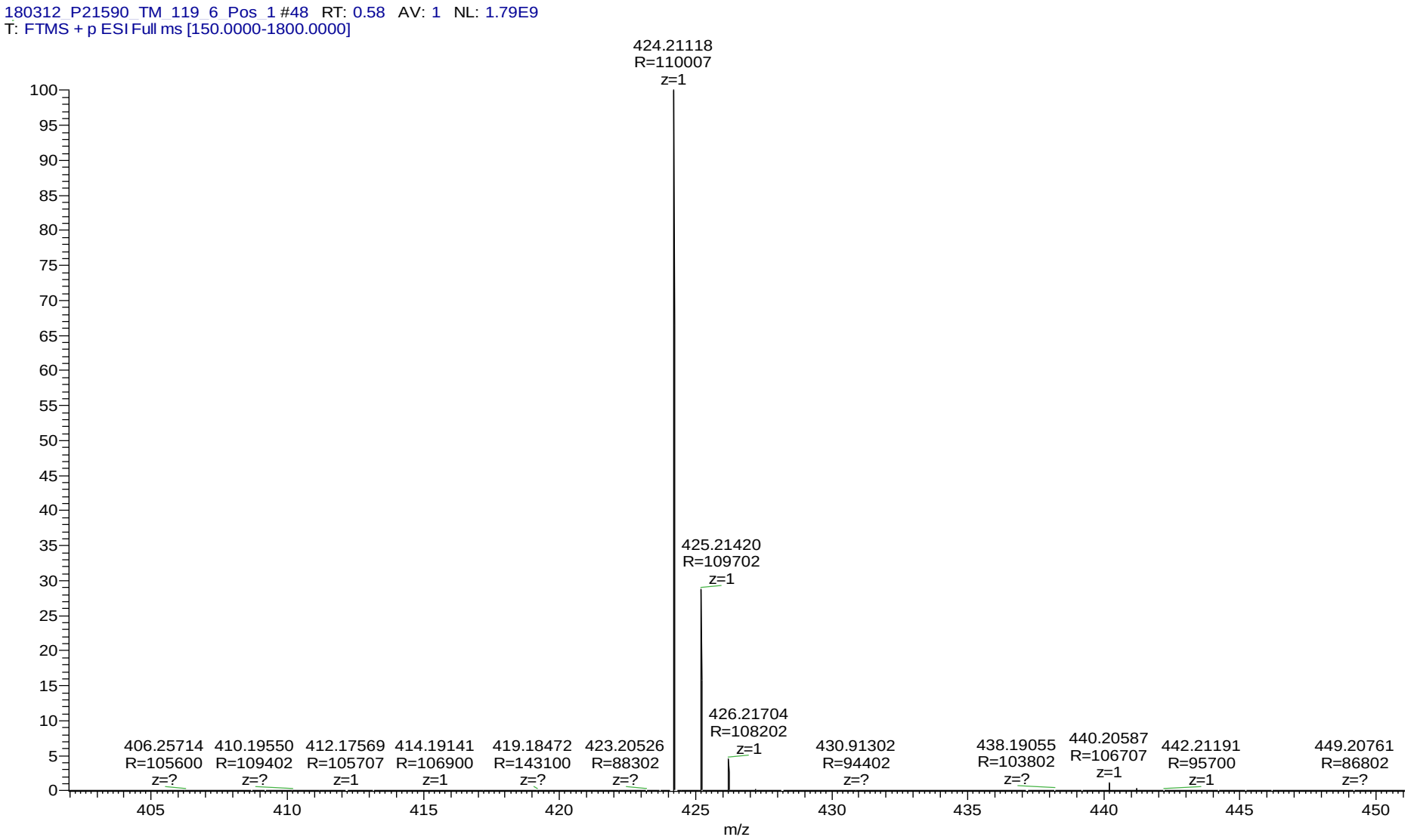

Figure S133. HRESI(+)-MS spectrum of 3-*O*-(1-pyrrolidinylethyl)unguinol (**7p**)

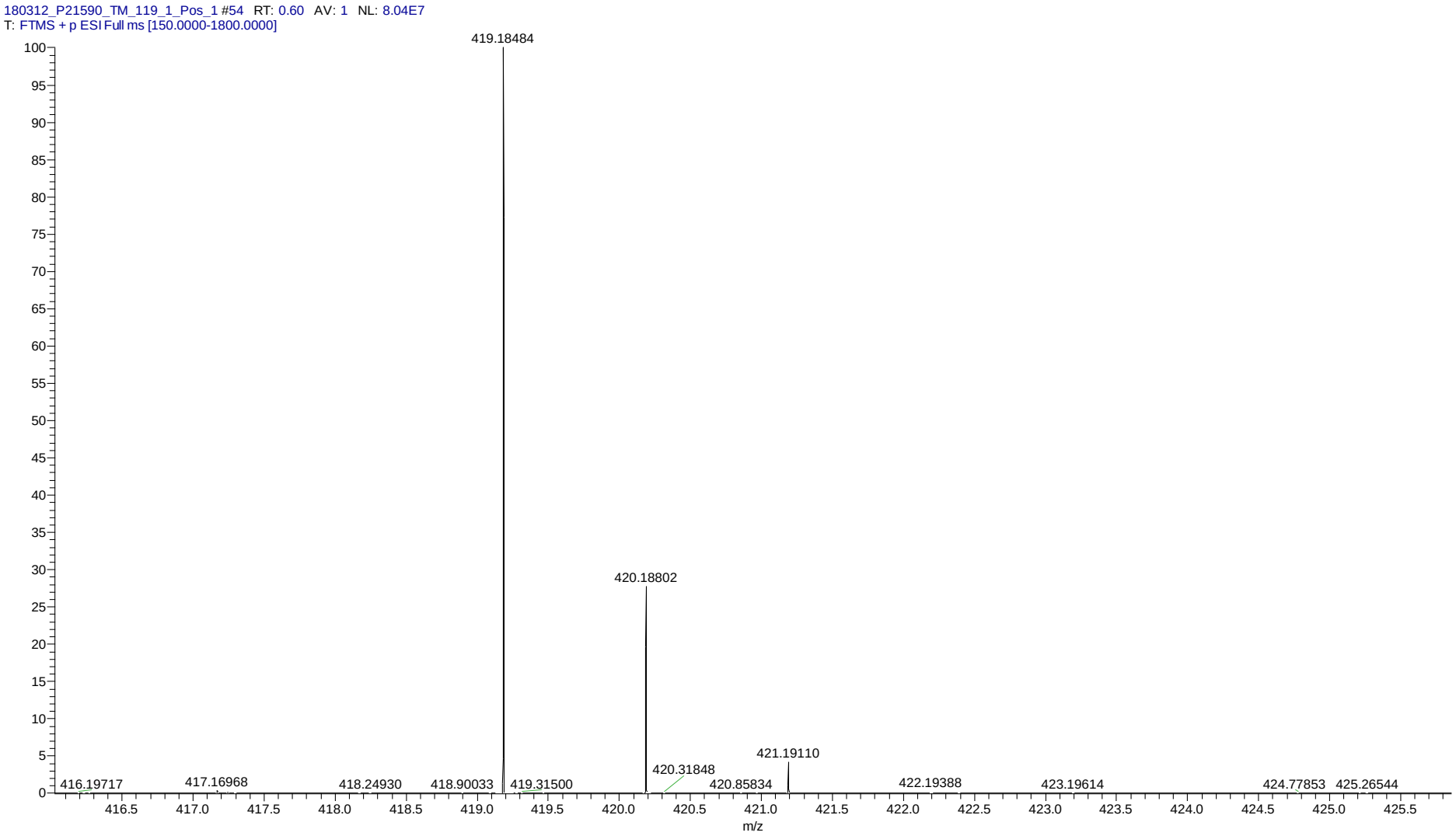

Figure S134. HRESI(+)-MS spectrum of 3-*O*-1′,2′-dihydrobenzylunguinol (**8a**)

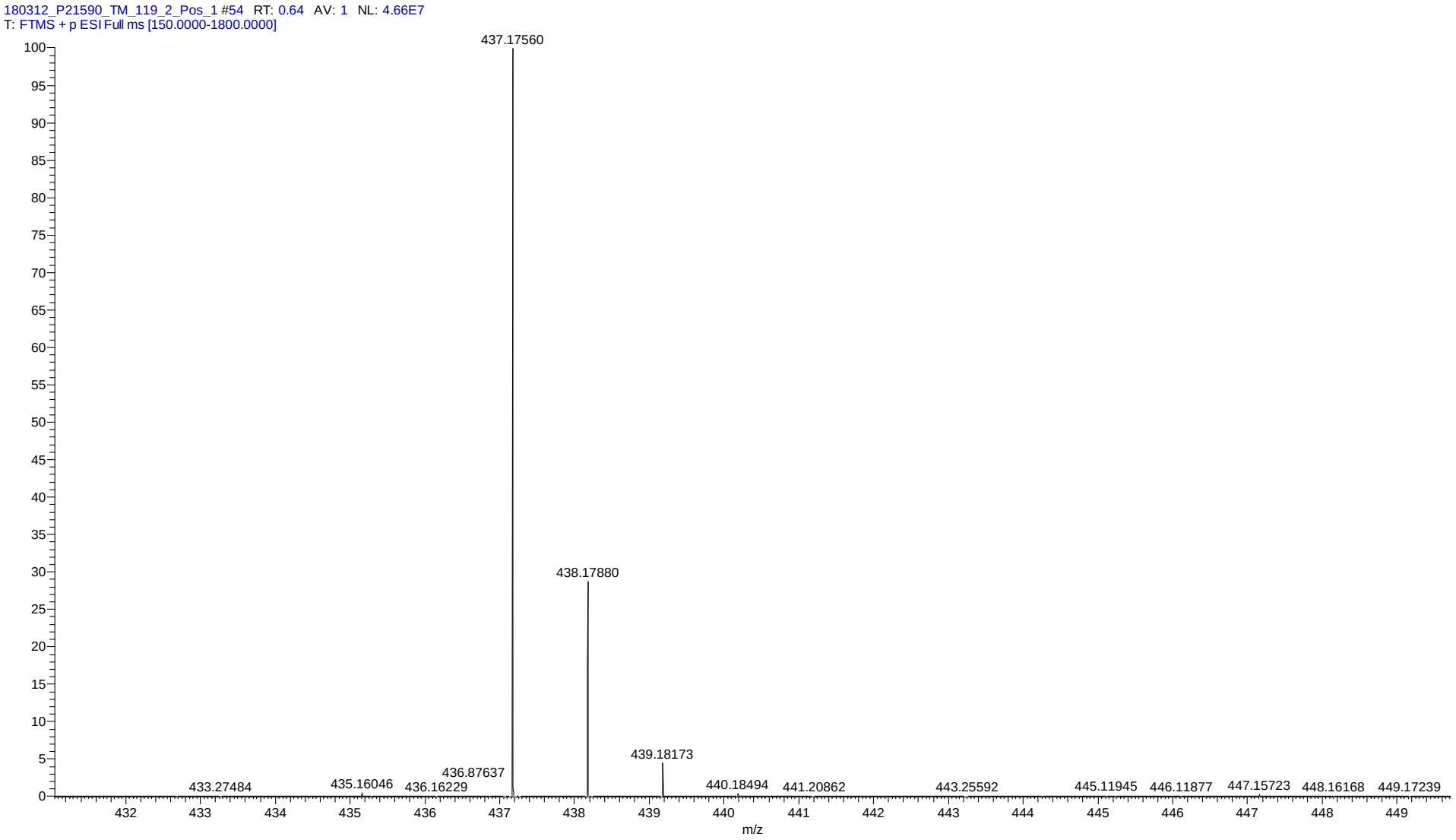

Figure S135. HRESI(+)-MS spectrum of 3-*O*-(2-fluorobenzyl)-1′,2′-dihydrounguinol (**8b**)

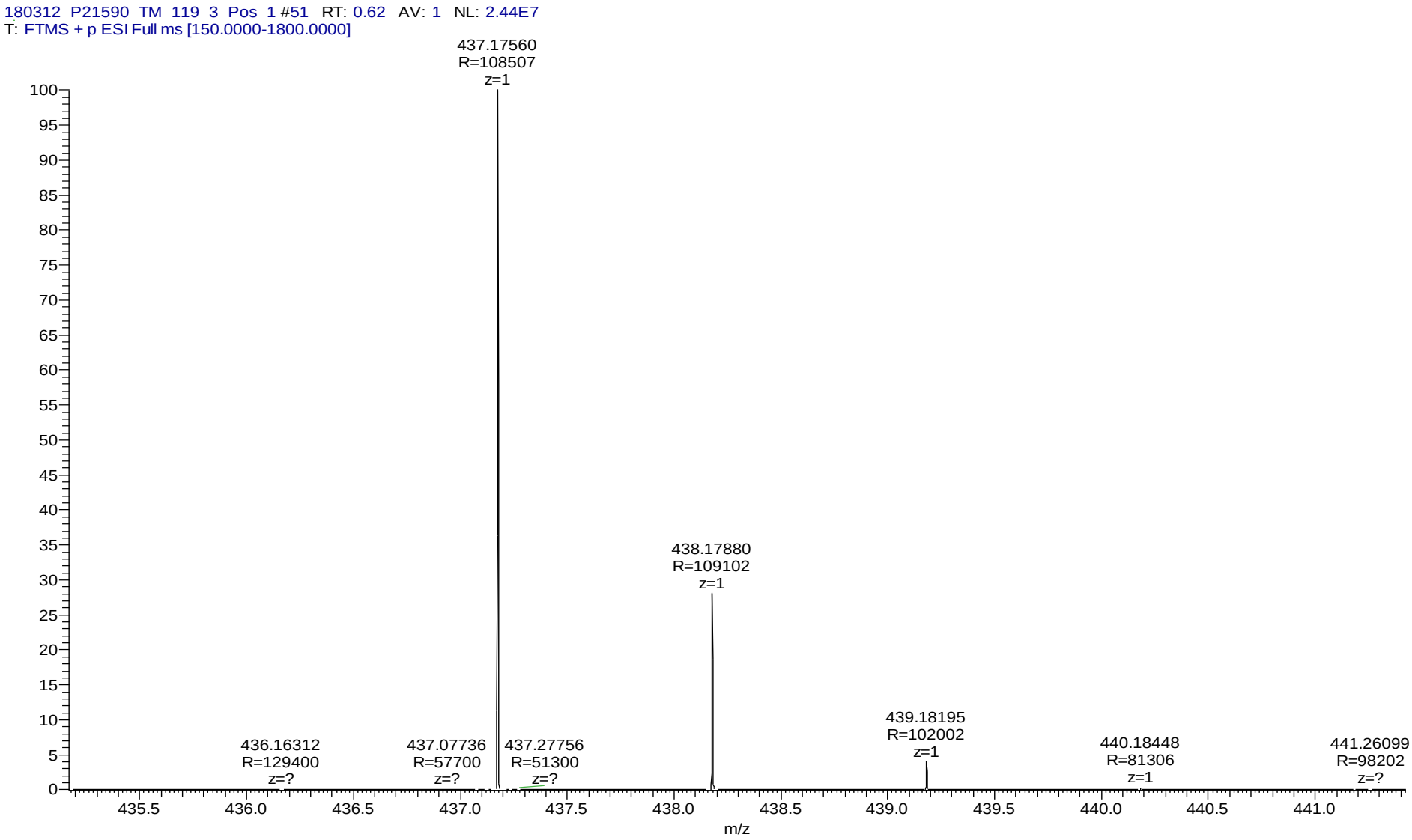

Figure S136. HRESI(+)-MS spectrum of 3-*O*-(4-fluorobenzyl)-1′,2′-dihydrounguinol (**8c**)