Supporting Information

Experimental and Computational Studies of the Diastereoselective Natural Based Meldrum Spiro Dibenzofuran Derivatives Synthesis

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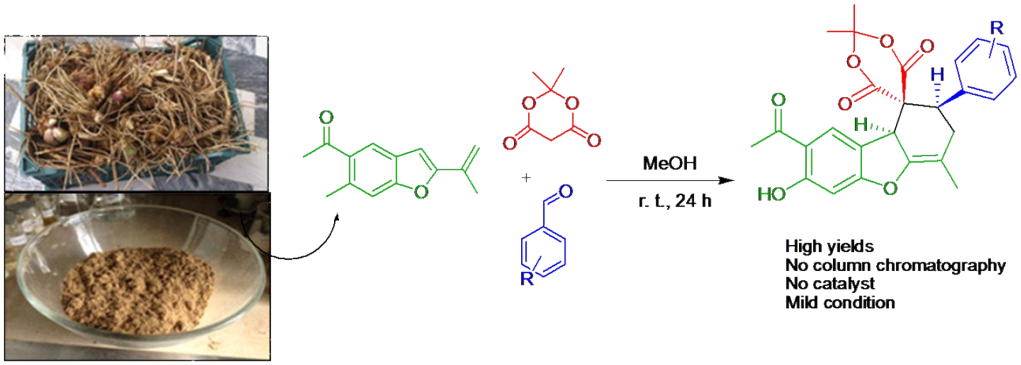

Experimental

General procedure for synthesis of Meldrum spiro dibenzofuran derivatives 4

A mixture of euparin **1** (1 mmol), aromatic aldehydes **2** (1 mmol) and Meldrum acid **3** (1 mmol) were dissolved in methanol (5 mL) and magnetically stirred for 24 hours at room temperature. After reaction completion, indicated by TLC, the solvent was evaporated under reduced pressure and the obtained solid was purified by recrystallization from dichloromethane to give products.

spiro[1-(3-Hydroxy-6-methyl-8-phenyl-7,7,8,9a-tetrahydro-dibenzofuran-2-yl)-ethanone(2,2-Dimethyl[1,3] Dioxane-4,6-Dione)] **(4a)**

White crystalline; yield: 84% (0.37 g), mp = 179–181˚C. IR (KBr) (ν_{max}, cm^{-1}): 3435 (OH), 1768, 1735, 1638 (3C=O); MS (EL, 70Ev): *m/z* (%): 448 (M^+, 7), 362 (31), 216 (100), 105 (21), 77 (18), 43 (93); ^1H NMR (400 MHz, $CDCl_3$): δ_H 0.61, 1.61 (2s, 6H, 2Me), 1.91, 2.50 (2s, 6H, 2Me), 2.64 (br dd, 1H, H-7'), 2.91 (br dd, 1H, H-7″), 3.97 (dd, 1H, *J*=10.8 Hz, *J*=6.4 Hz, H-8'), 4.82 (s, 1H, H-9'a), 6.51 (s, 1H, H_{Ar}), 7.28-7.35 (m, 5H, H_{Ar}), 7.43 (s, 1H, H_{Ar}), 13.06 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 14.9 (CH_3), 26.2 (CH_3), 28.9 (CH_3), 29.4 (CH_3), 35.3 (CH_2), 47.1 (CH), 49.9 (CH), 56.3 (C), 99.5, (C), 102.0, 105.9, 109.0, 114.6, 115.3, 126.0, 128.7,129.2, 129.4, 138.3, 144.6, 162.5, 164.8, 166.5, (14 C of Ar), 168.9 (Ester C=O), 170.8 (Ester C=O), 201.8 (Ketone C=O). Anal. Calcd for $C_{26}H_{24}O_7$: C, 69.63; H, 5.39. Found: C, 69.51; H, 5.17.

spiro[1-(3-Hydroxy-6-methyl-8-p-tolyl-7,7,8,9a-tetrahydro-dibenzofuran-2-yl)-ethanone(2,2-Dimethyl[1,3] Dioxane-4,6-Dione)] **(4b)**

White crystalline; yield: 86% (0.40 g), mp = 152–154˚C. IR (KBr) (ν_{max}, cm^{-1}): 3456 (OH), 1770, 1737, 1641 (3C=O); MS (EL, 70Ev): *m/z* (%): 462 (M^+, 3), 376 (15), 216 (100), 173 (37), 115 (58), 43 (98); ^1H NMR (400 MHz, $CDCl_3$): δ_H 0.65, 1.61 (2s, 6H, 2Me), 1.90, 2.32 (2s, 6H, 2Me), 2.50 (s, 3H, 1Me, 4-Methyl benzaldehyde), 2.61 (br dd, 1H, H-7'), 2.88 (br dd, 1H, H-7″), 3.93 (dd, 1H, *J*=10.8 Hz, *J*=6.4 Hz, H-8'), 4.82 (s, 1H, H-9'a), 6.51 (s, 1H, H_{Ar}), 7.14 (d, 2H, *J*=8 Hz, H_{Ar}), 7.21 (d, 2H, *J*=8 Hz, H_{Ar}), 7.43 (s, 1H, H_{Ar}), 13.06 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 14.9 (CH_3), 21.0 (CH_3), 26.2 (CH_3), 28.9 (CH_3), 29.4 (CH_3), 35.3 (CH_2), 46.8 (CH), 49.9 (CH), 56.3 (C), 96.2 (C), 99.4, 105.9, 109.0, 114.5, 126.0, 129.2, 129.5, 129.7, 135.2, 138.5, 149.8, 155.5, 158.1, 162.9 (14 C of Ar), 166.4 (Ester C=O), 169.6 (Ester

C=O), 202.1 (Ketone C=O). Anal. Calcd for $C_{27}H_{26}O_7$: C, 70.11; H, 5.66. Found: C, 70.83; H, 5.23.

spiro[1-[8-(3-Bromo-phenyl)-3-Hydroxy-6-methyl-7,7,8,9a-tetrahydro-dibenzofuran-2-yl])-ethanone(2,2-Dimethyl[1,3] Dioxane-4,6-Dione)] **(4c)**

White crystalline; yield: 70% (0.37 g), mp = 148–150˚C. IR (KBr) (ν_{max}, cm^{-1}): 3414 (OH), 1771, 1733, 1638 (3C=O); MS (EL, 70Ev): *m/z* (%): 528 (M^+, 9), 442 (10), 216 (97), 101 (24), 43 (100); ^1H NMR (400 MHz, $CDCl_3$): δ_H 0.76, 1.59 (2s, 6H, 2Me), 1.91, 2.51 (2s, 6H, 2Me), 2.64 (br dd, 1H, H-7'), 2.84 (br dd, 1H, H-7″), 3.93 (dd, 1H, *J*=10.8 Hz, *J*=6.8 Hz, H-8'), 4.80 (s, 1H, H-9'a), 6.52 (s, 1H, H_{Ar}), 7.21-7.50 (m, 4H, H_{Ar}), 7.45 (s, 1H, H_{Ar}), 13.06 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 14.9 (CH_3), 26.2 (CH_3), 29.1 (CH_3), 29.3 (CH_3), 35.3 (CH_2), 46.7 (CH), 50.1 (CH), 56.1 (C), 99.5 (C), 106.0, 108.9, 114.5, 114.9, 123.2, 126.1, 128.3, 130.7, 131.9, 132.2, 132.2, 140.7, 144.6, 162.6, 164.5 (14 C of Ar), 166.5 (Ester C=O), 168.9 (Ester C=O), 201.8 (Ketone C=O). Anal. Calcd for $C_{26}H_{23}BrO_7$: C, 59.21; H, 4.39. Found: C, 59.03; H, 4.86.

spiro[1-[8-(4-Chloro-phenyl)-3-Hydroxy-6-methyl-7,7,8,9a-tetrahydro-dibenzofuran-2-yl])-ethanone(2,2-Dimethyl[1,3] Dioxane-4,6-Dione)] **(4d)**

White crystalline; yield: 78% (0.38 g), mp = 144–146˚C. IR (KBr) (ν_{max}, cm^{-1}): 3463 (OH), 1771, 1737, 1640 (3C=O); MS (EL, 70Ev): *m/z* (%): 482 (M^+, 12), 424 (26), 396 (100), 351 (61), 294 (53), 268 (26), 248 (85), 216 (98), 43 (83); ^1H NMR (400 MHz, $CDCl_3$): δ_H 0.75, 1.63 (2s, 6H, 2Me), 1.91, 2.51 (2s, 6H, 2Me), 2.63 (br dd, 1H, H-7'), 2.84 (br dd, 1H, H-7″), 3.95 (dd, 1H, *J*=10.8 Hz, *J*=6.8 Hz, H-8'), 4.80 (s, 1H, H-9'a), 6.52 (s, 1H, H_{Ar}), 7.28-7.35 (m, 4H, H_{Ar}), 7.44 (s, 1H, H_{Ar}), 13.06 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 14.9 (CH_3), 26.2 (CH_3), 29.3 (CH_3), 29.3 (CH_3), 35.3 (CH_2), 46.5 (CH), 50.0 (CH), 56.2 (C), 99.5 (C), 105.9, 108.9, 114.5, 115.0 126.1, 129.1, 129.3, 129.9, 130.8, 134.6, 136.8, 144.6, 162.8, 164.5

(14 C of Ar), 166.5 (Ester C=O), 169.1 (Ester C=O), 201.8 (Ketone C=O). Anal. Calcd for $C_{26}H_{23}ClO_7$: C, 64.66; H, 4.80. Found: C, 65.07; H, 4.21.

spiro[1-[8-(4-Hydroxy-phenyl)-3-Hydroxy-6-methyl-7,7,8,9a-tetrahydro-dibenzofuran-2-yl])-ethanone(2,2-Dimethyl[1,3] Dioxane-4,6-Dione)] **(4e)**

White crystalline; yield: 80% (0.37 g), mp = 161–163˚C. IR (KBr) (ν_{max}, cm^{-1}): 3430, 3434 (2OH), 3434 (OH), 1764, 1735, 1639 (3C=O); MS (EL, 70Ev): *m/z* (%): 464 (M^+, 3), 349 (52), 248 (20), 216 (100), 146 (28), 77 (21), 43 (87); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.74, 1.63 (2s, 6H, 2Me), 1.90, 2.51 (2s, 6H, 2Me), 2.61 (br dd, 1H, H-7'), 2.84 (br dd, 1H, H-7″), 3.92 (dd, 1H, *J*=10.8 Hz, *J*=6.8 Hz, H-8'), 4.81 (s, 1H, H-9'a), 5.02 (s, 1H, OH), 6.51 (s, 1H, H_{Ar}), 6.80 (d, 2H, *J*=8,4 Hz, H_{Ar}), 7.21 (d, 2H, *J*=8.4 Hz, H_{Ar}), 7.43 (s, 1H, H_{Ar}), 13.06 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 14.9 (CH_3), 26.2 (CH_3), 29.1 (CH_3), 29.3 (CH_3), 35.5 (CH_2), 46.4 (CH), 49.9 (CH), 56.2 (C), 99.4 (C), 105.9, 109.1, 114.5, 115.3 115.8, 126.0, 130.4, 130.7, 142.3, 144.7, 156.3, 157.6, 158.4, 164.6 (14 C of Ar), 166.4 (Ester C=O), 171.0 (Ester C=O), 202.4 (Ketone C=O). Anal. Calcd for $C_{26}H_{24}O_8$: C, 67.23; H, 5.20. Found: C, 66.57; H, 5.02.

spiro[1-[8-(3,4-Dimethoxy-phenyl)-3-Hydroxy-6-methyl-7,7,8,9a-tetrahydro-dibenzofuran-2-yl])-ethanone(2,2-Dimethyl[1,3] Dioxane-4,6-Dione)] **(4f)**

White crystalline; yield: 77% (0.39 g), mp = 143–145˚C. IR (KBr) (ν_{max}, cm^{-1}): 3414 (OH), 1768, 1733, 1636 (3C=O); MS (EL, 70Ev): *m/z* (%): 508 (M^+, 2), 422 (8), 216 (100), 173 (15), 91 (16), 43 (73); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.74, 1.63 (2s, 6H, 2Me), 1.91, 2.51 (2s, 6H, 2Me), 2.63 (br dd, 1H, H-7'), 2.87 (br dd, 1H, H-7″), 3.87 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.92 (dd, 1H, *J*=11.2 Hz, *J*=6.8 Hz, H-8'), 4.81 (s, 1H, H-9'a), 6.51 (s, 1H, H_{Ar}), 6.82 (d, 1H, *J* = 8.4 Hz, ArH), 6.90 (d, 1H, *J* = 8.4 Hz, ArH), 7.44 (s, 1H, H_{Ar}), 13.06 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 14.9 (CH_3), 26.2 (CH_3), 29.2 (CH_3), 29.3 (CH_3), 35.5 (CH_2), 46.8 (CH), 50.1 (CH), 55.9 (OCH_3), 56.0 (OCH_3), 56.5 (C), 99.5 (C), 105.9, 109.1, 111.3, 112.4, 114.5, 115.2, 121.6, 126.0, 130.6, 144.7, 149.2, 161.7, 163.0, 164.6 (14 C of Ar), 166.5 (Ester C=O),

169.4 (Ester C=O), 201.9 (Ketone C=O). Anal. Calcd for $C_{28}H_{28}O_9$: C, 66.13; H, 5.54. Found: C, 65.63; H, 5.19.

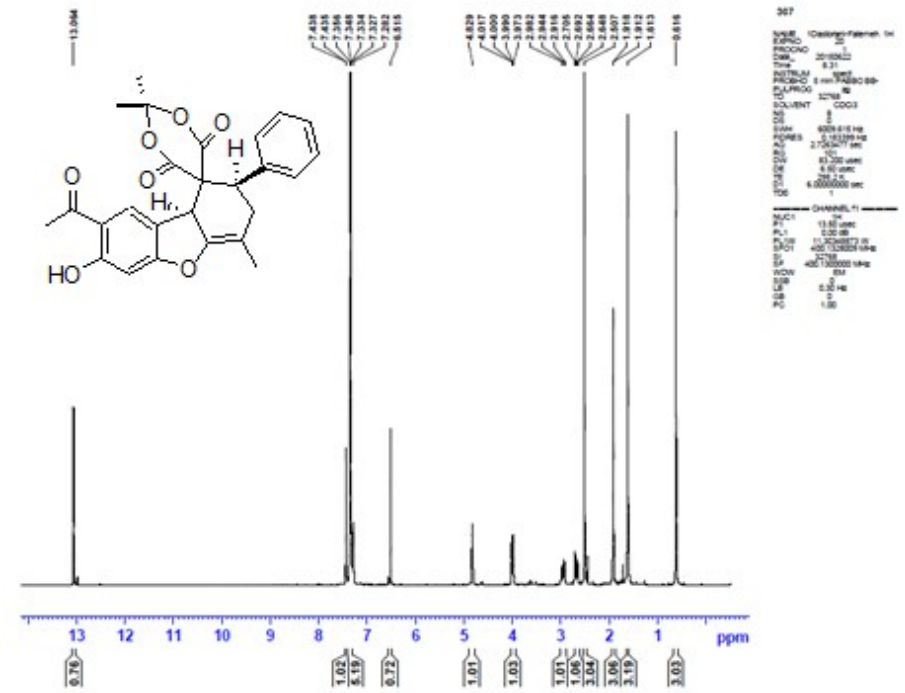

Figure 1. [1]H NMR spectra of compound **4a**

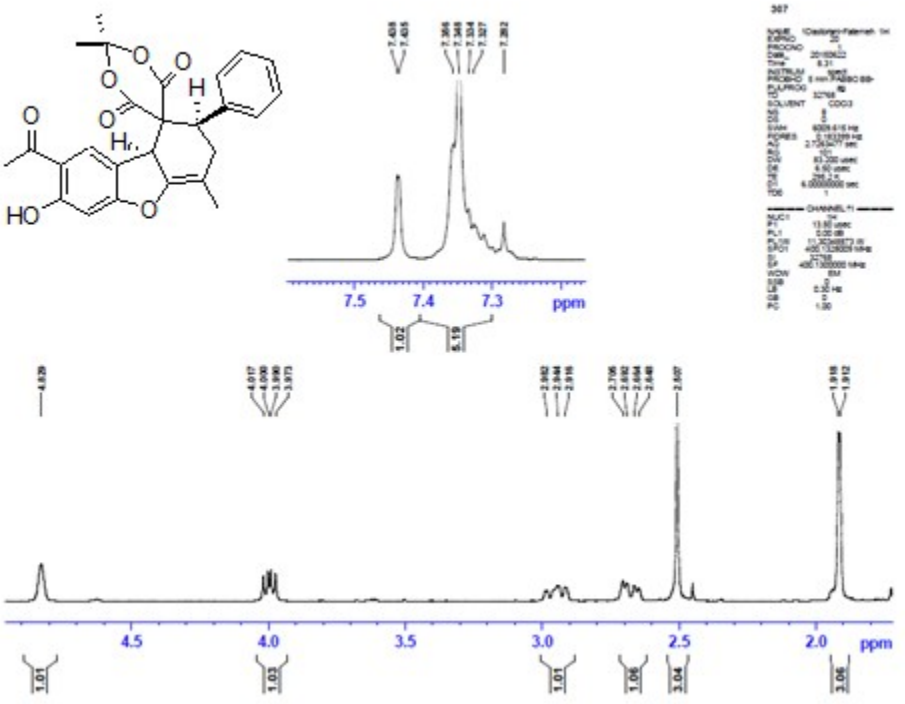

Figure 2. [1]H NMR spectra of compound **4a**

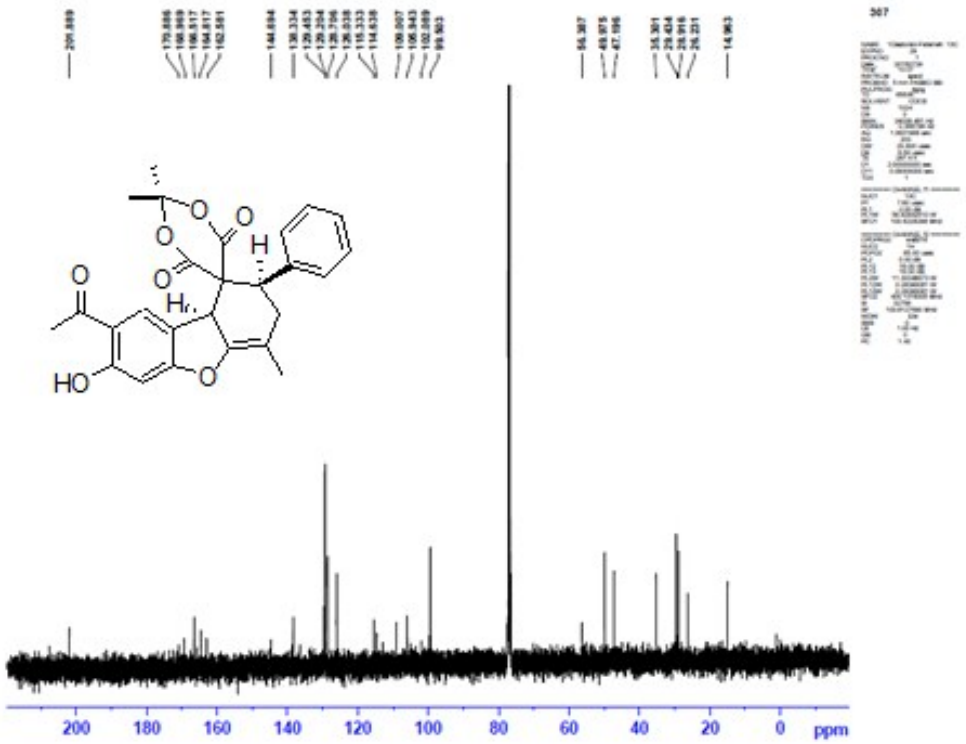

Figure 3. [13]C NMR spectra of compound **4a**

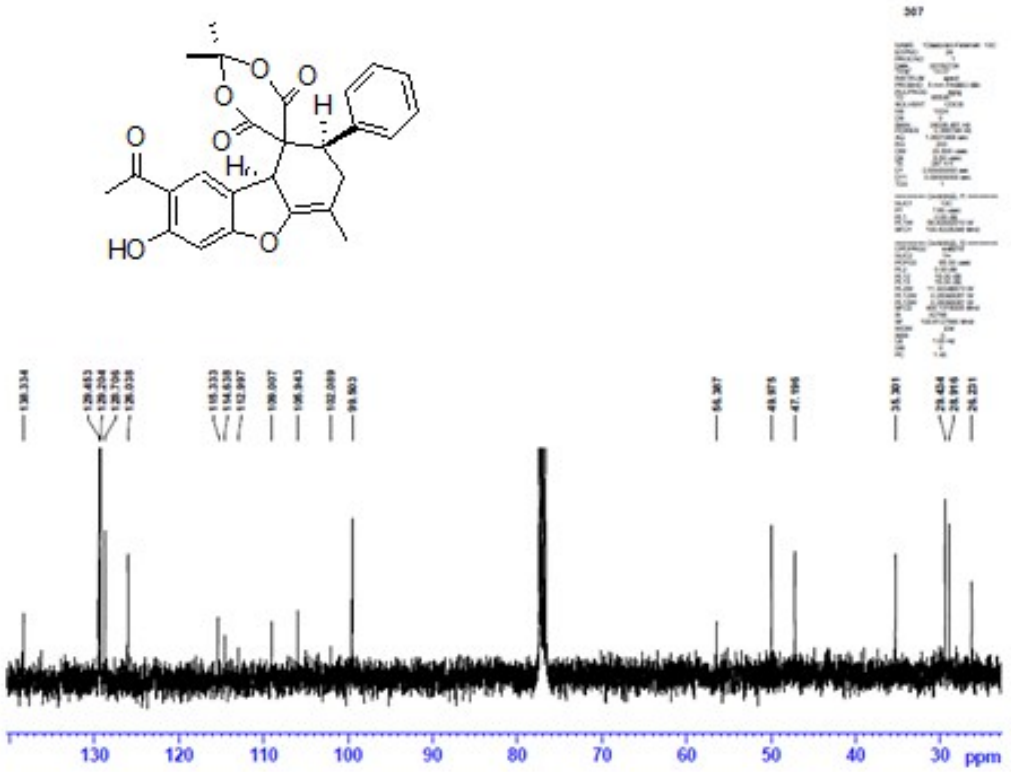

Figure 4. ^{13}C NMR spectra of compound **4a**

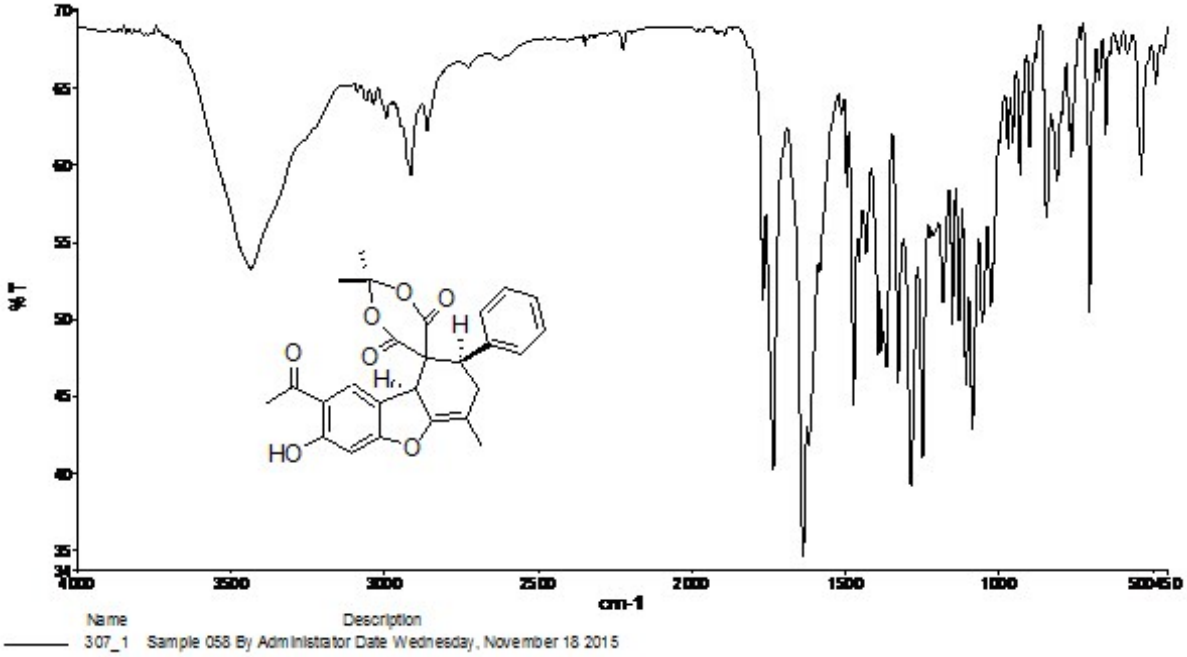

Figure 5. IR spectra of compound **4a**

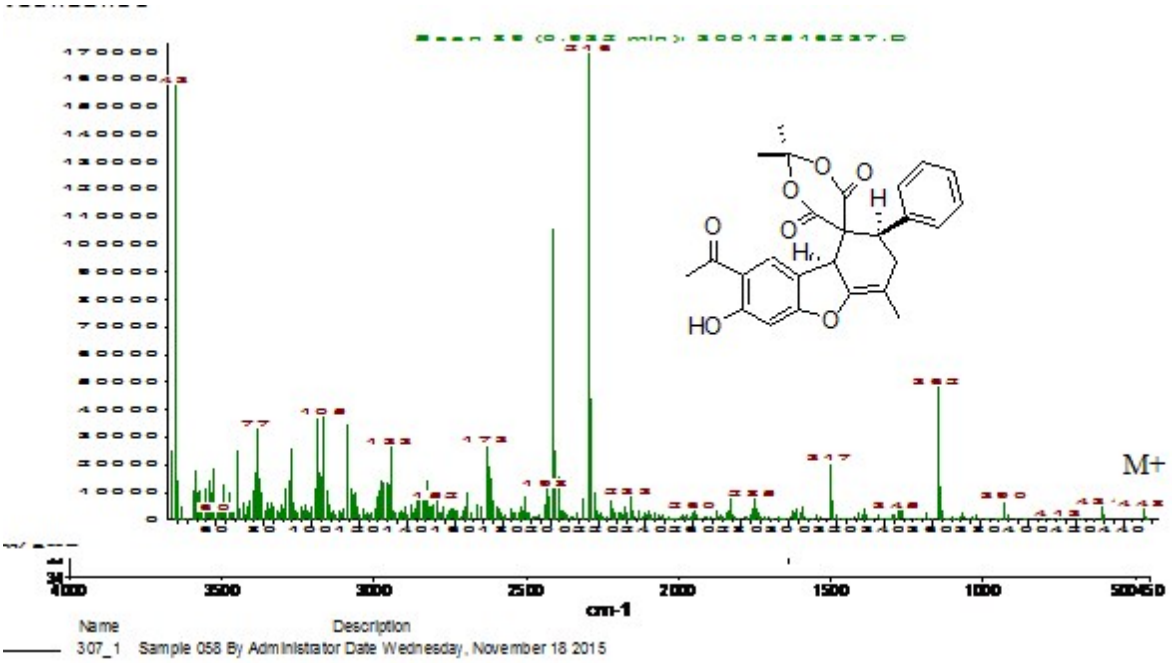

Figure 6. Mass spectra of compound **4a**

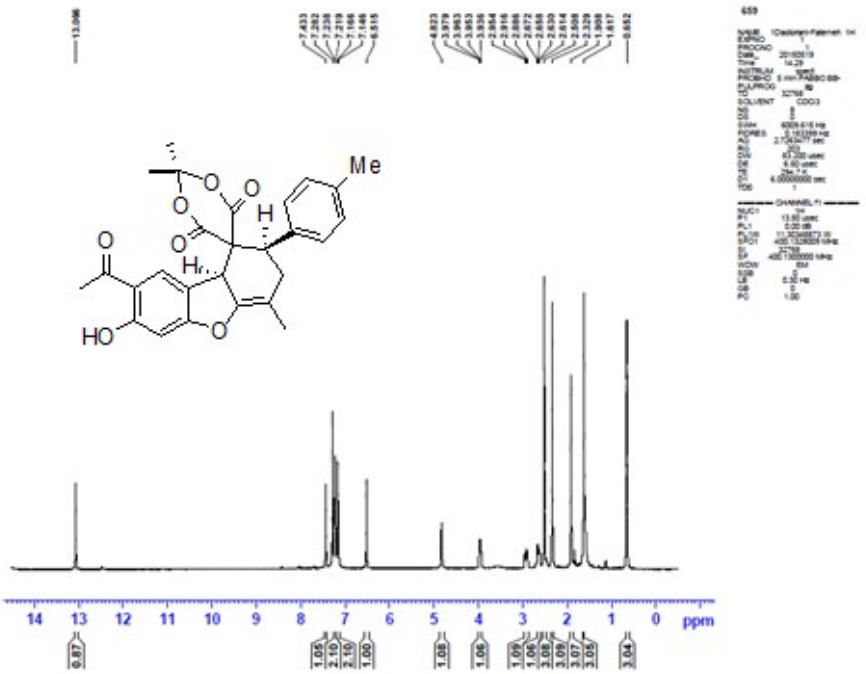

Figure 7. [1]H NMR spectra of compound **4b**

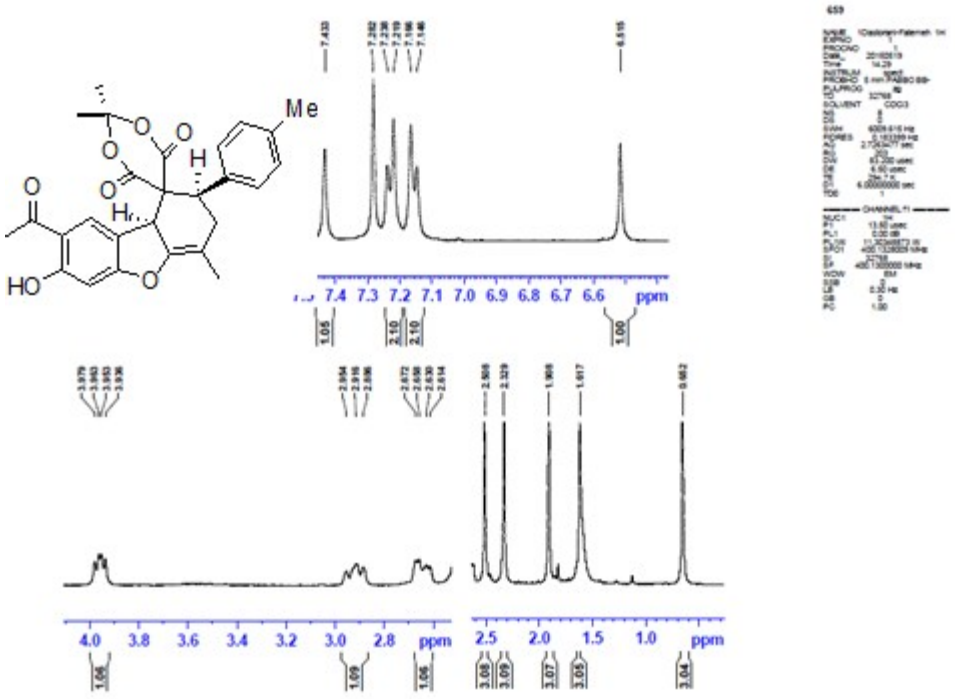

Figure 8. [1]H NMR spectra of compound **4b**

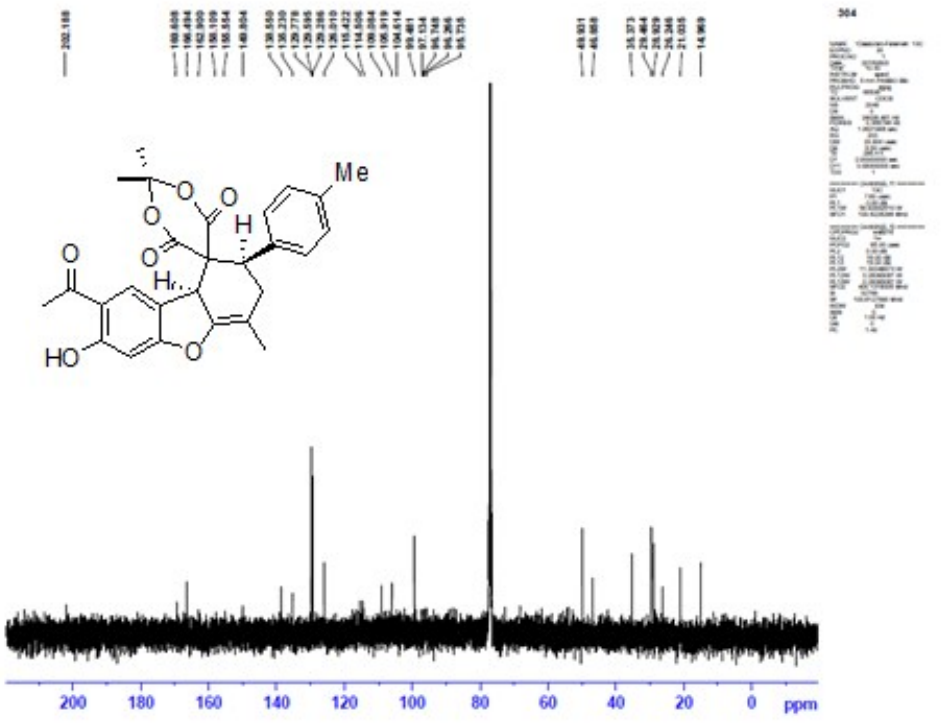

Figure 9. [13]C NMR spectra of compound **4b**

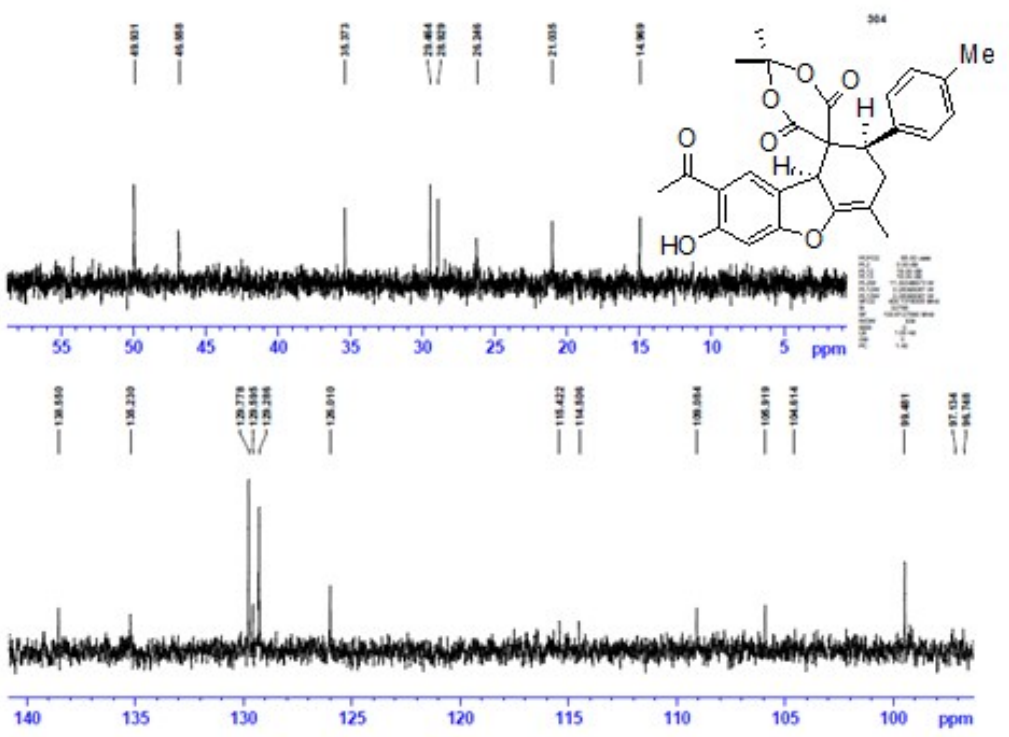

Figure 10. ^{13}C NMR spectra of compound **4b**

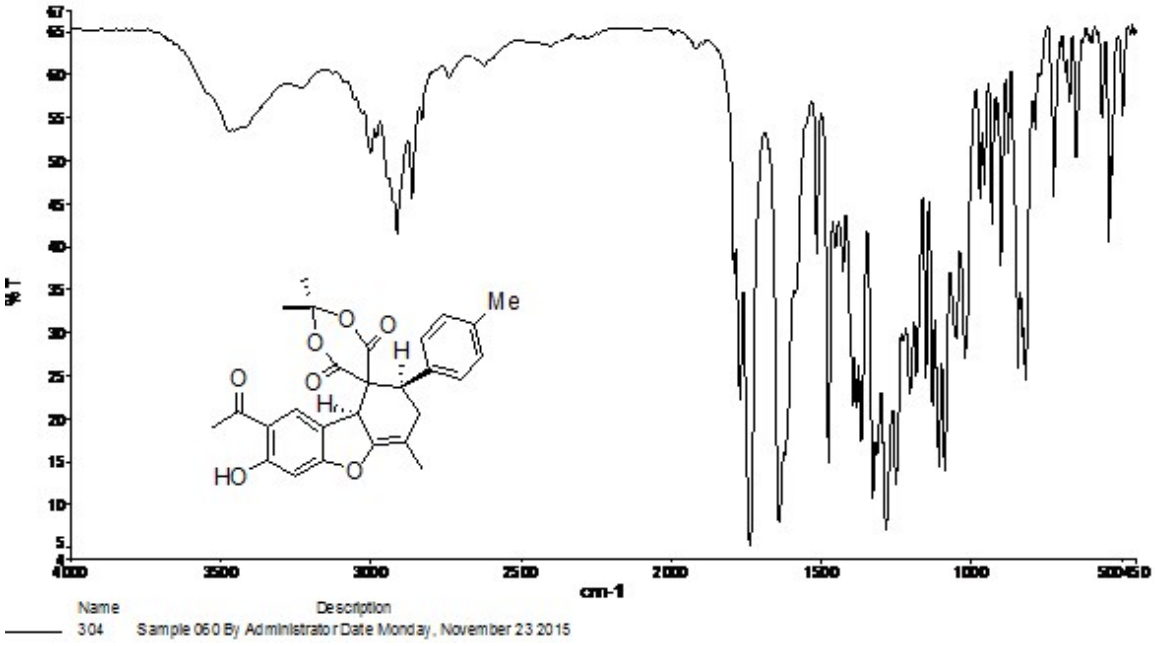

Figure 11. IR spectra of compound **4b**

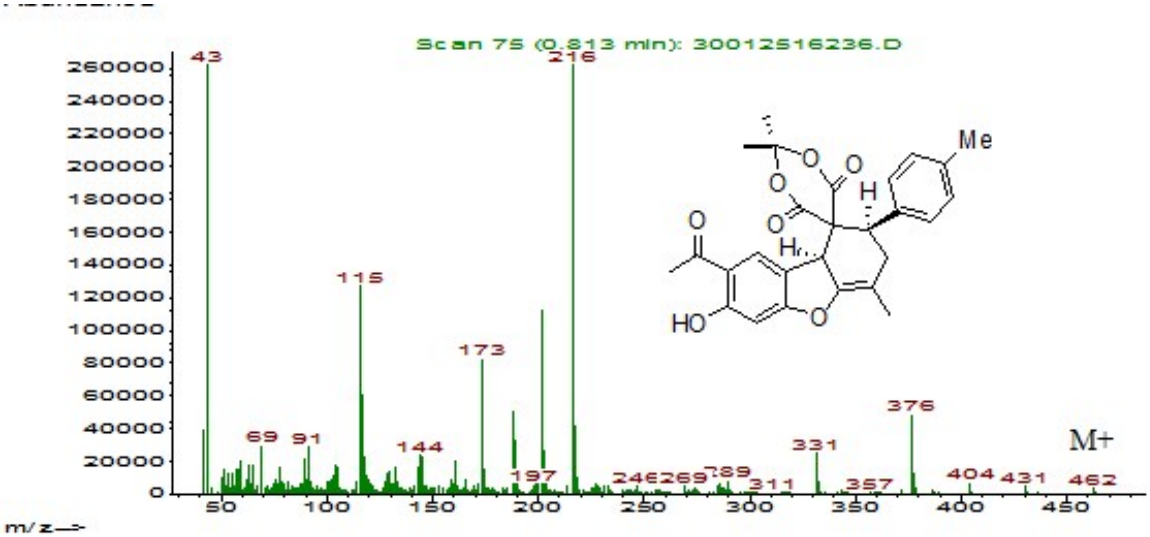

Figure 12. Mass spectra of compound **4b**

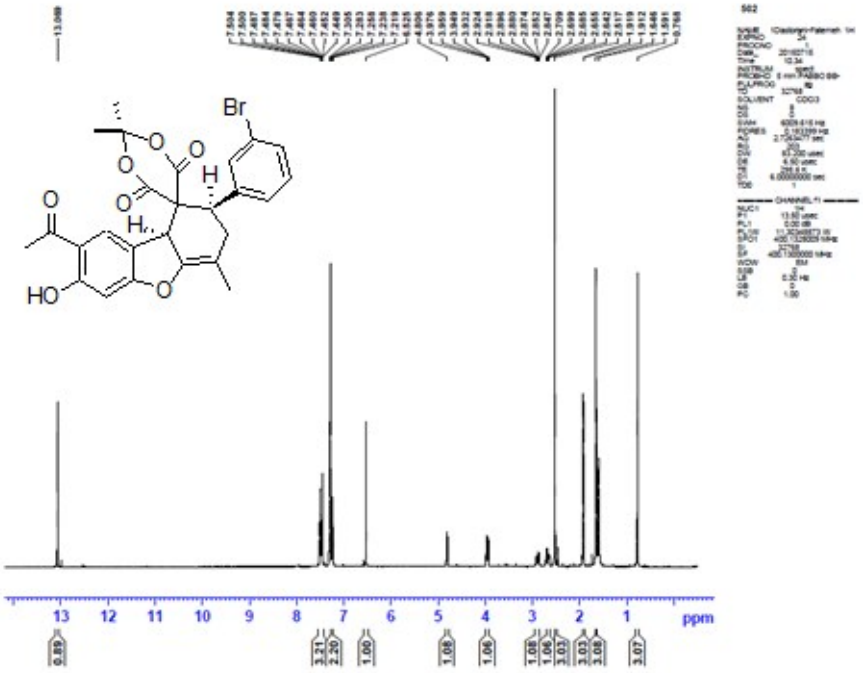

Figure 13. [1]H NMR spectra of compound **4c**

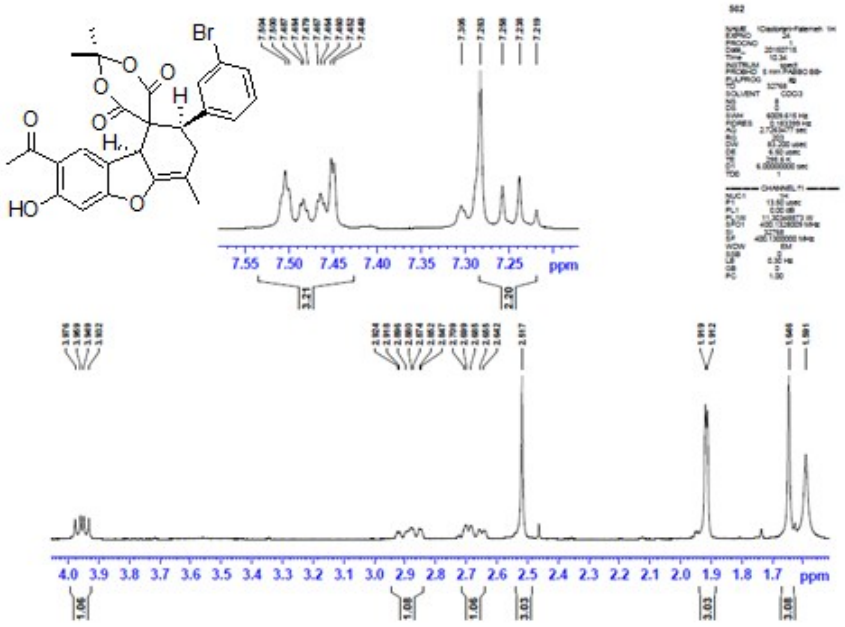

Figure 14. [1]H NMR spectra of compound **4c**

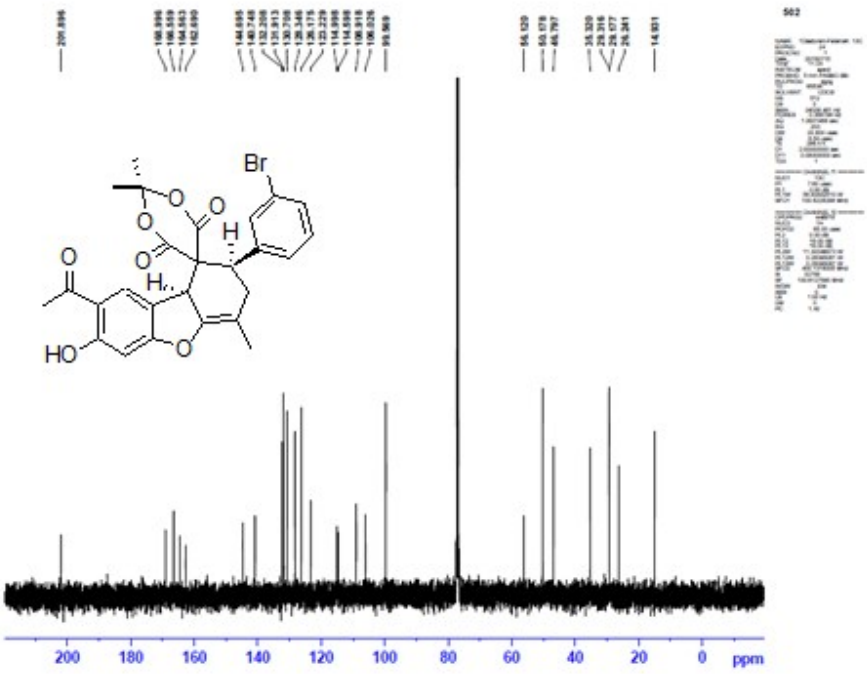

Figure 15. ^{13}C NMR spectra of compound **4c**

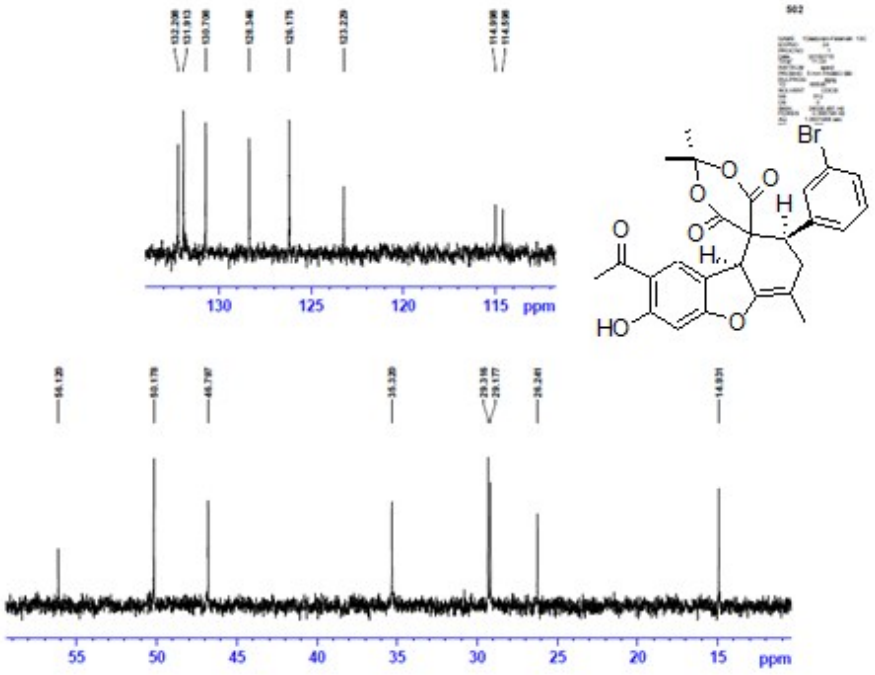

Figure 16. ^{13}C NMR spectra of compound **4c**

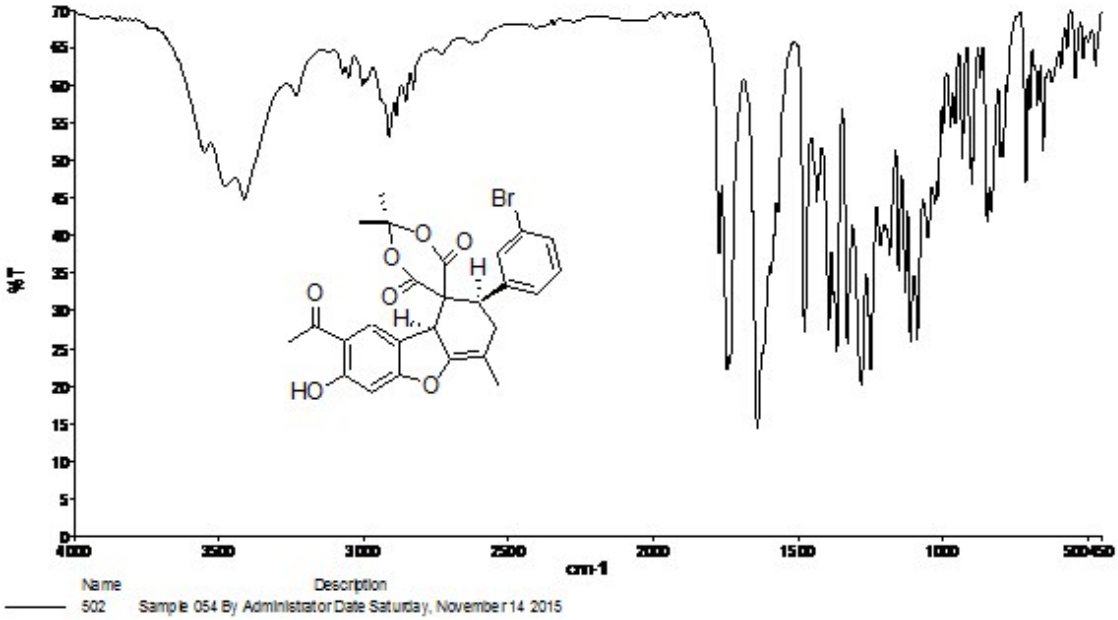

Figure 17. IR spectra of compound **4c**

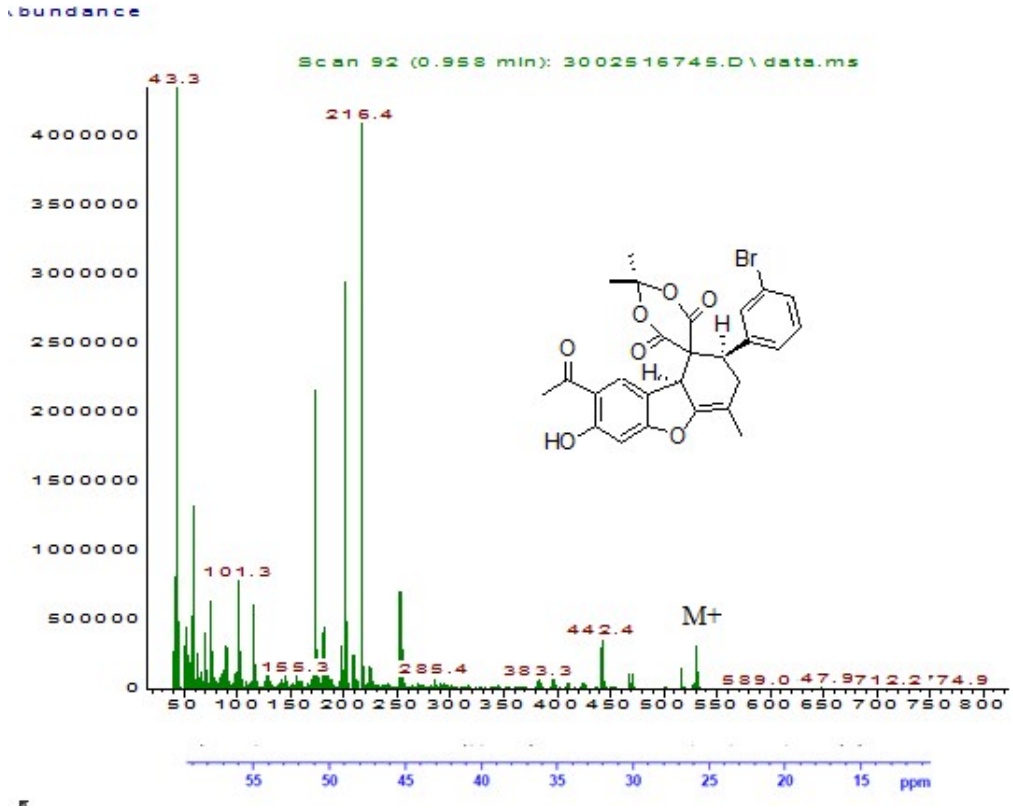

Figure 18. Mass spectra of compound **4c**

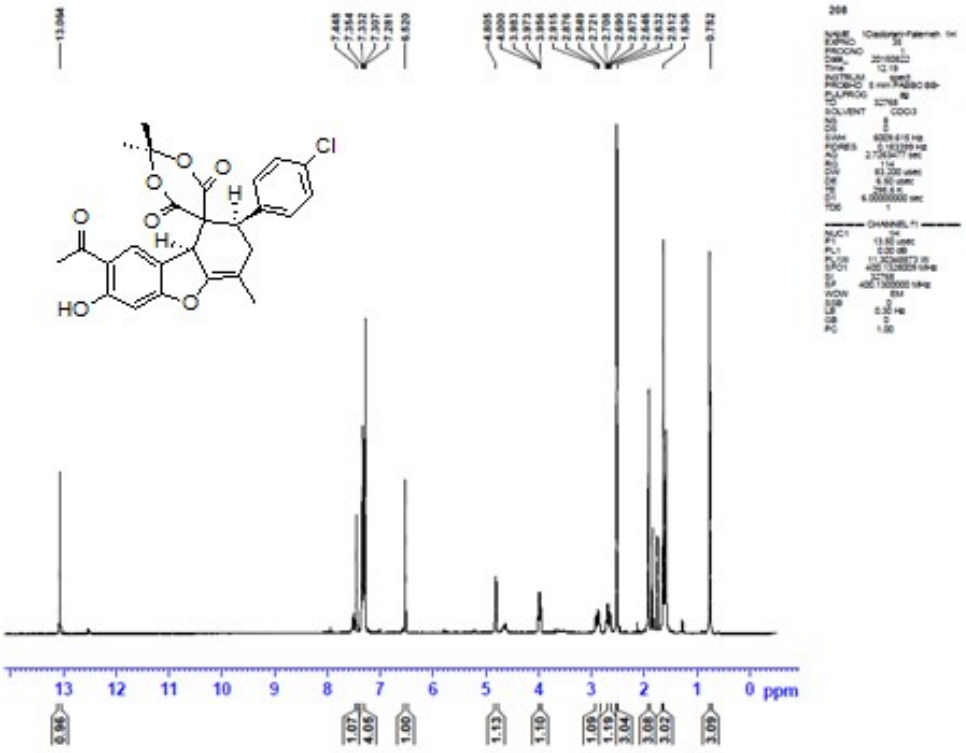

Figure 19. [1]H NMR spectra of compound **4d**

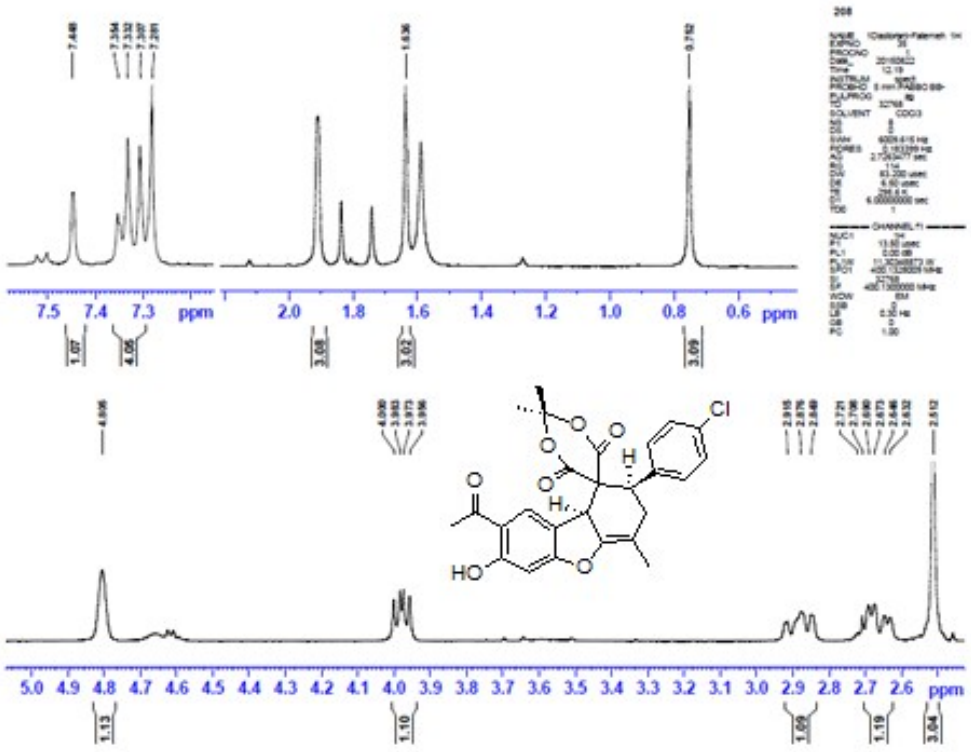

Figure 20. [1]H NMR spectra of compound **4d**

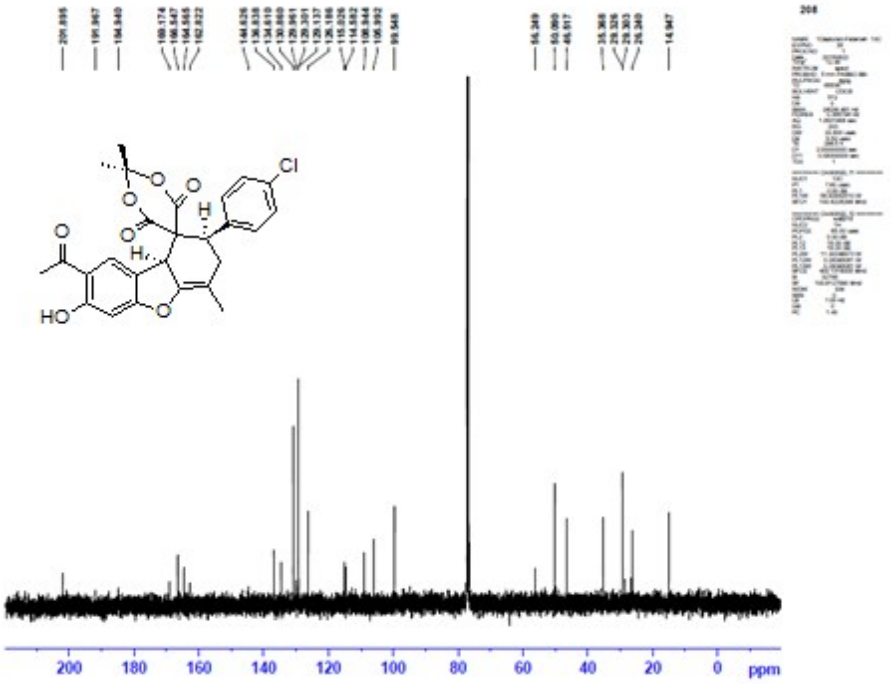

Figure 21. ^{13}C NMR spectra of compound **4d**

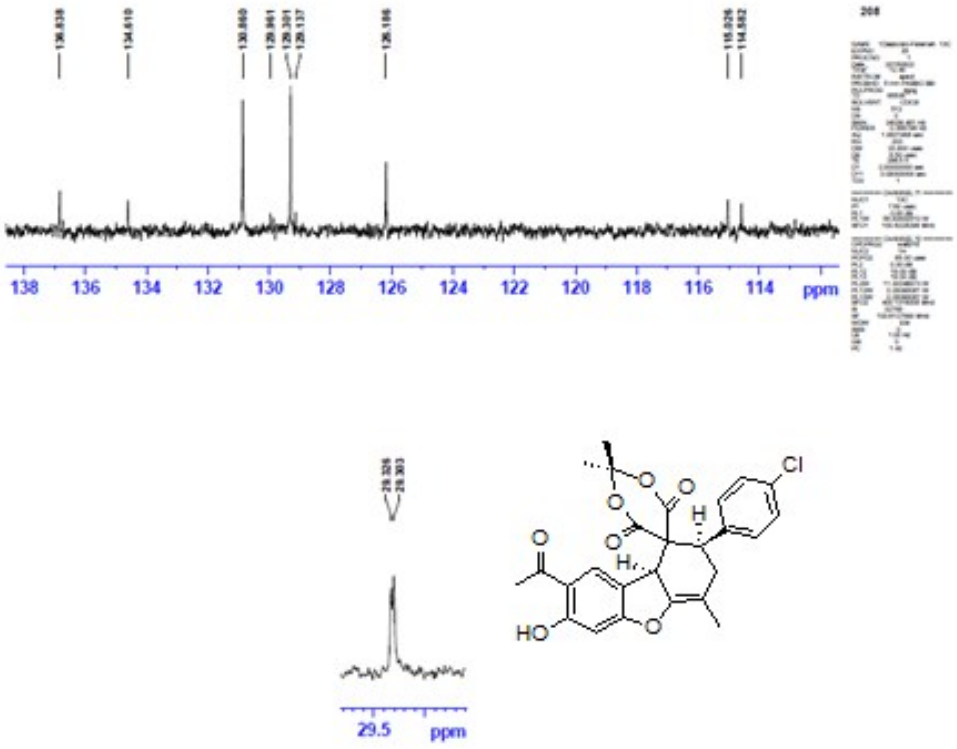

Figure 22. ^{13}C NMR spectra of compound **4d**

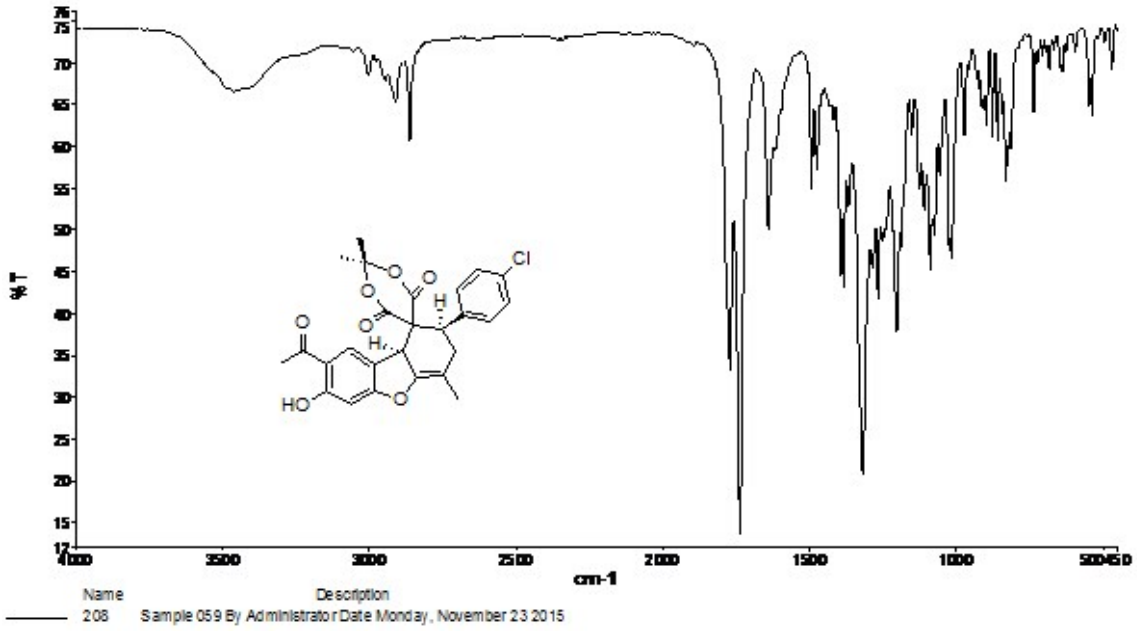

Figure 23. IR spectra of compound **4d**

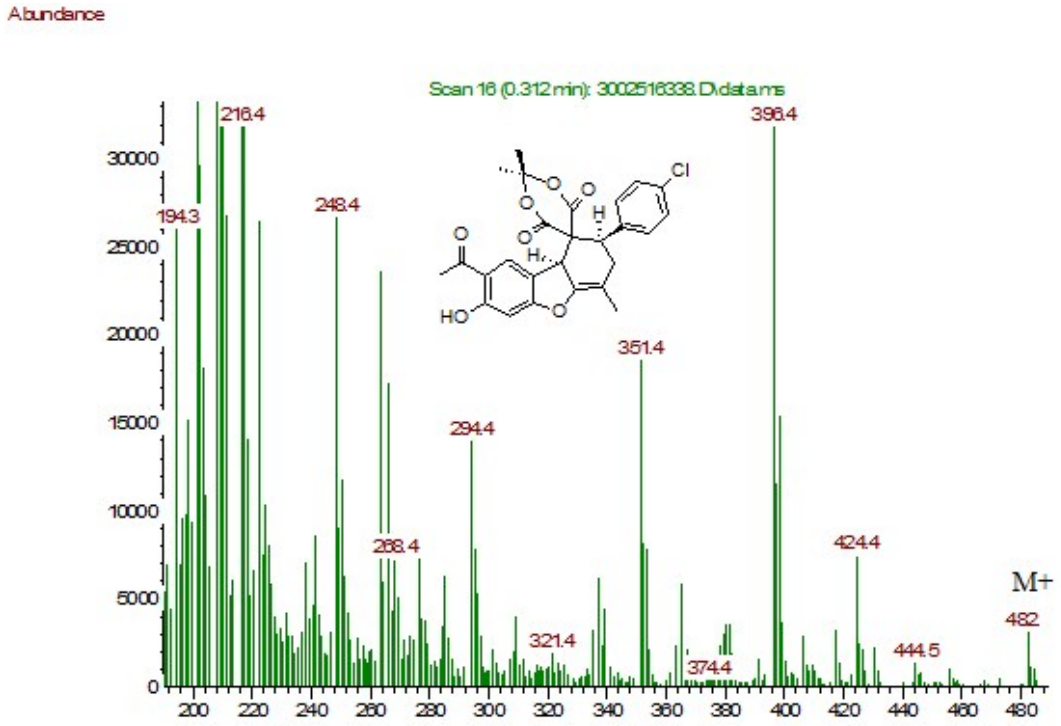

Figure 24. Mass spectra of compound **4d**

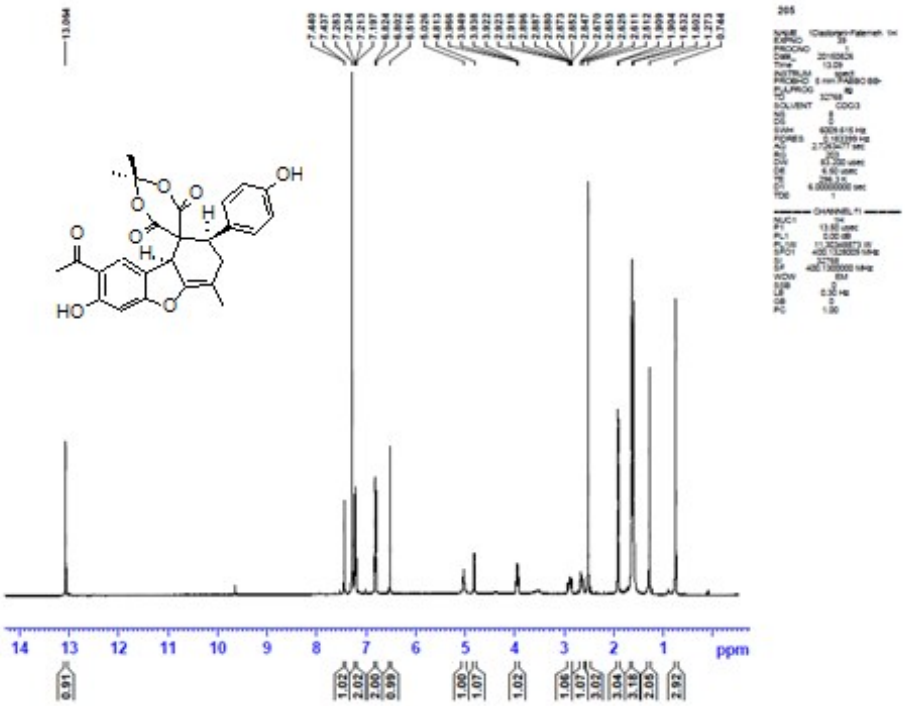

Figure 25. [1]H NMR spectra of compound **4e**

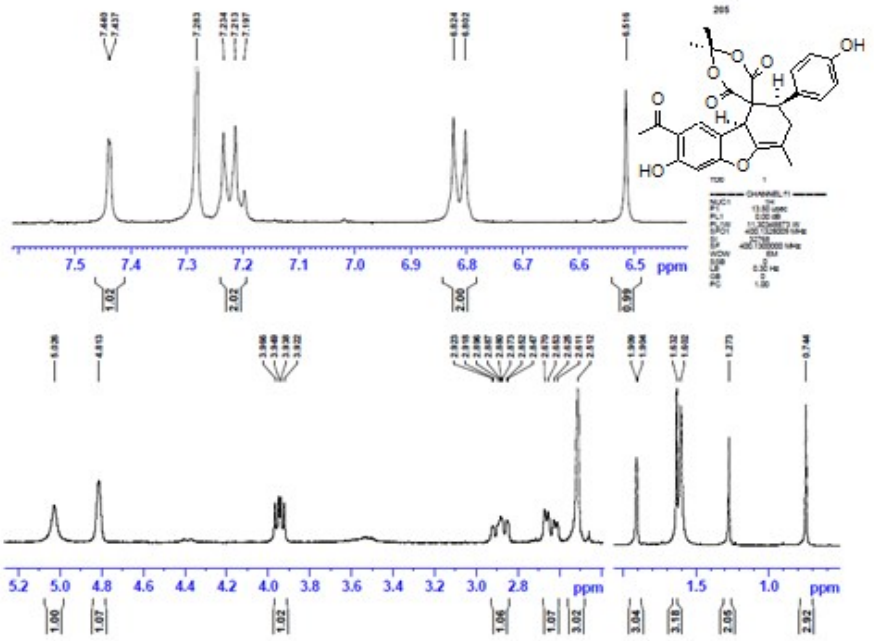

Figure 26. [1]H NMR spectra of compound **4e**

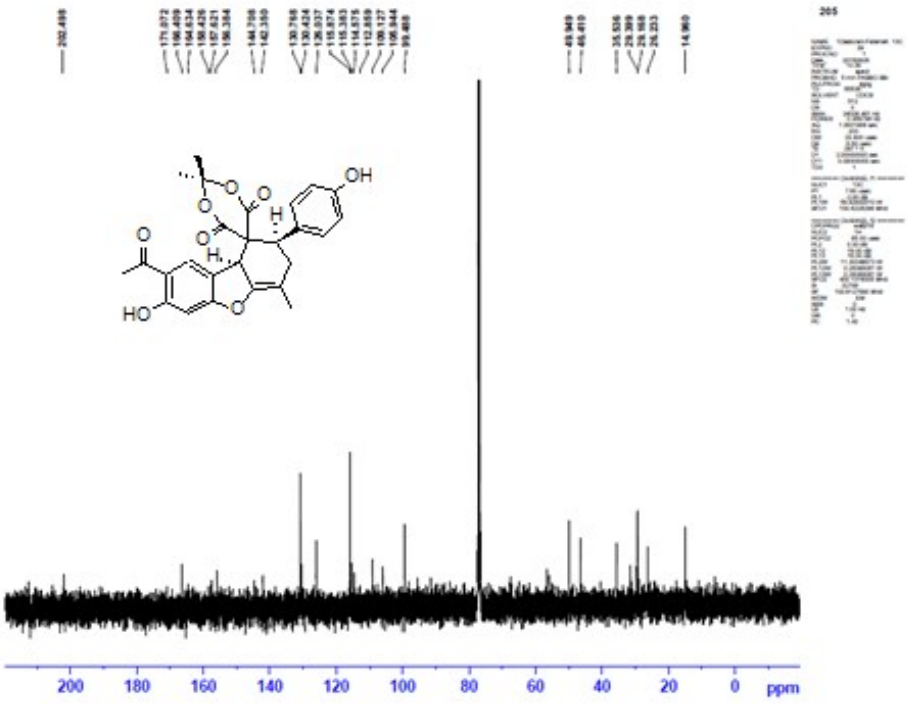

Figure 27. ^{13}C NMR spectra of compound **4e**

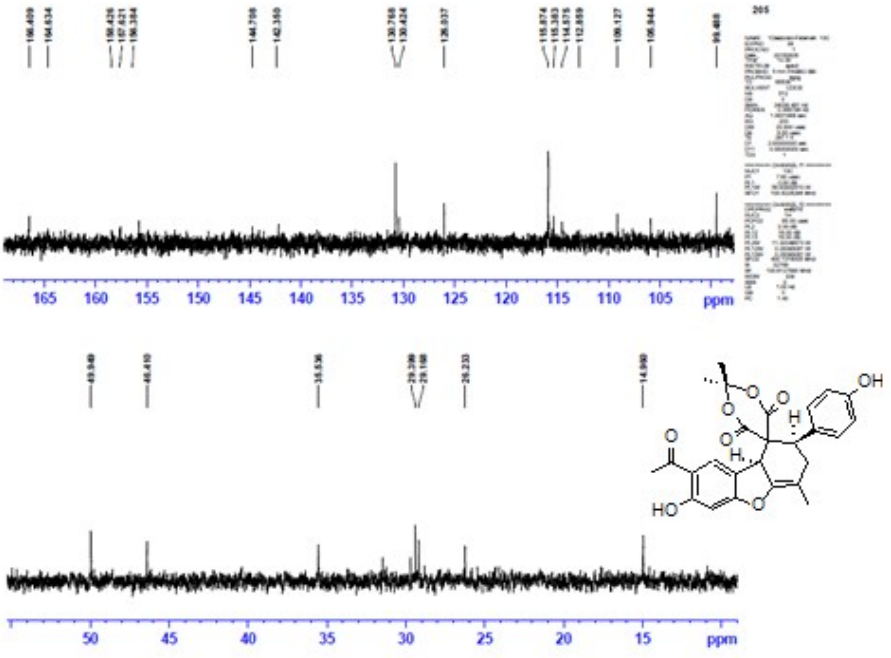

Figure 28. ^{13}C NMR spectra of compound **4e**

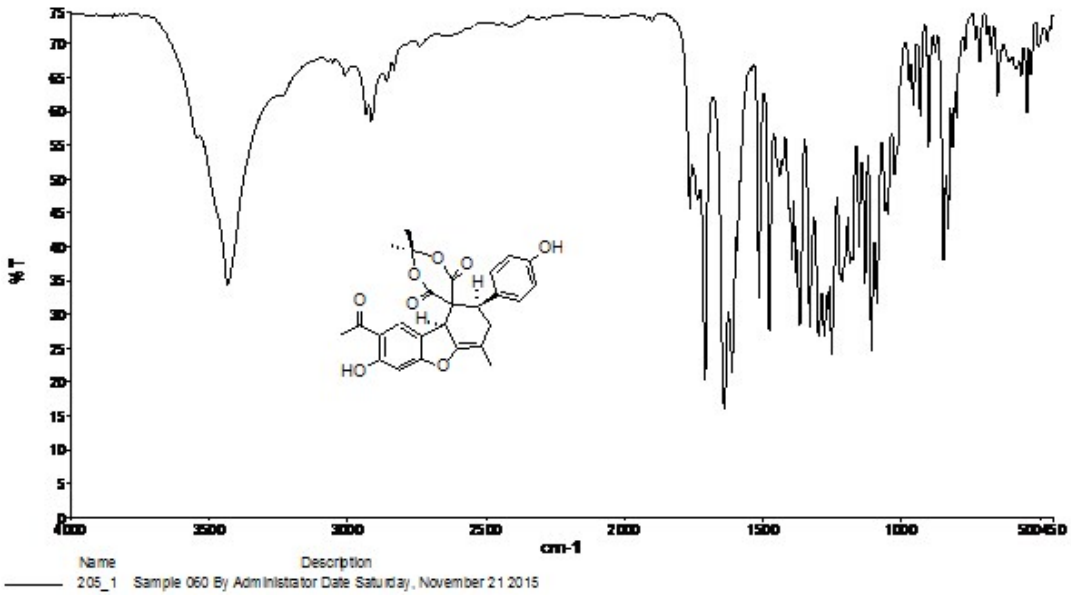

Figure 29. IR spectra of compound **4e**

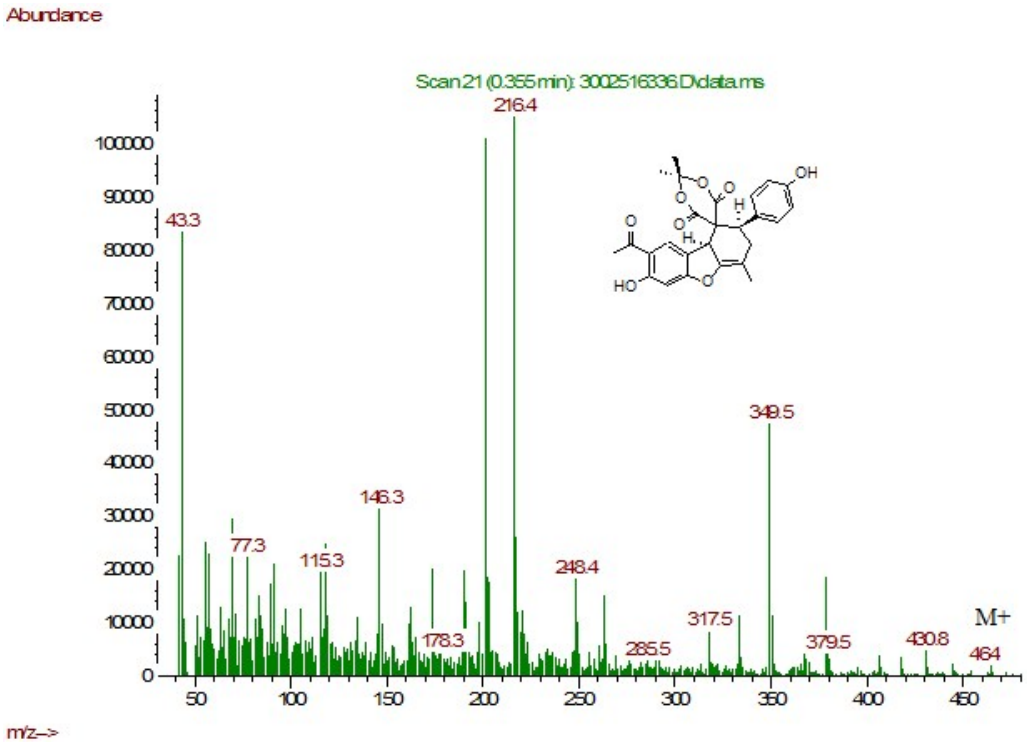

Figure 30. Mass spectra of compound **4e**

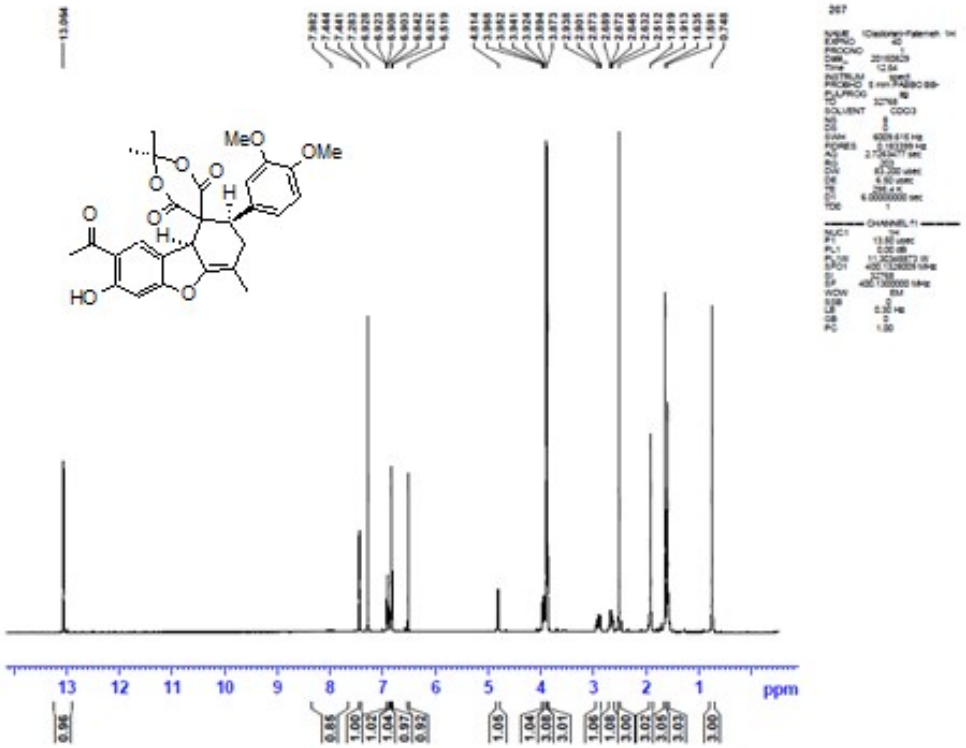

Figure 31. [1]H NMR spectra of compound **4f**

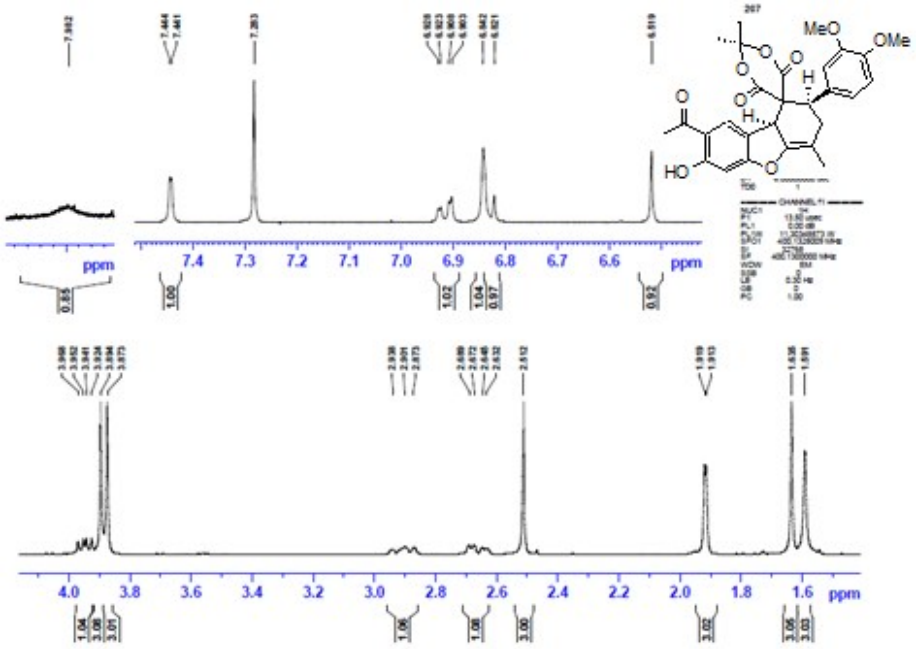

Figure 32. [1]H NMR spectra of compound **4f**

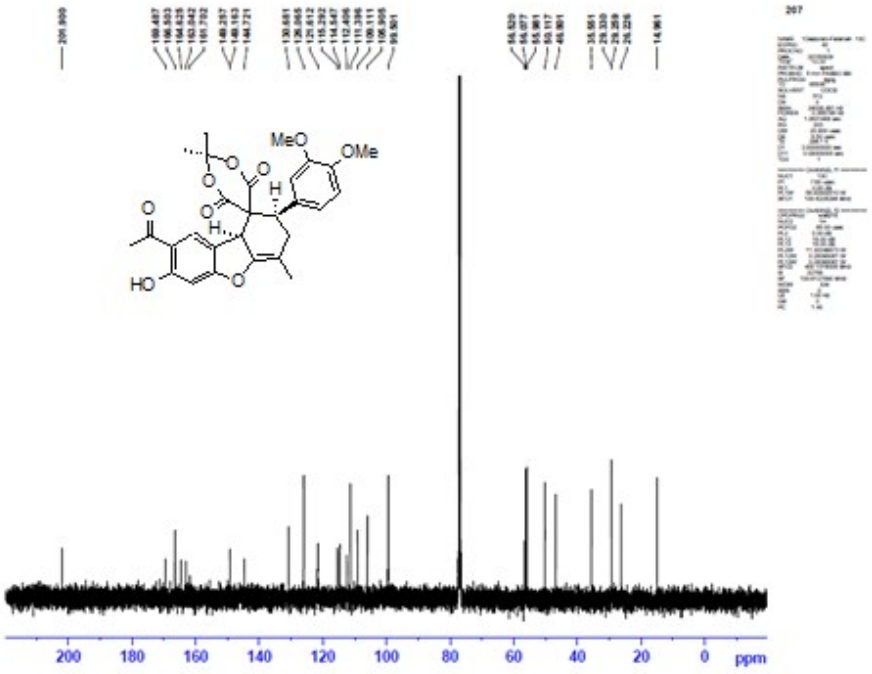

Figure 33. ^{13}C NMR spectra of compound **4f**

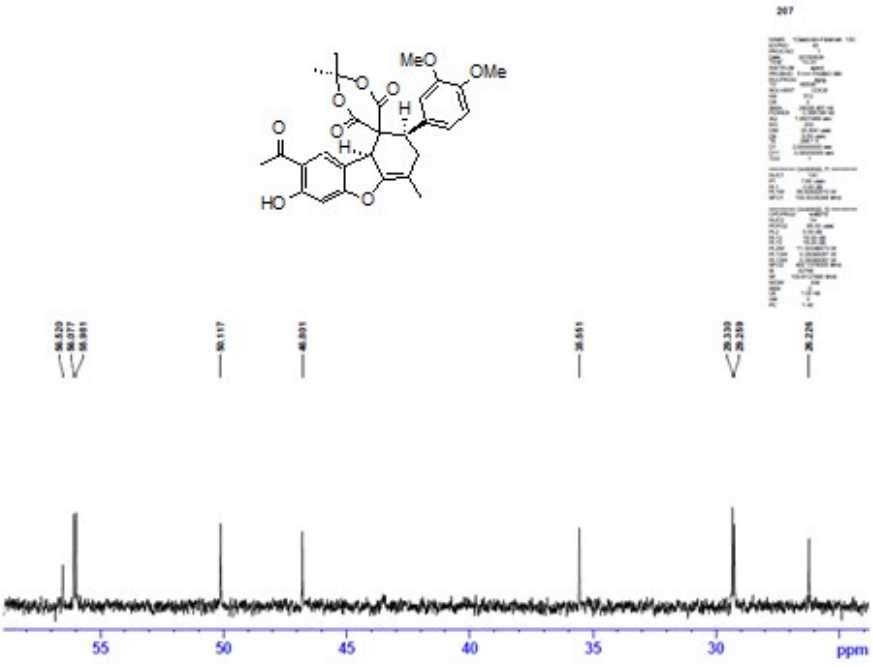

Figure 34. ^{13}C NMR spectra of compound **4f**

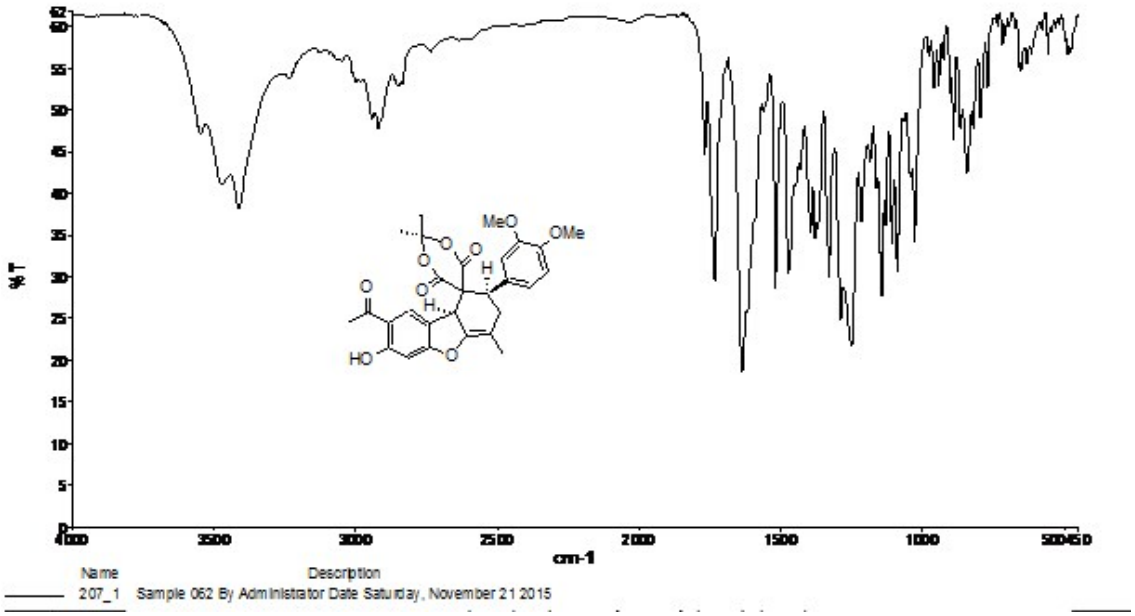

Figure 35. IR spectra of compound **4f**

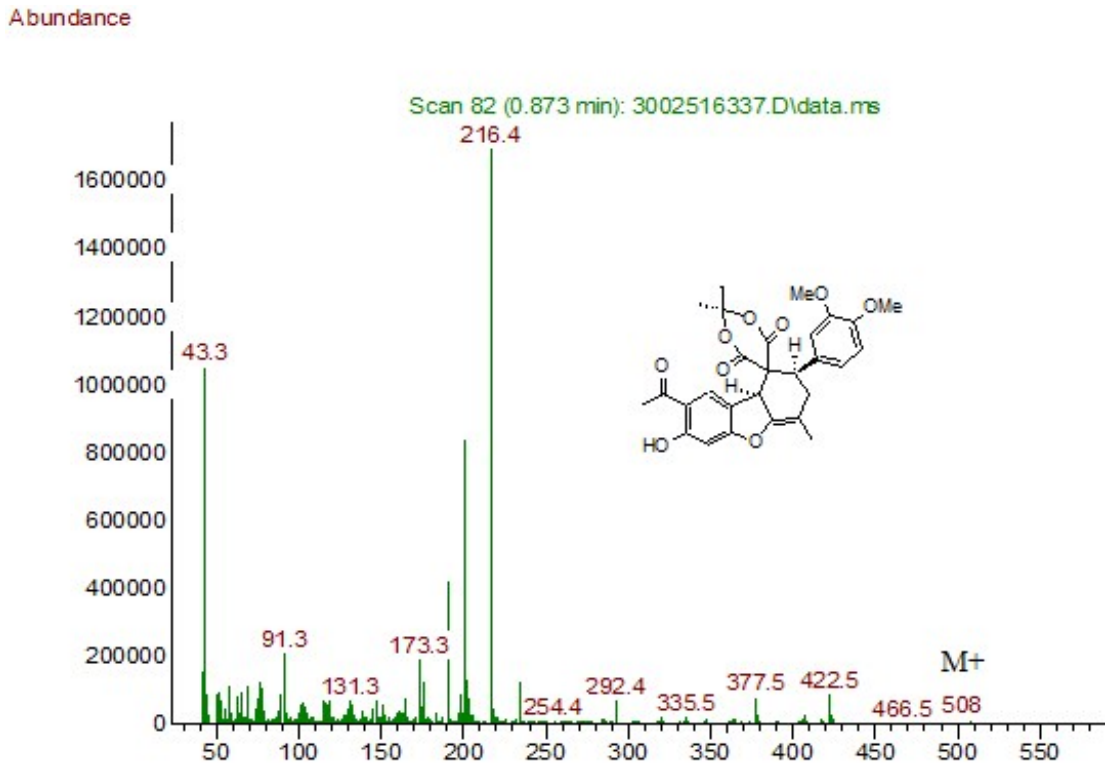

Figure 36. Mass spectra of compound **4f**