Supporting Information

Zanthosimuline and Related Pyranoquinolines as Antifungal Agents for Post-Harvest Fruits Disease Control

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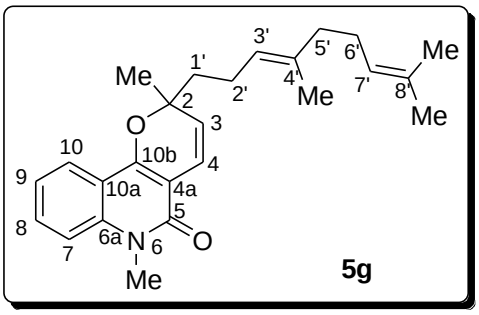
GENERAL INFORMATION

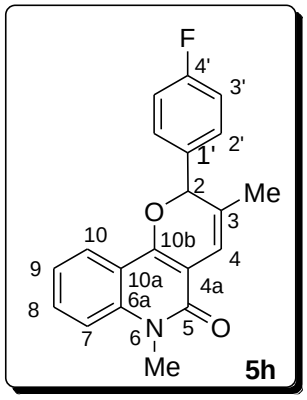
All reagents were purchased from commercial suppliers and used without further purification. Solvents were analytical grade or were purified by standard procedures prior to use. Yields were calculated for material judged homogeneous by thin layer chromatography (TLC) and nuclear magnetic resonance (^{1}H NMR). All reactions were monitored by thin layer chromatography performed on silica gel 60 F_{254} pre-coated aluminum sheets, visualized by a 254 nm UV lamp, and stained with an ethanolic solution of 4-anisaldehyde. Column flash chromatography was performed using silica gel 60 (230 – 400 mesh). Melting points (m.p.) were taken on an electrothermal melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were acquired at 300 MHz for ^{1}H and 75 MHz for ^{13}C using $CDCl_3$ as solvent. Chemical shifts for proton nuclear magnetic resonance spectra are reported in parts per million relative to the signal of tetramethylsilane (TMS) at 0 ppm (internal standard) and coupling constants (*J*) are reported in hertz (Hz). Chemical shifts for carbon nuclear magnetic resonance (^{13}C NMR) spectra are reported in parts per million relative to the center line of the $CDCl_3$ triplet at 77.0 ppm. The following abbreviations are used to indicate the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, quint = quintet, h = sextet, br = broad signal. IR spectra were obtained using an FT-IR spectrometer and only partial spectral data are listed. High-resolution mass spectra (HRMS) were recorded with a Q-TOF mass spectrometer equipped with an ESI source (detection of the ions was performed in electrospray ionization, positive ion mode). The structure of the products were determined by a combination of spectroscopic methods such as IR, 1D and 2D NMR (including NOE, DEPT, COSY, HSQC and HMBC experiments) and HRMS. NMR signals assignments were based on 2D NMR experiments performed.

(*E*)-2-(4,8-Dimethylnona-3,7-dienyl)-2,6-dimethyl-2*H*-pyrano[3,2-c]quinolin-5(6*H*)-one (5g)



Colorless to pale yellow liquid. **IR** (film) (cm^{-1}): 2966, 2922, 1643, 1633, 1362. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.96 (dd, *J* = 7.9; 1.3 Hz, 1H, 10-H), 7.54 (ddd, *J* = 8.6; 7.2; 1.4 Hz, 1H, 8-H), 7.31 (bd, *J* = 8.6 Hz, 1H, 7-H), 7.22 (ddd, *J* = 7.9; 7.0; 0.8 Hz, 1H, 9-H), 6.79 (d, *J* = 10.1 Hz, 1H, 4-H), 5.49 (d, *J* = 10.0 Hz, 1H, 3-H), 5.11 (bt, *J* = 7.1 Hz, 1H, 3'-H), 5.06 (bt, *J* = 6.9 Hz, 1H, 7'-H), 3.69 (s, 3H, N-CH_3), 2.21-2.09 (m, 2H, 2'-H), 2.09-1.97 (m, 2H, 6'-H), 1.97-1.87 (m, 2H, 5'-H), 1.87-1.68 (m, 2H, 1'-H), 1.66 (s, 3H, 8'-CH_3*), 1.58 (s, 3H, 9'-H*), 1.55 (s, 3H, 4'-CH_3), 1.48 (s, 3H, 2'-CH_3). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 160.9 (C, C-5), 155.2 (C, C-10b), 139.3 (C, C-6a), 135.5 (C, C-4'), 131.2 (C, C-8'), 130.7 (CH, C-8), 125.1 (CH, C-3), 124.1 (CH, C-7'), 123.4 (CH, C-3'), 122.9 (CH, C-10), 121.5 (CH, C-9), 118.3 (CH, C-4), 115.9 (C-10a), 113.9 (CH, C-7), 105.4 (C, C-4a), 81.2 (C, C-2), 41.4 (CH_2, C-1'), 39.5 (CH_2, C-5'), 29.1 (CH_3, N-CH_3), 26.9 (CH_3, C2'-CH_3), 26.5 (CH_2, C-6'), 25.5 (CH_3, C-9'*), 22.3 (CH_2, C-2'), 17.5 (CH_3, C8'-CH_3*), 15.8 (CH_3, C4'-CH_3). **HRMS** *m/z* 378.2411 [(M + Na^+) calcd. for $C_{25}H_{32}NO_2$ 378.2427].

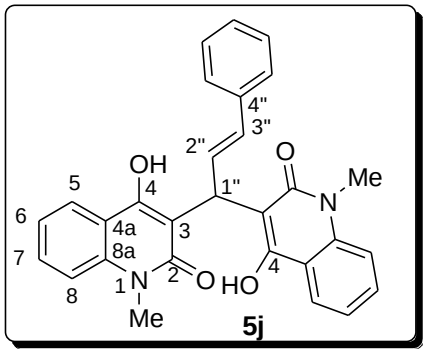
2-(4-Fluorophenyl)-3,6-dimethyl-2*H*-pyrano[3,2-c]quinolin-5(6*H*)-one (5h)



Yellow solid. M.p.: 128.0-130.0 ºC. **IR** (film) (cm^{-1}): 3071, 3051, 2993, 2938, 1632, 1508, 1223. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.81 (dd, *J* = 7.9; 1.4 Hz, 1H, 10-H), 7.48 (ddd, *J* = 8.6; 7.2; 1.6 Hz, 1H, 8-H), 7.47-7.38 (m, 2H, 2'-H), 7.27 (d, *J* = 8.6 Hz, 1H, 7-H), 7.14 (ddd, *J* = 8.1; 7.3; 0.9 Hz, 1H, 9-H), 7.06-6.96 (m, 2H, 3'-H), 6.85-6.82 (m, 1H, 4-H), 5.85 (bs, 1H, 2-H), 3.69 (s, 3H, N-CH_3), 1.80-1.77 (m, 3H, 3-CH_3). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 163.0 (C, d, *J* = 248.0 Hz, C-4'), 160.7 (C, C-5), 152.7 (C, C-10b), 138.9 (C, C-6a), 134.0 (C, d, *J* = 3.0 Hz, C-1'), 130.5 (CH, C-8),

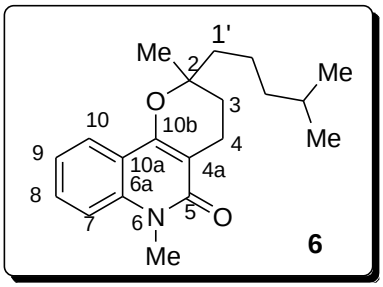
129.6 (2 × CH, d, *J* = 8.4 Hz, C-2'), 128.3 (C, C-3), 122.7 (CH, C-10), 121.6 (CH, C-9), 115.6 (2 × CH, d, *J* = 21.8 Hz, C-3'), 115.52 (C, C-10a), 115.46 (CH, C-4), 113.8 (CH, C-7), 106.4 (C, C-4a), 80,7 (CH, C-2), 29.2 (CH_3, N-CH_3), 19.7 (CH_3, C3-CH_3). **HRMS** *m/z* 665.2214 [(2M + Na^+) calcd. for $C_{40}H_{32}F_2N_2NaO_4$ 665.2222].

(*E*)-3,3'-(3-phenylprop-2-ene-1,1-diyl)bis(4-hydroxy-1-methylquinolin-2(1*H*)-one) (5j)



Yellow liquid. **IR** (film) (cm^{-1}): 3020, 2941, 1628, 1607, 1553, 1368. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 8.21 (d, *J* = 8.0 Hz, 2H, 5-H, 5'-H), 7.58 (ddd, *J* = 8.3; 7.2; 1.0 Hz, 2H, 7-H, 7'-H), 7.41-7.21 (m, 8H, 5''-H, 6''-H, 6-H, 6'-H, 8-H, 8'-H), 7.20-7.11 (m, 1H, 7''-H), 7.04 (dd, *J* = 16.0; 5.2 Hz, 1H, 2''-H), 6.47 (dd, *J* = 16.0; 1.6 Hz, 1H, 3''-H), 5.80 (dd, *J* = 5.2; 1.8 Hz, 1H, 1''-H), 3.80 (s, 3H, N-CH_3^*), 3.75 (s, 3H, N-CH_3^*). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 166.2 (C, C-2*), 164.9 (C, C-2'*), 160.53 (C, C-4*), 160.51 (C, C-4'*), 138.3 (C, C-8a*), 138.1 (C, C-8a'*), 137.5 (C, C-4''), 130.9 (2 × CH, C-7, C-7'), 130.5 (CH, C-3''), 128.3 (2 × CH, C-6''), 127.7 (CH, C-2''), 126.9 (CH, C-7''), 126.2 (2 × CH, C-5''), 124.6 (2 × CH, C-5, C-5'), 124.5 (CH, C-6*), 122.4 (CH, C-6'*), 118.1 (C, C-4a*), 117.6 (C, C-4a'*), 114.0 (CH, C-8*), 113.9 (CH, C-8'*), 112.3 (C, C-3*), 111.0 (C, C-3'*), 35.9 (CH, C-1''), 30.2 (CH_3, N-CH_3^*), 29.8 (CH_3, N-CH_3^*). **HRMS** *m/z* 465.1802 [(M + Na^+) calcd. for $C_{29}H_{25}N_2O_4$ 465.1809].

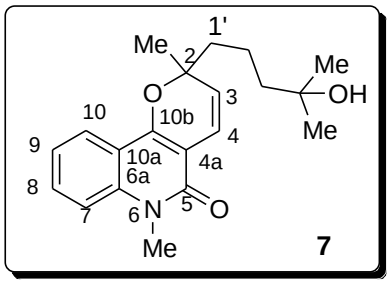
2,6-dimethyl-2-(4-methylpentyl)-3,4-dihydro-2H-pyrano[3,2-*c*]quinolin-5(6*H*)-one (6)



Colourless liquid. **IR** (film) (cm^{-1}): 2949, 2899, 2866, 1636, 1595, 1398, 1161. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.95 (dd, *J* = 8.0; 1.4 Hz, 1H, 10-H), 7.52 (ddd, *J* = 8.6; 7.2; 1.5 Hz, 1H, 8-H), 7.32 (d, *J* = 8.3 Hz, 1H, 7-H), 7.21 (ddd, *J* = 8.0; 7.2; 0.9 Hz, 1H, 9-H), 3.70 (s, 3H, N-CH_3), 2.75-2.53 (m, 2H, 4-H), 1.95-1.76 (m, 2H, 3-H), 1.76-1.39 (m, 5H, 1'-H, 2'-H, 4'-H), 1.35 (s, 3H, 2-CH_3), 1.29-1.12 (m, 2H, 3'-H), 0.88 (d, *J* = 6.6 Hz, 6H, 5'-H, 4'-CH_3). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 163.2 (C, C-5),

155.3 (C, C-10b), 138.5 (C, C-6a), 129.8 (CH, C-8), 122.5 (CH, C-10), 121.2 (CH, C-9), 116.6 (C, C-10a), 113.6 (CH, C-7), 105.5 (C, C-4a), 78,4 (C, C-2), 39.6 (CH_2, C-1'), 39.2 (CH_2, C-3'), 30.3 (CH_2, C-3), 29.0 (CH_3, N-CH_3), 27.7 (CH, C-4'), 23.6 (CH_3, C2-CH_3), 22.4 (2 × CH_3, C4'-CH_3, C-5'), 21.1 (CH_2, C-2'), 17.5 (CH_2, C-4). **HRMS** *m/z* 314.2100 [(M + H^+) calcd. for $C_{20}H_{28}NO_2$ 314.2114].

2-(4-hydroxy-4-methylpentyl)-2,6-dimethyl-2H-pyrano[3,2-*c*]quinolin-5(6*H*)-one (7)



Colourless solid. M.p.: 144.8-148.1 °C. Yield: 60%. **IR** (film) (cm^{-1}): 3416, 2966, 2945, 1649, 1618, 1161. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.95 (dd, *J* = 8.0; 1.3 Hz, 1H, 10-H), 7.54 (ddd, *J* = 8.6; 7.1; 1.5 Hz, 1H, 8-H), 7.31 (bd, *J* = 8.6 Hz, 1H, 7-H), 7.22 (ddd, *J* = 8.0; 7.2; 0.9 Hz, 1H, 9-H), 6.79 (d, *J* = 10.0 Hz, 1H, 4-H), 5.49 (d, *J* = 10.0 Hz, 1H, 3-H), 3.69 (s, 3H, N-CH_3), 1.92-1.64 (m, 2H, 1'-H), 1.62-1.42 (m, 4H, 2'-H, 3'-H), 1.47 (s, 3H, 2-CH_3), 1.19 (s, 6H, 5'-H, 4'-CH_3). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 160.8 (C, C-5), 155.1 (C, C-10b), 139.2 (C, C-6a), 130.7 (CH, C-8), 125.2 (CH, C-3), 122.9 (CH, C-10), 121.6 (CH, C-9), 118.3 (CH, C-4), 115.8 (C, C-10a), 113.9 (CH, C-7), 105.4 (C, C-4a), 81.2 (C, C-2), 70.7 (C, C-4'), 43.8 (CH_2, C-3'), 41.7 (CH_2, C-1'), 29.15 (CH_3, N-CH_3), 29.11 (2 × CH_3, C-5', C4'-CH_3), 26.7 (CH_3, C2-CH_3), 18.5 (CH_2, C-2'). **HRMS** *m/z* 350.1708 [(M + Na^+) calcd. for $C_{20}H_{25}NNaO_3$ 350.1727].

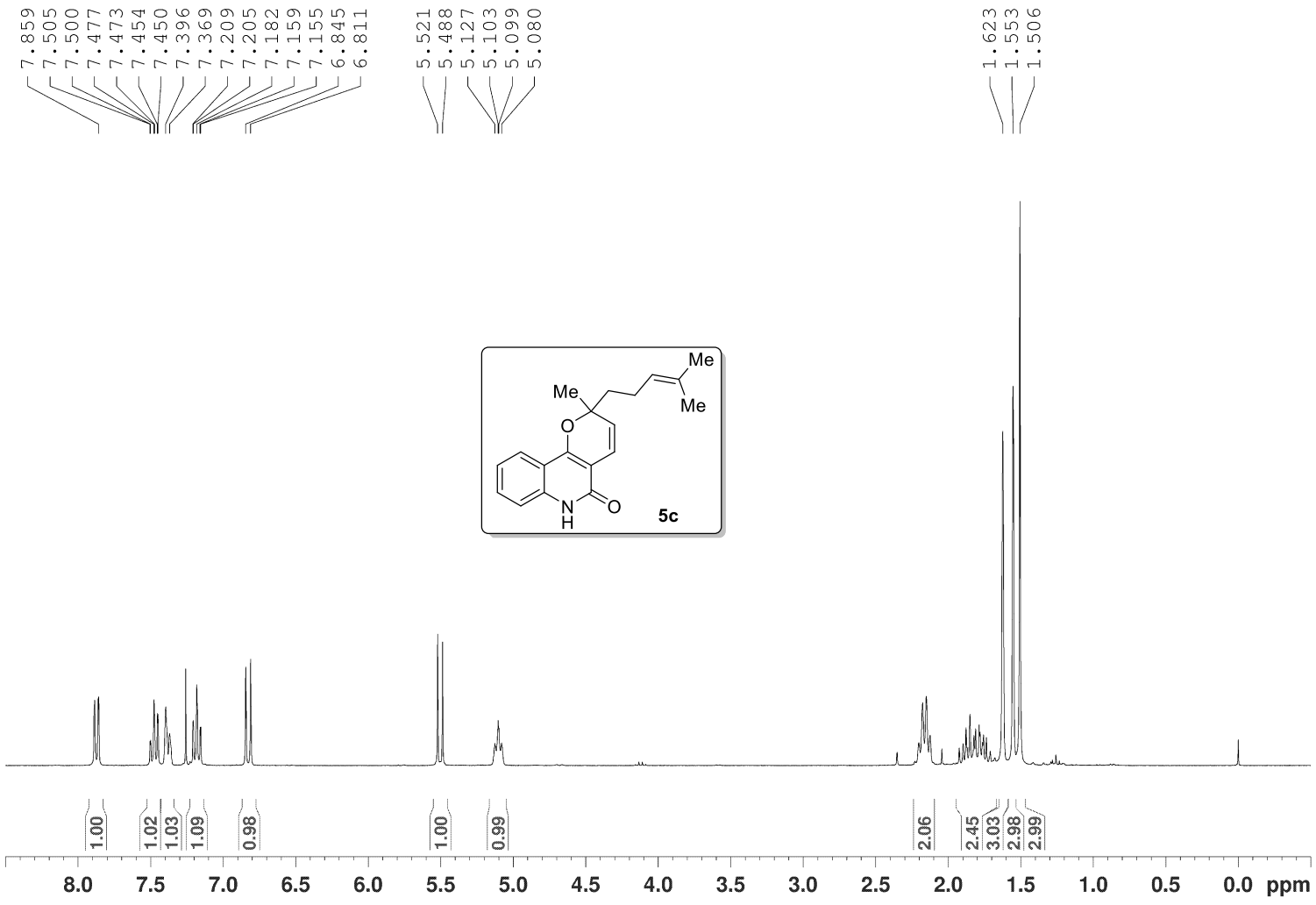


Figure S1.[1]H NMR Spectrum of Compound **5c** ($CDCl_3$, 300 MHz)

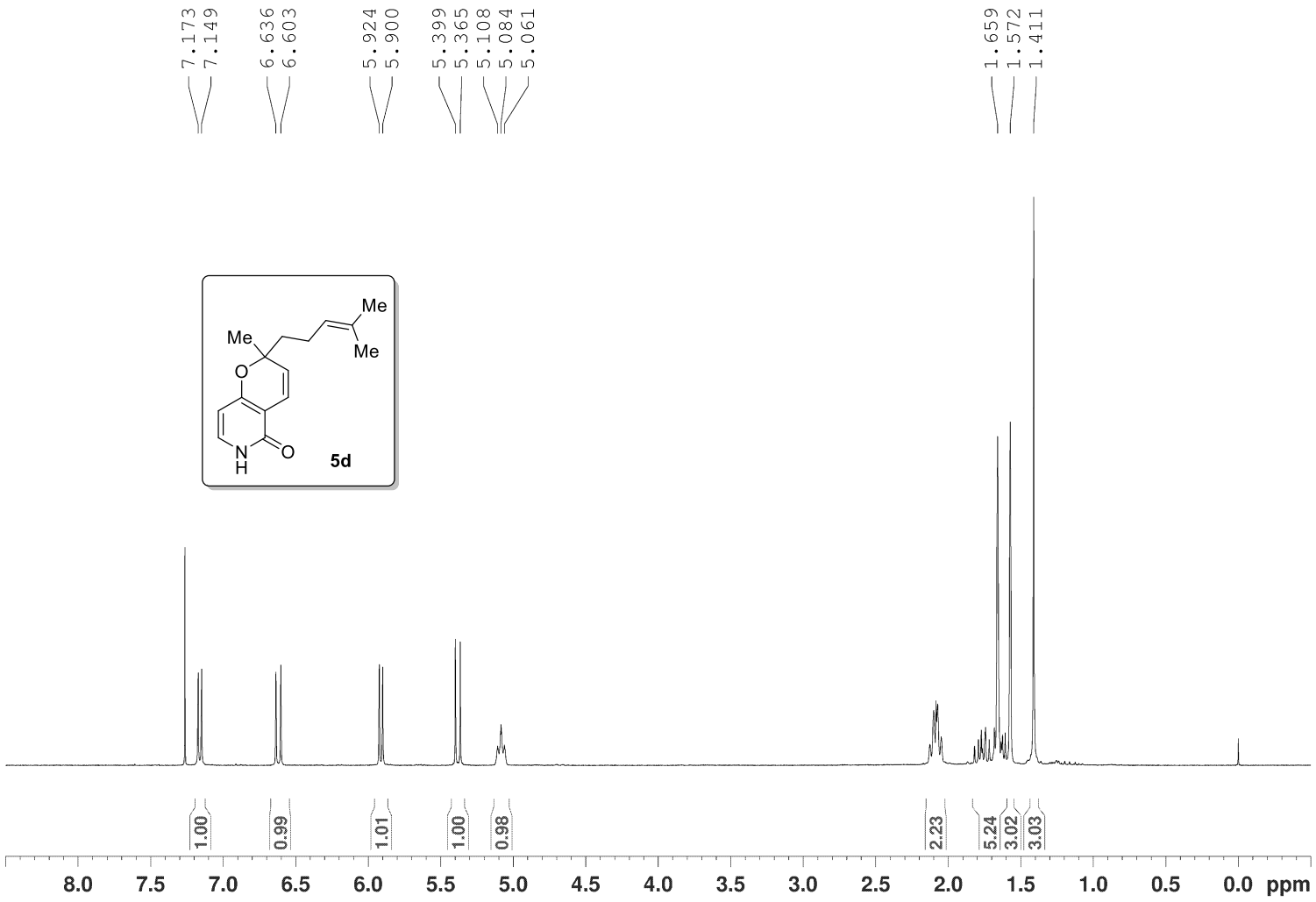


Figure S2. ^{1}H NMR Spectrum of Compound **5d** ($CDCl_3$, 300 MHz)

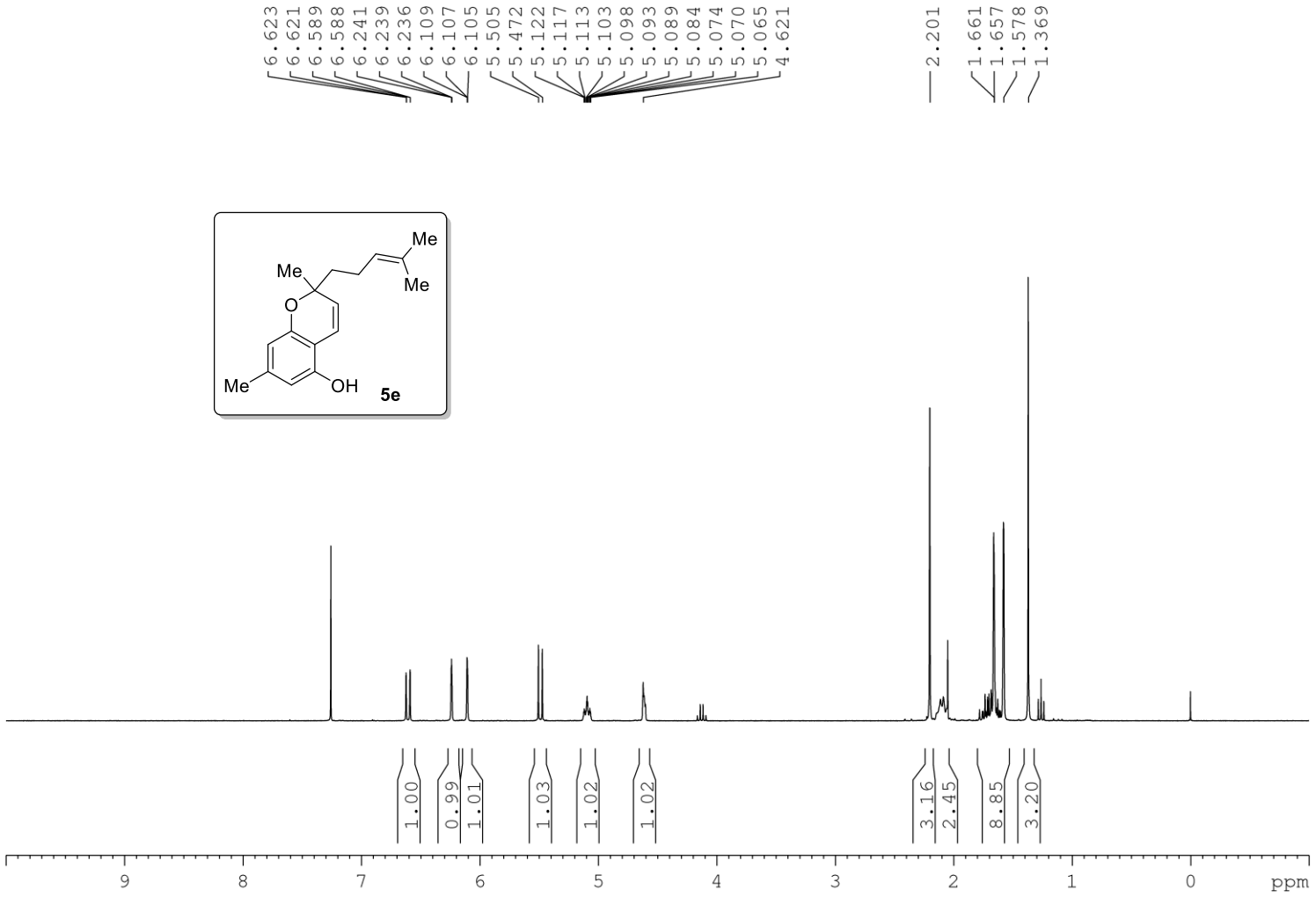


Figure S3. ^{1}H NMR Spectrum of Compound **5e** ($CDCl_3$, 300 MHz)

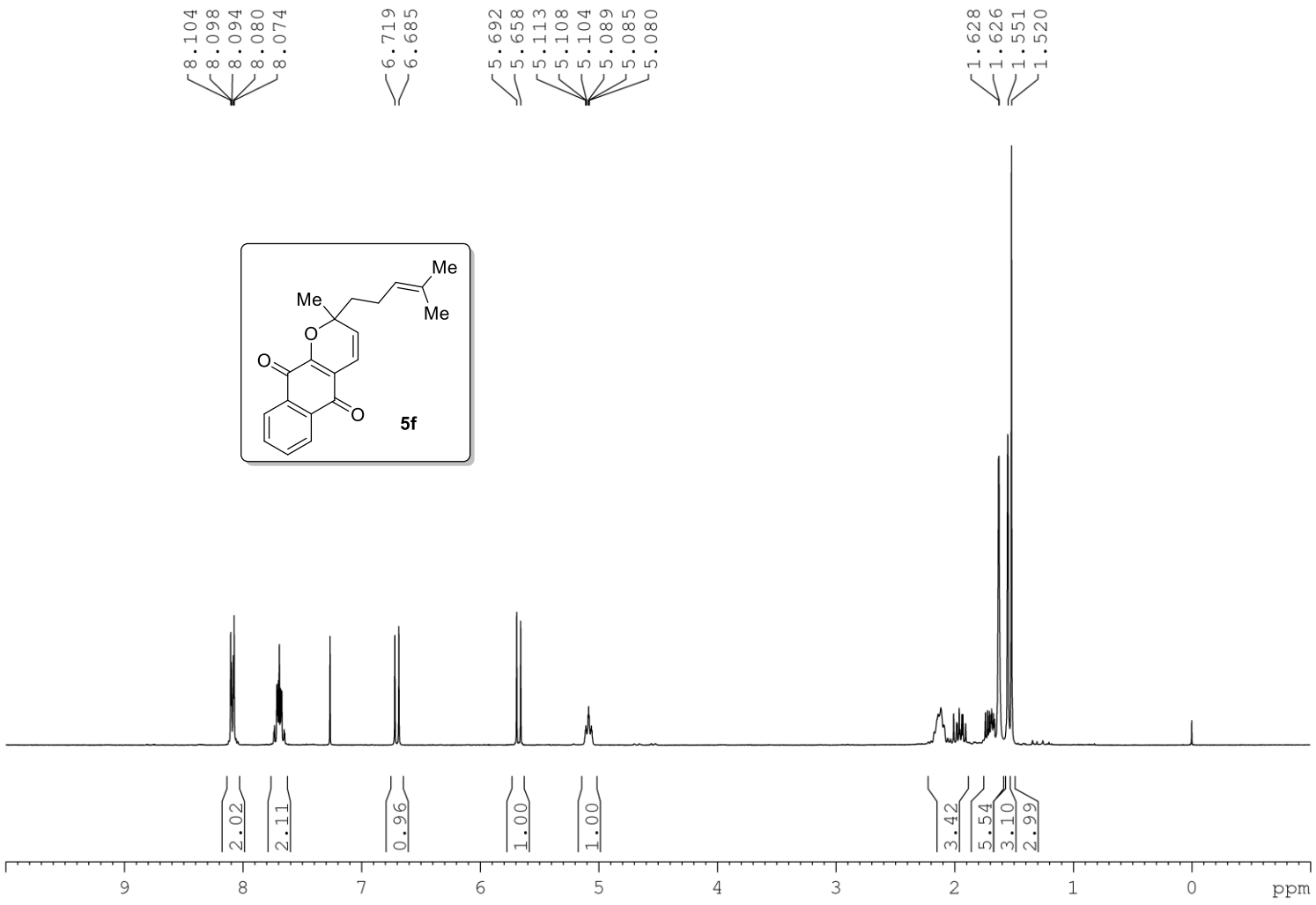


Figure S4. ^{1}H NMR Spectrum of Compound **5f** ($CDCl_3$, 300 MHz)

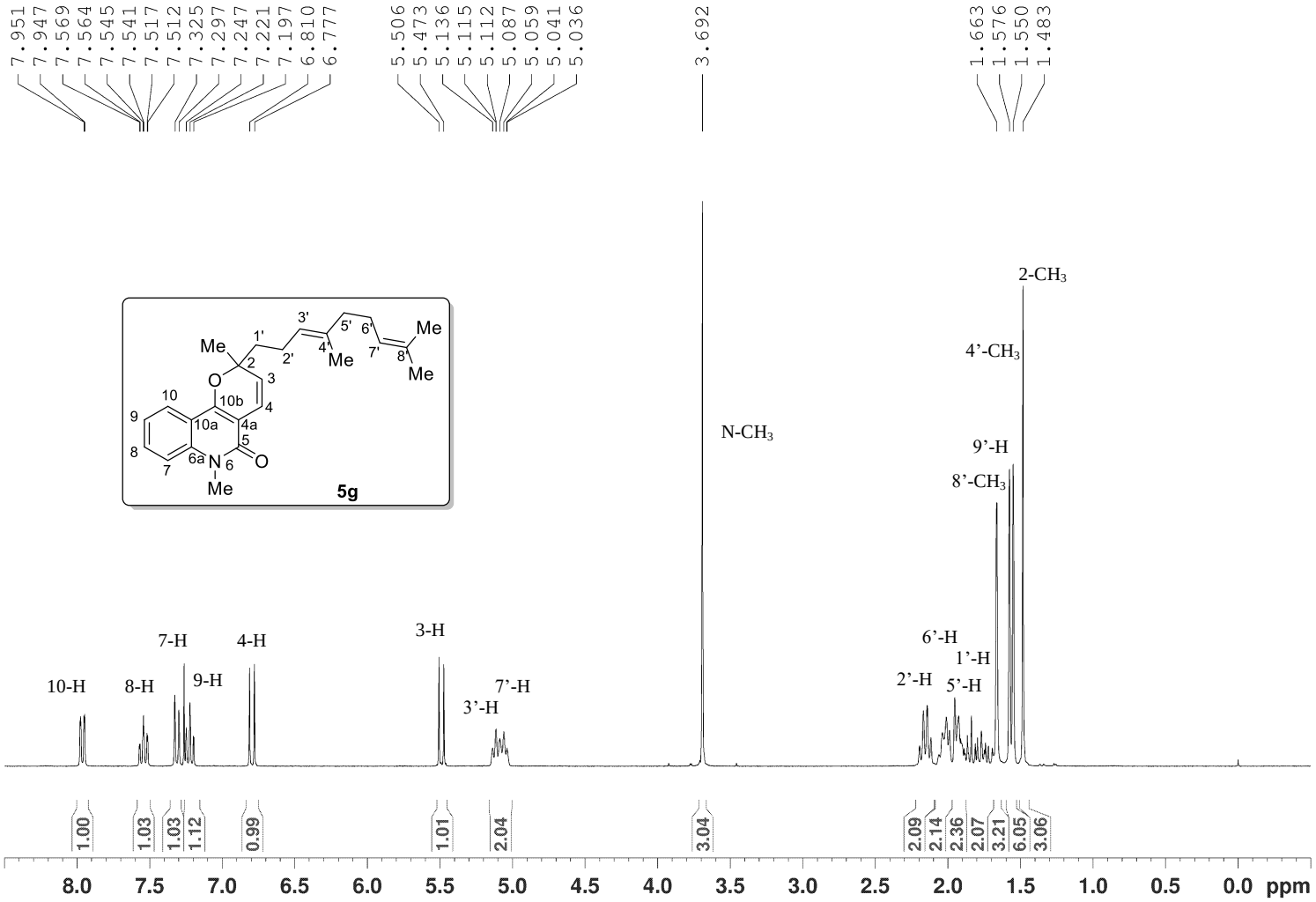


Figure S5. ^{1}H NMR Spectrum of Compound **5g** ($CDCl_3$, 300 MHz)

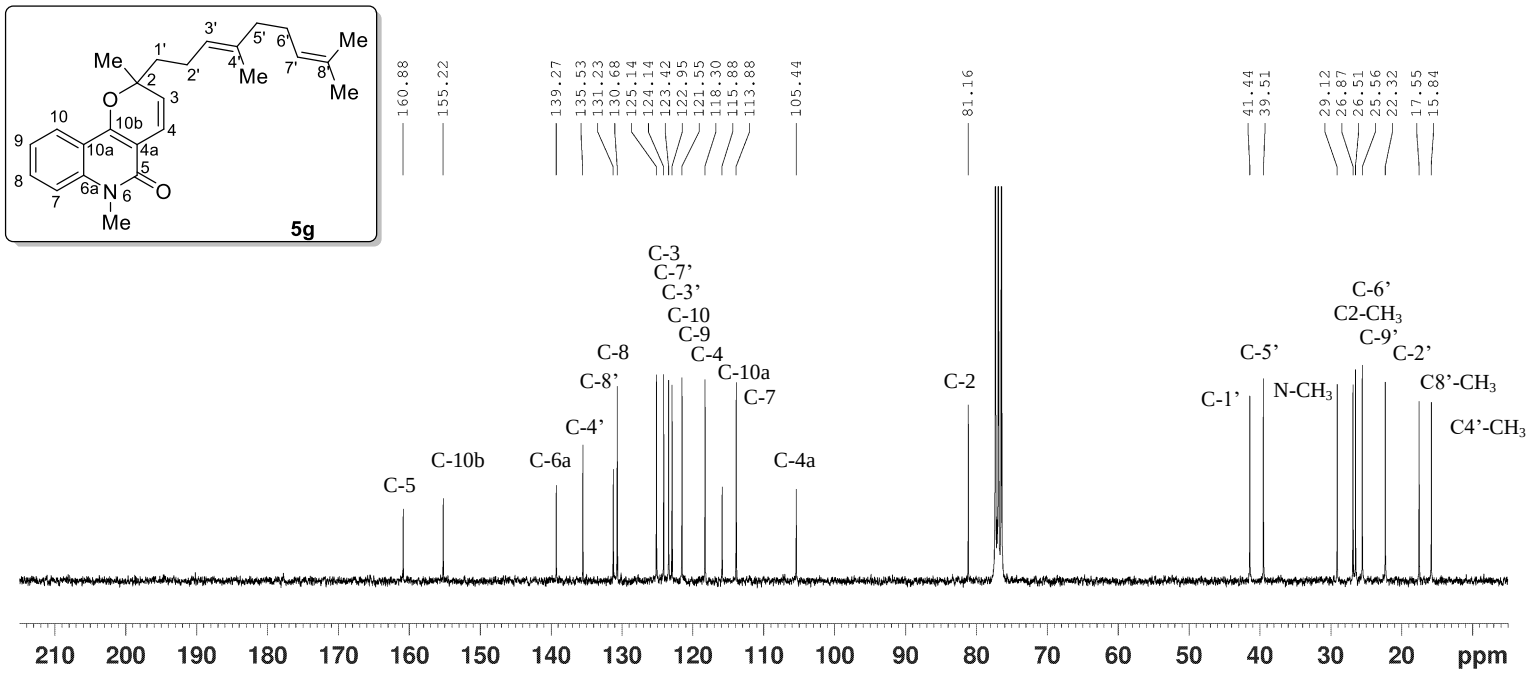


Figure S6. $^{13}C\{^{1}H\}$ NMR Spectrum of Compound **5g** ($CDCl_3$, 75 MHz)

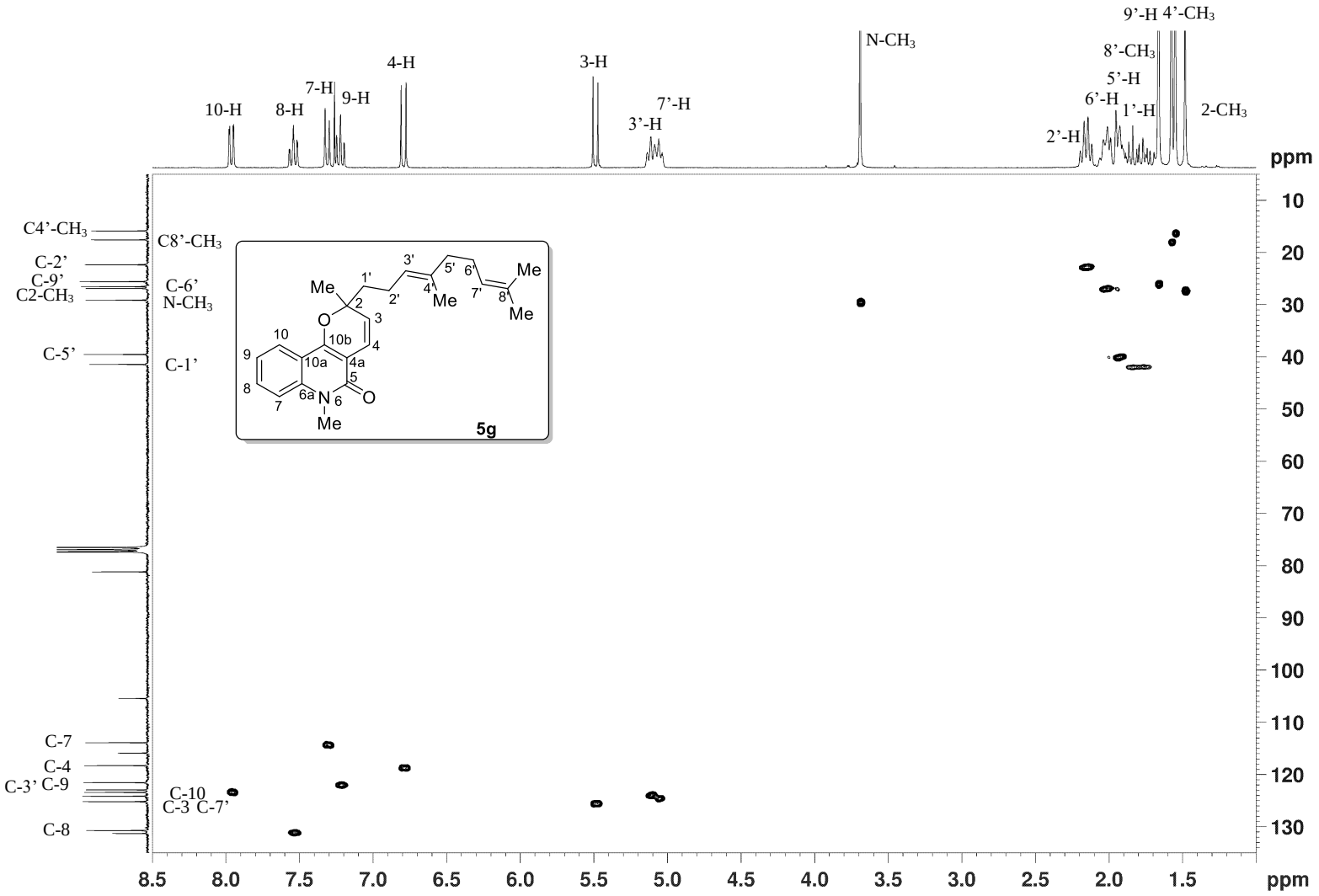


Figure S7. 2D ^{1}H-^{13}C HSQC Spectrum of Compound **5g** ($CDCl_3$)

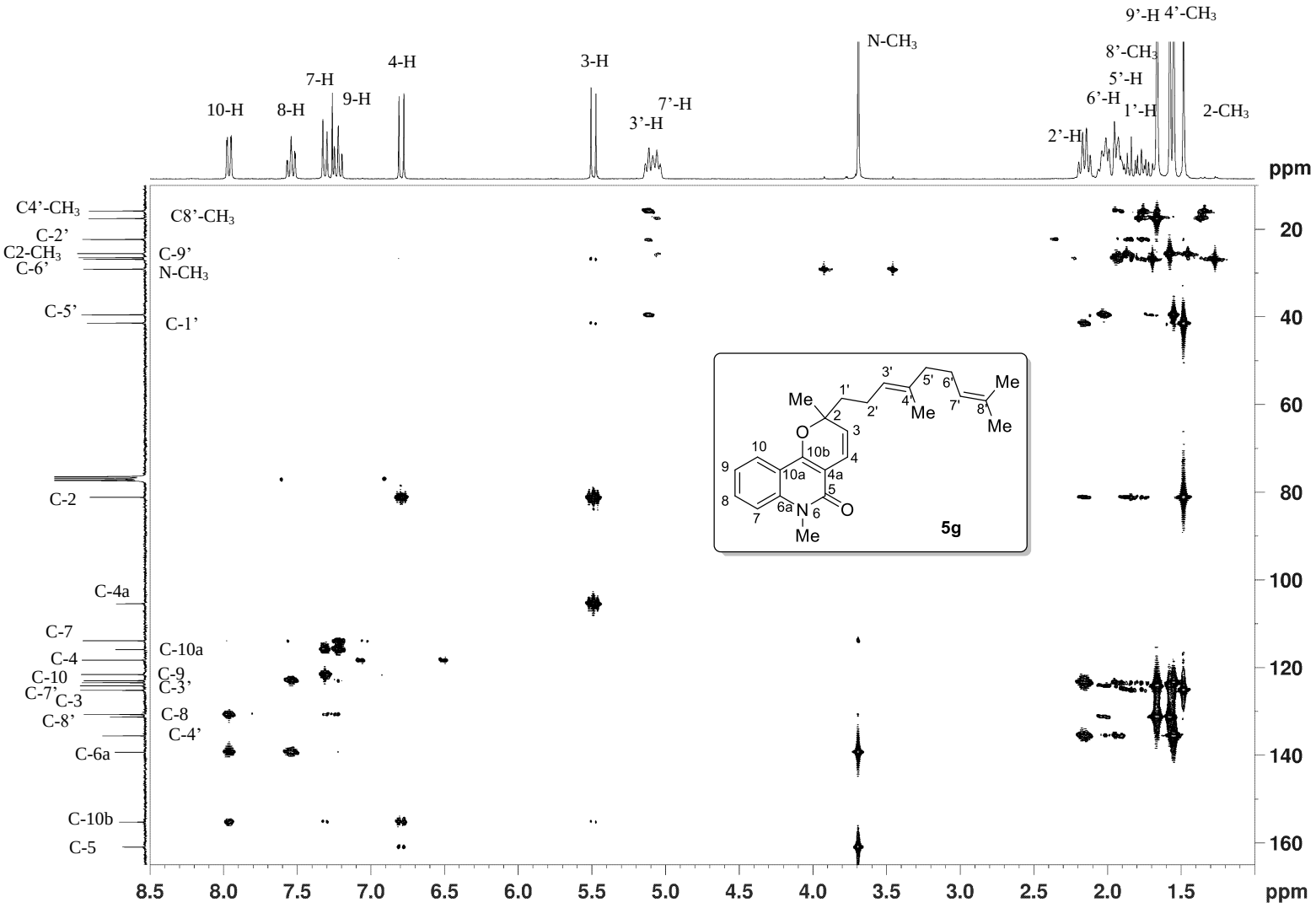


Figure S8. 2D ^{1}H-^{13}C HMBC Spectrum of Compound **5g** ($CDCl_3$)

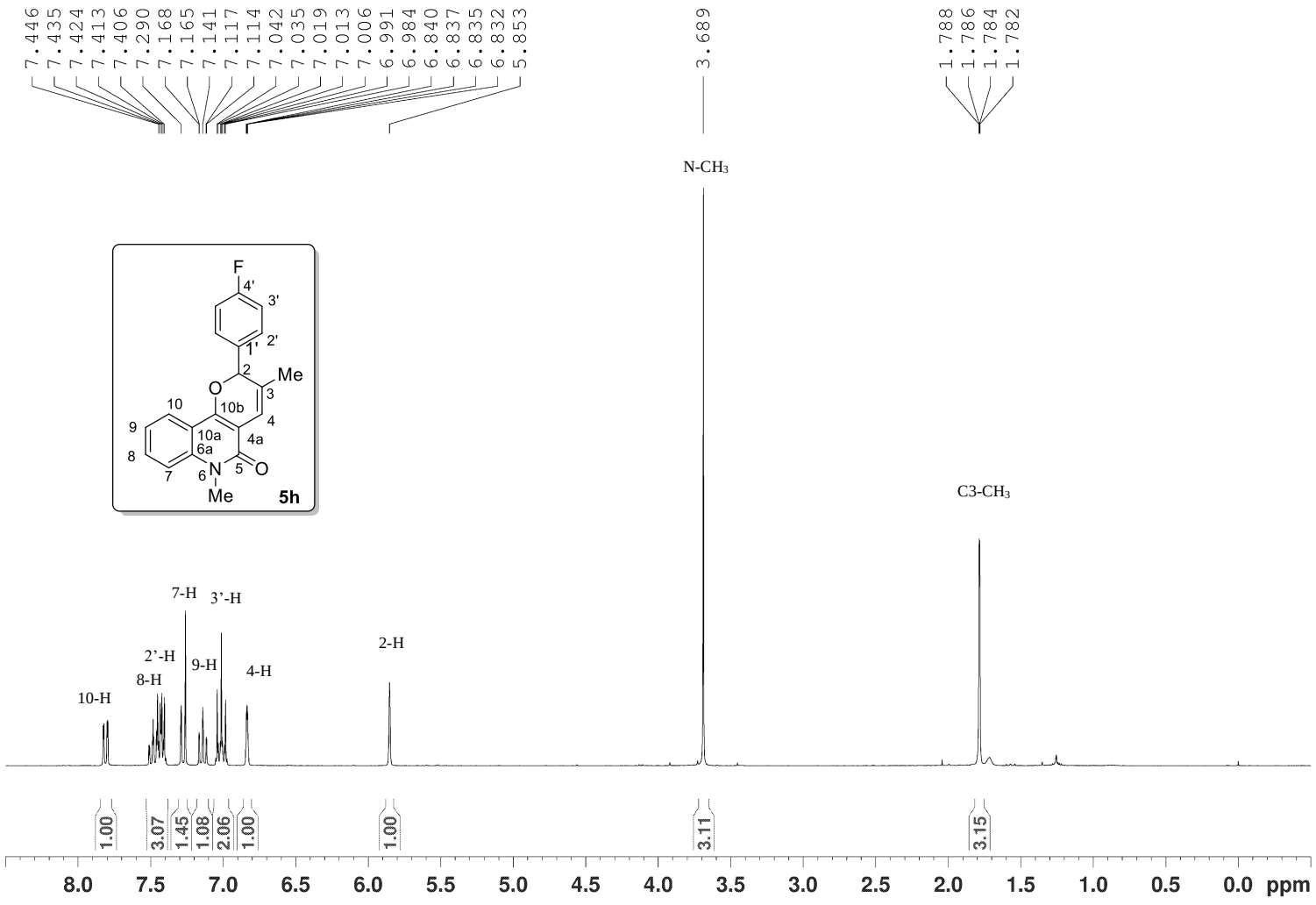


Figure S9. ^{1}H NMR Spectrum of Compound **5h** ($CDCl_3$, 300 MHz)

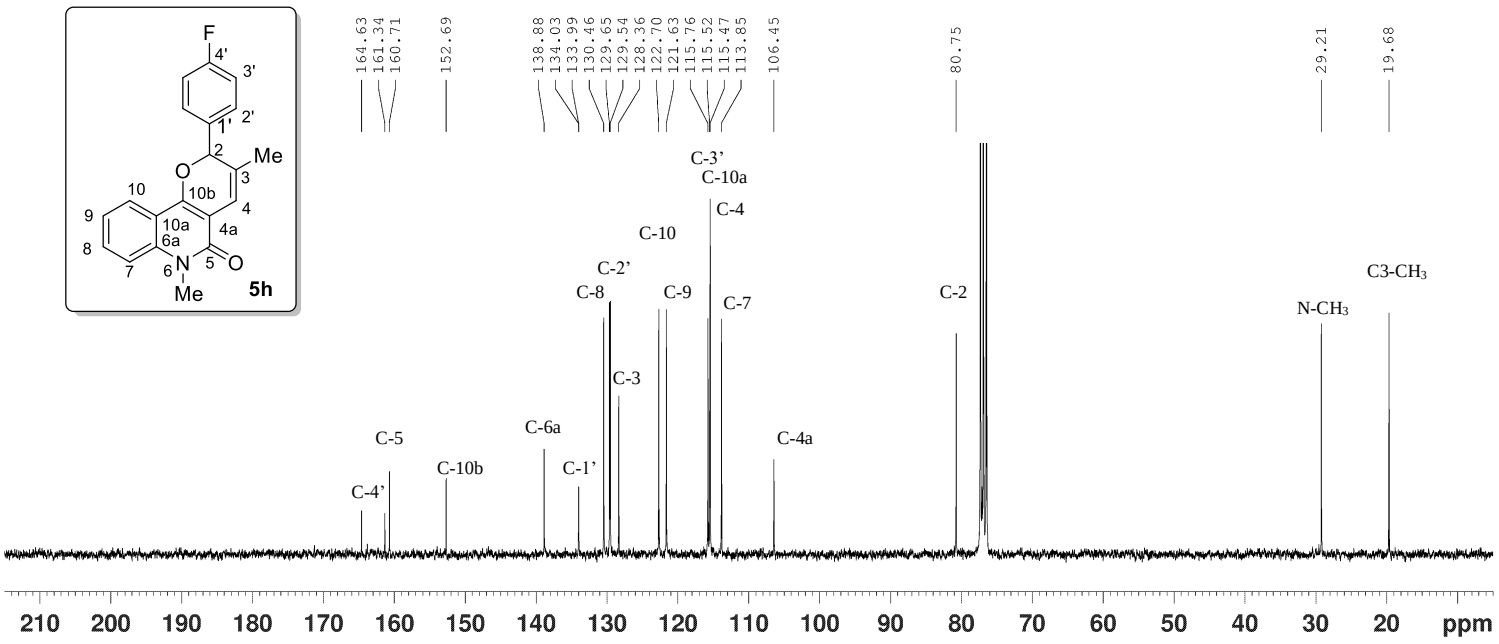


Figure S10. $^{13}C\{^{1}H\}$ NMR Spectrum of Compound **5h** ($CDCl_3$, 75 MHz)

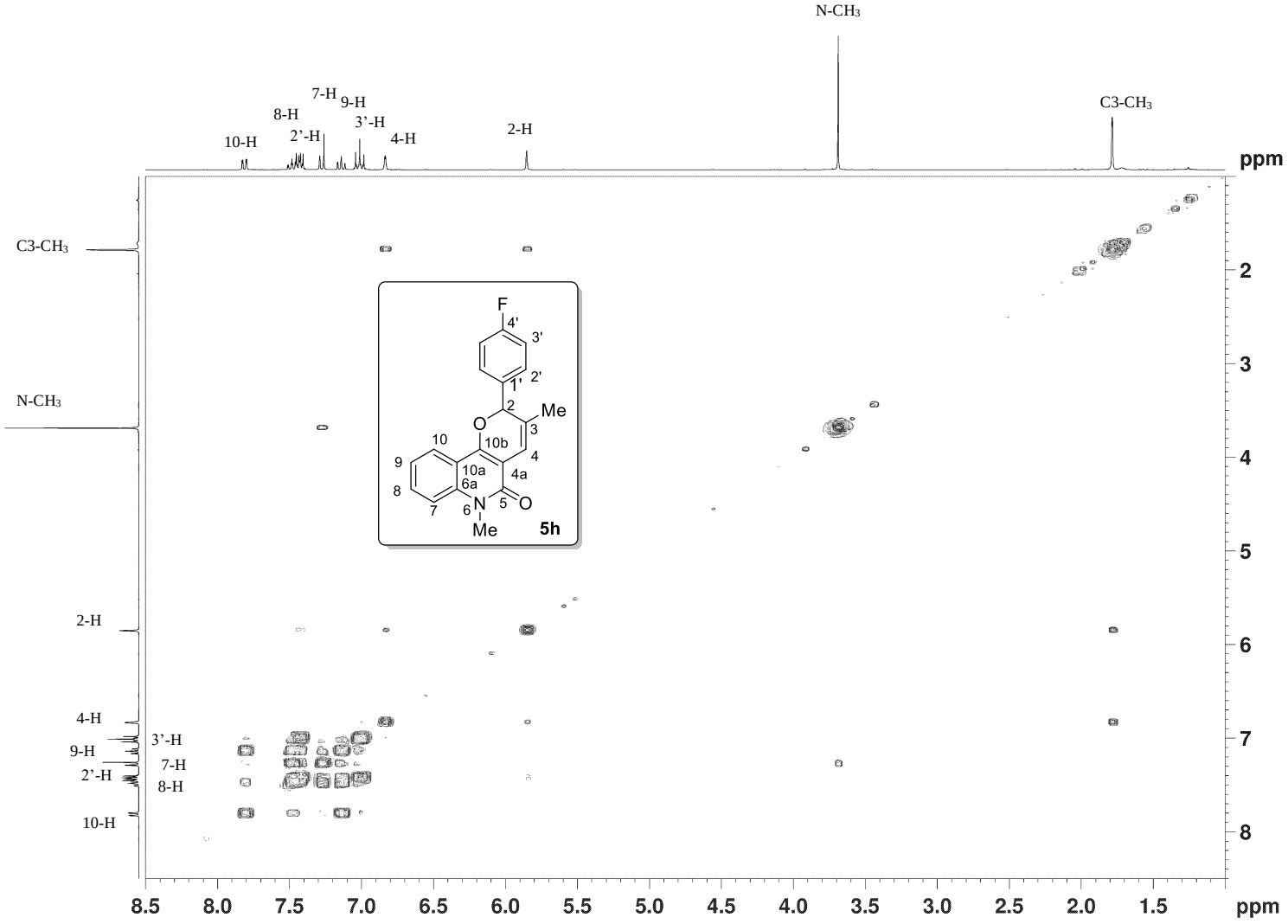


Figure S11. 2D ^{1}H-^{1}H COSY Spectrum of Compound **5h** ($CDCl_3$, 300 MHz)

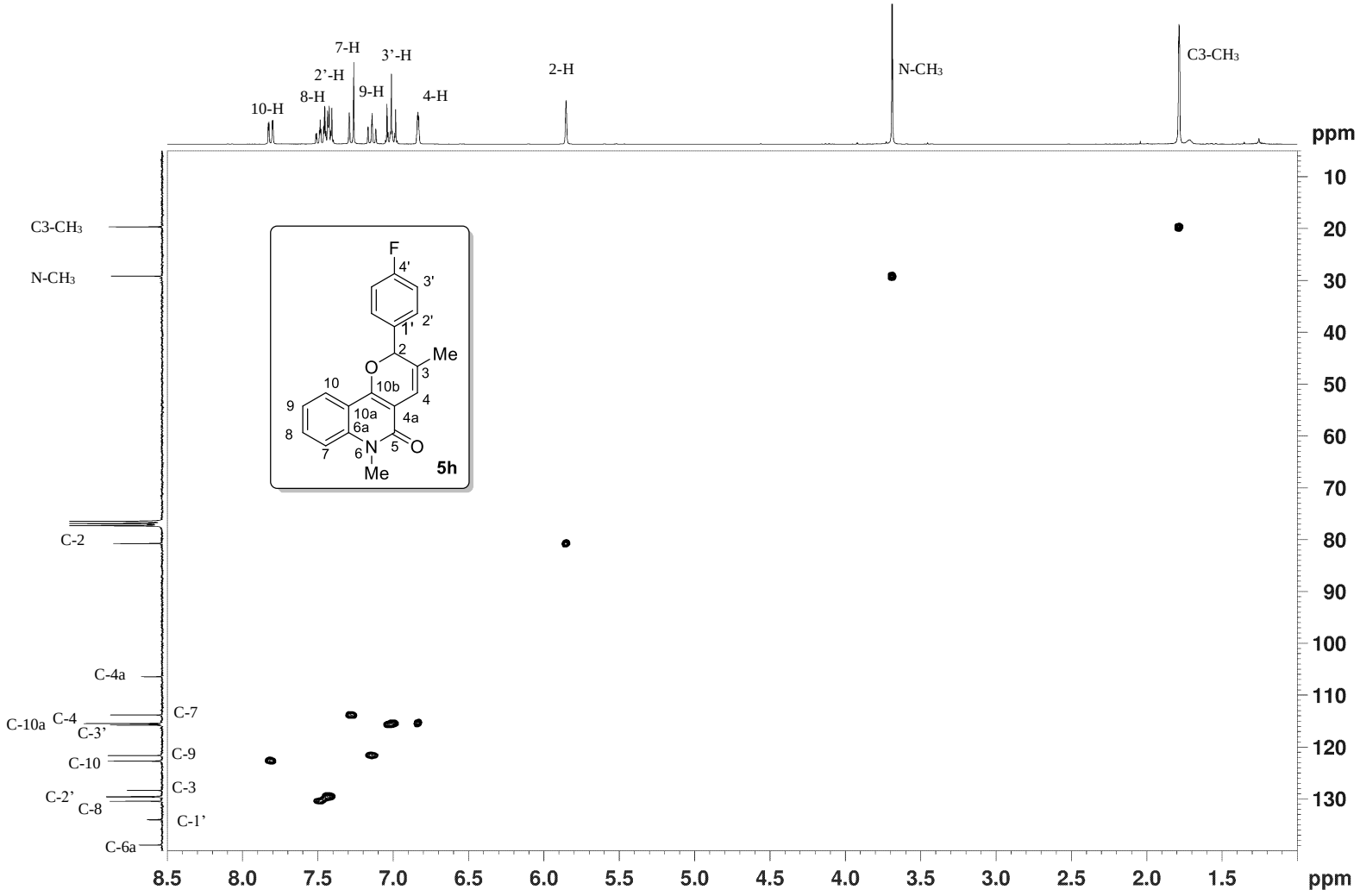


Figure S12. 2D ^{1}H-^{13}C HSQC Spectrum of Compound **5h** ($CDCl_3$)

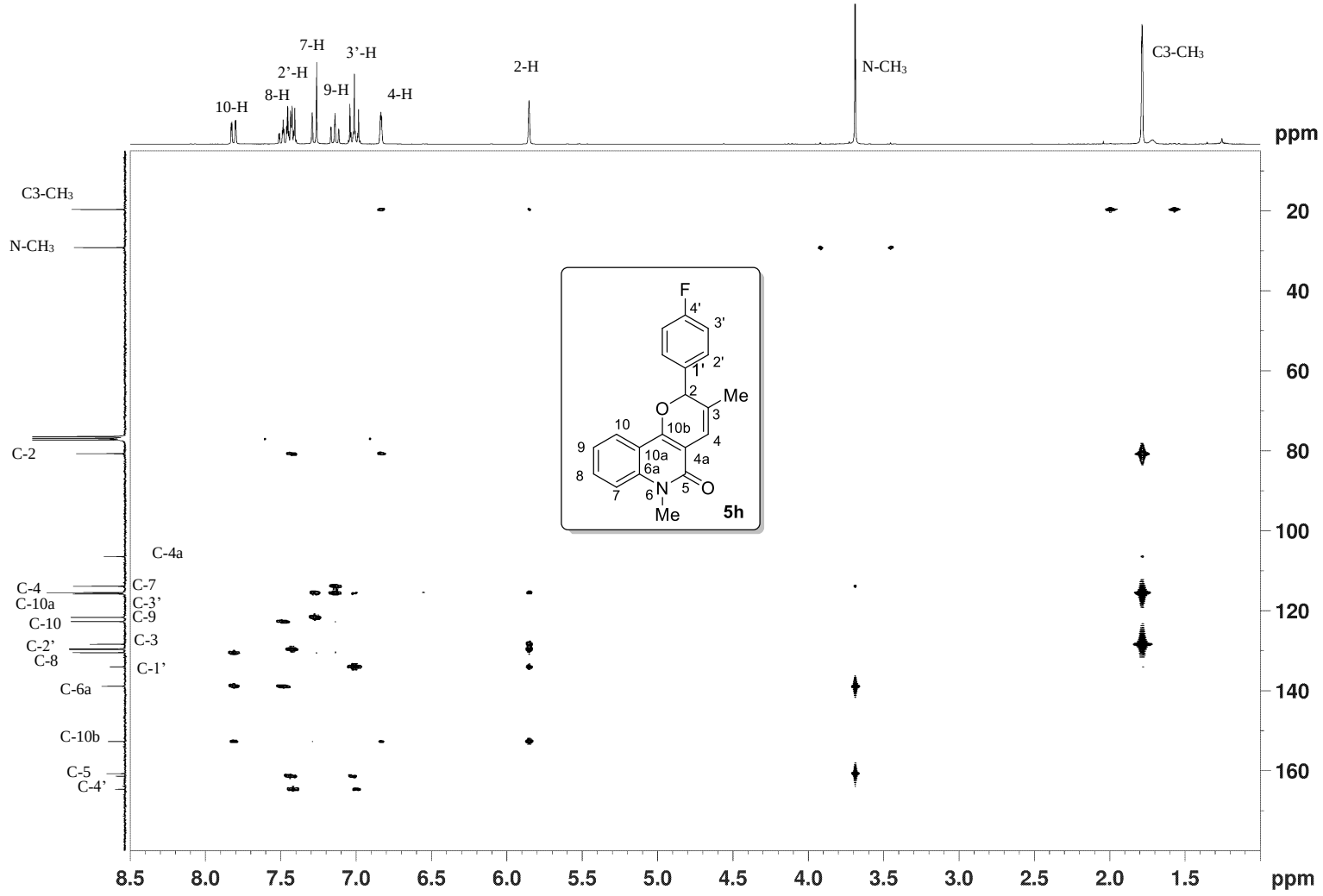


Figure S13. 2D ^{1}H-^{13}C HMBC Spectrum of Compound **5h** ($CDCl_3$)

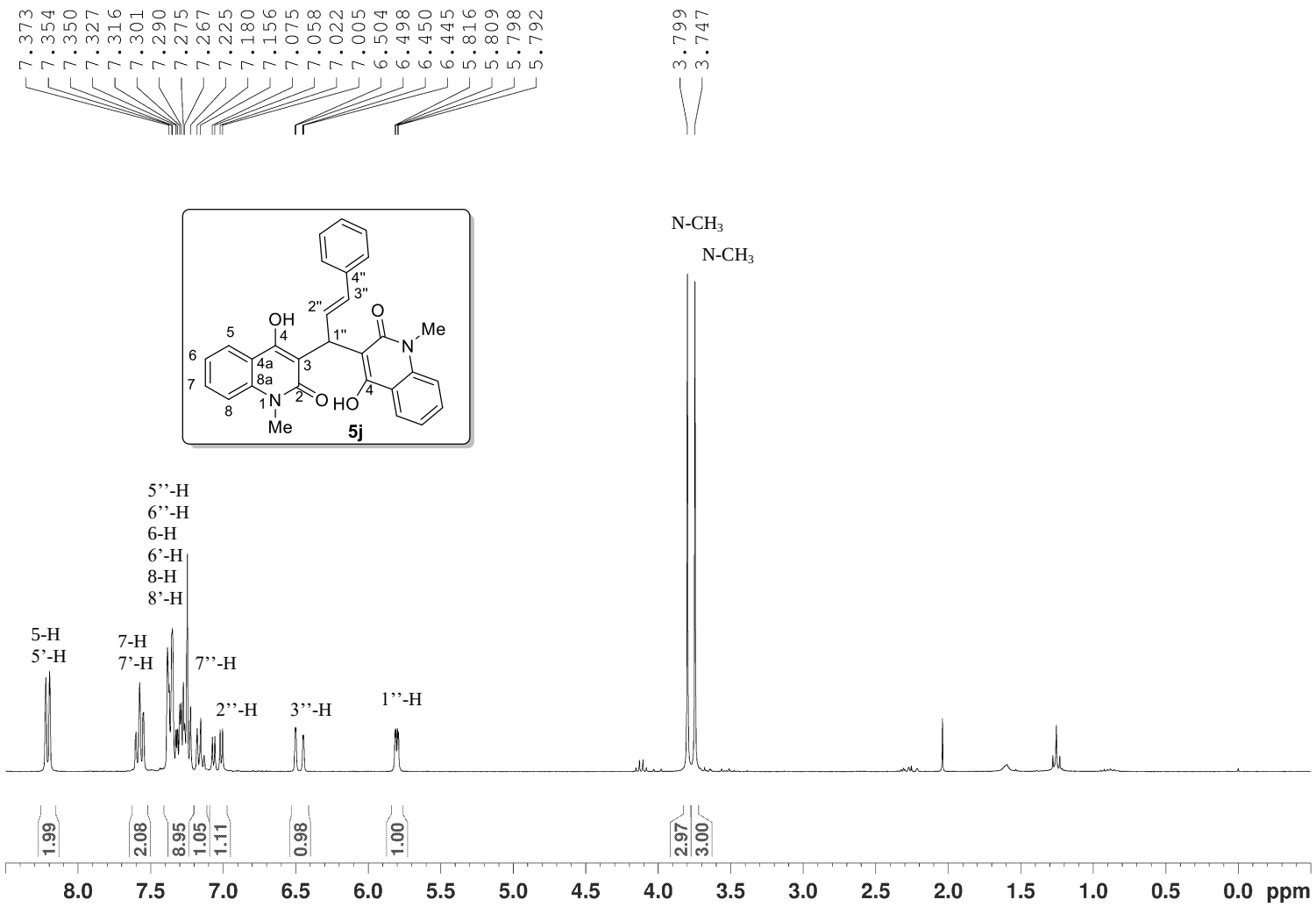


Figure S14. ^{1}H NMR Spectrum of Compound **5j** ($CDCl_3$, 300 MHz)

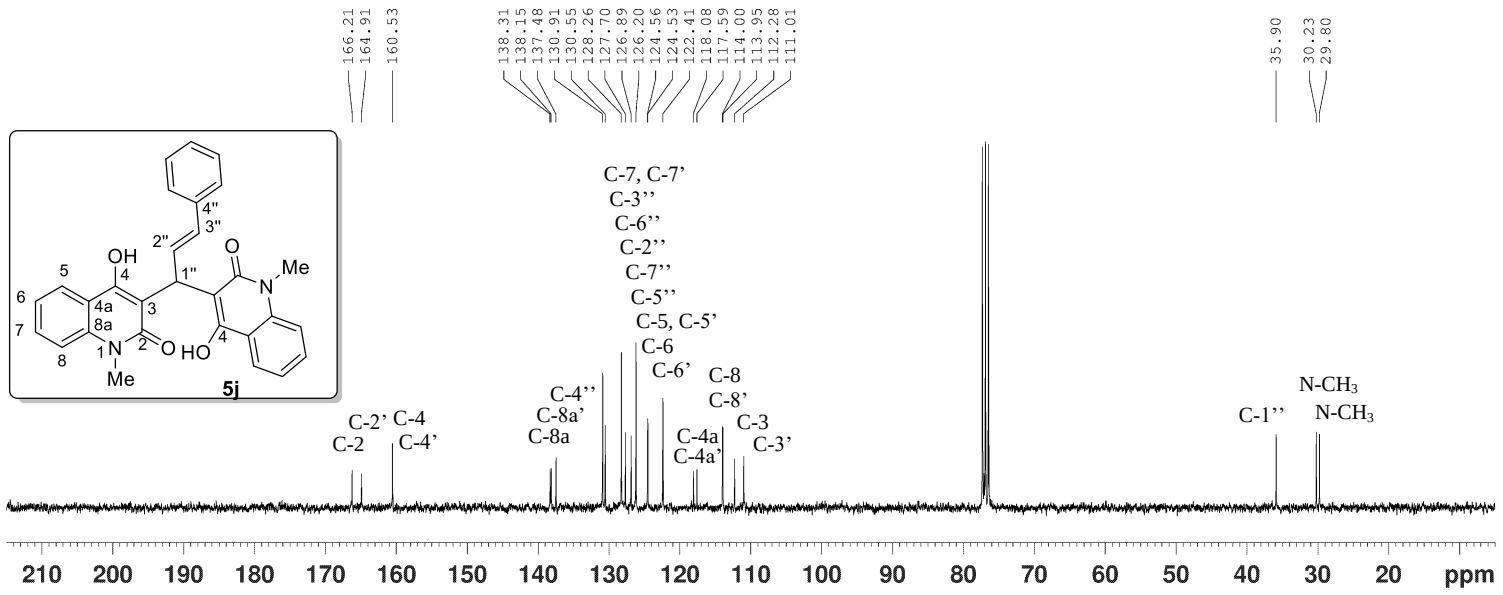


Figure S15. $^{13}C\{^{1}H\}$ NMR Spectrum of Compound **5j** ($CDCl_3$, 75 MHz)

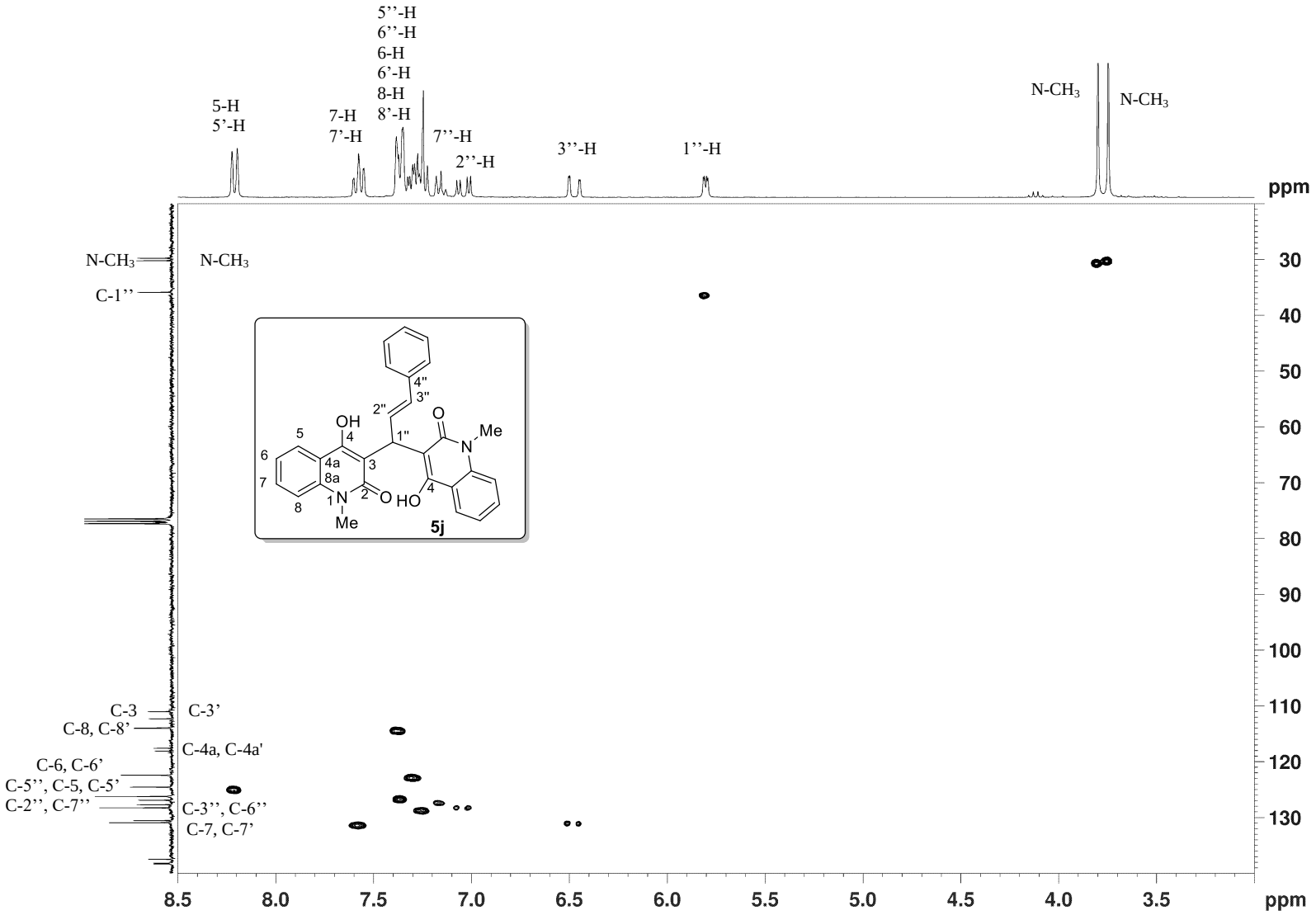


Figure S16. 2D ^{1}H-^{13}C HSQC Spectrum of Compound **5j** ($CDCl_3$)

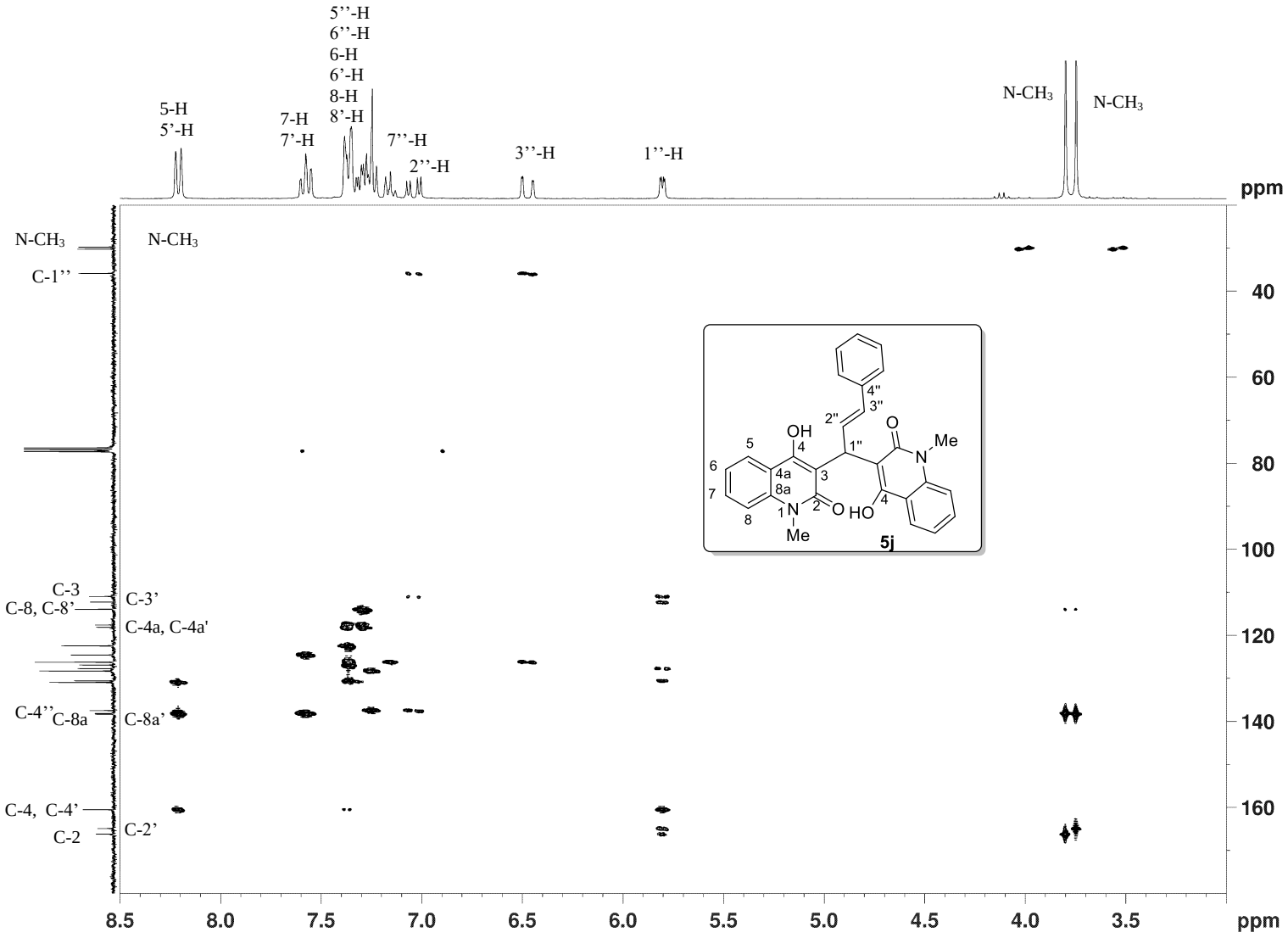


Figure S17. 2D ^{1}H-^{13}C HMBC Spectrum of Compound **5j** ($CDCl_3$)

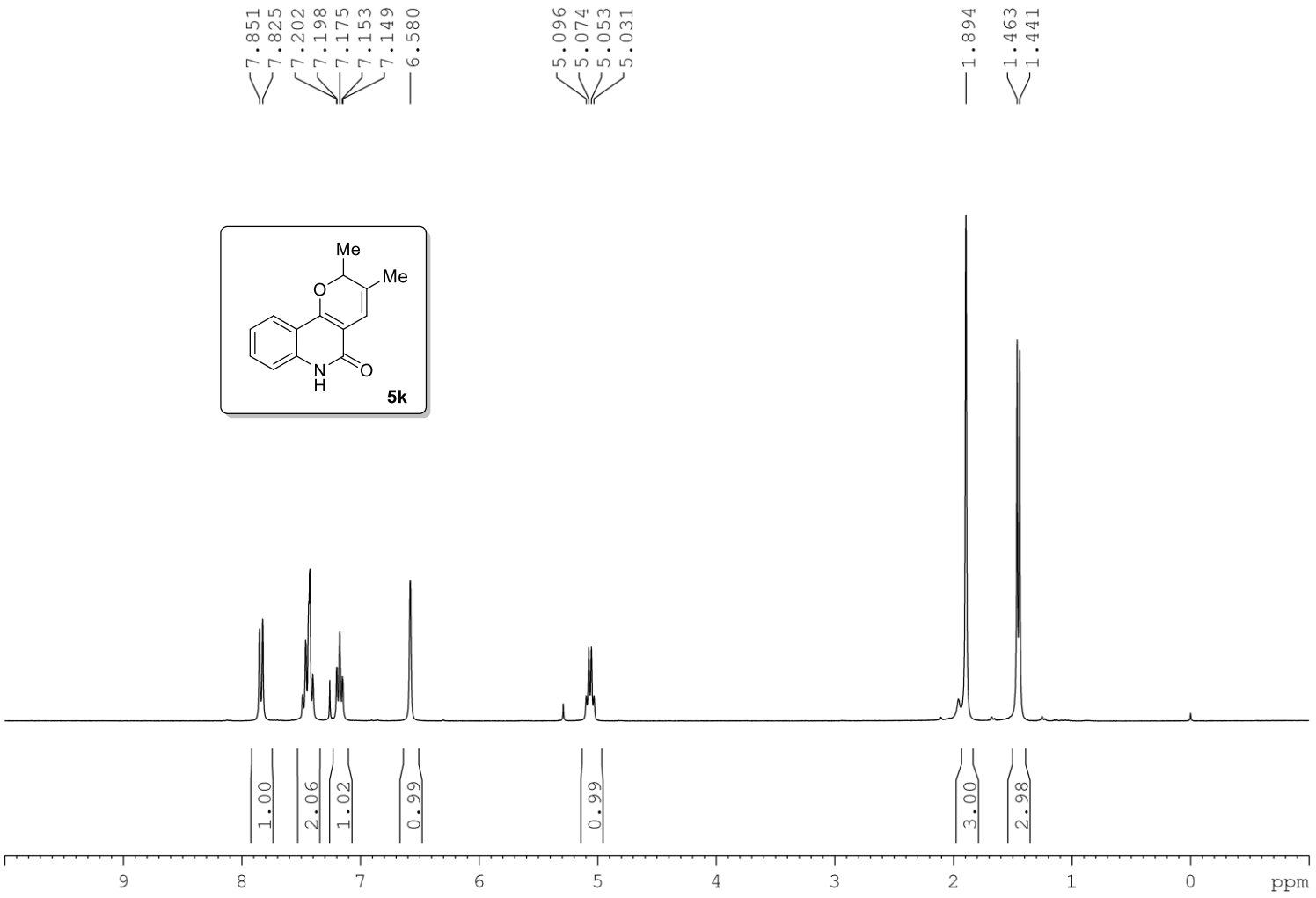


Figure S18. ^{1}H NMR Spectrum of Compound **5k** ($CDCl_3$, 300 MHz)

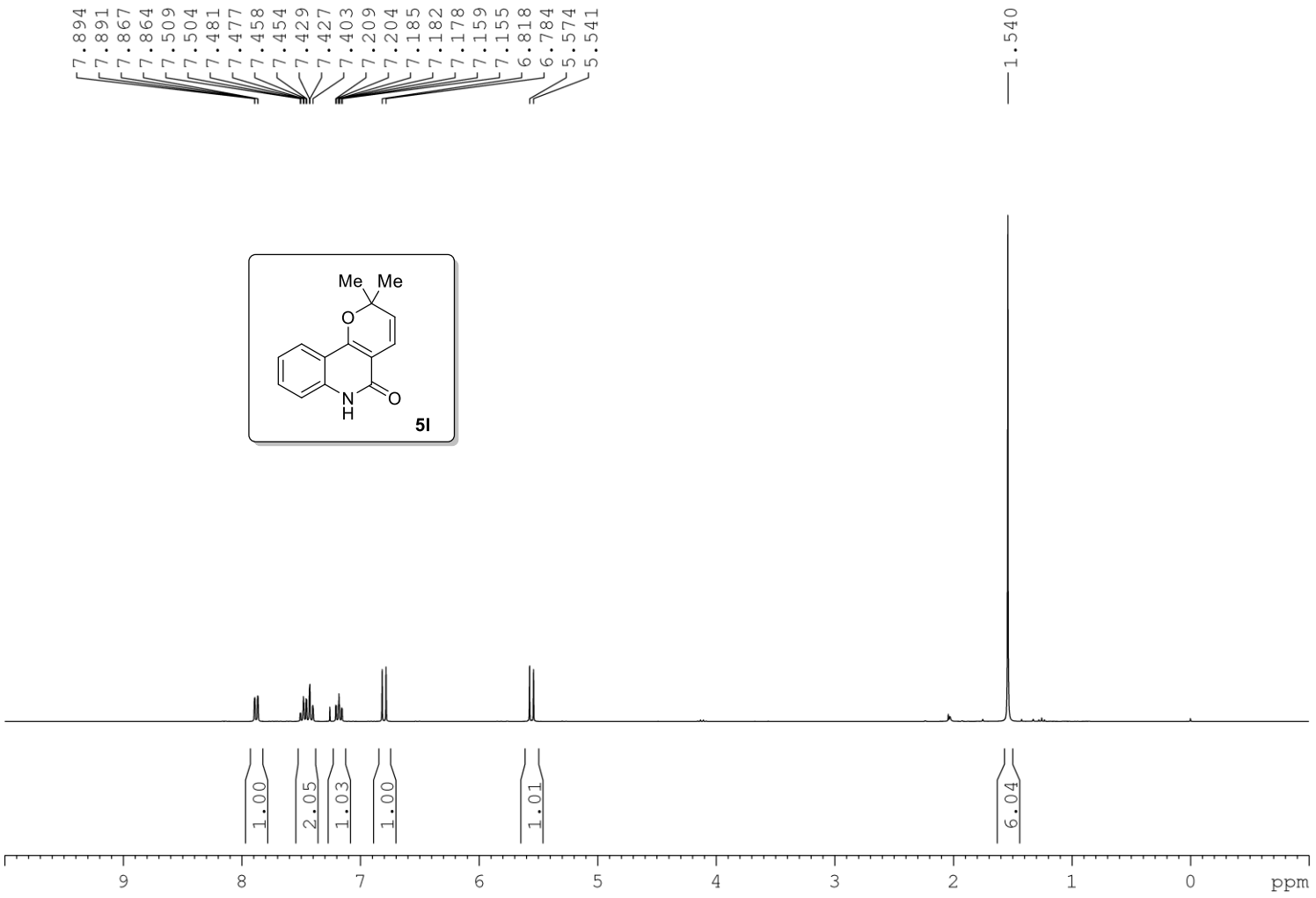


Figure S19. ^{1}H NMR Spectrum of Compound **5l** ($CDCl_3$, 300 MHz)

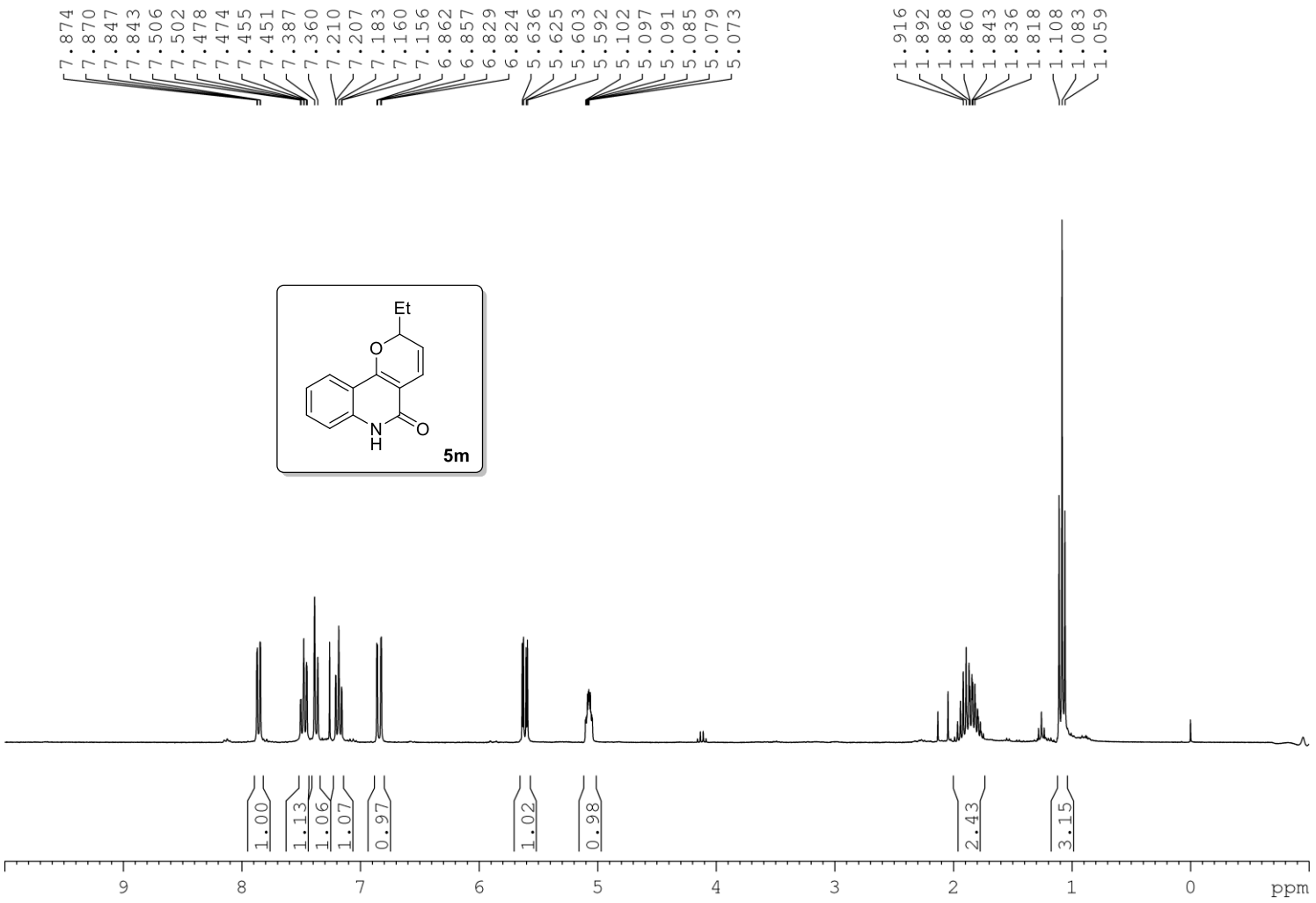


Figure S20. ^{1}H NMR Spectrum of Compound **5m** ($CDCl_3$, 300 MHz)

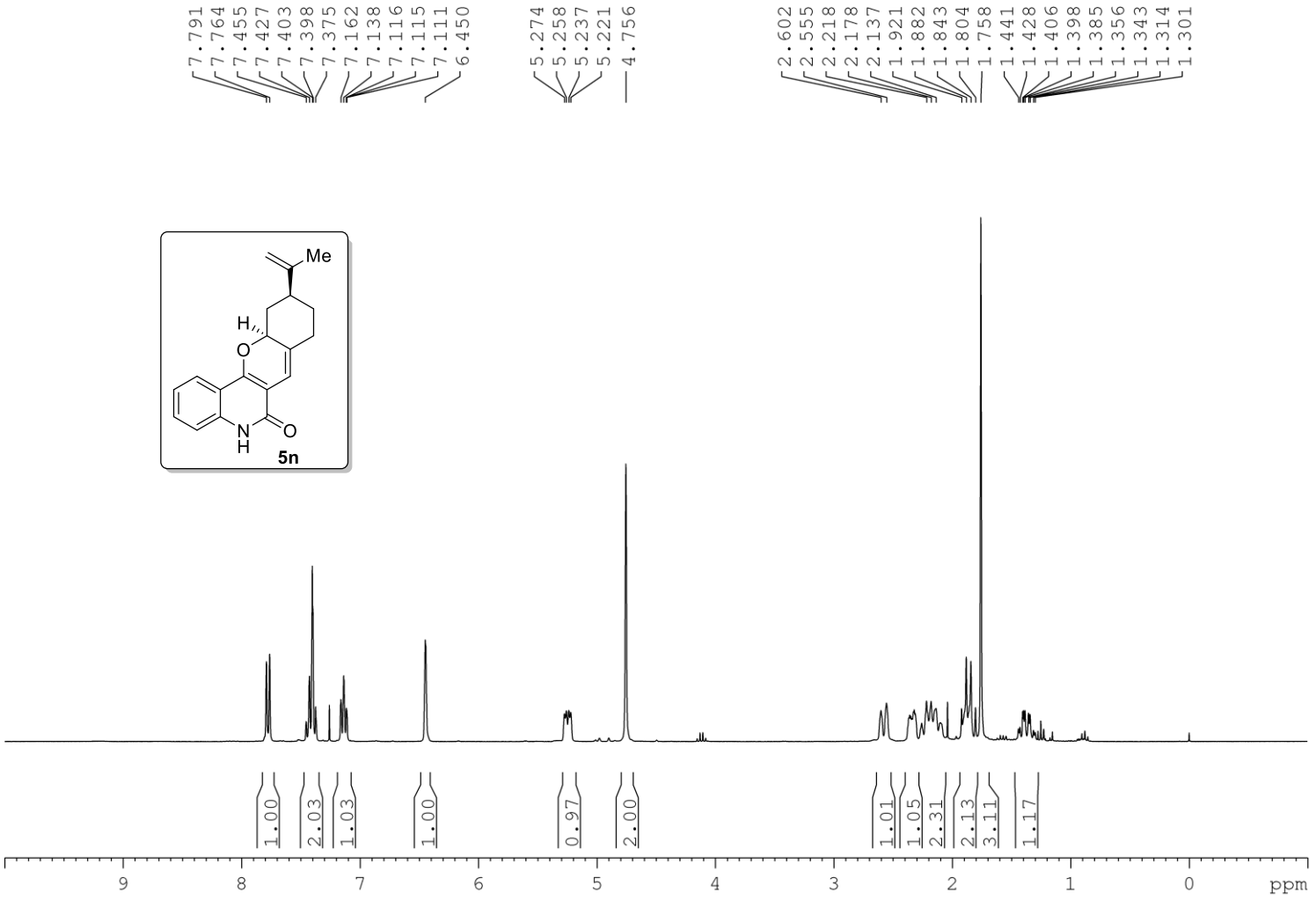


Figure S21. ^{1}H NMR Spectrum of Compound **5n** ($CDCl_3$, 300 MHz)

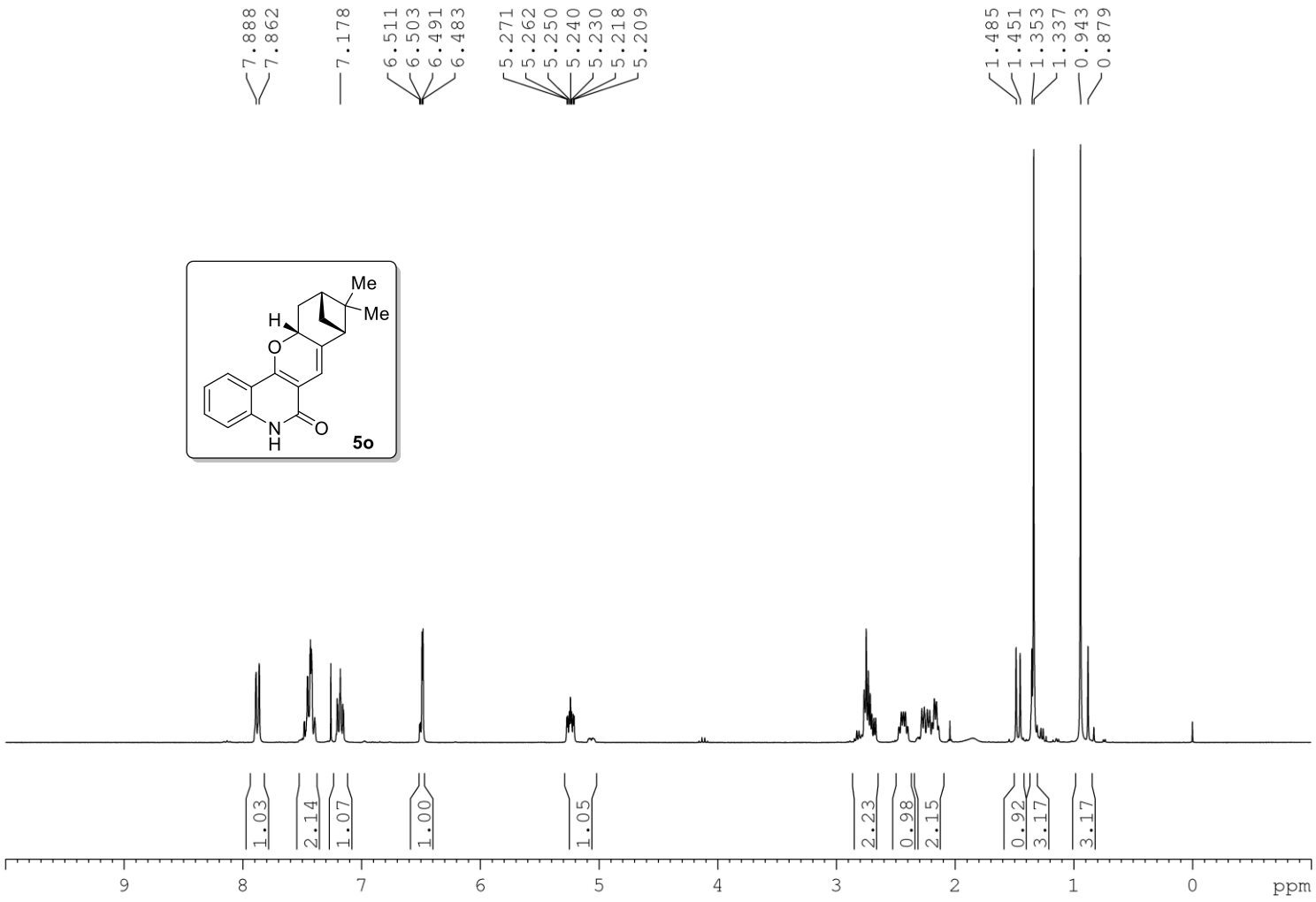


Figure S22.[1]H NMR Spectrum of Compound **5o** ($CDCl_3$, 300 MHz)

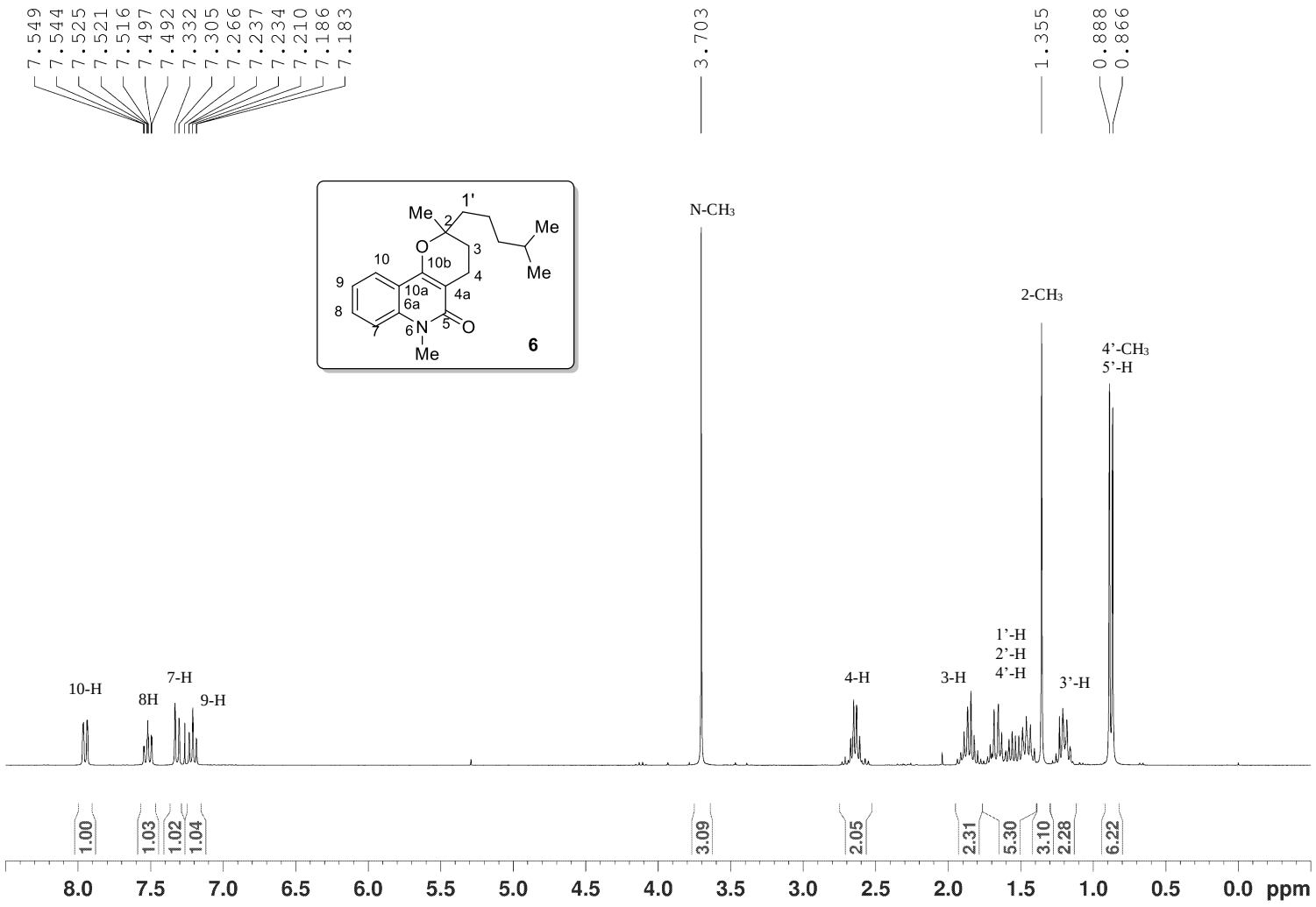


Figure S23. ^{1}H NMR Spectrum of Compound **6** ($CDCl_3$, 300 MHz)

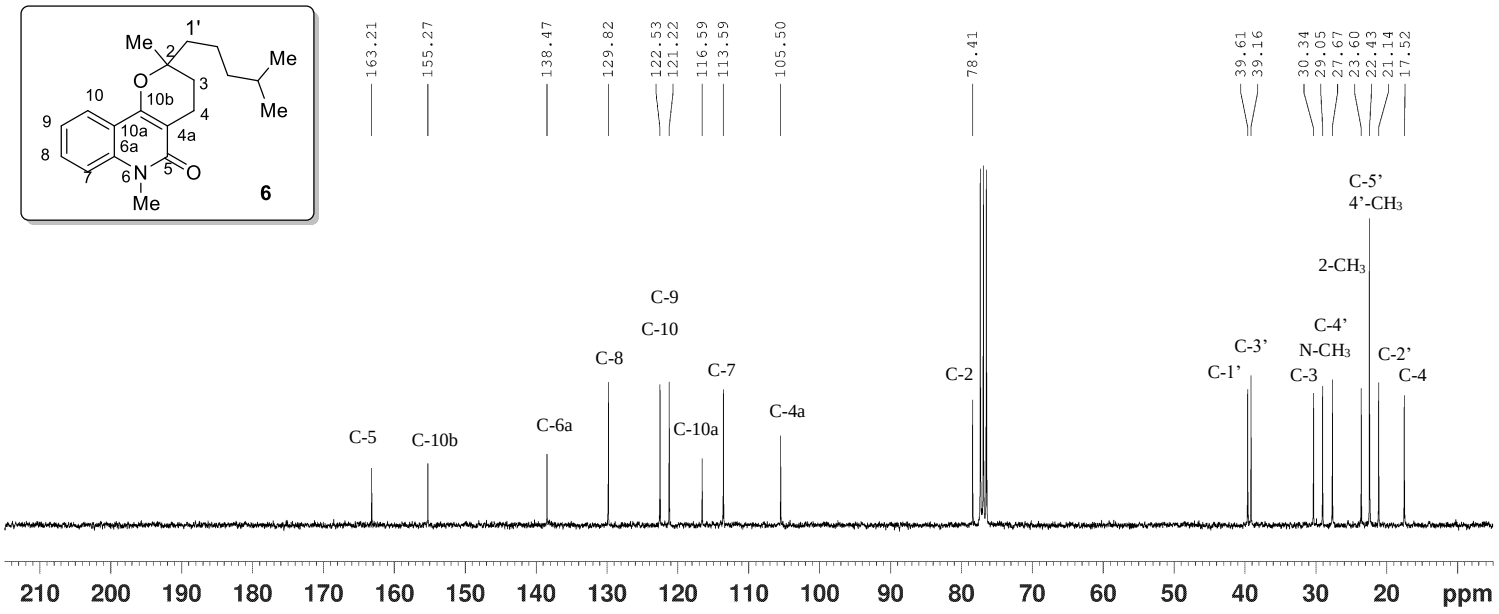


Figure S24. $^{13}C\{^{1}H\}$ NMR Spectrum of Compound **6** ($CDCl_3$, 75 MHz)

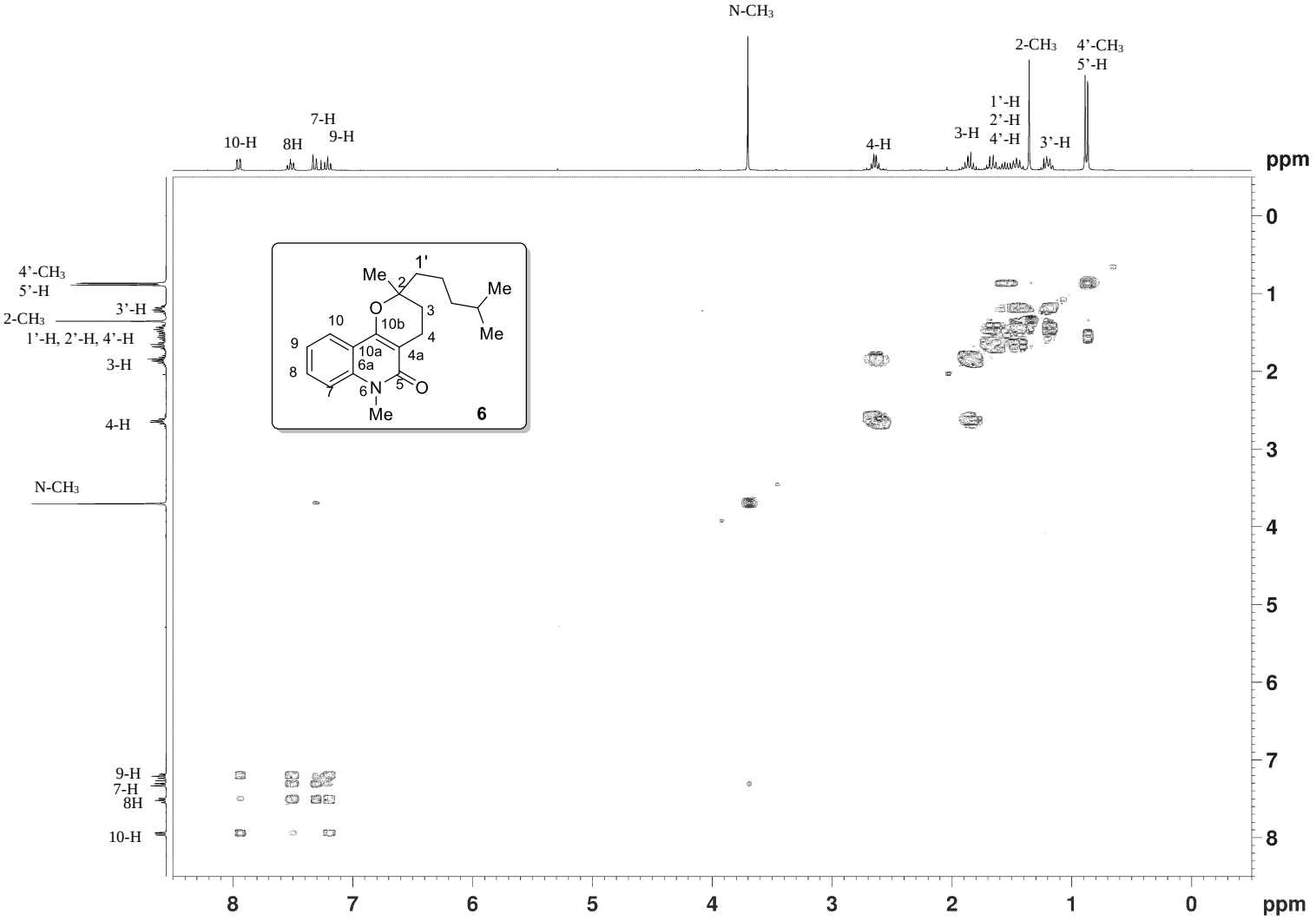


Figure S25. 2D ^{1}H-^{1}H COSY Spectrum of Compound **6** ($CDCl_3$, 300 MHz)

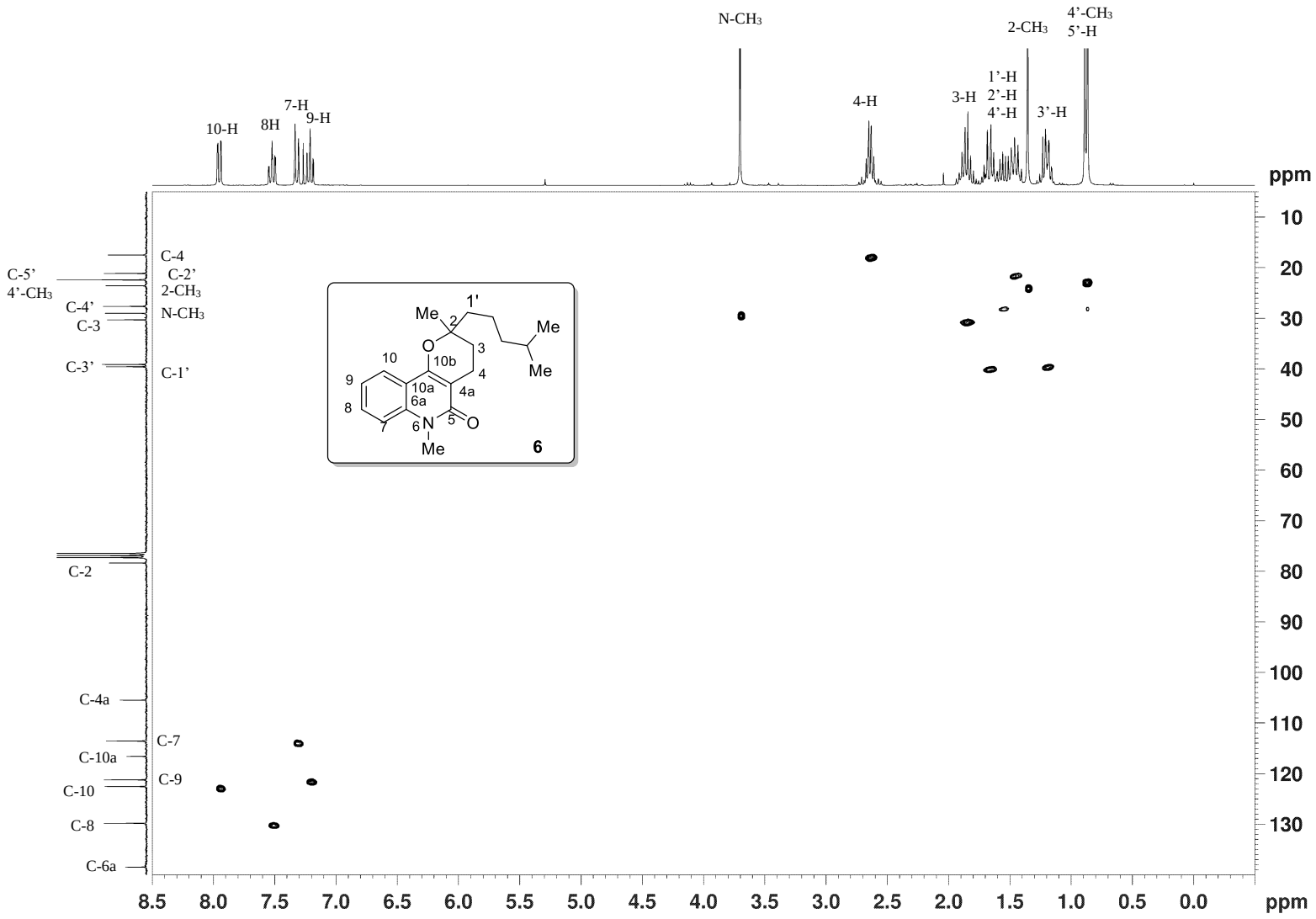


Figure S26. 2D ^{1}H-^{13}C HSQC Spectrum of Compound **6** ($CDCl_3$)

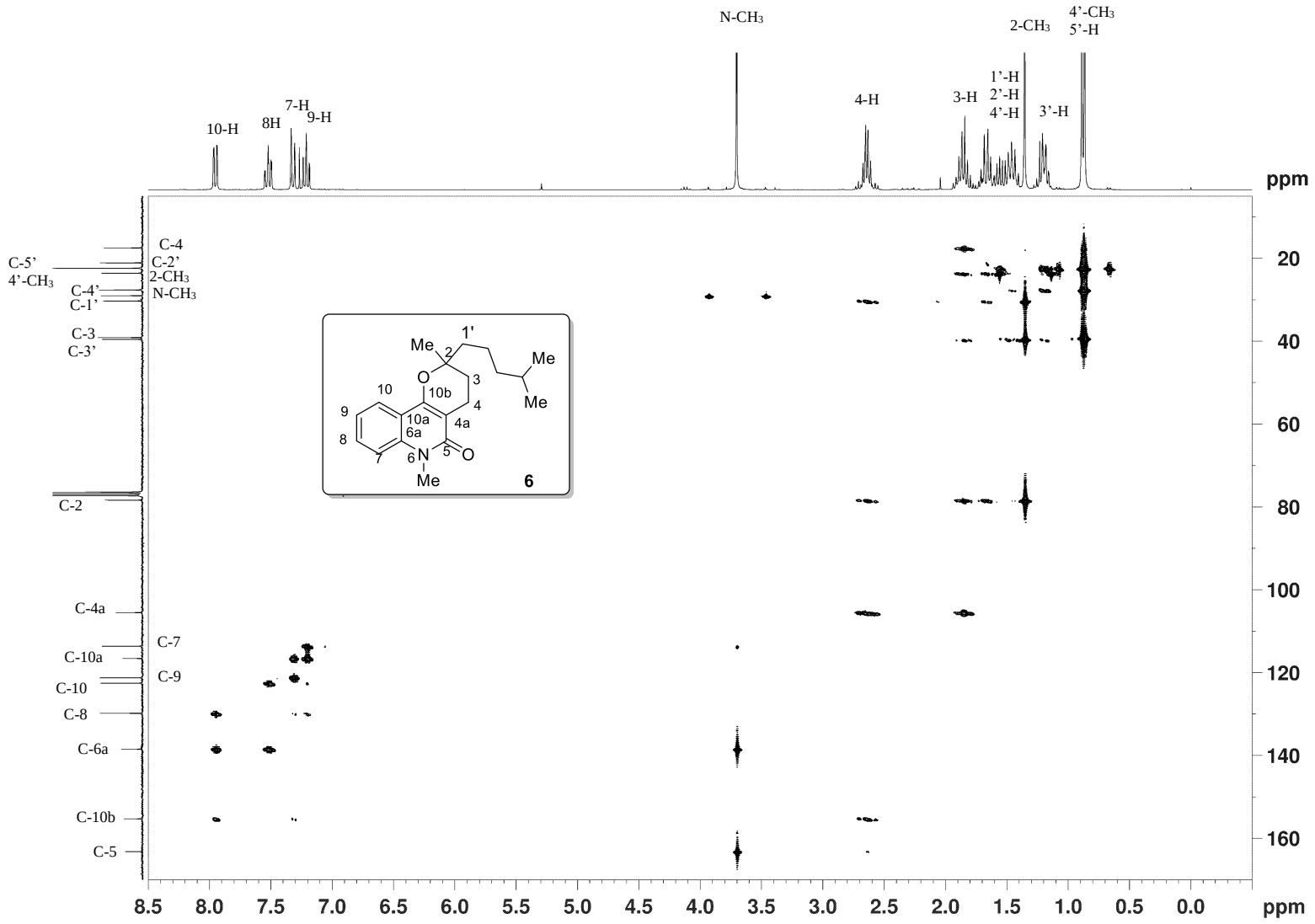


Figure S27. 2D ^{1}H-^{13}C HMBC Spectrum of Compound **6** ($CDCl_3$)

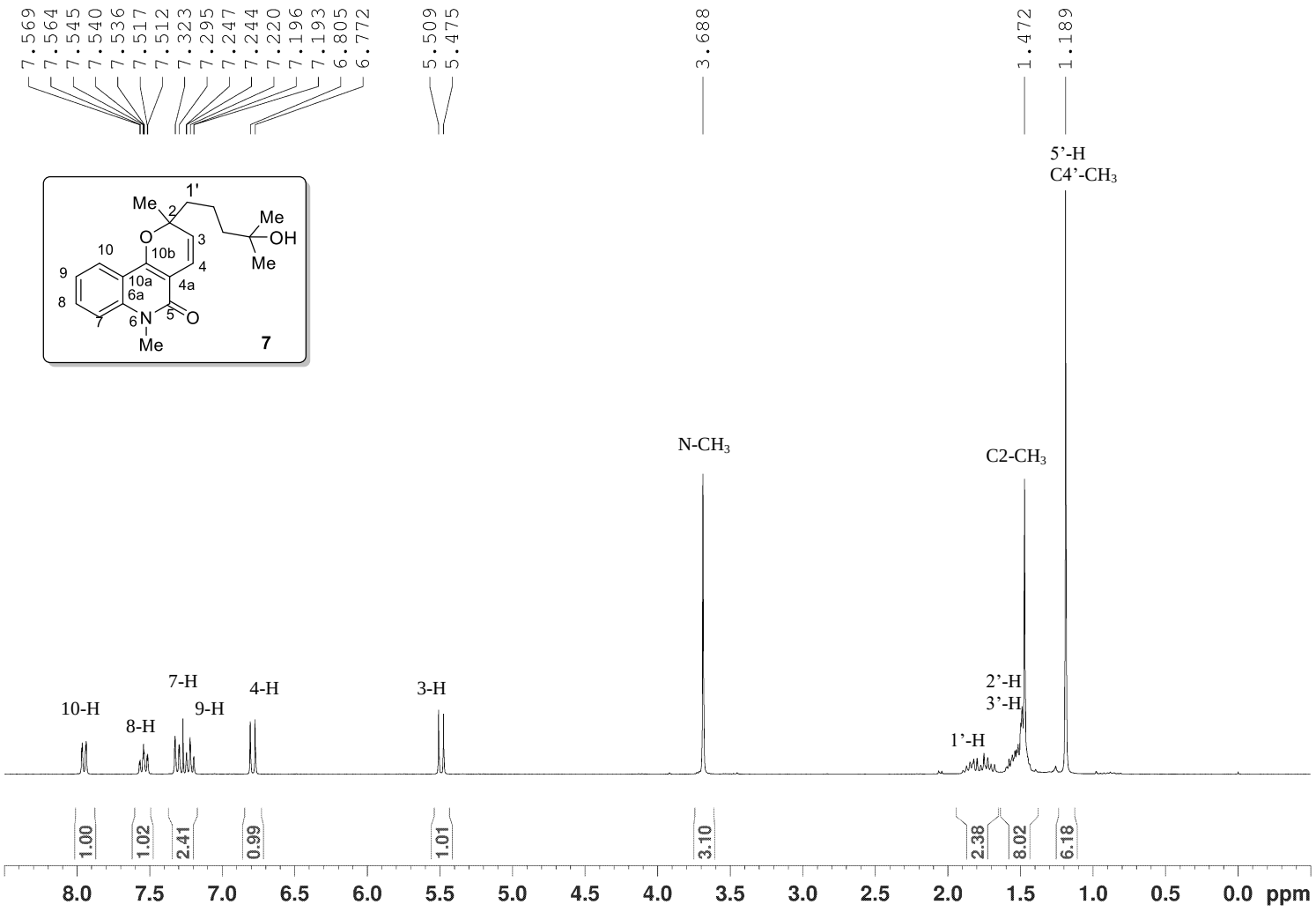


Figure S28. ^{1}H NMR Spectrum of Compound **7** ($CDCl_3$, 300 MHz)

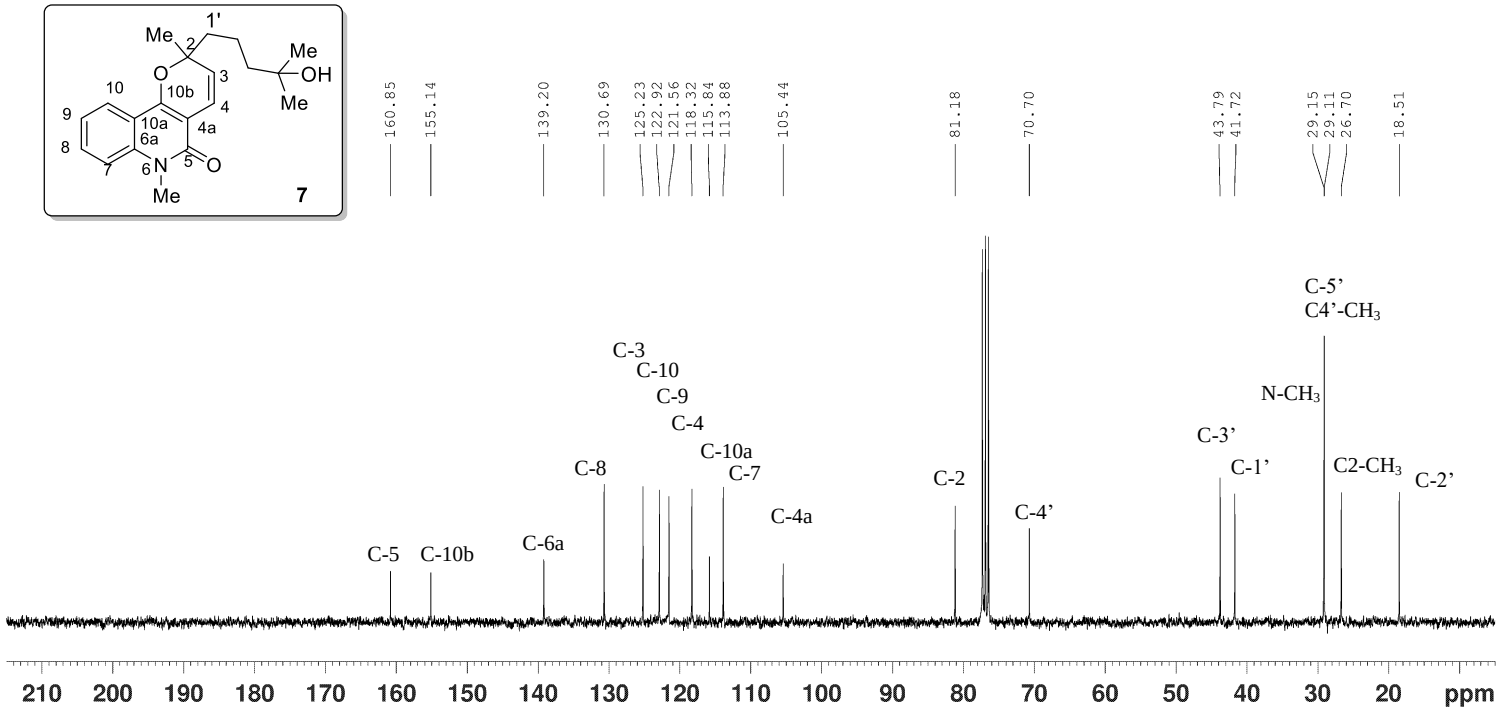


Figure S29. $^{13}C\{^{1}H\}$ NMR Spectrum of Compound **7** ($CDCl_3$, 75 MHz)

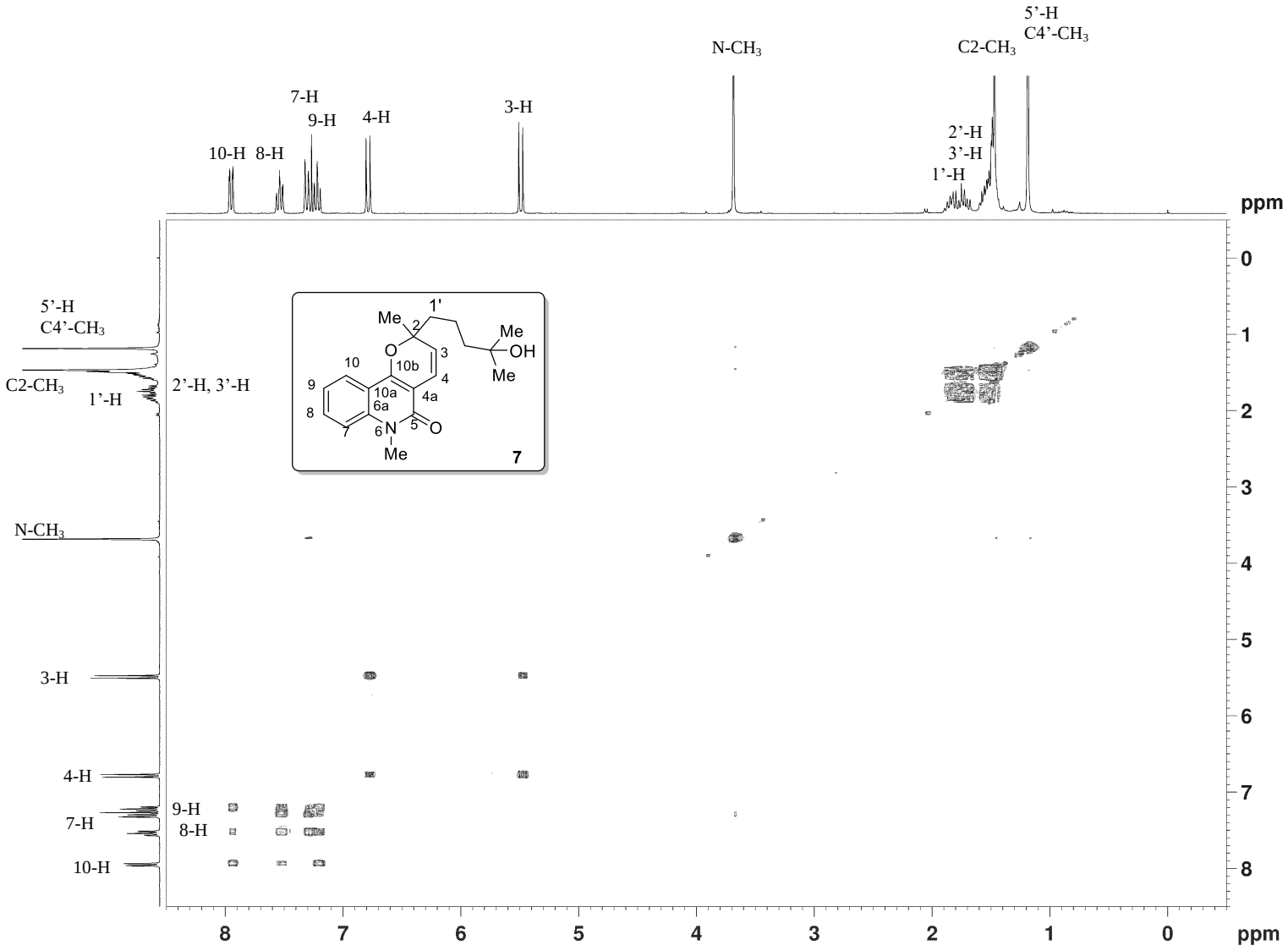


Figure S30. 2D ^{1}H-^{1}H COSY Spectrum of Compound **7** ($CDCl_3$, 300 MHz)

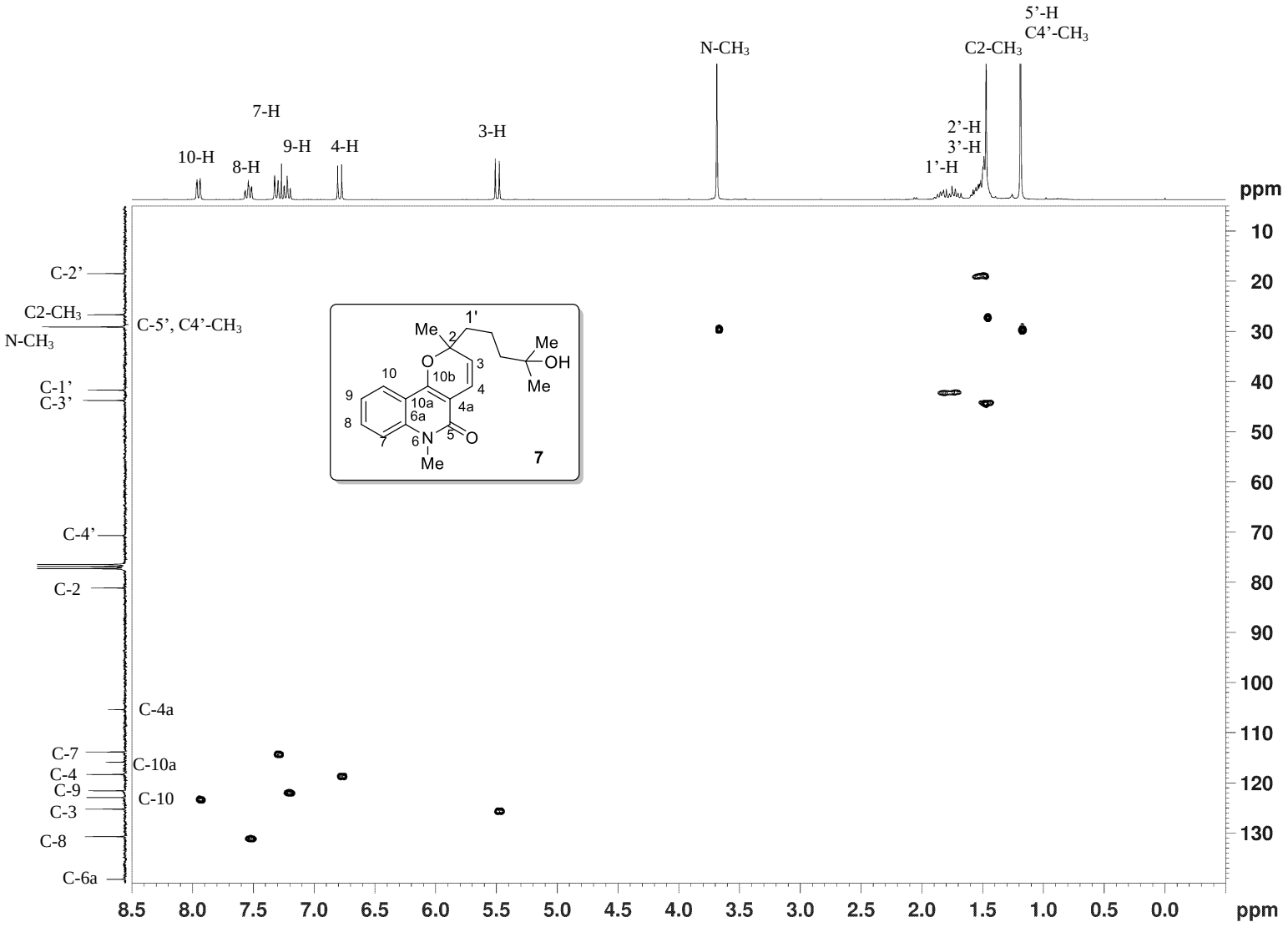


Figure S31. 2D ^{1}H-^{13}C HSQC Spectrum of Compound **7** ($CDCl_3$)

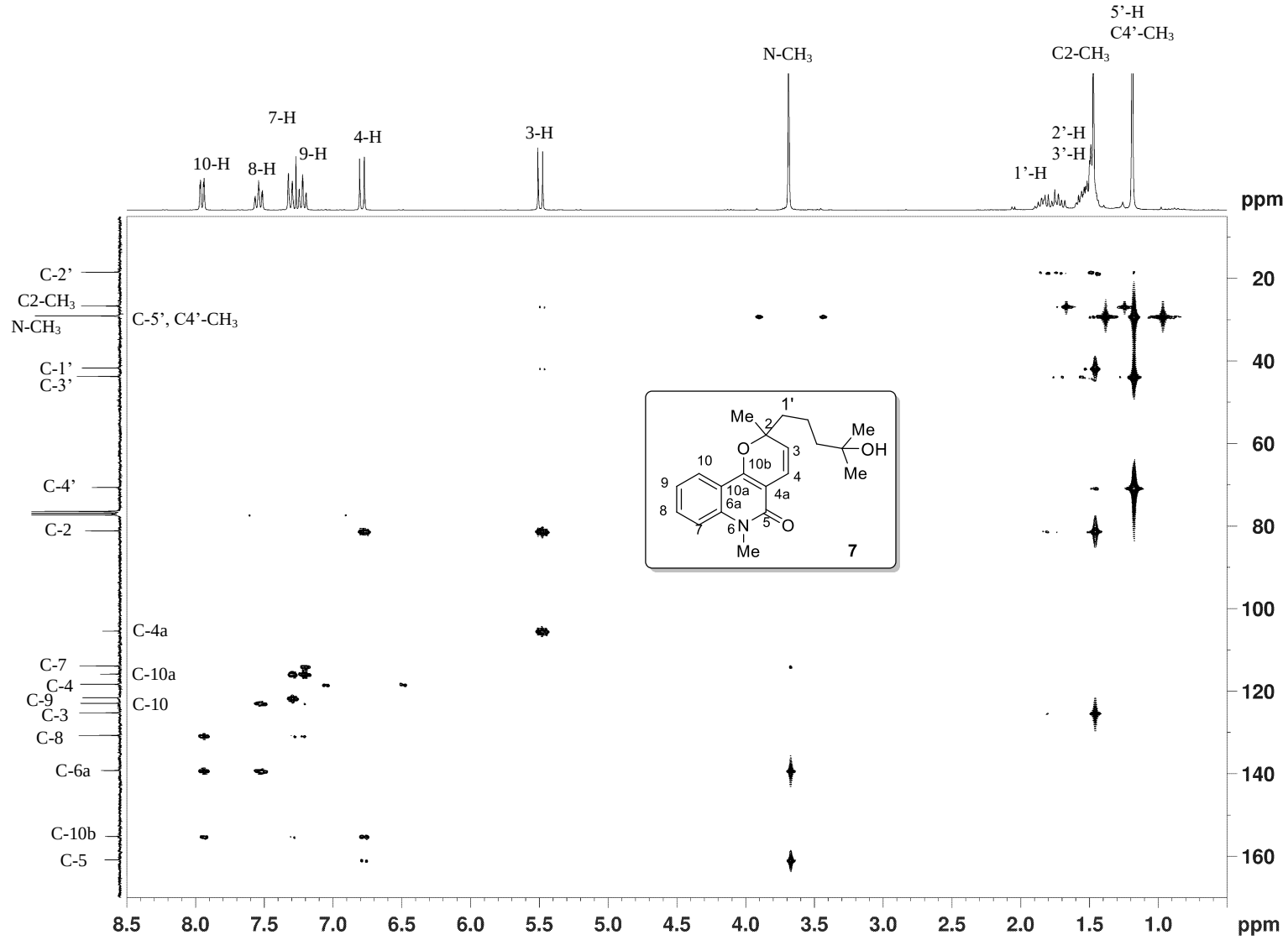


Figure S32. 2D ^{1}H-^{13}C HMBC Spectrum of Compound **7** ($CDCl_3$)

Treated with CBZ Control Treated with compound **5c**

Figure S33: Evaluation of *M. fructicola* sporulation index on wound-inoculated peaches treated with compound **5c** (right) and the commercial antifungal CBZ (left) against a control (center).