Synthesis of *cis*-fused-oxazolo/oxazino-isoquinolinones *via* photo-cascade reaction

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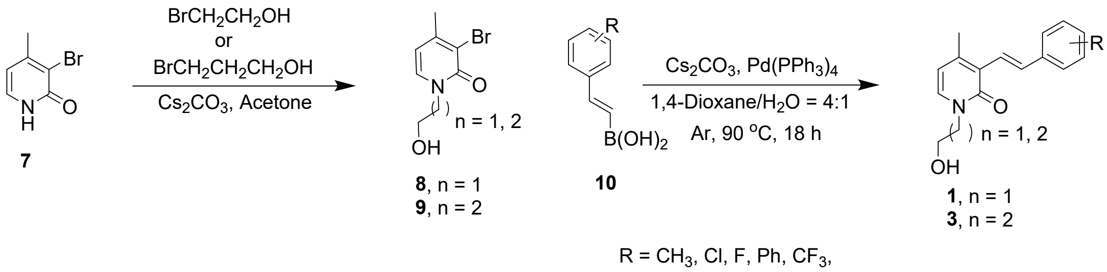
Contents

S1 General Information

^{1}H NMR and ^{13}C NMR were recorded on a Bruker-400MHz, 600 MHz Spectrometer (^{1}H: 400 MHz, ^{13}C: 101 MHz), (^{1}H: 600 MHz, ^{13}C: 151 MHz), using $CDCl_3$ as the solvent at room temperature. The chemical shifts (δ) were expressed in ppm. High-resolution mass spectra (HRMS) were recorded on a Bruker MAXIS spectrometer. All the irradiation experiments were performed in a photochemical reactor of LED 50 W light 410-415 nm.

S2. Synthetic schemes

General procedure for the synthesis of (*E*)-1-(2-hydroxyethyl/propyl)-4-methyl-3-styrylpyridin-2(1H)-ones 1 and **3**



Scheme S1 Synthesis of (*E*)-1-(2-hydroxyethyl/propyl)-4-methyl-3-styrylpyridin-2(1H)-one derivatives **1** and **3**

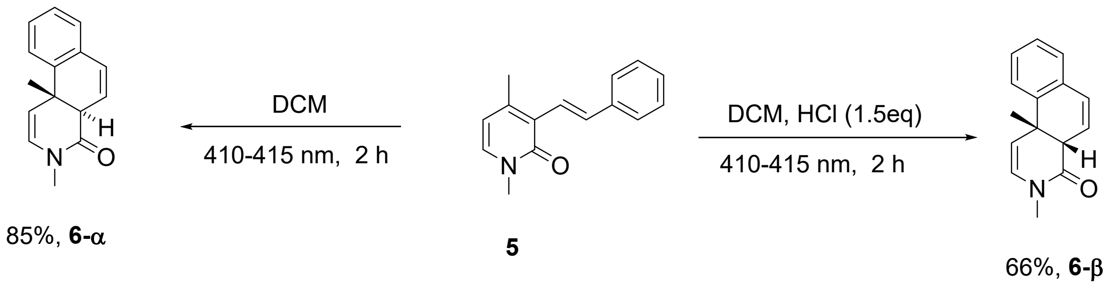
Synthesis of 3-bromo-1-(2-hydroxyethyl/propyl)-4-methylpyridin-2(1H)-ones 8 and **9**

3-bromopyridin-1(2H)-one **7** (4 mmol, 696 mg), 2-bromo-1-ethanol (2 eq, 8 mmol) or 3-bromopropan-1-ol, and Cs_2CO_3 (2 eq, 8 mmol, 2592 mg) were added to a 100 mL dry round-bottom flask, and 40 ml of acetone was added to the round-bottom flask as the reaction solvent. The mixture was stirred at room temperature for 12 hours. TLC showed that the raw material was completely consumed, and the reaction was stopped. The product was extracted with dichloromethane and water, the organic phases were combined and dried over anhydrous sodium sulfate, the organic solvent was removed by vacuum distillation, and the mixture was chromatographed on a silica gel column (CH_2Cl_2: CH_3OH = 50:1) to obtain pure 3-bromo-1-(2-hydroxyethyl/propyl)-4-

methylpyridin-2(1H)-ones **8** and **9**. [1]

Synthesis of (*E*)-1-(2-hydroxyethyl/propyl)-4-methyl-3-styrylpyridin-2(1H)-ones 1 and 3.

3-bromo-1-(2-hydroxyethyl/propyl)-4-methylpyridin-2(1H)-ones **8** or **9** (3 mmol, 782 mg), (*E*)-styrylboronic acid **10** (2 eq, 6 mmol, 296 mg), Cs_2CO_3 (2 eq, 6 mmol, 1944 mg), $Pd(PPh_3)_4$ (0.05 eq, 0.15 mmol, 173 mg) was placed in a dry 50 mL Schlenk round-bottom flask. The reaction flask was sealed and filled with argon, and the solvent dioxane and water (12 mL: 3 mL) were added to the reaction flask. The reaction mixture was reacted at 90 °C for 18 hours. TLC detected that the raw material was consumed entirely, and the reaction was stopped. After the reaction completion, the solution was cooled to room temperature. It was extracted with dichloromethane and water, and the organic phases were combined and dried over anhydrous sodium sulfate, then distilled under reduced pressure. The mixture was separated and purified by silica gel column chromatography (CH_2Cl_2: CH_3OH = 20:1) to obtain (*E*)-1-(2-hydroxyethyl/propyl)-4-methyl-3-styrylpyridin-2(1H)-ones **1** and **3**.[2]



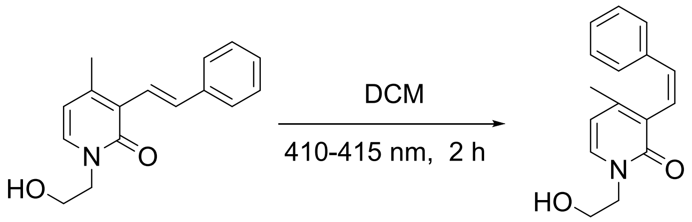
Scheme S2 Synthesis of **6(α, β)** under 410-415 nm LED 50 W light irradiation

General procedure for the synthesis of 6-α and 6-β

(*E*)-1-methyl-3-styrylpyridin-2(1H)-ones **5** (0.2 mmol) was dissolved in 40 mL of dichloromethane. The resulting mixture was deaerated (bubbling argon), degassed (ultrasound) for 30 minutes, and irradiated with 410-415 nm LED 50 W light for 2 hours to stop the reaction. The solvent was removed by vacuum distillation, and the mixture was separated and purified by silica gel column chromatography petroleum ether/ethyl acetate 4:3 to obtain product **6-α**.

A solution of **5** (0.2 mmol) in dichloromethane (40 mL) was treated with HCl (1.5 equiv). The mixture was deaerated by argon bubbling and degassed via sonication for

30 minutes. Subsequently, the reaction was irradiated with a 50 W LED (410–415 nm) for 2 hours before quenching. The solvent was then removed under reduced pressure, and the crude product was purified by silica gel column chromatography using a petroleum ether/ethyl acetate (4:3) eluent to afford the desired product **6-β**



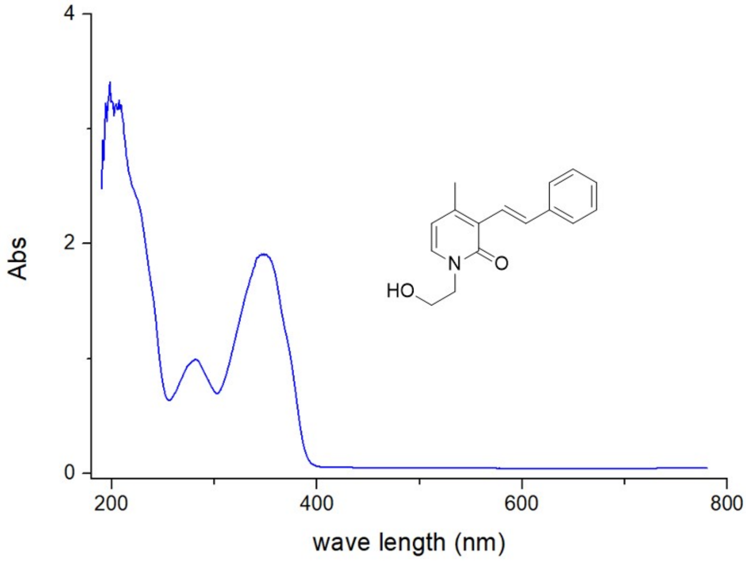
1a 80%, **A**

Scheme S3 Synthesis of **A** under 410-415 nm LED 50 W light irradiation

General procedure for the synthesis of A

(*E*)-1-(2-hydroxyethyl)-4-methyl-3-styrylpyridin-2(1H)-ones **1a** (0.2 mmol) and were dissolved in 40 mL of dichloromethane. The resulting mixture was deaerated (bubbling argon), degassed (ultrasound) for 30 minutes, and irradiated with 410-415 nm LED 50 W light for 2 hours to stop the reaction. The solvent was removed by vacuum distillation, and the mixture was separated and purified by silica gel column chromatography petroleum ether/ethyl acetate 4:3 to obtain product **A**.

S3. UV absorption spectra of 1a and 3a



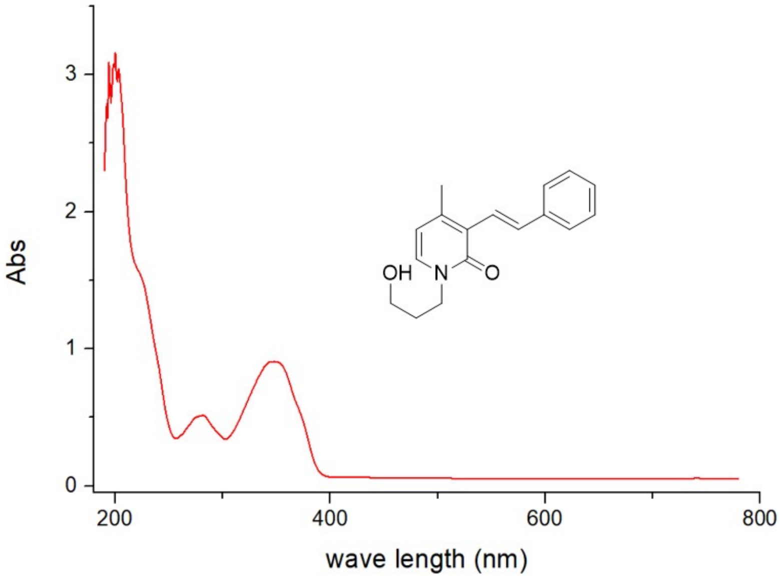


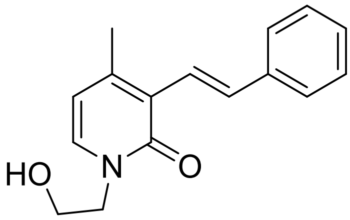
Figure S1. UV absorption spectra of **1a** and **3a** in CH_2Cl_2 (10^{-5}M).

References

[1] A. Modak, S. Rana, D. Maiti, *J. Org. Chem*., 2015, **80**, 296−303.

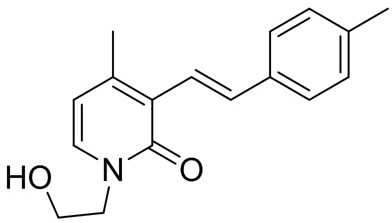
[2] F. Alonso, I. P. Beletskaya, M. Yus, *Tetrahedron*., 2008, **64**, 3047-3101.

S4. Characterisation Data



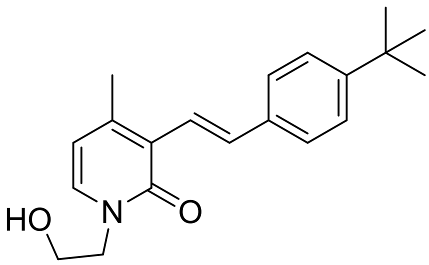
(*E*)-1-(2-hydroxyethyl)-4-methyl-3-styrylpyridin-2(1H)-one (1a)

Yield: 82% (310 mg). Yellow solid. m.p. 109.5 – 110.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 16.2 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.22 (d, *J* = 7.1 Hz, 1H), 7.11 (dd, *J* = 13.5, 12.0 Hz, 2H), 6.09 (d, *J* = 6.8 Hz, 1H), 4.18 – 4.05 (m, 2H), 3.93 (s, 2H), 3.76 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.4, 147.8, 138.5, 135.2, 133.9, 128.7, 127.7, 126.7, 125.1, 122.1, 110.5, 61.9, 53.8, 20.6. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{18}NO_2$ 256.1332, found 256.1324. IR (3395.5 cm^{-1}, 2921.45 cm^{-1}, 1638.71 cm^{-1}, 1554.87 cm^{-1}, 1355 cm^{-1})



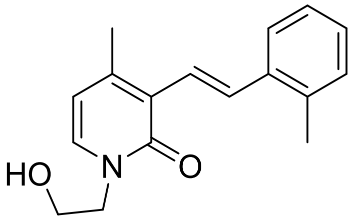
(*E*)-1-(2-hydroxyethyl)-4-methyl-3-(4-methylstyryl)pyridin-2(1H)-one (1b)

Yield: 75% (303 mg). Yellow solid. m.p. 97.2 – 98.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 16.2 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.12 (t, *J* = 7.0 Hz, 3H), 7.05 (d, *J* = 16.2 Hz, 1H), 6.08 (d, *J* = 6.8 Hz, 1H), 4.09 (d, *J* = 4.4 Hz, 2H), 3.93 (d, *J* = 4.2 Hz, 2H), 3.78 (s, 1H), 2.33 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.4, 147.4, 137.6, 135.7, 135.0, 133.9, 129.4, 126.6, 125.2, 121.1, 110.5, 61.9, 53.8, 21.4, 20.6. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1482.



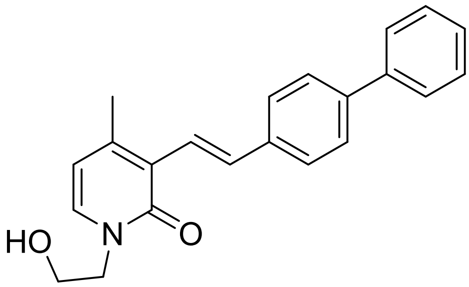
(*E*)-3-(4-(tert-butyl)styryl)-1-(2-hydroxyethyl)-4-methylpyridin-2(1H)-one (1c)

Yield: 79% (372 mg). Yellow solid. m.p. 139.7 – 140.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 16.2 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 6.9 Hz, 1H), 7.07 (d, *J* = 16.2 Hz, 1H). 6.06 (d, *J* = 6.8 Hz, 1H), 4.11 – 4.05 (m, 2H), 4.02 – 3.62 (m, 3H), 2.32 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.9, 150.8, 147.4, 135.8, 135.1, 133.6, 126.4, 125.6, 125.1, 121.4, 110.4, 61.5, 53.5, 34.7, 31.4, 20.6. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{26}NO_2$ 312.1958, found 312.1957.



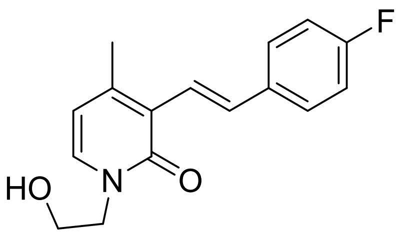
(*E*)-1-(2-hydroxyethyl)-4-methyl-3-(2-methylstyryl)pyridin-2(1H)-one (1d)

Yield: 80% (323 mg). Brown solid. m.p. 75.1 – 76.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 16.1 Hz, 1H), 7.59 (d, *J* = 7.2 Hz, 1H), 7.21 – 7.13 (m, 4H), 6.97 (d, *J* = 16.0 Hz, 1H), 6.06 (d, *J* = 6.9 Hz, 1H), 4.26 (s, 1H), 4.13 – 4.06 (m, 2H), 3.90 (t, *J* = 4.9 Hz, 2H), 2.42 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.1, 147.6, 137.6, 136.1, 135.3, 131.7, 130.2, 127.4, 126.1, 125.1, 125.0, 123.3, 110.2, 61.2, 53.2, 20.6, 20.1. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1480.



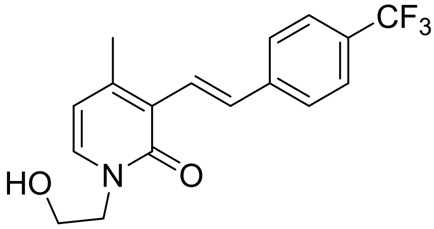
(*E*)-3-(2-([1,1'-biphenyl]-4-yl)vinyl)-1-(2-hydroxyethyl)-4-methylpyridin-2(1H)-one (1e)

Yield: 77% (386 mg). Yellow solid. m.p. 145.6 – 146.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 16.2 Hz, 1H), 7.64 – 7.58 (m, 6H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.35 (d, *J* = 7.3 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.14 (d, *J* = 6.8 H, 1Hz), 4.22 – 4.13 (m, 2H), 3.99 (s, 2H), 3.49 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.4, 147.8, 140.8, 140.3, 137.6, 135.2, 133.3, 128.9, 127.3, 127.1, 126.9, 125.1, 122.1, 110.5, 62.2, 53.8, 20.7. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{22}H_{22}NO_2$ 332.1645, found 332.1637.



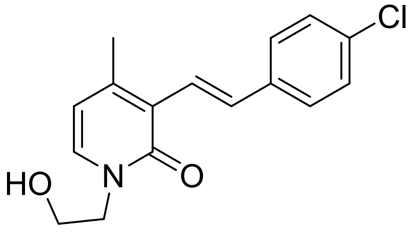
(*E*)-3-(4-fluorostyryl)-1-(2-hydroxyethyl)-4-methylpyridin-2(1H)-one (1f)

Yield: 72% (296 mg). Yellow solid. m.p. 119.8 – 120.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 16.2 Hz, 1H), 7.45 (dd, *J* = 8.0, 5.7 Hz, 2H), 7.13 (d, *J* = 6.7 Hz, 1H), 6.99 (dd, *J* = 16.6, 8.2 Hz, 3H), 6.06 (d, *J* = 6.8 Hz, 1H), 4.08 (s, 2H), 3.90 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.6 (d, *J* = 247.0 Hz), 162.1, 147.7, 135.3, 134.6 (d, *J* = 2.9 Hz), 132.5, 128.1 (d, *J* = 7.8 Hz), 124.7, 121.8, 115.6 (d, *J* = 21.5 Hz), 110.4, 61.5, 53.5, 20.5. ^{19}FNMR (376 MHz, Chloroform-*d*) δ -114.31– -114.37 (m). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{17}NO_2$ 274.1238, found 274.1230.



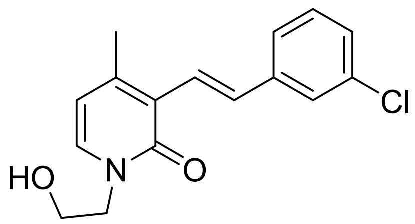
(*E*)-1-(2-hydroxyethyl)-4-methyl-3-(4-(trifluoromethyl)styryl)pyridin-2(1H)-one (1g)

Yield: 65% (315 mg). White solid. m.p. 85.4 – 86.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 16.2 Hz, 1H), 7.59 – 7.53 (m, 4H), 7.16 (t, *J* = 11.3 Hz, 2H), 6.08 (d, *J* = 6.8 Hz, 1H), 4.10 (t, *J* = 4.6 Hz, 2H), 3.93 (d, *J* = 4.5 Hz, 2H), 3.81 (s, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.1, 148.7, 142.1, 136.0, 132.0, 130.0 (q, *J* = 32.1 Hz), 126.7, 125.6 (q, *J* = 3.2 Hz), 124.4, 124.4 (q, *J* = 271.8 Hz), 124.2, 110.4, 61.4, 53.5, 20.5. ^{19}FNMR (376 MHz, Chloroform-*d*) δ -62.27 (s). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}NO_2$ 324.1206, found 324.1199.



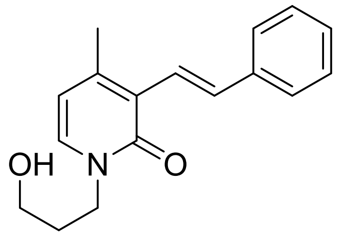
(*E*)-3-(4-chlorostyryl)-1-(2-hydroxyethyl)-4-methylpyridin-2(1H)-one (1h)

Yield: 57% (250 mg). Yellow solid. m.p. 116.5 – 116.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 16.2 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 7.12 (t, *J* = 7.0 Hz, 1H), 7.05 (d, *J* = 16.2 Hz, 1H), 6.08 (d, *J* = 6.8 Hz, 1H), 4.09 (d, *J* = 4.4 Hz, 2H), 3.93 (d, *J* = 4.2 Hz, 2H), 3.78 (s, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.4, 148.0, 137.0, 135.4, 133.2, 132.5, 128.8, 127.8, 124.7, 122.5, 110.5, 62.1, 53.8, 20.6. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{16}H_{17}NO_2$ 290.0942, found 290.0936.



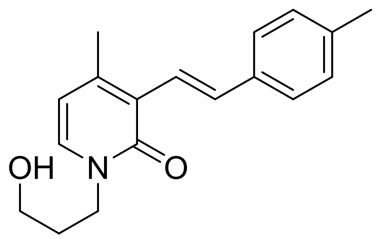
(*E*)-3-(3-chlorostyryl)-1-(2-hydroxyethyl)-4-methylpyridin-2(1H)-one. (1i)

Yield: 59% (258 mg). White solid. m.p. 104.9 – 105.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 16.1 Hz, 1H), 7.47 (s, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.7 Hz, 1H), 7.19 – 7.15 (m, 2H), 7.06 (d, *J* = 16.1 Hz, 1H), 6.08 (d, *J* = 6.8 Hz, 1H), 4.12 – 4.07 (m, 2H), 3.92 (d, *J* = 3.9 Hz, 3H), 2.32 (s, 3H).^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.1, 148.3, 140.5, 135.7, 134.5, 132.1, 129.9, 127.4, 126.2, 125.8, 124.3, 123.3, 110.4, 61.5, 53.5, 20.6. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{16}H_{17}NO_2$ 290.0942, found 290.0940.



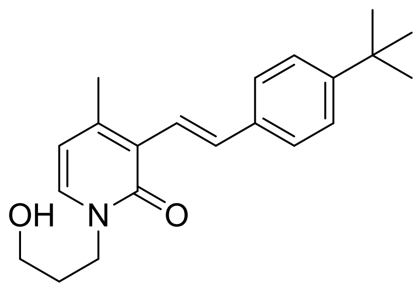
(*E*)-1-(3-hydroxypropyl)-4-methyl-3-styrylpyridin-2(1H)-one (3a)

Yield: 88% (356 mg). Yellow solid. m.p. 112.3 – 112.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 16.2 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.17 – 7.06 (m, 2H), 6.16 (d, *J* = 6.8 Hz, 1H), 4.15 (t, *J* = 6.1 Hz, 2H), 4.04 (s, 1H), 3.52 (t, *J* = 5.1 Hz, 2H), 2.37 (s, 3H), 1.92 (dt, *J* = 11.6, 5.8 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.3, 147.4, 138.5, 134.0, 134.2, 128.7, 127.7, 126.7, 125.0, 122.1, 111.2, 57.8, 45.9, 32.6, 20.7. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1480. IR (3347.31 cm^{-1}, 2922.08 cm^{-1}, 1636.02 cm^{-1}1562.09 cm^{-1}, 1322.15 cm^{-1})



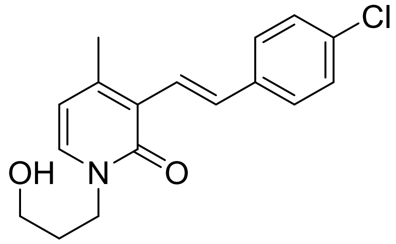
(*E*)-1-(3-hydroxypropyl)-4-methyl-3-(4-methylstyryl)pyridin-2(1H)-one (3b)

Yield: 86% (366 mg). Dark red solid. m.p. 70.2 – 70.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 16.2 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 7.09 (dd, *J* = 11.5, 8.0 Hz, 2H), 6.16 (d, *J* = 6.8 Hz, 1H), 4.23 – 4.11 (m, 2H), 3.99 (s, 1H), 3.52 (d, *J* = 4.7 Hz, 2H), 2.37 (s, 3H), 2.34 (s, 3H), 1.93 (dt, *J* = 11.5, 5.7 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.2, 147.2, 137.6, 135.7, 134.1, 129.4, 126.7, 125.2, 121.2, 111.2, 57.8, 46.1, 32.6, 21.4, 20.7. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{22}NO_2$ 284.1645, found 284.1640.



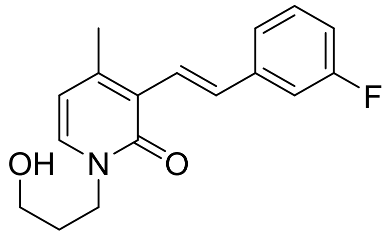
(*E*)-3-(4-(tert-butyl)styryl)-1-(3-hydroxypropyl)-4-methylpyridin-2(1H)-one (3c)

Yield: 84% (410 mg). Brown solid. m.p. 97.6 – 98.3 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 16.2 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.10 (dd, *J* = 11.5, 7.1 Hz, 2H), 6.14 (d, *J* = 6.3 Hz, 1H), 4.13 (t, *J* = 6.1 Hz, 3H), 3.53 (t, *J* = 5.3 Hz, 2H), 2.35 (s, 3H), 1.95 – 1.88 (m, 2H), 1.32 (s, 9H).^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.1, 150.8, 147.1, 135.7, 133.9, 126.4, 125.6, 125.2, 121.4, 111.1, 57.8, 46.1, 34.7, 32.5, 31.4, 20.6. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{28}NO_2$ 326.2115, found 326.2110.



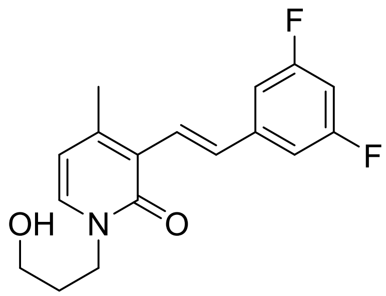
(*E*)-3-(4-chlorostyryl)-1-(3-hydroxypropyl)-4-methylpyridin-2(1H)-one (3d)

Yield: 65% (297 mg). Brown solid. m.p. 140.5 – 141.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 16.2 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.10 (dd, *J* = 19.6, 11.5 Hz, 2H), 6.16 (s, 1H), 4.15 (t, *J* = 6.1 Hz, 2H), 3.93 (s, 1H), 3.52 (t, *J* = 5.3 Hz, 2H), 2.36 (s, 3H), 1.96 – 1.90 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 163.1, 147.6, 137.0, 134.2, 133.1, 132.8, 128.7, 127.8, 124.7, 122.5, 111.1, 57.8, 45.9, 32.5, 20.5. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{17}H_{19}NO_2$ 304.1099, found 304.1093.



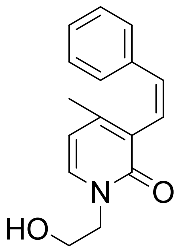
(*E*)-3-(3-fluorostyryl)-1-(3-hydroxypropyl)-4-methylpyridin-2(1H)-one (3e)

Yield: 74% (320 mg). Brown solid. m.p. 89.2 – 90.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 16.2 Hz, 1H), 7.23 (dd, *J* = 21.5, 6.8 Hz, 4H), 7.16 – 7.08 (m, 2H), 6.96 – 6.86 (m, 1H), 6.16 (d, *J* = 6.8 Hz, 1H), 4.14 (t, *J* = 6.2 Hz, 2H), 3.99 (s, 1H), 3.52 (t, *J* = 5.3 Hz, 2H), 2.36 (s, 3H), 1.94 – 1.90 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.5, 162.1, 148.1, 141.0 (d, *J* = 7.7 Hz), 134.5, 132.9, 130.0 (d, *J* = 8.4 Hz), 124.5, 123.3, 122.8, 114.5, 114.3, 112.7 (d, *J* = 21.8 Hz), 111.6, 57.9, 46.0, 32.5, 29.8, 20.6. ^{19}FNMR (376 MHz, Chloroform-*d*) δ -113.59 (d, *J* = 5.6 Hz). HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{17}H_{19}NO_2$ 288.1394, found 288.1384.



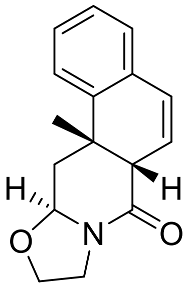
(*E*)-3-(3,5-difluorostyryl)-1-(3-hydroxypropyl)-4-methylpyridin-2(1H)-one (3f)

Yield: 72% (334 mg). Yellow solid. m.p. 128.1 – 129.2 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 16.0 Hz, 1H), 7.17 (d, *J* = 6.8 Hz, 1H), 7.09 (d, *J* = 16.0 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.70 – 6.62 (m, 1H), 6.16 (d, *J* = 6.8 Hz, 1H), 4.14 (t, *J* = 6.2 Hz, 2H), 3.55 (dd, *J* = 38.6, 33.2 Hz, 3H), 2.36 (s, 3H), 2.36 (s, 3H), 1.98 – 1.88 (m, 2H), 1.99 – 1.85 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 164.1 (d, *J* = 13.3 Hz), 162.5 (d, *J* = 13.1 Hz), 148.5, 142.2 (t, *J* = 9.2 Hz), 134.9, 131.7, 124.4, 124.0, 111.0, 109.1 (dd, *J* = 20.2, 5.0 Hz), 102.8, 102.6, 102.4, 57.8, 46.1, 32.5, 20.5. ^{19}FNMR (376 MHz, Chloroform-*d*) δ -110.44 (t, *J* = 8.0 Hz), -110.48 – -110.85 (m). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{18}NO_2$ 306.1300, found 306.1298.



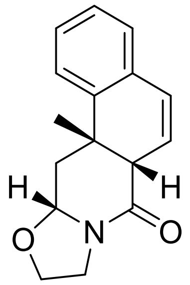
(Z)-1-(2-hydroxyethyl)-4-methyl-3-styrylpyridin-2(1H)-one (A)

Yield: 80% (103 mg). Yellow solid. m.p. 60. 1 – 61.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 (ddd, *J* = 17.8, 9.0, 4.9 Hz, 6H), 6.73 (d, *J* = 12.1 Hz, 1H), 6.39 (d, *J* = 12.2 Hz, 1H), 5.99 (t, *J* = 7.9 Hz, 1H), 4.09 (s, 2H), 3.89 (s, 3H), 1.79 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.6, 148.0, 137.8, 135.8, 133.2, 128.3, 128.1, 127.3, 127.1, 124.4, 109.8, 61.7, 53.4, 21.0. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{18}NO_2$ 256.1332, found 256.1322.



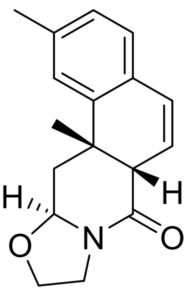
(6aS,11aS,12aS)-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b] isoquinolin-7-one (2a-α)

Yield: 36% (47 mg). Yellow solid. m.p. 64.1 – 65.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.15 (m, 2H), 7.09 (d, *J* = 6.8 Hz, 1H), 6.62 – 6.47 (m, 2H), 4.96 (d, *J* = 6.9 Hz, 1H), 4.21 – 4.00 (m, 2H), 3.89 – 3.78 (m, 1H), 3.36 (dd, *J* = 16.7, 9.9 Hz, 1H), 3.21 (s, 1H), 2.75 (d, *J* = 14.5 Hz, 1H), 2.48 (dd, *J* = 14.5, 7.0 Hz, 1H), 1.03 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.5, 132.2, 128.2, 127.7, 127.3, 127.0, 124.1, 123.4, 85.7, 63.7, 46.5, 42.9, 37.4, 36.5, 22.6. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{18}NO_2$ 256.1332, found 256.1331. IR (2923.15 cm^{-1}, 1649.74 cm^{-1}1600.76 cm^{-1}, 1302.04 cm^{-1}, 1033.41 cm^{-1}))



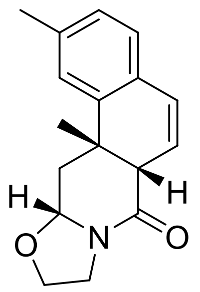
(6aS,11aR,12aS)-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b] isoquinolin-7-one (2a-β)

Yield: 34% (43 mg). Yellow solid. m.p. 104.2 – 104.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.18 (m, 3H), 7.18 – 7.11 (m, 1H), 6.62 (dd, *J* = 9.5, 3.2 Hz, 1H), 6.46 (d, *J* = 9.5 Hz, 1H), 4.93 (dd, *J* = 9.4, 5.4 Hz, 1H), 4.22 (dd, *J* = 13.9, 10.1 Hz, 1H), 4.05 – 3.88 (m, 1H), 3.43 (s, 2H), 3.41 (d, *J* = 3.1 Hz, 1H), 3.16 (s, 1H), 2.92 (dd, *J* = 12.4, 5.3 Hz, 1H), 1.92 – 1.82 (m, 1H), 1.14 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.3, 142.5, 132.9, 128.2, 128.0, 127.7, 127.1, 125.2, 121.9, 86.1, 65.1, 48.4, 42.5, 37.3, 36.5, 20.7. HRMS (ESI) m/z [M+H]$^{+}$ calcd for $C_{16}H_{18}NO_2$ 256.1332, found 256.1326. IR (2896.06 cm^{-1}, 1644.68 cm^{-1}1562.69 cm^{-1}, 1335.61 cm^{-1}, 1007.09 cm^{-1})



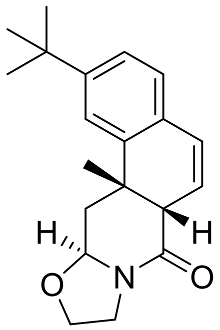
(6aS,11aS,12aS)-3,12a-dimethyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b] isoquinolin-7-one (2b-α)

Yield: 35% (47 mg). Yellow solid. m.p. 75.6 – 76.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 (d, *J* = 7.6 Hz, 3H), 6.50 (dd, *J* = 27.9, 9.9 Hz, 2H), 4.96 (d, *J* = 6.9 Hz, 1H), 4.17 – 4.05 (m, 2H), 3.88 – 3.78 (m, 1H), 3.35 (dd, *J* = 16.9, 9.8 Hz, 1H), 3.18 (s, 1H), 2.74 (d, *J* = 14.5 Hz, 1H), 2.46 (dd, *J* = 14.4, 7.0 Hz, 1H), 2.34 (s, 3H), 1.01 (s, 3H). ^{13}CNMR (101 MHz, Chloroform-*d*) δ 169.2, 142.6, 138.0, 129.6, 127.6, 127.2, 124.3, 123.0, 85.8, 63.8, 46.6, 42.9, 37.4, 36.5, 22.3, 21.7. HRMS (ESI) m/z [M+H]$^{+}$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1483.



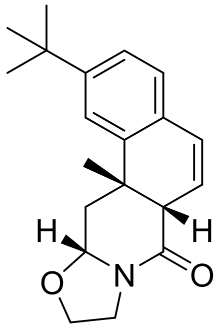
(6aS,11aR,12aS)-3,12a-dimethyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b] isoquinolin-7-one (2b-β)

Yield: 34% (46 mg). Yellow solid. m.p. 169.3 – 169.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.07 – 6.97 (m, 3H), 6.59 (d, *J* = 6.4 Hz, 1H), 6.39 (d, *J* = 9.5 Hz, 1H), 4.92 (dd, *J* = 9.4, 5.4 Hz, 1H), 4.21 (dd, *J* = 9.8, 5.9 Hz, 1H), 3.96 (dd, *J* = 13.7, 9.9 Hz, 2H), 3.42 (dd, *J* = 10.5, 7.0 Hz, 1H), 3.14 (s, 1H), 2.92 (dd, *J* = 12.4, 5.3 Hz, 1H), 2.35 (s, 3H), 1.84 (dd, *J* = 12.1, 9.7 Hz, 1H), 1.12 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.5, 142.5, 137.8, 130.3, 128.0, 127.62, 127.59, 124.1, 122.8, 86.1, 65.1, 48.5, 42.5, 37.3, 36.6, 21.7, 20.7. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1483.



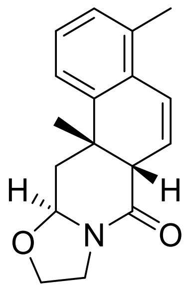
(6aS,11aS,12aS)-2-(tert-butyl)-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2c-α)

Yield: 34% (54 mg). Yellow solid. m.p. 142.1 – 142.7 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.26 – 7.22 (m, 2H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.55 (dd, *J* = 9.7, 2.9 Hz, 1H), 6.49 (dd, *J* = 9.7, 2.0 Hz, 1H), 4.98 (d, *J* = 6.8 Hz, 1H), 4.17 – 4.08 (m, 2H), 3.86 (t, *J* = 7.4 Hz, 1H), 3.41 – 3.34 (m, 1H), 3.21 (s, 1H), 2.80 (d, *J* = 14.4 Hz, 1H), 2.51 (dd, *J* = 14.4, 7.0 Hz, 1H), 1.32 (s, 9H), 1.04 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 169.2, 151.3, 142.2, 129.6, 127.5,126.9, 123.8, 123.2, 120.3, 85.8, 63.8, 46.7, 42.9, 37.5, 36.7, 35.0, 31.5, 22.4. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{20}H_{26}NO_2$ 312.1958, found 312.1954.



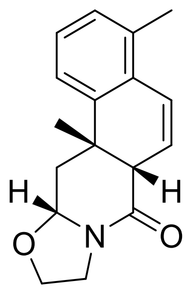
(6aS,11aR,12aS)-2-(tert-butyl)-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f] oxazolo[3,2-b]isoquinolin-7-one (2c-β)

Yield: 32% (52 mg). Yellow solid. m.p. 130.4 – 130.8 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.26 – 7.24 (m, 2H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.60 (dd, *J* = 9.5, 3.2 Hz, 1H), 6.42 (dd, *J* = 9.5, 2.6 Hz, 1H), 4.94 (dd, *J* = 9.4, 5.3 Hz, 1H), 4.28 – 4.18 (m, 1H), 4.02 – 3.95 (m, 2H), 3.46 – 3.40 (m, 1H), 3.16 (s, 1H), 2.98 (dd, *J* = 12.3, 5.4 Hz, 1H), 1.88 (dd, *J* = 12.2, 9.6 Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 167.5, 151.1, 142.2, 130.3, 127.9, 127.3, 124.3, 123.9, 118.8, 86.1, 65.2, 48.5, 42.5, 37.6, 36.6, 35.0, 31.5, 20.8. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{26}NO_2$ 312.1958, found 312.1952.



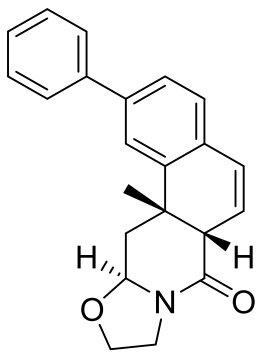
(6aS,11aS,12aS)-4,12a-dimethyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b] isoquinolin-7-one (2d-α)

Yield: 35% (48 mg). Yellow solid. m.p. 60.9 – 61.5 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.13 (t, *J* = 7.5 Hz, 1H), 7.04 (dd, *J* = 11.6, 7.5 Hz, 2H), 6.77 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.58 (dd, *J* = 10.0, 2.1 Hz, 1H), 4.95 (d, *J* = 6.9 Hz, 1H), 4.24 – 4.03 (m, 2H), 3.91 – 3.80 (m, 1H), 3.38 – 3.33 (m, 1H), 3.15 (s, 1H), 2.73 (d, *J* = 14.5 Hz, 1H), 2.45 (dd, *J* = 14.5, 7.0 Hz, 1H), 2.34 (s, 3H), 1.01 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.2, 142.8, 134.4, 130.4, 128.9, 127.8, 124.3, 124.0, 121.2, 85.8, 63.7, 45.9, 42.9, 37.6, 36.7, 22.0, 19.6. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1482.



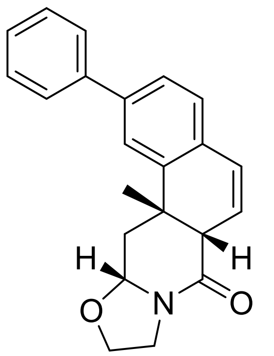
(6aS,11aR,12aS)-4,12a-dimethyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b] isoquinolin-7-one (2d-β)

Yield: 34% (47 mg). Yellow solid. m.p. 182.4 – 182.9 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.15 – 7.11 (m, 1H), 7.09 – 7.04 (m, 2H), 6.83 (dd, *J* = 9.8, 3.2 Hz, 1H), 6.48 (dd, *J* = 9.8, 2.7 Hz, 1H), 4.92 (dd, *J* = 9.4, 5.4 Hz, 1H), 4.20 (dd, *J* = 9.9, 6.0 Hz, 1H), 4.01 – 3.93 (m, 2H), 3.45 – 3.40 (m, 1H), 3.11 (t, *J* = 2.8 Hz, 1H), 2.90 (dd, *J* = 12.4, 5.4 Hz, 1H), 2.35 (s, 3H), 1.84 (dd, *J* = 12.3, 9.6 Hz, 1H), 1.12 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.5, 142.8, 134.9, 131.1, 129.0, 127.7, 125.2, 124.9, 119.7, 86.2, 65.2, 47.9, 42.4, 37.5, 36.8, 20.5, 19.6. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1491.



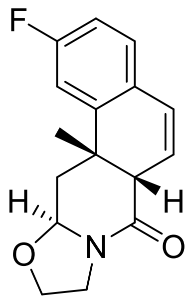
(6aS,11aS,12aS)-12a-methyl-2-phenyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2e-α)

Yield: 30% (50 mg). Yellow solid. m.p. 98.2 – 98.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 7.4 Hz, 2H), 7.44 (dd, *J* = 10.5, 5.1 Hz, 4H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 1H), 6.66 – 6.53 (m, 2H), 4.98 (d, *J* = 6.8 Hz, 1H), 4.22 – 4.05 (m, 2H), 3.85 (dd, *J* = 8.5, 4.1 Hz, 1H), 3.38 (dd, *J* = 13.2, 5.4 Hz, 1H), 3.25 (s, 1H), 2.83 (d, *J* = 14.4 Hz, 1H), 2.55 (dd, *J* = 14.4, 7.0 Hz, 1H), 1.08 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.0, 143.1, 141.1, 131.3, 128.9, 127.7, 127.5, 127.4, 127.1, 125.8, 124.3, 122.4, 85.7, 63.8, 46.6, 42.9, 37.5, 36.7, 22.4. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{22}H_{21}NNaO_2$ 354.1470, found 354.1465.



(6aS,11aR,12aS)-12a-methyl-2-phenyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo [3,2-b]isoquinolin-7-one (2e-β)

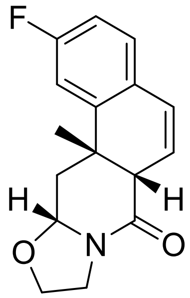
Yield: 28% (47 mg). Yellow solid. m.p. 108.1 – 108.7 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 4H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 6.68 (d, *J* = 9.5 Hz, 1H), 6.50 (d, *J* = 9.5 Hz,1H), 4.95 (dd, *J* = 9.4, 5.3 Hz, 1H), 4.27 – 4.18 (m, 1H), 3.98 (tt, *J* = 15.9, 7.9 Hz, 2H), 3.43 (dd, *J* = 16.7, 9.9 Hz, 1H), 3.22 (s, 1H), 3.01 (dd, *J* = 12.3, 5.3 Hz, 1H), 2.00 – 1.90 (m, 1H), 1.19 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.3, 143.0, 141.0, 140.9, 132.0, 129.0, 128.1, 127.8, 127.5, 127.1, 125.8, 125.3, 121.0, 86.1, 65.2, 48.5, 42.5, 37.5, 36.6, 20.8. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{22}H_{22}NO_2$ 332.1651, found 332.1656.



(6aS,11aS,12aS)-2-fluoro-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2f-α)

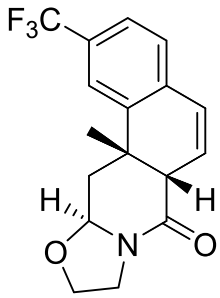
Yield: 30% (42 mg). Yellow solid. m.p. 62.6 – 63.4 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.08 – 7.03 (m, 1H), 6.88 (dt, *J* = 16.7, 6.6 Hz, 2H), 6.49 (dd, *J* = 11.1, 6.8 Hz, 2H), 4.94 (t, *J* = 6.5 Hz, 1H), 4.16 – 4.05 (m, 2H), 3.89 – 3.79 (m, 1H), 3.36 (dd, *J* = 13.2, 5.2 Hz, 1H), 3.17 (s, 1H), 2.66 (d, *J* = 14.4 Hz, 1H), 2.43 (dd, *J* = 14.4, 7.0 Hz, 1H), 1.00 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.7, 162.6 (d, *J* = 246.7 Hz), 145.0 (d, *J* = 6.8 Hz), 128.6 (dd, *J* = 24.3, 5.4 Hz), 128.49 (d, *J* = 2.7 Hz), 126.7, 123.3, 113.56 (d, *J* = 21.5 Hz), 111.05 (d, *J* = 22.9 Hz), 85.5, 63.8, 46.1, 42.9, 37.2, 36.7, 22.0. ^{19}FNMR

(376 MHz, Chloroform-*d*) δ -112.49 – -112.54 (m). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{17}NO_2$ 274.1238, found 274.1238.



(6aS,11aR,12aS)-2-fluoro-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2f-β)

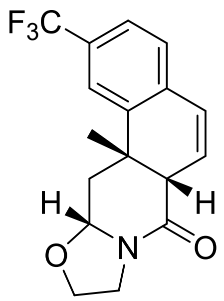
Yield: 28% (39 mg). Yellow solid. m.p. 92.4 – 92.8 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.10 (dd, *J* = 8.2, 5.9 Hz, 1H), 6.97 – 6.88 (m, 2H), 6.61 – 6.52 (m, 1H), 6.41 (dd, *J* = 9.5, 2.5 Hz, 1H), 4.91 (dd, *J* = 9.4, 5.4 Hz, 1H), 4.20 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.99 – 3.90 (m, 2H), 3.50 – 3.35 (m, 1H), 3.12 (s, 1H), 2.82 (dd, *J* = 12.3, 5.4 Hz, 1H), 1.90 – 1.82 (m, 1H), 1.12 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.7, 162.5 (d, *J* = 246.7 Hz), 145.0 (d, *J* = 6.8 Hz), 128.7 (d, *J* = 8.0 Hz), 128.5, 126.7, 123.3 (d, *J* = 2.1 Hz), 113.5 (d, *J* = 21.5 Hz), 111.0 (d, *J* = 22.9 Hz), 85.5, 63.7, 46.1, 42.9, 37.2, 36.7, 23.0. ^{19}FNMR (376 MHz, Chloroform-*d*) δ -102.97 – -103.04 (m). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{17}NO_2$ 274.1238, found 274.1240.



(6aS,11aS,12aS)-12a-methyl-2-(trifluoromethyl)-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f] oxazolo[3,2-b]isoquinolin-7-one (2g-α)

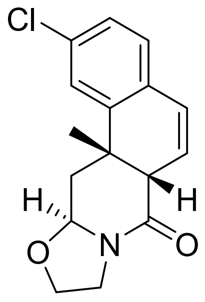
Yield: 26% (43 mg). Yellow solid. m.p. 110.2 – 110.9 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.46 – 7.39 (m, 2H), 7.17 (d, *J* = 7.7 Hz, 1H), 6.69 – 6.54 (m, 2H), 4.96 (d, *J* = 6.9 Hz, 1H), 4.14 – 4.05 (m, 2H), 3.84 (t, *J* = 10.0 Hz, 1H), 3.40 – 3.31 (m, 1H), 3.21 (s, 1H), 2.76 (d, *J* = 14.4 Hz, 1H), 2.48 (dd, *J* = 14.4, 7.0 Hz, 1H), 1.02 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.3, 143.2, 135.5, 130.0, 129.82 (d, *J* = 32.1 Hz), 129.7, 127.4, 127.0, 126.8, 125.6, 124.20 (d, *J* = 272.3 Hz), 124.1 (d, *J* = 3.7

Hz), 122.8, 120.4 (d, J = 3.5 Hz), 85.5, 63.7, 46.3, 42.9, 37.1, 36.6, 22.1.^{19}FNMR (376 MHz, Chloroform-d) δ -62.13 (s). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}NO_2$ 324.1206, found 324.1203.



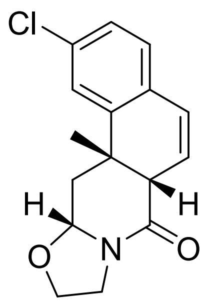
(6aS,11aR,12aS)-12a-methyl-2-(trifluoromethyl)-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f] oxazolo[3,2-b]isoquinolin-7-one (2g-β)

Yield: 24% (40 mg). Yellow solid. m.p. 130.5 – 131.2 °C. ^{1}HNMR (400 MHz, Chloroform-d) δ 7.70 – 7.50 (m, 2H), 7.46 (d, J = 7.9 Hz, 1H), 7.35 (t, J = 4.1 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 5.07 (dd, J = 9.8, 4.3 Hz, 1H), 4.24 (dd, J = 7.8, 4.5 Hz, 1H), 4.02 – 3.91 (m, 2H), 3.63 (d, J = 3.9 Hz, 2H), 3.55 – 3.49 (m, 1H), 2.93 (dd, J = 12.3, 4.3 Hz, 1H), 1.79 (dd, J = 12.2, 9.9 Hz, 1H), 1.32 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 161.2, 143.7, 137.3, 133.9, 132.9, 132.0, 130.79 (d, J = 251.2 Hz), 129.5, 128.9, 128.6 (d, J = 11.9 Hz), 123.4 (d, J = 3.4 Hz), 120.9 (d, J = 3.8 Hz), 84.9, 65.2, 43.3, 38.2, 36.7, 30.7, 28.1. ^{19}FNMR (376 MHz, Chloroform-d) δ -62.85 (s). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}NO_2$ 324.1206, found 324.1206.



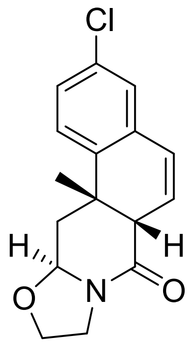
(6aS,11aS,12aS)-2-chloro-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2h-α)

Yield: 24% (35 mg). Yellow solid. m.p. 116.3 – 116.2 °C. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.16 (d, J = 7.1 Hz, 2H), 7.02 (d, J = 8.4 Hz, 1H), 6.59 – 6.48 (m, 2H), 4.96 (d, J = 6.9 Hz, 1H), 4.18 – 4.03 (m, 2H), 3.88 – 3.79 (m, 1H), 3.37 (dd, J = 13.4, 4.6 Hz, 1H), 3.18 (s, 1H), 2.70 (d, J = 14.4 Hz, 1H), 2.45 (dd, J = 14.4, 7.0 Hz, 1H), 1.02 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 144.3, 133.6, 130.6, 128.4, 127.1, 126.8, 124.6, 124.0, 85.5, 63.8, 46.2, 42.9, 37.2, 36.7, 22.1. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}NO_2$ 290.0942, found 290.0945.



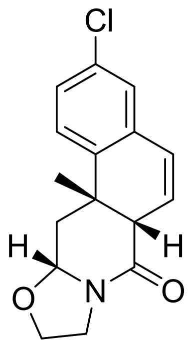
(6aS,11aR,12aS)-2-chloro-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2h-β)

Yield: 22% (32 mg). Yellow solid. m.p. 95.6 – 96.2 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.13 (d, *J* = 5.9 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.52 (dd, *J* = 9.5, 3.0 Hz, 1H), 6.42 (dd, *J* = 9.5, 1.9 Hz, 1H), 4.85 (dd, *J* = 9.3, 5.4 Hz, 1H), 4.17 – 4.13 (m, 1H), 3.94 – 3.88 (m, 2H), 3.38 – 3.34 (m, 1H), 3.06 (s, 1H), 2.80 (dd, *J* = 12.3, 5.3 Hz, 1H), 1.82 – 1.77 (m, 1H), 1.09 (d, *J* = 18.8 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.8, 144.2, 133.4, 131.3, 128.7, 127.2, 127.1, 125.6, 122.6, 85.8, 65.1, 48.0, 42.4, 37.4, 36.4, 20.4. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}NO_2$ 290.0942, found 290.0925.



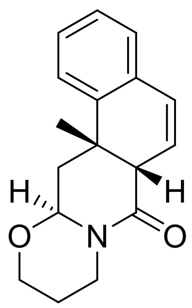
(6aS,11aS,12aS)-3-chloro-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2i-α)

Yield: 22% (33 mg). Yellow solid. m.p. 90.4 – 91.2 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.19 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.11 – 7.06 (m, 1H), 6.98 (dd, *J* = 7.4, 1.1 Hz, 1H), 6.56 (dd, *J* = 9.7, 2.1 Hz, 1H), 6.48 (dd, *J* = 9.7, 2.9 Hz, 1H), 4.93 (dd, *J* = 7.2, 2.6 Hz, 1H), 4.14 (td, *J* = 7.8, 3.6 Hz, 1H), 3.97 – 3.85 (m, 2H), 3.55 (dd, *J* = 14.7, 2.5 Hz, 1H), 3.47 – 3.42 (m, 1H), 3.25 (s, 1H), 2.64 (dd, *J* = 14.7, 7.2 Hz, 1H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.6, 140.9, 134.0, 132.7, 127.9, 127.0, 126.8, 125.8, 124.9, 85.6, 63.7, 46.4, 42.9, 37.2, 36.3, 22.2. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}NO_2$ 290.0942, found 290.0941.



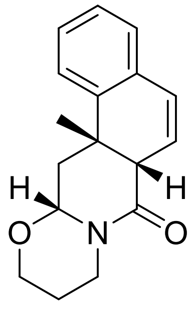
(6aS,11aR,12aS)-3-chloro-12a-methyl-6a,9,10,11a,12,12a-hexahydro-7H-benzo[f]oxazolo[3,2-b]isoquinolin-7-one (2i-β)

Yield: 20% (30 mg). Yellow solid. m.p. 110.5 – 111.2 °C. ^{1}H NMR ((400 MHz, Chloroform-*d*) δ 7.17 (d, *J* = 10.4 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.06 (d, *J* = 2.1 Hz, 1H), 6.59 (dd, *J* = 9.8, 2.1 Hz, 1H), 6.51 – 6.45 (m, 1H), 4.94 (d, *J* = 6.8 Hz, 1H), 4.08 (dd, *J* = 8.2, 4.0 Hz, 2H), 3.89 – 3.80 (m, 1H), 3.39 – 3.31 (m, 1H), 3.17 (s, 1H), 2.70 (d, *J* = 14.4 Hz, 1H), 2.42 (dd, *J* = 14.4, 7.0 Hz, 1H), 0.99 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.1, 138.5, 135.6, 132.8, 131.5, 128.1, 128.0, 126.8, 124.0, 85.6, 64.4, 47.4, 42.8, 39.4 (d, *J* = 5.6 Hz), 19.1. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}NO_2$ 290.0942, found 290.0940.



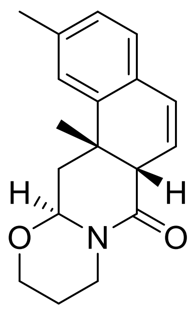
(6aS,12aS,13aS)-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3]oxazino[3,2-b]isoquinolin-7-one (4a-α)

Yield: 23% (32 mg). Yellow solid. m.p. 66.5 – 67.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.09 (m, 5H), 6.58 (s, 2H), 4.93 (dd, *J* = 26.2, 9.9 Hz, 2H), 4.16 (dd, *J* = 11.4, 4.4 Hz, 1H), 3.77 (t, *J* = 11.0 Hz, 1H), 3.11 (s, 1H), 2.81 (t, *J* = 11.5 Hz, 1H), 2.61 (d, *J* = 14.2 Hz, 1H), 2.35 (dd, *J* = 14.2, 6.2 Hz, 1H), 1.95 – 1.86 (m, 1H), 1.54 (d, *J* = 13.4 Hz, 1H), 1.21 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.1, 132.5, 128.0, 127.6, 127.4, 126.9, 125.2, 122.4, 85.5, 68.7, 47.5, 41.2, 38.9, 36.3, 25.7, 21.4. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1474. IR (2923.04 cm^{-1}, 1645.74 cm^{-1}1447.68 cm^{-1}, 1305.51 cm^{-1}, 1060.22 cm^{-1})



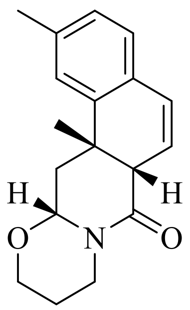
(6aS,12aR,13aS)-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3]oxazino [3,2-b]isoquinolin-7-one (4a-β)

Yield: 56% (56 mg). Yellow solid. m.p. 124.1 – 124.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.19 (m, 3H), 7.14 – 7.10 (m, 1H), 6.57 (dd, *J* = 11.7, 2.1 Hz, 2H), 4.91 – 4.77 (m, 2H), 4.14 (d, *J* = 11.4 Hz, 1H), 3.74 (t, *J* = 13.1 Hz, 1H), 3.24 (s, 1H), 2.82 (dd, *J* = 19.4, 6.3 Hz, 2H), 2.02 (d, *J* = 13.0 Hz, 1H), 1.96 – 1.85 (m, 1H), 1.61 (d, *J* = 13.7 Hz, 1H), 1.02 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.2, 147.5, 140.8, 140.3, 137.6, 134.1, 133.6, 128.9, 127.3, 127.8, 127.0, 125.0, 122.2, 111.2, 57.8, 46.0, 32.6, 20.7. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_2$ 270.1489, found 270.1476. IR (2922.93 cm^{-1}, 1641.76 cm^{-1}1450.05.76 cm^{-1}, 1344.04 cm^{-1}, 1075.13 cm^{-1}))



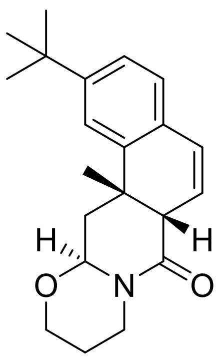
(6aS,12aS,13aS)-2,13a-dimethyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3]oxazino [3,2-b]isoquinolin-7-one (4b-α)

Yield: 20% (29 mg). Yellow solid. m.p. 140.3 – 140.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.00 (s, 3H), 6.59 – 6.49 (m, 2H), 4.92 (dd, *J* = 23.4, 9.7 Hz, 2H), 4.22 – 4.11 (m, 1H), 3.76 (t, *J* = 11.9 Hz, 1H), 3.08 (s, 1H), 2.81 (t, *J* = 11.5 Hz, 1H), 2.61 (d, *J* = 14.2 Hz, 1H), 2.33 (s, 3H), 1.89 (t, *J* = 17.0 Hz, 1H), 1.59 (s, 2H), 1.20 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7, 137.7, 129.9, 127.4, 127.4, 127.3, 124.1, 123.3, 85.5, 68.7, 47.6, 41.2, 38.9, 36.3, 25.7, 21.7, 21.3. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{22}NO_2$ 284.1645, found 284.1636.



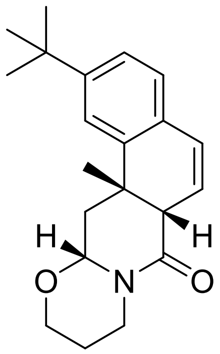
(6aS,12aR,13aS)-2,13a-dimethyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3]oxazino [3,2-b]isoquinolin-7-one (4b-β)

Yield: 50% (71 mg). Yellow solid. m.p. 170.2 – 170.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 (s, 3H), 6.52 (dt, J = 24.1, 6.3 Hz, 2H), 4.89 – 4.75 (m, 2H), 4.13 (d, J = 16.0 Hz, 1H), 3.74 (t, J = 12.0 Hz, 1H), 3.22 (s, 1H), 2.78 (d, J = 15.4 Hz, 2H), 2.34 (s, 3H), 2.04 – 1.87 (m, 2H), 1.61 (s, 1H), 1.00 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.8, 137.7, 130.0, 127.6, 127.5, 127.3, 124.3, 123.2, 85.7, 67.5, 47.4, 40.2, 39.1, 36.3, 25.4, 21.7, 20.4. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{22}NO_2$ 284.1645, found 284.1636.



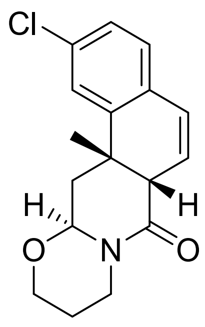
(6aS,12aS,13aS)-2-(tert-butyl)-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f] [1,3]oxazino[3,2-b]isoquinolin-7-one (4c-α)

Yield: 22% (37 mg). Yellow solid. m.p. 145.5 – 146.2 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.24 – 7.21 (m, 2H), 7.05 (d, J = 16 Hz, 1H), 6.58-6.55 (m, 2H), 4.98 (d, J = 6.2 Hz, 1H), 4.90 (d, J = 6.3 Hz, 1H), 4.20 – 4.12 (m, 1H), 3.81 – 3.72 (m, 1H), 3.11 (s, 1H), 2.85 – 2.77 (m, 1H), 2.68 (d, J = 14.2 Hz, 1H), 2.37 (dd, J = 14.1, 6.3 Hz, 1H), 1.94-190 (m, 1H), 1.52 (d, J = 13.6 Hz, 1H), 1.31 (s, 9H), 1.23 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7, 151.0, 142.7, 129.8, 127.3, 127.0, 124.3, 123.6, 119.3, 85.5, 68.7, 47.7, 41.1, 39.0, 36.5, 35.7, 31.4, 25.7, 21.4. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{28}NO_2$ 326.2115, found 326.2108.



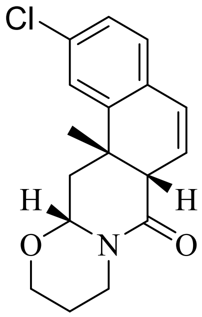
(6aS,12aR,13aS)-2-(tert-butyl)-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3]oxazino[3,2-b]isoquinolin-7-one (4c-β)

Yield: 52% (85 mg). Yellow solid. m.p. 145.5 – 146.2 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.26 – 7.21 (m, 2H), 7.06 (d, *J* = 16.5 Hz, 1H), 6.58-6.55 (m, 1H), 4.92 – 4.87 (m, 1H), 4.81 (dd, *J* = 13.3, 4.9 Hz, 1H), 4.20 – 4.12 (m, 1H), 3.81 – 3.72 (m, 1H), 3.24 (s, 1H), 2.90 (dd, *J* = 13.0, 6.3 Hz, 1H), 2.85 – 2.77 (m, 1H), 2.38 (dd, *J* = 14.1, 6.3 Hz, 1H), 2.04 (dd, *J* = 12.9, 9.1 Hz, 1H), 1.94-190 (m, 1H), 1.62 (d, *J* = 13.4 Hz, 1H), 1.31 (s, 9H), 1.03 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.8, 151.0, 141.9, 130.0, 127.2, 127.0, 124.5, 123.8, 119.2, 85.7, 67.7, 47.5, 40.1, 39.1, 36.5, 35.0, 31.4, 25.4, 20.5. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{28}NO_2$ 326.2115, found 326.2108.



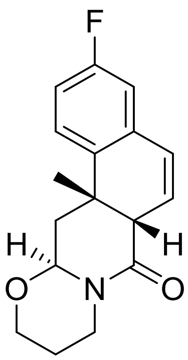
(6aS,12aS,13aS)-2-chloro-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3]oxazino[3,2-b]isoquinolin-7-one (4d-α)

Yield: 20% (31 mg). Yellow solid. m.p. 67.3 – 68.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.11 (d, *J* = 7.0 Hz, 2H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.58-6.49 (m, 2H), 4.92 – 4.72 (m, 2H), 4.11 (d, *J* = 15.9 Hz, 1H), 3.71 (t, *J* = 13.0 Hz, 1H), 3.03 (s, 1H), 2.77 (t, *J* = 13.1 Hz, 1H), 2.52 (d, *J* = 14.1 Hz, 1H), 2.29 (dd, *J* = 14.1, 6.2 Hz, 1H), 1.92-1.83 (m, 1H), 1.52 (d, *J* = 13.5 Hz, 1H), 1.17 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.0, 144.9, 133.3, 131.0, 128.4, 126.8, 126.6, 125.7, 123.0, 85.3, 68.7, 47.2, 41.2, 38.7, 36.5, 25.7, 21.2. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{19}NO_2$ 304.1099, found 304.1096.



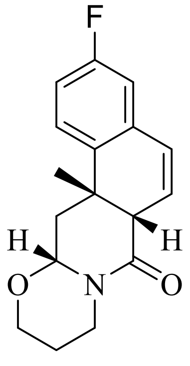
(6aS,12aR,13aS)-2-chloro-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3] oxazino[3,2-b]isoquinolin-7-one (4d-β)

Yield: 40% (62 mg) . Yellow solid. m.p. 67.3 – 68.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.13 (d, J = 7.0 Hz, 2H), 7.02 (d, J = 8.5 Hz, 1H), 6.59-6.50 (m, 2H), 4.84 (dd, J = 8.9, 6.5 Hz, 1H), 4.12 (m, 1H), 3.72 (m, 1H), 3.17 (s, 1H), 2.82-2.76 (m, 2H), 1.99-1.90 (m, 2H),1.59 (d, J = 13.5 Hz, 1H), 0.98 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.2, 144.0, 133.3, 131.1, 128.5, 127.0, 126.6, 125.9, 123.0, 85.4, 67.8, 47.0, 40.2, 38.9, 36.4, 25.4, 20.2. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{19}NO_2$ 304.1099, found 304.1096.



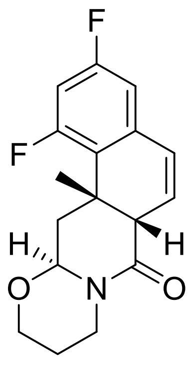
(6aS,12aS,13aS)-3-fluoro-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3] oxazino[3,2-b]isoquinolin-7-one (4e-α)

Yield: 18% (26 mg). Yellow solid. m.p. 195.2 – 195.9 °C. ^{1}HNMR (400 MHz, Chloroform-*d*) δ 7.10 (td, J = 8.6, 5.5 Hz, 1H), 6.90 – 6.82 (m, 1H), 6.78 (dd, J = 9.2, 2.7 Hz, 1H), 6.65 – 6.56 (m, 1H), 6.49 (dt, J = 9.7, 2.8 Hz, 1H), 4.92 (d, J = 6.2 Hz, 1H), 4.84 (dd, J = 8.9, 6.5 Hz, 1H), 4.11 (td, J = 11.5, 4.6 Hz, 1H), 3.72 (q, J = 13.5 Hz, 1H), 3.03 (s, 1H), 2.55 (d, J = 14.2 Hz, 1H), 2.29 (dd, J = 14.2, 6.3 Hz, 1H), 1.90 – 1.84 (m, 2H), 1.52 (d, J = 14.5 Hz, 1H), 1.16 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.1, 162.8, 160.4, 138.8 (d, J = 2.6 Hz), 134.4 (d, J = 7.8 Hz), 133.3, 131.0, 126.9, 123.8, 113.9, 113.8, 113.7, 85.3, 68.6, 47.5, 41.2, 39.0, 36.0, 25.6, 21.4. ^{19}FNMR (376 MHz, Chloroform-*d*)) δ -116.18 – -116.24 (m). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{19}NO_2$ 288.1394, found 288.1390.



(6aS,12aR,13aS)-3-fluoro-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3] oxazino[3,2-b]isoquinolin-7-one (4e-β)

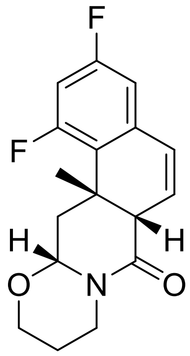
Yield: 45% (65 mg). Yellow solid. m.p. 195.2 – 195.9 °C. ^{1}HNMR (400 MHz, Chloroform-*d*) δ 7.10 (td, *J* = 8.6, 5.5 Hz, 1H), 6.90 – 6.82 (m, 1H), 6.78 (dd, *J* = 9.2, 2.7 Hz, 1H), 6.65 – 6.56 (m, 1H), 6.49 (dt, *J* = 9.7, 2.8 Hz, 1H), 4.84 (dd, *J* = 8.9, 6.5 Hz, 1H), 4.76 (dd, *J* = 13.4, 4.8 Hz, 1H), 4.11 (td, *J* = 11.5, 4.6 Hz, 1H), 3.72 (q, *J* = 13.5 Hz, 1H), 3.17 (s, 1H), 2.80 – 2.72 (m, 2H), 1.98-1.88 (m, 2H), 1.58 (d, *J* = 13.5 Hz, 1H), 0.97 (s). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.3, 162.9, 160.5, 138.0 (d, *J* = 2.8 Hz), 134.6 (d, *J* = 7.9 Hz), 133.3, 131.1, 127.0, 123.9, 114.18, 114.0, 114.0, 85.5, 67.8, 47.3, 40.1, 39.1, 35.9, 25.3, 20.4. ^{19}FNMR (376 MHz, Chloroform-*d*)) δ -116.49 – -116.55 (m) HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{19}NO_2$ 288.1394, found 288.1390.



(6aS,12aS,13aS)-1,3-difluoro-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3] oxazino[3,2-b]isoquinolin-7-one (4f-α)

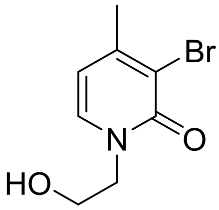
Yield: 22% (34 mg). Yellow solid. m.p. 154.5 – 155.2 °C.^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.70 (dd, *J* = 9.6, 2.3 Hz, 1H), 6.63 – 6.55 (m, 2H), 6.45 (ddd, *J* = 9.7, 6.3, 3.8 Hz, 1H), 4.86 (d, *J* = 6.2 Hz, 1H), 4.81 (dd, *J* = 17.3, 8.6 Hz, 1H), 4.12 (dd, *J* = 11.3, 2.9 Hz, 1H), 3.73-3.67(m, 1H)

3.11 (s, 1H), 3.04 (dd, *J* = 14.7, 4.2 Hz, 1H), 2.77 (qd, *J* = 13.2, 3.2 Hz, 1H), 2.44 (dd, *J* = 14.7, 6.3 Hz, 1H), 1.91 – 1.81 (m, 1H), 1.50 (d, *J* = 13.5 Hz, 1H), 1.22 (s, 3H), ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.4, 160.7 – 160.4 (m), 159.6 (dd, *J* = 11.9, 6.7 Hz), 136.6, 136.5, 127.5, 126.6, 124.6 (d, *J* = 3.7 Hz), 124.5 (d, *J* = 4.0 Hz), 110.2, 110.2 (t, *J* = 3.9 Hz), 103.65, 103.5 (d, *J* = 4.5 Hz), 103.3, 85.2 (d, *J* = 2.6 Hz), 68.5, 47.9, 41.1, 39.7, 36.9 (d, *J* = 3.2 Hz), 25.6, 19.5. ^{19}FNMR (376 MHz, Chloroform-*d*) δ -109.00 (t, *J* = 9.5 Hz), -109.12 (d, *J* = 6.2 Hz). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{18}NO_2$ 306.1300, found 306.1294.



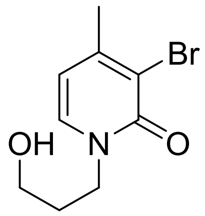
(6aS,12aR,13aS)-1,3-difluoro-13a-methyl-6a,10,11,12a,13,13a-hexahydro-7H,9H-benzo[f][1,3]oxazino[3,2-b]isoquinolin-7-one (4f-β)

Yield: 46% (70 mg). Yellow solid. m.p. 154.5 – 155.2 °C.^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.66 (dd, *J* = 9.6, 2.3 Hz, 1H), 6.63 – 6.55 (m, 2H), 6.45 (ddd, *J* = 9.7, 6.3, 3.8 Hz, 1H), 4.81 (dd, *J* = 17.3, 8.6 Hz, 1H), 4.73 (dd, *J* = 14.4, 3.8 Hz, 1H), 4.08 (dd, *J* = 11.4, 4.7 Hz, 1H), 3.74 – 3.66 (m, 1H), 3.29 (ddd, *J* = 13.6, 6.6, 3.4 Hz, 1H), 3.25 (s, 1H), 2.77 (qd, *J* = 13.2, 3.2 Hz, 1H), 2.07 (dd, *J* = 13.6, 8.8 Hz, 1H), 1.91 – 1.81 (m, 1H), 1.57 (d, *J* = 14.4 Hz, 1H), 1.03 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.6, 162.2 (t, *J* = 14.7 Hz), 161.3 (dd, *J* = 12.0, 6.7 Hz), 136.6, 136.8, 136.8 (d, *J* = 2.1 Hz), 136.7, 127.6, 126.6, 123.8 (d, *J* = 4.1 Hz), 123.8 (d, *J* = 4.1 Hz), 110.4, 110.3 (t, *J* = 3.1 Hz), 103.7, 103.6 (d, *J* = 4.6 Hz), 103.4, 85.3 (d, *J* = 2.8 Hz), 67.7, 47.8, 40.1, 39.6, 36.7 (d, *J* = 3.2 Hz), 25.3, 18.6. ^{19}FNMR (376 MHz, Chloroform-*d*) δ -112.65 – -112.77 (m), -113.00 – -113.00 (m). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{18}NO_2$ 306.1300, found 306.1294.



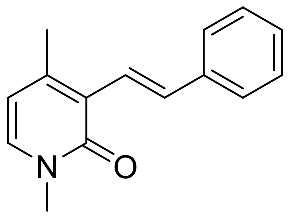
3-bromo-1-(2-hydroxyethyl)-4-methylpyridin-2(1H)-one (8)

Yield: 90% (415 mg). White solid. m.p. 109.5 – 110.4 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 6.8 Hz, 1H), 6.07 (d, *J* = 6.8 Hz, 1H), 4.14 – 4.02 (m, 2H), 3.92 (s, 1H), 3.87 – 3.81 (m, 2H), 2.25 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.4, 151.0, 136.5, 116.7, 108.7, 60.5, 53.8, 23.5. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_8H_{11}NO_2$ 231.9968, found 231.9962.



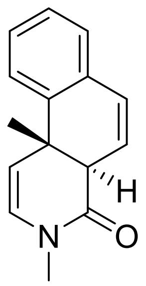
3-bromo-1-(3-hydroxypropyl)-4-methylpyridin-2(1H)-one (9)

Yield: 92% (45 mg). White solid. m.p. 103.4 – 104.2 °C. ^{1}HNMR (400 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 6.8 Hz, 1H), 6.14 (d, *J* = 6.8 Hz, 1H), 4.12 (t, *J* = 6.2 Hz, 2H), 3.75 (s, 1H), 3.49 (d, *J* = 5.0 Hz, 2H), 2.30 (s, 3H), 1.92 – 1.85 (m, 2H). ^{13}CNMR (101 MHz, Chloroform-*d*) δ 159.7, 150.9, 135.1, 117.1, 109.6, 57.8, 47.2, 32.3, 23.7. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_9H_{12}NNaO_2$ 267.9944, found 267.9940.



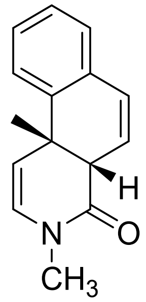
(E)-1,4-dimethyl-3-styrylpyridin-2(1H)-one (5)

Yield: 86% (450 mg). Yellow solid. m.p. 101.2 – 101.8 °C.^{1}HNMR (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 16.1 Hz, 1H), 7.51 (d, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.10 (dd, *J* = 15.8, 11.5 Hz, 2H), 6.03 (s, 1H), 3.52 (s, 3H), 2.33 (s, 3H). ^{13}CNMR (101 MHz, Chloroform-*d*) δ 161.9, 147.9, 138.8, 134.9, 133.6, 128.7, 127.5, 126.7, 124.7, 122.2, 110.1, 38.1, 20.5. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{15}H_{16}NO$ 226.1232, found 226.1230.



(4aR,10bS)-3,10b-dimethyl-4a,10b-dihydrobenzo[f]isoquinolin-4(3H)-one (6-α)

Yield: 85% (90 mg). Yellow solid. m.p. 115.3 – 115.9 °C.^{1}HNMR (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 7.4 Hz), 7.28 – 7.18 (m), 7.14 (d, *J* = 7.2 Hz), 6.62 – 6.55 (m), 6.14 (d, *J* = 7.8 Hz), 5.97 (d, *J* = 7.8 Hz), 3.42 (s), 3.15 (s), 1.01 (s). ^{13}CNMR (101 MHz, Chloroform-*d*) δ 169.4, 140.4, 133.0, 129.3, 128.2, 127.9, 127.7, 126.9, 123.7, 123.0, 114.8, 47.4, 37.9, 33.7, 21.1. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{16}NO$ 226.1232, found 226.1231.

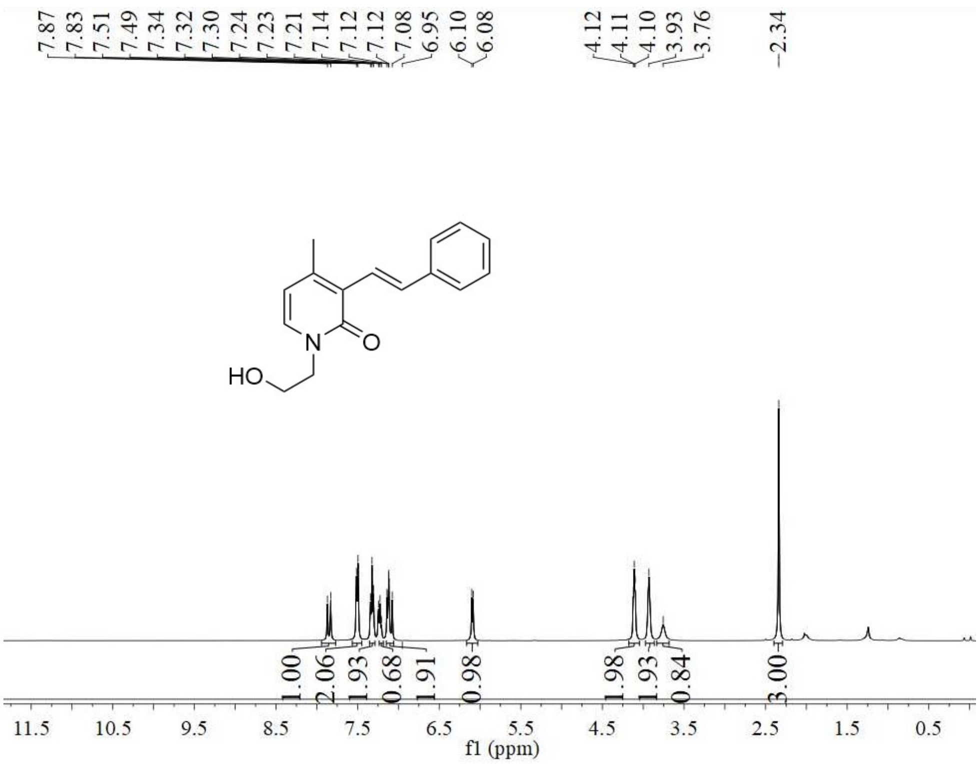


(4aS,10bS)-3,10b-dimethyl-4a,10b-dihydrobenzo[f]isoquinolin-4(3H)-one (6-β)

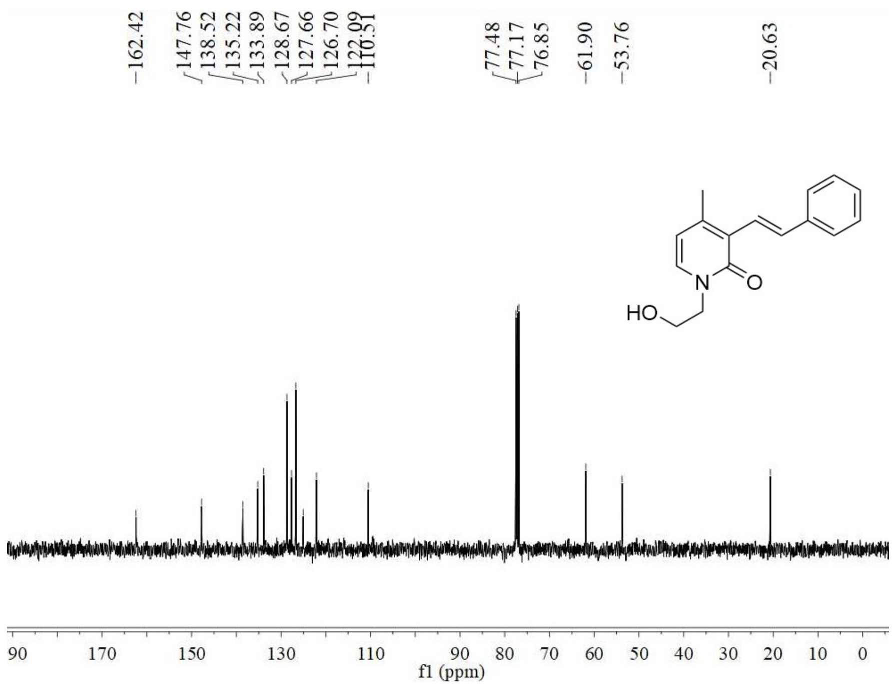
Yield: 66% (70 mg). Yellow solid. m.p. 130.3 – 130.9 °C . ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 1H), 7.19 (tt, *J* = 7.3, 5.9 Hz, 2H), 7.11 – 7.02 (m, 1H), 6.61 (d, *J* = 9.6 Hz, 1H), 6.13 – 5.86 (m, 2H), 5.15 (d, *J* = 7.8 Hz, 1H), 3.21 (d, *J* = 3.9 Hz, 1H), 3.02 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.8, 140.0, 132.1, 128.6, 128.3, 127.1, 124.4 (d, *J* = 8.2 Hz), 114.0, 48.6, 37.9, 34.2, 27.5. HRMS (ESI) m/z calcd for $C_{15}H_{15}NO$ $[M+H]^+$ 226.1232, found 226.1230

S5. ^{1}H NMR , ^{13}C NMR, 2D NMR and ^{19}F NMR Spectra

1a

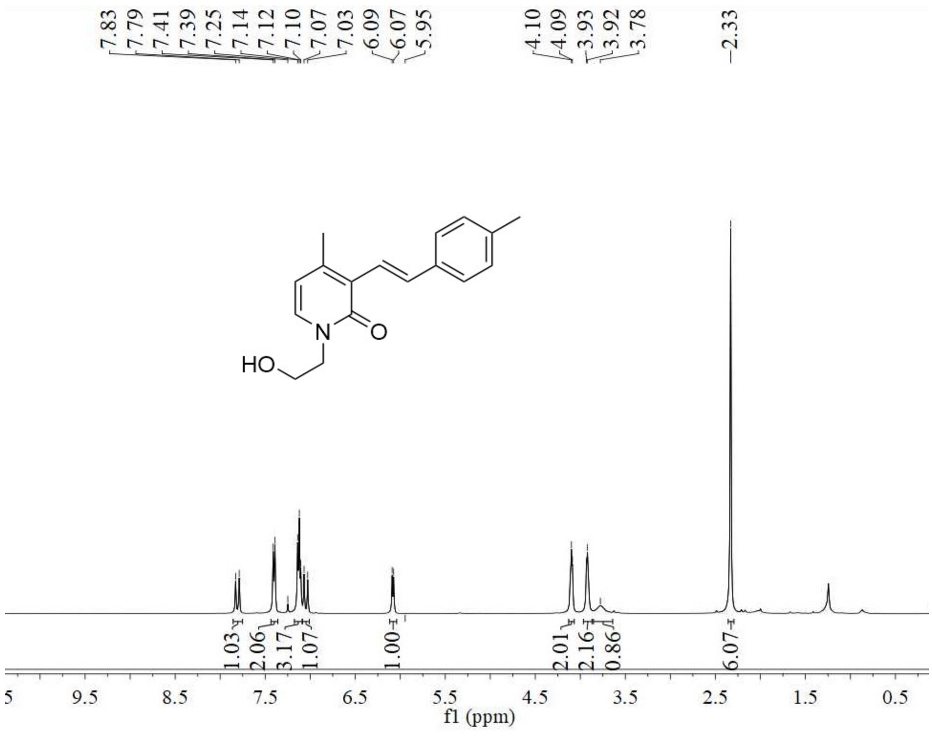


^{1}H NMR ($CDCl_3$)

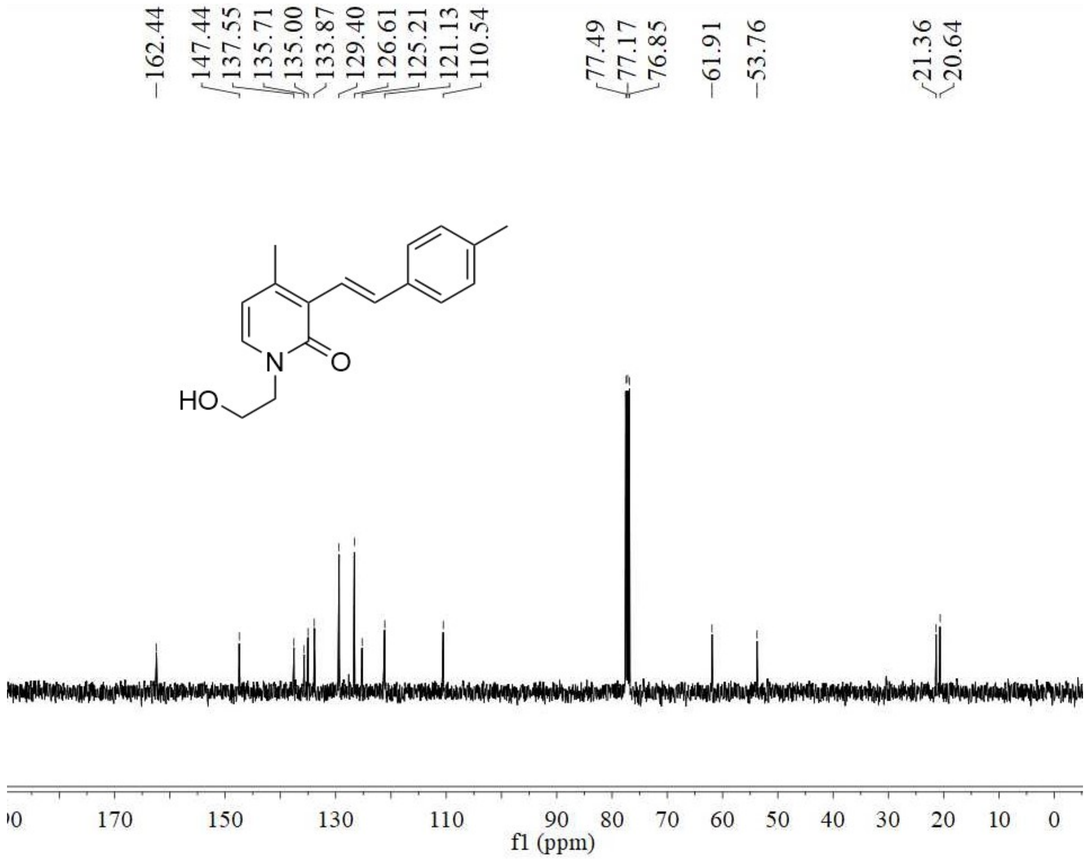


^{13}C NMR ($CDCl_3$)

1b

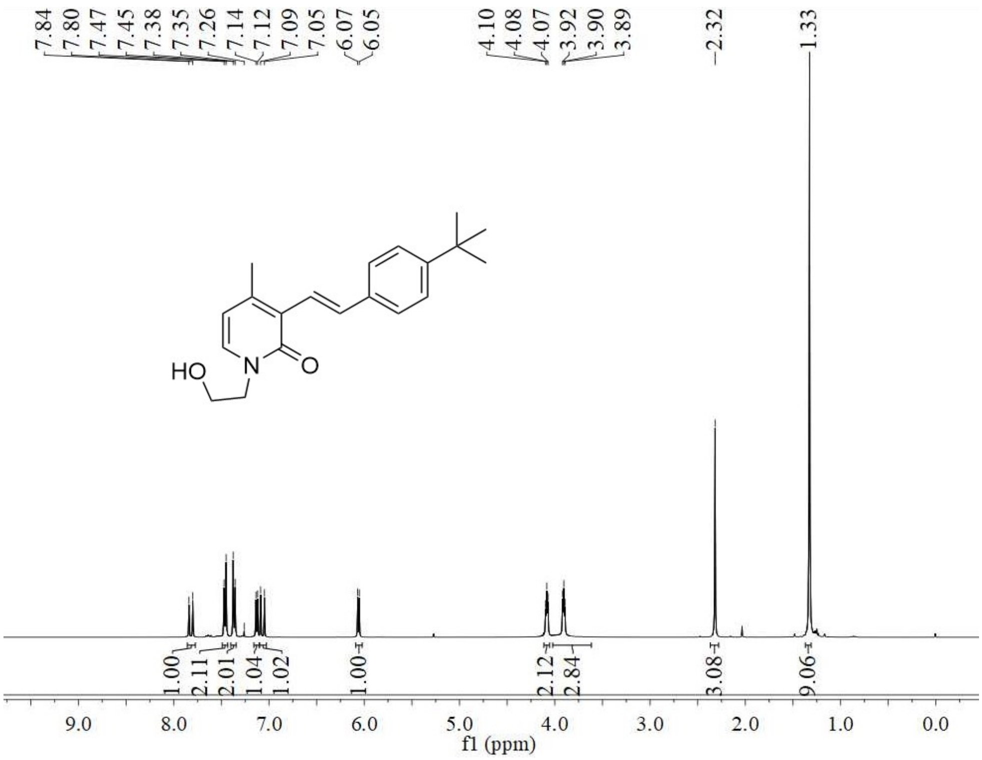


^{1}H NMR ($CDCl_3$)

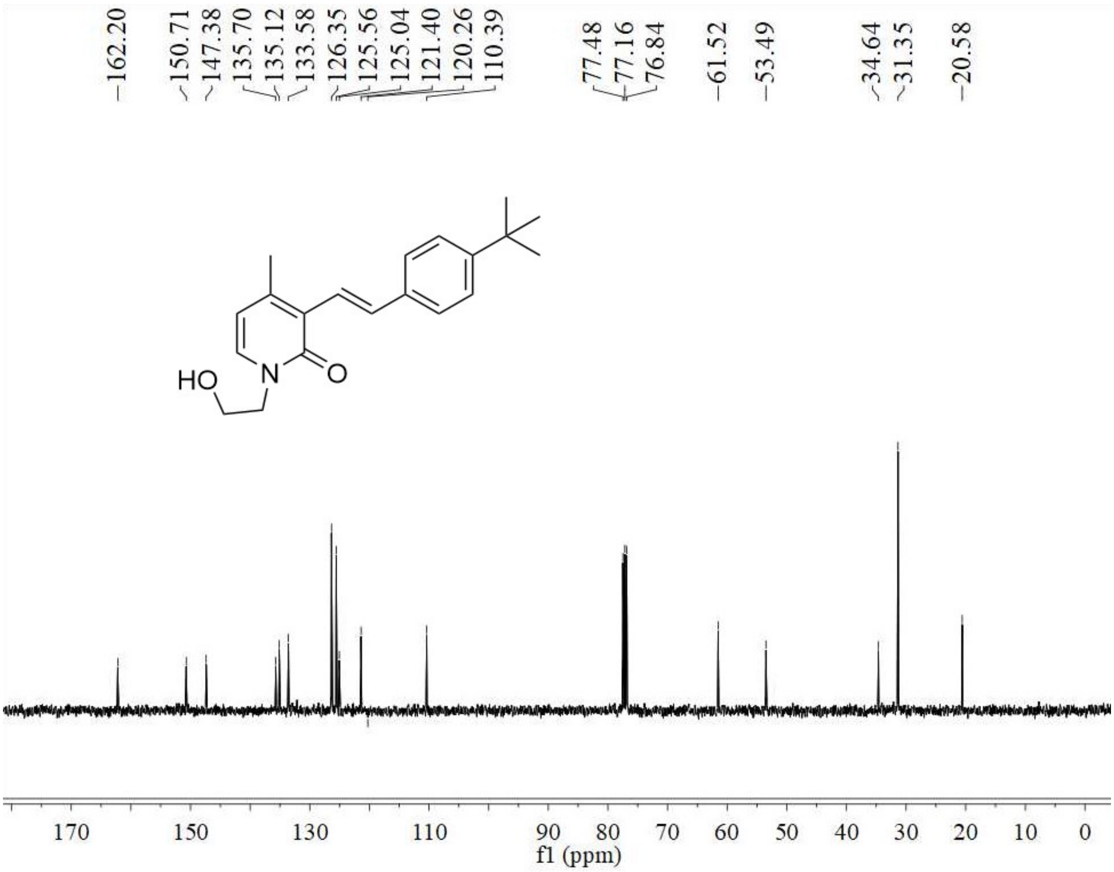


^{13}C NMR ($CDCl_3$)

1c

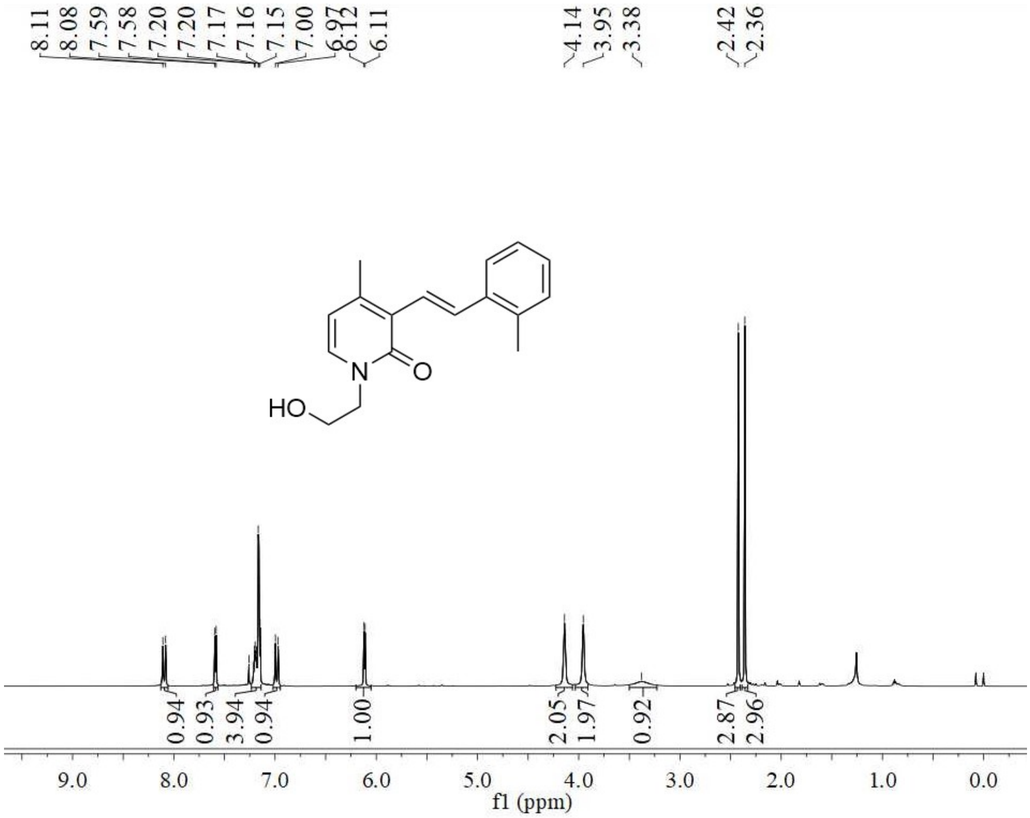


^{1}H NMR ($CDCl_3$)

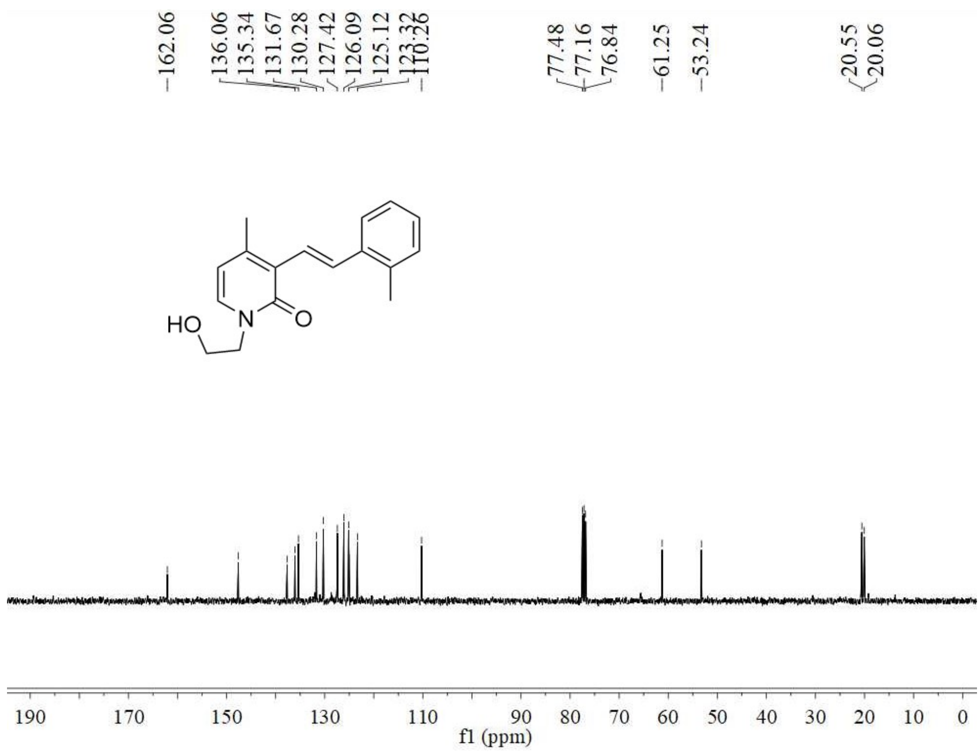


^{13}C NMR ($CDCl_3$)

1d

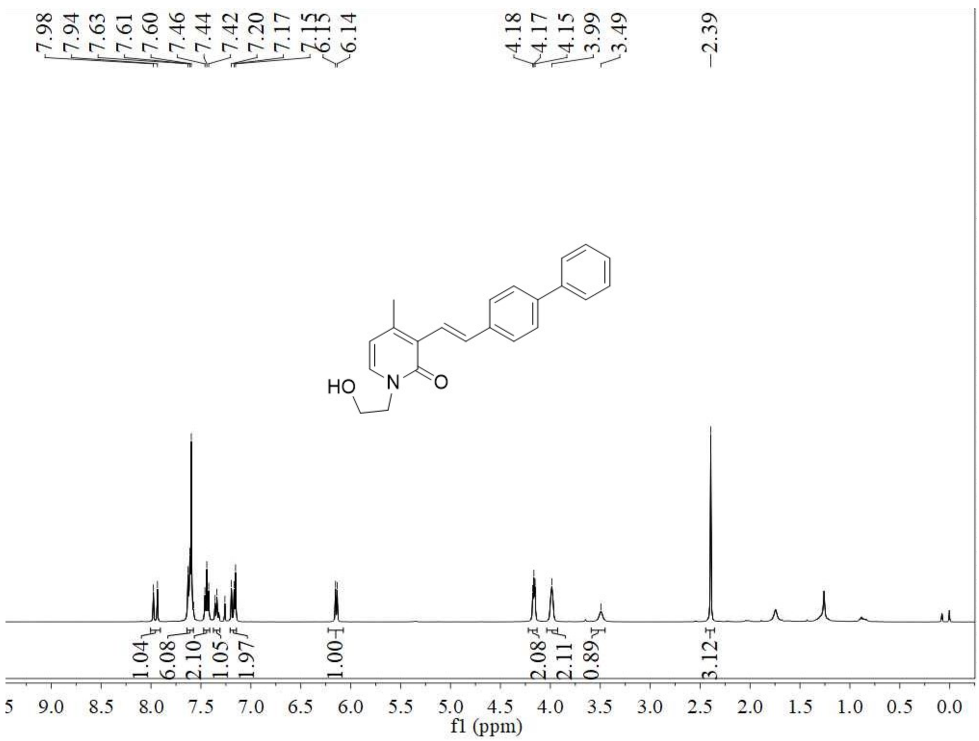


^{1}H NMR ($CDCl_3$)

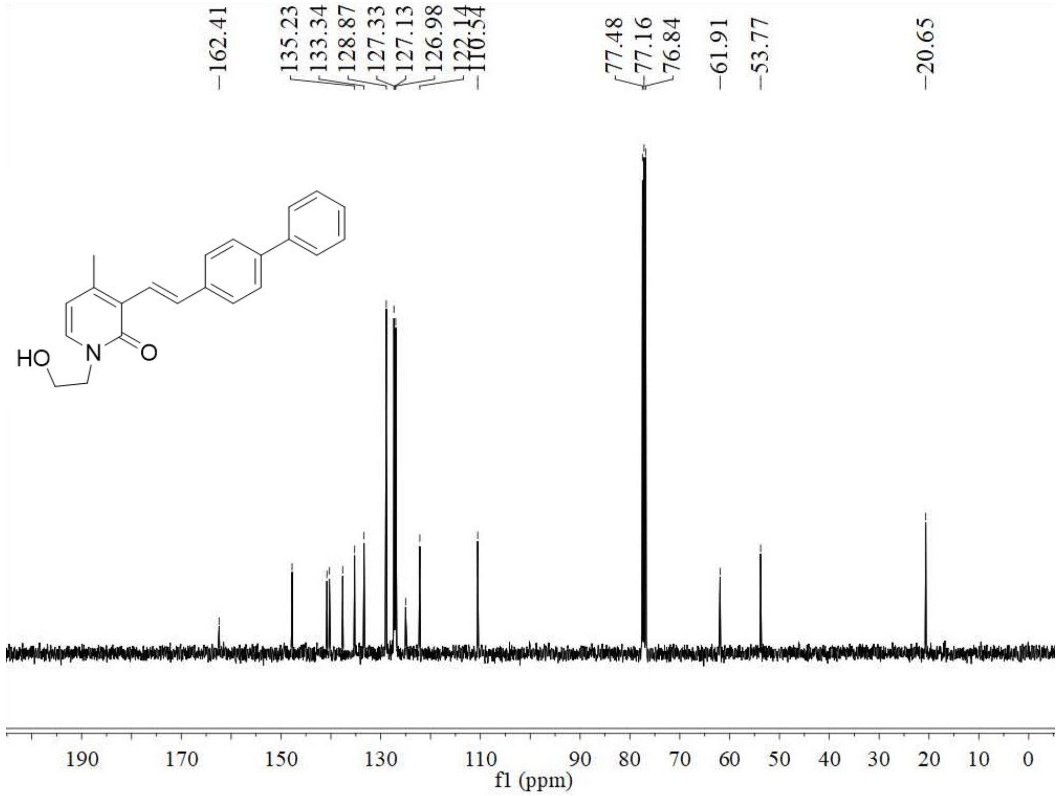


^{13}C NMR ($CDCl_3$)

1e

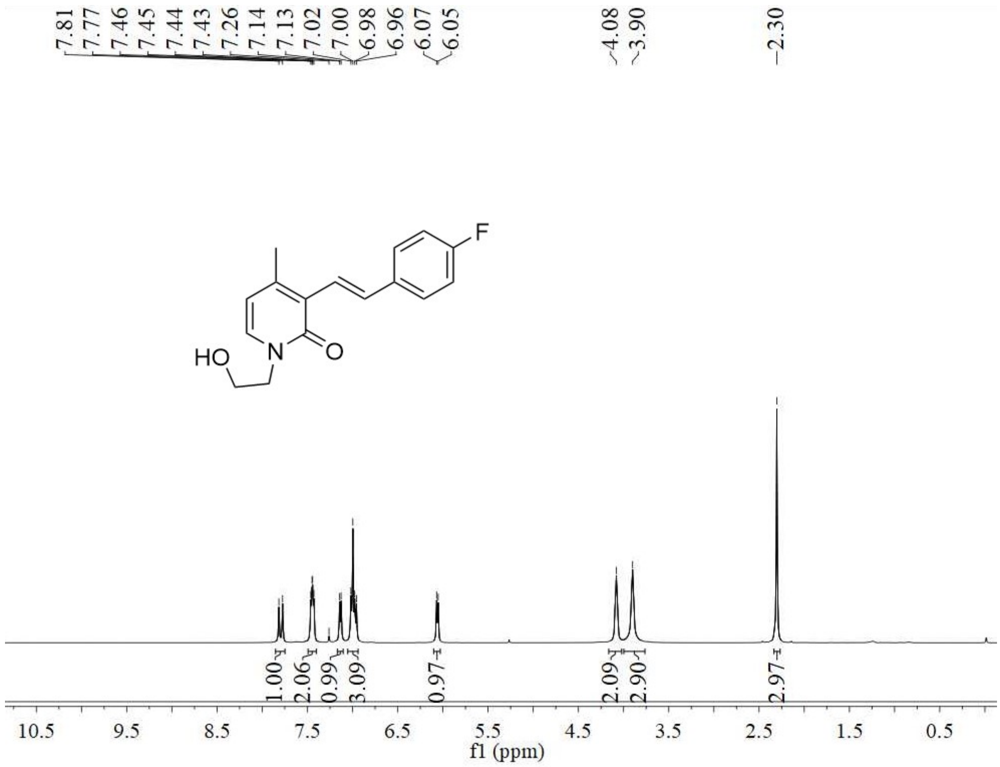


^{1}H NMR ($CDCl_3$)

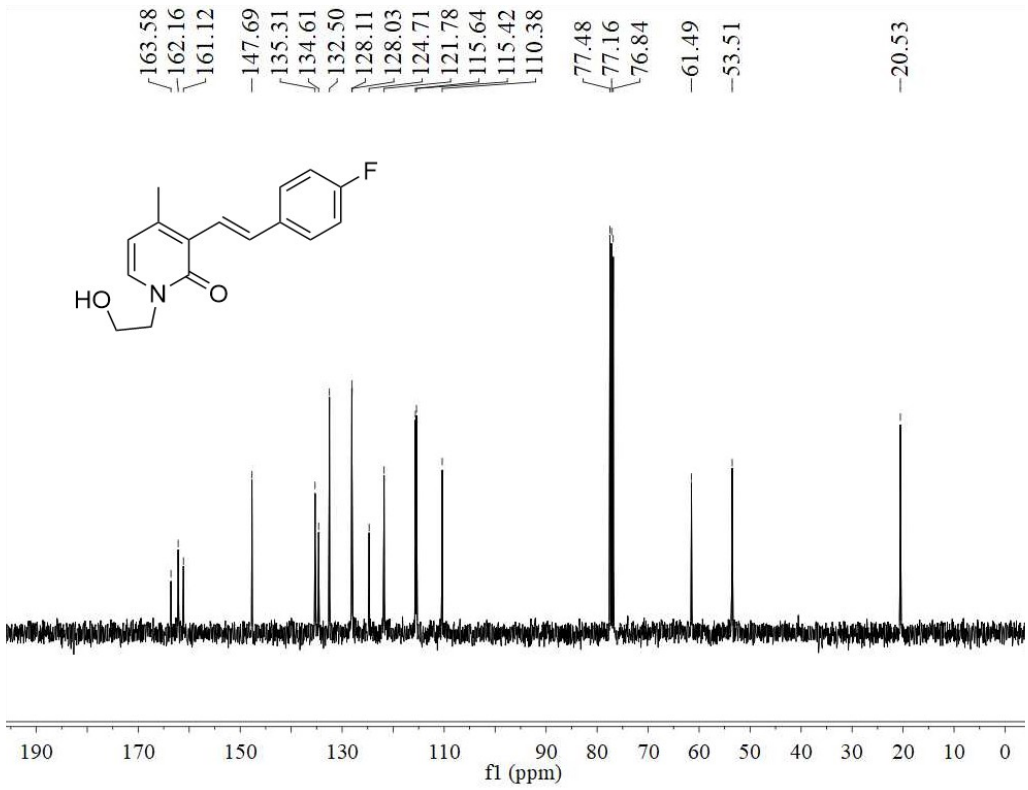


^{13}C NMR ($CDCl_3$)

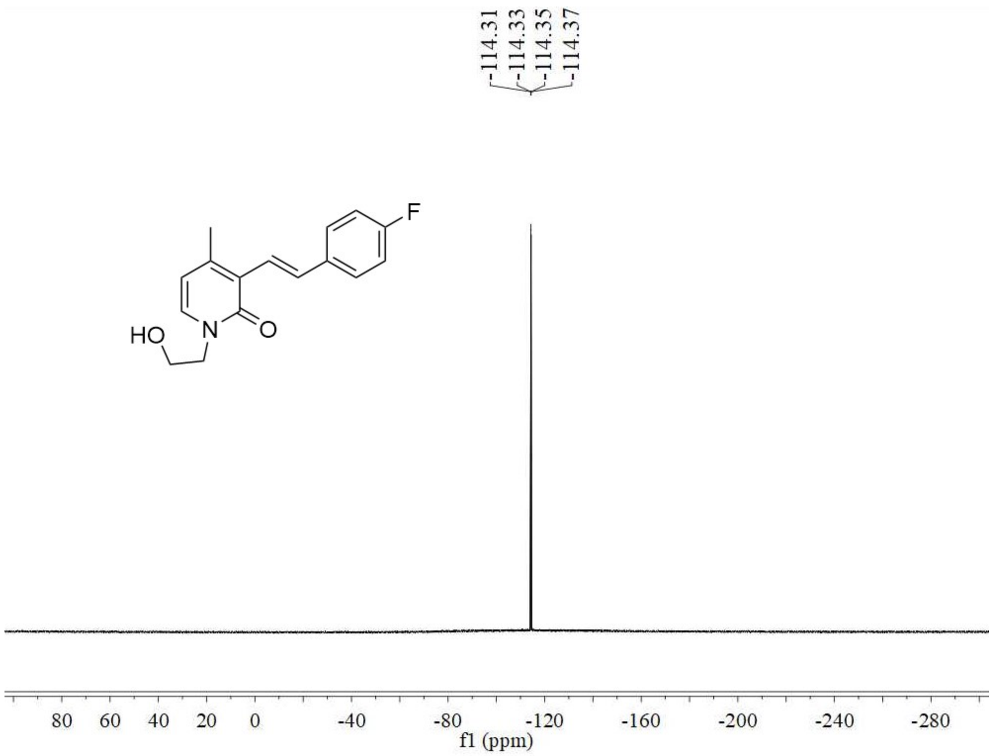
1f



^{1}H NMR ($CDCl_3$)

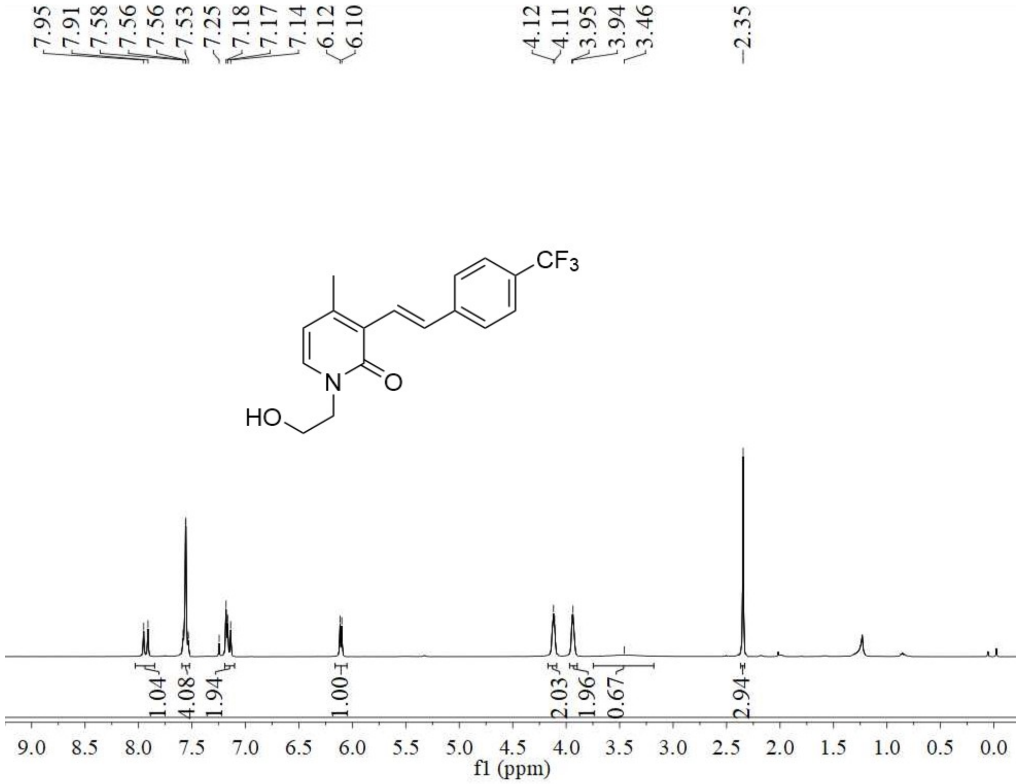


^{13}C NMR ($CDCl_3$)

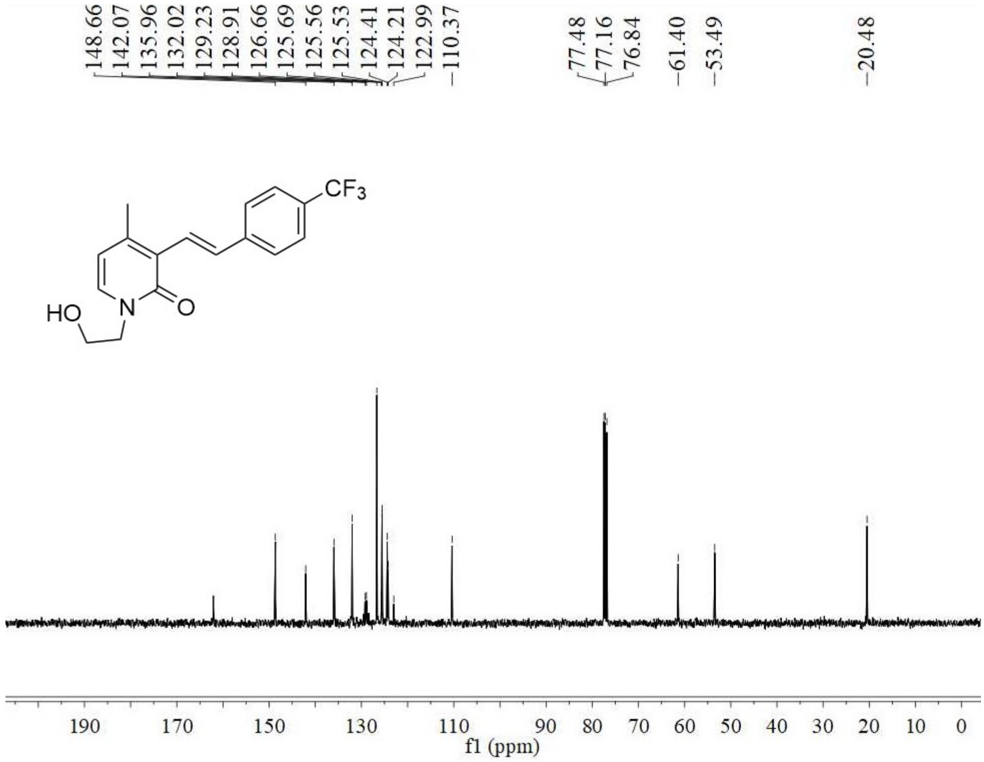


^{19}F NMR ($CDCl_3$)

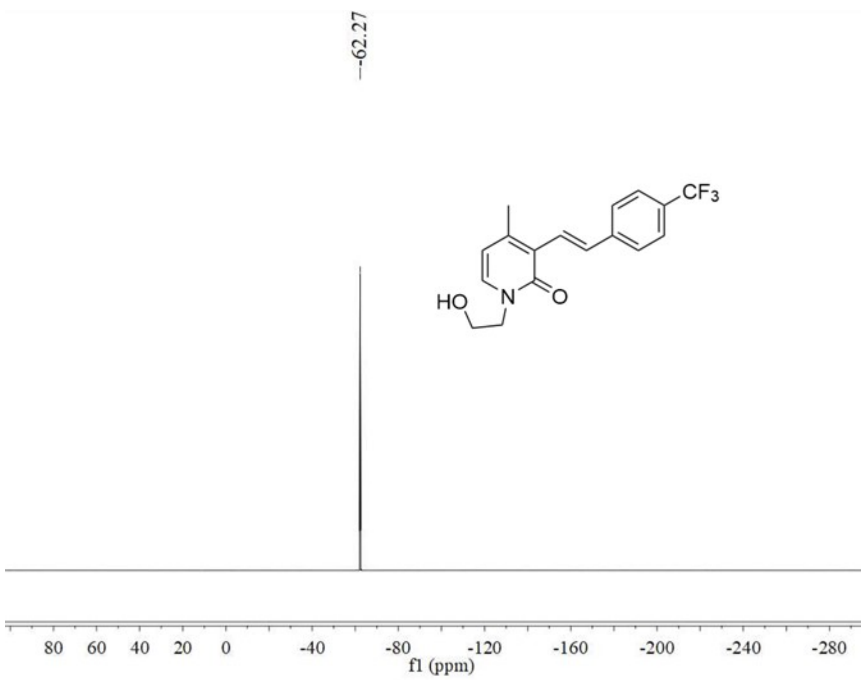
1g



^{1}H NMR ($CDCl_3$)

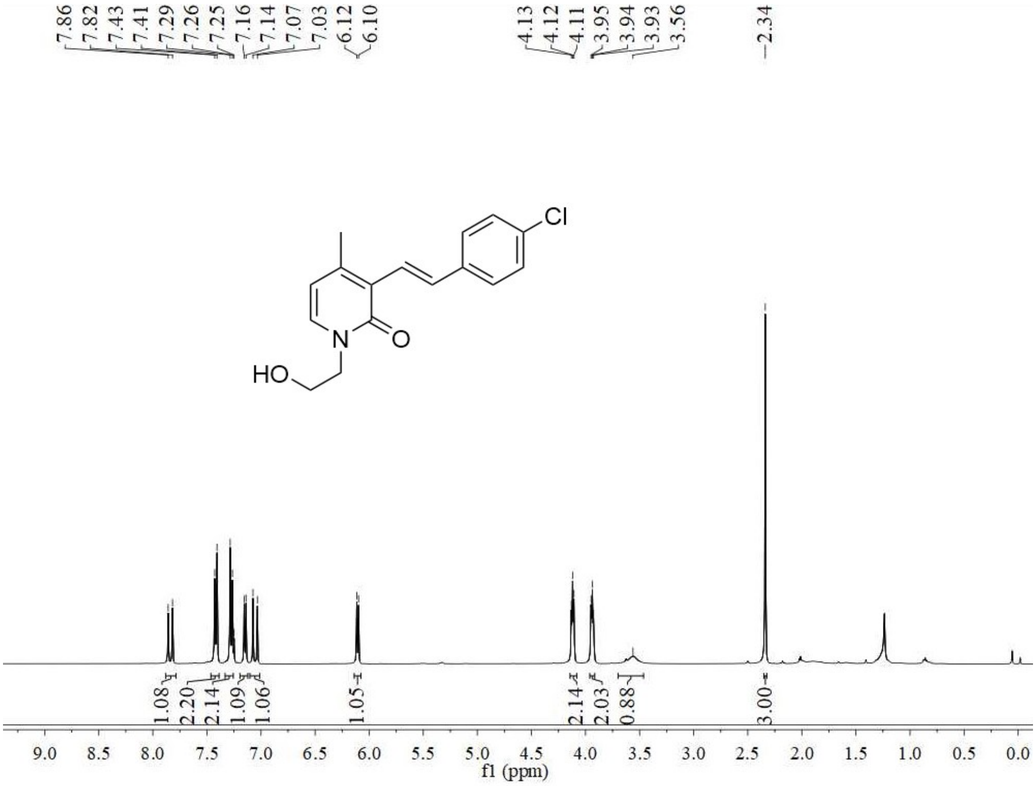


^{13}C NMR ($CDCl_3$)

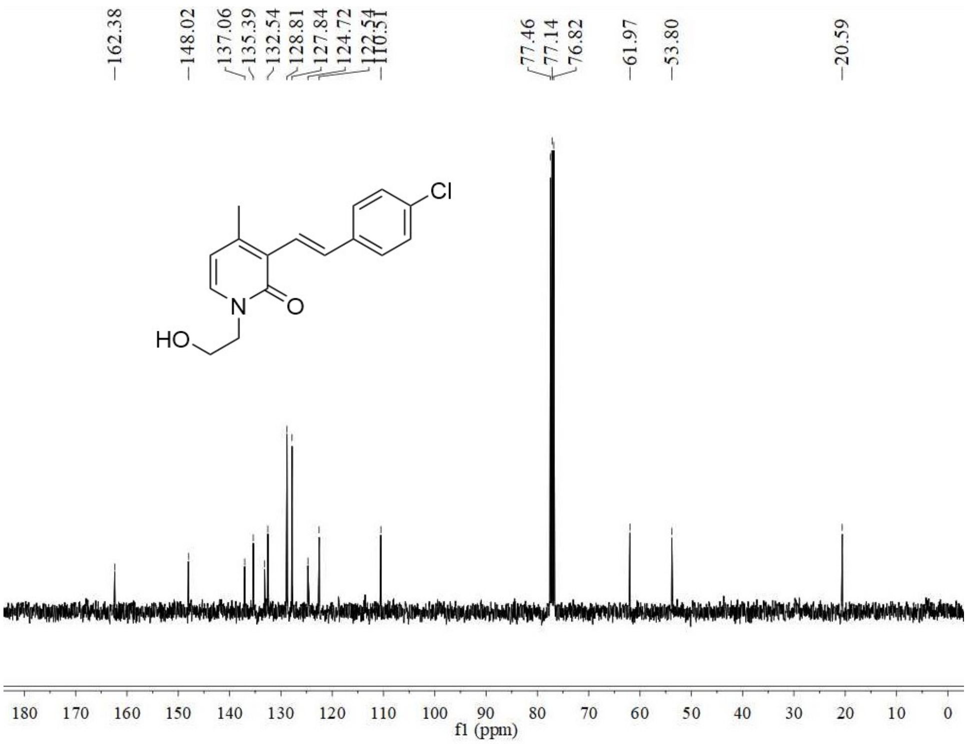


^{19}F NMR ($CDCl_3$)

1h

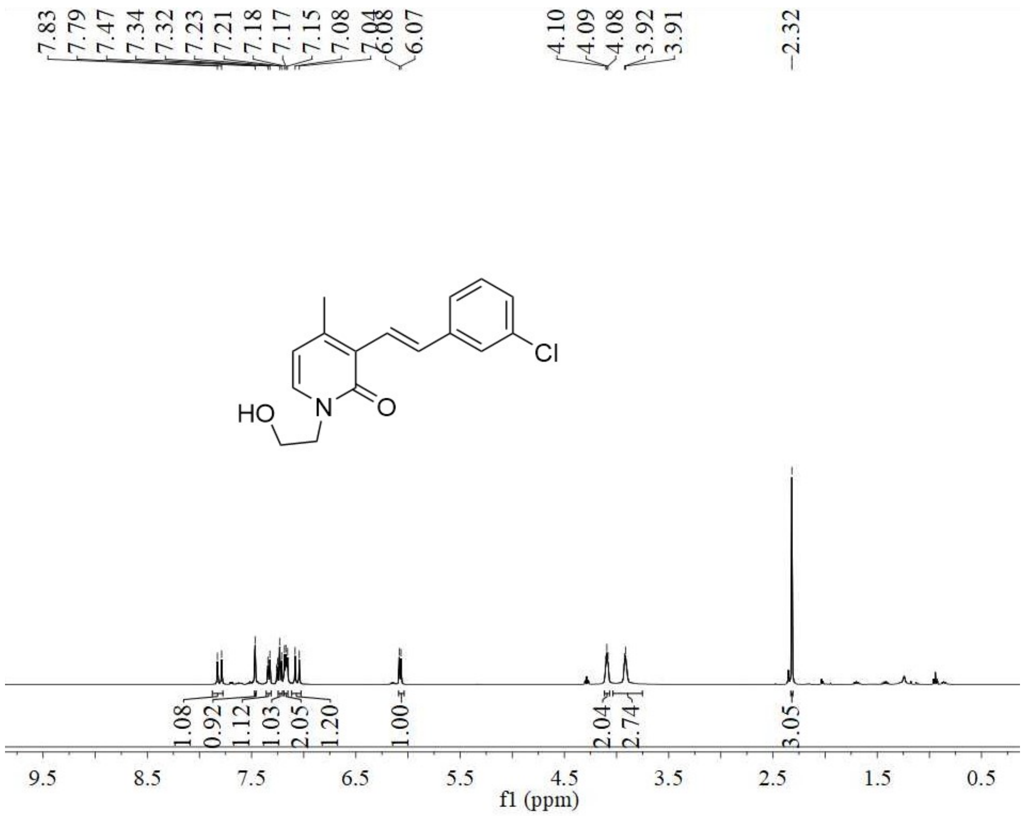


^{1}H NMR ($CDCl_3$)

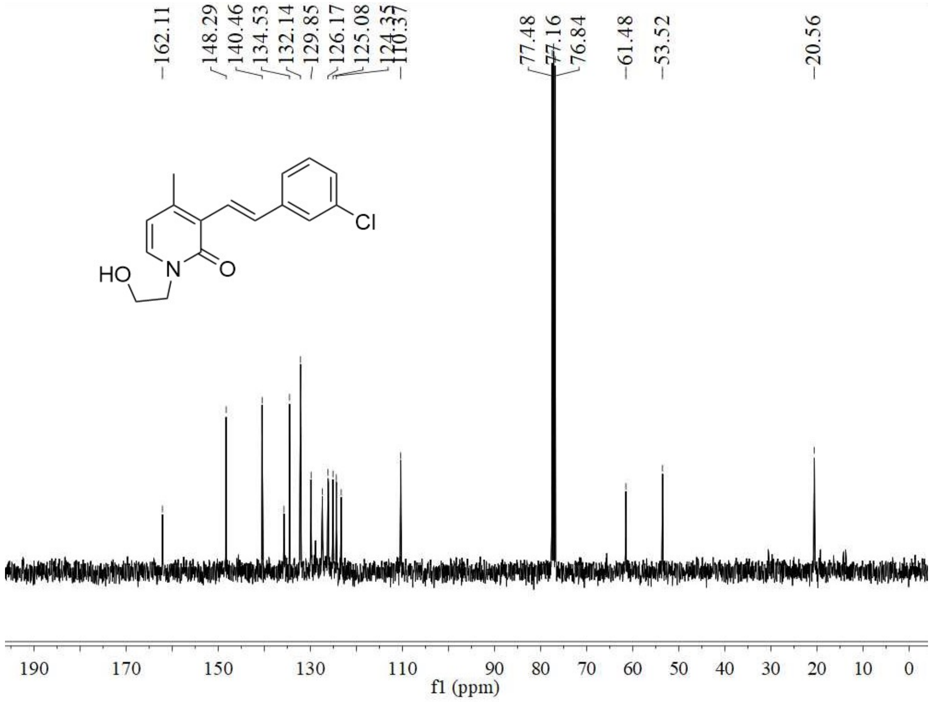


^{13}C NMR ($CDCl_3$)

1i

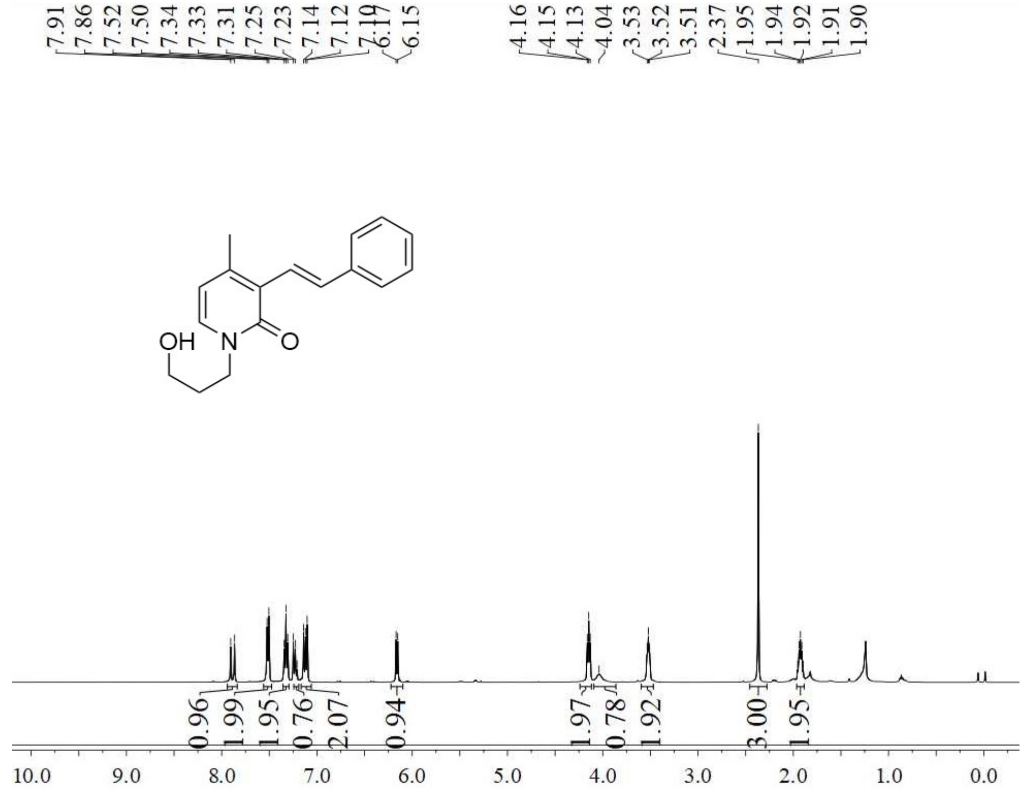


^{1}H NMR ($CDCl_3$)

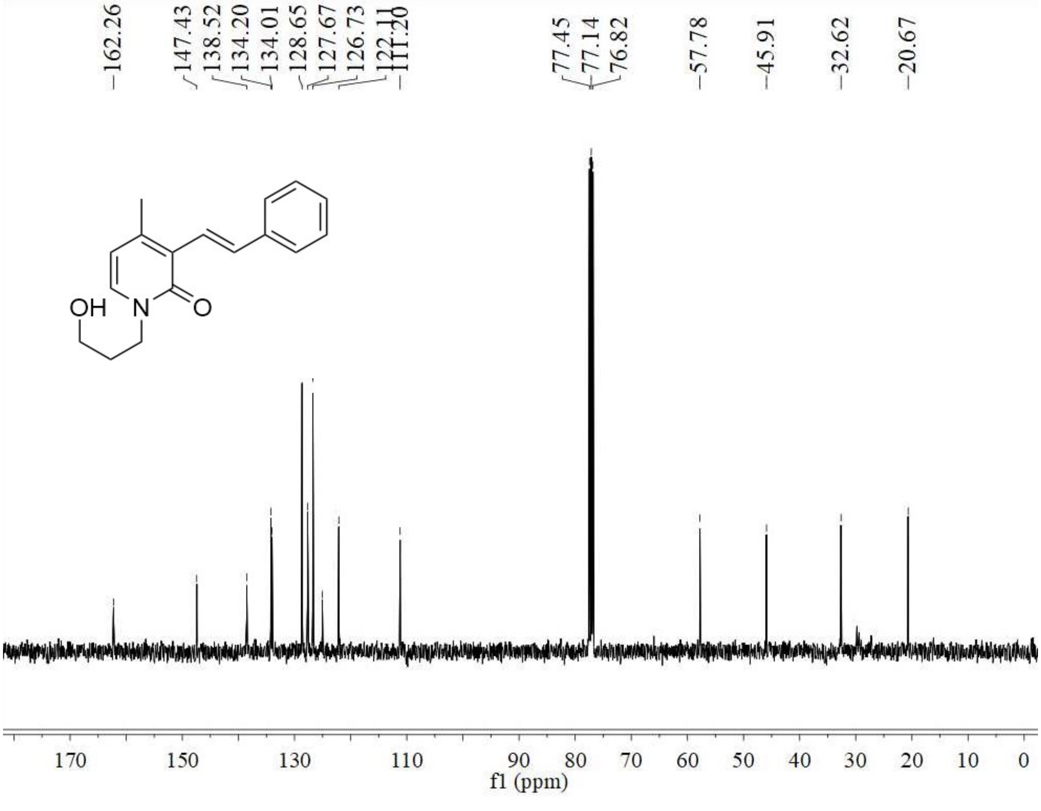


^{13}C NMR ($CDCl_3$)

3a

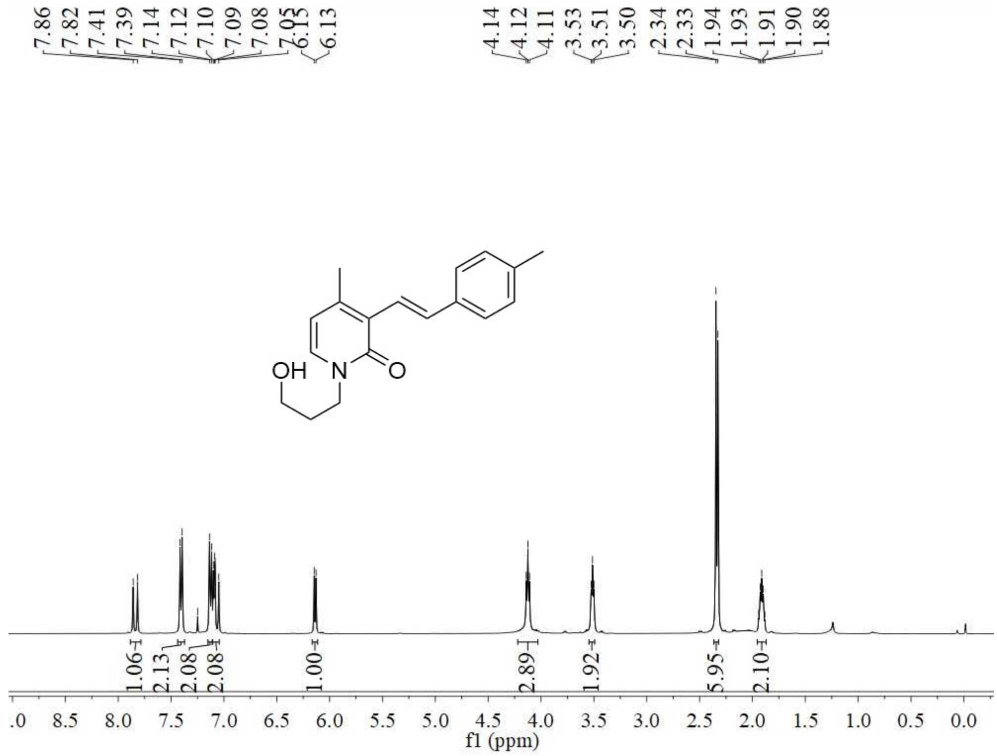


^{1}H NMR ($CDCl_3$)

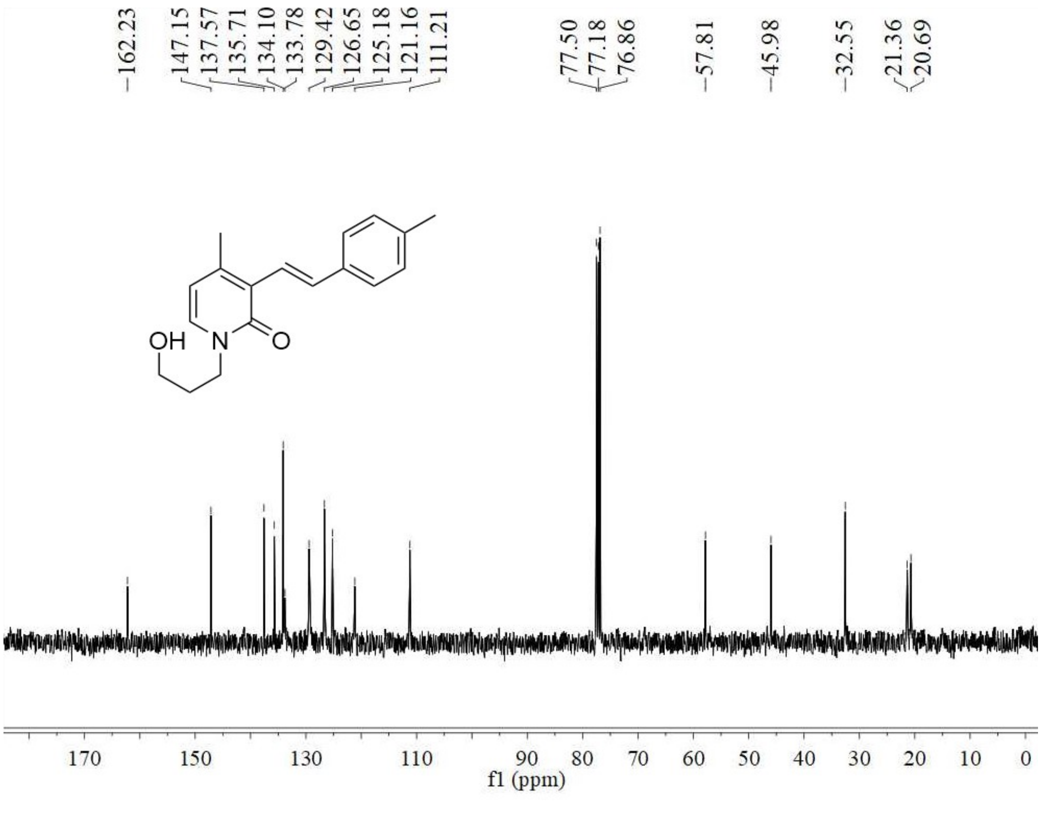


^{13}C NMR ($CDCl_3$)

3b

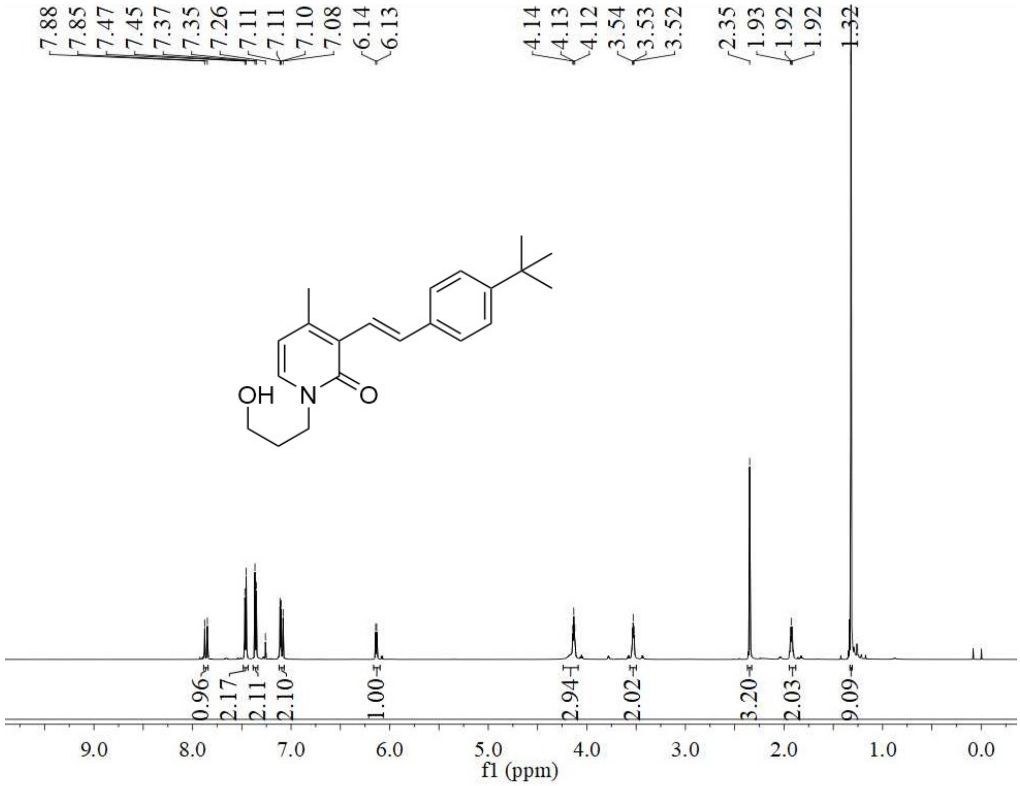


^{1}H NMR ($CDCl_3$)

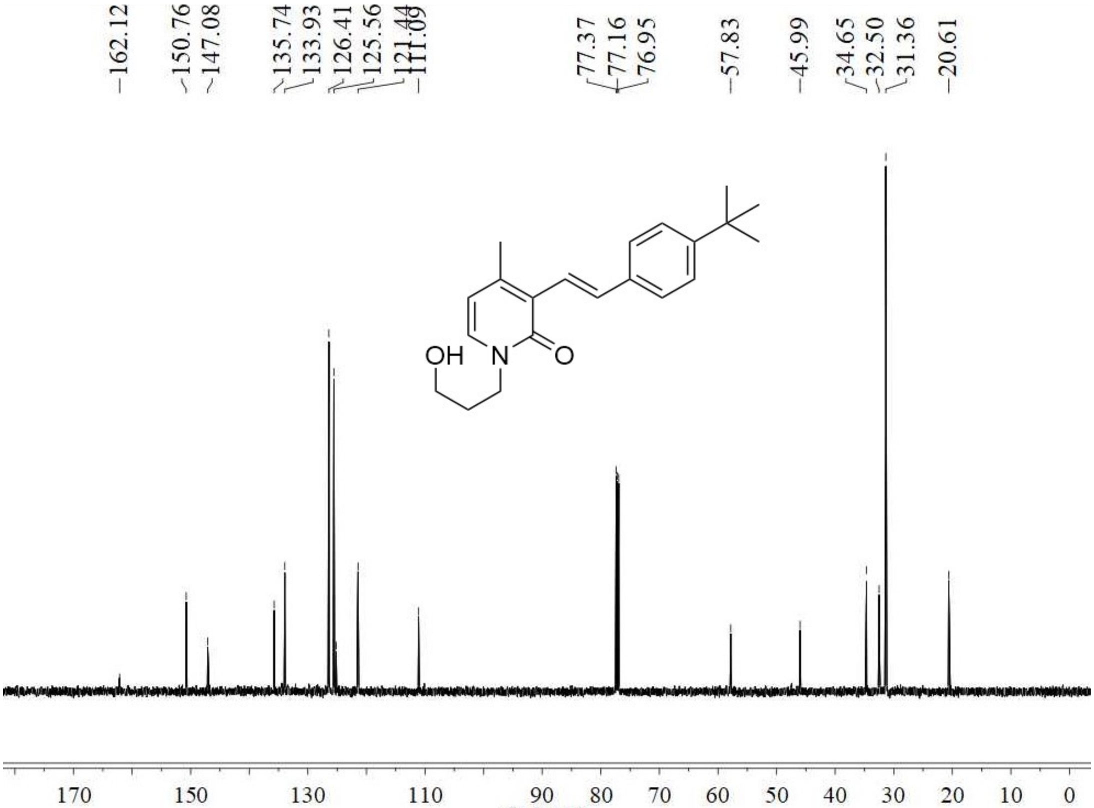


^{13}C NMR ($CDCl_3$)

3c

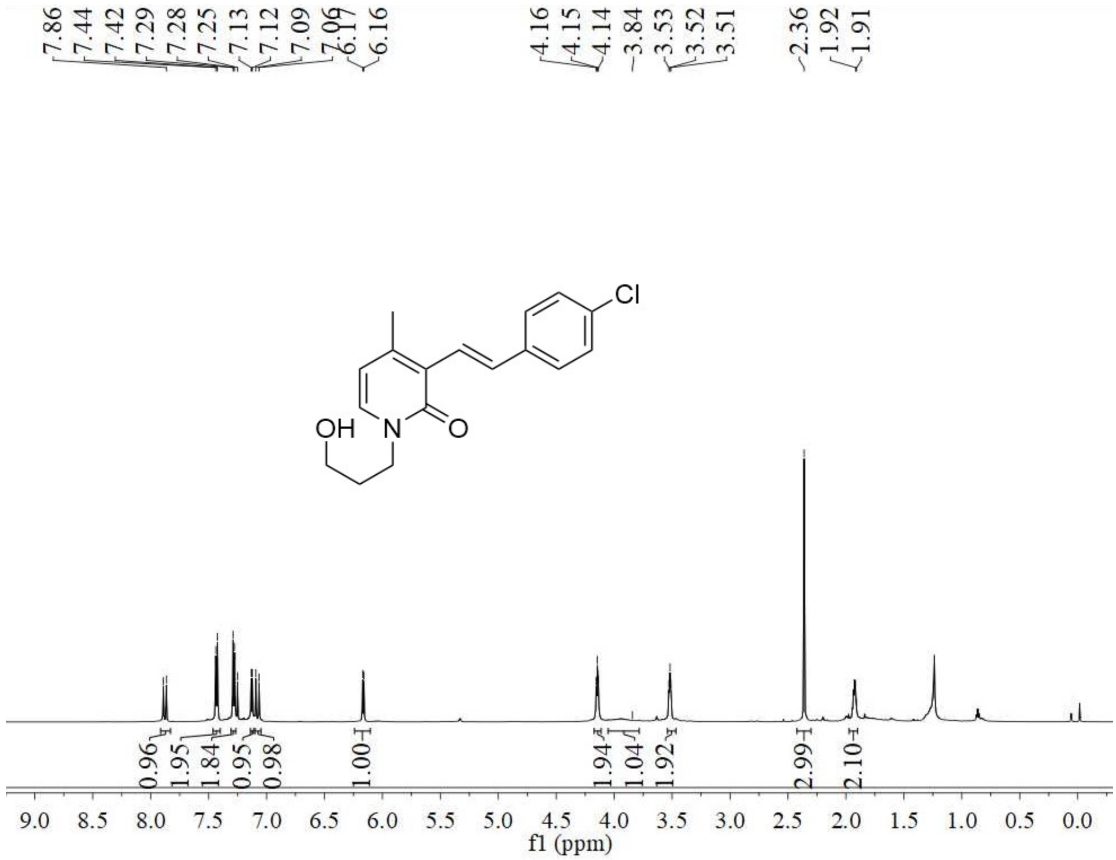


^{1}H NMR ($CDCl_3$)

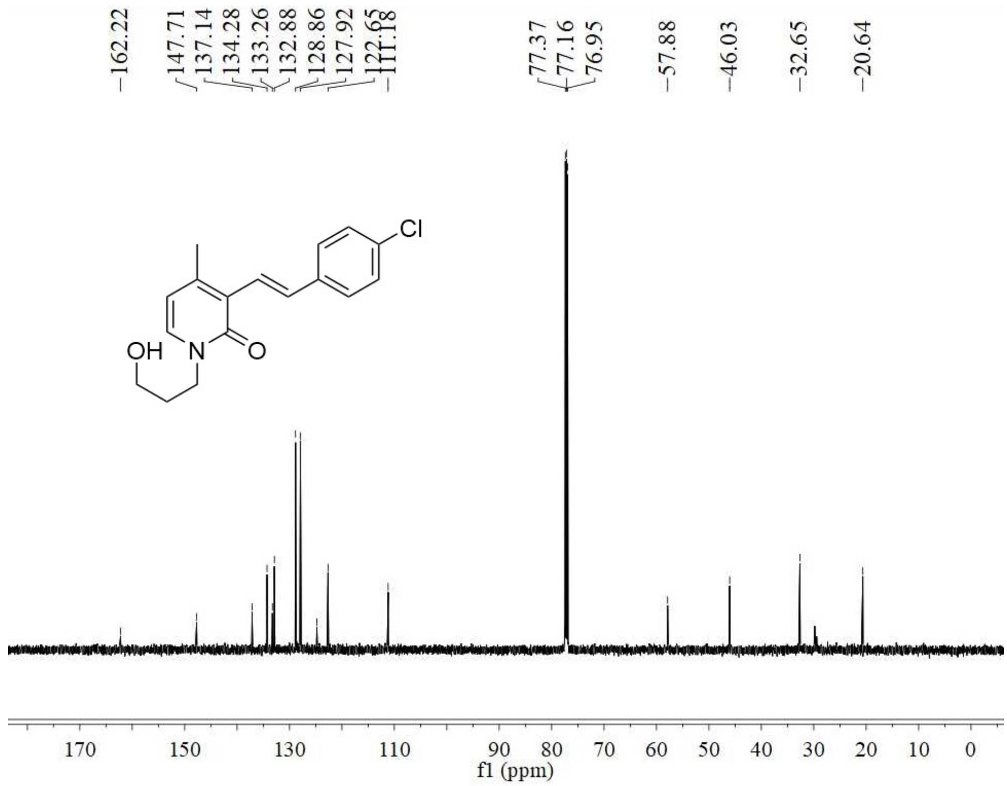


^{13}C NMR ($CDCl_3$)

3d

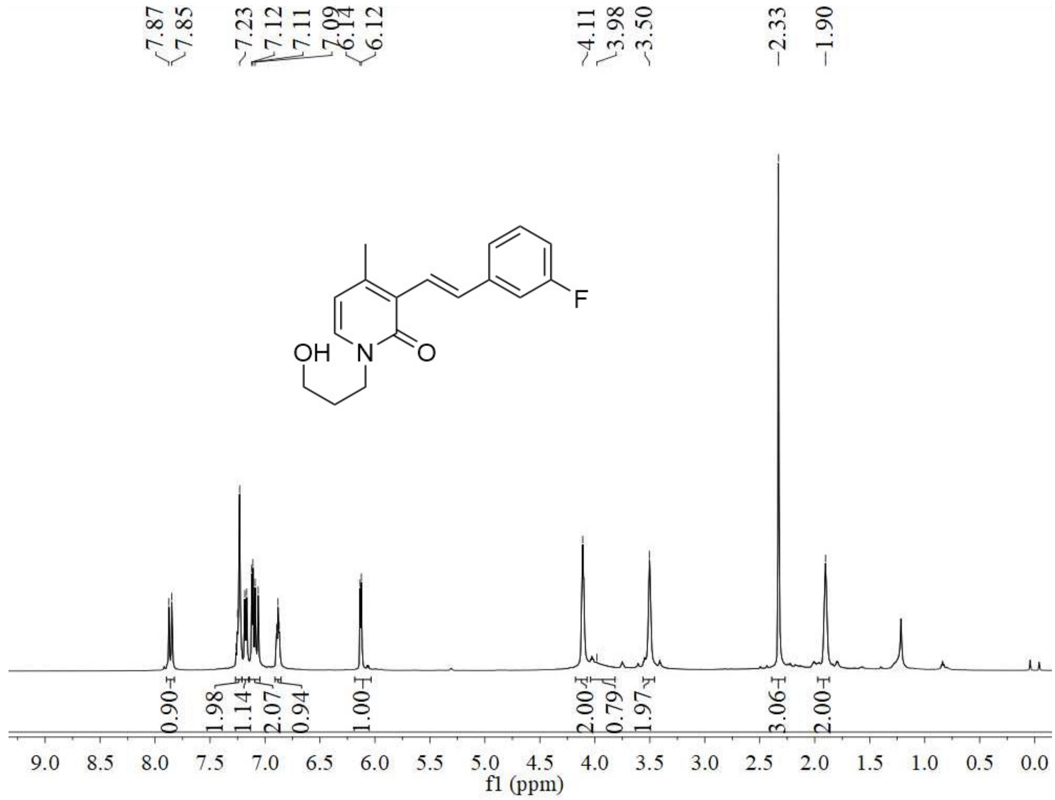


^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

3e



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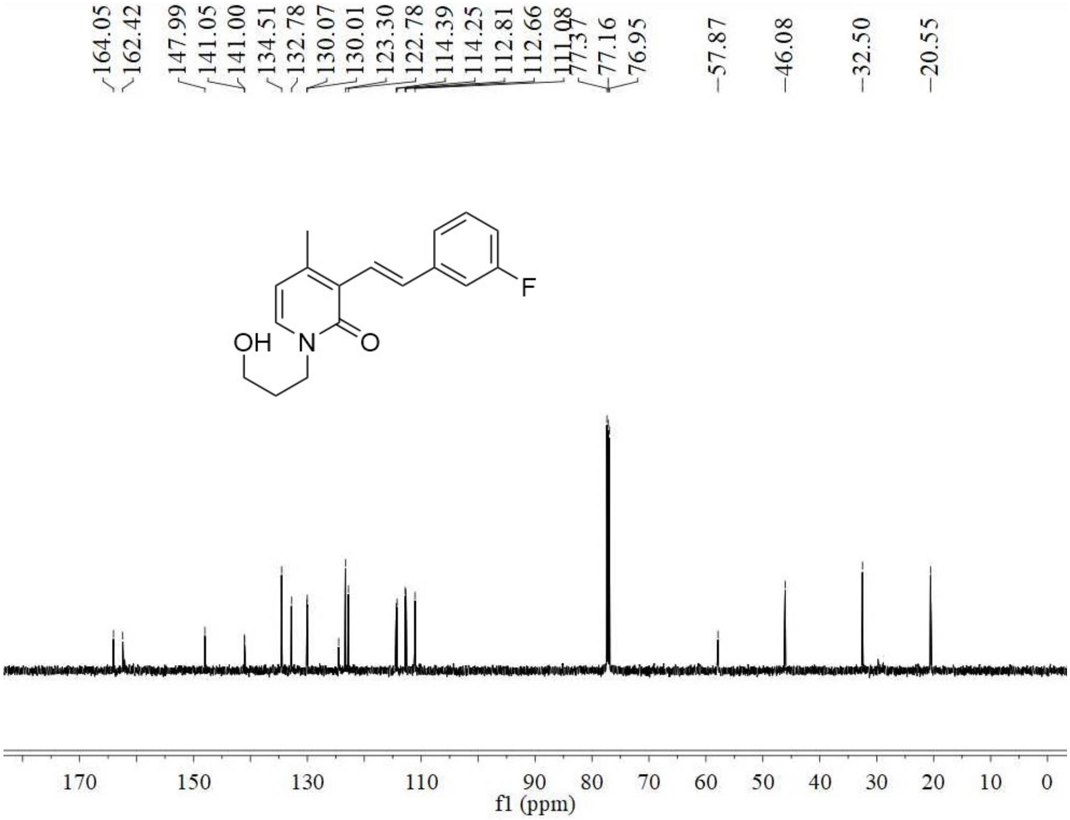
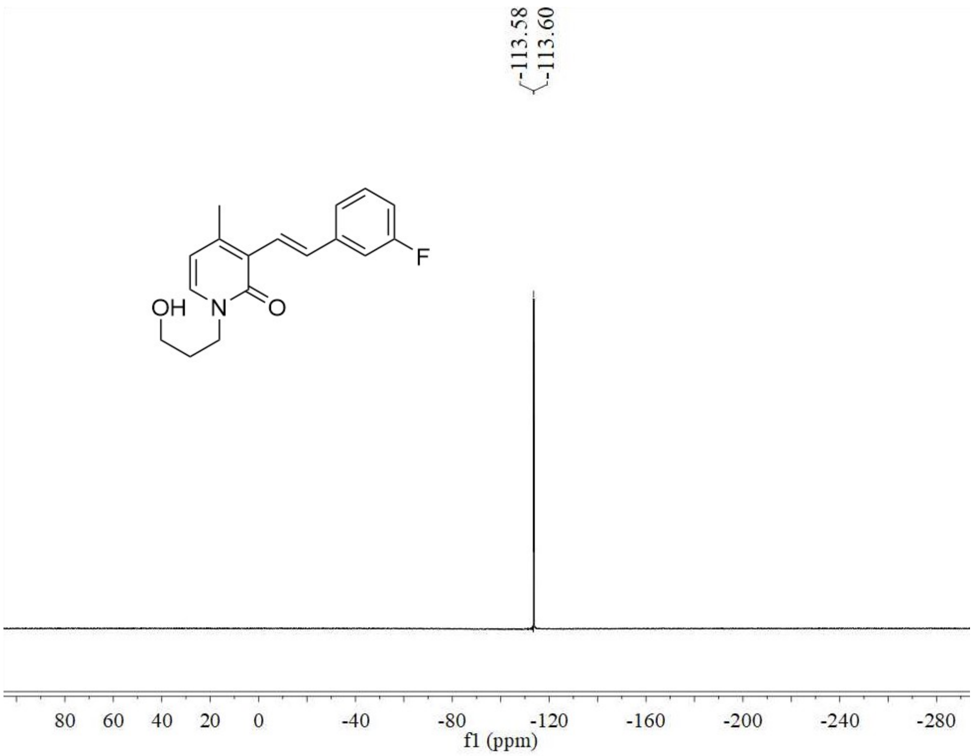
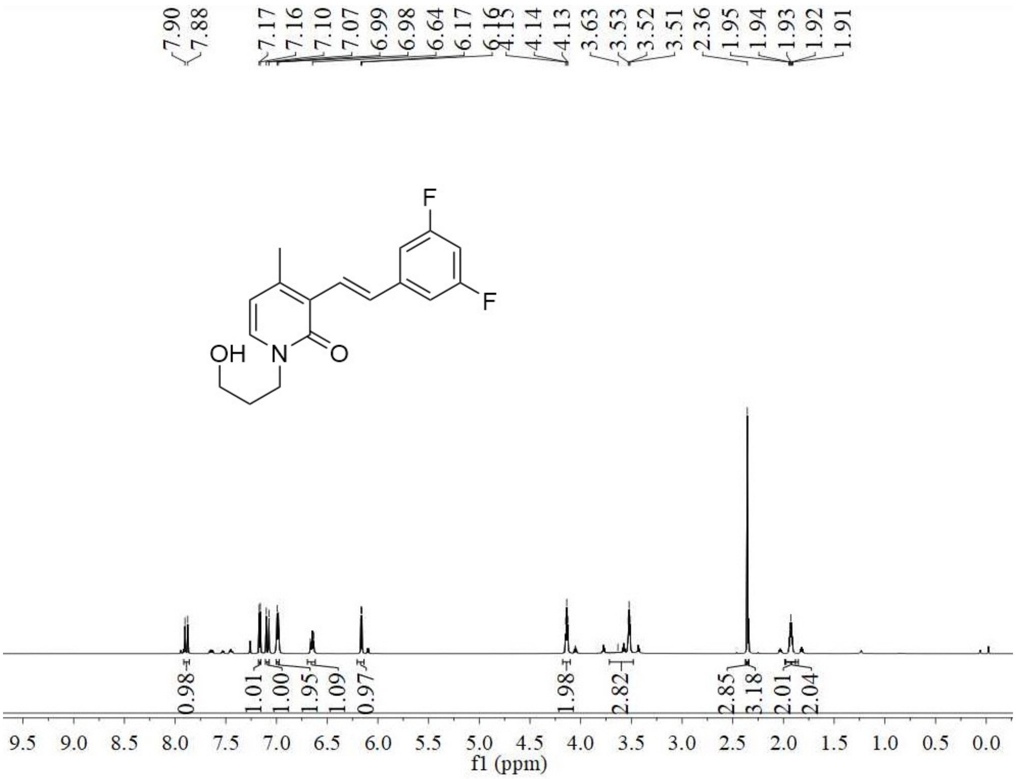


^{13}C NMR ($CDCl_3$)

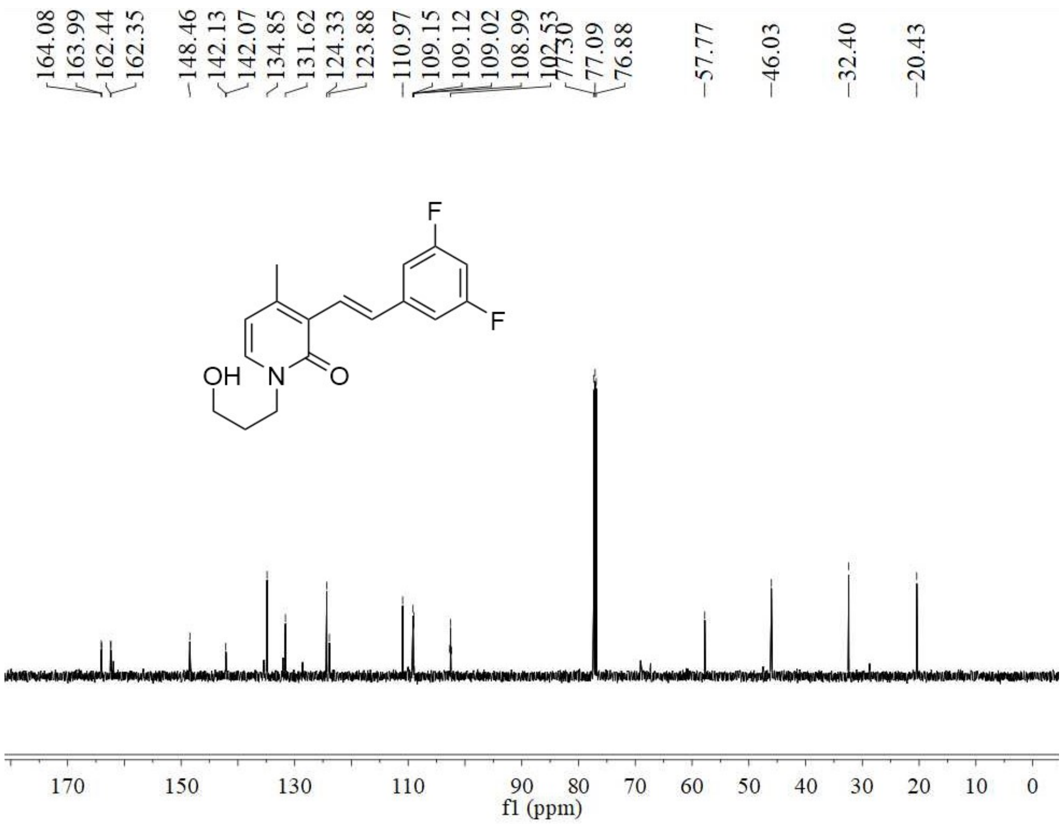


^{19}F NMR ($CDCl_3$)

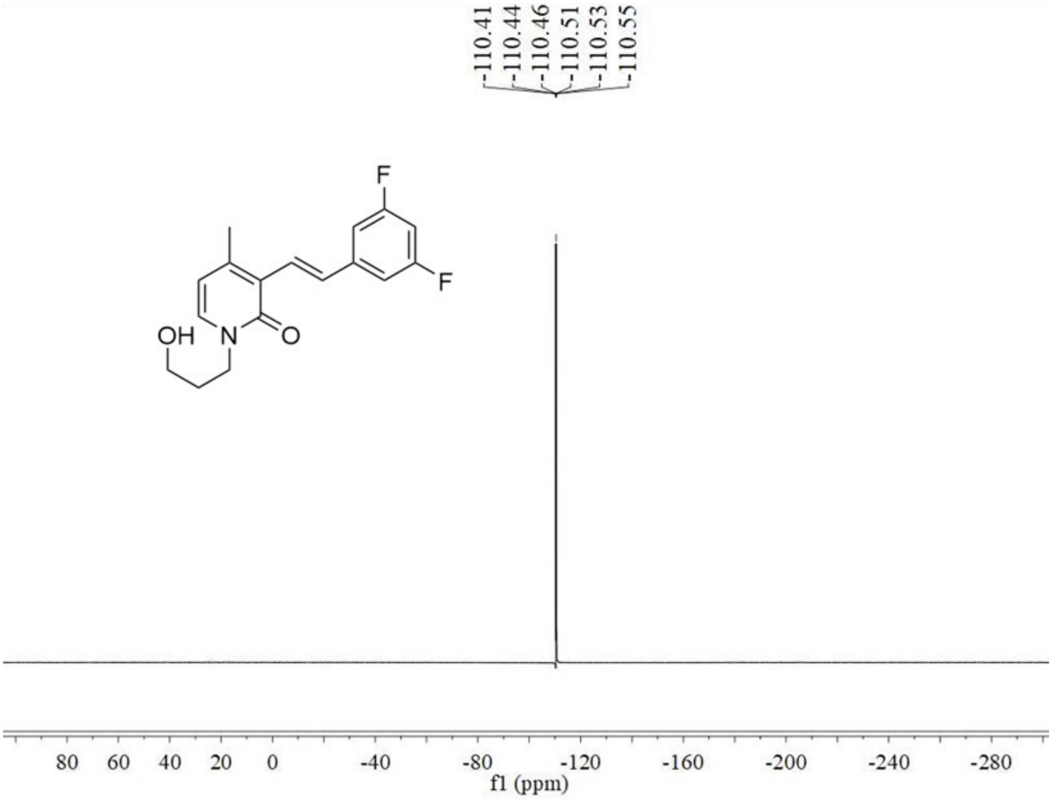
3f



^{1}H NMR ($CDCl_3$)

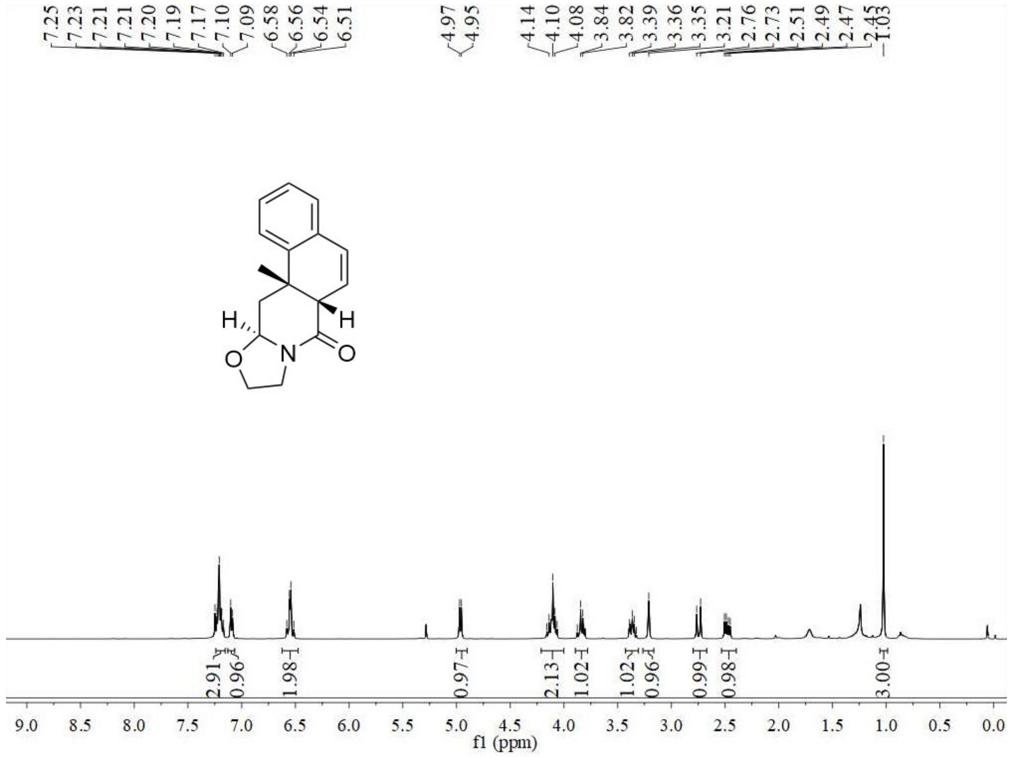


^{13}C NMR ($CDCl_3$)

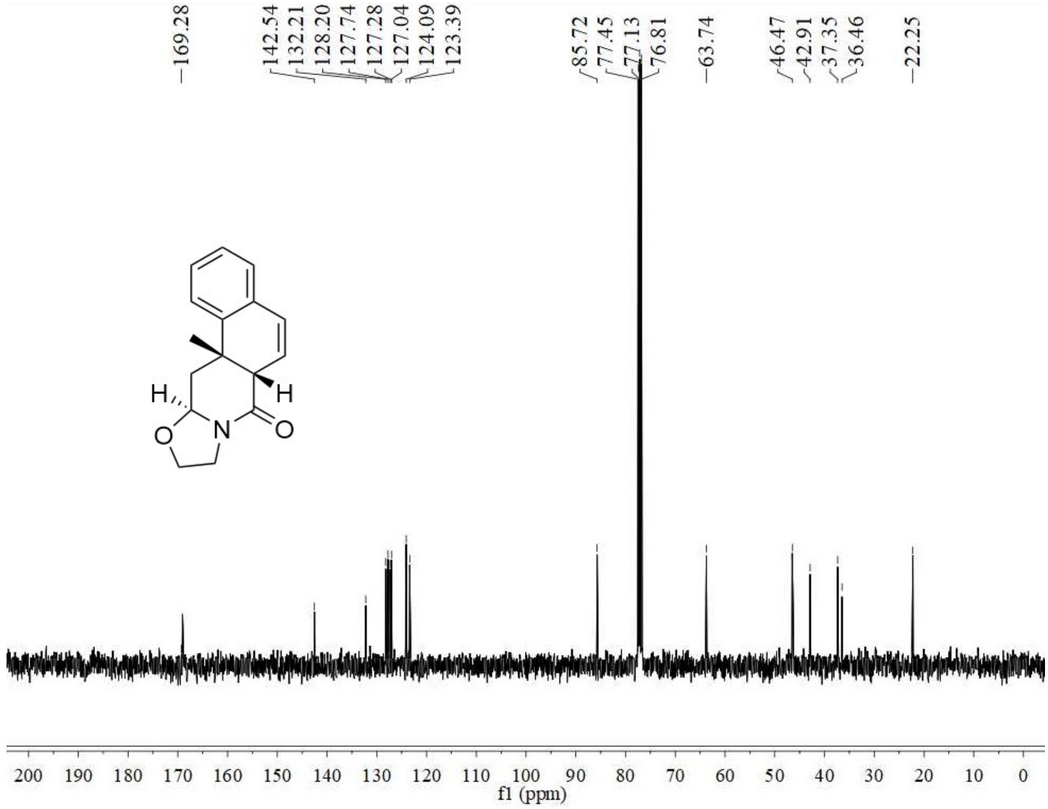


^{19}F NMR ($CDCl_3$)

2a-α

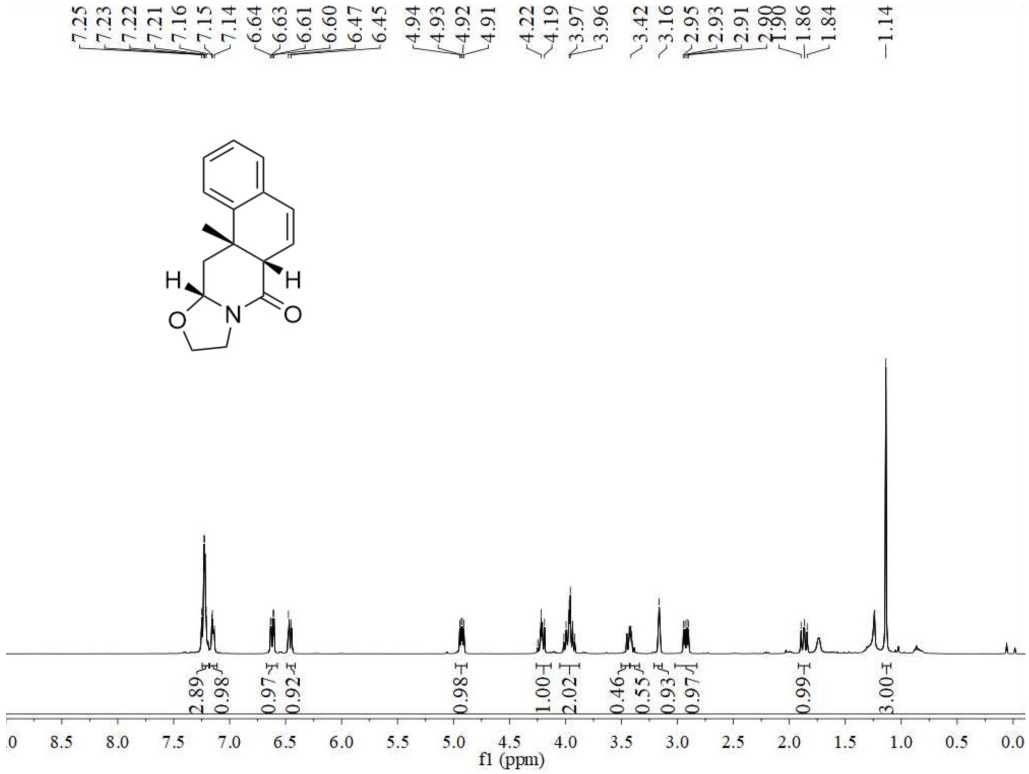


^{1}H NMR ($CDCl_3$)

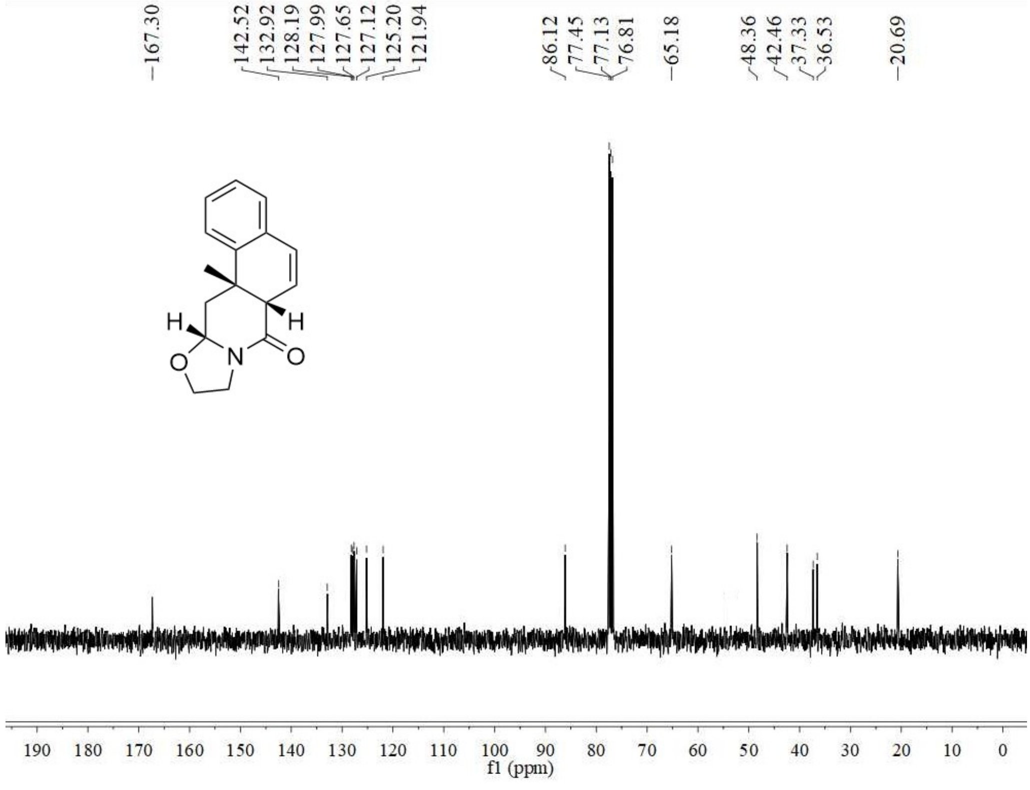


^{13}C NMR ($CDCl_3$)

2a-β

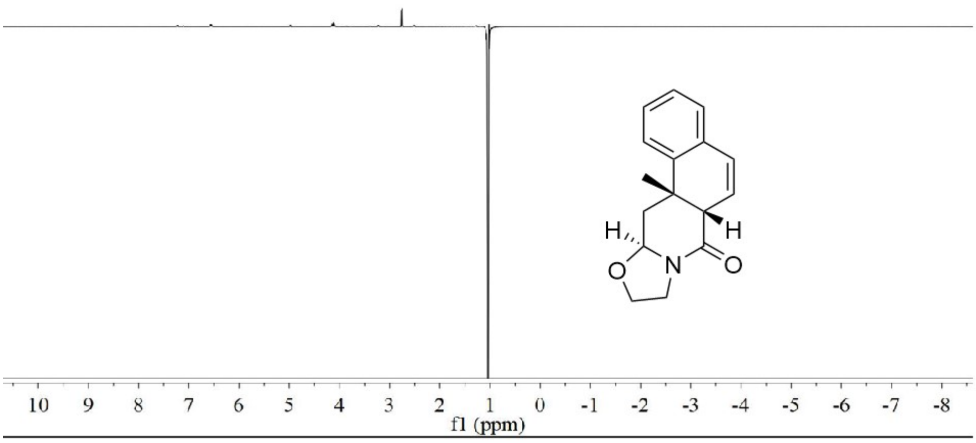


^{1}H NMR ($CDCl_3$)



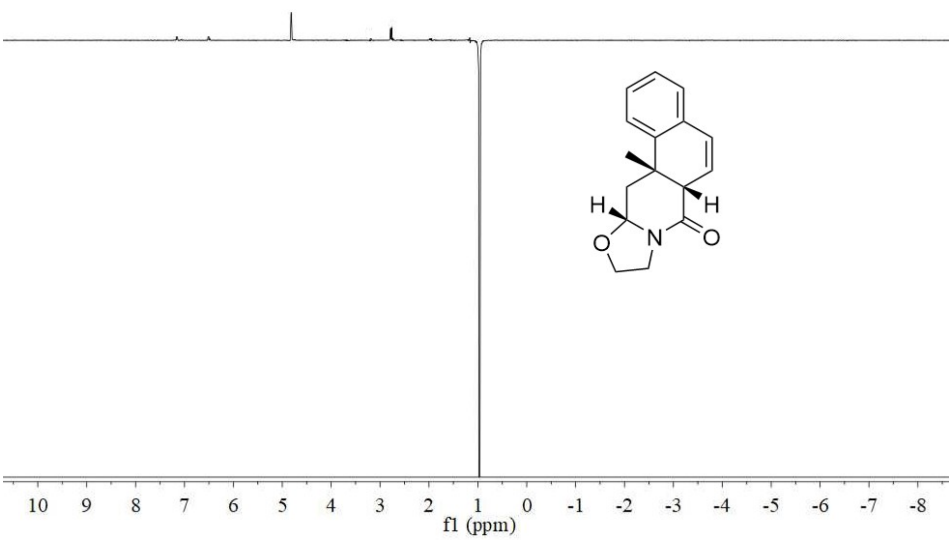
^{13}C NMR ($CDCl_3$)

2a-α



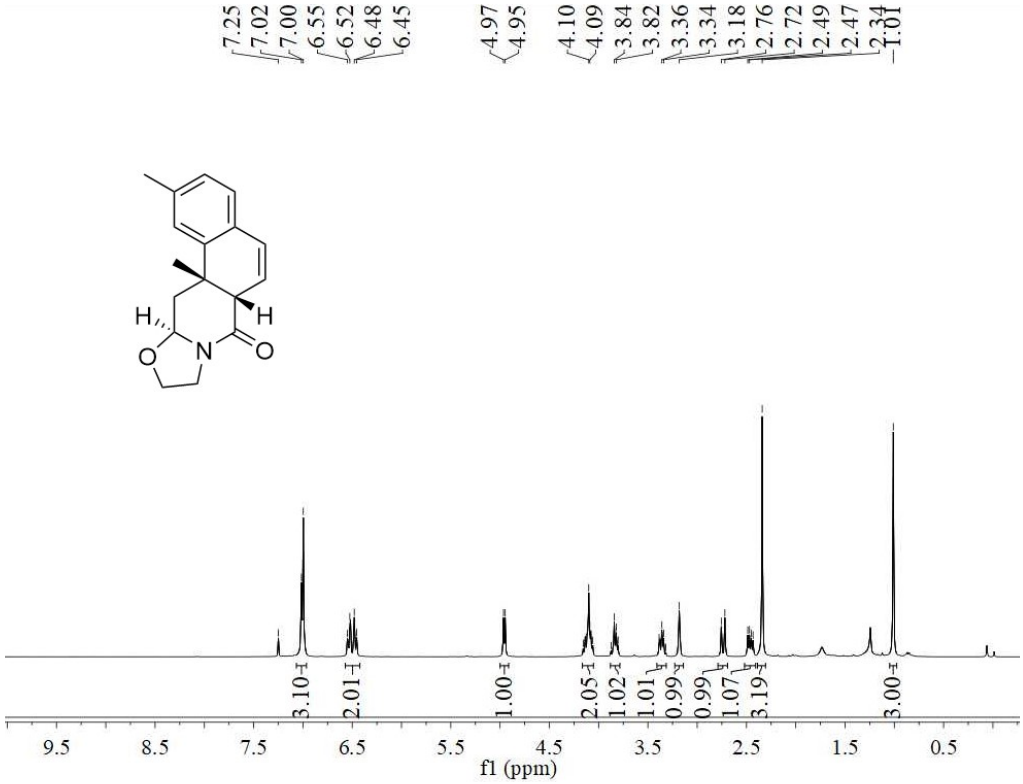
NOE NMR

2a-β

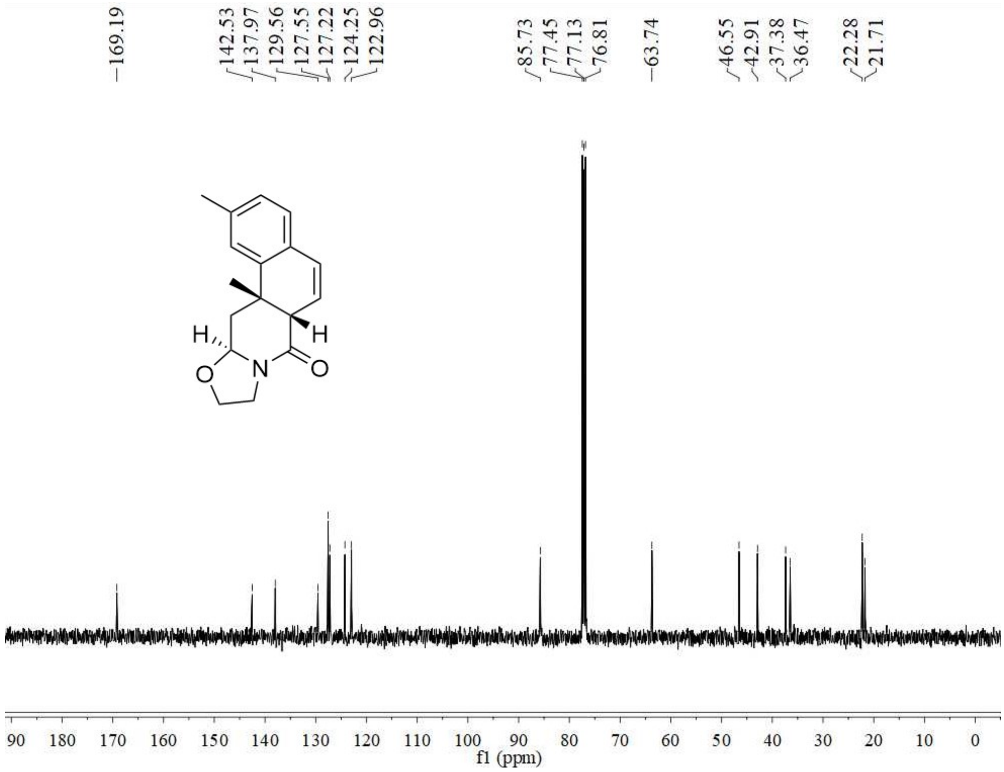


NOE NMR

2b-α

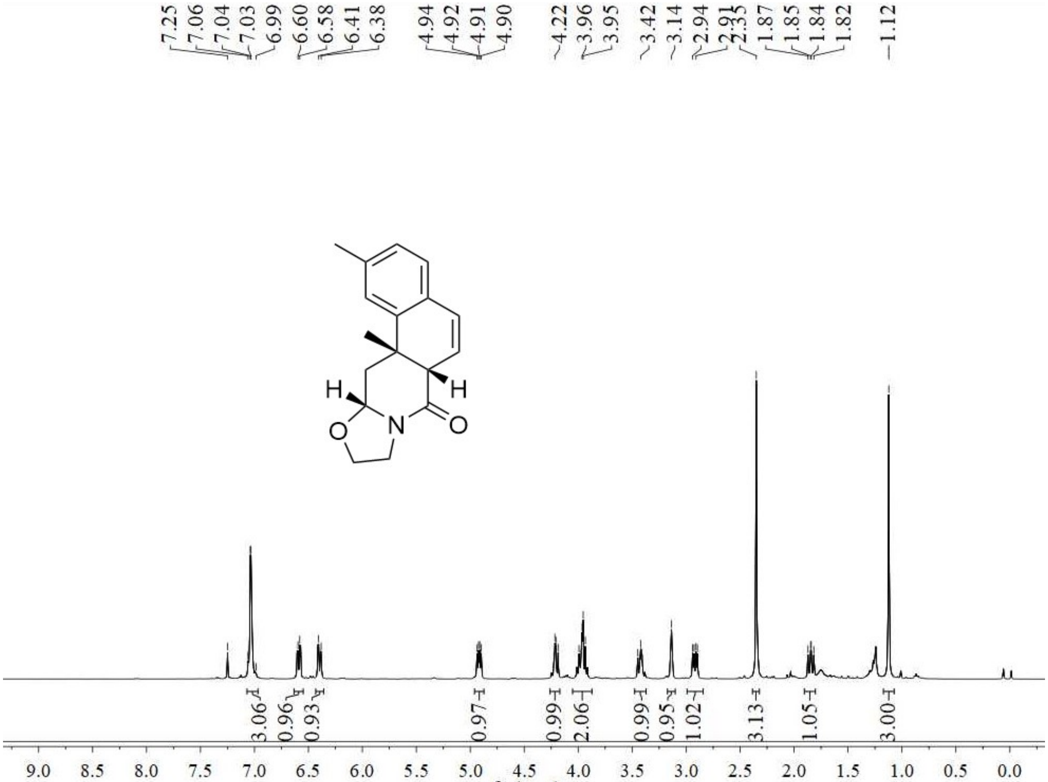


^{1}H NMR ($CDCl_3$)

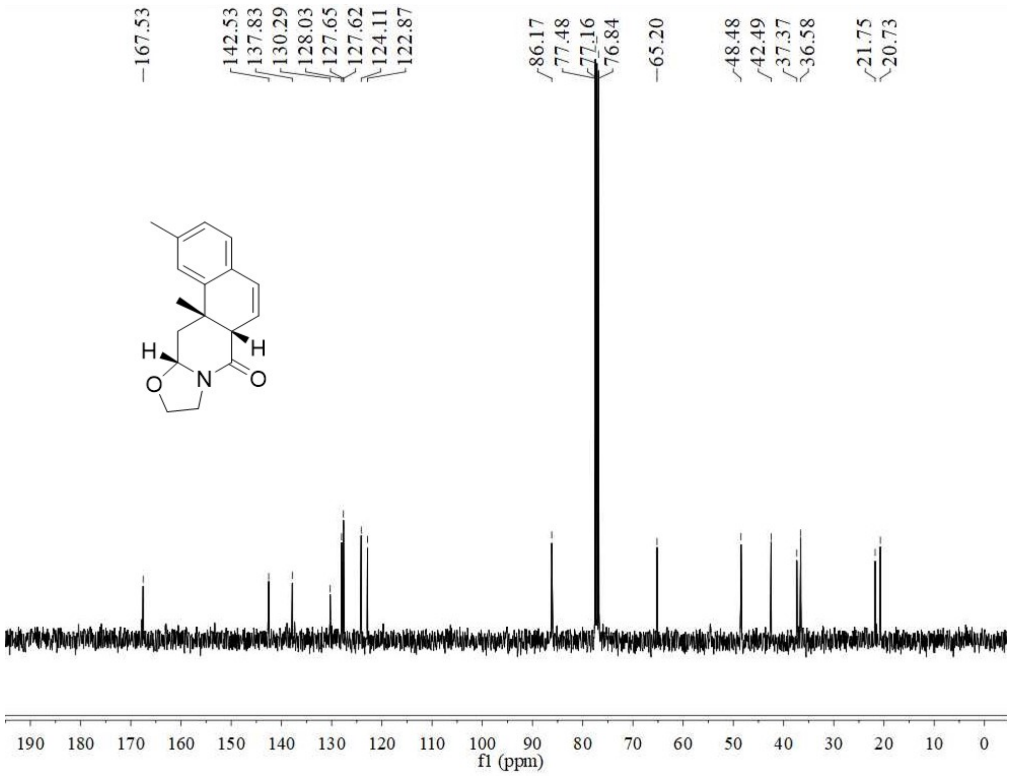


^{13}C NMR ($CDCl_3$)

2b-β

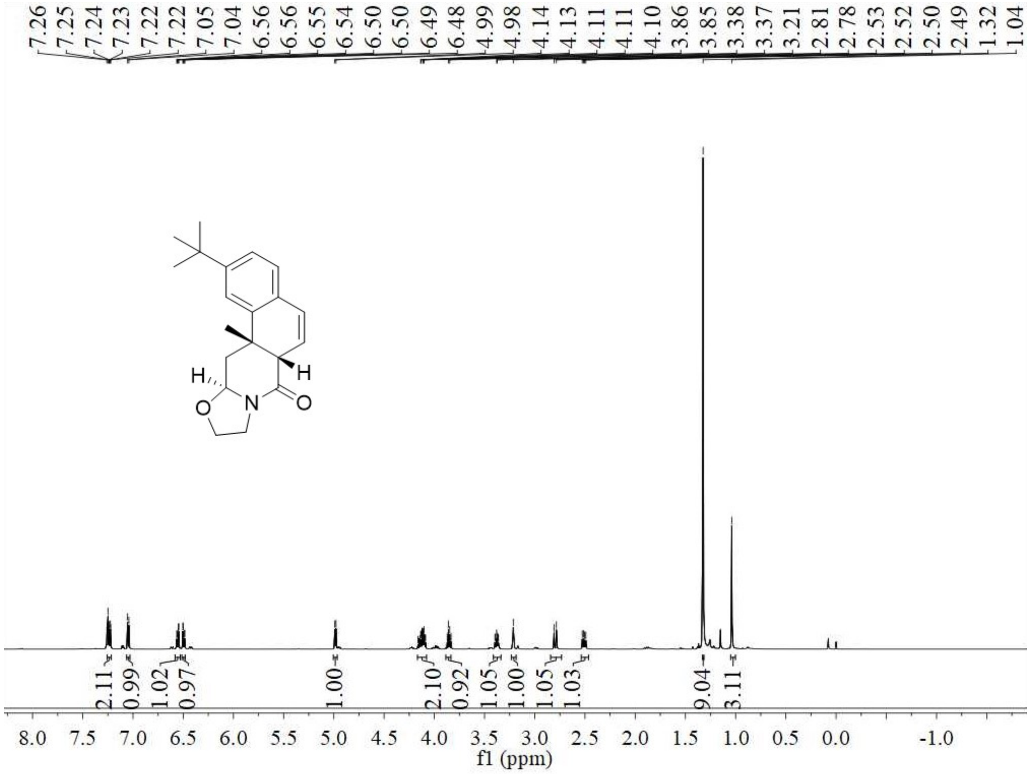


^{1}H NMR ($CDCl_3$)

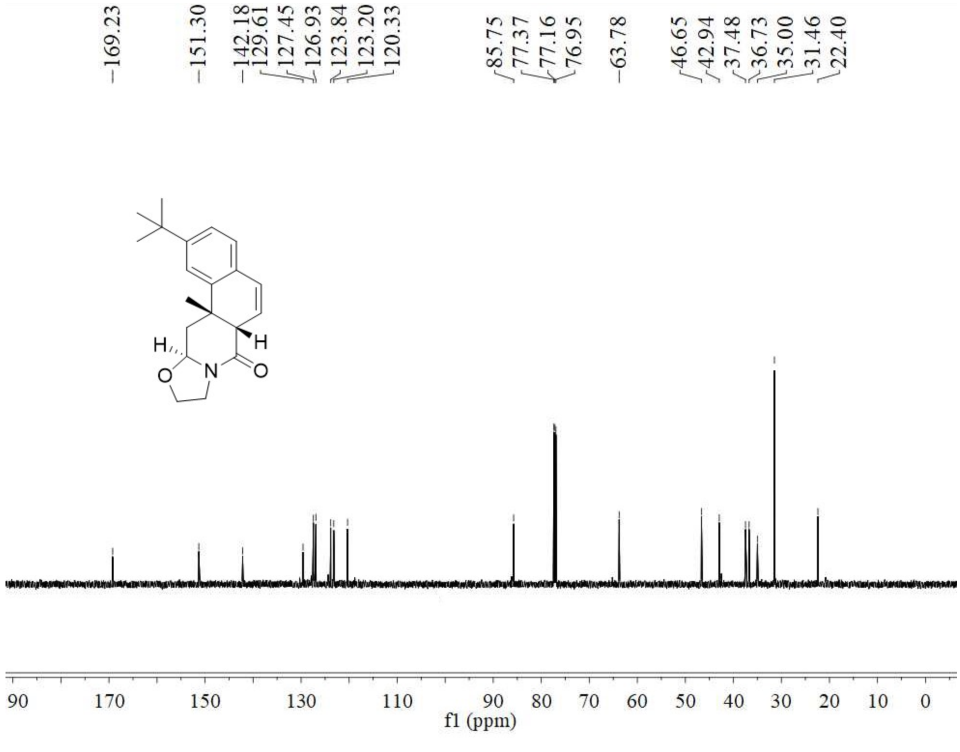


^{13}C NMR ($CDCl_3$)

2c-α

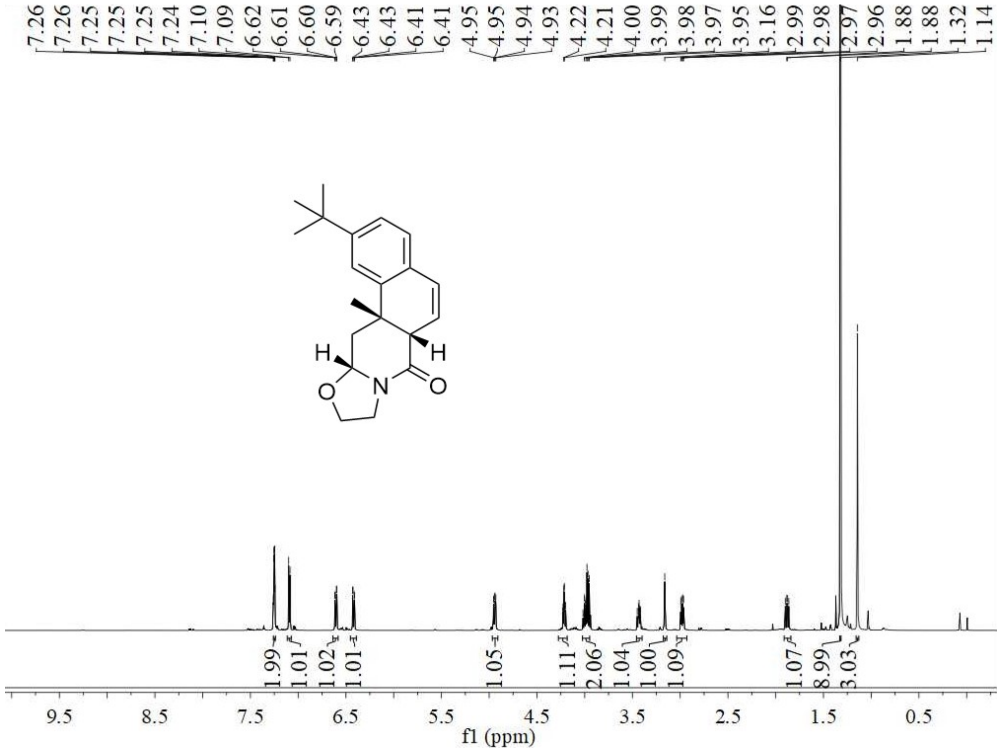


^{1}H NMR ($CDCl_3$)

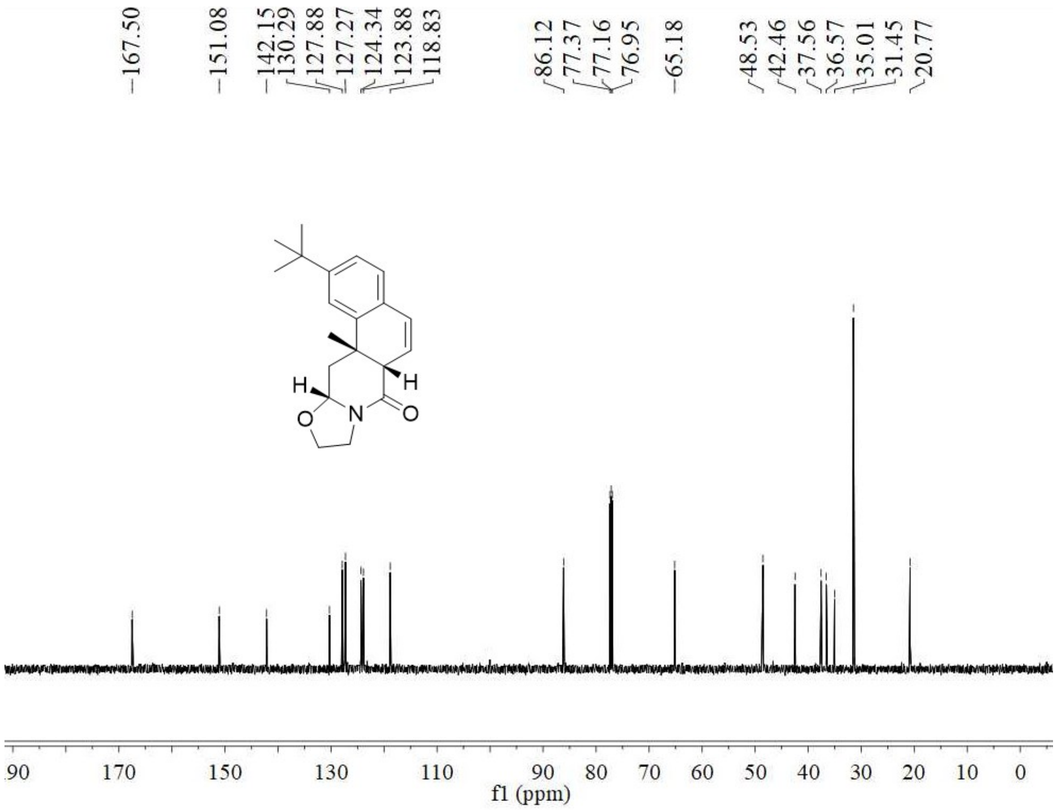


^{13}C NMR ($CDCl_3$)

2c-β

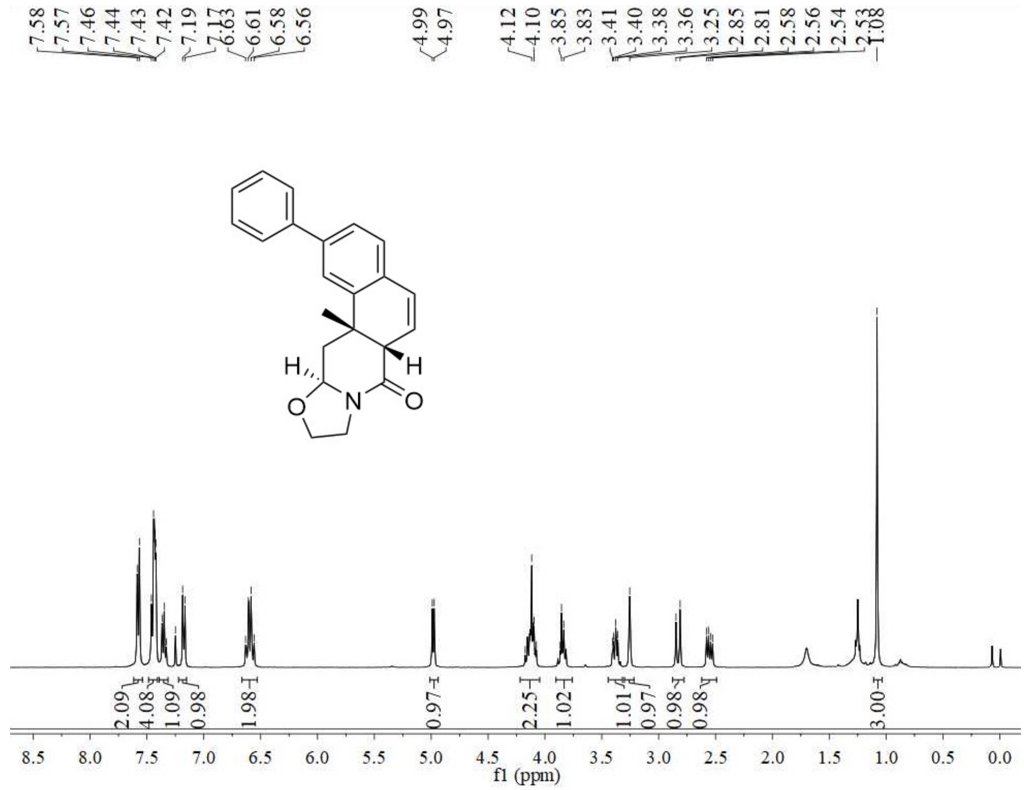


^{1}H NMR ($CDCl_3$)

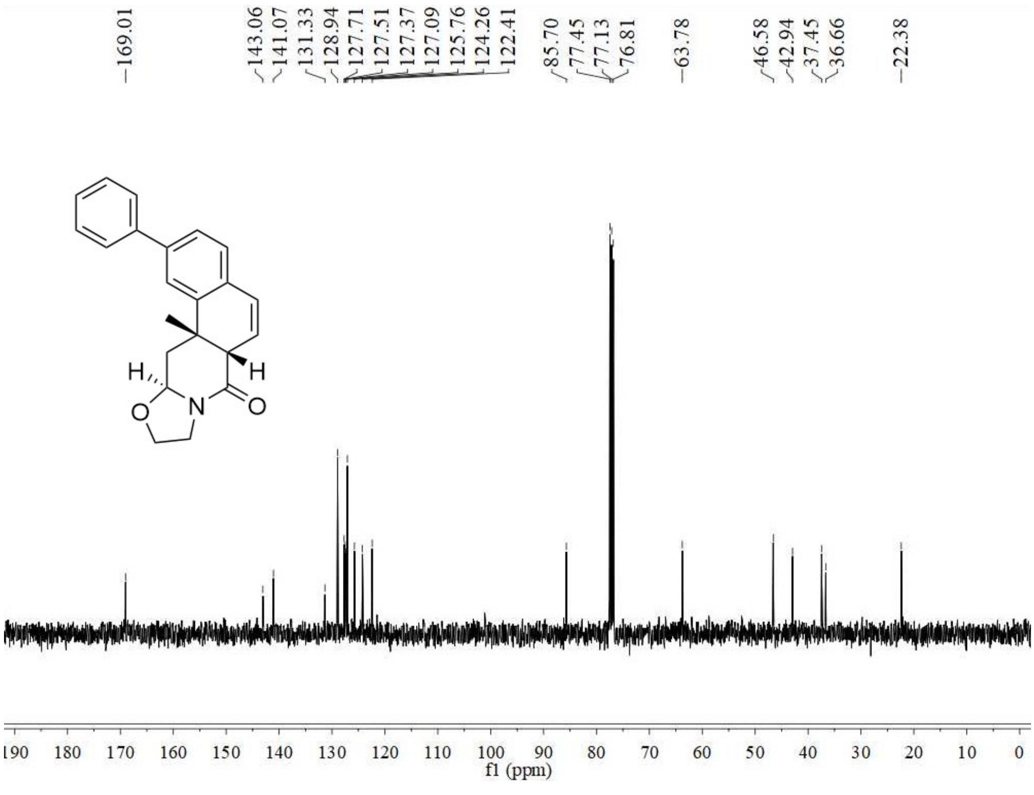


^{13}C NMR ($CDCl_3$)

2d-α

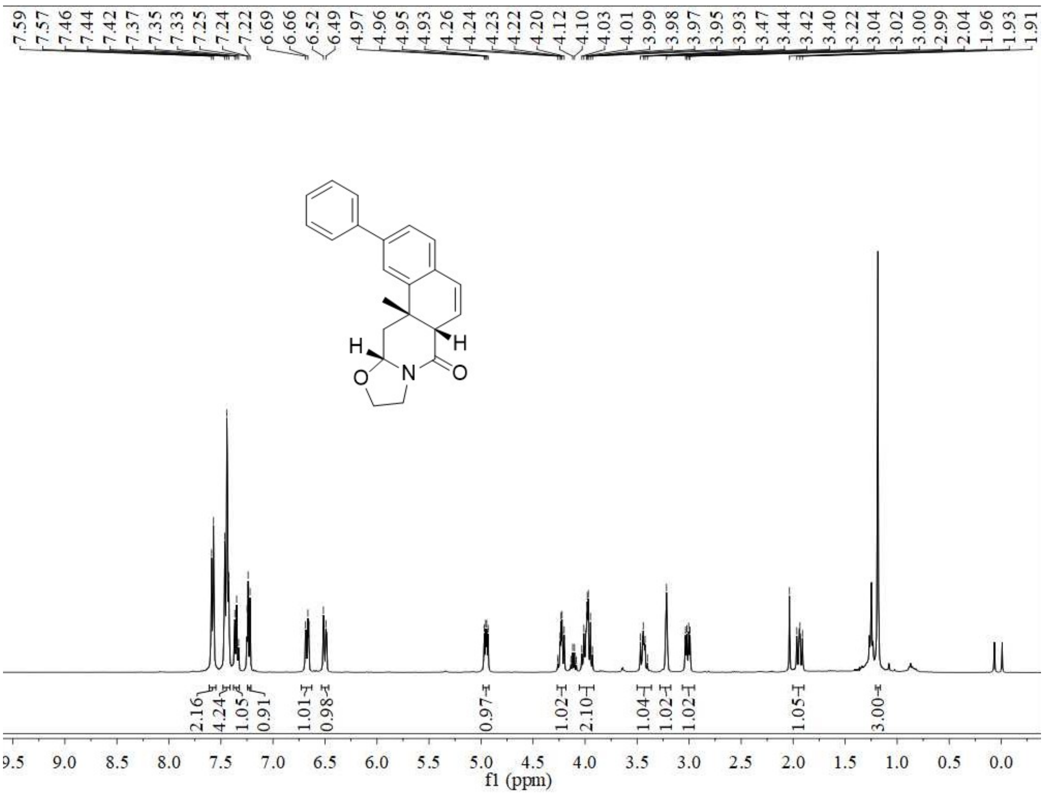


^{1}H NMR (CDCl$_3$)

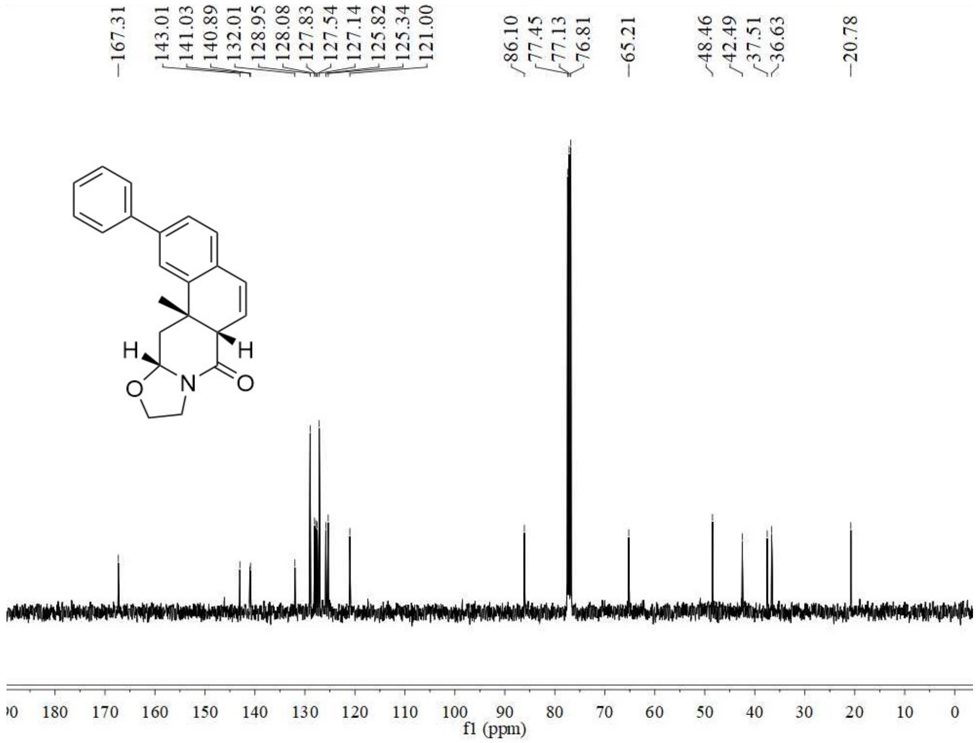


^{13}C NMR (CDCl$_3$)

2d-β

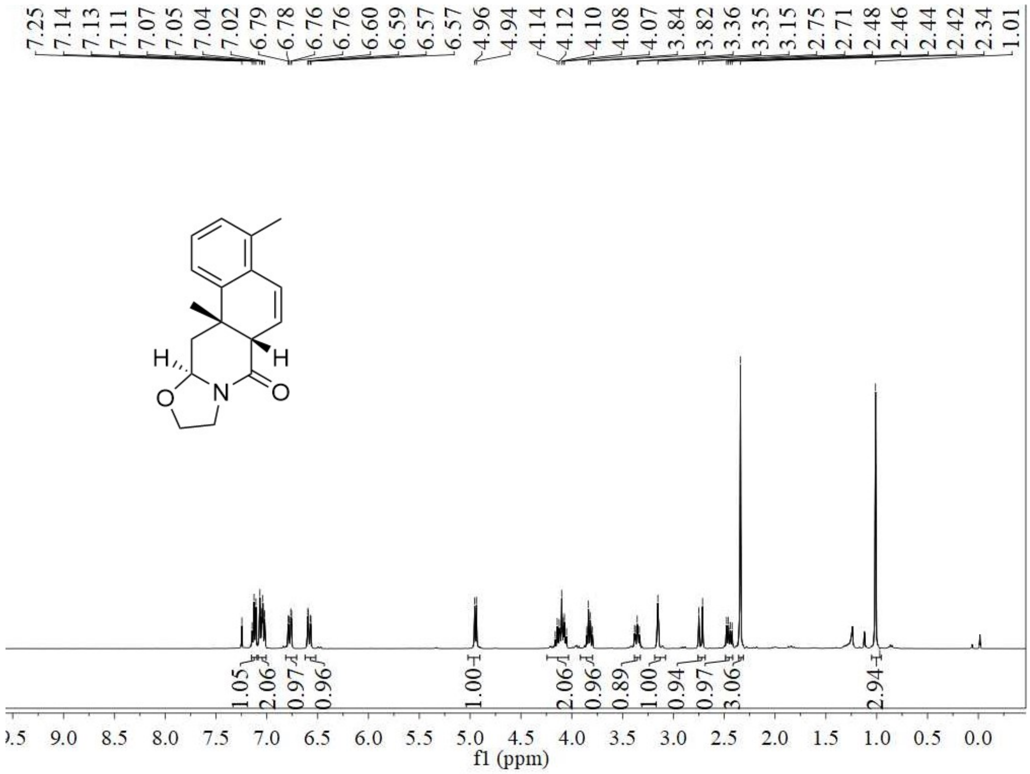


^1H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

2e-α



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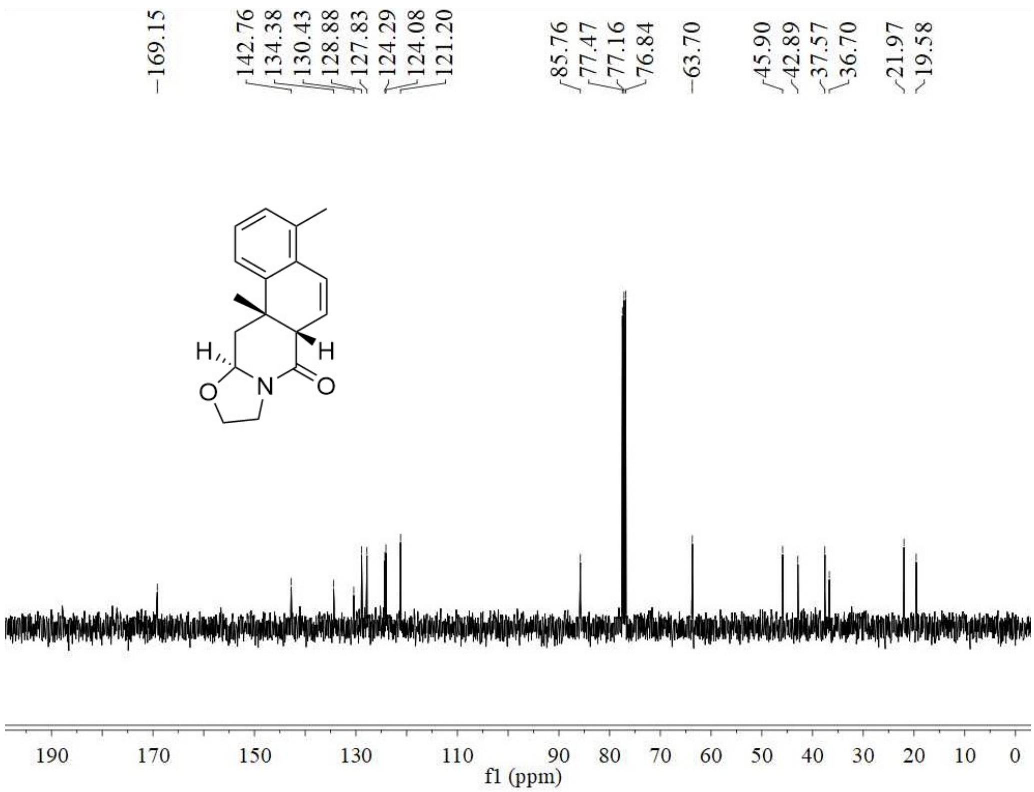
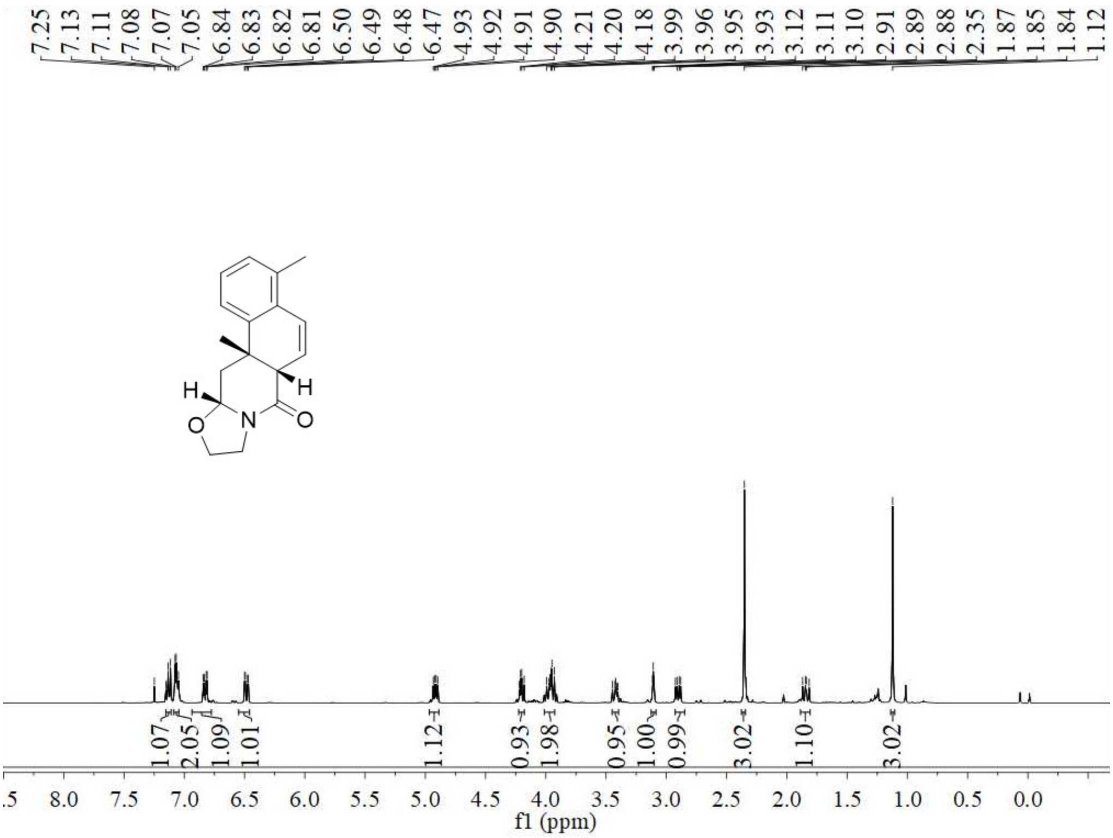


^{13}C NMR ($CDCl_3$)

2e-β



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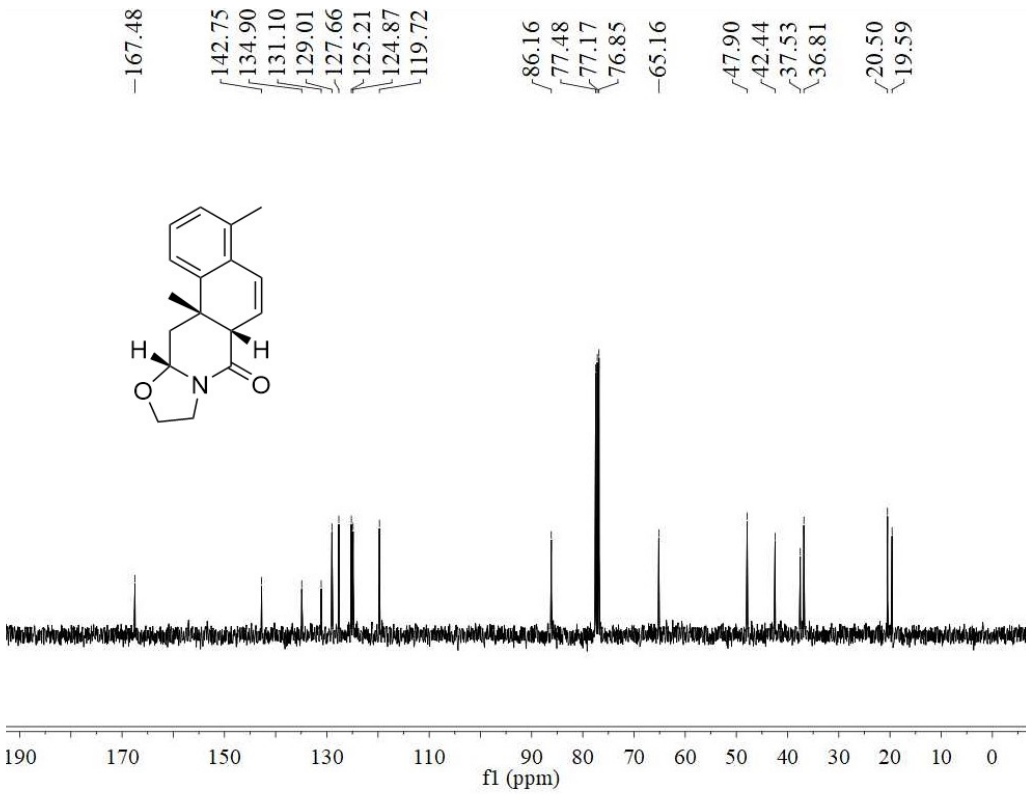
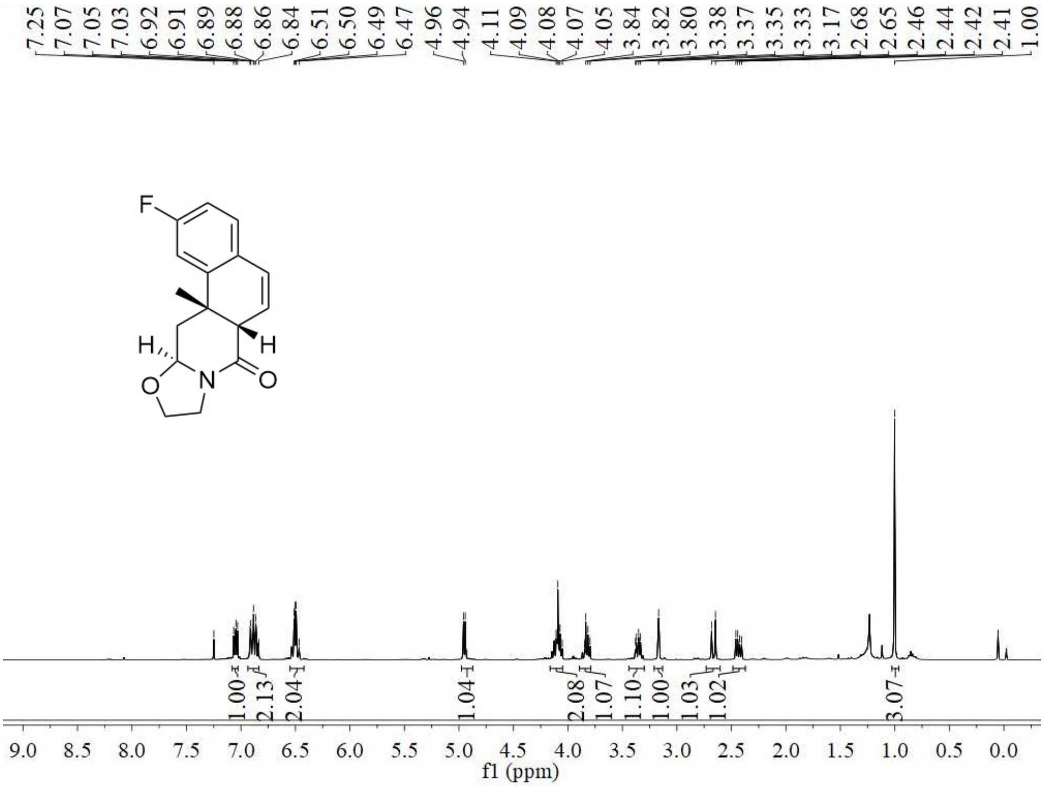
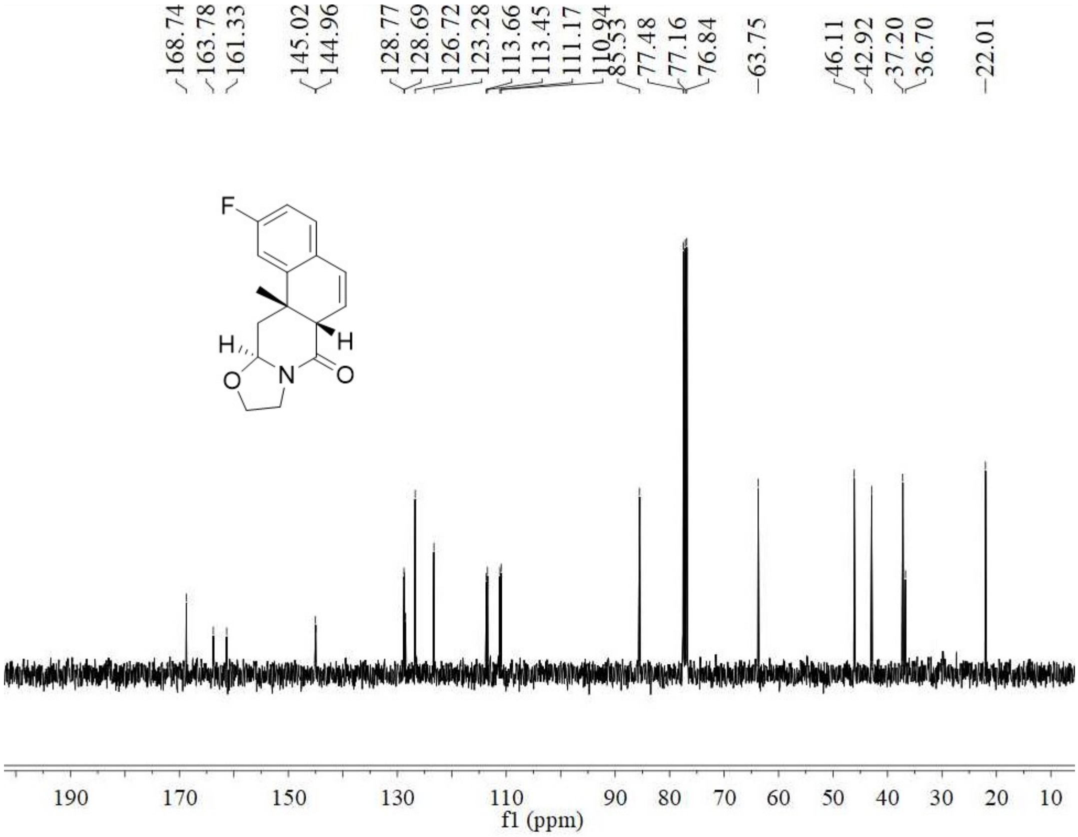


^{13}C NMR ($CDCl_3$)

2f-α

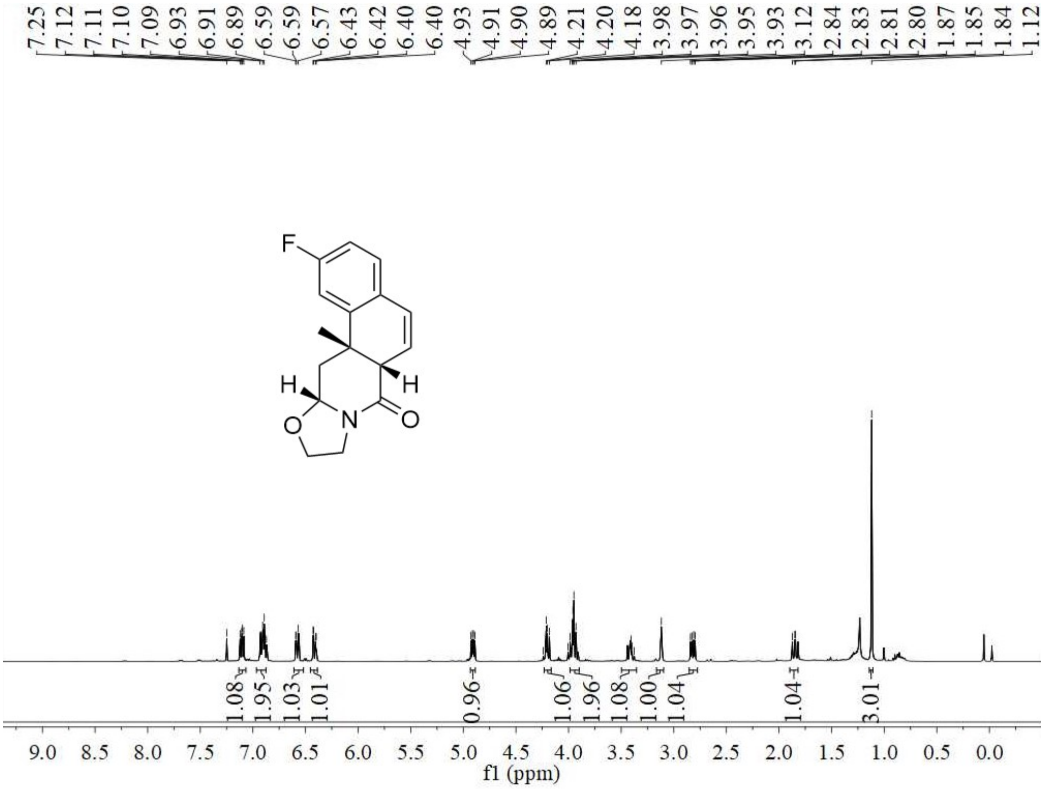


^{1}H NMR ($CDCl_3$)

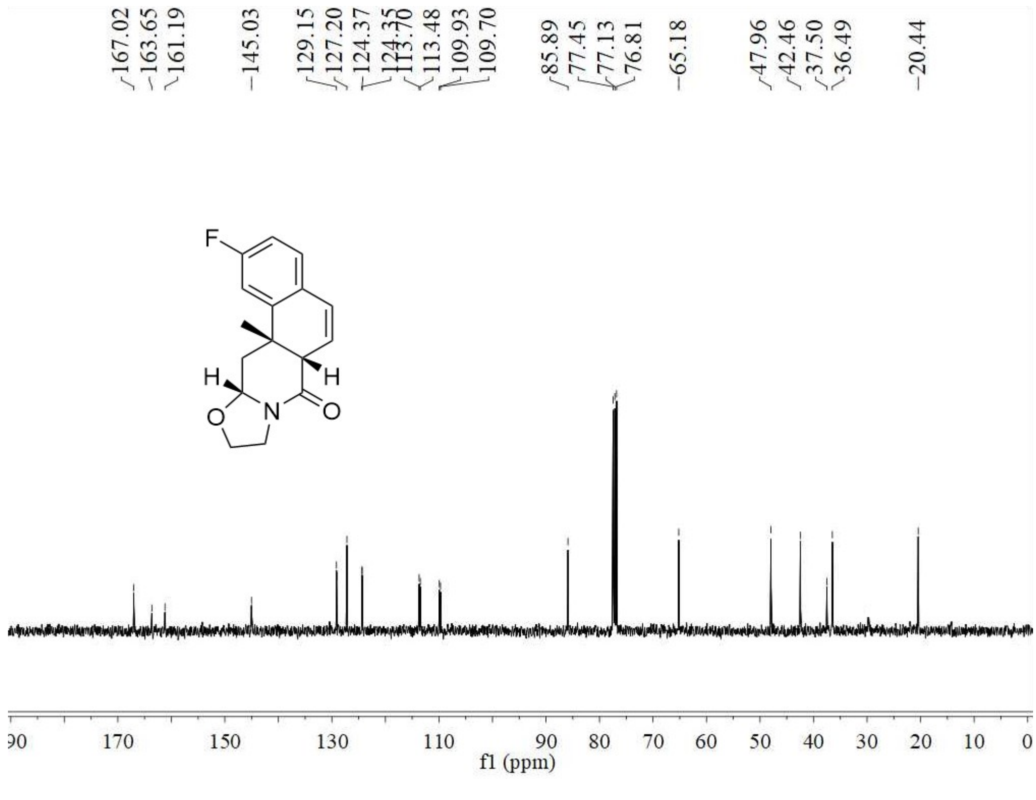


^{13}C NMR ($CDCl_3$)

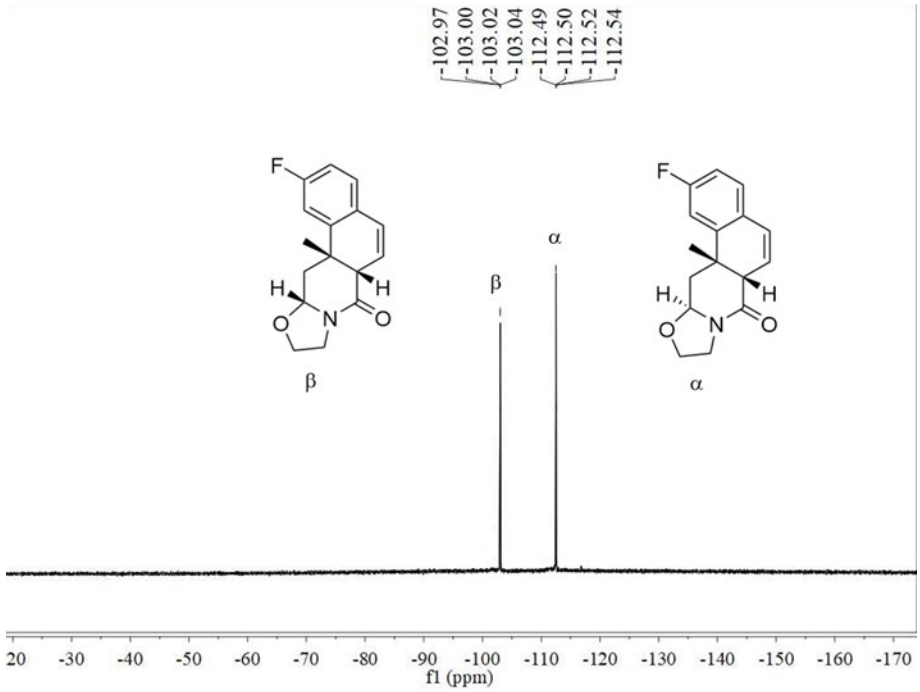
2f-β



^{1}H NMR ($CDCl_3$)

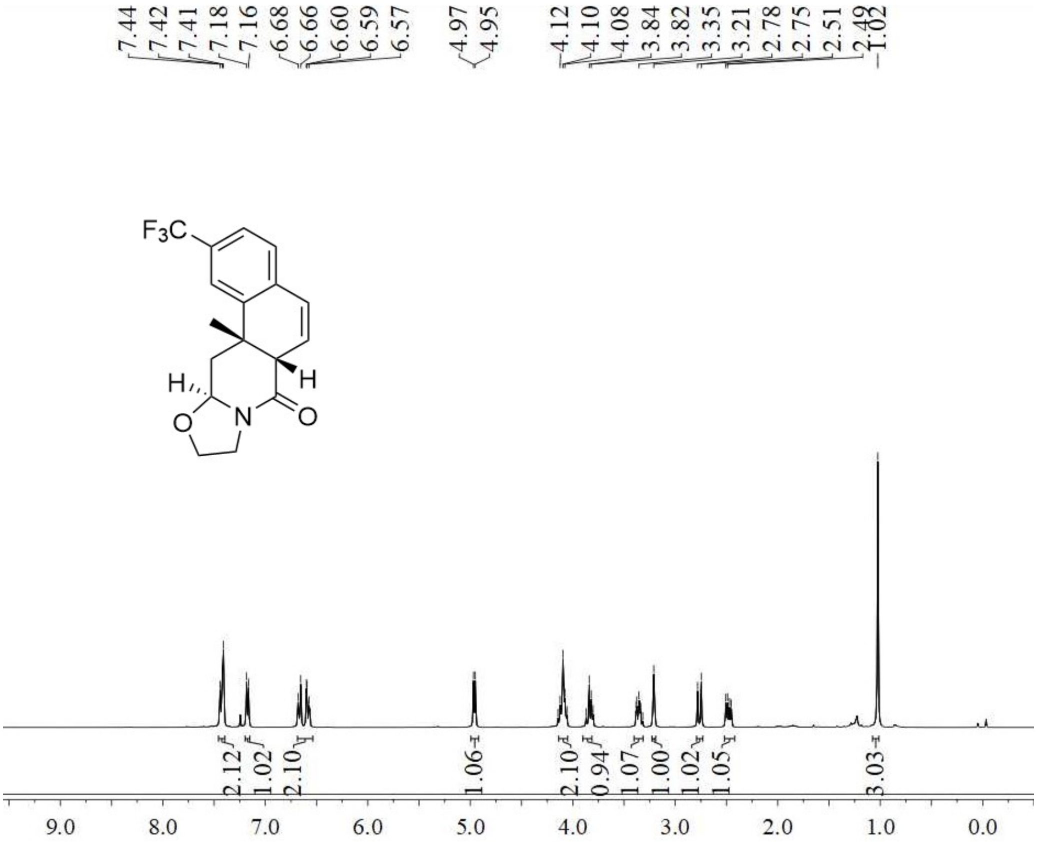


^{13}C NMR ($CDCl_3$)

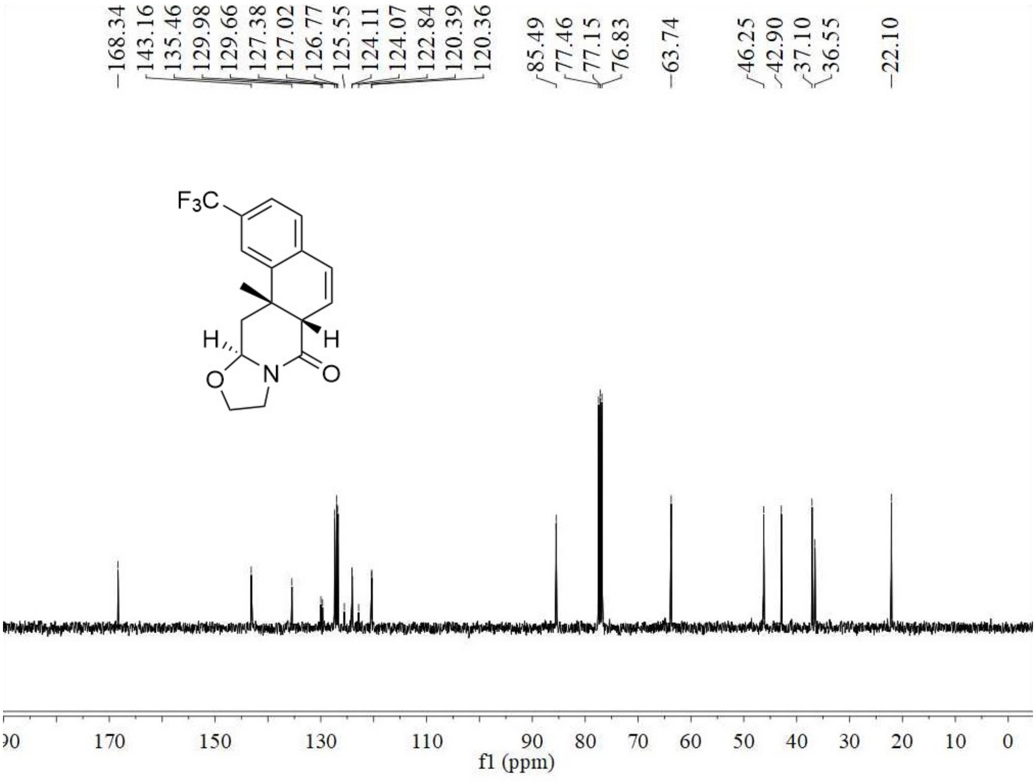


^{19}F NMR ($CDCl_3$)

2g-α

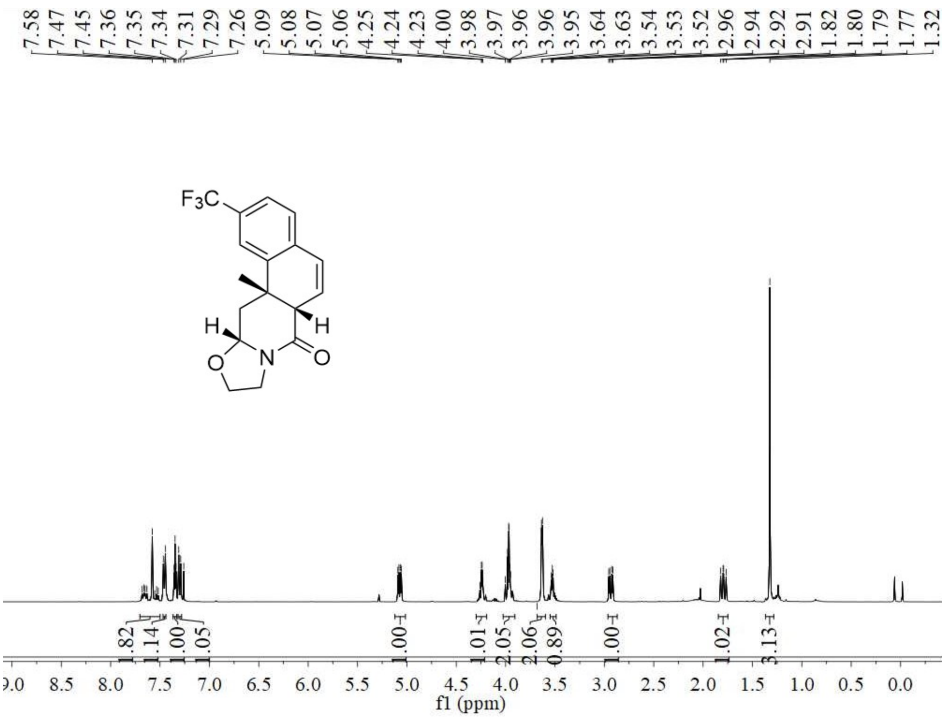


^{1}H NMR ($CDCl_3$)

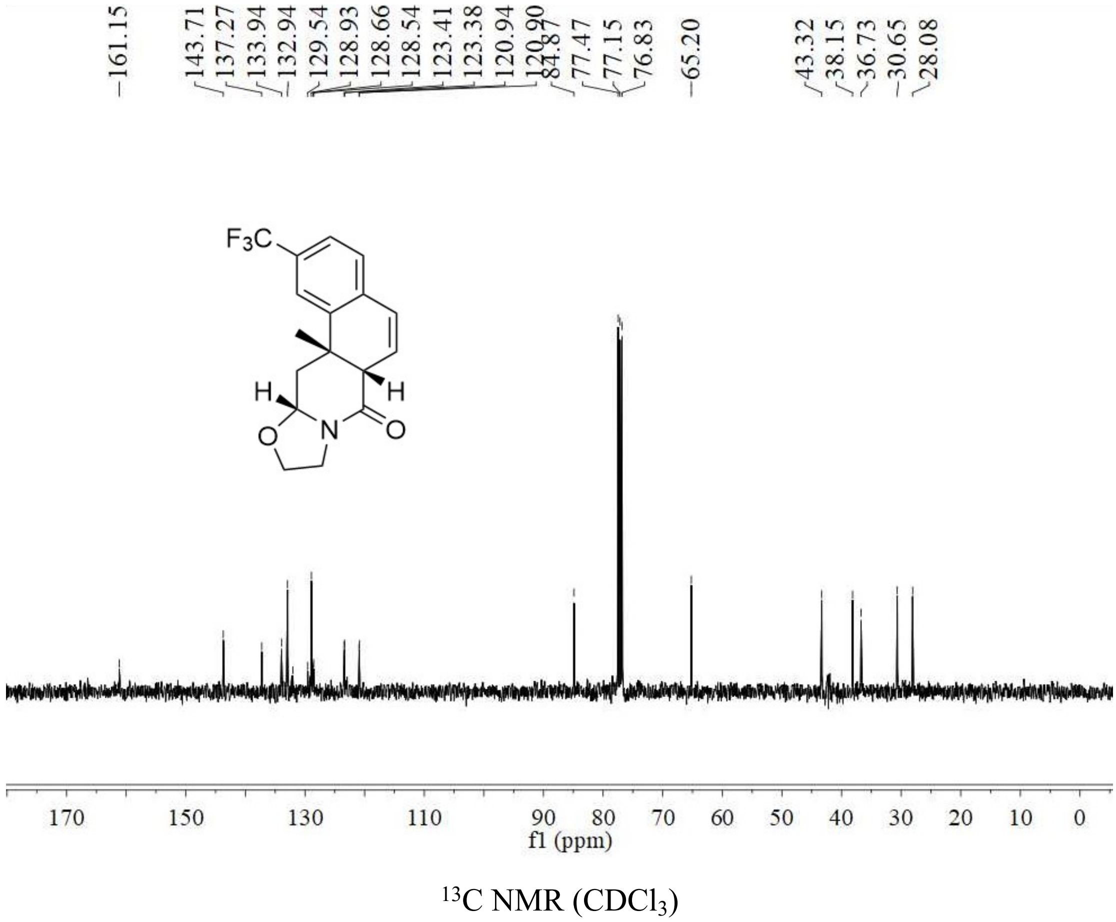


^{13}C NMR ($CDCl_3$)

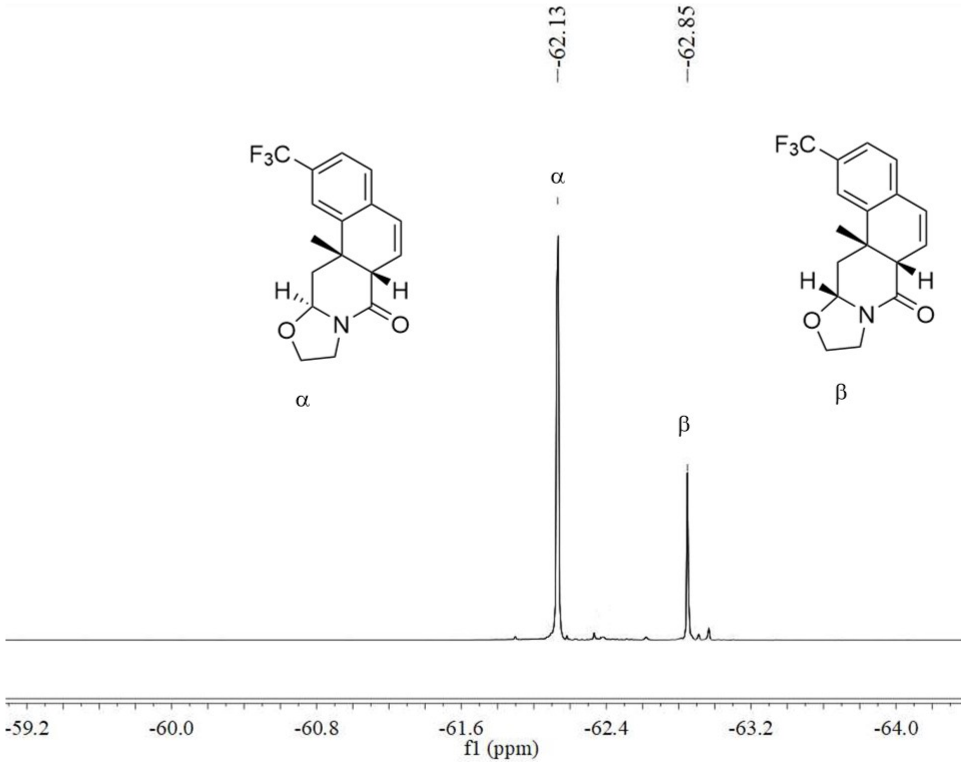
2g-β



^{1}H NMR ($CDCl_3$)

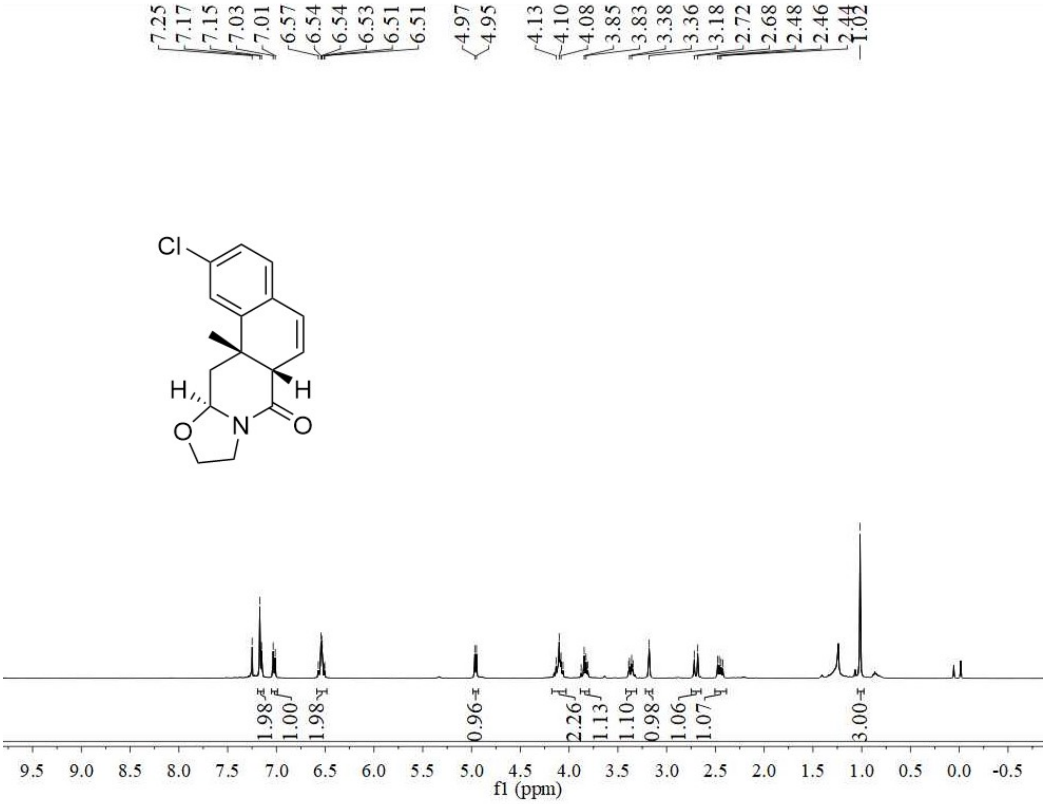


^{13}C NMR ($CDCl_3$)

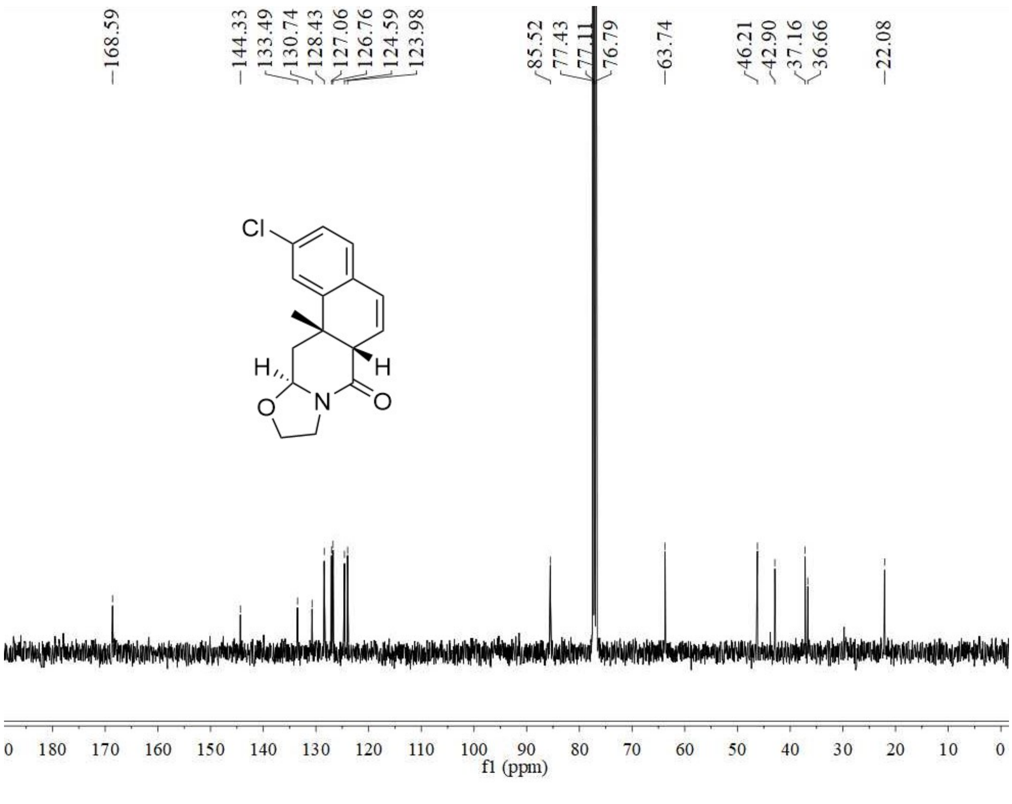


^{19}F NMR ($CDCl_3$)

2h-α

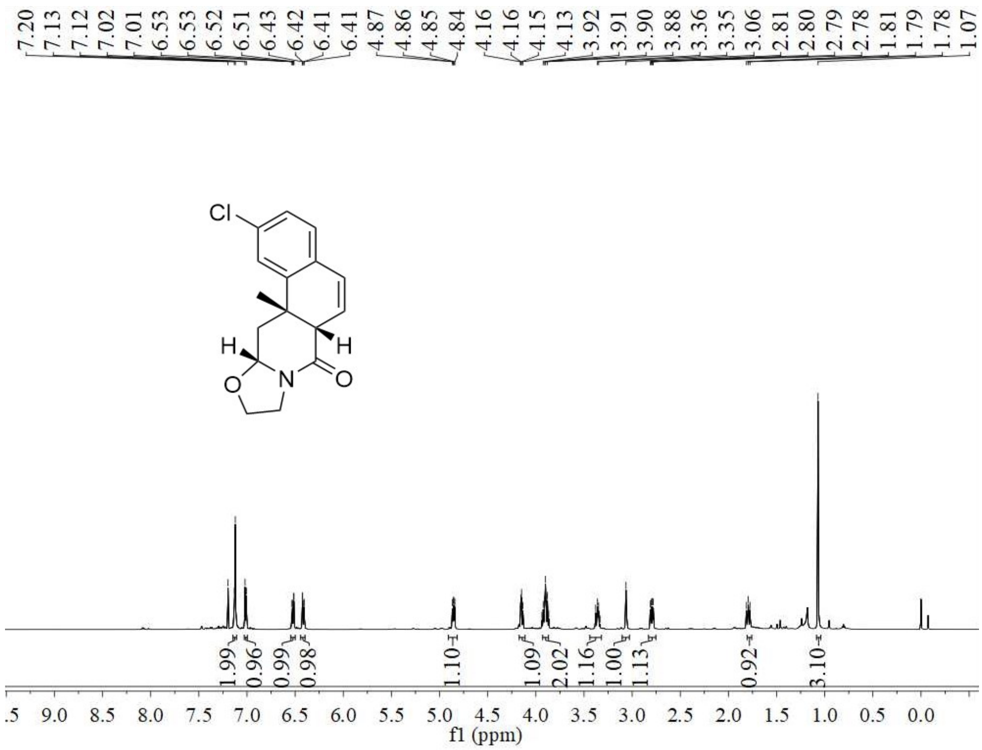


^{1}H NMR ($CDCl_3$)

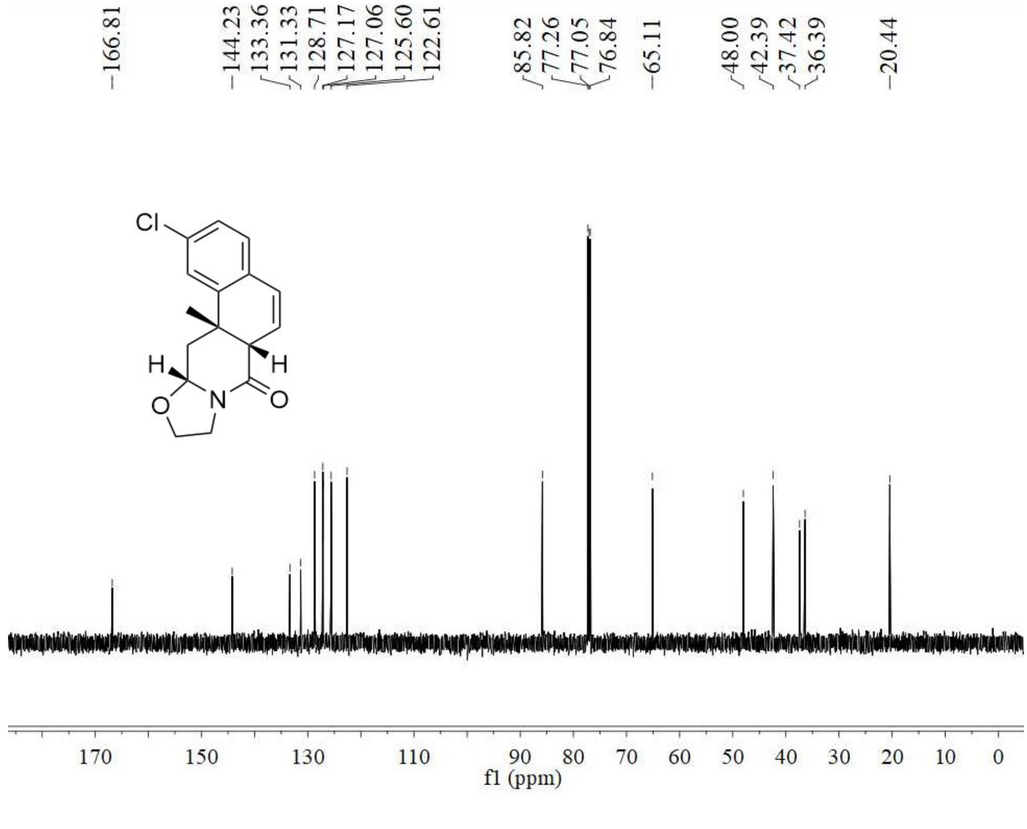


^{13}C NMR ($CDCl_3$)

2h-β

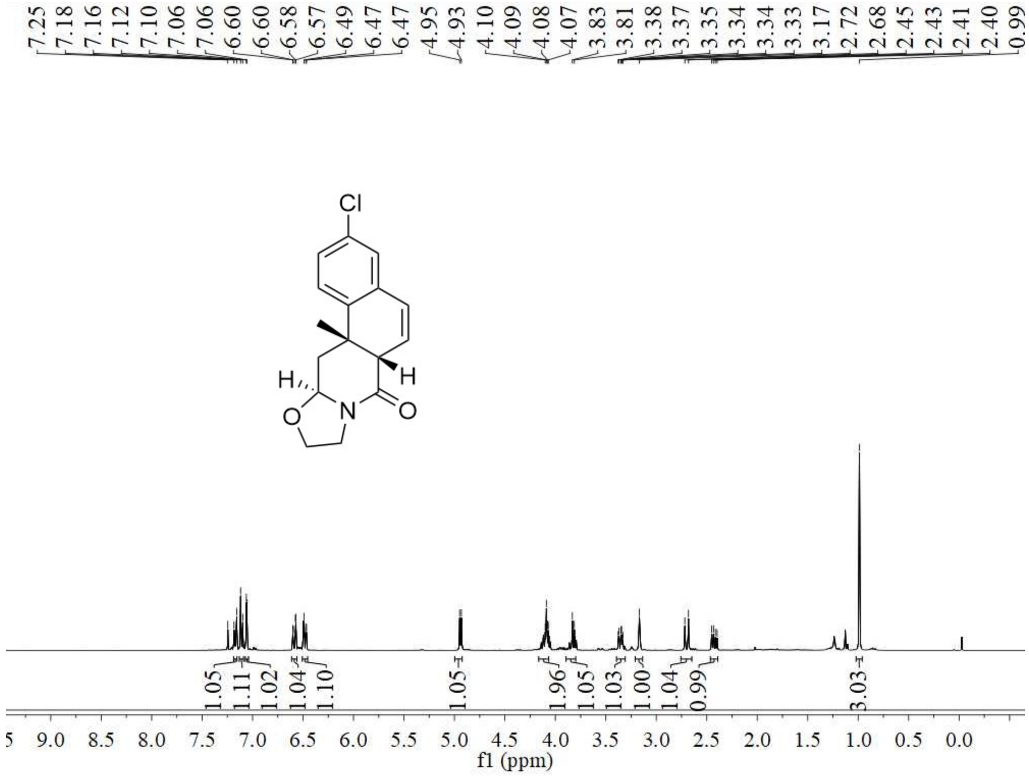


^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

2i-α



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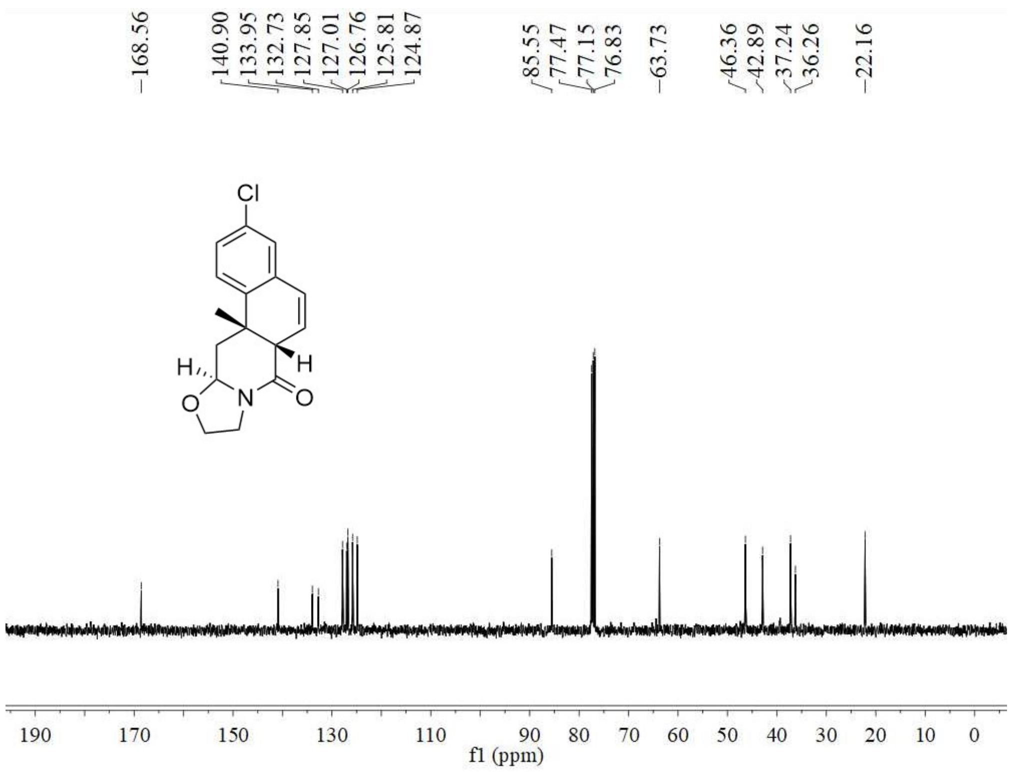
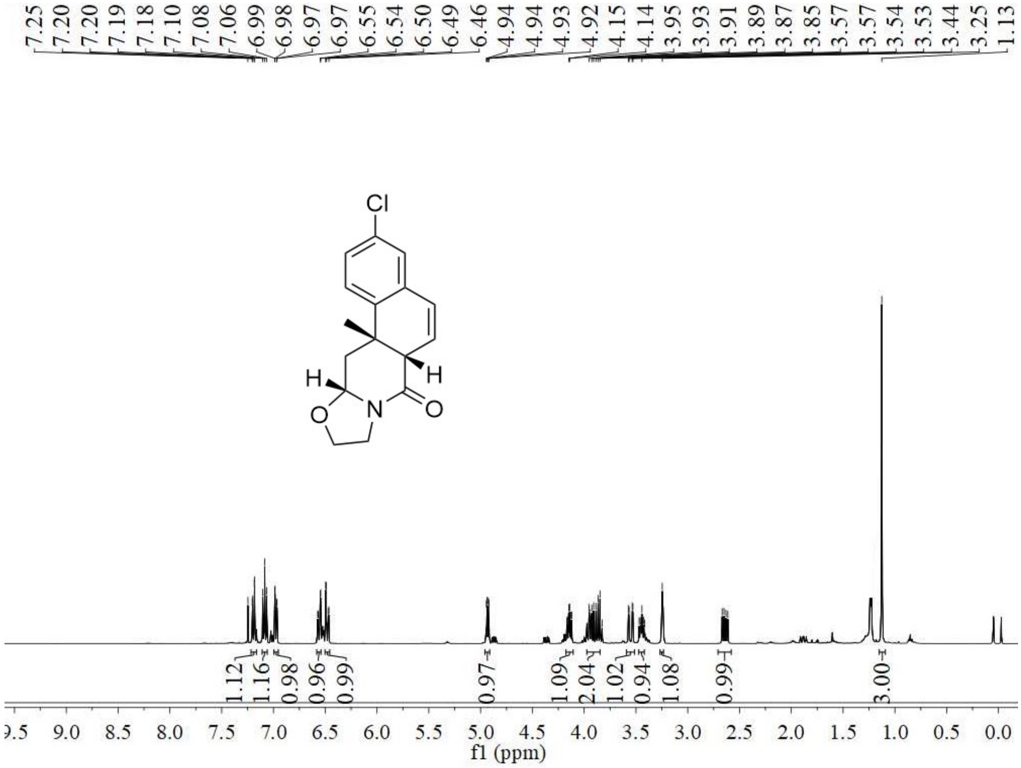
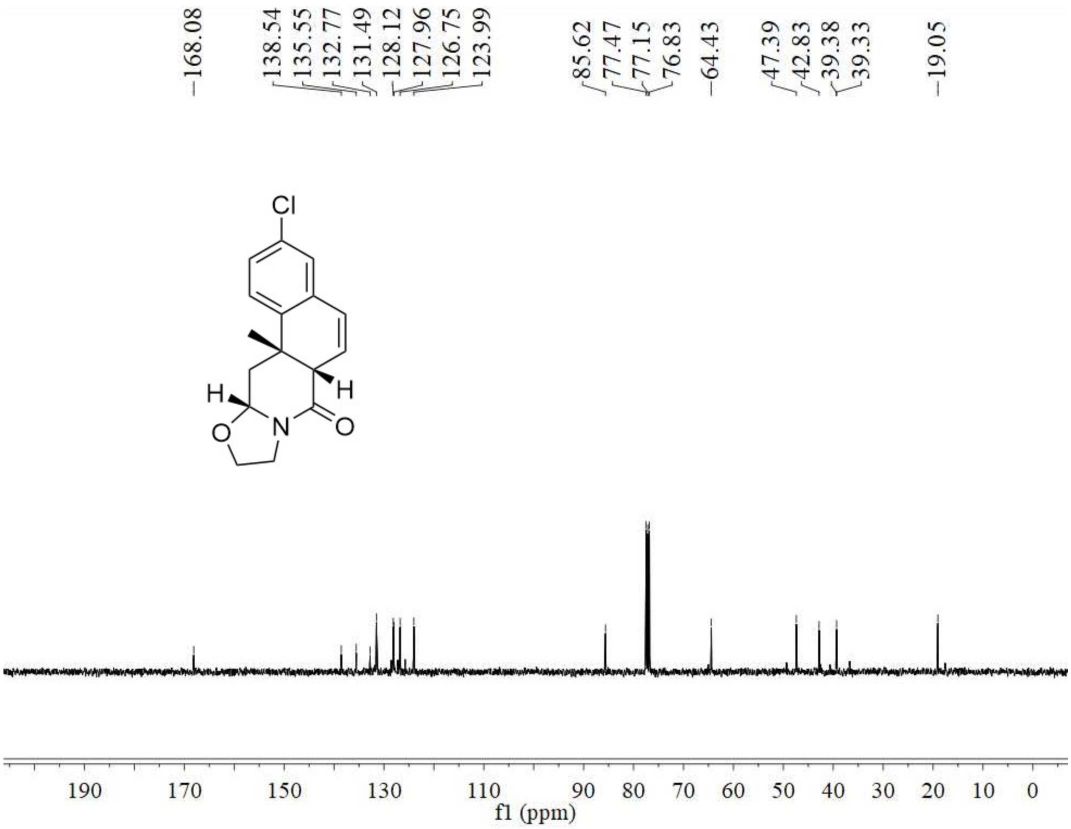


^{13}C NMR ($CDCl_3$)

2i-β

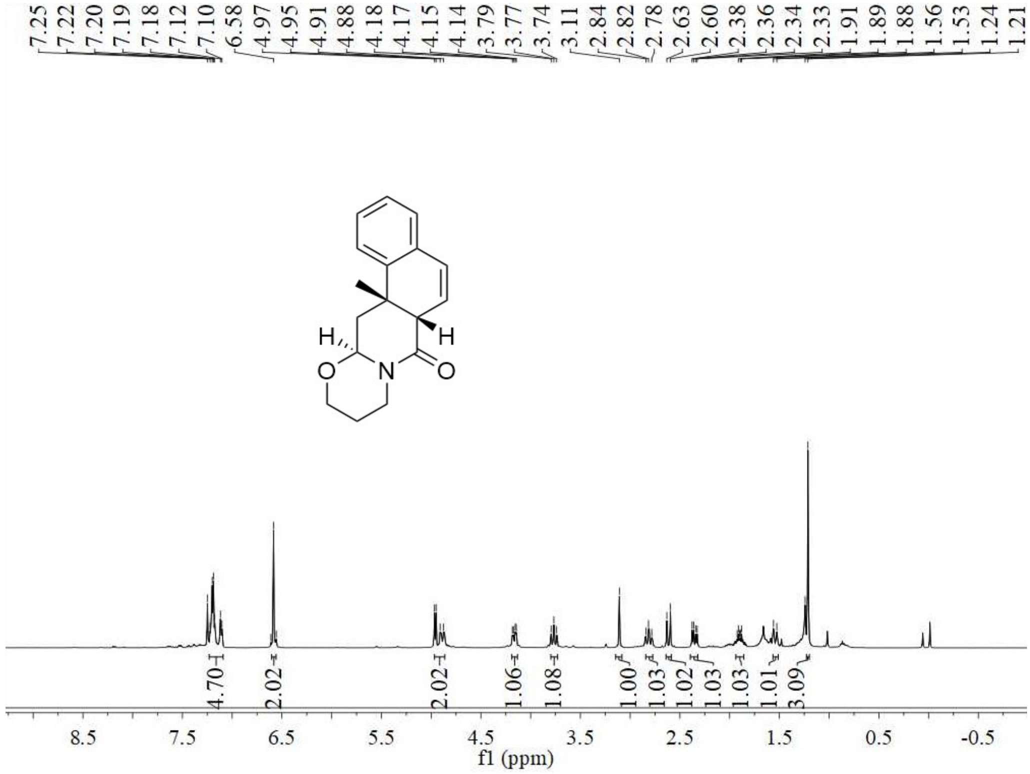


^{1}H NMR ($CDCl_3$)

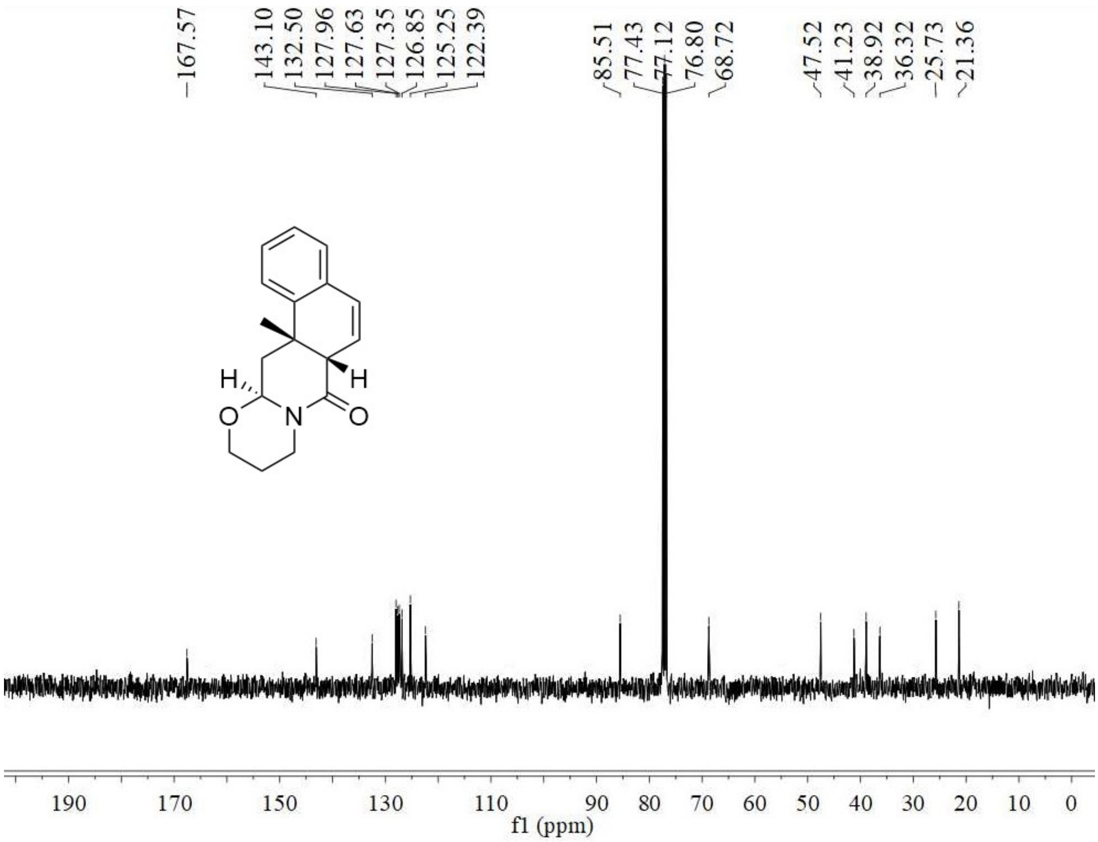


^{13}C NMR ($CDCl_3$)

4a-α

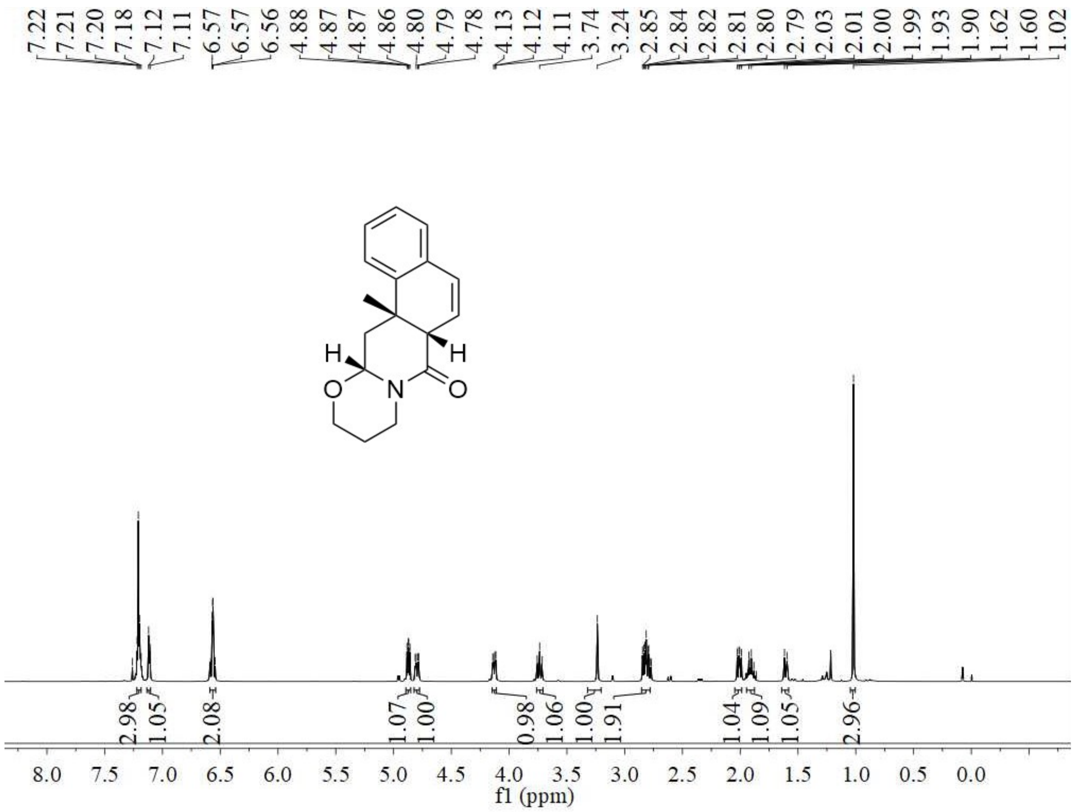


^{1}H NMR ($CDCl_3$)

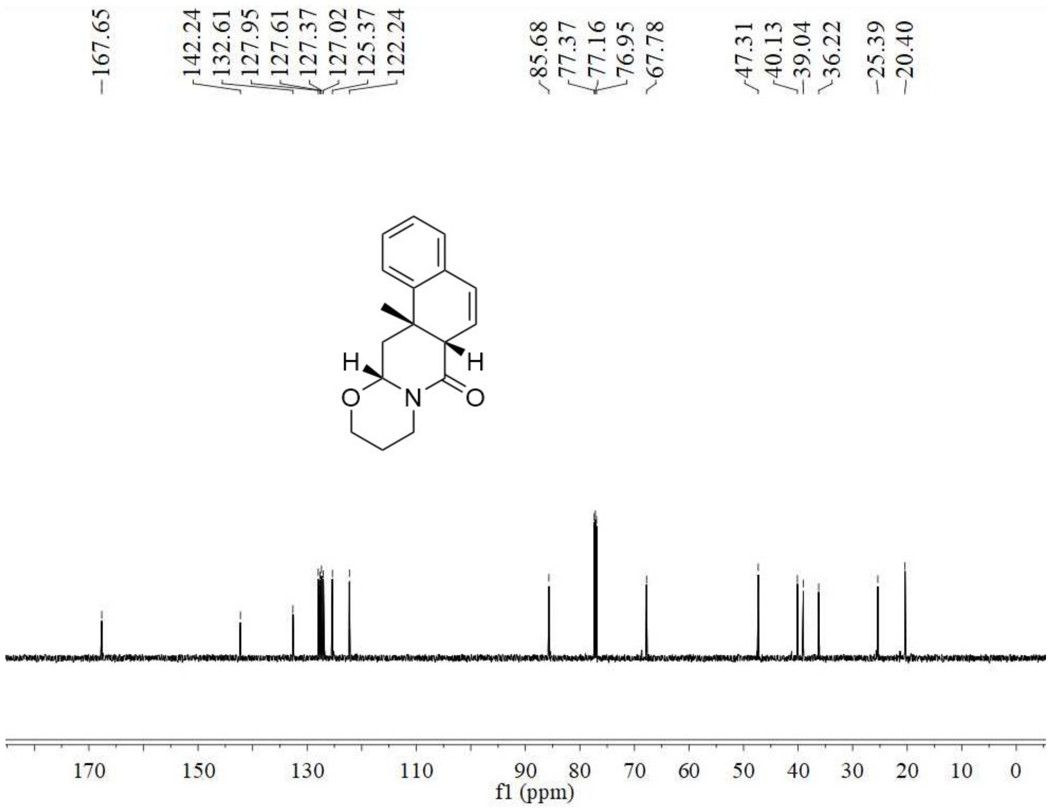


^{13}C NMR ($CDCl_3$)

4a-β

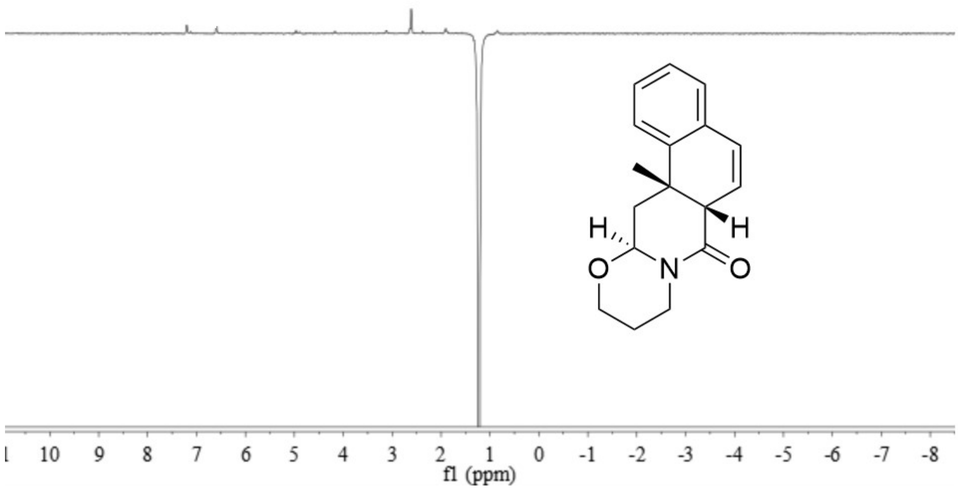


^{1}H NMR ($CDCl_3$)



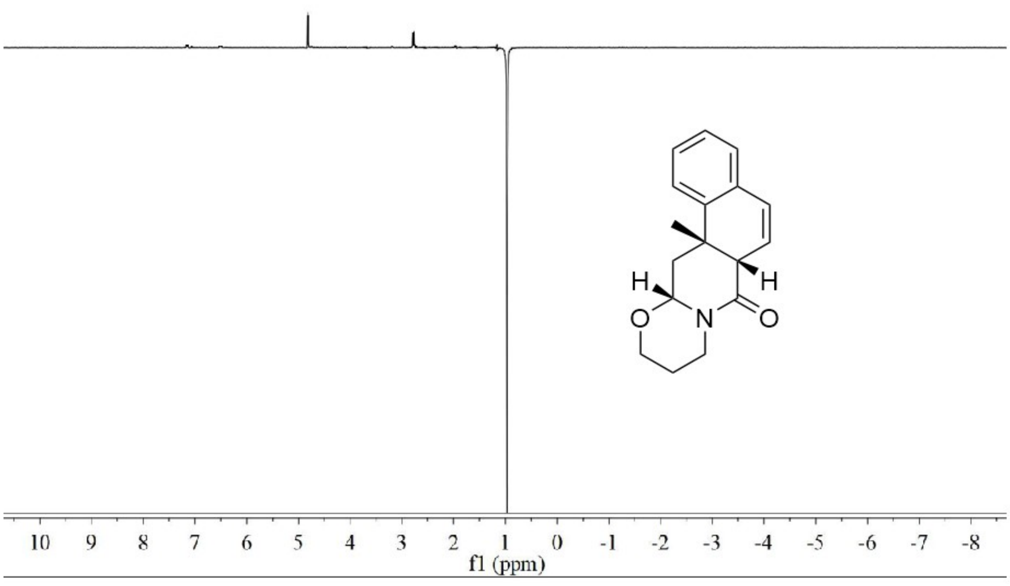
^{13}C NMR ($CDCl_3$)

4a-α



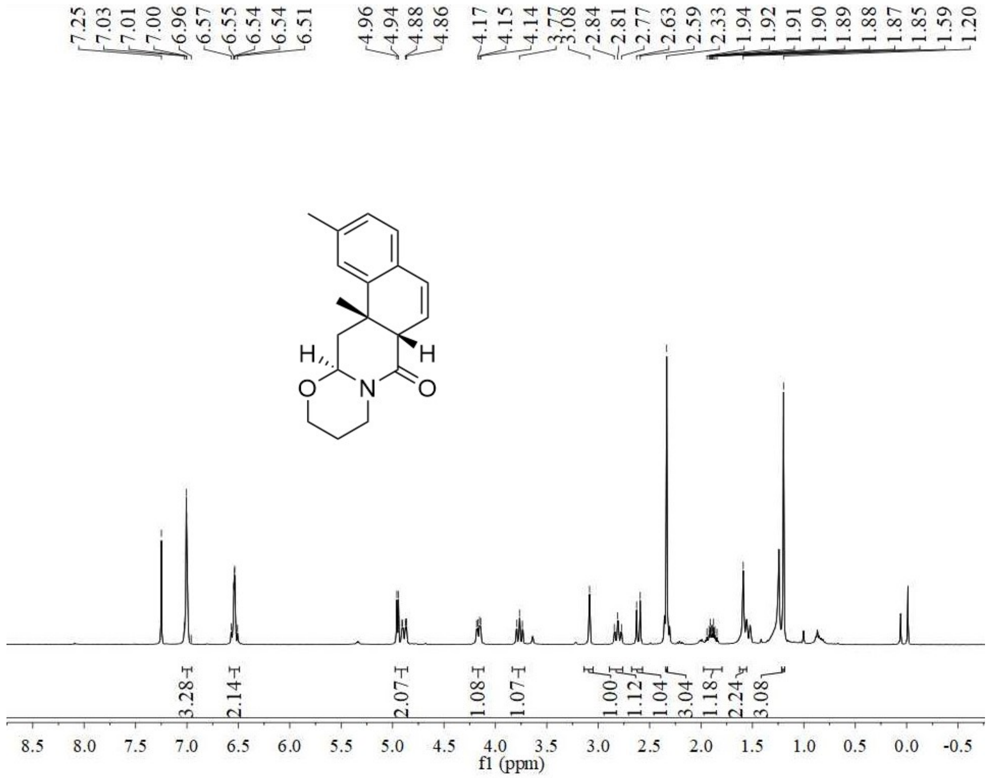
NOE NMR

4a-β

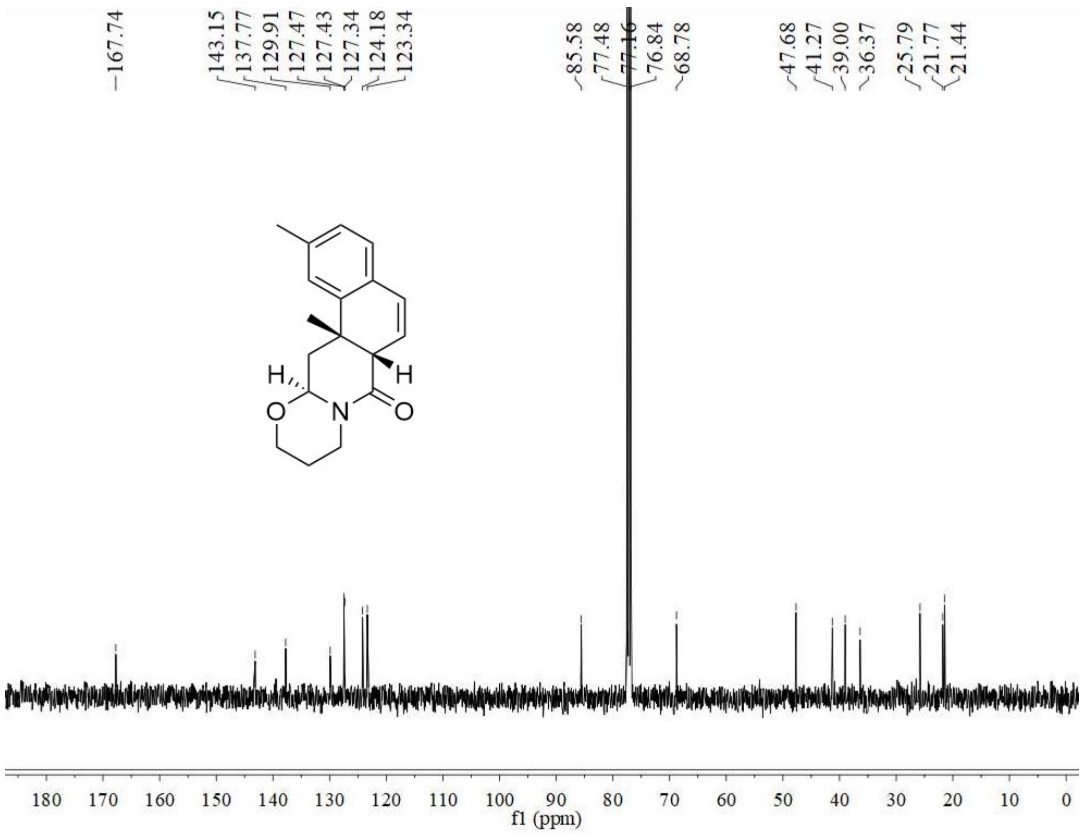


NOE NMR

4b-α

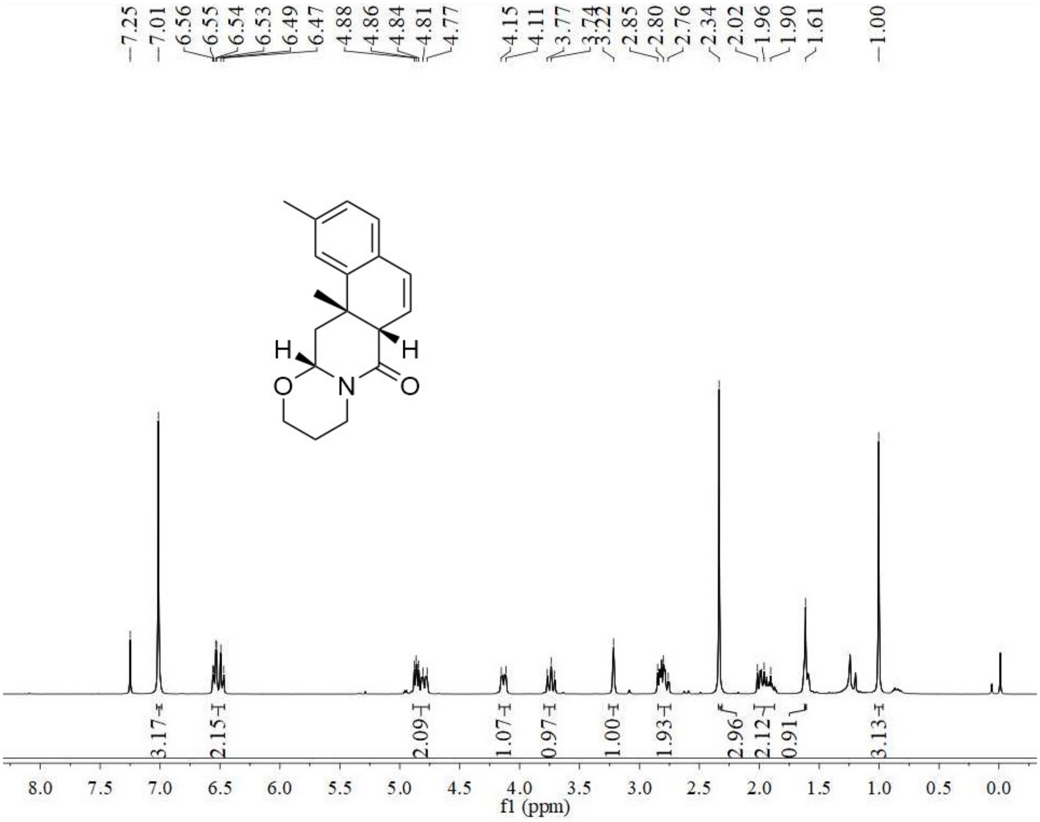


^{1}H NMR ($CDCl_3$)

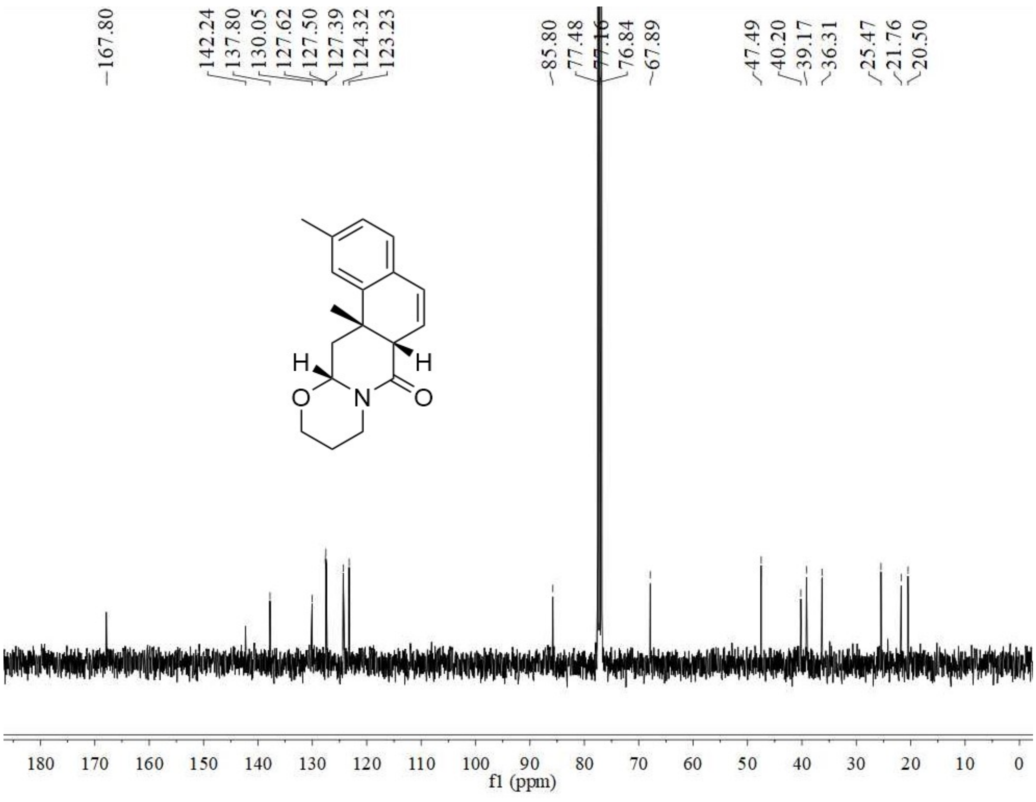


^{13}C NMR ($CDCl_3$)

4b-β

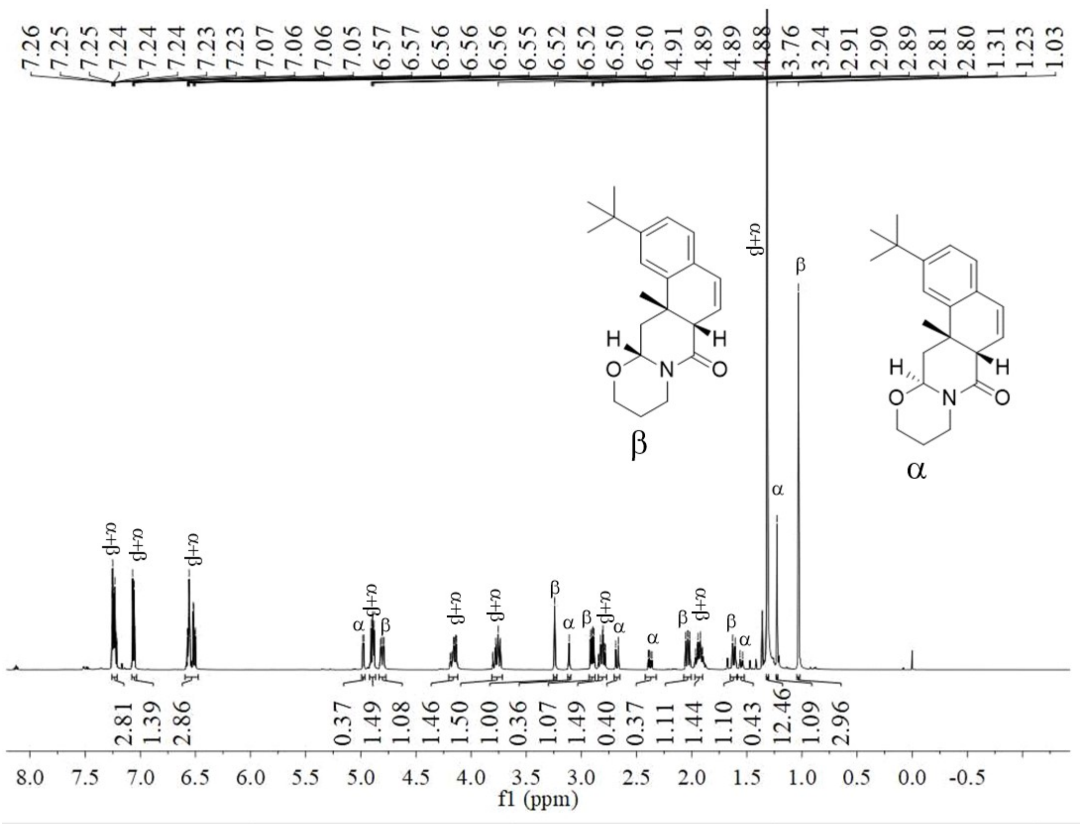


^{1}H NMR ($CDCl_3$)

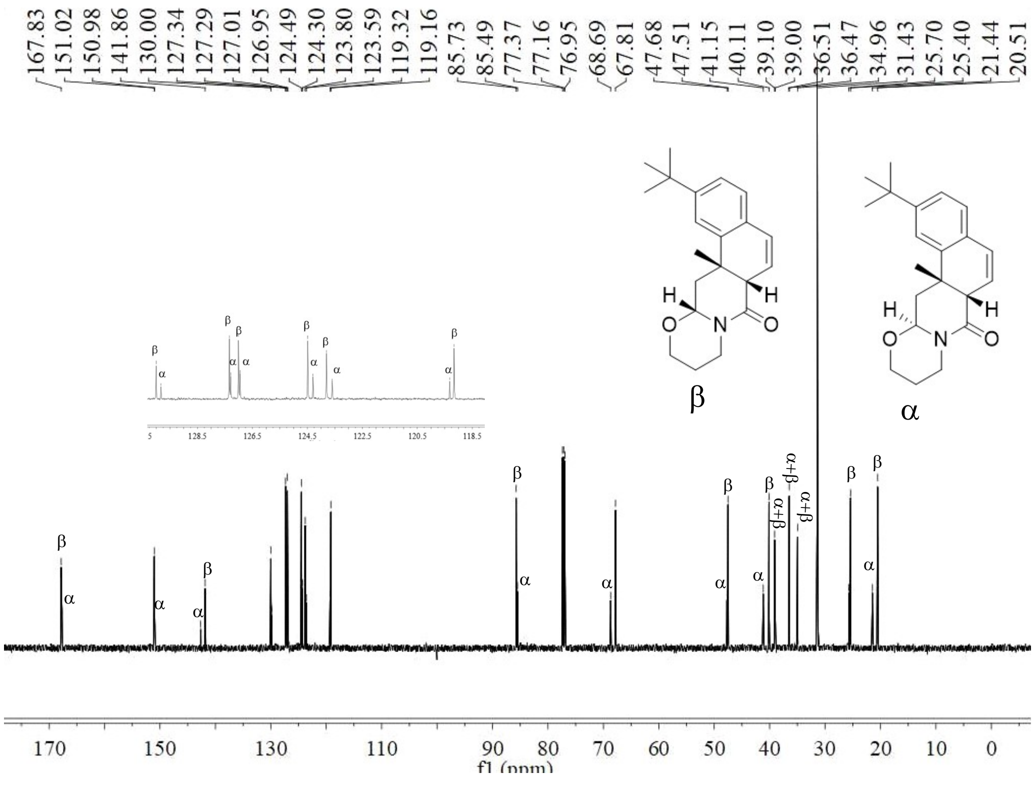


^{13}C NMR ($CDCl_3$)

4c-α, β

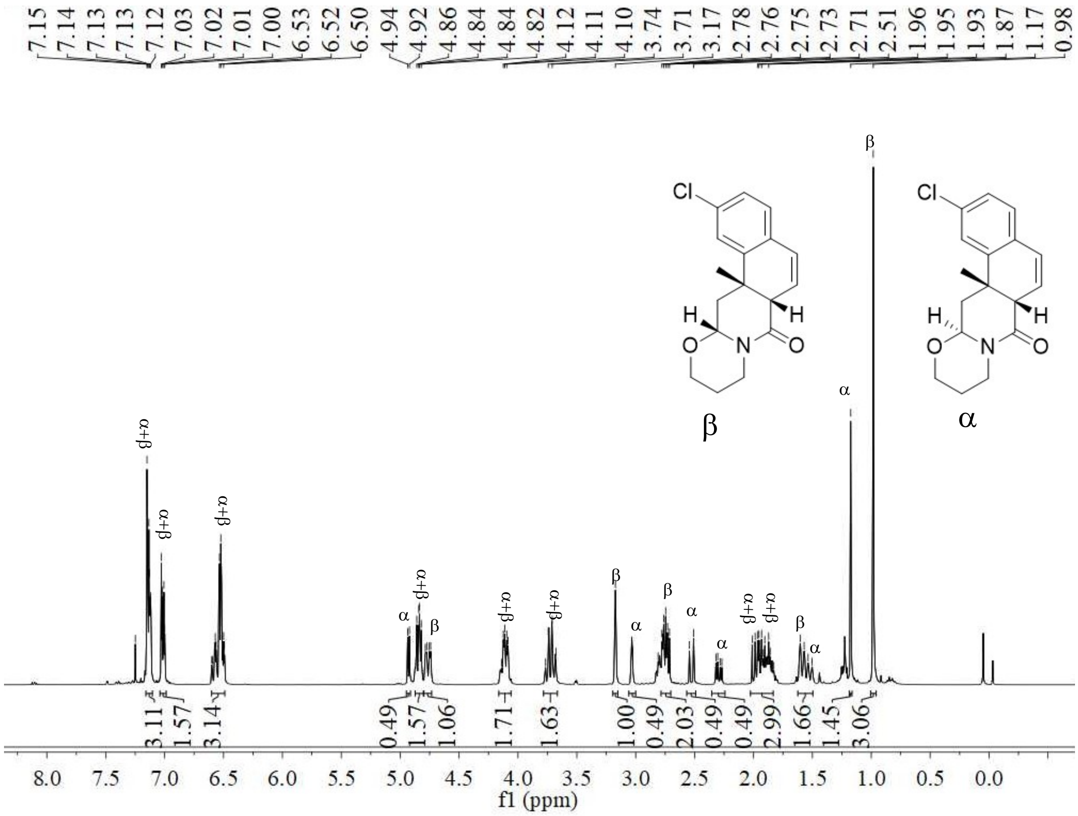


^{1}H NMR ($CDCl_3$)

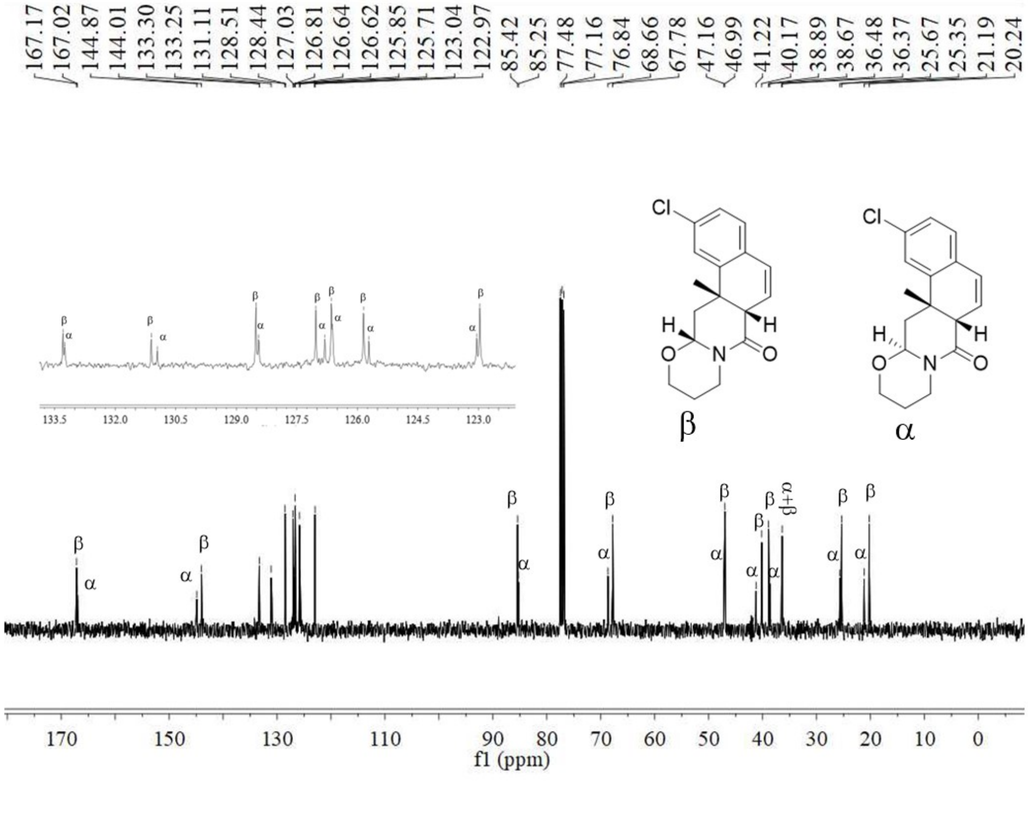


^{13}C NMR ($CDCl_3$)

4d-α, β

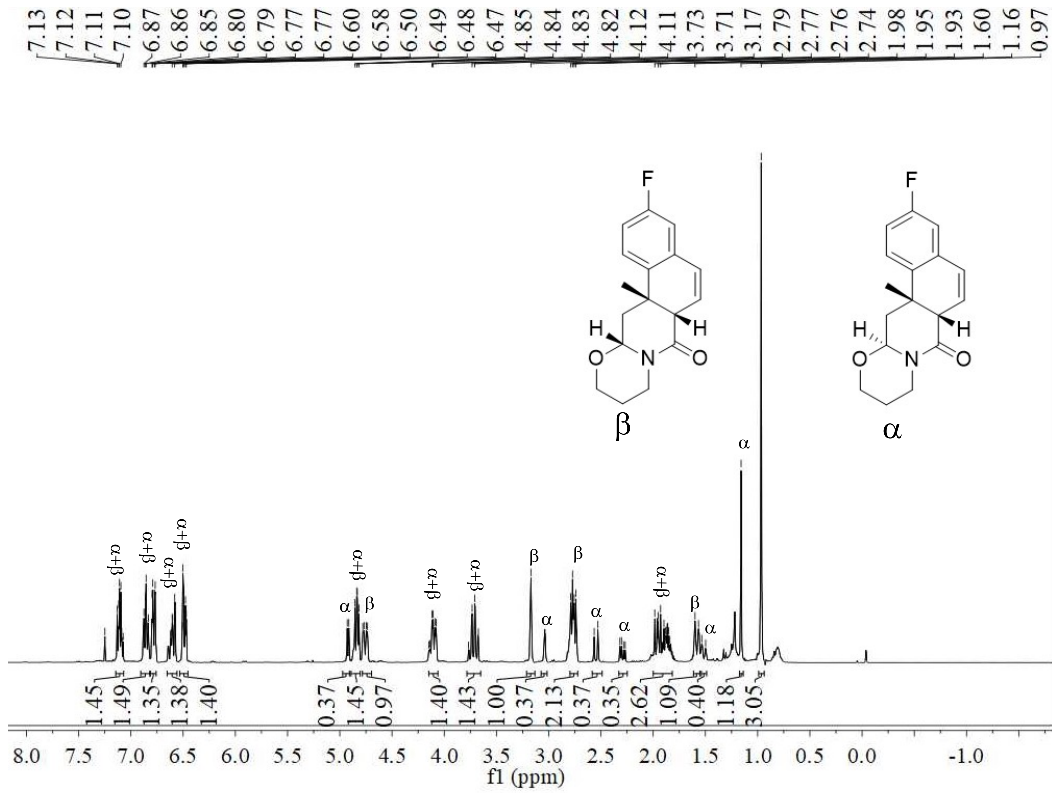


^{1}H NMR ($CDCl_3$)

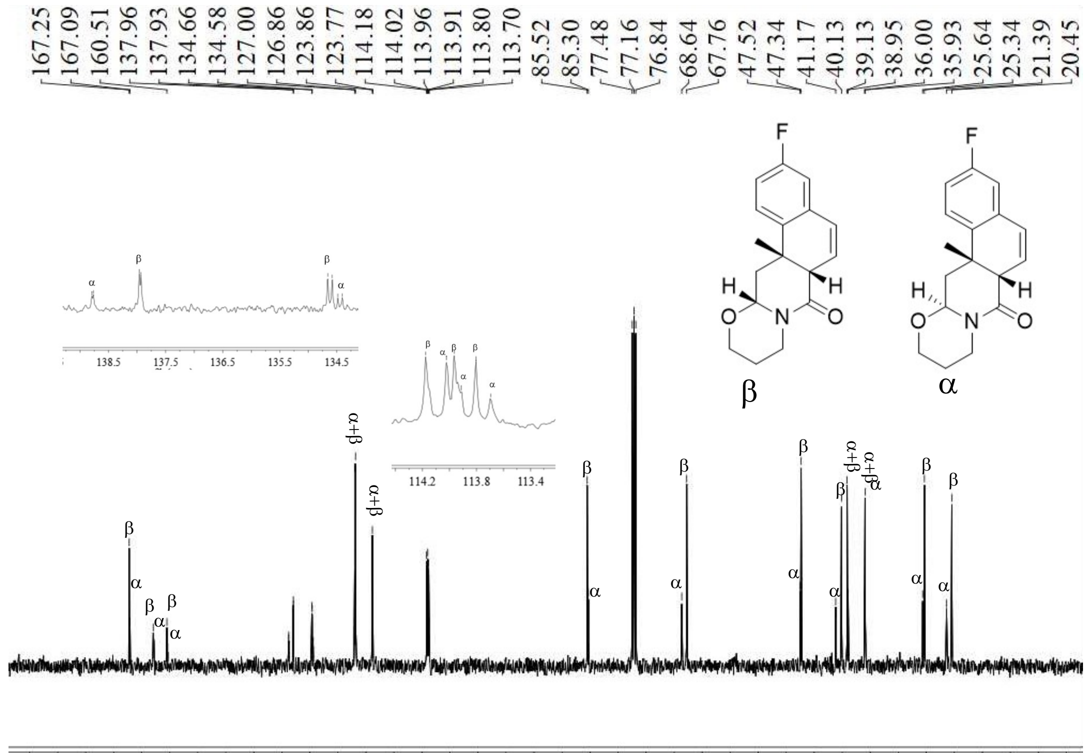


^{13}C NMR ($CDCl_3$)

4e-α, β

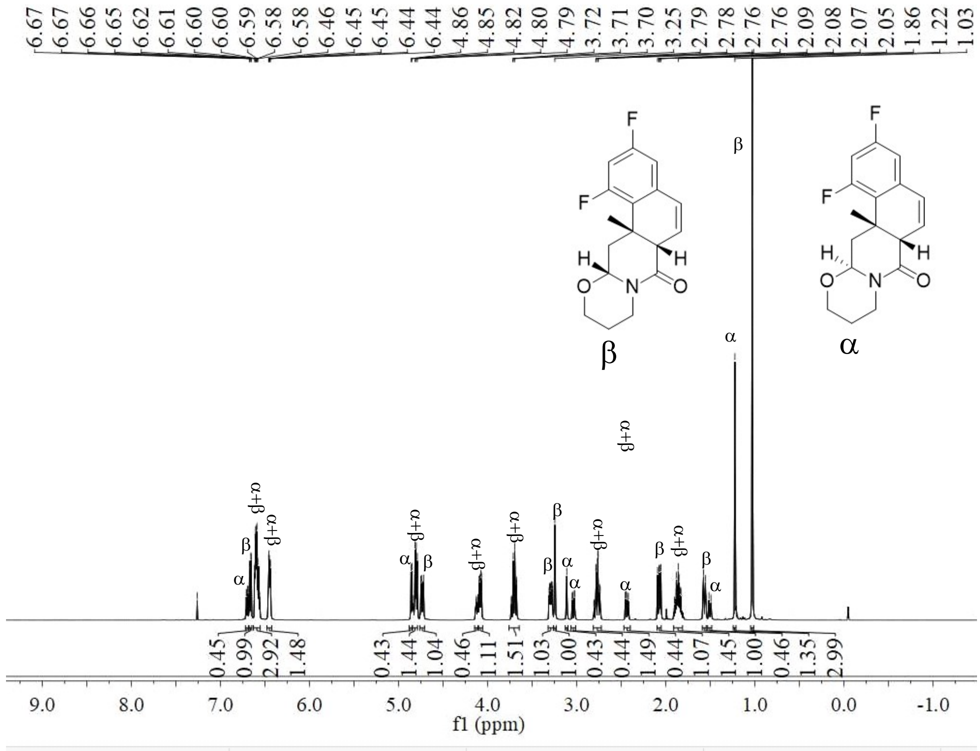


^{1}H NMR ($CDCl_3$)

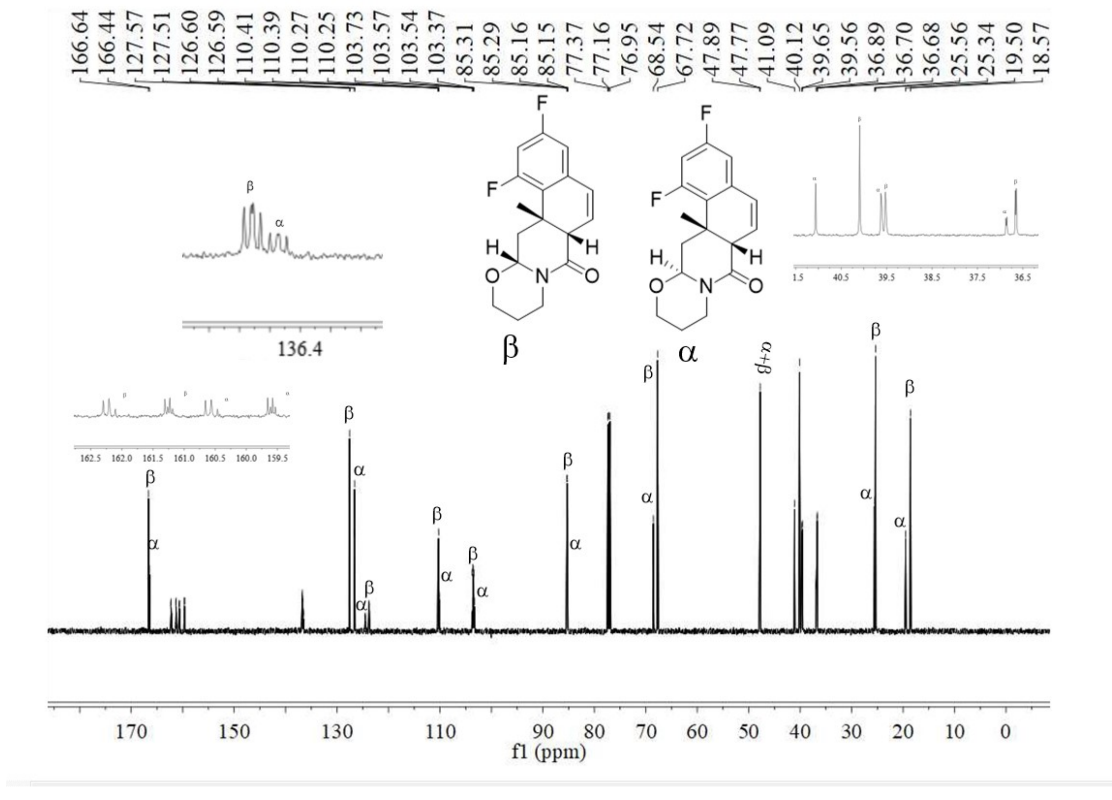


^{13}C NMR ($CDCl_3$)

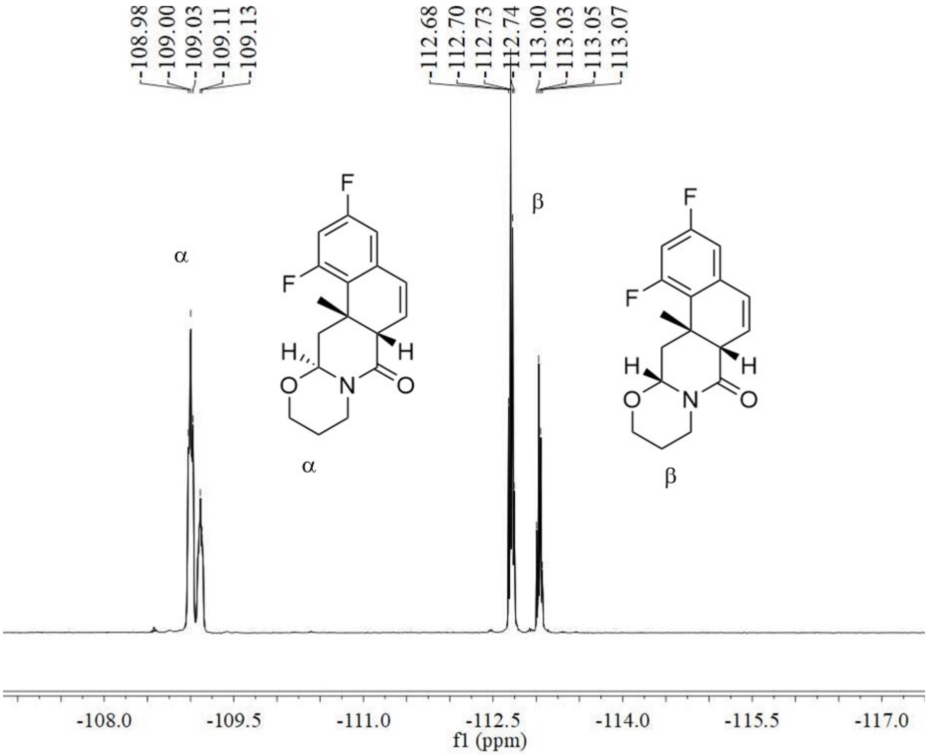
4f-α, β



^{1}H NMR ($CDCl_3$)

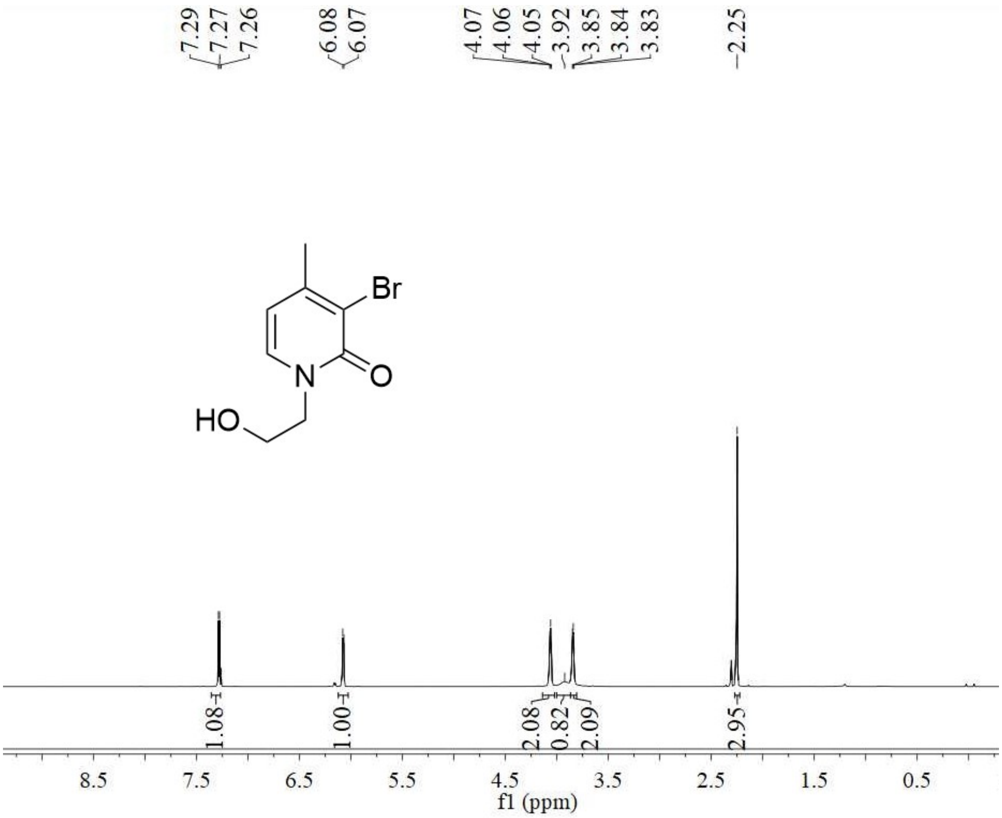


^{13}C NMR ($CDCl_3$)

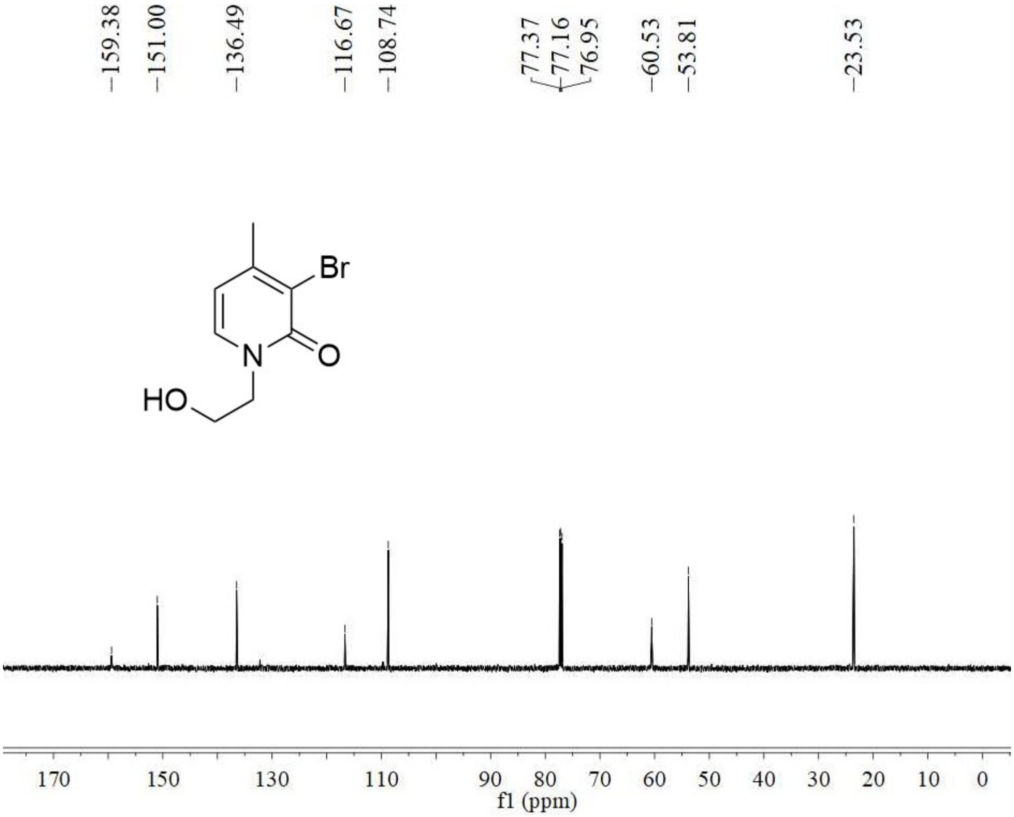


^{19}F NMR ($CDCl_3$)

8

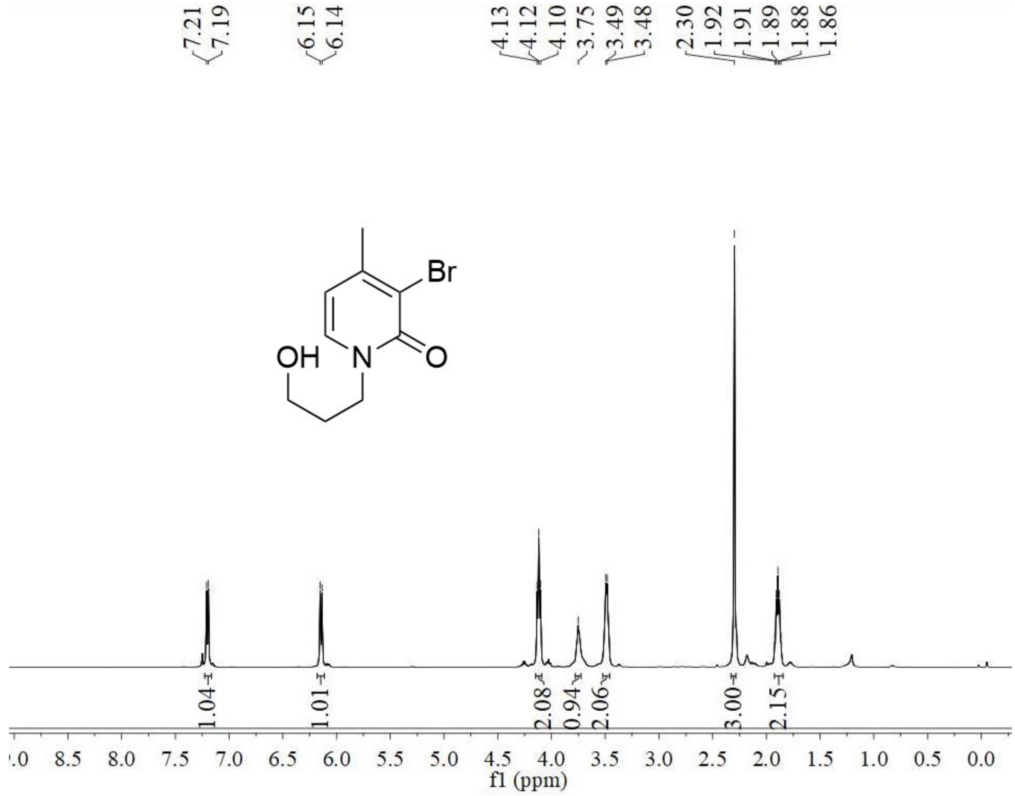


^{1}H NMR ($CDCl_3$)

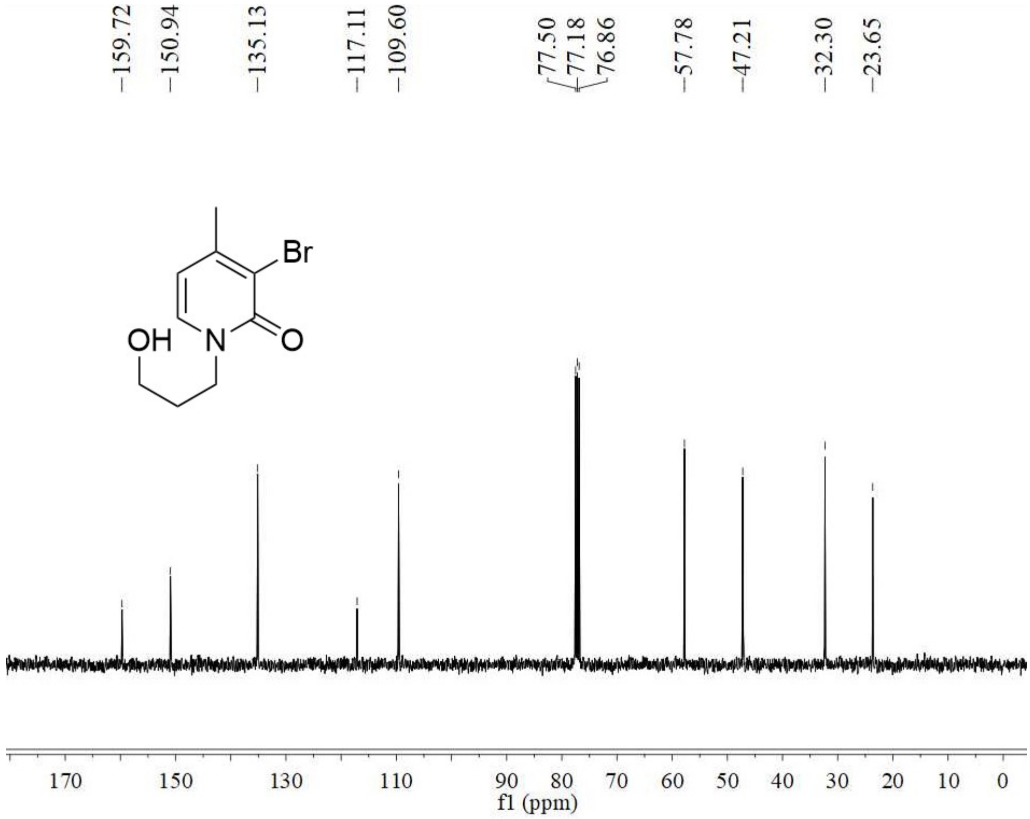


^{13}C NMR ($CDCl_3$)

9

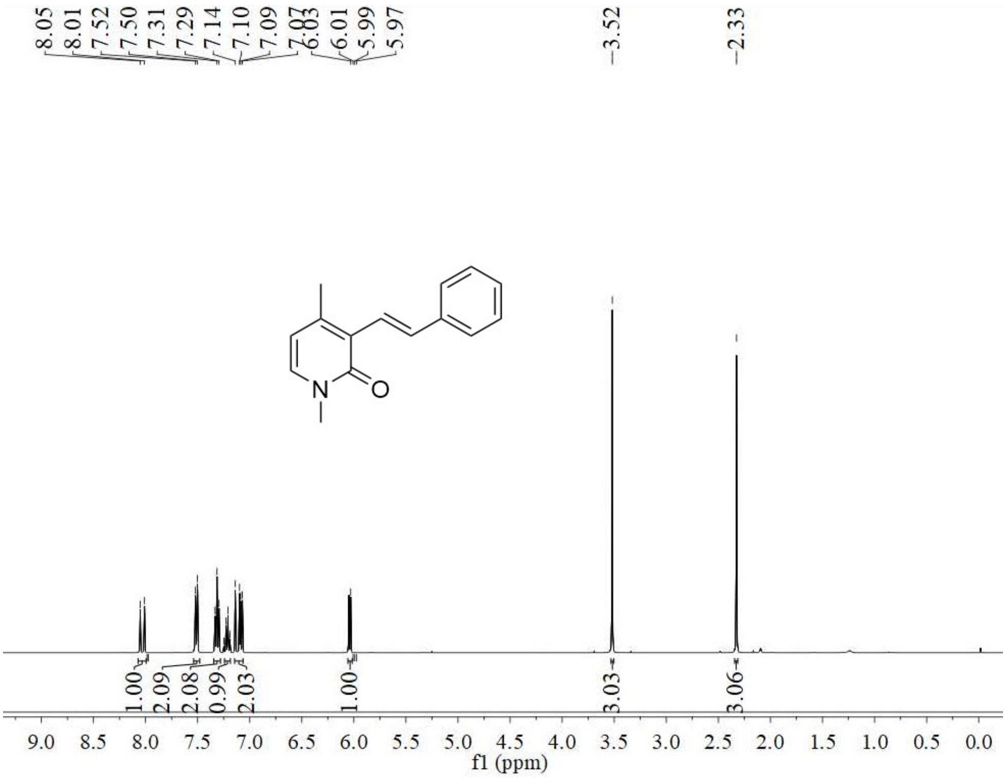


^1H NMR ($CDCl_3$)

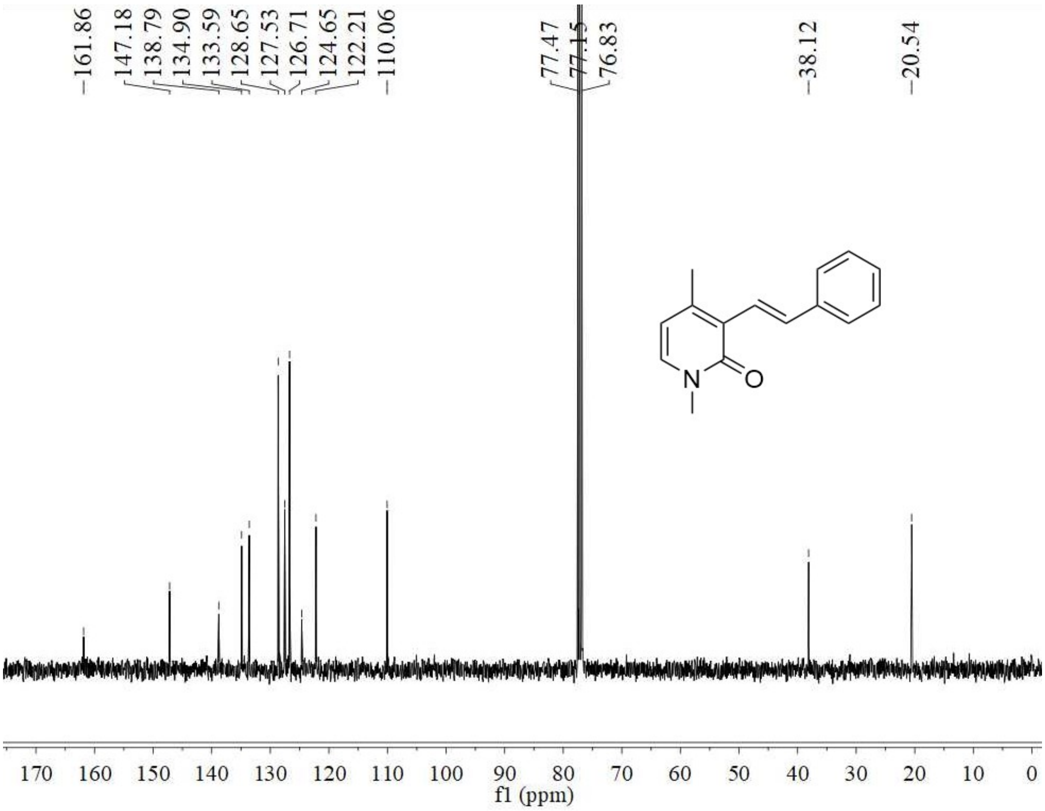


^{13}C NMR ($CDCl_3$)

5

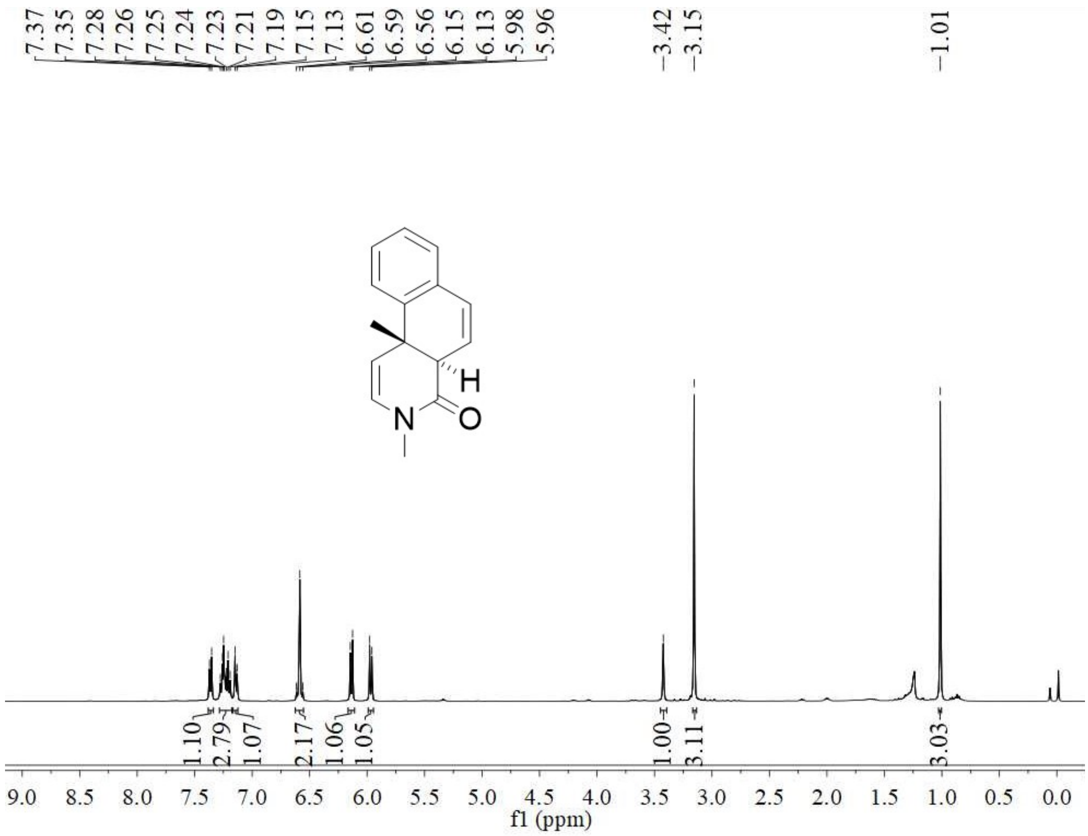


^{1}H NMR ($CDCl_3$)

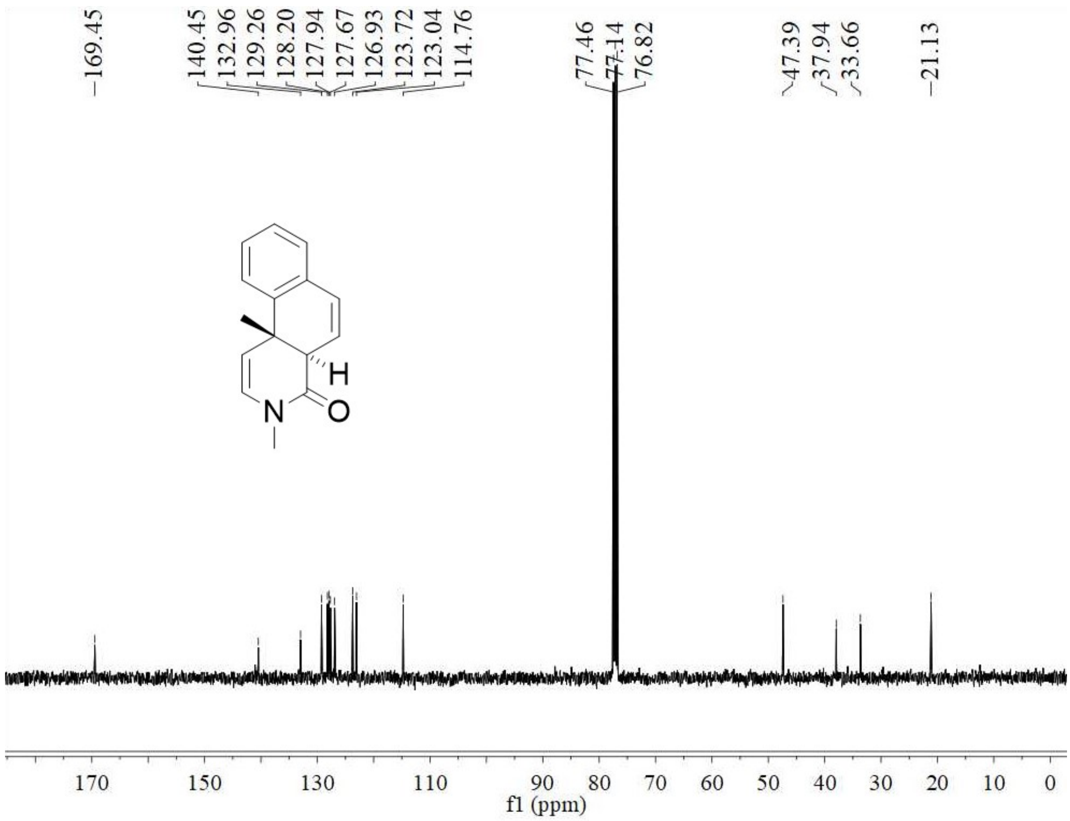


^{13}C NMR ($CDCl_3$)

6-α

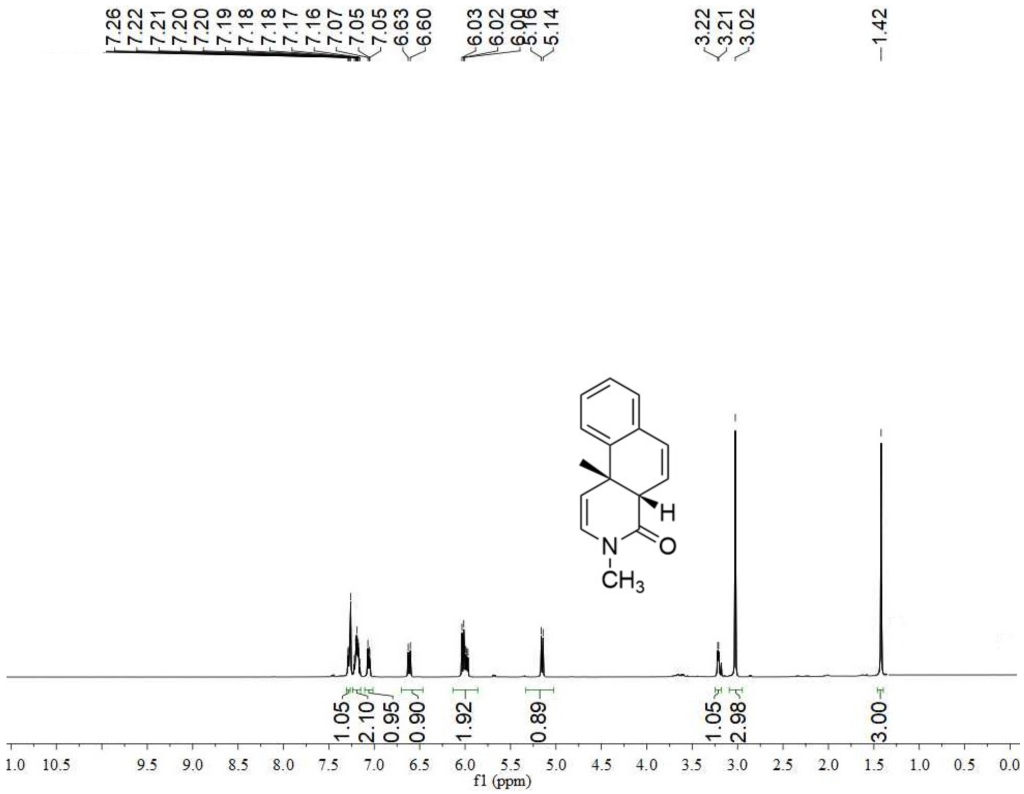


^{1}H NMR ($CDCl_3$)

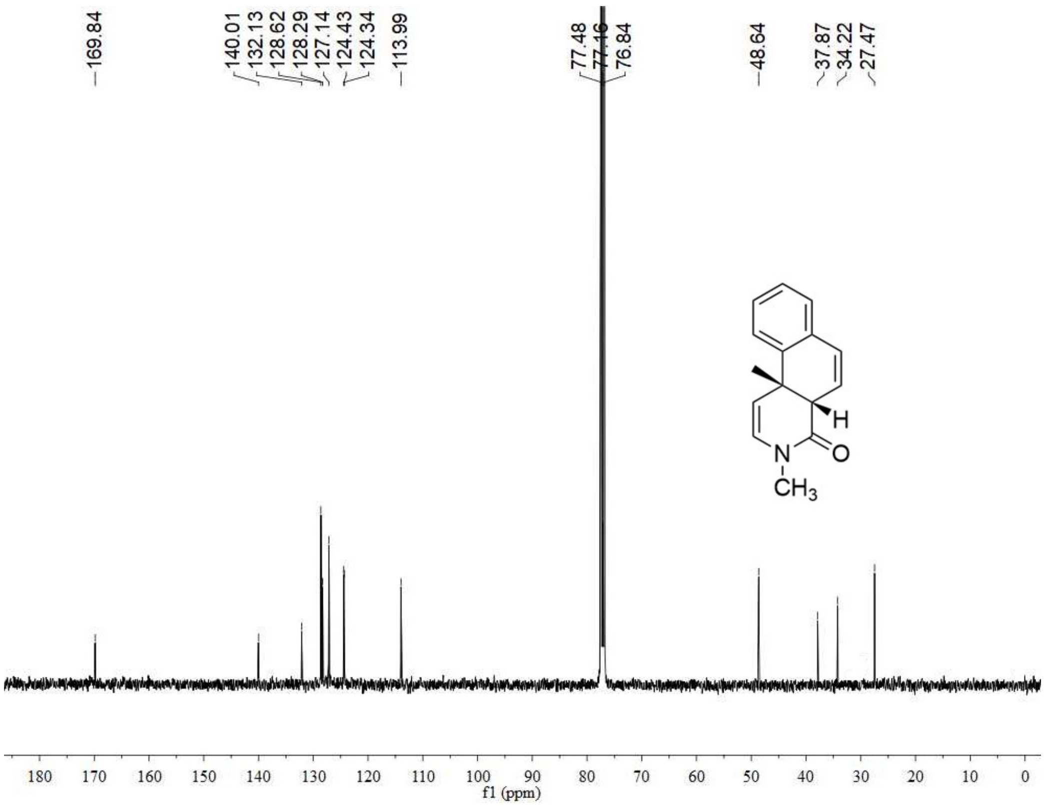


^{13}C NMR ($CDCl_3$)

6-β

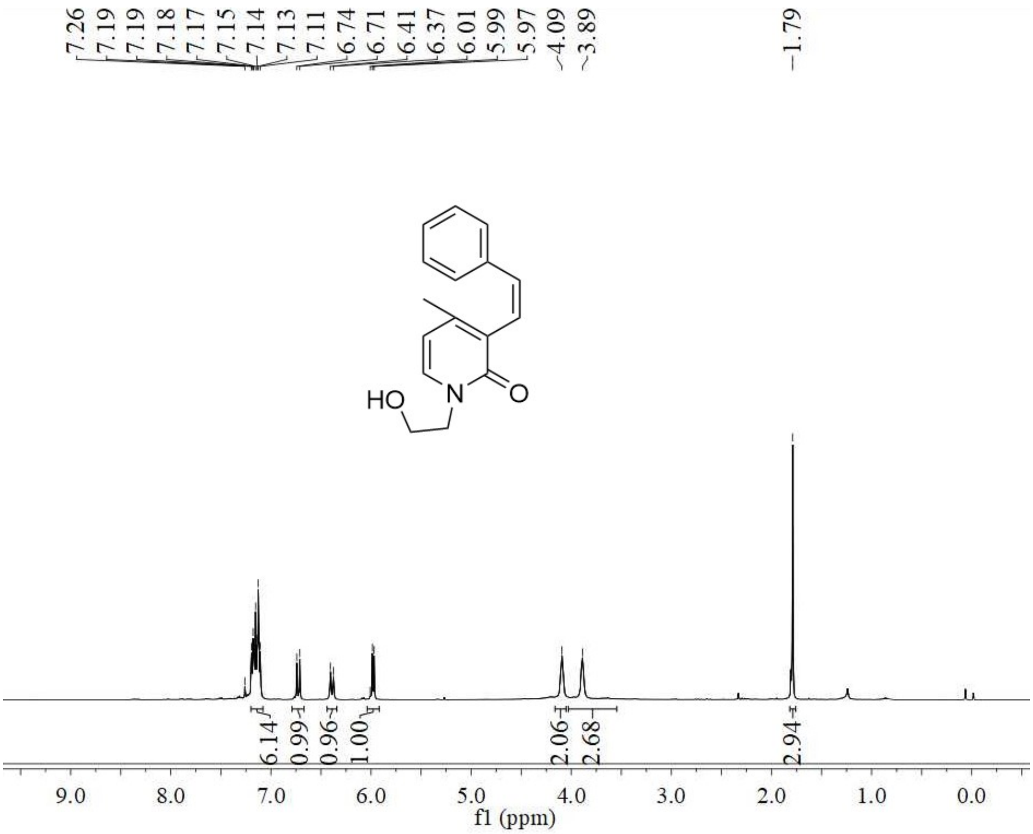


^{1}H NMR ($CDCl_3$)

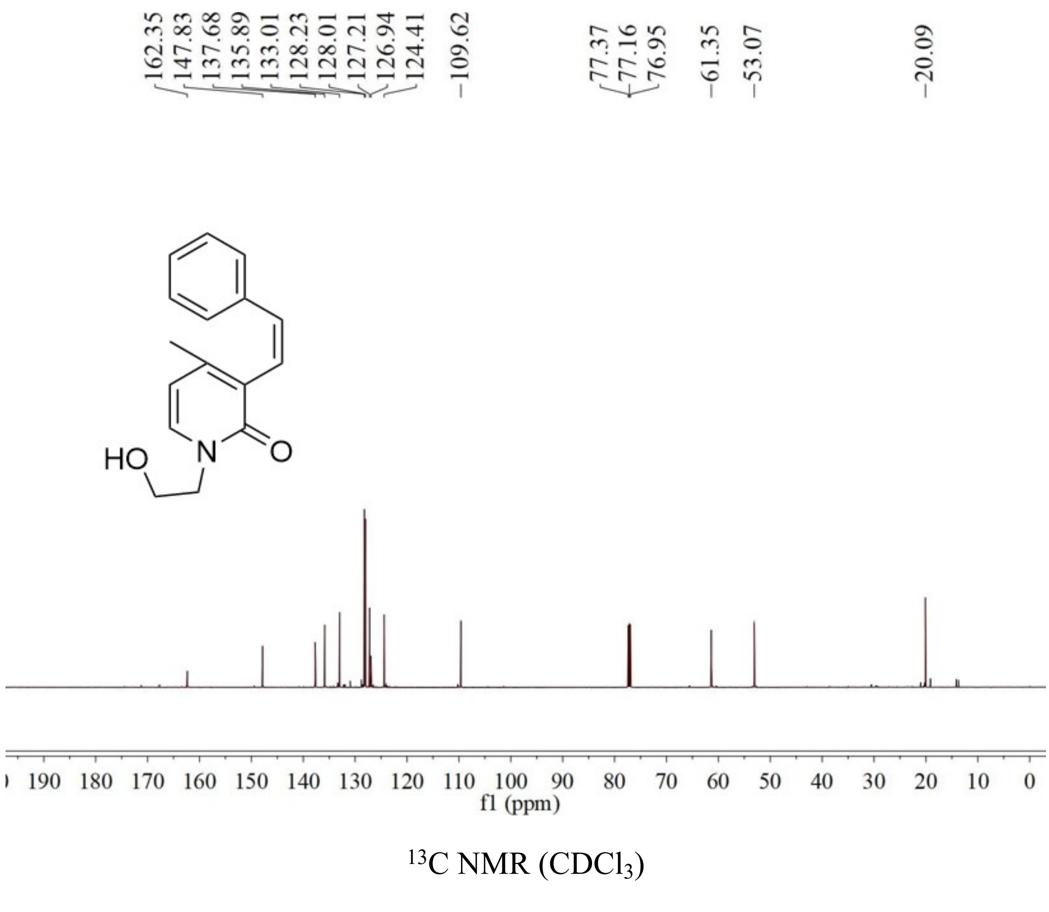


^{13}C NMR ($CDCl_3$)

A

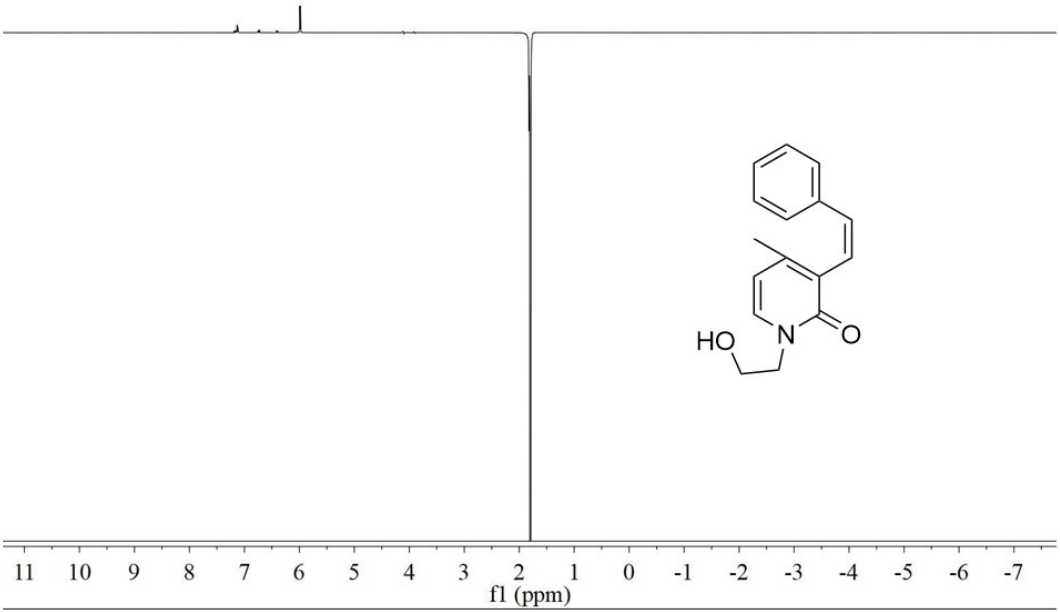


^{1}H NMR ($CDCl_3$)

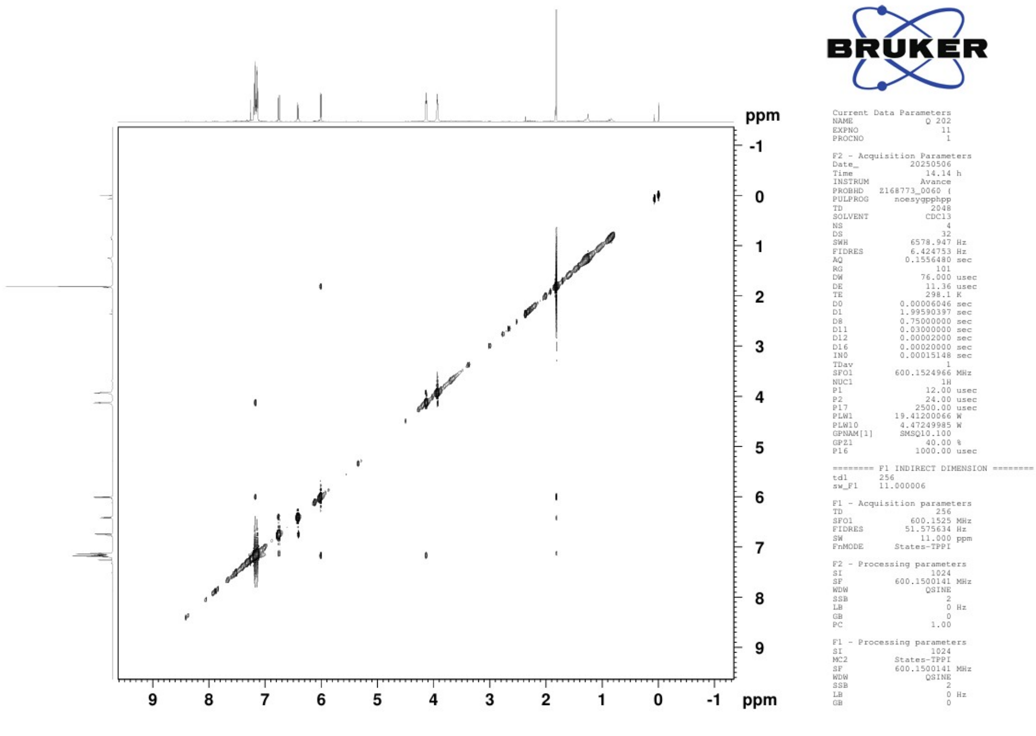


^{13}C NMR ($CDCl_3$)

A

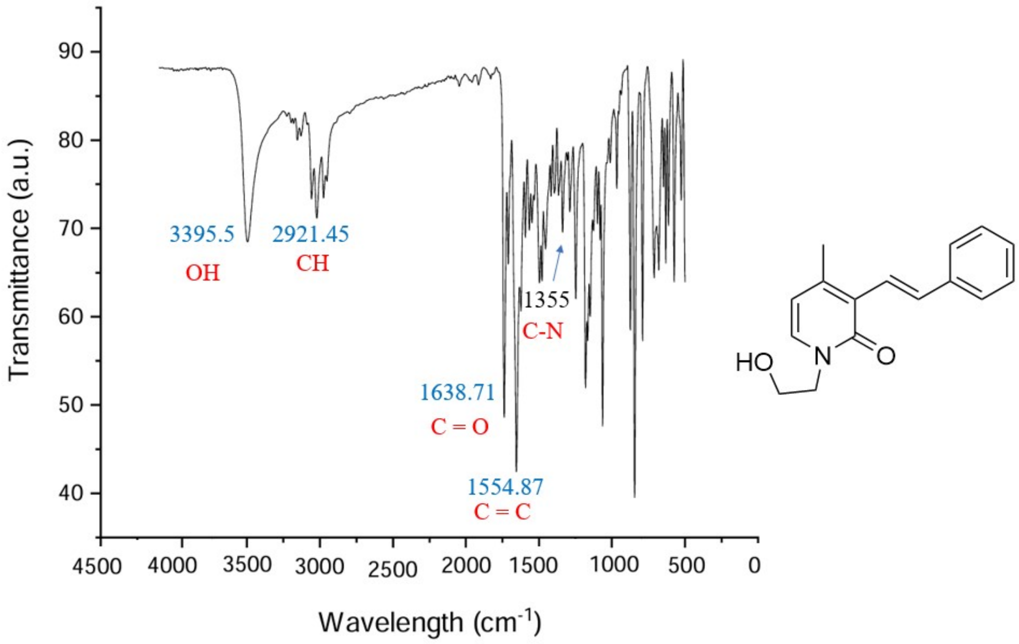


NOE NMR ($CDCl_3$)

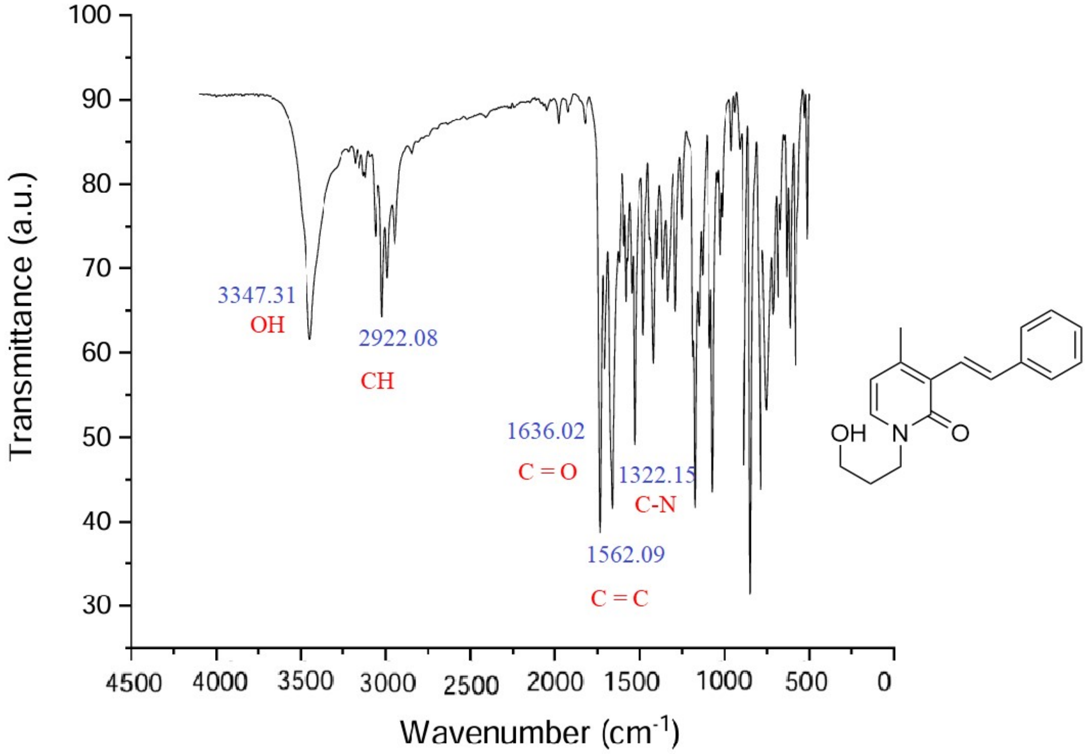


2D NMR ($CDCl_3$)

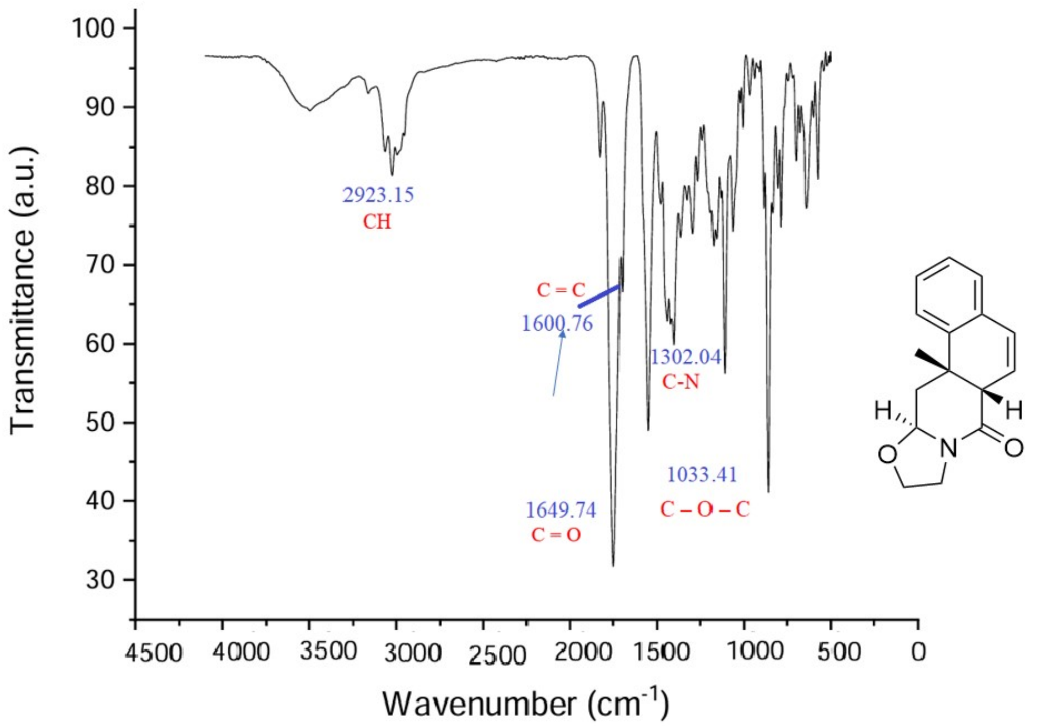
1a


Transmittance (a.u.)
Wavelength (cm-1)
3395.5
OH
2921.45
CH
1355
C-N
1638.71
C = O
1554.87
C = C
HO
N
O

3a

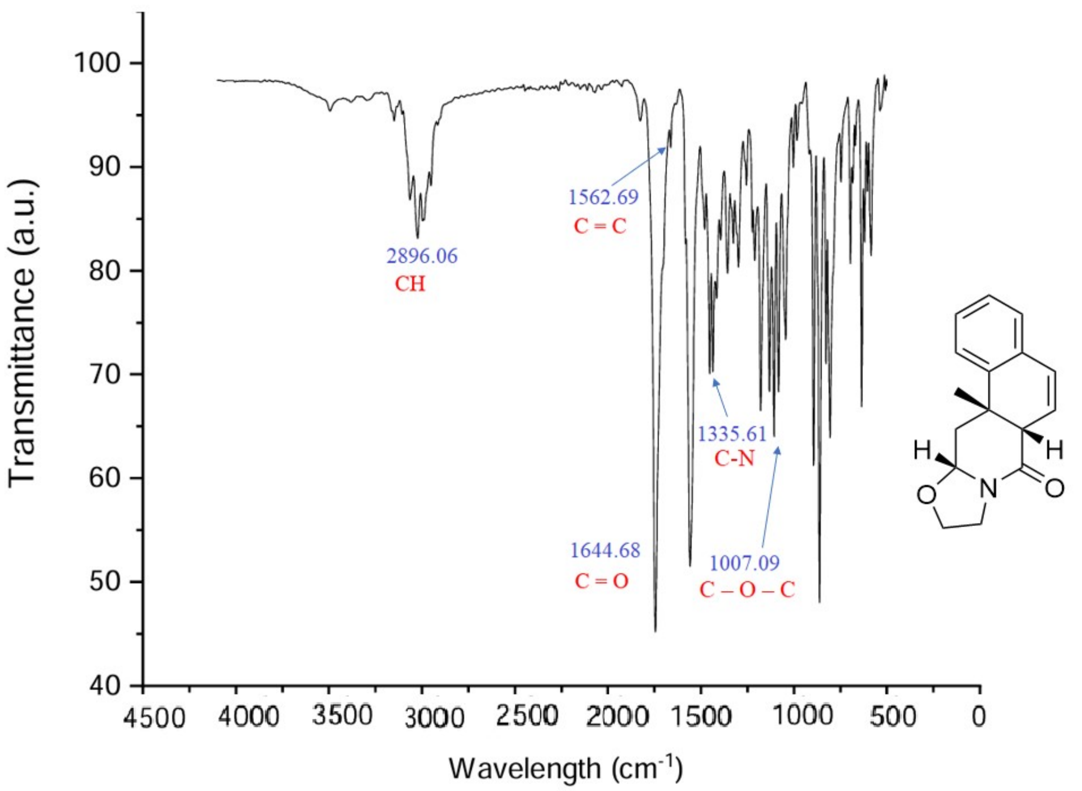

Transmittance (a.u.)
Wavenumber (cm-1)
3347.31
OH
2922.08
CH
1636.02
C = O
1322.15
C-N
1562.09
C = C
OH
N
O

2a-α



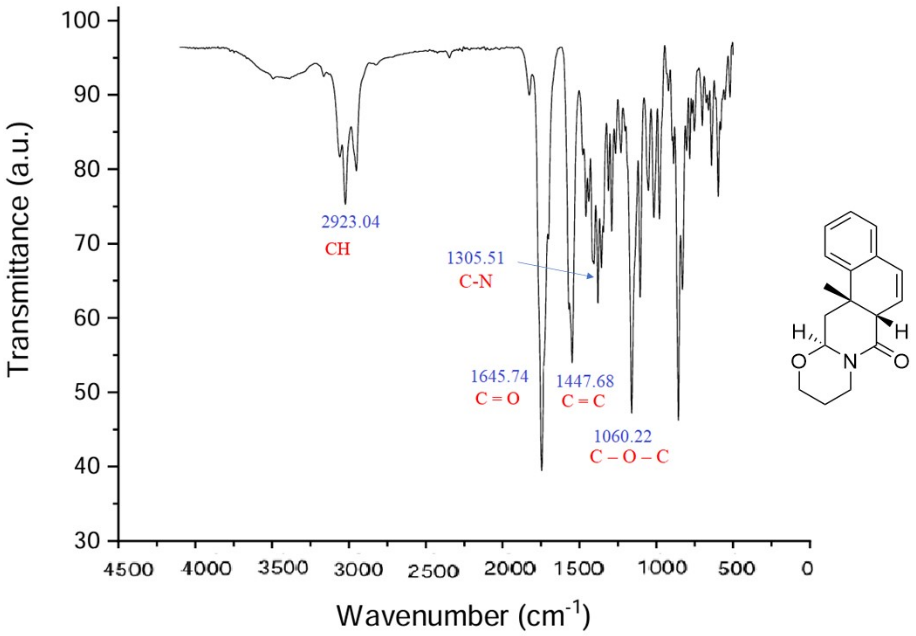
Transmittance (a.u.)
Wavenumber (cm⁻¹)
2923.15
CH
C = C
1600.76
1302.04
C-N
1033.41
C – O – C
1649.74
C = O

2a-β

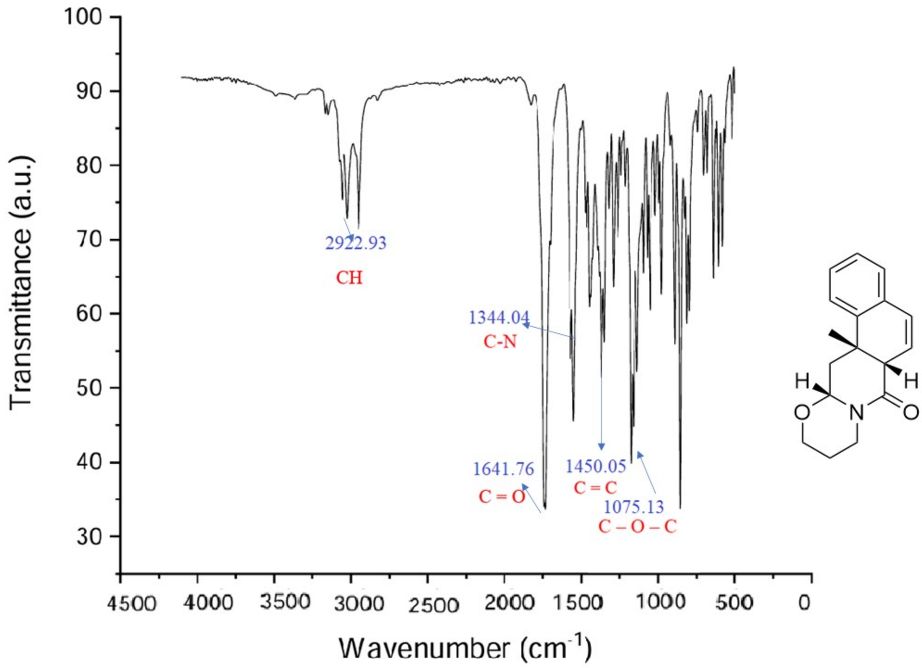


Transmittance (a.u.)
Wavelength (cm⁻¹)
2896.06
CH
1562.69
C = C
1335.61
C-N
1644.68
C = O
1007.09
C – O – C

4a-α


100
90
80
70
60
50
40
30
Transmittance (a.u.)
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Wavenumber (cm-1)
2923.04
CH
1305.51
C-N
1645.74
C = O
1447.68
C = C
1060.22
C – O – C
H
H
O
N
O

4a-β


100
90
80
70
60
50
40
30
Transmittance (a.u.)
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Wavenumber (cm-1)
2922.93
CH
1344.04
C-N
1641.76
C = O
1450.05
C = C
1075.13
C – O – C
H
H
O
N
O