Total Synthesis and Biological Studies of Cryptocin and Derivatives of Equisetin and Fusarisetin A

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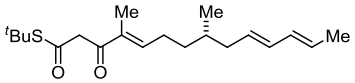
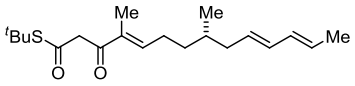
Supporting Information

General Experimental Procedures. All reactions were carried out under nitrogen except noted. Anhydrous dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl. Anhydrous toluene was prepared from sodium. Flash column chromatography was performed as described by Still (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925), employing Qingdao Haiyang silica gel 60 (200–300 mesh). TLC analyses were performed on EMD 250 μm Silica Gel $HSGF_{254}$ plates and visualized by quenching of UV fluorescence (λ_{max}= 254 nm), or by staining ceric ammonium molybdate, ammonium molybdate, or potassium permanganate. Preparative TLC purifications were performed on Yantai Jiangyou HouZhiBeiBan $HSGF_{254}$ (0.4 mm-0.5 mm). ^1H and ^{13}C NMR spectra were recorded on a Bruker-600, 500, 400 spectrometer. Chemical shifts for ^1H and ^{13}C NMR spectra are reported in ppm (δ) relative to residue protium in the solvent ($CDCl_3$: δ 7.26, 77.00 ppm; methanol-d_4: δ 3.31, 49.0 ppm) and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. The $[\alpha]_D$ was recorded using PolAAr 3005 High Accuracy Polarimeter. High-resolution mass spectra (HRMS) were acquired on a waters GCT premier, and Mass spectra at Agilent 5975C.

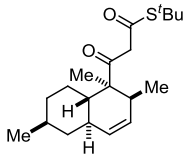


Polyenoyl β-keto thioester **20**: To a solution of phosphonate **19** (3.4 g, 8.70 mmol) in THF (80 mL, 0.2 M) was added *n*-BuLi (6.0 mL, 9.6 mmol) at –78 ^oC, The resulting mixture was allowed to warm to 0 ^oC over a period of 10 min before it was cooled to –78 ^oC, at which temperature a solution of aldehyde **18** (872 mg, 2.90 mmol) in THF (5 mL) was added dropwise via syringe. The mixture was allowed to -78 ^oC over a period of 30 min and warmed to 0 ^oC for 10 min before it was quenched with saturated aq. NH_4Cl solution (20 mL). Evaporation of the solvent and extracted with EtOAc (2 × 50 mL) and the combined organic phase was washed with NH_4Cl solution (20 mL ×2) and brine (50 mL), then dried over anhydrous Na_2SO_4, After filtration and evaporation of the solvent, the residue so obtained was purified by flash column chromatography (1% to 2% ethyl acetate-petroleum ether) to give **20** (812 mg, 83% for 2 steps) as

colorless oil as an inseparable E/Z isomeric mixture (E:Z = ca. 1:1): R_f = 0.40 (5% ethyl acetate-petroleum ether).



We followed the procedure, reported by Theodorakis and co-workers to isomerize Z isomer using a visible light-induced isomerization catalyzed with iodine.[1] To a solution of polyene **20** (100 mg, 0.30 mmol) in CH_2Cl_2 (15 mL, 0.02 M) was slowly added a solution of I_2 (3 mg, 5 mmol%) in CH_2Cl_2 (1 mL). The mixture was photolyzed with sunlamp (visible light) for 4 h. Evaporation of the solvent and the residue obtained was purified by preparative TLC on silica gel (2% ethyl acetate-petroleum ether) to give the pure polyenoyl β-keto thioester **20**; ^{1}H NMR (400 MHz, $CDCl_3$) (E:Z = ca. 6:1) δ 12.97 (enol form, OH), 6.64 (t, *J* = 7.2 Hz, 1H), 6.56 (t, *J* = 7.2 Hz, enol form), 6.32 (dd, *J* = 26.0, 12.0 Hz, enol form), 6.19 – 5.88 (m, 2H, keto/enol), 5.77 – 5.45 (m, 2H, keto/enol), 3.83 (s, 2H), 2.40 – 2.13 (m, 3H, keto/enol), 2.13 – 2.00 (m, 1H, keto/enol), 2.00 – 1.87 (m, 1H, keto/enol), 1.79 (s, 3H), 1.73 (d, *J* = 6.2 Hz, 3H), 1.52 (s, enol form), 1.46 (s, 9H), 1.37 – 1.20 (m, 2H, keto/enol), 1.00 – 0.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ196.4 (enol form), 193.6, 193.3, 169.9 (enol form), 146.0, 149.96 (enol form), 137.01 (enol form), 137.00, 131.92, 131.75 (enol form), 131.61 (enol form), 131.54, 130.0 (enol form), 129.7, 127.1, 124.3 (enol form), 97.29 (enol form), 53.8, 48.8, 48.23 (enol form), 48.18 (enol form), 39.9, 35.09 (enol form), 35.03, 33.01, 32.97 (enol form), 30.18 (enol form), 29.7 (3 C), 27.01 (enol form), 26.97, 19.41 (enol form), 19.35, 18.29 (enol form), 18.0, 12.0 (enol form), 11.3; HRMS (EI): Exact mass calcd for $C_{20}H_{32}SO_2[M]^+$: 336.2123; Found: 336.2122.

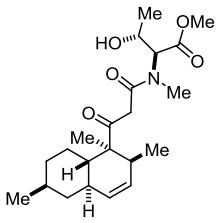


Decalin β-keto thioester **22**: To a solution of polyene **20** (100 mg, 0.30 mmol) in CH_2Cl_2 (15 mL, 0.02 M), a solution of I_2 (3 mg, 5 mmol%) in CH_2Cl_2 (1 mL) was added. The mixture was photolyzed with sunlamp (visible light) for 4 h. The mixture was then cooled down to –78 ^{o}C, and BF_3•OEt_2 (75 μL, 0.60 mmol) was slowly added. The reaction mixture was stirred for 30 min at same temperature. The reaction was then warmed to

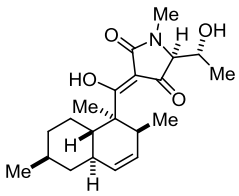
0 ^{o}C for 5 min before it was quenched with saturated NaCl solution (5 mL) and allowed to reach room temperature. Evaporation of the solvent and extracted with EtOAc (2 × 10 mL) and the combined organic phase was washed with $NaHCO_3$ solution (10 mL ×2) and brine (10 mL) ,then dried over anhydrous Na_2SO_4, After filtration and evaporation of the solvent, the residue (d.r. = 8:1) was purified by flash column chromatography (1% ethyl acetate-petroleum ether) to give the decalin β-keto thioester **22** (60 mg, 60%) as a viscous oil: R_f = 0.35 (2 % ethyl acetate-petroleum ether); $[a]_D^{21}$ =38.3 (*c* =1.05 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.39 (s, enol form), 5.56 – 5.41 (m, 1H, keto/enol), 5.33 (d, *J* = 9.9 Hz, 1H, keto/enol), 3.59 (q, *J* = 15.6 Hz, 2H), 2.16 – 1.98 (m, 1H) 1.97 – 1.89 (m, enol form), 1.83 – 1.65 (m, 4H, keto/enol), 1.68 – 1.54 (m, 2H keto/enol), 1.51 (s, enol form), 1.47 (s, 9H), 1.23 – 1.12 (m, 2H, keto/enol), 1.07 – 0.97 (m, 2H, keto/enol), 0.94 (d, *J* = 7.0 Hz, 1H), 0.92 – 0.86 (m, 3H, keto/enol), 0.86 – 0.78 (m, 4H, keto/enol); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.9, 196.2 (enol form) 193.1, 182.0 (enol form), 130.7 (enol form), 129.8, 130.7 (enol form), 129.2, 129.1 (enol form), 99.4 (enol form), 54.5, 53.1, 48.8, 48.1 (enol form), 42.0 (enol form), 41.9, 39.5, 38.9 (enol form), 38.7, 38.5, 38.4 (enol form), 35.6 (enol form), 35.5, 33.3, 33.2 (enol form), 30.17 (enol form), 29.6 (3 C), 27.4 (enol form), 27.0, 22.4, 19.1 (enol form), 18.7, 17.7, 17.2 (enol form); MS (m/z) (%): EI [M] (%) calcd for $C_{20}H_{32}SO_2$: 336; found 336 (1), 280 (22), 247 (57), 219 (100), 149 (59).

General procedure for the aminolysis: We followed the procedure of CF_3CO_2Ag-promoted aminolysis developed by Dixon, Ley and co-workers.[2] A solution of *N*-methyl amino ester (1.2 equiv) in THF was added via syringe to a solution of thioester (1.0 equiv) in THF and triethylamine (4.0 equiv) at 20 ^{o}C. The reaction mixture was cooled to 0 ^{o}C before silver trifluoroacetate (1.5 equiv) was added in one portion. The resulting solution was stirred for a further 20 min. The solvent was removed under reduced pressure and dichloromethane was added to the residue. The mixture was filtered through short celite pad and washed with dichloromethane. The collected filtrate was concentrated and the residue was purified

by silica gel column chromatography to give product.

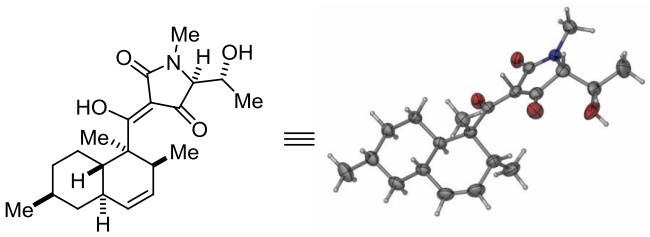


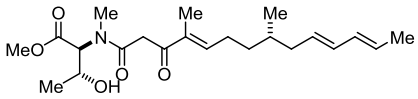
Ketoamide **24** was prepared according to the general procedure of aminolysis with **22** and N-methyl-L-threonine methyl ester **23**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **24** (50 mg, 71%) as colorless oil: R_f = 0.31 (40% ethyl acetate–petroleum ether); $[a]_D^{21}$ =11.8 (*c* =1.1 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 14.80 (s, enol form), 5.55 – 5.46 (m, 1H), 5.44 – 5.26 (m, 1H), 4.55 – 4.46 (m, 1H), 4.40 (d, *J* = 6.2 Hz, 1H), 3.97 – 3.69 (m, 4H), 3.65 – 3.39 (m, 1H), 3.21 – 2.93 (m, 3H), 2.16 – 2.05 (m, 1H), 1.73 (dd, *J* = 23.0, 11.8 Hz, 3H), 1.62 (t, *J* = 9.8 Hz, 3H), 1.52 – 1.41 (m, 1H), 1.32 (d, *J* = 6.2 Hz, 2H), 1.29 – 1.21 (m, 3H), 1.11 – 0.85 (m, 6H), 0.85 – 0.76 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.3, 169. 8, 169.0, 129.7, 129.2, 85.4 (enol form), 66.0, 65.2, 53.1, 52.2, 45.8, 41.8, 39.7, 38.7, 38.4, 37.3, 35.5, 33.2, 27.1, 22.3, 20.0, 18.6, 17.4; Exact mass calcd for $C_{22}H_{35}NO_5[M]^+$: 393.2515; Found: 393.2516。



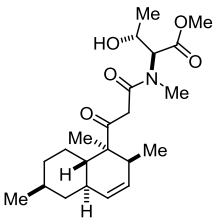
Cryptocin **4**: To a solution of ketoamide **24** (52 mg, 0.13 mmol) in methanol (2.5 mL, 0.05M) at 0 ^oC was added 0.5 ml of a solution of sodium methoxide (21 mg, 0.39mmol) in methanol via syringe. After 1.5 h the reaction was quenched by the addition of 1 N HCl (1 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4. After filtration and evaporation of the solvent, the residue obtained was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the pure cryptocin **4** (35 mg, 75%) as pale red foam: R_f = 0.37 (5 % methanol-dichloromethane); $[a]_D^{21}$ =90.4 (*c* =0.49 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.56-5.49 (m, 1H), 5.34 (d, *J* = 9.7 Hz, 1H), 4.19 (s, 1H), 4.04 – 3.58 (m, 2H), 2.98 (s, 3H), 2.84 (s, 1H), 2.08 – 1.90 (m, 1H), 1.90 – 1.72 (m, 3H), 1.67 (s, 1H), 1.46 (s, 4H), 1.20 – 0.98 (m, 5H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (s, 1H), 0.82 (d, *J* = 6.0 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 200.4, 192.4, 177.0,

129.3, 129.2, 100.5, 66.8, 66.5, 48.6, 42.3, 39.0, 38.6, 35.7, 33.4, 28.3, 27.2, 22.4, 18.3, 17.1, 14.3 (the peak at C16 is unavailable); HRMS (EI): Exact mass calcd for $C_{21}H_{31}NO_4$ $[M]^+$: 361.2253; Found: 361.2256. Recrystallization of **4** from ethyl acetate–hexanes gave single crystals suitable for X-ray analysis (CCDC: 1000587).



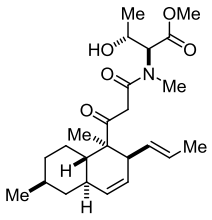


Polyenoylamino acid **25** was prepared according to the general procedure of aminolysis with **20** and N-methyl-L-threonine methyl ester **23**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **25** (21 mg, 79%) as colorless oil: R_f = 0.24 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -22.2 (*c* = 0.83 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.46 (s, enol form), 6.66 (t, *J* = 6.7 Hz, 1H), 6.30 (dd, *J* = 26.3, 11.9 Hz, enol form), 6.16 – 5.83 (m, 1H), 5.73 – 5.44 (m, , 2H), 4.85 (d, *J* = 5.7 Hz, 1H), 4.63 – 4.37 (m, 1H), 4.09 – 3.84 (m, 2H), 3.86 – 3.66 (m, 3H), 3.23 (br, 1H), 3.16 – 2.83 (m, 3H), 2.36 – 2.19 (m, 2H), 2.11 – 2.00 (m, 1H), 2.0 – 1.89 (m, 1H), 1.87 – 1.73 (m, 3H), 1.72 (d, *J* = 6.5 Hz, 2H), 1.53 – 1.41 (m, 2H), 1.36 – 1.17 (m, 5H), 1.02 – 0.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.1, 170.2, 169.3, 145.7, 136.7, 131.9, 131.5, 129.7, 127.2, 66.6, 63.2, 52.3, 44.5, 39.8, 35.7, 35.0, 33.1, 26.9, 19.6, 19.3, 18.0, 11.2. Exact mass calcd for $C_{22}H_{35}NO_5$[M]$^+$: 393.2515; Found: 393.2516。

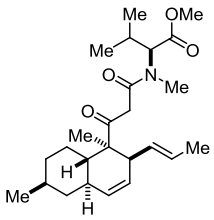


Ketoamide **24**: To a solution of polyenoylamino acid **25** (14 mg, 0.033 mmol) in CH_2Cl_2 (6 mL, 0.02 M), the mixture was then cooled down to –78 ^{o}C, and BF_3•OEt_2 (22 μL, 0.17 mmol) was slowly added. The reaction mixture was stirred for 8 h at same temperature before it was quenched with saturated NaCl solution (1 mL) and allowed to reach room temperature. Evaporation of the solvent and extracted with EtOAc (2 ×

3 mL) and the combined organic phase was washed with $NaHCO_3$ solution (3 mL ×2) and brine (3 mL), then dried over anhydrous Na_2SO_4, After filtration and evaporation of the solvent, the residue was purified by flash column chromatography (10%-30% ethyl acetate-petroleum ether) to give the ketoamide **24** (8 mg, 57%) as colorless oil.

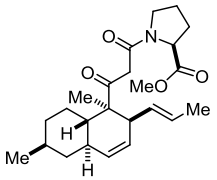


Ketoamide **32** was prepared according to the general procedure of aminolysis with **26** and **23**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **32** (85 mg, 85%) as colorless oil: R_f = 0.16 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 135.4 (*c* =0.50 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.67 (s, enol form), 5.59 – 5.28 (m, 3H), 5.25 – 5.05 (m, 1H), 4.71 (d, *J* = 6.2 Hz, 1H), 4.51 – 4.38 (m, 1H), 3.87 – 3.61 (m, 4H), 3.50 (d, *J* = 16.8 Hz, 1H), 3.09 – 2.83 (m, 3H), 2.62 – 2.50 (m, 1H), 2.40 (s, 1H), 1.86 – 1.62 (m, 5H), 1.59 (d, *J* = 6.4 Hz, 3H), 1.47 (br, 1H), 1.30 (d, *J* = 6.4 Hz, 2H), 1.27 – 1.15 (m, 4H), 1.13 – 0.94 (m, 2H), 0.93 – 0.75 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 170.0, 169.0, 130.9, 130.4, 126.6, 126.4, 66.2, 63.7, 53.3, 52.1, 49.7, 46.0, 41.8, 39.8, 38.3, 35.8, 35.4, 33.3, 27.1, 22.3, 19.7, 17.7, 17.3; HRMS (EI): Exact mass calcd for $C_{24}H_{37}NO_5[M]^+$: 419.2672; Found: 419.2676.

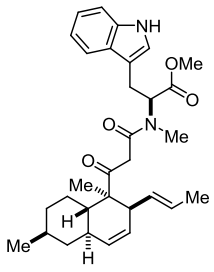


Ketoamide **33** was prepared according to the general procedure of aminolysis with **26** and N-methyl-L-valine methyl ester **28**, which was purified by silica gel column chromatography (5% to 15% ethyl acetate-petroleum ether) to give **33** (52 mg, 75%) as colorless oil: R_f = 0.14(10% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 85.2 (*c* =0.59 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.9 (1s, enol form), 5.48 – 5.28 (m, 3H), 5.27 – 5.06 (m, 1H), 4.97 – 4.89 (m, 1H), 3.87 – 3.56 (m, 4H), 3.53 – 3.34 (m, 1H), 3.02 – 2.71 (m, 3H), 2.54 (dd, *J* = 8.7, 4.7 Hz, 1H), 2.28 – 2.07 (m, 1H), 1.83 – 1.61 (m, 6H), 1.60 – 1.53 (m, 3H), 1.52 – 1.37 (m, 1H), 1.25 (d, *J* = 15.6 Hz, 2H), 1.16 – 1.04 (m, 2H), 1.04 – 0.96 (m, 3H), 0.96 – 0.92 (m, 3H), 0.91 – 0.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.7, 171.4, 168.4, 131.2, 130.4, 126.4, 126.1,

61.2, 53.3, 51.6, 49.6, 46.0, 41.8, 39.8, 38.3, 35.4, 33.2, 31.8, 27.4, 27.0, 22.3, 19.6, 18.7, 17.6, 17.3 (the peak at the C of enol form aren't obvious); HRMS (EI): Exact mass calcd for $C_{25}H_{39}NO_4[M]^+$: 417.2879; Found: 417.2877.

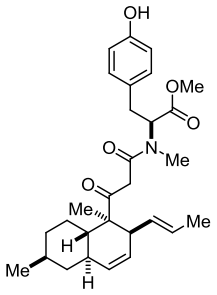


Ketoamide **34** was prepared according to the general procedure of aminolysis with **26** and L-proline methyl ester **29**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **34** (150 mg, 90%) as colorless oil: R_f = 0.25 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 108.2 (*c* =0.63 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.5(1s, enol form), 5.53 – 5.27 (m, 3H), 5.26 – 5.11 (m, 1H), 5.08 (s, enol form), 4.52 (dd, *J* = 8.3, 3.6 Hz, 1H), 3.82 – 3.54 (m, 4H), 3.54 – 3.41 (m, 2H), 3.31 (d, *J* = 15.8 Hz, 1H), 2.54 (dd, *J* = 9.1, 4.8 Hz, 1H), 2.36 (d, *J* = 7.8 Hz, enol form), 2.29 – 2.12 (m, 1H), 2.10 – 1.85 (m, 3H), 1.84 – 1.63 (m, 5H), 1.62 – 1.53 (dd, *J* = 8.7, 3.6 Hz, 3H), 1.52 – 1.40 (m, 1H), 1.29 – 1.20 (m, 2H), 1.11 – 0.93 (m, 3H), 0.94 – 0.74 (m, 4H).^{13}CNMR (100 MHz, $CDCl_3$) δ 207.0, 172.7, 166.3, 131.4, 130.5, 126.4, 126.0, 58.7, 53.2, 52.1, 49.5, 47.7, 46.5, 41.9, 39.8, 38.4, 35.5, 33.3, 29.4, 27.2, 24.8, 22.4, 17.7, 17.3 (the peaks at some C of enol form are unavailable); HRMS (EI): Exact mass calcd for $C_{24}H_{35}NO_4[M]^+$: 401.2566; Found: 401.2567.



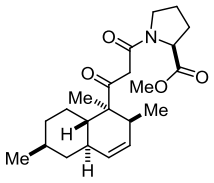
Ketoamide **35** was prepared according to the general procedure of aminolysis with **26** and *N*-methyl-L-tryptophan methyl ester **30**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **35** (203 mg, 98%) as colorless oil: R_f = 0.34 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ =90.9 (*c* =0.58 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ14.84 (1s, enol form) 8.45 – 8.05 (m, 1H), 7.64 (dd, *J* = 20.0, 7.6 Hz, 1H), 7.37 (dd, *J* = 20.0, 7.6 Hz, 1H), 7.24 – 7.06 (m, 3H), 7.02 (s, enol form), 5.46 – 5.21 (m, 3H), 5.20 – 5.06 (m, 1H), 5.06 – 4.82 (m, 1H), 4.65 (dd, *J* = 10.5, 4.4 Hz, enol form), 3.88 – 3.58 (m, 3H), 3.58 – 3.41 (m, 1H), 3.41 – 3.08 (m, 2H), 3.05 – 2.64 (m, 4H), 2.53 (dd, *J* = 8.5, 4.7 Hz, 1H), 1.86 – 1.59 (m, 5H), 1.60 – 1.31 (m, 5H), 1.24 – 0.97 (m, 3H), 0.97 – 0.68 (m, 5H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 206.7, 206.6 (enol form), 171.5, 170.6 (enol form), 168.42, 168.40 (enol form), 136.50 (enol form), 136.04, 131.0 (keto/enol), 130.4, 130.0 (enol form), 127.2, 126.5 (enol form), 126.43, 126.35, 126.3 (enol form), 125.68 (enol form), 123.7 (enol form), 122.7, 122.2 (enol form), 121.7, 119.9 (enol form), 119.1, 118.2, 117.6 (enol form), 112.0 (enol form), 111.2, 110.6, 109.6 (enol form), 60.5 (enol form), 57.6, 53.3, 52.9 (enol form), 52.5 (enol form), 52.1, 49.4, 48.0 (enol form), 45.9, 44.1 (enol form), 41.8 (keto/enol), 39.7, 39.2 (enol form), 38.3, 38.1 (enol form), 35.4, 35.3 (enol form), 33.3 (enol form), 33.23 (keto/enol), 33.19, 27.0, 26.8 (enol form), 25.1 (enol form), 24.4, 22.4 (keto/enol), 17.68 (enol form), 17.63, 17.1, 15.7 (keto/enol); HRMS (EI): Exact mass calcd for $C_{31}H_{40}N_2O_4[M]^+$: 504.2988; Found: 504.2984.

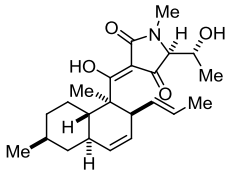


Ketoamide **36** was prepared according to the general procedure of aminolysis with **26** and *N*-methyl-L-tyrosine methyl ester **31**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **36** (20 mg, 77%) as colorless foam: R_f = 0.17 (20% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 123.7 (*c* = 0.29 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 14.64 (1s, enol form), 7.07 (d, *J* = 8.2 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, enol from), 6.80 – 6.64 (m, 2H), 5.54 – 5.20 (m, 4H), 5.20 – 4.97 (m, 1H), 4.45 (m, enol form), 3.90 – 3.54 (m, 4H), 3.43 –3.15 (m, 2H), 3.07 – 2.71 (m, 4H), 2.52 (s, 1H), 2.36 (s, enol form), 1.85 – 1.61 (m, 6H), 1.60 – 1.50 (m, 3H), 1.46 (br, 1H), 1.21 – 1.10 (m, 2H), 1.09 – 0.97 (m, 2H), 0.97 – 0.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8 (enol form), 206.4, 171.2, 170.3 (enol form), 168.9, 168.6 (enol form), 155.9 (enol form), 155.3, 131.08 (enol form), 130.95, 130.4, 130.1 (enol form), 129.8 (2 C), 127.9, 127.6 (enol form), 126.5 (keto/enol), 126.4, 126.3 (enol form), 115.8 (enol form), 115.5 (2 C), 63.04 (keto/enol), 58.5 (keto/enol), 53.44 (enol form), 53.40, 52.5 (enol form), 52.3, 49.5, 49.2 (enol form), 45.8, 45.3 (enol form), 41.8 (keto/enol), 39.7, 39.6 (enol form), 38.34, 38.28 (enol form), 35.4 (keto/enol), 34.7 (enol form), 34.0, 33.3, 33.2 (enol form), 30.1 (enol form), 27.1, 22.4 (keto/enol), 17.7 (keto/enol), 17.1, 16.9 (enol

form); HRMS (EI):Exact mass calcd for $C_{29}H_{39}NO_5[M]^+$: 481.2828; Found: 481.2824.

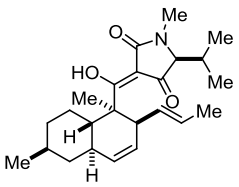


Ketoamide **37** was prepared according to the general procedure of aminolysis with **22** and L-proline methyl ester **29**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **37** (77 mg, 93%) as colorless oil: R_f = 0.36 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$=4.0 (*c* =1.48 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.84 (s, enol form), 14.61 (s, enol form) 5.56 – 5.43 (m, 1H), 5.40 – 5.23 (m, 1H), 5.13 (s, enol form) 4.64 – 4.42 (m, 1H), 3.85 – 3.26 (m, 6H), 2.34 – 1.83 (m, 5H), 1.83 – 1.65 (m, 4H), 1.64 – 1.52 (m, 1H), 1.53 –1.35 (m, 1H), 1.31 – 1.11 (m, 3H), 1.02 (dd, *J* = 18.4, 6.2 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 1H), 0.92 – 0.85 (m, 3H), 0.82 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 172.3, 166.0, 129.7, 129.2, 58.6, 53.0, 52.1, 47.5, 46.1, 45.0, 41.9, 39.3, 38.5, 35.5, 33.2, 29.2, 27.1, 24.6, 22.3, 18.7, 17.4. HRMS (EI): Exact mass calcd for $C_{22}H_{33}NO_4$ $[M]^+$: 375.2410; Found: 375.2412.

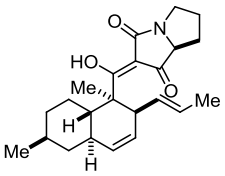


Derivative of cryptocin **38**: To a solution of ketoamide **32** (85 mg, 0.20 mmol) in methanol (12 mL, 0.02 M) at 0 ^{o}C was added sodium methoxide (38 mg, 0.70 mmol). After 2 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the pure derivative of cryptocin **38** (59 mg, 69%) as pale red foam: R_f = 0.24 (40% ethyl acetate-petroleum ether); $[a]_D^{21}$ = 315.9 (*c* = 0.77 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (s, 2H), 5.33 – 5.21 (m, 1H), 5.20 – 5.06 (m, 1H), 4.18 (s, 1H), 3.91 (s, 1H), 3.78 (s, 1H), 3.34 (s, 1H), 2.96 (s, 3H), 1.93 (d, *J* = 8.5 Hz, 1H), 1.88 – 1.62 (m, 4H), 1.59 – 1.34 (m, 7H), 1.18 – 0.96 (m, 5H), 0.97 – 0.78 (m, 4H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 199.6, 192.3, 177.0, 130.7, 129.8, 126.9, 126.6, 100.7, 66.6, 66.5, 48.7, 45.2, 42.2, 39.9, 38.4, 35.6, 33.4, 28.2, 27.2, 22.4, 17.7, 17.1, 13.8; HRMS (EI): Exact mass calcd for $C_{23}H_{33}NO_4[M]^+$: 387.2410; Found: 387.2411.

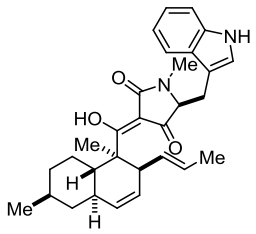


Derivative of cryptocin **39**: To a solution of ketoamide **33** (68 mg, 0.16 mmol) in methanol (3 mL, 0.05 M) at 0 ^oC was added sodium methoxide (26 mg, 0.48 mmol). After 5 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (10% ethyl acetate-petroleum ether) to give the pure derivative of cryptocin **39** (30 mg, 49%, d.r. =4:1) as pale red foam: R_f = 0.29 (10% ethyl acetate-petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 5.38 (s, 2H), 5.33 – 5.23 (m, 1H), 5.22 – 5.08 (m, 1H), 3.48 (s, 1H), 3.36 (s, 1H), 2.99 (s, 3H), 2.93 (s, isomer), 2.42 – 2.20 (m, 1H), 1.97 (br, 1H), 1.90 – 1.57 (m, 5H), 1.58 – 1.37 (m, 7H), 1.19 – 0.99 (m, 5H), 0.98 – 0.76 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0, 191.1, 176.8, 130.9, 129.7, 126.9, 126.7, 100.9, 70.2, 48.4, 45.0, 42.3, 40.1, 38.6, 35.7, 33.5, 29.1, 28.4, 27.9, 22.5, 17.7, 17.5, 17.0, 14.0 (peak at enol form aren't obvious); HRMS (EI): Exact mass calcd for $C_{24}H_{35}NO_3[M]^+$: 385.2617; Found: 385.2618.

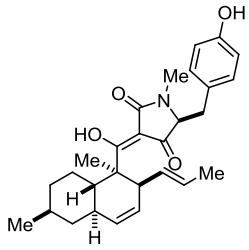


Derivative of cryptocin **40**: To a solution of ketoamide **34** (120 mg, 0.30 mmol) in methanol (15 mL, 0.01 M) at 60 ^oC was added 0.5 ml of a solution of sodium methoxide (80 mg, 1.50 mmol) in methanol via syringe. After 4 h the reaction was quenched by the addition of 1 N HCl (1 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (30% ethyl

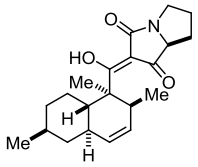
acetate-petroleum ether) to give the pure derivative of cryptocin **40** (79 mg, 71%, d.r. = 4:1) as pale red foam: R_f = 0.48 (40% ethyl acetate–petroleum ether); $[a]_D^{21}$ =318.3(*c* =0.63 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 – 5.32 (m, 2H), 5.28 – 5.00 (m, 2H), 3.90 (dd, *J* = 9.5, 7.2 Hz, 1H), 3.70 (ddd, *J* = 21.7, 12.6, 10.2 Hz, 1H), 3.36 (br, 1H), 3.32 – 3.11 (m, 1H), 2.26 – 2.16 (m, 1H), 2.18 – 2.00 (m, 2H), 1.99 – 1.88 (m, 1H), 1.63 (d, *J* = 29.2 Hz, 4H), 1.54 – 1.35 (m, 6H), 1.46 (d, *J* = 2.9 Hz, 1H); 1.20 – 0.96 (m, 3H), 0.96 – 0.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 192.8, 181.3, 131.1, 129.9, 126.6, 126.5, 101.9, 67.7, 48.9, 45.1, 43.9, 42.3, 39.9, 38.3, 35.7, 33.5, 28.3, 27.4, 26.8, 22.5, 17.9, 13.9; HRMS (EI): Exact mass calcd for $C_{23}H_{31}NO_3[M]^+$: 369.2304; Found: 369.2303.



Derivative of cryptocin **41**: To a solution of ketoamide **35** (132 mg, 0.26 mmol) in methanol (13 mL, 0.02M) at 0 ^{o}C was added sodium methoxide (42 mg, 0.78mmol). After 1 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the pure derivative of cryptocin **41** (100 mg, 82%, d.r. = 5:1) as pale red foam: R_f = 0.34 (30 % ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.63 (dd, *J* = 20.4, 7.8 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.12 (m, 2H), 6.98 – 6.89 (m, 1H), 5.42 – 5.04 (m, 2H), 4.75 (br, 1H), 4.61 (br, 1H), 4.07 – 3.80 (m, 1H), 3.49 – 3.21 (m, 2H), 3.16 – 2.77 (m, 4H), 2.01 – 1.77 (m, 3H), 1.69 – 1.55 (m, 2H), 1.55 – 1.41 (m, 4H), 1.33 (d, *J* = 5.6 Hz, 3H), 1.17 – 0.96 (m, 2H), 0.98 – 0.59 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 191.0, 176.6, 135.9, 130.5, 129.8, 127.4, 126.8, 126.4, 122.8, 122.0, 119.5, 118.7, 111.0, 109.1, 100.4 (enol form), 66.2, 62.5, 48.5, 44.7, 42.1, 39.7, 38.6, 35.6, 33.4, 28.1, 27.7, 24.6, 22.4, 17.9, 13.9; HRMS (EI):Exact mass calcd for $C_{30}H_{36}N_2O_3[M]^+$: 472.2726; Found: 472.2723.

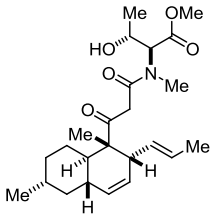


Derivative of cryptocin **42**: To a solution of ketoamide **36** (51 mg; 0.11 mmol) in methanol (2 mL, 0.05M) at 0 ^{o}C was added sodium methoxide (17 mg, 0.32mmol). After 1.5 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (20% ethyl acetate-petroleum ether) to give the pure derivative of cryptocin **42** (45 mg, 90%, d.r. = 3:1) as pale red foam: R_f = 0.22 (20% ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (d, 8.2 Hz, 2H), 6.69 (d, *J* = 8.2 Hz, 2H), 5.53 – 5.28 (m, 3H), 4.85 (s, 1H), 3.99 – 3.73 (m, 1H), 3.31 – 3.14 (m, 1H), 3.14 – 3.03 (m, 2H), 3.00 (s, 3H), 2.93 (s, isomer), 1.93 – 1.68 (m, 4H), 1.68 – 1.55 (m, 1H), 1.55 – 1.34 (m, 6H), 1.30 – 0.95 (m, 3H), 0.95 – 0.81 (m, 4H) (the peak at hydrogen of phenolic hydroxyl was not found); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 190.8, 176.6, 155.2, 130.7 (2 C), 130.5, 130.3, 130.0, 127.5, 126.3, 115.4 (2 C), 100.5 (enol form), 66.8, 63.4, 48.7, 44.7, 42.1, 39.7, 38.7, 35.6, 33.6, 33.4, 28.1, 27.9, 22.4, 17.9, 13.8; HRMS (EI):Exact mass calcd for $C_{28}H_{35}NO_4[M]^+$: 449.2566; Found: 449.2563.

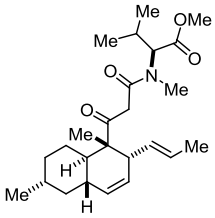


Derivative of cryptocin **43**: To a solution of ketoamide **37** (77 mg, 0.20 mmol) in methanol (10 mL, 0.02 M) at 60 ^{o}C was added 0.5 ml of a solution of sodium methoxide (61 mg, 1.00 mmol) in methanol via syringe. After 2 h the reaction was quenched by the addition of 1 N HCl (1 mL) at 25 ^{o}C. The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (20% ethyl acetate-petroleum ether) to give the pure derivative of cryptocin **43** (63 mg, 90%) as pale red foam: R_f = 0.25 (20% ethyl acetate-petroleum ether); $[a]_D^{21}$ =117.8 (*c* = 0.76 in

$CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.67 – 5.40 (m, 1H), 5.30 (d, *J* = 9.8 Hz, 1H), 3.90 (t, *J* = 8.6 Hz, 1H), 3.78 – 3.53 (m, 1H), 3.37 – 3.21 (m, 1H), 2.81 (s, 1H), 2.26 – 1.93 (m, 3H), 1.92 – 1.58 (m, 5H), 1.53 – 1.35 (m, 5H), 1.16 – 0.96 (m, 2H), 0.96 – 0.81 (m, 4H), 0.79 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 192.8, 180.6, 129.6, 129.0, 101.8, 67.8, 48.6, 43.6, 42.3, 38.9, 38.5, 36.0, 35.7, 33.4, 28.3, 27.2, 26.8, 22.4, 18.5, 14.2; HRMS (EI): Exact mass calcd for $C_{21}H_{29}NO_3$ $[M]^+$: 343.2147; Found: 343.2144.

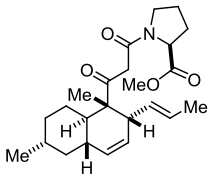


Ketoamide **44** was prepared according to the general procedure of aminolysis with **27** and N-methyl-L-threonine methyl ester **23**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **44** (170 mg, 86%) as colorless oil: R_f = 0.17 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -130.1 (*c* =0.43 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 14.65 (s, enol form), 5.50 – 5.27 (m, 3H), 5.26 – 5.03 (m, 1H), 4.79 (d, *J* = 6.0 Hz, 1H), 4.45 (d, *J* = 10.3, 1H), 3.87 – 3.67 (m, 4H), 3.63 – 3.42 (m, 1H), 3.19 (d, *J* = 3.9 Hz, 1H), 3.11 – 2.88 (m, 3H), 2.57 (dd, *J* = 9.0, 4.5 Hz, 1H), 1.87 – 1.64 (m, 5H), 1.64 – 1.53 (m, 3H), 1.45 (dd, *J* = 16.6, 9.6 Hz, 1H), δ 1.28 – 1.17 (m, 3H). 1.35 – 1.17 (m, 3H), 1.17 – 0.96 (m, 2H), 0.95 – 0.86 (m, 3H), 0.85 – 0.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 170.2, 169.0, 130.8, 130.4, 126.8, 126.4, 66.4, 63.3, 53.4, 52.1, 49.6, 46.0, 41.8, 39.8, 38.3, 35.6, 35.4, 33.3, 27.1, 22.4, 19.6, 17.7, 17.2; HRMS (EI): Exact mass calcd for $C_{24}H_{37}NO_5[M]^+$: 419.2672; Found: 419.2673.

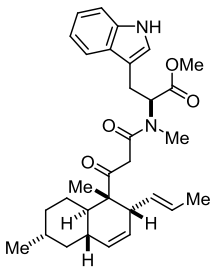


Ketoamide **45** was prepared according to the general procedure of aminolysis with **27** and N-methyl-L-valine methyl ester **28**, which was purified by silica gel column chromatography (5% to 10% ethyl acetate-petroleum ether) to give **45** (20 mg, 50%) as colorless oil: R_f = 0.41 (20% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 90.3 (*c* = 0.69 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 14.9(1s, enol form), 5.48 – 5.28 (m, 3H), 5.26 – 5.09 (m, 1H), 4.92 (dd, *J* = 10.6, 4.7 Hz, 1H), 3.87 – 3.56 (m, 4H), 3.53 – 3.30 (m, 1H), 3.02 – 2.71

(m, 3H), 2.54 (dd, *J* = 8.7, 4.7 Hz, 1H), 2.28 – 2.07 (m, 1H), 1.70 (ddd, *J* = 22.5, 18.8, 9.6 Hz, 6H), 1.60 – 1.53 (m, 3H), 1.52 – 1.37 (m, 1H), 1.24 (d, *J* = 15.6 Hz, 2H), 1.14 – 1.04 (m, 2H), 1.00 (t, *J* = 8.4 Hz, 3H), 0.96 – 0.92 (m, 3H), 0.91 – 0.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 171.5, 168.5, 130.8, 130.4, 126.8, 126.4, 61.2, 53.4, 51.7, 49.5, 46.2, 41.8, 39.7, 38.4, 35.4, 33.3, 31.7, 27.4, 27.1, 22.4, 19.6, 18.8, 17.7, 17.1; HRMS (EI): Exact mass calcd for $C_{25}H_{39}NO_4[M]^+$: 417.2879; Found: 417.2880.

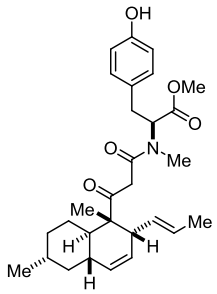


Ketoamide **46** was prepared according to the general procedure of aminolysis with **27** and L-proline methyl ester **29**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **46** (54 mg, 62%) as colorless oil: R_f = 0.34 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -104.9 (*c* = 0.43 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.45 (s, enol form), 5.48 – 5.25 (m, 3H), 5.30 – 5.13 (m, 1H), 5.06 (d, *J* = 6.1 Hz, enol form), 4.49 (dd, *J* = 8.6, 3.8 Hz, 1H), 4.42 – 4.34 (m, enol form), 3.86 – 3.66 (m, 3H), 3.65 – 3.51 (m, 2H), 3.51 – 3.38 (m, 2H), 3.30 (d, *J* = 15.8 Hz, enol form), 3.14 (d, *J* = 16.2 Hz, enol form), 2.55 (dd, *J* = 8.9, 4.3 Hz, 1H), 2.46 (dd, *J* = 9.0, 4.9 Hz, enol form), 2.29 – 2.10 (m, 1H), 2.09 – 1.87 (m, 3H), 1.82 – 1.66 (m, 3H), 1.66 – 1.52 (m, 4H), 1.51 – 1.39 (m, 1H), 1.27 – 1.16 (m, 3H), 1.12 – 0.94 (m, 3H), 0.94 – 0.76 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 172.6, 166.1, 130.8, 130.4, 126.8, 126.5, 58.7, 53.6, 52.2, 49.4, 47.6, 46.6, 41.9, 39.9, 38.4, 35.5, 33.4, 29.4, 27.2, 24.8, 22.4, 17.9, 17.0; EI [M] (%) calcd for $C_{24}H_{35}NO_4$: 401; found 401(8), 372 (7), 227 (20), 228 (57), 70 (100).



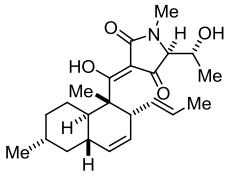
Ketoamide **47** was prepared according to the general procedure of aminolysis with **27** and *N*-methyl-L-tryptophan methyl ester **30**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **47** (74 mg, 80%) as colorless oil: R_f = 0.35 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -82.3 (*c* =0.14 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.82 (s, enol form), 8.60 – 8.21 (m, 1H), 7.87 – 7.50 (m, 1H), 7.44 – 7.30 (m, 1H), 7.22 – 7.07 (m, 3H), 7.00 (d,

J = 8.4 Hz, enol form), 5.46 – 5.22 (m, 4H), 5.21 – 5.08 (m, 1H), 5.01 – 4.84 (m, enol form), 4.45 (dd, *J* = 9.2, 5.4 Hz, enol form), 3.84 – 3.69 (m, 3H), 3.69 – 3.60 (m, 1H), 3.47 (dd, *J* = 15.5, 5.2 Hz, 1H), 3.38 – 3.13 (m, 2H), 2.97 – 2.74 (m, 3H), 2.49 (dd, *J* = 8.9, 4.9 Hz, 1H), 2.43 – 2.32 (m, enol form), 1.84 – 1.60 (m, 5H), 1.60 – 1.53 (m, 2H), 1.52 – 1.40 (m, 1H), 1.35 – 1.20 (m, 2H), 1.15 – 0.99 (m, 3H), 0.99 – 0.77 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9 (enol form), 206.7, 171.5, 170.8 (enol form), 168.41 (enol form), 168.35, 136.2 (enol form), 136.1, 132.2 (enol form), 131.0, 130.5, 130.0 (enol form), 127.8 (enol form), 127.7 (enol form), 127.4 (2 C), 126.8 (enol form), 126.4, 123.3 (enol form), 122.8, 122.2 (enol form), 121.8, 119.6 (enol form), 119.3 (enol form), 118.3, 118.0, 111.6 (enol form), 111.2, 110.9, 109.8 (enol form), 61.0, 57.7, 53.3, 53.0 (enol form), 52.3 (enol form), 52.2, 49.4, 49.3 (enol form), 45.8, 45.2 (enol form), 41.8, 39.7, 39.6 (enol form), 38.5 (enol form), 38.3, 35.53 (enol form), 35.45, 33.5 (enol form), 33.30, 29.1 (enol form), 27.1, 25.5 (enol form), 24.4, 22.4, 17.7, 17.3 (enol form), 17.0, 16.8 (enol form). HRMS (EI): Exact mass calcd for $C_{31}H_{40}N_2O_4[M]^+$: 504.2988; Found: 504.2992.

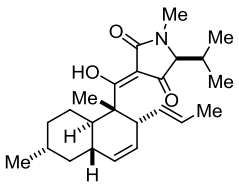


Ketoamide **48** was prepared according to the general procedure of aminolysis with **27** and *N*-methyl-L-tyrosine methyl ester **31**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **48** (120 mg, 89%) as colorless oil: R_f = 0.29 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -121.5 (*c* =0.44 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 7.4 Hz, enol form), 6.72 (d, *J* = 8.1 Hz, 2H), 5.46 – 5.22 (m, 4H), 5.21 – 5.04 (m, 1H), 4.29 (dd, *J* = 9.0, 5.5 Hz, enol form), 3.73 (d, *J* = 14.2 Hz, 3H), 3.65 – 3.55 (m, 1H), 3.36 – 3.15 (m, 2H), 3.01 – 2.75 (m, 4H), 2.48 (dd, *J* = 9.1, 5.0 Hz, 1H), 1.85 – 1.61 (m, 5H), 1.55 (t, *J* = 6.4 Hz, 3H), 1.46 (d, *J* = 6.4 Hz, 1H), 1.18 – 0.95 (m, 4H), 0.94 – 0.76 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 171.9, 171.2 (enol form), 169.7, 169.5 (enol form), 156.6 (enol form), 156.1, 132.0, 131.3, 130.8 (enol form), 130.6 (2 C), 128.8, 127.2, 127.0, 116.6 (enol form), 116.3 (2 C), 63.8, 59.5, 54.2, 54.1 (enol form), 53.1, 50.3, 46.4, 42.7, 40.5, 40.4 (enol form),

39.1, 36.3, 34.7, 34.2 (enol form), 34.1, 27.9, 23.2, 18.5, 18.4 (enol form), 17.9; HRMS (EI):Exact mass calcd for $C_{29}H_{39}NO_5[M]^+$: 481.2828; Found: 481.2827.

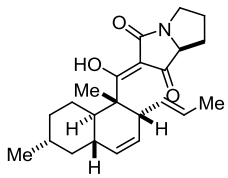


Derivative of (-)-equisetin **49**: To a solution of ketoamide **44** (170 mg, 0.41 mmol) in methanol (41 mL, 0.01M) at 0 ^oC was added sodium methoxide (66 mg, 1.22 mmol). After 1.5 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the pure derivative of (-)-equisetin **49** (115 mg, 74%, d.r. = 5:1) as pale red foam: R_f = 0.21 (40% ethyl acetate-petroleum ether); $[a]_D^{21}$ = -281.9 (*c* = 0.78 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.55 – 5.35 (m, 2H), 5.34 – 5.22 (m, 1H), 5.20 (s, 1H), 4.19 (s, 1H), 3.80 – 3.65 (m, 1H), 3.35 (br, 1H), 2.99 (s, 3H), 1.97 (s, 1H), 1.90 – 1.71 (m, 3H), 1.72 – 1.48 (m, 6H), 1.48 – 1.33 (m, 3H), 1.17 – 0.99 (m, 5H), 0.98 – 0.79 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 191.9, 177.2, 130.8, 129.9, 127.0, 126.5, 100.4 (enol form), 67.7, 66.6, 48.9, 44.9, 42.2, 39.9, 38.5, 35.6, 33.4, 29.6, 28.2, 27.6, 22.4, 17.9, 17.6, 14.0; HRMS (EI): Exact mass calcd for $C_{23}H_{33}NO_4[M]^+$: 387.2410; Found: 387.2407.



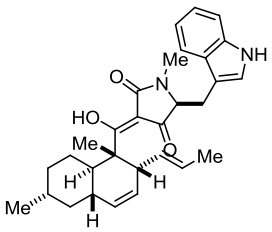
Derivative of (-)-equisetin **50**: To a solution of ketoamide **45** (32 mg, 0.074 mmol) in methanol (3.2 mL, 0.02 M) at 0 ^oC was added sodium methoxide (20 mg, 0.37 mmol). After 5 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (10% ethyl acetate-petroleum ether) to give the pure derivative of (-)-equisetin **50** (20 mg, 67%, d.r. =5:2) as pale red foam:

R_f = 0.52 (20% ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 – 5.13 (m, 3H), 5.06 – 4.74 (m, 1H), 3.87 – 3.60 (m, 1H), 3.59 – 3.30 (m, 1H), 2.99 (s, 3H), 2.90 (s, isomer), 2.38 – 2.18 (m, 1H), 2.13 – 1.94 (m, 1H), 1.94 – 1.63 (m, 4H), 1.64 – 1.35 (m, 8H), 1.18 – 0.97 (m, 5H), 0.97 – 0.80 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 191.6, 176.6, 131.3, 131.0, 129.8, 126.9, 70.4, 66.0, 48.4, 44.9, 42.3, 39.9, 38.6, 35.7, 33.5, 29.3, 28.4, 27.8, 22.5, 17.9, 17.1, 16.2, 13.7; HRMS (EI): Exact mass calcd for $C_{24}H_{35}NO_3[M]^+$: 385.2617; Found: 385.2615.

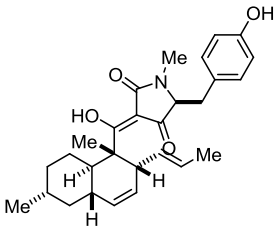


Derivative of (-)-equisetin **51**: To a solution of ketoamide **46** (34 mg, 0.085 mmol) in methanol (4 mL, 0.02 M) at 60 ^{o}C was added sodium methoxide (23 mg, 0.42 mmol). After 3 h the reaction was quenched by the addition of 1 N HCl (1 mL) at 20 ^{o}C. The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 10 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the inseparable derivative of (-)-equisetin (**51**) (22 mg, 71%, d.r. = 2:1) as pale red foam: R_f = 0.30 (30% ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.50 – 5.34 (m, 2H), 5.33 – 5.19 (m, 1H), 5.18 – 5.06 (m, 1H), 4.14 (t, J = 7.8 Hz, 1H), 3.92 – 3.78 (m, enol form), 3.76 – 3.58 (m, 1H), 3.44 – 3.24 (m, 1H), 3.24 – 3.09 (m, 1H), 2.32 – 2.15 (m, 1H), 2.16 – 2.00 (m, 2H), 1.94 – 1.71 (m, 4H), 1.67 (d, J = 4.6 Hz, 1H), 1.60 – 1.37 (m, 8H), 1.19 – 0.98 (m, 2H), 0.98 – 0.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.4, 198.6, 171.5, 131.3, 129.8, 126.7, 126.6, 107.1 (enol form), 67.7, 64.0, 50.4, 45.5, 43.7, 42.2, 39.9, 38.6, 38.2, 35.6, 33.4, 27.9, 27.4, 22.4, 17.8, 14.1 (some C of isomer in this spectrogram); HRMS (EI): Exact mass calcd for $C_{23}H_{31}NO_3[M]^+$: 369.2304; Found: 369.2303。

Derivative of (-)-equisetin **52**: To a solution of ketoamide **47** (32 mg, 0.067 mmol) in methanol (8.5 mL, 0.01M) at 0 ^{o}C was added sodium methoxide (11 mg, 0.20 mmol). After 3 h the reaction was quenched by the addition of 1 N HCl (1 mL). The mixture



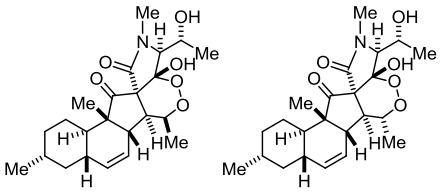
was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the inseparable derivative of (-)-equisetin **52** (25 mg, 78%, d.r. = 3:1) as pale red foam: R_f = 0.54 (40% ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.13 (dt, *J* = 14.9, 7.2 Hz, 2H), 6.94 (s, 1H), 5.48 – 5.31 (m, 2H), 5.30 – 5.21 (m, 1H), 5.21 – 5.09 (m, 1H), 3.90 (t, *J* = 4.7 Hz, 1H), 3.48 – 3.18 (m, 3H), 3.00 (s, isomer), 2.94 (s, 3H), 1.88 – 1.56 (m, 5H), 1.56 – 1.41 (m, 4H), 1.39 – 1.29 (m, 1H), 1.20 (s, 2H), 1.15 – 0.99 (m, 1H), 0.97 – 1.81 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 191.6, 176.6, 135.9, 131.0, 129.9, 127.3, 126.9, 126.7, 122.7, 122.1, 119.6, 119.5, 118.8, 111.1, 100.3, 66.4, 48.5, 45.0, 42.2, 39.8, 38.6, 35.6, 33.5, 28.2, 27.7, 25.4, 22.4, 17.9, 13.5； HRMS (EI):Exact mass calcd for $C_{30}H_{36}N_2O_3[M]^+$: 472.2726; Found: 472.2728.



Derivative of (-)-equisetin **53**: To a solution of ketoamide **48** (65 mg, 0.14 mmol) in methanol (4 mL, 0.05M) at 0 ^{o}C was added sodium methoxide (22 mg, 0.41 mmol). After 2.5 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give inseparable derivative of (-)-equisetin **53** (47 mg, 78%, d.r. = 3:1) as pale red foam: R_f = 0.34 (30% ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 5.46 – 5.30 (m, 2H), 5.29 – 4.93 (m, 2H), 4.02 – 3.61 (m, 1H), 3.55 – 3.19 (m, 1H), 3.14 – 3.00 (m, 2H), 3.00 – 2.80 (m, 3H), 1.81 (t, *J* = 11.3 Hz, 3H), 1.72 (d, *J* = 11.3 Hz, 1H),

1.68 – 1.57 (m, 2H), 1.56 – 1.39 (m, 4H), 1.35 (s, 2H), 1.15 – 0.92 (m, 2H), 0.92 – 0.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 191.5, 176.6, 155.1, 130.9, 130.5, 130.4 (2 C), 129.9, 126.9, 126.6, 115.4 (2 C), 100.3, 67.1, 48.9, 45.0, 42.2, 39.8, 38.6, 35.6, 33.5, 28.2, 27.9, 22.4, 17.9, 13.8; HRMS (EI):Exact mass calcd for $C_{28}H_{35}NO_4[M]^+$: 449.2566; Found: 449.2570.

1) **$Mn(OAc)_3$ method:**



Peroxide **54** and **54′**: A solution of Derivative of (-)-equisetin **49** (45 mg, 0.12 mmol) in AcOH (5 mL, 0.01 M) was added Manganous acetate (6.2 mg, 0.023 mmol) at 25 ^{o}C. The resulting solution was stirred for a further 4 h. The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The mixture was filtered through short celite pad and washed with ethyl acetate (10 mL). The collected filtrate was concentrated and the residue was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give the mixture of **54** and **54′** (43 mg, 88%, d.r. = 1.1:1) as colorless oil: R_f = 0.23 (30% ethyl acetate–petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) (dr =ca. 1.5:1) δ 5.77 (t, *J* = 10.1 Hz, 1H, **54**/**54′**), 5.56 (dd, *J* = 17.9, 10.1 Hz, 1H, **54**/**54′**), 4.76 (s, 1H, **54**), 4.62 (s, 1H, **54′**), 4.54 – 4.42 (m, 1H, **54**), 4.41 – 4.32 (m, 1H, **54**/**54′**), 4.30 – 4.25 (m, 1H, **54′**), 4.11 (s, 1H, **54′**), 4.01 (s, 1H, **54**), 3.06 (s, 3H, **54**), 3.05 (s, 3H, **54′**), 2.90 (s, 1H, **54**/**54′**), 2.78 (dd, *J* = 12.2, 2.1 Hz, 1H, **54′**), 2.71 (dd, *J* = 12.2, 3.5 Hz, 1H, **54**), 2.62 (dd, *J* = 12.2, 3.5 Hz, 1H, **54′**), 2.53 (d, *J* = 12.2 Hz, 1H, **54**), 1.85 (dd, *J* = 27.7, 12.2 Hz, 2H, **54**/**54′**), 1.72 (d, *J* = 12.2 Hz, 2H, **54**/**54′**), 1.62 – 1.30 (m, 9H, **54**/**54′**), 1.14 – 0.98 (m, 4H, **54**/**54′**), 0.98 – 0.76 (m, 4H, **54**/**54′**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.1 (**54′**), 215.8, 169.4 (**54′**), 168.4, 133.7 (**54′**), 133.2, 125.8, 123.3 (**54′**), 102.6, 102.1 (**54′**), 75.9, 74.7 (**54′**), 70.5 (**54′**), 70.4, 63.8 (**54′**), 63.7, 63.0, 59.8 (**54′**), 52.7, 51.6 (**54′**), 46.3, 44.7, 44.3 (**54′**), 43.3, 41.6 (**54′**), 41.5, 38.1, 37.9 (**54′**), 36.9, 36.8 (**54′**), 35.2, 35.1 (**54′**), 32.8 (**54**/**54′**), 31.21, 31.1 (**54′**), 25.0, 24.9 (**54′**), 23.5, 23.2 (**54′**), 22.20 (**54′**), 22.18, 19.0 (**54′**), 17.0,

15.04 (**54′**), 14.63; ESI $[M+Na]^+$ calcd for $[C_{23}H_{33}NO_6Na]^+$ 442.22; found 442.17.

2) **CAN method:** (We followed the procedure, reported by Theodorakis and co-workers in the synthesis of fusarisetin A.[1])

A solution of **49** (9.8 mg, 0.025 mmol) and ceric ammonium nitrate (13.9 mg, 0.025 mmol) in acetic acid (2.5 mL, 0.01 M) was stirred under oxygen atmosphere (1 atm) for 6 h, the solvent was removed and ethyl acetate (5 mL) was added. The mixture was filtered through short celite column and washed with ethyl acetate (5 mL). The collected filtrate was concentrated and the residue was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the mixture of **54** and **54′** (5.4 mg, 51%, d.r. = 1.3: 1) as colorless oil: R_f = 0.23 (30% ethyl acetate–petroleum ether).

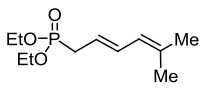
3) **$Ru(bpy)_3Cl_2$•$6H_2O$ method:**

To a solution of **49** (7.7 mg, 0.027 mmol) in acetonitrile (2.6 mL, 0.01 M) was added $Ru(bpy)_3Cl_2$•$6H_2O$ [tris(2,2'-bipyridyl) ruthenium(II) chloride hexahydrate] (2.0 mg, 0.0027 mmol) and triethylamine (14.0 μL, 0.10 mmol) at 25 ^oC. The mixture was stirred and irradiated with a 23 W household compact fluorescence lamp at 25 ^oC for 3.5 hours under 1 atm air. (The distance between the lamp and the reaction bottle is about 10 cm). The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The organic phase was washed with water (5 mL×2) , brine (5 mL), and dried over anhydrous sodium sulfate, filtered, concentrated, purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the mixture of **54** and **54′** (2.3 mg, 47% (brsm), d.r. = 1.5:1)

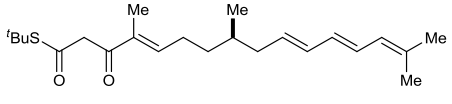
4) **Methylene blue method:**

To a solution of **49** (10.3 mg, 0.027 mmol) in acetonitrile (2.7 mL, 0.01 M) was added methylene blue (0.85 mg, 0.0027 mmol) and triethylamine (14.0 μL, 0.10 mmol) at 25 ^oC. The mixture was stirred and irradiated with a 23 W household compact fluorescence lamp at 25 ^oC for 5 hours under 1 atm air. (The distance

between the lamp and the reaction bottle is about (10 cm). The solvent was removed under reduced pressure and ethyl acetate (80 mL) was added to the residue. The organic phase was washed with water (5 mL × 2), brine (5 mL) and dried over anhydrous sodium sulfate, filtered, concentrated, purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the mixture of **54** and **54′** (3.8 mg, 41%, d.r. = 1:1) as colorless oil: R_f = 0.23 (30% ethyl acetate–petroleum ether).

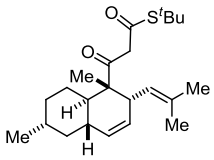


We followed the procedure reported by Nagorny and co-workers for the preparation of **57**.[3] To a solution of sulfonylphosphonate **55** (398 mg, 1.0 mmol) in THF (5 mL, 0.2 M) was slowly added KHMDS (1.2 mL, 1.2 mmol) at -78 ℃. After stirring for 20 minutes at this temperature, aldehyde **56** (126 mg, 1.5 mmol) was added to the mixture. After another 20 minutes, the reaction mixture was warmed up to 0 ℃ and stirred for 1 hour. The reaction was then quenched by addition of aqueous NH_4Cl solution (1 mL) and the product was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and then concentrated in vacuo. The unpurified reaction mixture was purified by column chromatography (15%–30% ethyl acetate–petroleum ether) to afford phosphonate **57** (160 mg, 70%, *E:Z* = 8:1) as a colorless oil: R_f = 0.41 (40% ethyl acetate–petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 – 6.21 (m, 1H), 6.01 (d, *J* = 11.6 Hz, Z), 5.80 (d, *J* = 11.6 Hz, 1H), 5.52 – 5.38 (m, 1H), 5.37 – 5.23 (m, Z isomer), 4.29 – 3.90 (m, 4H), 2.62 (dd, *J* = 22.3, 7.5 Hz, 2H), 1.73 (d, *J* = 8.6 Hz, 6H), 1.28 (t, *J* = 7.0, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.9 (d, *J* = 4.5 Hz), 131.5 (d, *J* = 15.0 Hz), 124.3 (d, *J* = 4.5 Hz), 118.6 (d, *J* = 12.7 Hz), 61.8 (d, *J* = 6.7 Hz), 31.4, 30.0, 25.8 (d, *J* = 1.0 Hz), 18.1(d, *J* = 0.9 Hz), 16.30, 16.24.



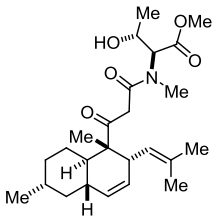
Polyenoyl β-keto thioester **59:** To a solution of diethyl 2,4-hexadiene-1-yl-phosphonate **57**[2-3](2 g, 8.6 mmol) in tetrahydrofuran (43 mL, 0.2 M) was added dropwise a solution of LiHMDS (9.5 mL, 9.5 mmol) in THF at -78 ^{o}C. After stirring at -78 ^{o}C for 30 minutes, a solution of aldehyde **32** (730 mg, 2.87 mmol) in anhydrous tetrahydrofuran (10 mL)

was added dropwise to the above solution. After stirring at -78 ^{o}C for 30 minutes, the reaction mixture was warmed to 30 ^{o}C and stirred for 16 hours. The reaction was quenched with saturated ammonium chloride solution (4 mL). The solvent was removed under reduced pressure and ethyl acetate (40 mL) and water (40 mL) was added to the residue. The organic phase was separated and the aqueous phase was extracted with ethyl acetate (15 mL × 2). The combined organic phase was washed with water (30 mL), brine (30 mL), and dried over anhydrous sodium sulfate, filtered, concentrated. The crude product was purified by silica gel column chromatography (1% to 3% ethyl acetate-petroleum ether) to give **59** (630 mg, 70% for 2 steps, *E/Z* = 15:1) as colorless oil: R_f = 0.34 (2% ethyl acetate-petroleum ether); $[a]_D^{21}$ = -60.3 (*c* = 0.20 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.97 (enol form, OH), 6.63 (t, *J* = 7.2 Hz, 1H), 6.56 (t, *J* = 7.8 Hz, enol form), 6.39 – 6.23 (m, 1H), 6.17 – 6.01 (m, 2H, keto/enol), 5.86 (dd, *J* = 21.8, 11.2 Hz, 1H, keto/enol), 5.70 – 5.50 (m, 1H, keto/enol), 5.50 (s, enol form), 3.82 (s, 2H), 2.36 – 2.15 (m, 2H, keto/enol), 2.15 – 2.05 (m, 1H, keto/enol), 2.04 – 1.91 (m, 1H, keto/enol), 1.83 (s, 1H), 1.79 (s, 6H), 1.76 (s, 3H), 1.73 (s, 1H), 1.51 (s, enol form), 1.46 (s, 9H), 0.96 – 0.84 (m, 4H, keto/enol); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 193.2, 146.0, 137.0, 135.2, 132.5, 131.4, 130.1, 127.6, 125.2, 53.6, 48.7, 40.1, 35.0, 33.0, 29.6 (3 C), 26.9, 26.1, 19.3, 18.3, 11.2; HRMS (m/z): EI [M] calcd for $C_{23}H_{36}O_2S$ 376.2436; found 376.2439.

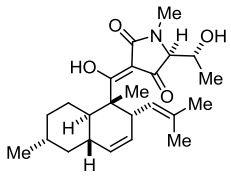


Decalin β-keto thioester **60**: To a solution of polyene **59** (100 mg, 0.27 mmol) in CH_2Cl_2 was added dropwise a solution of borontrifluoride ethyl ether complex (67 μL，0.53 mmol), The solution was stirred at -82 ^{o}C for 1 hours. The reaction mixture was stirred at 0 ^{o}C for 2 min, and saturated sodium bicarbonate solution (10 mL) was added to the above solution. The mixture was stirred at 25 ^{o}C for 3 minutes. The organic phase was washed with saturated sodium bicarbonate solution (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate, filtered, concentrated. The crude product was purified by silica gel column chromatography (1% ethyl acetate-petroleum ether) to give **60** (63.0 mg, 63%) as colorless foam: R_f = 0.40 (2% ethyl acetate-petroleum ether); $[a]_D^{21}$

= -118.0 (*c* = 0.54 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.28 (enol form, OH), 5.38 (d, *J* = 10.2 Hz, 1H), 5.30 (ddd, *J* = 10.2, 4.8, 2.4 Hz, 1H), 4.98 (d, *J* = 10.2 Hz, enol form), 4.81 (d, *J* = 10.2 Hz, 1H), 3.48 (dd, *J* = 71.6, 15.6 Hz, 2H), 2.82 (dd, *J* = 10.2, 4.7 Hz, 1H), 2.73 (dd, *J* = 10.2, 3.5 Hz, enol form), 1.85 – 1.69 (m, 5H, keto/enol), 1.65 (d, *J* = 1.1 Hz, 7H, keto/enol), 1.50 (s, enol form), 1.45 (s, 9H), 1.19 (d, *J* = 10.9 Hz, 3H, keto/enol), 1.18 – 0.95 (m, 2H, keto/enol), 0.94 – 0.84 (m, 4H, keto/enol); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.2, 195.9 (enol form), 193.3, 181.7 (enol form), 132.0, 131.2 (enol form), 130.0, 129.4 (enol form), 127.7 (enol form), 125.9, 125.3 (enol form), 124.1, 99.5 (enol form), 54.0, 53.0, 48.5, 48.0 (enol form), 47.2 (enol form), 46.0 (enol form), 44.4, 42.06, 42.03 (enol form), 39.80, 39.76 (enol form), 38.3 (enol form), 38.2, 35.60 (enol form), 35.56, 33.39, 33.37 (enol form), 30.2 (enol form), 29.7 (3 C), 27.4 (enol form), 27.3, 26.03, 25.93 (enol form), 22.49 (keto/enol), 17.83, 17.80 (enol form), 17.1 (keto/enol); HRMS (m/z): EI [M] calcd for $C_{23}H_{36}O_2S$ 376.2436; found 376.2435.

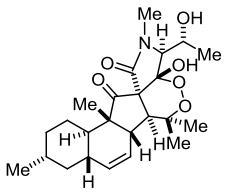


Ketoamide **61** was prepared according to the general procedure of aminolysis with **60** and *N*-methyl-L-threonine methyl ester **23**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **61** (110 mg, 75%) as colorless oil: R_f = 0.21 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -116.9 (*c* = 0.45 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.64 (enol form, OH), 5.37 (d, *J* = 9.6 Hz, 1H), 5.30 (ddd, *J* = 6.9, 4.6, 2.0 Hz, 1H), 4.91 – 4.80 (m, 1H), 4.64 (d, *J* = 6.1 Hz, 1H), 4.51 – 4.34 (m, 1H), 3.81 – 3.64 (m, 4H), 3.45 (dd, *J* = 16.7, 4.1 Hz, 1H), 3.07 – 2.90 (m, 3H), 2.84 (dd, *J* = 9.9, 4.7 Hz, 1H), 1.82 – 1.68 (m, 5H), 1.69 – 1,62 (m, 4H), 1.60 (s, 3H), 1.51 – 1.36 (m, 2H), 1.29 (d, *J* = 6.6 Hz, 3H), 1.21 – 0.98 (m, 3H), 0.98 – 0.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.7, 170.1, 169.0, 131.8, 129.9, 125.7, 124.3, 66.2, 64.0, 52.9, 52.2, 45.3, 44.6, 41.9, 39.9, 38.2, 35.7, 35.5, 33.3, 27.2, 25.8, 22.4, 19.7, 17.7, 17.6; HRMS (EI): Exact mass calcd for $C_{25}H_{39}NO_5[M]^+$: 433.2828; Found: 433.2829.



Derivative of (-)-equisetin **62**: To a solution of ketoamide **61** (50 mg, 0.12 mmol) in methanol (12 mL, 0.01M) at 0 ^{o}C was added sodium methoxide (19 mg, 0.36 mmol). After 1.5 h the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (60% ethyl acetate-petroleum ether) to give the pure **62** (32 mg, 70%, d.r. = 4:1) as pale red foam: R_f = 0.27 (60 % ethyl acetate-petroleum ether); $[a]_D^{21}$ = -182.4 (*c* = 0.28 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (s, 2H), 4.88 (s, 1H), 4.17 (s, 1H), 3.86 – 3.49 (m, 2H), 2.98 (s, 3H), 1.99 (s, 1H), 1.91 – 1.68 (m, 5H), 1.64 – 1.53 (m, 4H), 1.46 (s, 6H), 1.14 – 1.02 (m, 5H), 0.98 – 0.71 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 192.1, 177.2, 132.2, 129.2, 126.3, 124.4, 67.5, 66.6, 48.6, 42.3, 41.1, 39.9, 38.4, 35.7, 33.5, 29.7, 28.3, 27.4, 25.9, 22.5, 17.9, 17.6, 13.8. HRMS (EI): Exact mass calcd for $C_{24}H_{35}NO_4[M]^+$: 401.2566; Found: 401.2568.

1) **$Mn(OAc)_3$ method**



Peroxide **63**: A solution of **62** (18 mg, 0.045 mmol) in AcOH (4.5 mL, 0.01 M) was added Manganous acetate (6.2 mg, 0.022 mmol) at 25 ^{o}C. The resulting solution was stirred for a further 1 h. The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The mixture was filtered through short celite pad and washed with ethyl acetate (10 mL). The collected filtrate was concentrated and the residue was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **63** (18 mg, 93%) as colorless oil: R_f = 0.36 (40% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 115.2 (*c* = 0.43 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 10.2, 4.6, 2.4 Hz, 1H), 5.55 (d, *J* = 10.2 Hz, 1H), 4.82 (s, 1H), 4.54 – 4.28 (m, 1H), 4.01 (s, 1H), 3.07 (s, 3H), 3.02 (d, *J* = 2.0 Hz, 1H), 2.69 (d, *J* = 11.9 Hz, 1H), 2.61 (dd, *J* = 11.9, 4.6 Hz, 1H), 1.81 (d, *J* = 7.1 Hz, 3H), 1.71 (d, *J* = 13.0 Hz, 1H), 1.52 – 1.40 (m, 3H), 1.40 – 1.31 (m, 5H), 1.27 (s, 3H), 1.10 – 0.93 (m,

4H), 0.93 – 0.80 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.6, 169.3, 133.6, 126.0, 102.0, 79.1, 70.5, 63.7, 62.2, 52.5, 47.8, 45.1, 41.3, 37.7, 36.9, 35.2, 32.8, 31.2, 26.6, 25.5, 25.0, 23.6, 22.2, 14.5; ESI $[M+Na]^+$ calcd for $[C_{24}H_{35}NO_6Na]^+$ 456.24; found 456.39.

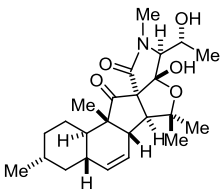
2) **CAN method:**

A solution of **62** (7.0 mg, 0.017 mmol) and ceric ammonium nitrate (9.6 mg, 0.017 mmol) in acetic acid (1.7 mL, 0.01 M) was stirred under oxygen atmosphere (1 atm) for 2 h. The solvent was removed under reduced pressure and ethyl acetate (5 mL) was added to the residue. The mixture was filtered through short celite pad and washed with ethyl acetate (10 mL). The collected filtrate was concentrated and the residue was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **63** (5.2 mg, 80%) as colorless oil: R_f = 0.36 (40% ethyl acetate–petroleum ether).

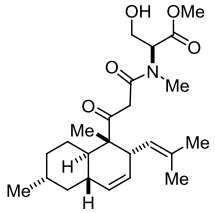
3) **$Ru(bpy)_3Cl_2$•$6H_2O$ method:**

To a solution of **62** (6.2 mg, 0.015 mmol) in acetonitrile (1.5 mL, 0.01 M) was added $Ru(bpy)_3Cl_2$•$6H_2O$ [tris(2,2'-bipyridyl) ruthenium(II) chloride hexahydrate] (17.0 mg, 0.023 mmol) and triethylamine (9.0 μL, 0.060 mmol) at 25 ^oC. The mixture was stirred and irradiated with a 23 W household compact fluorescence lamp at 25 ^oC for 7 hours under 1 atm air. (The distance between the lamp and the reaction bottle is about 10 cm). The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The organic phase was washed with water (5 mL × 2) , brine (5 mL), and dried over anhydrous sodium sulfate, filtered, concentrated, and purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give the pure **63** (2.3 mg, 34%) as colorless oil: R_f = 0.36 (40% ethyl acetate–petroleum ether).

Derivative (+)-fusarisetin A **64**: To a solution of peroxide **63** (13 mg, 0.028 mmol) in acetonitrile (2.8 mL, 0.01M) was added trimethyl phosphite (98 μL, 0.83 mmol). The

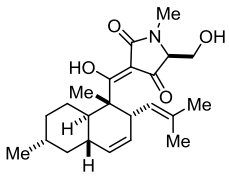


solution was heated to 80 °C for 1 h. The solvent was removed under reduced pressure. The crude product was purified by preparative TLC on silica gel (40% ethyl acetate-petroleum ether) to give **64** (12 mg, 92%) as colorless solid: R_f = 0.22 (40% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 68.6 (*c* = 0.53 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (ddd, *J* = 10.0, 4.7, 2.4 Hz, 1H), 5.54 (d, *J* = 10.0 Hz, 1H), 4.34 – 4.24 (m, 1H), 3.91 (s, 1H), 3.82 – 3.64 (m, 1H), 3.45 (d, *J* = 2.0 Hz, 1H), 3.01 (s, 3H), 2.89 (d, *J* = 10.9 Hz, 1H), 2.59 (dd, *J* = 10.9, 4.7 Hz, 1H), 1.82 (d, *J* = 11.2 Hz, 2H), 1.77 – 1.58 (m, 3H), 1.58 – 1.44 (m, 4H), 1.39 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 15.0 Hz, 3H), 1.09 – 1.00 (m, 2H), 0.97 (s, 3H), 0.94 – 0.80 (m, 4H);^{13}C NMR (101 MHz, $CDCl_3$) δ 213.6, 170.4, 132.9, 125.0, 108.8, 86.7, 74.9, 73.2, 65.3, 59.7, 54.8, 45.2, 41.5, 37.0, 36.5, 35.1, 32.9, 31.42, 31.38, 25.5, 25.2, 22.3, 21.2, 14.0; ESI $[M-H]^-$ calcd for $[C_{24}H_{34}NO_5]^-$ 417.25; found 416.49.

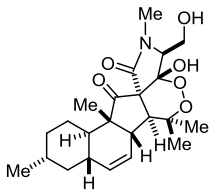


Ketoamide **S1** was prepared according to the general procedure of aminolysis with **60** *N*-methyl-L-serine methyl ester **S4**, which was purified by silica gel column chromatography (10% to 40% ethyl acetate-petroleum ether) to give **S1** (118 mg, 82%) as colorless oil: R_f = 0.21 (40% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -69.8 (*c* = 0.68 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.53(enol form, OH), 5.37 (d, *J* = 9.8 Hz, 1H), 5.30 (dd, *J* = 9.8, 2.5 Hz, 1H), 4.96 – 4.80 (m, 1H), 4.67 (t, *J* = 6.6 Hz, 1H), 4.08 – 3.84 (m, 2H), 3.82 – 3.63 (m, 4H), 3.44 (d, *J* = 16.9 Hz, 1H), 2.96 – 2.77 (m, 4H), 1.82 – 1.68 (m, 5H), 1.64 (s, 3H), 1.60 (s, 3H), 1.53 – 1.38 (m, 1H), 1.33 – 1.17 (m, 3H), 1.15 – 0.91 (m, 2H), 0.94 – 0.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.9, 169.8, 168.6, 131.8, 129.9, 125.6, 124.3, 61.3, 59.9, 52.9, 52.2, 45.3, 44.5, 41.9, 39.92, 39.88, 38.2, 35.5, 33.3, 27.2, 25.8, 22.4, 17.7, 17.6; HRMS (EI): Exact mass calcd for $C_{24}H_{37}NO_5[M]^+$: 419.2672; Found: 419.2676.

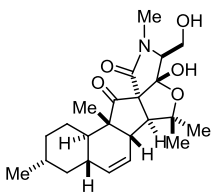
Derivative of (-)-equisetin **65**: To a solution of ketoamide **S1** (68 mg, 0.16 mmol) in methanol (16 mL, 0.01M) at 0 °C was added sodium methoxide (26 mg, 0.48 mmol).



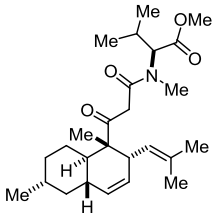
After 1.5 h the reaction was quenched by the addition of 1 N HCl (1 mL). The mixture was then partitioned between brine (10 mL) and CH_2Cl_2 (25 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (60% ethyl acetate-petroleum ether) to give the pure **65** (32 mg, 51%, d.r. = 1.5:1) as pale red foam: R_f = 0.13 (60 % ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (s, 2H), 4.90 (s, *J* = 8.5 Hz, 1H), 3.99 (d, *J* = 8.9 Hz, 1H), 3.89 (s, 1H), 3.63 (d, *J* = 7.5 Hz, 1H), 3.56 (s, 1H), 3.03 (s, 3H), 1.97 (s, 1H), 1.92 – 1.68 (m, 4H), 1.67 – 1.35 (m, 10H), 1.19 – 1.02 (m, 2H), 0.98 – 0.81 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 190.6, 177.1, 132.1, 129.2, 126.4, 124.6, 99.6, 66.7, 60.3, 48.5, 42.3, 41.2, 34.0, 38.4, 35.7, 33.5, 28.3, 27.3, 25.9, 22.5, 17.9, 14.0.



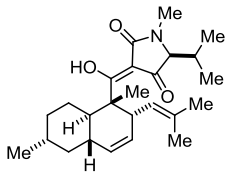
Peroxide **66**: A solution of **65** (40 mg, 0.10 mmol) in AcOH (10 mL, 0.01 M) was added Manganous acetate (20 mg, 0.08 mmol) at 25 ^{o}C. The resulting solution was stirred for a further 4 h. The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The mixture was filtered through short celite pad and washed with ethyl acetate (10 mL). The collected filtrate was concentrated and the residue was purified by preparative TLC on silica gel (60% ethyl acetate-petroleum ether) to give the pure **66** (23 mg, 54%) as colorless oil: R_f = 0.33 (60% ethyl acetate–petroleum ether); $[a]_D^{21}$ =139.8 (*c* = 0.40 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 – 5.72 (m, 1H), 5.55 (d, *J* = 10.4 Hz, 1H), 4.36 – 4.19 (m, 1H), 3.99 (dd, *J* = 10.4, 3.1 Hz, 1H), 3.26 (dd, *J* = 8.9, 3.2 Hz, 1H), 2.97 (s, 3H), 2.66 (s, 2H), 1.81 (d, *J* = 10.8 Hz, 2H), 1.71 (d, *J* = 12.8 Hz, 1H), 1.50 – 1.39 (m, 3H), 1.39 – 1.32 (m, 3H), 1.29 (s, 3H), 1.09 – 0.96 (m, 4H), 0.93 – 0.83 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.6, 169.8, 133.5, 126.2, 101.7, 78.8, 65.81, 62.8, 59.3, 52.1, 47.6, 45.0, 41.3, 37.9, 36.9, 35.2, 32.8, 29.2, 26.6, 25.6, 25.0, 22.2, 14.5; ESI $[M+Na]^+$ calcd for $[C_{23}H_{33}NO_6Na]^+$ 442.22; found 442.18.



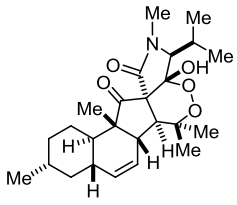
Derivative (+)-fusarisetin A **67**: To a solution of peroxide **66** (15 mg, 0.036 mmol) in acetonitrile (4 mL, 0.01 M) was added trimethyl phosphite (127 μL, 1.07 mmol). The solution was heated to 80 ^{o}C for 2 hours. The solvent was removed under reduced pressure. The crude product was purified by preparative TLC on silica gel (40% ethyl acetate-petroleum ether) to give **67** (8 mg, 55%) as colorless solid: R_f = 0.13 (40% ethyl acetate–petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ5.75 (ddd, *J* = 9.3, 4.5, 2.4 Hz, 1H), 5.54 (d, *J* = 9.3 Hz, 1H), 4.05 – 3.84 (m, 2H), 3.61 – 3.46 (m, 1H), 3.10 (s, 1H), 2.94 (s, 3H), 2.92 – 2.79 (m, 1H), 2.60 (dd, *J* = 10.9, 4.5 Hz, 1H), 1.89 – 1.78 (m, 2H), 1.72 (d, *J* = 12.7 Hz, 1H), 1.68 – 1.57 (m, 2H), 1.54 (s, 2H), 1.52 – 1.39 (m, 3H), 1.18 (s, 2H), 1.13 – 0.95 (m, 4H), 0.95 – 0.77 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.0, 170.1, 132.9, 125.1, 108.6, 86.8, 75.3, 68.9, 59.2, 59.1, 54.7, 45.2, 41.5, 37.0, 36.5, 35.1, 32.9, 31.5, 28.9, 25.4, 25.3, 22.3, 13.9; HRMS (EI): Exact mass calcd for $C_{23}H_{33}NO_5[M]^+$: 403.2359; Found: 403.2362.



Ketoamide **S2** was prepared according to the general procedure of aminolysis with **60** and *N*-methyl-L-valine methyl ester **28**, which was purified by silica gel column chromatography (5% to 10% ethyl acetate-petroleum ether) to give **S2** (32 mg, 76%) as colorless oil: R_f = 0.47 (20% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -149.2 (*c* = 0.81 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.82 (enol form, OH), 5.37 (d, *J* = 9.7 Hz, 1H), 5.34 – 5.25 (m, 1H), 4.97 – 4.81 (m, 2H), 3.77 – 3.64 (m, 4H), 3.43 – 3.30 (m, 1H), 3.05 – 2.73 (m, 4H), 2.34 (s, 1H), 2.30 – 2.03 (m, 1H), 1.74 (t, *J* = 15.1 Hz, 5H), 1.68 – 1.56 (m, 6H), 1.53 – 1.40 (m, 1H), 1.30 – 1.18 (m, 3H), 1.15 – 1.02 (m, 2H), 1.02 – 0.94 (m, 3H), 0.95 – 0.90 (m, 3H), 0.88 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 171.5, 168.5, 131.8, 129.9, 125.9, 124.4, 61.2, 53.0, 51.7, 45.5, 44.6, 41.9, 40.0, 38.2, 35.5, 33.3, 31.4, 27.4, 27.2, 25.8, 22.4, 19.6, 18.8, 17.7, 17.4; HRMS (EI): Exact mass calcd for $C_{26}H_{41}NO_4[M]^+$: 431.3036; Found: 431.3038.

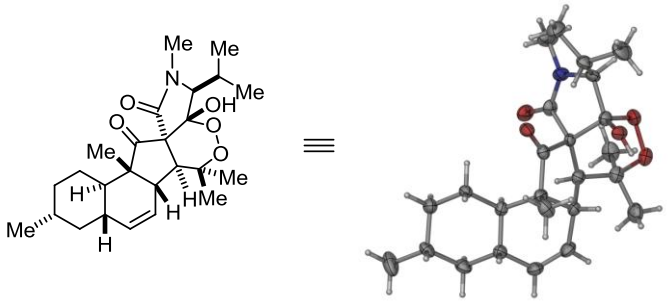


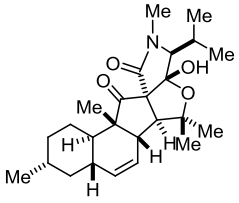
Derivative of (-)-equisetin **68**: To a solution of ketoamide **S2** (61 mg, 0.14 mmol) in methanol (14 mL, 0.01 M) at 10 ^{o}C was added sodium methoxide (38 mg, 0.70 mmol). After 10 h the reaction was quenched by the addition of 1 N HCl (1 mL). The mixture was then partitioned between brine (5 mL) and CH_2Cl_2 (10 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 10 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel (10% ethyl acetate-petroleum ether) to give inseparable **68** (47 mg, 84%, d.r. = 3:1) as pale red foam: R_f = 0.50 (10 % ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 – 5.22 (m, 2H), 5.03 – 4.75 (m, 1H), 3.98 (d, *J* = 9.5 Hz, isomer), 3.88 – 3.59 (m, 1H), 3.39 (d, *J* = 2.2 Hz, 1H), 2.99 (s, 1H), 2.89 (s, isomer), 2.31 – 2.17 (m, 1H), 2.10 – 1.92 (m, 1H), 1.90 – 1.66 (m, 4H), 1.56 (s, 3H), 1.50 (d, *J* = 12.4 Hz, 3H), 1.44 (s, 4H), 1.18 – 0.99 (m, 5H), 0.89 (t, *J* = 10.2 Hz, 6H), 0.79 (d, *J* = 7.0 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 191.6, 176.5, 131.9, 129.1, 126.7, 124.6, 70.3, 66.1, 48.2, 42.3, 41.2, 39.9, 38.4, 35.7, 33.5, 29.3 28.3, 27.7, 25.9, 22.5, 17.9, 17.2, 17.0, 13.6. HRMS (EI): Exact mass calcd for $C_{25}H_{37}NO_3[M]^+$: 399.2773; Found: 399.2776.



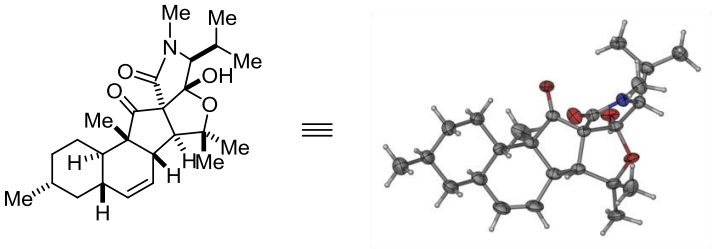
Peroxide **69**: A solution of **50** (22 mg, 0.055 mmol) in AcOH (5.5 mL, 0.01 M) was added Manganous acetate (15 mg, 0.055 mmol) at 25 ^{o}C. The resulting solution was stirred for a further 20 min. The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The mixture was filtered through short celite pad and washed with ethyl acetate (10 mL). The collected filtrate was concentrated and the residue was purified by silica gel column chromatography (10% to 20% ethyl acetate-petroleum ether) to give **69** (18 mg, 94%) as colorless oil: R_f = 0.46 (20% ethyl acetate–petroleum ether); $[a]_D^{21}$ =139.7 (*c* = 0.49 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 10.2, 4.0, 2.4 Hz, 1H), 5.54 (d, *J* = 10.2 Hz, 1H), 3.18 – 3.10 (m, 1H), 3.00 (s, 3H), 2.73 – 2.67 (m, 1H), 2.65 (s, 1H), 2.64 – 2.54 (m, 2H), 1.80 (d, *J* = 10.8 Hz, 2H), 1.70 (d, *J* = 12.8 Hz, 1H), 1.53 (dd, *J* = 12.7, 2.9 Hz,

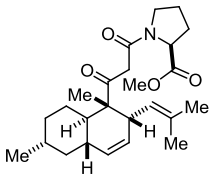
1H), 1.46 – 1.32 (m, 5H), 1.24 (d, *J* = 8.0 Hz, 3H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.08 – 0.95 (m, 8H), 0.94 – 0.79 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.0, 170.3, 133.5, 126.2, 102.7, 79.2, 72.5, 62.4, 51.8, 47.2, 45.3, 41.3, 38.1, 37.0, 35.2, 33.5, 32.8, 29.8, 26.6, 25.7, 25.0, 22.9, 22.3, 20.2, 14.7; HRMS (EI): Exact mass calcd for $C_{25}H_{37}NO_5$ $[M]^+$: 431.2672; Found: 431.2671. Recrystallization of **69** from chloroform–hexanes gave single crystals suitable for X-ray analysis (CCDC: 1000588).



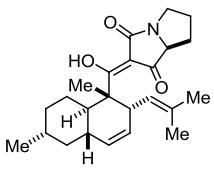


Derivative (+)-fusarisetin A **70**: To a solution of peroxide **69** (18 mg, 0.042 mmol) in acetonitrile (4.2 mL, 0.01 M) was added trimethyl phosphite (152 μL, 1.26 mmol). The solution was heated to 80 ^{o}C for 3 hours. The solvent was removed under reduced pressure. The crude product was purified by preparative TLC on silica gel (40% ethyl acetate-petroleum ether) to give **70** (13 mg, 76%) as colorless solid: R_f = 0.21 (20% ethyl acetate–petroleum ether); $[a]_D^{21}$ =123.4 (*c* = 0.23 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 (ddd, *J* = 10.0, 4.7, 2.5 Hz, 1H), 5.53 (d, *J* = 10.0 Hz, 1H), 3.23 (d, *J* = 5.5 Hz, 1H), 2.94 (s, 3H), 2.85 (d, *J* = 11.0 Hz, 1H), 2.54 (dd, *J* = 11.0, 4.7 Hz, 1H), 2.41 (s, 1H), 2.30 – 2.19 (m, 1H), 1.82 (t, *J* = 12.4 Hz, 2H), 1.71 (d, *J* = 12.4 Hz, 1H), 1.65 – 1.54 (m, 2H), 1.54 – 1.49 (m, 3H), 1.48 – 1.37 (m, 1H), 1.14 (s, 3H), 1.09 (t, *J* = 6.6 Hz, 6H), 1.06 – 0.93 (m, 5H), 0.93 – 0.84 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.3, 170.7, 133.0, 125.1, 109.4, 86.4, 75.7, 75.0, 59.6, 54.2, 45.3, 41.5, 37.2, 36.5, 35.1, 32.9, 31.7, 31.0, 29.2, 25.4, 25.2, 22.3, 21.0, 18.7, 14.2; HRMS (EI): Exact mass calcd for $C_{25}H_{37}NO_4$ $[M]^+$: 415.2723; Found: 415.2721. Recrystallization of **70** from chloroform–hexanes gave single crystals suitable for X-ray analysis (CCDC: 1000589).



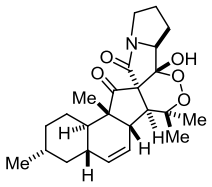


Ketoamide **S3** was prepared according to the general procedure of aminolysis with **60** and *N*-methyl-L-proline methyl ester **29**, which was purified by silica gel column chromatography (10% to 30% ethyl acetate-petroleum ether) to give **S3** (70 mg, 80%) as colorless oil: R_f = 0.24 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = -134.9 (*c* = 0.30 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.44 (enol form, OH), 5.38 (d, *J* = 10.1 Hz, 1H), 5.34 – 5.26 (m, 1H), 5.04 (s, enol form), 4.87 (d, *J* = 10.1 Hz, 1H), 4.50 (dd, *J* = 8.6, 3.7 Hz, 1H), 4.40 – 4.27 (m, enol form), 3.76 – 3.63 (m, *J* = 3.5 Hz, 4H), 3.63 – 3.50 (m, 2H), 3.46 – 3.31 (m, 1H), 3.26 (d, *J* = 16.0 Hz, enol form), 2.89 – 2.73 (m, 1H), 2.35 – 2.12 (m, 2H), 2.12 – 1.88 (m, 3H), 1.83 – 1.69 (m, 6H), 1.69 – 1.55 (m, 3H), 1.55 – 1.42 (m, 1H), 1.35 – 1.17 (m, 3H), 1.15 – 0.95 (m, 3H), 0.94 – 0.85 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.1, 172.6, 166.2, 131.8, 129.8, 126.1, 124.4, 58.7, 53.2, 52.2, 47.4, 46.7, 44.6, 41.9, 40.1, 38.3, 35.6, 33.4, 29.4, 27.2, 25.9, 24.8, 22.4, 17.8, 17.2; HRMS (EI): Exact mass calcd for $C_{25}H_{37}NO_4[M]^+$: 415.2723; Found: 415.2725.

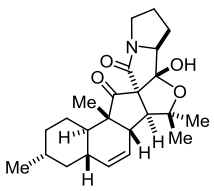


Derivative of (-)-equisetin **71**: To a solution of ketoamide **S3** (37 mg, 0.089 mmol) in methanol (9 mL, 0.01M) at 60 ^{o}C was added sodium methoxide (24 mg, 0.45 mmol). After 3 h the reaction was quenched by the addition of 1 N HCl (1 mL) at 25 ^{o}C. The mixture was then partitioned between brine (5 mL) and CH_2Cl_2 (10 mL), and the aqueous phase was extracted with CH_2Cl_2 (5 × 5 mL). The combined organic portions were dried over Na_2SO_4 After filtration and evaporation of the solvent, the residue so obtained was purified by preparative TLC on silica gel 10% ethyl acetate-petroleum ether) to give inseparable **71** (17 mg, 68%, d.r. = 1.3 :1) as pale red foam: R_f = 0.45

(30 % ethyl acetate-petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (s, 2H), 4.88 (s, 1H), 4.11 (s, isomer), 3.85 (s, 1H), 3.66 (s, 1H), 3.24 (s, 1H), 2.37 – 2.00 (m, 3H), 2.00 – 1.66 (m, 5H), 1.65 – 1.36 (m, 11H), 1.18 – 1.01 (m, 2H), 0.98 – 0.87 (m, 4H); HRMS (EI): Exact mass calcd for $C_{24}H_{33}NO_3[M]^+$: 383.2460; Found: 383.2459.

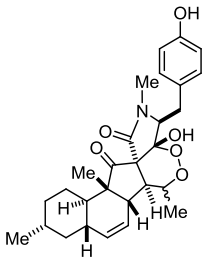


Peroxide **72**: A solution of **71** (7.5 mg, 0.02 mmol) in AcOH (2 mL, 0.01 M) was added Manganous acetate (2.7 mg, 0.01 mmol) at 25 ^{o}C. The resulting solution was stirred for a further 1 h. The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The mixture was filtered through short celite pad and washed with ethyl acetate (10 mL). The collected filtrate was concentrated and the residue was purified by silica gel column chromatography (10% to 20% ethyl acetate-petroleum ether) to give **72** (7 mg, 99%) as colorless oil: R_f = 0.31 (20% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 15.4 (*c* = 0.2 in C HCl$_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (d, *J* = 10.4 Hz, 1H), 5.55 (d, *J* = 10.4 Hz, 1H), 3.88 (ddd, *J* = 11.5, 8.6, 6.8 Hz, 1H), 3.48 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.22 (s, 1H), 3.14 (ddd, *J* = 11.5, 9.7, 4.7 Hz, 1H), 2.60 (s, 2H), 2.44 – 2.30 (m, 1H), 2.27 – 2.15 (m, 1H), 2.06 – 1.87 (m, 1H), 1.87 – 1.75 (m, 3H), 1.75 – 1.60 (m, 2H), 1.56 – 1.43 (m, 2H), 1.39 (d, *J* = 10.4 Hz, 6H), 1.10 – 0.94 (m, 5H), 0.94 – 0.77 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.2, 173.4, 133.6, 126.2, 100.4, 79.0, 68.0, 65.2, 52.2, 48.2, 45.3, 44.1, 41.3, 37.7, 36.8, 35.2, 32.8, 26.6, 25.4, 25.0, 24.8, 24.4, 22.3, 14.5; HRMS (EI): Exact mass calcd for $C_{24}H_{33}NO_5[M]^+$: 415.2359; Found: 415.2356.

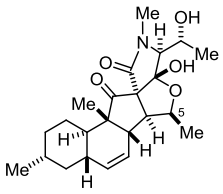


Derivative (+)-fusarisetin A **73**: To a solution of peroxide **72** (12 mg, 0.029 mmol) in acetonitrile (3 mL, 0.01 M) was added trimethyl phosphite (102 μL, 0.87 mmol). The solution was heated to 80 ^{o}C for 2.5 hours. The solvent was removed under reduced pressure. The crude product was purified by preparative TLC on silica gel (30% ethyl acetate-petroleum ether) to give **73** (9 mg, 82%) as colorless solid. R_f = 0.14 (20% ethyl acetate–petroleum ether), $[a]_D^{21}$ =58.1 (*c* = 0.37 in $CHCl_3$); ^{1}H NMR (400 MHz,

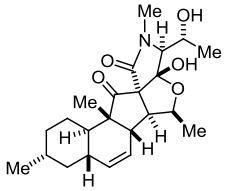
$CDCl_3$) δ 5.75 (ddd, *J* = 10.0, 4.7, 2.5 Hz, 1H), 5.54 (d, *J* = 10.0 Hz, 1H), 3.87 (dt, *J* = 11.8, 8.4 Hz, 1H), 3.72 (dd, *J* = 10.7, 5.8 Hz, 1H), 3.25 – 3.01 (m, 1H), 2.80 (d, *J* = 10.7 Hz, 1H), 2.64 (s, 1H), 2.50 (dd, *J* = 10.7, 4.6 Hz, 1H), 2.28 – 2.08 (m, 1H), 1.99 – 1.78 (m, 4H), 1.78 – 1.69 (m, 2H), 1.69 – 1.57 (m, 2H), 1.52 (s, 3H), 1.44 (s, 1H), 1.31 (s, 3H), 1.14 – 0.99 (m, 2H), 0.96 (s, 3H), 0.94 – 0.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.6, 173.6, 133.0, 125.1, 108.3, 86.6, 71.8, 59.1, 54.3, 45.3, 43.3, 41.5, 37.0, 36.5, 35.1, 32.9, 30.9, 26.7, 26.2, 25.4, 25.3, 24.7, 22.3, 13.9; HRMS (EI): Exact mass calcd for $C_{24}H_{33}NO_4[M]^+$: 399.2410; Found: 399.2408.



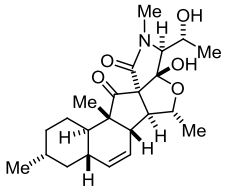
Peroxide **74** and **74′**: A solution of **53** (31 mg, 0.069 mmol) in CH_3CN (7 mL, 0.01 M)) was added Methylene blue (4.4 mg, 0.014 mmol) and triethylamine (38 µL, 0.28 mmol) at 30 ^oC. The resulting solution was stirred for a further 2 h. The solvent was removed under reduced pressure and ethyl acetate (10 mL) was added to the residue. The mixture was filtered through short celite pad and washed with ethyl acetate (10 mL). The collected filtrate was concentrated and the residue was purified by TLC chromatography (30% ethyl acetate-petroleum ether) to give a mixture of **74** and **74′** (12 mg, 53%, dr = 2.0 : 1.0*) as colorless oil: R_f = 0.23 (40% ethyl acetate–petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (**74**, major; **74′***, minor, d, *J* = 8.3 Hz, 2H), 6.76 (d, *J* = 8.3 Hz, 2H), 5.84 – 5.70 (m, 1H), 5.55 (dd, *J* = 18.2, 10.2 Hz, 1H), 4.45 (m, 1H), 3.35 (t, *J* = 7.1 Hz, 1H), 3.27 – 3.12 (m, 2H), 2.83 – 2.60 (m, 4H), 1.83 (dd, *J* = 22.6, 11.5 Hz, 3H), 1.75 – 1.53 (m, 3H), 1.51 – 1.36 (m, 2H), 1.33 (dd, *J* = 10.2, 6.5 Hz, 3H), 1.08 – 1.01 (m, 4H), 0.94 – 0.84 (d, *J* = 6.5 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.9*, 212.2, 169.9*, 168.9, 155.1, 133.7*, 133.2, 130.3, 129.0, 128.9*, 126.1, 123.6*, 116.0, 102.8, 102.3*, 76.0, 74.6*, 68.0*, 67.8, 63.5, 60.1*, 52.1, 51.0*, 46.1*, 44.3, 43.7*, 43.4, 41.6*, 41.5, 38.5, 38.4*, 37.0, 36.9*, 35.2, 35.1*, 35.0*, 34.8, 32.8, 30.2, 30.1*, 25.1, 25.0*, 22.3, 20.0*, 17.1, 15.2*, 14.73. ESI $[M-H]^-$ calcd for $[C_{28}H_{34}NO_6]^-$ 480.25; found 480.29.



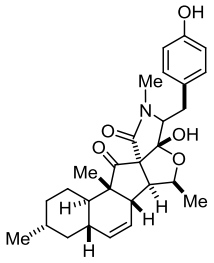
Derivative (+)-fusarisetin A **75** and derivative C_5-*epi*-fusarisetin A **76**: To a solution of inseparable mixture of peroxide **54** and peroxide **54′** (dr = 1.5:1) (9 mg, 0.024 mmol) in acetonitrile (2.4 mL, 0.01 M) was added trimethyl phosphite (85 μL, 0.71 mmol, 30 equiv.). The solution was heated to 80 ^{o}C for 2 hours. The solvent was removed under reduced pressure. The crude product was purified by preparative TLC on silica gel (40% ethyl acetate-petroleum ether) to give **75** (4.1 mg, 48%) and **76** (2.1 mg, 25%) as colorless solid.



Derivative (+)-fusarisetin A **75**: R_f = 0.11 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ = 60.8 (*c* = 0.50 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 (ddd, *J* = 10.0, 4.8, 2.5 Hz, 1H), 5.53 (d, *J* = 10.0 Hz, 1H), 4.46 – 4.26 (m, 2H), 4.15 (s, 1H), 3.55 (d, *J* = 2.7 Hz, 1H), 3.44 (br, 1H), 2.97 (s, 3H), 2.94 (d, *J* = 5.7 Hz, 1H), 2.56 (dd, *J* = 11.0, 4.7 Hz, 1H), 1.90 – 1.77 (m, 2H), 1.77 – 1.69 (m, 2H), 1.68 – 1.51 (m, 2H), 1.45 (d, *J* = 6.7 Hz, 3H), 1.39 (d, *J* = 6.7 Hz, 3H), 1.16 – 0.93 (m, 5H), 0.93 – 0.74 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.1, 169.8, 132.9, 125.0, 108.9, 78.2, 74.4, 72.5, 65.9, 55.0, 54.2, 43.3, 41.7, 37.5, 36.5, 35.1, 32.9, 30.7, 25.2, 22.3, 20.1, 17.0, 14.0; ESI $[M+H]^+$ calcd for $[C_{23}H_{33}NO_5H]^+$ 404.24; found 404.22.



Derivative (+)-fusarisetin A **76**: R_f = 0.15 (30% ethyl acetate–petroleum ether); $[a]_D^{21}$ =68.8 (*c* =0.39 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (ddd, *J* = 9.7, 4.8, 2.3 Hz, 1H), 5.52 (d, *J* = 9.7 Hz, 1H), 4.58 – 4.50 (m, 1H), 4.31 (d, *J* = 7.6 Hz, 2H), 3.95 (s, 1H), 3.43 (s, 1H), 3.00 (s, 3H), 2.74 (dd, *J* = 10.0, 3.9 Hz, 1H), 2.36 (dd, *J* = 10.0, 4.7 Hz, 1H), 1.78 (dt, *J* = 40.4, 11.0 Hz, 4H), 1.50 – 1.36 (m, 4H), 1.23 (d, *J* = 6.3 Hz, 4H), 1.11 – 0.99 (m, 2H), 0.96 (s, 3H), 0.93 – 0.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.9, 170.0, 132.5, 124.4, 109.3, 83.6, 74.4, 72.0, 65.1, 58.4, 55.6, 50.2, 41.6, 36.7, 36.4, 35.1, 32.9, 31.6, 25.3, 22.3, 22.3, 21.5, 14.1; ESI $[M+K]^+$ calcd for $[C_{23}H_{33}NO_5K]^+$ 442.20; found 442.17.



Derivative (+)-fusarisetin A **77**: To a solution of inseparable mixture of peroxide **74** and peroxide **74′** (d.r. = 1.5:1) (15 mg, 0.03 mmol) in acetonitrile (3 mL) was added trimethyl phosphite (111 μL, 0.9 mmol). The solution was heated to 80 ^{o}C for 1 hours. The solvent was removed under reduced pressure. The crude product was purified by preparative TLC on silica gel (40% ethyl acetate-petroleum ether) to give **77** (9.5 mg, 66 %) as colorless solid: R_f = 0.32 (40% acetate-petroleum ether); $[a]_D^{21}$ = 85.8 (*c* =0.10 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 2H), 5.70 (ddd, *J* = 10.0, 4.6, 2.4 Hz, 1H), 5.52 (d, *J* = 10.0 Hz, 1H), 4.59 – 4.36 (m, 1H), 3.88 – 3.62 (m, 1H), 3.16 – 2.92 (m, 3H), 2.72 (s, 3H), 2.61 (dd, *J* = 11.0, 4.7 Hz, 2H), 1.91 – 1.77 (m, 2H), 1.71 (d, *J* = 12.6 Hz, 1H), 1.65 – 1.52 (m, 3H), 1.43 (d, *J* = 6.5 Hz, 4H), 1.17 – 0.94 (m, 5H), 0.92 – 0.85 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.5, 169.1, 154.6, 132.8, 130.4, 129.7, 125.2, 115.8, 108.9, 79.3, 75.0, 70.2, 54.2, 54.0, 43.5, 41.7, 37.4, 36.6, 35.7, 35.1, 33.0, 29.7, 25.3, 22.3, 17.6, 14.0; HRMS (EI): Exact mass calcd for $C_{28}H_{35}NO_5[M]^+$: 465.2515; Found: 465.2518.

Biological studies of derivatives of cryptocin, equisetin and fusarisetin A

Cell line and Cell culture

The high metastatic MDA-MB-231 breast cancer cells were purchased from American Type Culture Collection (Manassas, VA) and cultured in L-15 medium (Life Technologies Inc Gibco/Brl Division, Grand Island, NY) supplemented with 10% fetal bovine serum (FBS; Gibco/Brl Division) . MDA-MB-231 cells were incubated at 37 ℃ under a humidified 95%: 5% (v/v) mixture of air and CO_2.

Cell viability assay

MDA-MB-231 cells were seeded in 96-well plates at a density of 5×10^3 cells per well and treated with indicated concentrations of different compounds for 48 h. Cell

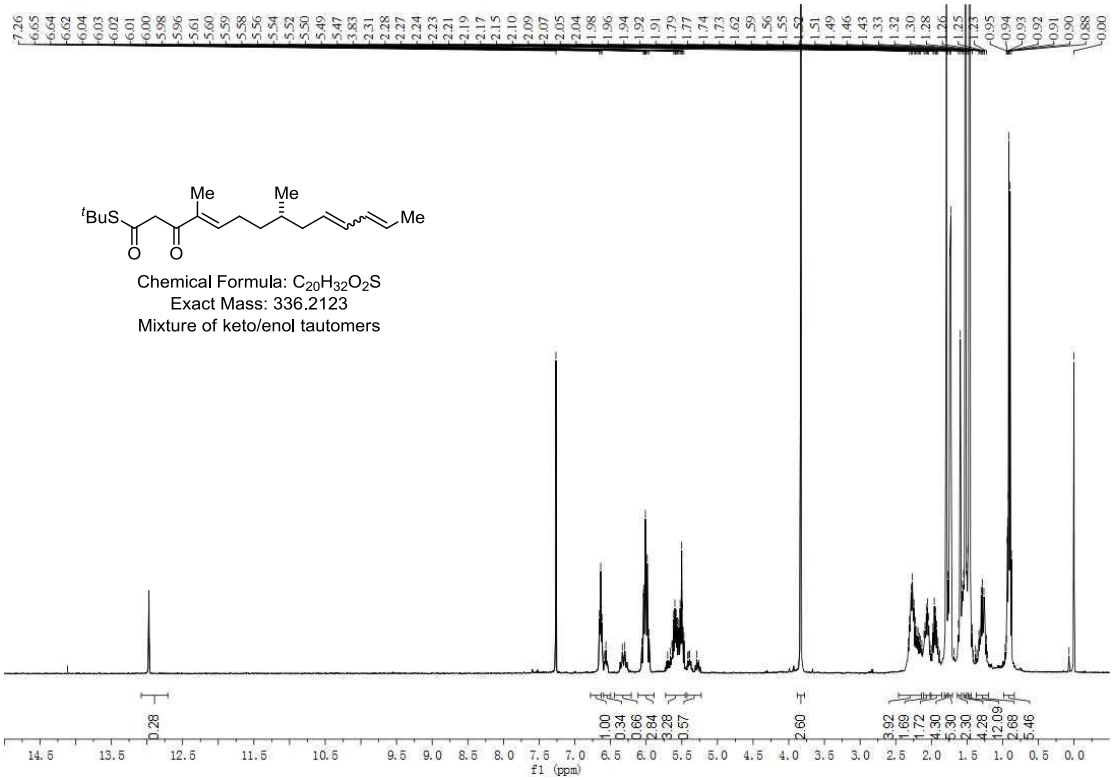
viability was determined by MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetr azolium, inner salt] (Promega, Madison, WI) method, as described previously (Pang X, et al. 2009). Half-inhibitory concentration (IC_{50}) values were calculated by Origin software (Version 8.0; OriginLab Corporation, Northampton, MA).

Cell migration assay

Boyden chamber migration assay was performed as previously described (Fang Y, et al. 2013). The cells were starved and pre-incubated with indicated concentrations of different compounds at 37 ℃ for 1 h. A total of 5×10^4 cells in 100 μL were seeded on the upper chamber and 500 μL of medium supplemented with FBS was added in the lower chamber as a chemo-attractant. Cells were then incubated for additional 18-20 h. Non-migrated cells were removed with a cotton swab. Those migrated cells on the lower surface of the membrane were fixed in 4% paraformaldehyde, stained with 0.5% crystal and counted under an inverted microscope (Olympus, Center Valley, PA; magnification, ×100).

Reference:

1. a) J. Xu, E. J. E. Caro-Diaz, L. Trzoss, E. A. Theodorakis, *J. Am. Chem. Soc.* **2012**, *134*, 5072–5075; b) J. Xu, E. J. E. Caro-Diaz, M. H. Lacoske, C.-I. Hung, C. Jamora, E. A. Theodorakis, *Chem. Sci.*, **2012**, *3*, 3378–3386;
2. Burke, L. T., Dixon, D. J. Ley, S. V. & Rodr ǵuez, F. *Org. Biomol. Chem.* **2005**, *3*, 724.
3. N. R. Cichowicz, P. Nagorny, *Org. Lett.* **2012**, *14*, 1058–1061.
4. For preparation of amino acids **23**, **28-31,** see: White, K. N.; Konopelski, J. P. *Org. Lett*. **2005**, *7*, 41.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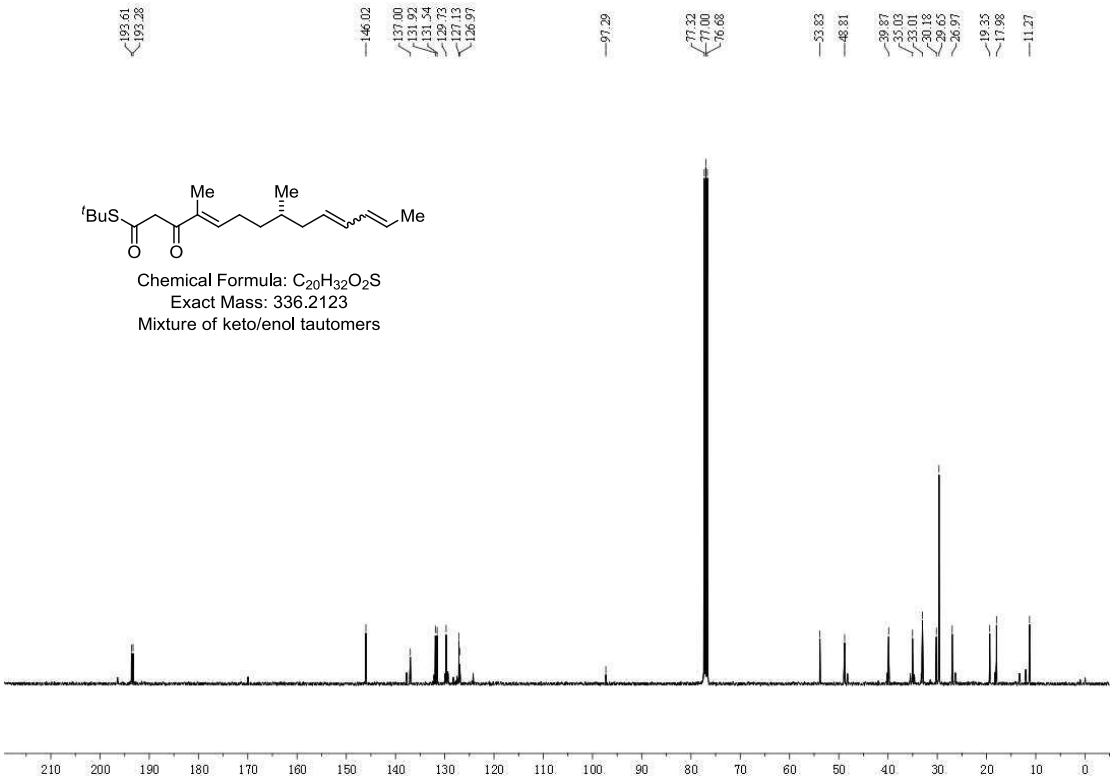
tBuS
Me
O
O
Chemical Formula: C20H32O2S
Exact Mass: 336.2123
Mixture of keto/enol tautomers
f1 (ppm)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tBuS
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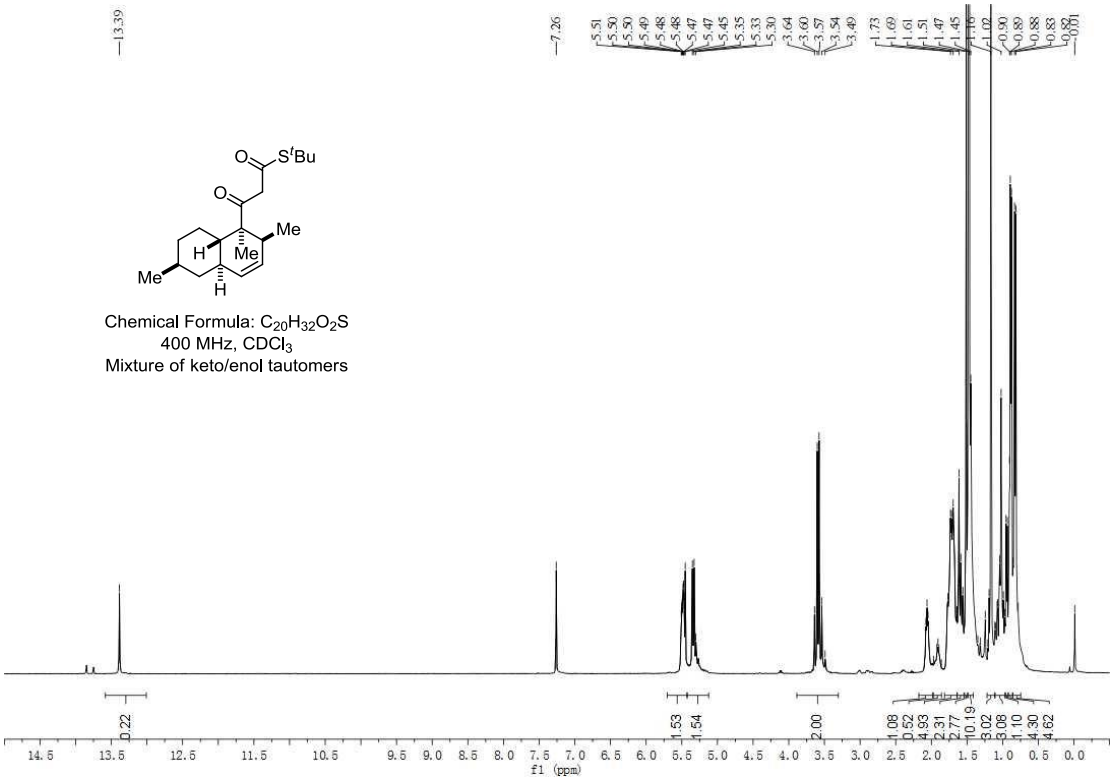
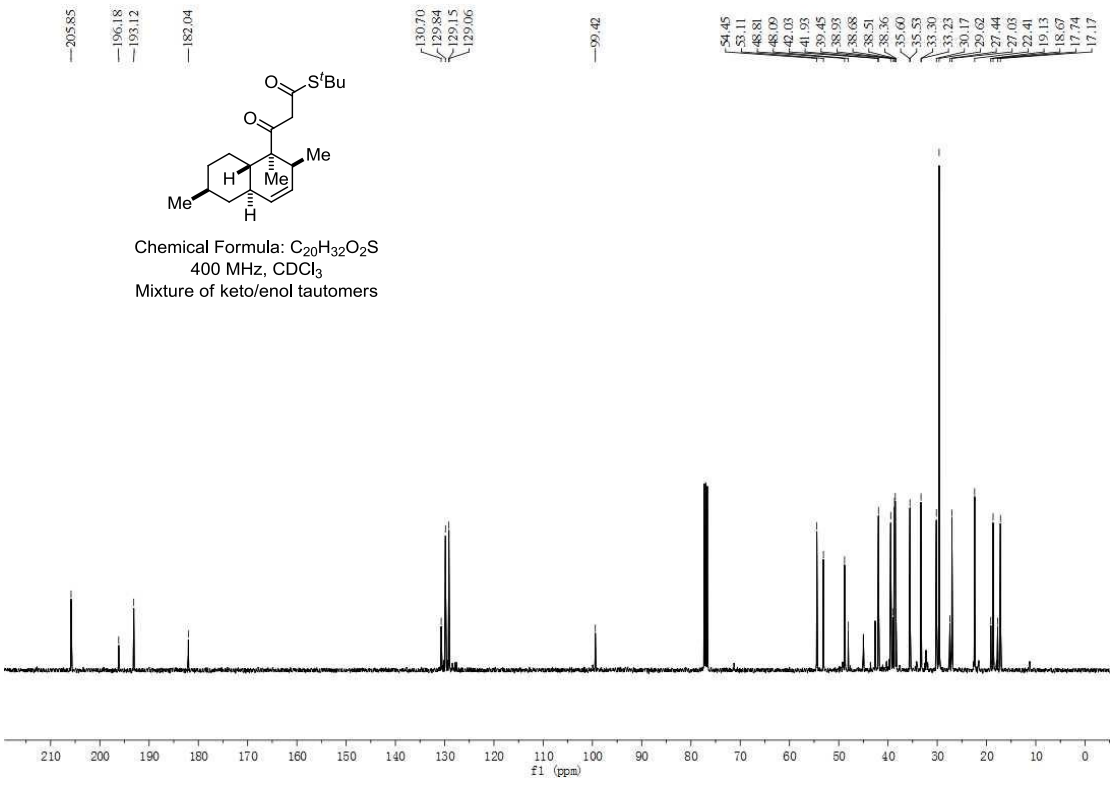
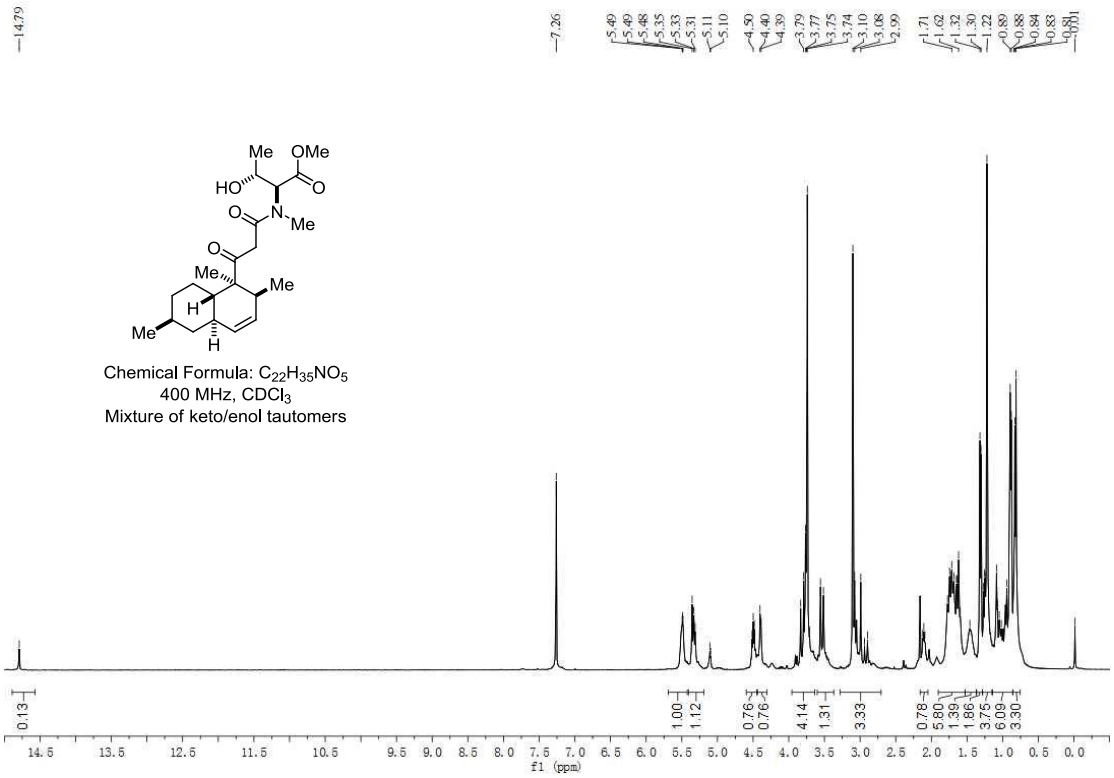
Chemical Formula: C20H32O2S
Exact Mass: 336.2123
Mixture of keto/enol tautomers



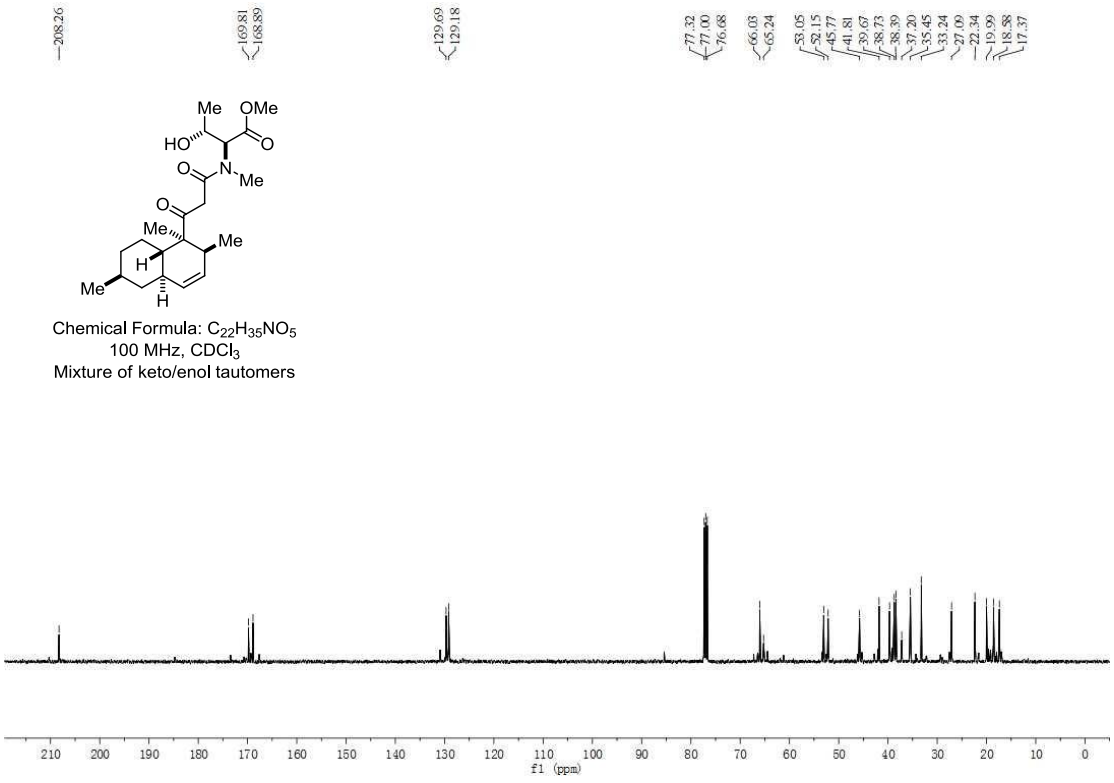
Chemical Formula: $C_{20}H_{32}O_2S$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers



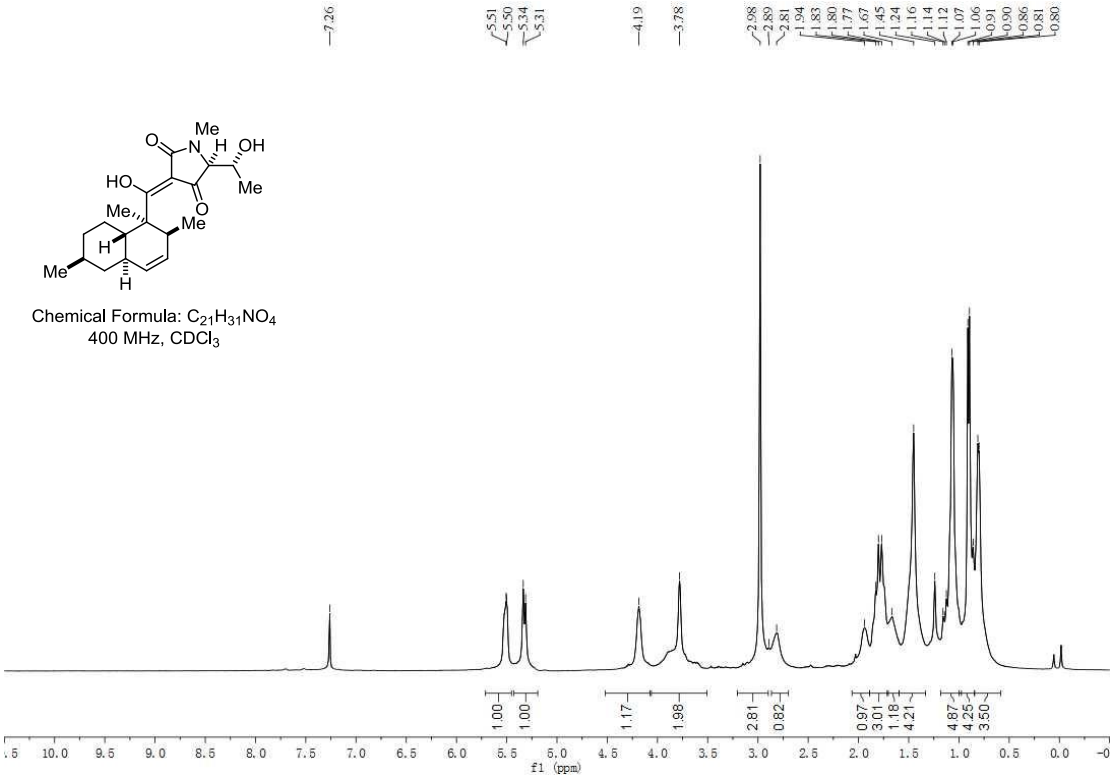
Chemical Formula: $C_{20}H_{32}O_2S$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers



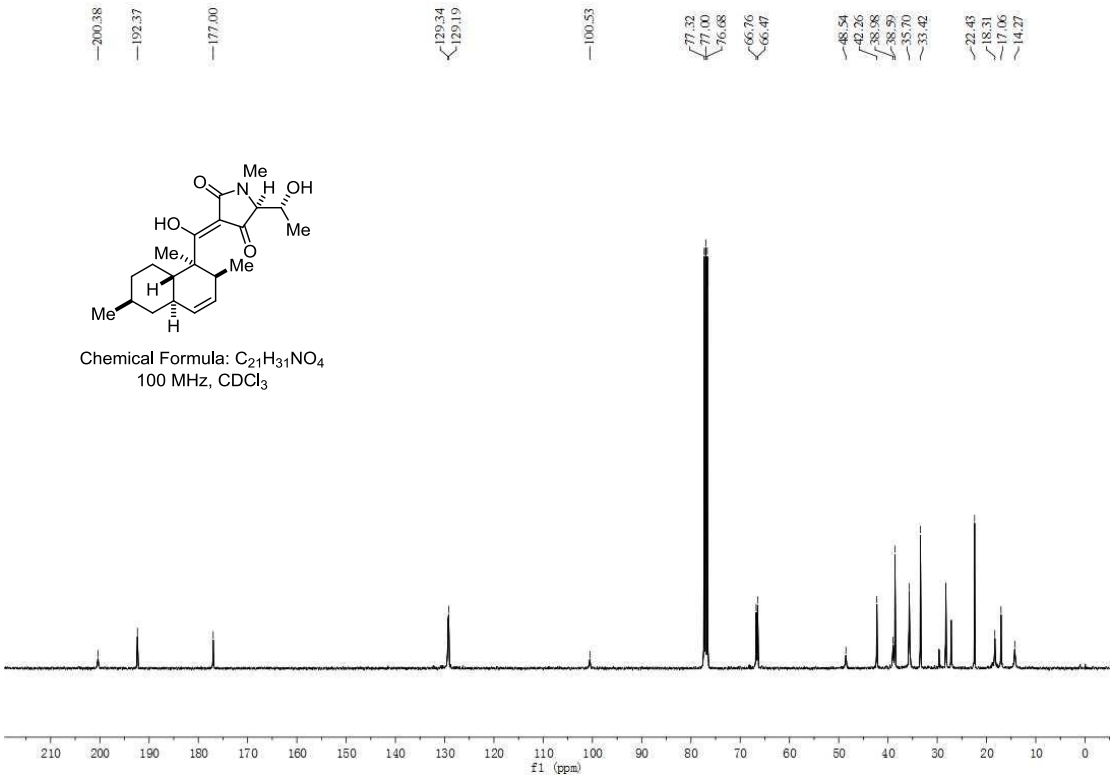
Chemical Formula: $C_{22}H_{35}NO_5$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers



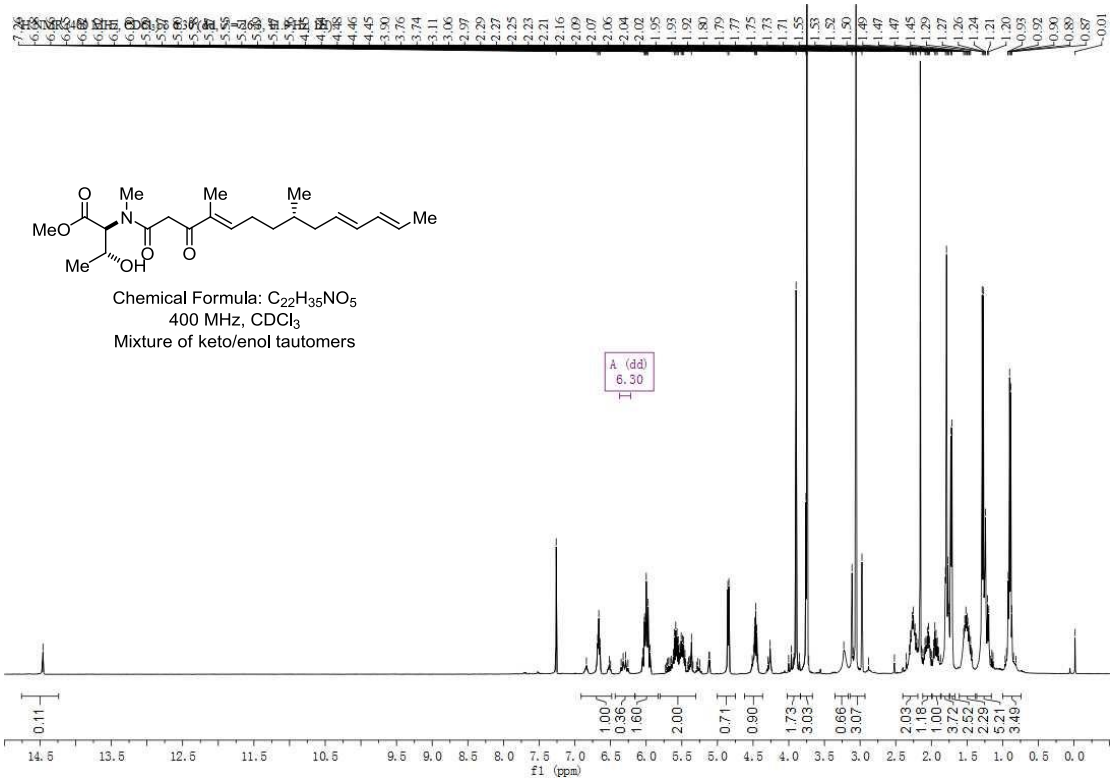
Chemical Formula: $C_{22}H_{35}NO_5$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers



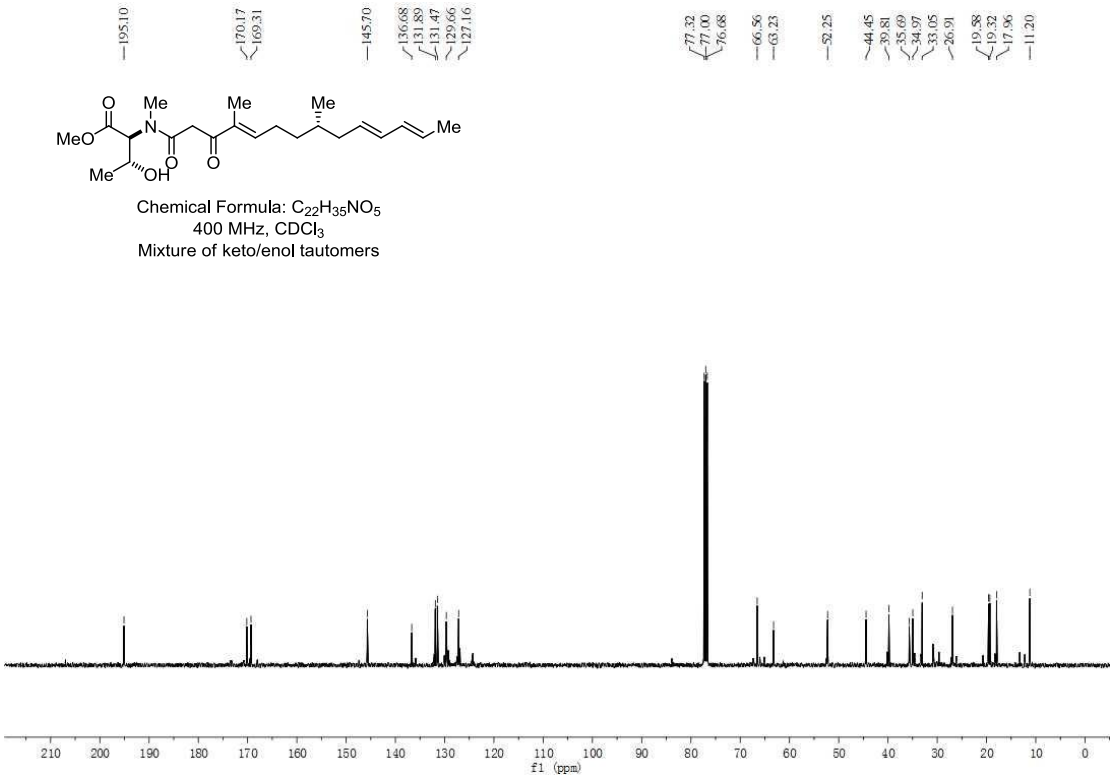
Chemical Formula: $C_{21}H_{31}NO_4$
400 MHz, $CDCl_3$



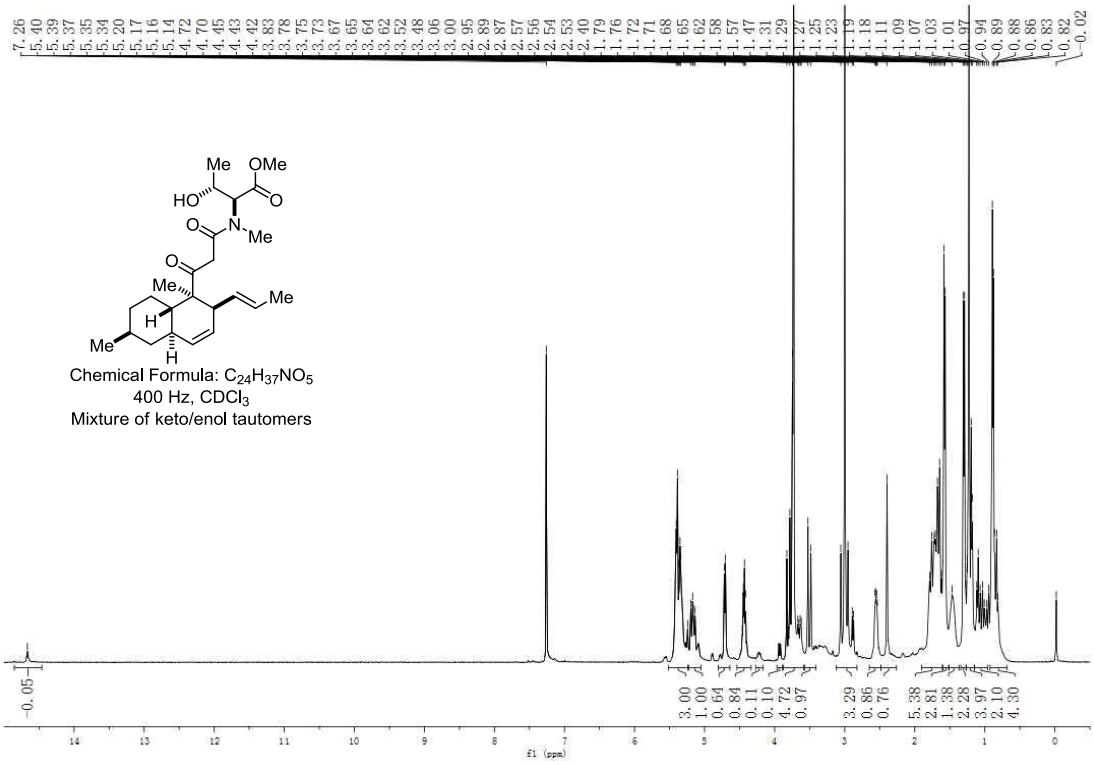
Chemical Formula: $C_{21}H_{31}NO_4$
100 MHz, $CDCl_3$



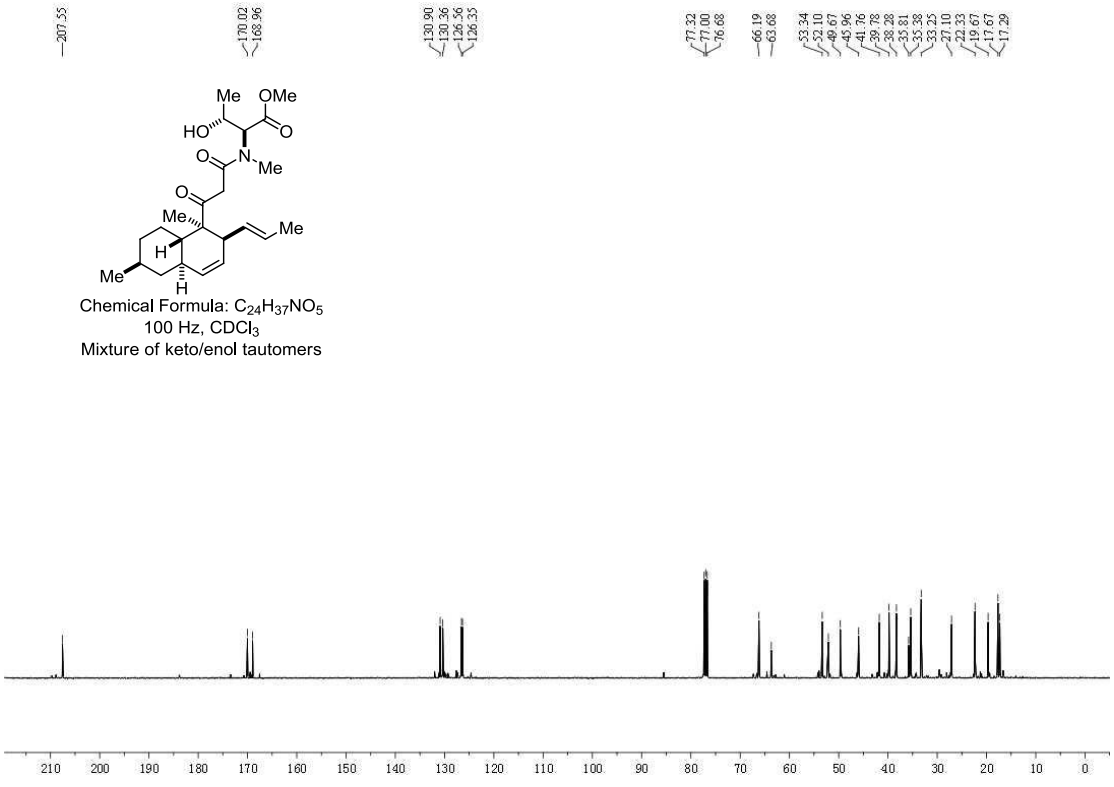
Chemical Formula: $C_{22}H_{35}NO_5$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers



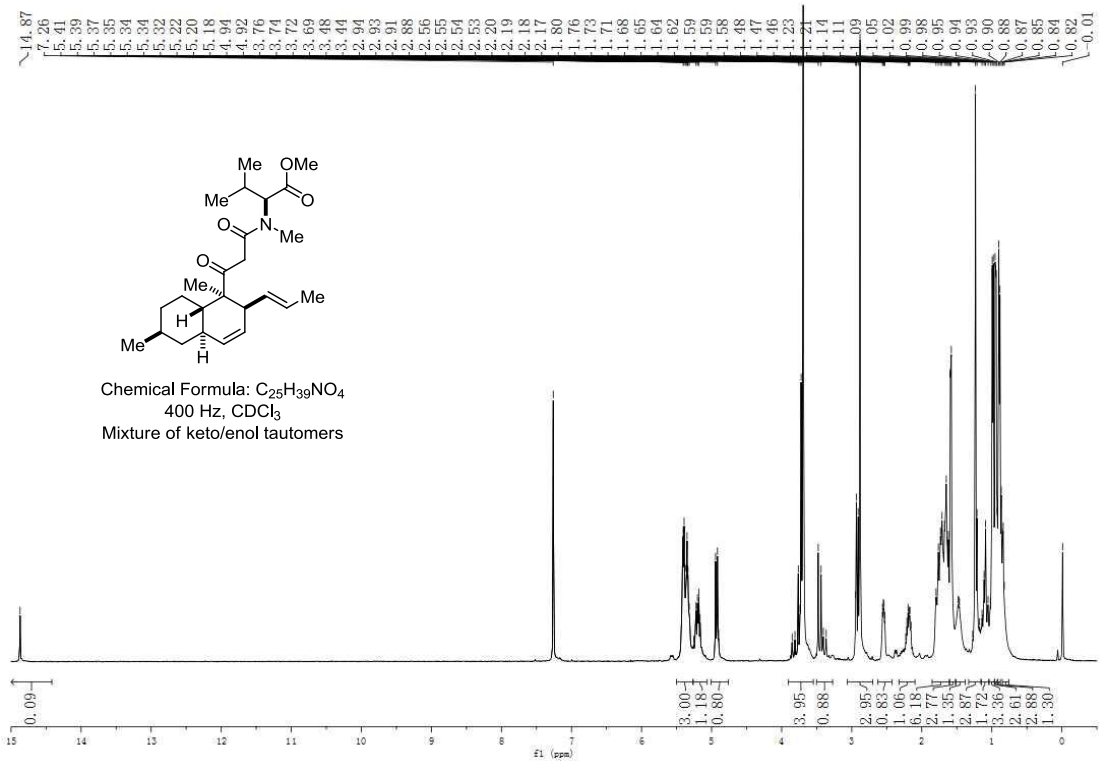
Chemical Formula: $C_{22}H_{35}NO_5$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers



Chemical Formula: $C_{24}H_{37}NO_5$
400 Hz, $CDCl_3$
Mixture of keto/enol tautomers



Chemical Formula: $C_{24}H_{37}NO_5$
100 Hz, $CDCl_3$
Mixture of keto/enol tautomers


Me
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N
Me
O
Me
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Me
H
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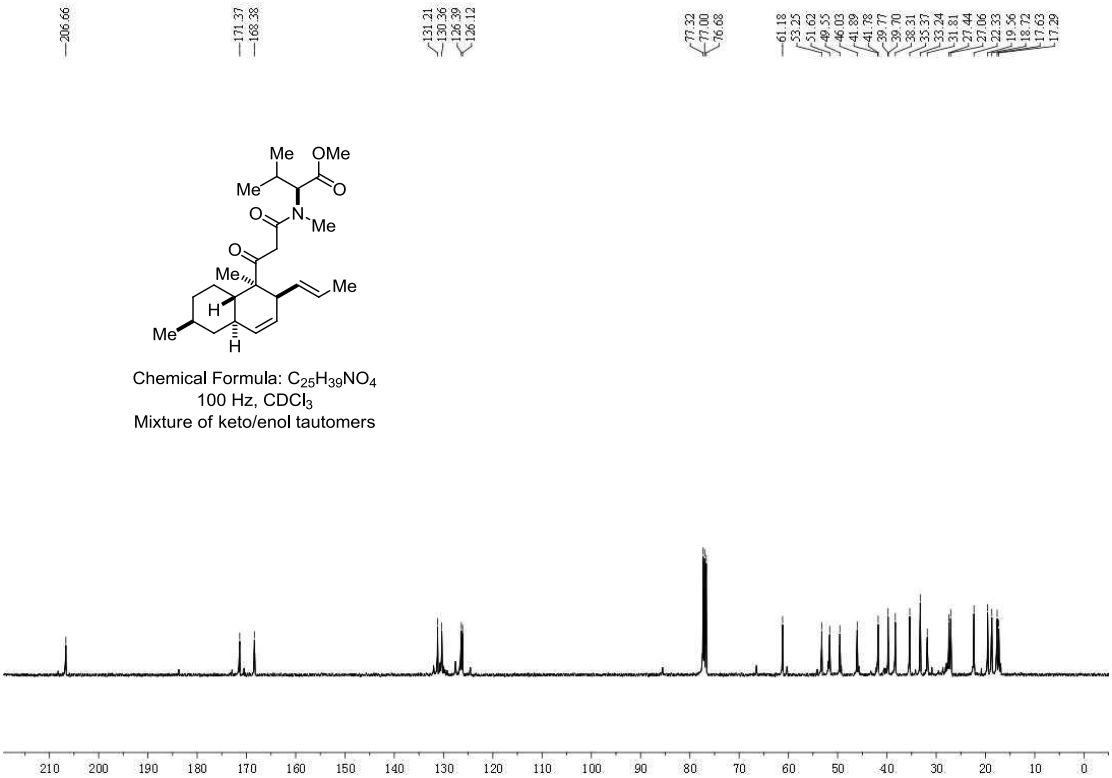
400 Hz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)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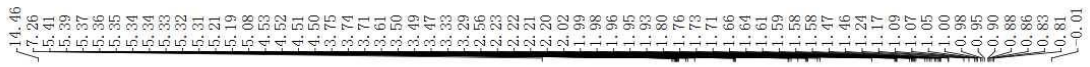
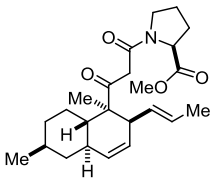
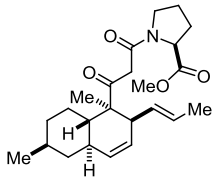
H
Chemical Formula: $C_{25}H_{39}NO_4$
100 Hz, $CDCl_3$
Mixture of keto/enol tautomers

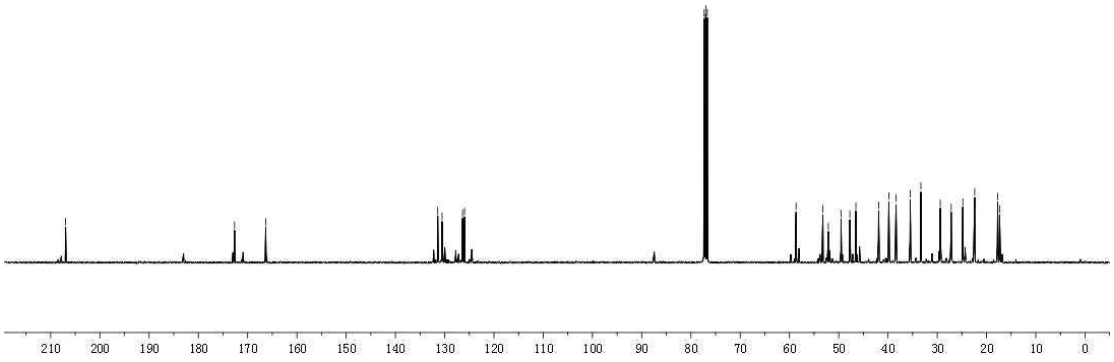


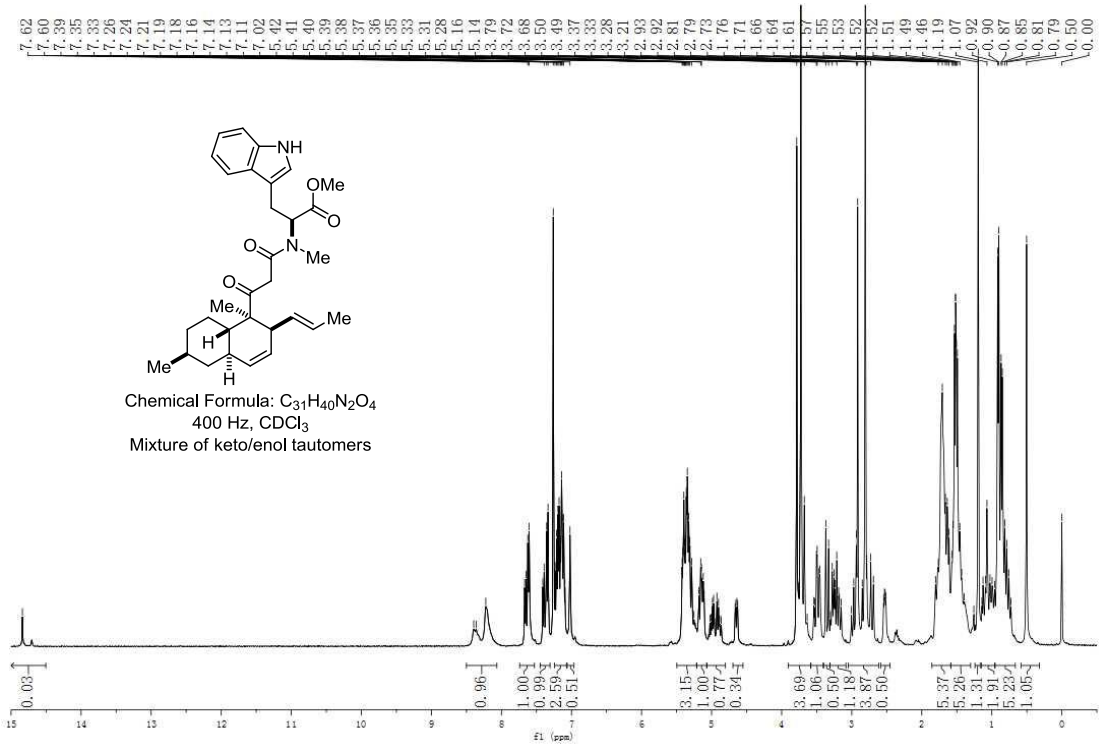


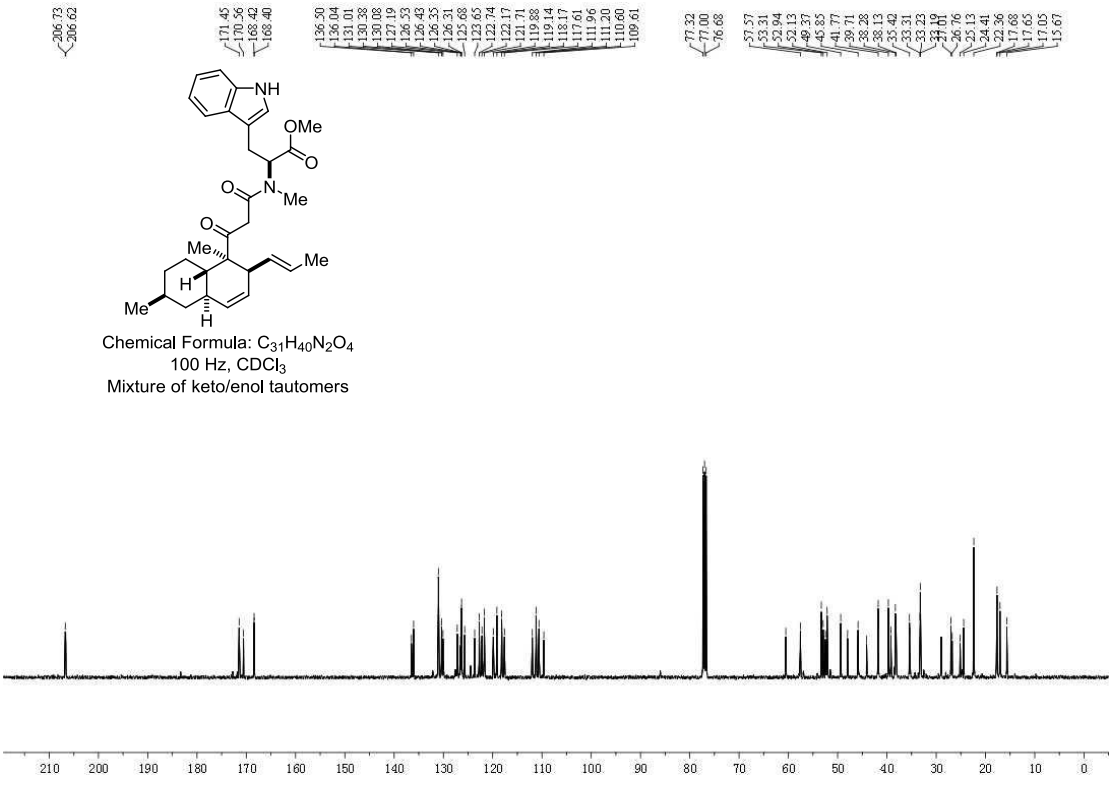
Chemical Formula: $C_{24}H_{35}NO_4$
400 Hz, $CDCl_3$
Mixture of keto/enol tautomers

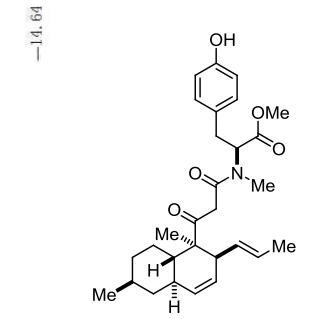


Chemical Formula: $C_{24}H_{35}NO_4$
100 Hz, $CDCl_3$
Mixture of keto/enol tautomers

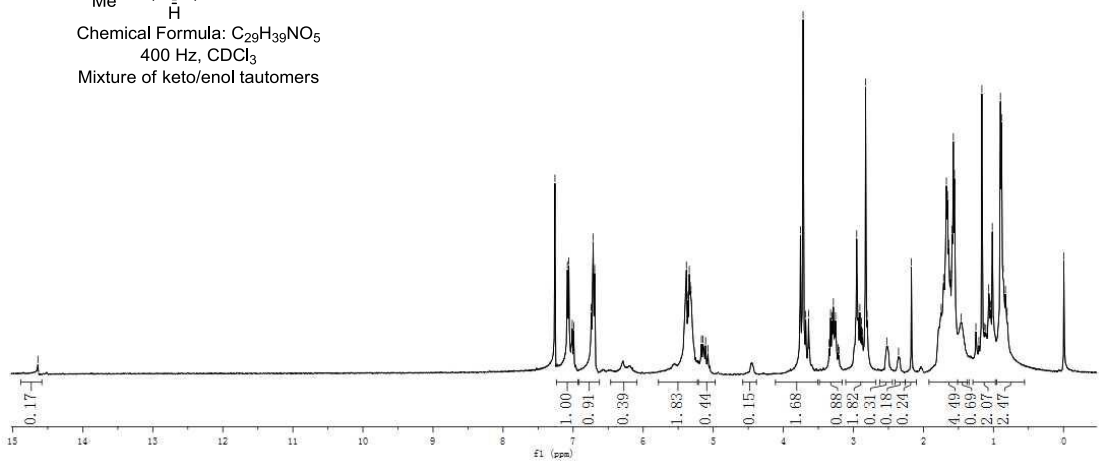


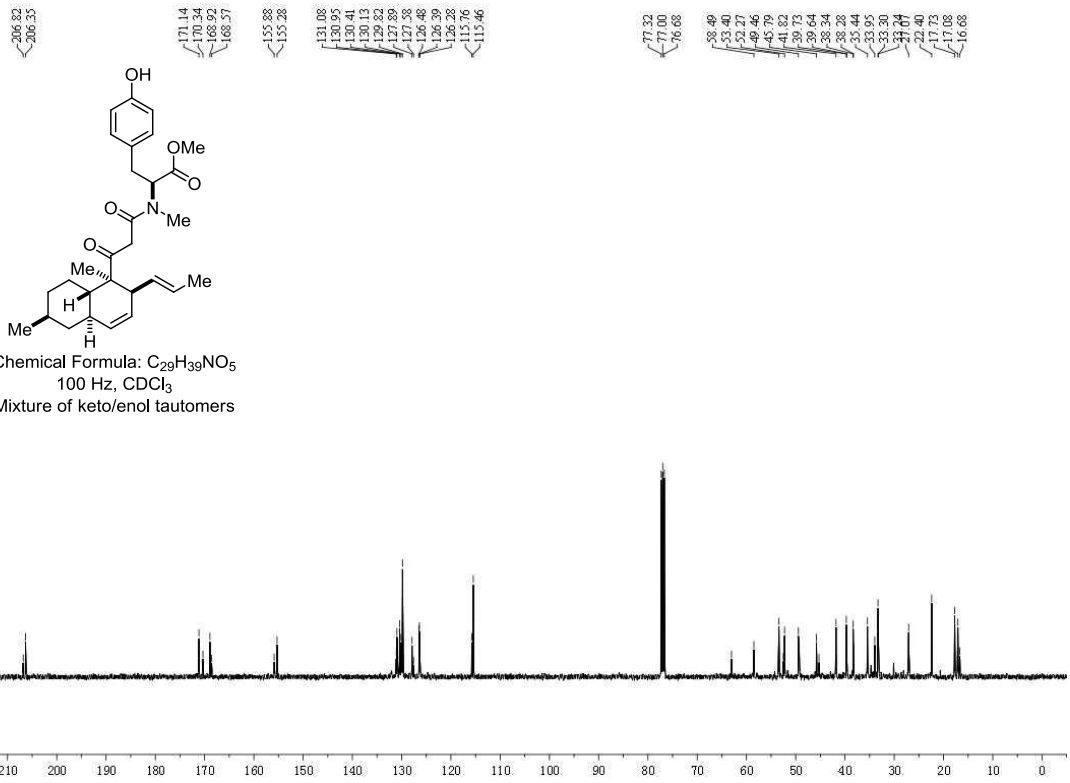

NH
OMe
O
N
Me
O
O
Me
H
Me
Me
H
Chemical Formula: $C_{31}H_{40}N_2O_4$
400 Hz, $CDCl_3$
Mixture of keto/enol tautomers


NH
OMe
O
N
Me
O
O
Me
H
Me
Me
H
Chemical Formula: $C_{31}H_{40}N_2O_4$
100 Hz, $CDCl_3$
Mixture of keto/enol tautomers

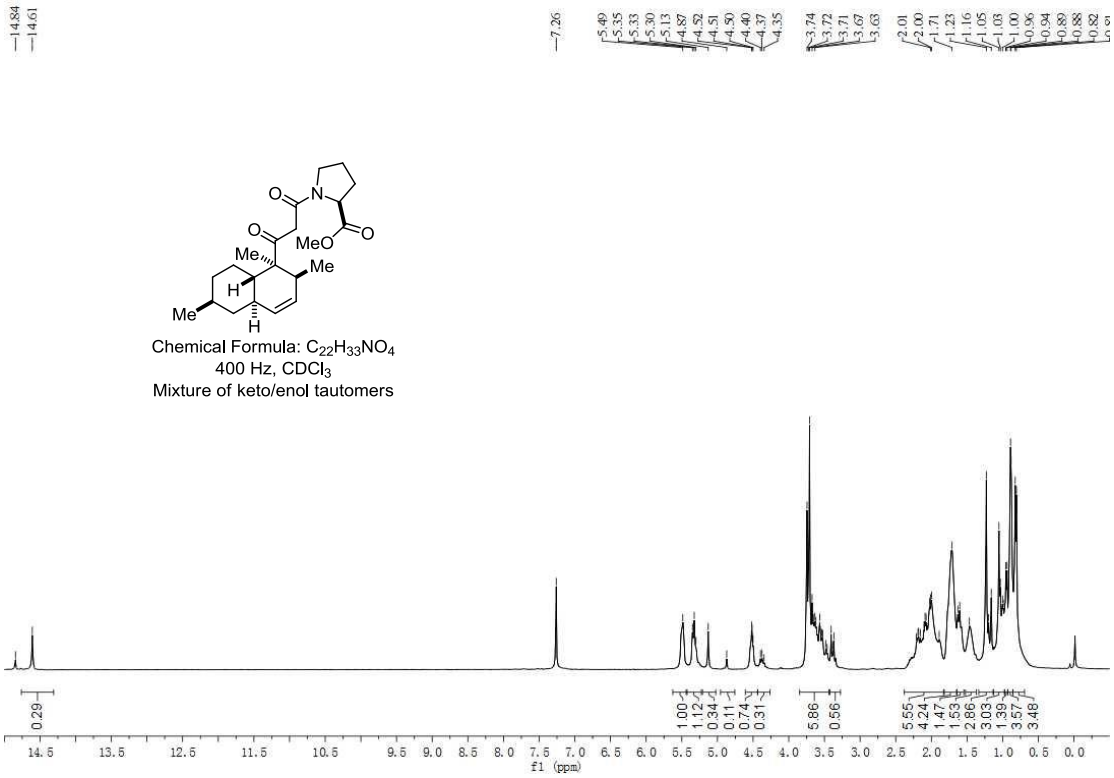


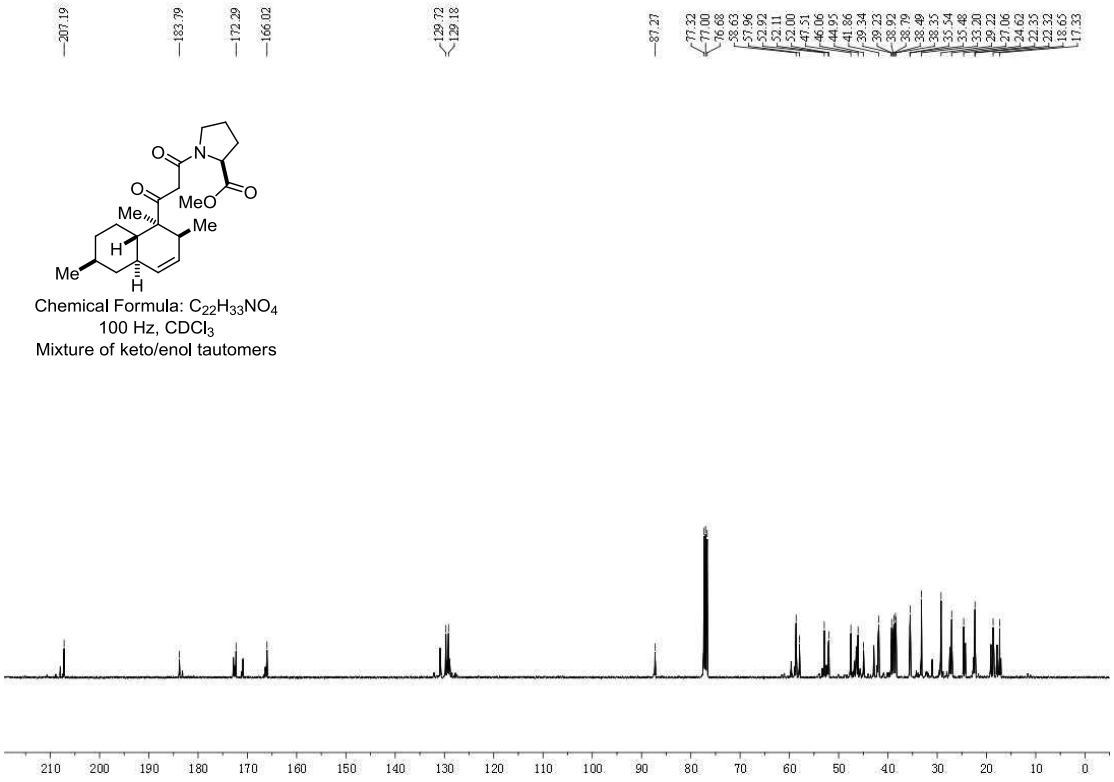
Chemical Formula: $C_{29}H_{39}NO_5$
400 Hz, $CDCl_3$
Mixture of keto/enol tautomers

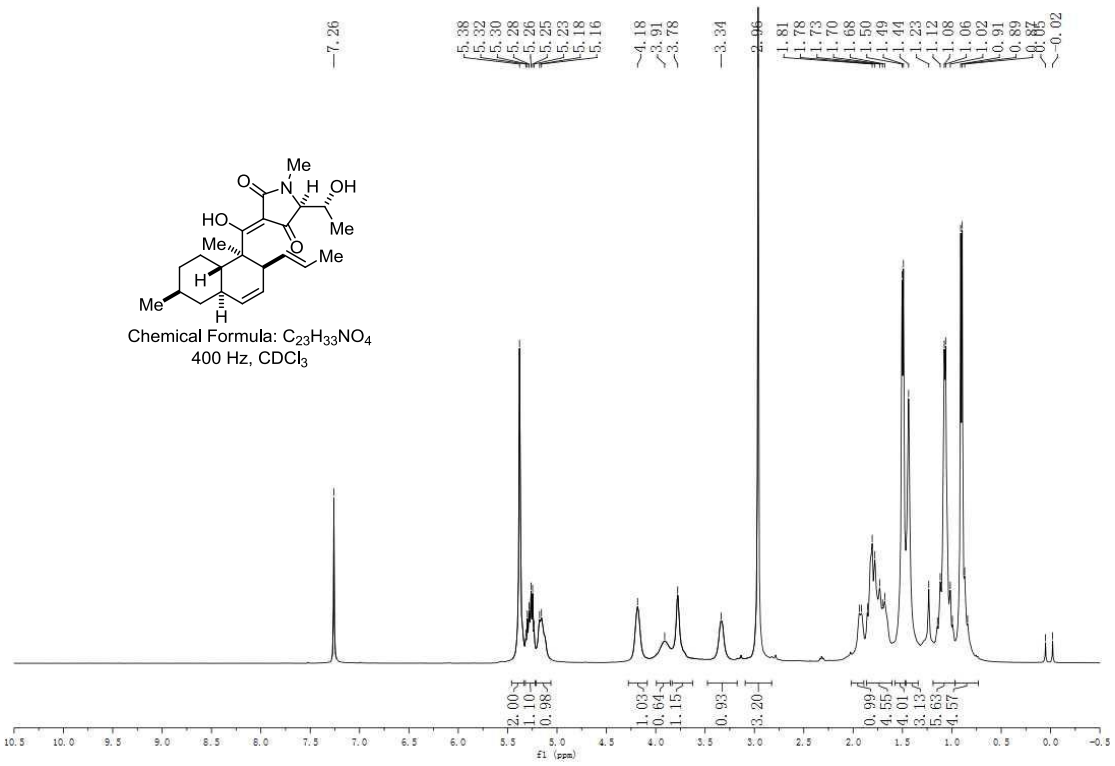


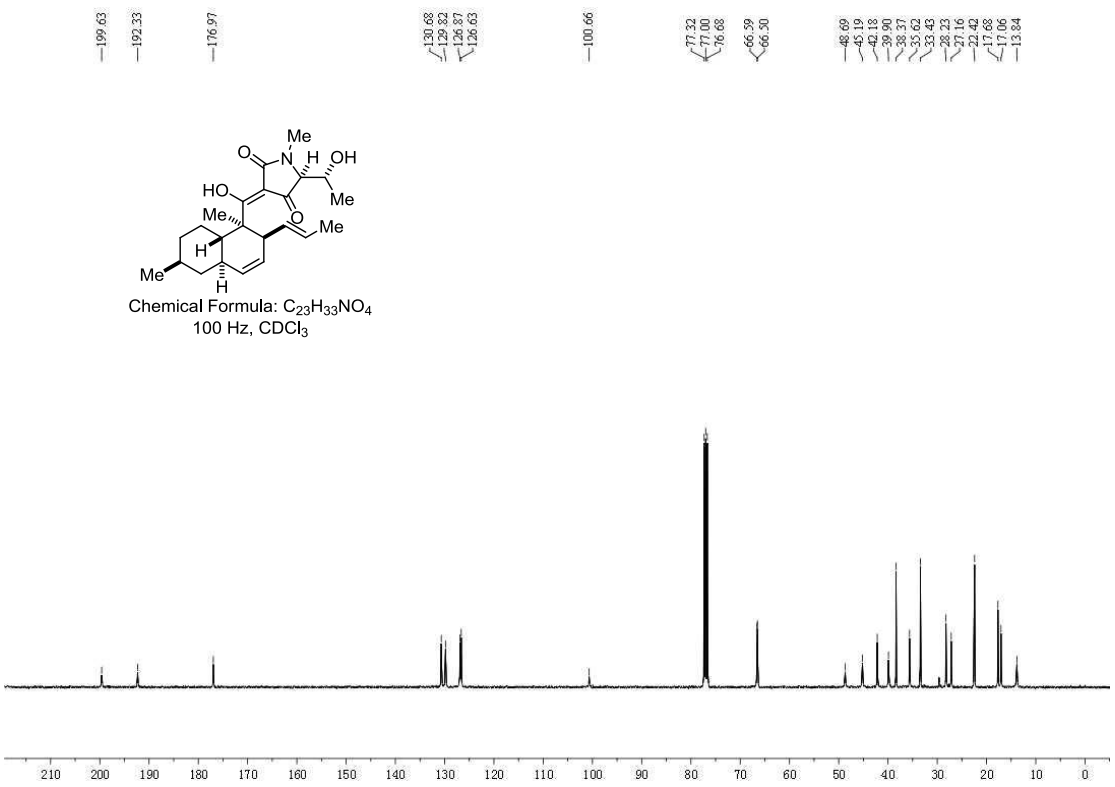


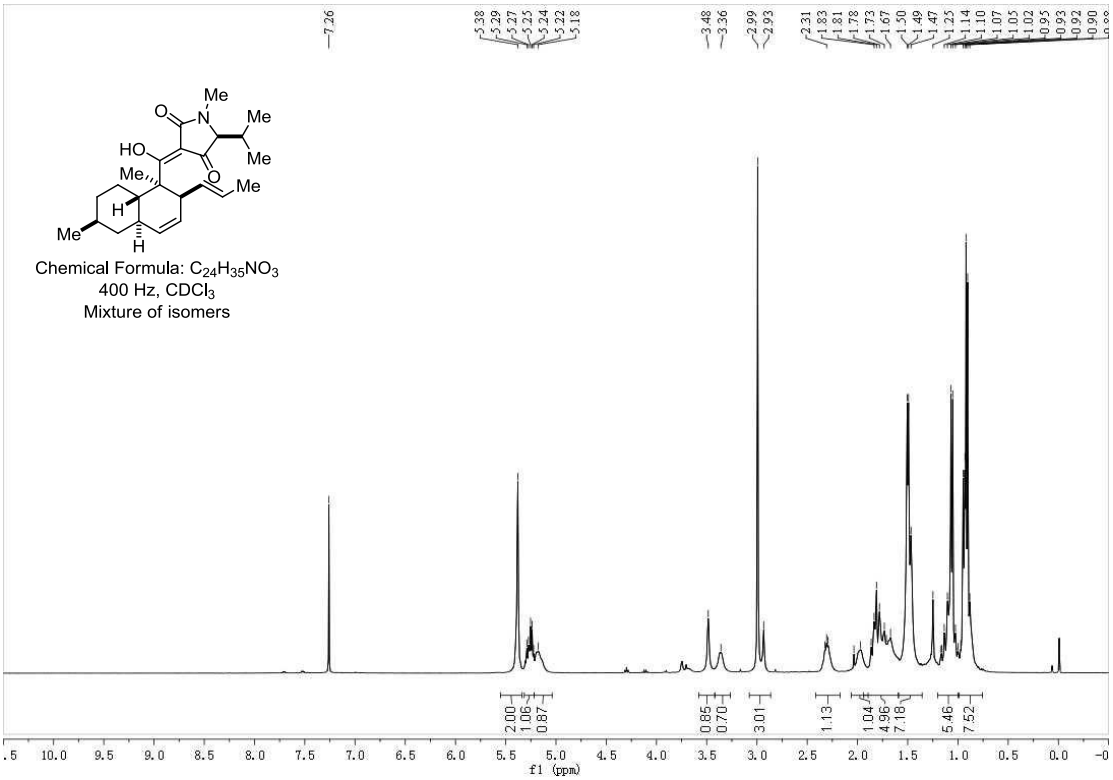
Chemical Formula: $C_{29}H_{39}NO_5$
100 Hz, $CDCl_3$
Mixture of keto/enol tautomers

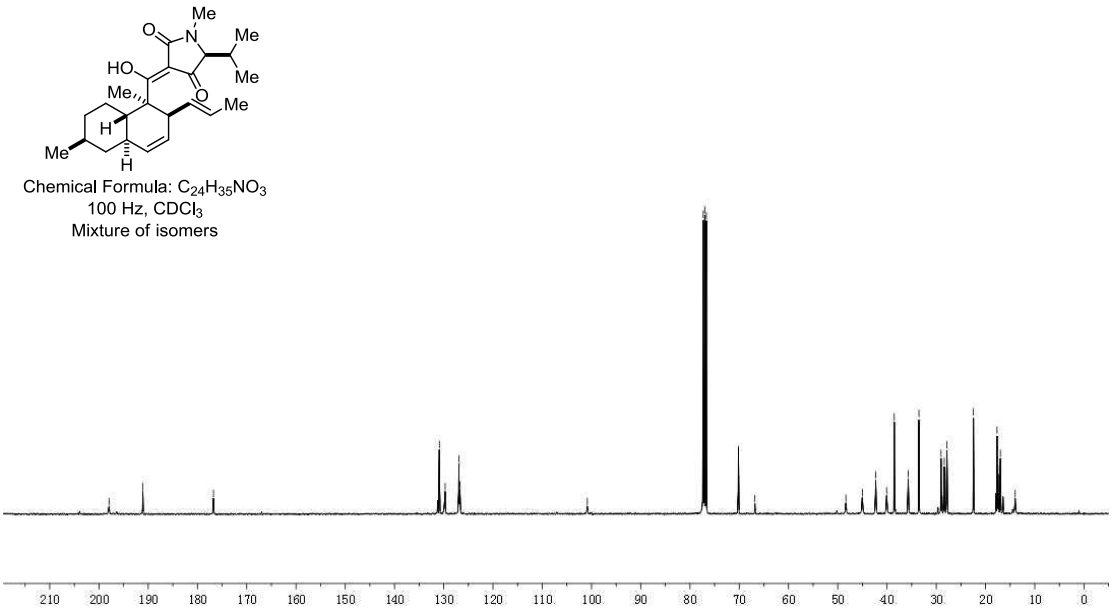

14.84
14.61
7.26
5.49
5.35
5.33
5.30
5.13
4.87
4.52
4.51
4.50
4.40
4.37
4.35
3.74
3.72
3.71
3.67
3.63
2.01
2.00
1.71
1.23
1.16
1.05
1.03
1.00
0.96
0.94
0.89
0.88
0.82
O
N
O
MeO
O
Me
Me
H
Me
H
Chemical Formula: C22H33NO4
400 Hz, CDCl3
Mixture of keto/enol tautomers
0.29
1.00
1.12
0.34
0.11
0.74
0.31
5.86
0.56
5.55
4.24
1.47
1.53
2.86
3.03
1.39
3.57
3.48
14.5
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

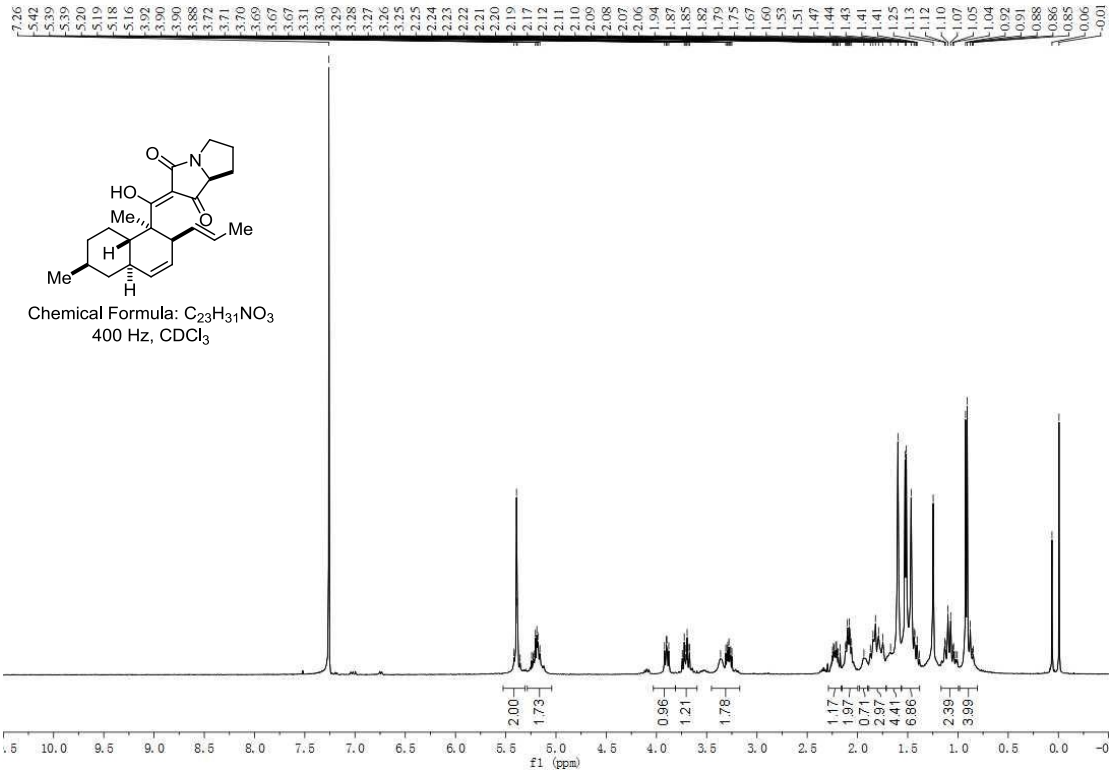

207.19
183.79
172.29
166.02
129.72
129.18
87.27
77.32
77.00
76.68
58.63
57.96
52.92
52.11
52.00
47.51
46.06
44.95
41.86
39.34
39.23
38.92
38.79
38.49
38.35
35.54
35.48
33.20
29.22
27.06
24.62
22.35
22.32
18.65
17.33
O
N
O
MeO
O
Me
Me
H
Me
H
Chemical Formula: C22H33NO4
100 Hz, CDCl3
Mixture of keto/enol tautomers
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

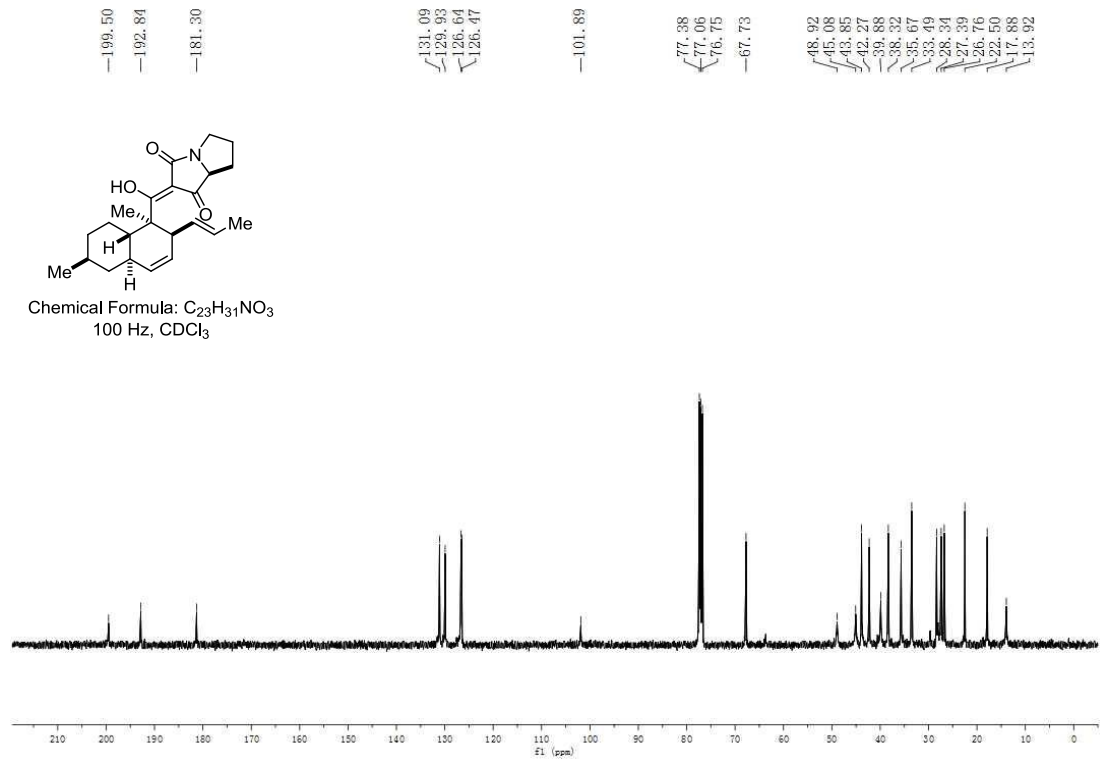

Me
O
N
H
OH
HO
Me
Me
O
Me
H
Me
H
Chemical Formula: C23H33NO4
400 Hz, CDCl3
7.26
5.38
5.32
5.30
5.28
5.26
5.25
5.23
5.18
5.16
4.18
3.91
3.78
3.34
2.06
1.81
1.78
1.73
1.70
1.68
1.50
1.49
1.44
1.23
1.12
1.08
1.06
1.02
0.91
0.89
0.87
0.05
-0.02
2.00
1.10
0.98
1.03
0.64
1.15
0.93
3.20
0.99
4.55
4.01
3.13
5.63
4.57
f1 (ppm)

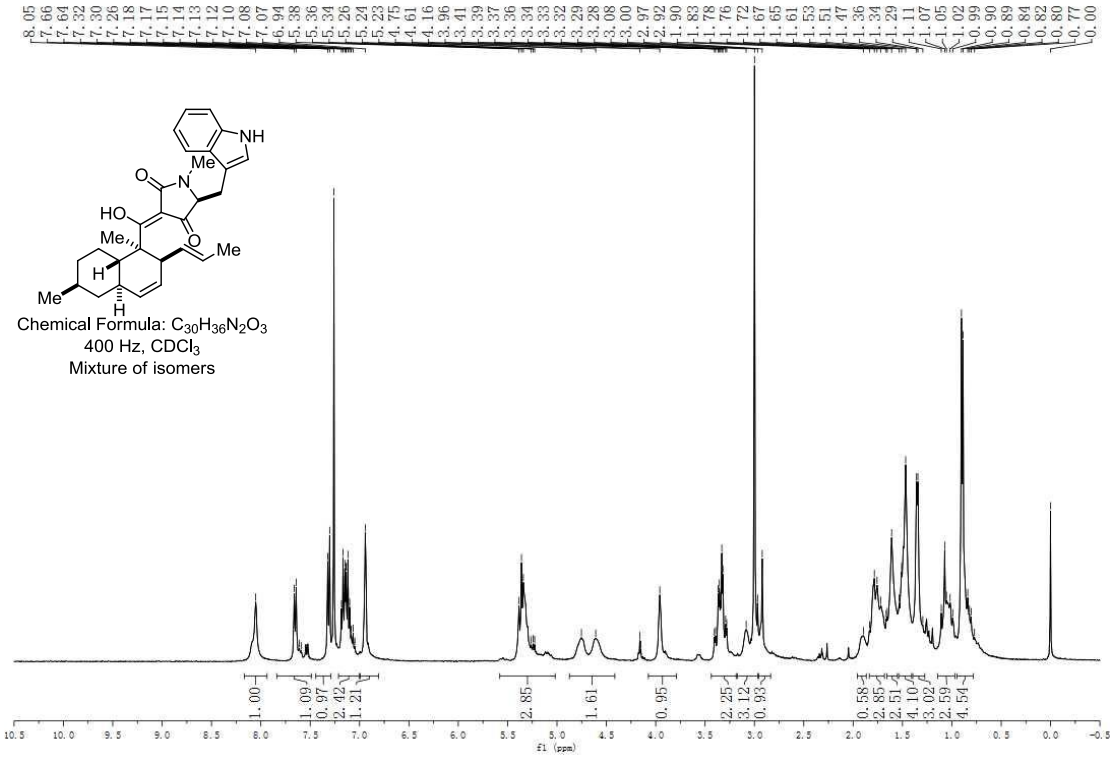

199.63
192.33
176.97
130.68
129.82
126.87
126.63
100.66
77.32
77.00
76.68
66.59
66.50
48.69
45.19
42.18
39.90
38.37
35.62
33.43
28.23
27.16
22.42
17.68
17.06
13.84
Me
O
N
H
OH
HO
Me
Me
O
Me
H
Me
H
Chemical Formula: C23H33NO4
100 Hz, CDCl3

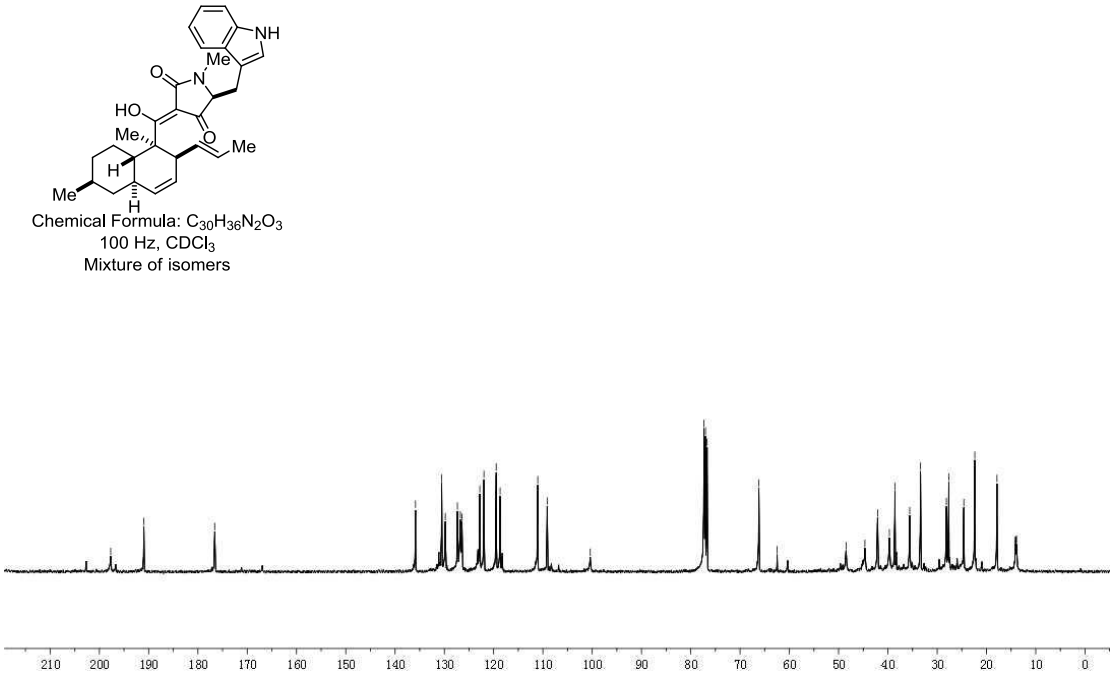

Chemical Formula: $C_{24}H_{35}NO_3$
400 Hz, $CDCl_3$
Mixture of isomers
f1 (ppm)

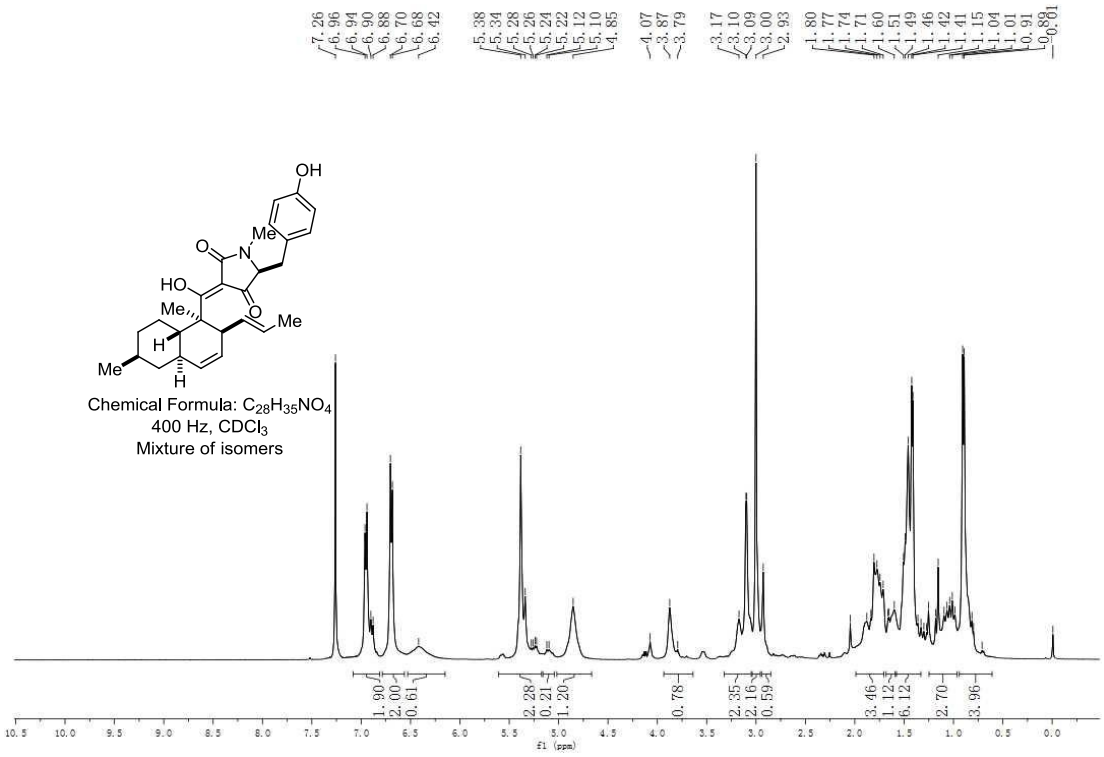

Chemical Formula: $C_{24}H_{35}NO_3$
100 Hz, $CDCl_3$
Mixture of isomers

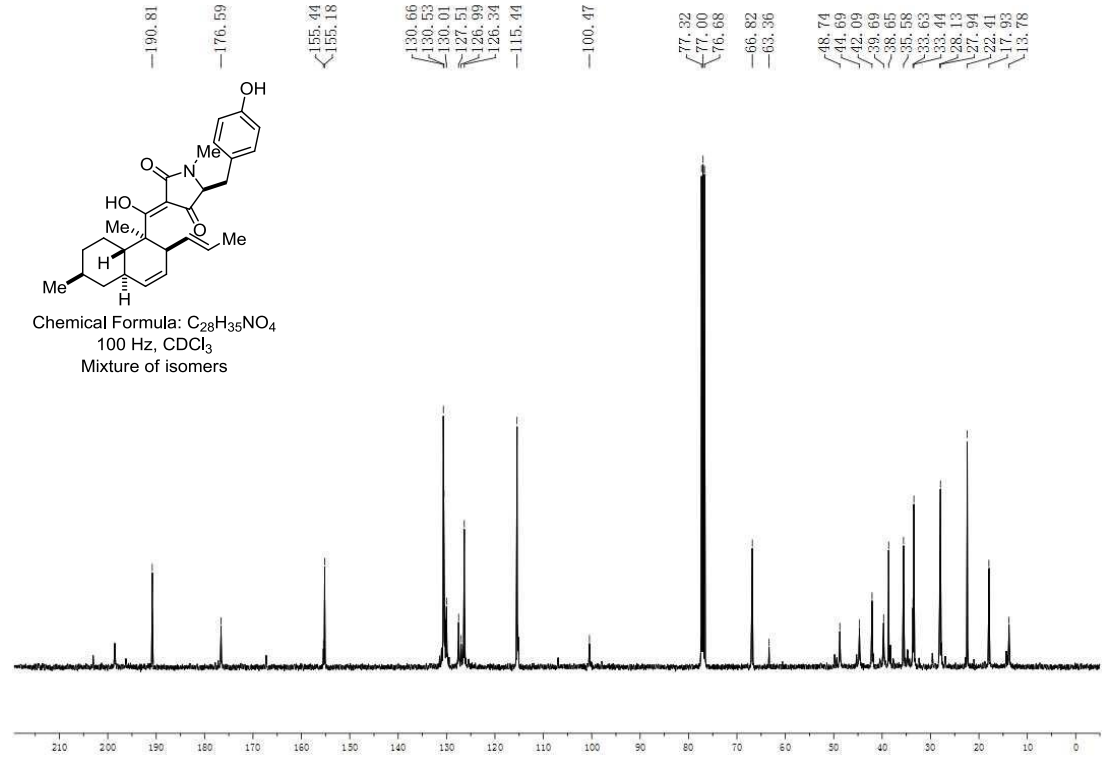

Chemical Formula: $C_{23}H_{31}NO_3$
400 Hz, $CDCl_3$
f1 (ppm)

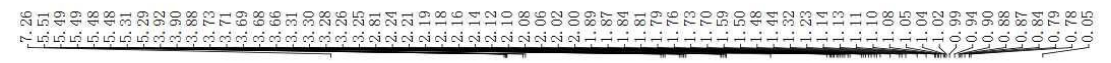

Chemical Formula: $C_{23}H_{31}NO_3$
100 Hz, $CDCl_3$
f1 (ppm)

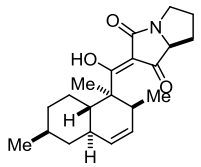

Chemical Formula: $C_{30}H_{36}N_2O_3$
400 Hz, $CDCl_3$
Mixture of isomers


Chemical Formula: $C_{30}H_{36}N_2O_3$
100 Hz, $CDCl_3$
Mixture of isomers

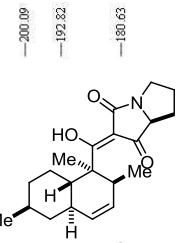

Chemical Formula: $C_{28}H_{35}NO_4$
400 Hz, $CDCl_3$
Mixture of isomers
f1 (ppm)


Chemical Formula: $C_{28}H_{35}NO_4$
100 Hz, $CDCl_3$
Mixture of isomers

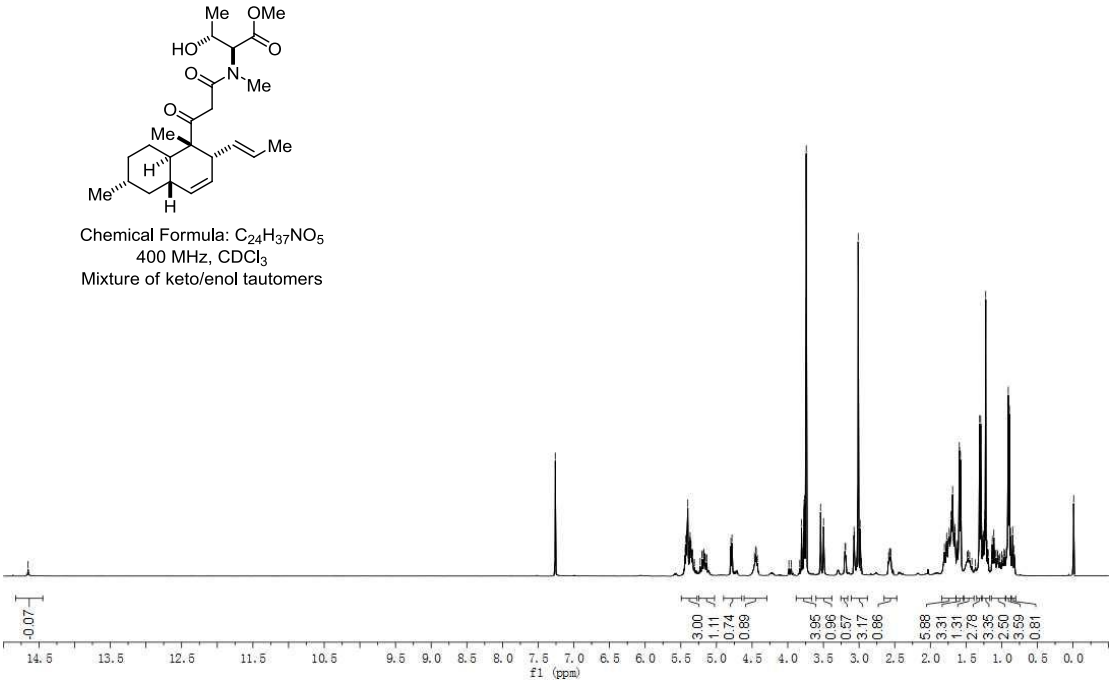




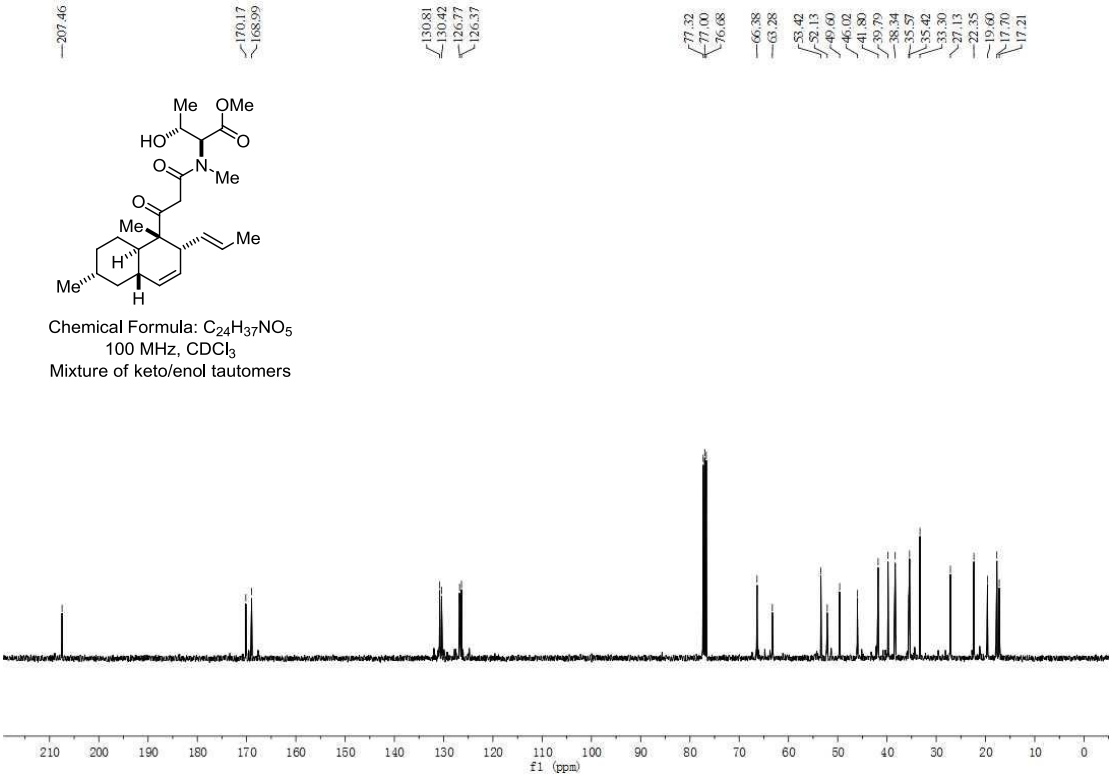
Chemical Formula: $C_{21}H_{29}NO_3$
400 Hz, $CDCl_3$



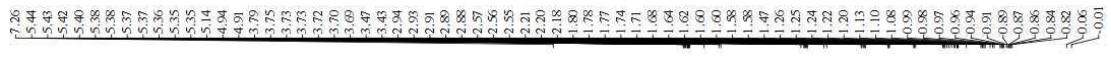
Chemical Formula: $C_{21}H_{29}NO_3$
100 Hz, $CDCl_3$

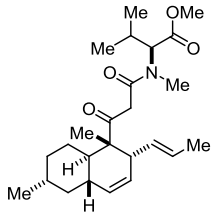


Chemical Formula: $C_{24}H_{37}NO_5$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers

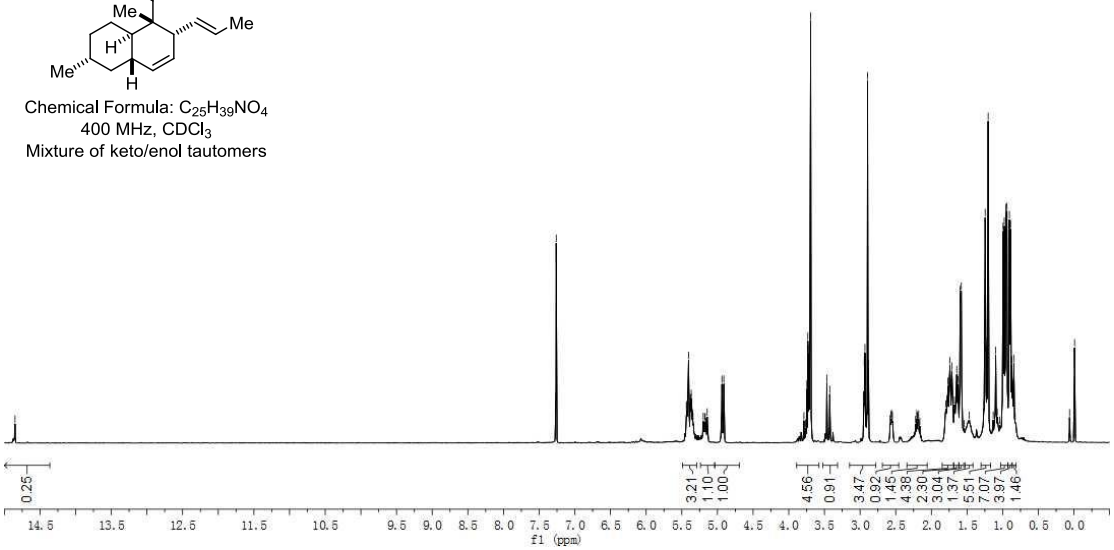


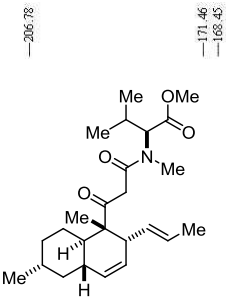
Chemical Formula: $C_{24}H_{37}NO_5$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers



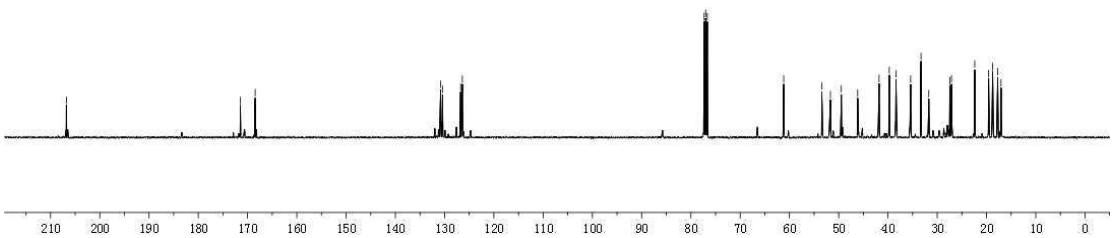


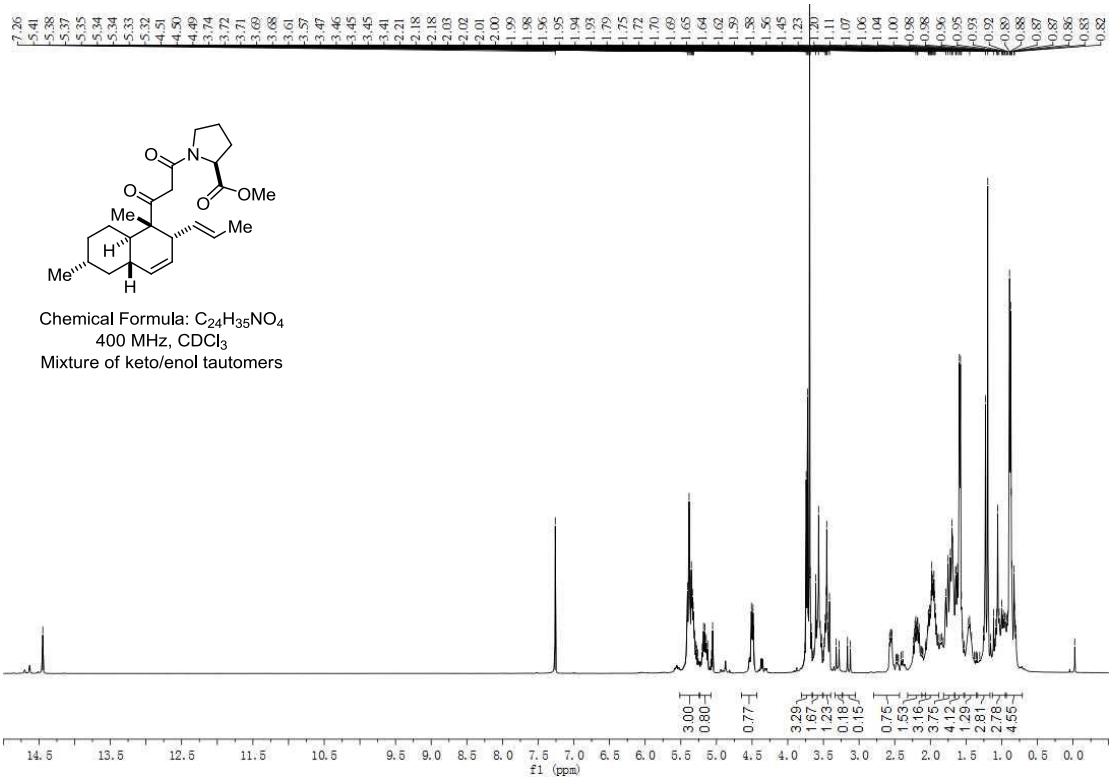
Chemical Formula: $C_{25}H_{39}NO_4$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers



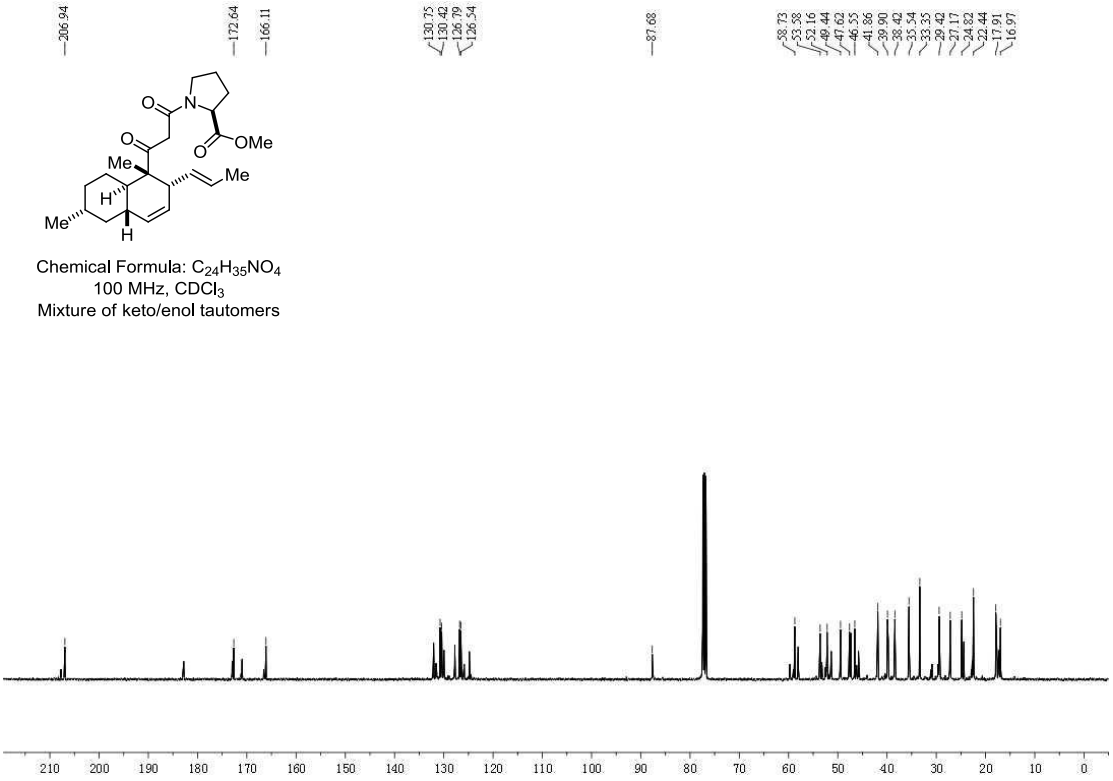


Chemical Formula: $C_{25}H_{39}NO_4$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers

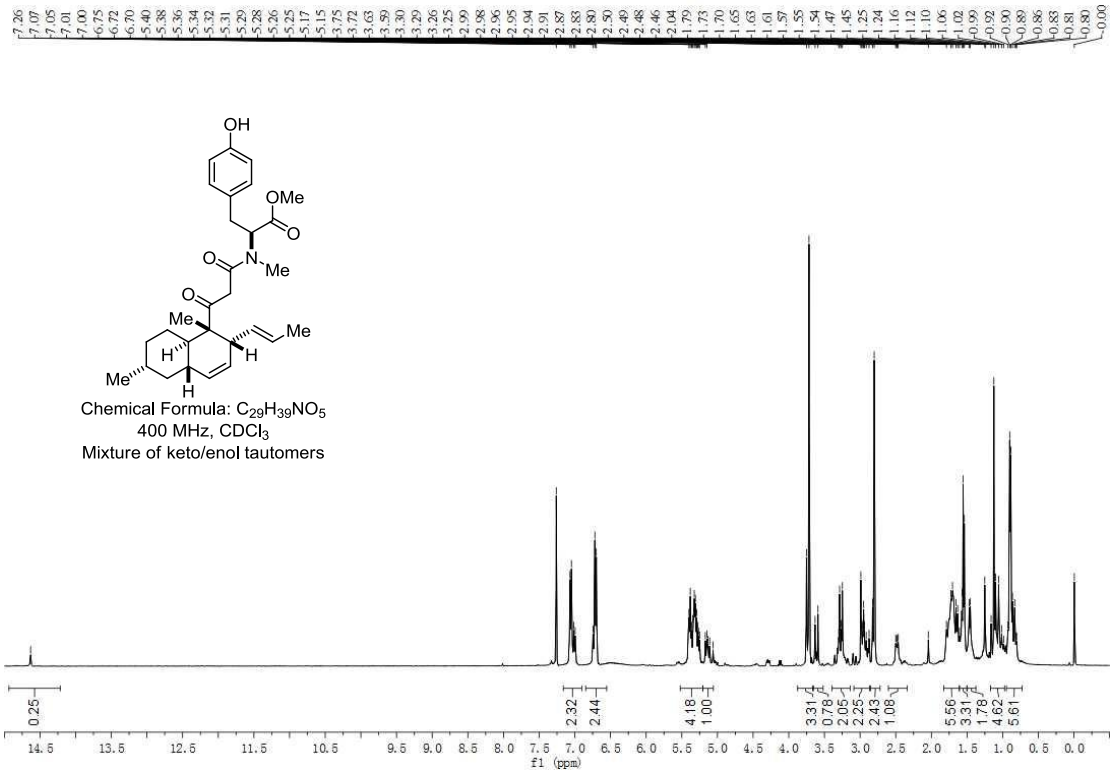


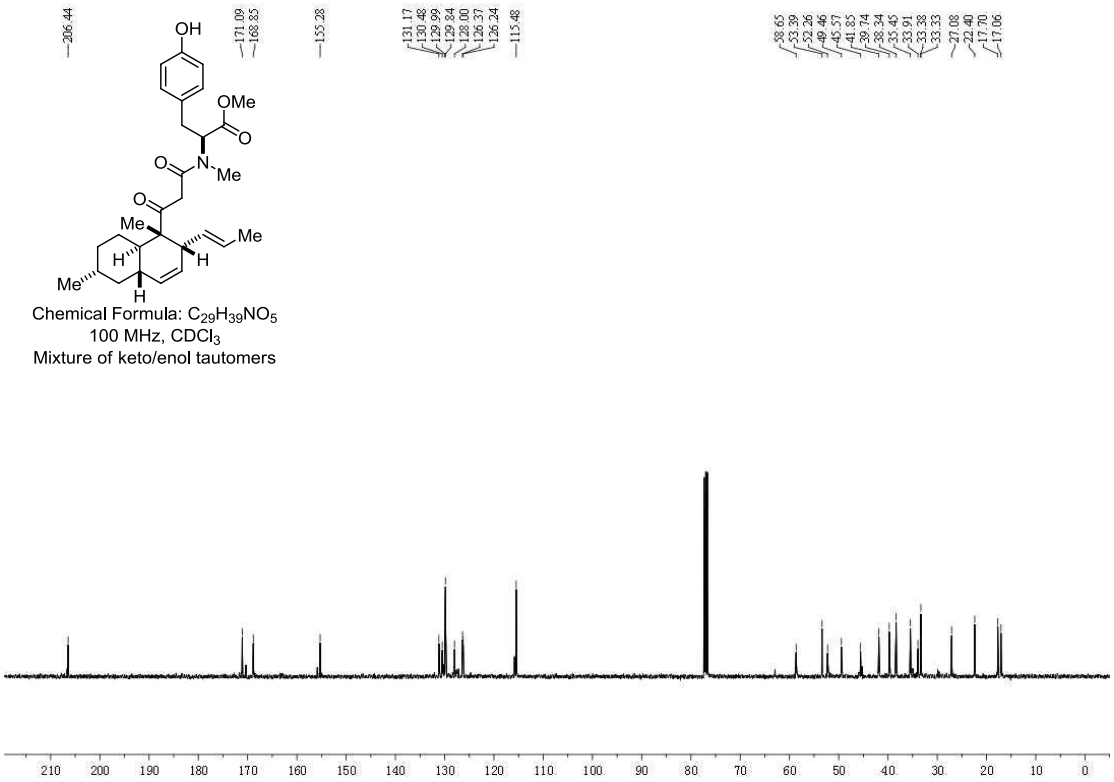


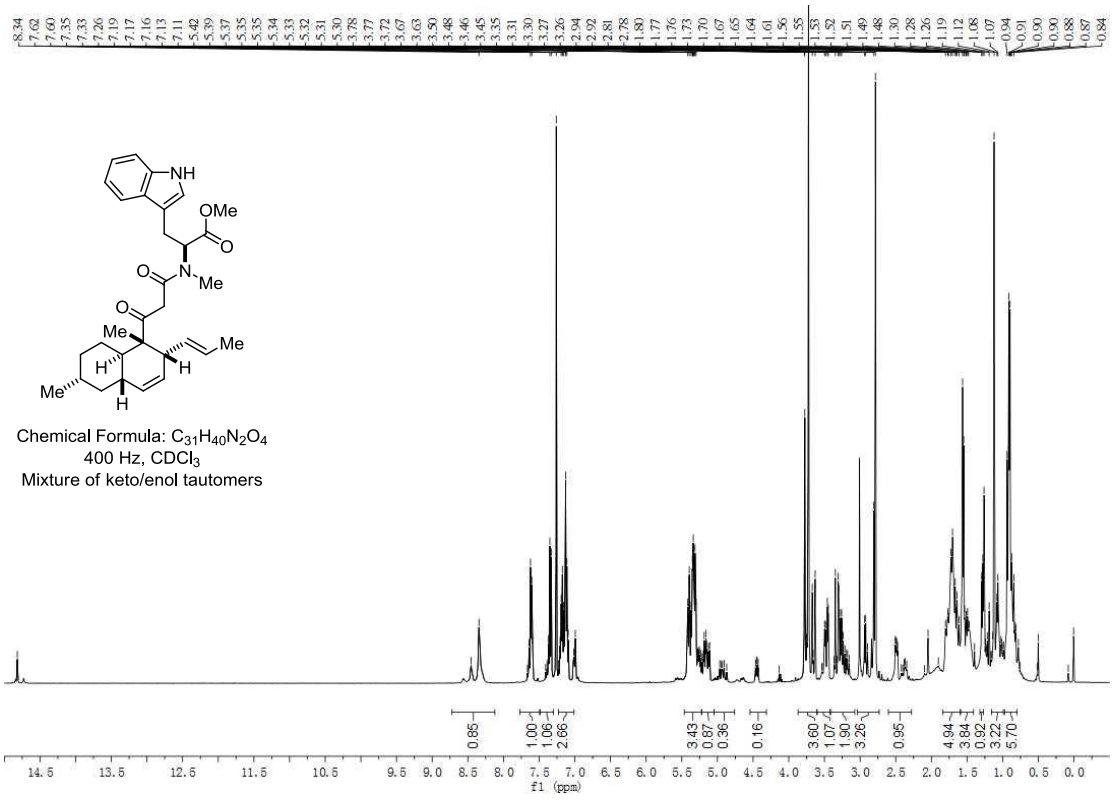
Chemical Formula: $C_{24}H_{35}NO_4$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers

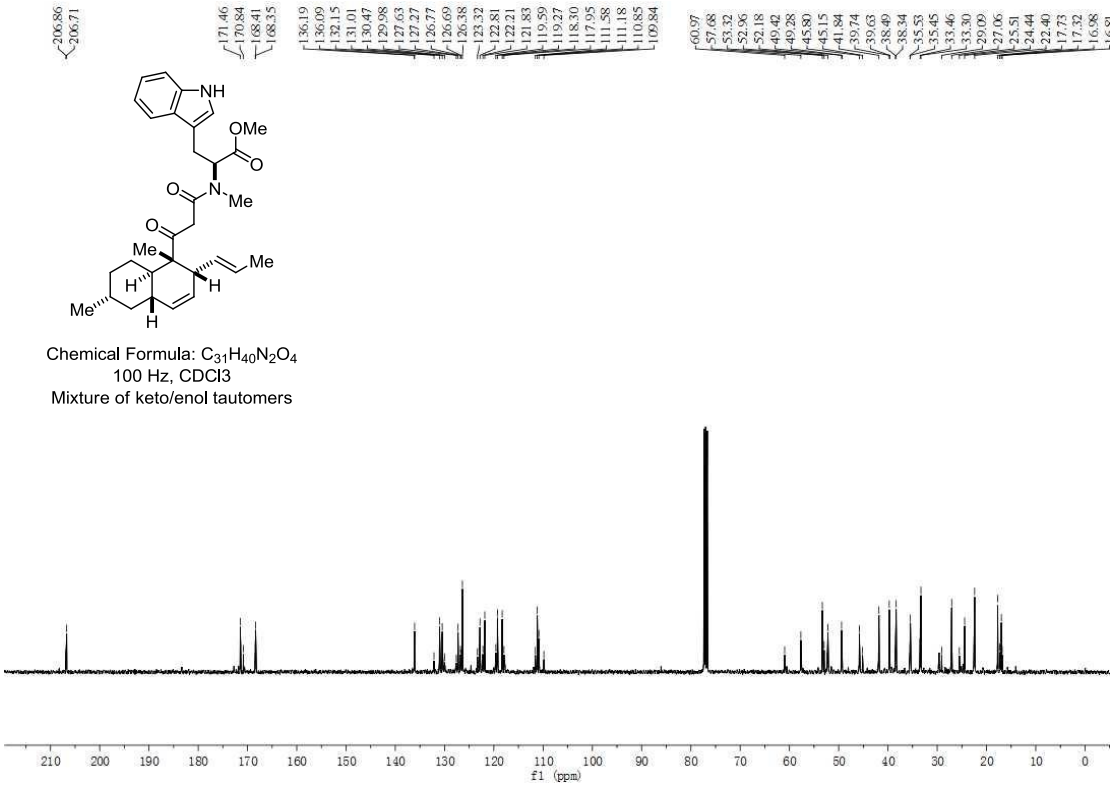


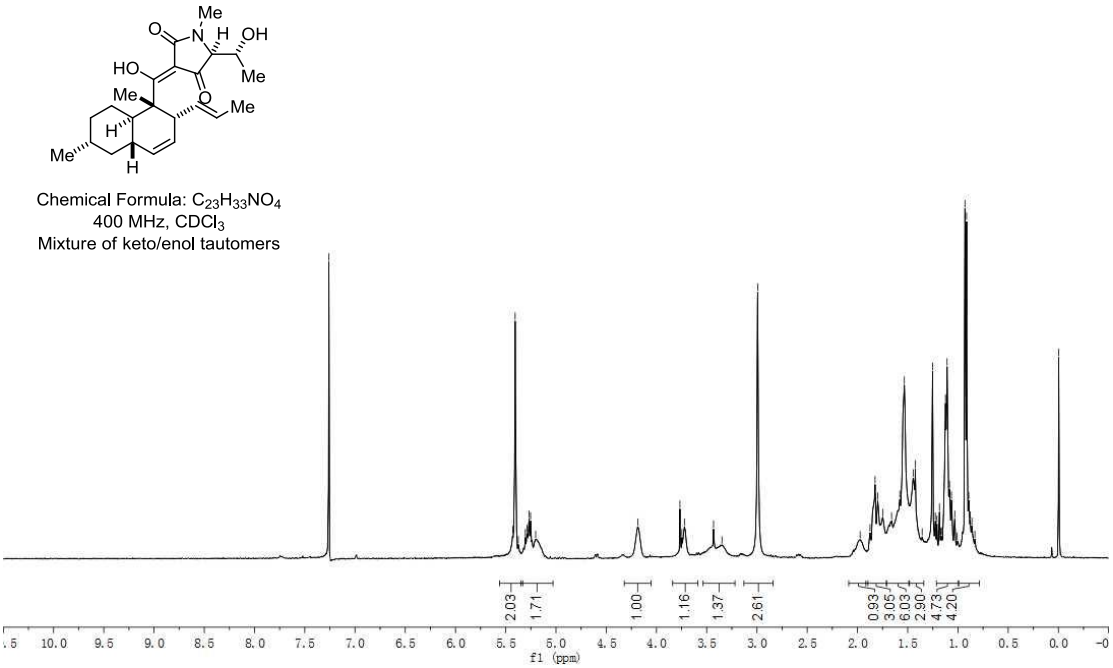
Chemical Formula: $C_{24}H_{35}NO_4$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers


Chemical Formula: $C_{29}H_{39}NO_5$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)

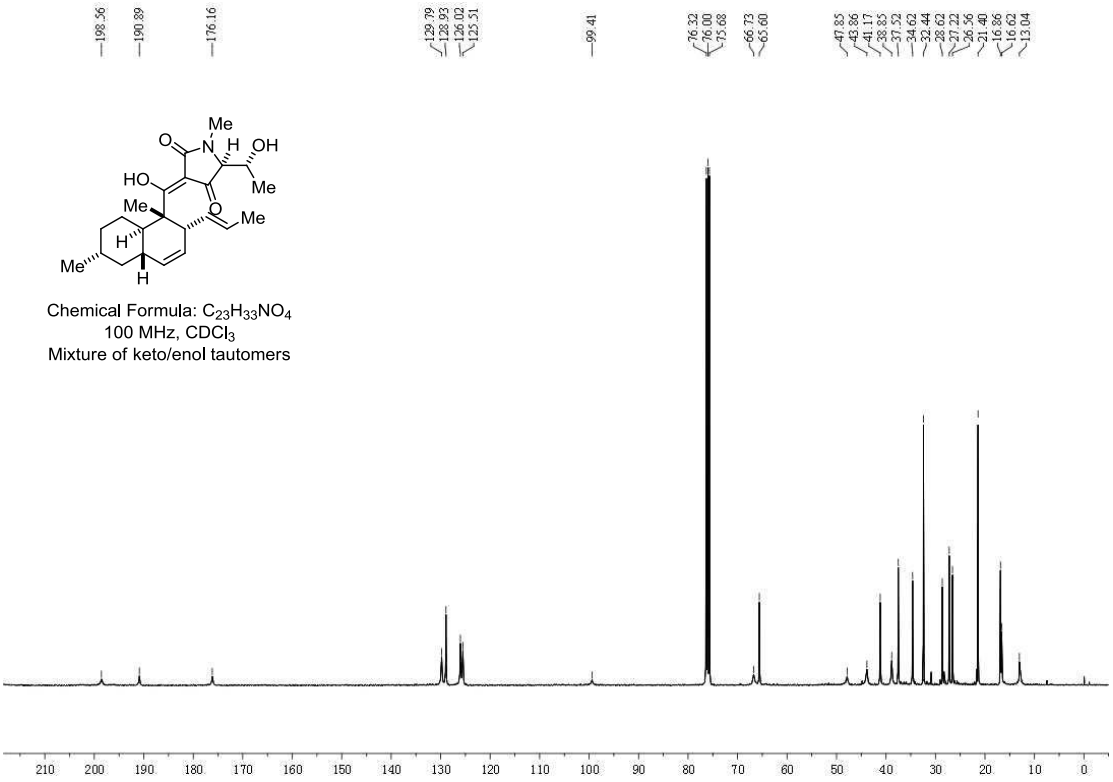

Chemical Formula: $C_{29}H_{39}NO_5$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers


Chemical Formula: $C_{31}H_{40}N_2O_4$
400 Hz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)

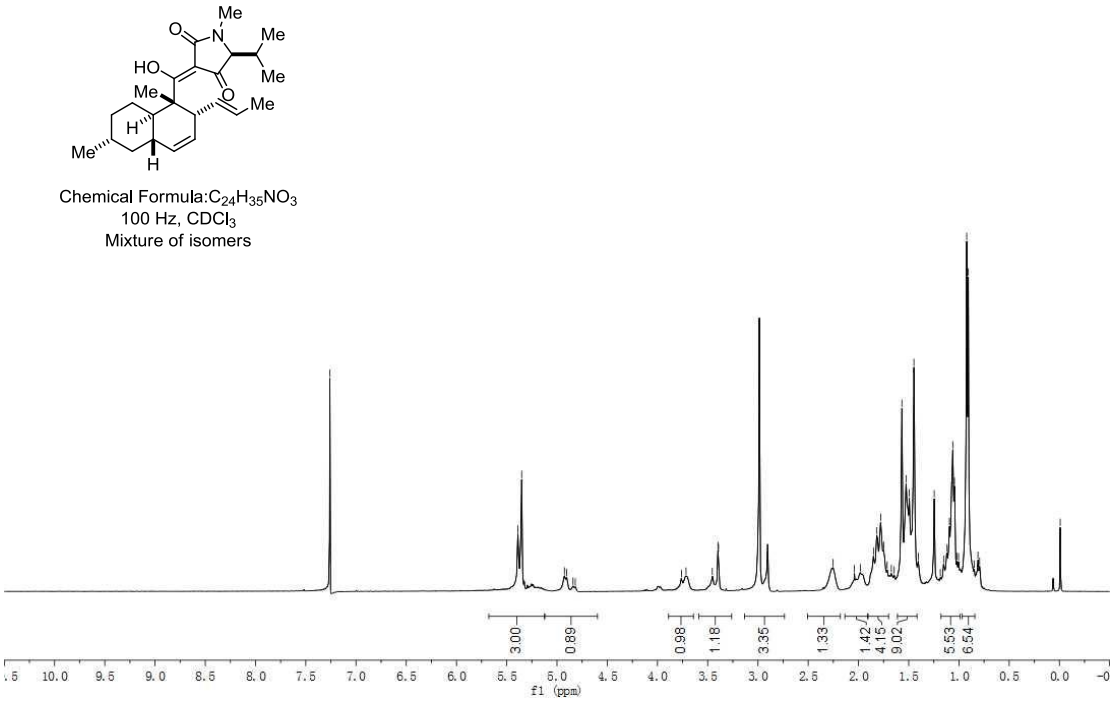

Chemical Formula: $C_{31}H_{40}N_2O_4$
100 Hz, CDCl3
Mixture of keto/enol tautomers
f1 (ppm)

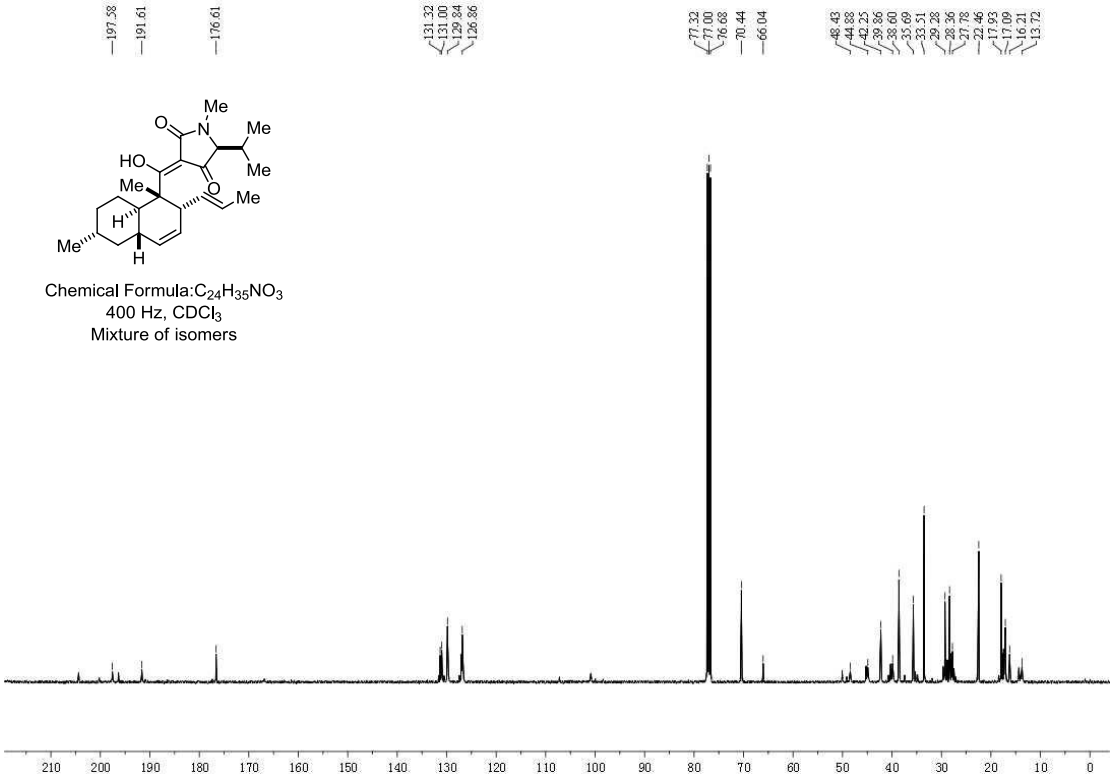


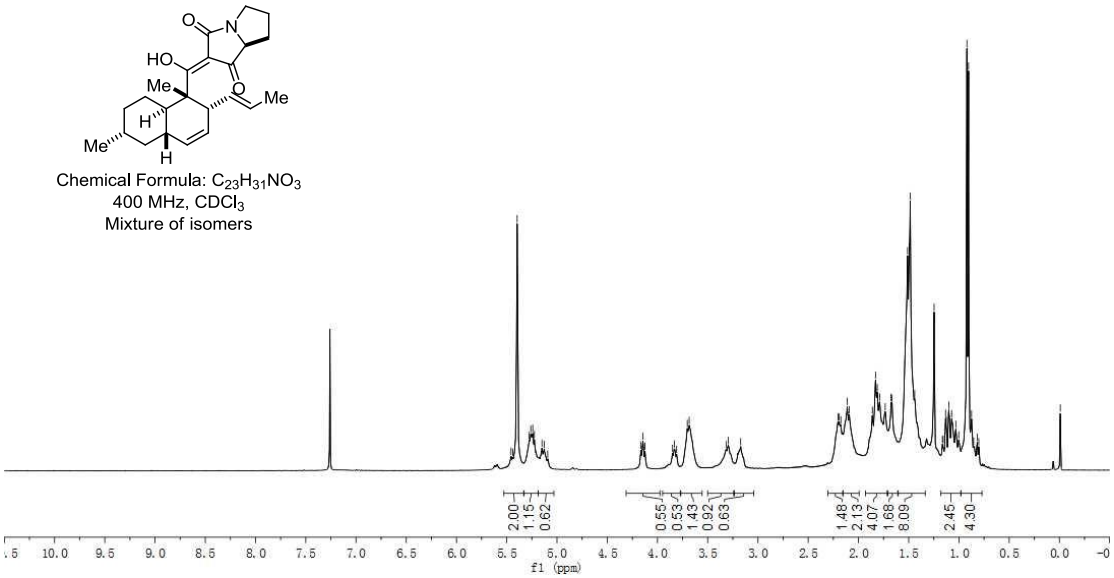
Chemical Formula: $C_{23}H_{33}NO_4$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers

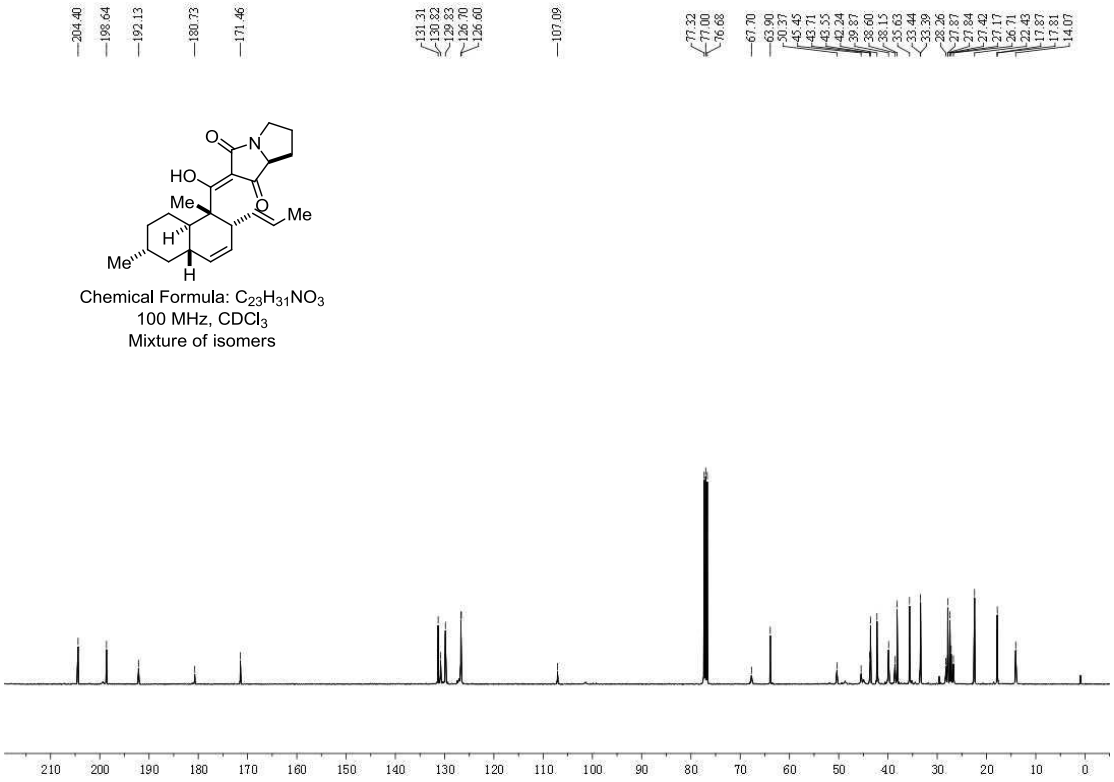


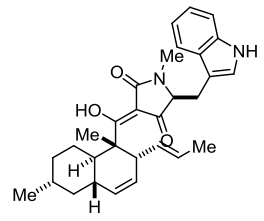
Chemical Formula: $C_{23}H_{33}NO_4$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers


Chemical Formula:C24H35NO3
100 Hz, CDCl3
Mixture of isomers
f1 (ppm)

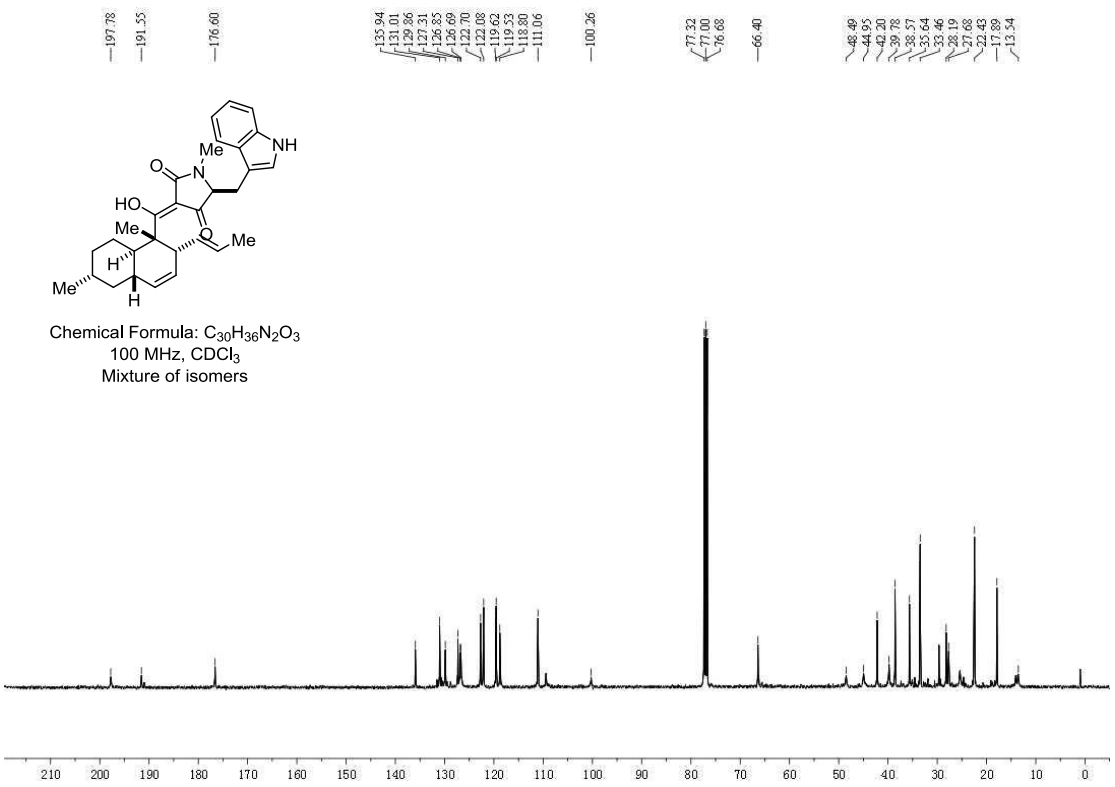

Chemical Formula:C24H35NO3
400 Hz, CDCl3
Mixture of isomers


HO
Me
O
N
O
Me
H
Me
H
Chemical Formula: $C_{23}H_{31}NO_3$
400 MHz, $CDCl_3$
Mixture of isomers
f1 (ppm)

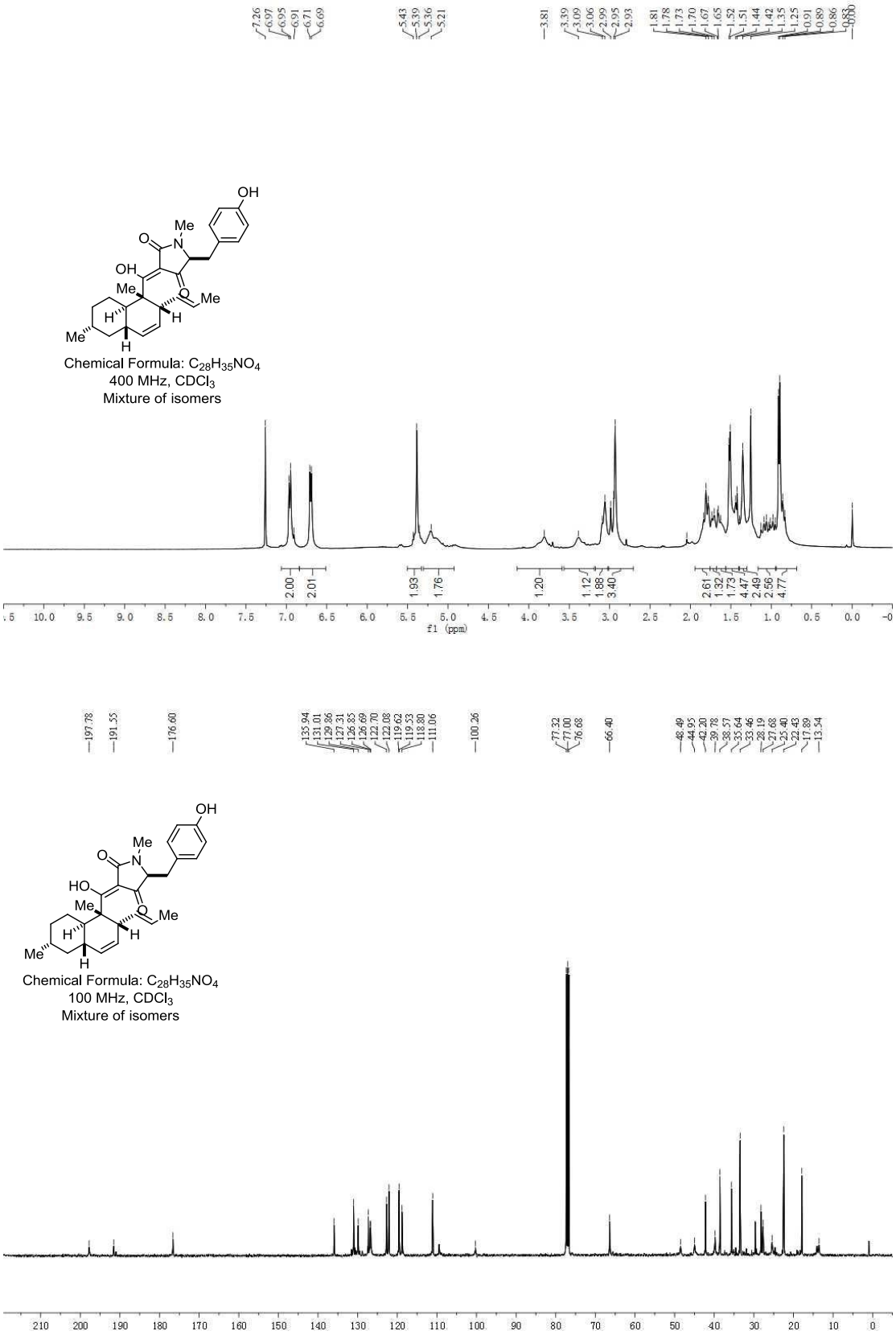

HO
Me
O
N
O
Me
H
Me
H
Chemical Formula: $C_{23}H_{31}NO_3$
100 MHz, $CDCl_3$
Mixture of isomers

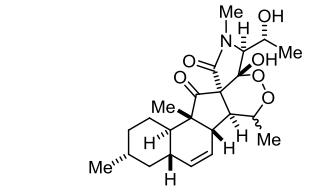


Chemical Formula: $C_{30}H_{36}N_2O_3$
400 MHz, $CDCl_3$
Mixture of isomers

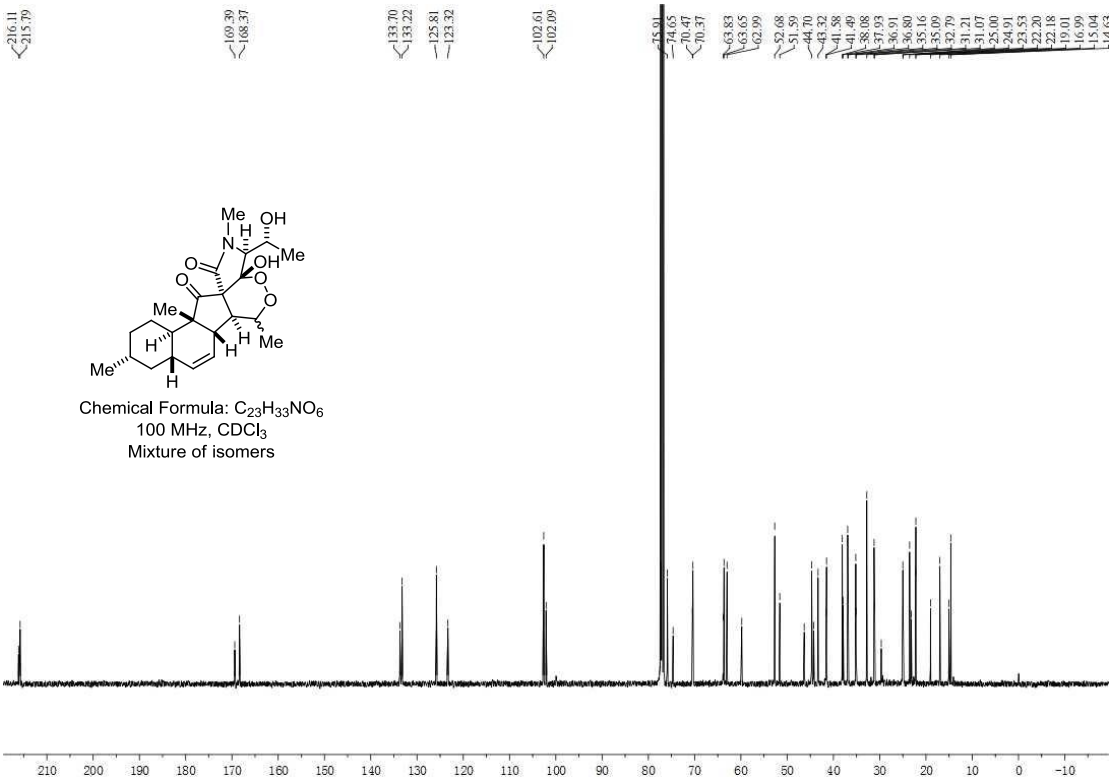


Chemical Formula: $C_{30}H_{36}N_2O_3$
100 MHz, $CDCl_3$
Mixture of isomers

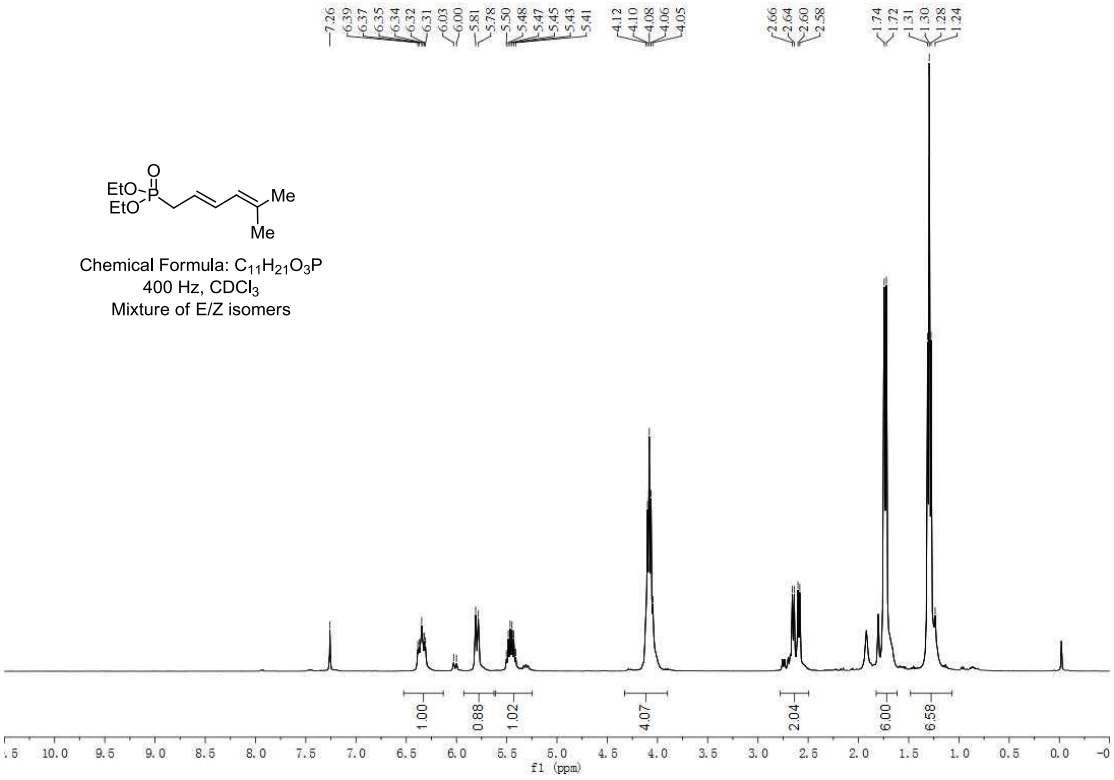

Chemical Formula: $C_{28}H_{35}NO_4$
400 MHz, $CDCl_3$
Mixture of isomers
f1 (ppm)
Chemical Formula: $C_{28}H_{35}NO_4$
100 MHz, $CDCl_3$
Mixture of isomers



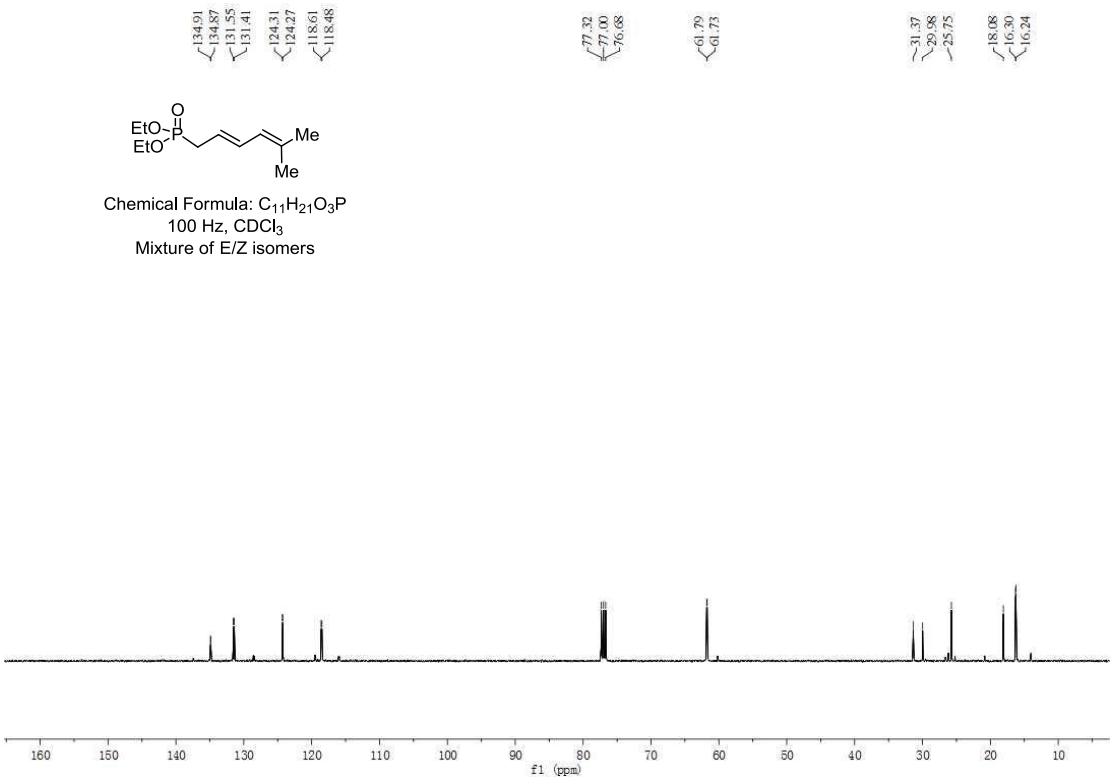
Chemical Formula: $C_{23}H_{33}NO_6$
400 MHz, $CDCl_3$
Mixture of isomers



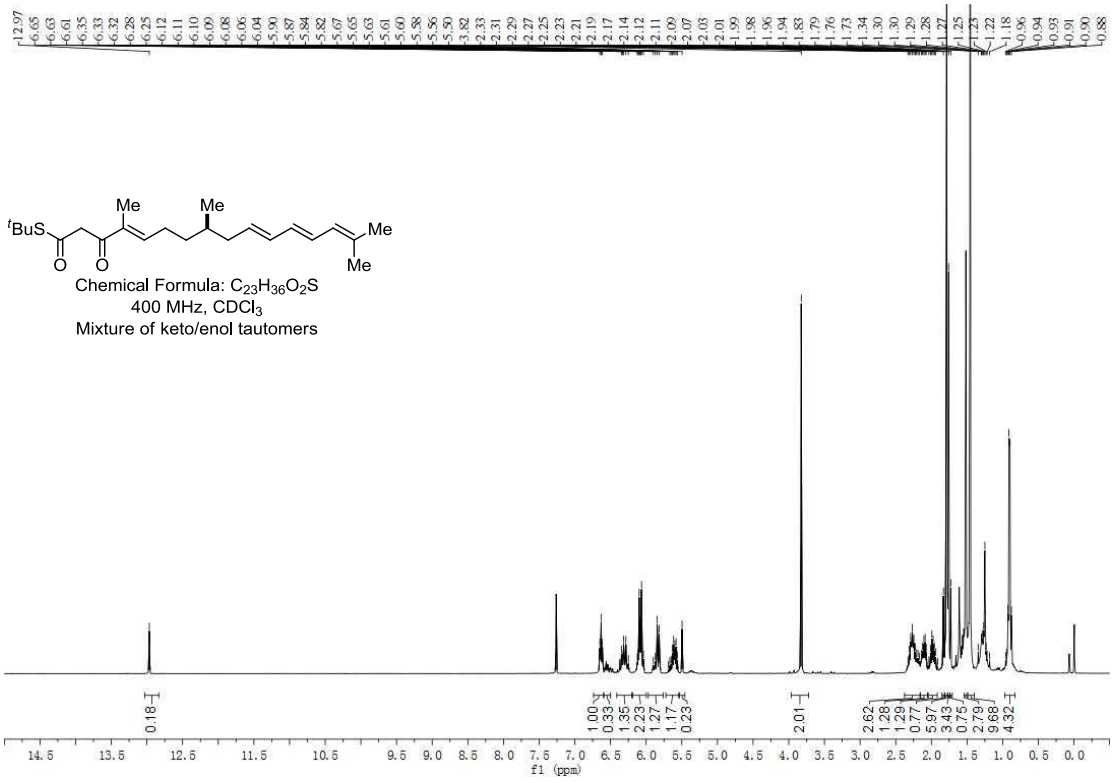
Chemical Formula: $C_{23}H_{33}NO_6$
100 MHz, $CDCl_3$
Mixture of isomers



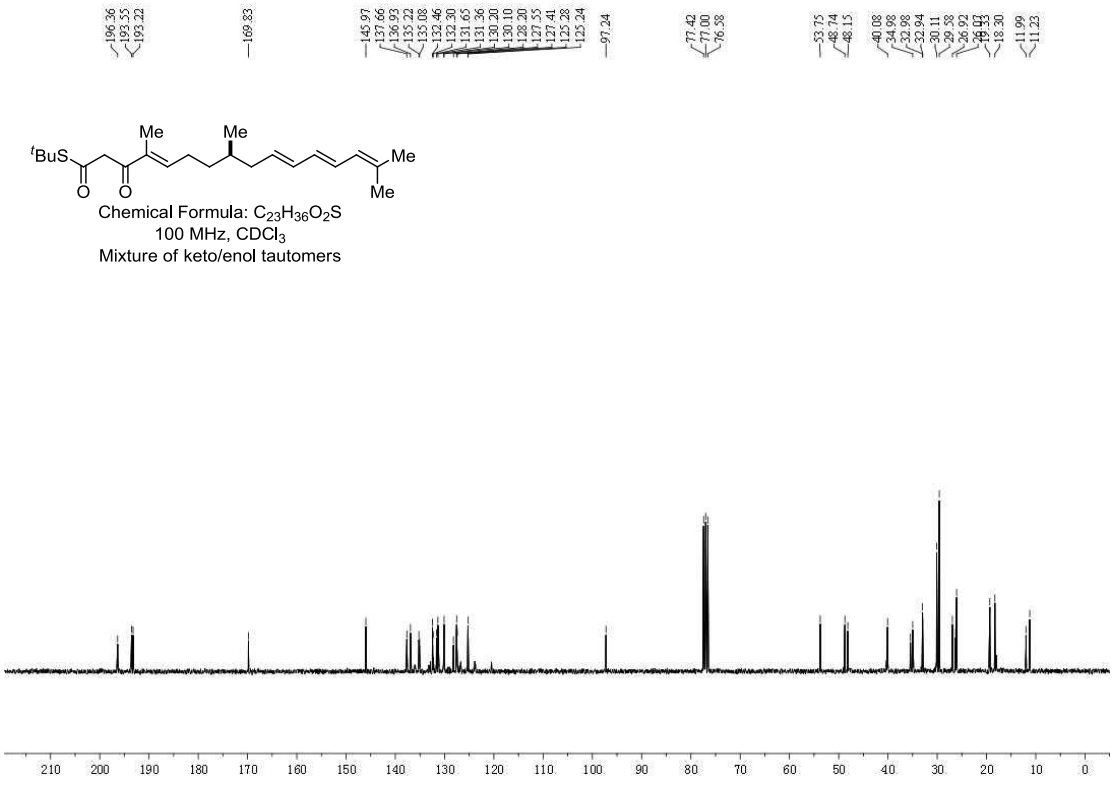
Chemical Formula: $C_{11}H_{21}O_3P$
400 Hz, $CDCl_3$
Mixture of E/Z isomers



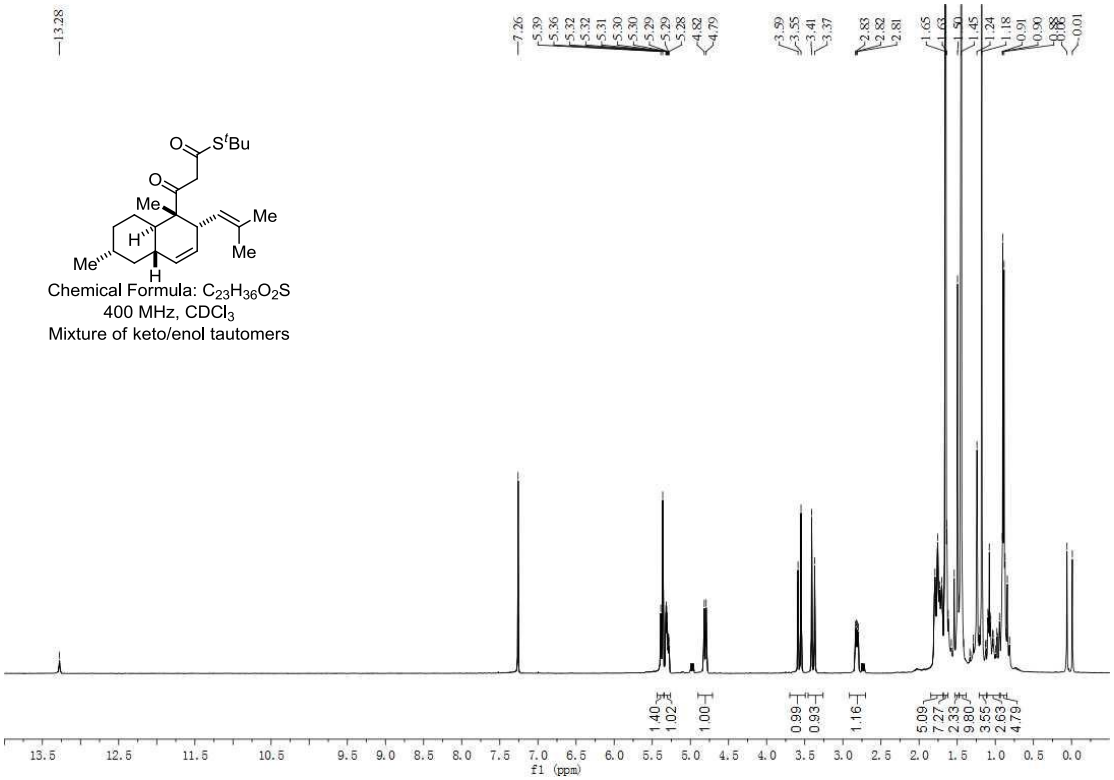
Chemical Formula: $C_{11}H_{21}O_3P$
100 Hz, $CDCl_3$
Mixture of E/Z isomers

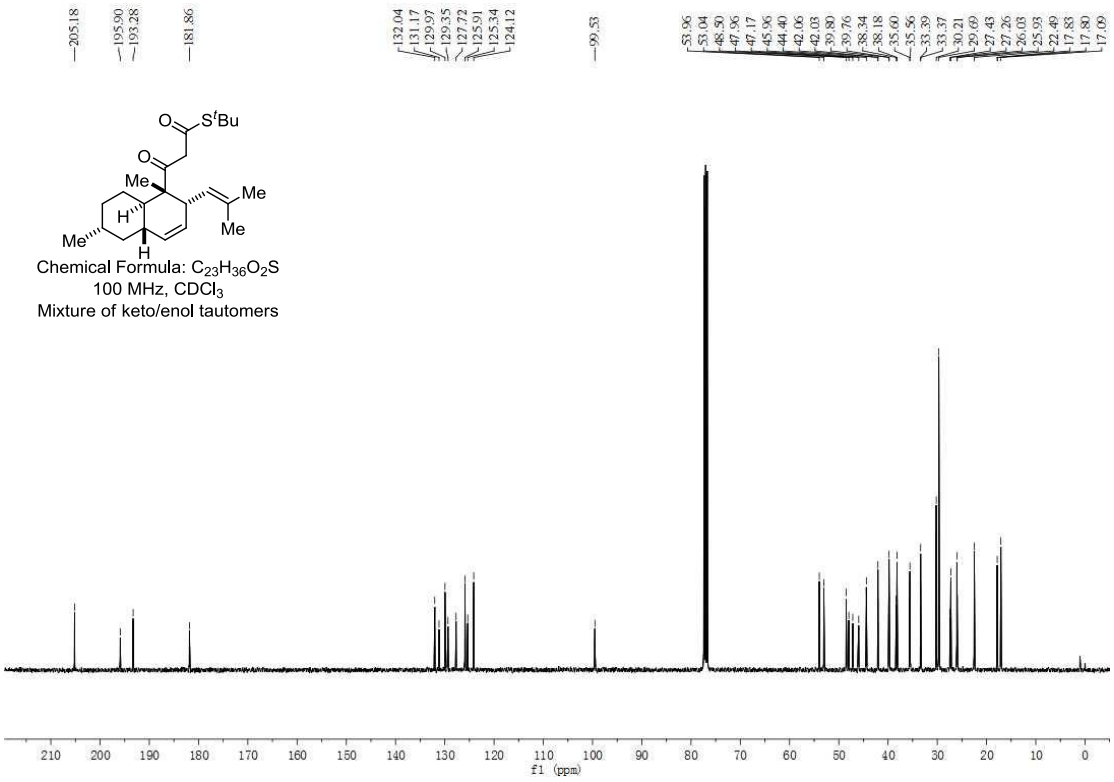


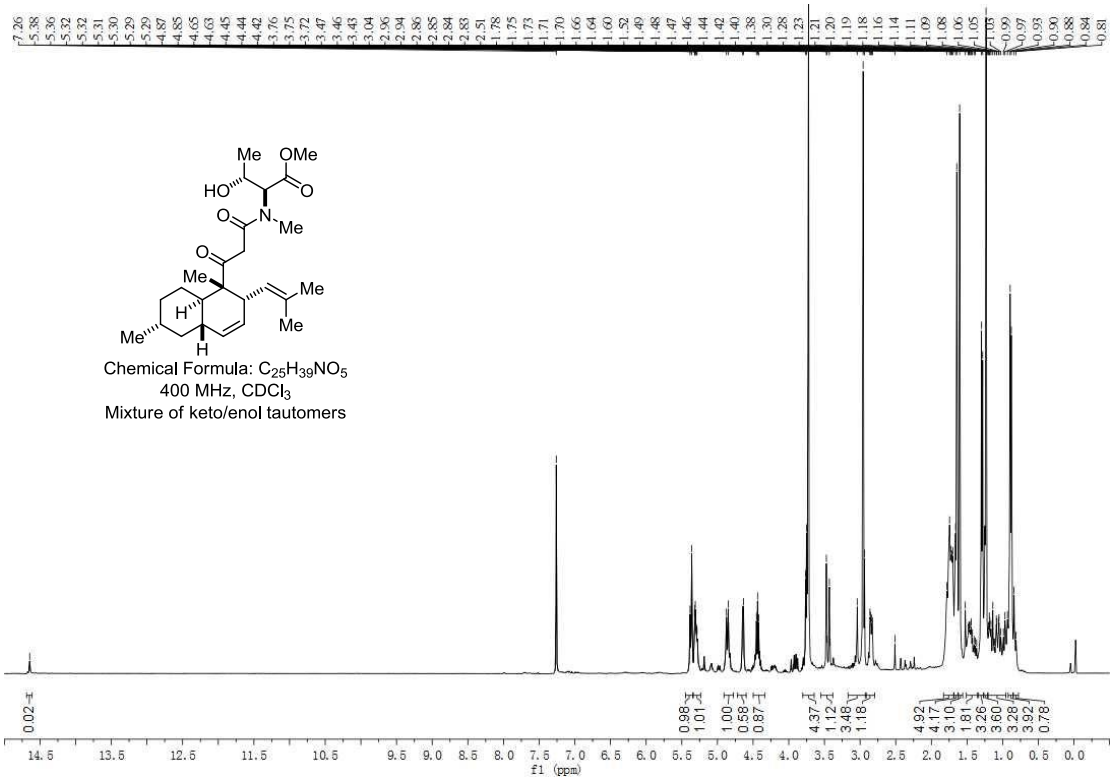
Chemical Formula: $C_{23}H_{36}O_2S$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers

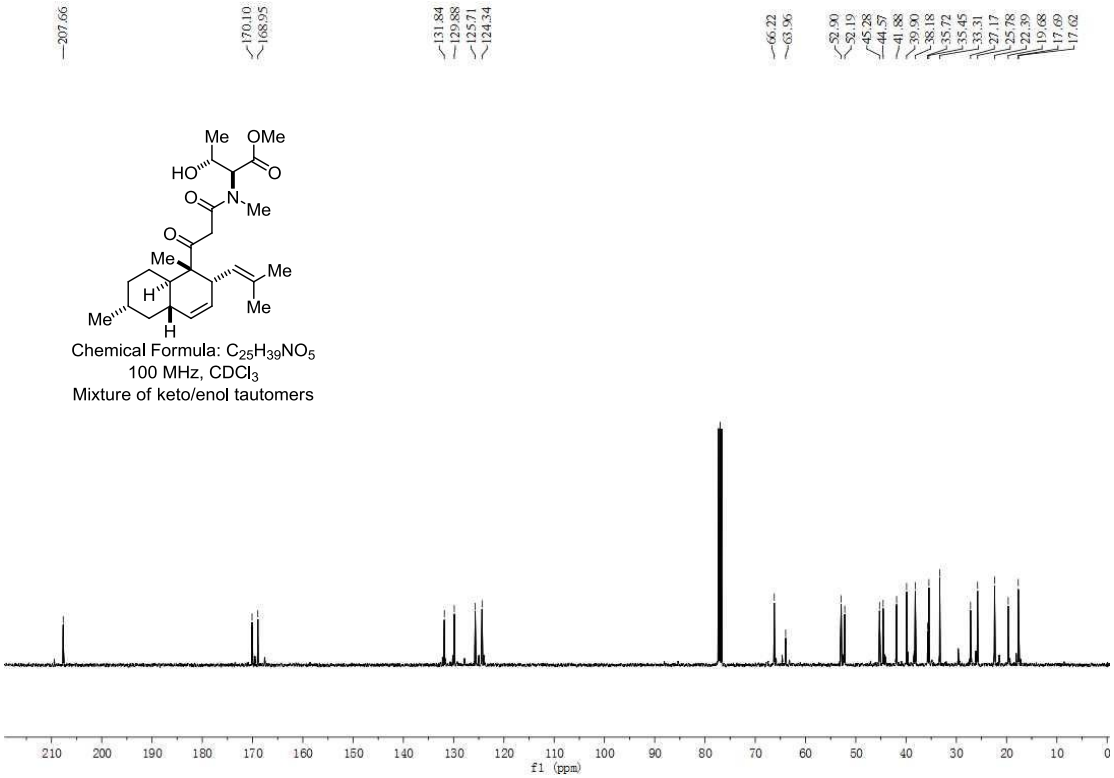


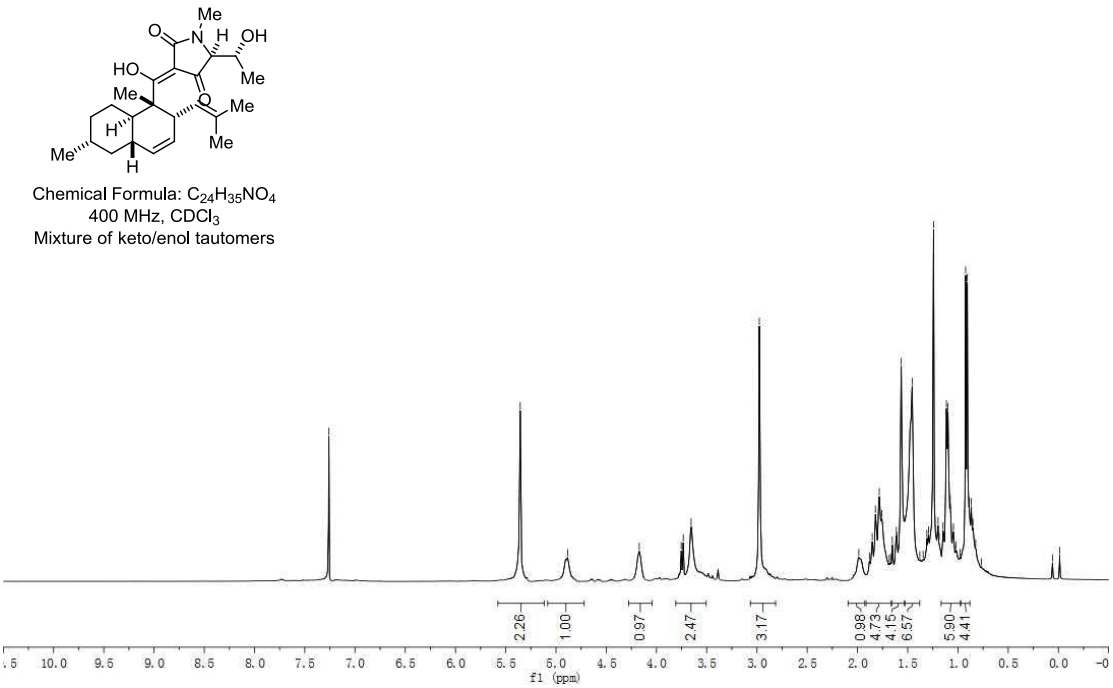
Chemical Formula: $C_{23}H_{36}O_2S$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers

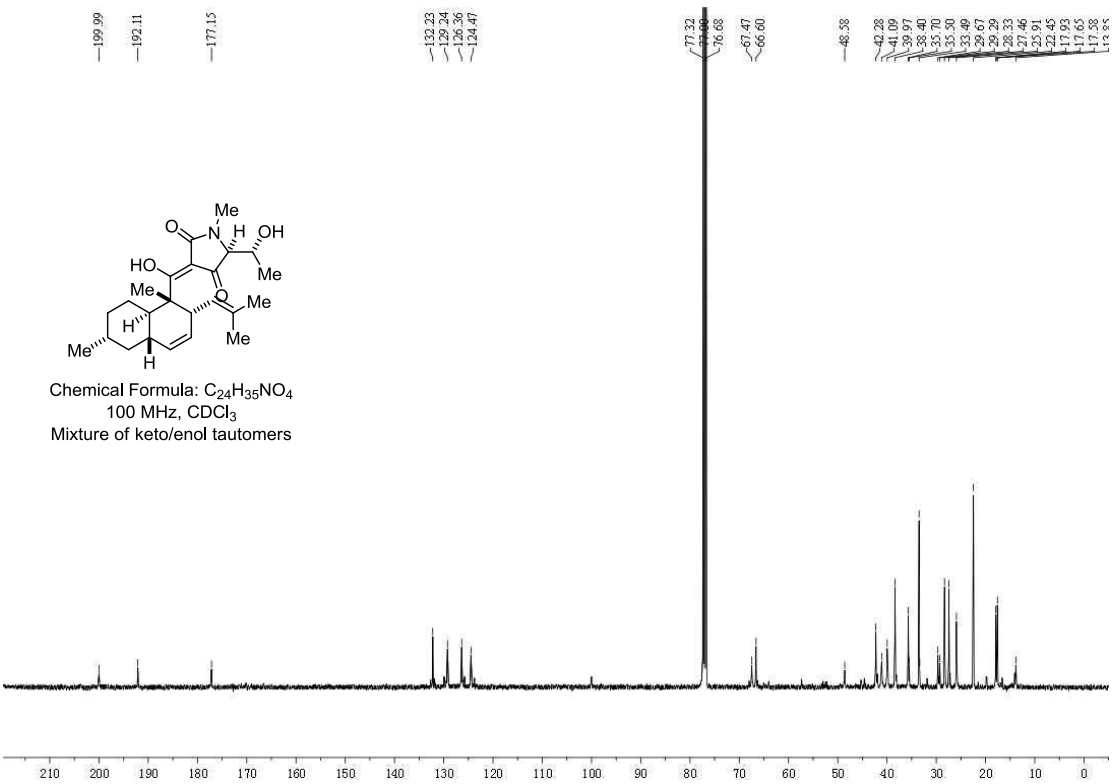

Chemical Formula: $C_{23}H_{36}O_2S$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)

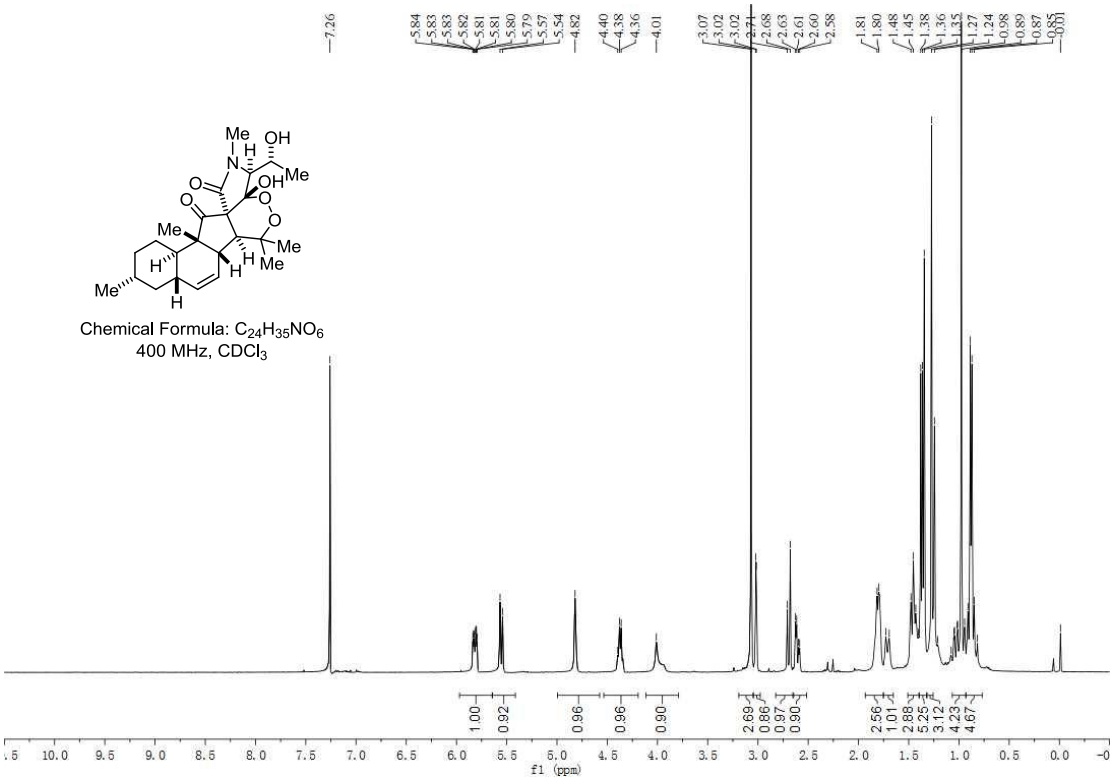

Chemical Formula: $C_{23}H_{36}O_2S$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)

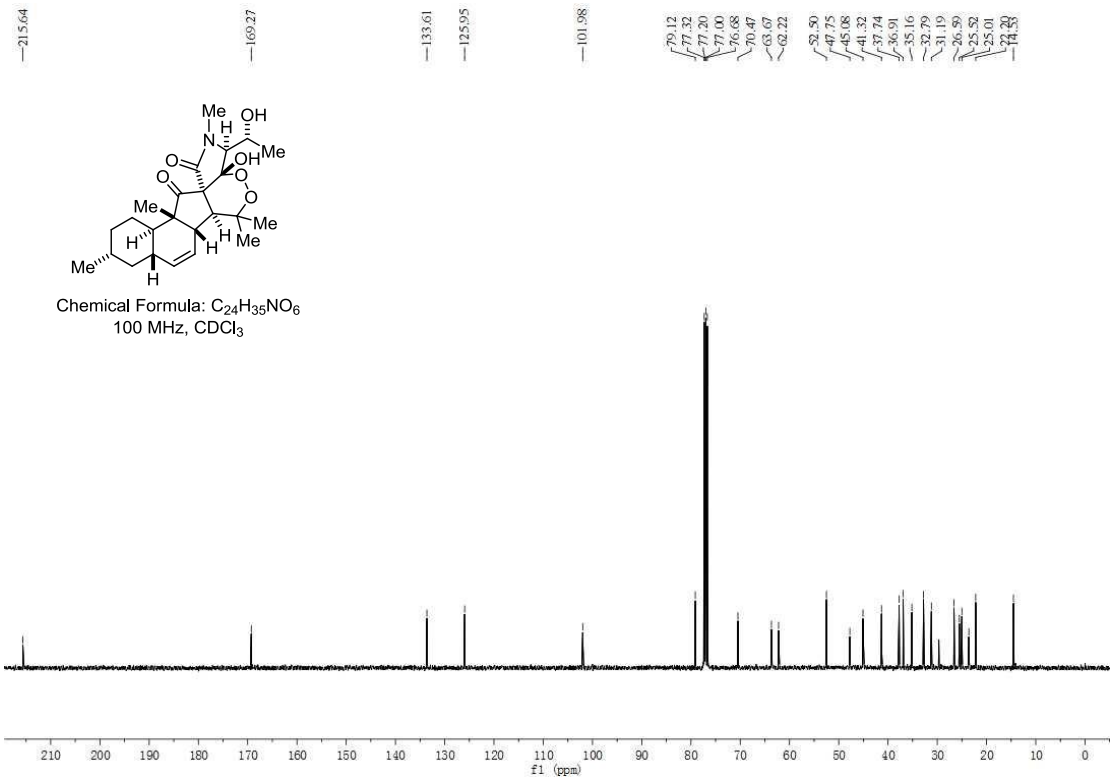

Chemical Formula: $C_{25}H_{39}NO_5$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)

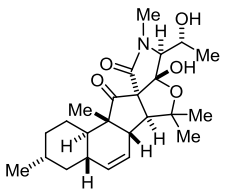

Chemical Formula: $C_{25}H_{39}NO_5$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)


Me
O
N
H
OH
HO
Me
Me
O
Me
H
Me
Me
H
Chemical Formula: C24H35NO4
400 MHz, CDCl3
Mixture of keto/enol tautomers
f1 (ppm)

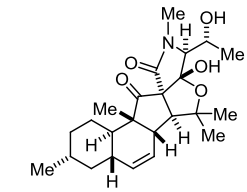

Me
O
N
H
OH
HO
Me
Me
O
Me
H
Me
Me
H
Chemical Formula: C24H35NO4
100 MHz, CDCl3
Mixture of keto/enol tautomers


Chemical Formula: $C_{24}H_{35}NO_6$
400 MHz, $CDCl_3$
f1 (ppm)

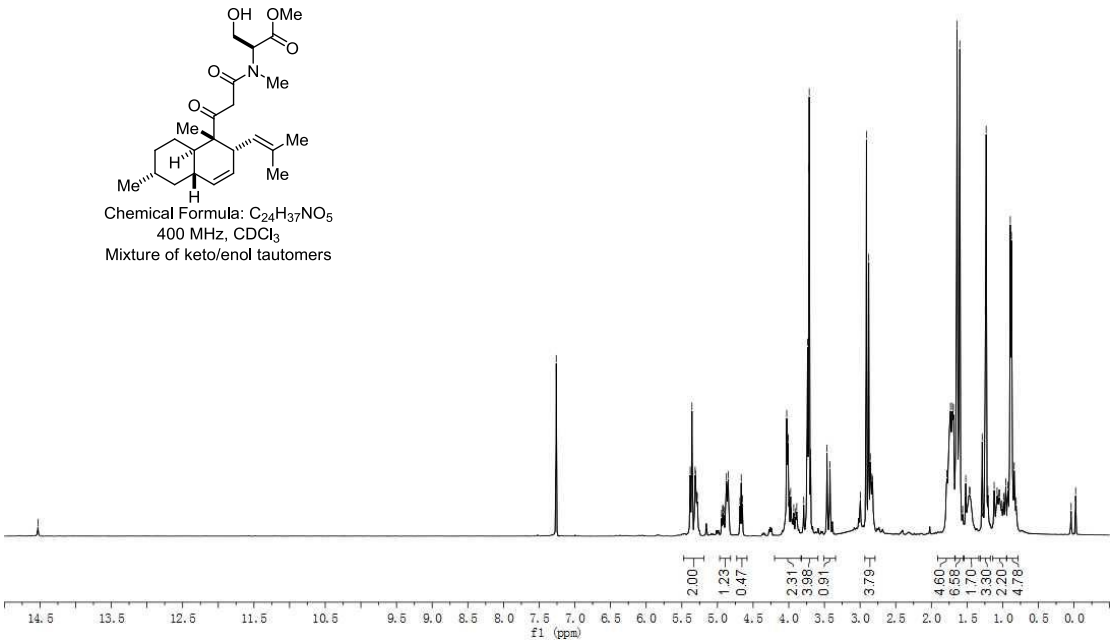

Chemical Formula: $C_{24}H_{35}NO_6$
100 MHz, $CDCl_3$
f1 (ppm)

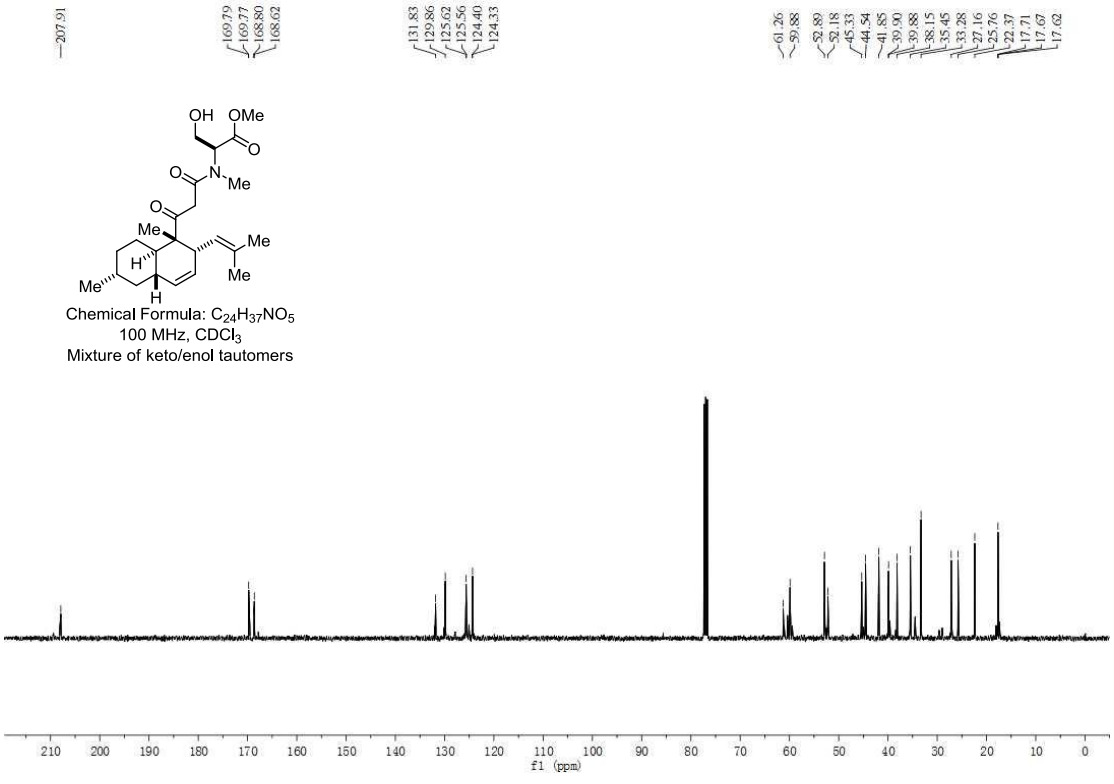


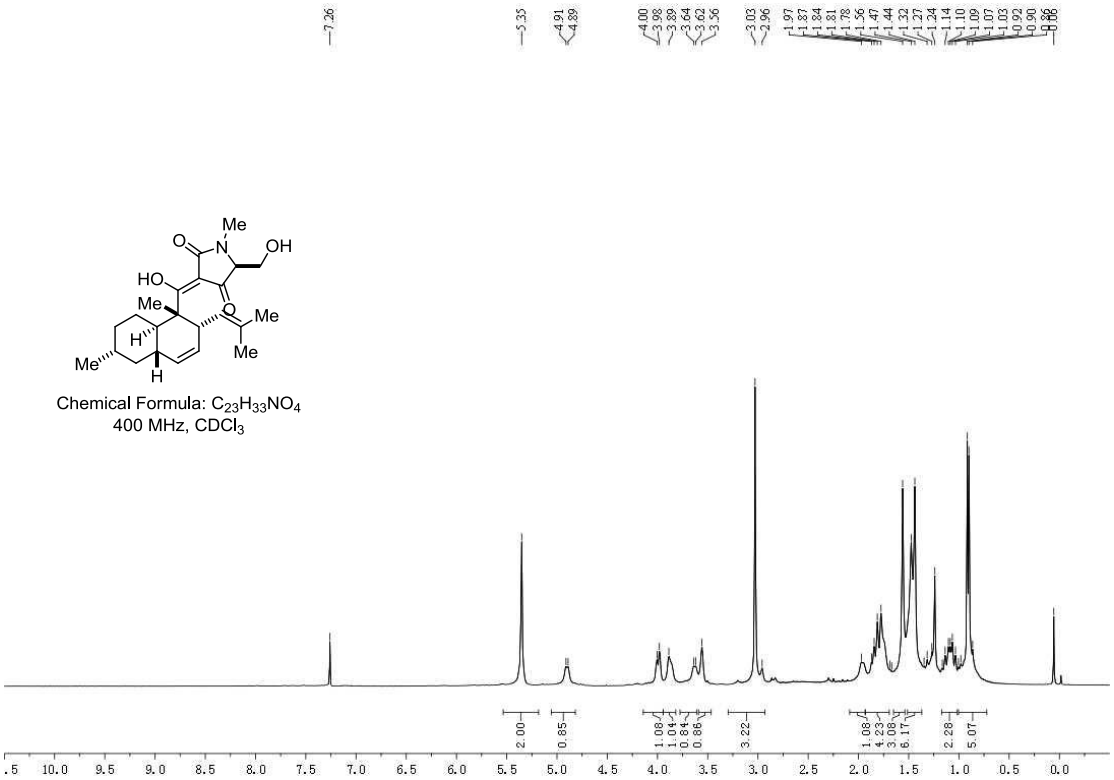
Chemical Formula: $C_{24}H_{35}NO_5$
400 MHz, $CDCl_3$

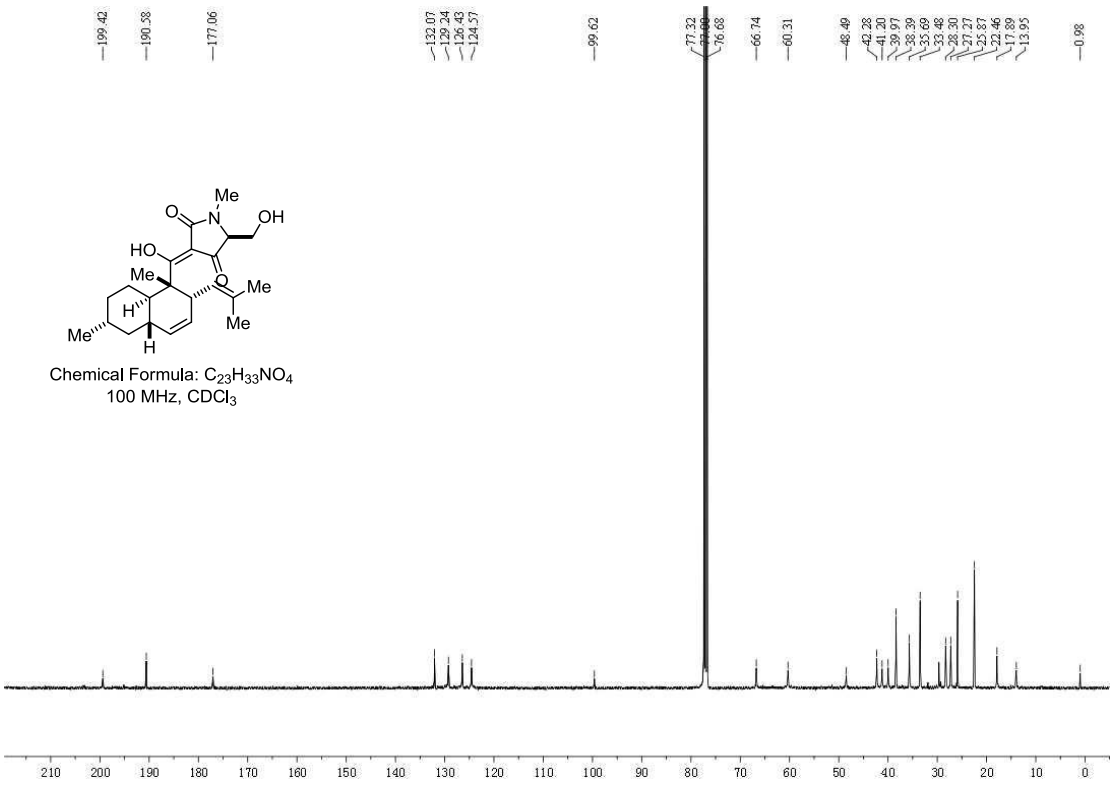


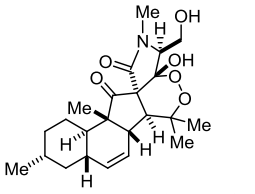
Chemical Formula: $C_{24}H_{35}NO_5$
100 MHz, $CDCl_3$


OH
OMe
O
O
N
Me
O
Me
H
Me
Me
Me
H
Chemical Formula: C24H37NO5
400 MHz, CDCl3
Mixture of keto/enol tautomers
14.53
7.26
5.38
5.36
5.31
5.31
5.29
5.28
4.92
4.87
4.85
4.68
4.67
4.65
4.03
4.01
4.01
3.74
3.72
3.71
3.46
2.91
2.88
1.73
1.70
1.69
1.64
1.60
1.24
1.23
0.89
0.88
0.02
2.00
1.23
0.47
2.31
3.98
0.91
3.79
4.60
6.58
1.70
3.30
2.20
4.78
f1 (ppm)

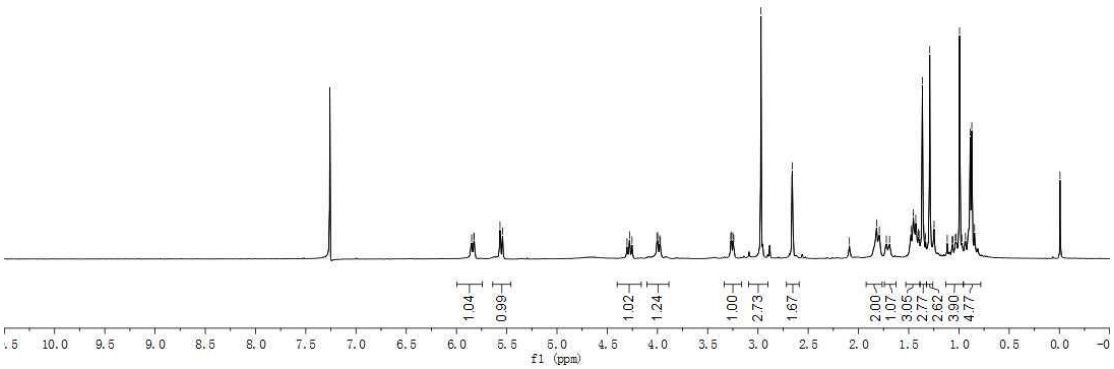

207.91
169.79
169.77
168.80
168.62
131.83
129.86
125.62
125.56
124.40
124.33
61.26
59.88
52.89
52.18
45.33
44.54
41.85
39.90
39.88
38.15
35.45
33.28
27.16
25.76
22.37
17.71
17.67
17.62
OH
OMe
O
O
N
Me
O
Me
H
Me
Me
Me
H
Chemical Formula: C24H37NO5
100 MHz, CDCl3
Mixture of keto/enol tautomers
f1 (ppm)

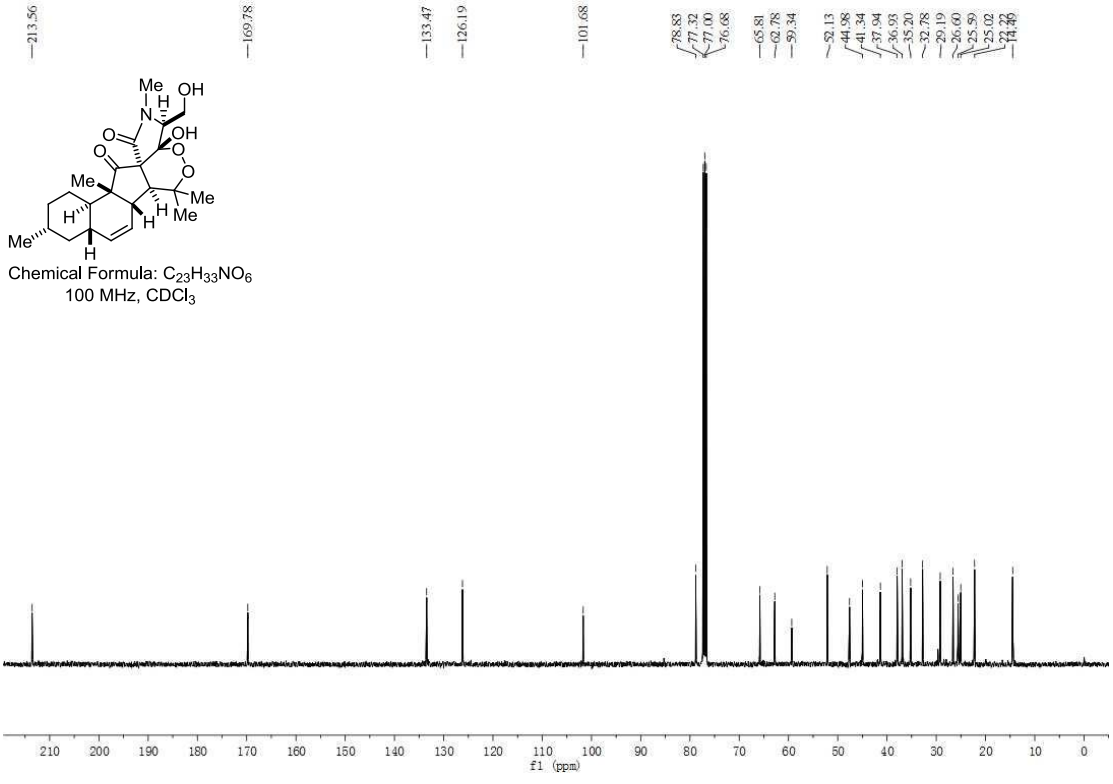

Me
O
N
OH
HO
Me
O
Me
H
Me
Me
H
Chemical Formula: C23H33NO4
400 MHz, CDCl3


Me
O
N
OH
HO
Me
O
Me
H
Me
Me
H
Chemical Formula: C23H33NO4
100 MHz, CDCl3

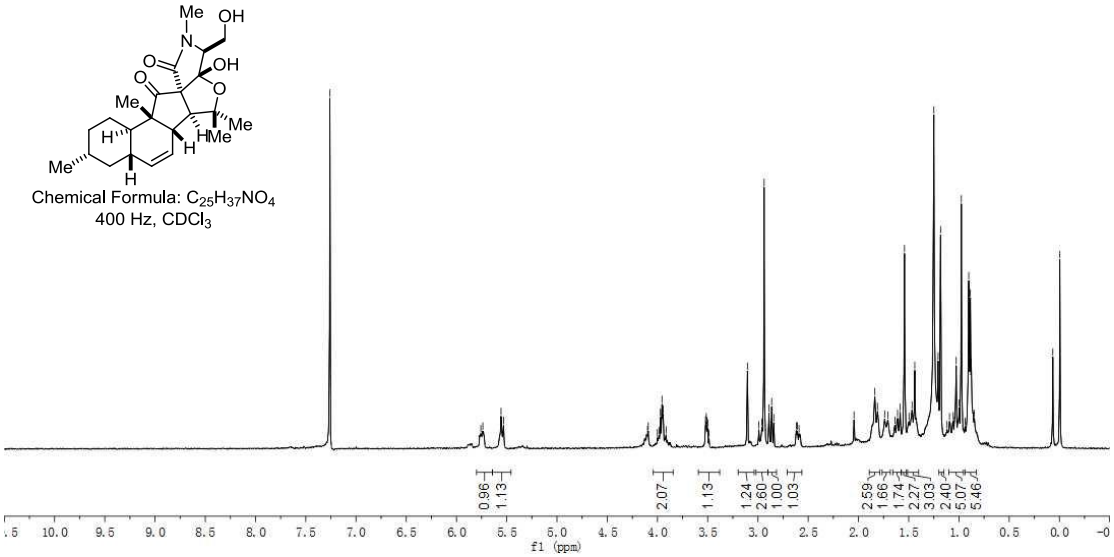


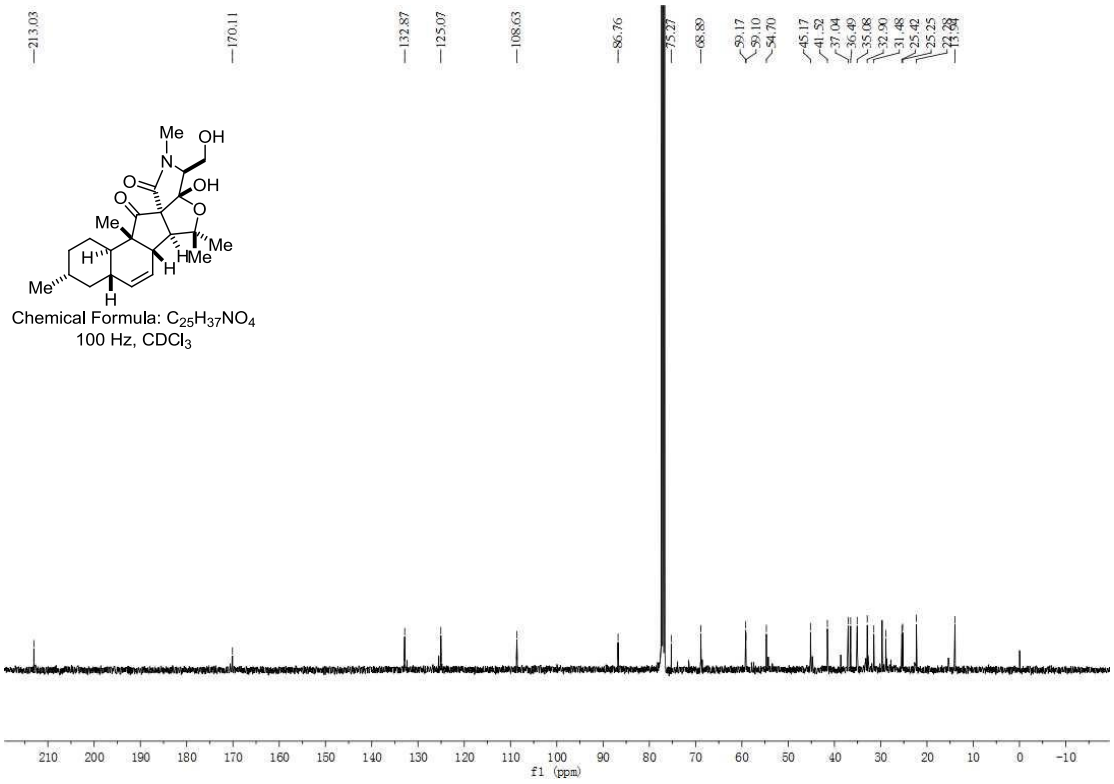
Chemical Formula: $C_{23}H_{33}NO_6$
400 MHz, $CDCl_3$

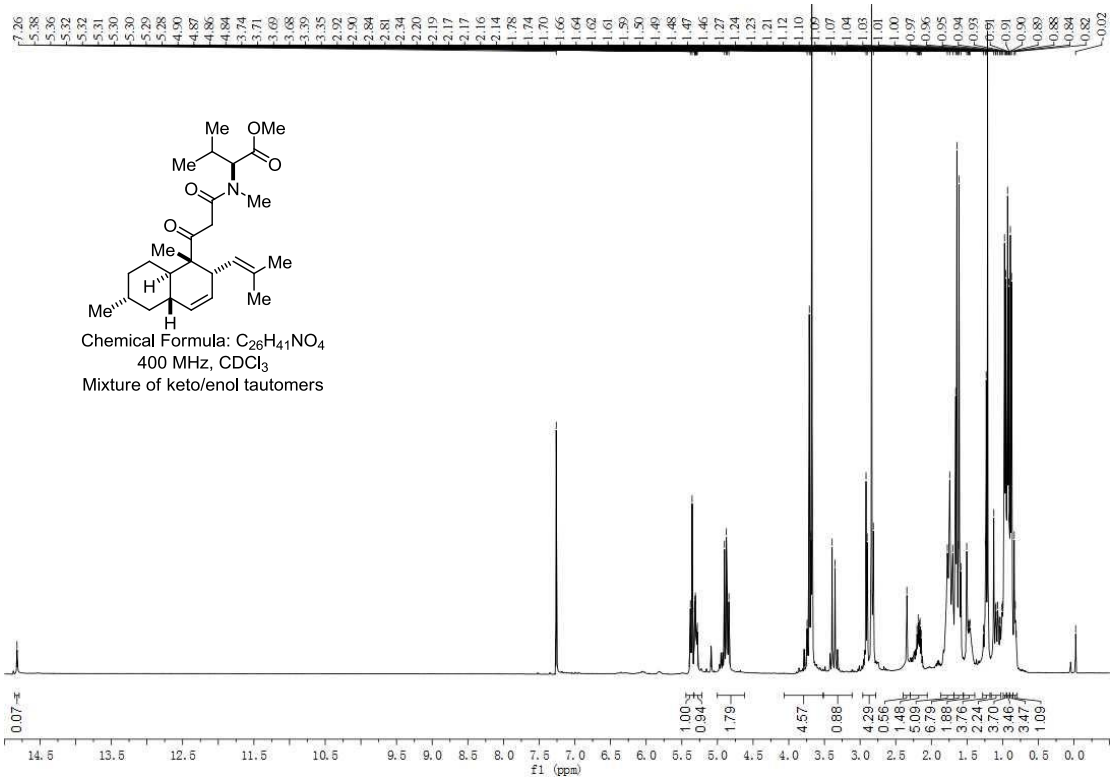


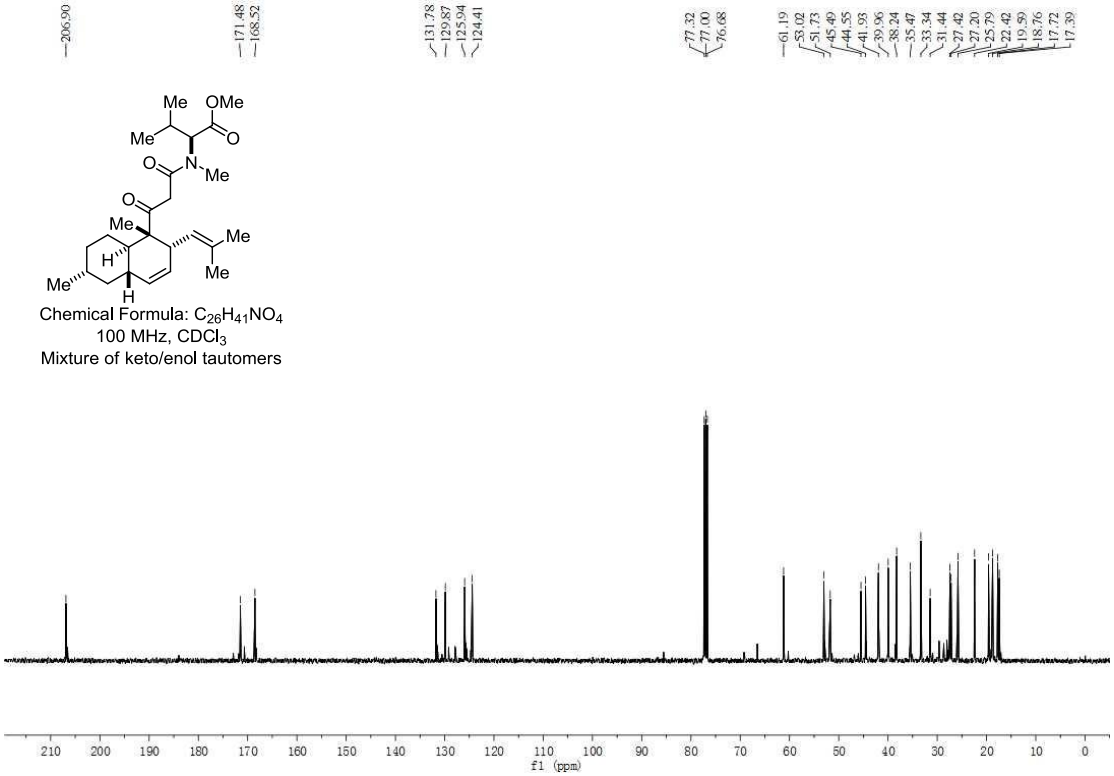


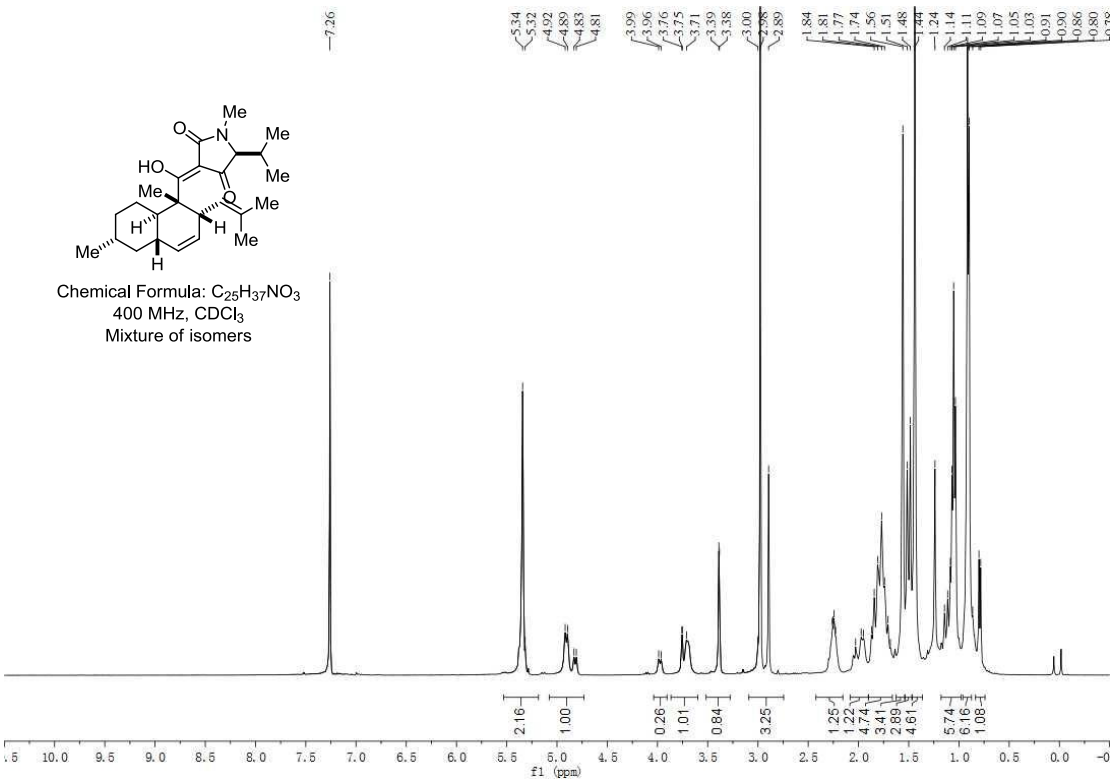
Chemical Formula: $C_{23}H_{33}NO_6$
100 MHz, $CDCl_3$

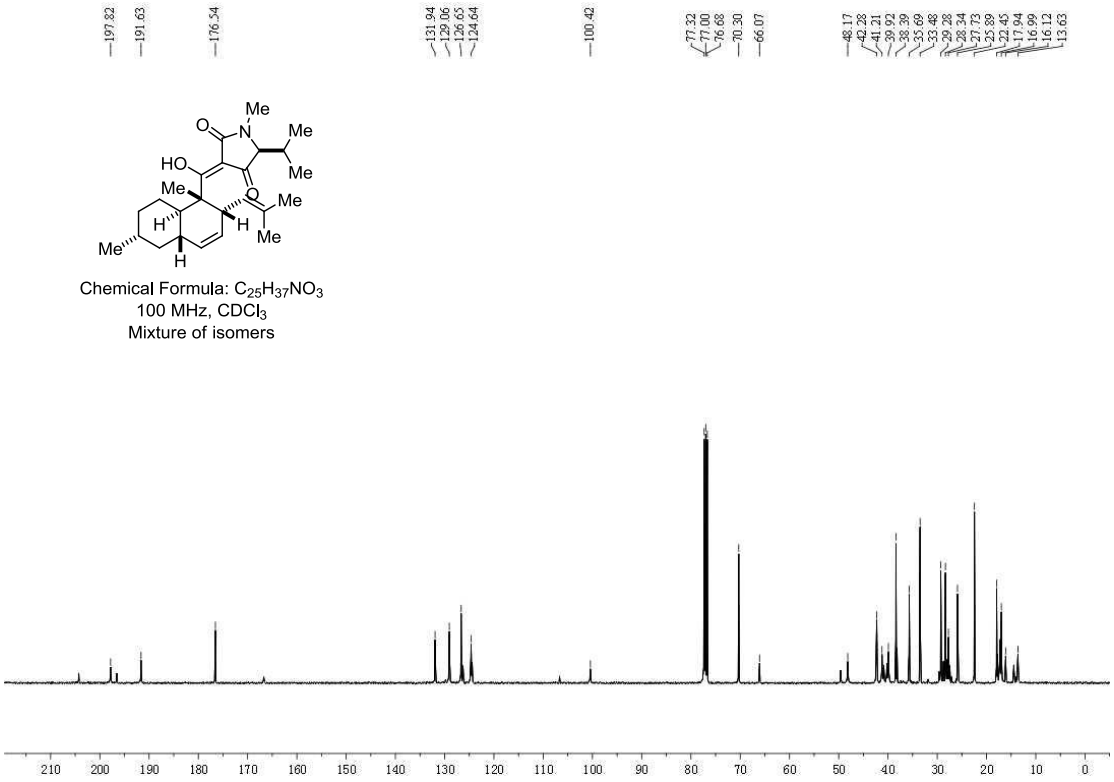

Chemical Formula: $C_{25}H_{37}NO_4$
400 Hz, $CDCl_3$
f1 (ppm)

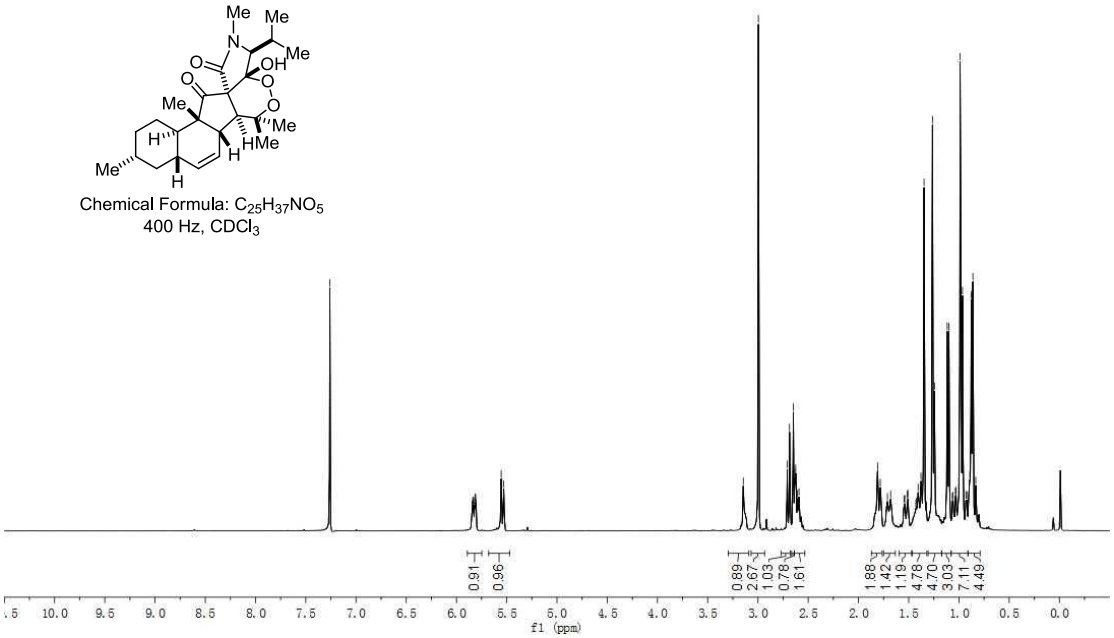

Chemical Formula: $C_{25}H_{37}NO_4$
100 Hz, $CDCl_3$
f1 (ppm)

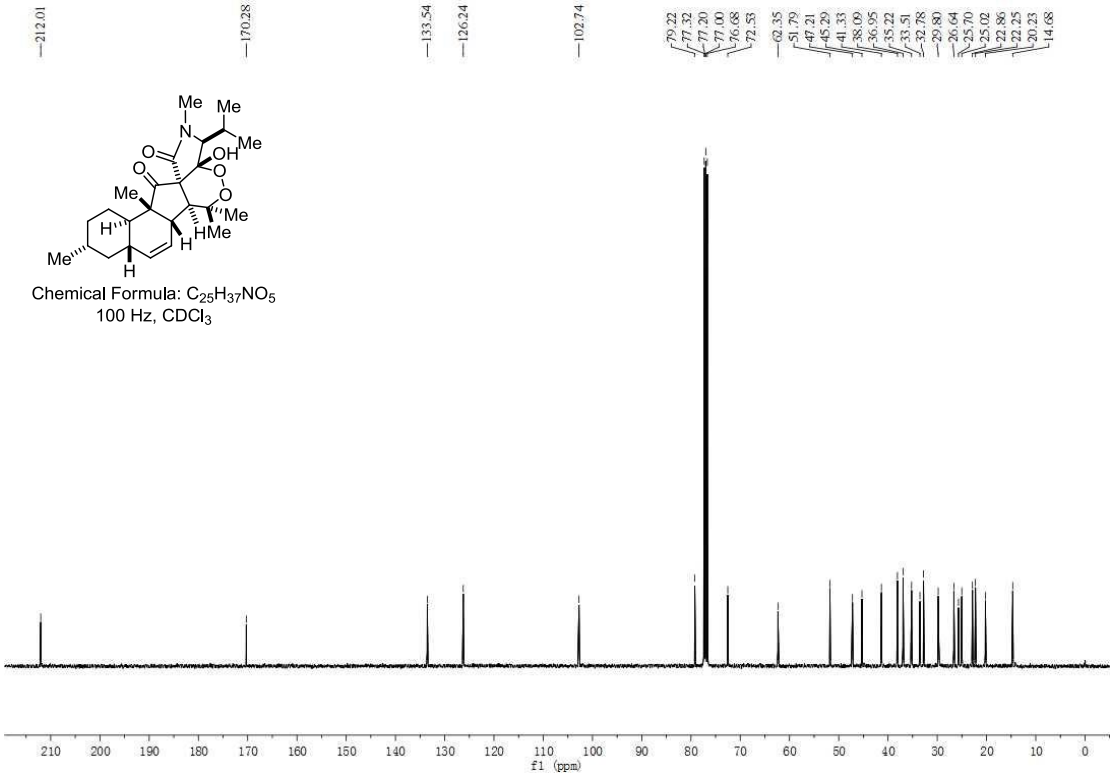

Me
OMe
Me
O
O
N
Me
O
Me
Me
H
Me
H
Chemical Formula: $C_{26}H_{41}NO_4$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)

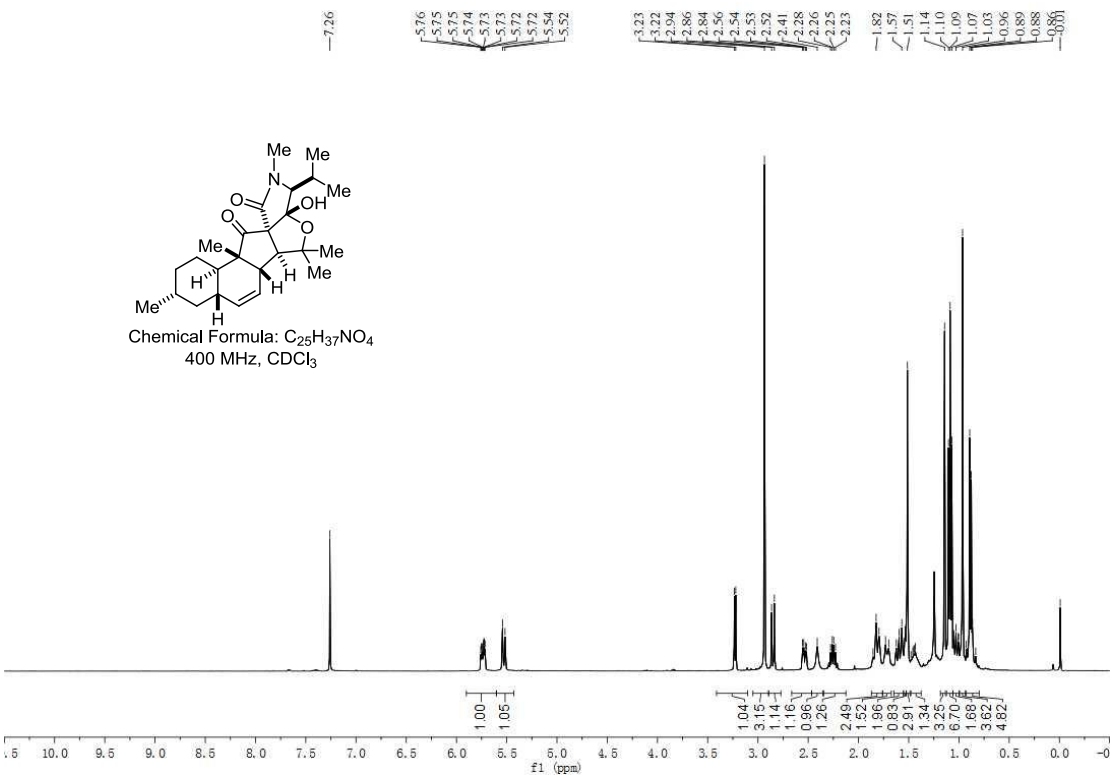

Me
OMe
Me
O
O
N
Me
O
Me
Me
H
Me
H
Chemical Formula: $C_{26}H_{41}NO_4$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)

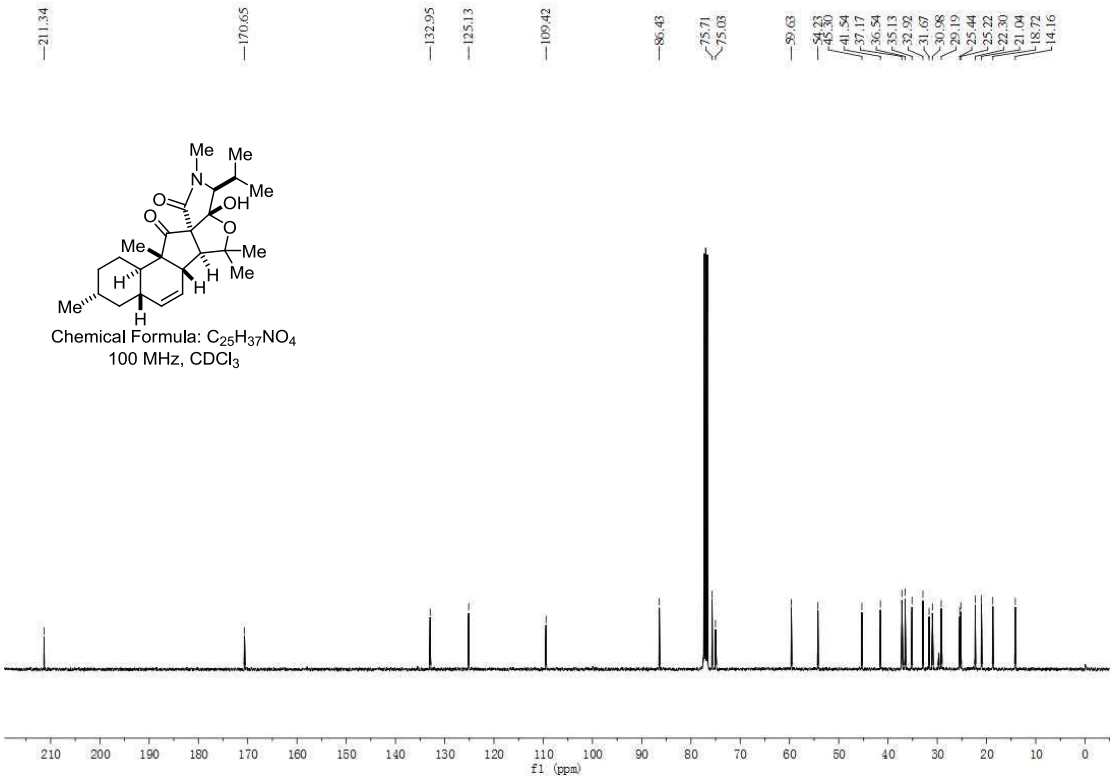

Chemical Formula: $C_{25}H_{37}NO_3$
400 MHz, $CDCl_3$
Mixture of isomers
f1 (ppm)

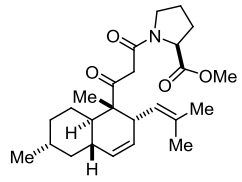

Chemical Formula: $C_{25}H_{37}NO_3$
100 MHz, $CDCl_3$
Mixture of isomers


Chemical Formula: $C_{25}H_{37}NO_5$
400 Hz, $CDCl_3$
f1 (ppm)

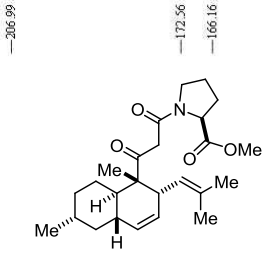

Chemical Formula: $C_{25}H_{37}NO_5$
100 Hz, $CDCl_3$
f1 (ppm)


Chemical Formula: C25H37NO4
400 MHz, CDCl3
f1 (ppm)

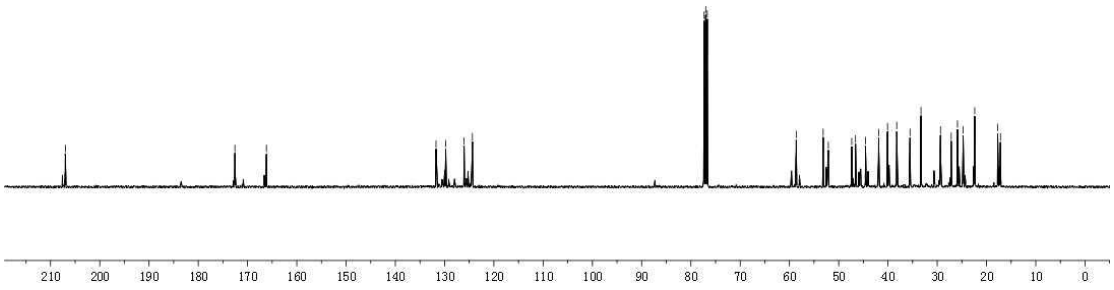

Chemical Formula: C25H37NO4
100 MHz, CDCl3
f1 (ppm)

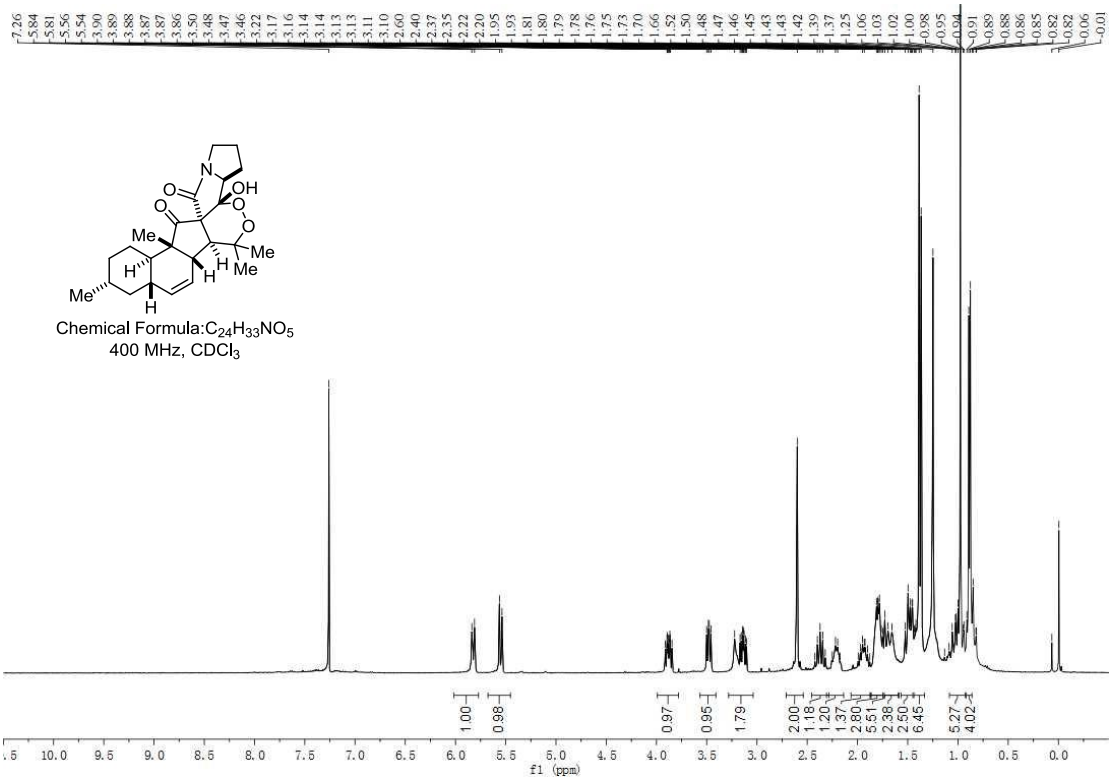


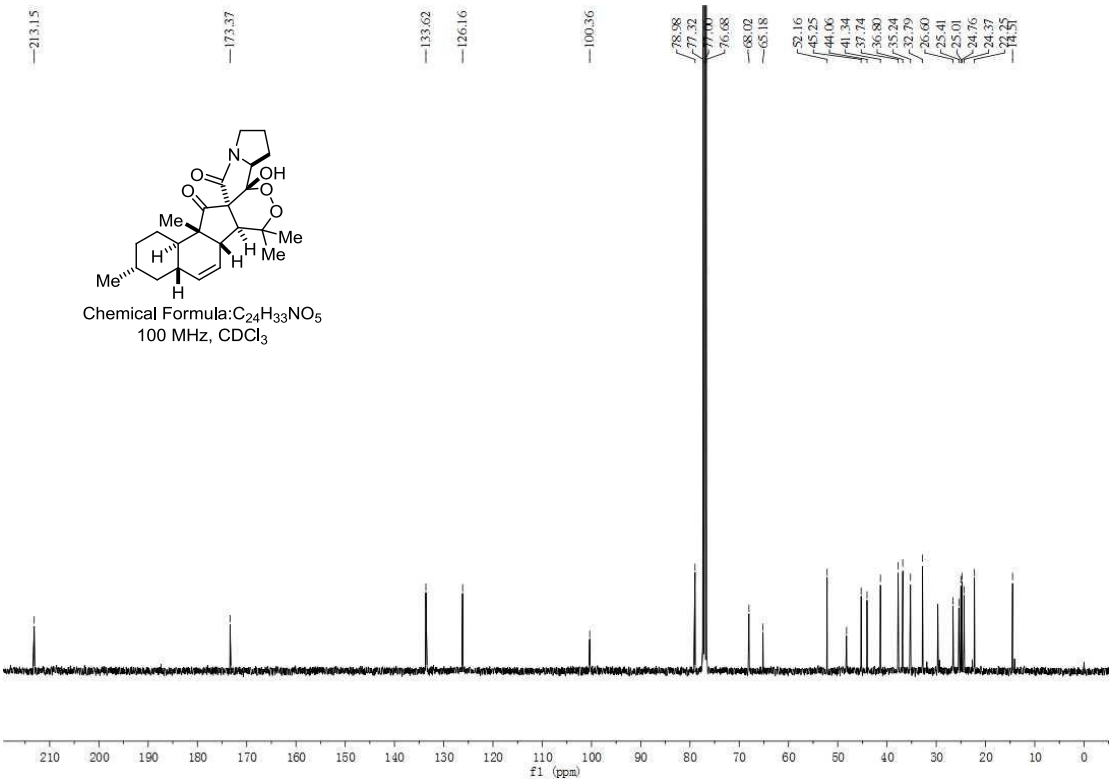
Chemical Formula: $C_{25}H_{37}NO_4$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers

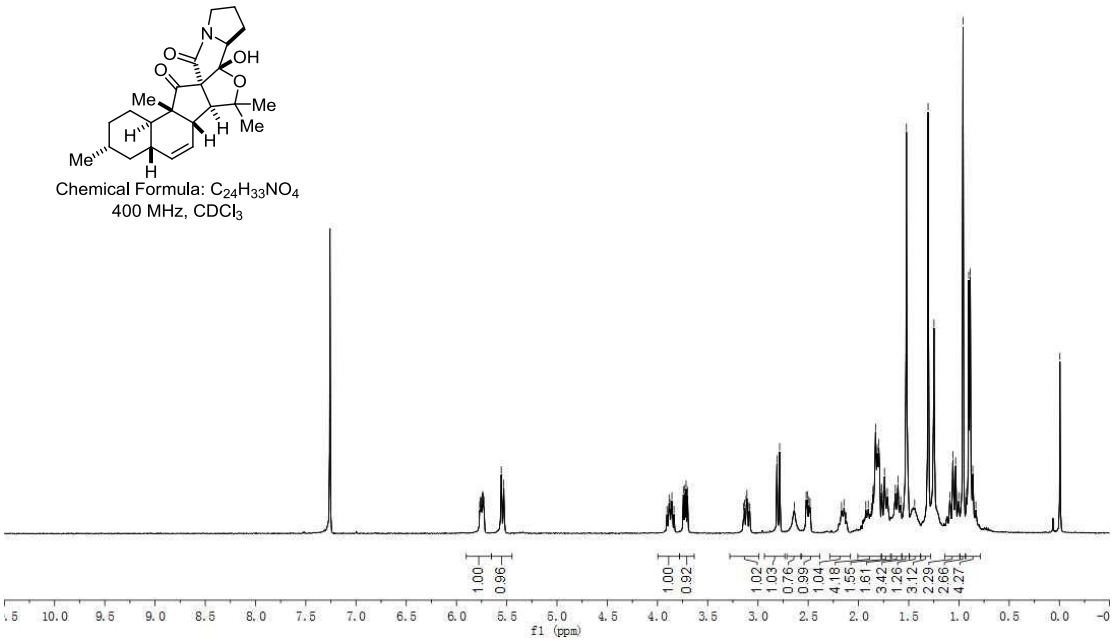


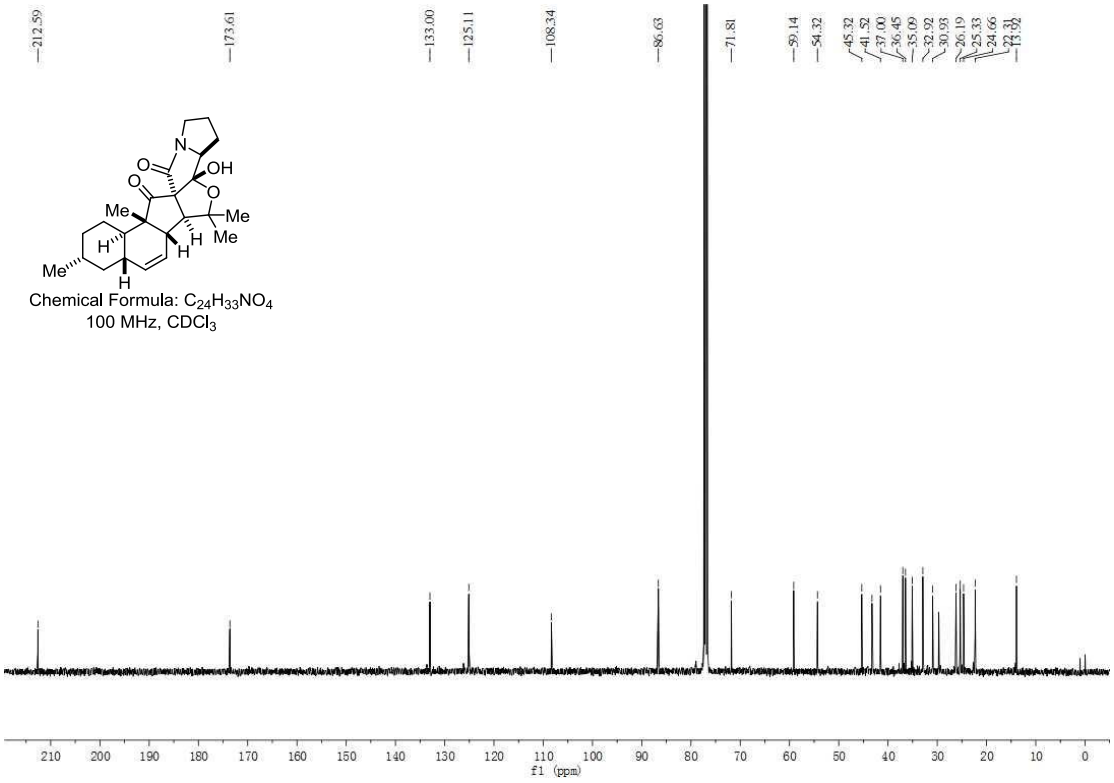
Chemical Formula: $C_{25}H_{37}NO_4$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers

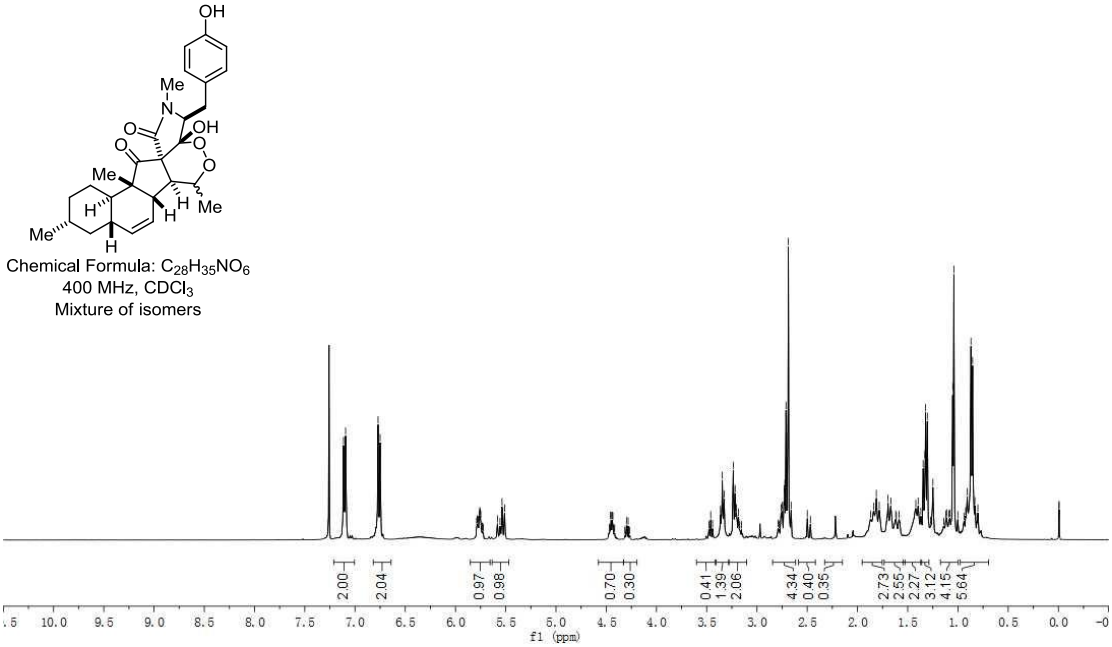


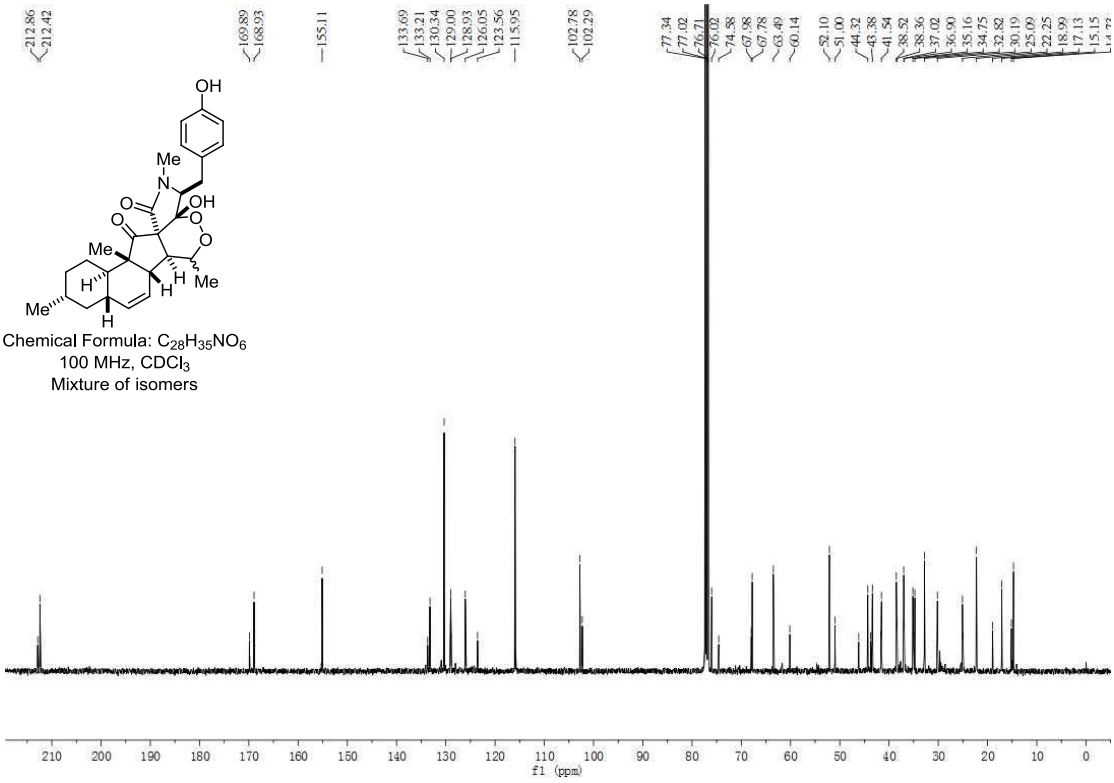

Chemical Formula:C24H33NO5
400 MHz, CDCl3
f1 (ppm)

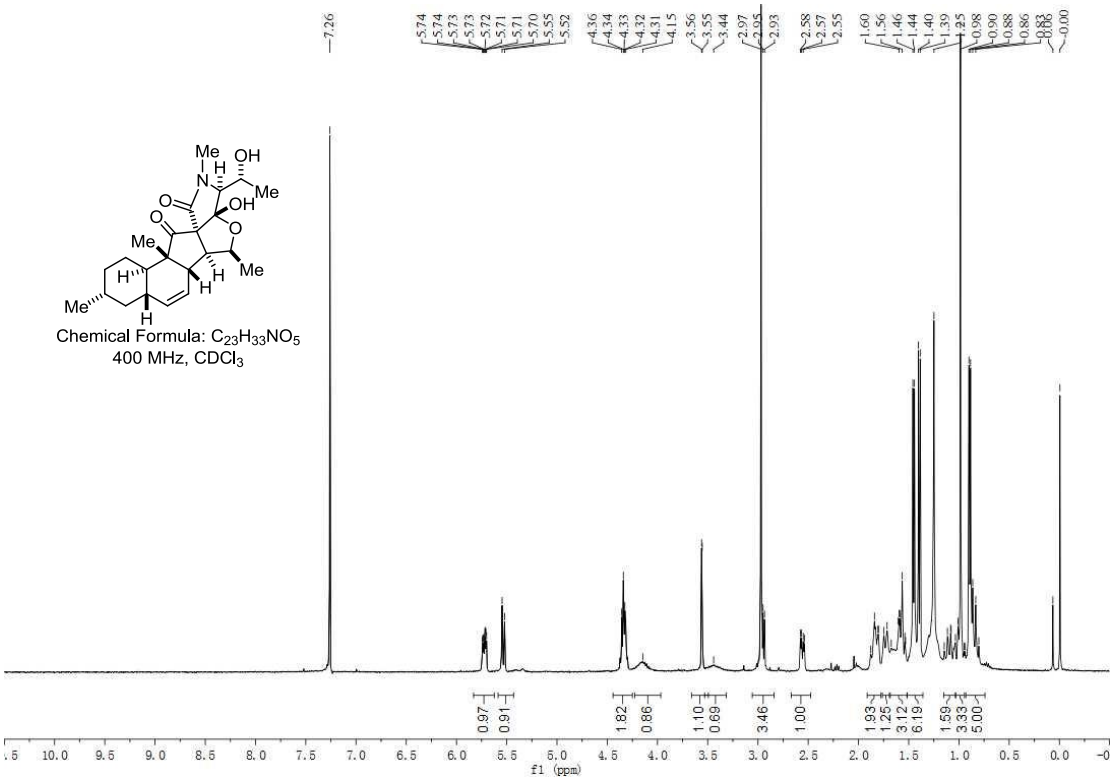

Chemical Formula:C24H33NO5
100 MHz, CDCl3
f1 (ppm)

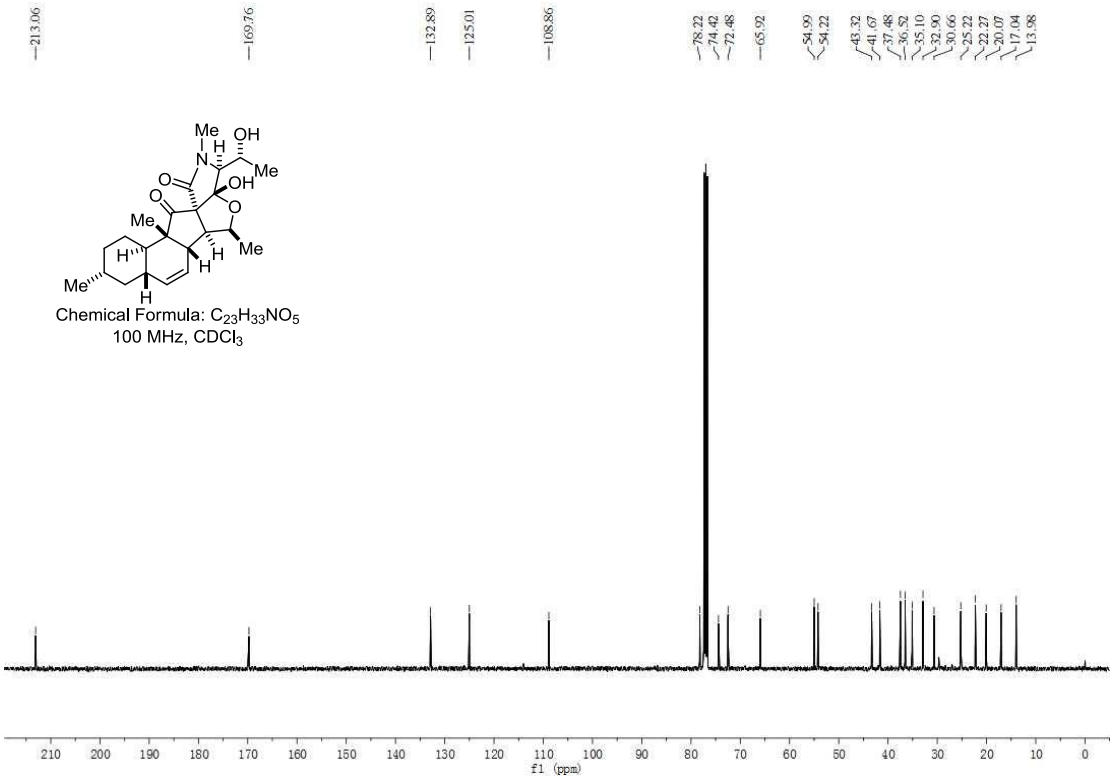

Chemical Formula: $C_{24}H_{33}NO_4$
400 MHz, $CDCl_3$
f1 (ppm)

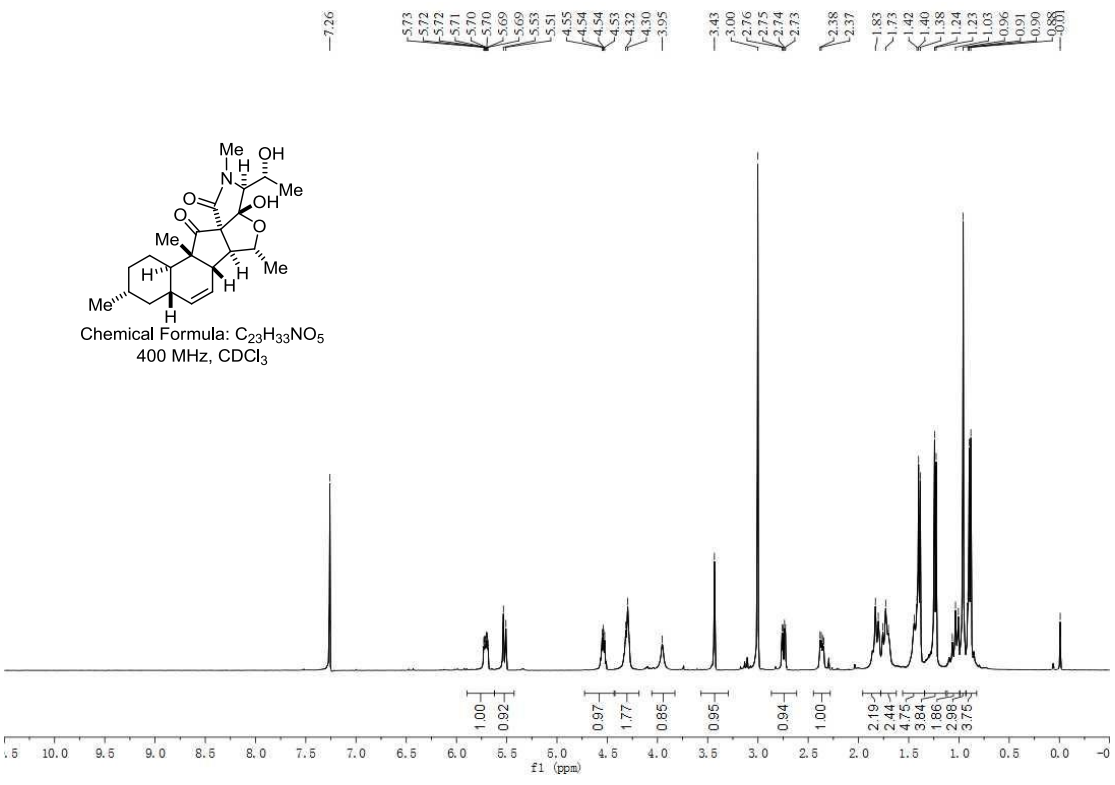

Chemical Formula: $C_{24}H_{33}NO_4$
100 MHz, $CDCl_3$
f1 (ppm)

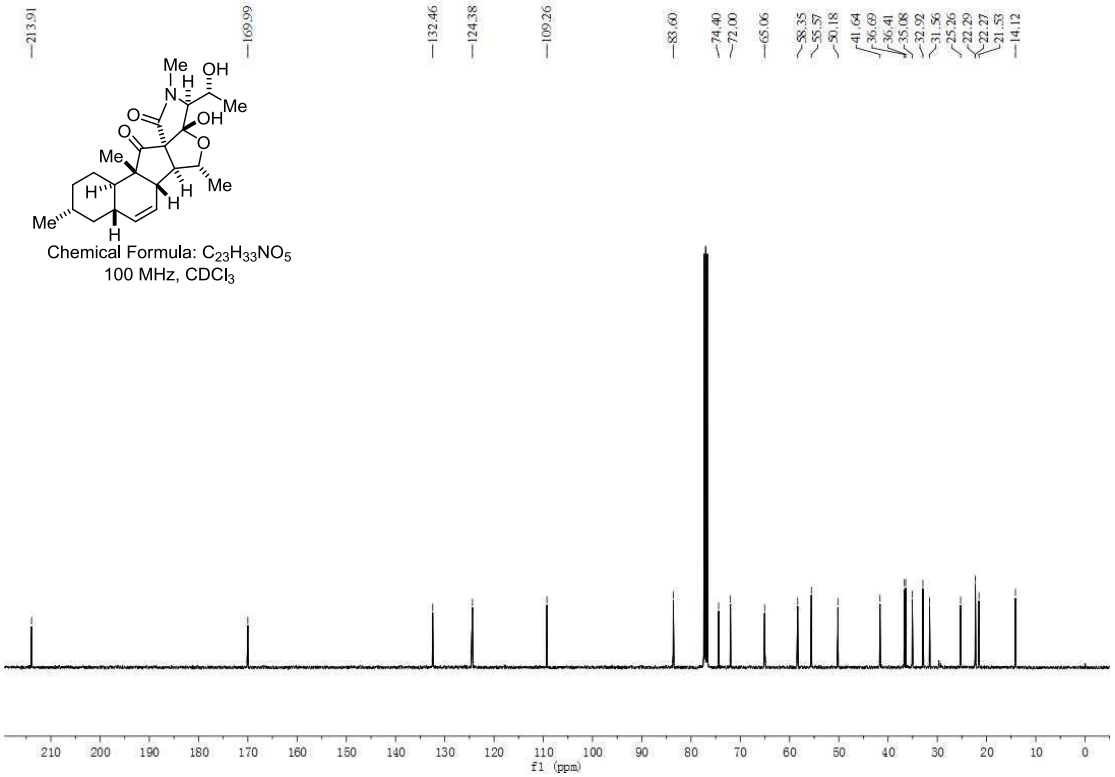

Chemical Formula: $C_{28}H_{35}NO_6$
400 MHz, $CDCl_3$
Mixture of isomers
f1 (ppm)

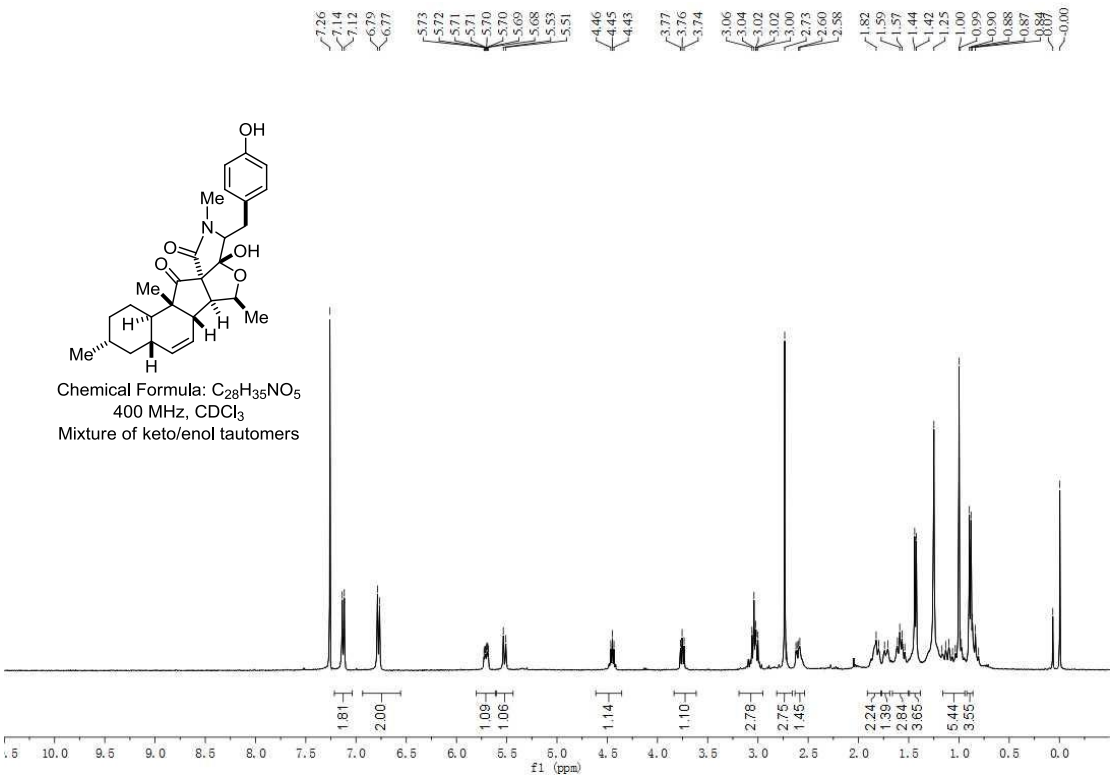

Chemical Formula: $C_{28}H_{35}NO_6$
100 MHz, $CDCl_3$
Mixture of isomers
f1 (ppm)

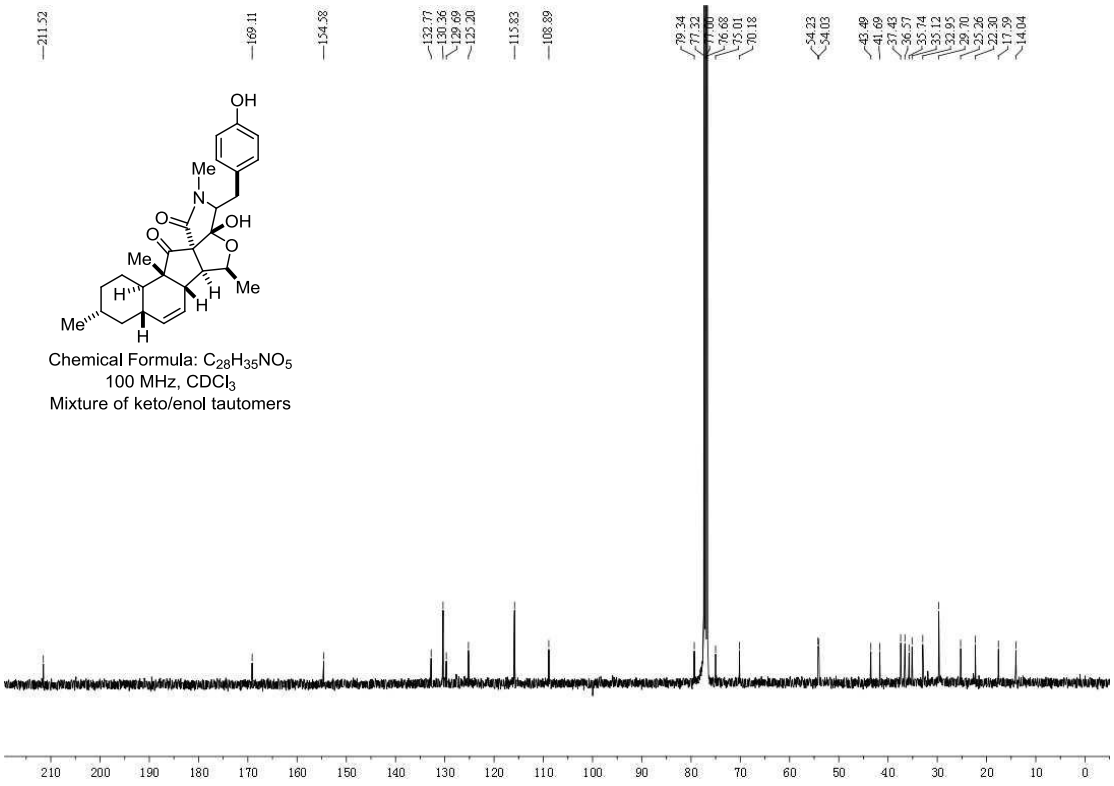

Chemical Formula: $C_{23}H_{33}NO_5$
400 MHz, $CDCl_3$
f1 (ppm)


Chemical Formula: $C_{23}H_{33}NO_5$
100 MHz, $CDCl_3$
f1 (ppm)


Chemical Formula: $C_{23}H_{33}NO_5$
400 MHz, $CDCl_3$
f1 (ppm)


Chemical Formula: $C_{23}H_{33}NO_5$
100 MHz, $CDCl_3$
f1 (ppm)


Chemical Formula: $C_{28}H_{35}NO_5$
400 MHz, $CDCl_3$
Mixture of keto/enol tautomers
f1 (ppm)


Chemical Formula: $C_{28}H_{35}NO_5$
100 MHz, $CDCl_3$
Mixture of keto/enol tautomers