Rapid Construction of the Common [5-5-6] Tricyclic Ring Skeleton in Polycyclic Cembranoids and Norcembranoids via Intramolecular 1, 3-Dipolar Cycloaddition

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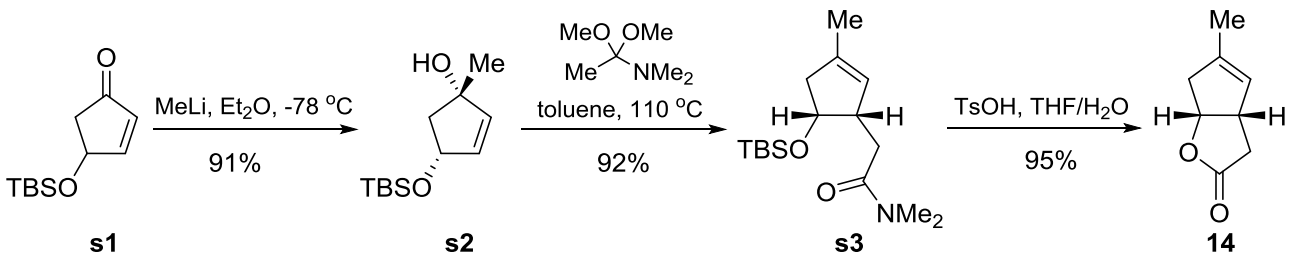
General Information.

All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Reagents were purchased at the highest commercial quality and used without further purification. Tetrahydrofuran (THF), diethyl ether (Et_2O), toluene and 1, 4-dioxane were distilled from sodium/benzophenone ketyl immediately before use. Methylene chloride (CH_2Cl_2), triethylamine (Et_3N) and acetonitrile (CH_3CN) were distilled from calcium hydride and stored under an argon atmosphere. Methanol (MeOH) and ethanol (EtOH) were distilled form magnesium and stored under an argon atmosphere. Reactions were monitored by thin layer chromatography (TLC) carried out on silica gel GF254 plates using UV light as visualizing agent or basic aqueous potassium permanganate as developing agent. Column chromatography was performed on silica gel (200–300 mesh). ^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX-400 spectrometers (at 400 MHz and 101 MHz respectively) and calibrated by using residual undeuterated chloroform (δ_H = 7.26 ppm) and $CDCl_3$ (δ_C = 77.16 ppm) as internal references. The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Bruker 550 spectrometer. Melting points (m.p.) were recorded on a RY-1A apparatus. High-resolution mass spectra (HRMS) were acquired using Varian 7.0T FTMS or Agilent 6520 Q-TOF LC/MS with electrospray ionization (ESI) source.

Experimental Procedures and Spectroscopic Data

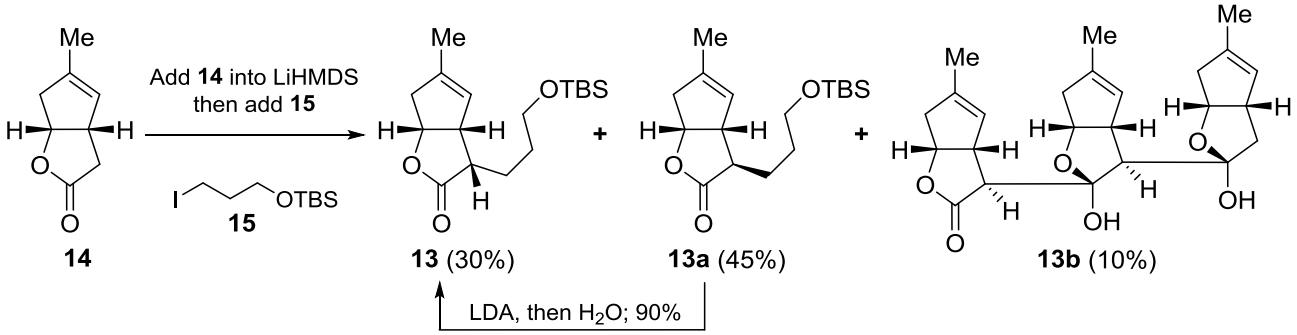


Preparation of Mulzer bicyclolactone 14: To a stirred solution of **s1**[1] (21.2 g, 100 mmol) in Et_2O (300 mL) at −78 °C was slowly added MeLi (68.8 mL, 1.6 M in Et_2O, 110 mmol) via syringe over a period of 30 min. The resulting mixture was stirred at −78 °C for 2 h before it was quenched with saturated aq. NH_4Cl solution (60 mL) and extracted with *t*BuOMe (3 × 100 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:10 → 1:5) to give the known tertiary alcohol **s2** (20.8 g, 91.1 mmol, 91%) as a colorless oil. R_f = 0.50

(silica, EtOAc:petroleum ether 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.86 (d, *J* = 5.5 Hz, 1 H), 5.76 (d, *J* = 5.5 Hz, 1 H), 4.74–4.65 (m, 1 H), 2.30 (dd, *J* = 13.6, 6.6 Hz, 1 H), 2.16 (brs, 1 H), 1.78 (dd, *J* = 13.6, 3.5 Hz, 1 H), 1.32 (s, 3 H), 0.88 (s, 9 H), 0.07 (s, 6 H) ppm; The other characterization data were in agreement with these reported in the literature.[2]

To a stirred solution of **s2** (74.0 g, 324 mmol) in toluene (400 mL) was added *N*, *N*-dimethlyacetamide dimethoxy acetal (95.9 g, 90% in MeOH, 648 mmol) at room temperature. The resulting mixture was heated to reflux for 60 h, during which time the generated MeOH was concomitantly distilled out. After removing the volatiles under vacuum, the residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:10 → 1:5) to give the known amide **s3** (88.7 g, 298 mmol, 92%) as a light yellow oil. R_f = 0.40 (silica, EtOAc:petroleum ether 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.28 (s, 1 H), 4.55–4.48 (m, 1 H), 3.17–3.09 (m, 1 H), 2.98 (s, 3 H), 2.92 (s, 3 H), 2.61 (dd, *J* = 16.0, 6.9 Hz, 1 H), 2.43 (dd, *J* = 16.2, 6.5 Hz, 1 H), 2.23–2.10 (m, 2 H), 1.68 (s, 3 H), 0.86 (s, 9 H), 0.03 (s, 3 H), 0.00 (s, 3 H) ppm; The other characterization data were in agreement with these reported in the literature.[3]

To a stirred solution of **s3** (88.7 g, 298 mmol) in THF/H_2O (400 mL/200 mL) was slowly added TsOH•H_2O (113 g, 596 mmol). The resulting mixture was stirred at room temperature for 8 h before it was quenched with anhydrous $NaHCO_3$ powder (50.1 g, 596 mmol) and extracted with *t*BuOMe (3 × 200 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:10 → 1:5) to give the known bicyclolactone **14**[4] (39.1 g, 283 mmol, 95%) as a light yellow oil. R_f = 0.40 (silica, EtOAc:petroleum ether 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.16 (s, 1 H), 5.09 (t, *J* = 5.8 Hz, 1 H), 3.52–3.43 (m, 1 H), 2.74–2.61 (m, 2 H), 2.54 (d, *J* = 17.9 Hz, 1 H), 2.39 (d, *J* = 17.9 Hz, 1 H), 1.74 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.0, 139.4, 124.93, 83.8, 45.4, 43.1, 33.5, 15.9 ppm; HRMS (ESI): calcd for $C_8H_{10}O_2Na$ $[M+Na]^+$ 161.0573, found: 161.0576.



The alkylation of 14: To a stirred solution of LiHMDS (400 mL, 0.3 M in THF, 120 mmol) was slowly added bicyclolactone **14** (13.8 g, 100 mmol) in THF (50 mL) at −78 °C before a solution of

alkyl iodide **15** (30.0 g, 100 mmol) in THF (50 mL) was added. The resulting mixture was stirred at −40 °C to −20 °C for 8 h before it was quenched with aq. HOAc solution (240 mL, 1.0 M in water) and extracted with EtOAc/petroleum ether (1:1, 3 × 200 mL). The combined organic phases were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:12 → 1:6) to give alkylate **13a** (colorless oil, 13.9 g, 44.8 mmol, 45%), **13** (colorless oil, 9.20 g, 29.6 mmol, 30%) and trimer **13b** (white solid, 1.39 g, 3.35 mmol, 10%) sequentially.

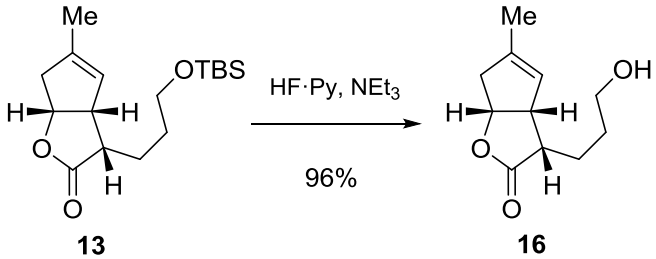
The deprotonation/kinetic protonation procedure of 13a: To a stirred solution of **13a** (9.60 g, 30.9 mmol) in THF (150 mL) was slowly added LDA (18.6 mL, 2.0 M in THF, 37.1 mmol) at −78 °C. The resulting mixture was stirred at that temperature for 1 h before it was quenched with water (4.5 mL). After vigorously stirred at −78 °C for 10 min, HOAc (4.2 mL, 74.0 mmol) was added and the mixture was warmed to room temperature, diluted with brine (100 mL), and extracted with EtOAc/petroleum ether (1:1, 3 × 100 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:12 → 1:6) to give alkylate **13** (colorless oil, 8.61 g, 27.7 mmol, 90%).

Data for **13**: R_f = 0.40 (silica, EtOAc:petroleum ether 1:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.25 (s, 1 H), 4.96 (t, *J* = 5.4 Hz, 1 H), 3.72–3.58 (m, 2 H), 3.52 (s, 1 H), 2.70–2.58 (m, 2 H), 2.52 (d, *J* = 17.8 Hz, 1 H), 1.92–1.82 (m, 1 H), 1.74 (d, *J* = 0.8 Hz, 3 H), 1.71–1.63 (m, 2 H), 1.60–1.49 (m, 1 H), 0.89 (s, 9 H), 0.04 (s, 6 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.5, 141.1, 121.0, 81.8, 62.8, 49.7, 43.7, 43.1, 31.0, 26.0, 24.2, 18.4, 16.5, -5.2 ppm; IR (thin film): ν_{max} = 2954, 2930, 2858, 1770, 1472, 1256, 1162, 1097, 1005, 953, 836, 776 cm^{-1}; HRMS (ESI): calcd for $C_{17}H_{31}O_3Si$ [M+H]$^+$ 311.2037, found: 311.2040.

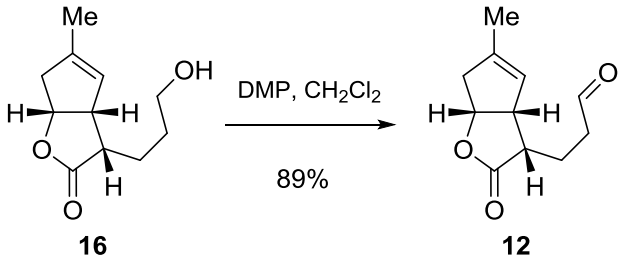
Data for **13a**: R_f = 0.50 (silica, EtOAc:petroleum ether 1:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.16 (s, 1 H), 5.06 (t, *J* = 5.9 Hz, 1 H), 3.64 (dd, *J* = 5.8, 3.8 Hz, 2 H), 3.21–3.15 (m, 1 H), 2.64 (dd, *J* = 17.8, 4.7 Hz, 1 H), 2.51 (d, *J* = 17.8 Hz, 1 H), 2.42 (t, *J* = 6.0 Hz, 1 H), 1.81–1.75 (m, 1 H), 1.73 (s, 3 H), 1.69–1.62 (m, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.8, 139.7, 125.2, 82.7, 62.6, 52.3, 45.6, 43.5, 30.4, 28.5, 26.1, 18.4, 16.3, -5.2 ppm; IR (thin film): ν_{max} = 2954, 2930, 2858, 1770, 1472, 1255, 1170, 1101, 1007, 837, 777 cm^{-1}; HRMS (ESI): calcd for $C_{17}H_{31}O_3Si$ [M+H]$^+$ 311.2037, found: 311.2041.

Data for **13b**: R_f = 0.38 (silica, EtOAc:petroleum ether 1:8); m.p. 162–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52 (s, 1 H), 5.27 (s, 1 H), 5.20 (s, 1 H), 5.12–5.05 (m, 3 H), 4.90–4.82 (m, 2 H), 3.52–3.36 (m, 2 H), 3.32 (d, *J* = 3.5 Hz, 1 H), 3.17 (s, 1 H), 2.65 (dd, *J* = 18.1, 6.1 Hz, 1 H), 2.58–2.45 (m,

3 H), 2.30–2.17 (m, 3 H), 1.91 (d, J = 7.7 Hz, 1 H), 1.71 (d, J = 11.9 Hz, 9 H), 1.55–1.48 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.8, 139.2, 139.0, 137.6, 127.7, 126.0, 124.9, 107.4, 106.6, 84.1, 82.4, 81.8, 58.5, 51.4, 49.1, 44.2, 43.5, 43.2, 42.9, 16.6, 16.3 ppm; IR (thin film): ν_{max} = 3436, 2928, 1736, 1656, 1616, 1433, 1281, 1200, 1137, 1065, 1043, 964, 920, 859, 802, 600 cm^{-1}; HRMS (ESI): Calcd for $C_{24}H_{30}O_6Na$ [M+Na]$^+$ 437.1935, found: 437.1938; CCDC 1871342 contains the supplementary crystallographic data for **13b** and is available free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

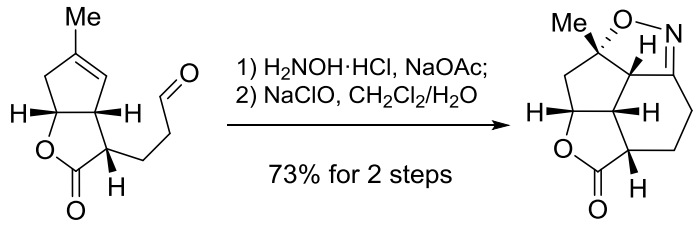


Primary alcohol 16: To a stirred solution of **13** (7.60 g, 24.5 mmol) in THF (120 mL) was added HF•Py (content 65 %，7.50 g，49.0 mmol) and NEt_3 (3.4 mL, 24.5 mmol). The resulting mixture was stirred at room temperature for 6 h before it was quenched with brine (120 mL) and extracted with EtOAc (3 × 100 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:2 → 1:1) to give alcohol **16** (4.62 g, 23.5 mmol, 96%) as a colorless oil. Data for **16**: R_f = 0.60 (silica, EtOAc:petroleum ether 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.23 (s, 1 H), 4.96 (t, J = 5.3 Hz, 1 H), 3.66 (td, J = 6.3, 2.4 Hz, 2 H), 3.52 (s, 1 H), 2.73–2.57 (m, 2 H), 2.50 (d, J = 17.9 Hz, 1 H), 2.32 (brs, 1 H), 1.93–1.83 (m, 1 H), 1.76–1.68 (m, 5 H), 1.59–1.48 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.8, 141.3, 120.8, 82.0, 62.3, 49.8, 43.6, 43.1, 30.8, 23.9, 16.5 ppm; IR (thin film): ν_{max} = 3448, 2936, 2871, 1761, 1446, 1349, 1181, 1159, 1055, 1003, 828 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{16}O_3Na$ [M+Na]$^+$ 219.0992, found: 219.0995.



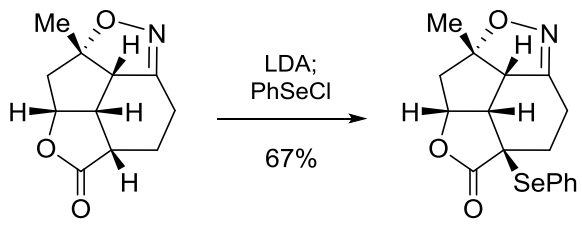
Aldehyde 12: To a stirred solution of **16** (3.20 g, 16.3 mmol) in CH_2Cl_2 (80 mL) was added Dess–Martin periodinane (8.31 g，19.6 mmol). After stirring at room temperature for 3 h, the reaction mixture was directly subjected to flash column chromatography using EtOAc/petroleum ether (1:5 → 1:2) as eluent to give aldehyde **12** (2.82 g, 14.5 mmol, 89%) as a colorless oil. Data for **12**: R_f = 0.60

(silica, EtOAc:petroleum ether 1:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.80 (s, 1 H), 5.21 (s, 1 H), 4.96 (t, J = 5.3 Hz, 1 H), 3.52 (s, 1 H), 2.81–2.65 (m, 3 H), 2.65–2.58 (m, 1 H), 2.52 (d, J = 17.9 Hz, 1 H), 2.04 (td, J = 14.5, 7.3 Hz, 1 H), 1.85 (td, J = 14.6, 7.5 Hz, 1 H), 1.75 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.6, 178.0, 141.8, 120.4, 81.8, 49.9, 43.6, 42.1, 41.7, 20.2, 16.5 ppm; IR (thin film): ν_{max} = 2915, 1762, 1721, 1446, 1349, 1274, 1182, 1162, 1004, 983, 958, 901 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{14}O_3Na$ [M+Na]$^+$ 217.0835, found: 217.0838.



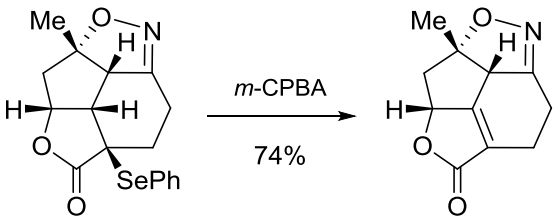
12 **10**

Tetracyclic isoxazoline 10: To a stirred solution of **12** (2.82 g, 14.5 mmol) in *t*-BuOH/H_2O (70 mL/7 mL) was added hydroxylamine hydrochloride (1.11 g，16.0 mmol) and NaOAc (2.62 g，31.9 mmol). After stirring at room temperature for 1 h, the reaction mixture was concentrated under vacuum, diluted with brine (80 mL) and extracted with CH_2Cl_2 (3 × 80 mL). The organic phases were combined, added with water (80 mL) and aq. NaClO solution (10% in water, 29 mL, 43.5 mmol). The resulting mixture was stirred at room temperature for 4 h before it was diluted with brine (100 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/CH_2Cl_2 (1:4 → 1:1) to give tetracyclic isoxazoline **10** (2.19 g, 10.6 mmol, 73% for 2 steps) as a white solid. Data for **10**: R_f = 0.40 (silica, EtOAc 100%); m.p. 194–195 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.88 (t, J = 5.4 Hz, 1 H), 3.40–3.32 (m, 1 H), 3.28 (d, J = 9.8 Hz, 1 H), 3.04–2.90 (m, 1 H), 2.69 (dd, J = 17.3, 8.8 Hz, 1 H), 2.61 (d, J = 16.5 Hz, 1 H), 2.44 (dd, J = 16.2, 9.7 Hz, 1 H), 2.30 (t, J = 11.7 Hz, 1 H), 2.17 (dd, J = 16.5, 5.6 Hz, 1 H), 2.02–1.90 (m, 1 H), 1.51 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.8, 156.1, 95.2, 84.5, 57.9, 47.7, 47.5, 39.3, 25.5, 20.7, 19.3 ppm; IR (thin film): ν_{max} = 2966, 2927, 1760, 1632, 1450, 1355, 1340, 1185, 1157, 1089, 1001, 905, 869, 807 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{13}NO_3Na$ [M+Na]$^+$ 230.0788, found: 230.0792; CCDC 1871751 contains the supplementary crystallographic data for **10** and is available free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



10 **17**

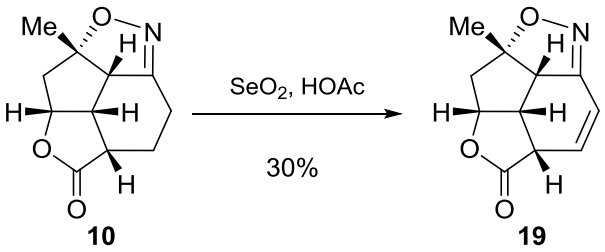
The α-selenylated product 17: To a stirred solution of **10** (207 mg, 1.00 mmol) in THF (20 mL) was slowly added LDA (1.2 mL, 1.0 M in THF, 1.20 mmol) at −78 °C. After stirred at that temperature for 1 h, PhSeCl (230 mg, 1.2 mmol) in THF (5 mL) was added. The resulting mixture was gradually warmed to 0 ℃ in 4 h before it was quenched with saturated aq. NH_4Cl solution (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:6 → 1:2) to give α-selenylated product **17** (243 mg, 0.67 mmol, 67%) as a white solid. Data for **17**: R_f = 0.50 (silica, EtOAc:petroleum ether 1:1); m.p. 180–182 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73–7.60 (m, 2 H), 7.46 (t, *J* = 7.4 Hz, 1 H), 7.36 (t, *J* = 7.5 Hz, 2 H), 4.67 (t, *J* = 5.5 Hz, 1 H), 3.37 (d, *J* = 9.7 Hz, 1 H), 3.21 (dd, *J* = 9.8, 5.4 Hz, 1 H), 2.77–2.61 (m, 2 H), 2.54–2.44 (m, 1 H), 2.38 (dd, *J* = 13.8, 8.9 Hz, 1 H), 2.23 (dt, *J* = 13.9, 9.8 Hz, 1 H), 2.11 (dd, *J* = 16.6, 5.8 Hz, 1 H), 1.51 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.7, 154.6, 138.2, 130.4, 129.5, 124.9, 95.2, 83.1, 59.1, 55.0, 47.9, 47.4, 29.0, 25.7, 21.1 ppm; IR (thin film): ν_{max} = 2970, 2930, 1757, 1439, 1354, 1308, 1221, 1170, 1136, 1064, 1001, 896, 744, 693 cm^{-1}; HRMS (ESI): calcd for $C_{17}H_{18}NO_3Se$ $[M+H]^+$ 364.0446, found: 364.0450; CCDC 1871341 contains the supplementary crystallographic data for **17** and is available free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



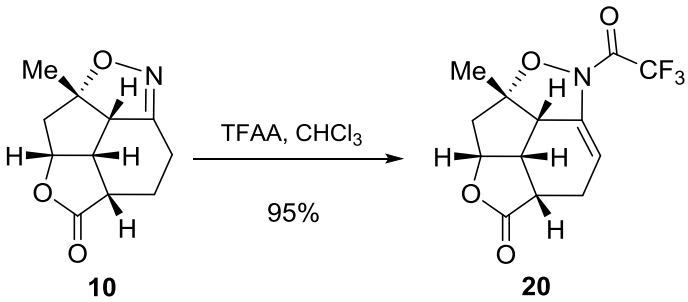
17 **18a**

Unsaturated lactone 18a: To a stirred solution of **17** (18 mg, 0.05 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (content 70 %，25 mg，0.10 mmol) and $NaHCO_3$ (25 mg, 0.3 mmol). The resulting mixture was stirred at 0 °C for 2 h before it was quenched with brine (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:2 → 1:1) to give unsaturated tetracyclic lactone **18a** (8 mg, 0.035 mmol,

74%) as an amorphous solid. Data for **18a**: R_f = 0.40 (silica, EtOAc:petroleum ether 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.23 (td, *J* = 8.1, 3.7 Hz, 1 H), 3.88 (s, 1 H), 2.96–2.84 (m, 2 H), 2.78–2.57 (m, 3 H), 1.70 (s, 3 H), 1.62–1.48 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.3, 172.0, 160.3, 127.2, 94.3, 81.4, 56.6, 46.9, 25.0, 24.0, 18.7 ppm; IR (thin film): ν_{max} = 2973, 2932, 1757, 1682, 1437, 1337, 1309, 1287, 1264, 1128, 1069, 1032, 1014, 855, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{11}NO_3Na$ $[M+Na]^+$ 228.0631, found: 228.0635.

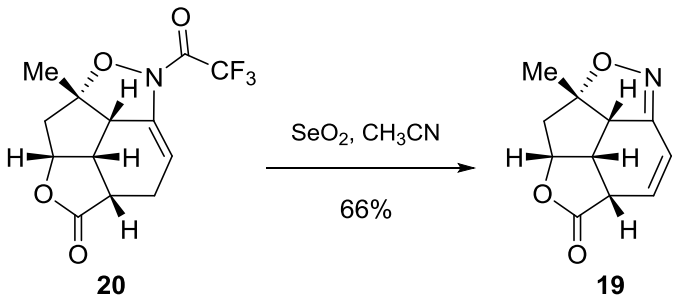


Unsaturated isoxazoline 19: To a stirred solution of **10** (50 mg, 0.24 mmol) in 1,4-dioxane (5 mL) was added SeO_2 (535 mg，4.83 mmol) and HOAc (580 mg, 9.66 mmol). The resulting mixture was stirred at 110 ℃ for 36 h before it was quenched with brine (10 mL) and extracted with $CHCl_3$ (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:1 → 2:1) to give unsaturated tetracyclic isoxazoline **19** (15 mg, 0.073 mmol, 30%) as a pale yellow foam. Data for **19**: R_f = 0.40 (silica, EtOAc:petroleum ether 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.79 (d, *J* = 10.0 Hz, 1 H), 6.45 (dd, *J* = 10.0, 6.0 Hz, 1 H), 5.02 (td, *J* = 8.3, 6.5 Hz, 1 H), 3.63 (ddd, *J* = 10.7, 6.0, 1.4 Hz, 1 H), 3.52 (dd, *J* = 19.8, 9.5 Hz, 1 H), 3.22 (d, *J* = 9.5 Hz, 1 H), 2.50 (dd, *J* = 15.2, 8.1 Hz, 1 H), 2.18 (dd, *J* = 15.3, 6.3 Hz, 1 H), 1.62 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.8, 156.5, 134.1, 121.5, 94.6, 82.1, 55.4, 45.3, 40.2, 39.8, 22.8 ppm; IR (thin film): ν_{max} = 2927, 2855, 1761, 1362, 1323, 1243, 1172, 1067, 1035, 1008, 880, 864, 846, 741, 693 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{11}NO_3Na$ $[M+Na]^+$ 228.0631, found: 228.0635.

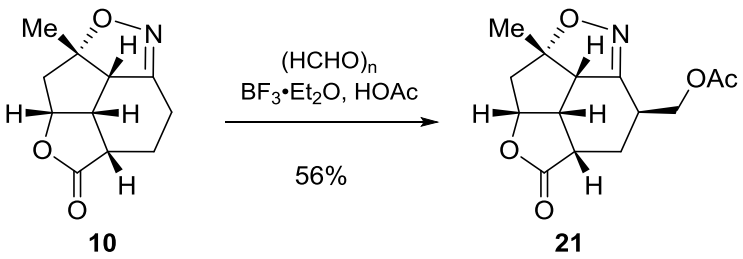


Trifluoroacetylated enamine 20: To a stirred solution of **10** (226 mg, 1.09 mmol) in $CHCl_3$ (23 mL) was added trifluoroacetic anhydride (0.62 mL，4.36 mmol). The resulting mixture was stirred at 60 ℃ for 2 h before it was concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:2 → 2:1) to give trifluoroacetylated enamine **20** (314

mg, 1.04 mmol, 95%) as a white solid. Data for **20**: R_f = 0.55 (silica, EtOAc 100%); m.p. 136–138 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.41 (dd, *J* = 4.8, 3.3 Hz, 1 H), 4.98 (td, *J* = 8.2, 5.4 Hz, 1 H), 3.47 (dt, *J* = 10.6, 8.5 Hz, 1 H), 3.11 (ddd, *J* = 10.7, 5.2, 2.1 Hz, 1 H), 2.87–2.84 (m, 1 H), 2.81 (dd, *J* = 8.2, 2.1 Hz, 1 H), 2.45 (ddd, *J* = 15.4, 7.9, 0.8 Hz, 1 H), 2.29–2.21 (m, 1 H), 2.01 (dd, *J* = 15.5, 5.3 Hz, 1 H), 1.56 (d, *J* = 0.5 Hz, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.2, 150.8 (q, *J* = 40.0 Hz), 135.5, 115.5 (q, *J* = 286.4 Hz), 108.8, 92.4, 81.3, 49.8, 41.9, 40.7, 39.2, 25.2, 22.1 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = -72.9 ppm; IR (thin film): ν_{max} = 2980, 1770, 1691, 1659, 1465, 1245, 1209, 1160, 1040, 1008, 905, 818, 734, 716 cm^{-1}; HRMS (ESI): Calcd for $C_{13}H_{12}F_3NO_4Na$ $[M+Na]^+$ 326.0611, found: 326.0615; CCDC 1871339 contains the supplementary crystallographic data for **20** and is available free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

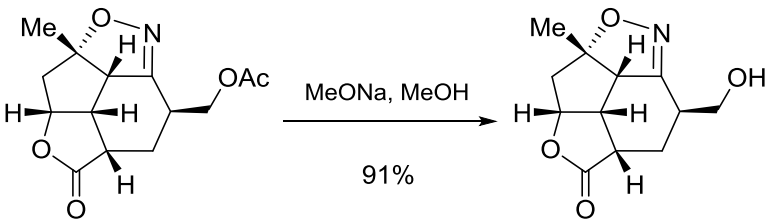


Unsaturated isoxazoline 19, a revised procedure: To a stirred solution of **20** (60 mg, 0.198 mmol) in CH_3CN (6 mL) was added 4Å molecular sieve (120 mg, over dried) and SeO_2 (89 mg，0.802 mmol). After stirring at 81 °C for 2 h, the reaction mixture was filtered, concentrated under vacuum and subjected to flash column chromatography using EtOAc/petroleum ether (1:2 → 2:1) as eluent to give unsaturated isoxazoline **19** (27 mg, 0.132 mmol, 66%) as a pale yellow foam. The spectral and physical properties of compound **19** are identical as above.



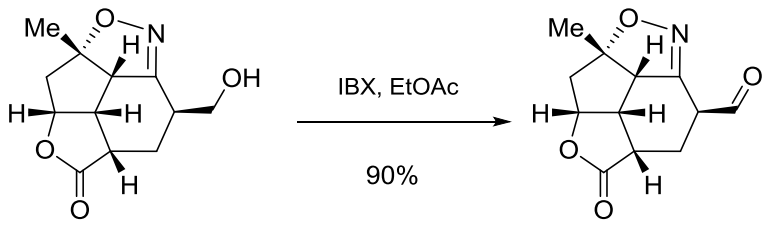
Acetate 21: To a stirred solution of **10** (320 mg, 1.54 mmol) in AcOH (7.0 mL) was added paraformaldehyde (139 mg，4.63 mmol) and BF_3•Et_2O (437 mg, 3.08 mmol). The resulting mixture was stirred at 60 ℃ for 30 h before it was quenched with saturated aq. $NaHCO_3$ solution (100 mL) and extracted with $CHCl_3$ (3 × 50 mL). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:2 → 1:0) to give acetate

21 (240 mg, 0.86 mmol, 56%) as an amorphous solid. Data for **21**: R_f = 0.40 (silica, EtOAc 100%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.86 (t, *J* = 5.0 Hz, 1 H), 4.18 (dd, *J* = 11.0, 7.6 Hz, 1 H), 4.00 (dd, *J* = 11.0, 5.8 Hz, 1 H), 3.36–3.30 (m, 2 H), 3.13 (dd, *J* = 15.4, 7.9 Hz, 1 H), 2.98 (dd, *J* = 5.2, 2.8 Hz, 1 H), 2.58 (d, *J* = 16.5 Hz, 1 H), 2.36 (ddd, *J* = 14.1, 8.6, 3.4 Hz, 1 H), 2.15 (dd, *J* = 16.4, 5.5 Hz, 1 H), 1.99 (s, 3 H), 1.65 (ddd, *J* = 14.0, 10.0, 3.7 Hz, 1 H), 1.48 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.5, 170.8, 156.1, 95.8, 84.7, 64.3, 56.4, 47.6, 47.4, 38.9, 31.4, 25.3, 24.4, 20.8 ppm; IR (thin film): ν_{max} = 2969, 2933, 1764, 1740, 1449, 1364, 1317, 1236, 1183, 1160, 1092, 1042, 1000, 897, 735 cm^{-1}; HRMS (ESI): calcd for $C_{14}H_{18}NO_5$ $[M+H]^+$ 280.1179, found: 280.1179.



21 **s4**

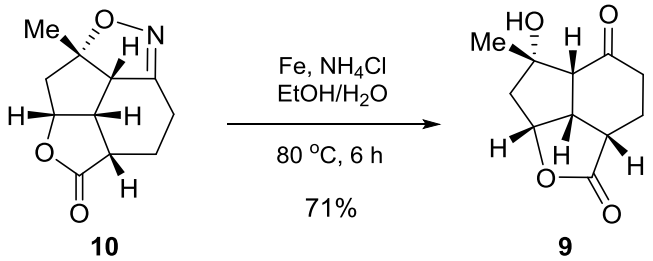
Alcohol S1: To a stirred solution of **21** (200 mg, 0.716 mmol) in MeOH (10 mL) was added MeONa (39 mg，0.716 mmol). After stirring at room temperature for 20 min, the reaction mixture was quenched with HCO_2H (54 μL, 1.43 mmol) and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/MeOH (40:1 → 10:1) to give alcohol **s4** (154 mg, 0.649 mmol, 91%) as a white solid. Data for **s4**: R_f = 0.50 (silica, EtOAc/MeOH = 20:1); m.p. 160–161 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.91 (t, *J* = 5.6 Hz, 1 H), 3.82 (dd, *J* = 10.6, 4.9 Hz, 1 H), 3.66 (dd, *J* = 10.6, 6.0 Hz, 1 H), 3.44–3.28 (m, 2 H), 3.14–2.95 (m, 2 H), 2.69 (d, *J* = 16.6 Hz, 1 H), 2.39 (ddd, *J* = 14.0, 8.3, 3.5 Hz, 1 H), 2.22 (dd, *J* = 16.6, 5.9 Hz, 1 H), 2.04 (brs, 1 H), 1.83 (ddd, *J* = 14.1, 10.5, 3.6 Hz, 1 H), 1.56 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.6, 157.6, 95.4, 84.3, 64.2, 57.4, 48.0, 47.5, 39.2, 34.4, 25.6, 24.2 ppm; IR (thin film): ν_{max} = 3469, 2931, 2782, 1761, 1446, 1357, 1342, 1182, 1159, 1156, 1000, 893, 878, 734 cm^{-1}; HRMS (ESI): calcd for $C_{12}H_{15}NO_4Na$ $[M+Na]^+$ 260.0893, found: 260.0898.



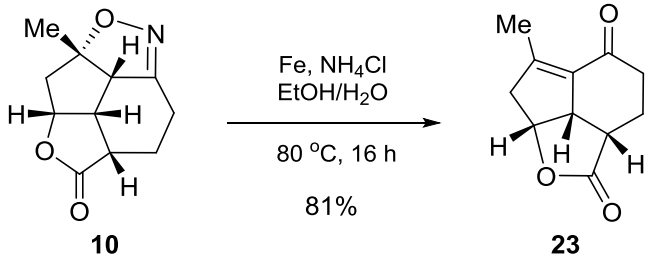
s4 **22**

Aldehyde 22: To a stirred solution of **s4** (154 mg, 0.649 mmol) in EtOAc (14 mL) was added *o*-iodoxybenzoic acid (545 mg, 1.947 mmol). The resulting mixture was stirred at 77 °C for 6 h before it was filtered and concentrated under vacuum to give aldehyde **22** (153 mg, NMR purity: ca. 90%) as

a pale yellow oil. Data for **22**: R_f = 0.40 (silica, EtOAc 100%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.68 (s, 1 H), 4.92 (t, *J* = 5.5 Hz, 1 H), 3.94 (t, *J* = 9.4 Hz, 1 H), 3.35 (td, *J* = 9.0, 5.6 Hz, 1 H), 3.19 (d, *J* = 9.6 Hz, 1 H), 3.13–3.03 (m, 1 H), 2.70 (d, *J* = 16.6 Hz, 1 H), 2.46–2.29 (m, 2 H), 2.21 (dd, *J* = 16.6, 5.6 Hz, 1 H), 1.54 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.5, 176.3, 151.7, 96.6, 84.6, 56.4, 47.7, 47.5, 45.4, 38.5, 25.4, 20.8 ppm; IR (thin film): ν_{max} = 2969, 2931, 1763, 1724, 1446, 1342, 1322, 1181, 1159, 1091, 999, 904, 732 cm^{-1}; HRMS (ESI): calcd for $C_{12}H_{14}NO_4$ $[M+H]^+$ 236.0917, found: 236.0921.

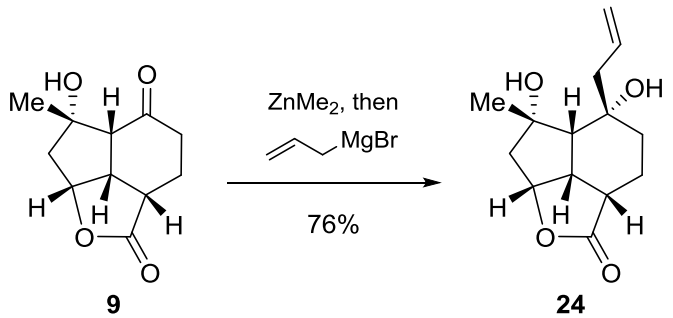


Tricyclic β-hydroxy ketone 9: To a stirred solution of **10** (725 mg, 3.50 mmol) in EtOH/H_2O (1:1, 120 mL) was added Fe dust (1.96 g，35.0 mmol) and NH_4Cl (1.87 g, 35.0 mmol). The resulting mixture was stirred at 80 ℃ for 6 h before it was quenched with brine (60 mL) and extracted with EtOAc (6 × 50 mL). The combined organic phases were washed with brine (60 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/CH_2Cl_2 (1:10 → 1:1) to give tricyclic β-hydroxy ketone **9** (522 mg, 2.48 mmol, 71%) as a white solid. Data for **9**: R_f = 0.55 (silica, EtOAc 100%); m.p. 174–176 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.14–5.03 (m, 1 H), 3.41 (td, *J* = 10.6, 6.4 Hz, 1 H), 3.08–2.96 (m, 1 H), 2.63–2.46 (m, 3 H), 2.33 (d, *J* = 15.1 Hz, 2 H), 2.10 (ddd, *J* = 18.5, 9.2, 5.3 Hz, 1 H), 1.93 (dd, *J* = 15.1, 4.9 Hz, 1 H), 1.63 (s, 1 H), 1.47 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 209.8, 177.8, 83.4, 82.4, 58.3, 47.3, 43.7, 43.6, 38.8, 38.1, 27.1, 22.7 ppm; IR (thin film): ν_{max} = 3458, 2966, 2931, 1758, 1698, 1368, 1237, 1179, 1152, 1107, 1005, 945 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{14}O_4Na$ $[M+Na]^+$ 233.0784, found: 233.0788; CCDC 1871340 contains the supplementary crystallographic data for **9** and is available free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



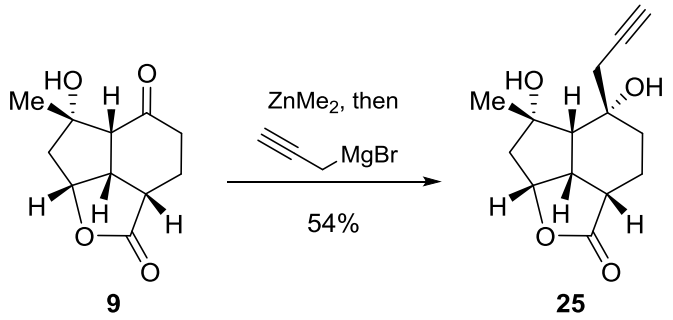
Tricyclic enone 23: To a stirred solution of **10** (1.62 g, 7.83 mmol) in EtOH/H_2O (1:1, 120 mL) was

added Fe dust (4.38 g，78.3 mmol) and NH_4Cl (4.19 g, 78.3 mmol). The resulting mixture was stirred at 80 °C for 16 h before it was quenched with brine (60 mL) and extracted with EtOAc (6 × 50 mL). The combined organic phases were washed with brine (60 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:4 → 1:1) to give tricyclic enone **23** (1.22 g, 6.34 mmol, 81%) as a pale yellow oil. Data for **23**: R_f = 0.45 (silica, EtOAc/petroleum ether 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.01 (t, *J* = 5.4 Hz, 1 H), 3.71 (ddd, *J* = 7.3, 3.7, 1.8 Hz, 1 H), 3.16 (dd, *J* = 17.1, 9.3 Hz, 1 H), 3.02–2.90 (m, 1 H), 2.71 (d, *J* = 19.4 Hz, 1 H), 2.46–2.26 (m, 3 H), 2.11 (s, 3 H), 1.93–1.81 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.0, 178.6, 151.8, 129.6, 80.5, 48.8, 46.1, 39.0, 38.4, 22.1, 15.8 ppm; IR (thin film): ν_{max} = 2959, 2931, 1765, 1688, 1631, 1419, 1349, 1238, 1164, 1060, 994, 938, 859, 592 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{12}O_3Na$ $[M+Na]^+$ 215.0679, found: 215.0682.



Allylated tricyclic core 24: To a stirred solution of **9** (170 mg, 0.809 mmol) in THF (20 mL) was slowly added $ZnMe_2$ (0.89 mL, 1.0 M in toluene, 0.890 mmol) at −78 °C. After stirred at that temperature for 30 min, allylmagnesium bromide (0.89 mL, 1.0 M in diethyl ether, 0.890 mmol) was added. The resulting mixture was gradually warmed to 0 °C in 2 h before it was quenched with saturated aq. NH_4Cl solution (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:2 → 2:1) to give allylated tricyclic core **24** (156 mg, 0.618 mmol, 76%) as a white solid. Data for **24**: R_f = 0.60 (silica, EtOAc:petroleum ether 2:1); m.p. 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.92 (ddt, *J* = 17.3, 10.2, 7.3 Hz, 1 H), 5.23–5.09 (m, 2 H), 4.92 (dd, *J* = 6.4, 5.2 Hz, 1 H), 3.07 (td, *J* = 10.7, 6.7 Hz, 1 H), 2.79 (ddd, *J* = 10.3, 6.9, 3.0 Hz, 1 H), 2.51 (s, 1 H), 2.32–2.23 (m, 3 H), 2.20–2.12 (m, 1 H), 1.99 (d, *J* = 10.8 Hz, 1 H), 1.92–1.82 (m, 2 H), 1.80–1.70 (m, 1 H), 1.65 (s, 1 H), 1.52 (s, 3 H), 1.50–1.46 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.9, 133.3, 119.3, 82.6, 82.3, 73.5, 52.1, 48.0, 46.3, 41.7, 38.3, 33.1, 30.1, 20.7 ppm; IR (thin film): ν_{max} = 3443, 2932, 1758, 1457, 1370, 1260, 1176, 1109, 1026, 1005, 951, 920, 798 cm^{-1}; HRMS (ESI): Calcd for $C_{14}H_{20}O_4Na$ $[M+Na]^+$ 275.1254, found:

275.1258.



Propargylated tricyclic core 25: To a stirred solution of **9** (50 mg, 0.238 mmol) in THF (10 mL) was slowly added $ZnMe_2$ (0.24 mL, 1.0 M in toluene, 0.240 mmol) at −78 °C. After stirred at that temperature for 30 min, propargyl magnesium bromide (0.71 mL, 0.40 M in diethyl ether, 0.286 mmol) was added. The resulting mixture was gradually warmed to 0 °C in 2 h before it was quenched with saturated aq. NH_4Cl solution (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:2 → 2:1) to give propargylated tricyclic core **25** (32 mg, 0.128 mmol, 54%) as a white solid. Data for **25**: R_f = 0.55 (silica, EtOAc:petroleum ether 2:1); m.p. 177–179 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.94 (dd, *J* = 6.5, 5.0 Hz, 1 H), 3.10 (td, *J* = 10.7, 6.6 Hz, 1 H), 2.80 (ddd, *J* = 10.3, 7.2, 3.1 Hz, 1 H), 2.74 (s, 1 H), 2.55–2.42 (m, 2 H), 2.29 (d, *J* = 15.3 Hz, 1 H), 2.26–2.18 (m, 1 H), 2.14 (dd, *J* = 6.3, 3.7 Hz, 2 H), 2.08 (s, 1 H), 1.95 (d, *J* = 16.4 Hz, 1 H), 1.87 (dd, *J* = 15.3, 5.0 Hz, 1 H), 1.73 (t, *J* = 22.0 Hz, 2 H), 1.55 (s, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.7, 82.5, 82.2, 80.0, 73.1, 72.2, 51.7, 47.9, 41.7, 38.2, 33.1, 32.7, 29.9, 20.6 ppm; IR (thin film): ν_{max} = 3441, 3296, 2929, 1759, 1456, 1370, 1232, 1176, 1126, 1110, 1005, 949, 856, 828, 735, 649 cm^{-1}; HRMS (ESI): calcd for $C_{14}H_{18}O_4Na$ $[M+Na]^+$ 273.1097, found: 273.1100; CCDC 1884458 contains the supplementary crystallographic data for **25** and is available free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

II References

[1] The racemate and either enantiomer of **s1** are commercially available [(±)-**s1**: CAS No. 56745-67-6; (+)-**s1**: CAS No. 61305-35-9; (−)-**s1**: CAS No. 61305-36-0]. Racemic **s1** could also be conveniently prepared via a two-step procedure from furfuryl alcohol, see: Watson, T. J. N.; Curran, T. T.; Hay, D. A.; Shah, R. S.; Wenstrup, D. L.; Webster, M. E. *Org. Process Res. Dev.* **1998**, *2*, 357.

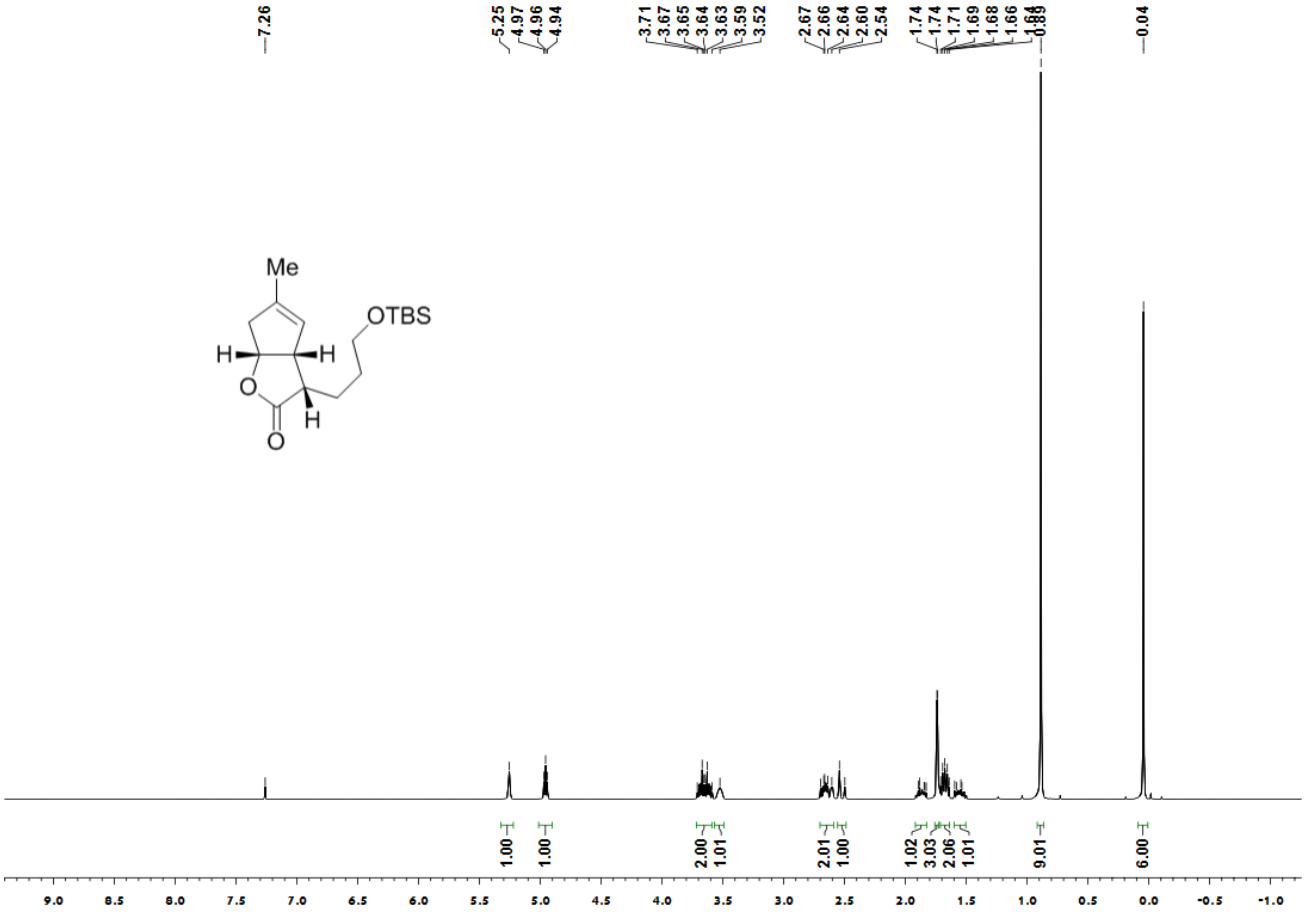
[2] Roy, A.; Schneller, S. W. *J. Org. Chem.* **2003**, *68*, 9269.

[3] Gilbert, M. W.; Galkina, A.; Mulzer, J. *Synlett* **2004**, *14*, 2558.

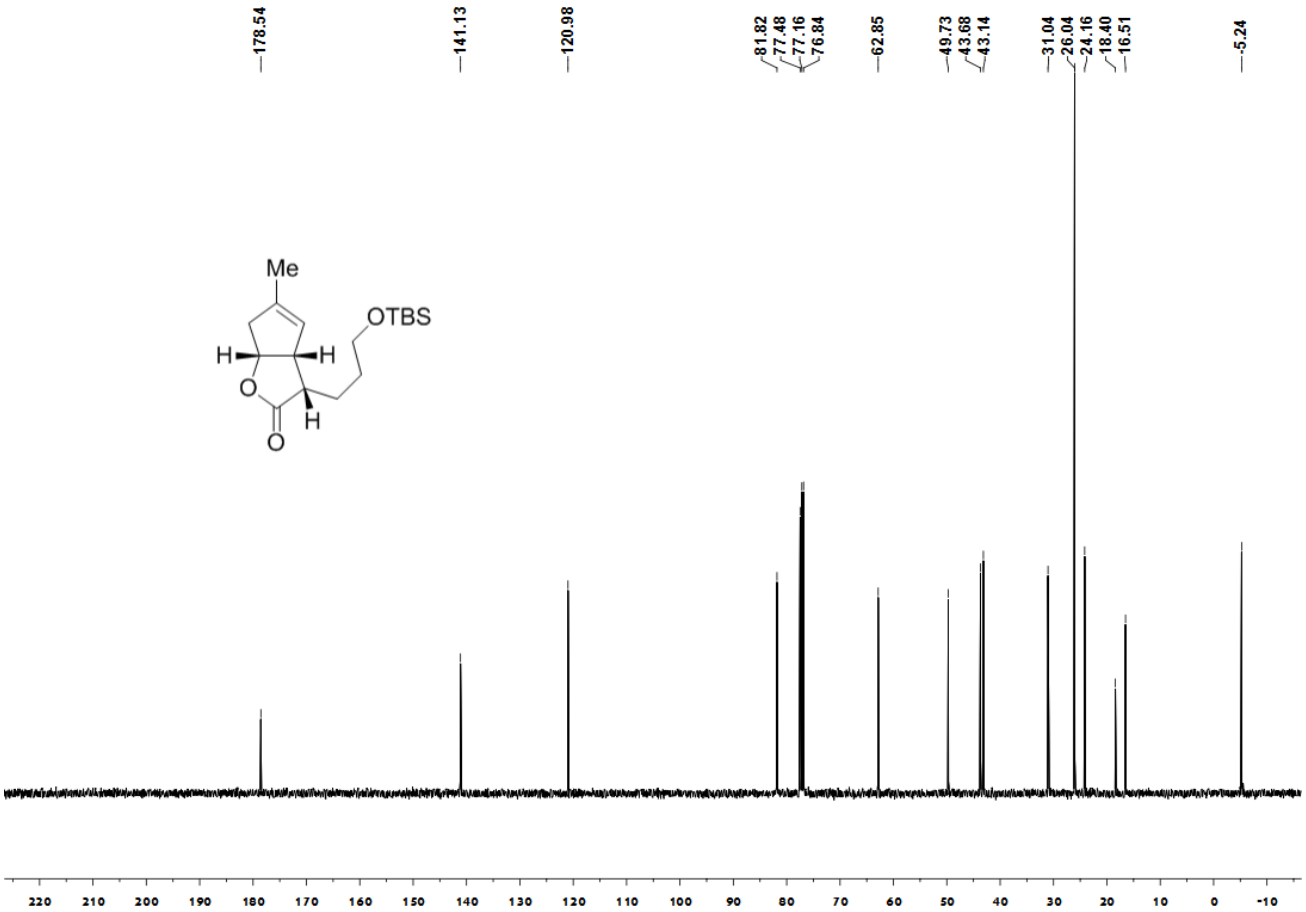
[4] Mulzer, J.; Giester, G.; Gilbert, M. *Helvetica Chimica Acta* **2005**, *88*, 1560.

III ^{1}H and ^{13}C NMR Spectra of Compounds

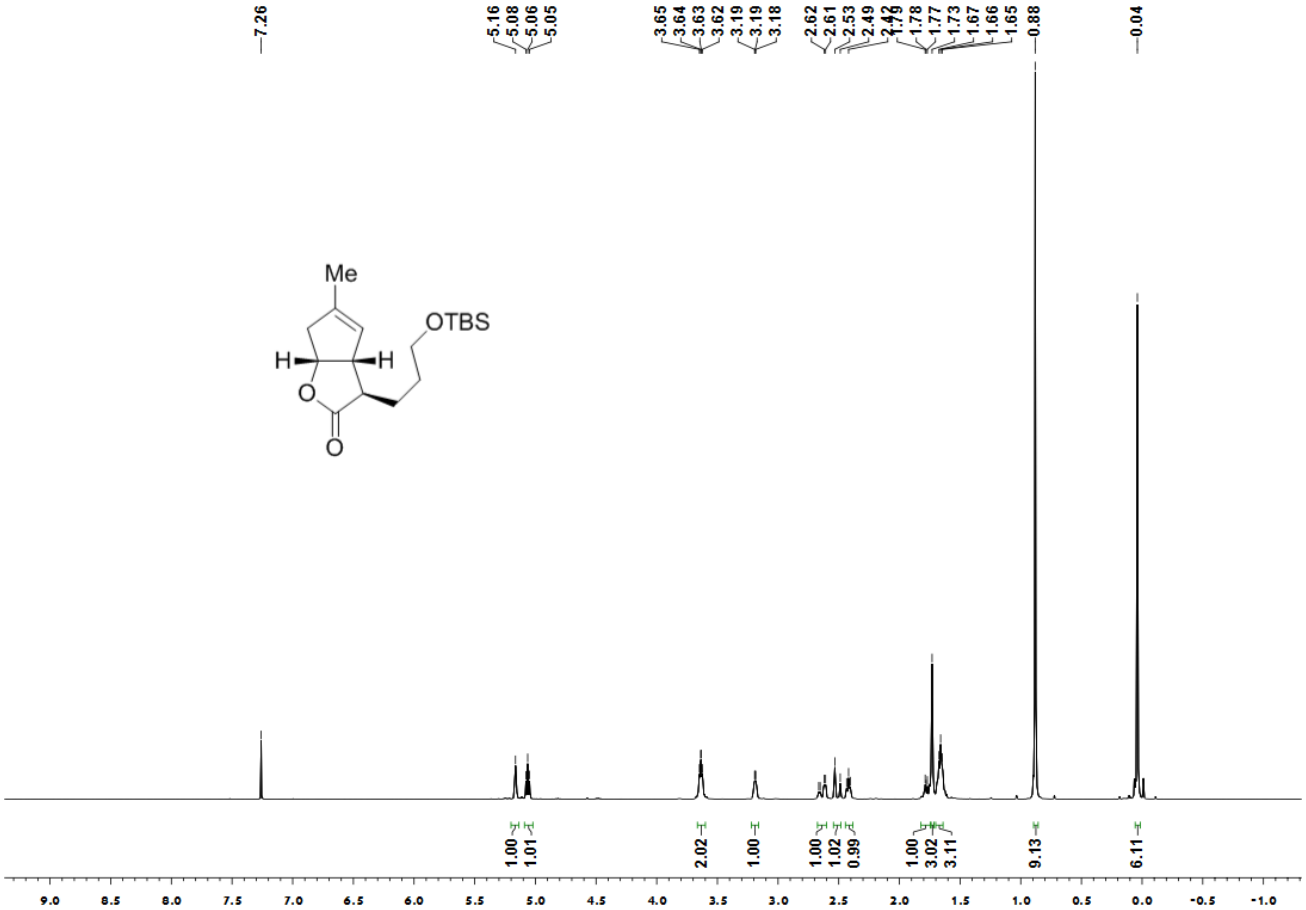
^{1}H NMR Spectra of **13** (400 MHz, $CDCl_3$)



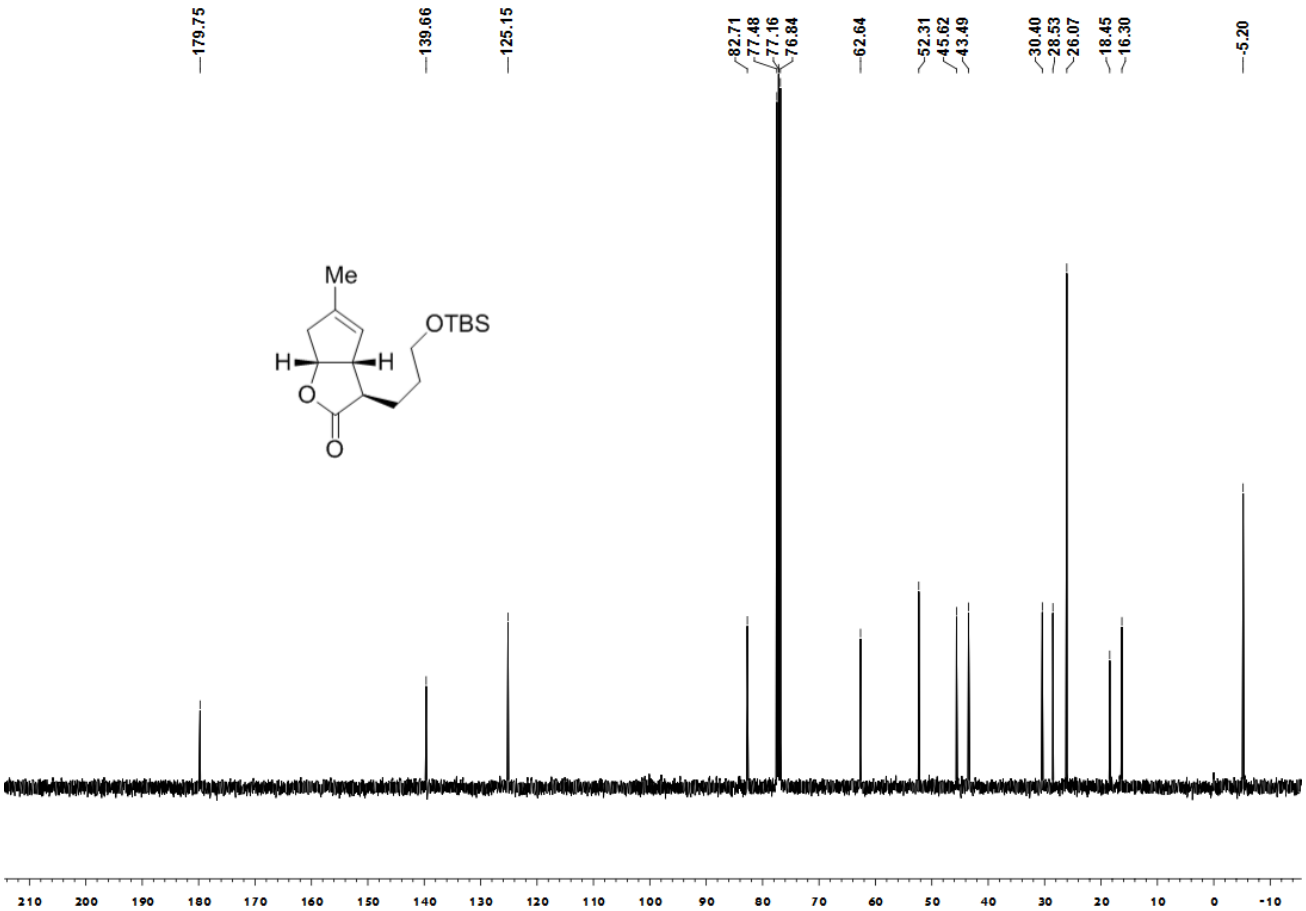
^{13}C NMR Spectra of **13** (101 MHz, $CDCl_3$)



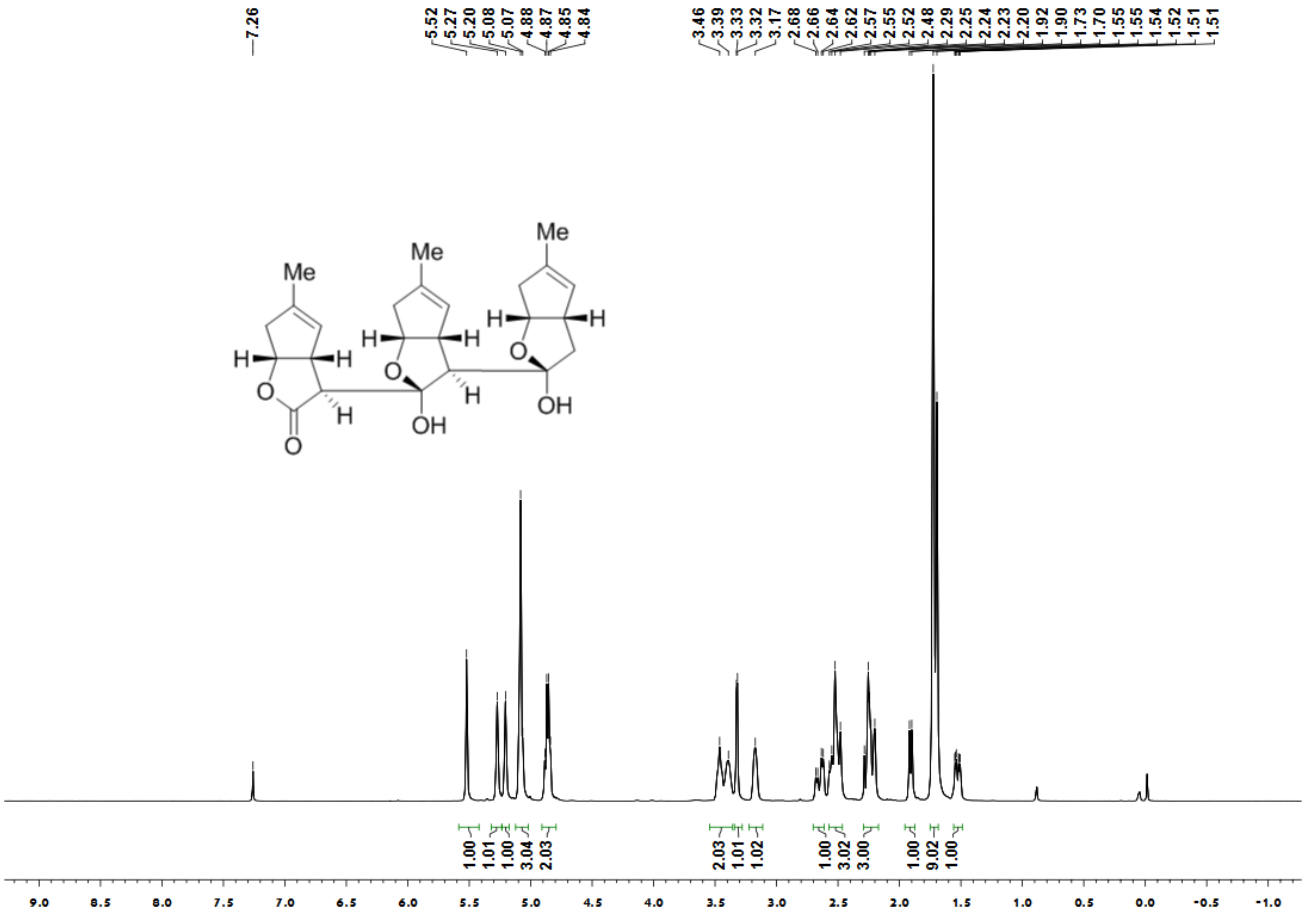
^{1}H NMR Spectra of **13a** (400 MHz, $CDCl_3$)



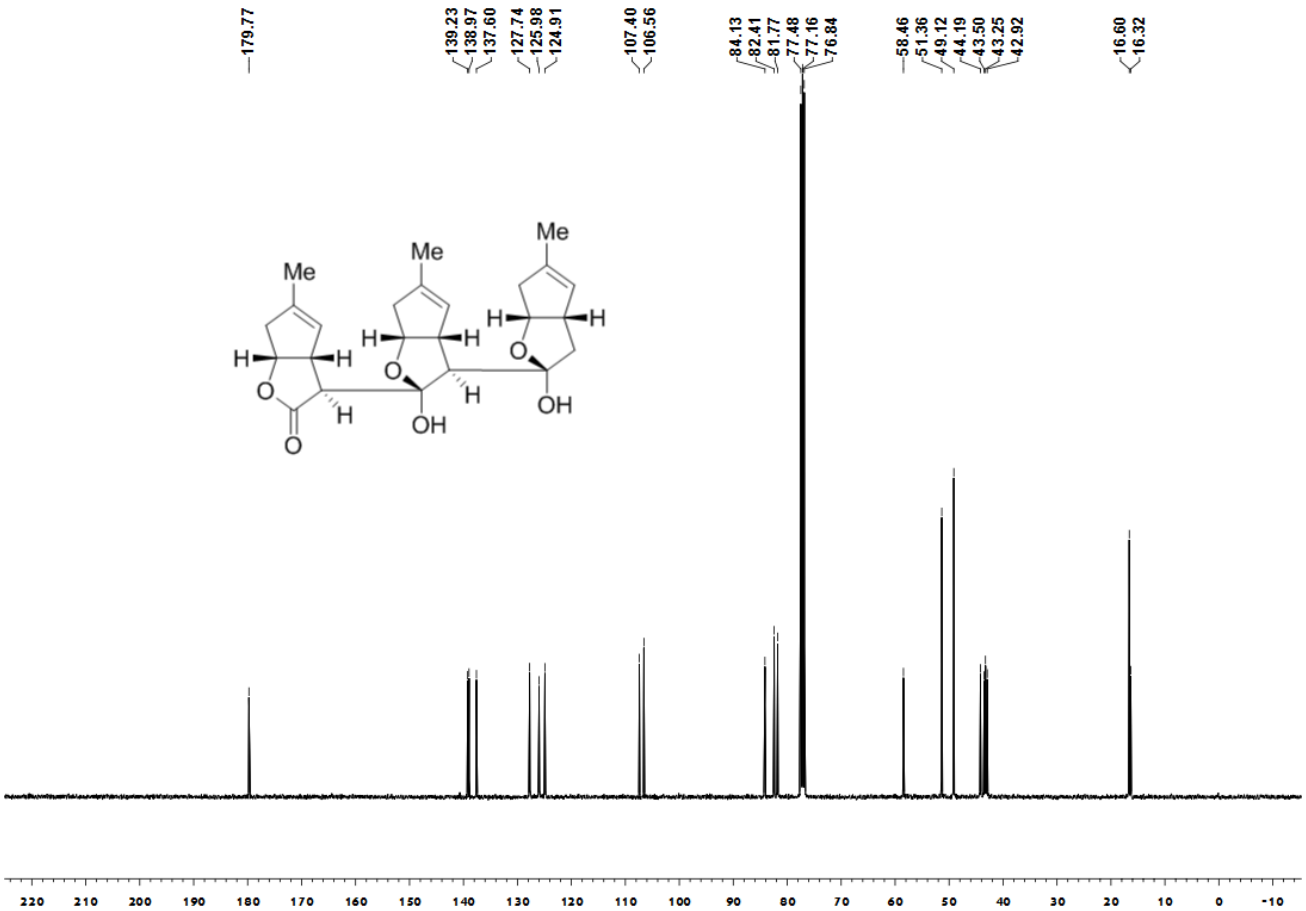
^{13}C NMR Spectra of **13a** (101 MHz, $CDCl_3$)



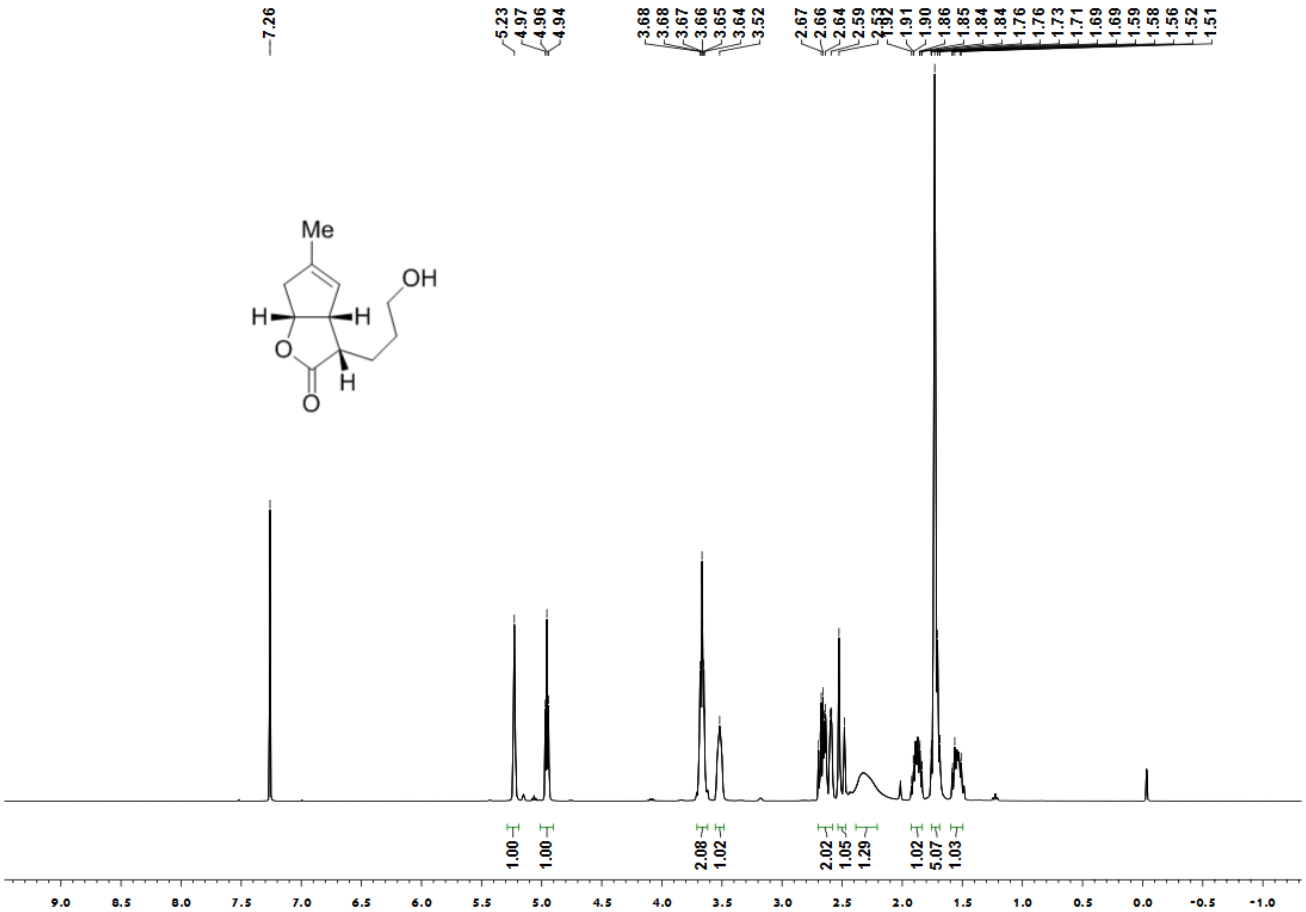
^{1}H NMR Spectra of **13b** (400 MHz, $CDCl_3$)



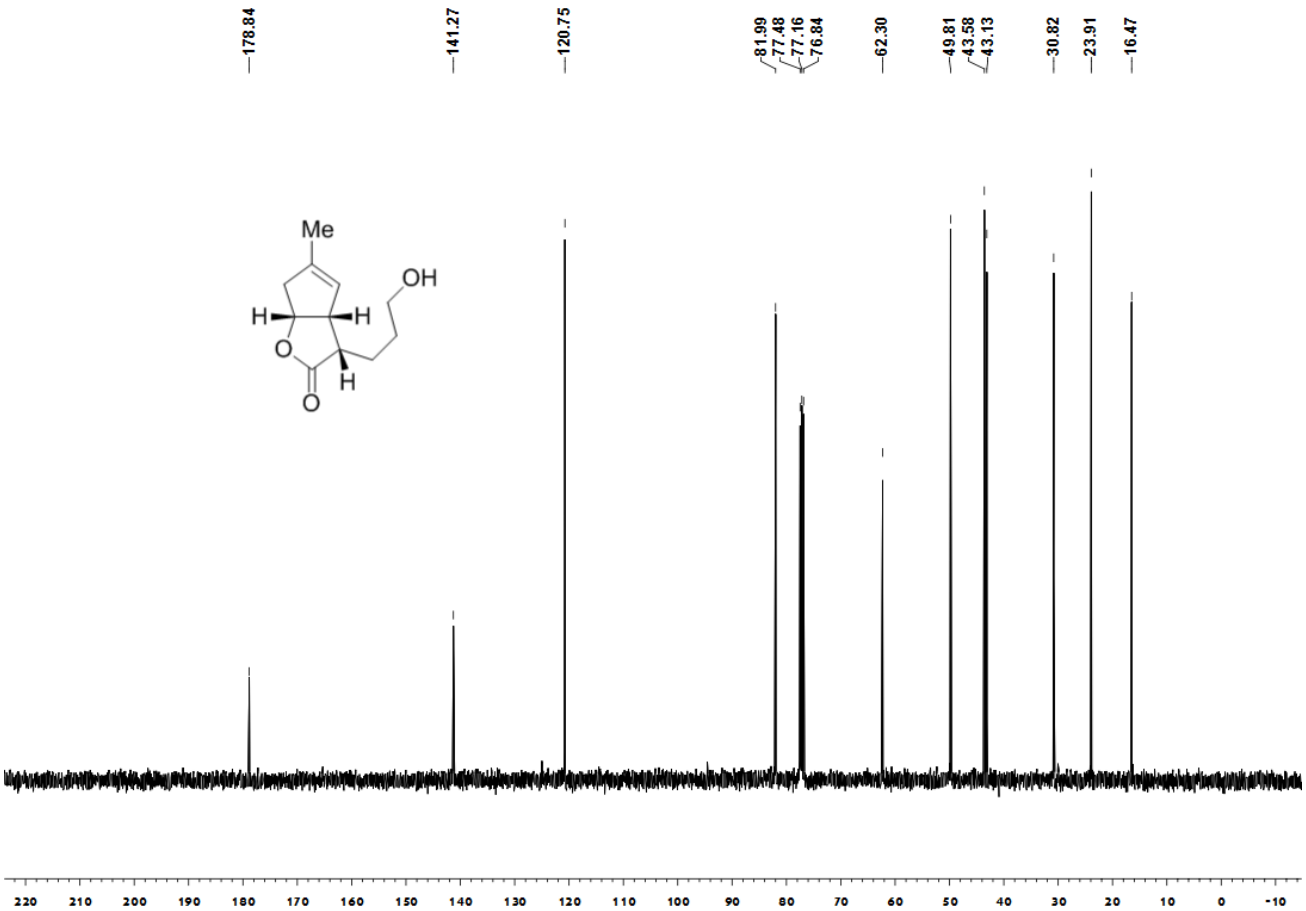
^{13}C NMR Spectra of **13b** (101 MHz, $CDCl_3$)



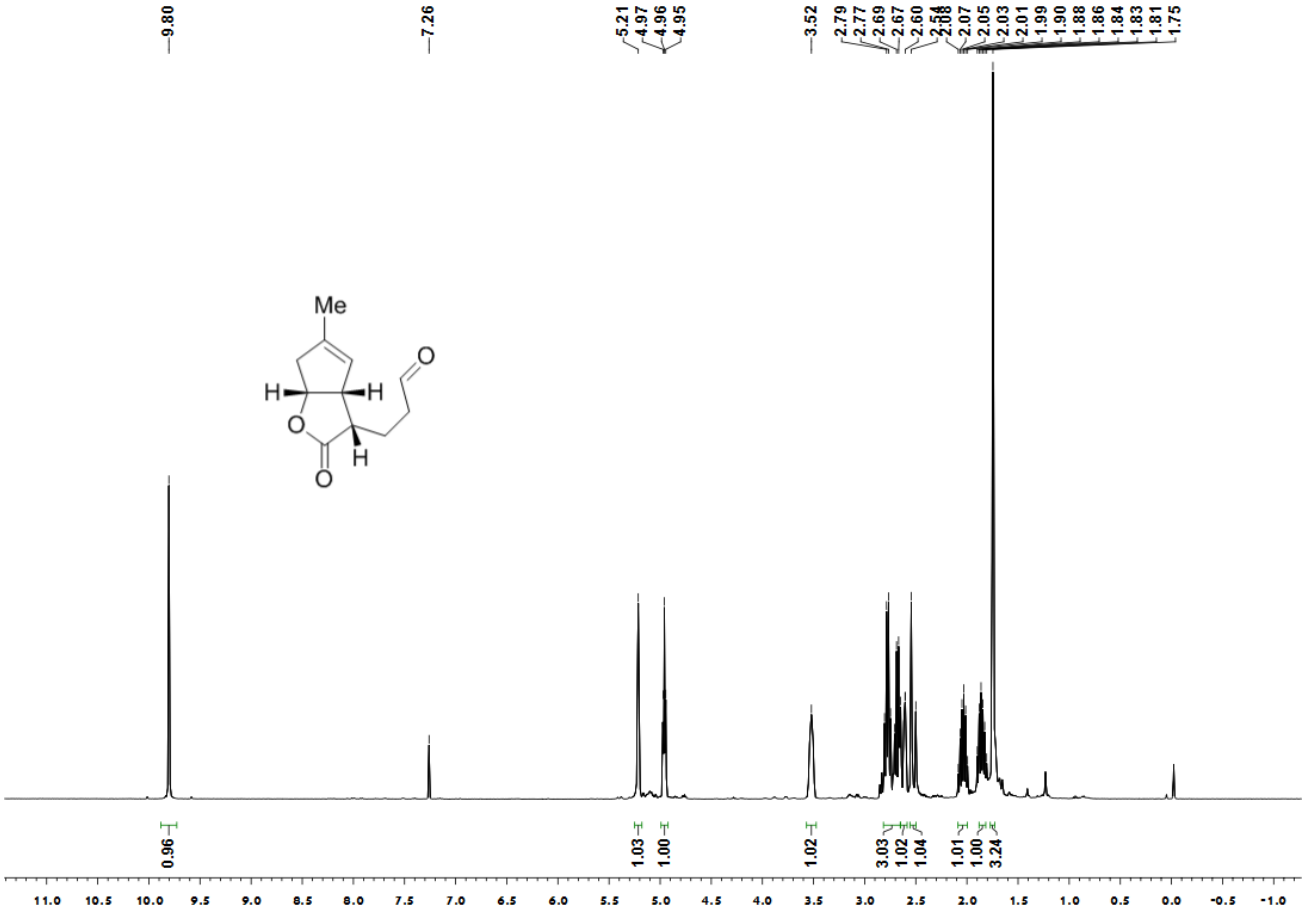
^{1}H NMR Spectra of **16** (400 MHz, $CDCl_3$)



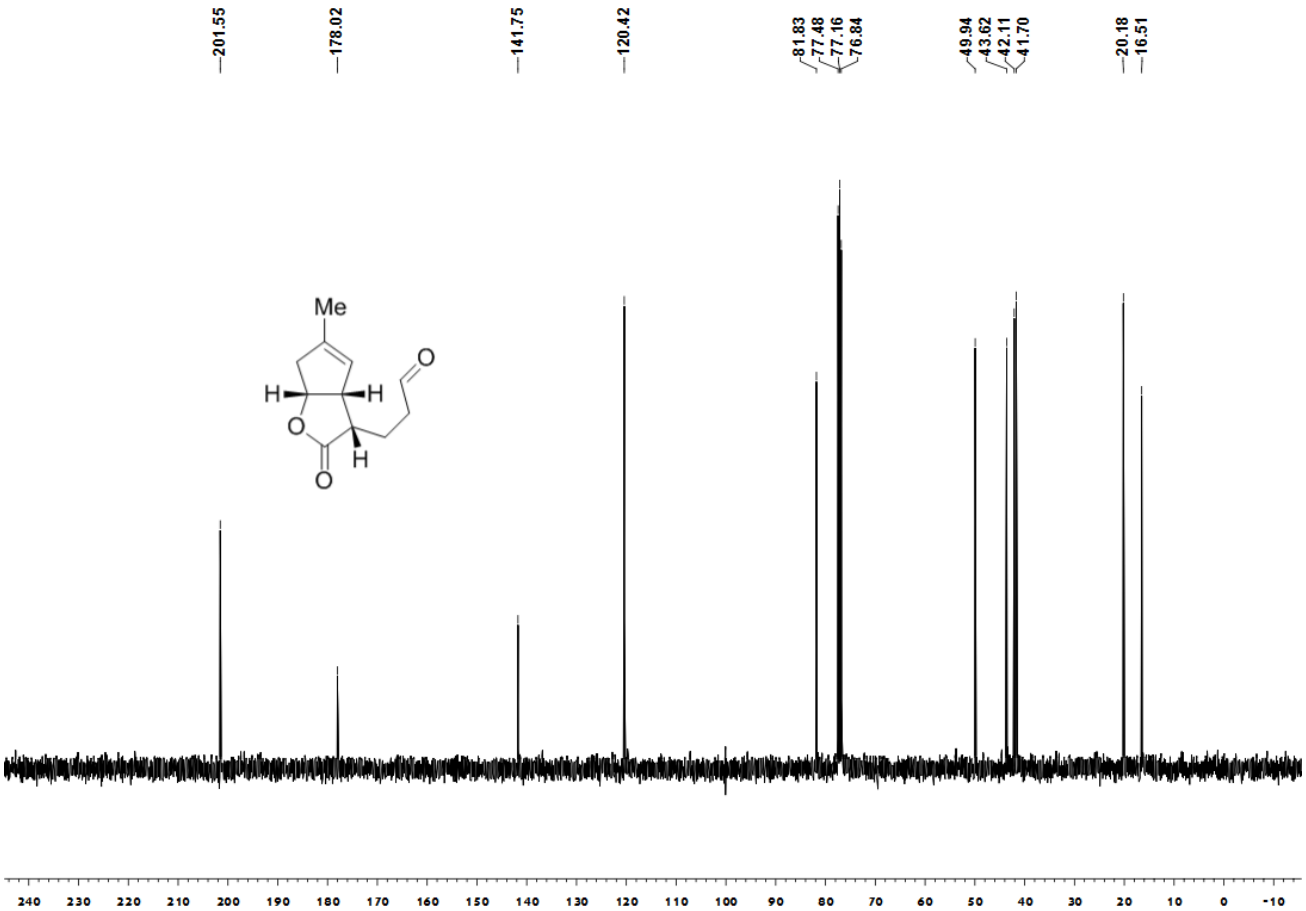
^{13}C NMR Spectra of **16** (101 MHz, $CDCl_3$)



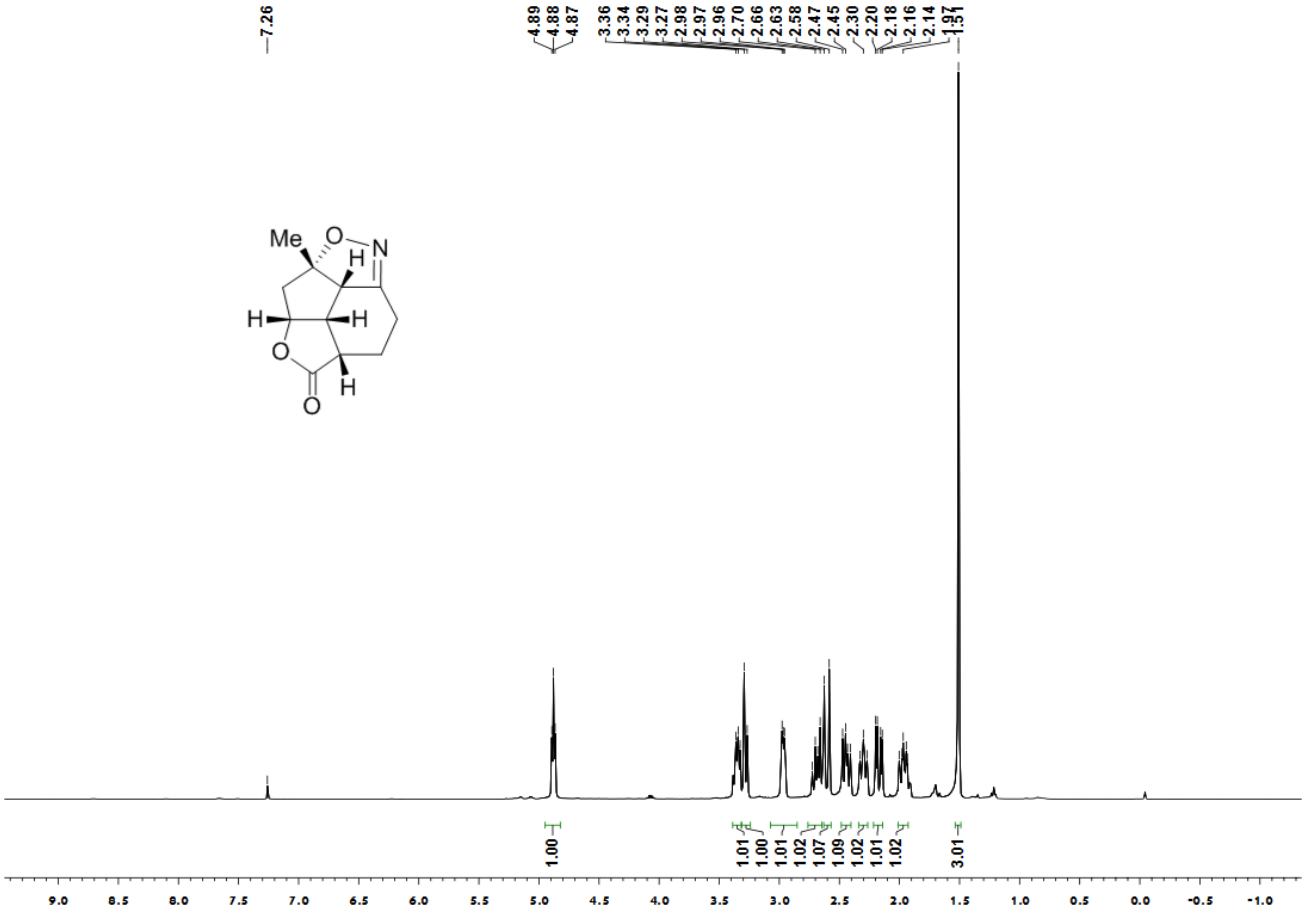
^{1}H NMR Spectra of **12** (400 MHz, $CDCl_3$)



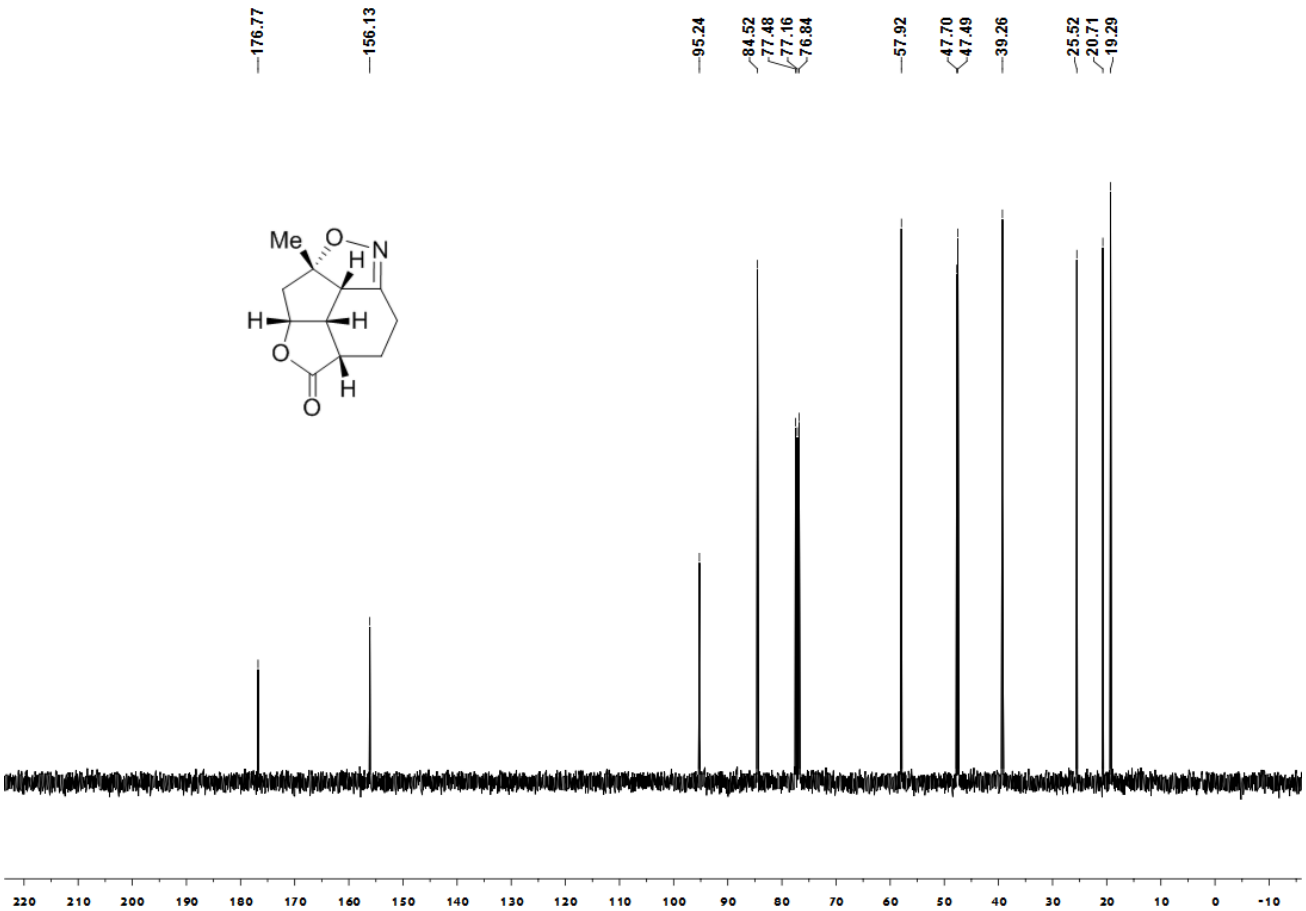
^{13}C NMR Spectra of **12** (101 MHz, $CDCl_3$)



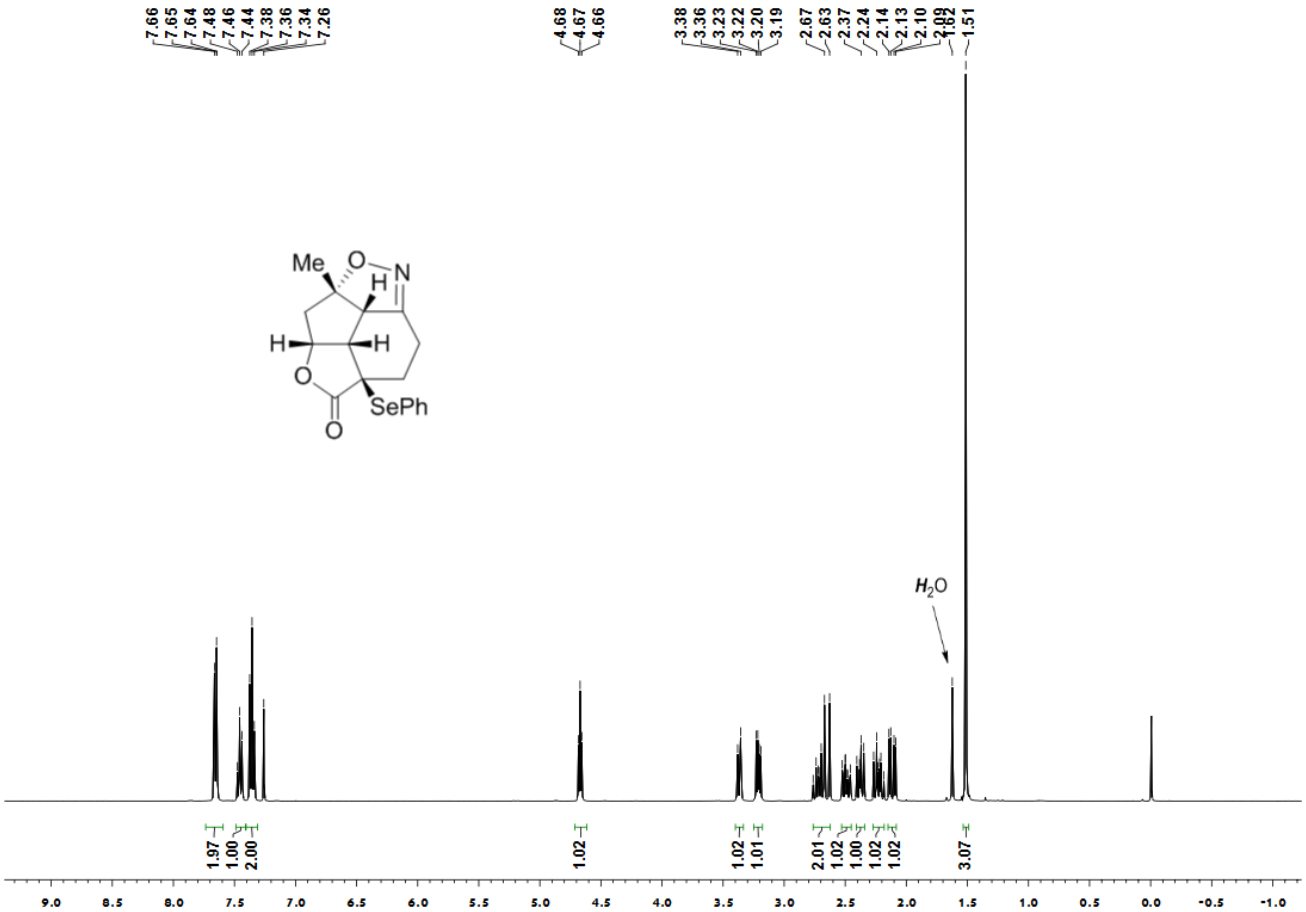
^{1}H NMR Spectra of **10** (400 MHz, $CDCl_3$)



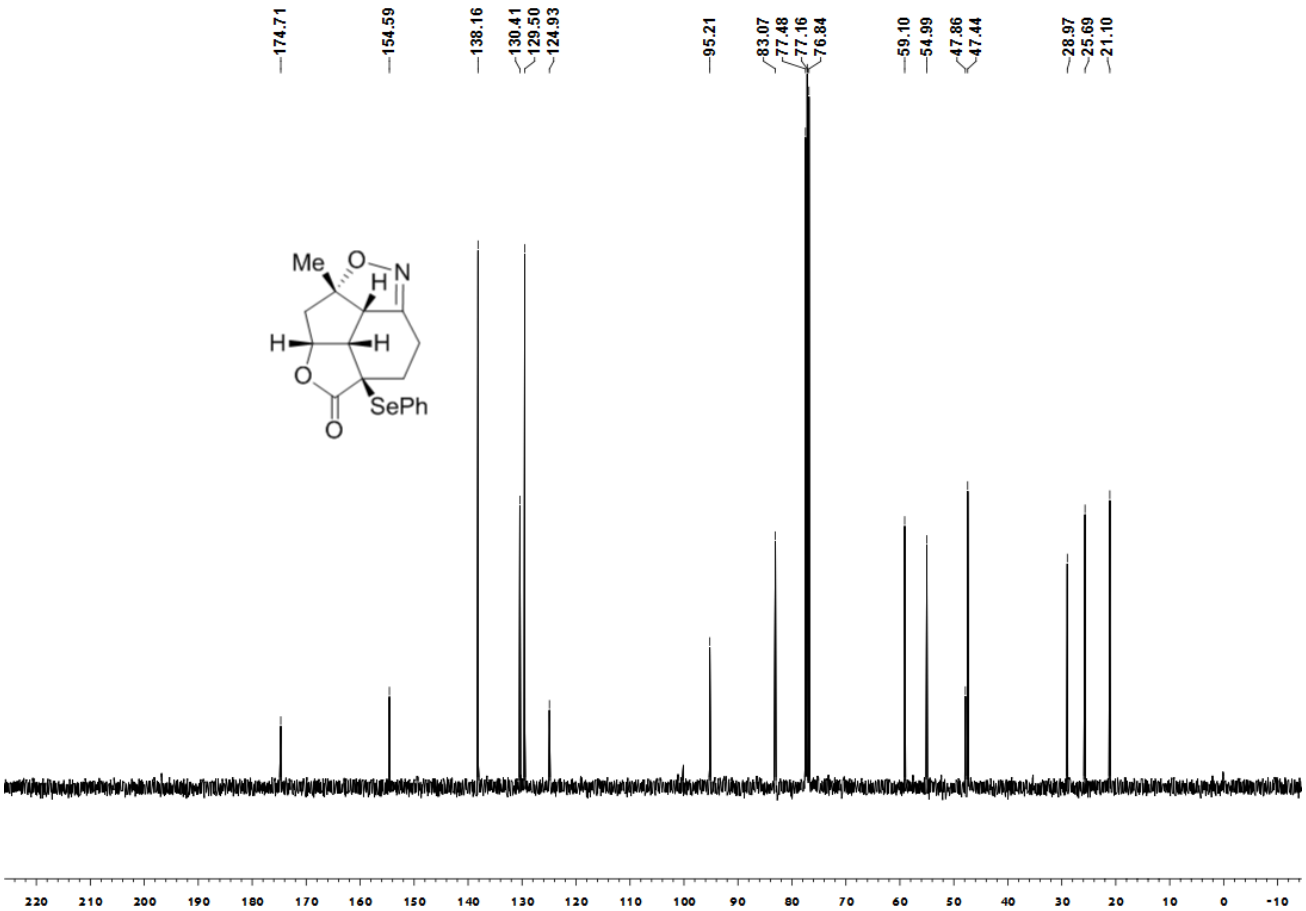
^{13}C NMR Spectra of **10** (101 MHz, $CDCl_3$)



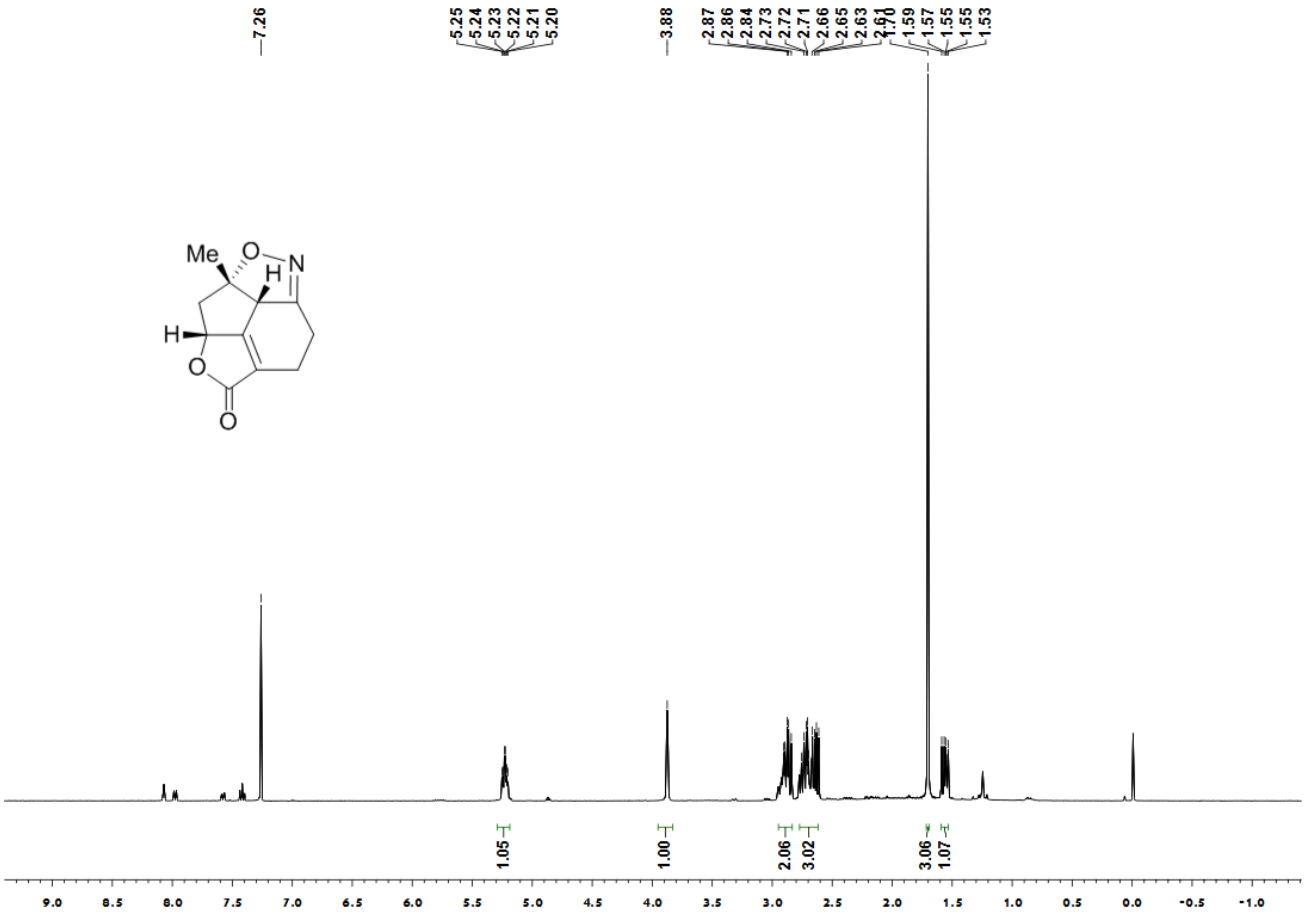
^{1}H NMR Spectra of **17** (400 MHz, $CDCl_3$)



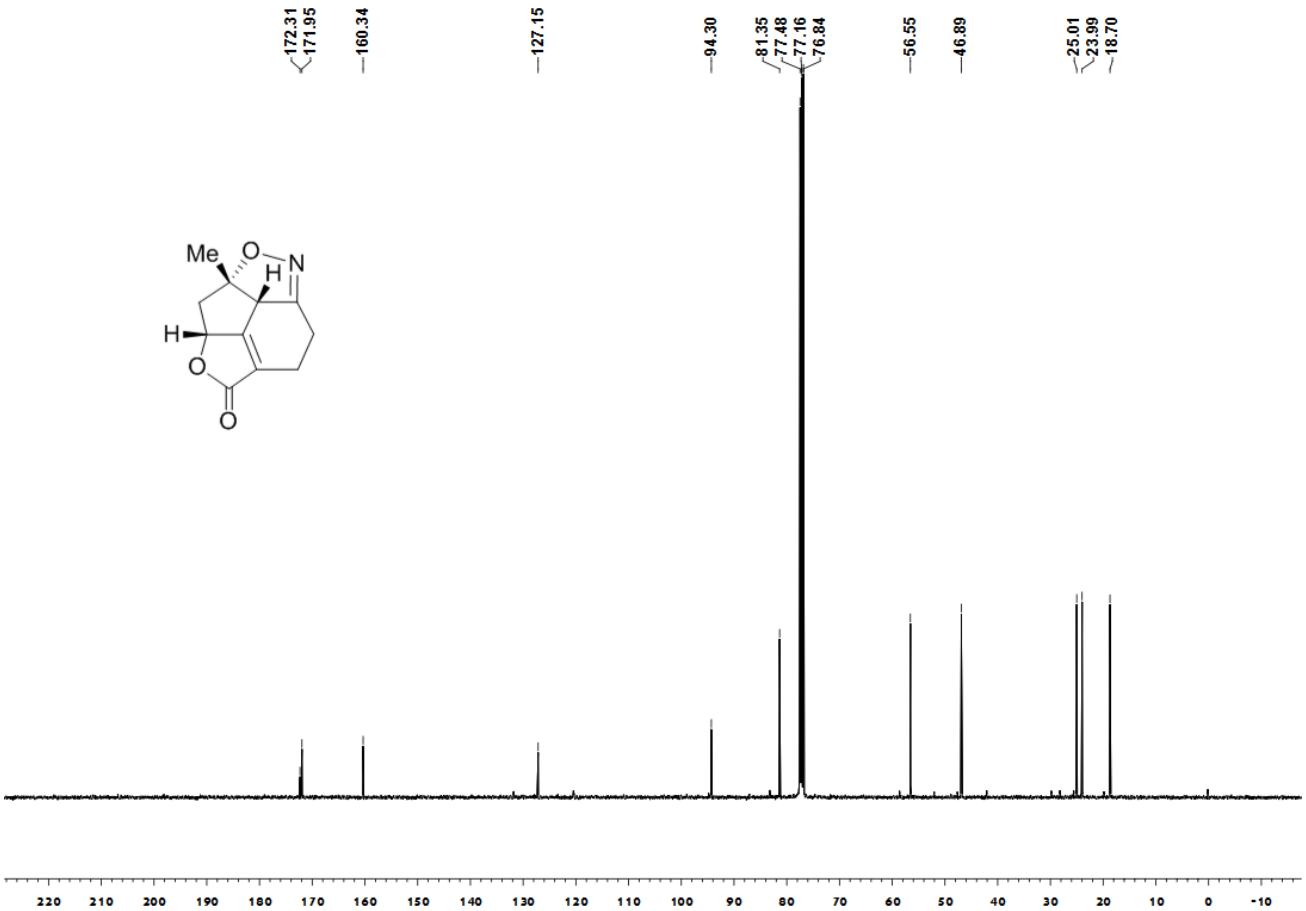
^{13}C NMR Spectra of **17** (101 MHz, $CDCl_3$)



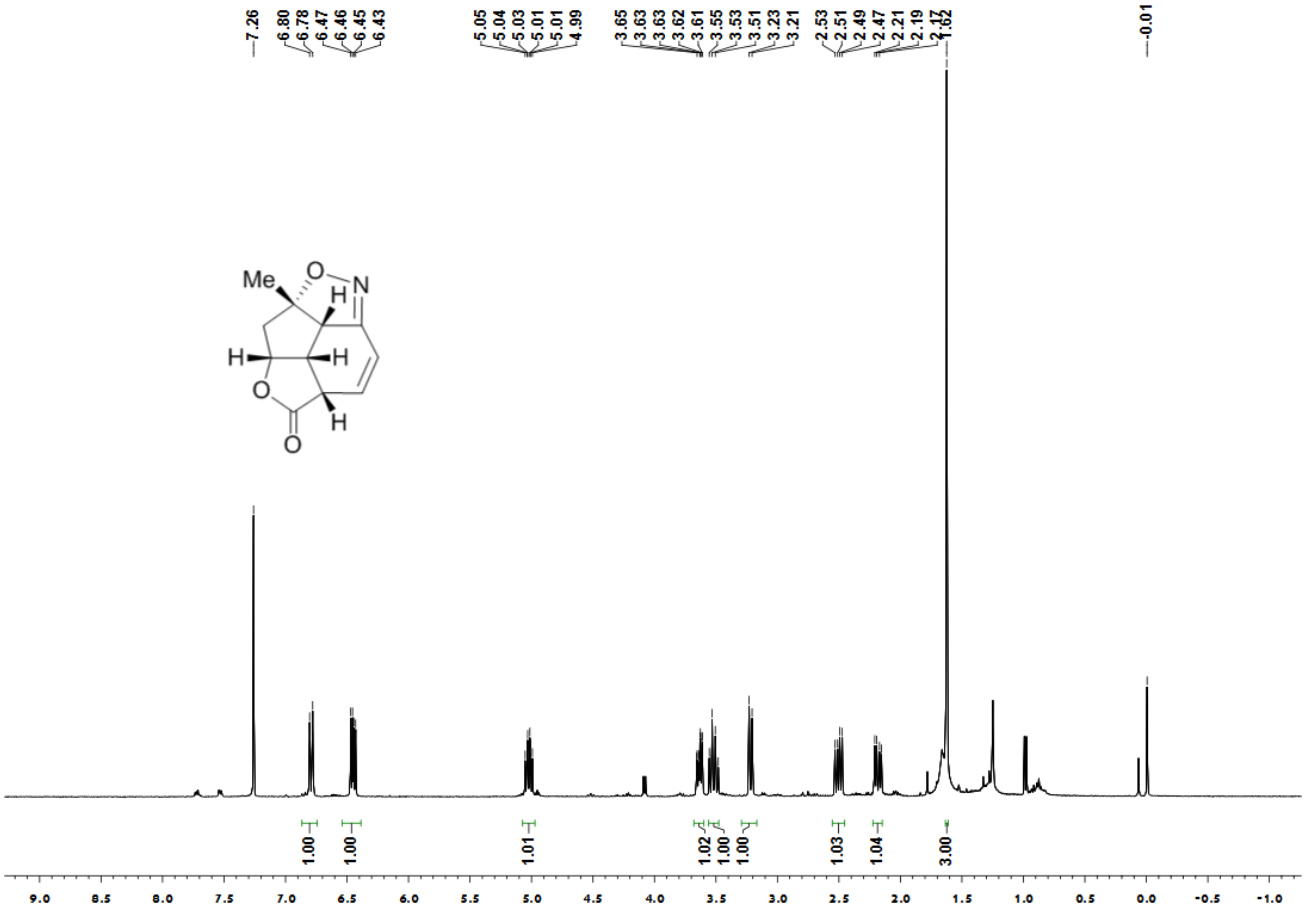
^{1}H NMR Spectra of **18a** (400 MHz, $CDCl_3$)



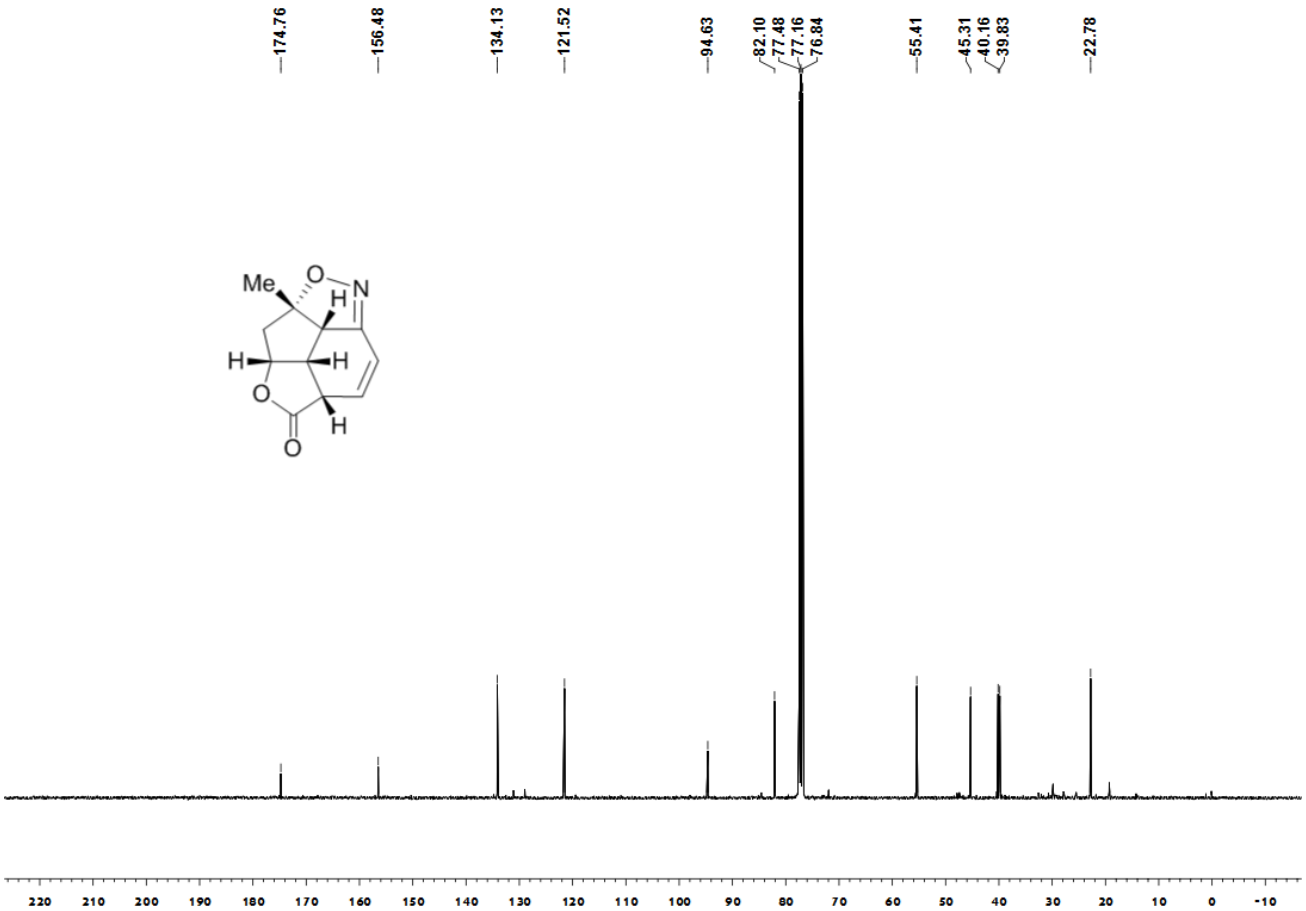
^{13}C NMR Spectra of **18a** (101 MHz, $CDCl_3$)



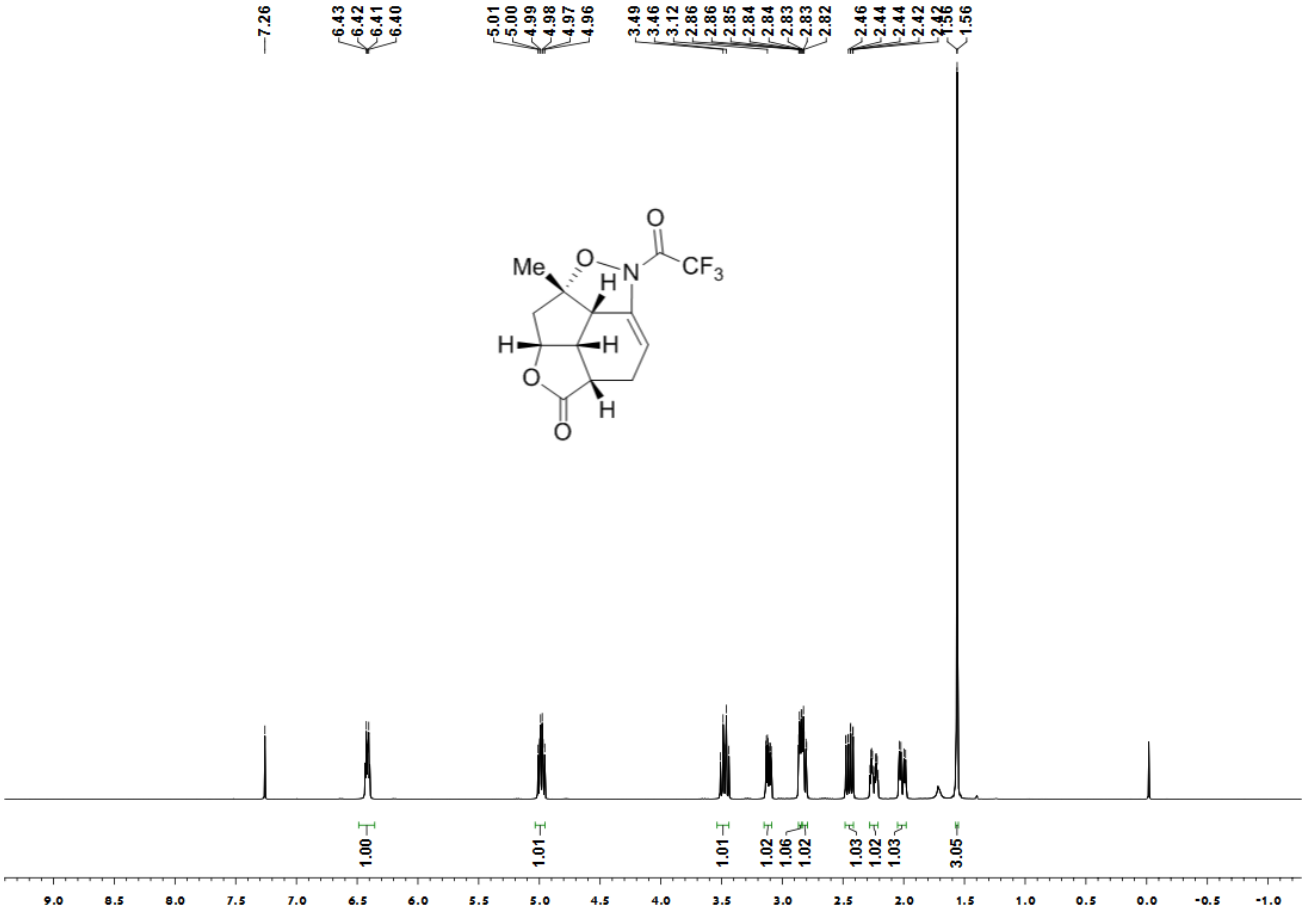
^{1}H NMR Spectra of **19** (400 MHz, $CDCl_3$)



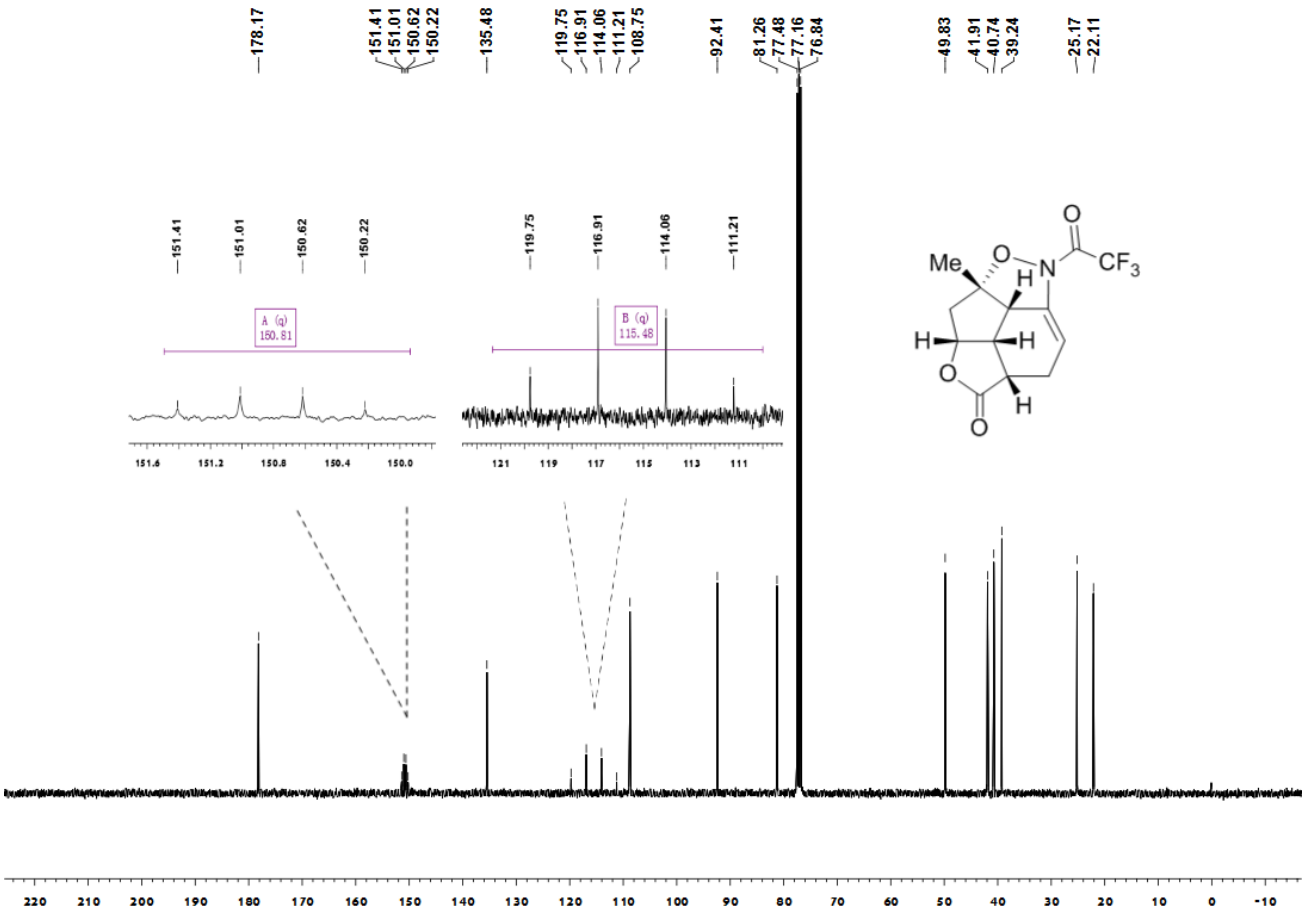
^{13}C NMR Spectra of **19** (101 MHz, $CDCl_3$)



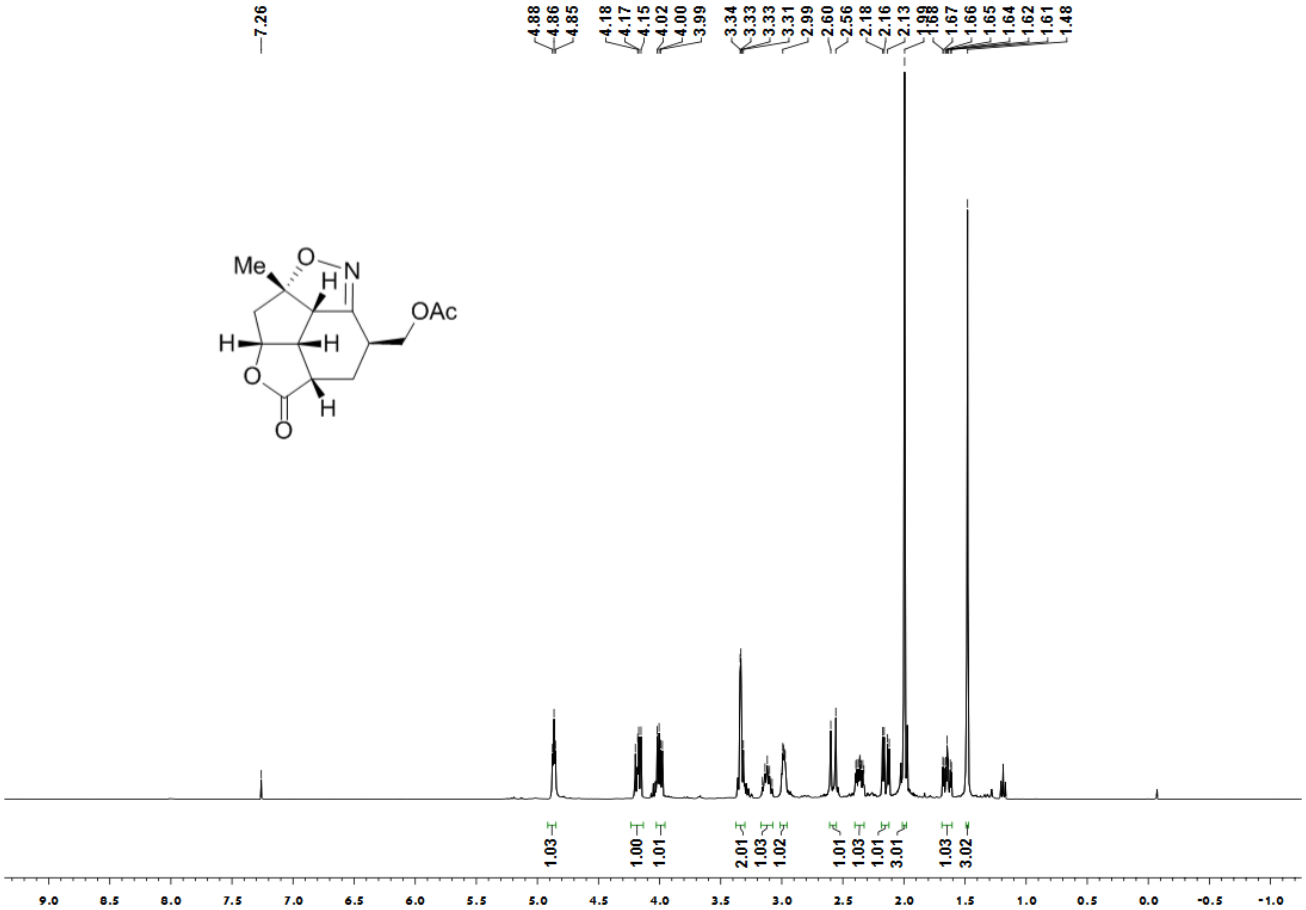
^{1}H NMR Spectra of **20** (400 MHz, $CDCl_3$)



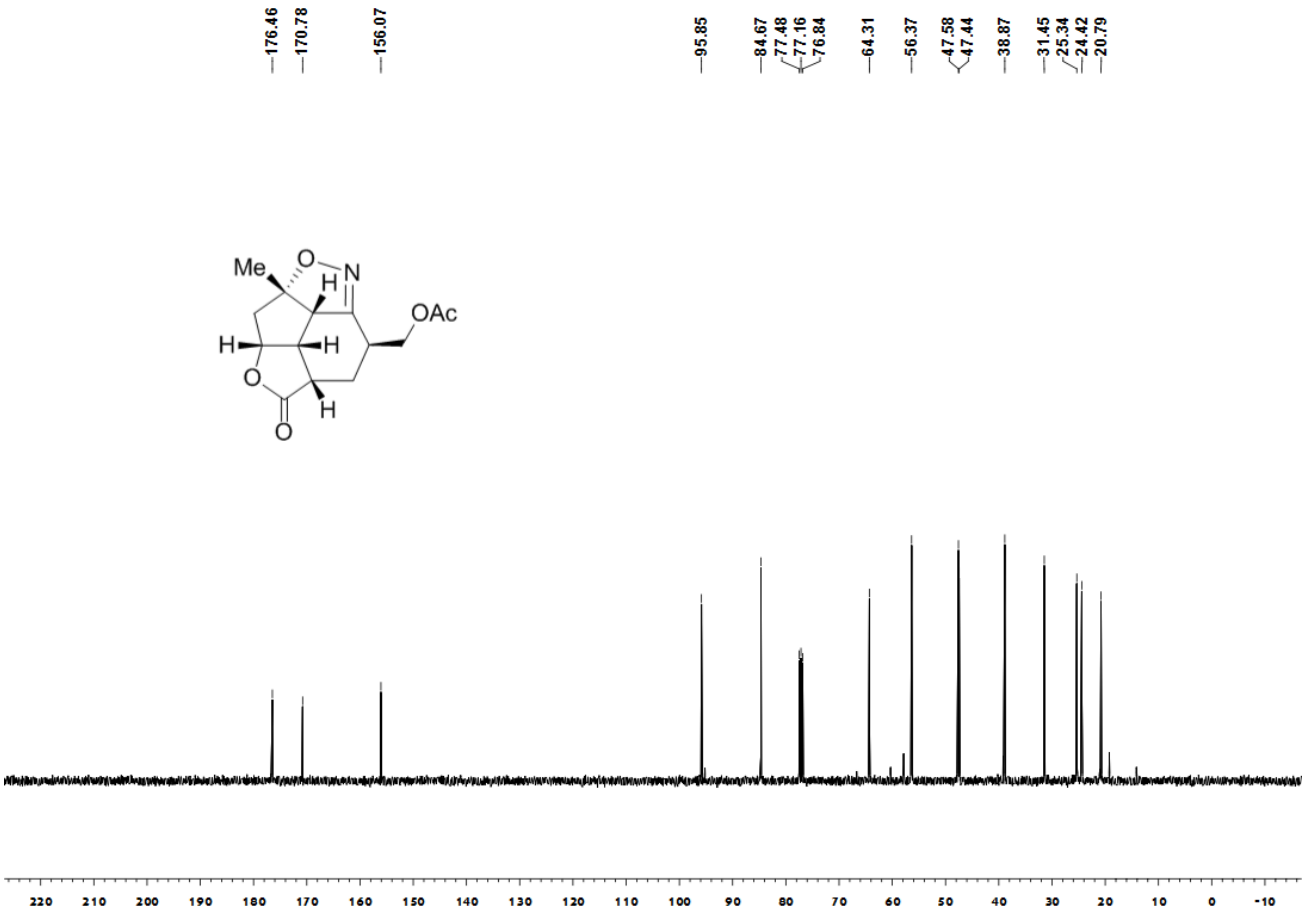
^{13}C NMR Spectra of **20** (101 MHz, $CDCl_3$)



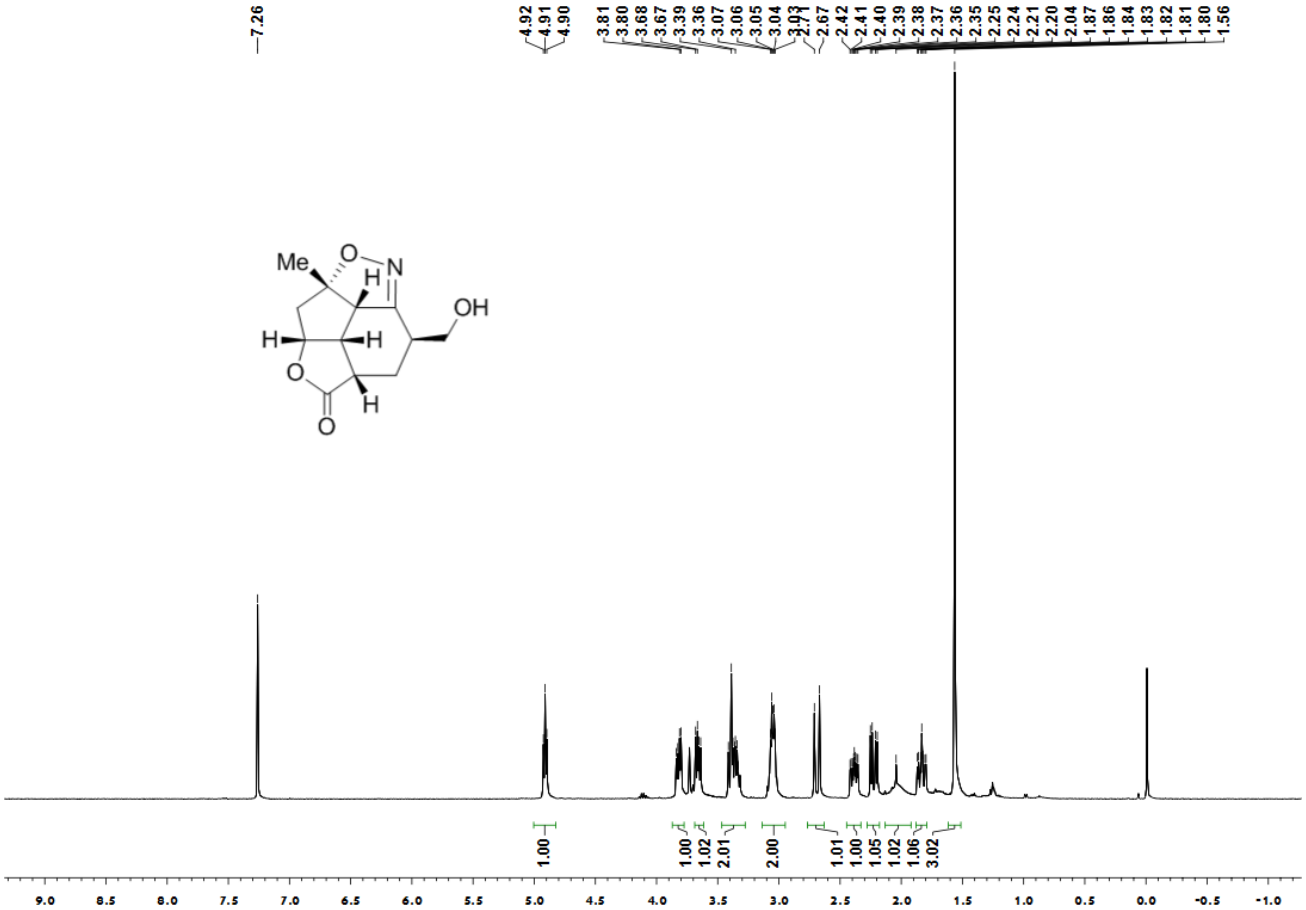
^{1}H NMR Spectra of **21** (400 MHz, $CDCl_3$)



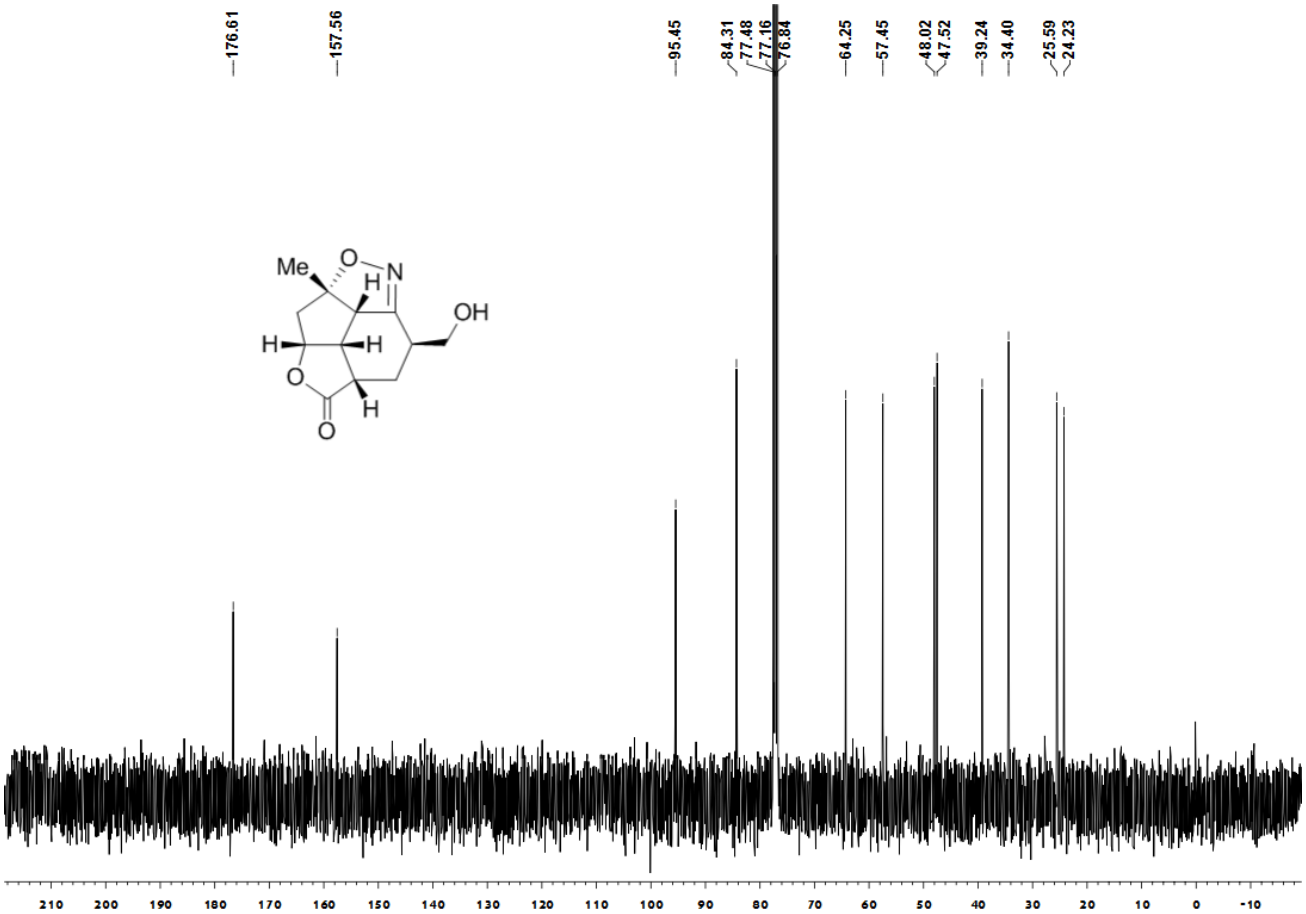
^{13}C NMR Spectra of **21** (101 MHz, $CDCl_3$)



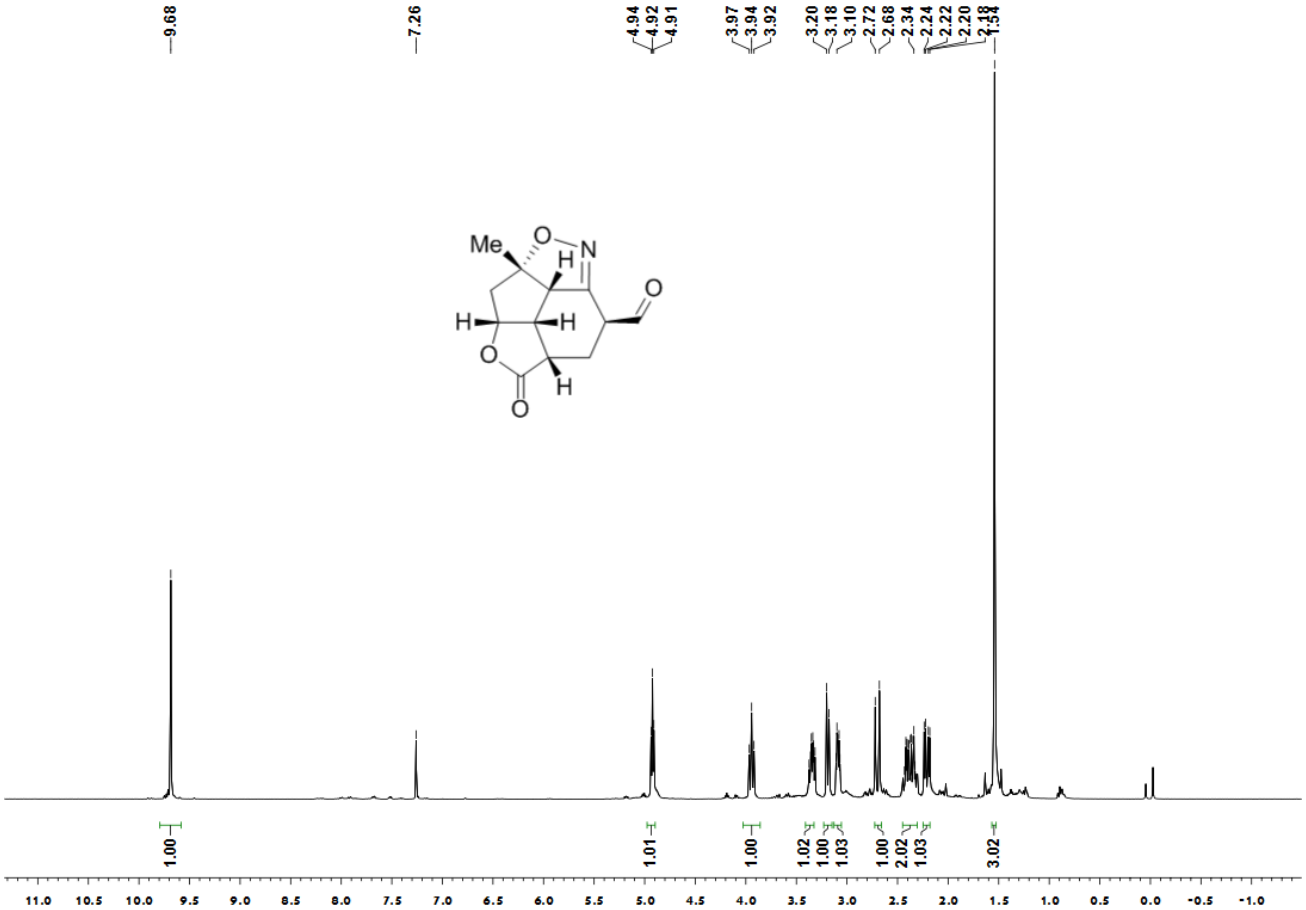
^{1}H NMR Spectra of **s4** (400 MHz, $CDCl_3$)



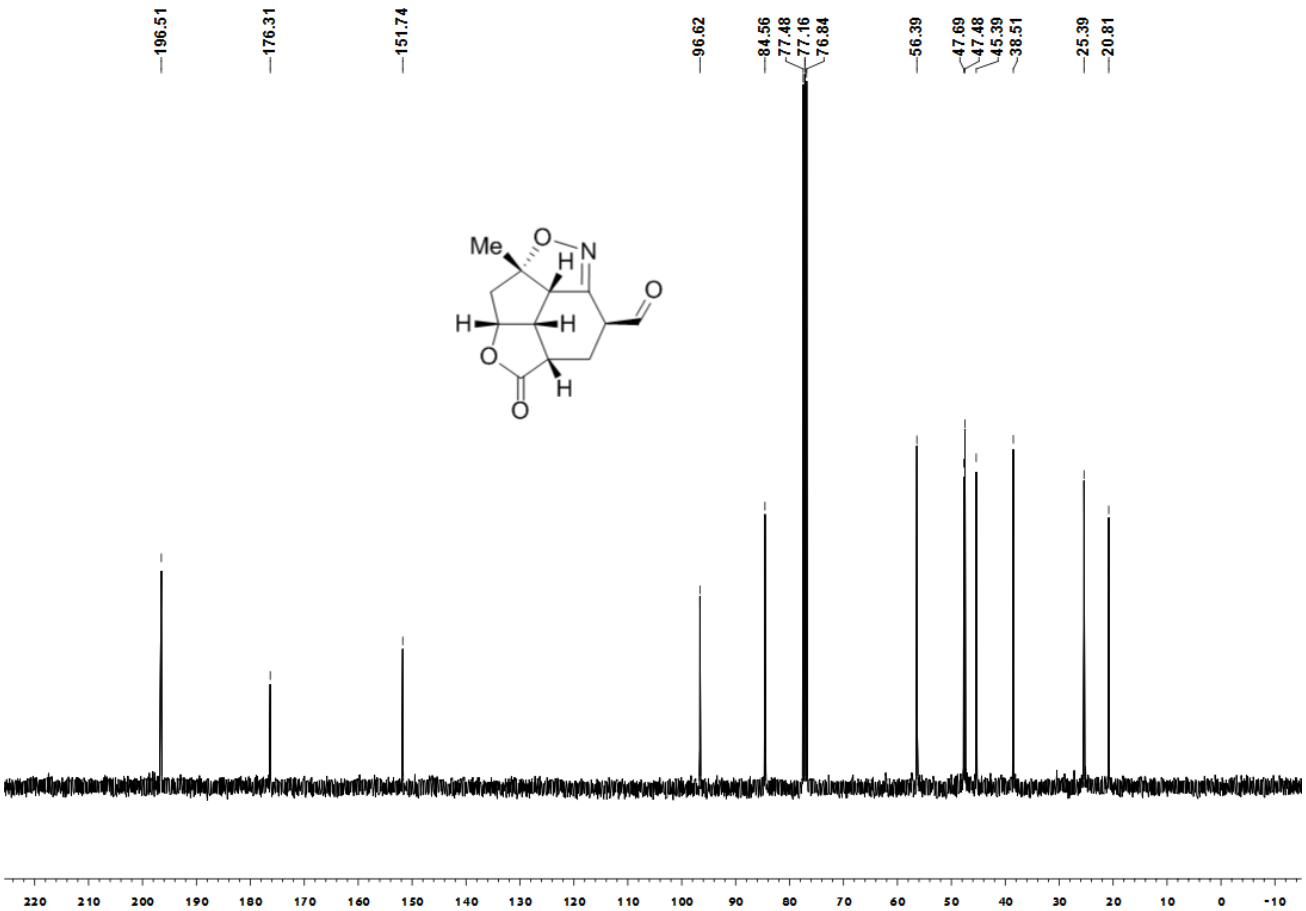
^{13}C NMR Spectra of **s4** (101 MHz, $CDCl_3$)



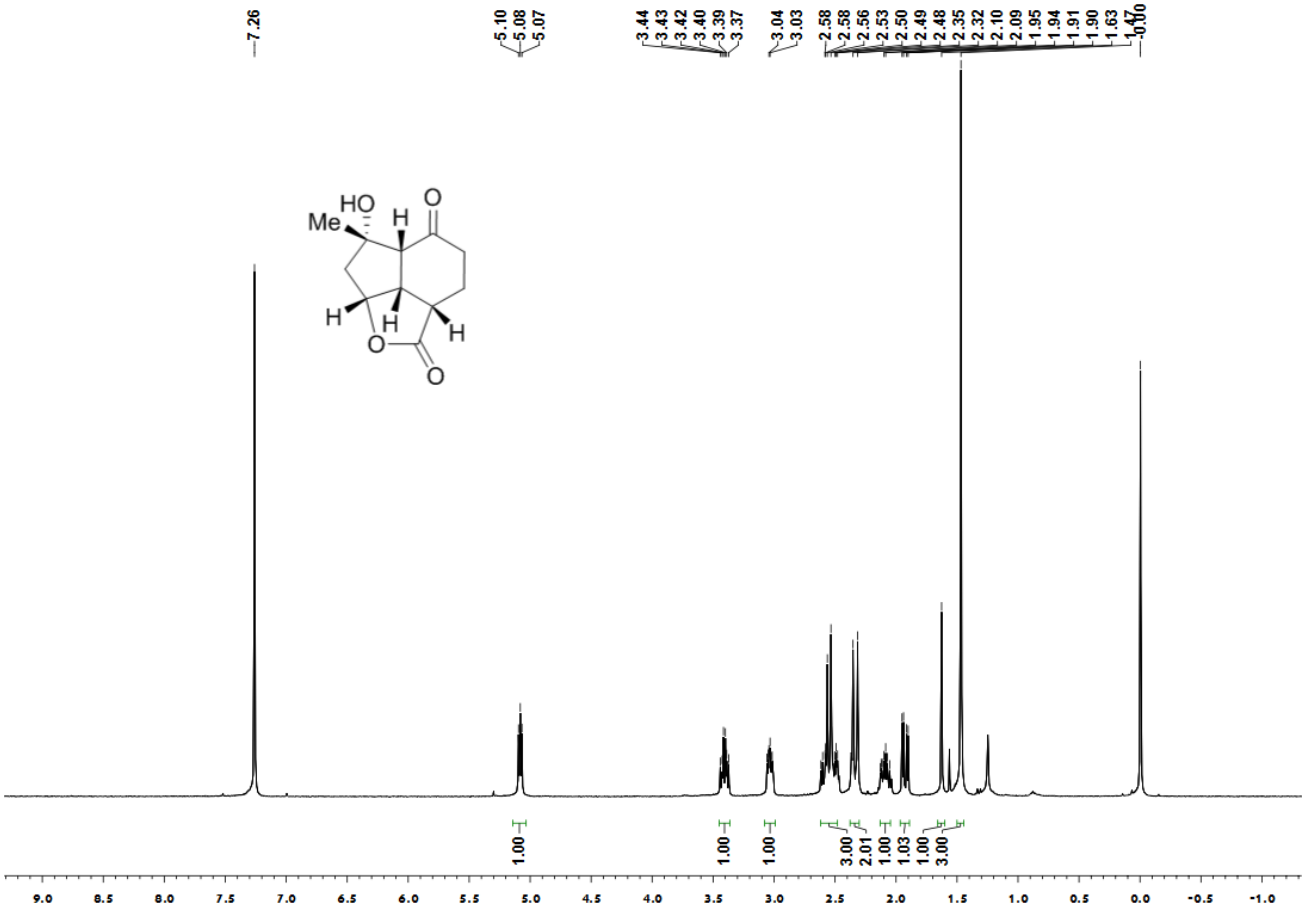
^{1}H NMR Spectra of **22** (400 MHz, $CDCl_3$)



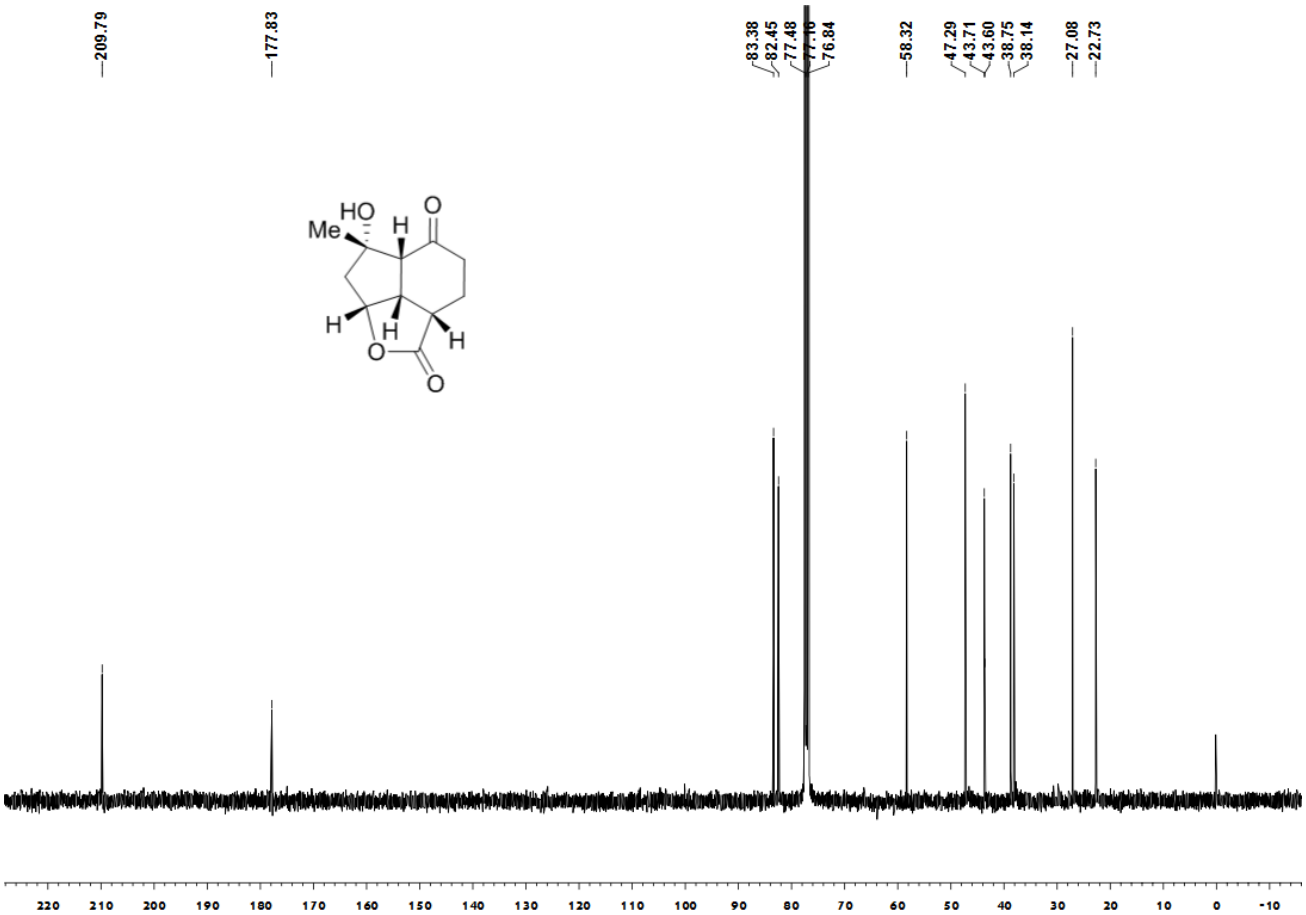
^{13}C NMR Spectra of **22** (101 MHz, $CDCl_3$)



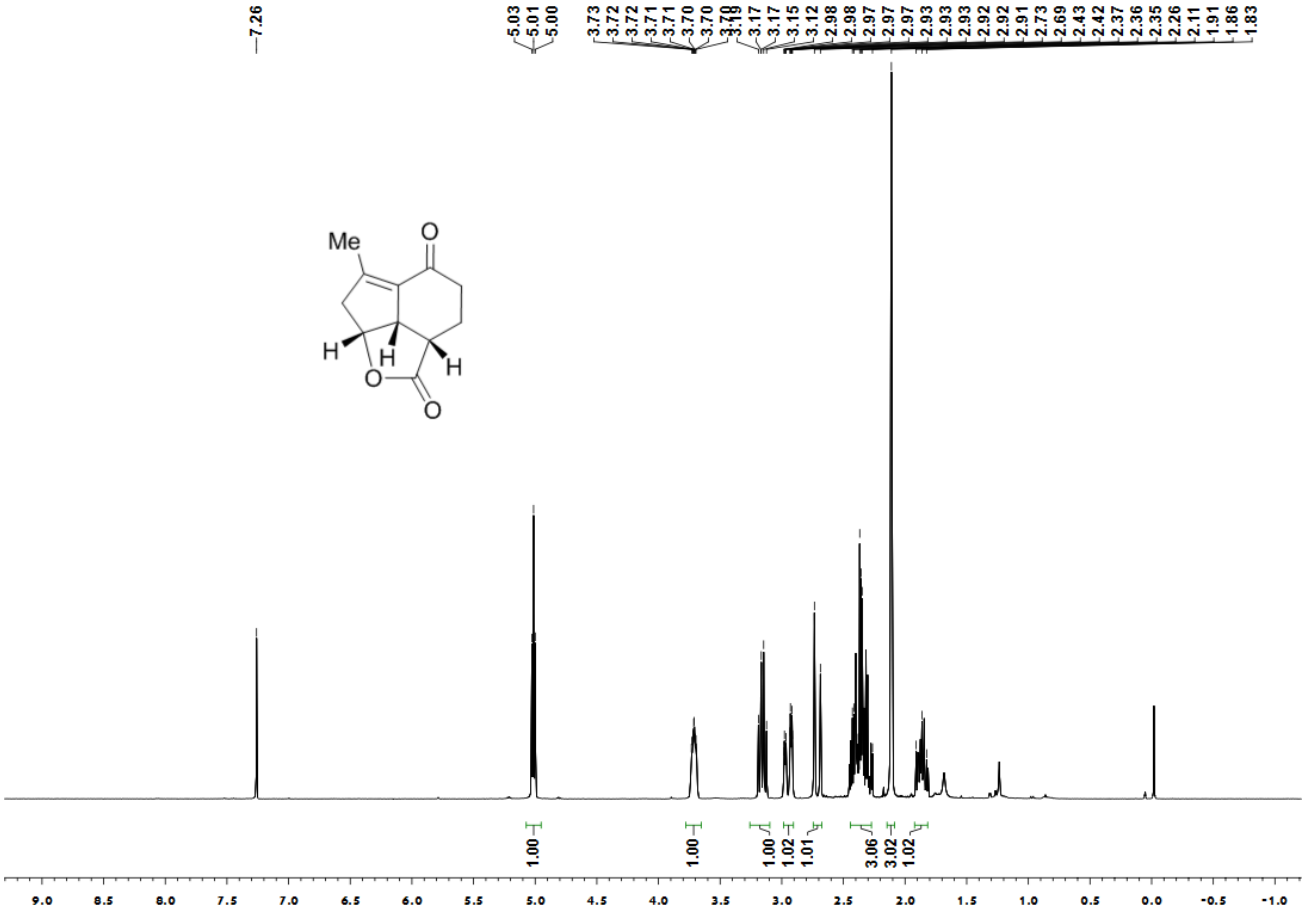
^{1}H NMR Spectra of **9** (400 MHz, $CDCl_3$)



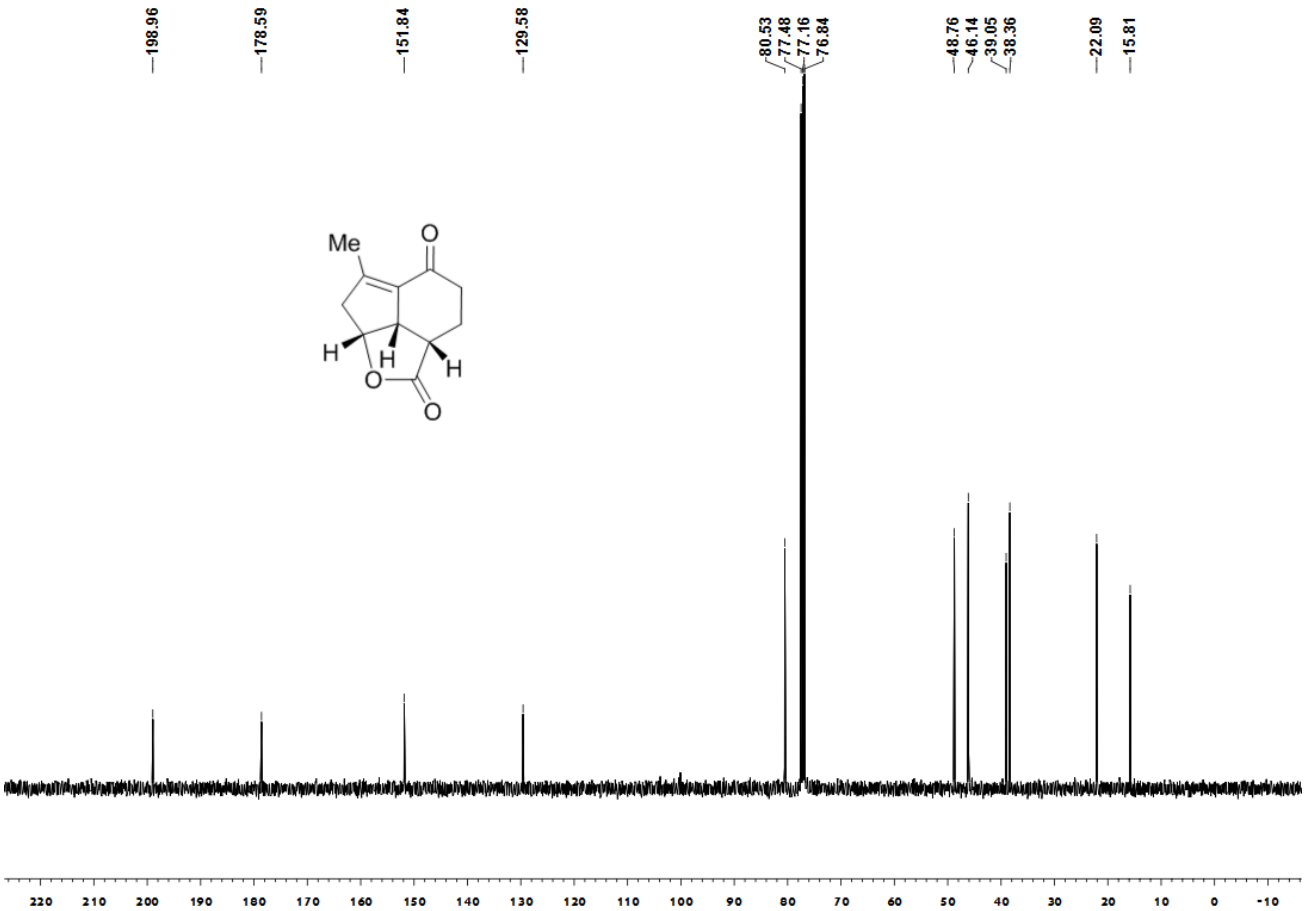
^{13}C NMR Spectra of **9** (101 MHz, $CDCl_3$)



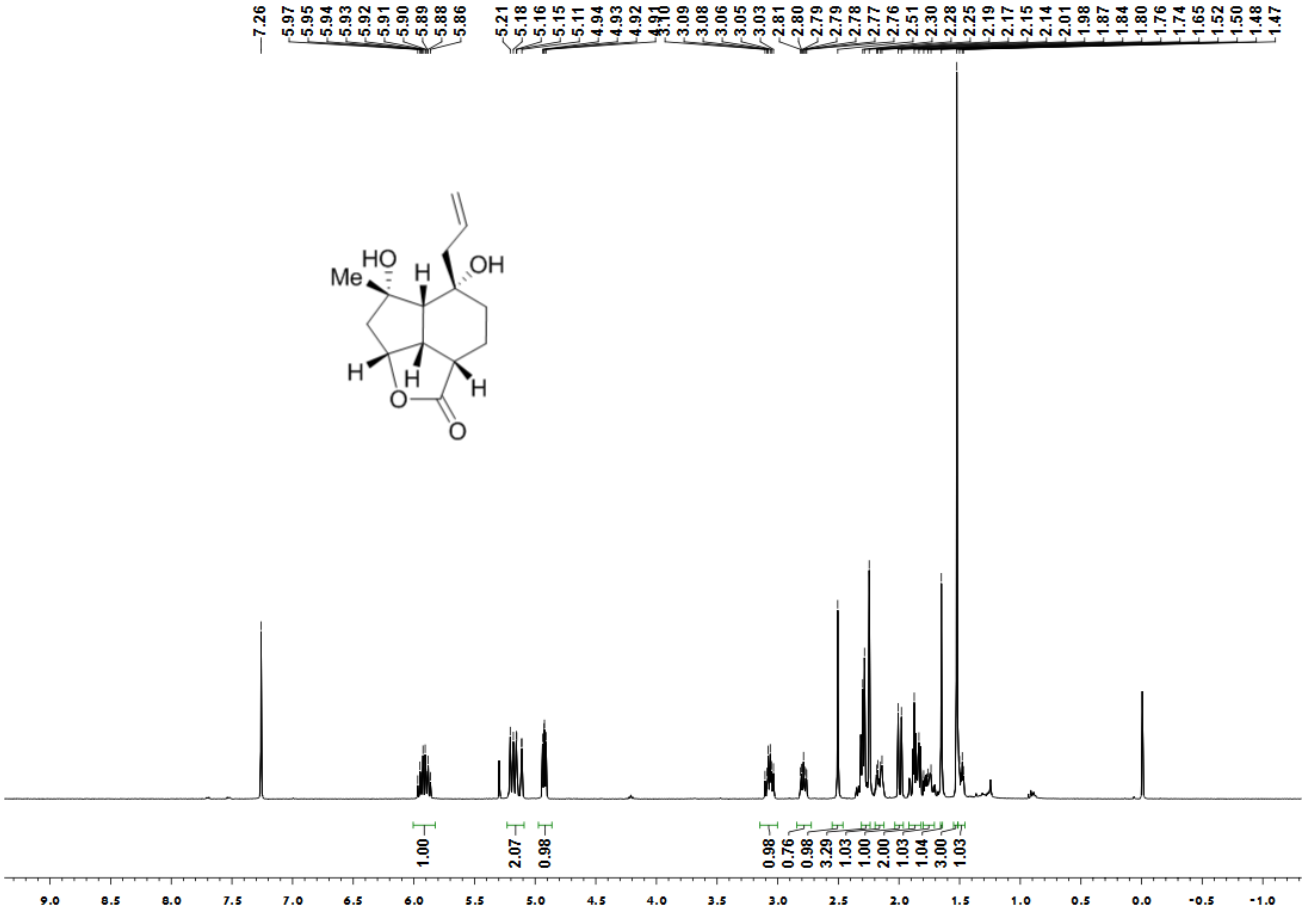
^{1}H NMR Spectra of **23** (400 MHz, $CDCl_3$)



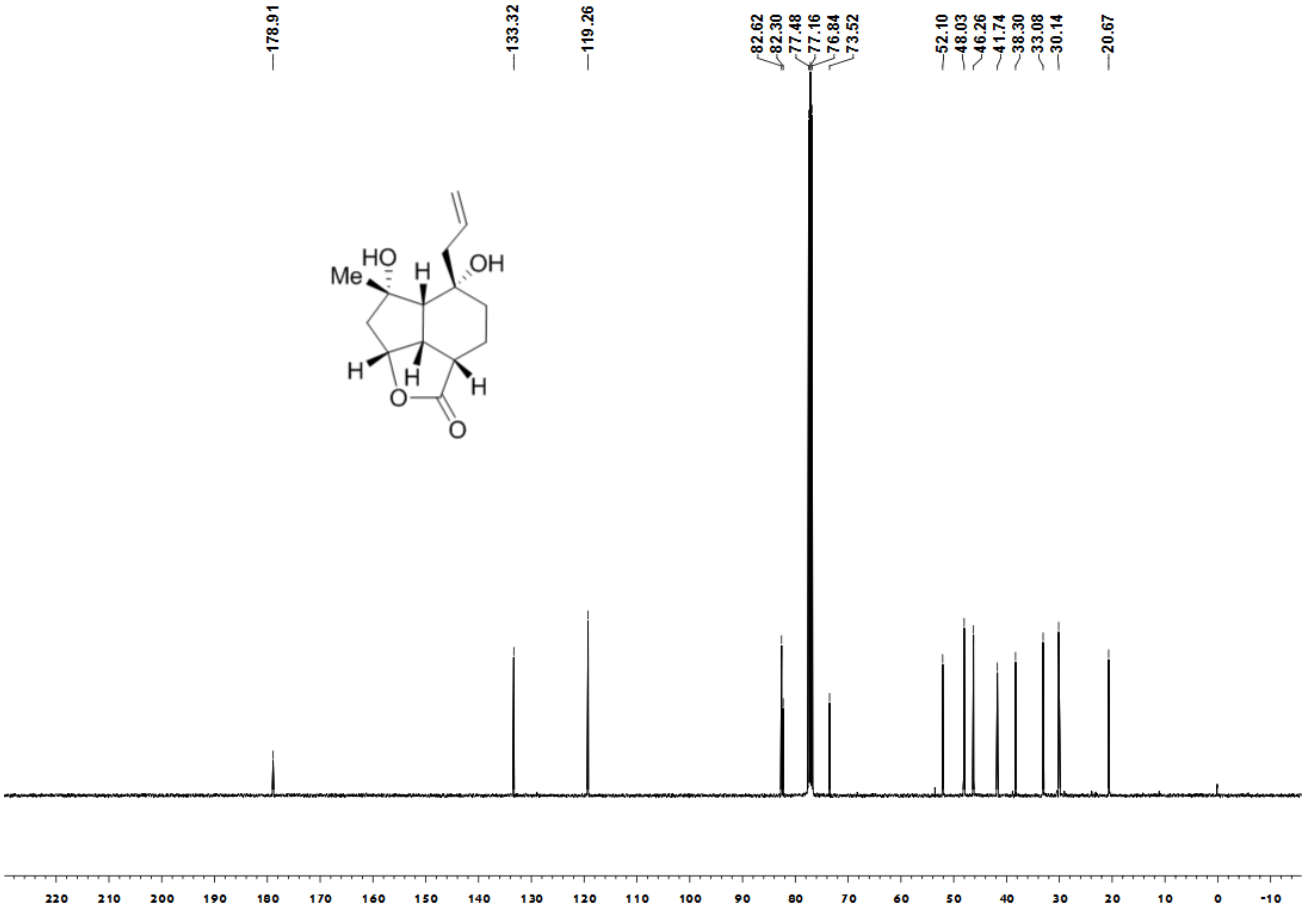
^{13}C NMR Spectra of **23** (101 MHz, $CDCl_3$)



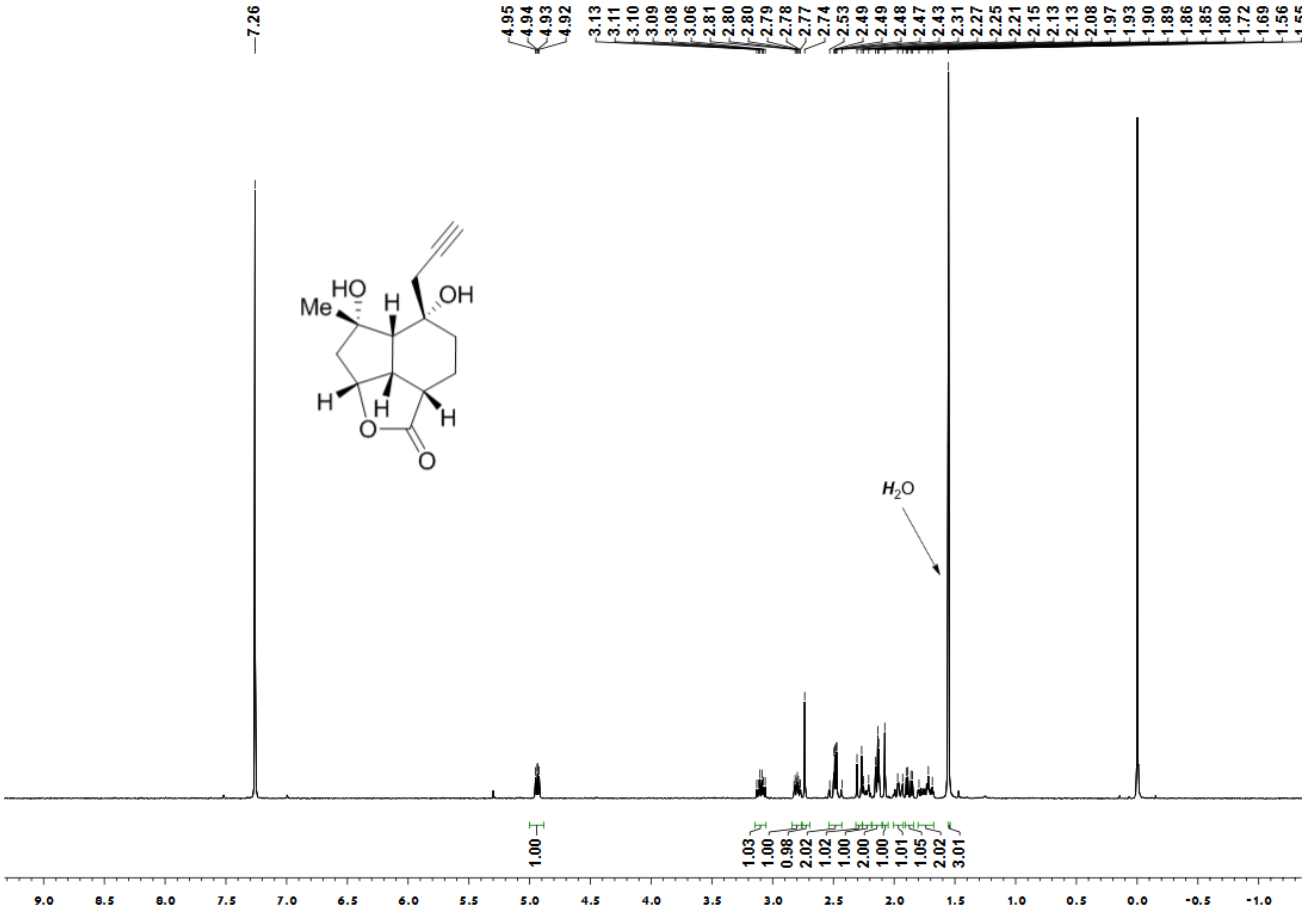
^{1}H NMR Spectra of **24** (400 MHz, $CDCl_3$)



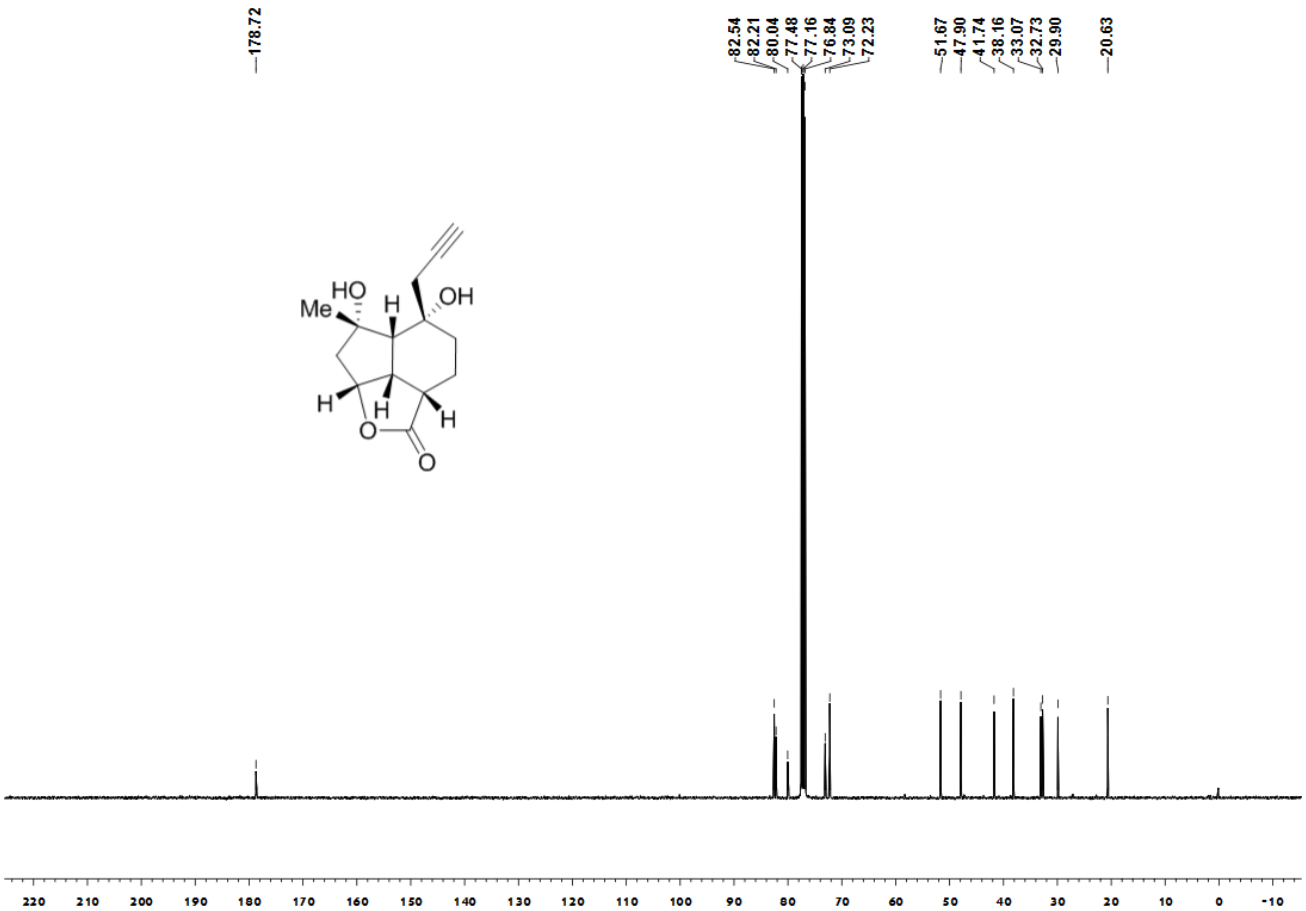
^{13}C NMR Spectra of **24** (101 MHz, $CDCl_3$)



^{1}H NMR Spectra of **25** (400 MHz, $CDCl_3$)

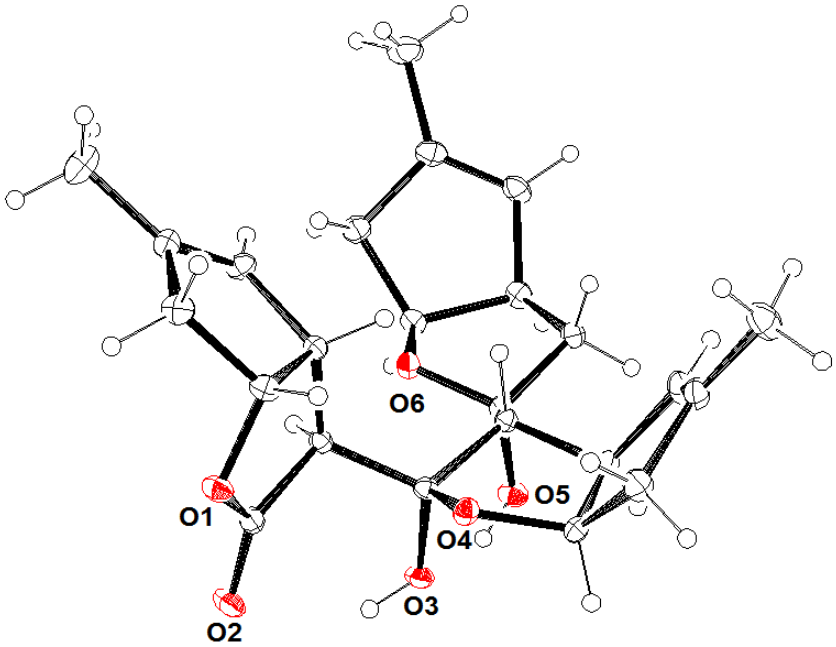


^{13}C NMR Spectra of **25** (101 MHz, $CDCl_3$)



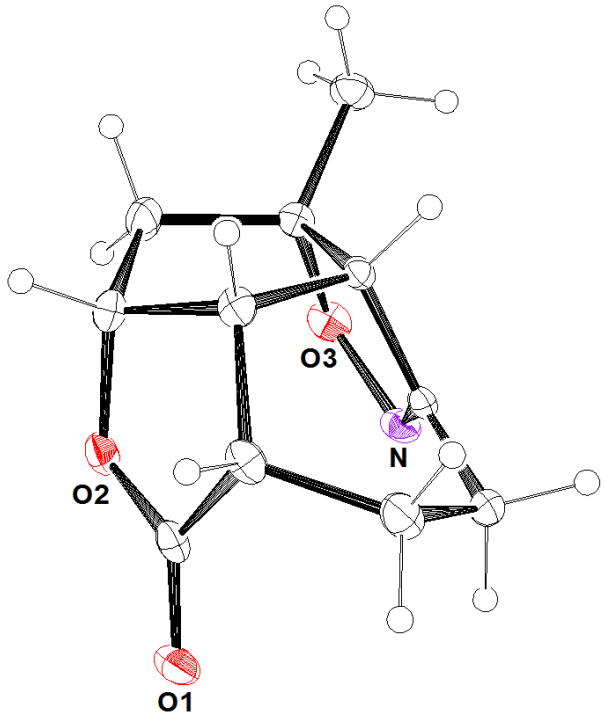
IV ORTEP Drawings and Crystallographic Data of Compounds

ORTEP Drawing and Crystallographic Data of Compound **13b** (CCDC 1871342)



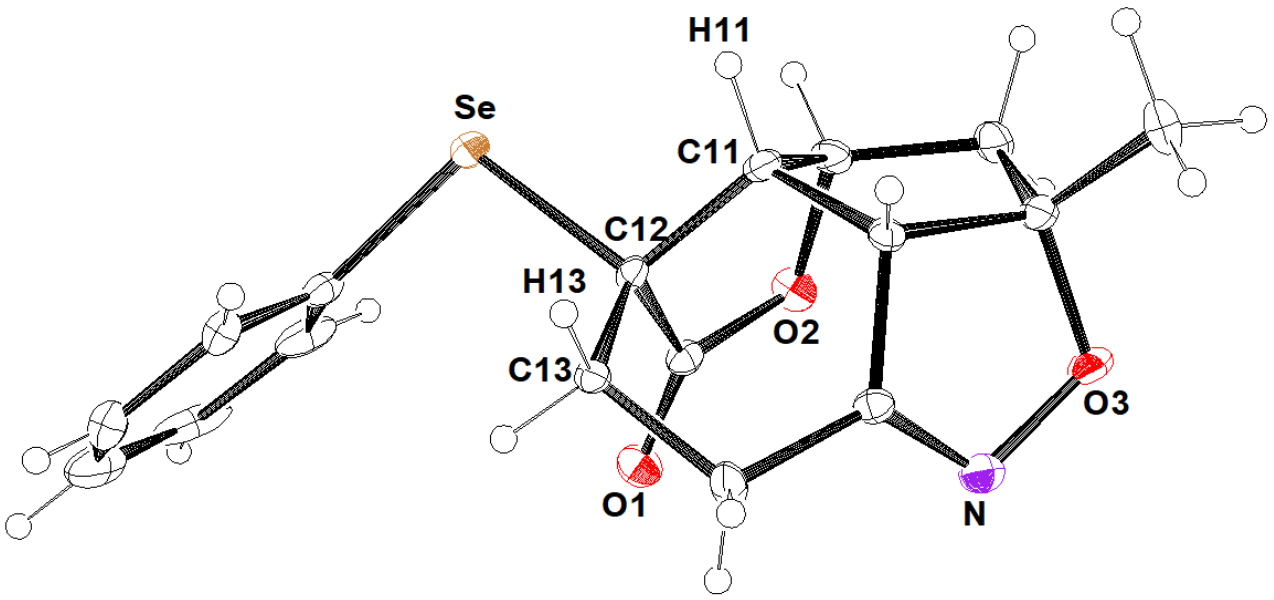
Empirical formula	$C_{24}H_{30}O_6$
Formula weight	414.48
Temperature	293(2) K
Crystal system	monoclinic
Space group	$P2_1/n$
Unit cell dimensions	a = 11.488(2) Å α = 90 °
	b = 9.975(2) Å β = 96.11(3) °
	c = 18.524(4) Å γ = 90 °
Volume	2110.8(7) $Å^3$
Z	4
ρ_{calc}	1.304 g/cm^3
μ	0.093 mm^{-1}
F(000)	888.0
Crystal size	0.2 × 0.18 × 0.12 mm^3
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection	5.71 to 55.76 °
Index ranges	$-15 \leq h \leq 13$, $-13 \leq k \leq 13$, $-24 \leq l \leq 24$
Reflections collected	20549
Independent reflections	5006 [R_{int} = 0.0389, R_{sigma} = 0.0357]
Data/restraints/parameters	5006/0/276
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R_1 = 0.0442, wR_2 = 0.1046
Final R indexes [all data]	R_1 = 0.0564, wR_2 = 0.1117
Largest diff. peak/hole	0.27/-0.22 e $Å^{-3}$

ORTEP Drawing and Crystallographic Data of Compound **10** (CCDC 1871751)



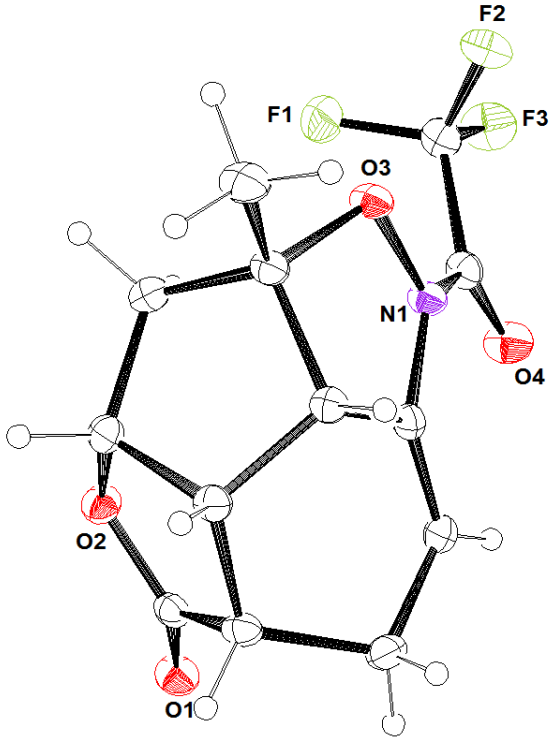
Empirical formula	$C_{11}H_{13}NO_3$
Formula weight	207.22
Temperature/K	113.15
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.6996(13)
b/Å	9.779(2)
c/Å	14.849(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	972.8(3)
Z	4
ρ_{calc}g/cm^3	1.415
μ/mm^{-1}	0.103
F(000)	440.0
Crystal size/mm^3	0.2 ×0.18 ×0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/ °	6.672 to 55.706
Index ranges	$-8 \leq h \leq 8$, $-12 \leq k \leq 12$, $-19 \leq l \leq 19$
Reflections collected	11517
Independent reflections	2318 [R_{int} = 0.0451, R_{sigma} = 0.0346]
Data/restraints/parameters	2318/0/137
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0352, wR_2 = 0.0816
Final R indexes [all data]	R_1 = 0.0398, wR_2 = 0.0845
Largest diff. peak/hole / e Å^{-3}	0.23/-0.14
Flack parameter	0.5

ORTEP Drawing and Crystallographic Data of Compound **17** (CCDC 1871341)



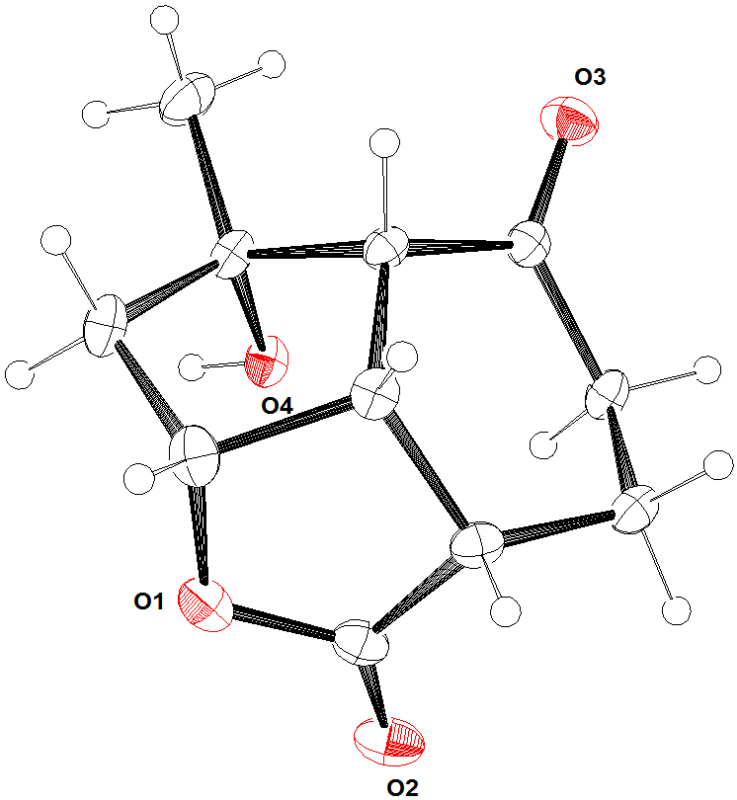
Empirical formula	$C_{17}H_{17}NO_3Se$
Formula weight	362.27
Temperature	113.15 K
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 11.583(2) Å α = 90°
	b = 6.049(12) Å β = 114.53(3)°
	c = 11.729(2) Å γ = 90°
Volume	747.7(3) $Å^3$
Z	2
ρ_{calc}	1.609 g/cm^3
μ	2.523 mm^{-1}
F(000)	368.0
Crystal size	0.2 × 0.18 × 0.12 mm^3
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection	3.818 to 55.736 °
Index ranges	$-15 \leq h \leq 15$, $-7 \leq k \leq 7$, $-15 \leq l \leq 15$
Reflections collected	9015
Independent reflections	3536 [R_{int} = 0.0622, R_{sigma} = 0.1321]
Data/restraints/parameters	3536/1/200
Goodness-of-fit on F^2	0.763
Final R indexes [I>=2σ (I)]	R_1 = 0.0318, wR_2 = 0.0558
Final R indexes [all data]	R_1 = 0.0501, wR_2 = 0.0581
Largest diff. peak/hole	0.37/-0.51 e $Å^{-3}$
Flack parameter	0.047(10)

ORTEP Drawing and Crystallographic Data of Compound **20** (CCDC 1871339)



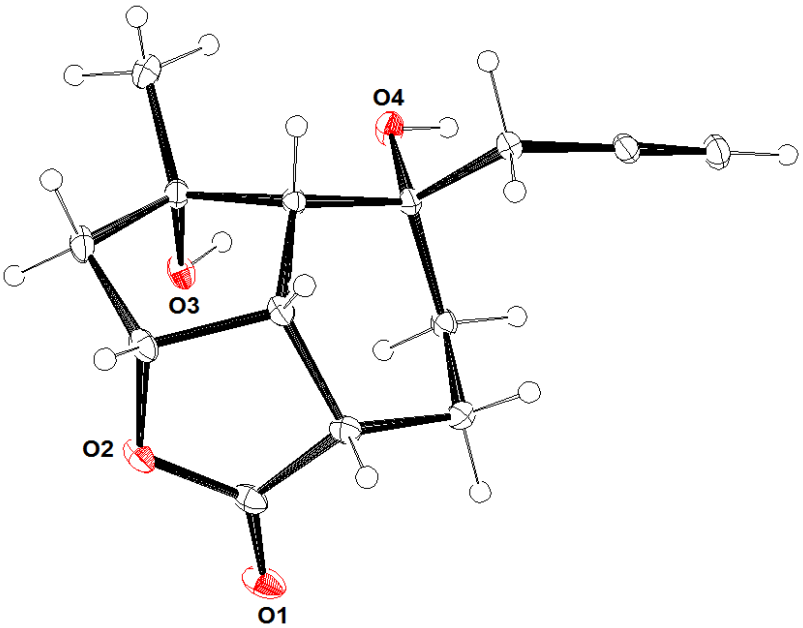
Empirical formula	$C_{13}H_{12}F_3NO_4$
Formula weight	303.24
Temperature	213.15 K
Crystal system	orthorhombic
Space group	$Pna2_1$
Unit cell dimensions	a = 15.0383(18) Å α = 90 °
	b = 10.0768(13) Å β = 90 °
	c = 8.2471(10) Å γ = 90 °
Volume	1249.7(3) $Å^3$
Z	4
ρ_{calc}	1.612 g/cm^3
μ	0.148 mm^{-1}
F(000)	624.0
Crystal size	0.2 × 0.18 × 0.12 mm^3
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection	6.384 to 54.914 °
Index ranges	$-19 \leq h \leq 19$, $-13 \leq k \leq 13$, $-10 \leq l \leq 10$
Reflections collected	13565
Independent reflections	2842 [R_{int} = 0.0302, R_{sigma} = 0.0198]
Data/restraints/parameters	2842/1/191
Goodness-of-fit on F^2	1.049
Final R indexes [I>=2σ (I)]	R_1 = 0.0270, wR_2 = 0.0726
Final R indexes [all data]	R_1 = 0.0280, wR_2 = 0.0735
Largest diff. peak/hole	0.26/-0.13 e $Å^{-3}$
Flack parameter	0.05(16)

ORTEP Drawing and Crystallographic Data of Compound **9** (CCDC 1871340)



Empirical formula	$C_{11}H_{14}O_4$
Formula weight	210.22
TemperatureK	113.15 K
Crystal system	monoclinic
Space group	$P2_1/n$
Unit cell dimensions	a = 11.5648(6) Å α = 90°
	b = 6.3244(3) Å β = 105.105(5)°
	c = 13.9396(6) Å γ = 90°
Volume	984.32(8) $Å^3$
Z	4
ρ_{calc}	1.419 g/cm^3
μ	0.108 mm^{-1}
F(000)	448.0
Crystal size	0.24 × 0.2 × 0.18 mm^3
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection	5.314 to 54.196 °
Index ranges	$-14 \leq h \leq 14$, $-8 \leq k \leq 8$, $-17 \leq l \leq 17$
Reflections collected	9128
Independent reflections	2159 [R_{int} = 0.0294, R_{sigma} = 0.0198]
Data/restraints/parameters	2159/0/139
Goodness-of-fit on F^2	1.036
Final R indexes [I>=2σ (I)]	R_1 = 0.0417, wR_2 = 0.1037
Final R indexes [all data]	R_1 = 0.0473, wR_2 = 0.1081
Largest diff. peak/hole	0.33/-0.20 e $Å^{-3}$

ORTEP Drawing and Crystallographic Data of Compound **25** (CCDC 1884458)



Empirical formula	$C_{14}H_{18}O_4$
Formula weight	250.28
Temperature/K	113.15
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	6.3851(4)
b/Å	10.5141(5)
c/Å	18.2943(12)
α/°	90
β/°	94.679(6)
γ/°	90
Volume/Å^3	1224.08(12)
Z	4
ρ_{calc}g/cm^3	1.358
μ/mm^{-1}	0.099
F(000)	536.0
Crystal size/mm^3	0.2 × 0.18 × 0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.468 to 52.734
Index ranges	$-7 \leq h \leq 7$, $-13 \leq k \leq 13$, $-21 \leq l \leq 22$
Reflections collected	10439
Independent reflections	2410 [R_{int} = 0.0329, R_{sigma} = 0.0241]
Data/restraints/parameters	2410/0/166
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0378, wR_2 = 0.0886
Final R indexes [all data]	R_1 = 0.0440, wR_2 = 0.0924
Largest diff. peak/hole / e Å^{-3}	0.29/-0.17