

Supporting Information for:

**Tandem Iodine-Mediated Oxidations of Tetrahydro- β -Carbolines:
Total Synthesis of Eudistomins Y₁-Y₇**

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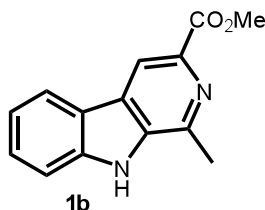
Methods and Materials

Tetrahydrofuran, diethyl ether, dichloromethane, benzene, toluene, and acetonitrile were dried using a Glass Contour solvent purification system by SG Water USA, LLC. Commercially available starting materials and reagents were purchased from Aldrich or Acros Organics and were used as received.

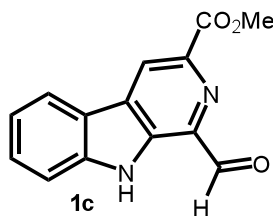
Analytical thin layer chromatography (TLC) was performed on Whatman Partisil® KF6 0.25 mm silica gel plates with UV indicator. Visualization was accomplished by irradiation under a 254 nm UV lamp followed by staining with either an aqueous solution of ceric ammonium molybdate (CAM) or iodine. Column chromatography on silica gel was performed using a forced flow of the indicated solvent system on EM Reagents Silica Gel 60 (230-400 mesh).

¹H NMR spectra were recorded on a Bruker ARX 500 (500 MHz) or a Varian Unity Inova 500 (500 MHz) spectrometer. ¹³C NMR spectra were recorded on a Bruker ARX 500 (125 MHz) or a Varian Unity Inova 500 (125 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane (0 ppm) or with the solvent resonance as the internal standard (CDCl₃ 7.26 ppm, DMSO-d₆ 2.49 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and number of protons. IR spectra were recorded on a Thermo Nicolet FT200 FT-IR spectrometer with an attenuated total reflectance (ATR) head. Melting points were obtained on a Mel-Temp apparatus and are uncorrected.

Experimental Procedures



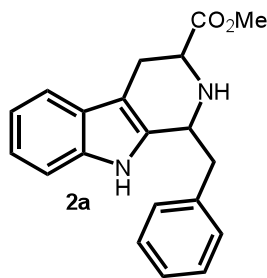
Methyl 1-methyl-9H-pyrido[3,4-*b*]indole-3-carboxylate (1b). A 25 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tetrahydro- β -carboline **1a** (286 mg, 1.2 mmol). To this flask was added 2-iodoxybenzoic acid (656 mg, 2.3 mmol), tetra-*n*-butylammonium bromide (189 mg, 0.6 mmol), and acetonitrile (10 mL). The mixture was stirred open to air at rt. After 2 h, the acetonitrile was removed under reduced pressure. Purification of the residue by flash chromatography (8:2 EtOAc:hexanes to 5% MeOH:EtOAc) afforded β -carboline **1b** (241 mg, 86% yield) as an off-white solid: mp 215-218 °C; R_f = 0.34 (8:2 EtOAc:hexanes); IR (neat) 3264, 2360, 1712, 1350, 1249, 740 cm^{-1} ; ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$) δ 12.02 (s, 1H), 8.76 (s, 1H), 8.35 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.58 (t, J = 7.1 Hz, 1H), 7.30 (t, J = 7.2 Hz, 1H), 3.90 (s, 3H), 2.81 (s, 3H); ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$) δ 171.4, 147.4, 146.0, 141.4, 141.2, 133.6, 132.0, 127.4, 126.6, 125.4, 121.2, 117.6, 57.1, 25.6; HRMS (ESI) m/z 241.0975 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_2^+$: 241.0977].



Methyl 1-formyl-9H-pyrido[3,4-*b*]indole-3-carboxylate (1c). To a stirred solution of tetrahydro- β -carboline **1a** (234 mg, 1.0 mmol) in DMSO (5 mL) was added 2-iodoxybenzoic

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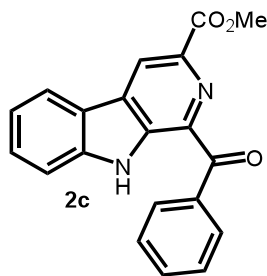
acid (1.1 g, 4.0 mmol). The reaction mixture was stirred in the open at 65 °C. After 2 h, the reaction mixture was allowed to reach rt. The solids were filtered and washed with EtOAc (10 mL). The filtrate was partitioned with brine (35 mL). The product was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried (MgSO₄) and filtered. To the filtrate was added silica gel (1.0 g) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (EtOAc) to provide aldehyde **1c** (90 mg, 37% yield) as a yellow solid: mp 219-222 °C; *R_f* = 0.71 (EtOAc); IR (neat) 3363, 2947, 1720, 1681, 1265, 740 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.41 (s, 1H), 10.25 (s, 1H), 9.11 (s, 1H), 8.43 (d, *J* = 8.1 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 3.95 (s, 3H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 193.1, 165.2, 142.3, 136.5, 135.2, 134.6, 131.4, 129.5, 122.3, 121.2 (2C), 120.0, 113.3, 52.2; HRMS (ESI) *m/z* 255.0772 [(M+H)⁺; calcd for C₁₄H₁₁N₂O₃⁺: 255.0770].



Methyl 1-benzyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylate (2a). To a stirred solution of tryptophan methyl ester hydrochloride (6.5 g, 25.7 mmol) in methanol (80 mL) was added phenylacetaldehyde (2.2 mL, 18.9 mmol) at rt. The reaction mixture was stirred at rt for 30 min, then at 65 °C for 20 h. An additional aliquot of phenylacetaldehyde (2.2 mL, 18.9 mmol) was added, and stirring was continued. After 21 h, the majority of solvent was removed under

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reduced pressure. The residue was washed with 14% aqueous NH_4OH (50 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by recrystallization (48:49:3 Et_2O /hexanes/methanol) afforded β -carboline **2a** (7.1 g, 86% yield) as a mixture of diastereomers (3:2 *cis:trans*). The *cis*-isomer¹ was obtained in pure form after purification on silica gel (3:7 EtOAc:hexanes) as a white solid: mp 86-90 °C; R_f = 0.11 (3:7 EtOAc:hexanes); IR (neat) 2360, 2337, 1867, 1720, 1512, 1435, 1219, 740 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.48 (d, J = 7.3 Hz, 1H), 7.42-7.35 (m, 5H), 7.19 (d, J = 7.6 Hz, 1H), 7.14 (t, J = 7.0 Hz, 1H), 7.09 (t, J = 7.7 Hz, 1H), 4.53 (t, J = 6.2 Hz, 1H), 3.81 (s, 3H), 3.80 (dd, J = 11.4, 4.3 Hz, 1H), 3.23 (dd, J = 13.6, 6.3 Hz, 1H), 3.14 (ddd, J = 15.0, 4.1, 1.8 Hz, 1H), 3.05 (dd, J = 13.4, 7.8 Hz, 1H), 2.85 (ddd, J = 14.9, 11.1, 2.4 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.4, 137.6, 135.7, 135.0, 129.4 (2C), 129.0 (2C), 127.2, 126.7, 121.8, 119.6, 118.0, 110.8, 108.4, 56.5, 54.1, 52.2, 41.7, 25.9; HRMS (ESI) m/z 343.1419 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2\text{Na}^+$: 343.1422].

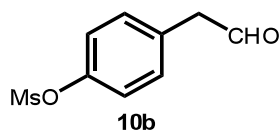


Methyl 1-benzoyl-9H-pyrido[3,4-*b*]indole-3-carboxylate (2c). A 100 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tetrahydro- β -carboline **2a** (360 mg, 1.1 mmol). To this flask was added iodine (2.0 g, 7.9 mmol), potassium carbonate (1.0 g, 7.9 mmol), and ethyl acetate (56 mL). The mixture was stirred in the open at rt. After 2 h, the

¹ Determined by ^{13}C and ^1H NMR according to the method of Cook: Ungemach, F.; Soerens, D.; Weber, R.; DiPierro, M.; Campos, O.; Mokry, P.; Cook, J. M.; Silverton, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 6976-6984.

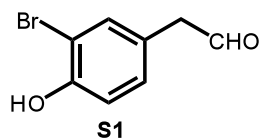
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reaction mixture was partitioned with saturated $\text{Na}_2\text{S}_2\text{O}_3$ (25 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by recrystallization (ethanol) afforded ketone **2c** (365 mg, 98% yield) as a yellow solid: mp 140-142 °C; R_f = 0.57 (3:7 EtOAc:hexanes); IR (neat) 3726, 3342, 2356, 2334, 1693, 1638, 1435, 1358, 1336, 1260, 1123, 991, 717 cm^{-1} ; ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$) δ 12.40 (s, 1H), 9.13 (s, 1H), 8.45 (d, J = 7.7 Hz, 1H), 8.39 (d, J = 7.3 Hz, 2H), 7.84 (d, J = 8.2 Hz, 1H), 7.70 (t, J = 7.2 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.7 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$) δ 192.3, 165.2, 136.6 (2C), 135.7, 135.0, 132.7, 131.3, 131.1 (2C), 129.3, 128.0 (2C), 122.1, 120.9, 120.5, 120.3, 113.2, 52.2; HRMS (ESI) m/z 357.1219 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_3\text{Na}^+$: 357.1215].

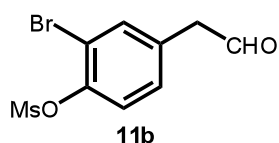


4-(2-oxoethyl)phenyl methanesulfonate (10b). A 100 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with alcohol **10a** (953 mg, 4.4 mmol). To this flask was added *o*-iodoxybenzoic acid (3.7 g, 13.2 mmol) and ethyl acetate (35 mL). The mixture was stirred at 80 °C. After 3 h, the reaction mixture was allowed to reach rt, whereby it was filtered over a sintered glass funnel. The filtrate was concentrated under reduced pressure. Purification of the residue by flash chromatography (1:1 EtOAc:hexanes) afforded β -aldehyde **10b** (863 mg, 91% yield) as a yellow oil: R_f = 0.48 (1:1 EtOAc:hexanes); IR (neat) 1742, 1375, 1210 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.76 (t, J = 2.0 Hz, 1H), 7.28-7.27 (m, 4H), 3.73 (d, J = 2.0 Hz, 2H), 3.14 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 198.4, 148.4, 131.2 (2C), 122.5 (2C), 49.7, 37.4; HRMS (ESI) m/z 237.0193 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_9\text{H}_{10}\text{O}_4\text{SNa}^+$: 237.0197].

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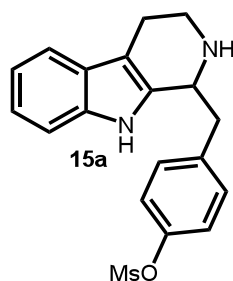
2-(3-bromo-4-hydroxyphenyl)acetaldehyde (S1). A 15 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with bromophenol **11a** (217 mg, 1.0 mmol). To this flask was added triethylamine (0.28 mL) and DMSO (1.1 mL). A solution of SO₃ •pyridine (318 mg, 2.0 mmol) in DMSO (1.1 mL) was added dropwise at rt. After 1 h, the reaction was brought to 0 °C and H₂O (6 mL) was added. The mixture was then stirred at rt. After 15 min, the product was extracted with CH₂Cl₂ (3 x 15 mL). The combined organic layers were washed with brine (15 mL), dried (MgSO₄), and concentrated under reduced pressure. For characterization purposes, a small amount was purified by flash chromatography (1:1 EtOAc:hexanes) to provide aldehyde **S1** as a white solid: mp 30-31 °C; *R_f* = 0.60 (1:1 EtOAc:hexanes); IR (neat) 1709, 1490, 1287, 1172, 1041, 816 cm⁻¹; ¹H NMR (500 MHz, (CDCl₃) δ 9.70 (t, *J* = 2.1 Hz, 1H), 7.32 (d, *J* = 1.8 Hz, 1H), 7.04 (dd, *J* = 1.8, 8.3 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 5.80 (s, 1H), 3.61 (d, *J* = 2.1 Hz, 2H); ¹³C NMR (125 MHz, (CDCl₃) δ 199.1, 151.7, 132.9, 130.3, 125.1, 116.5, 110.4, 49.0; HRMS (ESI) *m/z* 236.9530 [(M+Na)⁺; calcd for C₈H₇O₂BrNa⁺: 236.9527].



2-bromo-4-(2-oxoethyl)phenyl methanesulfonate (11b). A flask containing crude aldehyde **S1** was placed under an inert nitrogen atmosphere. To the flask was added CH₂Cl₂ (5 mL) and triethylamine (0.15 mL). The flask was cooled to 0 °C and methanesulfonyl chloride (0.09 mL) was added. The reaction mixture was allowed to reach rt. After 15 min, the reaction mixture was partitioned with H₂O (10 mL) and the product was extracted with CH₂Cl₂ (3 x 10 mL). The

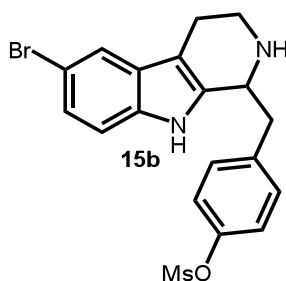
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combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography (3:7 EtOAc:hexanes) afforded mesylate **11b** (126 mg, 43% yield) as a yellow oil: R_f = 0.48 (1:1 EtOAc:hexanes); IR (neat) 1715, 1484, 1353, 1167, 969, 816 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.76 (t, J = 1.8 Hz, 1H), 7.51 (d, J = 2.0 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.21 (dd, J = 2.0, 8.3 Hz, 1H), 3.73 (d, J = 1.8 Hz, 2H), 3.27 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 197.7, 145.6, 134.8, 132.7, 130.1, 124.4, 116.0, 49.0, 38.8; HRMS (ESI) m/z 314.9310 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_9\text{H}_9\text{O}_4\text{BrSNa}^+$: 314.9303].



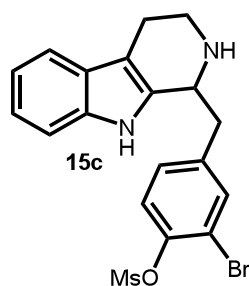
4-((2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)methyl)phenyl methanesulfonate (15a). A 25 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tryptamine hydrochloride (108 mg, 0.6 mmol). To this flask was added aldehyde **10b** (98 mg, 0.5 mmol) and isopropyl alcohol (5 mL). The reaction mixture was stirred at 87 °C. After 19 h, the reaction mixture was concentrated under reduced pressure. The residue was partitioned with saturated NaHCO_3 (10 mL) and extracted with CH_2Cl_2 (5 x 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography (10% MeOH:EtOAc) afforded β -carboline **15a** (130 mg, 72% yield) as a white solid: mp >260 °C; R_f = 0.15 (10% MeOH:EtOAc); IR (neat) 3238, 2937, 2794, 1495, 1353, 1167, 1139, 975, 865, 734, 663 cm^{-1} ; ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$) δ 11.30 (s, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.13 (t, J = 7.7 Hz, 1H), 7.03 (t, J = 7.7 Hz, 1H), 4.85 (d, J = 8.1 Hz, 1H), 3.70 (dd, J = 2.5, 14.3

Hz, 1H), 3.42 (d, $J = 12.9$ Hz, 1H), 3.38 (s, 3H), 3.19-3.13 (m, 2H), 3.00-2.95 (m, 1H), 2.86 (d, $J = 15.9$ Hz, 1H); ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$) δ 148.2, 136.0, 135.2, 131.3 (2C), 130.4, 125.9, 122.2 (2C), 121.6, 118.8, 118.0, 111.3, 106.4, 53.6, 41.3, 37.2, 36.8, 18.5; HRMS (ESI) m/z 357.1269 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}_3\text{S}^+$: 357.1273].



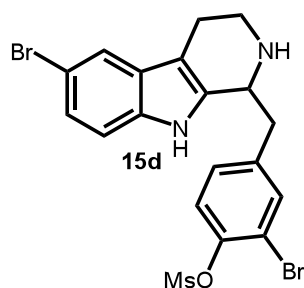
4-((6-bromo-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)methyl)phenyl

methanesulfonate (15b). A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with 5-bromotryptamine hydrochloride (52 mg, 0.2 mmol). To this flask was added aldehyde **10b** (82 mg, 0.4 mmol) and isopropyl alcohol (3 mL). The reaction mixture was stirred at 87 °C. After 45 h, the reaction mixture was concentrated under reduced pressure. The residue was diluted with saturated NaHCO_3 (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography (10% $\text{MeOH}:\text{CH}_2\text{Cl}_2$) afforded β -carboline **15b** (37 mg, 45% yield) as a brown tack; $R_f = 0.44$ (10% $\text{MeOH}:\text{CH}_2\text{Cl}_2$); IR (neat) 1501, 1358, 1145, 964, 871, 668 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.60 (d, $J = 1.3$ Hz, 1H), 7.59 (s, 1H), 7.31 (d, $J = 8.5$ Hz, 2H), 7.27-7.25 (m, 3H), 7.21 (dd, $J = 1.8, 8.5$ Hz, 1H), 7.11 (d, $J = 8.5$ Hz, 1H), 4.32 (t, $J = 7.0$ Hz, 1H), 3.30 (dt, $J = 4.8, 12.7$ Hz, 1H), 3.18 (s, 3H), 3.12 (dd, $J = 5.9, 13.7$ Hz, 1H), 3.05-2.99 (m, 2H), 2.75-2.2.64 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 147.8, 137.4, 136.4, 134.2, 130.7 (2C), 129.0, 124.2, 122.2 (2C), 120.7, 112.5, 112.2, 109.2, 53.6, 41.9, 40.5, 37.5, 22.3; HRMS (ESI) m/z 435.0374 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_3\text{BrS}^+$: 435.0378].



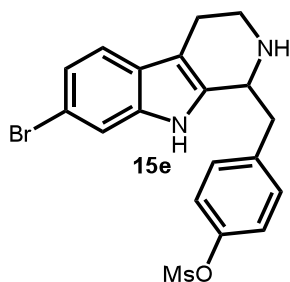
2-bromo-4-((2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)methyl)phenyl

methanesulfonate (15c). A 25 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tryptamine hydrochloride (236 mg, 1.2 mmol). To this flask was added aldehyde **11b** (293 mg, 1.0 mmol) and isopropyl alcohol (5 mL). The reaction mixture was stirred at 85 °C. After 24 h, the reaction mixture was concentrated under reduced pressure. The residue was partitioned with saturated NaHCO₃ (15 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc) afforded β -carboline **15c** (301 mg, 69% yield) as a yellow tack: R_f = 0.13 (EtOAc); IR (neat) 1726, 1649, 1556, 1452, 800 cm⁻¹; ¹H NMR (500 MHz, (CDCl₃) δ 7.79 (s, 1H), 7.57 (d, J = 2.0 Hz, 1H), 7.51 (d, J = 7.7 Hz, 1H), 7.38 (d, J = 8.2 Hz, 1H), 7.29 (d, J = 7.9 Hz, 1H), 7.21 (dd, J = 2.0, 8.3 Hz, 1H), 7.17 (dt, J = 1.0, 7.1 Hz, 1H), 7.12 (dt, J = 1.0, 7.8 Hz, 1H), 4.26 (dd, J = 5.0, 8.9 Hz, 1H), 3.31-3.26 (m, 4H), 3.09 (dd, J = 4.9, 13.8 Hz, 1H), 3.03 (ddd, J = 5.1, 7.6, 12.7 Hz, 1H), 2.89 (dd, J = 8.9, 13.8 Hz, 1H), 2.78 (ddd, J = 1.5, 5.0, 15.3 Hz, 1H), 2.72 (ddd, J = 1.5, 5.0, 15.4 Hz, 1H); ¹³C NMR (125 MHz, (CDCl₃) δ 145.0, 139.4, 135.6, 134.7, 134.5, 129.6, 127.2, 124.2, 121.8, 119.4, 118.2, 115.9, 110.8, 109.6, 53.5, 41.9, 40.4, 38.9, 22.5; HRMS (ESI) m/z 435.0381 [(M+H)⁺; calcd for C₁₉H₂₀N₂O₃BrS⁺: 435.0378].



2-bromo-4-((6-bromo-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)methyl)phenyl

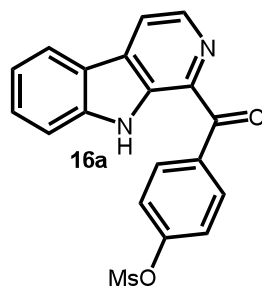
methanesulfonate (15d). A 15 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with 5-bromotryptamine hydrochloride (110 mg, 0.4 mmol). To this flask was added aldehyde **11b** (303 mg, 1.0 mmol) and isopropyl alcohol (3 mL). The reaction mixture was stirred at 85 °C. After 15 h, methanol (1.5 mL) and EtOAc (1.5 mL) were added. Stirring was continued at 85 °C. After 24 h, the reaction mixture was concentrated under reduced pressure. The residue was partitioned with saturated NaHCO₃ (15 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc) afforded β -carboline **15d** (110 mg, 53% yield) as a yellow tack: R_f = 0.11 (EtOAc); IR (neat) 1704, 1479, 1358, 1172, 969, 854 cm⁻¹; ¹H NMR (500 MHz, (CDCl₃) δ 8.07 (s, 1H), 7.58 (d, J = 0.7 Hz, 1H), 7.51 (d, J = 1.5 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 7.19 (dd, J = 1.5, 8.5 Hz, 1H), 7.14 (dd, J = 1.5, 8.2 Hz, 1H), 7.10 (d, J = 8.5 Hz, 1H), 4.21 (dd, J = 4.2, 8.3 Hz, 1H), 3.27-3.22 (m, 4H), 3.05 (dd, J = 4.5, 13.8 Hz, 1H), 2.98 (ddd, J = 5.0, 7.3, 12.5 Hz, 1H), 2.83 (dd, J = 9.0, 13.7 Hz, 1H), 2.69 (dt, J = 5.7, 14.8 Hz, 1H), 2.62 (dt, J = 4.0, 15.6 Hz, 1H); ¹³C NMR (125 MHz, (CDCl₃) δ 144.9, 139.2, 136.1, 134.4, 134.2, 129.5, 129.0, 124.3, 124.1, 120.7, 115.9, 112.5, 112.3, 109.2, 53.3, 41.7, 40.1, 38.9, 22.2; HRMS (ESI) m/z 512.9489 [(M+H)⁺; calcd for C₁₉H₁₉N₂O₃Br₂S⁺: 512.9483].



4-((7-bromo-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)methyl)phenyl

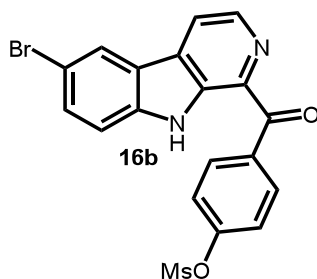
methanesulfonate (15e). A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with 6-bromotryptamine hydrochloride (67 mg, 0.2 mmol). To this flask was added aldehyde **10b** (130 mg, 0.6 mmol) and isopropyl alcohol (3 mL). The reaction mixture was stirred at 87 °C. After 15 h, the reaction mixture was concentrated under reduced pressure. The residue was diluted with saturated NaHCO₃ (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc) afforded β -carboline **15e** (78 mg, 73% yield) as a brown tack; R_f = 0.11 (EtOAc); IR (neat) 1501, 1356, 1146, 964, 871 cm⁻¹; ¹H NMR (500 MHz, (CDCl₃/(CD₃)₂SO) δ 10.69 (s, 1H), 7.42 (s, 1H), 7.30 (d, J = 7.9 Hz, 2H), 7.24 (d, J = 8.7 Hz, 1H), 7.18 (d, J = 7.3 Hz, 2H), 7.02 (d, J = 7.9 Hz, 1H), 4.18 (d, J = 8.4 Hz, 1H), 3.33 (dd, J = 1.8, 13.6 Hz, 1H), 3.20-3.14 (m, 4H), 2.89-2.79 (m, 2H), 2.64-2.54 (m, 2H); ¹³C NMR (125 MHz, (CDCl₃/(CD₃)₂SO) δ 147.2, 137.8, 136.5, 136.2, 130.3 (2C), 125.7, 121.4 (2C), 120.8, 118.5, 113.2, 113.1, 107.8, 53.2, 41.3, 39.2, 36.7, 21.9; HRMS (ESI) m/z 457.0191 [(M+Na)⁺; calcd for C₁₉H₁₉N₂O₃BrSNa⁺: 457.0197].

Supporting Information Panarese and Waters*



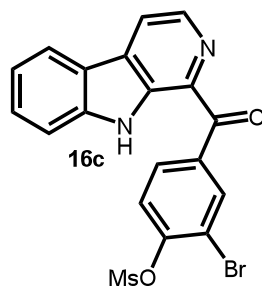
4-(9H-pyrido[3,4-b]indole-1-carbonyl)phenyl methanesulfonate (16a). A 250 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tetrahydro- β -carboline **15a** (656 mg, 1.8 mmol). To this flask was added iodine (3.28 g, 12.9 mmol), potassium carbonate (1.78 g, 12.9 mmol), and ethyl acetate (92 mL). The mixture was stirred in the open at rt. After 2 h, the reaction mixture was brought to 80 °C for 60 h then allowed to cool to rt, whereby it was concentrated under reduced pressure. The residue was partitioned with saturated Na₂S₂O₃ (25 mL). The product was extracted with 1% MeOH:CH₂Cl₂ (3 x 25 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (3.0 g) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide ketone **16a** (485 mg, 72% yield) as a yellow solid: mp 166-167 °C; *R_f* = 0.70 (7:3 EtOAc:hexanes); IR (neat) 3397, 2931, 2356, 1704, 1583, 1495, 1364, 1205, 1145, 964, 871, 734 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.10 (s, 1H), 8.53 (d, *J* = 4.8 Hz, 1H), 8.45 (d, *J* = 4.8 Hz, 1H), 8.33-8.31 (m, 3H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 3.50 (s, 3H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 192.5, 151.5, 141.6, 137.1, 136.3, 135.8 (2C), 132.8 (2C), 131.1, 128.9, 121.7, 121.6 (2C), 120.2, 119.9, 119.0, 112.9, 37.7; HRMS (ESI) *m/z* 389.0566 [(M+Na)⁺; calcd for C₁₉H₁₄N₂O₄SNa⁺: 389.0572].

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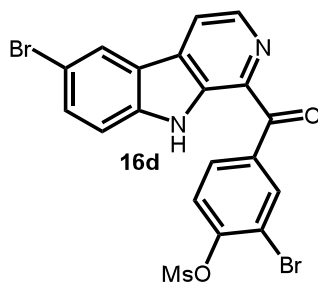
4-(6-bromo-9H-pyrido[3,4-b]indole-1-carbonyl)phenyl methanesulfonate (16b). A 50 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tetrahydro- β -carboline **15b** (231 mg, 0.5 mmol). To this flask was added iodine (943 mg, 3.7 mmol), potassium carbonate (513 mg, 3.7 mmol), and ethyl acetate (27 mL). The mixture was stirred in the open at rt. After 2 h, the reaction mixture was brought to 80 °C for 60 h then allowed to cool to rt, whereby it was concentrated under reduced pressure. The residue was partitioned with saturated $\text{Na}_2\text{S}_2\text{O}_3$ (25 mL) and extracted with 1% MeOH: CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4) and filtered. To the filtrate was added silica gel (1.0 g) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide ketone **16b** (162 mg, 69% yield) as a yellow solid: mp 201-203 °C; R_f = 0.68 (1:1 EtOAc:hexanes); IR (neat) 2920, 1726, 1610, 1210, 964, 800 cm^{-1} ; ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$) δ 12.20 (s, 1H), 8.56 (s, 1H), 8.53 (d, J = 5.0 Hz, 1H), 8.47 (d, J = 5.0 Hz, 1H), 8.31 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8.5 Hz, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.55 (d, J = 8.5 Hz, 2H), 3.50 (s, 3H); ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$) δ 192.3, 151.6, 140.3, 137.4, 136.1, 136.0, 135.9, 132.8 (2C), 131.3, 130.0, 124.3, 121.9, 121.6 (2C), 119.4, 114.9, 112.2, 37.7; HRMS (ESI) m/z 466.9681 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{19}\text{H}_{13}\text{N}_2\text{O}_4\text{BrSNa}^+$: 466.9677].

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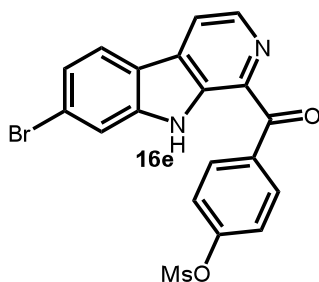
2-bromo-4-(9H-pyrido[3,4-*b*]indole-1-carbonyl)phenyl methanesulfonate (16c). A 50 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tetrahydro- β -carboline **15c** (173 mg, 0.4 mmol). To this flask was added iodine (705 mg, 2.8 mmol), potassium carbonate (384 mg, 2.8 mmol), and ethyl acetate (20 mL). The mixture was stirred in the open at rt. After 2 h, the reaction mixture was brought to 80 °C for 50 h then allowed to cool to rt. The residue was partitioned with 10% aqueous Na₂S₂O₃ (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (500 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide ketone **16c** (104 mg, 58% yield) as a yellow solid: mp 183-185 °C; R_f = 0.63 (1:1 EtOAc:hexanes); IR (neat) 2350, 1621, 1369, 1216, 1172, 882 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.11 (s, 1H), 8.56 (d, J = 1.5 Hz, 1H), 8.54 (d, J = 5.0 Hz, 1H), 8.44 (d, J = 4.9 Hz, 1H), 8.30 (d, J = 7.8 Hz, 1H), 8.27 (dd, J = 1.5, 8.5 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.73 (d, J = 8.3 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 3.63 (s, 3H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 191.1, 148.5, 141.7, 137.5, 137.2, 135.9, 135.8, 135.3, 131.7, 131.2, 129.0, 123.3, 121.7, 120.3, 119.9, 119.3, 115.3, 113.0, 39.1; HRMS (ESI) m/z 466.9683 [(M+Na)⁺; calcd for C₁₉H₁₃N₂O₄BrSNa⁺: 466.9677].

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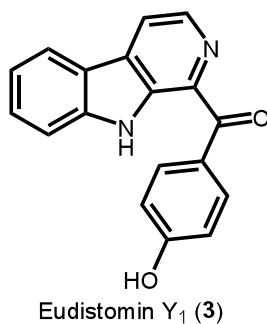
2-bromo-4-(6-bromo-9H-pyrido[3,4-b]indole-1-carbonyl)phenyl methanesulfonate (16d). A 50 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tetrahydro- β -carboline **15d** (90 mg, 0.2 mmol). To this flask was added iodine (311 mg, 1.2 mmol), potassium carbonate (169 mg, 1.2 mmol), and ethyl acetate (9 mL). The mixture was stirred in the open at rt. After 2 h, the reaction mixture was brought to 80 °C for 50 h then allowed to cool to rt. The residue was partitioned with 10% aqueous Na₂S₂O₃ (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (500 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide ketone **16d** (59 mg, 64% yield) as a yellow solid: mp 198-200 °C; R_f = 0.54 (1:1 EtOAc:hexanes); IR (neat) 1698, 1638, 1437, 1358, 1210, 1172, 969, 865 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.27 (s, 1H), 8.64 (s, 1H), 8.59 (dd, J = 1.2, 4.9 Hz, 1H), 8.56-8.55 (m, 2H), 8.26 (d, J = 8.7 Hz, 1H), 7.79-7.75 (m, 2H), 7.73 (dd, J = 1.0, 8.7 Hz, 1H), 3.63 (d, J = 1.0 Hz, 3H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 191.1, 148.6, 140.4, 137.6, 137.4, 135.9 (2C), 135.7, 131.7, 131.5, 130.2, 124.5, 123.3, 121.9, 119.8, 115.3, 115.0, 112.3, 39.1; HRMS (ESI) m/z 544.8779 [(M+Na)⁺; calcd for C₁₉H₁₂N₂O₄Br₂SNa⁺: 544.8782].

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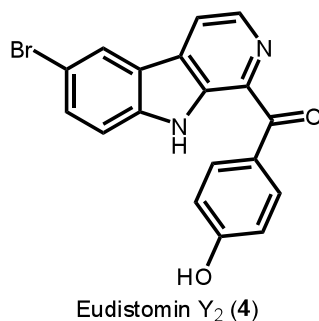
4-(7-bromo-9H-pyrido[3,4-b]indole-1-carbonyl)phenyl methanesulfonate (16e). A 50 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with tetrahydro- β -carboline **15e** (64 mg, 0.15 mmol). To this flask was added iodine (262 mg, 1.0 mmol), potassium carbonate (143 mg, 1.0 mmol), and ethyl acetate (8 mL). The mixture was stirred in the open at rt. After 2 h, the reaction mixture was brought to 80 °C for 60 h then allowed to cool to rt, whereby it was concentrated under reduced pressure. The residue was partitioned with saturated Na₂S₂O₃ (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (1.0 g) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide ketone **16e** (30 mg, 46% yield) as a yellow solid: mp 198-200 °C; *R_f* = 0.54 (1:1 EtOAc:hexanes); IR (neat) 2920, 1726, 1611, 1210, 961, 799 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.18 (s, 1H), 8.55 (d, *J* = 4.9 Hz, 1H), 8.46 (d, *J* = 5.0 Hz, 1H), 8.31 (d, *J* = 8.5 Hz, 2H), 8.27 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 1.3 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 1,3 8.2 Hz, 1H), 3.50 (s, 3H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 192.4, 151.6, 142.4, 137.7, 136.1, 135.9, 132.9 (2C), 130.5, 123.6, 123.1, 121.7, 121.6 (2C), 119.2, 119.1, 115.5, 37.7; HRMS (ESI) *m/z* 466.9672 [(M+Na)⁺; calcd for C₁₉H₁₃N₂O₄BrSNa⁺: 466.9677].

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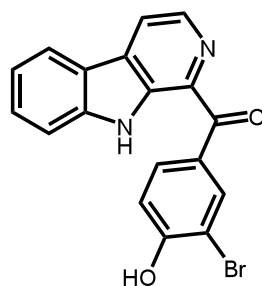
Eudistomin Y₁ (3). A 25 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with ketone **16a** (324 mg, 0.9 mmol). To this flask was added 1 M NaOH (5.3 mL) and ethanol (5.3 mL). The mixture was stirred at 90 °C for 1 h then allowed to cool to rt, whereby it was partitioned between saturated NaHCO₃ (10 mL) and EtOAc (20 mL). The product was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (1.0 g) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide eudistomin Y₁ (**3**) (241 mg, 94% yield) as a yellow solid: mp 220-221 °C; *R_f* = 0.52 (1:1 EtOAc:hexanes); IR (neat) 3331, 1594, 1238, 1216, 1161, 964, 663 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 11.94 (s, 1H), 10.38 (s, 1H), 8.52 (d, *J* = 5.0 Hz, 1H), 8.41 (d, *J* = 4.9 Hz, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 8.26 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.59 (t, *J* = 7.1 Hz, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 2H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 191.2, 161.7, 141.4, 137.3, 136.8, 135.5, 133.6 (2C), 130.6, 128.7, 128.2, 121.7, 120.0, 119.9, 118.1, 114.7 (2C), 112.8; HRMS (ESI) *m/z* 289.0978 [(M+H)⁺; calcd for C₁₈H₁₃N₂O₂⁺: 289.0974].

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Eudistomin Y₂ (4). A 25 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with ketone **16b** (120 mg, 0.3 mmol). To this flask was added 1 M NaOH (1.6 mL) and ethanol (1.6 mL). The mixture was stirred at 90 °C for 1 h then allowed to cool to rt, whereby it was partitioned between saturated NaHCO₃ (10 mL) and EtOAc (15 mL). The product was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (500 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide eudistomin Y₂ (**4**) (89 mg, 90% yield) as a yellow solid: mp >260 °C; *R_f* = 0.69 (1:1 EtOAc:hexanes); IR (neat) 3364, 1594, 1468, 1265, 1210, 1161, 969 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.07 (s, 1H), 10.41 (s, 1H), 8.53 (s, 1H), 8.51 (d, *J* = 4.9 Hz, 1H), 8.40 (d, *J* = 4.9 Hz, 1H), 8.27 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.68 (d, *J* = 8.8 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 191.1, 161.9, 140.1, 137.7, 137.0, 135.7, 133.7 (2C), 131.1, 129.6, 128.1, 124.2, 122.0, 118.5, 114.8 (2C), 114.8, 112.0; HRMS (ESI) *m/z* 367.0083 [(M+H)⁺; calcd for C₁₈H₁₂N₂O₂Br⁺: 367.0082].

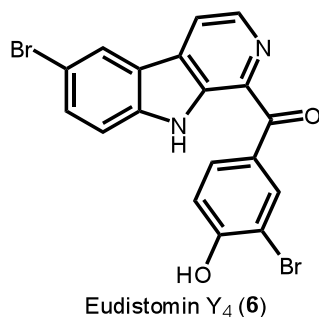
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Eudistomin Y₃ (**5**)

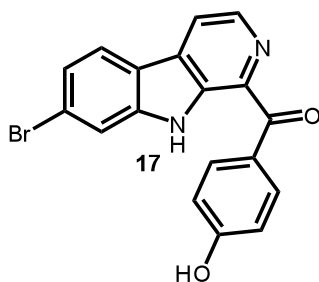
Eudistomin Y₃ (5). A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with ketone **16c** (20 mg, 0.04 mmol). To this flask was added 1 M NaOH (0.3 mL) and ethanol (0.3 mL). The mixture was stirred at 90 °C for 1 h then allowed to cool to rt, whereby it was partitioned between saturated NaHCO₃ (5 mL) and EtOAc (5 mL). The product was extracted with EtOAc (5 x 5 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (100 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide eudistomin Y₃ (**5**) (15 mg, 91% yield) as a yellow solid: mp 231-234 °C; *R_f* = 0.49 (1:1 EtOAc:hexanes); IR (neat) 1736, 1594, 1304, 1205, 734 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 11.99 (s, 1H), 11.29 (s, 1H), 8.57 (d, *J* = 2.0 Hz, 1H), 8.55 (d, *J* = 4.9 Hz, 1H), 8.44 (d, *J* = 5.0 Hz, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 8.24 (dd, *J* = 2.1, 8.5 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.60 (ddd, *J* = 1.0, 7.2, 8.2 Hz, 1H), 7.31 (ddd, *J* = 0.7, 7.2, 7.8 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 1H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 190.0, 158.1, 141.5, 136.9, 136.6, 136.3, 135.7, 132.4, 130.9, 129.5, 128.8, 121.7, 120.0, 120.0, 118.6, 115.5, 112.8, 108.7; HRMS (ESI) *m/z* 367.0081 [(M+H)⁺; calcd for C₁₈H₁₂N₂O₂Br⁺: 367.0082].

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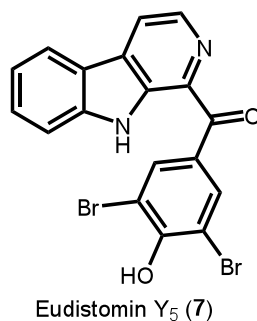
Eudistomin Y₄ (6). A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with ketone **16d** (37 mg, 0.1 mmol). To this flask was added 1 M NaOH (0.4 mL) and ethanol (0.4 mL). The mixture was stirred at 90 °C for 1 h then allowed to cool to rt, whereby it was partitioned between saturated NaHCO₃ (5 mL) and EtOAc (5 mL). The product was extracted with EtOAc (5 x 5 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (100 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide eudistomin Y₄ (**6**) (29 mg, 90% yield) as a yellow solid: mp >260 °C; *R_f* = 0.53 (1:1 EtOAc:hexanes); IR (neat) 1589, 1468, 1194, 980, 794 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.13 (s, 1H), 11.30 (s, 1H), 8.61 (s, 1H), 8.57 (d, *J* = 4.8 Hz, 1H), 8.56 (s, 1H), 8.49 (d, *J* = 4.8 Hz, 1H), 8.24 (dd, *J* = 2.1, 8.7 Hz, 1H), 7.75 (d, *J* = 8.7 Hz, 1H), 7.73 (dd, *J* = 1.6, 8.7 Hz, 1H), 7.13 (d, *J* = 8.7 Hz, 1H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 189.8, 158.2, 140.2, 137.2, 137.0, 136.3, 135.8, 132.5, 131.3, 129.8, 129.4, 124.4, 121.9, 119.0, 115.6, 114.9, 112.1, 108.7; HRMS (ESI) *m/z* 444.9186 [(M+H)⁺; calcd for C₁₈H₁₁N₂O₂Br₂⁺: 444.9187].

Supporting Information Panarese and Waters*



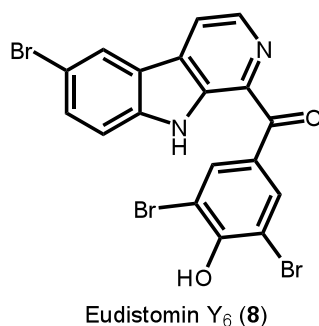
(7-bromo-9H-pyrido[3,4-b]indol-1-yl)(4-hydroxyphenyl)methanone (17). A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with ketone **16e** (47 mg, 0.1 mmol). To this flask was added 1 M NaOH (1 mL) and ethanol (1 mL). The mixture was stirred at 90 °C for 1 h then allowed to cool to rt, whereby it was partitioned between saturated NaHCO₃ (10 mL) and EtOAc (10 mL). The product was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (500 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (7:3 EtOAc:hexanes) to provide phenol **17** (37 mg, 96% yield) as a yellow solid: mp 236-239 °C; *R_f* = 0.82 (7:3 EtOAc:hexanes); IR (neat) 3360, 1594, 1468, 1263, 1210, 1159, 972 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.05 (s, 1H), 10.41 (s, 1H), 8.54 (d, *J* = 5.1 Hz, 1H), 8.42 (d, *J* = 5.0 Hz, 1H), 8.27 (d, *J* = 8.8 Hz, 1H), 8.26 (d, *J* = 8.7 Hz, 2H), 7.95 (d, *J* = 1.6 Hz, 1H), 7.44 (dd, *J* = 1.6, 8.3 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 2H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 191.1, 161.9, 142.2, 137.6, 137.3, 135.7, 133.7 (2C), 130.1, 128.0, 123.5, 122.9, 121.5, 119.2, 118.3, 115.3, 114.8 (2C); HRMS (ESI) *m/z* 367.0080 [(M+H)⁺; calcd for C₁₈H₁₂N₂O₂Br⁺: 367.0082].

Supporting Information Panarese and Waters*



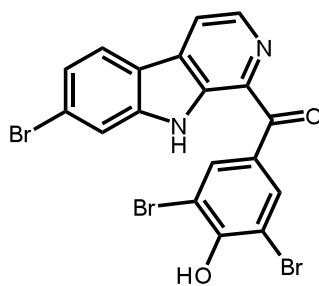
Eudistomin Y₅ (7). A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with eudistomin Y₁ (**3**) (50 mg, 0.2 mmol). To this flask was added phenyltrimethylammonium tribromide (131 mg, 0.4 mmol), CH₂Cl₂ (1 mL) and methanol (0.4 mL). The mixture was stirred at rt for 20 min, whereby it was partitioned with saturated NaHCO₃ (5 mL). The product was extracted with 2% triethylamine:chloroform (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (500 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide eudistomin Y₅ (**7**) (74 mg, 95% yield) as a yellow amorphous solid: mp >260 °C; *R_f* = 0.68 (1:1 EtOAc:hexanes); IR (neat) 1704, 1621, 1572, 1463, 1304, 1243, 1210, 800 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.01 (s, 1H), 8.55 (d, *J* = 5.0 Hz, 1H), 8.53 (s, 2H), 8.44 (d, *J* = 5.0 Hz, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.31 (t, *J* = 7.3 Hz, 1H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 188.7, 155.0, 141.6, 137.0, 136.1, 135.8, 135.3, 131.0, 130.3, 128.9, 121.7, 120.1, 119.9, 118.9, 112.9, 110.9 (2C); HRMS (ESI) *m/z* 466.9006 [(M+Na)⁺; calcd for C₁₈H₁₀N₂O₂Br₂Na⁺: 466.9007].

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Eudistomin Y₆ (8). A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with eudistomin Y₂ (**4**) (47 mg, 0.1 mmol). To this flask was added phenyltrimethylammonium tribromide (97 mg, 0.2 mmol), CH₂Cl₂ (1 mL) and methanol (0.4 mL). The mixture was stirred at rt for 20 min, whereby it was partitioned with saturated NaHCO₃ (5 mL) and extracted with 2% triethylamine:chloroform (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (500 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (1:1 EtOAc:hexanes) to provide eudistomin Y₆ (**8**) (74 mg, 95% yield) as a yellow amorphous solid: mp >260 °C; *R_f* = 0.82 (1:1 EtOAc:hexanes); IR (neat) 1468, 1271, 1243, 1189, 1046, 986, 673 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.16 (s, 1H), 10.96 (s, 1H), 8.61 (s, 1H), 8.59 (d, *J* = 4.9 Hz, 1H), 8.52 (s, 2H), 8.52 (d, *J* = 4.9 Hz, 1H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.74 (dd, *J* = 1.2, 8.7 Hz, 1H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 188.6, 154.6, 140.3, 137.3, 136.4, 135.9, 135.3 (2C), 131.4, 130.6, 130.0, 124.4, 121.9, 119.4, 114.9, 112.2, 110.8 (2C); HRMS (ESI) *m/z* 522.8289 [(M+H)⁺; calcd for C₁₈H₁₀N₂O₂Br₃⁺: 522.8292].

Supporting Information Panarese and Waters*



Eudistomin Y₇ (**9**)

Eudistomin Y₇ (9**).** A 10 mL round-bottom flask equipped with a teflon-coated magnetic stirbar was charged with phenol **17** (37 mg, 0.1 mmol). To this flask was added phenyltrimethylammonium tribromide (76 mg, 0.2 mmol), CH₂Cl₂ (1 mL) and methanol (0.4 mL). The mixture was stirred at rt for 20 min, whereby it was partitioned with saturated NaHCO₃ (5 mL) and extracted with 2% triethylamine:chloroform (5 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. To the filtrate was added silica gel (500 mg) and the solvent was removed under reduced pressure. Further drying on a vacuum pump gave a free flowing powder. This material was loaded onto a dry packed silica gel column, topped with a layer of sand (1 cm), and eluted (EtOAc) to provide eudistomin Y₇ (**9**) (46 mg, 86% yield) as a yellow amorphous solid: mp >260 °C; *R_f* = 0.85 (EtOAc); IR (neat) 1468, 1270, 1245, 1189, 1046, 988 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 12.05 (s, 1H), 10.92 (s, 1H), 8.55 (d, *J* = 4.9 Hz, 1H), 8.53 (s, 2H), 8.41 (d, *J* = 3.8 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 1.5 Hz, 1H), 7.42 (dd, *J* = 1.5, 8.2 Hz, 1H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 188.4, 154.4, 142.2, 137.3, 136.2, 135.7, 135.1 (2C), 130.5, 130.3, 123.2, 122.9, 121.5, 119.0, 118.7, 115.3, 110.6 (2C); HRMS (ESI) *m/z* 522.8290 [(M+H)⁺; calcd for C₁₈H₁₀N₂O₂Br₃⁺: 522.8292].

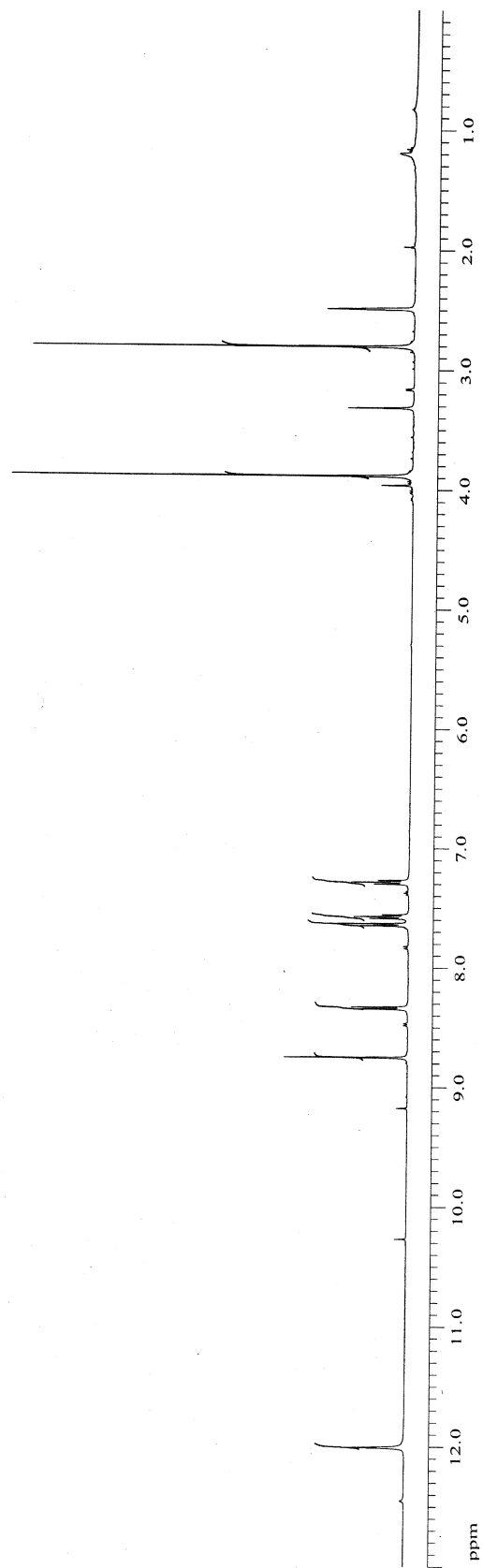
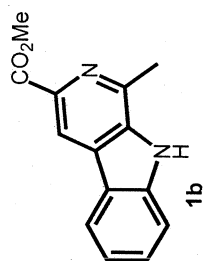


Figure S1. The 500 MHz ¹H NMR Spectrum of Compound **1b** in DMSO-*d*₆

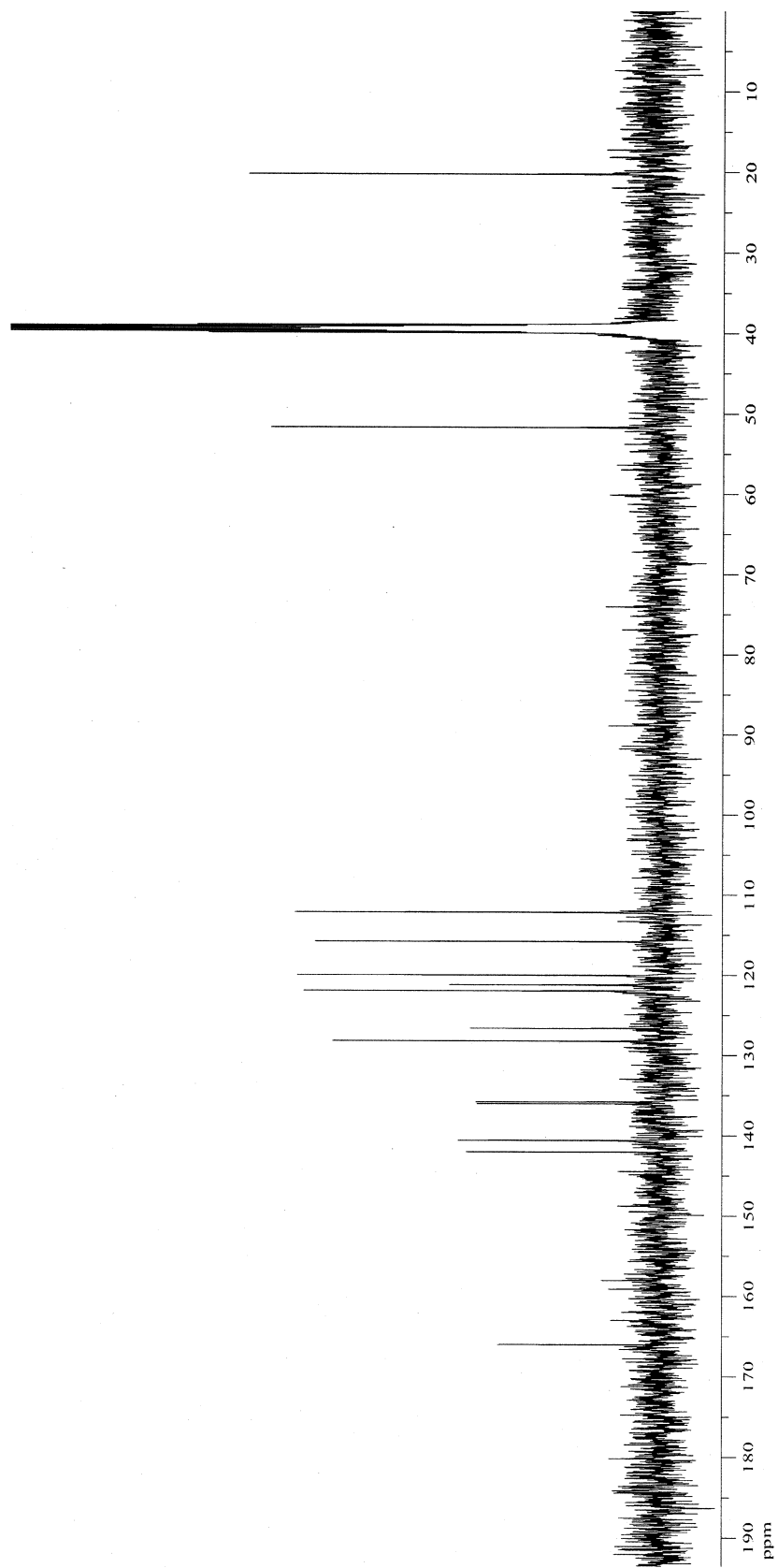
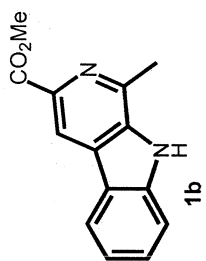


Figure S2. The 125 MHz ^{13}C NMR Spectrum of Compound **1b** in $\text{DMSO-}d_6$

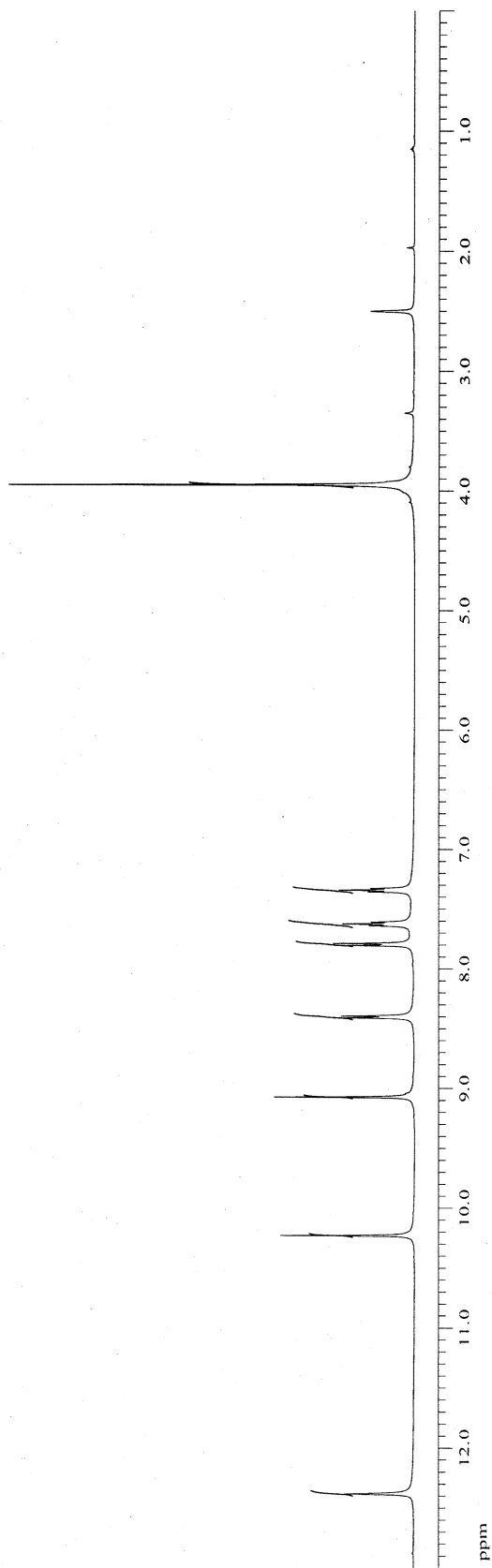
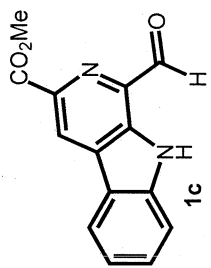


Figure S3. The 500 MHz ¹H NMR Spectrum of Compound 1c in DMSO-d₆

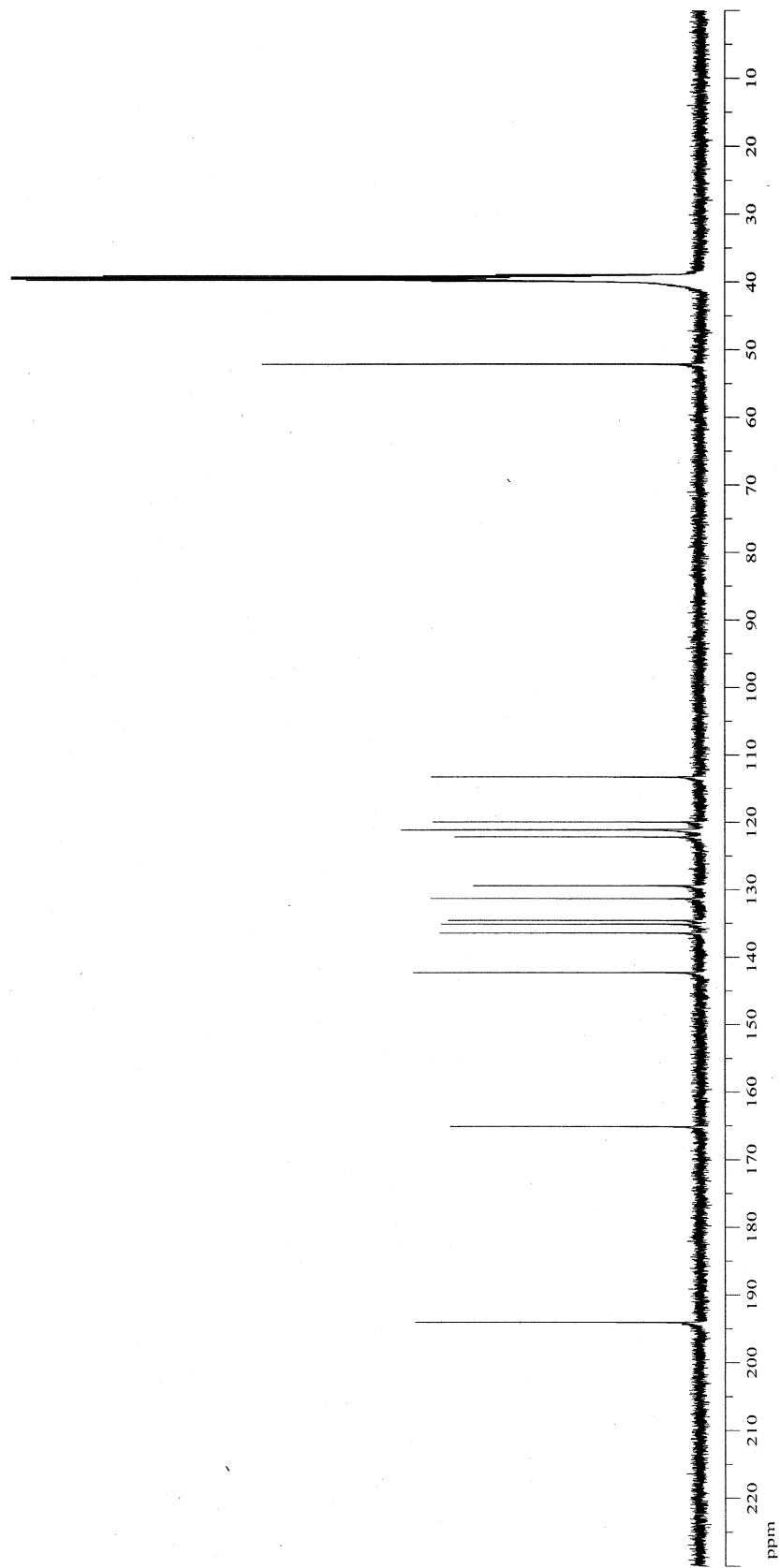
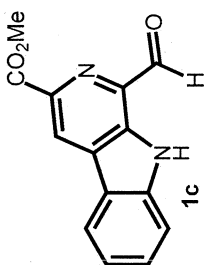


Figure S4. The 125 MHz ^{13}C NMR Spectrum of Compound **1c** in $\text{DMSO-}d_6$

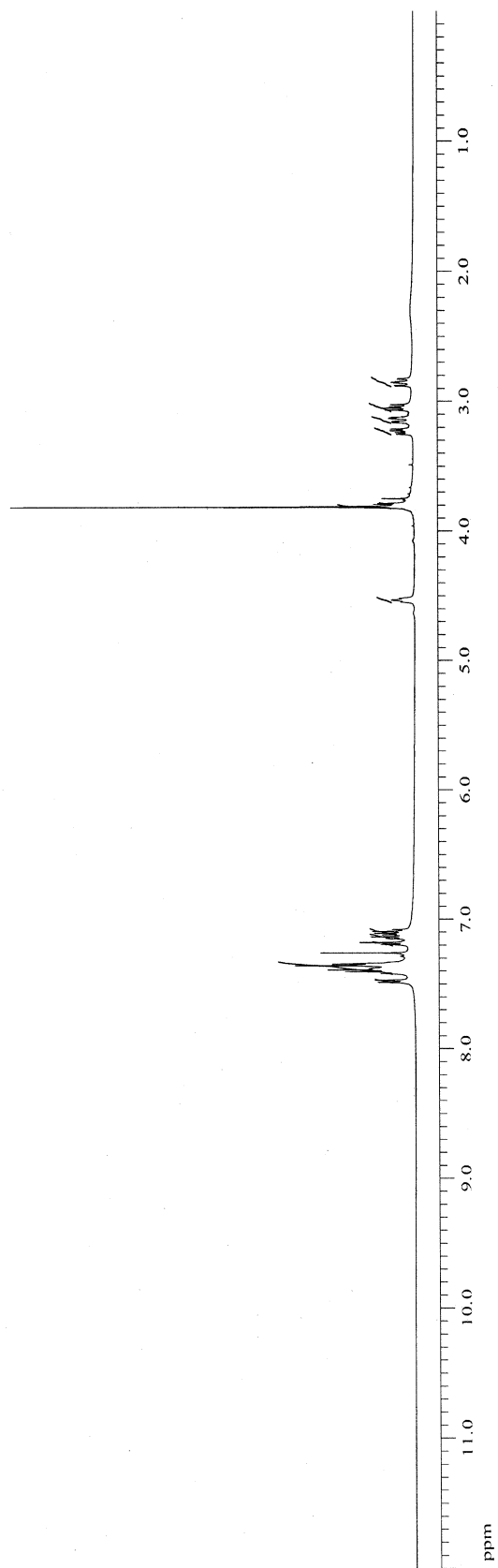
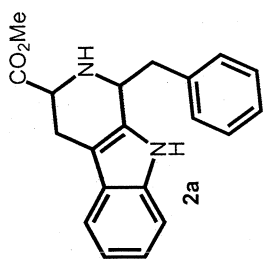


Figure S5. The 500 MHz ¹H NMR Spectrum of Compound 2a in CDCl₃

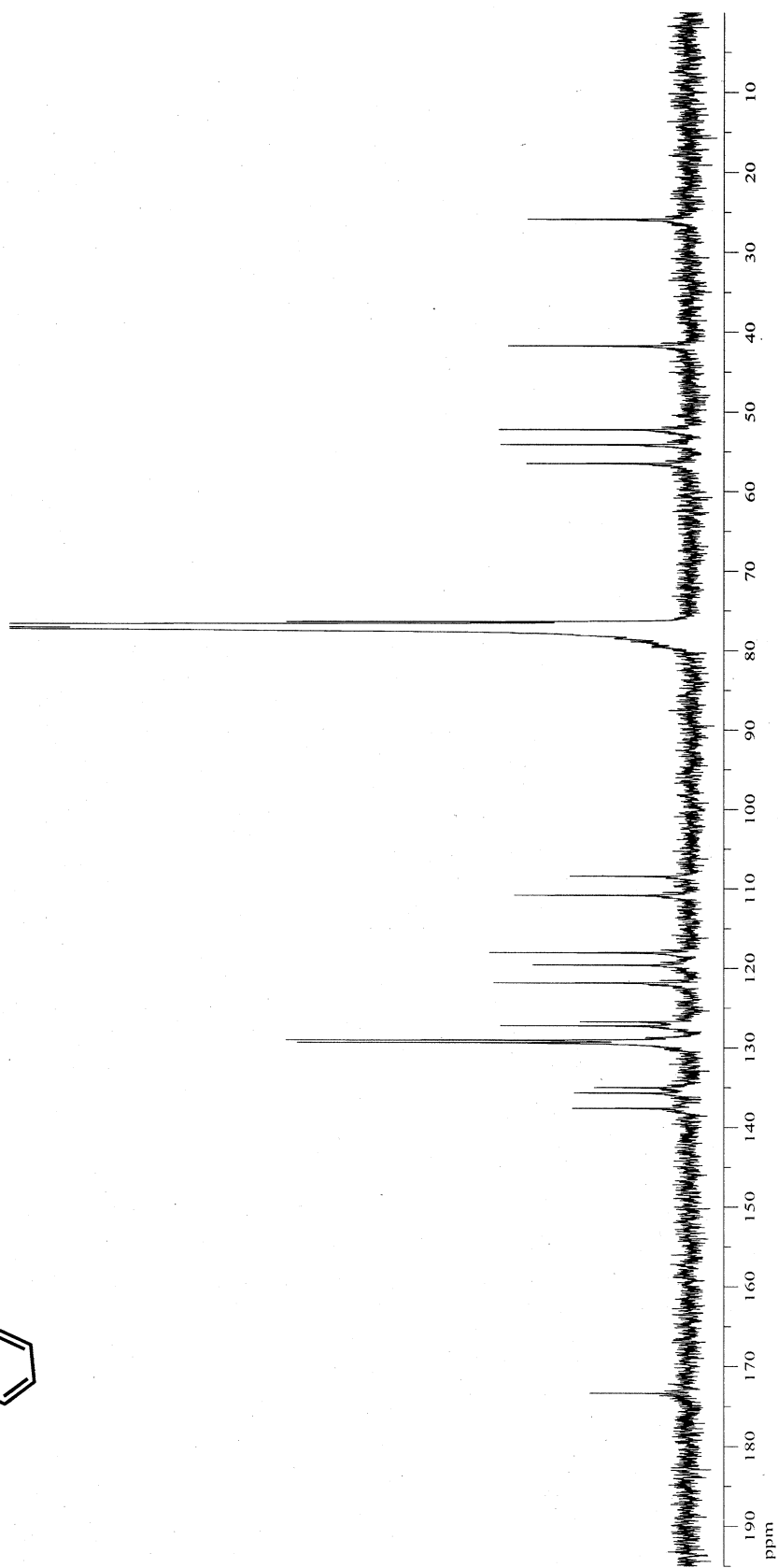
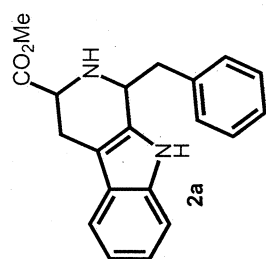


Figure S6. The 125 MHz ¹³C NMR Spectrum of Compound 2a in CDCl₃

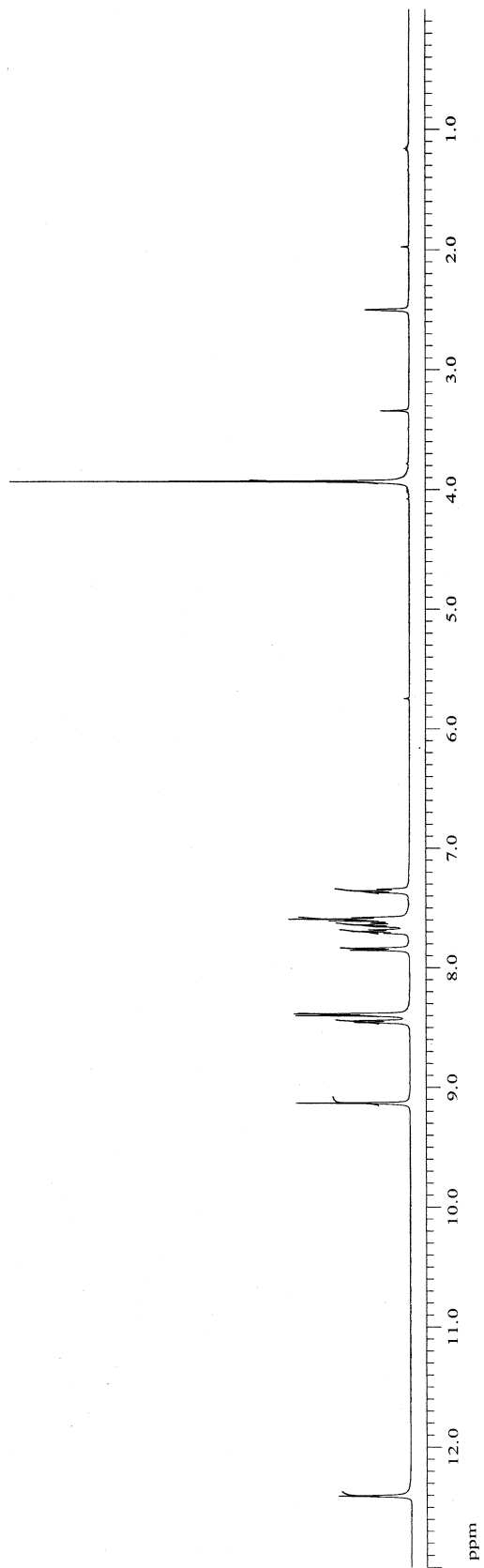
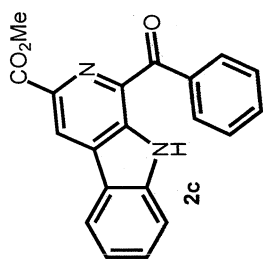


Figure S7. The 500 MHz ¹H NMR Spectrum of Compound 2c in DMSO-d₆

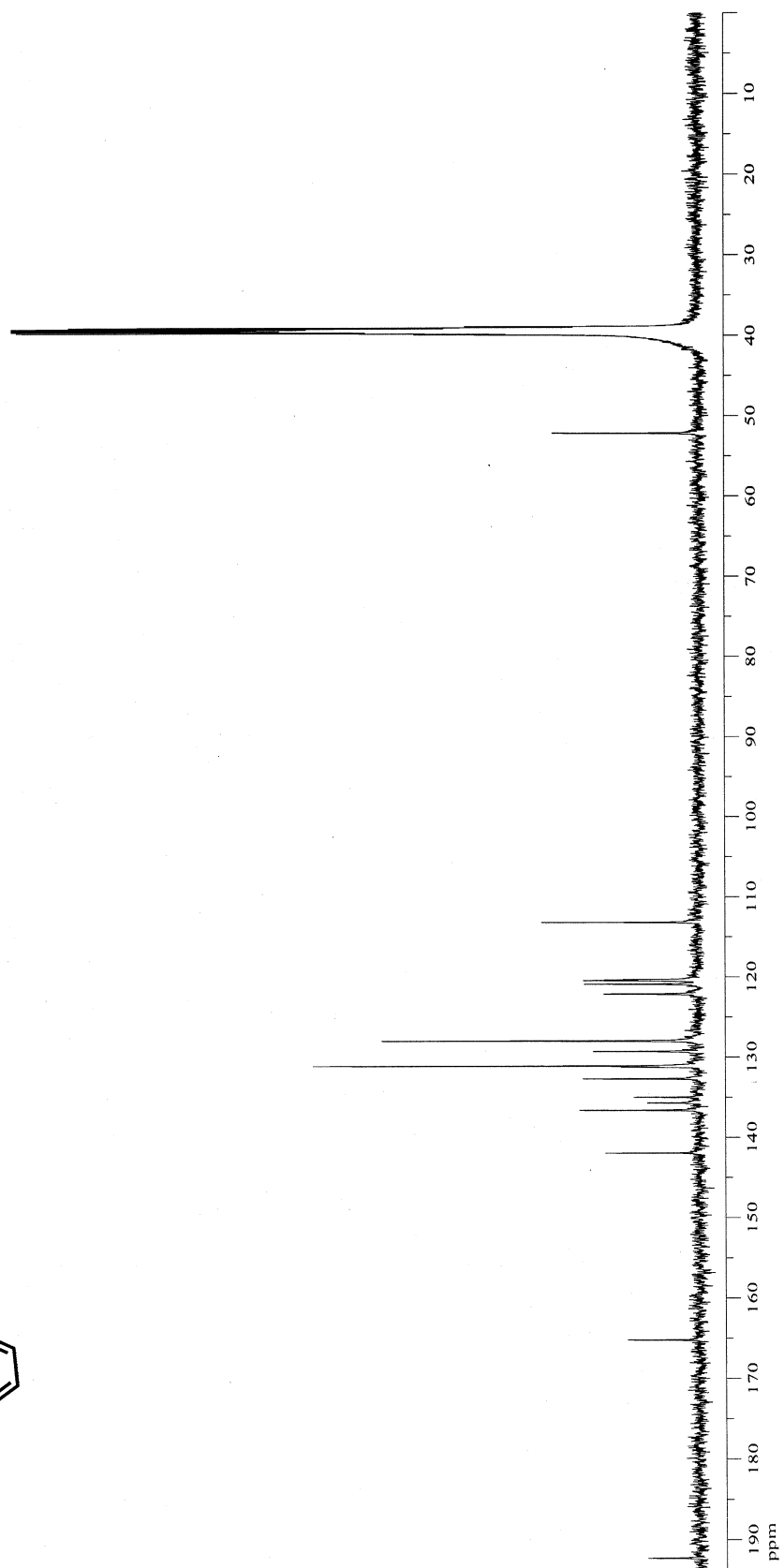
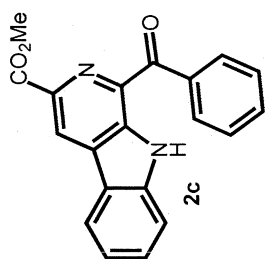


Figure S8. The 125 MHz ^{13}C NMR Spectrum of Compound **2c** in $\text{DMSO}-d_6$

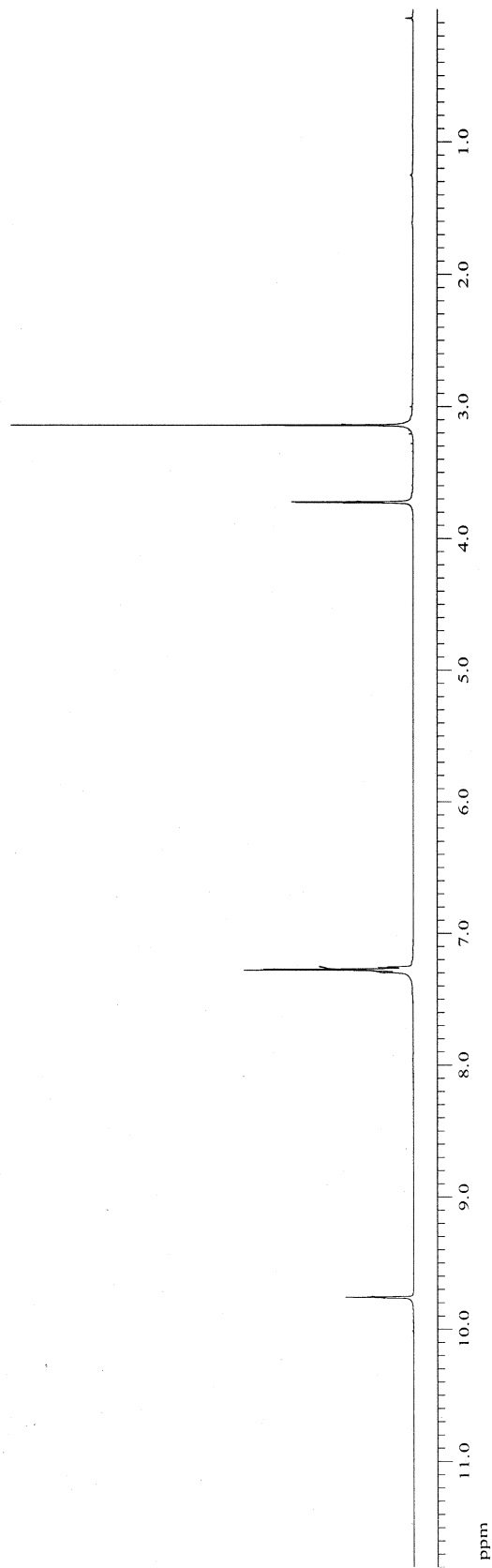
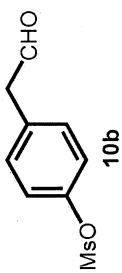


Figure S9. The 500 MHz ^1H NMR Spectrum of Compound **10b** in CDCl_3

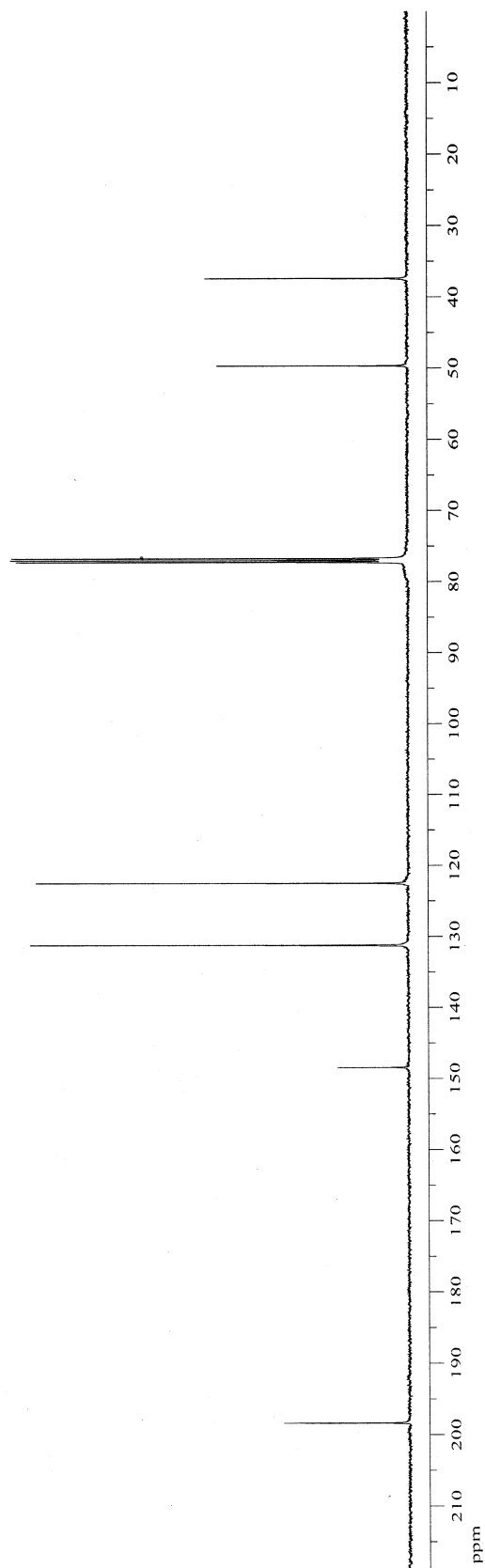
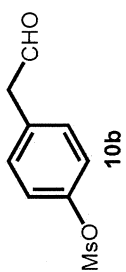


Figure S10. The 125 MHz ¹³C NMR Spectrum of Compound **10b** in CDCl₃

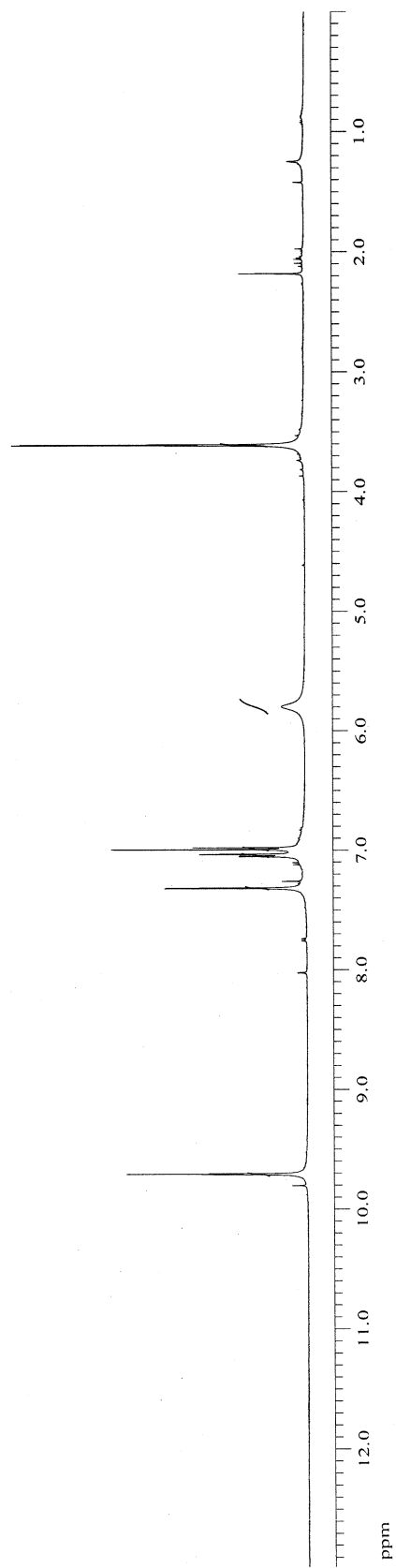
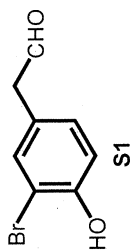


Figure S11. The 500 MHz ^1H NMR Spectrum of Compound S1 in CDCl_3

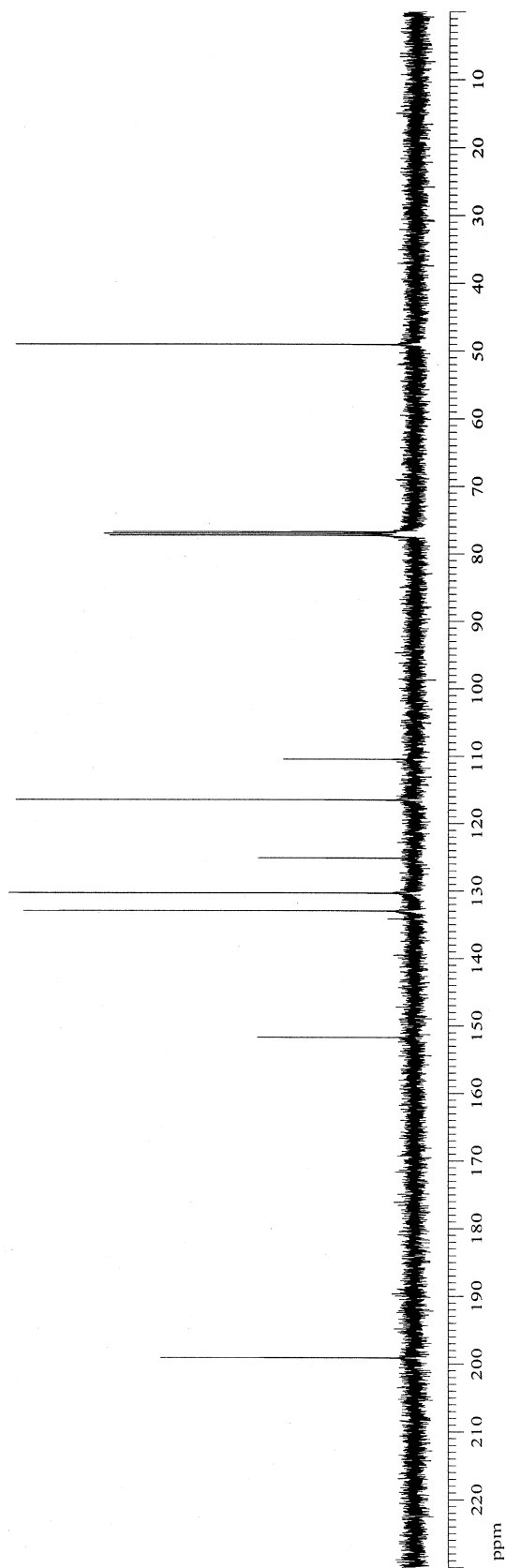
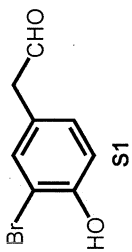


Figure S12. The 125 MHz ¹³C NMR Spectrum of Compound S1 in CDCl₃

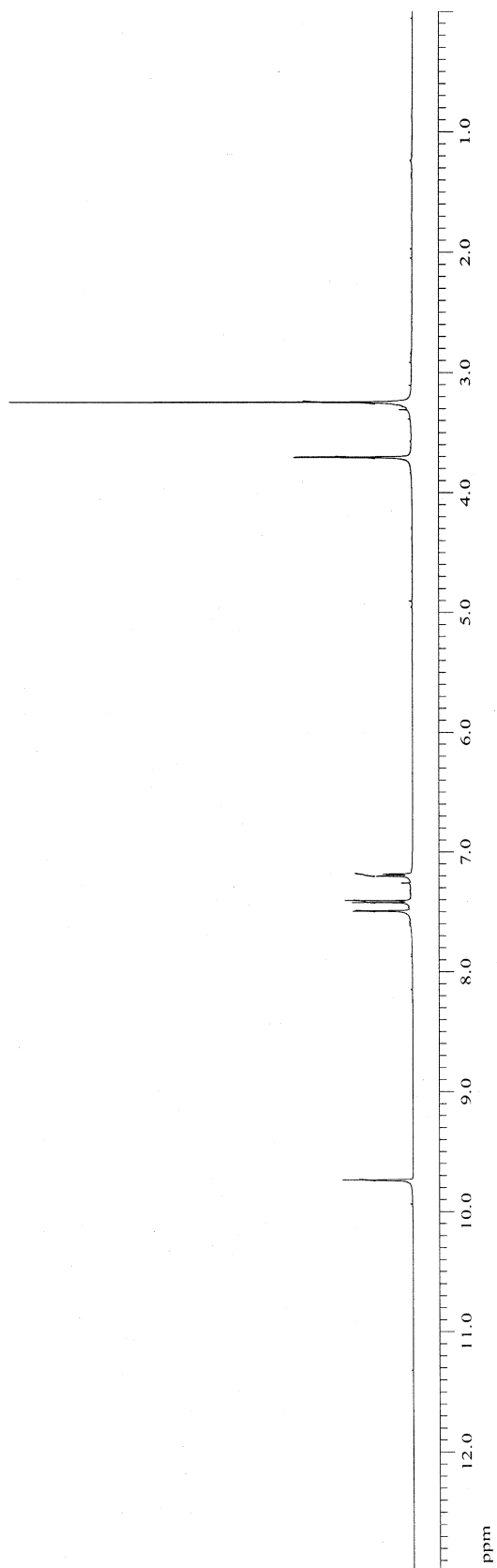
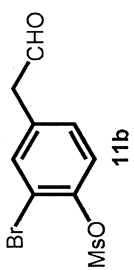


Figure S13. The 500 MHz ¹H NMR Spectrum of Compound 11b in CDCl₃

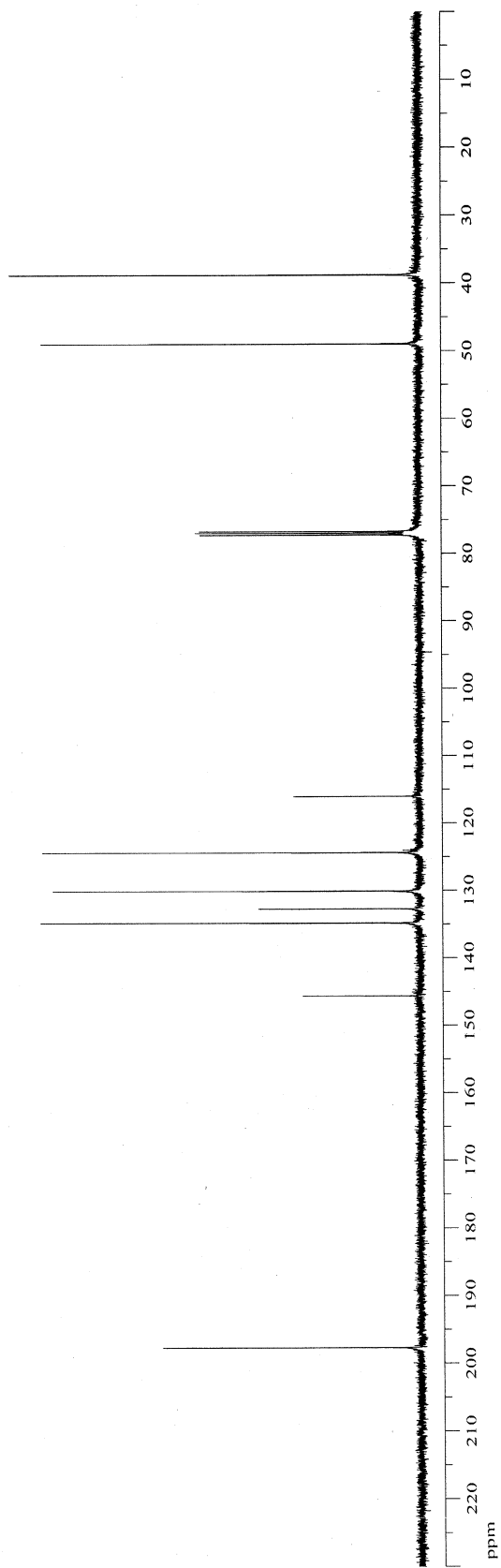
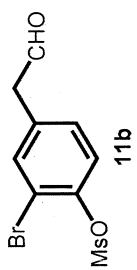


Figure S14. The 125 MHz ¹³C NMR Spectrum of Compound 11b in CDCl₃

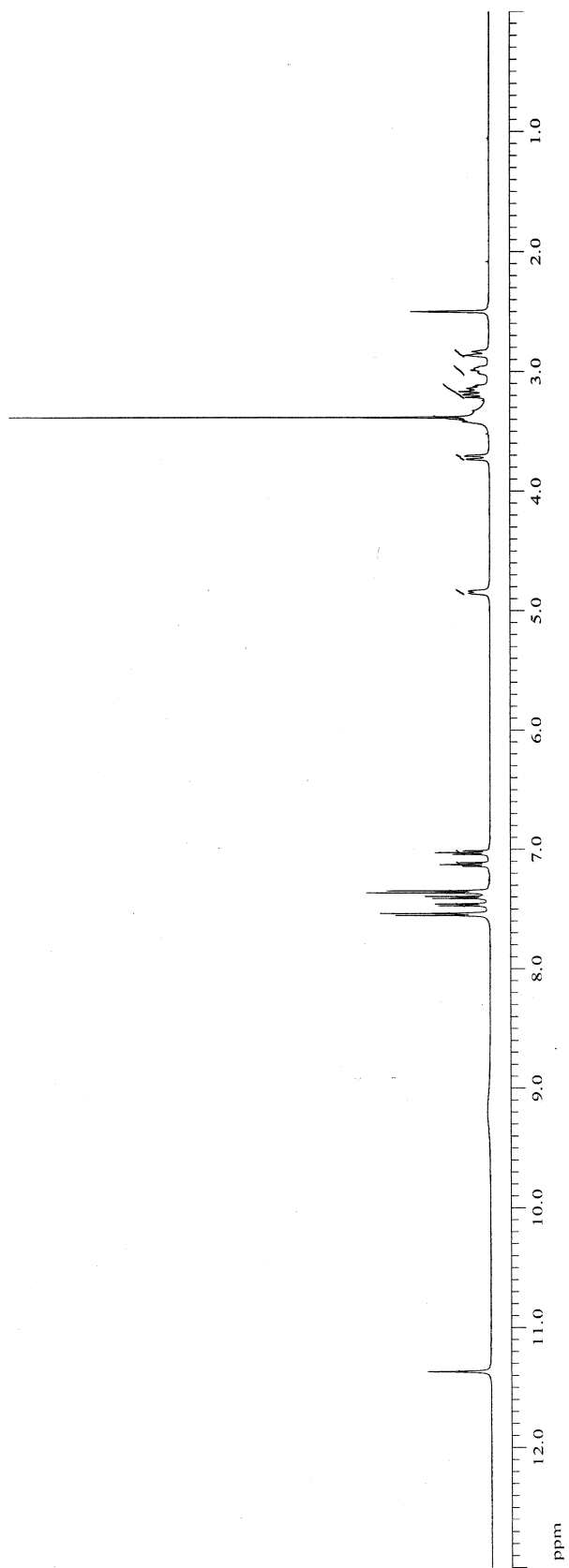
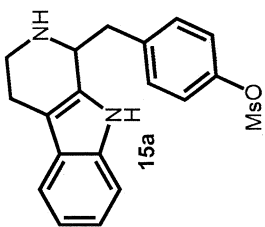


Figure S15. The 500 MHz ¹H NMR Spectrum of Compound 15a in DMSO-d₆

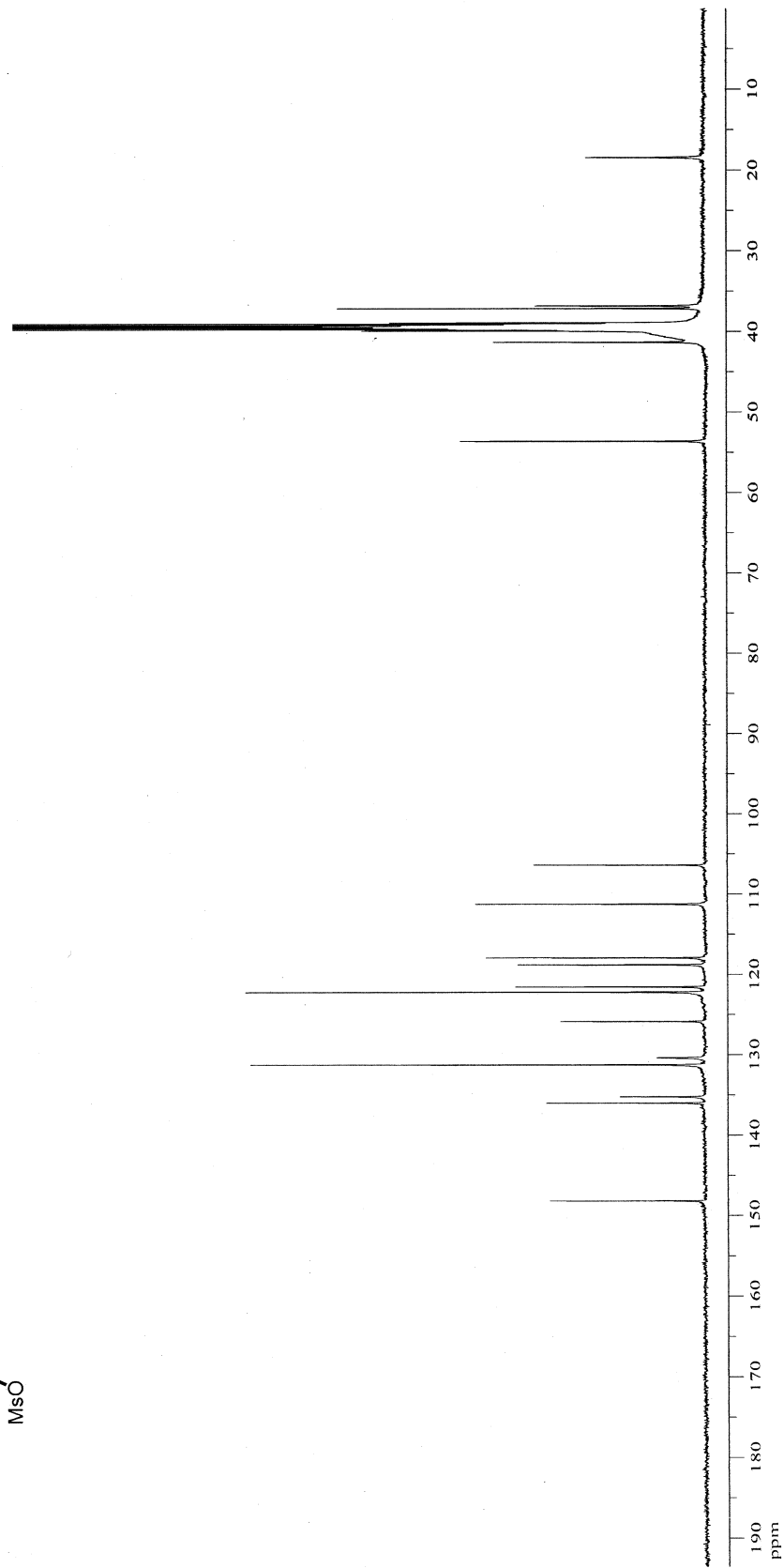
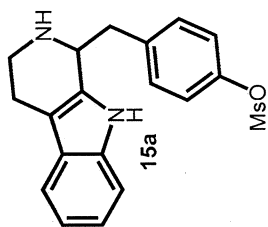


Figure S16. The 125 MHz ^{13}C NMR Spectrum of Compound 15a in $\text{DMSO-}d_6$

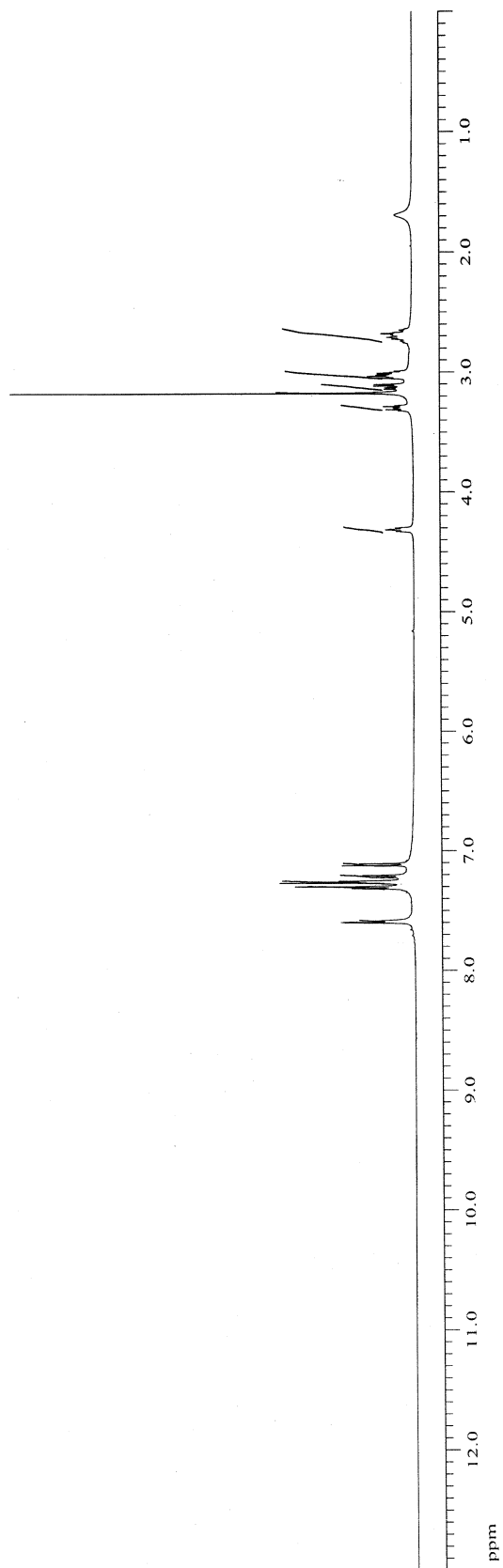
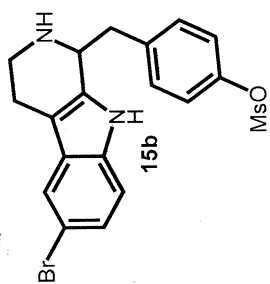


Figure S17. The 500 MHz ¹H NMR Spectrum of Compound **15b** in CDCl₃

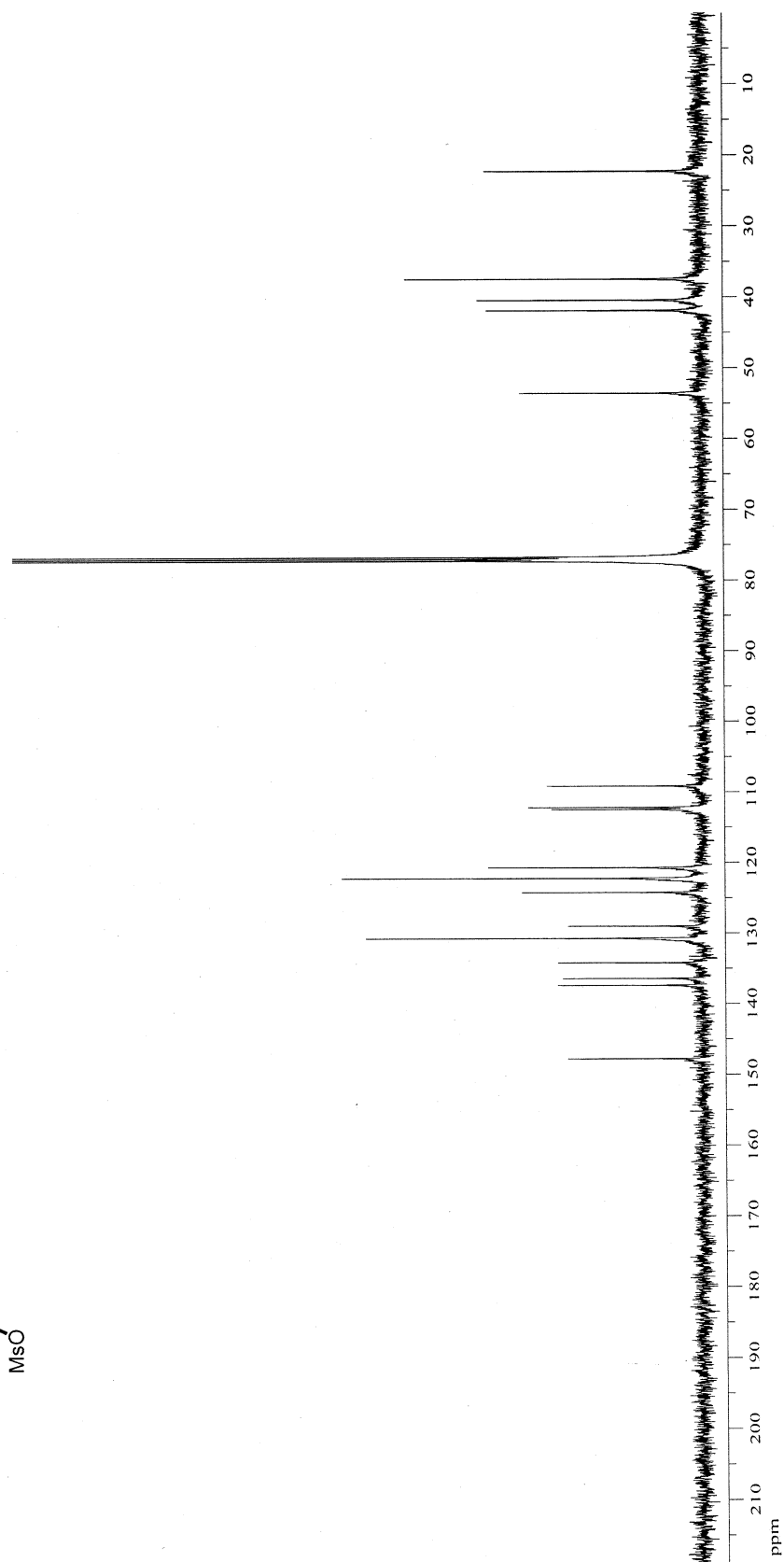
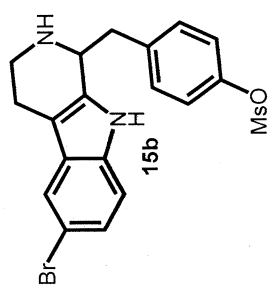


Figure S18. The 125 MHz ¹³C NMR Spectrum of Compound **15b** in CDCl₃

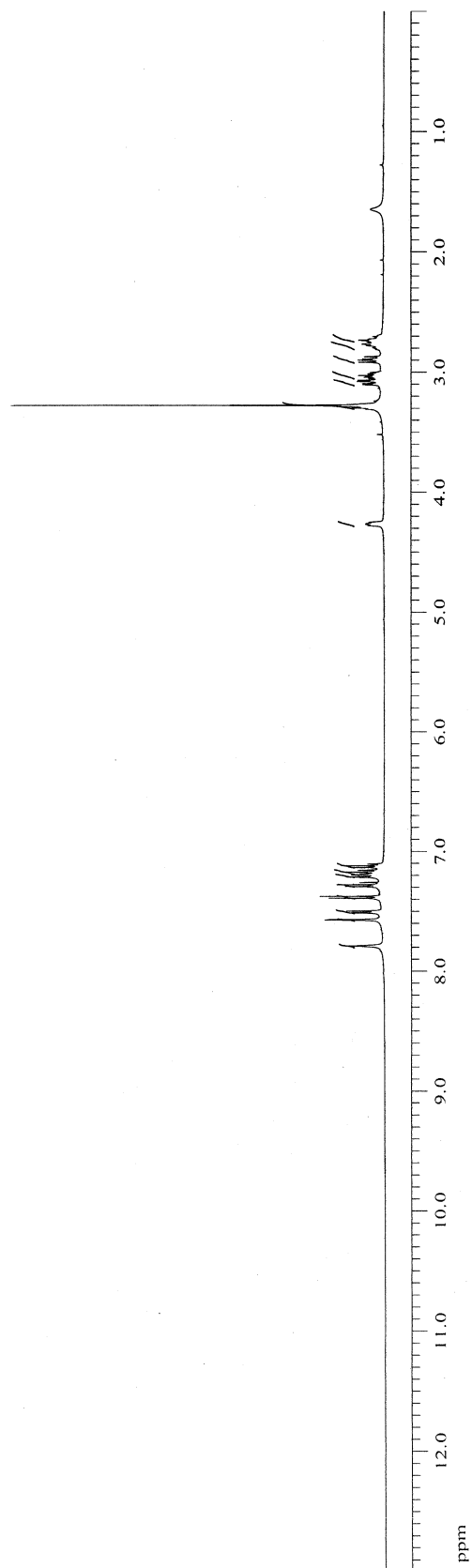
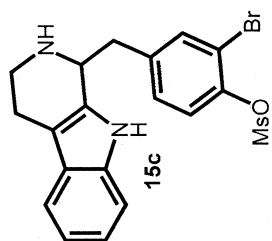


Figure S19. The 500 MHz ^1H NMR Spectrum of Compound 15c in CDCl_3

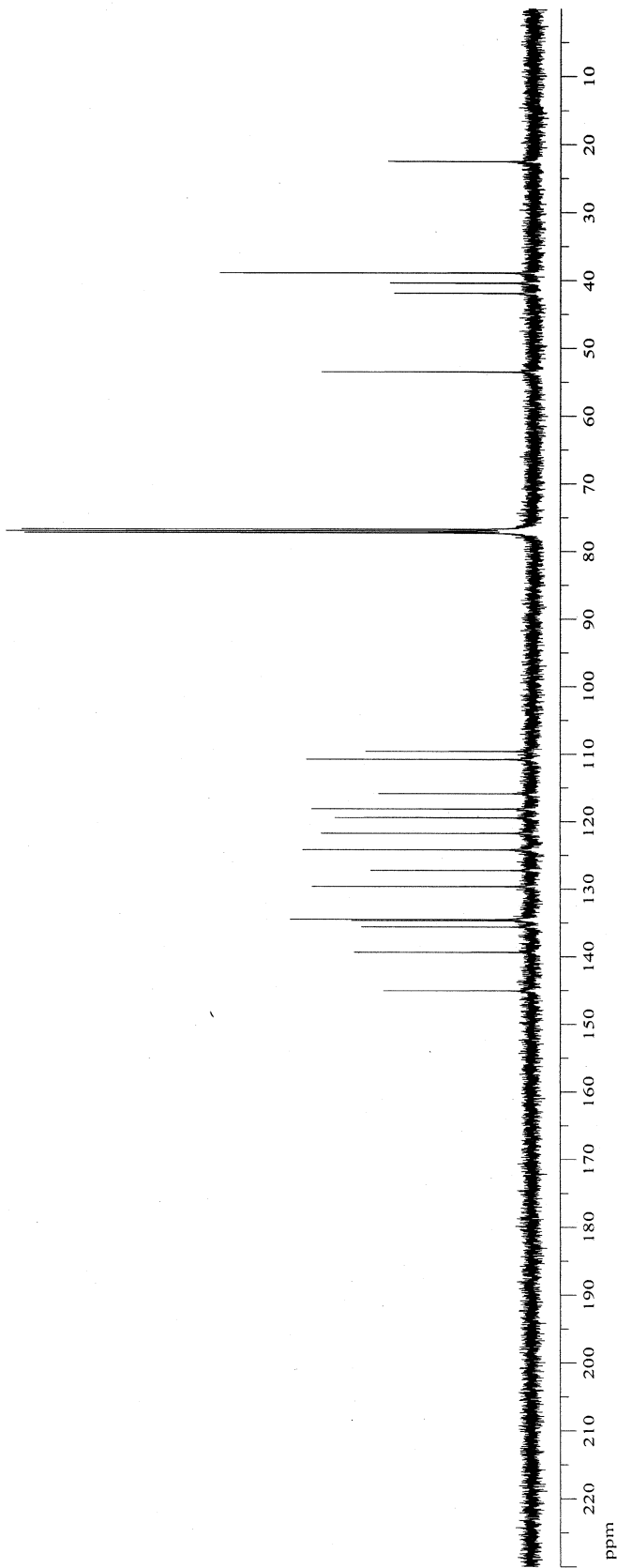
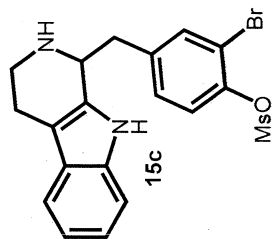


Figure S20. The 125 MHz ^{13}C NMR Spectrum of Compound **15c** in CDCl_3

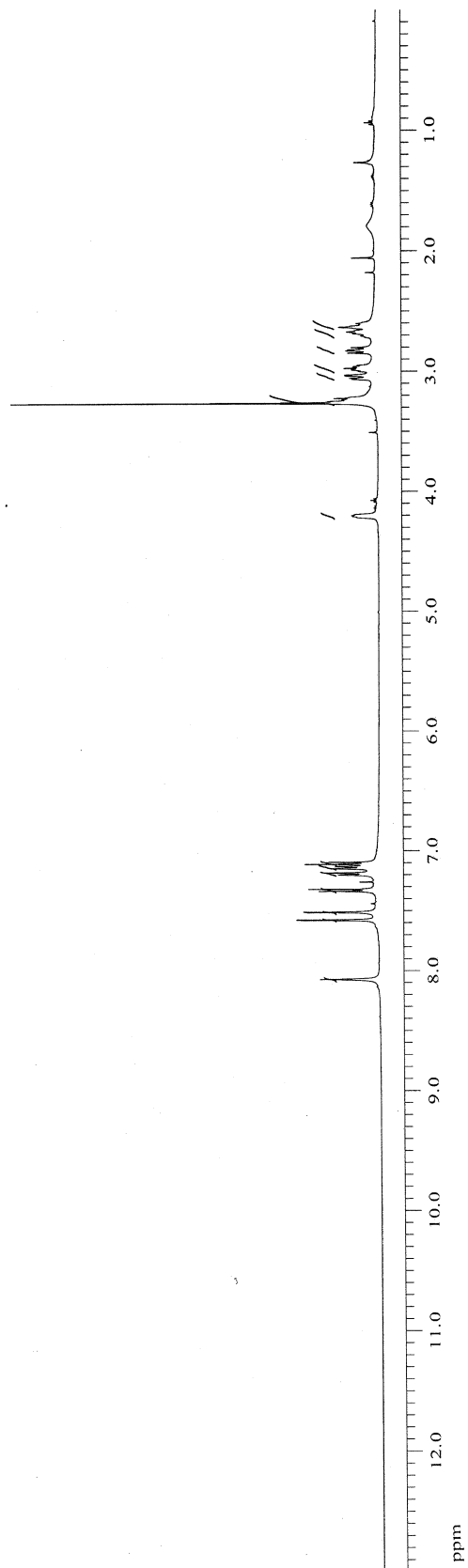
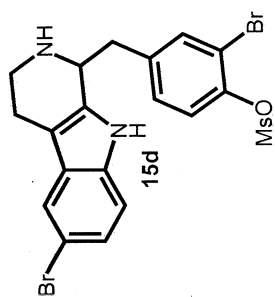


Figure S21. The 500 MHz ^1H NMR Spectrum of Compound 15d in CDCl_3

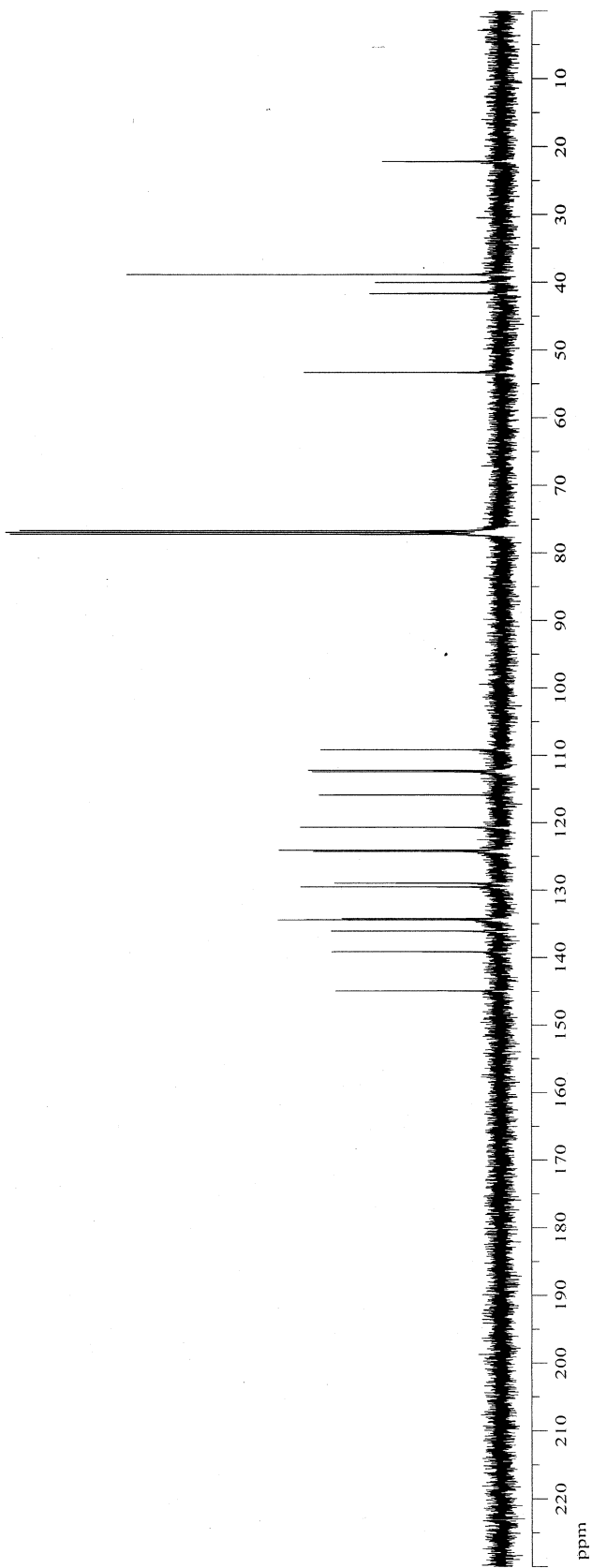
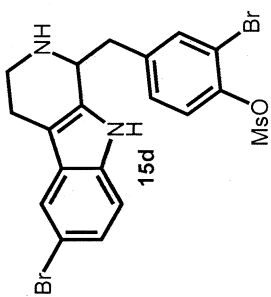


Figure S22. The 125 MHz ^{13}C NMR Spectrum of Compound 15d in CDCl_3

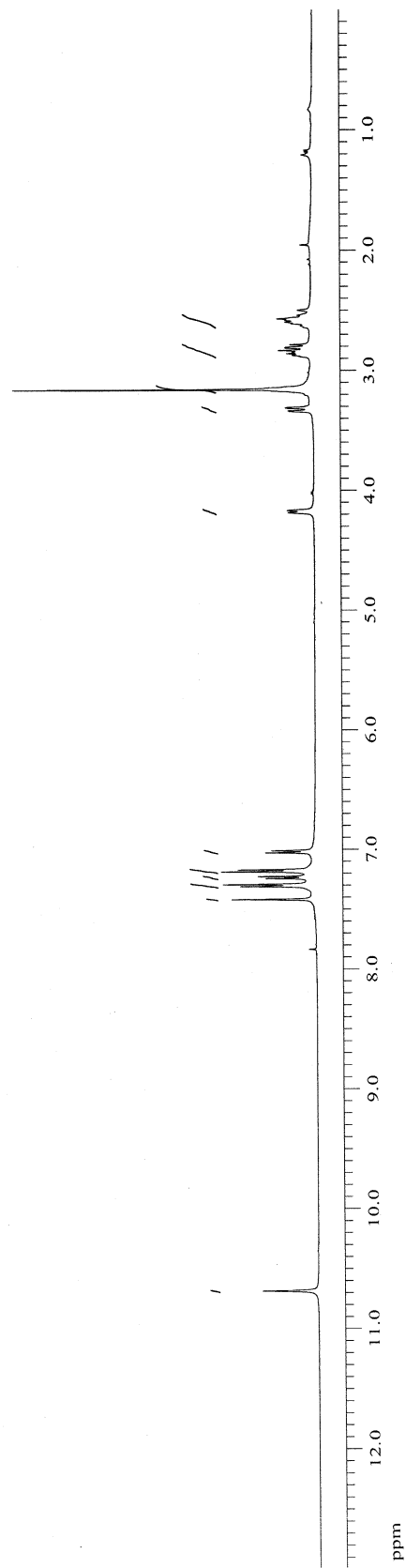
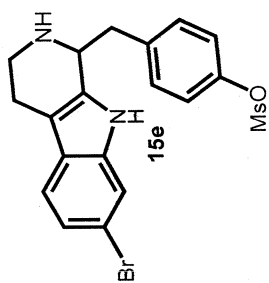


Figure S23. The 500 MHz ¹H NMR Spectrum of Compound **15e** in CDCl₃/DMSO-*d*₆

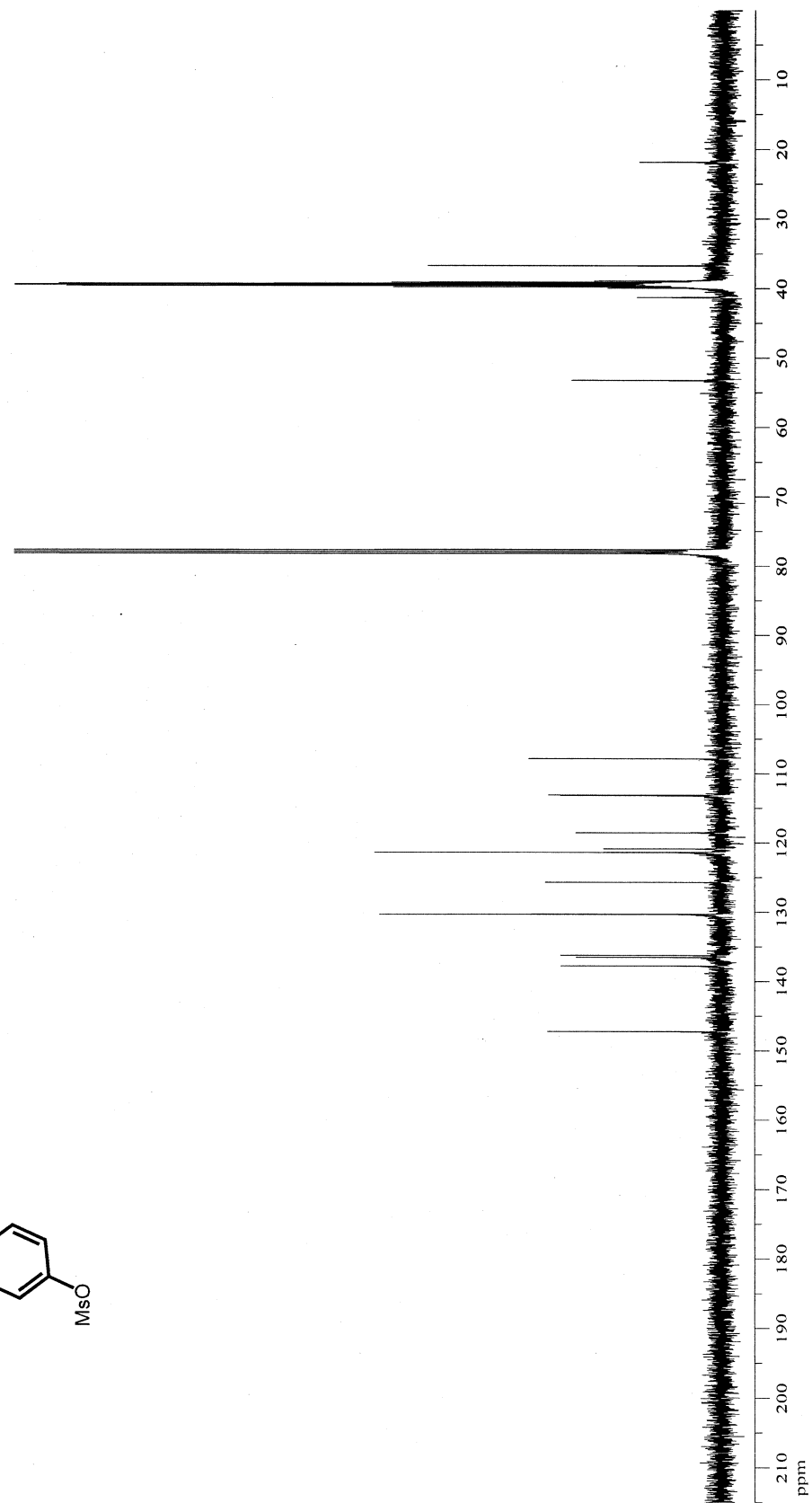
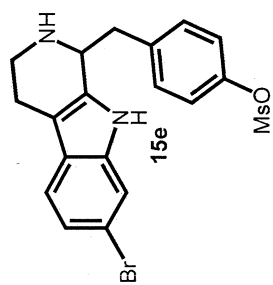


Figure S24. The 125 MHz ^{13}C NMR Spectrum of Compound **15e** in $\text{CDCl}_3/\text{DMSO-}d_6$

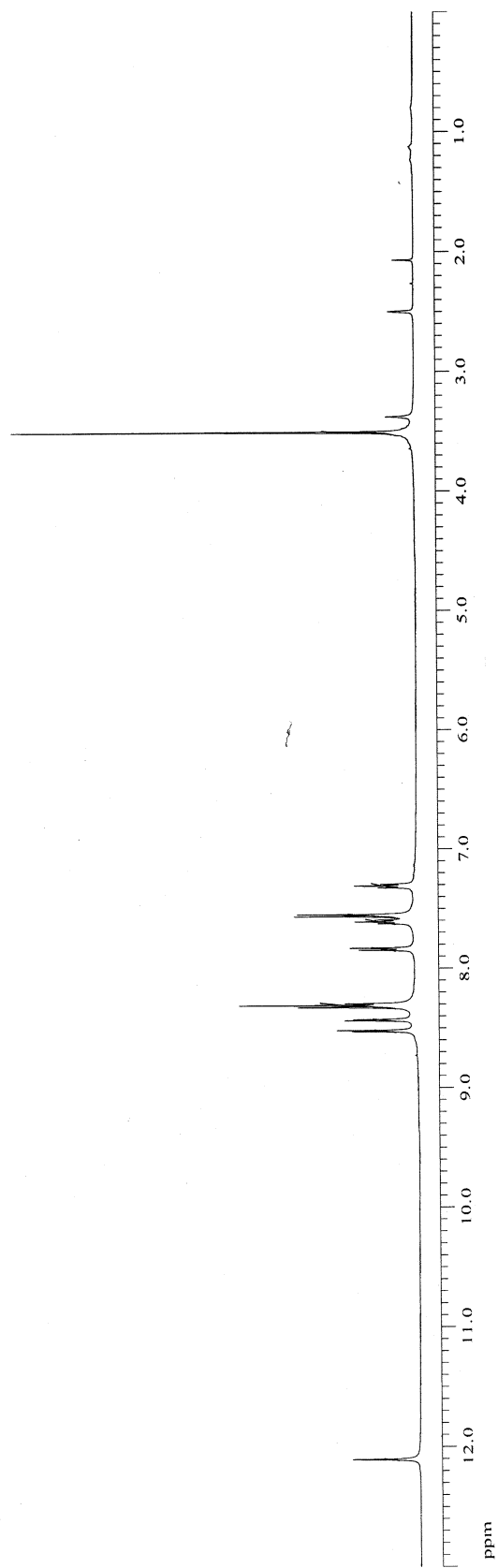
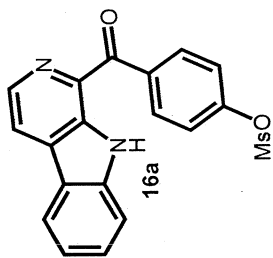


Figure S25. The 500 MHz ^1H NMR Spectrum of Compound 16a in $\text{DMSO}-d_6$

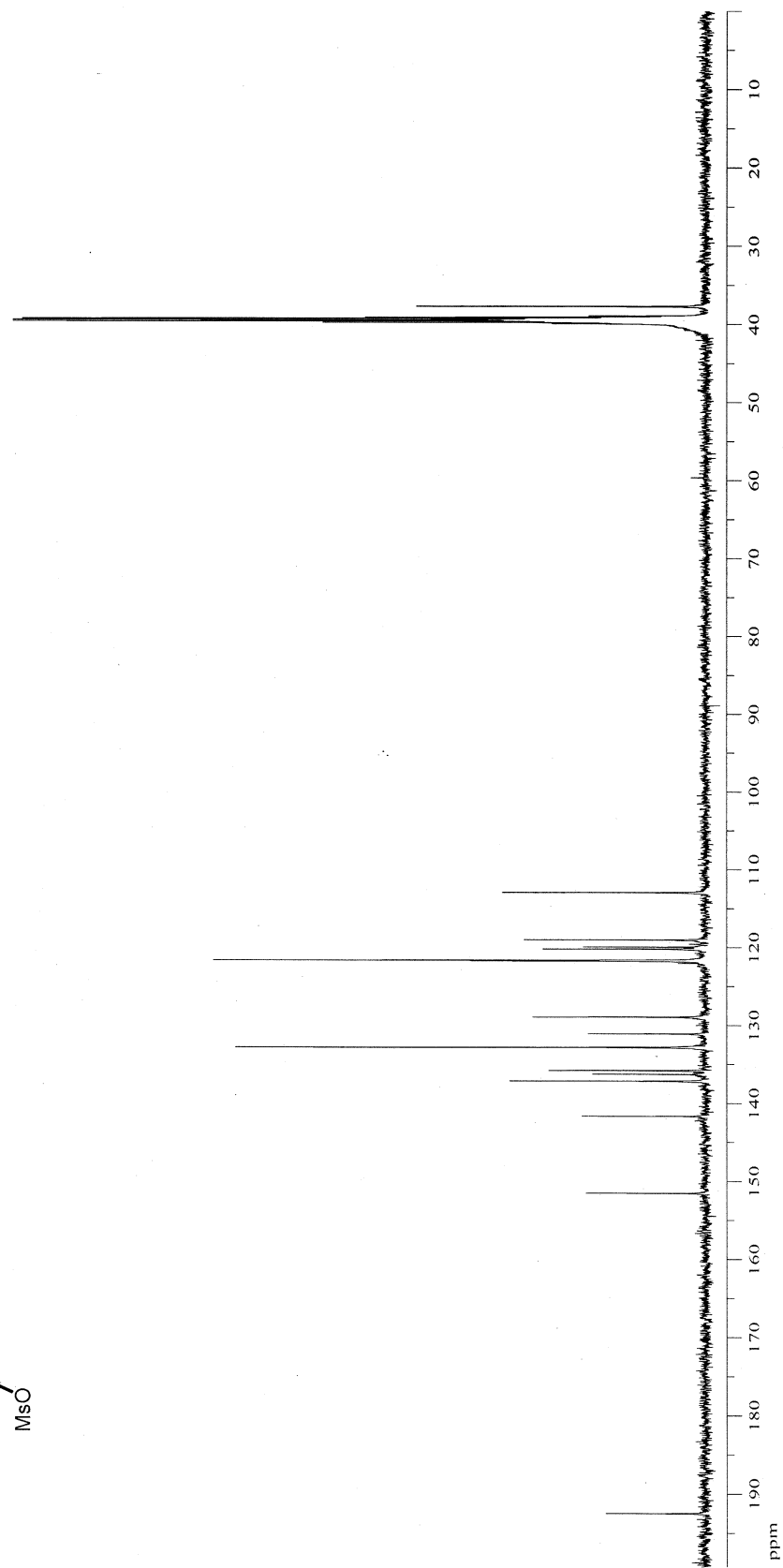
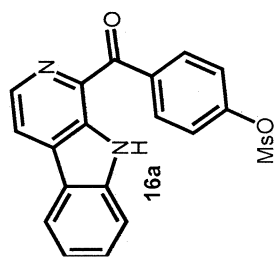


Figure S26. The 125 MHz ^{13}C NMR Spectrum of Compound **16a** in $\text{DMSO-}d_6$

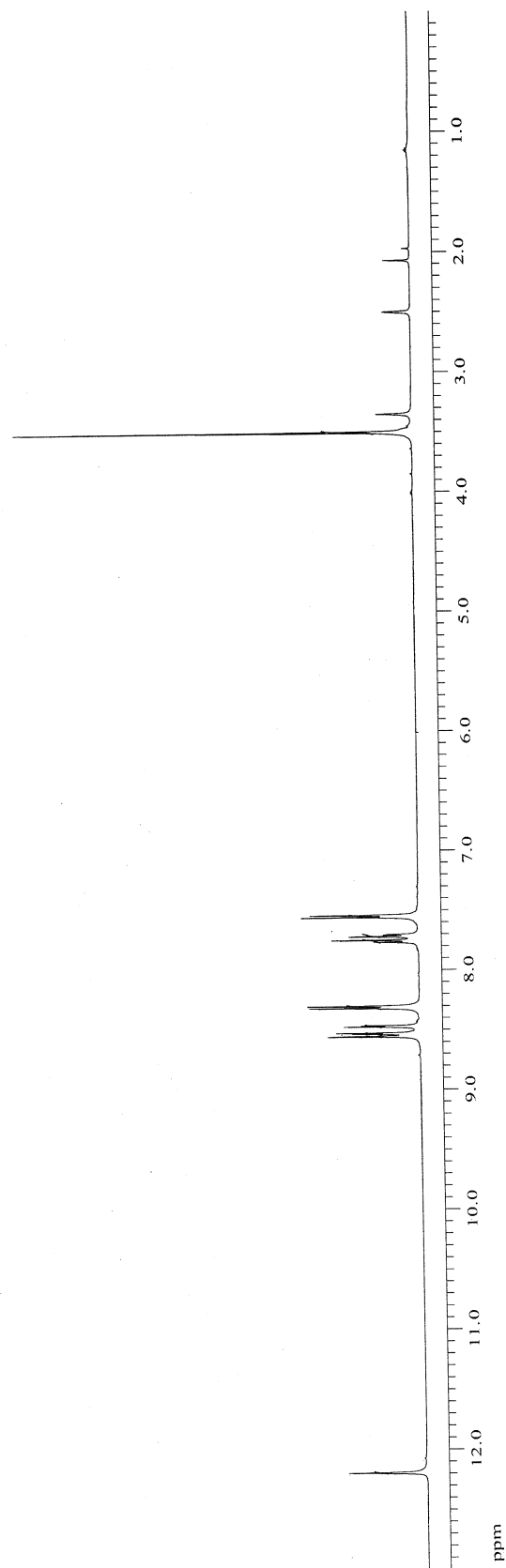
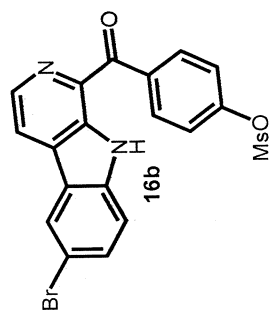


Figure S27. The 500 MHz ¹H NMR Spectrum of Compound 16b in DMSO-d₆

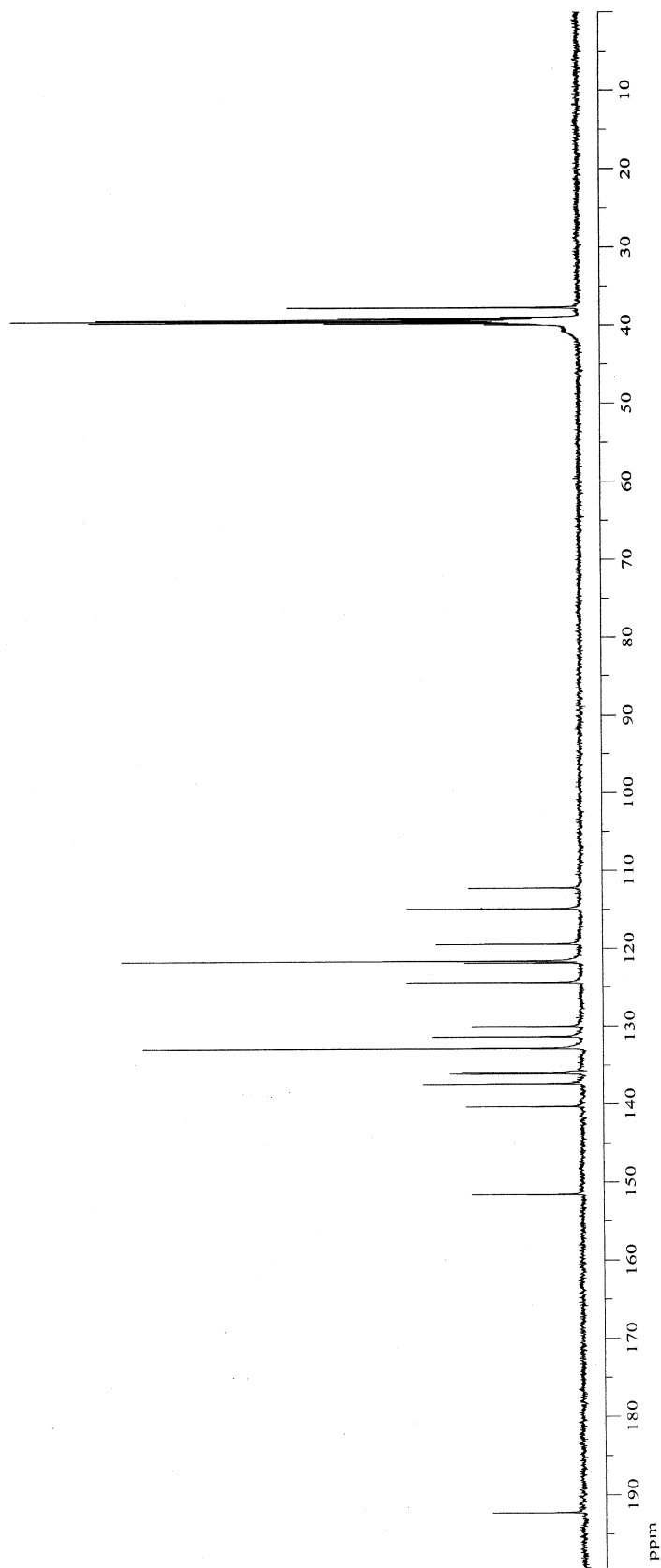
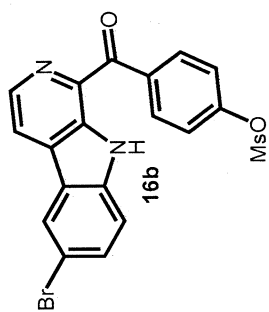


Figure S28. The 125 MHz ^{13}C NMR Spectrum of Compound **16b** in $\text{DMSO-}d_6$

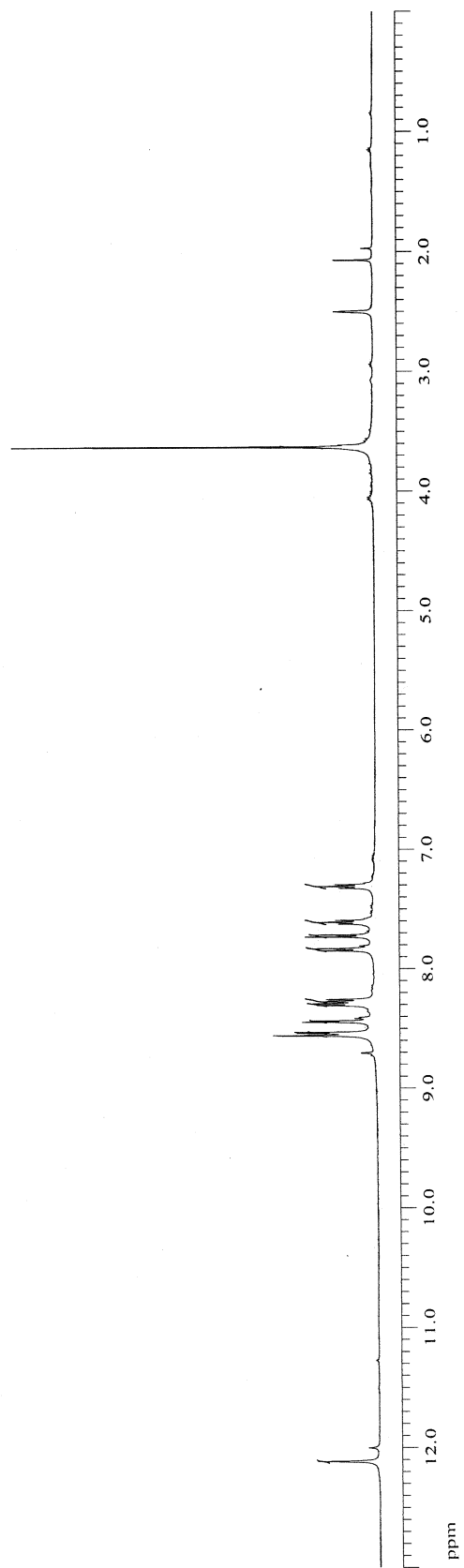
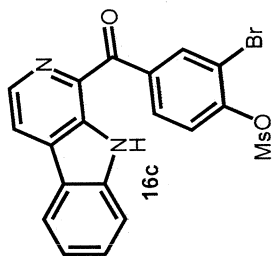


Figure S29. The 500 MHz ¹H NMR Spectrum of Compound 16c in DMSO-d₆

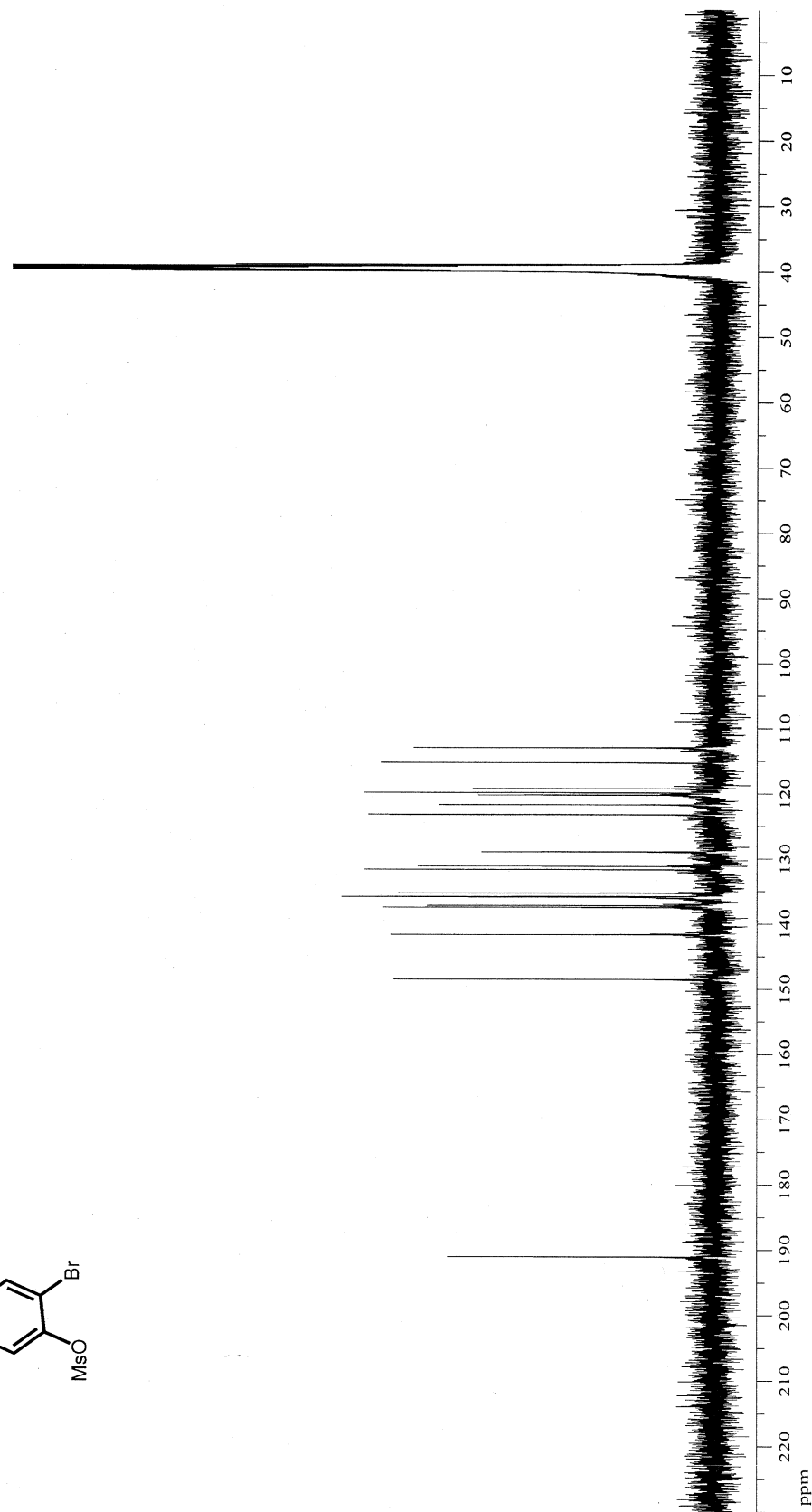
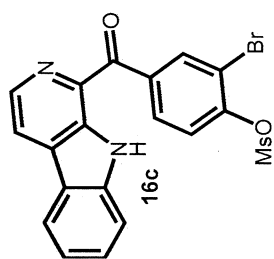


Figure S30. The 125 MHz ¹³C NMR Spectrum of Compound **16c** in DMSO-*d*₆

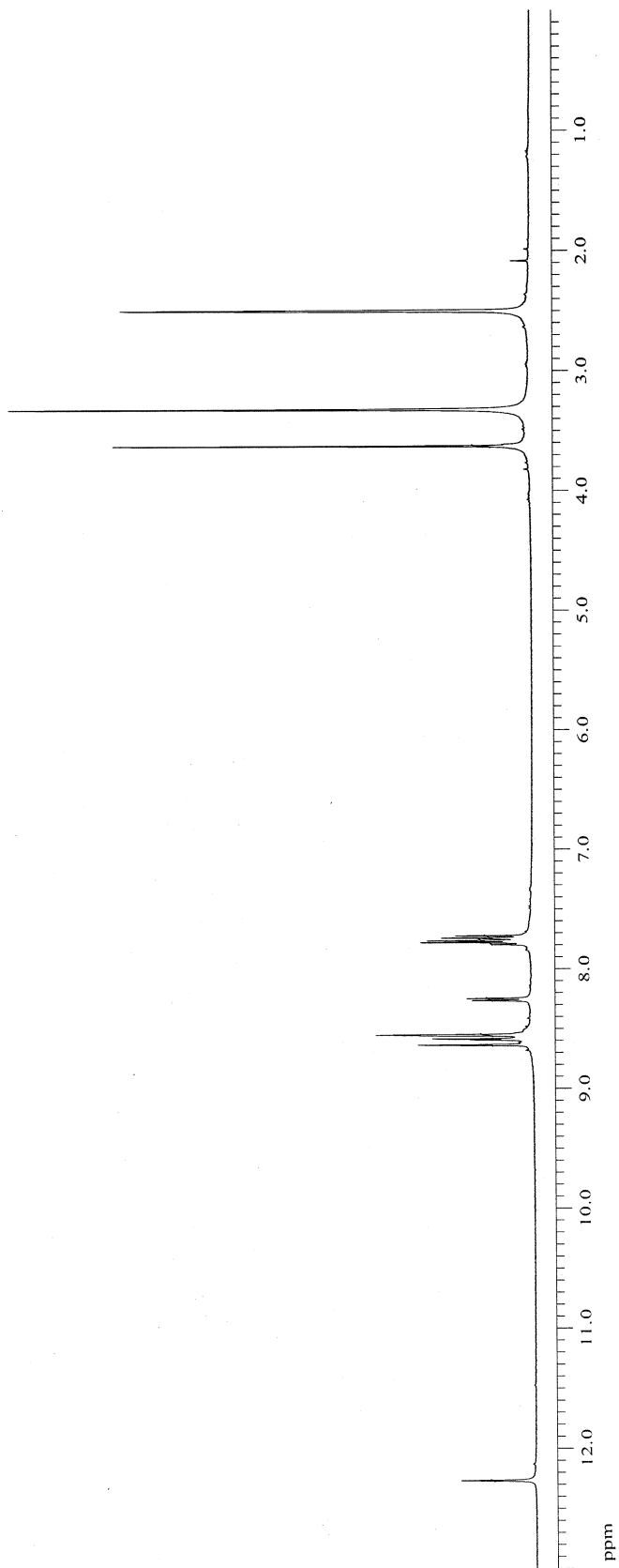
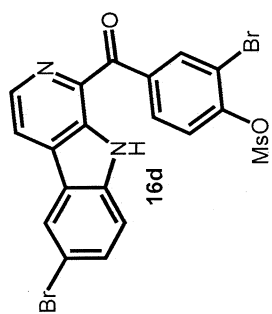


Figure S31. The 500 MHz ^1H NMR Spectrum of Compound **16d** in $\text{DMSO}-d_6$

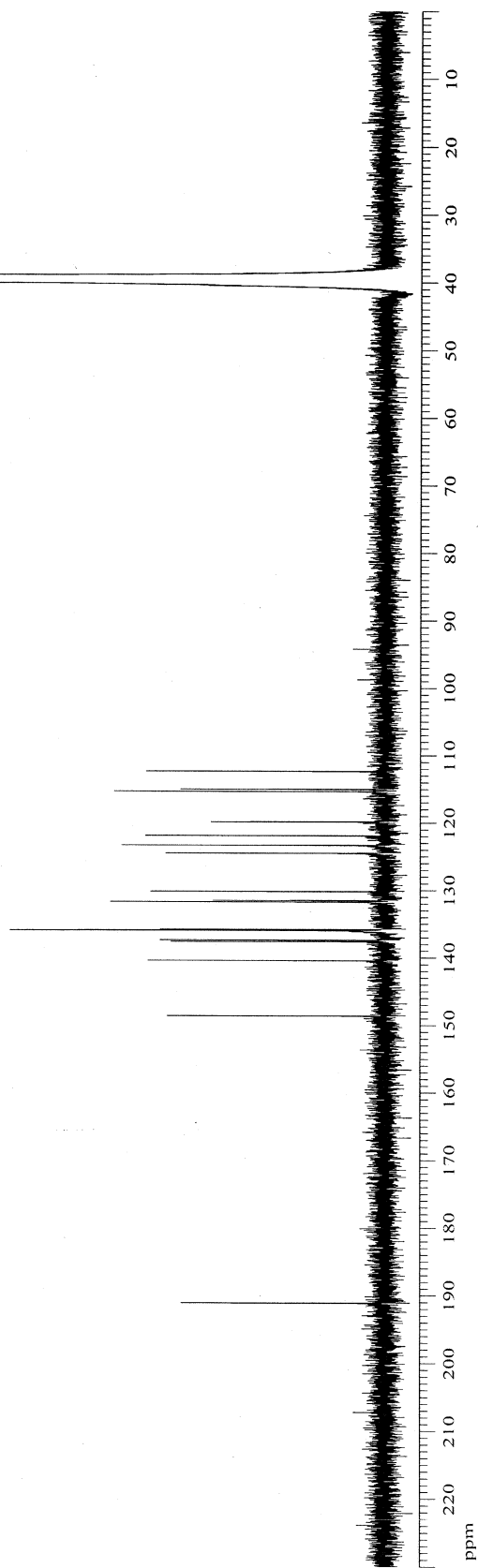
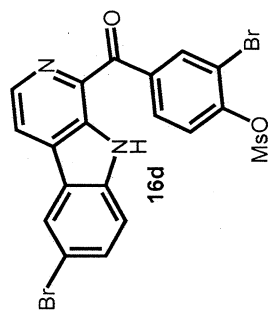


Figure S32. The 125 MHz ^{13}C NMR Spectrum of Compound 16d in $\text{DMSO-}d_6$

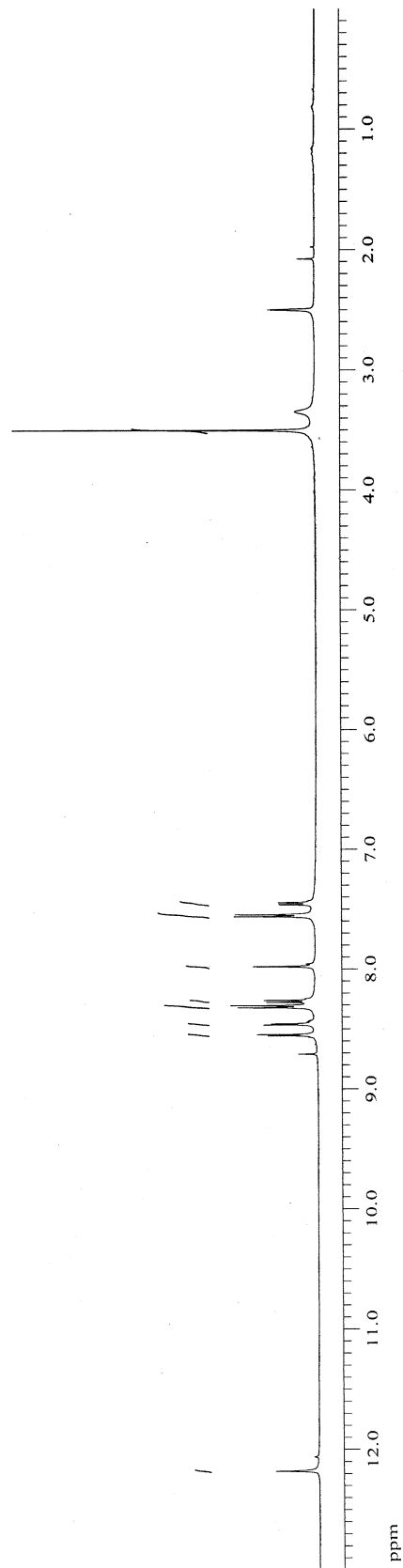
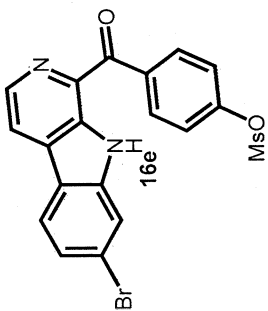


Figure S33. The 500 MHz ^1H NMR Spectrum of Compound **16e** in $\text{DMSO-}d_6$

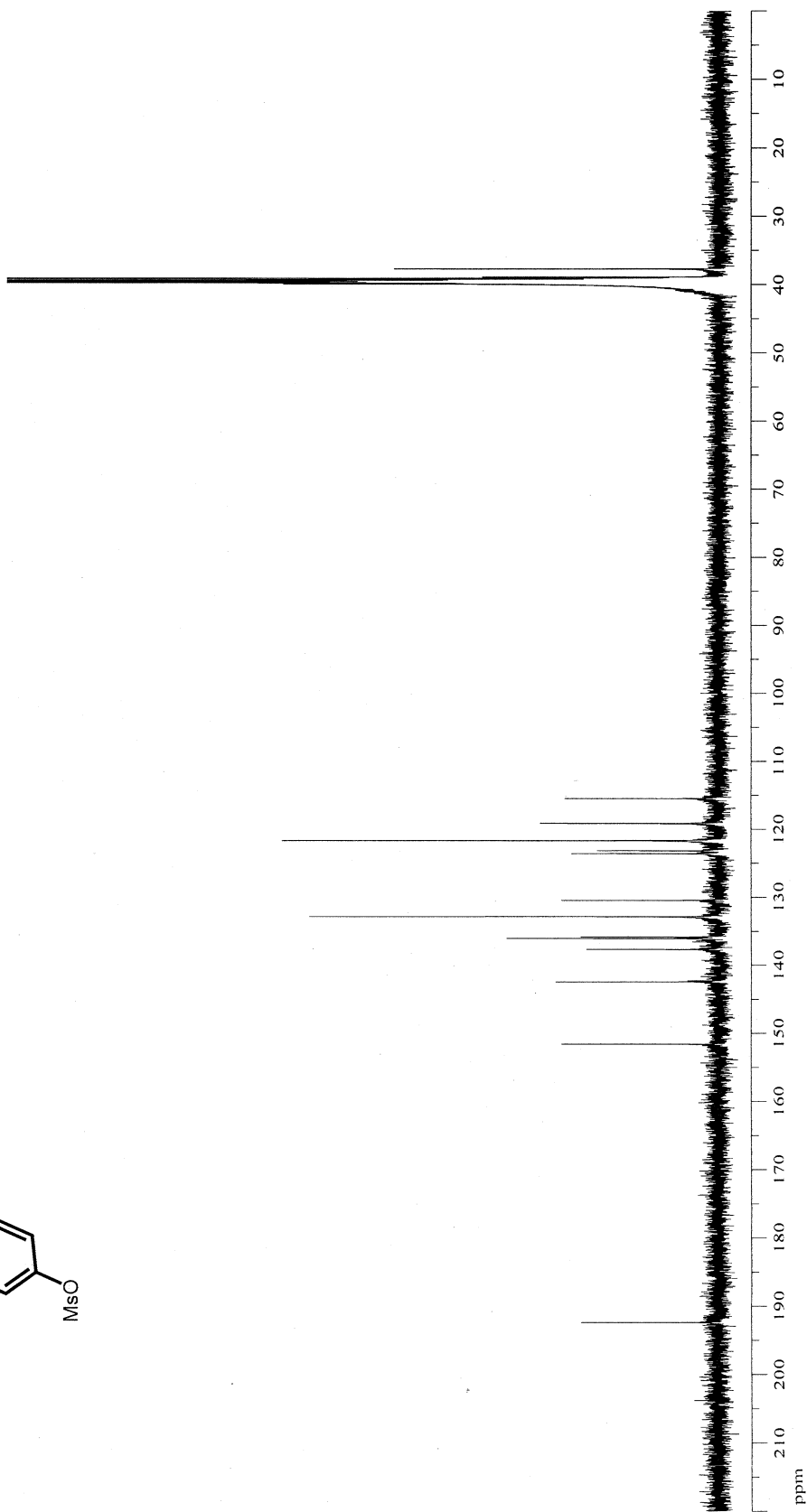
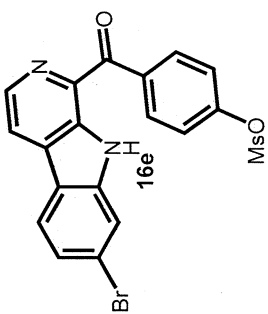


Figure S34. The 125 MHz ^{13}C NMR Spectrum of Compound 16e in $\text{DMSO-}d_6$

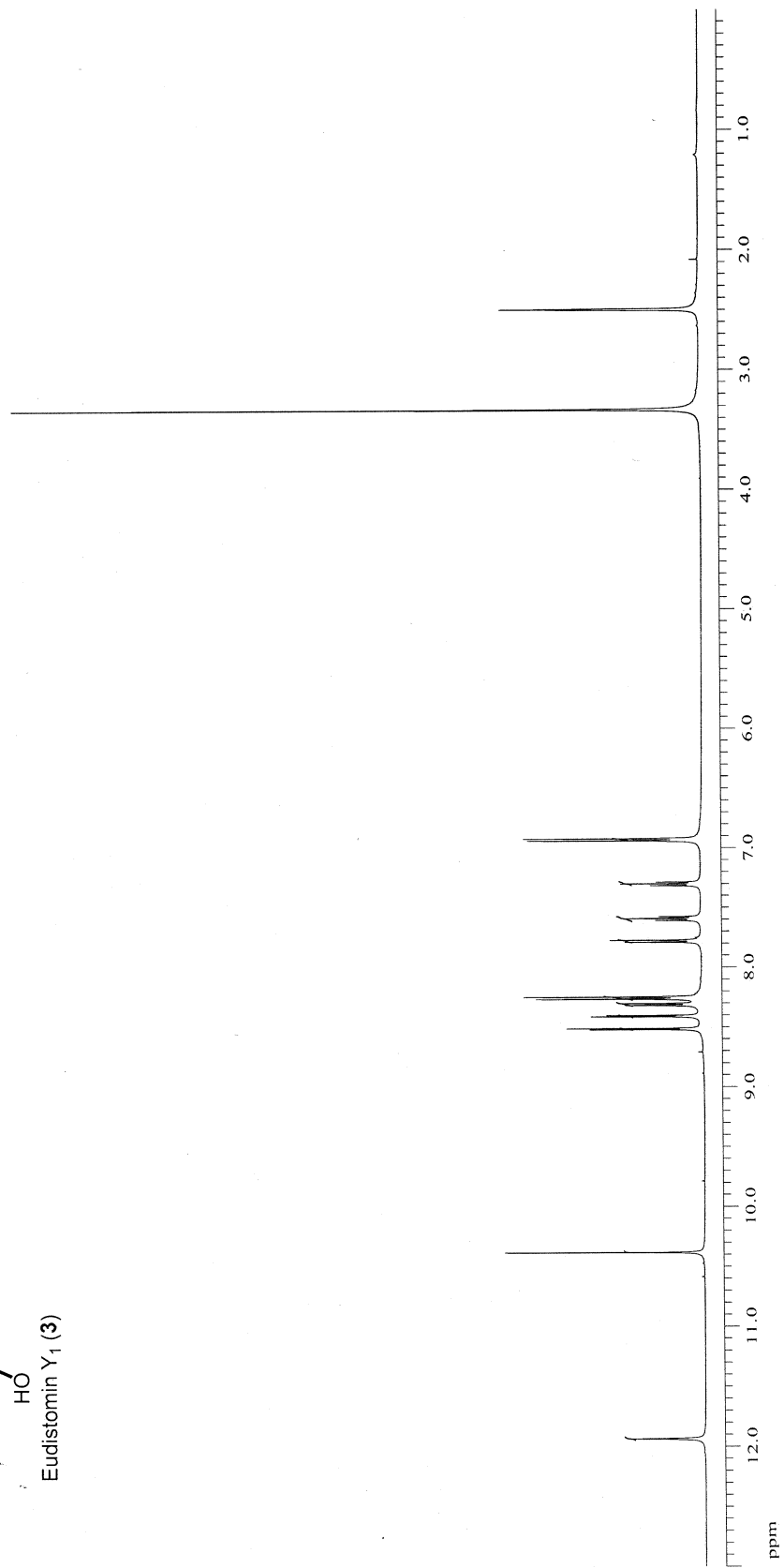
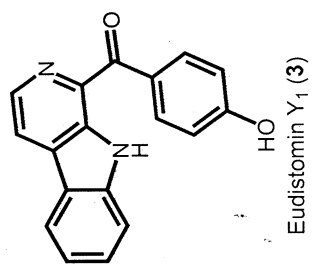


Figure S35. The 500 MHz ¹H NMR Spectrum of Compound Eudistomin Y₁ (3) in DMSO-d₆

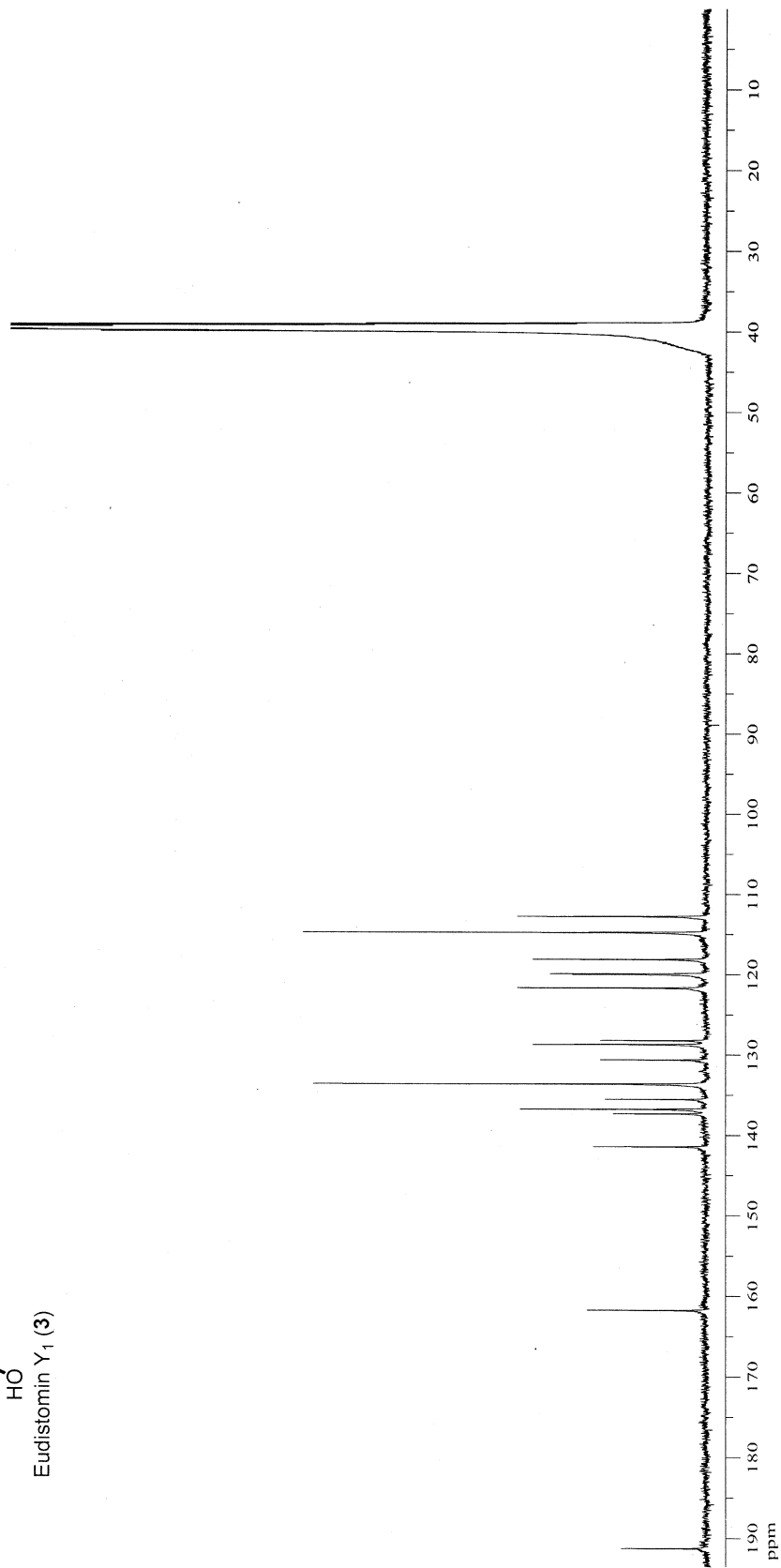
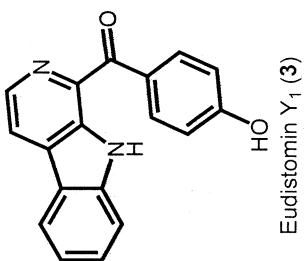


Figure S36. The 125 MHz ¹³C NMR Spectrum of Compound Eudistomin Y₁ (3) in DMSO-*d*₆

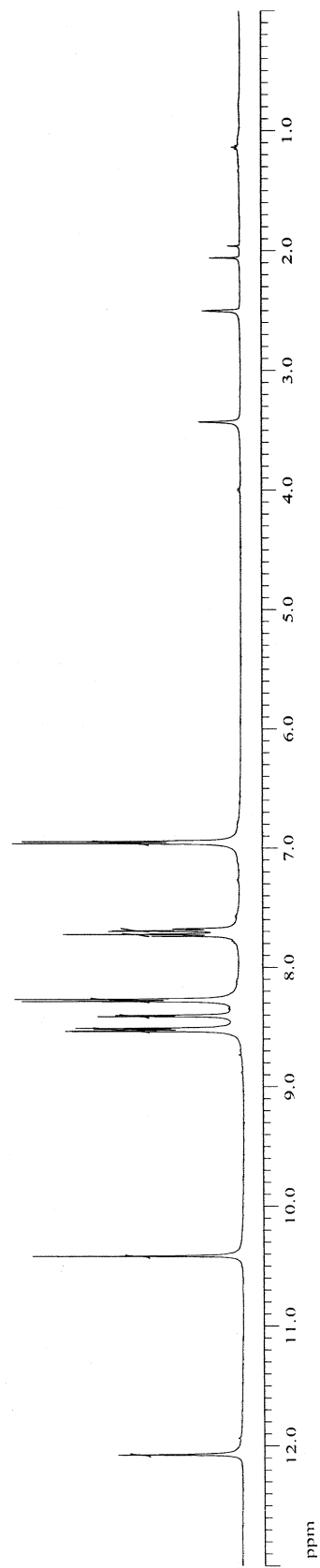
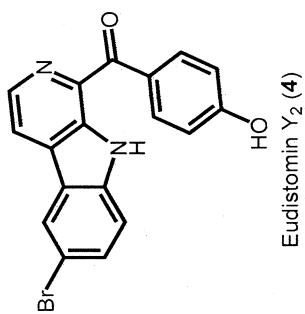


Figure S37. The 500 MHz ¹H NMR Spectrum of Compound Eudistomin Y₂ (4) in DMSO-*d*₆

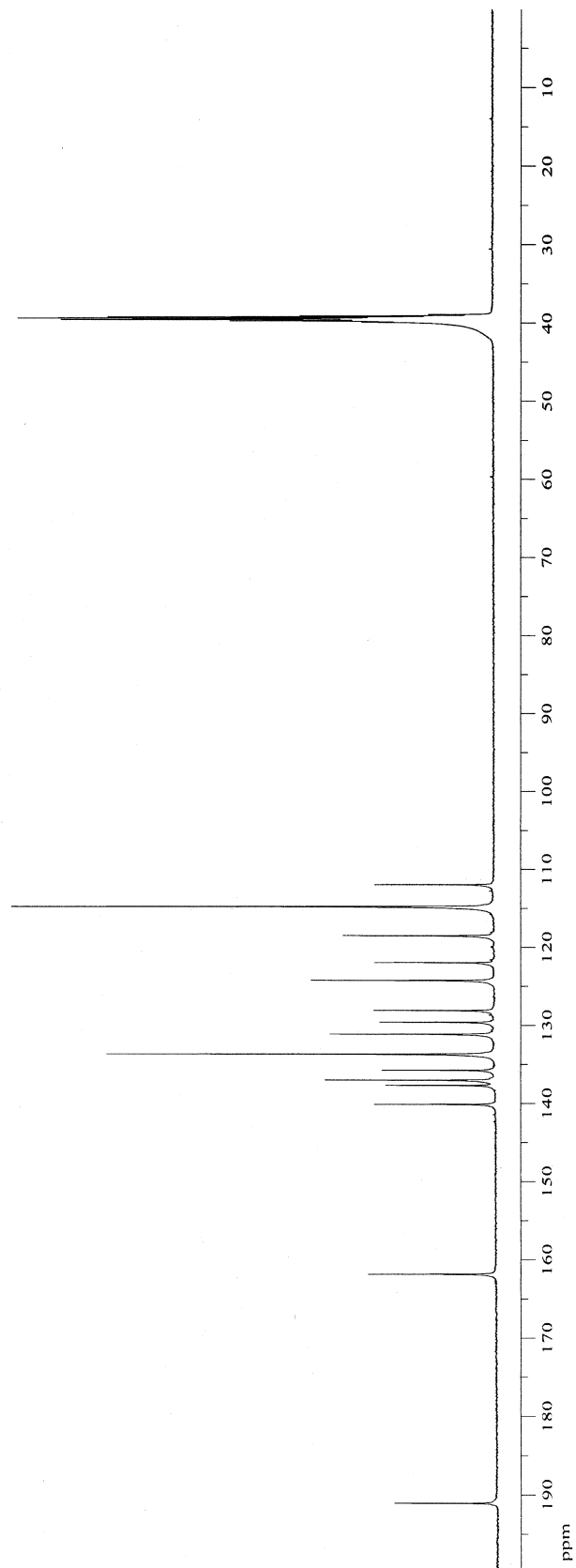
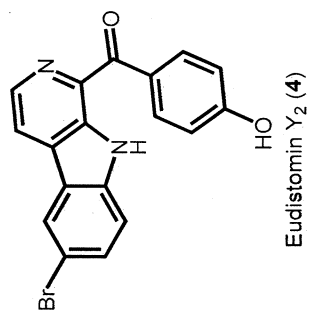


Figure S38. The 125 MHz ¹³C NMR Spectrum of Compound Eudistomin Y₂ (4) in DMSO-d₆

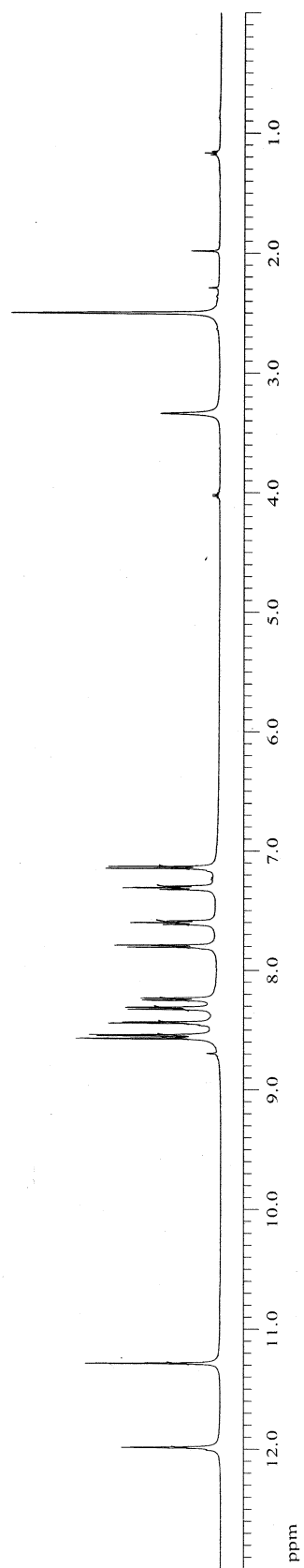
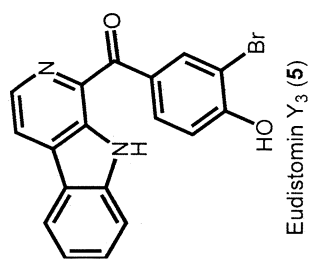


Figure S39. The 500 MHz ¹H NMR Spectrum of Eudistomin Y₃ (5) in DMSO-d₆

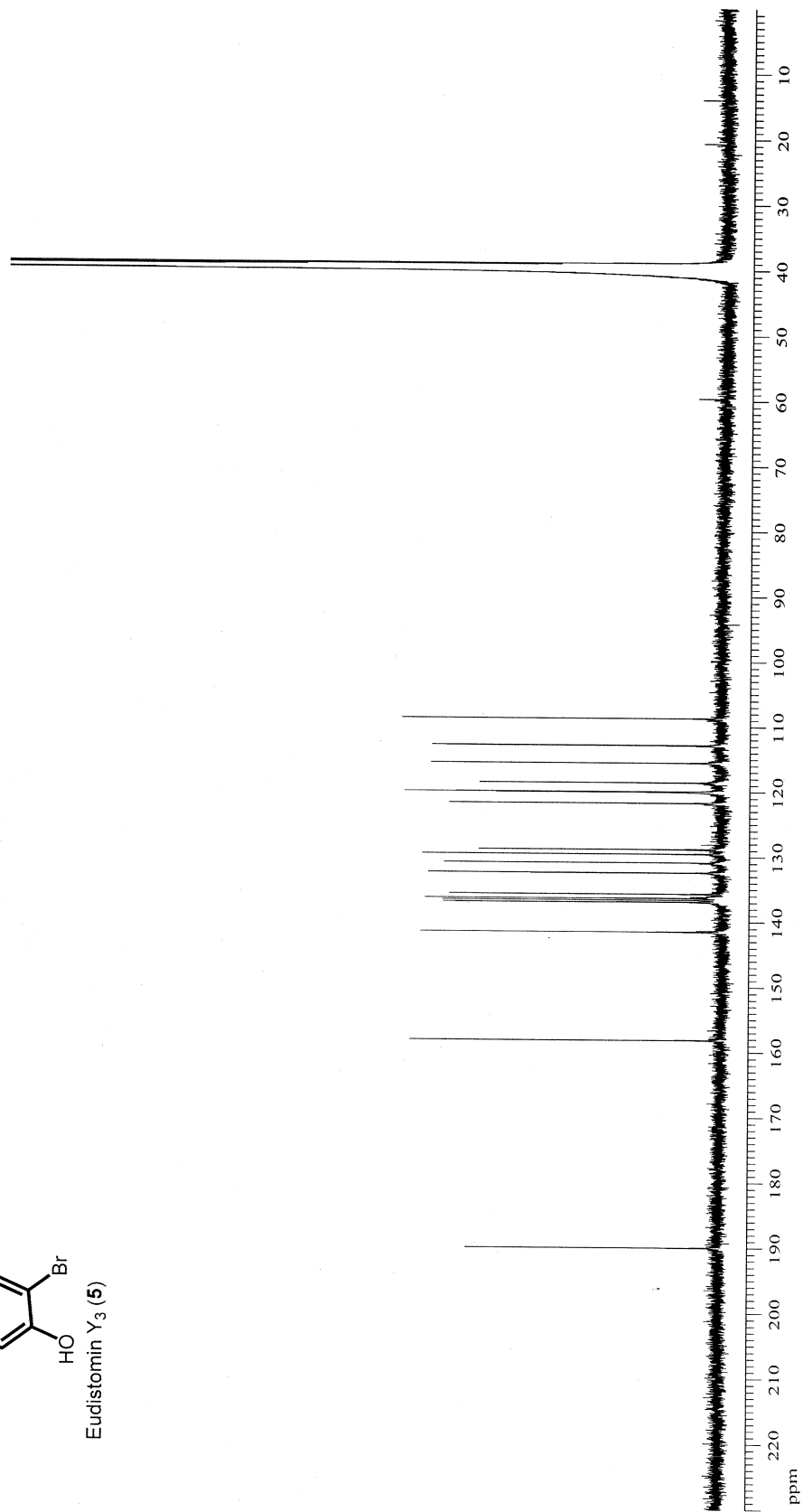
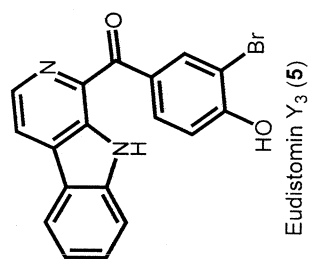


Figure S40. The 125 MHz ¹³C NMR Spectrum of Eudistomin Y₃ (5) in DMSO-*d*₆

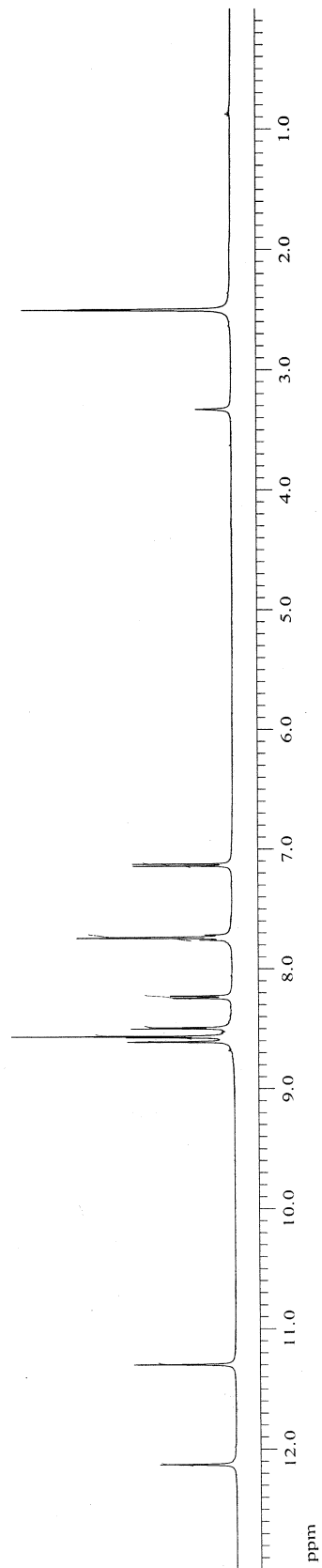
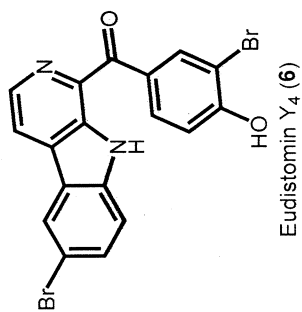


Figure S41. The 500 MHz ¹H NMR Spectrum of Eudistomin Y₄ (**6**) in DMSO-*d*₆

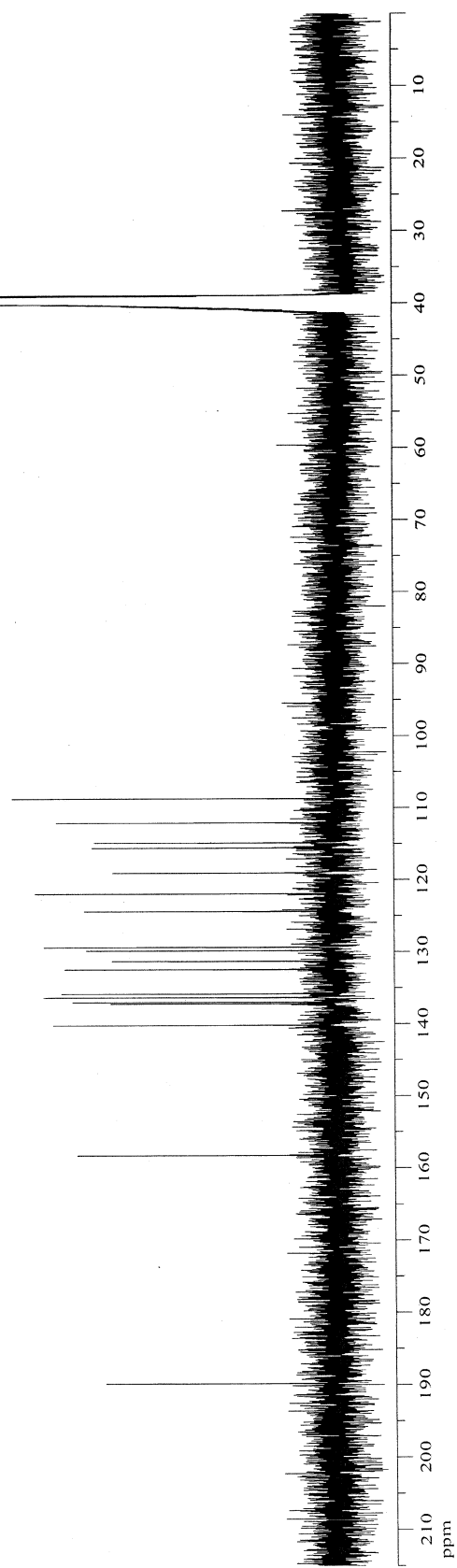
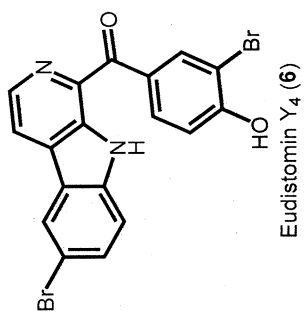


Figure S42. The 125 MHz ¹³C NMR Spectrum of Eudistomin Y₄ (6) in DMSO-d₆

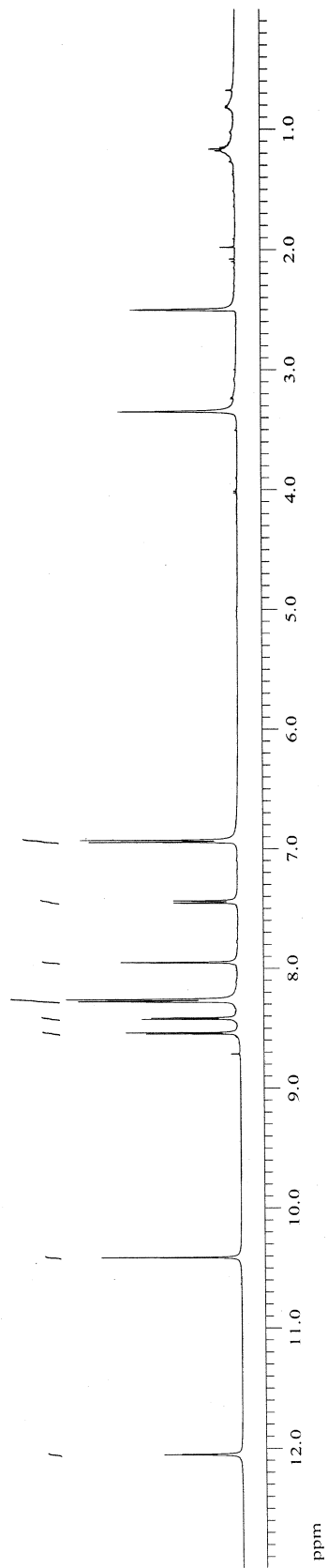
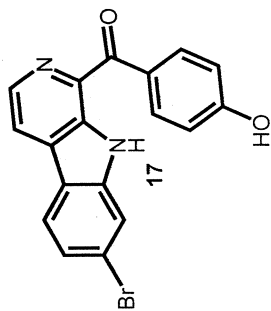


Figure S43. The 500 MHz ¹H NMR Spectrum of Compound 17 in DMSO-d₆

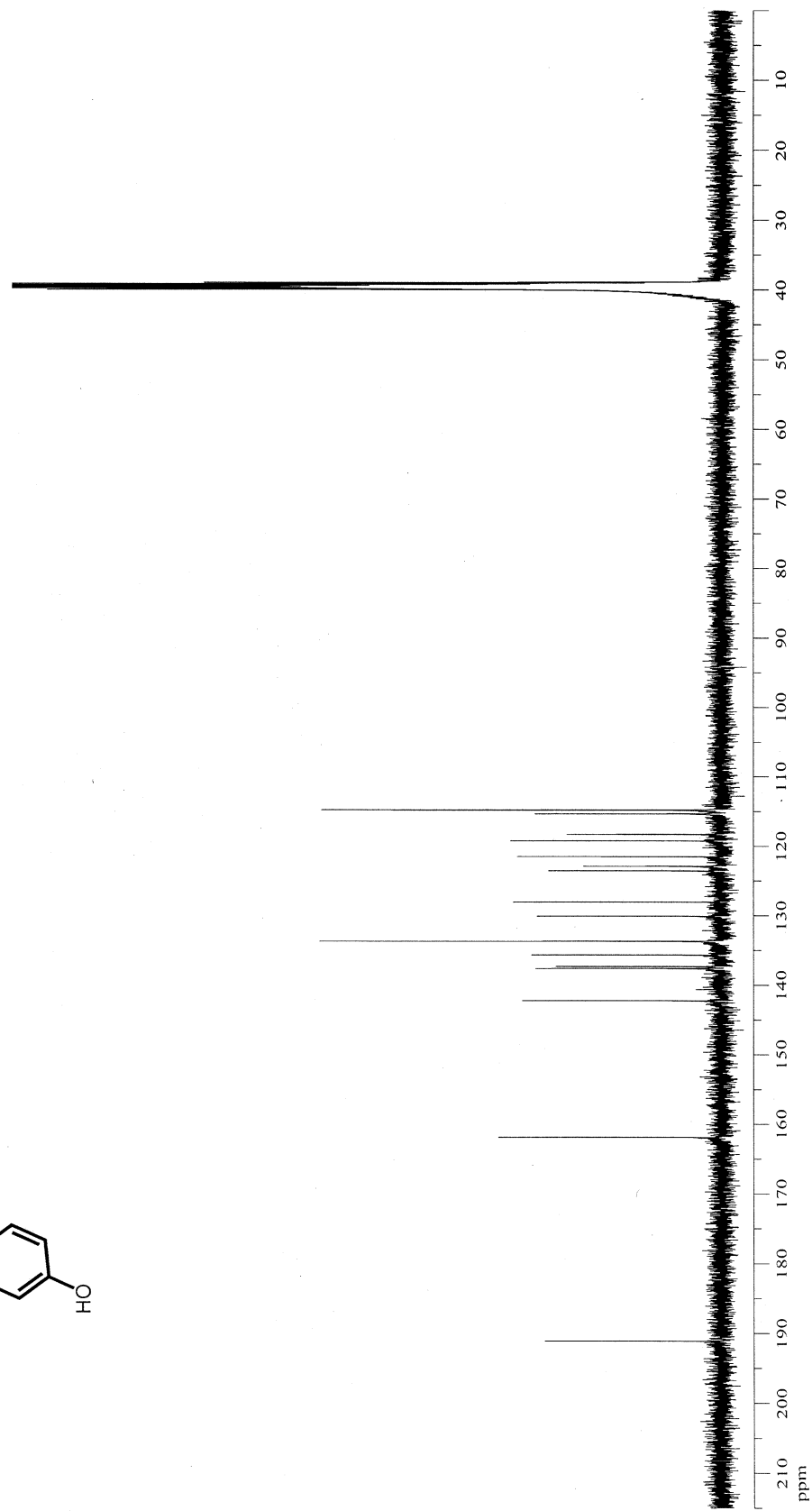
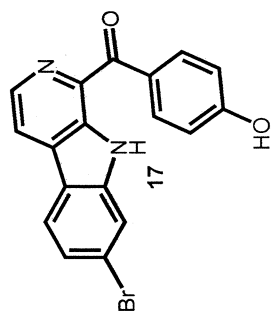


Figure S44. The 125 MHz ^{13}C NMR Spectrum of Compound 17 in $\text{DMSO-}d_6$

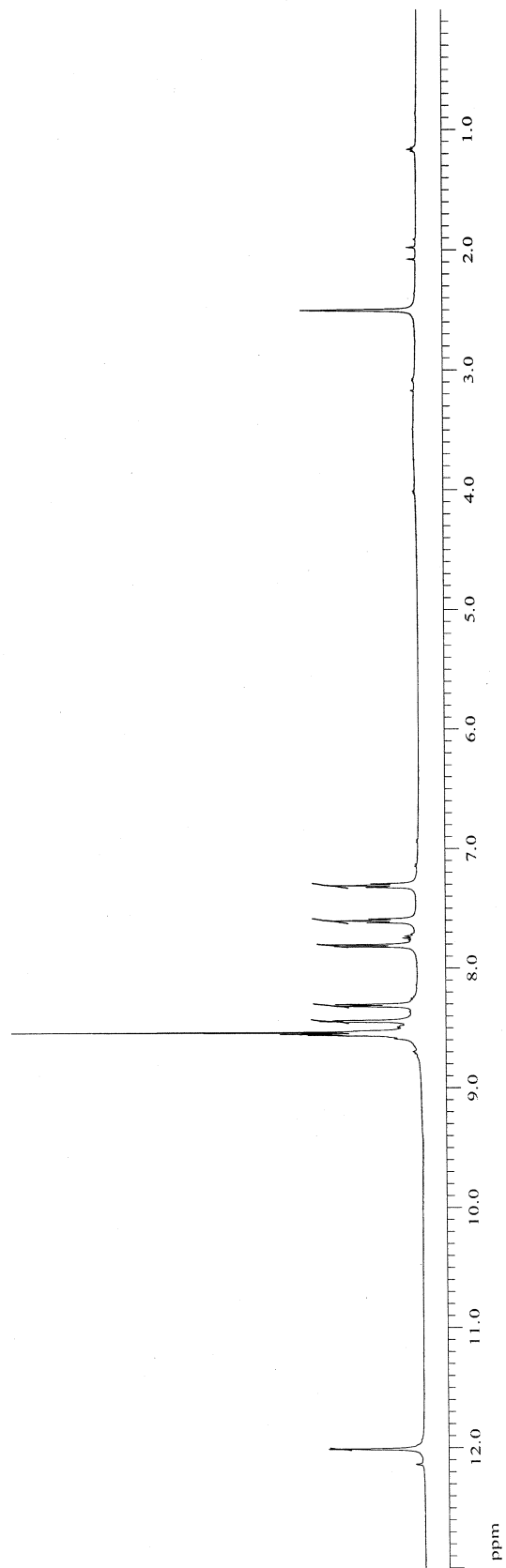
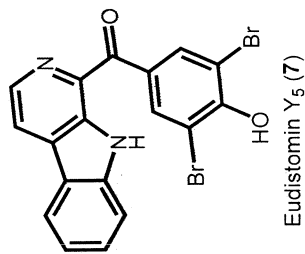


Figure S45. The 500 MHz ¹H NMR Spectrum of Compound Eudistomin Y₅ (7) in DMSO-*d*₆

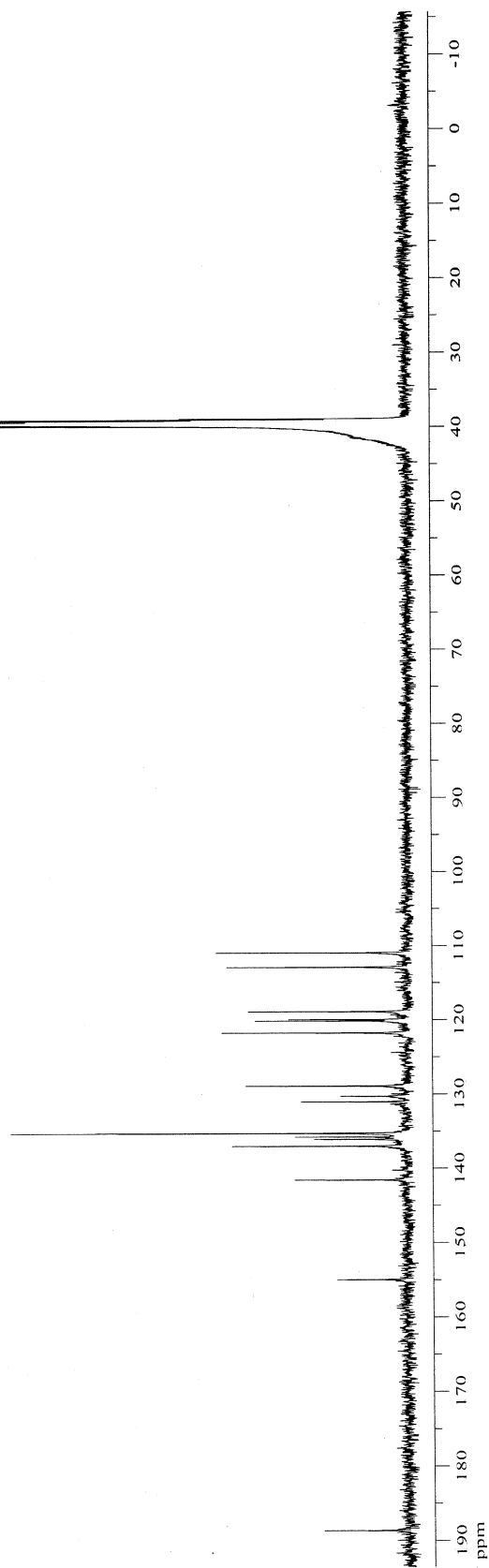
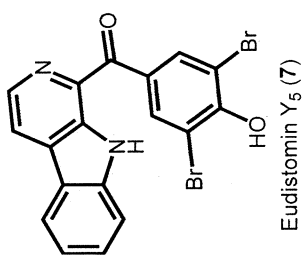


Figure S46. The 125 MHz ¹³C NMR Spectrum of Compound Eudistomin Y₅ (7) in DMSO-*d*₆

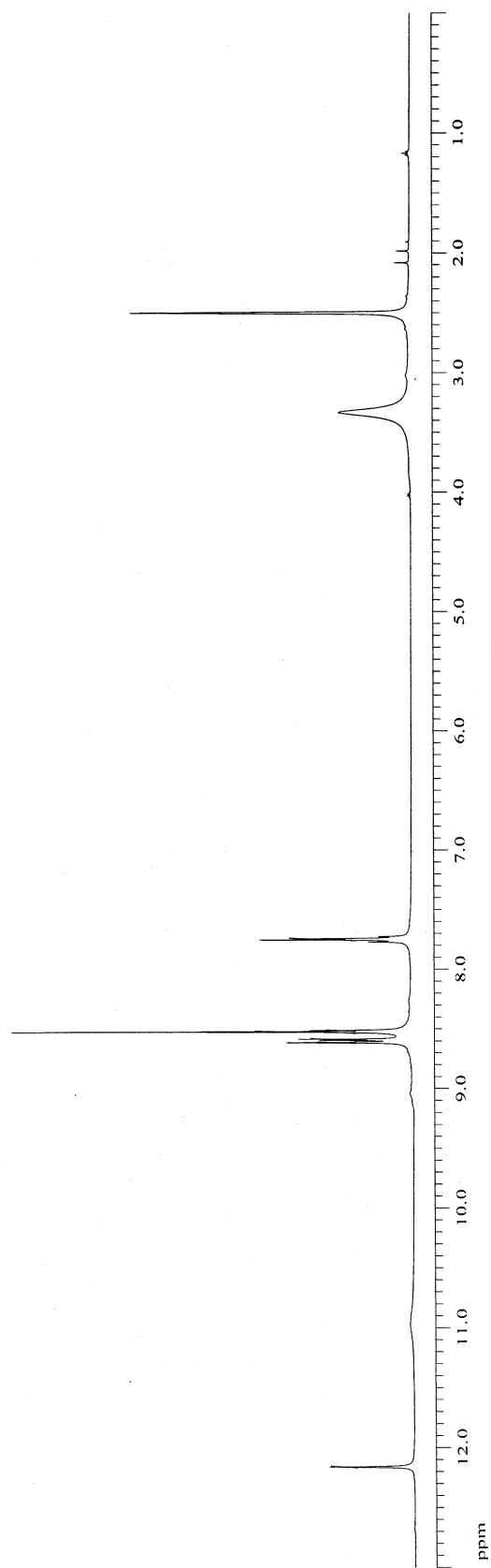
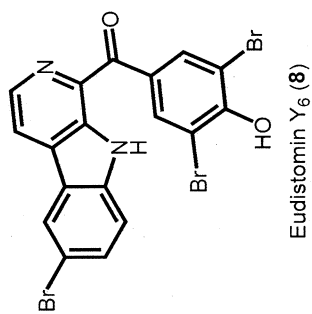


Figure S47. The 500 MHz ¹H NMR Spectrum of Compound Eudistomin Y₆ (8) in DMSO-*d*₆

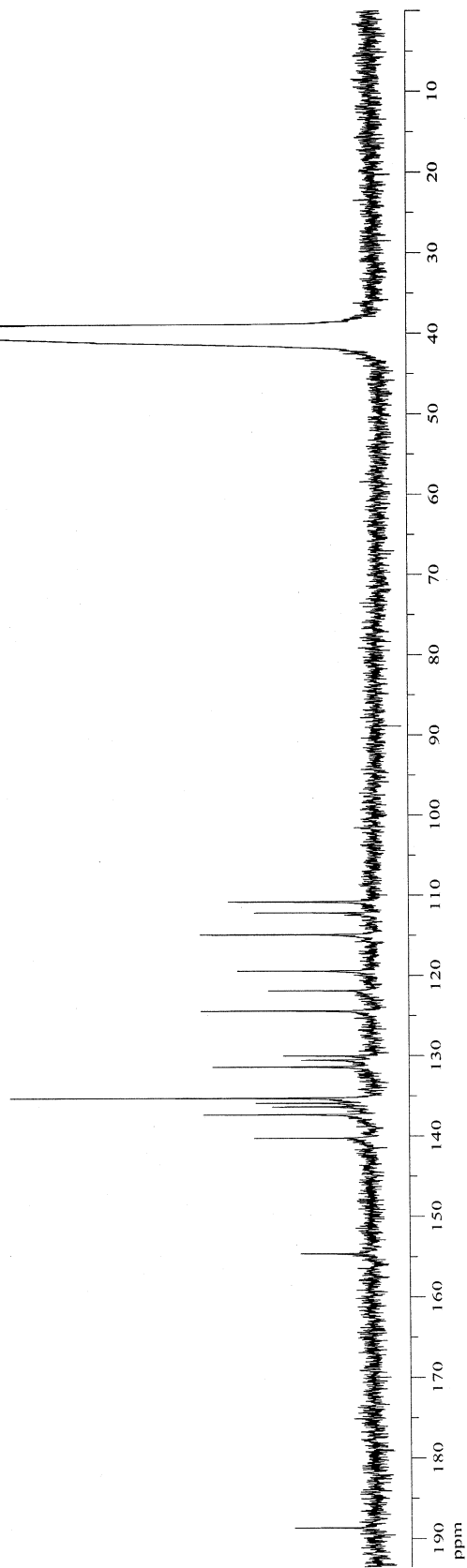
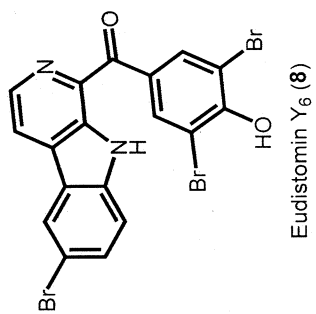


Figure S48. The 125 MHz ¹³C NMR Spectrum of Compound Eudistomin Y₆ (**8**) in DMSO-d₆

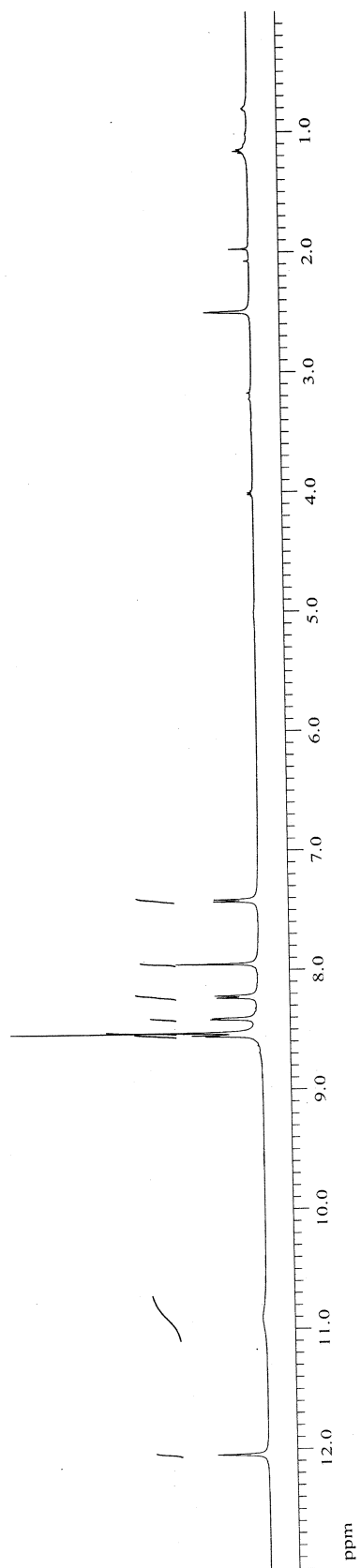
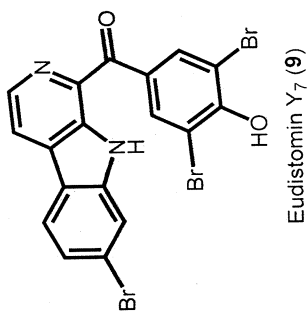


Figure S49. The 500 MHz ¹H NMR Spectrum of Compound Eudistomin Y₇ (9) in DMSO-*d*₆

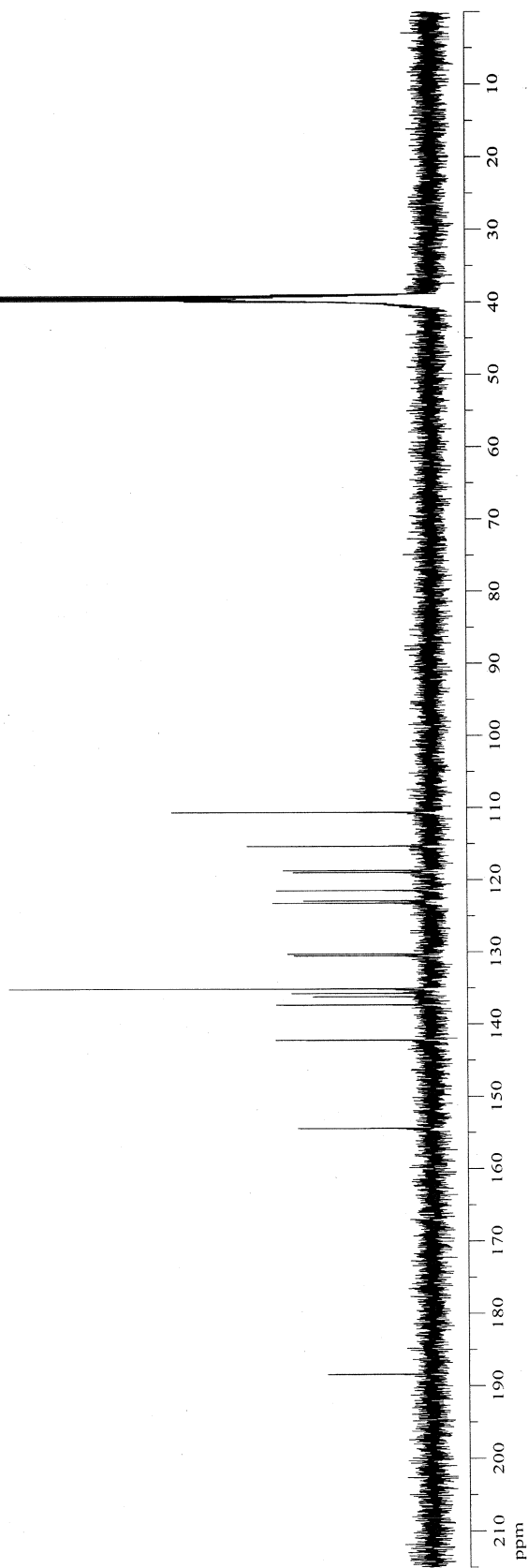
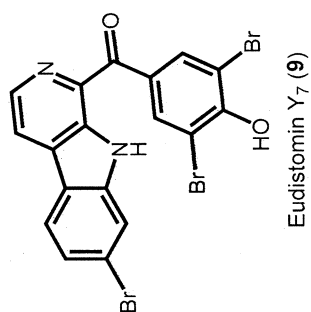


Figure S50. The 125 MHz ¹³C NMR Spectrum of Compound Eudistomin Y₇ (9) in DMSO-*d*₆