Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Enantioselective First Total Syntheses of Antiviral Natural Products Xiamycins D and E

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1. General Information

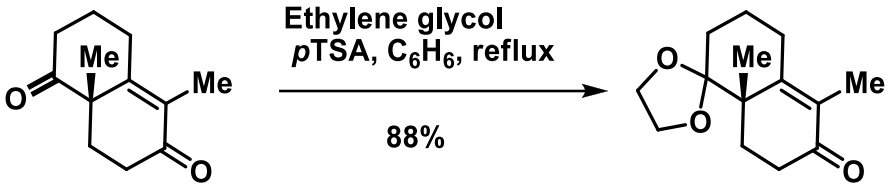
All reactions were carried out under nitrogen and argon atmosphere with dry solvents under anhydrous conditions, unless otherwise mentioned. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF and diethyl ether were distilled from sodium-benzophenone and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically pure material, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as a visualizing agent and an p-anisaldehyde or ninhydrine stain, and heat as developing agents. Merck silica gel (particle size 100-200 and 230-400 mesh) was used for flash column chromatography.

Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. NMR spectra were recorded on Bruker Avance 500 (^{1}H: 400 & 500MHz, ^{13}C: 100 & 125MHz) in $CDCl_3$ & CD_3OD having TMS 0.03% as internal standard. Mass spectrometric data were obtained using WATERS-Q-T and Agilent of Premier-ESI-MS. Optical rotation were measured using a polarimeter (AUTOPOL II) at 20 °C.

The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of a doublet of a doublet.

2. Experimental Procedures:

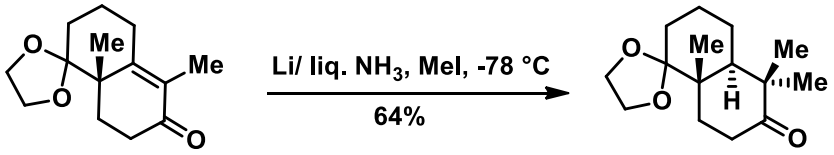
Synthesis of compound 6a:



Wieland Miescher derivative ketone 6 **6a**

Ethylene glycol (6.6 mL, 110 mmol) was refluxed in benzene (30 mL) for 2 hours using Dean-Stark trap. Upon cooling, a solution of Wieland-Miescher ketone derivative **6** (4.2 g, 21.84 mmol) in benzene and *p*-toluene sulfonic acid (376 mg, 2.18 mmol) were added to the solution. Then the resulting reaction mixture was refluxed under condenser for 2 hours. After 2 hours, reaction mixture was cooled to room temperature and quenched with saturated solution of $NaHCO_3$ (20 mL). The resulting mixture was extracted with ethyl acetate and washed with water and brine solution, dried over Na_2SO_4 and concentrated. The obtained crude was purified by column chromatography (15 – 20%) EtOAc in hexanes to obtain pure ketal compound **6** (4.56 g, 88 % yield) as a white solid. *Rf* = 0.5 (35% EtOAc-hexane); Spectral data (^1H, ^{13}C, IR, HRMS) were consistent with those previously reported.[1]

Synthesis of compound 6b:

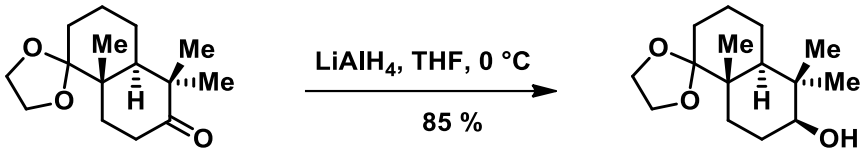


6a **6b**

A solution of enone **6a** (2 g, 8.46 mmol) in THF (15 mL), was added portion wise to a stirring solution of Li metal (253 mg, 36.5 mmol) in NH_3 (140 mL), the mixture (radical anion) was stirred for 25 min at -78 °C. A solution of MeI (5.77 mL, 84.69 mmol) in THF (10 mL) was added drop wise by syringe to the reaction mixture and continued for 40 min. After 40 min, the reaction mixture was quenched with solid NH_4Cl (2 g) and cooled to room temperature for evaporation of ammonia. Then, water (20 mL) was added and extracted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. The crude product was purified by column chromatography (10 – 15%) EtOAc in hexanes to obtain of the pure dimethylated ketal compound **6b** (1.380 g, 64 % yield) as a yellow

solid. *Rf* = 0.5 (30% EtOAc-hexane); Spectral data (^{1}H, ^{13}C, IR, HRMS) were consistent with those previously reported.[1]

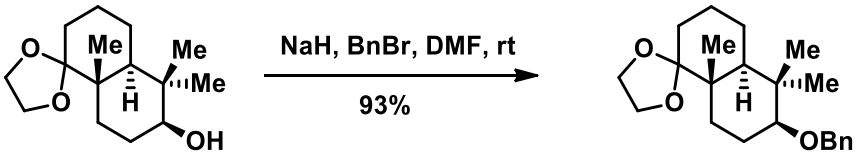
Synthesis of compound 6c:



6b **6c**

To solution of **6b** (3 g, 11.88 mmol) in THF (30 mL) at 0 °C was added $LiAlH_4$ (516 mg 13.06 mmol) and allowed to stirred at room temperature for 2 hours. After completion of reaction, the reaction was quenched with ice water at 0 °C and diluted with ethyl acetate. The organic layer was washed with 1N HCl solution and extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (20 – 25%) EtOAc in hexanes to obtain of the pure hydroxyl ketal compound **6c** (2.64 g, 85 % yield) as white solid. *Rf* = 0.5 (40% EtOAc-hexane); Spectral data (^{1}H, ^{13}C, IR, HRMS) were consistent with those previously reported.[1]

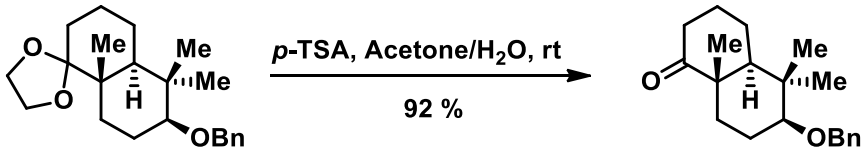
Synthesis of compound 6d:



6c **6d**

To a magnetically stirred solution of alcohol **6c** (3.7 g, 14.5 mmol) in DMF (30 mL) at 0 °C were added benzyl bromide (5.3 mL, 21.8 mmol) and sodium hydride (944 mg, 24.65 mmol, 60% in oil hexane) sequentially. The reaction mixture was stirred at room temperature for 12 hours. After completion of the reaction, the reaction mixture was quenched with 1N HCl solution and ice water was added to the solution. The organic layer was extracted with ethyl acetate, dried over Na_2SO_4 and concentrated and crude was purified by silica gel column chromatography using (5 – 7%) EtOAc in hexanes as an eluent. The desired compound benzylic ether **6d** as a colourless oil (4.7 g, 93% yield), *Rf* = 0.5 (10% EtOAc-hexane); Spectral data (^{1}H, ^{13}C, IR, HRMS) were consistent with those previously reported.[1]

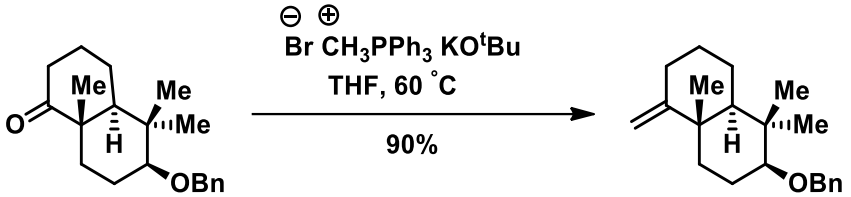
Synthesis of compound 7:



6d **7**

To a solution of **6d** (3 g, 8.7 mmol) in acetone/H_2O (1:1) was added a *p*-TSA (1.64 g, 9.57 mmol) at room temperature. The reaction mixture was continued with stirring for 6 hours. Then solvent (acetone) was removed by rota-vapour followed by quenched with saturated solution of $NaHCO_3$, extracted with ethyl acetate and organic layer was separated. The organic layer was dried over anhydrous Na_2SO_4, concentrated and the crude was purified by silica gel column chromatography using (7 – 10%) EtOAc in hexanes as an eluent. The desired compound benzylic ether **7**[1] was obtained as white solid (2.42 g, 92% yield). *Rf* = 0.5 (15 % EtOAc-hexane); $[\alpha]_D^{20}$ = + 17 (*c* 0.416, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3088, 3063, 3029, 2940, 2867, 1705, 1605, 1454, 1358, 1255, 1103, 1071, 735, 697; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 4 H), 7.25 – 7.20 (m, 1 H), 4.64 (d, *J* = 11.8 Hz, 1 H), 4.39 (d, *J* = 11.8 Hz, 1 H), 2.87 (dd, *J* = 11.1, 4.1 Hz, 1 H), 2.53 (td, *J* = 14.0, 6.9 Hz, 1 H), 2.16 (dd, *J* = 13.7, 4.4 Hz, 1 H), 2.04 (ddt, *J* = 13.0, 6.5, 3.0 Hz, 1 H), 1.91 (dt, *J* = 12.1, 3.9 Hz, 1 H), 1.74 – 1.63 (m, 3 H), 1.57 – 1.44 (m, 3 H), 1.13 (s, 3 H), 1.11 – 1.08 (m, 1 H), 0.98 (s, 3 H), 0.92 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ) δ 215.3, 139.0, 128.1, 127.3, 127.2, 85.4, 71.3, 52.9, 48.5, 39.7, 37.4, 31.0, 28.0, 26.1, 22.3, 20.5, 18.5, 16.7; **HRMS**: m/z calcd. for $C_{20}H_{28}NaO_2$ $[M+Na]^+$: 323.1987; found: 323.1984.

Synthesis of compound 8:

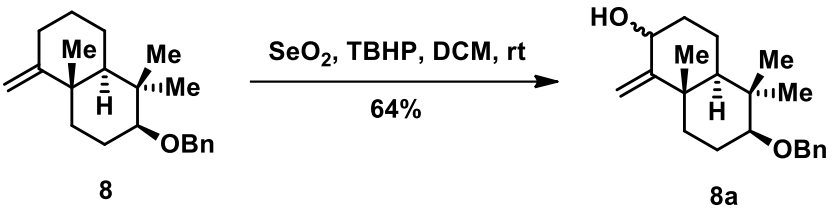


7 **8**

To a suspension of methyltriphenylphosphonium bromide (12.1 g, 29 mmol) in dry THF (40 mL) at 0 °C under argon atmosphere was added potassium tert-butoxide (3.25 g, 29 mmol) and the mixture stirred for 30 min. After 30 min, ketone **7** (3 g, 10 mmol) in THF (10 mL) was added dropwise to the reaction mixture and stirring was continued at 60 °C for 2 hours. Then the reaction mixture was cooled to room temperature, quenched with water and diluted with ethyl acetate. The organic layer was separated and the aqueous layer was extracted two more times with EtOAc (2 x 50 mL). Combined extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (3 – 5%) EtOAc in hexanes to obtain olefin compound 8[2a] as a

colorless oil (2.7 g, 90% yield). *Rf* = 0.5 (5% EtOAc-hexane). $[\alpha]_D^{20}$ = −18.0 (*c* 0.10, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3086, 3064, 3030, 2936, 1718, 1634, 1496, 1453, 1100, 1070, 891, 733, 696; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 4 H), 7.26 (m, 1 H), 4.69 (d, *J* = 11.8 Hz, 1 H), 4.50 (d, *J* = 1.8 Hz, 2 H), 4.44 (d, *J* = 11.9 Hz, 1 H), 2.93 (dd, *J* = 11.2, 4.2 Hz, 1 H), 2.33 – 2.27 (m, 1 H), 2.10 (dd, *J* = 13.6, 4.5 Hz, 1 H), 1.96 – 1.87 (m, 2 H), 1.69 – 1.61 (m, 3 H), 1.49 (dd, *J* = 14.6, 10.9 Hz, 2 H), 1.25 (dd, *J* = 13.5, 4.3 Hz, 2 H), 1.07 (s, 3 H), 0.97 (s, 3 H), 0.89 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 160.0, 139.6, 128.3, 127.6, 127.3, 102.7, 86.6, 71.5, 53.7, 39.9, 39.6, 35.4, 33.1, 28.7, 28.4, 23.3, 21.9, 20.4, 16.5; **HRMS**: m/z calcd. for $C_{21}H_{30}NaO$ $[M+Na]^+$: 321.2194; found: 321.2197.

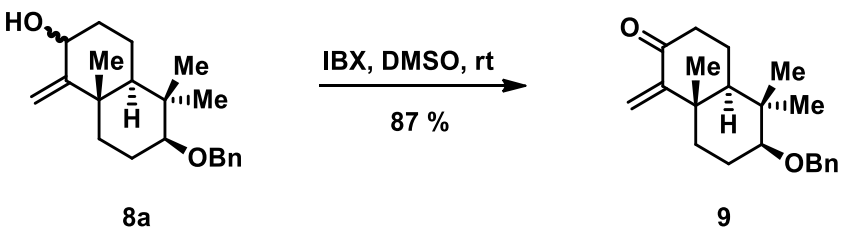
Synthesis of compound 8a:



8 **8a**

A mixture of olefin **8** (1.5 g, 5.03 mmol), SeO_2 (280 mg, 2.515 mmol), TBHP (5 M in decane, 1.8 mL, 10.06 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 12 hours. The solution was quenched with saturated solution of $Na_2S_2O_3$ (10 mL) and extracted with CH_2Cl_2. The organic layer was separated, dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography (10 – 13%) EtOAc in hexanes to give alcohol **8a**[2b] (1.012 g, 64% yield) as a colorless oil: *Rf* = 0.5 (20% EtOAc-hexane). $[\alpha]_D^{20}$ = −31.0 (*c* 1.28, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3417, 2944, 2871, 1716, 1633, 1454, 1326, 1209, 1100, 1043, 950, 734, 697; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 4 H), 7.28 – 7.23 (m, 1 H), 4.81 (dd, *J* = 25.9, 1.3 Hz, 2 H), 4.68 (d, *J* = 11.9 Hz, 1 H), 4.44 (d, *J* = 11.9 Hz, 1 H), 4.31 (t, *J* = 3.0 Hz, 1 H), 2.92 (dd, *J* = 11.6, 4.3 Hz, 1 H), 2.04 – 1.99 (m, 1 H), 1.93 (dd, *J* = 13.1, 4.0 Hz, 1 H), 1.84 – 1.75 (m, 2 H), 1.70 – 1.60 (m, 2 H), 1.57 – 1.42 (m, 3 H), 1.25 (s, 3 H), 1.00 (s, 3 H), 0.93 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.2, 139.4, 128.3, 127.5, 127.3, 109.5, 86.3, 74.6, 71.5, 53.6, 39.5, 36.1, 34.9, 28.5, 25.9, 22.9, 22.3, 16.9, 16.6; **HRMS**: m/z calcd. for $C_{21}H_{34}NO_2$ $[M+NH_4]^+$: 332.2590; found: 332.2586.

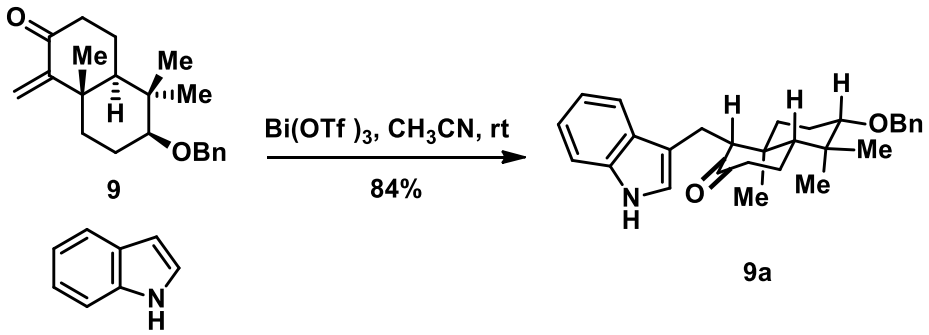
Synthesis of compound 9



8a **9**

The compound **8a** allylic alcohol (1.0 g, 3.18 mmol) was dissolved in DMSO (10 mL) and IBX (890 mg, 3.18 mmol) was added. After stirring for 20 min at room temperature, the reaction mixture was quenched with saturated solution of $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 10 mL). Combined extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (7 – 10%) EtOAc in hexanes to give enone **9**[2b] (870 mg, 87% yield) as a pale yellow oil: *Rf* = 0.5 (15% EtOAc-hexane); $[\alpha]_D^{20}$ **=** −10.12 (*c* 0.58, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3063, 2939, 2871, 1717, 1694, 1584, 1454, 1386, 1273, 1110, 1069, 931, 878, 697, 458; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 4 H), 7.29 – 7.20 (m, 1 H), 5.55 (s, 1 H), 5.00 (s, 1 H), 4.69 (d, *J* = 11.8 Hz, 1 H), 4.44 (d, *J* = 11.8 Hz, 1 H), 3.00 (dd, *J* = 11.2, 3.9 Hz, 1 H), 2.65 (ddd, *J* = 17.0, 5.4, 1.8 Hz, 1 H), 2.29 (ddd, *J* = 17.0, 12.5, 7.7 Hz, 1 H), 2.00 – 1.90 (m, 2 H), 1.82 (dd, *J* = 12.5, 5.7 Hz, 2 H), 1.55 (dtd, *J* = 27.2, 13.7, 12.7, 2.9 Hz, 2 H), 1.39 (dd, *J* = 12.5, 3.0 Hz, 1 H), 1.06 (s, 3 H), 1.03 (s, 3 H), 0.93 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 203.7, 158.4, 139.2, 128.3, 127.5, 127.4, 114.1, 85.9, 71.5, 50.2, 40.6, 40.4, 39.5, 35.2, 28.4, 22.9, 21.5, 20.2, 16.5; **HRMS**[ESI]: m/z calcd. for $C_{21}H_{29}O_2$ $[M+H]^+$: 313.2168; found: 313.2161.

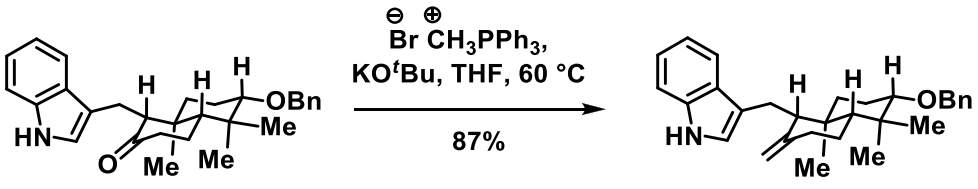
Synthesis of compound 9a:



To a solution of indole moiety (750 mg, 6.41 mmol), and the enone **9** (2 g, 6.41 mmol) in dry CH_3CN (20 mL) was added bismuth triflate (24 mg, 0.19 mmol, 3 mol%) and the reaction mixture was stirred at room temperature for 5 hours. Then the reaction mixture was diluted with saturated solution of $NaHCO_3$ (5 mL) and extracted with EtOAc (3 x 25 mL). Combined extracts were dried over Na_2SO_4 and concentrated in vacuo. Purification of crude compound by silica gel column chromatography (15 – 20%) EtOAc in hexanes afforded Michael adduct **9a**[3] (2.3 g, 84% yield) as a brownish foam: *Rf* = 0.5 (30% EtOAc/hexane); $[\alpha]_D^{20}$ **=** +66 (*c* 0.1, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3414, 3058, 2934, 2853, 1706, 1618, 1455, 1356, 1256, 1113, 1097, 927, 740, 697,424; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (s, 1 H), 7.62 (d, *J* = 7.8 Hz, 1 H), 7.43 – 7.38 (m, 3 H), 7.35 – 7.28 (m, 2 H), 7.18 (dt, *J* = 14.6, 6.5 Hz, 2 H), 7.00 (d, *J* = 1.8 Hz, 1 H), 4.76 (d, *J* = 11.9 Hz, 1 H), 4.52 (d, *J* = 11.8 Hz, 1 H), 3.25 (dd, *J* = 14.1, 9.9 Hz, 1 H), 3.11 (dd, *J* = 11.2, 3.9 Hz, 1 H), 2.72 (d, *J* = 13.9 Hz, 1 H), 2.47 (d, *J* = 9.5 Hz, 1 H), 2.43 – 2.34 (m, 1 H),

2.27 – 2.13 (m, 2 H), 2.05 (dd, *J* = 7.7, 4.0 Hz, 2 H), 1.77 – 1.53 (m, 4 H), 1.11 (s, 3 H), 0.94 (d, *J* = 11.2 Hz, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 211.8, 139.3, 136.1, 128.4, 127.6, 127.5, 127.4, 123.4, 121.7, 119.1, 118.5, 115.5, 111.3, 86.1, 71.6, 65.0, 53.9, 42.9, 42.4, 39.5, 37.2, 28.7, 23.7, 23.2, 17.2, 16.5, 14.7; **HRMS**: m/z calcd. for $C_{29}H_{36}NO_2$ $[M+H]^+$: 430.2746; found: 430.2749.

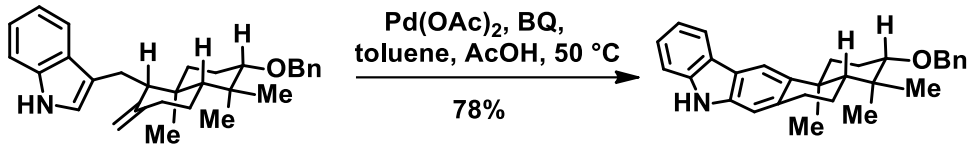
Synthesis of compound 10:



9a **10**

To a suspension of methyltriphenylphosphonium bromide (2.24 g, 5.394 mmol) in THF (20 mL) at 0 °C was added potassium tert-butoxide (604 mg, 5.394 mmol) and reaction mixture was stirred for 30 min. The Michael adduct **9a** (800 mg, 1.86 mmol) in THF (5 mL) was added dropwise to the above solution and the resulting mixture was stirred at 60 °C for 2 hours. Then the reaction mixture was cooled to room temperature, quenched with water and diluted with ethyl acetate. The organic layer was separated and the aqueous layer was extracted two more times with EtOAc (2 x 10 mL). Combined extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (10 – 15%) EtOAc in hexanes to afford indolosespene **10**[2a] (690 mg, 87% yield) as a brownish foam: *Rf* = 0.5 (20% EtOAc-hexane); $[\alpha]_D^{20}$ **= +**15.2 (*c* 1.75, $CHCl_3$); **IR** (neat): *ν*max/cm^{-1} 3419, 2928, 2851, 1719, 1642, 1455, 1361, 1226, 1097, 887, 739, 697, 422; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 (s, 1 H), 7.65 (d, *J* = 7.7 Hz, 1 H), 7.34 (ddt, *J* = 28.4, 14.8, 7.2 Hz, 6 H), 7.16 (dt, *J* = 26.5, 7.1 Hz, 2 H), 6.89 (s, 1 H), 4.86 (s, 1 H), 4.72 (d, *J* = 11.7 Hz, 2 H), 4.48 (d, *J* = 11.9 Hz, 1 H), 3.06 − 2.98 (m, 2 H), 2.84 (dd, *J* = 15.4, 10.7 Hz, 1 H), 2.41 (d, *J* = 12.4 Hz, 1 H), 2.21 (d, *J* = 10.4 Hz, 1 H), 2.11 (d, *J* = 13.1 Hz, 1 H), 2.03 – 1.95 (m, 2 H), 1.77 (d, *J* = 12.9 Hz, 1 H), 1.65 – 1.45 (m, 2 H), 1.36 – 1.19 (m, 2 H), 1.05 (s, 3 H), 0.90 (d, *J* = 7.5 Hz, 6 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.3, 139.6, 136.2, 128.3, 127.9, 127.6, 127.4, 121.9, 119.1, 118.9, 116.3, 111.2, 107.9, 86.58, 71.5, 56.4, 55.3, 39.8, 39.5, 38.2, 37.4, 28.7, 24.0, 23.7, 19.8, 16.7, 14.5; **HRMS**: m/z calcd. for $C_{30}H_{38}NO$ $[M+H]^+$: 428.2953; found: 428.2950.

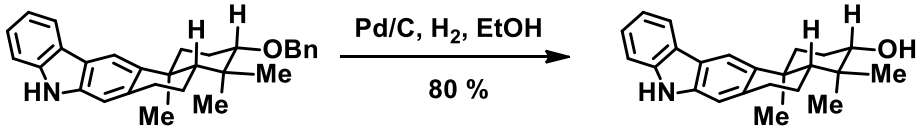
Synthesis of compound 10a:



10 **10a**

To a stirred solution of indolosespene **10** (500 mg, 1.17 mmol) in AcOH/toluene (1:4) were sequentially added p-benzoquinone (252 mg, 2.34 mmol) and $Pd(OAc)_2$ (13 mg, 0.058 mmol, 5 mol%) at room temperature. The resulting mixture was heated to 50 °C and stirred for 3 hours, before it was cooled to room temperature and quenched with saturated aq. $NaHCO_3$. And extraction with EtOAc (3 × 10 mL), the combined extracts were dried over anhydrous Na_2SO_4. The residue was purified by silica gel column chromatography using (15 – 20%) EtOAc in hexanes as an eluent to give pentacyclic indole compound **10a**[4a-b] (389 mg, 78% yield) as a brownish foam: *Rf* = 0.5 (20% EtOAc-hexane); $[\alpha]_D^{20}$ **= +**55 (*c* 0.75, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3412, 3027, 2964, 2867, 1723, 1611, 1465, 1376, 1242, 1100, 1071, 973, 879, 746, 571, 444; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.7 Hz, 1 H), 7.95 (s, 1 H), 7.71 (s, 1 H), 7.45 −7.25 (m, 7 H), 7.21 (s, 1 H), 7.03 (s, 1 H), 4.74 (d, *J* = 11.9 Hz, 1 H), 4.49 (d, *J* = 11.8 Hz, 1 H), 3.19 − 2.98 (m, 3 H), 2.58 (dt, *J* = 12.7, 2.9 Hz, 1 H), 2.08 (dd, *J* = 13.0, 3.7 Hz, 1 H), 1.98 − 1.75 (m, 3 H), 1.64 (t, *J* = 11.9 Hz, 1 H), 1.43 (dd, *J* = 11.9, 2.6 Hz, 1 H), 1.31 (s, 3 H), 1.11 (s, 3 H), 1.02 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.0, 140.1, 139.5, 138.1, 134.0, 128.3, 127.6, 127.4, 125.4, 123.8, 121.9, 120.0, 119.2, 115.7, 110.5, 109.9, 86.4, 71.6, 50.7, 39.3, 37.9, 37.8, 31.5, 28.5, 25.7, 23.8, 19.0, 16.0; **HRMS**: m/z calcd. for $C_{30}H_{34}NO$ $[M+H]^+$: 424.2640; found: 424.2640.

Synthesis of compound 11:

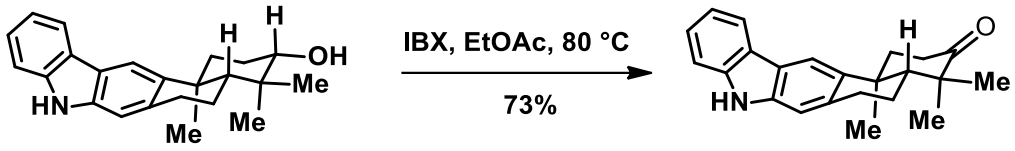


10a **11**

To a solution of **10a** (1.0 g, 2.36 mmol) in dry ethanol (15 mL) was added (10% Pd/C, 100 mg) and the reaction mixture was stirred at room temperature under a hydrogen atmosphere (1 atm) for 12 hours. The Pd/C was removed by filtration through a pad of celite and the filtrate was concentrated in vacuo and purified by column chromatography (15 – 20%) EtOAc in hexanes to provide **11**[4c] (630 mg, 80% yield) as a brownish foam. *Rf* = 0.4 (30% EtOAc/hexane); $[\alpha]_D^{20}$ **= +**20.12 (*c* 1.55, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3410, 2931, 2869, 1713, 1610, 1512, 1465, 1317, 1241, 1004, 935, 828, 735, 613, 424; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.8 Hz, 1 H), 7.94 (s, 1 H), 7.80 (s, 1 H), 7.40 − 7.28 (m, 2

H), 7.19 (dt, *J* = 8.0, 6.5, 1.6 Hz, 1 H), 7.04 (s, 1 H), 3.35 (dd, *J* = 10.9, 5.1 Hz, 1 H), 3.21 – 3.01 (m, 2 H), 2.55 (dt, *J* = 12.8, 3.3 Hz, 1 H), 1.94 – 1.70 (m, 5 H), 1.43 (dd, *J* = 12.0, 2.7 Hz, 1 H), 1.28 (s, 3 H), 1.10 (s, 3 H), 0.95 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.9, 140.1, 138.2, 133.9, 125.4, 123.8, 122.0, 120.0, 119.2, 115.8, 110.5, 109.9, 79.0, 50., 39.2, 38.0, 37.9, 31.5, 28.4, 28.3, 25.7, 19.2; **HRMS**: m/z calcd. for $C_{23}H_{27}NNaO$ $[M+Na]^+$: 356.1990; found: 356.1988.

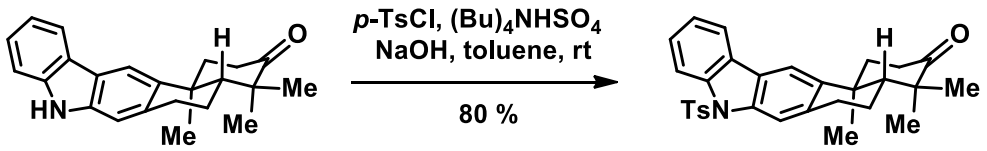
Synthesis of compound 11a:



11 **11a**

The compound **11** (1.3 g, 3.9 mmol) was dissolved in EtOAc (20 mL) and IBX (1.6 g, 5.86 mmol) was added. The reaction mixture was reflux for 2 hours, poured to water and extracted with EtOAc (2 x 30 mL). Combined extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (10 – 15%) EtOAc in hexanes to give keto compound **11a**[2a] (945 mg, 73% yield) as a brownish foam. *Rf* = 0.5 (20% EtOAc/hexane); $[\alpha]_D^{20}$ **= +**30.3 (*c* 0.033, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3406, 2926, 2854, 1701, 1611, 1466, 1318, 1244, 1116, 737, 614, 442; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.0 Hz, 1 H), 7.95 (s, 1 H), 7.86 (s, 1 H), 7.36 (dd, *J* = 3.9, 1.0 Hz, 2 H), 7.20 (dt, *J* = 8.0, 5.0, 3.1 Hz, 1 H), 7.09 (s, 1 H), 3.19 − 3.04 (m, 2 H), 2.81 − 2.62 (m, 3 H), 2.13 – 1.99 (m, 2 H), 1.93 − 1.86 (m, 2 H), 1.41 (s, 3 H), 1.19 (d, *J* = 8.2 Hz, 6 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 217.6, 140.2, 139.8, 138.4, 133.6, 125.7, 123.6, 122.4, 120.1, 119.4, 117.5, 116.8, 110.6, 109.9, 51.2, 47.6, 38.5, 37.8, 35.0, 31.8, 27.0, 25.5, 21.4, 20.6; **HRMS**: m/z calcd. for $C_{23}H_{25}ClNO$ $[M+Cl]^+$: 366.1625; found: 366.1628.

Synthesis of compound 11b:

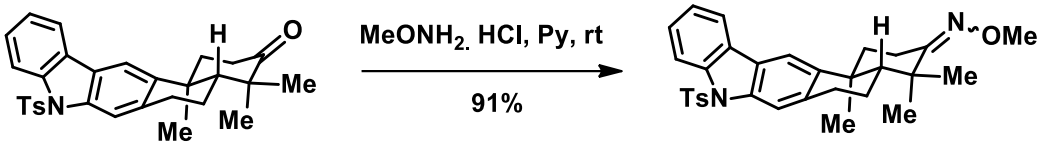


11a **11b**

To a stirred mixture of **11a** (200 mg, 0.604 mmol) and tetrabutylammoniumhydrogensulfate (20.37 mg, 0.06 mmol) in toluene (10 mL) was added aq. NaOH (50 %, 10 mL) at 0 °C followed by paramethyl tosyl chloride (184 mg, 0.970 mmol). The resulting suspension was warm to room temperature and vigorously stirred for 1 hours at same temperature. The reaction mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 30 mL). The combine extracts were washed

with brine (10 mL), separated, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (20 – 25%) EtOAc in hexanes to afford tosyl carbazole **11b**[5] (235 mg, 80% yield) as a brownish foam: Rf = 0.5 (35% EtOAc-hexane); $[\alpha]_D^{20}$ **= +**84 (*c* 0.033, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3297, 2924, 2854, 1738, 1465, 1376, 1261, 1175, 1018, 810, 668, 542, 417; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.3 Hz, 1 H), 7.99 (s, 1 H), 7.83 (d, *J* = 7.6 Hz, 1 H), 7.76 (s, 1 H), 7.70 (d, *J* = 8.4 Hz, 2 H), 7.42 (t, *J* = 8.2 Hz, 1 H), 7.31 (t, *J* = 7.4 Hz, 1 H), 7.10 (d, *J* = 8.2 Hz, 2 H), 3.25 – 3.18 (m, 1 H), 3.13 – 3.05 (m, 1 H), 2.79 – 2.72 (m, 1 H), 2.66 − 2.58 (m, 2 H), 2.26 (s, 3 H), 2.05 − 1.96 (m, 2 H), 1.89 (dd, *J* = 10.4, 4.7 Hz, 2 H), 1.35 (s, 3 H), 1.19 (s, 3 H), 1.17 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 217.2, 144.9, 143.9, 138.6, 136.9, 135.3, 129.8, 127.1, 126.6, 126.6, 124.9, 123.9, 119.7, 116.6, 115.1, 114.8, 50.8, 47.6, 38.1, 37.7, 34.8, 31.9, 26.9, 25.3, 21.7, 21.3, 20.4; **HRMS**: m/z calcd. for $C_{30}H_{31}NNaO_3S$ $[M+Na]^+$: 508.1922; found: 508.1922.

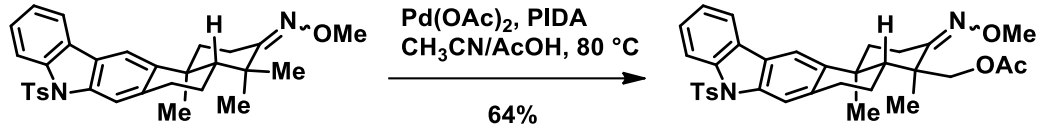
Synthesis of compound 12:



11b **12**

To a magnetically stirred solution of Tosyl carbazole **11b** (300 mg, 0.618 mmol) in pyridine (5 ml) was added $MeONH_2$·HCl (77 mg, 0.927 mmol) at room temperature. The resulting solution was stirred for 2 hours. After completion of reaction, the reaction was diluted with EtOAc and poured to 10% aqueous AcOH (4 mL) and neutralized with water followed by saturated solution of $NaHCO_3$. The organic layer was separated and aqueous layer was extracted with EtOAc, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography using (10 – 15%) EtOAc in hexanes as an eluent to furnish the desired oxime **12**[5] (291 mg, 91%) as a pale yellow foam; *Rf* = 0.5 (20% EtOAc-hexane); $[\alpha]_D^{20}$ **= +**66.06 (*c* 0.033, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 2955, 2854, 1738, 1465, 1376, 1261, 1176, 1053, 882, 746, 666, 542, 419; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.4 Hz, 1 H), 7.97 (s, 1 H), 7.83 (d, *J* = 7.6 Hz, 1 H), 7.73 (s, 1 H), 7.69 (d, *J* = 8.4 Hz, 2 H), 7.41 (t, *J* = 7.9 Hz, 1 H), 7.31 (t, *J* = 7.7 Hz, 1 H), 7.10 (d, *J* = 8.2 Hz, 2 H), 3.84 (s, 3 H), 3.20 (dd, *J* = 17.1, 5.4 Hz, 1 H), 3.12 −3.04 (m, 2 H), 2.49 (dt, *J* = 6.7, 3.3 Hz, 1 H), 2.44 – 2.40 (m, 1 H), 2.26 (s, 3 H), 1.98 (dd, *J* = 13.1, 7.0 Hz, 1 H), 1.88 – 1.80 (m, 1 H), 1.71 – 1.65 (m, 2 H), 1.33 (s, 3 H), 1.26 (s, 3 H), 1.19 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 165.1, 145.0, 144.7, 138.5, 136.7, 135.4, 135.2, 129.7, 126.9, 126.7, 126.6, 124.6, 123.7, 119.6, 116.1, 115.1, 114.6, 61.2, 50.7, 40.1, 37.9, 37.5, 31.7, 27.7, 25.0, 23.3, 21.6, 19., 18.5; **HRMS**: m/z calcd. for $C_{31}H_{35}N_2O_3S$ $[M+H]^+$: 515.2368; found: 515.2368.

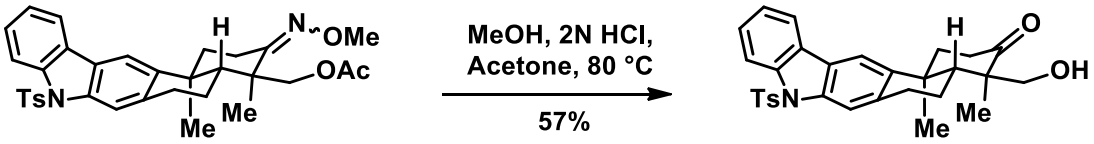
Synthesis of compound 13:



12 **13**

Compound **12** O-Methyloxime carbazole (100 mg, 0.194 mmol) was dissolved in 1:9 ratio of AcOH: CH_3CN (5 mL) at room temperature. Then $PhI(OAc)_2$ (125 mg, 0.39 mmol) and $Pd(OAc)_2$ (2.24 mg, 0.05 mmol, 5 mol%), were added sequentially and the resulting solution was heated at 80 °C for 1 hours. Then, the reaction was cooled, diluted with EtOAc, washed with sat. aq. $NaHCO_3$, brine and organic layer was separated, dried over Na_2SO_4. Evaporation of the solvent and purification of the residue by silica gel column chromatography using (12 – 16%) EtOAc in hexanes as a eluent furnished the compound **13**[6c] (1:3 distereomer, 72 mg, 64 %) as a yellow colour foam. *Rf* = 0.5 (25% EtOAc-hexane); $[\alpha]_D^{20}$ **= +**85 (*c* 0.2, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3380, 2924, 2854, 1739, 1598, 1465, 1372, 1234, 1174, 1050, 945, 811, 768, 666, 584, 439; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 8.3, 4.7 Hz, 1 H), 7.96 (s, 1 H), 7.83 (t, *J* = 8.6 Hz, 1 H), 7.78 (s, 1 H), 7.71 (p, *J* = 8.5 Hz, 3 H), 7.42 (t, *J* = 7.8 Hz, 1 H), 7.31 (t, *J* = 7.4 Hz, 1 H), 7.11 (t, *J* = 8.9 Hz, 3 H), 4.25 (d, *J* = 10.8 Hz, 1 H), 4.16 (d, *J* = 10.8 Hz, 1 H), 3.83 (d, *J* = 4.9 Hz, 4 H), 3.37 – 2.96 (m, 3 H), 2.92 (ddd, *J* = 17.0, 6.9, 2.9 Hz, 1 H), 2.66 – 2.43 (m, 3 H), 2.27 (d, *J* = 5.0 Hz, 4 H), 2.01 (s, 4 H), 1.90 – 1.78 (m, 3 H), 1.67 (dd, *J* = 14.7, 9.9 Hz, 1 H), 1.39 (s, 1 H), 1.33 (s, 1 H), 1.31 (s, 3 H), 1.20 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.1, 160.7, 144.8, 143.9, 138.6, 136.8, 135.4, 129.8, 127.1, 126.7, 126.6, 126.6, 124.8, 123.8, 119.7, 116.7, 115.1, 114.7, 69.2, 61.6, 44.2, 43.0, 37.8, 36.3, 32.0, 25.0, 21.7, 21.2, 20.1, 19.9, 19.7; **HRMS**: m/z calcd. for $C_{33}H_{37}N_2O_5S$ $[M+H]^+$: 573.2423; found: 573.2423.

Synthesis of compound 13a:

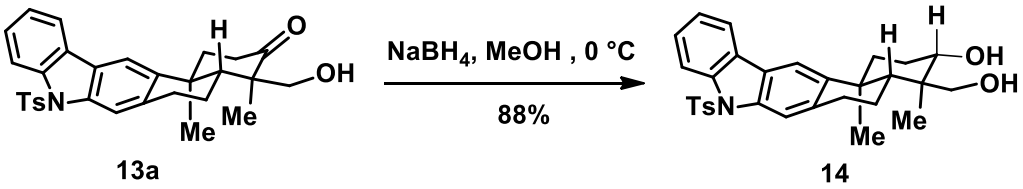


13 **13a**

To a magnetically stirred solution of compound **13** (500 mg, 0.998 mmol) was dissolved in mixture of acetone (0.5 mL), MeOH (3 mL) and aqueous 2 N HCl (3 mL). The contents were heated to 80 °C and reaction progress was monitored by TLC. After completion of reaction, the reaction mixture was diluted with ethyl acetate, washed with H_2O and sat. aq. $NaHCO_3$. The organic layer was separated, dried over Na_2SO_4, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography using (30 – 40%) EtOAc in hexanes as an eluent gave the desired

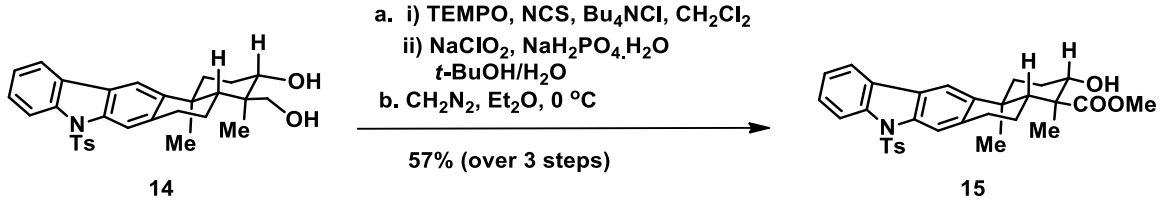
keto-alcohol **13a**[7] (251 mg, 57%) as a pale yellow foam. *Rf* = 0.5 (60% EtOAc-hexane); $[\alpha]_D^{20}$ = +40.7 (*c* 0.216, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3422, 2923, 2853, 1737, 1698, 1465, 1368, 1242,1173, 1018, 945, 882, 748, 667, 583, 404; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1 H), 8.00 (s, 1 H), 7.83 (d, *J* = 7.6 Hz, 1 H), 7.76 (s, 1 H), 7.68 (d, *J* = 8.3 Hz, 2 H), 7.42 (t, *J* = 8.1 Hz, 1 H), 7.31 (t, *J* = 7.4 Hz, 1 H), 7.10 (d, *J* = 8.2 Hz, 2 H), 3.76 (d, *J* = 11.3 Hz, 1 H), 3.50 (d, *J* = 11.3 Hz, 1 H), 3.19 (ddt, *J* = 24.3, 13.3, 6.2 Hz, 2 H), 2.87 (dt, *J* = 15.7, 13.3, 6.5 Hz, 1 H), 2.68 (dt, *J* = 13.0, 6.4, 2.6 Hz, 1 H), 2.52 (dt, *J* = 15.8, 5.2, 2.7 Hz, 1 H), 2.33 (dd, *J* = 12.2, 2.2 Hz, 1 H), 2.26 (s, 3 H), 1.95 (dq, *J* = 18.3, 6.5, 5.3 Hz, 2 H), 1.85 (dd, *J* = 13.1, 7.1 Hz, 1 H), 1.45 (s, 3 H), 1.13 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 218.1, 144.9, 143.8, 138.7, 137.0, 135.4, 135.2, 129.8, 127.1, 126.6, 124.7, 123.9, 119.7, 115.9, 115.2, 115.0, 66.9, 52.7, 44.3, 37.7, 37.5, 36.1, 31.4, 25.2, 21.7, 19.9; **HRMS**: m/z calcd. for $C_{30}H_{31}NNaO_4S$ $[M+Na]^+$: 524.1871; found: 524.1868.

Synthesis of compound 14:



The compound **13a** (150 mg, 0.299 mmol) was dissolved in MeOH (4 mL) and cooled to 0 °C. $NaBH_4$ (34 mg, 0.898 mmol) was added, and the solution was stirred at 0 °C for 30 min. The reaction mixture was diluted with EtOAc and quenched with aqueous 1 M HCl. The organic layer was washed with water and the aqueous was extracted with ethylacetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude material was purified by silica gel column chromatography using (40 – 50%) EtOAc in hexanes as an eluent to furnish the required diol **14**[7] (133 mg, 88% yield) as a yellow oil. *Rf* = 0.4 (80% EtOAc-hexane); $[\alpha]_D^{20}$ = +14 (*c* 0.1, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 2924, 2853, 1738, 1465, 1376, 1260, 1186, 1091, 908, 883, 747, 665, 585, 442; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1 H), 8.00 (s, 1 H), 7.83 (d, *J* = 7.6 Hz, 1 H), 7.76 (s, 1 H), 7.68 (d, *J* = 8.3 Hz, 2 H), 7.42 (t, *J* = 8.1 Hz, 1 H), 7.31 (t, *J* = 7.4 Hz, 1 H), 7.10 (d, *J* = 8.2 Hz, 2 H), 3.76 (d, *J* = 11.4 Hz, 1 H), 3.50 (d, *J* = 11.3 Hz, 1 H), 3.26 − 3.11 (m, 2 H), 2.92 − 2.83 (m, 1 H), 2.68 (dt, *J* = 13.0, 6.4, 2.6 Hz, 1 H), 2.52 (dt, *J* = 15.8, 5.2, 2.7 Hz, 1 H), 2.34 – 2.30 (m, 1 H), 2.26 (s, 3 H), 2.05 − 1.77 (m, 4 H), 1.45 (s, 3 H), 1.13 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.7, 144.8, 138.6, 136.8, 135.3, 129.8, 126.9, 126.8, 126.7, 124.6, 123.8, 119.7, 115.5, 115.1, 114.7, 76.5, 71.8, 44.4, 42.4, 37.8, 37.2, 31.3, 29.8, 27.7, 25.7, 21.7, 19.2; **HRMS**: m/z calcd. for $C_{30}H_{37}N_2O_4S$ $[M+NH_4]^+$: 521.2474; found: 521.2474.

Synthesis of compound 15:



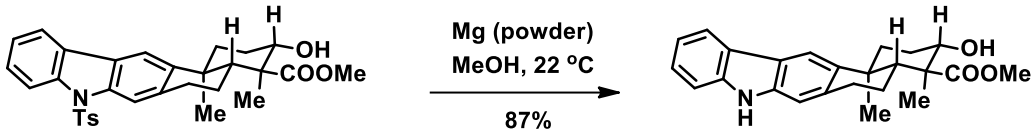
To a magnetically stirred solution of TEMPO (28 mg, 0.176 mmol), N-chlorosuccinimide (475 mg, 3.57 mmol), and Bu_4NCl (50 mg, 0.176 mmol) was added a solution of diol **14** (600 mg, 1.19 mmol) in CH_2Cl_2 (10 mL), aq. $NaHCO_3$ (0.5 M, 69 mg) and K_2CO_3 (0.05 M, 420 mg) sequentially. The mixture was stirred for 3 hours at room temperature and the time where both organic and aqueous layers were separated in the reaction mixture. The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give crude aldehyde as an orange colour oil which was immediately used for next step without further purification[8]. *Rf* = 0.5 (40% EtOAc/hexane).

To a magnetically stirred solution of aldehyde **14a** (597 mg, 1.19 mmol) in t-BuOH (10 mL) and H_2O (3 mL), 2-methyl-2-butene was added (0.54 mL, 11.91 mmol) $NaClO_2$ (643 mg, 7.18 mmol) and $NaH_2PO_4.H_2O$ (1.418 g, 11.91 mmol) were added in one portion into the solution. The reaction mixture was stirred for 50 min and then quenched by the addition of 5% aqueous $Na_2S_2O_3$ solution. Ethylacetate was added, the organic layer was separated and the aqueous layer was extracted with ethylacetate (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give crude acid as a yellow colour oil which was immediately used for next step without further purification[8]. *Rf* = 0.4 (7% MeOH/CH_2Cl_2).

The crude acid **14b** (616 mg, 1.19 mmol) was dissolved in dry Et_2O (10 mL) and cooled to 0 °C. The freshly prepared diazomethane solution in dry Et_2O (20 mL) was added at 0 °C. The reaction mixture was then stirred at the same temperature and reaction progress was monitor by TLC. After completion of the reaction, solvent was removed under reduced pressure at a temperature below 25 °C to get a yellow colored crude product which was passed through a silica gel column chromatography using (45 – 50%) EtOAc in hexanes as an eluent to give required methyl ester **15**[8] as a yellow oil (362 mg, overall 3 steps 57% yield); *Rf* = 0.5 (60% EtOAc/hexanes), $[\alpha]_D^{20}$ **=** −115 (*c* 0.033, $CHCl_3$); **IR** (neat): *ν*max/cm^{-1} 3444, 2926, 2855, 1713, 1598, 1465, 1369, 1245, 1174, 1091, 997, 812, 703, 668, 585; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.4 Hz, 1 H), 7.95 (s, 1 H), 7.82 (d, *J* = 7.6 Hz, 1 H), 7.78 − 7.58 (m, 3 H), 7.42 (t, *J* = 7.5 Hz, 1 H), 7.31 (t, *J* = 7.5 Hz, 1 H), 7.10 (d, *J* = 8.2 Hz, 2 H), 4.06 (dd, *J* = 11.6, 4.5 Hz, 1 H), 3.75 (s, 3 H), 3.13 (dt, *J* = 24.3, 13.8, 7.1 Hz, 2 H), 2.47 (dt, *J* = 12.7, 2.9 Hz,

1 H), 2.27 (s, 3 H), 2.16 (dd, *J* = 12.5, 2.1 Hz, 1 H), 1.99 – 1.81 (m, 3 H), 1.72 (d, *J* = 3.6 Hz, 1 H), 1.51 (dd, *J* = 14.1, 6.6 Hz, 1 H), 1.27 (d, *J* = 16.8 Hz, 6 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.9, 145.3, 144.8, 138.6, 136.9, 135.3, 135.2, 129.8, 127.0, 126.7, 126.6, 124.7, 123.8, 119.7, 115.6, 115.2, 114.8, 75.3, 53.9, 52.5, 45.7, 37.4, 37.1, 31.0, 27.4, 25.7, 21.7, 21.5, 10.8; **HRMS**: m/z calcd. for $C_{31}H_{33}NNaO_5S$ $[M+Na]^+$: 554.1977; found: 554.1983.

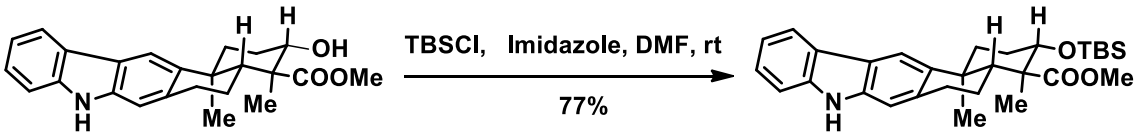
Synthesis of Xiamycin A methyl ester 2:



15 **Xiamycin A methyl ester 2**

To a solution of methyl ester **15** (100 mg, 0.188 mmol) in MeOH (3 mL) were added magnesium powder (36 mg, 1.5 mmol) at 22 °C. The resulting mixture was subjected for sonication at the same temperature about 30 min and then quenched with saturated aq. NH_4Cl (5 mL) solution. The reaction mixture was extracted with ethylacetate (3 × 10 mL) and the combined organic phases were washed with brine (5 mL), separated and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum, and residue was purified by silica gel column chromatography using (35 – 40%) EtOAc in hexanes to give xiamycin A methyl ester **2**[9a] (62 mg, 87% yield) as a pale yellow colour amorphous solid. *Rf* = 0.5 (55% EtOAc-hexane); $[\alpha]_D^{20}$ **= +**75.9 (*c* 0.216, $CHCl_3$); **IR** (neat): *ν*max/cm^{-1} 3409, 2926, 2854, 1715, 1612, 1466, 1320, 1244, 1133, 1069, 940, 800, 735, 606, 536; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.8 Hz, 1 H), 7.92 (s, 1 H), 7.84 (s, 1 H), 7.36 – 7.32 (m, 2 H), 7.18 (dt, *J* = 8.0, 5.5, 2.6 Hz, 1 H), 7.04 (s, 1 H), 4.08 (dd, *J* = 11.2, 4.4 Hz, 1 H), 3.73 (s, 3 H), 3.11 – 3.04 (m, 2 H), 2.57 (d, *J* = 12.7 Hz, 1 H), 2.21 (dd, *J* = 12.5, 2.3 Hz, 1 H), 2.03−1.93 (m, 2 H), 1.87 − 1.78 (m, 2 H), 1.48 (dd, *J* = 11.7, 5.2 Hz, 1 H), 1.29 (s, 6 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.8, 141.0, 139.9, 138.1, 133.3, 125.4, 123.5, 121.9, 119.8, 119.1, 115.6, 110.44, 109.80, 75.28, 53.79, 52.25, 45.86, 37.37, 37.24, 30.74, 27.42, 25.81, 21.48, 10.71; **HRMS**: m/z calcd. for $C_{24}H_{28}NO_3$ $[M+H]^+$: 378.2069; found: 378.2070.

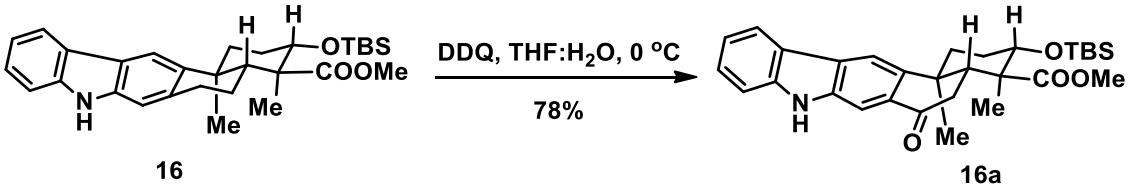
Synthesis of compound 16:



Xiamycin A methyl ester 2 **16**

To a stirred solution of Xiamycin A methyl ester **2** (80 mg, 0.212 mmol), imidazole (36 mg, 0.530 mmol) in DMF (1.0 mL) at 0 °C was added tert-butyldimethylsilyl chloride (38 mg, 0.254 mmol). The solution was allowed to stired at room temperature for 10 hours. The solvent was removed in vacuo and the residue was dissolved in diethyl ether, washed with saturated solution of $NaHCO_3$ and aqueous layer was extracted three times with diethyl ether. The combined organic extracts were washed with brine, separated and dried over Na_2SO_4. Solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (10 – 15%) EtOAc in hexanes to afford the TBS ether **16**[9b] as pale yellow oil (81 mg, 77%). *Rf* = 0.5 (20% EtOAc-hexane); $[\alpha]_D^{20}$ **= +**58 (*c* 0.20, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3346, 2938, 2851, 1732, 1607, 1476, 1301, 1211, 1167, 1057, 967, 806,753, 643, 521; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.7 Hz, 1 H), 7.91 (s, 1 H), 7.79 (s, 1 H), 7.34 (d, *J* = 6.4 Hz, 2 H), 7.18 (t, *J* = 7.6 Hz, 1 H), 7.01 (s, 1 H), 4.14 (dd, *J* = 10.9, 4.5 Hz, 1 H), 3.67 (s, 3 H), 3.10 – 3.00 (m, 2 H), 2.52 (d, *J* = 9.8 Hz, 1 H), 2.18 (dd, *J* = 12.6, 2.3 Hz, 1 H), 1.98 (dd, *J* = 11.6, 8.5 Hz, 1 H), 1.81 (q, *J* = 13.7, 13.1 Hz, 3 H), 1.42 – 1.37 (m, 1 H), 1.27 (d, *J* = 7.5 Hz, 6 H), 0.86 (s, 9 H), 0.05 (s, 3 H), -0.04 (s, 3 H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.9, 141.3, 139.9, 138.1, 133.4, 125.3, 123.6, 121.9, 119.8, 119.1, 115.5, 110.4, 109.7, 76.0, 54.7, 51.8, 46.2, 37.4, 37.0, 30.6, 28.1, 25.6, 21.3, 17.8, 10.9, - 3.9, - 5.3; **HRMS**: m/z calcd. for $C_{30}H_{42}NO_3Si$ $[M+H]^+$: 492.2934; found: 492.2934.

Synthesis of compound 16a:

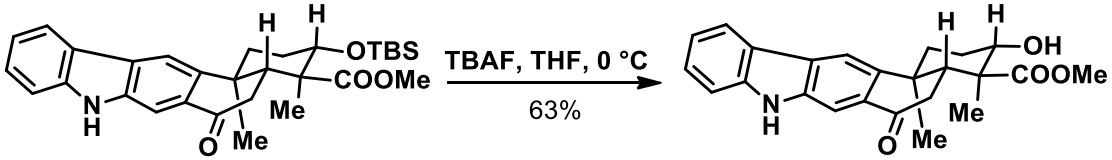


16 **16a**

Compound **16** (41 mg, 0.083 mmol) was dissolved in THF: H_2O (9:1) 3 mL and cooled to 0 °C. DDQ (104 mg, 0.459 mmol) was added and stirred at 0 °C for 2 hours. The reaction mixture was poured into ethyl acetate and washed with excess saturated solution aq. $NaHCO_3$ (3×5 mL). The organic fraction was dried over Na_2SO_4, filtered and evaporated to get a dark red coloured residue which was purified by silica gel column chromatography (15 – 20%) EtOAc in hexanes to get ketone **16a**[10] as a yellow oil (33 mg, 78% yield). R_f = 0.6 (30% EtOAc/hexane); $[\alpha]_D^{20}$ **= +**48.8 (*c* 0.250, $CHCl_3$); **IR** (neat): *v*max/cm^{-1} 3399, 2961, 2874, 1726, 1629, 1567, 1404, 1345, 1249, 1157, 1025, 924, 880, 775, 666; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.68 (s, 1 H), 8.14 (s, 1 H), 8.07 (d, *J* = 7.5 Hz, 1 H), 7.98 (s, 1 H), 7.50 − 7.39 (m, 2 H), 7.26 – 7.21 (m, 1 H), 4.18 (dd, *J* = 9.2, 4.7 Hz, 1 H), 3.66 (s, 3 H), 2.95 − 2.86 (m, 1 H), 2.68 (d, *J* = 13.3 Hz, 1 H), 2.58 (d, *J* = 11.4 Hz, 1 H), 2.30 (d, *J* = 18.1 Hz, 1 H), 1.94 (dd, *J* = 25.8, 13.0 Hz, 3 H), 1.33 (d, *J* = 16.1 Hz, 6 H), 0.86 (s, 9 H), 0.08 (s, 3 H), -0.03 (s, 3 H); **^{13}C NMR** (125 MHz,

$CDCl_3$) δ 198.7, 176.8, 146.3, 141.7, 137.6, 128.5, 128.3, 127.5, 122.4, 121.0, 119.6, 114.6, 111.1, 109.7, 75.6, 53.9, 52.1, 45.0, 37.6, 37.2, 36.5, 27.7, 25.6, 24.5, 17.8, 10.6, - 4.0, - 5.3; **HRMS**: m/z calcd. for $C_{30}H_{43}N_2O_4Si$ $[M+NH_4]^+$: 523.2992; found: 523.2995.

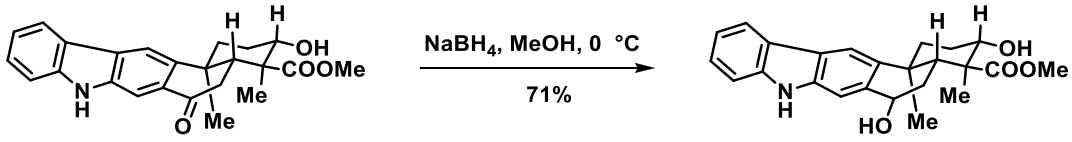
Synthesis of Xiamycin E (5):



16a **Xiamycin E, 5**

To a solution of compound **16a** (30 mg, 0.059 mmol) in THF (2.0 mL) was added TBAF (1 M in THF) (0.1 mL, 0.118 mmol) at 0 °C. The resulting mixture was stirred at same temperature for 1 hours and reaction progress was monitored by TLC. After completion of the reaction, the reaction mixture was quenched with saturated solution of $NaHCO_3$ and extracted with ethyl acetate. The organic fraction was dried over Na_2SO_4, filtered and solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography using (30 – 40%) EtOAc in hexanes to give xiamycin E **5**[9b] as a yellow oil (15 mg, 63% yield). R_f = 0.5 (60% EtOAc/hexane); $[\alpha]_D^{20}$ = +22 (*c* 0.2, MeOH); **IR** (neat): *v*max/cm^{-1} 3363, 2942, 2853, 1717, 1628, 1473, 1327, 1250, 1069, 741, 667; **^{1}H NMR** (500 MHz, CD_3OD) δ 8.15 (d, *J* = 7.0 Hz, 1 H), 8.14 (s, 1 H), 8.06 (s, 1 H), 7.48 – 7.44 (m, 2 H), 7.20 (ddd, *J* = 8.0, 5.2, 2.8 Hz, 1 H), 4.13 – 4.10 (m, 1 H), 3.72 (s, 3 H), 3.00 – 2.94 (m, 1 H), 2.75 – 2.72 (m, 1 H), 2.65 – 2.61 (m, 1 H), 2.19 (dd, *J* = 18.0, 3.5 Hz, 1 H), 1.99 – 1.94 (m, 3 H), 1.36 (s, 3 H), 1.35 (s, 3 H); **^{13}C NMR** (125 MHz, CD_3OD) δ 200.7, 178.5, 147.4, 143.9, 139.5, 129.9, 129.2, 128.6, 123.6, 122.2, 120.3, 116.0, 112.2, 110.6, 75.9, 54.7, 52.8, 46.8, 38.7, 38.6, 38.0, 28.1, 24.8, 11.0; **HRMS**: m/z calcd. for $C_{24}H_{24}NO_4$ $[M-H]^-$: 390.1705; found: 390.1707.

Synthesis of Xiamycin D (4):

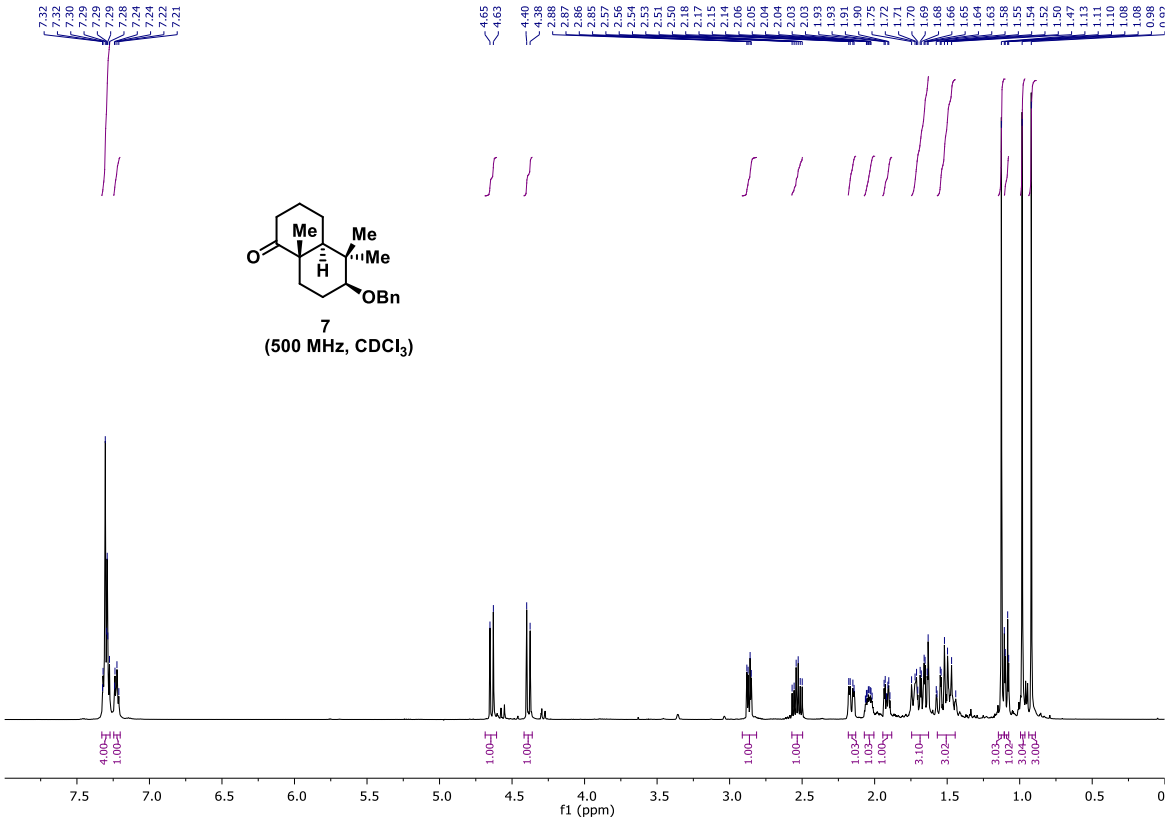


Xiamycin E, 5 **Xiamycin D, 4**

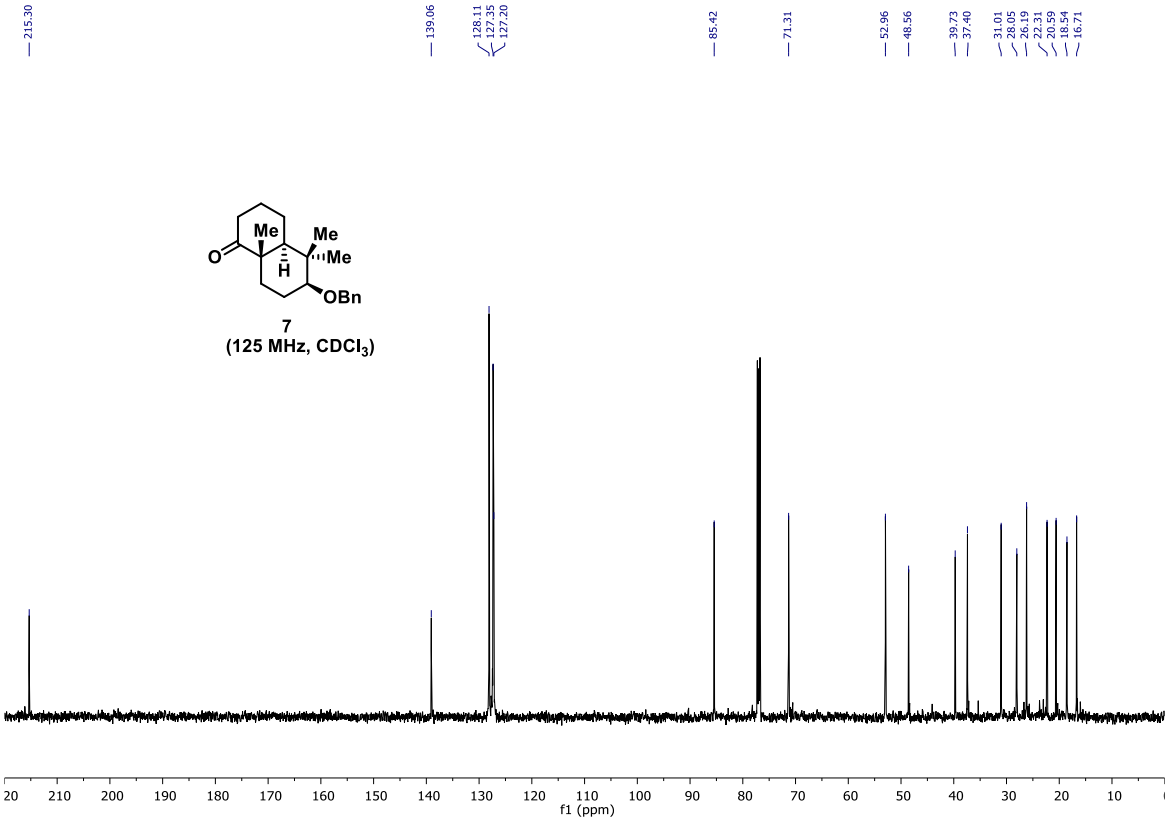
To a magnetically stirred solution of xiamycin E, **5** (14 mg, 0.35 mmol) in dry MeOH (1.5 mL) was added sodium borohydride (3.9 mg, 0.107 mmol) at 0 °C. The reaction mixture was stirring at same temperature for 10 min. After completion reaction, solvent was removed under reduced pressure, diluted with water and extracted using ethyl acetate. The organic fraction was separated, dried over Na_2SO_4 and crude residue was purified by flash chromatography using (40 – 50%) EtOAc in hexanes

to get xiamycin D **4**[7] (10 mg, 71% yield) as a yellow oil. R_f = 0.5 (80% EtOAc/hexane); $[\alpha]_D^{20}$ **= +**134 (*c* 0.1, MeOH); **IR** (neat): *ν*max/cm^{-1} 3407, 2924, 2853, 1714, 1612, 1464, 1379, 1243, 1132, 1088, 927, 876, 743, 429; **^{1}H NMR** (500 MHz, CD_3OD) δ 8.00 (d, *J* = 8.0 Hz, 1 H), 7.94 (s, 1 H), 7.57 (s, 1 H), 7.38 (d, *J* = 7.9 Hz, 1 H), 7.34 – 7.30 (m, 1 H), 7.12 – 7.09 (m, 1 H), 4.85-4.83 (m, 1 H), 4.10 – 4.05 (m, 1 H), 3.74 (s, 3 H), 2.64 (d, *J* = 12.8 Hz, 1H), 2.17 (d, *J* = 12.7 Hz, 1H), 2.03 – 1.95 (m, 1 H), 1.89 (dd, *J* = 8.0, 2.6 Hz, 2 H), 1.70 (dd, *J* = 11.4, 6.8 Hz, 2 H), 1.38 (s, 3 H), 1.28 (s, 3 H); **^{13}C NMR** (126 MHz, CD_3OD) δ 179.4, 142.3, 141.2, 140.2, 137.2, 126.5, 124.3, 124.2, 120.8, 119.4, 116.3, 111.5, 110.0, 76.1, 71.9, 55.3, 52.6, 46.3, 39.1, 38.9, 33.2, 28.4, 26.7, 11.4; **HRMS**: m/z calcd. for $C_{24}H_{26}NO_4$ $[M-H]^-$: 392.1862; found: 392.1864.

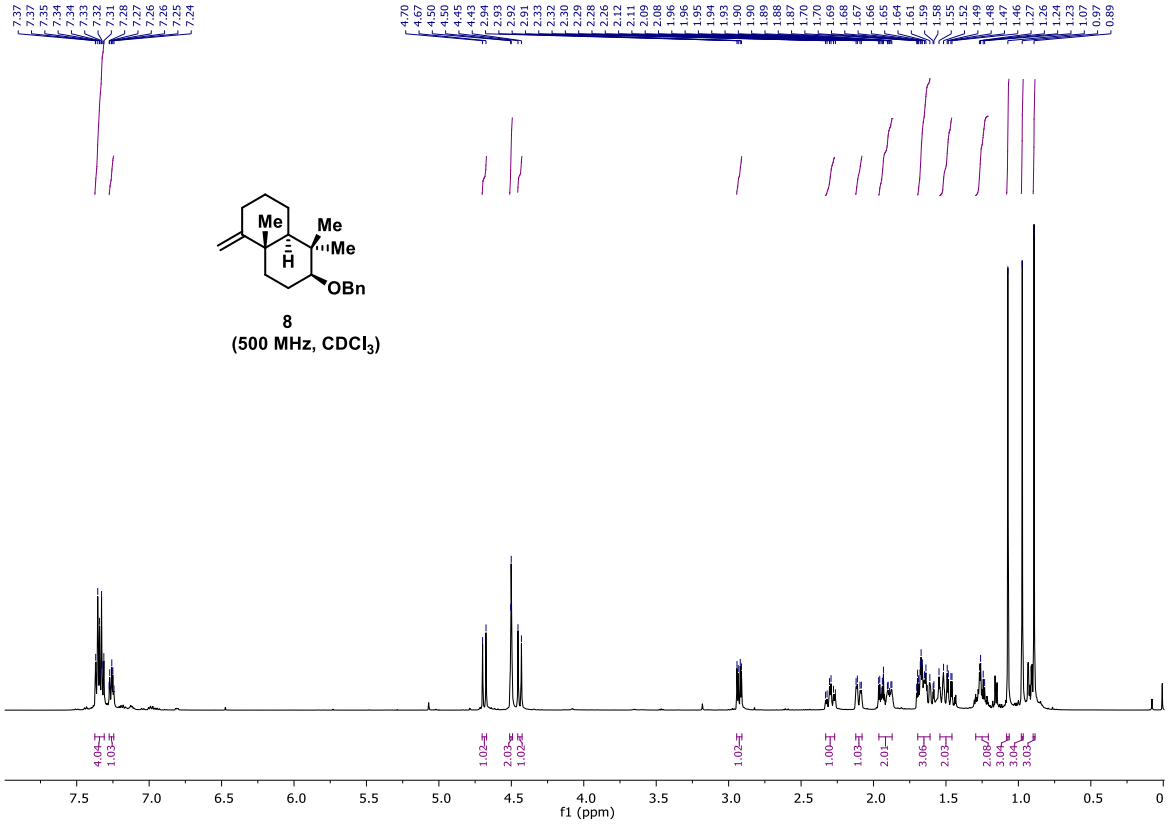
3. ^{1}H and ^{13}CNMR Spectra:



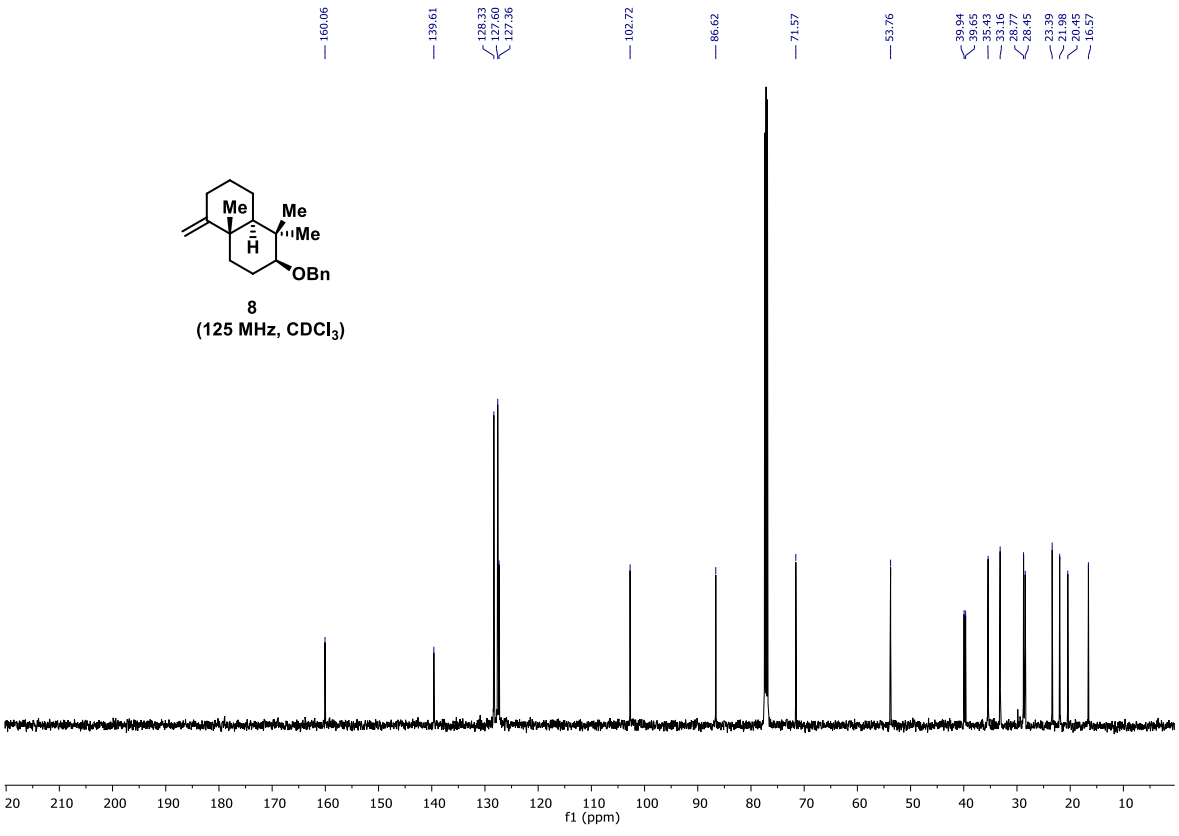
7
(500 MHz, $CDCl_3$)



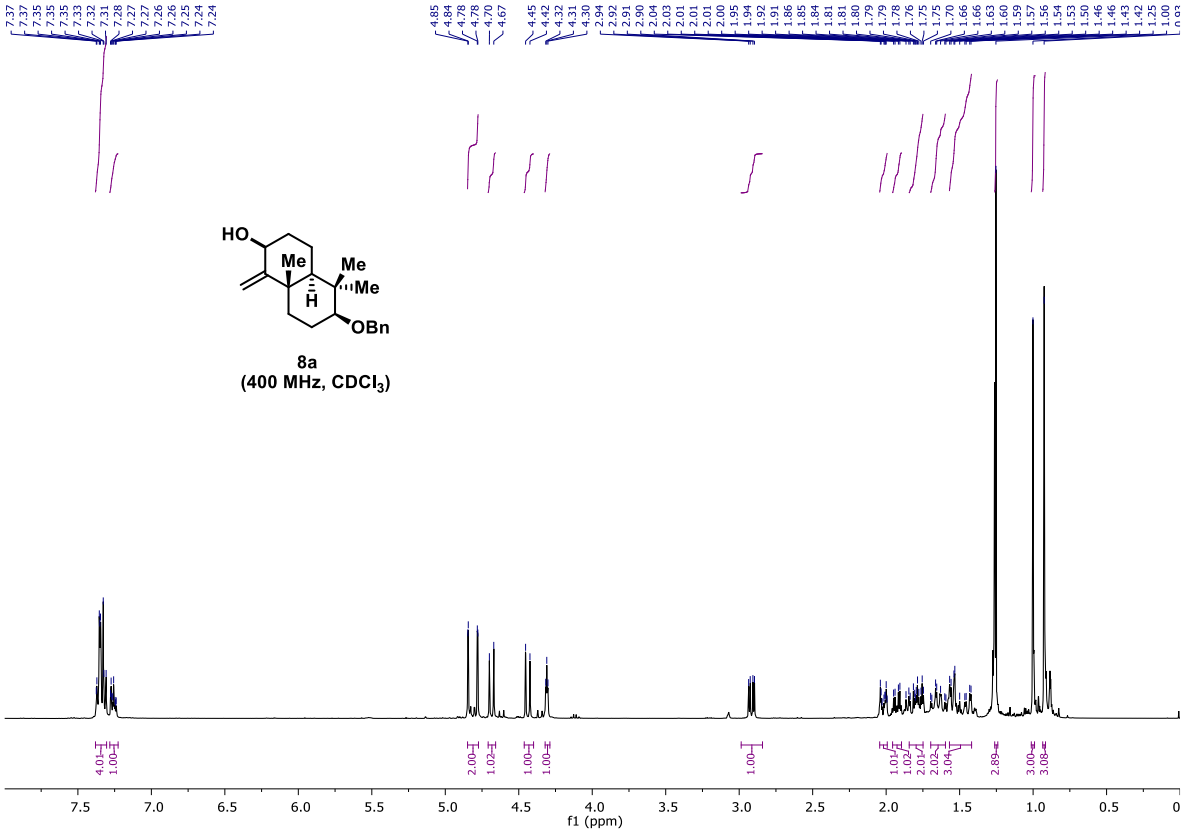
7
(125 MHz, $CDCl_3$)



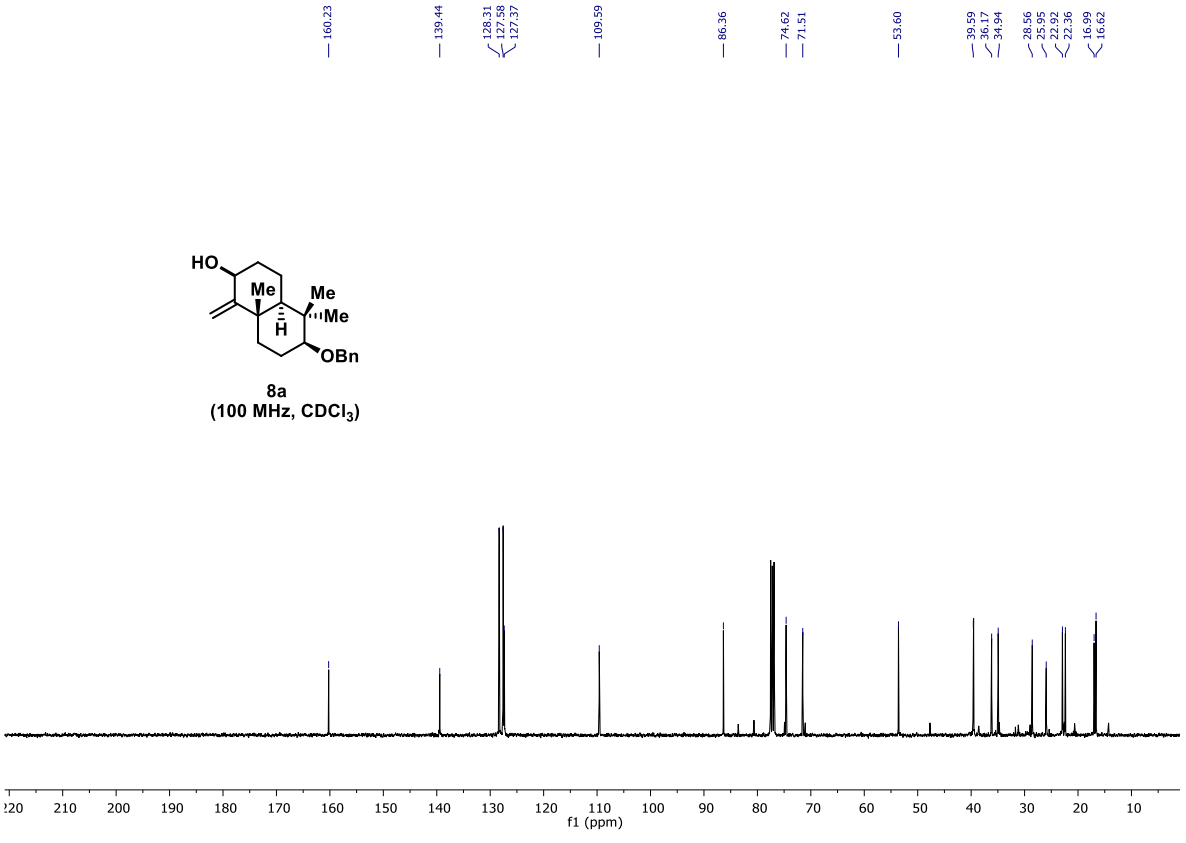
8
(500 MHz, $CDCl_3$)



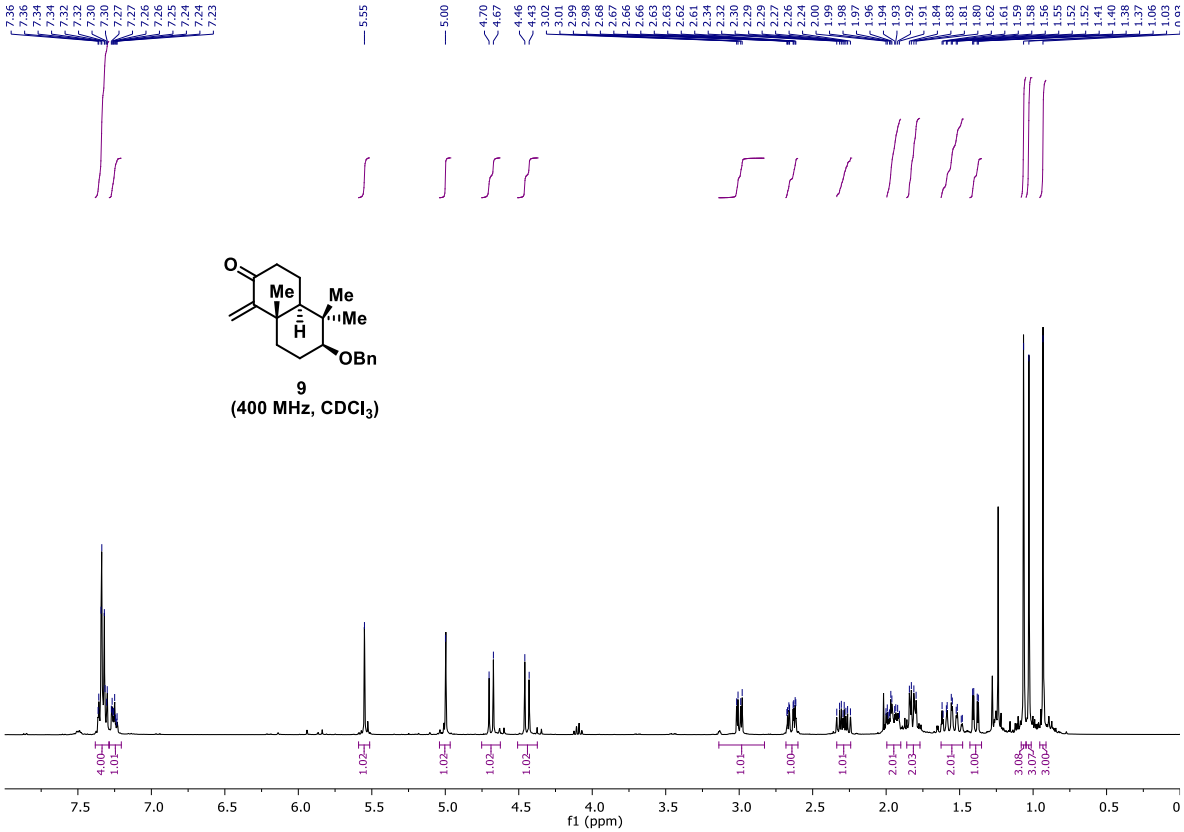
8
(125 MHz, $CDCl_3$)



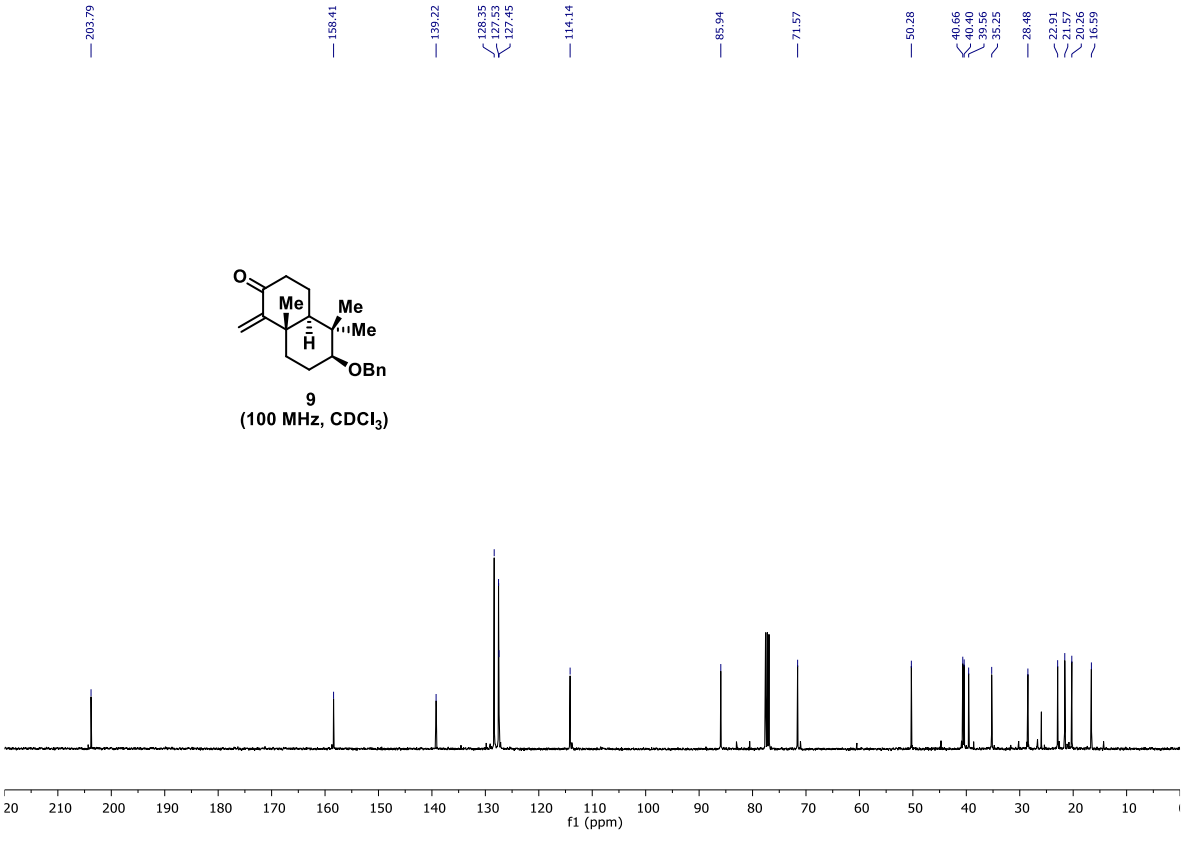
8a
(400 MHz, $CDCl_3$)



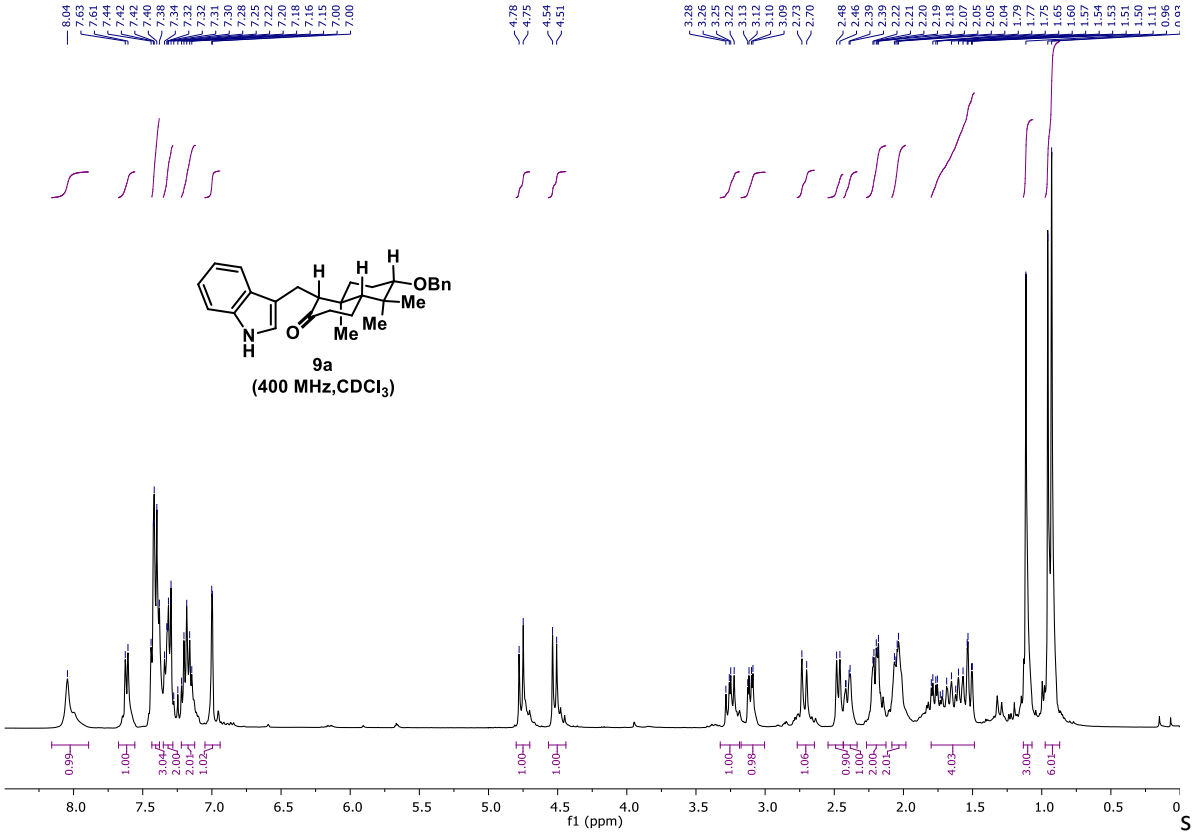
8a
(100 MHz, $CDCl_3$)

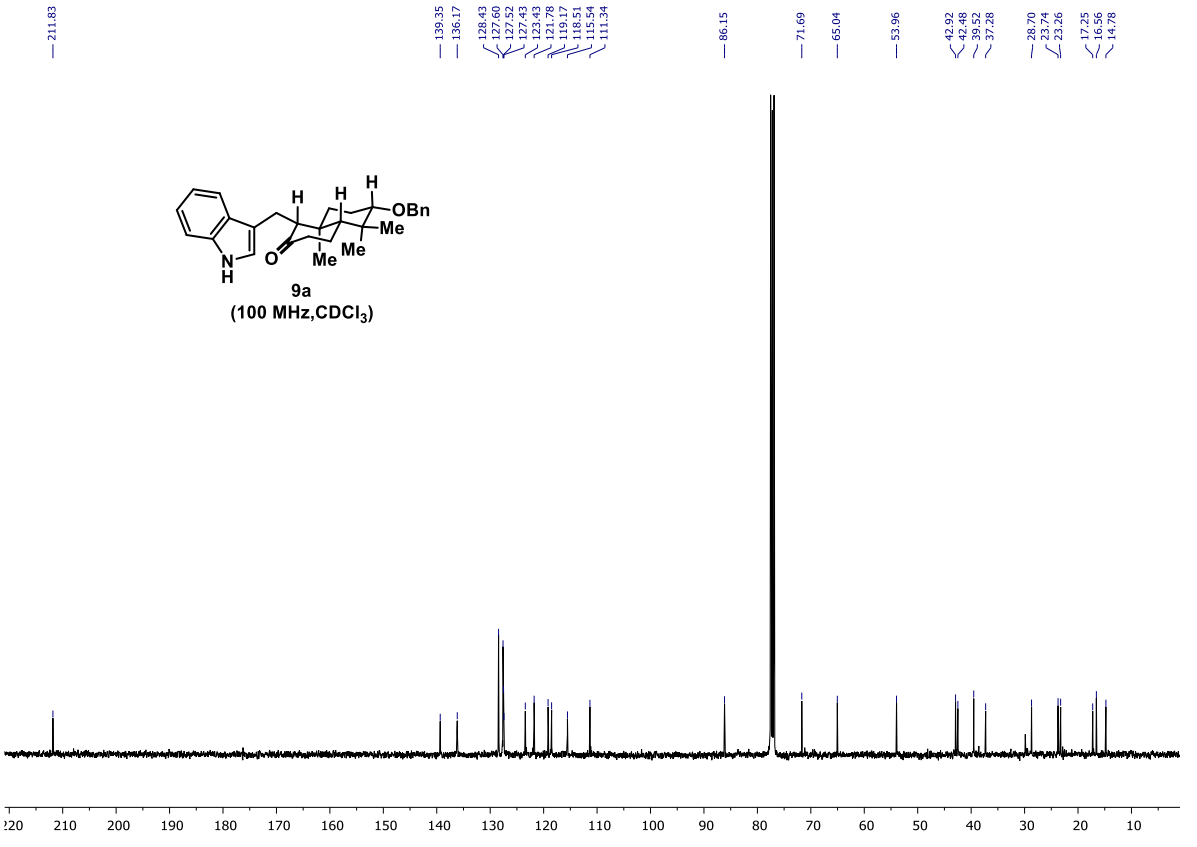


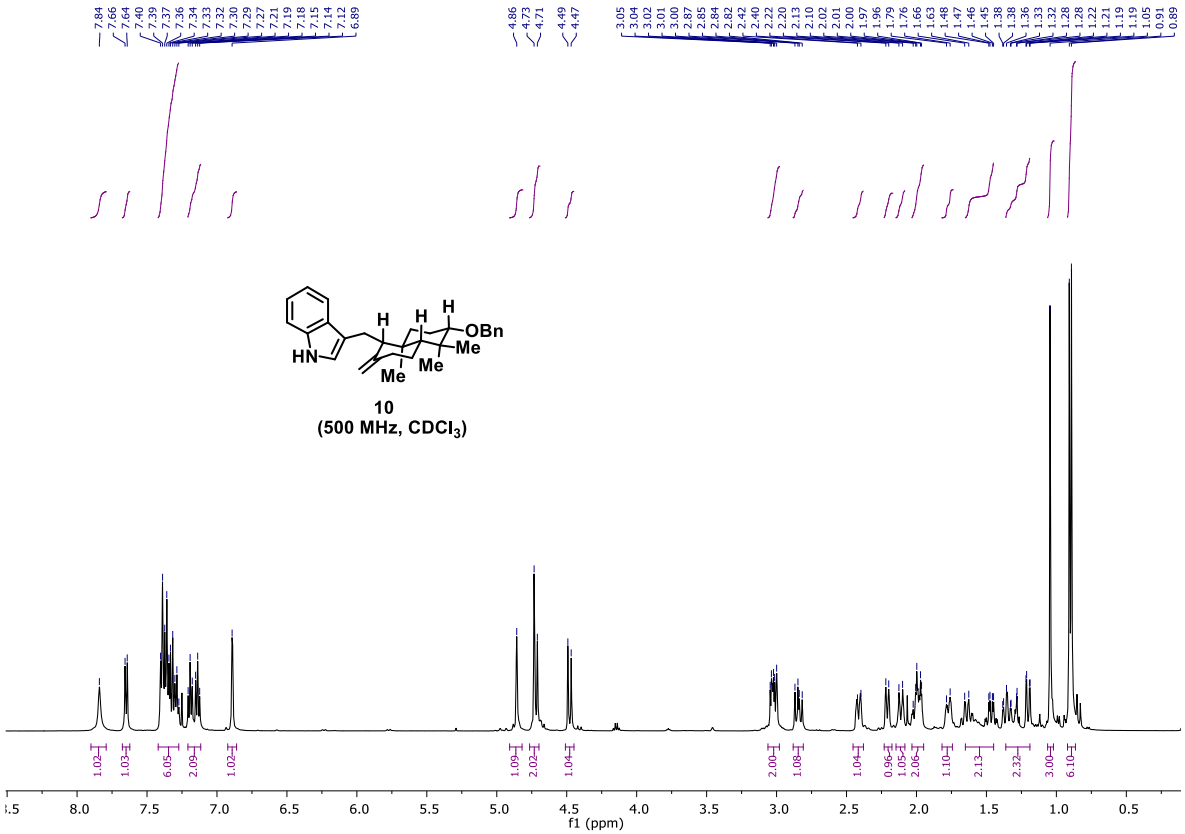
9
(400 MHz, $CDCl_3$)



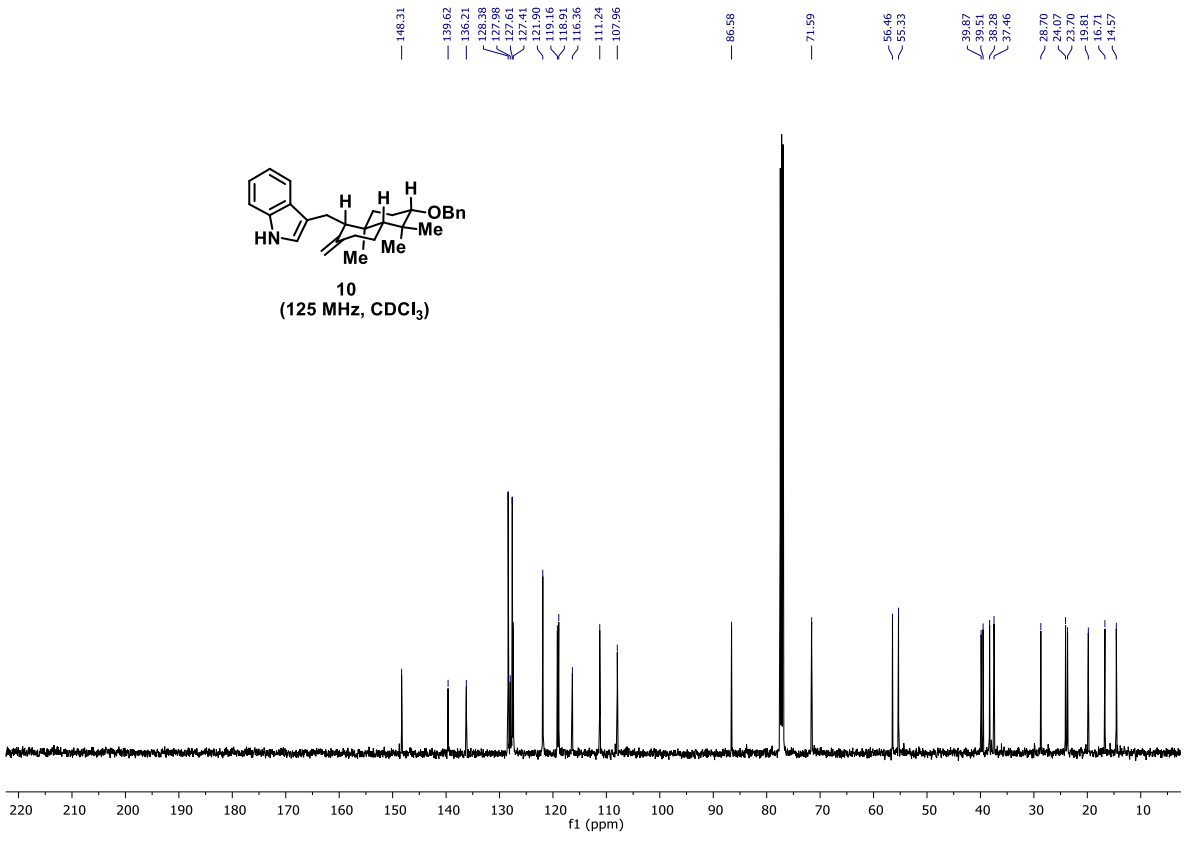
9
(100 MHz, $CDCl_3$)


9a
(400 MHz,CDCl3)
f1 (ppm)

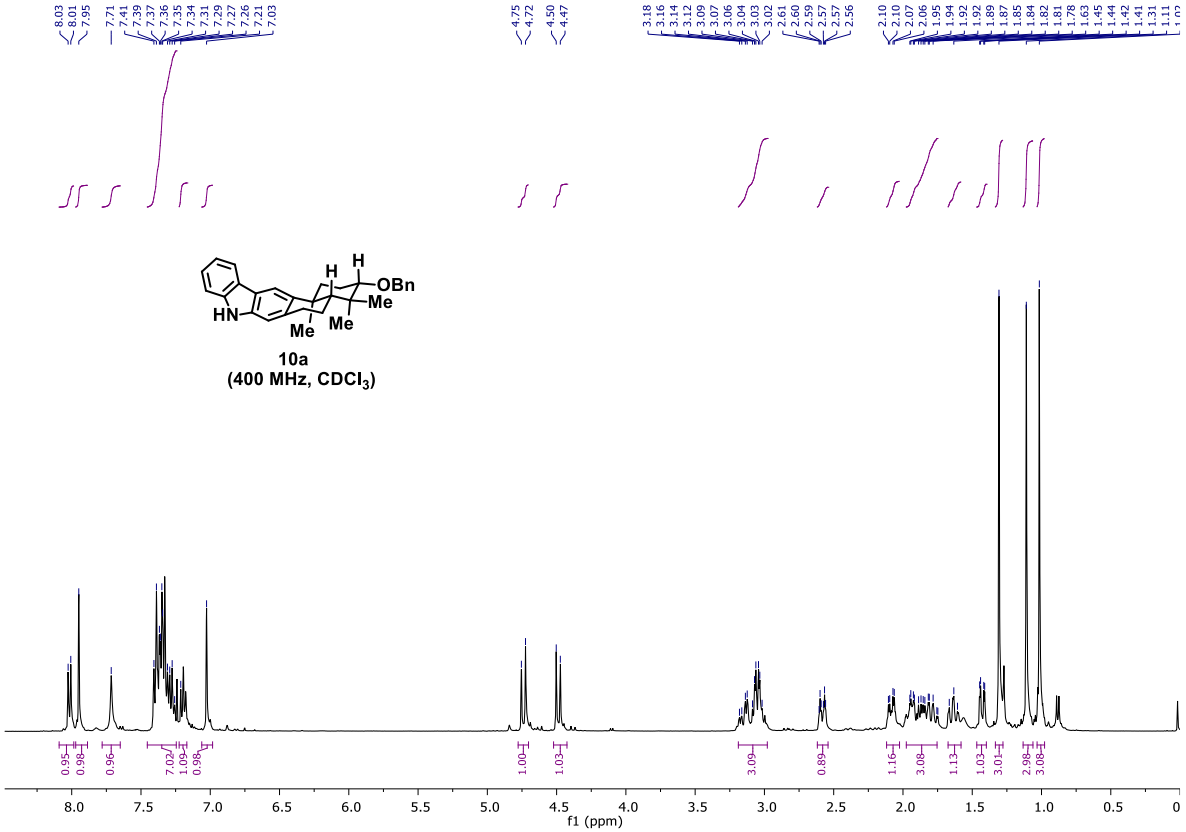

9a
(100 MHz,CDCl3)



10
(500 MHz, $CDCl_3$)



10
(125 MHz, $CDCl_3$)


8.03
8.01
7.95
7.71
7.41
7.39
7.37
7.36
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7.34
7.31
7.29
7.27
7.26
7.21
7.03
4.75
4.72
4.50
4.47
3.18
3.16
3.14
3.12
3.09
3.07
3.06
3.04
3.03
3.02
2.61
2.60
2.59
2.57
2.57
2.56
2.10
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2.07
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1.84
1.82
1.81
1.78
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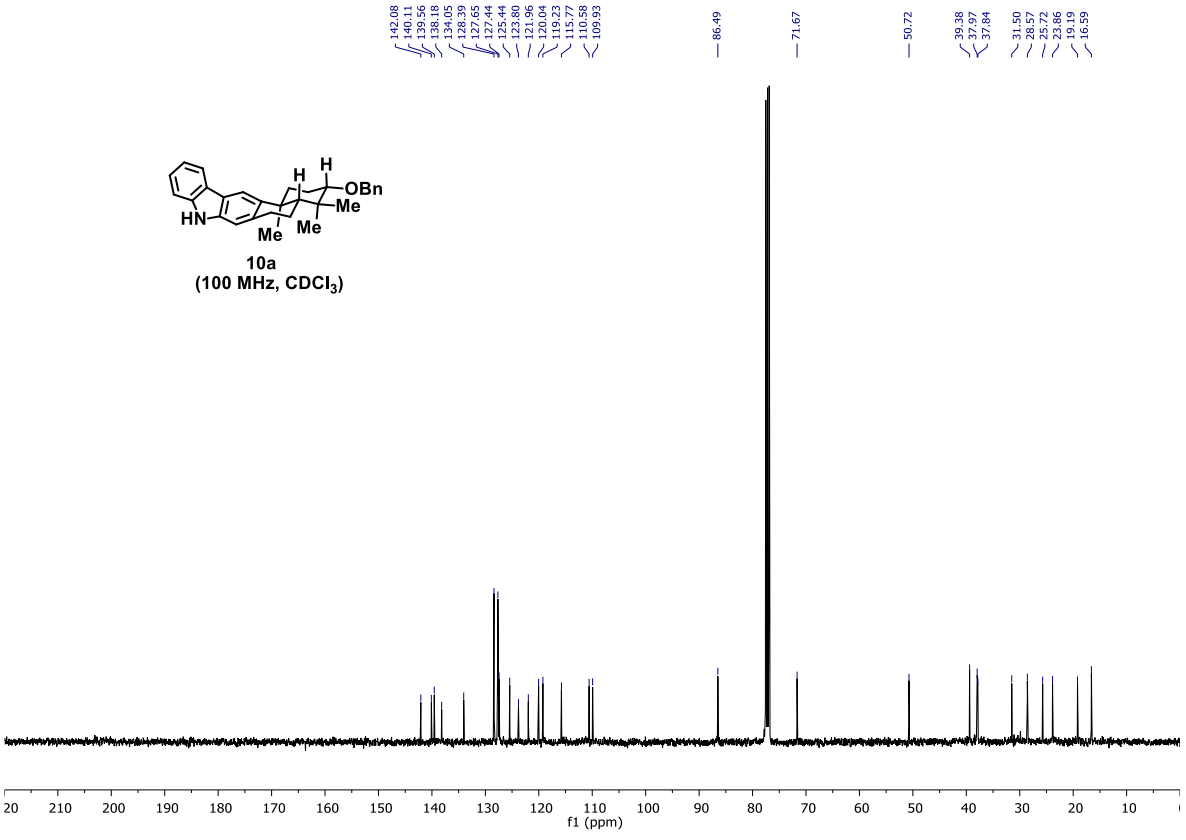
1.44
1.42
1.41
1.31
1.11
H
H
OBn
Me
HN
Me
Me
10a
(400 MHz, CDCl3)
0.95
0.98
0.96
7.02
1.09
0.98
1.00
1.03
3.09
0.89
1.16
3.08
1.13
1.03
3.01
2.98
3.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)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123.80
121.96
120.04
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115.77
110.58
109.93
86.49
71.67
50.72
39.38
37.97
37.84
31.50
28.57
25.72
23.86
19.19
16.59
H
H
OBn
Me
HN
Me
Me
10a
(100 MHz, CDCl3)
220
210
200
190
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140
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120
110
100
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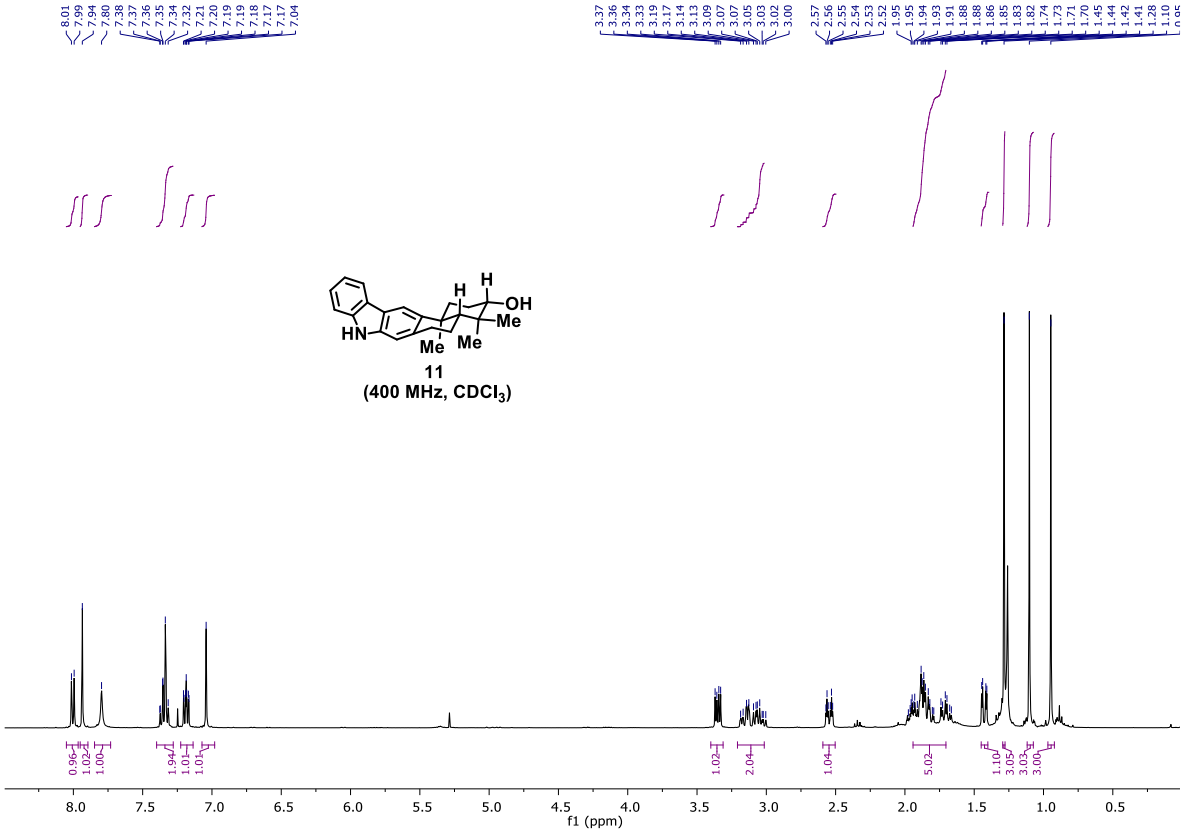
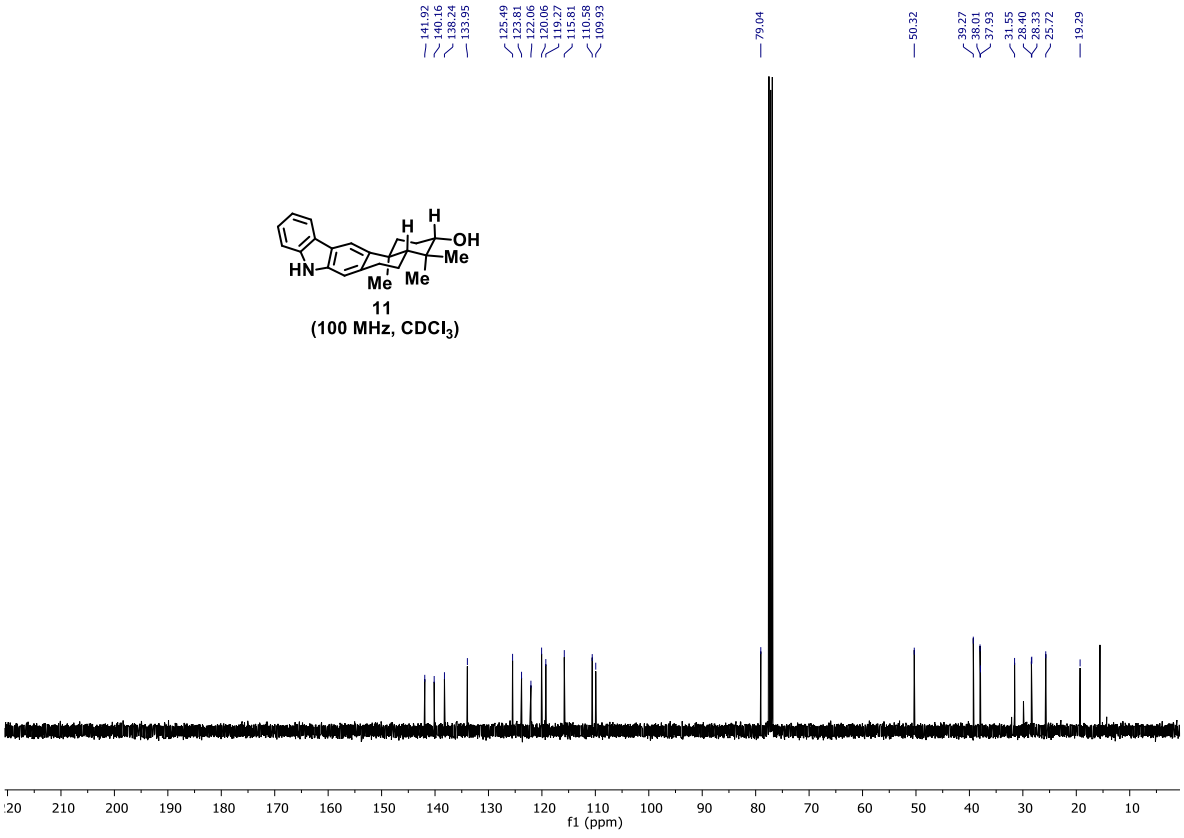
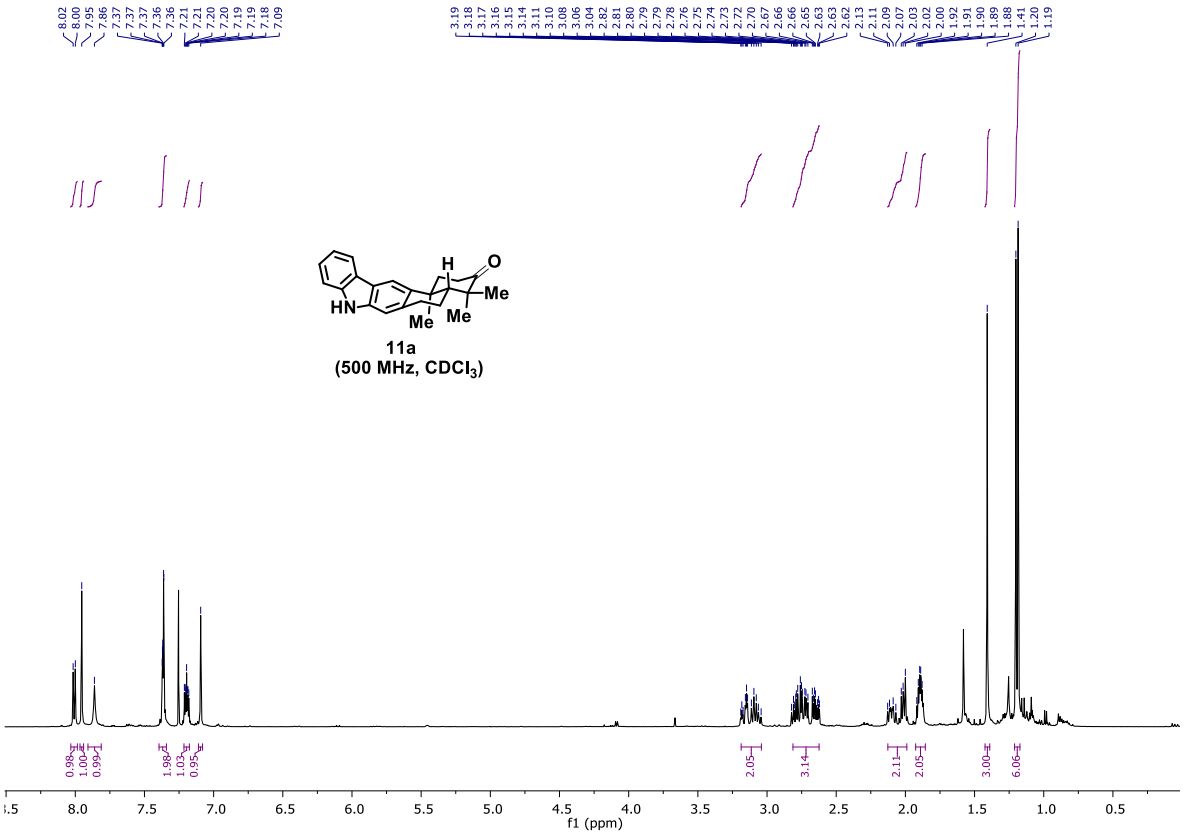
60
50
40
30
20
10
f1 (ppm)

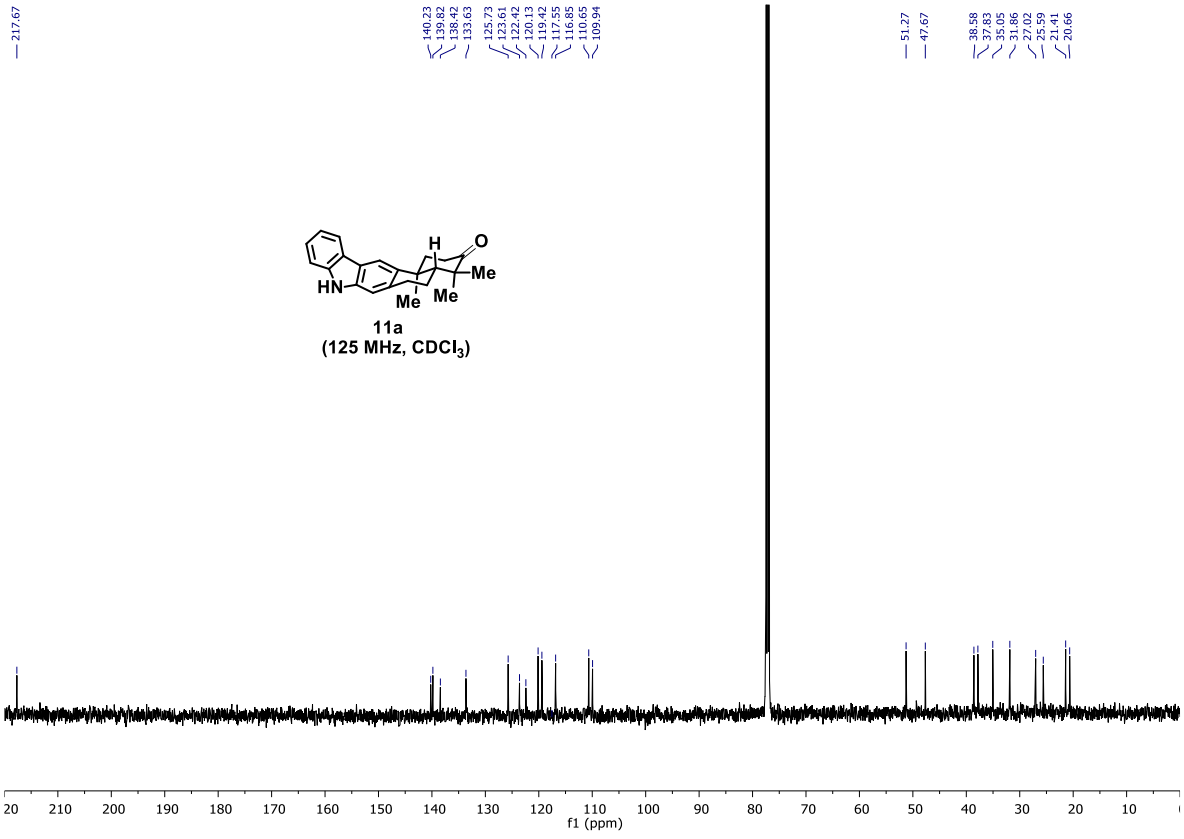


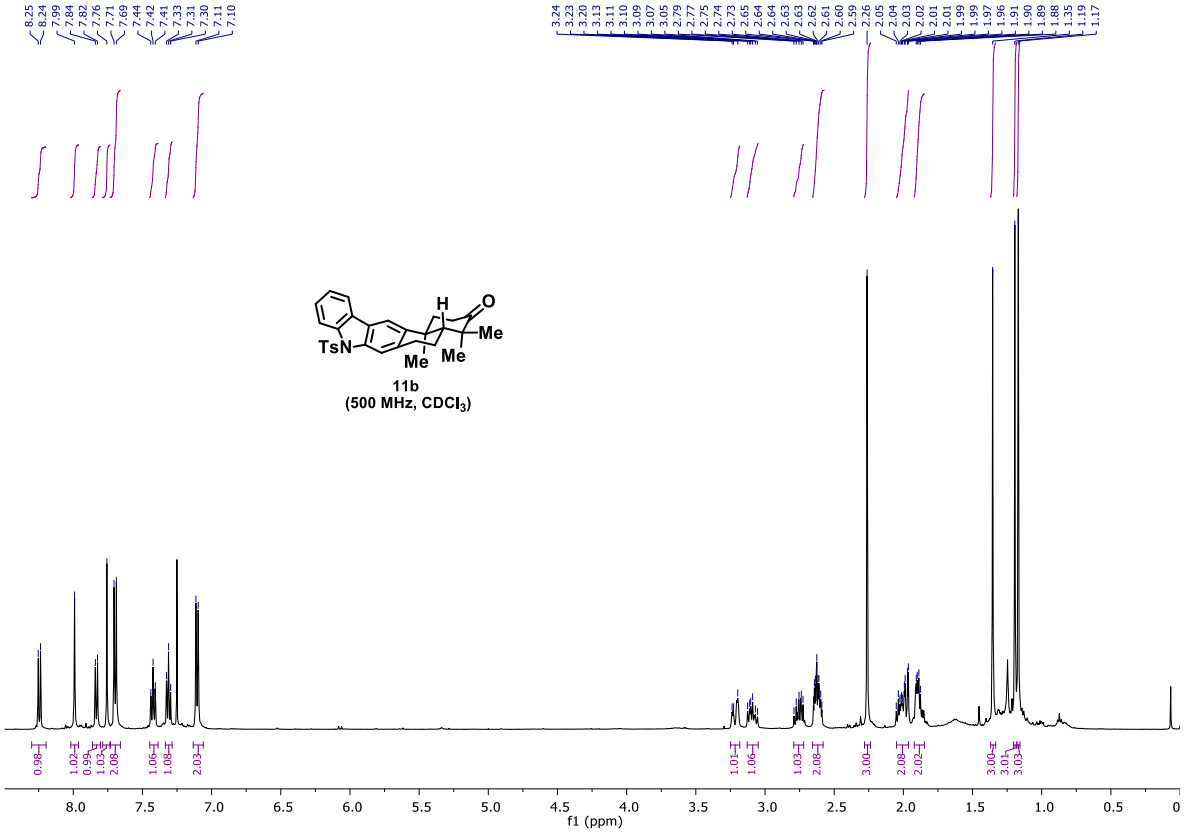
11
(400 MHz, $CDCl_3$)



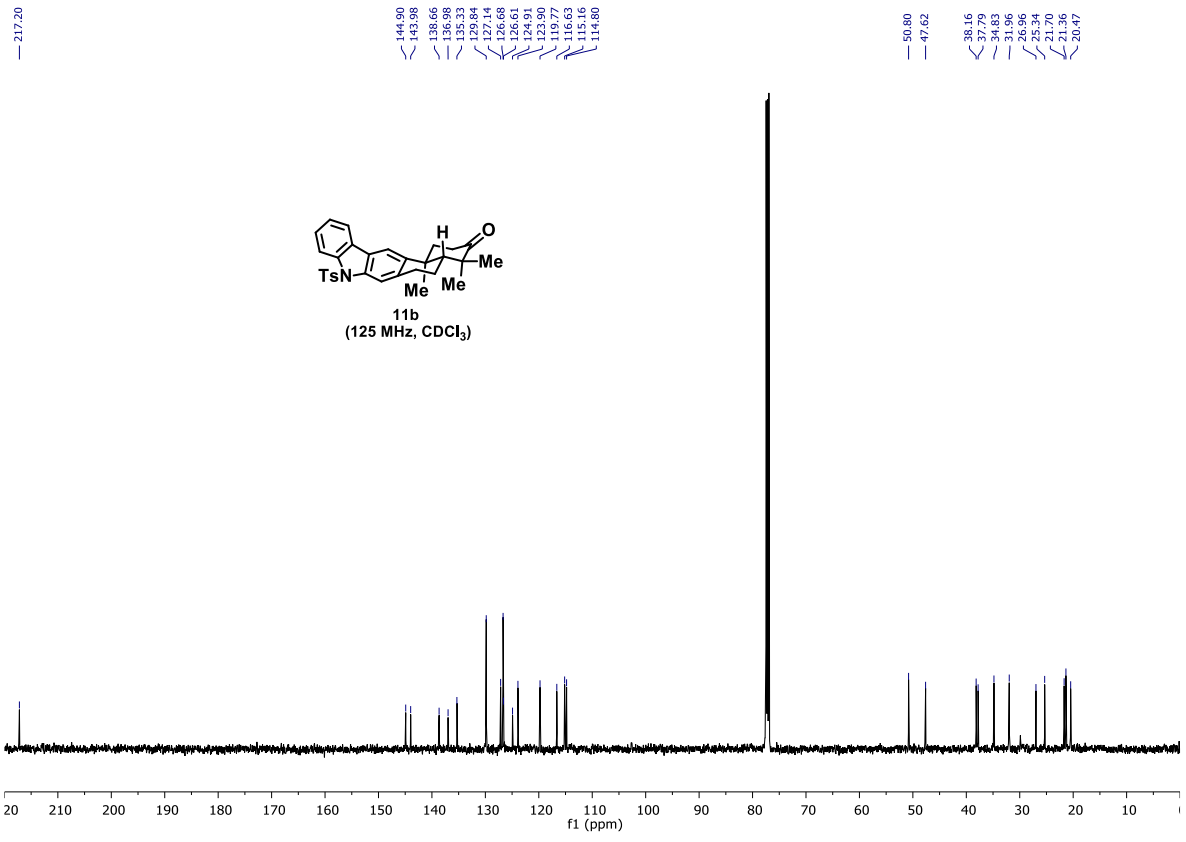
11
(100 MHz, $CDCl_3$)


11a
(500 MHz, CDCl3)
f1 (ppm)

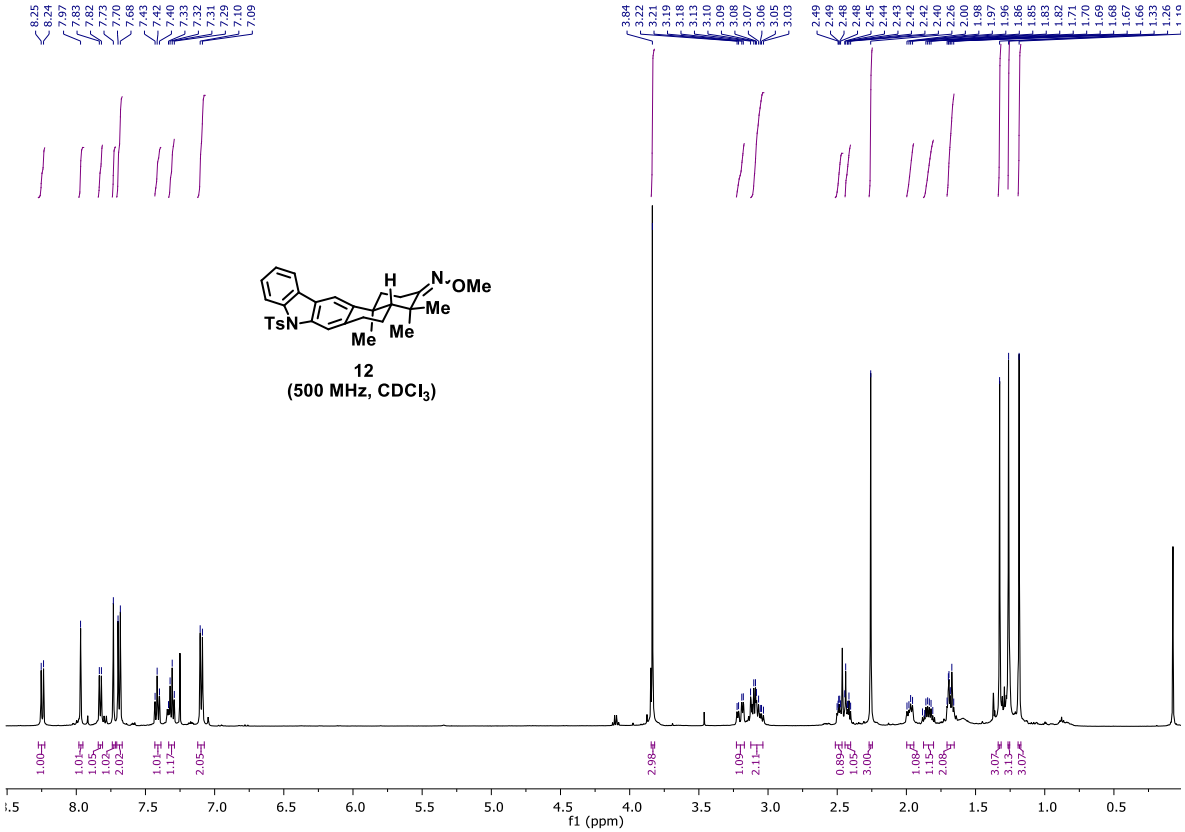

11a
(125 MHz, CDCl3)
f1 (ppm)



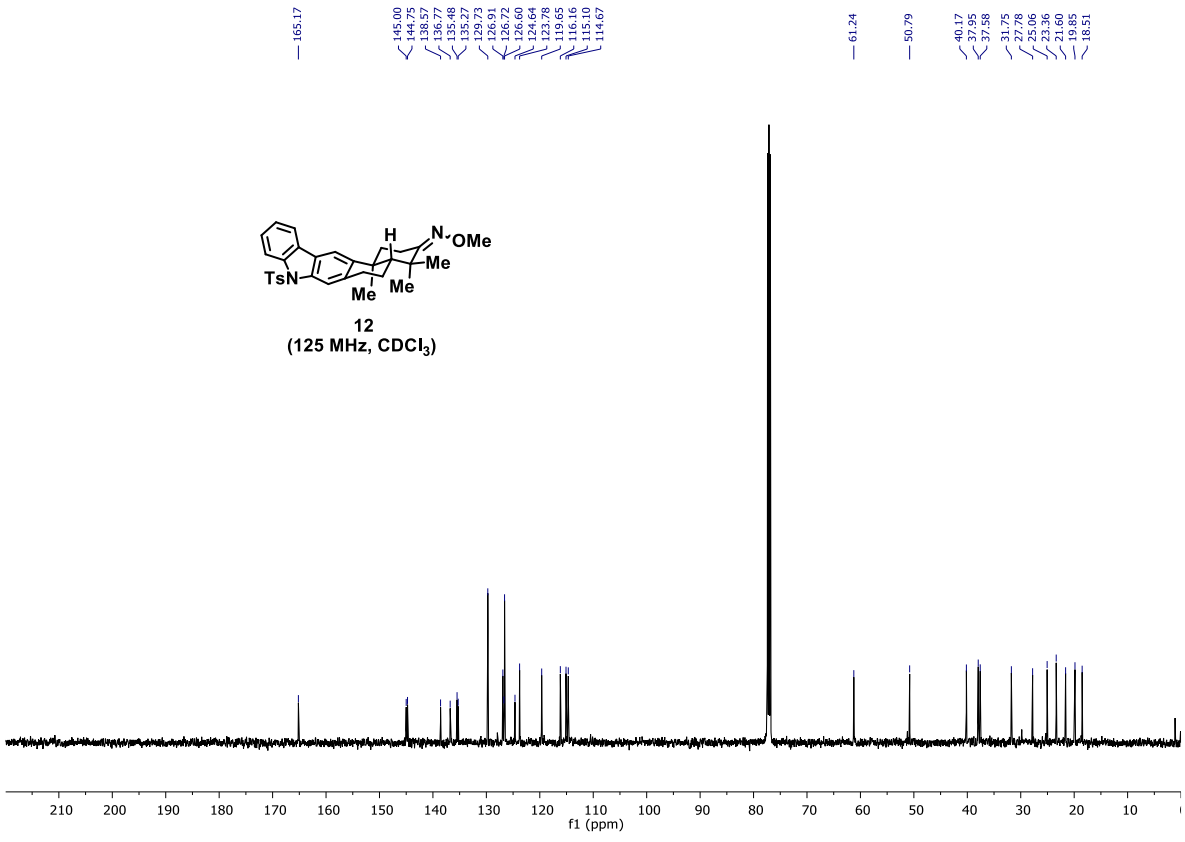
11b
(500 MHz, $CDCl_3$)



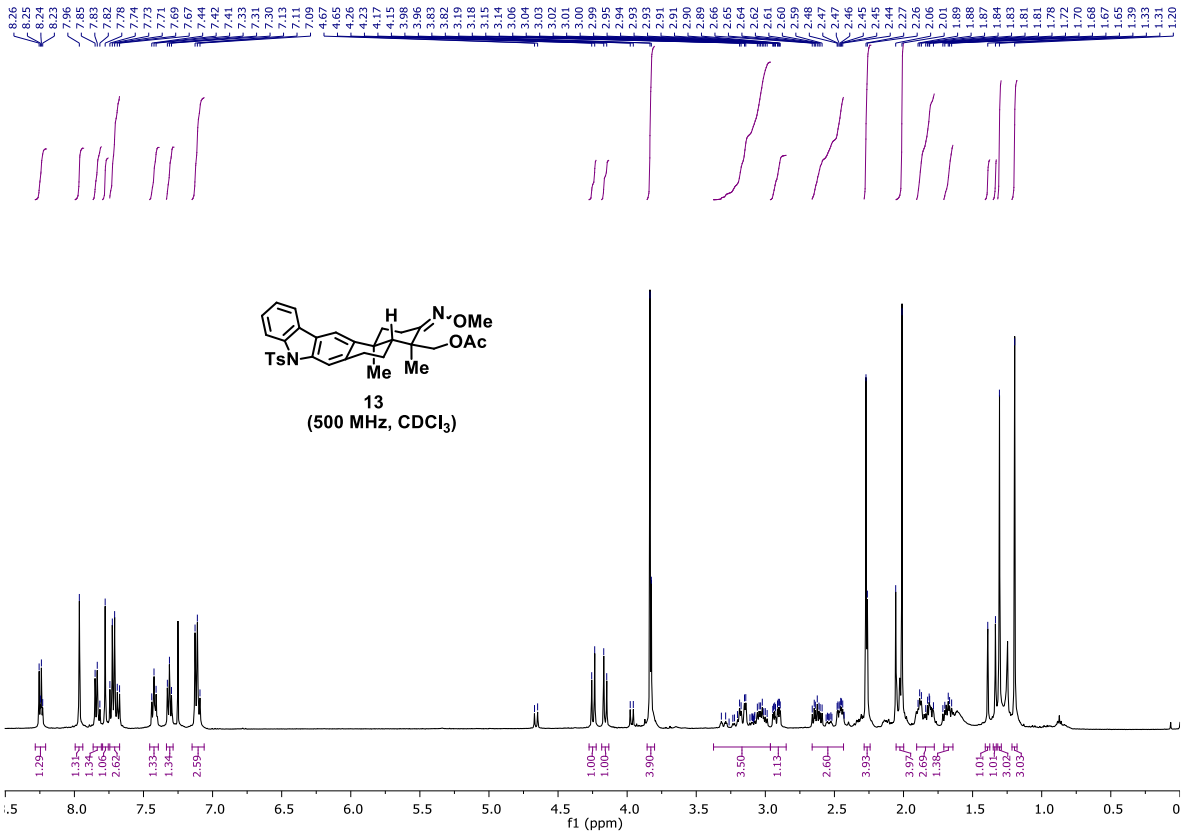
11b
(125 MHz, $CDCl_3$)



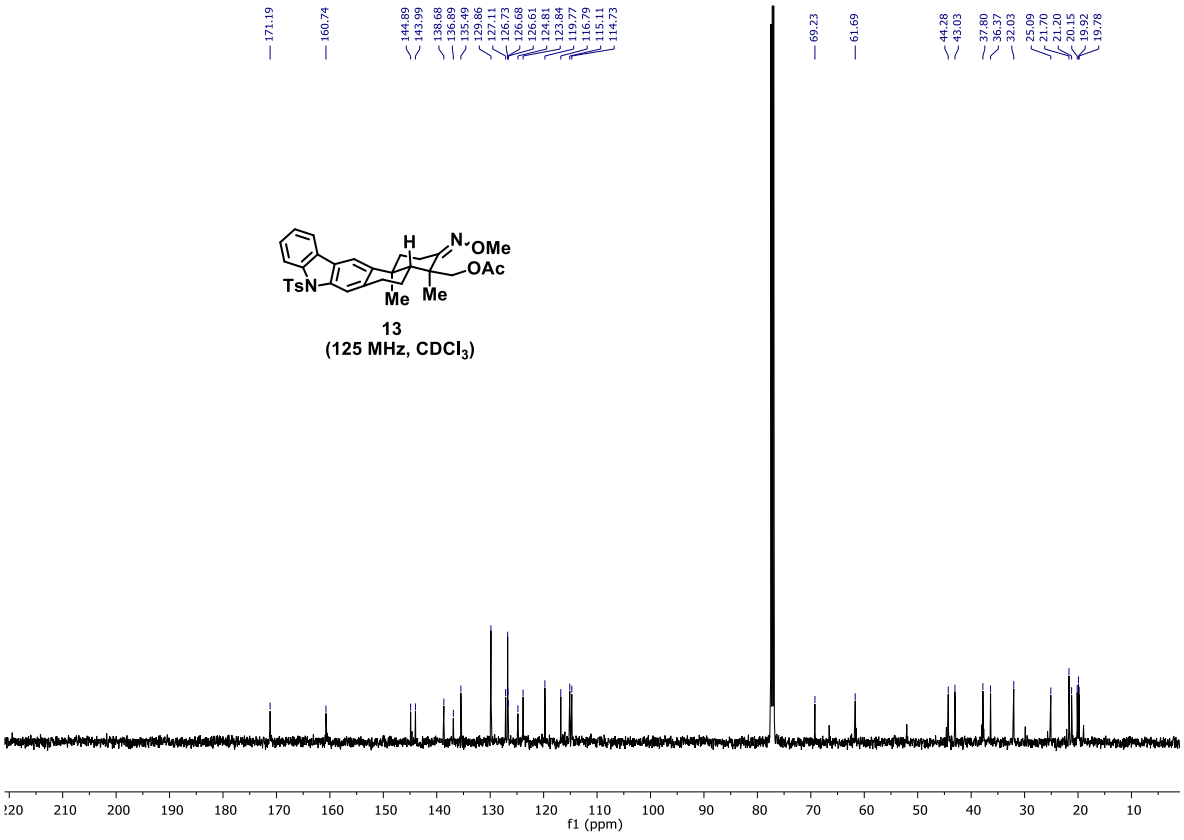
12
(500 MHz, $CDCl_3$)



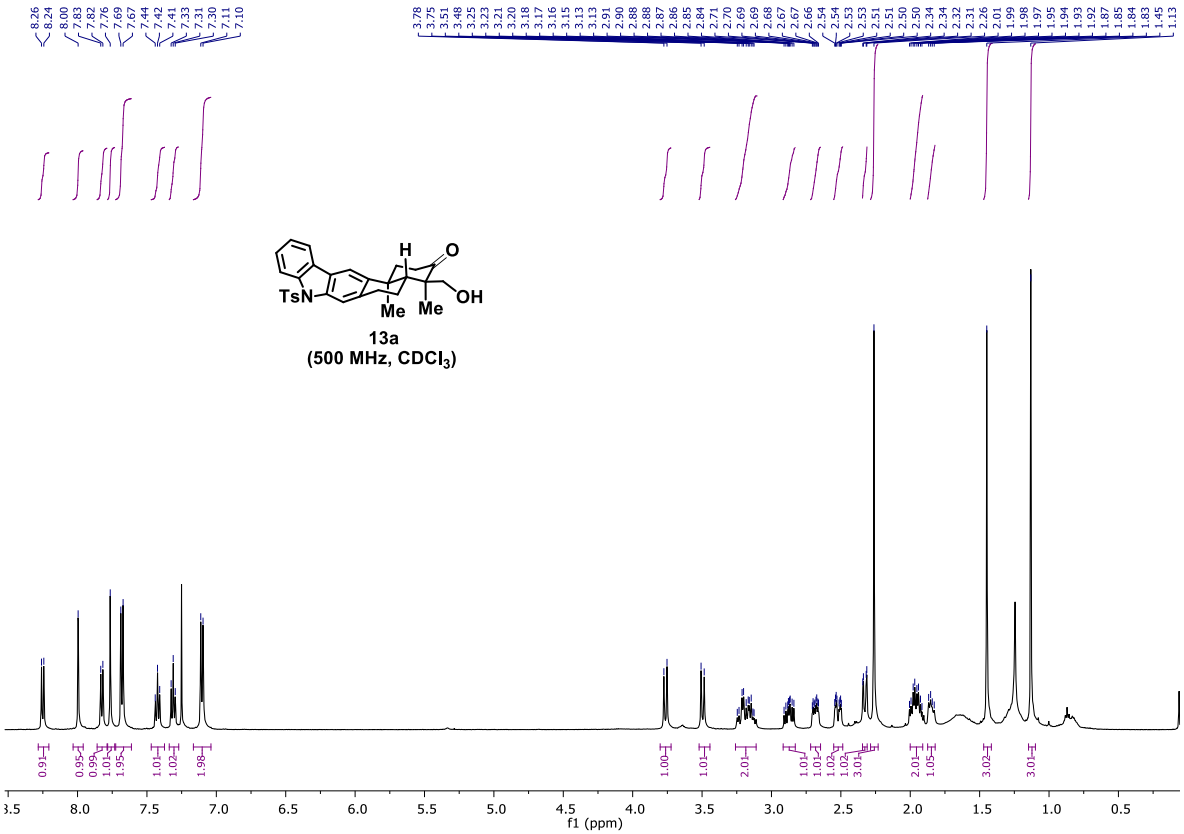
12
(125 MHz, $CDCl_3$)



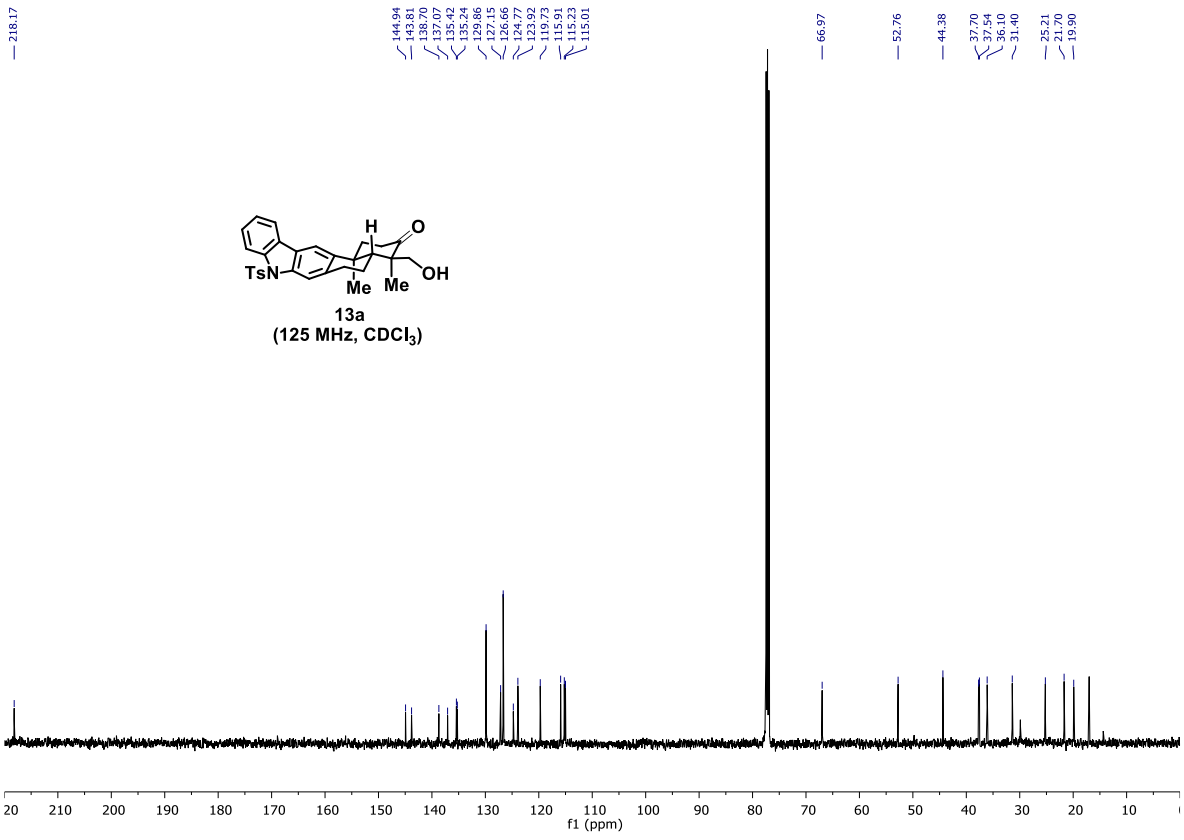
13
(500 MHz, $CDCl_3$)



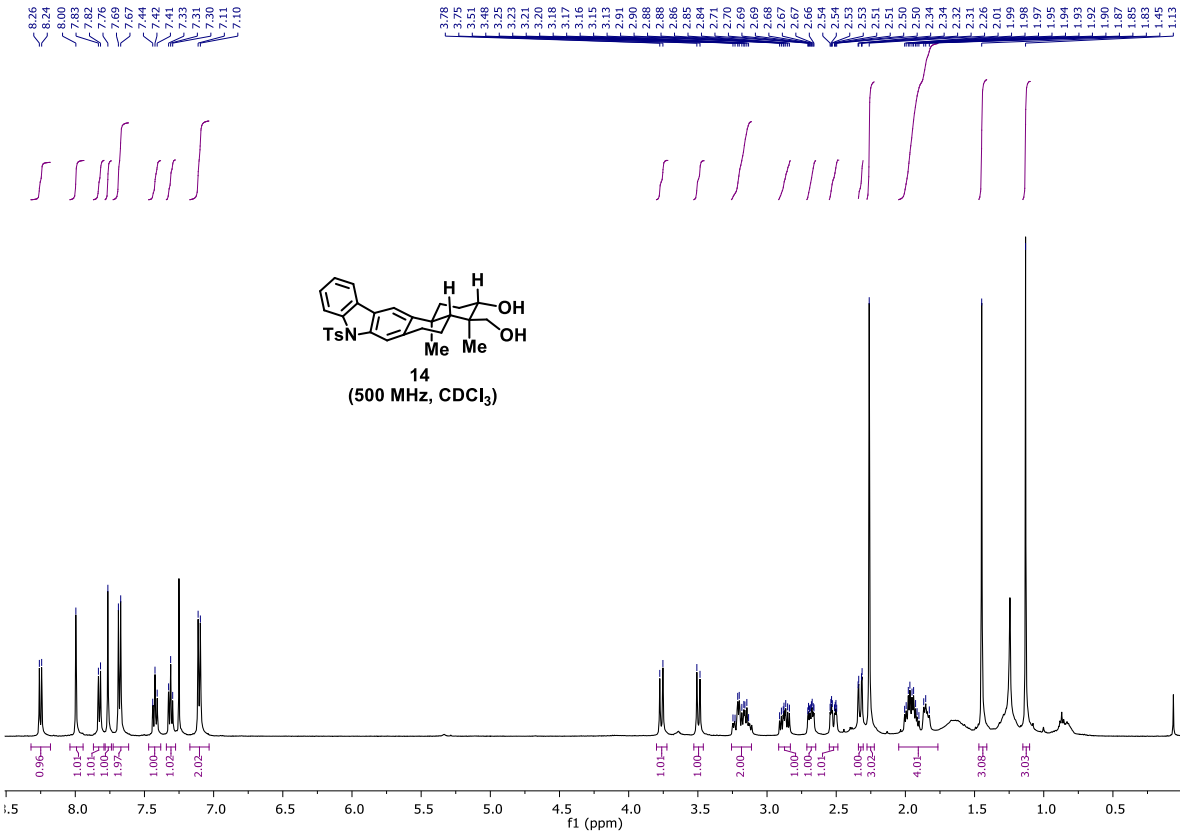
13
(125 MHz, $CDCl_3$)

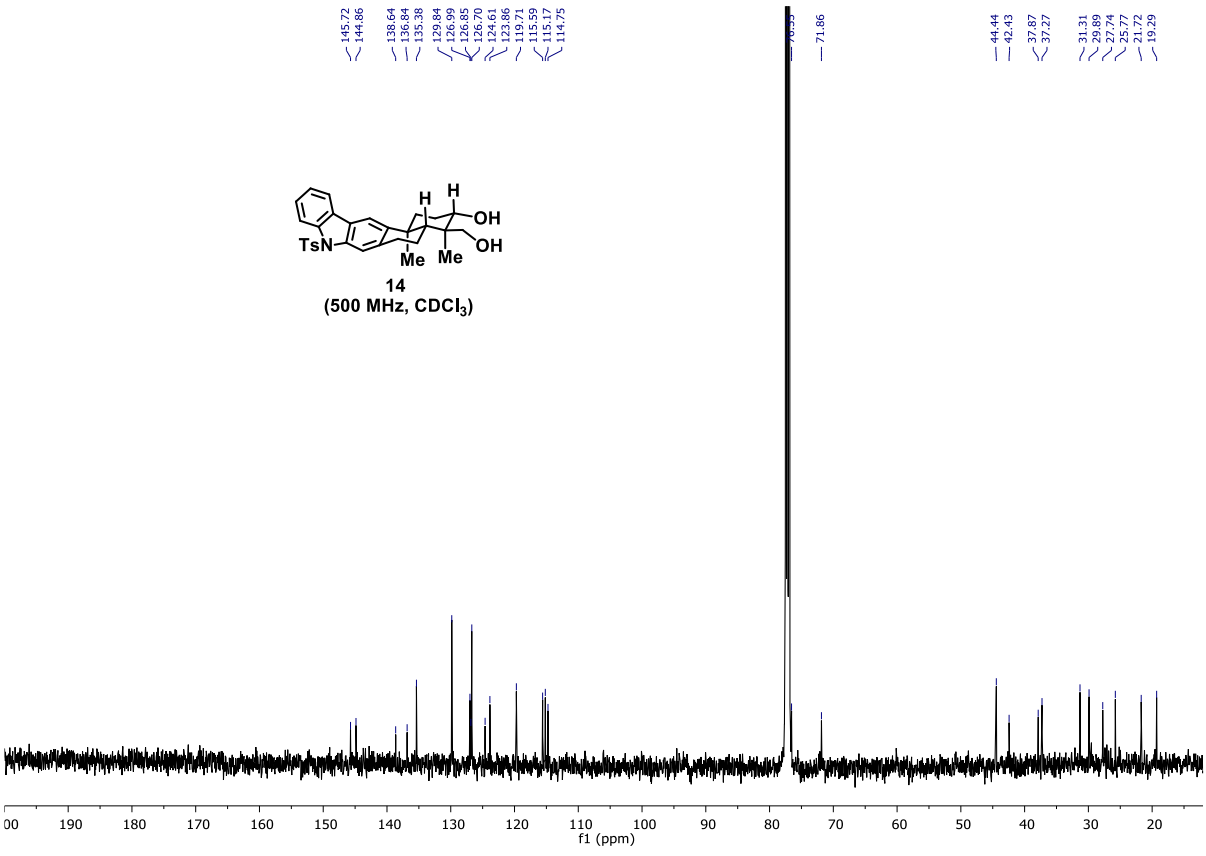


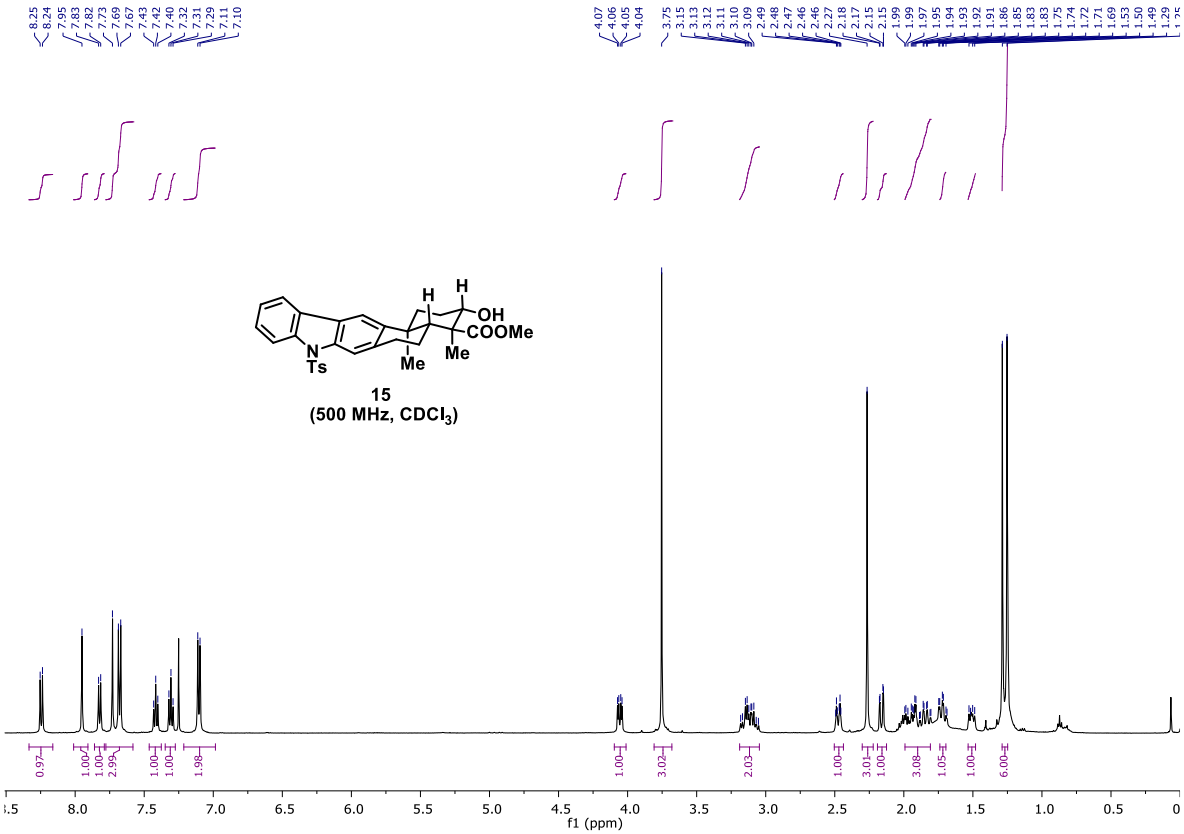
13a
(500 MHz, $CDCl_3$)



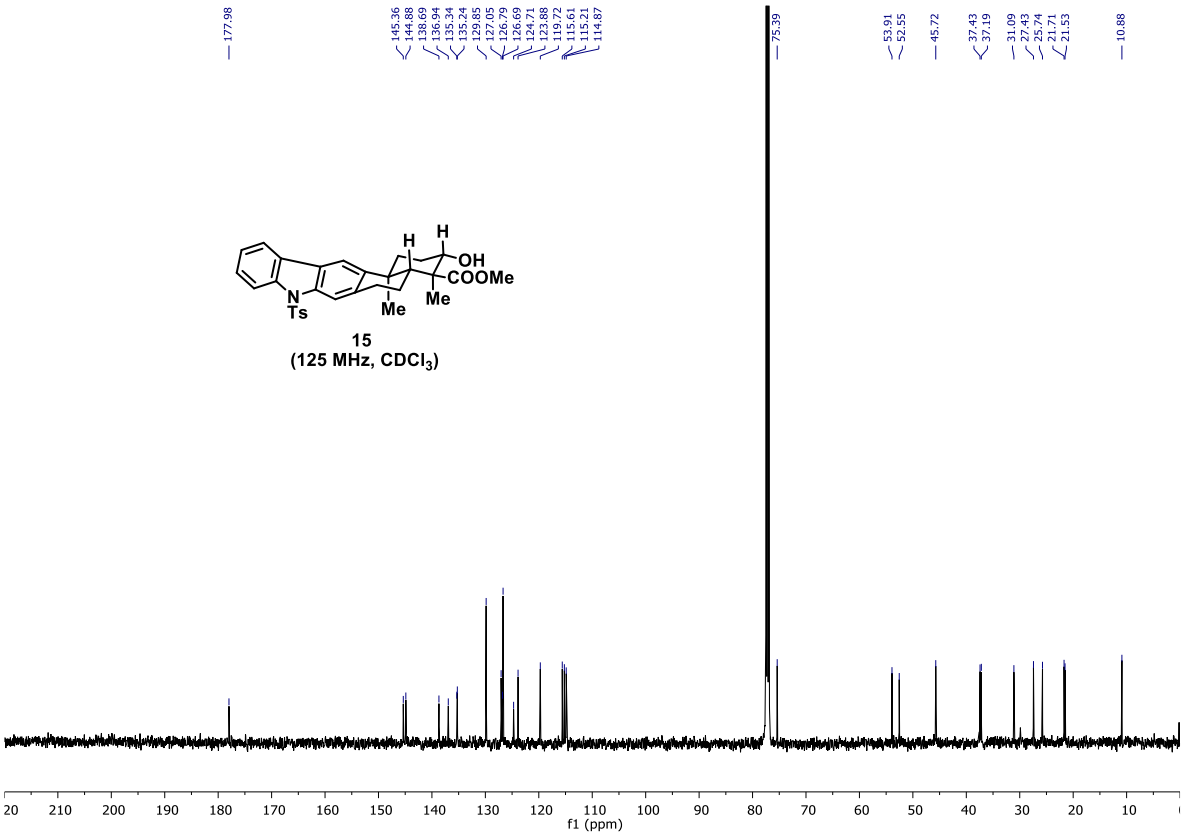
13a
(125 MHz, $CDCl_3$)


8.26 8.24 8.00 7.83 7.82 7.76 7.69 7.67 7.44 7.42 7.41 7.33 7.31 7.30 7.11 7.10
3.78 3.75 3.51 3.48 3.25 3.23 3.21 3.20 3.18 3.17 3.16 3.15 3.13 2.91 2.90 2.88 2.88 2.86 2.85 2.84 2.71 2.70 2.69 2.69 2.68 2.67 2.67 2.66 2.54 2.54 2.53 2.53 2.51 2.51 2.50 2.50 2.34 2.32 2.31 2.26 2.01 1.99 1.98 1.97 1.95 1.94 1.93 1.92 1.90 1.87 1.85 1.83 1.45 1.13
H
H
OH
OH
TsN
Me
Me
14
(500 MHz, CDCl3)
0.96 1.01 1.01 1.00 1.97 1.00 1.02 2.02 1.01 1.00 2.00 1.00 1.00 1.00 3.02 4.01 3.08 3.03
f1 (ppm)

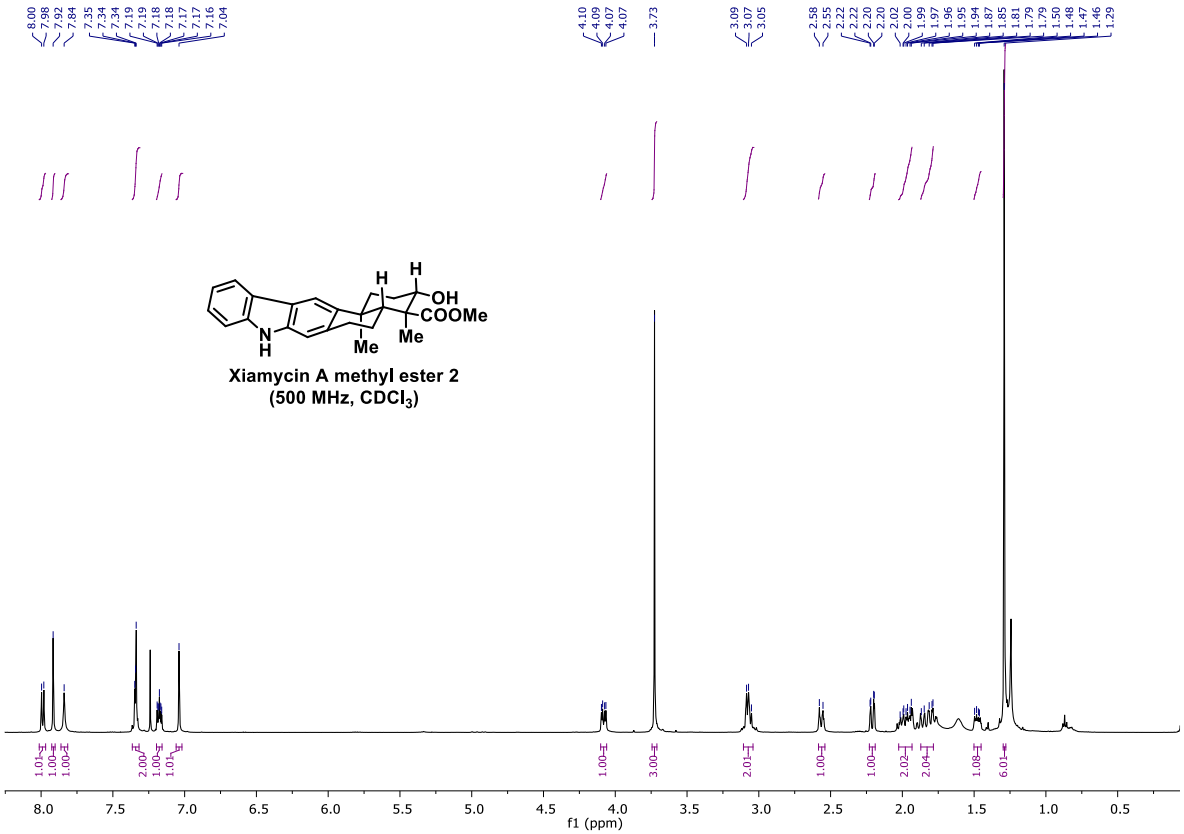

145.72 144.86 138.64 136.84 135.38 129.84 126.99 126.85 126.70 124.61 123.86 119.71 115.59 115.17 114.75
77.53 71.86
44.44 42.43 37.87 37.27 31.31 29.89 27.74 25.77 21.72 19.29
H
H
OH
OH
TsN
Me
Me
14
(500 MHz, CDCl3)
f1 (ppm)



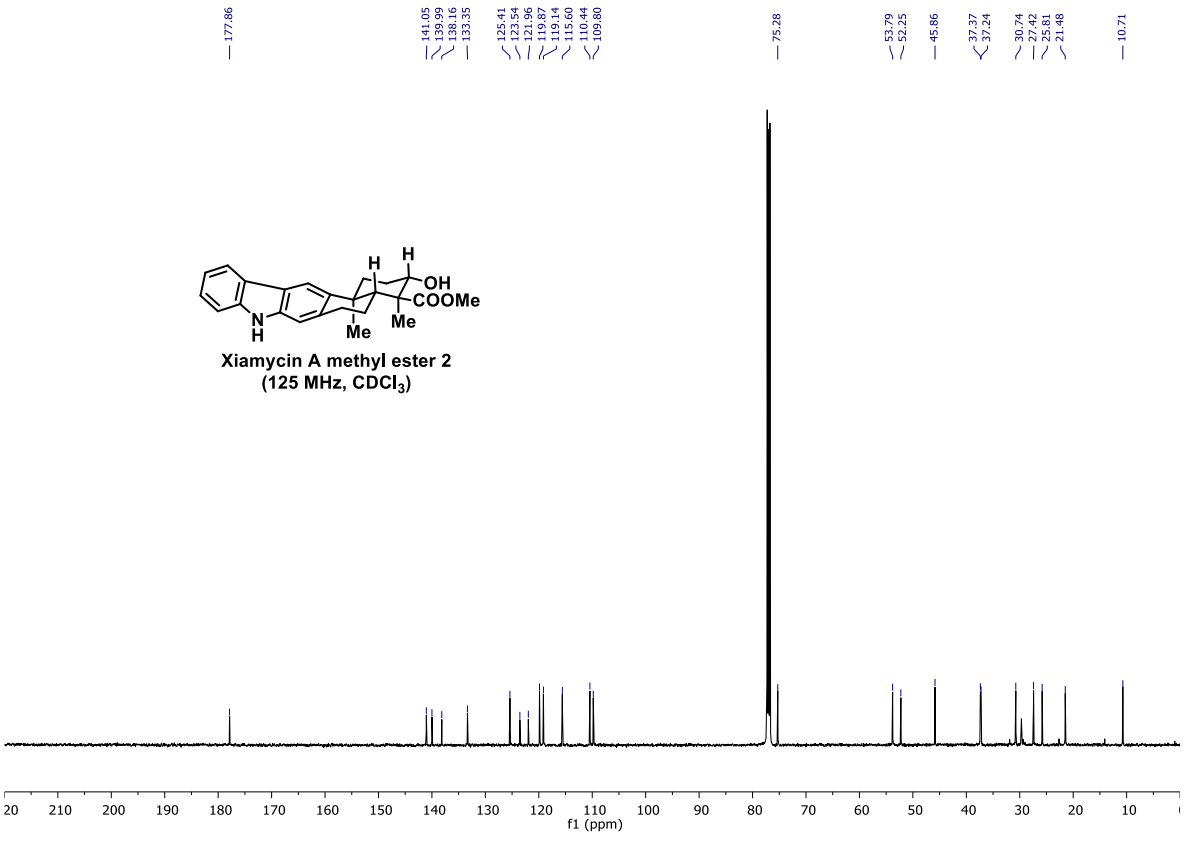
15
(500 MHz, $CDCl_3$)



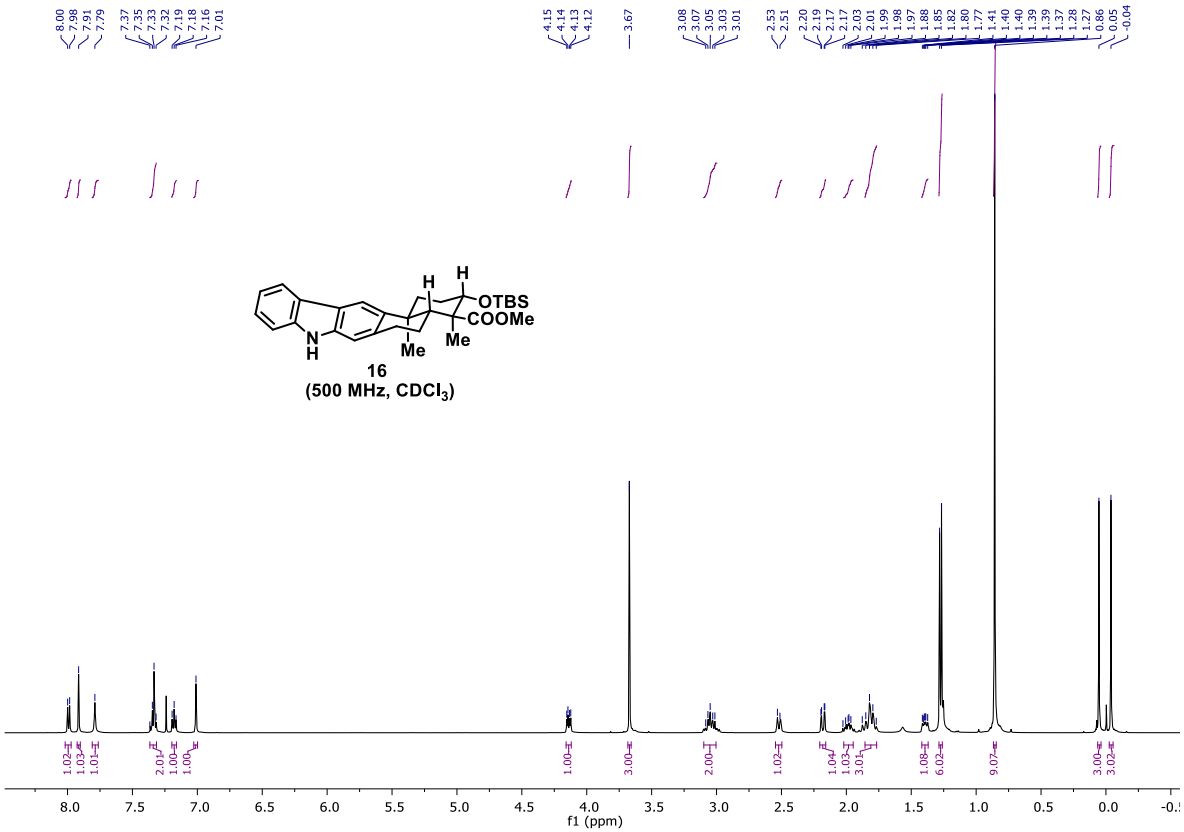
15
(125 MHz, $CDCl_3$)

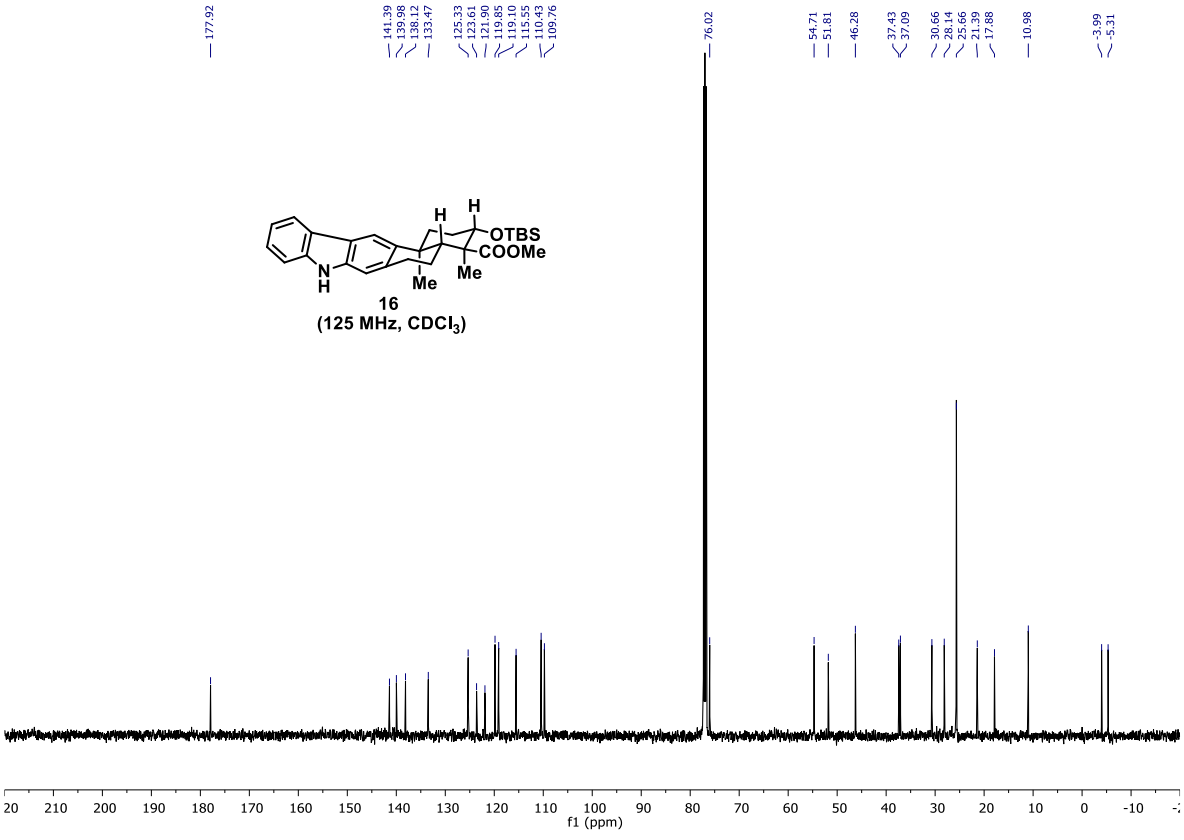


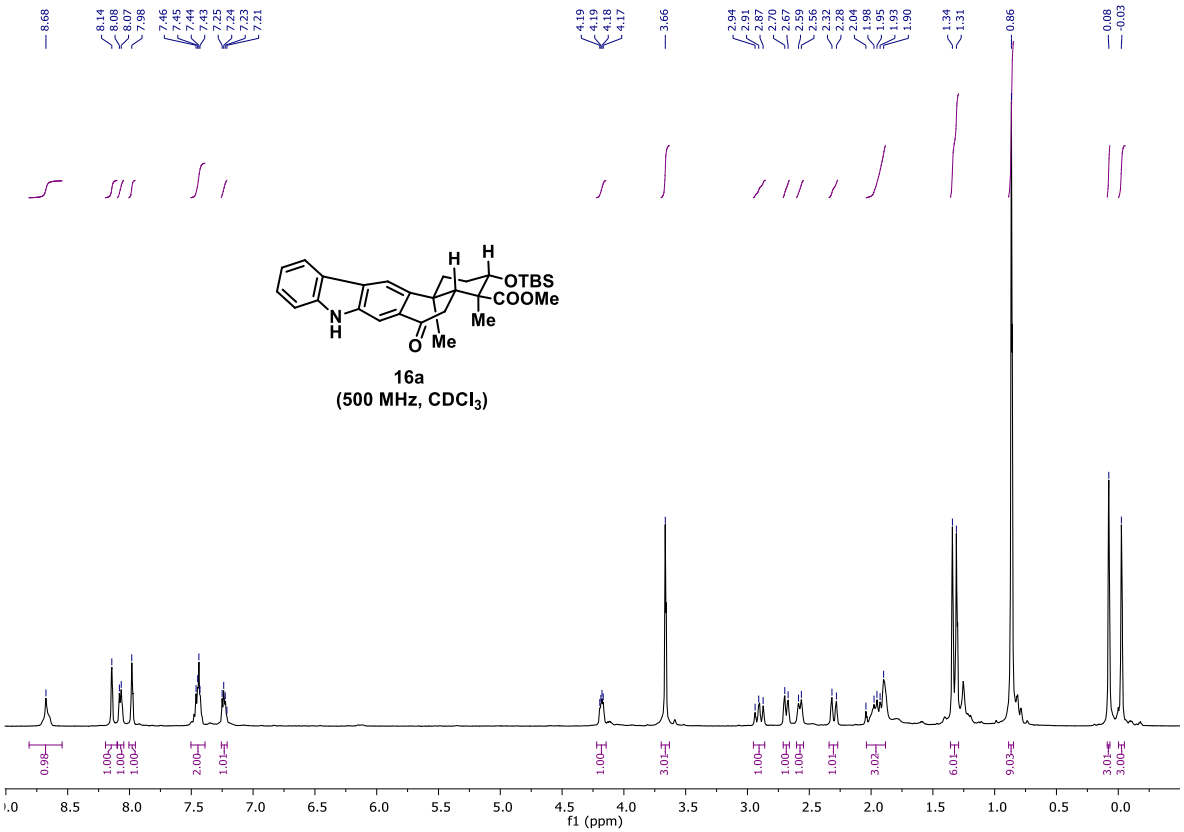
Xiamycin A methyl ester 2
(500 MHz, $CDCl_3$)



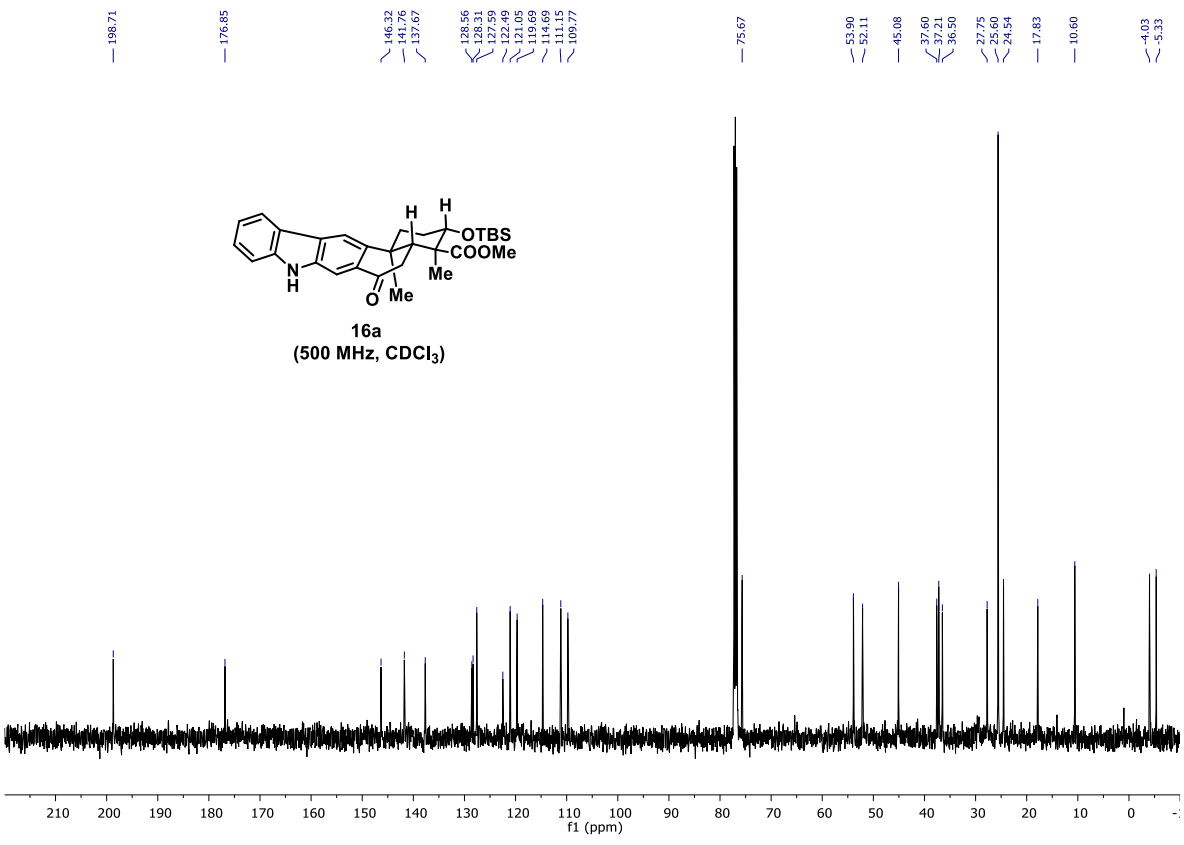
Xiamycin A methyl ester 2
(125 MHz, $CDCl_3$)


8.00
7.98
7.91
7.79
7.37
7.35
7.33
7.32
7.19
7.18
7.16
7.01
4.15
4.14
4.13
4.12
3.67
3.08
3.07
3.05
3.03
3.01
2.53
2.51
2.20
2.19
2.17
2.17
2.03
2.01
1.99
1.98
1.97
1.88
1.85
1.82
1.80
1.77
1.41
1.40
1.40
1.39
1.39
1.37
1.28
1.27
1.06
0.05
-0.04
H
H
OTBS
COOMe
N
H
Me
Me
16
(500 MHz, CDCl3)
1.02
1.03
1.01
2.01
1.00
1.00
1.00
3.00
2.00
1.02
1.04
1.03
3.01
1.08
6.02
9.07
3.00
3.02
f1 (ppm)


177.92
141.39
139.98
138.12
133.47
125.33
123.61
121.90
119.85
119.10
115.55
110.43
109.76
76.02
54.71
51.81
46.28
37.43
37.09
30.66
28.14
25.66
21.39
17.88
10.98
-3.99
-5.31
H
H
OTBS
COOMe
N
H
Me
Me
16
(125 MHz, CDCl3)
f1 (ppm)

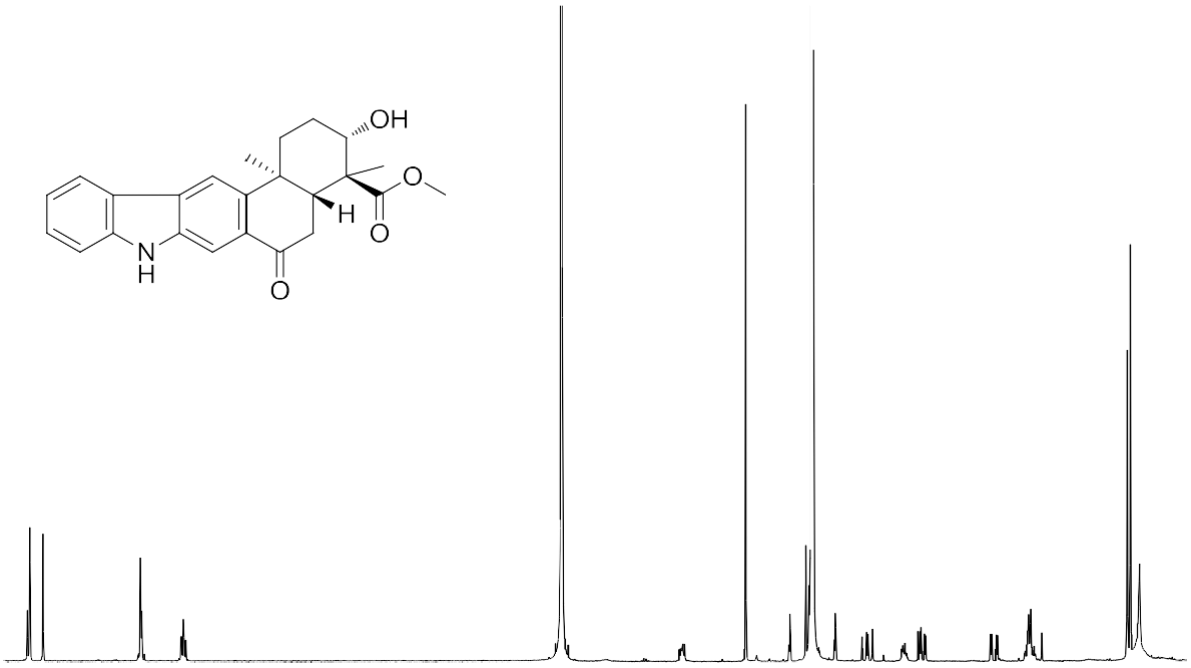


16a
(500 MHz, $CDCl_3$)

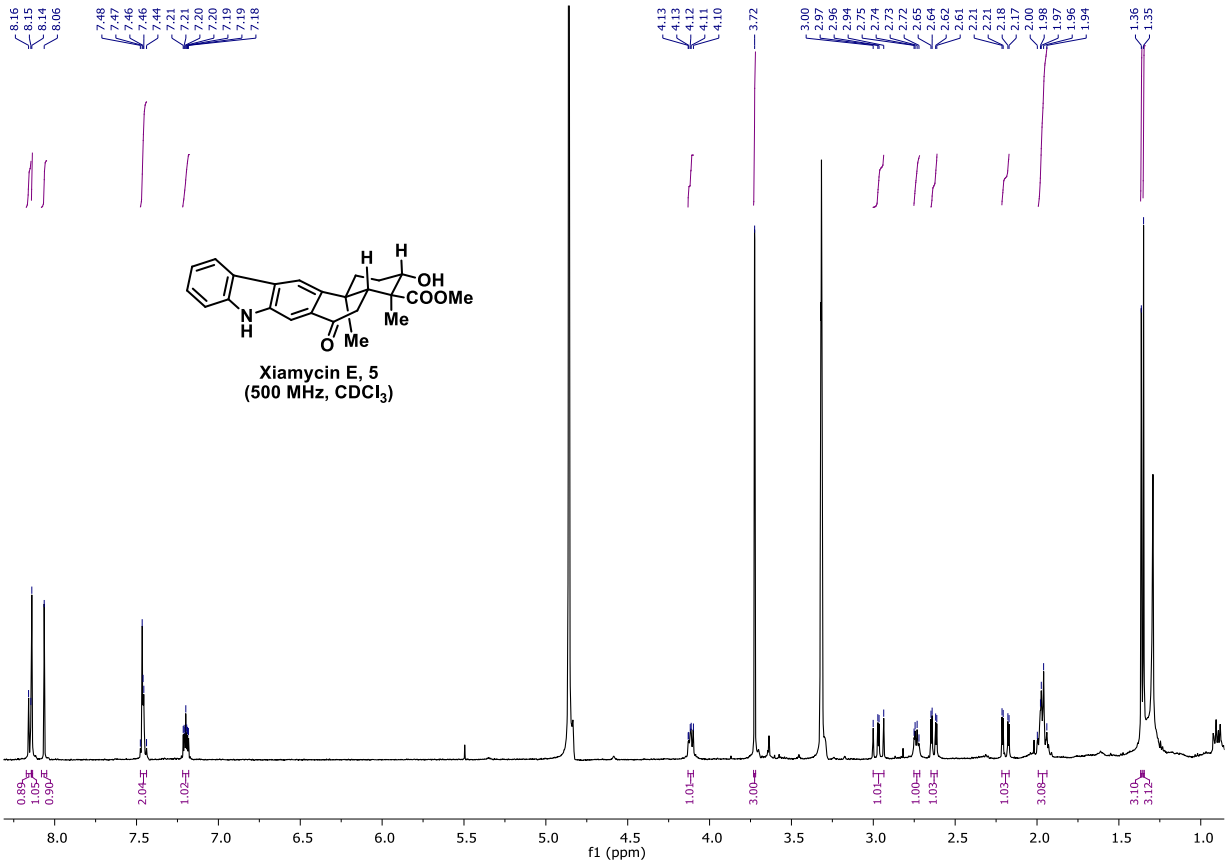


16a
(500 MHz, $CDCl_3$)

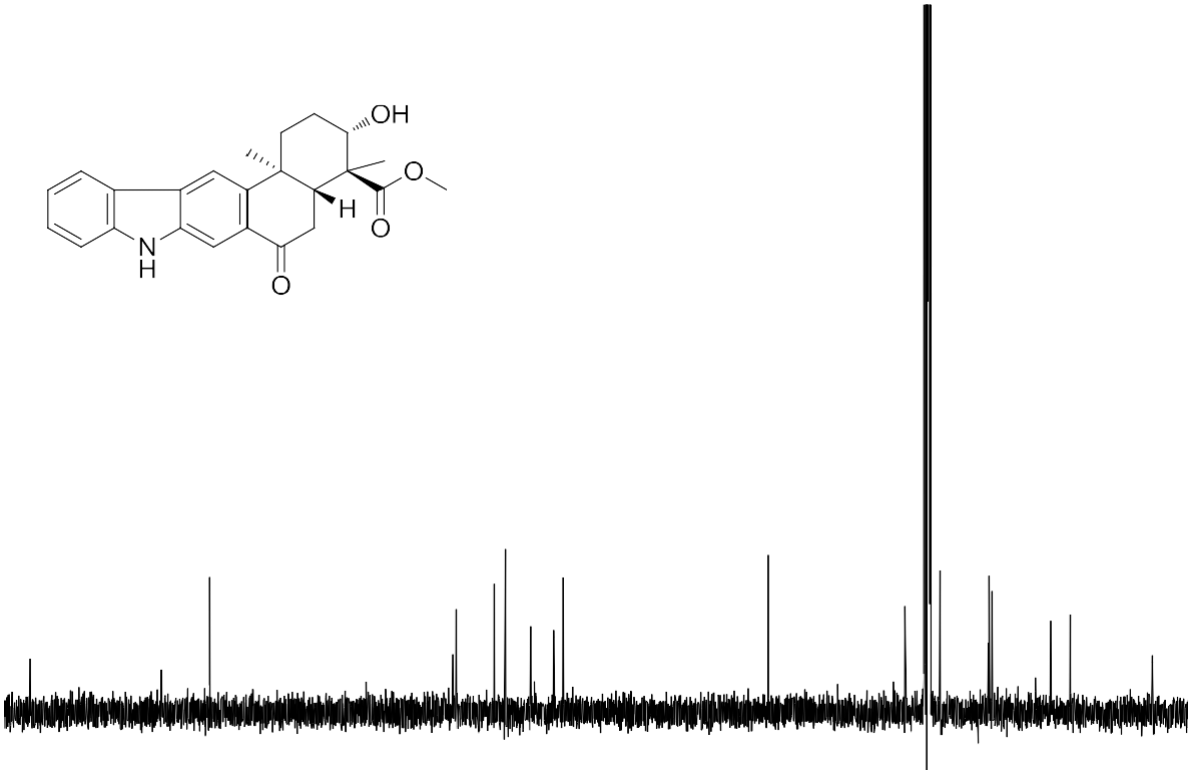
Reported: ^{1}H NMR spectrum (600 MHz) of xiamycin E in CD_3OD.



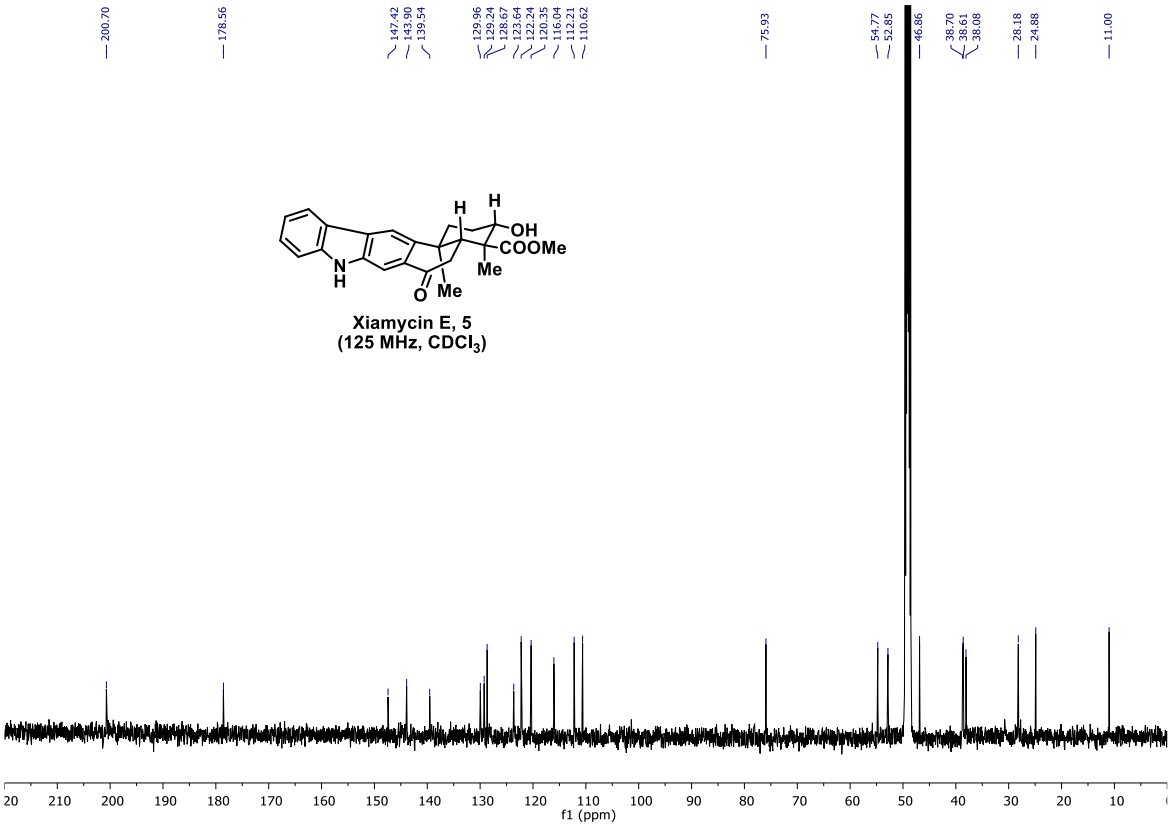
Synthesis: ^{1}H NMR spectrum (500 MHz) of xiamycin E (5) in CD_3OD.



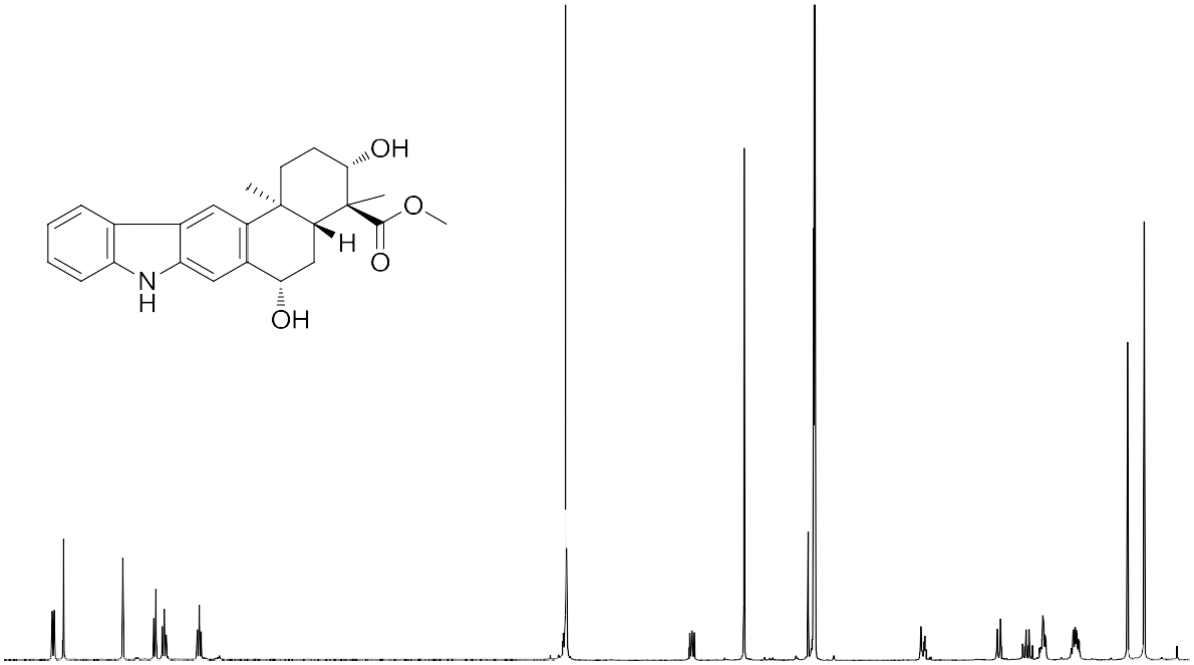
Reported: ^{13}C NMR spectrum (150 MHz) of Xiamycin E in CD_3OD.



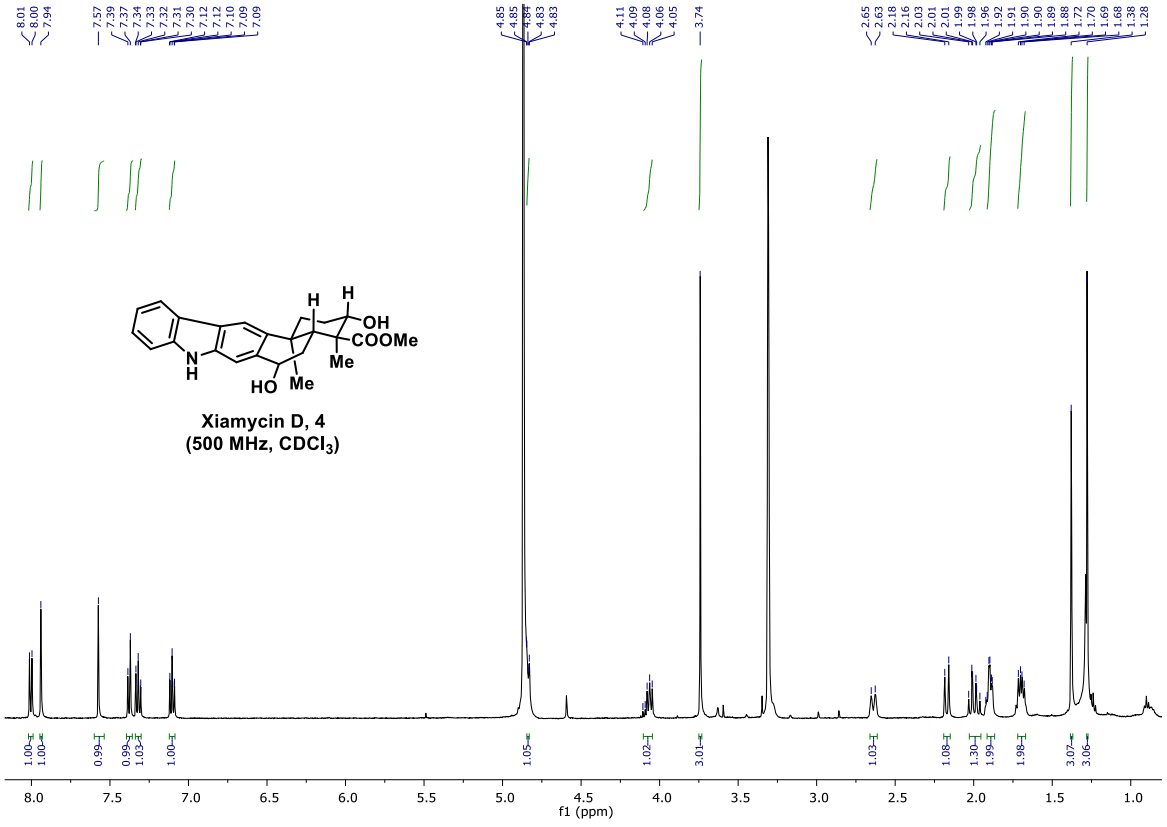
Synthesis: ^{13}C NMR spectrum (150 MHz) of Xiamycin E in CD_3OD.



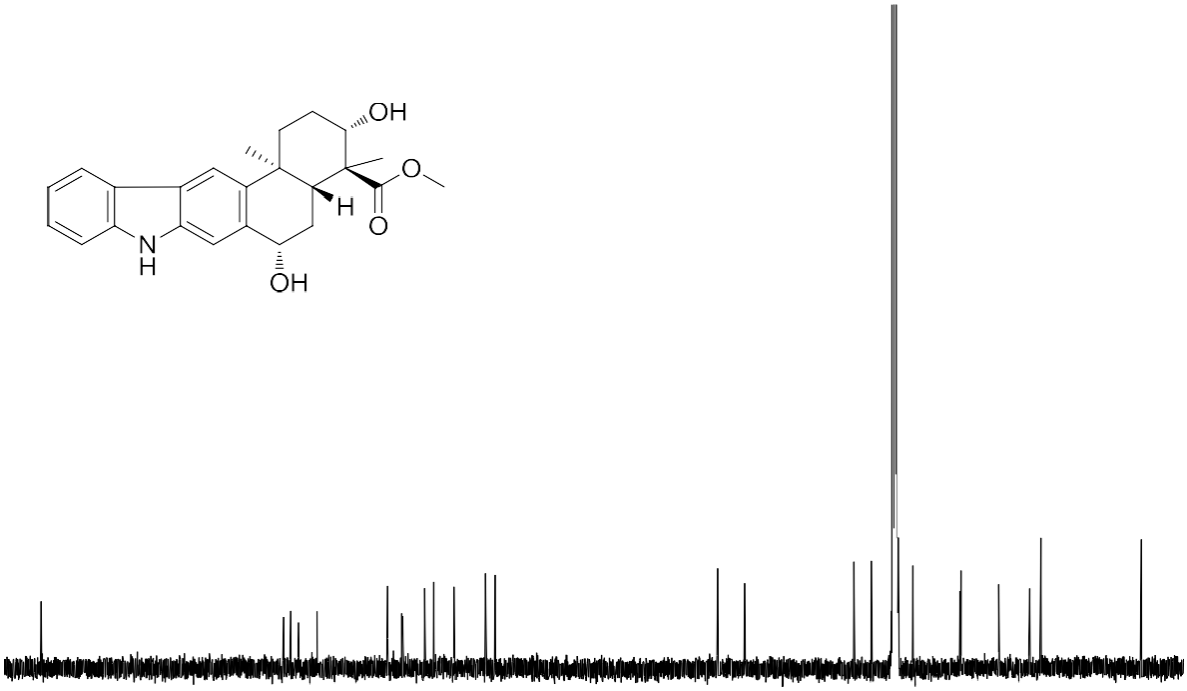
Reported: ^{1}H NMR spectrum (600 MHz) of Xiamycin D in CD_3OD.



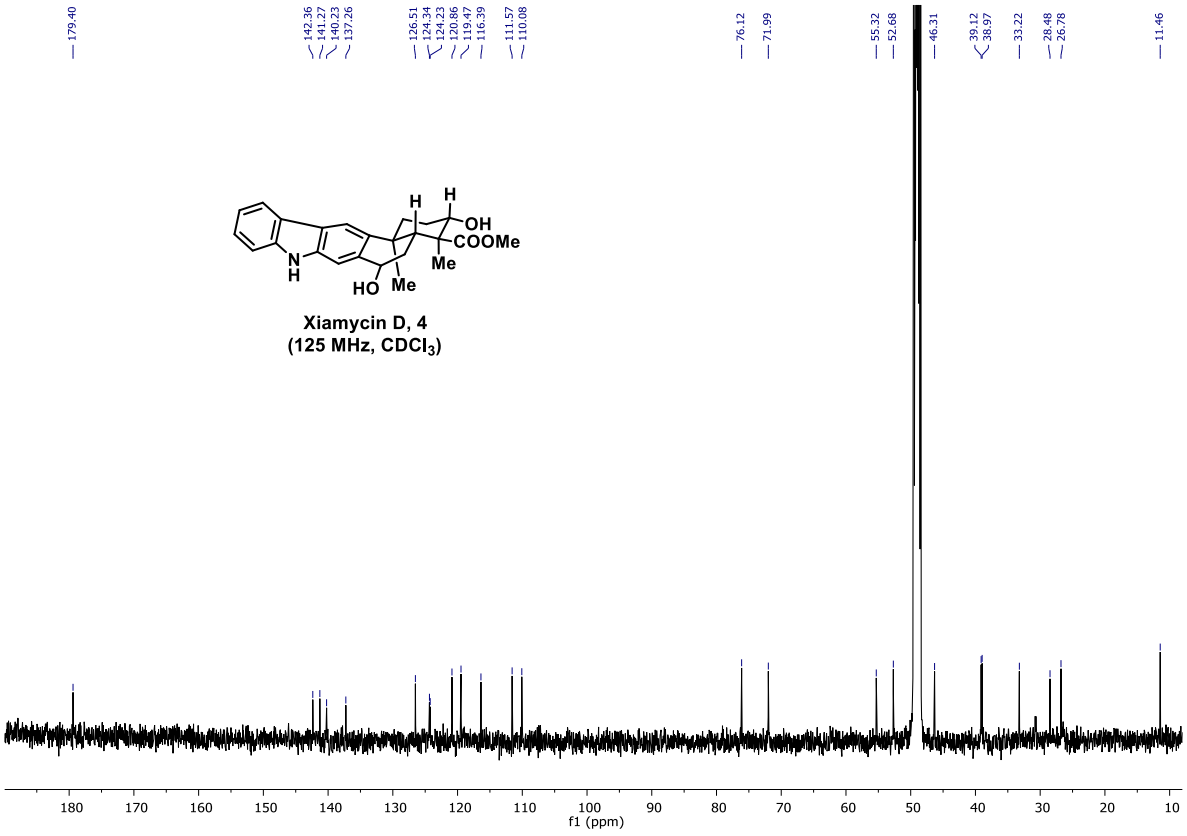
Synthesis: ^{1}H NMR spectrum (500 MHz) of Xiamycin D (4) in CD_3OD.



Reported: ^{13}C NMR spectrum (150 MHz) of Xiamycin D in CD_3OD.



Synthesis: ^{13}C NMR spectrum (125 MHz) of Xiamycin D (4) in CD_3OD.



SS

4. ^{1}H and ^{13}C NMR comparison tables:

4.1: (+)-Xiamycin D (4):

^{1}H-NMR in CD_3OD		**^{13}C-NMR in CD_3OD**	
Literature[11] 600 MHz	Synthetic 500 MHz	Literature[11] 150 MHz	Synthetic 125 MHz
1.28 (s, 3 H)	1.28 (s, 3 H)	11.4	11.4
1.38 (s, 3 H)	1.38 (s, 3 H)	26.8	26.7
1.70 (m, 2 H)	1.70 (dd, J = 11.4, 6.8, Hz, 2 H)	28.5	28.4
1.92 (m, 2 H)	1.89 (dd, *J* = 8.0, 2.6, Hz, 2 H)	33.2	33.2
2.00 (m, 1 H) (1.68, m)	2.03-1.95 (m, 1 H)	39.0	38.9
2.18 (dd, *J* = 13.0, 1.5, Hz, 1 H)	2.17 (d, *J* = 12.7 Hz, 1 H)	39.1	39.1
2.64 (ddd, *J* = 13.0, 3.5, 3.5, Hz, 1 H) (1.70 m)	2.64 (d, *J* = 12.8 Hz, 1 H)	46.3	46.3
3.74 (s, 3 H)	3.74 (s, 3 H)	52.7	52.6
4.07 (dd, *J* = 9.5, 6.5, Hz, 1 H)	4.10−4.05 (m, 1 H)	55.3	55.3
4.85 (m, 1 H)	4.85−4.83 (m, 1 H)	72.0	71.9
7.11 (dd, *J* = 8.0, 8.0, Hz, 1 H)	7.12-7.09 (m, 1 H)	76.1	76.1
7.32 (dd, *J* = 8.0, 8.0 Hz, 1 H)	7.34-7.30 (m, 1 H)	110.1	110.0
7.38 (d, *J* = 8.0, Hz, 1 H)	7.38 (d, *J* = 7.9 Hz, 1 H)	111.6	111.5
7.58 (s, 1 H)	7.57 (s, 1 H)	116.4	116.3
7.94 (s, 1 H)	7.94 (s, 1 H)	119.5	119.4
8.01 (d, 8.0, 1 H)	8.00 (d, *J* = 8.0 Hz, 1 H)	120.9	120.8
		124.2	124.2
		124.4	124.3
		126.5	126.5
		137.3	137.2
		140.2	140.2
		141.3	141.2
		142.4	142.3
		179.4	179.4

4.2: (+)-Xiamycin E (5):

^{1}H-NMR in CD_3OD		**^{13}C-NMR in CD_3OD**	
Literature[11] 600 MHz	Synthetic 500 MHz	Literature[11] 150 MHz	Synthetic 125 MHz
1.35 (s, 3 H)	1.35 (s, 3 H)	10.9	11.0
1.37 (s, 3 H)	1.36 (s, 3 H)	24.8	24.8
1.98 (m, 2 H) 1.95 (m, 1 H)	1.99-1.94 (m, 3 H)	28.1	28.1
2.19 (dd, *J* = 18.0, 3.5, 1 H)	2.19 (dd, *J* = 18.0, 3.5 Hz, 1 H)	38.1	38.0
2.63 (dd, *J* = 14.0, 3.5 1 H)	2.65-2.61 (m, 1 H)	38.6	38.6
2.74 (m, 1 H)	2.75-2.72 (m, 1 H)	38.7	38.7
2.97 (dd, *J* = 18.0, 14.0, Hz, 1 H)	3.0-2.94 (m, 1 H)	46.8	46.8
3.72 (s, 3 H)	3.72 (s, 3 H)	52.8	52.8
4.11 (m, 1 H)	4.13-4.10 (m, 1 H)	54.7	54.7
7.20 (dd, *J* = 8.0, 8.0, Hz, 1 H)	7.20 (ddd, *J* = 8.0, 5.2, 2.8 Hz, 1 H)	75.9	75.9
7.45 (dd, *J* = 8.0, 8.0 Hz, 1 H) 7.46 (d, *J* = 8.0, Hz, 1 H)	7.48-7.44 (m, 2 H)	110.6	110.6
8.06 (s, 1 H)	8.06 (s, 1 H)	112.7	112.2
8.14 (s, 1 H)	8.14 (s, 1 H)	116.0	116.0
8.15 (d, 8.0, 1 H)	8.15 (d, *J* = 7.0 Hz, 1 H)	120.3	120.3
		122.2	122.2
		123.6	123.6
		128.6	128.6
		129.2	129.2
		129.9	129.9
		139.5	139.5
		143.9	143.9
		147.4	147.4
		178.5	178.5
		200.7	200.7

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