Synthesis of Alkaloid (–)-205B via Stereoselective Reductive Cross-Coupling and Intramolecular [3+2] Annulation

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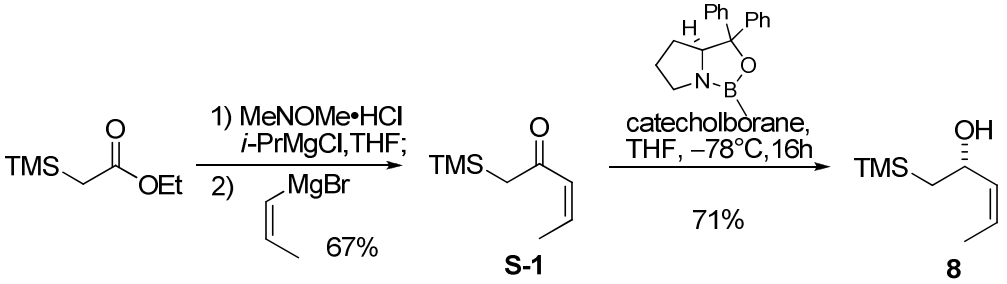
Supporting Information

General Information: All reactions were carried out in flame-dried flasks under an atmosphere of dry argon unless otherwise specified. Toluene and dichloromethane were dried over activated alumina columns and sparged with argon prior to use. Diethyl ether and tetrahydrofuran were dried and distilled from sodium-benzophenone. Ti(O*i*-Pr)$_4$ (Aldrich, 97%) was distilled prior to use (69-70 °C, < 1 Torr). *sec*-Butyllithium and *i*-PrMgCl (Aldrich) were titrated by the method of Love *et al.*[1] Enantiomeric excess of chiral alcohol **(+)-8** was determined by using Mosher's ester analysis.[2] Enantiomeric excess of homoallylic amine **(+)-9** was determined by using Mosher's amide analysis.[3] All other solvents and reagents were used as received from commercial suppliers. Thin-layer chromatography was performed on 250 μm E. Merck silica gel plates (60F-254). Flash column chromatography was performed using Silicycle SiliaFlash P60 silica gel, 40-63 μm particle size. ^{1}H NMR data were recorded at 400 MHz on a Bruker AM-400 in CD_3Cl, DMSO (D6) or C_6D_6. ^{13}C NMR data were recorded at 100 MHz on a Bruker AM-400. ^{13}C NMR data are reported by listing the chemical shift along with a parenthetical description of the substitution (q = three attached protons, t = two attached protons, d = one attached proton, s = no attached proton). Infrared spectra were recorded on a PerkinElmer SpectrumOne FT-IR instrument. LRMS spectra were acquired on a Varian 500-MS mass spectrometer under soft ionization mode. HRMS (ESI-TOF-MS) was performed on Thermo LTQ Orbitrap Mass Spectrometry at Scripps Florida. Optical rotations were measured using a quartz cell with a 0.5 mL capacity and a 10 cm path length.

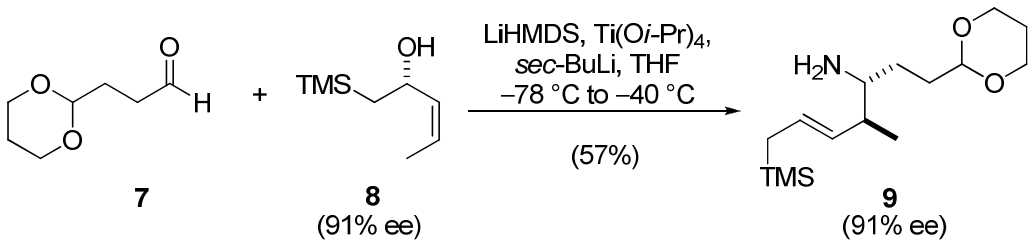


Preparation of (+)-(*R*,*Z*)-1-(trimethylsilyl)pent-3-en-2-ol (8): To a flame-dried 200 mL 3-neck round bottom flask was charged 2.4 g (100 mmol) of magnesium turnings and 2 mg of iodine followed by 10 mL of anhydrous THF under argon. The mixture was refluxed at 60 °C until it changed from brown to water white. A solution of 7.2 g (60.0 mmol) of (*Z*)-1-bromopropene in 60 mL of anhydrous THF was added via a syringe at a rate to maintain reflux. The resulting gray solution was heated at 60 °C for 2 h. In the meanwhile, to a suspension of *N*,*O*-dimethylhydroxyamine hydrochloride (4.9 g, 52.5 mmol) in 100 mL of THF was sequentially added isopropyl magnesium chloride (52.5 mL, 105 mmol, 2.0 M in THF) and ethyl 2-(trimethylsilyl)acetate (8.0 g, 50.0 mmol) via cannula at –20 °C under argon. The reaction mixture was stirred at –10 °C for 30 minutes, resulting in a gray suspension. The freshly prepared (*Z*)-propenyl magnesium bromide was cooled to rt and added via a cannula at –20 °C over 30 min. After stirring for additional 2 h at 0 °C, the reaction was quenched with saturated aqueous NH_4Cl, and then diluted with 200 mL of diethyl ether. The aqueous phase was extracted with 100 mL of diethyl ether (2×). The combined organic extracts were washed with saturated aqueous NaCl, dried ($MgSO_4$) and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 100 g of silica gel (2.5% ethyl acetate in hexanes) to give 5.2 g of ketone **S-1** as a water white oil.

To a solution of (*S*)-CBS[4] (1.3 g, 5.0 mmol) in 100 mL of anhydrous THF was added 5.0 mL (5.0 mmol, 1.0 M in toluene) of catecholborane at 0 °C under argon. After stirring for 0.5 h, the reaction mixture was cooled to –78 °C. A solution of enone **S-1** (0.77 g, 5.0 mmol) in 10 mL of THF was added via a syringe pump over 1 h, and resulting colorless solution was stirred at –50 °C for 16 h. The reaction was quenched by sequential addition of 1 mL of methanol and 20 mL of saturated aqueous NH_4Cl. The aqueous phase was extracted with 100 mL of diethyl ether (2×). The combined organic extracts

were dried ($MgSO_4$), concentrated *in vacuo* and chromatographed over 50 g of silica gel (10% EtOAc in hexanes) to give give 0.55 g (71% yield, d:r ≥ 20:1, *E*:*Z* ≥ 20:1, 91% ee by Mosher's ester[2]) of allylic alcohol **8** as a colorless oil.

Data for alcohol **8**: IR (neat) 3365, 2956, 2872, 1658, 1461, 1380 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 9H, TMS), 0.86 (ABq, *J* = 14.0, 8.4 Hz, 1H, CH_2TMS), 1.01 (ABq, *J* = 14.0, 6.0 Hz, 1H, CH_2TMS), 1.35 (br, 1H, OH), 1.67 (dd, *J* = 6.8, 1.2 Hz, 3H, CH_3), 4.63 (td, *J* = 8.4, 6.4 Hz, 1H, C<u>H</u>OH), 5.41 (m, 2H, CH=CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.00 (q), 14.04 (q), 27.74 (t), 65.96 (d), 125.70 (d), 136.45 (d); $[\alpha]_D^{25}$ = 23.0° (*c* 0.10, $CHCl_3$).

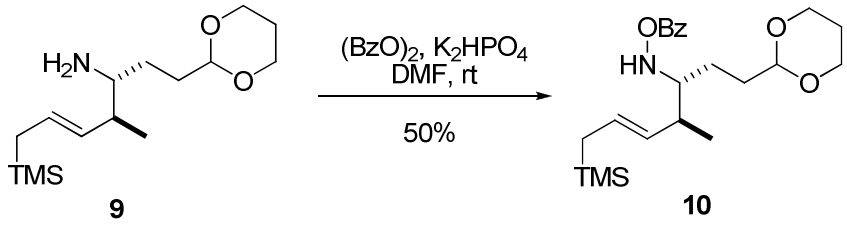


7 **8** (91% ee) **9** (91% ee)

Preparation of (+)-(3*R*,4*S*,*E*)-1-(1,3-dioxan-2-yl)-4-methyl-7-(trimethylsilyl)hept-5-en-3-amine (9): To a solution of 1.44 g (10.0 mmol) of aldehyde **7** in 10 mL of anhydrous THF was added 10.0 mL (10.0 mmol, 1.0 M in THF) of LiHMDS via cannula over 20 min at –78 °C under argon. The reaction mixture turned into a clear pale yellow solution. After 20 min, a solution of 2.96 mL (2.84 g, 10.0 mmol) of Ti(O*i*-Pr)$_4$ in 20 mL of anhydrous diethyl ether was added via cannula over 20 min. After stirring for 5 min, 14.3 mL (20.0 mmol, 1.4 M in cyclohexane) of *sec*-BuLi was added via cannula over 20 min. The temperature of the orange solution was raised to –40 °C over 15 min, then the mixture was stirred at –40 °C for an additional 0.5 h, resulting in a dark brown suspension. Next, the reaction mixture was cooled back to –78 °C, and a solution of 0.78 g (5.0 mmol) of alcohol **8** in 5 mL of THF was added to the brown suspension via cannula over 10 min. The mixture was allowed to rise to room temperature and stirred for 16 h. Finally, sequential addition of 10 mL of diethyl ether and 10 mL of saturated aqueous NH_4Cl was followed by vigorous stirring for 0.5 h. The aqueous phase was separated and extracted with 2 portions of 20 mL of diethyl ether. The combined organic extracts were washed sequentially with 20 mL of saturated aqueous $NaHCO_3$, 20 mL of

brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified immediately via chromatography over 50 g of silica gel (300 mL of EtOAc, 210 mL of CH_2Cl_2:MeOH:NH_4OH = 200:10:1, 220 ml of CH_2Cl_2:MeOH:NH_4OH = 200:10:1 and 230 mL of CH_2Cl_2:MeOH:NH_4OH = 200:30:1) to give 0.47 g (57%, d:r ≥ 20:1, *E*:*Z* ≥ 20:1, 91% ee by Mosher's amide[3]) of homoallylic amine **9** as a colorless oil. The relative stereochemistry of **9** was assigned by analogy to our previous studies.[5]

Data for amine **9**: IR (neat) 2954, 2849, 1654, 1450, 1246 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 9H, TMS), 1.06 (d, *J* = 7.2 Hz, 3H, CH_3), 1.28 and 2.10 (m, 2H, dioxane), 1.34 and 1.60 (m, 2H, C(2)H_2), 1.44 (2H, d, *J* = 8.0 Hz, 2H, TMSCH_2), 1.45 (br, 2H, NH_2), 1.62 and 1.74 (m, 2H, C(1)H_2), 2.05 (m, 1H, C(4)$\underline{H}CH_3$), 2.49 (m, 1H, C$\underline{H}NH_2$), 3.75 (m, 2H, dioxane), 4.10 (m, 2H, dioxane), 4.53 (t, *J* = 4.8 Hz, 1H, C$\underline{H}(OCH_2)_2$), 5.14 (dd, *J* = 15.2, 8.4 Hz, 1H, -CH_2CH=C$\underline{H}$-), 5.42 (td, *J* = 14.8, 8.4 Hz, 1H, -CH_2C$\underline{H}$=CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.004 (q), 19.72 (q), 24.83 (t), 27.76 (t), 31.37 (t), 34.05 (t), 45.22 (d), 57.47 (d), 68.82 (t), 104.45 (d), 129.36 (d), 132.72 (d); HRMS $C_{15}H_{31}NO_2Si$ + H^+ calcd. *m*/*z* 286.2202, found *m*/*z* 286.2194; $[\alpha]_D^{25}$ = 7.2° (*c* 0.10, $CHCl_3$).

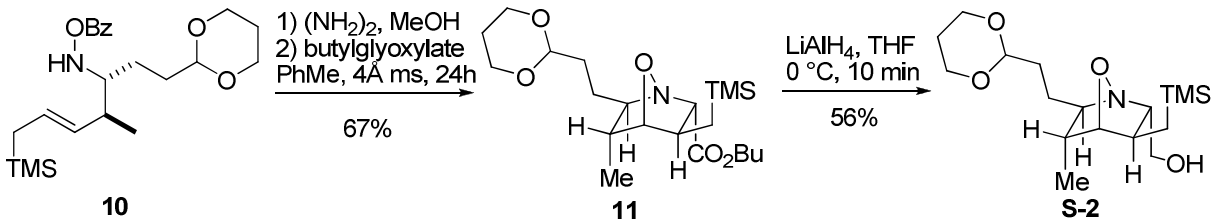


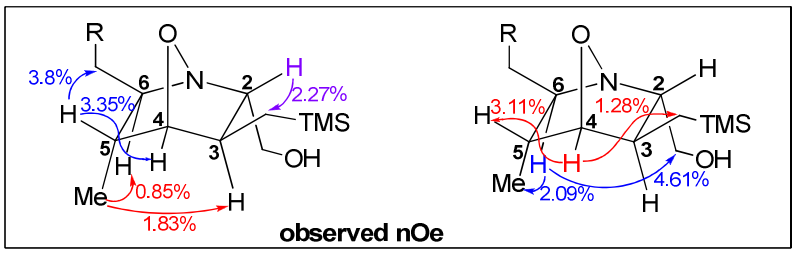
9 **10**

Preparation of (+)-*N*-((3*R*,4*S*,*E*)-1-(1,3-dioxan-2-yl)-4-methyl-7-(trimethylsilyl)hept-5-en-3-yl)-*O*-benzoylhydroxylamine (10): To a suspension of 0.73 g (3.03 mmol) of dibenzoyl peroxide and 0.66 g (3.78 mmol) of potassium phosphate dibasic in 10 mL of degassed anhydrous DMF was added a solution of 0.72 g (2.52 mmol) of amine **9** in 5 mL of DMF under argon.[6] The suspension was stirred at room temperature for 8 h. When NMR spectra indicated complete consumption of starting material, the reaction mixture was poured into 50 mL of deionized water and stirred for 30 min until the suspension turned clear. The mixture was extracted with 2 portions of 50 mL of ethyl

acetate. The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution, 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography over 50 g of silica gel (5% to 10% ethyl acetate in hexanes) to give 510 mg (50%) of benzoylamine **10** as a colorless oil.

Data for benzoylamine **10**: IR (neat) 2957, 1722, 1451, 1270, 1145 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 9H, TMS), 1.08 (d, *J* = 6.8 Hz, 3H, CH_3), 1.33 and 2.08 (m, 2H, dioxane), 1.46 (2H, dd, *J* = 8.0, 0.8 Hz, 2H, $TMSCH_2$), 1.63 and 1.74 (m, 2H, $C(2)H_2$), 1.79 (m, 2H, $C(1)H_2$), 2.40 (qd, *J* = 7.2, 6.8 Hz, 1H, $C(4)\underline{H}CH_3$), 2.90 (m, 1H, $C\underline{H}NH_2$), 3.75 (m, 2H, dioxane), 4.10 (m, 2H, dioxane), 4.57 (t, *J* = 4.8 Hz, 1H, $C\underline{H}(OCH_2)_2$), 5.21 (ddd, *J* = 15.2, 8.4, 1.2 Hz, 1H, $-CH_2CH{=}C\underline{H}-$), 5.42 (tdd, *J* = 14.8, 8.4, 0.8 Hz, 1H, $-CH_2C\underline{H}{=}CH$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.004 (q), 19.21 (q), 24.84 (t), 25.47 (t), 27.76 (t), 33.63 (t), 40.73 (d), 66.98 (d), 68.80 (t), 68.81 (t), 104.19 (d), 130.18 (d), 130.40 (d), 130.75 (s), 131.24 (d), 132.24 (d), 135.01 (d), 168.42 (s); $[\alpha]_D^{25}$ = 20.0° (*c* 0.10, $CHCl_3$).





Preparation of (–)-(2*S*,3*R*,4*S*,5*R*,6*S*)-butyl 6-(2-(1,3-dioxan-2-yl)ethyl)-5-methyl-3-((trimethylsilyl)methyl)-7-oxa-1-azabicyclo[2.2.1]heptane-2-carboxylate (11): To a solution of 390 mg (0.96 mmol) of benzoylamine **10** in 10 mL of degassed anhydrous methanol was added 0.5 mL of hydrazine hydrate at rt under argon. After stirring for 10 h, methanol was removed *in vacuo* and the residual colorless oil was dissolved in 20 mL

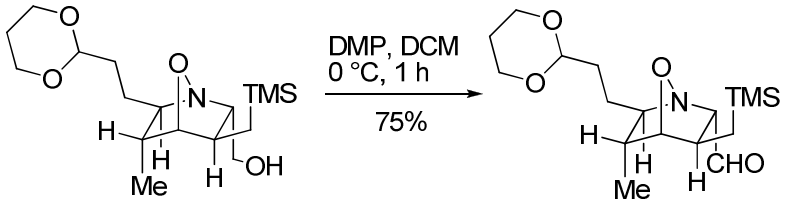
of degassed anhydrous toluene, dried ($MgSO_4$) and transferred to a 200 mL sealed tube already charged with 1.0 g of activated 4 Å molecular sieves, followed by addition of a solution of freshly prepared *n*-butyl blyoxylate (374 mg, 2.88 mmol) in 5 mL of anhydrous toluene. (Note: As the intermediate hydroxylamine can be oxidized to oximes in air, and decomposes on silica gel, it must be used immediately without purification.) The reaction mixture was diluted with 100 mL of anhydrous toluene, stirred at 100 °C for 1 h, then was heated at 120 °C for 48 h. The crude was concentrated *in vacuo* and the residue was purified by chromatography over 50 g of silica gel (5% to 10% ethyl acetate in hexanes) to give 265 mg (67%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptane **11** as a pale yellow oil. Since **11** has the same Rf as the hydrazine derivative, full characterization was delayed until after the next step.

Preparation of (–)-((2*S*,3*R*,4*S*,5*R*,6*S*)-6-(2-(1,3-dioxan-2-yl)ethyl)-5-methyl-3-((trimethylsilyl)methyl)-7-oxa-1-azabicyclo[2.2.1]heptan-2-yl)methanol (S-2): To a solution of 265 mg (0.64 mmol) of **11** in 10 mL of anhydrous THF was added 0.5 mL (0.5 mmol, 1.0 M in THF) of lithium aluminum hydride via a syringe at 0 °C under argon. After 10 min, TLC analysis indicated that the reaction was complete. The reaction was quenched by sequential addition of 5 drops of H_2O, 5 drops of 1.0 N NaOH and 15 drops of H_2O. After stirring for 1 h, the organic layer was collected, dried ($MgSO_4$) and concentrated *in vacuo*. The crude was chromatographed over 10 g of silica gel (10% to 50% EtOAc in hexanes) to give 128 mg (56%) of alcohol **S-2** as a colorless oil.

Data for oxazabicyclo[2.2.1]heptane **11**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 9H, TMS), 0.70 and 0.81 (ABq, *J* = 14.8 Hz, 2H, TMSC$\underline{H}_2$), 0.92 (t, *J* = 5.7 Hz, 3H, C$\underline{H}_3$(CH$_2$)$_3$), 1.06 (d, *J* = 6.8 Hz, 3H, CH_3), 1.30 and 2.00 (m, 2H, dioxane), 1.40 (m, 4H, CH_3(C$\underline{H}_2$)$_2$), 1.57 (m, 1H, C(3)H), 1.63 and 1.72 (m, 4H, (CH$_2$)$_2$), 2.00 (m, 1H, C(5)H), 2.30 (td, *J* = 6.4, 2.8 Hz, 1H, C(6)H), 2.63 (m, 1H, C(2)H), 3.63 (d, *J* = 5.2 Hz, 1H, C(4)H), 3.72 (m, 2H, dioxane), 4.06 (m, 2H, dioxane), 4.26 (t, *J* = 6.8 Hz, 2H, OC$\underline{H}_2$), 4.50 (t, *J* = 4.8 Hz, 1H, C$\underline{H}$(OCH$_2$)$_2$); HRMS $C_{21}H_{39}NO_5Si$ + H^+ calcd *m*/*z* 414.2676, found *m*/*z* 414.2665; $[\alpha]_D^{25}$ = –7.5° (*c* 0.10, $CHCl_3$).

Data for alcohol **S-2:** IR (neat) 3429, 2955, 2856, 1739, 1671, 1430, 1404, 1374, 1244 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 9H, TMS), 0.60 (ABq, *J* = 14.8, 4.0 Hz, 1H, TMSC$\underline{H}_2$), 0.81 (ABq, *J* = 14.8, 10.4 Hz, 1H, TMSC$\underline{H}_2$), 1.04 (d, *J* = 6.8 Hz, 3H, CH_3),

1.33 and 2.03 (m, 2H, dioxane), 1.55 (m, 2H, C<u>H</u>$_2$), 1.71 and 1.82 (m, 2H, C<u>H</u>$_2$), 1.75 (m, 1H, C(3)H), 1.90 (m, 1H, C(5)H), 2.52 (br, 1H, OH), 2.72 (td, *J* = 9.2, 4.0 Hz, 1H, C(6)H), 3.21 (td, *J* = 10.0, 5.2 Hz, 1H, C(2)H), 3.70 (m, 2H, C<u>H</u>$_2$OH), 3.78 (m, 2H, dioxane), 4.08 (m, 2H, dioxane), 4.19 (d, *J* = 4.8 Hz, 1H, C(4)H), 4.50 (dd, *J* = 5.2, 3.6 Hz, 1H, C<u>H</u>(OCH$_2$)$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.004 (q), 12.98 (q), 23.00 (t), 26.71 (t), 31.02 (t), 33.03 (t), 37.09 (d), 47.14 (d), 61.73 (t), 65.17 (d), 67.77 (t), 67.83 (t), 79.71 (d), 91.84 (d), 103.74 (d); HRMS $C_{17}H_{33}NO_4Si$ + H^+ calcd *m*/*z* 344.2257, found *m*/*z* 344.2246; $[\alpha]_D^{25}$ = –13.0° (*c* 0.10, $CHCl_3$).

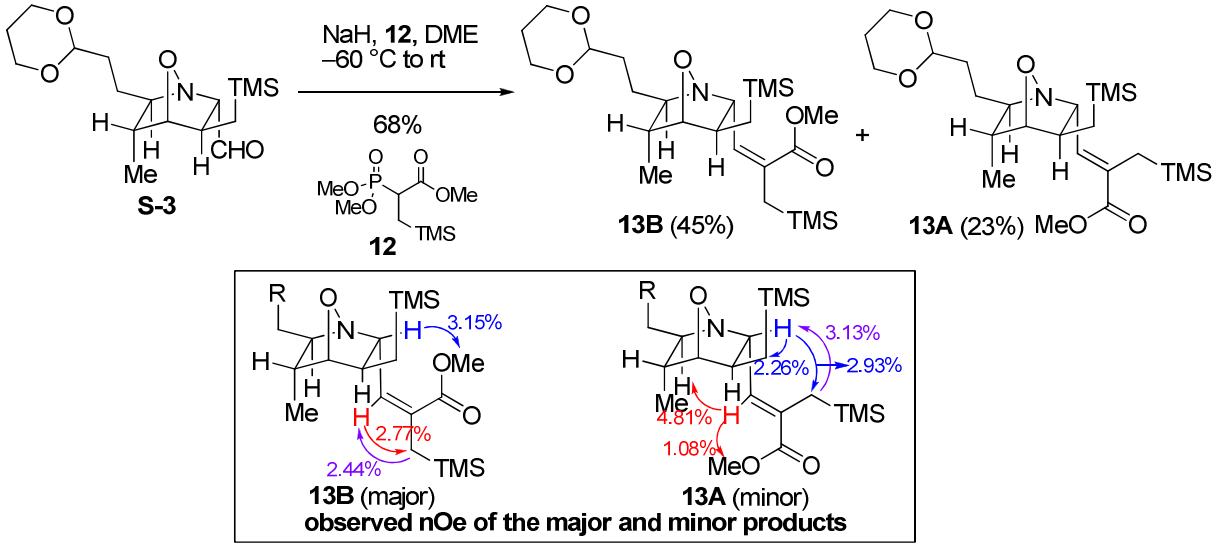


S-2 **S-3**

Preparation of (–)-(2*S*,3*R*,4*S*,5*R*,6*S*)-6-(2-(1,3-dioxan-2-yl)ethyl)-5-methyl-3-((trimethylsilyl)methyl)-7-oxa-1-azabicyclo[2.2.1]heptane-2-carbaldehyde (S-3): To a solution of 64 mg (0.19 mmol) of alcohol **S-2** in 10 mL of anhydrous CH_2Cl_2 was added a solution of 127 mg (0.2 mmol) of Dess-Martin periodinane in 2 mL of CH_2Cl_2 via a syringe at 0 °C under argon. After 1 h, TLC analysis indicated that the reaction was complete. To the reaction mixture was sequential added 10 mL of CH_2Cl_2 and 2 mL of saturated aqueous $NaHCO_3$. After stirring for 0.5 h, the white suspension turned clear. The organic layer was collected, dried ($MgSO_4$) and concentrated *in vacuo*. The crude was chromatographed over 10 g of silica gel (10% to 20% EtOAc in hexanes) to give 51 mg (75%) of aldehyde **S-3** as a colorless oil.

Data for aldehyde **S-3:** IR (neat) 2955, 2850, 1724, 1447, 1379, 1247 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 9H, TMS), 0.64 (ABq, *J* = 14.8, 6.0 Hz, 1H, TMSC<u>H</u>$_2$), 0.80 (ABq, *J* = 14.8, 9.2 Hz, 1H, TMSC<u>H</u>$_2$), 0.98 (d, *J* = 7.2 Hz, 3H, CH_3), 1.31 and 2.02 (m, 2H, dioxane), 1.47, 1.62, 1.75 (m, 4H, (C<u>H</u>$_2$)$_2$), 1.95 (m, 1H, C(5)H), 2.14 (td, *J* = 8.0, 5.2 Hz, 1H, C(6)H), 2.57 (m, 1H, C(3)H), 3.61 (d, *J* = 4.8 Hz, 1H, C(2)H), 3.71 (m, 2H, dioxane), 4.05 (m, 2H, dioxane), 4.24 (d, *J* = 4.8 Hz, 1H, C(4)H), 4.51 (t, *J* = 4.8 Hz, 1H,

C<u>H</u>(OCH$_2$)$_2$), 9.78 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.004 (q), 13.29 (q), 23.72 (t), 26.86 (t), 31.13 (t), 33.46 (t), 35.08 (d), 46.96 (d), 66.90 (t), 71.52 (d), 87.14 (d), 93.24 (d), 103.14 (d), 198.69 (d); LRMS $C_{17}H_{31}NO_4Si$ + H^+ calcd *m*/*z* 342.2, found *m*/*z* 342.4; $[\alpha]_D^{25}$ = –8.0° (*c* 0.10, $CHCl_3$).

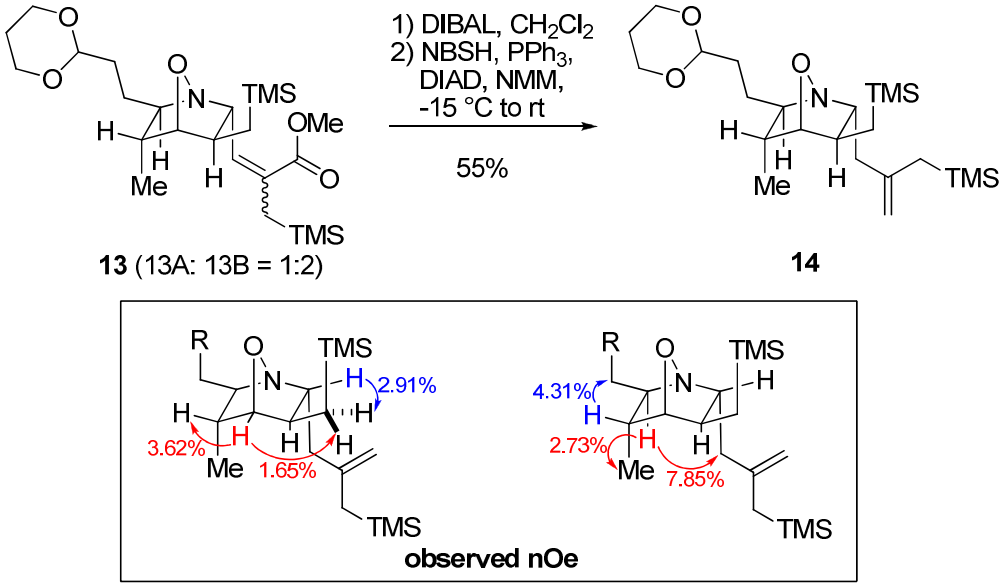


Preparation of (*E*)-methyl 3-((2*R*,3*R*,4*S*,5*R*,6*S*)-6-(2-(1,3-dioxan-2-yl)ethyl)-5-methyl-3-((trimethylsilyl)methyl)-7-oxa-1-azabicyclo[2.2.1]heptan-2-yl)-2-((trimethylsilyl)methyl)acrylate (13B) and (*Z*)-methyl 3-((2*R*,3*R*,4*S*,5*R*,6*S*)-6-(2-(1,3-dioxan-2-yl)ethyl)-5-methyl-3-((trimethylsilyl)methyl)-7-oxa-1-azabicyclo-[2.2.1]heptan-2-yl)-2-((trimethylsilyl)methyl)acrylate (13A): To a stirred suspension of NaH (12 mg, 0.3 mmol, 60% in mineral oil) in 4 mL of anhydrous dimethoxyethane (DME) was added a solution of 81 mg (0.3 mmol) of methyl 2-(dimethoxyphosphoryl)-3-(trimethylsilyl)propanoate **12**[7] in 1 mL of DME at 0 °C under argon. After 10 min, the ice-bath was removed and the reaction mixture was stirred at rt for an additional 10 min. The resulting pale-yellow suspension was filtered through a syringe filter and added dropwise to a solution of 51 mg (0.15 mmol) of aldehyde **S-3** in 4 mL of anhydrous DME at –60 °C via syringe over 10 min. The reaction was monitored by NMR. After 0.5 h, when no aldehyde **S-3** remained, the resulting yellow solution was poured into a mixture of 5mL of saturated aqueous $NaHCO_3$ and 40 mL of diethyl ether with stirring. The

organic layer was collected, dried ($MgSO_4$), concentrated *in vacuo*, and chromatographed over 10 g of silica gel (2.5% to 20% EtOAc in hexanes) to give 17 mg (23%) of *Z* isomer **13A** and 33 mg (45%) of *E* isomer **13B** as products. Although the products were used as a mixture in the following steps, 10 mg of the major product **13B** was purified for full characterization.

Data for **13B:** IR (neat) 2954, 2852, 1723, 1435, 1247 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ –0.02 (s, 9H, TMS), 0.00 (s, 9H, TMS), 0.68 (ABq, *J* = 15.2, 4.8 Hz, 1H, TMSC$\underline{H}_2$), 0.77 (ABq, *J* = 14.8, 10.0 Hz, 1H, TMSC$\underline{H}_2$), 1.07 (d, *J* = 7.2 Hz, 3H, CH_3), 1.32 and 2.02 (m, 2H, dioxane), 1.48, 1.52, 1.69 (m, 4H, (C$\underline{H}_2$)$_2$), 1.75 and 1.86 (ABq, *J* = 13.2 Hz, 2H, TMSC$\underline{H}_2$C=), 1.87 (m, 1H, C(3)H), 1.97 (m, 1H, C(5)H), 2.29 (td, *J* = 7.2, 5.6 Hz, 1H, C(6)H), 3.71 (m, 2H, dioxane), 3.72 (s, 3H, OMe), 4.05 (m, 2H, dioxane), 4.11 (dd, *J* = 9.6, 4.8 Hz, 1H, C(2)H), 4.22 (d, *J* = 4.8 Hz, 1H, C(4)H), 4.48 (t, *J* = 4.8 Hz, 1H, C$\underline{H}$(OCH$_2$)$_2$), 5.38 (d, *J* = 9.6 Hz, 1H, =CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ –0.71 (q), –0.10 (q), 13.63 (q), 22.25 (t), 26.64 (t), 26.82 (t), 31.39 (t), 33.51 (t), 42.56 (d), 46.78 (d), 52.60 (q), 67.43 (d), 67.80 (t), 74.97 (d), 92.56 (d), 103.29 (d), 130.24 (d), 138.06 (s), 169.27 (s); HRMS $C_{24}H_{45}NO_5Si_2 + H^+$ calcd *m*/*z* 484.2915, found *m*/*z* 484.2899; $[\alpha]_D^{25}$ = –9.0° (*c* 0.10, $CHCl_3$).

Data for **13A**: IR (neat) 2926, 2853, 1717, 1432, 1249 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ –0.02 (s, 9H, TMS), 0.00 (s, 9H, TMS), 0.57 (ABq, *J* = 14.8, 3.6 Hz, 1H, TMSC$\underline{H}_2$), 0.79 (ABq, *J* = 14.8, 10.8 Hz, 1H, TMSC$\underline{H}_2$), 1.07 (d, *J* = 7.2 Hz, 3H, CH_3), 1.28 and 2.00 (m, 2H, dioxane), 1.49, 1.50, 1.66 (m, 4H, (C$\underline{H}_2$)$_2$), 1.95 and 2.15 (ABq, *J* = 13.6 Hz, 2H, TMSC$\underline{H}_2$C=), 1.96 (m, 1H, C(3)H), 2.05 (m, 1H, C(5)H), 2.40 (td, *J* = 7.2, 5.6 Hz, 1H, C(6)H), 3.59 (dd, *J* = 8.4, 3.2 Hz, 1H, C(2)H), 3.69 (m, 2H, dioxane), 3.72 (s, 3H, OMe), 4.05 (m, 2H, dioxane), 4.24 (d, *J* = 4.8 Hz, 1H, C(4)H), 4.44 (t, *J* = 4.8 Hz, 1H, C$\underline{H}$(OCH$_2$)$_2$), 6.38 (d, *J* = 8.4 Hz, 1H, =CH); LRMS $C_{24}H_{45}NO_5Si_2 + H^+$ calcd *m*/*z* 484.2915, found *m*/*z* 484.2899.



Preparation of (2*S*,3*R*,4*S*,5*R*,6*R*)-2-(2-(1,3-dioxan-2-yl)ethyl)-3-methyl-5-((trimethylsilyl)methyl)-6-(2-((trimethylsilyl)methyl)allyl)-7-oxa-1-azabicyclo[2.2.1]-heptane (14): To a mixture of 44 mg (0.091 mmol) of esters **13A** and **13B** in 5 mL of anhydrous DCM was added 0.4 mL (0.4 mmol, 1.0 M in hexanes) of DIBAL via a syringe at 0 °C under argon. After 10 min, TLC analysis indicated that the reaction were complete. The reaction was quenched by sequential addition of 0.1 mL of methanol (dissolved in 1 mL of DCM) and 1 mL of saturated aqueous Rochelle's salt. After stirring for 1 h, the organic layer was collected, dried ($MgSO_4$) and concentrated *in vacuo*. The crude was chromatographed over 10 g of silica gel (10% to 50% EtOAc in hexanes) to give 41 mg (99%) of alcohols (inseparable mixture of alkene isomers with a ratio of 2:1) as a colorless oil which was used directly in the following deoxygenation step. The oil was first dissolved in 2 mL of anhydrous *N*-methylmorpholine (NMM) and then transferred to a 10 mL round bottom flask charged with 0.2 g of activated 4 Å molecular sieves. After cooling to −15 °C, a solution of 78 mg (0.3 mmol) of PPh_3 in 1 mL of anhydrous NMM was added via a syringe under argon. After 5 min, a solution of 61 mg (0.3 mmol) of DIAD in 1 mL of anhydrous NMM was introduced to the suspension dropwise. After 10 more min, a solution of 65 mg (0.3 mmol) of freshly prepared 2-nitrobenzenesulfonylhydrazide (NBSH)[8] in 1 mL of NMM was added to the reaction mixture promptly to avoid decomposition. The resulting pale yellow suspension was

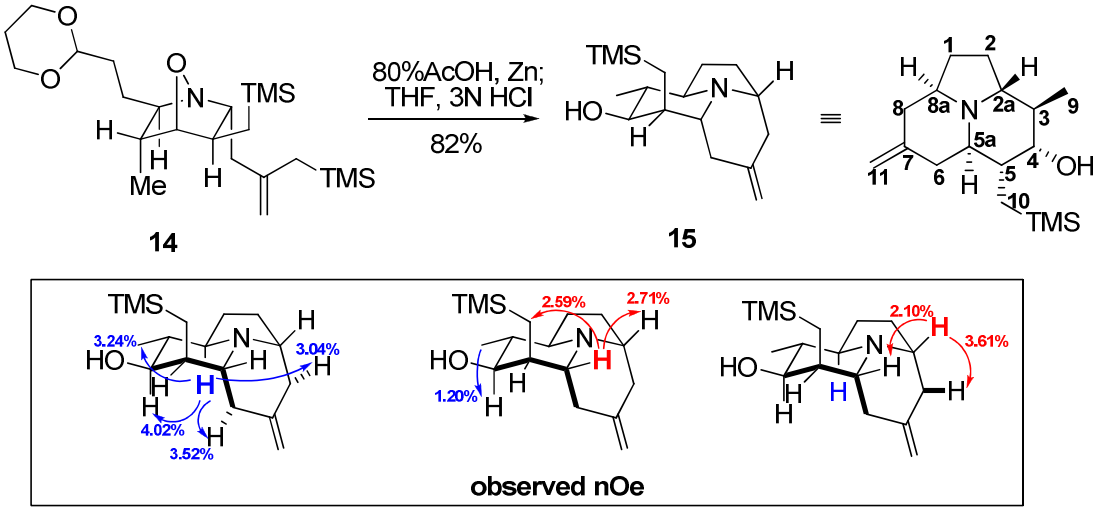
stirred at – 15 °C for 3 h. When mass spectrum of reaction mixture indicated that the starting material was consumed, the temperature of the reaction mixture was allowed to rise gradually to rt and the resulting suspension was stirred for 16 h. The yellow suspension was filtered through a celite pad, concentrated and chromatographed over 10 g of silica gel (2% to 10% EtOAc in hexanes) to give 22 mg (55%) of **14** as a pale yellow oil.

Data for **14:** IR (neat) 2954, 2850, 1633, 1378, 1247 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ –0.02 (s, 9H, TMS), 0.00 (s, 9H, TMS), 0.49 (ABq, *J* = 14.8, 2.8 Hz, 1H, TMSC$\underline{H}_2$), 0.75 (ABq, *J* = 14.8, 11.6 Hz, 1H, TMSC$\underline{H}_2$), 1.04 (d, *J* = 7.2 Hz, 3H, CH_3), 1.32 and 2.03 (m, 2H, dioxane), 1.43, 1.72, 1.76 (m, 4H, (C$\underline{H}_2$)$_2$), 1.52 and 1.61 (ABq, 2H, TMSC$\underline{H}_2$C=), 1.75 (m, 1H, C(3)H), 1.92 (m, 1H, C(5)H), 2.13 (d, *J* = 8.0 Hz, 2H, CH_2C=), 2.44 (td, *J* = 7.2, 5.2 Hz, 1H, C(6)H), 4.11 (td, *J* = 7.6, 5.2 Hz, 1H, C(2)H), 3.72 (m, 2H, dioxane), 4.05 (m, 2H, dioxane), 4.14 (d, *J* = 4.8 Hz, 1H, C(4)H), 4.48 (t, *J* = 4.8 Hz, 1H, C$\underline{H}$(OCH$_2$)$_2$), 4.56 (s, 1H, =CH_2), 4.71 (s, 1H, =CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ –0.42 (q), –0.004 (q), 13.55 (q), 23.24 (t), 26.80 (t), 26.98 (t), 31.22 (t), 33.64 (t), 39.65 (t), 40.68 (d), 46.88 (d), 66.25 (d), 67.80 (t), 76.01 (d), 91.65 (d), 103.36 (d), 111.04 (t), 145.05 (s); HRMS $C_{23}H_{45}NO_3Si_2$ + H^+ calcd *m*/*z* 440.3016, found *m*/*z* 440.3002; $[\alpha]_D^{25}$ = –26.0° (*c* 0.10, $CHCl_3$).

***o*-Nitrobenzenesulfonylhydrazide (NBSH).** NBSH was prepared according to Myers's procedure[8(b)] without modification: To a stirred solution *o*-nitrobenzenesulfonyl chloride (11.1 g, 0.05 mol, 1 equiv) in THF (50 mL) was added hydrazine monohydrate (6.05 mL, 0.125 mol, 2.5 equiv, from Aldrich) dropwise via a syringe at –30 °C (cooled by a Cryocool with *i*-PrOH as coolant) under argon. After stirring at –30 °C for 30 min, the reaction mixture changed from water white to orange and hydrazine hydrochloride precipitated out. Thin-layer chromatographic (TLC) analysis indicated no sulfonyl chloride left. Ethyl acetate (100 mL, 25 °C) was added to the cold reaction mixture and the resulting suspension was washed repeatedly with ice-cold 10% aqueous sodium chloride (5 × 100 mL). (*A 500 mL separation funnel and 500 mL of 10% aqueous sodium chloride was cooled in 10 lbs of ice for 30 min prior to use.*) The organic extract was dried over sodium sulfate at 0 °C and then was added slowly to a stirred solution of

hexanes (600 mL) at 25 °C over 5 min. Within 10 min, *o*-nitrobenzenesulfonylhydrazide precipitated as an off-white solid which was collected by vacuum filtration. The filter cake was washed with hexanes (2 × 30 mL, 25 °C) and then dried in vacuo (1 mm Hg) at 25 °C for 48 h to afford pure NBSH as an off-white powder (8.2 g, 76%): mp 98-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.11 (1H, m), 7.82-7.91 (3H, m), 6.94 (1H, bs), 4.02 (2H, bs); Rf 0.20 (2:1 ethyl acetate:hexanes).

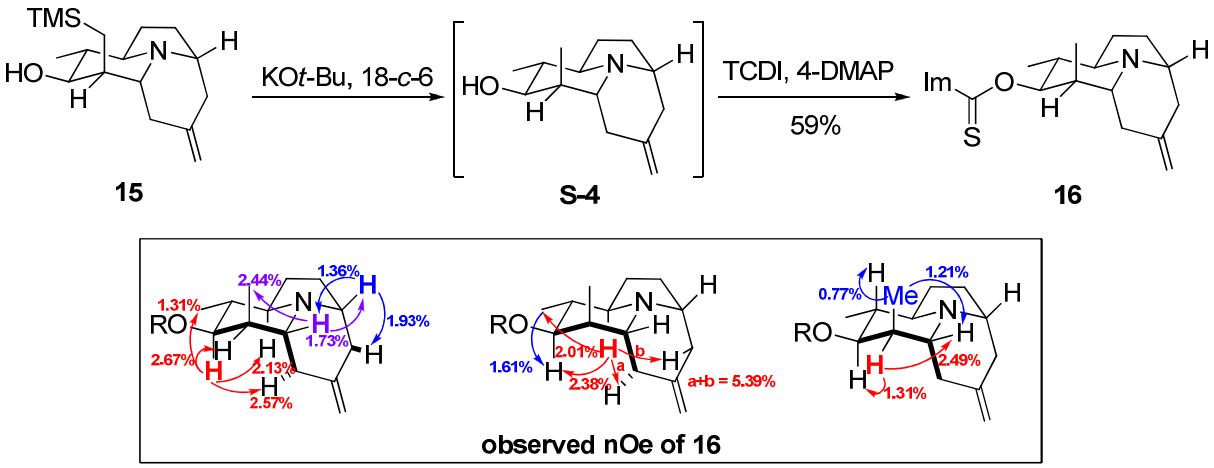
Note: According to Myers's procedure, NBSH was dried in vacuo (< 1.5 mm Hg) for 14 h. We have prepared NBSH 3 times according to this procedure without trouble. However, one attempt at preparing this reagent was complicated by environmental conditions (high humidity). In an attempt to thoroughly dry one batch of material (in order to prepare material with a similar melting point to that described in the literature) we dried the sample under high vacuum for 48h. The material produced by this procedure proved to be quite unstable. For example, a slight tap of a vial containing this material on the benchtop resulted in the initial generation of yellow smoke followed by a red flame.



Preparation of (2a*R*,3*R*,4*S*,5*R*,5a*R*,8a*R*)-3-methyl-7-methylene-5-((trimethylsilyl)methyl)decahydro-1H-pyrrolo[2,1,5-de]quinolizin-4-ol (15): To a solution of 22 mg (0.05 mmol) of allylsilane **14** in 1 mL of 80% acetic acid in H_2O was

added 6.4 mg (0.1 mmol) of zinc powder (Aldrich, < 10 micro) under argon at rt. After stirring for 10 min, mass spectra of the reaction mixture indicated complete consumption of starting material. The suspension was filtered through a syringe filter and the filtrate was transferred into a 10 mL round bottom flask. After concentration *in vacuo* (< 1 mm Hg) for 10 min, the residue was treated with 2.5 mL of THF and 0.5 mL of 3 N HCl at 40 °C for 16 h under argon with stirring. When cooled to rt, the reaction mixture was poured into 50 mL of degassed ether suspended with 1 g of pulverized KOH. The organic phase was collected, dried (K_2CO_3), and concentrated *in vacuo*. The crude was chromatographed over 10 g of silica gel (2.5% to 20% EtOAc in hexanes) to give 12 mg (82%) of olefin **15** as a pale yellow oil. It is worth mentioning that product **15** is easily oxidized to *N*-oxide. So it is suggested that all operations should be conducted under argon.

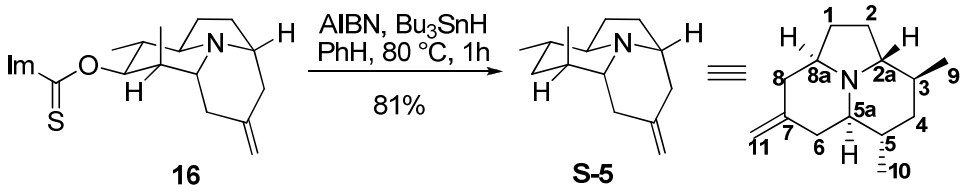
Data for **15:** IR (neat) 3370, 2951, 2928, 1716, 1647, 1454, 1246 cm^{-1}; ^1H NMR (DMSO, 400 MHz) δ 0.00 (s, 9H, TMS), 0.65 (ABq, *J* = 14.4, 10.8 Hz, 1H, TMSC$\underline{H}_2$), 0.89 (d, *J* = 7.2 Hz, 3H, CH_3), 0.94 (ABq, *J* = 14.4, 2.4 Hz, 1H, TMSC$\underline{H}_2$), 1.31 and 2.01 (m, 4H, C(1)H_2 and C(2)H_2), 1.34 (m, 1H, C(3)H), 1.72 and 1.86 (m, 2H, C(8)H_2), 1.75 (m, 1H, C(5)H), 1.78 (m, 1H, C(6)H), 2.41 (t, *J* = 12.4 Hz, 1H, C(6)H), 2.64 (m, 1H, C(2a)H), 2.80 (dd, *J* = 12.8, 2.0 Hz, 1H, C(5a)H), 2.97 (m, 1H, C(8a)H), 3.37 (m, 1H, C(4)H), 4.38 (d, *J* = 5.2 Hz, 1H, OH), 4.62 (s, 1H, =CH_2), 4.65 (s, 1H, =CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −0.004 (q), 14.36 (t), 15.06 (q), 29.24 (t), 29.41 (t), 34.43 (t), 37.26 (t), 39.28 (d), 41.45 (d), 58.30 (d), 61.01 (d), 61.77 (d), 72.87 (d), 107.20 (t), 149.13 (s); HRMS $C_{17}H_{31}NO_2Si + H^+$ calcd *m*/*z* 294.2253, found *m*/*z* 294.2246; $[\alpha]_D^{25}$ = −4.7° (*c* 0.10, $CHCl_3$).



Preparation of (2a*R*,3*R*,4*S*,5*R*,5a*R*,8a*R*)-3,5-dimethyl-7-methylenedecahydro-1H-pyrrolo[2,1,5-de]quinolizin-4-ol (15) and *O*-(2a*R*,3*R*,4*S*,5*R*,5a*R*,8a*R*)-3,5-dimethyl-7-methylenedecahydro-1H-pyrrolo[2,1,5-de]quinolizin-4-yl 1H-imidazole-1-carbothioate (16): To a solution of 12 mg (0.04 mmol) of alcohol **15** in 1 mL of wet DMSO (with 5% H_2O) was added 45 mg (0.2 mmol) of KO*t*-Bu and 53 mg (0.2 mmol) of 18-*c*-6 under argon. The reaction mixture was heated at 90 °C for 16 h. After cooling to rt, the reaction mixture was transferred into 50 mL of degassed ether and 5 mL of 1.0 N NaOH. After vigorous stirring under argon, the organic phase was collected, dried (K_2CO_3), and concentrated *in vacuo*. The crude was chromatographed over 10 g of silica gel (10% to 50% EtOAc in hexanes) to give alcohol **S-4** a pale yellow oil. As this intermediate is easily oxidized to the *N*-oxide by exposure to air, it was immediately dissolved in 3 mL of anhydrous DCM and introduced to a 10 mL sealed tube under argon. To the pale yellow solution was added 36 mg (0.2 mmol) of 1, 1'-thiocarbonyldiimidazole (TCDI) and 24 mg (0.2 mmol) of 4-DMAP under argon. The reaction mixture was heated at 60 °C for 16 h, then was cooled to rt and concentrated *in vacuo* with 1 g of silica gel. The crude was chromatographed over 10 g of silica gel (20% EtOAc in hexanes) to give 8 mg (59% for 2 steps) of thioester **16** as a pale yellow oil.

Data for **16:** IR (neat) 3133, 3069, 2930, 1758, 1647, 1462, 1284 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (d, *J* = 6.8 Hz, 3H, CH_3), 1.09 (d, *J* = 7.2 Hz, 3H, CH_3), 1.33, 1.48 and 2.06 (m, 4H, C(1)H_2 and C(2)H_2), 1.90 and 1.96 (m, 3H, C(6)H_2 and C(8)H_2), 1.98 (m,

1H, C(3)H), 2.32 (td, *J* = 10.4 and 1.6 Hz, 1H, C(5)H), 2.41 (t, *J* = 12.8 Hz, 1H, C(6)H), 2.78 (td, *J* = 9.6, 3.6 Hz, 1H, C(2a)H), 2.93 (d, *J* = 12.0 Hz, 1H, C(5a)H), 3.07 (m, 1H, C(8a)H), 4.61 (s, 1H, $=CH_2$), 4.62 (s, 1H, $=CH_2$), 5.49 (dd, J = 10.8, 5.2 Hz, 1H, C(4)H), 6.98 (s, 1H, im), 7.58 (s, 1H, im), 8.29 (s, 1H, im); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.26 (q), 14.46 (q), 28.80 (t), 28.90 (t), 33.87 (t), 35.44 (d), 36.82 (t), 37.30 (d), 58.12 (d), 60.58 (d), 61.70 (d), 87.45 (d), 107.50 (t), 130.84 (d), 147.15 (s), 183.90 (s); HRMS $C_{18}H_{25}N_3OS + H^+$ calcd *m*/*z* 332.1797, found *m*/*z* 332.1789; $[\alpha]_D^{25} = 51°$ (*c* 0.10, $CHCl_3$).

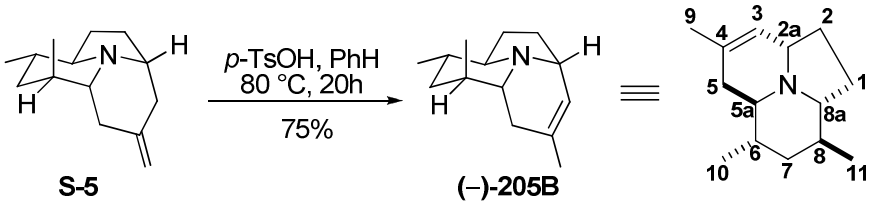


16 **S-5**

Preparation of (2a*R*,3*R*,5*R*,5a*R*,8a*R*)-3,5-dimethyl-7-methylenedecahydro-1H-pyrrolo[2,1,5-de]quinolizin (S-5): To a solution of 8 mg (0.024 mmol) of thioester **16** in 2 mL of degassed anhydrous benzene was added a solution of 15 mg (0.05 mmol) of Bu_3SnH and 2 mg (0.01 mmol) of AIBN in 1 mL of degassed benzene at 80 °C under argon over 0.5 h. When the reaction was judged to be complete (in 2 h, analyzed by TLC), the solution was cooled to rt and washed with 1 mL of 1.0 N DCl in D_2O (3×) under argon. The aqueous phases were collected, neutralized with several drops of concentrated KOH in D_2O, then was extracted with 1 mL of $CDCl_3$ (3×). The organic extracts were dried (K_2CO_3), concentrated to give 4 mg (81%) of **S-5** as a pale yellow oil which was dissolved in $CDCl_3$ immediately for NMR experiments and the following reaction.

Data for **S-5:** IR (neat) 3069, 2958, 2926, 1651, 1459, 1261 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.85 (d, *J* = 6.8 Hz, 3H, CH_3), 1.12 (d, *J* = 7.2 Hz, 3H, CH_3), 1.30-1.37 (m, 4H, $C(1)H_2$ and $C(2)H_2$), 1.49-1.58 (m, 1H, C(5)H), 1.71 (br, 1H), 1.83 (dd, *J* = 8.4, 2.0 Hz, 1H), 1.94-2.03 (m, 4H), 2.29 (t, *J* = 12.0 Hz, 1H, C(6)H), 2.57 (q, *J* = 7.2 Hz, 1H, C(2a)H), 2.71 (td, *J* = 12.0, 2.8 Hz, 1H, C(5a)H), 3.03 (m, 1H, C(8a)H), 4.629 (s, 1H, $=CH_2$), 4.633 (s, 1H, $=CH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.69 (q), 20.40 (q), 28.51 (t),

28.06 (t), 32.29 (d), 33.22 (d), 35.10 (t), 36.50 (t), 37.59 (t), 59.43 (d), 61.57 (d), 61.92 (d), 106.50 (t), 148.60 (s); HRMS $C_{14}H_{23}N + H^+$ calcd *m*/*z* 206.1909, found *m*/*z* 206.1903; $[\alpha]_D^{25} = -12.1°$ (*c* 0.10, $CHCl_3$).



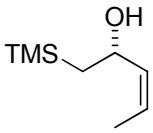
S-5 (–)-205B

Preparation of (–)-205B: To a solution of alkene (–)-**S-5** (4 mg, 0.024 mmol) in 3 mL of benzene (D6) was added 24 mg (0.12 mmol) of *p*-TsOH•H2O under argon. The reaction mixture was heated at 80 °C for 20 h. After cooling to rt, the benzene solution was washed with 1 mL of 1.0 N DCl in D_2O (3×) under argon. The aqueous phases were collected, neutralized with several drops of concentrated solution of KOH in D_2O, then was extracted with 1 mL of $CDCl_3$ (3×). The organic extracts were dried (K_2CO_3) and concentrated *in vacuo* to give 3 mg (75%) of a pale yellow oil with alkaloid (–)-205B as the major isomer (6:1 as shown in ^1H NMR in $CDCl_3$). After filtering through a silica gel pad (1 cm), alkaloid (–)-205B is the only product (^1H NMR in C_6D_6). The natural product can be stored as a solution in C_6D_6 or $CDCl_3$ for several weeks at – 80 °C. However, neat product is easily oxidized to N-oxide in a couple of days.

Data for (–)-205B: IR (neat) 2956, 2839, 1648, 1456, 1393, 1175 cm^{-1}; 1H NMR (400 MHz, C_6D_6) δ 0.81 (d, *J* = 6.8 Hz, 3H, CH_3), 1.29 (d, *J* = 7.2 Hz, 3H, CH_3), 1.23-1.36 (m, 6H), 1.53-1.60 (m, 1H), 1.59 (s, 3H), 1.78-1.82 (m, 1H), 1.95-2.01 (td, *J* = 10.0, 2.4 Hz, 1H), 2.06 (t, *J* = 14.8 Hz, 1H), 2.15 (td, *J* = 9.6, 4.8 Hz, 1H), 2.95 (dd, *J* = 11.6, 4.4 Hz, 1H), 3.87 (br, 1H), 5.19 (d, *J* = 1.2 Hz, 1H, CH=); 1H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, *J* = 6.4 Hz, 3H, CH_3), 1.17 (d, *J* = 7.2 Hz, 3H, CH_3), 1.25-1.48 (m, 6H), 1.62 (s, 3H), 1.68-1.70 (m, 1H), 1.88-1.91 (m, 1H), 2.09-2.13 (m, 3H), 2.98 (dd, *J* = 12.0, 4.4 Hz, 1H), 3.76 (br, 1H), 5.18 (s, 1H, CH=); ^{13}C NMR (C_6D_6, 100 MHz) δ 19.42 (q), 20.79 (q), 24.17 (q), 28.73 (t), 29.20 (t), 30.19 (t), 33.16 (d), 33.36 (d), 36.38 (t), 57.01(d), 59.00 (d), 60.98 (d), 126.85 (d), 129.9 (s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.83 (q), 20.21 (q),

23.54 (q), 28.38 (t), 28.41 (t), 29.29 (t), 32.51 (d), 32.58 (d), 35.48 (t), 56.34(d), 58.09 (d), 60.47 (d), 125.61 (d), 129.54 (s); HRMS $C_{14}H_{23}N + H^+$ calcd *m*/*z* 206.1909, found *m*/*z* 2056.1899; $[\alpha]_D^{25} = -8.0°$ (*c* 0.1, $CHCl_3$).

1 Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755.
2 Hoye, T. R.; Jeffrey, C. S.; Shao, F., *Nature Protocols*, **2007**, *2*, 2451.
3 Pearson, A.J.; Sun, H.; Wang, X. *J. Org. Chem.* **2007**, *72*, 2547.
4 Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551.
5 (a) Yang, D.; Micalizio, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 9216. (b) Takahashi, M.; McLaughlin, M.; Micalizio, G. C. *Angew. Chem. Int. Ed.* 2009, *48*, 3648. (c) Chen, M. Z.; McLaughlin, M.; Takahashi, M.; Tarselli, M. A.; Yang, D.; Umemura, S.; Micalizio, G. C. *J. Org. Chem.*, 2010, *75*, 8048.
6 Berman A. M.; Johnson J. S. *J. Org. Chem*. **2006**, *71*, 219.
7 Hoffmann, H. M. R.; Hennig, R. *Helv. Chim. Acta.* **1983**, *66*, 828.
8 (a) Zheng, B.; Myers, A. G. *Tetrahedron Lett.* **1996**, *37*, 4841. (b) Myers, A. G.; Zheng, B.; Movassaghi, M. *J. Org. Chem.* **1997**, *62*, 7507.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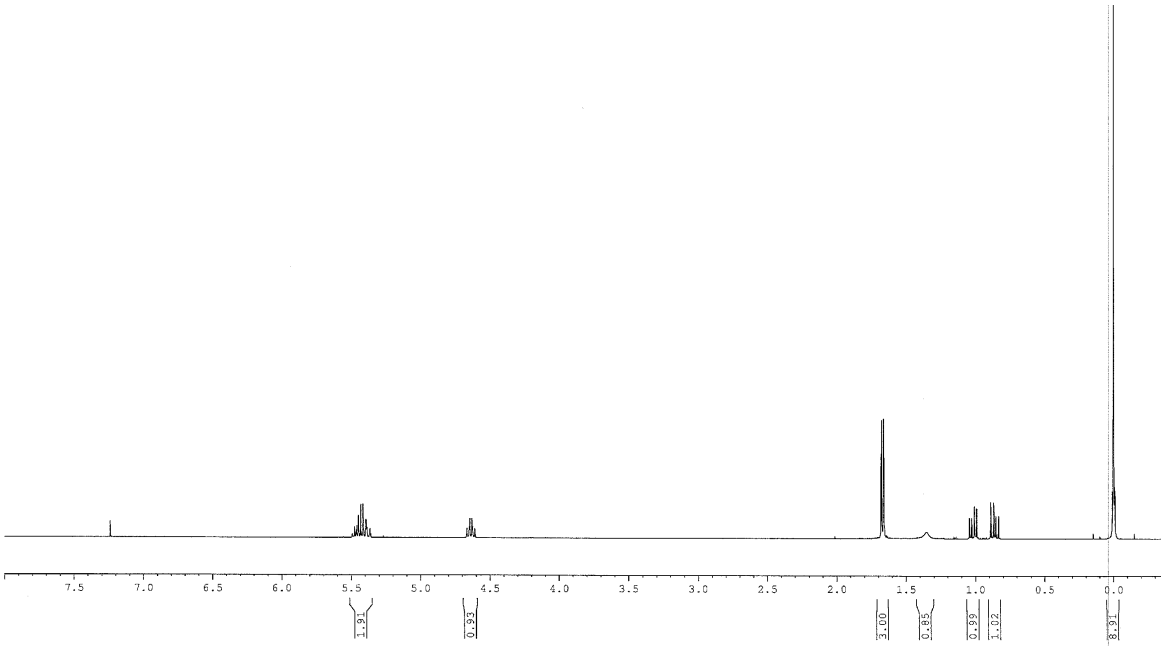
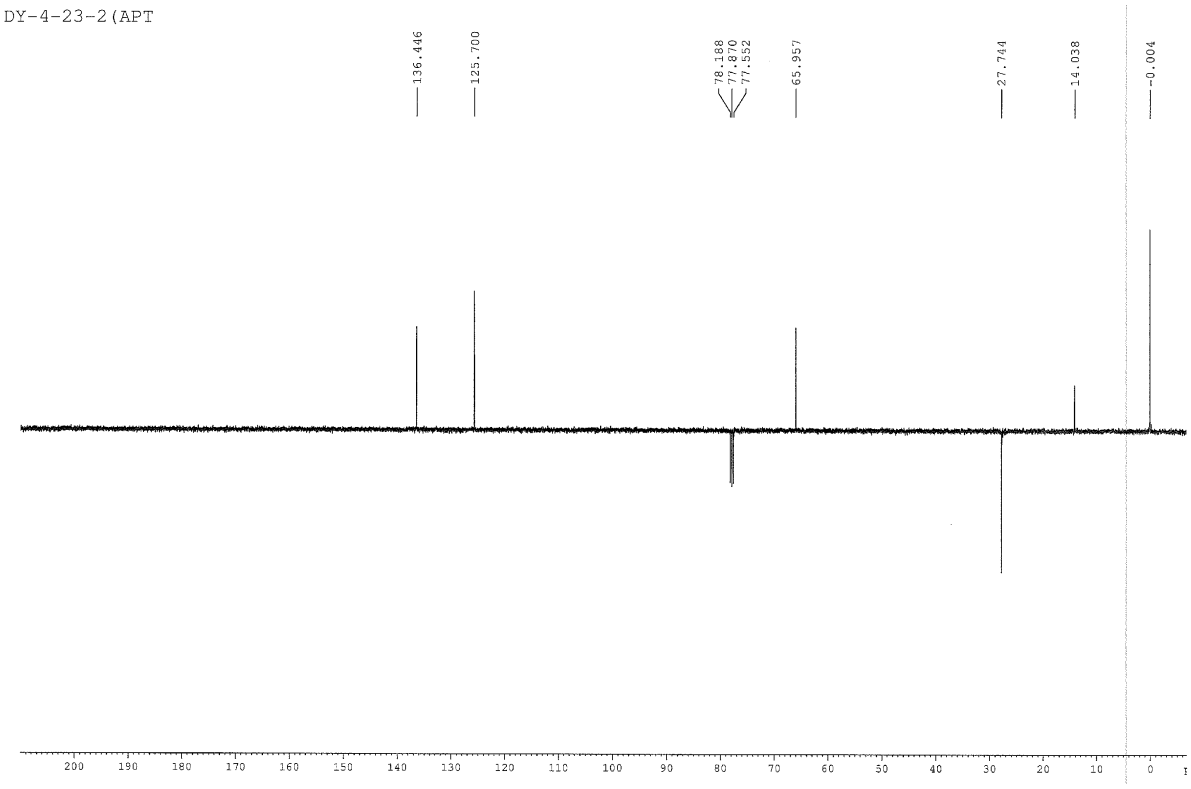
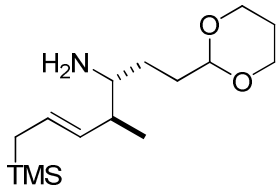
TMS

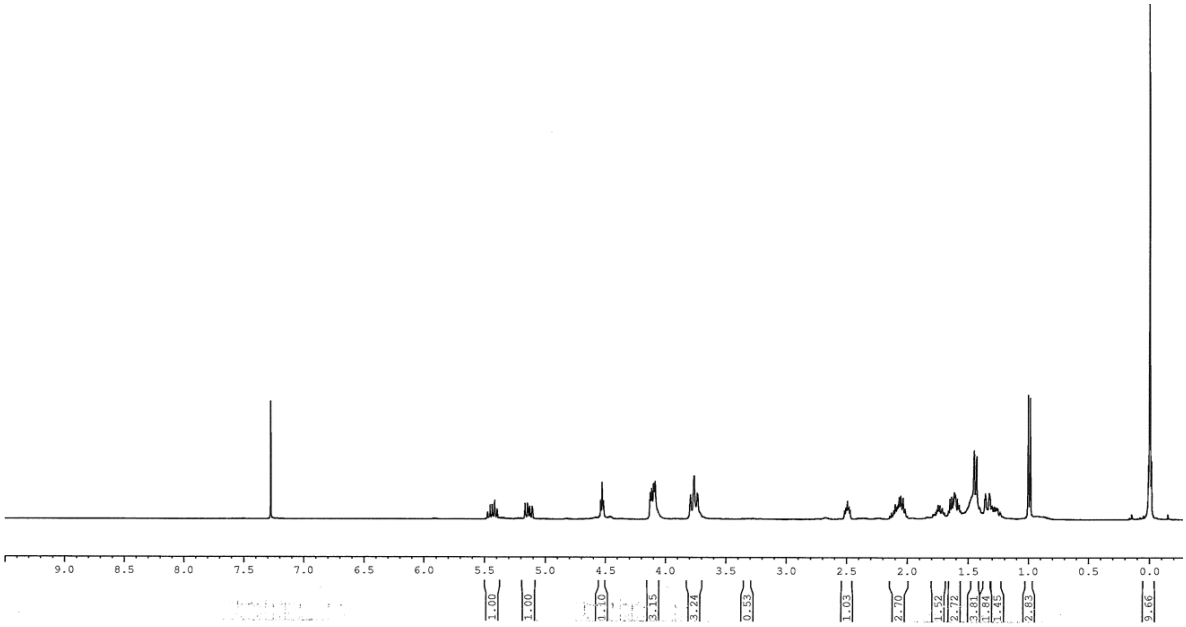
8 (DY-4-23)


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.91
0.93
3.00
0.85
0.99
1.02
8.91

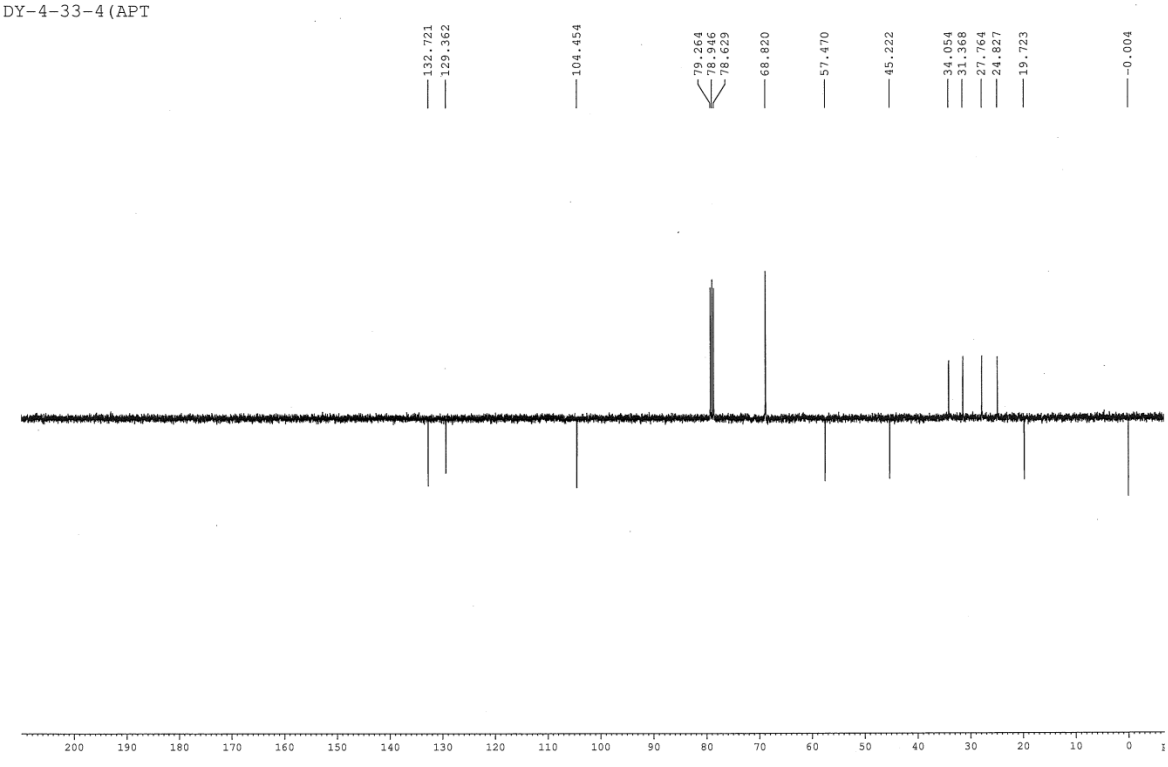

DY-4-23-2(APT
136.446
125.700
78.188
77.870
77.552
65.957
27.744
14.038
-0.004
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

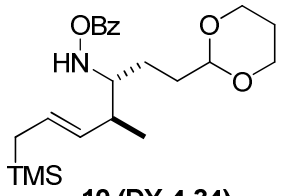


9 (DY-4-33)

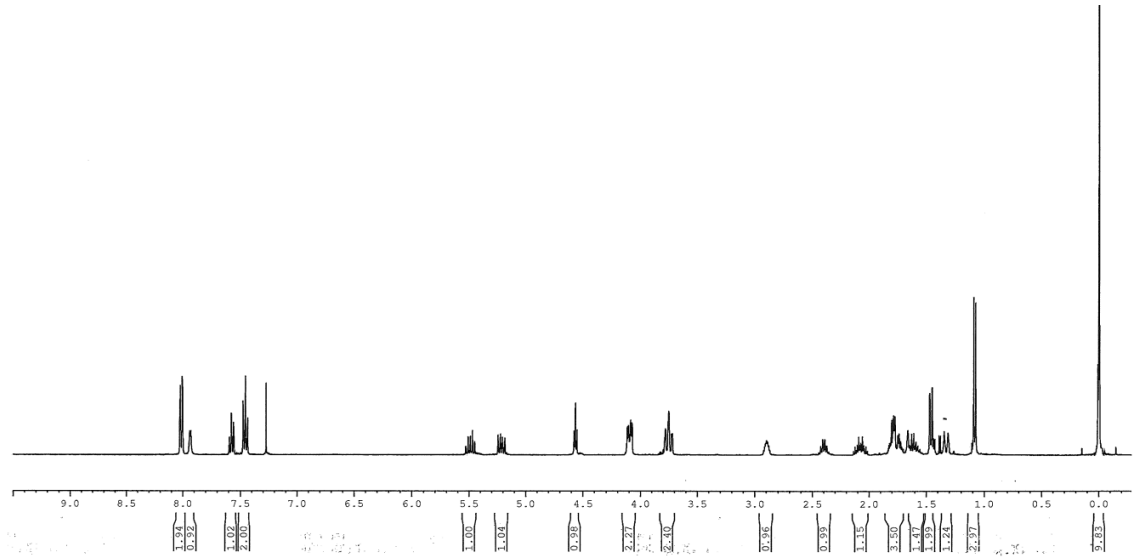


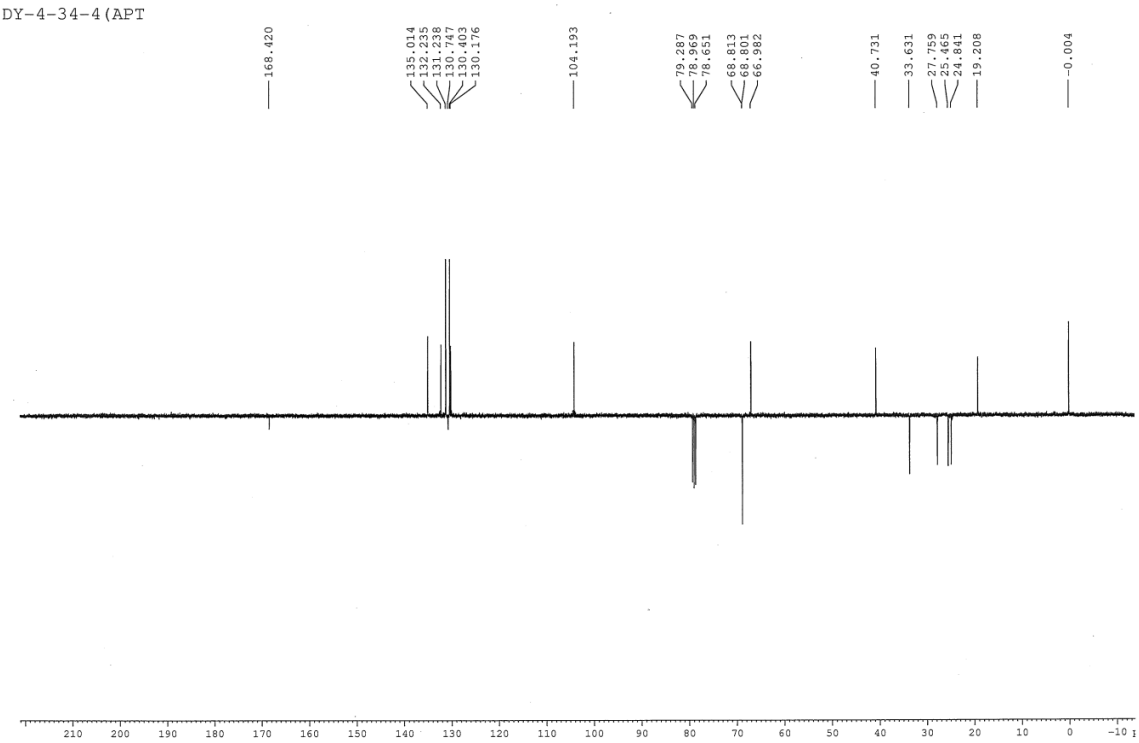
DY-4-33-4(APT

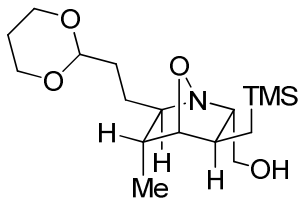



OBz
HN
O
O
TMS

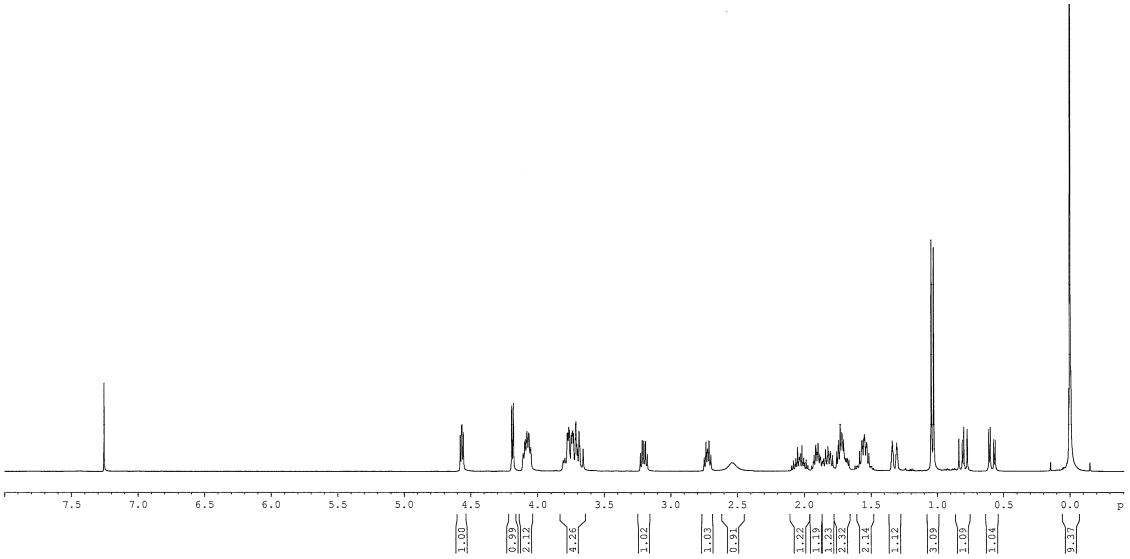
10 (DY-4-34)


9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.94
0.92
1.02
2.00
1.00
1.04
0.98
2.27
2.40
0.96
0.99
1.15
3.50
1.47
1.69
1.24
2.97
9.83

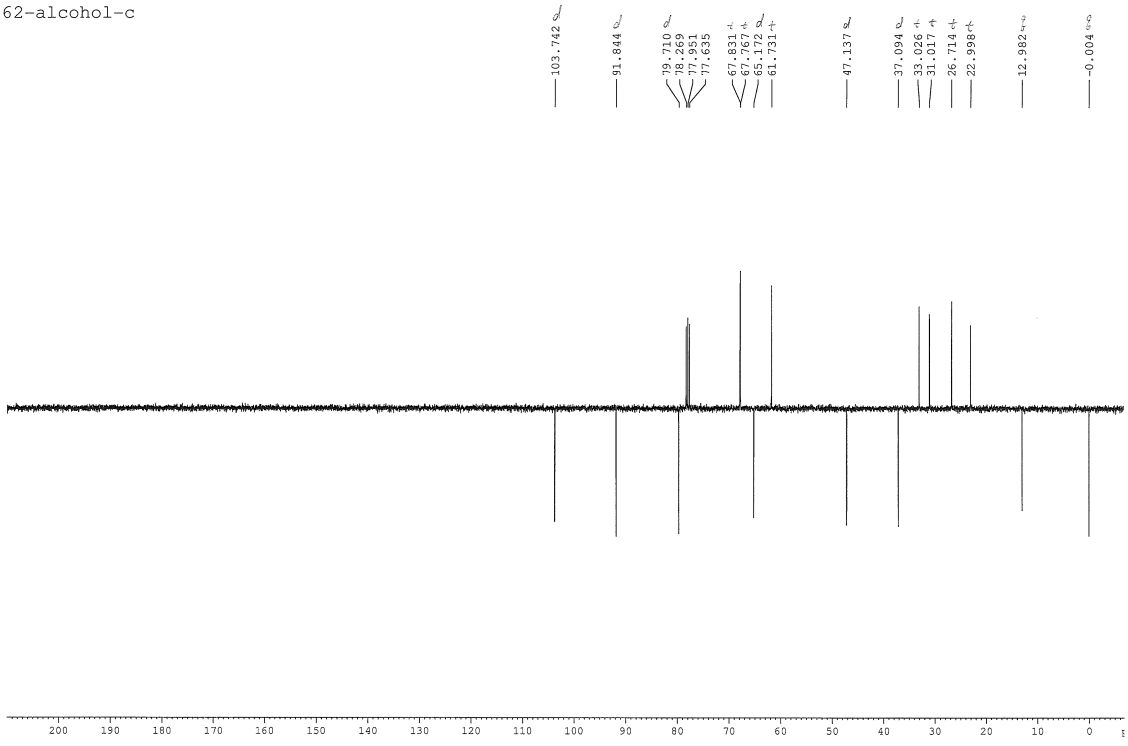

DY-4-34-4(APT
168.420
135.014
132.235
131.238
130.747
130.403
130.176
104.193
79.287
78.969
78.651
68.813
68.801
66.982
40.731
33.631
27.759
25.465
24.841
19.208
-0.004
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

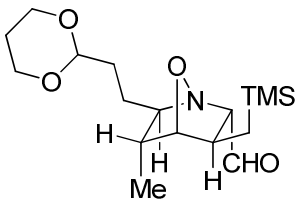


S-2 (DY-3-262)

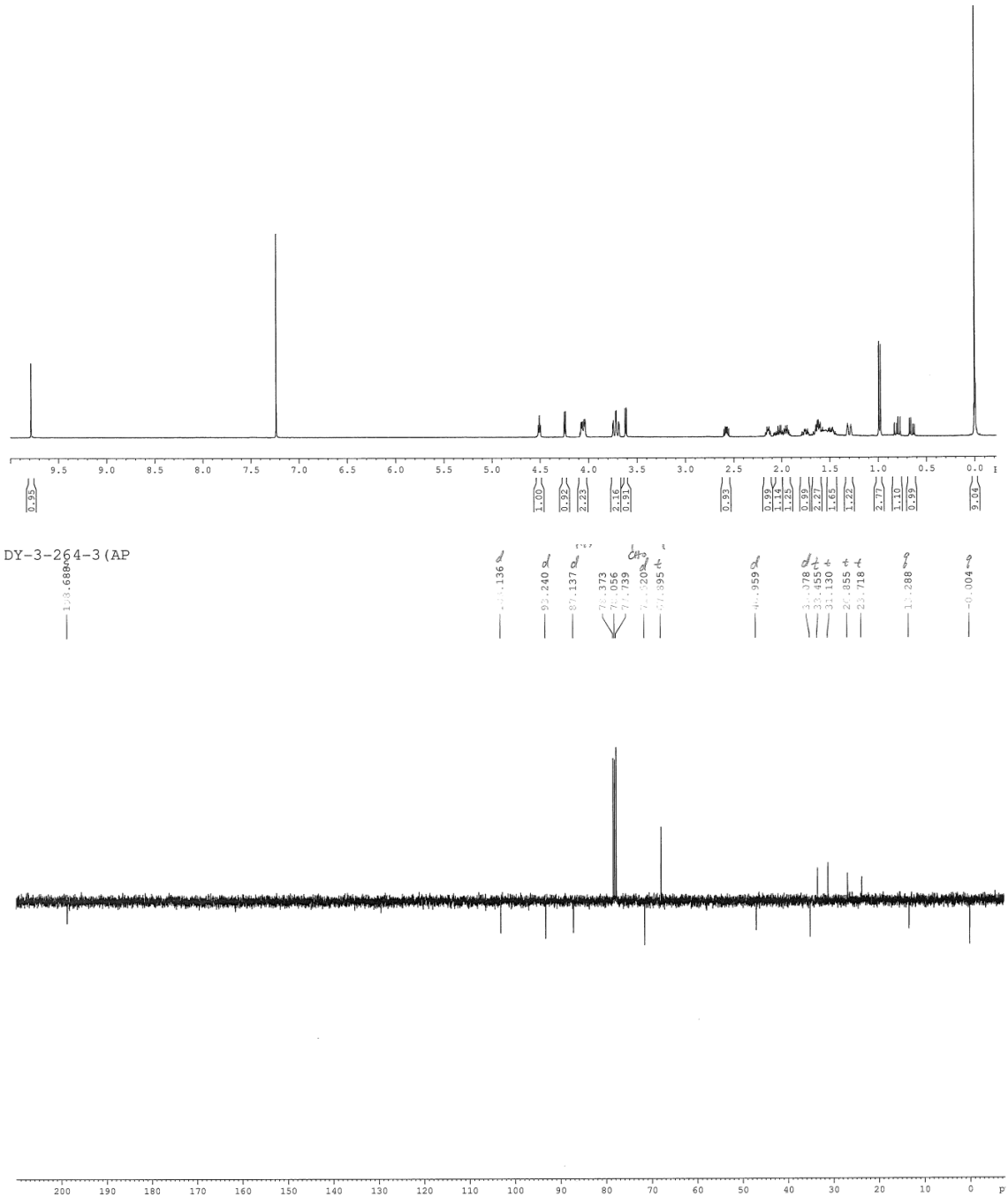


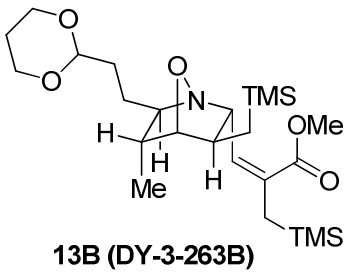
262-alcohol-c



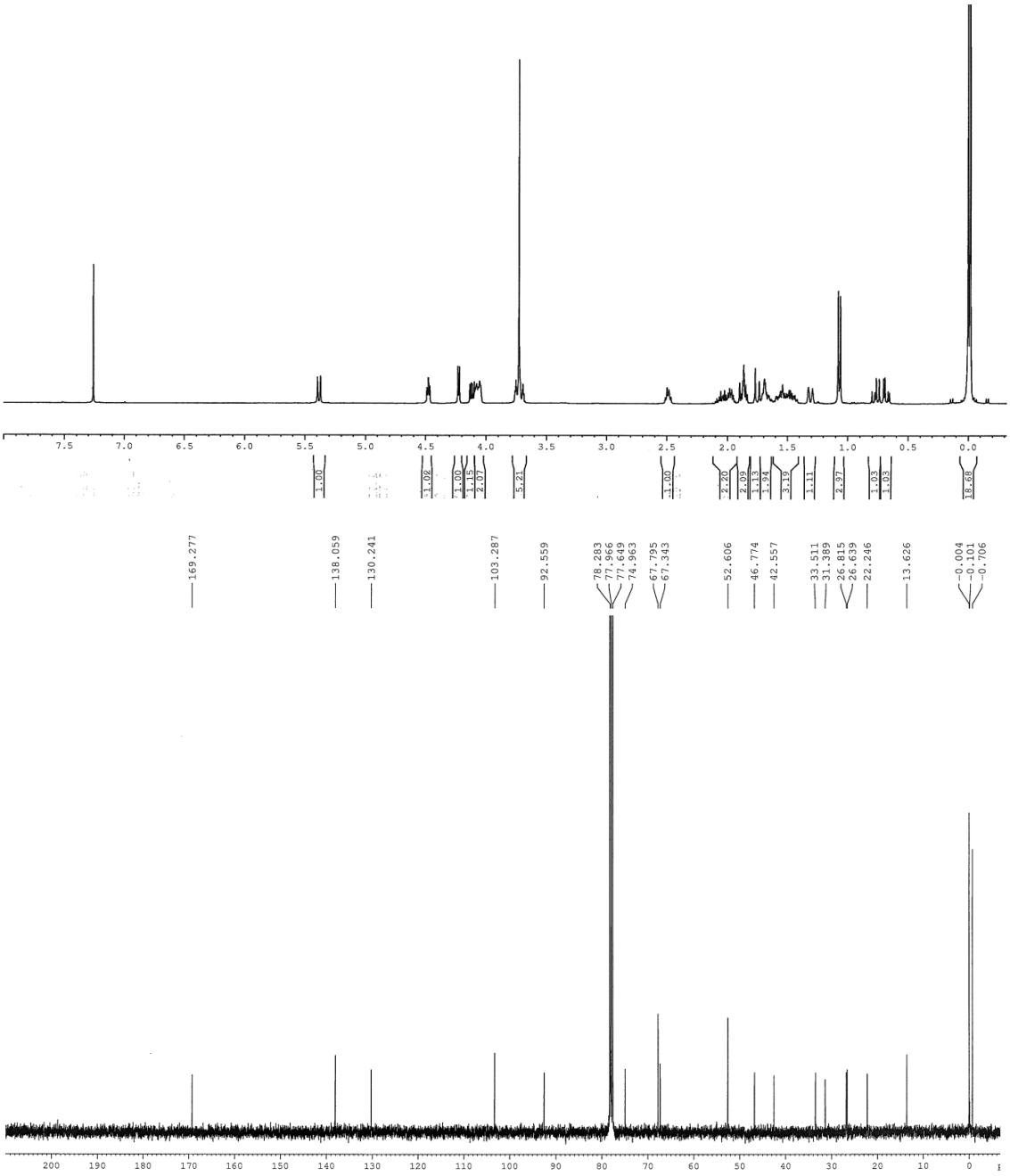


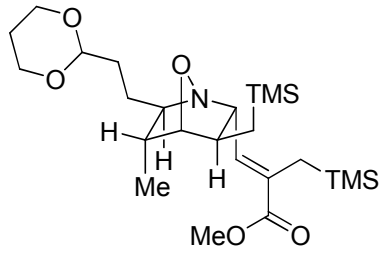
S-3 (DY-3-264)



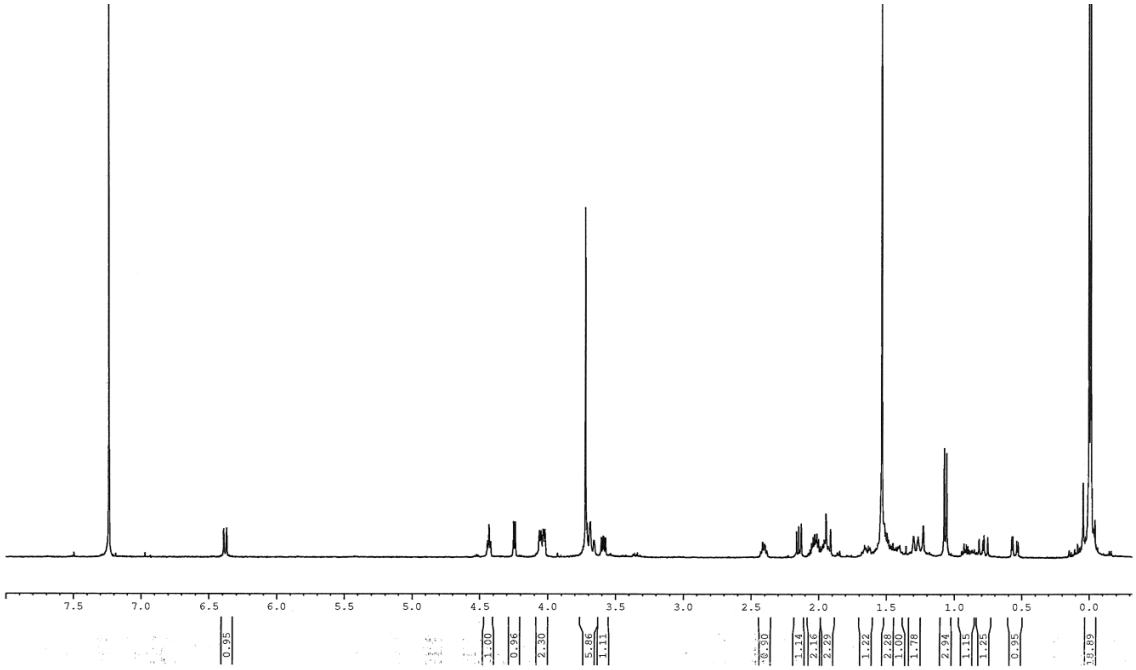

O
O
O
N
TMS
OMe
H
H
Me
H
O
TMS

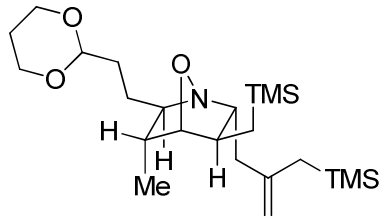
13B (DY-3-263B)


7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.00 1.08 1.00 1.15 2.07 5.21 1.00 2.20 2.09 1.13 1.04 3.19 1.11 2.97 1.03 1.03 18.68
169.277 138.059 130.241 103.287 92.559 78.283 77.966 77.649 74.963 67.795 67.343 52.606 46.774 42.557 33.511 31.389 26.815 26.639 22.246 13.626 -0.004 -0.101 -0.706
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

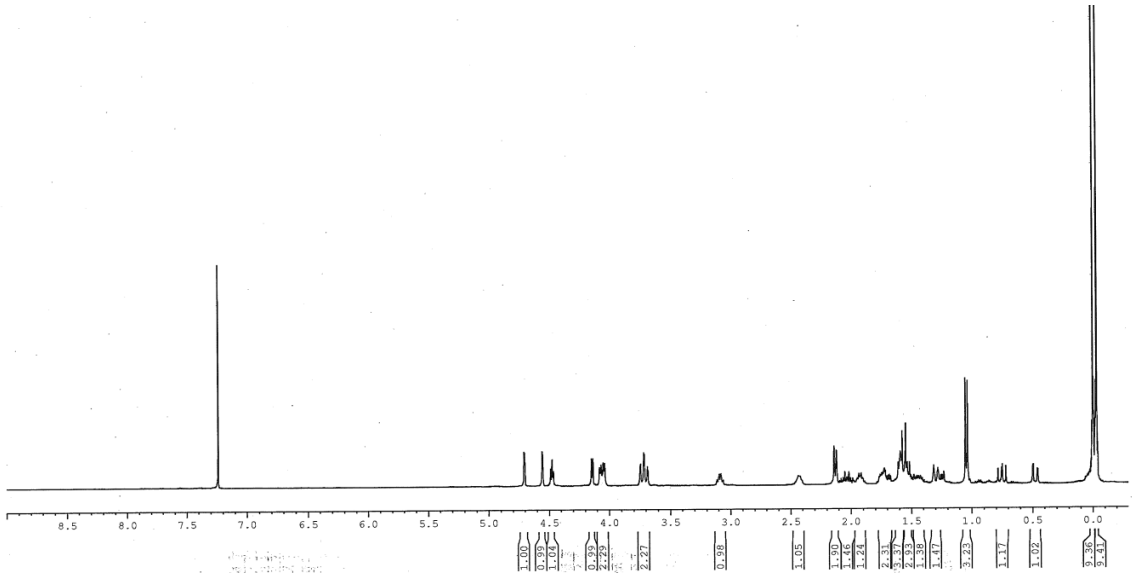

O
O
O
N
TMS
H
H
Me
H
TMS
MeO
O

13A (DY-3-263A)

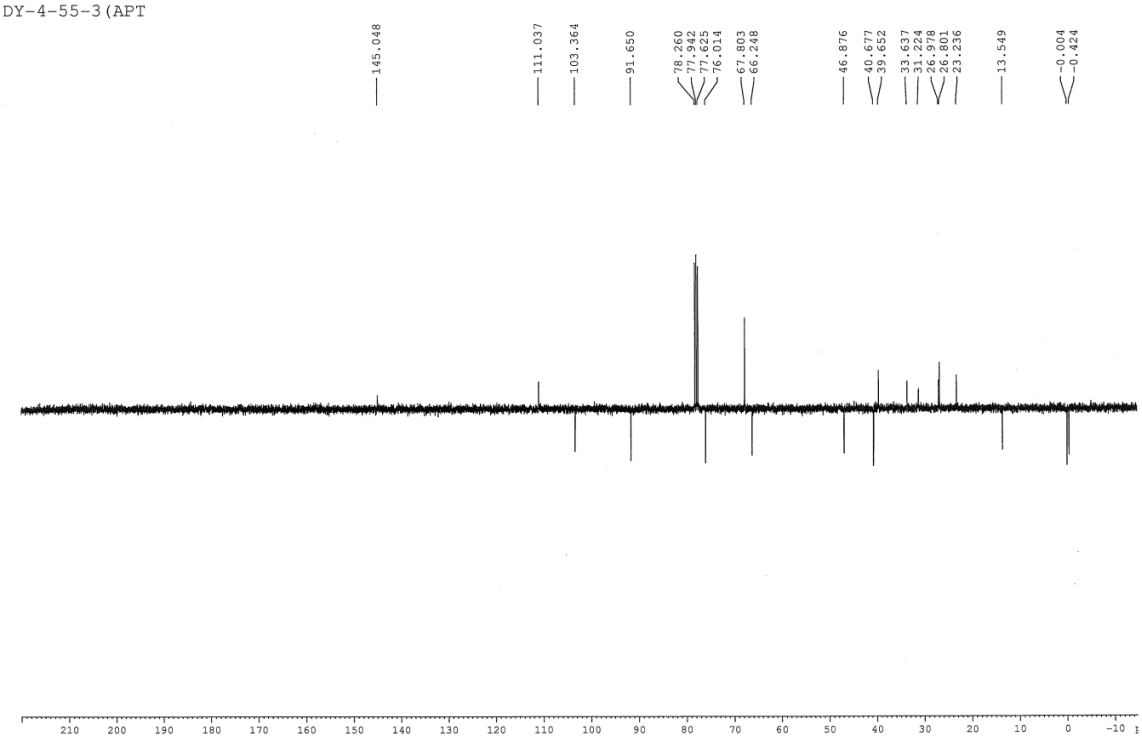

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.95
1.00
0.96
2.30
5.86
1.11
0.90
1.14
2.16
2.29
1.22
2.28
1.00
1.78
2.94
1.15
1.25
0.95
10.89

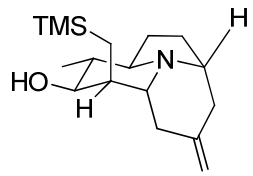


14 (DY-4-55)

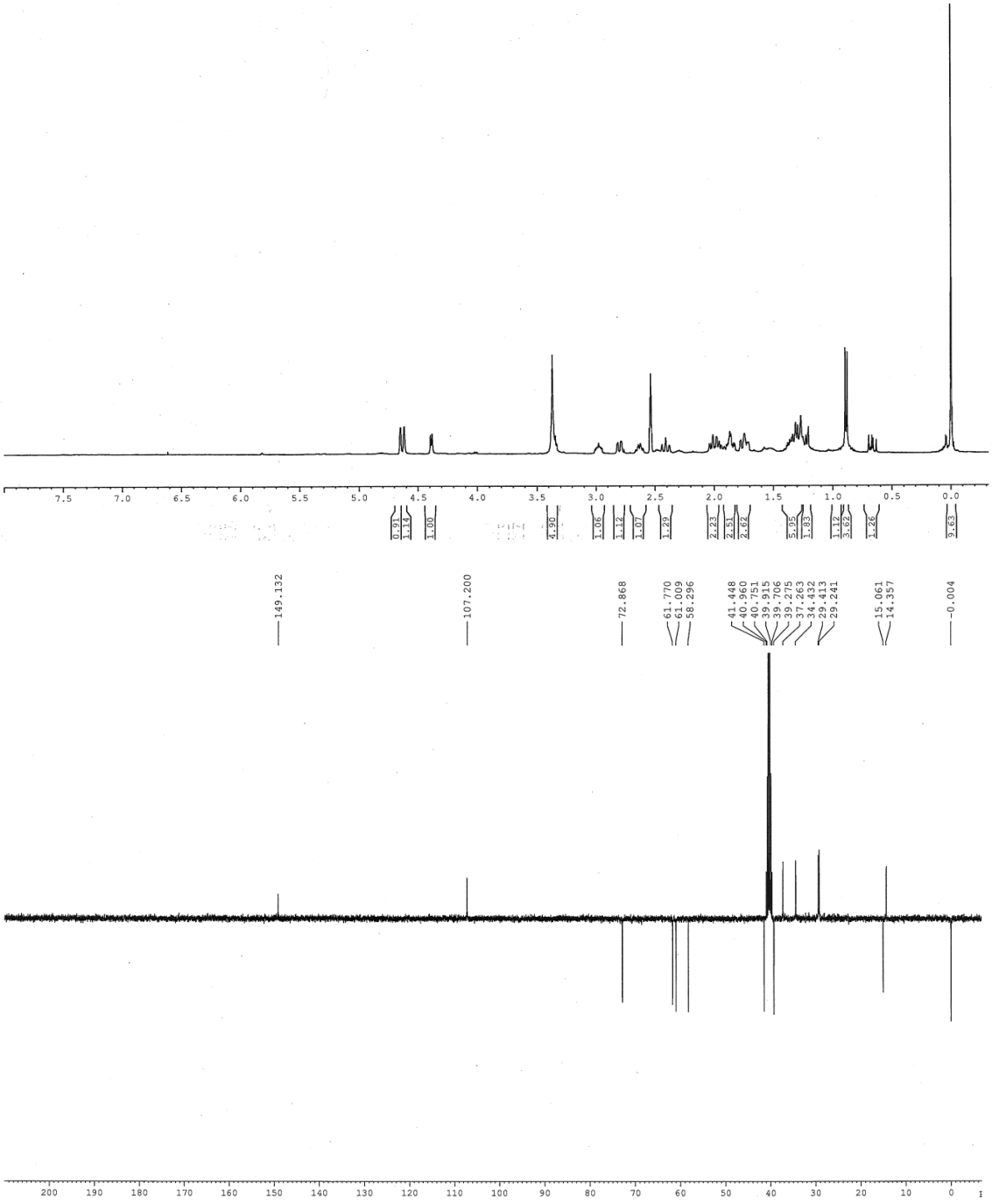


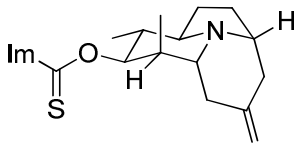
DY-4-55-3(APT



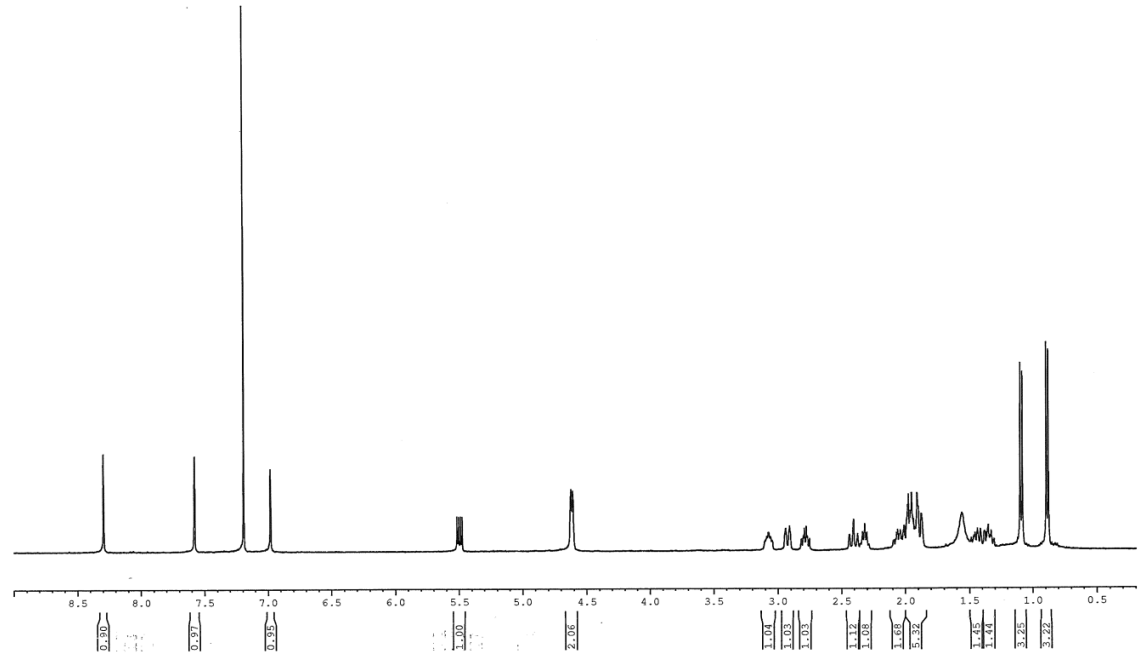


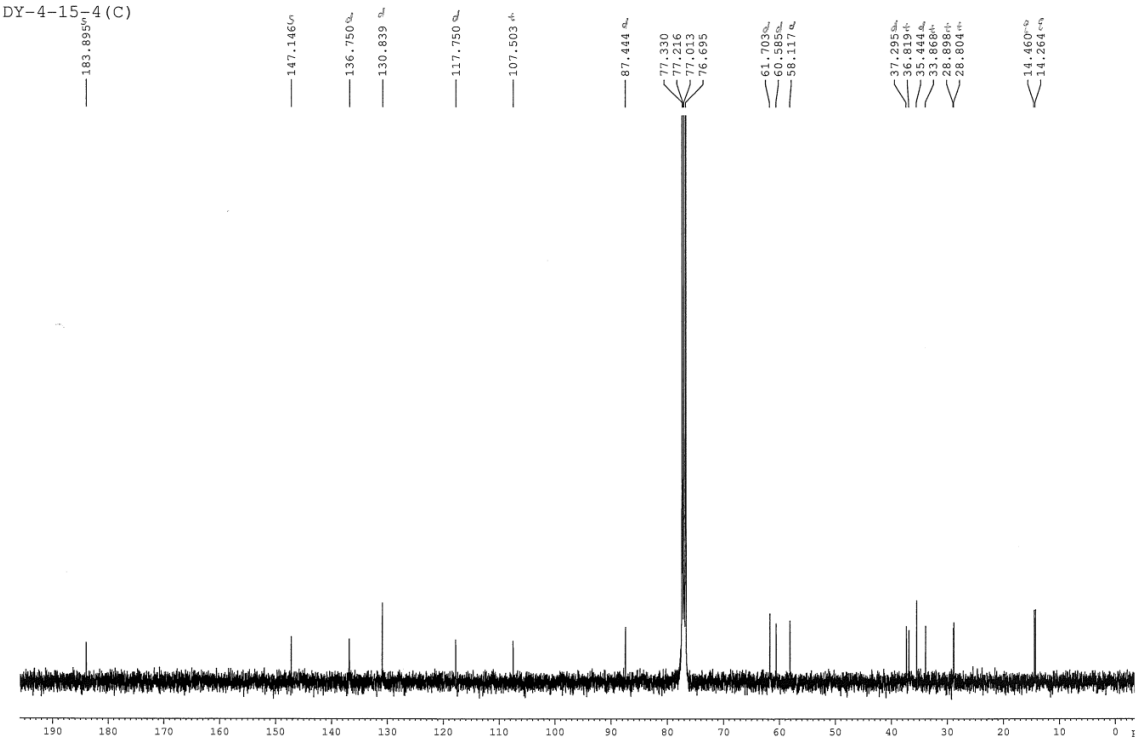
15 (DY-4-56 in DMSO)

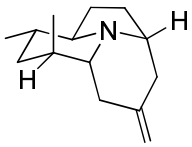



Im
O
S
H
N
H

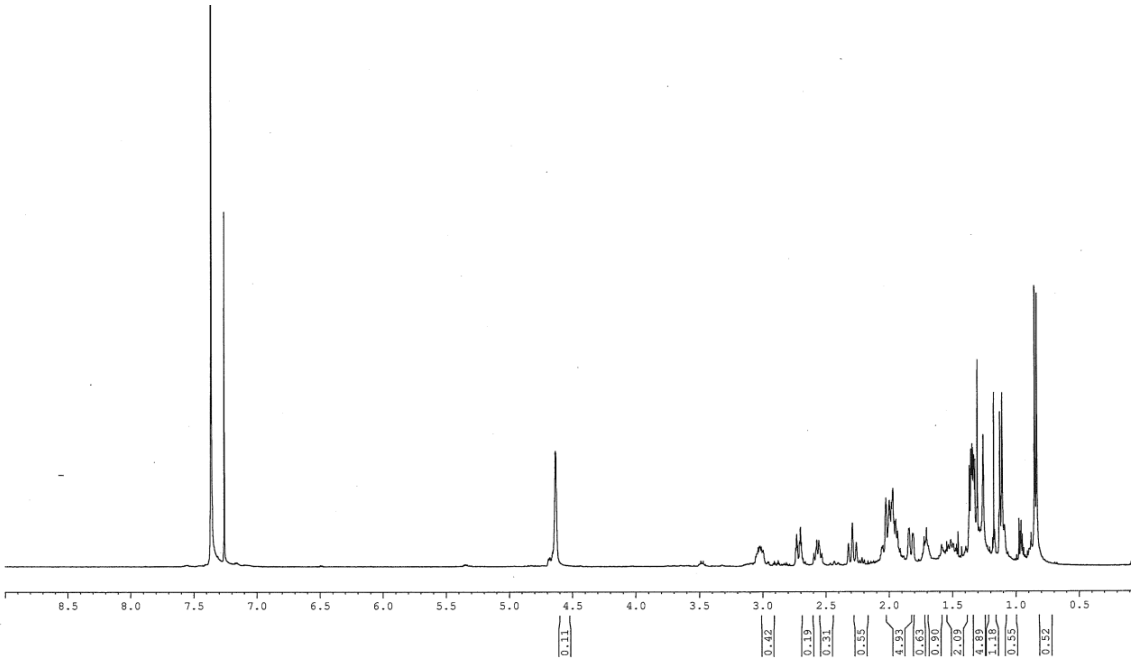
16 (DY-4-15)

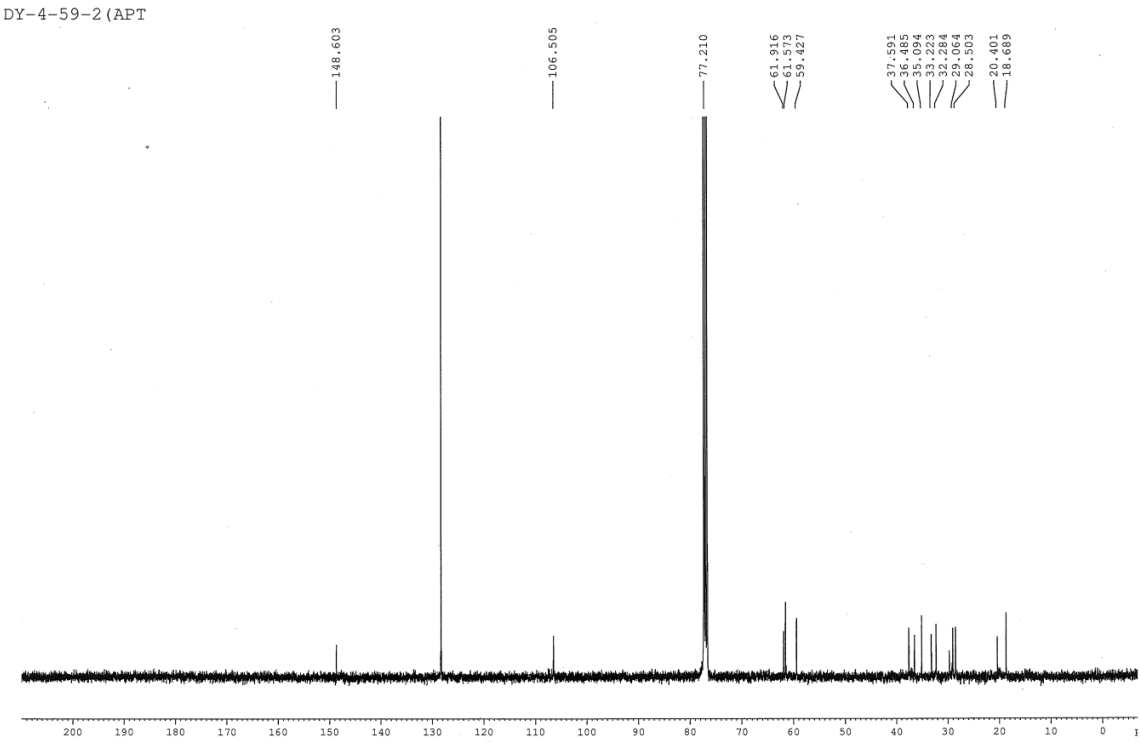

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.90
0.97
0.95
1.00
2.06
1.04
1.03
1.03
1.12
1.08
1.68
5.32
1.45
1.44
3.25
3.22

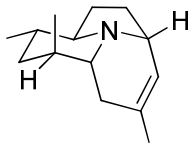

DY-4-15-4(C)
183.895
147.146
136.750
130.839
117.750
107.503
87.444
77.330
77.216
77.013
76.695
61.703
60.585
58.117
37.295
36.819
35.444
33.868
28.898
28.804
14.460
14.264
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


N
H
H

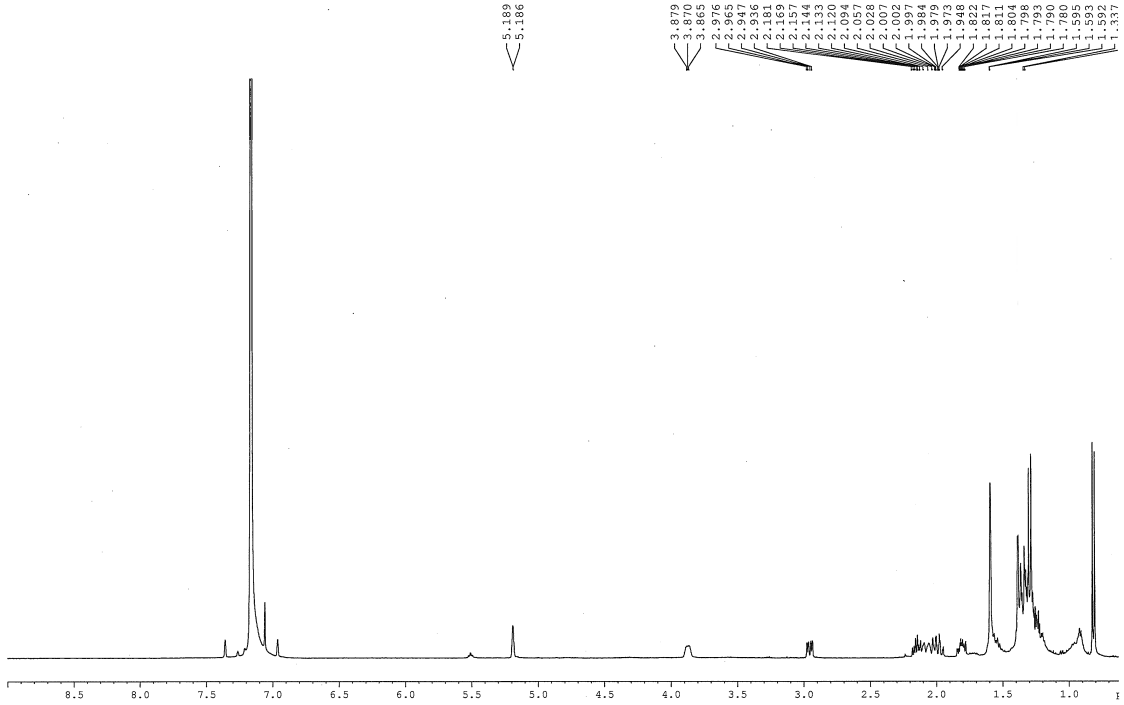
S-5 (DY-4-59)

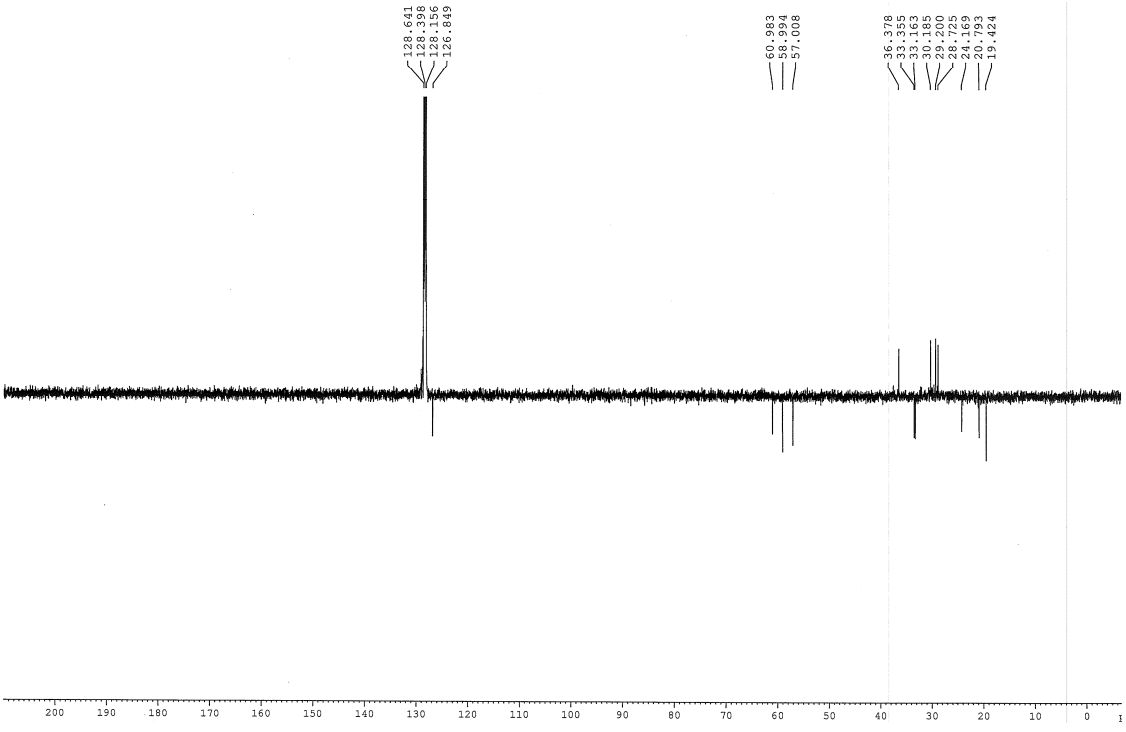

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.11
0.42
0.19
0.31
0.55
4.93
0.63
0.90
2.09
4.89
1.18
0.55
0.52

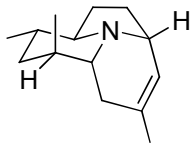

DY-4-59-2(APT
148.603
106.505
77.210
61.916
61.573
59.427
37.591
36.485
35.094
33.223
32.284
29.064
28.503
20.401
18.689
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


N
H
H

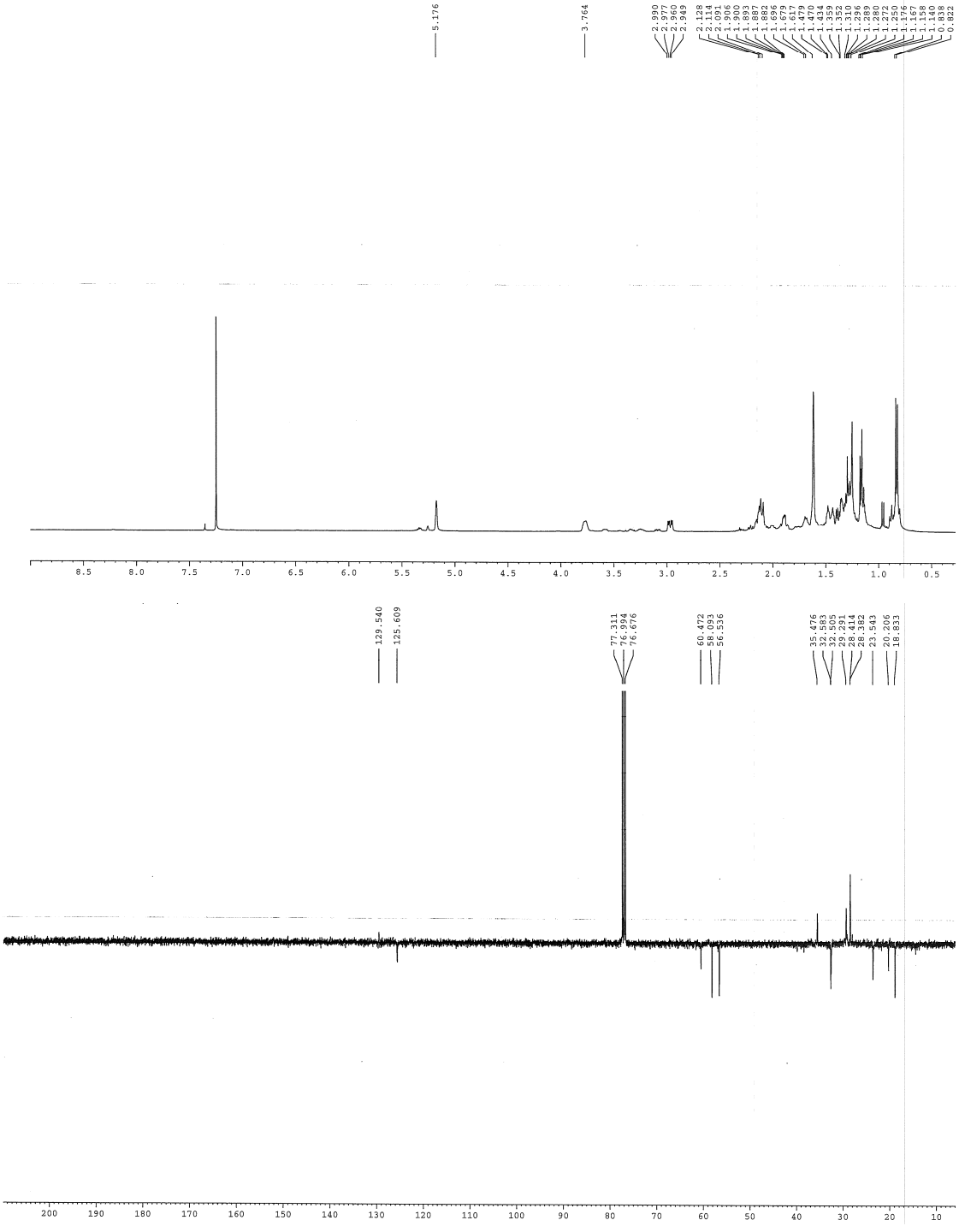
(–)-205B (C_6D_6)


5.189
5.186
3.879
3.870
3.865
2.976
2.965
2.947
2.936
2.181
2.169
2.157
2.144
2.133
2.120
2.094
2.057
2.028
2.007
2.002
1.997
1.984
1.979
1.973
1.948
1.922
1.817
1.811
1.804
1.798
1.793
1.790
1.780
1.595
1.593
1.592
1.337
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0


128.641
128.398
128.156
126.849
60.983
58.994
57.008
36.378
33.355
33.163
30.185
29.200
28.725
24.169
20.793
19.424
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

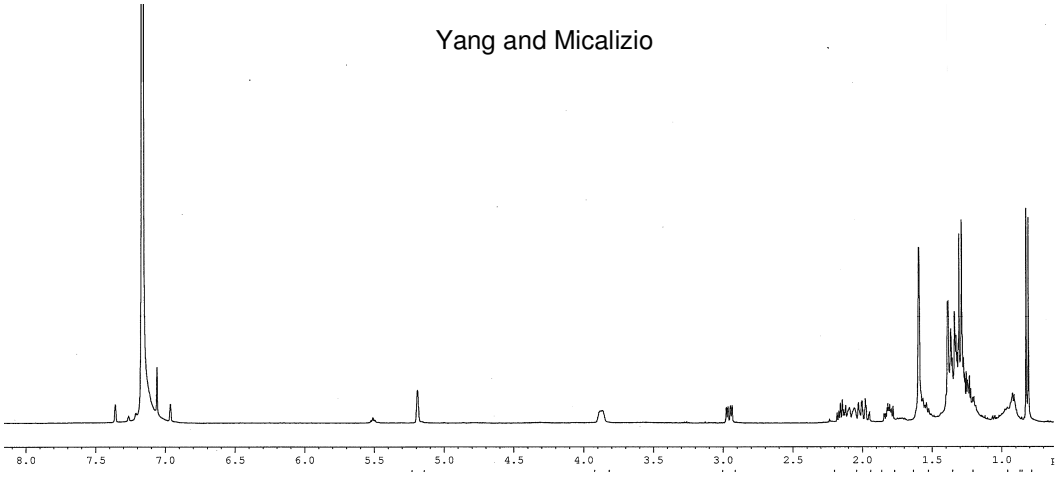

N
H
H

(–)-205B ($CDCl_3$)

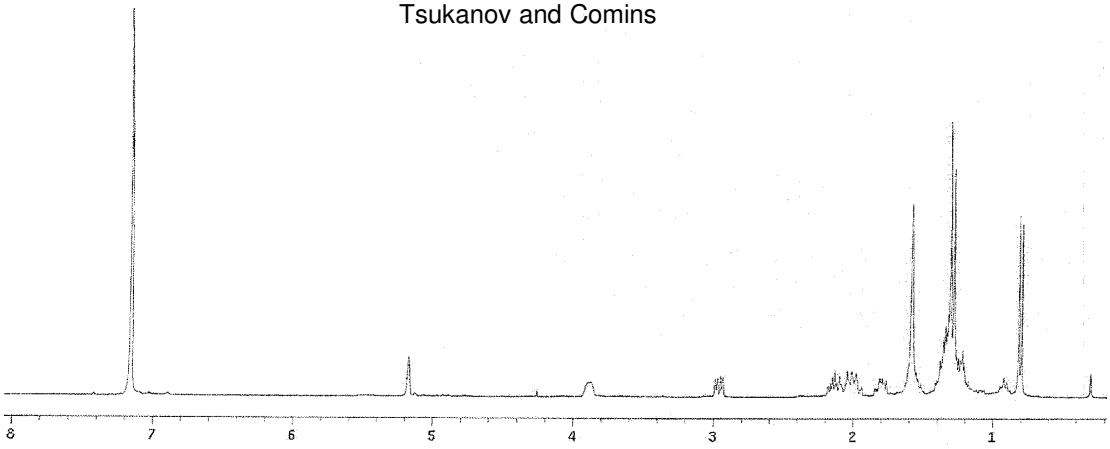

5.176
3.764
2.990
2.977
2.960
2.949
2.128
2.114
2.091
1.906
1.900
1.893
1.887
1.882
1.676
1.673
1.617
1.479
1.470
1.464
1.359
1.352
1.310
1.296
1.289
1.280
1.272
1.250
1.176
1.167
1.158
1.140
0.838
0.822
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
129.540
125.609
77.311
76.994
76.676
60.472
58.093
56.536
35.476
32.583
32.505
29.291
28.414
28.382
23.543
20.206
18.833
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

Comparison of ^{1}H NMR of (–)-205B

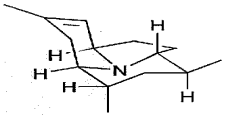
Yang and Micalizio



Tsukanov and Comins



Kim and Smith



(-)-2

500 MHz ^{1}H NMR in C_6D_6

Comparison Table of Characterization Data

^{1}H NMR					
$CDCl_3$			C_6D_6		
400 MHz	400 MHz[1]	500 MHz[2]	400 MHz	400 MHz[1]	500 MHz[2]
5.18 (bs, 1H)	5.18 (bs, 1H)	5.18 (bs, 1H)	5.19 (d, *J* = 1.2 Hz, 1H)	5.19 (bs, 1H)	5.19 (bs. 1H)
3.76 (bs, 1H)	3.79 (bs, 1H)	3.79 (bs, 1H)	3.87 (bs, 1H)	3.87 (bs, 1H)	3.87 (bs, 1H)
2.98 (dd, *J* = 12.0, 4.4 Hz, 1H)	2.98 (dd, *J* = 4.6, 11.2 Hz, 1H)	2.98 (dd, *J* = 11.4, 4.6, 1H)	2.95 (dd, *J* = 11.6 Hz, 4.4, 1H)	2.95 (dd, *J* = 14.2, 4.8 Hz, 1H)	2.95 (dd, *J* = 11.5, 4.6 Hz, 1H)
2.13 - 2.09 (m,3H)	2.17 - 2.10 (m,3H)	2.17 - 2.10 (m,3H)	2.15 (td, *J* = 9.8, 4.8 Hz, 1H)	2.15 (dt, *J* = 9.8, 5.1 Hz, 1H)	2.15 (dd, *J* = 9.8, 5.2 Hz, 1H)
1.91 - 1.88 (m, 1H)	1.94 - 1.86 (m, 1H)	1.93 - 1.88 (m, 1H)	2.06 (t, *J* = 14.8 Hz, 1H)	2.05 (bt, *J* = 15.0, 1H)	2.06 (bt, *J* = 14.3 Hz, 1H)
1.74 - 1.66 (m, 1H)	1.78 - 1.68 (m, 1H)	1.79 - 1.71 (m, 1H)	2.01 - 1.95 (td, *J* = 10.0, 2.4 Hz,1H)	2.02 - 1.95 (m, 1H)	2.02 - 1.95 (m, 1H)
1.62 (s, 3H)	1.63 (s, 3H)	1.62 (s, 3H)	1.82 -1.78 (m, 1H)	1.84 - 1.78 (m, 1H)	1.84 -1.79 (m, 1H)
1.48 - 1.25 (m, 6H)	1.51 - 1.23(m, 6H)	1.49 - 1.26 (m, 6H)	1.60-1.53 (m, 1H)	1.60 - 1.52 (m, 1H)	1.60-1.53 (m, 1H)
1.17 (d, *J* = 7.2 Hz, 3H)	1.17 (d, *J* = 7.3 Hz, 3H)	1.18 (d, *J* = 7.2 Hz, 3H)	1.59 (s, 3H)	1.59 (s, 3H)	1.59 (s, 3H)
0.83 (d, *J* = 6.4 Hz, 3H)	0.84 (d, *J* = 6.6 Hz, 3H)	0.84 (d, *J* = 6.4 Hz, 3H)	1.36 - 1.23 (m, 6H)	1.40 - 1.23 (m, 6H)	1.39 - 1.21 (m, 6H)
			1.29 (d, *J* = 7.2 Hz, 3H)	1.29 (d, *J* = 7.0 Hz, 3H)	1.29 (d, *J* = 7.1 Hz, 3H)
			0.81 (d, *J* = 6.8 Hz, 3H)	0.81 (d, *J* = 6.6 Hz, 3H)	0.81 (d, *J* = 6.6 Hz, 3H)
^{13}C NMR					
$CDCl_3$			C_6D_6		
100 MHz	100 MHz[1]	125 MHz[2]	100 MHz	100 MHz[1]	125 MHz[2]
129.54 (s)	129.48	129.54	129.90 (s)	129.92	129.94
125.61 (d)	125.33	125.56	126.85 (d)	126.81	126.85
60.47 (d)	60.54	60.53	60.98 (d)	60.96	60.99
58.09 (d)	57.99	58.12	59.00 (d)	58.96	59.00
56.34(d)	56.41	56.24	57.01 (d)	56.97	57.02
35.48 (t)	35.39	35.51	36.38 (t)	36.34	36.39
32.58 (d)	32.57	32.61	33.36 (d)	33.34	33.36
32.51 (d)	32.31	32.43	33.16 (d)	33.14	33.16
29.29 (t)	29.09	29.23	30.19 (t)	30.15	30.18
28.41 (t)	28.38	28.43	29.20 (t)	29.18	29.20
28.38 (t)	28.34	28.43	28.73 (t)	28.70	28.74
23.54 (q)	23.53	23.52	24.17 (q)	24.18	24.15
20.21 (q)	20.11	20.19	20.79 (q)	20.79	20.79
18.83 (q)	18.84	18.82	19.42 (q)	19.43	19.43
IR			**Optical Rotation**		
Found	Ref 1	Ref 2	Found	Ref 1	Ref 2
2956 2939 2852 1648 1456 1393 1175	2956 2925 2852 1647 1458 1377 1171	2959 2924 2841 1655 1458 1376 1169	$[\alpha]_D^{25} = -8.0°$ (c 0.10, $CHCl_3$)	$[\alpha]_D^{25} = -8.6°$ (c 0.45, $CHCl_3$)	$[\alpha]_D^{25} = -8.3°$ (c 0.23, $CHCl_3$)

References:

(1) Tsukanov, S. V.; Comins, D. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 8626.

(2) Smith, A. B.; Kim, D.-S. *J. Org. Chem.* **2006**, *71*,2547.