Supporting Information

Enantioselective Total Synthesis of the Unnatural Enantiomer of Quinine

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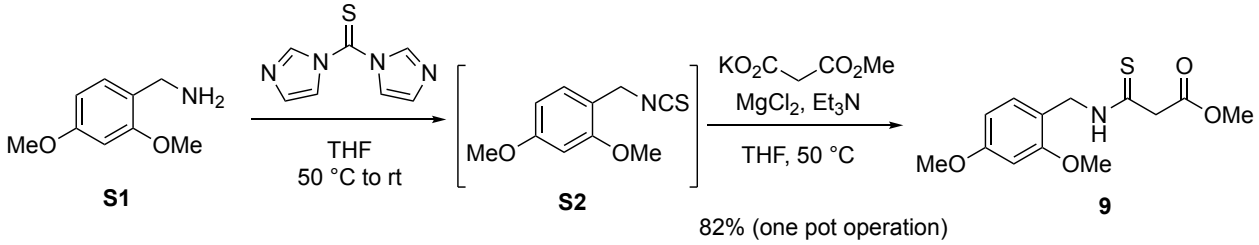
General Remarks: All reactions were monitored by thin-layer chromatography using Merck 60 F254 precoated silica gel plates (0.25 mm thickness). Specific optical rotations were measured using a JASCO P-1020 polarimeter. FT-IR spectra were recorded on a SHIMADZU IR Affinity-IS. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECX 500 FT-NMR spectrometer (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR) instrument. Data for ^{1}H NMR are reported as chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, dd = doubledoublet, ddd = doubledoubledoublet, dt = doubletriplet, q = quartet, quint. = quintet, m = multiplet, br = broad), coupling constant (Hz), integration, and assignment. Data for ^{13}C NMR are reported as chemical shift. The high-resolution mass spectra were recorded on a BRUKER impact II. Preparative thin layer chromatography was performed using Merck 60 F254 precoated silica gel plates (0.25 mm thickness). Flash chromatography was performed using silica gel 60N of Kanto Chemical Co. Int., Tokyo, Japan and amino silica gel (SiO_2–NH) of Fuji Silysia Co. Int., Japan. HPLC analysis was performed on a SHIMAZU Prominence series, UV detection monitored at appropriate wavelength respectively, using DAICEL Chiralpak IC (0.46 cm × 25 cm) and DAICEL Chiralpak AS-H (0.46 cm × 25 cm).

Preparation of thiomalonamate **9**



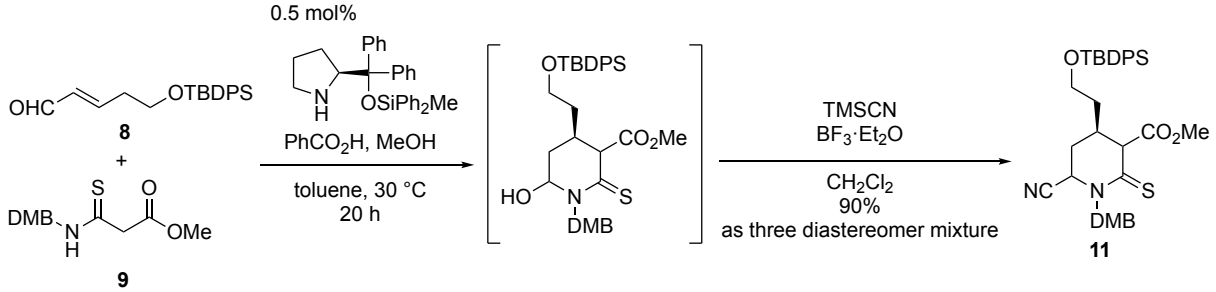
To a solution of 1,1-thiocarbonyldiimidazole (9.09 g, 0.051 mol) in dry THF (170 mL), 2,4-dimethoxybenzylamine (**S1**, 5.65 g, 0.034 mol) was added at 50 °C under Ar atmosphere. The reaction mixture was stirred for 2 h at room temperature to provide 1-(isothiocyanatomethyl)-2,4-dimethoxybenzene (**S2**) solution.

In another flask, to a solution of monomethyl potassium malonate (15.9 g, 0.102 mol) in dry THF (113 mL), $MgCl_2$ (12.3 g, 0.129 mol) was added at 0 °C under Ar atmosphere. Et_3N (22.7 mL, 0.163 mol) was slowly added to the resulting mixture at 0 °C. The resulting suspension mixture was stirred for 1 h at room temperature. The resulting solution of **S2** was added to the resulting monomethyl potassium malonate suspension. The reaction mixture was stirred for 120 h at 50 °C under Ar atmosphere. The resulting mixture was slowly quenched with excess amount of water at 0 °C. The yielded suspension was filtrated with Celite pad and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 20% EtOAc / *n*-hexane) provided thiomalonamate **9** (7.87 g, 82%) as a pale yellow oil.

Thiomalonamate **9**

^{1}H NMR (500MHz, $CDCl_3$) δ 9.54 (br s, 1H), 7.25 (m, 1H, overlapped to $CDCl_3$), 6.48 (s, 1H), 4.45 (d, J = 8.0 Hz, 1H), 4.81 (d, J = 5.5 Hz, 2H), 3.86 (s, 3H), 3.86 (s, 2H), 3.80 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 192.3, 170.2, 161.1, 158.9, 131.3, 116.5, 104.1, 98.8, 55.5 (2C), 52.5, 48.4, 46.1; IR (neat) ν_{max} 3194, 2964, 1734, 1608, 1558, 1506, 1456, 1423, 1346, 1265, 1213, 1155, 1116, 1031, 1008, 842, 812, 786, 696 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{13}H_{18}NO_4S]^+$: 284.0951 found : 284.0950.

Organocatalytic formal aza [3+3] cycloaddition reaction and Strecker reaction



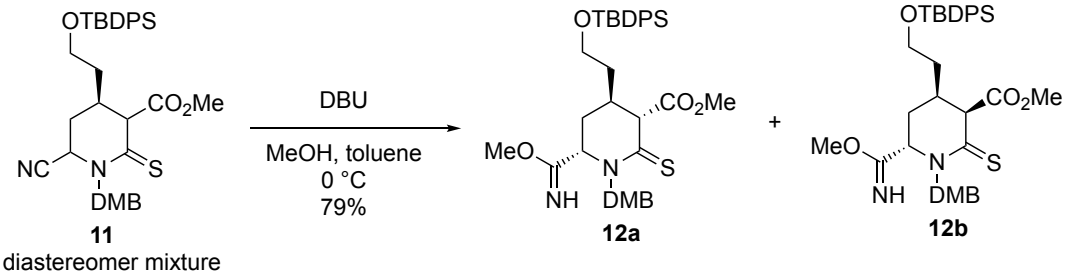
Diphenylprolinol diphenylmethyl silyl ether (**10**, 2.0 mg, 0.0044 mmol) was added to the solution of α, β-

unsaturated aldehyde **8**[s1] (331 mg, 0.98 mmol), thiomalonamate **9** (252 mg, 0.89 mmol) and benzoic acid (108.6 mg, 0.89 mmol) in toluene (1 mL) at 30 °C in open flask. To the resulting mixture, MeOH (108 μL, 2.67 mmol) was added. The reaction mixture was stirred for 20 h at 30 °C. The resulting mixture was slowly quenched with saturated aqueous $NaHCO_3$ at 0 °C. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. To the crude mixture, TMSCN (533 μL, 5.34 mmol) was added at room temperature under Ar atmosphere. The reaction mixture was stirred for 30 min at room temperature. CH_2Cl_2 was added to the resulting mixture and cooled at –20 °C under Ar atmosphere. To the resulting mixture, $BF_3 \cdot Et_2O$ (135 μL, 1.07 mmol) was slowly added at – 20 °C. The reaction mixture was stirred for 1.5 h at – 20 °C under Ar atmosphere before being quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 20% EtOAc / *n*-hexane) provided thiolactam **11** (508 mg, 90% as three diastereomers mixture; dr = 5 : 3 : 2) as a pale yellow oil.

Compound **11** (three diastereomer mixture)

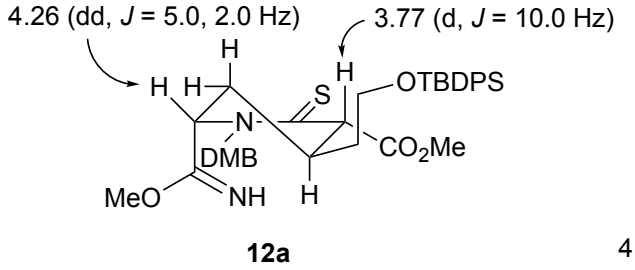
^{1}H NMR (500MHz, $CDCl_3$) δ 7.58–7.67 (m), 7.34–7.46 (m), 7.29 (d, *J* = 9.0 Hz), 6.46–6.50 (m), 6.21 (d, *J* = 14.5 Hz), 6.11 (d, *J* = 14.5 Hz), 6.06 (d, *J* = 14.5 Hz), 4.69 (dd, *J* = 15.0, 1.5 Hz), 4.56–4.63 (m), 4.32 (t, *J* = 6.0 Hz), 4.26 (d, *J* = 6.0 Hz), 3.90 (d, *J* = 8.0 Hz), 3.85 (s), 3.84 (s), 3.82 (s), 3.82 (s), 3.81 (s), 3.78 (s), 3.77 (s), 3.70–3.80 (m), 3.70 (s), 2.68-2.81 (m), 2.39–2.50 (m), 2.22–2.28 (m), 2.12 (d, *J* = 13.5 Hz), 1.90 (dt, *J* = 13.5, 6.5 Hz), 1.73–1.79 (m), 1.62–1.72 (m), 1.36–1.43 (m), 1.03–1.06 (m); ^{13}C NMR (125MHz, $CDCl_3$) δ 197.7, 197.0 (2C), 191.8, 170.9, 170.6, 170.4, 161.7, 161.6, 161.5, 159.4, 159.2, 150.8, 135.9 (3C), 133.7 (2C), 133.6 (3C), 132.4, 131.8, 130.5, 130.2, 128.2, 128.1, 117.1, 116.9, 116.6, 114.5, 114.4, 114.3, 105.1, 105.0, 99.0 (2C), 91.8, 63.8, 62.3, 61.0, 60.9, 60.3, 55.9 (2C), 53.2, 53.0, 52.9, 51.0, 50.8, 49.8, 47.7, 36.3,36.2, 35.0, 31.8, 31.3, 31.0, 30.1, 30.0, 28.3, 27.3, 27.2 (2C), 19.6, 19.5 (2C); IR (neat) ν_{max} 3070, 2931, 2856, 1732, 1612, 1587, 1508, 1463, 1427, 1290, 1207, 1157, 1109, 1033, 937, 821, 736 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{35}H_{43}N_2O_5SSi]^+$: 631.2656 found : 631.2659.

Imidate formation

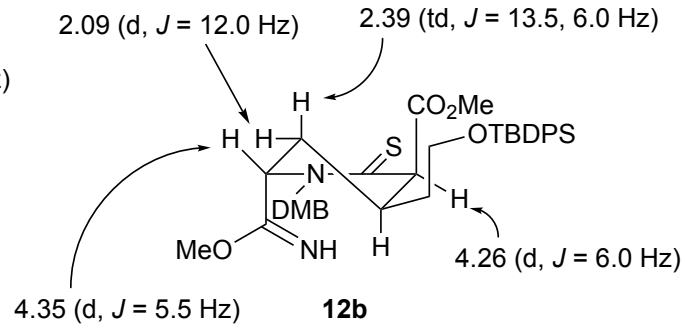


To a solution of diastereomer mixture of **11** (100 mg, dr = 5 : 3 : 2, 0.159 mmol) in toluene (159 μL) and MeOH (634 μL), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 47.4 mL, 0.317 mmol) was added at 0 °C under

Ar atmosphere. The reaction mixture was stirred for 22 h at 0 °C under Ar atmosphere before being quenched with aqueous NH_4Cl. The aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 30–50% EtOAc / *n*-hexane gradient) provided imidate **12** (82.2 mg, 79% as two major diastereomers mixture; **12a** : **12b** = 3 : 1) as a pale yellow oil. The diastereomer mixture was partially separated by PTLC (35% EtOAc / *n*-hexane). The relative stereochemistry of partially isolated **12a** and **12b** were determined by coupling constant in ^{1}H-NMR. In addition, enantiomeric excess of **12a** and **12b** were determined by HPLC with DAICEL Chiralpak IC (each 94% *ee*). For **12a**: 10% *i*-PrOH/*n*-hexane, 0.5 mL/min; major enantiomer t_R = 53.2 min, minor enantiomer t_R = 43.9 min (see page S18); For **12b**: 20% *i*-PrOH/*n*-hexane, 0.75 mL/min; major enantiomer t_R = 13.7 min, minor enantiomer t_R = 36.0 min (see page S20).



12a



12b

Imidate **12a**

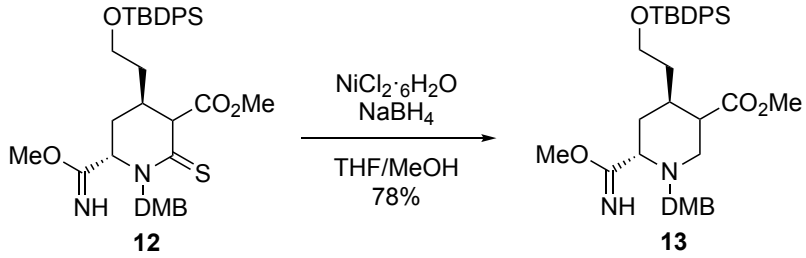
^{1}H NMR (500MHz, $CDCl_3$) δ 7.75 (br s, 1H), 7.59–7.61 (m, 4H), 7.36–7.44 (m, 6H), 7.28 (d, *J* = 9.5 Hz, 1H), 6.43–6.44 (m, 2H), 5.96 (d, *J* = 14.5 Hz, 1H), 4.47 (d, *J* = 14.5 Hz, 1H), 4.26 (dd, *J* = 5.0, 2.0 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.77 (d, *J* = 10.0 Hz, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.61–3.65 (m, 2H), 2.33–2.36 (m, 2H), 1.74–1.76 (m, 1H), 1.67 (br s, 1H), 1.59 (dt, *J* = 6.5, 13.0 Hz, 1H), 1.39–1.41 (m, 1H), 1.01 (s, 9H); ^{13}C NMR (125MHz, $CDCl_3$) δ 197.4, 171.3, 168.9, 161.0, 158.9, 135.6, 135.5, 133.6, 133.4, 129.8, 127.8, 114.9, 104.5, 98.5, 63.7, 61.0, 60.7, 55.5, 55.4, 53.9, 52.9, 51.1, 36.6, 30.6, 26.9, 19.2; IR (neat) ν_{max} 2949, 2856, 1737, 1662, 1612, 1587, 1508, 1427, 1207, 1109, 1033, 970, 821, 750 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{36}H_{47}N_2O_6SSi]^+$: 663.2919 found : 663.2902; $[\alpha]^{27}_D$ +103.5 (*c* 2.92, $CHCl_3$).

Imidate **12b**

^{1}H NMR (500MHz, $CDCl_3$) δ 7.64–7.67 (m, 4H), 7.40–7.49 (m, 6H), 7.31, (d, *J* = 8.5 Hz, 1H), 6.52 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.49 (d, *J* = 2.0 Hz, 1H), 6.18 (d, *J* = 15.5 Hz, 1H), 4.35 (d, *J* = 5.5 Hz, 1H), 4.30 (d, *J* =15.5 Hz, 1H), 4.26 (d, *J* = 6.0 Hz, 1H), 3.83 (s, 3H), 3.74 (s, 3H), 3.68 (s, 3H), 3.60–3.80 (m, 5H), 2.46 (m, 1H), 2.39 (td, *J* = 13.5, 6.0 Hz, 1H), 2.09 (d, *J* = 12.0 Hz, 1H), 1.57–1.63 (m, 1H), 1.30–1.38 (m, 1H), 1.06 (s, 9H); ^{13}C NMR (125MHz, $CDCl_3$) δ 197.6, 170.8, 160.9, 161.0, 158.9, 135.9, 135.8, 133.9, 133.7, 130.2, 130.1, 129.3, 128.2, 128.1, 115.0,

104.7, 98.9, 62.5, 60.9, 60.5, 55.8, 55.7, 52.7, 51.6, 35.4, 28.5, 27.9, 27.2, 19.5; IR (neat) ν_{max} 2931, 2856, 1732, 1652, 1614, 1589, 1508, 1456, 1427, 1207, 1157, 1109, 1033, 821, 750 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{36}H_{47}N_2O_6SSi]^+$: 663.2919 found : 663.2908; $[\alpha]^{27}_D$ +92.3 (*c* 1.34, $CHCl_3$).

Reduction of thiocarbonyl group



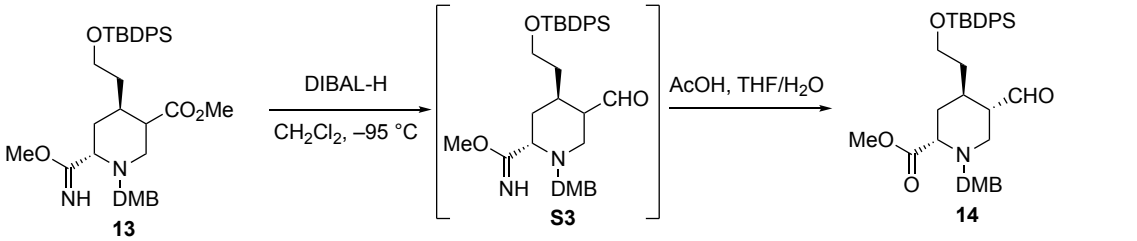
α-CO_2Me (**12a**) : β-CO_2Me (**12b**) = 3 : 1 α-CO_2Me (**13a**) : β-CO_2Me (**13b**) = 3 : 1

To a solution of **12** (**12a** : **12b** = 3 : 1, 211 mg, 0.318 mmol) in THF (5.3 mL) and MeOH (5.3 mL), $NaBH_4$ (144 mg, 3.82 mmol) was added at –20 °C under Ar atmosphere. To the resulting mixture, $NiCl_2$ (227 mg, 0.955 mmol) was added at –20 °C. The reaction mixture was stirred for 5 min before being quenched with saturated aqueous $NaHCO_3$. The yielded suspension was filtrated with Celite pad and the aqueous layer was extracted three times with $CHCl_3$. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 30% EtOAc / *n*-hexane) provided compound **13** (157.1 mg, 78% as two diastereomers mixture; **13a** : **13b** = 3 : 1) as a pale yellow oil. The NMR chart of diastereomer mixture was shown in page S21.

Major piperidine **13a** which was partially isolated by PTLC

^{1}H NMR (500MHz, $CDCl_3$) δ 7.97 (br s, 1H), 7.65–7.67 (m, 4H), 7.36–7.43 (m, 6H), 7.20 (d, *J* = 8.0 Hz, 1H), 6.43–6.47 (m, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.64–3.76 (m, 7H), 3.60 (s, 3H), 3.54 (d, *J* = 14.0 Hz, 1H), 3.21–3.23 (m, 1H), 2.99 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.67 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.43 (td, *J* = 4.0, 8.5 Hz, 1H), 20.7–2.11 (m, 1H), 1.42–1.53 (m, 2H), 1.04 (s, 9H); ^{13}C NMR (125MHz, $CDCl_3$, major diastereomer) δ 174.8, 173.9, 160.4, 159.1, 135.9 (2C), 134.2, 134.1, 130.9, 129.9 (2C), 128.0, 119.2, 104.3, 98.7, 61.7, 59.9, 55.7, 55.6, 53.6, 52.5, 51.8, 49.2, 44.3, 36.8, 31.2, 28.3, 27.1, 19.5; IR (neat) ν_{max} 2931, 2854, 1732, 1651, 1612, 1587, 1506, 1427, 1290, 1207, 1155, 1105, 1035, 821, 752 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{36}H_{49}N_2O_6Si]^+$: 633.3554 found : 633.3341; $[\alpha]^{26}_D$ –4.7 (*c* 5.35, $CHCl_3$).

DIBAL reduction, isomerization, hydrolysis of imidate



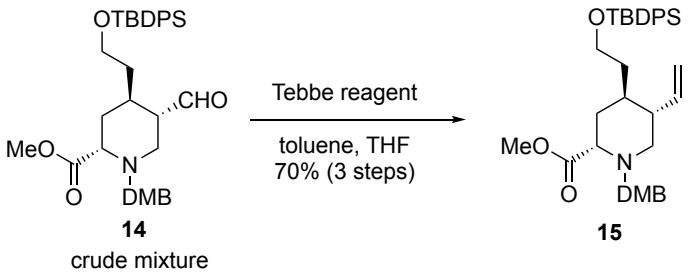
α-CO_2Me (**13a**) : β-CO_2Me (**13b**) = 3 : 1

Single isomer determined by crude NMR

To a solution of **13** (265 mg, 0.419 mmol, **13a** : **13b** = 3 : 1) in CH_2Cl_2 (10 mL), DIBAL-H (1.0 M solution in *n*-hexane, 2.1 mL, 2.1 mmol) was added slowly at –95 °C under Ar atmosphere. The reaction mixture was stirred for 2 h before being quenched with dry MeOH (1.5 mL) at –95 °C. To the resulting mixture, saturated aqueous Rochelle's salt was added at room temperature. The aqueous layer was extracted six times with $CHCl_3$. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. The crude materials of **S3** was directly employed next hydrolysis.

To a solution of the crude materials of aldehyde **S3** in THF (4.2 mL), acetic acid (0.14 mL) and H_2O (0.84 mL) were added via syringe at room temperature under Ar atmosphere. The reaction mixture was stirred for 5 h at room temperature before being quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted four times with EtOAc. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. Aldehyde **14** was unstable in silica gel column chromatography, thus, the crude materials of **14** was directly employed to next Tebbe olefination. The ^{1}H-NMR of the crude materials of **14** strongly indicated isomerization reaction on acid hydrolysis condition to thermodynamically stable **14** (see page S23).

Tebbe olefination



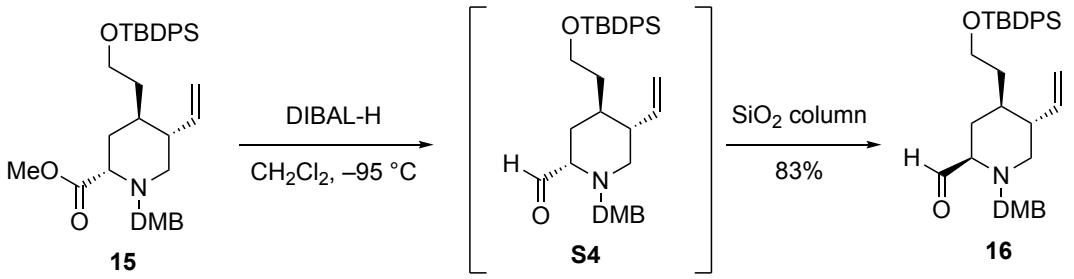
To a solution of the crude materials of **14** in dry toluene (4.2 mL) and dry THF (1.4 mL), μ-chlorobis(η^5-cyclopentadienyl)(dimethylaluminum)-μ-methylenetitanium (Tebbe reagent, 0.5 M solution in toluene, 0.85 mL, 0.461 mmol) was added at 0 °C under Ar atmosphere. The reaction mixture was stirred for 2 h at room temperature before being quenched with saturated aqueous Rochelle's salt at 0 °C. The aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 10%

EtOAc / *n*-hexane) provided compound **15** (176 mg, 70%) as a pale yellow oil.

Piperidine **15** (single isomer)

^{1}H NMR (500MHz, $CDCl_3$) δ 7.64–7.66 (m, 4H), 7.36–7.42 (m, 6H), 7.22 (d, *J* = 8.5 Hz, 1H), 6.43–6.47 (m, 2H), 5.51–5.59 (m, 1H), 4.98–5.01 (m, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 3.65–3.80 (m, 3H), 3.66 (s, 6H), 3.52–3.62 (m, 1H), 3.01(t, *J* = 11.5 Hz, 1H), 2.62 (dd, *J* = 12.0, 4.5 Hz, 1H), 2.13–2.15 (m, 1H), 1.93–2.00 (m, 1H), 1.84–1.90 (m, 1H), 1.48–1.51 (m, 2H), 1.15–1.21 (m, 1H), 1.02–1.04 (m, 10H); ^{13}C NMR (125MHz, $CDCl_3$) δ; 174.2, 159.9, 158.9, 40.4, 135.7, 134.1, 134.0, 130.1, 129.6, 119.9,116.2, 104.1, 98.5, 61.7, 59.9, 58.5, 55.5, 55.4, 52.9,52.8,51.0, 47.1, 36.3,33.2, 32.6, 26.9, 19.3, 18.5; IR (neat) ν_{max} 2929, 2856, 1734, 1612, 1587, 1506, 1563, 1427, 1292, 1207, 1155, 1109, 1037, 1004, 918, 821, 754 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{36}H_{48}NO_5Si]^+$: 602.3296 found : 602.3284; $[\alpha]^{27}_D$ –6.5 (*c* 1.29, $CHCl_3$).

DIBAL reduction and isomerization



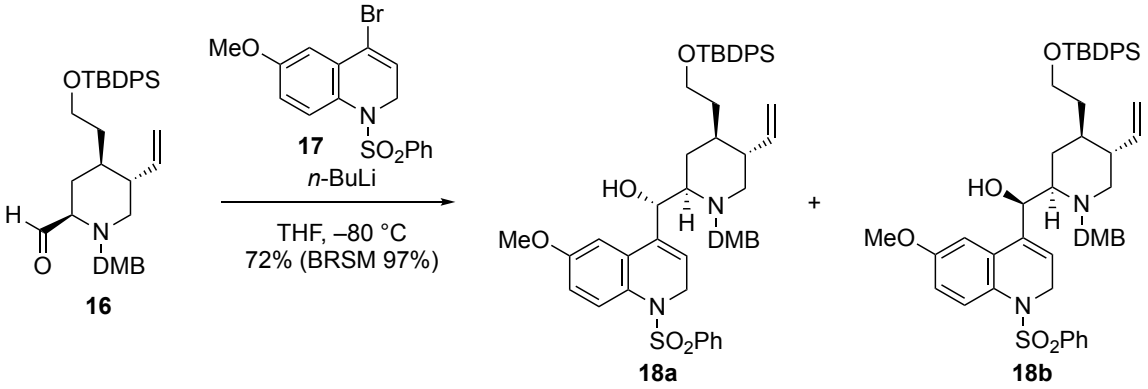
To a solution of ester **15** (1.05 g, 1.75 mmol) in CH_2Cl_2 (25 mL), DIBAL-H (1.0 M solution in *n*-hexane, 5.2 mL, 5.2 mmol) was added slowly at –95 °C under Ar atmosphere. The reaction mixture was stirred for 2.5 h before being quenched with EtOAc (3.6 mL) followed by addition of MeOH (3.6 mL) at –95 °C. To the resulting mixture, saturated aqueous Rochelle's salt was added at room temperature. The aqueous layer was extracted four times with $CHCl_3$. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 1% Et_3N/ 20%EtOAc–*n*-hexane solution) provided compound **16** (826 mg, 83%) as a colorless oil. The ^{1}H-NMR of crude materials indicated **S4**. After SiO_2 column chromatography, C6 aldehyde was isomerized to thermodynamically stable form. As a result, **16** was obtained as single isomer. ^{1}H-NMR of the crude mixture; See page S25. ^{1}H-NMR of isolated **16**; see page S26.

Piperidine-2-carbaldehyde **16**

^{1}H NMR (500MHz, $CDCl_3$) δ 9.47 (s, 1H), 7.62–7.64 (m, 4H), 7.36–7.42 (m, 6H), 7.15 (d, *J* = 8.0 Hz, 1H), 6.43–6.46 (m, 2H), 5.41–5.48 (m, 1H), 4.98–5.02 (m, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 3.61–3.68 (m, 3H), 3.58 (d, *J* =14.0 Hz, 1H), 3.45 (d, *J* = 13.5 Hz, H), 2.85 (dd, *J* = 11.5, 3.5 Hz, 1H), 2.68–2.72 (m, 1H), 1.83–1.97 (m, 3H), 1.64–1.68 (m, 1H), 1.27–1.36 (m, 2H), 1.14–1.21 (m, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ; 204.1, 159.1, 139.6, 135.8, 135.7,

134.0, 132.2, 130.9, 129.8, 127.9, 116.9, 104.0, 98.1, 70.7, 61.6, 57.2, 55.4, 54.6, 52.9, 46.5, 36.7, 36.2, 35.7, 31.9, 29.9, 27.0, 19.3; IR (neat) ν_{max} 2929, 2856, 1730, 1614, 1506, 1463, 1427, 1290, 1263, 1209, 1157, 1110, 1039, 920, 823, 738, 702 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{35}H_{46}NO_4Si]^+$: 572.3191 found : 572.3177; $[\alpha]^{26}_D$ –6.4 (*c* 0.93, $CHCl_3$).

Coupling reaction with dihydroquinoline derivative **17**



To a solution of dihydroquinoline **17**[S2] (79.9 mg, 0.21 mmol) in dry THF (1 mL), *n*-BuLi (2.5M solution in *n*-hexane, 84 μL, 0.21 mmol) was slowly added at –90 °C under Ar atmosphere. The reaction mixture was stirred for 30 min at –90 °C. To the resulting mixture, a solution of aldehyde **16** (100 mg, 0.175 mmol) in dry THF (1 mL) was slowly added at –90 °C under Ar atmosphere. The reaction mixture was stirred for 22 h at –80 °C before being quenched with benzoic acid (26 mg, 0.21 mmol). To the resulting mixture, excess amount of 20% aqueous NH_3 solution was added at 0 °C. The aqueous layer was extracted four times with EtOAc. The combined organic layer was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 1% Et_3N/ 20%EtOAc–*n*-hexane solution to 1% Et_3N/ 90%EtOAc–*n*-hexane solution gradient) provided compound **19** (110.1 mg, 72%, **18a** : **18b** = 1 : 1) as a pale yellow oil and 25.8 mg of **16** was recovered (25%). The diastereomer mixture (**18a** and **18b**) was partially separated by PTLC (35% EtOAc / *n*-hexane).

Coupling product **18a**

^{1}H NMR (500MHz, C_6D_6, VT 70 °C) δ 7.85 (d, *J* = 9.0 Hz, 1H), 7.75–7.77 (m, 4H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.23–7.27 (m, 6H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.63 (d, *J* = 9.5 Hz, 1H), 6.35–6.38 (m, 2H), 5.92 (br s, 1H), 5.26–5.35 (m, 1H), 4.85–4.89 (m, 2H), 4.35–4.39 (m, 2H), 4.24 (d, *J* = 18.0 Hz, 1H), 3.68–3.77 (m, 3H), 3.37–3.40 (m, 9H), 2.94 (d, *J* = 9.5 Hz, 1H), 2.05–2.18 (m, 2H),1.83–1.87 (m, 1H), 1.43 (d, *J* = 11.6 Hz, 1H), 1.26–1.30 (m, 3H), 1.18–1.25 (m, 2H), 1.15 (s, 9H); ^{13}C NMR (125MHz, C_6D_6, VT 70 °C) δ; 159.6, 158.6, 141.6, 136.2, 134.9, 132.4, 131.6, 130.2, 129.8, 122.8 (br), 116.5 (br), 112.9, 111.8, 105.0, 99.7, 70.8 (br), 65.8, 62.5, 55.4, 55.3, 55.2, 45.8, 42.3 (br), 37.9 (br), 37.6, 30.3 (br), 27.5, 19.7, several aromatic carbons were overlapped to C_6D_6; IR (neat) ν_{max} 2929, 2854, 1735, 1612, 1508, 1427, 1352, 1290, 1242, 1209, 1159, 1089, 1037, 918, 821, 727 cm^{-1};

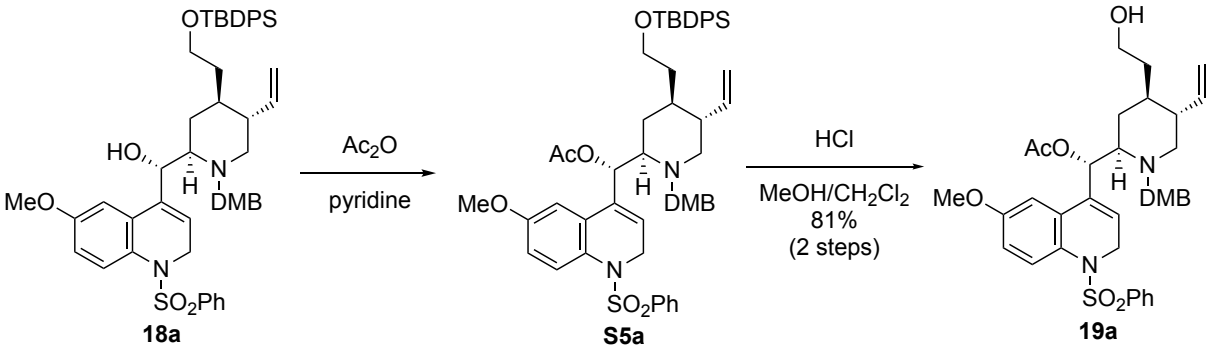
HRMS (ESI) $[M+H]^+$ calculated for $[C_{51}H_{61}N_2O_7SSi]^+$: 873.3963 found : 873.3944; $[\alpha]^{26}_D$ –4.1 (*c* 0.76, $CHCl_3$).

Coupling product **18b**

^1H NMR (500MHz, $CDCl_3$) δ 7.51–7.53 (m, 4H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.29–7.32 (m, 3H), 7.22–7.25 (m, 3H), 6.95 (br s, 1H), 6.82 (br s, 1H), 6.71 (dd, *J* = 9.5, 3.5 Hz, 1H), 6.33–6.36 (m, 2H), 5.83 (br s, 1H), 5.20–5.27 (m, 1H), 4.82–4.85 8m, 2H), 4.39 (d, *J* = 18.0 Hz, 1H), 4.17–4.22 (m, 2H), 3.71 (s, 6H), 3.64 (s, 3H), 3.48–3.58 (m, 4H), 2.65 (d, *J* = 14.5 Hz, 1H), 2.50 (br s, 1H), 1.92–1.97 (m, 1H), 1.11–1.24 (m, 5H), 0.91 (s, 9H); ^{13}C NMR (125MHz, $CDCl_3$) δ 158.8, 157.8, 140.1, 135.6, 134.0, 132.7, 131.9, 130.5, 129.9, 129.7, 129.1, 128.9, 128.2, 127.8, 127.4, 122.8 (br), 116.5 (br), 112.2, 110.7, 104.0, 98.8, 70.8 (br), 65.4, 64.9, 61.7, 55.5, 55.4, 46.1(br), 45.3, 41.0, 37.3, 36.8 (br), 29.8 (br), 27.0, 19.2; IR (neat) ν_{max} 2966, 2860, 1716, 1456, 1033, 871, 773 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{51}H_{61}N_2O_7SSi]^+$: 873.3963 found : 873.3970; $[\alpha]^{26}_D$ +7.6 (*c* 0.05, $CHCl_3$).

Optimization to complete total synthesis of (+)-quinine using isolated 19a

Acetylation and removal of TBDPS group



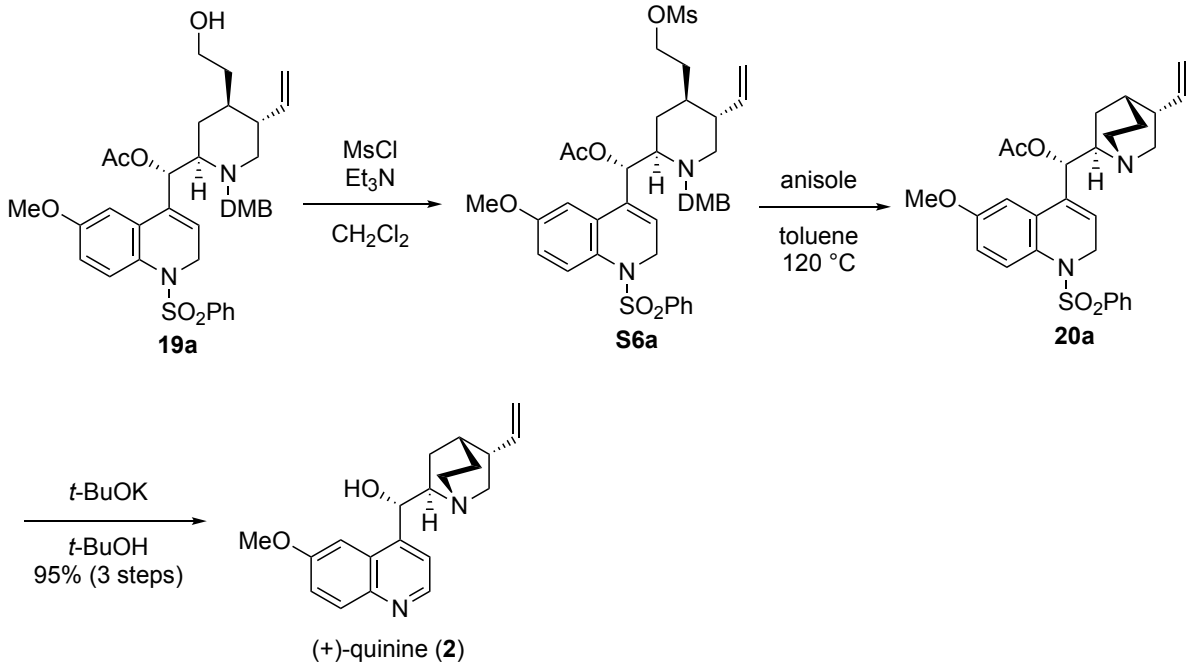
To a solution of **18a** (21.8 mg, 0.0259mmol) in pyridine (0.5 mL), acetic anhydride (5.5 μL, 0.059 mmol) and dimethylaminopyridine (DMAP, 0.2 mg, 0.00016 mmol) were added at 0 °C under Ar atmosphere. The reaction mixture was stirred for 68 h at room temperature before being quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layer was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained crude material was directly employed to next reaction.

To a solution of the crude mixture of **S5a** in CH_2Cl_2 (160 μL) and MeOH (160 μL), 2M HCl/MeOH (82 μL, 0.16 mmol) was slowly added at 0 °C under Ar atmosphere. The reaction mixture was stirred for 6 h at room temperature before being quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 40%EtOAc–*n*-hexane) provided compound **19a** (13.7 mg, 81%) as a pale yellow oil.

Compound **19a**

^{1}H NMR (500MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, 2H), 7.53 (t, *J* = 7.0 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.24–7.27 (m, 1H, overlapped to $CDCl_3$), 7.20 (d, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.78 (dd, *J* = 8.5, 3.0 Hz, 1H), 6.43–6.45 (m, 2H), 6.25 (s, 1H), 5.93 (s, 1H), 5.40–5.47 (m, 1H), 4.96–4.99 (m, 2H), 4.50 (dd, *J* = 17.5, 4.5 Hz, 1H), 4.22 (d, *J* = 15.5 Hz, 1H), 4.14 (d, *J* = 14.0 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.63–3.69 (m, 2H), 3.22 (d, *J* = 13.5 Hz, 1H), 2.82 (d, *J* = 9.0 Hz, 1H), 2.38 (d, *J* = 10.5 Hz, 1H), 2.05 (s, 3H), 1.76–1.91 (m, 3H), 1.14–1.25 (m, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ; 169.5, 159.9, 158.6, 158.3, 140.1, 139.7, 134.0, 133.1, 131.0, 130.1,.129.0 (2C), 128.2, 127.6, 127.5, 122.5, 119.4, 116.5, 113.4, 109.3, 104.3, 98.5, 77.4 (2C), 77.2, 76.9, 70.7, 69.8, 63.5, 60.0, 59.2, 55.6, 55.5, 50.4, 45.9, 45.0, 36.8, 36.4, 29.9, 29.8, 29.5, 29.4, 28.9, 21.3; IR (neat) ν_{max} 2922, 2845, 1743, 1508, 1456, 1163, 1033 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{37}H_{45}N_2O_8S]^+$: 677.2891 found : 677.2895; $[\alpha]^{27}_D$ +28.4(*c* 0.28, $CHCl_3$).

Quinuclidine formation and complete total synthesis of (+)-quinine



To a solution of **19a** (9.5 mg, 0.014 mmol) and Et_3N (20 μL, 0.14 mmol) in CH_2Cl_2 (0.3 mL), methanesulfonyl chloride (MsCl, 4.4 μL, 0.056 mmol) was added at 0 °C under Ar atmosphere. The reaction mixture was stirred for 20 min at 0 °C before being quenched with 20% aqueous NH_3 solution. The aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude materials of **S6a** was directly employed to the next quinuclidine formation.

To a solution of the crude materials of **S6a** in toluene (0.4 mL), anisole (4.9 μL, 0.042 mmol) was added at room temperature under Ar atmosphere. The reaction mixture was refluxed for 21 h at 120 °C before being quenched with 20% aqueous NH_3 solution. The aqueous layer was extracted four times with EtOAc. The

combined organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude materials of **20a** was directly employed to the next reaction.

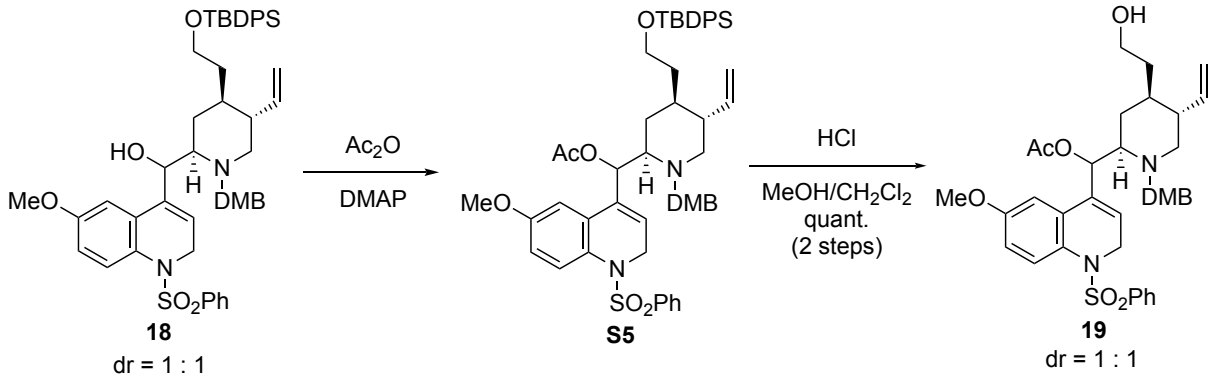
To a solution of the crude materials of **20a** in *t*-BuOH (0.6 mL), *t*-BuOK (7.6 mg, 0.33 mmol) was added at room temperature under Ar atmosphere. The reaction mixture was stirred for 3 h at 60 °C before being quenched with 20% aqueous NH_3 solution. The aqueous layer was extracted four times with EtOAc. The combined organic layer was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2–NH, 1%MeOH–$CHCl_3$) provided (+)-quinine (**2**, 4.3 mg, 95%) as white amorphous powder. All spectral data of (+)-quinine (**2**) except sign of rotation were identified with authentic (–)-quinine; see page S31, 32.

Unnatural (+)-quinine (**2**)

^{1}H NMR (500MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.0 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 4.0 Hz, 1H), 7.28 (dd, *J* = 9.3, 2.8 Hz, 1H), 7.19 (d, *J* = 2.5 Hz, 1H), 5.70 (ddd, *J* = 17.0, 10.5, 7.5 Hz, 1H), 5.54 (d, *J* = 3.5 Hz, 1H), 4.93 (dt, *J* = 16.5, 1.5 Hz, 1H), 4.90 (br d, *J* = 15.5 Hz, 1H), 3.85 (s, 3H), 3.45–3.51 (m, 1H), 3.02–3.07 (m, 2H), 2.59–2.64 (m, 2H), 2.25 (br s, 1H), 1.70–1.79 (m, 3H), 1.45–1.50 (m, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ; 158.2, 148.3, 147.9, 144.5, 142.3, 131.9, 126.7, 122.0, 118.9, 114.9, 101.7, 73.3, 60.3, 57.4, 56.1, 43.6, 40.4, 28.3, 28.0, 21.9; IR (neat) ν_{max} 2935, 2862, 1622, 1508, 1240, 1031, 717 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{20}H_{25}N_2O_2]^+$: 325.1911 found : 325.1902; $[\alpha]^{26}_D$ +142.2 (*c* 1.18, EtOH), [natural (–)-quinine $[\alpha]^{25}_D$ –150.0 (*c* 1.38, EtOH)].

Total syntheses of (+)-quinine and (–)-9-*epi*-quinine

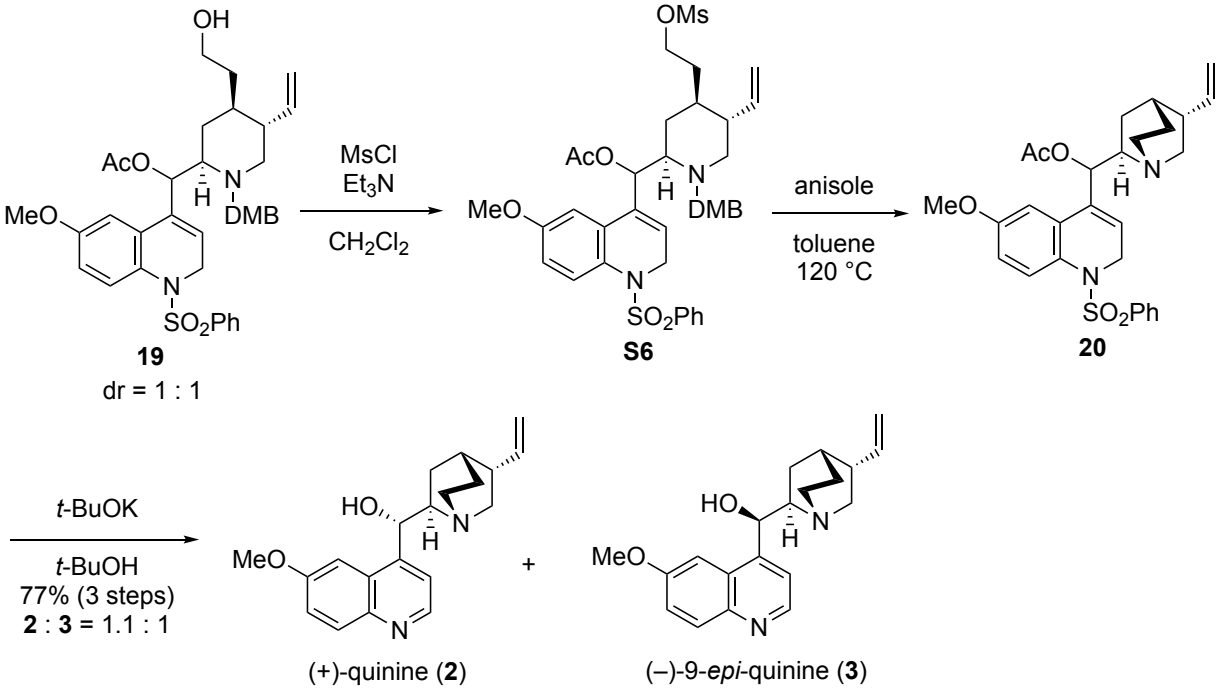
Acetylation and removal of TBDPS group



To a solution of **18** (9α-OH : 9β-OH = 1 : 1, 2.10 g, 2.04 mmol) in acetic anhydride (24 mL), dimethylaminopyridine (DMAP, 58.8 mg, 0.48 mmol) was added at 0 °C under Ar atmosphere. The reaction mixture was stirred for 30 min at room temperature before being quenched with 15% aqueous NaOH solution at 0 °C. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layer was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The crude materials of **S5** was directly employed to next removal of TBDPS group.

To a solution of the crude mixture of **S5** in CH_2Cl_2 (24 mL) and MeOH (24 mL), 2M HCl/MeOH (6.0 mL, 10.2 mmol) was slowly added at 0 °C under Ar atmosphere. The reaction mixture was stirred for 12 h at room temperature before being quenched with saturated aqueous $NaHCO_3$ at 0 °C. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2, 40%EtOAc–*n*-hexane) provided compound **19** (9α-OH : 9β-OH = 1 : 1, 1.67 g, quant.) as a pale yellow oil. The NMR chart of diastereomer mixture **19** was shown page S30.

Quinuclidine formation and complete total synthesis of (+)-quinine and (–)-9-*epi*-quinine



To a solution of **19** (1.59 g, 2.35 mmol) and Et_3N (1.85 mL, 11.75 mmol) in CH_2Cl_2 (29 mL), methanesulfonyl chloride (MsCl, 273 μL, 3.53 mmol) was added at 0 °C under Ar atmosphere. The reaction mixture was stirred for 5 min at 0 °C before being quenched with 20% aqueous NH_3 solution. The aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude materials of **S6** was directly employed to the next quinuclidine formation.

To a solution of the crude materials of **S6** in toluene (34 mL), anisole (798 μL, 7.05 mmol) was added at room temperature under Ar atmosphere. The reaction mixture was refluxed for 7 h at 120 °C before being quenched with 20% aqueous NH_3 solution. The aqueous layer was extracted four times with EtOAc. The combined organic layer was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The crude materials of **20** was directly employed to the next reaction.

To a solution of the crude materials of **20** in *t*-BuOH (34 mL), *t*-BuOK (791 mg, 7.05 mmol) was added at room temperature under Ar atmosphere. The reaction mixture was stirred for 1.5 h at 60 °C before being

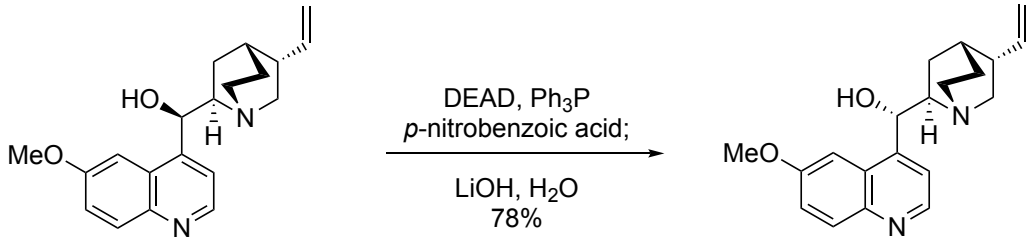
quenched with 20% aqueous NH_3 solution. The aqueous layer was extracted four times with EtOAc. The combined organic layer was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2–NH, 1–10%MeOH–$CHCl_3$) provided (+)-quinine (**2**, 310 mg, 41%) as a white amorphous powder and (–)-9-*epi*-quinine (**3**, 272 mg, 36%) as a white amorphous powder. All spectral data of (–)-9-*epi*-quinine (**3**) except sign of rotation were identified with reported data[S3)].

(–)-9-*epi*-quinine

^{1}H NMR (500MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.0 Hz, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.63 (s, 1H), 7.35–7.39 (m, 2H), 5.72 (dt, *J* = 17.0, 9.0 Hz, 1H), 4.91–5.01 (m, 3H), 3.91 (s, 3H), 3.24 (dd, *J* = 13.0, 10.0 Hz, 1H), 3.16 (dt, *J* = 14.0, 7.5 Hz, 1H), 3.09 (q, *J* = 8.5, 1H), 2.75–2.77 (m, 2H), 2.29 (br s, 1H), 1.58–1.69 (m, 3H), 1.43 (t, *J* = 5.5, 1H), 0.93 (dd, *J* = 12.5, 7.5 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ; 157.4, 147.5, 144.7, 144.4, 141.4, 131.5, 128.1, 121.3, 120.1, 114.6, 102.5, 71.3, 61.5, 55.9, 55.4, 40.7, 39.9, 27.9, 27.2, 25.1; IR (neat) ν_{max} 2933, 2864, 1620, 1506, 1240, 1028, 852,715 cm^{-1}; HRMS (ESI) $[M+H]^+$ calculated for $[C_{20}H_{25}N_2O_2]^+$: 325.1911 found : 325.1903; $[\alpha]^{28}_D$ –29.3 (*c* 3.60, EtOH); [for (+)-9-*epi*-quinine: lit[S3b)] $[\alpha]^{22}_D$ +23 (*c* 1.0, EtOH)]

Synthetic (–)-9-*epi*-quinine	Reported (+)-9-*epi*-quinine [S3b)]
^{13}C-NMR (125 MHz, $CDCl_3$)	^{13}C-NMR (100 MHz, $CDCl_3$)
157.4	157.6
147.5	147.5
144.7	144.8
144.4	143.9
141.4	140.3
131.5	131.6
128.1	128.0
121.3	121.5
120.1	120.1
114.6	115.3
102.5	102.5
71.3	70.7
61.5	61.6
55.9	55.7
55.4	55.3
40.7	40.9
39.9	39.1
27.9	27.1
27.2	27.0
25.1	24.7

Mitsunobu conversion from (–)-9-*epi*-quinine to (+)-quinine



(–)-9-*epi*-quinine (**3**) (+)-quinine (**2**)

To a solution of (–)-9-*epi*-quinine (**3**, 25.5 mg, 0.079 mmol), triphenylphosphine (26.8 mg, 0.10 mmol) and *p*-nitrobenzoic acid (PNBA, 14.4 mg, 0.087 mmol) in dry THF (786 μL), diethyl azodicarboxylate (DEAD, 39.3 μL, 0.087 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred for 7 h at room temperature. The resulting mixture was cooled at 0 °C, then aqueous 1M LiOH solution (393 μL) and MeOH (79 μL) were added to the reaction mixture. The reaction mixture was stirred for 17 h at room temperature under Ar atmosphere. The resulting mixture was extracted four times with $CHCl_3$. The combined organic layer was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (SiO_2–NH, 1–10%MeOH–$CHCl_3$) provided (+)-quinine (**2**, 19.9 mg, 78%) as white amorphous powder.

Recrystallization of (+)-quinine

100 mg of (+)-quinine was dissolved to a solution of H_2SO_4 (14.8 mL, 0.28 mmol) in H_2O (5 mL). After colorless crystals were formed, the suspension was filtrated. As a result, (+)-quinine sulfate hydrate was obtained in 76% yield (92.1 mg) as colorless crystals. The part of crystals was added to 20% aqueous NH_3 solution and the resulting mixture was extracted with $CHCl_3$. The organic layer was concentrated and enantiomeric excess was determined using the crude materials. The enantiomeric excess was over 99% *ee*. DAICEL ChiralPak AS-H column; 10% *i*-PrOH/*n*-hexane, 0.25 mL/min; synthetic unnatural (+)-quinine t_R = 32.7 min, natural (–)-quinine t_R = 19.8 min (see page S34).

Reference;

S1) a) S. BouzBouz, C. Roche, J. Cossy, *Synlett* **2009**, *5*, 803–807; b) H. Zhang, X. Ma, H. Kang, R. Wang, *Chem. Asian. J.* **2013**, *8*, 542–545.

S2) a) H. Murase, K. Senda, M. Senoo, T. Hata, H. Urabe, *Chem. Eur. J.* **2014**, *20*, 317–322; b) L. Alonso-Marañón, L. A. Sarandeses, M. M. Martínez, J. P. Sestelo, *Org. Chem. Front.* **2017**, *4*, 500–505.

S3) a) T. M. Lipińska, K. Piechocka, M. Denisiuk, B. Chmiel, A. Skórska-Stania, *ARKIVOC* **2012**, 264–280; b) A. P. Gorka, K. S. Sherlach, A. C. de Dios, P. D. Roepe, *Antimicrob. Agents Chemother.* **2013**, *57, 365–364.*

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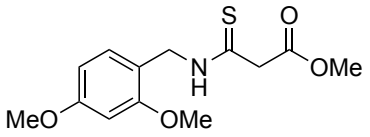

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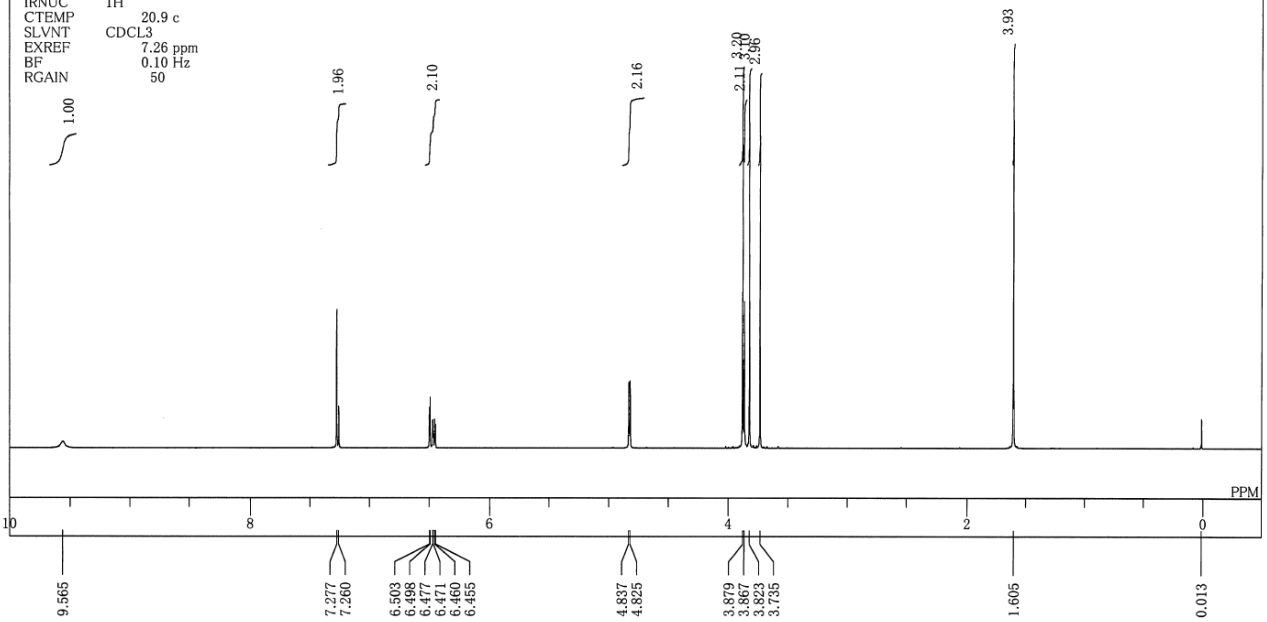

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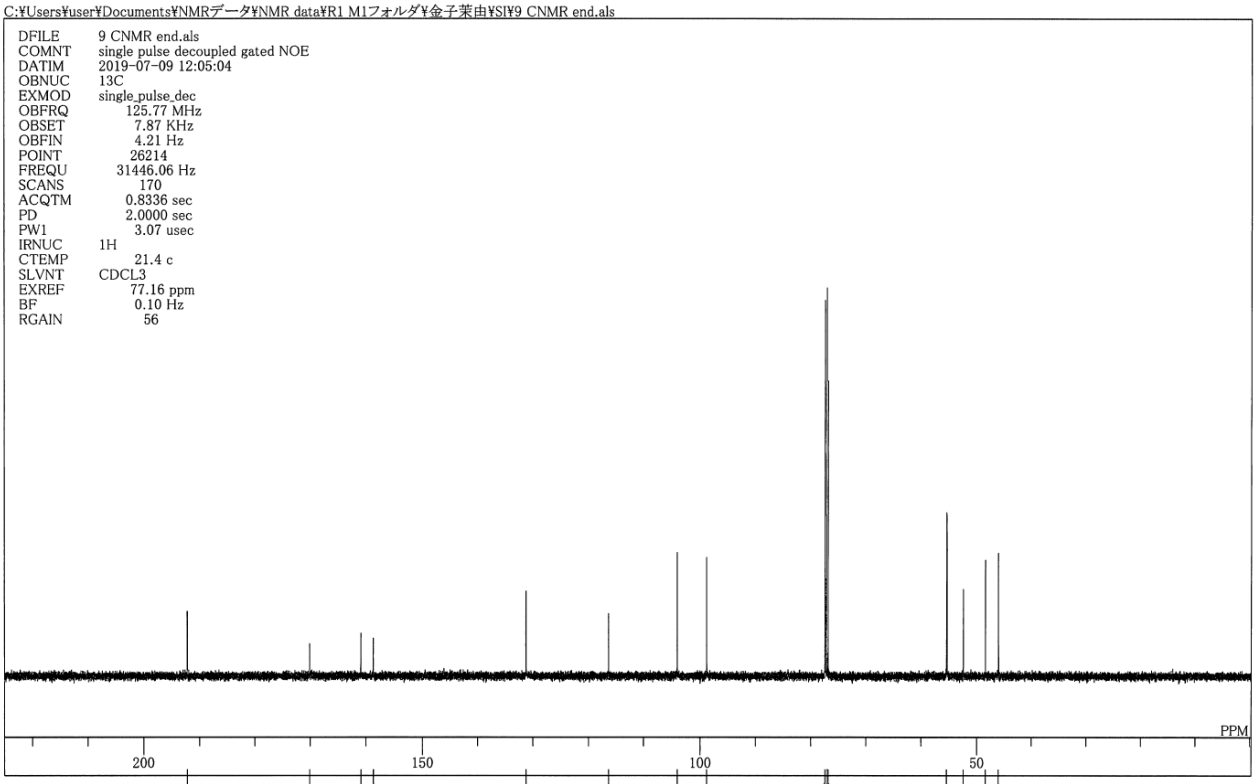

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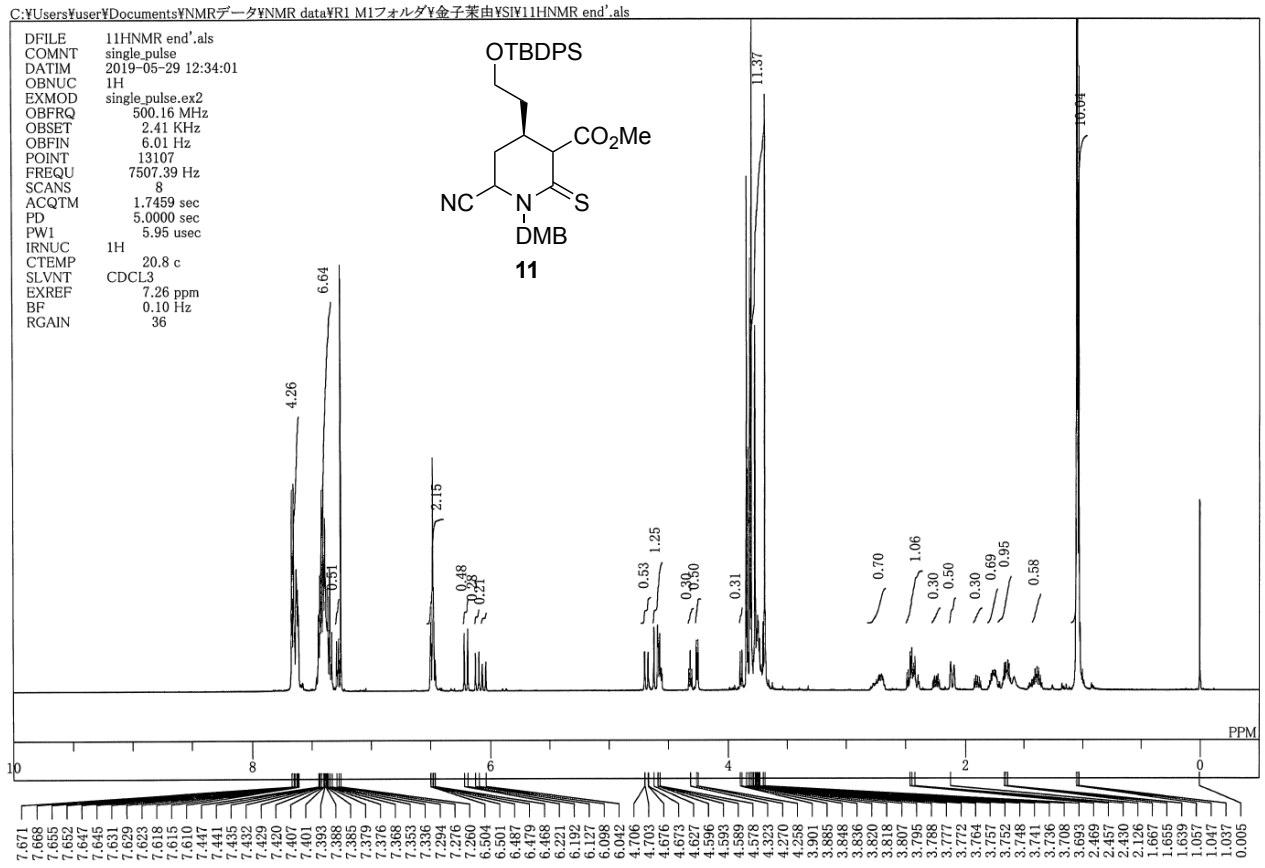
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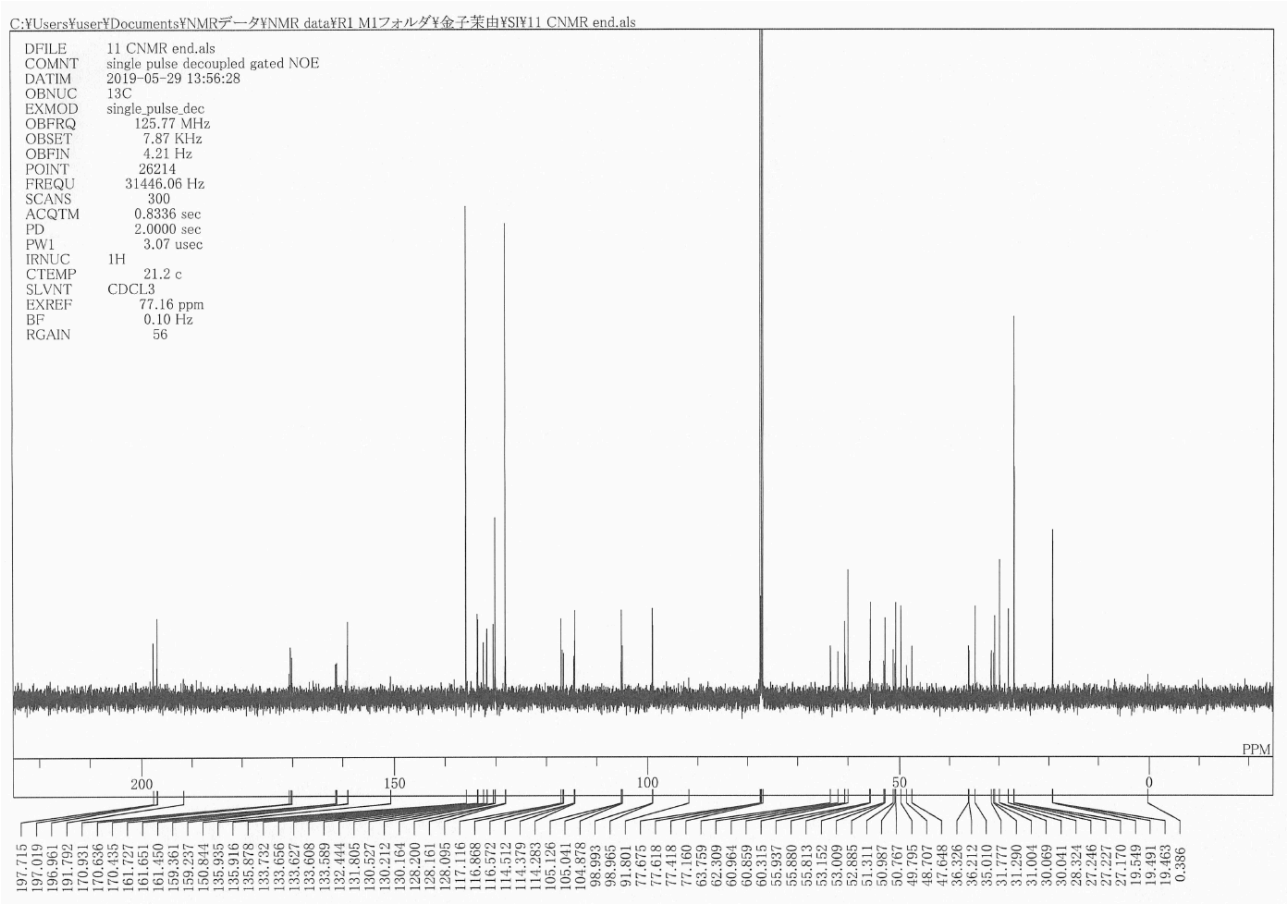
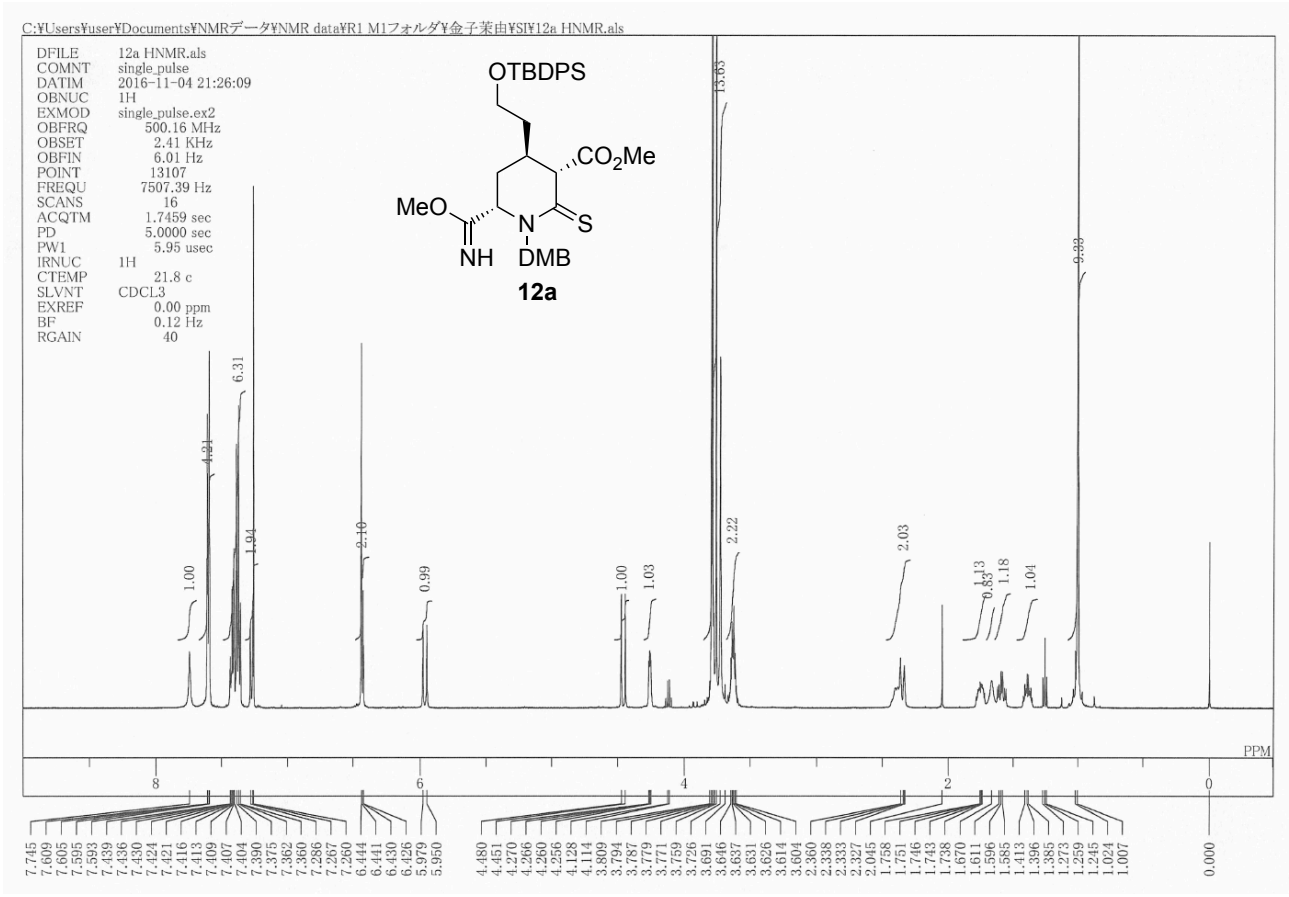
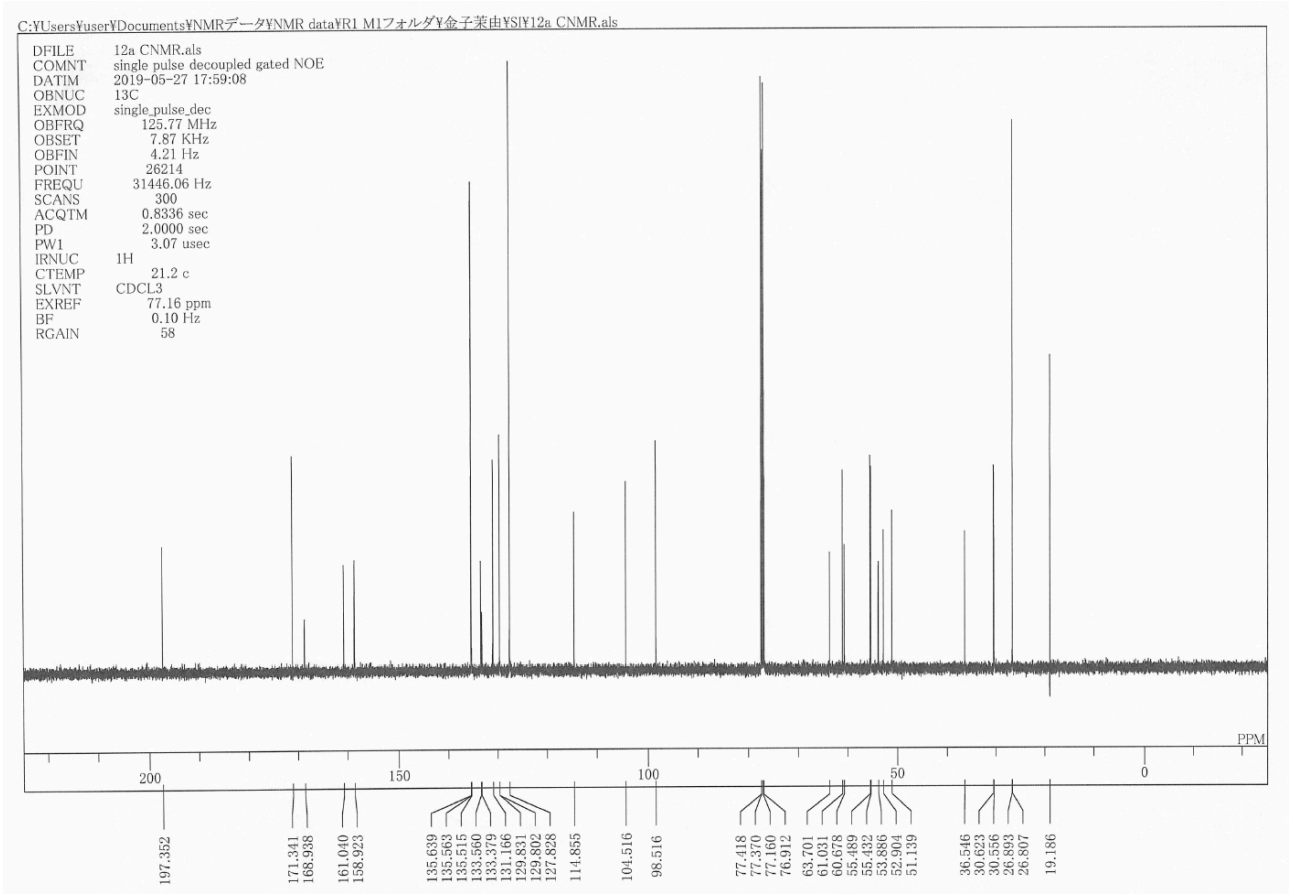
BF 0.10 Hz
RGAIN 36
OTBDPS
CO2Me
NC
N
S
DMB
11
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥11 CNMR end.als
DFILE 11 CNMR end.als
COMNT single pulse decoupled gated NOE
DATIM 2019-05-29 13:56:28
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 300
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 21.2 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 56
PPM

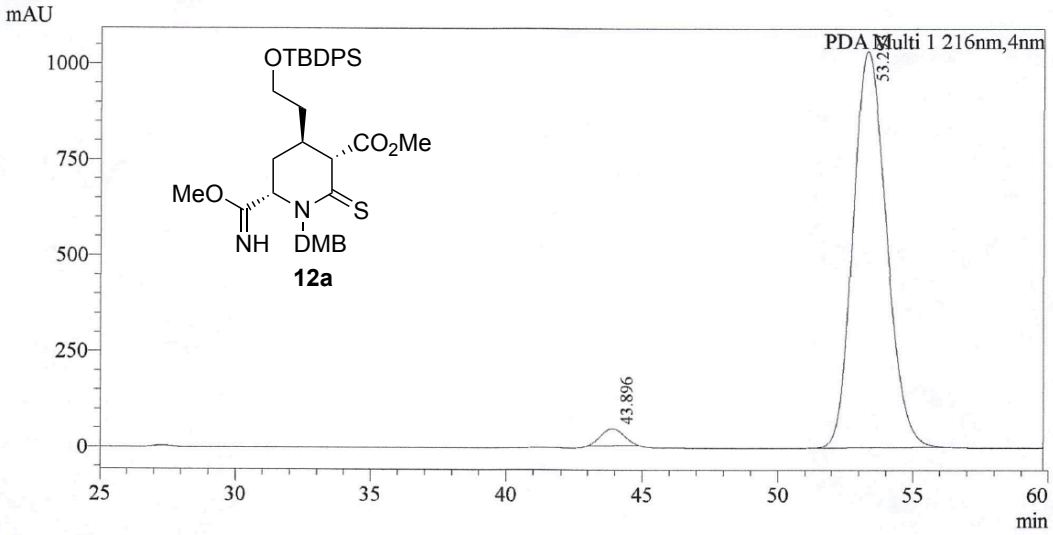

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥12a HNMR.als
DFILE 12a HNMR.als
COMNT single_pulse
DATIM 2016-11-04 21:26:09
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 16
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 21.8 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 40
OTBDPS
CO2Me
MeO
N
S
NH
DMB
12a
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥12a CNMR.als
DFILE 12a CNMR.als
COMNT single pulse decoupled gated NOE
DATIM 2019-05-27 17:59:08
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 300
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 21.2 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 58
PPM

=== Shimadzu LabSolutions Report ===

Sample Name	: TKP33 ee major 4			
Sample ID	: kaneko			
Data Filename	: TKP33 ee major 4.lcd			
Method Filename	: 10%iPrOH-Hex-flow0.5.lcm			
Batch Filename	:			
Vial#	: 1-1		Sample Type	: –é'm
Injection Volume	: 2000 uL			
Date Acquired	: 2018/04/23 18:08:49	Acquired by	: System Administrator	
Date Processed	: 2018/04/23 22:48:21	Processed by	: System Administrator	

<Chromatogram>

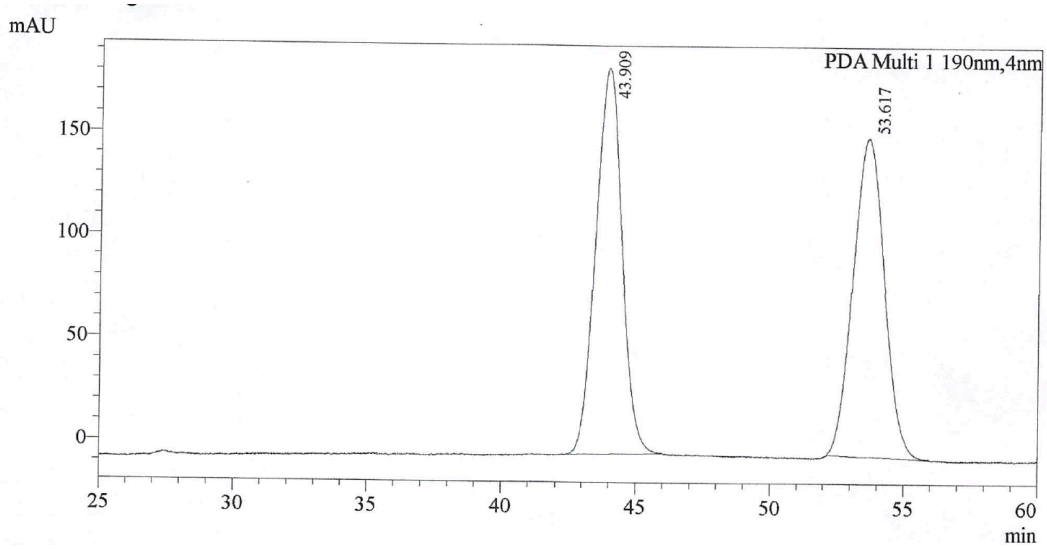


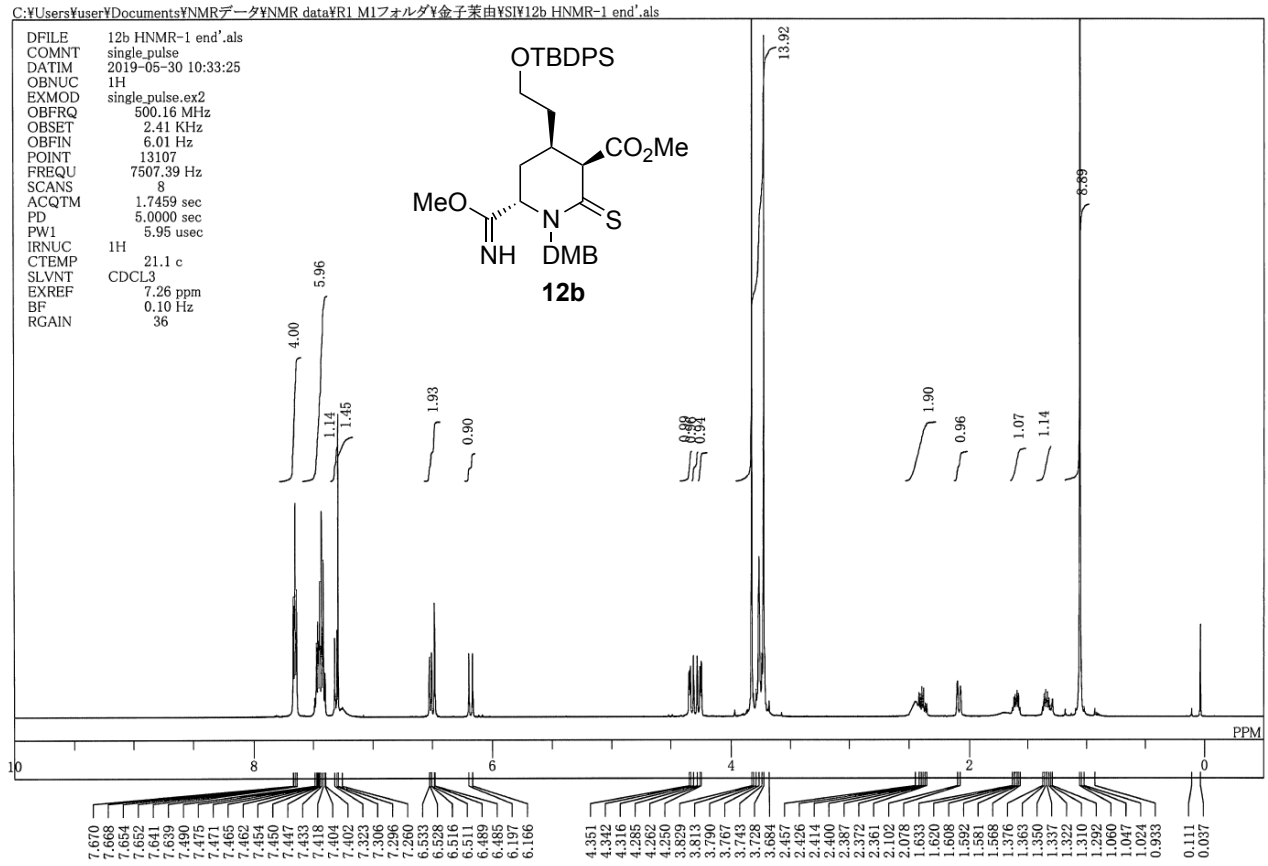
<Peak Table>

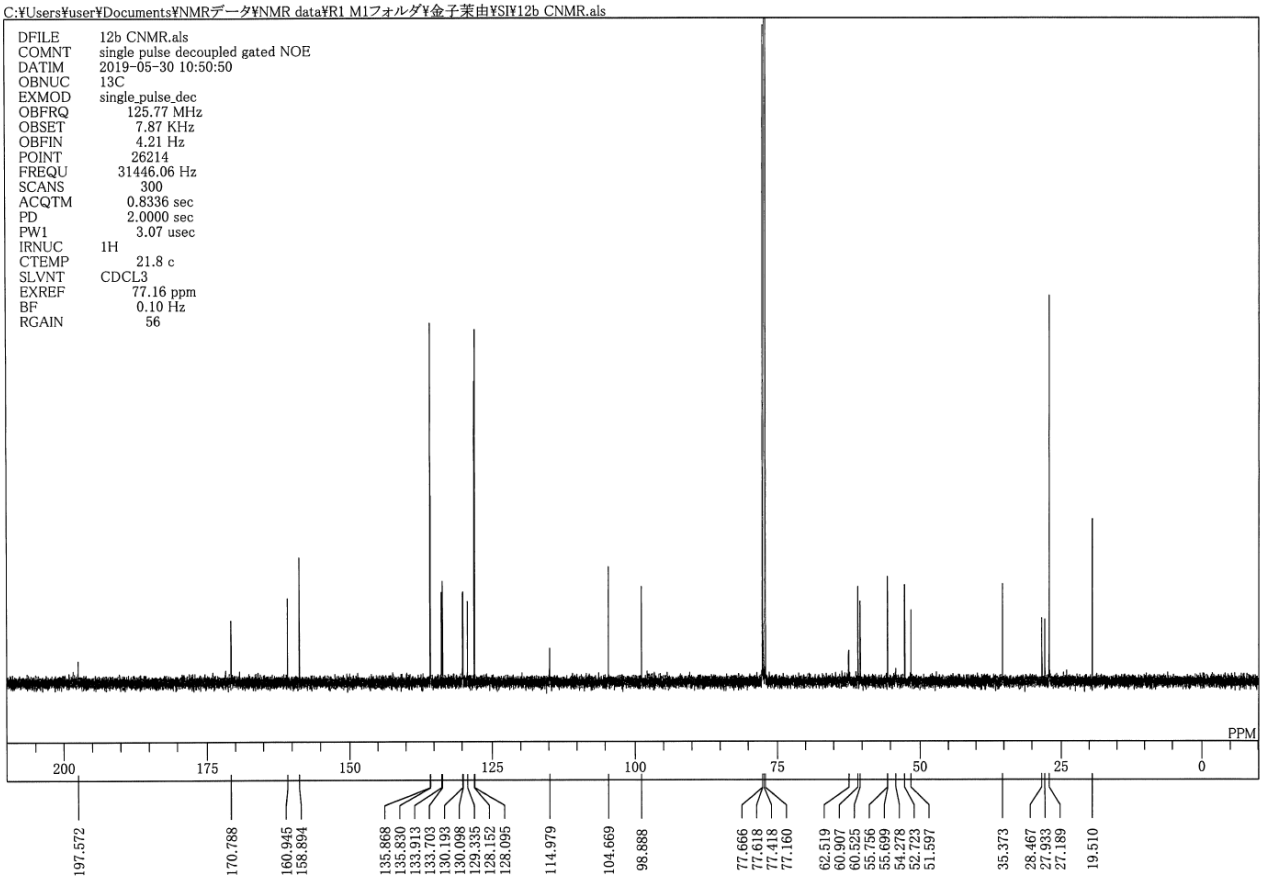
PDA Ch1 216nm

Peak#	Ret. Time	Area	Height	Conc.	Name
1	43.896	2611281	44203	2.866	
2	53.293	88506909	1032774	97.134	
‡Œv		91118190	1076977		

Racemic 12a



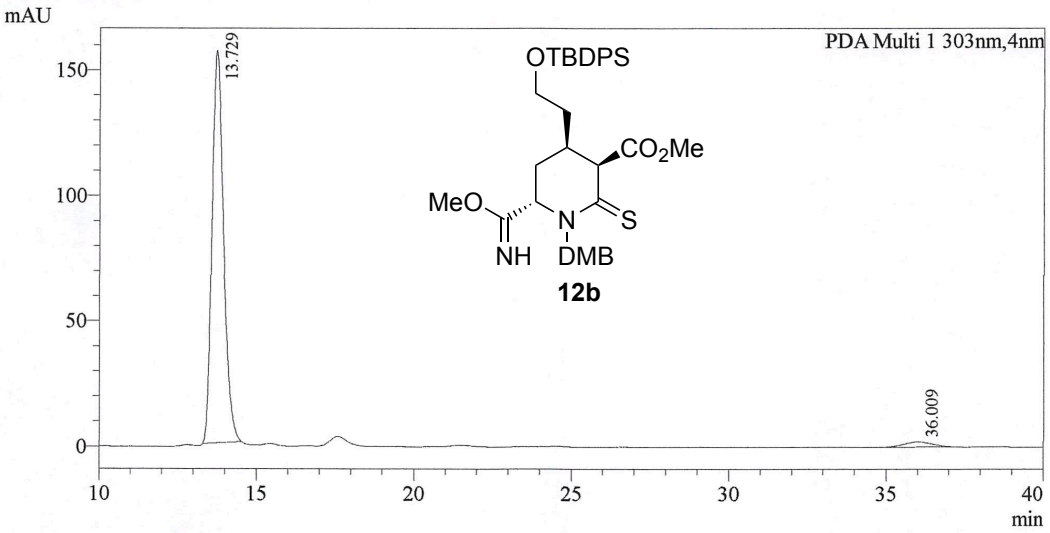

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥12b HNMR-1 end'.als
DFILE 12b HNMR-1 end'.als
COMNT single_pulse
DATIM 2019-05-30 10:33:25
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 21.1 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.10 Hz
RGAIN 36
OTBDPS
CO2Me
MeO
N
S
NH
DMB
12b
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥12b CNMR.als
DFILE 12b CNMR.als
COMNT single pulse decoupled gated NOE
DATIM 2019-05-30 10:50:50
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 300
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 21.8 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 56
PPM

=== Shimadzu LabSolutions Report ===

Sample Name	: compound 12b chiral IC		
Sample ID	: kaneko		
Data Filename	: compound 12b chiral IC.lcd		
Method Filename	: 20%iPrOH-Hex-flow0.75.lcm		
Batch Filename	:		
Vial#	: 1-1	Sample Type	: –¢'m
Injection Volume	: 20 uL		
Date Acquired	: 2019/07/12 16:34:38 Acquired by		: System Administrator
Date Processed	: 2019/07/12 17:17:06 Processed by		: System Administrator

<Chromatogram>

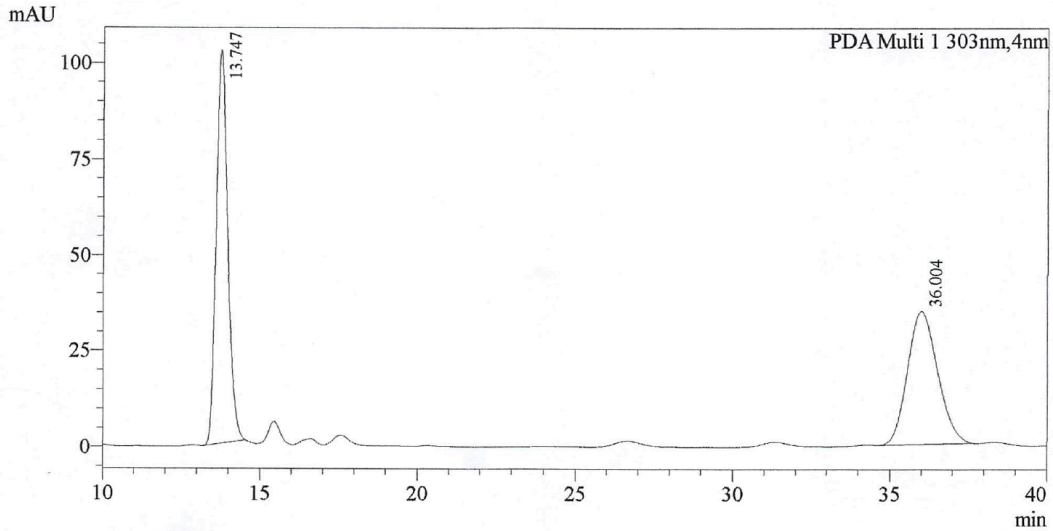


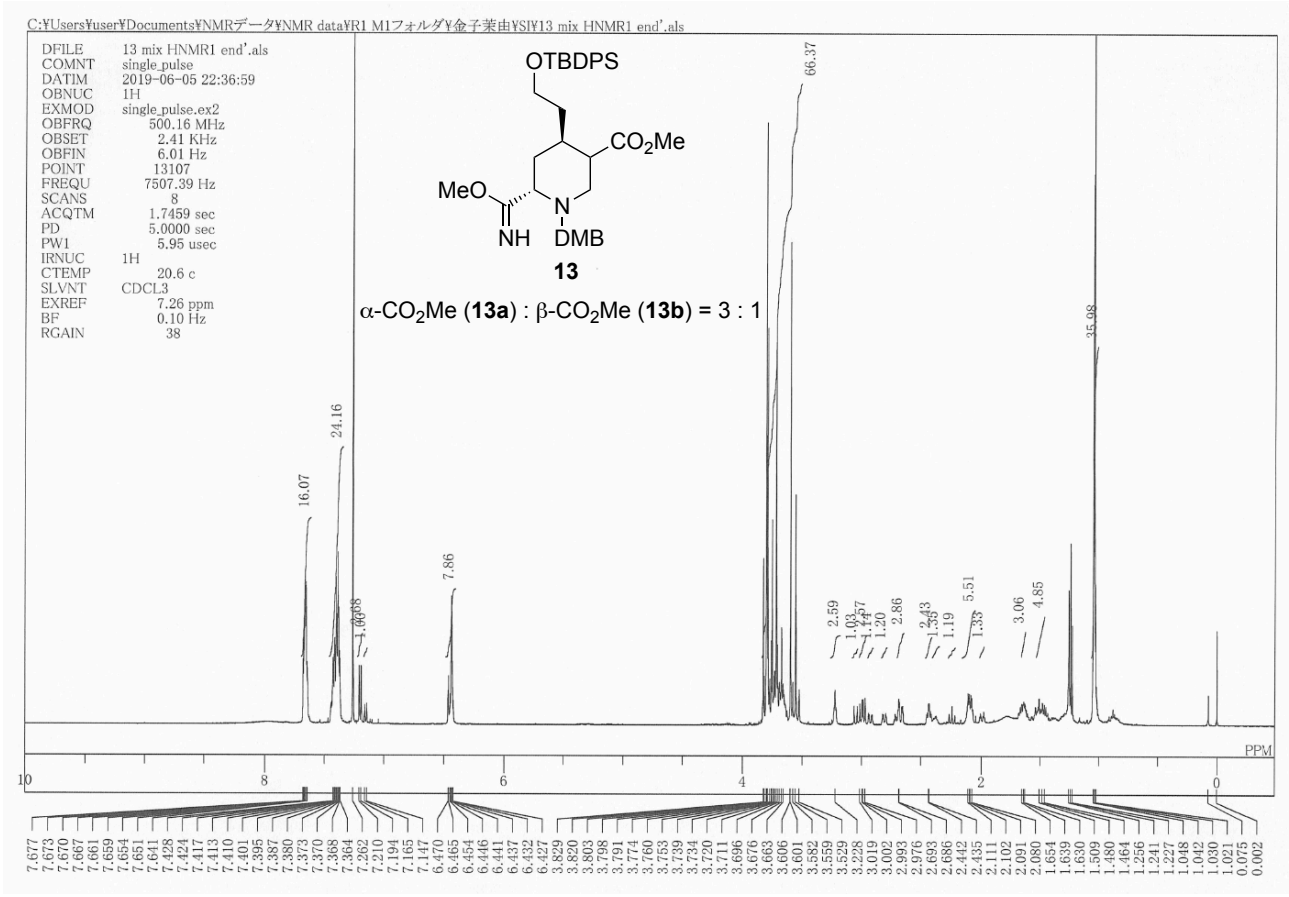
<Peak Table>

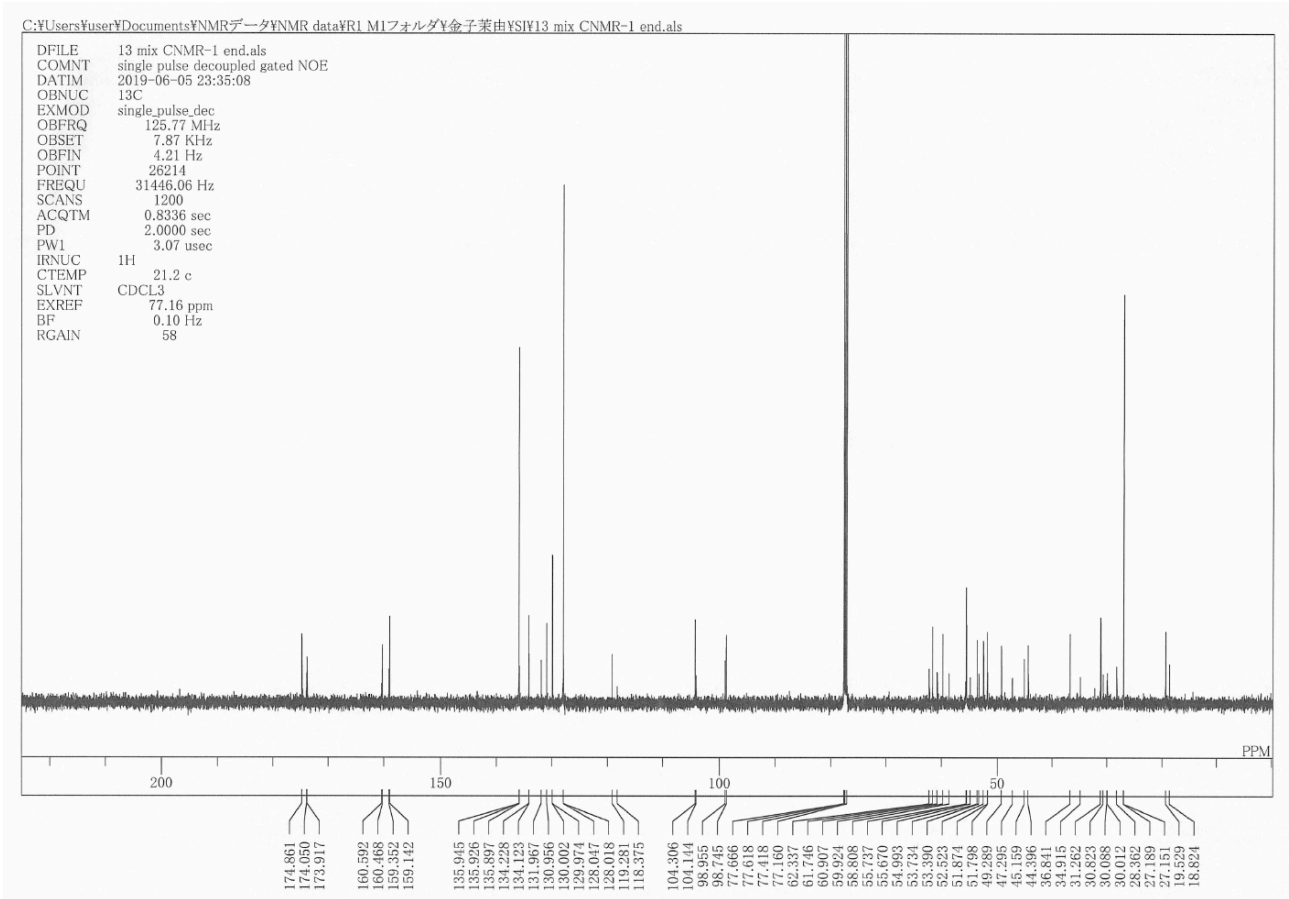
PDA Ch1 303nm

Peak#	Ret. Time	Area	Height	Conc.	Name
1	13.729	3983503	156496	96.861	
2	36.009	129109	2000	3.139	
‡Œv		4112611	158497		

Racemic 12b

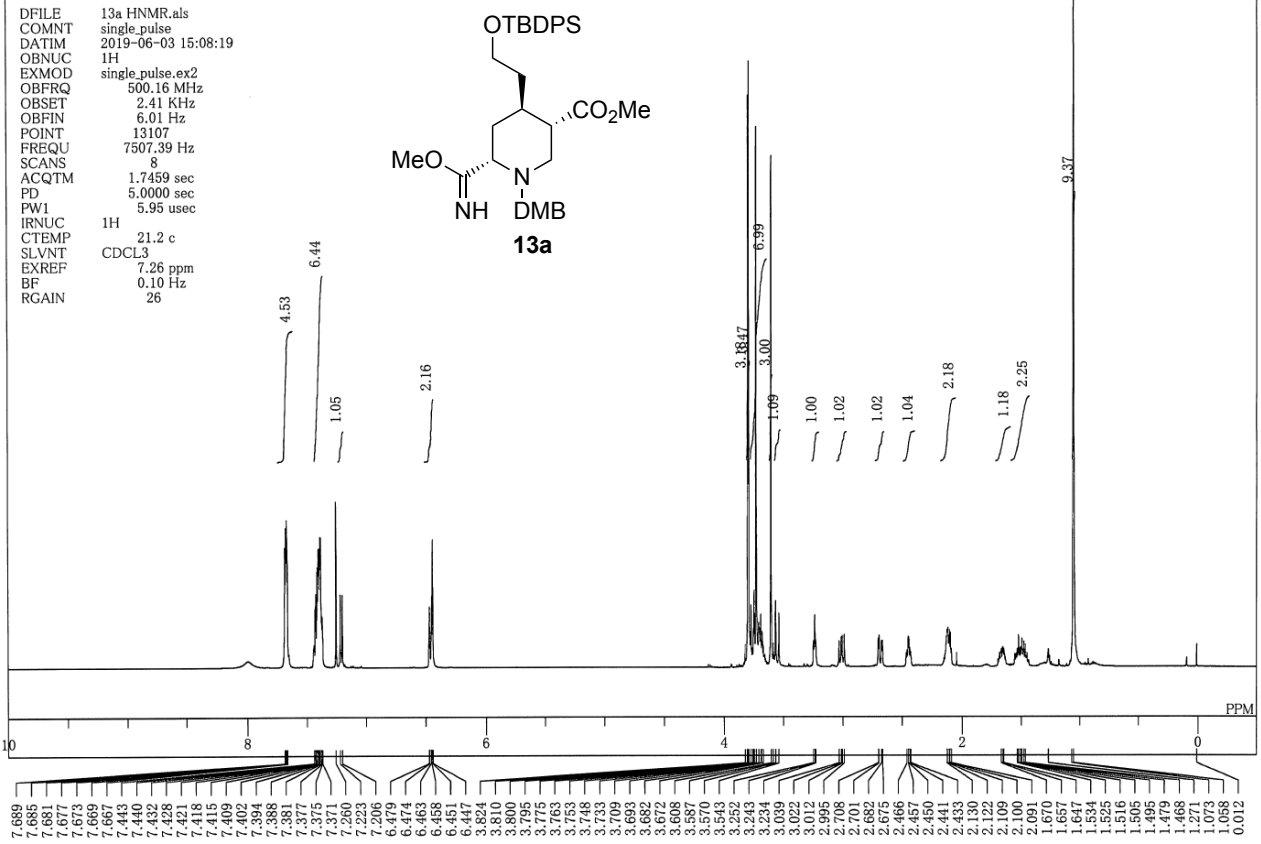



C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥13 mix HNMR1 end'.als
DFILE 13 mix HNMR1 end'.als
COMNT single_pulse
DATIM 2019-06-05 22:36:59
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 20.6 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.10 Hz
RGAIN 38
OTBDPS
CO2Me
MeO
N
NH
DMB
13
α-CO2Me (13a) : β-CO2Me (13b) = 3 : 1
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥13 mix CNMR-1 end.als
DFILE 13 mix CNMR-1 end.als
COMNT single pulse decoupled gated NOE
DATIM 2019-06-05 23:35:08
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1200
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 21.2 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 58
PPM

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥13a HNMR.als

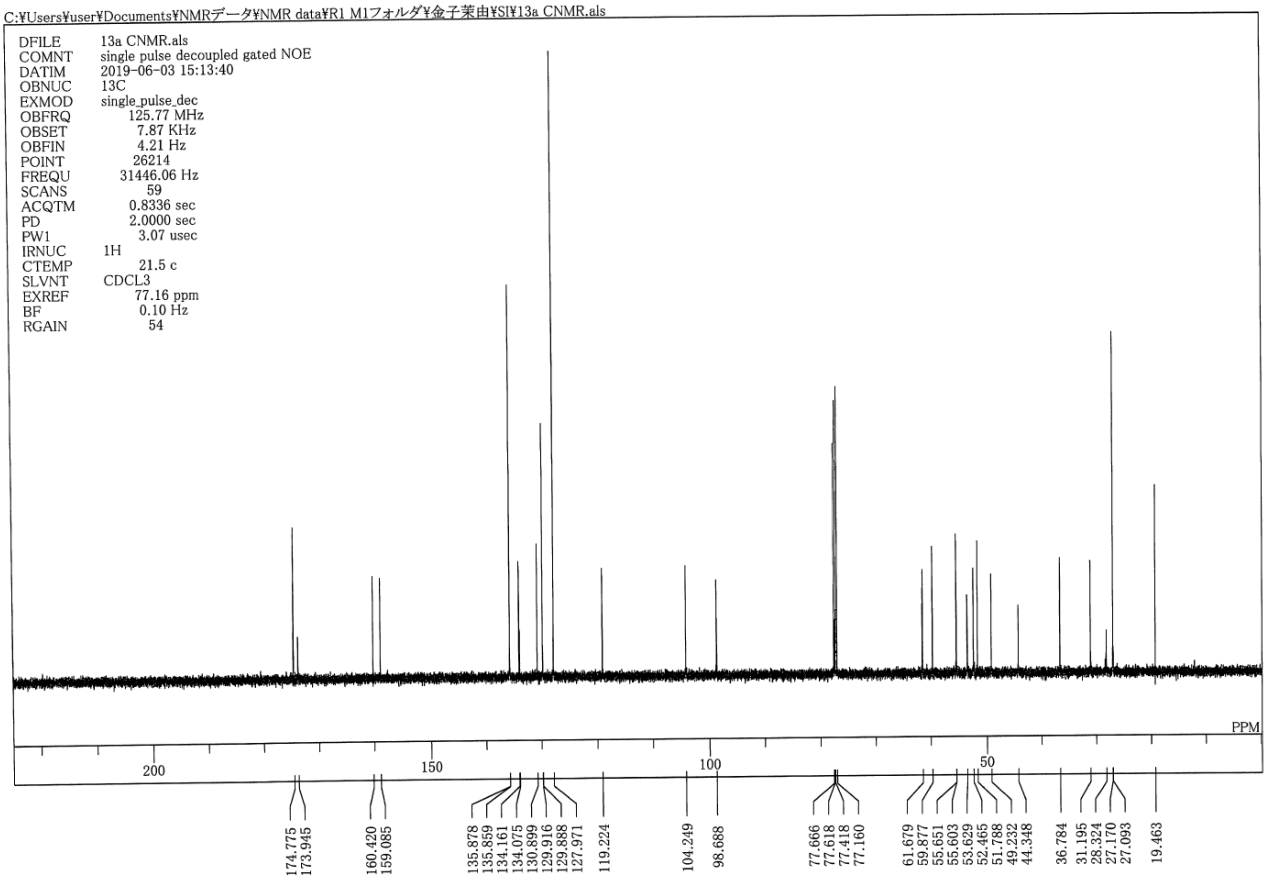
DFILE 13a HNMR.als
COMNT single_pulse
DATIM 2019-06-03 15:08:19
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 21.2 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.10 Hz
RGAIN 26



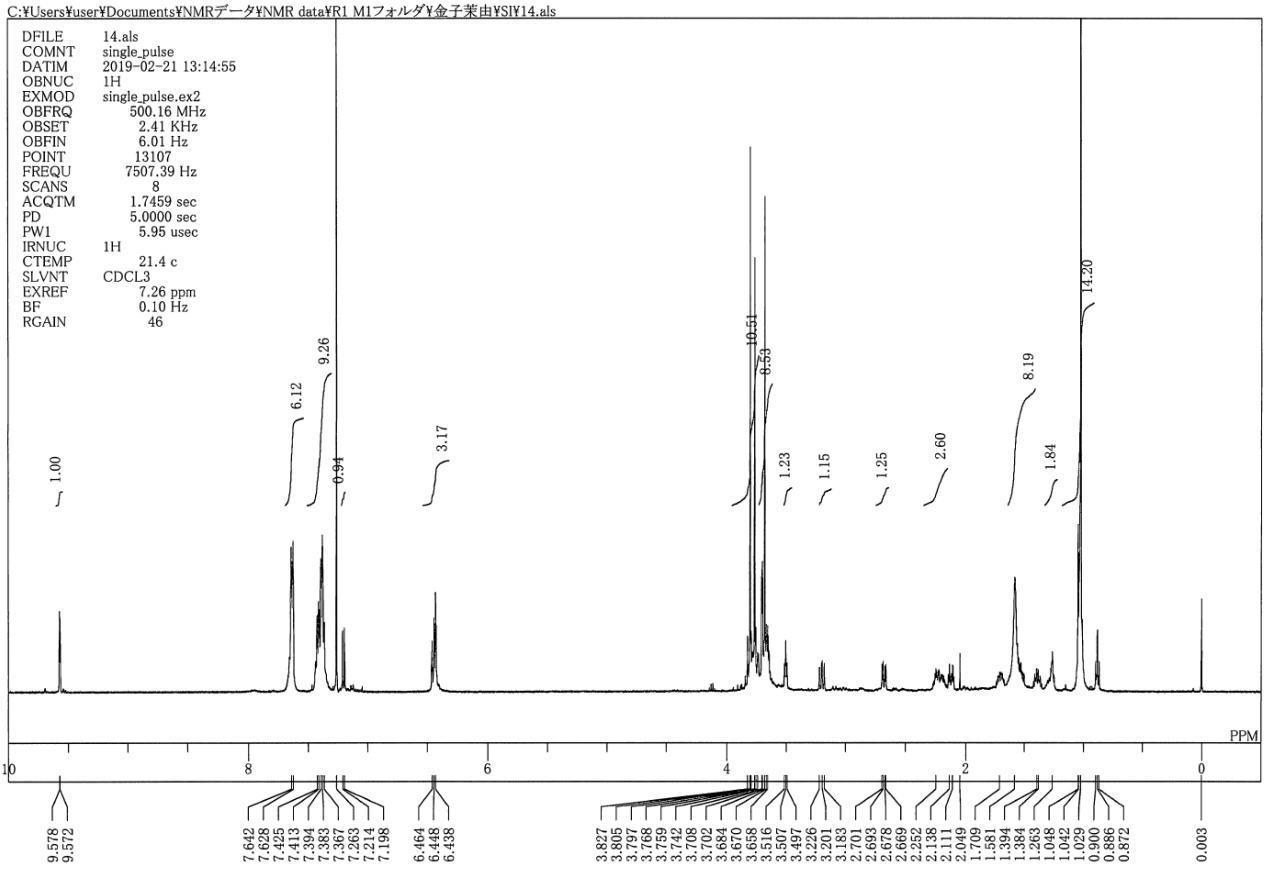
7.689 7.685 7.681 7.677 7.673 7.669 7.667 7.443 7.440 7.432 7.428 7.421 7.418 7.415 7.409 7.402 7.394 7.388 7.381 7.377 7.375 7.371 7.260 7.223 7.206 6.479 6.474 6.463 6.458 6.451 6.447 3.824 3.810 3.800 3.795 3.775 3.763 3.753 3.748 3.733 3.709 3.693 3.682 3.672 3.608 3.587 3.570 3.543 3.252 3.243 3.234 3.039 3.022 3.012 2.995 2.708 2.701 2.682 2.675 2.466 2.457 2.450 2.441 2.433 2.130 2.122 2.109 2.100 2.091 1.670 1.657 1.647 1.534 1.525 1.516 1.505 1.495 1.479 1.468 1.271 1.073 1.058 0.012

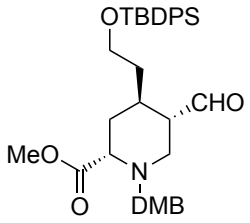
C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥13a CNMR.als

DFILE 13a CNMR.als
COMNT single pulse decoupled gated NOE
DATIM 2019-06-03 15:13:40
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 59
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 21.5 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 54



174.775 173.945 160.420 159.085 135.878 135.859 134.161 134.075 130.899 129.916 129.888 127.971 119.224 104.249 98.688 77.666 77.618 77.418 77.160 61.679 59.877 55.651 55.603 53.629 52.465 51.788 49.232 44.348 36.784 31.195 28.324 27.170 27.093 19.463



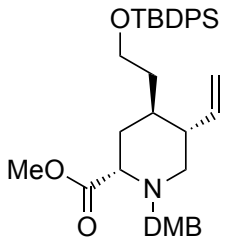


14

Single isomer determined by crude ^{1}H-NMR

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥15 HNMR-1 end.als

DFILE	15 HNMR-1 end.als
COMNT	single_pulse
DATIM	2019-06-10 10:37:18
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	13107
FREQU	7507.39 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	5.95 usec
IRNUC	1H
CTEMP	21.4 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.10 Hz
RGAIN	24

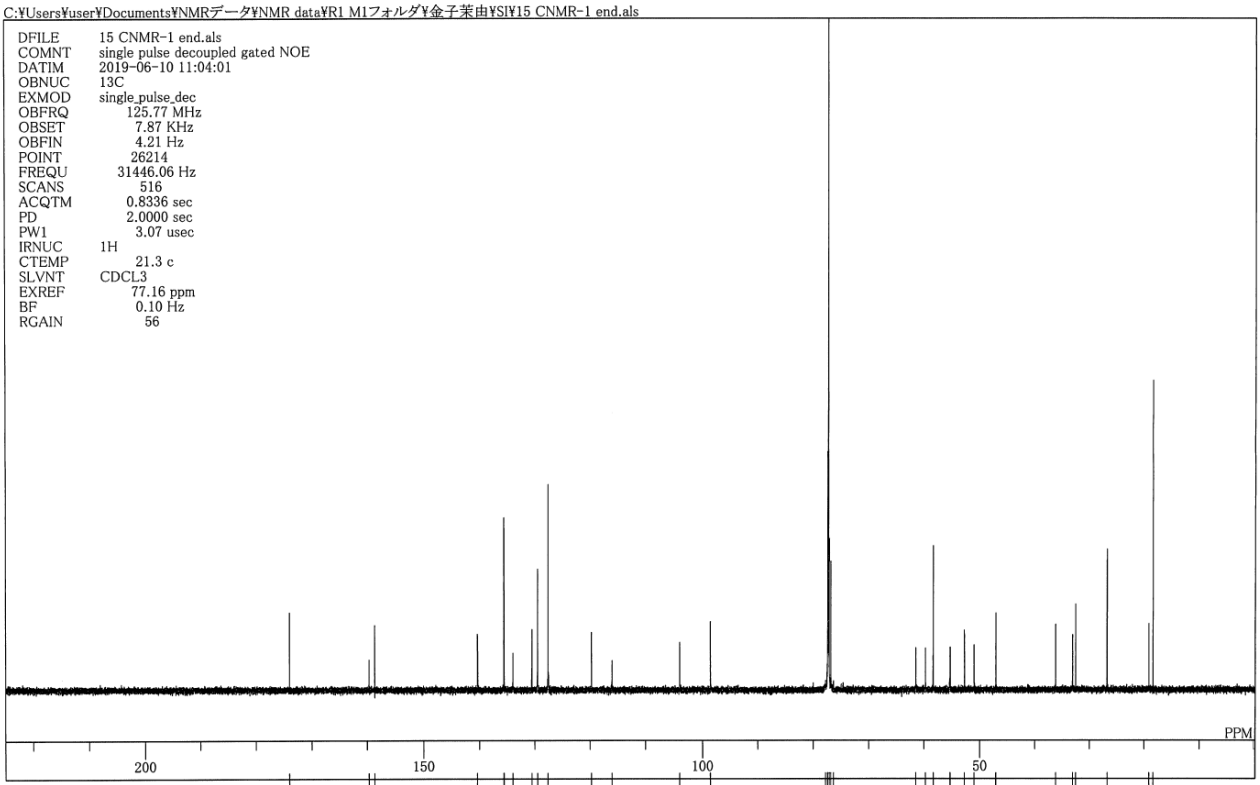


15

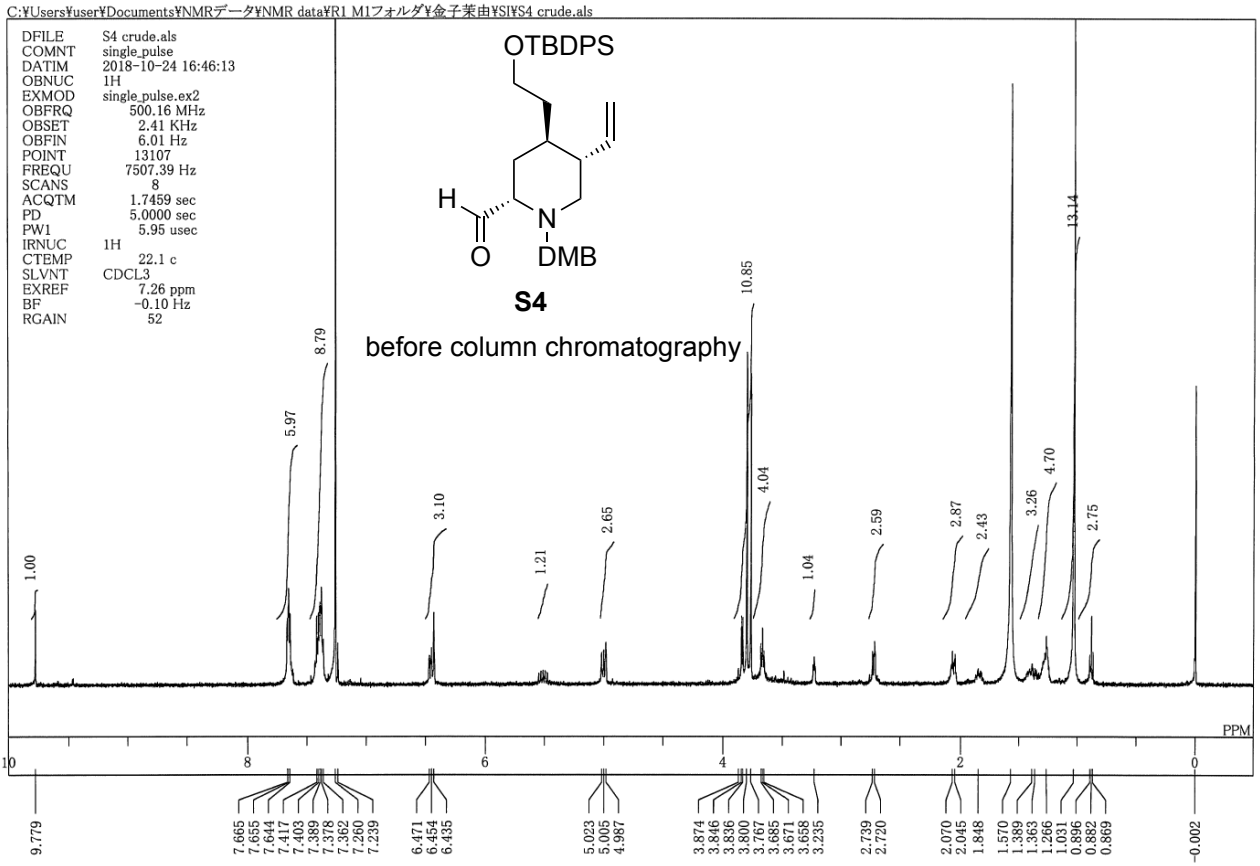
7.649 7.646 7.633 7.630 7.466 7.424 7.410 7.397 7.395 7.381 7.369 7.367 7.356 7.353 7.318 7.289 7.260 7.231 7.212 7.196 7.048 6.458 6.454 6.442 6.437 6.426 6.422 5.572 5.551 5.538 5.534 5.520 5.500 5.154 5.005 4.988 4.985 4.967 3.790 3.768 3.756 3.726 3.724 3.712 3.698 3.685 3.658 3.647 3.634 3.625 3.576 3.504 3.025 3.002 2.979 2.623 2.614 2.600 2.591 2.135 2.120 1.964 1.872 1.858 1.849 1.572 1.495 1.473 1.245 1.232 1.218 1.188 1.173 1.162 1.029 1.026 1.019 −0.004

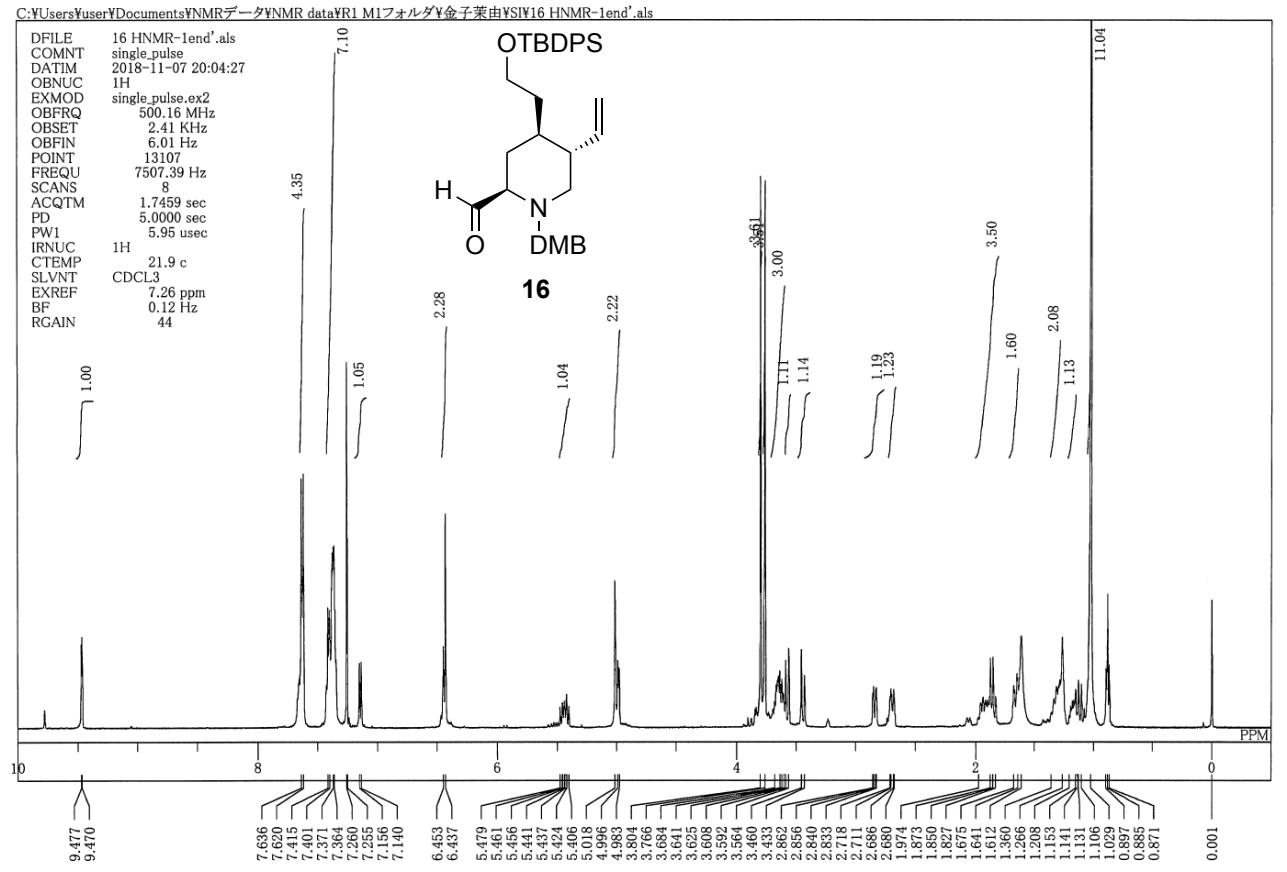
C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥15 CNMR-1 end.als

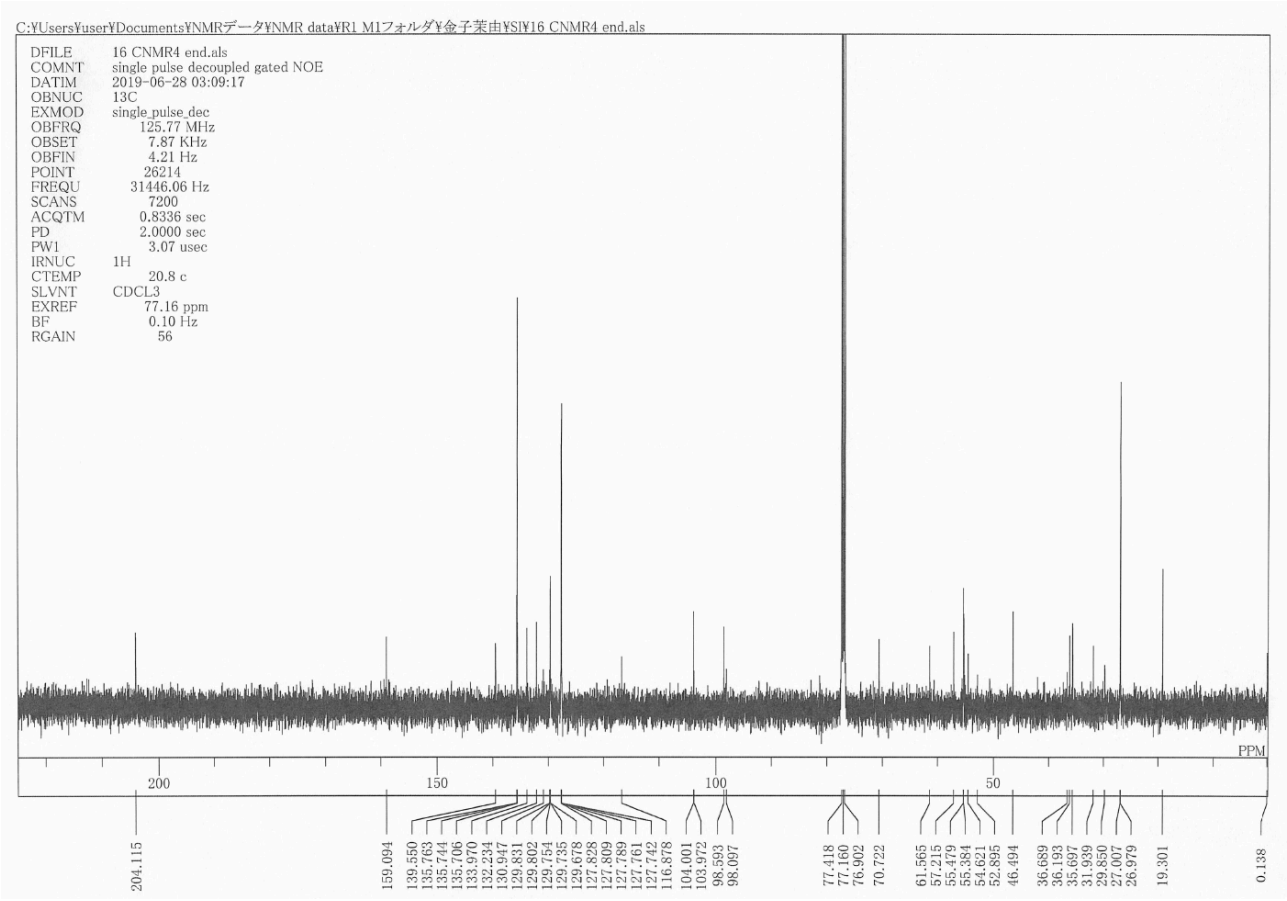
DFILE	15 CNMR-1 end.als
COMNT	single pulse decoupled gated NOE
DATIM	2019-06-10 11:04:01
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	26214
FREQU	31446.06 Hz
SCANS	516
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	3.07 usec
IRNUC	1H
CTEMP	21.3 c
SLVNT	CDCL3
EXREF	77.16 ppm
BF	0.10 Hz
RGAIN	56

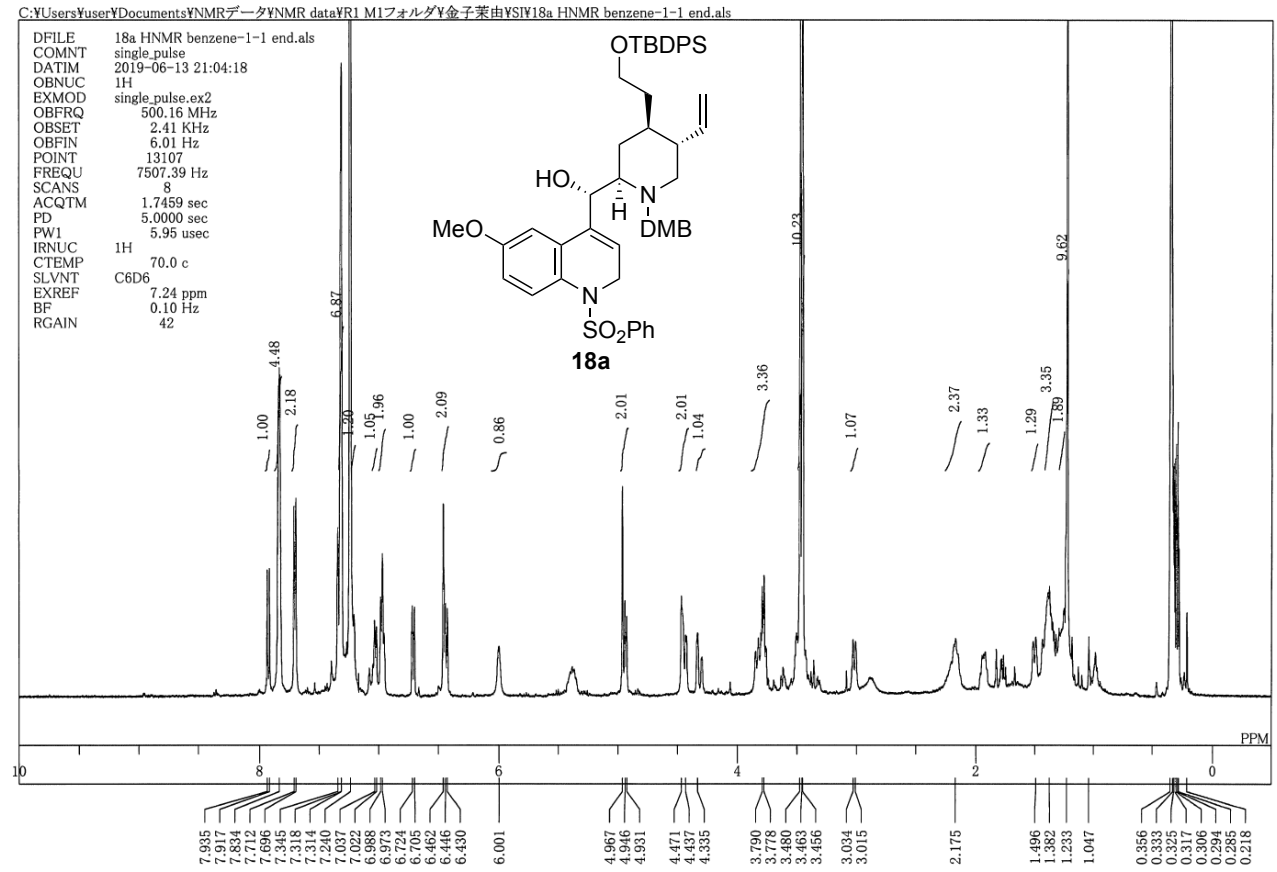


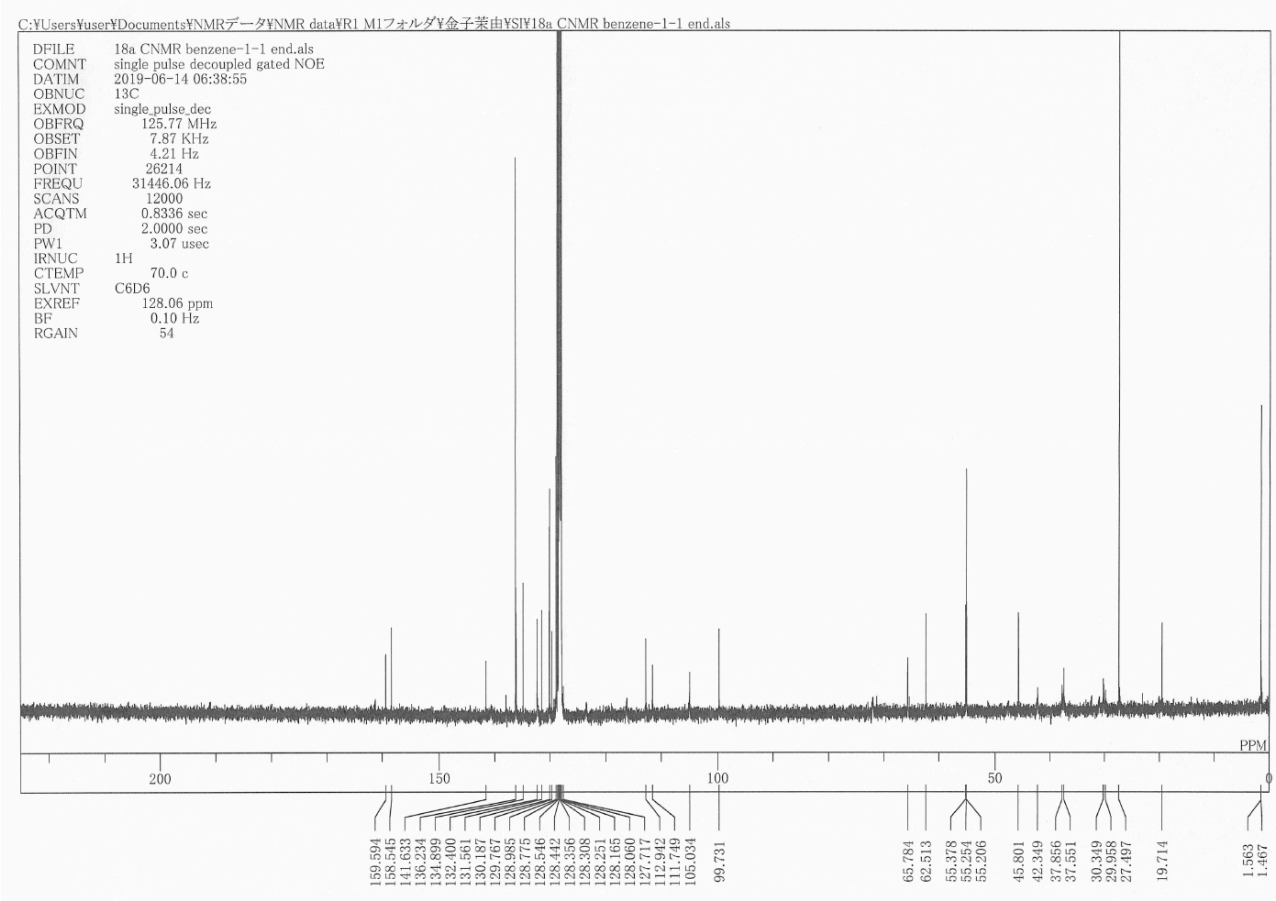
174.174 159.905 158.865 140.409 135.668 135.639 134.066 134.018 130.670 129.640 127.713 119.882 116.200 104.096 98.535 77.818 77.418 77.370 77.160 76.912 76.464 61.651 59.896 58.513 55.498 55.441 52.856 52.837 51.044 47.105 36.298 33.226 32.654 26.903 19.272 18.509

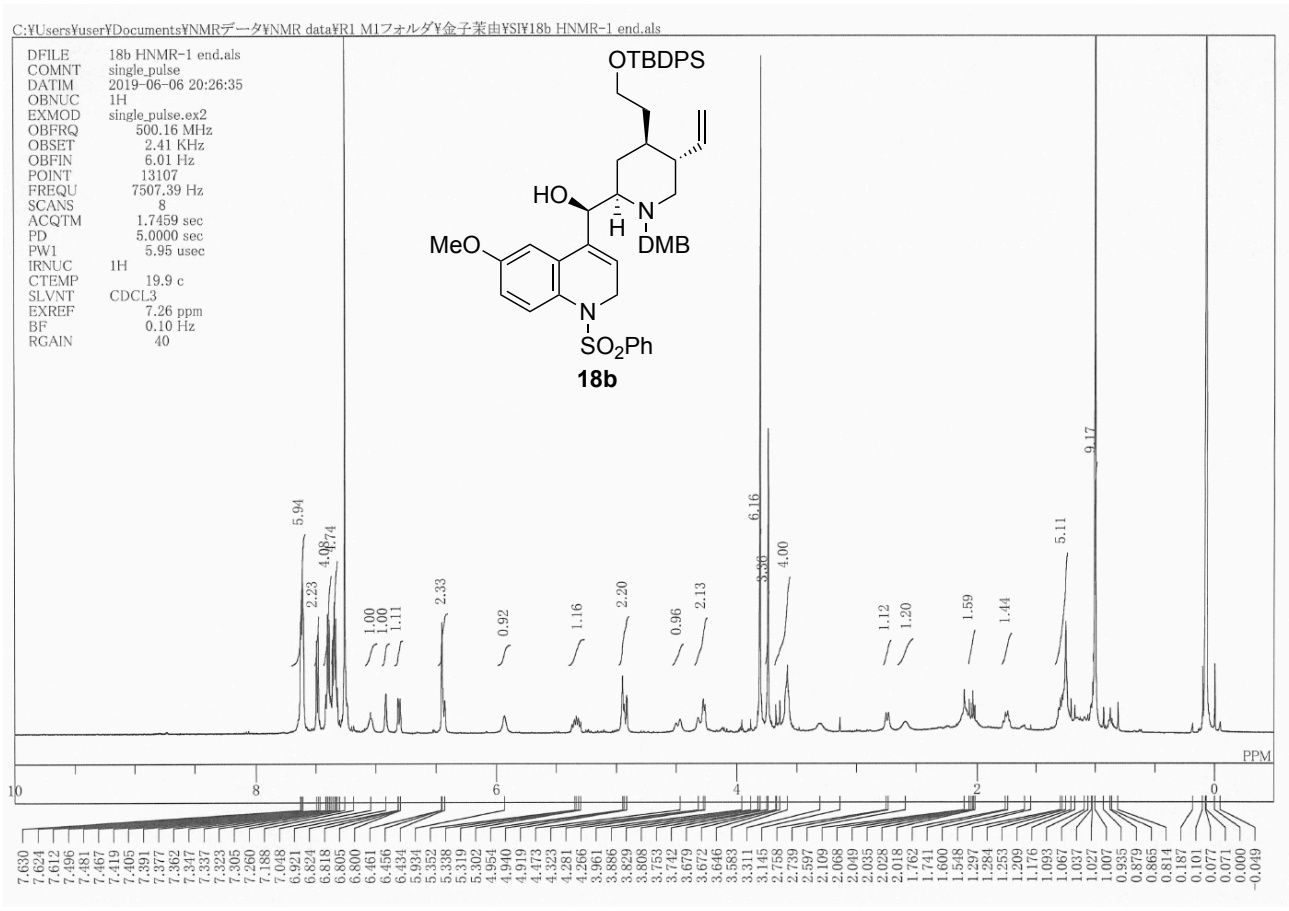

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥S4 crude.als
DFILE S4 crude.als
COMNT single_pulse
DATIM 2018-10-24 16:46:13
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 22.1 c
SLVNT CDCL3
EXREF 7.26 ppm
BF -0.10 Hz
RGAIN 52
OTBDPS
H
N
O
DMB
S4
before column chromatography
1.00
5.97
8.79
3.10
1.21
2.65
10.85
4.04
1.04
2.59
2.87
2.43
3.26
4.70
13.14
2.75
PPM
10
8
6
4
2
0
9.779
7.665
7.655
7.644
7.417
7.403
7.389
7.378
7.362
7.260
7.239
6.471
6.454
6.435
5.023
5.005
4.987
3.874
3.846
3.836
3.800
3.767
3.685
3.671
3.658
3.235
2.739
2.720
2.070
2.045
1.848
1.570
1.389
1.363
1.266
1.031
0.896
0.882
0.869
-0.002

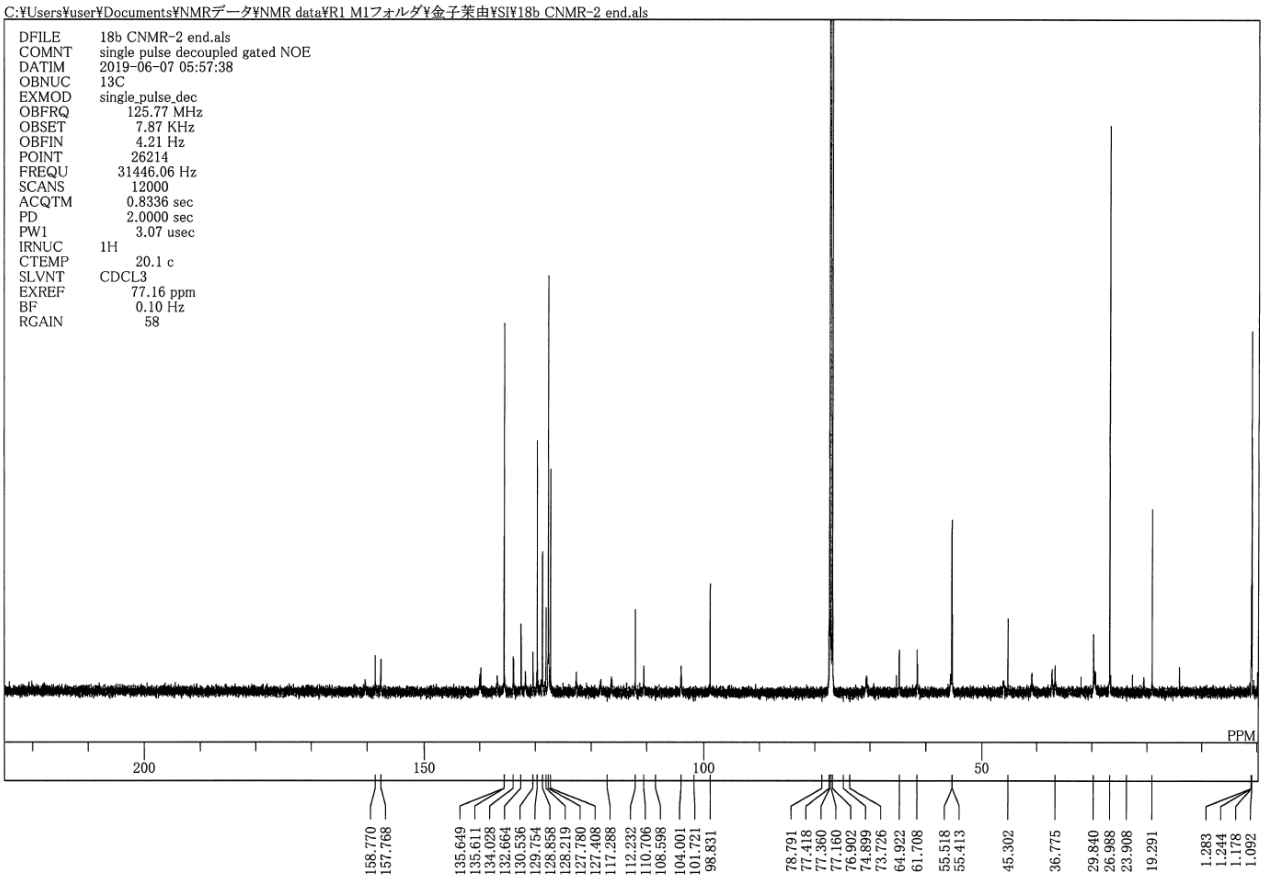

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥16 HNMR-1end'.als
DFILE 16 HNMR-1end'.als
COMNT single_pulse
DATIM 2018-11-07 20:04:27
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 21.9 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.12 Hz
RGAIN 44
OTBDPS
H
N
O
DMB
16
PPM

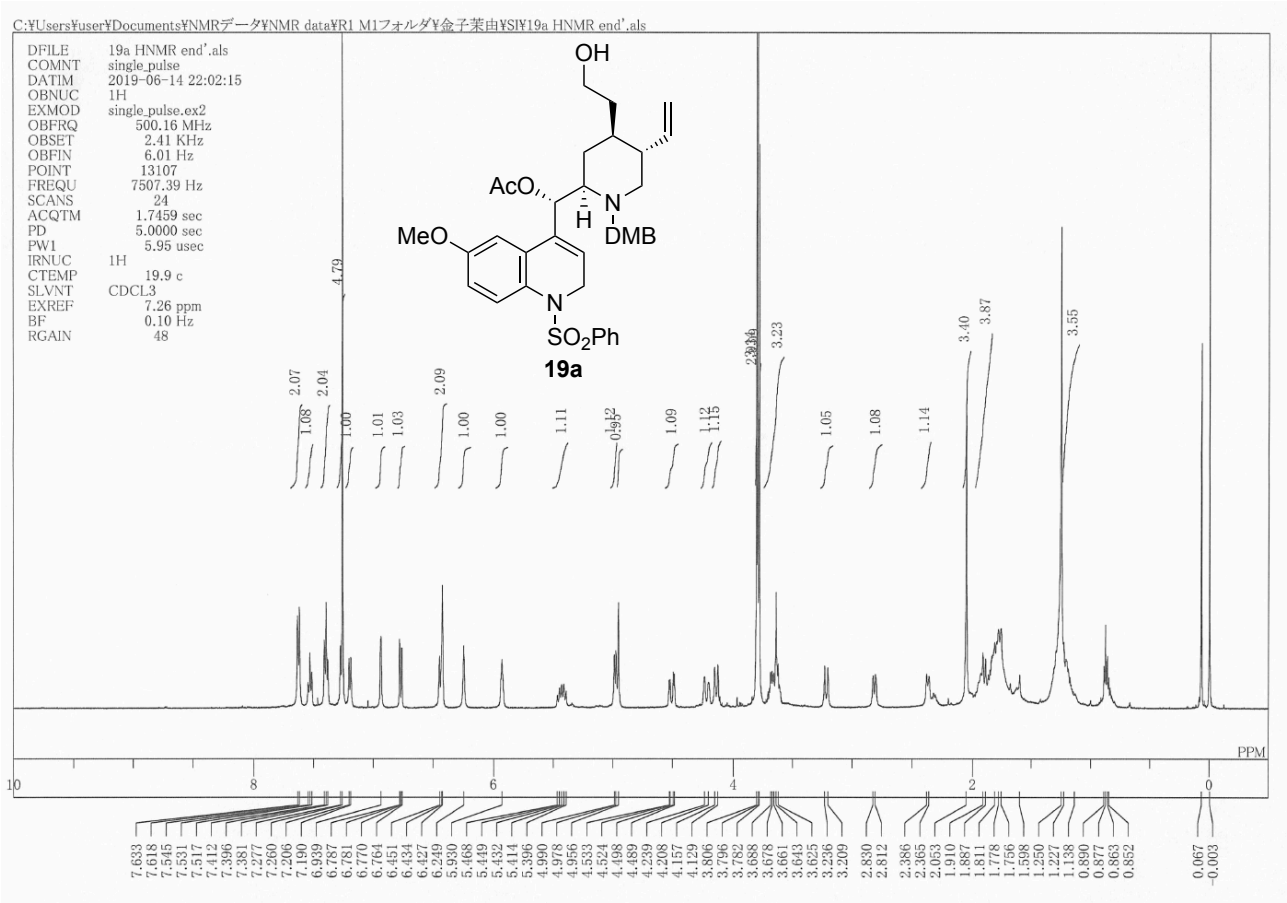

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥16 CNMR4 end.als
DFILE 16 CNMR4 end.als
COMNT single pulse decoupled gated NOE
DATIM 2019-06-28 03:09:17
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 7200
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 20.8 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 56
PPM

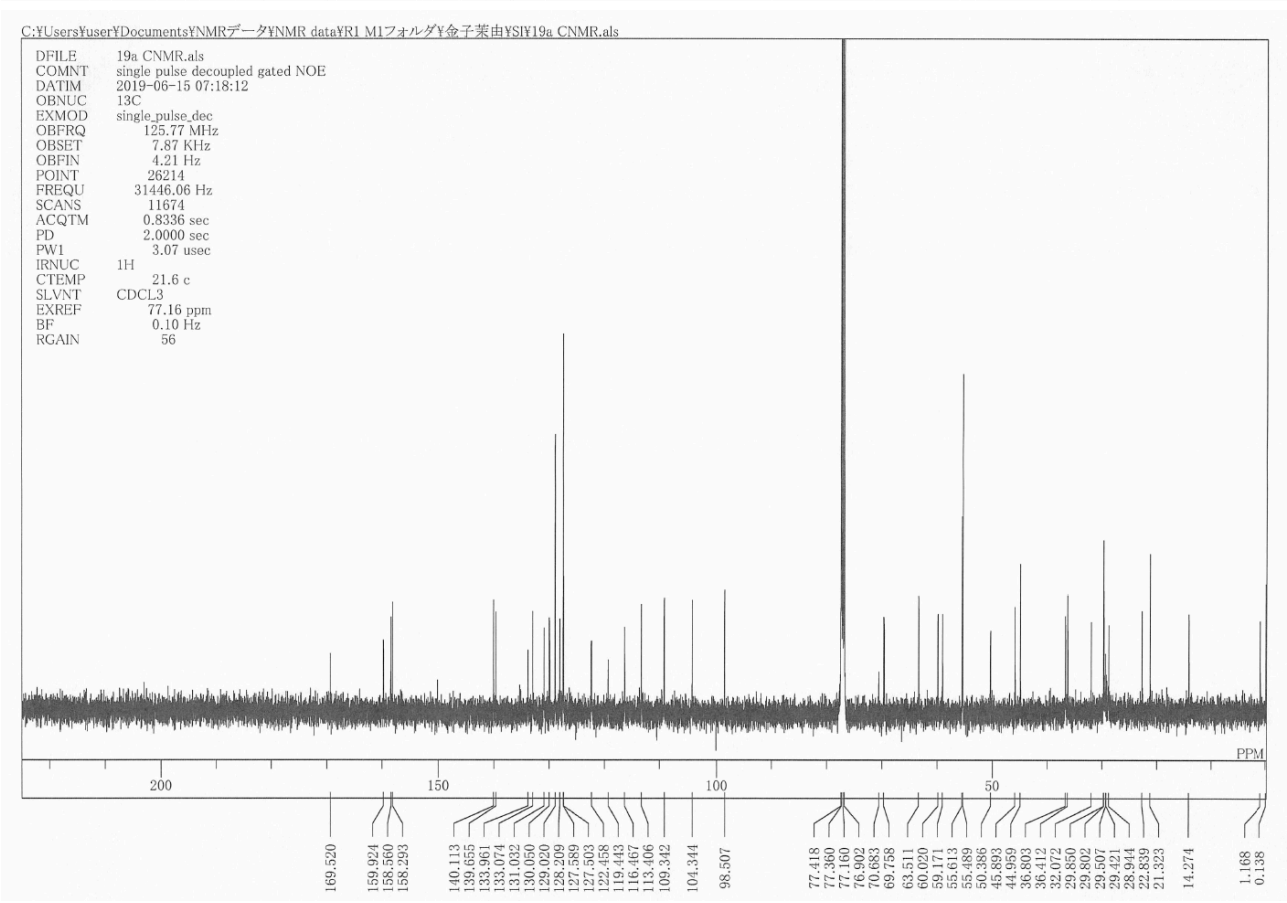

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥18a HNMR benzene-1-1 end.als
DFILE 18a HNMR benzene-1-1 end.als
COMNT single_pulse
DATIM 2019-06-13 21:04:18
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 70.0 c
SLVNT C6D6
EXREF 7.24 ppm
BF 0.10 Hz
RGAIN 42
OTBDPS
HO
H
N
DMB
MeO
N
SO2Ph
18a
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥18a CNMR benzene-1-1 end.als
DFILE 18a CNMR benzene-1-1 end.als
COMNT single pulse decoupled gated NOE
DATIM 2019-06-14 06:38:55
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 12000
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 70.0 c
SLVNT C6D6
EXREF 128.06 ppm
BF 0.10 Hz
RGAIN 54
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥18b HNMR-1 end.als
DFILE 18b HNMR-1 end.als
COMNT single_pulse
DATIM 2019-06-06 20:26:35
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 19.9 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.10 Hz
RGAIN 40
OTBDPS
HO
H
N
DMB
MeO
N
SO2Ph
18b
PPM

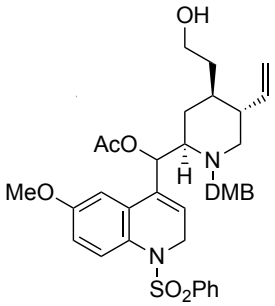

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥18b CNMR-2 end.als
DFILE 18b CNMR-2 end.als
COMNT single pulse decoupled gated NOE
DATIM 2019-06-07 05:57:38
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 12000
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 20.1 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 58
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥19a HNMR end',als
DFILE 19a HNMR end',als
COMNT single_pulse
DATIM 2019-06-14 22:02:15
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 24
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 5.95 usec
IRNUC 1H
CTEMP 19.9 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.10 Hz
RGAIN 48
OH
AcO
H
N
DMB
MeO
N
SO2Ph
19a
PPM


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥19a CNMR.als
DFILE 19a CNMR.als
COMNT single pulse decoupled gated NOE
DATIM 2019-06-15 07:18:12
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 11674
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 21.6 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 56
PPM

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥19 mix HNMR-2-2 end.als

DFILE	19 mix HNMR-2-2 end.als
COMNT	single_pulse
DATIM	2019-06-07 22:42:49
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16384
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	5.95 usec
IRNUC	1H
CTEMP	20.1 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.10 Hz
RGAIN	36

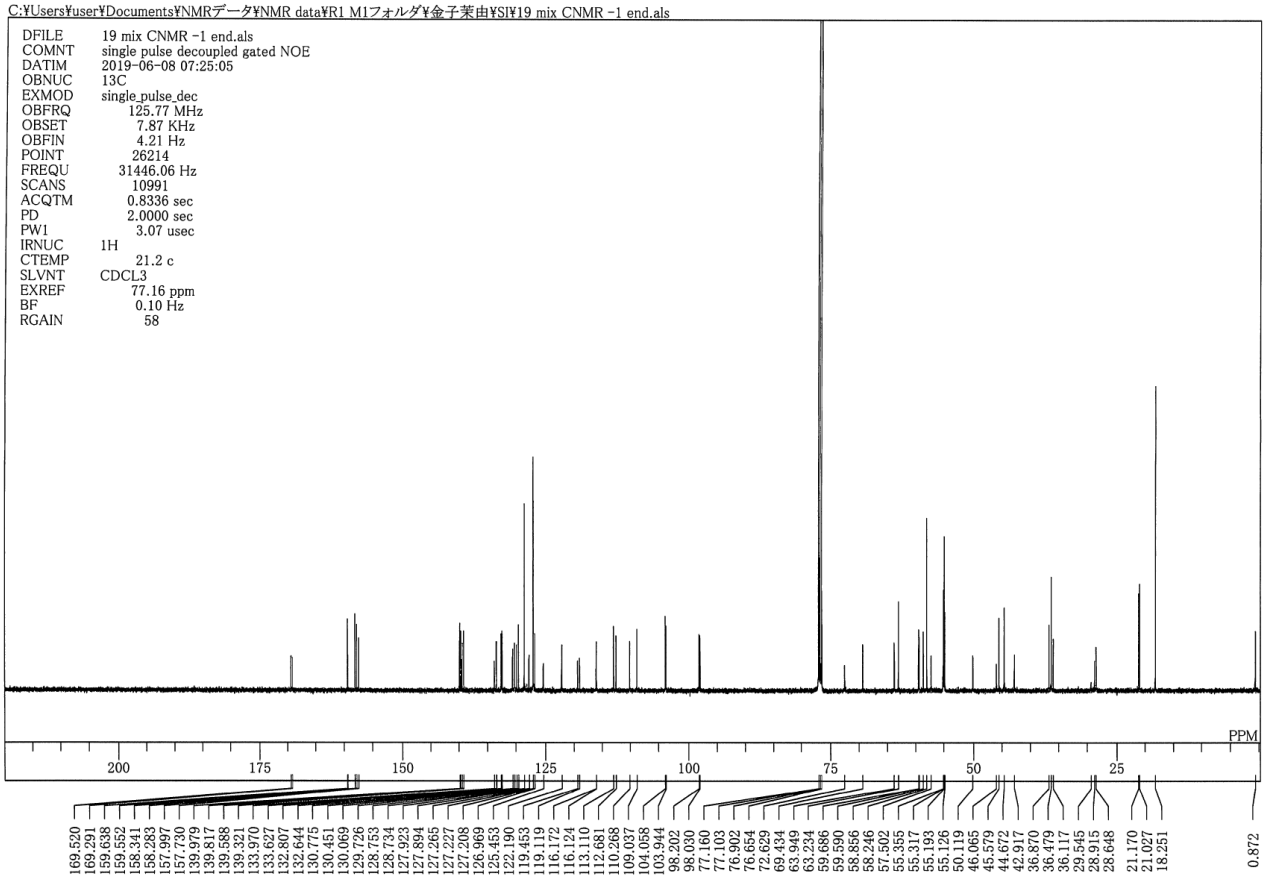


19

dr = 1 : 1

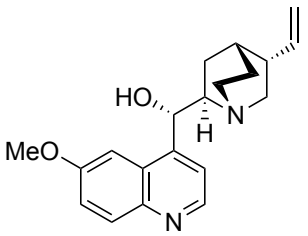
C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥19 mix CNMR -1 end.als

DFILE	19 mix CNMR -1 end.als
COMNT	single pulse decoupled gated NOE
DATIM	2019-06-08 07:25:05
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	26214
FREQU	31446.06 Hz
SCANS	10991
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	3.07 usec
IRNUC	1H
CTEMP	21.2 c
SLVNT	CDCL3
EXREF	77.16 ppm
BF	0.10 Hz
RGAIN	58

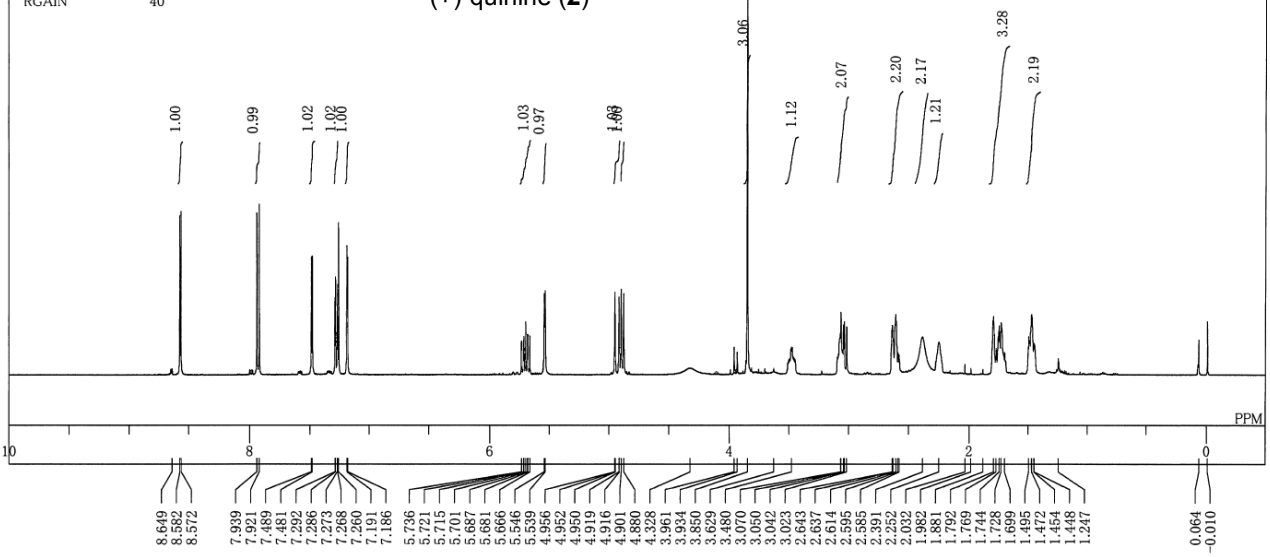


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥ent-quinine HNMR-1 end.als

DFILE	ent-quinine HNMR-1 end.als
COMNT	single_pulse
DATIM	2019-06-28 07:33:25
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	13107
FREQU	7507.39 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	5.95 usec
IRNUC	1H
CTEMP	20.2 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.10 Hz
RGAIN	40

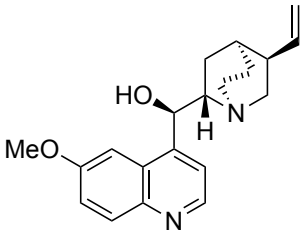


synthetic unnatural
(+)-quinine (**2**)

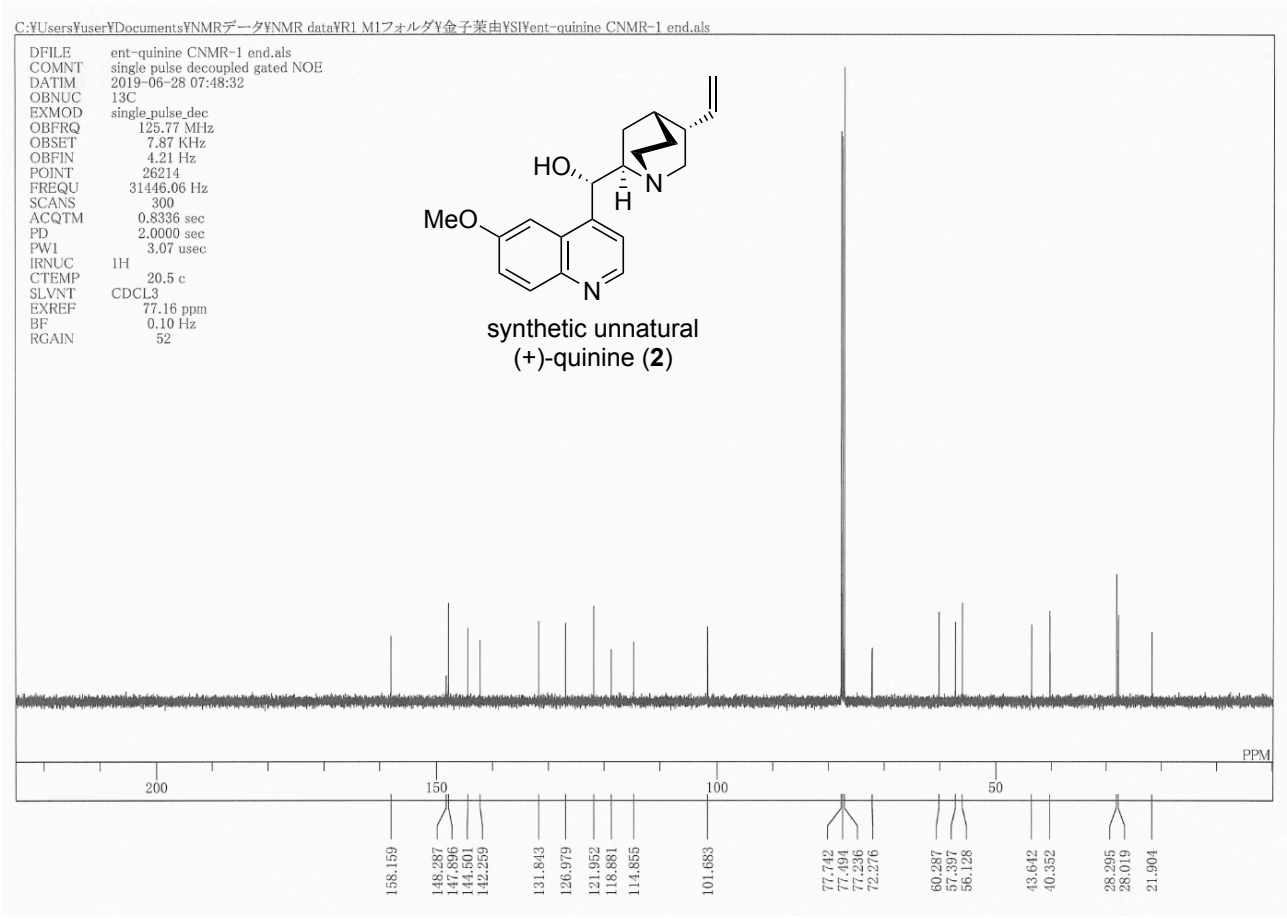


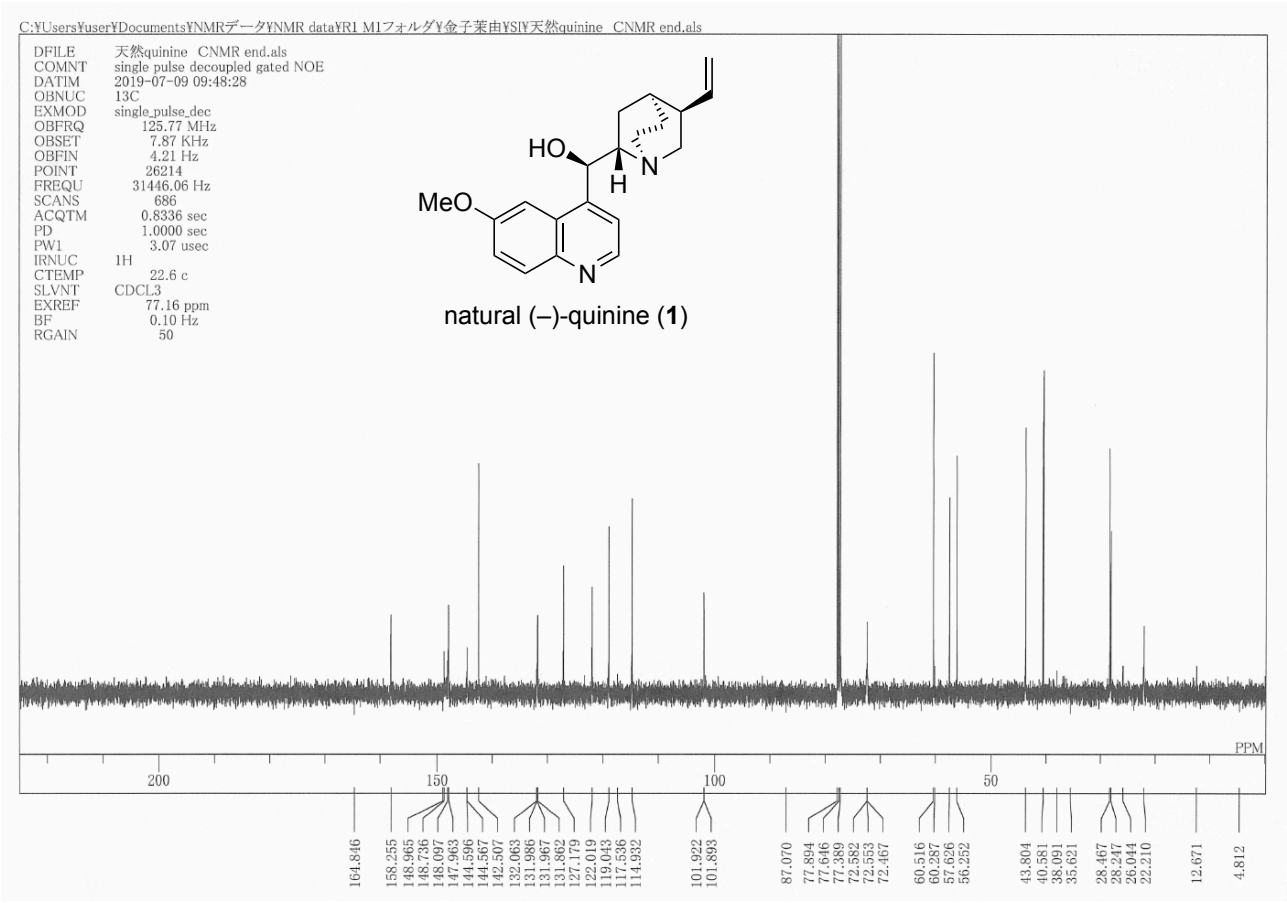
C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥天然quinine HNMR end.als

DFILE	天然quinine HNMR end.als
COMNT	single_pulse
DATIM	2019-07-09 11:45:25
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	13107
FREQU	7507.39 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	5.95 usec
IRNUC	1H
CTEMP	20.9 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.10 Hz
RGAIN	42

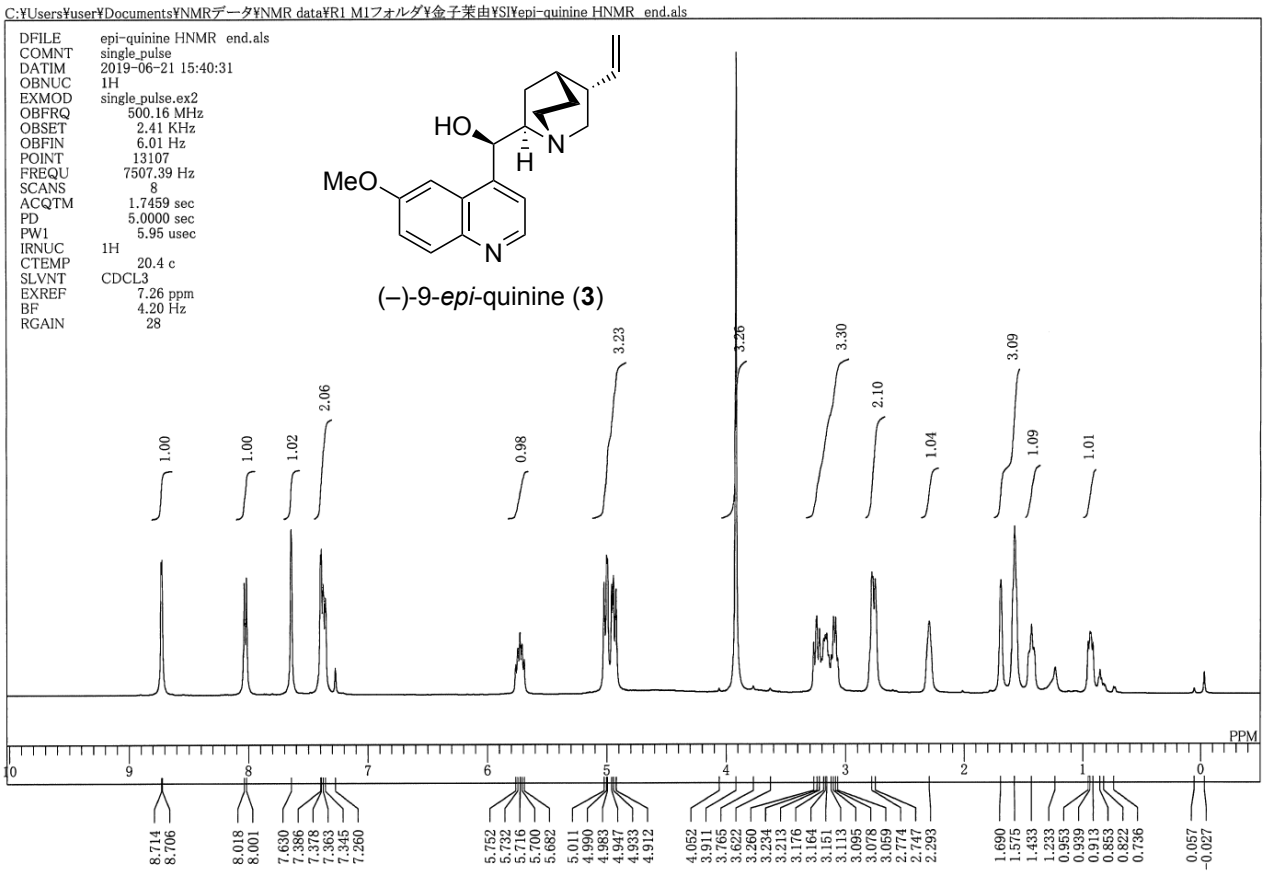


natural (–)-quinine (**1**)

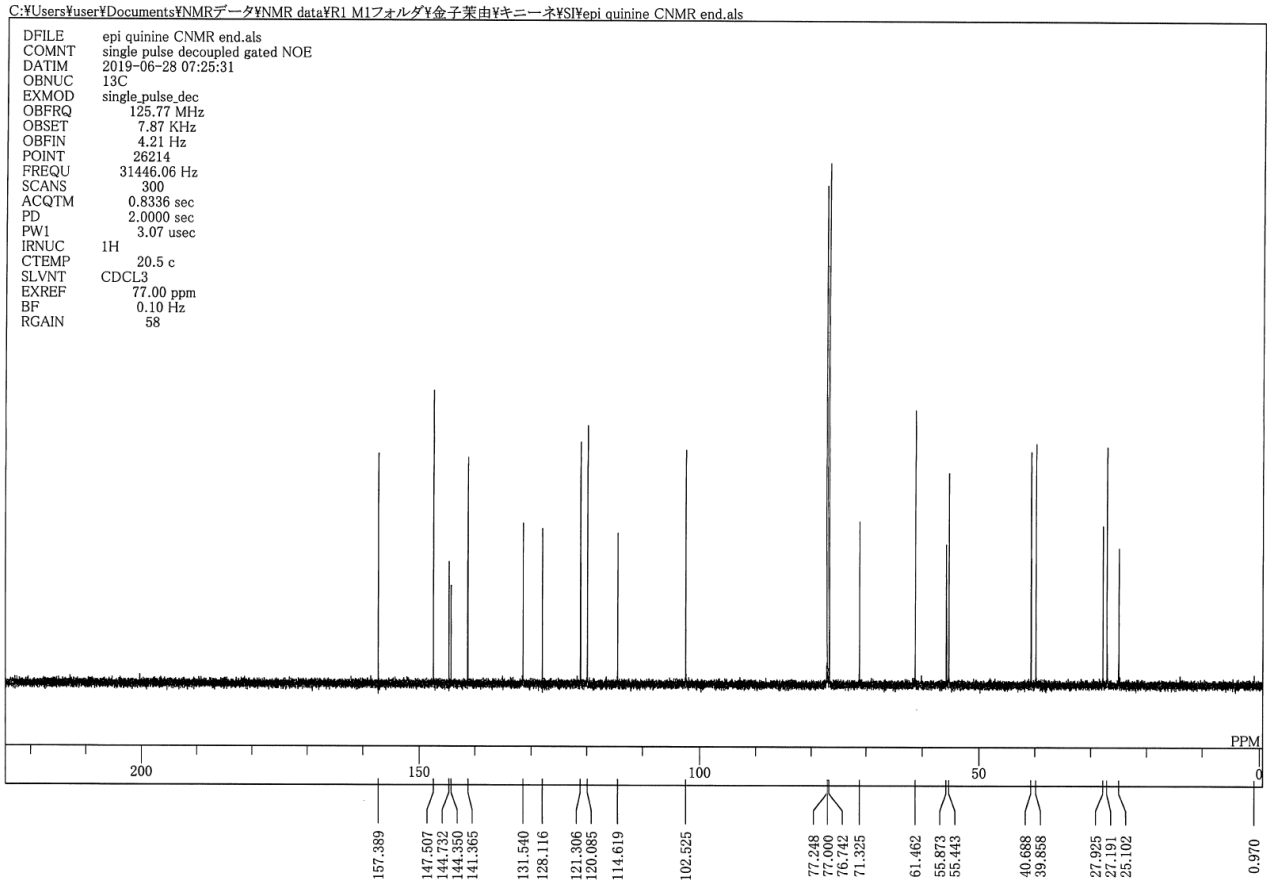

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥ent-quinine CNMR-1 end.als
DFILE ent-quinine CNMR-1 end.als
COMNT single pulse decoupled gated NOE
DATIM 2019-06-28 07:48:32
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 300
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 20.5 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 52
HO
H
N
MeO
N
synthetic unnatural
(+)-quinine (2)
PPM
200
150
100
50
158.159
148.287
147.896
144.501
142.259
131.843
126.979
121.952
118.881
114.855
101.683
77.742
77.494
77.236
72.276
60.287
57.397
56.128
43.642
40.352
28.295
28.019
21.904


C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥天然quinine CNMR end.als
DFILE 天然quinine CNMR end.als
COMNT single pulse decoupled gated NOE
DATIM 2019-07-09 09:48:28
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 686
ACQTM 0.8336 sec
PD 1.0000 sec
PW1 3.07 usec
IRNUC 1H
CTEMP 22.6 c
SLVNT CDCL3
EXREF 77.16 ppm
BF 0.10 Hz
RGAIN 50
HO
H
N
MeO
N
natural (–)-quinine (1)
PPM
200
150
100
50
164.846
158.255
148.965
148.736
148.097
147.963
144.596
144.567
142.507
132.063
131.986
131.967
131.862
127.179
122.019
119.043
117.536
114.932
101.922
101.893
87.070
77.894
77.646
77.389
72.582
72.553
72.467
60.516
60.287
57.626
56.252
43.804
40.581
38.091
35.621
28.467
28.247
26.044
22.210
12.671
4.812

C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥SI¥epi-quinine HNMR end.als



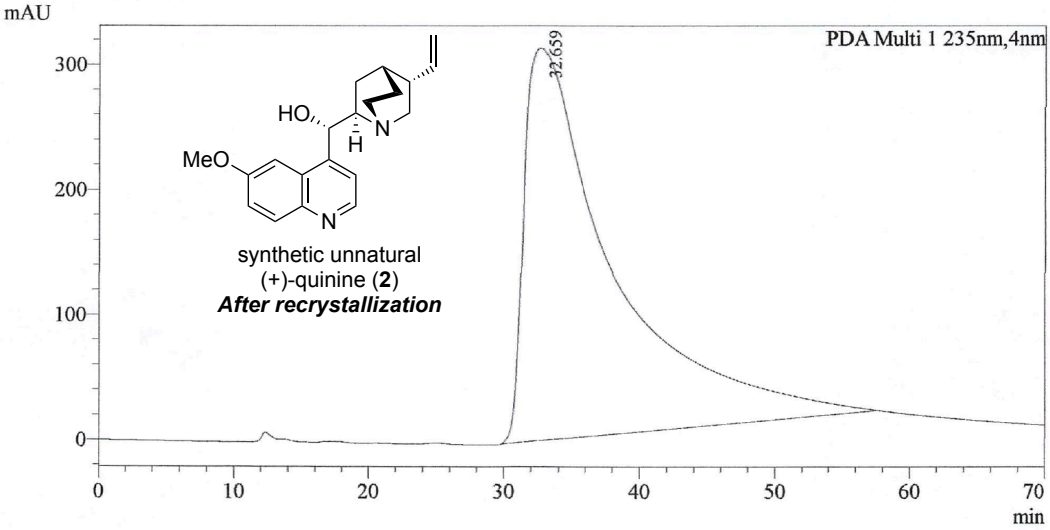
C:¥Users¥user¥Documents¥NMRデータ¥NMR data¥R1 M1フォルダ¥金子茉由¥キニーネ¥SI¥epi quinine CNMR end.als



=== Shimadzu LabSolutions Report ===

Sample Name	: kini unnat 10 ih		
Sample ID	: kaneko		
Data Filename	: kini unnat 10 ih.lcd		
Method Filename	: 10%iPrOH-Hex-floe0.25.lcm		
Batch Filename	:		
Vial#	: 1-1	Sample Type	: –¢'m
Injection Volume	: 20 uL		
Date Acquired	: 2019/07/16 19:41:38 Acquired by	: System Administrator	
Date Processed	: 2019/07/16 21:02:24 Processed by	: System Administrator	

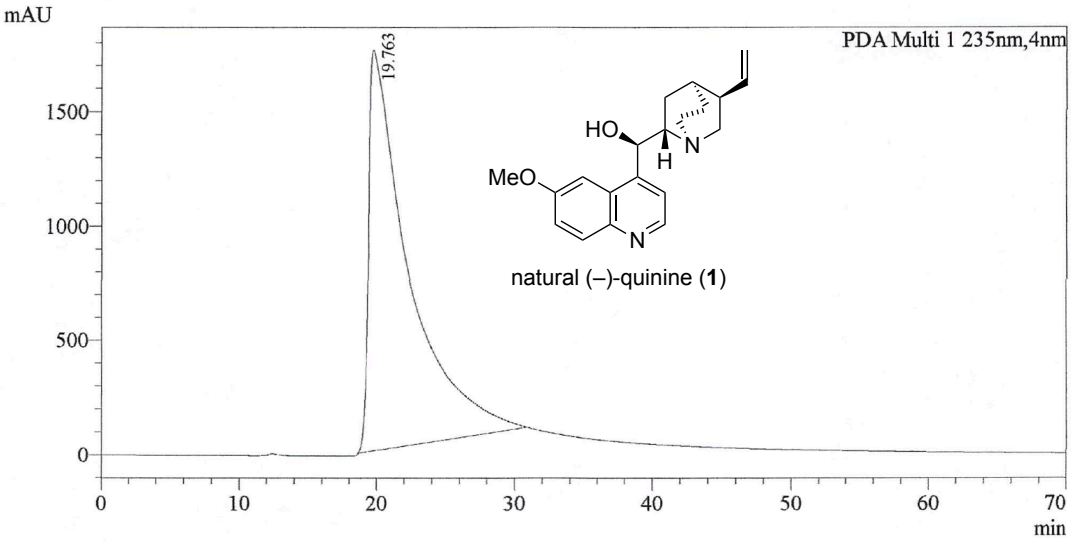
<Chromatogram>



<Peak Table>

PDA Ch1 235nm

Peak#	Ret. Time	Area	Height	Conc.	Name
1	32.659	144074762	313968	100.000	
‡Œv		144074762	313968		



<Peak Table>

PDA Ch1 235nm

Peak#	Ret. Time	Area	Height	Conc.	Name
1	19.763	351504692	1750259	100.000	
‡Œv		351504692	1750259		