

Supporting Information

Formal Total Synthesis of (\pm)-Strictamine Based on a Gold-Catalyzed Cyclization

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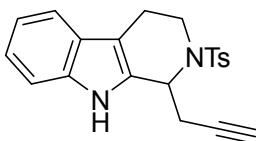
Experimental Section

General Methods. Unless otherwise stated, reagents and anhydrous solvents (except for THF) were used as purchased from commercial suppliers. THF was distilled from sodium and benzophenone prior to use. Dess-Martin periodinane was prepared according to the known literature procedures.¹ For workup, the organic layer was washed once with the specified aqueous solutions. Glassware were dried at 65 °C prior to use. IR spectra were determined on a JASCO FT/IR-4100 spectrometer. Exact mass (HRMS) spectra were recorded on Shimadzu LC-ESI-IT-TOF-MS equipment. ¹H NMR spectra were recorded using a JEOL AL-500 spectrometer at 500 MHz. Chemical shifts are reported in δ (ppm) relative to Me₄Si (in CDCl₃) as internal standard. ¹³C NMR spectra were recorded using a JEOL AL-500 and referenced to the residual solvent signal. Melting points were measured by a hot stage melting points apparatus (uncorrected). For flash chromatography, silica gel (Wakogel C-300E; Wako Pure Chemical Industries, Ltd) was employed.

The known compounds **11**², **12**², and **21**³ were synthesized according to the literature.

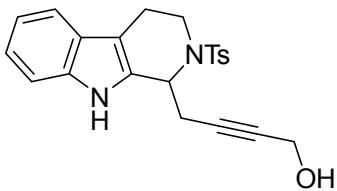
- (1) Stevenson, P. J.; Treacy, A. B.; Nieuwenhuyzen, M. *J. Chem. Soc., Perkin Trans. 2*, **1997**, 589.
- (2) Kolundžić, F.; Murali, A.; Pérez-Galán, P.; Bauer, J. O.; Strohmann, C.; Kumar, K.; Waldmann, H. *Angew. Chem., Int. Ed.* **2014**, 53, 8122.
- (3) Yin, W.; Kabir, S.; Wang, Z.; Rallapalli, S. K.; Ma, J.; Cook, J. M. *J. Org. Chem.* **2010**, 75, 3339.

1. Preparation of the Substrates for Gold-Catalyzed Reaction (Compounds **8a** and **8b**)



rac-1-(Prop-2-yn-1-yl)-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (13)

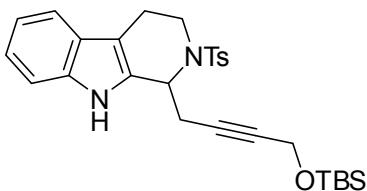
To a solution of the known tetrahydro- β -carboline (THBC) derivative **12¹** (1.47 g, 5.19 mmol) in CH₂Cl₂ (26 mL) were added Et₃N (2.2 mL, 15.6 mmol), TsCl (1.49 g, 7.79 mmol), *N,N*-dimethylaminopyridine (DMAP; 318 mg, 2.60 mmol) at 0 °C, and the mixture was stirred at the same temperature for 1 h. Saturated NaHCO₃ was added to the mixture, and the aqueous layer was extracted with CH₂Cl₂ twice. The combined organic layer was washed with saturated NaHCO₃ and brine, dried over MgSO₄, and concentrated in vacuo. The residue was dissolved in THF (51.9 mL), and tetrabutylammonium fluoride (TBAF; 1.0 M in THF; 7.8 mL, 7.79 mmol) was added to the mixture at 0 °C. After stirring at room temperature for 1 h, saturated NH₄Cl was added to the mixture, and the whole was extracted with EtOAc twice. The combined organic layer was washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10/1 to 2/1) to give **13** (2.14 g, 93%). Recrystallization from CH₂Cl₂/hexane gave pure **9** as colorless crystals (1.32 g from 1.50 g, 88%): mp 164–165 °C; IR (neat) 3394 (NH), 3279 (C≡CH), 2360 (C≡CH), 1330, 1151 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ: 2.28 (t, *J* = 2.6 Hz, 1H), 2.33 (s, 3H), 2.42–2.49 (m, 1H), 2.59 (dd, *J* = 15.5, 2.9 Hz, 1H), 2.77 (ddd, *J* = 16.3, 10.0, 2.6 Hz, 1H), 2.93–2.97 (m, 1H), 3.36–3.42 (br m, 1H), 4.19 (dd, *J* = 14.6, 4.9 Hz, 1H), 5.26 (dd, *J* = 10.0, 4.3 Hz, 1H), 7.06–7.09 (m, 1H), 7.16–7.19 (m, 3H), 7.33 (d, *J* = 8.6 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.67–7.69 (m, 2H), 8.38 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ: 20.4, 21.4, 26.3, 40.3, 51.3, 72.3, 81.2, 108.6, 111.1, 118.3, 119.6, 122.4, 126.1, 126.7 (2C), 129.7 (2C), 131.8, 135.8, 137.9, 143.5. *Anal.* calcd for C₂₁H₂₀N₂O₂S: C, 69.42; H, 5.53; N, 7.69. Found: C, 69.08; H, 5.52; N, 7.58.



rac-4-(2-Tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)but-2-yn-1-ol (8a)

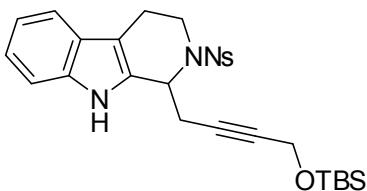
To a solution of **13** (2.45 g, 6.72 mmol) in dry THF (134 mL) was added a solution of *i*-PrMgCl (2.0 M in THF; 16.8 mL, 33.6 mmol) at 0 °C under argon. After stirring at 60 °C for 1 h, a suspension of paraformaldehyde (808 mg, 26.9 mmol) in dry THF (13.5 mL) was added to the mixture at the same temperature. After stirring at 60 °C for 1 h, NaOH (1 M, 96.5 mL) was added to the mixture at room temperature. After stirring for 30 min, saturated NH₄Cl was added to the mixture. The whole was extracted with EtOAc three times, and the combined organic layer was washed with distilled water and brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5/1 to 1/1) to give **8a** (1.76 g, 66%) as a pale yellow

solid: mp 110 °C; IR (neat): 3394 (OH), 2231 (C≡CH), 1323, 1152 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ: 2.25 (t, *J* = 5.7 Hz, 1H), 2.32 (s, 3H), 2.40-2.46 (m, 1H), 2.57 (dd, *J* = 15.5, 4.0 Hz, 1H), 2.78-2.81 (m, 1H), 2.91-2.95 (m, 1H), 3.37-3.44 (m, 1H), 4.16 (dd, *J* = 14.6, 5.4 Hz, 1H), 4.28-4.37 (br m, 2H), 5.30-5.32 (br m, 1H), 7.05-7.08 (m, 1H), 7.15-7.18 (m, 3H), 7.32-7.37 (m, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 8.63 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ: 20.2, 21.4, 26.5, 40.0, 51.3, 51.8, 82.2, 83.0, 108.3, 111.2, 118.2, 119.4, 122.3, 126.0, 126.7 (2C), 129.7 (2C), 131.7, 135.9, 137.8, 143.5; HRMS (ESI) calcd for C₂₂H₂₃N₂O₃S (MH⁺) 395.1424, found 395.1420.



***rac*-1-{4-[(tert-Butyldimethylsilyl)oxy]but-2-yn-1-yl}-2-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (14)**

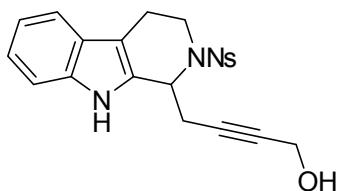
To a solution of **8a** (1.66 g, 4.21 mmol) in dry CH₂Cl₂ (42.1 mL) were added imidazole (573 mg, 8.42 mmol) and TBSCl (953 mg, 6.32 mmol) at 0 °C. After stirring at 0 °C for 1 h, the mixture was quenched with saturated NH₄Cl and extracted with CH₂Cl₂ twice. The combined organic layer was washed with distilled water and brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10/1 to 4/1) to give **14** (1.85 g, 86%). Recrystallization from CHCl₃/hexane gave pure **14** as colorless crystals: mp 122 °C; IR (neat): 3383 (NH), 2310 (C≡CH), 1353, 1159 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ: 0.156 (s, 3H), 0.163 (s, 3H), 0.95 (s, 9H), 2.33 (s, 3H), 2.43-2.49 (br m, 1H), 2.59 (dd, *J* = 15.5, 3.4 Hz, 1H), 2.74-2.80 (m, 1H), 2.94-2.98 (br m, 1H), 3.35-3.41 (m, 1H), 4.19 (dd, *J* = 14.3, 5.2 Hz, 1H), 4.36-4.38 (br m, 2H), 5.23 (dd, *J* = 10.3, 4.0 Hz, 1H), 7.05-7.08 (m, 1H), 7.15-7.18 (m, 3H), 7.31 (d, *J* = 8.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 8.57 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ: -5.2, -5.1, 18.4, 20.4, 21.4, 25.9 (3C), 26.6, 40.3, 51.6, 52.0, 82.0, 82.5, 108.5, 111.1, 118.2, 119.4, 122.2, 126.1, 126.7 (2C), 129.7 (2C), 132.0, 135.8, 137.9, 143.4. *Anal.* calcd for C₂₈H₃₆N₂O₃SSi: C, 66.10; H, 7.13; N, 5.51. Found: C, 66.04; H, 6.97; N, 5.53.



***rac*-1-{4-[(tert-Butyldimethylsilyl)oxy]but-2-yn-1-yl}-2-[(2-nitrophenyl)sulfonyl]-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (15)**

To a stirred solution of **14** (1.88 g, 3.69 mmol) in MeOH (36.9 mL) was added magnesium (2.70 g, 111 mmol) at room temperature. After stirring at 40 °C for 2 h, the mixture was allowed to cool to room temperature, quenched with saturated NH₄Cl, and extracted with EtOAc three times. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated in vacuo. After the residue was dissolved in CH₂Cl₂ (36.9 mL), diisopropylethylamine (DIPEA; 0.97 mL, 5.54 mmol) and NsCl

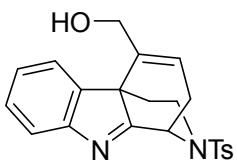
(858 mg, 3.87 mmol) were added to the mixture at room temperature. After stirring at room temperature for 1 h, the mixture was quenched with saturated NaHCO₃ and extracted with CH₂Cl₂ twice. The combined organic layer was washed with saturated NaHCO₃, saturated NH₄Cl and brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5/1 to 2/1) to give **15** (1.33 g, 67%). Recrystallization from EtOAc/hexane gave pure **15** as pale yellow crystals: mp 111–112 °C; IR (neat): 3384 (NH), 2360 (C≡CH), 1541 (NO₂), 1362, 1163 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ: 0.15 (s, 3H), 0.16 (s, 3H), 0.95 (s, 9H), 2.67–2.72 (m, 2H), 2.80–2.86 (m, 1H), 2.92–2.96 (m, 1H), 3.49–3.55 (m, 1H), 4.25–4.28 (m, 1H), 4.35–4.37 (br m, 2H), 5.31 (dd, *J* = 10.0, 4.3 Hz, 1H), 7.07–7.09 (m, 1H), 7.18 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.57–7.65 (m, 3H), 8.00–8.02 (m, 1H), 8.57 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ: –5.2, –5.1, 18.4, 20.9, 25.8 (3C), 26.5, 40.7, 52.0, 52.2, 81.5, 82.8, 108.2, 111.2, 118.2, 119.6, 122.4, 124.4, 126.0, 130.2, 131.8, 131.9, 133.6, 134.0, 135.9, 147.9; HRMS (FAB) calcd for C₂₇H₃₄N₃O₅SSi (MH⁺) 540.1983, found 540.1978.



***rac*-4-{2-[(2-Nitrophenyl)sulfonyl]-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-yl}but-2-yn-1-ol (8b)**

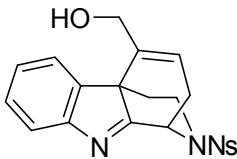
To a solution of **15** (1.15 g, 2.13 mmol) in THF (21.3 mL) was added a solution of TBAF (1.0 M in THF; 3.20 mL, 3.20 mmol) at room temperature. After stirring at room temperature for 1 h, saturated NH₄Cl was added to the mixture, and the whole was extracted with EtOAc twice. The combined organic layer was washed with distilled water and brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 4/1 to 1/2) to give **8b** (857 mg, 95%). Recrystallization from CH₂Cl₂/hexane to give pure **8b** as pale yellow crystals: mp 125 °C; IR (neat): 3396 (OH), 2345 (C≡CH), 1540 (NO₂), 1339, 1160 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ: 2.21 (t, *J* = 5.7 Hz, 1H), 2.59–2.66 (m, 1H), 2.69–2.73 (m, 1H), 2.82–2.87 (m, 1H), 2.90–2.94 (m, 1H), 3.51–3.57 (m, 1H), 4.23–4.26 (m, 1H), 4.28–4.35 (m, 2H), 5.36–5.38 (br m, 1H), 7.06–7.09 (m, 1H), 7.16–7.19 (m, 1H), 7.35–7.40 (m, 2H), 7.56–7.64 (m, 3H), 8.01–8.03 (m, 1H), 8.62 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ: 20.7, 26.4, 40.5, 51.3, 52.4, 82.4, 82.6, 108.0, 111.3, 118.2, 119.6, 122.4, 124.4, 126.0, 130.2, 131.7, 132.0, 133.7, 134.0, 136.0, 147.9; HRMS (ESI) calcd for C₂₁H₂₀N₃O₅S (MH⁺) 426.1118, found 426.1119.

2. Gold-Catalyzed Cyclization



***rac*-[(*1R,4aR*)-12-Tosyl-1,2-dihydro-1,4a-(epiminoethano)carbazol-4-yl]methanol (rac-7a)** (Table 1, entry 6)

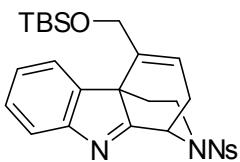
To a solution of **8a** (20.0 mg, 0.051 mmol) in EtOH (510 μ L) was added AgNTf₂ (1.97 mg, 5.1 μ mol) and SPhosAuCl (3.26 mg, 5.10 μ mol) at room temperature. After stirring at 60 °C for 5 h, the mixture was concentrated in vacuo and the residue was purified by column chromatography (silica gel, hexane/EtOAc = 2/3) to give **7a** (13.7 mg, 69%) as a yellow solid: mp 168–169 °C; IR (neat): 2955 (OH), 1676 (C=N), 1343, 1154 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ 1.10 (dt, *J* = 12.9, 5.0 Hz, 1H), 1.61–1.63 (m, 1H), 2.34 (s, 3H), 2.44 (d, *J* = 13.7 Hz, 1H), 2.74–2.78 (br s, 2H), 3.57 (dt, *J* = 13.2, 3.1 Hz, 1H), 3.76 (dd, *J* = 13.7, 4.6 Hz, 1H), 4.13 (d, *J* = 12.6 Hz, 1H), 4.28 (dd, *J* = 12.6, 5.2 Hz, 1H), 5.29 (t, *J* = 3.4 Hz, 1H), 5.95–5.99 (m, 1H), 7.19–7.25 (m, 3H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 21.4, 35.6, 35.7, 38.6, 52.0, 55.5, 65.0, 121.3, 124.2, 125.6, 126.2, 127.2 (2C), 128.5, 129.7 (2C), 135.0, 136.8, 139.4, 143.6, 155.0, 181.2; HRMS (FAB) calcd for C₂₂H₂₃N₂O₃S (MH⁺): 395.1429; found: 395.1434.



***rac*-12-[*(1R,4aR*)-(2-Nitrophenyl)sulfonyl]-1,2-dihydro-1,4*a*-(epiminoethano)carbazol-4-yl]methanol (rac-7b)** (Table 1, entry 7)

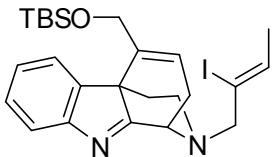
By a procedure identical with that described for the synthesis of **7a**, **8b** (50.0 mg, 0.118 mmol) was converted to **7b** (38.1 mg, 76%) by the reaction with SPhosAuCl (3.26 mg, 11.2 μ mol) and AgNTf₂ (1.97 mg, 11.2 μ mol) in EtOH (1.2 mL) at 60 °C for 5 h. The reaction using a large amount of **8b** (845 mg, 1.99 mmol) gave **7b** (543 mg, 64%) by treatment with SPhosAuCl (128 mg, 0.199 mmol) and AgNTf₂ (77.2 mg, 0.199 mmol) in EtOH (19.9 mL) at 60 °C for 5 h. Column chromatography: silica gel, hexane/EtOAc = 2/3; pale yellow crystals; mp 119 °C; IR (neat): 3091 (OH), 1540 (NO₂), 1627 (C=N), 1364, 1162 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ : 1.43–1.49 (m, 1H), 1.58–1.61 (m, 1H), 2.60 (d, *J* = 13.2 Hz, 1H), 2.84–2.93 (br m, 2H), 3.67–3.73 (m, 1H), 3.92 (dd, *J* = 13.7, 4.6 Hz, 1H), 4.15–4.18 (m, 1H), 4.30–4.34 (m, 1H), 5.19–5.20 (m, 1H), 6.02–6.04 (m, 1H), 7.26–7.29 (m, 1H), 7.38–7.41 (m, 1H), 7.58–7.62 (m, 1H), 7.64–7.69 (m, 4H), 8.09–8.13 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ : 36.1, 36.3, 39.3, 52.4, 55.6, 65.1, 121.5, 124.3 (2C), 125.9, 126.2, 128.6, 130.9, 131.9, 133.0, 133.8, 135.1, 139.3, 147.7, 155.1, 180.7; HRMS (FAB) calcd for C₂₁H₂₀N₃O₅S (MH⁺): 426.1118, found 426.1118.

3. Preparation of Compounds 6a and 26



***rac*-(1*R*,4*aR*)-4-{[(tert-Butyldimethylsilyl)oxy]methyl}-12-[(2-nitrophenyl)sulfonyl]-1,2-dihydro-1,4*a*-(epiminoethano)carbazole (*rac*-20)**

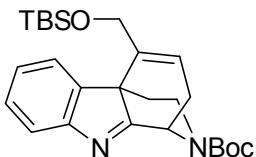
To a solution of **7b** (530 mg, 1.25 mmol) in dry CH₂Cl₂ (12.5 mL) were added imidazole (170 mg, 2.50 mmol) and TBSCl (283 mg, 1.88 mmol) at 0 °C. After stirring at 0 °C for 1 h, the mixture was quenched with saturated NH₄Cl and extracted with CH₂Cl₂ twice. The combined organic layer was washed with distilled water and brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10/1 to 4/1) to give **20** (434 mg, 64%) as a pale yellow solid: mp 126–127 °C; IR (neat): 1629 (C=N), 1541 (NO₂), 1361, 1162 (O=S=O); ¹H NMR (500 MHz, CDCl₃) δ: 0.09 (s, 3H), 0.12 (s, 3H), 0.94 (s, 9H), 1.38–1.44 (m, 1H), 2.67 (d, *J* = 13.2 Hz, 1H), 2.82–2.93 (m, 2H), 3.68–3.74 (br m, 1H), 3.89 (dd, *J* = 14.0, 4.3 Hz, 1H), 4.03 (d, *J* = 12.0 Hz, 1H), 4.29 (d, *J* = 12.0 Hz, 1H), 5.17 (d, *J* = 5.2 Hz, 1H), 5.95–5.97 (br m, 1H), 7.24–7.28 (m, 1H), 7.38 (dd, *J* = 8.3, 7.2 Hz, 1H), 7.59–7.62 (m, 1H), 7.64–7.69 (m, 4H), 8.10–8.13 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ: –5.4, –5.3, 18.2, 25.9 (3C), 36.1, 36.5, 39.3, 52.5, 55.8, 66.0, 121.5, 124.2, 124.3, 125.4, 125.7, 128.5, 131.0, 131.9, 133.2, 133.7, 134.9, 139.5, 147.8, 155.2, 180.8; HRMS (FAB) calcd for C₂₇H₃₄N₃O₅SSi (MH⁺) 540.1983, found 540.1984.



***rac*-(1*R*,4*aR*)-4-{[(tert-Butyldimethylsilyl)oxy]methyl}-12-[(*Z*)-2-iodobut-2-en-1-yl]-1,2-dihydro-1,4*a*-(epiminoethano)carbazole (*rac*-6a)**

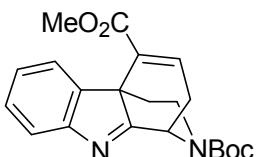
To a solution of **20** (41.6 mg, 0.0771 mmol) in dry DMF (0.77 mL) were added K₂CO₃ (32.0 mg, 0.231 mmol) and thiophenol (39 μL, 0.385 mmol) at 0 °C. After stirring at 0 °C for 1 h, the mixture was added saturated NaHCO₃ and extracted with EtOAc twice. The combined organic layer was washed with 1N NaOH, distilled water and brine, dried over Na₂SO₄ and concentrated in vacuo. The remaining thiophenol in the residue was removed by short column chromatography (silica gel, CHCl₃ to CHCl₃/MeOH = 10/1) to afford the corresponding amine as crude product. To this amine in DMF (0.77 mL) were added K₂CO₃ (69.2 mg, 0.501 mmol) and (*Z*)-1-bromo-2-iodobut-2-ene (**21**) (60.3 mg, 0.231 mmol) at room temperature. After stirring at 50 °C for 1 h, distilled water was added to the mixture, and the whole was extracted with EtOAc twice. The combined organic layer was washed with distilled water and brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10/1 to 3/1) to give **6a** (30.8 mg, 75%) as a colorless oil: IR (neat): 2976 (C=C-H), 2955 (C=C-H), 1684 (C=N), 1626 (C=C), 1598 (C=C); ¹H

NMR (500 MHz, CDCl₃) δ: 0.08 (s, 3H), 0.11 (s, 3H), 0.94 (s, 9H), 1.49-1.54 (m, 1H), 1.79 (d, *J* = 6.3 Hz, 3H), 2.49 (d, *J* = 12.6 Hz, 1H), 2.62-2.69 (m, 2H), 2.82 (d, *J* = 16.6 Hz, 1H), 3.19-3.28 (m, 2H), 3.39 (d, *J* = 14.3 Hz, 1H), 3.88 (d, *J* = 6.0 Hz, 1H), 4.02 (d, *J* = 12.6 Hz, 1H), 4.30 (d, *J* = 12.6 Hz, 1H), 5.88 (q, *J* = 6.3 Hz, 1H), 5.93-5.95 (br m, 1H), 7.22-7.25 (m, 1H), 7.37-7.40 (m, 1H), 7.66-7.69 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ: -5.4, -5.2, 18.3, 21.7, 25.9 (3C), 33.7, 36.5, 42.6, 55.3, 56.6, 65.0, 65.9, 109.0, 120.9, 124.2, 124.9, 125.8, 128.0, 132.5, 134.6, 140.7, 155.7, 185.3; HRMS (ESI) calcd for C₂₅H₃₆IN₂OSi (MH⁺) 535.1636, found 535.1637.



tert-Butyl *rac*-(1*R*,4*aR*)-4-{{[(tert-Butyldimethylsilyl)oxy]methyl}-1,2-dihydro-1,4a-(epiminoethano)carbazole-12-carboxylate (*rac*-23)}

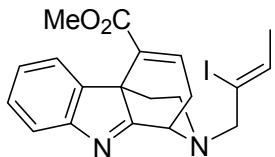
To a solution of **20** (540 mg, 1.00 mmol) in dry DMF (10 mL) were added K₂CO₃ (415 mg, 3.00 mmol) and thiophenol (255 μL, 2.50 mmol) at 0 °C. After stirring at 0 °C for 1 h, saturated NaHCO₃ was added to the mixture, and the whole was extracted with EtOAc twice. The combined organic layer was washed with 1N NaOH, distilled water and brine, dried over Na₂SO₄ and concentrated in vacuo. The remaining thiophenol in the residue was removed by short column chromatography (silica gel, CHCl₃ to CHCl₃/MeOH = 10/1) to afford the corresponding amine (343 mg) as crude product. To this amine (150 mg, 0.423 mmol) in CH₂Cl₂ (4.2 mL) were added Et₃N (295 μL, 2.12 mmol) and Boc₂O (185 mg, 0.846 mmol) at room temperature. After stirring at room temperature for 1 h, the mixture was concentrated in vacuo. The residue was purified by column chromatography (silica gel, Hexane/EtOAc = 10/1 to 3/1) to give **23** (188 mg, 98%). Recrystallization from EtOAc/hexane gave pure **23** as colorless crystals: mp 147–148 °C; IR (neat): 2976 (C=C-H), 1684 (C=O), 1625 (C=N); ¹H NMR (500 MHz, CDCl₃, 60 °C) δ: 0.09 (s, 3H), 0.12 (s, 3H), 0.94 (s, 9H), 1.29-1.35 (m, 1H), 1.48 (br s, 9H), 2.60-2.75 (m, 3H), 3.36-3.42 (br m, 1H), 3.92-4.13 (m, 2H), 4.34 (d, *J* = 12.6 Hz, 1H), 5.34-5.49 (br m, 1H), 5.93 (s, 1H), 7.22-7.25 (m, 1H), 7.36-7.39 (m, 1H), 7.64-7.67 (m, 2H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ: -5.34, -5.26, 18.3, 25.9 (3C), 28.5 (3C), 35.6, 36.8, 37.3, 50.6, 56.4, 66.0, 80.4, 121.4, 124.3, 125.3 (2C), 128.3, 135.2, 140.2, 154.5, 155.9, 183.5; HRMS (ESI) calcd for C₂₆H₃₉N₂O₃Si (MH⁺) 455.2724, found 455.2724.



12-tert-Butyl 4-Methyl *rac*-(1*R*,4*aR*)-1,2-dihydro-1,4a-(epiminoethano)carbazole-4,12-dicarboxylate (*rac*-25)

To a solution of **23** (180 mg, 0.395 mmol) in THF (4.0 mL) was added a solution of TBAF (1.0 M in THF; 0.593 mL, 0.593 mmol) at room temperature. After stirring at room temperature for 1 h,

saturated NH₄Cl was added to the mixture, and the whole was extracted with EtOAc twice. The combined organic layer was washed with distilled water and brine, dried over Na₂SO₄ and concentrated in vacuo. The resulting crude alcohol in CH₂Cl₂ (4.0 mL) was added Dess-Martin periodinane (252 mg, 0.593 mmol) at room temperature. After stirring at room temperature for 1 h, to the mixture was added saturated NaHCO₃/saturated sodium thiosulfate (1/1), and the whole was extracted with CH₂Cl₂ twice. The combined organic layer was washed with saturated sodium thiosulfate, distilled water and brine, dried over MgSO₄ and concentrated in vacuo. To the resulting crude aldehyde in *tert*-butanol (6.4 mL) and CH₂Cl₂ (1.6 mL) were added 2-methyl-2-butene (0.628 mL, 5.93 mmol), sodium dihydrogenphosphate dihydrate (493 mg, 3.16 mmol) and sodium chlorite (80%, 135 mg, 1.19 mmol) in distilled water (1.2 mL) at 0 °C. After stirring at 0 °C for 1 h, the mixture was extracted with CH₂Cl₂ twice. The combined organic layer was washed with saturated sodium thiosulfate and brine, dried over MgSO₄ and concentrated in vacuo. To the crude acid in MeOH (7.9 mL) was added a solution of trimethylsilyldiazomethane (0.6 M in hexane; 4.00 mL, 2.37 mmol) at 0 °C. After stirring at room temperature for 1 h, the mixture was concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5/1 to 2/1) to give **25** (95.0 mg, 69% in 4 steps) as a colorless oil; IR (neat): 2976 (C=C-H), 1691 (C=O), 1636 (C=N); ¹H NMR (500 MHz, CDCl₃, 60 °C) δ: 1.37 (dt, *J* = 12.9, 6.4 Hz, 1H), 1.48 (s, 9H), 2.77-2.89 (m, 3H), 3.20-3.26 (m, 1H), 3.77 (s, 3H), 4.06 (br s, 1H), 5.43 (br s, 1H), 7.04 (t, *J* = 3.7 Hz, 1H), 7.22-7.27 (m, 1H), 7.36-7.39 (m, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.90 (d, *J* = 7.4 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ: 28.4 (3C), 34.8, 37.1, 37.8, 50.3, 51.6, 55.0, 80.7, 121.2, 125.9, 126.2, 128.7, 130.3, 139.5, 140.2, 154.4, 156.1, 165.5, 181.5; HRMS (ESI) calcd for C₂₁H₂₅N₂O₄ (MH⁺) 369.1809, found 369.1809.

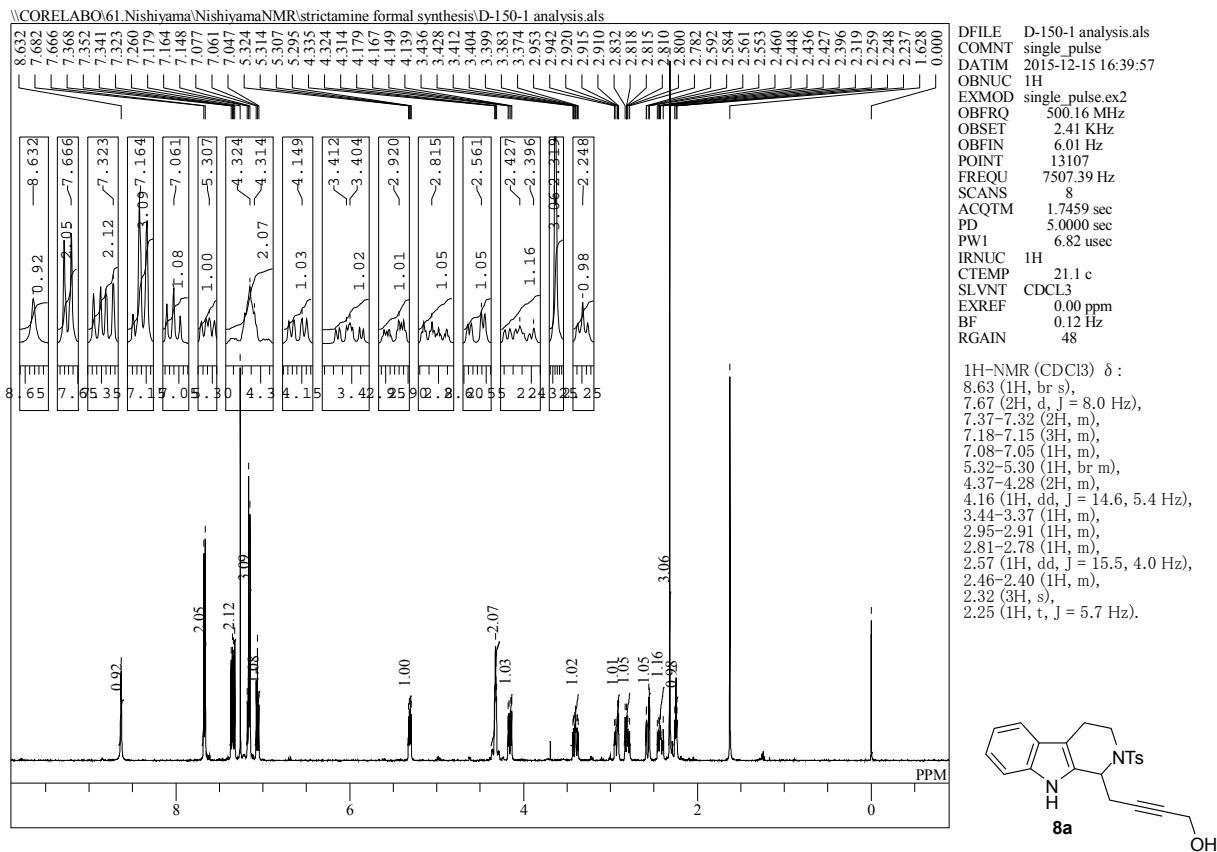


Methyl (1*R*,4*aR*)-12-[(*Z*)-2-Idobut-2-en-1-yl]-1,2-dihydro-1,4*a*-(epiminoethano)carbazole-4-carboxylate (*rac*-**26**)**

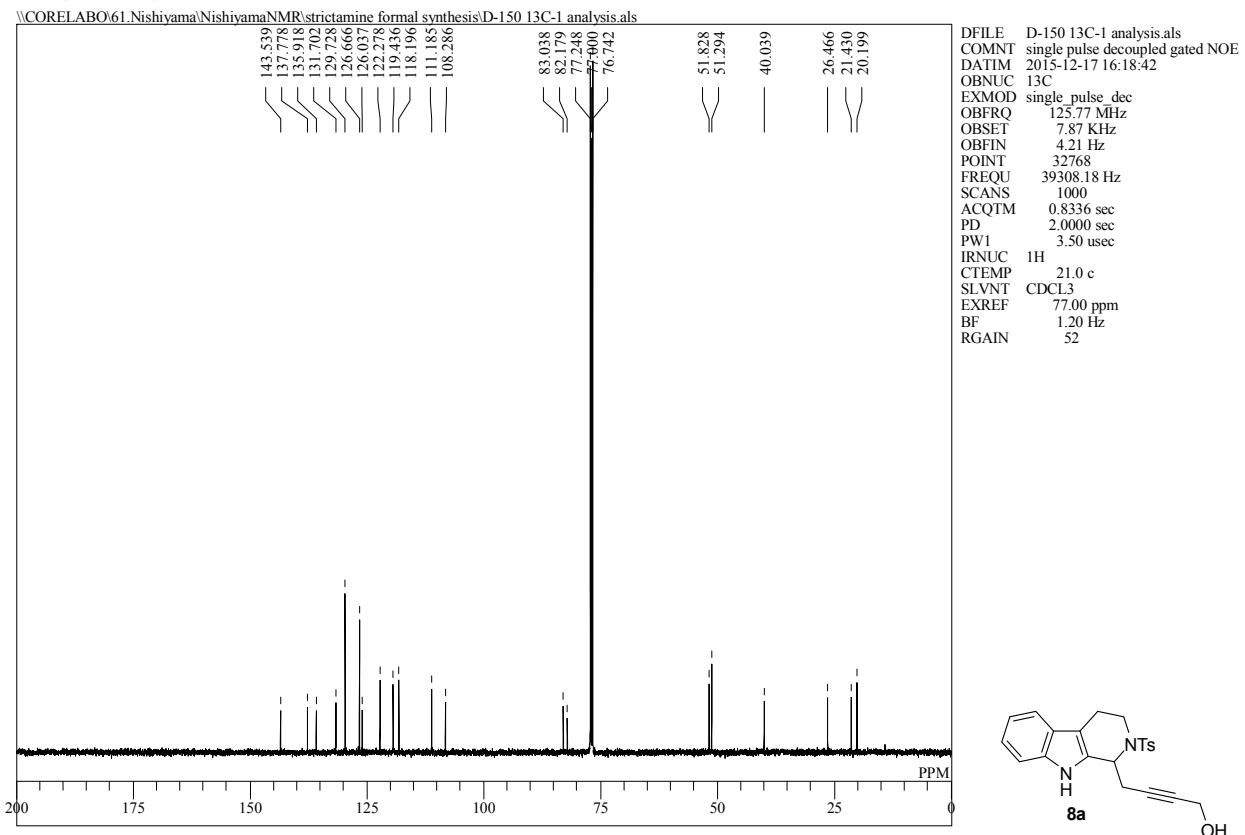
To a solution of **25** (35.0 mg, 0.0950 mmol) in CH₂Cl₂ (0.95 mL) was added HCl in 1,4-dioxane (4.0 M, 120 μL, 0.475 mmol) at room temperature. After stirring at room temperature for 1 h, the mixture was quenched with saturated NaHCO₃ and extracted with EtOAc twice. The combined organic layer was washed with distilled water and brine, dried over Na₂SO₄ and concentrated in vacuo. The resulting crude amine in DMF (0.95 mL) were added K₂CO₃ (85.4 mg, 0.618 mmol) and (*Z*)-1-bromo-2-iodobut-2-ene (**21**) (76.9 mg, 0.285 mmol) at room temperature. After stirring at room temperature for 1.5 h, the mixture was diluted with distilled water and extracted with EtOAc twice. The combined organic layer was washed with distilled water and brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5/1 to 1/1) to give **26** (20.2 mg, 47%) as a colorless oil; IR (CDCl₃): 2947 (C=C-H), 2914 (C=C-H), 1714 (C=O), 1630 (C=C), 1597 (C=C); ¹H NMR (500 MHz, CDCl₃) δ: 1.57 (dt, *J* = 12.5, 4.0 Hz, 1H), 1.79 (d, *J* = 6.3

Hz, 3H), 2.64-2.70 (m, 2H), 2.78 (ddd, J = 20.5, 6.5, 3.0 Hz, 1H), 2.90-2.95 (m, 1H), 3.03-3.09 (m, 1H), 3.23 (d, J = 13.7 Hz, 1H), 3.39 (d, J = 13.7 Hz, 1H), 3.76 (s, 3H), 3.95 (d, J = 6.3 Hz, 1H), 5.89 (q, J = 6.5 Hz, 1H), 7.06 (t, J = 3.4 Hz, 1H), 7.22-7.25 (m, 1H), 7.37-7.40 (m, 1H), 7.67 (d, J = 7.4 Hz, 1H), 7.92 (d, J = 7.4 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 21.7, 33.9, 35.8, 43.1, 51.7, 54.7, 55.2, 65.0, 108.5, 120.8, 125.5, 126.3, 128.3, 129.7, 132.9, 140.1, 141.1, 155.9, 165.8, 183.0; HRMS (FAB) calcd for $\text{C}_{20}\text{H}_{22}\text{IN}_2\text{O}_2$ (MH^+) 449.0720, found 449.0720.

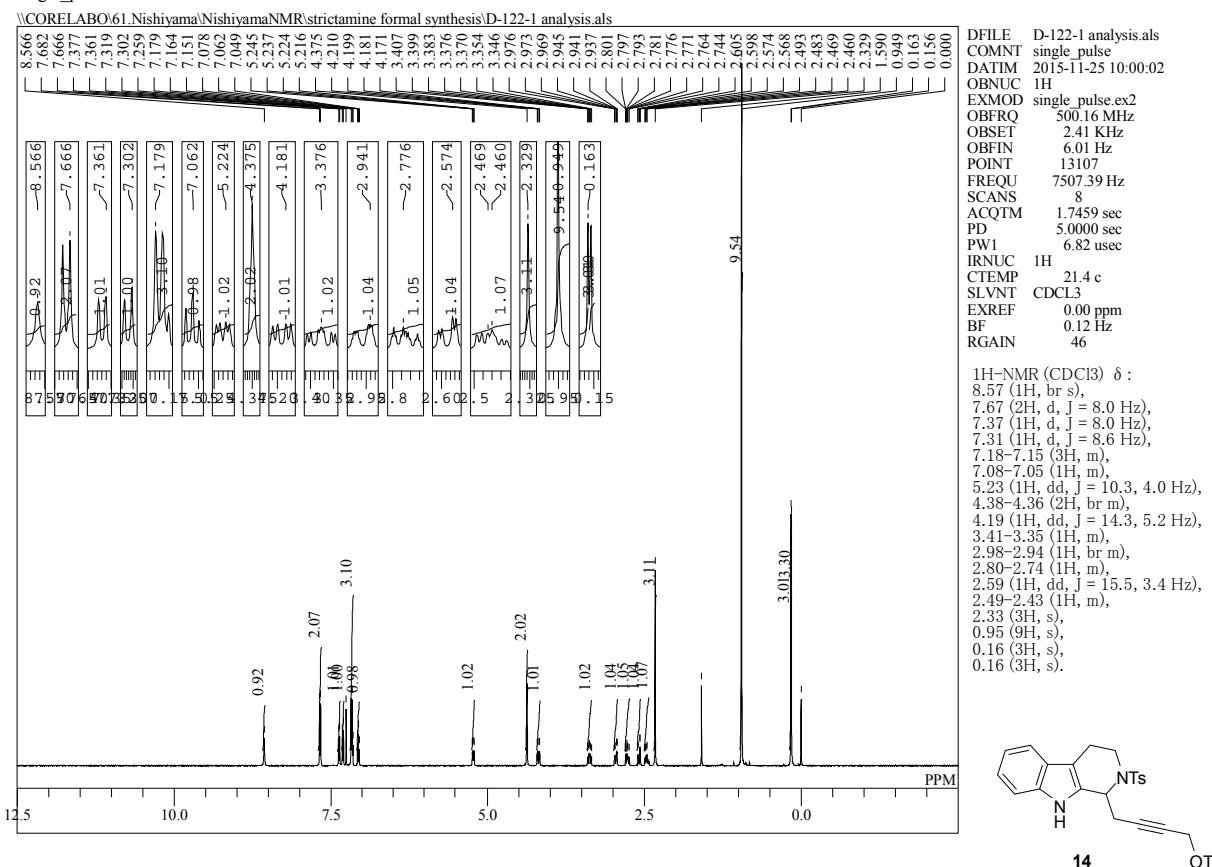
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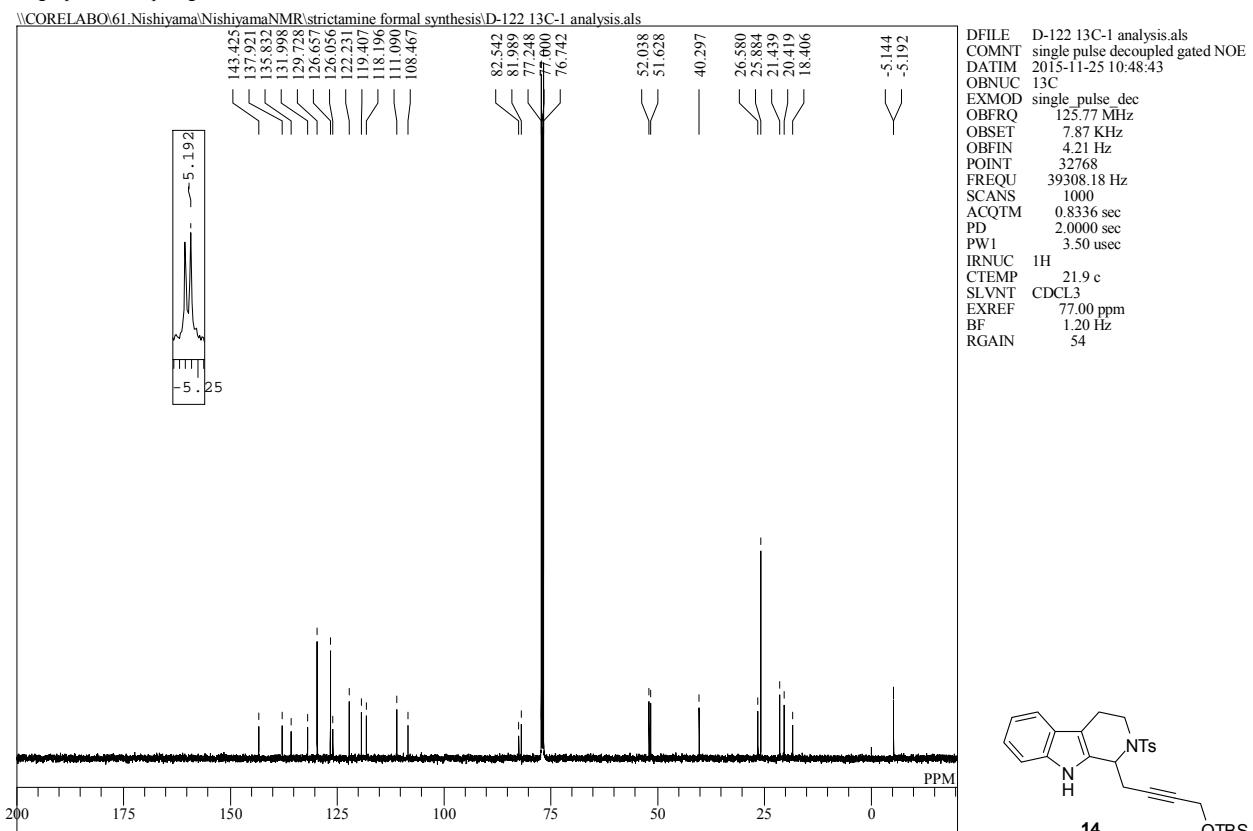
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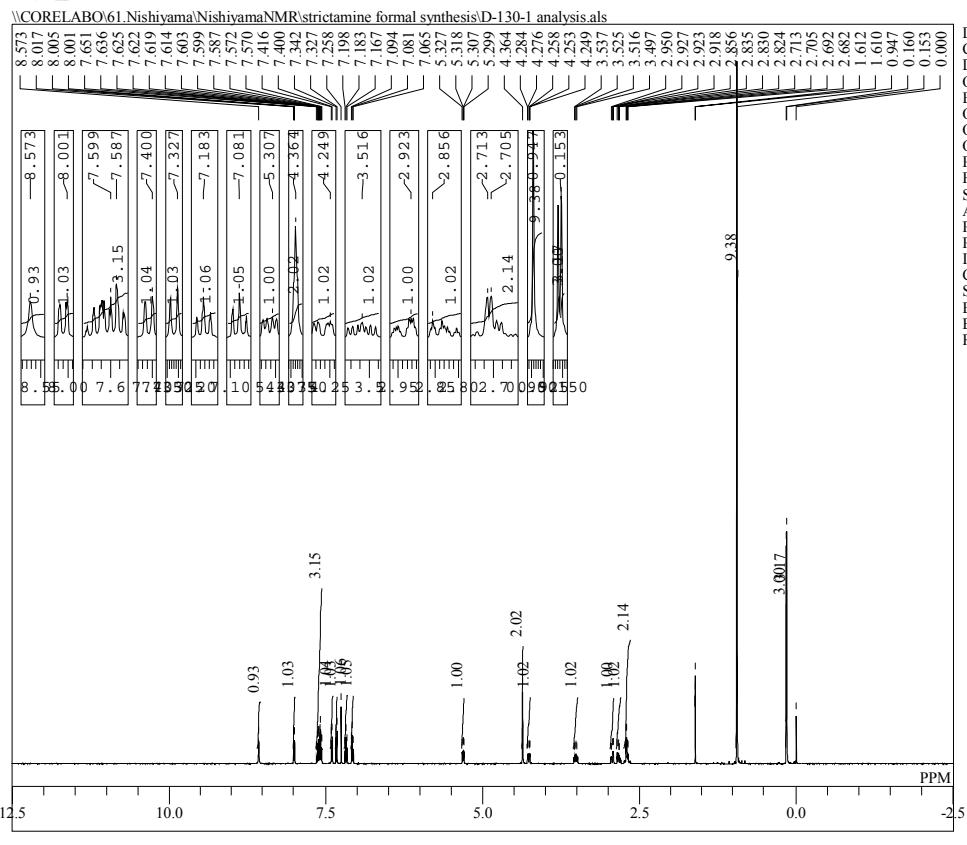
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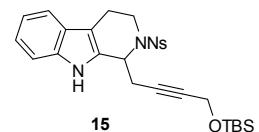
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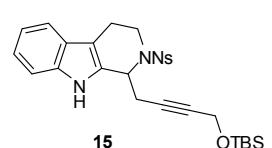
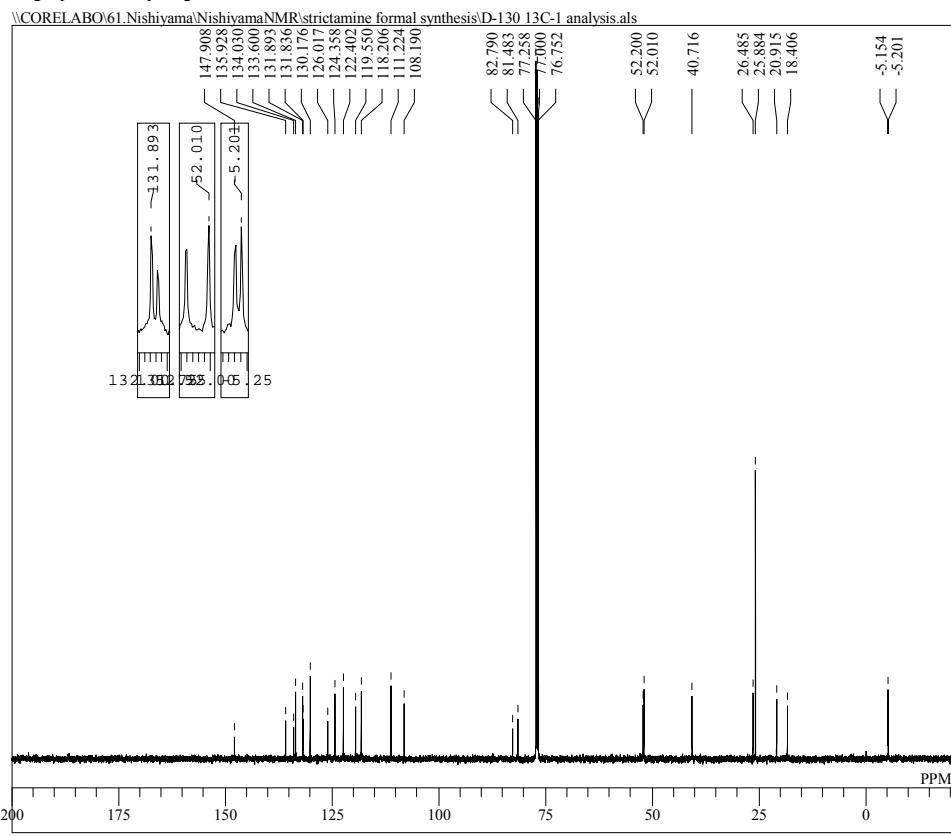
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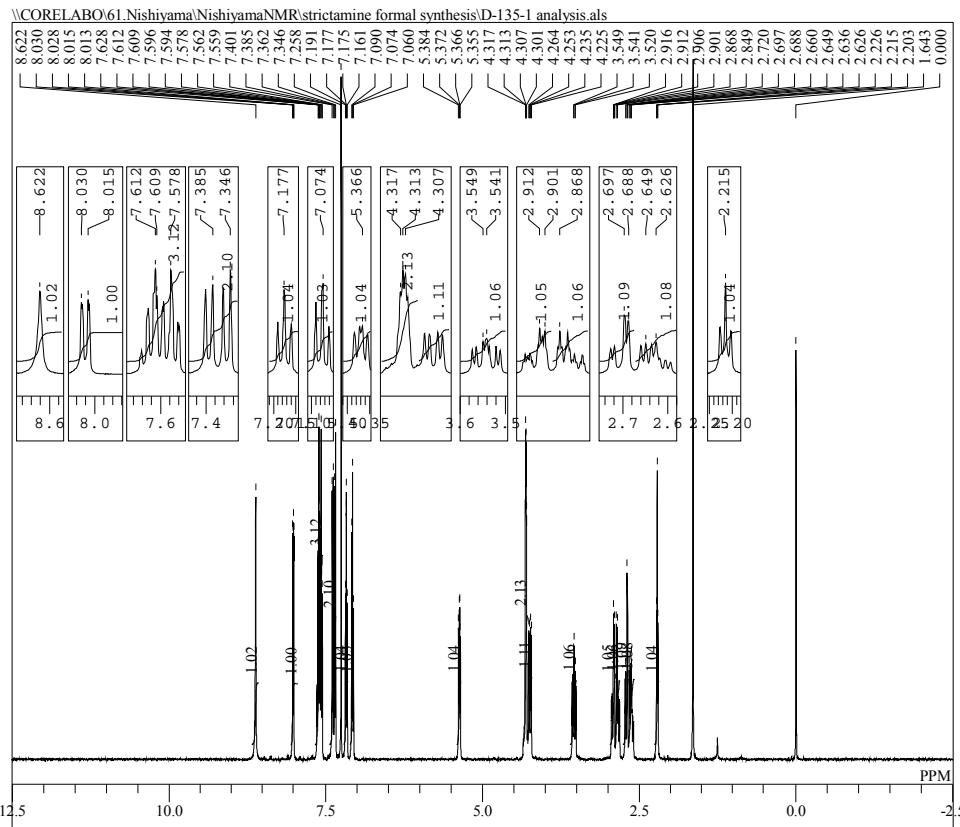
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 0.15 (3H, s).



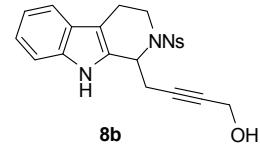
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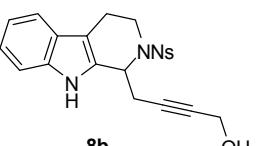
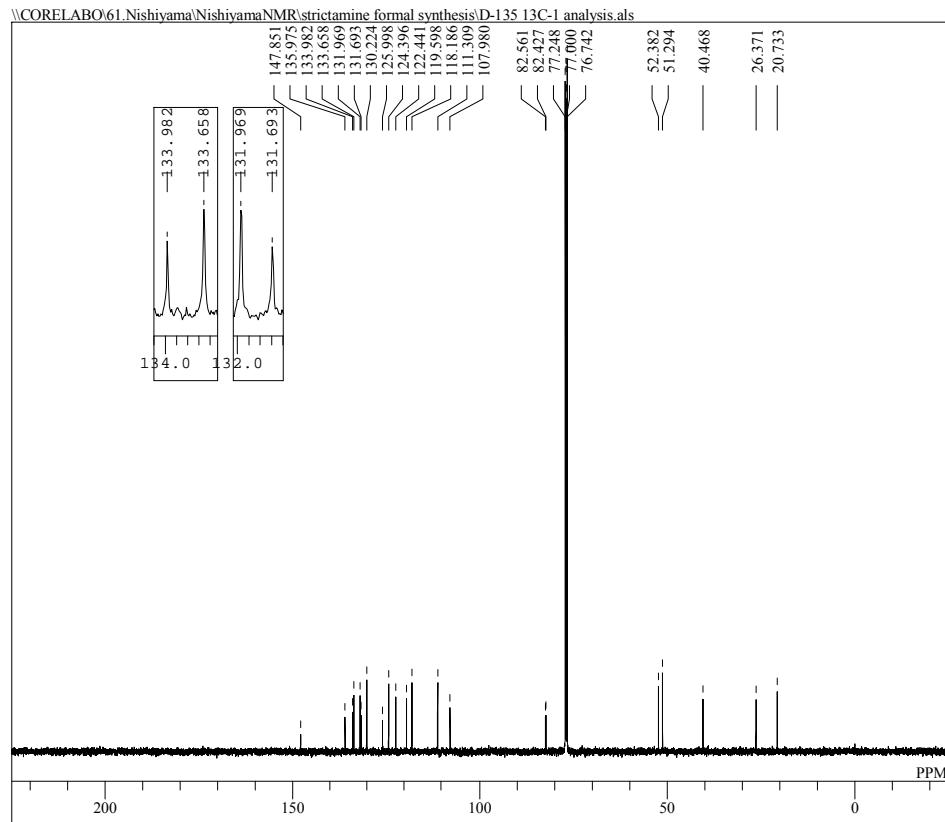
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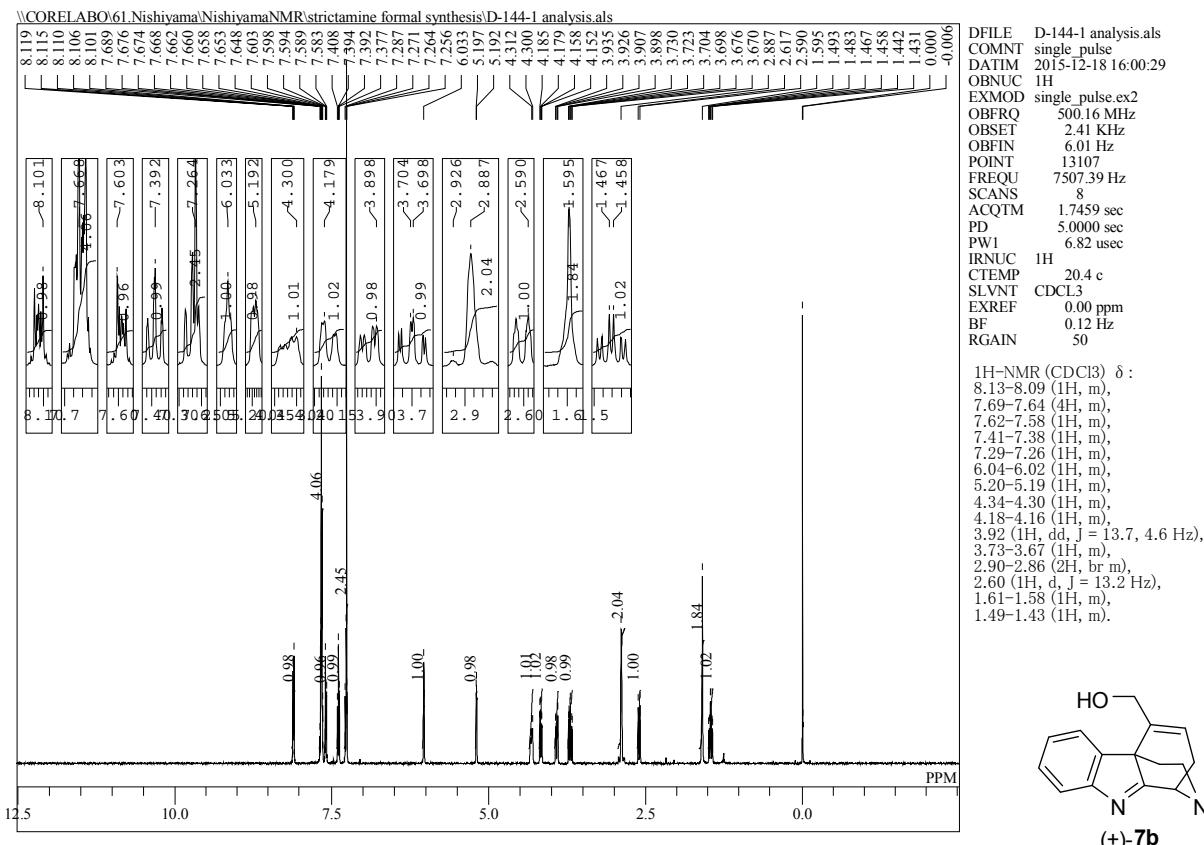
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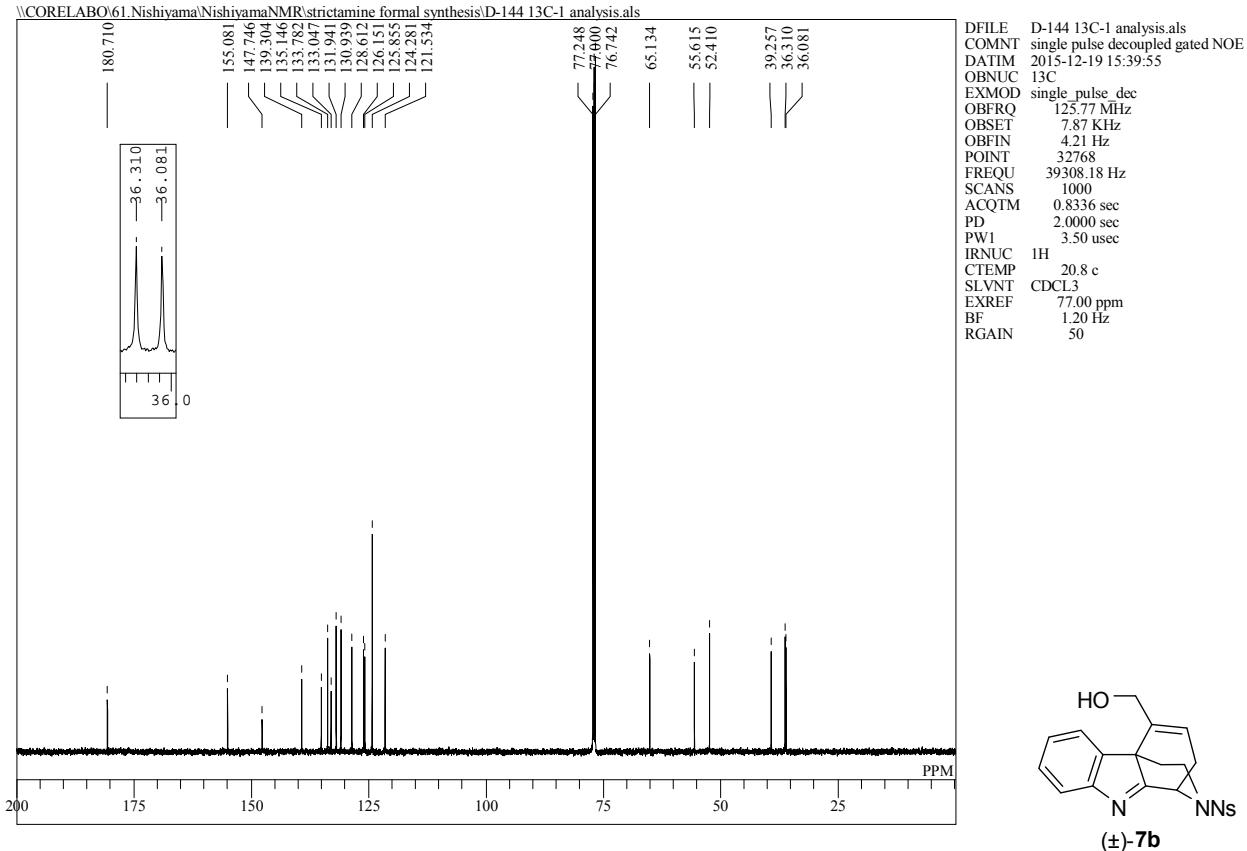
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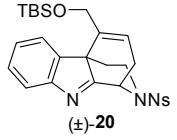
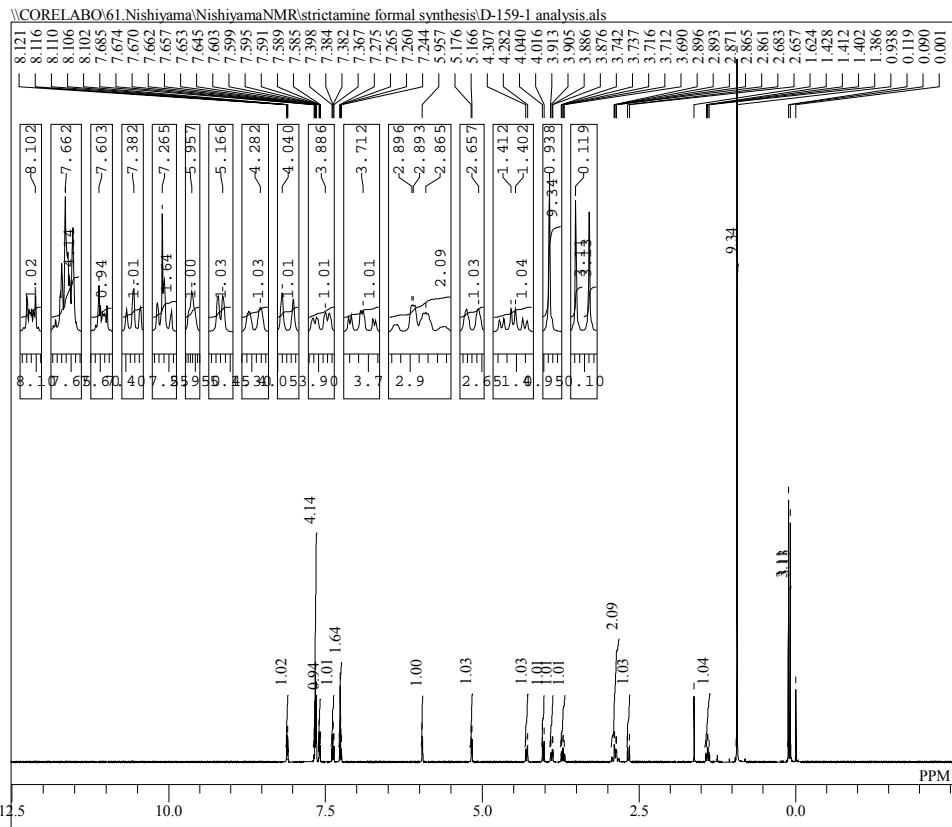
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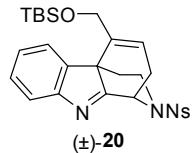
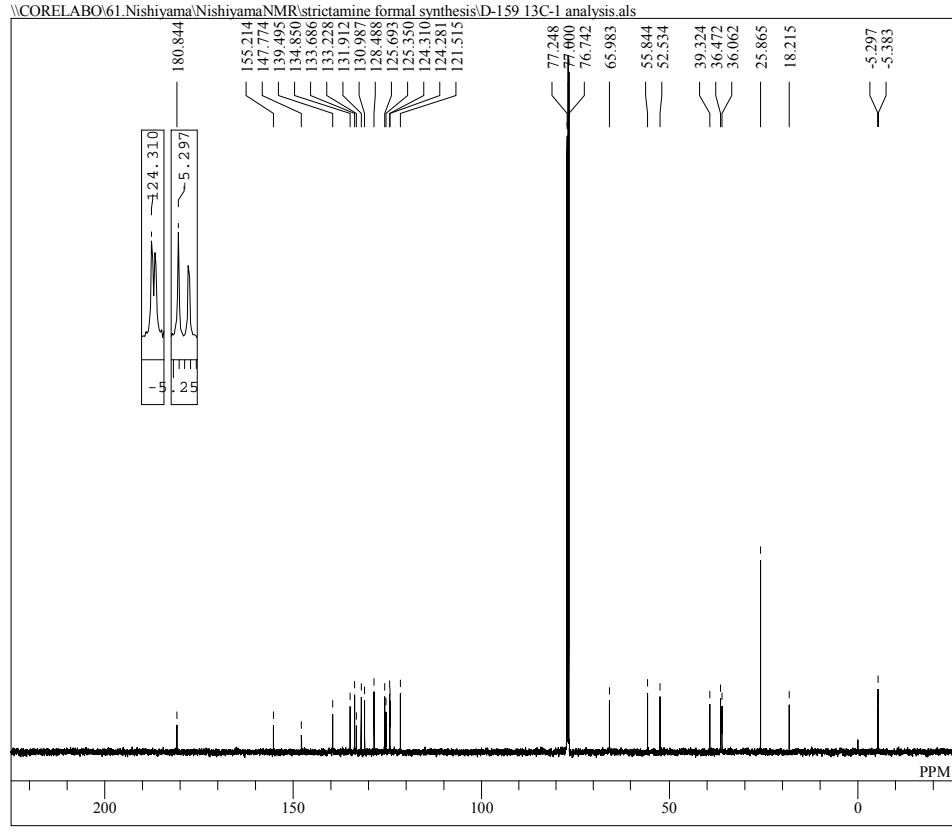
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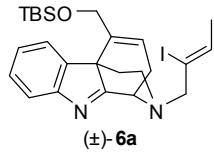
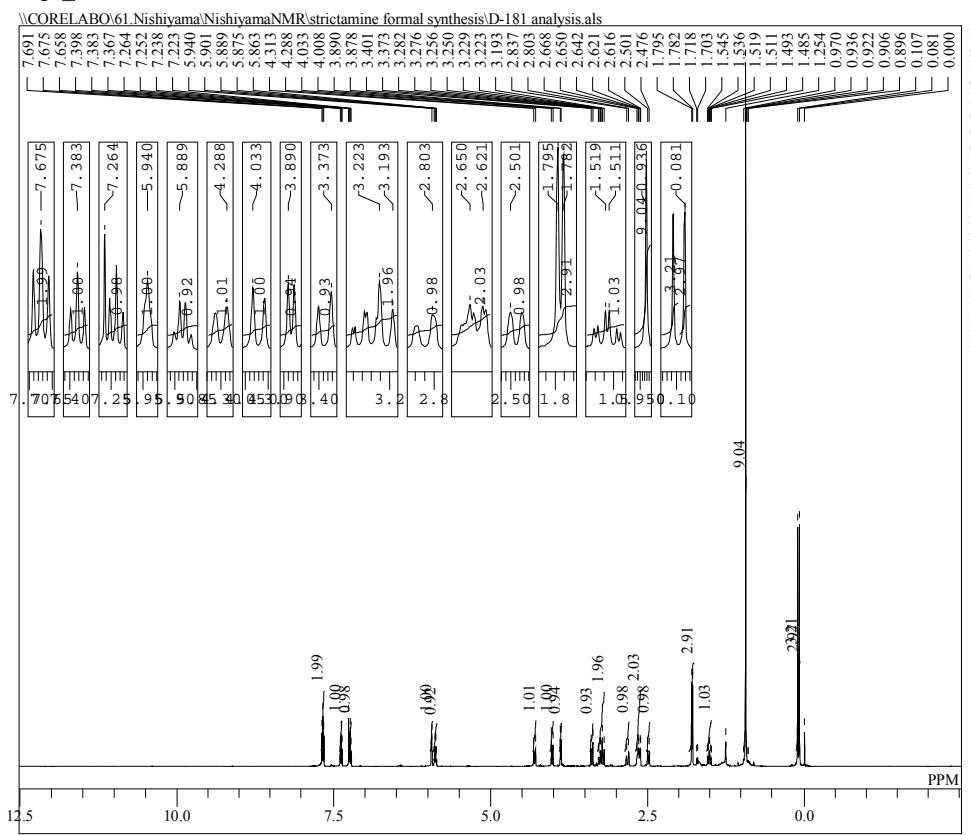
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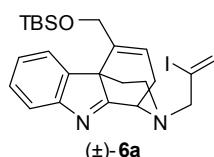
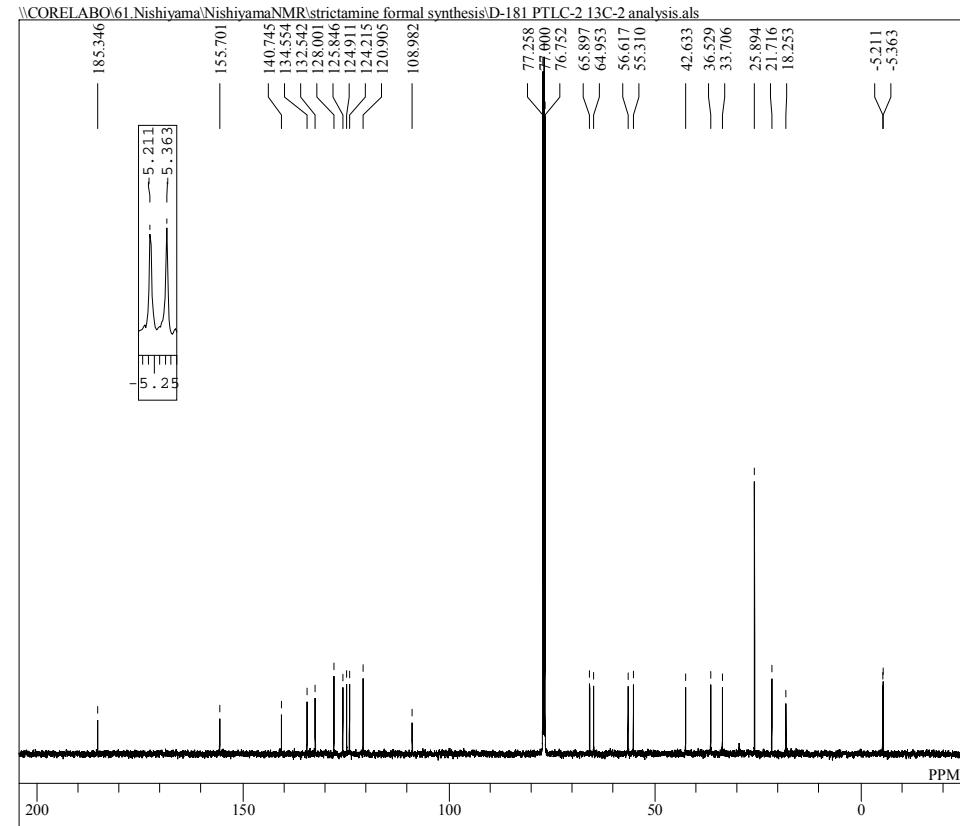
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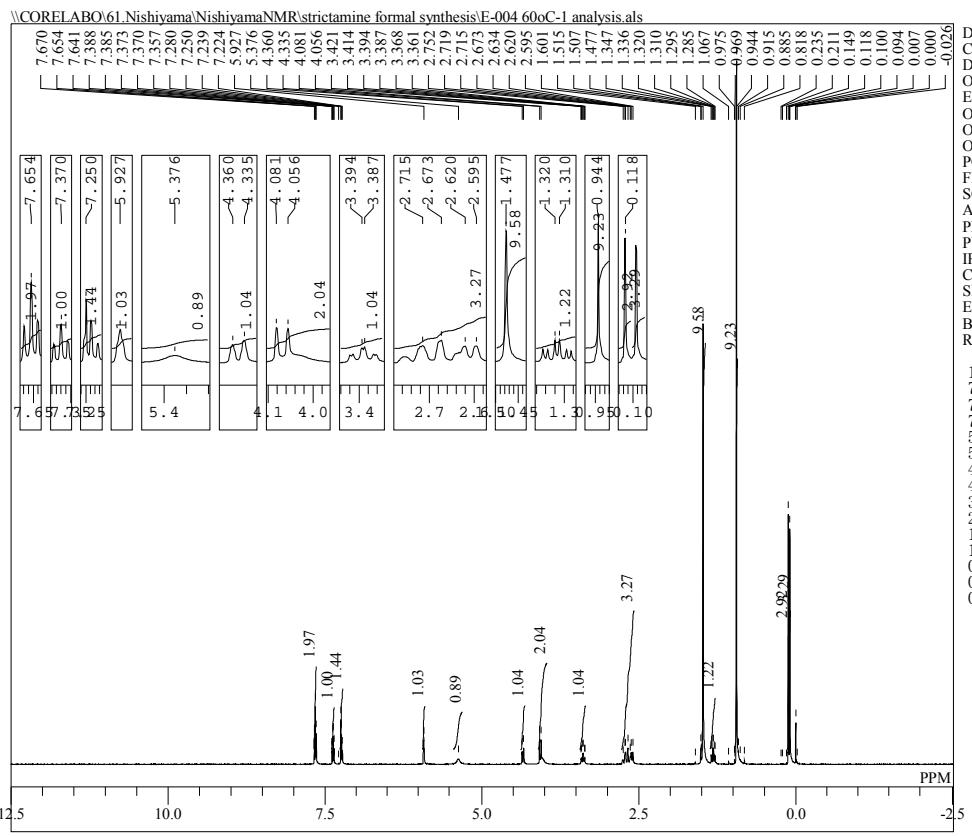
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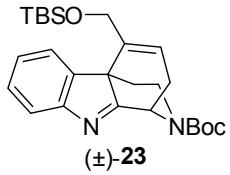
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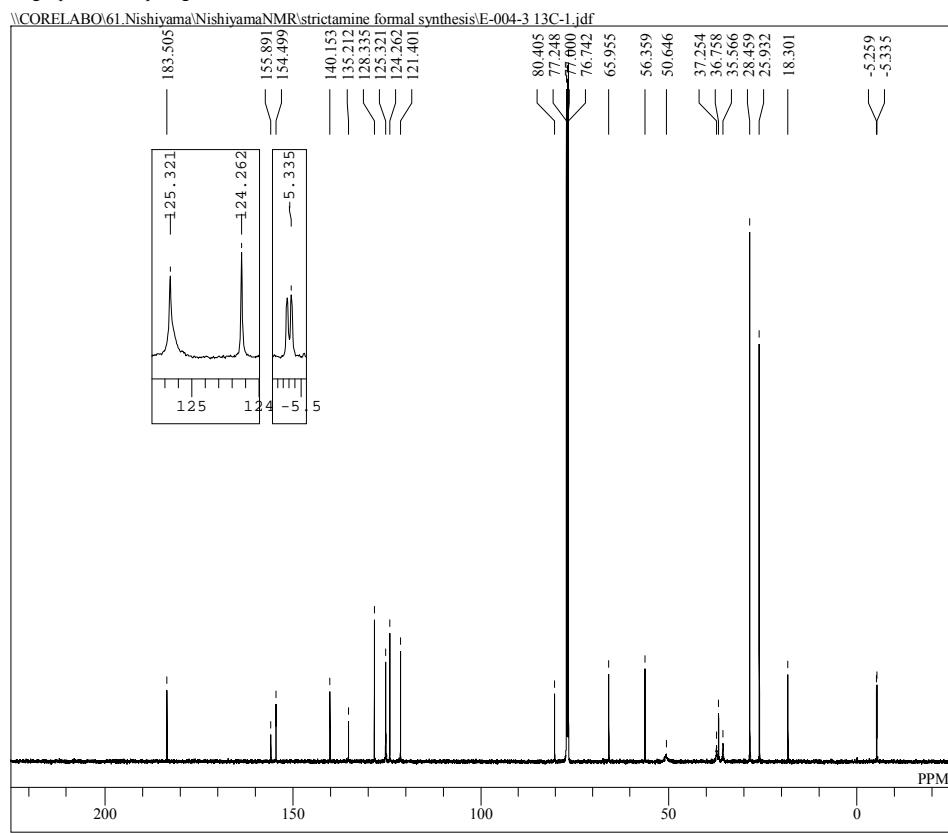
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¹H-NMR (CDCl₃) δ :

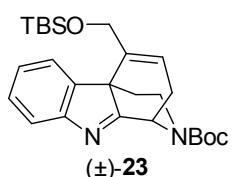
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3.42–3.36 (1H, br m),
2.75–2.60 (3H, m),
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0.12 (3H, s),
0.09 (3H, s).



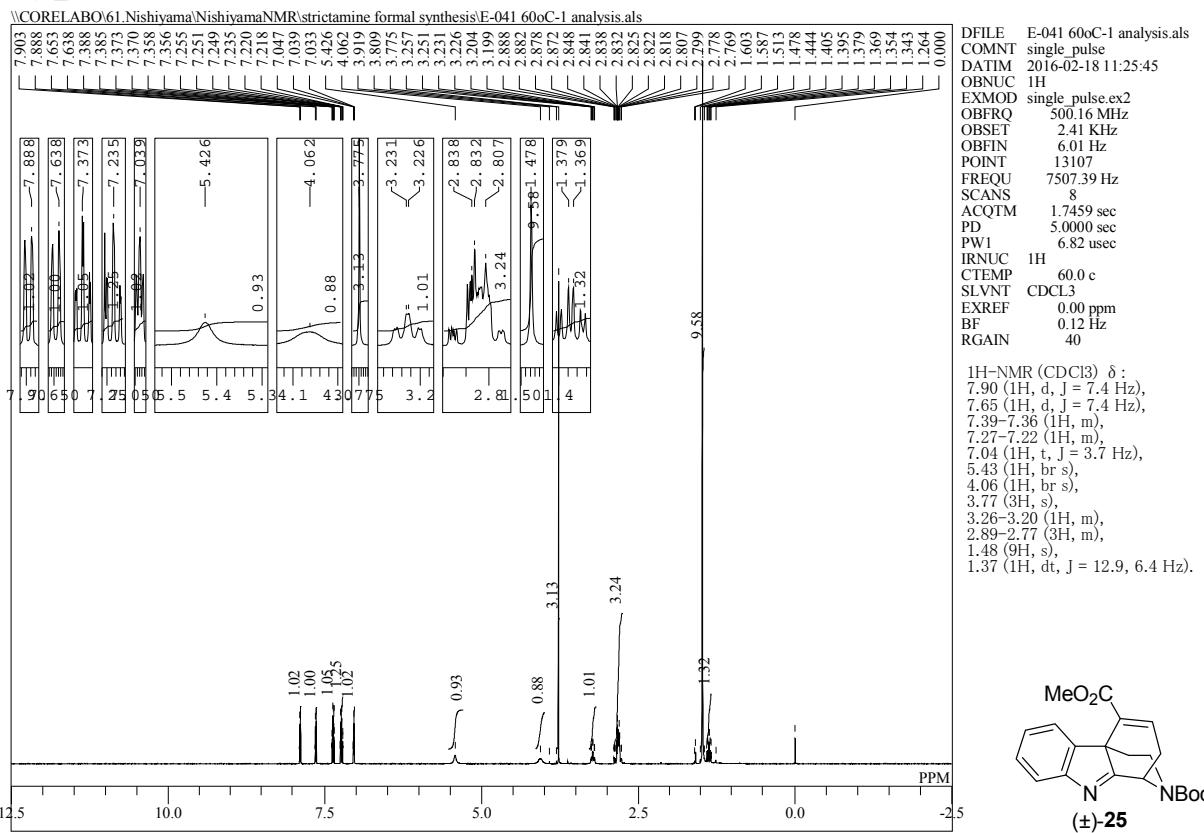
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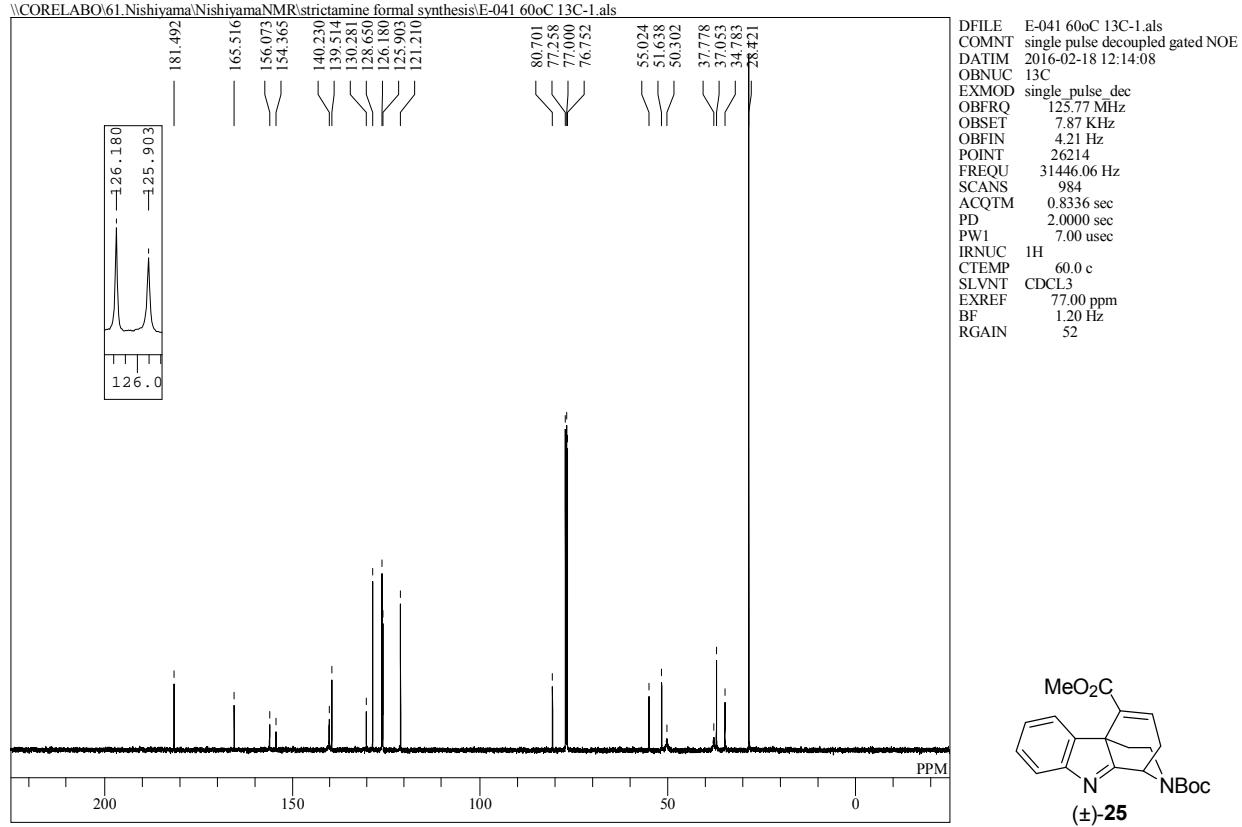
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RGAIN 54



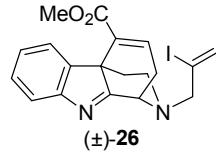
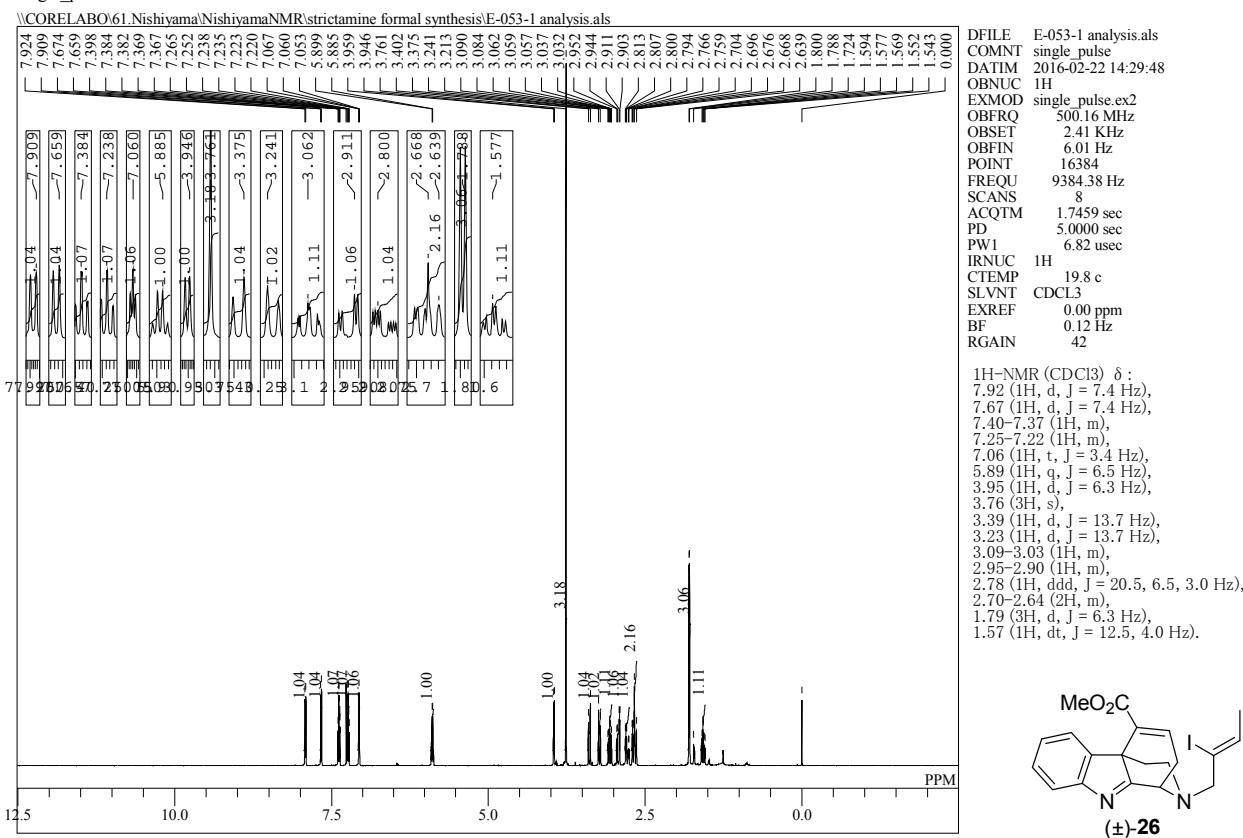
single_pulse



single pulse decoupled gated NOE



single_pulse



single pulse decoupled gated NOE

