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Supporting Information

Organocatalytic multicomponent coupling to access a highly functionalised tetracyclic furoindoline: Interrupted Passerini/Joullié–Ugi cascade reaction

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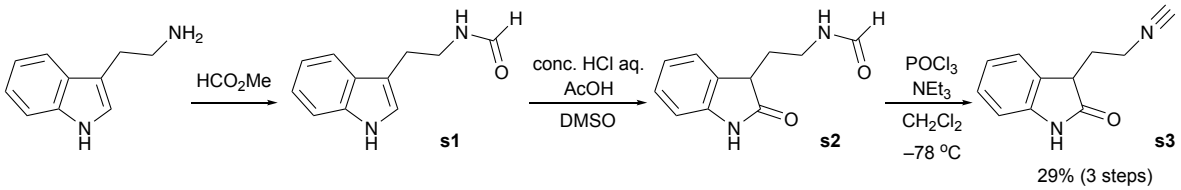
1. General Information

All reagents and solvents were purchased from either Tokyo Chemical Industry Co., Ltd., or FUJIFILM Wako Pure Chemical Corporation, Kanto Chemical Co., Ltd., Sigma-Aldrich Co. LLC and used without further purification. $CDCl_3$ was treated with K_2CO_3 prior to use. Chromatography was carried out with Wakogel® C-200 silica gel (FUJIFILM Wako Pure Chemical Corporation, granule, 0.075-0.150 mm). Melting points were measured using the micro melting point equipment (J-SCIENCE LAB Co., Ltd., RFS-10). NMR spectra were recorded at 600 and 400 MHz for ^{1}H and 150 and 100 MHz for ^{13}C on JEOL JNM-ECA600 and -ECZ400R spectrometers, respectively. Chemical shifts are reported in part per million (ppm, δ) relative to residual solvent peaks of $CDCl_3$ (7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR), CD_3OD (3.31 ppm for ^{1}H NMR, 49.0 ppm for ^{13}C NMR) and DMSO-d6 (2.50 ppm for ^{1}H NMR, 39.5 ppm for ^{13}C NMR) and coupling constant (*J* values) are given in Hertz. IR spectra were recorded on a JASCO IR FT/IR 4100 spectrometer. High-resolution mass spectra (HRMS) were measured on a JEOL Accu TOF T-100 equipped with an ESI ionization unit.

2. Preparation of Isocyanide

Compounds **11a**,[1] **11b**[2], **11e**[1], **19a**,[3,4] **20a**[5] and **20b**[6] were prepared as known method. Experimental procedures for preparing isocyanide **11c, 11d** and **11f** are described below.

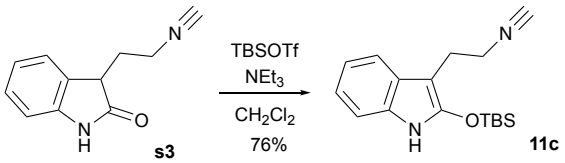
3-(2-isocyanoethyl)indolin-2-one (s3)



A suspension of tryptamine (1.6 g, 10 mmol) in HCO_2Me (10 ml) was stirred at room temperature under Ar atmosphere for 48 h. The mixture was filtrate through a pad of silica gel and wash with a 10% MeOH in CH_2Cl_2. Resulting solution was concentrated *in vacuo* to provide a crude product **s1** as a pale brown oil. To a solution of crude product **s1** in AcOH (50 mL) was added DMSO (2.0 mL) and conc. aqueous HCl (17 mL) at room temperature. After being stirred at room temperature for 1 h, the mixture was poured into a saturated aqueous Na_2CO_3 (180 mL) and extracted with AcOEt (100 mL x 3). The combined organic extracts were washed with brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to provide a crude product **s2** as a dark brown oil. To a solution of crude indolidone **s2** and NEt_3 (3.8 mL, 27 mmol) in CH_2Cl_2 (60 ml) was added $POCl_3$ (750 µL, 8.3 mmol) dropwise at –78 °C under Ar atmosphere. After being stirred at –78 °C for 3 h, the mixture was quenched by icy water (100 mL) and extracted with CH_2Cl_2 (100 mL x 3). The combined organic extracts were washed with water (100 ml) and brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 2/1 to 1.5/1) to provide corresponding isocyanide **s3** as a pale brown solid (545 mg, 29% yield (3 steps)).

mp 123-124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (m, 1H), 7.31-7.21 (2H), 7.07 (m, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 3.77 (ddd, *J* = 14.9, 7.6, 7.2 Hz, 1H), 3.67-3.57 (2H), 2.35 (m, 1H), 2.26 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.0, 157.1, 141.3, 128.6, 127.7, 124.0, 122.7, 110.1, 42.5, 38.5, 30.2. IR (neat, ATR) 3189, 2360, 2149, 1694, 1620, 1470, 1336, 1235, 750, 665 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M–H]^-$ calcd for $[C_{11}H_9N_2O]^-$ 185.0715, found 185.0175.

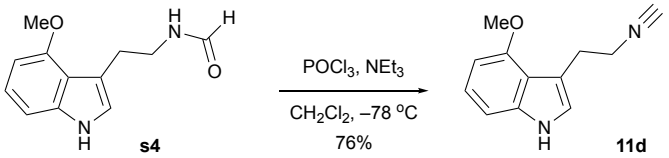
3-(2-isocyanoethyl)-2-*t*-butyldimethylsilyloxyindole (11c)



To a solution of isocyanide **s3** (489 mg, 2.6 mmol) and NEt_3 (1.1 mL, 7.8 mmol) in CH_2Cl_2 (13 ml) was added TBSOTf (0.9 mL, 3.9 mmol) dropwise at 0 °C under Ar atmosphere. After being stirred at 0 °C for 1 h, the mixture was quenched by saturated aqueous $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (20 mL x 3). The combined organic extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 8/1 to 2.5/1) to provide corresponding isocyanide **11c** as a colorless solid (592 mg, 76% yield).

mp 166-168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (brs, 1H), 7.25 (m, 1H), 7.02 (m, 1H), 6.97-6.88 (2H), 4.47 (ddd, *J* = 16.6, 8.6, 4.7 Hz, 1H), 4.34 (ddd, *J* = 16.6, 8.2, 7.1 Hz, 1H), 2.47 (ddd, *J* = 12.8, 8.6, 7.1 Hz, 1H), 2.13 (ddd, *J* = 12.8, 8.2, 4.7 Hz, 1H), 0.86 (s, 9H), –0.13 (s, 3H), –0.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 179.9, 140.8, 131.4, 128.8, 123.6, 122.8, 110.1, 71.4, 65.5, 36.1, 26.4, 16.9 (3C), –5.3 (d, *J* = 2.8 Hz), –5.9 (d, *J* = 2.8 Hz). IR (neat, ATR) 3193, 2934, 2858, 2360, 1710, 1619, 1470, 1330, 1252, 1210, 937, 811, 751, 681, 515 cm^{-1}. HRMS (ESI-TOF) *m*/*z* $[M+H]^+$ calcd for $[C_{17}H_{25}N_2OSi]^+$ 301.1736, found 301.1727.

3-(2-isocyanoethyl)-4-methoxyindole (11d)

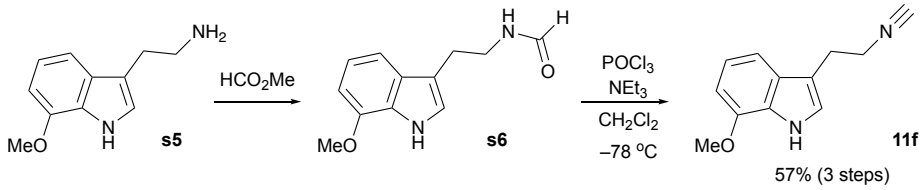


To a solution of *N*-formyl-4-methoxytryptamine **s4**[7] (874.7 mg, 4.0 mmol) and NEt_3 (2.8 mL, 20.0 mmol) in CH_2Cl_2 (8.0 mL) was added $POCl_3$ (550 µL, 6.0 mmol) dropwise at –78 °C under Ar atmosphere. After being stirred at –78 °C for 3 h, the mixture was quenched by icy water (50 mL) and extracted with CH_2Cl_2 (30 mL x 3). The combined organic extracts were washed with H_2O (100 mL) and brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 4/1) to provide 3-(2-isocyanoethyl)-4-methoxyindole **11d** as a pale brown solid (607 mg, 76% yield).

mp 71-73 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 7.03-6.92 (3H), 6.46 (m, 1H), 3.89 (m, 3H), 3.71 (m, 2H), 3.17 (m, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 155.5, 154.3, 140.0, 123.4, 123.2, 117.9, 111.5, 105.9, 99.9, 55.5, 44.6, 28.8. IR (neat, ATR) 3404, 2937, 2837, 2531, 2360, 2150, 1583, 1503, 1437, 1355, 1254, 1086, 973, 935, 779, 736, 679 cm^{-1}. HRMS

(ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{12}H_{12}N_2NaO]^+$ 223.0847, found 223.0848.

Preparation of 3-(2-isocyanoethyl)-7-methoxyindole 11f



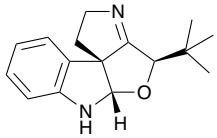
A suspension of 7-methoxytryptamine **s5**[8] (510 mg, 2.68 mmol) in HCO_2Me (2 mL) was stirred at room temperature under Ar atmosphere. After being stirred for 26 h, the mixture was filtrate through a pad of silica gel and wash with a 10% MeOH in CH_2Cl_2. Resulting solution was concentrated *in vacuo* to provide a crude **s6** as a pale brown solid. To a solution of crude product **s6** and NEt_3 (3.0 mL, 22 mmol) in CH_2Cl_2 (24 mL) was added $POCl_3$ (320 µL, 3.5 mmol) dropwise at –78 °C under Ar atmosphere. After being stirred at –78 °C for 6 h, the mixture was quenched by icy water (50 mL) and extracted with CH_2Cl_2 (30 mL x 3). The combined organic extracts were washed with H_2O (100 mL) and brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 4/1) to provide 3-(2-isocyanoethyl)-7-methoxyindole **11f** as a colorless powder (303 mg, 57% yield (2 steps)).

mp 119-120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (brs, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 2.4 Hz, 1H), 7.07 (dd, *J* = 8.0, 7.2 Hz, 1H), 6.68 (d, *J* = 7.2 Hz, 1H), 3.97 (s, 3H), 3.66 (m, 2H), 3.16 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 128.0, 126.8, 122.1, 120.2, 111.4, 110.8, 102.1, 55.3, 42.3 (t, *J* = 6.2 Hz, 1H), 26.0. IR (neat, ATR) 3295, 2935, 2360, 2159, 1626, 1577, 1499, 1448, 1374, 1348, 1260, 1097, 1056, 935, 783, 732, 685, 614, 554 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M–H]^-$ calcd for $[C_{12}H_{11}N_2O]^-$ 199.0871, found 199.0872.

3. General Procedure for Interrupted Passerini Reaction of 3-(2-isocyanoethyl)indole

To a solution of isocyanide (0.2 mmol) and aldehyde (0.3 mmol) in toluene (300 μL) was added 3,5,6-trifluoro-2-pyridone (**8**, 3.0 mg, 0.04 mmol) at room temperature under Ar atmosphere. After complete consumption of isocyanide, 300 μL of eluent (0.5% NEt_3 in Hexane/AcOEt = 3/1) was added to the reaction mixture. The mixture was put on a silica gel and purified by column chromatography (0.5% NEt_3 in Hexane/AcOEt = 3/1) to provide corresponding tetracyclic furoindoline **21-23**.

4-(*tert*-butyl)-2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indole (21a)



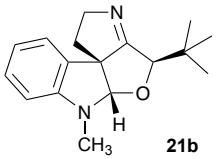
21a

Colorless powder (43.5 mg, 85% yield). mp 112-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (m, 1H), 7.08 (m, 1H), 6.78 (m, 1H), 6.71 (m, 1H), 5.24 (m, 1H), 4.90 (brs, 1H), 4.58-4.42 (2H), 3.87 (m, 1H), 2.33-2.16 (2H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 148.2, 130.1, 128.9, 123.0, 119.7, 109.7, 93.2, 80.9, 70.5, 67.6, 36.5, 34.0, 25.5 (3C). IR (neat, ATR) 3334, 2952, 2869, 1672, 1605, 1472, 1358, 1259, 1213, 1174, 1063, 1023, 975, 941, 882, 741 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{16}H_{20}N_2ONa]^+$ 279.1475, found 279.1474.

Large Scale synthesis of 21a

The reaction of isocyanide **19** (513 mg, 3.0 mmol), pivalaldehyde (510 μL, 4.5 mmol) in the presence of catalyst **8** (90 mg, 0.6 mmol) in toluene (4.5 mL) provided corresponding tetracyclic furoindoline **21a** (642 mg, 83% yield).

4-(*tert*-butyl)-6-methyl-2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indole (21b)



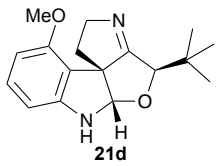
21b

After reaction for 6 h, the reaction mixture was purified by silica gel column chromatography (0.5% NEt_3 in Hexane/AcOEt = 4/1).

Colorless solid (16.0 mg, 30% yield). mp 108-110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (m, 1H), 7.04 (m, 1H), 6.70 (m, 1H), 6.49 (d, *J* = 7.6 Hz, 1H), 5.12 (s, 1H), 4.57-4.39 (2H), 3.75 (m, 1H), 3.01 (s, 3H), 2.32-2.17 (2H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.1, 150.0, 130.7, 128.9, 122.6, 118.0, 106.3, 97.6, 80.1, 69.1, 67.4, 36.7, 33.8, 30.6, 25.4 (3C). IR (neat, ATR) 2951, 2870, 1674, 1603, 1488, 1388, 1361, 1305, 1273, 1238, 1174, 1120, 1003, 973, 938,

881, 743 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $[C_{17}H_{23}N_2O]^+$ 271.1810, found 271.1814.

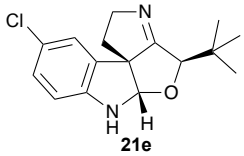
4-(*tert*-butyl)-10-methoxy-2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indole (21d)



21d

Pale yellow solid (42.9 mg, 75%). mp 139-140 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.10 (dd, *J* = 8.4, 7.8 Hz, 1H), 6.39-6.34 (2H), 5.13 (s, 1H), 4.88 (brs, 1H), 4.70 (m, 1H), 4.39 (m, 1H), 3.89 (m, 1H), 3.78 (s, 3H), 2.18-2.09 (2H), 1.03 (s, 9H).^{13}C NMR (150 MHz, $CDCl_3$) δ 180.9, 156.5, 150.5, 130.1, 116.3, 103.3, 102.2, 94.3, 80.7, 69.3, 67.9, 55.2, 34.4, 34.0, 25.5 (3C). IR (neat, ATR) 3331, 2950, 1674, 1602, 1464, 1278, 1251, 1099, 975, 941, 885, 773, 728 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{17}H_{22}N_2O_2Na]^+$ 309.1579, found 309.1573.

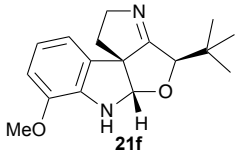
4-(*tert*-butyl)-9-chloro-2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indole (21e)



21e

Pale yellow solid (47.6 mg, 82% yield). mp 125-126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (dd, *J* = 8.4, 2.0 Hz 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 5.24 (s, 1H), 4.90 (brs, 1H), 4.57-4.42 (2H), 3.87 (m, 1H), 2.33-2.16 (2H), 1.02 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 184.3, 146.9, 131.7, 128.8, 124.1, 123.2, 110.4, 93.4, 80.9, 70.4, 67.6, 36.3, 34.0, 25.4 (3C). IR (neat, ATR) 3330, 2955, 2870, 1675, 1606, 1479, 1257, 1173, 1073, 978, 945, 886, 813, 733 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $[C_{16}H_{20}ClN_2O]^+$ 291.1264, found 291.1268.

4-(*tert*-butyl)-7-methoxy-2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indole (21f)



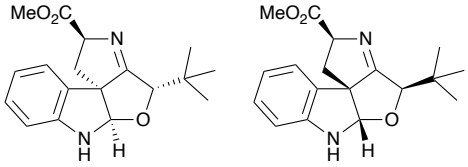
21f

The reaction was performed in 400 µL of toluene.

Colorless oil (48.7 mg, 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.81-6.68 (3H), 5.26 (s, 1H), 4.95 (brs, 1H), 4.51 (m, 1H), 4.45 (dd, *J* = 15.3, 8.4 Hz, 1H), 3.87 (m, 1H), 3.83 (s, 3H), 2.26 (ddd, *J* = 12.6, 10.1, 8.4 Hz, 1H), 2.19 (dd, *J* = 12.6, 5.4 Hz, 1H), 1.02 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 185.3, 145.0, 137.6, 130.8, 120.3, 115.2, 110.4, 93.5, 80.9, 71.4, 67.6, 55.3, 36.2, 34.1, 25.4 (3C). IR (neat, ATR) 3321, 2952, 1672, 1616, 1592, 1490, 1463, 1283, 1255,

1217, 1181, 1051, 977, 947, 907, 732 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{17}H_{22}N_2O_2Na]^+$ 309.1579, found 309.1577.

Methyl 4-(*tert*-butyl)-2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indole-2-carboxylate (22)



22a **22b**

The reaction was performed in 500 µL of toluene. After reaction for 48 h, the reaction mixture was purified by silica gel column chromatography (0.5% NEt_3 in Hexane/AcOEt = 2.5/1 to 1/1).

Characteristic data of major diastereomer 22a

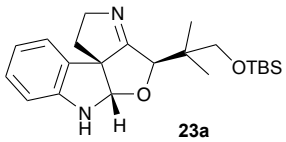
Major diastereomer **22a** could not isolated due to the instability. Therefore, the yield was calculated by ^{1}H NMR spectroscopy using nitrobenzene as the internal standard (41% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.11 (2H), 6.81 (m, 1H), 6.72 (m, 1H), 5.39 (ddd, *J* = 10.4, 1.8, 1.8 Hz, 1H), 5.17 (s, 1H), 4.89 (brs, 1H), 3.91 (m, 1H), 3.86 (s, 3H), 2.64 (dd, *J* = 14.0, 10.4 Hz, 1H), 2.37 (dd, *J* = 14.0, 1.8 Hz, 1H), 1.03 (s, 9H). HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{18}H_{22}N_2NaO_3]^+$ 337.1528, found 337.1530.

Characteristic data of minor diastereomer 22b

Pale yellow amorphous solid (16.3 mg, 26% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16 (ddd, *J* = 7.8, 7.3, 1.1 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.80 (ddd, *J* = 7.8, 7.8, 1.1 Hz, 1H), 6.72 (d, *J* = 7.3 Hz, 1H), 5.42 (ddd, *J* = 8.7, 6.9, 3.3 Hz, 1H), 5.30 (s, 1H), 4.92 (brs, 1H), 3.91 (d, *J* = 3.3 Hz, 1H), 3.83 (s, 3H), 2.50-2.41 (2H), 1.04 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.8, 172.3, 148.3, 129.4, 129.0, 122.9, 119.9, 110.0, 92.8, 81.0, 80.4, 71.3, 52.4, 39.7, 34.3, 25.4 (3C). IR (neat, ATR) 3385, 2954, 2361, 2335, 1740, 1675, 1607, 1475, 1363, 1270, 1210, 1177, 1070, 1029, 973, 910, 744 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{18}H_{22}N_2NaO_3]^+$ 337.1528, found 337.1541.

4-((*tert*-butyldimethylsilyl)oxy)-2-methylpropan-2-yl)-2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indole (23a)



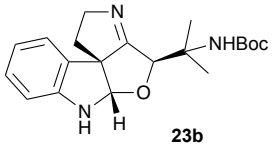
23a

Product **23a** could not be isolated due to the instability. Therefore, the yield was calculated by ^{1}H NMR spectroscopy using nitrobenzene as the internal standard (69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (ddd, *J* =7.6, 7.2, 1.1 Hz, 1H), 7.06 (d, *J* =7.2 Hz, 1H), 6.76 (m, 1H), 6.68 (d, *J* =7.6

Hz, 1H), 5.23 (s, 1H), 4.83 (brs, 1H), 4.57-4.40 (2H), 4.08 (m, 1H), 3.52 (d, *J* = 9.4 Hz, 1H), 3.45 (d, *J* = 9.4 Hz, 1H), 2.33-2.18 (2H), 1.03 (s, 3H), 0.93 (s, 3H), 0.80 (s, 9H), -0.02 (s, 3H), -0.03 (s, 3H). HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $[C_{22}H_{35}N_2O_2Si]^+$ 387.2468, found 387.2461.

tert-butyl (2-(2,4,5a,6-tetrahydro-1*H*-pyrrolo[3',2':3,4]furo[2,3-*b*]indol-4-yl)propan-2-yl)carbamate (23b)

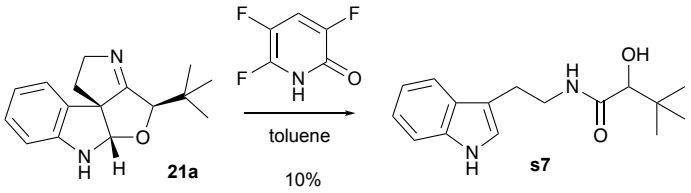


23b

After reaction for 3.5 h, the reaction mixture was purified by silica gel column chromatography (0.5% NEt_3 in Hexane/AcOEt = 2/1). Product **23b** could not be isolated due to the instability. Therefore, the yield was calculated by ^1H NMR spectroscopy using nitrobenzene as the internal standard (36% yield).

^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (ddd, *J* = 7.9, 7.8, 1.5 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 6.79 (ddd, *J* = 7.8, 7.2, 1.0 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 5.27 (s, 1H), 5.17 (brs, 1H), 4.90 (brs, 1H), 4.61-4.41 (2H), 4.30 (m, 1H), 2.36-2.18 (2H), 1.42 (s, 3H), 1.40 (s, 9H), 1.38 (s, 3H). HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{20}H_{27}N_3NaO_3]^+$ 380.1950, found 380.1945.

4. Study of Stability of Tetracyclic Furoindoline 21a



To a solution of tetracyclic furoindoline **21a** (13.8 mg, 0.054 mmol) in toluene (500 µL) was added 3,5,6-trifluoro-2-pyridone (5.0 mg, 0.03 mmol) at room temperature under Ar atmosphere. After stirred for 40 h, the mixture was put on a silica gel and purified by column chromatography (Hexane/AcOEt = 2/1) to provide the α-hydroxyamide **s7** as a pale brown oil (1.5 mg, 10% yield).

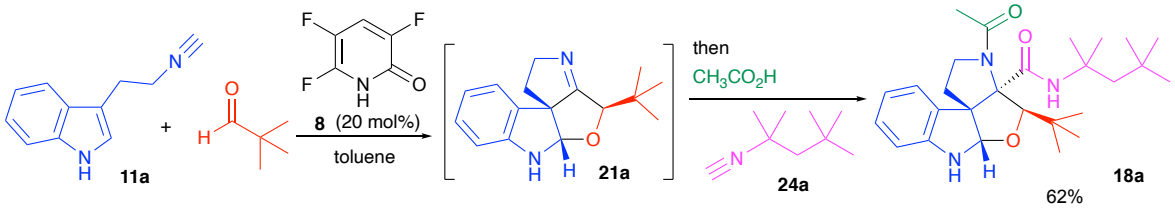
Characteristic data of *N*-(2-hydroxy-3,3-dimethylbutanoyl)tryptamine (s7)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (brs, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.21 (m ,1H), 7.13 (m, 1H), 7.05 (brs, 1H), 6.18 (m, 1H), 3.70-3.61 (2H), 3.63 (s, 1H), 3.07-2.93 (2H), 0.93 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 136.4, 127.3, 122.3, 122.0, 119.5, 118.7, 112.9, 111.3, 79.6, 39.4, 34.9, 25.9 (3C), 25.4. IR (neat, ATR) 3401, 3323, 2957, 1650, 1529, 1458, 1363, 1231, 1079, 1017, 743 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{16}H_{22}N_2NaO_2]^+$ 297.1579, found 297.1582.

5. General Procedure for One-pot Interrupted Passerini/Joullié-Ugi Reaction of 3-(2-isocyanoethyl)indole

To a solution of isocyanide **11** (0.1 mmol) and aldehyde (0.15 mmol) in toluene (150 μL) was added 3,5,6-trifluoro-2-pyridone (**8**, 1.5 mg, 0.02 mmol) at room temperature under Ar atmosphere. After isocyanide **11** was completely consumed, isocyanide **24** (0.15 mmol) (or a solution of **11a** (0.15 mmol) in toluene (150 μL)) and carboxylic acid (0.15 mmol) were added. The reaction mixture was stirred at same temperature for 12 h. The mixture was then put on a silica gel and purified by column chromatography to provide corresponding highly functionalised tetracyclic furoindoline **18**.

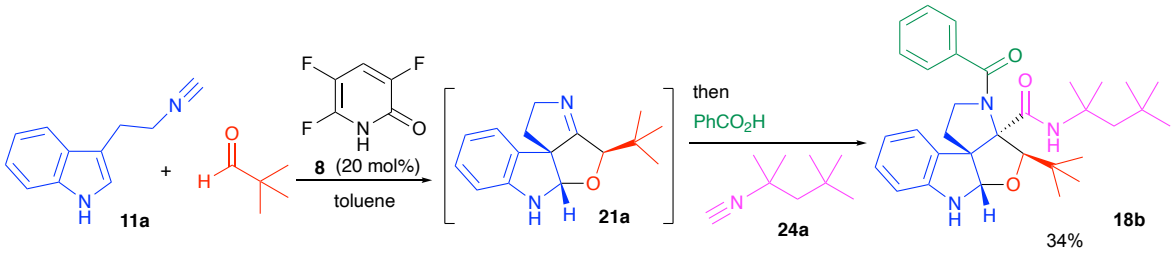
Tetracyclic furoindoline (18a)



Purified by silica gel column chromatography (Hexane/AcOEt = 1.5/1 to 1/2).

Colorless amorphous solid (28.0 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (brd, *J* = 7.6 Hz, 1H), 7.07 (ddd, *J* = 8.0, 7.4, 1.3 Hz, 1H), 6.69 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 5.58 (s, 1H), 5.24 (brs, 1H), 4.55 (brs, 1H), 3.88 (dd, *J* = 10.0, 8.4 Hz, 1H), 3.80 (brs, 1H), 3.61 (m, 1H), 2.67 (brm, 1H), 2.11 (s, 3H), 1.97 (m, 1H), 1.55-1.20 (8H), 1.12 (s, 9H), 0.72 (brs, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 166.1, 150.3, 129.4, 127.3, 125.3, 118.8, 107.9, 97.6, 86.0, 80.7, 70.3, 56.1, 55.8, 48.4, 35.6, 34.6, 31.5 (4C), 29.4, 27.8 (3C), 25.5, 24.3. IR (neat, ATR) 3315, 2952, 1650, 1519, 1478, 1408, 1358, 1269, 1224, 1072, 996, 913, 734 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{27}H_{41}N_3O_3Na]^+$ 478.3046, found 478.3034.

Tetracyclic furoindoline (18b)

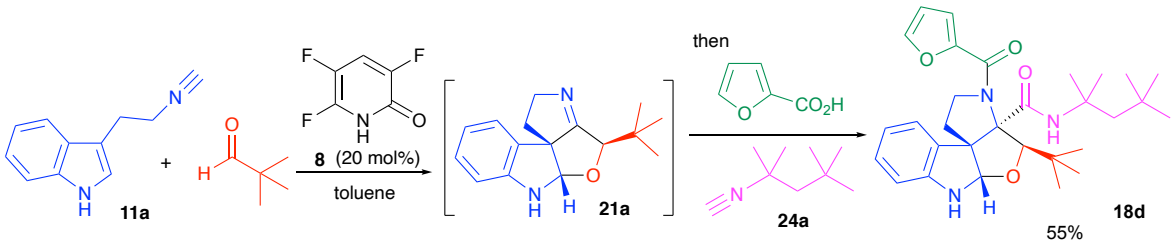


Purified by silica gel column chromatography (Hexane/AcOEt = 3/1).

Pale brown amorphous solid (17.6 mg, 34% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (m, 2H), 7.47-7.32 (5H), 7.27 (m, 1H), 7.09 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 6.71 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.55 (d, *J* = 7.6 Hz, 1H), 5.63 (s, 1H), 5.30 (brs, 1H), 4.59 (s, 1H), 3.87 (brm, 1H), 3.83-3.60 (2H), 2.67 (brm, 1H), 1.89 (brd, *J* = 8.8 Hz, 1H), 1.55-1.29 (8H), 1.21

(s, 9H), 0.73 (brs, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 165.9, 150.4,137.5, 129.9, 129.5, 128.2 (2C), 127.5, 127.1 (2C), 125.1, 118.9, 108.9, 97.3, 85.9, 81.2, 70.5, 56.3, 55.8, 50.8, 35.4, 34.8, 31.6 (4C), 29.5, 28.1 (3C), 25.5. IR (neat, ATR) 3336, 2953, 2361, 1643, 1516, 1479, 1393, 1270, 1226, 1069, 744 cm^{-1}. HRMS (ESI-TOF) *m/z* [M+Na]$^+$ calcd for $[C_{32}H_{43}N_3O_3Na]^+$ 540.3202, found 540.3205.

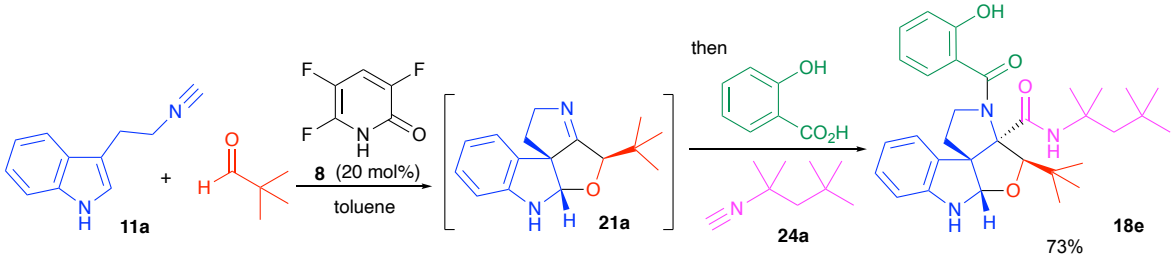
Tetracyclic furoindoline (18d)



Purified by silica gel column chromatography (Hexane/AcOEt = 2/1).

Pale yellow oil (27.9 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.28 (brs, 1H), 7.08 (m, 1H), 6.99 (brs, 1H), 6.70 (brdd, *J* = 7.4, 7.4, Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 6.47 (brs, 1H), 5.64 (m, 1H), 5.25 (brs, 1H), 4.61 (brs, 1H), 4.23 (brm, 1H), 4.09-3.69 (2H), 2.74 (m, 1H), 2.01 (m, 1H), 1.60-1.23 (2H), 1.42 (s, 3H), 1.36 (brs, 3H), 1.12 (s, 9H), 0.72 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 159.3, 150.4, 148.6, 144.1, 129.5, 127.5, 125.0, 118.8, 115.7, 111.1, 107.8, 97.2, 86.1, 81.3, 69.7, 56.2, 55.9, 49.3, 35.6, 34.6, 31.6 (4C), 29.6, 28.0 (3C), 25.5. IR (neat, ATR) 3329, 2952, 1670, 1631, 1518, 1477, 1401, 1366, 1271, 1226, 1069, 914, 733 cm^{-1}. HRMS (ESI-TOF) *m/z* [M+Na]$^+$ calcd for $[C_{30}H_{41}N_3O_4Na]^+$ 530.2995, found 530.3001.

Tetracyclic furoindoline (18e)

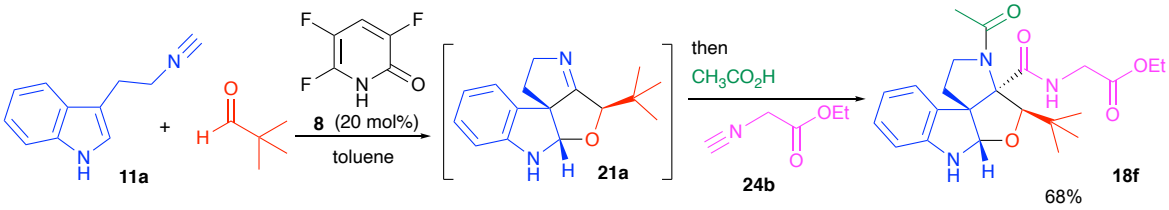


Purified by silica gel column chromatography (Hexane/AcOEt = 2/1).

Colorless solid (39.0 mg, 73%). mp 228-229 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 7.29 (m, 1H), 7.24 (d, *J* = 7.5, 1H), 7.20 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.10 (ddd, *J* = 8.0, 7.6, 1.3 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.85 (dd, *J* = 7.5, 7.4 Hz, 1H), 6.72 (dd, *J* = 7.7, 7.6, Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 5.64 (m, 1H), 5.43 (s, 1H), 4.61 (s, 1H), 3.95 (dd, *J* = 11.2, 8.2 Hz, 1H), 3.87 (s, 1H), 3.67 (ddd, *J* = 12.6, 11.2, 4.9 Hz, 1H), 2.68 (ddd, *J* = 12.8, 12.6, 8.2 Hz, 1H), 1.95 (dd, *J* = 12.8, 4.9 Hz, 1H), 1.42 (d, *J* = 15.2 Hz, 1H), 1.39 (s, 3H), 1.32 (s, 3H), 1.32 (d, *J* = 15.2 Hz, 1H), 1.21 (s, 9H),

0.73 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 167.0, 156.2, 150.4, 131.6, 129.6, 127.2, 126.6, 124.8, 121.5, 119.0, 118.8, 117.3, 108.0, 97.4, 85.7, 81.8, 70.6, 56.7, 55.6, 50.5, 35.8, 34.9, 31.5 (4C), 29.2, 27.8 (3C), 25.3. IR (neat, ATR) 3331, 2952, 1632, 1521, 1480, 1419, 1361, 1265, 1215, 1069, 910, 735 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{32}H_{43}N_3O_4Na]^+$ 556.3152, found 556.3163.

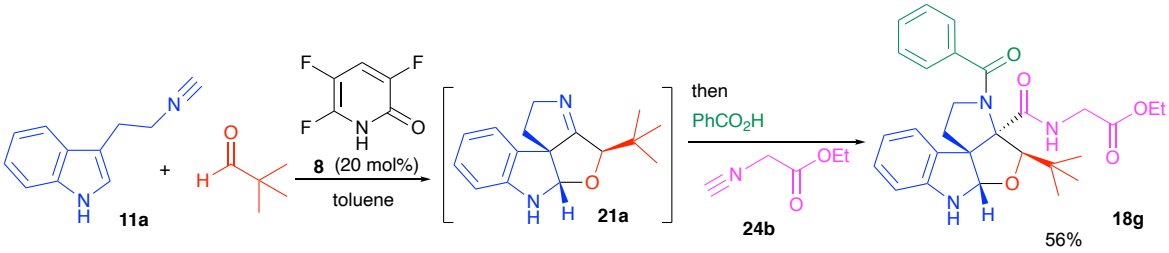
Tetracyclic furoindoline (18f)



Purified by silica gel column chromatography (Hexane/AcOEt = 1/2 to 0/1).

Pale yellow amorphous solid (29.3 mg, 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.05 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.03 (m, 1H), 6.62 (dd, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 5.91 (brs, 1H), 5.62 (d, *J* = 3.6 Hz, 1H), 4.59 (s, 1H), 4.27-4.00 (2H), 4.08 (dd, *J* =18.6, 4.8 Hz, 1H), 3.94 (dd, *J* = 10.5, 8.1, 1H), 3.8-3.50 (2H), 2.59 (m, 1H), 2.14 (s, 3H), 2.04 (m, 1H), 1.72 (brs, 1H), 1.25 (m, 3H), 1.10 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 169.2, 167.2, 150.1, 129.5, 125.0 (2C), 118.4, 108.3, 97.5, 86.4, 80.4, 70.7, 61.5, 48.5, 41.6, 35.2, 34.2, 27.3 (3C), 24.4, 14.1. IR (neat, ATR) 3352, 2959, 1739, 1656, 1517, 1482, 1403, 1354, 1270, 1204, 1071, 915, 735 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{23}H_{31}N_3O_5Na]^+$ 452.2162, found 452.2170.

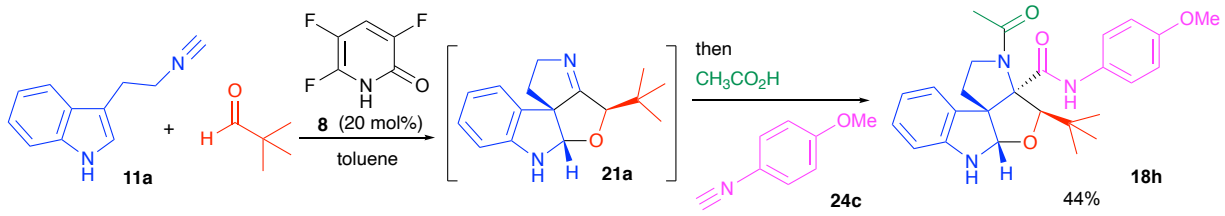
Tetracyclic furoindoline (18g)



Purified by silica gel column chromatography (Hexane/AcOEt = 1.5/1 to 0/1).

Colorless solid (27.5 mg, 56% yield). mp 184-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (m, 2H), 7.49-7.35 (3H), 7.16-6.95 (2H), 6.64 (ddd, *J* = 7.6, 7.6, 0.9 Hz, 1H), 6.59 (d, *J* = 7.2 Hz, 1H), 5.89 (brm, 1H), 5.67 (s, 1H), 4.65 (brs, 1H), 4.44-3.87 (4H), 3.90-3.42 (3H), 2.58 (brm, 1H), 1.95 (brm, 1H), 1.27 (brm, 3H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8 (2C), 167.1, 150.2, 137.2, 130.2, 129.6, 128.3 (2C), 127.2 (2C), 125.2, 124.8, 118.5, 108.3, 97.1, 86.3, 80.7, 70.9, 61.5, 51.0, 41.7, 35.0, 34.4, 27.6 (3C), 14.1. IR (neat, ATR) 3345, 2958, 1739, 1641, 1483, 1396, 1270, 1206, 1067, 743 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{28}H_{33}N_3O_5Na]^+$ 514.2318, found 514.2327.

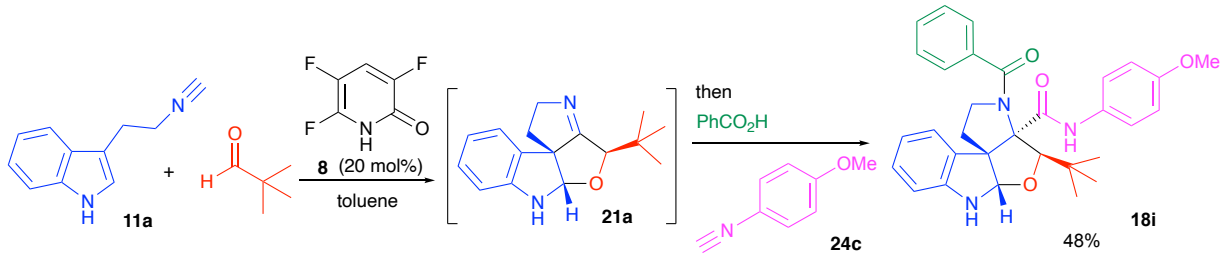
Tetracyclic furoindoline (18h)



Purified by silica gel column chromatography (Hexane/AcOEt = 1/1.5 to 1/3).

Pale yellow amorphous solid (20.2 mg, 44% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18-7.00 (4H), 6.95 (brs, 1H), 6.78 (d, *J* = 9.0 Hz, 2H), 6.63 (dd, *J* = 7.2, 7.8, 1H), 6.59 (d, *J* = 7.2Hz, 1H), 5.65 (d, *J* = 3.6 Hz, 1H), 4.61 (d, *J* = 3.0 Hz, 1H), 4.25 (brs, 1H), 3.96 (dd, *J* = 10.2, 8.4 Hz, 1H), 3.76 (s, 3H), 3.72 (m, 1H), 2.62 (m, 1H), 2.18 (s, 3H), 2.08 (dd, *J* = 12.0, 4.8 Hz, 1H), 1.13 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.6, 166.2, 157.0, 150.3, 130.2, 129.8, 125.9, 125.2, 123.7 (2C), 119.0, 114.1 (2C), 108.5, 97.9, 86.8, 80.8, 71.0, 55.6, 48.8, 35.7, 34.5, 27.6 (3C), 24.7. IR (neat, ATR) 3349, 2957, 1644, 1513, 1408, 1354, 1238, 1076, 1034, 912, 827, 736 cm^{-1}. HRMS (ESI-TOF) *m/z* [M+Na]$^{+}$ calcd for $[C_{26}H_{31}N_3O_4Na]^{+}$ 472.2213, found 472.2220.

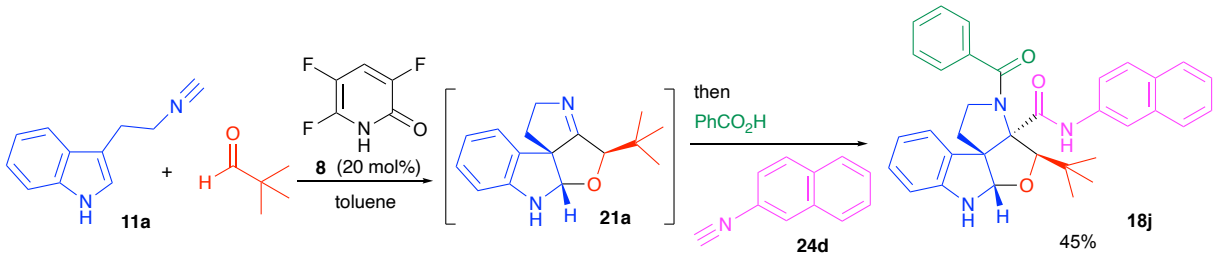
Tetracyclic furoindoline (18i)



Purified by silica gel column chromatography (Hexane/AcOEt = 2/1 to 1.5/1).

Pale brown amorphous solid (24.4 mg, 48% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.2 Hz, 2H), 7.59-7.38 (3H), 7.23-7.11 (3H), 7.09 (dd, *J* = 8.1, 7.4 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.64 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.61 (d, *J* = 8.1 Hz, 1H), 5.70 (brd, *J* = 3.0 Hz, 1H), 4.69 (brd, *J* = 2.4 Hz, 1H), 4.28 (brm, 1H), 3.86 (brm, 1H), 3.84 (brm, 1H), 3.78 (s, 3H), 2.61 (brm, 1H), 2.01 (brd, *J* = 9.0 Hz, 1H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 165.7, 156.8, 150.2, 137.1, 130.4, 130.0 (2C), 128.4 (2C), 127.3 (2C), 125.9, 124.7, 123.5 (2C), 118.8, 114.0 (2C), 108.2, 97.2, 86.4, 81.0, 70.9, 55.4, 51.1, 35.3, 34.5, 27.7 (3C). IR (neat, ATR) 3348, 2956, 1682, 1635, 1512, 1399, 1239, 1069, 1035, 914, 731 cm^{-1}. HRMS (ESI-TOF) *m/z* [M+Na]$^{+}$ calcd for $[C_{31}H_{33}N_3O_4Na]^{+}$ 534.2369, found 534.2362.

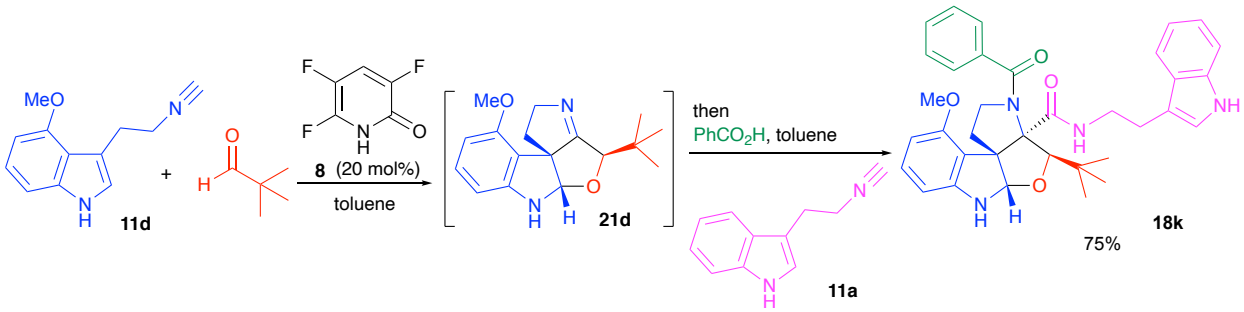
Tetracyclic furoindoline (18j)



Purified by silica gel column chromatography (Hexane/AcOEt = 2.5/1).

Colorless amorphous solid (23.7 mg, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 2.0 Hz, 1H), 7.83-7.70 (3H), 7.70-7.58 (2H), 7.54-7.36 (5H), 7.31 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.17 (brd, *J* = 7.2 Hz, 1H), 7.07 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.57 (dd, *J* = 7.6, 7.6 Hz, 1H), 5.73 (d, *J* = 3.0 Hz, 1H), 4.69 (d, *J* = 3.0 Hz, 1H), 4.36 (brs, 1H), 3.90 (d, *J* = 8.4 Hz, 2H), 2.65 (m, 1H), 2.05 (d, *J* = 12.4 Hz, 1H), 1.25 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 165.9, 150.2, 137.0, 134.5, 133.7, 130.9, 130.6, 129.7, 128.5, 128.4 (2C), 127.7, 127.5, 127.4 (2C), 126.3, 125.7, 125.0, 124.6, 121.0, 119.0, 118.2, 108.3, 97.3, 86.5, 81.2, 71.1, 51.1, 35.3, 34.5, 27.7 (3C). IR (neat, ATR) 3360, 2958, 2360, 1690, 1633, 1529, 1493, 1396, 1271, 1070, 737 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{34}H_{33}N_3O_3Na]^+$ 554.2420, found 554.2427.

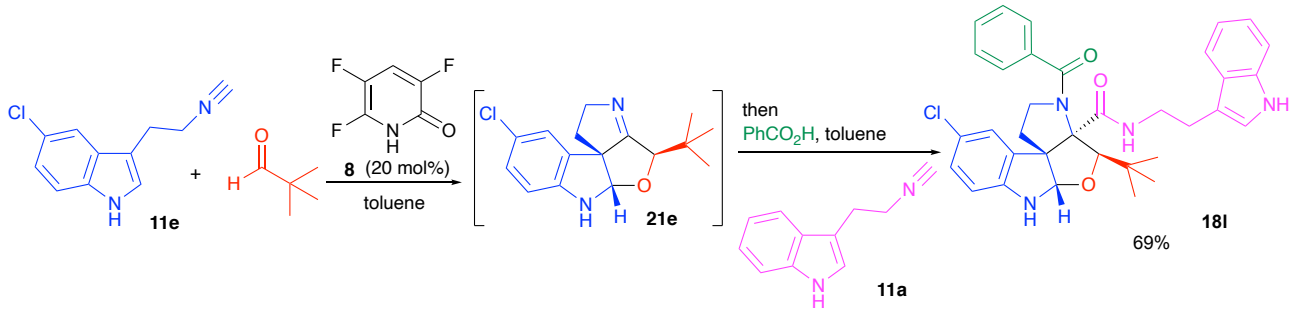
Tetracyclic furoindoline (18k)



Purified by silica gel column chromatography (Hexane/AcOEt = 1/1 to 1/2).

Pale brown amrophous solid (43.5 mg, 75% yield). ^{1}H NMR (600 MHz, DMSO-d_6, 100 °C) δ 10.5 (brs, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.51-7.39 (5H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.16 (brs, 1H), 7.07 (m, 1H), 6.98 (m, 1H), 6.93 (m, 1H), 6.26 (brs, 1H), 6.15 (brs, 1H), 6.14 (m, 1H), 5.57 (d, *J* = 3.6 Hz, 1H), 4.49 (m, 1H), 3.67 (m, 1H), 3.61 (s, 3H), 3.57 (m, 2H), 3.12 (m, 2H), 2.93 (m, 1H), 2.86 (m, 1H), 1.74 (dd, *J* = 12.0, 4.8 Hz, 1H), 1.08 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.6, 165.8, 158.1, 153.0, 138.5, 136.3, 130.0, 129.5, 127.8 (2C), 127.3, 127.2 (2C), 122.7, 120.8, 118.2, 118.1, 112.5, 111.4, 111.2, 101.2, 100.5, 97.4, 86.4, 80.0, 71.7, 54.9, 50.8, 40.4, 33.9, 30.4, 27.8 (3C), 24.9. IR (neat, ATR) 3312, 2954, 1730, 1640, 1604, 1519, 1465, 1396, 1250, 1082, 741 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{35}H_{38}N_4O_4Na]^+$ 601.2791, found 601.2781.

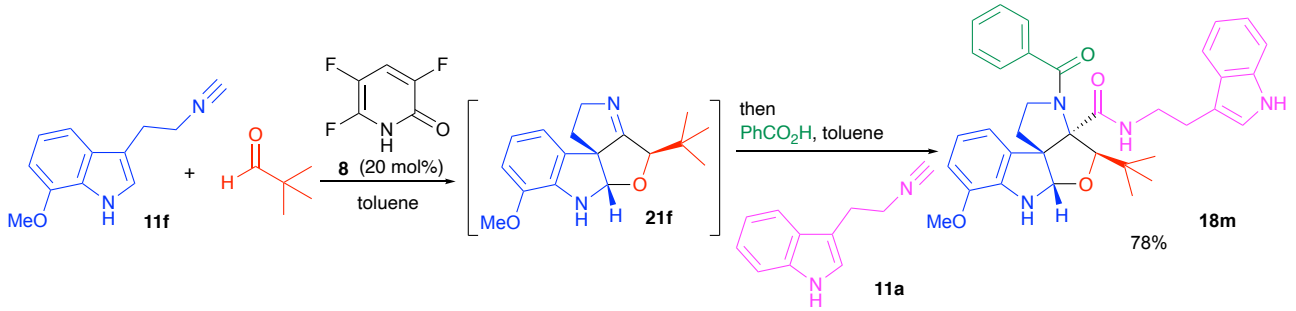
Tetracyclic furoindoline (18l)



Purified by silica gel column chromatography (Hexane/AcOEt = 1/1 to 1/2, AcOEt/MeOH = 9/1).

Pale brown amorphous solid (40.2 mg, 69% yield). ^{1}H NMR (400 MHz, DMSO-d_6, 100 °C) δ 10.6, (brs, 1H), 7.55 (brs, *J* = 8.0 Hz, 1H), 7.52-7.42 (5H), 7.36 (m, 1H) 7.15 (m, 1H), 7.70 (m, 1H), 7.00 (m, 1H), 7.00-6.91 (2H), 6.58 (m, 1H), 6.50 (d, *J* = 8.4 Hz, 1H), 5.66 (d, *J* = 3.2 Hz, 1H), 4.25 (m, 1H), 3.73 (ddd, *J* = 12.5, 10.3, 5.3 Hz, 1H), 3.62 (dd, *J* = 10.3, 8.0 Hz, 1H), 3.43 (m, 1H), 3.30 (m, 1H), 2.96 (m, 1H), 2.88 (m, 1H), 2.37 (ddd, *J* = 12.5, 12.4, 8.0 Hz, 1H), 1.95 (dd, *J* = 12.4, 5.3 Hz, 1H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.9, 166.7, 150.3, 137.5, 136.3, 130.0, 128.4, 128.0 (2C), 127.6 (2C), 127.2, 126.8, 124.5, 122.7, 120.9, 120.0, 118.2 (2C), 112.1, 111.4, 108.2, 97.1, 86.0, 80.1, 69.4, 50.6, 40.3, 34.4, 33.8, 27.6 (3C), 25.0. IR (neat, ATR) 3329, 2954, 1636, 1487, 1401, 1269, 1071, 814, 741 cm^{-1}. HRMS (ESI-TOF) *m/z* [M+Na]$^{+}$ calcd for [$C_{34}H_{35}ClN_4O_3Na$]$^{+}$ 605.2296, found 605.2289.

Tetracyclic furoindoline (18m)

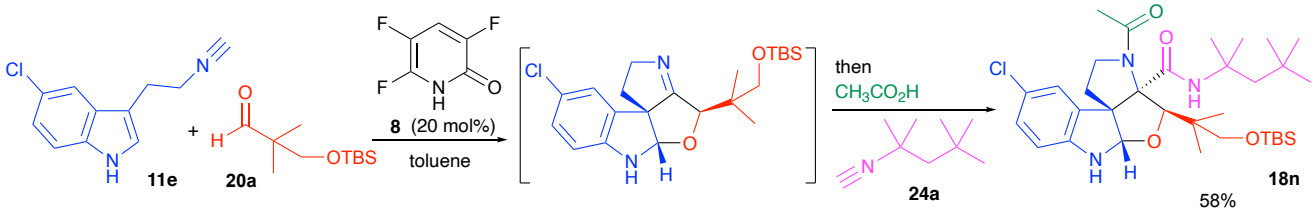


Purified by silica gel column chromatography (Hexane/AcOEt = 1/1 to 1/2).

Colorless amporphous solid (45.2 mg, 78% yield). ^{1}H NMR (400 MHz, DMSO-d_6, 100 °C) δ 10.6, (brs, 1H), 7.63-7.41 (6H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.16 (brs, 1H), 7.07 (m, 1H), 6.98 (m, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.61 (m, 1H), 6.48 (m, 1H), 5.91 (m, 1H), 5.62 (d, *J* = 3.6 Hz, 1H), 4.25 (m, 1H), 3.78 (s, 3H), 3.72 (m, 1H), 3.61 (m, 1H), 3.41 (m, 1H), 3.27 (m, 1H), 2.91 (m, 1H), 2.84 (m, 1H), 2.39 (m, 1H), 1.88 (dd, *J* = 12.4, 4.8 Hz, 1H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6, 80 °C) δ 167.6, 166.2, 142.8, 140.0, 137.6, 136.1, 129.3, 127.6 (2C), 127.0, 126.7 (2C), 126.3, 122.2, 120.5, 117.8, 117.8 (2C), 117.2, 111.9, 111.0, 110.9, 97.1, 85.4, 80.0, 70.3, 54.9, 50.1, 39.8, 34.4, 33.5, 27.2 (3C), 24.3. IR (neat, ATR) 3324, 2934, 1728, 1637, 1496, 1451, 1400, 1255, 1227, 1066, 1009, 736 cm^{-1}. HRMS (ESI-TOF)

m/z [M+Na]$^+$ calcd for [$C_{35}H_{38}N_4O_4Na$]$^+$ 601.2791, found 601.2804.

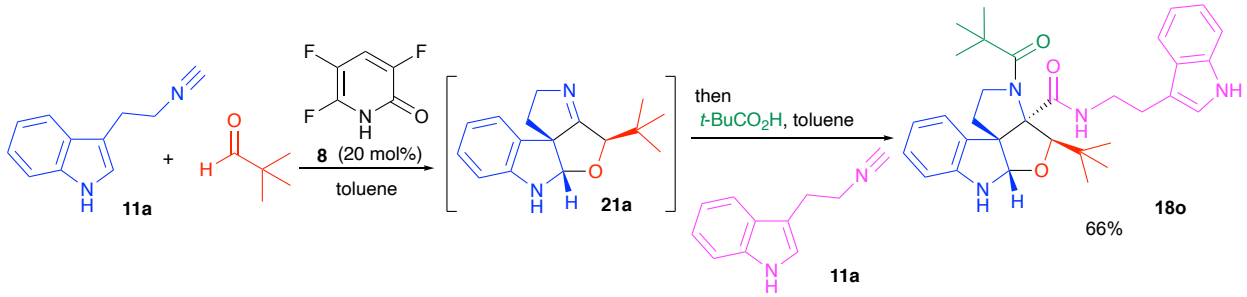
Tetracyclic furoindoline (18n)



Purified by silica gel column chromatography (Hexane/AcOEt = 1.5/1 to 1:1).

Colorless amorphous solid (36.0 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 1.8 Hz, 1H), 7.02 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.38 (d, *J* = 8.0 Hz, 1H), 5.53 (d, *J* = 3.2 Hz, 1H), 5.21 (brs, 1H), 4.43 (d, *J* = 3.2 Hz, 1H), 4.15 (brs, 1H), 3.89 (dd, *J* = 10.5, 8.2 Hz, 1H), 3.65 (d, *J* = 8.8 Hz, 1H), 3.59 (ddd, *J* = 12.4, 10.5, 5.2 Hz, 1H), 2.98 (d, *J* = 8.4 Hz, 1H), 2.66 (m, 1H), 2.11 (s, 3H), 1.96 (dd, *J* = 12.4, 5.2 Hz, 1H), 1.43 (s, 3H), 1.37 (s, 2H), 1.33 (s, 3H), 1.31 (s, 3H), 0.88 (s, 9H), 0.81 (s, 3H), 0.75 (brs, 9H), 0.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 166.2, 148.8, 129.2, 127.2, 126.9, 123.2, 108.3, 97.3, 80.8, 80.3, 72.4, 70.2, 56.5, 55.7, 48.3, 38.9, 35.3, 31.6 (3C), 31.5, 29.1, 26.0 (3C), 25.6, 24.3, 22.4, 18.6, 16.6, -5.3, -5.4. IR (neat, ATR) 3325, 2952, 2864, 1657, 1520, 1481, 1405, 1358, 1254, 1082, 841, 777, 733 cm^{-1}. HRMS (ESI-TOF) *m/z* [M+Na]$^+$ calcd for [$C_{33}H_{54}ClN_3O_4SiNa$]$^+$ 642.3470, found 642.3479.

Tetracyclic furoindoline (18o)

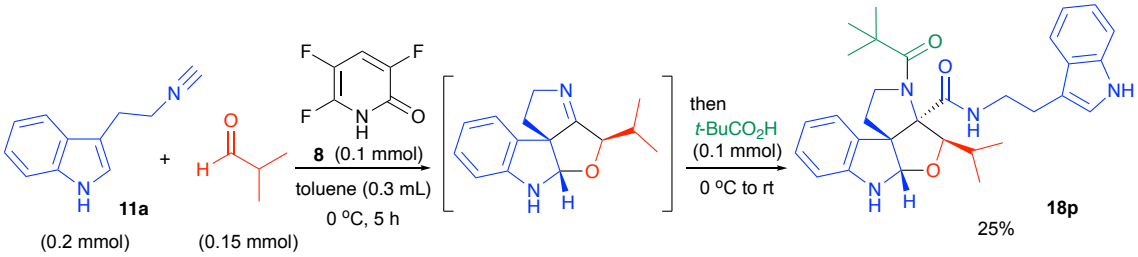


Purified by silica gel column chromatography (Hexane/AcOEt = 1/1).

Colorless powder (34.9 mg, 66%). mp 323 °C (decomp.). ^{1}H NMR (400 MHz, DMSO-d_6, 100 °C) δ 10.51 (brs, 1H), 7.45 (brd, *J* = 7.2 Hz, 1H), 7.34 (m, 1H), 7.20-7.01 (2H), 7.03-6.81 (3H), 6.49 (d, *J* = 7.6 Hz, 1H), 6.45 (brdd, *J* = 7.2, 7.2 Hz, 1H), 6.29 (brm, 1H), 6.05 (brs, 1H), 5.52 (d, *J* = 3.6 Hz, 1H), 4.13 (dd, *J* = 10.6, 7.9 Hz, 1H), 4.05 (brm, 1H), 3.54 (ddd, *J* = 12.5, 10.6, 5.1 Hz, 1H), 3.32 (m, 1H), 3.21 (m, 1H), 2.81 (m, 1H), 2.67 (brm, 1H), 2.43 (ddd, *J* = 12.5, 12.5, 7.9 Hz, 1H), 1.96 (dd, *J* = 12.5, 5.1 Hz, 1H), 1.21 (s, 9H), 0.94 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6, 100 °C) δ 173.9, 166.6, 151.0, 136.1, 128.0, 126.9, 125.5, 124.6, 122.1, 120.5, 117.8, 117.7, 116.4, 111.6, 110.9, 106.9, 96.3,

85.2, 81.4, 67.8, 47.3, 39.3, 38.2, 34.8, 33.6, 27.0 (3C), 26.8 (3C), 24.1. IR (neat, ATR) 3310, 2961, 2360, 1731, 1613, 1475, 1410, 1358, 1239, 1067, 743 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{32}H_{40}N_4O_3Na]^+$ 551.2998, found 551.3011.

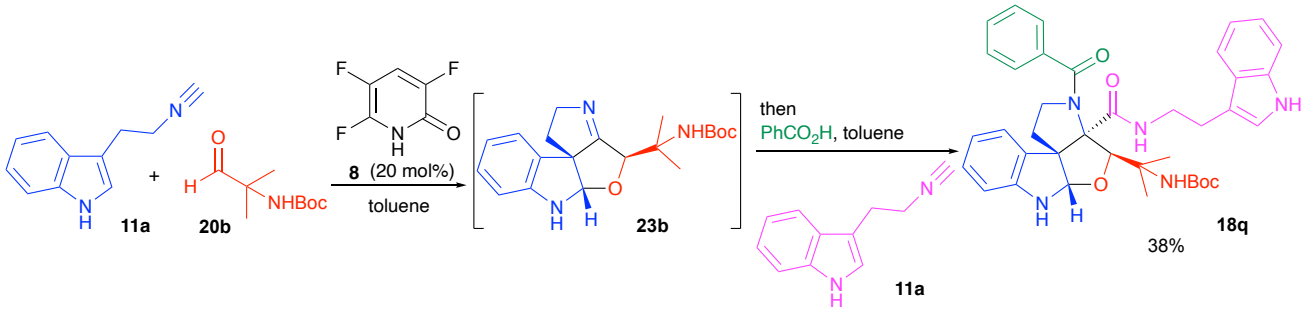
Tetracyclic furoindoline (18p)



To a solution of isocyanide **11a** (34.2 mg, 0.2 mmol) and isobutyraldehyde (14.9 µL, 0.15 mmol) in toluene (300 µL) was added 3,5,6-trifluoro-2-pyridone (**8**, 14.9 mg, 0.1 mmol) at 0 °C under Ar atmosphere. After being stirred at 0 °C for 5 h, pivalic acid (10.2 mg, 0.10 mmol) was added. The reaction mixture was gently warmed to room temperature and keep stirring for 8 h. The mixture was then put on a silica gel and purified by column chromatography (Hexane/AcOEt = 1/1) to provide corresponding highly functionalised tetracyclic furoindoline **18p** as a pale brown solid (12.9 mg, 25% yield).

mp 257 °C (decomp.). ^{1}H NMR (400 MHz, DMSO-d_6, 100 °C) δ 10.5 (brs, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 6.34 (d, *J* = 8.0 Hz, 1H), 7.13-7.03 (2H), 7.03-6.91 (3H), 6.47 (d, *J* = 8.4 Hz, 1H), 6.46 (m, 1H), 6.41-6.29 (2H), 5.54 (d, *J* = 3.6 Hz, 1H), 4.20 (d, *J* = 4.0 Hz, 1H), 4.12 (dd, *J* = 10.2, 8.0 Hz ,1H), 3.59 (ddd, *J* = 12.2, 10.2, 5.3 Hz, 1H), 3.36 (m, 1H), 3.21 (m, 1H), 2.83 (ddd, *J* = 14.5, 8.5, 5.7 Hz, 1H), 2.70 (m, 1H), 2.48 (ddd, *J* = 12.6, 12.2, 8.0 Hz, 1H), 2.18 (m, 1H), 2.00 (dd, *J* = 12.6, 5.3 Hz, 1H), 1.23 (s, 9H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, 100 °C) δ 174.2, 167.0, 150.7, 136.1, 127.9, 126.8, 125.3, 124.4, 122.0, 120.4, 117.7, 117.6, 116.3, 111.6, 110.8, 106.8, 97.2, 84.0, 81.6, 66.1, 47.0, 39.3, 38.3, 34.8, 26.9 (3C), 26.5, 24.2, 22.5, 17.6. IR (neat, ATR) 3303, 2962, 2929, 2875, 1620, 1515, 1478, 1406, 1358, 1268, 1053, 1023, 743 cm^{-1}. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $[C_{31}H_{38}N_4O_3Na]^+$ 537.2842, found 537.2853.

Tetracyclic furoindoline (18q)



To a solution of isocyanide **11a** (34.2 mg, 0.2 mmol) and aldehyde **20b** (28.1 mg, 0.15 mmol) in toluene (300 µL) was added 3,5,6-trifluoro-2-pyridone (**8**, 3.0 mg, 0.02 mmol) at room temperature under Ar atmosphere. After being stirred at same temperature for 3.5 h, benzoic acid (12.2 mg, 0.1 mmol) was added and stirred for 12 h. The mixture was then put on a silica gel and purified by column chromatography (Hexane/AcOEt = 1/1) to provide corresponding highly functionalised tetracyclic furoindoline **18q** as a pale brown amorphous solid (24.7 mg, 38% yield).

^{1}H NMR (400 MHz, DMSO-d_6, 100 °C) δ 10.6 (brs, 1H), 7.62-7.51 (3H), 7.52-7.43 (3H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.16 (brs, 1H), 7.08 (brdd, *J* = 8.4, 6.8 Hz, 1H), 6.98 (dd, *J* = 7.6, 7.2 Hz, 2H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 2H), 6.48 (dd, *J* = 8.0, 7.2 Hz, 1H), 6.14 (brs, 1H), 5.68 (d, *J* = 3.2 Hz, 1H), 4.46, (brs, 1H), 3.80 (ddd, *J* = 11.2, 11.2, 5.2 Hz, 1H), 3.68 (dd, *J* = 10.4, 8.0 Hz, 1H), 3.49 (m, 1H), 3.26 (m, 1H), 3.02 (m, 1H), 2.98 (m, 1H), 2.88 (m, 1H), 2.46 (ddd, *J* = 12.5, 12.5, 8.2 Hz, 1H), 1.96 (dd, *J* = 12.8, 4.8 Hz, 1H), 1.56 (s, 3H), 1.36 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6, 100 °C) δ 168.0, 166.4, 153.6, 150.7, 136.9, 136.1, 129.3, 128.3, 127.4 (2C), 126.9, 126.7 (2C), 124.8, 124.3, 122.1, 120.4, 117.7 (2C), 116.6, 111.9, 110.9, 107.0, 96.5, 83.2, 79.7, 76.4, 69.3, 53.8, 49.9, 39.9, 33.9, 27.8 (3C), 25.9, 24.2, 22.8. IR (neat, ATR) 3315, 1650, 1524, 1392, 1363, 1272, 1168, 1054, 1026, 745 cm^{-1}. HRMS (ESI-TOF) *m/z* [M+Na]$^{+}$ calcd for [$C_{38}H_{43}N_5O_5Na$]$^{+}$ 672.3162, found 672.3160.

4. Reference

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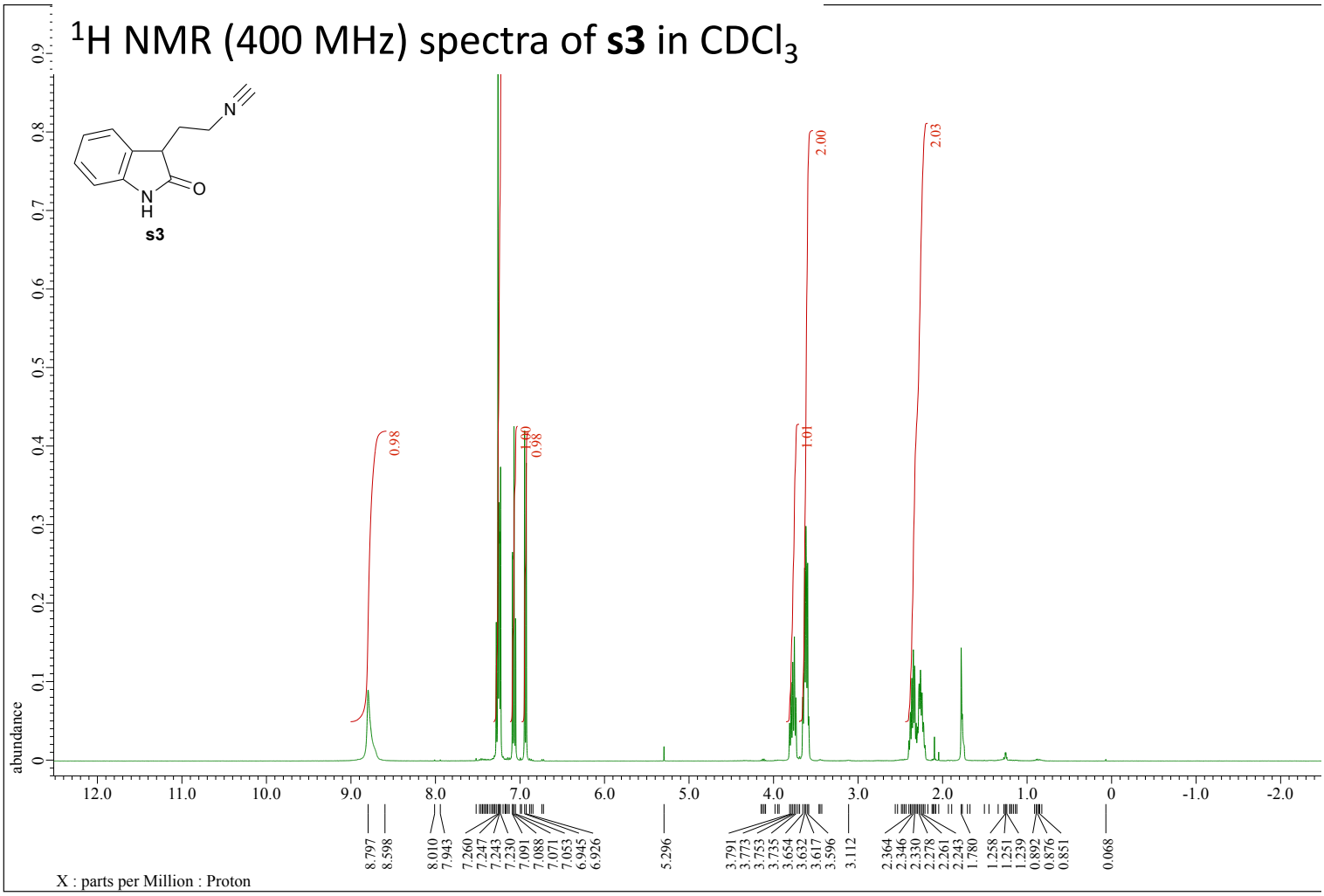
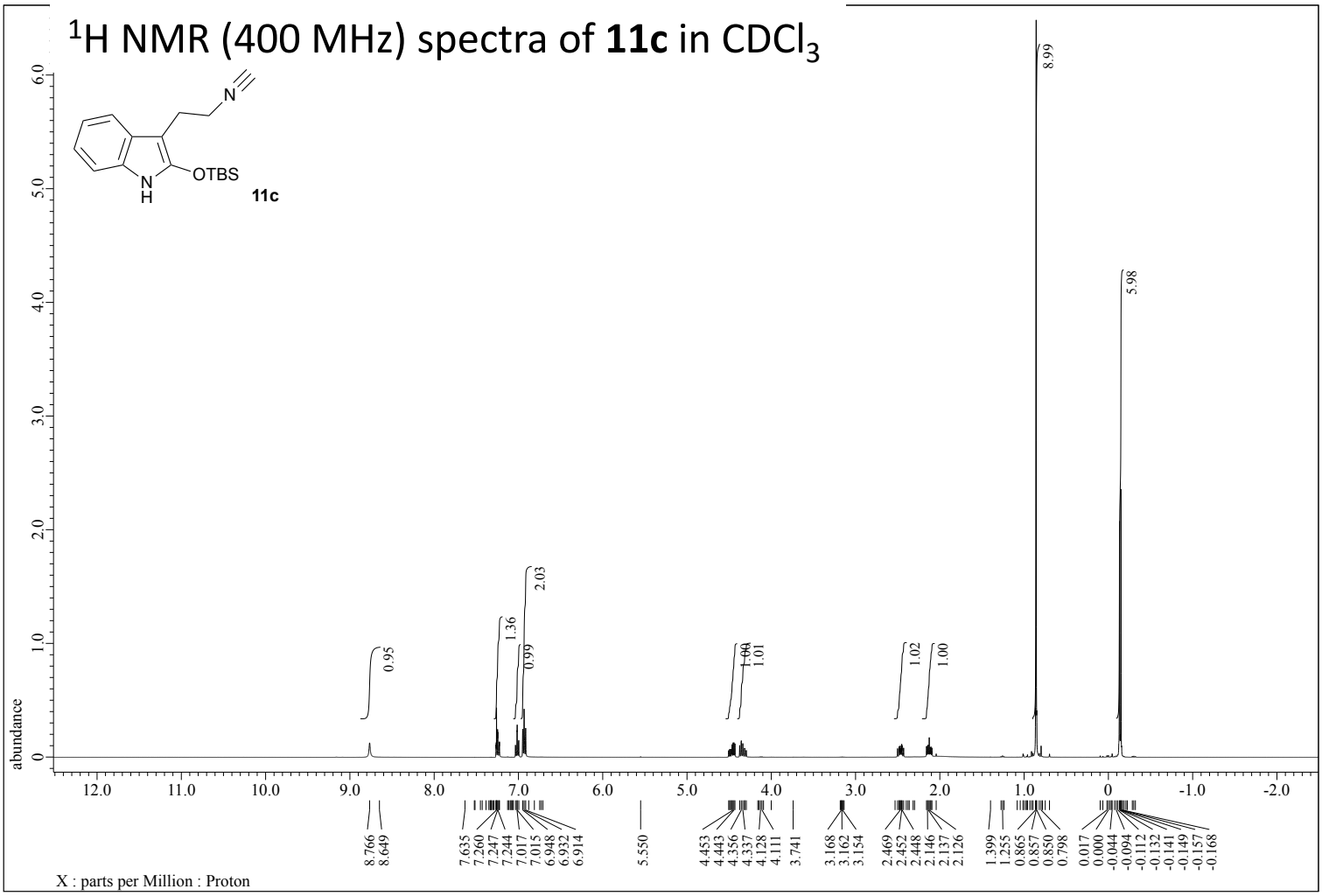
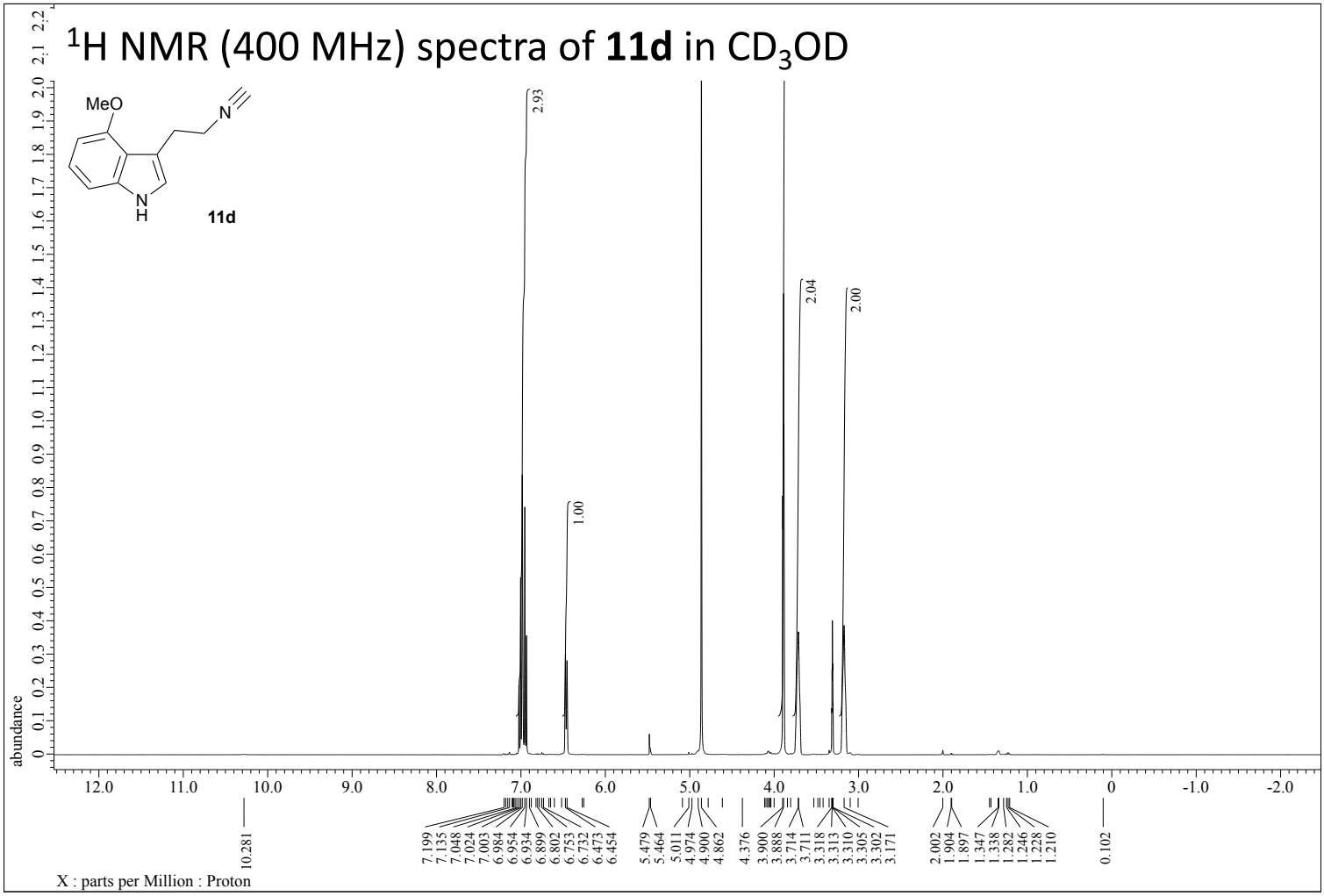
7. ^{1}H NMR Spectra

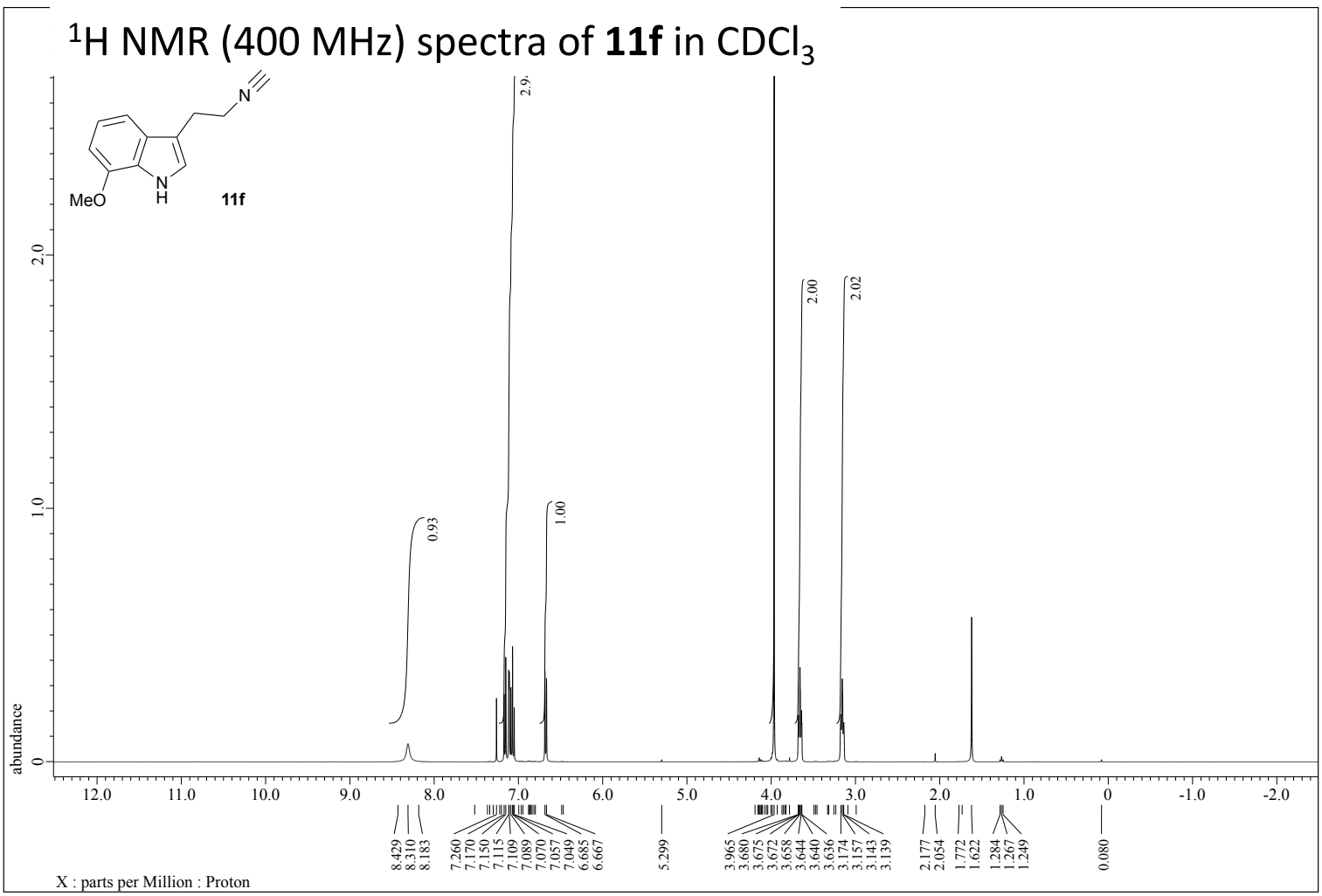




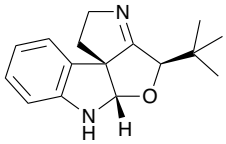
^{1}H NMR (400 MHz) spectra of **11d** in CD_3OD



^{1}H NMR (400 MHz) spectra of **11f** in $CDCl_3$

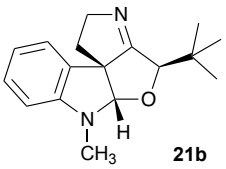


^{1}H NMR (400 MHz) spectra of **21a** in $CDCl_3$



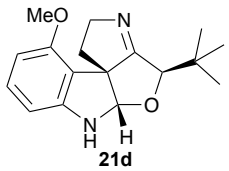
21a

^{1}H NMR (400 MHz) spectra of **21b** in $CDCl_3$



21b

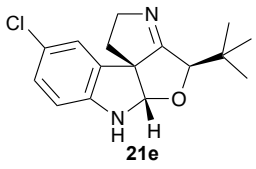
^{1}H NMR (600 MHz) spectra of **21d** in $CDCl_3$



21d

X : parts per Million : 1H

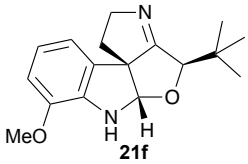
^{1}H NMR (400 MHz) spectra of **21e** in $CDCl_3$



21e

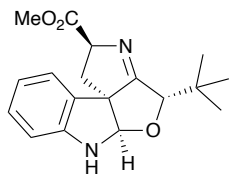
X : parts per Million : Proton

^{1}H NMR (600 MHz) spectra of **21f** in $CDCl_3$



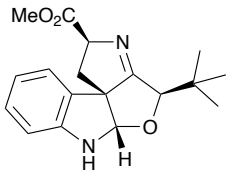
21f

^{1}H NMR (400 MHz) spectra of **22a** in $CDCl_3$



22a

^{1}H NMR (600 MHz) spectra of **22b** in $CDCl_3$

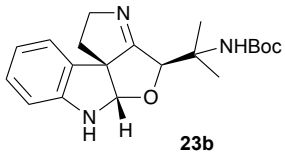


22b

^{1}H NMR (400 MHz) spectra of **23a** in $CDCl_3$

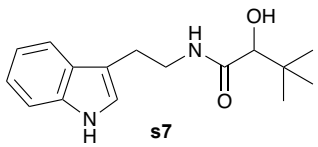
23a

^{1}H NMR (400 MHz) spectra of **23b** in $CDCl_3$



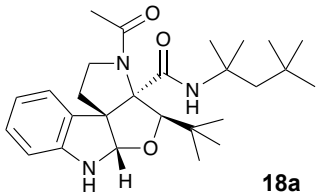
23b

^{1}H NMR (400 MHz) spectra of **s7** in $CDCl_3$



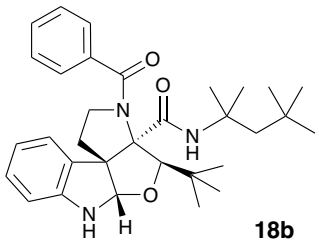
s7

^{1}H NMR (400 MHz) spectra of **18a** in $CDCl_3$



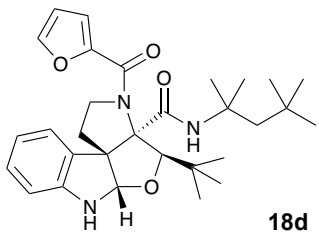
18a

^{1}H NMR (400 MHz) spectra of **18b** in $CDCl_3$



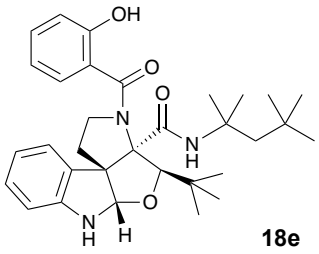
18b

^{1}H NMR (400 MHz) spectra of **18d** in $CDCl_3$



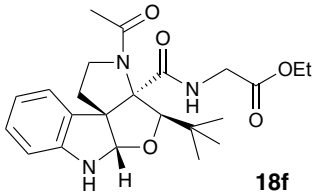
18d

^{1}H NMR (400 MHz) spectra of **18e** in $CDCl_3$



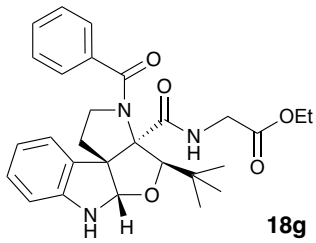
18e

^{1}H NMR (600 MHz) spectra of **18f** in $CDCl_3$



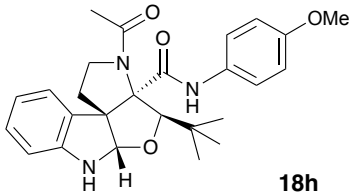
18f

^{1}H NMR (400 MHz) spectra of **18g** in $CDCl_3$



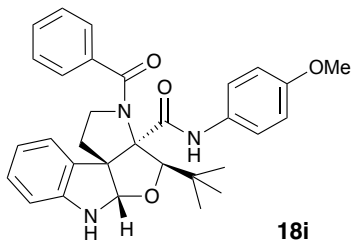
18g

^{1}H NMR (600 MHz) spectra of **18h** in $CDCl_3$



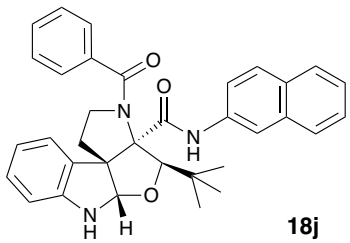
18h

^{1}H NMR (600 MHz) spectra of **18i** in $CDCl_3$



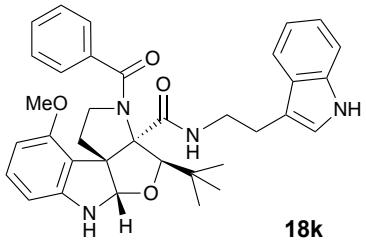
18i

^{1}H NMR (400 MHz) spectra of **18j** in $CDCl_3$



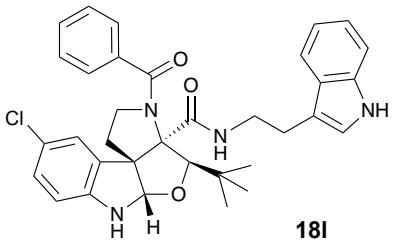
18j

^{1}H NMR (600 MHz, 100 °C) spectra of **18k** in DMSO-d_6



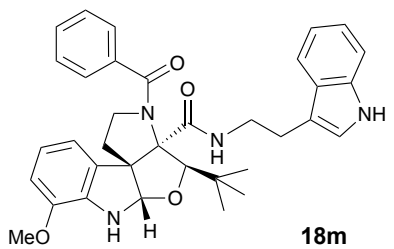
18k

^{1}H NMR (400 MHz, 100 °C) spectra of **18l** in DMSO-d_6



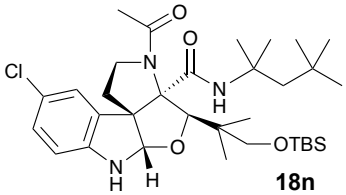
18l

^{1}H NMR (400 MHz, 100 °C) spectra of **18m** in DMSO-d_6



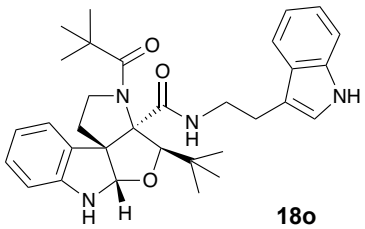
18m

^{1}H NMR (400 MHz) spectra of **18n** in $CDCl_3$



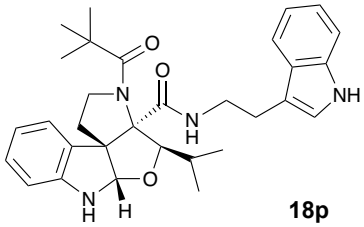
18n

^{1}H NMR (400 MHz, 100 °C) spectra of **18o** in DMSO-d_6



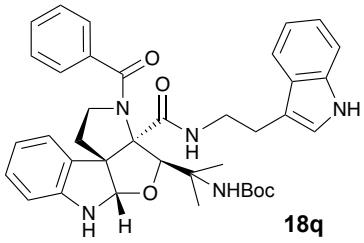
18o

^{1}H NMR (400 MHz, 100 °C) spectra of **18p** in DMSO-d_6



18p

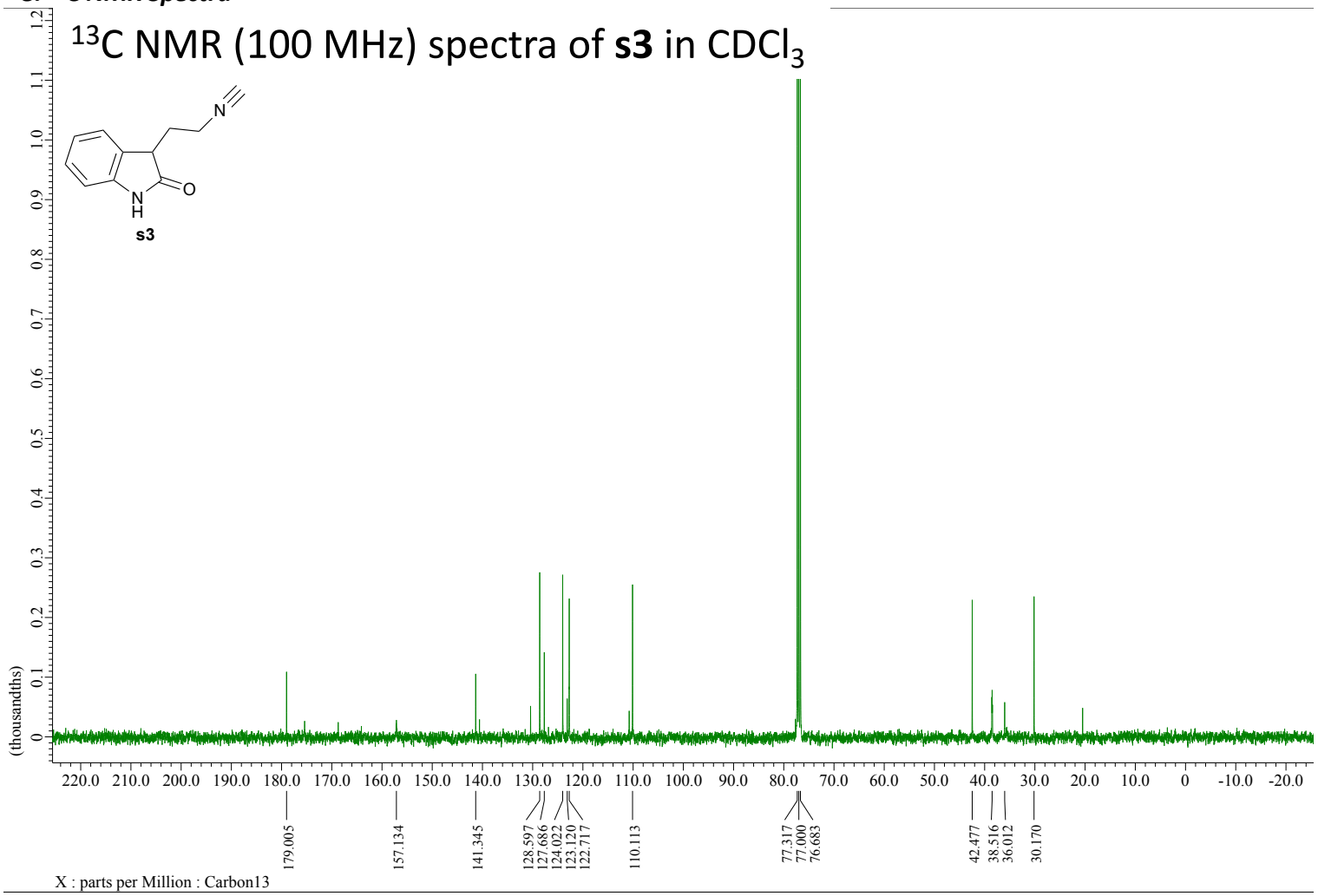
^{1}H NMR (400 MHz, 100 °C) spectra of **18q** in DMSO-d_6



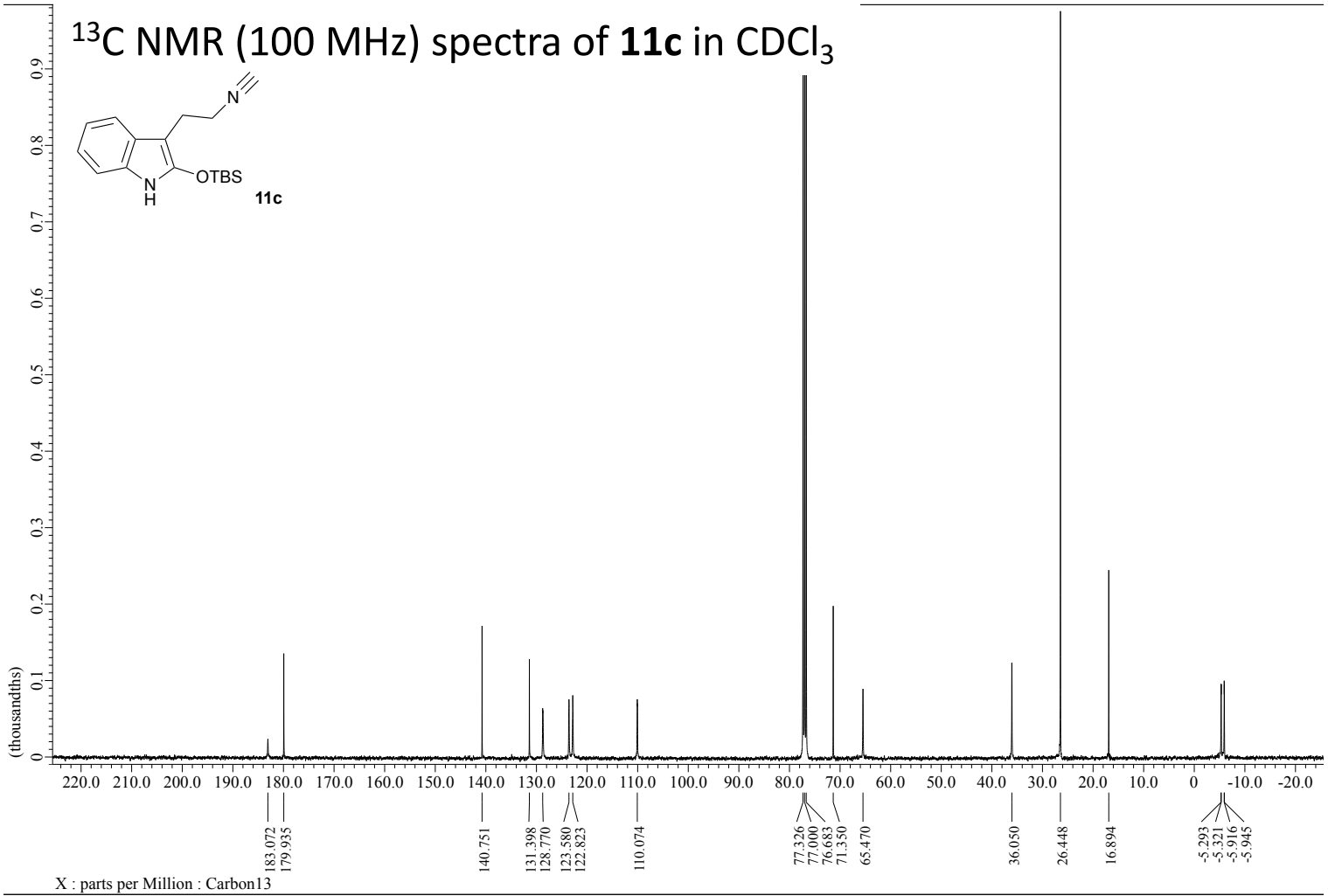
18q

8. ^{13}C NMR Spectra

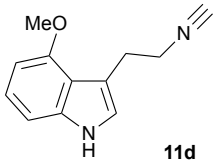
^{13}C NMR (100 MHz) spectra of **s3** in $CDCl_3$



^{13}C NMR (100 MHz) spectra of **11c** in $CDCl_3$



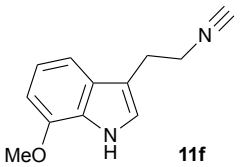
^{13}C NMR (100 MHz) spectra of **11d** in CD_3OD



11d

X : parts per Million : Carbon13

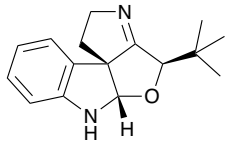
^{13}C NMR (100 MHz) spectra of **11f** in $CDCl_3$



11f

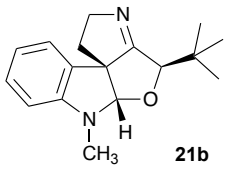
X : parts per Million : Carbon13

^{13}C NMR (100 MHz) spectra of **21a** in $CDCl_3$



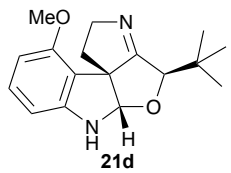
21a

^{13}C NMR (100 MHz) spectra of **21b** in $CDCl_3$



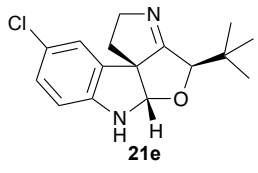
21b

^{13}C NMR (150 MHz) spectra of **21d** in $CDCl_3$



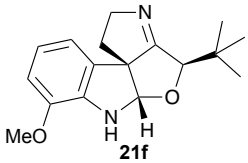
21d

^{13}C NMR (150 MHz) spectra of **21e** in $CDCl_3$



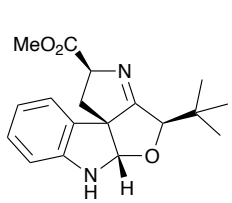
21e

^{13}C NMR (150 MHz) spectra of **21f** in $CDCl_3$



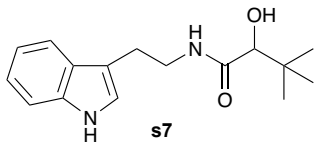
21f

^{13}C NMR (150 MHz) spectra of **22b** in $CDCl_3$



22b

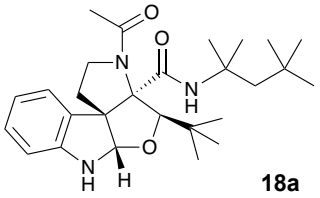
^{13}C NMR (100 MHz) spectra of **s7** in $CDCl_3$



s7

X : parts per Million : Carbon13

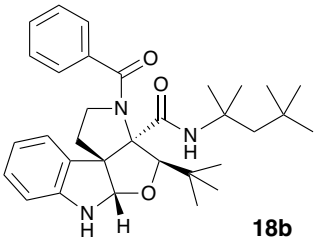
^{13}C NMR (100 MHz) spectra of **18a** in $CDCl_3$



18a

X : parts per Million : Carbon13

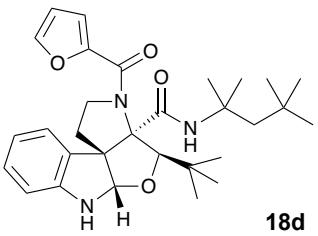
^{13}C NMR (100 MHz) spectra of **18b** in $CDCl_3$



18b

X : parts per Million : Carbon13

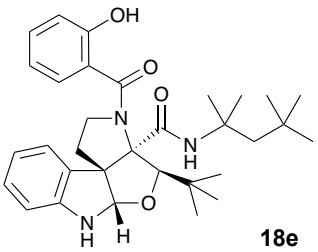
^{13}C NMR (100 MHz) spectra of **18d** in $CDCl_3$



18d

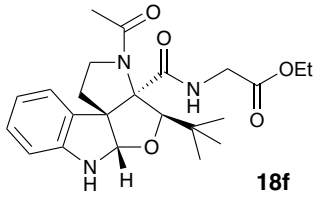
X : parts per Million : Carbon13

^{13}C NMR (100 MHz) spectra of **18e** in $CDCl_3$



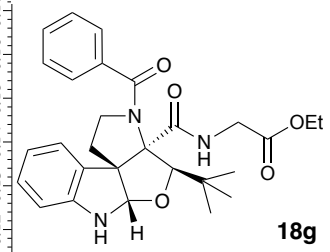
18e

^{13}C NMR (100 MHz) spectra of **18f** in $CDCl_3$



18f

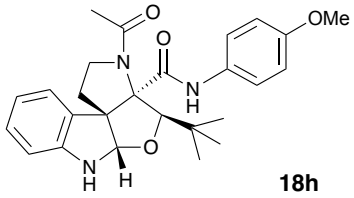
^{13}C NMR (100 MHz) spectra of **18g** in $CDCl_3$



18g

X : parts per Million : Carbon13

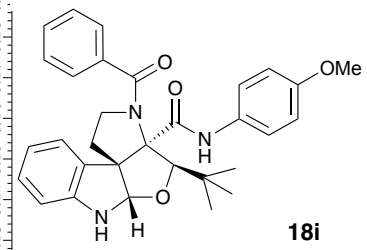
^{13}C NMR (150 MHz) spectra of **18h** in $CDCl_3$



18h

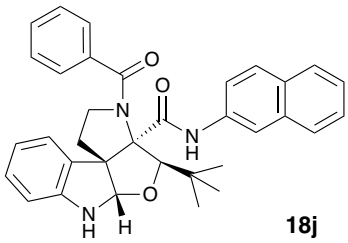
X : parts per Million : 13C

^{13}C NMR (100 MHz) spectra of **18i** in $CDCl_3$



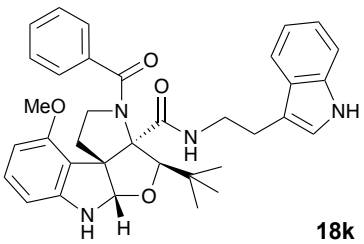
18i

^{13}C NMR (100 MHz) spectra of **18j** in $CDCl_3$



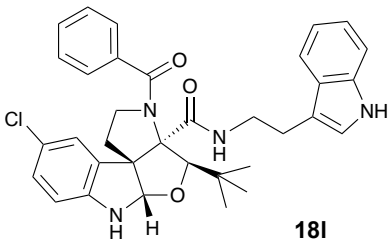
18j

^{13}C NMR (100 MHz) spectra of **18k** in DMSO-d_6



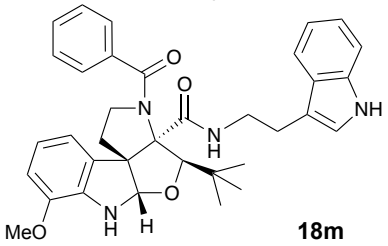
18k

^{13}C NMR (100 MHz) spectra of **18l** in DMSO-d_6



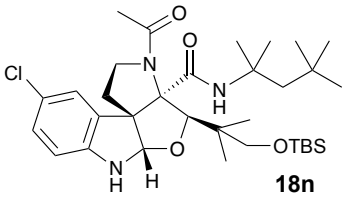
18l

^{13}C NMR (100 MHz, 80 °C) spectra of **18m** in DMSO-d_6



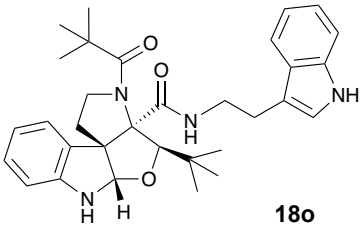
18m

^{13}C NMR (100 MHz) spectra of **18n** in $CDCl_3$



18n

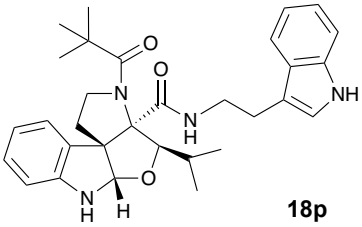
^{13}C NMR (100 MHz, 100 ^{o}C) spectra of **18o** in DMSO-d_6



18o

X : parts per Million : Carbon13

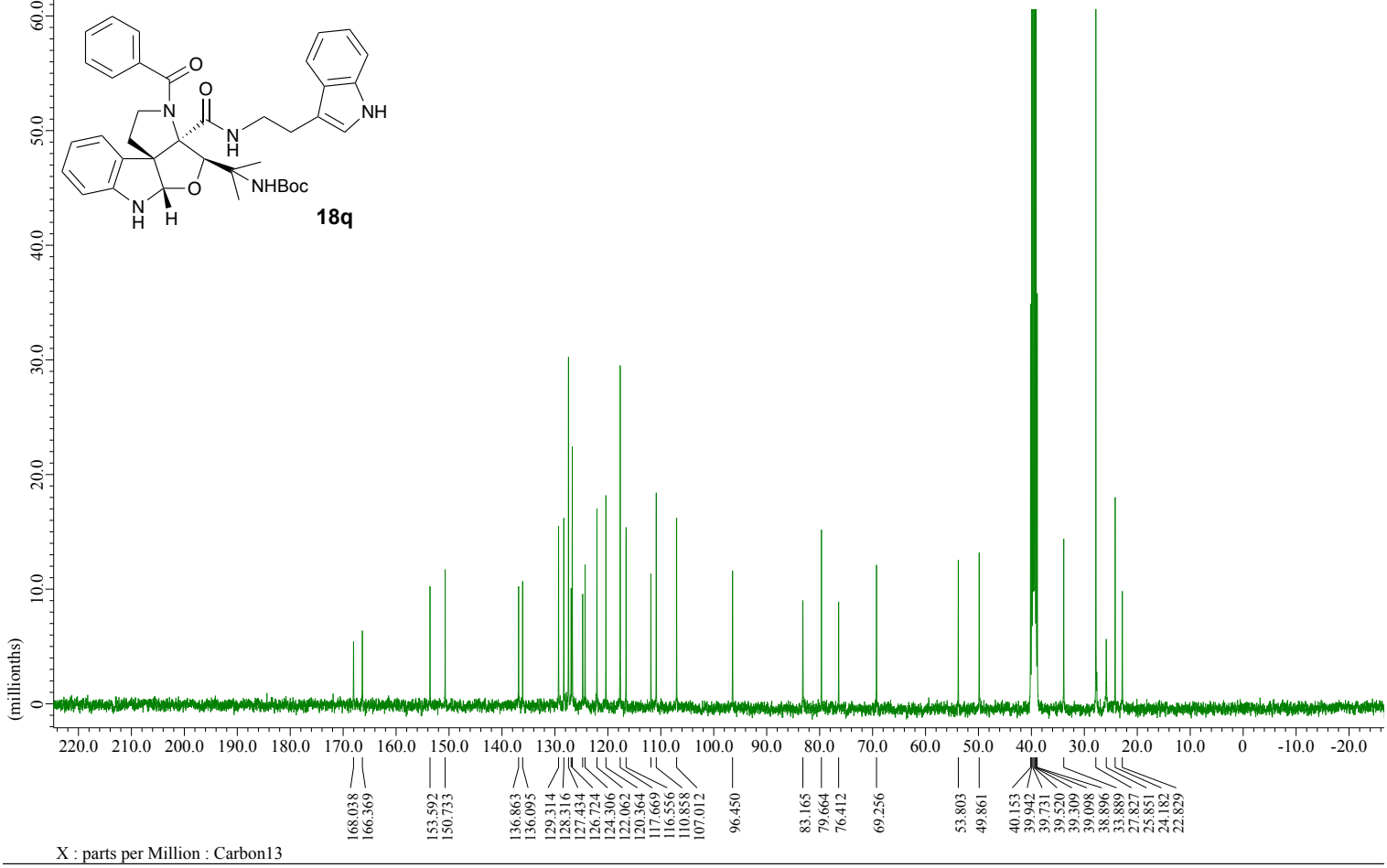
^{13}C NMR (100 MHz, 100 ^{o}C) spectra of **18p** in DMSO-d_6



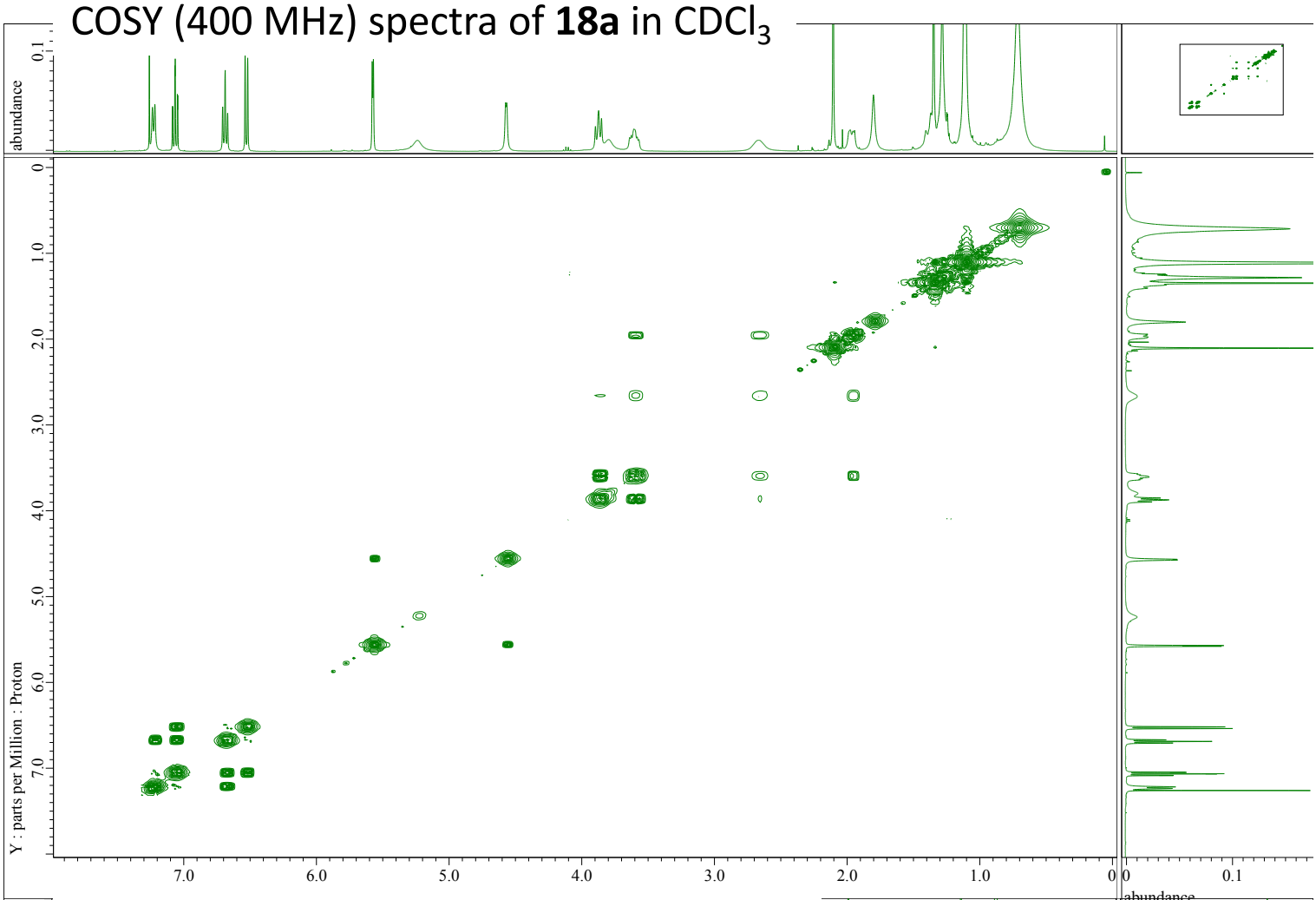
18p

X : parts per Million : Carbon13

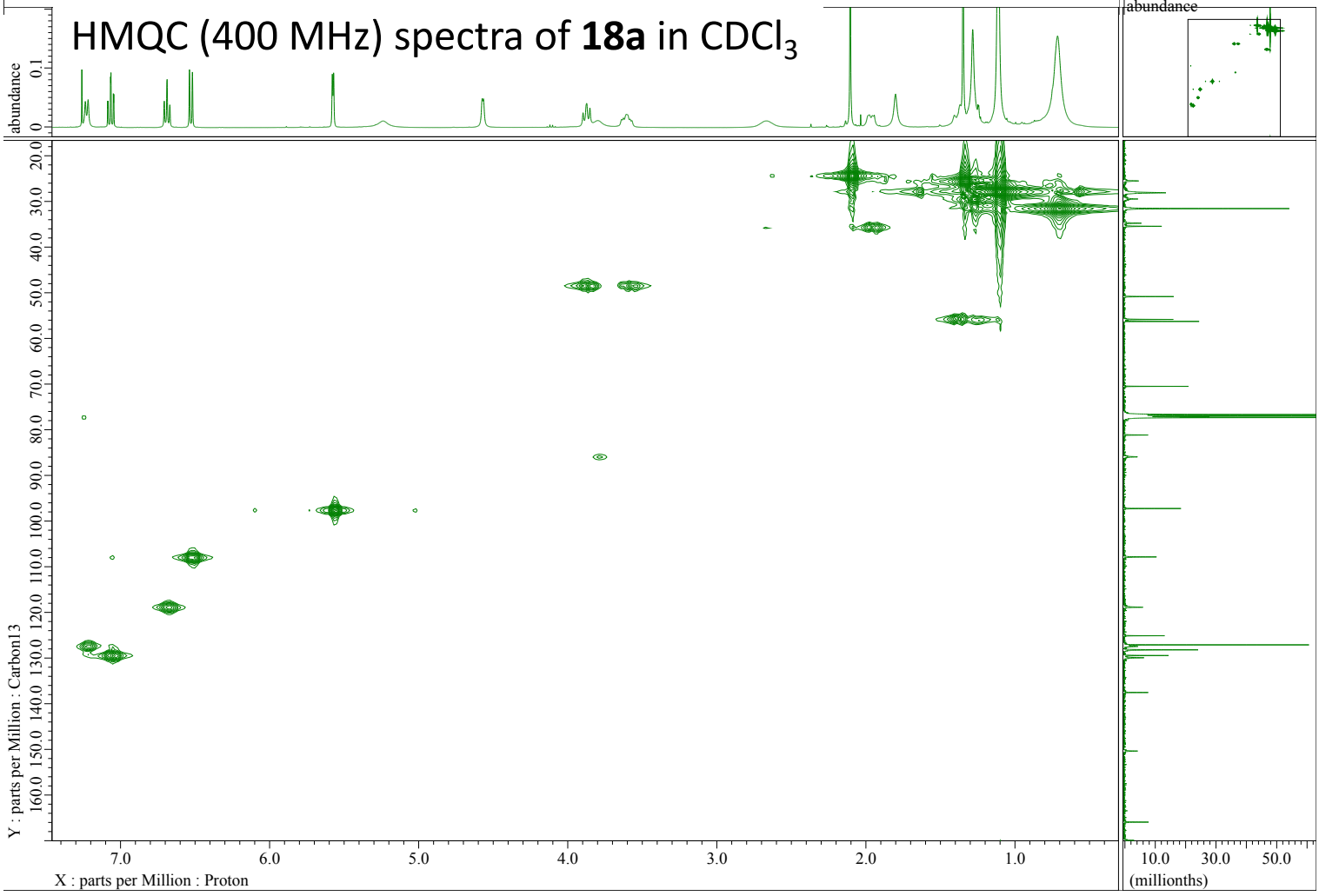
^{13}C NMR (100 MHz, 100 °C) spectra of **18q** in DMSO-d_6



9. COSY, HMQC, HMBC, NOESY Spectra of 18a

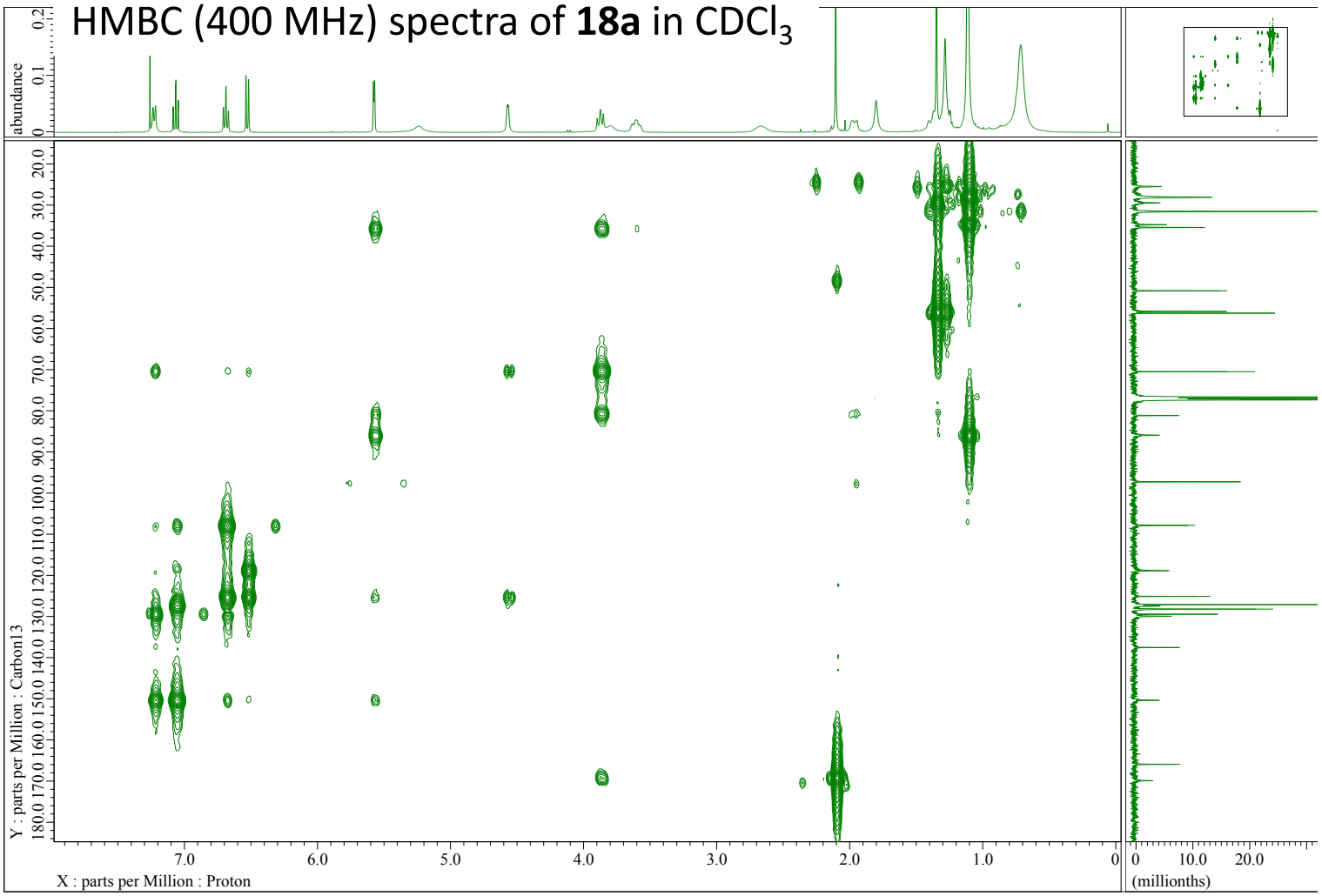


COSY (400 MHz) spectra of **18a** in $CDCl_3$

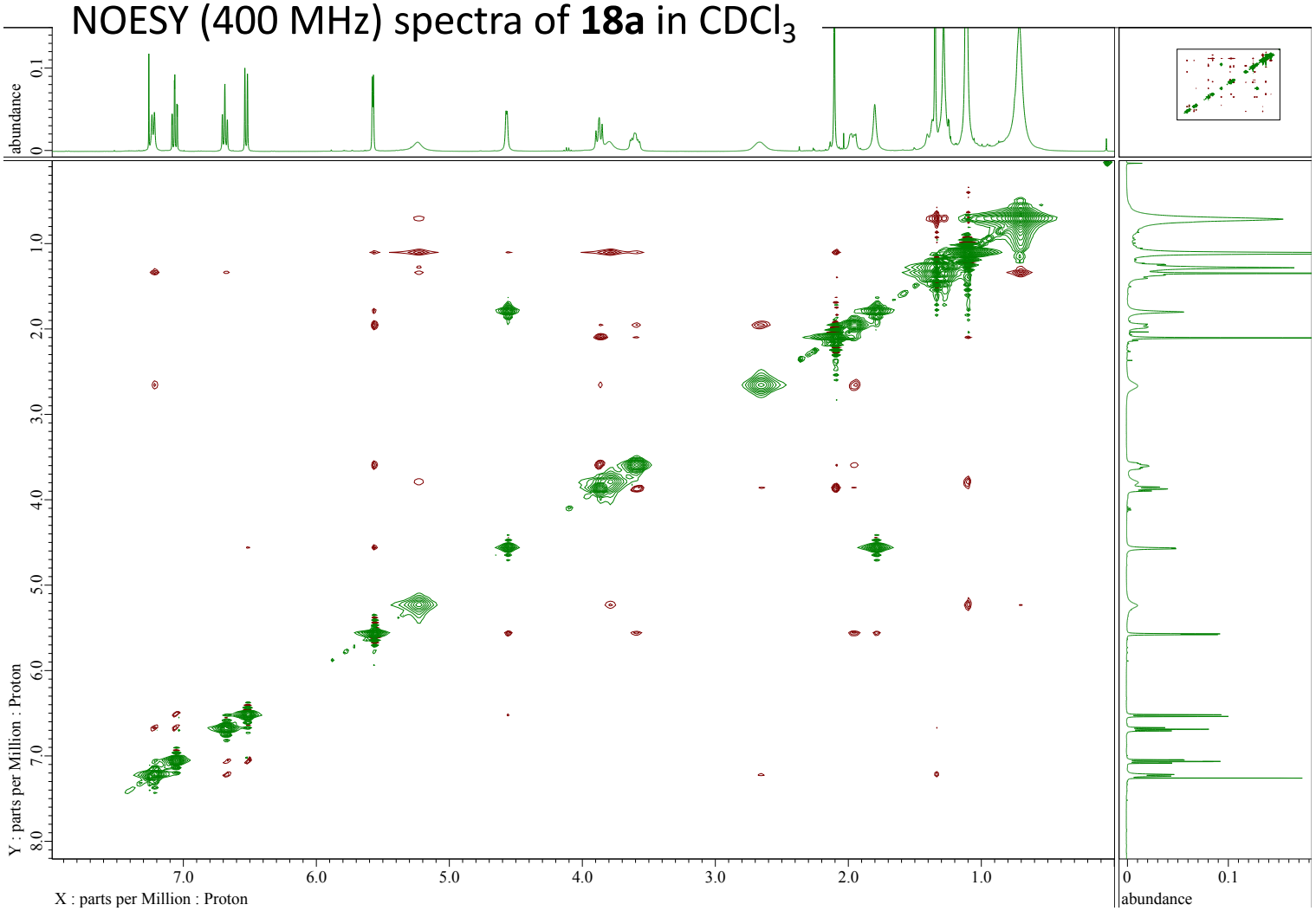


HMQC (400 MHz) spectra of **18a** in $CDCl_3$

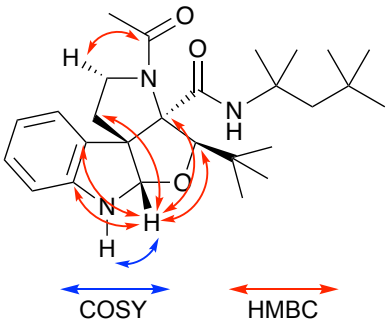
HMBC (400 MHz) spectra of **18a** in $CDCl_3$

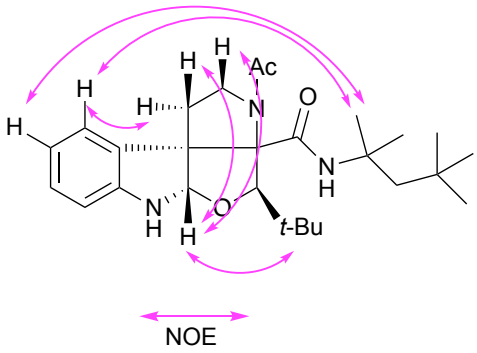


NOESY (400 MHz) spectra of **18a** in $CDCl_3$



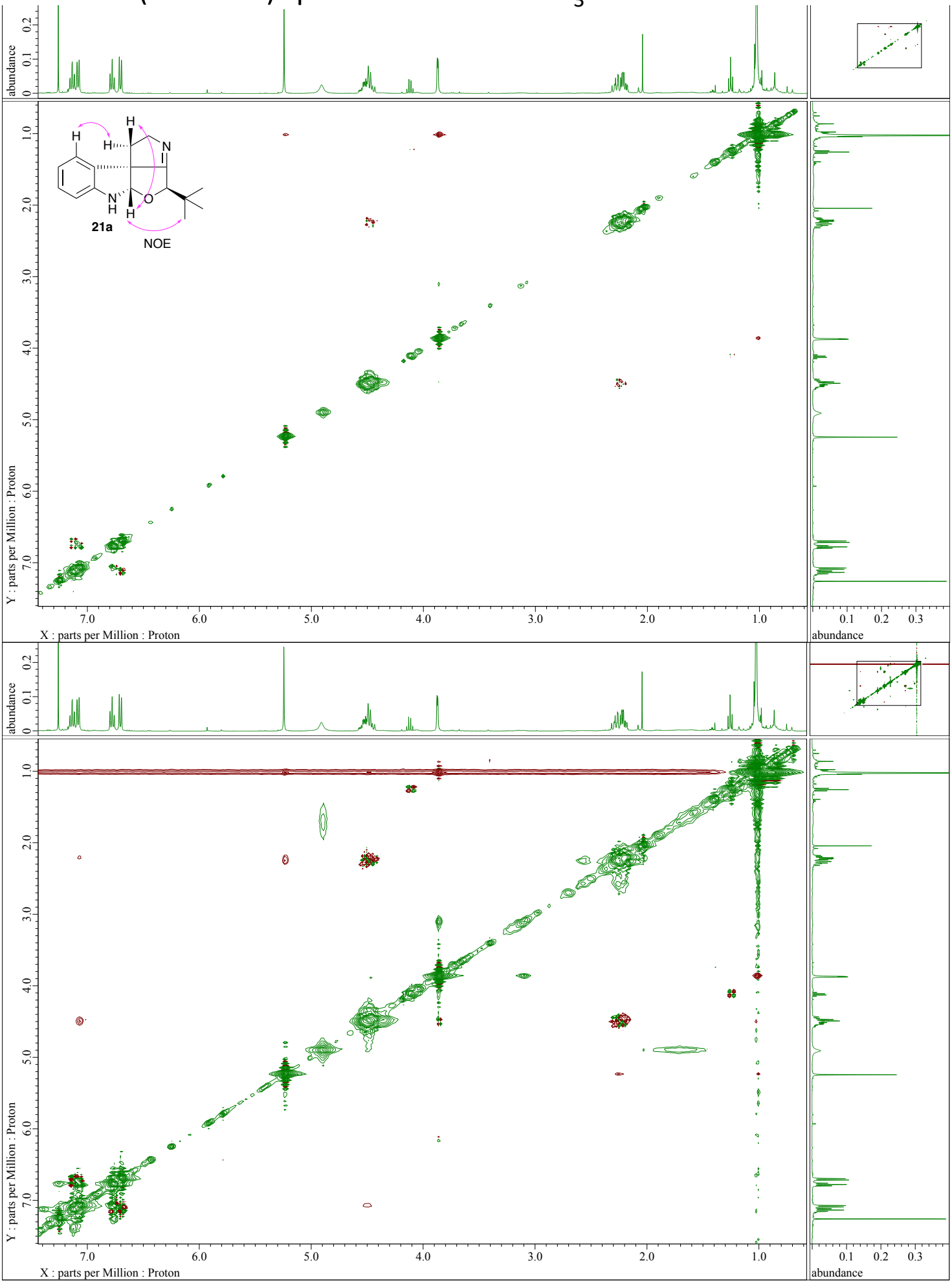
COSY, HMBC and NOESY correlation of **18a** in $CDCl_3$



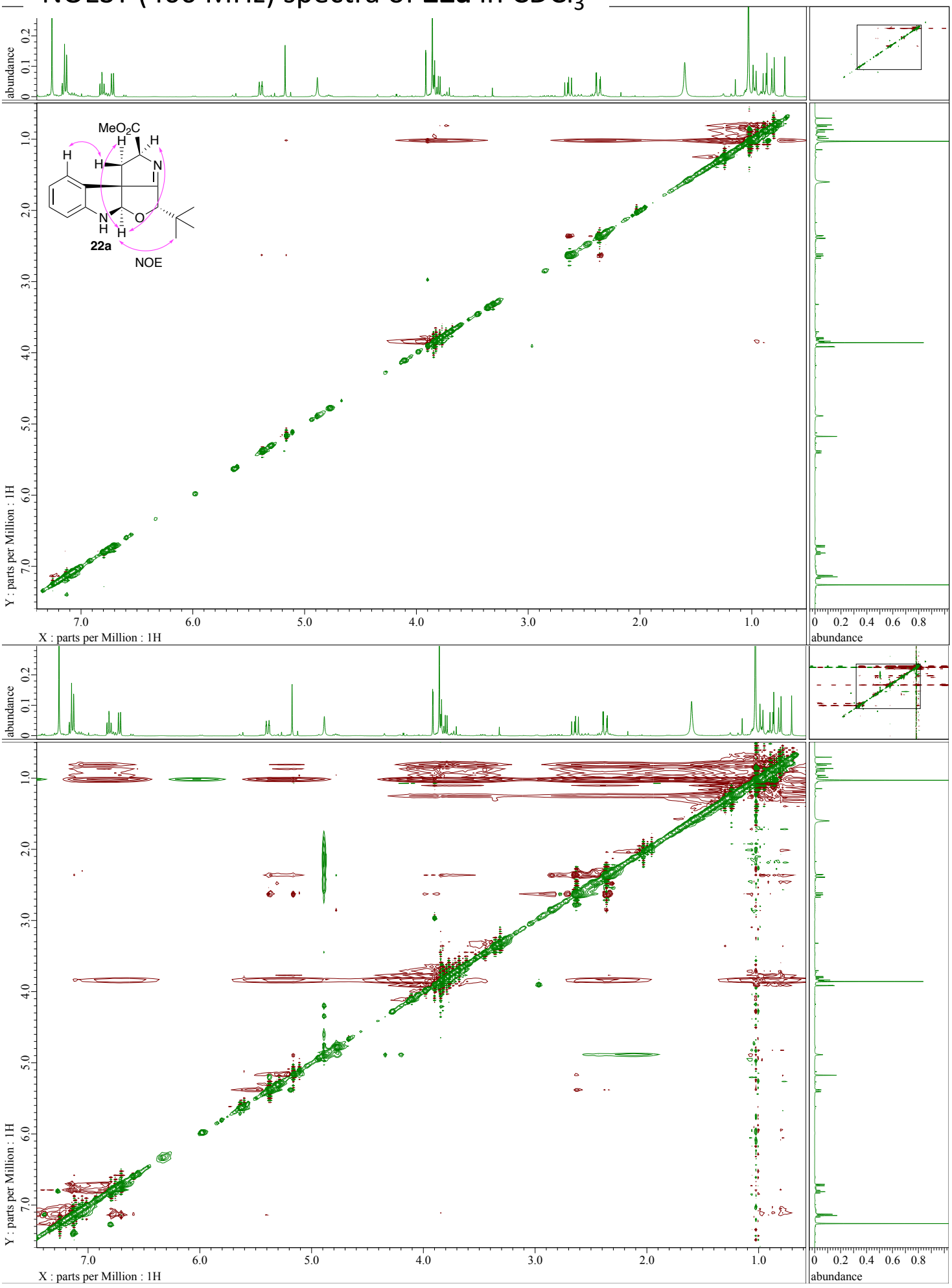


10. NOESY Spectra 0f 21a, 22a and 22b

NOESY (400 MHz) spectra of **21a** in $CDCl_3$



NOESY (400 MHz) spectra of **22a** in $CDCl_3$



NOESY (400 MHz) spectra of **22b** in $CDCl_3$