Electronic Supplementary Information

Synthesis of Tryptophan-containing 2,5-Diketopiperazines via Sequential C–H Activation: Total Syntheses of Tryprostatin A, Maremycins A and B

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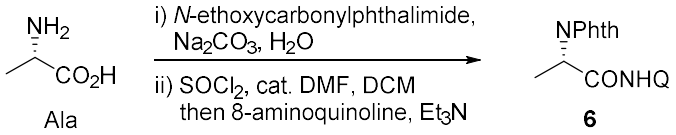
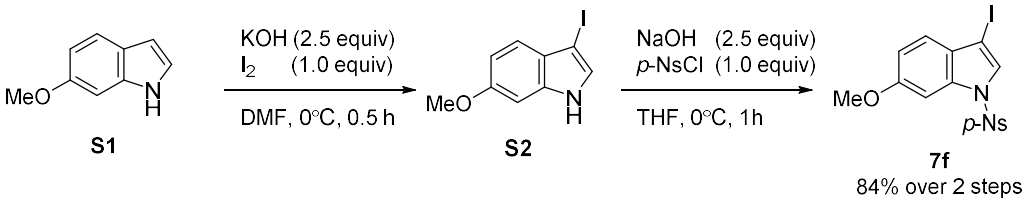
1. General Information

NaOCN and *t*-BuOH was obtained from Aladdin®, $Pd(OAc)_2$ was obtained from Strem®, $AgBF_4$ was obtained from J&K Chemical®, 1,4-Dioxane and 1,2-Dichloroethane was from Energy® without purification. The other materials and solvents were purchased from Adamas® and other commercial suppliers and used without additional purification. Nuclear magnetic resonance (NMR) spectra were recorded with BrukerAVANCE 400 MHz. ^{1}H and ^{13}C chemical shifts are reported in ppm downfield of tetramethylsilane and referenced to residual solvent peak as following: $CDCl_3$= 7.26 (^{1}H NMR), $(CD_3)_2CO$ = 2.05 (^{1}H NMR), $(CD_3)_2SO$ = 2.50 (^{1}H NMR), $CDCl_3$= 77.16 (^{13}C NMR), $(CD_3)_2CO$ = 29.84, 206.26 (^{13}C NMR), $(CD_3)_2SO$ = 39.52 (^{13}C NMR). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, dd = doublet of doublets, ddd = do*u*blet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) for new compounds were recorded on EI-TOF or ESI-TOF. Optical rotations were measured using a 1 mL cell with a 1 dm path length on Perkin Elmer 341 at 589 nm at 20 ºC. Infrared spectra were recorded on a Bruker Vector 22 FT-Infrared spectrometer.

2. Experiment Details and Characterization Data



Compound **6** is a known compound prepared from alanine according to the literature procedure.[1]



To a stirred solution of 6-methoxyindole **S1** (2.94 g, 20 mmol) in DMF (50 mL) was added KOH (2.80 g, 50 mmol). The suspension was then cooled to 0ºC. After 5 min, I_2 (5.10 g, 20 mmol) was added by 5 portions. The mixture was stirred at 0ºC for 30 min under nitrogen, and poured into ice-cold saturated $Na_2S_2O_3$ aqueous. A mass of light brown solid was separated out immediately. Filtered and resolve the residue by EtOAc, dired over $MgSO_4$, filtered and concentrated in vacuo to afford the crude 3-iodo-6-methoxyindole **S2**, which was unstable under air. Dissolved the crude iodo-indole with THF (60 mL) instantly, NaOH (2.0 g, 50 mmol) was added to the stirred solution. The mixture was cooled to 0ºC for 10 min under N_2, *p*-NsCl (5.5 g, 26 mmol) added by portions and the suspension was stirred at 0ºC for 1 hour. The reaction mixture was quenched by glacial acetic acid (5.0 mL), and the aqueous phase was extracted with EtOAc for twice. The combined organic extract was washed three times with saturated $NaHCO_3$ aq., brine, and dried over Na_2SO_4, filtered and concentrated in vacuo. MeOH (10 mL) was added to the brown residue, the suspension stirred under room temperature by 10 min, which was filtered to afford the **7f** (7.6 g, 84% over 2 steps) as a yellow solid.

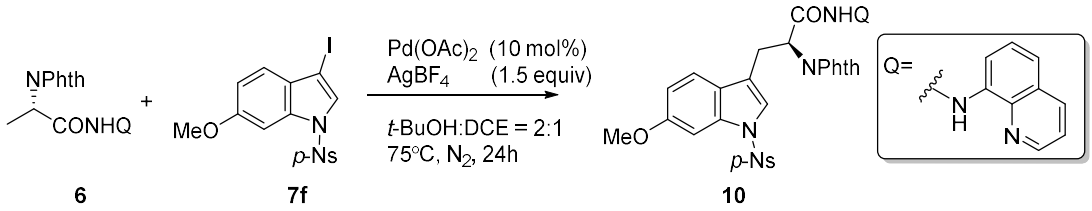
mp 156-157 ºC (decomp.).

IR (neat, cm^{-1}) 2998, 2360, 1531, 1381, 1269, 1106, 1025, 755.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.25 (m, 2H), 8.09 – 8.01 (m, 2H), 7.54 (s, 1H), 7.49 (d, *J* = 2.3 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 6.96 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.90 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 150.9, 143.1, 135.3, 128.2, 128.1, 126.6, 124.8, 123.2, 113.6, 97.9, 69.1, 56.1.

HRMS (EI-TOF) calcd. for $C_{15}H_{11}IN_2O_5S$ (M^+): 457.9436, found: 457.9433.



According to the procedure reported by our group,[1] to a 50 mL-Schlenk reactor was added **6** (2.76 g, 8.0 mmol), **7f** (4.76 g, 10.4 mmol, 1.3 equiv), $AgBF_4$ (2.34 g, 12 mmol, 1.5 equiv) and $Pd(OAc)_2$ (179.6 mg, 0.8 mmol), followed by *t*-BuOH (60 mL) and DCE (30 mL). Nitrogen was charged and the mixture was heated up to 75°C for 24 hours. The suspension was cooled to room temperature and quenched by Et_3N (10 mL). The reaction mixture was filtered through a pad of Celite, concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc/DCM = 4/1/1) to afford **10** (4.32 g, 80%) as a yellow oil.

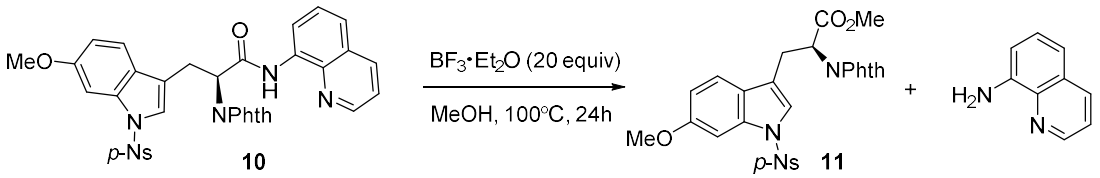
IR (neat, cm^{-1})**:** 3115, 3064, 3019, 2942, 2780, 2701, 2369, 2334, 1776, 1715, 1531, 1378, 1270, 1110, 987, 759.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.76 – 8.63 (m, 1H), 8.52 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.92 (d, *J* = 8.9 Hz, 2H), 7.88 – 7.81 (m, 2H), 7.82 – 7.76 (m, 2H), 7.78 – 7.70 (m, 2H), 7.58 – 7.49 (m, 3H), 7.48 (d, *J* = 2.2 Hz, 1H), 7.43 (s, 1H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.91 (dd, *J* = 8.7, 2.2 Hz, 1H), 5.47 (dd, *J* = 9.3, 6.7 Hz, 1H), 3.91 (dd, *J* = 15.4, 6.6 Hz, 1H), 3.86 (s, 3H), 3.77 (dd, *J* = 15.3, 9.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 165.8, 158.8, 150.4, 148.5, 143.2, 138.5, 136.5, 136.5, 134.6, 133.7, 131.6, 127.9, 127.8, 127.4, 124.4, 124.4, 123.8, 123.1, 122.4, 121.8, 120.5, 120.0, 116.9, 112.9, 98.6, 55.9, 54.3, 24.9.

$[\alpha]^{20}_D$ = -9.0 (*c*=1.0, in $CHCl_3$)

HRMS (ESI) m/z: 698.1306 ($M+Na^+$); calcd. for $C_{35}H_{25}N_5NaO_8S$: 698.1322.



According to the procedure reported by our group,[1] to a 50 mL-Schlenk reactor was added **10** (761 mg, 1.13 mmol), followed by MeOH (15 mL) and $BF_3 \cdot Et_2O$ (2.84 mL, 22.5 mmol). The mixture was heated up to 100°C for 24 hours. After cooled to room temperature saturated $NaHCO_3$ aqueous was added to quench the reaction. The aqueous phase was washed by DCM three times. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc/DCM = 5/1/1) to afford **11** (565 mg, 89%) as a yellow oil, and 8-Aminoquinoline (130 mg, 80%) was recovered.

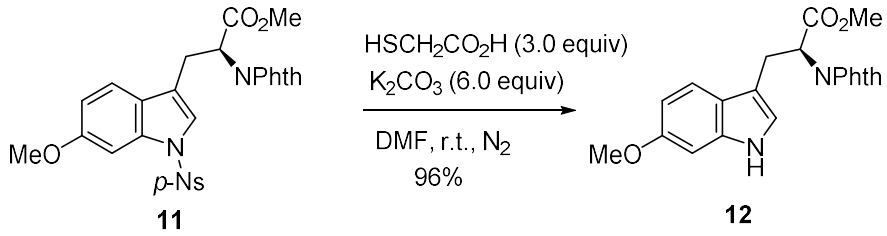
IR (neat, cm^{-1}) 3011, 2944, 2860, 2362, 2336, 2200, 2154, 1715, 1614, 1533, 1382, 1271, 1108, 770, 732.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.05 (m, 2H), 7.92 – 7.84 (m, 2H), 7.84 – 7.74 (m, 4H), 7.48 (d, *J* = 2.3 Hz, 1H), 7.42 (d, *J* = 8.7 Hz, 1H), 7.28 (s, 1H), 6.90 (dd, *J* = 8.7, 2.3 Hz, 1H), 5.23 (dd, *J* = 11.0, 5.0 Hz, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 3.77 – 3.57 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 167.4, 158.7, 150.4, 143.2, 136.3, 134.6, 131.5, 127.8, 124.4, 124.4, 123.7, 122.6, 120.2, 119.9, 112.9, 98.5, 55.9, 53.2, 51.6, 24.7.

$[\alpha]^{20}_D$ = -119.6 (*c*=0.86, in $CHCl_3$).

HRMS (ESI) m/z: 586.0894 ($M+Na^+$); calcd. for $C_{27}H_{21}N_3NaO_9S$: 586.0896.



According to the procedure reported by Dumas,[3] to a stirred solution of **11** (563.5 mg, 1.0 mmol) in DMF (10 mL) was added K_2CO_3 (839.3 mg, 6.0 mmol) and mercaptoacetic acid (276.4 mg, 3.0 mmol). The suspension was stirred under nitrogen for another 1 h at ambient temperature. Acetic acid glacial (0.5 mL) was added to quench the reaction. The suspension was diluted by EtOAc and washed by $NaHCO_3$ aqueous for three times. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc = 2/1) to afford **12** (363.3 mg, 96%) as a yellow oil.

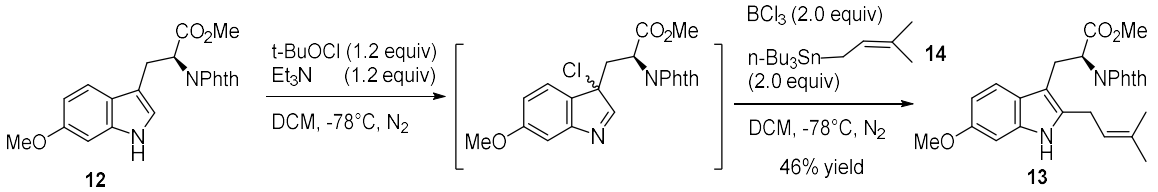
IR (neat, cm^{-1}) 3058, 3011, 2925, 2861, 2699, 2448, 2361, 1711, 1628, 1555, 1457, 1388, 1263, 1160, 1098, 806, 750.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.77-7.72 (m, 2H), 7.69 – 7.60 (m, 2H), 7.44 (d, *J* = 8.5 Hz, 1H), 6.86 (d, *J* = 1.5 Hz, 1H), 6.78 – 6.65 (m, 2H), 5.25 (dd, *J* = 9.7, 6.3 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.74 – 3.63 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 167.7, 156.6, 136.9, 134.1, 131.8, 123.5, 121.7, 121.4, 119.2, 111.2, 109.6, 94.7, 55.7, 52.9, 52.8, 24.9.

$[\alpha]^{20}_D$ = -38.6 (*c*=1.0, in $CHCl_3$).

HRMS (EI-TOF) calcd. for $C_{21}H_{18}N_2O_5$ (M^+): 378.1219, found: 378.1216.



According to the procedure reported by Danishefsky,[4] to a -78ºC solution of **12** (319.4 mg, 0.84 mmol) and Et_3N (140 μL，1.0 mmol) in CH_2Cl_2 (5.0 mL) was added tert-butylhypochlorite (114 μL, 1.0 mmol) slowly via syringe. The solution was then stirred for another 30 min. Organic tin reagent **14** (1.20 g，3.36 mmol) was added followed by rapid addition of BCl_3 (1M in hexane, 1.68 mL). After 2 hours, the solution was quenched by $NaHCO_3$ aqueous, and extracted with EtOAc for three times. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give **13** (172.5 mg, 46%) as a yellow oil.

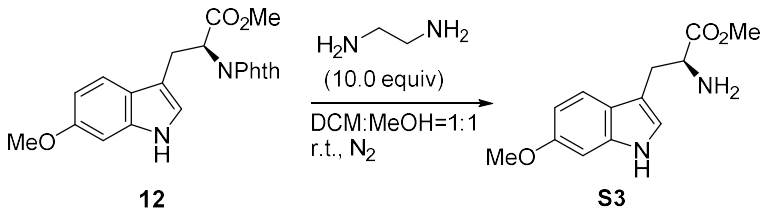
IR (neat, cm^{-1}) 3011, 2405, 2362, 1715, 1445, 1352, 1268, 1100, 756.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 2H), 7.67-7.61 (m, 2H), 7.62 (s, 1H), 7.33 (d, *J* = 8.6 Hz, 1H), 6.68 (d, *J* = 2.2 Hz, 1H), 6.62 (dd, *J* = 8.6, 2.3 Hz, 1H), 5.18 (dd, *J* = 10.2, 5.5 Hz, 1H), 5.14 – 5.03 (m, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 3.67 – 3.56 (m, 2H), 3.41 (dd, *J* = 16.4, 7.4 Hz, 1H), 3.28 (dd, *J* = 16.4, 7.0 Hz, 1H), 1.65 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 167.5, 155.8, 135.9, 134.6, 134.5, 134.0, 131.9, 123.4, 123.0, 120.5, 118.5, 108.8, 105.8, 94.6, 55.7, 52.8, 52.6, 25.7, 25.0, 24.1, 17.8.

$[\alpha]^{20}_D$ = -4.0 (*c*=1.0, in $CHCl_3$).

HRMS (ESI) m/z: 469.1726 ($M+Na^+$); calcd. for $C_{26}H_{26}N_2NaO_5$: 469.1739.



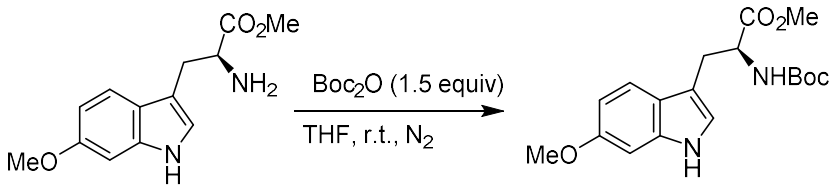
To a solution of **12** (378.4 mg, 1.0 mmol) in CH_2Cl_2 (2.5 mL) and MeOH (2.5 mL) was added ethylenediamine (670 μL, 10.0 mmol) in one portion. The mixture was stirred at 25°C for 2 hours. Concentrated in vacuo, and the residue was purified with flash column chromatography on silica gel (DCM/MeOH = 10:1) to give amino compound **S3** (243.3 mg, 98%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.47 (d, *J* = 8.6 Hz, 1H), 6.93 (d, *J* = 2.0 Hz, 1H), 6.83 (d, *J* = 2.1 Hz, 1H), 6.79 (dd, *J* = 8.6, 2.2 Hz, 1H), 3.83 (s, 3H), 3.83 – 3.78 (m, 1H), 3.71 (s, 3H), 3.24 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.02 (dd, *J* = 14.4, 7.6 Hz, 1H), 1.65 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.9, 156.7, 137.1, 122.0, 121.8, 119.4, 111.2, 109.7, 94.8, 55.7, 55.0, 52.1, 30.9.

$[\alpha]_D^{20}$ = +8.2 (*c*=0.96, in $CHCl_3$).

HRMS (ESI) m/z: 271.1041 ($M+Na^+$); calcd. for $C_{13}H_{16}N_2NaO_3$: 271.1059.



S3 **15**

To a solution of amino substrate **S3** (243.3 mg, 0.98 mmol) in THF (10.0 mL) was added Boc_2O (320.8 mg, 1.47 mmol) in one portion. The mixture was stirred at 25 ºC for 4 hours. Concentrated in vacuo, and the residue was purified with flash column chromatography on silica gel (hexane/ethyl acetate = 2:1) to give **15** (331.0 mg, 97%) as a yellow solid.

mp 105-106 ºC.

IR (neat, cm^{-1}) 3016, 2929, 2853, 2771, 2697, 2370, 2338, 1703, 1630, 1506, 1454, 1365, 1163, 1026.

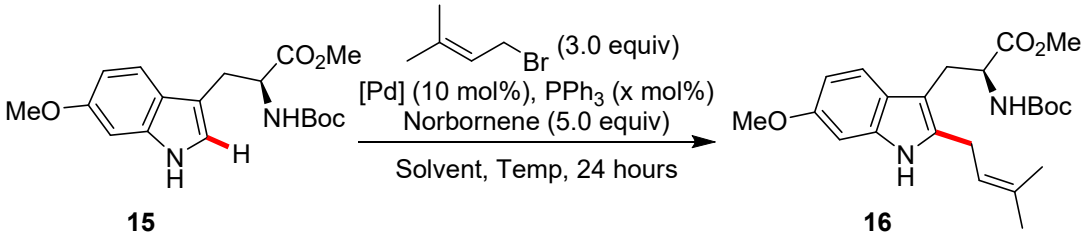
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.40 (d, *J* = 8.6 Hz, 1H), 6.88 (d, *J* = 2.3 Hz, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.78 (dd, *J* = 8.6, 2.3 Hz, 1H), 5.09 (d, *J* = 8.2 Hz, 1H), 4.62 (dt, *J* = 8.4, 5.5 Hz, 1H), 3.83 (s, 3H), 3.67 (s, 3H), 3.24 (d, *J* = 5.5 Hz, 2H), 1.43 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 156.7, 155.4, 137.1, 122.1, 121.6, 119.4, 110.1, 109.8, 94.7, 79.9, 55.7, 54.2, 52.3, 28.4, 28.1.

$[\alpha]^{20}_D$ = +10.3(*c*=0.73, in $CHCl_3$).

HRMS (ESI) m/z: 371.1577 ($M+Na^+$); calcd. for $C_{18}H_{24}N_2NaO_5$: 371.1583.

Table S1. Optimization reaction conditions of Pd-catalyzed C-H prenylation



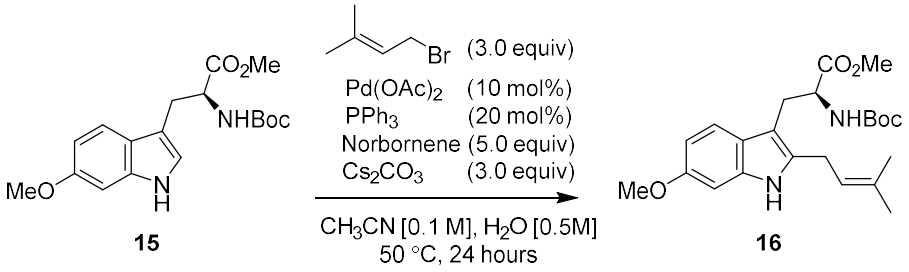
15 **16**

Entry	[Pd] (10 mol%)	PPh_3 (x mol%)	Additive (3.0 equiv)	Solvent	Temp /°C	yield /%
1	$PdCl_2$	20	Cs_2CO_3	Dioxane:DMF=1:1	90	0
2	$PdCl_2$	20	Cs_2CO_3	Dioxane:DMF=1:1	70	0
3	$PdCl_2$	0	K_2CO_3	DMF [0.2 M], H_2O [0.5 M]	90	0
4	$PdCl_2$	0	K_2CO_3	Dioxane [0.2 M], H_2O [0.5 M]	70	0
5	$PdCl_2$	0	K_2CO_3	DMF [0.2 M], H_2O [0.5 M]	50	trace
6	$Pd(OAc)_2$	20	Cs_2CO_3	DMF [0.1 M], H_2O [0.5 M]	50	0
7	$Pd(OAc)_2$	20	Cs_2CO_3	Dioxane [0.1 M], H_2O [0.5 M]	50	0
8	$Pd(OAc)_2$	20	Cs_2CO_3	DMSO [0.1 M], H_2O [0.5 M]	50	0
9	$Pd(OAc)_2$	20	Cs_2CO_3	DMAc [0.1 M], H_2O [0.5 M]	50	0
10	**$Pd(OAc)_2$**	**20**	**Cs_2CO_3**	**CH_3CN [0.1 M], H_2O [0.5 M]**	**50**	**68[a]**
11	$Pd(OAc)_2$	20	Cs_2CO_3	CH_3CN [0.1 M], H_2O [0.5 M]	40	trace
12	$Pd(OAc)_2$	20	Cs_2CO_3	CH_3CN [0.1 M], H_2O [0.5 M]	60	22

[a]Isolated yield and 32% of **15** was recovered

General procedure for the optimization of Pd-catalyzed C-H prenylation:

To a 10 mL-Schlenk reactor was added **15** (34.5 mg, 0.1 mmol), additive (0.3 mmol), PPh_3 (x mol%) and [Pd] (10 mol%), followed by solvents. Prenyl bromide (35.0 μl, 0.3 mmol) and norbornene (47.0 mg, 0.5 mmol) were added to the suspension finally. Nitrogen was charged and the mixture was heated up to indicated Temp for 24 hours. The suspension was cooled to room temperature and extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/ethyl acetate = 4:1) to give **16.**



To a 10 mL-Schlenk reactor was added **15** (69 mg, 0.2 mmol), Cs_2CO_3 (200 mg, 0.6 mmol), PPh_3 (10.4 mg, 0.04 mmol) and $Pd(OAc)_2$ (4.6 mg, 0.04 mmol), followed by CH_3CN (2.0 mL), H_2O (0.4 mL). Prenyl bromide (70.0 µl, 0.6 mmol) and norbornene (94.0 mg, 1 mmol) were added to the suspension finally. Nitrogen was charged and the mixture was heated up to 50ºC for 24 hours. The suspension was cooled to room temperature and extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/ethyl acetate = 4:1) to give **16** (56 mg, 68%) as a colorless oil and **15** was recovered by 32%.

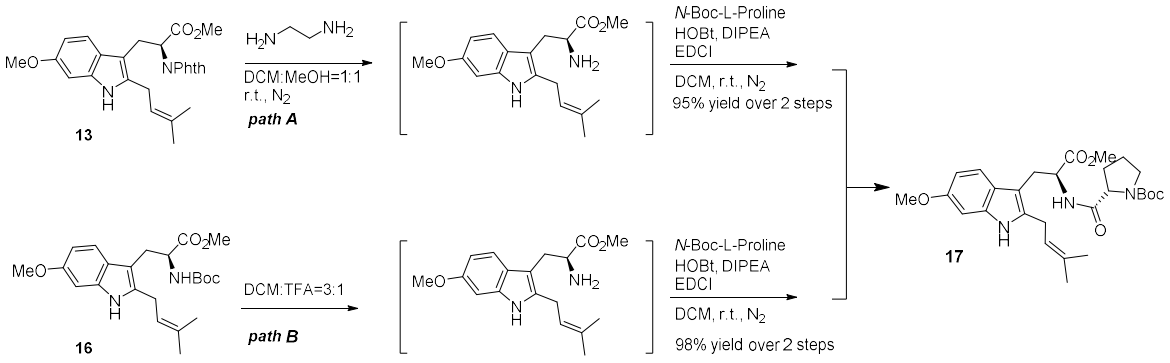
IR (neat, cm^{-1}) 3006, 2378, 2331, 1717, 1463, 1368, 1267, 1164, 754.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.30 (d, *J* = 8.7 Hz, 1H), 6.78 (d, *J* = 2.0 Hz, 1H), 6.73 (dd, *J* = 8.7, 2.0 Hz, 1H), 5.32-5.25 (m, 1H), 5.07 (d, *J* = 7.9 Hz, 1H), 4.58 (dd, *J* = 13.3, 5.5 Hz, 1H), 3.82 (s, 3H), 3.65 (s, 3H), 3.42-3.36 (m, 2H), 3.22-3.17 (m, 2H), 1.79 (s, 3H), 1.76 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 155.9, 155.1, 135.8, 134.7, 123.2, 120.4, 118.7, 108.9, 104.9, 94.4, 79.7, 55.7, 54.1, 52.2, 29.3, 28.3, 27.2, 25.8, 25.0, 17.8.

$[\alpha]^{20}_D$ = +42.0 (*c*=0.39, in $CHCl_3$).

HRMS (ESI) m/z: 439.2188 ($M+Na^+$); calcd. for $C_{23}H_{32}N_2NaO_5$: 439.2209.



Path A: To a solution of **13** (80.0 mg, 0.18 mmol) in CH_2Cl_2 (2.5 mL) and MeOH (2.5 mL) was added ethylenediamine (120.2 μL，1.8 mmol) in one portion. The mixture was stirred at 25ºC for 2 hours. Concentrated in vacuo, brine was added and the residue was extracted with DCM for three times. The organic layer dried over Na_2SO_4 and concentrated in vacuo. The crude product dissolved in dry DCM (4.0 ml) and to the stirred solution was added *N*-Boc-L-Proline (42.6 mg，0.2 mmol), DIPEA (44.6 μL，0.27 mmol), HOBt (24.3 mg, 0.18 mmol), followed by EDCI (44.9 mg，0.24 mmol). The reaction mixture was stirred over night at ambient temperature. Concentrated in vacuo, the residue was purified with flash column chromatography on silica gel (hexane/ethyl acetate = 1:1) to give **17** (87.8 mg, 95% over 2 steps) as a colorless oil.

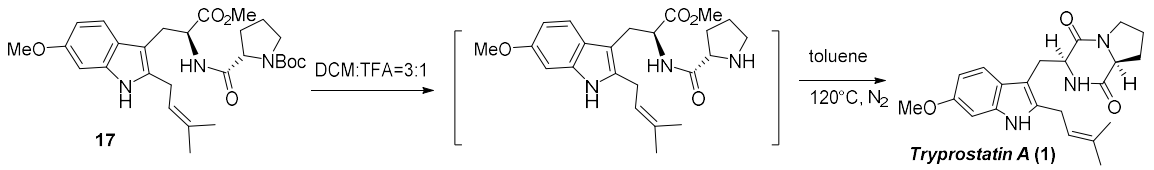
Path B: To a solution of **16** (41.6 mg, 0.1 mmol) in CH_2Cl_2 (3.0 mL) was added TFA (1.0 mL). The mixture was stirred under N_2 atmosphere for 2 hours. Na_2CO_3 aqueous was added to adjust the pH between 7.0~8.0. The solution was extracted with DCM for three times, dried over $MgSO_4$ and concentrated in vacuo. The crude product dissolved in dry DCM (4.0 mL) and to the stirred solution was added *N*-Boc-*L*-Proline (23.7 mg，0.11 mmol), DIPEA (25.0 μL，0.15 mmol), HOBt (HOBt，13.6 mg, 0.1 mmol), followed by EDCI (25.1 mg，0.13 mmol). The reaction mixture was stirred over night at ambient temperature. Concentrated in vacuo, the residue was purified with flash column chromatography on silica gel (hexane/ethyl acetate = 1:1) to give **17** (50.3 mg, 98% over 2 steps) as a colorless oil.

IR (neat, cm^{-1}) 3015, 2380, 2336, 1742, 1676, 1512, 1458, 1389, 1266, 1164, 1032, 914, 752.

^{1}H NMR (400 MHz, CD_3COCD_3) δ 9.69 (s, 1H), 7.36 (d, *J* = 8.6 Hz, 1H), 7.12 (s, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.67 (dd, *J* = 8.6, 2.2 Hz, 1H), 5.32 (t, *J* = 7.2 Hz, 1H), 4.74 (s, 1H), 4.16 (s, 1H), 3.76 (s, 3H), 3.59 (s, 3H), 3.46 (d, *J* = 7.1 Hz, 2H), 3.30 (dd, *J* = 7.6, 6.0 Hz, 2H), 3.25-3.08 (m, 2H), 2.97-2.88 (m, 2H), 2.09 – 1.90 (m, 2H), 1.76 (s, 3H), 1.72 (s, 3H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, Acetone) δ 173.9, 157.4, 138.2, 136.4, 1343, 124.8, 123.0, 119.7, 110.0, 106.4, 96.0, 80.6, 62.0, 56.4, 54.7, 52.9, 48.2, 32.4, 30.6, 29.2, 28.6, 26.6, 26.5, 24.8, 18.7. ; **$[\alpha]^{20}_{D}$** = -30.8 (*c*=0.66, in $CHCl_3$).

HRMS (ESI) m/z: 536.2731 ($M+Na^+$); calcd. for $C_{28}H_{39}N_3NaO_6$: 536.2737.



To a solution of **17** (77.0 mg，0.15 mmol) in CH_2Cl_2 (3.0 mL) was added TFA (1.0 mL). The mixture was stirred under N_2 atmosphere for 2 hours. Na_2CO_3 aqueous was added to adjust the pH between 7.0~8.0. The solution was extracted with DCM for three times, dried over $MgSO_4$ and concentrated in vacuo to afford the crude product. To a 50 mL-Schlenk reactor was added the crude dipeptide, followed by toluene (2.0 mL). Nitrogen was charged and the mixture was heated up to 120 ºC overnight. The suspension was cooled to room temperature and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/acetone = 2:3) to give **1** (39.7 mg，69% over 2 steps) as a colorless oil.

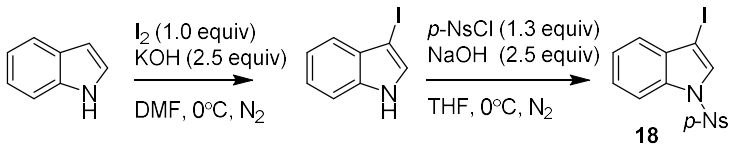
IR (neat, cm^{-1}) 3003, 2931, 2331, 1659, 1458, 1265, 1204, 1158, 1032, 913, 811, 755.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.76 (dd, *J* = 8.6, 2.3 Hz, 1H), 5.66 (s, 1H), 5.32-5.25 (m, 1H), 4.34 (dd, *J* = 11.2, 2.5 Hz, 1H), 4.06 (t, *J* = 7.4 Hz, 1H), 3.82 (s, 3H), 3.72 – 3.54 (m, 3H), 3.46 (dd, *J* = 16.3, 7.6 Hz, 1H), 3.38 (dd, *J* = 15.9, 6.7 Hz, 1H), 2.91 (dd, *J* = 15.0, 11.2 Hz, 1H), 2.41 – 2.28 (m, 1H), 2.09 – 1.97 (m, 2H), 1.95 – 1.85 (m, 1H), 1.76 (s, 3H), 1.73(s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 165.9, 156.4, 136.4, 135.2, 135.2, 122.4, 120.1, 118.4, 109.4, 104.5, 95.0, 59.3, 55.8, 54.7, 45.5, 28.4, 25.8, 25.8, 25.2, 22.7, 18.0.

$[\alpha]^{20}_D$ = -67.5 (*c*=0.825, $CHCl_3$). Lit:[8] **$[\alpha]^{27}_D$** = -69.7 (*c* 0.70, $CHCl_3$).

HRMS (ESI) m/z: 404.1940 ($M+Na^+$); calcd. for $C_{22}H_{27}N_3NaO_3$: 404.1950.



18

To a stirred solution of indole (2.34 g, 20 mmol) in DMF (50 mL) was added KOH (2.80 g, 50 mmol). The suspension was then cooled to 0°C. After 5 min, I_2 (5.10 g, 20 mmol) was added by 5 portions. The mixture was stirred at 0°C for 30 min under nitrogen, and poured into ice-cold saturated $Na_2S_2O_3$ aqueous. A mass of light brown solid was separated out immediately. Filtered and resolve the residue by EtOAc, dired over $MgSO_4$, filtered and concentrated in vacuo to afford the crude 3-Iodo-indole, which was unstable under air. Dissolved the crude iodo-indole with THF (60 mL) instantly, NaOH (2.0 g, 50 mmol) was added to the stirred solution. The mixture was cooled to 0°C for 10 min under N_2, *p*-NsCl (5.5 g, 26 mmol) added by portions and the suspension was stirred at 0°C for 1 hour. The reaction mixture was quenched by glacial acetic acid (5.0 mL), and the aqueous phase was extracted with EtOAc twice. The combined organic extract was washed three times with saturated $NaHCO_3$ aq., brine, and dried over Na_2SO_4, filtered and concentrated in vacuo. MeOH (10 mL) was added to the brown residue, the suspension stirred under room temperature by 10 min, which was filtered to afford the **18** (7.54 g, 88% over 2 steps) as a yellow solid.

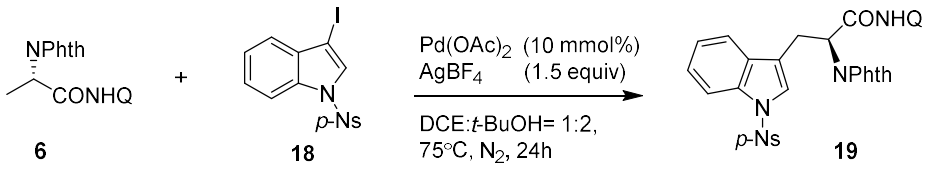
mp 187-190 °C (decomp.).

IR (neat, cm^{-1}) 2332, 1542, 1444, 1380, 1179, 1126, 748.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.25 (m, 2H), 8.12 – 8.03 (m, 3H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.68 (s, 1H), 7.45-7.33 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.9, 143.1, 134.3, 132.8, 129.4, 128.3, 126.5, 124.9, 124.8, 122.6, 113.3, 69.2.

HRMS (EI-TOF) calcd. for $C_{14}H_9IN_2O_4S$ (M^+): 427.9328, found: 427.9328.



To a 500 mL flask was added **6** (6.9 g, 20 mmol), **18** (12.8g, 30 mmol) and $Pd(OAc)_2$ (449 mg, 2 mmol), $AgBF_4$ (5.84 g, 30 mmol), followed by *t*-BuOH (140 mL) and DCE (70 mL). Nitrogen was charged and the mixture was heated up to 75ºC for 24 hours. The suspension was cooled to room temperature and quenched by Et_3N (40 mL). The reaction mixture was filtered through a pad of Celite, concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc/DCM = 4/1/1) to afford **19** (10.55 g, 82%) as a yellow oil.

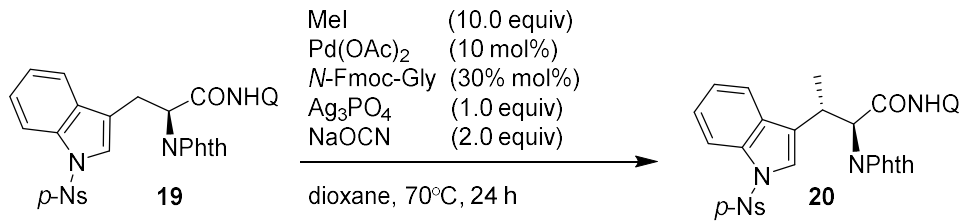
IR (neat, cm^{-1}) 3067, 3020, 2932, 2695, 2585, 2467, 2339, 1946, 1890, 1775, 1715, 1602, 1533, 1380, 1179, 977, 783.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33 (s, 1H), 8.78 – 8.71 (m, 1H), 8.51 (dd, *J* = 4.4, 1.7 Hz, 1H), 8.16 (d, *J* = 8.3 Hz, 1H), 7.98 – 7.94 (m, 1H), 7.94 – 7.89 (m, 2H), 7.83 (td, *J* = 6.2, 2.6 Hz, 4H), 7.79 – 7.74 (m, 2H), 7.69 (d, *J* = 7.3 Hz, 1H), 7.58 (s, 1H), 7.57 – 7.53 (m, 2H), 7.44 – 7.28 (m, 3H), 5.52 (dd, *J* = 9.2, 6.7 Hz, 1H), 3.98 (ddd, *J* = 15.2, 6.7, 1.1 Hz, 1H), 3.81 (ddd, *J* = 15.2, 9.2, 1.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 165.8, 150.3, 148.4, 143.1, 138.3, 136.4, 135.2, 134.6, 133.6, 131.6, 130.7, 127.9, 127.8, 127.3, 125.7, 124.4, 124.3, 124.3, 123.8, 122.3, 121.8, 119.9, 119.9, 116.8, 113.7, 54.2, 24.9.

$[\alpha]^{20}_D$ = -34.6 (*c*=0.96, in $CHCl_3$).

HRMS (ESI) m/z: 668.1213 ($M+Na^+$); calcd. for $C_{34}H_{23}N_5NaO_7S$: 668.1216.



According to the procedure reported by our group [6], to a 250 mL-Schlenk reactor was added **19** (2.58 g, 4 mmol), NaOCN (520 mg, 8 mmol)，*N*-Fmoc-Glycine (356 mg, 1.2 mmol), $Pd(OAc)_2$ (90 mg, 0.4 mmol) and Ag_3PO_4 (1.67 g, 4 mmol) , followed by Dioxane (70 mL) and MeI (2.5 mL，40 mmol). Nitrogen was charged and the mixture was heated up to 70ºC for 24 hours. The suspension was cooled to room temperature and quenched by Et_3N (2 mL). The reaction mixture was filtered through a pad of Celite, concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc/DCM = 4/1/1) to afford **20** (2.3 g，84%) as a yellow oil.

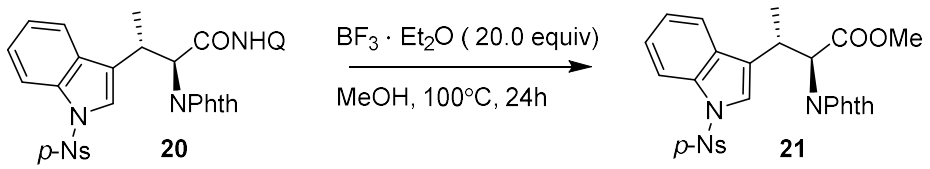
IR (neat, cm^{-1}) 3107, 3063, 2929, 2694, 2625, 2443, 2336, 1718, 1607, 1531, 1377, 1179, 1126, 780, 731.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (s, 1H), 8.87 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.82-8.76 (m, 1H), 8.19 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.94 (d, *J* = 8.9 Hz, 2H), 7.91 – 7.86 (m, 1H), 7.82 (d, *J* = 8.9 Hz, 2H), 7.78 – 7.73 (m, 1H), 7.69 – 7.64 (m, 2H), 7.64-7.59 (m, 2H), 7.59 – 7.53 (m, 2H), 7.49 (s, 1H), 7.47 (d, *J* = 4.3 Hz, 1H), 7.30 – 7.25 (m, 2H), 5.38 (d, *J* = 11.3 Hz, 1H), 4.77-4.67 (m, 1H), 1.63 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 165.8, 150.2, 148.7, 143.1, 138.7, 136.3, 135.1, 134.5, 134.0, 131.1, 129.8, 127.9, 127.7, 127.3, 125.7, 125.5, 124.3, 124.1, 123.6, 122.7, 122.6, 121.8, 120.5, 117.2, 113.5, 60.7, 30.2, 19.7.

$[\alpha]^{20}_D$ = -62.1 (*c*=0.98, in $CHCl_3$).

HRMS (ESI) m/z: 682.1364 ($M+Na^+$); calcd. for $C_{35}H_{25}N_5NaO_7S$: 682.1372.



To a 100 mL-Schlenk reactor was added **20** (1.1 g, 1.67 mmol), followed by MeOH (40 mL) and $BF_3 \cdot Et_2O$ (3.3 mL, 30.4 mmol). The mixture was heated up to 100 ^oC for 24 hours. After cooled to room temperature saturated $NaHCO_3$ aqueous was added to quench the reaction. The aqueous phase was washed by DCM three times. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc/DCM = 5/1/1) to afford **21** (594 mg, 65%) as a yellow oil.

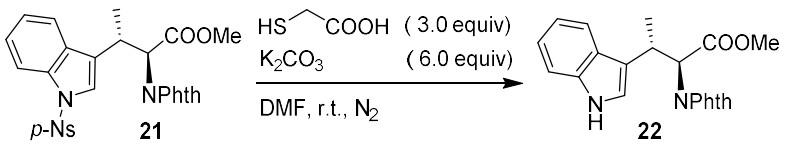
IR (neat, cm^{-1}) 3066, 3029, 2936, 2759, 2693, 2595, 2469, 2360, 1719, 1533, 1382, 1181, 1007, 858, 743.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.01 (m, 2H), 7.91-7.85 (m, 2H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.65-7.57 (m, 5H), 7.41 (s, 1H), 7.27 – 7.16 (m, 2H), 5.05 (d, *J* = 10.0 Hz, 1H), 4.28-4.16 (m, 1H), 3.73 (s, 3H), 1.63 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 167.2, 150.4, 143.2, 134.9, 134.4, 131.2, 130.0, 128.0, 125.6, 125.5, 124.4, 124.0, 123.5, 123.2, 120.5, 113.5, 56.2, 52.9, 31.1, 19.8.

$[\alpha]^{20}_D$ = -104.2 (*c*=0.95, in $CHCl_3$).

HRMS (ESI) m/z: 570.0944 ($M+Na^+$); calcd. for $C_{27}H_{21}N_3NaO_8S$: 570.0947.



To a stirred solution of **21** (547.5 mg, 1.0 mmol) in DMF (10 mL) was added K_2CO_3 (839.3 mg, 6.0 mmol) and mercaptoacetic acid (276.4 mg, 3.0 mmol). The suspension was stirred under nitrogen for another 1 h at ambient temperature. Acetic acid glacial (0.5 mL) was added to quench the reaction. The suspension was diluted by EtOAc and washed by $NaHCO_3$ aqueous for three times. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc = 2/1) to afford **22** (337.0 mg, 93%) as a yellow oil.

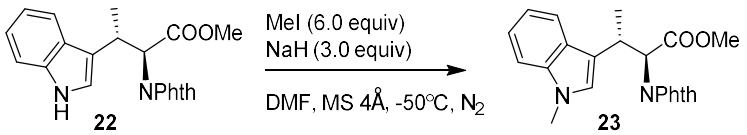
IR (neat, cm^{-1}) 3001, 2927, 2374, 2329, 1713, 1614, 1462, 1385, 1267, 1117, 1096, 1011, 755.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.60-7.54 (m, 2H), 7.54-7.47 (m, 2H), 7.16 – 7.11 (m, 1H), 7.04 – 6.93 (m, 3H), 5.09 (d, *J* = 10.1 Hz, 1H), 4.33-4.22 (m, 1H), 3.74 (s, 3H), 1.65 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 167.3, 136.0, 133.8, 131.3, 126.3, 123.1, 122.0, 121.7, 119.3, 119.2, 117.0, 111.0, 57.1, 52.5, 31.2, 20.2.

$[\alpha]^{20}_D$ = -105.7 (*c*=0.92, in $CHCl_3$).

HRMS (ESI) m/z: 385.1152 ($M+Na^+$); calcd. for $C_{21}H_{18}N_2NaO_4$: 385.1164.



To a 50 mL flask was added **22** (181 mg, 0.5 mmol), 4 A molecular sieve (75.0 mg), followed by dry DMF (5 mL). The stirred mixture was charged with nitrogen and cooled to -50°C for 10 min. NaH (60% dispersion in mineral oil, 60 mg, 1.5 mmol) was added cautiously. After 10 min, MeI (187 μL，3 mmol) was added by one portion. The reaction stirred for another 30 min, which was quenched by glacial acetic acid (0.2 mL). The mixture was extracted with EtOAc and $NaHCO_3$ aqueous. The water layer was washed by EtOAc for three times. The combined organic layer washed by brine and dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/EtOAc = 4/1) to afford **23** (144.9 mg，77%) as a yellow oil.

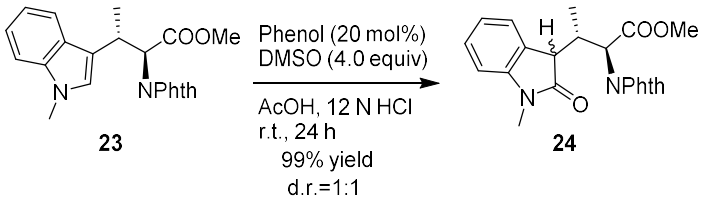
IR (neat, cm^{-1}) 3060, 2937, 2693, 2637, 2473, 2361, 1714, 1614, 1466, 1383, 1265, 1199, 1008, 735.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 3H), 7.58-7.51 (m, 2H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.01 – 6.95 (m, 1H), 6.87 (s, 1H), 5.08 (d, *J* = 10.0 Hz, 1H), 4.31-4.21 (m, 1H), 3.74 (s, 3H), 3.60 (s, 3H), 1.64 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 167.4, 136.7, 133.8, 131.5, 126.8, 126.6, 123.2, 121.4, 119.5, 118.8, 115.7, 109.0, 57.1, 52.5, 32.7, 31.2, 20.3.

$[\alpha]^{20}_D$ = -106.1 (*c*=0.93, in $CHCl_3$).

HRMS (ESI) m/z: 399.1311 ($M+Na^+$); calcd. for $C_{22}H_{20}N_2NaO_4$: 399.1321.



According to the procedure reported by Jia[7], to a solution of **23** (682.0 mg, 1.81 mmol) in acetic acid (3.6 mL) at ambient temperature was added 12 N aq. HCl (0.5 mL), DMSO (565.7 mg, 7.2 mmol) and phenol (34.1 mg，0.36 mmol) successively. The reaction mixture was stirred at room temperature for 24 h and then neutralized by Na_2CO_3 aqueous. The suspension extracted with EtOAc for three times. The combined organic layer dried over $MgSO_4$, filtered and the solvent was removed under pressure and the residue was purified with flash column chromatography on silica gel (hexane/EtOAc = 2/1) to afford **24** as a 1:1 diastereomer mixture (703.1 mg, 99%) as a colorless oil.

A sample of pure diastereomer of **24** was obtained by preparative TLC and the spectroscopic data were as follows, the absolute configuration of C3-position of oxindole was not determined since the configuration would not be retained during the oxidation (**25 →26**).

IR (neat, cm^{-1}) 3018, 2927, 2368, 1719, 1613, 1464, 1382, 1268, 1211, 753.

One diastereomer of **24:**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.84 (m, 2H), 7.77 – 7.69 (m, 2H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.29-7.23 (m , 1H), 7.09 (t, *J* = 7.3 Hz, 1H), 6.72 (d, *J* = 7.7 Hz, 1H), 5.20 (d, *J* = 8.5 Hz, 1H), 3.73 (s, 3H), 3.69-3.66 (m, 1H), 3.63 – 3.53 (m, 1H), 3.00 (s, 3H), 0.99 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.7, 169.8, 167.9, 144.6, 134.2, 132.1, 128.2, 128.0, 123.9, 123.7, 122.7, 107.9, 55.3, 52.8, 47.1, 35.0, 25.9, 14.2;

$[\alpha]^{20}_D$ = -1.7 (*c*=0.95, in $CHCl_3$).

HRMS (ESI) m/z: 415.1259 ($M+Na^+$); calcd. for $C_{22}H_{20}N_2NaO_5$: 415.1270.

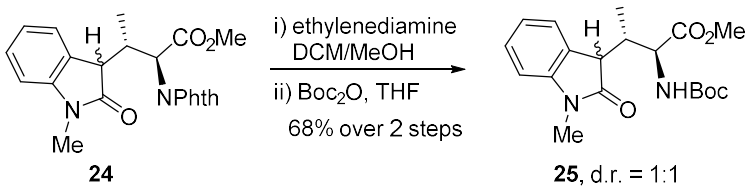
The other diastereomer of **24:**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.59 (m, 4H), 7.24 (d, *J* = 6.2 Hz, 1H), 6.96 – 6.78 (m, 1H), 6.39 (dd, *J* = 8.0, 1.6 Hz, 1H), 4.96 (d, *J* = 11.2 Hz, 1H), 3.75 – 3.60 (m, 4H), 3.43-3.36 (m, 1H), 3.09 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.9, 168.9, 167.1, 143.8, 134.0, 131.5, 127.6, 126.5, 124.6, 123.4, 122.3, 107.6, 54.4, 52.7, 48.7, 33.7, 26.2.

$[\alpha]^{20}_{D}$ = -49.4 (*c*=0.98, in $CHCl_3$).

HRMS (ESI) m/z: 415.1265 ($M+Na^+$); calcd. for $C_{22}H_{20}N_2NaO_5$: 415.1270.



24 **25**, d.r. = 1:1

To a solution of **24** (703.1 mg, 1.79 mmol, d.r. = 1:1) in CH_2Cl_2 (5.0 mL) and MeOH (5.0 mL) was added ethylenediamine (1.2 ml，17.9 mmol) in one portion. The mixture was stirred at 25 °C for 2 hours. Concentrated in vacuo, brine was added and the residue was extracted with THF (5 mL × 4). To the combined organic layer was added Boc_2O (586.0 mg, 2.7 mmol). The reaction was stirred at ambient temperature under nitrogen. After 4 hours, the mixture was concentrated in vacuo and the residue was purified with flash column chromatography on silica gel (hexane/EtOAc = 2/1) to afford **25** as a 1:1 diastereomer mixture (441.1 mg, 68% over 2 steps, d.r. = 1:1) as a colorless oil.

A sample of pure diastereomer of **25** was obtained by preparative TLC and the spectroscopic data were as follows, the absolute configuration of C3-position of oxindole was not determined since the configuration would not be retained during the oxidation (**25 →26**).

IR (neat, cm^{-1}) 2932, 2337, 1701, 1612, 1519, 1466, 1364, 1264, 1165, 1083, 1016, 758.

One diastereomer of **25:**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 2H), 7.19 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 4.47 (dd, *J* = 8.2, 4.8 Hz, 1H), 3.78 (s, 3H), 3.48 (s, 1H), 3.21 (s, 3H), 2.95-2.84 (m, 1H), 1.46 (s, 9H), 0.86 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 173.1, 156.6, 144.4, 128.5, 127.9, 126.8, 123.4, 123.1, 108.3, 79.6, 58.4, 52.4, 48.1, 36.7, 28.6, 26.4, 12.9.

$[\alpha]^{20}_D$ = -17.9 (*c*=0.85, in $CHCl_3$).

HRMS (ESI) m/z: 385.1726 ($M+Na^+$); calcd. for $C_{19}H_{26}N_2NaO_5$: 385.1739.

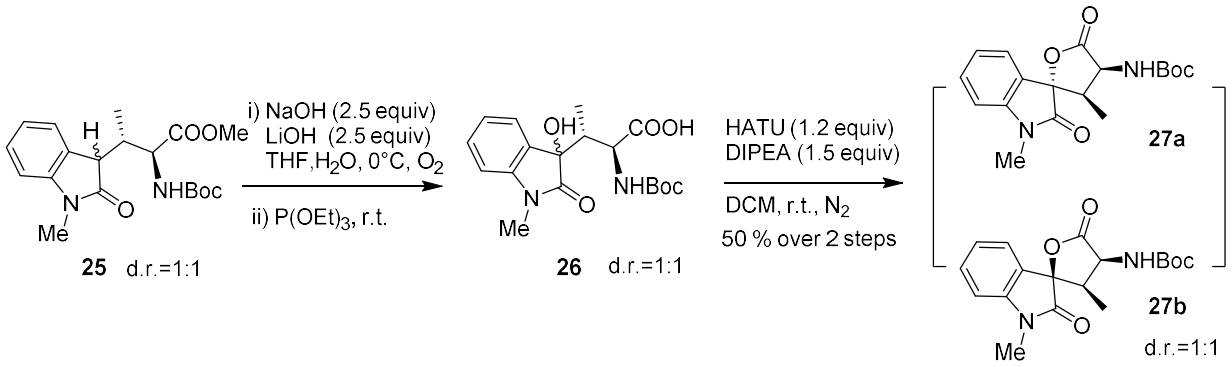
The other diastereomer of **25:**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.7 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 5.33 (d, *J* = 9.7 Hz, 1H), 4.60-4.50 (m, 1H), 3.70 (s, 3H), 3.63 (d, *J* = 2.4 Hz, 1H), 3.21 (s, 3H), 2.66-2.56 (m, 1H), 1.44 (s, 9H), 0.69 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.24, 172.55, 155.41, 144.59, 128.19, 126.06, 125.29, 122.76, 108.05, 80.27, 56.52, 52.15, 46.87, 38.59, 28.29, 26.25, 12.79.

$[\alpha]^{20}_{D}$ = -17.5 (*c*=0.53, in $CHCl_3$).

HRMS (ESI) m/z: 385.1718 ($M+Na^+$); calcd. for $C_{19}H_{26}N_2NaO_5$: 385.1739.



According to the procedure reported by Jia[7], to a solution of **25** (332.4 mg, 0.92 mmol, d.r. = 1:1) in THF/H_2O (5.0 mL/2.5 mL) was added NaOH (92.0 mg，2.3 mmol) and LiOH (55.1 mg, 2.3 mmol) at 0ºC. The mixture was bubbled with oxygen for 6 hours at the same temperature. $P(OEt)_3$ (631.0 μL, 3.68 mmol) was added and the resulting mixture was allowed to warm to room temperature and stirred for 2 hours. The reaction solution was adjusted to pH 7.0 with AcOH and extracted with EtOAc. The organic layer dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product **26** was dissolved in DCM (10.0 mL), to which was added DIPEA (304.1μl, 1.84 mmol) and HATU (524.7 mg，1.38 mmol). The reaction was stirred at amient temperature overnight under nitrogen. The mixture was concentrated in vacuo and the residue was separated with flash column chromatography on silica gel (hexane/EtOAc = 3/1) to afford **27** as a 1:1 diastereomer mixture (159.3 mg，50 % over 2 steps, d.r. = 1:1) as a colorless oil.

A sample of pure **27a** and **27b** were obtained by preparative TLC and the spectroscopic data were as follows. The absolute configuration of C3-position of oxindole in **27a** and **27b** was determined by the transformation to maremycins A and B.

27a:

IR (neat, cm^{-1}) 3067, 2987, 2924, 2377, 2339, 1792, 1717, 1617, 1506, 1466, 1376, 1319, 1266, 1160, 1009, 754.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (td, *J* = 7.8, 1.0 Hz, 1H), 7.35 (d, *J* = 7.2 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.22 (d, *J* = 10.7 Hz, 1H), 4.89 (dd, *J* = 10.7, 9.0 Hz, 1H), 3.22 (s, 3H), 2.90-2.80 (m, 1H), 1.47 (s, 9H), 0.88 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 173.8, 155.8, 144.5, 131.7, 124.5, 124.3, 124.2, 109.2, 86.5, 80.4, 52.3, 41.5, 28.5, 26.6, 7.6.

$[\alpha]^{20}_D$ = -8.3 (*c*=0.67, in $CHCl_3$).

HRMS (ESI) m/z: 369.1419 ($M+Na^+$); calcd. for $C_{18}H_{22}N_2NaO_5$: 369.1426.

27b：

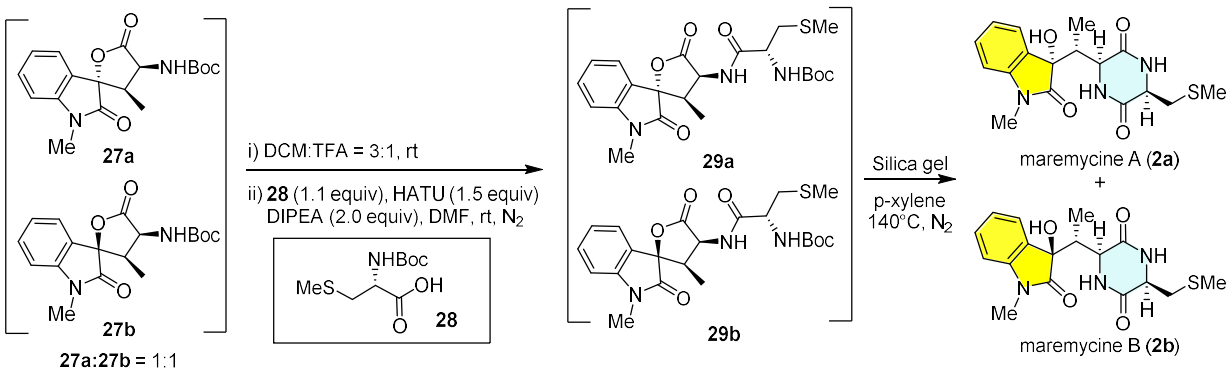
IR (neat, cm^{-1}) 3064, 3011, 2928, 2372, 2333, 1795, 1716, 1616, 1517, 1467, 1370, 1266, 1166, 1095, 994, 752.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (td, *J* = 7.8, 1.1 Hz, 1H), 7.31 (d, *J* = 7.0 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 5.73 – 5.56 (m, 1H), 5.07 (d, *J* = 3.0 Hz, 1H), 3.18 (s, 3H), 3.17 – 3.04 (m, 1H), 1.46 (s, 9H), 1.05 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 174.4, 155.1, 144.4, 131.2, 126.8, 123.0, 122.8, 109.0, 84.0, 80.5, 53.2, 41.1, 28.2, 26.3, 11.4.

$[\alpha]^{20}_D$ = -11.9 (*c*=0.46, in $CHCl_3$).

HRMS (ESI) m/z: 369.1416 ($M+Na^+$); calcd. for $C_{18}H_{22}N_2NaO_5$: 369.1426.



To a solution of **27** (159.3 mg，0.46 mmol， d.r.=1:1) in CH_2Cl_2 (3.0 mL) was added TFA (1.0 mL). The mixture was stirred under nitrogen for 2 hours. Na_2CO_3 aqueous was added to adjust the pH between 7.0~8.0. The solution was extracted with DCM for three times, dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in DMF (3.0 mL), to which was added DIPEA (152.0 μL, 0.92 mmol) and *N*-Boc-*S*-methyl-L-cysteine **28**[11] (119.1 mg，0.51 mmol) followed by HATU (262.4 mg， 0.69 mmol). The reaction was stirred at ambient temperature under nitrogen for 4 hours. The mixture was extracted with EtOAc and the organic layer washed with 1 M HCl, Na_2CO_3 aqueous and brine in sequence. The solvent was removed under reduced pressure and the residue **29** was transferred to a 50 mL-Schlenk reactor with *p*-xylene (3.0 mL), to which was added SiO_2 (240.0 mg) and charged with nitrogen. The suspension was heated up to 140°C and stirred overnight. The solvent was removed under reduced pressure and the residue was purified with flash column chromatography on silica gel (hexane/DCM/acetone = 1/1/1) to afford maremycin A **2a** (60.1 mg, 36% over 3 steps) and maremycin B **2b** (63.6 mg, 38% over 3 steps) separately as a white solid.

Maremycin A (**2a**):

mp 228-230 °C.

IR (neat, cm^{-1}) 3005, 2926, 2473, 2333, 1710, 1464, 1268, 912, 755.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8ZJDN 7.93 (s, 1H), 7.58 (s, 1H), 7.37 (d, *J*= 7.3 Hz, 1H), 7.32 (t, *J*= 7.7 Hz, 1H), 7.05 (t, *J*= 7.6 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 4.89 (s, 1H), 4.31-4.22 (m, 1H), 3.10 (s, 3H), 2.98 (dd, *J*= 4.0, 14.0 Hz, 1H), 2.80 (dd, *J*= 14.0, 4.0 Hz, 1H), 2.09 (s, 3H), 2.08-2.01 (m, 1H), 1.12 (d, *J*= 7.2 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 178.0, 168.0, 165.7, 143.0, 130.6, 129.2, 125.0, 121.9, 108.5, 76.4, 54.3, 53.6, 43.1, 36.4, 25.9, 16.4, 8.3.

[α]$^{20}_{D}$ = -111.3 (*c* 0.24, MeOH); Lit:[9] **[α]$^{25}_{D}$** = -120.95 (*c* 0.21, MeOH); Lit:[7] **[α]$^{25}_{D}$** = -115.5 (*c* 0.30, MeOH).

HRMS (ESI) m/z: 386.1146 ($M+Na^+$); calcd. for $C_{17}H_{21}N_3NaO_4S$: 386.1150.

Maremycin B (**2b**):

mp 211-214 ºC

IR (neat, cm^{-1}) 3111, 3065, 3011, 2921, 2703, 2622, 2361, 1664, 1461, 1375, 1095, 783.

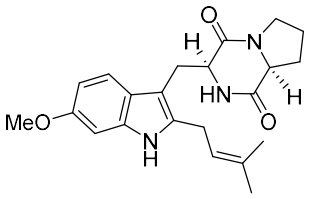
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (d, *J* = 2 Hz, 1H), 7.70 (d, *J* = 2 Hz, 1H), 7.38-7.26 (m, 2H), 7.08 (t, *J*= 7.6 Hz, 1H), 7.02 (d, *J*= 7.6 Hz, 1H), 6.91 (s, 1H), 4.57-4.52 (m, 1H), 4.20-4.13 (m, 1H), 3.11 (s, 3H), 2.97 (dd, *J* = 14.0, 4.8 Hz, 1H), 2.83 (dd, *J*= 14.0, 3.9 Hz, 1H), 2.32 (qd, *J* = 7.2, 6.8 Hz, 1H), 2.11 (s, 3H), 0.86 (d, *J*= 7.1 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 176.3, 167.4, 166.2, 143.0, 131.4, 129.2, 123.9, 122.4, 108.6, 77.2, 55.5, 54.4, 43.6, 36.9, 25.8, 16.2, 9.8.

[α]$^{20}_{D}$ = +69.8 (*c* 0.78, MeOH); Lit:[9] **[α]$^{25}_{D}$** = +2.94 (*c* 0.21, MeOH); Lit:[7] **[α]$^{25}_{D}$** = +78.3 (*c* 0.28, MeOH).

HRMS (ESI) m/z: 386.1175 ($M+Na^+$); calcd. for $C_{17}H_{21}N_3NaO_4S$: 386.1150.

3. Comparison of NMR Data of Natural and Synthetic Compounds



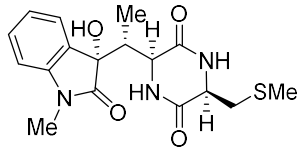
1: *Tryprostatin A*

Table S1. NMR data comparison of synthetic and natural[8] **Tryprostatin A**[a]

^{1}H NMR		^{13}C NMR	
Natural[b]	**This work**[c]	**Natural**[d]	**This work**[e]
7.88 (brs, 1H)	7.97 (s, 1H)	169.35	169.43
7.34 (d, *J* = 8.8Hz, 1H)	7.34 (d, *J* = 8.6 Hz, 1H)	165.82	165.94
6.83 (d, *J* = 2.4Hz, 1H)	6.83 (d, *J* = 2.2 Hz, 1H)	156.37	156.48
6.76 (dd, *J* = 8.8, 2.4 Hz, 1H)	6.76 (dd, *J* = 8.6, 2.3 Hz, 1H)	136.28	136.43
5.65 (brs, 1H)	5.66 (s, 1H)	135.25	135.25
5.29 (br dd, *J* = 7.0, 6.5 Hz, 1H)	5.32-5.25 (m, 1H)	135.11	135.25
4.34 (br dd, *J* = 11.2, 3.5 Hz, 1H)	4.34 (dd, *J* = 11.2, 2.5 Hz, 1H)	122.30	122.44
4.06 (br dd, *J* = 7.8, 7.3Hz, 1H)	4.06 (t, *J* = 7.4 Hz, 1H)	119.97	120.14
3.83 (s, 3H)	3.82 (s, 3H)	118.36	118.45
3.67 (ddd, *J* = 12.7, 8.8, 2.9 Hz, 1H)	3.72 – 3.54 (m, 3H)	109.35	109.43
3.63 (dd, *J* = 15.1, 3.5Hz, 1H)		104.46	104.55
3.58 (ddd, *J* = 12.7, 8.8, 2.9 Hz, 1H)		94.89	95.06
3.46 (dd, *J* = 16.5, 7.0 Hz, 1H)	3.46 (dd, *J* = 16.3, 7.6 Hz, 1H)	59.29	59.39
3.40 (dd, *J* = 16.5, 6.5 Hz, 1H)	3.38 (dd, *J* = 15.9, 6.7 Hz, 1H)	55.77	55.89
2.91 (dd, *J* = 15.1, 11.2 Hz, 1H)	2.91 (dd, *J* = 15.0, 11.2 Hz, 1H)	54.57	54.73
2.33 (m, 1H)	2.41 – 2.28 (m, 1H)	45.43	45.52
2.08-1.97 (m, 2H)	2.09 – 1.97 (m, 2H),	28.38	28.48
1.95-1.85 (m, 1H)	1.95 – 1.85 (m, 1H),	25.76	25.83
1.78 (s, 3H)	1.76 (s, 3H)	25.68	25.80
1.75 (s, 3H)	1.73 (s, 3H)	25.10	25.23

		22.65	22.75
		17.98	18.06

[a] All data were recorded in $CDCl_3$ and to the solvent signal (7.26 ppm for ^{1}H, 77.16 ppm for ^{13}C); [b] Measured at 500 MHz, δ [ppm, mult, *J* (Hz)]; [c] Measured at 125 MHz, δ (ppm); [d] Measured at 400 MHz, δ [ppm, mult, *J* (Hz)]; [e] Measured at 101 MHz, δ (ppm).



maremycine A (2)

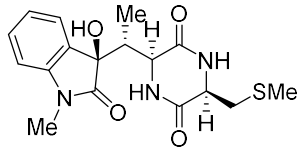
Table S2. NMR data comparison of synthetic and published Maremycin A [a]

^{1}H NMR			**^{13}C NMR**		
Natural[b]	**Synthesized by Jia[c]**	**This work[d]**	**Natural[e]**	**Synthesized by Jia[f]**	**This work[g]**
8.60 (s, br, 1H)	8.64 (br s, 1H)	8.65 (s, 1H)	177.9	178.0	178.0
7.88 (s, 1H)	7.92 (br s, 1H)	7.93 (s, 1H)	167.9	168.0	168.0
7.53 (s, 1H)	7.59 (br s, 1H)	7.58 (s, 1H)	165.6	165.7	165.7
7.37 (m, 2H)	7.37 (d, *J* = 7.6 Hz, 1H)	7.37 (d, *J*= 7.3 Hz, 1H)	143.0	143.0	143.0
	7.33 (t, *J* = 7.6 Hz, 1H),	7.32 (t, *J*= 7.7 Hz, 1H)	130.6	130.6	130.6
7.01 (dd, *J* = 7.5 Hz, 1H)	7.05 (t, *J* = 7.6 Hz, 1H)	7.05 (t, *J*= 7.6 Hz, 1H)	129.0	129.1	129.2
6.99 (d, *J* = 7.5 Hz, 1H)	7.00 (d, *J* = 7.6 Hz, 1H)	7.00 (d, *J* = 7.6 Hz, 1H)	124.9	125.0	125.0
4.88 (s, br, 1H)	4.89 (br s, 1H),	4.89 (s, 1H)	121.7	121.8	121.9
4.25 (ABX, 1H)	4.27 (d, *J* = 2.0 Hz, 1H)	4.31-4.22 (m, 1H)	108.5	108.5	108.5
3.09 (s, 3H)	3.10 (s, 3H)	3.10 (s, 3H)	76.4	76.4	76.4
2.96 (ABX, *J* = 14.0, 4.0Hz, 1H)	2.98 (dd, *J* = 4.0, 14.0 Hz, 1H)	2.98 (dd, *J*= 4.0, 14.0 Hz, 1H)	54.2	54.3	54.3
2.83 (ABX, *J* = 14.0, 4.0Hz, 1H)	2.80 (dd, *J* = 4.0, 14.0 Hz, 1H)	2.80 (dd, *J*= 14.0, 4.0 Hz, 1H)	53.6	53.6	53.6
2.08 (s, 3H)	2.09 (s, 3H)	2.09 (s, 3H)	43.0	43.1	43.1
2.05 (m, 1H)	2.05 (m, 1H)	2.08-2.01 (m, 1H)	36.4	36.4	36.4
1.11 (d, *J* = 7.0 Hz,	1.12 (d, *J* = 7.2	1.12 (d, *J*= 7.2	25.8	25.9	25.9

1H)	Hz, 3H)	Hz, 3H)			
			16.3	16.4	16.4
			8.3	8.3	8.3

[a] All data were recorded in d6-DMSO and to the solvent signal (2.50 ppm for ^{1}H, 39.52 ppm for ^{13}C);

[b] See reference 9, Measured at 500 MHz, δ [ppm, mult, *J* (Hz)]; [c] See reference 7, Measured at 400 MHz, δ [ppm, mult, *J* (Hz)]; [d] Measured at 400 MHz, δ [ppm, mult, *J* (Hz)]; [e] See reference 9, Measured at 125 MHz, δ (ppm); [f] See reference 7, Measured at 101 MHz, δ (ppm); [g]Measured at 101 MHz, δ (ppm);



maremycine B (3)

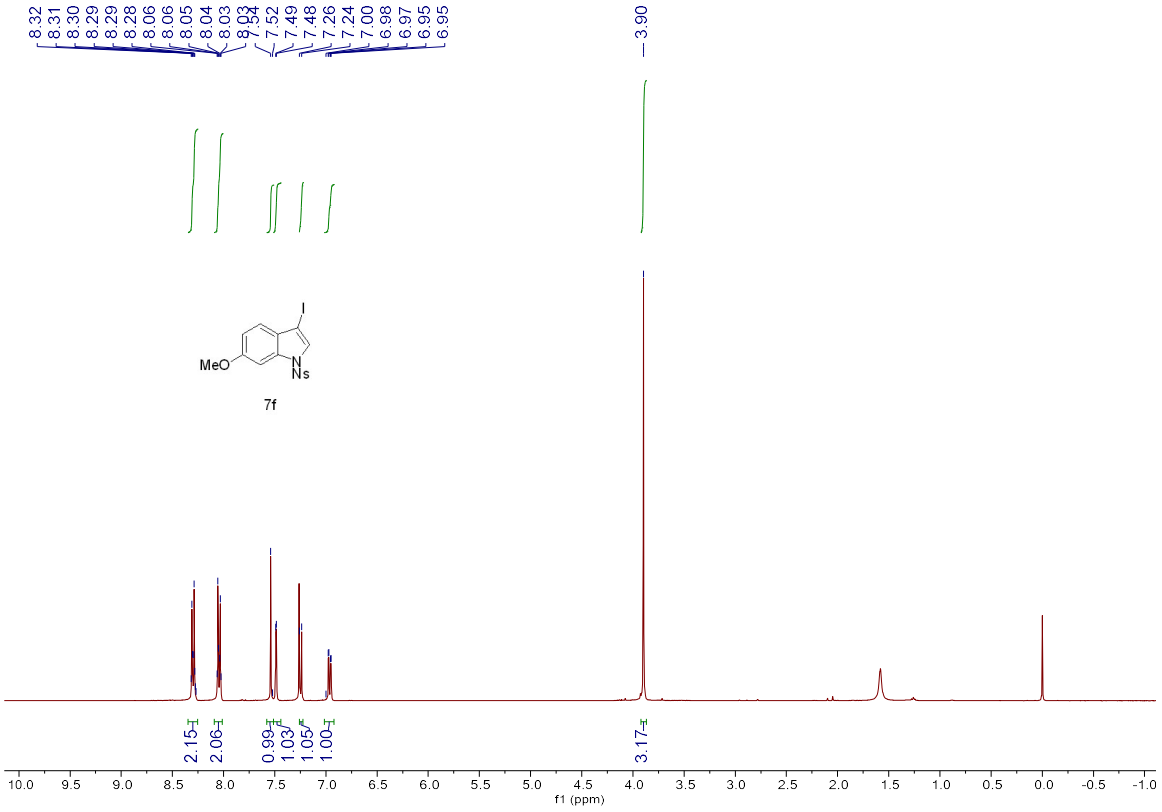
Table S2. NMR data comparison of synthetic and published Maremycin B [a]

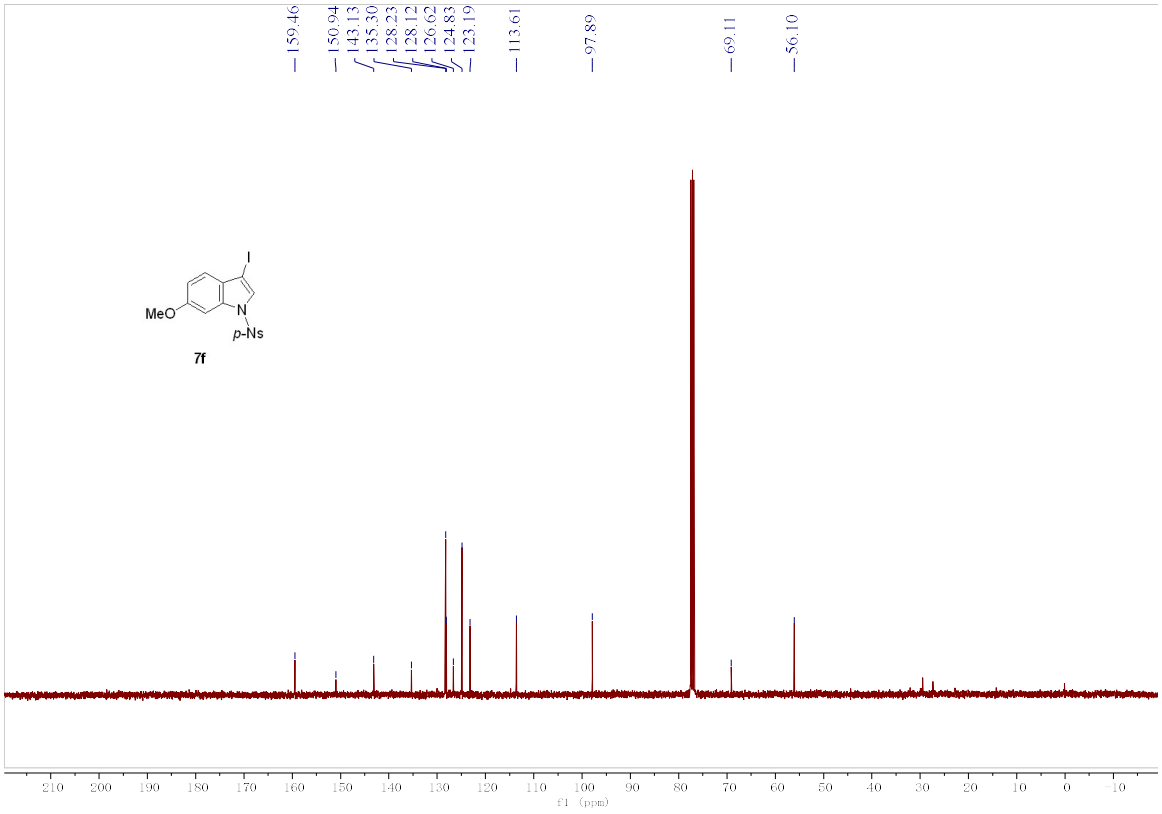
^{1}H NMR			**^{13}C NMR**		
Natural[b]	**Synthesized by Jia[c]**	**This work[d]**	**Natural[e]**	**Synthesized by Jia[f]**	**This work[g]**
8.42 (d, br, *J* = 2Hz, 1H)	8.49 (br s, 1H)	8.48 (d, *J* = 2Hz, 1H)	176.2	176.3	176.3
7.67(d, br, *J* = 1.5 Hz, 1H)	7.70 (br s, 1H)	7.70 (d, *J* = 2Hz, 1H)	167.3	167.4	167.4
7.34 (ddd, *J* = 7.5, 7.5, 1 Hz, 1H)	7.36-7.31 (m, 2H)	7.38-7.26 (m, 2H)	166.1	166.2	166.2
7.31(dd, *J* = 7.5, 1 Hz, 1H)			142.9	143.0	143.0
7.07 (ddd, *J* = 7.5, 7.5, 1 Hz, 1H)	7.08 (t, *J* = 7.6 Hz, 1H)	7.08 (t, *J*= 7.6 Hz, 1H)	131.4	131.4	131.4
7.01 (dd, *J* = 7.5, 1 Hz, 1H)	7.02 (d, *J* = 7.6 Hz, 1H)	7.02 (d, *J*= 7.6 Hz, 1H)	129.2	129.2	129.2
6.88 (s, 1H)	6.92 (br s, 1H)	6.91 (s, 1H)	123.7	123.8	123.9
4.52 (ddd, J = 5.5, 1.5, 1.5 Hz, 1H)	4.54 (d, *J* = 4.0 Hz,1H)	4.57-4.52 (m, 1H)	122.3	122.4	122.4
4.15 (ABX, 1H)	4.17 (s, 1H),	4.20-4.13 (m, 1H)	108.5	108.6	108.6
3.10 (s, 3H)	3.11 (s, 3H)	3.11 (s, 3H)	77.2	77.2	77.2
2.96 (ABX, *J* = 5.5 Hz, 1H)	2.96 (dd, *J* = 4.8, 14.0 Hz, 1H)	2.97 (dd, *J* = 14.0, 4.8 Hz, 1H)	55.5	55.5	55.5
2.85 (ABX, *J* = 13.5, 4.2 Hz, 1H)	2.83 (dd, *J* = 3.6, 14.0 Hz, 1H)	2.83 (dd, *J*= 14.0, 3.9 Hz, 1H)	54.3	54.4	54.4
2.33 (qd, *J* = 7, 5.5 Hz,	2.31 (m, 1H)	2.32 (qd, *J* = 7.2, 6.8	43.5	43.6	43.6

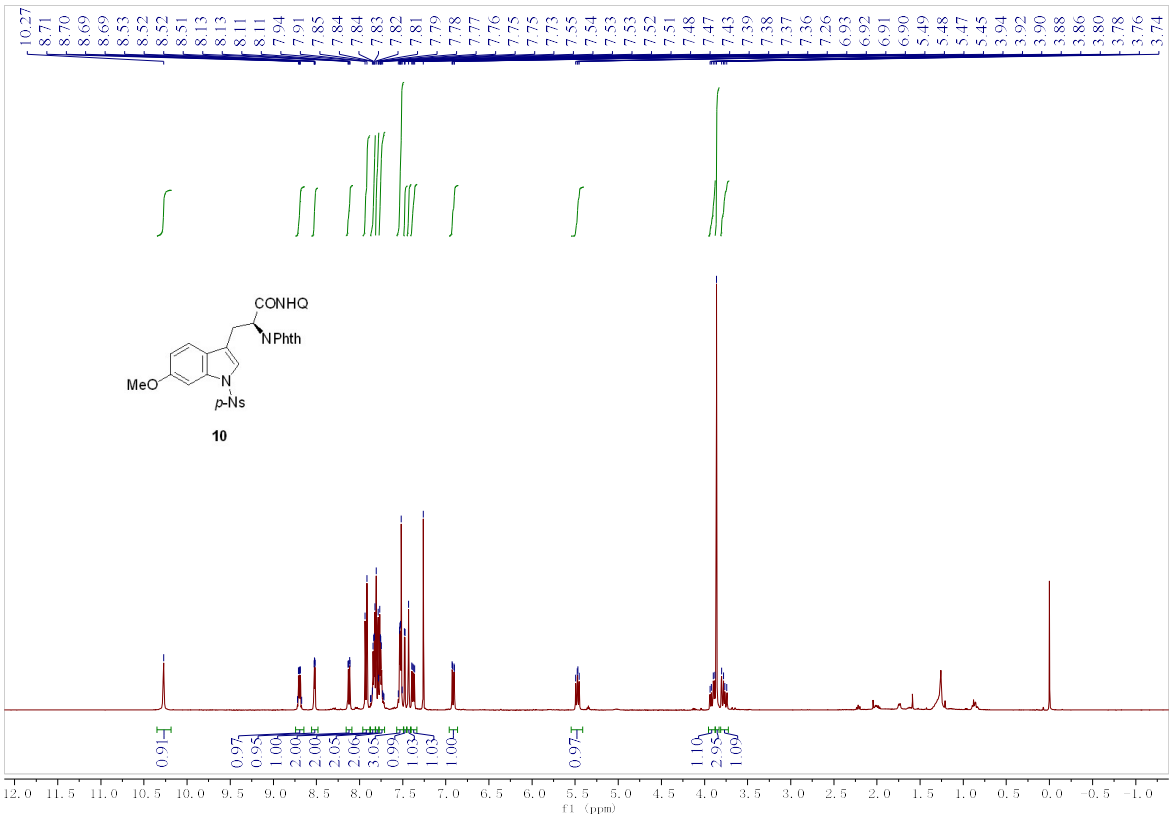
1H)		Hz, 1H)			
2.12 (s, 3H)	2.12 (s, 3H)	2.11 (s, 3H)	36.9	36.9	36.9
0.83 (d, *J*= 7 Hz, 3H)	0.87 (d, *J*= 6.8 Hz, 3H)	0.86 (d, *J*= 7.1 Hz, 3H)	25.7	25.8	25.8
			16.1	16.2	16.2
			9.8	9.8	9.8

[a] All data were recorded in d6-DMSO and to the solvent signal (2.50 ppm for ^{1}H, 39.52 ppm for ^{13}C); [b] See reference 9, Measured at 500 MHz, δ [ppm, mult, *J* (Hz)]; [c] See reference 7, Measured at 400 MHz, δ [ppm, mult, *J* (Hz)]; [d] Measured at 400 MHz, δ [ppm, mult, *J* (Hz)]; [e] See reference 9, Measured at 125 MHz, δ (ppm); [f] See reference 7, Measured at 101 MHz, δ (ppm); [g]Measured at 101 MHz, δ (ppm);

4. Copies of ^{1}H and ^{13}C NMR Spectra



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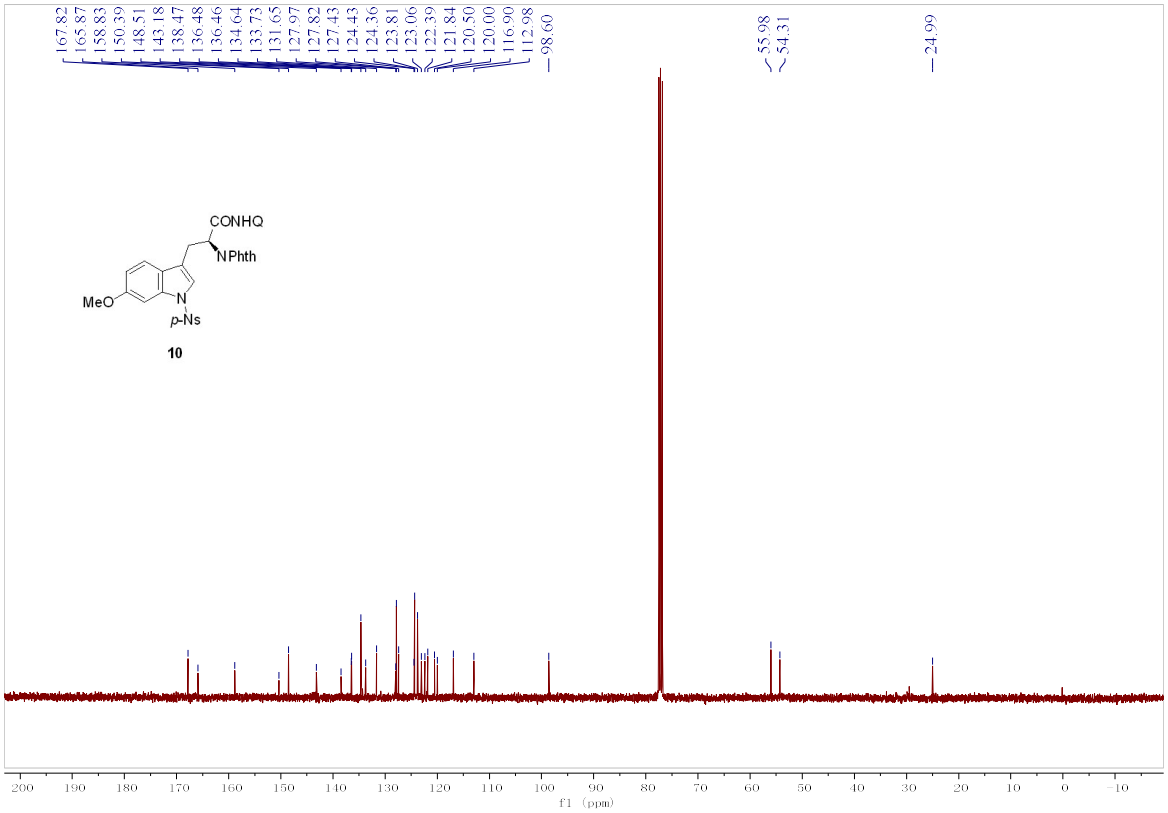
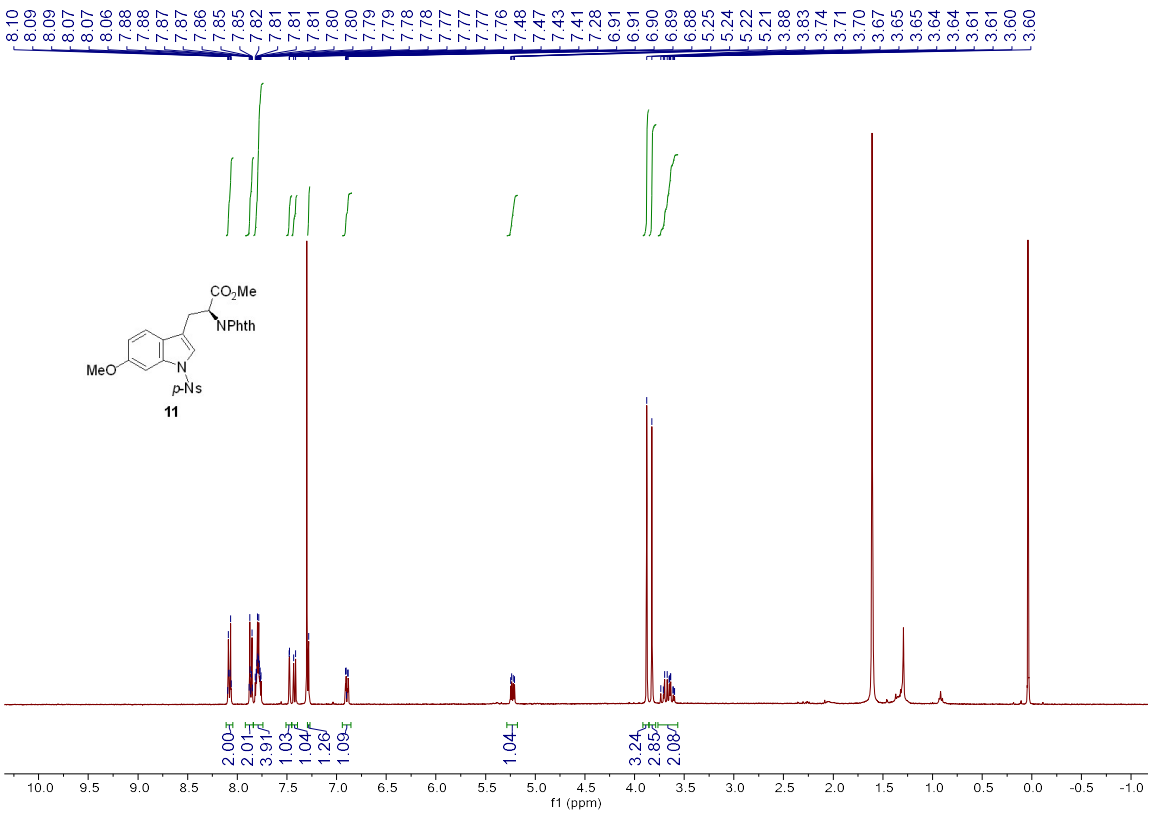
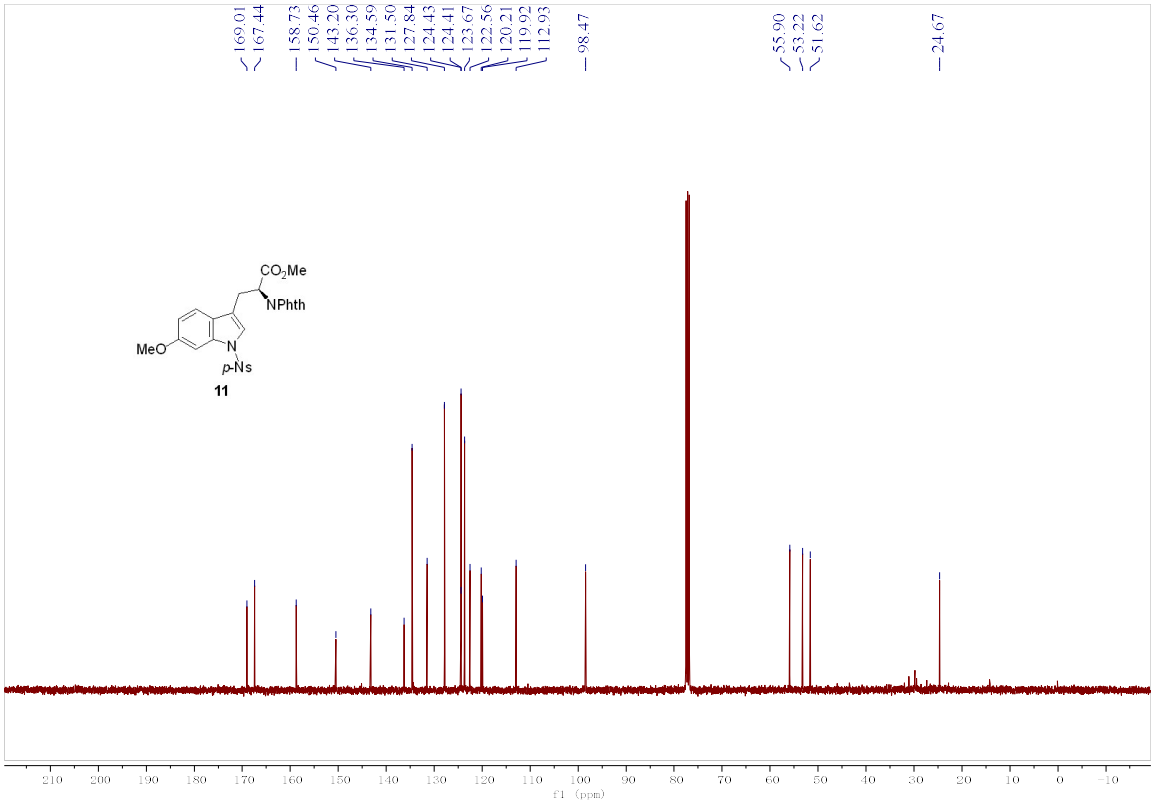
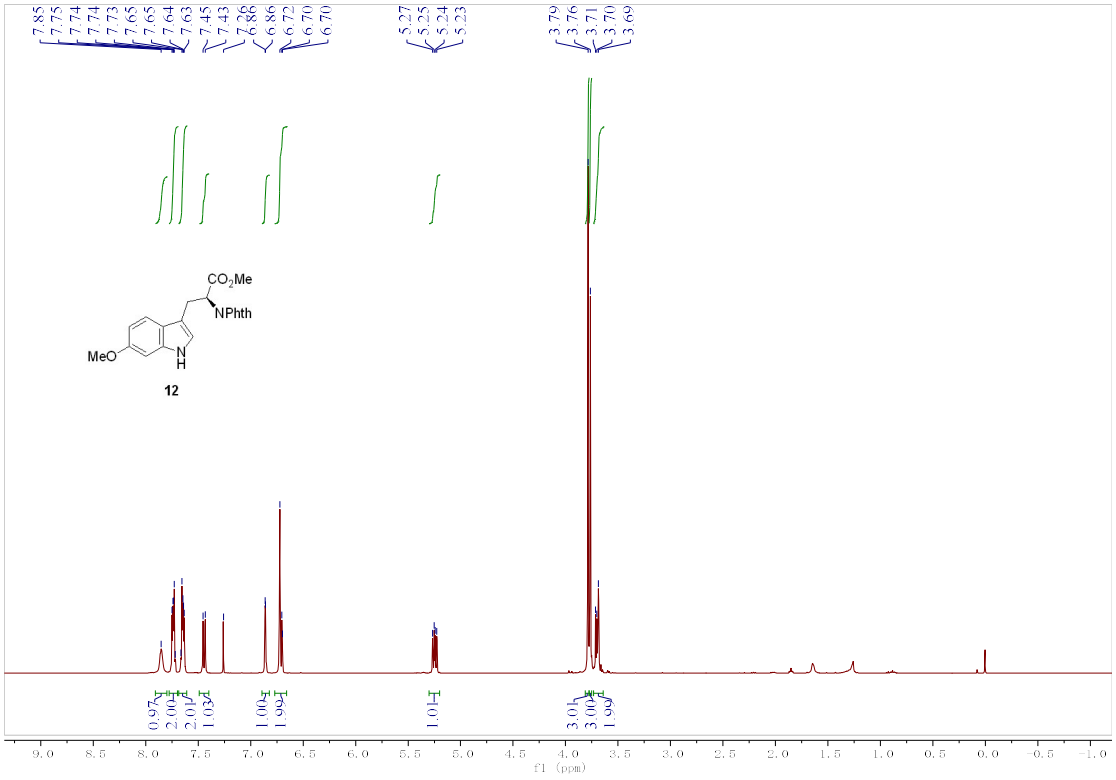
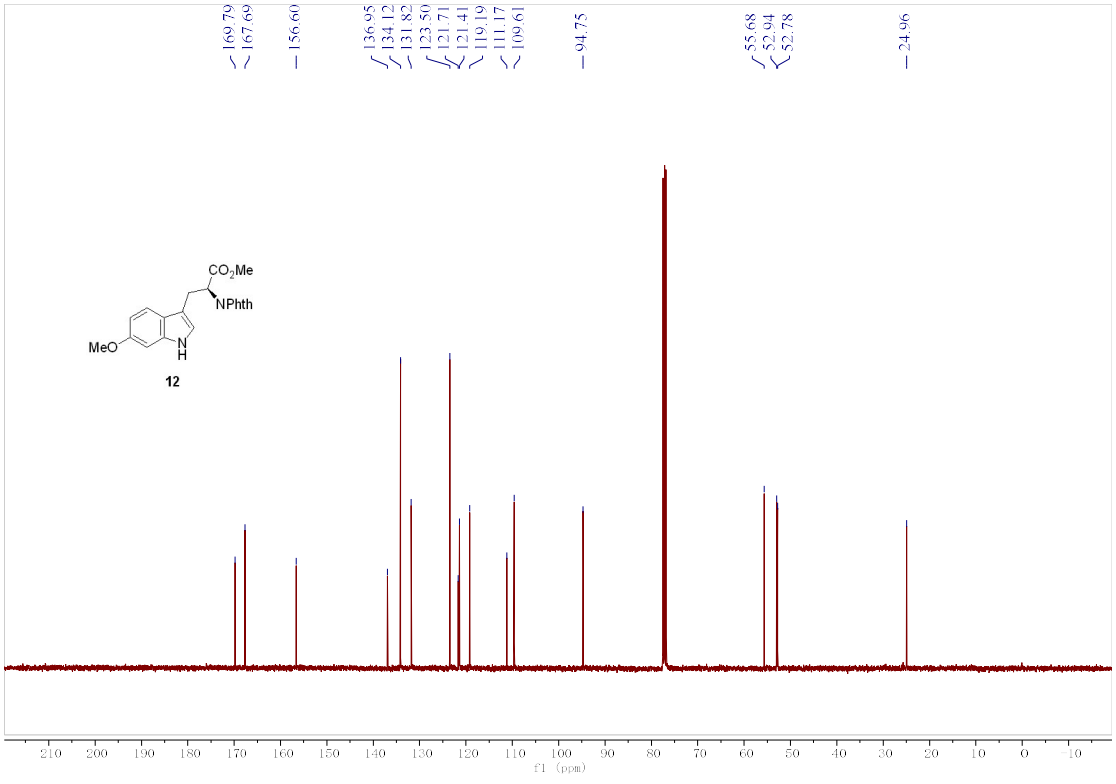
p-Ns
10

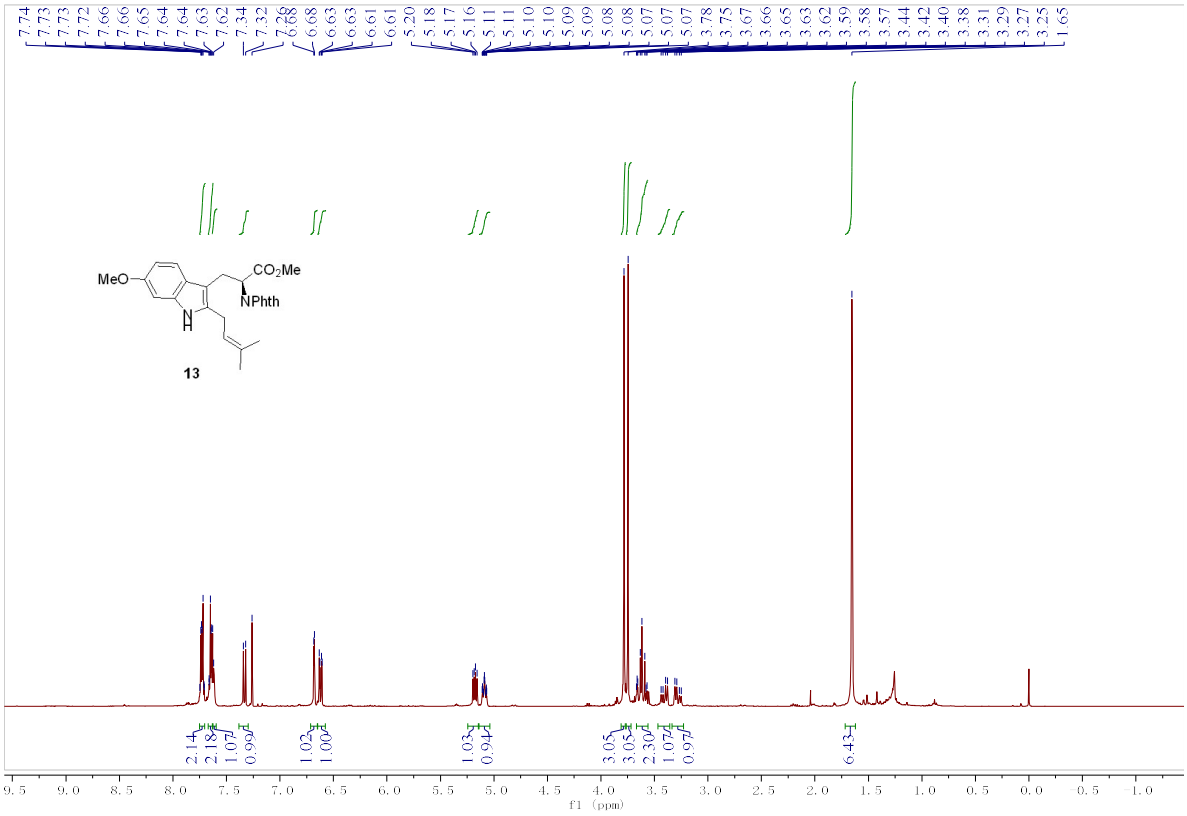

CONHQ
NPhth
MeO
N
p-Ns
10

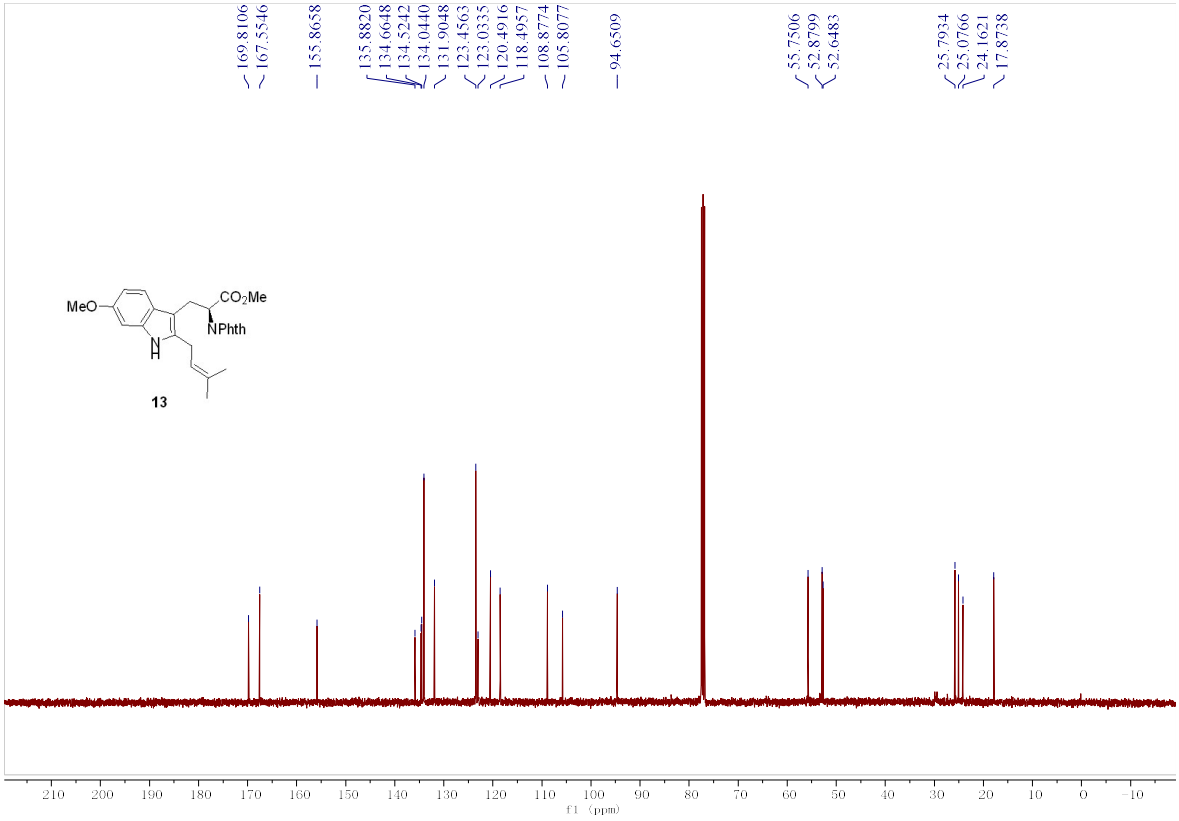

8.10 8.09 8.09 8.07 8.07 8.06 7.88 7.88 7.87 7.87 7.86 7.85 7.85 7.82 7.81 7.81 7.81 7.80 7.80 7.79 7.79 7.78 7.78 7.77 7.77 7.77 7.76 7.48 7.47 7.43 7.41 7.28 6.91 6.91 6.90 6.89 6.88 5.25 5.24 5.22 5.21 3.88 3.83 3.74 3.71 3.70 3.67 3.65 3.65 3.64 3.64 3.61 3.61 3.60 3.60
CO2Me
NPhth
MeO
N
p-Ns
11
2.00 2.01 3.91 1.03 1.04 1.26 1.09 1.04 3.24 2.85 2.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

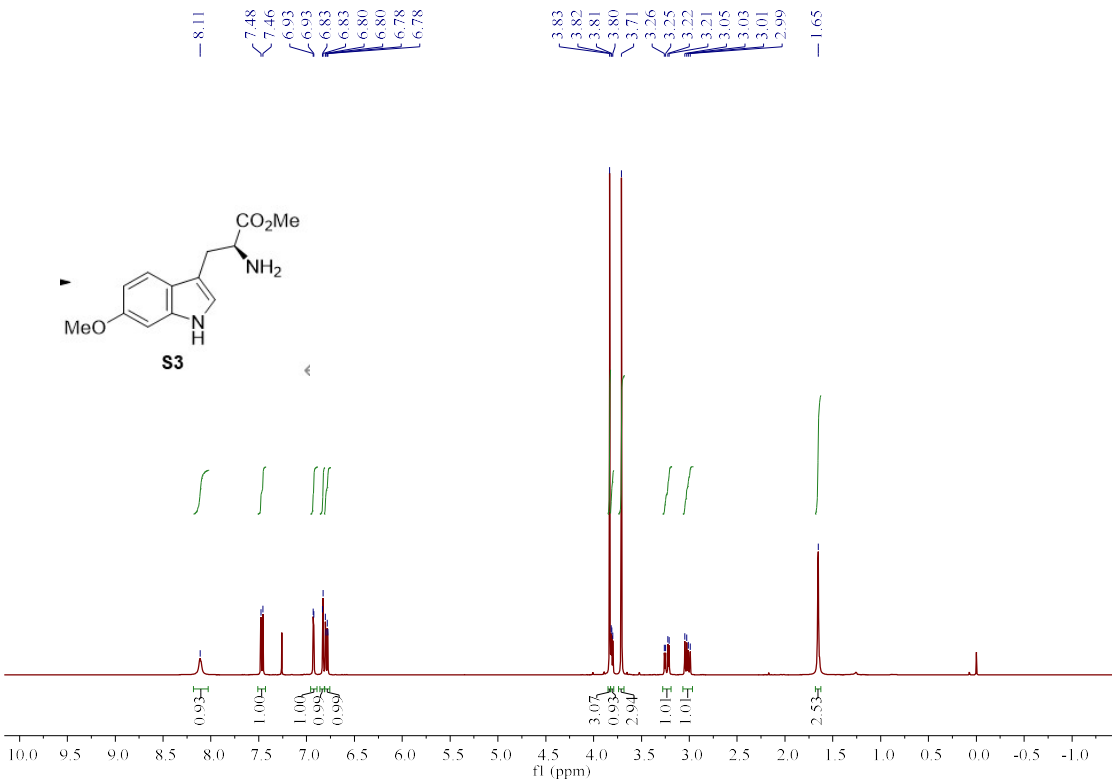

169.01 167.44 158.73 150.46 143.20 136.30 134.59 131.50 127.84 124.43 124.41 123.67 122.56 120.21 119.92 112.93 98.47 55.90 53.22 51.62 24.67
CO2Me
NPhth
MeO
N
p-Ns
11
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

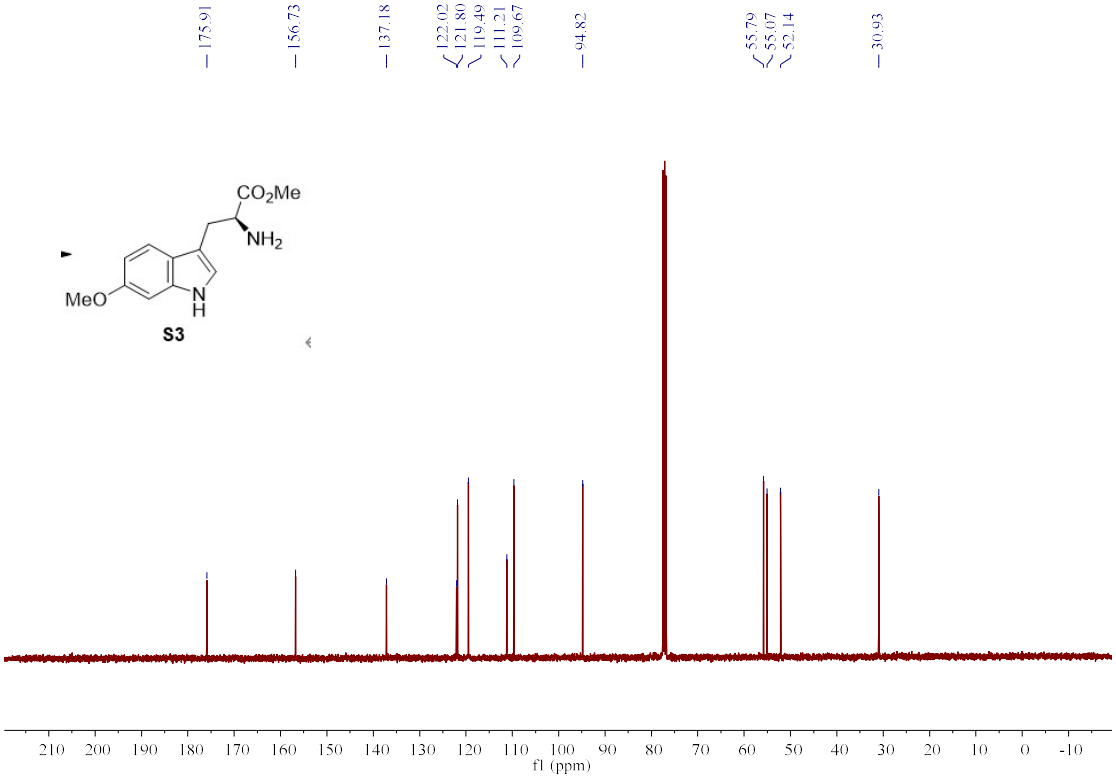

7.85
7.75
7.74
7.74
7.73
7.65
7.65
7.64
7.63
7.45
7.43
7.26
6.86
6.86
6.72
6.70
6.70
5.27
5.25
5.24
5.23
3.79
3.76
3.71
3.70
3.69
CO2Me
NPhth
MeO
N
H
12
0.97
2.00
2.01
1.03
1.00
1.99
1.01
3.01
3.00
1.99
f1 (ppm)

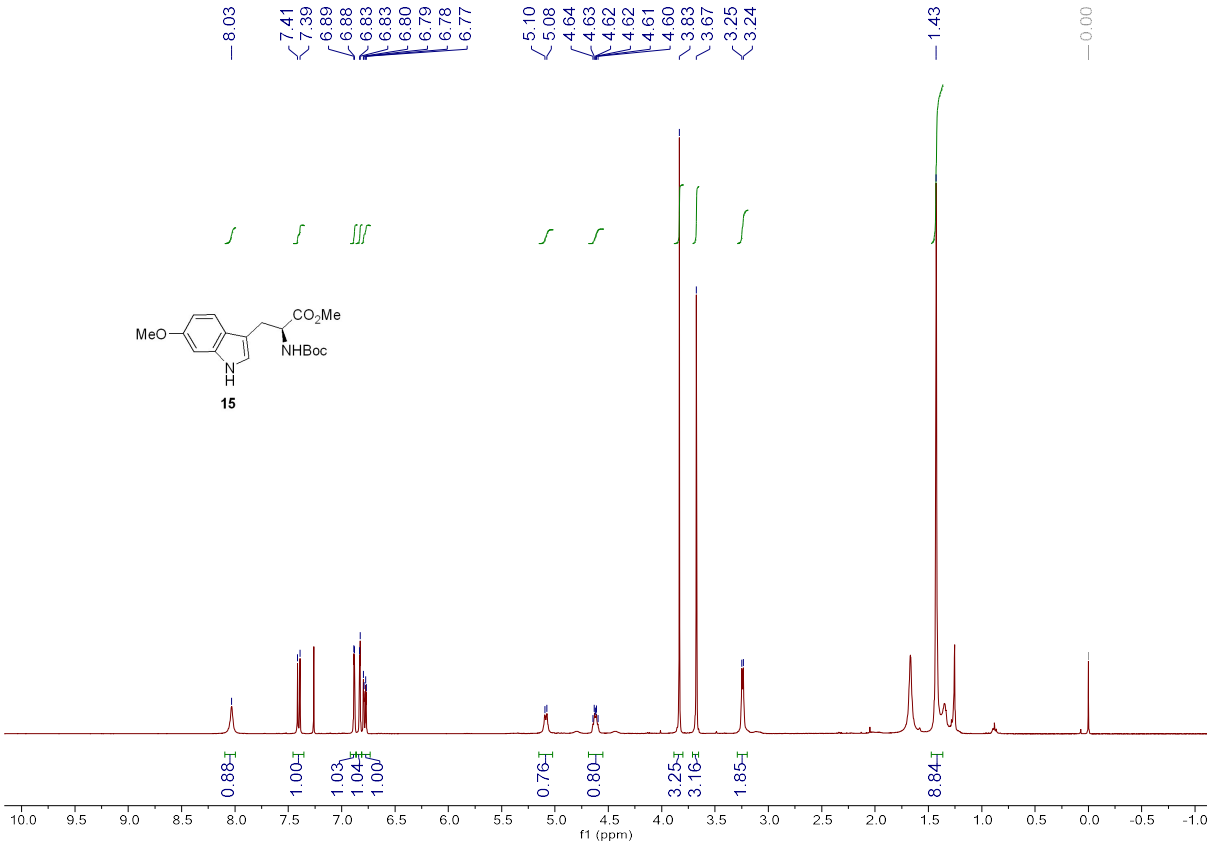

169.79
167.69
156.60
136.95
134.12
131.82
123.56
121.71
121.41
119.19
111.17
109.61
94.75
55.68
52.94
52.78
24.96
CO2Me
NPhth
MeO
N
H
12
f1 (ppm)

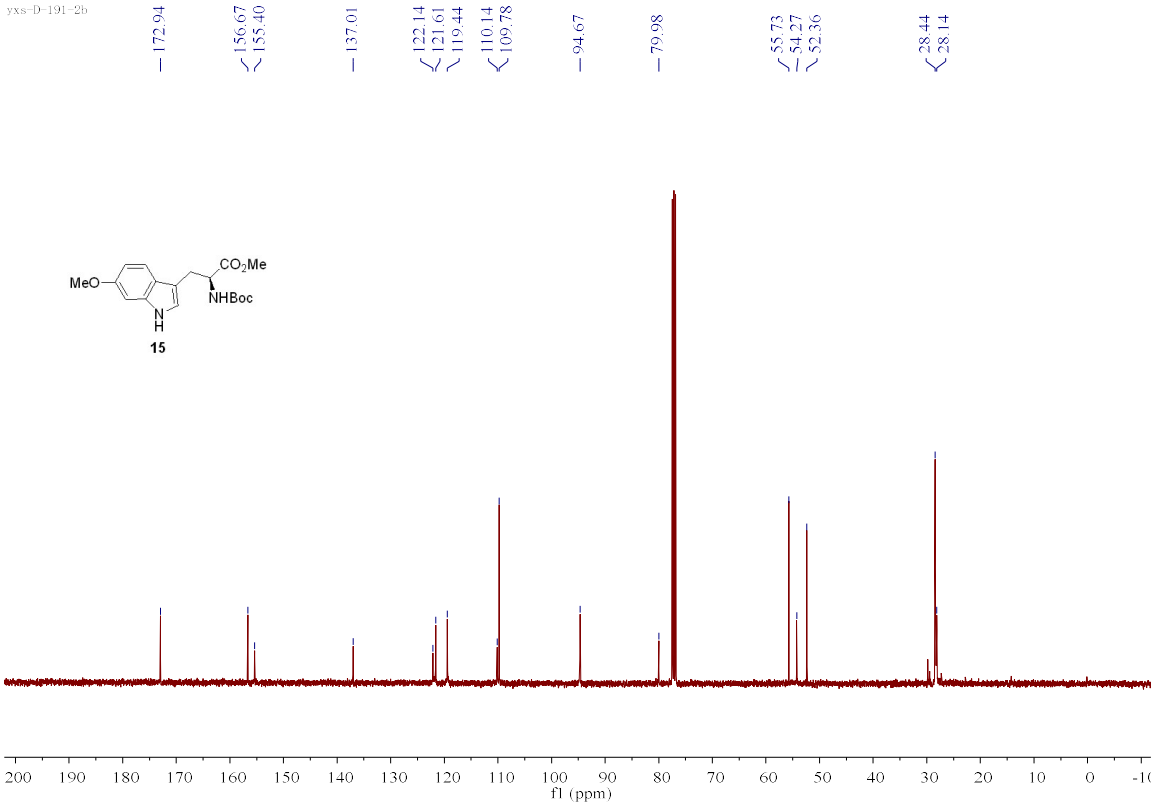

MeO
CO2Me
NPhth
13

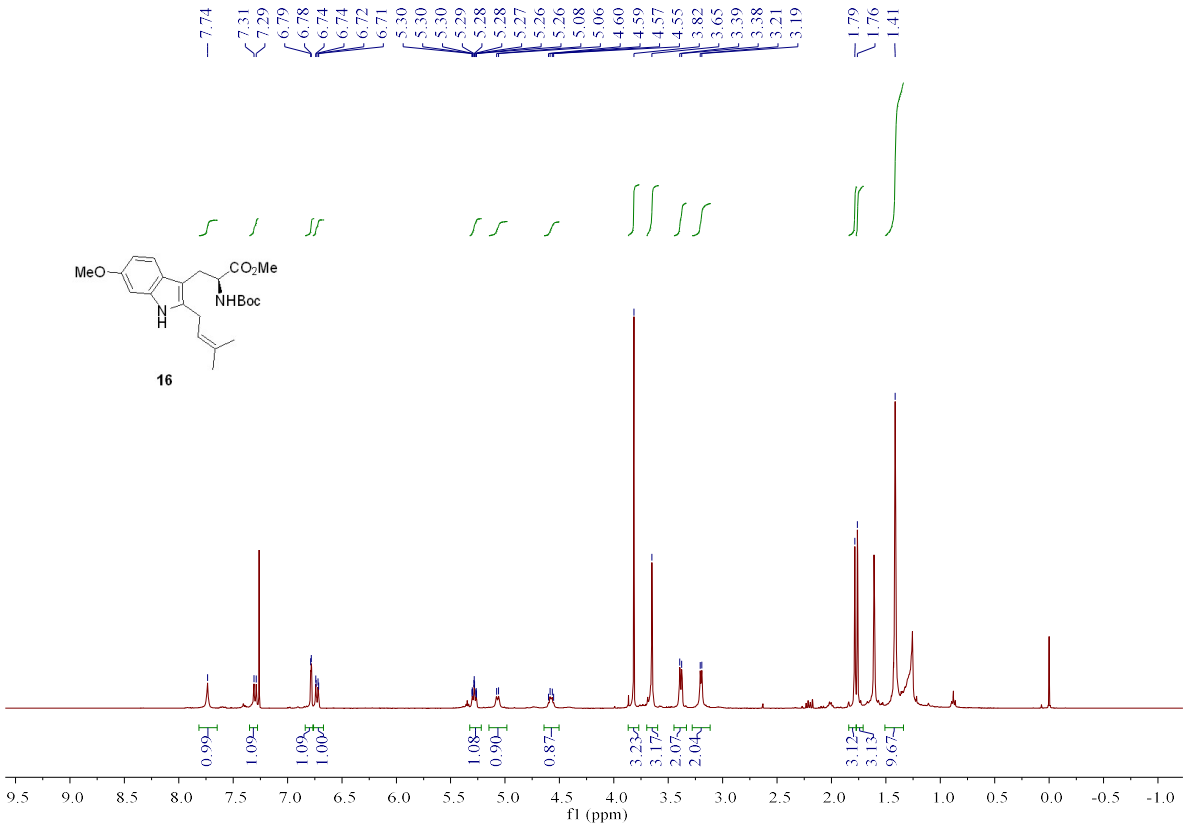

MeO
CO2Me
NPhth
13

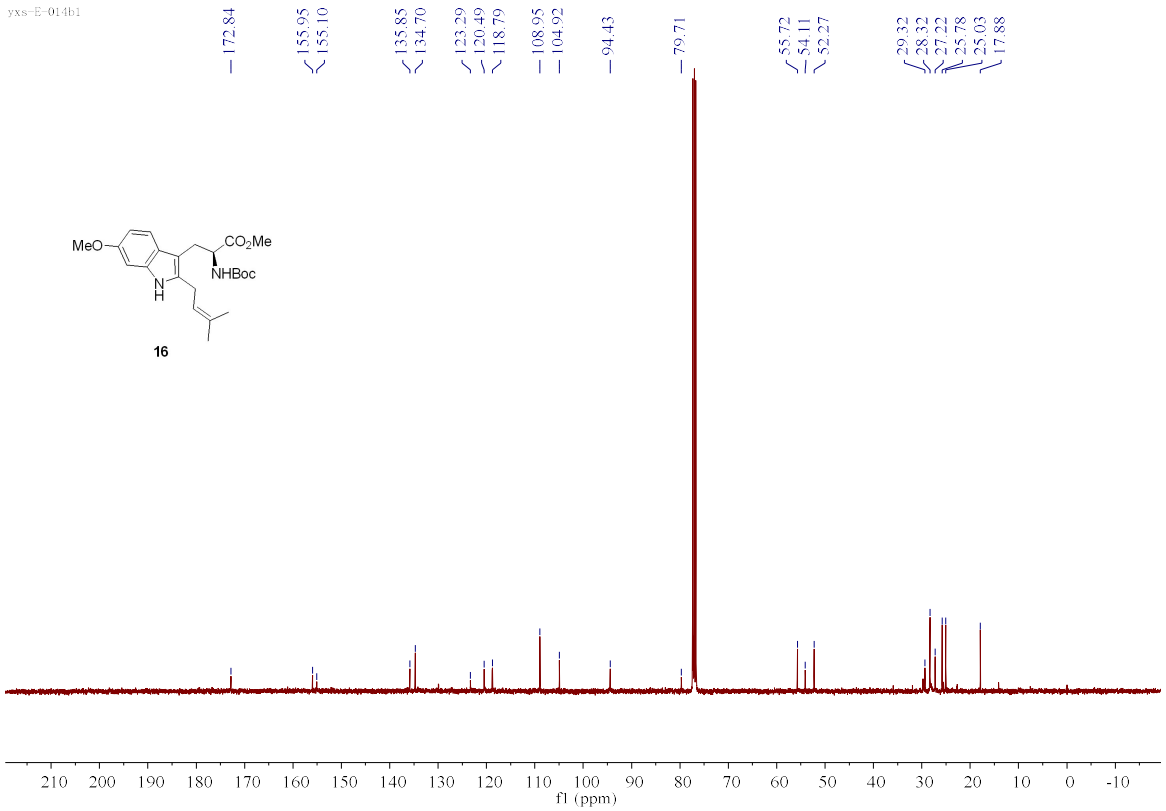

8.11
7.48
7.46
6.93
6.93
6.83
6.83
6.80
6.80
6.78
6.78
3.83
3.82
3.81
3.80
3.71
3.26
3.25
3.22
3.21
3.05
3.03
3.01
2.99
1.65
CO2Me
NH2
MeO
N
H
S3
0.93
1.00
1.00
0.99
0.99
3.07
0.93
2.94
1.01
1.01
2.53
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

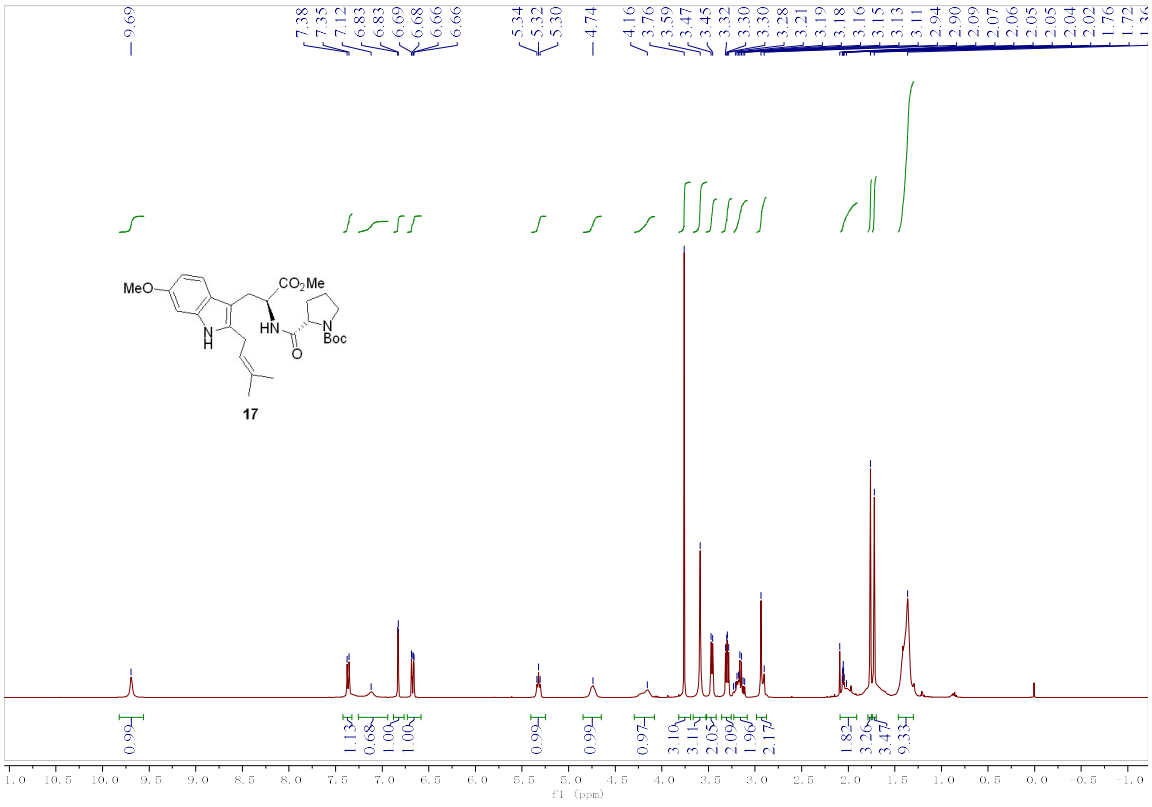

175.91
156.73
137.18
122.02
121.80
119.49
111.21
109.67
94.82
55.79
55.07
52.14
30.93
CO2Me
NH2
MeO
N
H
S3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

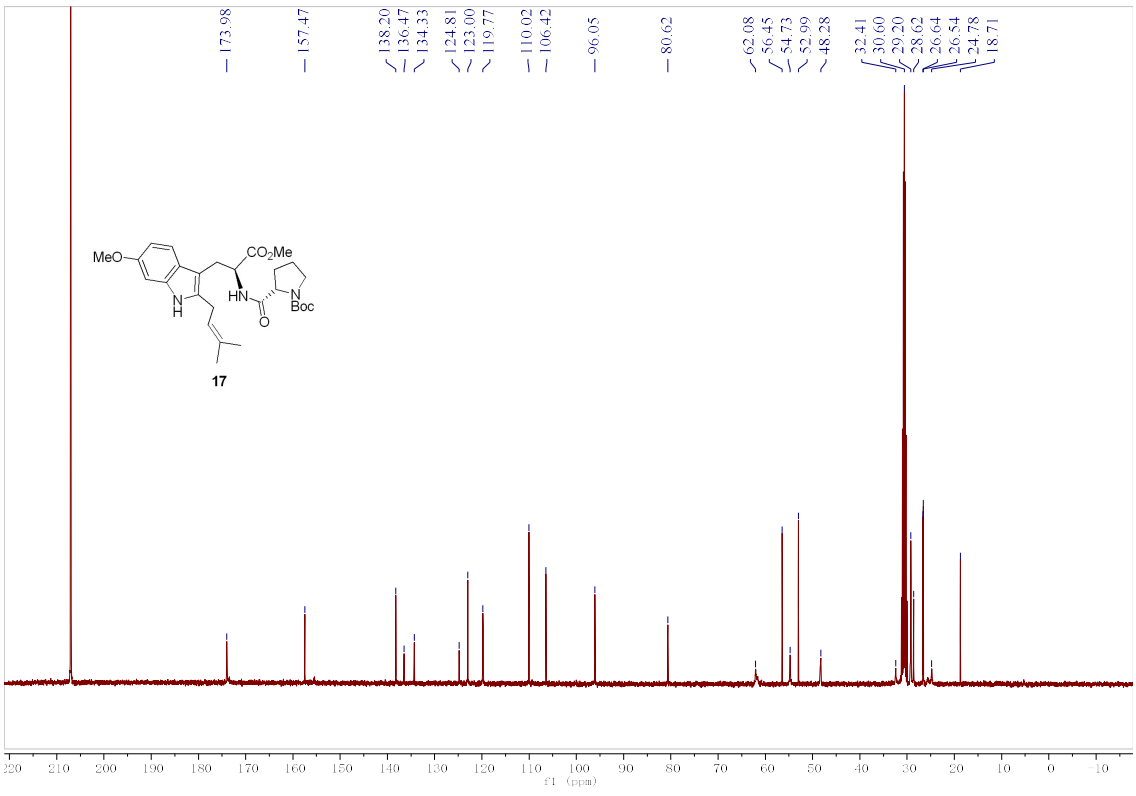

8.03
7.41
7.39
6.89
6.88
6.83
6.83
6.80
6.79
6.78
6.77
5.10
5.08
4.64
4.63
4.62
4.62
4.61
4.60
3.83
3.67
3.25
3.24
1.43
0.00
MeO
CO2Me
NHBoc
N
H
15
0.88
1.00
1.03
1.04
1.00
0.76
0.80
3.25
3.16
1.85
8.84
f1 (ppm)


yxs-D-191-2b
172.94
156.67
155.40
137.01
122.14
121.61
119.44
110.14
109.78
94.67
79.98
55.73
54.27
52.36
28.44
28.14
MeO
CO2Me
NHBoc
N
H
15
f1 (ppm)

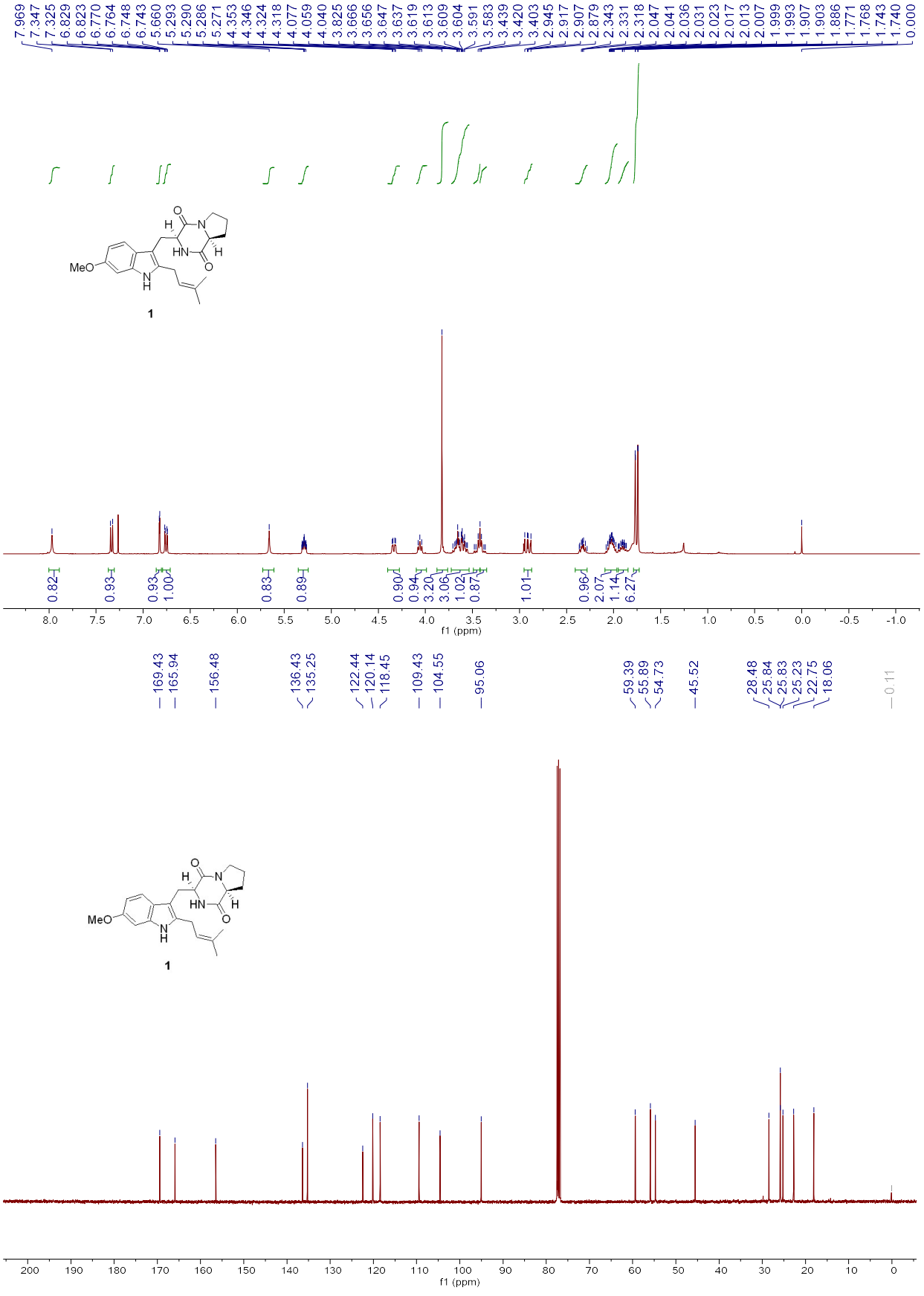

7.74
7.31
7.29
6.79
6.78
6.74
6.74
6.72
6.71
5.30
5.30
5.30
5.29
5.28
5.28
5.27
5.26
5.26
5.08
5.06
4.60
4.59
4.57
4.55
3.82
3.65
3.39
3.38
3.21
3.19
1.79
1.76
1.41
MeO
CO2Me
NHBoc
16
0.99
1.09
1.09
1.00
1.08
0.90
0.87
3.23
3.17
2.07
2.04
3.12
3.13
9.67
f1 (ppm)

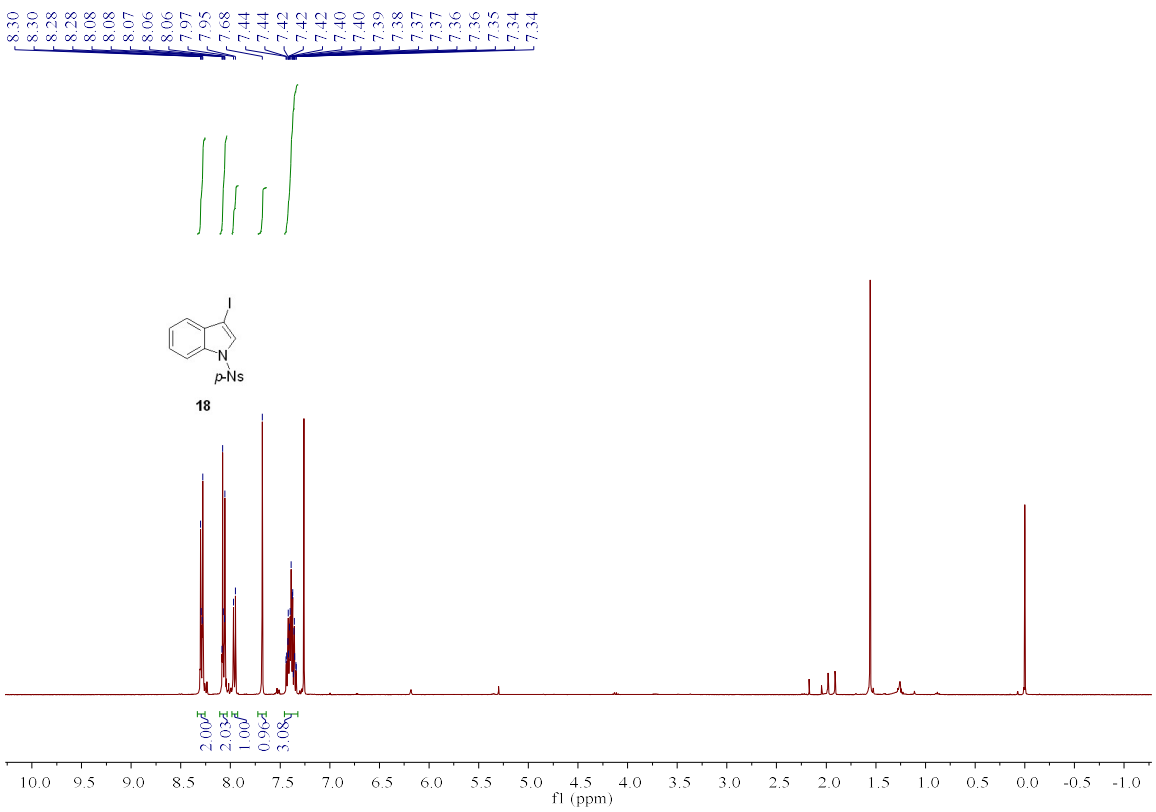

yxs-E-014b1
172.84
155.95
155.10
135.85
134.70
123.29
120.49
118.79
108.95
104.92
94.43
79.71
55.72
54.11
52.27
29.32
28.32
27.22
25.78
25.03
17.88
MeO
CO2Me
NHBoc
16
f1 (ppm)

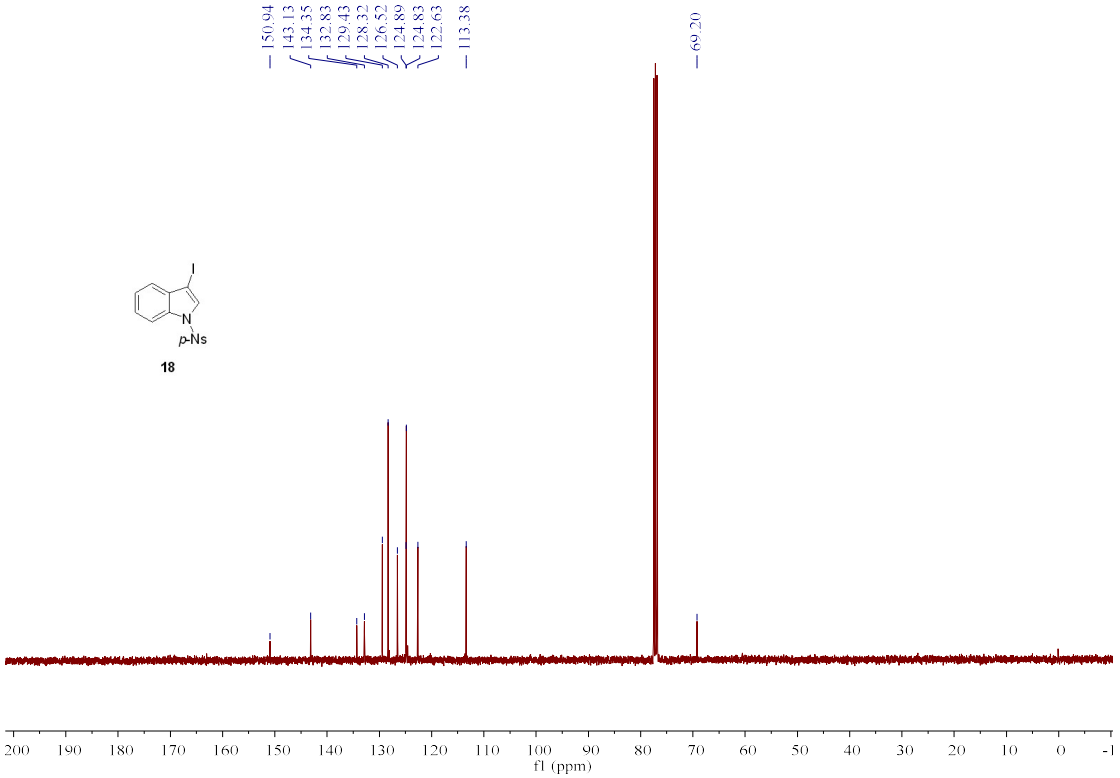

MeO
CO2Me
HN
N
Boc
O
H
17

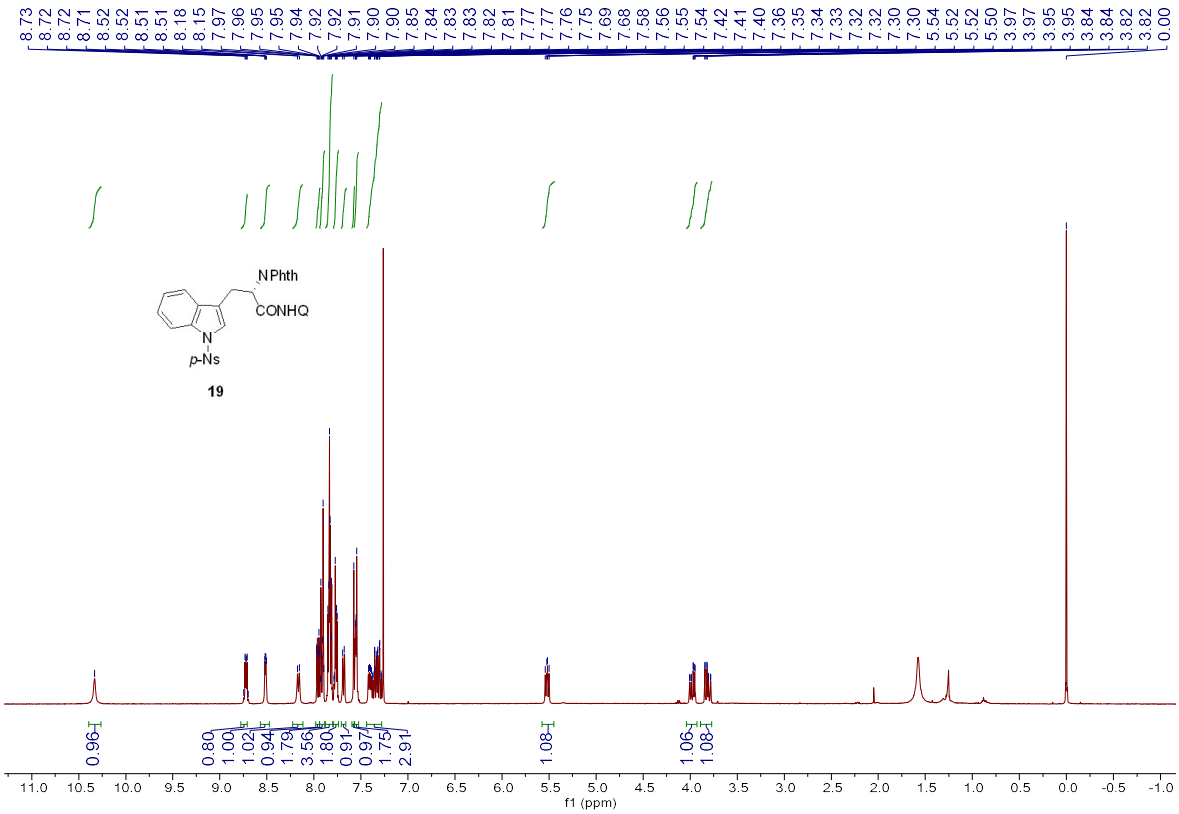

MeO
CO2Me
HN
N
Boc
O
H
17

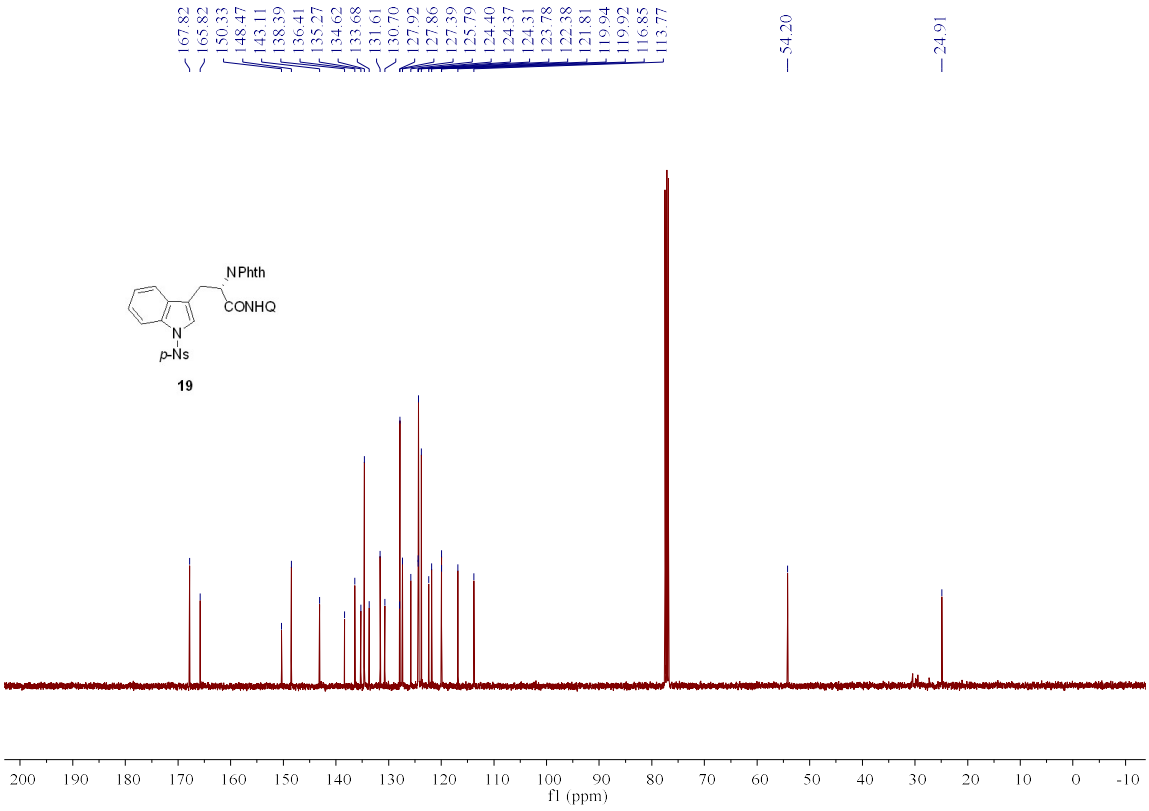
Tryprostatin A (**1**)

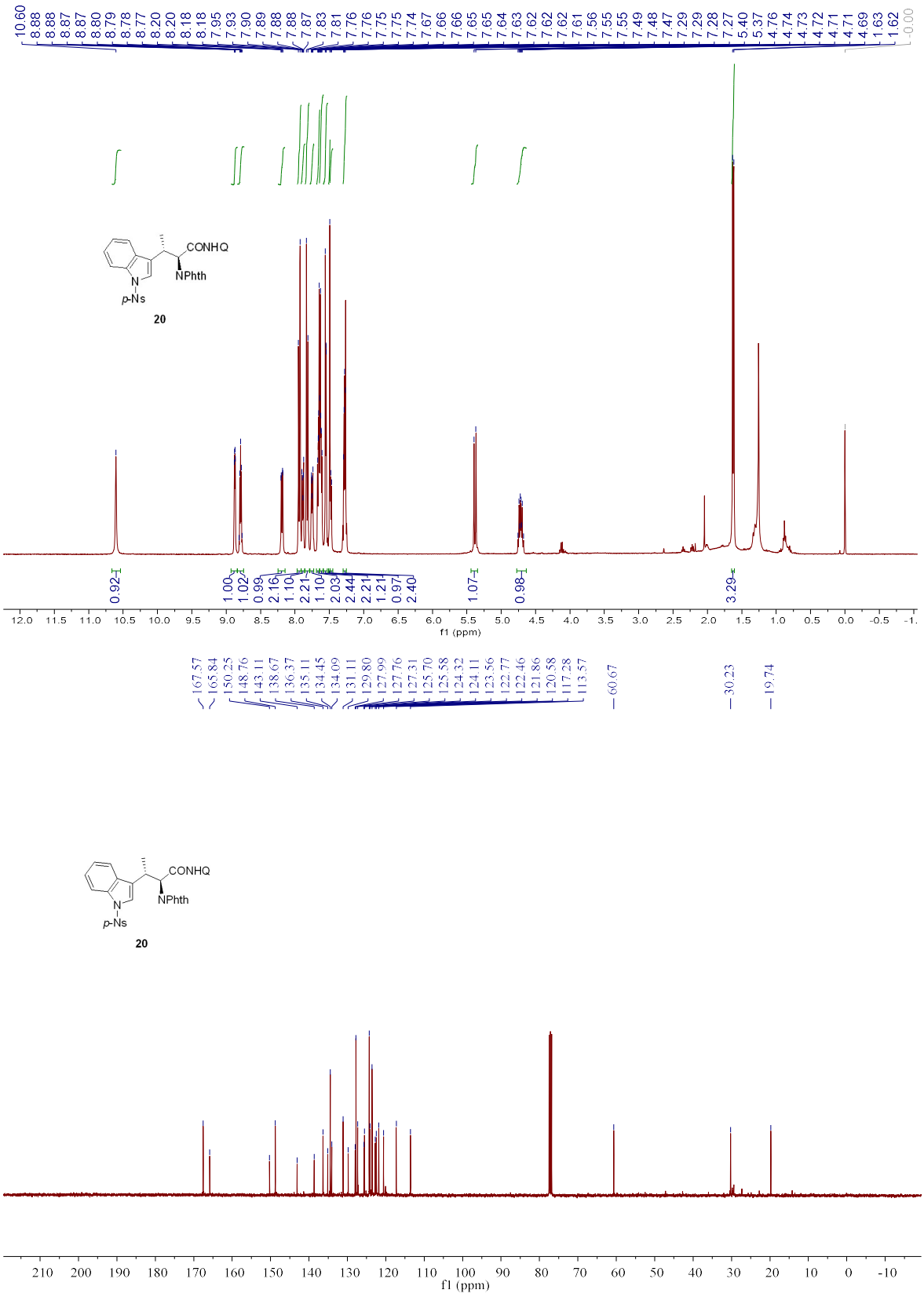


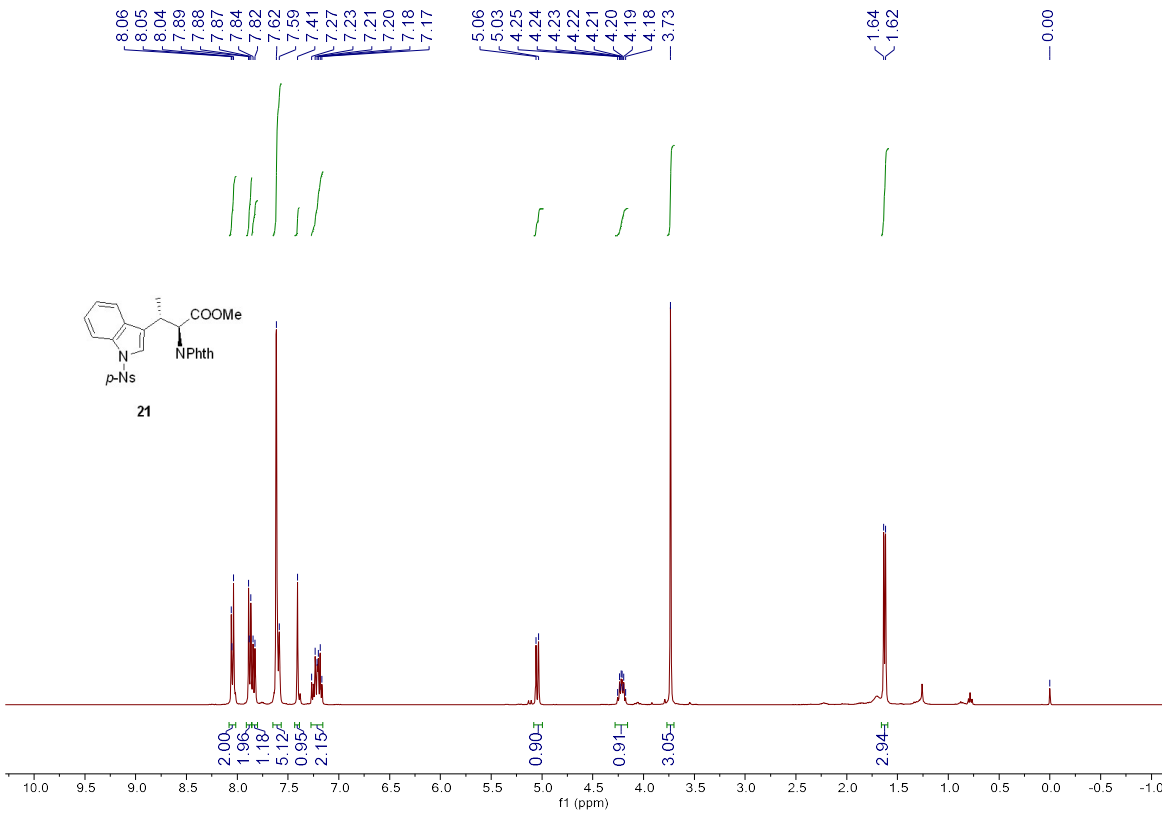

8.30
8.30
8.28
8.28
8.08
8.08
8.07
8.06
8.06
7.97
7.95
7.68
7.44
7.44
7.42
7.42
7.42
7.40
7.40
7.39
7.38
7.37
7.37
7.36
7.35
7.34
7.34
I
N
p-Ns
18
2.00
2.03
1.00
0.96
3.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

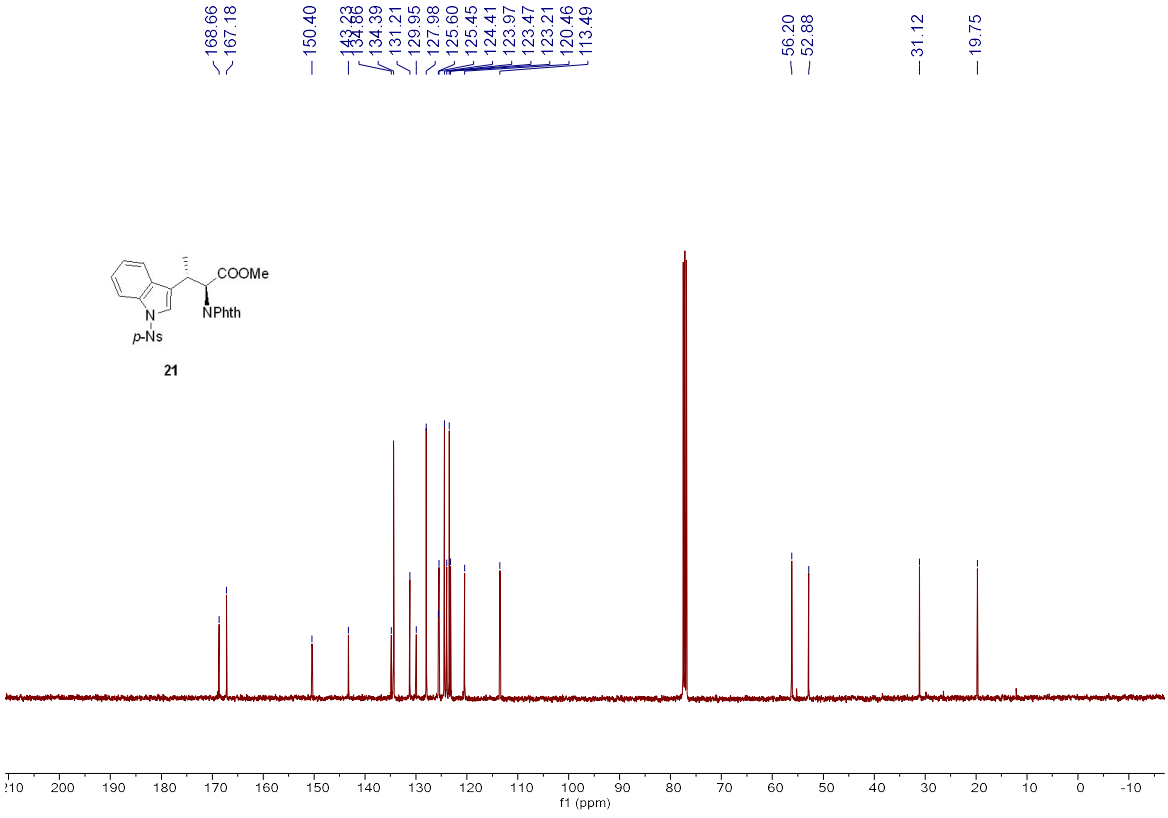

150.94
143.13
134.35
132.83
129.43
128.32
126.52
124.89
124.83
122.63
113.38
69.20
I
N
p-Ns
18
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

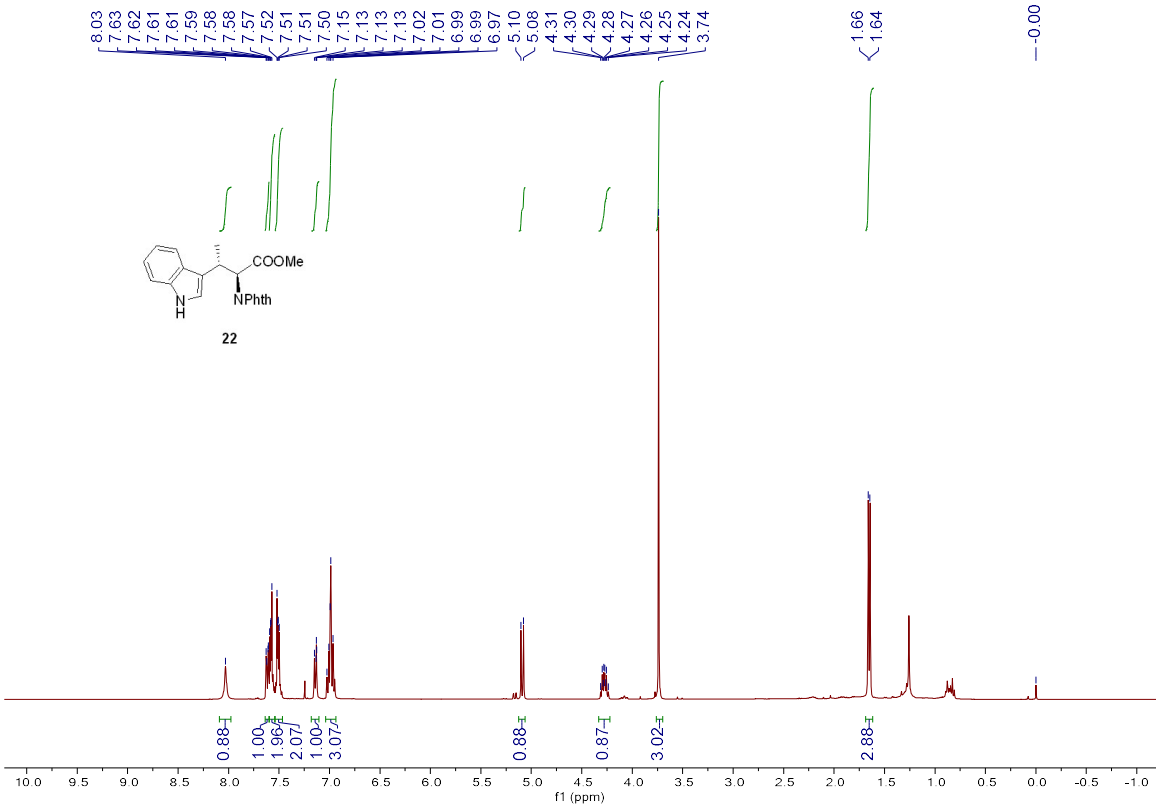

NPhth
CONHQ
N
p-Ns
19
f1 (ppm)

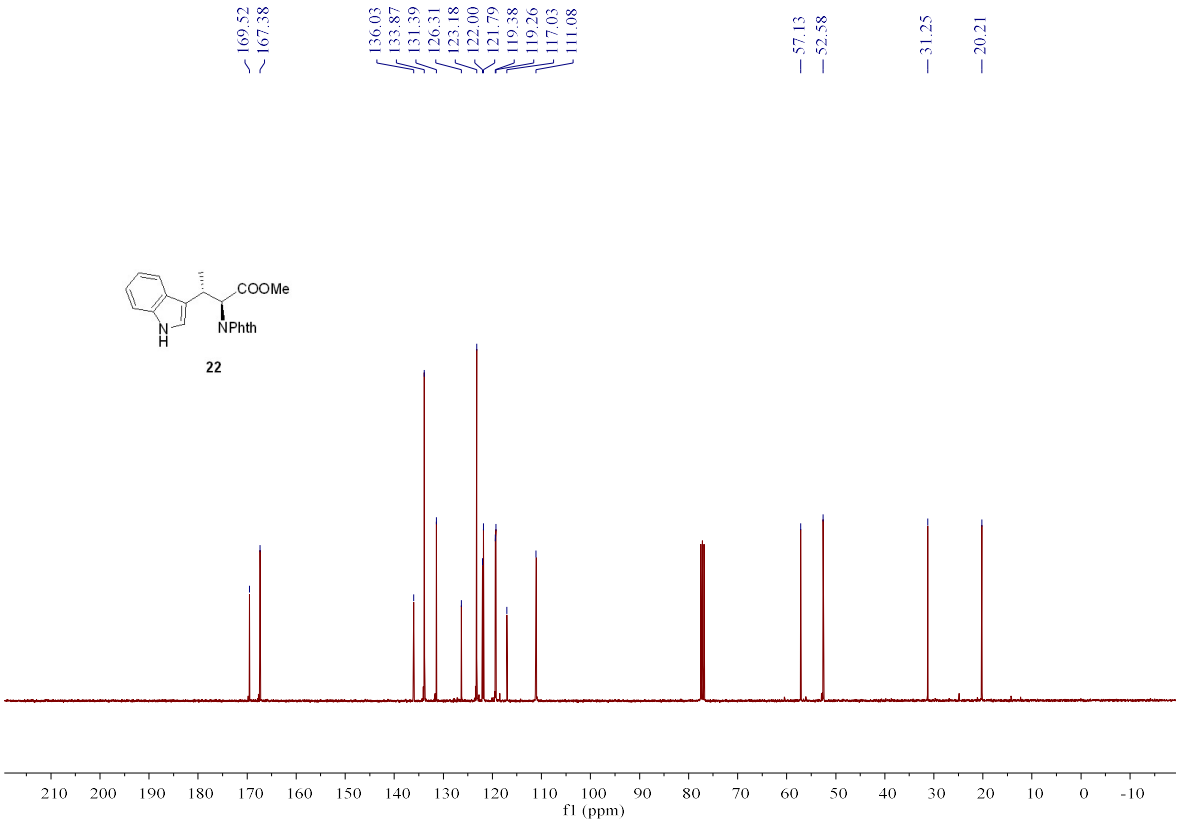

NPhth
CONHQ
N
p-Ns
19
f1 (ppm)

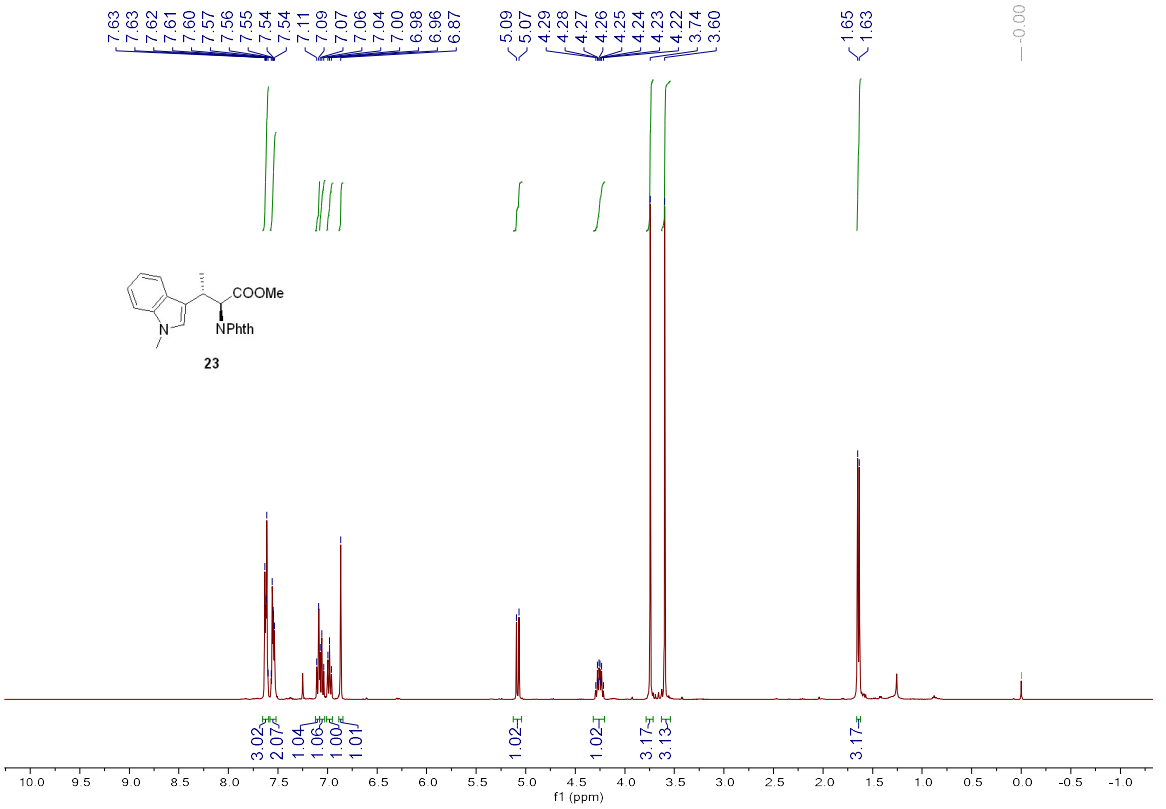

CONHQ
NPhth
p-Ns
20
f1 (ppm)


8.06
8.05
8.04
7.89
7.88
7.87
7.84
7.82
7.62
7.59
7.41
7.27
7.23
7.21
7.20
7.18
7.17
5.06
5.03
4.25
4.24
4.23
4.22
4.21
4.20
4.19
4.18
3.73
1.64
1.62
0.00
COOMe
NPhth
p-Ns
21
2.00
1.96
1.18
5.12
0.95
2.15
0.90
0.91
3.05
2.94
f1 (ppm)


168.66
167.18
150.40
143.23
134.86
134.39
131.21
129.95
127.98
125.60
125.45
124.41
123.97
123.47
123.21
120.46
113.49
56.20
52.88
31.12
19.75
COOMe
NPhth
p-Ns
21
f1 (ppm)


8.03
7.63
7.62
7.61
7.61
7.59
7.58
7.58
7.57
7.52
7.51
7.51
7.50
7.15
7.13
7.13
7.02
7.01
6.99
6.99
6.97
5.10
5.08
4.31
4.30
4.29
4.28
4.27
4.26
4.25
4.24
3.74
1.66
1.64
0.00
COOMe
NPhth
N
H
22
0.88
1.00
1.96
2.07
1.00
3.07
0.88
0.87
3.02
2.88
f1 (ppm)


169.52
167.38
136.03
133.87
131.39
126.31
123.18
122.00
121.79
119.38
119.26
117.03
111.08
57.13
52.58
31.25
20.21
COOMe
NPhth
N
H
22
f1 (ppm)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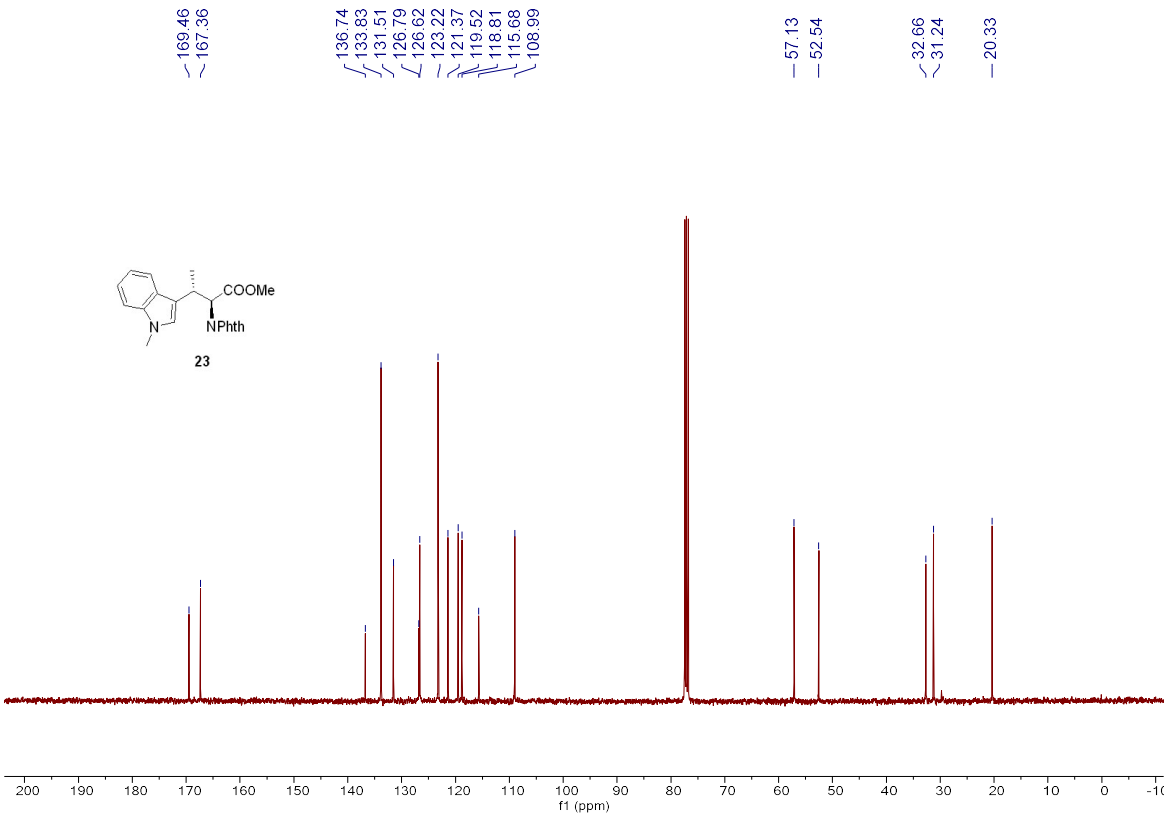
7.63
7.62
7.61
7.60
7.57
7.56
7.55
7.54
7.54
7.11
7.09
7.07
7.06
7.04
7.00
6.98
6.96
6.87
5.09
5.07
4.29
4.28
4.27
4.26
4.25
4.24
4.23
4.22
3.74
3.60
1.65
1.63
-0.00
COOMe
NPhth
N
23
3.02
2.07
1.04
1.06
1.00
1.01
1.02
1.02
3.17
3.13
3.17
f1 (ppm)


169.46
167.36
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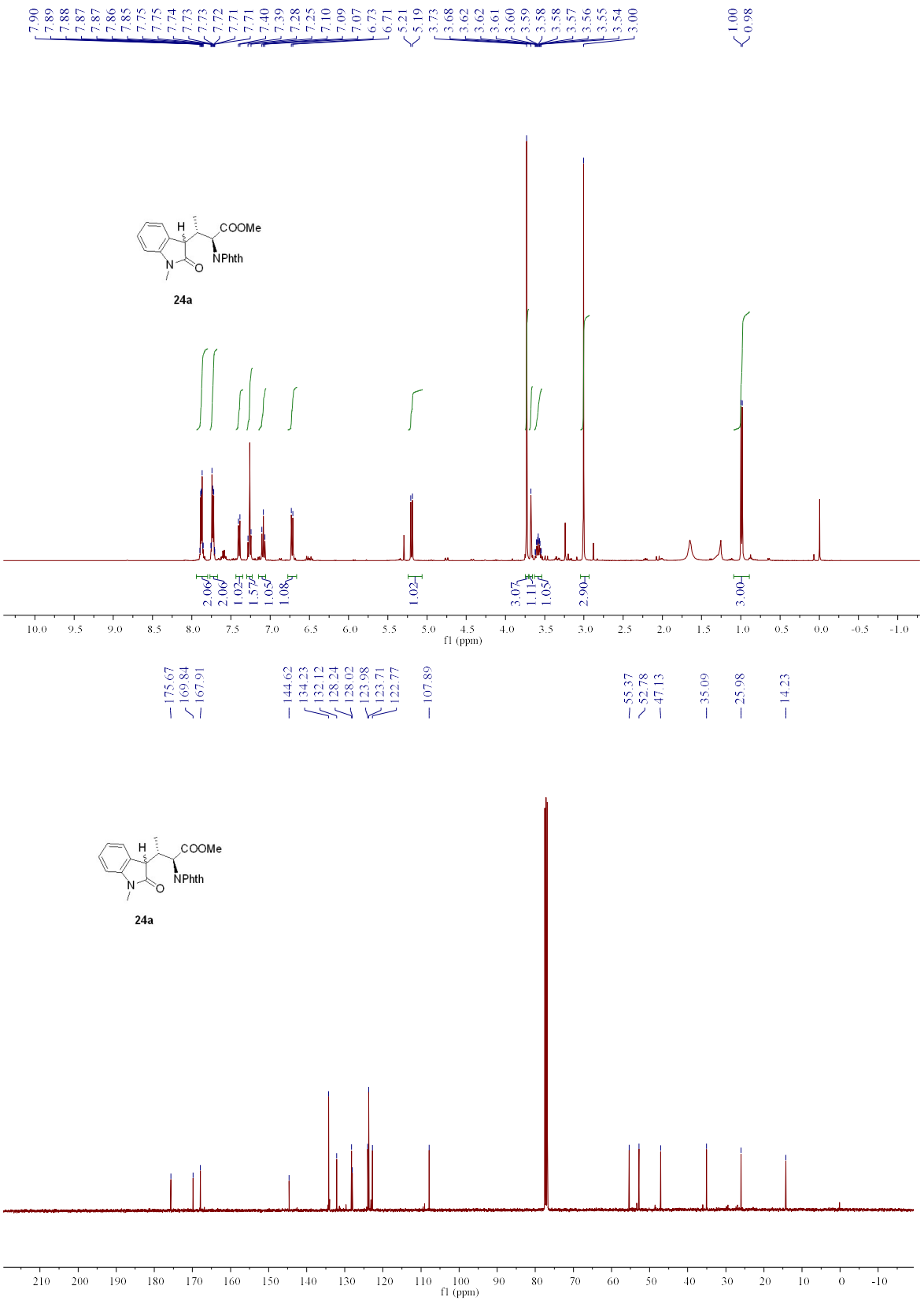
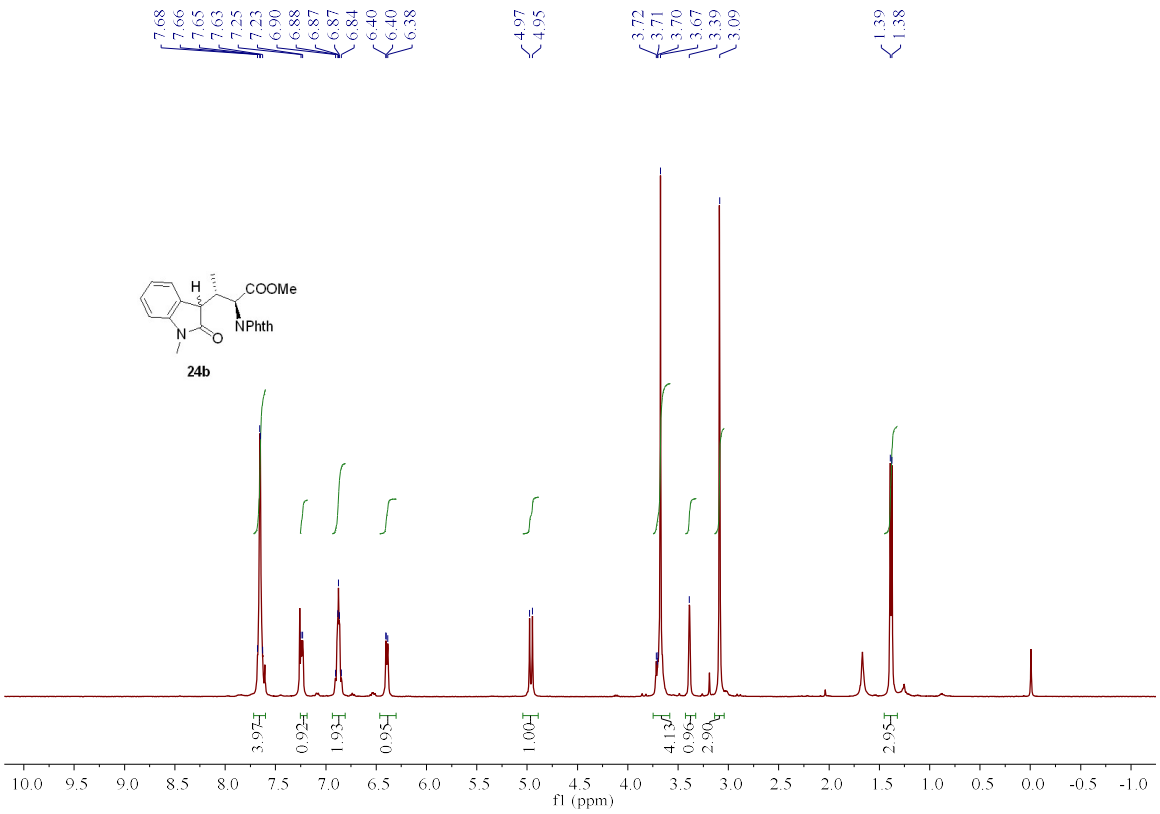
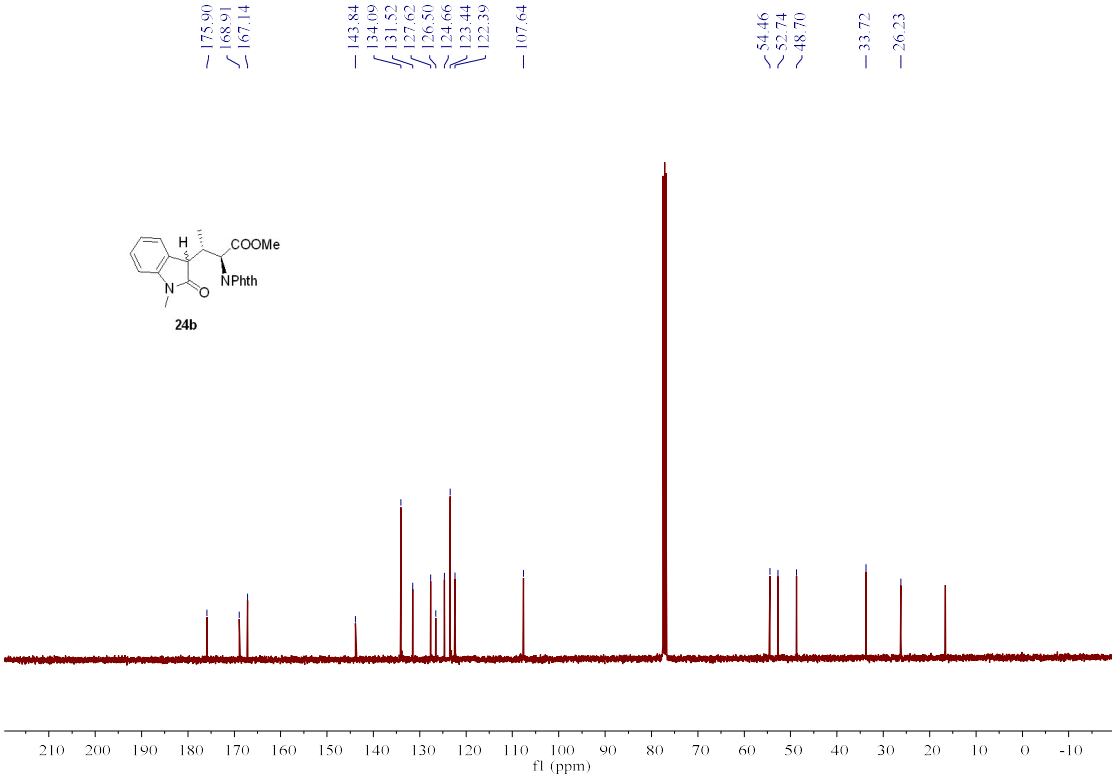
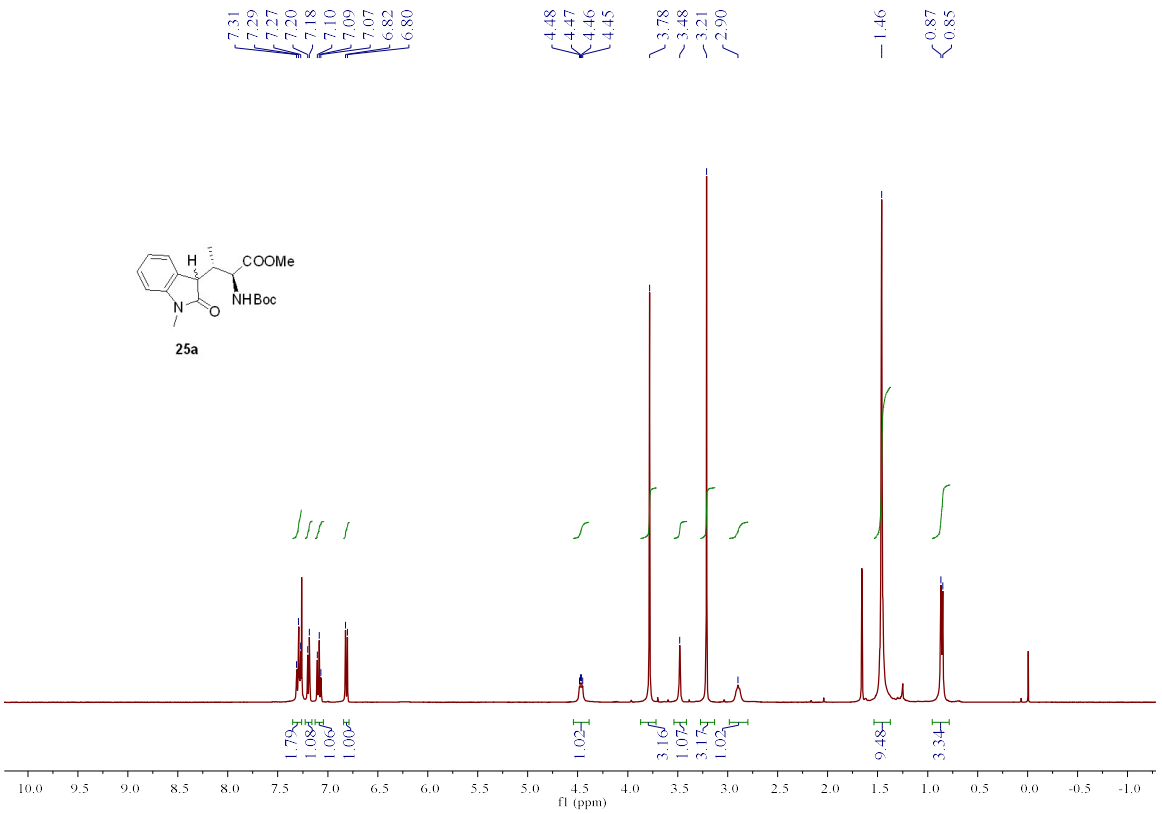
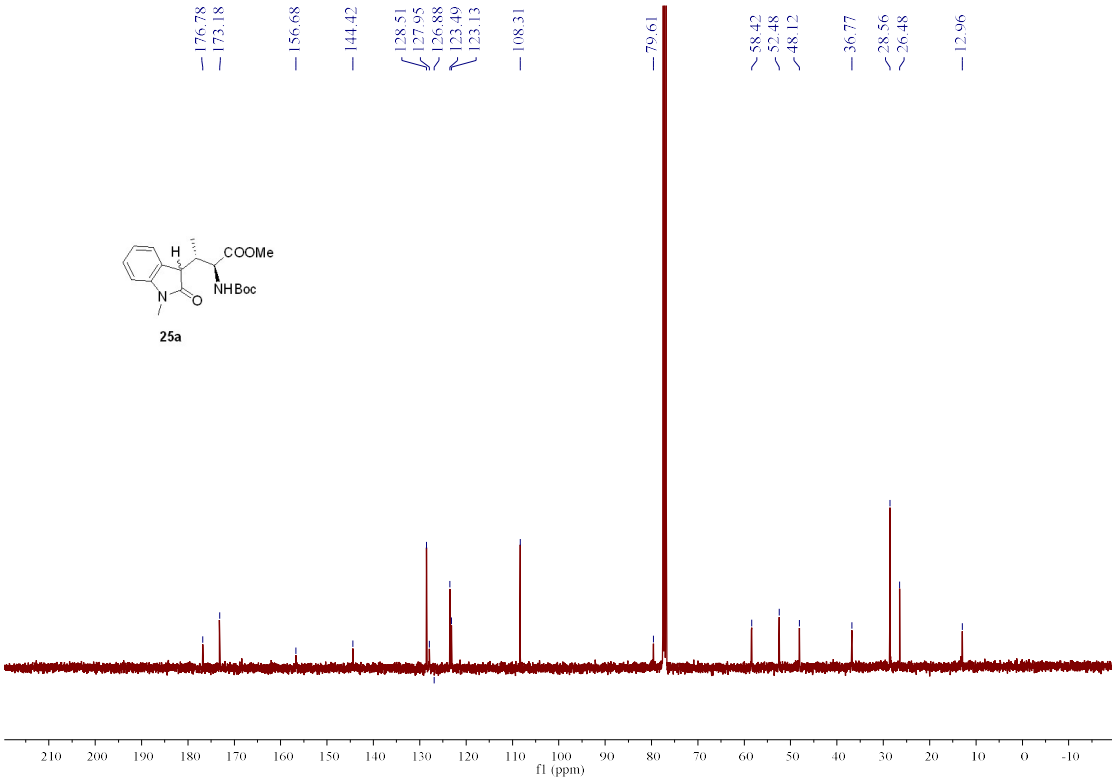
133.83
131.51
126.79
126.62
123.22
121.37
119.52
118.81
115.68
108.99
57.13
52.54
32.66
31.24
20.33
COOMe
NPhth
N
23
f1 (ppm)

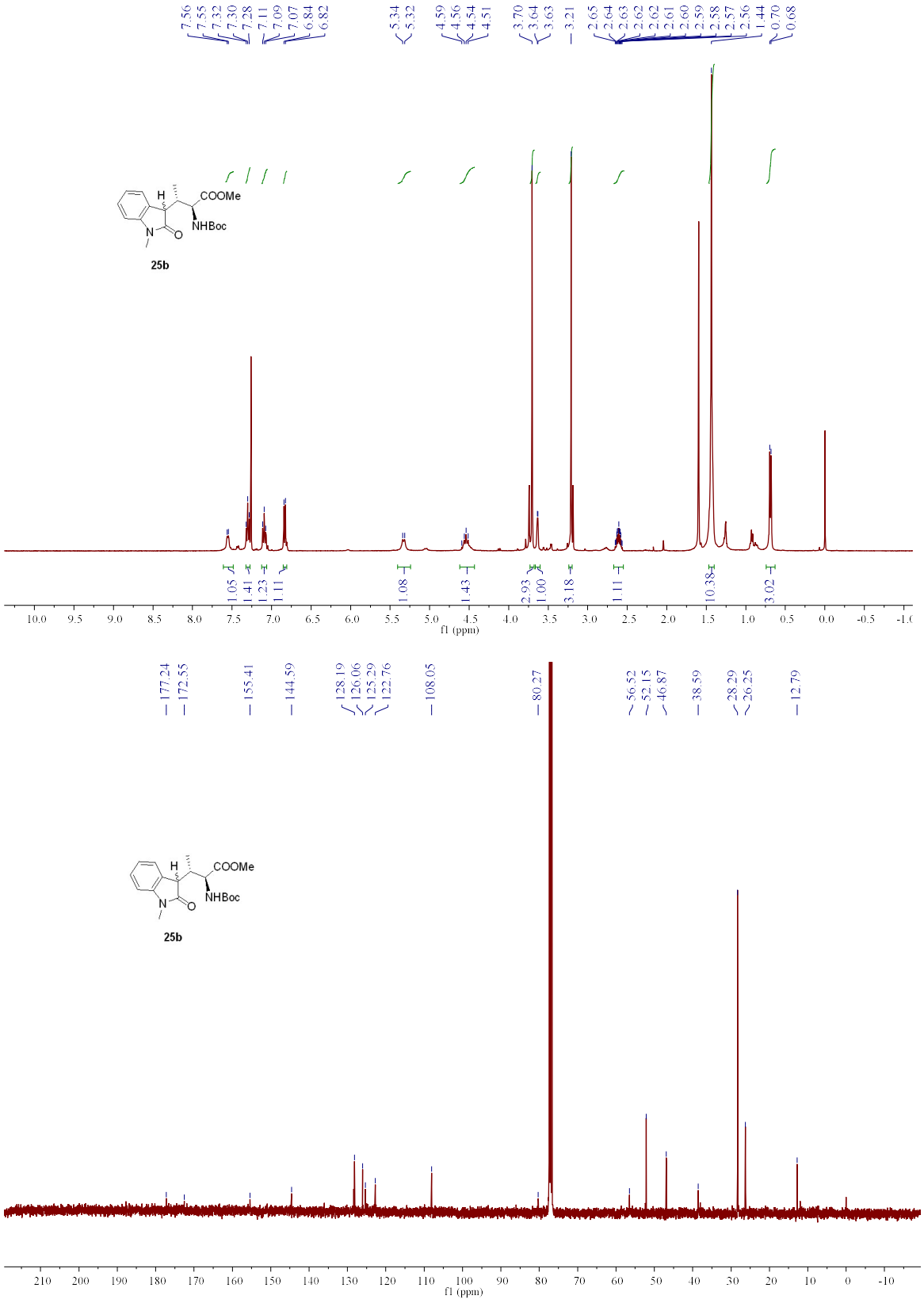

7.90
7.89
7.88
7.87
7.87
7.86
7.85
7.75
7.75
7.74
7.73
7.73
7.72
7.71
7.71
7.40
7.39
7.28
7.25
7.10
7.09
7.07
6.73
6.71
5.21
5.19
3.73
3.68
3.62
3.62
3.61
3.60
3.59
3.58
3.58
3.57
3.56
3.55
3.54
3.00
1.00
0.98
H
COOMe
NPhth
N
O
24a
2.06
2.06
1.02
1.57
1.05
1.08
1.02
3.07
1.11
1.03
2.90
3.00
f1 (ppm)
175.67
169.84
167.91
144.62
134.23
132.12
128.24
128.02
123.98
123.71
122.77
107.89
55.37
52.78
47.13
35.09
25.98
14.23
f1 (ppm)

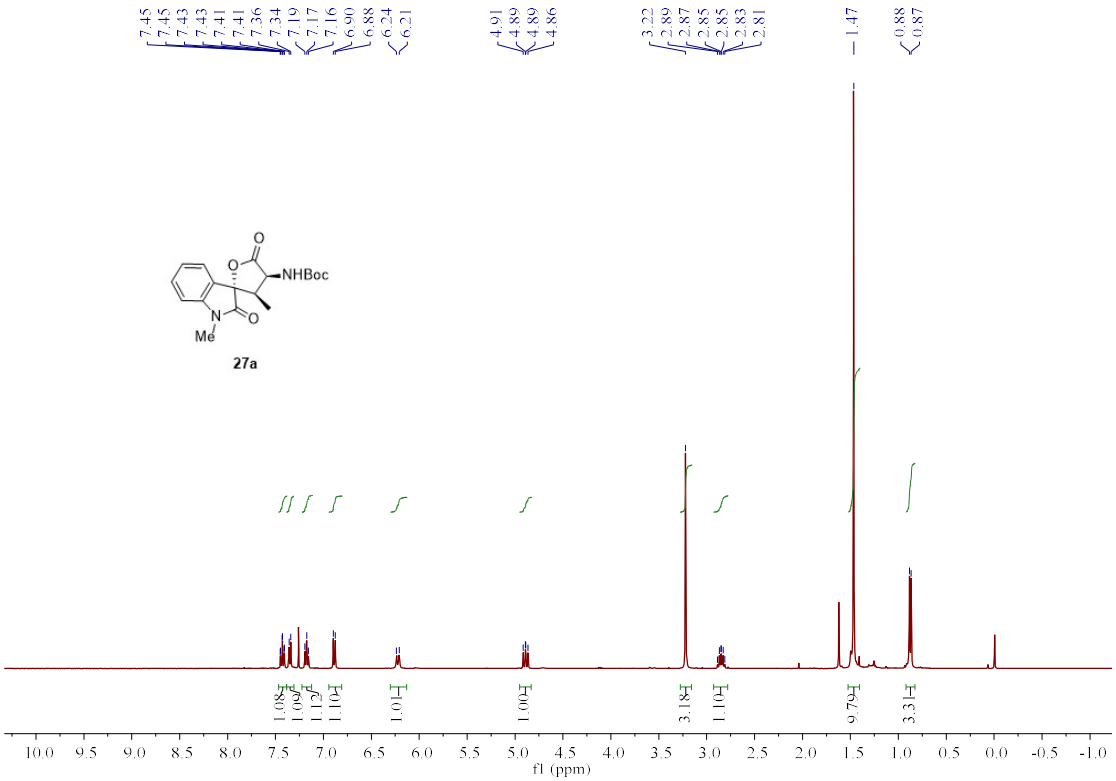

7.68
7.66
7.65
7.63
7.25
7.23
6.90
6.88
6.87
6.87
6.84
6.40
6.40
6.38
4.97
4.95
3.72
3.71
3.70
3.67
3.39
3.09
1.39
1.38
H
COOMe
NPhth
N
O
24b
3.97
0.92
1.93
0.95
1.00
4.13
0.96
2.90
2.95
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


175.90
168.91
167.14
143.84
134.09
131.52
127.62
126.50
124.66
123.44
122.39
107.64
54.46
52.74
48.70
33.72
26.23
H
COOMe
NPhth
N
O
24b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

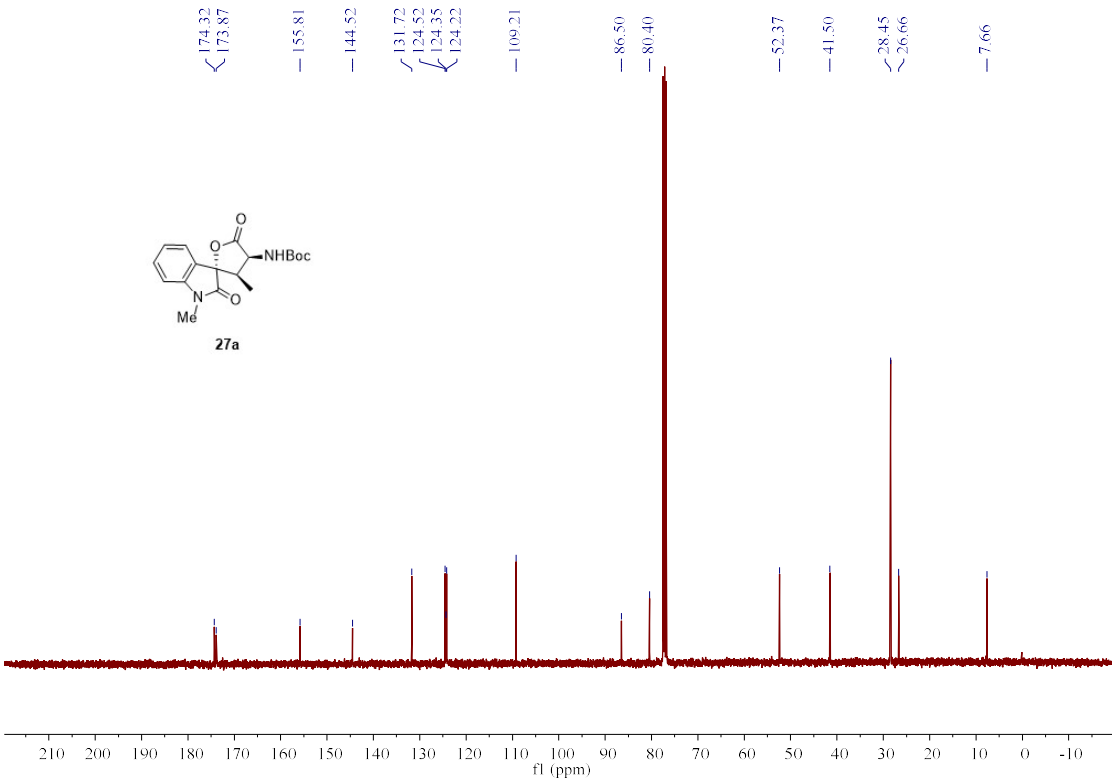

7.31
7.29
7.27
7.20
7.18
7.10
7.09
7.07
6.82
6.80
4.48
4.47
4.46
4.45
3.78
3.48
3.21
2.90
1.46
0.87
0.85
COOMe
NHBoc
25a
1.79
1.08
1.06
1.00
1.02
3.16
1.07
3.17
1.02
9.48
3.34
f1 (ppm)


176.78
173.18
156.68
144.42
128.51
127.95
126.88
123.49
123.13
108.31
79.61
58.42
52.48
48.12
36.77
28.56
26.48
12.96
COOMe
NHBoc
25a
f1 (ppm)

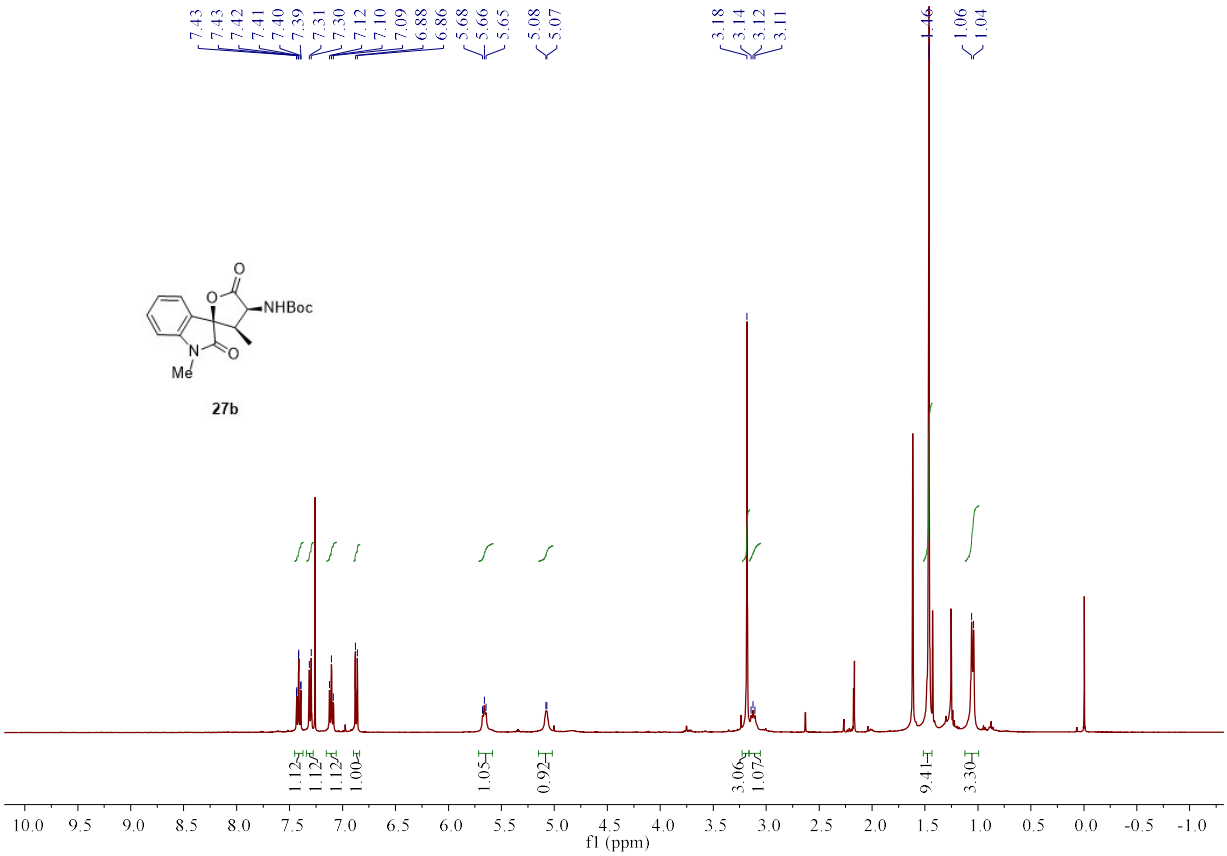

7.56
7.55
7.32
7.30
7.28
7.11
7.09
7.07
6.84
6.82
5.34
5.32
4.59
4.56
4.54
4.51
3.70
3.64
3.63
3.21
2.65
2.64
2.63
2.62
2.62
2.61
2.60
2.59
2.58
2.57
2.56
1.44
0.70
0.68
COOMe
NHBoc
25b
1.05
1.41
1.23
1.11
1.08
1.43
2.93
1.00
3.18
1.11
10.38
3.02
f1 (ppm)
177.24
172.55
155.41
144.59
128.19
126.06
125.29
122.76
108.05
80.27
56.52
52.15
46.87
38.59
28.29
26.25
12.79
COOMe
NHBoc
25b
f1 (ppm)

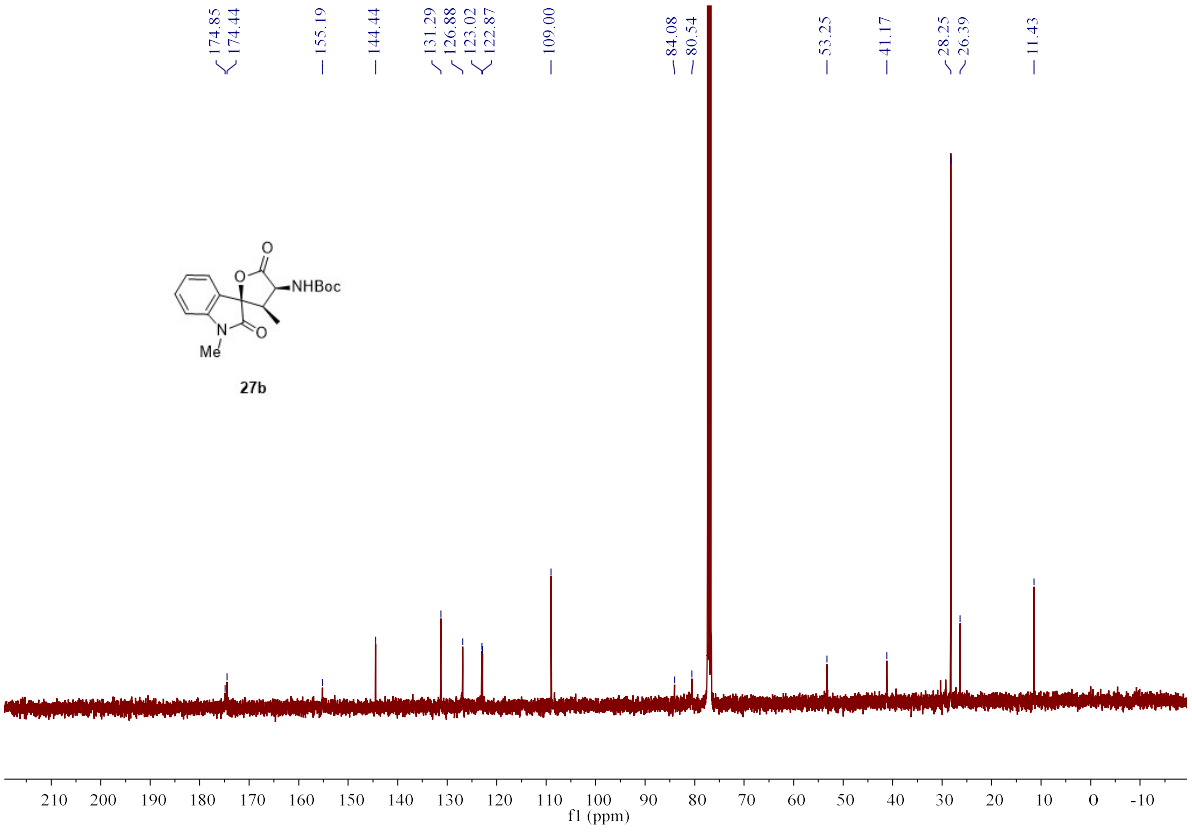

7.45
7.45
7.43
7.43
7.41
7.41
7.36
7.34
7.19
7.17
7.16
6.90
6.88
6.24
6.21
4.91
4.89
4.89
4.86
3.22
2.89
2.87
2.85
2.85
2.83
2.81
1.47
0.88
0.87
NHBoc
O
O
N
Me
O
1.08
1.09
1.13
1.10
1.01
1.00
3.18
1.10
9.79
3.31
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

27a

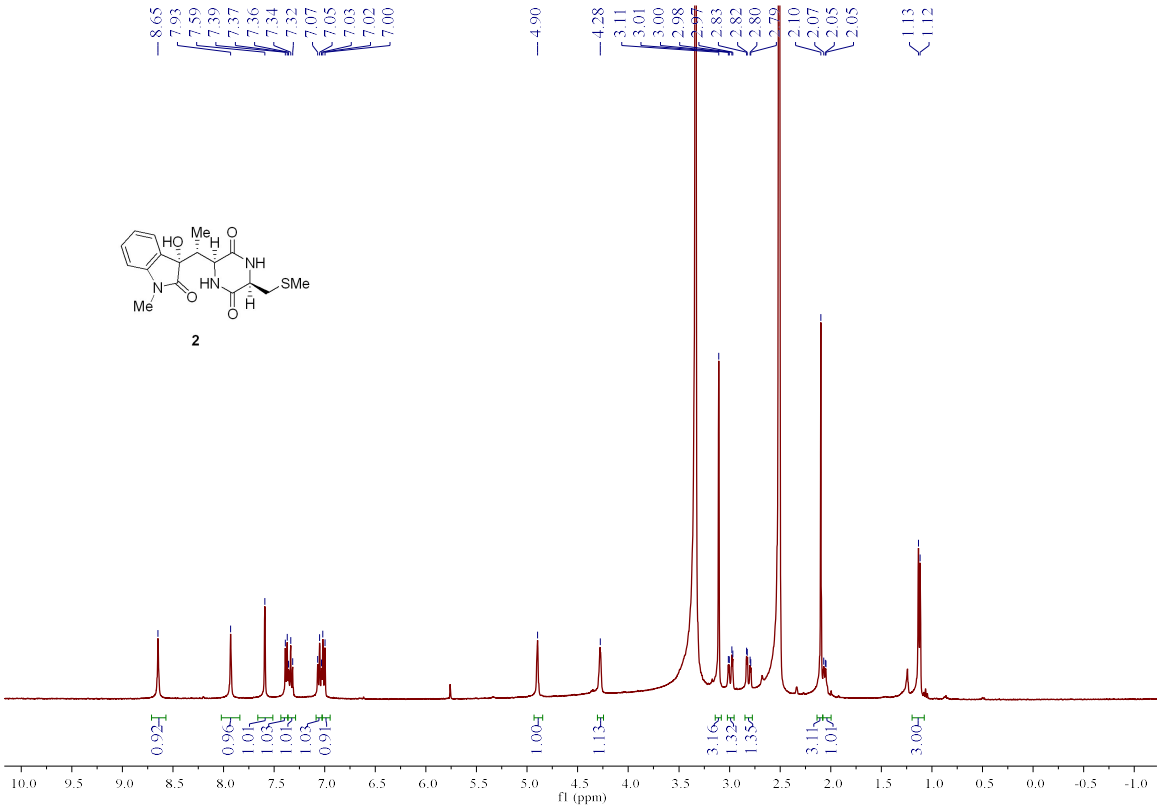

174.32
173.87
155.81
144.52
131.72
124.52
124.35
124.22
109.21
86.50
80.40
52.37
41.50
28.45
26.66
7.66
NHBoc
O
O
N
Me
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

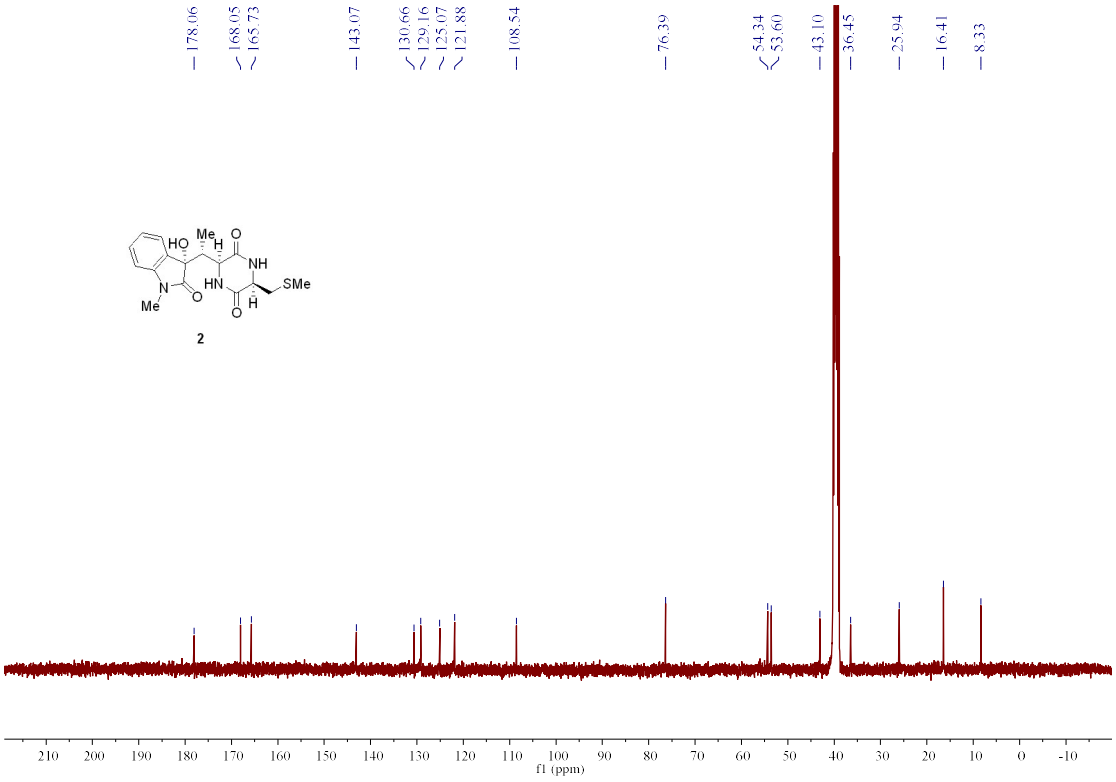
27a


7.43
7.43
7.42
7.41
7.40
7.39
7.31
7.30
7.12
7.10
7.09
6.88
6.86
5.68
5.66
5.65
5.08
5.07
3.18
3.14
3.12
3.11
1.46
1.06
1.04
NHBoc
O
O
N
Me
O
27b
1.12
1.12
1.12
1.00
1.05
0.92
3.06
1.07
9.41
3.30
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

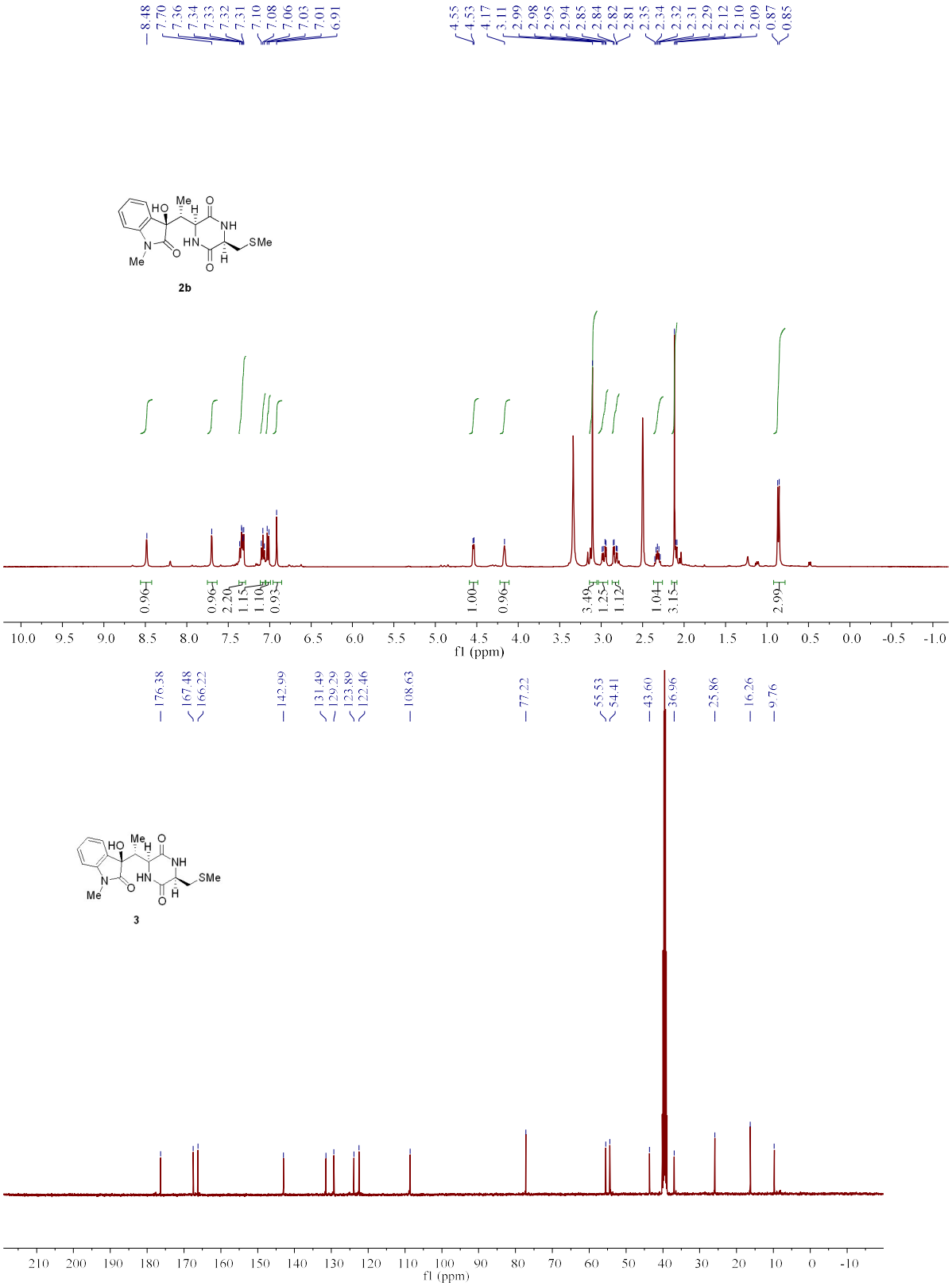

174.85
174.44
155.19
144.44
131.29
126.88
123.02
122.87
109.00
84.08
80.54
53.25
41.17
28.25
26.39
11.43
NHBoc
O
O
N
Me
O
27b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

Maremycin A (**2a**)





Maremycin B (**2b**)



5. X-ray Crystallographic Data

Crystal Data and Structure for **20**

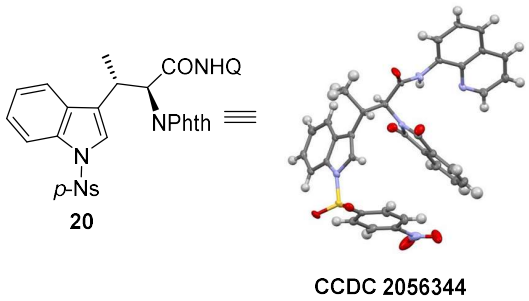


Figure S1. X-Ray crystallographic data of **20.** The ellipsoids drawn at 30% probability level.

Table S2. Crystal data and structure refinement for **20**

Bond precision:	C-C = 0.0092 A		Wavelength=1.54184
Cell:	a=10.5548(4)	b=27.6947(9)	c=10.8041(4)
	alpha=90	beta=101.966(4)	gamma=90
Temperature:	170 K		
	Calculated		Reported
Volume	3089.5(2)		3089.5(3)
Space group	P 21		P 1 21 1
Hall group	P 2yb		P 2yb
Moiety formula	C35 H25 N5 O7 S		C35 H25 N5 O7 S
Sum formula	C35 H25 N5 O7 S		C35 H25 N5 O7 S
Mr	659.66		659.66
Dx,g cm-3	1.418		1.418
Z	4		4
Mu (mm-1)	1.440		1.440
F000	1368.0		1368.0
F000’	1373.63		
h,k,lmax	12,33,12		12,32,12
Nref	11119[5684]		10748
Tmin,Tmax	0.526,0.562		0.385,1.000
Tmin’	0.477		

Correction method= # Reported T Limits: Tmin=0.385 Tmax=1.000

AbsCorr = MULTI-SCAN

Data completeness= 1.89/0.97 Theta(max)= 67.425

R(reflections)= 0.0692(9415) wR2(reflections)= 0.1795(10748)

S = 1.031 Npar= 867

6. References

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