Supplemental material for:

# Catalytic Asymmetric Formal Total Syntheses of (+)- and (–)-Cycloclavine

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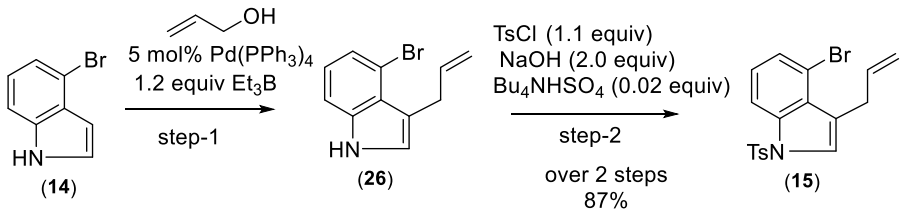
## Materials and Methods

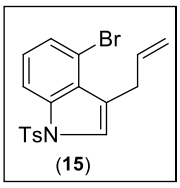
Unless otherwise stated, reactions were performed in oven-dried glassware fitted with rubber septa under a nitrogen atmosphere and were stirred with Teflon-coated magnetic stirring bars. Liquid reagents and solvents were transferred *via* syringe using standard Schlenk techniques. Tetrahydrofuran (THF), diethyl ether ($Et_2O$) was distilled over sodium/benzophenone ketyl. Acetonitrile, dichloromethane ($CH_2Cl_2$), toluene, and benzene were distilled over calcium hydride. All other solvents such as chloroform, methanol, ethanol, DMSO and reagents such as tryptamine, phthalic anhydride, succinic anhydride, sodium borohydride, methyl chloroformate, benzyl chloroformate,p-toluenesulfonyl chloride, $LiAlH_4$, triethylamine, acetic acid, Di-tert-butyl dicarbonate, paraformaldehyde, etc. were used as received, unless otherwise noted.Thin layer chromatography was performed using Merck Silicagel 60 F-254 precoated plates (0.25 mm) and visualized by UV irradiation, 2,4-DNP, anisaldehyde stain and other stains. Silicagel (particle size 100-200 mesh) was used for flash chromatography. Melting points were recorded on a digital melting point apparatus and are uncorrected. $^1H$ and $^{13}C$ NMR spectra were recorded 400, 500 MHz spectrometers with $^{13}C$ operating frequencies of 100, 125 MHz, respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (δ = 7.24 for $^1H$ NMR and δ = 77.0 for $^{13}C$ NMR). Data for $^1H$ NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, and number of hydrogen). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). IR spectra were recorded on a FT-IR system (Spectrum BX) and are reported in frequency of absorption ($cm^{-1}$). Only selected IR absorbencies are reported. High-resolution mass spectrometry (HRMS) data were recorded on MicrOTOF-Q-II mass spectrometer using methanol as solvent. High resolution mass spectra and NMR data were obtained from the Central Instrumentation Facility (CIF) at the Indian Institute of Science Education and Research (IISER) Bhopal.




**Synthesis of compound 15**:

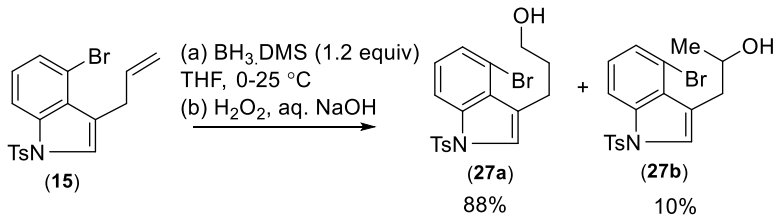
**Step 1**: In a resealable round-bottom flask, 4-bromoindole **14** (25.0 g, 127.52 mmol; 1.0 equiv) was taken in dry THF (200 mL) and degassed under argon atmosphere for 10 minutes. To this solution allyl alcohol (8.7 mL, 127.52 mmol; 1.0 equiv), triethyl borane [1(M) in hehane)] (38.3 mL, 38.3 mmol; 0.3equiv), and $Pd(PPh_3)_4$ (2.95 gm, 2.55 mmol; 0.02 equiv) were added successively and stirred the reaction mixture after placing in an oil bath maintain 50 ºC for 12 h. Upon completion of the reaction, (TLC showed complete consumption of starting material) the reaction mixture was concentrated under reduced pressure to afford crude allylated product **26** as brown oil, which was used for next step without purification.

**Step 2**: To the stirred solution of 3-allylated-4-bromo indole **26** (~30.1 g, 127.52 mmol; 1.0 equiv) in $CH_2Cl_2$ (250 mL), *p*-TsCl (26.7 g, 140.3 mmol; 1.1 equiv), NaOH (10.2 gm, 255.0 mmol; 2 equiv) in 5 mL water, and $Bu_4NHSO_4$ (865 mg, 2.55 mmol; 0.02 equiv) were added respectively at RT and stirred vigorously for 1h. Upon completion of reaction, the organic layer was washed with water (2 X 100 mL), dried over $Na_2SO_4$ and concentrated under vacco to get white solid, which was purified by column chromatography with *n*-Hexane-EtOAc (9:1) to afford compound (**15**) as colorless solid.

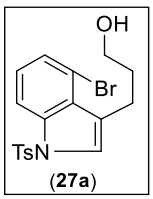



**3-Allyl-4-bromo-1-tosyl-1H-indole** (**15**): 43.3 g (87% yield) as colorless solid. $R_f$ = 0.45 (5% EtOAc in hexane). **$^1$H NMR**(400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.2 Hz, 1H), 7.71 (m, 2H), 7.39 (s, 1H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.19 (m, 2H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.02 -

6.12 (m, 1H), 5.03 - 5.14 (m, 2H), 3.69-3.17 (m, 2H), 2.31 (s, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 145.2, 136.6, 135.8, 134.9, 128.8, 127.8, 126.8, 125.0, 122.0, 116.8, 114.6, 112.9, 30.9, 21.6; **IR** (film) $\upsilon_{max}$ 2920, 2725, 1596, 1411, 1372, 1189, 1172, 1087, 982, 773 $cm^{-1}$.

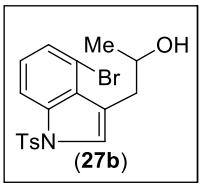



**Synthesis of primary alcohol 27a**: In an oven dried round-bottom flask, the compound **15** (22.0 g, 56.4 mmol; 1.0 equiv) was taken in dry THF (250 mL) under argon atmosphere at 0 °C. To this solution, $BH_3.SMe_2$ [5 M in $Et_2O$] (6.4 mL, 67.6 mmol; 1.2 equiv) was added drop wise for 15 minutes and stirring was continued for 12 h [temperature gradually increases to 25 °C]. Upon completion of the reaction (judged by running TLC) the reaction mixture was placed over an ice bath and excess borane was quenched by careful addition of EtOH (50 mL), then 10% (W/V) aqueous NaOH (30 mL) and followed by 30 % (W/V) $H_2O_2$ (30 mL). Then the mixture was stirred for another 6 h at 25 °C and was diluted with $CH_2Cl_2$ (250 mL) and water (200 mL). The organic layer was separated through separatory funnel, washed with water twice and dried over anhydrous $Na_2SO_4$. The organic layer was concentrated under reduced pressure. The crude mixtures were purified by column chromatography by using n-Hexane/EtOAc (3:2) mixture as eluent to afford **27a** as colorless solid.



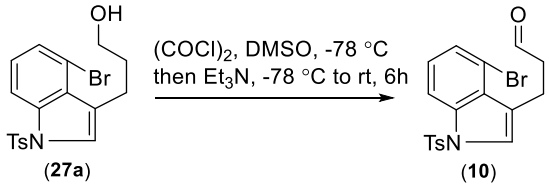

**3-(4-Bromo-1-tosyl-1H-indol-3-yl)propan-1-ol** (**27a**): 20.3 g (88% yield) as colorless solid. $R_f$ = 0.45 (40% EtOAc in hexane). **$^1$H NMR** (500 MHz, $CDCl_3$) δ: 7.98 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.74 (m, 2H), 7.40 (s, 1H), 7.39 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.25 (m, 2H),

7.13 (t, *J* = 8.1 Hz, 1H), 3.76 (t, *J* = 6.3 Hz, 2H), 3.04 (m, 2H), 2.36 (s, 3H), 1.96-2.01 (m, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) δ: 145.2, 136.6, 134.9, 129.9, 128.9, 127.8, 126.8, 125.4, 124.6, 123.1, 114.6, 112.9, 62.2, 33.1, 22.6, 21.6; **IR** (film) $\upsilon_{max}$ 3374, 2928, 1595, 1412, 1244, 1172, 1088, 979, 776 $cm^{-1}$; **MP**143–145°C; **HRMS** (ESI) m/z 408.0217 $[M + H]^+$; calculated for $[C_{18}H_{18}BrNO_3S + H]^+$: 408.0264.



(**27b**)

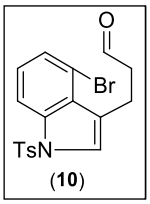
**1-(4-Bromo-1-tosyl-1H-indol-3-yl)propan-2-ol** (**27b**): 2.3 g (10% yield) as brownish gel. $R_f$ = 0.50 (40% EtOAc in hexane). **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 7.99 (d, *J* = 8.3 Hz, 1H), 7.79 – 7.70 (m, 2H), 7.53 (s, 1H), 7.41 – 7.32 (m, 1H), 7.24 – 7.17 (m, 2H), 7.16 – 7.09 (m, 1H), 4.17 (ddd, *J* = 8.6, 6.4, 4.7 Hz, 1H), 3.80 – 3.48 (m, 1H), 3.20 (dt, *J* = 14.7, 3.7 Hz, 1H), 2.42 – 2.17 (m, 4H), 1.28 (dd, *J* = 6.2, 1.9 Hz, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 145.3, 136.6, 134.7, 130.0, 128.7, 128.0, 126.8, 126.2, 125.5, 119.9, 114.5, 113.0, 67.5, 35.9, 22.7, 21.6; **IR** (film) $\upsilon_{max}$ 3365, 2965, 2901, 1576, 1452, 1270, 1135, 1098, 985, 779 $cm^{-1}$; **HRMS** (ESI) m/z 430.0109 $[M + Na]^+$; calculated for $[C_{18}H_{18}BrNO_3S + Na]^+$: 430.0083.



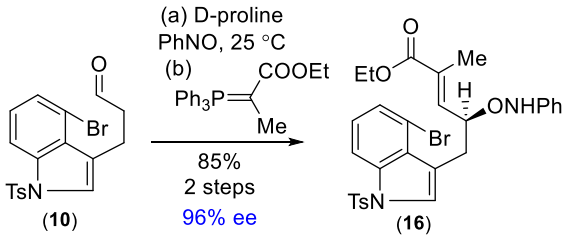
(**27a**) (**10**)

**Synthesis of aldehyde 10**: In an oven-dried long neck round-bottom flask, DMSO (11.2 mL, 156.3 mmol; 5.0 equiv) was charged in dry $CH_2Cl_2$ (100 mL) and the reaction vessel was cooled to -78 ºC. To that solution oxalyl chloride (4.0 mL, 46.9 mmol, 1.5 equiv) in 20 mL $CH_2Cl_2$ was transferred drop-wise over a period of 15 minutes and stirring was continued for additional 30 minutes at same temperature. After that, a solution of alcohol **27a** (12.7 g, 31.3 mmol; 1.0 equiv) in $CH_2Cl_2$ (80 mL) was added to the reaction mixture drop-wise through a syringe and stirring was continued at same temperature for another

additional 2 h. Next, $Et_3N$ (22.0 mL, 156.3 mmol, 5.0 equiv) was added to the reaction mixture at -78 ºC and allowed to increase the temperature gradually to 25 °C. Upon completion of reaction, (TLC showed complete consumption of starting material) the reaction mixture was quenched with water and diluted with $CH_2Cl_2$. The organic layer was separated, washed with brine and dried over anhydrous $Na_2SO_4$.The organic layer was concentrated under reduced pressure and the crude was then purified by flash chromatography by using n-Hexane/EtOAc (17:3) as eluent to afford the desired aldehyde (**10**) as yellow solid.

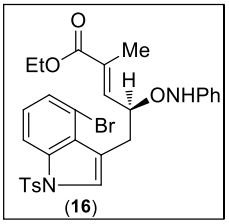



**3-(4-Bromo-1-tosyl-1H-indol-3-yl)propanal** (**10**): The compound was obtained as yellow solid in 12.1 g (95% yield). $R_f$ = 0.50 (20% EtOAc in hexane). **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 9.85 (t, *J* = 1.2 Hz, 1H), 7.79 (dd, *J* = 8.4, 0.7 Hz, 1H), 7.74 (m, 2H), 7.40 (s, 1H), 7.39 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.25 (m, 2H), 7.14 (t, *J* = 8.1 Hz, 1H), 3.29 (td, *J* = 7.5, 0.7 H, 2H), 2.87-2.91 (td, *J* = 7.6, 1.0 Hz, 2H), 2.40 (s, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 201.1, 145.3, 136.6, 134.8, 130.0, 128.6, 127.8, 126.8, 125.6, 125.1, 121.6, 114.4, 113.0, 44.4, 21.6, 18.9; **IR** (film) $\upsilon_{max}$ 2920, 1716, 1595, 1558, 1412, 1372, 1172, 1131, 1087, 982, 745 $cm^{-1}$; **MP** 136–138°C, **HRMS** (ESI) m/z 406.0093 $[M + H]^+$; calculated for $[C_{18}H_{16}BrNO_3S + H]^+$: 406.0107.




**Synthesis of** (–)-(**16**)**:** In an oven-dried round-bottom flask was charged with aldehyde (**10**) (8.0 g, 19.9 mmol, 1.0 equiv) in DMSO (50 mL) under argon atmosphere. To this

solution, nitrosobenzene (2.1 g, 19.9 mmol, 1.0equiv) and D-proline (918 mg, 7.97 mmol, 0.4 equiv) were added successively and stirred for 10 minutes at 25 °C until color of the solution changed from green to yellow (color change is indicated the completion of reaction). Upon completion of the reaction, (judged by running a TLC) a solution of stabilized Wittig salt (10.8 g, 35.9 mmol, 1.5 equiv) and anhydrous LiCl (1.5 g, 35.9 mmol, 1.5 equiv) in 100 mL MeCN was transferred to the reaction mixture at once at 0 ºC and continued for another additional 2 h at same temperature. Upon completion of the reactions (judged by TLC analysis), the reaction mixture was quenched by addition of water and the reaction mixture was partitioned between water and EtOAc. Then organic layer was separated through separatory funnel and water layer was washed twice with EtOAc (100 mL). The combined organic layer was washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude was then purified by flash chromatography by using n-Hexane/EtOAc (4:1) as eluents to afford compound (**16**) as yellow gel.

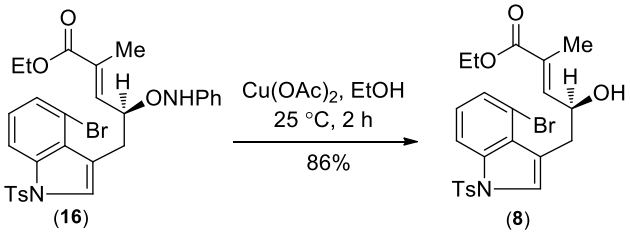


(**16**)

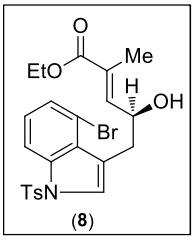
**Ethyl (*S*,E)-5-(4-bromo-1-tosyl-1H-indol-3-yl)-2-methyl-4-((phenylamino)oxy)pent-2-enoate** (–)-**16**: 10.1 g (85% yields) as yellow gel. $R_f$ = 0.52 (20% EtOAc in hexane). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.5 Hz, 1H), 7.68 (m, 2H), 7.50 (s, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.15 (m, 2H), 7.08-7.13 (m, 2H), 6.88 (m, 2H), 6.72-6.78 (m, 3H), 5.00-5.06 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.47 (dd, *J* = 14.5, 7.0 Hz, 1H), 3.20 (dd, *J* = 14.5, 6.6 Hz, 1H), 2.30 (s, 3H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.31 (t, *J* = 7.05 Hz, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 167.6, 148.2, 145.3, 139.1, 136.3, 134.8, 132.1, 130.0, 128.8, 128.6, 127.9, 126.9, 126.8, 125.4, 122.0, 117.6, 114.5, 114.3, 112.9, 79.3, 60.9, 29.9, 21.5, 14.3, 13.2; **IR** (film) $\upsilon_{max}$3392, 1705, 1596, 1436, 1373, 1174, 1120, 721 $cm^{-1}$;**HRMS** (ESI) m/z 597.1000 $[M + H]^+$; calculated for $[C_{29}H_{29}BrN_2O_5S + H]^+$: 597.1053. Enantiomeric excess was determined to be 96% ee *via* HPLC analysis using a Chiralpak AD-H column; solvent: 2-propanol/ hexane = 1/3; flow rate: 1.0 mL/min; detection: at

254 nm): $t_R$ major = 16.19 min, $t_R$ minor = 24.23 min.;$[\alpha]_{589}^{23.2\ ^{\circ}C}$ = – 84.0 (*c* = 0.10, $CH_2Cl_2$).

[Compound (+)-**16** was synthesized in 86% yield from the compound **10** using L-proline as catalyst by using the similar procedure as explained above. Rotation of the compound (+)-**16**; $[\alpha]_{589}^{24.0}$ = +80 (*c* = 0.15, $CH_2Cl_2$).]



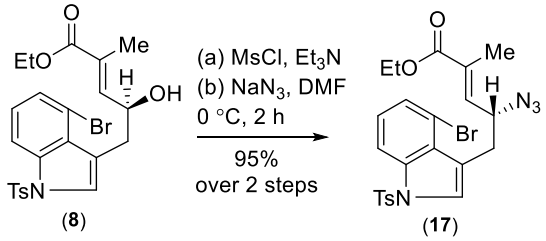

**Synthesis of allylic alcohol** (–)-(**8**): In an oven-dried round-bottom flask, compound **16** (7.0 g, 11.7mmol, 1.0 equiv) was dissolved in 70 mL of EtOH under argon atmosphere at 0 ºC. To that solution anhydrous $Cu(OAc)_2$ (319 mg, 1.76 mmol, 0.15 equiv) was added. Then the reaction mixture was stirred at same for 2 h until starting material completely consumed (judged by running TLC). After that, the reaction mixture was concentrated under reduced pressure and the crude mixture was directly purified through column chromatography using n-Hexane/EtOAc (7:3) as eluents to afford the compound (**8**) as yellow gel.




**Ethyl (*S*,E)-5-(4-bromo-1-tosyl-1H-indol-3-yl)-4-hydroxy-2-methylpent-2-enoate** (**8**): 5.1 g (86% yield) as yellow gel. $R_f$ = 0.3 (20% EtOAc in hexane). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.2 Hz, 1H), 7.69 (m, 2H), 7.47 (s, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.21 (m, 2H), 7.10 (t, *J* = 8.1 Hz, 1H), 6.68 (m, 1H), 4.81 (m, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.11- 3.24 (m, 2H), 2.32 (s, 3H), 1.79 (brs, 1H), 1.64 (d, *J* = 1.1 Hz, 3H), 1.28 (t, *J* =

7.0 Hz, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 167.7, 145.4, 141.1, 136.4, 134.7, 130.0, 129.9, 129.7, 128.5, 127.9, 126.8, 125.5, 117.8, 114.3, 113.0, 68.1, 60.9, 33.4, 21.6, 14.2, 13.1; **IR** (film) $\upsilon_{max}$3375, 2929, 1717, 1412, 1373, 1248, 1174, 983, 949 $cm^{-1}$;**HRMS** (ESI) m/z 506.0612 $[M + H]^+$; calculated for $[C_{23}H_{24}BrNO_5S+ H]^+$: 506.0631. Enantiomeric excess was determined to be 96.5% ee *via* HPLC analysis using a Chiralpak AD-H column; solvent: 2-propanol/ hexane = 1/3; flow rate: 1.0 mL/min; detection: at 254 nm): $t_R$ major = 9.62 min, $t_R$ minor = 15.90 min.; $[\alpha]_{589}^{21.1\ ^oC}$= – 9.2 (*c* = 0.53, $CH_2Cl_2$).

[Compound (+)-**8** was synthesized from (+)-**16** in 84% yield, by using the similar procedure as described above. Rotation of the compound (+)-**8**; $[\alpha]_{589}^{23.1}$ = +10.1 (*c* = 0.42, $CH_2Cl_2$).]

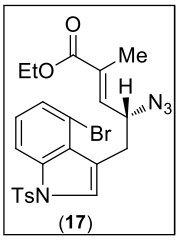



**Synthesis of azide** (+)-(**17**):

**Step 1**: The enantioenriched compound **8** (3.5 g, 6.9 mmol, 1.0 equiv) was charged in 40 mL $CH_2Cl_2$ under argon atmosphere and $Et_3N$ (1.2 mL, 8.53 mmol, 1.2 equiv) and DMAP (88 mg, 0.72 mmol, 0.1 equiv) were added at 0 ºC. To this solution, MsCl (0.67 mL, 8.53 mmol, 1.2 equiv.) was added dropwise over 2 minutes. The reaction mixture was then allowed to stir at same temperature for 30 minutes. After complete consumption of starting material (judged by running TLC), the reaction mixture was quenched with 30 mL water and diluted with 50 mL $CH_2Cl_2$. The organic layer was separated through separatory funnel, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude product was directly treated for next step without further purification.

**Step 2**: The crude mixtures were dissolved in DMF (20 mL) under argon atmosphere. To this reaction solution, $NaN_3$ (2.30 g, 35.55 mmol, 5 equiv.) was added at 0 ºC and stirred

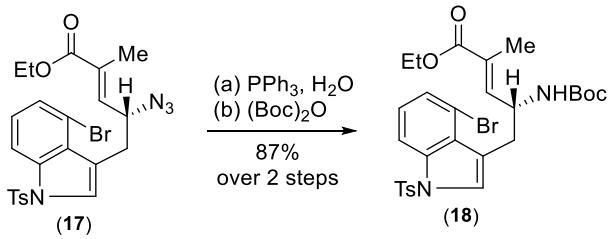
the reaction mixture for 2 h. Upon completion of the reactions, (TLC showed complete consumption of starting material) the reaction mixture was diluted with 60 mL EtOAc and water (60 mL). The organic layer was separated and washed the aqueous layer with 2 X 30 mL EtOAc. The combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure. The crude reaction mixture was purified by flash chromatography with *n*-Hexane/EtOAc (9:1) to afford azide **17** as colourless gel.



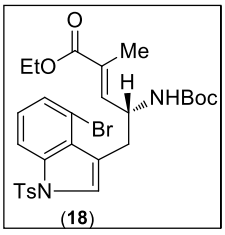
(**17**)

**Ethyl (*R*,*E*)-4-azido-5-(4-bromo-1-tosyl-1H-indol-3-yl)-2-methylpent-2-enoate** (**17**): 3.5 g (95% yields) as colourless gel. $R_f$ = 0.4 (10% EtOAc in hexane).**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.94, (d, *J* = 8.3 Hz, 1H), 7.69 (m, 2H), 7.46 (s, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.20 (m, 2H), 7.11 (t, *J* = 7.9 Hz, 1H), 6.61 (d, *J* = 9.7 Hz, 1H), 4.61-4.67 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.17 (d, *J* = 6.8 Hz, 2H), 2.32 (s, 3H), 1.67 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 167.2, 145.4, 136.4, 134.7, 132.1, 130.0, 128.3, 127.9, 127.1, 126.8, 125.6, 117.3, 114.1, 113.1, 61.1, 59.6, 31.1, 21.6, 14.2, 13.2; **IR** (film) $\upsilon_{max}$2928, 2097, 1712, 1596, 1412, 1373, 1248, 1174, 1097, 984, 749 $cm^{-1}$; **HRMS** (ESI) m/z 553.0545 $[M + Na]^+$; calculated for $[C_{23}H_{23}BrN_4O_4S + Na]^+$: 553.0516 ; $[\alpha]_{589}^{21.5\,^{\circ}C}$ = +10.0 (*c* = 0.23, $CHCl_3$).

[Compound (**–**)-**17** was synthesized in 93% yield from (+)-**8** applying similar procedure as described above. Rotation of the compound (–)-**17**; $[\alpha]_{5589}^{23.2}$ = –8.9 (*c* = 0.12, $CH_2Cl_2$).]



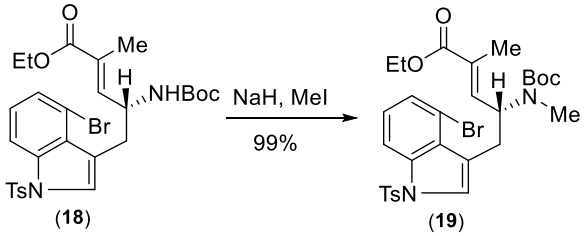

**Synthesis of compound** (+)-(**18**): In a round-bottom flask, the compound **17** (2.8 g, 5.27 mmol, 1.0 equiv) was taken THF (30 mL) at 25 °C. To this solution, $PPh_3$ (1.7 g, 6.33 mmol, 1.2 equiv) and 2 mL water were added. Then the reaction mixture was heated to 70 ºC for 3 h. Upon completion of the reactions (judged by TLC analysis), the reaction mixture was concentrated under vacuo. The reaction mixture was diluted with 15 mL of $CH_2Cl_2$ and $Na_2SO_4$ (~2 g) was added to remove majority of water. The organic layer was transferred to another round-bottom flask. To this solution was added $Et_3N$ (1.1 mL, 7.90 mmol, 1.5 equiv) followed by $(Boc)_2O$ (1.5 mL, 6.33 mmol, 1.2 equiv) simultaneously at 25 °C. It was stirred for 30 minutes for completion of the reaction (judged by TLC analysis). The crude reaction was then concentrated under reduced pressure and purified by flash chromatography with *n*-hexane-EtOAc (4:1) to afford Boc-protected amine **18** as yellow gel.



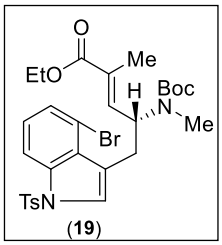

**Ethyl (*R*,*E*)-5-(4-bromo-1-tosyl-1H-indol-3-yl)-4-((*tert*-butoxycarbonyl)amino)-2-methylpent-2-enoate** (**18**): 2.78 g (87% yields) as yellow gel. $R_f$ = 0.4 (20% EtOAc in hexane). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.3 Hz, 1H), 7.68 (m, 2H), 7.44 (s, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.19 (m, 2H), 7.07 (t, *J* = 8.2 Hz, 1H), 6.58 (d, *J* = 8.8 Hz, 1H), 4.76 (m, 2H), 4.17 (q, *J* = 6.9 Hz, 2H), 3.17 (m, 2H), 2.30 (s, 3H), 1.70 (s, 3H), 1.26 (m, 12H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 167.8, 154.9, 145.3, 130.0, 129.7, 128.7, 127.9, 126.8, 126.3, 125.4, 118.1, 114.4, 112.8, 79.7, 60.8, 49.4, 31.4, 28.2, 21.6, 14.2, 13.0; **IR** (film) $\upsilon_{max}$3366, 2978, 2928, 1703, 1505, 1367, 1174, 1097, 982, 737 $cm^{-1}$;

**HRMS** (ESI) m/z 605.1288 $[M + H]^+$; calculated for $[C_{28}H_{33}BrN_2O_6S + H]^+$: 605.1315. Enantiomeric excess was determined to be 96% ee *via* HPLC analysis using a Chiralpak AD-H column; solvent: 2-propanol/ hexane = 1/3; flow rate: 1.0 mL/min; detection: at 254 nm): $t_R$ minor = 9.50 min, $t_R$ major = 13.08 min.; $[\alpha]_{589}^{21.3\ ^oC}$= +3.9 (*c* = 0.28, $CHCl_3$).

[Compound (–)-**18** was synthesized in 88% overall yield in 2 steps from (–)-**17**, applying similar procedure as described above. Rotation of the compound (–)-**18**; $[\alpha]_{589}^{23.1}$ = –3.5 (*c* = 0.20, $CH_2Cl_2$).]

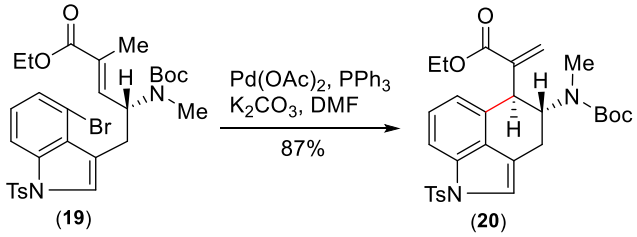



**Synthesis of compound** (+)-(**19**): In an oven dried round-bottom flask compound **18** (2.0 g, 3.30 mmol, 1.0 equiv) was dissolved in dry DMF (12 mL) under nitrogen atmosphere at 0 °C. To this solution, NaH (264 mg, 6.60 mmol, 1.2 equiv) was added pinch wise and stirred for 5 minutes. After stirring for 5 minutes, MeI (454 µL, 7.26 mmol, 1.1 equiv) was added to the reaction mixture drop wise at 0 °C and stirring continued for another 30 minutes. After complete consumption of starting material, reaction was quenched with water and partitioned between water and EtAOc. Then organic layer was separated through separatory funnel and aqueous layer was washed twice with EtOAc. The combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The crude product was then purified by flash chromatography using *n*-hexane-EtOAc (3:1) mixture as eluent to afford compound **19** as yellow gel.



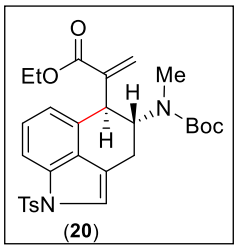

**Ethyl (*R*,*E*)-5-(4-bromo-1-tosyl-1H-indol-3-yl)-4-((*tert*-butoxycarbonyl)(methyl)amino)-2-methylpent-2-enoate** (**19**): 2.02 g (99% yield) as yellow gel. $R_f$ = 0.42 (20% EtOAc in hexane).**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* =8.4 Hz, 1H), 7.67 (m, 2H), 7.40 (brs, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.21 (m, 2H), 7.10 (t, *J* = 8.1 Hz, 1H), 6.74 (brs, 1H), 5.29 (m, 1H), 3.08- 3.23 (m, 2H), 2.71 (s, 1H), 2.30 (s, 3H), 1.78 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.01 (brs, 9H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 167.8, 154.9, 145.2, 138.1, 136.3, 134.7, 131.3, 130.1, 128.8, 127.7, 126.9, 126.2, 125.4, 118.2, 114.4, 112.9, 79.7, 60.9, 53.6, 29.1, 29.0, 27.9, 21.5, 14.3, 13.1; **IR** (film) $\upsilon_{max}$2914, 1690, 1457, 1368, 1248, 1174, 1123, 1022, 983, 750 $cm^{-1}$; **HRMS** (ESI) m/z 619.1477 $[M + H]^+$; calculated for $[C_{29}H_{35}BrN_2O_6S + H]^+$: 619.1472; $[\alpha]_{589}^{21.5\ ^oC}$= + 37.9 (*c* = 0.38, $CHCl_3$).

[Compound (–)-**19** was synthesized in 98% yield from (–)-**18**, applying similar procedure as described above. Rotation of the compound (–)-**19**; $[\alpha]_{589}^{23.2}$ = –23.4 (*c* = 0.15, $CH_2Cl_2$).]




**Procedure for unprecedented Heck cyclization** (–)-**20**: In a re-sealable tube, compound **19** (1.6 g, 2.58 mmol, 1.0 equiv) was charged in dry DMF (8 mL) and degassed by using argon balloon. To this solution, anhydrous $K_2CO_3$ (1.1 g, 7.75 mmol, 3.0 equiv), $Pd(OAc)_2$ (58 mg, 0.26 mmol, 0.1 equiv) and $PPh_3$ (203 mg, 0.77 mmol, 0.3 equiv) were added successively under argon atmosphere at 25 °C. Then the reaction mixture was

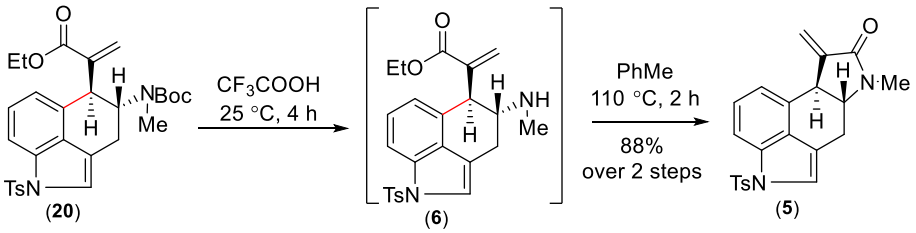
sealed and placed over an oil bath maintaining temperature 110 ºC for 12 h. Upon completion of the reaction (monitoring by TLC), reaction mixture was diluted with 30 mL EtOAc and partitioned between EtOAc and $H_2O$. The organic layer was then separated, dried over anhydrous $Na_2SO_4$, and concentrated under reduced pressure. The crude material was directly purified through column chromatography using *n*-hexane/EtOAc (4:1) as eluents to afford the desired product **20** as colorless gel.



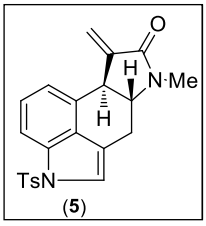
(**20**)

**Ethyl 2-((4R,5S)-4-((*tert*-butoxycarbonyl)(methyl)amino)-1-tosyl-1,3,4,5-tetrahydrobenzo[cd]indol-5-yl)acrylate** (−)-**20**: 1.20 g (87% yield) as colourless gel. $R_f$ = 0.4 (20% EtOAc in hexane). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.73 (m, 3H), 7.13 (m, 4H), 6.74 (brs, 1H), 4.47 (d, *J* = 10.9 Hz, 1H), 5.70 (s, 1H), 4.70 (brs, 1H), 4.08-4.26 (m, 3H), 2.88 (m, 2H), 2.76 (m, 3H), 2.28 (s, 3H), 1.38 (m, 9H), 1.03 (t, *J* = 6.4 Hz, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) (**rotamer**) δ 166.5, 166.1, 155.5, 155.4, 144.7, 139.1, 135.4, 13.9, 133.6, 133.2, 133.1, 129.8, 129.7, 128.4, 128.3, 126.8, 126.6, 125.6, 119.8, 119.5, 113.5, 111.5, 79.9, 79.5, 61.4, 60.7, 53.5, 43.5, 43.2, 28.5, 28.3, 25.5, 25.4, 21.9, 17.9, 13.9; **IR** (film) $\upsilon_{max}$2977, 1692, 1363, 1301, 1253, 1177, 1116, 1088, 1024 $cm^{-1}$;**HRMS** (ESI) m/z 539.2240 $[M + H]^+$; calculated for $[C_{29}H_{34}N_2O_6S + H]^+$: 539.2210 ;$[\alpha]_{589}^{21.4}$ $^{oC}$= – 33.7 (*c* = 0.27, $CHCl_3$).

[Compound (+)-**20** was synthesized in 84% yield from (−)-**19**, applying similar procedure as described above. Rotation of the compound (+)-**20**; $[\alpha]_D^{23.2}$ = +30.2 (*c* = 0.10, $CH_2Cl_2$).]

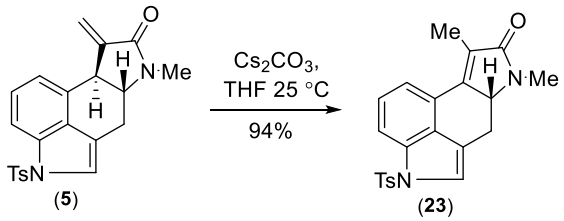



**Synthesis of lactone** (**–**)-(**5**): To a round-bottom flask, Boc-protected amine **20** (1.0 g, 1.86 mmol; 1.0 equiv.) was reacted with $CF_3CO_2H$ (8 mL) at 25 °C until starting material fully consumed (monitored by TLC analysis). Upon completion of reaction, the excess acid was removed under reduced pressure and diluted with $CHCl_3$.The organic layer was washed with saturated $NaHCO_3$, dried over anhydrous $Na_2SO_4$ and evaporated to dryness under reduced pressure. The crude was then dissolved in toluene and transferred the solution to a re-sealable tube and heated to 110 °C for 24 h until starting material fully consumed (judged by TLC analysis). Then the reaction mixture was concentrated under reduced pressure and purified through column chromatography using *n*-hexane/EtOAc (1:3) to afford tetracyclic γ-lactam **5** as colorless gel.

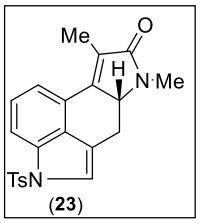



**(6a*R*,9a*S*)-7-Methyl-9-methylene-4-tosyl-4,6,6a,7,9,9a-hexahydro-8H-indolo[6,5,4-cd]indol-8-one** (**5**): 662 mg (88% overall yield) as colourless gel. $R_f$ = 0.35 (75% EtOAc in hexane).**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.7 Hz, 1H), 7.74 (m, 2H), 7.24-7.31 (m, 3H), 7.18 (m, 2H), 6.16 (d, *J* = 3.4 Hz, 1H), 5.85 (d, *J* = 3.0 Hz, 1H), 3.86 (m, 1H), 3.35 (m, 1H), 3.29 (m, 1H), 2.95 (s, 3H), 2.71 (m, 1H), 2.29 (s, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 169.8, 145.0, 139.7, 135.4, 133.2, 130.1, 130.0, 129.7, 126.8, 125.7, 121.1, 117.4, 116.9, 114.7, 112.4, 61.6, 45.6, 27.8, 27.1, 21.6; **IR** (film) $\upsilon_{max}$2921, 1682, 1430, 1373, 1358, 1178, 1112, 1089, 968, 768 cm$^{-1}$;**HRMS** (ESI) m/z 293.1295 [M + H]$^+$; calculated for [$C_{22}H_{20}N_2O_3S$ + H]$^+$: 293.1267 ; $[\alpha]_{589}$ $^{23.0\ °C}$= – 56.7 (*c* = 0.18, $CH_2Cl_2$).

[Compound (+)-**5** was synthesized in 90% overall yield in 2 steps from (+)-**20**, applying similar procedure as described above. Rotation of the compound (+)-**5**; $[\alpha]_{589}^{23.2}$ = +52.9 (*c* = 0.20, $CH_2Cl_2$).]



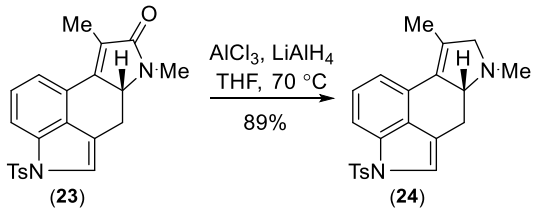

**Isomerization of double bond** (+)-(**23**): An oven dried round-bottom flask was charged with compound (**5**) (200 mg, 0.51 mmol, 1.0 equiv) in dry THF (7 mL). To this solution, anhydrous $Cs_2CO_3$ (497 mg, 1.53 mmol, 3.0 equiv) was added at rt and stirred the reaction mixture for 1 h, until the starting material fully consumed. Upon completion of the reaction (monitoring by TLC), it was filtered through celite pad and washed with EtOAc. The combined organic layers were concentrated under vacco and crude was purified through column chromatography using hexane/EtOAc (1:3) to afford the desired product **23** as colorless gel.



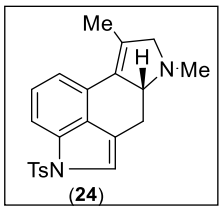

(***R***)**-7,9-Dimethyl-4-tosyl-4,6,6a,7-tetrahydro-8H-indolo[6,5,4-cd]indol-8-one** (**23**): 188 mg (94% yield) as colorless gel. $R_f$ = 0.3 (75% EtOAc in hexane).**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.75 (m, 2H), 7.34-7.40 (m, 2H), 7.30 (d, *J* = 1.7 Hz, 1H), 7.20 (m, 2H), 4.08 (m, 1H), 3.47 (dd, *J* = 14.7, 6.3 Hz, 1H), 3.05 (s, 3H), 2.46(m, 1H), 2.31 (s, 3H), 2.14 ( d, *J* = 1.5 Hz, 1H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 172.4, 145.2, 144.4, 135.4, 133.5, 130.1, 129.9, 128.7, 126.9, 126.1, 124.9, 121.6, 119.7, 116.3, 114.1, 60.6, 27.5, 26.7, 21.7, 10.1; **IR** (film) $\upsilon_{max}$2919, 1683, 1436, 1373, 117,

1112, 1088, 986 $cm^{-1}$; **HRMS** (ESI) m/z 393.1274 $[M + H]^+$; calculated for $[C_{22}H_{20}N_2O_3S + H]^+$: 393.1267 ;$[\alpha]_{589}{}^{21.8\,°C}$= +28.0 (*c* = 0.10, $CHCl_3$).

[Compound (–)-**23** was synthesized from (+)-**5** in ~94% yield, applying similar procedure as described above. Rotation of the compound, (–)-**23**; $[\alpha]_{589}{}^{23.2}$ = –27.5 (*c* = 0.25, $CH_2Cl_2$).]




**Synthesis of cyclic allyl amine** (+)-(**24**): To an oven dried round-bottom flask, suspension of $LiAlH_4$ (73 mg, 1.90 mmol, 5.0 equiv) in dry THF (3 mL) was cooled at 0 ºC. To that a solution of anhydrous $AlCl_3$ (51 mg, 0.38 mmol; 1.0 equiv.) in THF (2 mL) was added drop-wise at same temperature and stirring was continued for 30 minutes. Afterwards a solution of (**23**) (150 mg, 0.38 mmol, 1.0 equiv.) in THF (3 mL) drop wise. After that stirring was continued for another 1.5 h at 0 ºC. Upon completion of reaction, reaction mixture was quenched by careful addition of ethyl acetate and followed by addition of water. Then the whole mixture was filtered through a celite pad. The clear organic layer was dried over anhydrous $Na_2SO_4$, concentrated under reduced pressure and then purified through column chromatography using methanol/ethyl acetate (1:9) mixture as eluents to afford the desired product (**24**) as yellow gel.

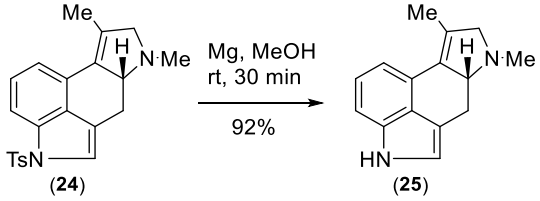



**(*R*)-7,9-Dimethyl-4-tosyl-6,6a,7,8-tetrahydro-4H-indolo[6,5,4-cd]indole** (**24**)**:** 127 mg (89% yield) as colourless gel. $R_f$ = 0.3 (10% MeOH in EtOAc). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.69-7.75 (m, 3H), 7.26-7.34 (m, 2H), 3.19 (m, 3H), 3.85 (dd, *J* = 14.3, 3.3 Hz,

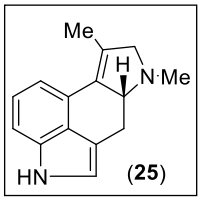
1H), 3.55 (m, 1H), 3.46 (m, 1H), 3.21 (dd, *J* = 14.9, 6.0 Hz, 1H), 2.51-2.56 (s, 3H; m, 1H), 2.30 (s, 3H), 2.05 (s, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 144.7, 135.5, 133.6, 132.2, 129.8, 129.7, 128.6, 126.7, 126.6, 125.6, 119.9, 118.8, 118.7, 112.0, 71.4, 68.2, 40.4, 29.0, 21.5, 13.5;**IR** (film) $\upsilon_{max}$2918, 2852, 1558, 1357, 1165, 1112, 763 $cm^{-1}$; **HRMS** (ESI) m/z 379.1499 $[M + H]^+$; calculated for $[C_{22}H_{22}N_2O_2S + H]^+$: 379.1475; $[\alpha]_{589}^{21.4\,°C}$= +48.8 (*c* = 0.86, $CHCl_3$).

[Compound (–)-**24** was synthesized from (–)-**23** in 87% yield, applying similar procedure as described above. Rotation of the compound (–)-**24**; $[\alpha]_{589}^{23.2}$ = –50.0 (*c* = 0.10, $CH_2Cl_2$).]

**Synthesis of** (+)**-25 [Formal total synthesis of** (+)**-cyclocavine** (**1**)**]:**



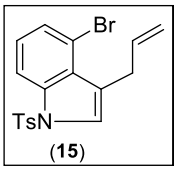

To an oven dried screw capped vial, compound **24** (15 mg, 0.039 mmol; 1.0 equiv.) was dissolved in 1.5 mL dry MeOH and dry Mg powder (38 mg, 1.58 mmol; 40.0 equiv.) was added to it at 25 ºC. The reaction was stirred vigorously for 30 minutes. Upon completion of de-tosylation (monitoring by running TLC), dichloromethane (5 mL) and water (2 mL) were added to the reaction mixture and it was poured into a separatory funnel. The organic layer was separated, dried over $K_2CO_3$ and concentrated under reduced pressure. The crude was purified by column chromatography with methanol-ethyl acetate (1: 9) to afford **25** as brown gel.



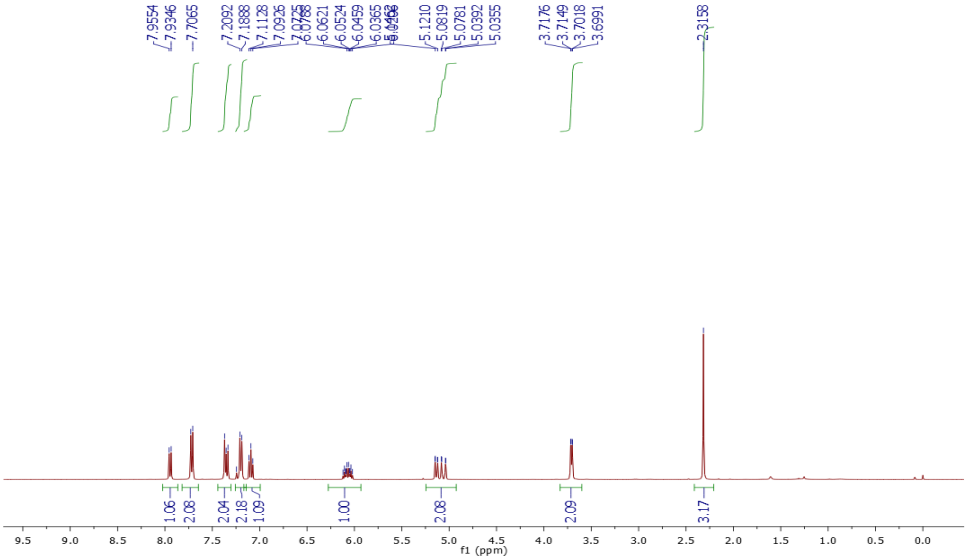
**(*R*)-7,9-dimethyl-6,6a,7,8-tetrahydro-4H-indolo[6,5,4-cd]indole** (**25**)**:** 8.0 mg (92% yield) as colourless solid. $R_f$ = 0.2 (10% MeOH in EtOAc).**$^1$H NMR** (700 MHz, $CDCl_3$) δ: 8.03 (brs, 1H), 7.26 (m, 1H), 7.20 (m, 2H), 6.90 (t, *J* = 1.8 Hz, 1H), 3.90 (dd, *J* = 13.6, 3.1 Hz, 1H), 3.68 (m, 1H), 3.50 (m,1H), 3.34 (dd, *J* = 14.3, 6.2 Hz, 1H), 2.68 (m, 1H), 2.58 (s, 3H), 2.14 (s, 3H); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 134.1, 130.8, 130.2, 127.3, 126.0, 123.0, 118.3, 114.7, 112.3, 109.2, 72.3, 68.3, 40.3, 29.5, 13.7; **IR** (film) $\upsilon_{max}$ 3048, 2972, 1642, 1545, 1520, 1312, 1032, 936, 745 $cm^{-1}$; **HRMS** (ESI) m/z 225.1386 $[M + H]^+$; calculated for $[C_{15}H_{16}N_2 + H]^+$: 225.1386; $[\alpha]_{589}^{21.3\,°C}$ = +57.0 (*c* = 0.8, $CHCl_3$).

[Compound (–)-**25** was synthesized from (–)-**24** in 94% yield, applying similar procedure as described above. Rotation of the compound (–)-**25**; $[\alpha]_{589}^{23.2}$ = –54.0 (*c* = 0.18, $CH_2Cl_2$).]

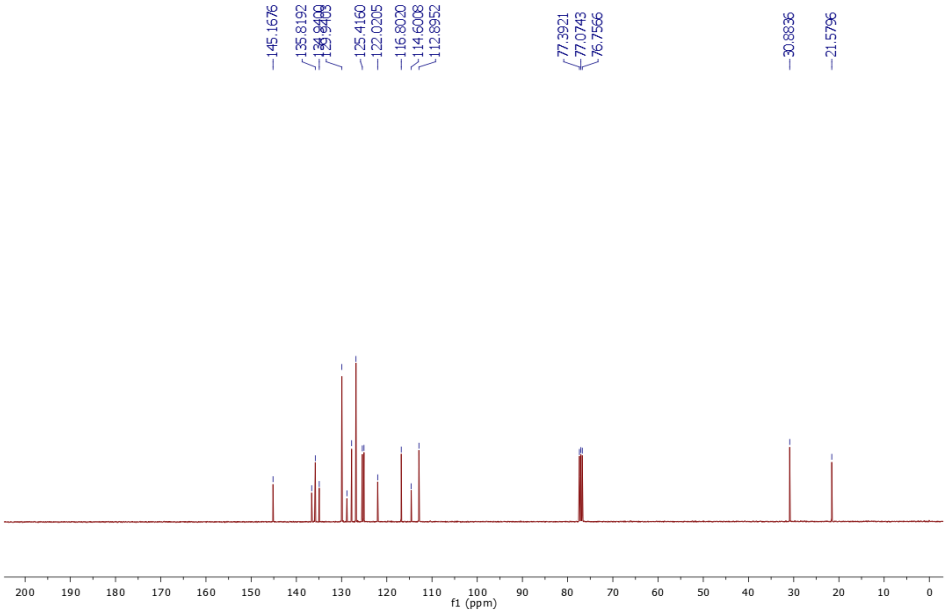
# Spectral Graphics



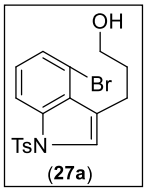
(**15**)

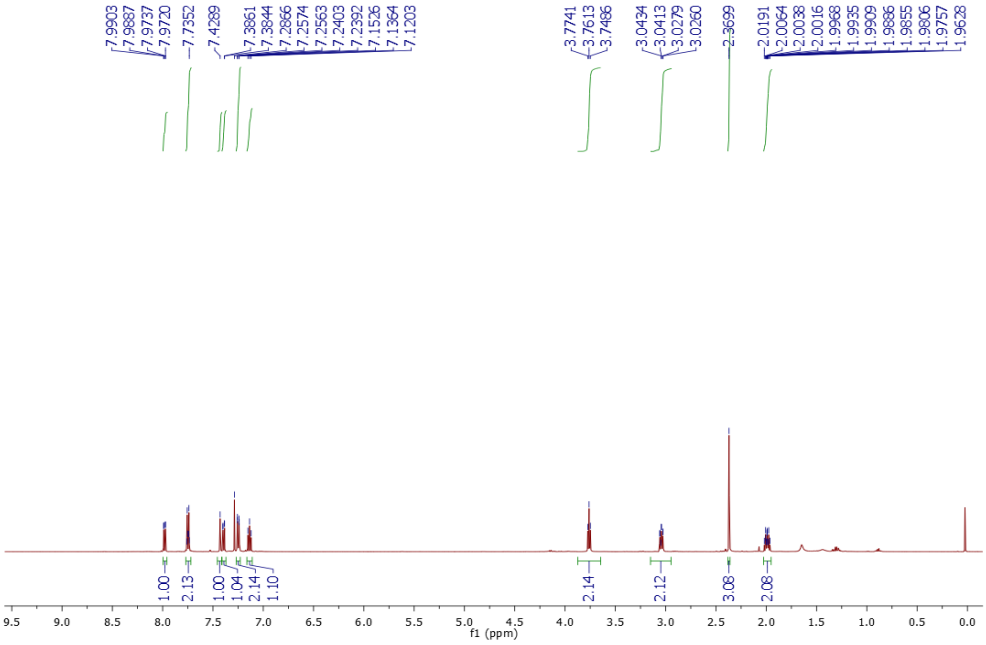



$^{1}$H NMR (400 MHz, $CDCl_3$) of (**15**)

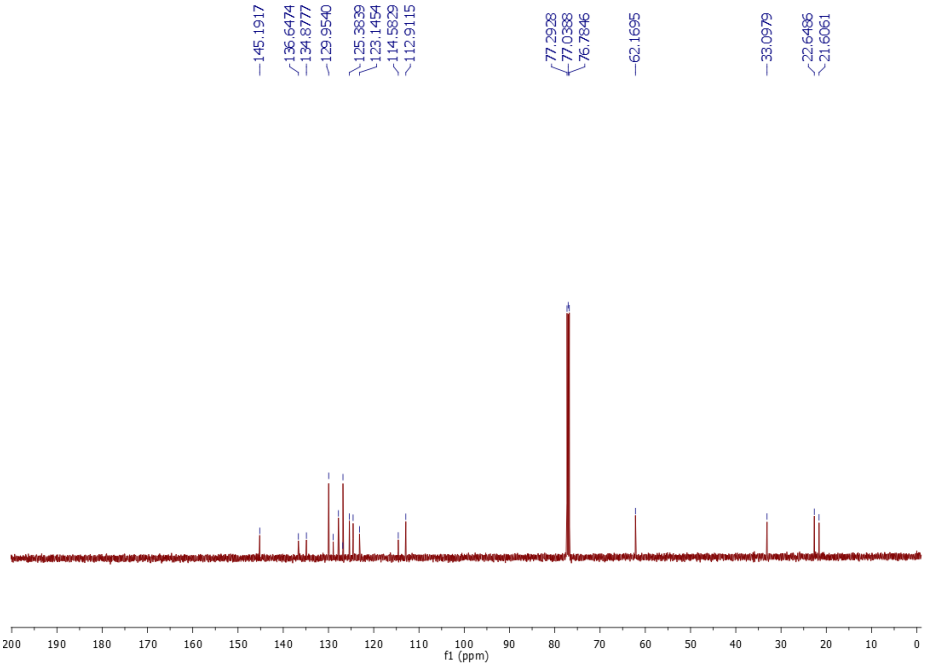


$^{13}$C NMR (100 MHz, $CDCl_3$) of compound (**15**)




$^{1}$H NMR (400 MHz, $CDCl_3$) of (**27a**)




$^{13}$C NMR (100 MHz, $CDCl_3$) of (**27a**)

# Display Report

**Analysis Info**

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| Method | HRLCMS-20 Sept tune wide.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SG8-130 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
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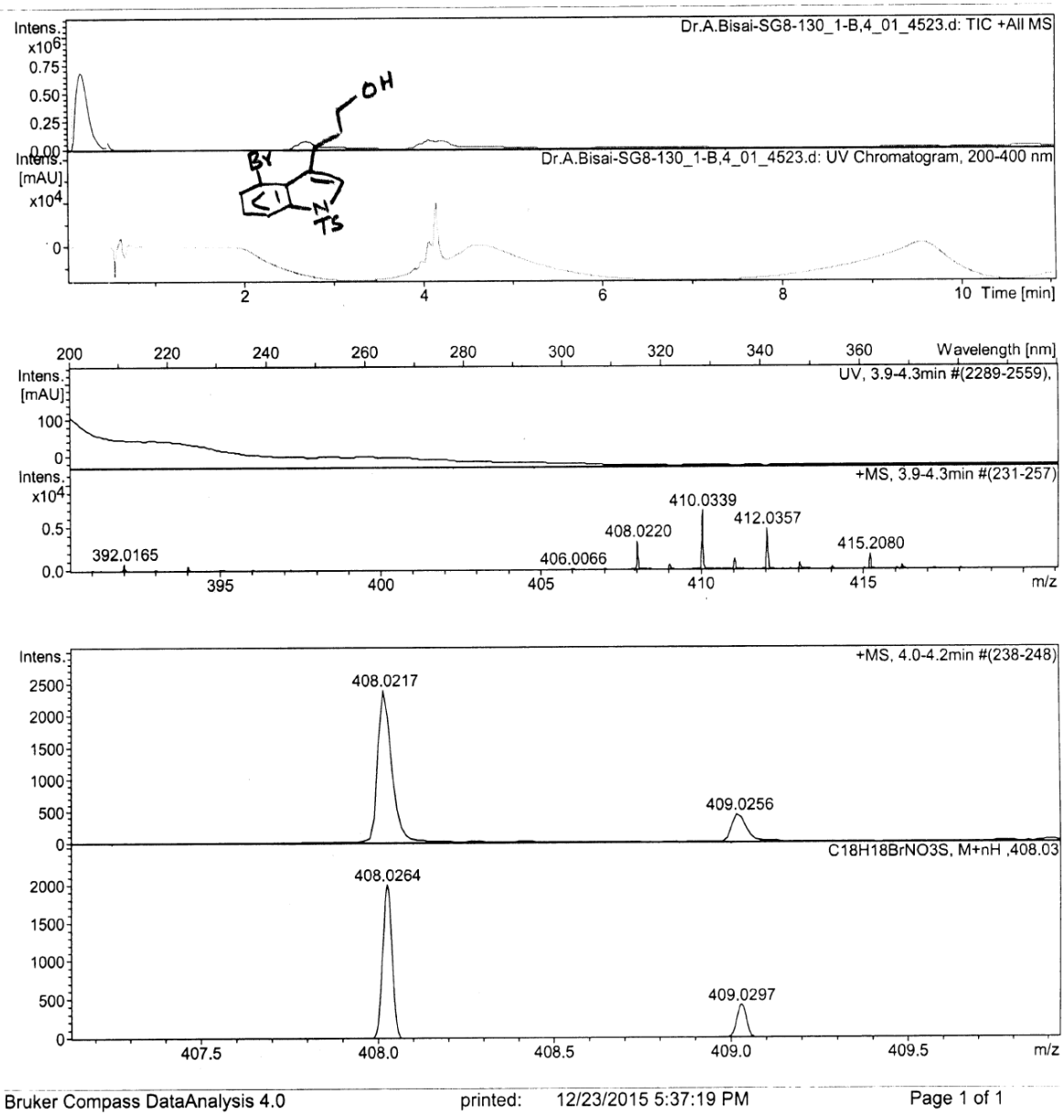
| Scan End | 3000 m/z | Set Collision Cell RF | 600.0 Vpp | Set Divert Valve | Waste |

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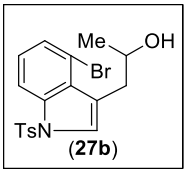
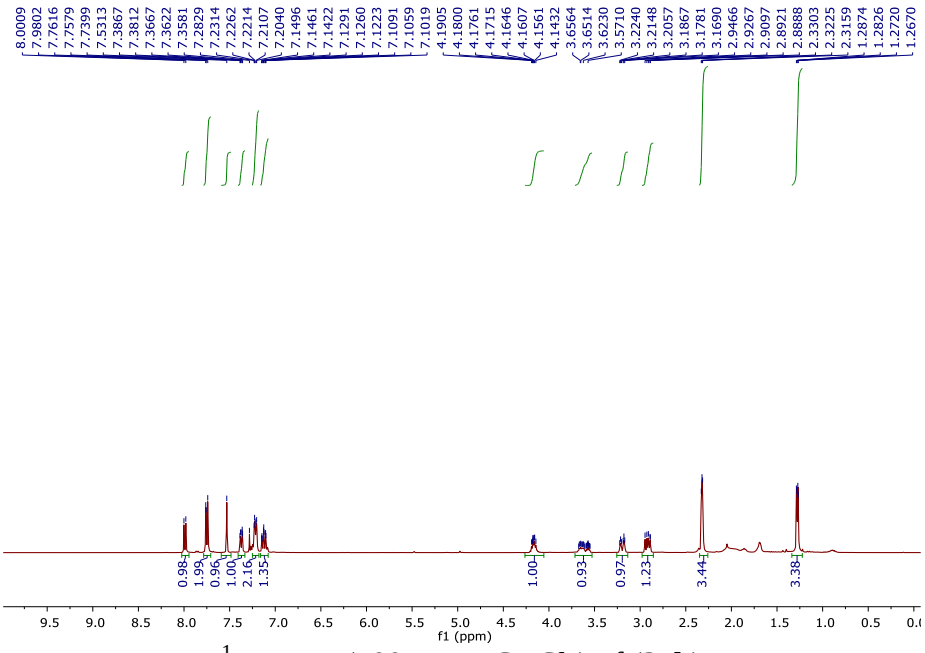
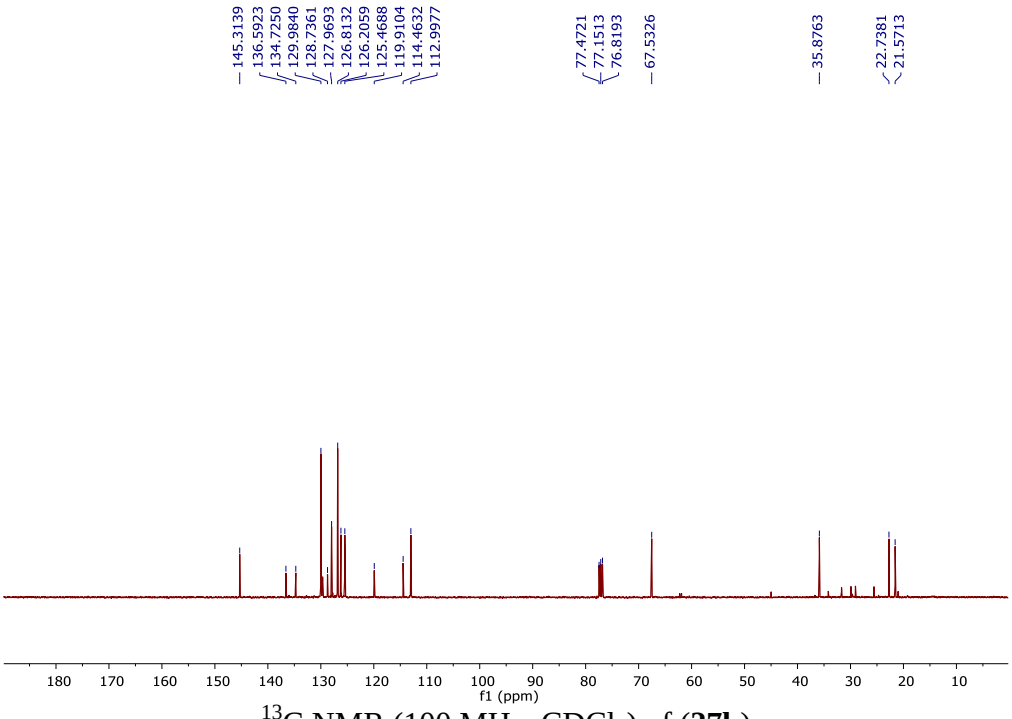
Scanned copy of mass spectrum of (**27a**)

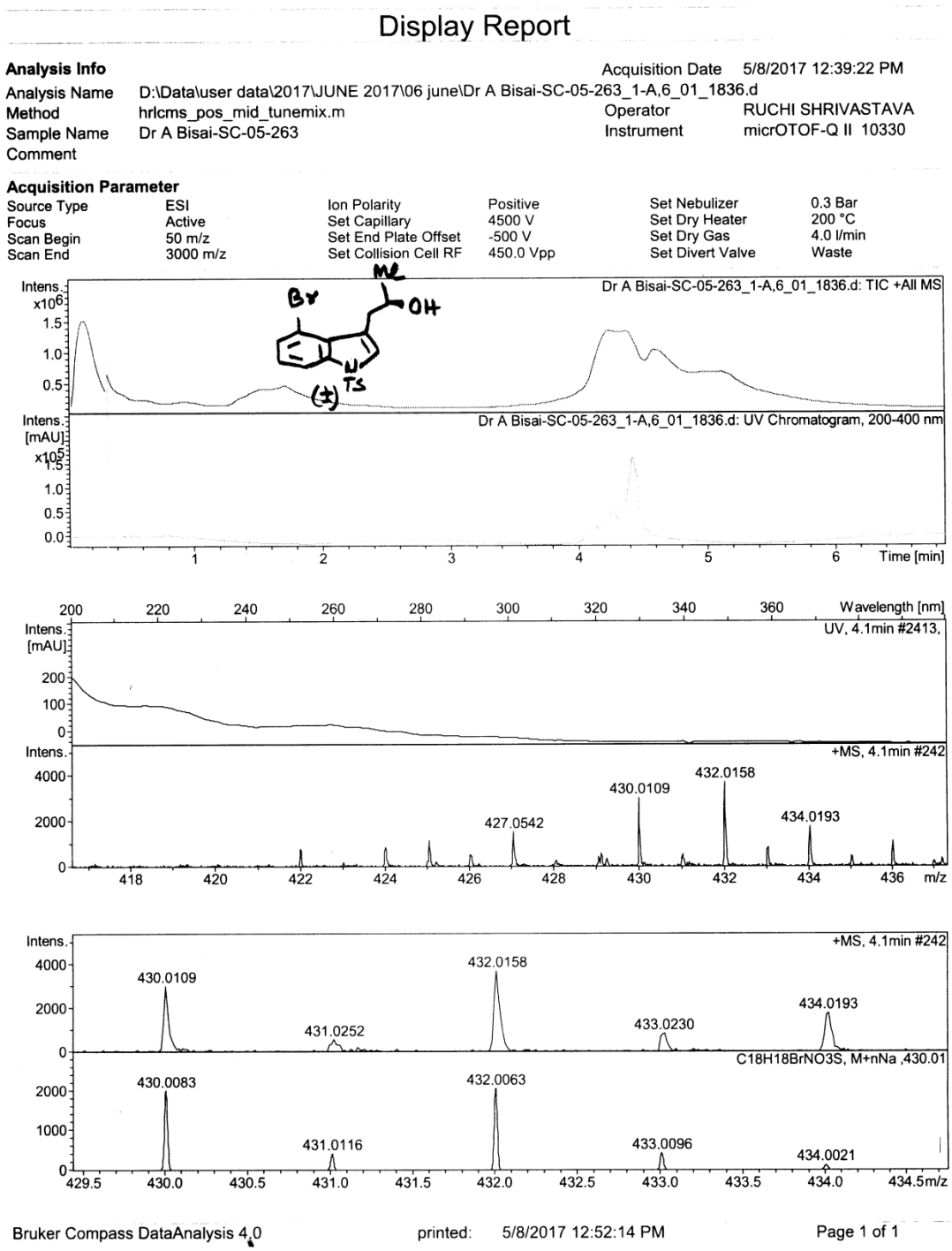


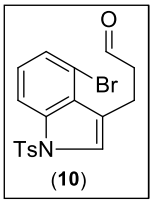

$^{1}$H NMR (400 MHz, $CDCl_3$) of (**27b**)

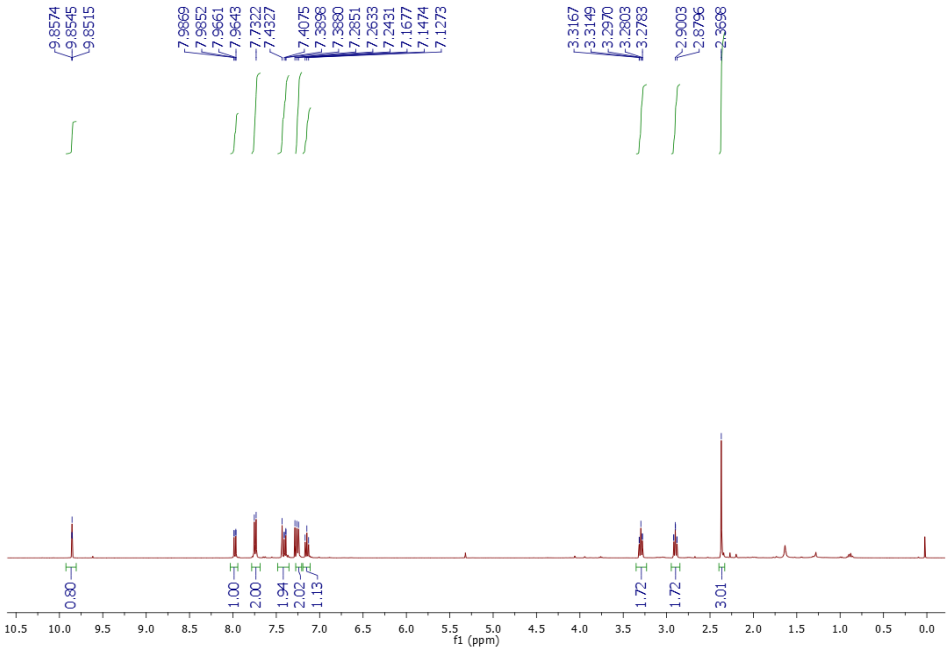



$^{13}$C NMR (100 MHz, $CDCl_3$) of (**27b**)

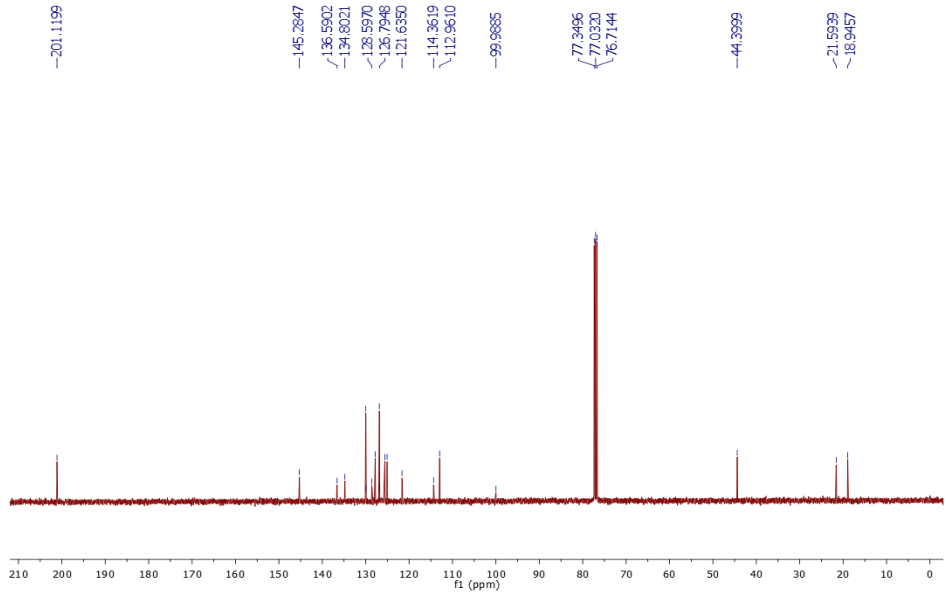



Scanned copy of mass spectrum of (**27b**)

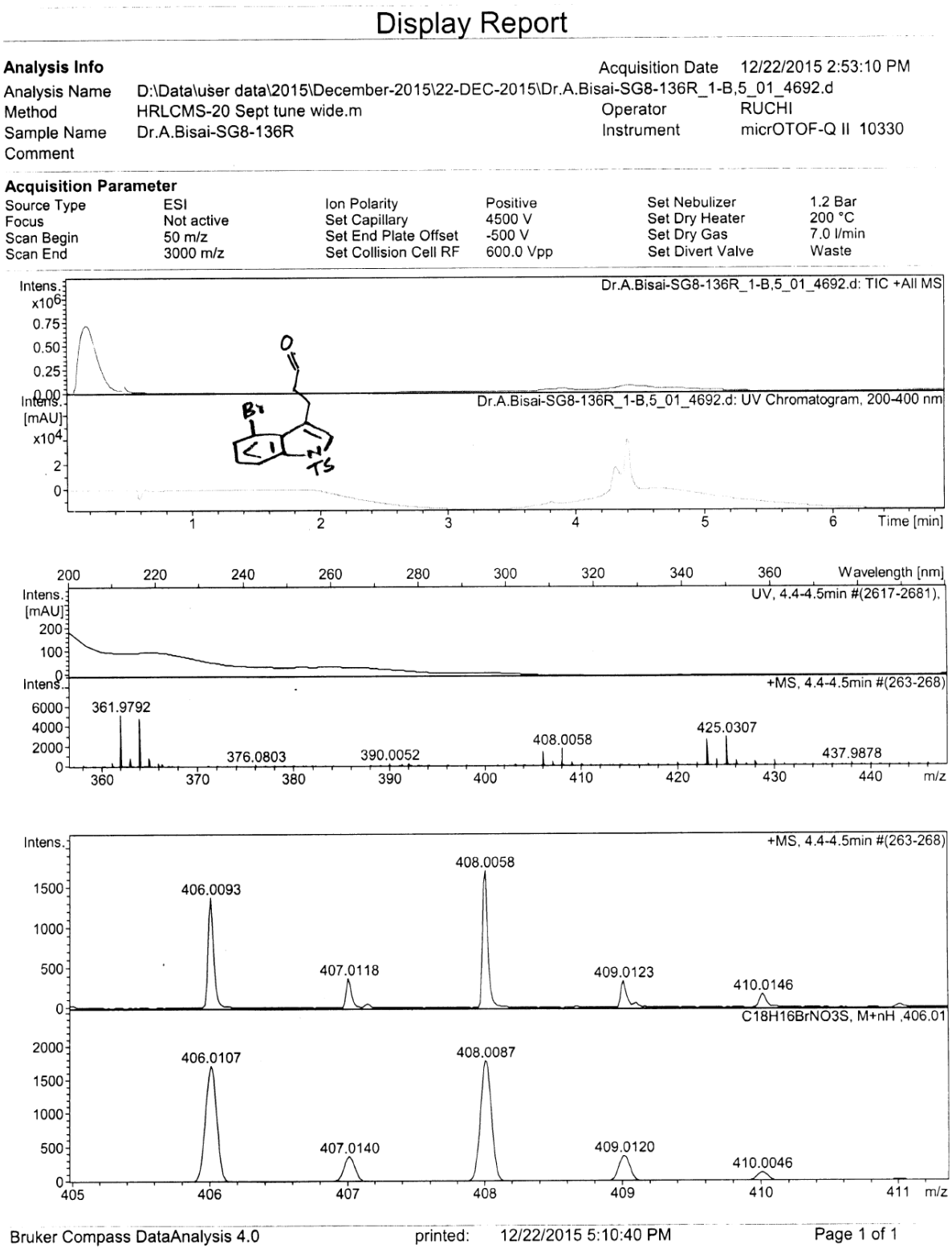


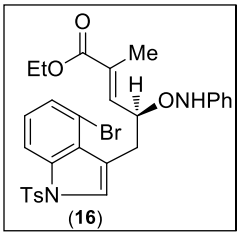

$^{1}$H NMR (400 MHz, $CDCl_3$) of (**10**)

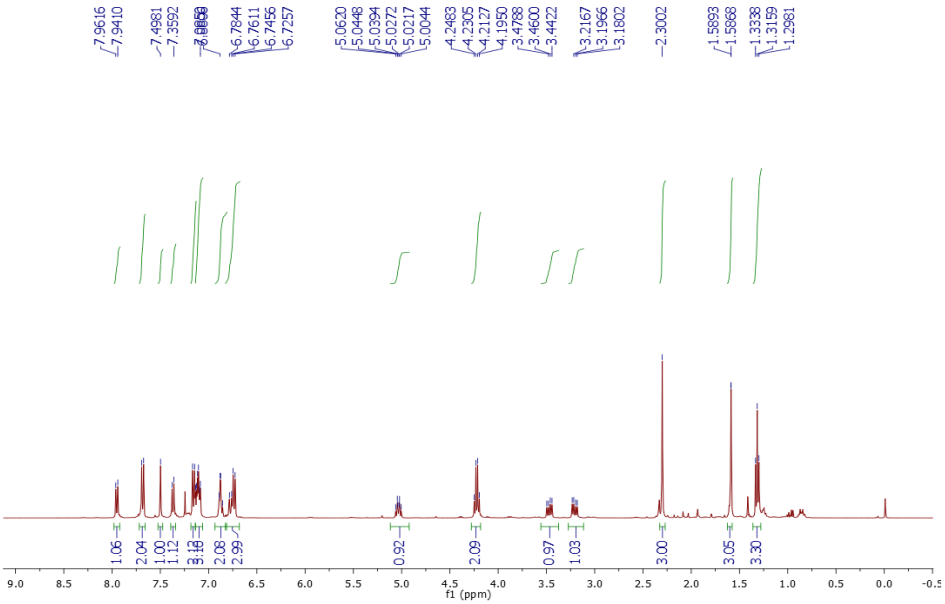



$^{13}$C NMR (100 MHz, $CDCl_3$) of (**10**)

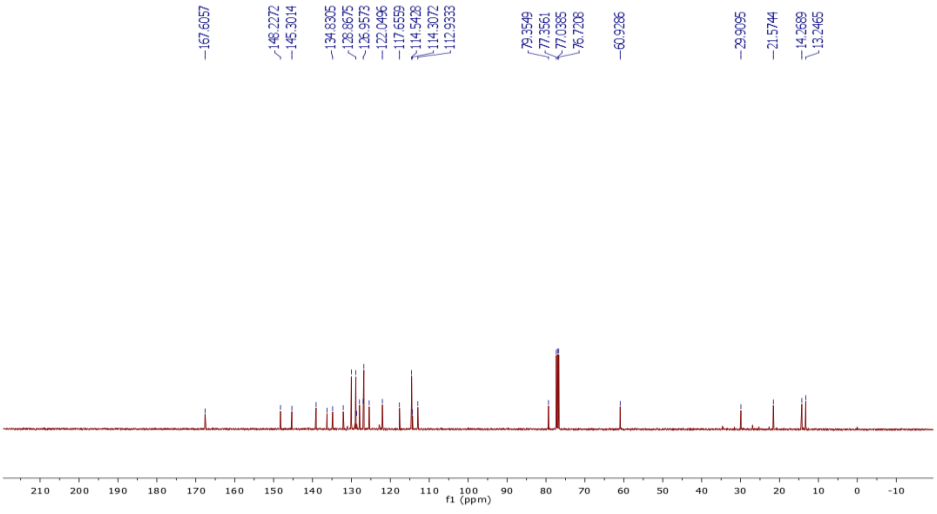



Scanned copy of mass spectrum of (**10**)




$^{1}$H NMR (400 MHz, $CDCl_3$) of (–)-**16**




$^{13}$C NMR (100 MHz, $CDCl_3$) of (–)-**16**

# Display Report

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| Method | HRLCMS-20 Sept tune wide.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SC-03-253 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

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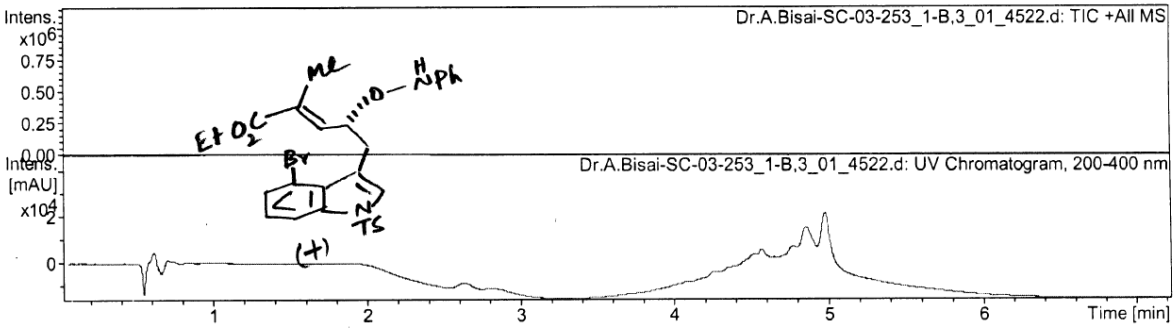
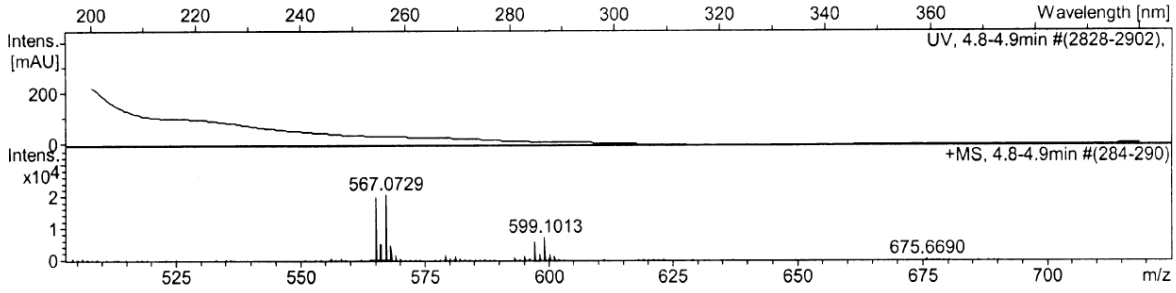
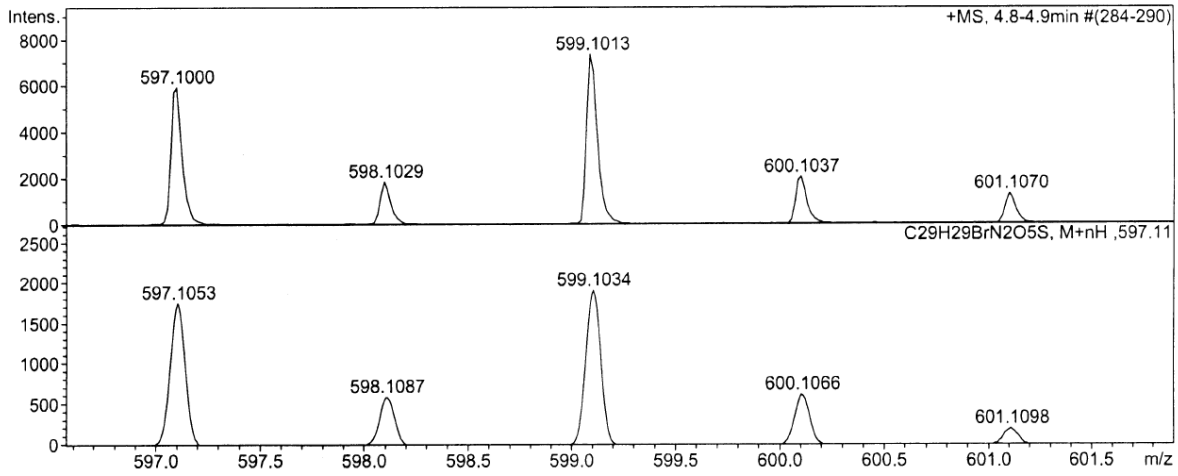
| Focus | Not active | Set Capillary | 4500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 7.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 600.0 Vpp | Set Divert Valve | Waste |

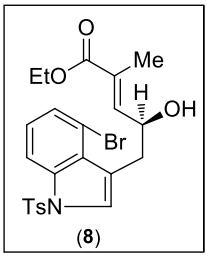


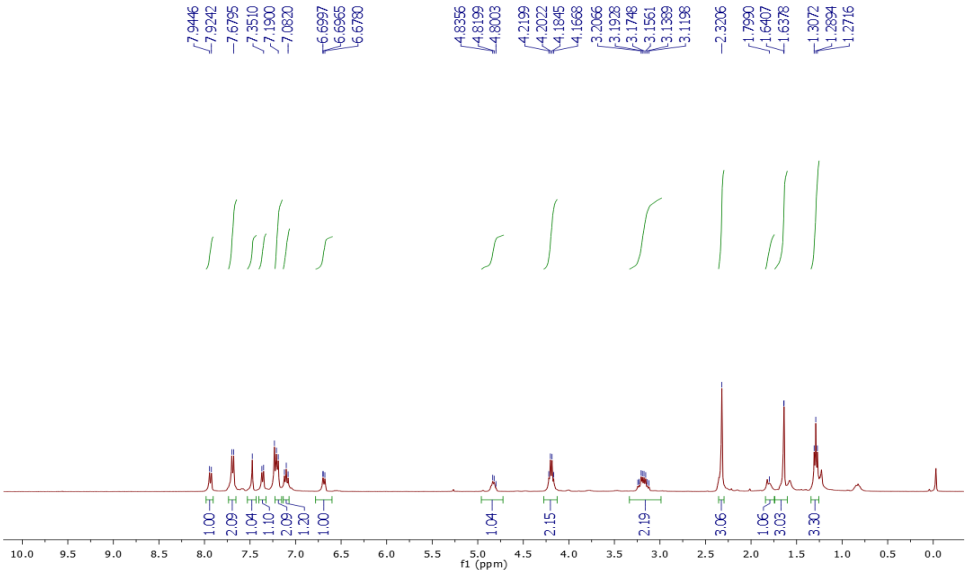





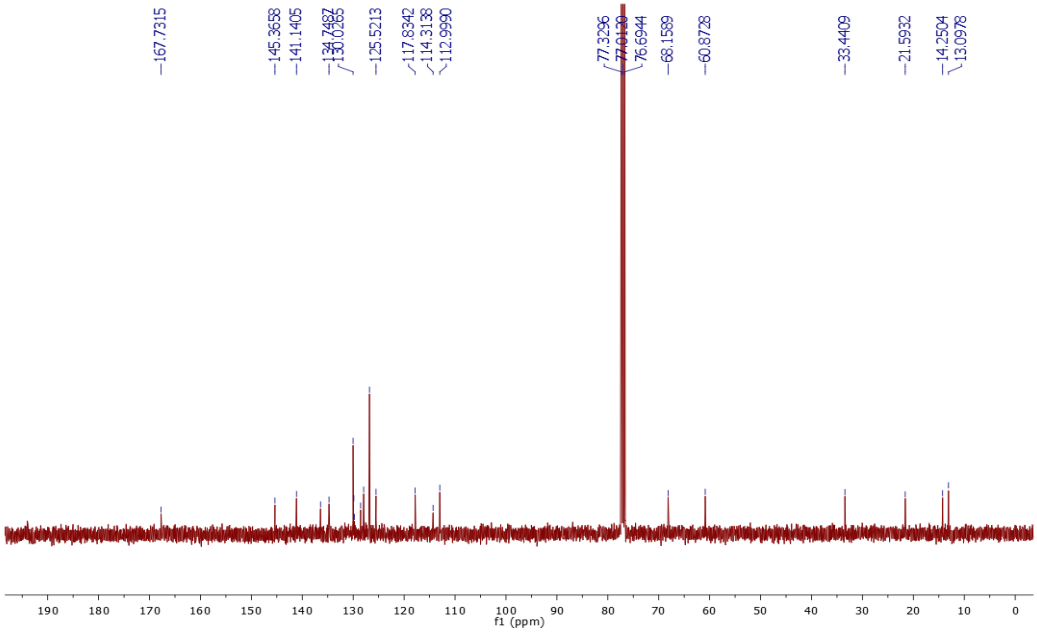

Scanned copy of mass spectrum of (+)-**16**




(**8**)




$^{1}$H NMR (400 MHz, $CDCl_3$) of (–)-**8**




$^{13}$C NMR (100 MHz, $CDCl_3$) of (–)-**8**

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| Analysis Name | D:\Data\user data\2015\December-2015\08-DEC-2015\Dr.A.Bisai-SB7-160_1-A,5_01_4464.d | | |
| Method | HRLCMS-20 Sept tune wide.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SB7-160 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

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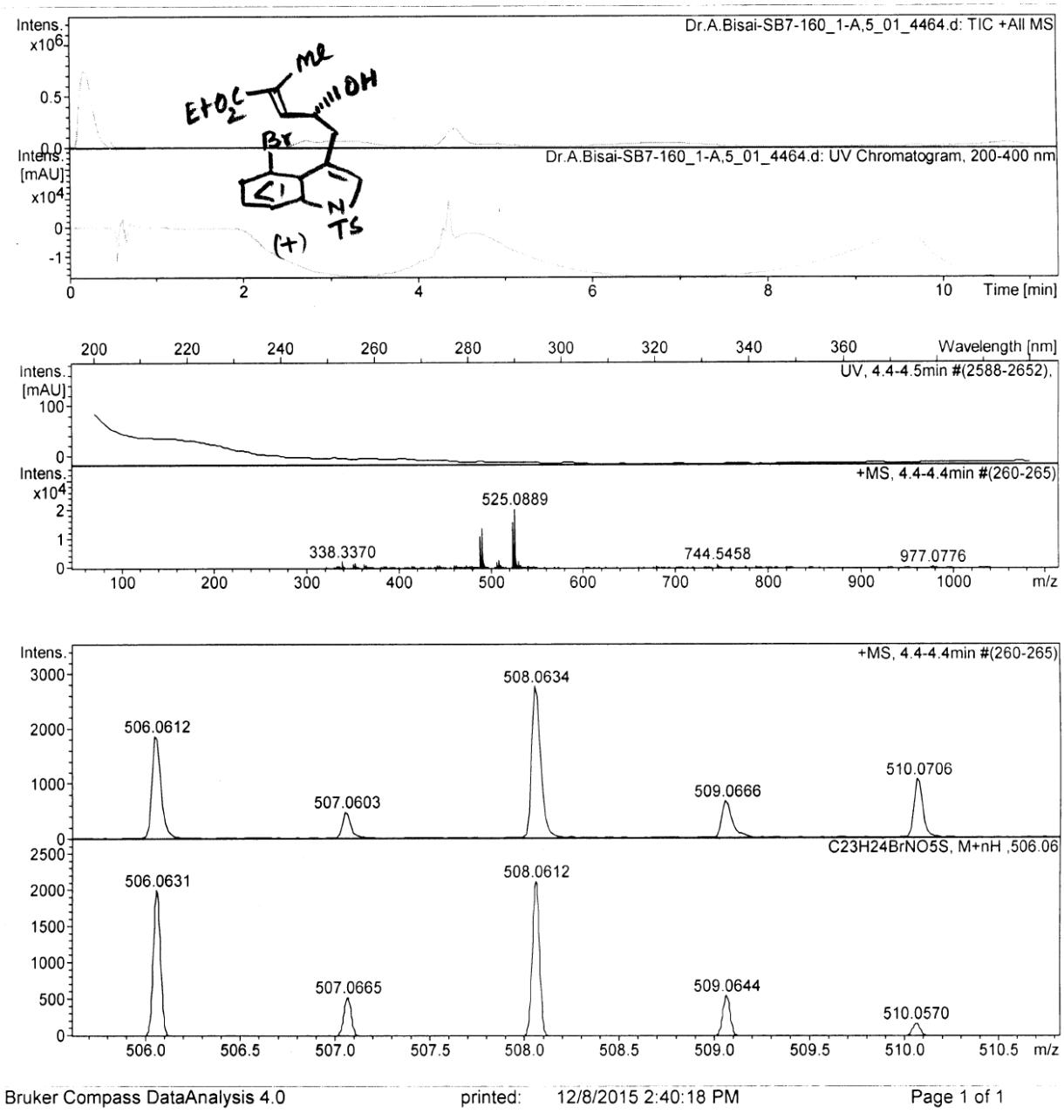


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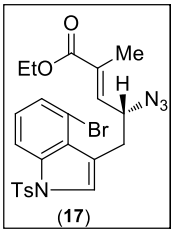
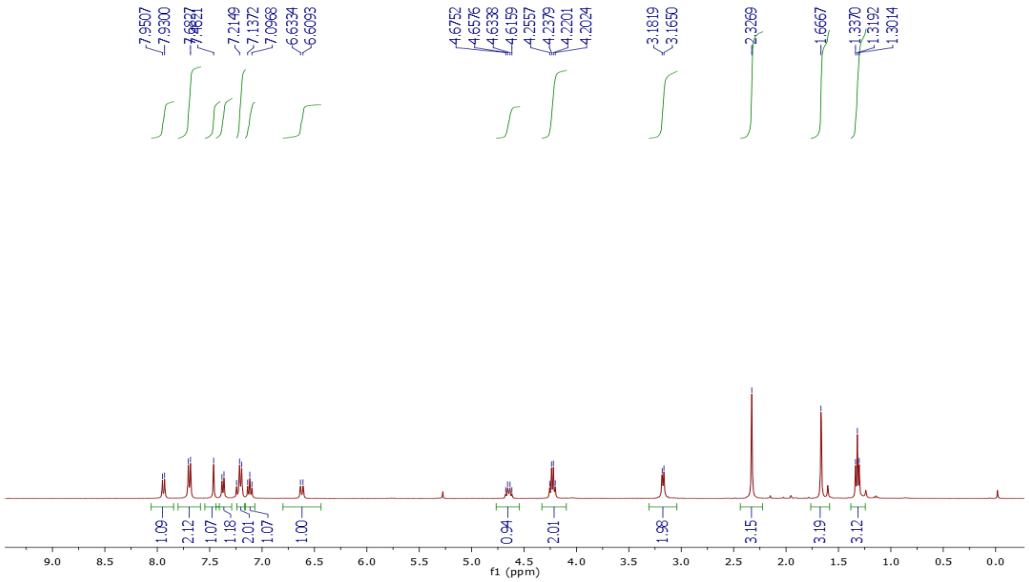
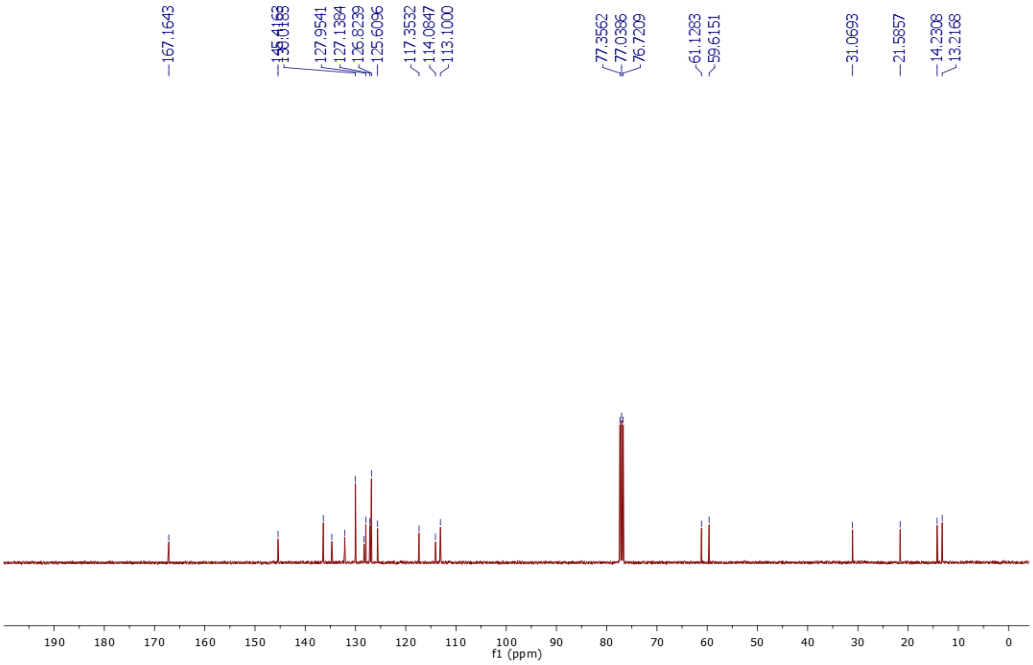
Scanned copy of mass spectrum of (+)-**8**

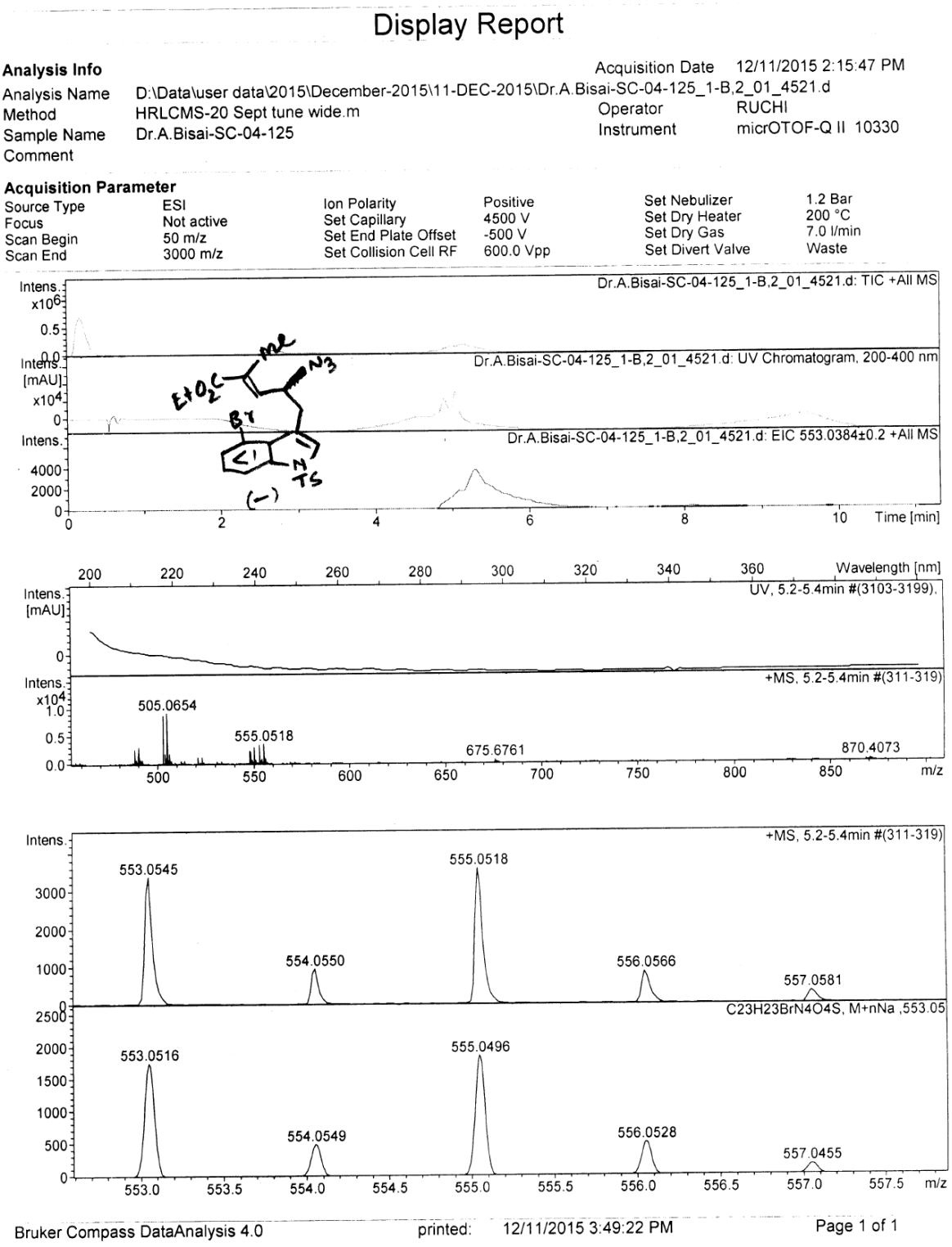


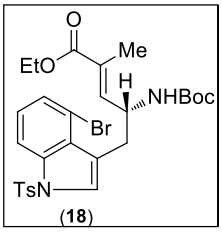

$^{1}$H NMR (400 MHz, $CDCl_3$) of (+)-**17**



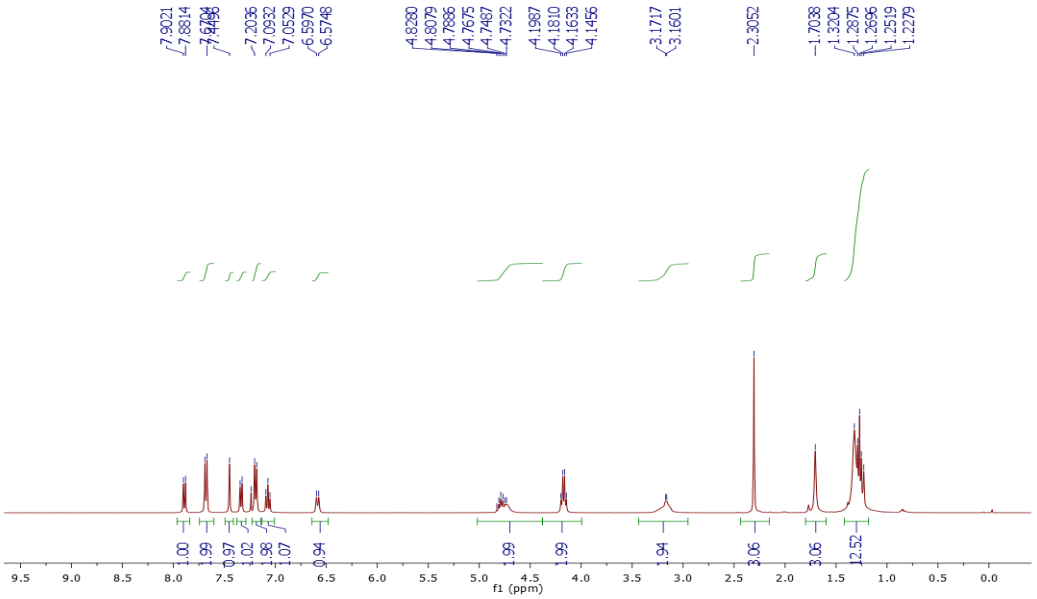

$^{13}$C NMR (100 MHz, $CDCl_3$) of (+)-**17**



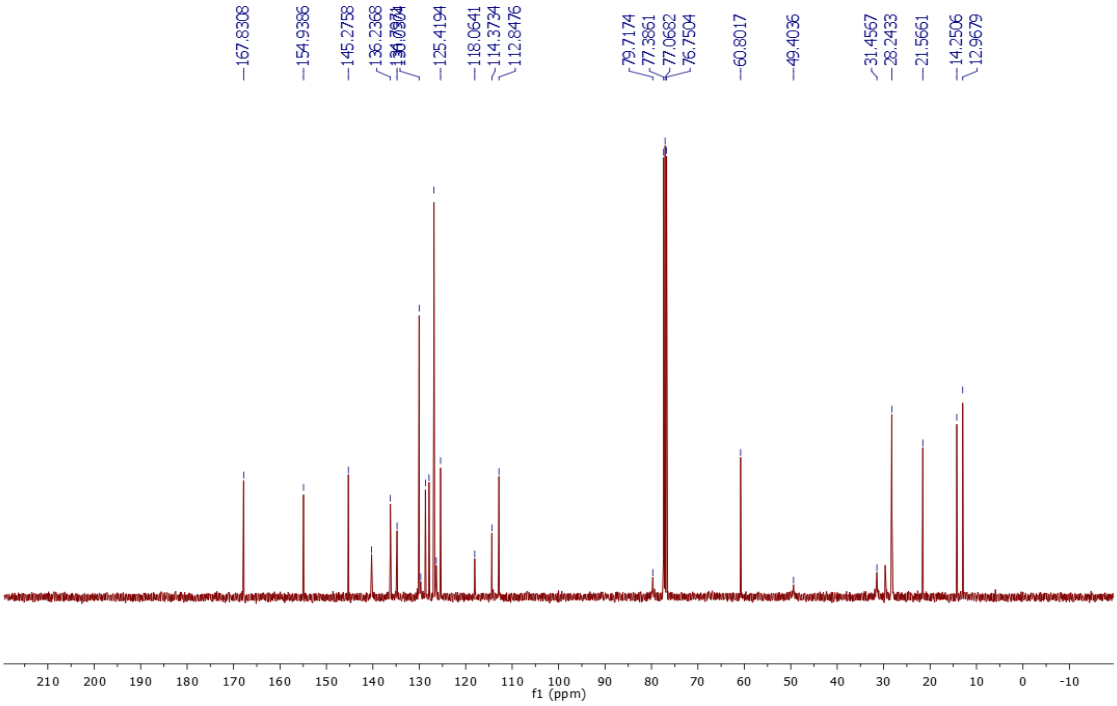

Scanned copy of mass spectrum of (–)-**17**




(**18**)




$^{1}$H NMR (400 MHz, $CDCl_3$) of (+)-**18**




$^{13}$C NMR (100 MHz, $CDCl_3$) of (+)-**18**

# Display Report

**Analysis Info**

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| Analysis Name | D:\Data\user data\2015\December-2015\08-DEC-2015\Dr.A.Bisai-SC-04-265_1-A,7_01_4467.d | | |
| Method | HRLCMS-20 Sept tune wide.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SC-04-265 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

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| Focus | Not active | Set Capillary | 4500 V | Set Dry Heater | 200 °C |
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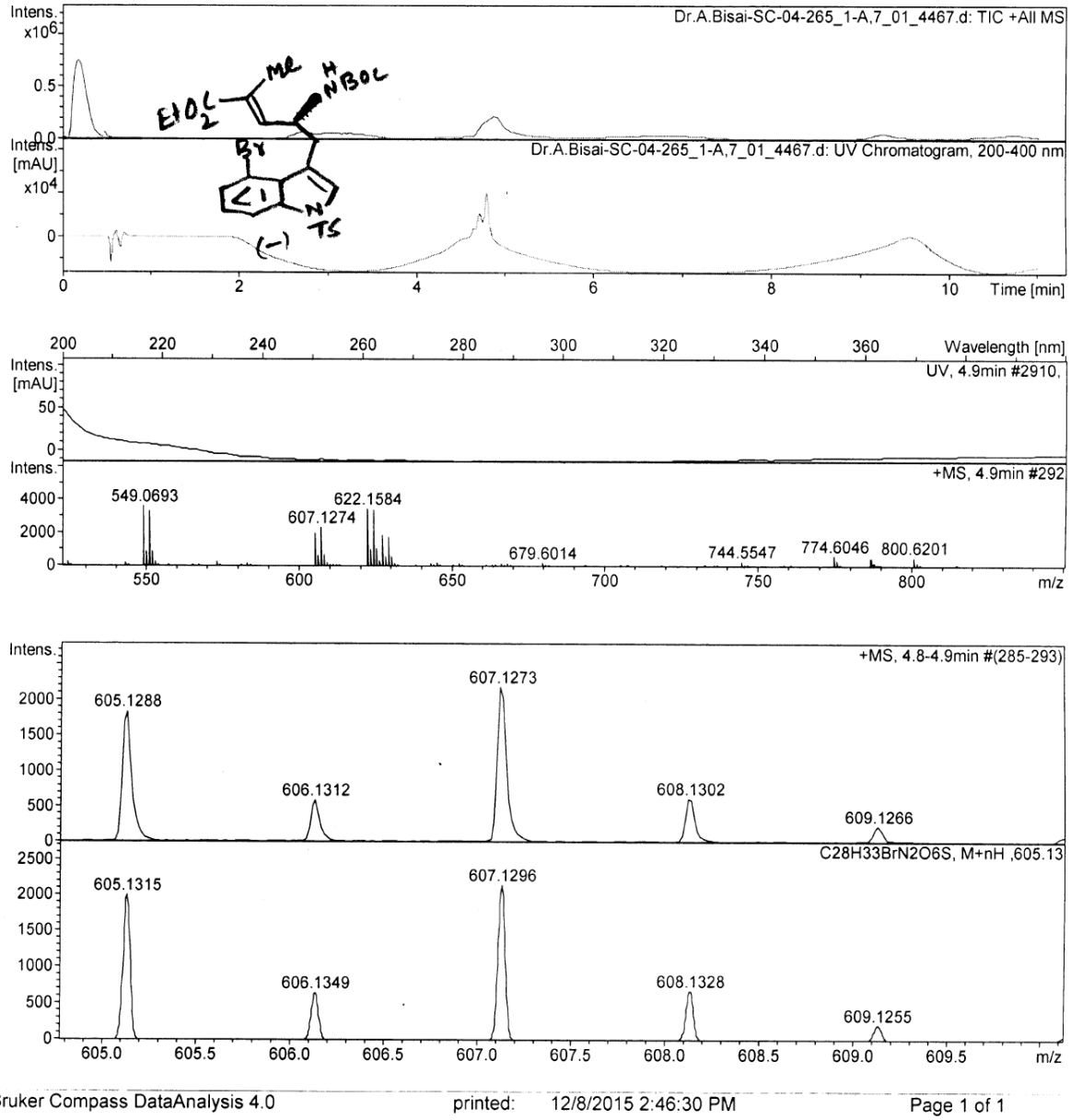
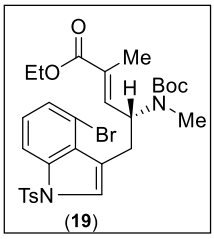





Scanned copy of mass spectrum of (–)-**18**



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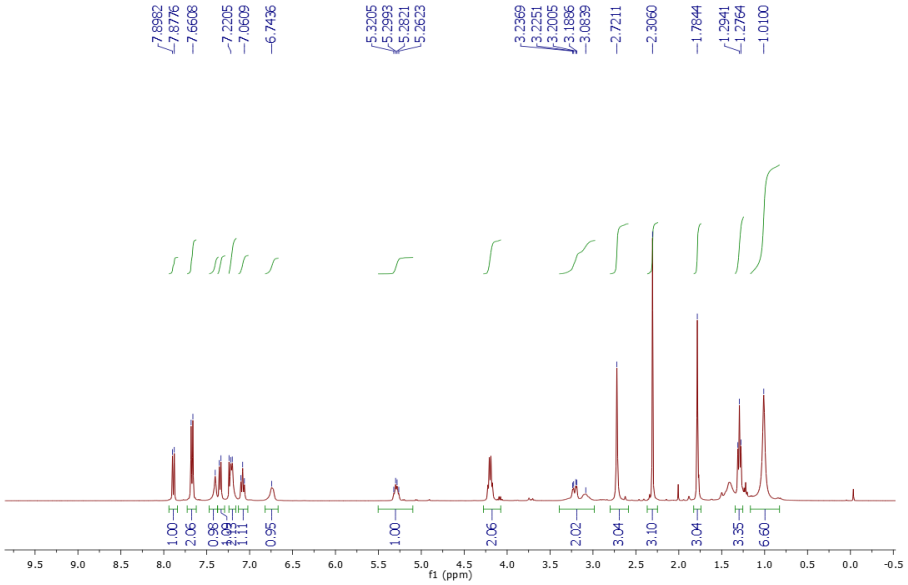
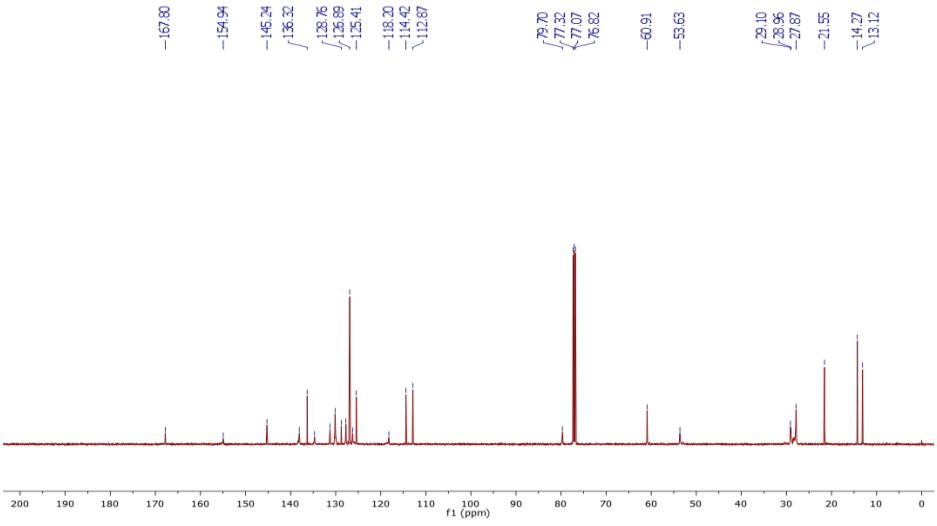



$^{1}$H NMR (400 MHz, $CDCl_3$) of (+)-**19**




$^{13}$C NMR (100 MHz, $CDCl_3$) of (+)-**19**

# Display Report

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| Method | HRLCMS-20 Sept tune wide.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SC-04-266 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

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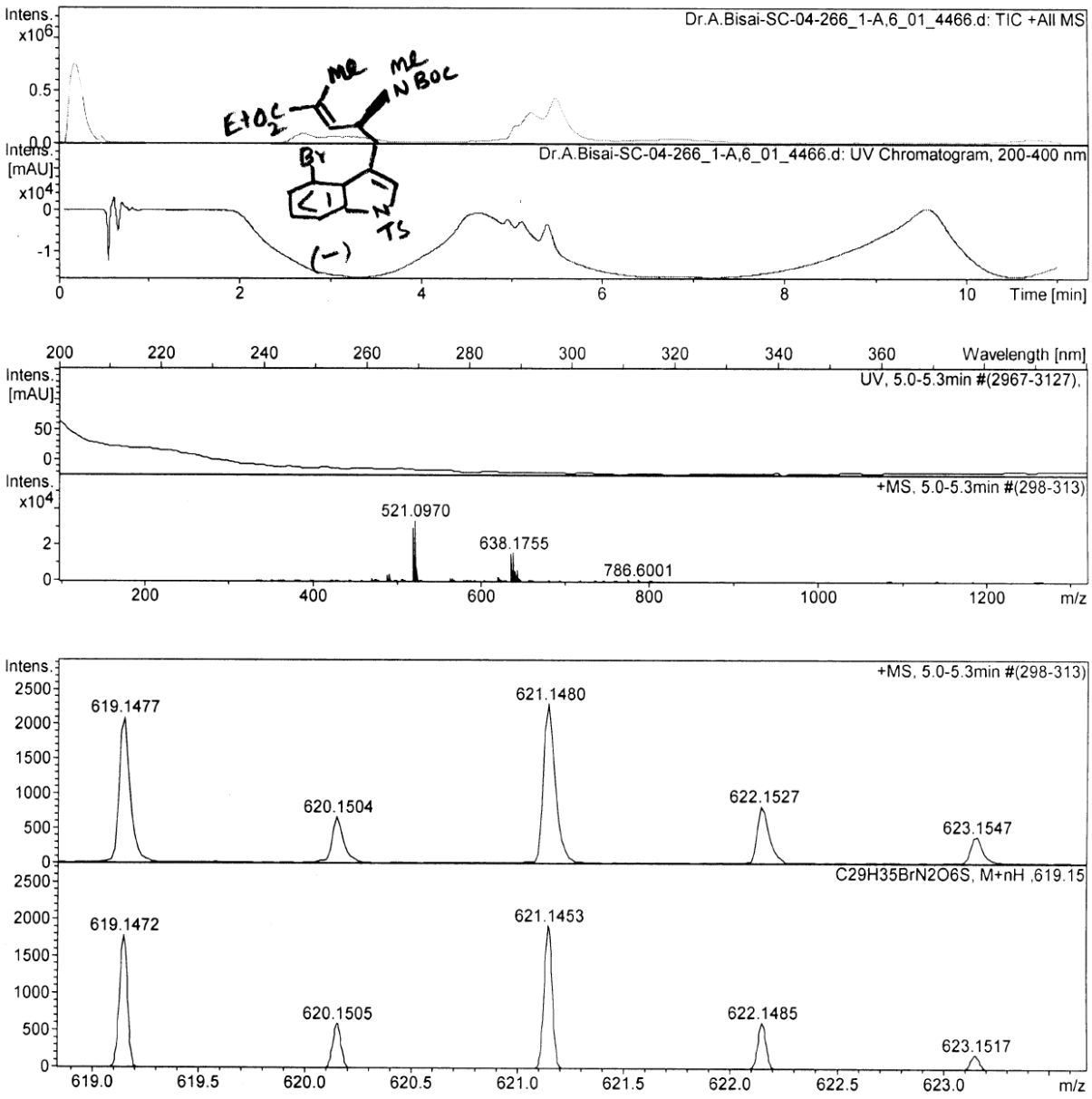


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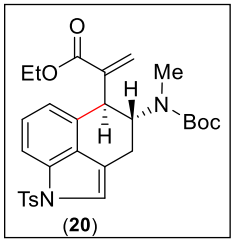
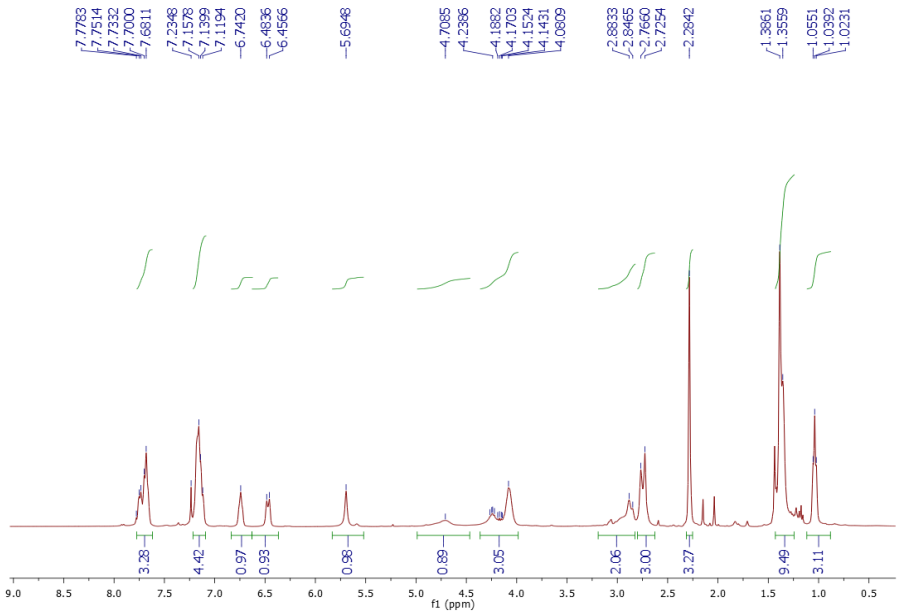
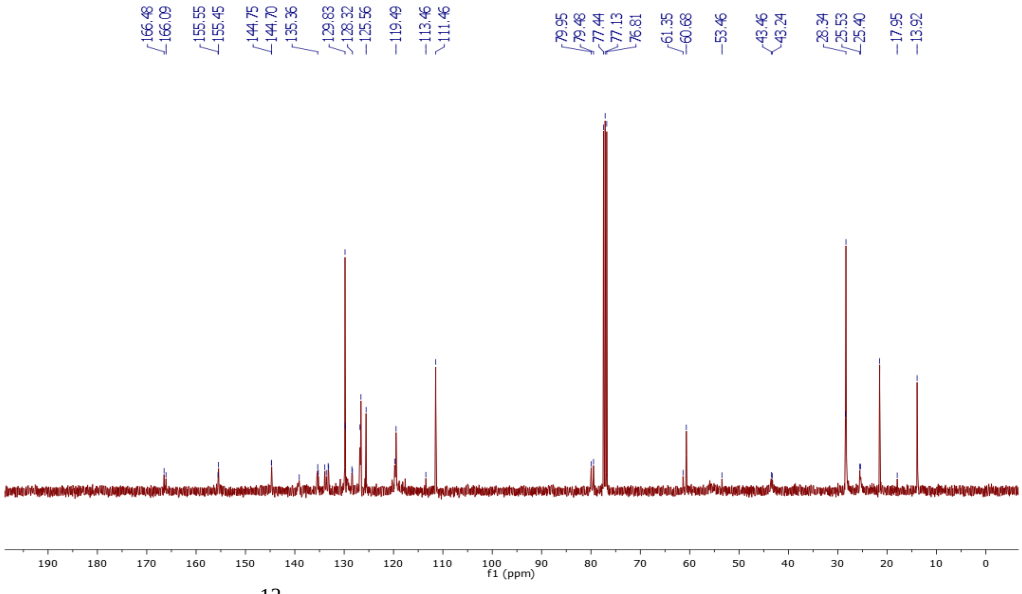
Scanned copy of mass spectrum of (–)-**19**




(**20**)




$^{1}$H NMR (400 MHz, $CDCl_3$) of (**–**)-**20**




$^{13}$C NMR (100 MHz, $CDCl_3$) of (**–**)-**20**

# Display Report

**Analysis Info**

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| Sample Name | Dr.A.BISAI-AB-SG9-195 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

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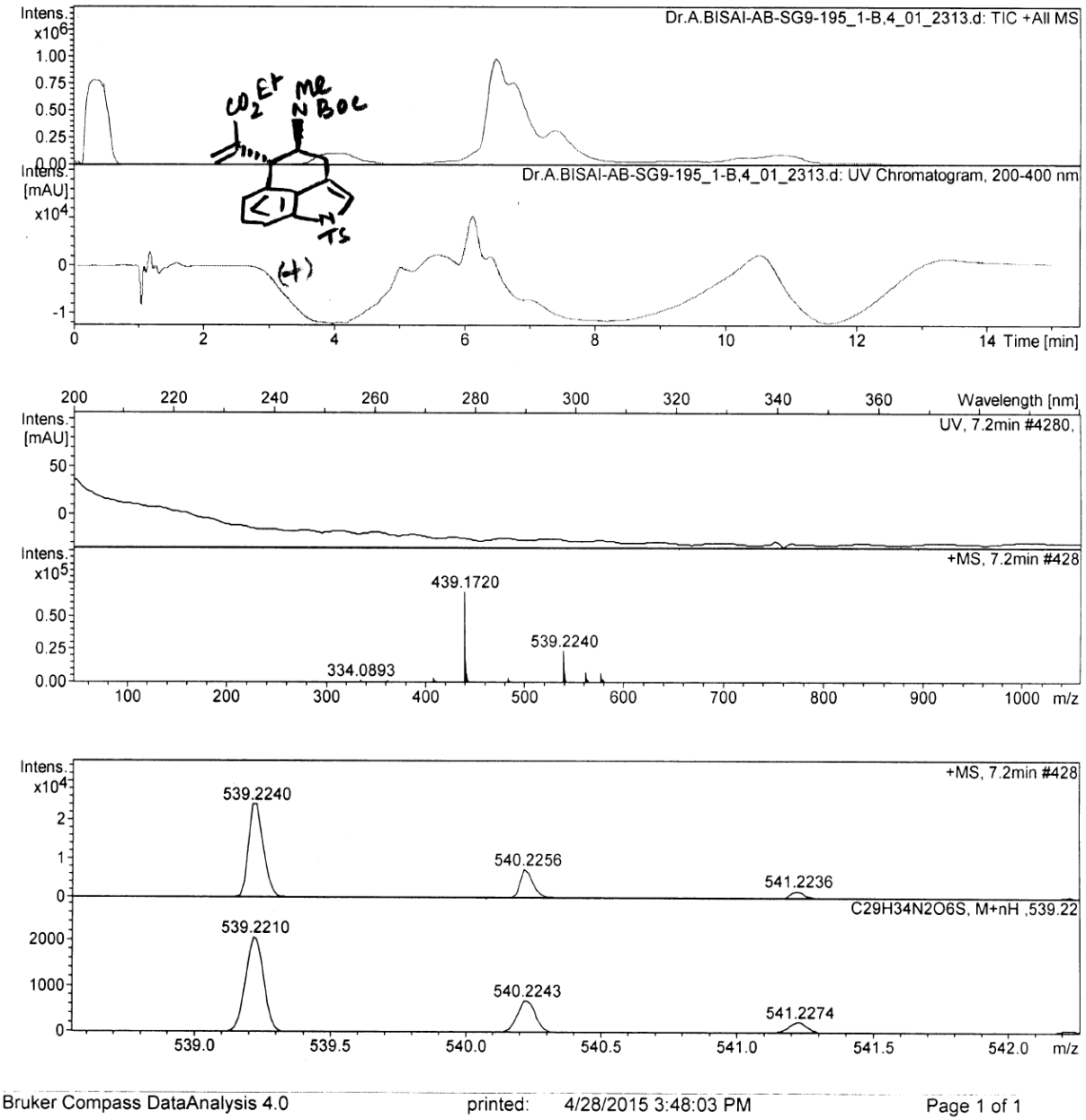
| Scan End | 3000 m/z | Set Collision Cell RF | 600.0 Vpp | Set Divert Valve | Waste |

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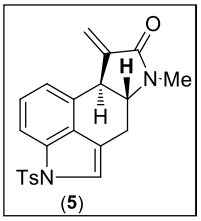
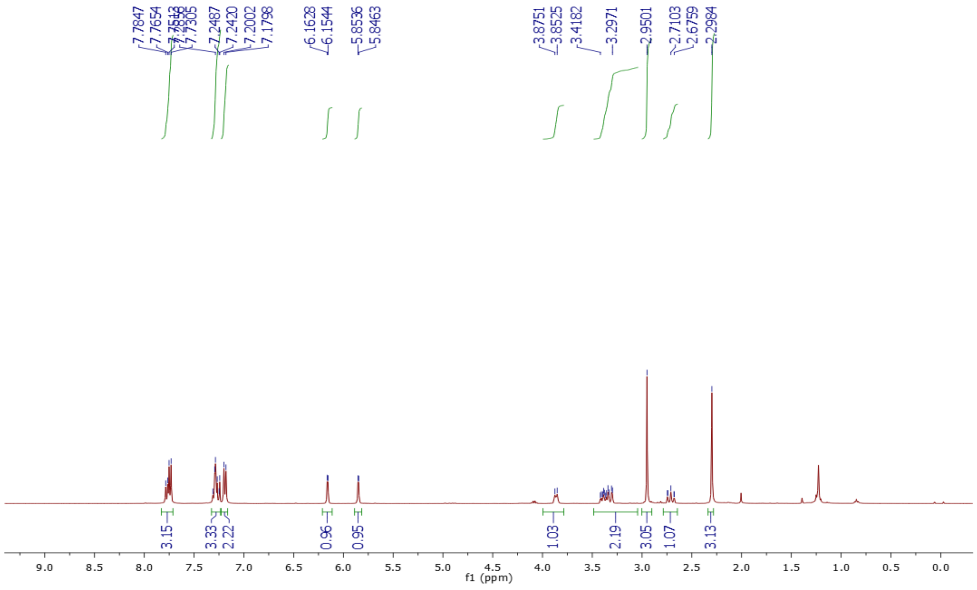
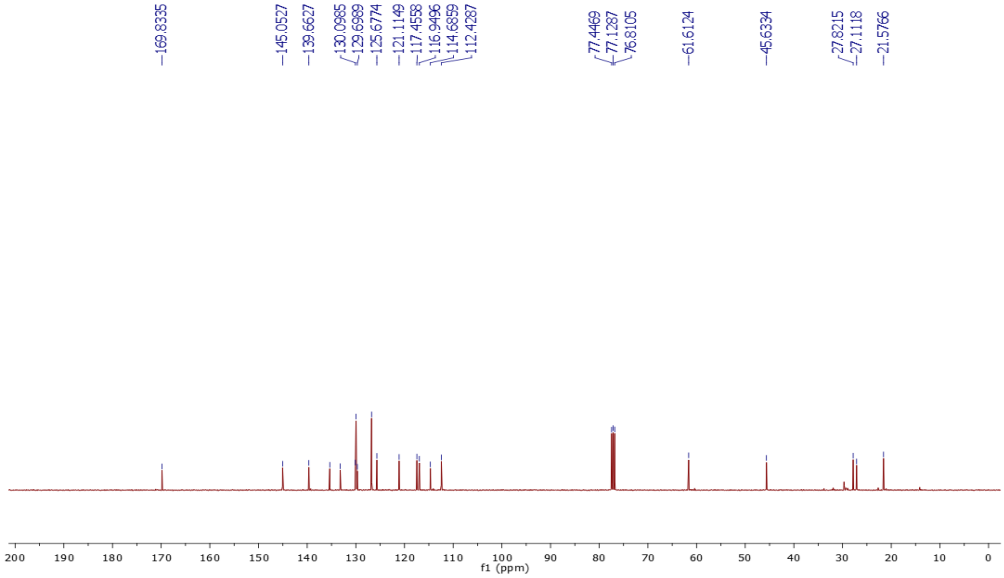
Scanned copy of mass spectrum of (+)-**20**




$^{1}$H NMR (400 MHz, $CDCl_3$) of (−)-**5**




$^{13}$C NMR (100 MHz, $CDCl_3$) of (−)-**5**

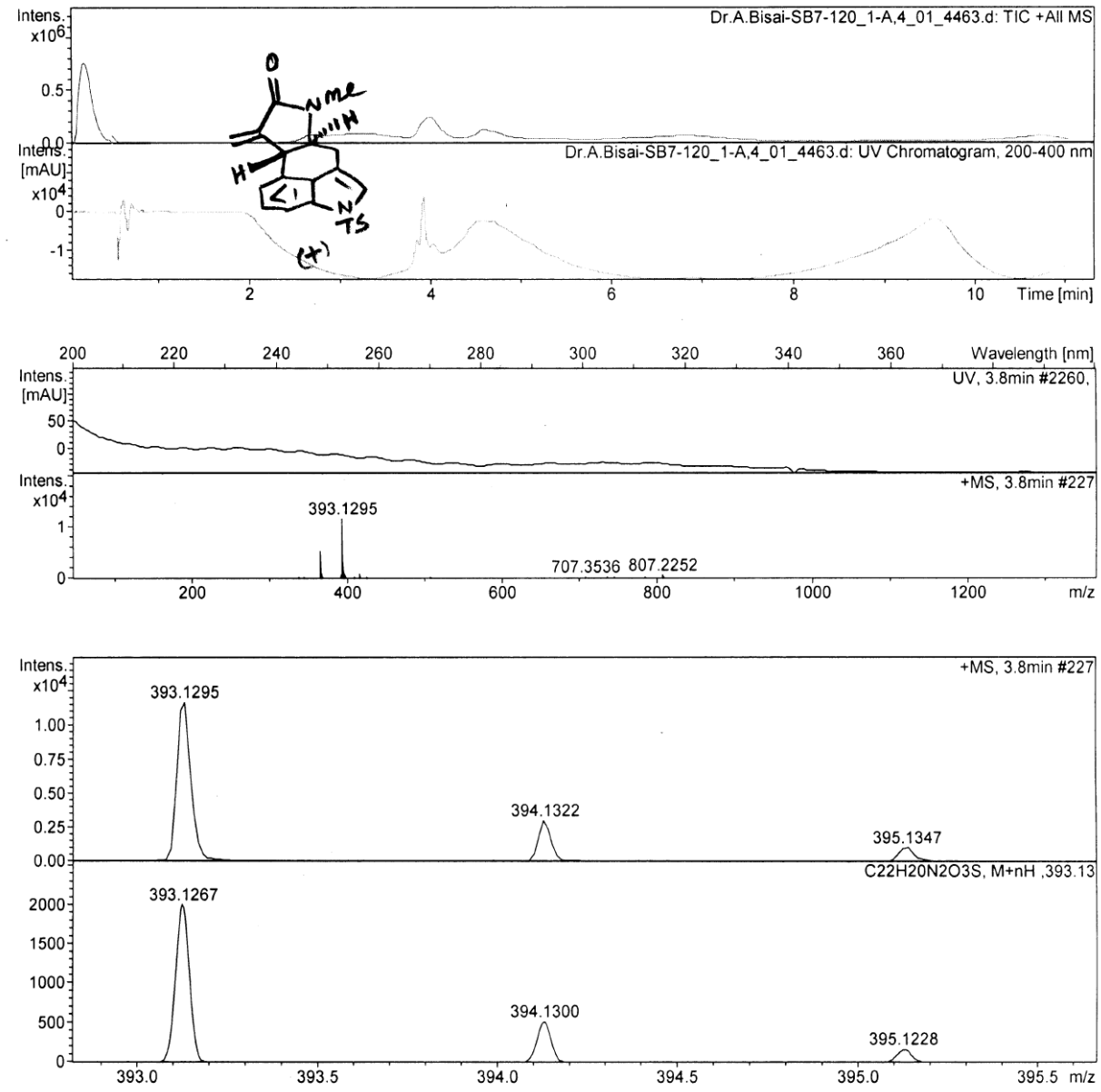
# Display Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\user data\2015\December-2015\08-DEC-2015\Dr.A.Bisai-SB7-120_1-A,4_01_4463.d | Acquisition Date | 12/8/2015 1:04:34 PM |
| Method | HRLCMS-20 Sept tune wide.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SB7-120 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 1.2 Bar |
| Focus | Not active | Set Capillary | 4500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 7.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 600.0 Vpp | Set Divert Valve | Waste |

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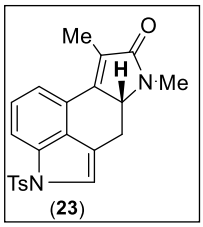
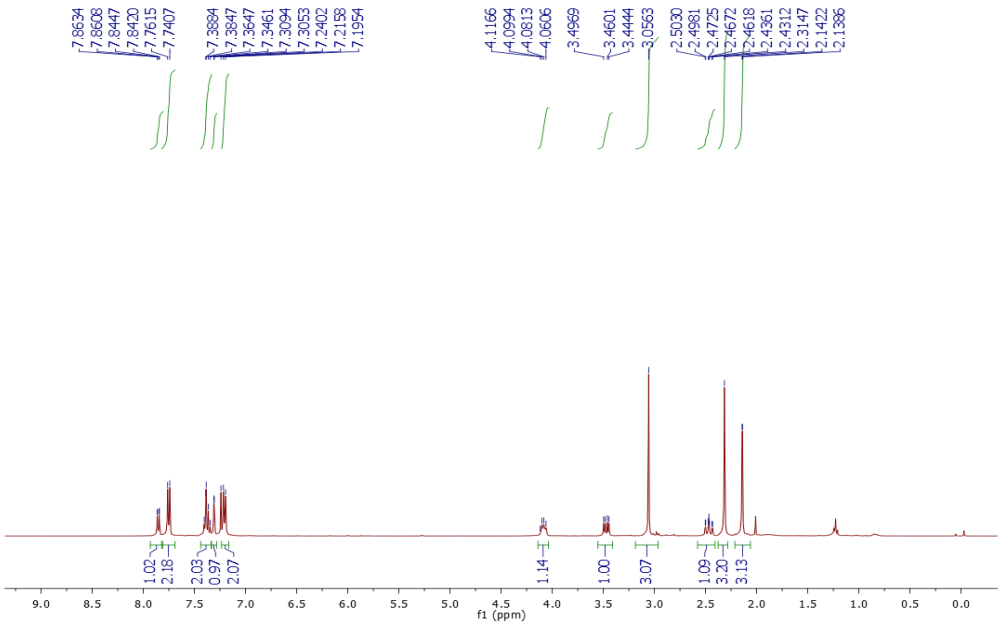
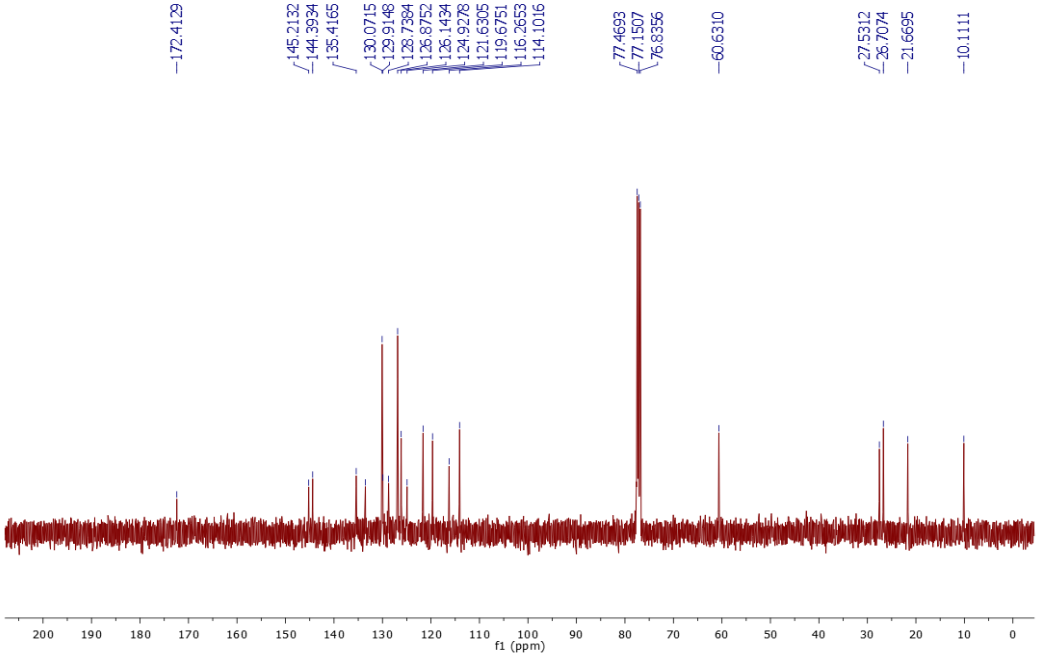
Scanned copy of mass spectrum of (+)-**5**



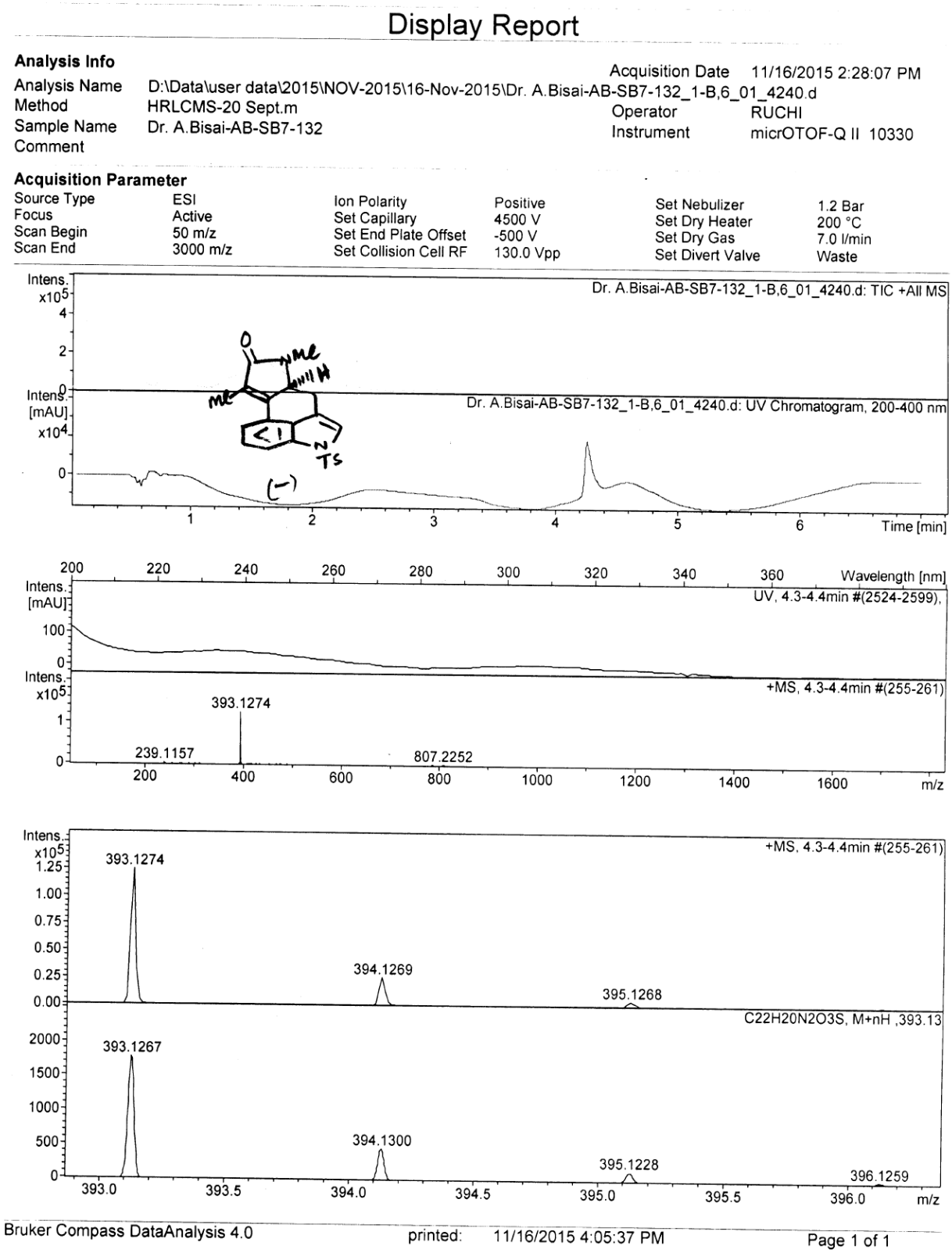

(**23**)



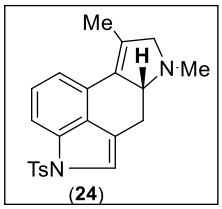

$^{1}$H NMR (400 MHz, $CDCl_3$) of (+)-**23**

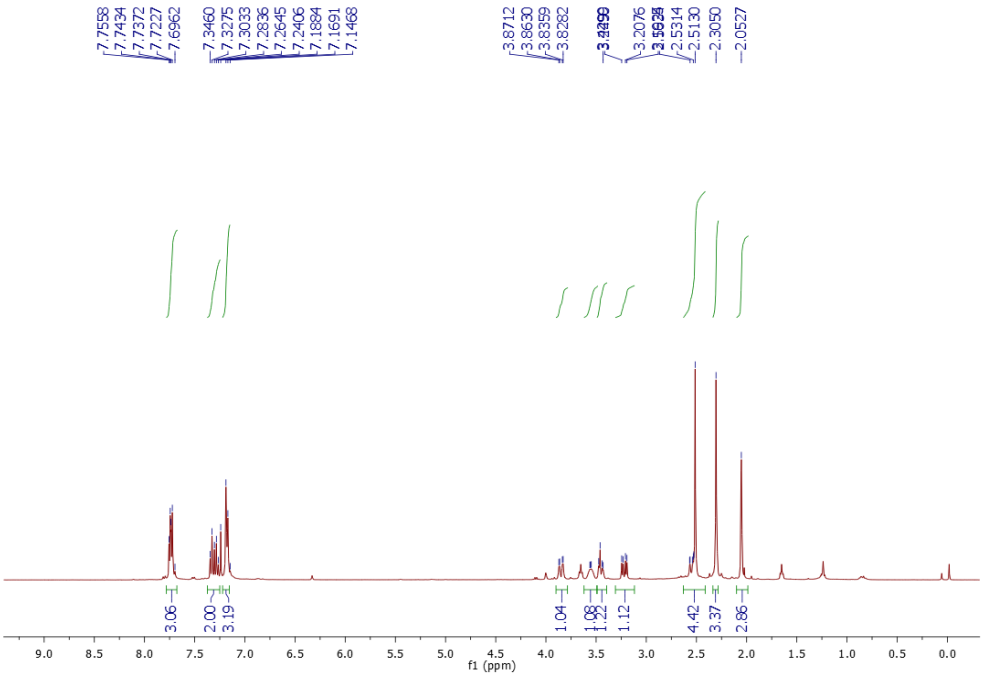



$^{13}$C NMR (100 MHz, $CDCl_3$) of (+)-**23**

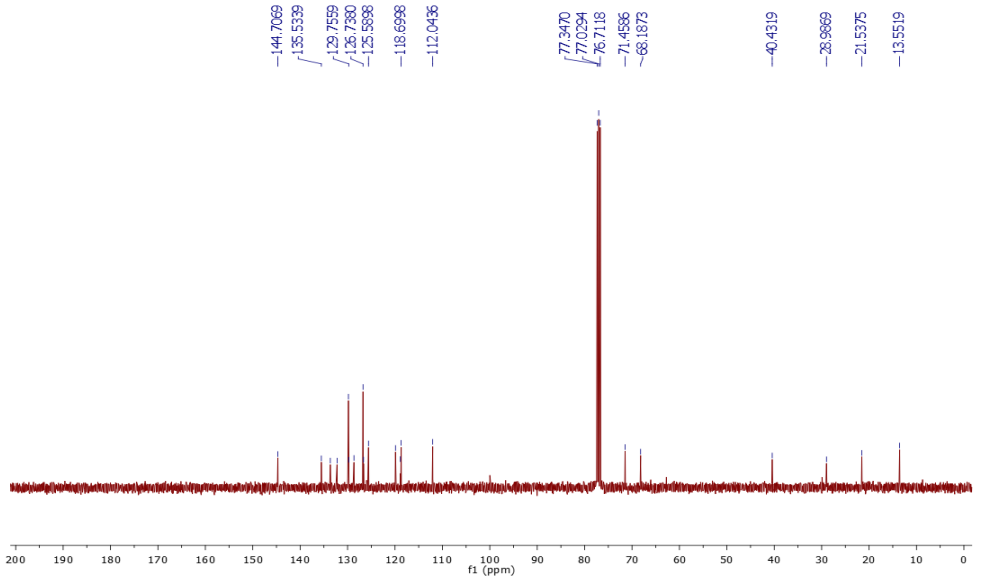



Scanned copy of mass spectrum of (–)-**23**




$^{1}$H NMR (400 MHz, $CDCl_3$) of (+)-**24**




$^{13}$C NMR (100 MHz, $CDCl_3$) of (+)-**24**

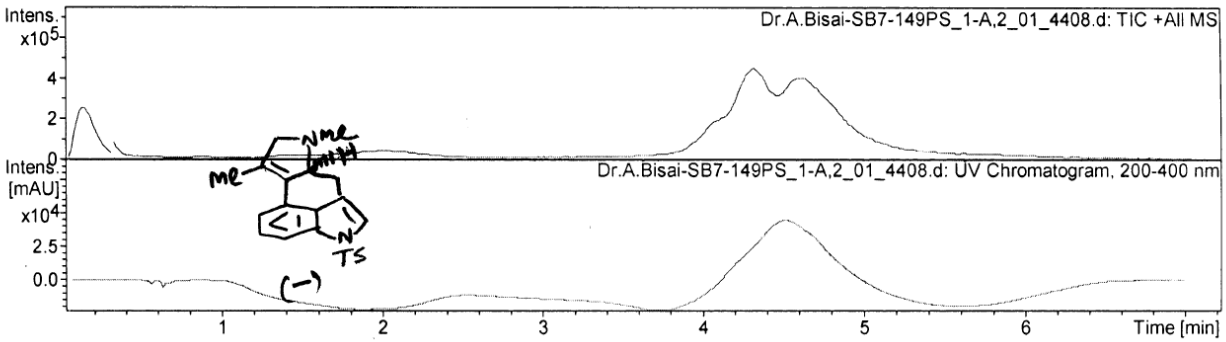
# Display Report

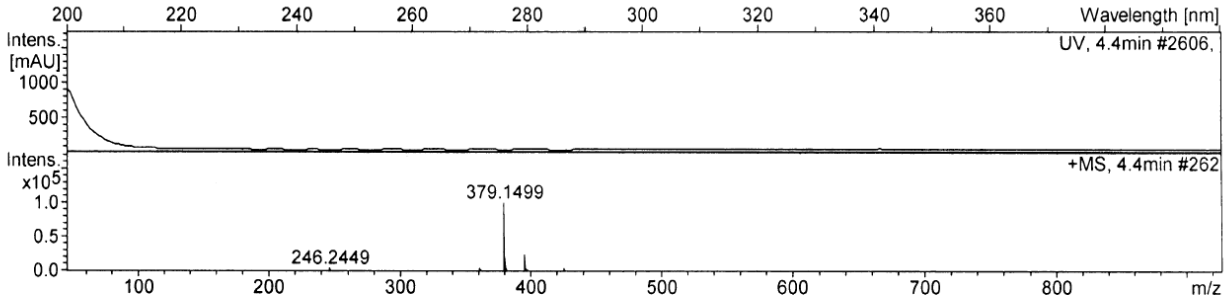
**Analysis Info**

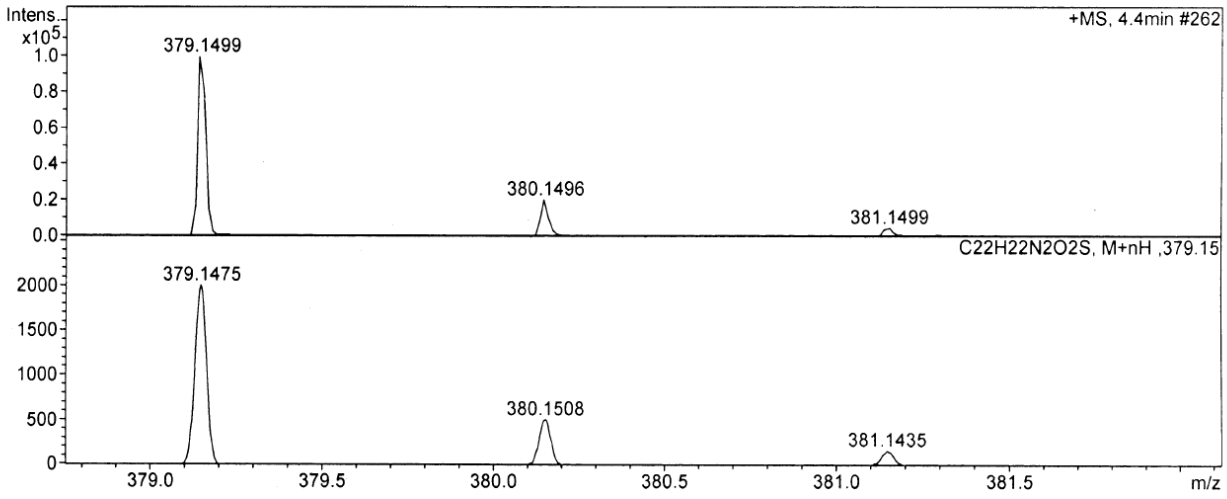
| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\user data\2015\DEC-2015\02-DEC-2015\Dr.A.Bisai-SB7-149PS_1-A,2_01_4408.d | Acquisition Date | 12/2/2015 12:23:06 PM |
| Method | HRLCMS-20 Sept.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SB7-149PS | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 1.2 Bar |
| Focus | Active | Set Capillary | 4500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 7.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 130.0 Vpp | Set Divert Valve | Waste |

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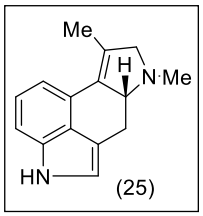
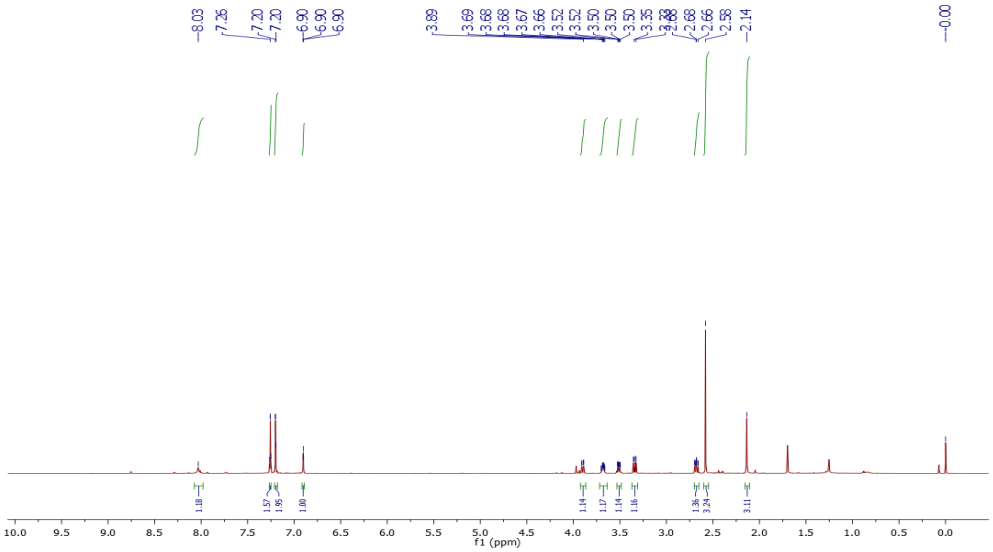
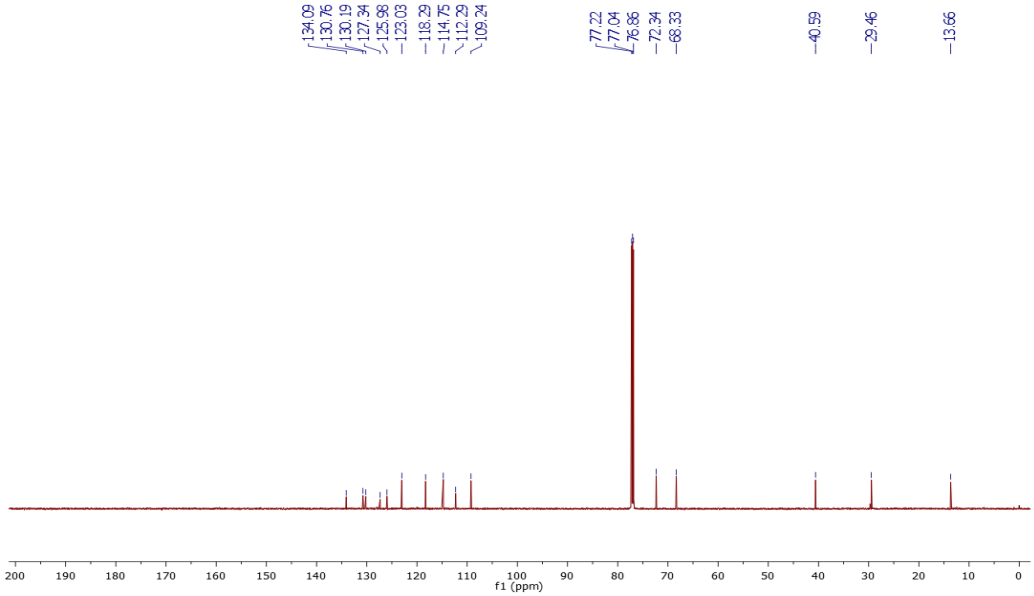
Scanned copy of mass spectrum of (–)-**24**




$^{1}$H NMR(400 MHz, $CDCl_3$) of (+)-**25**




$^{13}$C NMR(100 MHz, $CDCl_3$) of (+)-**25**

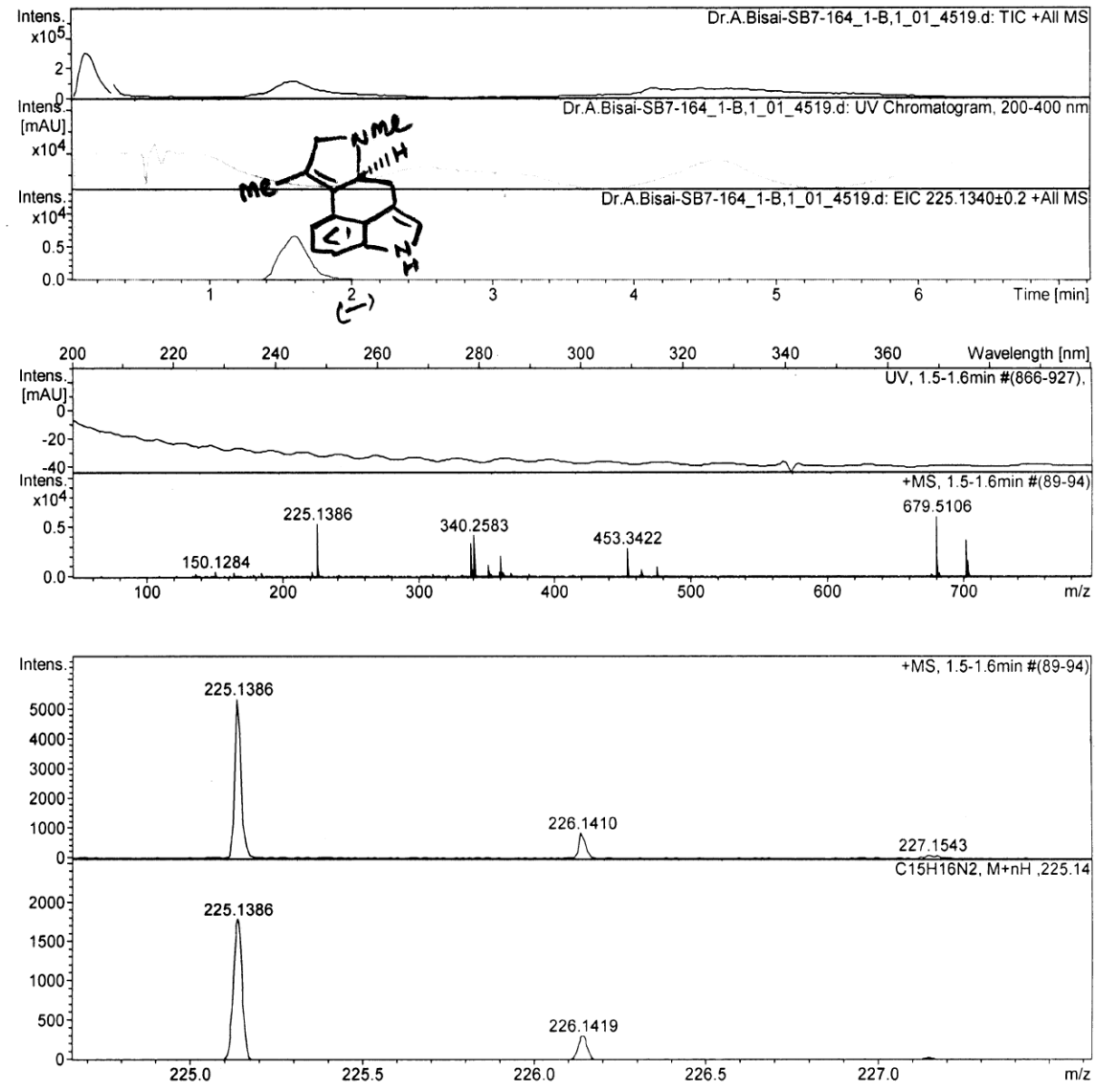
# Display Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Acquisition Date | 12/11/2015 1:59:26 PM | | |
| Analysis Name | D:\Data\user data\2015\December-2015\11-DEC-2015\Dr.A.Bisai-SB7-164_1-B,1_01_4519.d | | |
| Method | HRLCMS-20 Sept.m | Operator | RUCHI |
| Sample Name | Dr.A.Bisai-SB7-164 | Instrument | micrOTOF-Q II 10330 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 1.2 Bar |
| Focus | Active | Set Capillary | 4500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 7.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 130.0 Vpp | Set Divert Valve | Waste |

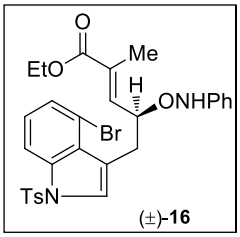




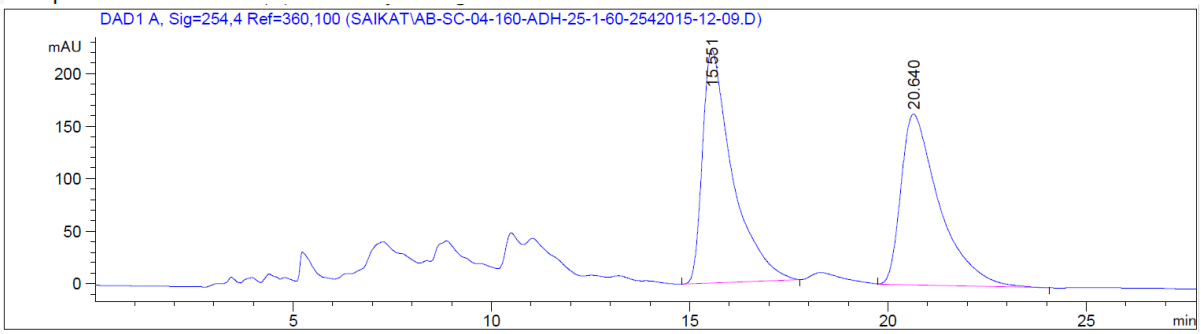

Scanned copy of mass spectrum of (–)-**25**

# HPLC Trace

HPLC data of compound (±)-**16**:

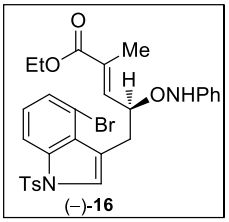



Data File C:\CHEM32\1\DATA\SAIKAT\AB-SC-04-160-ADH-25-1-60-2542015-12-09.D
Sample Name: AB-SC-04-160-ADH-25-1-60-254

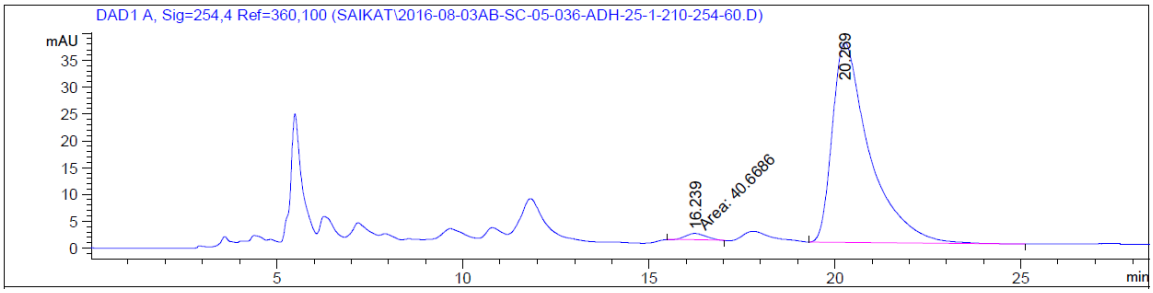



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.551 | BB | 0.7615 | 1.16828e4 | 222.17804 | 51.7444 |
| 2 | 20.640 | BB | 0.9870 | 1.08951e4 | 162.33562 | 48.2556 |
| Totals : | | | | 2.25778e4 | 384.51366 | |

HPLC data of compound (–)-**16**:



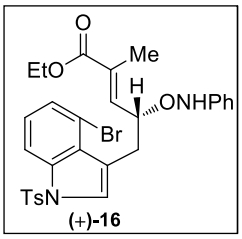

Data File C:\CHEM32\1\DATA\SAIKAT\2016-08-03AB-SC-05-036-ADH-25-1-210-254-60.D
Sample Name: AB-SC-05-036-ADH-25-1-210-254-60



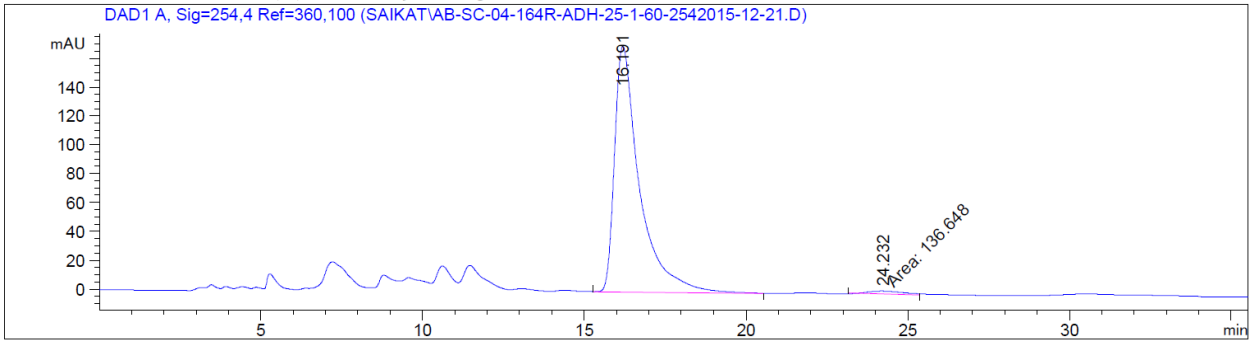

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.239 | MM | 0.6091 | 40.66863 | 1.11287 | 1.5506 |
| 2 | 20.269 | BB | 1.0027 | 2582.10376 | 37.25105 | 98.4494 |
| Totals : | | | | 2622.77239 | 38.36392 | |

HPLC data of compound (+)-**16**:

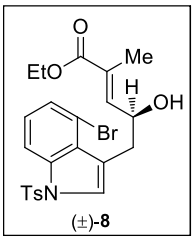



Data File C:\CHEM32\1\DATA\SAIKAT\AB-SC-04-164R-ADH-25-1-60-2542015-12-21.D
Sample Name: AB-SC-04-164R-ADH-25-1-60-254

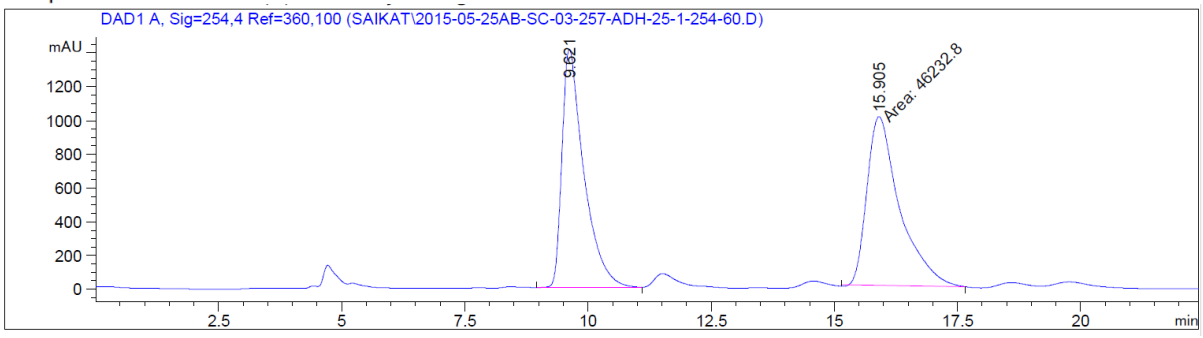



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.191 | BB | 0.7829 | 9143.63477 | 170.15610 | 98.5275 |
| 2 | 24.232 | MM | 1.1993 | 136.64833 | 1.89893 | 1.4725 |
| Totals : | | | | 9280.28310 | 172.05503 | |

HPLC data of compound (±)-**8**:

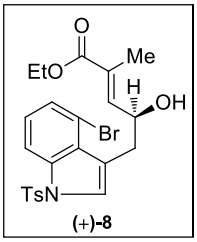



Data File C:\CHEM32\1\DATA\SAIKAT\2015-05-25AB-SC-03-257-ADH-25-1-254-60.D
Sample Name: AB-SC-03-257-ADH-25-1-254-60



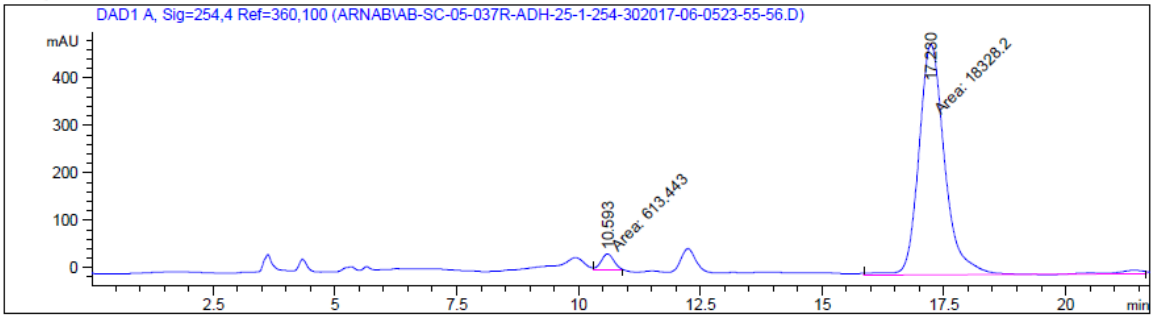
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.621 | BV | 0.4496 | 4.37290e4 | 1410.99182 | 48.6084 |
| 2 | 15.905 | MM | 0.7714 | 4.62328e4 | 998.86591 | 51.3916 |
| Totals : | | | | 8.99618e4 | 2409.85773 | |

HPLC data of compound (–)-**8**:



(+)-**8**

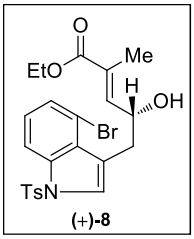
Data File C:\CHEM32\1\DATA\ARNAB\AB-SC-05-037R-ADH-25-1-254-302017-06-0523-55-56.D
Sample Name: AB-SC-05-037R-ADH-25-1-254-30



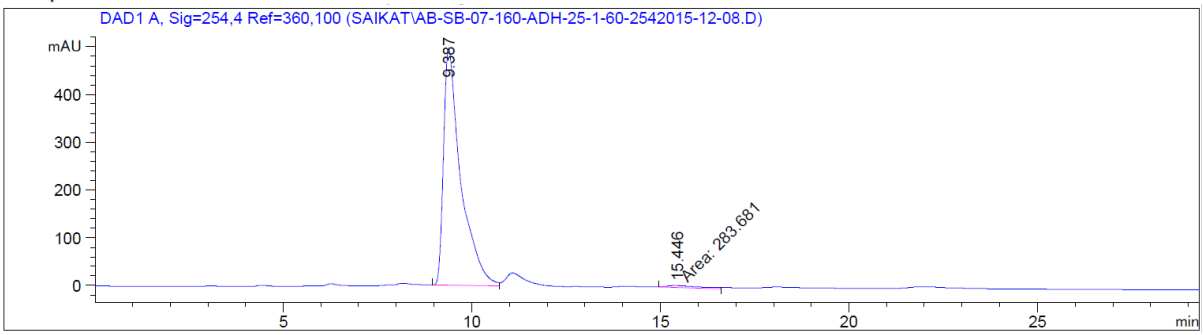

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.593 | MM | 0.3039 | 613.44250 | 33.64640 | 3.2386 |
| 2 | 17.230 | MM | 0.6266 | 1.83282e4 | 487.46713 | 96.7614 |
| Totals : | | | | 1.89416e4 | 521.11353 | |

HPLC data of compound (+)-**8**:

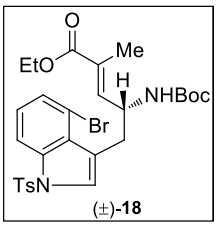



Data File C:\CHEM32\1\DATA\SAIKAT\AB-SB-07-160-ADH-25-1-60-2542015-12-08.D
Sample Name: AB-SB-07-160-ADH-25-1-60-254

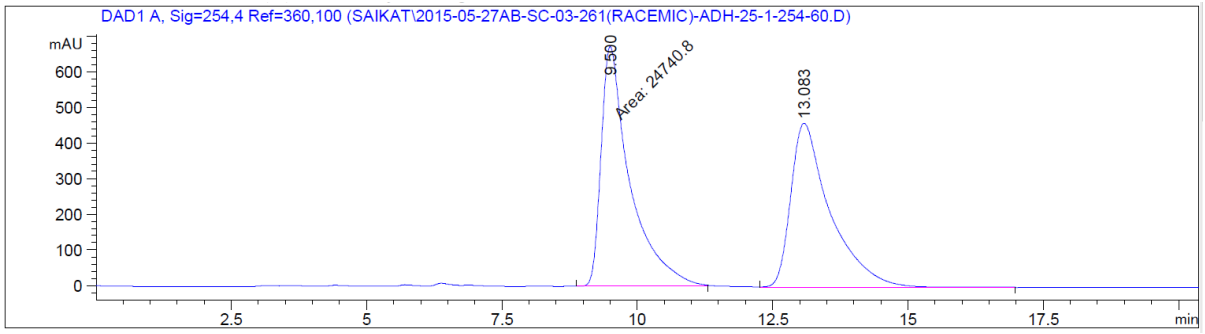



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.387 | BV | 0.4584 | 1.57166e4 | 495.02777 | 98.2270 |
| 2 | 15.446 | MM | 1.1425 | 283.68088 | 4.13844 | 1.7730 |
| Totals : | | | | 1.60003e4 | 499.16621 | |

HPLC data of compound (±)-**18**:

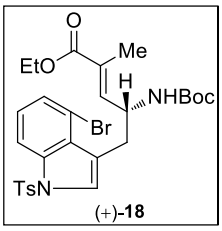



Data File C:\CHEM32\1\DATA\SAIKAT\2015-05-27AB-SC-03-261(RACEMIC)-ADH-25-1-254-60.D
Sample Name: AB-SC-03-261(Racemic)-ADH-25-1-254-60

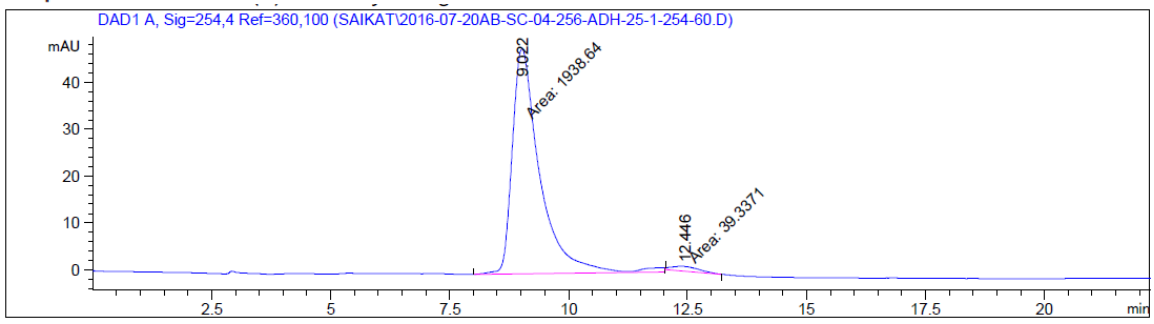



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.500 | MM | 0.6141 | 2.47408e4 | 671.42346 | 51.6950 |
| 2 | 13.083 | BB | 0.7228 | 2.31183e4 | 459.61508 | 48.3050 |
| Totals : | | | | 4.78591e4 | 1131.03854 | |

HPLC data of compound (+)-**18**:



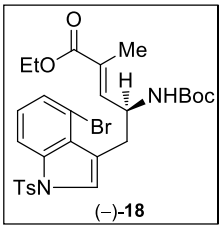

Data File C:\CHEM32\1\DATA\SAIKAT\2016-07-20AB-SC-04-256-ADH-25-1-254-60.D
Sample Name: AB-SC-04-256-ADH-25-1-254-60



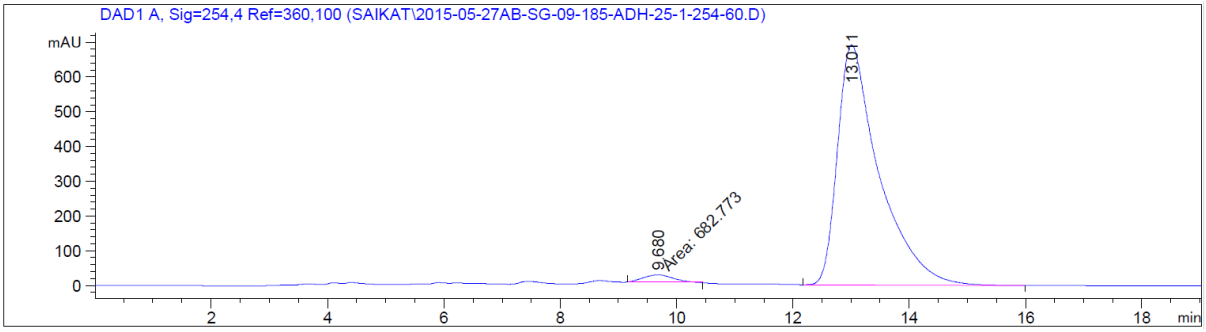
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.022 | MM | 0.6727 | 1938.63586 | 48.03125 | 98.0112 |
| 2 | 12.446 | MM | 0.6658 | 39.33714 | 9.84652e-1 | 1.9888 |
| Totals : | | | | 1977.97300 | 49.01590 | |

HPLC data of compound (–)-**18**:




Data File C:\CHEM32\1\DATA\SAIKAT\2015-05-27AB-SG-09-185-ADH-25-1-254-60.D
Sample Name: AB-SG-09-185-ADH-25-1-254-60




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.680 | MM | 0.5584 | 682.77289 | 20.37837 | 1.9527 |
| 2 | 13.011 | BB | 0.7203 | 3.42828e4 | 689.21088 | 98.0473 |
| Totals : | | | | 3.49655e4 | 709.58924 | |