Supporting Information

Concise Total Syntheses of Bis(cyclotryptamine) Alkaloids via Thio-Urea Catalyzed One-Pot Sequential Michael Addition

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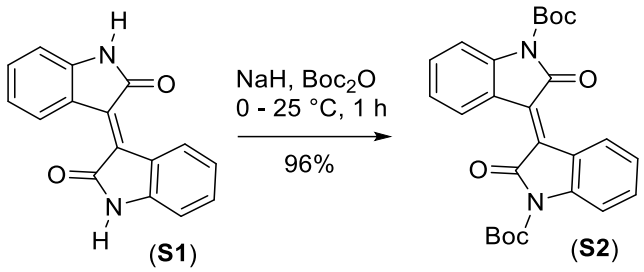
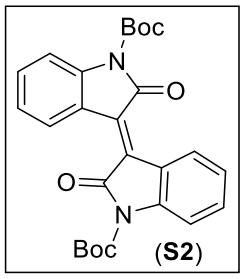
Materials and Methods

Unless otherwise stated, reactions were carried out using oven dried glassware with Teflon-coated magnetic stirring bars were used to stir the reactions. The Syringe was used to transfer the solvents and liquid reagents. Tetrahydrofuran (THF), Diethyl ether (Et_2O) were distilled over sodium/benzophenone ketyl. Dichloromethane CH_2Cl_2) was distilled over calcium hydride. All other solvents like Nitromethane, MeOH, EtOAc, DMF, Dichloroethane (DCE) and reagents were used as received. Reaction temperatures above 25 °C were maintained by using oil-bath on a magnetic stirrer. Thin layer chromatography (TLC) analysis was performed by using silicagelprecoated plates (0.25 mm) 60 (F-254), Visualized by UV irradiation, yellow dip stain and other stains. Silicagel of particle size 230-400 and 100-200 mesh were used to perform flash chromatography. Digital melting point apparatus is used to record the melting points.^{1}H NMR spectra were recorded by using 400, 500 700 MHz spectrometers, ^{13}C NMR operating frequencies are 100, 125 175 MHz respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvents ($CDCl_3$) signal (δ = 7.24 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR) and (DMSO-D_6) signal (δ = 2.50 for ^{1}H NMR and δ = 39.5 for ^{13}C NMR). Data for ^{1}H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, number of hydrogen). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). IR spectra were recorded on an 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.

Preparation of Boc-protected iso-indigo compound (S2):



In an oven dry round bottom flask, compound **S1** (10 gm, 38.13 mmol, 1.0 equiv.) was taken in dry THF (100 ml) and then allowed to stir for 5 min. Then NaH (2.0 gm, 83.9 mmol, 2.2 equiv.) was added portion-wise to the reaction mixture and allowed to stir for another 30 mins followed by the addition of di-*tert*-butyl decarbonate (17.4 ml, 83.9 mmol, 2.2 equiv.). After complete consumption of starting materials (as judged by running TLC), saturated NH_4Cl (20 mL) was added at 0 ºC followed by the addition of brine (20 mL) and it was extracted with EtOAC (25 mL X 2). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under the reduced pressure. The crude mixture was purified by flush chromatography using ethyl acetate and n-hexane (1:9) as eluents.

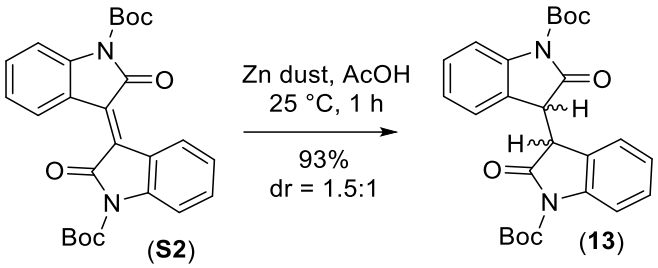


Di-*tert*-butyl (*E*)-2,2'-dioxo-[3,3'-biindolinylidene]-1,1'-dicarboxylate (**S2)**: Compound **S2** was obtained as red foam (38.13 mmol scale of reaction, 16.9 g of product, 96% yield); R_f = 0.6 (10% EtOAc in hexane).

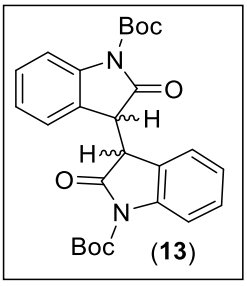
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, *J* = 7.9 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.15 (t, *J* = 7.7 Hz, 1H), 1.66 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 148.8, 141.3, 133.3, 132.8, 129.2, 124.2, 121.9, 114.4, 84.9, 28.2.

Reduction of compound S2:



An oven dried round bottom flask was charged with compound **S2** (15 gm, 32.43 mmol, 1.0 equiv.) in acetic acid (80 ml). To this solution was added Zn dust (10.6 gm, 162.2 mmol, 5.0 equiv.) portion-wise and allowed to stir at room temperature for another 1 h. After complete consumption of starting materials (monitored by running TLC), the reaction mixture was quenched with saturated $NaHCO_3$ (15 mL) and then extracted with EtOAc (30 mL X 2). The organic layers were separated and washed with brine (30 mL X 1). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under the reduced pressure. The crude mixture was purified using column chromatography (15% EtOAc in Petroleum Ether) to afford the desired mixture of diastereomers as an orange foam.



Di-*tert*-butyl 2,2'-dioxo-[3,3'-biindoline]-1,1'-dicarboxylate (13): Compound **13** was obtained as a mixture of 1.5:1 diastereomers (32.43 mmol scale of reaction, 14.0 gm of product, 93% yield); R_f = 0.42 (30% EtOAc in hexane).

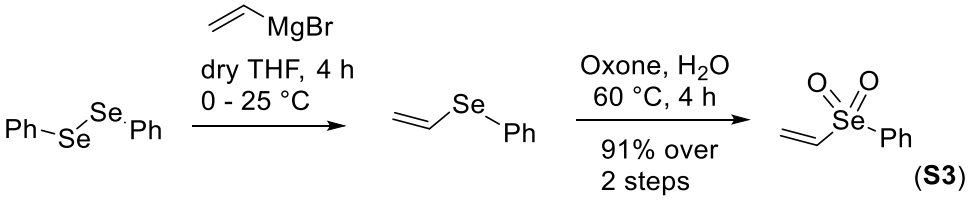
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.30 (td, *J* = 7.9, 1.5 Hz, 1H), 7.16 – 7.11 (m, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.88 (m, 1H), 6.79 (d, *J* = 7.4 Hz, 1H), 4.42 (s, 1H), 4.32 (s, 1H), 1.66 (s, 6H), 1.56 (d, *J* = 5.0 Hz, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 172.8, 148.9, 148.9, 141.0, 140.2, 129.1, 128.9, 124.5, 124.5, 124.3, 123.2, 123.2, 123.1, 115.5, 114.9, 84.8, 84.4, 47.5, 47.3, 28.1, 28.0.

IR (film)υ_{max}: 2981, 1765, 1731, 1481, 1466, 1370, 1351, 1299, 1252, 1150, 1091, 753 cm^{-1}.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $[C_{26}H_{28}N_2O_6 + H]^+$ 465.2045; Found 465.2033.

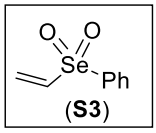
Preparation of the Michael acceptor phenyl vinyl selenone S3:



(**S3**)

In an oven dried RB flask, diphenyl di-selenide (PhSe-SePh, 9.0 gm, 2.88 mmol, 1.0 equiv.) was taken in THF (80 mL) and 1.0 (M) solution of vinyl magnesium bromide in THF (6.3 ml, 6.34 mmol, 2.2 equiv.) was added slowly to the reaction vessel over a period of 5 minutes maintaining the temperature at 0 °C. The reaction mixture was warmed to room temperature and stirring continued for another 4 h. The reaction mixture was quenched with aqueous NH_4Cl (15 mL), diluted with water (10 mL) and extracted with EtOAc (15 mL X 3). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (2% EtOAc in *n*-hexane) on silica gel to afford the pure product.

To a solution of the phenyl vinyl selenide (2.88 mmol, 1.0 equiv.) in water (20 mL) oxone ($2KHSO_5.KHSO_4.K_2SO_4$) (965 mg, 6.33 mmol, 2.2 equiv.) was added portion wise at room temperature over a period of 10 min. The reaction mixture was warmed to 60 °C and stirred until complete consumption of the starting material (judged by running TLC, 4 h). The reaction mixture was extracted with EtOAc (15 mL X 2). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel to afford the desired phenyl vinyl selenone **S3**.



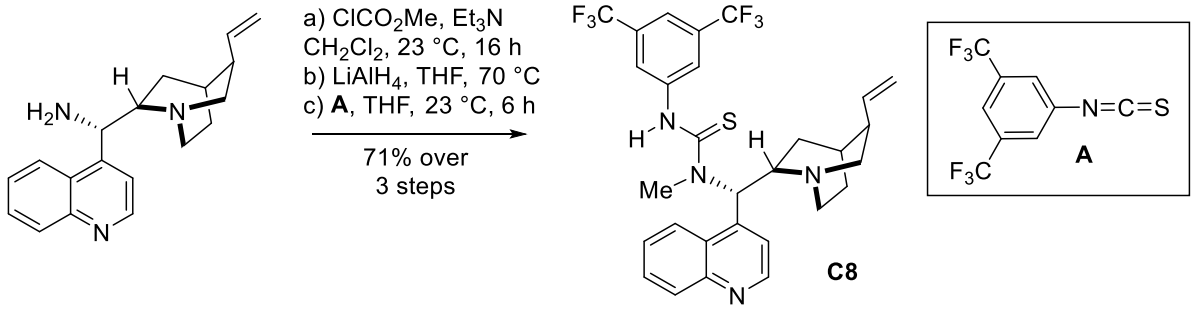
(**S3**)

(Vinylselenonyl)benzene (**S3)**: Compound **S3** was obtained as white solid (mp: 110-112 ºC) (563 mg of product, 91% yield); R_f = 0.55 (3% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 2H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 6.64 (dd, *J* = 16.5, 9.9 Hz, 1H), 6.43 (d, *J* = 16.5 Hz, 1H), 6.02 (d, *J* = 9.7 Hz, 1H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 138.5, 133.8, 129.5, 127.9, 127.9.

IR (film)υ_{max}: 3043, 1448, 1370, 1221, 1064, 980, 929, 880, 761, 685 cm^{-1}.

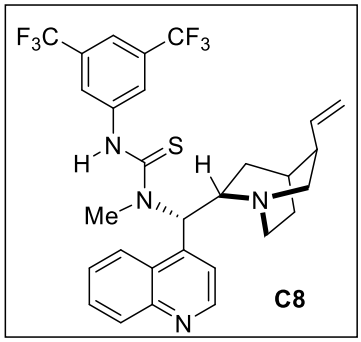
Preparation of catalyst C8 from C3:



A flame-dried sealed tube (25 mL) was charged with amine (0.886 mmol, 1 equiv.) in dichloromethane (10 mL) and triethylamine was (0.886 mmol, 1 equiv.) added to it. Chloromethylformate [ClCOOMe (0.886 mmol, 1 equiv.)] was added drop-wise to the reaction mixture ay room temperature and stirring continued for 16 h. After completion of the reaction (as monited by running TLC), water (10 mL) was added and extracted with CH_2Cl_2 (20 mL X 2). Next, the combined organic phases were dried over Na_2SO_4 and evaporated under reduced pressure. The crude carbamate was charged for the next step without further purification. [For the preparation of the amine, please see, Dixon *et. al. Chem. Eur. J*. 2013, **19**, 14286.]

In a flame-dried 100 mL round-bottom, carbamate (0.886 mmol, 1.0 equiv.) was taken in dry THF (20 mL). The mixture was cooled to 0 °C and $LiAlH_4$ (1.33 mmol, 1.5 equiv.) was slowly added to the reaction mixture in portions. Then the reaction mixture was refluxed at 70 °C for 1 h and then cooled again to 0 °C. Then, the reaction mixture was successively quenched with dropwise addition of EtOAC (3 mL), water (2 mL), 20% KOH aqueous solution (5 mL) and stirred until the slurry changed colour from grey to white (1 h). The whole mixture was filtered through a celite pad and the solid was washed with Et_2O (3 X 30 mL) and concentrated in rotary evaporator under reduced pressure. Next, the filtrate was dried over Na_2SO_4 and evaporated yielding a crude product.

To a solution of *N*-methylated secondary amine (0.886 mmol, 1.0 equiv.) in dry THF (10 mL) was added 3,5-bis(trifluoromethyl)phenyl isothiocyanate (**A**) (0.945 mmol, 1.1 equiv.) at room temperature. The mixture was stirred overnight at the same temperature to completion of the reaction. The solvents were evaporated and the residue was purified by flash chromatography (5% to 10% MeOH in CH_2Cl_2) to give **C8** as a white foam (71% yield).



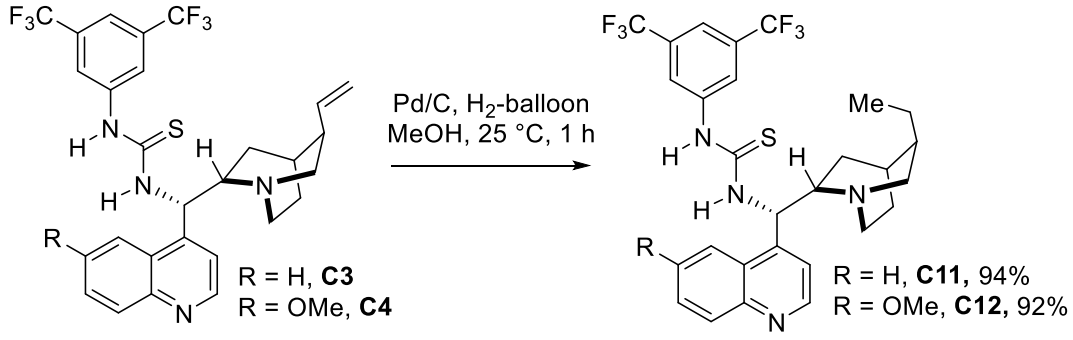
3-(3,5-Bis(trifluoromethyl)phenyl)-1-methyl-1-((1*S*)-quinolin-4-yl((2*S*)-5-vinylquinuclidin-2-yl)methyl)thiourea (**C8)**: Compound **C8** was obtained as white solid (mp: 170-171 ºC) (364 mg of product, 71% yield); R_f = 0.35 (10% MeOH in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.7 Hz, 1H), 8.16 – 8.13 (m, 2H), 8.11 (d, *J* = 7.7 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.61 (d, *J* = 4.4 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.52 – 7.47 (m, 1H), 7.43 – 7.40 (m, 1H), 5.80 (ddd, *J* = 17.0, 10.4, 6.2 Hz, 1H), 5.55 (d, *J* = 9.6 Hz, 1H), 5.30 – 5.14 (m, 2H), 3.89 – 3.78 (m, 1H), 3.70 (dt, *J* = 13.0, 9.3 Hz, 1H), 3.40 – 3.27 (m, 2H), 3.17 (q, *J* = 9.5 Hz, 1H), 2.78 – 2.68 (m, 1H), 2.19 – 2.09 (m, 2H), 2.00 (s, 3H), 1.86 – 1.75 (m, 2H), 1.01 – 0.73 (m, 1H).

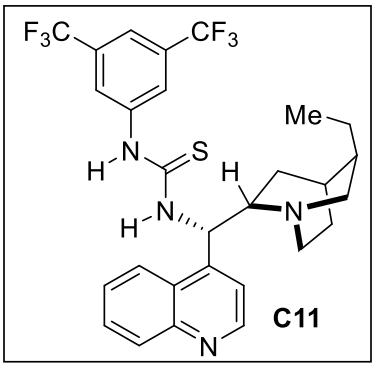
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 152.9, 138.5, 135.3, 133.0, 130.4, 130.0, 127.7, 126.9, 123.9, 123.4, 111.9, 60.6, 56.0, 51.8, 38.9.

IR (film)υ_{max}: 3212, 1654, 1125, 889, 681 cm^{-1}.

General procedure for the preparation of C11 and C12:



To an oven dried round bottom flask catalyst **C3** (0.887 mmol, 1.0 equiv.) was taken in MeOH and the mixture was purged with N_2 atmosphere for 15 min and then Pd-C (50 mg of 10% Pd-C) was added to the reaction mixture portion-wise. After an additional 5 min of stirring the reaction vessel was charged with H_2-balloon and allowed to stir for another 1 h. After complete consumption of starting material (judged by running TLC) H_2-balloon was removed very cautiously, and then mixture was concentrated under reduced pressure. The crude mixture was purified by flash chromatography using methanol and dichloromethane as eluents [2-3% $MeOH/CH_2Cl_2$].

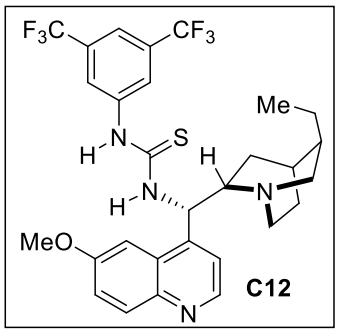


1-(3,5-*Bis*(trifluoromethyl)phenyl)-3-((1*S*)-((2*S*)-5-ethylquinuclidin-2-yl)(quinolin-4-yl)methyl)thiourea (**C11)**: Compound **C11** was obtained as white solid (mp: 174-175 ºC) (472 mg of product, 94% yield); R_f = 0.25 (5% MeOH in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J* = 4.5 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.71 – 7.53 (m, 2H), 7.49 – 7.38 (m, 2H), 7.29 – 6.95 (m, 1H), 3.40 – 3.30 (m, 2H), 3.28 – 3.19 (m, 1H), 2.95 – 2.83 (m, 2H), 2.34 – 2.26 (m, 1H), 1.67 – 1.55 (m, 3H), 1.44 – 1.35 (m, 1H), 1.29 – 1.23 (m, 1H), 0.76 (dd, *J* = 13.9, 7.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 150.1, 148.9, 142.3, 141.4, 132.6, 132.1, 130.8, 129.6, 129.1, 128.7, 127.3, 126.7, 114.6, 60.4, 59.7, 56.1, 41.0, 39.5, 29.7, 28.0, 27.3, 26.2, 14.2.

IR (film)υ_{max}: 3244, 1634, 752, 681 cm^{-1}.



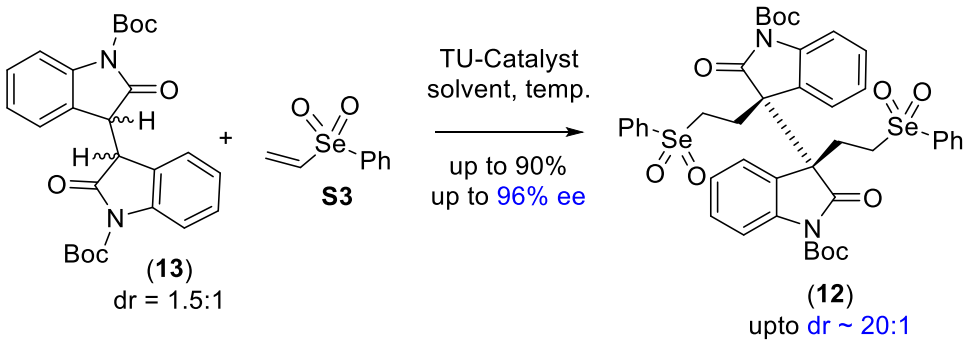
1-(3,5-*Bis*(trifluoromethyl)phenyl)-3-((1*S*)-((2*S*)-5-ethylquinuclidin-2-yl)(6-methoxyquinolin-4-yl)methyl)thiourea (**C12)**: Compound **C12** was obtained as white solid (mp: 171-173 ºC) (0.887 mmol scale of reaction, 462 mg of product, 92% yield); R_f = 0.20 (5% MeOH in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.05 (s, 1H), 7.97 (d, *J* = 9.3 Hz, 1H), 7.86 (s, 1H), 7.60 (s, 1H), 7.57 (s, 1H), 7.48 – 7.46 (m, 1H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 4.6 Hz, 1H), 3.96 (s, 3H), 3.68 (d, *J* = 7.9 Hz, 1H), 3.15 – 3.09 (m, 1H), 2.96 (dd, *J* = 14.2, 9.8 Hz, 2H), 2.90 – 2.79 (m, 2H), 2.32 (q, *J* = 7.9 Hz, 1H), 1.65 (s, 1H), 1.62 – 1.46 (m, 3H), 1.24 (s, 3H), 1.22 (d, *J* = 2.3 Hz, 1H), 0.98 – 0.83 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 141.2, 140.1, 138.3, 133.5, 125.5, 125.0, 123.7, 123.1, 122.1, 120.0, 119.3, 115.7, 110.5, 110.4, 109.9, 108.5, 75.4, 53.9, 52.4, 46.0, 37.5, 30.8, 29.8, 27.5, 25.9, 21.6, 10.8.

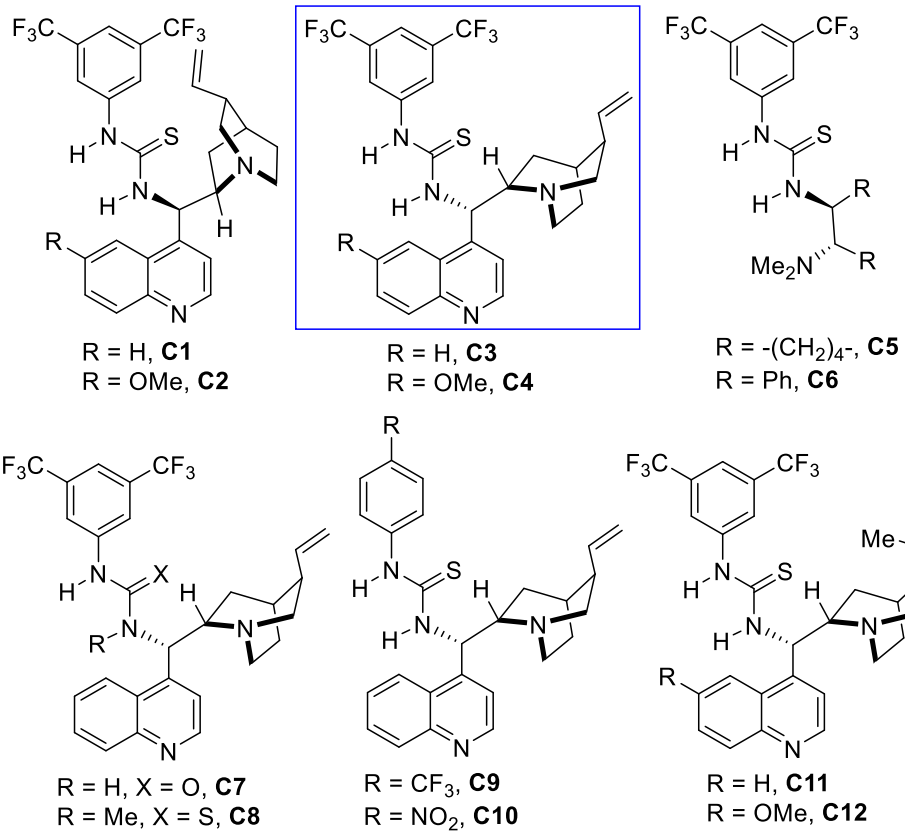
IR (film)υ_{max}: 3244, 1634, 752, 681 cm^{-1}.

Experimental Procedure for a One-Pot Sequential Michael addition of Dimeric 2-Oxindoles onto Phenylvinylselenone:



The diastereomeric mixture (*ca.* 1.5:1) of dimeric 2-oxindole (**13**) (115 mg, 0.25 mmol, 1.0 equiv.) was taken in solvent (6 mL; see optimization table) and thio-urea catalyst (**C1-C12**) (0.025 mmol) was added to the reaction mixture at room temperature and stirred for 5 minutes. To this reaction mixture was added phenylvinyl selenone (**S3**) (118 mg, 0.55 mmol, 2.2 equiv.) slowly over a period of 2 minutes. Then, the reaction mixture was allowed to stir till the complete consumption of the starting material (judged by running TLC) at specified temperature (see optimization table). The reaction mixture was concentrated under reduced pressure and the crude product was purified by flush chromatography using silica as a stationary phase and ethyl acetate and *n*-hexane as mobile phase. (For details about the reaction conditions please see the optimization table)

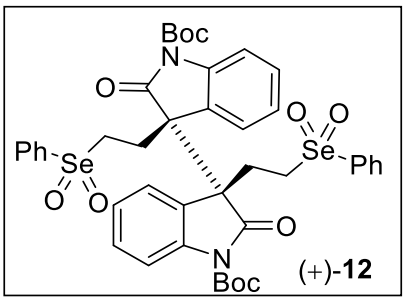
Catalyst screening for the Sequential Michael addition of dimeric 2-oxindoles:



Detailed optimization of sequential Michael addition of dimeric 2-oxindoles onto phenylvinyl selenone:

S. N.	Substrate /Cat.	solvent	Temp (°C)	dr	Time/product	Yield (%)	ee
1	**15a/C1**	CH_2Cl_2	25 °C	---	5d/**16a**	---	---
2	**15b/C1**	CH_2Cl_2	25 °C	---	5d/**16b**	---	---
3	**15c/C1**	CH_2Cl_2	25 °C	---	5d/**16c**	---	---
4	**13/C1**	CH_2Cl_2	25 °C	~20:1	72 h/**12**	79%	-84%
5	**13/C1**	PhMe	25 °C	~12:1	72 h/**12**	62%	-87%
6	**13/C1**	MeCN	25 °C	~20:1	72 h/**12**	88%	-89%
7	**13/C2**	MeCN	25 °C	~20:1	72 h/**12**	86%	-93%
8	**13/C2**	MeCN	0 °C	~20:1	96 h/**12**	64%	-90%
9	**13/C3**	MeCN	25 °C	~20:1	72 h/**12**	90%	96%
10	**13/C3**	MeCN	0 °C	~20:1	96 h/**12**	72%	93%
11	**13/C3**	$CHCl_3$	0 °C	~20:1	96 h/**12**	72%	91%
12	**13/C4**	MeCN	25 °C	~20:1	72 h/**12**	84%	87%
13	**13/C5**	MeCN	25 °C	~9:1	96 h/**12**	72%	70%

14	**13/C6**	MeCN	25 °C	~12:1	96 h/**12**	81%	67%
15	**13/C7**	MeCN	25 °C	~20:1	96 h/**12**	80%	78%
16	**13/C8**	MeCN	25 °C	~9:1	96 h/**12**	41%	ND
17	**13/C9**	MeCN	25 °C	~20:1	72 h/**12**	82%	76%
18	**13/C10**	MeCN	25 °C	~20:1	72 h/**12**	76%	72%
19	**13/C11**	MeCN	25 °C	~20:1	72 h/**12**	82%	91%
20	**13/C12**	MeCN	25 °C	~20:1	72 h/**12**	79%	83%



Di-*tert*-butyl (3*R*,3'*R*)-2,2'-dioxo-3,3'-*bis*(2-(phenylselenonyl)ethyl)-[3,3'-biindoline]-1,1'-dicarboxylate [(+)-**12**]: Compound (+)-**12** was obtained as white foam (0.25 mmol scale of reaction, 201 mg of product, 90% yield); R_f = 0.35 (20% EtOAc in Hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 5.5 Hz, 2H), 7.28 (d, *J* = 6.4 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.05 – 6.98 (m, 2H), 6.86 (d, *J* = 7.8 Hz, 1H), 3.40 – 3.34 (m, 1H), 3.33 – 3.28 (m, 1H), 2.17 – 2.12 (m, 1H), 2.09 – 2.05 (m, 1H), 1.41 (s, 9H).

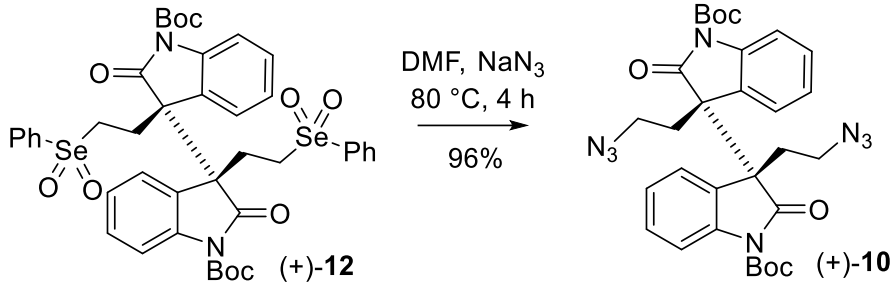
^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 157.9, 155.4, 129.6, 129.1, 128.5, 126.9, 125.4, 120.4, 109.4, 79.9, 49.5, 33.7, 28.4, 25.6, 24.9.

IR (film)υ_{max}: 3244, 2546, 2078, 1634, 1105, 752, 681 cm^{-1}.

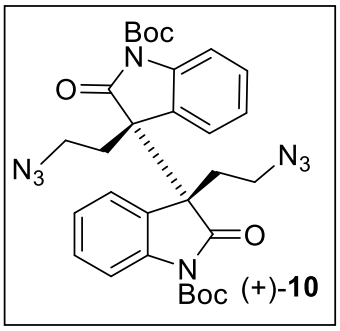
HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ Calcd for $[C_{42}H_{44}N_2O_{10} + H]^+$ 897.1420; Found 897.1431.

$[\alpha]_D^{24.0}$ = +113.89 (*c* = 2.0, $CHCl_3$) for (+)-**12** and $[\alpha]_D^{24.0}$ = –109.73 (*c* = 1.5, $CHCl_3$) for (–)-**12**.

Preparation of *bis*-azide [(+)-**10**] **from compound** (+)-**12:**



In an oven dried round-bottom flask, compound (+)-**12** (195 mg, 0.22 mmol, 1.0 equiv.) was taken in DMF (5 mL). To this solution was added NaN_3 (32 mg, 0.48 mmol, 2.2 equiv.) at room temperature. Then, the mixture was allowed to at a pre-heated oil-bath at 80 °C for about 4 h. After complete conversion of starting material (monitored by TLC) the reaction mixture was then extracted with EtOAc (10 mL X 2). Next, the organic layers were collected and dried with Na_2SO_4 and it was concentrated in a rotary evaporated under reduced pressure. The crude mixture was purified by column chromatography to afford the *bis*-azide (+)-**10** as a yellow gel.



Di-*tert*-butyl (3*R*,3'*R*)-3,3'-*bis*(2-azidoethyl)-2,2'-dioxo-[3,3'-biindoline]-1,1'-dicarboxylate [(+)-**10**]: Compound (+)-**10** was obtained as yellow gel (120 mg of product, 90% yield); R_f = 0.30 (20% EtOAc in Hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.15 (m, 1H), 7.10 – 7.03 (m, 1H), 6.94 (dd, *J* = 9.1, 6.1 Hz, 1H), 3.22 – 3.06 (m, 1H), 3.00 (ddt, *J* = 16.6, 14.0, 4.7 Hz, 2H), 2.84 – 2.55 (m, 1H), 2.55 – 2.33 (m, 1H), 1.61 (s, 9H).

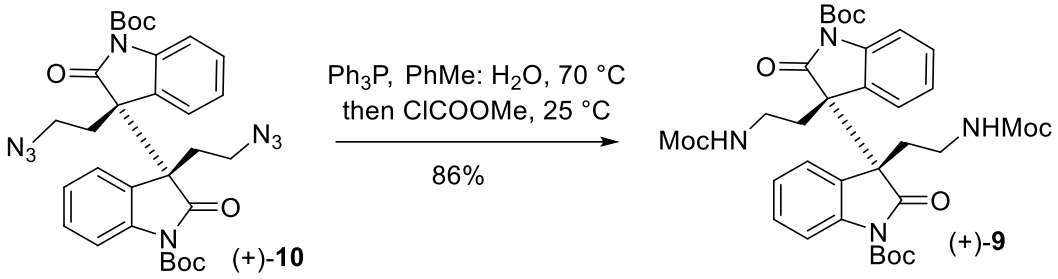
^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 157.9, 155.4, 129.6, 129.1, 128.5, 126.9, 125.4, 120.4, 109.4, 79.9, 49.5, 33.7, 28.4, 25.6, 24.9.

IR (film)υ_{max}: 3244, 2546, 2078, 1634, 1105, 752, 681 cm^{-1}.

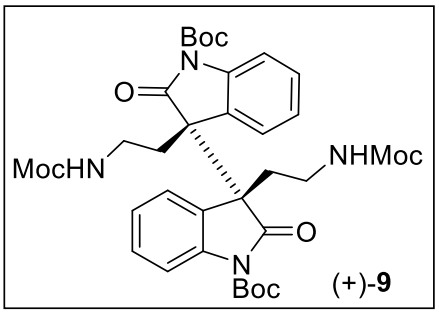
HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $[C_{18}H_{24}O_4 + Na]^+$ 327.1548; Found 327.1567.

$[\alpha]_D^{24.0}$ = +157.56 (*c* = 1.5, $CHCl_3$) for (+)-**10** and $[\alpha]_D^{24.0}$ = –125.41 (*c* = 2.0, $CHCl_3$) for (–)-**10**.

Preparation of *bis*-Moc protected compound [(+)-8)] from *bis*-azide [(+)-10)] via Staudinger Reaction:



In a round bottom flask compound (+)-**10** (100 mg, 0.166 mmol, 1.0 equiv.) was taken in a mixture of toluene and water (2:1; 9 mL) and triphenyl phosphene (131 mg, 0.498 mmol, 3.0 equiv.) was added to the reaction mixture. The reaction mixture was placed on a pre-heated oil-bath at 70 ºC for 3 h. The mixture was allowed to stir until gas stopped evolving. Upon complete consumption of starting material (monitored by TLC), the reaction mixture was cooled to room temperature and saturated sodium bicarbonate ($NaHCO_3$) solution (5 mL) was added to it. Next, chloromethyl formate (32.0 µL, 0.415 mmol, 2.5 equiv.) was added to the reaction mixture at 25 ºC dropwise and the reaction mixture was allowed to stir for an additional 1 h. After completion of starting material, the reaction mixture was extracted with EtOAc (8 mL X 2) and washed with brine (10 mL X 1). The crude product was purified through column chromatography with EtOAc and *n*-hexane as eluents.



Di-*tert*-butyl (3*R*,3'*R*)-3,3'-*bis*(2-((methoxycarbonyl)amino)ethyl)-2,2'-dioxo-[3,3'-biindoline]-1,1'-dicarboxylate [(+)-**9**]: Compound (+)-**9** was obtained as colourless foam (90 mg of product, 90% yield); R_f = 0.20 (30% EtOAc in Hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 2H), 7.13 (t, *J* = 7.5 Hz, 2H), 4.94 (s, 2H), 3.55 (s, 6H), 3.29 (d, *J* = 6.7 Hz, 2H), 2.20 (dt, *J* = 14.0, 6.8 Hz, 2H), 2.07 (dt, *J* = 14.0, 6.8 Hz, 2H), 1.28 (s, 18H).

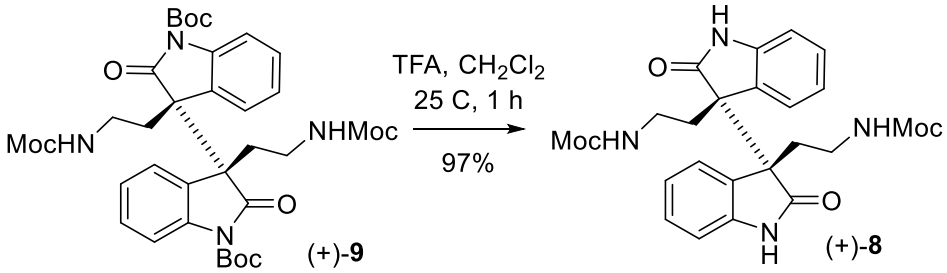
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 148.6, 132.5, 131.1, 130.6, 129.9, 129.4, 125.4, 119.7, 80.3, 67.7, 66.1, 53.9, 52.6, 41.1.

IR (film)υ_{max}: 3244, 2546, 2078, 1634, 1105, 752, 681 cm^{-1}.

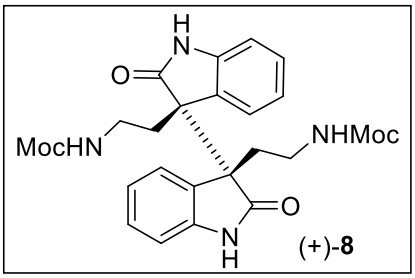
HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ Calcd for $[C_{30}H_{35}N_8O_6 + H]^+$ 603.2690; Found 603.2684.

$[\alpha]_D^{24.0}$ = +136.23 (*c* = 2.5, $CHCl_3$) for (+)-**9** and $[\alpha]_D^{24.0}$ = +132.75 (*c* = 2.0, $CHCl_3$) for (–)-**10**.

Boc-deprotection of dimeric 2-oxindole, (+)-8:



To a solution of compound (+)-**9** (90 mg, 0.149 mmol, 1.0 equiv.) in dichloromethane (5 mL), trifluoroacetic acid (70 μL, 0.88 mmol, 6.0 equiv.) was added dropwise at room temperature and allowed to stir at same temperature for 1 h. Then the reaction mixture was quenched with saturated $NaHCO_3$ solution (5 mL) and extracted with dichloromethane (10 mL X 2). The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography using EtOAc and *n*-hexane (2:3) to afford the desired product.



Dimethyl (((3*R*,3'*R*)-2,2'-dioxo-[3,3'-biindoline]-3,3'-diyl)*bis*(ethane-2,1-diyl))dicarbamate (+)-**8**: Compound (+)-**8** was obtained as yellow oil (67 mg of product, 97% yield); R_f = 0.33 (50% EtOAc in Hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 2H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 2H), 6.99 (t, *J* = 7.7 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 2H), 5.42 (s, 2H), 3.53 (s, 6H), 3.24 (t, *J* = 6.9 Hz, 4H), 2.06 (dd, *J* = 10.3, 4.8 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 180.6, 157.1, 139.7, 129.7, 124.2, 123.1, 110.7, 75.8, 52.1, 37.6, 36.0, 29.7.

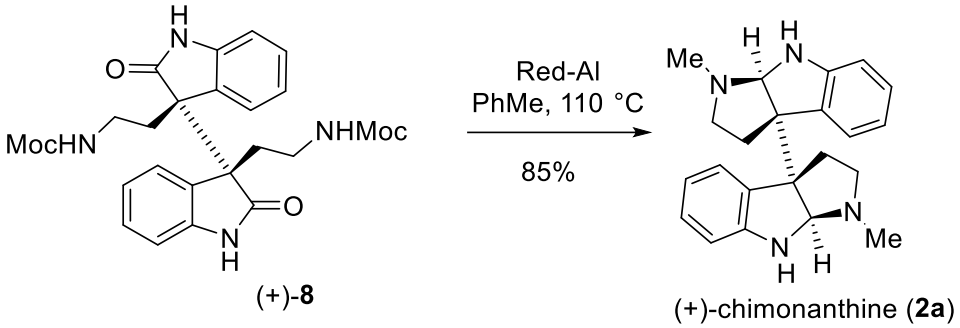
IR (film)υ_{max}: 3244, 2546, 2078, 1634, 1105, 752, 681 cm^{-1}.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $[C_{24}H_{26}N_4O_6 + H]^+$ 467.1925; Found 467.1920.

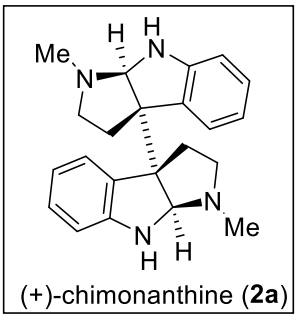
Enantiomeric excess of pure compound was determined *via* HPLC analysis using a Chiralpak IA column; solvent: hexane/2-propanol = 90/10; flow rate: 1.0 mL/min; detection: at 254 nm): t_R minor = 11.78 min, t_R major = 15.29 min. $[\alpha]_D^{24.0}$ = +289. 71 (*c* = 0.7, EtOH for 96% ee).

Enantiomeric excess of pure compound was determined *via* HPLC analysis using a Chiralpak IA column; solvent: hexane/2-propanol = 90/10; flow rate: 1.0 mL/min; detection: at 254 nm): t_R major = 10.89 min, t_R minor = 15.20 min. $[\alpha]_D^{24.0}$ = (–)-265. 28 (*c* = 0.7, EtOH for 93% ee).

Total Synthesis of Chimonanthine (2a):



In an oven-dried round-bottom flask was charged with compound (+)-**8** (65 mg, 0.139 mmol, 1.0 equiv.) in 4 mL of dry toluene (PhMe) under nitrogen atmosphere. To this solution, Red-Al (2.3 mL, 1.39 mmol, 10.0 equiv.) was added drop-wise at 0 ºC over a period of 2 minutes. After 15 minutes of stirring at room temperature, it was placed over an oil-bath maintaining temperature at 110 °C and stirring continued for 10 h. Then the reaction mixture was slowly cooled to room temperature and then placed it over an ice-bath, and quenched by the careful addition of MeOH (1 mL) and saturated aqueous solution of Rochelle's salt (5 mL). The resulting mixture was extracted with EtOAc (8 mL X 2) and the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in a rotary evaporator under the reduced pressure. The crude product was purified by flash chromatography using 2% ($MeOH/CH_2Cl_2$, saturated with ammonia) as eluent to afford of the desired product.



(3a*R*,3'a*R*,8a*R*,8'a*R*)-1,1'-Dimethyl-2,2',3,3',8,8a,8',8'a-octahydro-1*H*,1'*H*-3a,3'a-bipyrrolo[2,3-*b*]indole (**2a)**: (+)-Chimonanthine [(+)-**2a**] was obtained as white solid (mp: 177-180 ºC) (41 mg of **2a**, 85% yield); R_f = 0.30 (5 % MeOH in CH_2Cl_2 saturated with NH_3).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.3 Hz, 2H), 6.99 (dd, *J* = 7.5 Hz, 2H), 6.66 (dd, *J* = 7.5 Hz, 2H), 6.53 (d, *J* = 7.5 Hz, 2H), 4.29 (s, 2H), 4.21 (s, 2H), 2.58 - 2.46 (m, 6H), 2.33 (s, 6H), 2.05 (dd, J = 10.5, 5.1 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 150.5, 133.7, 128.2, 124.9, 118.7, 109.4, 85.6, 63.7, 52.7, 37.4, 35.9.

IR (film)υ_{max}: 3423, 2902, 1589, 1452, 1321 cm^{-1}.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $[C_{22}H_{26}N_4 + H]^+$ 347.2230; Found 347.2243.

$[\alpha]_D^{24.0}$ = +265.11 (*c* = 1.0, EtOH) for (+)-chimonanthine (**2a**) [lit.[1] $[\alpha]_D^{24.0}$ = +254.0 (*c* = 1.0, EtOH)].

Following a similar procedure as described for (+)-Chimonanthine [(+)-**2a**], the total synthesis of (–)-Chimonanthine [(–)-**2a**] was accomplished.

$[\alpha]_D^{24.0}$ = –309.11 (*c* = 1.0, EtOH) for (–)-Chimonanthine [(–)-**2a**] [lit.[3] $[\alpha]_D^{25.0}$ = –328.11 (*c* = 1.0, EtOH)].

Comparison of NMR Data of (+)-Chimonanthine [(+)-**2a**] of this report with literature of (+)-(**2a**) by Movassaghi[1] and Kanai.[2]

Comparison of ^{1}H-NMR Data:

Movassaghi's report (+)-chimonanthine (**2a**) (^{1}H-NMR, 500 MHz, $CDCl_3$)[1]			
δ (ppm)	Int.	mult.	*J* (Hz)
7.19	2H	d	*J* = 7.5 Hz
6.98	2H	t	*J* = 7.3 Hz
6.66	2H	t	*J* = 7.3 Hz
6.53	2H	d	*J* = 7.5 Hz
4.40	2H	br-s	-
4.23	2H	s	-
2.57-2.51	6H	m	-
2.33	6H	s	-
2.05	2H	app dd	*J* = 10.5, 5.0 Hz

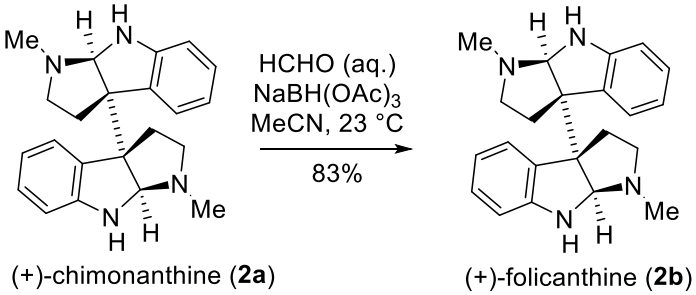
Matsunaga's report (+)-chimonanthine (**2a**) (^{1}H-NMR, 500 MHz, $CDCl_3$)[2]			
δ (ppm)	Int.	mult.	*J* (Hz)
7.18	2H	d	*J* = 7.5 Hz
6.98	2H	dd	*J* = 7.3 Hz
6.65	2H	dd	*J* = 7.5, 7.5 Hz
6.53	2H	d	*J* = 7.5 Hz
4.39	2H	s	-
4.23	2H	s	-
2.58-2.48	6H	m	-
2.32	6H	s	-
2.05	2H	m	-

This report: (+)-chimonanthine (**2a**) (^{1}H-NMR, 500 MHz, $CDCl_3$)			
δ (ppm)	Int.	mult.	*J* (Hz)
7.18	2H	d	*J* = 7.3 Hz
6.99	2H	dd	*J* = 7.5 Hz
6.66	2H	dd	*J* = 7.5 Hz
6.53	2H	d	*J* = 7.5 Hz
4.30	2H	s	-
4.21	2H	s	-
2.58-2.46	6H	m	-
2.33	6H	s	-
2.05	2H	dd	*J* = 10.5, 5.1 Hz

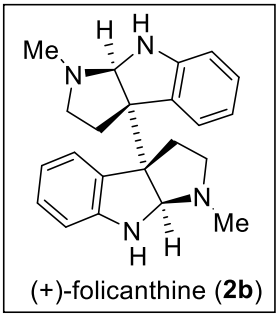
Comparison of ^{13}C-NMR Data:

Movassaghi's report of (+)-chimonanthine (**2a**) (^{13}C-NMR, 125 MHz, $CDCl_3$)[1]	Matsunaga's report of (+)-chimonanthine (**2a**) (^{13}C-NMR, 125 MHz, $CDCl_3$)[2]	This report: (+)-chimonanthine (**2a**) (^{13}C-NMR, 125 MHz, $CDCl_3$)
151.08	150.8	150.5
133.79	133.5	133.7
128.22	128.0	128.2
124.64	124.4	124.9
118.78	118.5	118.7
109.39	109.1	109.4
85.52	85.2	85.6
63.81	63.5	63.7
52.94	52.7	52.7
37.40	37.1	37.4
36.06	35.8	35.9

Total Synthesis of (+)-Folicanthine [(+)-2b]:



An over-dried round-bottom flask was charged with (+)-chimonanthine [(+)-**2a**] (45.0 mg, 0.13 mmol, 1.0 equiv.) in acetonitrile (5 ml). To this solution was added formalin (37% aqueous solution, 47 µL, 1.17 mmol, 5.0 equiv.) at room temperature and stirred for 5 minutes. Next, sodium triacetoxyborohydride (140 mg, 0.66 mmol, 5.2 equiv.) was added at the same temperature and stirring was continued until the complete consumption of the starting material (judged by running TLC). After 30 minutes of stirring, a solution of methanol (1:19) in dichloromethane (saturated with ammonia) was added slowly to the reaction mixture. After 5 minutes of stirring, the resulting slurry was concentrated under reduced pressure and the residue was purified by flash column chromatography (1% MeOH in CH_2Cl_2 saturated with ammonia) to afford (+)-folicanthine [(+)-**2b**] as a white solid.



(3a*R*,3'a*R*,8a*R*,8'a*R*)-1,1'-Dimethyl-2,2',3,3',8,8a,8',8'a-octahydro-1H,1'H-3a,3'a-bipyrrolo[2,3-*b*]indole (2b): (+)-Folicanthine [(+)-**2b**] was obtained as white solid (mp: 187-190 ºC) (37 mg of product, 83% yield); R_f = 0.42 (5 % MeOH in CH_2Cl_2 saturated with NH_3).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 – 6.89 (dd, *J* = 7.5 Hz, 4H), 6.53 (t, *J* = 7.6 Hz, 2H), 6.29 (d, *J* = 7.8 Hz, 2H), 4.71 (s, 2H), 3.02 (s, 6H), 2.83 (m, 2H), 2.50 – 2.42 (m, 10H), 2.05 – 1.99 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 128.2, 128.1, 126.9, 116.6, 105.8, 91.9, 62.6, 52.5, 37.0, 35.2.
IR (film)υ_{max}: 3128, 2908, 1689, 1508, 1177, 798 cm^{-1}.

HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ Calcd for $[C_{24}H_{30}N_4 + H]^+$ 375.2543; Found 375.2565.

$[\alpha]_D^{24.0}$ = +215.13 (*c* = 0.70, MeOH) for (+)-folicanthine (**2a**) [lit.[1] $[\alpha]_D^{24.0}$ = +207 (*c* = 0.75, MeOH)]

Following a similar procedure as described for (+)-Folicanthine [(+)-**2b**], the total synthesis of (–)-Folicanthine [(–)-**2b**] was accomplished.

$[\alpha]_D^{24.0}$ = –251.54 (*c* = 1.0, EtOH) for (–)-Folicanthine [(–)-**2b**].

Comparison of NMR Data of (+)-Folicanthine [(+)-**2b**] of this report with literature of (+)-(**2b**) prepared independently by Movassaghi[1] and Kanai.[2]

Comparison of ^{1}H-NMR Data:

Movassaghi's report of (+)-folicanthine (**2b**) (^{1}H-NMR, 500 MHz, $CDCl_3$)[1]			
6.98	2H	t	*J* = 7.5 Hz
6.94	2H	d	*J* = 6.5 Hz
6.51	2H	t	*J* = 7.0 Hz
6.27	2H	d	*J* = 7.5 Hz
4.37	2H	s	-
3.00	6H	s	-
2.64 – 2.62	2H	m	-
2.50 – 2.41	10H	m	-
1.99 – 1.95	2H	m	-

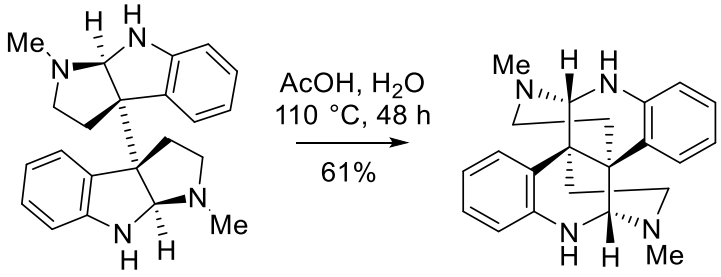
Matsunaga's report (+)-folicanthine (**2b**) (^{1}H-NMR, 500 MHz, $CDCl_3$)[2]			
δ (ppm)	Int.	mult.	*J* (Hz)
7.00 – 6.90	4H	m	-
6.50	2H	dd	*J* = 7.3, 7.3 Hz
6.26	2H	d	*J* = 8.0 Hz
4.36	2H	s	-
2.99	6H	s	-
2.64	2H	m	-
2.50 – 2.38	10H	m	-
2.50 – 2.38	2H	m	-
2.00 – 1.92	2H	m	-

This report (+)-folicanthine (**2b**) (^{1}H-NMR, 400 MHz, $CDCl_3$)[1]			
7.07 – 6.89	4H	dd	*J* = 7.5 Hz
6.53	2H	t	*J* = 7.6 Hz
6.29	2H	d	*J* = 7.8 Hz
6.27	2H	d	*J* = 7.5 Hz
4. 71	2H	s	-
3.02	6H	s	-
2.83	2H	m	-
2.50 – 2.42	10H	m	-
2.05 – 1.99	2H	m	-

Comparison of ^{13}C-NMR Data:

Movassaghi's report of (+)-Folicanthine [(+)-**2b**] (^{13}C-NMR, 125 MHz, $CDCl_3$)[1]	Matsunaga's report of (+)-Folicanthine [(+)-**2b**] (^{13}C-NMR, 125 MHz, $CDCl_3$)[2]	This report: (+)-Folicanthine [(+)-**2b**] (^{13}C-NMR, 125 MHz, $CDCl_3$)
153.21	152.9	152.9
133.16	132.8	128.2
128.29	128.0	128.1
123.95	123.7	126.9
116.85	116.6	116.6
106.05	105.8	105.8
92.34	92.0	91.9
63.00	62.7	62.6
52.94	52.7	52.5
38.25	37.9	37.0
35.58	35.2	35.2

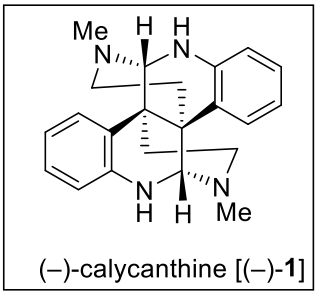
Total Synthesis of (–)-Calycanthine (1):



(+)-chimonanthine (**2a**) (–)-calycanthine (**1**)

A sealed tube was charged with (+)-chimonanthine (**2a**) (40.0 mg, 0.115 mmol, 1.0 equiv.) in a mixture (1:1) of acetic acid in water (2.5 mL) under an atmosphere of nitrogen and heated to 110 ºC. Upon completion of the reaction (48 h), as monitored by running TLC, the reaction mixture was cooled to room temperature and partitioned between dichloromethane (10 mL)

and saturated aqueous sodium bicarbonate (10 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (10 mL X 2). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and were concentrated under the reduced pressure to afford a brown residue. The residue was purified by flash column chromatography (1% methanol in dichloromethane saturated with ammonia) to afford (–)-Calycanthine [(–)-**1**].



(4b*R*,5*S*,10b*R*,11*S*)-13,18-dimethyl-5,6,11,12-tetrahydro-5,10b:11,4b-bis(epiminoethano) dibenzo[c,h][2,6]naphthyridine (**3**): (–)-Calycanthine [(–)-**1**] was obtained as white solid (mp: 228-229 ºC) (24 mg of product, 61% yield); R_f = 0.49 (5% MeOH in CH_2Cl_2 saturated with NH_3).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 7.5 Hz, 2H), 6.51 (d, *J* = 7.7 Hz, 2H), 6.29 (d, *J* = 7.8 Hz, 2H), 4.57 (d, *J* = 12.1 Hz, 2H), 4.32 (s, 2H), 3.15 (td, *J* = 13.5, 5.7 Hz, 2H), 2.63 (dd, *J* = 11.7, 5.1 Hz, 1H), 2.43 (s, 6H), 2.24 (dd, *J* = 7.8, 4.9 Hz, 2H), 1.28 (d, *J* = 7.4 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 145.5, 126.6, 125.1, 124.5, 116.4, 112.1, 71.1, 46.2, 42.7, 36.1, 31.8.

^{1}H NMR (400 MHz, DMSO-d_6) δ 6.94 (d, *J* = 7.5 Hz, 2H), 6.81 (t, *J* = 7.5 Hz, 2H), 6.57 (d, *J* = 20.0 Hz, 2H), 6.43 (t, *J* = 7.4 Hz, 2H), 4.16 (d, *J* = 4.1 Hz, 2H), 3.27 (s, 2H), 2.11 (s, 6H), 2.02 – 1.87 (m, 4H), 0.98 – 0.88 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 145.9, 127.0, 126.2, 124.3, 115.9, 111.5, 69.8, 46.1, 42.5, 36.3, 34.3.

IR (film)υ_{max}: 3425, 2913, 1656, 1623, 1495, 1109, 785 cm^{-1}.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $[C_{22}H_{26}N_4 + H]^+$ 347.2230; Found 347.2244.

$[\alpha]_D^{24.0} = -617.82$ (*c* = 0.20, EtOH) for (–)-Calycanthine [(–)-**1**] [lit.[1] $[\alpha]_D^{24.0} = -612$ (*c* = 0.18, EtOH)]

Following a similar procedure as described for (–)-Calycanthine [(–)-**1**], the total synthesis of (+)-Calycanthine [(+)-**1**] was accomplished.

$[\alpha]_D^{24.0} = +646.25$ (*c* = 1.0, $CHCl_3$) for (+)-Calycanthine [(+)-**1**] [lit.[3] $[\alpha]_D^{24.0} = +675$ (*c* = 1.0, $CHCl_3$)].

Comparison of NMR Data of (–)-Calycanthine [(–)-**1**] of this report with literature by Movassaghi *et. al.*[1] and Kanai *et. al.*[2]

Comparison of ^{1}H-NMR Data:

Movassaghi's report of (–)-Calycanthine [(–)-**1**] (^{1}H-NMR, 500 MHz, $CDCl_3$)[1]			
7.01	2H	d	*J* = 7.5 Hz
6.82	2H	app t	*J* = 7.5 Hz
6.55	2H	t	*J* = 7.5 Hz
6.27	2H	d	*J* = 8.0 Hz
4.58	2H	br s	-
4.32	2H	s	-
3.13	2H	td	*J* = 13.3, 5.3 Hz
2.62	2H	dd	*J* = 11.3, 5.3 Hz
2.42	6H	s	-
2.27	2H	dt	*J* = 12.5, 3.6 Hz
1.29	2H	dd	*J* = 13.3, 3.8 Hz

Matsunaga's report of (–)-Calycanthine [(–)-**1**] (^{1}H-NMR, 500 MHz, $CDCl_3$)[1]			
7.00	2H	d	*J* = 7.5 Hz
6.80	2H	dd	*J* = 7.7, 7.7 Hz
6.53	2H	dd	*J* = 7.7, 7.7 Hz
6.26	2H	d	*J* = 7.7 Hz
4.55	2H	br d	*J* = 4.0 Hz
4.30	2H	d	*J* = 4.0 Hz
3.12	2H	ddd	*J* = 13.2, 4.0, 4.0 Hz
2.60	2H	ddd	*J* = 11.6, 4.0, 4.0 Hz
2.40	6H	s	-
2.26	2H	ddd	*J* = 11.6, 4.0, 4.0 Hz
1.29	2H	m	-

This report: (–)-Calycanthine [(–)-**1**] (^{1}H-NMR, 500 MHz, $CDCl_3$)			
7.05	2H	d	*J* = 8.4 Hz
6.82	2H	dd	*J* = 7.5 Hz
6.51	2H	d	*J* = 7.7 Hz
6.29	2H	d	*J* = 7.8 Hz
4.57	2H	d	*J* = 12.1 Hz
4.32	2H	s	-
3.15	2H	td	*J* = 13.5, 5.7 Hz
2.63	2H	dd	*J* = 11.7, 5.1, 4.0 Hz
2.43	6H	s	-
2.24	2H	dd	*J* = 7.8, 4.9 Hz
1.28	2H	d	*J* = 7.4 Hz

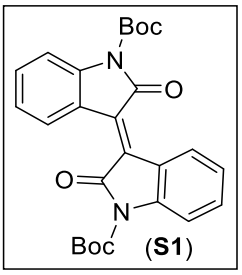
Comparison of ^{13}C-NMR Data:

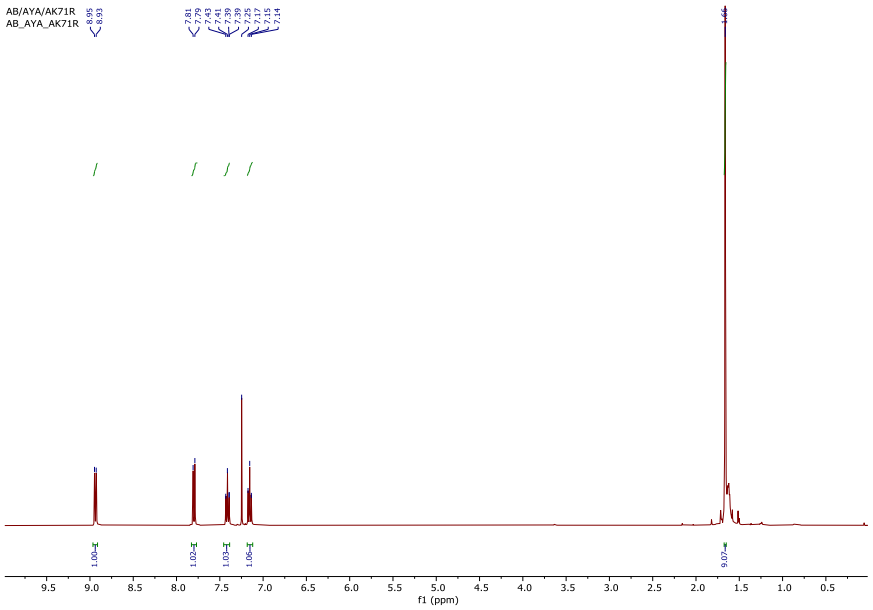
Movassaghi's report of (–)-Calycanthine [(–)-**1**] (^{13}C-NMR, 125 MHz, $CDCl_3$)[1]	Matsunaga's report of (–)-Calycanthine [(–)-**1**] (^{13}C-NMR, 125 MHz, $CDCl_3$)[2]	This report: (–)-Calycanthine [(–)-**1**] (^{13}C-NMR, 125 MHz, $CDCl_3$)
145.56	145.7	145.5
126.72	126.8	126.6
125.21	125.4	125.1
124.61	124.6	124.5
116.51	116.6	116.4
112.18	112.3	112.1
71.20	71.3	71.1
46.72	46.8	46.2
42.78	42.8	42.7
36.13	36.2	36.1
31.90	32.0	31.8

References:

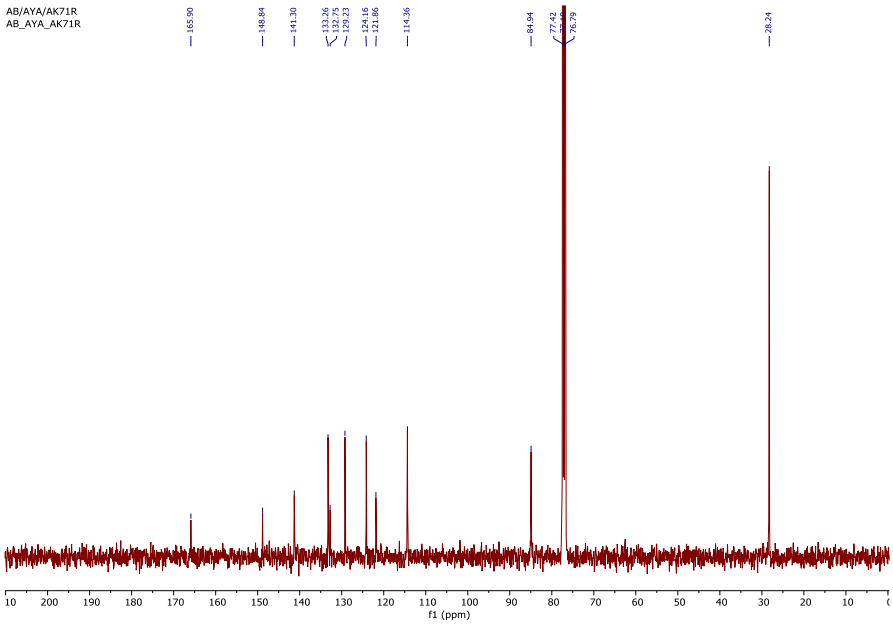
1) M. Movassaghi, and M. A. Schmidt, *Angew. Chem. Int. Ed*. 2007, **46**, 3725–3728.
2) H. Mitsunuma, M. Shibasaki, M. Kanai, and S. Matsunaga *Angew. Chem. Int. Ed*. 2012, **51**, 5217–5221.
3) R. K. Duke, R. D. Allan, G. A. R. Johnston, K. N. Mewett and D. Mitrovic, *J. Nat. Prod*. 1995, **58**, 1200–1208.

Spectral Data

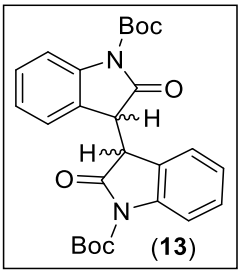


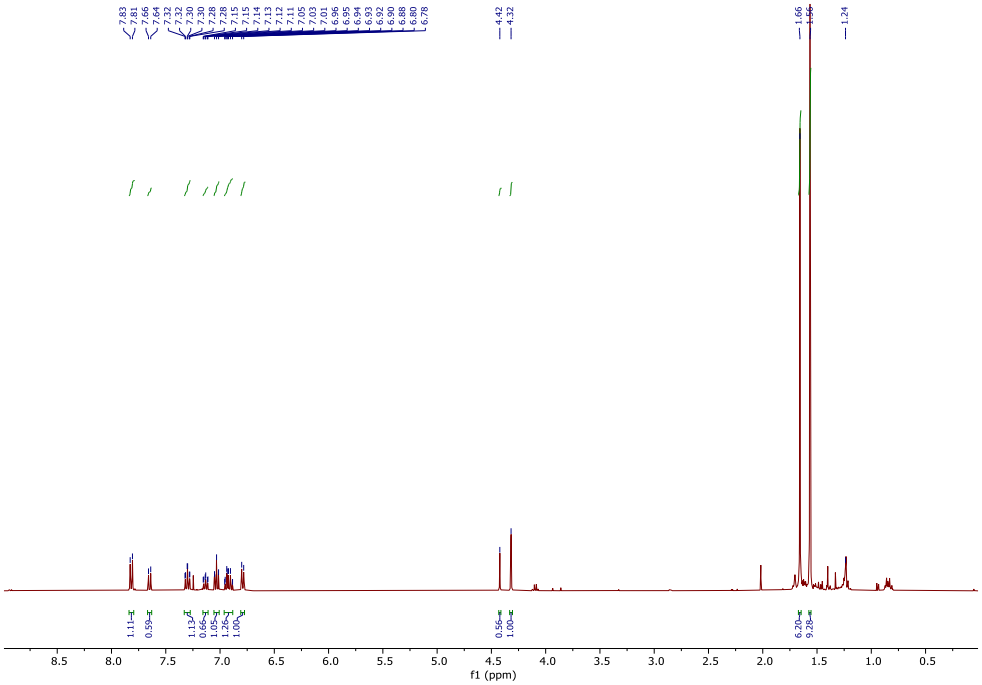


^{1}H NMR (400 MHz, $CDCl_3$) of **S1**

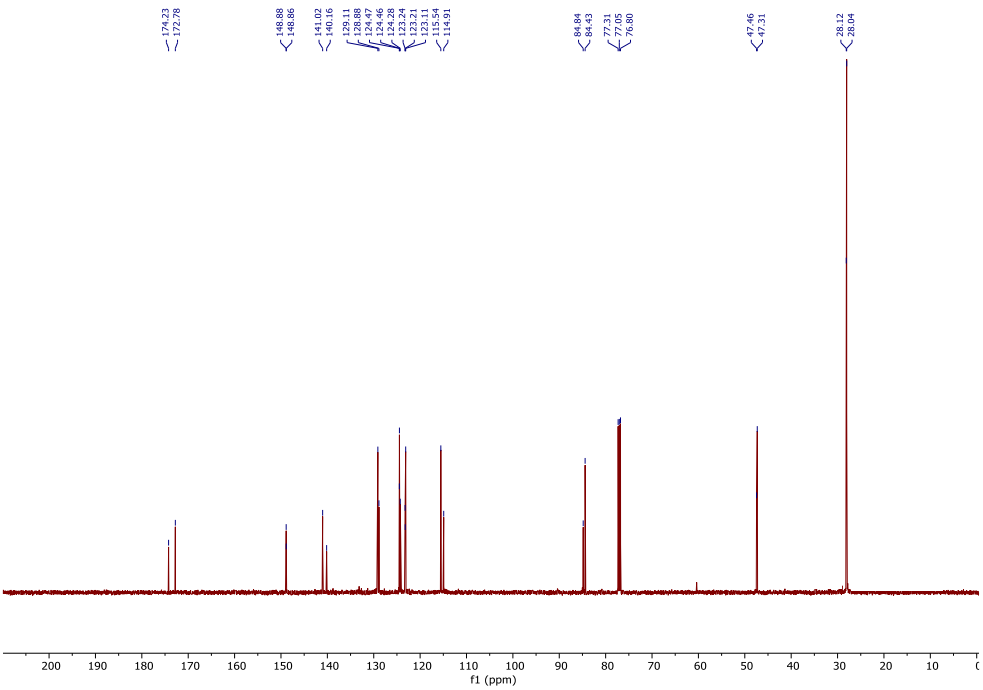


^{13}C NMR (100 MHz, $CDCl_3$) of **S1**





^{1}H NMR (400 MHz, $CDCl_3$) of **13**



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

Display Report

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Sample Name	AB_AK_242	Instrument	maXis impact 8282001.00127
Comment			

Acquisition Parameter

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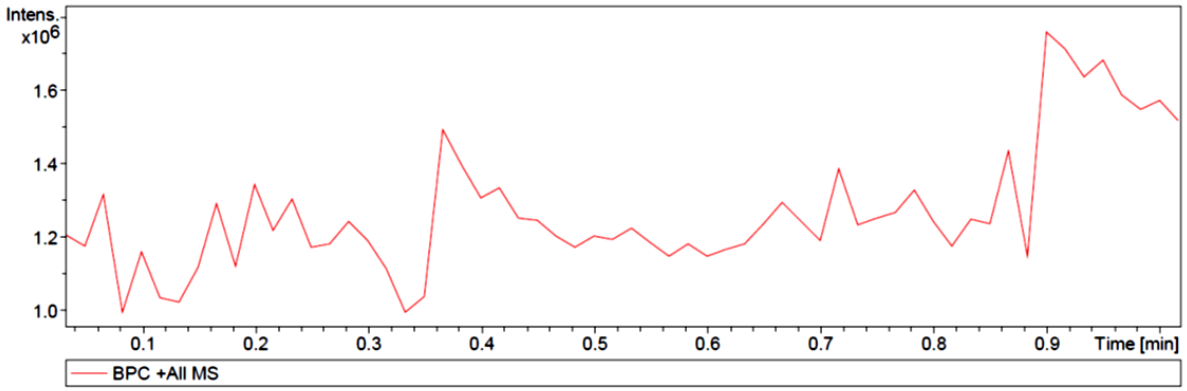

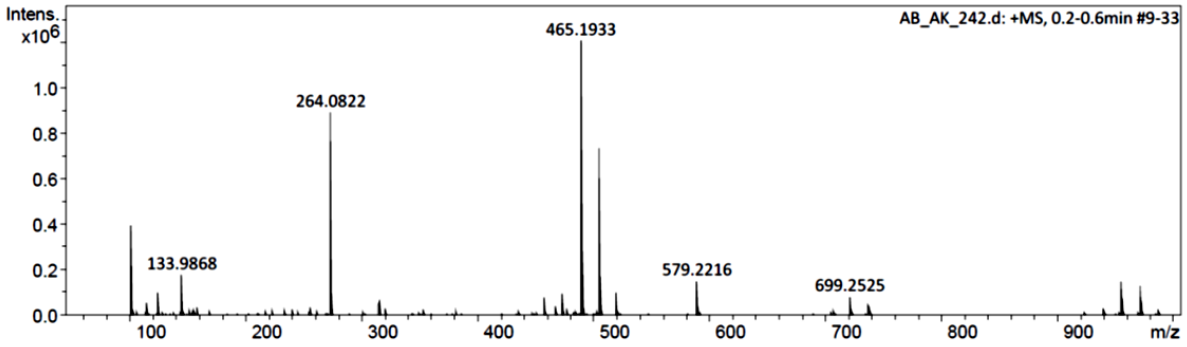

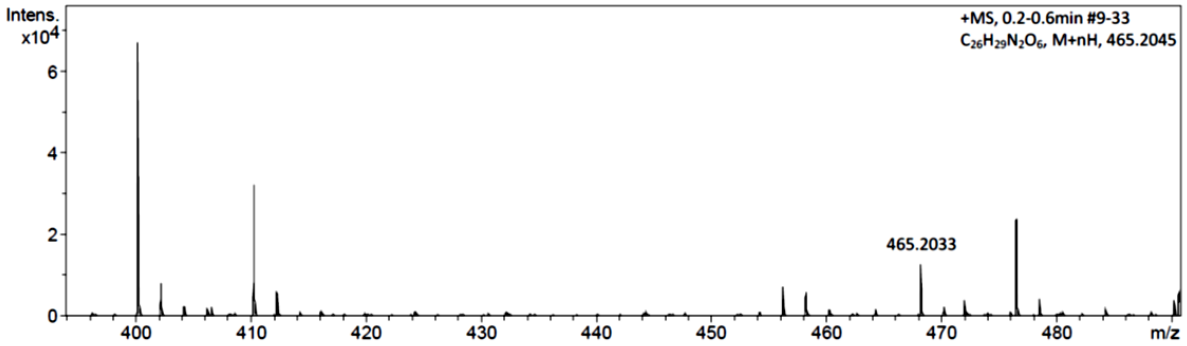

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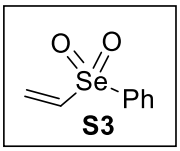
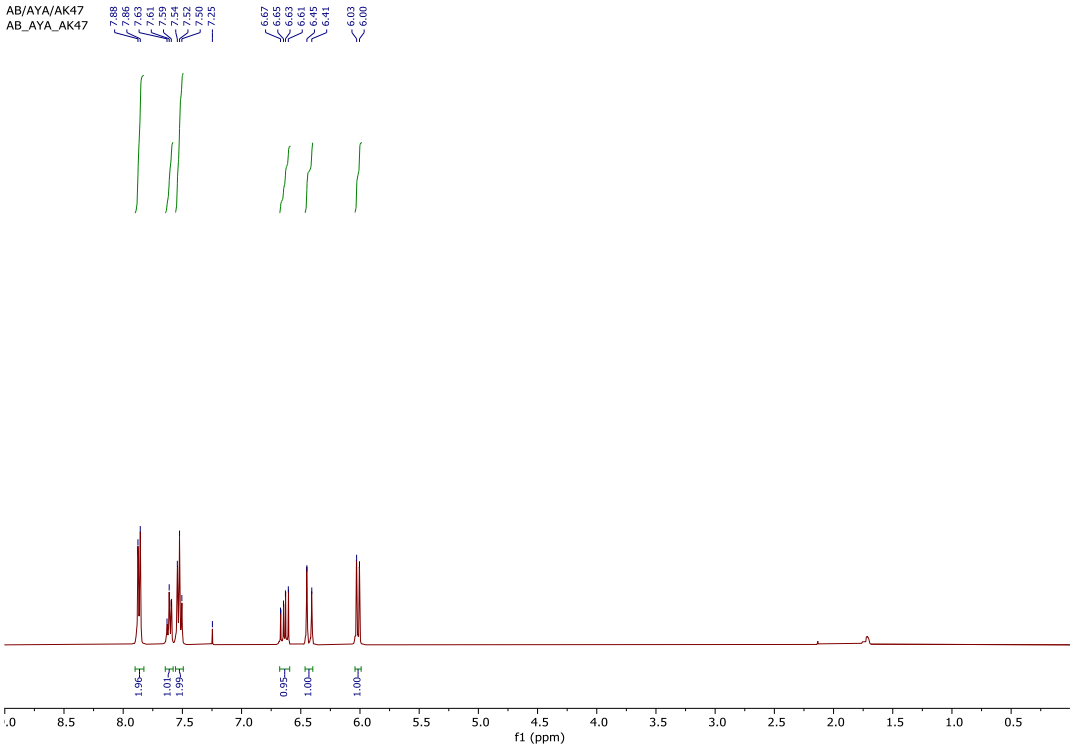
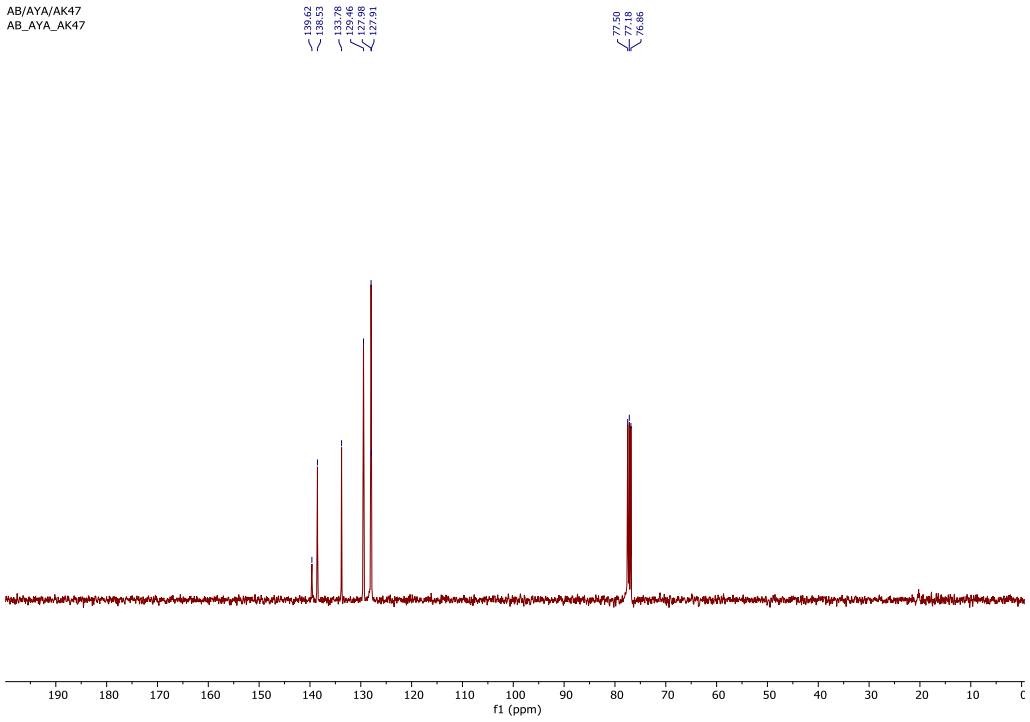
HRMS of **10d**



S3



^{1}H NMR (400 MHz, $CDCl_3$) of **S3**



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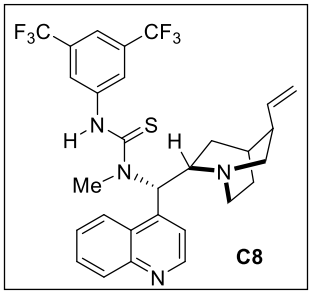
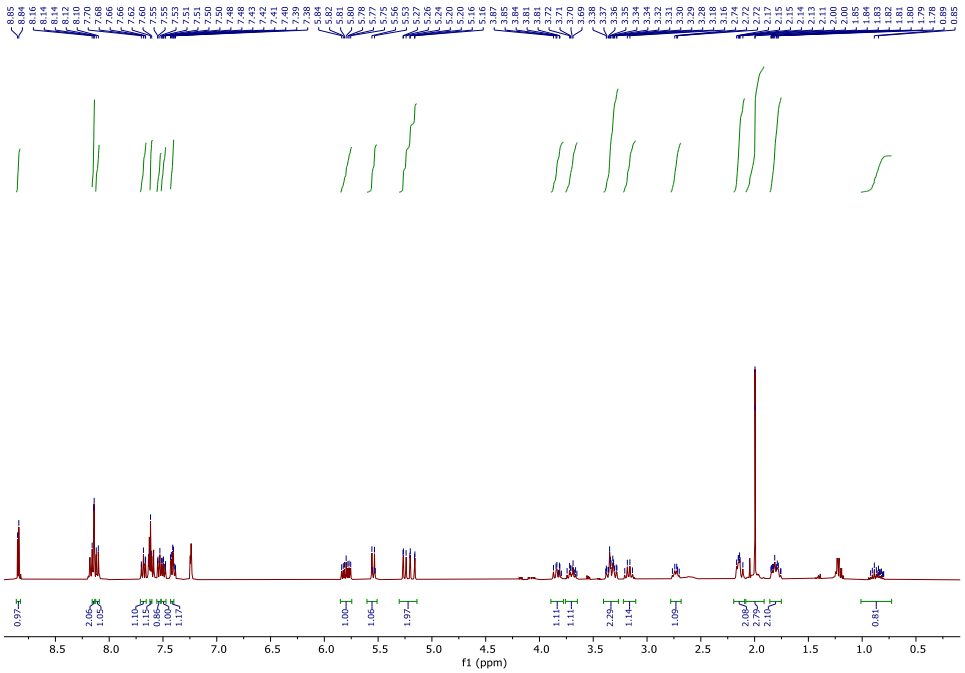
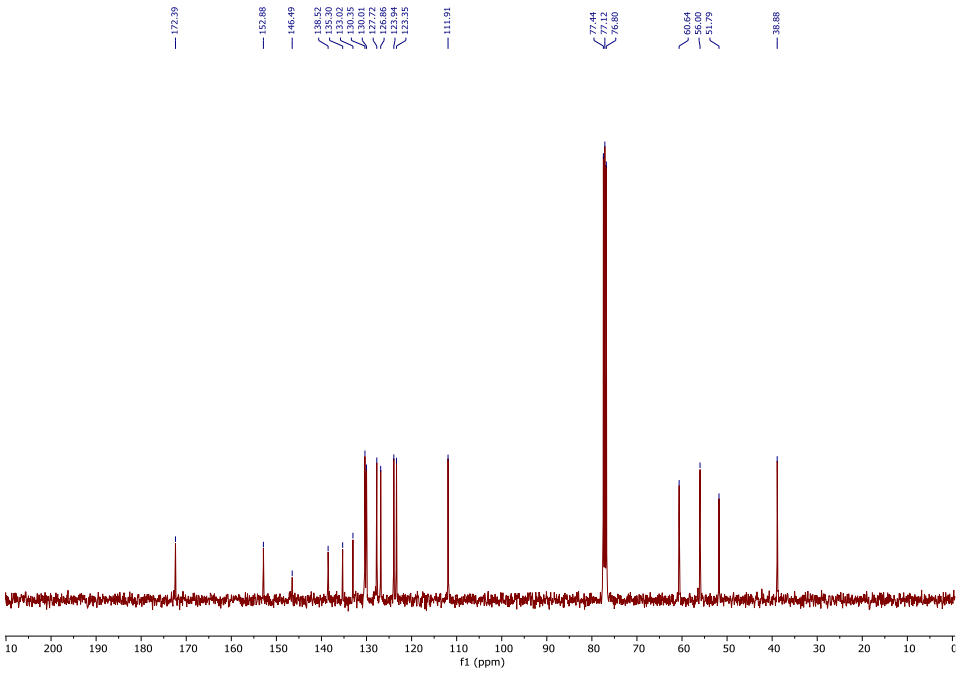
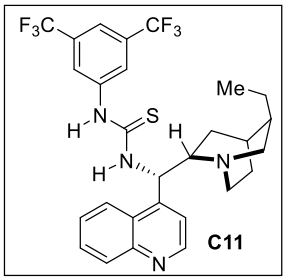


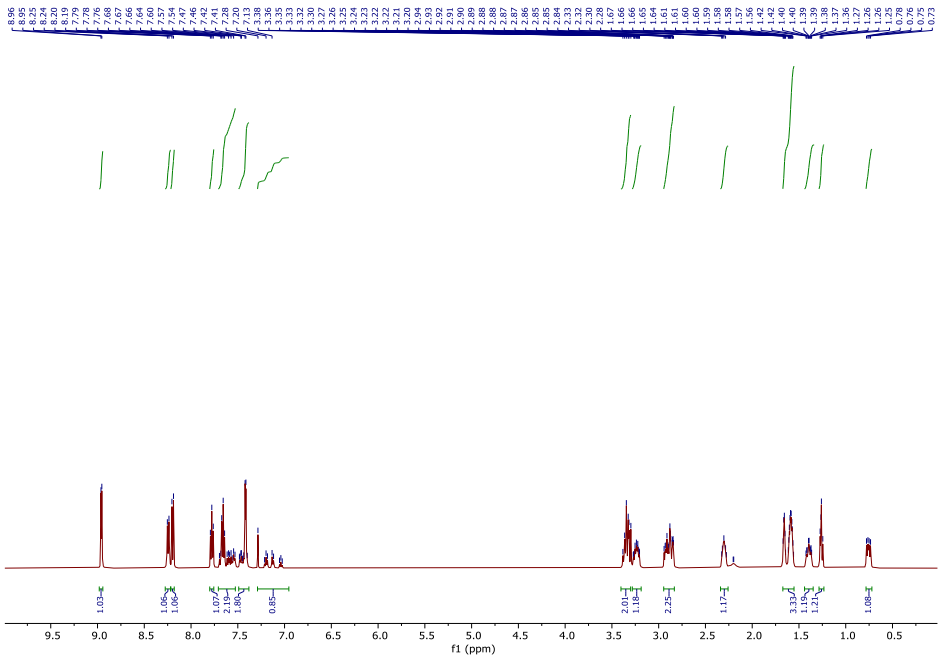


^{1}H NMR (400 MHz, $CDCl_3$) of **C8**

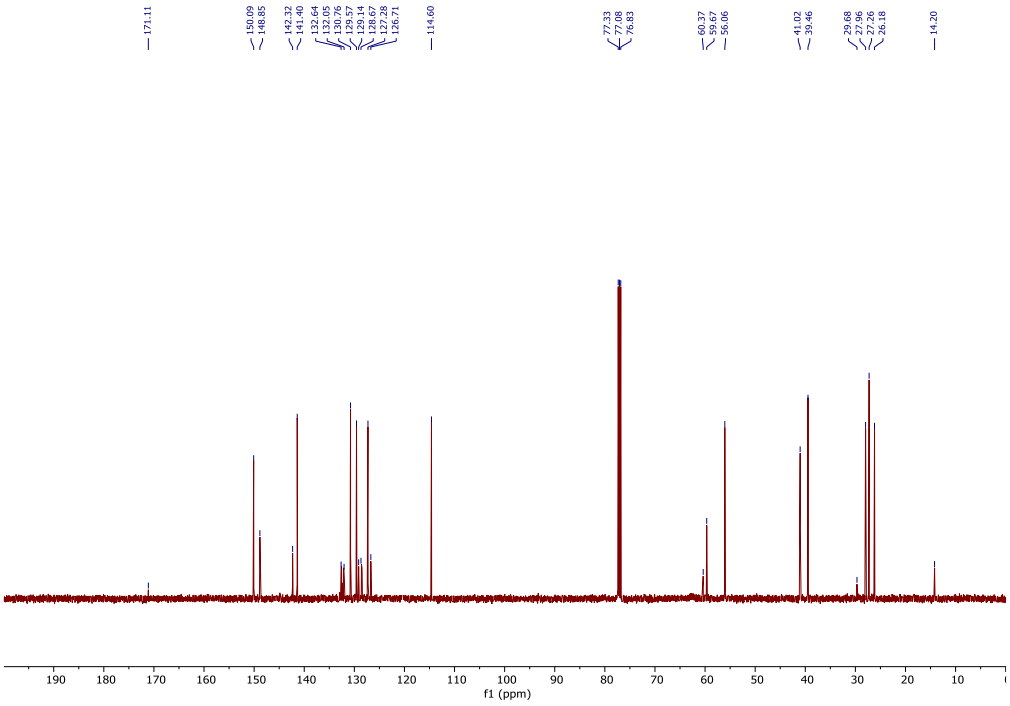


^{13}C NMR (100 MHz, $CDCl_3$) of **C8**

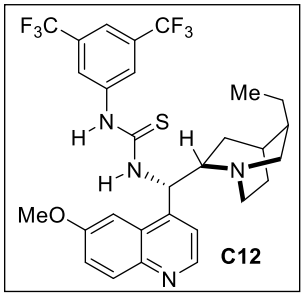


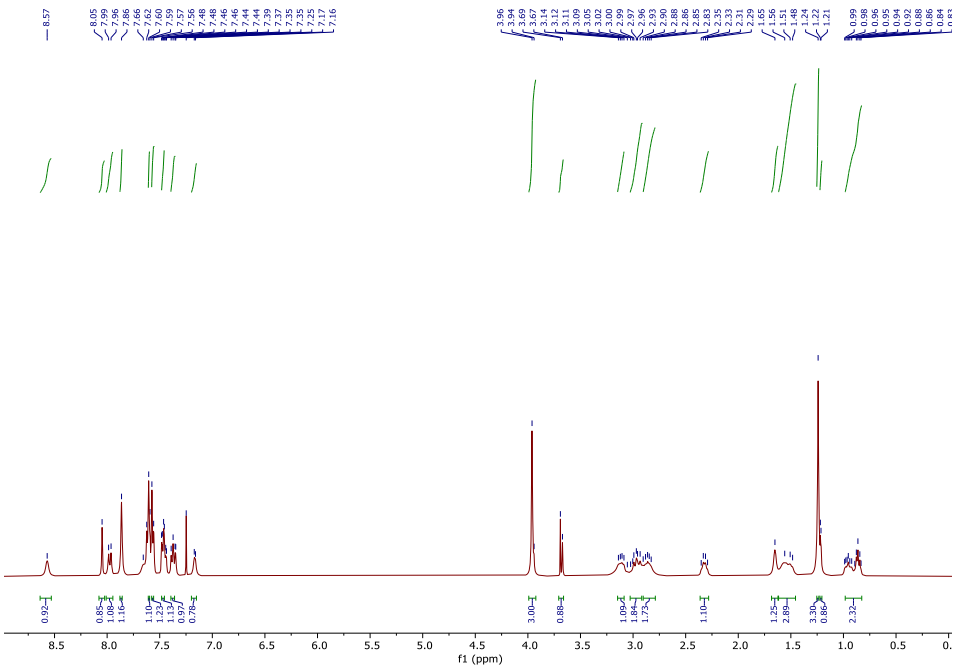


^{1}H NMR (400 MHz, $CDCl_3$) of **C11**

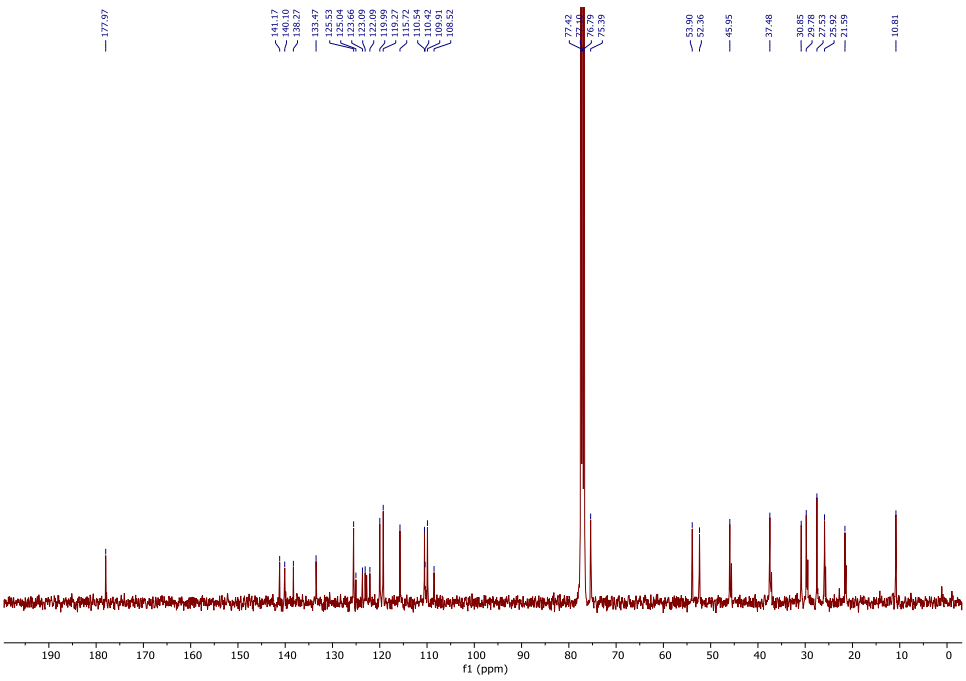


^{13}C NMR (100 MHz, $CDCl_3$) of **C11**

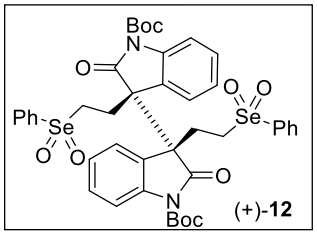


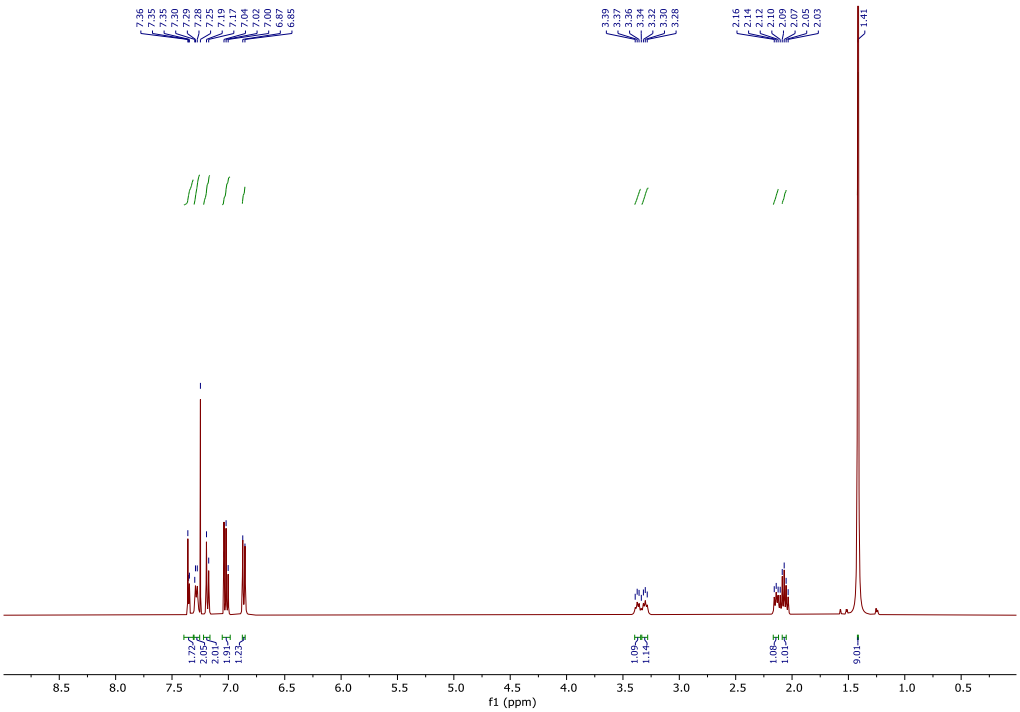


^{1}H NMR (400 MHz, $CDCl_3$) of **C12**

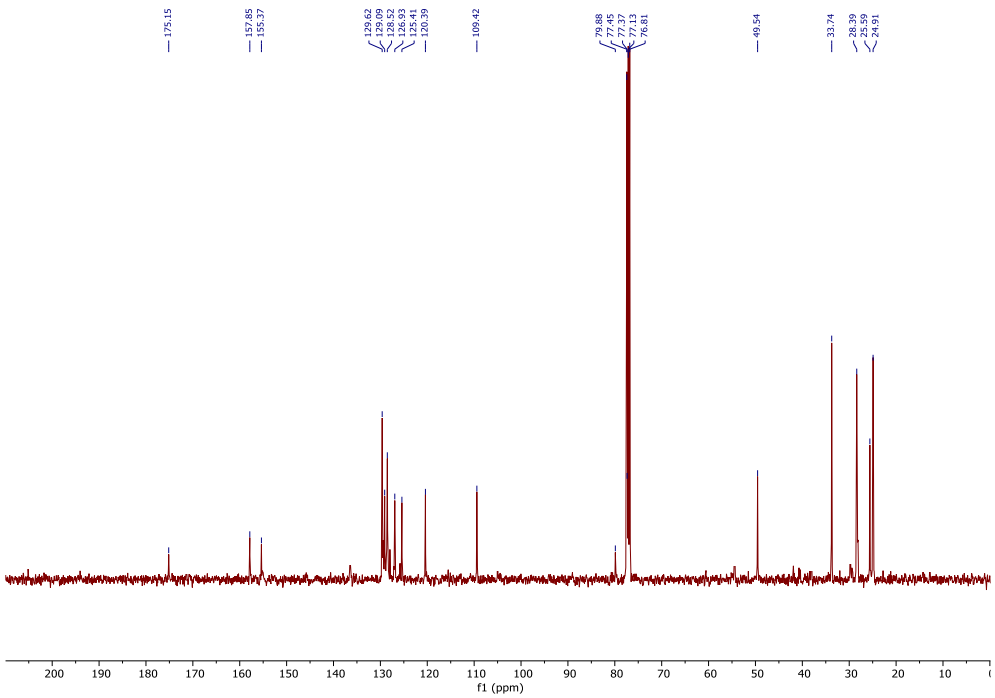


^{13}C NMR (100 MHz, $CDCl_3$) of **C12**





^{1}H NMR (400 MHz, $CDCl_3$) of (+)-**12**



^{13}C NMR (100 MHz, $CDCl_3$) of (+)-**12**

Display Report

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Comment			

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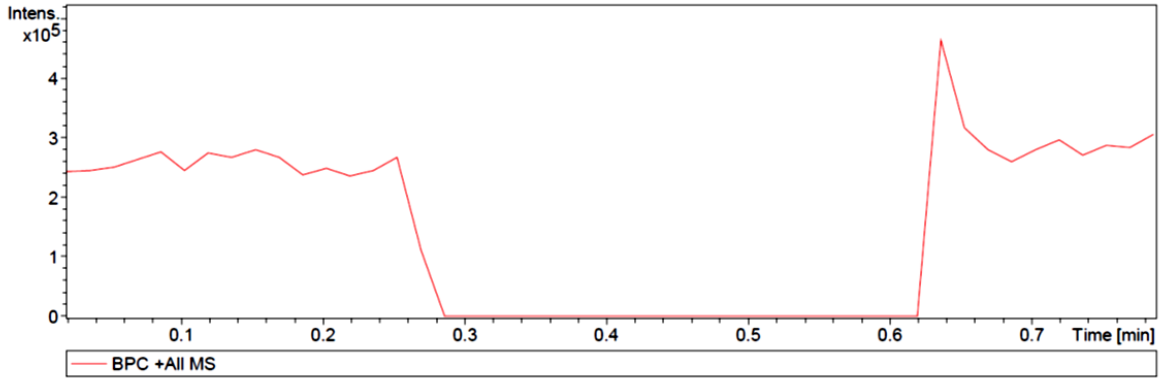

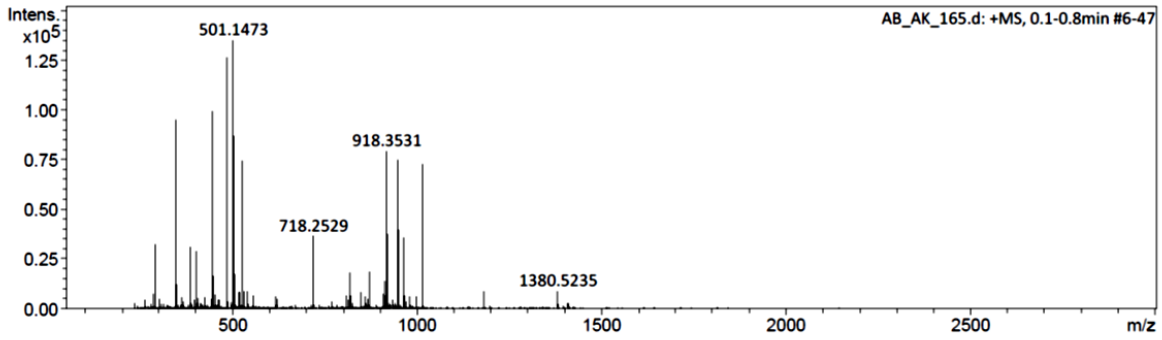

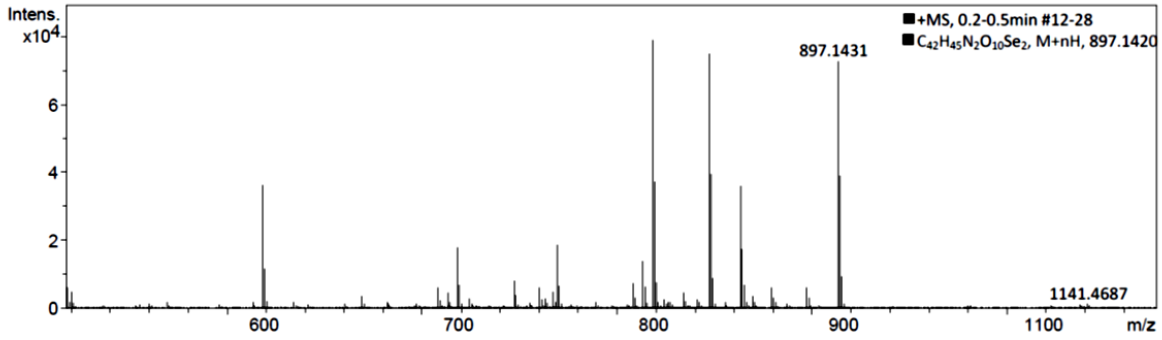

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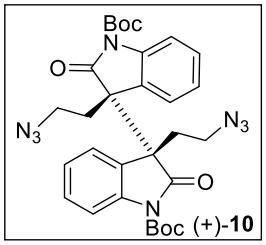
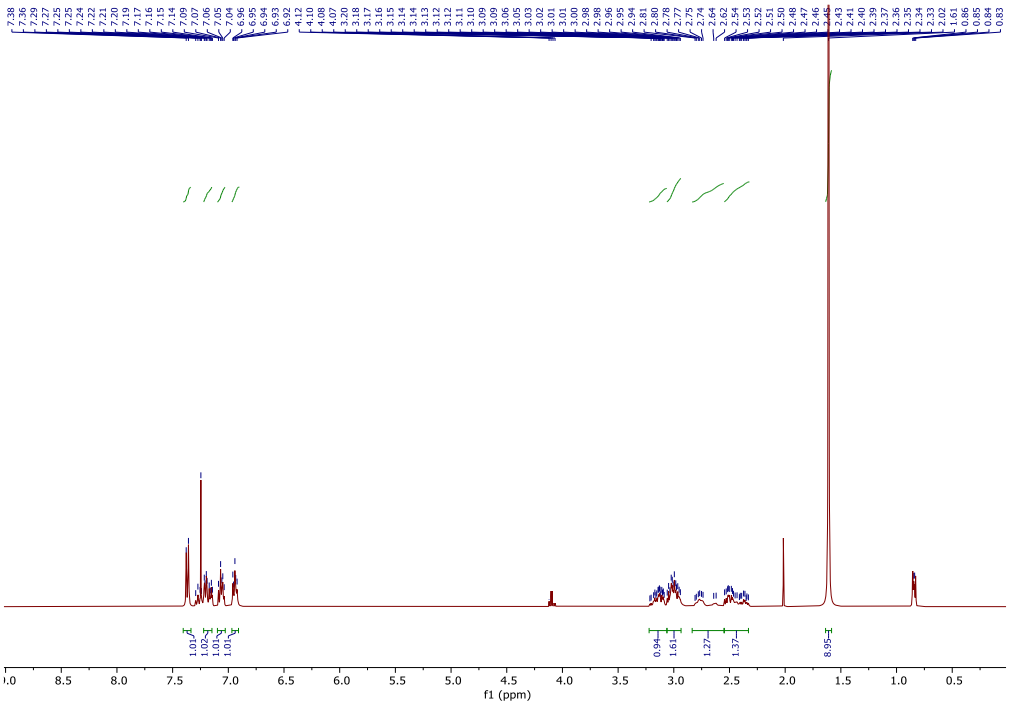
Bruker Compass DataAnalysis 4.1 printed: 3/9/2021 12:46:03 PM by: IISER Kolkata Page 1 of 1

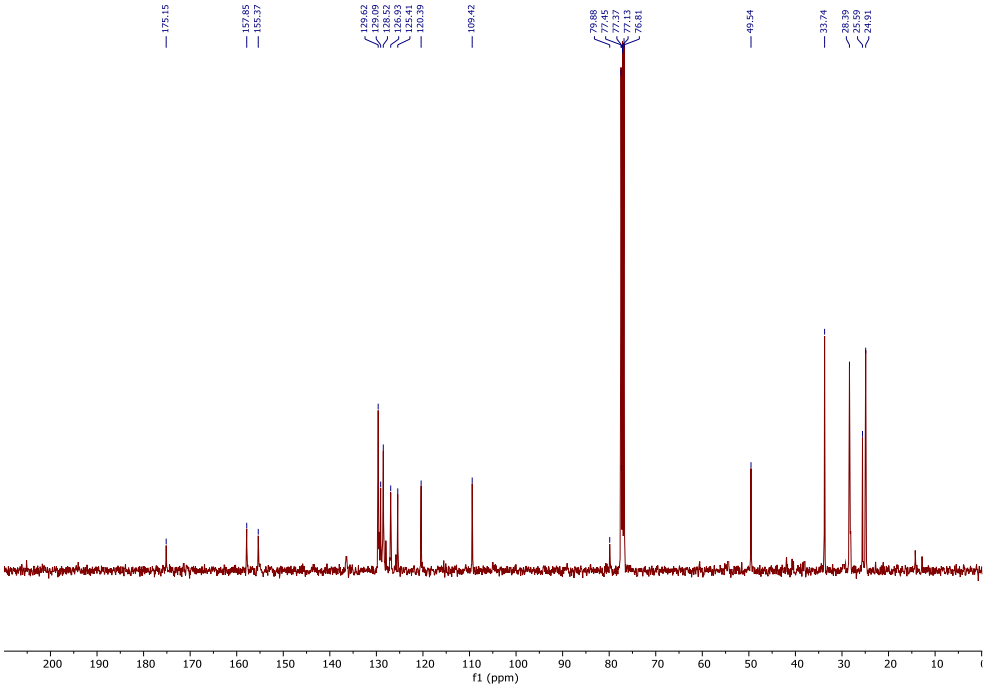
HRMS of (+)-**12**



(+)-**10**



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



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

Display Report

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Comment			

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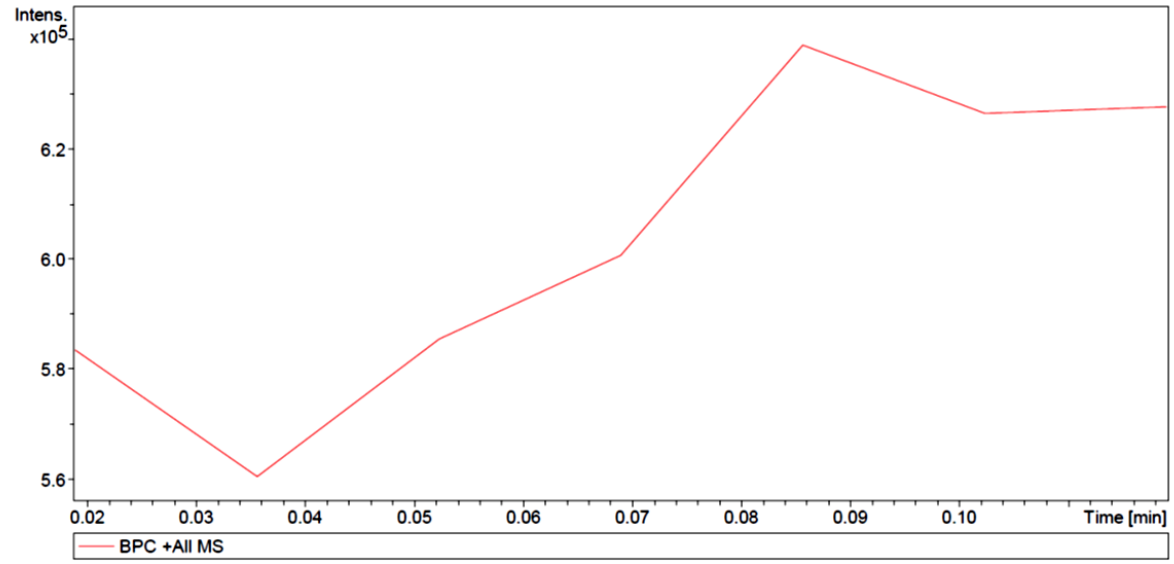

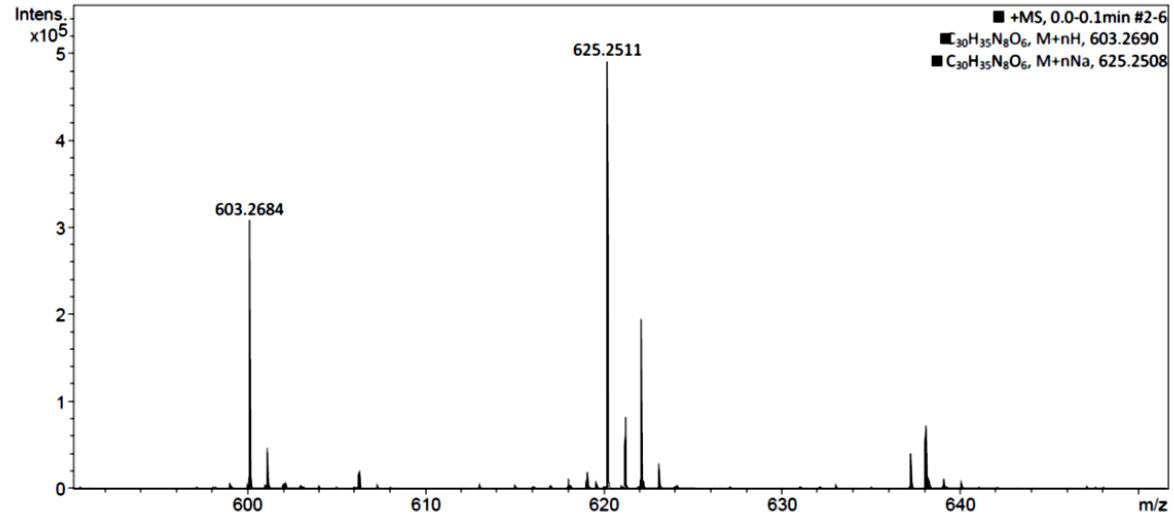

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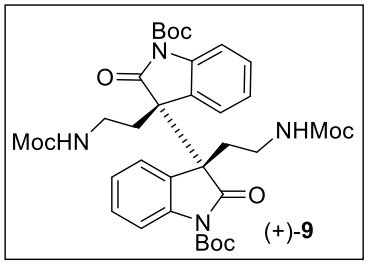
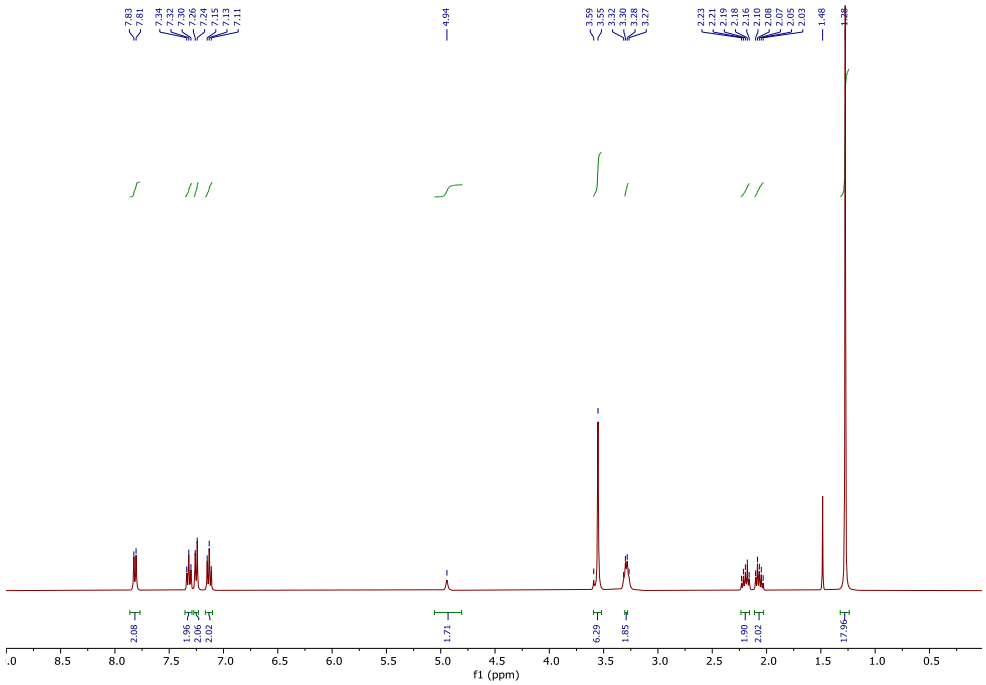
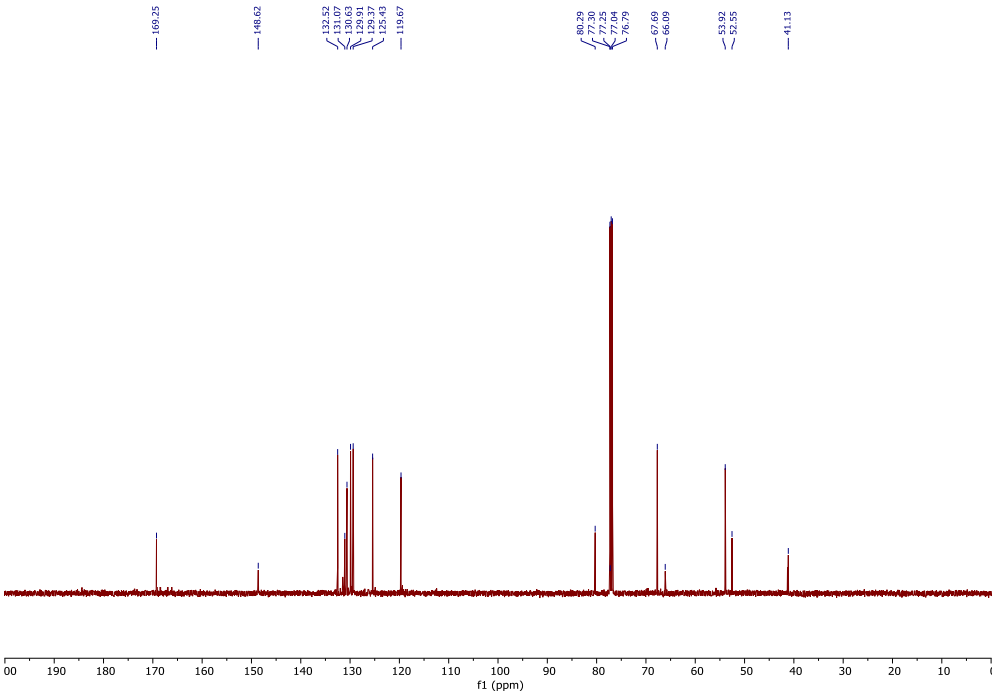
Bruker Compass DataAnalysis 4.1 printed: 8/27/2021 12:37:28 PM by: IISER Kolkata Page 1 of 1

HRMS of (+)-**10**





^{1}H NMR (400 MHz, $CDCl_3$) of (+)-**9**



^{13}C NMR (100 MHz, $CDCl_3$) of (+)-**9**

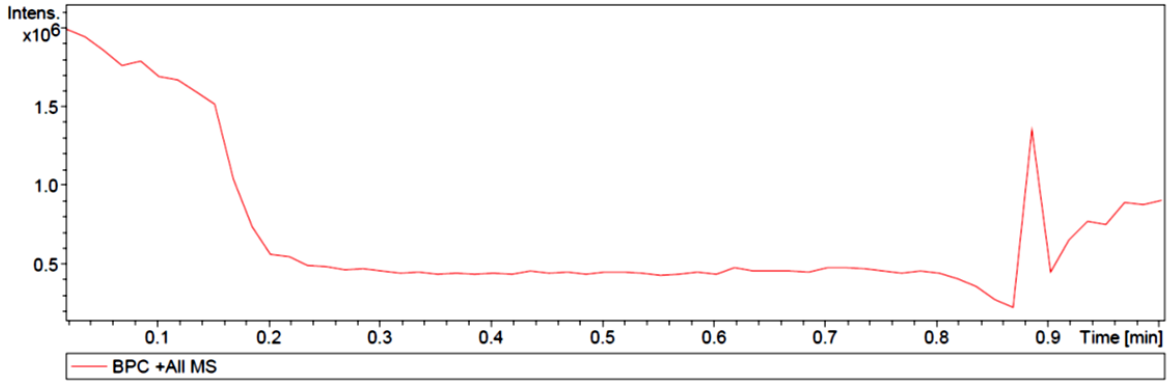
Display Report

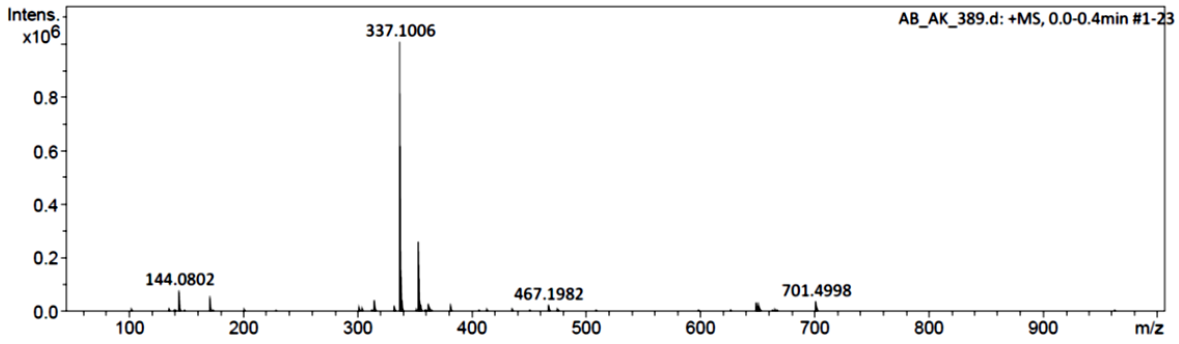
Analysis Info

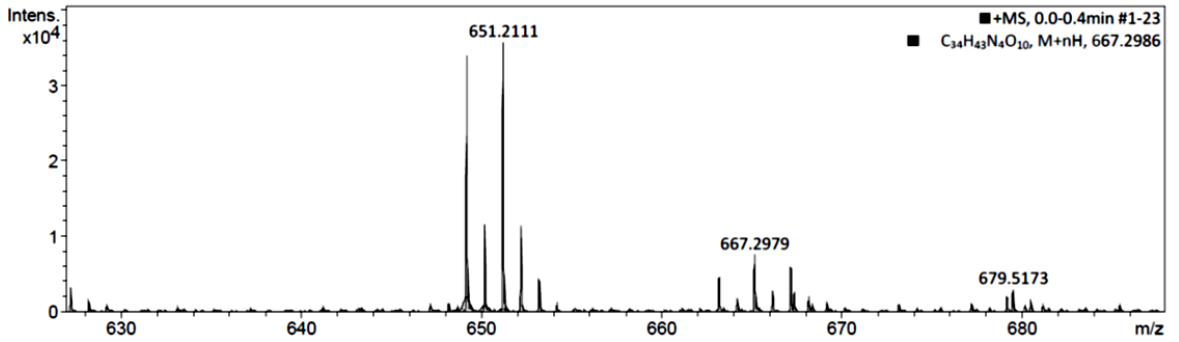
Analysis Name	D:\Data\User data\2021\NOV\AB_AK_389.d	Acquisition Date	11/1/2021 11:18:39 AM
Method	Tune_pos_Standard.m	Operator	IISER Kolkata
Sample Name	AB_AK_389	Instrument	maXis impact 8282001.00127
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.5 Bar
Focus	Active	Set Capillary	3400 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



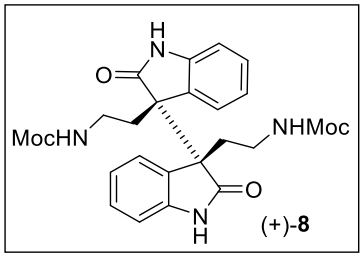


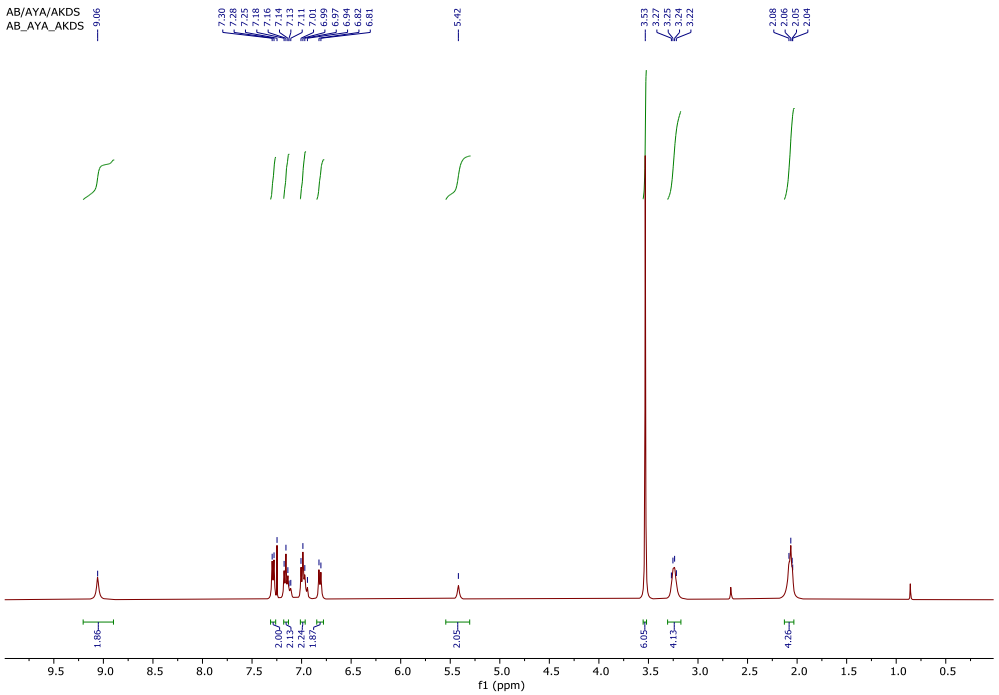


AB_AK_389.d

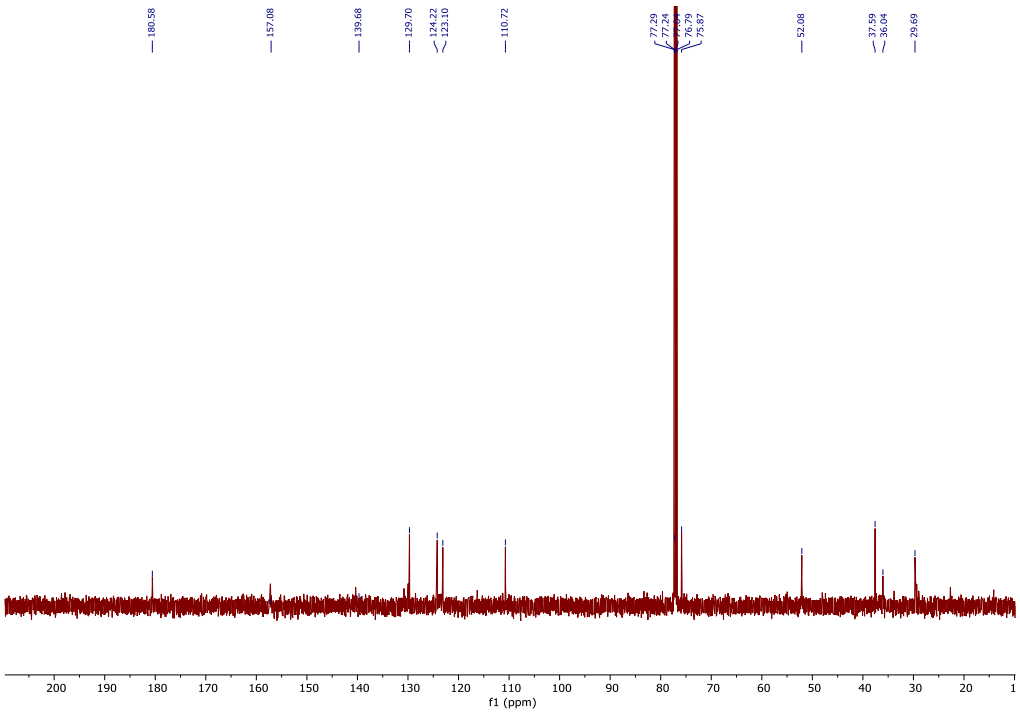
Bruker Compass DataAnalysis 4.1 printed: 11/1/2021 11:25:14 AM by: IISER Kolkata Page 1 of 1

HRMS of (+)-**9**





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



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

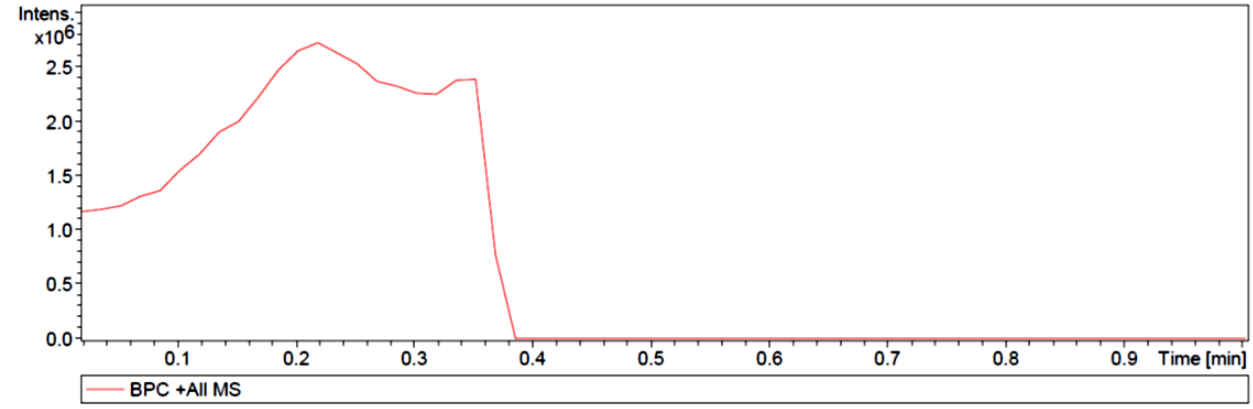
Display Report

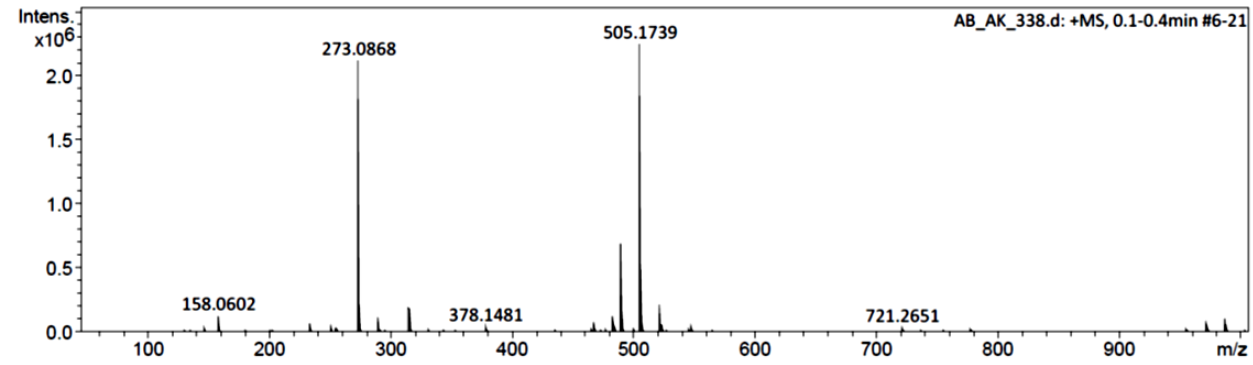
Analysis Info

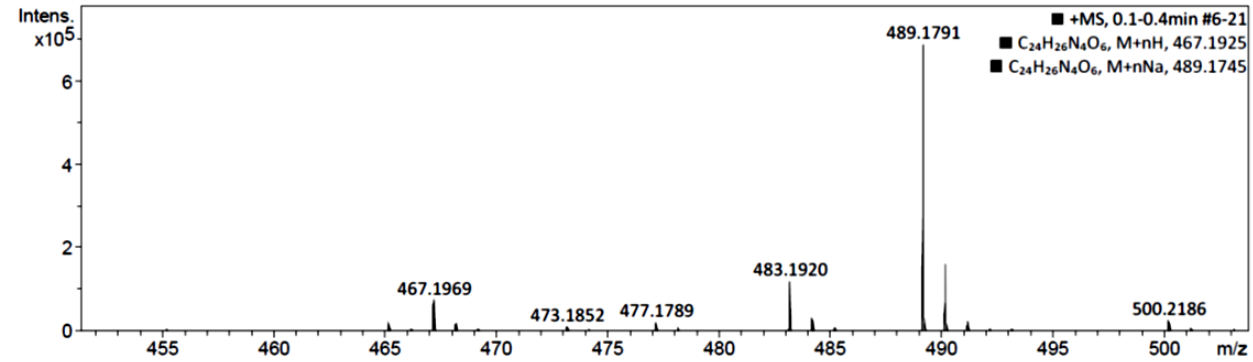
Analysis Name	D:\Data\User data\2021\OCTOBER\AB_AK_338.d	Acquisition Date	10/4/2021 11:49:24 AM
Method	Tune_pos_Standard.m	Operator	IISER Kolkata
Sample Name	AB_AK_338	Instrument	maXis impact 8282001.00127
Comment	SIGNAL DROPPIN WHILE WASHING WITH MEOH		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.5 Bar
Focus	Active	Set Capillary	3400 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C







AB_AK_338.d

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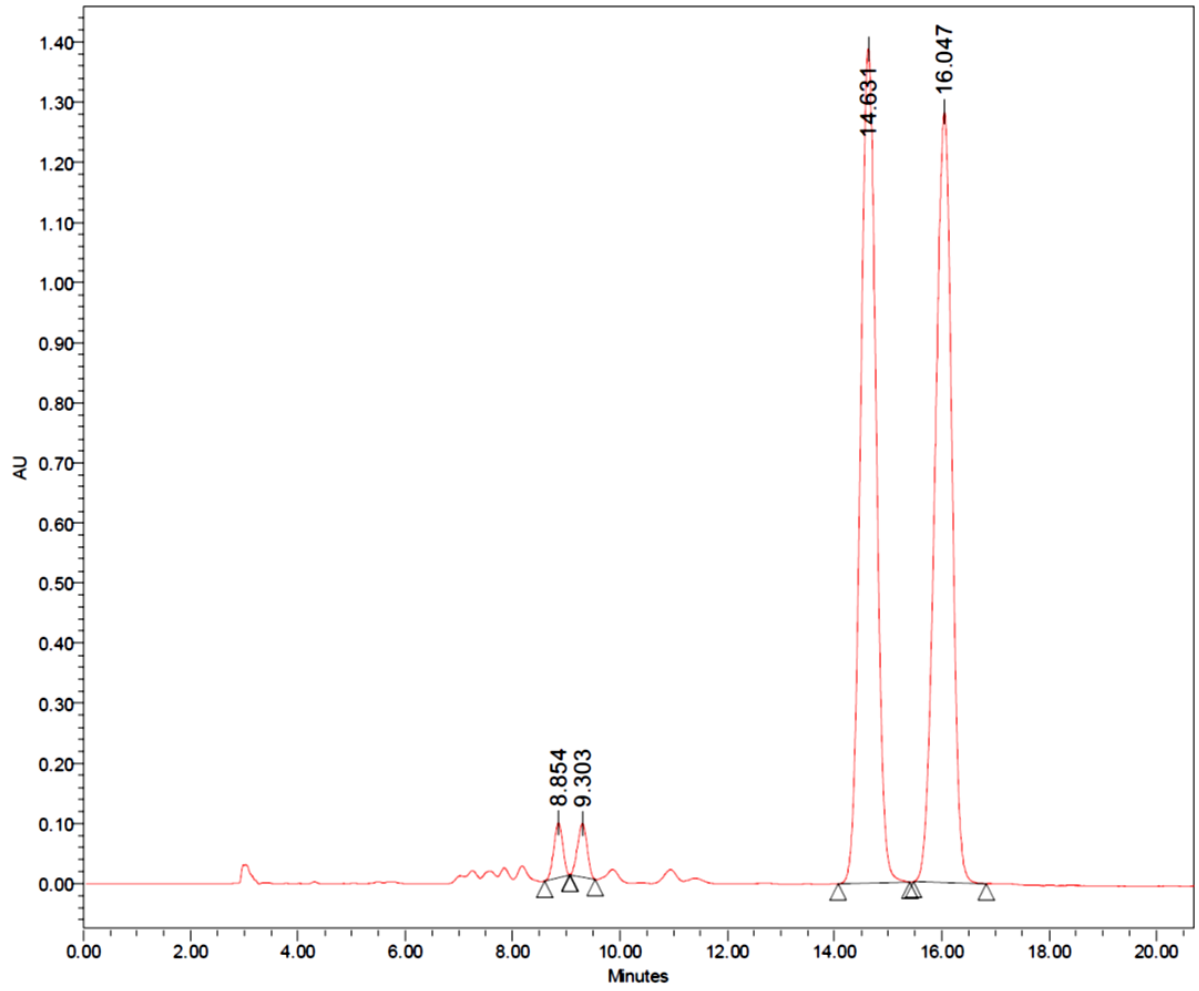
HRMS of (+)-**8**

Empower™ 3 SOFTWARE

Peak Summary Report



Sample Name: AB_AK_NHMoc_IA-10-1-rac; Date Acquired: 18-03-2021 19:17:41 IST; Vial: 1; Injection:

Peak Summary with Statistics
Name:

	Sample Name	Vial	Inj	Retention Time (min)	Area	% Area	Height
1	AB_AK_NHMoc_IA-10-1-rac	1	1	8.854	1066128	1.84	91223
2	AB_AK_NHMoc_IA-10-1-rac	1	1	16.047	27778392	47.99	1281813
3	AB_AK_NHMoc_IA-10-1-rac	1	1	14.631	27923303	48.24	1387564
4	AB_AK_NHMoc_IA-10-1-rac	1	1	9.303	1120173	1.94	89221

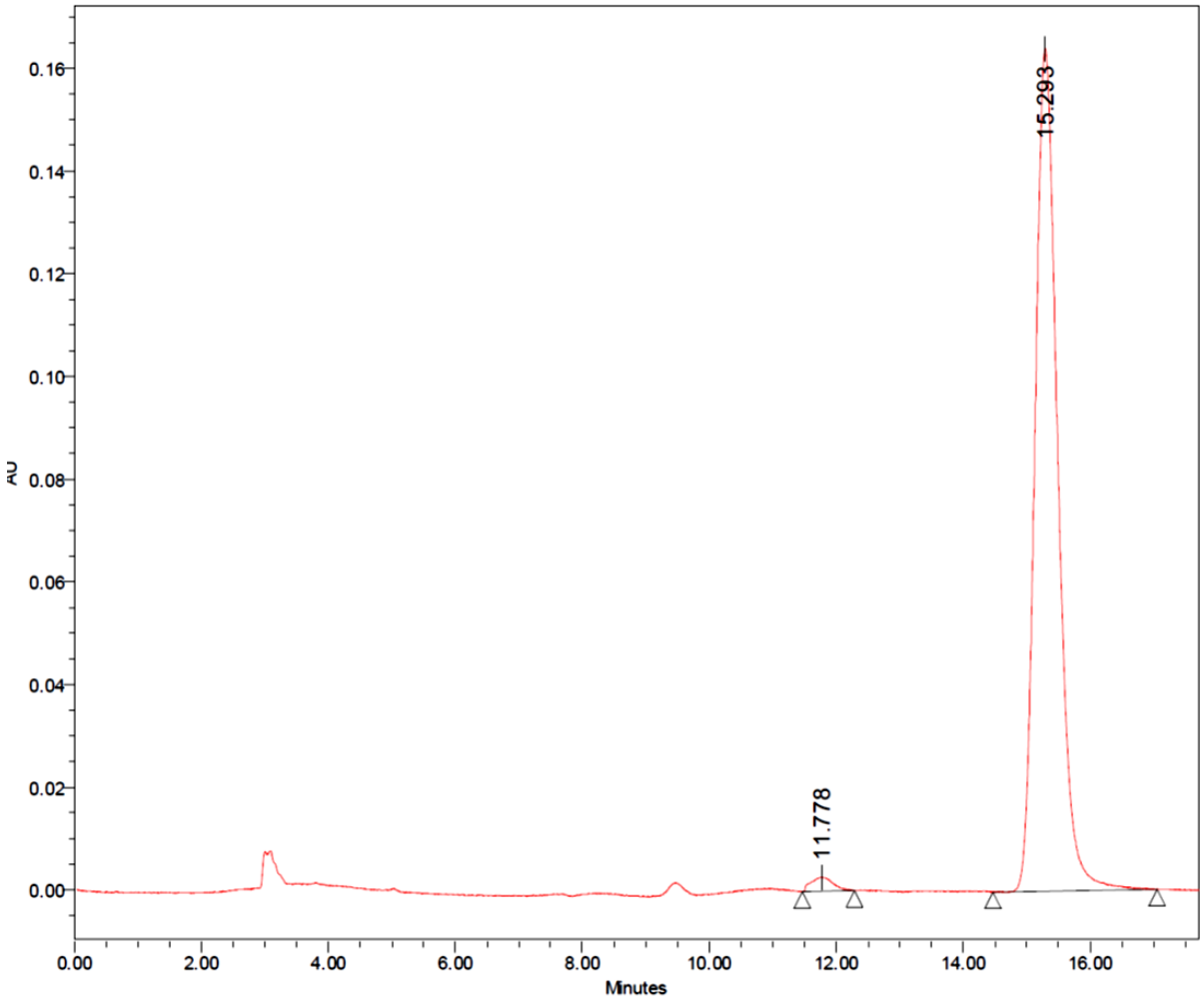
Reported by User: System
Report Method: Peak Summary Report
Report Method ID 1009
Page: 1 of 2

Project Name: AB Research Group
Date Printed:
18-03-2021
22:27:05 Asia/Calcutta

HPLC data of (±)-**8**

Empower 3 SOFTWARE

Peak Summary Report



Sample Name: AB_AK_C/MeCN_IA-10-1; Date Acquired: 25-03-2021 22:57:45 IST; Vial: 1; Injection:

Peak Summary with Statistics

Name:

	Sample Name	Vial	Inj	Retention Time (min)	Area	% Area	Height
1	AB_AK_C/MeCN_IA-10-1	1	1	15.293	4073856	98.41	164093
2	AB_AK_C/MeCN_IA-10-1	1	1	11.778	65950	1.59	2765
Mean				13.536			
Std. Dev.				2.486			

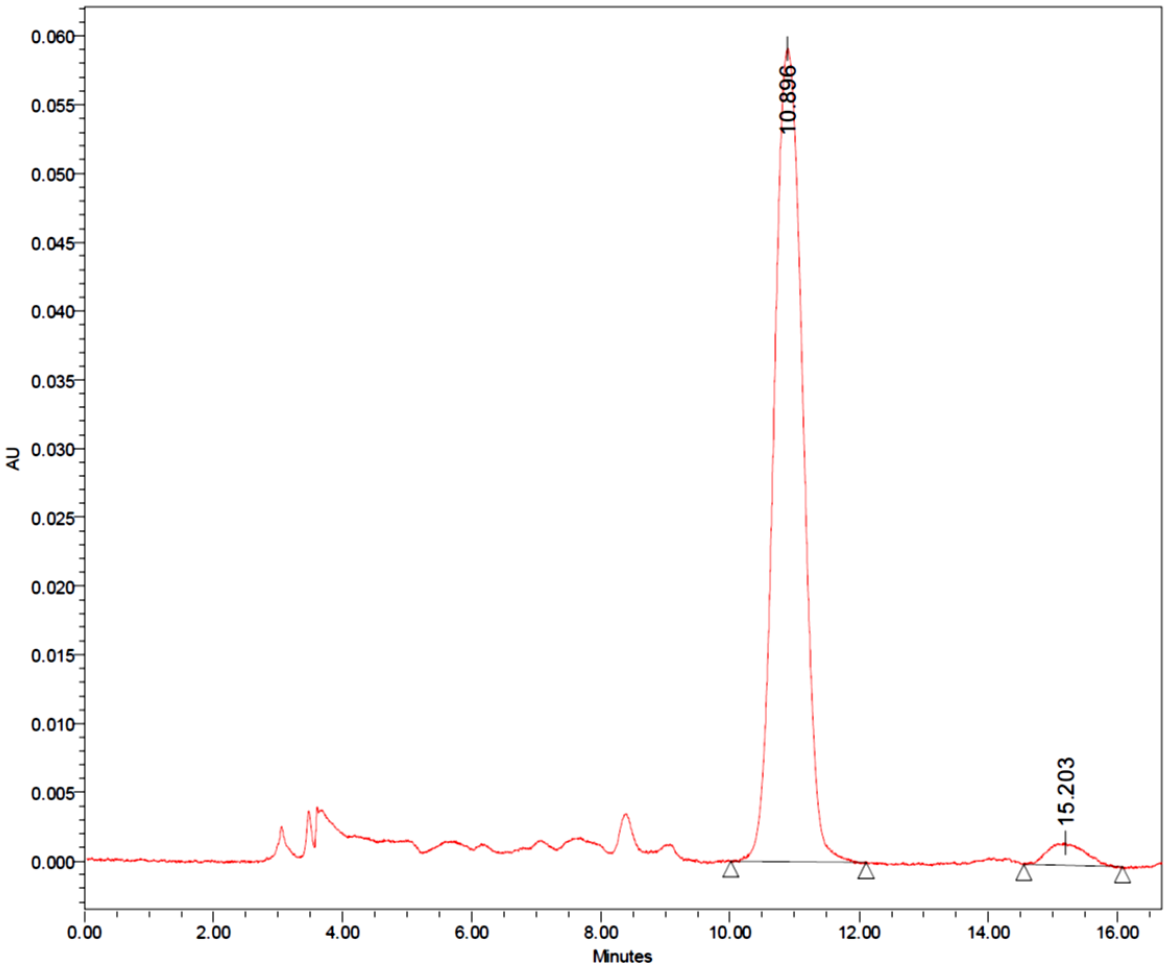
Reported by User: System
Report Method: Peak Summary Report
Report Method ID 1009
Page: 1 of 2

Project Name: AB Research Group
Date Printed:
25-03-2021
23:17:58 Asia/Calcutta

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

Empower™ 3 SOFTWARE

Peak Summary Report



Sample Name: AB_AK_QD/PhMe_IA-10-1; Date Acquired: 26-03-2021 01:53:04 IST; Vial: 1; Injection:

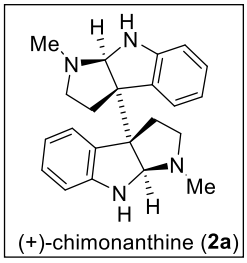
Peak Summary with Statistics
Name:

	Sample Name	Vial	Inj	Retention Time (min)	Area	% Area	Height
1	AB_AK_QD/PhMe_IA-10-1	1	4	15.203	65121	3.46	1614
2	AB_AK_QD/PhMe_IA-10-1	1	4	10.896	1819348	96.54	59154
Mean				13.049			
Std. Dev.				3.046			

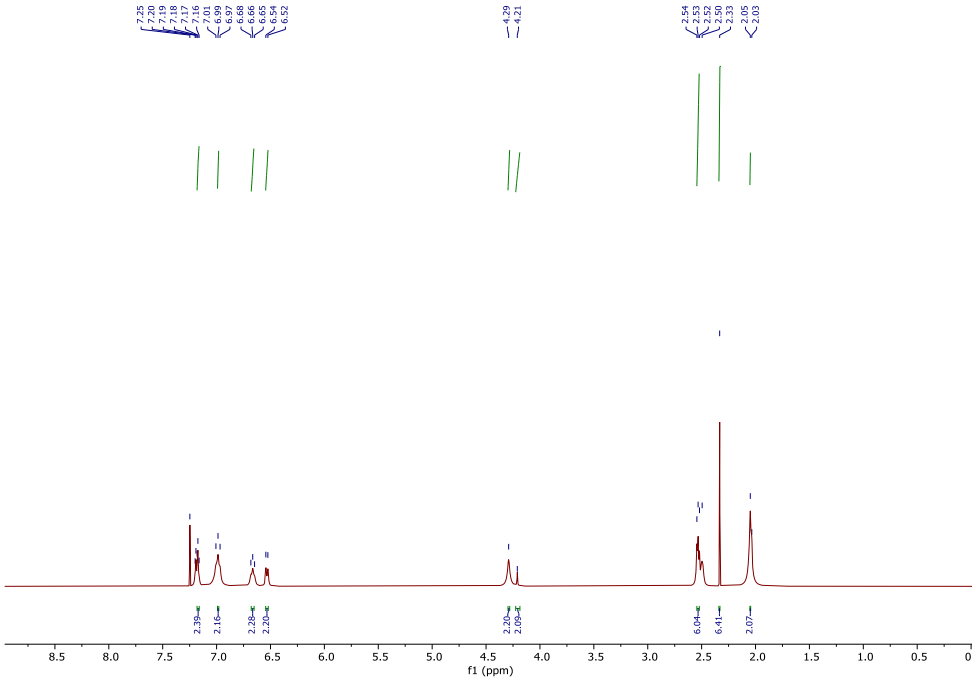
Reported by User: System
Report Method: Peak Summary Report
Report Method ID 1009
Page: 1 of 2

Project Name: AB Research Group
Date Printed:
13-12-2021
14:22:44 Asia/Calcutta

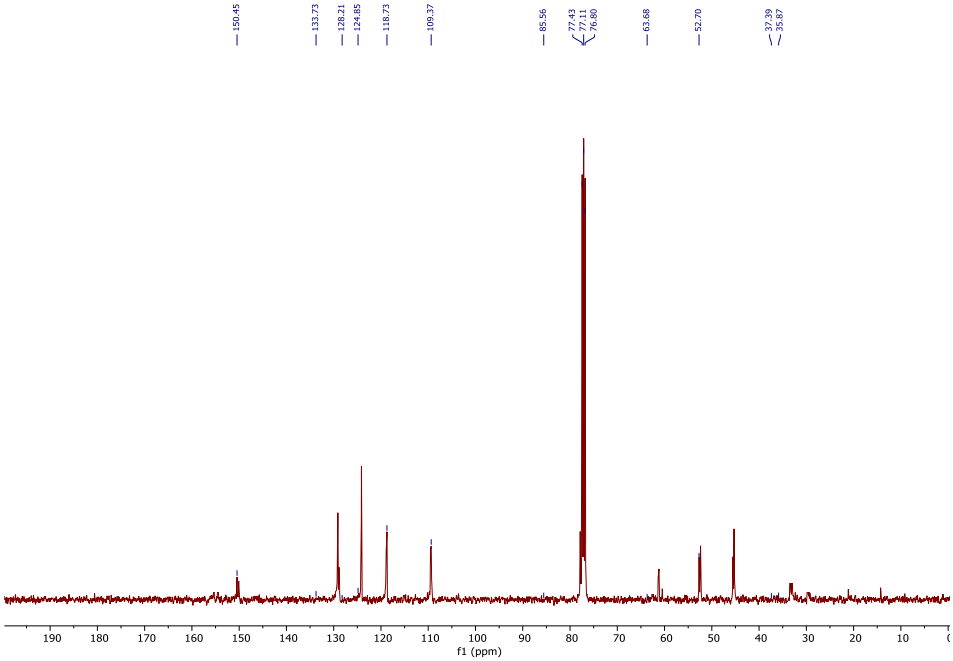
HPLC data of (–)-**8**



(+)-chimonanthine (**2a**)



^{1}H NMR (400 MHz, $CDCl_3$) of (+)-Chimonanthine [(+)-**2a**]



^{13}C NMR (100 MHz, $CDCl_3$) of (+)-Chimonanthine [(+)-**2a**]

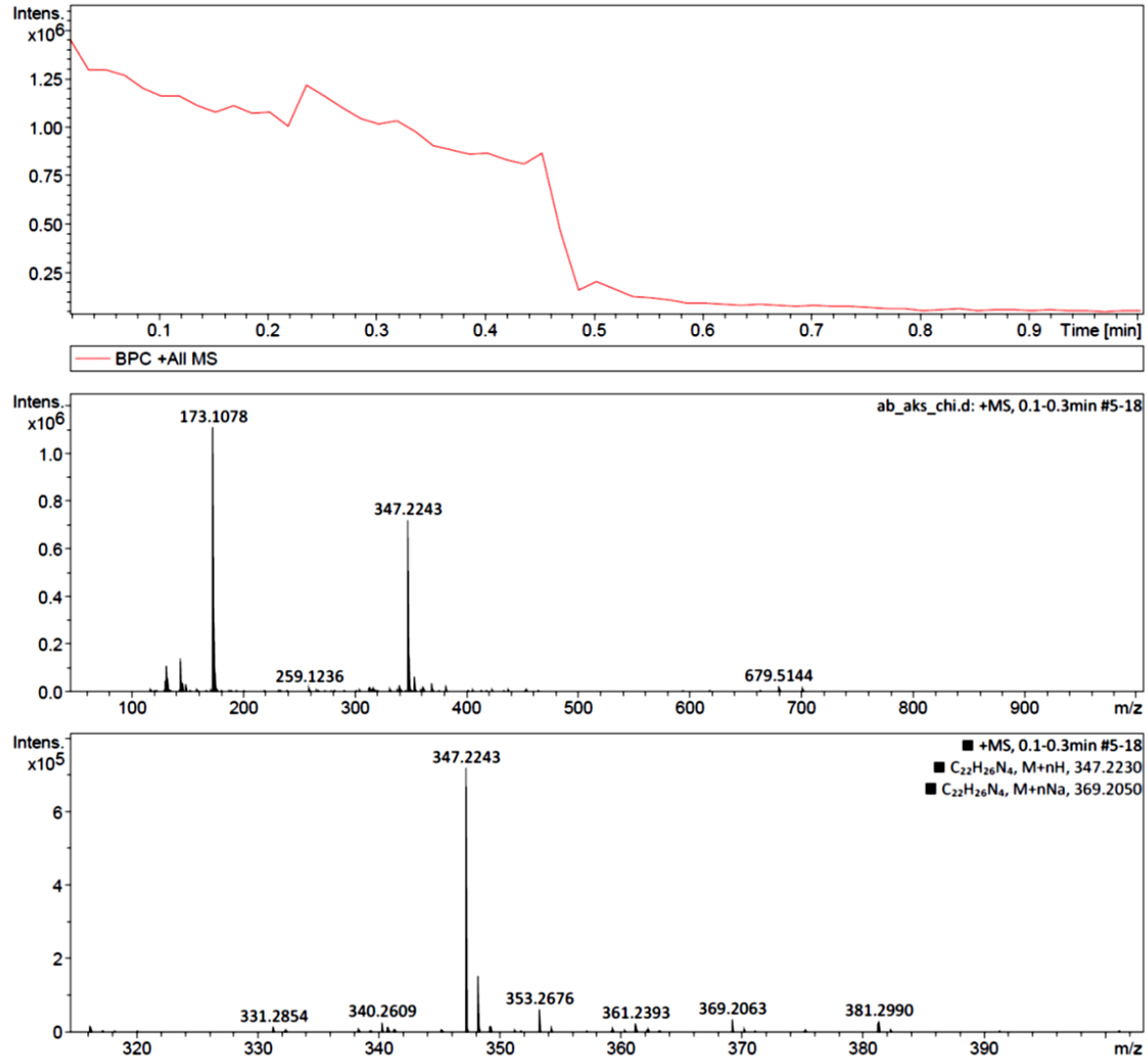
Display Report

Analysis Info

Analysis Name	D:\Data\User data\2021\OCTOBER\ab_aks_chi.d	Acquisition Date	10/18/2021 1:57:23 PM
Method	Tune_pos_Standard.m	Operator	IISER Kolkata
Sample Name	ab_aks_chi	Instrument	maXis impact 8282001.00127
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.5 Bar
Focus	Active	Set Capillary	3400 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



ab_aks_chi.d

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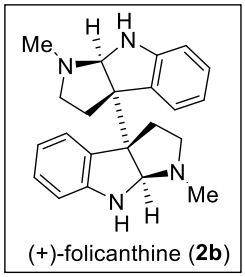
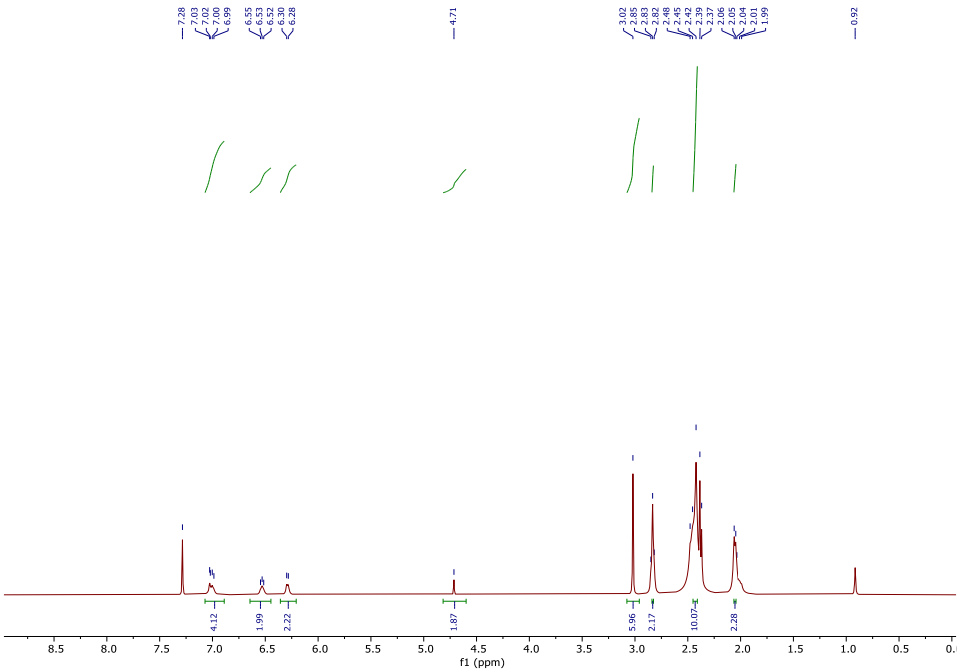
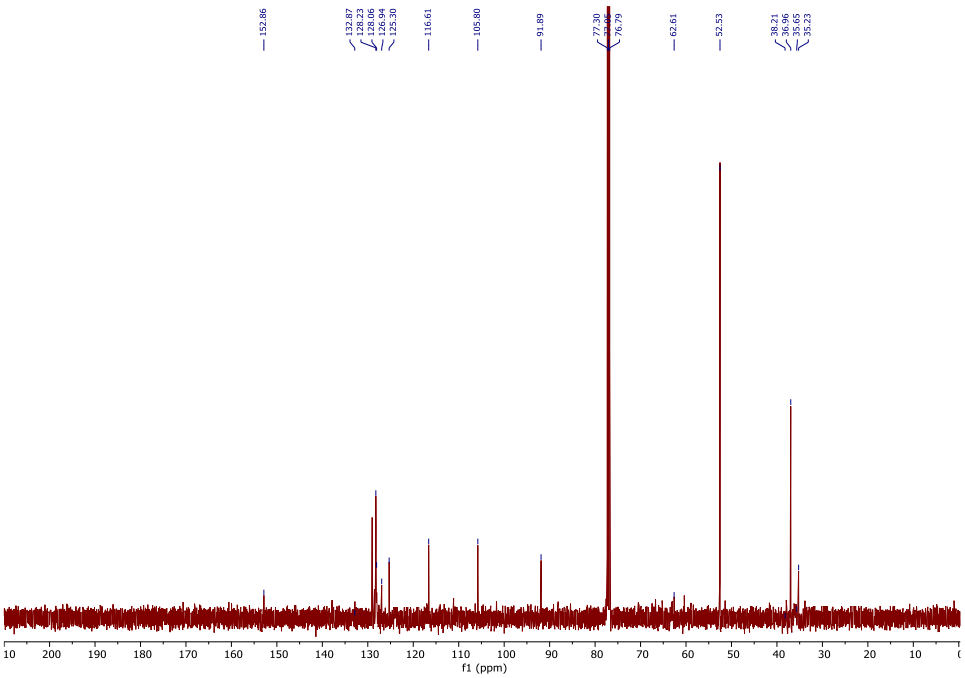
Scanned copy of mass spectrum of (+)-Chimonanthine [(+)-**2a**]



(+)-folicanthine (**2b**)



^{1}H NMR (400 MHz, $CDCl_3$) of (+)-Folicanthine [(+)-**2b**]



^{13}C NMR (100 MHz, $CDCl_3$) of (+)-Folicanthine [(+)-**2b**]

Display Report

Analysis Info

Analysis Name	D:\Data\new user data 2021\august-2021\11-augAK-foli.d	Acquisition Date	8/11/2021 1:45:13 PM
Method	tune_wide.m	Operator	RUCHI
Sample Name	AK-foli	Instrument	micrOTOF-Q II 10330
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
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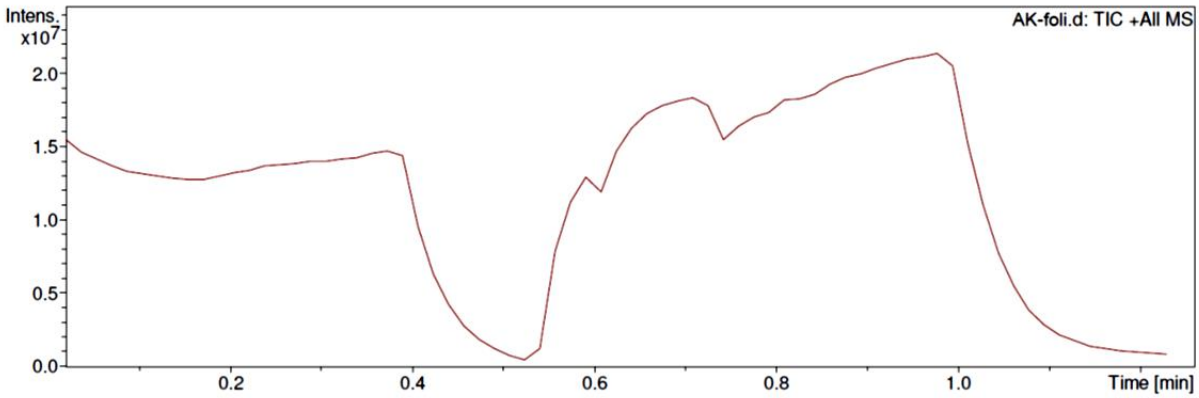
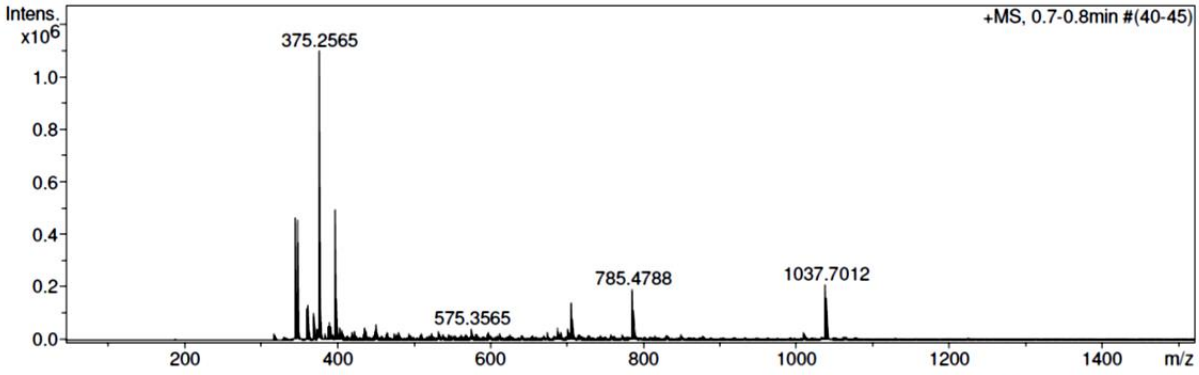
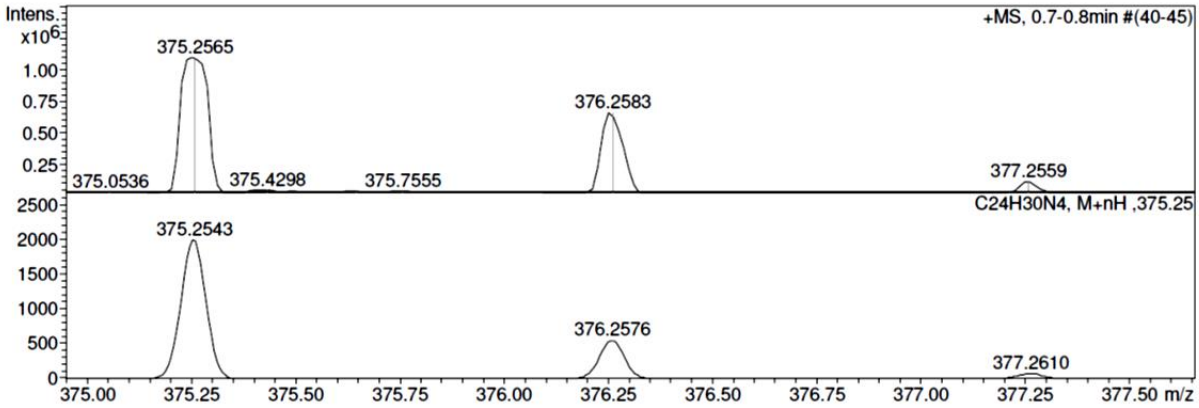
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste

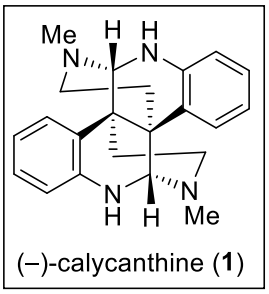




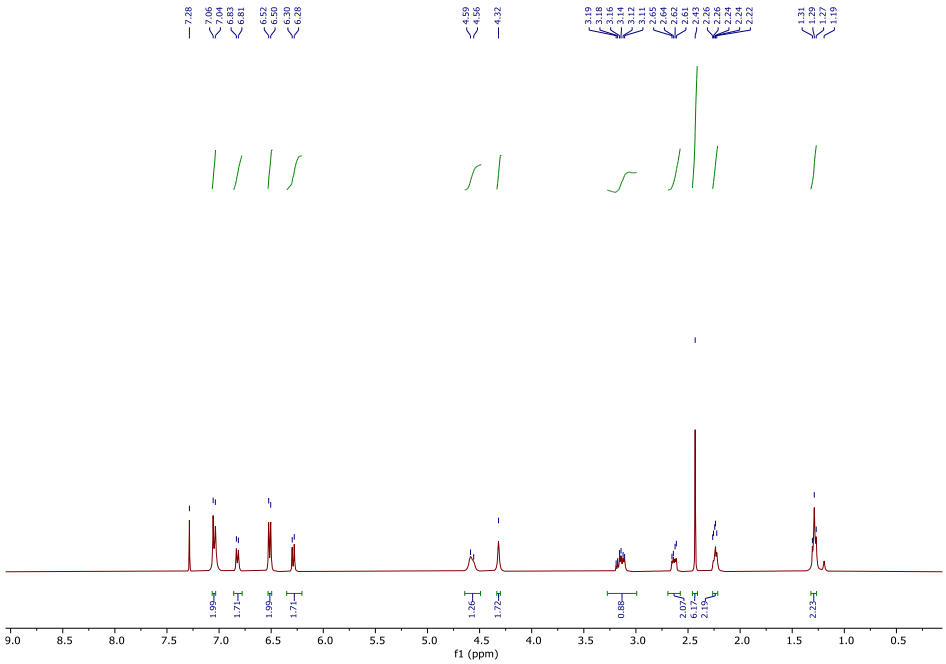


Bruker Compass DataAnalysis 4.0 printed: 8/11/2021 1:45:13 PM Page 1 of 1

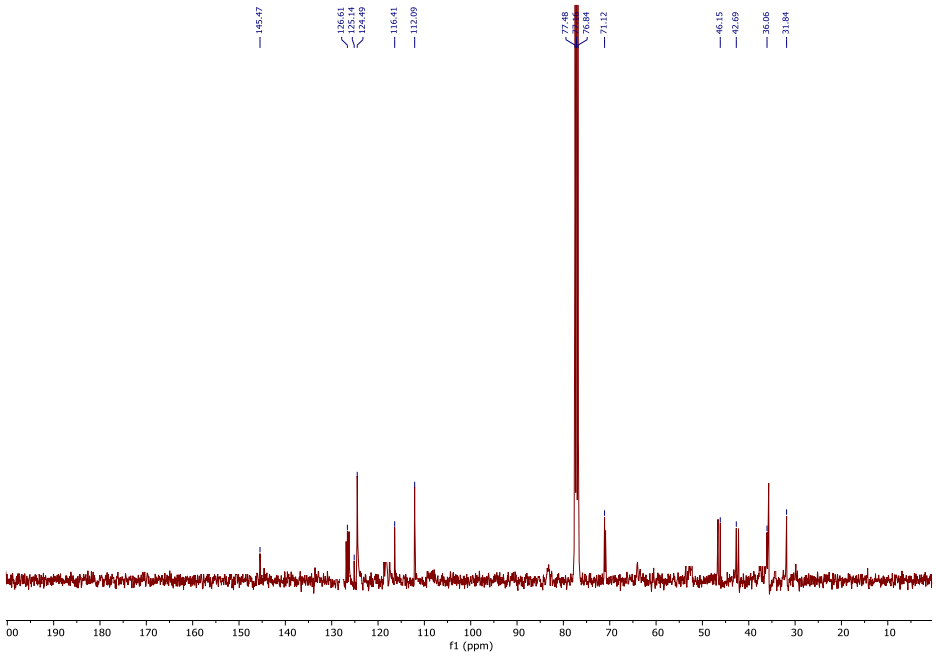
HRMS of (+)-Folicanthine [(+)-**2b**]



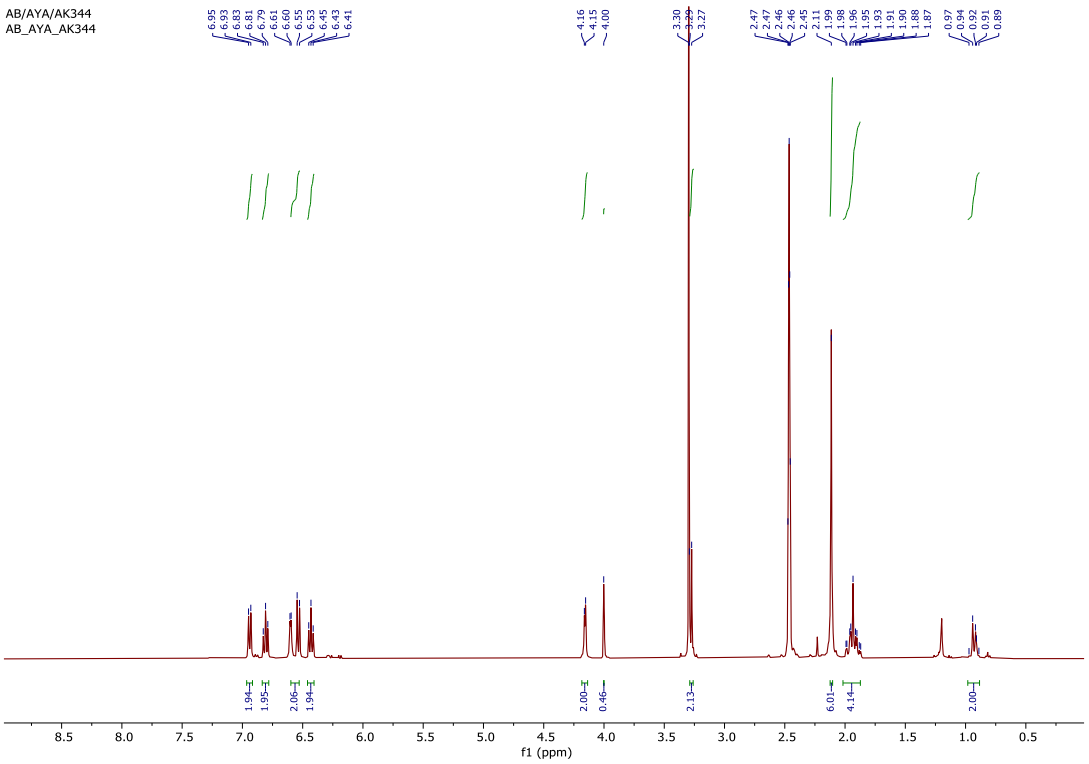
(–)-calycanthine (**1**)



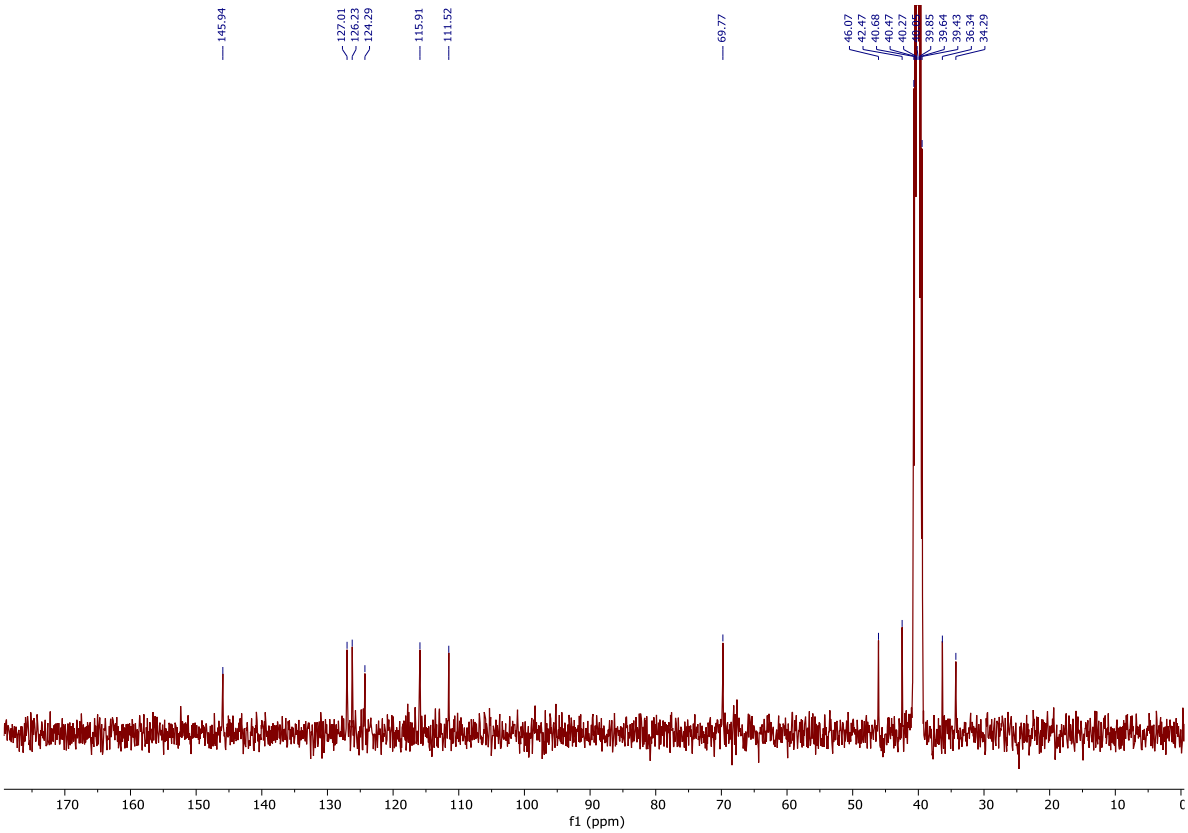
^{1}H NMR (400 MHz, $CDCl_3$) of (–)-Calycanthine [(–)-**1**]



^{13}C NMR (100 MHz, $CDCl_3$) of (–)-Calycanthine [(–)-**1**]



^{1}H NMR (400 MHz, DMSO-d_6) of (–)-Calycanthine [(–)-**1**]



^{13}C NMR (100 MHz, DMSO-d_6) of (–)-Calycanthine [(–)-**1**]

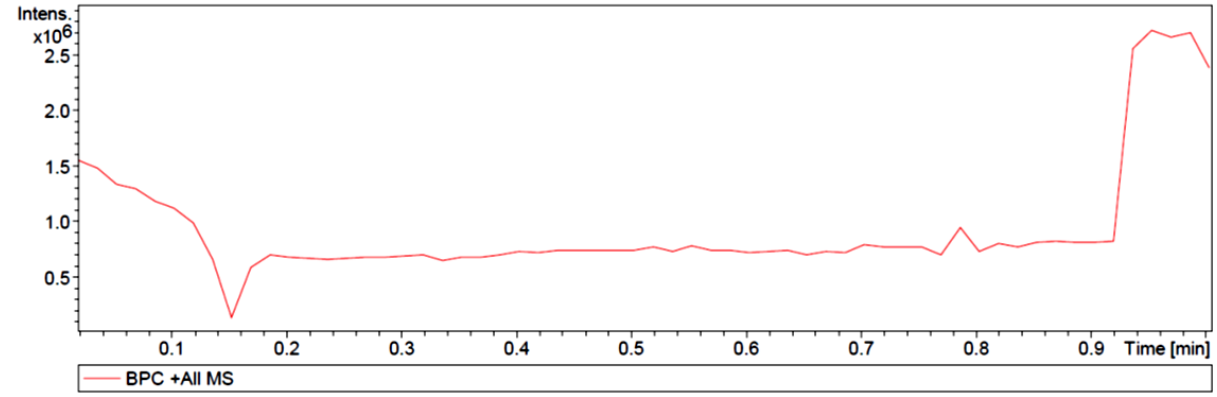
Display Report

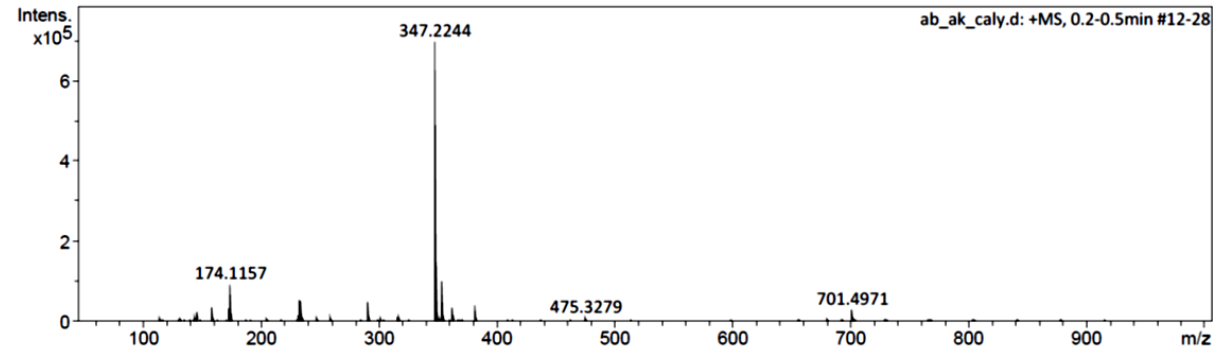
Analysis Info

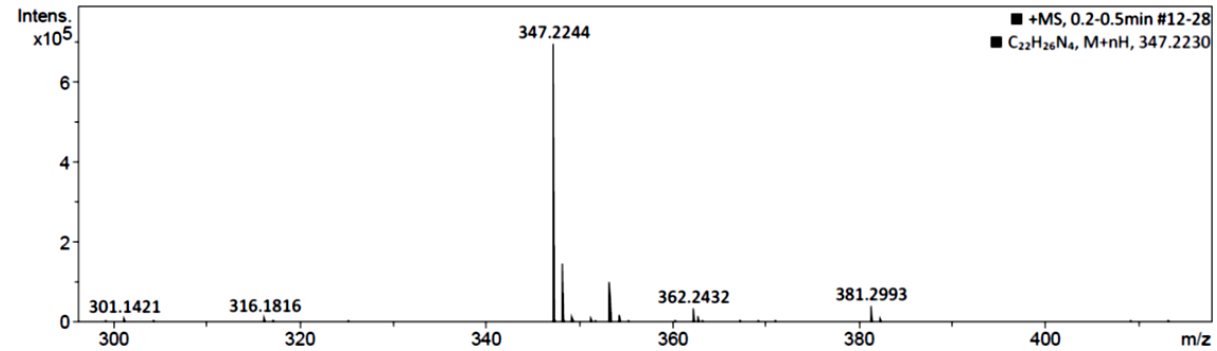
Analysis Name	D:\Data\User data\2021\OCTOBER\ab_ak_caly.d	Acquisition Date	10/18/2021 2:12:20 PM
Method	Tune_pos_Standard.m	Operator	IISER Kolkata
Sample Name	ab_ak_caly	Instrument	maXis impact 8282001.00127
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.5 Bar
Focus	Active	Set Capillary	3400 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C







ab_ak_caly.d

Bruker Compass DataAnalysis 4.1 printed: 10/18/2021 2:14:36 PM by: IISER Kolkata Page 1 of 1

HRMS of (–)-Calycanthine [(–)-**1**]