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Supplemental material for:

Total Synthesis of (+)-Xiamycin G *via* Acetanilide Assisted Two-Fold Csp2-H Functionalization

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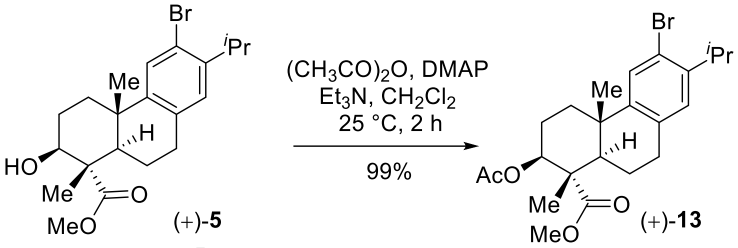
Materials and Methods

Unless otherwise stated, reactions were carried out using oven dried glass ware 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 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 silica gel precoated plates (0.25 mm) 60 (F-254), Visualized by UV irradiation, yellow dip stain and other stains. Silica gel 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 was recorded by using 400, 500 MHz spectrometers, ^{13}C-NMR operating frequencies are 100, 125 MHz respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvents ($CDCl_3$) signal ($\delta = 7.29$ for 1H NMR and $\delta = 77.0$ for ^{13}C NMR) and (CD_3OD) signal ($\delta = 3.33$ for ^{1}H NMR and $\delta = 49.0$ for ^{13}C NMR). Data for ^{1}H 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 was recorded on MicrOTOF-Q-II mass spectrometer using methanol as solvent. Optical rotations were measured on an automatic polarimeter.

Acetylation of (+)**-5:**

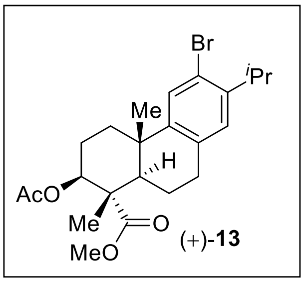


(+)-**5**

(for synthesis of **5** see ref 1)

(+)-**13**

Carbotricyclic compound (+)**-5** (5 g, 12.2 mmol, 1.0 equiv.) was taken in CH_2Cl_2 (30 mL) under an inert atmosphere. To this solution was added Et_3N (2.61 mL, 18.3 mmol., 1.5 equiv.) followed by the addition of catalytic amount of DMAP (149 mg, 1.22 mmol, 0.1 equiv.) at room temperature. After 5 minutes of stirring, acetic anhydride (Ac_2O, 1.4 mL, 14.64 mmol, 1.2 equiv.) was added to the reaction mixture dropwise at 25 ºC and the stirring was continued till the consumption of starting material (2 h). Upon completion of the reaction (TLC analysis), water (10 mL) was added and the reaction mixture was extracted CH_2Cl_2 (30 mL X 2). The organic layers were dried over Na_2SO_4 and concentrated on a rotary evaporator under reduced pressure. The crude product was purified by flash column chromatography with 10% EtOAc in *n*-hexane to furnish acetate (+)-**13** as yellow foam (5.45 g, 99% yield).



(+)-**13**

Methyl (1*S*,2*S*,4a*S*,10a*R*)**-2-acetoxy-6-bromo-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate** [(+)**-13]:** (+)**-13** was obtained as yellow foam (12.2 mmol scale, 5.45 g, 99% yield). $R_f = 0.3$ (10% EtOAc in *n*-hexane).

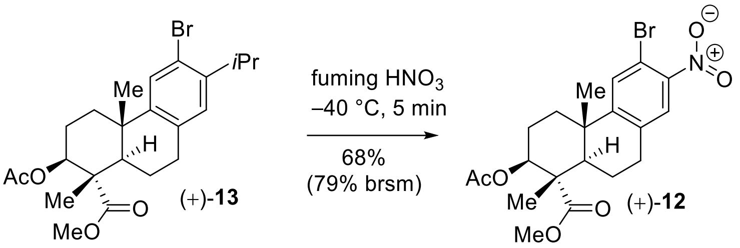
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (s, 1H), 6.93 (s, 1H), 5.22 (dd, *J* = 11.9, 4.6 Hz, 1H), 3.68 (s, 3H), 3.28 (p, *J* = 6.8 Hz, 1H), 2.94 – 2.75 (m, 2H), 2.31 (dt, *J* = 13.2, 3.5 Hz, 1H), 2.20 (dd, *J* = 12.5, 2.2 Hz, 1H), 2.02 (s, 3H), 2.02 – 1.95 (m, 1H), 1.90 (ddd, *J* = 12.9, 6.6, 4.7 Hz, 1H), 1.86 – 1.80 (m, 1H), 1.72 (ddd, *J* = 13.8, 10.1, 3.5 Hz, 1H), 1.39 (ddt, *J* = 13.7, 7.5, 2.3 Hz, 1H), 1.31 (s, 3H), 1.23 (s, 3H), 1.21 (d, *J* = 7.3 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 170.0, 147.8, 144.4, 134.1, 128.7, 127.1, 121.7, 76.7, 52.4, 52.0, 45.3, 36.7, 36.2, 32.3, 29.5, 25.0, 23.9, 23.0, 22.8, 21.1, 21.0, 11.7.

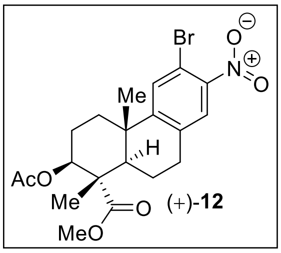
IR (neat) υ_{max} 3307, 2887, 2792, 1702, 1687, 1531, 1414, 1208, 1051, 946, 787 cm^{-1}.
HRMS (ESI) *m/z*: $[M+ Na]^+$ calcd. for $[C_{23}H_{31}O_4Br+ Na]^+$ 473.1298, found 473.1288.

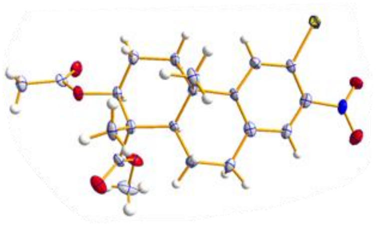
$[\alpha]^{25}_{589}$ = +66.42 (*c* = 0.85, $CHCl_3$).

***ipso*-Nitration of (+)-13:**



An oven-dried round-bottom flask was charged with 2 mL of fuming nitric acid and it was cooled to – 40 °C. Then compound (+)**-13** (800 mg, 1.8 mmol, 1.0 equiv.) was directly charged into the reaction vessel and scratched well with a spatula (5 minutes) maintaining the – 40 °C temperature. After 5 minutes (TLC analysis showed product formation), the reaction mixture was quenched with water (5 mL) and saturated $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (20 mL X 2). The organic layers were dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure and purified by column chromatography 10% EtOAc in *n*-hexane to afford compound (+)**-12** as white foam [547 mg, 68% yield (79% BRSM)]. Compound (+)**-12** was prepared in 2.1 g following several batches.





XRD data of (+)-**12**
CCDC: 2496283

Methyl (1*S*,2*S*,4a*S*,10a*R*)**-2-acetoxy-6-bromo-1,4a-dimethyl-7-nitro-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate** [(+)**-12**]**:** (+)**-12** was obtained as a white foam. (1.8 mmol scale, 547 mg, 68% yield); R$_f$ = 0.27 (20% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.57 (s, 1H), 5.21 (dd, *J* = 11.9, 4.5 Hz, 1H), 3.70 (d, *J* = 1.5 Hz, 3H), 2.97 (dd, *J* = 17.8, 7.0 Hz, 1H), 2.92 – 2.83 (m, 1H), 2.35 (dt, *J* = 13.2, 3.2 Hz, 1H), 2.25 – 2.17 (m, 1H), 2.04 (s, 3H), 2.03 (s, 1H), 1.97 – 1.81 (m, 2H), 1.75 (td, *J* = 13.4, 3.5 Hz, 1H), 1.46 (dd, *J* = 13.8, 7.5 Hz, 1H), 1.33 (s, 3H), 1.26 (s, 3H).

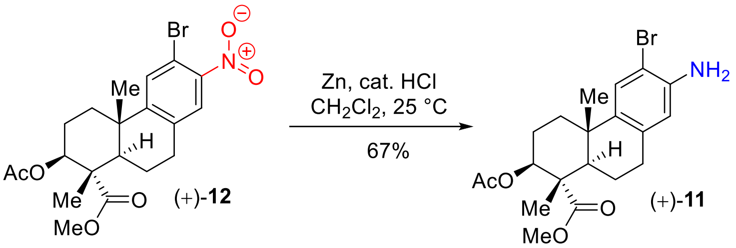
^{13}C NMR (125 MHz, $CDCl_3$) δ 175.7, 169.8, 154.5, 147.5, 135.7, 131.3, 126.2, 111.4, 76.0, 53.0, 51.7, 44.6, 37.3, 35.8, 29.1, 24.7, 23.6, 20.9, 20.3, 11.6.

IR (neat) υ_{max} 1857, 1705, 1690, 1621, 1363, 1301, 1203, 891,741 cm^{-1}.

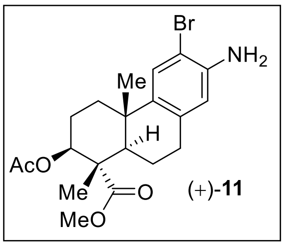
HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $[C_{20}H_{24}O_6NBr + Na]^+$ 476.0679, found 476.0667.

$[\alpha]^{25}_{589}$ = +37.5 (*c* = 0.69, $CHCl_3$).

Synthesis of (+)-**11:**



In a round-bottom flask *o*-bromo nitroarene (+)**-12** (945 mg, 2.08 mmol, 1 equiv.) was taken in 15 mL CH_2Cl_2. Next, Zn dust (1.36 g, 20.80 mmol, 10 equiv.) was added to the reaction solution followed by addition of catalytic amount of Conc. HCl was added to the reaction mixture at 0 °C in dropwise manner. Upon completion of the reaction (3 h), as monitored by TLC analysis, it was extracted with CH_2Cl_2 (25 mL X 3). The combined organic layers were washed with sodium bicarbonate (15 mL X 1) and dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude product was purified by flash chromatography with 25- 35% EtOAc in *n*-hexane to furnish (+)-**11** as a colourless liquid (591 mg, 67% yield).



Methyl (1*S*,2*S*,4a*S*,10a*R*)-2-acetoxy-7-amino-6-bromo-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**11**]**:** (+)-**11** was obtained as colorless liquid; (2.08 mmol scale, 591 mg, 67% yield); R$_f$ = 0.3 (20% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.24 (s, 1H), 6.47 (s, 1H), 5.22 (dd, *J* = 11.9, 4.6 Hz, 1H), 3.93 (s, 2H), 3.68 (s, 3H), 2.80 – 2.72 (m, 2H), 2.26 (dt, *J* = 13.3, 3.5 Hz, 1H), 2.17 (dd, *J* = 12.5, 2.3 Hz, 1H), 2.02 (s, 3H), 2.00 – 1.94 (m, 1H), 1.91 – 1.83 (m, 1H), 1.83 – 1.76 (m, 1H), 1.68 (td, *J* = 13.3, 3.5 Hz, 1H), 1.34 (ddt, *J* = 13.2, 6.7, 2.2 Hz, 1H), 1.30 (s, 3H), 1.22 – 1.19 (m, 3H).

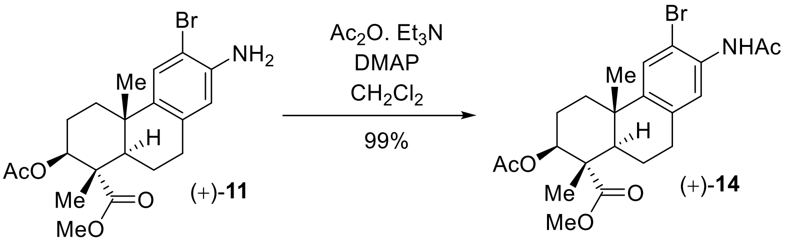
^{13}C NMR (125 MHz, CDCl$_3$) δ 176.4, 170.1, 141.7, 140.6, 135.1, 128.5, 115.5, 107.5, 77.2, 52.4, 52.0, 45.6, 36.4, 36.3, 29.5, 25.2, 24.0, 21.1, 21.0, 11.6.

IR (neat) υ_{max} 3441, 3357, 1843, 1703, 1687, 1609, 1473, 1278, 883 cm^{-1}.

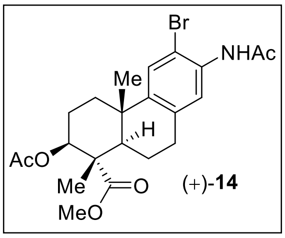
HRMS (ESI) *m/z*: [M + H]$^+$ calcd. for [C$_{20}$H$_{26}$BrO$_4$N + H]$^+$ 424.1123, found 424.1132.

$[\alpha]^{25}_{589}$ = +41.32 (*c* = 0.78, CHCl$_3$).

Synthesis of (+)-**14:**



In an oven dried round-bottom flask, (+)-**11** (42 mg, 0.098 mmol, 1.0 equiv.) was taken in dry CH$_2$Cl$_2$ (6 mL). To the solution was added Et$_3$N (21 μL, 0.147 mmol., 1.5 equiv.) and catalytic amount of DMAP (1.1 mg, 0.009 mmol., 0.1 equiv.) at 25 °C. Acetic anhydride (13 μL, 0.127 mmol., 1.3 equiv.) was added at 25 ºC and it was allowed to stir until the full consumption of starting material (3 h). Upon completion of the reaction (as monitored by TLC analysis), water (4 mL) was added and then extracted with CH_2Cl_2 (6 mL X 2). The organic layers were separated and dried over Na_2SO_4 and concentrated on a rotary evaporator under the reduced pressure. The crude bis-acetate was purified by flash column chromatography with 40% EtOAc in *n*-hexane to afford (+)-**14** as yellow liquid (45 mg, 99% yield).



Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-acetamido-2-acetoxy-6-bromo-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**14**]**:** (+)-**14** was obtained as colorless liquid; (0.098mmol scale, 45 mg, 99% yield); R_f = 0.2 (30% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.49 (s, 1H), 7.36 (s, 1H), 5.21 (dd, *J* = 11.9, 4.5 Hz, 1H), 3.68 (s, 3H), 2.95 – 2.78 (m, 2H), 2.31 – 2.24 (m, 1H), 2.22 (s, 3H), 2.19 – 2.15 (m, 1H), 2.02 (s, 3H), 1.84 (dtd, *J* = 37.3, 12.5, 4.0 Hz, 2H), 1.70 (ddd, *J* = 17.1, 10.6, 3.9 Hz, 2H), 1.39 (dt, *J* = 13.3, 6.8 Hz, 1H), 1.30 (s, 3H), 1.21 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 176.3, 170.1, 168.3, 146.2, 135.5, 133.3, 128.2, 124.2, 122.4, 76.7, 52.5, 52.1, 45.4, 36.9, 36.4, 29.8, 25.1, 24.9, 24.0, 21.2, 21.0, 11.8.

IR (neat) υ_{max} 3387, 3271, 3093, 2804, 1709, 1687, 1564, 1267, 762, 655 cm^{-1}.
$[\alpha]^{25}_{589}$ = +41.62 (*c* = 0.28, $CHCl_3$).

Our first-generation approach towards xiamycin G (1b):

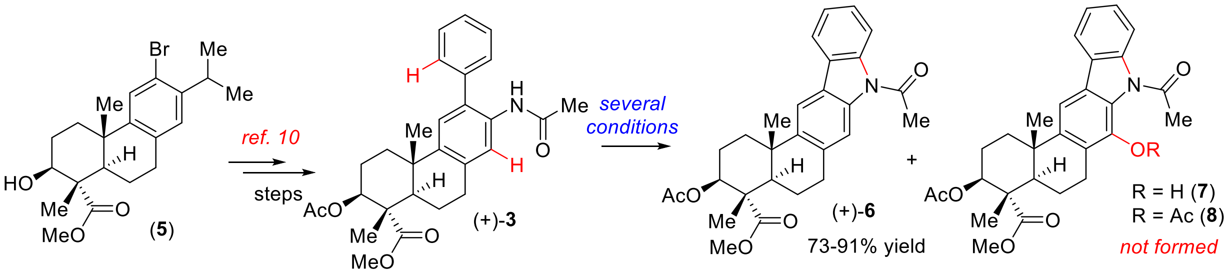
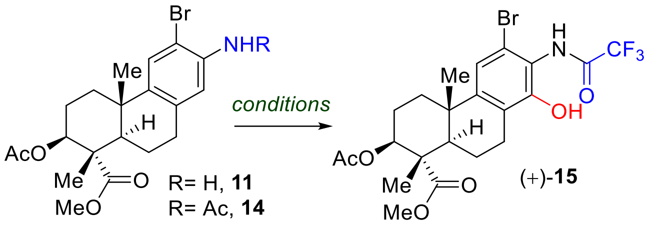


Table 1: Optimization Table for directed double Csp^2-H activation

Entry	Reagent	Solvent	Temp.	Time	Result
1	$Pd(OAc)_2$, $PhI(OAc)_2$, O_2	AcOH: Ac_2O (3:1)	100 °C	9 h	13% of **6**
2	$Pd(OAc)_2$, $K_2S_2O_8$	TFA: TFAA (9:1)	100 °C	8 h	86% of **6**
3	BBr_3 then $NaBO_3.4H_2O$	CH_2Cl_2 then THF: H_2O (1:1)	25 °C	3 h	Multitude of spots
4	$Pd(OAc)_2$, $K_2S_2O_8$	DCE: AcOH (2:1)	80 °C	12 h	89% of **6**
5	$Pd(OAc)_2$, TBHP in decane	Toluene	100 °C	10 h	73% of **6**
6	$Pd(OAc)_2$, TFA, TBHP in H_2O	-	25 °C	24 h	Multitude of spots
7	AgOTf, PIFA	DCE	25 °C	1 h	91% of **6**
8	[Ru(*p*-cymene)Cl_2]$_2$, $K_2S_2O_8$	TFA: TFAA (9:1)	80 °C	8 h	Multitude of spots

[a] all reactions were done using 0.1 mmol of 2-phenyl acetanilide **3** and yields are reported after column purification.

Table 2: Optimization for aniline/ acetanilide directed *o*-hydroxylation

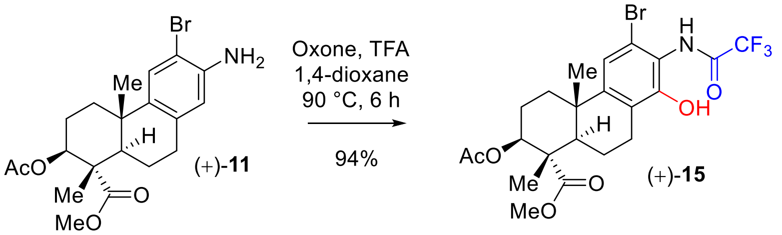


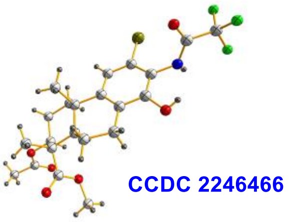
Entry	Substrate	Reagent	Solvent	Temp.	Time	Result
1	**14**	[Ru(*p*-cymene)Cl_2]$_2$, $K_2S_2O_8$	TFA: TFAA (3:1)	80 °C	12 h	83% of **15**
2	**11**	Oxone, TFA	CH_3CN	80 °C	10 h	21% of **15**
3	**11**	Oxone, TFA	DMSO	120 °C	10 h	29% of **15**
4	**11**	Oxone, TFA	1,4-dioxane	90 °C	6 h	94% of **15**
5	**11**	$K_2S_2O_8$, TFA	1,4-dioxane	90 °C	6 h	33% of **15**
6	**11**	TBHP, TFA	1,4-dioxane	90 °C	17 h	NR
7	**11**	Oxone, AcOH	1,4-dioxane	90 °C	6 h	decomposition

8	**11**	H_2O_2, TFA	1,4-dioxane	90 ºC	6 h	19% of **15**

[a]all reactions were done using 0.1 mmol of substrate and yields are reported after column purification. [b]starting materials were recovered in 15-37% yield.

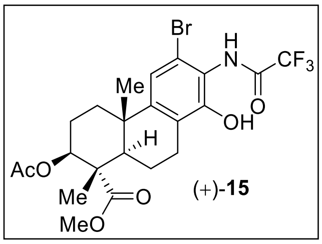
Aniline directed *o*-hydroxylation (+)-15:





XRD Data of (+)-**15**

In an oven dried sealed tube oxone (302 mg, 0.981 mmol, 1.2 equiv.) was taken in 1,4-dioxane (4 mL) under argon atmosphere and TFA (158 mL, 2.045 mmol, 2.5 equiv.) was added to it and stirred the reaction mixture for another 10 min. After that 2-bromo aniline derivative (+)-**11** (347 mg, 0.818 mmol, 1.0 equiv.) dissolved in 1,4-dioxane (3 mL) was added to the mixture dropwise manner. The reaction mixture was sonicated and degassed and refilled with N_2 from the double manifold (this sequence was carried out 3 times). The sealed tube was set into a pre-heated oil bath at 90 °C and stirred for 6 h (complete consumption of starting materials). After cooling it to room temperature, the reaction mixture was diluted with water (4 mL) and extracted with EtOAc (6 mL X 3). The combined organic layers were washed with aqueous saturated $Na_2S_2O_3$ solution (3 mL) and dried over anhydrous Na_2SO_4, and concentrated in a rotary evaporator under reduced pressure. The residue was purified by silica gel column chromatography with 23% EtOAc in *n*-hexane to afford to provide (+)-**15** as yellow foam (412 mg, 94% yield).



(+)-**15**

Methyl (1*S*,2*S*,4a*S*,10a*R*)-2-acetoxy-6-bromo-8-hydroxy-1,4a-dimethyl-7-(2,2,2-trifluoroacetamido)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-15]: (+)-**15** was obtained as a yellow foam (0.818 mmol scale, 412 mg, 94% yield); $R_f = 0.2$ (20% EtOAc in *n*-hexane).

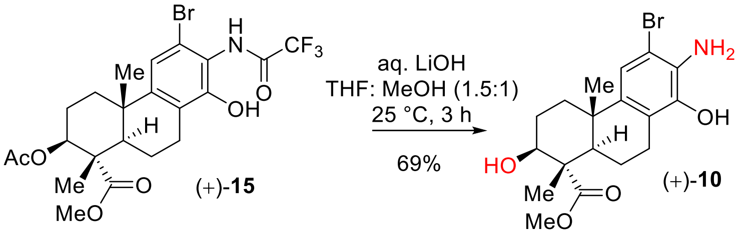
^{1}H NMR (500 MHz, $CDCl_3$): 8.41 (s, 1H), 7.57 (s, 1H), 7.13 (s, 1H), 5.22 (dd, J = 11.9, 4.5 Hz, 1H), 3.70 (s, 3H), 2.94 (ddd, J = 18.5, 6.9, 1.3 Hz, 1H), 2.66 (ddd, J = 19.0, 11.4, 8.1 Hz, 1H), 2.28 (dt, J = 13.1, 3.5 Hz, 1H), 2.17 (dd, J = 12.7, 2.2 Hz, 1H), 2.03 (s, 3H), 2.02 – 1.98 (m, 1H), 1.91 – 1.79 (m, 2H), 1.70 (td, J = 13.4, 3.6 Hz, 1H), 1.49 – 1.43 (m, 1H), 1.31 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 176.1, 170.1, 157.0 – 155.6 (m), 150.9, 148.3, 127.0, 120.9, 118.4, 116.8, 114.4, 76.5, 52.5, 51.9, 44.9, 37.0, 36.2, 24.8, 24.5, 23.8, 21.1, 20.2, 11.7.

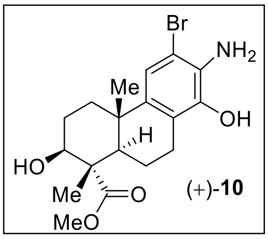
^{19}F NMR (470 MHz, $CDCl_3$) δ -74.54.

IR (neat) υ_{max} 3293, 2805, 1821, 1701, 1697, 1645, 1357, 1178, 965, cm^{-1}.
HRMS (ESI) *m/z*: $[M+ Na]^+$ calcd. for $[C_{22}H_{25}BrF_3O_6N + Na]^+$ 558.0710, found 558.0727.
$[\alpha]^{25}{}_{589}$= +28.0 (c = 0.89, CH_3OH).

Synthesis of (+)-10:



Trifluoro acetamido derivative (+)-**15** (390 mg, 0.727 mmol, 1.0 equiv.) was dissolved in THF: MeOH (1.5:1) (6 mL) and 2 M solution of aq. LiOH solution (727 µL, 1.45 mmol, 2 equiv.) was added to it at room temperature and stirred the reaction mixture for another 3 h at the same temperature. Upon completion of the reaction, as monitored by TLC analysis, THF: MeOH solvent mixture was evaporated and it was extracted with CH_2Cl_2 (6 mL X 3). The combined organic layers were dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude product was purified by flash chromatography with 25- 50- 60% EtOAc in *n*-hexane to furnish (+)-**10** as a colourless liquid (199 mg, 69% yield).



(+)-**10**

Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-amino-6-bromo-2,8-dihydroxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**10**]**:** (+)-**10** was obtained as a red oil (0.727 mmol scale, 199 mg, 69% yield); $R_f = 0.25$ (50% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (s, 1H), 4.02 (dd, *J* = 11.6, 4.6 Hz, 1H), 3.76 (s, 3H), 2.80 – 2.70 (m, 1H), 2.58 (dt, *J* = 17.4, 9.0 Hz, 1H), 2.26 (d, *J* = 13.0 Hz, 1H), 2.07 (s, 1H), 1.91 (s, 1H), 1.88 (d, *J* = 3.9 Hz, 1H), 1.79 (d, *J* = 11.8 Hz, 1H), 1.62 (d, *J* = 12.3 Hz, 1H), 1.58 – 1.50 (m, 1H), 1.26 (s, 3H), 1.21 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 177.7, 142.7, 142.2, 125.0, 120.3, 119.9, 109.9, 75.1, 53.6, 52.3, 45.1, 36.8, 36.6, 27.2, 25.3, 24.0, 20.5, 10.6.

IR (neat) υ_{max} 3498, 3437, 3387, 1809, 1699, 1653, 1598, 1481, 1262, 798 cm^{-1}.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{18}H_{24}BrO_4N + H]^+$ 398.0967, found 398.0966.
$[\alpha]^{25}_{589} = +88.0$ (*c* = 0.67, $CHCl_3$).

Chemoselective methylation of (+)-10:

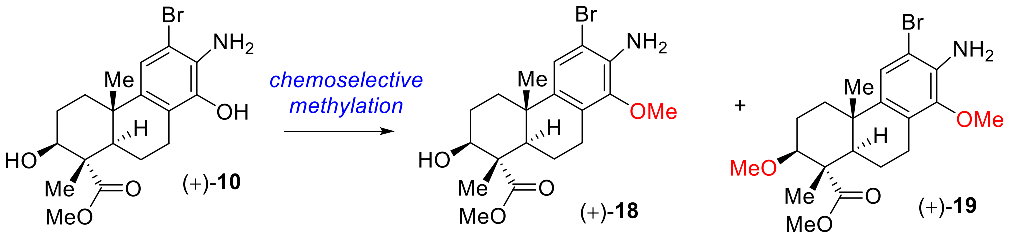
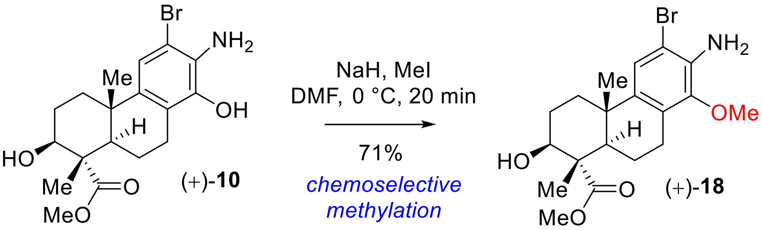


Table 3: Optimization table

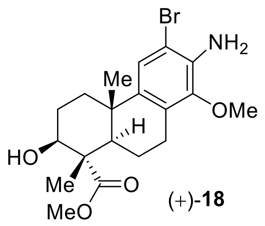
Entry	Methylating Reagent	Base	Solvent	Temp.	Time	Yield
1	Me_2SO_4	K_2CO_3	Acetone	55 °C	5 h	28% of **18** + multitude of spots
2	Me_2SO_4	K_2CO_3	Acetone	55 °C	1.5 h	17% of **18** + other spots
3	MeI	Et_3N	CH_2Cl_2	25 °C	4 h	Multitude of spots
4	MeI	NaH	DMF	25 °C	2 h	15% (**18**)+ 31% (**19**)

5	MeI	NaH	DMF	0 °C	20 min	71% of **18**
6	MeI	NaH	DMF	0 °C	45 min	32% (**18**)+ 27% (**19**)
7	MeI	KO^{t}Bu	THF	25 °C	2 h	7% (**18**)+ 13% (**19**)
8	MeI	KO^{t}Bu	1,4-dioxane	25 °C	2 h	11% (**18**)+ multitude of spots

[a]all reactions were done using 0.12 mmol of substrate and yields are reported after column purification.



In an oven dried round-bottom flask (+)-**10** (179 mg, 0.449 mmol, 1.0 equiv.) was taken in dry DMF (4 mL) under argon atmosphere and to it NaH (48.5 mg, 2.022 mmol, 4.5 equiv.) was added at 0 °C. After 10 min. MeI (31.2 µL, 0.494 mmol, 1.1 equiv.) was added to the reaction mixture in dropwise manner at 0 °C and the reaction mixture was stirred at the same temperature for another 20 min. After complete consumption of starting materials the reaction mixture was diluted with water (2 mL) and extracted with 50% EtOAc in *n*-hexane (6 mL X 2). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in a rotary evaporator under reduced pressure. The residue was purified by silica gel column chromatography with 25% EtOAc in *n*-hexane to afford (+)-**18** as yellow oil (131 mg, 71% yield).



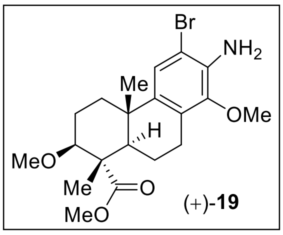
Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-amino-6-bromo-2-hydroxy-8-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**18**]**:** (+)-**18** was obtained as a yellow oil (0.449 mmol scale, 131 mg, 71% yield); $R_f = 0.3$ (30% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.09 (s, 1H), 4.04 (dd, *J* = 11.8, 4.5 Hz, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 2.97 – 2.90 (m, 1H), 2.71 – 2.62 (m, 1H), 2.25 (dt, *J* = 13.1, 3.4 Hz, 1H), 2.09 – 2.02

(m, 1H), 1.92 – 1.86 (m, 1H), 1.86 – 1.81 (m, 1H), 1.80 – 1.76 (m, 1H), 1.62 (dd, *J* = 13.3, 3.6 Hz, 1H), 1.46 (ddt, *J* = 13.4, 7.9, 1.9 Hz, 1H).1.25 (s, 3H), 1.19 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 177.8, 144.7, 140.7, 135.8, 128.0, 123.8, 107.5, 75.2, 58.5, 53.6, 52.3, 45.4, 36.9, 36.7, 27.3, 25.4, 24.3, 20.7, 10.7.

IR (neat) υ_{max} 3501, 3435, 3379, 1778, 1702, 1656, 1452, 1248, 693 cm^{-1}.
HRMS (ESI) *m/z*: $[M+ H]^+$ calcd. for $[C_{19}H_{26}BrO_4N + H]^+$ 412.1123, found 412.1136.
$[\alpha]^{25}_{589}$ = +34.0 (*c* = 0.97, $CHCl_3$).



(+)-**19**

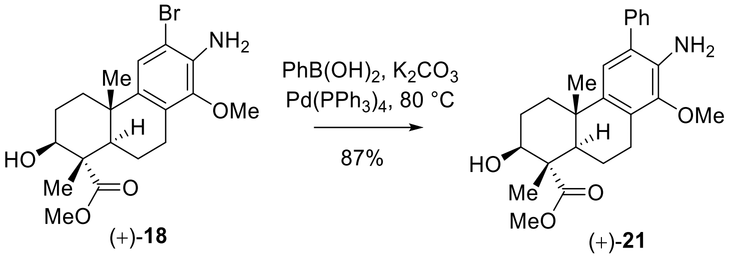
Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-amino-6-bromo-2,8-dimethoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**19**]: (+)-**19** was obtained as a colorless oil (0.449 mmol scale, 24.8 mg, 13% yield); R$_f$ = 0.28 (30% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.10 (s, 1H), 4.22 – 3.92 (m, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 3.66 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.32 (s, 3H), 2.96 – 2.87 (m, 1H), 2.67 – 2.58 (m, 1H), 2.31 – 2.24 (m, 1H), 2.09 – 2.02 (m, 1H), 2.00 (dd, *J* = 12.6, 2.2 Hz, 1H), 1.87 – 1.77 (m, 1H), 1.68 – 1.58 (m, 2H), 1.41 – 1.34 (m, 1H), 1.22 (s, 3H), 1.18 (s, 3H).

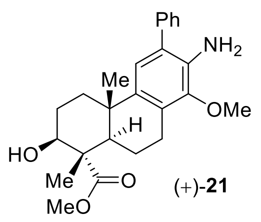
^{13}C NMR (125 MHz, $CDCl_3$): δ 178.1, 144.7, 140.8, 135.8, 127.9, 123.8, 107.5, 84.5, 58.5, 57.0, 53.1, 52.1, 46.3, 36.8, 36.8, 25.4, 24.2, 22.8, 20.2, 11.2.

IR (neat) υ_{max} 3498, 3415, 3356, 1793, 1710, 1656, 1452, 1248, 1179, 721 cm^{-1}.
HRMS (ESI) *m/z*: $[M+ H]^+$ calcd. for $[C_{20}H_{28}BrO_4N + H]^+$ 426.1280, found 426.1274.
$[\alpha]^{25}_{589}$ = +49.0 (*c* = 0.63, $CHCl_3$).

Suzuki-Miyaura Coupling of (+)-**18:**



A round-bottom flask was charged with (+)-**18** (172 mg, 0.417 mmol, 1.0 equiv.) and benzene boronic acid (61 mg, 0.501 mmol, 1.2 equiv.) in a mixture of benzene (4 mL), EtOH (1 mL), and water (1 mL) at room temperature under argon atmosphere. Next, potassium carbonate (231 mg, 1.67 mmol, 4.0 equiv.) was added to the reaction mixture followed by the addition of catalyst, tetrakis(triphenylphosphine)palladium(0) (9.6 mg, 0.008 mmol, 0.02 equiv.) at the same temperature. Then the reaction mixture was placed on a pre-heated oil bath maintaining temperature of 80 °C. Upon completion of the reaction (10 h), as monitored by TLC analysis, it was extracted with 50% EtOAc in *n*-hexane (6 mL X 3). The combined organic layers were washed with brine (4 mL X 1) and dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude product was purified by flash chromatography with 30% EtOAc in *n*-hexane to furnish (+)-**21** as white foam (148.5 g, 87% yield).



Methyl (1S,2S,4aS,10aR)-7-amino-2-hydroxy-8-methoxy-1,4a-dimethyl-6-phenyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**21**]**:** (+)-**21** was obtained as a white foam (0.417 mmol scale, 148.5 mg, 87% yield); R_f = 0.32 (30% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 – 7.85 (m, 1H), 7.48 – 7.45 (m, 3H), 7.40 – 7.34 (m, 2H), 6.86 (s, 1H), 4.10 – 4.04 (m, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.07 – 3.00 (m, 1H), 2.79 (ddd, *J* = 17.7, 11.5, 7.7 Hz, 1H), 2.31 (dt, *J* = 13.2, 3.4 Hz, 1H), 2.15 (dd, *J* = 12.5, 2.1 Hz, 1H), 1.90 – 1.85 (m, 2H), 1.81 – 1.76 (m, 1H), 1.69 – 1.66 (m, 1H), 1.53 – 1.48 (m, 1H), 1.28 (s, 3H), 1.25 (s, 3H).

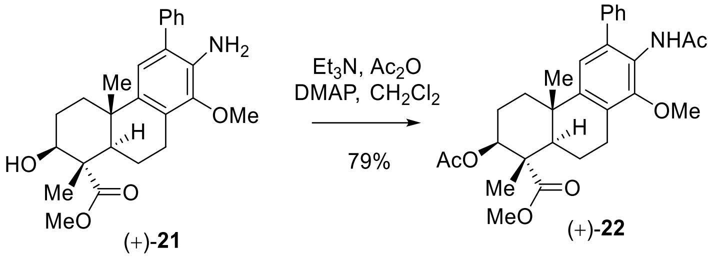
^{13}C NMR (125 MHz, $CDCl_3$): δ 177.9, 144.4, 139.7, 139.6, 134.7, 129.1, 128.8, 128.6, 127.8, 127.1, 126.8, 121.7, 119.8, 75.3, 58.4, 53.7, 52.3, 45.6, 37.0, 36.6, 27.4, 25.5, 24.5, 20.9, 10.7.

IR (neat) υ_{max} 3496, 3389, 2913, 2863, 1710, 1569, 1455, 1243, 915, 540 cm^{-1}.

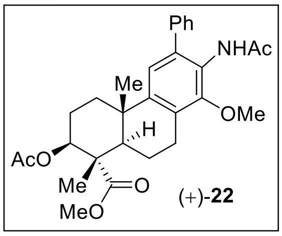
HRMS (ESI) *m/z*: [M+ H]$^+$ calcd. for [$C_{25}H_{31}O_4N$ + H]$^+$ 410.2331, found 410.2345.

$[\alpha]^{25}_{589}$ = +30.5 (*c* = 0.79, $CHCl_3$)

Synthesis of 2-phenylacetanilide [(+)-22]:



In an oven dried round-bottom flask, (+)-**21** (132 mg, 0.322 mmol, 1.0 equiv.) was taken in dry CH_2Cl_2 (6 mL). To the solution was added Et_3N (139 µL, 0.998 mmol., 3.1 equiv.) and catalytic amount of DMAP (4 mg, 0.032 mmol., 0.1 equiv.) at 25 °C. Acetic anhydride (82 µL, 0.805 mmol., 2.5 equiv.) was added at 25 ºC and it was allowed to stir until the full consumption of starting material (8 h). Upon completion of the reaction (as monitored by TLC analysis), water (4 mL) was added and then extracted with CH_2Cl_2 (6 mL X 2). The organic layers were separated and dried over Na_2SO_4 and concentrated on a rotary evaporator under the reduced pressure. The crude bis-acetate was purified by flash column chromatography with 45- 50% EtOAc in *n*-hexane to afford (+)-**22** as yellow liquid (125.6 mg, 79% yield).



Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-acetamido-2-acetoxy-8-methoxy-1,4a-dimethyl-6-phenyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**22**]**:** (+)-**22** was obtained as a yellow liquid (0.322 mmol scale, 125.6 mg, 79% yield); R$_f$ = 0.25 (40% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.30 (m, 5H), 7.00 (s, 1H), 6.67 (s, 1H), 5.20 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.03 – 2.96 (m, 1H), 2.79 – 2.70 (m, 1H), 2.31 (d, *J* = 11.9 Hz, 1H), 2.23 – 2.20 (m, 1H), 1.99 (s, 3H), 1.97 (s, 3H), 1.81 (s, 1H), 1.75 (s, 2H), 1.65 (s, 2H), 1.29 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 176.4, 170.1, 169.6, 153.6, 149.2, 139.7, 138.8, 129.0, 128.6, 128.3, 127.2, 124.8, 122.2, 76.7, 60.0, 52.5, 52.0, 45.2, 37.1, 36.4, 25.1, 24.5, 24.0, 23.2, 21.1, 20.5, 11.7.

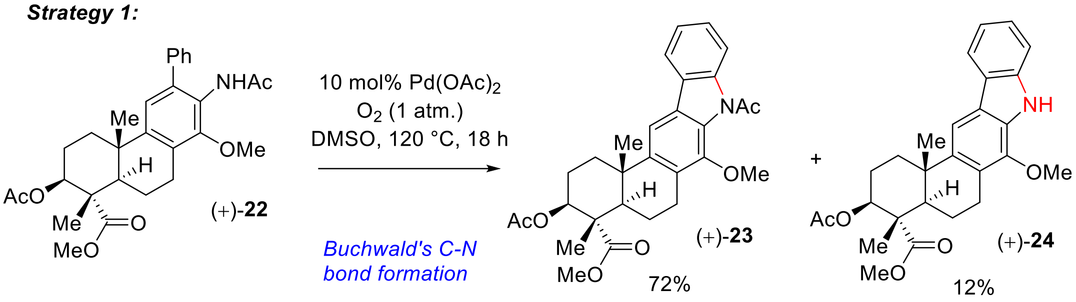
IR(neat) υ_{max} 2971, 2755, 1816, 1739, 1627, 1201, 1069, 981 cm^{-1}.

HRMS(ESI) *m/z*: $[M+ H]^+$ calcd. for $[C_{29}H_{35}NO_6 + H]^+$ 494.2543, found 494.2564.

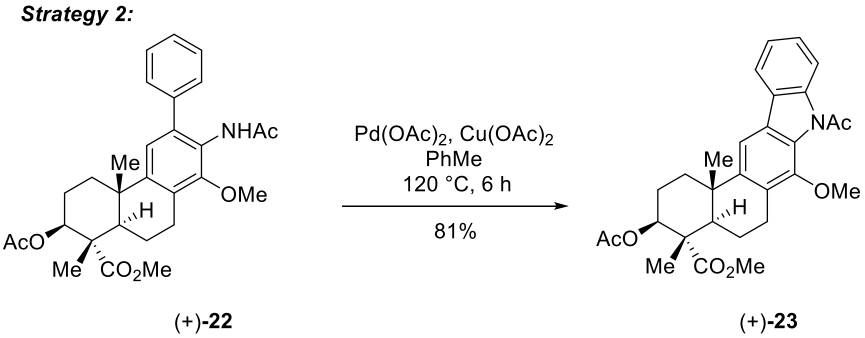
$[\alpha]^{25}_{589} = +91.0$ ($c = 0.73$, $CHCl_3$)

Buchwald's Oxidative C-N bond Formation of (+)-22:

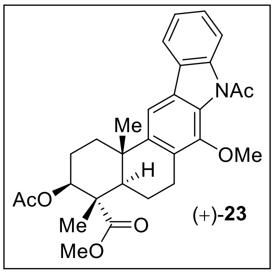
Strategy 1:



2-Phenyl acetanilide derivative (+)-**22** (102 mg, 0.207 mmol, 1.0 equiv.) was taken in DMSO (5 mL) under argon atmosphere and $Pd(OAc)_2$ (4.7 mg, 0.021 mmol, 0.1 equiv.) was added to it. The reaction mixture was sonicated and degassed and refilled with O_2 from the double manifold (this sequence was carried out 3 times). The sealed tube was set into a pre-heated oil bath at 120 °C and stirred for 18 h (complete consumption of starting materials). After cooling it to room temperature, the reaction mixture was diluted with water (6 mL) and extracted with 50% EtOAc in *n*-hexane (8 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in a rotary evaporator under reduced pressure. The residue was purified by silica gel column chromatography with 10% EtOAc in *n*-hexane to afford to provide (+)-**23** as brown foam (67 mg, 72% yield) and (+)-**24** as white foam (10 mg, 12% yield).



In an oven-dried sealed tube, compound (+)-**22** (40.0 mg, 0.081 mmol, 1.0 equiv.) was taken in dry toluene (2 mL). The reaction mixture was degassed by purging Argon gas for 10 min after that purged with O_2 gas for 20 min. Next, $Pd(OAc)_2$ (2.0 mg, 0.0081 mmol, 0.1 equiv.), and $Cu(OAc)_2$ (3.0 mg, 0.016 mmol, 0.2 equiv.) were added to the solution and the tube was sealed. Then the reaction mixture was allowed to heat to 120 °C on a preheated oil bath for 6 h. After completion of the reaction (monitored by TLC) the crude reaction mixture was diluted with water (3 mL) and EtOAc (3 mL). The resulting biphasic mixture was then transferred to a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with EtOAc (5 mL X 2). The combined organic layer was concentrated under vacuum and the crude product was purified by column chromatography (10% Ethyl acetate in *n*-hexane) to afford (+)-**23**.

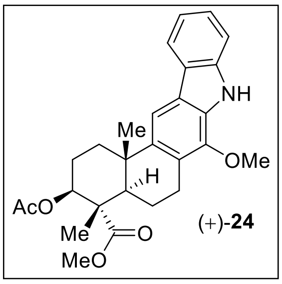


Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-acetoxy-8-acetyl-7-methoxy-4,13*b*-dimethyl-2,3,4,4*a*,5,6,8,13*b*-octahydro-1*H*-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**23**]: (+)-**23** was obtained as light yellow coloured liquid (strategy 1: 0.207 mmol scale, 67 mg, 72% yield and strategy 2: 0.081 mmol scale of reaction; 32.0 mg; 81% yield); R_f = 0.30 (15% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 – 8.27 (m, 1H), 7.88 (ddd, *J* = 7.6, 1.4, 0.7 Hz, 1H), 7.64 (s, 1H), 7.45 – 7.41 (m, 1H), 7.35 – 7.31 (m, 1H), 5.27 – 5.23 (m, 1H), 3.69 (s, 3H), 3.68 (s, 3H), 3.13 (ddd, *J* = 18.1, 6.8, 1.5 Hz, 1H), 2.89 – 2.80 (m, 1H), 2.61 (s, 3H), 2.53 (dd, *J* = 9.8, 3.5 Hz, 1H), 2.29 – 2.25 (m, 1H), 2.06 – 2.03 (m, 1H), 2.02 (s, 3H), 1.95 – 1.91 (m, 1H), 1.86 (d, *J* = 10.1 Hz, 2H), 1.52 – 1.47 (m, 1H), 1.34 (s, 3H), 1.32 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 176.4, 172.7, 170.1, 146.7, 145.1, 140.6, 129.0, 128.0, 127.7, 127.5, 125.9, 123.5, 119.2, 115.6, 111.3, 76.8, 59.0, 52.5, 52.1, 45.4, 37.3, 37.0, 26.6, 25.5, 24.7, 24.1, 21.12, 20.6, 11.8.

IR(neat) υ_{max} 3410, 2873, 2847, 1745, 1683, 1499, 1278, 968 cm^{-1}.
HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{29}H_{33}NO_6 + H]^+$ 492.2386, found 492.2384.
$[\alpha]^{25}_{589}$ = +53.0 (*c* = 0.63, $CHCl_3$)



(+)-**24**

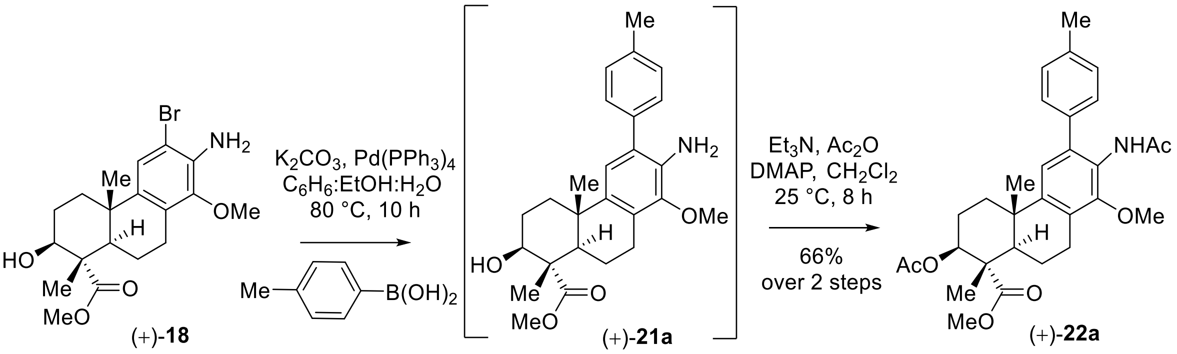
Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-hydroxy-7-methoxy-4,13b-dimethyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-b]carbazole-4-carboxylate [(+)-**24**]**:** (+)-**24** was obtained as a white foam (0.207 mmol scale, 10 mg, 12% yield); R_f = 0.3 (30% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.35 (s, 1H), 8.61 (d, *J* = 8.3 Hz, 1H), 8.28 (s, 1H), 8.10 (d, *J* = 7.9 Hz, 1H), 7.90 (q, *J* = 6.2, 5.0 Hz, 1H), 7.79 – 7.71 (m, 1H), 5.30 (dd, *J* = 11.5, 4.7 Hz, 1H), 4.15 (s, 3H), 3.73 (s, 3H), 3.72 – 3.68 (m, 1H), 3.36 – 3.28 (m, 1H), 3.04 (ddd, *J* = 18.6, 11.1, 8.1 Hz, 1H), 2.69 (dd, *J* = 9.4, 3.3 Hz, 1H), 2.37 (dd, *J* = 12.7, 2.3 Hz, 1H), 2.06 (s, 3H), 2.04 – 1.96 (m, 3H), 1.57 (dd, *J* = 13.4, 8.0 Hz, 1H), 1.40 (d, *J* = 3.4 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 176.3, 170.1, 151.6, 133.4, 129.9, 127.8, 125.5, 123.6, 121.9, 120.1, 119.4, 115.3, 112.8, 111.5, 76.7, 61.9, 52.5, 52.1, 45.1, 37.8, 36.9, 25.6, 24.5, 24.1, 21.1, 20.4, 11.8.

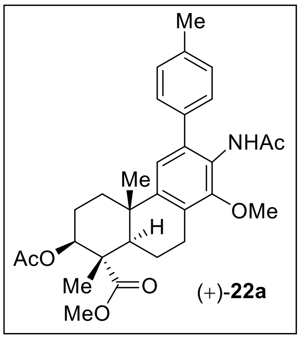
IR (neat) υ_{max} 3403, 3387, 2947, 2858, 1705, 1596, 1193, 783 cm^{-1}.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{27}H_{32}O_5N + H]^+$ 450.2281, found 450.2263.
$[\alpha]^{25}_{589}$ = +36.5 (*c* = 0.52, $CHCl_3$)

Synthesis of acetanilide (+)-**22a:**



A round-bottom flask was charged with (+)-**18** (50 mg, 0.121 mmol, 1.0 equiv.) and *p*-tolylboronic acid (20 mg, 0.146 mmol, 1.2 equiv.) in a mixture of benzene (3 mL), EtOH (1 mL), and water (1 mL) at room temperature under argon atmosphere. Next, potassium carbonate (67 mg, 0.49 mmol, 4.0 equiv.) was added to the reaction mixture followed by the addition of catalyst, tetrakis(triphenylphosphine)palladium(0) (2.8 mg, 0.0025 mmol, 0.02 equiv.) at the same temperature. Then the reaction mixture was placed on a pre-heated oil bath maintaining temperature of 80 °C. Upon completion of the reaction (10 h), as monitored by TLC analysis, it was extracted with 50% EtOAc in *n*-hexane (4 mL X 3). The combined organic layers were washed with brine (2 mL X 1) and dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude product was charged for next step.

In an oven dried round-bottom flask, (+)-**21a** (0.121 mmol, 1.0 equiv.) was taken in dry CH_2Cl_2 (3 mL). To the solution was added Et_3N (52 µL, 0.375 mmol., 3.1 equiv.) and catalytic amount of DMAP (1.5 mg, 0.0121 mmol., 0.1 equiv.) at 25 °C. Acetic anhydride (29 µL, 0.303 mmol., 2.5 equiv.) was added at 25 °C and it was allowed to stir until the full consumption of starting material (8 h). Upon completion of the reaction (as monitored by TLC analysis), water (2 mL) was added and then extracted with CH_2Cl_2 (4 mL X 2). The organic layers were separated and dried over Na_2SO_4 and concentrated on a rotary evaporator under the reduced pressure. The crude bis-acetate was purified by flash column chromatography with 45-50% EtOAc in *n*-hexane to afford (+)-**22a** as yellow liquid (41 mg, 66% yield over two steps).



Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-acetamido-2-acetoxy-8-methoxy-1,4a-dimethyl-6-(p-tolyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**21a**]**:** (+)-**21a** was obtained as yellow liquid (0.121 mmol scale, 41 mg, 66% yield over two steps); R*f* = 0.25 (40% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, *J* = 10.0 Hz, 4H), 6.98 (s, 1H), 6.72 (s, 1H), 5.20 (dd, *J* = 11.1, 4.4 Hz, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 3.02 – 2.95 (m, 1H), 2.77 – 2.69 (m, 1H), 2.36 (s, 3H), 2.32 – 2.27 (m, 1H), 2.22 – 2.18 (m, 1H), 1.99 (s, 6H), 1.82 – 1.70 (m, 4H), 1.46 – 1.40 (m, 1H), 1.29 (s, 3H), 1.23 (s, 3H).

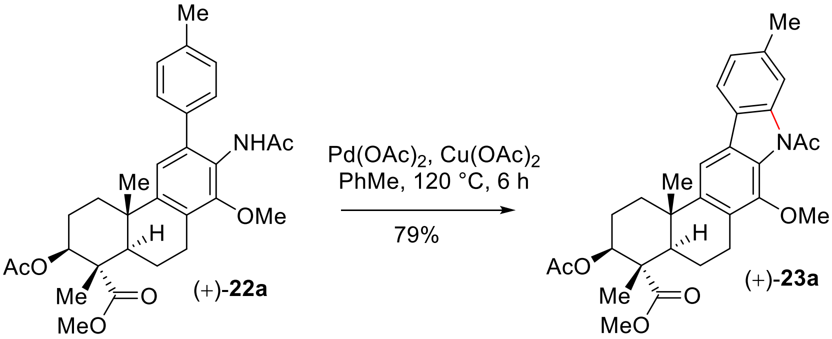
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 176.4, 170.1, 169.6, 153.6, 149.2, 138.7, 136.9, 136.8, 129.4, 129.0, 128.4, 124.8, 122.2, 77.3, 59.9, 52.4, 52.1, 45.2, 37.1, 36.7, 36.4, 25.1, 24.7, 24.5, 23.99, 23.2, 21.2, 21.2, 20.5, 11.7.

IR (neat) υ_{max}: 3491, 3384, 2917, 2863, 1730, 1579, 1465, 1246, 928, 565 cm^{-1}.

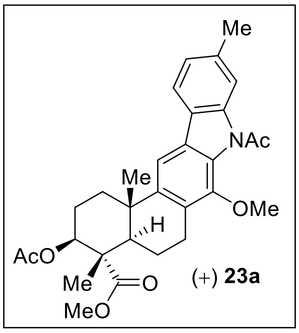
HRMS (ESI) *m/z*: $[M+ H]^+$ calcd. for $[C_{30}H_{37}O_6N + H]^+$ 508.2699, found 508.2695.

$[\alpha]^{25}_{589}$ = +36.8 (*c* = 0.79, $CHCl_3$).

Synthesis of (+)-**22a through oxidative C-N bond formation of** (+)-**22a:**



In an oven-dried sealed tube, compound (+)-**22a** (30.0 mg, 0.059 mmol, 1.0 equiv.) was taken in dry toluene (2 mL). The reaction mixture was degassed by purging Argon gas for 10 min after that purged with O_2 gas for 20 min. Next, $Pd(OAc)_2$ (1.3 mg, 0.0059 mmol, 0.1 equiv.), and $Cu(OAc)_2$ (2.1 mg, 0.012 mmol, 0.2 equiv.) were added to the solution and the tube was sealed. Then the reaction mixture was allowed to heat to 120 °C on a preheated oil bath for 6 h. After completion of the reaction (monitored by TLC) the crude reaction mixture was diluted with water (2 mL) and EtOAc (3 mL). The resulting biphasic mixture was then transferred to a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with EtOAc (3 mL X 2). The combined organic layer was concentrated under vacuum and the crude product was purified by column chromatography (15% Ethyl acetate in *n*-hexane) to afford (+)-**23a (**23.5 mg, 79% yield).



Methyl (3*S*,4*S*,4a*R*,13b*S*)-8-acetyl-3-hydroxy-7-methoxy-4,10,13b-trimethyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**23a**]: (+)-**23a** was obtained as light yellow coloured liquid (0.059 mmol scale of reaction; 23.5 mg; 79% yield); R_f = 0.30 (15% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 – 8.10 (m, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.59 (s, 1H), 7.15 (ddt, *J* = 7.8, 1.5, 0.6 Hz, 1H), 5.28 – 5.21 (m, 1H), 3.68 (s, 3H), 3.67 (s, 3H), 3.11 (ddd, *J* = 18.1, 6.9, 1.6 Hz, 1H), 2.84 (ddd, *J* = 18.4, 11.3, 7.9 Hz, 1H), 2.60 (s, 3H), 2.54 – 2.51 (m, 1H), 2.50 (s, 3H), 2.27 (dd, *J* = 12.6, 2.3 Hz, 1H), 2.07 – 2.02 (m, 1H), 2.01 (s, 3H), 1.97 – 1.84 (m, 3H), 1.52 – 1.46 (m, 1H), 1.34 (s, 3H), 1.31 (s, 3H).

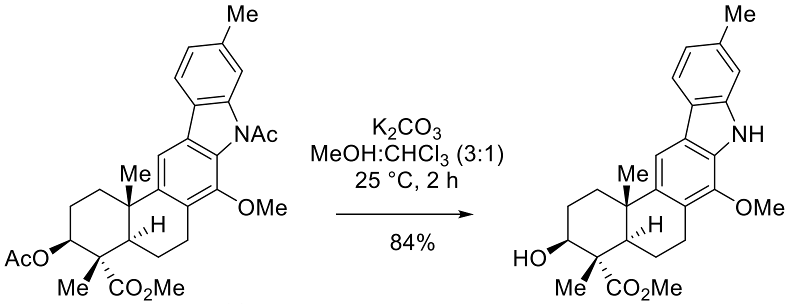
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 176.4, 172.9, 170.1, 146.6, 145.1, 140.9, 137.8, 129.0, 127.8, 127.4, 124.7, 123.5, 118.8, 115.8, 111.0, 76.8, 58.9, 52.4, 52.1, 45.4, 37.3, 37.0, 26.6, 25.5, 24.6, 24.1, 22.2, 21.1, 20.7, 11.8.

IR(neat) υ_{max} :3417, 2853, 2897, 1725, 1689, 1501, 1278, 978 cm^{-1}.

HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{30}H_{35}O_6N + H]^+$ 506.2543, found 506.2547.

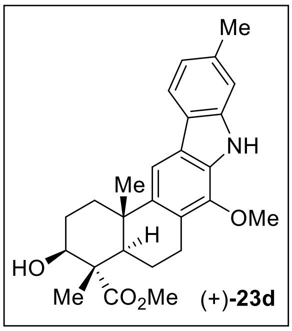
$[\alpha]^{25}_{589} = +56.0$ ($c = 0.63$, $CHCl_3$).

Synthesis of pentacyclic carbazole derivative (+)-**23a:**



(+)-**23a** (+)-**23d**

In an oven-dried round bottom flask compound (+)-**23a** (15.0 mg, 0.030 mmol, 1.0 equiv.) was taken in a mixture of methanol and chloroform [MeOH: $CHCl_3$ (3:1)]. To the solution K_2CO_3 (9.0 mg, 0.065 mmol, 2.2 equiv.) was added and then the reaction mixture was stirred at 25 °C for 2 h. After completion of the reaction (monitored by TLC) the reaction mixture was directly evaporated under reduced pressure. The mixture was then extracted with EtOAc (5 mL X 3). The combined organic layers were washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. Then the crude product was purified by flash chromatography with 30% EtOAc in *n*-hexane to afford (+)-**23d** as yellow liquid.



(+)-**23d**

Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-hydroxy-7-methoxy-4,10,13b-trimethyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**23d**]**:** (+)-**23d** was obtained as yellow liquid (0.030 mmol scale of reaction; 10.6 mg, 85% yields). $R_f = 0.3$ (30% EtOAc in *n*-hexane).

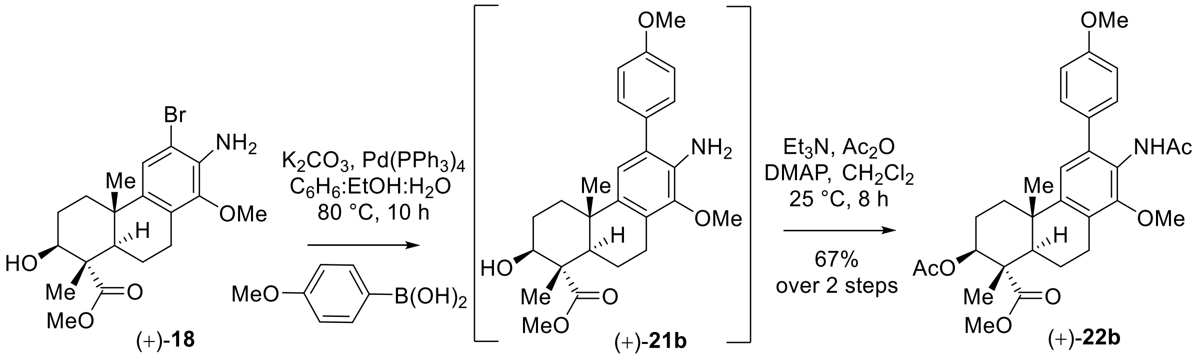
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.67 (s, 1H), 7.19 (s, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 4.08 (dd, *J* = 11.1, 4.5 Hz, 1H), 3.91 (s, 3H), 3.74 (s, 3H), 3.16 (dd, *J* = 17.5, 6.6 Hz, 1H), 2.91 (ddd, *J* = 18.1, 11.2, 7.8 Hz, 1H), 2.56 – 2.51 (m, 1H), 2.50 (s, 3H), 2.19 (dd, *J* = 12.5, 2.3 Hz, 1H), 1.96 – 1.91 (m, 2H), 1.81 (s, 2H), 1.55 – 1.50 (m, 1H), 1.29 (s, 3H), 1.29 (s, 3H).

IR(neat) υ_{max}: 3525, 2944, 1655, 1460, 1445, 1172, 823, 776, 665 cm^{-1}.

HRMS(ESI) *m/z*: $[M+ Na]^+$ calcd. for $[C_{26}H_{31}NO_5 + H]^+$ 422.2331, found 422.2325.

$[\alpha]^{25}_{589}$ = +38.7 (*c* = 0.43, CH_3OH).

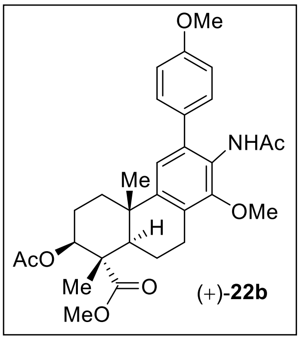
Synthesis of acetanilide (+)-**22b:**



A round-bottom flask was charged with (+)-**18** (50 mg, 0.121 mmol, 1.0 equiv.) and benzene boronic acid (22 mg, 0.146 mmol, 1.2 equiv.) in a mixture of benzene (3 mL), EtOH (1 mL), and water (1 mL) at room temperature under argon atmosphere. Next, potassium carbonate (67 mg, 0.49 mmol, 4.0 equiv.) was added to the reaction mixture followed by the addition of catalyst, tetrakis(triphenylphosphine)palladium(0) (2.8 mg, 0.0025 mmol, 0.02 equiv.) at the same temperature. Then the reaction mixture was placed on a pre-heated oil bath maintaining temperature of 80 °C. Upon completion of the reaction (10 h), as monitored by TLC analysis, it was extracted with 60% EtOAc in *n*-hexane (4 mL X 3). The combined organic layers were washed with brine (2 mL X 1) and dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude product was charged for next step.

Next, in an oven dried round-bottom flask, (+)-**21b** (0.121 mmol, 1.0 equiv.) was taken in dry CH_2Cl_2 (3 mL). To the solution was added Et_3N (52 μL, 0.375 mmol., 3.1 equiv.) and catalytic amount of DMAP (1.5 mg, 0.0121 mmol., 0.1 equiv.) at 25 °C. Acetic anhydride (29 μL, 0.303 mmol., 2.5 equiv.) was added at 25 ºC and it was allowed to stir until the full consumption of starting material (8 h). Upon completion of the reaction (as monitored by TLC analysis), water

(2 mL) was added and then extracted with CH_2Cl_2 (4 mL X 2). The organic layers were separated and dried over Na_2SO_4 and concentrated on a rotary evaporator under the reduced pressure. The crude bis-acetate was purified by flash column chromatography with 45- 50% EtOAc in *n*-hexane to afford (+)-**22b** as yellow liquid (41.6 mg, 67% yield over two steps).



(+)-**22b**

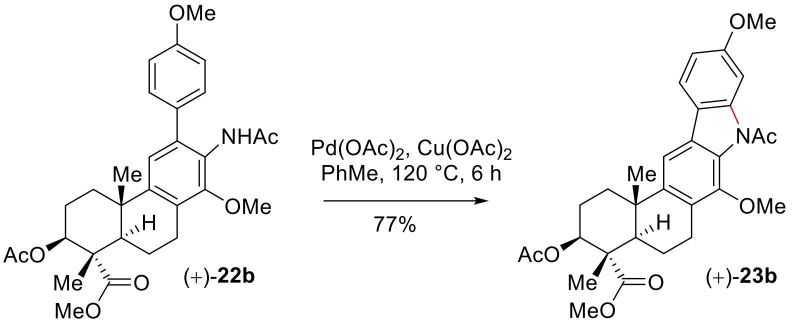
Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-acetamido-2-acetoxy-8-methoxy-6-(4-methoxyphenyl)-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**22b**]: (+)-**22b** was obtained as a white foam (0.121 mmol scale, 41.6 mg, 67% yield); R_f = 0.35 (60% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (s, 1H), 7.06 – 6.90 (m, 4H), 6.78 (s, 1H), 5.23 (dd, *J* = 11.4, 4.4 Hz, 1H), 3.85 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.02 (dd, *J* = 18.0, 6.5 Hz, 1H), 2.77 (td, *J* = 11.0, 5.7 Hz, 1H), 2.34 (d, *J* = 12.1 Hz, 1H), 2.24 (d, *J* = 12.3 Hz, 1H), 2.02 (s, 6H), 1.90 – 1.81 (m, 2H), 1.77 (d, *J* = 11.2 Hz, 2H), 1.56 – 1.45 (m, 1H), 1.32 (s, 3H), 1.27 (s, 3H).

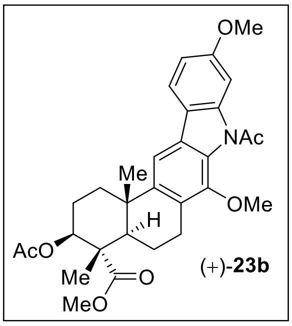
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 176.4, 170.1, 169.7, 158.7, 153.7, 149.2, 138.5, 132.1, 130.1, 129.7, 128.3, 124.9, 122.1, 114.2, 113.7, 77.3, 59.9, 55.3, 52.4, 52.1, 45.2, 37.1, 36.4, 25.1, 24.7, 24.5, 24.0, 21.1, 20.5, 11.7.

IR (neat) υ_{max} :3466, 3359, 2933, 2763, 1750, 1519, 1475, 1293, 955, 520 cm^{-1}.
HRMS (ESI) *m/z*: [M+ H]$^+$ calcd. for $[C_{30}H_{37}O_7N + H]^+$ 524.2648, found 524.2645.
$[\alpha]^{25}_{589}$ = +40.5 (*c* = 0.79, $CHCl_3$).

Synthesis of (+)-23b through oxidative C-N bond formation of (+)-22b:



In an oven-dried sealed tube, compound (+)-**22b** (30.0 mg, 0.057 mmol, 1.0 equiv.) was taken in dry toluene (2 mL). The reaction mixture was degassed by purging Argon gas for 10 min after that purged with O_2 gas for 20 min. Next, $Pd(OAc)_2$ (1.3 mg, 0.0057 mmol, 0.1 equiv.), and $Cu(OAc)_2$ (2.1 mg, 0.012 mmol, 0.2 equiv.) were added to the solution and the tube was sealed. Then the reaction mixture was allowed to heat to 120 °C on a preheated oil bath for 6 h. After completion of the reaction (monitored by TLC) the crude reaction mixture was diluted with water (2 mL) and EtOAc (3 mL). The resulting biphasic mixture was then transferred to a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with EtOAc (3 mL X 2). The combined organic layer was concentrated under vacuum and the crude product was purified by column chromatography (20% Ethyl acetate in *n*-hexane) to afford (+)-**23b (**22.8 mg, 77% yield).



Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-acetoxy-8-acetyl-7,10-dimethoxy-4,13b-dimethyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**23b**]: (+)-**23b** was obtained as light yellow coloured liquid (0.057 mmol scale of reaction; 22.8 mg; 77% yield); R_f = 0.25 (20% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, *J* = 2.3 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.57 (s, 1H), 6.96 (dd, *J* = 8.5, 2.3 Hz, 1H), 5.28 (dd, *J* = 11.3, 4.5 Hz, 1H), 3.94 (s, 3H), 3.72 (s, 3H), 3.70 (s, 3H), 3.13 (ddd, *J* = 17.8, 6.8, 1.5 Hz, 1H), 2.87 (ddd, *J* = 18.4, 11.3, 7.8 Hz, 1H), 2.64 (s, 3H), 2.57 – 2.53 (m, 1H), 2.30 (dd, *J* = 12.6, 2.3 Hz, 1H), 2.10 – 2.06 (m, 1H), 2.05 (s, 3H), 1.96 – 1.87 (m, 3H), 1.52 (dq, *J* = 5.8, 2.0 Hz, 1H).

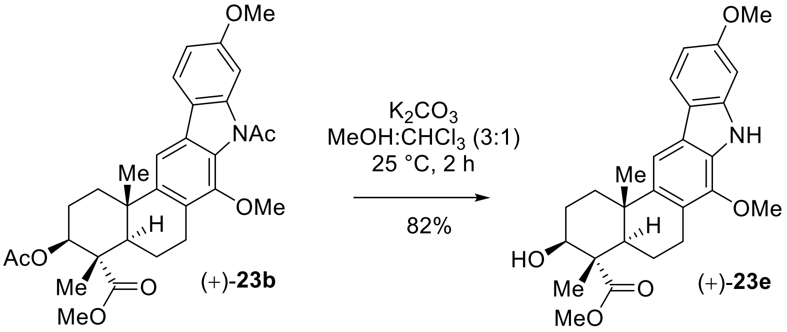
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 176.4, 173.0, 170.1, 159.9, 146.7, 145.1, 141.8, 128.9, 127.8, 126.5, 119.8, 119.2, 111.9, 110.5, 100.0, 59.0, 55.7, 52.4, 52.1, 45.4, 37.3, 37.0, 26.6, 25.5, 24.6, 24.1, 21.1, 20.7, 11.8.

IR(neat) υ_{max} :3430, 2868, 2797, 1795, 1653, 1539, 1278, 978 cm^{-1}.

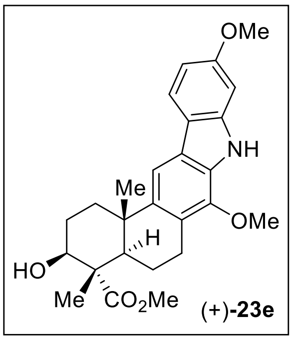
HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{30}H_{35}O_7N + H]^+$ 522.2492, found 522.2496.

$[\alpha]^{25}_{589} = +49.0$ (*c* = 0.63, $CHCl_3$).

Synthesis of pentacyclic carbazole derivative (+)-**23b:**



In an oven-dried round bottom flask compound (+)-**23b** (15.0 mg, 0.029 mmol, 1.0 equiv.) was taken in a mixture of methanol and chloroform [MeOH: $CHCl_3$ (3:1)]. To the solution K_2CO_3 (8.7 mg, 0.063 mmol, 2.2 equiv.) was added and then the reaction mixture was stirred at 25 °C for 2 h. After completion of the reaction (monitored by TLC) the reaction mixture was directly evaporated under reduced pressure. The mixture was then extracted with EtOAc (5 mL X 3). The combined organic layers were washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. Then the crude product was purified by flash chromatography with 40% EtOAc in *n*-hexane to afford (+)-**23e** as yellow liquid.



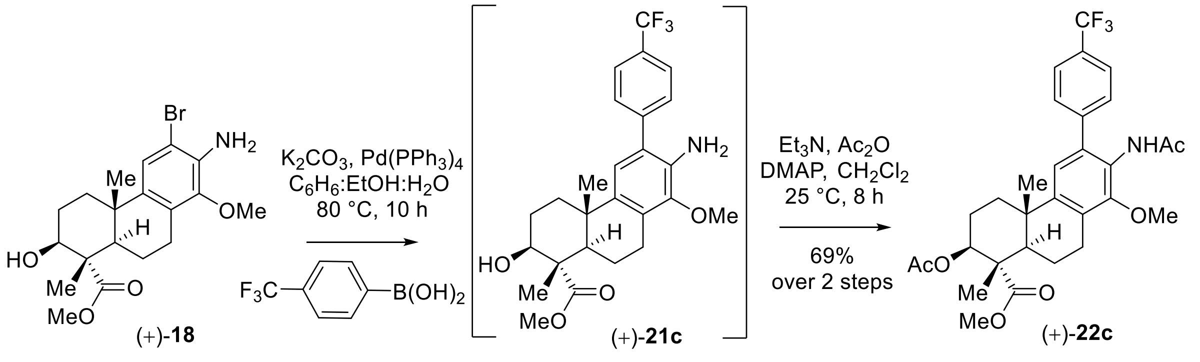
Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-hydroxy-7,10-dimethoxy-4,13b-dimethyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**23e**]**:** (+)-**23e** was obtained as colorless liquid (0.029 mmol scale of reaction; 10.4 mg, 82% yields). R*f* = 0.3 (40% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.62 (s, 1H), 6.90 (d, *J* = 2.2 Hz, 1H), 6.80 (dd, *J* = 8.5, 2.2 Hz, 1H), 4.08 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.74 (s, 3H), 3.19 – 3.11 (m, 1H), 2.90 (ddd, *J* = 18.1, 11.2, 7.8 Hz, 1H), 2.57 – 2.50 (m, 1H), 2.18 (dd, *J* = 12.5, 2.3 Hz, 1H), 1.96 – 1.89 (m, 2H), 1.84 – 1.77 (m, 2H), 1.54 – 1.49 (m, 1H), 1.29 (s, 3H), 1.29 (s, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 178.0, 158.9, 142.5, 141.8, 141.2, 130.9, 124.2, 123.8, 120.8, 118.0, 110.7, 107.9, 95.1, 59.8, 55.6, 53.8, 52.3, 45.6, 37.6, 37.4, 27.5, 25.9, 24.4, 21.0, 10.8.

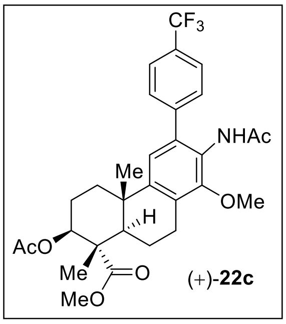
IR(neat) υ_{max}: 3537, 2964, 1685, 1360, 1475, 1272, 803, 746, 655 cm^{-1}.
HRMS(ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{26}H_{31}NO_5 + H]^+$ 438.2281, found 438.2275.
$[\alpha]^{25}_{589}$ = +42.7 (*c* = 0.43, CH_3OH).

Synthesis of acetanilide (+)-**22c:**



A round-bottom flask was charged with (+)-**18** (50 mg, 0.121 mmol, 1.0 equiv.) and benzene boronic acid (27.7 mg, 0.146 mmol, 1.2 equiv.) in a mixture of benzene (3 mL), EtOH (1 mL), and water (1 mL) at room temperature under argon atmosphere. Next, potassium carbonate (67 mg, 0.49 mmol, 4.0 equiv.) was added to the reaction mixture followed by the addition of catalyst, tetrakis(triphenylphosphine)palladium(0) (2.8 mg, 0.0025 mmol, 0.02 equiv.) at the same temperature. Then the reaction mixture was placed on a pre-heated oil bath maintaining temperature of 80 °C. Upon completion of the reaction (10 h), as monitored by TLC analysis, it was extracted with 60% EtOAc in *n*-hexane (4 mL X 3). The combined organic layers were washed with brine (2 mL X 1) and dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude product was charged for next step.

Next, In an oven dried round-bottom flask, (+)-**21C** (0.121 mmol, 1.0 equiv.) was taken in dry CH_2Cl_2 (3 mL). To the solution was added Et_3N (52 µL, 0.375 mmol., 3.1 equiv.) and catalytic amount of DMAP (1.5 mg, 0.0121 mmol., 0.1 equiv.) at 25 °C. Acetic anhydride (29 µL, 0.303 mmol., 2.5 equiv.) was added at 25 °C and it was allowed to stir until the full consumption of starting material (8 h). Upon completion of the reaction (as monitored by TLC analysis), water (2 mL) was added and then extracted with CH_2Cl_2 (4 mL X 2). The organic layers were separated and dried over Na_2SO_4 and concentrated on a rotary evaporator under the reduced pressure. The crude bis-acetate was purified by flash column chromatography with 45- 50% EtOAc in *n*-hexane to afford (+)-**22c** as yellow liquid (46.8 mg, 69% yield over two steps).



Methyl (1*S*,2*S*,4a*S*,10a*R*)-7-acetamido-2-acetoxy-8-methoxy-1,4a-dimethyl-6-(4-(trifluoromethyl)phenyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate [(+)-**22c**]**:** (+)-**22c** was obtained as yellow liquid (0.121 mmol scale, 46.8 mg, 69% yield); $R_f = 0.3$ (50% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 6.97 (s, 1H), 6.86 (s, 1H), 5.19 (dd, *J* = 11.3, 4.5 Hz, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.99 (dd, *J* = 18.1, 6.5 Hz, 1H), 2.74 (ddd, *J* = 18.3, 11.2, 7.7 Hz, 1H), 2.30 (d, *J* = 12.3 Hz, 1H), 2.20 (dd, *J* = 12.5, 2.1 Hz, 1H), 1.99 (s, 3H), 1.96 (s, 3H), 1.85 – 1.71 (m, 4H), 1.42 (dd, *J* = 13.7, 7.7 Hz, 1H), 1.29 (s, 3H), 1.24 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.28.

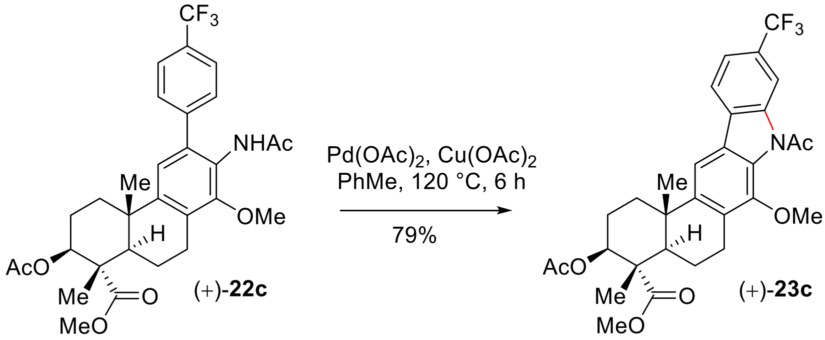
^{13}C{^{19}F} {^{1}H} NMR (101 MHz, $CDCl_3$): δ 176.4, 170.2, 169.6, 153.5, 149.5, 143.7, 137.6, 129.6, 129.3, 128.9, 125.2, 124.9, 124.3, 122.2, 76.7, 60.1, 52.6, 52.1, 45.3, 37.2, 36.4, 25.2, 24.6, 24.0, 23.3, 21.2, 20.5, 11.8.

IR (neat) υ_{max} :3445, 3369, 2913, 2863, 1710, 1569, 1455, 1320, 1243, 915, 540 cm^{-1}.

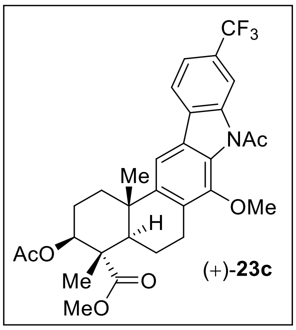
HRMS (ESI) *m/z*: $[M+ H]^+$ calcd. for $[C_{30}H_{34}O_6NF_3 + H]^+$ 562.2416, found 562.2426.

$[\alpha]^{25}_{589}$ = +48.5 (*c* = 0.79, $CHCl_3$).

Synthesis of (+)**-23c through oxidative C-N bond formation of** (+)**-22c:**



In an oven-dried sealed tube, compound (+)-**22c** (30.0 mg, 0.053 mmol, 1.0 equiv.) was taken in dry toluene (2 mL). The reaction mixture was degassed by purging Argon gas for 10 min after that purged with O_2 gas for 20 min. Next, $Pd(OAc)_2$ (1.2 mg, 0.0053 mmol, 0.1 equiv.), and $Cu(OAc)_2$ (2.0 mg, 0.011 mmol, 0.2 equiv.) were added to the solution and the tube was sealed. Then the reaction mixture was allowed to heat to 120 °C on a preheated oil bath for 6 h. After completion of the reaction (monitored by TLC) the crude reaction mixture was diluted with water (2 mL) and EtOAc (3 mL). The resulting biphasic mixture was then transferred to a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with EtOAc (3 mL X 2). The combined organic layer was concentrated under vacuum and the crude product was purified by column chromatography (20% Ethyl acetate in *n*-hexane) to afford (+)-**23c (**23.4 mg, 79% yield).



Methyl (3*S*,4*S*,4a*R*,13b*S*)-8-acetyl-3-hydroxy-7-methoxy-4,13b-dimethyl-10-(trifluoromethyl)-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**23c**]: (+)-**23c** was obtained as light yellow coloured liquid (0.053 mmol scale of reaction; 23.4.0 mg; 79% yield); R*f* = 0.30 (15% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 – 8.58 (m, 1H), 7.99 – 7.95 (m, 1H), 7.69 (s, 1H), 7.59 (ddd, *J* = 8.1, 1.6, 0.7 Hz, 1H), 5.25 (dd, *J* = 11.4, 4.7 Hz, 1H), 3.69 (s, 3H), 3.69 (s, 3H), 3.18 – 3.11 (m, 1H), 2.87 (ddd, *J* = 18.5, 11.2, 7.9 Hz, 1H), 2.64 (s, 3H), 2.53 (dd, *J* = 9.7, 3.4 Hz, 1H), 2.29 – 2.25 (m, 1H), 2.07 – 2.03 (m, 1H), 2.02 (s, 3H), 1.95 – 1.85 (m, 3H), 1.54 – 1.49 (m, 1H), 1.34 (s, 3H), 1.32 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$): δ -61.14.

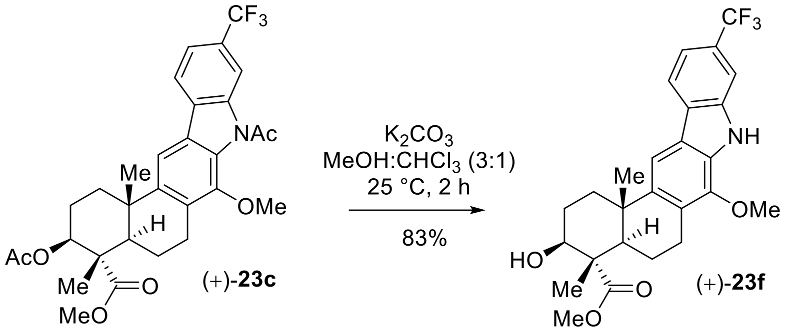
^{13}C{^{19}F} {^{1}H} NMR (101 MHz, $CDCl_3$): δ 176.5, 172.7, 170.2, 147.3, 145.2, 140.0, 129.9, 129.6, 129.3, 128.7, 126.5, 124.6, 120.4, 119.6, 113.1, 112.1, 59.2, 52.6, 52.1, 45.4, 37.5, 37.0, 26.7, 25.6, 24.8, 24.1, 21.2, 20.6, 11.8.

IR(neat) υ_{max} :3422, 2854, 2847, 1745, 1783, 1449, 1278, 958 cm^{-1}.

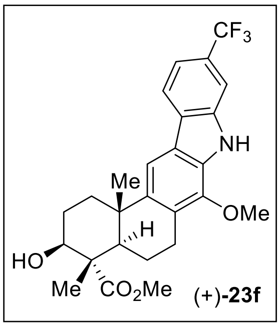
HRMS(ESI) *m/z*: [M+ H]$^+$ calcd. for $[C_{30}H_{32}O_6NF_3 + H]^+$ 560.2260, found 560.2258.

$[\alpha]^{25}_{589}$ = +53.0 (*c* = 0.63, $CHCl_3$).

Synthesis of pentacyclic carbazole derivative (+)-**23f:**



In an oven-dried round bottom flask compound (+)-**23c** (15.0 mg, 0.027 mmol, 1.0 equiv.) was taken in a mixture of methanol and chloroform [MeOH: $CHCl_3$ (3:1)]. To the solution K_2CO_3 (8.2 mg, 0.058 mmol, 2.2 equiv.) was added and then the reaction mixture was stirred at 25 °C for 2 h. After completion of the reaction (monitored by TLC) the reaction mixture was directly evaporated under reduced pressure. The mixture was then extracted with EtOAc (5 mL X 3). The combined organic layers were washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. Then the crude product was purified by flash chromatography with 30% EtOAc in *n*-hexane to afford (+)-**23f** as yellow liquid.


(+)-**23f**

Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-hydroxy-7-methoxy-4,13b-dimethyl-10-(trifluoromethyl)-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-28]: (+)-**28** was obtained as colorless liquid (0.027 mmol scale of reaction; 10.6 mg, 83% yields). R$_f$ = 0.3 (30% EtOAc in *n*-hexane).

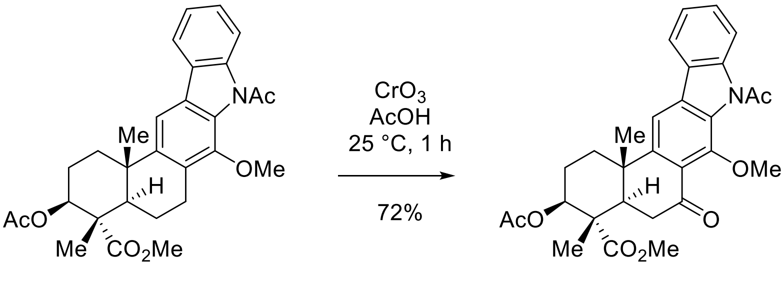
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.76 (s, 1H), 7.68 – 7.66 (m, 1H), 7.46 – 7.41 (m, 1H), 4.08 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.92 (s, 3H), 3.75 (s, 3H), 3.19 (ddd, *J* = 17.9, 6.9, 1.7 Hz, 1H), 2.93 (ddd, *J* = 18.2, 11.1, 7.9 Hz, 1H), 2.59 – 2.52 (m, 1H), 2.19 (dd, *J* = 12.5, 2.3 Hz, 1H), 1.99 – 1.92 (m, 2H), 1.84 (d, *J* = 11.1 Hz, 2H), 1.58 – 1.52 (m, 1H), 1.30 (s, 6H).

^{19}F NMR (376 MHz, $CDCl_3$): δ -60.83.

^{13}C{^{19}F} {^{1}H} NMR (101 MHz, CDCl$_3$): δ 178.0, 143.4, 142.1, 139.0, 132.1, 127.5, 127.1, 126.8, 125.0, 122.7, 120.4, 116.2, 112.1, 108.2, 75.3, 60.0, 53.8, 52.4, 45.6, 37.7, 37.6, 27.5, 26.0, 24.5, 20.9, 10.8.

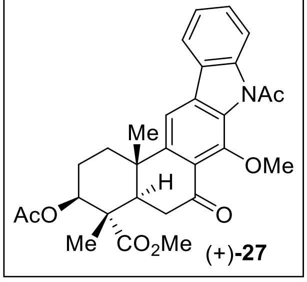
IR(neat) υ_{max} :3515, 2974, 1655, 1460, 1425, 1201, 823, 780, 681 cm^{-1}.
HRMS(ESI) *m/z*: [M+ H]$^+$ calcd. for [$C_{26}H_{28}NF_3O_4$ + H]$^+$ 476.2049, found 476.2034.
$[\alpha]^{25}_{589}$ = +29.7 (*c* = 0.43, CH$_3$OH).

Benzylic Oxidation of Compound (+)**23:**



(+)-**23** (+)-**27**

In an oven-dried round bottom flask, the compound (+)-**23** (32.0 mg, 0.065 mmol, 1.0 equiv.) was taken in 2 mL of AcOH. To the solution CrO$_3$ (13.0 mg, 0.131 mmol, 2 equiv.) was added and the reaction mixture was allowed to stir at 25 °C for 1 h. After completion of reaction (monitored by TLC) the reaction mixture was diluted with ethyl acetate and quenched with saturated aqueous sodium bicarbonate solution. The mixture was extracted with EtOAc (5 mL X 3). The combined organic layers were washed with brine and dried over Na$_2$SO$_4$ and concentrated under reduced pressure. Then the crude product was purified by flash chromatography with 25% EtOAc in *n*-hexane to afford (+)-**27**.



(+)-**27**

Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-acetoxy-8-acetyl-7-methoxy-4,13*b*-dimethyl-6-oxo-2,3,4,4*a*,5,6,8,13*b*-octahydro-1*H*-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**27**]: (+)-**27**

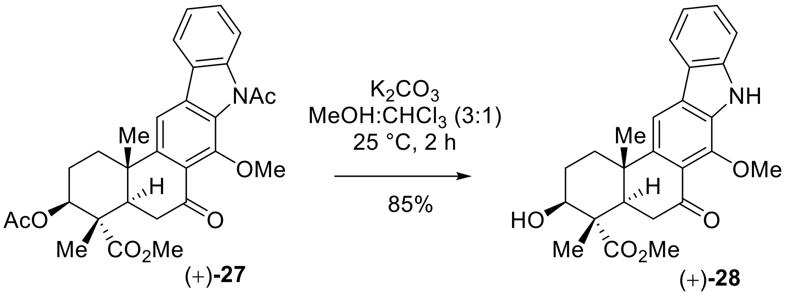
was obtained as yellowish liquid (0.065 mmol scale of reaction; 24.0 mg, 72% yield). $R_f = 0.3$ (25% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 – 8.25 (m, 1H), 7.98 – 7.95 (m, 1H), 7.70 (s, 1H), 7.55 – 7.51 (m, 1H), 7.38 (dd, *J* = 7.4, 1.0 Hz, 1H), 5.25 (d, *J* = 7.8 Hz, 1H), 3.83 (s, 3H), 3.66 (s, 3H), 2.87 – 2.80 (m, 1H), 2.75 – 2.70 (m, 1H), 2.62 (s, 3H), 2.57 – 2.54 (m, 1H), 2.38 (d, *J* = 13.5 Hz, 1H), 2.13 – 2.08 (m, 2H), 2.03 (s, 3H), 1.92 (d, *J* = 11.9 Hz, 1H), 1.41 (s, 3H), 1.33 (s, 3H).

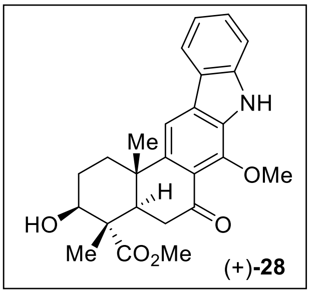
^{13}C NMR (101 MHz, $CDCl_3$): δ 196.5, 175.2, 172.9, 170.0, 151.9, 148.9, 141.7, 133.0, 130.5, 129.5, 124.5, 123.7, 123.0, 120.4, 115.4, 110.0, 76.3, 62.0, 52.7, 50.9, 43.6, 38.4, 37.7, 36.5, 27.2, 24.0, 23.7, 21.1, 11.4.

IR (neat) υ_{max} 3500, 3410, 2924, 1725, 1660, 1460, 1243, 1132, 823, 767, 528 cm^{-1}.
HRMS(ESI) *m/z*: $[M+ Na]^+$ calcd. for $[C_{29}H_{31}NO_7 + Na]^+$ 528.1998, found 528.1996.
$[\alpha]^{25}_{589} = +21.3$ (*c* = 0.24, $CHCl_3$).

Synthesis of Compound (+)-**28:**



In an oven-dried round bottom flask compound (+)-**27** (24.0 mg, 0.047 mmol, 1.0 equiv.) was taken in a mixture of methanol and chloroform [MeOH: $CHCl_3$ (3:1)]. To the solution K_2CO_3 (15.0 mg, 0.104 mmol, 2.2 equiv.) was added and then the reaction mixture was stirred at 25 ºC for 2 h. After completion of the reaction (monitored by TLC) the reaction mixture was directly evaporated under reduced pressure. The mixture was then extracted with EtOAc (5 mL X 3). The combined organic layers were washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. Then the crude product was purified by flash chromatography with 50% EtOAc in *n*-hexane to afford (+)-**28** as yellow liquid.



(+)-**28**

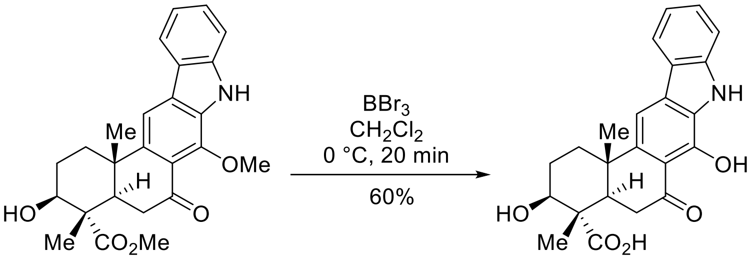
Methyl (3*S*,4*S*,4a*R*,13b*S*)-3-hydroxy-7-methoxy-4,13*b*-dimethyl-6-oxo-2,3,4,4*a*,5,6,8,13*b*-octahydro-1*H*-naphtho[2,1-*b*]carbazole-4-carboxylate [(+)-**28**]**:** (+)-**28** was obtained as colorless liquid (0.047 mmol scale of reaction; 17 mg, 85% yields). $R_f = 0.25$ (50% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (s, 1H), 8.09 – 8.07 (m, 1H), 7.78 (s, 1H), 7.51 – 7.50 (m, 2H), 7.27 (s, 1H), 4.15 – 4.12 (m, 1H), 4.06 (s, 3H), 3.75 (s, 3H), 2.92 – 2.86 (m, 1H), 2.66 – 2.63 (m, 1H), 2.61 – 2.58 (m, 1H), 2.47 (d, *J* = 13.7 Hz, 1H), 2.05 – 2.02 (m, 2H), 1.95 (d, *J* = 2.4 Hz, 1H), 1.39 (s, 3H), 1.33 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 197.6, 176.9, 147.3, 146.2, 141.0, 132.0, 128.7, 127.7, 123.2, 121.2, 121.0, 120.0, 111.3, 110.2, 74.8, 62.0, 52.6, 52.5, 43.7, 38.7, 37.8, 37.0, 24.6, 22.7, 10.5.

IR(neat) υ_{max} 3525, 2944, 1655, 1460, 1445, 1172, 823, 776, 665 cm^{-1}.
HRMS(ESI) *m/z*: $[M + Na]^+$ calcd. for $[C_{25}H_{27}NO_5 + Na]^+$ 444.1787, found 444.1770.
$[\alpha]^{25}_{589} = +29.7$ (*c* = 0.43, CH_3OH).

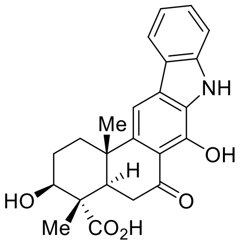
Total Synthesis of Xiamycin G (+)-**1b:**



(+)-**28**

(+)-**1b**

In an oven-dried round bottom flask compound (+)-**28** (17 mg, 0.040 mmol, 1.0 equiv.) was taken in 2 mL dry CH_2Cl_2. To it BBr_3 (8.4 μL, 0.088 mmol, 2.2 equiv.) was added at 0 °C and allowed to stir for 20 min. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water (2 mL). The resulting biphasic mixture was transferred to a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with CH_2Cl_2 (5 mL X 2). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude product was purified by flash column chromatography with 70% EtOAc in *n*-hexane to afford compound (+)-**1b** as yellow liquid.



xiamycin G [(+)-**1b**]

(3*S*,4*S*,4a*R*,13b*S*)**-3,7-dihydroxy-4,13*b*-dimethyl-6-oxo-2,3,4,4*a*,5,6,8,13*b*-octahydro-1*H*-naphtho[2,1-*b*]carbazole-4-carboxylic acid** [(+)-**1b**]**:** (+)-**1b** was obtained as yellow liquid (0.040 mmol scale of reaction; 10 mg; 60%). R_f = 0.3 (70% EtOAc in *n*-hexane).

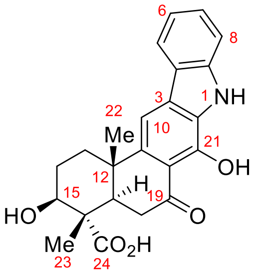
^{1}H NMR (500 MHz, CD_3OD) δ 8.06 (d, *J* = 7.9 Hz, 1H), 7.55 (s, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.43 (dd, *J* = 8.3, 6.9 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 4.12 – 4.08 (m, 1H), 3.02 (dd, *J* = 18.2, 14.1 Hz, 1H), 2.63 (dd, *J* = 8.7, 2.9 Hz, 1H), 2.57 (dd, *J* = 14.1, 3.6 Hz, 1H), 2.32 (dd, *J* = 18.2, 3.5 Hz, 1H), 1.97 – 1.90 (m, 3H), 1.32 (s, 3H), 1.30 (s, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 206.8, 180.4, 152.5, 147.5, 143.5, 130.9, 128.9, 128.4, 124.5, 122.4, 120.8, 113.1, 112.5, 107.1, 76.2, 54.5, 46.9, 39.0, 38.8, 38.4, 28.6, 25.1, 11.5.

IR(neat) υ_{max} 3402, 2937, 2203, 1697, 1633, 1453, 1190, 1013 cm^{-1}.

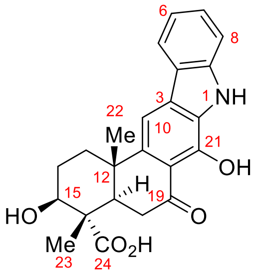
HRMS(ESI) *m/z*: $[M + H]^+$ calcd. for $[C_{23}H_{23}NO_5 + H]^+$ 394.1654, found 394.1645.

$[\alpha]^{25}_{589}$ = +25.0 (*c* = 0.1, $CHCl_3$).



Comparison of ^{1}H-NMR Data:

No.	**This report of Xiamycin G (500 MHz, CD_3OD)**	**Zhang's report of Xiamycin G (600 MHz, CD_3OD)** [2]
5	8.06 (d, *J* = 7.9 Hz, 1H)	8.07 (d, *J* =7.8 Hz, 1H)
6	7.17 (t, *J* = 7.4 Hz, 1H)	7.18 (dd, *J* = 7.8, 7.2 Hz, 1H)
7	7.43 (dd, *J* = 8.3, 6.9 Hz, 1H)	7.44 (dd, *J* = 7.8, 7.2 Hz, 1H)
8	7.49 (d, *J* = 8.2 Hz, 1H)	7.50 (d, *J* = 8.4 Hz, 1H)
10	7.55 (s, 1H)	7.55 (s, 1H)
13	2.63 (dd, *J* = 8.7, 2.9 Hz, 1H)	2.62 (m, 1H)
	1.97-1.90 (m, 1H)	1.93 (m, 1H)
14	1.97-1.90 (m, 2H)	1.93 (m, 2H)
15	4.12-4.08 (m, 1H)	4.10 (m, 1H)
17	2.57 (dd, *J* = 14.1, 3.6 Hz, 1H)	2.58 (m, 1H)
18	3.02 (dd, *J* = 18.2, 14.1 Hz, 1H)	3.01 (dd, *J* = 12, 14.5 Hz, 1H)
19	2.32 (dd, *J* = 18.2, 3.5 Hz, 1H)	2.39 (dd, *J* = 12, 14.5 Hz, 1H)
22	1.32 (s, 3H)	1.32 (s, 3H)
23	1.30 (s, 3H)	1.30 (s, 3H)



Comparison of ^{13}C-NMR Data:

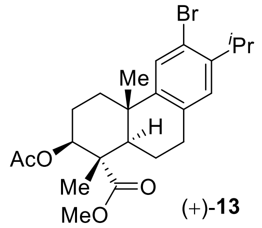
No.	**This report of Xiamycin G (126 MHz, CD_3OD)**	**Zhang's report of Xiamycin G (150 MHz, CD_3OD)**[2]
2	128.4 C	128.1 C
3	130.9 C	130.8 C
4	124.5 C	124.2 C
5	122.4 CH	122.2 CH

6	120.8 CH	120.5 CH
7	128.9 CH	128.6 CH
8	113.1 CH	112.8 CH
9	143.5 C	143.3 C
10	107.1 CH	106.7 CH
11	147.5 C	147.4 C
12	38.8 C	38.7 C
13	38.4 CH_2	38.2 CH_2
14	28.6 CH_2	28.3 CH_2
15	76.2 CH	76.2 CH
16	54.5 C	54.3 C
17	46.9 CH	46.6 CH
18	39.0 CH_2	38.6 CH_2
19	206.8 C	206.9 C
20	112.5 C	112.4 C
21	152.5 C	152.2 C
22	25.1 CH_3	24.9 CH_3
23	11.5 CH_3	11.5 CH_3
24	180.4 C	181.3 C

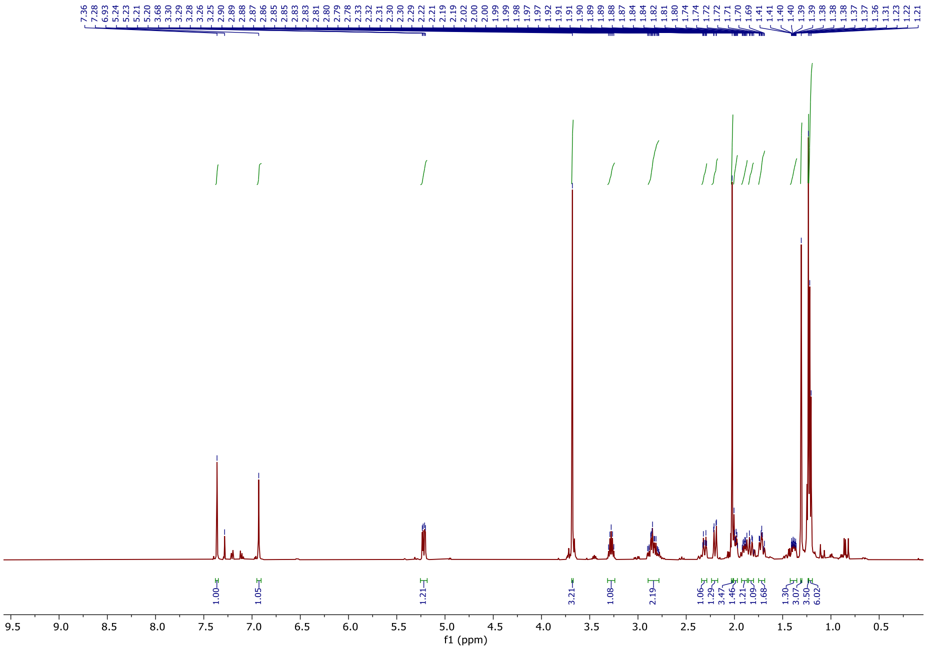
References:

1. Nandi, R.; Niyogi, S.; Kundu, S.; Gavit, V. R.; Mumda, M.; Murmu, M.; Bisai, A. *Chem. Sci.* **2023**, *14*, 8047.
2. Zhang, Q.; Li, H.; Yu, L.; Sun, Y.; Zhu, Y.; Zhu, H.; Zhang, L.; Li, S.; Shen, Y.; Tian, C.; Li, A.; Liu, H.; Zhang C. *Chem. Sci*. **2017**, *8*, 5067.

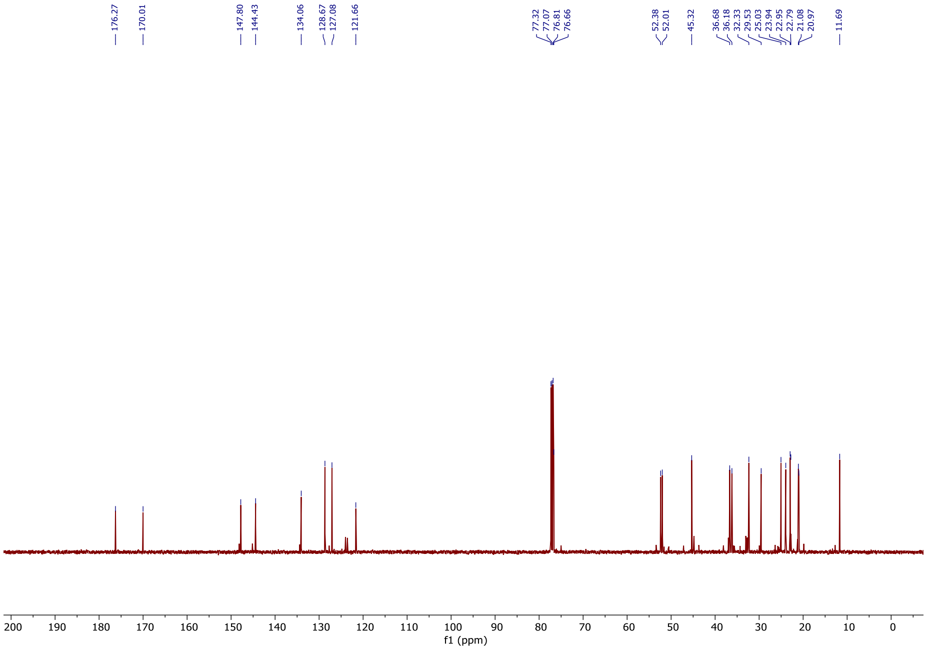
Spectral Traces



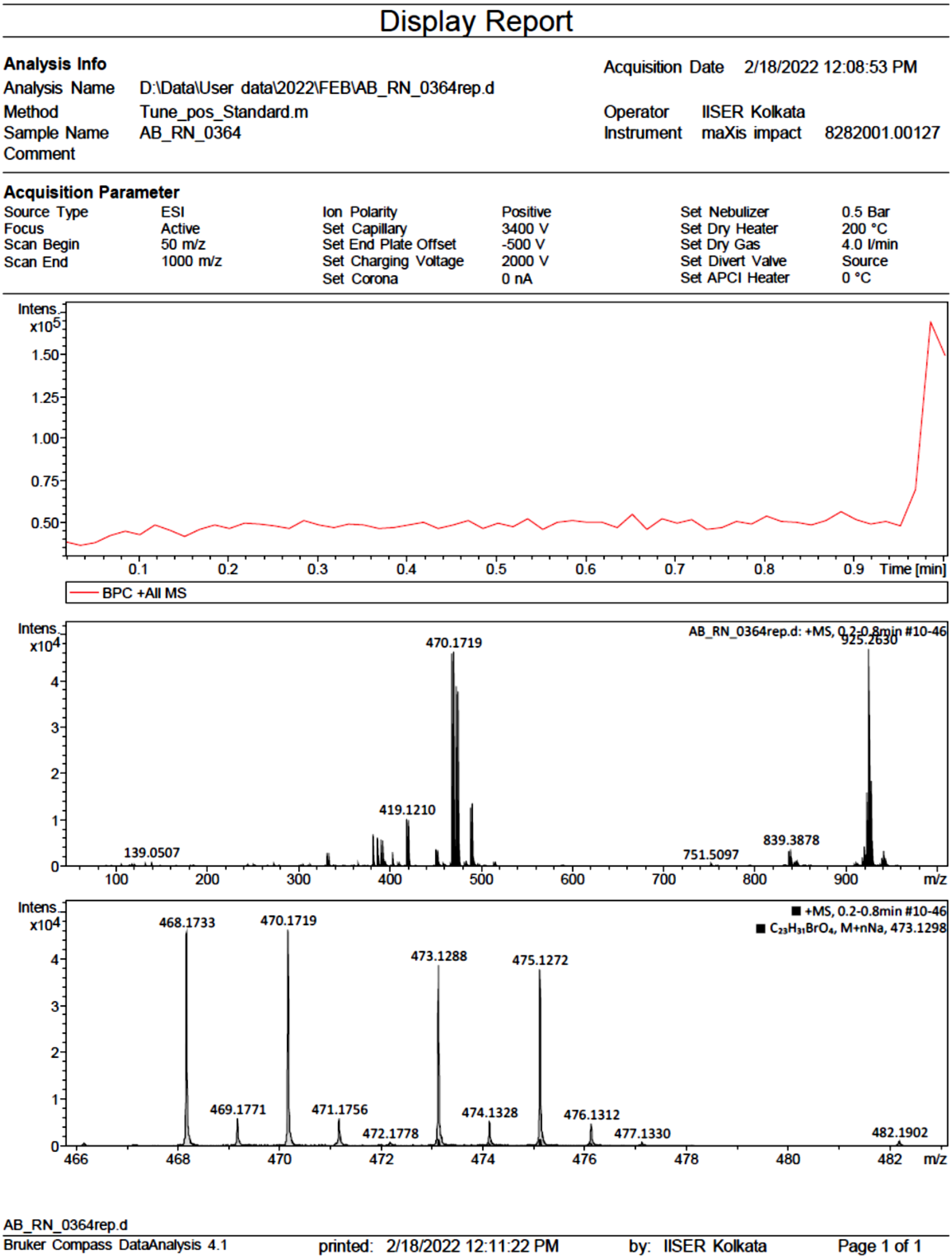
(+)-**13**



^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**13**



^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**13**



Display Report

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Sample Name	AB_RN_0364	Instrument	maXis impact 8282001.00127
Comment			

Acquisition Parameter

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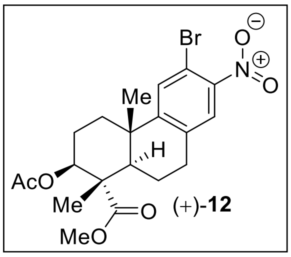
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C

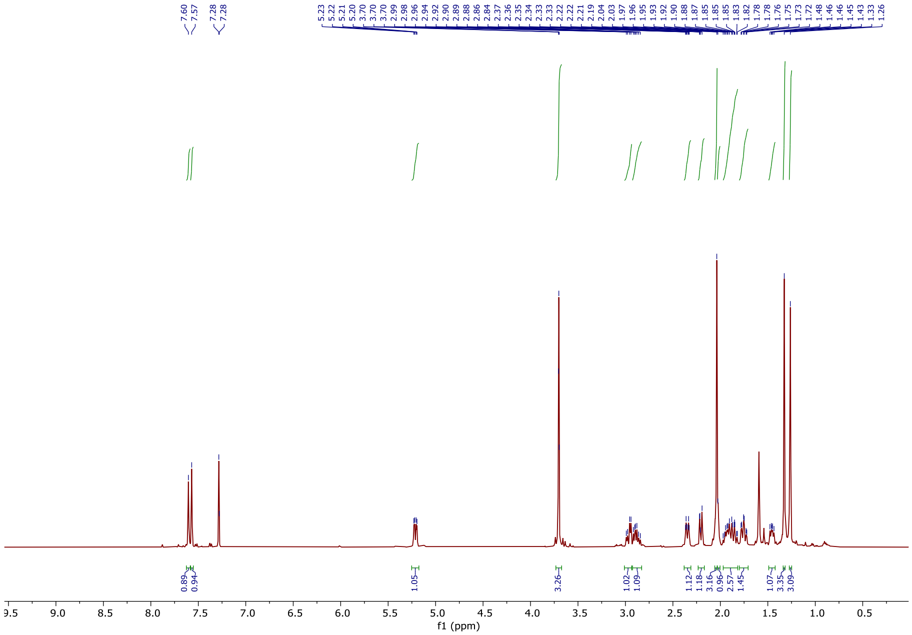
AB_RN_0364rep.d

Bruker Compass DataAnalysis 4.1 printed: 2/18/2022 12:11:22 PM by: IISER Kolkata Page 1 of 1

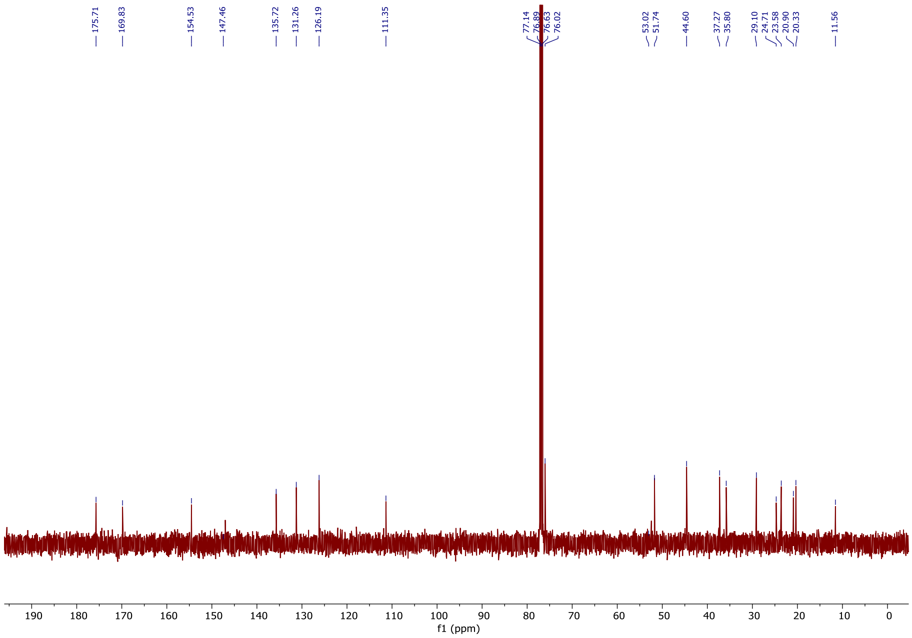
HRMS data of (+)-**13**



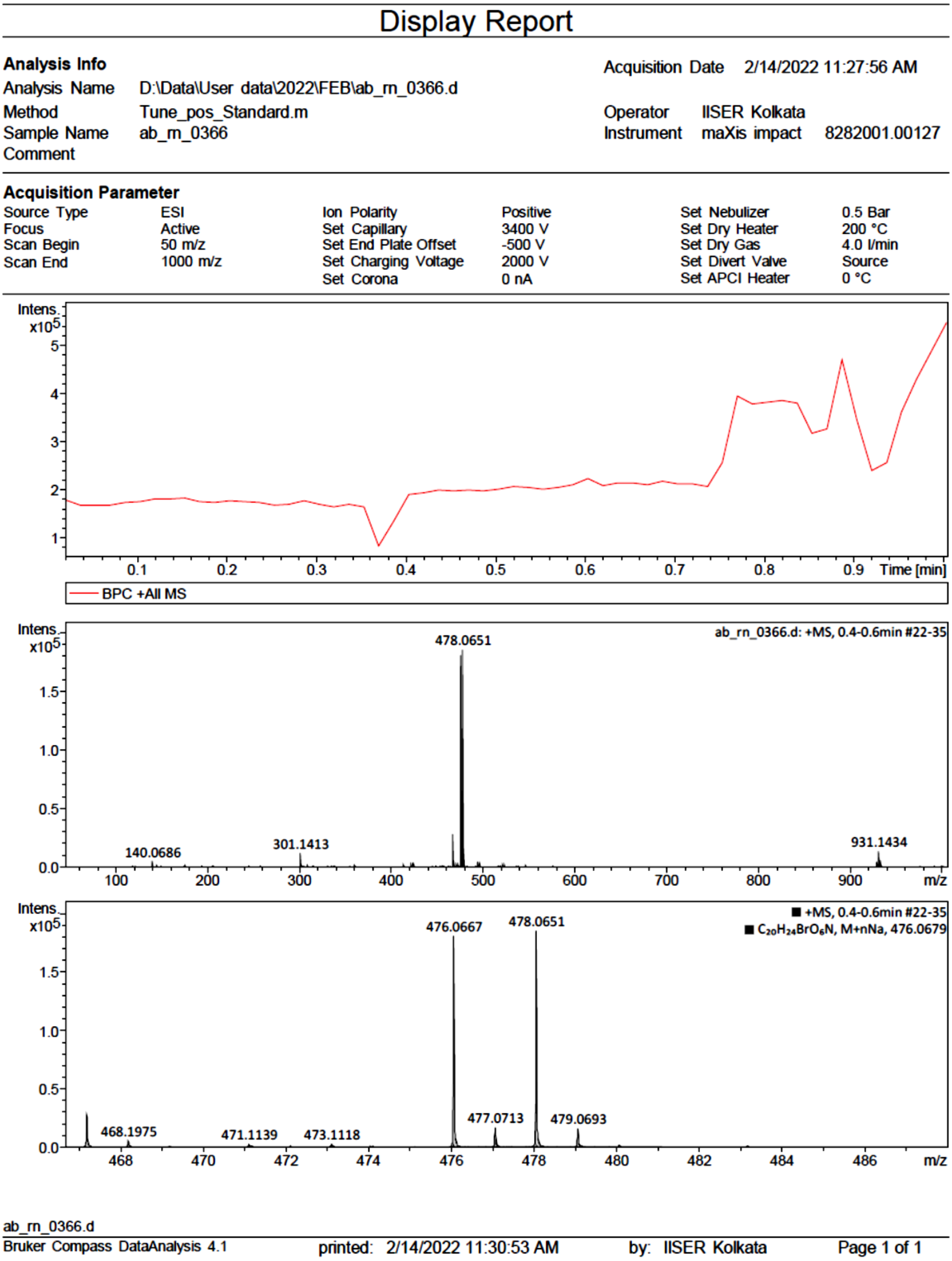
(+)-**12**



^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**12**



^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**12**



Display Report

Analysis Info

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Comment			

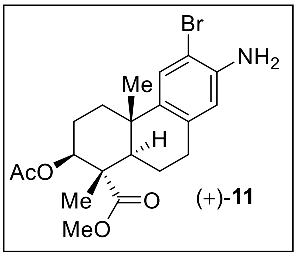
Acquisition Parameter

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

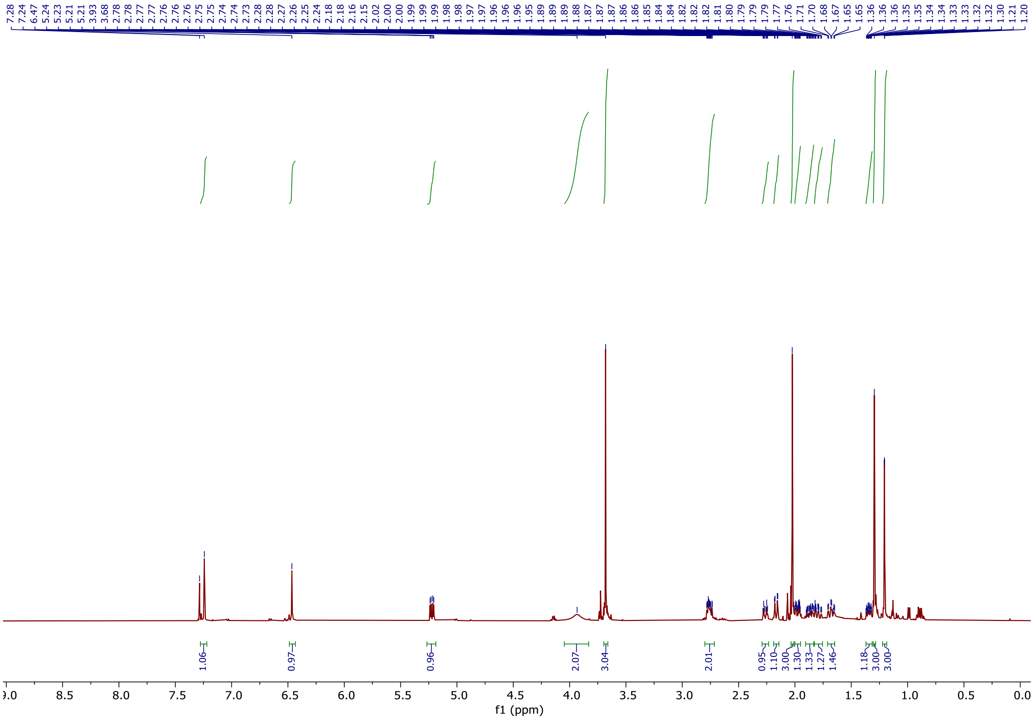
ab_rn_0366.d

Bruker Compass DataAnalysis 4.1 printed: 2/14/2022 11:30:53 AM by: IISER Kolkata Page 1 of 1

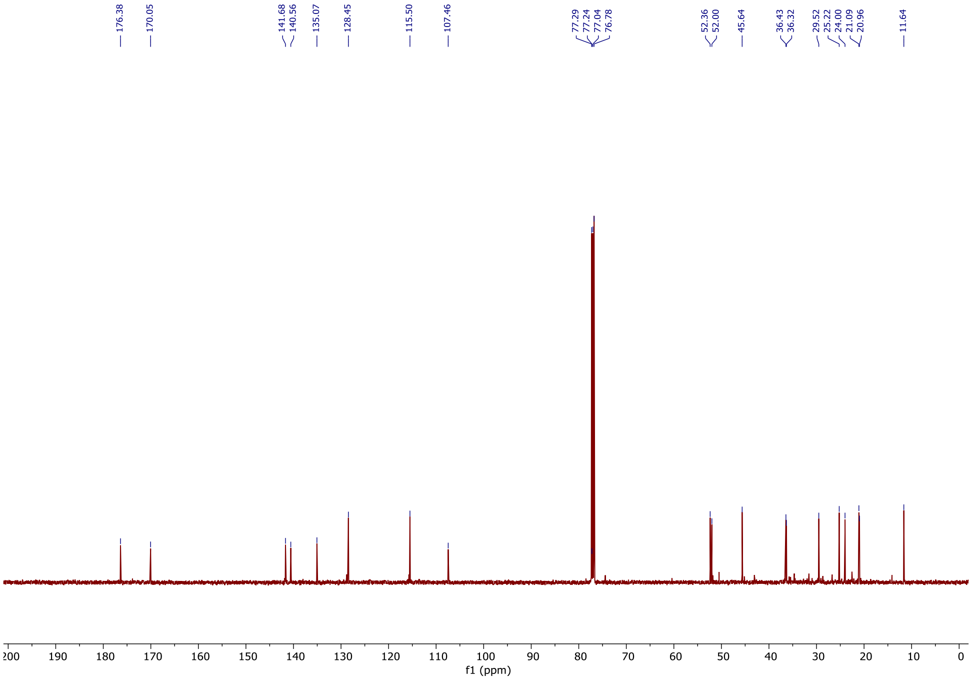
HRMS data of (+)-**12**



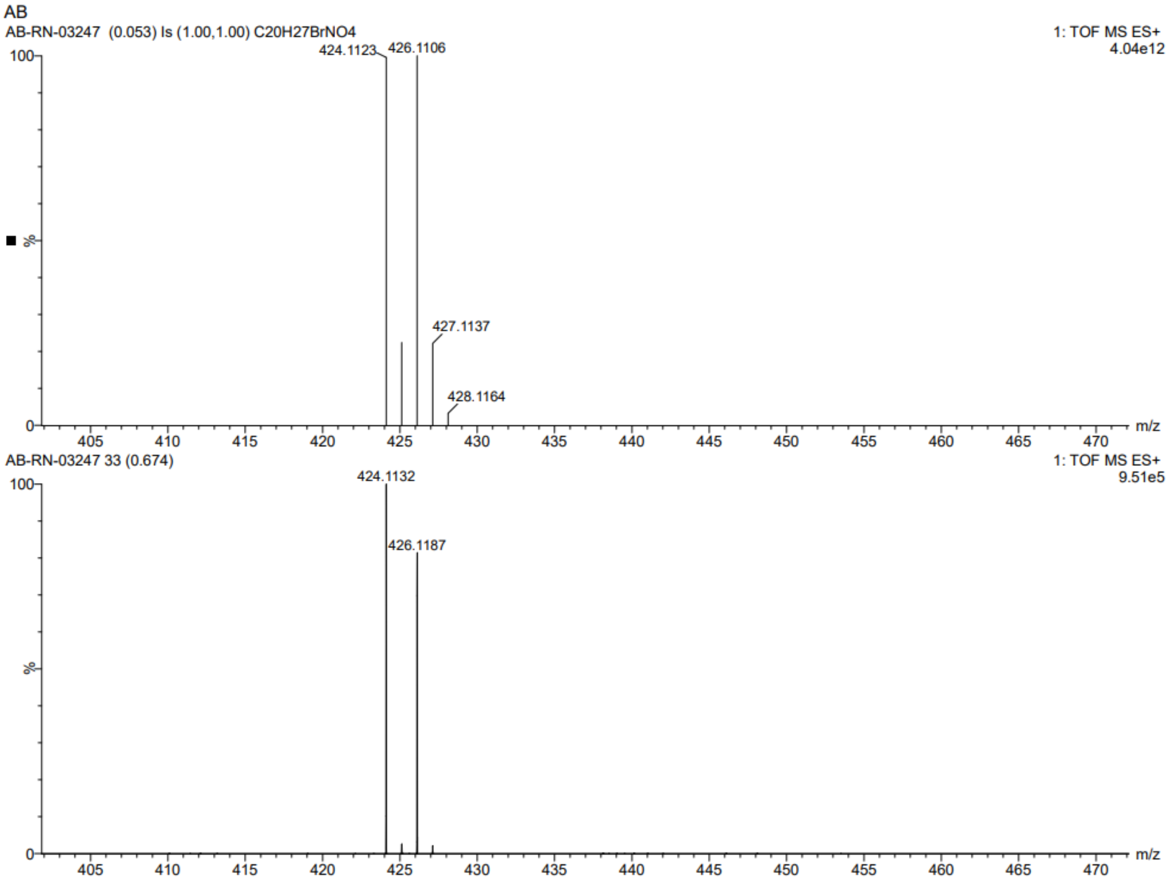
(+)-**11**



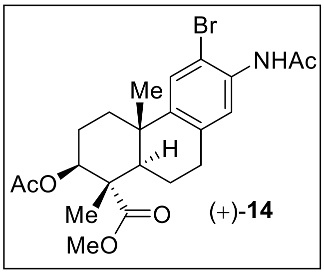
^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**11**



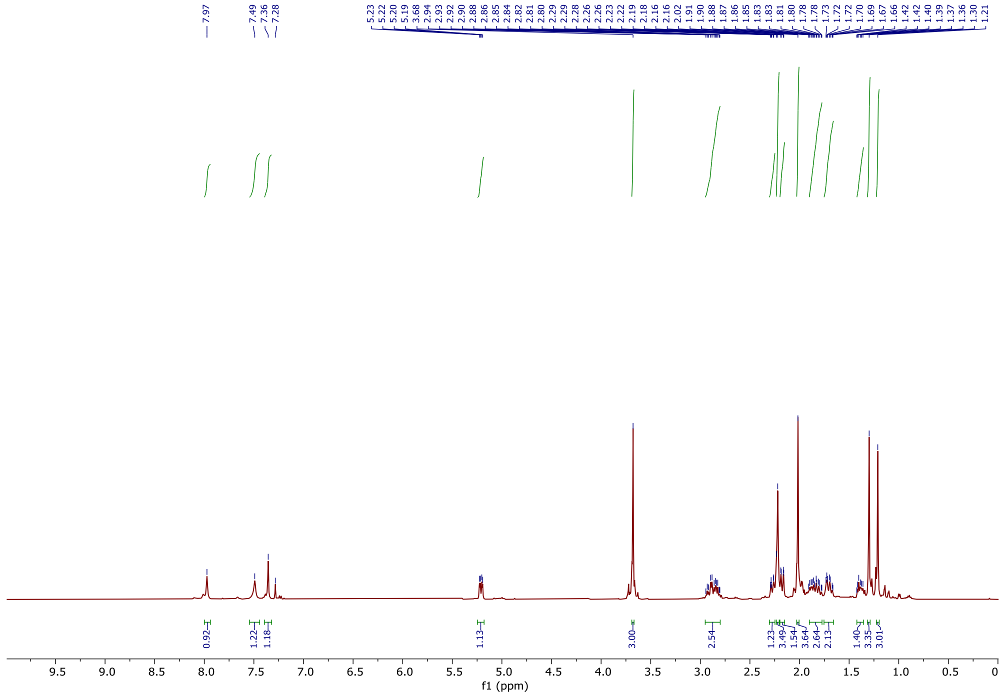
^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**11**



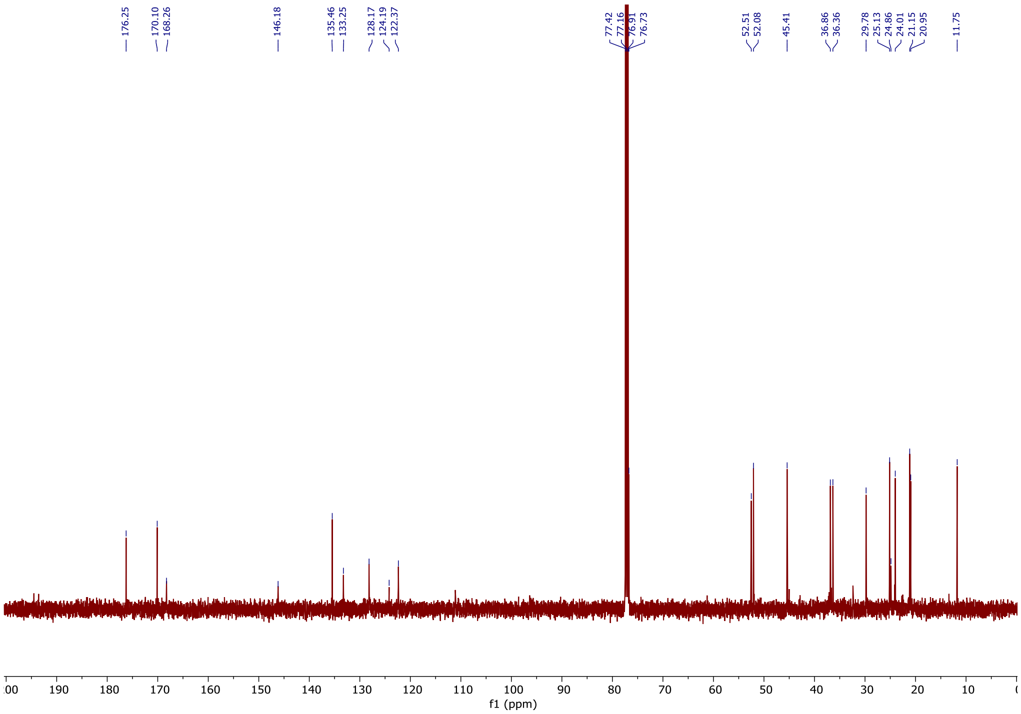
HRMS data of (+)-**11**



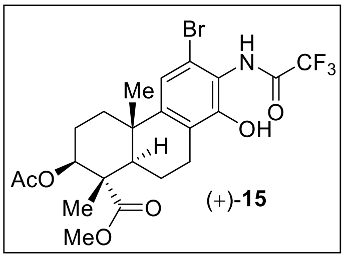
(+)-**14**



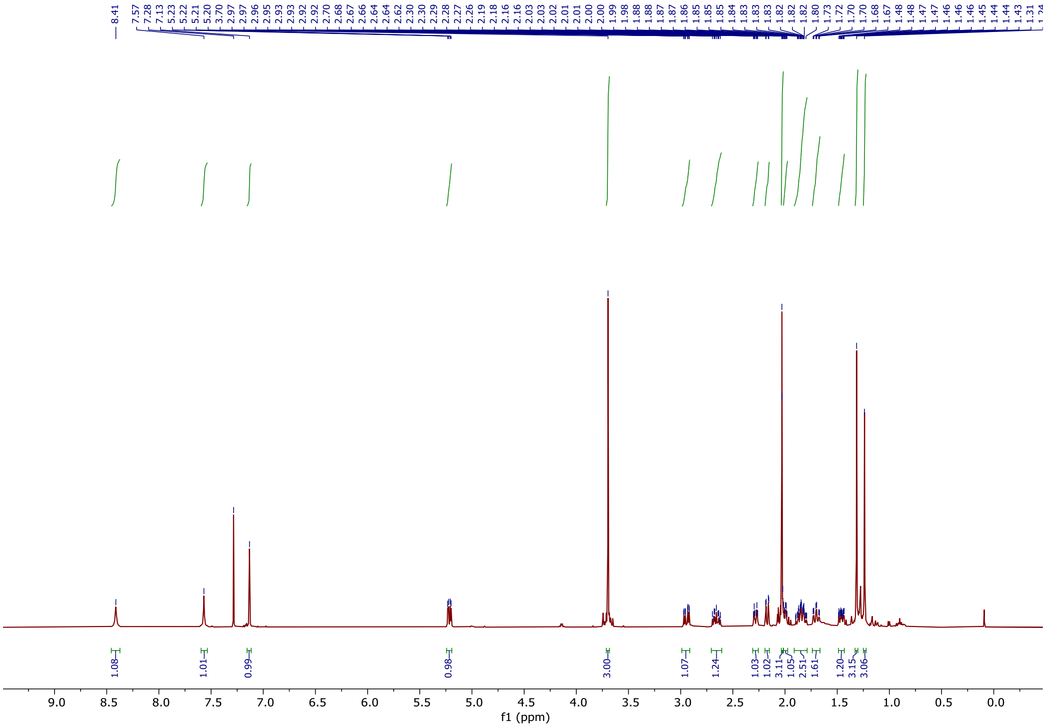
^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**14**



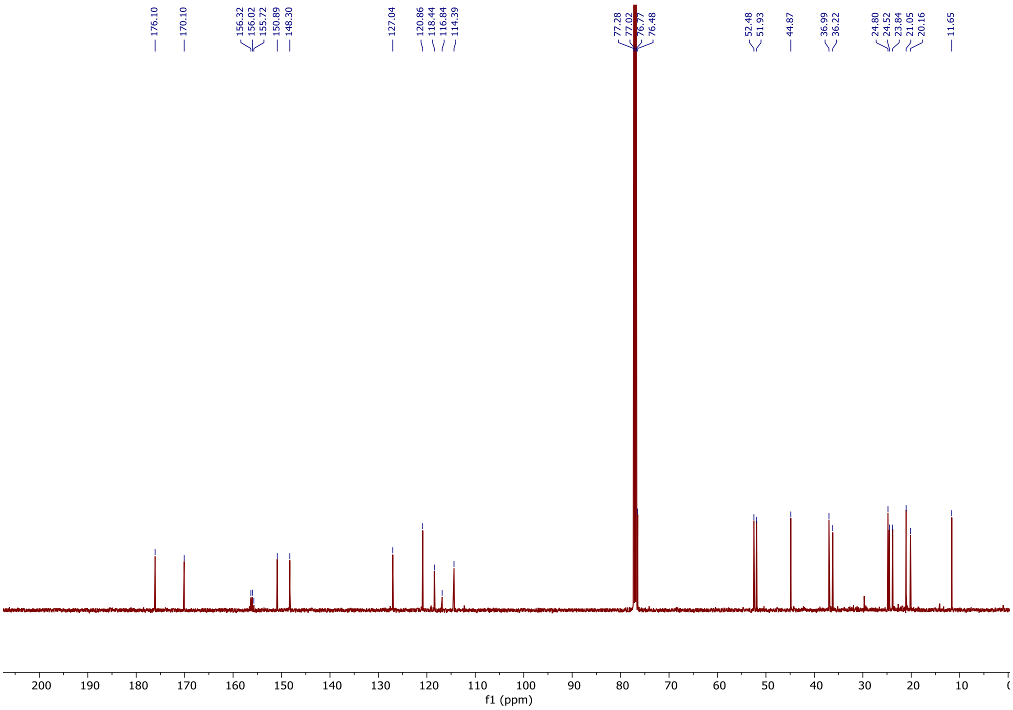
^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**14**



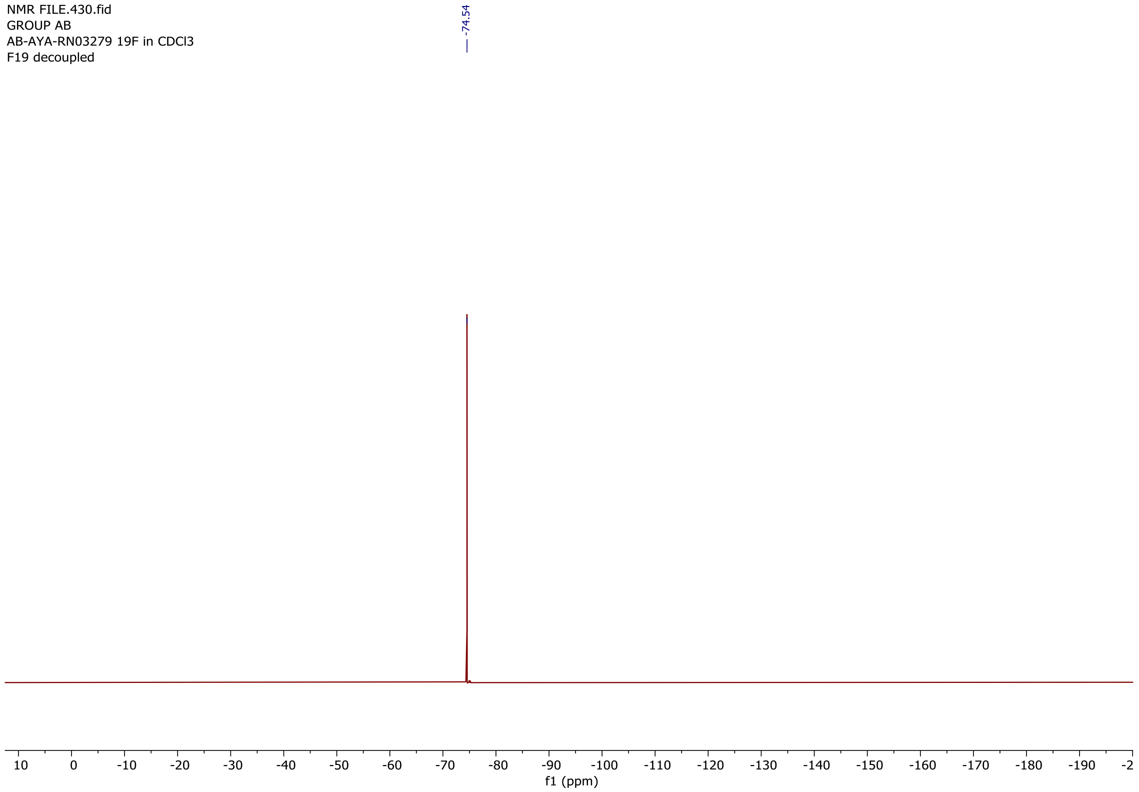
(+)-**15**



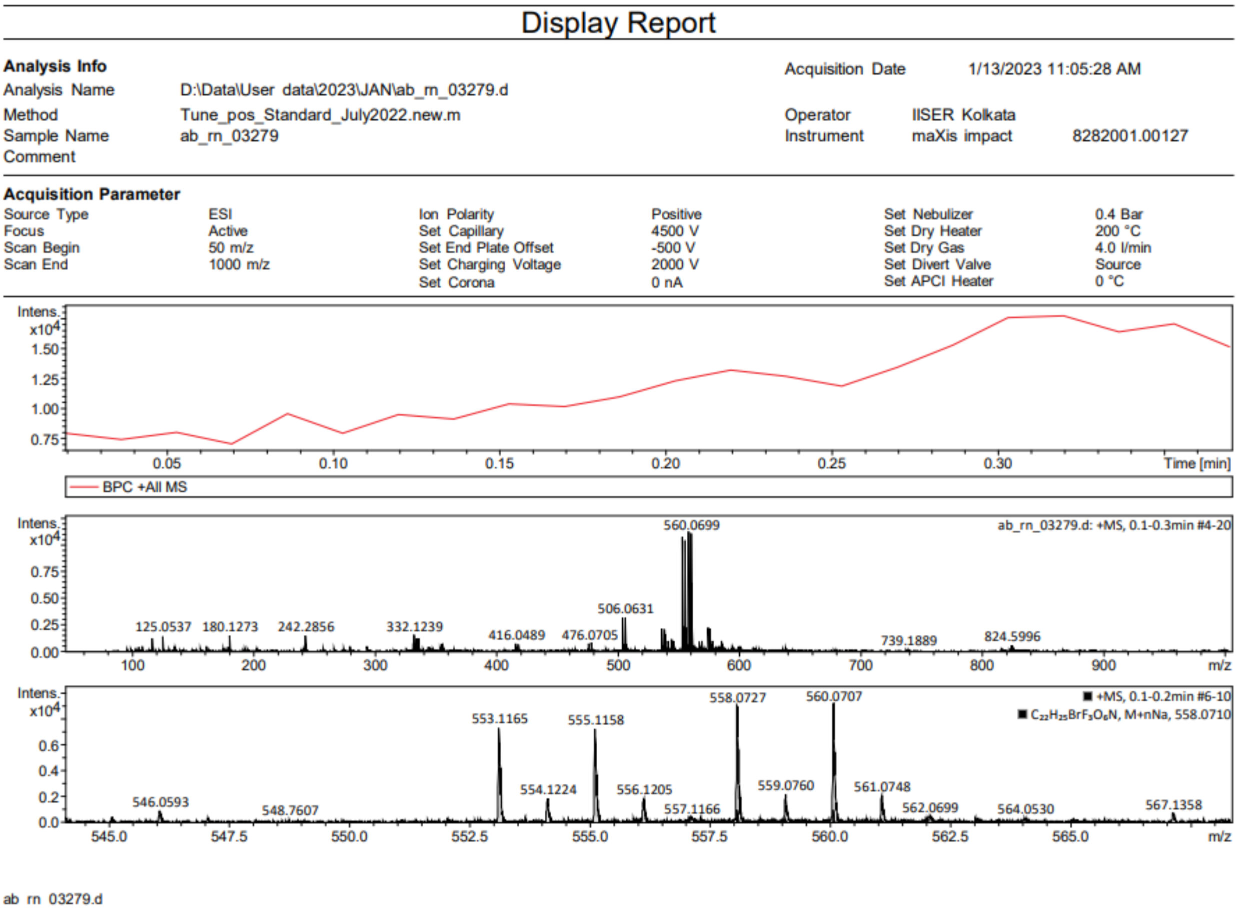
^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**15**



^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**15**



^{19}F NMR (470 MHz, CDCl$_3$) of (+)-**15**



Display Report

Analysis Info

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Sample Name	ab_rn_03279	Instrument	maXis impact	8282001.00127
Comment				

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
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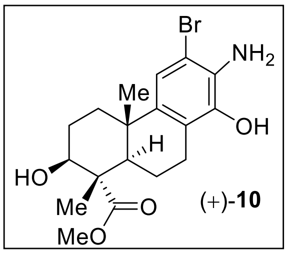
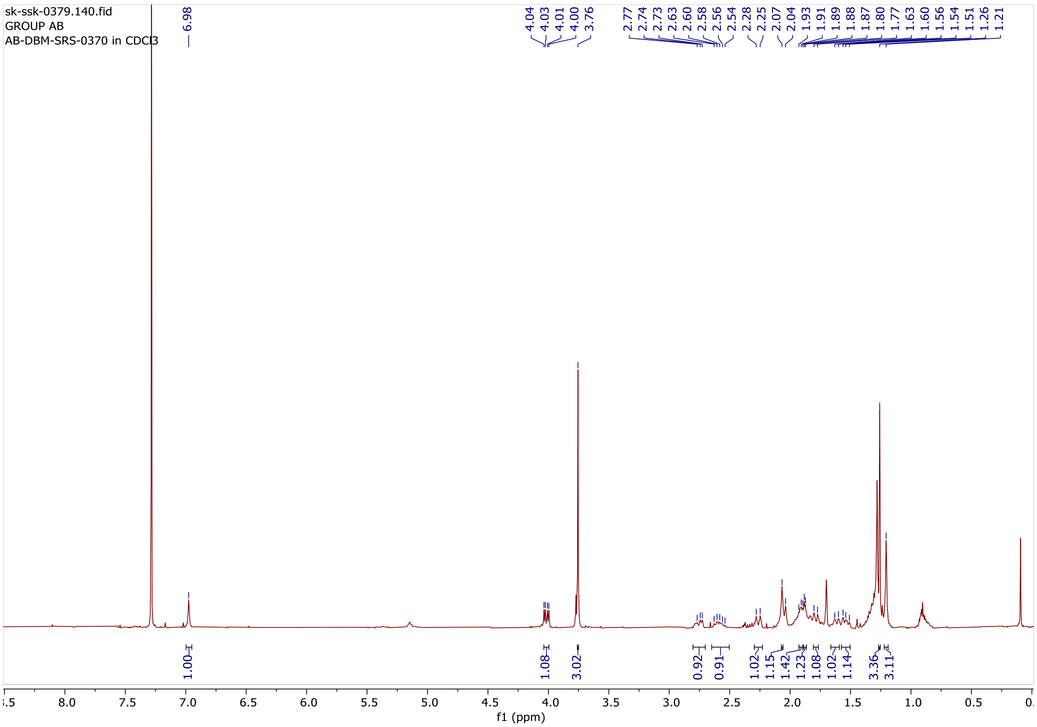
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C

ab rn 03279.d

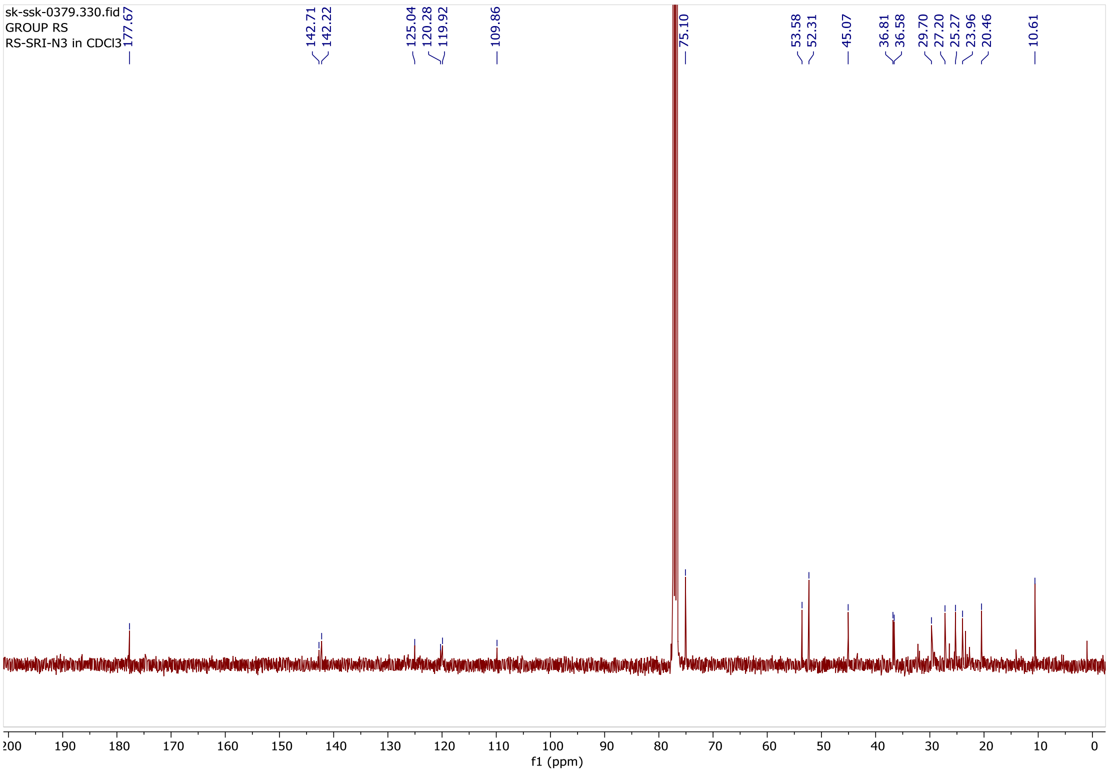
HRMS data of (+)-**15**



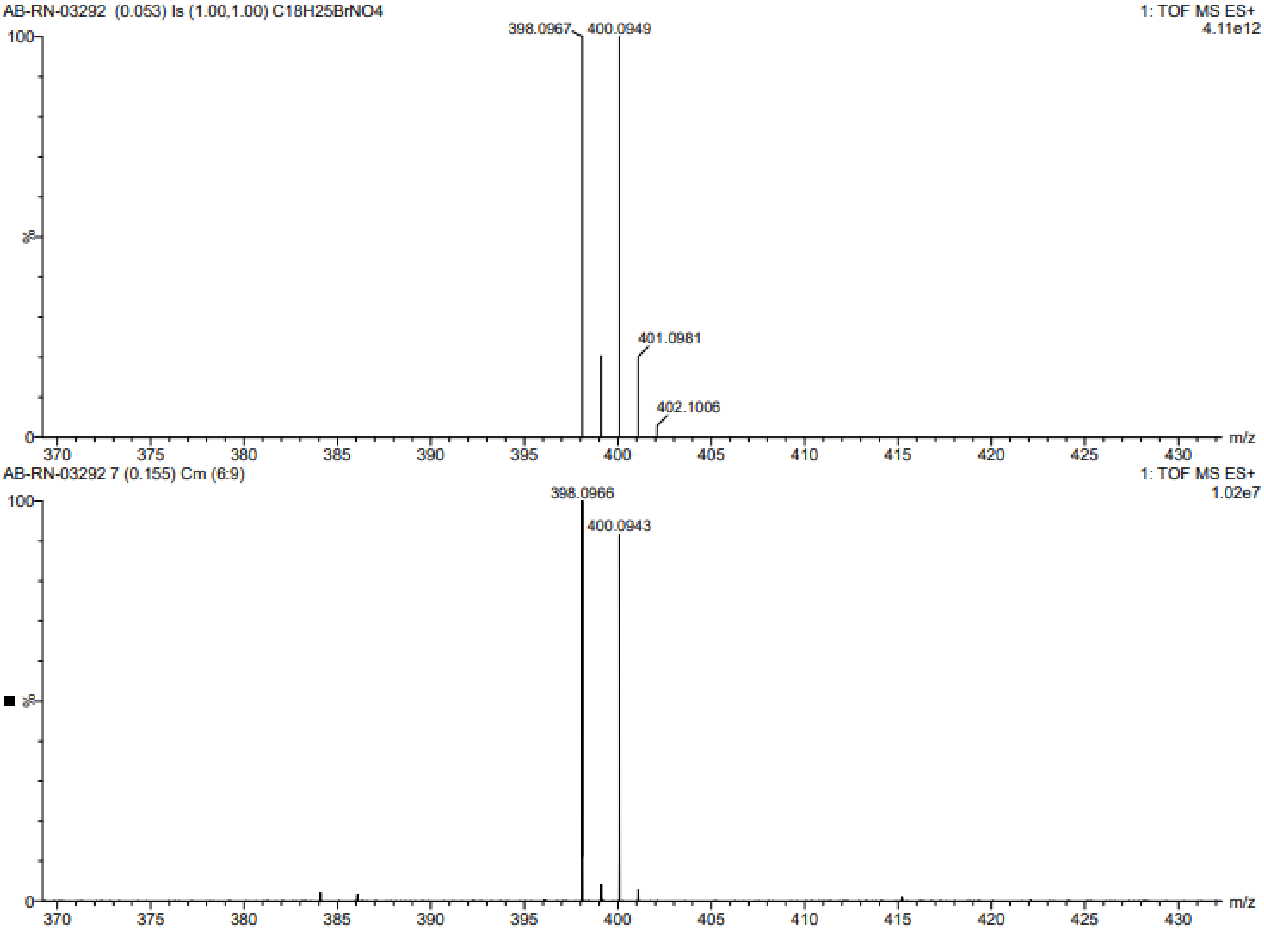
(+)-**10**



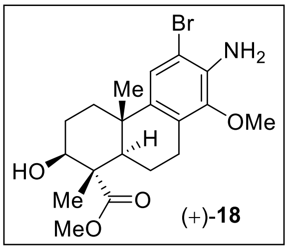
^{1}H NMR (400 MHz, CDCl$_3$) of [(+)-**10**]



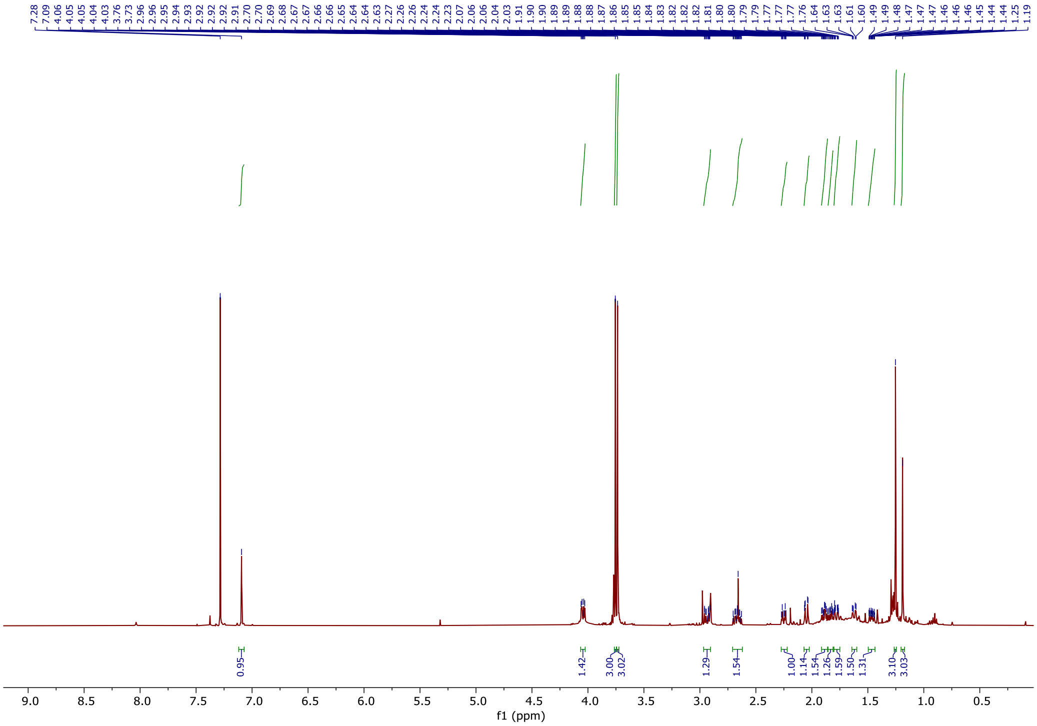
^{13}C NMR (126 MHz, CDCl$_3$) of [(+)-**10**]



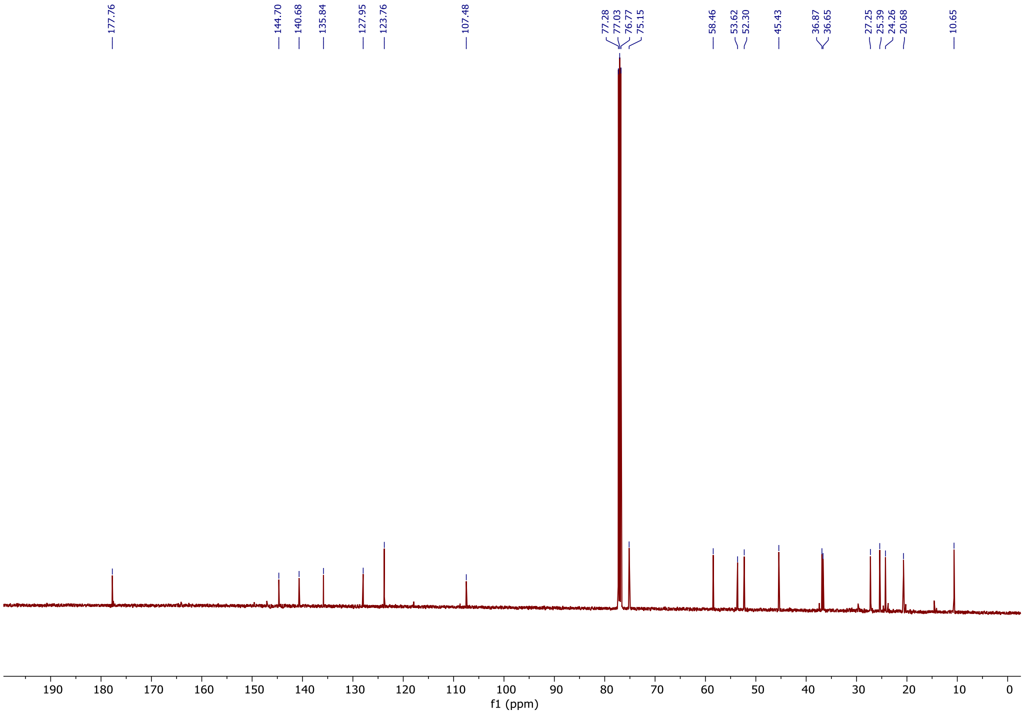
HRMS data of (+)**-10**



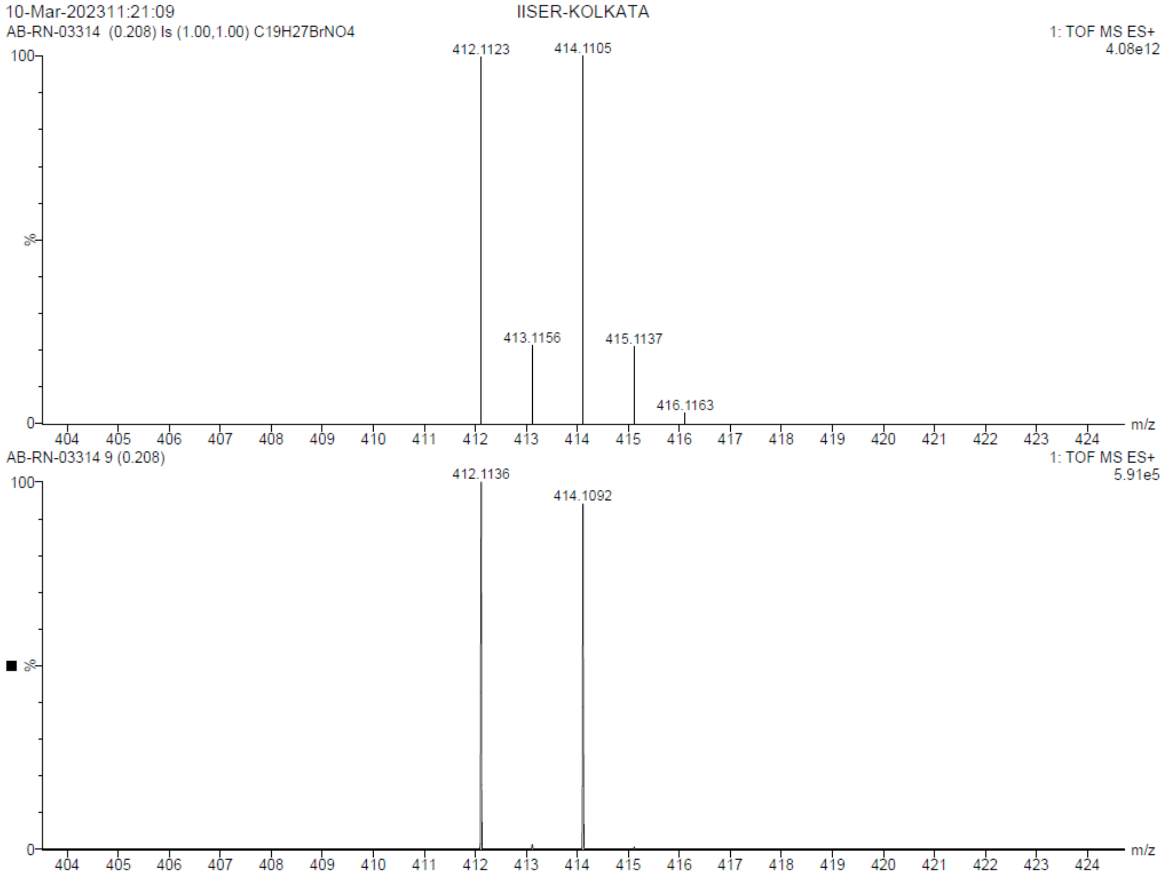
(+)-**18**



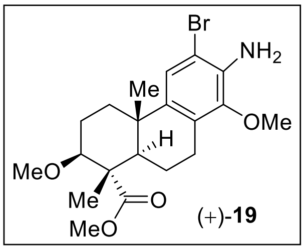
^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**18**

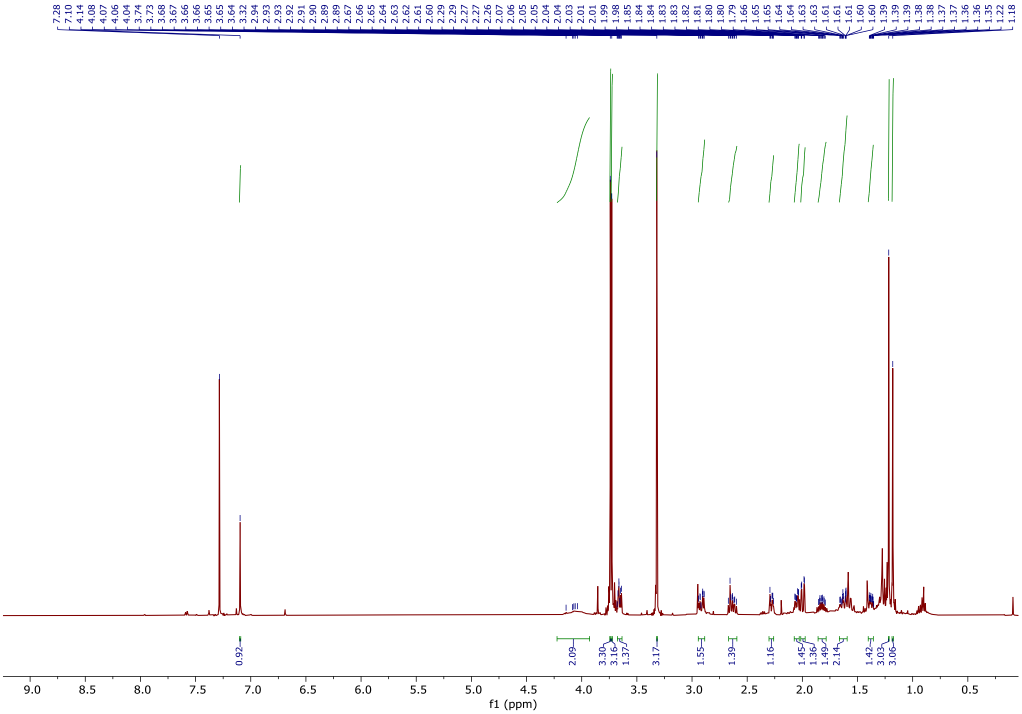


^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**18**

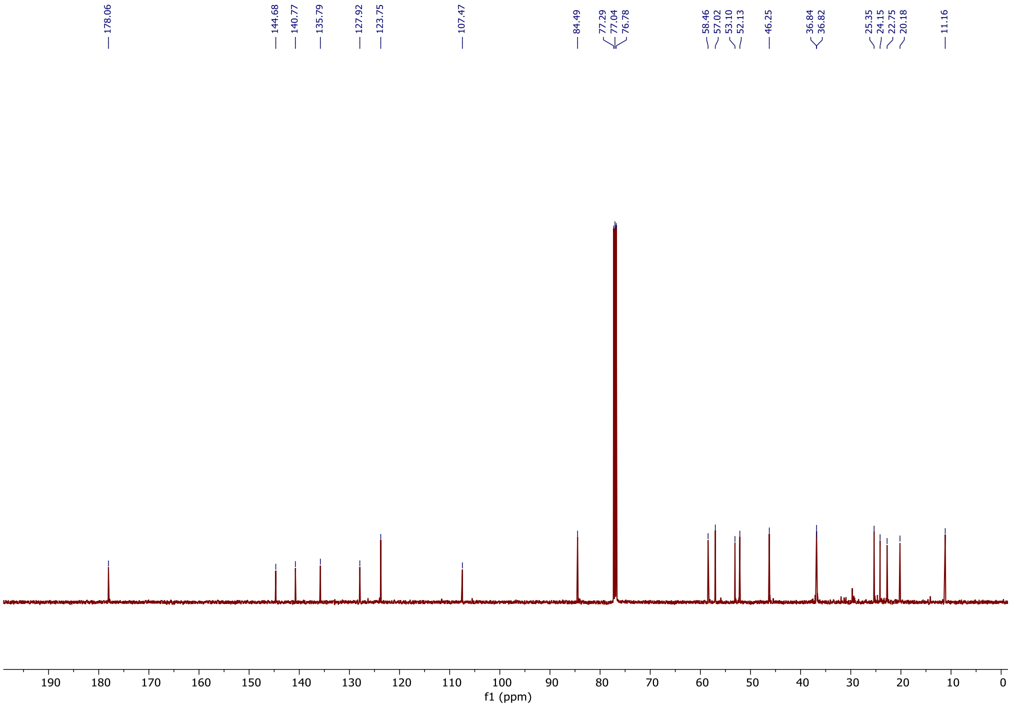


HRMS data of (+)-**18**

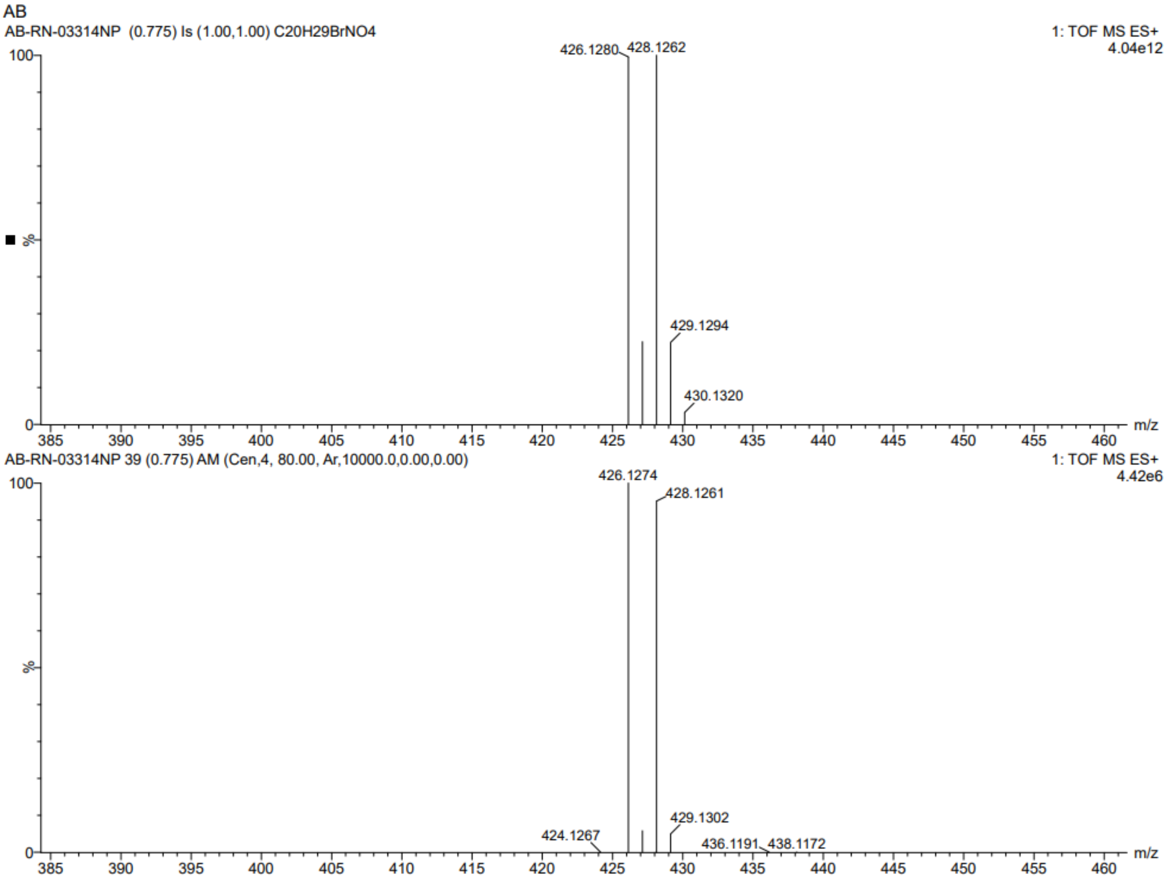




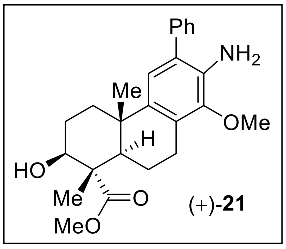
^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**19**



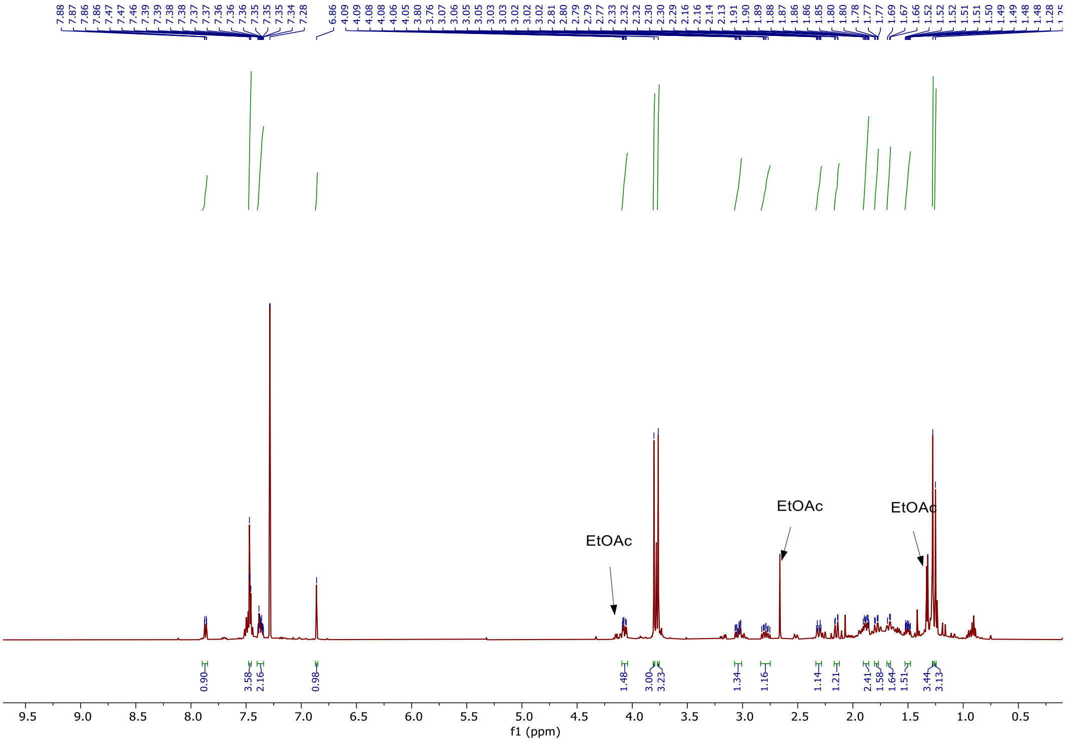
^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**19**



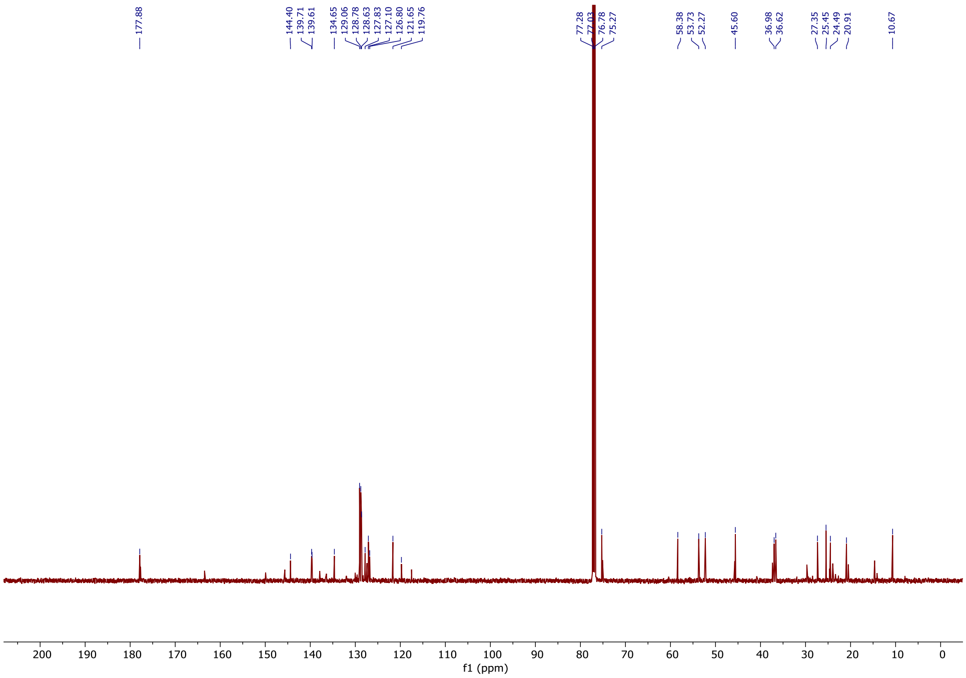
HRMS data of (+)-**19**



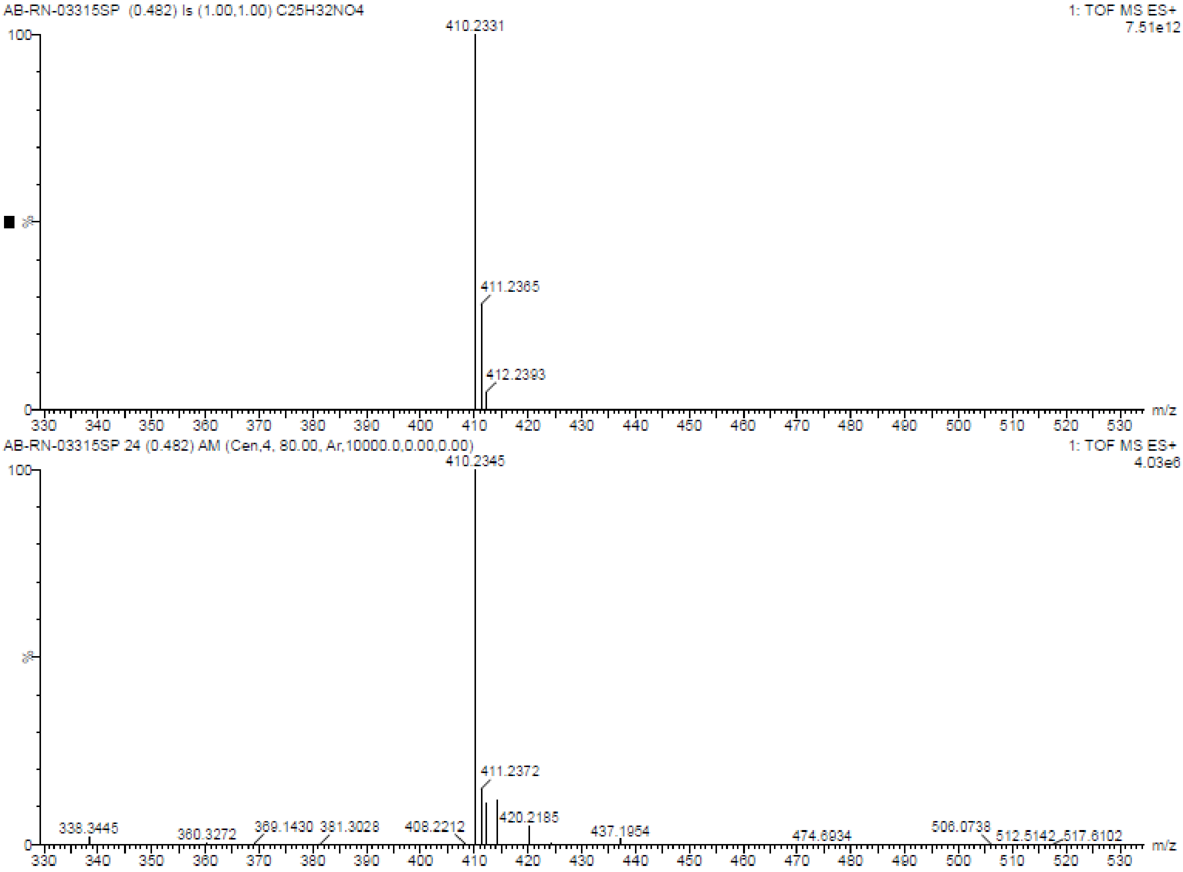
(+)-**21**



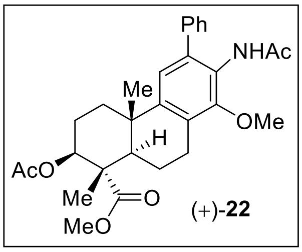
^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**21**



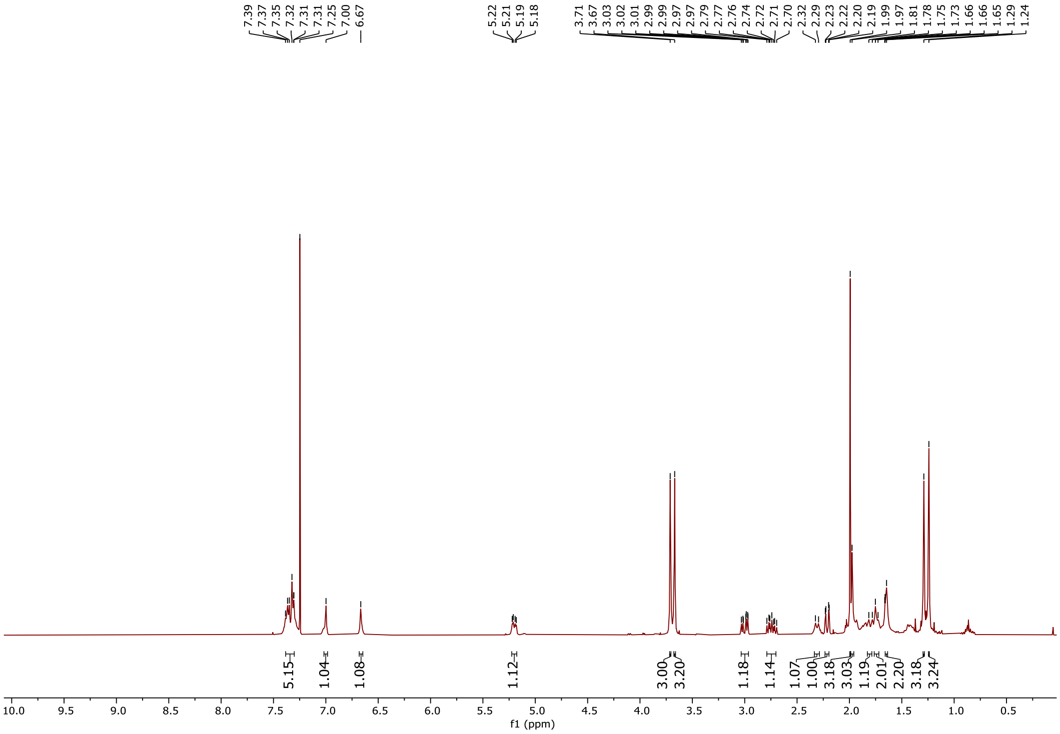
^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**21**



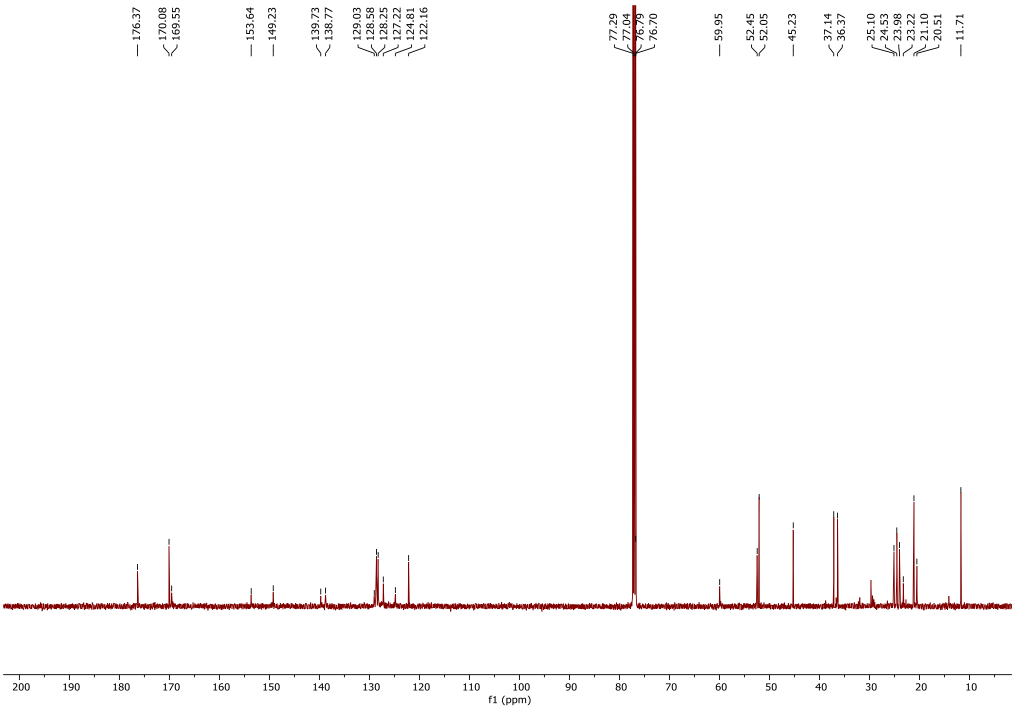
HRMS data of (+)**-21**



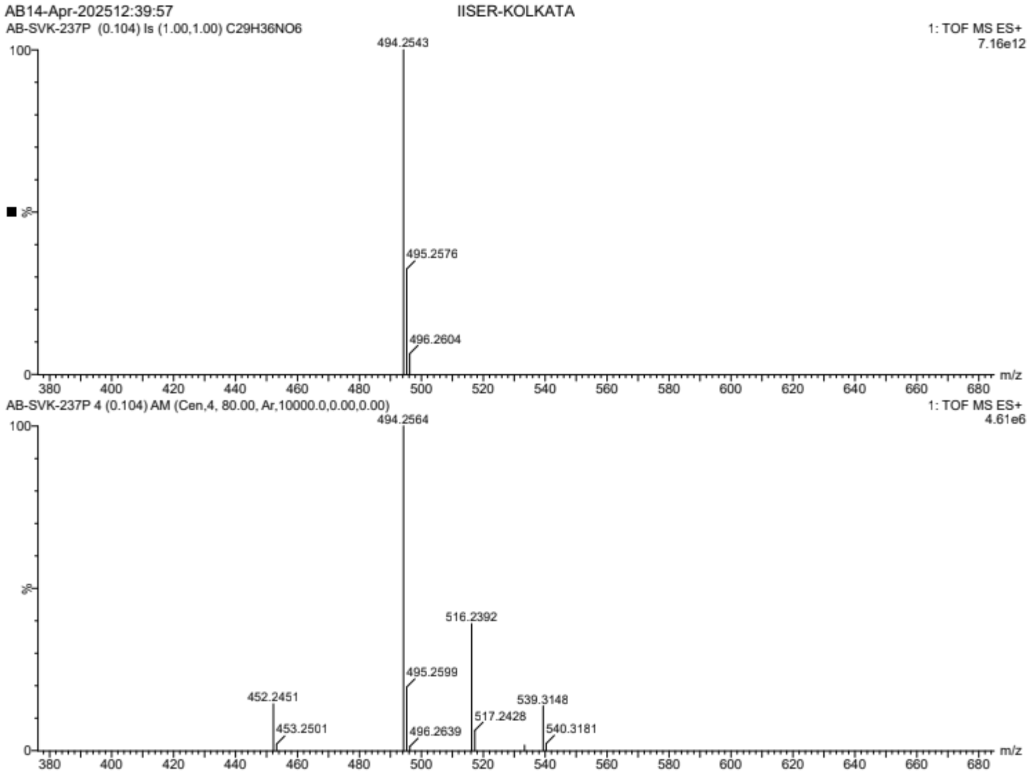
(+)-**22**



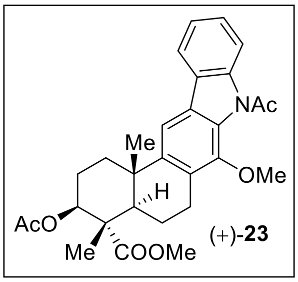
^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**22**



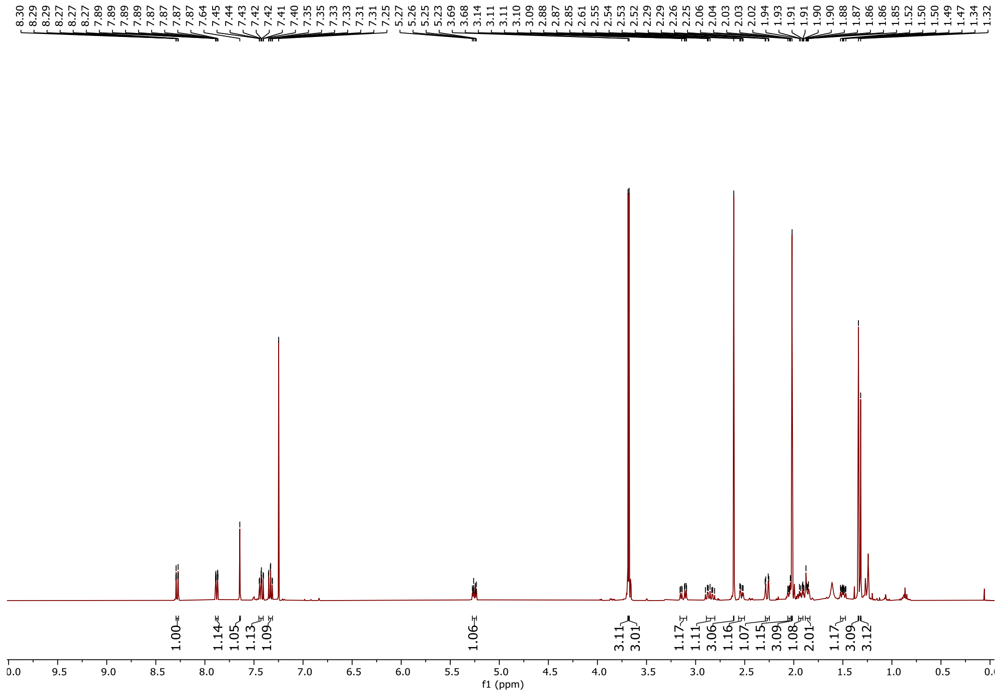
^{13}C NMR (101 MHz, CDCl$_3$) of (+)-**22**



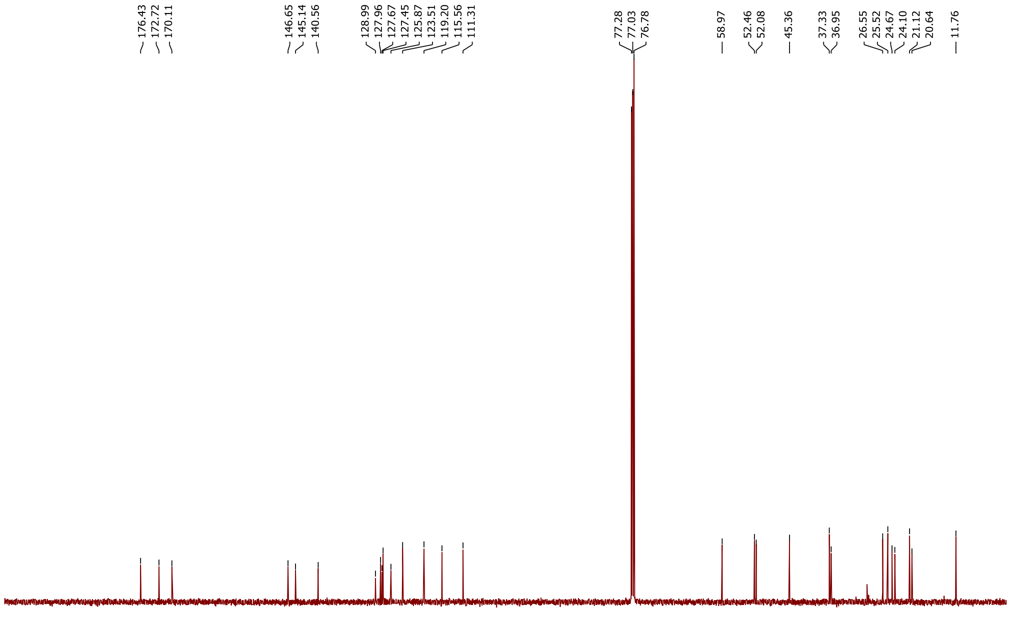
HRMS data of (+)-**22**



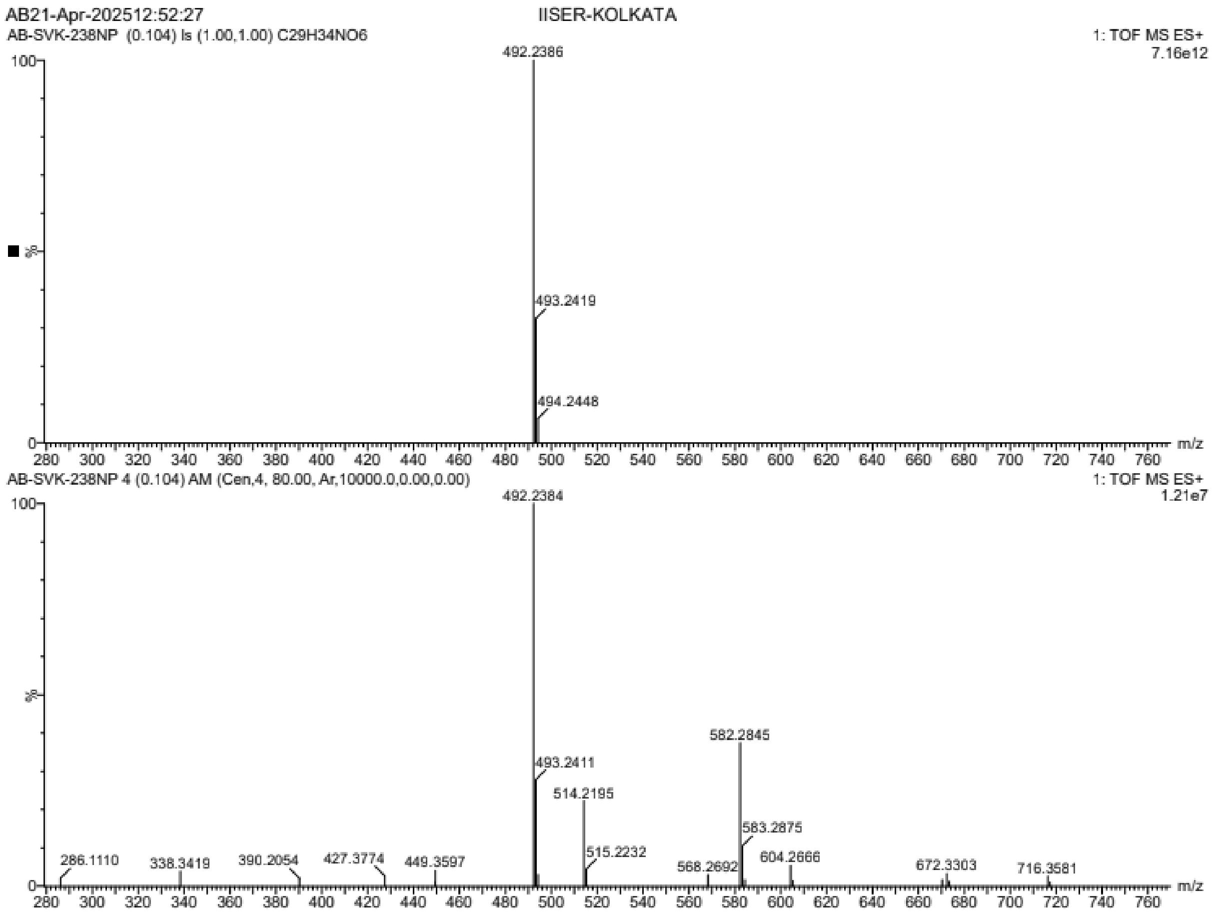
(+)-**23**



^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**23**



^{13}C NMR (126 MHz, CDCl$_3$) of (+)-**23**



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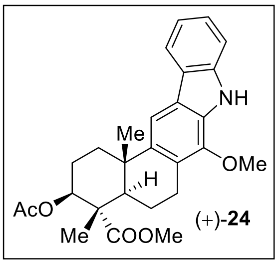
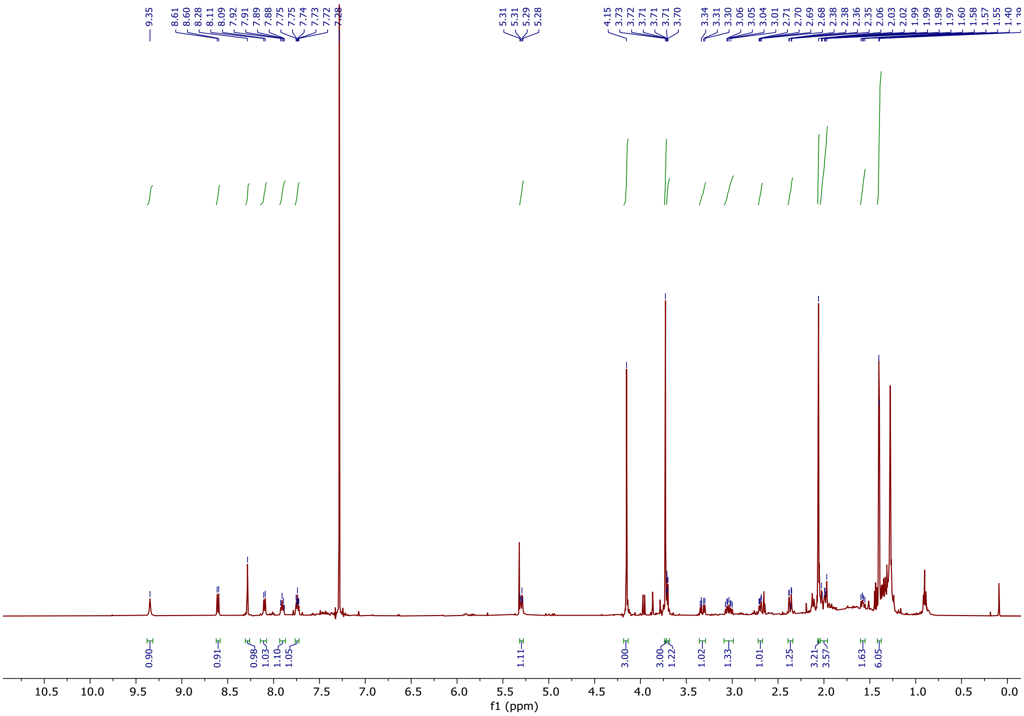
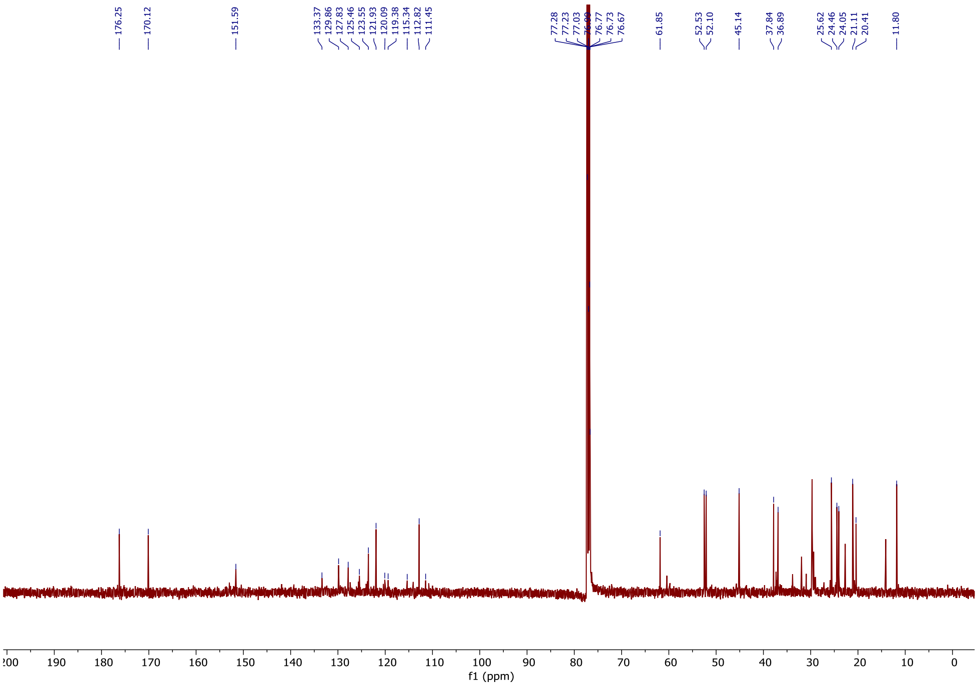


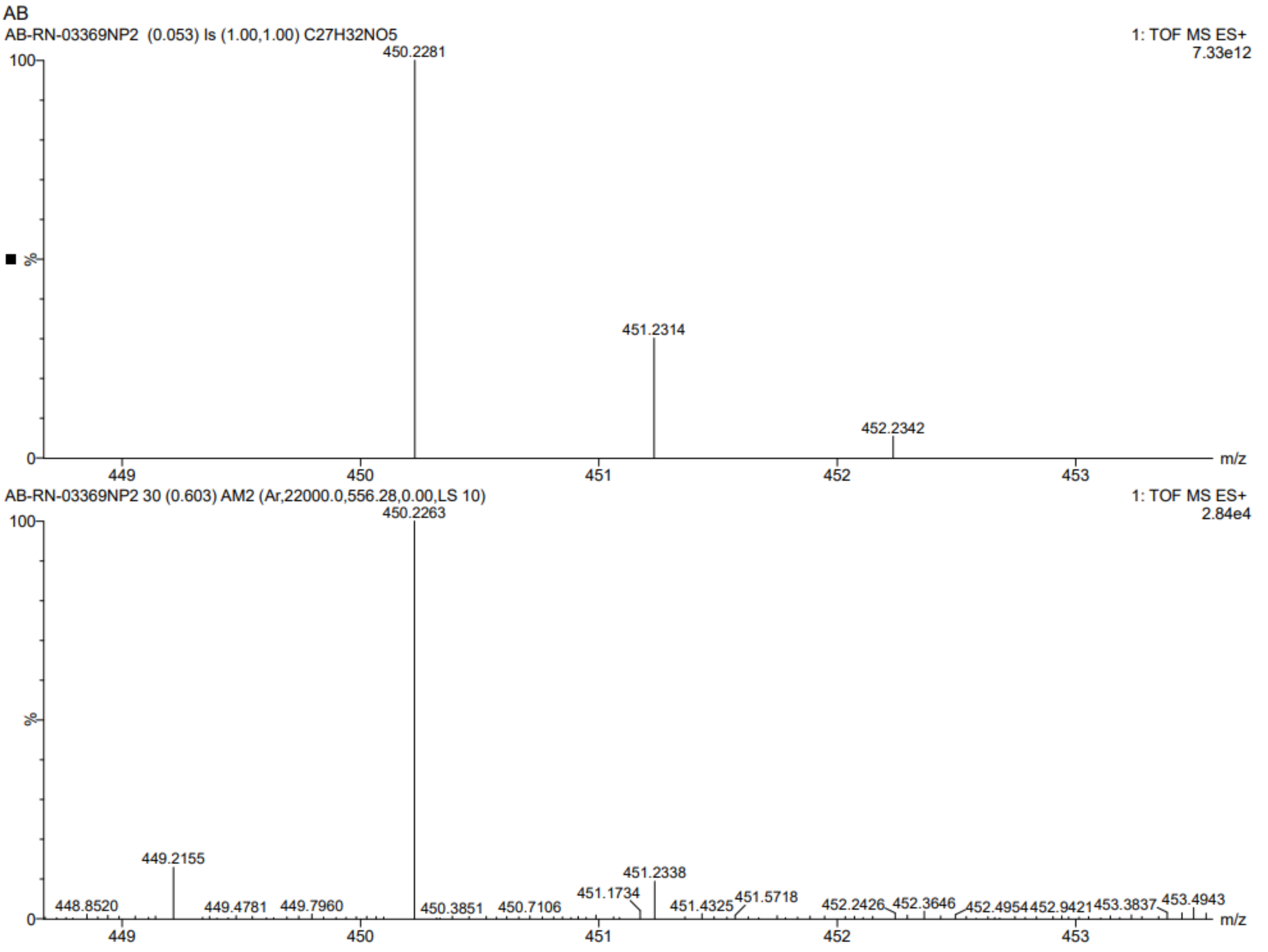
(+)-**24**



^{1}H NMR (500 MHz, CDCl$_3$) of (+)-**24**



^{13}C NMR (125 MHz, CDCl$_3$) of (+)-**24**



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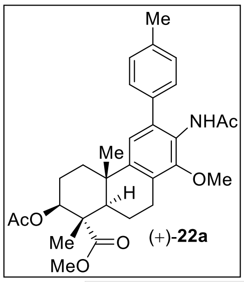
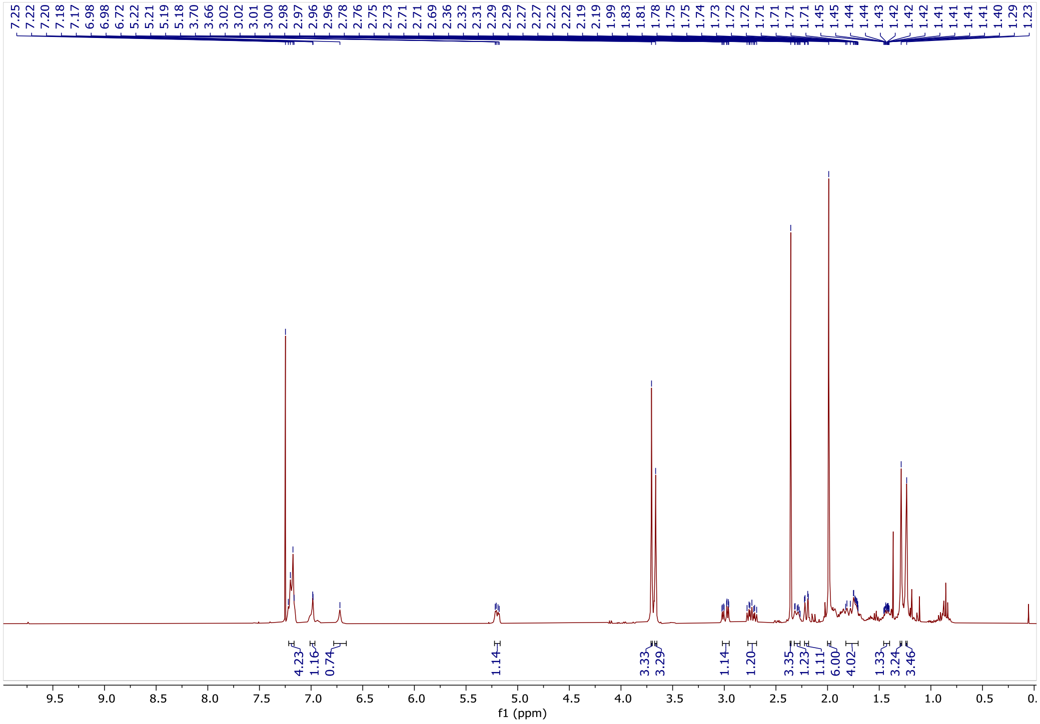
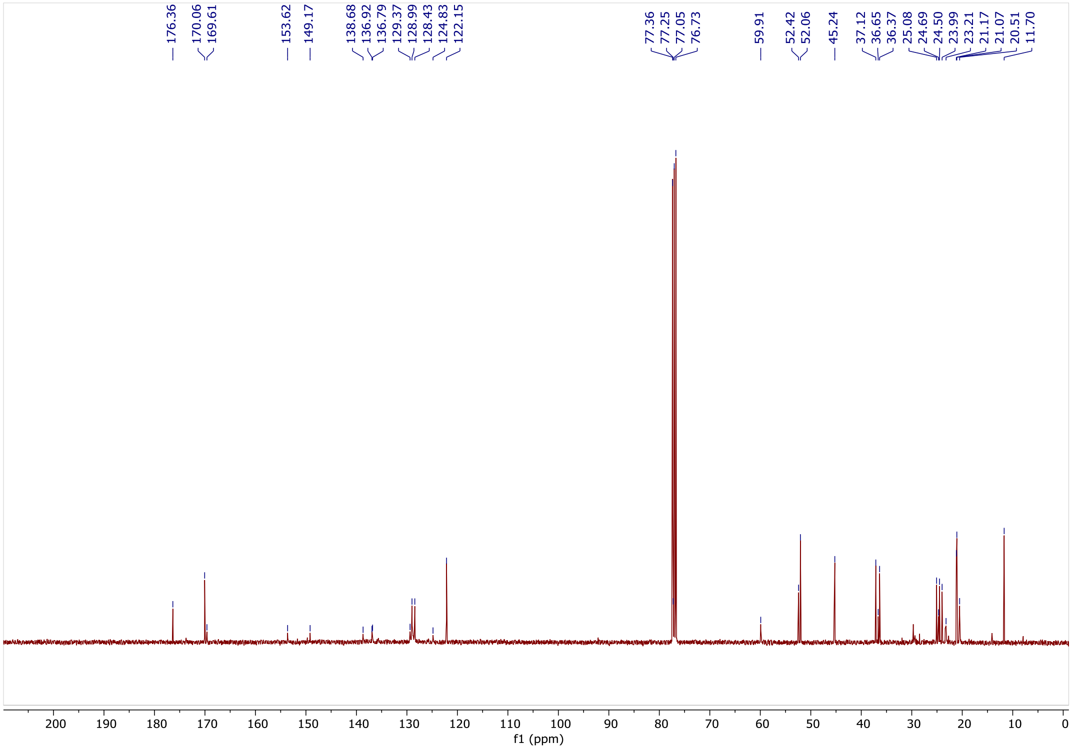


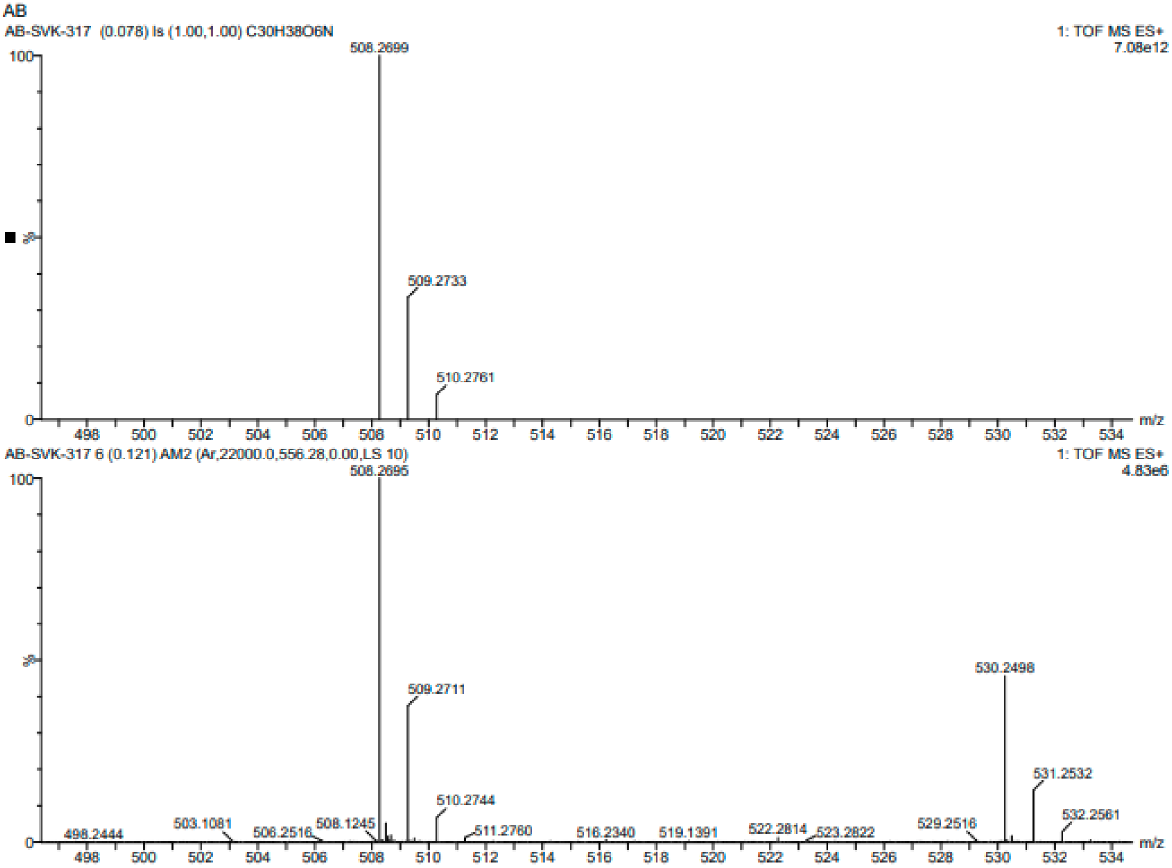
(+)-**22a**



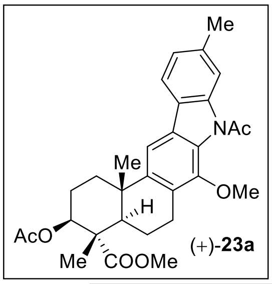
^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**22a**



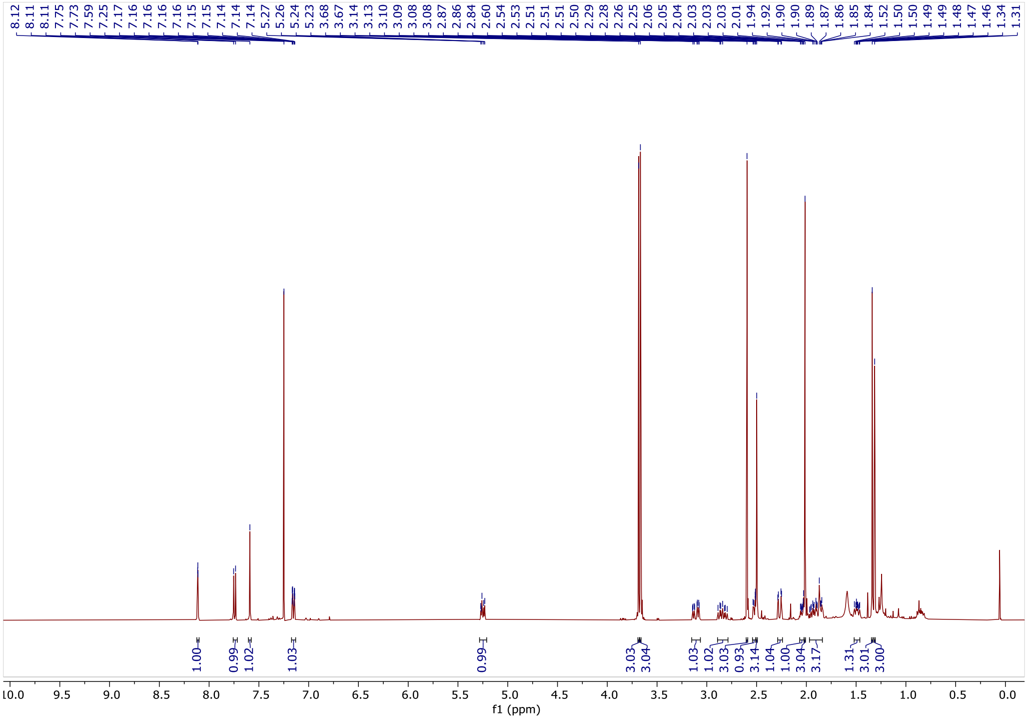
^{13}C NMR (101 MHz, CDCl$_3$) of (+)-**22a**



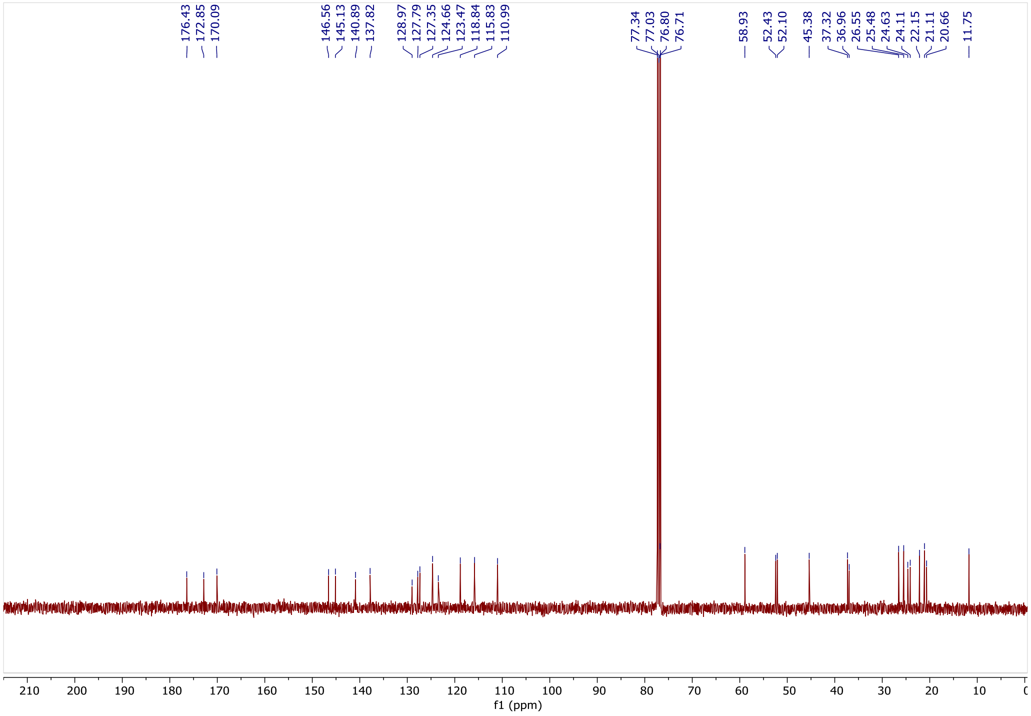
HRMS data of (+)-**22a**



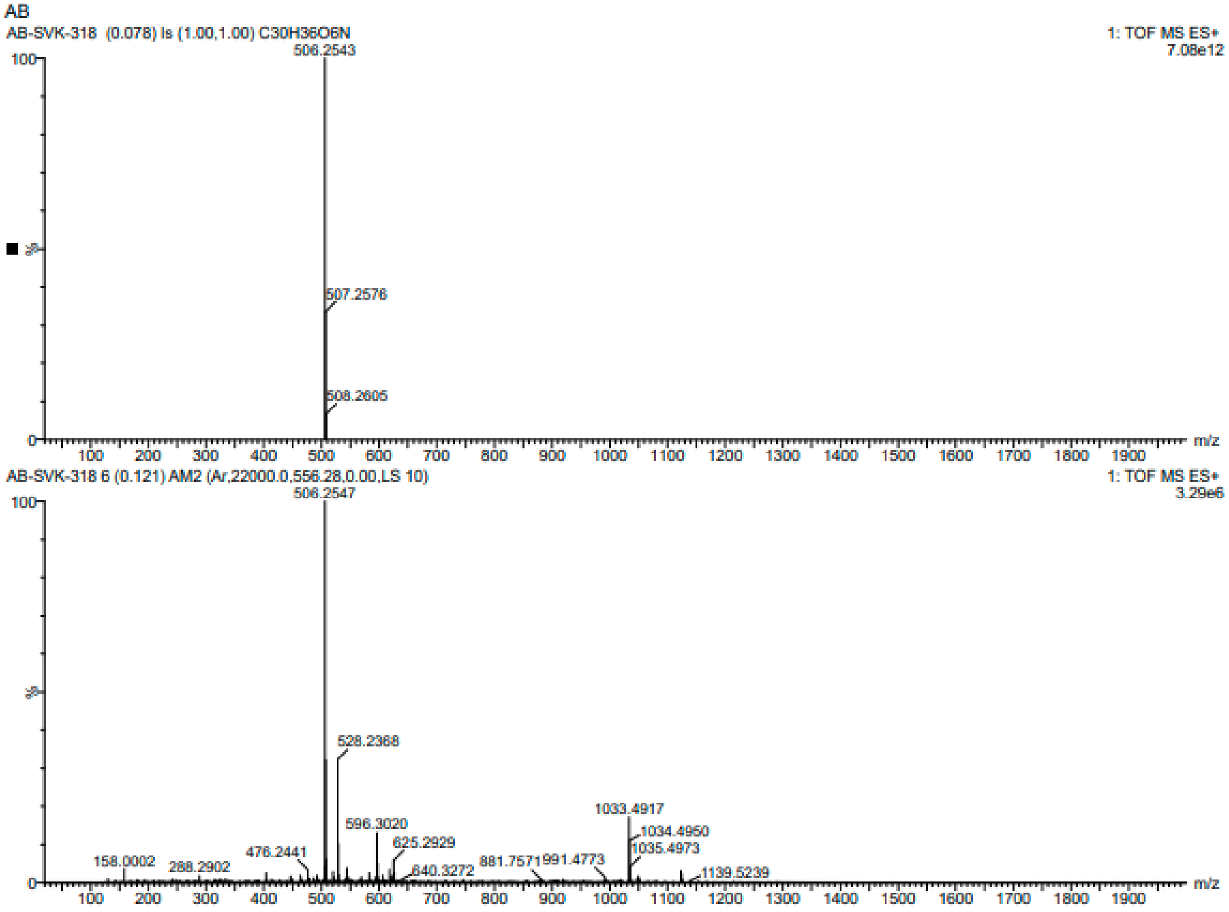
(+)-**23a**



^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**23a**



^{13}C NMR (101 MHz, CDCl$_3$) of (+)-**23a**



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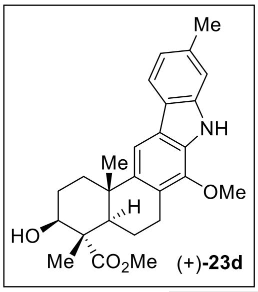
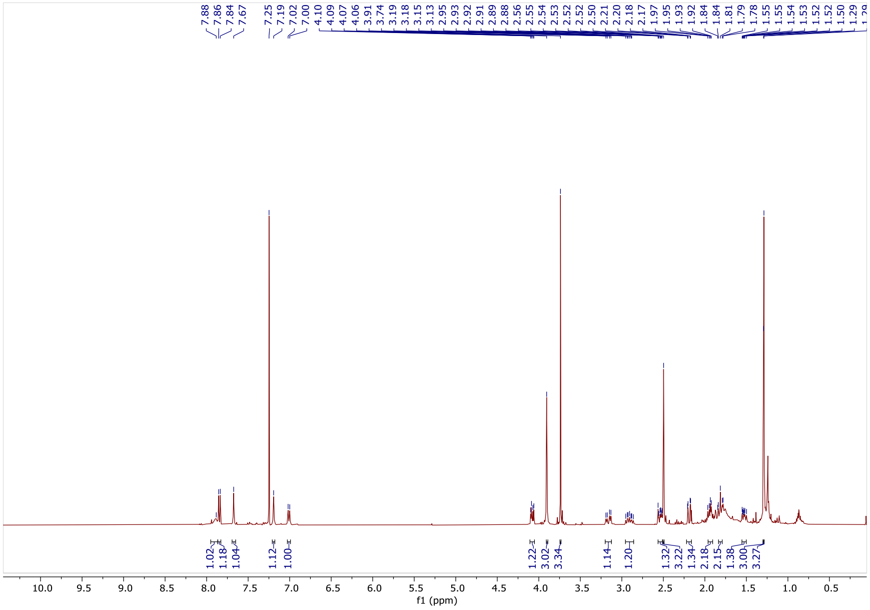
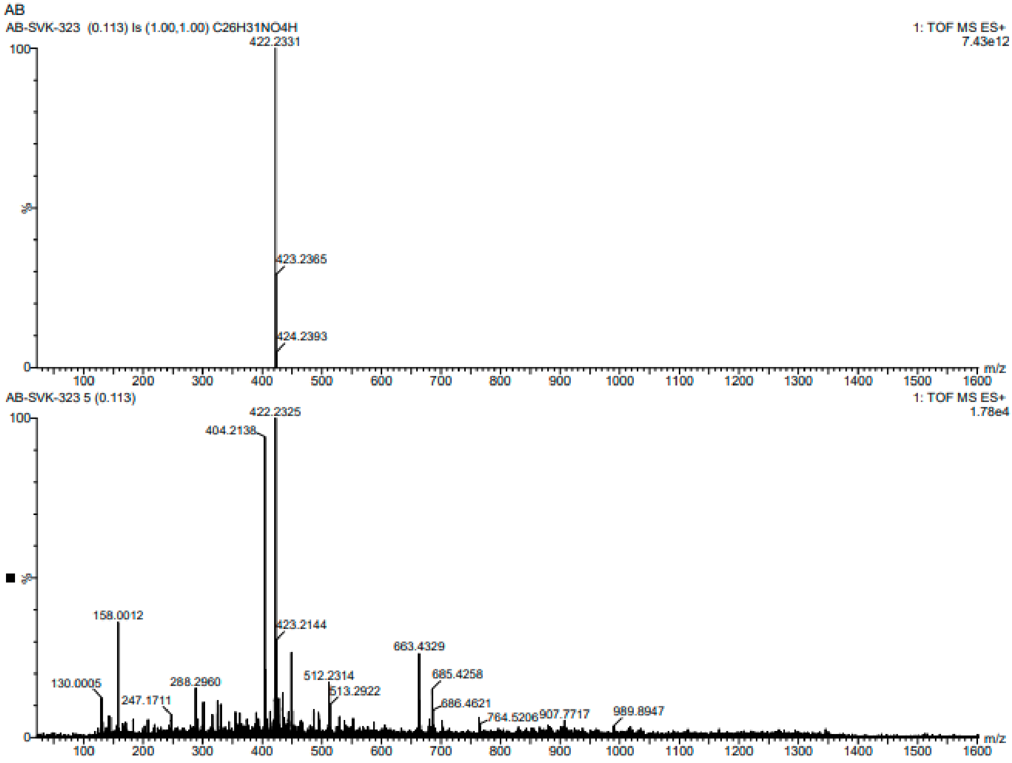


(+)-**23d**



^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**23d**



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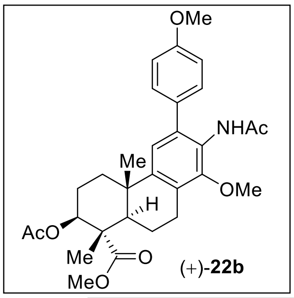
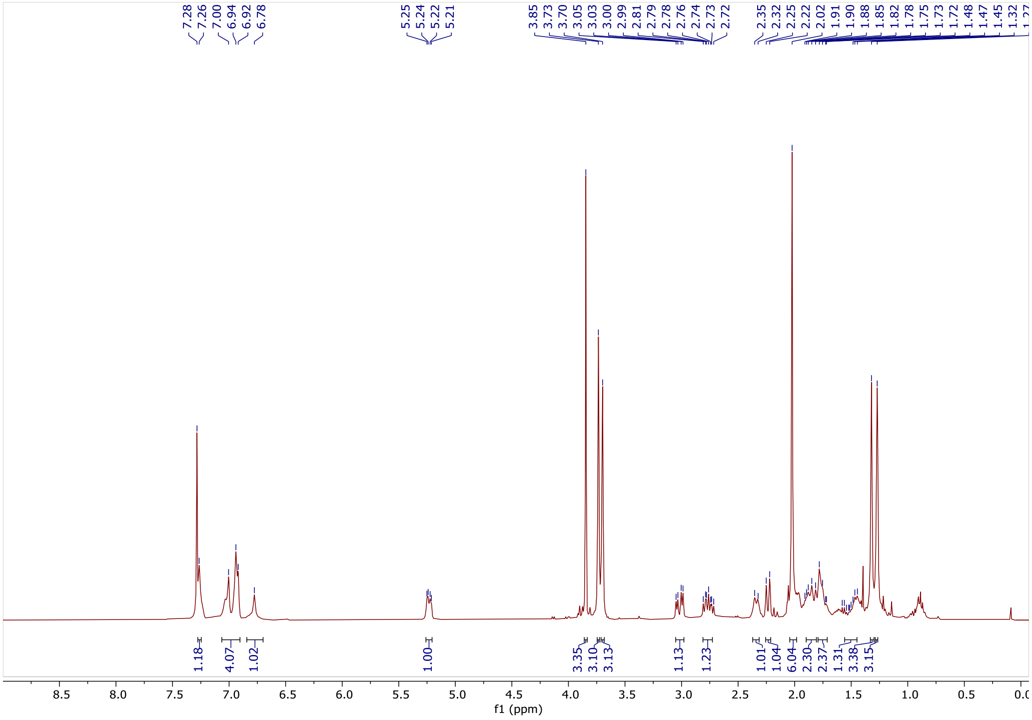
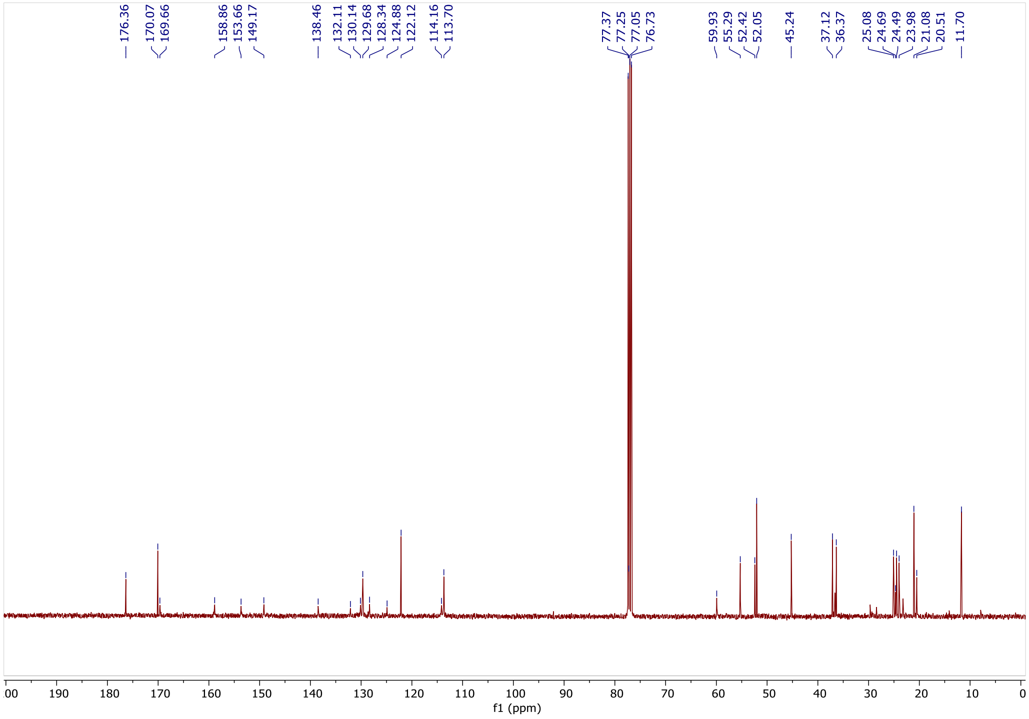


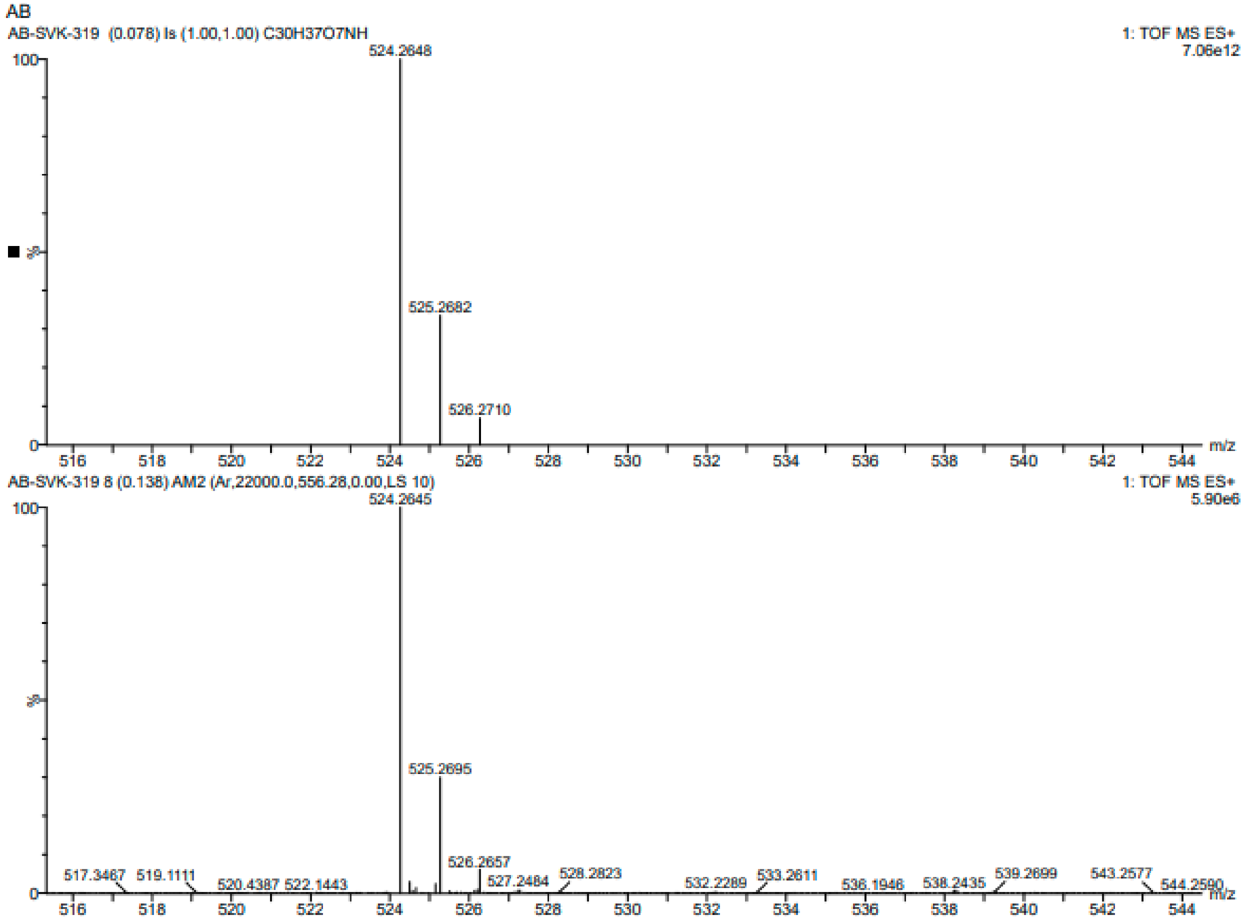
(+)-**22b**



^{1}H NMR (400 MHz, $CDCl_3$) of (+)-**22b**



^{13}C NMR (101 MHz, $CDCl_3$) of (+)-**22b**



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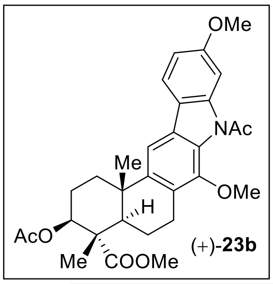
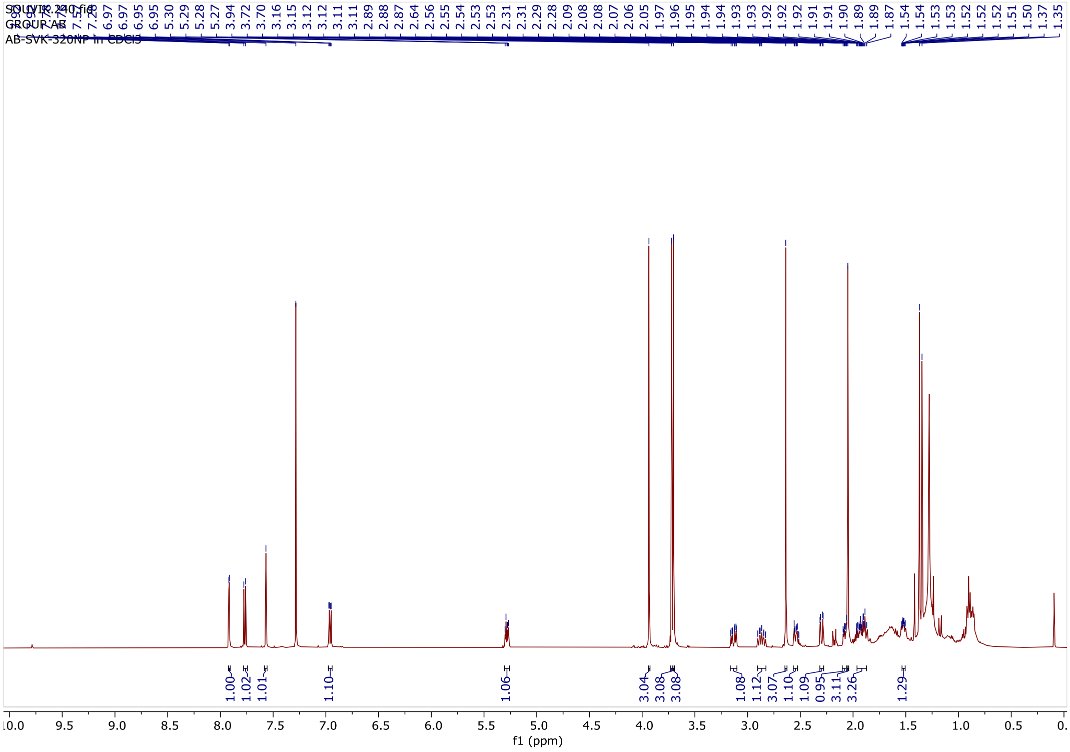
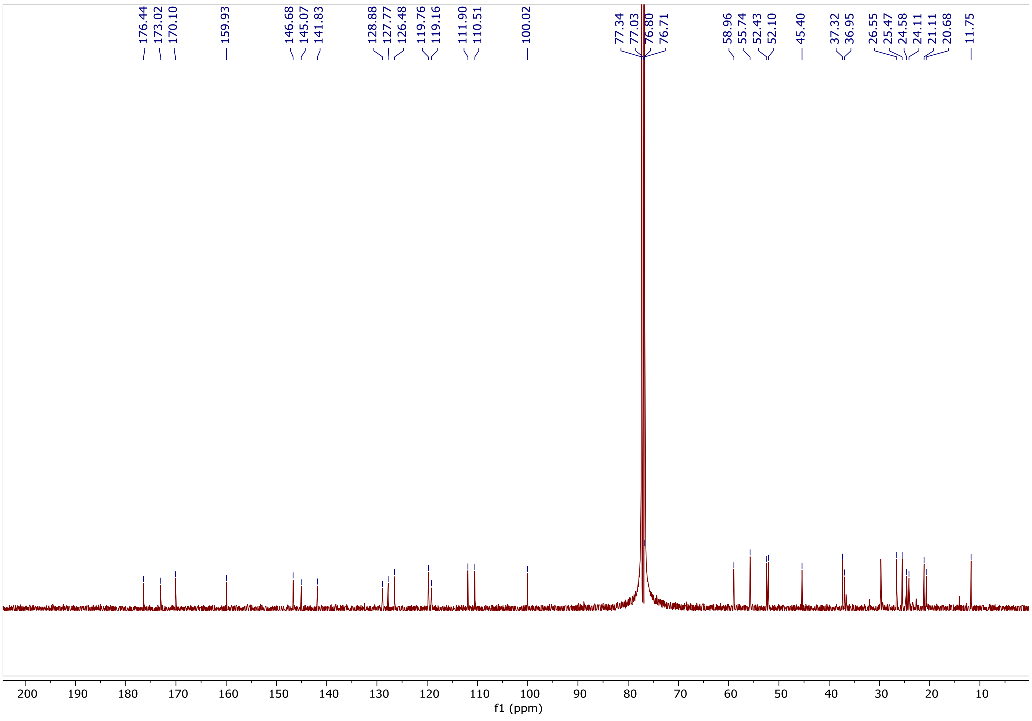


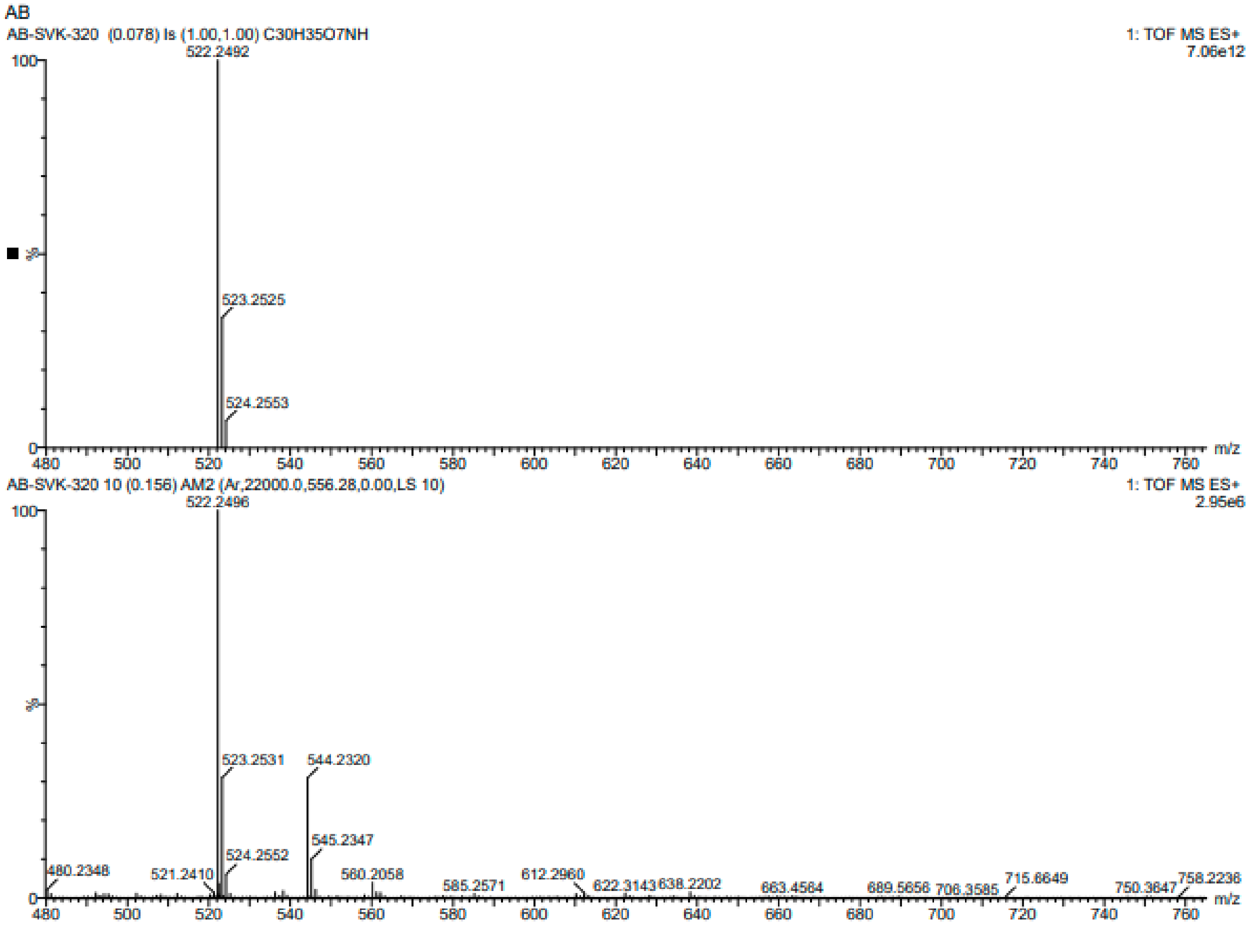
(+)-**23b**



^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**23b**



^{13}C NMR (101 MHz, CDCl$_3$) of (+)-**23b**



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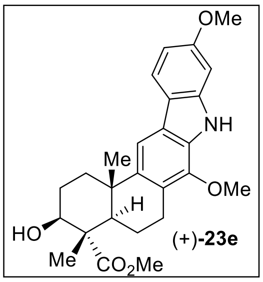
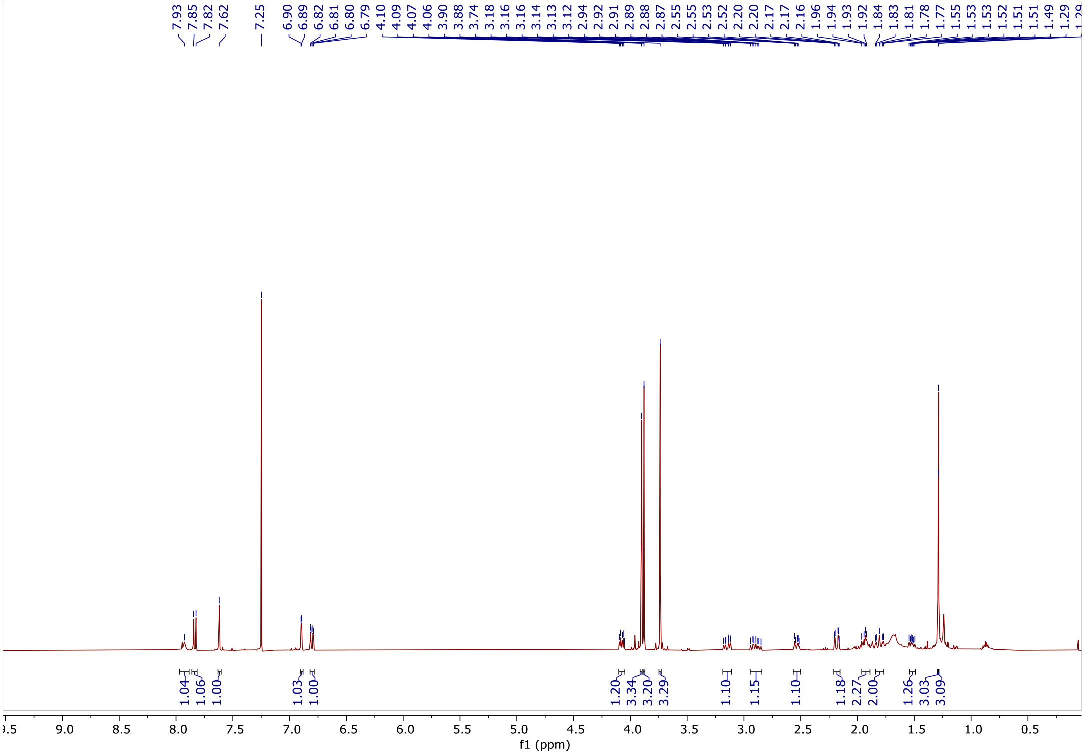
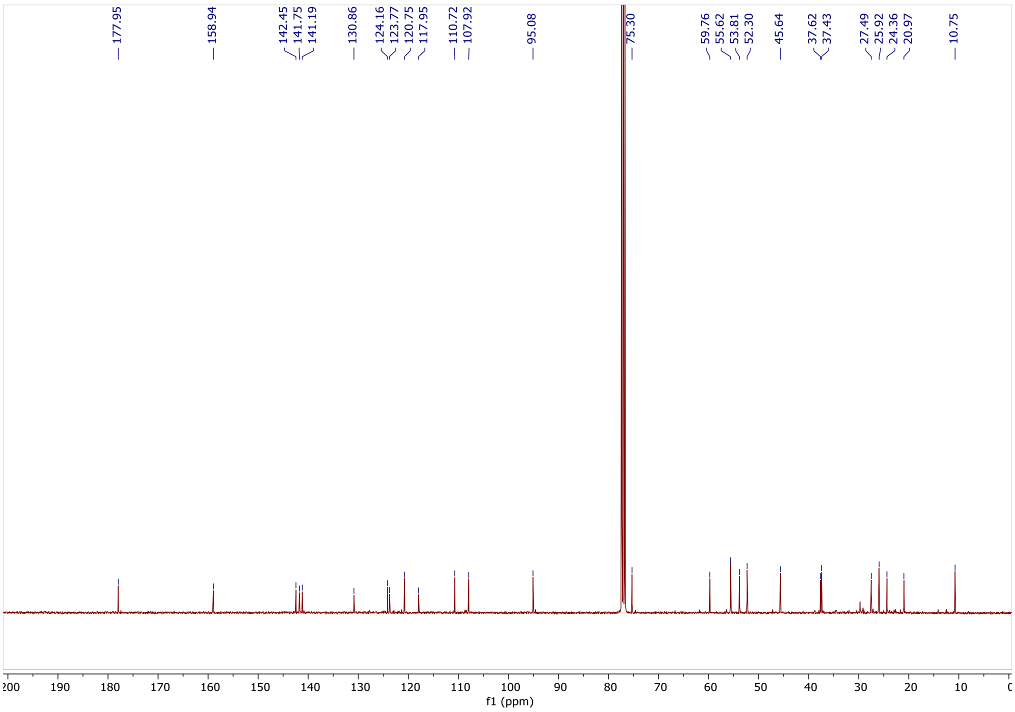
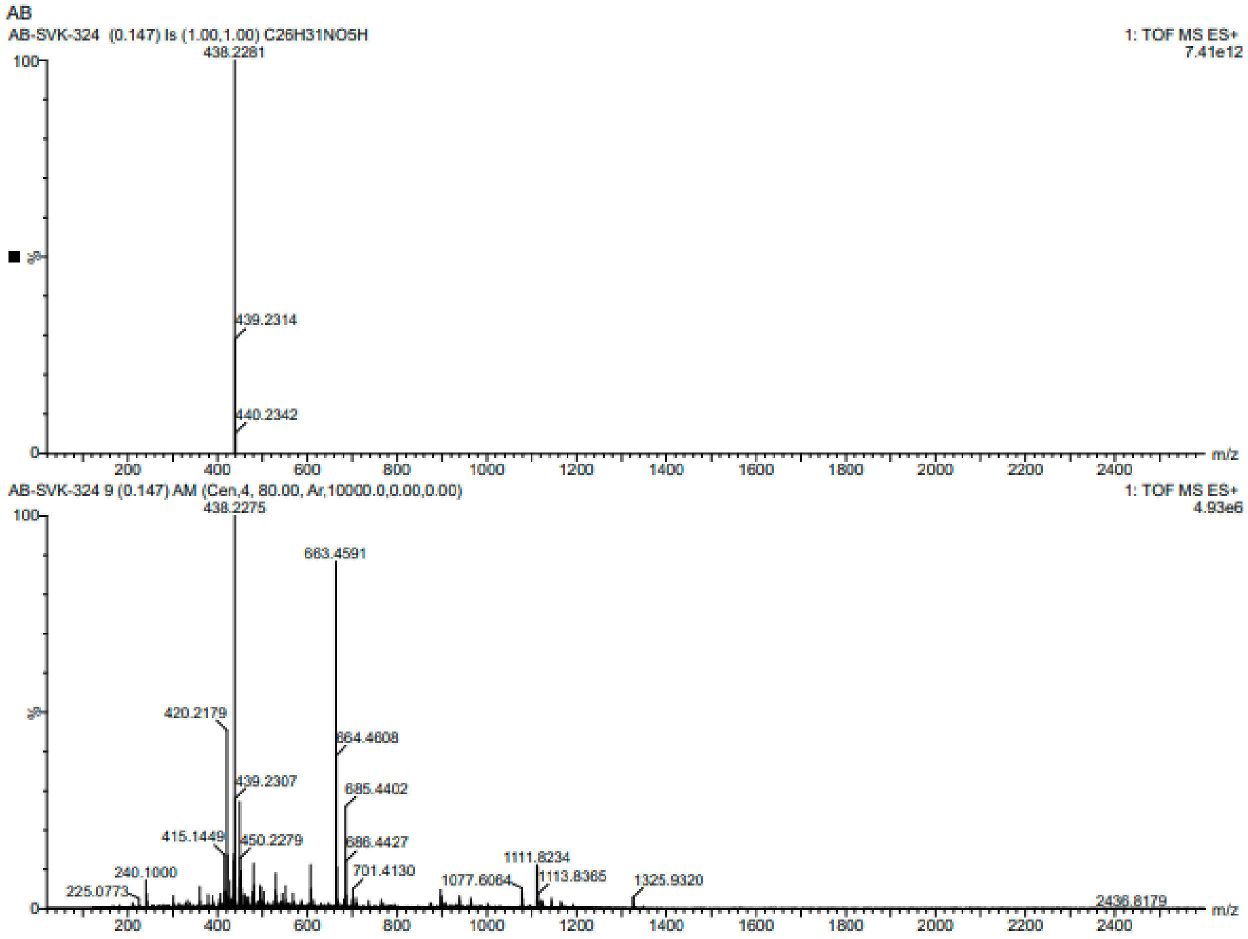




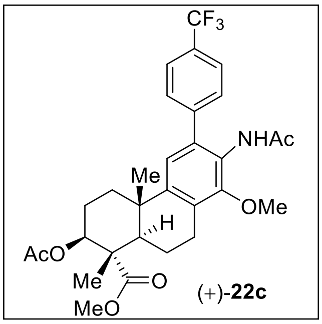
^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**23e**



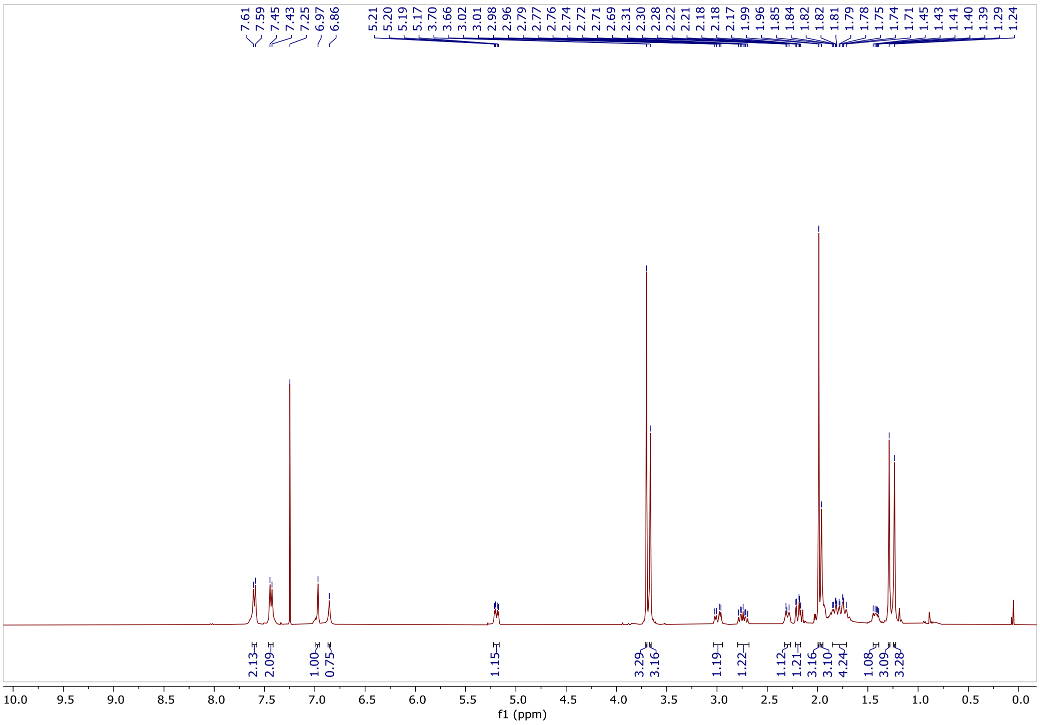
^{13}C NMR (101 MHz, CDCl$_3$) of (+)-**23e**



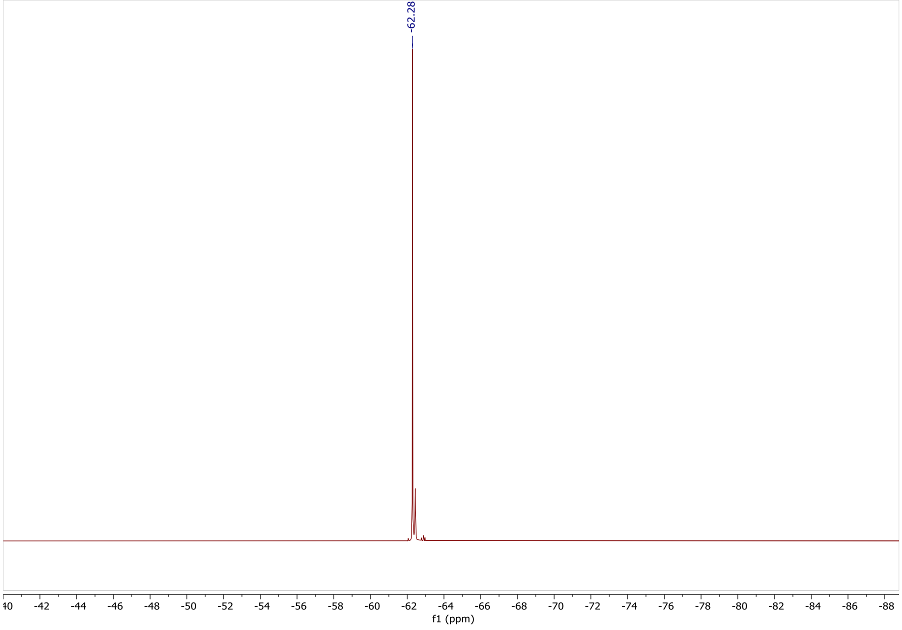
HRMS data of (+)-**23e**



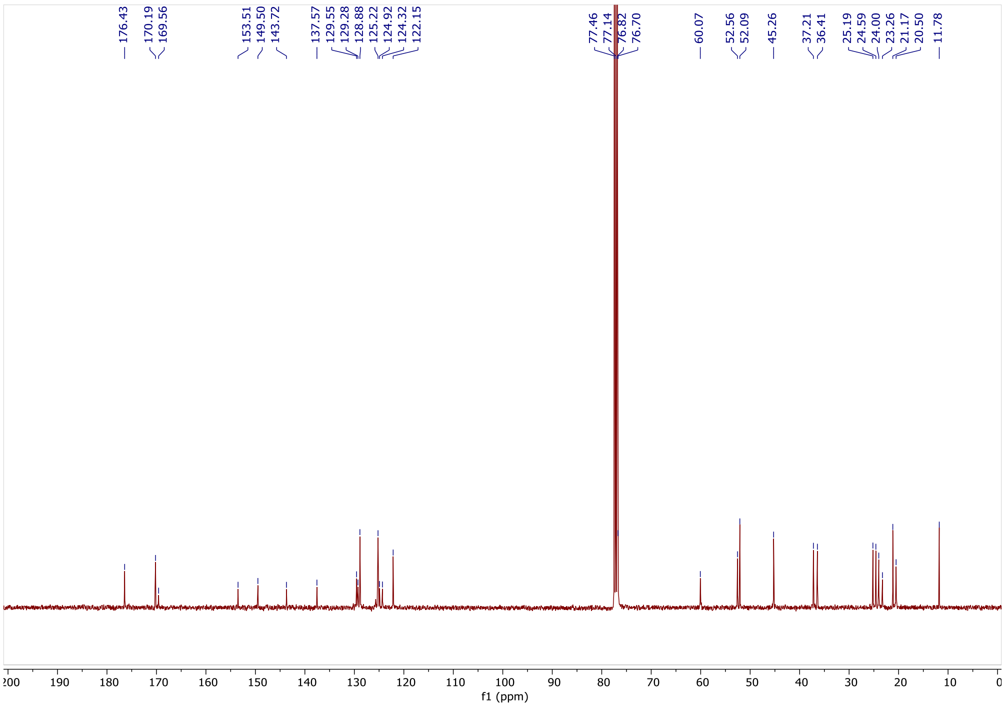
(+)-**22c**



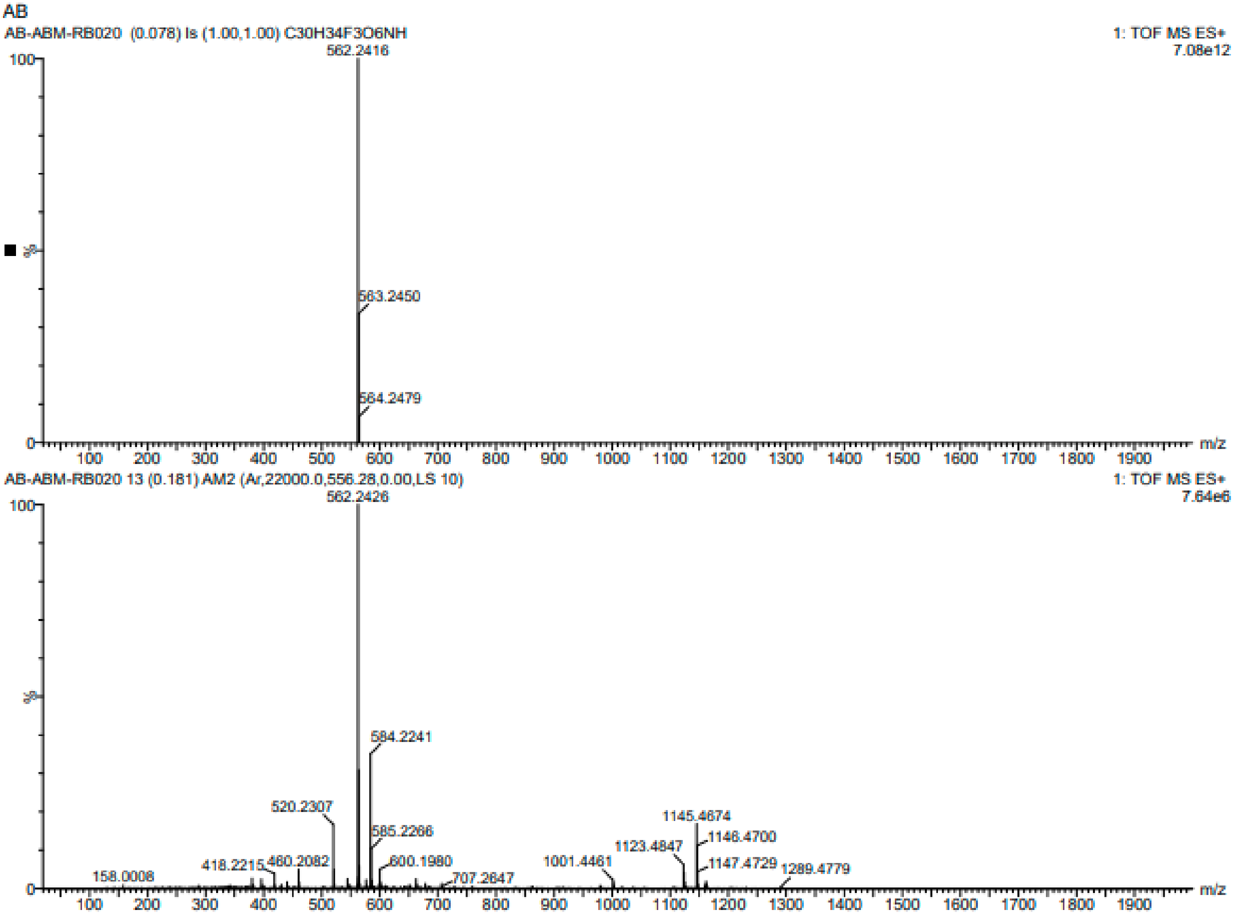
^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**22c**



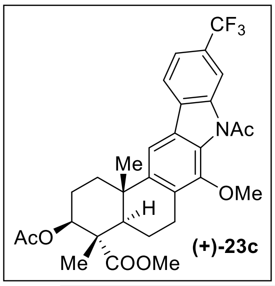
^{19}F NMR (376 MHz, CDCl$_3$) of (+)-**22c**



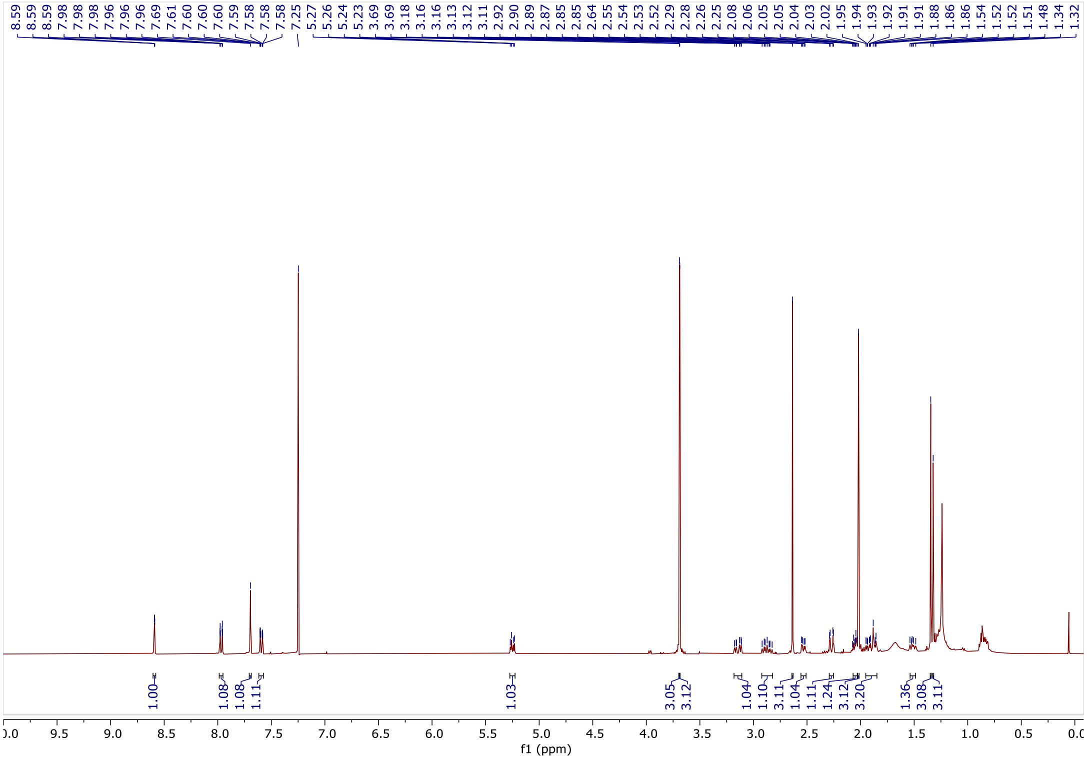
^{13}C{^{19}F} {^{1}H} NMR (101 MHz, CDCl$_3$) of (+)-**22c**



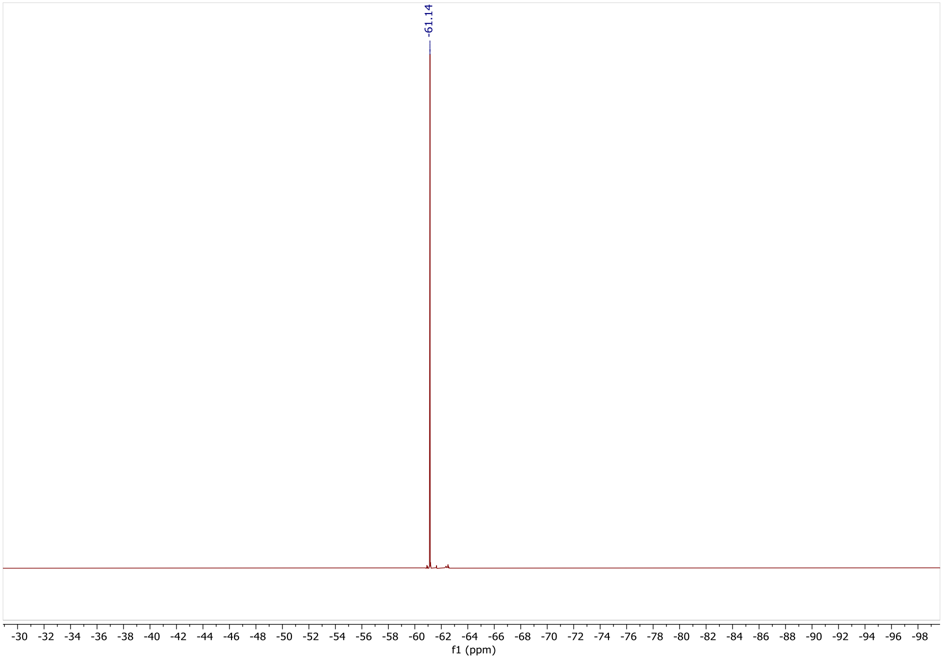
HRMS data of (+)-**22c**



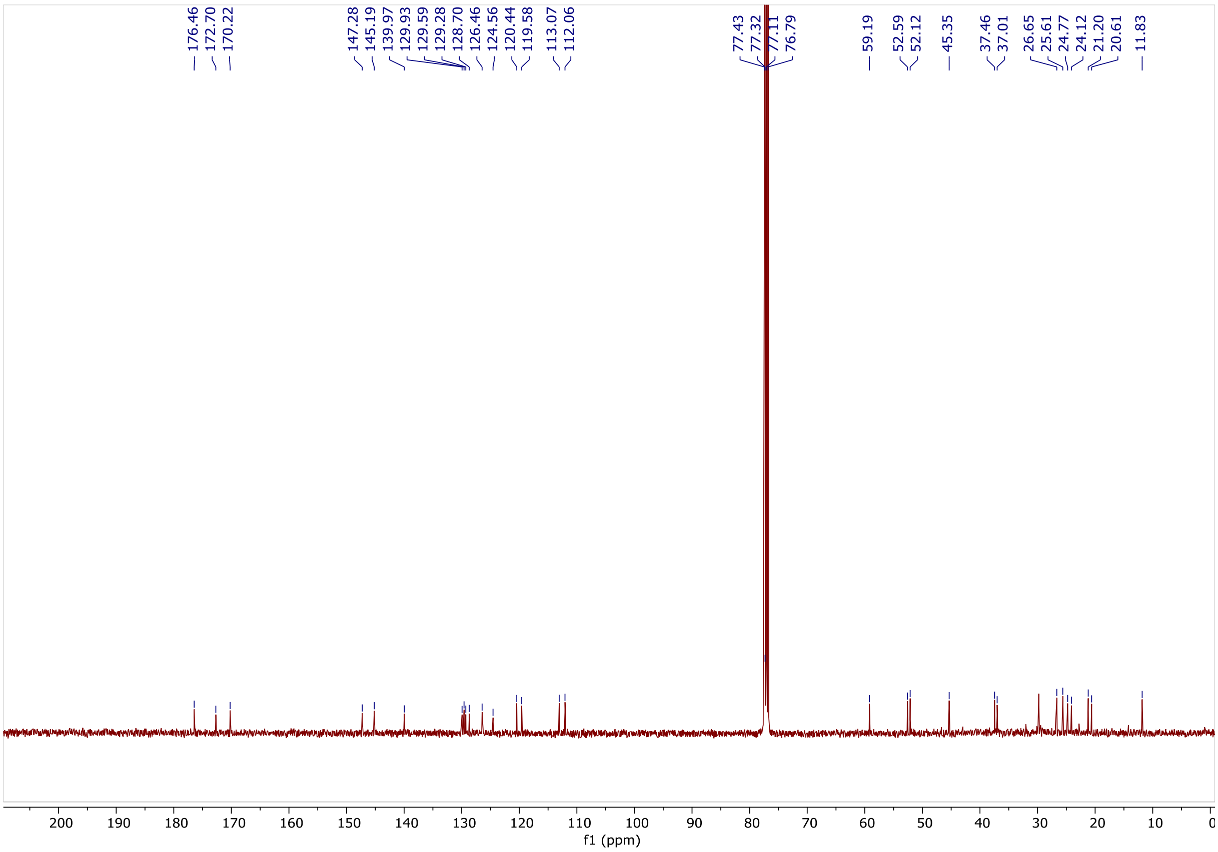
(+)-23c



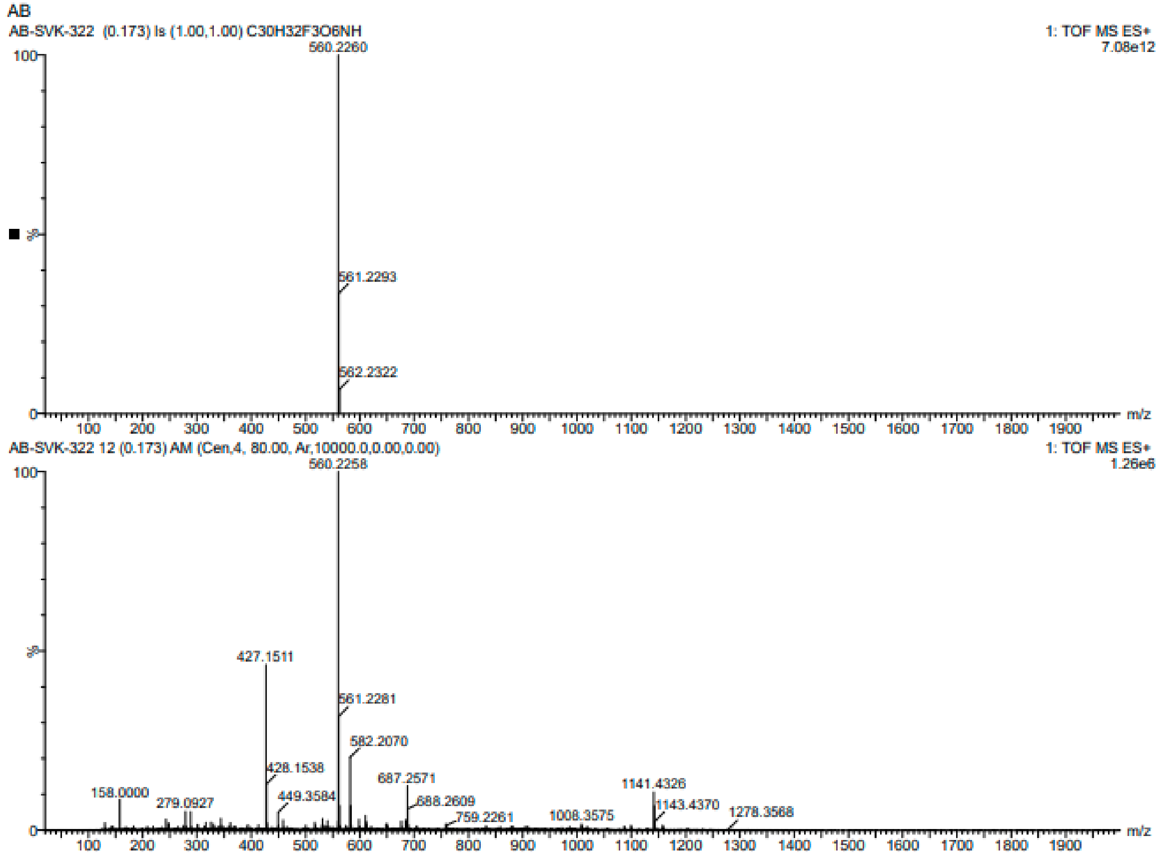
^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**23c**



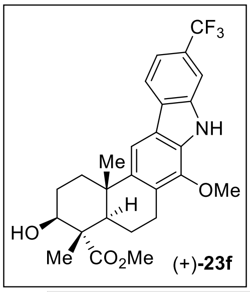
^{19}F NMR (376 MHz, CDCl$_3$) of (+)-**23c**



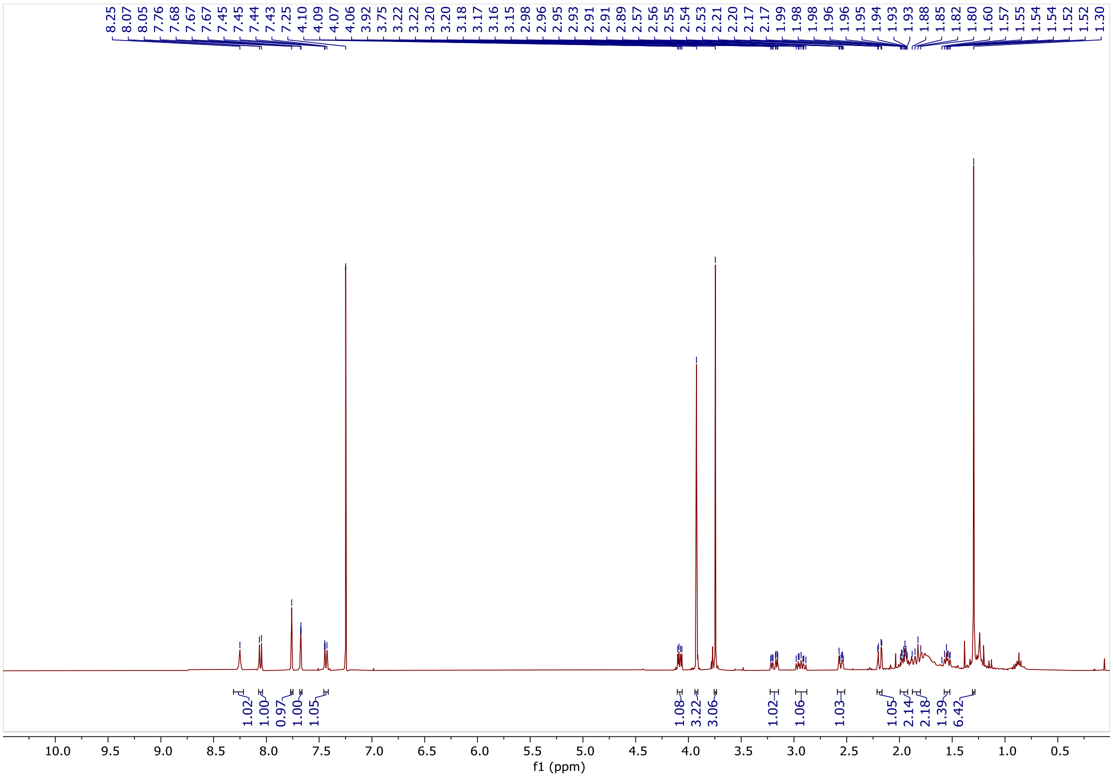
^{13}C{^{19}F} {^{1}H} NMR (101 MHz, CDCl$_3$) of (+)-**23c**



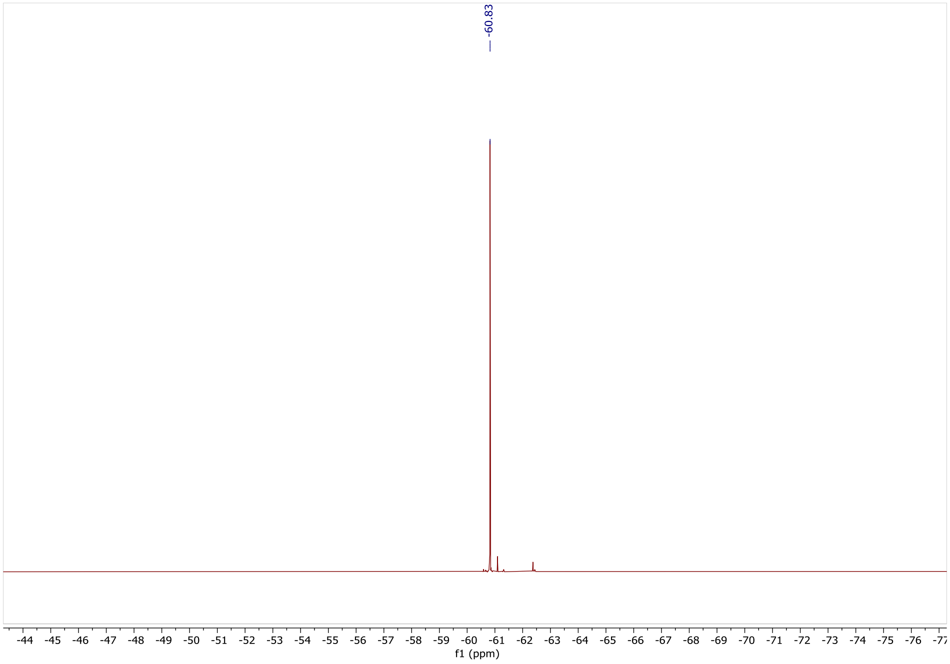
HRMS data of (+)-**23c**



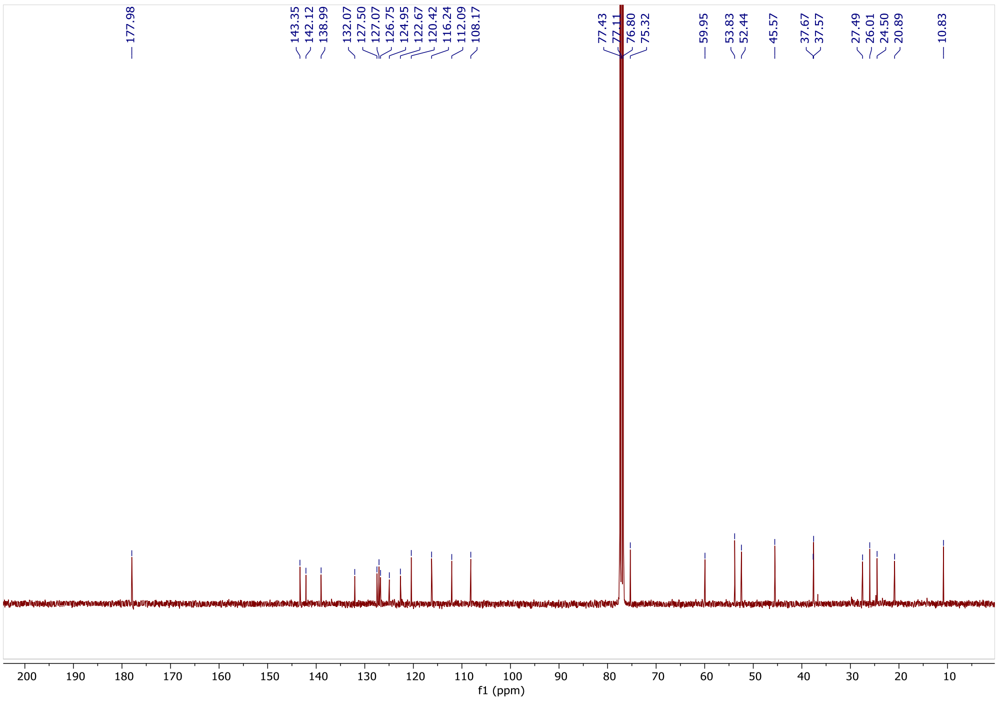
(+)-**23f**



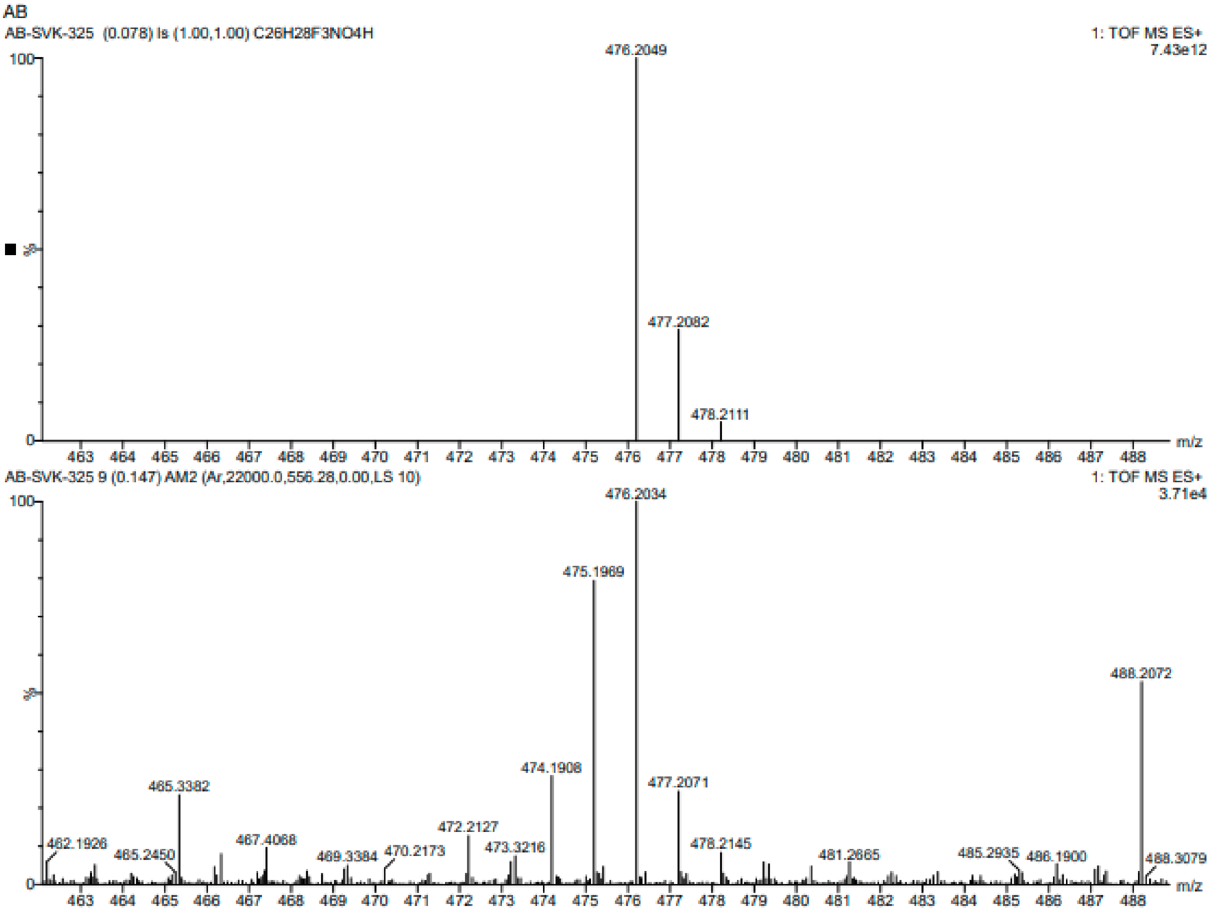
^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**23f**



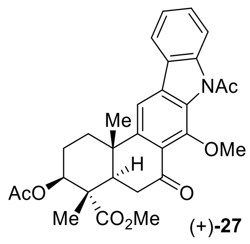
^{19}F NMR (376 MHz, CDCl$_3$) of (+)-**23f**



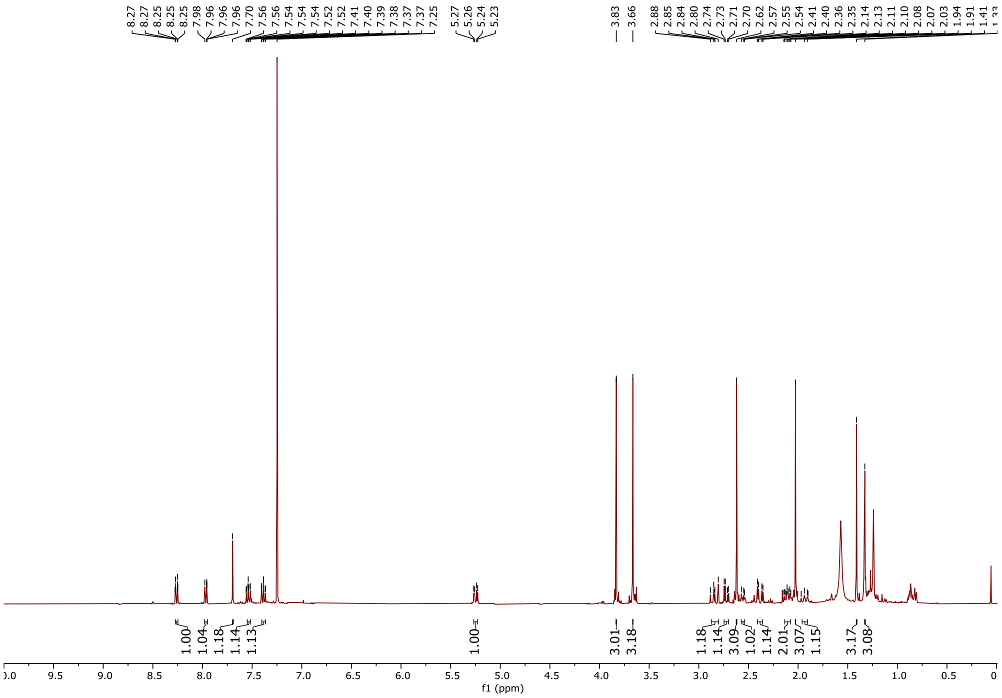
$^{13}C\{^{19}F\}\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of (+)-**23f**



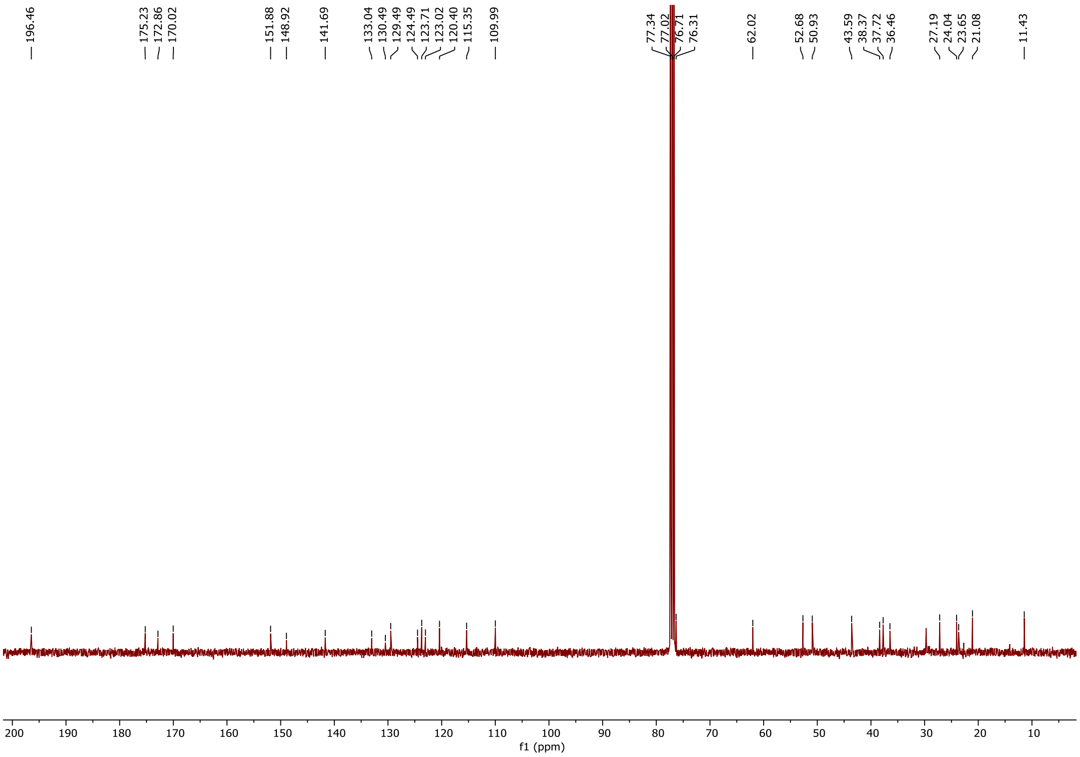
HRMS data of (+)-**23f**



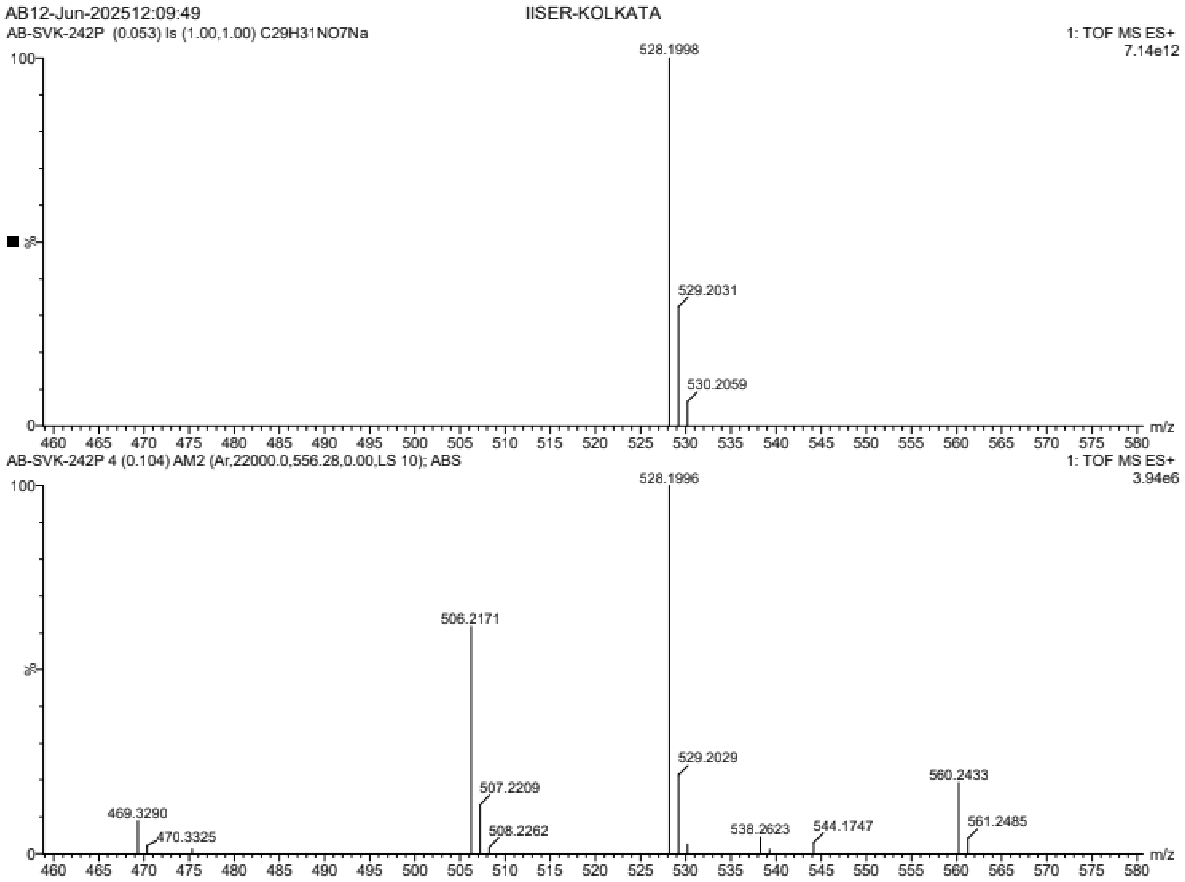
(+)-**27**



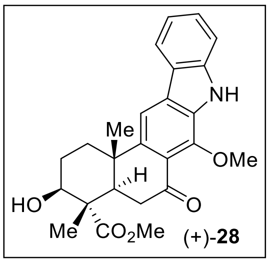
^{1}H NMR (400 MHz, CDCl$_3$) of (+)-**27**



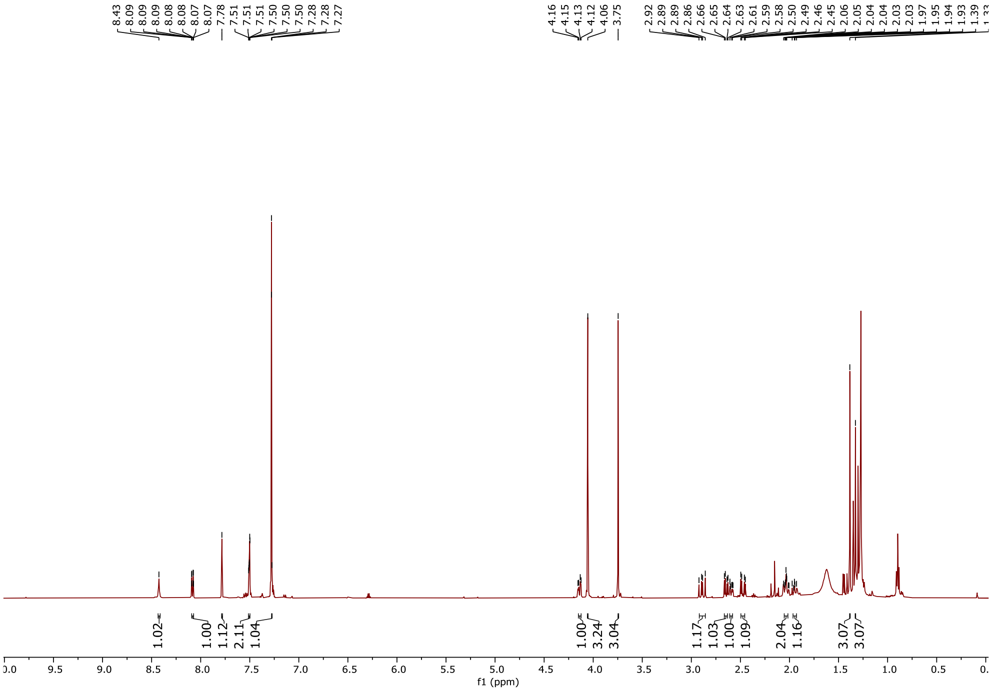
^{13}C NMR (101 MHz, CDCl$_3$) of (+)-**27**



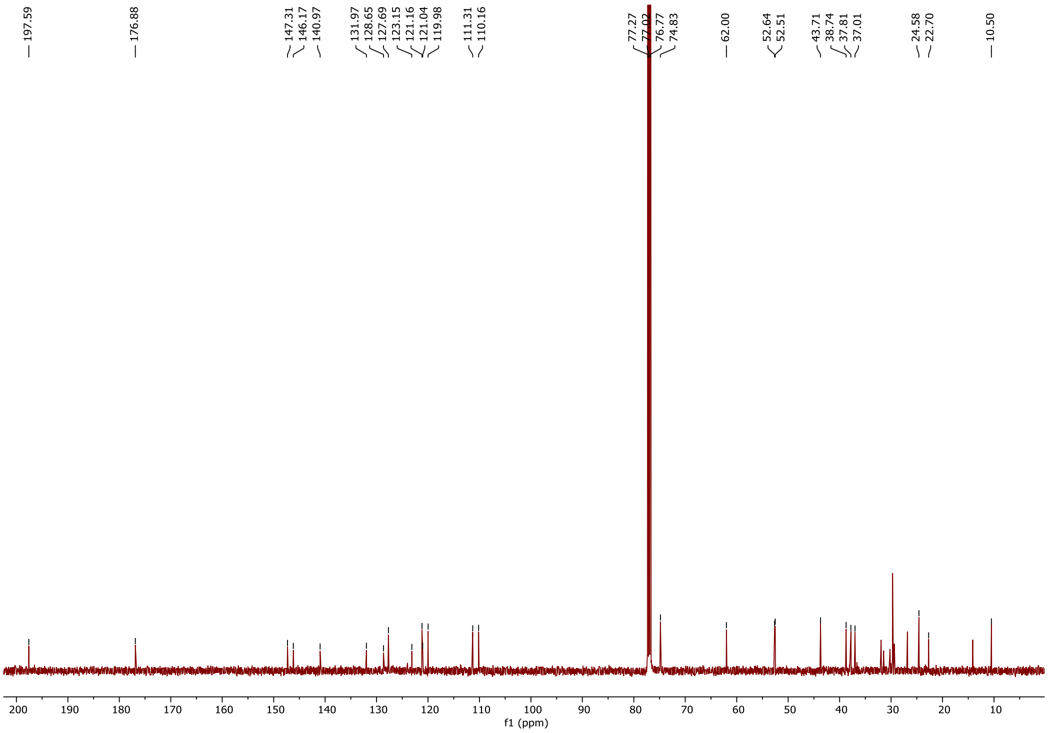
HRMS data of (+)-**27**



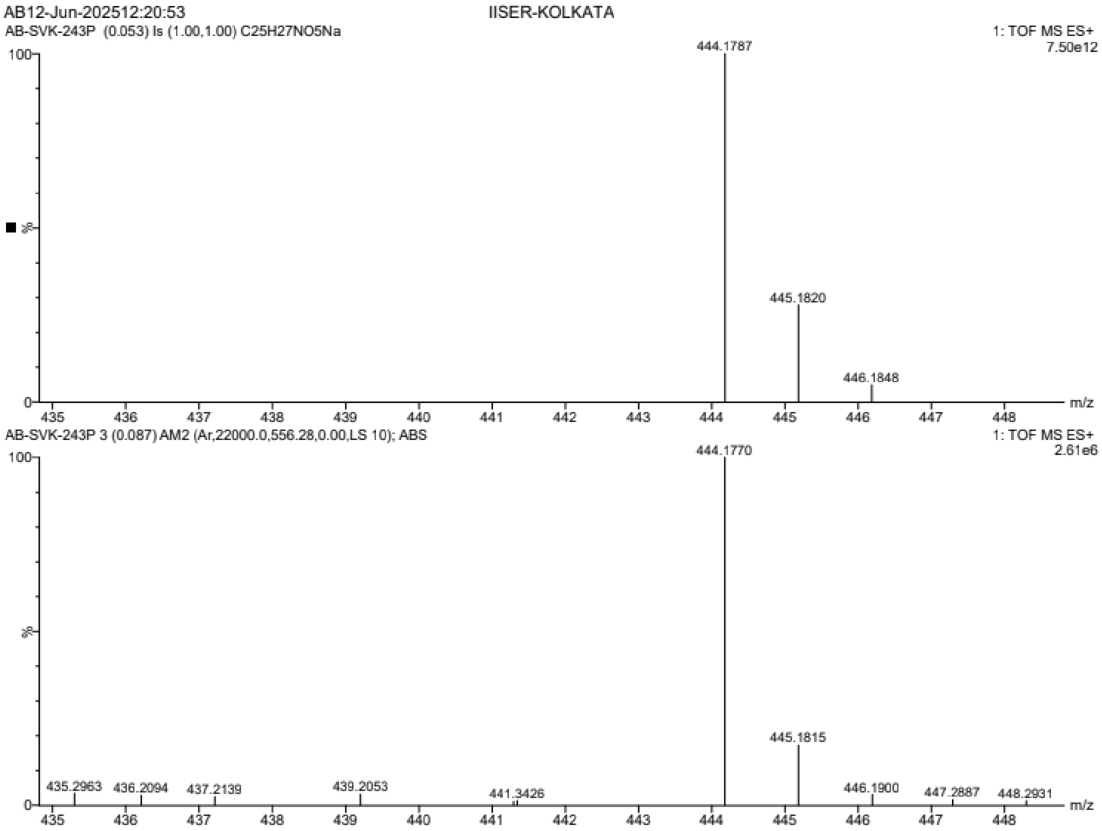
(+)-**28**



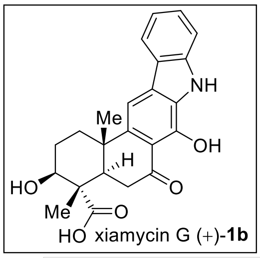
^{1}H NMR (500 MHz, $CDCl_3$) of (+)-**28**



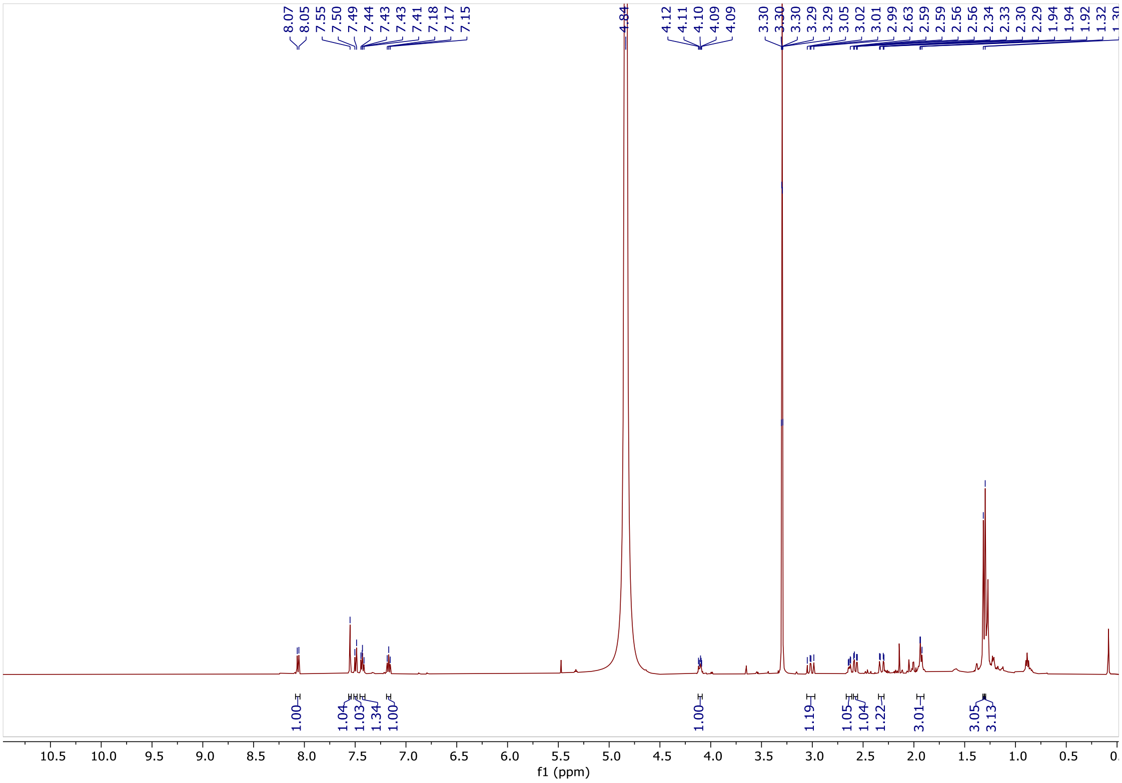
^{13}C NMR (126 MHz, $CDCl_3$) of (+)-**28**



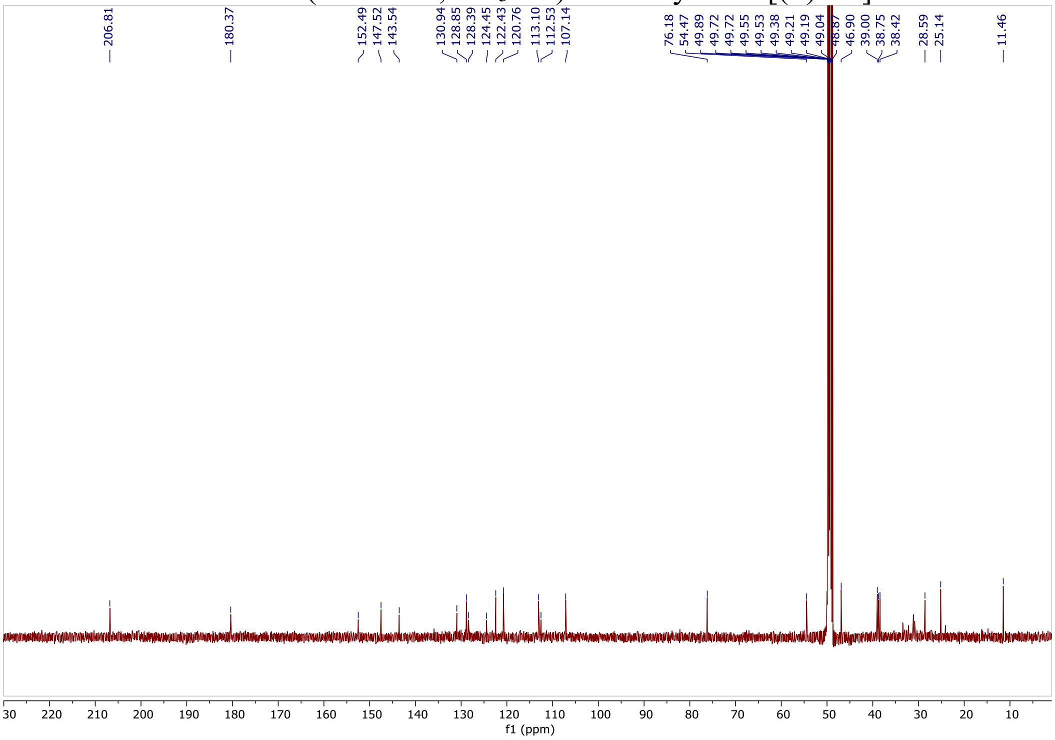
HRMS data of (+)-**28**



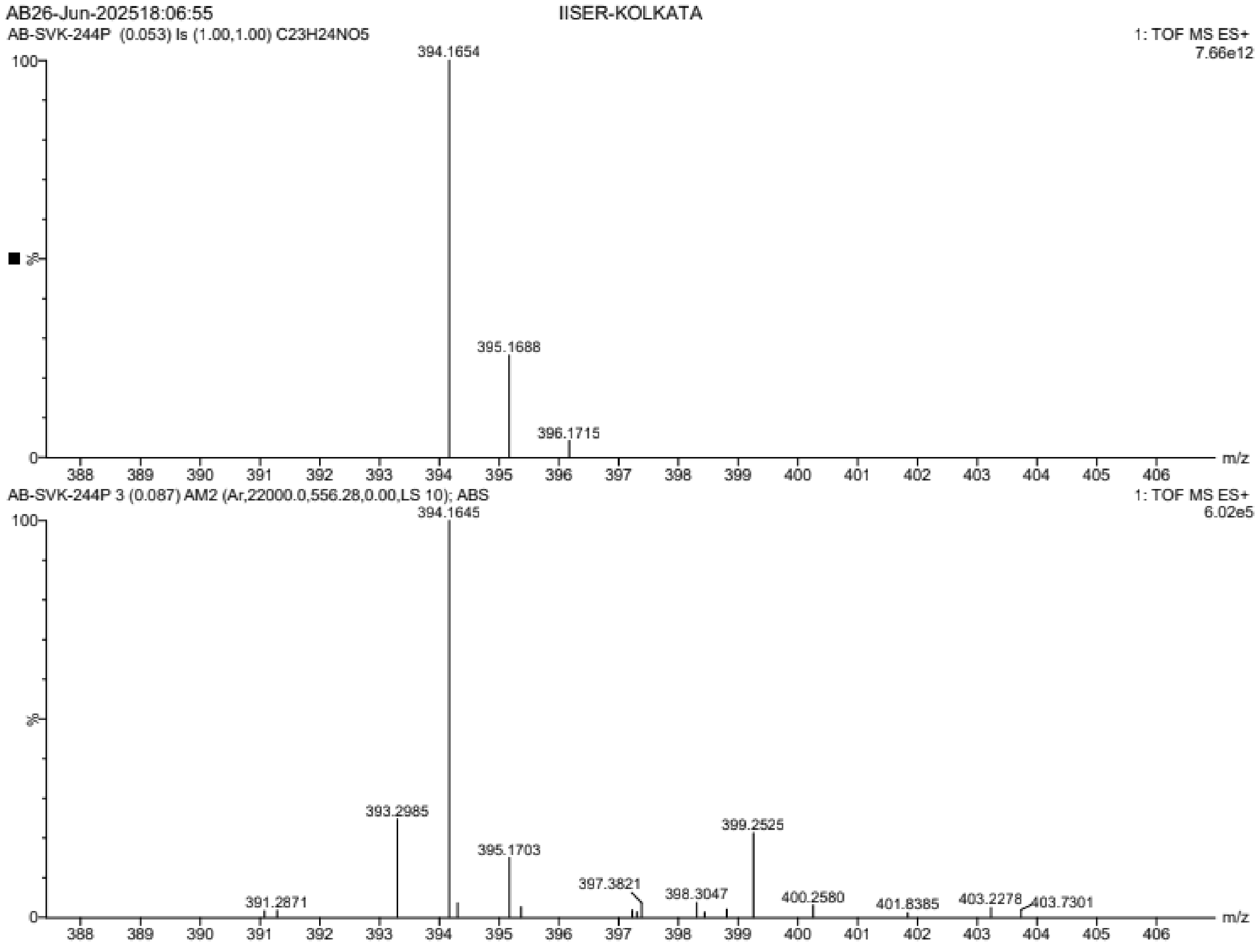
xiamycin G (+)-**1b**



^{1}H NMR (500 MHz, CD$_3$OD) of xiamycin G [(+)-**1b**]



^{13}C NMR (126 MHz, CD$_3$OD) of xiamycin G [(+)-**1b**]



HRMS data of xiamycin G [(+)-**1b**]

Crystal Data and Structure Refinement of (+)-**12 (CCDC 2496283):**

A colorless block 0.04 × 0.04 × 0.02 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100.15 K using omega scans. Crystal-to-detector distance was 43.92 mm and exposure time was 0.50 seconds per frame at low angles and 2.00 seconds at high angles, using a scan width of 0.5°. The 2Θ range for data collection /° 4.25 to 50.73. A total of 66388 reflections were collected covering the $-18 \leq h \leq 18$, $-8 \leq k \leq 8$, $-23 \leq l \leq 23$. 7124 reflections were founded to be symmetry independent, with an R_{int} of 0.0561. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be $P2_1$. Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2018/2) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by least-squares (SHELXL-2018/3). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2018/3.

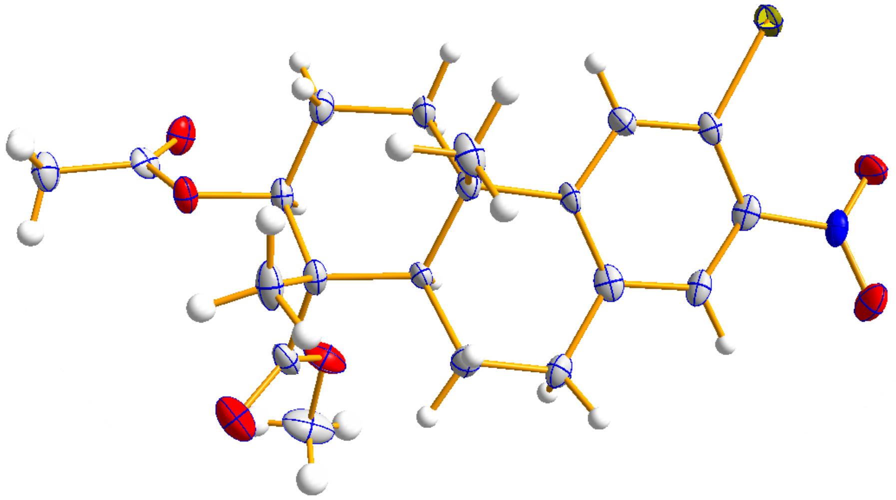


Figure S1. Single crystal XRD structure of compound (+)-**12**.

Crystal Data and Structure Refinement of (+)-**15** (CCDC **2246466**):

A colorless block 0.45 × 0.12 × 0.05 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100.15 K using omega scans. Crystal-to-detector distance was 43.92 mm and exposure time was 0.50 seconds per frame at low angles and 2.00 seconds at high angles, using a scan width of 0.5°. The 2Θ range for data collection /° 7.912 to 137.188. A total of 45519 reflections were collected covering the indices $-10 \leq h \leq 10$, $-18 \leq k \leq 18$, $-19 \leq l \leq 19$. 4131 reflections were founded to be symmetry independent, with an R_{int} of 0.0685. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be $P2_12_12_1$. CrysAlis^{Pro} 1.171.41.115a (Rigaku Oxford Diffraction, 2021) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2018/2) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by least-squares (SHELXL-2018/3). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2018/3.

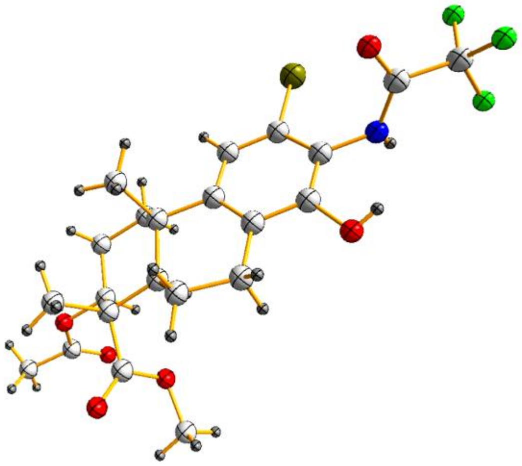


Figure S2. Single crystal XRD structure of compound (+)-**15**.