Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Total Synthesis of (-)-δ-Lycorane

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Supporting Information

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1. General Information

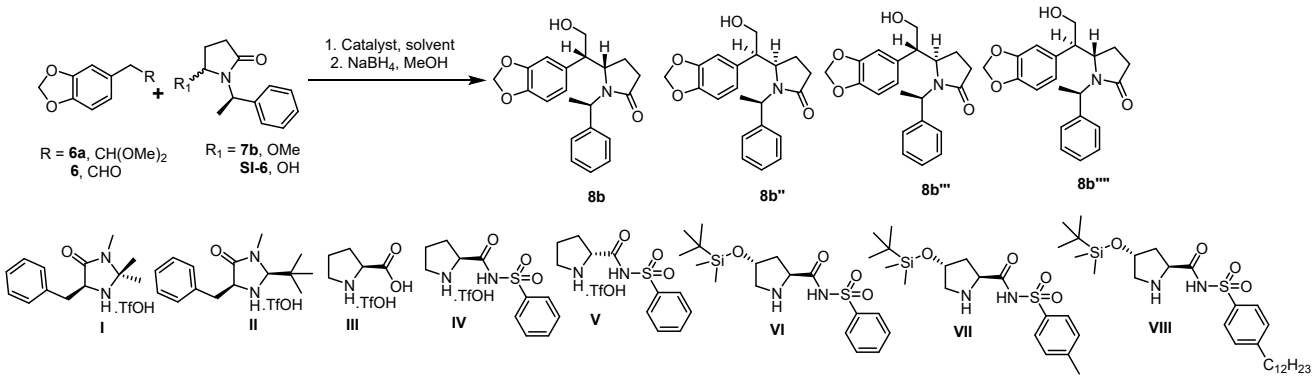
Unless otherwise stated, all oxygen or moisture sensitive reactions were conducted in flame-dried glassware under an atmosphere of Argon. All solvents were purified and dried according to the standard methods prior in use. The Proline-sulphonamide based catalysts were synthesized according to published procedure[1]. Reagents were purchased from Aldrich, Alfa Aesar, TCI and other commercial sources and used without further purification unless otherwise noted. Column chromatography was done in 60Å-120Å and 100Å-200Å silica gel of Merck Company. NMR data was acquired on Bruker Avance 400 spectrometer in $CDCl_3$ (TMS as internal reference) at rt and chemicals shifts (δ) are given in ppm; calibrated with the residual $CHCl_3$ for ^1H NMR (δ = 7.26 ppm) and the deuterated solvent signals for ^{13}C NMR (δ = 77.11 ppm). Chemical shift assignments were carried out using various 1-d (^1H, ^{13}C) and 2D NMR experiments (DEPT, COSY, NOESY, HSQC, HMBC) for compound **19** and **(-)-1,** multiplicities of NMR signal are designated as s (singlet), d (doublet), t (triplet), br (broad) and m (multiplet). ^{13}C spectra were recorded at 100 MHz. Coupling constants, *J*, were reported in Hertz (Hz). Important correlations were analyzed using HMBC, COSY and NOESY. NOESY was acquired using mixing time of 0.5 s and 4096x500 or 4096x256 FIDs with 16 transients and relaxation delay of 1-2s. HRMS analysis was performed using Q-TOF mass spectrometer of the SAIF Division in CSIR-CDRI Lucknow. Optical rotations were measured on an Automatic Polarimeter Anton Par MCP 5100.

2. Experimental Procedure

[1] S. Fu, X. Fu, S. Zhang, X. Zou. X. Wu, Highly diastereo- and enantioselective direct aldol reactions by 4-tert-butyldimethylsiloxy-substituted organocatalysts derived from N-prolylsulfonamides in water, *Tetrahedron: Asymmetry,* 2009, **20**, 2390–2396.

2. (i) Synthesis of 5-(1'-aryl) substituted-2-pyrrolidone via Mannich reaction

Table SI-1; Optimisation of Mannich reaction



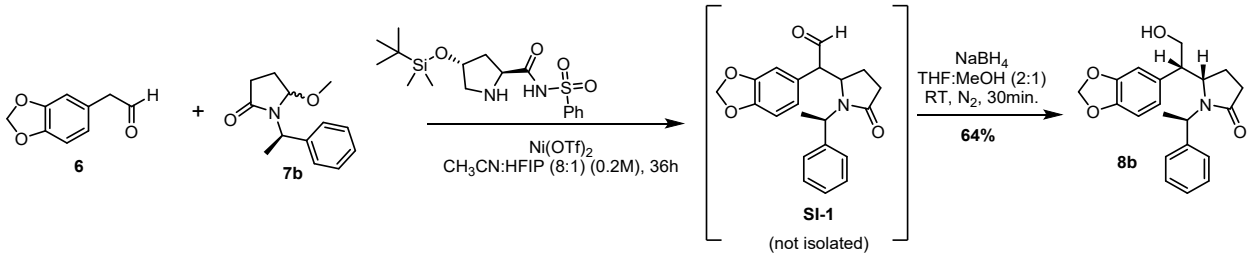
S.No.	Reaction conditions	8b:8b'':8b''':8b''''	Conversion
1	**6a** + **SI-6**, CSA/ *p*-TSA/TfOH/BF_3.OEt_2, DCM 4 days	-	Decomposition of **6a** & **SI-6**
2	**6a** + **SI-6**, Cat. **I/II/III**, CH_3CN, 4 days	-	No rxn
3	**6a** + **SI-6**, Cat. **IV**, CH_3CN, 4 days	9:4:1:2	42%
4	**6a** + **SI-6**, Cat. **IV**, DCM, DCE, $CHCl_3$, Acetone, THF, Ether, Dioxane	-	No rxn
5	**6a** + **SI-6**, Cat. **IV**, CH_3CN:HFIP (9:1) (0.1 M), 36h	9:4:1:2	91%
6	**6a** + **SI-6**, Cat. **V**, CH_3CN:HFIP (9:1) (0.1 M), 36h	1.6:6.3:1:0.6	20%
7	**6a** + **SI-6**, Cat. **VI**, CSA, CH_3CN:HFIP (9:1) (0.1 M), 36h	8:2:1:1	93%
8	**6a** + **SI-6**, Cat. **VII**, CSA, CH_3CN:HFIP (9:1) (0.1 M), 36h	8:2:1:1	93%
9	**6a** + **SI-6**, Cat. **VIII**, CSA, CH_3CN:HFIP (9:1) (0.1 M), 36h	8:2:1:1.5	89%
10	**6a** + **SI-6**, Cat. **VI**, CSA, CH_3CN, Variation in conc. of HFIP, 36h	No change	No change
11	**6a** + **SI-6**, Cat. **VI**, CSA, Additive (LiCl, $MgBr_2$.OEt_2, $Ni(OTf)_2$, $In(OTf)_3$, $Yb(OTf)_3$, $Sc(OTf)_3$, CH_3CN:HFIP (9:1) (0.1 M), 36h	No change	No change
12	**6a** + **SI-6**, Cat. **VI**, BF_3.OEt_2, CH_3CN (0.1 M), 12h	1:2:1:1	100%
13	**6a** + **SI-6**, Cat. **VI**, CSA, $B(C_6F_5)_3$, CH_3CN:HFIP (9:1) (0.1 M), 36h	13.5:2.6:1:2	100%
14	**6** + **7b**, Cat. **VI**, CSA, CH_3CN:HFIP (9:1) (0.1 M), 36h	3.3:2:1:1	96%
15	**6** + **7b**, Cat. **VI**, $Yb(OTf)_3$, CH_3CN:HFIP (9:1) (0.1 M), 36h	10.5:2.2:1:1.5	94%
16	**6** + **7b**, Cat. **VI**, $Sc(OTf)_3$, CH_3CN:HFIP (9:1) (0.1 M), 36h	5:2.5:1:1	96%
17	**6 + 7b,** Cat. **VI**, $Ni(OTf)_2$, CH_3CN:HFIP (9:1) (0.1 M), 36h	38:4:1:1	92%
18	**6** + **7b**, Cat. **VI**, $La(OTf)_2$, CH_3CN:HFIP (9:1) (0.1 M), 36h	10.6:1.8:1:1.8	92%
19	**6** + **7b**, Cat. **VI**, $MgBr_2$.OEt_2/ $Bi(OTf)_3$/$Sn(OTf)_2$/ $Cu(OTf)_2$/ Cu(OTf)/ $In(OTf)_3$/ CH_3CN:HFIP (9:1) (0.1 M), 36h	-	No rxn

20	**6a**+**7b**, Cat. **VI**, CSA, CH_3CN:HFIP (9:1) (0.1 M), 36h	-	No rxn
21	**6**+**SI-6**, Cat. **VI**, CSA, CH_3CN:HFIP (9:1) (0.1 M), 36h	-	No rxn
22	Entry 10 & 14 at 0°C	-	No rxn

Reaction condition; 6a/6 (0.1 mmol), 7b/SI-6 (0.2 mmol), Cat. (10 mol%), CSA/p-TSA/TfOH *(10 mol%), $BF_3.OEt_2$ (0.1 mmol), Additive (5 mol%), CH_3CN:HFIP (0.9mL:0.1mL), rt*

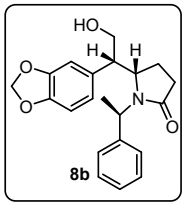
Synthesis of **8b** [(*S*)-5-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-hydroxyethyl)-1-((*R*)-1-(4methoxyphenyl)ethyl)pyrrolidin-2-one]

Scheme SI-1; Mannich reaction between aldehyde **6** and hydroxylactam **7b**



General procedure 1; A vial charged with **6** (165 mg, 1.0 mmol), **7b** (438 mg, 2.0 mmol), and catalyst **VI** (38 mg, 0.1 mmol). In the mixture solution of CH_3CN: HFIP (4 mL:0.5 mL) was added. Then $Ni(OTf)_2$ (18 mg, 0.05 mmol) was added and stirred the reaction mixture for 36 h at rt. After completion of the reaction, reaction mixture was quenched with sat. aqueous solution of sodium bicarbonate. Then the solvent was evaporated and reaction mixture was diluted with ethyl acetate. The aqueous layer was extracted with ethyl acetate, combined organic layer washed with brine and dried over sodium sulfate. Evaporation of solvent gave crude reaction mixture which was used in next step without further purification.

Crude aldehyde **SI-1** dissolved in THF:MeOH (4 mL:2 mL) solution and $NaBH_4$ (80 mg, 2 mmol) was added in portion wise at 0 °C, after 1 h, reaction mixture was quenched with aq. ammonium chloride solution and solvent was evaporated. The mixture was diluted with ethyl acetate and aqueous layer was extracted with ethyl acetate (x 2). Combine organic layer washed with brine and dried over sodium sulfate, after evaporation of solvent, compound was purified via column chromatography using silica gel 100-200 mesh (40-50% Acetone:Hexane as eluent) that gave product **8b** as colorless viscous oil (226 mg, 64% yield).



R_f : 0.6 (10% Acetone:DCM (x2))

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.44 (m, 5H), 6.74 (d, *J* = 7.9 Hz, 1H), 6.56-6.61 (m, 2H), 5.94 (s, 2H), 5.41 (q, *J* = 7.3 Hz, 1H), 3.80-3.87 (m, 1H), 3.64-3.73 (m, 2H), 3.15-3.20 (m, 1H), 1.86 (d, *J* = 7.3 Hz, 3H), 1.75-1.83 (m, 2H), 1.36-1.40 (m, 1H), 1.26-1.33 (m, 1H).

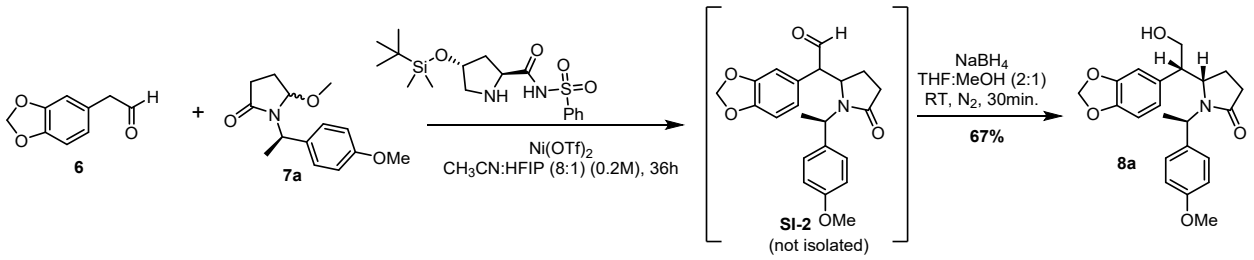
^{13}C NMR (100 MHz, $CDCl_3$): δ 176.64, 147.80, 146.79, 140.87, 130.74, 128.64, 127.71, 127.56, 121.87, 108.73, 108.43, 101.02, 62.91, 58.53, 52.64, 49.75, 30.54, 21.77, 19.28.

HRMS (ESI): m/z calcd for $C_{21}H_{24}NO_4^+$ $[M+H]^+$: 354.1700, found: 354.1694,

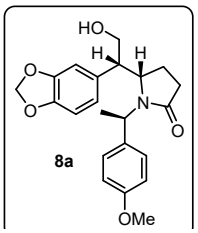
$[\alpha]_D^{23}$: -27.6° (c 0.3, $CHCl_3$),

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3361.2, 3008.5, 1657.6, 1444.1, 1372.2, 1245.4, 1181.5, 1035.1, 932.1, 809.6, 744.4, 698.5.

Synthesis of **8a** [(*S*)-5-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-hydroxyethyl)-1-((*R*)-1-(4-methoxyphenyl)ethyl)pyrrolidin-2-one]



Substrate **8a** was prepared according to general procedure **1**, using **6** (165 mg, 1.0 mmol), **7a** (498 mg, 2.0 mmol), $Ni(OTf)_2$ (18 mg, 0.05 mmol) and Catalyst **VI** (38 mg, 0.1 mmol), in CH_3CN:HFIP (4mL:0.5 mL). The product **8a** obtained as colorless viscous oil (256 mg, 67% yield, d.r. = 40:4:1:1) after $NaBH_4$ reduction.



R_f : 0.6 (10% Acetone:DCM (x2))

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.73 (d, *J* = 7.9 Hz, 1H), 6.61 (d, *J* = 1.5 Hz, 1H), 6.58 (dd, *J* = 1.5 Hz, 7.9 Hz, 1H), 5.92 (s, 2H), 5.36 (q, *J* = 7.3 Hz, 1H), 3.81-3.86 (m, 1H), 3.81 (s, 3H), 3.64-3.72 (m, 2H), 3.14-3.20 (m, 1H), 1.83-1.88 (m, 1H), 1.82 (d, *J* = 7.3 Hz, 3H), 1.77-1.79 (m, 1H), 1.74-1.77 (m, 1H) 1.18-1.25 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.39, 159.04, 147.86, 146.85, 132.83, 130.56, 128.78, 121.86, 113.95, 108.73, 108.49, 101.04, 63.07, 58.26, 55.28, 51.94, 49.88, 30.57, 21.82, 19.46.

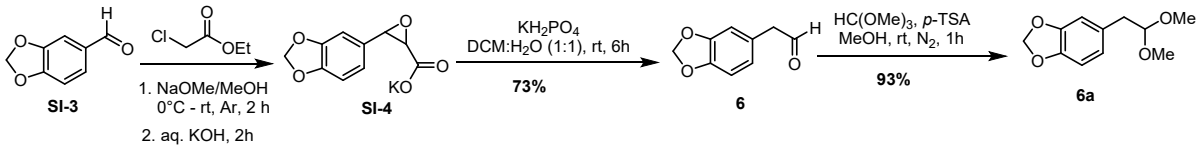
HRMS (ESI): m/z calcd for $C_{22}H_{25}NO_5Na^+$ $[M+Na]^+$: 406.1630, found: 406.1586.

$[\alpha]_D^{23}$: -4.10° (c 0.6, $CHCl_3$)

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3016.8, 1660.7, 1501.7, 1442.1, 1248.2, 1181.1, 1036.5, 933.7, 741.9, 667.9.

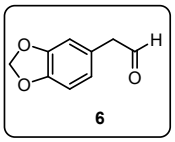
2. (ii) Synthesis of (-)-δ-Lycorane

Synthesis of **6** [2-(benzo[d][1,3]dioxol-5-yl)acetaldehyde] & **6a** [5-(2,2-dimethoxyethyl)benzo[d][1,3]dioxole]



Sodium metal (3 g, 133 mmol) was carefully added to methanol (130 mL) through stage-wise addition and was stirred at rt until whole sodium metal gets completely dissolved. Then this clear solution was refluxed

for about 15 min then NaOMe/MeOH solution was added drop wise to stir mixture of piperonal **SI-3** (10 g, 67 mmol) and ethyl chloroacetate (9.5 mL, 100 mmol) at 5-10 ˚C, under an argon atmosphere and was stirred it for 1 h. After that without any separation, the aqueous solution of KOH (5.6 g, 100 mmol in 33 mL of water) was added and the resulting solution was stirred at rt for 3 h to obtain a pale yellow precipitate and this reaction mixture was kept in ice bath for about 30 min and the resultant precipitate was filtered off from the solution. Filtrate was washed with methanol and DCM. **SI-4** was obtained as white & floppy solid. Sequentially, the white solid was added to the 1:1 mixture of water & DCM. Next, mono potassium phosphate (10 g, 73 mmol) was added to resulting solution and the reaction mixture was stirred for 12 h. Finally, the aqueous layer was extracted with DCM (x 2) and the combined organic phase was dried over anhydrous sodium sulfate. After three steps 3,4-methylenedioxy phenyl acetaldehyde **6** (8.0 g) was obtained in 73% overall yield.



6

R_f : 0.5 (10% EtOAc:Hexane)

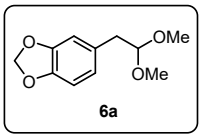
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (t, *J* = 2.3 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.69 (d, *J* = 1.5 Hz, 1H), 6.66 (dd, *J* = 1.5, 7.8 Hz, 1H), 5.96 (s, 2H), 3.60 (d, *J* = 2.3 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 199.31, 148.19, 147.02, 125.27, 122.80, 109.90, 108.74, 101.16, 50.17.

HRMS (ESI): m/z calcd for $C_9H_9O_3^+$ $[M+H]^+$: 165.0552, found: 165.0447.

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 2622.3, 2316.4, 1993.8, 1710.1, 1620.1, 1542.6, 1441.7, 1313.4, 1094.5, 912.6, 799.5.

p-TSA (1.7 g, 9.8 mmol) was added to reaction mixture of **6** (8 g, 49 mmol) and trimethyl orthoformate (10.8 mL, 98 mmol) in methanol (100 mL) at 0 ˚C and stirred the reaction mixture for 1 h. After completion of reaction, saturated solution of sodium bicarbonate was added and methanol was evaporated, after that aqueous layer was extracted by ethyl acetate (x 3) and combined organic layer dried over sodium sulfate, concentrated and purified by column chromatography using silica gel 60-120 mesh (10% Acetone: Hexane as eluent) and product was obtained as colorless oil **6a** (9.5 g, 93% yield).



6a

R_f : 0.5 (10% EtOAc:Hexane)

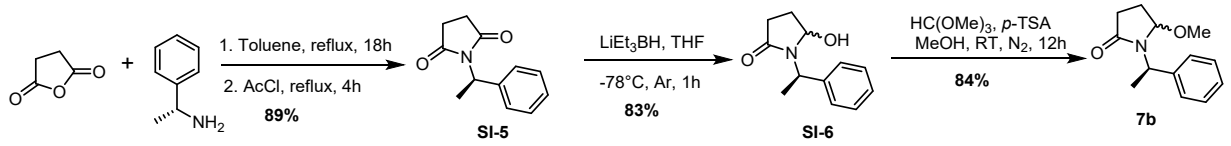
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.75 (d, *J* = 1.6 Hz, 1H), 6.73 (s, 1H), 6.66-6.69 (m, 1H), 5.92 (s, 2H), 4.48 (t, *J* = 5.5 Hz, 1H), 3.34 (s, 6H), 2.82 (d, *J* = 5.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 147.53, 146.09, 130.73, 122.35, 109.86, 108.13, 105.44, 100.82, 53.40, 39.32.

HRMS (ESI): m/z calcd for $C_{10}H_{11}O_3^+$ $[M\text{-}OMe]^+$: 179.0708, found: 179.0607.

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 2896.3, 2832.5, 1852.1, 1608.9, 1492.4, 1361.3, 1244.1, 1115.6, 1036.6, 861.5, 721.3.

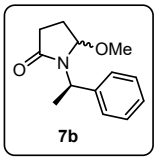
Synthesis of **7b [**5-methoxy-1-((*R*)-1-phenylethyl)pyrrolidin-2-one]



General Procedure 2; Substrate **SI-6** was prepared according to reported procedure[2], (*R*)-(-)-1-phenylethane-1-amine (5 g, 41.3 mmol) was added to a suspension of succinic anhydride (4.2 g, 42 mmol) in toluene (50 mL) and the mixture was heated under reflux for 18 h. The solvent was removed in *vacuo* and the residue was re-dissolved in acetyl chloride (20 mL). The resulting solution was heated under reflux for 4 h, after that acetyl chloride was evaporated on KOH trap and the mixture was dissolved in ethyl acetate. The mixture was washed thoroughly with saturated $NaHCO_3$ solution and dried over Na_2SO_4. The solvent was removed in *vacuo* affording the compound **SI-5** (7.5 g, 89% yield) as pure colorless oil.

$LiEt_3BH$ (22 mL of 1.0 M solution in THF, 22 mmol) was added drop wise to a solution of imide (4 g, 19.7 mmol) in THF (66 mL) at −78 ˚C. The mixture was allowed to stir for 1 h at same temperature. Then residue was cooled to 0 ˚C and the reaction was quenched with drop wise addition of saturated aqueous $NaHCO_3$ solution. THF was removed under vacuum and the mixture was extracted with CH_2Cl_2, washed with brine and dried over Na_2SO_4. The solvent was removed in *vacuo* affording the title compound **SI-6** (3.3 g, 83% yield) as an inseparable mixture of diastereoisomers (2:1).

A solution of 5-hydroxy-1-((R)-1-phenylethyl)pyrrolidin-2-one (5 g, 24.4 mmol) in MeOH (75 mL) was treated with *p*-TSA·H_2O (0.84 g, 4.9 mmol) and trimethylorthoformate (5.4 mL, 48.8 mmol), the solution was allowed to stand for 12 h. After completion of reaction, saturated solution of sodium bicarbonate was added and methanol was evaporated, after that aqueous layer was extracted by ethyl acetate (x 3) and combined organic layer dried over sodium sulfate, concentrated and purified by column chromatography using silica gel 60-120 mesh (40% Acetone: Hexane as eluent) and product was obtained as colorless oil **7b** (4.5 g, 84% yield) as inseparable mixture of diastereoisomers (3:1).



R_f : 0.5 (40% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.49 (m, 10H, major + minor), 7.20-7.33 (m, *J* = 3.2 Hz, 10H, major + minor), 5.36 (q, *J* = 7.1 Hz, 3H, major), 5.14 (q, *J* = 7.3 Hz, 1H, minor), 5.02-5.06 (m, 1H, minor), 4.45-4.49 (m, 3H, major), 3.14 (s, 9H, major), 2.94 (s, 3H, minor), 2.50-2.66 (m, 4H, major + minor), 2.26-2.37 (m, 4H, major + minor), 2.04-2.17 (m, 1H, minor), 1.94-2.01 (m, 1H, minor), 1.87-1.94 (m, 6H, major), 1.66 (d, *J* = 7.2 Hz, 3H, minor), 1.62 (d, *J* = 7.1 Hz, 9H, major).

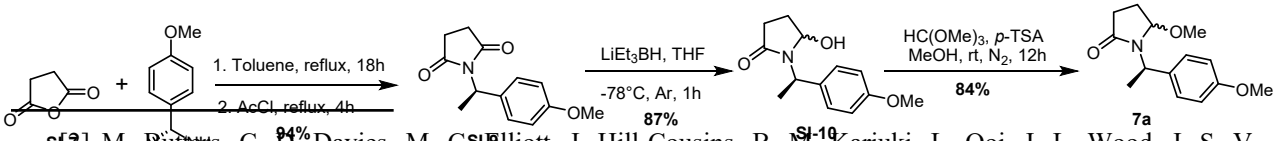
^{13}C NMR (100 MHz, $CDCl_3$): δ 175.01, 174.77, 141.75, 139.91, 128.55, 128.13, 127.77, 127.70, 127.46, 127.22, 88.90, 89.09, 52.51, 51.97, 51.31, 50.51, 29.55, 29.25, 24.23, 24.02, 18.14, 17.62.

$[\alpha]_D^{23}$: +46.30° (c 0.6, $CHCl_3$)

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3747.8, 3630.1, 3002.9, 2377.1, 1682.6, 1491.9, 1374.7, 1195.1, 1009.9, 766.1, 697.4.

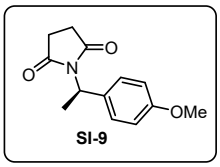
Synthesis of **7a [**5-methoxy-1-((*R*)-1-(4-methoxyphenyl)ethyl)pyrrolidin-2-one]

7a was prepared according to General Procedure **2,** (*R*)-(-)-4-Methoxy-α-methylbenzylamine **SI-8** (2.9 mL, 20 mmol) and succinic anhydride **SI-7** (2 g, 20 mmol) in toluene (50 mL) refluxed for 18 h.



[2] M. Buttress, C. D. Davies, M. C. Elliott, J. Hill-Cousins, B. M. Kariuki, L. Ooi, J. L. Wood, J. S. V. Wordingham, Synthesis and stereochemical determination of batzelladine C methyl ester, *Org. Biomol. Chem.* 2009, **7**, 5001–5009.

Toluene was evaporated and crude was redissolved in acetyl chloride (30 mL) and again refluxed for 4 h to get imide **SI-9** (4 g, 94% yield) as pure colorless oil. Treating imide **SI-9** (4.4 g, 18.9 mmol) in THF (63 mL) with $LiEt_3BH$ (22 mL of 1.0 M solution in THF, 22 mmol) at −78 ℃, substrate **SI-10** (3.7 g, 87% yield) was obtained as inseparable mixture of diastereoisomers (2:1) as colorless oil. A solution of 5-hydroxy-1-((R)-1-phenylethyl)pyrrolidin-2-one **SI-10** (5 g, 24.4 mmol) in MeOH (75 mL) was treated with *p*-TSA·H_2O (0.84 g, 4.9 mmol) and trimethylorthoformate (5.4 mL, 48.8 mmol), **7a** (4.5 g, 84% yield) was obtained as colorless oil and as inseparable mixture of diastereoisomers (3:1).



SI-9

R_f : 0.6 (40% Acetone:Hexane)

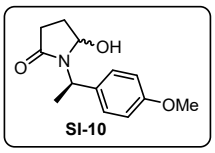
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.38 (q, *J* = 7.3 Hz, 1H), 3.78 (s, 3H), 2.62 (q, *J* = 0.8 Hz, 4H), 1.79 (d, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.04, 159.13, 131.85, 129.00, 113.68, 55.25, 49.89, 28.08, 16.71.

HRMS (ESI): m/z calcd for $C_{13}H_{15}NaNO_3^+$ $[M+Na]^+$: 256.0950, found: 256.0911.

$[\alpha]_D^{23}$: +146.101° (c 1.0, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3020.8, 1700.4, 1214.5, 742.7, 668.5.



SI-10

R_f: 0.4 (40% Acetone:Hexane)

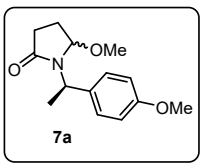
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.4 Hz, 2H, minor), 7.28 (d, *J* = 8.4 Hz, 4H, major), 6.89 (d, *J* = 8.4 Hz, 6H, major + minor), 5.29-5.40 (m, 4H, major + minor), 4.89-4.94 (m, 2H, major), 3.81 (s, 6H, major), 3.80 (s, 3H, minor), 2.57-2.70 (m, 3H, major + minor), 2.27-2.36 (m, 3H, major + minor), 2.07-2.18 (m, 3H, major + minor), 1.77-1.89 (m, 3H, major + minor), 1.65 (d, *J* = 7.2 Hz, 6H, major), 1.59 (d, *J* = 7.2 Hz, 3H, minor).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.46, 166.04, 159.20, 148.10, 147.09, 131.14, 129.44, 128.21, 123.16, 121.70, 114.26, 108.69, 108.47, 101.23, 60.65, 59.73, 55.30, 49.54, 44.55, 29.51, 21.76, 14.25.

HRMS (ESI): m/z calcd for $C_{13}H_{18}NO_3^+$ $[M+H]^+$: 236.1287, found: 236.1277.

$[\alpha]_D^{23}$: +45.10° (c 0.7, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3015.7, 1669.3, 1513.2, 1427.8, 1249.7, 1214.9, 1180.2, 1035.7, 915.3, 742.6, 668.2, 634.8.



7a

R_f : 0.5 (40% Acetone:Hexane)

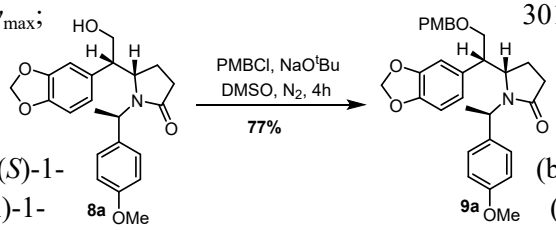
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 8.5 Hz, 2H, minor), 7.26 (d, *J* = 8.5 Hz, 6H, major), 6.89 (d, *J* = 8.8 Hz, 6H, major), 6.83 (d, *J* = 8.8 Hz, 2H, minor), 5.31 (q, *J* = 7.1 Hz, 3H, major), 5.11 (q, *J* = 7.2 Hz, 1H, minor), 5.03-5.06 (m, 1H, minor), 4.43-4.47 (m, 3H, major), 3.81 (s, 9H, major), 3.78 (s, 3H, minor), 3.14 (s, 9H, major), 2.94 (s, 3H, minor), 2.48-2.65 (m, 4H, major + minor), 2.26-2.36 (m, 4H, major + minor), 2.03-2.14 (m, 1H, minor), 1.93-2.00 (m, 1H, minor), 1.94-1.99 (m, 6H, major), 1.63 (d, *J* = 7.2 Hz, 3H, minor), 1.59 (d, *J* = 7.1 Hz, 9H, major).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.95, 174.68, 159.06, 158.69, 133.97, 131.88, 128.97, 128.81, 128.69, 128.57, 114.24, 113.94, 113.85, 113.41, 89.04, 88.80, 55.27, 55.22, 52.46, 51.84, 50.66, 50.03, 29.59, 29.35, 24.17, 23.95, 18.37, 17.70.

HRMS (ESI): m/z calcd for $C_{13}H_{15}NO_2^+$ $[M\text{-}MeOH]^+$: 217.1103, found: 217.1045.

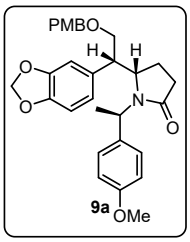
$[\alpha]_D^{23}$: +63.501° (c 0.6, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3014.3, 1682.6, 1613.2, 1513.1, 1420.4, 1373.0, 1249.2, 1215.5, 1181.2, 1077.1, 1043.8, 886.8, 741.4, 668.2.



Synthesis of **9a** [(*S*)-5-((*S*)-1-((4-methoxybenzyl)oxy)ethyl)-1-(benzo[d][1,3]dioxol-5-yl)-2-((*R*)-1-(4-methoxyphenyl)ethyl)pyrrolidin-2-one]

8a (50 mg, 0.13 mmol) was dissolved in 2 mL of DMSO and sodium tert-butoxide (25 mg, 0.26 mmol) was added in portion at rt, after stirring the reaction mixture for 15 min. add PMBCl (35 µL, 0.26 mmol). After 4 h the reaction mixture was quenched by sat. solution of NH_4Cl and the aqueous layer was extracted with ethyl acetate (x 2), washed with brine solution, dried over sodium sulfate, concentrate the solvent in *vacuo*. The crude reaction mixture was purified by column chromatography using silica gel 60-120 mesh (30% Acetone:Hexane as eluent) to obtain the product **9a** as light yellowish oil (50 mg, 77% yield).



R_f : 0.5 (40% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$); δ 7.30 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.58 (d, *J* = 1.6 Hz, 1H), 6.55 (dd, *J* = 1.6, 8.0 Hz, 1H), 5.92 (q, *J* = 1.4 Hz, 2H), 5.40 (q, *J* = 7.3 Hz, 1H), 4.41 (q, *J* = 12.7 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.71-3.75 (m, 1H), 3.51-3.63 (m, 2H), 3.23-3.29 (m, 1H), 1.80 (d, *J* = 7.4 Hz, 3H), 1.64-1.77 (m, 3H), 1.11-1.19 (m, *J* = 3.9 Hz, 1H).

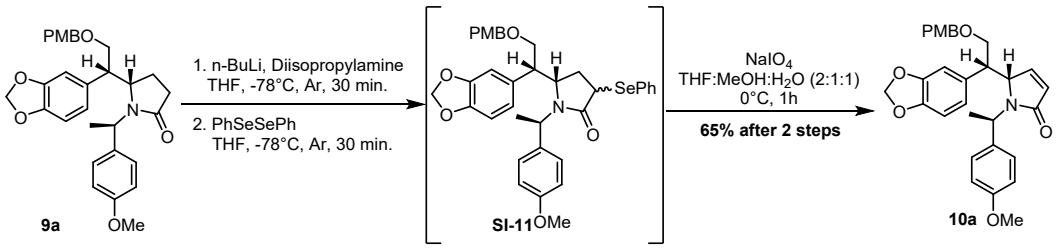
^{13}C NMR (100 MHz, $CDCl_3$); δ 176.42, 159.24, 158.96, 147.61, 146.66, 132.96, 131.11, 130.08, 129.14, 128.84, 121.81, 113.85, 113.78, 108.74, 108.29, 100.96, 72.83, 70.33, 58.28, 55.28, 51.66, 47.37, 30.54, 21.67, 19.53.

HRMS (ESI): m/z calcd for $C_{30}H_{34}NO_6^+$ $[M+H]^+$: 504.2386, found: 504.2378.

$[\alpha]_D^{23}$: -2.6° (c 0.7, $CHCl_3$).

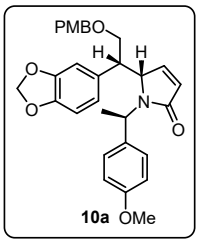
IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3012.5, 1612.4, 1445.9, 1363.3, 1217.7, 1179.5, 1098.1, 932.4, 821.0, 668.3.

Synthesis of **10a** [(*S*)-5-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-((4-methoxybenzyl)oxy)ethyl)-1-((*R*)-1-(4-methoxyphenyl)ethyl)-1,5-dihydro-2H-pyrrol-2-one]



A solution of *n*-butyl lithium (2.5 M in hexane) (0.12 mL, 0.3 mmol) was added into solution of diisopropyl amine (freshly distilled, 42 µL, 0.3 mmol) in dry THF (6 mL) at 0 ˚C under argon atmosphere and allowed to stir for 15 mins at same temperature. In another flame dried R.B., solution of starting material **9a** (50 mg, 0.1 mmol) in THF (2 mL) was subjected to –78 ˚C, into this reaction mixture LDA solution was added in dropwise manner and the solution was allowed to stir for 30 min. After 30 min, a solution of diphenyl diselenide (31 mg, 0.1 mmol) in dry THF (2 mL) was slowly added. After 30 mins reaction mixture was quenched with sat. solution of ammonium chloride, aqueous layer was extracted with ethyl acetate (x 2), combined organic layer was washed with brine, dried on sodium sulfate and evaporated, and the oily residue was purified by flash chromatography using silica gel 60-120 mesh (30 % acetone:hexane as eluent) to give the selenide **SI-11.**

In second step selenide **SI-11** was dissolved in THF:MeOH:H_2O (2:1:1, 4 mL) and the solution was cooled to 0 ˚C. Sodium metaperiodate (88 mg, 0.4 mmol) was then added portionwise and the mixture was stirred at 0 ˚C for 1 h. The mixture was diluted with water and extracted with ethylacetate (x 3). The organic layer was washed with brine, dried on sodium sulfate, and evaporated. The product **10a** (33 mg, 65% yield after two steps) was obtained after purification by flash chromatography using silica gel 60-120 mesh (40% Acetone:Hexane as eluent) as yellow oil.



R_f : 0.4 (40% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$); δ 7.24 (d, *J* = 8.6 Hz, 2H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.02 (dd, *J* = 1.7, 6.0 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.41 (d, *J* = 1.7 Hz, 1H), 6.37 (dd, *J* = 1.7, 8.0 Hz, 1H), 5.97 (dd, *J* = 1.7, 6.0 Hz, 1H), 5.88 (s, 2H), 5.23 (q, *J* = 7.2 Hz, 1H), 4.32-4.42 (m, 3H), 3.81 (s, 3H), 3.78 (s, 3H), 3.52-3.64 (m, 2H), 3.37-3.42 (m, 1H), 1.70 (d, *J* = 7.2 Hz, 3H).

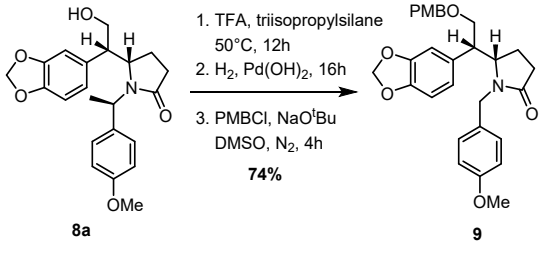
^{13}C NMR (100 MHz, $CDCl_3$); δ 173.11, 159.33, 158.82, 147.07, 146.59, 146.52, 133.45, 130.39, 129.81, 129.20, 128.56, 127.78, 122.15, 113.84, 113.82 109.01, 107.75, 100.90, 72.82, 71.66, 64.61, 55.28, 52.21, 46.45, 19.49.

HRMS (ESI): m/z calcd for $C_{30}H_{32}NO_6^+$ $[M+H]^+$: 502.2230, found: 502.2184.

$[\alpha]_D^{23}$: -123° (c 0.7, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3014.1, 1672.9, 1507.8, 1359.2, 1245.0, 1179.7, 1036.0, 934.1, 812.2, 742.5, 666.7.

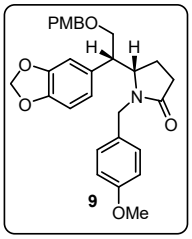
Synthesis of **9** [(*S*)-5-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-((4-methoxybenzyl)oxy)ethyl)-1-(4-methoxybenzyl)pyrrolidin-2-one]



A solution of the starting material **8a** (2 g, 5.2 mmol) in TFA (10 mL) and triisopropylsilane (3.2 mL, 15.6 mmol) was stirred at 50 ℃ for 12 h. After evaporating the TFA, the residue was dissolved in EtOAc and washed with sat. $NaHCO_3$, brine, dried by sodium sulfate, and concentrated in *vacuo*. The resulting crude material was purified by column chromatography using silica gel 60-120 mesh (40-50% Acetone:Hexane as eluent) to provide the product as yellow oil.

After that the obtained product was dissolved in MeOH (20 mL) and $Pd(OH)_2$ on carbon (20 wt.%) (200 mg) was added under nitrogen atmosphere. The resulting reaction mixture was stirred for 16 h at rt under 1 atm pressure of Hydrogen. After completion, the reaction mixture was filtered over Celite and concentrated in *vacuo* to afford white solid compound (1.0 g).

Sequentially, this white solid was dissolved in 20 mL of DMSO and sodium *tert*-butoxide (1.1 g, 12 mmol) was added in portion, after stirring the reaction mixture for 15 min add PMBCl (1.65 mL, 12 mmol). After 4h quench the reaction mixture by sat. solution of NH_4Cl and extract the aqueous layer via ethyl acetate (x 2), organic layer was washed with brine solution and dried over sodium sulfate. After concentration the obtained crude reaction mixture was purified by column chromatography using silica gel 60-120 mesh (40% Acetone:Hexane as eluent) to obtain light product **9** as yellow oil (1.9 g in overall yield of 74% after three steps).



R_f : 0.5 (40% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.58 (d, *J* = 1.2 Hz, 1H), 6.51 (dd, *J* = 1.2, 8.0 Hz, 1H), 5.93 (q, *J* = 1.4 Hz, 2H), 5.13 (d, *J* = 14.6 Hz, 1H), 4.43 (q, *J* = 10.5 Hz, 2H), 3.97 (d, *J* = 14.6 Hz, 1H), 3.83-3.89 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.74-3.68 (m, 1H), 3.60-3.67 (m,1H), 3.24-3.29 (m, 1H), 1.90-2.00 (m, 1H), 1.76-1.87 (m, 2H), 1.37-1.52 (m,1H).

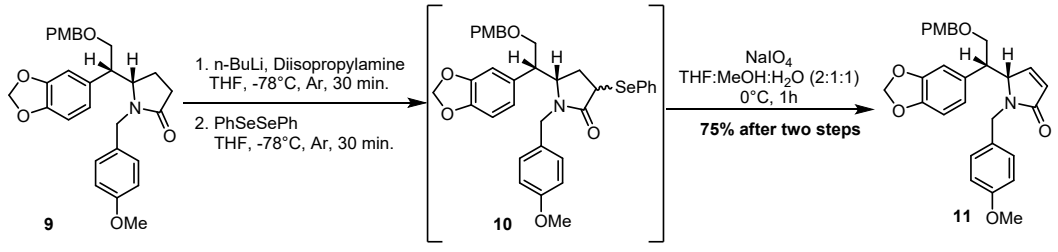
^{13}C NMR (100 MHz, $CDCl_3$): δ 159.26, 159.09, 147.74, 146.73, 131.10, 129.97, 129.77, 129.16, 128.77, 121.73, 114.05, 113.79, 108.61, 108.36, 101.01, 72.89, 69.91, 57.74, 55.28, 55.26, 44.42, 43.80, 29.88, 20.39.

HRMS (ESI): m/z calcd for $C_{29}H_{32}NO_6^+$ $[M+H]^+$: 490.2230, found: 490.2221.

$[\alpha]_D^{23}$: -9.6° (c 0.6, $CHCl_3$)

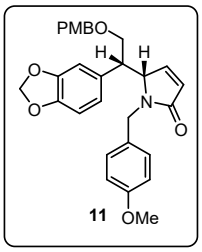
IR (in $CHCl_3$, cm^{-1}): ν_{max}; 1670.1, 1508.6, 1449.3, 1246.3, 1177.3, 1035.2, 812.6, 744.6.

Synthesis of **11** [(*S*)-5-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-((4-methoxybenzyl)oxy)ethyl)-1-(4-methoxybenzyl)-1,5-dihydro-2H-pyrrol-2-one]



A solution of *n*-butyl lithium (2.5 M in hexane) (1.4 mL, 3.68 mmol) was added into solution of diisopropyl amine (freshly distilled, 260 µL, 3.68 mmol) in dry THF (6 mL) at 0 ˚C under argon atmosphere and allowed to stir for 15 mins at same temperature. In another flame dried R.B., solution of starting material **9** (900 mg, 1.84 mmol) in THF (6 mL) was subjected to –78 ˚C, into this reaction mixture LDA solution was added in drop wise manner and the solution was allowed to stir for 30 min. After 30 min. a solution of diphenyl diselenide (0.574 g, 1.84 mmol) in dry THF (6 mL) was slowly added. After 30 min. reaction mixture was quenched by sat. solution of ammonium chloride, aqueous layer was extracted with ethyl acetate (x 2), combined organic layer was washed with brine, dried on sodium sulfate and evaporated, and the oily residue was purified by flash column chromatography using silica gel 60-120 mesh (30 % acetone:hexane as eluent) to give the selenide **10** (1.0 g, 84% yield).

In second step selenide **10** (1.0 g, 1.55mmol) was dissolved in THF:MeOH:H_2O (2:1:1, 50 mL) and the solution was cooled to 0 ˚C. Sodium metaperiodate (1.3 g, 6.2 mmol) was then added portion wise and the mixture was stirred at 0 ˚C for 1 h. The mixture was diluted with water and extracted with ethyl acetate (x 3). The organic layer was washed with brine, dried on sodium sulfate, and evaporated. The product **11** (673 mg, 89% yield) was obtained after purification by flash column chromatography (50% Acetone:Hexane as eluent) as yellow oil.



R_f : 0.5 (50% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, *J* = 2.0 Hz, 2H), 7.13 (d, *J* = 2.1 Hz, 2H), 7.05 (dd, *J* = 1.6, 6.0 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.64 (d, *J* = 8.5 Hz 1H), 6.42-6.45 (m, 2H), 6.04 (dd, *J* = 1.6, 6.0 Hz, 1H), 5.90 (s, 2H), 5.08 (d, *J* = 15.0 Hz, 1H), 4.36-4.46 (m, 3H), 4.01 (d, *J* = 15.0 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.65-3.72 (m, 2H), 3.39-3.44 (m, 1H).

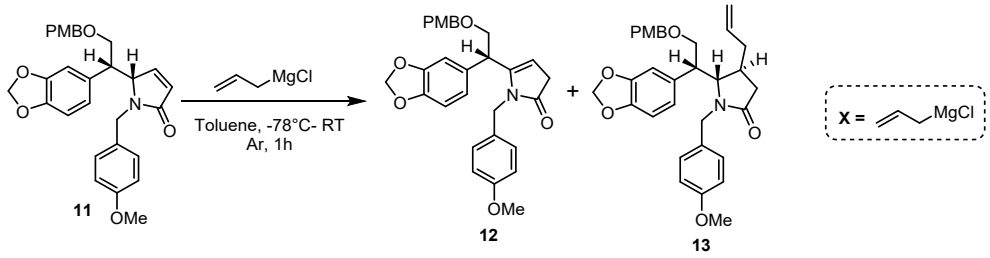
^{13}C NMR (100 MHz, $CDCl_3$): δ 171.72, 159.35, 159.04, 147.30, 146.78, 145.96, 129.94, 129.74, 129.52, 129.39, 129.28, 127.93, 121.75, 114.11, 113.85, 108.63, 107.98, 100.99, 72.91, 70.95, 62.99, 55.27, 45.42, 43.49.

HRMS (ESI): m/z calcd for $C_{29}H_{30}NO_6^+$ $[M+H]^+$: 488.2073, found: 488.2076.

$[\alpha]_D^{23}$: -37.5° (c 0.5, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3018.1, 1675.2, 1510.4, 1441.4, 1247.2, 1099.2, 1037.6, 932.9, 741.4, 668.3.

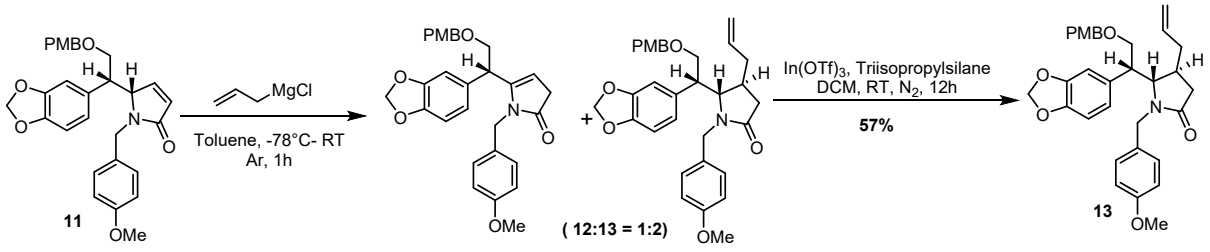
Table SI-2; Optimisation of 1, 4-conjugate Grignard addition



S.No.	Conditions	Temp.	Solvent	Conversion	12:13
1.	X (2.0 eq)	-78 ˚C	THF	100%	2:1
2.	X (3.0 eq), CuBr.DMS (3.0 eq), HMPA (3.0 eq), TMSCl (3.0eq)	-78 ˚C	THF	No Rxn	-
3.	Bu_4NCl (3.0 eq), Diglyme (3.0 eq), X (1.5 eq)	-78 ˚C	THF	100%	2:1
4.	$CeCl_3$ (3.0 eq), X (3.0 eq)	-78 ˚C	THF	No Rxn	-
5.	Allyltributyltin (3.0 eq), n-BuLi (3.0 eq), HMPA (3.0 eq), TMSCl (3.0 eq), CuI (3.0 eq)	-78 ˚C	THF	Sluggish reaction	
6.	Allyltributyltin (3.0 eq), n-BuLi (3.0 eq), HMPA (3.0 eq), TMSCl (3.0 eq), CuI (3.0 eq), LiCl (3.0 eq)	-78 ˚C	THF	Unidentified product	
7.	X (3.0 eq), CuBr.DMS (3.0 eq), HMPA (3.0 eq), TMSCl (3.0eq), LiCl (3.0 eq)	-78 ˚C	THF	Unidentified product	
8.	X (2.0 eq)	-78 ˚C	MTBE	No Rxn	
9.	X (2.0 eq)	0 ˚C	Dioxane	No Rxn	
10.	X (2.0 eq)	-78 ˚C	DCM	No Rxn	
11.	X (2.0 eq)	-78 ˚C – rt	Toluene	100%	(1:1)
12.	**X (6.0 eq)**	**-78 ˚C – rt**	**Toluene**	**100%**	**(1:2)**

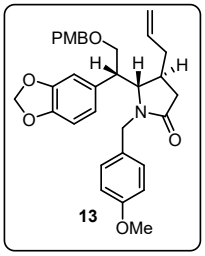
*Reaction condition; Substrate **11** (0.02 mmol), solvent 1 mL, time 1h, Ar atmosphere*

Synthesis of **13** [(4*S*,5*S*)-4-allyl-5-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-((4-methoxybenzyl)oxy)ethyl)-1-(4-methoxybenzyl)pyrrolidin-2-one]



Allylmagnesium chloride (1.0 M in THF, 17 mL), was added into a solution of enamide **11** (1.4 g, 2.87 mmol) in toluene (70 mL) at -78 ˚C, stir the reaction mixture for 30 min. at -78 ˚C and then stir at rt for 30 min. Carefully quenched the reaction mixture at 0 ˚C by dropwise addition of sat. ammonium chloride solution and extract the aqueous layer by ethyl acetate (x 2), combined organic layer was washed with brine and dried over sodium sulfate. After evaporation of solvent, the product was obtained as an inseparable

mixture (**12**:**13** = 1:2), to obtain pure addition product, crude mixture was re-dissolved in dry DCM (20 mL), then $In(OTf)_3$ (161 mg, 0.287 mmol) and triisopropylsilane (0.588 mL, 2.87 mmol) was added at 0 ℃ and stir the reaction mixture for 12 h at rt. After completion of reaction, the reaction mixture was quenched with sat. solution of sodium bicarbonate and was extracted with DCM (x 2). Combined organic layer was washed with sat. brine solution and dried over sodium sulphate. Evaporated the solvent and the crude product was purified by column chromatography using silica gel 60-120 mesh (40% Acetone:Hexane as eluent) to obtain product **13** as yellow oil (860 mg, 57% yield).



R_f : 0.6 (40% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.57 (d, *J* = 1.6 Hz, 1H), 6.50 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H), 5.93 (dd, *J* = 1.3, 3.8 Hz, 2H), 5.33-5.45 (m, 1H), 5.15 (d, *J* = 14.3 Hz, 1H), 4.85 (dd, *J* = 1.7, 10.2 Hz, 1H), 4.64 (dd, *J* = 1.7, 17.0 Hz, 1H), 4.42 (q, *J* = 9.3 Hz, 2H), 3.86 (d, *J* = 14.4 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.70-3.75 (m, 1H), 3.57-3.64 (m, 1H), 3.52 (d, *J* = 3.5 Hz, 1H), 3.16-3.22 (m, 1H), 2.01 (q, *J* = 7.6 Hz, 1H), 1.75-1.82 (m, 1H), 1.68-1.74 (m, 2H), 1.51-1.59 (m, 1H).

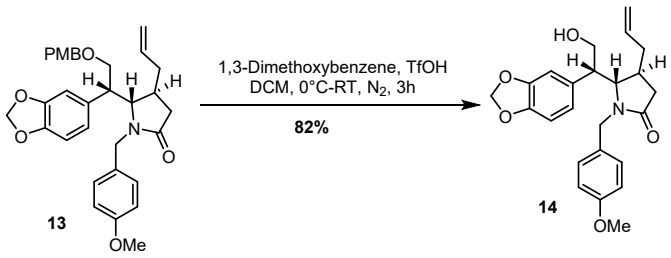
^{13}C NMR (100 MHz, $CDCl_3$): δ 174.49, 159.27, 159.15, 147.72, 146.69, 134.93, 131.53, 130.17, 129.97, 129.22, 128.73, 121.66, 117.67, 113.98, 113.78, 108.53, 108.34, 101.02, 72.94, 69.84, 62.35, 55.28, 44.69, 43.77, 39.32, 36.25, 32.66.

HRMS (ESI): m/z calcd for $C_{32}H_{36}NO_6^+$ $[M+H]^+$: 530.2543, found: 530.2535.

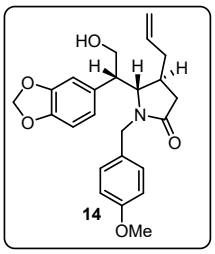
$[\alpha]_D^{23}$: +4.2° (c 0.7, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 2850.1, 2313.4, 1754.6, 1616.4, 1541.2, 1445.3, 1300.3, 1100.8, 1035.4, 928.8, 756.7.

Synthesis of **14** [(4*S*,5*S*)-4-allyl-5-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-hydroxyethyl)-1-(4-methoxybenzyl)pyrrolidin-2-one]



To a solution of the PMB ether **13** (450 mg, 0.85 mmol) and 1,3-dimethoxybenzene (0.335 mL, 2.55 mmol) in dichloromethane (5 mL) was added TfOH (75 µL, 0.85 mmol). The reaction mixture was stirred for 3 h at 0 ℃. After completion of the reaction, sat. aqueous solution of sodium bicarbonate was added. Extract the aqueous layer by DCM (x 2), washed with brine, dried over sodium sulfate. The product **14** was obtained by column chromatography using silica gel 60-120 mesh (50% Acetone:Hexane as eluent) as yellow oil (285 mg, 82% yield).

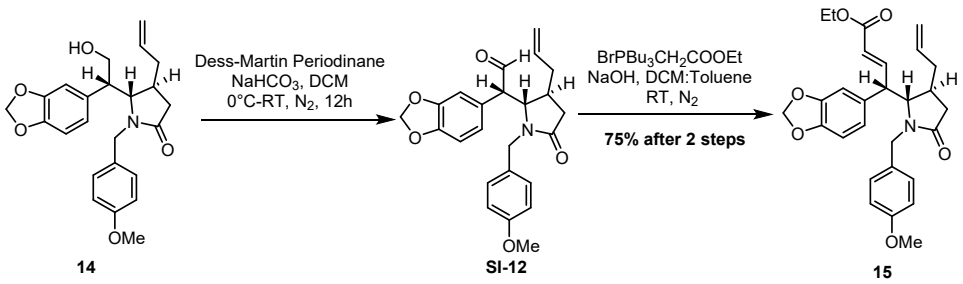


R_f : 0.4 (40% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 1.5 Hz, 1H), 6.54 (dd, *J* = 1.5, 8.0 Hz, 1H), 5.94 (s, 2H), 5.38-5.51 (m, 1H), 5.18 (d, *J* = 14.4 Hz, 1H), 4.90 (dd, *J* = 1.4, 10.1 Hz, 1H), 4.62

(dd, *J* = 1.4, 17.0 Hz, 1H), 3.92-3.97 (m, 1H), 3.89 (d, *J* = 14.4 Hz, 1H), 3.81 (s, 3H), 3.76-3.80 (m, 1H), 3.42 (d, *J* = 4.3 Hz, 1H), 3.07-3.13 (m, 1H), 1.97-2.01 (m, 1H), 1.81-1.89 (m, 1H), 1.69-1.74 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 174.54, 159.25, 148.00, 146.93, 135.09, 130.99, 130.08, 128.69, 121.67, 117.89, 114.08, 108.58, 108.51, 101.12, 62.58, 61.82, 55.31, 47.67, 44.12, 39.21, 36.33, 32.98.
HRMS (ESI): m/z calcd for $C_{24}H_{28}NO_5^+$ $[M+H]^+$: 410.1967, found: 410.1965.
$[\alpha]_D^{23}$: +12.40° (c 0.6, $CHCl_3$).
IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3392.5, 2923.1, 2313.7, 1660.2, 1614.8, 1541.8, 1446.3, 1298.0, 1177.8, 1034.4, 812.3, 665.9.

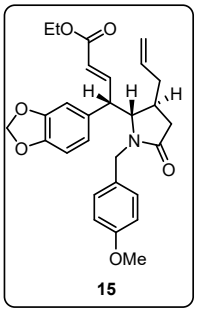
Synthesis of **15** [Ethyl-(*S*,*E*)-((2*S*,3*S*)-3-allyl-1-(4-methoxybenzyl)-5-oxopyrrolidin-2-yl)-4-(benzo[d][1,3]dioxol-5-yl)but-2-enoate]



To a solution of the mixture of **14** (250 mg, 0.62 mmol) in DCM (5 mL) was added Dess-Martin periodinane (394 mg, 0.93 mmol) and solid sodium bicarbonate (156 mg, 1.86 mmol) at 0 °C. The reaction mixture was stirred for 12 h at rt. The suspension was filtered through a Celite pad. The filter cake was sequentially washed with DCM (20 mL x 2). The filtrate was washed with sat. solution of sodium thiosulfate, brine and dried over sodium sulfate. After that organic layer was concentrated in *vacuo* and the obtained colorless oil used for next step without further purification.

To prepare tributyl(ethoxycarbonylmethyl)phosphnium bromide, a solution of bromoethyl acetate (1 g, 6 mmol) in dry ethyl acetate (5 mL) was treated with *n*-tributyl phosphine (50% sol. in ethyl acetate) (3.6 mL, 7.2 mmol) and stirred the reaction mixture for 24 h in nitrogen atmosphere. After evaporation of solvent, resulting white solid is filtered and washed with ether (10 mL x 2) to obtain 2.2 g white solid Wittig salt in quantative yield.

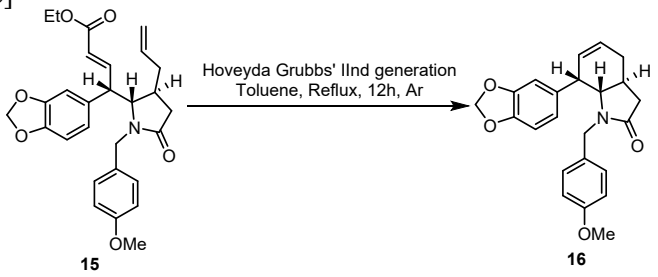
A solution of tributyl(ethoxycarbonylmethyl)phosphnium bromide (450 mg, 1.22 mmol) in DCM (5 mL) was washed with aq. solution of NaOH (1 M, 2x10 mL), dried on sodium sulfate and dilute with toluene (2 mL). The DCM was successively evaporated in *vacuo*. This solution of Wittig reagent in toluene was then transferred via cannula to a solution of aldehyde **SI-12** in DCM (6 mL) and stirred it at rt for 1 h. After that reaction mixture was evaporated and crude mixture was purified via column chromatography using silica gel 60-120 mesh (30% Acetone:Hexane as eluent) to get product **15** (218 mg, 75% yield) as red-orange oil.



R_f: 0.5 (30% Acetone:Hexane)

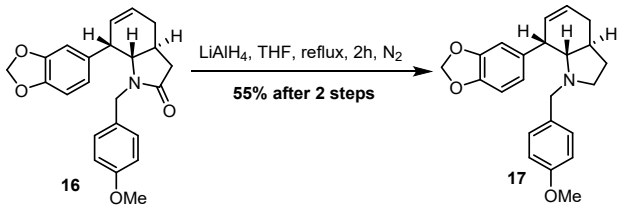
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, *J* = 8.5 Hz, 2H), 7.12 (dd, *J* = 8.5 Hz, 15.7 Hz, 1H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.51-6.57 (m, 2H), 5.95 (s, 2H), 5.89 (dd, *J* = 1.1, 15.6 Hz, 1H), 5.30-5.42 (m, 1H), 5.17 (d, *J* = 14.6 Hz, 1H), 4.86-4.93 (m, 1H), 4.61-4.69 (m, 1H), 4.17-4.24 (m, 2H), 3.82 (s, 3H), 3.78 (d, *J* = 14.6 Hz, 1H), 3.57-3.63 (m, 1H), 3.38 (d, *J* = 6.2 Hz, 1H), 2.02-2.15 (m, 2H), 1.89 (d, *J* = 16.3 Hz, 1H), 1.71-1.85 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 174.53, 166.02, 159.30, 148.07, 147.03, 134.64, 131.58, 130.00, 128.17, 123.36, 121.58, 118.03, 114.19, 108.67, 108.40, 101.23, 64.44, 60.63, 55.32, 50.40, 44.78, 38.98, 35.81, 33.72, 14.25.
HRMS (ESI): m/z calcd for $C_{28}H_{32}NO_6^+$ $[M+H]^+$: 478.2230, found: 478.2226.
$[\alpha]_D^{23}$: -2.30° (c 0.1, $CHCl_3$).
IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3017.6, 1709.6, 1675.9, 1504.6, 1442.6, 1364.8, 1217.8, 1176.1, 1106.7, 9281.8, 741.8, 667.6.

Synthesis of **16** [(3a*S*,7*S*,7a*S*)-7-(benzo[d][1,3]dioxol-5-yl)-1-(4-methoxybenzyl)-1,3,3a,4,7,7a-hexahydro-2H-indol-2-one]

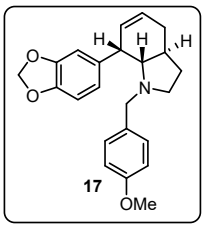


Dialkene product **15** (175 mg, 0.37 mmol) was dissolved in dry Toluene (18 mL) followed by the addition of the Hoveyda Grubbs' 2nd generation catalyst (11 mg, 0.0185 mmol) and this mixture was degassed under argon atmosphere. After stirring for 12 h at reflux, the mixture was concentrated in *vacuo* and redissolved in ethyl acetate. The residue was filtered over Celite pad. Evaporation of solvent provided **16** as a light brown liquid which was used in next step without further purification.

Synthesis of **17** [(3a*S*,7*S*,7a*S*)-7-(benzo[d][1,3]dioxol-5-yl)-1-(4-methoxybenzyl)-2,3,3a,4,7,7a-hexahydro-1H-indole]



Grubbs' product **16** was dissolved in THF (10 mL) and LAH (40 mg, 1 mmol) was added at once at 0 ℃. The solution was stirred at reflux for 2 h. The reaction mixture was quenched with 1N NaOH (1 mL) sol. at 0 ℃ and stirs the reaction mixture until grey ppt converted to white. The ppt was filtered off on a short Celite pad and the filtrate was concentrated under reduced pressure to give the crude product. The crude product was purified by flash chromatography on basic alumina (4-6% EtOAc:Hexane as eluent) to afford **17** (75 mg, 55% yield after two steps) as colorless oil.



R_f : 0.6 (40% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, *J* = 8.4 Hz, 2H), 6.79-6.81 (m, 1H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 1.0 Hz, 2H), 5.94 (q, *J* = 1.5 Hz, 2H), 5.90-5.93 (m, 1H), 5.72-5.78 (m, 1H), 4.35 (d, *J* = 12.8 Hz, 1H), 3.77 (s, 3H), 2.99 (d, *J* = 12.8 Hz, 1H), 2.76-2.84 (m, 1H), 2.40-2.49 (m, 1H), 2.30-2.37 (m, 1H), 2.05-2.12 (m, 1H), 1.97-2.03 (m, 1H), 1.90-1.97 (m, 1H), 1.76-1.85 (m, 1H), 1.27-1.36 (m, 2H).

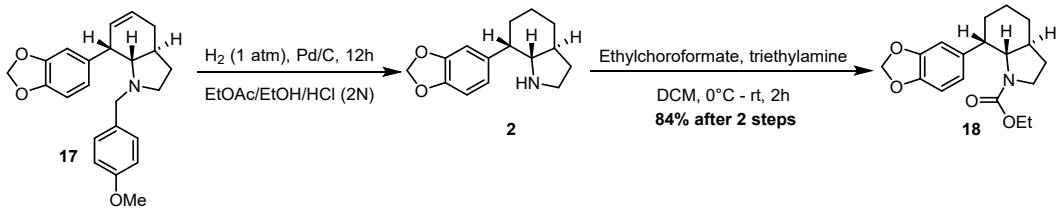
^{13}C NMR (100 MHz, $CDCl_3$): δ 158.48, 147.16, 146.12, 133.74, 131.73, 129.68, 128.98, 128.40, 123.45, 113.52, 110.77, 107.45, 100.84, 69.97, 58.34, 55.25, 52.53, 43.80, 33.61, 32.88, 28.06.

HRMS (ESI): m/z calcd for $C_{23}H_{26}NO_3^+$ $[M+H]^+$: 364.1913, found: 364.1913.

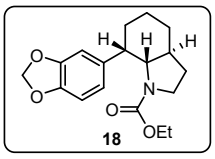
$[\alpha]_D^{23}$: -66.201° (c 0.2, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3847.1, 3701.4, 3604.5, 3518.5, 2361.7, 1855.6, 1742.8, 1622.1, 1513.2, 1448.6, 1348.7, 1097.3, 809.2, 682.1.

Synthesis of **18** Ethyl (3a*S*,7*S*,7a*S*)-7-(benzo[d][1,3]dioxol-5-yl)octahydro-1H-indole-1-carboxylate



17 (75 mg, 0.205 mmol) was dissolved in EtOAc:EtOH:HCl (6:2:0.4 mL) solution and 10% Pd/C (20 mg) was added at once under nitrogen atmosphere. The solution was stirred under ambient pressure of H_2 at rt for 12 h. After completion of reaction, 2 g potassium carbonate was added to the reaction mixture and was stirred for 30 min. The palladium catalyst and solid potassium carbonate was filtered off on a short Celite pad and the filtrate was concentrated under reduced pressure to give the product **2**. The crude product **2** was dissolved in DCM (3 mL). Then triethylamine (92 µL, 0.66 mmol) and ethyl chloroformate (31 µL, 0.33 mmol) was added sequentially at 0 °C. The reaction mixture was stirred at rt for 2 h. After completion of reaction, the mixture was quenched with aq. ammonium chloride and aq. layer was extracted by DCM (x 2), combined organic layer washed with brine sol. and dried over sodium sulfate. The crude product obtained after evaporation of organic solvent was purified by flash column chromatography using silica gel 60-120 mesh (20-30% EtOAc:Hexane as eluent) on silica gel to afford **18** (55 mg, 84% yield after two steps) as yellow oil.



R_f : 0.5 (30% EtOAc:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.74-6.89 (m, 2H), 6.71 (d, *J* = 8.1 Hz, 1H), 5.90 (s, 2H), 4.09-4.2 (m, 2H), 3.80-4.01 (m, 1H), 3.54-3.76 (m, 1H), 3.3 (dd, *J* = 4.4, 11.2 Hz, 1H), 2.87-3.05 (m, 1H), 2.11-2.21 (m, 1H), 1.94-2.01 (m, 1H), 1.79-1.92 (m, 2H), 1.69-1.76 (m, 3H), 1.31-1.37 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H).

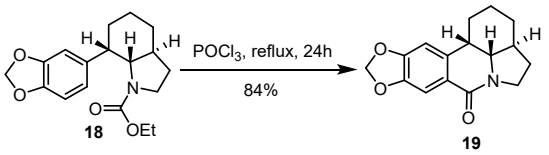
^{13}C NMR (100 MHz, $CDCl_3$): δ 147.15, 145.34, 122.10, 109.93, 109.64, 107.56, 100.63, 67.16, 60.75, 47.23, 39.76, 38.29, 30.71, 29.72, 22.65, 14.86.

HRMS (ESI): m/z calcd for $C_{18}H_{24}NO_4^+$ $[M+H]^+$: 318.1705, found: 318.1791.

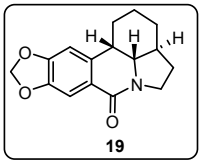
$[\alpha]_D^{23}$: -55.401° (c 0.3, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3091.5, 1682.3, 1493.9, 1427.5, 1214.6, 1123.8, 1039.4, 932.2, 742.5, 668.9, 628.5.

Synthesis of **19** [(3a*S*,3a^1*S*,12b*S*)-1,2,3,3a,3a^1,4,5,12b-octahydro-7H-[1,3]dioxolo[4,5-j]pyrrolo[3,2,1-de]phenanthridin-7-one]



The urethane **18** (37 mg, 0.115 mmol) was dissolved in freshly distilled $POCl_3$, (2 mL) and heated at 90 °C (preheated oil bath) for 20 h in a sealed glass tube. The mixture was cooled to rt and slowly poured into cold water (10 mL) with stirring. The aqueous solution was made slightly alkaline using sodium hydroxide pellets, and the aqueous mixture was then extracted with CH_2Cl_2 (x 3). The combined extracts were dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The Crude reaction mixture compound was purified by column chromatography using silica gel 60-120 mesh (30% Acetone:Hexane as eluent) to get product **19** (26 mg, 84% yield) as yellow oil.



R_f : 0.5 (30% Acetone:Hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 6.80 (d, *J* = 0.8 Hz, 1H), 5.99 (q, *J* = 1.3 Hz, 2H), 4.18-4.29 (m, 1H), 3.48-3.55 (m, 1H), 3.19-3.29 (m, 1H), 2.95 (dd, *J* = 7.4, 11.1 Hz, 1H), 2.37-2.46 (m, 1H), 1.86-2.01 (m, 2H), 1.64-1.78 (m, 2H), 1.35-1.47 (m, 1H), 1.26-1.34 (m, 1H), 1.16-1.23 (m, 1H), 1.06-1.14 (m, 1H).

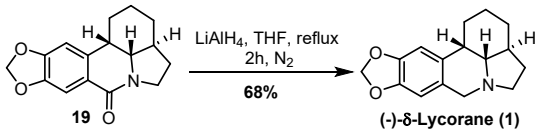
^{13}C NMR (100 MHz, $CDCl_3$): δ 166.81, 151.41, 146.57, 134.42, 122.91, 109.23, 104.65, 101.58, 63.64, 45.19, 38.52, 33.26, 29.26, 28.72, 26.01, 21.87.

HRMS (ESI): m/z calcd for $C_{16}H_{18}NO_3^+$ $[M+H]^+$: 272.1287, found: 272.1255.

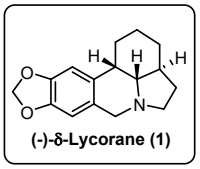
$[\alpha]_D^{23}$: -9.7° (c 0.3, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3748.9, 2929.8, 1641.8, 1477.8, 1418.4, 1214.7, 1039.1, 744.2.

Synthesis of **(-)-1** [(3a*S*,3a^1*S*,12b*S*)-2,3,3a,3a^1,4,5,7,12b-octahydro-1H-[1,3]dioxolo[4,5-j]pyrrolo[3,2,1-de]phenanthridine]



19 (17 mg, 0.086 mmol) dissolved in THF (5 mL) and LAH (14 mg, 0.344 mmol) was added at once at 0 °C. The solution was stirred at reflux for 2 h. The reaction mixture was quenched with 1N NaOH sol. at 0 °C and was stirred until the grey ppt converted to white. The ppt was filtered off on a short Celite pad and the filtrate was washed with brine sol. and concentrated under reduced pressure to give the crude product. The crude product was purified by flash chromatography on basic alumina (10-20% Acetone:Hexane as eluent) to afford (-)-**1** (11 mg, 68% yield) as colorless oil.



R_f: 0.4 (10% MeOH:DCM)

^{1}H NMR (400 MHz, $CDCl_3$); δ 6.82 (s, 1H), 6.61 (s, 1H), 5.91 (dd, *J* = 1.4, 8.2 Hz, 2H), 3.94 (d, *J* = 15.2 Hz, 1H), 3.34 (d, *J* = 15.3 Hz, 1H), 3.25 (t, *J* = 8.3 Hz, 1H), 3.11 (t, *J* = 5.1 Hz, 1H), 2.91 (dd, *J* = 5.2, 10.8 Hz, 1H), 2.33-2.40 (m, 2H), 1.78-1.81 (m, 1H), 1.71-1.76 (m, 1H), 1.62-1.68 (m, 1H), 1.59-1.61 (m, 1H), 1.27-1.37 (m, 2H), 1.07-1.12 (m, 1H), 0.96-1.03 (m, 1H).

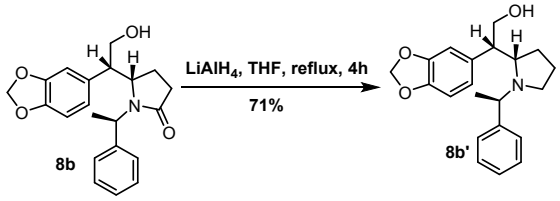
^{13}C NMR (100 MHz, $CDCl_3$); δ 146.68, 145.08, 132.45, 128.67, 108.14, 106.39, 100.62, 66.65, 54.71, 52.25, 39.83, 35.51, 30.0, 29.51, 25.69, 21.60.

HRMS (ESI): m/z calcd for $C_{16}H_{20}NO_2^+$ $[M+H]^+$: 258.1494, found: 258.1462.

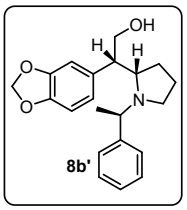
$[\alpha]_D^{23}$: -43.33° (c 0.12, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3020.1, 2927.6, 1477.2, 1214.5, 1040.5, 741.6, 668.7, 631.5.

Synthesis of **8b'** [(*S*)-2-(benzo[d][1,3]dioxol-5-yl)-2-((S)-1-((*R*)-1-phenylethyl)pyrrolidin-2-yl)ethan-1-ol]



8b (20 mg, 0.056 mmol) was dissolved in THF (3 mL) and LAH (9 mg, 0.226 mmol) was added at once at 0 °C. The solution was stirred at reflux for 4 h (TLC analysis showed the reaction completed). The reaction mixture was quenched with 1N NaOH sol. (1 mL) at 0 °C and the reaction mixture was stirred until grey ppt converted to white. The ppt was filtered off on a short Celite pad and the filtrate was concentrated under reduced pressure to give the crude product. The crude product was purified by flash chromatography on basic alumina (20-30 % Acetone:Hexane as eluent) to afford **8b'** (13.5 mg, 71%) as colorless oil.



R_f: 0.4 (10% MeOH:DCM x 2)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (m, *J* = 4.4 Hz, 5H), 6.64 (d, *J* = 7.9 Hz, 1H), 6.33 (dd, *J* = 1.6, 8.0 Hz, 1H), 6.27 (d, *J* = 1.6 Hz, 1H), 5.88 (q, *J* = 1.4 Hz, 2H), 3.63 (q, *J* = 6.5 Hz, 1H), 3.56 (t, *J* = 10.6 Hz, 1H), 3.40-3.47 (m, 1H), 3.30-3.37 (m, 1H), 3.00-3.15 (m, 2H), 2.51-2.60 (m, 1H), 1.77-1.87 (m, 2H), 1.51-1.59 (m, 1H), 1.46 (d, *J* = 6.5 Hz, 3H), 1.24-1.35 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 147.52, 146.09, 143.99, 135.09, 128.71, 128.08, 127.62, 121.18, 108.27, 108.04, 100.81, 68.39, 68.09, 62.55, 49.86, 48.99, 27.71, 23.11, 20.61.

HRMS (ESI): m/z calcd for $C_{21}H_{26}NO_3^+$ $[M+H]^+$: 340.1913, found: 340.1875.

$[\alpha]_D^{23}$: -17.3° (c 0.15, $CHCl_3$).

IR (in $CHCl_3$, cm^{-1}): ν_{max}; 3019.8, 1491.5, 1215.1, 1038.3, 932.7, 741.5, 668.9, 630.9.

3. NMR spectra Data comparison

Table SI-3; Comparison of ^{1}H-NMR spectroscopic data of (-)-δ-lycorane with other lycoranes

α-lycorane[3]	δ = 6.69 (s, 1 H), 6.64 (s,1 H), 5.91 (s, 2H), 4.27 (d, *J* = 14.8 Hz, 1H), 3.74 (d, *J* = 14.8 Hz, 1 H), 3.40 (m, 1 H), 2.91 (m, 1H), 2.70 (m, 1H), 2.49 (brs, 1H), 2.38 (m,1H), 2.25 (m, 1 H), 1.88 (m, 2 H), 1.68 (m, 3 H), 1.58 (m, 1 H),1.22 (m, 1H).
β-lycorane[4]	δ = 6.72 (s, 1H), 6.51 (s, 1H), 5.93-5.91 (m, 2H), 4.02 (d, *J* = 15.4 Hz, 1H), 3.22-3.12 (m, 2H), 2.54-2.51 (m, 1H), 2.23-2.21 (m, 2H), 2.10- 1.98 (m, 3H), 1.88-1.58 (m, 4H), 1.42-1.38 (m, 2H).
γ-lycorane[5]	δ = 6.61 (s, 1H), 6.49 (s, 1H), 5.89 (d, J = 2.8 Hz, 2H), 4.01 (d, *J* = 14.4 Hz, 1H), 3.38 (td, *J* = 9.2, 3.8 Hz, 1H), 3.21 (d, *J* = 14.3 Hz, 1H), 2.82– 2.65 (m, 1H), 2.37 (t, *J* = 4.7 Hz, 1H), 2.20–2.12 (m, 2H), 2.03–2.00 (m, 1H), 1.77–1.61 (m, 3H), 1.53–1.38 (m, 2H), 1.36–1.25 (m, 2H).
δ-lycorane[6]	δ = 6.82 (s, 1 H), 6.60 (s, 1 H), 5.90 (s, 2H), 3.94 (d, 1H, *J* = 15 Hz), 3.32 (d, 1H, *J* = 15 Hz), 1.07-3.37 (comp, 13 H).
δ-lycorane (our data)	δ 6.82 (s, 1H), 6.61 (s, 1H), 5.91 (dd, *J* = 1.4, 8.2 Hz, 2H), 3.94 (d, *J* = 15.2 Hz, 1H), 3.34 (d, *J* = 15.3 Hz, 1H), 3.25 (t, *J* = 8.3 Hz, 1H), 3.11 (t, *J* = 5.1 Hz, 1H), 2.91 (dd, *J* = 5.2, 10.8 Hz, 1H), 2.33-2.40 (m, 2H), 1.78-1.81 (m, 1H), 1.71-1.76 (m, 1H), 1.62-1.68 (m, 1H), 1.59-1.61 (m, 1H), 1.27-1.37 (m, 2H), 1.07-1.12 (m, 1H), 0.96-1.03 (m, 1H).

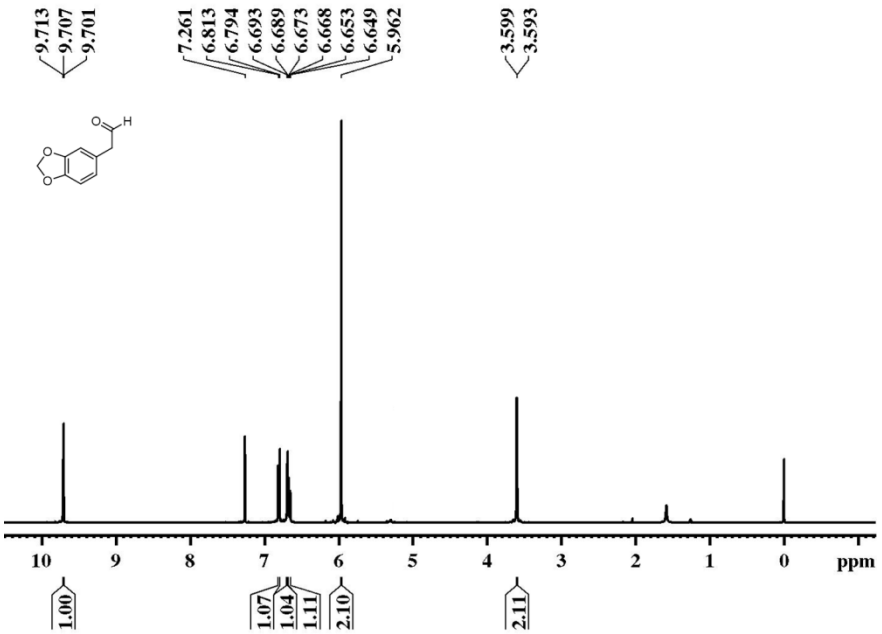
4. ^{1}H and ^{13}C NMR spectra

[3] Sun, Z. W.; Zhou, M. T.; Li, X.; Meng, X. L.; Peng, F. Z.; Zhang, H. B.; Shao, Z. H. Catalytic Asymmetric Assembly of Octahydroindolones:Divergent Synthesis of Lycorine-type Amaryllidaceae Alkaloids(+)-a-Lycorane and (+)-Lycorine. *Chem. – Eur. J.*, **2014**, *20*, 6112-6119.

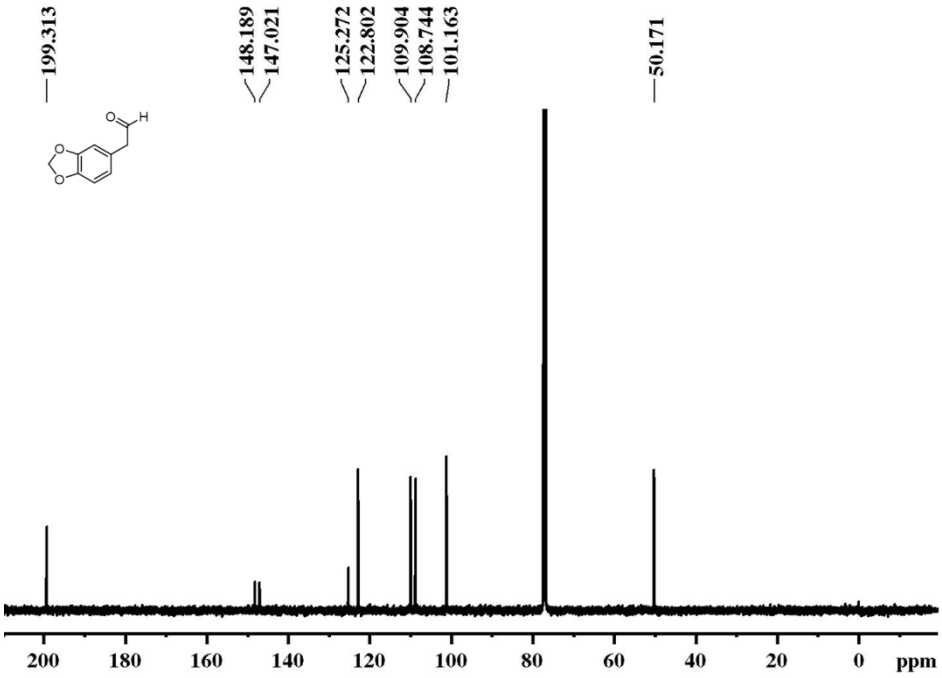
[4] Rana, N. K.; Huang, H. C.; Zhao, J. C. G. Highly Diastereodivergent Synthesis of Tetrasubstituted CyclohexanesCatalyzed by Modularly Designed Organocatalysts. *Angew. Chem., Int. Ed*., **2014**, *53*, 7619-7623.

[5] Meng, X. L.; Liu, T.; Sun, Z. W.; Wang, J. C.; Peng, F. Z.; Shao, Z. H. Asymmetric catalytic conjucate addition of acetaldehyde to nitrodienynes/nitroenynes: Application to the synthesis of (+)-α-Lycorane and Chiral β-alkynyl acids. *Org. Lett*., 2014, *16*, 3044-3047.

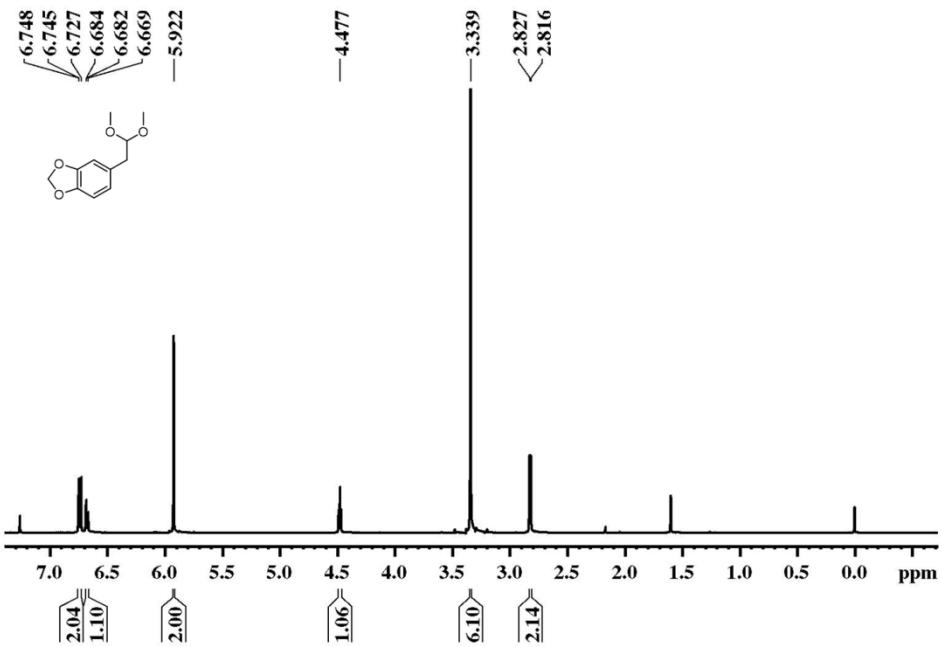
[6] Martin, S. F.; Tu, C. Y.; Kimura, M.; Simonsen, S. H. Intramolecular [4 + 2]Cycloadditions as a General Strategy for Alkaloid Synthesis. A Novel Formal Synthesis of Lycorine. *J. Org. Chem.* **1982**, *47*, 3634-3643.



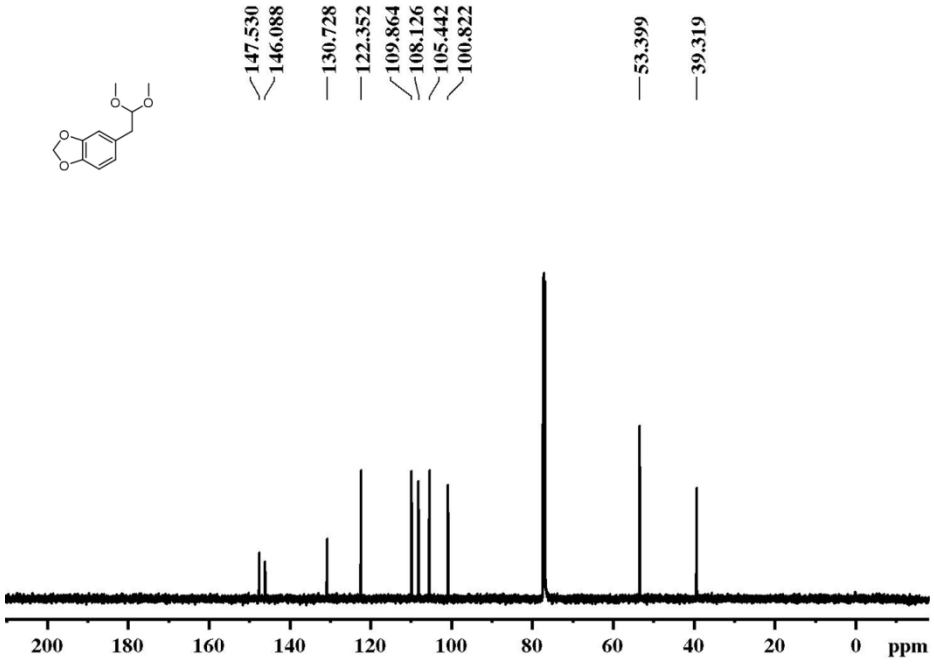
^{1}H NMR of Compound **6** in $CDCl_3$; 303K (400 MHz)



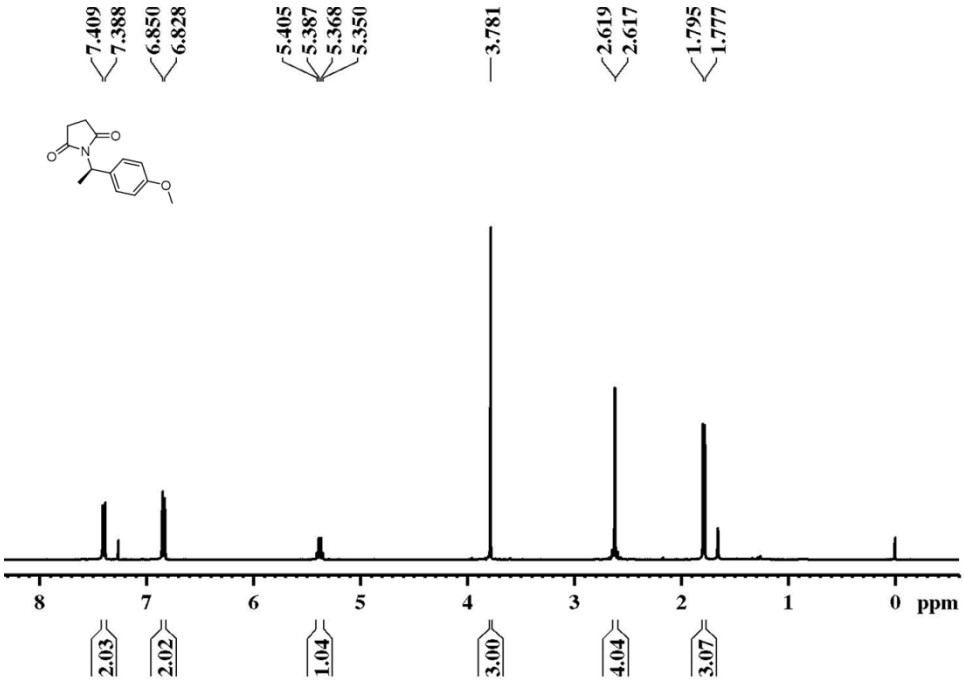
^{13}C NMR of Compound **6** in $CDCl_3$; 303K (100 MHz)



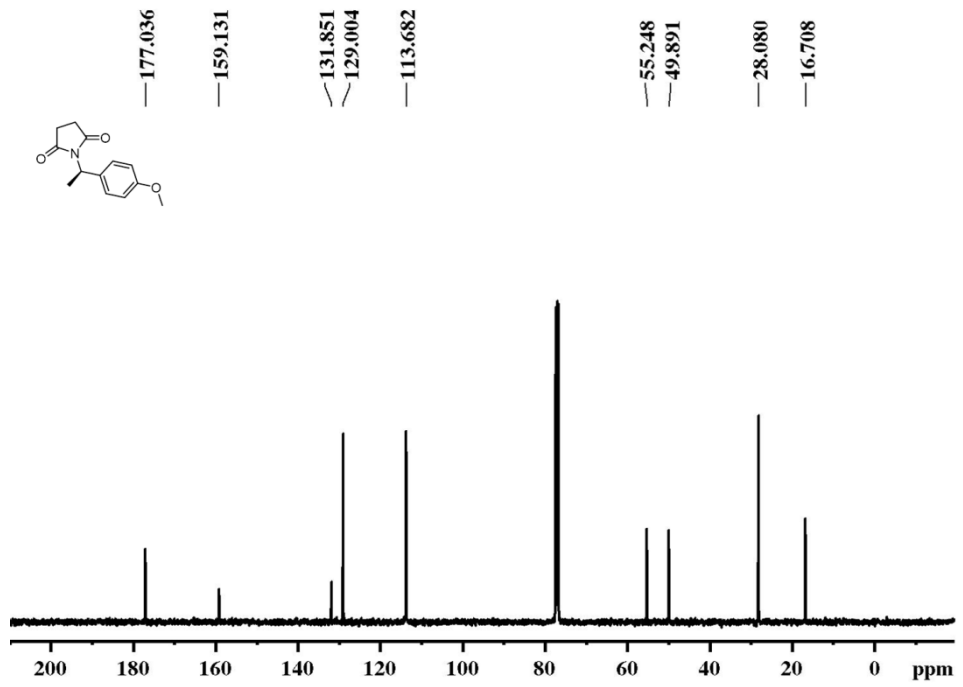
^{1}H NMR of Compound **6a** in $CDCl_3$; 303K (400 MHz)



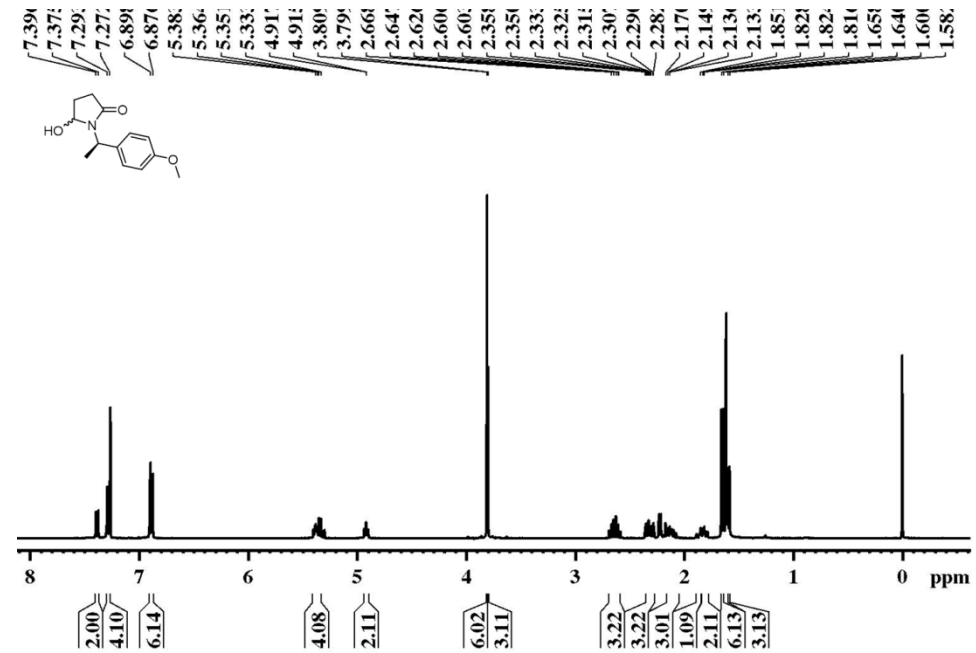
^{13}C NMR of Compound **6a** in $CDCl_3$; 303K (100 MHz)



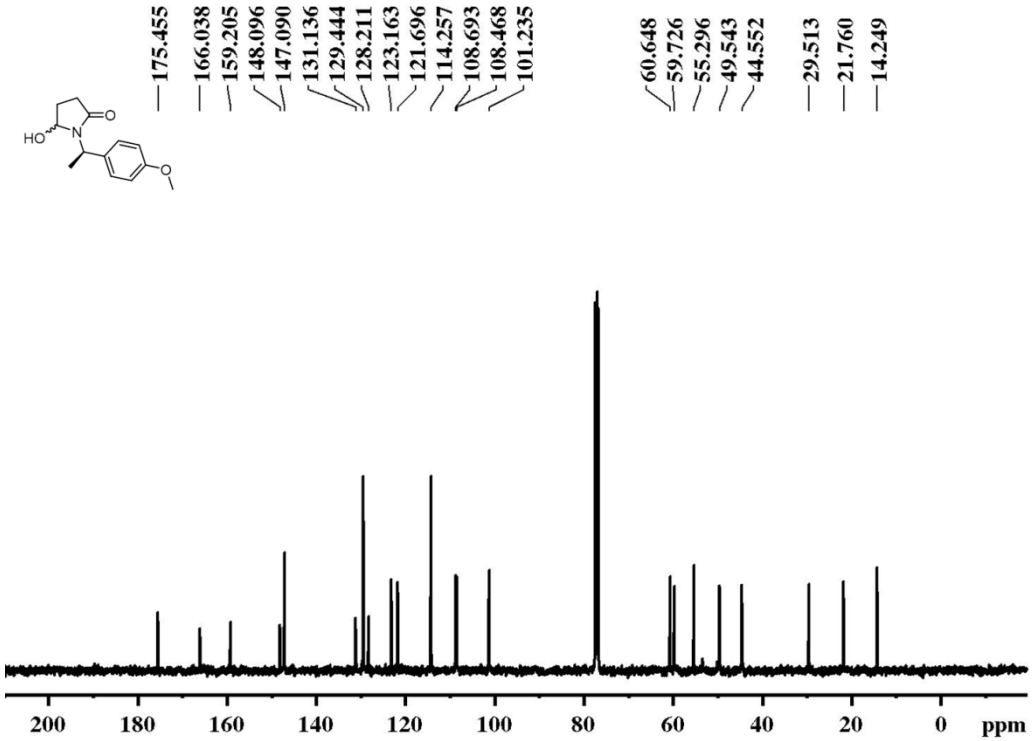
^{1}H NMR of Compound **SI-9** in $CDCl_3$; 303K (400 MHz)



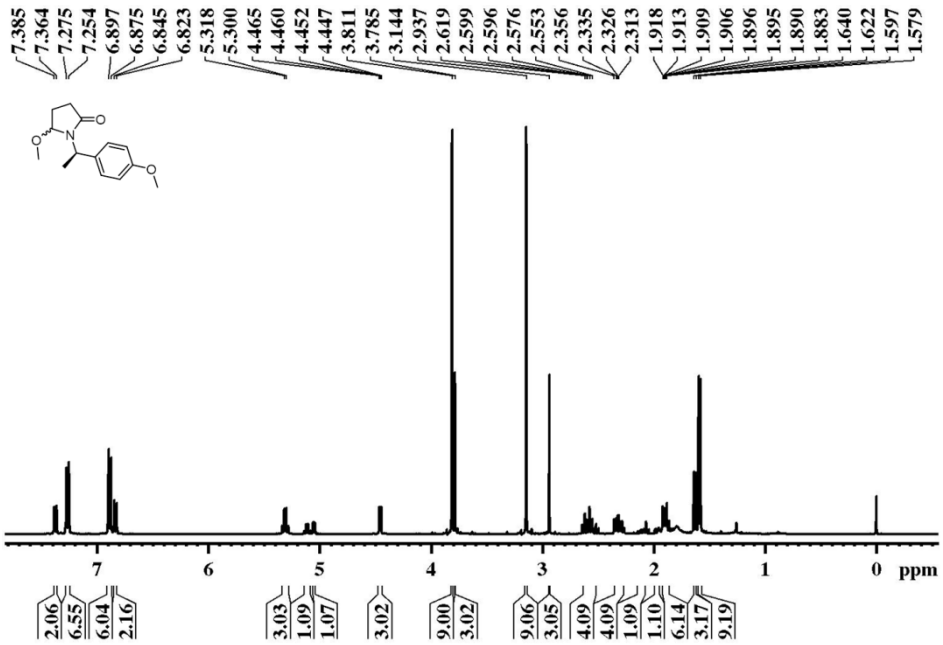
^{13}C NMR of Compound **SI-9** in $CDCl_3$; 303K (100 MHz)



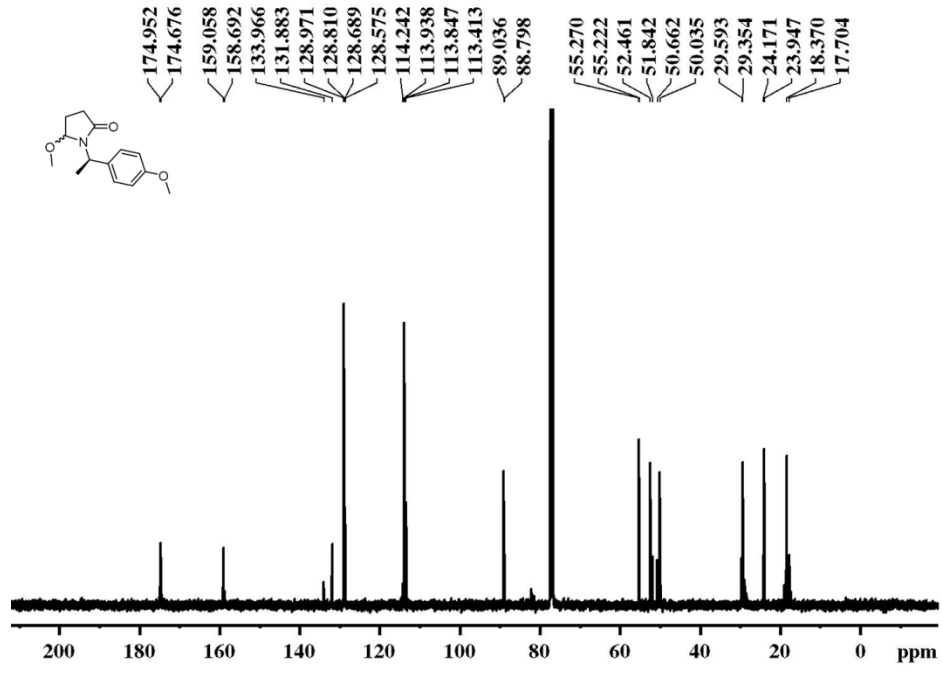
^{1}H NMR of Compound **SI-10** in $CDCl_3$; 303K (400 MHz)



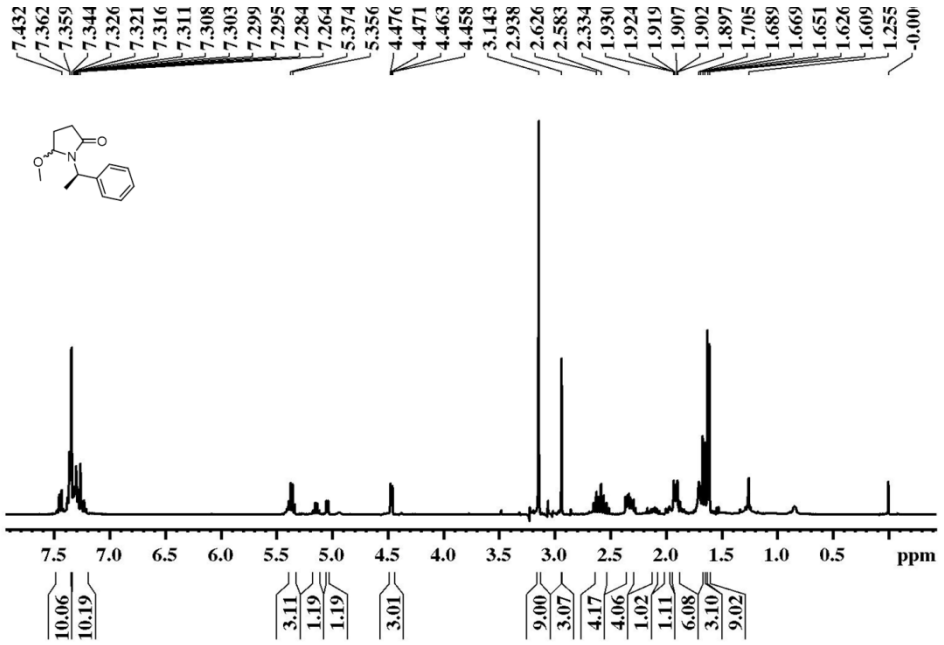
^{13}C NMR of Compound **SI-10** in $CDCl_3$; 303K (100 MHz)



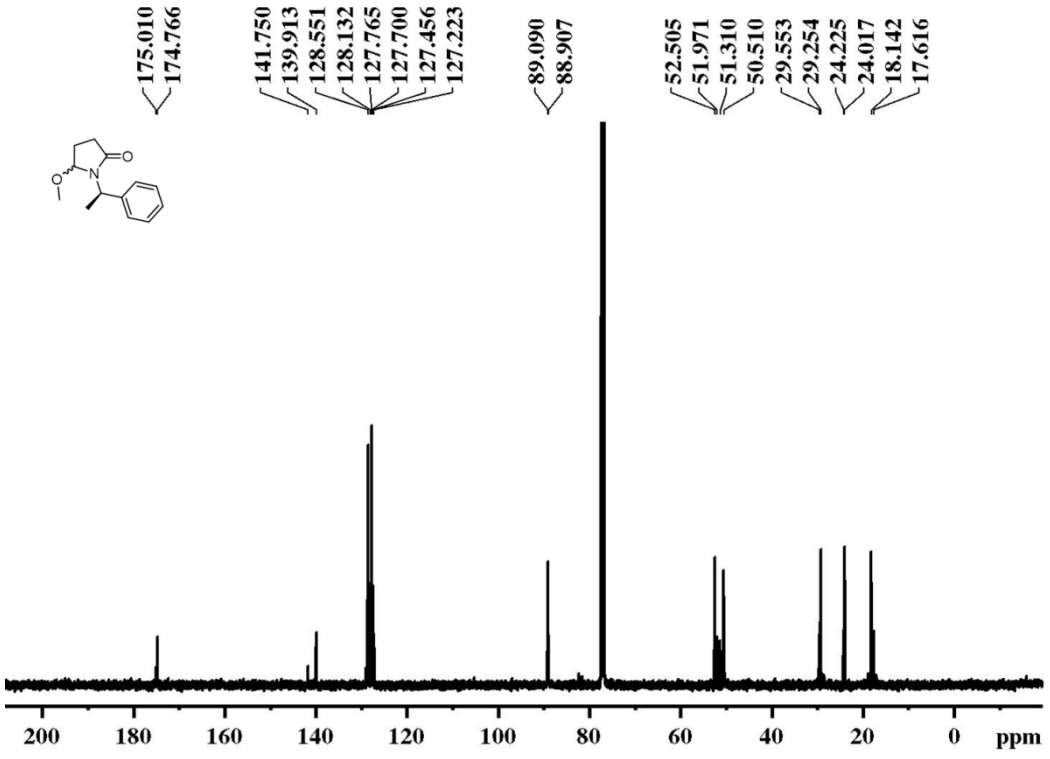
^{1}H NMR of Compound **7a** in $CDCl_3$; 303K (400 MHz)



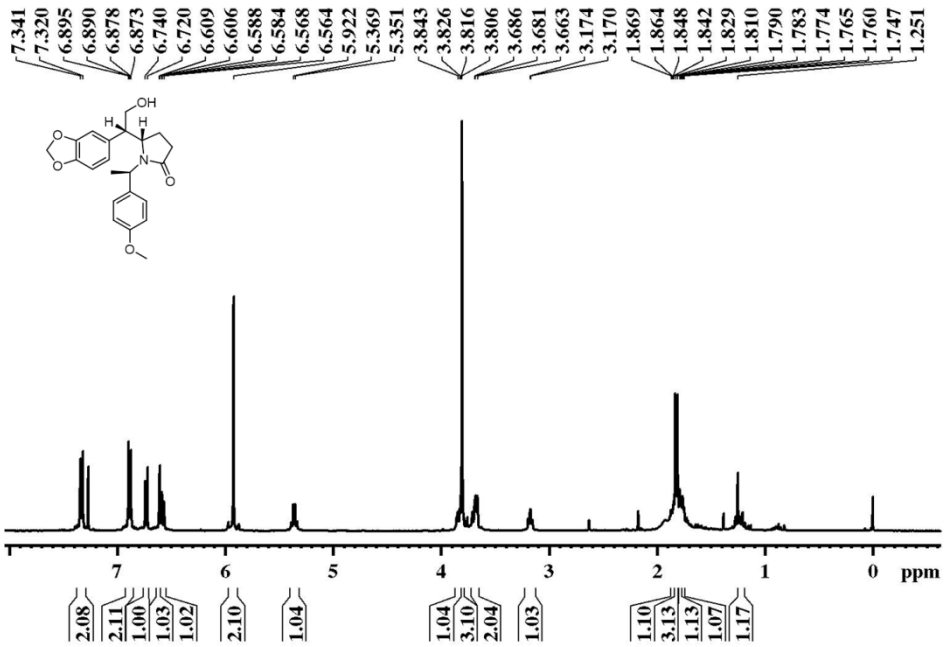
^{13}C NMR of Compound **7a** in $CDCl_3$; 303K (100 MHz)



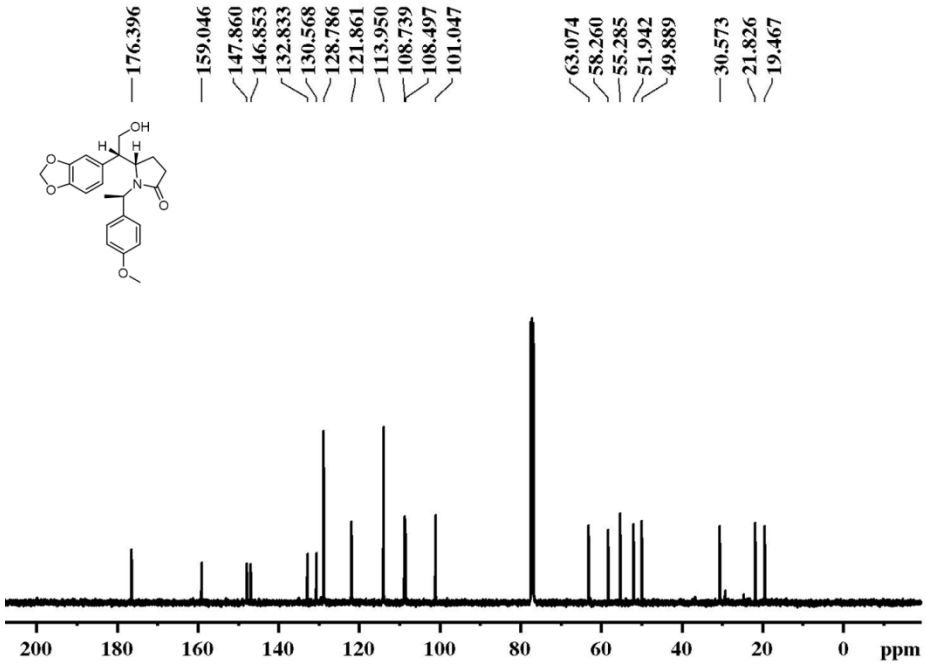
^{1}H NMR of Compound **7b** in $CDCl_3$; 303K (400 MHz)



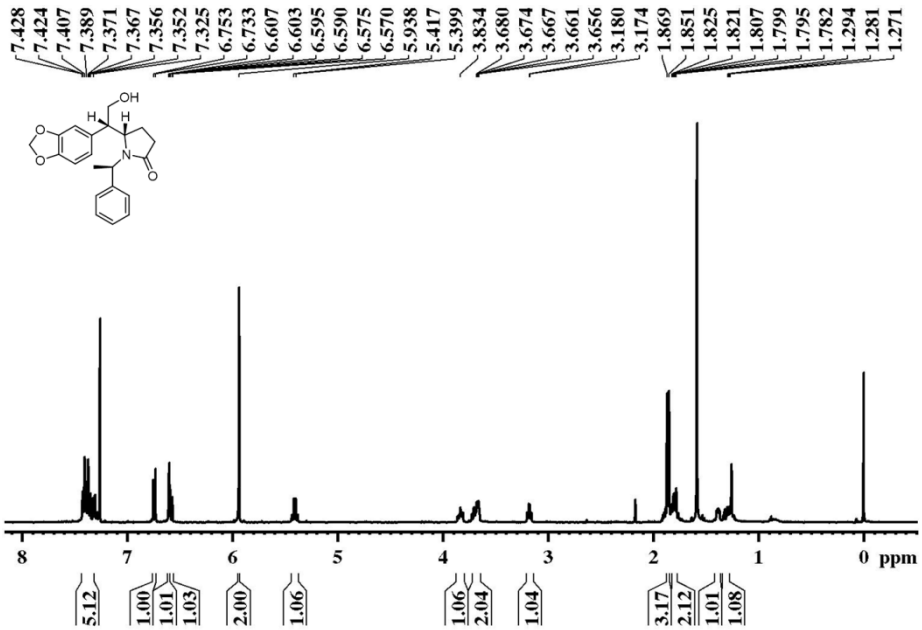
^{13}C NMR of Compound **7b** in $CDCl_3$; 303K (100 MHz)



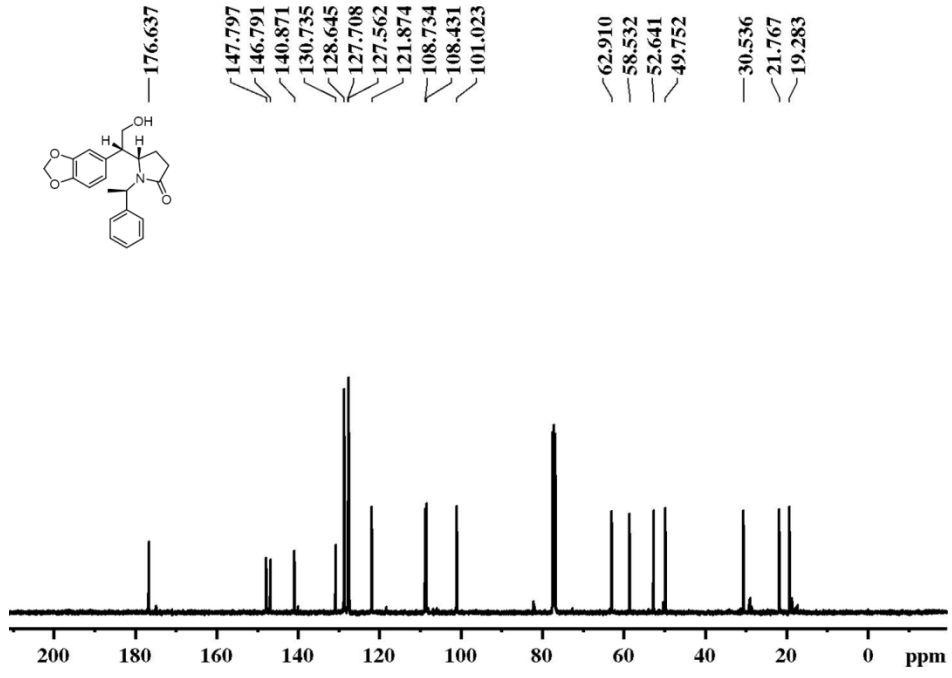
^{1}H NMR of Compound **8a** in $CDCl_3$; 303K (400 MHz)



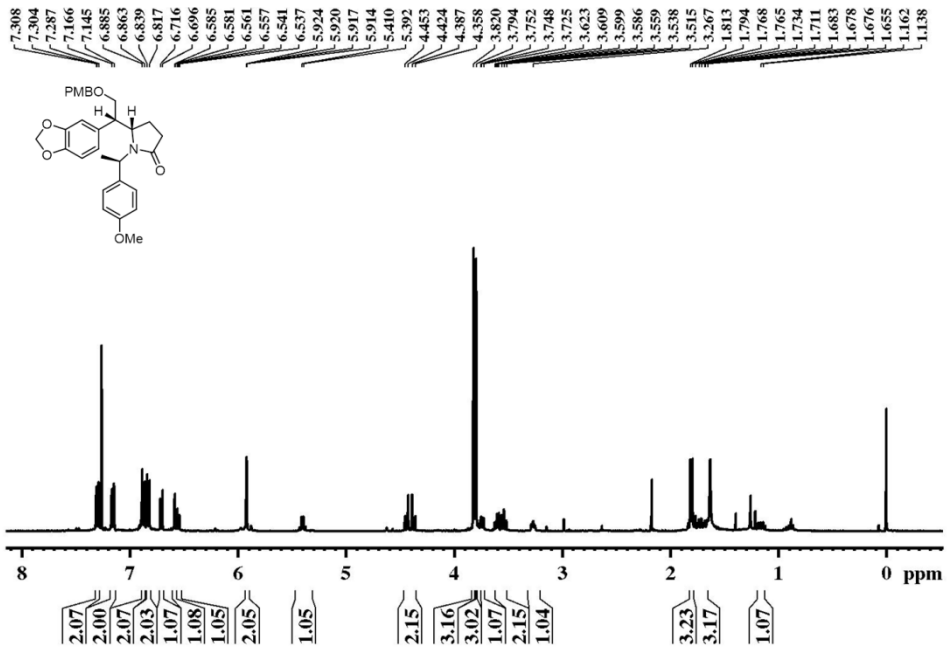
^{13}C NMR of Compound **8a** in $CDCl_3$; 303K (100 MHz)



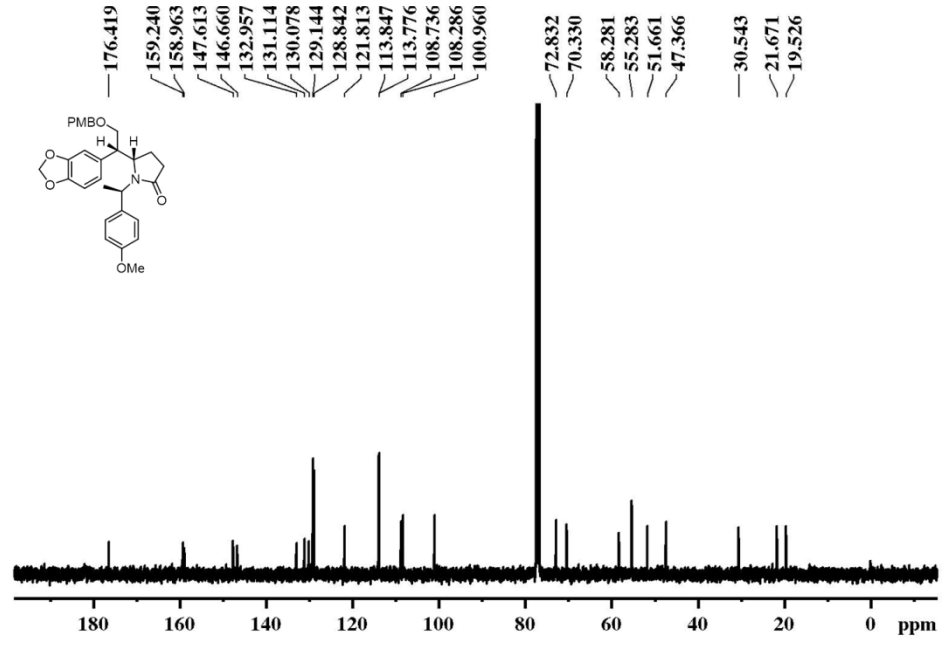
^{1}H NMR of Compound **8b** in $CDCl_3$; 303K (400 MHz)



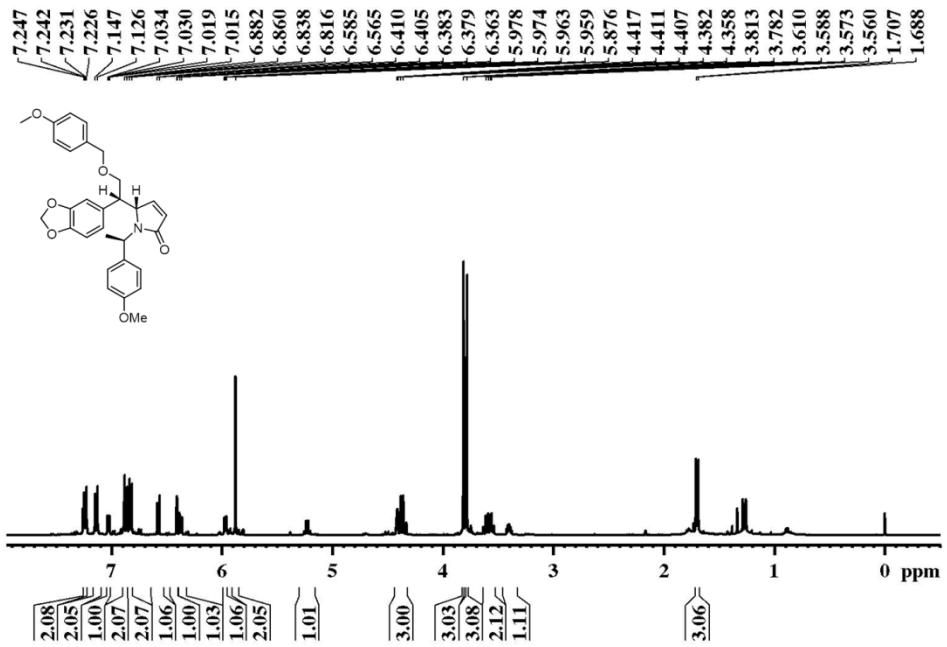
^{13}C NMR of Compound **8b** in $CDCl_3$; 303K (100 MHz)



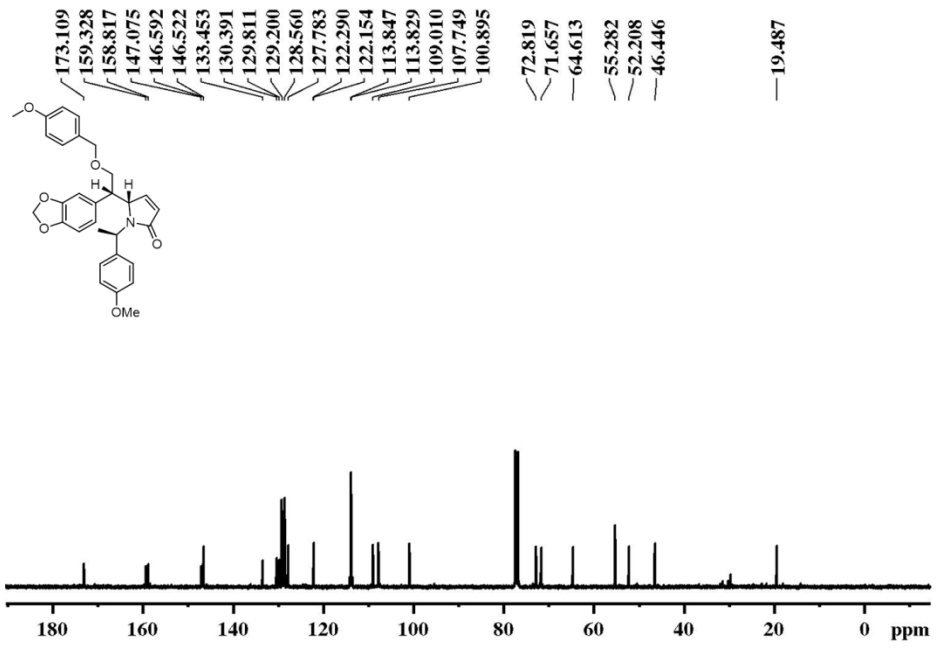
^{1}H NMR of Compound **9a** in $CDCl_3$; 303K (400 MHz)



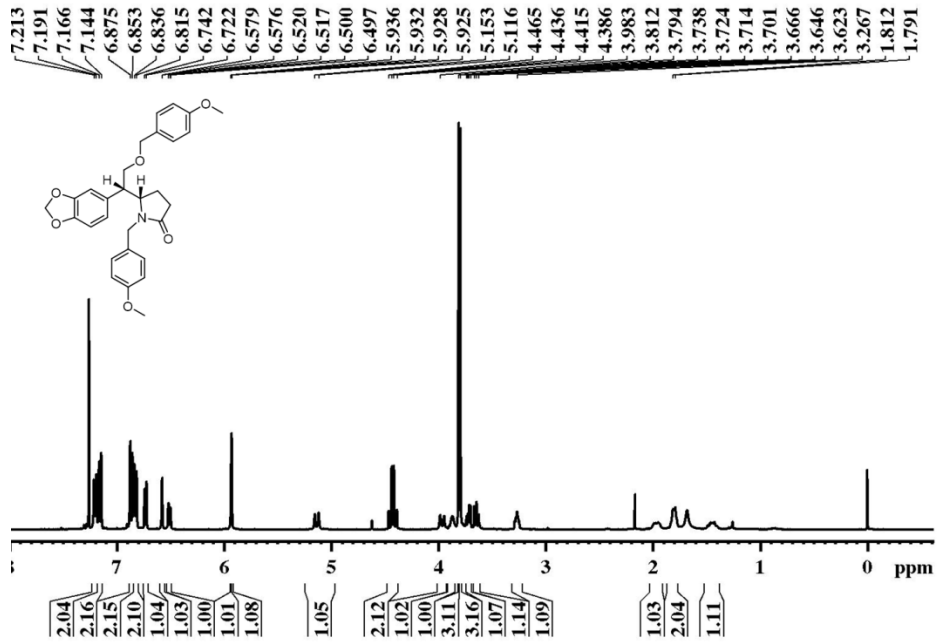
^{13}C NMR of Compound **9a** in $CDCl_3$; 303K (100 MHz)



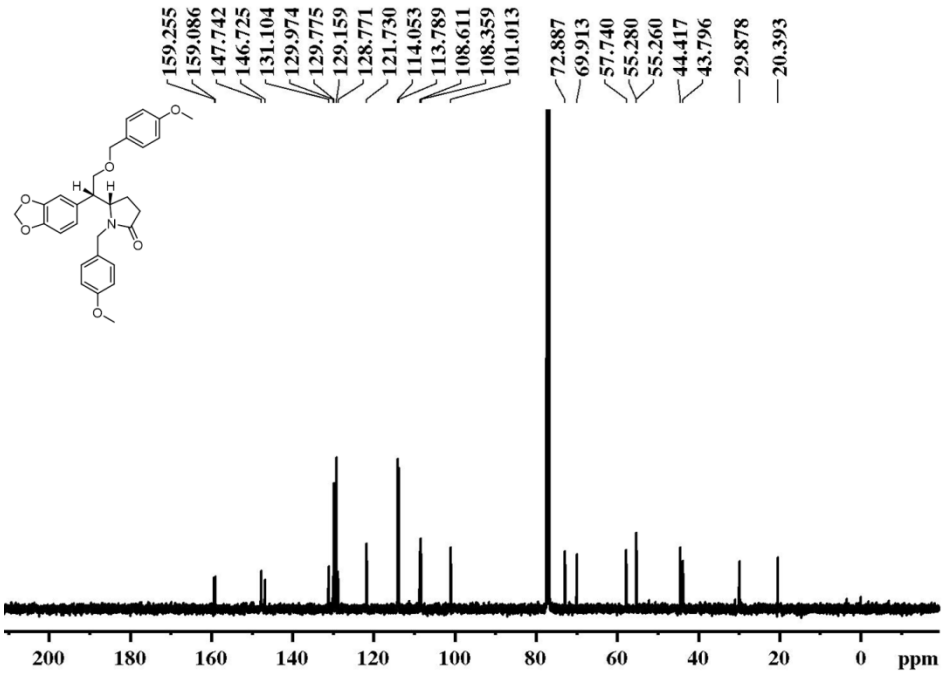
^{1}H NMR of Compound **10a** in $CDCl_3$; 303K (400 MHz)



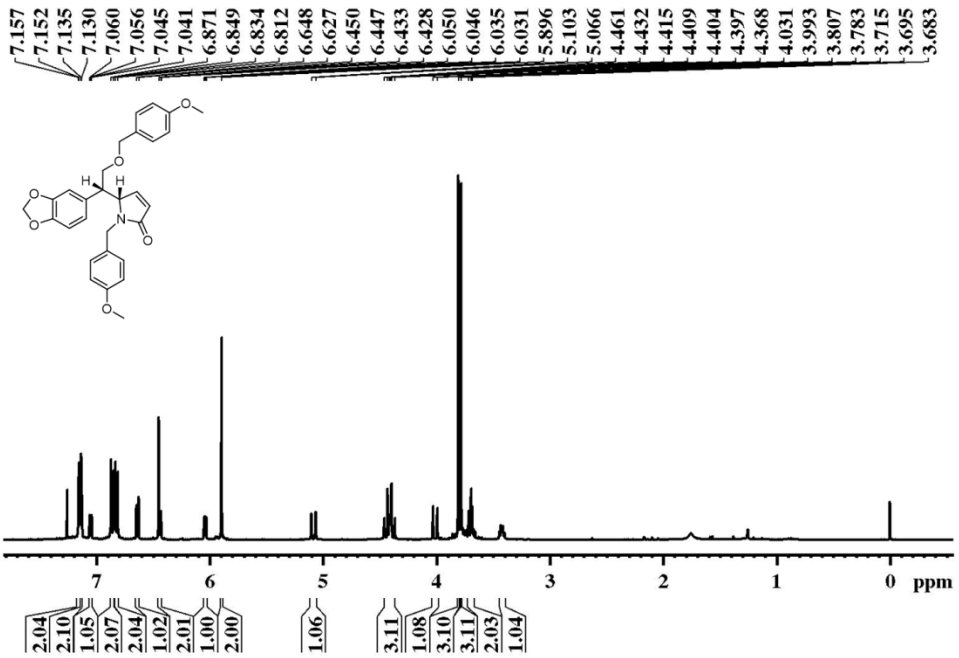
^{13}C NMR of Compound **10a** in $CDCl_3$; 303K (100 MHz)



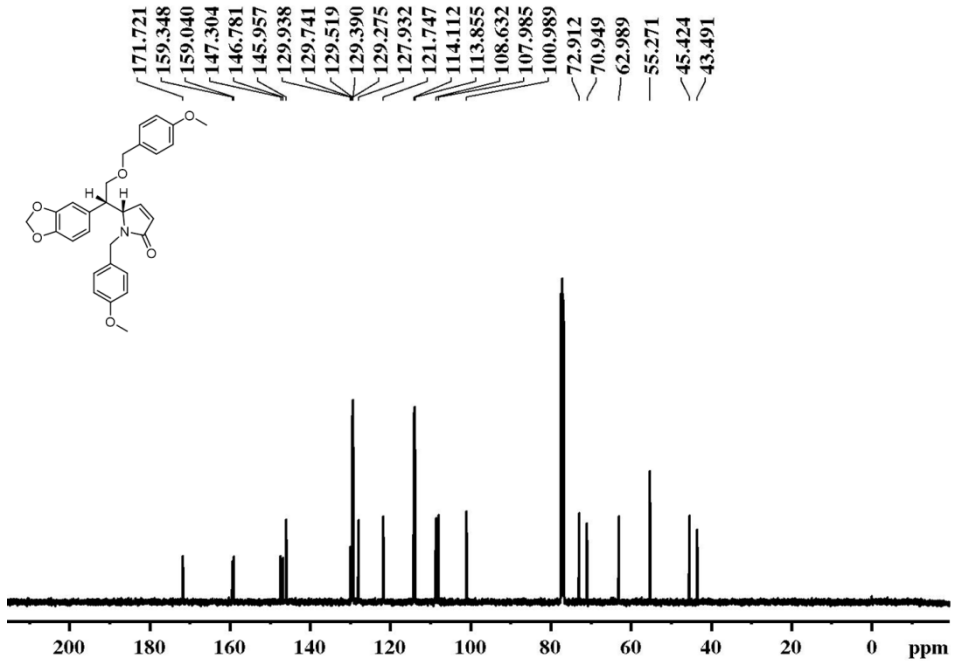
^{1}H NMR of Compound **9** in $CDCl_3$; 303K (400 MHz)



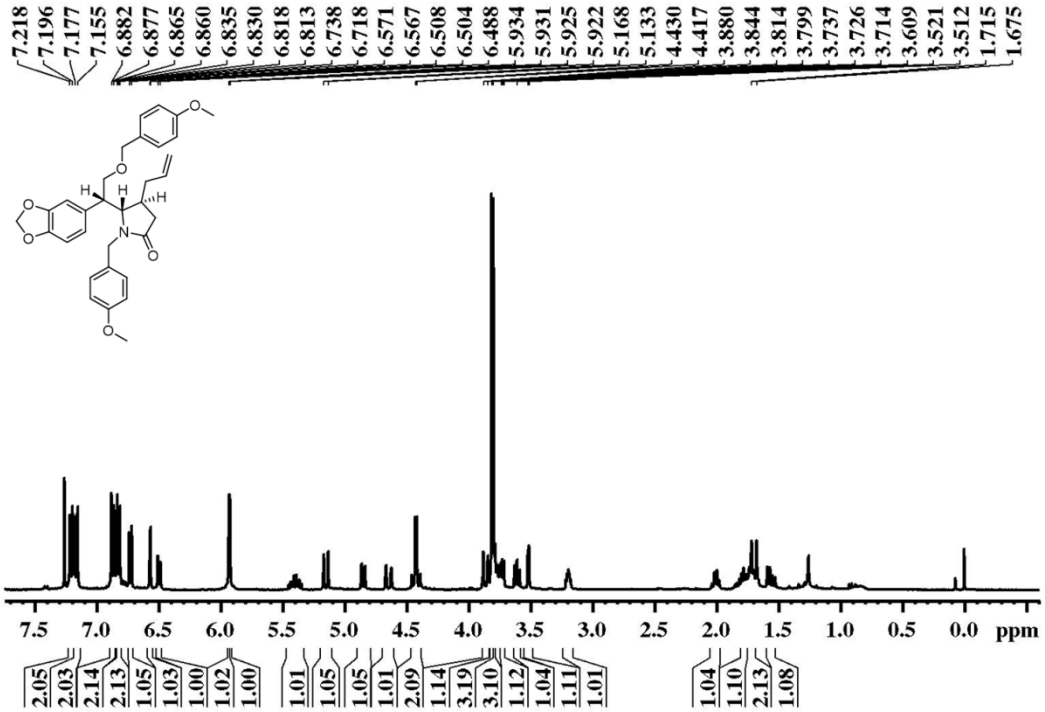
^{13}C NMR of Compound **9** in $CDCl_3$; 303K (100 MHz)



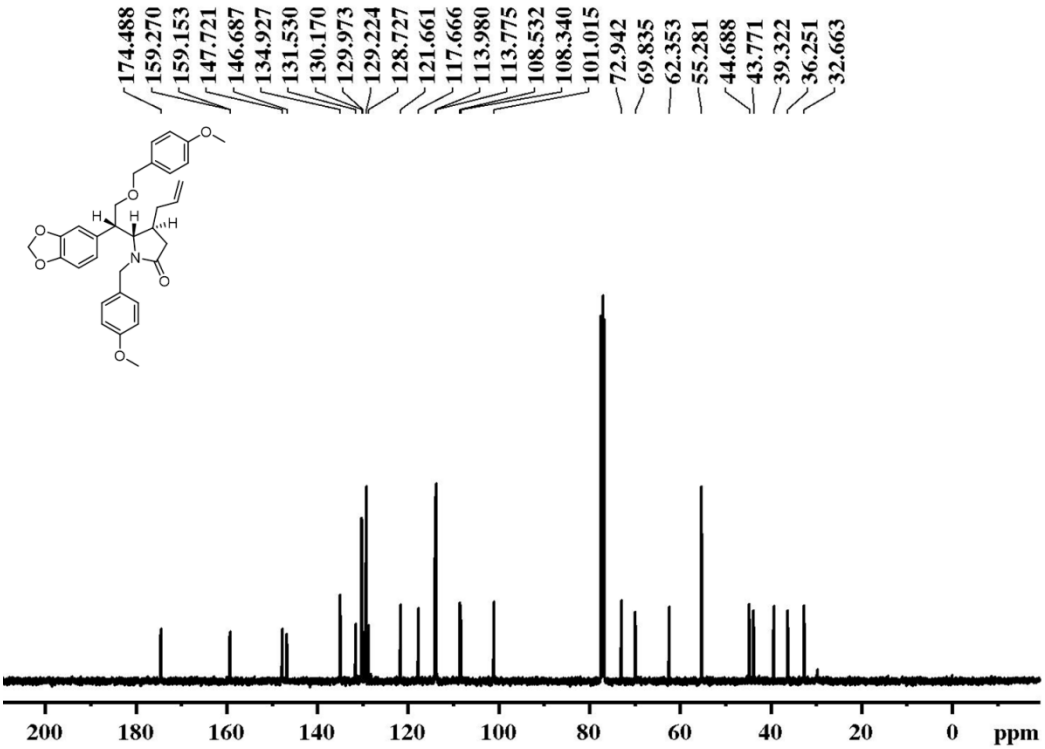
^{1}H NMR of Compound **11** in $CDCl_3$; 303K (400 MHz)



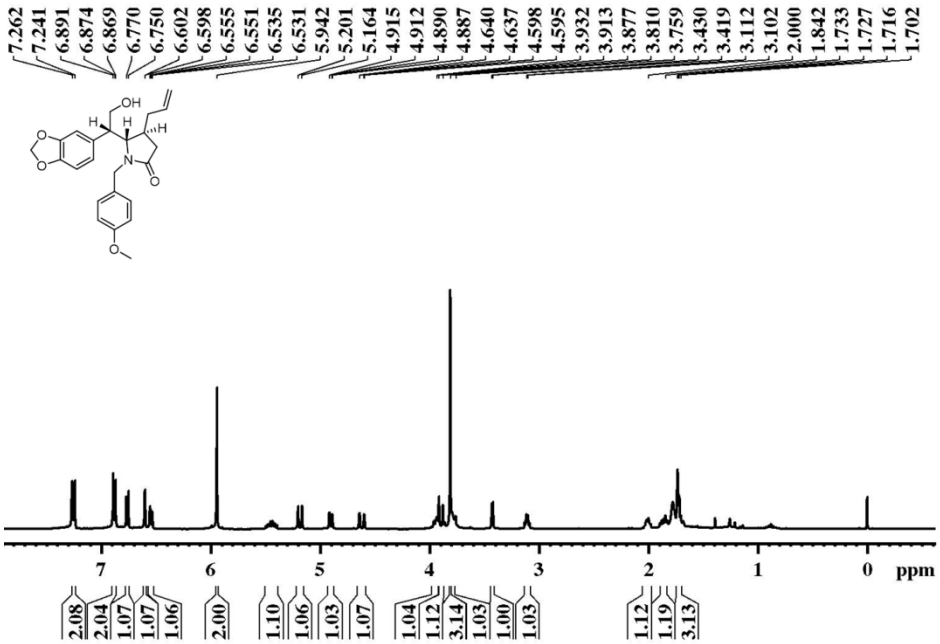
^{13}C NMR of Compound **11** in $CDCl_3$; 303K (100 MHz)



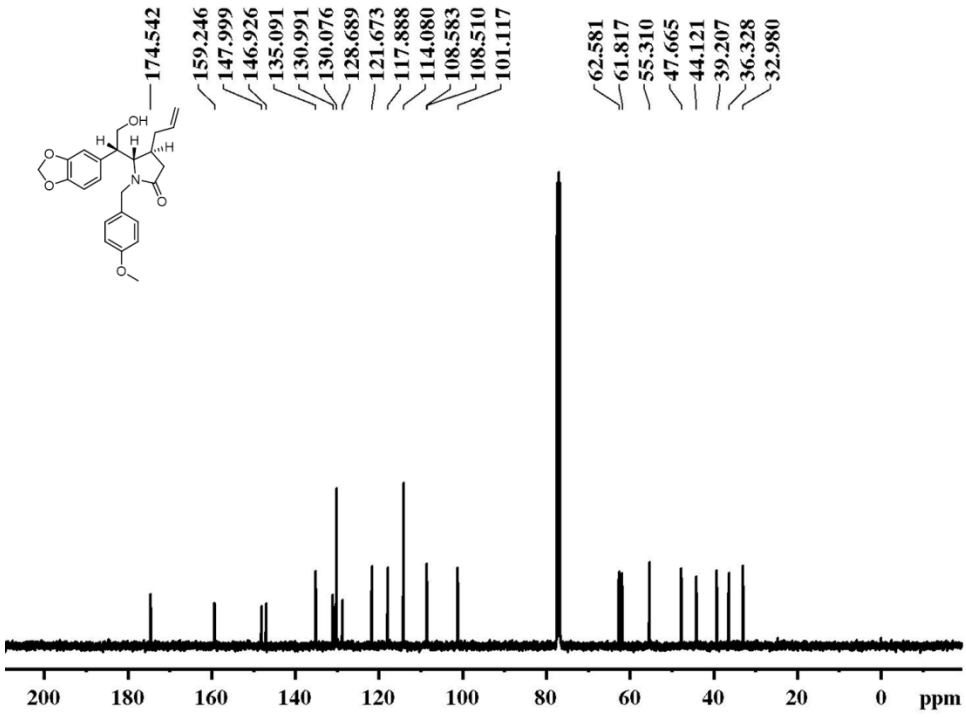
^{1}H NMR of Compound **13** in $CDCl_3$; 303K (400 MHz)



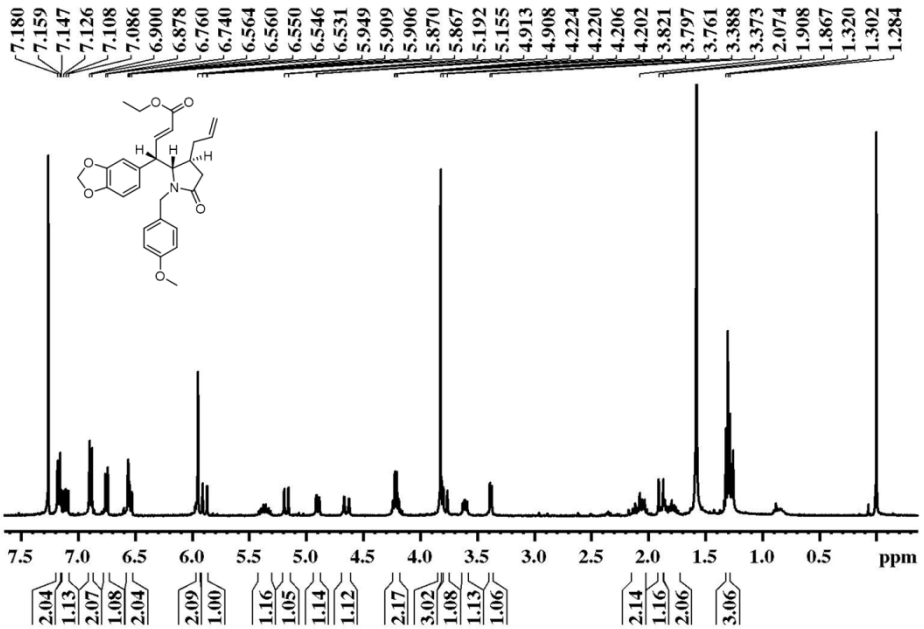
^{13}C NMR of Compound **13** in $CDCl_3$; 303K (100 MHz)



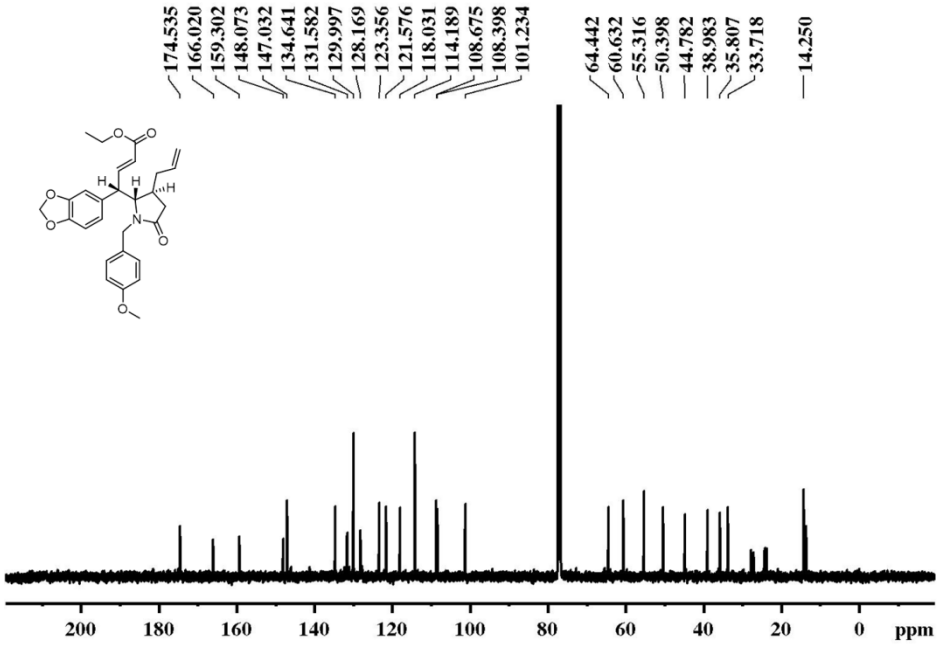
^{1}H NMR of Compound **14** in $CDCl_3$; 303K (400 MHz)



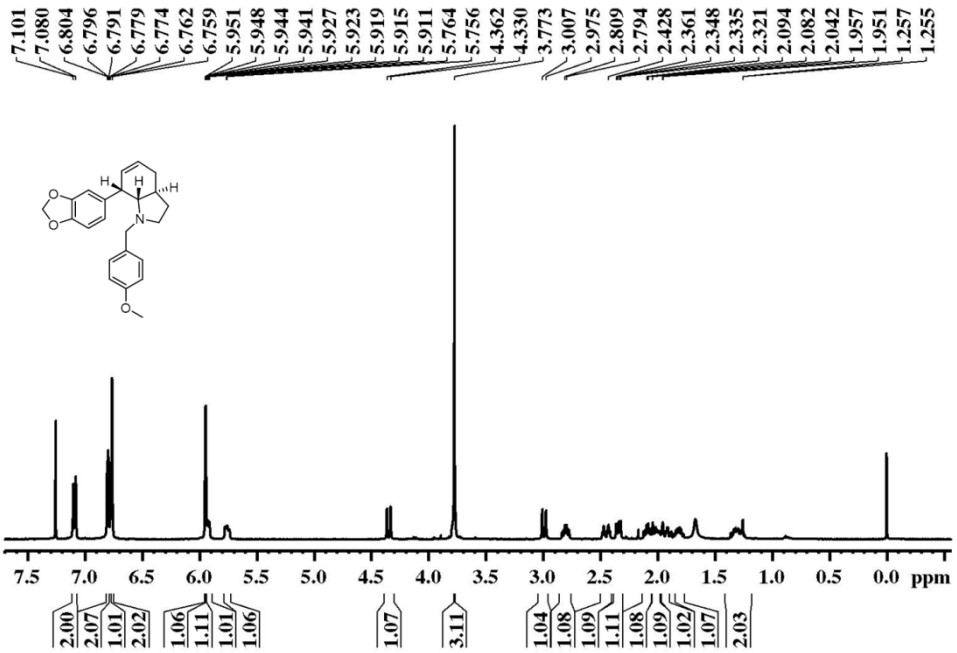
^{13}C NMR of Compound **14** in $CDCl_3$; 303K (100 MHz)



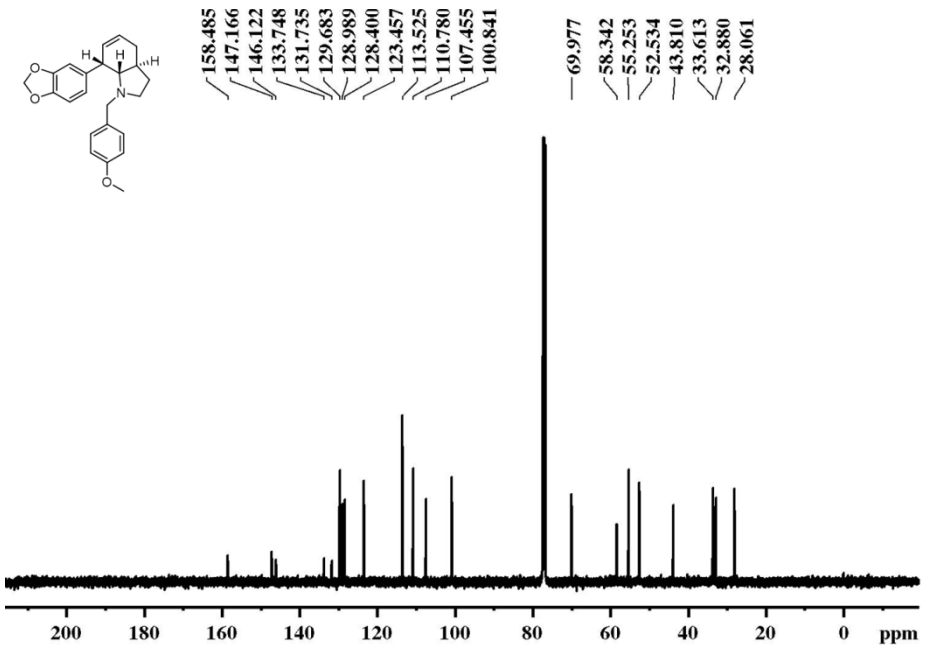
^{1}H NMR of Compound **15** in $CDCl_3$; 303K (400 MHz)



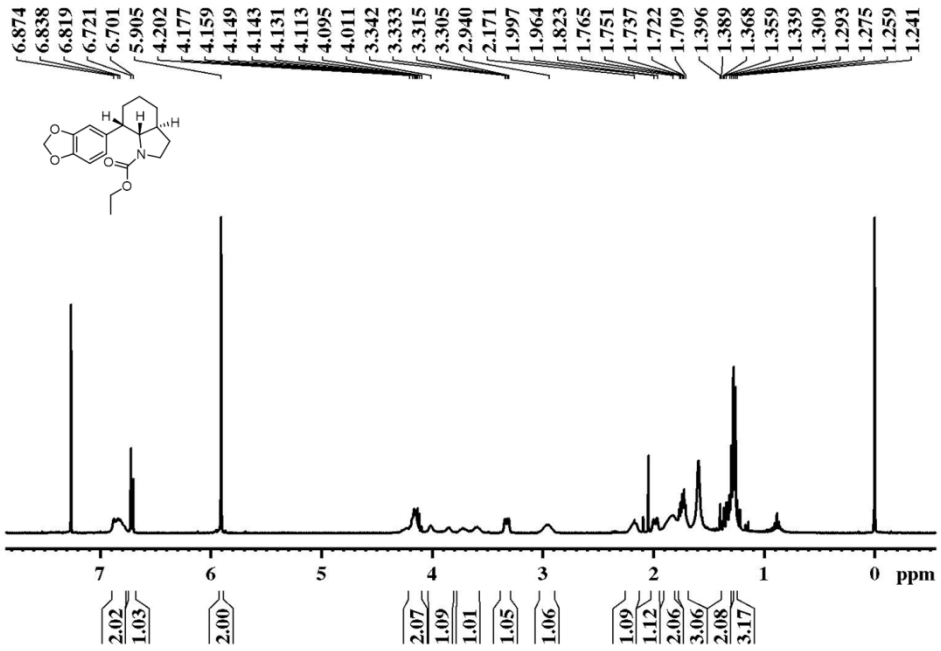
^{13}C NMR of Compound **15** in $CDCl_3$; 303K (100 MHz)



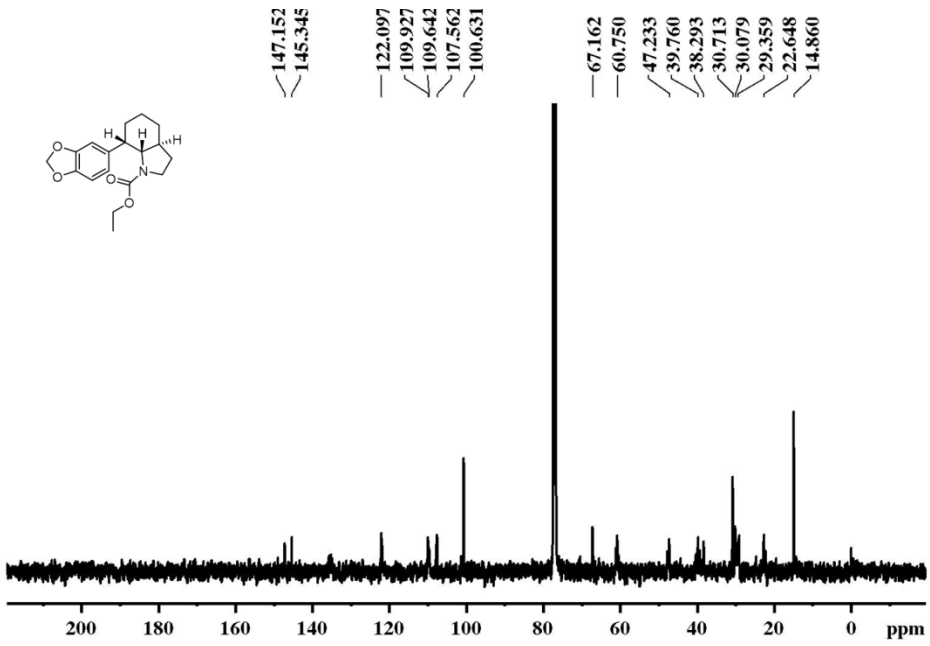
^{1}H NMR of Compound **17** in $CDCl_3$; 303K (400 MHz)



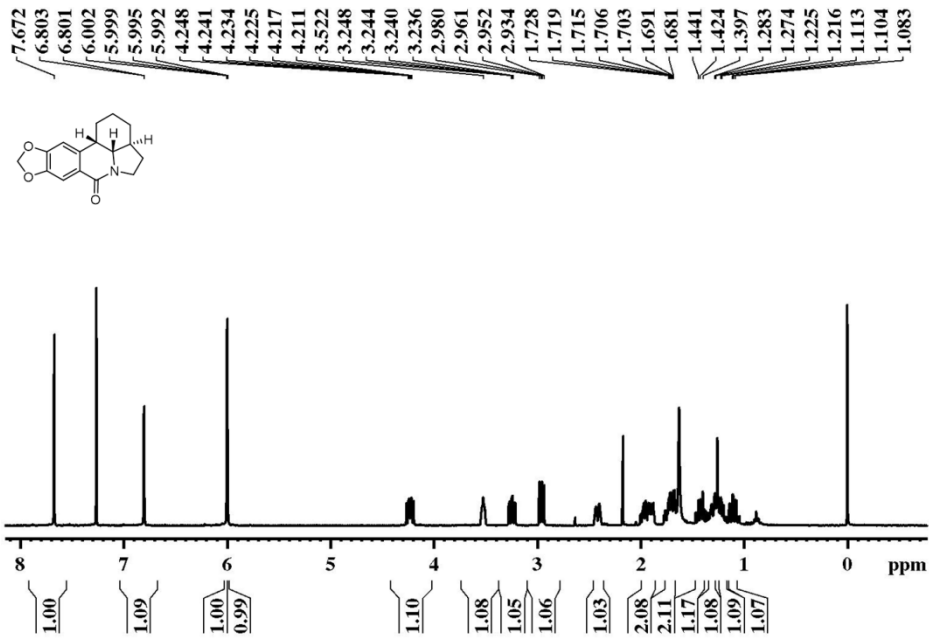
^{13}C NMR of Compound **17** in $CDCl_3$; 303K (100 MHz)



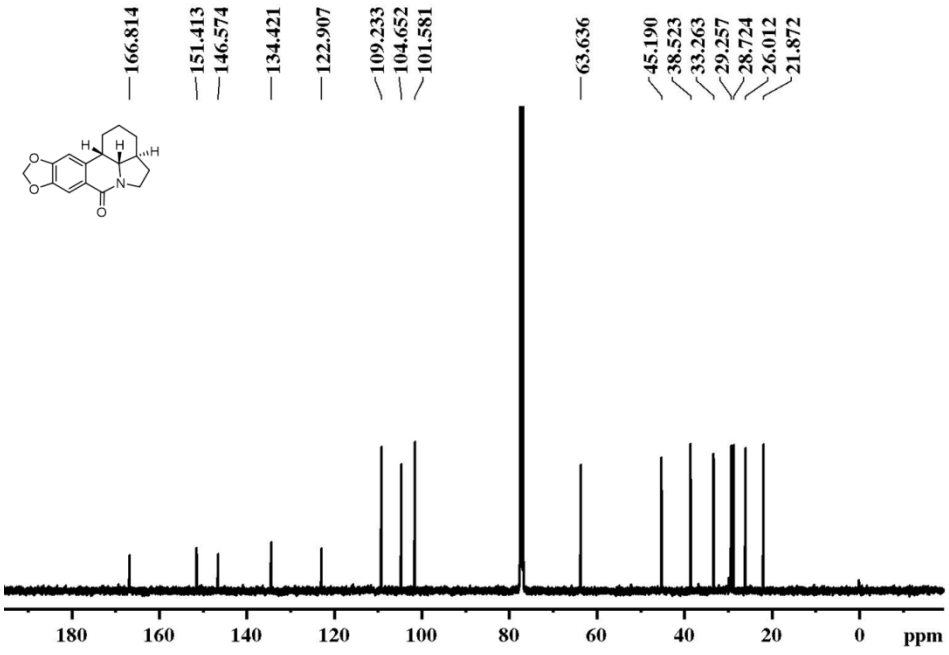
^{1}H NMR of Compound **18** in $CDCl_3$; 303K (400 MHz)



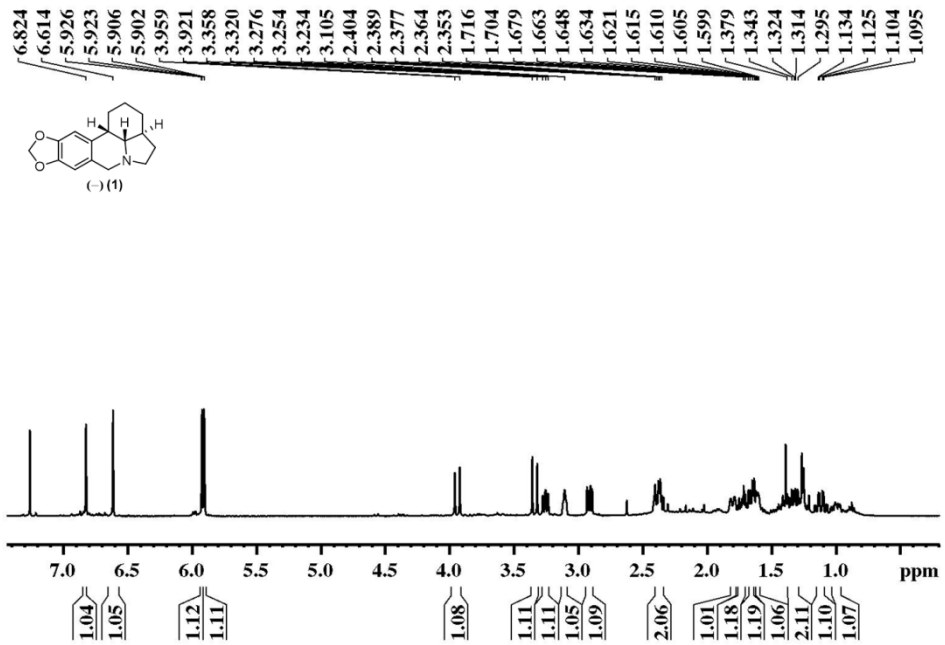
^{13}C NMR of Compound **18** in $CDCl_3$; 303K (100 MHz)



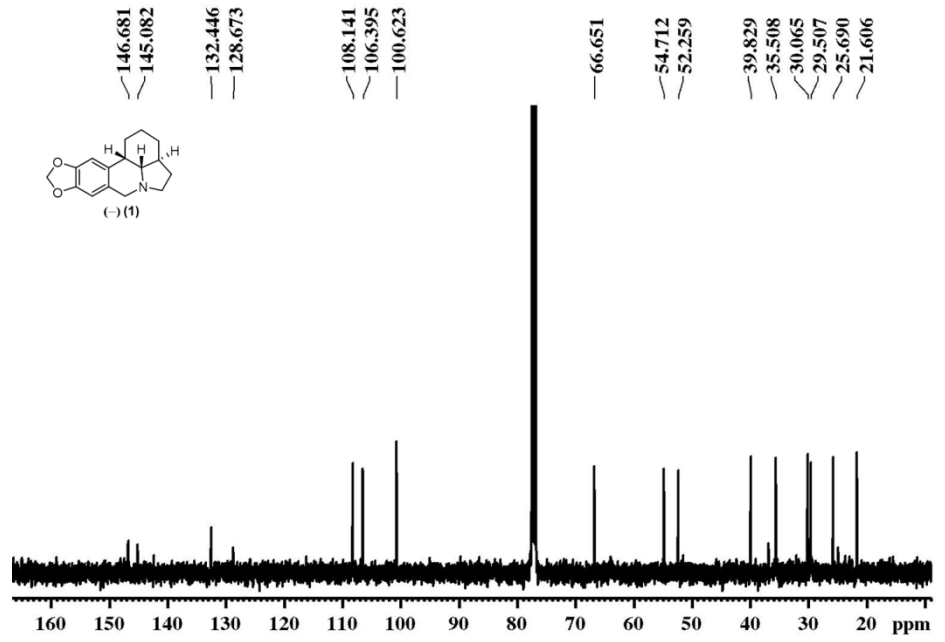
^{1}H NMR of Compound **19** in $CDCl_3$; 303K (400 MHz)



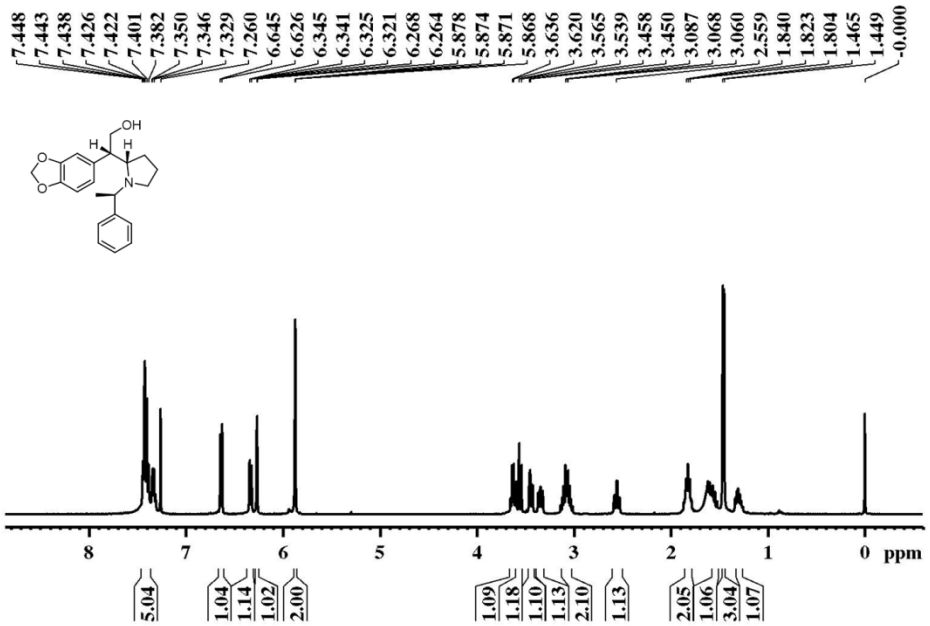
^{13}C NMR of Compound **19** in $CDCl_3$; 303K (100 MHz)



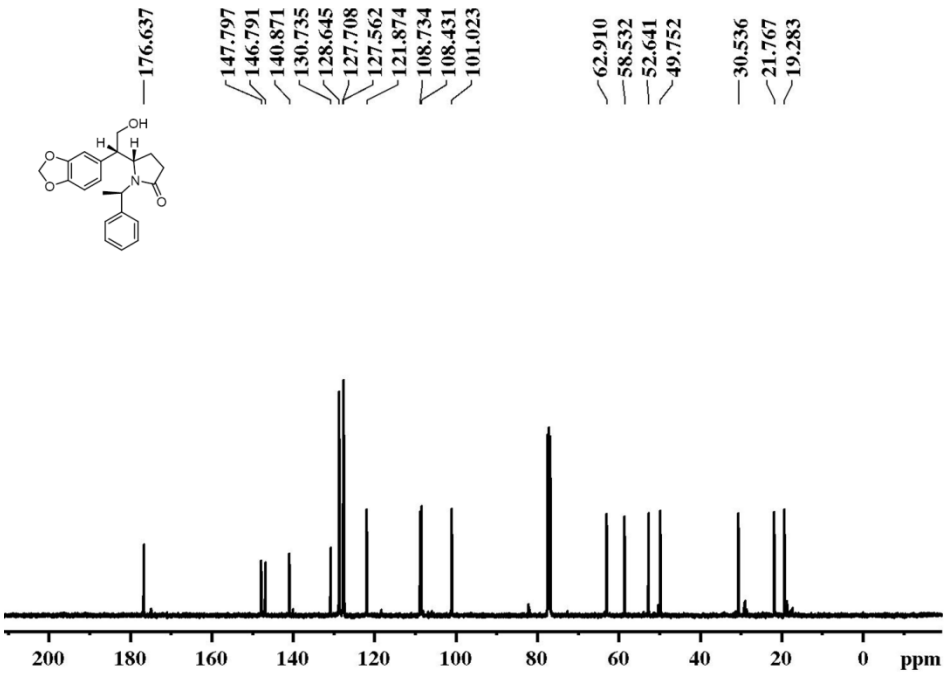
^{1}H NMR of Compound **(-)-1** in $CDCl_3$; 303K (400 MHz)



^{13}C NMR of Compound **(-)-1** in $CDCl_3$; 303K (100 MHz)



^{1}H NMR of Compound **8b'** in $CDCl_3$; 303K (400 MHz)



^{13}C NMR of Compound **8b'** in $CDCl_3$; 303K (100 MHz)

5. 2D-NMR analysis & spectra

(i) 2D-NMR of compound 19

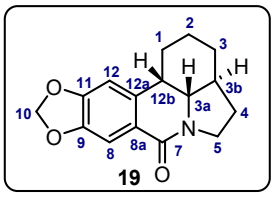
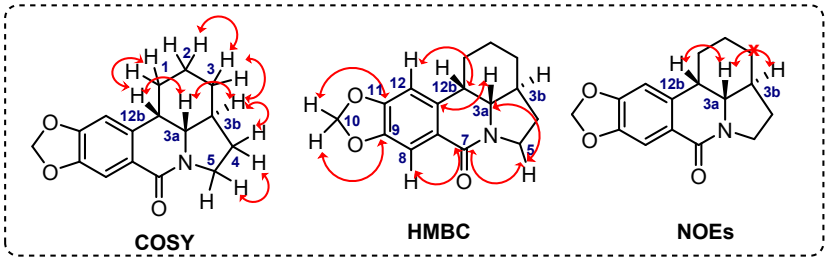
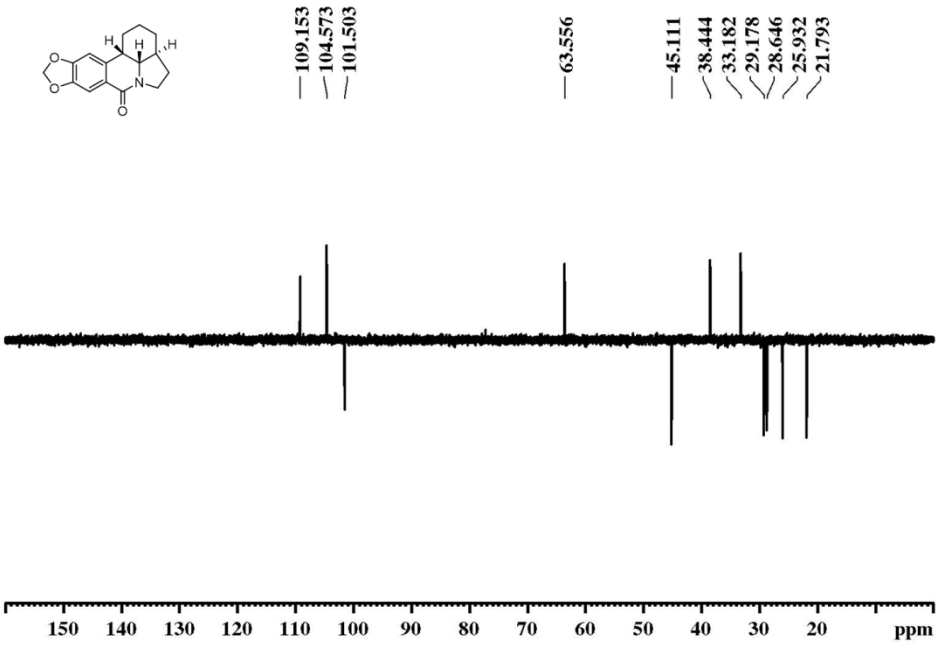


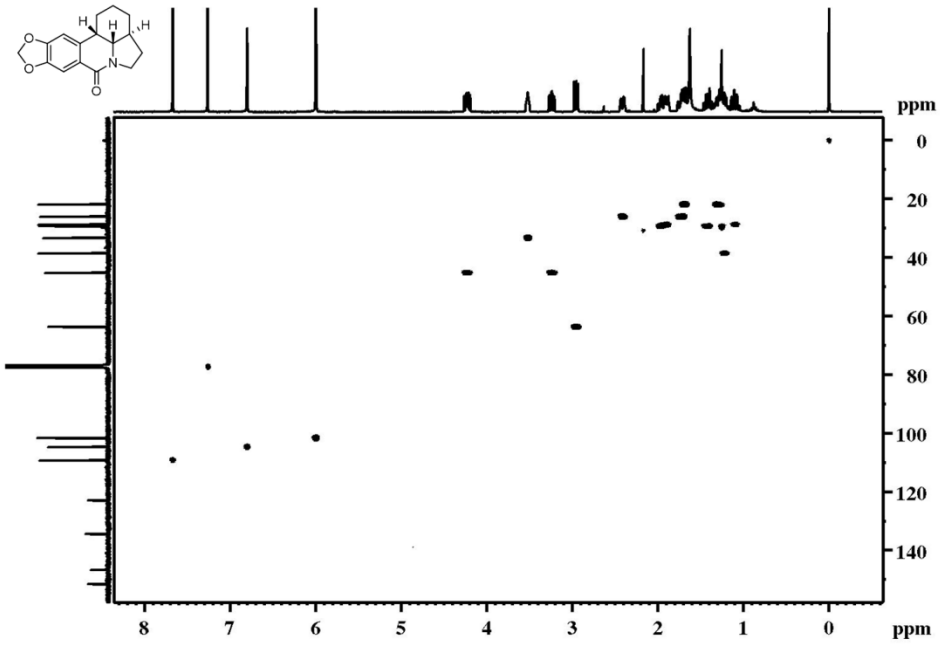
Table 1: Chemical Shifts (δ in ppm) and coupling constant values (*J* in Hz) for **19** in $CDCl_3$, 303K (400 MHz):

Position	Atoms	^{1}H	^{13}C	Important correlations
1	CH_2	2.37-2.46, m, 1H 1.64-1.78, m, 1H	26.01	• In HMBC, H_{12} proton shows relationship with C_{12b}, C_{8a}, C_{11}, C_9, and weak relationship with C_8 & C_7. H_{10} protons with C_9 & C_{11}. H_8 proton shows relationship with C_{12a}, C_9, & C_7. H_{3a} with C_7, C_{12a}. H_5 with C_7, C_4, C_{3a}, C_{3b}. • In COSY, H_{12b} shows relationship with H_{3a} & H_1 protons, H_{3a} proton with H_{12b} & H_{3b}, H_{3b} with H_4, H_3, H_{3a} and H_5 with H_4. H_1& H_3 shows relationship with H_2. • In NOEs, H_{12b} proton shows NOEs relationship with H_{3a}.
2	CH_2	1.64-1.78, m, 1H 1.26-1.34, m, 1H	21.87	
3	CH_2	1.86-1.93, m, 1H 1.06-1.14, m, 1H	28.72	
3a	CH	2.95, dd, *J* = 7.4, 11.1 Hz, 1H	63.64	
3b	CH	1.16-1.23, m, 1H	38.52	
4	CH_2	1.93-2.01, m, 1H 1.35-1.47, m, 1H	29.26	
5	CH_2	4.18-4.29, m, 1H 3.19-3.29, m, 1H	45.19	
8	CH	7.67, s, 1H	109.23	
10	CH_2	5.99, q, *J* = 1.3 Hz, 2H	101.50	
12	CH	6.8, d, *J* = 0.8 Hz, 1H	104.65	
12b	CH	3.48-3.55, m, 1H	33.26	
Chemical shift (other carbons): 166.81(C_7), 122.91(C_{8a}), 146.57(C_9), 151.41(C_{11}), 134.42(C_{12a}).				

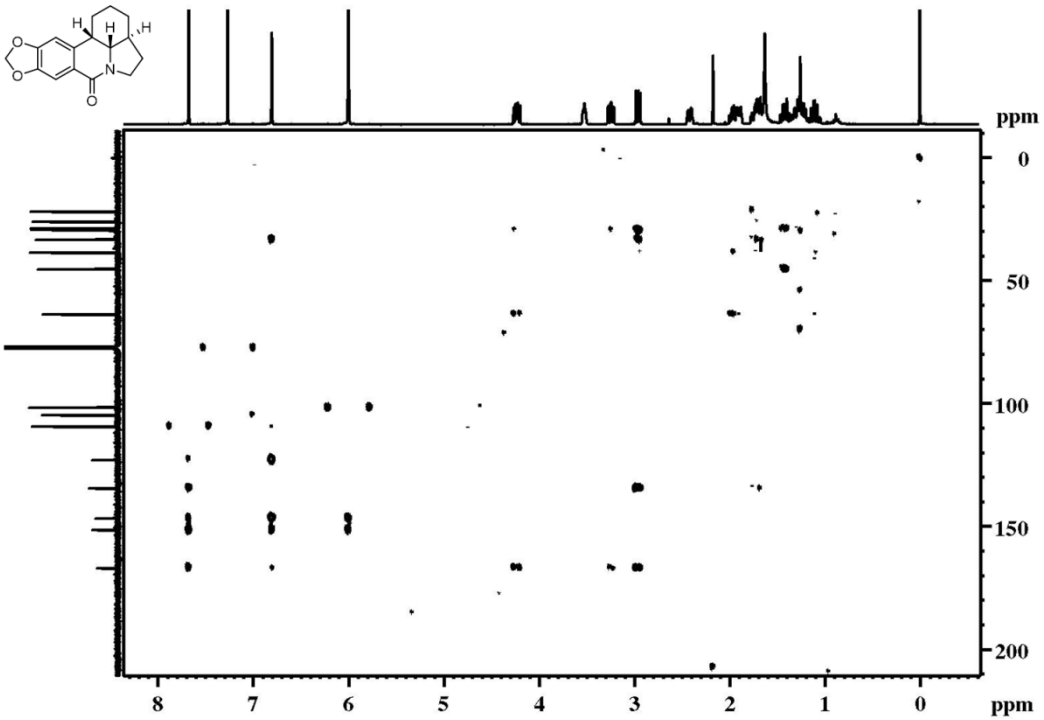




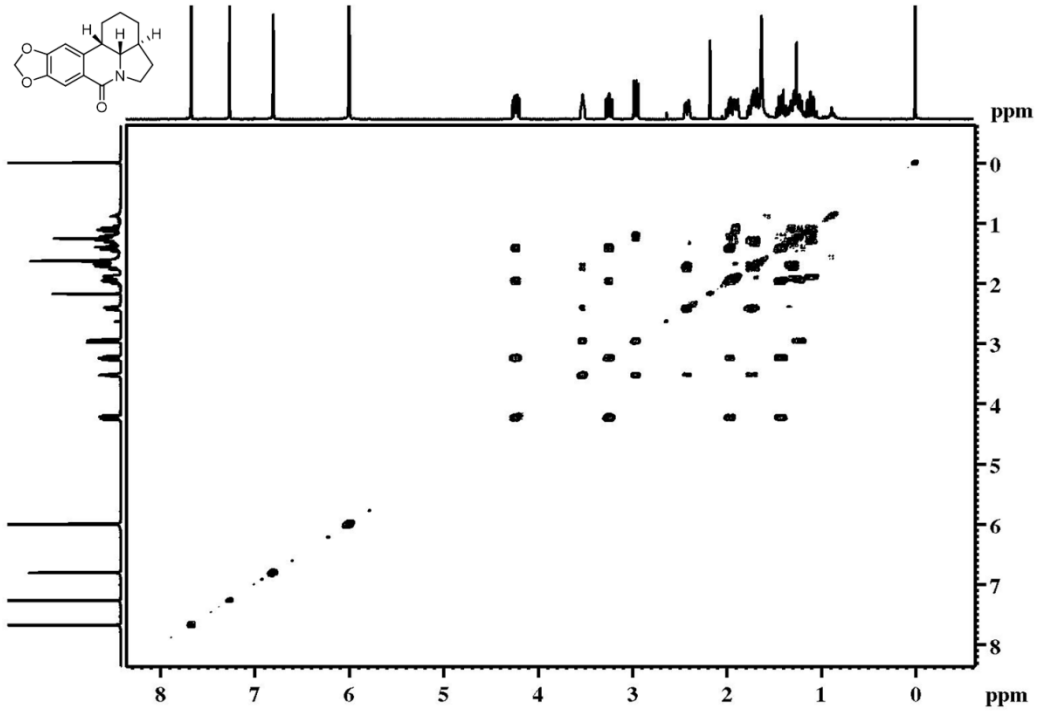
^{13}C DEPT 135 NMR spectrum of **19** in $CDCl_3$; 303K (100 MHz)



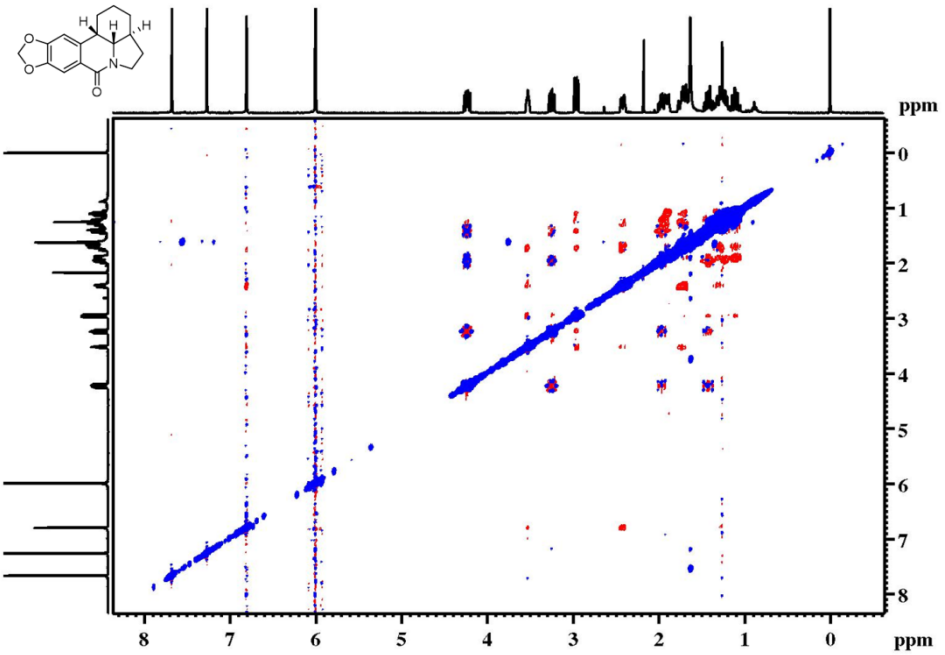
2D ^{1}H-^{13}C HSQC NMR spectrum of **19** in $CDCl_3$; 303K (400 MHz)



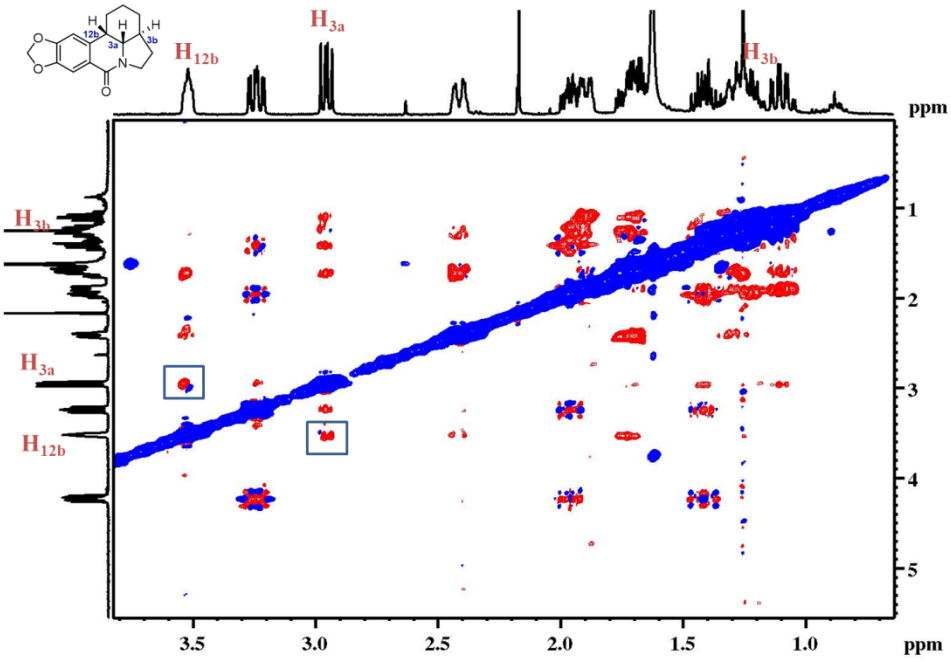
2D ^{1}H-^{13}C HMBC NMR spectrum of **19** in $CDCl_3$; 303K (400 MHz)



2D ^{1}H-^{1}H COSY NMR spectrum of **19** in $CDCl_3$; 303K (400 MHz)



2D ^{1}H-^{1}H NOEs NMR spectrum of **19** in $CDCl_3$; 303K (400MHz)



2D ^{1}H-^{1}H NOEs NMR spectrum of **19** in $CDCl_3$; 303K (400MHz)

(i) 2D-NMR of compound (-)-1

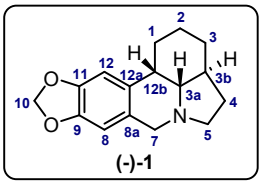
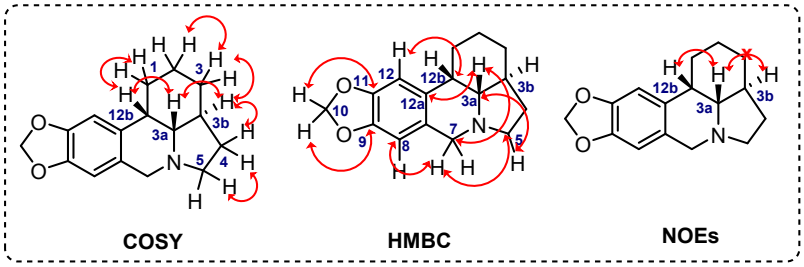
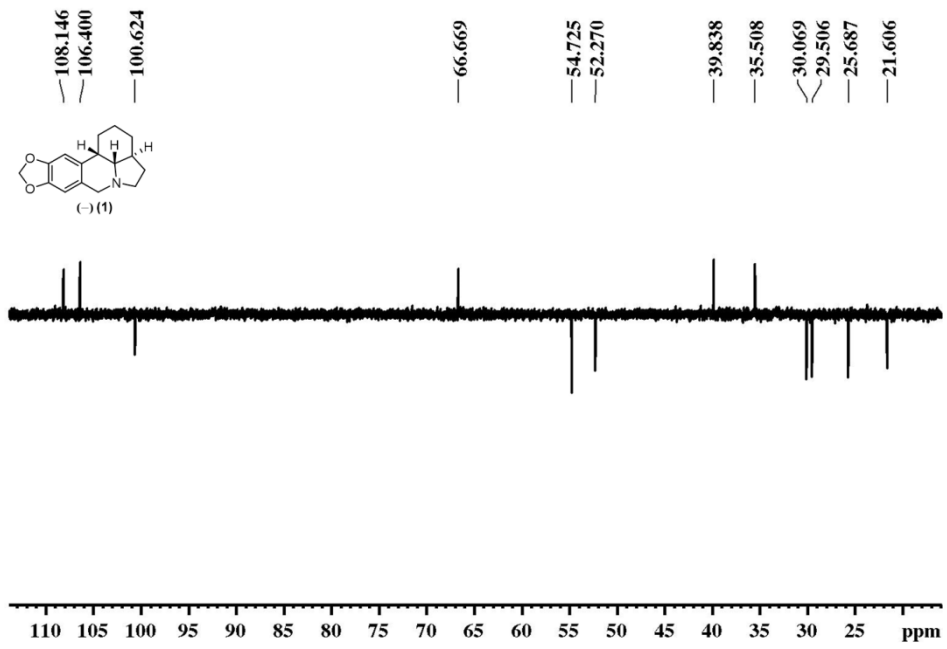


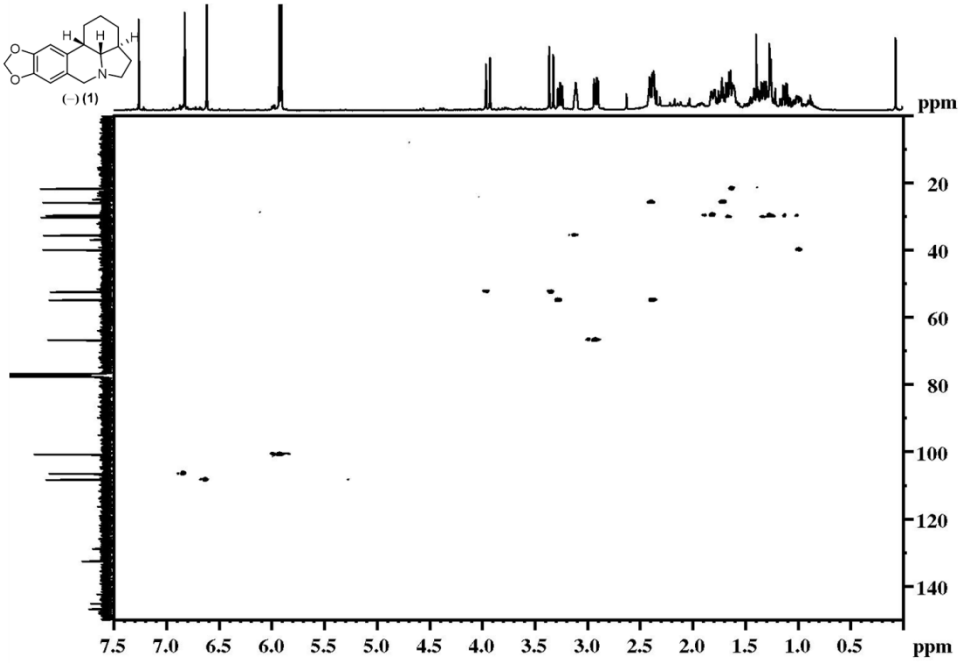
Table 1: Chemical Shifts (δ in ppm) and coupling constant values (*J* in Hz) for **(-)-1** in $CDCl_3$, 303K (400 MHz):

Position	Atoms	^{1}H	^{13}C	Important correlations
1	CH_2	1.71-1.76, m, 1H 2.33-2.40, m, 1H	25.69	• In HMBC, H_{12} proton shows relationship with C_{12b}, C_{8a}, C_9. H_{10} proton shows relationship with C_{11}, & C_9. H_8 proton shows relationship with C_{12a}, C_{11}, & C_7. H_{3a} with C_{12a}. H_5 with C_{3a}, C_{3b}, H_7 with C_5, C_8, C_{8a}, C_{3a}, C_{12a}. • In COSY, H_{12b} shows relationship with H_{3a} & H_1 protons, H_{3a} proton with H_{12b} & H_{3b}, H_{3b} with H_4, H_3, H_{3a} and H_5 with H_4. H_1& H_3 shows relationship with H_2. • In NOEs, H_{12b} proton shows NOEs relationship with H_{3a}.
2	CH_2	1.78-1.81, m, 1H 1.07-1.12, m, 1H	21.60	
3	CH_2	1.27-1.37, m, 1H 1.62-1.68, m, 1H	29.51	
3a	CH	2.91, dd, *J* = 5.2, 10.8 Hz, 1H	66.65	
3b	CH	0.96-1.03, m, 1H	39.83	
4	CH_2	1.27-1.37, m, 1H 1.59-1.61, m, 1H	30.06	
5	CH_2	3.25, t, *J* = 8.3 Hz, 1H 2.33-2.40, m, 1H	54.71	
7	CH_2	3.94, d, *J* = 15.2 Hz, 1H 3.34, d, *J* = 15.2 Hz, 1H	52.25	
8	CH	6.61, s, 1H	108.14	
10	CH_2	5.91, dd, *J* = 1.4, 8.2 Hz, 2H	100.62	
12	CH	6.82, s, 1H	106.39	
12b	CH	3.11, t, *J* = 5.1 Hz, 1H	35.51	
Chemical shift (other carbons): 128.67(C_{8a}), 145.08(C_9), 146.68(C_{11}), 132.45 (C_{12a}).				

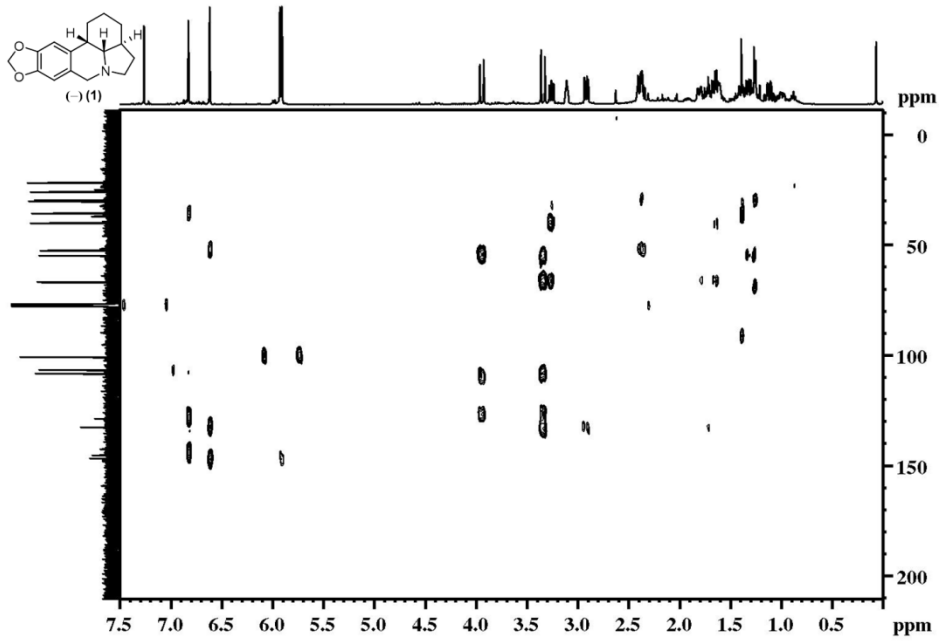




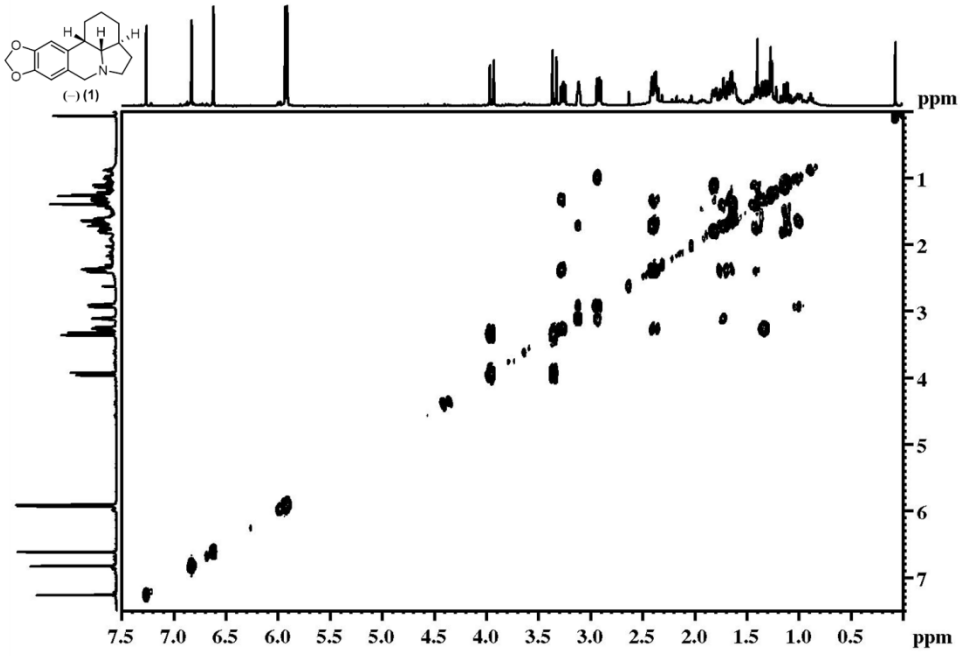
^{13}C DEPT 135 NMR spectrum of **(-)-1** in $CDCl_3$; 303K (100 MHz)



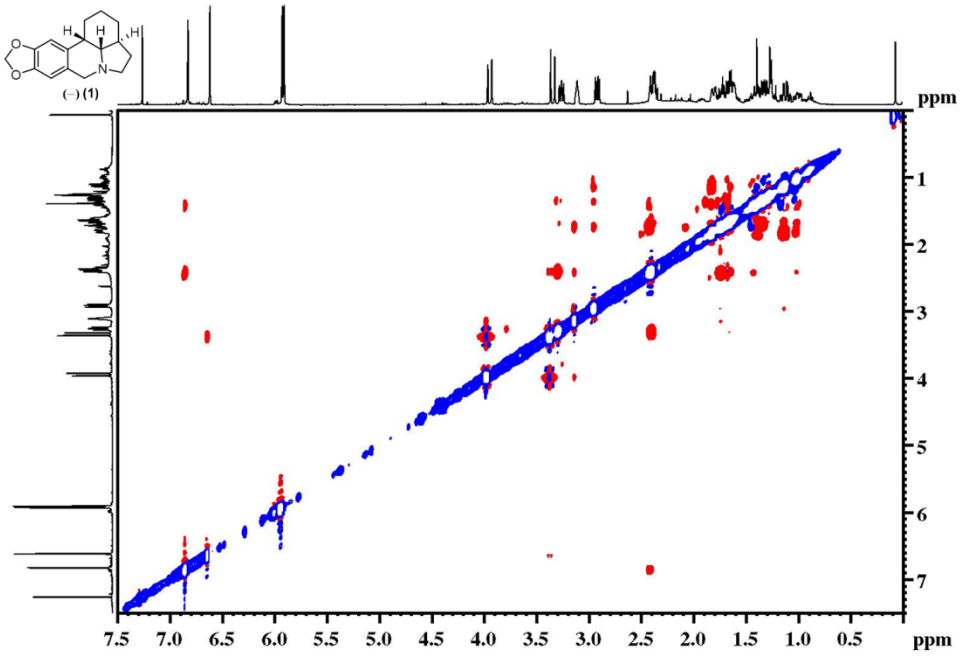
2D ^{1}H-^{13}C HSQC NMR spectrum of **(-)-1** in $CDCl_3$; 303K (400 MHz)



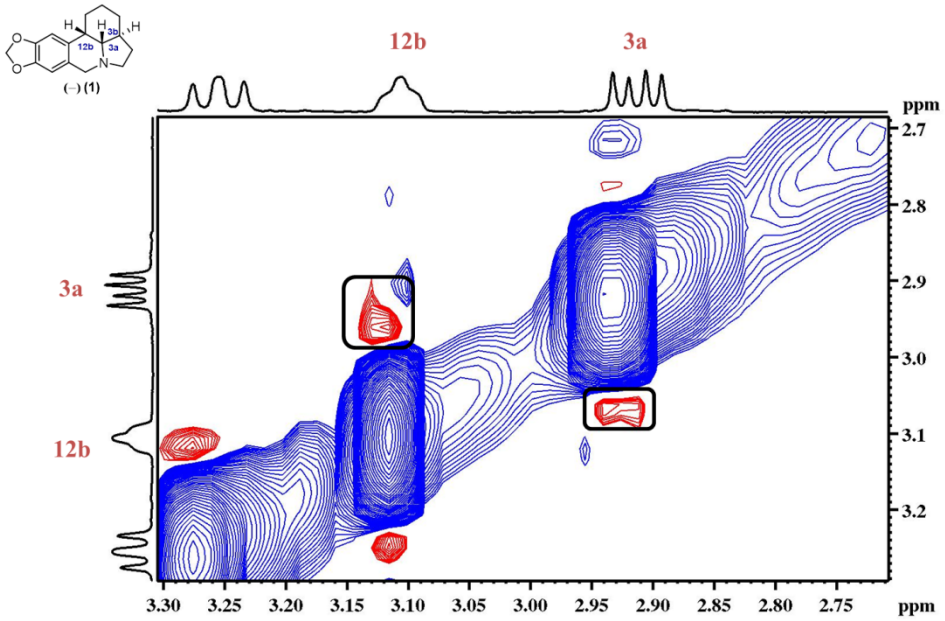
2D ^{1}H-^{13}C HMBC NMR spectrum of **(-)-1** in $CDCl_3$; 303K (400 MHz)



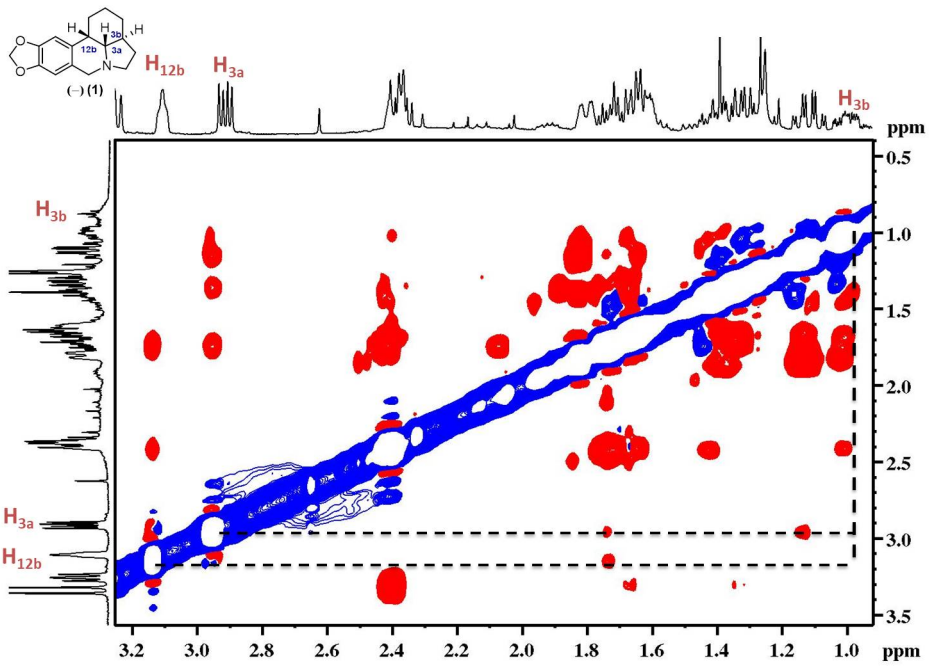
2D ^{1}H-^{1}H COSY NMR spectrum of **(-)-1** in $CDCl_3$; 303K (400 MHz)



2D ^{1}H-^{1}H NOEs NMR spectrum of **(-)-1** in $CDCl_3$; 303K (400MHz)



2D ^{1}H-^{1}H NOEs NMR spectrum of **(-)-1** in $CDCl_3$; 303K (400MHz)



2D ^{1}H-^{1}H NOEs NMR spectrum of **(-)-1** in $CDCl_3$; 303K (400MHz)

6. X-Ray Crystallographic Data

Crystallographic summary of compound 8b', in figure 1 and table 1

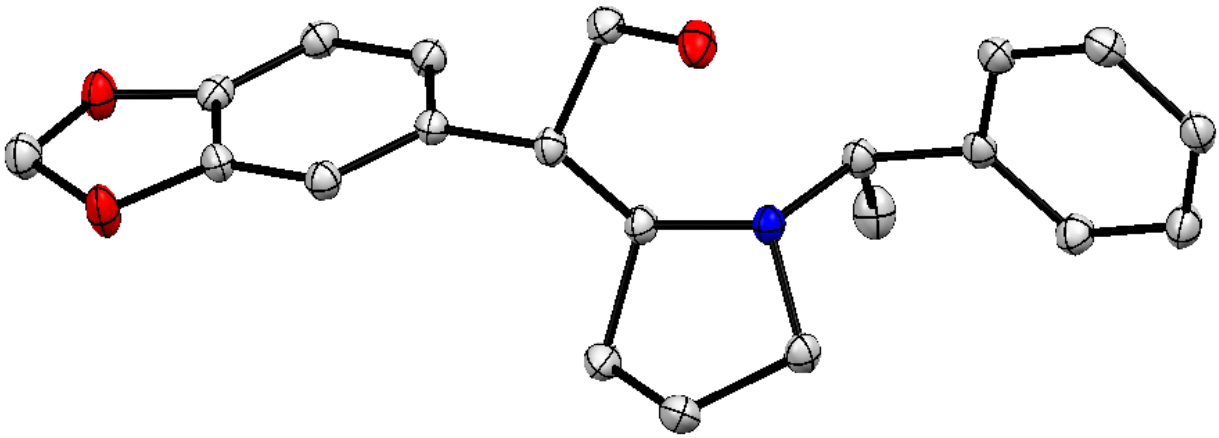


Figure1. ORTEP diagram drawn with 50% ellipsoid probability for non-H atoms of the crystal Structure of compound **8b'** determined at 423 K.

Crystallization: Crystals of compound **8b',** was grown from the solvent 30% (Ethyl acetate/Hexane) by slow evaporation method.

X-Ray Data Collection and Structure Refinement Details:

A good quality single crystal of size 0.35 x 0.30 x 0.20 mm was selected under a polarizing microscope and was mounted on a glass fiber for data collection. Single crystal X-ray data for compound **8b'**, was collected on a CCD Bruker SMART APEX-II 3 circle diffractometer equipped with the APEX2 goniometer. Single crystal X-ray diffraction data were collected on a Bruker D8 Quest diffractometer equipped with a PHOTON II CPAD detector and an Oxford Cryostream 800 Series cryostat. Multilayer monochromators with Mo/Kα radiation (λ = 0.71073 Å) from Incoatec IμS microsources were used. Data reduction was carried out by means of standard procedures using the Bruker software package SAINT[7]. Absorption corrections and the 4correction of other systematic errors were performed using SADABS.[8] The structures were solved by direct methods using SHELXT[9] and refined using SHELXL-2018.3.[10] Hydrogen atoms were placed in calculated positions using riding models.

Table 1. X-ray crystallographic data for compound (**A**).

Compound	**8b'**
Empirical formula	$C_{21}\ H_{26}\ N\ O_3$
Formula weight	340.43
Crystal System	Triclinic
Space group	*P 1*
a (Å)	5.8887(8)
b (Å)	8.3187(12)
c (Å)	9.4843(13)
α (°)	108.948(3)
β (°)	94.920(4)
γ (°)	93.497(4)
V (Å^3)	435.86(11)
Z	1
D_c (g/cm^3)	1.2969

[7] Herbert, S. A.; Janiak, A.; Thallapally, P. K.; Atwood, J. L.; Barbour, L. J. *Chem. Commun*., **2014**, *50*, 15509-15512.

[8] Dawson, A.; Allan, D. R.; Clark, S. J.; Parsons, S.; Ruf, M. *J. Appl. Crystallogr*. **2004**, *37*, 410.

[9] Sheldrick, G. M. Acta Crystallogr., *Sect. A* **2008**, *64*, 112–122.

[10] Sheldrick, G. M. Acta Crystallogr., *Sect. C: Struct. Chem.* **2015**, *71*, 3−8.

F_{000}	183.0889
Temperature (K)	423.15
Radiation (λ,Å)	0.71073
θ_{max} (°)	28.40
Total reflections	4263
Unique reflections	3925
Reflections [$I > 2\sigma(I)$]	4263
Parameters	228
R_{int}	0.0428
Goodness-of-fit	1.0500
R [$F^2 > 2\sigma(F^2)$]	0.0490
wR (F^2, all data)	0.1025
CCDC No.	**2210096**