Synthesis of (-)-Uniflorine A, (+)-Casuarine, (+)-Australine, (-)-3-*Epi*-australine and (-)-3,7-*Diepi*-australine

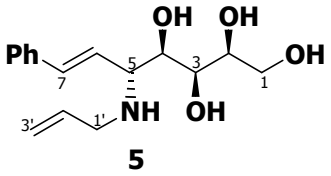
Thunwadee Ritthiwigrom, Anthony C. Willis and Stephen G. Pyne

SUPPORTING INFORMATION

1. Davis, A. S.; Pyne, S. G.; Skelton, B. W.; White, A. H., *J. Org. Chem.* **2004,** *69*, 3139-3143.

General methods: All IR spectra were run as neat samples. NMR assignments were made on the basis of COSY, DEPT, HSQC and sometimes HMBC experiments. In the case of epoxide compounds NMR assignments are given based on the numbering system of the parent pyrrolidine, pyrrolizine or indolizine and not the systematic numbering. Petrol refers to the hydrocarbon fraction of bp 40-60 °C

(6*E*)-5-(Allylamino)-5,6,7-trideoxy-7-phenyl-D-*gluco*-hept-6-enitol (5).



5

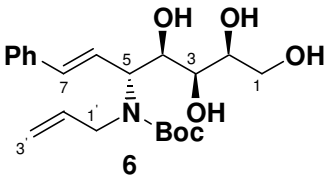
To a mixture of L-xylose (11.00 g, 73.3 mmol) and *trans*-2-phenylvinyl boronic acid (11.93 g, 80.6 mmol) was added absolute ethanol (110 mL) and allylamine (6.05 mL, 80.6 mmol). The reaction mixture was stirred at rt for 3 days, followed by the evaporation of all volatiles *in vacuo*. The residue was dissolved in 1 M HCl (*ca* 20 mL), applied to a column of DOWEX resin (H^+ form, 150 mL) and washed with distilled H_2O (2 L). The product was eluted with 7 M NH_4OH (2 L) and 14 M NH_4OH (2 L). The fractions containing the product were combined and concentrated to a brown foamy solid (19.78 g, 92%).

$[\alpha]_D^{25}$ +27 (*c* 0.06, MeOH).

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported earlier.[1]

1. Davis, A. S.; Pyne, S. G.; Skelton, B. W.; White, A. H., *J. Org. Chem.* **2004,** *69*, 3139-3143.

***tert*-Butyl allyl((2*S*,3*S*,4*R*,5*R*,*E*)-1,2,3,4-tetrahydroxy-7-phenylpent-6-en-5-yl)carbamate (6).**



6

To a solution of **5** (21.49 g, 73.34 mmol) in anhydrous MeOH (300 mL) was added anhydrous Et_3N (20.45 mL, 14.67 mmol) and di-*tert*-butyl-dicarbonate (47.44 g, 16.87 mmol). The reaction mixture was stirred at rt under an atmosphere of N_2 for 3

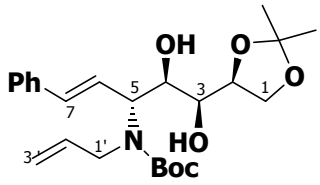
days, followed by the evaporation of all volatiles *in vacuo*. The residue was purified by flash column chromatography (FCC) (80:20 to 100:0 EtOAc/petrol and then 20:80 MeOH/EtOAc) to give a brown oil (23.1 g, 80%).

$[\alpha]_D^{25}$ -50 (*c* 3.0, $CHCl_3$).

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported earlier.[1]

1. Davis, A. S.; Pyne, S. G.; Skelton, B. W.; White, A. H., *J. Org. Chem.* **2004,** *69*, 3139-3143.

tert-Butyl allyl((2*S*,3*S*,4*R*,5*R*,*E*)-1,2-*O*-(1-methylethylidene)-3,4-dihydroxy-7-phenylpent-6-en-5-yl)carbamate (7).



7

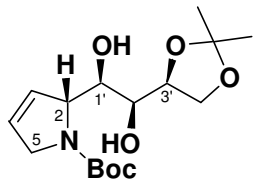
To a solution of **6** (4.957 g, 12.61 mmol) in anhydrous acetone (70 mL) was added 2,2-dimethoxypropane (1.86 mL, 15.13 mmol) and pyridinium *p*-toluenesulfonate (0.317 g, 1.261 mmol). The reaction mixture was stirred under an atmosphere of N_2 for 22 h, followed by the evaporation of all volatiles *in vacuo* to give a brown oil. The residue was purified by FCC (30:70 to 50:50 EtOAc/petrol) to give **7** (3.485 g, 64%) as a white solid, foamy solid. A small amount of another regioisomeric compound was also isolated (1.759 g, 19%). This compound was not further characterized.

$[\alpha]_D^{22}$ -36 (*c* 6.5, $CHCl_3$). [Lit.[2] for (+)-**7**; $[\alpha]_D^{23}$ +41 (*c* 10.1, $CHCl_3$)].

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported for (+)-**7**.[2]

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

(2*R*)-*tert*-Butyl 2-((1*R*,2*S*,3*S*)-1,2,3,4-tetrahydroxybutyl-3,4-*O*-(1-methylethylidene))-2,5-dihydro-1*H*-pyrrole-1-carboxylate (8).



8

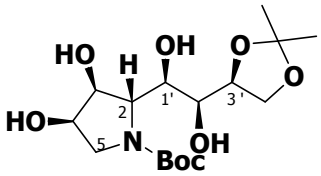
To a solution of **7** (5.553 g, 12.82 mmol) in anhydrous CH_2Cl_2 (260 mL) was added Grubbs' I catalyst (1.055 g, 1.282 mmol). The reaction mixture was stirred and heated at reflux for 18 h under an atmosphere of N_2 followed by the removal of all volatiles *in vacuo*. The residue was purified by FCC (50:50 to 70:30 EtOAc/petrol) to give **8** as a dark brown viscous oil (4.09 g, 97%).

$[\alpha]_D^{21}$ +125 (*c* 4.5, $CHCl_3$). [Lit.[2] for (-)-**8**; $[\alpha]_D^{22}$ -37 (*c* 5.75, $CHCl_3$)].

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported for (-)-**8**.[2]

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

(2*R*,3*S*,4*R*)-*tert*-Butyl 2-((1*R*,2*S*,3*S*)-1,2,3,4-tetrahydroxybutyl-3,4-*O*-(1-methylethylidene))-3,4-dihydroxypyrrolidine-1-carboxylate (9).



9

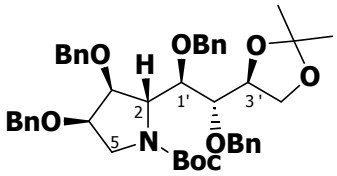
To a solution of **8** (4.00 g, 12.16 mmol) in acetone (60 mL) and water (60 mL) was added potassium osmate·dihydrate (223.7 mg, 0.608 mmol) and 4-morpholine-*N*-oxide (2.987 g, 25.53 mmol). The reaction mixture was stirred for 18 h at rt and evaporated to give a dark brown oil which was purified by FCC (100% EtOAc to 4:96 MeOH/EtOAc) to give **9** as a brown foamy solid (3.174 g, 72%).

$[\alpha]_D^{22}$ +32 (*c* 4.9, $CHCl_3$). [Lit.[2] for (-)-**9**; $[\alpha]_D^{22}$ -32 (*c* 4.8, $CHCl_3$).

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported for (-)-**9**.[2]

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

(2*R*,3*S*,4*R*)-*tert*-Butyl 3,4-bis(benzyloxy)-2-((1*R*,2*S*,3*S*)- 1,2-bis(benzyloxy)-3,4-*O*-(1-methylethylidene))- 3,4-dihydroxybutylpyrrolidine-1-carboxylate (10).



10

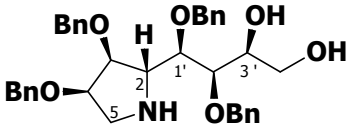
To a solution of **9** (3.077 g, 8.477 mmol) in dry THF (85 mL) was added *n*-Bu_4NI (313.1 mg, 0.848 mmol) and BnBr (8.07 mL, 67.81 mmol) follow by NaH (2.441 g, 50.86 mmol, 50 % in mineral oil) at 0 ^oC. After H_2 evolution had ceased (15 min) the reaction mixture was stirred at rt for 24 h. MeOH (50 mL) was then added followed by evaporation of all volatiles *in vacuo*. The residue was dissolved in EtOAc and filtered through celite, followed by further washings of the solids with EtOAc. The solvent was evaporated and the residue was purified by FCC (10:90 to 15:85 EtOAc/petrol) to give **10** as a pale yellow syrup (5.89 g, 96%).

$[\alpha]_D^{23}$ -50 (*c* 5.4, $CHCl_3$). [Lit.[2] for (+)-**10**; $[\alpha]_D^{23}$ +45 (*c* 4.26, $CHCl_3$).

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported for (+)-**10**.[2]

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

1-[(2*S*,3*R*,4*R*)-3,4-Bisbenzyloxy-2-pyrrolidinyl]-(1*R*,2*S*,3*R*)-1,2-dibenzyloxy-butane-3,4-diol (11).



11

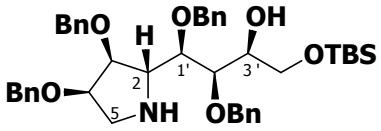
To a solution of **10** (5.78 g, 7.994 mmol) in MeOH (200 mL) was added dropwise conc. HCl solution (40 mL) and the mixture was stirred at rt for 18 h. The reaction mixture was basified at 0 ^0C with aqueous NH_3 solution (28%). The mixture was extracted with EtOAc, dried (Na_2CO_3), evaporated and purified by FCC (100% EtOAc to 93:5:2 EtOAc/MeOH/NH_3) to give **11** (3.788 g, 81%) as a yellow viscous oil.

$[\alpha]_D^{22}$ -27 (*c* 3.7, $CHCl_3$). [Lit.[2] for (+)-**11**; $[\alpha]_D^{21}$ +35 (*c* 1.45, $CHCl_3$).

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported for (+)-**11**.[2] It should be noted that the reported assignments for H-3 and H-4 and C-3 and C-4 should be interchanged.

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

1-[(2*S*,3*R*,4*R*)-3,4-Bisibenzyloxy-2-pyrrolidinyl]-(1*R*,2*S*,3*R*)-1,2-dibenzyloxy-4-(*tert*-butyldimethylsilyloxy)-butan-3-ol (12).



12

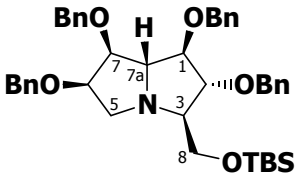
To a solution of the diol **11** (0.312 g, 0.535 mmol), imidazole (0.77 mg, 1.123 mmol) and 4-dimethylaminopyridine (6.5 mg, 0.053 mmol) in THF (6 mL) under N_2 at rt was added TBSCl (0.97 g, 0.642 mmol). The reaction mixture was stirred for 2 days and the reaction was quenched by the addition of water. The solvent was removed under reduced pressure and the residue was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were combined and washed with brine, dried (Na_2CO_3) and then evaporated to leave a residue which was chromatographed on silica gel by FCC (30:70 EtOAc/petrol to 2:98 MeOH /EtOAc). This gave **12** (0.316 g, 85%) as a yellow viscous oil.

$[\alpha]_D^{22}$ -17 (*c* 4.6, $CHCl_3$). [Lit.[2] for (+)-**12**; $[\alpha]_D^{22}$ +21 (*c* 0.7, $CHCl_3$).

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported for (+)-**12**.[2] It should be noted that the reported assignments for H-3 and H-4 and C-3 and C-4 should be interchanged.

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

(1*R*,2*R*,3*R*,6*R*,7*S*,7a*R*)-1,2,6,7-Tetrabenzyloxy-3-((*tert*-butyldimethylsilyloxy)methyl)-hexahydro-1*H*-pyrrolizine (13).



13

To a solution of **12** (0.792 g, 1.136 mmol) in pyridine (11 mL) was added triphenylphosphine (0.301 g, 1.148 mmol), triethylamine·hydrochloride (0.156 g, 1.136 mmol) and diisopropyl azodicarboxylate (0.56 mL, 2.841 mmol). The mixture was stirred at rt for 3 days. The volatiles were removed in *vacuo* then satd. $CuSO_4$ solution (20 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 x 25 mL). The combined CH_2Cl_2 extracts were washed with satd. $CuSO_4$ solution (20 mL) and water (20 mL), dried (Na_2CO_3), filtered and then evaporated. FCC (100% petrol to 20:80 EtOAc/petrol) gave **13** as a yellow viscous oil (0.587 g, 76%).

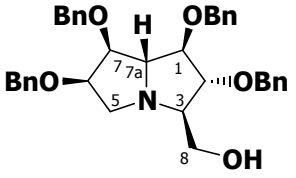
$[\alpha]_D^{20}$ -34 (*c* 0.4, $CHCl_3$).

IR υ_{max} (cm^{-1}): 3070, 3040, 2924, 2852, 1454, 1120, 1097.

This compound had the same R_f, MS and NMR spectroscopic data as reported for (+)-**13**.[2]

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

((1*R*,2*R*,3*R*,6*R*,7*S*,7a*R*)-1,2,6,7-Tetrabenzyloxy-hexahydro-1*H*-pyrrolizin-3-yl)methanol (14).



14

To a solution of **13** (1.417 g, 2.087 mmol) in MeOH (50 mL) was added dropwise conc. HCl solution (12.5 mL) and the mixture was stirred at rt for 18 h. The mixture was basified at 0 ^{0}C with aqueous NH_3 solution (28%). The mixture was extracted with EtOAc, dried (Na_2CO_3), evaporated and purified by FCC (50:50 EtOAc/petrol) to give **14** (1.058 g, 90%) as a pale yellow viscous oil. R_f 0.11 (50:50 EtOAc/petrol).

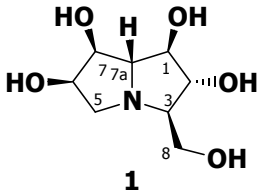
$[\alpha]_D^{20}$ -35 (*c* 1.3, $CHCl_3$). [Lit.[2] for (+)-**14**; $[\alpha]_D^{23}$ +34 (*c* 1.3, $CHCl_3$).

IR υ_{max} (cm^{-1}): 3446, 3050, 2893, 2858, 1449, 1107, 1097.

This compound had the same R_f, MS and NMR spectroscopic data as reported for (+)-**14**.[2]

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

(1*R*,2*R*,3*R*,6*R*,7*S*,7a*R*)-Hexahydro-3-(hydroxymethyl)-1*H*-pyrrolizine-1,2,6,7-tetraol (uniflorine A) (1).



1

To a solution of **14** (0.636 g, 1.126 mmol) in MeOH (12 mL) was added $PdCl_2$ (0.300 g, 1.690 mmol). The mixture was stirred at rt under an atmosphere of H_2 (balloon) for 1 day. The mixture was filtered through a celite pad and the solids were washed with MeOH. The combined filtrates were evaporated *in vacuo* and the residue was dissolved in water (3 mL) and applied to a column of Amberlyst (OH^-) A-26 resin (7 cm). Elution with water followed by evaporation *in vacuo* gave uniflorine A **1** (0.201 g, 87%) as a white solid. mp. 163.2-164.8 °C, (Lit.[3] mp. 174 - 178 °C).

$[\alpha]_D^{23}$ -3.7 (*c* 1.2, H_2O). [Lit.[3] for (-)-uniflorine A; $[\alpha]_D$ -4.4 ° (*c* 1.2, H_2O).

This compound had the same R_f, MS, IR and NMR spectroscopic data as reported for (+)-**1**.[2]

2. Ritthiwigrom, T.; Pyne, S. G., *Org. Lett.* **2008,** *10*, 2769-2771.

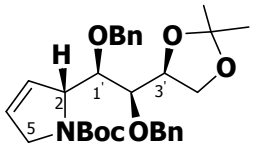
3. Matsumura, T.; Kasai, M.; Hayashi, T.; Arisawa, M.; Momose, Y.; Arai, I.; Amagaya, S.; Komatsu, Y., *Pharmaceutical Biol.* **2000,** *38*, 302-307.

Table 1 Physical and spectral Data for (-)-Uniflorine A[3] and **1**.

	Uniflorine A [3]	Synthetic **1**	
Physical Appearance	Colourless Microcrystals	White solid	
Optical Rotation	$[\alpha]_D$ -4.4 ° (*c* 1.2, H_2O)	$[\alpha]_D^{23}$ -3.7 (*c* 1.2, H_2O)	
Melting Point	174 - 178 °C	163.2-164.8 °C	
Mass Spectrometry	ISMS *m/z* 206 (M^+ + H)	ESI +ve *m/z* 206 (M + H^+, 100%)	
^{1}H NMR	500 MHz, D_2O	500 MHz, D_2O	
	4.35 (m, 1H, H-2)	4.34 (dt, 1H, $J_{5\alpha,6} = J_{5\beta,6} = J_{6,7}$ = 4.8 Hz, H-6)	
	4.18 (t, 1H, $J_{1,8a} = J_{1,2}$ = 4.5 Hz, H-1)	4.17 (t, 1H, $J_{6,7} = J_{6,7a}$ = 4.5 Hz, H-7)	
	3.94 (t, 1H, $J_{7,8} = J_{8,8a}$ = 7.7 Hz , H-8)	3.92 (t, 1H, $J_{1,2} = J_{1.7a}$ = 7.5 Hz, H-1)	
	3.81 (dd, 1H, $J_{6,7}$ = 9.0, $J_{7,8}$ = 7.7 Hz, H-7)	3.79 (t, 1H, $J_{1,2} = J_{2,3}$ = 8.5 Hz, H-2)	
	3.76 (dd, 1H, $J_{5\beta,6}$ = 3.8, $J_{5\alpha,5\beta}$ = 11.8 Hz, H-5β)	3.76 (dd, 1H, $J_{8,8'}$ = 11.8 Hz, $J_{3,8'}$ = 3.8 Hz, H-8')	
	3.61 (dd, 1H, $J_{5\alpha,6}$ = 6.4, $J_{5\alpha,5\beta}$ = 11.8 Hz, H-5α)	3.61 (dd, 1H, $J_{3,8}$ = 6.5, $J_{8,8'}$ = 11.5 Hz, H-8)	
	3.14 (dd, 1H, $J_{8,8a}$ = 7.7, $J_{1,8a}$ = 4.5 Hz, H-8a)	3.12 (dd, 1H, $J_{1,7a}$ = 7.5, $J_{7,7a}$ = 5.0 Hz, H-7a)	
	3.04 (dd, 1H, $J_{2,3\alpha}$ = 5.1, $J_{3\alpha,3\beta}$ = 12.1 Hz, H-3α)	3.02 (dd, 1H, $J_{5\beta,6}$ = 5.8, $J_{5\alpha,5\beta}$ = 11.8 Hz, H-5β)	
	2.98 (dd, 1H, $J_{2,3\beta}$ = 5.1, $J_{3\alpha,3\beta}$ = 12.1 Hz, H-3β)	2.96 (dd, 1H, $J_{5\alpha,6}$ = 5.3, $J_{5\alpha,5\beta}$ = 12.3 Hz, H-5α)	
	2.76 (m, 1H, $J_{5\alpha,6}$ = 6.4, $J_{5\beta,6}$ = 3.8, $J_{6,7}$ = 9.0 Hz, H-6)	2.74 (m, 1H, H-3)	
^{13}C NMR	125 MHz, D_2O (ref. TMS?)	125 MHz, D_2O (ref. MeCN, δ 1.47)	Δδ (ppm)
	81.2 (d, C-8)	79.1 (C-1)	2.1
	79.9 (d, C-7)	77.8 (C-2)	2.1
	78.1 (d, C-1)	76.0 (C-7)	2.1
	74.2 (d, C-2)	72.1 (C-6)	2.1
	73.6 (d, C-8a)	71.5 (C-7a)	2.1
	72.5 (d, C-6)	70.3 (C-3)	2.2
	65.3 (t, C-5)	63.2 (C-8)	2.1
	60.0 (t, C-3)	57.8 (C-5)	2.2

3. Matsumura, T.; Kasai, M.; Hayashi, T.; Arisawa, M.; Momose, Y.; Arai, I.; Amagaya, S.; Komatsu, Y., *Pharmaceutical Biol.* **2000,** *38*, 302-307.

(*R*)-*tert*-Butyl 2-((1*R*,2*S*)-1,2-bis(benzyloxy)-2-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,5-dihydro-1*H*-pyrrole-1-carboxylate (15).



15

To a solution of the diol **8** (8.55 g, 25.84 mmol) in dry THF (260 mL) was added *n*-Bu_4NI (954.3 mg, 2.58 mmol) and BnBr (9.27 mL, 78.0 mmol) follow by NaH (3.74 g, 78.0 mmol, 50 % in mineral oil) at 0 ^oC. After H_2 evolution had ceased (15 min) the reaction mixture was stirred at rt for 18 h. MeOH (50 mL) was then added followed by evaporation of all volatiles *in vacuo*. The residue was dissolved in EtOAc and filtered through celite, followed by further washings of the solids with EtOAc. The solvent was evaporated and the residue was purified by FCC (10:90 to 40:60 EtOAc/petrol) to give **15** as a yellow syrup (12.21 g, 92%). R_f 0.21 (15:85 EtOAc/petrol).

$[\alpha]_D^{22}$ +56 (*c* 1.4, $CHCl_3$).

MS (ESI +ve) *m/z* 510 ($M + H^+$, 30%).

HRMS (ESI +ve) calculated for $C_{30}H_{40}NO_6$ ($M+H^+$) 510.2856, found 510.2854.

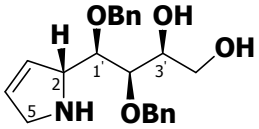
IR υ_{max} (cm^{-1}): 2980, 2929, 1696, 1393, 1107, 1060.

^1H NMR (500 MHz, $CDCl_3$) δ (major rotamer) 7.36-7.22 (m, 10H, Ar), 5.88 (app. t, 2H, *J* 8.5 Hz, H-3 and H-4), 4.81 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.74 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.55 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.50 (d, 1H, *J* 5.0 Hz, H-2), 4.35-4.25 (m, 2H, H-1' or H-2' and C*H*HPh), 4.16-3.98 (m, 2H, 2xH-5), 3.91 (d, 1H, *J* 4.5 Hz, H-1' or H-2'), 3.60-3.42 (m, 3H, 2xH-4' and H-3'), 1.45 (s, 9H, *t*-Bu), 1.42 (s, 3H, CH_3), 1.35 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (major rotamer) 153.9 (CO), 138.1 (C), 137.6(C), 128.48 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.7 (CH), 127.6 (C-3 or C-4), 126.3 (C-3 or C-4), 109.1 (C), 80.8 (C-3'), 79.9 (C), 79.3 (C-1' or C-2'), 77.1 (C-1' or C-2'), 74.1 (CH_2), 73.7 (CH_2), 67.5 (C-2), 65.5 (C-4'), 53.2 (C-5), 28.5 (C(CH_3)$_3$), 26.6 (CH_3), 25.5 (CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (minor rotamer) 154.2, 138.4, 137.9, 128.42, 128.39 128.3, 128.1, 127.8, 127.5, 126.9, 125.7, 109.0, 81.4, 79.7, 79.5, 77.5, 73.9, 73.5, 67.9, 65.8, 53.3, 28.4, 26.6, 25.6.

(2*S*,3*R*,4*R*)-3,4-Bis(benzyloxy)-4-((*R*)-2,5-dihydro-1*H*-pyrrol-2-yl)butane-1,2-diol (16).



16

To a solution of **15** (10.93 g, 21.47 mmol) in MeOH (500 mL) was added dropwise conc. HCl solution (95 mL) and the mixture was stirred at rt for 30 h. The reaction mixture was basified at 0 ^{0}C with aqueous NH_3 solution (28%). The mixture was extracted with EtOAc and the combined extracts were dried (Na_2CO_3), evaporated and purified by FCC (100% EtOAc to 8:2:1 EtOAc/MeOH/NH_3) to give **16** (6.0 g, 76%) as a brown foamy solid. R_f 0.34 (9:0.8:0.2 EtOAc/MeOH/NH_3).

$[\alpha]_D^{21}$ +122 (*c* 3.2, $CHCl_3$).

MS (ESI +ve) *m/z* 370 (M + H^+, 100%).

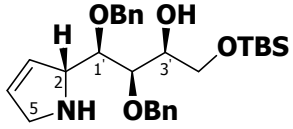
HRMS (ESI +ve) calculated for $C_{22}H_{28}NO_4$ (M+H^+) 370.2018, found 370.2009.

IR υ_{max} (cm^{-1}): 3390, 3288, 3062, 3027, 2955, 2909, 1078, 1059.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.3.4-7.27 (m, 10H, Ar), 5.97 (dd, 1H, *J* 6.0, 1.5 Hz, H-4), 5.89 (dd, 1H, *J* 6.0, 1.5 Hz, H-3), 4.73 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.67 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.60 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.53 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.27 (brs, 1H, H-2), 3.90-3.88 (m, 1H, H-3'), 3.76-3.70 (m, 3H, 2xH-5 and H-4'), 3.65-3.63 (m, 1H, H-2'), 3.61-3.56 (m, 2H, H-1' and H-4').

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0 (C), 137.9 (C), 129.9 (C-4), 128.8 (C-3), 128.42 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 81.6 (C-1'), 80.9 (C-2'), 74.4 (CH_2), 74.2 (CH_2), 70.6 (C-3'), 66.4 (C-2), 63.7 (C-4'), 52.7 (C-5).

(2*S*,3*R*,4*R*)-3,4-Bis(benzyloxy)-1-(*tert*-butyldimethylsilyloxy)-4-((*R*)-2,5-dihydro-1*H*-pyrrol-2-yl)butan-2-ol (17).



17

To a solution of the diol **16** (0.302 g, 0.816 mmol) and a crystal of 4-dimethylaminopyridine in THF (8 mL) under N_2 at rt was added imidazole (0.121 g, 1.776 mmol) and TBSCl (0.153 g, 1.02 mmol). The reaction mixture was stirred for

24 h and the reaction was quenched by the addition of water. The solvent was removed under reduced pressure and the residue was extracted with EtOAc. The combined extracts were washed with brine, dried (Na_2CO_3) and then evaporated to leave a residue which was chromatographed on silica gel by FCC (100% EtOAc to 10:2:1 EtOAc/MeOH/NH_3) to give **17** (0.320 g, 81%) as a brown viscous oil. R_f 0.65 (9:0.8:0.2 EtOAc/MeOH/NH_3).

$[\alpha]_D^{21}$ +93 (*c* 2.3, $CHCl_3$).

MS (ESI +ve) *m/z* 484 ($M + H^+$, 100%).

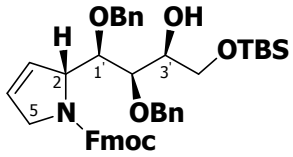
HRMS (ESI +ve) calculated for $C_{28}H_{42}NO_4Si$ ($M+H^+$) 484.2883, found 484.2906.

IR υ_{max} (cm^{-1}): 3390, 3288, 3062, 3021, 2955, 2929, 1077, 1062.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.3.6-7.27 (m, 10H, Ar), 5.98 (dd, 1H, *J* 5.5, 1.5 Hz, H-4), 5.92 (dd, 1H, *J* 6.0, 2.0 Hz, H-3), 4.75 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.73 (d, 1H, *J* 10.0 Hz, C*H*HPh), 4.69 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.52 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.21-4.18 (m, 1H, H-2), 3.88-3.85 (m, 2H, H-2' and H-3'), 3.74-3.70 (m, 4H, 2xH-5 and 2xH-4'), 3.57 (app. t, 1H, *J* 7.0 Hz, H-1'), 0.91 (s, 9H, *t*-Bu), 0.08 (s, 3H, CH_3), 0.07 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6 (C), 138.2 (C), 130.2 (C-4), 129.4 (C-3), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.5 (CH), 82.6 (C-1'), 79.8 (C-2'), 74.6 (CH_2), 74.0 (CH_2), 70.3 (C-3'), 66.2 (C-2), 63.2 (C-4'), 53.1 (C-5), 25.9 (C*(CH₃)₃*), 18.1 (C), -5.4 (CH_3), -5.5 (CH_3).

(*R*)-(9*H*-Fluoren-9-yl)methyl 2-((1*R*,2*R*,3*S*)-1,2-bis(benzyloxy)-4-(*tert*-butyldimethylsilyloxy)-3-hydroxybutyl)-2,5-dihydro-1*H*-pyrrole-1-carboxylate (18).



18

To a solution of **1**7 (6.05 g, 0.013 mol) in THF (125 mL) and satd. Na_2CO_3 solutiuon (60 mL) was added 9-fluorenylmethylchloroformate (3.89 g, 15.03 mmol) at 0 ^oC. The reaction mixture was stirred at 0 ^oC for 3 h. Water (20 mL) was added and the solvent was removed under reduced pressure and the residue was extracted with CH_2Cl_2 (3x70 mL). The combined extracts were washed with brine, dried (Na_2CO_3) and then evaporated to leave a residue which was chromatographed on silica gel by

FCC (10:90 to 30:70 EtOAc/petrol) to give **18** (8.31 g, 94%) as a colourless viscous oil. R_f 0.47 (20:80 EtOAc/petrol).

$[\alpha]_D^{24}$ +125 (*c* 2.0, $CHCl_3$).

MS (ESI +ve) *m/z* 706 ($M + H^+$, 20%).

HRMS (ESI +ve) calculated for $C_{43}H_{52}NO_6Si$ ($M+H^+$) 706.3564, found 706.3537.

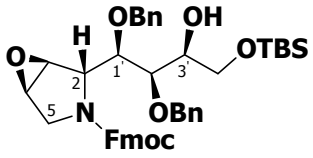
IR υ_{max} (cm^{-1}): 3061, 3028, 2945, 2924, 1700, 1413, 1107.

^{1}H NMR (500 MHz, $CDCl_3$) δ (major rotamer) 7.78-7.59 (m, 4H, Ar), 7.42-7.16 (m, 14H, Ar), 5.97-5.95 (m, 1H, H-3), 5.92-5.89 (m, 1H, H-4), 4.90 (d, 2H, *J* 11.0 Hz, 2xC*H*HPh), 4.91-4.89 (m, 1H, H-2), 4.67-4.63 (m, 1H, C*H*HPh), 4.47 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.45 (d, 1H, *J* 8.0 Hz, H-1' or H-2'), 4.39 (dd, 2H, *J* 7.0, 2.3 Hz, CH_2 (Fmoc)), 4.26-4.20 (m, 1H, C*H* (Fmoc)), 4.26-4.07 (m, 2H, 2xH-5), 3.88 (dd, 1H, *J* 13.5, 7.5 Hz, H-3'), 3.77 (d, 1H, *J* 7.5 Hz, H-1' or H-2'), 0.90 (s, 9H, *t*-Bu), 0.07 (s, 3H, CH_3), 0.06 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (major rotamer) 154.3 (CO), 144.0 (C), 143.9 (C), 141.3 (C), 141.2 (C), 138.4 (C), 138.2 (C), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 126.9 (CH), 125.0 (CH), 119.9 (CH), 78.3 (C-1'), 77.8 (C-2'), 74.7 (CH_2), 74.3 (CH_2), 70.8 (C-3'), 66.9 (*C*H_2 (Fmoc)), 66.2 (C-2), 63.6 (C-4'), 53.4 (C-5), 47.2 (*C*H (Fmoc)), 25.8 (C*(CH$_3$)$_3$*), 18.1 (C), -5.4 (CH_3), -5.5 (CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (minor rotamer) 154.3, 144.0, 143.8, 141.3, 141.2, 138.3, 138.2, 128.2, 127.8, 127.7, 127.6, 126.7, 126.5, 125.5, 124.7, 119.9, 80.2, 78.6, 74.9, 74.8, 71.0, 65.9, 65.5, 63.5, 54.2, 47.7, 25.7, 18.0, -5.4.

(1*S*,2*S*,5*R*)-(9*H*-Fluoren-9-yl)methyl 2-((1*R*,2*R*,3*S*)-1,2-bis(benzyloxy)-4-(*tert*-butyldimethylsilyloxy)-3-hydroxybutyl)-6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate (19).



19

To a solution of the olefin **18** (2.37 g, 3.37 mmol) in MeCN (35 mL) was added Na_2EDTA (13.5 mL, 4 x 10^{-4} M) and $CF_3C(O)CH_3$ (6.8 mL, 7.60 mmol). The reaction was chilled to 0 ^oC before the portionwise addition of a mixture of $NaHCO_3$ (4.24 g, 50.47 mmol) and oxone (4.14 g, 6.73 mmol) over 15 min. After stirring for 2 h at 0

^{o}C, the mixture was poured into water followed by removed of the volatiles under reduced pressure. The residue was extracted with CH_2Cl_2 (3x40 mL) and the combined organic extracts were washed with brine, dried (Na_2CO_3) and then evaporated to leave a residue which was chromatographed on silica gel by FCC (10:90 to 20:80 EtOAc/petrol) to give **19** (1.95 g, 81%) as a pale yellow oil. R_f 0.42 (20:80 EtOAc/petrol).

$[\alpha]_D^{25}$ +99 (*c* 1.1, $CHCl_3$).

MS (ESI +ve) *m/z* 744 (M + Na^+, 100%).

HRMS (ESI +ve) calculated for $C_{43}H_{51}NO_7SiNa$ (M+Na^+) 744.3333, found 744.3360.

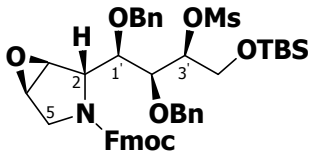
IR υ_{max} (cm^{-1}): 3062, 2945, 2924, 2858, 1700, 1454, 1110.

^{1}H NMR (500 MHz, $CDCl_3$) δ (major rotamer) 7.76-7.54 (m, 4H, Ar), 7.41-7.16 (m, 14H, Ar), 4.86 (d, 1H, *J* 10.5 Hz, C*H*HPh), 4.67 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.64 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.36 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.36-4.30 (m, 3H, C*H*$_2$ (Fmoc) and H-2), 4.26 (brs, 1H, H-1'), 4.19-4.15 (m, 1H, C*H* (Fmoc)), 3.91-3.86 (m, 1H, H-3'), 3.86-3.80 (m, 2H, H-2' and H-3), 3.74-3.67 (m, 2H, H-4' and H-5), 3.63 (d, 1H, *J* 2.0 Hz, H-4), 3.59-3.53 (m, 1H, H-4'), 3.24-3.20 (m, 1H, H-5), 0.88 (s, 9H, *t*-Bu), 0.04 (s, 3H, CH_3), 0.03 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (major rotamer) 154.9 (CO), 143.7 (C), 141.3 (C), 138.0 (C), 137.8 (C), 128.7 (CH), 128.2 (CH), 127.9 (CH), 127.8 (CH), 127.6 (CH), 127.1 (CH), 127.0 (CH), 125.0 (CH), 124.9 (CH), 119.9 (CH), 79.1 (C-1'), 77.2 (C-2'), 74.9 (CH_2), 74.4 (CH_2), 70.6 (C-3'), 67.1 (*C*H_2 (Fmoc)), 63.5 (C-4'), 60.1 (C-2), 56.3 (C-3), 55.6 (C-4), 47.8 (C-5), 47.1 (*C*H (Fmoc)), 25.8 (C*(CH$_3$)$_3$*), 18.1 (C), -5.4 (CH_3), -5.5 (CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (minor rotamer) 155.0, 144.0, 141.2, 137.9, 137.7, 127.8, 127.7, 127.69, 127.64, 127.63, 127.5, 127.4, 125.0, 124.7, 120.0, 80.6, 78.0, 75.0, 74.8, 70.8, 66.2, 63.4, 59.8, 56.4, 54.9, 48.2, 47.6, 25.7, 18.07, -5.45, -5.48.

(1*S*,2*S*,5*R*)-(9*H*-Fluoren-9-yl)methyl 2-((1*R*,2*S*,3*S*)-1,2-bis(benzyloxy)-4-(*tert*-butyldimethylsilyloxy)-3-(methylsulfonyloxy)butyl)-6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate (20).



20

To a solution of **19** (0.414 g, 0.574 mmol) in anhydrous CH_2Cl_2 (6 mL) was added anhydrous Et_3N (0.24 mL, 1.723 mmol) and methanesulfonyl chloride (0.089 mL, 1.148 mmol). The reaction mixture was stirred at 0 ^oC under an atmosphere of N_2 for 3 h, followed by the evaporation of all volatiles *in vacuo*. Water (20 mL) was added and the residue was extracted with CH_2Cl_2 (3x20 mL). The combined organic extracts were washed with brine, dried (Na_2CO_3) and then evaporated to leave a residue which was chromatographed on silica gel by FCC (10:90 to 30:70 EtOAc/petrol) to give **20** (0.433 g, 94%) as a pale yellow oil. R_f 0.5 (30:70 EtOAc/petrol).

$[\alpha]_D^{25}$ +64 (*c* 1.1, $CHCl_3$)

MS (ESI +ve) *m/z* 822 (M + Na^+, 100%).

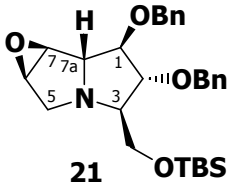
HRMS (ESI +ve) calculated for $C_{44}H_{54}NO_9SSi$ (M+H^+) 800.3289, found 800.3273.

IR υ_{max} (cm^{-1}): 2950, 2924, 2888, 2852, 1695, 1360, 1328, 1175, 1110.

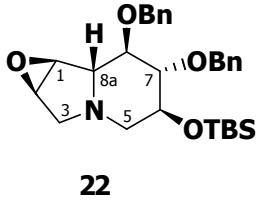
^{1}H NMR (500 MHz, $CDCl_3$) δ (major rotamer) 7.70-7.66 (m, 2H, Ar), 7.45 (app. t, 2H, *J* 6.8 Hz, Ar), 7.35-7.11 (m, 14H, Ar), 4.76-4.73 (m, 1H, H-3'), 4.64 (d, 1H, *J* 10.5 Hz, C*H*HPh), 4.64-4.61 (m, 2H, 2xC*H*HPh), 4.34 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.31-4.29 (m, 2H, CH_2 (Fmoc)), 4.16 (brs, 1H, H-2), 4.13 (app. t, 1H, *J* 7.0 Hz, C*H* (Fmoc)), 4.02-4.00 (m, 2H, H-1' and H-2'), 3.97-3.94 (m, 2H, 2x H-4'), 3.74-3.72 (m, 1H, H-3), 3.68 (d, 1H, *J* 12.0 Hz, H-5), 3.58-3.56 (m, 1H, H-4), 3.20 (d, 1H, *J* 13.0 Hz, H-5), 3.04 (s, 3H, CH_3 (Ms)), 0.82 (s, 9H, *t*-Bu), 0.04 (s, 6H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (major rotamer) 154.9 (CO), 144.0 (C), 143.7 (C), 141.3 (C), 141.2 (C), 137.9 (C), 137.5 (C), 128.5 (CH), 128.4 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 127.0 (CH), 125.0 (CH), 124.9 (CH), 120.0 (CH), 81.5 (C-3'), 79.1 (C-1'), 78.6 (C-2'), 75.7 (CH_2), 75.0 (CH_2), 67.1 (*C*H_2 (Fmoc)), 61.1 (C-4'), 60.6 (C-2), 56.0 (C-3), 55.6 (C-4), 47.8 (C-5), 47.2 (*C*H (Fmoc)) , 38.4 (CH_3 (Ms)), 25.8 (C(*CH_3*)$_3$), 18.1 (C), -5.4 (CH_3), -5.5 (CH_3).

(1a*R*,4*R*,5*R*,6*R*,6a*S*,6b*S*)-5,6-Bis(benzyloxy)-4-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1a*H*-oxireno[2,3-a]pyrrolizine (21) and (1a*R*,5*S*,6*S*,7*R*,7a*S*,7b*S*)-6,7-bis(benzyloxy)-5-(*tert*-butyldimethylsilyloxy)octahydrooxireno[2,3-a]indolizine (22).



21



22

To a solution of **20** (470.3 mg, 0.589 mmol) in MeCN (6 mL) was added piperidine (0.12 mL, 1.12 mmol). The reaction was stirring for 15 h at rt, the volatiles were removed under reduced pressure and the residue was purified by FCC (10:90 to 30:70 EtOAc/petrol) to give a mixture of **21** and **22** (91:9) as a pale yellow oil (271.0 mg, 96%). A pure sample of **21** was obtained by further purification of this mixture by FCC to give **21** as yellow needles.

21: R_f 0.27 (30:70 EtOAc/petrol).

mp. 40.9-43.1 ^{o}C (yellow needles)

$[\alpha]_D^{24}$ +12 (*c* 1.0, $CHCl_3$).

MS (ESI +ve) *m/z* 482 ($M + H^+$, 100%).

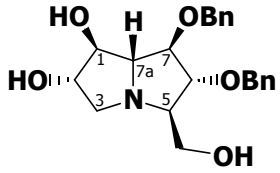
HRMS (CI +ve) calculated for $C_{28}H_{40}NO_4Si$ ($M+H^+$) 482.2727, found 482.2729.

IR υ_{max} (cm^{-1}): 3032, 2945, 2924, 2858, 1255, 1109.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.24 (m, 10H, Ar), 4.61 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.60 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.54 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.51 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.15 (app. t, 1H, *J* 3.8 Hz, H-2), 3.91 (dd, 1H, *J* 7.3, 3.8 Hz, H-1), 3.69-3.68 (m, 1H, H-6), 3.66 (dd, 1H, *J* 10.0, 6.0 Hz, H-8), 3.64-3.62 (m, 2H, H-7 and H-7a), 3.50 (app. t, 1H, *J* 10.0 Hz, H-8), 3.45 (d, 1H, *J* 11.5 Hz, H-5), 3.08-3.04 (m, 1H, H-3), 2.98 (d, 1H, *J* 12.0 Hz, H-5), 0.88 (s, 9H, *t*-Bu), 0.04 (s, 3H, CH_3), 0.03 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1 (C), 137.7 (C), 128.4 (CH), 128.3 (CH), 127.8 (CH), 127.7 (CH), 127.64 (CH), 127.6 (CH), 88.7 (C-2), 85.9 (C-1), 72.1 (CH_2), 71.8 (CH_2), 70.8 (C-3), 69.0 (C-7a), 64.4 (C-8), 58.5 (C-7), 57.0 (C-6), 55.6 (C-5), 25.9 (C(*CH_3*)$_3$), 18.2 (C), -5.4 (CH_3), -5.43 (CH_3).

(1*S*,2*S*,5*R*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-(hydroxymethyl)hexahydro-1*H*-pyrrolizine-1,2-diol (23).



23

To a solution of the epoxide **21** (37.4 mg, 0.078 mmol) in anhydrous CH_2Cl_2 (4 mL) was added $NaHSO_4$ (46.7 mg, 0.389 mmol). The reaction mixture was stirred and heated at reflux for 2 days under an atmosphere of N_2. The reaction was quenched by the addition of water (5 mL) and stirred for 1 h. The solvent was removed under reduced pressure and the residue was extracted with EtOAc (3x10 mL). The combined extracts were dried (Na_2CO_3) and evaporated. NMR analysis of this crude reaction mixture showed an 86:14 mixture of regioisomers. The crude mixture was purified by FCC (100% EtOAc to 8.5:1:0.5 EtOAc/MeOH/NH_3) to give **23** (a 92:8 mixture of diastereomers) as a pale yellow oil (15.3 mg, 51%).

23 (on a 92:8 mixture of diastereomers)**:**

R_f 0.34 (8.6:1.0:0.4 / EtOAc:MeOH:NH_3).

$[\alpha]_D^{23}$ +19 (*c* 1.1, $CHCl_3$).

MS (ESI +ve) *m/z* 386 ($M + H^+$, 100%).

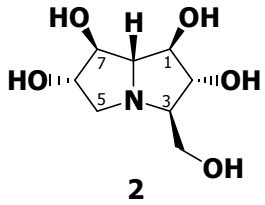
HRMS (ESI +ve) calculated for $C_{22}H_{28}NO_5$ ($M+H^+$) 386.1967, found 386.1967.

IR υ_{max} (cm^{-1}): 3390, 3027, 2929, 2873, 1449, 1103, 1063.

^{1}H NMR (500 MHz, CD_3OD) δ 7.36-7.24 (m, 10H, Ar), 4.68 (d, 2H, *J* 12.0 Hz, 2xC*H*HPh), 4.60 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.54 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.19 (app. t, 1H, *J* 5.3 Hz, H-1), 4.08 (dd, 1H, *J* 10.5, 5.5 Hz, H-2), 4.04 (app. t, 1H, *J* 5.3 Hz, H-7), 3.98 (dd, 1H, *J* 6.5, 5.5 Hz, H-6), 3.62 (dd, 1H, *J* 11.0, 4.8 Hz, H-8), 3.51 (dd, 1H, *J* 11.3, 5.8 Hz, H-8), 3.30 (m, 1H, H-5), 3.27 (app. t, 1H, *J* 5.0 Hz, H-7a), 3.18 (app. dt, 1H, *J* 5.8, 5.0 Hz, H-3), 2.87 (dd, 1H, *J* 11.3, 5.8 Hz, H-5).

^{13}C NMR (125 MHz, CD_3OD) δ 139.6 (C), 139.5 (C), 129.4 (CH), 129.3 (CH), 128.95 (CH), 129.5 (CH), 128.7 (CH), 128.5 (CH), 87.2 (C-1), 85.6 (C-6), 81.4 (C-7), 79.2 (C-2), 75.2 (C-7a), 73.3 (CH_2), 72.9 (CH_2), 72.6 (C-3), 63.5 (C-8), 60.1 (C-5).

(1*R*,2*R*,3*R*,6*S*,7*S*)-3-(Hydroxymethyl)hexahydro-1*H*-pyrrolizine-1,2,6,7-tetraol (casuarine) (2).



2

To a solution of 92% diastereomerically pure **23** (21.0 mg, 0.055 mmol) in MeOH (2 mL) was added $PdCl_2$ (10.0 mg, 0.055 mmol). The mixture was stirred at rt under an atmosphere of H_2 (balloon) for 1.5 h. The mixture was filtered through a celite pad and the solids were washed with MeOH. The combined filtrates were evaporated *in vacuo* and the residue was dissolved in water (1 mL) and applied to a column of Amberlyst (OH^-) A-26 resin (3 cm). Elution with water followed by evaporation *in vacuo* gave casuarine **2** (dr = 95:5) as a brown foamy solid (10.4 mg, 93%).

$[\alpha]_D^{23}$ +18.1 (*c* 1.0, H_2O). [Lit.[4] ; $[\alpha]_D^{24}$ +16.9 ° (*c* 0.8, H_2O)].

MS (ESI +ve) *m/z* 206 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_8H_{16}NO_5$ ($M+H^+$) 206.1028, found 206.0953.

IR υ_{max} (cm^{-1}): 3284, 2919, 1378, 1128, 1102, 1029.

^{1}H NMR (500 MHz, D_2O) δ 4.22-4.18 (m, 2H, H-6 and H-7), 4.16 (t, 1H, $J_{1,2} = J_{1,7a}$ = 8.7 Hz, H-1), 3.79 (t, 1H, $J_{1,2} = J_{2,3}$ = 8.0 Hz, H-2), 3.77 (dd, 1H, $J_{8,8'}$ = 10.0, $J_{3,8}$ = 3.5 Hz, H-8), 3.61 (dd, 1H, $J_{8,8'}$ = 11.3, $J_{3,8'}$ = 6.8 Hz, H-8'), 3.27 (dd, 1H, $J_{5\alpha,5\beta}$ = 12.3, $J_{5\beta,6}$ = 4.3 Hz, H-5β), 3.06 (dd, 1H, $J_{1,7a}$ = 8.0, $J_{7,7a}$ = 3.0 Hz, H-7a), 3.04-3.00 (m, 1H, H-3), 2.90 (dd, 1H, $J_{5\alpha,5\beta}$ = 11.8, $J_{5\alpha,6}$ = 4.3 Hz, H-5α).

^{13}C NMR (125 MHz, D_2O) δ 79.9 (C-7), 78.9 (C-1), 78.5 (C-6), 77.8 (C-2), 73.1 (C-7a), 71.0 (C-3), 63.5 (C-8), 59.0 (C-5).

4. Nash, R. J.; Thomas, P. I.; Waigh, R. D.; Fleet, G. W. J.; Wormald, M. R.; de Q. Lilley, P. M.; Watkin, D. J., *Tetrahedron Lett.* **1994,** *35*, 7849-7852.

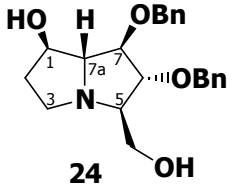
Table 2 Physical and spectral Data for (+)-Casuarine [4] and **2**.

	Casuarine [4]	Synthetic **2**	
Physical Appearance	Crystallize solid	Brown foamy solid	
Optical Rotation	$[\alpha]_D^{24}$ +16.9 ° (*c* 0.8, H_2O)	$[\alpha]_D^{23}$ +18.1 (*c* 1.0, H_2O)	
Melting Point	181-182 °C	-	
^{1}H NMR	500 MHz, D_2O (pH = 8.35)	500 MHz, D_2O	
	4.21 (m, 1H, *J* = 4.7, 4.0 Hz, H-6)	4.22-4.18 (m, 2H, H-6 and H-7)	
	4.19 (m, 1H, *J* =3.5 Hz, H-7)		
	4.162 (t, 1H, *J* = 8.0 Hz, H-1)	4.16 (t, 1H, $J_{1,2} = J_{1,7a}$ = 8.7 Hz, H-1)	
	3.796 (t, 1H, *J* = 8.0 Hz, H-2)	3.79 (t, 1H, $J_{1,2} = J_{2,3}$ = 8.0 Hz, H-2)	
	3.771 (dd, 1H, *J* = 11.9, 3.8 Hz, H-8)	3.77 (dd, 1H, $J_{8,8'}$ = 10.0, $J_{3,8}$ = 3.5 Hz, H-8)	
	3.611 (dd, 1H, *J* = 11.9, 6.6 Hz, H-8')	3.61 (dd, 1H, $J_{8,8'}$ = 11.3, $J_{3,8'}$ = 6.8 Hz, H-8')	
	3.270 (dd, 1H, *J* = 12.2, 4.7 Hz, H-5β)	3.27 (dd, 1H, $J_{5\alpha,5\beta}$ = 12.3, $J_{5\beta,6}$ = 4.3 Hz, H-5β)	
	3.071 (dd, 1H, *J* = 8.0, 3.5 Hz, H-7a)	3.06 (dd, 1H, $J_{1,7a}$ = 8.0, $J_{7,7a}$ = 3.0 Hz, H-7a)	
	3.04-3.00 (m, 1H, *J* = 8.0, 6.6, 3.8 Hz, H-3)	3.04-3.00 (m, 1H, H-3)	
	2.911 (dd, 1H, *J* = 12.2, 4.0 Hz, H-5α)	2.90 (dd, 1H, $J_{5\alpha,5\beta}$ = 11.8, $J_{5\alpha,6}$ = 4.3 Hz, H-5α)	
^{13}C NMR	125 MHz, D_2O (ref acetone δ 29.8)	125 MHz, D_2O (ref acetone δ 29.8)	Δδ (ppm)
	78.8 (C-7)	79.9 (C-7)	-1.1
	77.8 (C-1)	78.9 (C-1)	-1.1
	77.4 (C-6)	78.5 (C-6)	-1.1
	76.6 (C-2)	77.8 (C-2)	-1.2
	72.1 (C-7a)	73.1 (C-7a)	-1.0
	70.0 (C-3)	71.0 (C-3)	-1.0
	62.2 (C-8)	63.5 (C-8)	-1.3
	58.0 (C-5)	59.0 (C-5)	-1.0

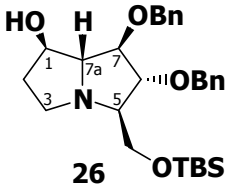
4. Nash, R. J.; Thomas, P. I.; Waigh, R. D.; Fleet, G. W. J.; Wormald, M. R.; de Q. Lilley, P. M.; Watkin, D. J., *Tetrahedron Lett.* **1994,** *35*, 7849-7852.

(1*R*,5*R*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-(hydroxymethyl)hexahydro-1*H*-pyrrolizin-1-ol (24),

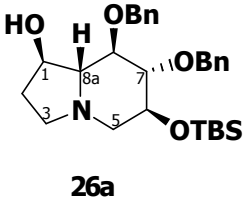
(1*R*,5*R*,6*R*,7*R*,7a*R*)-6,7-bis(benzyloxy)-5-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1*H*-pyrrolizin-1-ol (26) and (1*R*,6*S*,7*S*,8*R*,8a*R*)-7,8-bis(benzyloxy)-6-(*tert*-butyldimethylsilyloxy)octahydroindolizin-1-ol (26a)



24



26



26a

To solution of a 91:9 mixture of **21** and **22** (611.5 mg, 1.271 mmol) in anhydrous THF (13 mL) was added dropwise a solution of lithium aluminium hydride (1M in THF, 1.53 mL, 1.526 mmol). The reaction mixture was stirring for 8 h at 0 ^{o}C. The solvent was evaporated and the mixture was chromatographed on silica gel by FCC (50:50 EtOAc/petrol to 8.5:1.0:0.5 EtOAc/MeOH/NH_3) to give a mixture of **24** and **25** (**24**:**25** = 88:12) as a yellow viscous oil (106 mg, 27%), a mixture of **26** and **27** (**26**:**27** = 92:8) as a yellow viscous oil (330 mg, 64%), **26a** (10.3 mg, 2%) as a pale yellow oil and unreacted starting material (97.5 mg, 16%).

24 (on 88:12 mixture): R_f 0.40 (9:1:0.2 EtOAc/MeOH/NH_3).

$[\alpha]_D^{22}$ +6 (*c* 1.1, $CHCl_3$).

MS (ESI +ve) *m/z* 370 ($M + H^+$, 100%).

HRMS (CI +ve) calculated for $C_{22}H_{28}NO_4$ ($M+H^+$) 370.2018, found 370.2000.

IR υ_{max} (cm^{-1}): 3385, 2924, 2873, 1449, 1362, 1105.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.28 (m, 10H, Ar), 4.73 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.65 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.62 (d, 2H, *J* 10.0 Hz, 2xC*H*HPh), 4.19-4.17 (m, 1H, H-7), 4.07 (app. t, 1H, *J* 6.8 Hz, H-2), 3.80 (app. t, 1H, *J* 6.0 Hz, H-1), 3.56 (app. t, 2H, *J* 3.3 Hz, 2xH-8), 3.29 (dd, 1H, *J* 6.0, 3.5 Hz, H-7a), 3.17-3.12 (m, 1H, H-5), 2.82-2.79 (m, 1H, H-3), 2.78-2.73 (m, 1H, H-5), 2.04-1.97 (m, 1H, H-6), 1.78-1.73 (m, 1H, H-6).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1 (C), 138.0 (C), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.8 (CH), 127.78 (CH), 127.7 (CH), 86.6 (C-1), 83.7 (C-2), 76.7 (C-7), 75.7 (C-7a), 72.9 (CH_2), 72.2 (CH_2), 69.3 (C-3), 60.5 (C-8), 51.6 (C-5), 33.7 (C-6).

To a solution of the diol **24** (0.145 g, 0.039 mmol) and a crystal of 4-dimethylaminopyridine in THF (4 mL) under N_2 at rt was added imidazole (0.056 g, 0.083 mmol) and TBSCl (0.071 g, 0.047 mmol). The reaction mixture was stirred for

2 days and the reaction was quenched by the addition of water (10 mL). The solvent was removed under reduced pressure and the residue was extracted with EtOAc (3x20 mL). The combined extracts were washed with brine, dried (Na_2CO_3) and then evaporated to leave a residue which was chromatographed on silica gel by FCC (100% EtOAc to 10:2:1 EtOAc/MeOH/NH_3) to give a mixture of **26** and **27** (**26**:**27** = 82:18) (0.056 g, 61%) as a yellow viscous oil.

26 (on 92:8 mixture): R_f 0.44 (70:30 EtOAc/petrol).

$[\alpha]_D^{22}$ -16 (*c* 2.3, $CHCl_3$).

MS (ESI +ve) *m/z* 484 ($M + H^+$, 100%).

HRMS (CI +ve) calculated for $C_{28}H_{42}NO_4Si$ ($M+H^+$) 484.2883, found 484.2891.

IR υ_{max} (cm^{-1}): 3380, 2929, 2852, 1454, 1244, 1098.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.25 (m, 10H, Ar), 4.64 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.63 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.59 (d, 2H, *J* 12.0 Hz, 2xC*H*HPh), 4.17 (app. dt, 1H, *J* 5.0, 5.0 Hz, H-7), 3.95 (app. t, 1H, *J* 5.3 Hz, H-2), 3.86 (app. t, 1H, *J* 4.8 Hz, H-1), 3.65 (dd, 1H, *J* 10.0, 6.0 Hz, H-8), 3.59 (dd, 1H, *J* 9.8, 6.3 Hz, H-8), 3.26 (app. t, 1H, *J* 4.8 Hz, H-7a), 3.24-3.19 (m, 1H, H-5), 2.91-2.83 (m, 2H, H-3 and H-5), 2.09-2.03 (m, 1H, H-6), 1.74-1.67 (m, 1H, H-6), 0.88 (s, 9H, *t*-Bu), 0.04 (s, 3H, CH_3), 0.03 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4 (C), 138.2 (C), 128.4 (CH), 128.3 (CH), 127.74 (CH), 127.7 (CH), 127.61 (CH), 127.6 (CH), 86.9 (C-1), 85.5 (C-2), 76.6 (C-7), 76.4 (C-7a), 72.2 (CH_2), 71.9 (CH_2), 70.8 (C-3), 65.6 (C-8), 53.2 (C-5), 34.3 (C-6), 26.0 (C*(CH$_3$)$_3$*), 18.3 (C), -5.4 (2xCH_3).

26a: R_f 0.38 (40:60 EtOAc/petrol).

$[\alpha]_D^{25}$ +13.5 (*c* 0.7, $CHCl_3$).

MS (ESI +ve) *m/z* 484 ($M + H^+$, 100%).

HRMS (CI +ve) calculated for $C_{28}H_{42}NO_4Si$ ($M+H^+$) 484.2883, found 484.2892.

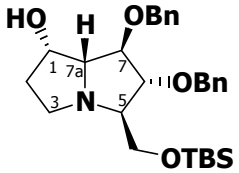
IR υ_{max} (cm^{-1}): 3349, 2922, 2850, 1248, 1069.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.26 (m, 10H, Ar), 4.98 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.88 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.81 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.66 (d, 1H, *J* 11.0 Hz, C*H*HPh), 3.93-3.89 (m, 1H, H-1), 3.84-3.79 (m, 1H, H-6), 3.44-3.38 (m, 2H, H-7 and H-8), 2.99 (dd, 1H, *J* 10.3, 5.3 Hz, H-5), 2.91 (app. t, 1H, *J* 8.3 Hz, H-3), 2.42 (app. dt, 1H, *J* 9.0, 8.5 Hz, H-3), 2.25-2.17 (m, 1H, H-2), 2.10 (app. t, 1H,

J 10.5 Hz, H-5), 1.96 (app. t, 1H, *J* 7.8 Hz, H-8a), 1.65-1.58 (m, 1H, H-2), 0.90 (s, 9H, *t*-Bu), 0.09 (s, 3H, CH_3), 0.07 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9 (C), 138.3 (C), 128.7 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.5 (CH), 127.4 (CH), 88.7 (C-7 or C-8), 81.9 (C-7 or C-8), 75.5 (CH_2), 75.1 (C-1), 74.8 (CH_2), 73.3 (C-8a), 72.8 (C-6), 57.5 (C-5), 51.7 (C-3), 32.0 (C-2), 25.8 (C*(CH₃)*$_3$), 17.9 (C), -4.6 (2xCH_3).

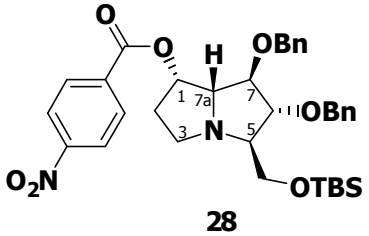
(1*S*,5*R*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1*H*-pyrrolizin-1-ol (29).



29

To a solution of 92% diastereomerically pure **26** (0.164 g, 0.34 mmol) in toluene (7 mL) was added triphenylphosphine (0.223 g, 0.85 mmol) and *para*-nitrobenzoic acid (0.142 g, 0.85 mmol). The mixture was stirred and cooled to 0 ^{o}C and diisopropyl azodicarboxylate (0.17 mL, 0.85 mmol) was added. The mixture was heated and stirred at 80 ^{o}C for 1.5 h. The volatiles were removed in *vacuo* then satd. $CuSO_4$ solution (20 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined CH_2Cl_2 extracts were washed with satd. $CuSO_4$ solution (20 mL) and water (20 mL), dried (Na_2CO_3), filtered and then evaporated to give **28** as a brown oil that was used in the next step without further purification.

(1*S*,5*R*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1*H*-pyrrolizin-1-yl 4-nitrobenzoate (28).



28

28: R_f 0.42 (30:70 EtOAc/petrol).

$[\alpha]_D^{22}$ +39 (*c* 0.9, $CHCl_3$).

MS (ESI +ve) *m/z* 633 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_{35}H_{45}N_2O_7Si$ ($M+H^+$) 633.2996, found 633.3007.

IR υ_{max} (cm^{-1}): 2924, 2858, 1724, 1528, 1270, 1102.

^1H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, 2H, *J* 8.5 Hz, Ar), 8.07 (d, 2H, *J* 8.5 Hz, Ar), 7.38-7.16 (m, 10H, Ar), 5.46-5.43 (m, 1H, H-7), 4.65 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.62 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.55 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.46 (d, 1H, *J* 12.5 Hz, C*H*HPh), 4.20 (app. t, 1H, *J* 5.0 Hz, H-1), 4.07 (dd, 1H, *J* 7.8, 5.3 Hz, H-2), 3.78 (dd, 1H, *J* 10.3, 3.8 Hz, H-8), 3.66 (app. t, 1H, *J* 4.5 Hz, H-7a), 3.63 (dd, 1H, *J* 10.5, 7.0 Hz, H-8), 3.30-3.26 (m, 1H, H-5), 3.00 (app. dt, 1H, *J* 7.5, 4.0 Hz, H-3), 2.90-2.84 (m, 1H, H-5), 2.20-2.16 (m, 2H, 2xH-6), 0.90 (s, 9H, *t*-Bu), 0.08 (s, 3H, CH_3), 0.07 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ163.9 (CO), 150.7 (C), 138.2 (C), 137.7 (C), 135.2 (C), 130.7 (CH), 128.4 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 123.5 (CH), 87.4 (C-2), 82.0 (C-1), 76.5 (C-7), 72.7 (CH_2), 72.1 (CH_2), 71.8 (C-3), 71.5 (C-7a), 66.1 (C-8), 52.7 (C-5), 34.5 (C-6), 26.0 (C*(CH₃)₃*), 18.3 (C), -5.3 (2xCH_3).

To a solution of crude **28** (0.34 mmol) in MeOH (7 mL) was added K_2CO_3 (0.075 g, 0.510 mmol). After stirring at rt for 2 h, the mixture was evaporated and dissolved in CH_2Cl_2 (15 mL) and the solution was washed with water (15 mL). The aqueous layer was extracted further with CH_2Cl_2 (3x10 mL) and the combined CH_2Cl_2 extracts were washed with brine, dried (Na_2CO_3) and evaporated. The residue was purified by FCC (50:50 EtOAc/petrol to 100% EtOAc) to give diastereomerically pure **29** as a yellow oil (93 mg, 57%). R_f 0.30 (80:20 EtOAc/petrol).

$[\alpha]_D^{22}$ -2.3 (*c* 1.8, $CHCl_3$).

MS (ESI +ve) *m/z* 484 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_{28}H_{42}NO_4Si$ ($M+H^+$) 484.2883, found 484.2873.

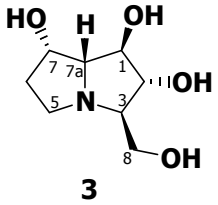
IR υ_{max} (cm^{-1}): 3402, 2923, 2850, 1256, 1100, 1047.

^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.28 (m, 10H, Ar), 4.63 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.59 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.56 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.52 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.27 (app. t, 1H, *J* 3.0 Hz, H-1), 4.16-4.14 (m, 1H, H-7), 4.11 (app. t, 1H, *J* 3.0 Hz, H-2), 3.67-3.57 (m, 3H, H-7a and 2xH-8), 3.22 (app. t, 1H,

J 8.5 Hz, H-5), 3.04 (dd, 1H, *J* 11.3, 7.3 Hz, H-3), 2.86-2.80 (m, 1H, H-5), 196-1.87 (m, 2H, 2xH-6), 0.87 (s, 9H, *t*-Bu), 0.02 (s, 3H, CH_3), 0.01 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2 (C), 137.6 (C), 128.5 (CH), 128.4 (CH), 127.84 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 85.4 (C-2), 81.9 (C-1), 74.0 (C-7a), 72.3 (C-3), 71.94 (C-7), 71.9 (CH_2), 71.8 (CH_2), 65.1 (C-8), 53.2 (C-5), 36.9 (C-6), 26.0 (C*(CH₃)₃*), 18.2 (C), -5.3 (CH_3), -5.4 (CH_3).

(1*R*,2*R*,3*R*,7*S*,7a*R*)-3-Hydroxymethyl-hexahydro-*1H*-pyrrolizine-1,2,7-triol (australine) (3).



3

To a solution of **29** (74.6 mg, 0.155 mmol) in MeOH (3 mL) was added $PdCl_2$ (41.1 mg, 0.232 mmol). The mixture was stirred at rt under an atmosphere of H_2 (balloon) for 3 h, follow by the dropwise addition of conc. HCl (10 drops) and stirring was continued at rt for 21 h. The mixture was filtered through a celite pad and the solids were washed with MeOH. The combined filtrates were evaporated *in vacuo* and the residue was dissolved in water (2 mL) and applied to a column of Amberlyst (OH^-) A-26 resin (4 cm). Elution with water followed by evaporation *in vacuo* gave australine **3** as a yellow oil (25.1 mg, 86%).

$[\alpha]_D^{22}$ +9.4 (*c* 2.4, H_2O). [Lit.[5]; $[\alpha]_D^{25}$ +8 ° (*c* 0.35, H_2O).

MS (ESI +ve) *m/z* 190 ($M + H^+$, 100%).

HRMS (EI) calculated for $C_8H_{15}NO_4$ (M^+) 189.1001, found 189.0994.

IR υ_{max} (cm^{-1}): 3318, 2944, 2873, 2484, 1388, 1332, 1123, 1041.

^{1}H NMR (500 MHz, D_2O) δ 4.37-4.35 (m, 1H, H-7), 4.22 (t, 1H, $J_{1,2} = J_{1,7a}$ = 7.8 Hz, H-1), 3.89 (dd, 1H, $J_{2,3}$ = 9.5, $J_{1,2}$ = 8.0 Hz, H-2), 3.79 (dd, 1H, $J_{8,8'}$ = 12.0 Hz, $J_{3,8}$ = 3.5 Hz, H-8), 3.61 (dd, 1H, $J_{8,8'}$ = 11.5 Hz, $J_{3,8'}$ = 7.0 Hz, H-8'), 3.17 (dd, 1H, $J_{1,7a}$ = 7.8 Hz, $J_{7,7a}$ = 4.8 Hz, H-7a), 3.15-3.12 (m, 1H, H-5), 2.74-2.69 (m, 2H, H-3 and H-5), 2.05-2.00 (m, 1H, H-6), 1.97-1.89 (m, 1H, H-6).

^{13}C NMR (125 MHz, D_2O) δ 79.5 (C-2), 73.7 (C-1), 71.3 (C-7a), 71.1 (C-3), 70.1 (C-7), 63.5 (C-8), 52.4 (C-5), 35.8 (C-6).

3·HCl salt: ^{1}H NMR (500 MHz, D_2O) δ 4.72-4.69 (m, 1H, H-7), 4.51 (app. t, 1H, *J* = 7.5 Hz, H-1), 4.18 (dd, 1H, *J* = 10.0, 8.0 Hz, H-2), 4.02 (dd, 1H, *J* = 13.0, 2.5 Hz, H-

8), 3.95-3.92 (m, 1H, H-7a), 3.92 (dd, 1H, J = 13.8, 4.3 Hz, H-8), 3.84 (app. brt, 1H, J = 9.8 Hz, H-5), 3.45-3.38 (m, 2H, H-5 and H-3), 2.36-2.31 (m, 1H, H-6), 2.05-2.00 (m, 1H, H-6), 2.29-2.27 (m, 1H, H-6).

^{13}C NMR (125 MHz, D_2O) δ 76.2 (C-2), 73.3 (C-7a), 72.1 (C-1), 71.4 (C-3), 68.7 (C-7), 56.5 (C-8), 52.9 (C-5), 35.0 (C-6).

5. Pearson, W. H.; Hines, J. V., *J. Org. Chem.* **2000,** *65*, 5785-5793.

Table 3 Physical and spectral Data for (+)-Australine[6, 7, 8, 9] and **3**.

	Natural Product	Synthetic	
		Denmark[9]	**3** (This work)
Physical Appearance	Colourless prisms[6]	Yellow oil	Yellow oil
Optical Rotation	$[\alpha]_D^{26}$ +19.3 ° (c 2.09, MeOH)[6]	$[\alpha]_D^{25}$ +8 ° (c 0.35, H_2O)[5]	$[\alpha]_D^{22}$ +9.4 (*c* 2.4, H_2O)
Melting Point	148-149 °C[6]	-	-
^{1}H NMR	500 MHz, D_2O, pH = 8.6[7]	500 MHz, D_2O	500 MHz, D_2O
	4.43 (ddd, 1H, $J_{7,7a}$ = 4.4, $J_{6,7}$ = 4.2, $J_{6,7}$ = 2.4 Hz, H-7)	4.19 (dt, 1H, J_d = 2.2, J_t = 4.2 Hz, H-7)	4.37-4.35 (m, 1H, H-7)
	4.29 (dd, 1H, $J_{1,2}$ = 8.2, $J_{1,7a}$ = 7.4 Hz, H-1)	4.04 (t, 1H, J = 7.8 Hz, H-1)	4.22 (t, 1H, $J_{1,2}$ = $J_{1,7a}$ = 7.8 Hz, H-1)
	3.96 (dd, 1H, $J_{2,3}$ = 9.5, $J_{1,2}$ = 8.2 Hz, H-2)	3.71 (dd, 1H, J = 9.5, 8.3 Hz, H-2)	3.89 (dd, 1H, $J_{2,3}$ = 9.5, $J_{1,2}$ = 8.0 Hz, H-2)
	3.85	3.60 (AB_x, dd, 1H, J = 12.0, 3.7 Hz, H-8)	3.79 (dd, 1H, $J_{8,8'}$ = 12.0, $J_{3,8}$ = 3.5 Hz, H-8)
	3.68	3.43 (AB_x, dd, 1H, J = 12.0, 6.6 Hz, H-8')	3.61 (dd, 1H, $J_{8,8'}$ = 11.5, $J_{3,8'}$ = 7.0 Hz, H-8')
	3.27 (dd, 1H, $J_{1,7a}$ = 7.4, $J_{7,7a}$ = 4.4 Hz, H-7a)	3.02 (dd, 1H, J = 7.6, 4.4 Hz, H-7a)	3.17 (dd, 1H, $J_{1,7a}$ = 7.8, $J_{7,7a}$ = 4.8 Hz, H-7a)
	3.23 (dd, 1H, $J_{5,6}$ = 11.5, $J_{5,6}$ = 6.0 Hz, H-5a)	2.98 (ddd, 1H, J = 9.8, 7.6, 2.2 Hz, H-5)	3.15-3.12 (m, 1H, H-5)
	2.80 (m, 2H, H-3 and H-5b)	2.58-2.52 (m, 2H, H-3 and H-5)	2.74-2.69 (m, 2H, H-3 and H-5)
	2.10 (ddd, 1H, $J_{5,6}$ = 6.0, $J_{6,7}$ = 2.4, $J_{5,6}$ = 2.1 Hz, H-6a)	1.87-1.82 (m, 1H, H-6)	2.05-2.00 (m, 1H, H-6)
	2.00 (ddd, 1H, $J_{5,6}$ = 11.5, $J_{5,6}$ = 7.5, $J_{6,7}$ = 4.2 Hz, H-6b)	1.79-1.71 (m, 1H, H-6).	1.97-1.89 (m, 1H, H-6).

Table 3 continued

	Natural Product[8] (Original assignment / reassignment)	**Synthetic**		
		Denmark[9]	Pearson[5*]	**3** (This work)
^{13}C NMR	125 MHz, D_2O (ref TSP δ 0.0)	100 MHz, D_2O (not given)	90 MHz, D_2O (ref dioxane)	125 MHz, D_2O (ref MeCN δ 1.47)
	81.8 (C-7 / C-2)	78.4 (C-2)	79.5	79.5 (C-2)
	75.9 (C-1)	72.7 (C-1)	73.9	73.7 (C-1)
	73.5 (C-2 / C-7a)	70.5 (C-7a)	71.7	71.3 (C-7a)
	73.3 (C-3)	70.2 (C-3)	71.4	71.1 (C-3)
	72.3 (C-7a / C-7)	69.1 (C-7)	70.3	70.1 (C-7)
	65.5 (C-8)	62.2 (C-8)	63.1	63.5 (C-8)
	54.6 (C-5)	51.6 (C-5)	52.7	52.4 (C-5)
	38.0 (C-6)	34.9 (C-6)	35.9	35.8 (C-6)

* Signals were not assigned.

5. Pearson, W. H.; Hines, J. V., *J. Org. Chem.* **2000,** *65*, 5785-5793.

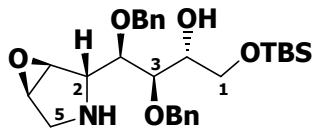
6. Molyneux, R. J.; Benson, M.; Wong, R. Y.; *J. Nat. Prod.* **1988,** *51*, 1198-1206.

7.Wormald, M. R.; Nash, R. J.; Hrnciar, P.; White, J. D.; Molyneux, R. J.; Fleet, G. W. J., *Tetrahedron: Asym.* **1998,** *9*, 2549-2558.

8. Kato, A.; Kano, E.; Adachi, I.; Molyneux, R. J.; Watson, A. A.; Nash, R. J.; Fleet, G. W. J.; Wormald, M. R.; Kizu, H.; Ikeda, K.; Asano, N., *Tetrahedron: Asym.* **2003,** *14*, 325-331.

9. Denmark, S. E.; Martinborough, E. A., *J. Am. Chem. Soc.* **1999,** *121*, 3046-3056.

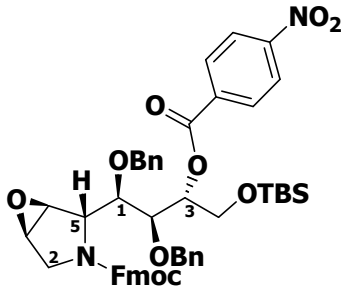
(2*R*,3*R*,4*R*)-3,4-Bis(benzyloxy)-4-((1*S*,2*S*,5*R*)-6-oxa-3-azabicyclo[3.1.0]hexan-2-yl)-1-(*tert*-butyldimethylsilyloxy)butan-2-ol (30).



30

To a solution of **19** (0.095 g, 0.131 mmol) in toluene (2 mL) was added triphenylphosphine (0.086 g, 0.328 mmol) and *para*-nitrobenzoic acid (0.055 g, 0.328 mmol). The mixture was cooled to 0 ^{o}C and diisopropyl azodicarboxylate (64.5 μL, 0.28 mmol) was added. The mixture was stirred at rt for 5 h. The volatiles were removed in *vacuo* then satd. $CuSO_4$ solution (20 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined CH_2Cl_2 extracts were washed with water (5 mL), dried (Na_2CO_3), filtered and then evaporated to give **30a** as a pale yellow oil that was used in the next step without further purification.

(1*S*,2*S*,5*R*)-(9*H*-Fluoren-9-yl)methyl 2-((1*R*,2*S*,3*R*)-1,2-bis(benzyloxy)-4-(*tert*-butyldimethylsilyloxy)-3-(4-nitrobenzoyloxy)butyl)-6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate (30a).



30a

30a: R_f 0.41 (30:70 EtOAc/petrol).

$[\alpha]_D^{22}$ +35 (*c* 2.6, $CHCl_3$).

MS (ESI +ve) *m/z* 870 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_{50}H_{55}N_2O_{10}Si$ ($M+H^+$) 871.3626, found 871.3611.

IR υ_{max} (cm^{-1}): 2950, 2940, 2857, 1720, 1701, 1529, 1271, 1101.

^{1}H NMR (500 MHz, $CDCl_3$) δ (major rotamer) 8.29-8.23 (m, 2H, Ar), 7.79-7.57 (m, 2H, Ar), 7.42-7.20 (m, 18H, Ar), 5.45 (dd, 1H, *J* 9.0, 5.5 Hz, H-3'), 4.91 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.84 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.60 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.45 (d, 2H, *J* 6.5 Hz, CH_2 (Fmoc)), 4.37 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.28-4.14 (m, 5H, H-1' or H-2', H-3 or H-4, 2xH-4' and C*H* (Fmoc)), 4.07 (d, 1H, *J* 3.0 Hz, H-3 or

H-4), 3.78 (brs, 1H, H-1' or H-2'), 3.76 (d, 1H, *J* 12.0, Hz, H-5), 3.68 (brd, 1H, *J* 2.0 Hz, H-2), 3.25 (d, 1H, *J* 11.5 Hz, H-5), 0.91 (s, 9H, *t*-Bu), 0.08 (s, 3H, CH_3), 0.07 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ (major rotamer) 163.9 (CO), 154.8 (CO), 150.5 (C), 143.8 (C), 143.5 (C), 141.2 (C), 141.1 (C), 137.6 (C), 137.4 (C), 135.2 (C), 130.7 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.5 (CH), 127.0 (CH), 126.9 (CH), 124.7 (CH), 123.4 (CH), 119.9 (CH), 80.7 (C-1'), 79.0 (C-2'), 75.8 (C-3'), 74.5 (CH_2), 74.8 (CH_2), 67.0 (*C*H_2 (Fmoc)), 61.8 (C-2), 60.5 (C-4'), 56.4 (C-3 or C-4), 55.7 (C-3 or C-4), 47.6 (C-5), 47.1 (*C*H (Fmoc)), 25.7 (C*(CH₃)₃*), 18.0 (C), -5.4 (CH_3), -5.5 (CH_3).

To a solution of crude **30a** (0.131 mmol) in MeOH (2 mL) was added K_2CO_3 (0.015 g, 0.109 mmol). After stirring at rt for 1 day, the mixture was evaporated and dissolved in CH_2Cl_2. The solution was washed with water (5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3x10 mL). The combined CH_2Cl_2 extracts were washed with brine, dried (Na_2CO_3) and evaporated. The residue was purified by FCC (50:50 EtOAc/petrol to 100% EtOAc) to give **30** as a yellow oil (36 mg, 55%). R_f 0.08 (30:70 EtOAc/petrol).

$[\alpha]_D^{23}$ +53 (*c* 2.8, $CHCl_3$).

MS (ESI +ve) *m/z* 500 ($M + H^+$, 100%).

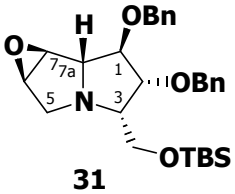
HRMS (ESI +ve) calculated for $C_{28}H_{42}NO_5Si$ ($M+H^+$) 500.2832, found 500.2836.

IR υ_{max} (cm^{-1}): 3362, 2930, 1449, 1250, 1100.

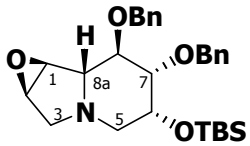
^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.25 (m, 10H, Ar), 4.86 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.71 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.62 (d, 1H, *J* 11.0 Hz, C*H*HPh), 4.57 (d, 1H, *J* 11.0 Hz, C*H*HPh), 3.81 (brs, 3H, H-2', H-3' and H-4'), 3.73 (dd, *J* 9.5, 3.5 Hz, 1H, H-4'), 3.67 (d, 1H, *J* 2.5 Hz, H-3 or H-4), 3.55 (dd, 1H, *J* 9.5, 2.0 Hz, H-1') 3.42 (d, 1H, *J* 9.5 Hz, H-2), 3.39 (d, 1H, *J* 2.5 Hz, H-3 or H-4), 3.02 (d, 1H, *J* 13.5 Hz, H-5), 2.70 (d, 1H, *J* 13.0 Hz, H-5), 0.91 (s, 9H, *t*-Bu), 0.08 (s, 6H, 2xCH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3 (C), 138.2 (C), 128.4 (CH), 128.3 (CH), 128.22 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 79.4 (C-2'), 78.5 (C-1'), 74.52 (CH_2), 74.5 (CH_2), 71.7 (C-3'), 64.4 (C-4'), 59.9 (C-2), 58.0 (C-3 or C-4), 55.8 (C-3 or C-4), 46.9 (C-5), 25.9 (C*(CH₃)₃*), 18.3 (C), -5.28 (CH_3), -5.3 (CH_3).

(1a*R*,4*S*,5*R*,6*R*,6b*S*)-5,6-Bis(benzyloxy)-4-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1a*H*-oxireno[2,3-a]pyrrolizine (31) and (1a*R*,5*R*,6*S*,7*R*,7a*S*,7b*S*)-6,7-bis(benzyloxy)-5-(*tert*-butyldimethylsilyloxy)octahydrooxireno[2,3-a]indolizine (32).



31



32

To a solution of **30** (0.500 g, 1.002 mmol) in toluene (10 mL) was added triphenylphosphine (0.657 g, 2.505 mmol). The mixture was cooled to 0 ^{o}C and diisopropyl azodicarboxylate (0.49 mL, 2.505 mmol) was added. The mixture was heated and stirred at 80 ^{o}C for 12 h. The volatiles were removed in *vacuo* then satd. $CuSO_4$ solution (20 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 x 25 mL). The combined CH_2Cl_2 extracts were washed with water (20 mL), dried (Na_2CO_3), filtered and then evaporated. The residue was purified by FCC (50:50 EtOAc/petrol to 100% EtOAc) to give to give **31** as a yellow oil (0.337 g, 70%) and **32** as a yellow oil (0.02 g, 4%).

31: R_f 0.26 (70:30 EtOAc/petrol).

$[\alpha]_D^{25}$ +43 (c 1.6, $CHCl_3$).

MS (ESI +ve) *m/z* 482 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_{28}H_{40}NO_4Si$ ($M+H^+$) 482.2727, found 482.2717.

IR υ_{max} (cm^{-1}): 2952, 2930, 2850, 1447, 1250, 1095.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.25 (m, 10H, Ar), 4.55 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.53 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.51 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.48 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.09 (d, 1H, *J* 4.0 Hz, H-2), 3.99 (app. t, 1H, *J* 9.3 Hz, H-8), 3.91 (dd, 1H, *J* 10.0, 5.0 Hz, H-8), 3.80 (d, 1H, *J* 4.5 Hz, H-1), 3.68-3.66 (m, 2H, H-6 or H-7 and H-7a), 3.60 (d, 1H, *J* 2.0 Hz, H-6 or H-7), 3.39 (app. dt, 1H, *J* 8.5, 4.3 Hz, H-3), 3.19 (d, 1H, *J* 10.5 Hz, H-5), 3.03 (d, 1H, *J* 11.5 Hz, H-5), 0.09 (s, 9H, *t*-Bu), 0.06 (s, 6H, 2xCH_3).

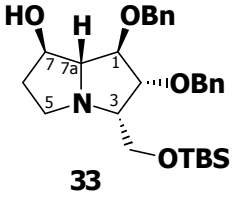
^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3 (C), 137.6 (C), 128.5 (CH), 128.3 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 127.3 (CH), 86.9 (C-2), 85.3 (C-1), 72.2 (CH_2), 71.9 (C-7a), 71.7 (CH_2), 65.7 (C-3), 58.5 (C-8), 57.6 (C-6 or C-7), 57.3 (C-6 or C-7), 48.1 (C-5), 25.9 (C*(CH$_3$)$_3$*), 18.2 (C), -5.4 (CH_3), -5.5 (CH_3).

32: R_f 0.25 (70:30 EtOAc/petrol).

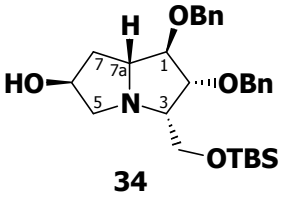
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.26 (m, 10H, Ar), 4.97 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.73 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.65 (d, 2H, *J* 11.5 Hz, 2xC*H*HPh), 4.15 (m, 1H, H-6), 3.63 (app. t, 1H, *J* 7.8 Hz, H-8), 3.55 (d, 1H, *J* 3.0 Hz, H-1 or H-2), 3.52 (d, 1H, *J* 10.5 Hz, H-3), 3.45 (d, 1H, *J* 3.0 Hz, H-1 or H-2), 3.38 (dd, 1H, *J* 10.0, 3.0 Hz, H-7), 3.20 (d, 1H, *J* 10.5 Hz, H-3), 3.15 (d, 1H, *J* 9.5 Hz, H-8a), 2.96 (dd, 1H, *J* 15.0, 1.5 Hz, H-5), 2.86 (brd, 1H, *J* 15.0 Hz, H-5), 0.91 (s, 9H, *t*-Bu), 0.10 (s, 3H, CH_3), 0.07 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5 (C), 138.3 (C), 133.2 (CH), 133.0 (CH), 128.6 (CH), 128.4 (CH), 128.2 (CH), 127.8 (CH), 127.6 (CH), 127.5 (CH), 84.1 (C-7), 75.0 (CH_2), 72.7 (C-8), 72.2 (CH_2), 71.3 (C-6), 61.8 (C-8a), 57.8 (C-1 or C-2), 54.7 (C-1 or C-2), 52.0 (C-3), 50.3 (C-5), 28.6 (C*(CH$_3$)$_3$*), 18.2 (C), -4.6 (CH_3), -4.7 (CH_3).

(1*R*,5*S*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1*H*-pyrrolizin-1-ol (33) and (2*S*,5*S*,6*R*,7*R*,7a*R*)-6,7-bis(benzyloxy)-5-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1*H*-pyrrolizin-2-ol (34).



33



34

To a solution of crude **31** (0.037 mg, 0.098 mmol) in anhydrous THF (2 mL) was added dropwise a solution of lithium aluminium hydride (1M in THF, 0.1 mL, 0.1 mmol). The mixture was stirred at rt for 12 h. The solvent was evaporated and the mixture was chromatographed on silica gel by FCC (80:20 EtOAc/petrol to 10:90 MeOH/EtOAc) to give **33** as a pale yellow oil (15.3 mg, 41%) and **34** (3.3 mg, 9%) as a pale yellow oil.

33: R_f 0.31 (5:95 MeOH/EtOAc).

$[\alpha]_D^{22}$ -4 (*c* 1.4, $CHCl_3$).

MS (ESI +ve) *m/z* 484 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_{28}H_{42}NO_4Si$ ($M+H^+$) 484.2883, found 484.2868.

IR υ_{max} (cm^{-1}): 3390, 2923, 2858, 1260, 1095.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.25 (m, 10H, Ar), 4.59 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.57 (d, 1H, *J* 10.5 Hz, C*H*HPh), 4.52 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.48 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.16 (app. dt, 1H, *J* 6.5, 5.5 Hz, H-7), 4.04 (dd, 1H, *J* 4.5, 2.0 Hz, H-2), 3.95 (dd, 1H, *J* 10.0, 7.3 Hz, H-8), 3.89-3.86 (m, 2H, H-1 and H-8), 3.35 (app. dt, 1H, *J* 6.5, 4.8 Hz, H-3), 3.30 (app. t, 1H, *J* 4.5 Hz, H-7a), 3.09 (ddd, 1H, *J* 9.3, 7.0, 6.5 Hz, H-5), 2.91-2.87 (m, 1H, H-5), 2.19-2.13 (m, 1H, H-6), 1.84-1.78 (m, 1H, H-6), 0.88 (s, 9H, *t*-Bu), 0.40 (s, 6H, 2xCH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4 (C), 138.1 (C), 128.4 (CH), 128.3 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.3 (CH), 85.9 (C-1), 85.6 (C-2), 77.7 (C-7a), 75.6 (C-7), 72.1 (CH_2), 71.4 (CH_2), 65.3 (C-3), 58.8 (C-8), 46.1 (C-5), 35.6 (C-6), 25.9 (C*(CH$_3$)$_3$*), 18.3 (C), -5.4 (CH_3), -5.5 (CH_3).

34: R_f 0.11 (5:95 MeOH/EtOAc).

$[\alpha]_D^{25}$ +10.3 (*c* 1.1, $CHCl_3$).

MS (ESI +ve) *m/z* 484 (M + H^+, 100%).

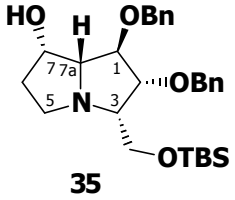
HRMS (ESI +ve) calculated for $C_{28}H_{42}NO_4Si$ ($M+H^+$) 484.2883, found 484.2863.

IR υ_{max} (cm^{-1}): 3236, 2952, 2923, 1250, 1096.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.24 (m, 10H, Ar), 4.56 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.53 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.48 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.45 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.43 (brt, 1H, *J* 4.0 Hz, H-6), 4.10 (dd, 1H, *J* 4.5, 2.0 Hz, H-2), 3.91 (d, 2H, *J* 6.0 Hz, 2xH-8), 3.88-3.83 (m, 2H, H-1 and H-7a), 3.54 (app. dt, 1H, *J* 6.0, 5.0 Hz, H-3), 3.23 (dd, 1H, *J* 10.0, 3.5 Hz, H-5), 2.96 (d, 1H, *J* 10.0 Hz, H-5), 2.18 (dd, 1H, *J* 13.0, 7.3 Hz, H-7), 1.86-1.81 (m, 1H, H-7), 0.89 (s, 9H, *t*-Bu), 0.05 (s, 6H, 2xCH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0 (C), 137.9 (C), 128.5 (CH), 128.4 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.4 (CH), 86.8 (C-1), 85.7 (C-2), 73.7 (C-6), 72.4 (CH_2), 71.5 (CH_2), 68.7 (C-7a), 64.5 (C-3), 58.5 (C-8), 56.2 (C-5), 39.5 (C-7), 25.9 (C*(CH$_3$)$_3$*), 18.3 (C), -5.4 (CH_3), -5.5 (CH_3).

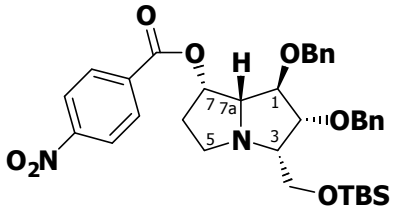
(1*S*,5*S*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1*H*-pyrrolizin-1-ol (35).



35

To a solution of **33** (0.040 g, 0.083 mmol) in toluene (2 mL) was added triphenylphosphine (0.055 g, 0.021 mmol) and *para*-nitrobenzoic acid (0.035 g, 0.021 mmol). The mixture was stirred at 0 ^{o}C and diisopropyl azodicarboxylate (41.1 μL, 0.021 mmol) was added. The mixture was stirred at rt for 8 h. The volatiles were removed in *vacuo* then satd. $CuSO_4$ solution (20 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined CH_2Cl_2 extracts were washed with water (5 mL), dried (Na_2CO_3), filtered and then evaporated to give **35a** as a brown oil that was used in the next step without further purification.

(1*S*,5*S*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyloxy)methyl)hexahydro-1*H*-pyrrolizin-1-yl 4-nitrobenzoate (35a).



35a

35a: R_f 0.39 (50:50 EtOAc/petrol).

$[\alpha]_D^{26}$ +31 (*c* 3.0, $CHCl_3$).

MS (ESI +ve) *m/z* 633 ($M + H^+$, 70%).

HRMS (ESI +ve) calculated for $C_{35}H_{45}N_2O_7Si$ ($M+H^+$) 633.2996, found 633.2986.

IR υ_{max} (cm^{-1}): 2926, 2853, 1726, 1528, 1272, 1096.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 4H, Ar), 7.37-7.12 (m, 10H, Ar), 5.63 (app. t, 1H, *J* 5.8 Hz, H-7), 4.56 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.51 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.49 (d, 1H, *J* 13.0 Hz, C*H*HPh), 4.47 (d, 1H, *J* 13.5 Hz, C*H*HPh), 4.13 (dd, 1H, *J* 4.5, 1.5 Hz, H-2), 4.07 (dd, 1H, *J* 10.3, 7.3 Hz, H-8), 4.05 (dd, 1H, *J* 4.3, 2.3 Hz, H-1), 4.00 (dd, 1H, *J* 10.3, 6.8 Hz, H-8), 3.68 (app. t, 1H, *J* 4.8 Hz, H-7a), 3.40 (app. dt, 1H, *J* 6.0, 5.0 Hz, H-3), 3.30-3.25 (m, 1H, H-5), 2.81 (app. brt, 1H, *J* 6.5 Hz, H-5), 2.30-

2.23 (m, 1H, H-6), 2.05 (brd, 1H, *J* 12.0 Hz, H-6), 0.90 (s, 9H, *t*-Bu), 0.08 (s, 3H, CH_3), 0.07 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8 (CO), 150.4 (C), 138.3 (C), 137.7 (C), 135.2 (C),130.6 (CH), 128.4 (CH), 128.3 (CH), 127.6 (CH), 127.5 (CH), 126.9 (CH), 123.3 (CH), 86.9 (C-2), 81.7 (C-1), 74.3 (C-7), 73.7 (C-7a), 72.3 (CH_2), 71.7 (CH_2), 65.4 (C-3), 59.9 (C-8), 46.2 (C-5), 34.7 (C-6), 25.9 (C*(CH$_3$)$_3$*), 18.3 (C), -5.3 (CH_3), -5.4 (CH_3).

To a solution of crude **35a** (0.083 mmol) in MeOH (2 mL) was added K_2CO_3 (0.023 g, 0.1669 mmol). After stirring at rt for 4 h, the mixture was evaporated and dissolved in CH_2Cl_2 then washed with water. The aqueous layer was extracted with CH_2Cl_2 and the combined CH_2Cl_2 extracts were washed with brine, dried (Na_2CO_3) and evaporated. The residue was purified by FCC (80:20 EtOAc/petrol to 10:90 MeOH/EtOAc) to give **35** as a pale yellow oil (26 mg, 64%). R_f 0.19 (10:90 MeOH/EtOAc).

$[\alpha]_D^{24}$ -5.3 (*c* 1.2, $CHCl_3$).

MS (ESI +ve) *m/z* 484 (M + H^+, 100%).

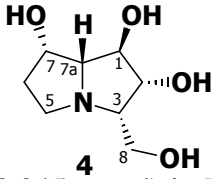
HRMS (ESI +ve) calculated for $C_{28}H_{42}NO_4Si$ (M+H^+) 484.2883, found 484.2882.

IR υ_{max} (cm^{-1}): 3418, 2930, 2850, 1673, 1250, 1089.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.26 (m, 10H, Ar), 4.68 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.62 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.57 (d, 1H, *J* 11.5 Hz, C*H*HPh), 4.56 (d, 1H, *J* 12.0 Hz, C*H*HPh), 4.25 (app. t, 1H, *J* 5.0 Hz, H-1), 4.23 (app. t, 1H, *J* 5.0 Hz, H-2), 4.12 (app. brt, 1H, *J* 2.5 Hz, H-7), 3.97 (dd, 1H, *J* 10.8, 5.3 Hz, H-8), 3.82 (dd, 1H, *J* 10.8, 5.3 Hz, H-8), 3.49 (app. t, 1H, *J* 4.3 Hz, H-7a), 3.31 (app. dt, 1H, *J* 4.8, 4.0 Hz, H-3), 3.04-2.99 (m, 1H, H-5), 2.81 (brt, 1H, *J* 7.8 Hz, H-5), 1.96-1.94 (m, 2H, 2xH-6), 0.88 (s, 9H, *t*-Bu), 0.05 (s, 3H, CH_3), 0.04 (s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4 (C), 137.9 (C), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.5 (CH), 85.5 (C-2), 79.5 (C-1), 73.2 (C-7a), 73.0 CH_2), 71.9 (CH_2), 71.2 (C-7), 62.5 (C-3), 59.3 (C-8), 43.9 (C-5), 36.9 (C-6), 26.0 (C*(CH$_3$)$_3$*), 18.6 (C), -5.3 (CH_3), -5.8 (CH_3).

(1*R*,2*R*,3*S*,7*S*,7a*R*)-3-(Hydroxymethyl)hexahydro-1*H*-pyrrolizine-1,2,7-triol (3-*epi*-australine) (4).



4

To a solution of **35** (21 mg, 0.045 mmol) in MeOH (1 mL) was added $PdCl_2$ (12 mg, 0.065 mmol). The mixture was stirred at rt under an atmosphere of H_2 (balloon) for 3 h, follow by the dropwise addition of conc. HCl (5 drops). Stirring at rt was continued for 21 h. The mixture was filtered through a celite pad and the solids were washed with MeOH. The combined filtrates were evaporated *in vacuo* and the residue was dissolved in water (1 mL) and applied to a column of Amberlyst (OH^-) A-26 resin (3 cm). Elution with water followed by evaporation *in vacuo* gave 3-*epi*-australine **4** as a brown viscous oil (7.2 mg, 88%).

$[\alpha]_D^{23}$ -10.5 (*c* 0.7, H_2O).

MS (ESI +ve) *m/z* 190 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_8H_{16}NO_4$ ($M+H^+$) 190.1079, found 190.1086.

IR υ_{max} (cm^{-1}): 3279, 2924, 2888, 1429, 1357, 1058.

^{1}H NMR (500 MHz, D_2O) δ 4.41 (brt, 1H, $J_{6,7} = J_{7,7a}$ = 4.0 Hz, H-7), 4.30 (t, 1H, $J_{1,2} = J_{1,7a}$ = 3.3 Hz, H-1), 4.15 (t, 1H, $J_{1,2} = J_{2,3}$ = 4.0 Hz, H-2), 4.01 (dd, 1H, $J_{8,8'}$ = 11.8 Hz, $J_{3,8}$ = 5.8 Hz, H-8), 3.92 (dd, 1H, $J_{8,8'}$ = 11.8 Hz, $J_{3,8'}$ = 6.3 Hz, H-8'), 3.38 (t, 1H, $J_{1,7a} = J_{7,7a}$ = 4.3 Hz, H-7a), 3.30 (dt, 1H, $J_{3,8'}$ = 5.3 Hz, $J_{2,3} = J_{3,8}$ = 4.5 Hz, H-3), 3.15-3.10 (m, 1H, H-5α), 2.88 (t, 1H, $J_{5,5} = J_{5,6}$ = 8.0 Hz, H-5β), 2.00-1.87 (m, 2H, 2xH-6).

^{13}C NMR (125 MHz, D_2O) δ 79.3 (C-2), 75.2 (C-7a), 74.7 (C-1), 70.4 (C-7), 63.9 (C-3), 57.8 (C-8), 45.3 (C-5), 35.6 (C-6).

4·HCl salt: $[\alpha]_D^{23}$ -37 (*c* 0.7, H_2O). [Lit.[10]; $[\alpha]_D^{20}$ -3.5 ° (*c* 1.35, H_2O).

^{1}H NMR (500 MHz, D_2O) δ 4.77-4.73 (m, 1H, H-7), 4.65 (s, 1H, H-1), 4.34 (d, 1H, *J* = 3.5 Hz, H-2), 4.29 (d, 1H, *J* = 5.5 Hz, H-7a), 4.16 (dd, 1H, *J* = 12.0, 4.5 Hz, H-8), 4.13-4.04 (m, 2H, H-8 and H-3), 3.74 (dd, 1H, *J* = 11.3, 5.3 Hz, H-5), 3.71-3.65 (m, 1H, H-5), 2.28 (dd, 1H, *J* = 14.0, 5.0 Hz, H-6), 2.21-2.13 (m, 1H, H-6).

^{13}C NMR (125 MHz, D_2O) δ 79.3 (C-7a), 77.4 (C-2), 74.2 (C-1), 69.3 (C-7), 67.1 (C-3), 56.1 (C-8), 48.4 (C-5), 35.0 (C-6).

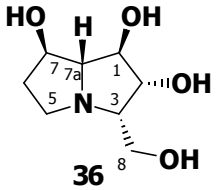
10. Nash, R. J.; Fellows, L. E.; Dring, J. V.; Fleet, G. W. J.; Derome, A. E.; Hamor, T. A.; Scofield, A. M.; Watkin, D. J., *Tetrahedron Lett.* **1988,** *29*, 2487-2490.

Table 4 Physical and spectral Data for (-)-3-*Epi*-australine[10] and **4**.

	3-*Epi*-australine[10]	Synthetic **4**	
Physical Appearance	oil	brown viscous oil	
Optical Rotation	$[\alpha]_D^{20}$ -3.5 ° (*c* 1.35, H_2O), HCl salt.	$[\alpha]_D^{23}$ -37 (*c* 0.7, H_2O), HCl salt	
^{1}H NMR	500 MHz, D_2O	500 MHz, D_2O	
	4.24 (dt, 1H, *J* = 4.5, 2.0 Hz, H-7)	4.41 (brt, 1H, $J_{6,7} = J_{7,7a} = 4.0$ Hz, H-7)	
	4.12 (t, 1H, *J* = 3.5 Hz, H-1)	4.30 (t, 1H, $J_{1,2} = J_{1,7a} = 3.3$ Hz, H-1)	
	3.96 (dd, 1H, *J* = 4.5, 3.5 Hz, H-2)	4.15 (t, 1H, $J_{1,2} = J_{2,3} = 4.0$ Hz, H-2)	
	3.80-3.70 (2H, AB part of ABX, CH_2OH)	4.01 (dd, 1H, $J_{8,8'} = 11.8$ Hz, $J_{3,8} = 5.8$ Hz, H-8)	
		3.92 (dd, 1H, $J_{8,8'} = 11.8$ Hz, $J_{3,8'} = 6.3$ Hz, H-8')	
	3.25 (dd, 1H, *J* = 4.5, 4.0 Hz, H-7a)	3.38 (t, 1H, $J_{1,7a} = J_{7,7a} = 4.3$ Hz, H-7a)	
	3.16 (dt, 1H, *J* = 6.0, 4.5 Hz, H-3)	3.30 (dt, 1H, $J_{3,8'} = 5.3$ Hz, $J_{2,3} = J_{3,8} = 4.5$ Hz, H-3)	
	2.96 (ddd, 1H, *J* = 11.5, 9.0, 6.0 Hz, H-5)	3.15-3.10 (m, 1H, H-5)	
	2.74 (m, 1H, H-5)	2.88 (t, 1H, $J_{5,5} = J_{5,6} = 8.0$ Hz, H-5)	
	1.82 (m, 2H, 2xH-6)	2.00-1.87 (m, 2H, 2xH-6)	
^{13}C NMR	125 MHz, D_2O (ref not given)	125 MHz, D_2O (ref MeCN δ 1.47)	Δδ (ppm)
	78.5 (C-2)	79.3 (C-2)	0.8
	74.8 (C-7a)	75.2 (C-7a)	0.4
	74.0 (C-1)	74.7 (C-1)	0.7
	69.6 (C-7)	70.4 (C-7)	0.8
	63.5 (C-3)	63.9 (C-3)	0.4
	56.9 (C-8)	57.8 (C-8)	0.9
	44.9 (C-5)	45.3 (C-5)	0.4
	34.8 (C-6)	35.6 (C-6)	0.8

10. Nash, R. J.; Fellows, L. E.; Dring, J. V.; Fleet, G. W. J.; Derome, A. E.; Hamor, T. A.; Scofield, A. M.; Watkin, D. J., *Tetrahedron Lett.* **1988,** *29*, 2487-2490.

(1*R*,2*R*,3*S*,7*R*,7a*R*)-3-(Hydroxymethyl)hexahydro-1H-pyrrolizine-1,2,7-triol (3,7-D*iepi*-australine) (36).



To a solution of **33** (20 mg, 0.041 mmol) in MeOH (1 mL) was added $PdCl_2$ (11 mg, 0.062 mmol). The mixture was stirred at rt under an atmosphere of H_2 (balloon) for 3 h, follow by the dropwise addition of conc. HCl (5 drops) at rt for 15 h. The mixture was filtered through a celite pad and the solids were washed with MeOH. The combined filtrates were evaporated *in vacuo* and the residue was dissolved in water (1 mL) and applied to a column of Amberlyst (OH^-) A-26 resin (3 cm). Elution with water followed by evaporation *in vacuo* gave 3,7-di*epi*-australine **36** as a white solid (7.0 mg, 90%).

$[\alpha]_D^{24}$ -9.3 (*c* 1.1, H_2O).

MS (ESI +ve) *m/z* 190 ($M + H^+$, 100%).

HRMS (ESI +ve) calculated for $C_8H_{16}NO_4$ ($M+H^+$) 190.1079, found 190.1074.

IR υ_{max} (cm^{-1}): 3370, 3309, 2509, 1454, 1202, 1060.

^{1}H NMR (500 MHz, D_2O) δ 4.30 (dt, 1H, $J_{6,7} = J_{7,7a} = 6.5$ Hz, $J_{6,7} = 6.0$ Hz, H-7), 4.16 (brd, 1H, $J_{2,3} = 3.5$ Hz, H-2), 4.13 (s, 1H, H-1), 3.97 (dd, 1H, $J_{8,8'} = 11.8$ Hz, $J_{3,8} = 7.0$ Hz, H-8), 3.92 (dd, 1H, $J_{8,8'} = 12.0$ Hz, $J_{3,8'} = 7.0$ Hz, H-8'), 3.28 (ddd, 1H, $J_{2,3} = 9.0$, $J_{3,8} = 7.0$, $J_{2,3} = 4.0$ Hz, H-3), 3.11 (ddd, 1H, $J_{5,5} = 10.0$, $J_{5,6} = 10.0$, $J_{5,6} = 6.0$ Hz, H-5α), 3.06 (dd, 1H, $J_{7,7a} = 2.0$, $J_{1,7a} = 5.5$ Hz, H-7a), 2.98 (t, 1H, $J_{5,5} = J_{5,6} = 8.5$ Hz, H-5β), 2.23-2.18 (m, 1H, H-6α), 1.80-1.72 (m, 1H, H-6β).

^{13}C NMR (125 MHz, D_2O) δ 80.5 (C-1), 79.8 (C-2), 78.2 (C-7a), 75.1 (C-7), 64.9 (C-3), 57.6 (C-8), 46.4 (C-5), 34.5 (C-6).

36·HCl salt: $[\alpha]_D^{21}$ -21 (*c* 0.63, H_2O), HCl salt. [Lit.[11] for *ent*-**36**·HCl; $[\alpha]_D^{20}$ +33° (*c* 0.1, H_2O).

^{1}H NMR (500 MHz, D_2O) δ 4.63 (dt, 1H, $J_{6,7} = 8.0$ Hz, $J_{6,7} = J_{7,7a} = 6.0$ Hz, H-7), 4.41 (brs, 1H, H-1), 4.35 (d, 1H, $J_{1,2} = 2.5$ Hz H-2), 4.13 (dd, 1H, $J_{8,8'} = 12.5$ Hz, $J_{3,8} = 5.0$ Hz, H-8), 4.10 (d, 1H, $J_{8,8'} = 9.0$ Hz, H-8), 4.06-4.02 (m, 1H, H-3), 3.84 (d, 1H, $J_{7,7a} = 6.5$ Hz, H-7a), 3.75 (dd, 1H, $J_{5,5} = 11.3$ Hz, $J_{5,6} = 6.3$ Hz, H-5), 3.73 (dd, 1H, $J_{5,5} = 10.8$ Hz, $J_{5,6} = 6.3$ Hz, H-5), 2.54-2.48 (m, 1H, H-6), 2.07-1.99 (m, 1H, H-6).

^{13}C NMR (125 MHz, D_2O) δ 80.1 (C-7a), 77.6 (C-1), 77.1 (C-2), 73.1 (C-7), 67.7 (C-3), 55.8 (C-8), 48.6 (C-5), 33.1 (C-6).

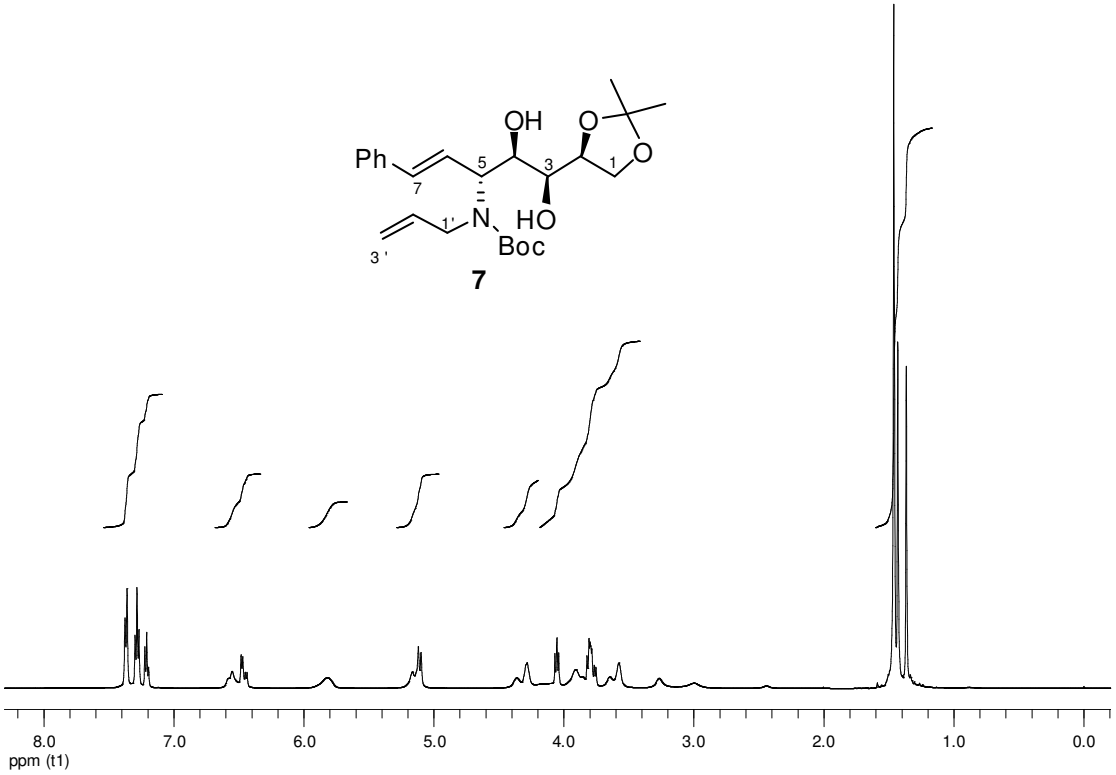
11. Chikkanna, D.; Singh, O. V.; Kong, S. B.; Han, H.,. *Tetrahedron Lett.* **2005,** *46*, 8865-8868.

Table 5 Physical and spectral Data for (+)-1,2-Di*epi*-alexine·HCl salt [ent-**36**][11] and **36**·HCl salt [3,7-di*epi*-australine·HCl salt].

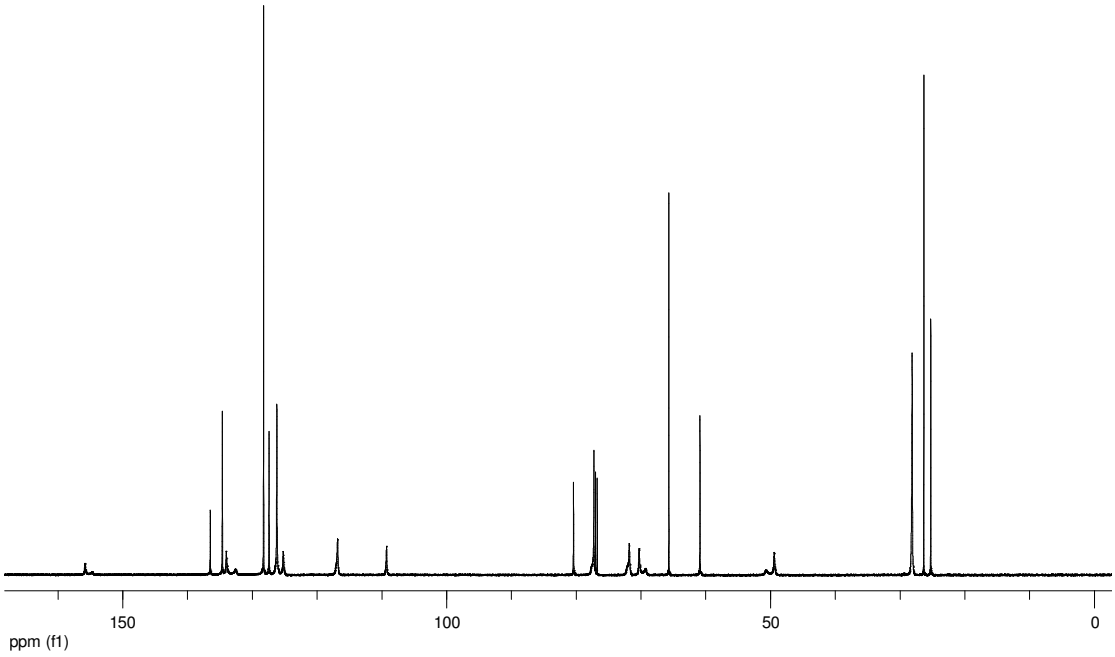
	1,2-Di*epi*-alexine·HCl salt [11]	Synthetic **36**·HCl salt	
Physical Appearance	Not reported	Pale yellow viscous oil	
Optical Rotation	$[\alpha]_D^{20}$ +33° (*c* 0.1, H_2O), HCl salt	$[\alpha]_D^{21}$ -21 (*c* 0.63, H_2O), HCl salt	
^{1}H NMR	500 MHz, D_2O	500 MHz, D_2O	
	4.62-4.58 (m, 1H)	4.63 (dt, 1H, $J_{6,7}$ = 8.0 Hz, $J_{6,7}$ = $J_{7,7a}$ = 6.0 Hz, H-7)	
	4.37 (brs, 1H)	4.41 (brs, 1H, H-1)	
	4.32 (brs, 1H)	4.35 (d, 1H, $J_{1,2}$ = 2.5 Hz H-2)	
	4.12-3.98 (m, 3H)	4.13 (dd, 1H, $J_{8,8'}$ = 12.5 Hz, $J_{3,8}$ = 5.0 Hz, H-8) 4.10 (d, 1H, $J_{8,8'}$ = 9.0 Hz, H-8) 4.06-4.02 (m, 1H, H-3)	
	3.80 (d, 1H, *J* = 5.8 Hz)	3.84 (d, 1H, $J_{7,7a}$ = 6.5 Hz, H-7a)	
	3.75-3.60 (m, 2H)	3.75 (dd, 1H, $J_{5,5}$ = 11.3 Hz, $J_{5,6}$ = 6.3 Hz, H-5α)	
		3.73 (dd, 1H, $J_{5,5}$ = 10.8 Hz, $J_{5,6}$ = 6.3 Hz, H-5β)	
	2.51-2.44 (m, 1H)	2.54-2.48 (m, 1H, H-6)	
	2.04-1.96 (m, 1H)	2.07-1.99 (m, 1H, H-6)	
^{13}C NMR	75 MHz, D_2O (ref not given)	125 MHz, D_2O (ref MeCN δ 1.47)	Δδ (ppm)
	81.8	80.1 (C-7a)	1.7
	79.4	77.6 (C-1)	1.8
	78.9	77.1 (C-2)	1.8
	74.8	73.1 (C-7)	1.7
	69.8	67.7 (C-3)	2.1
	57.6	55.8 (C-8)	1.8
	50.3	48.6 (C-5)	1.7
	34.9	33.1 (C-6)	1.8

11. Chikkanna, D.; Singh, O. V.; Kong, S. B.; Han, H.,. *Tetrahedron Lett.* **2005,** *46*, 8865-8868.

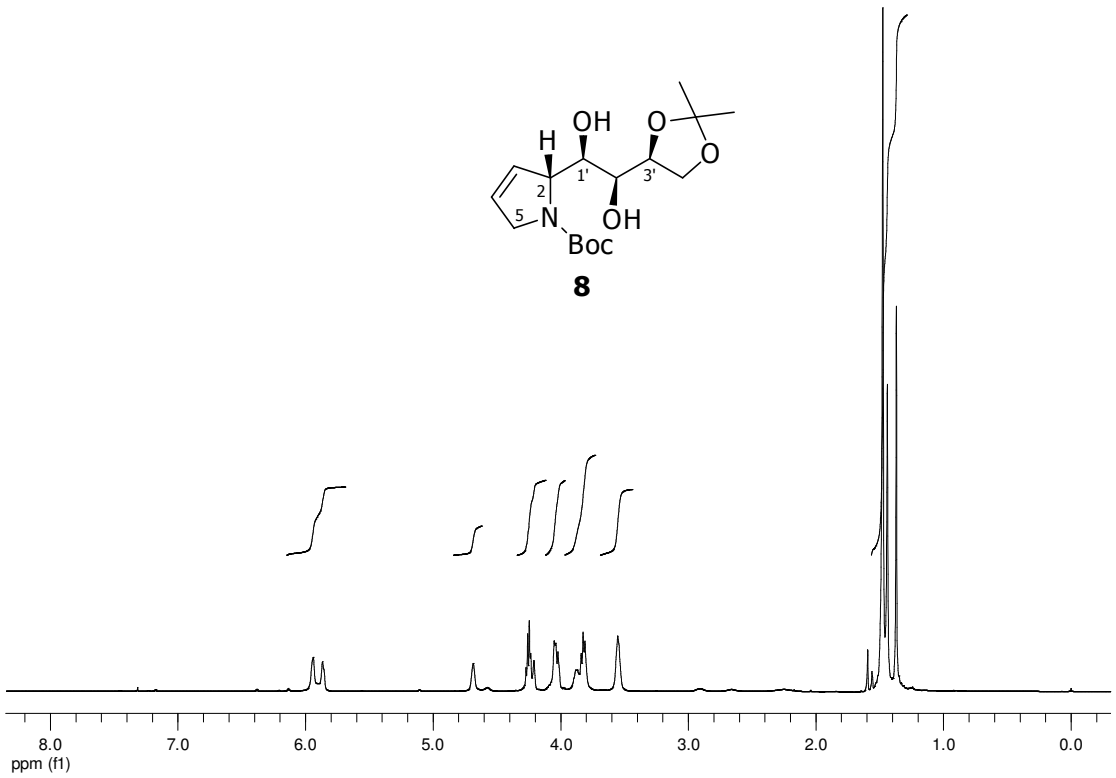
^{1}H NMR (5OO MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (5OO MHz, $CDCl_3$)



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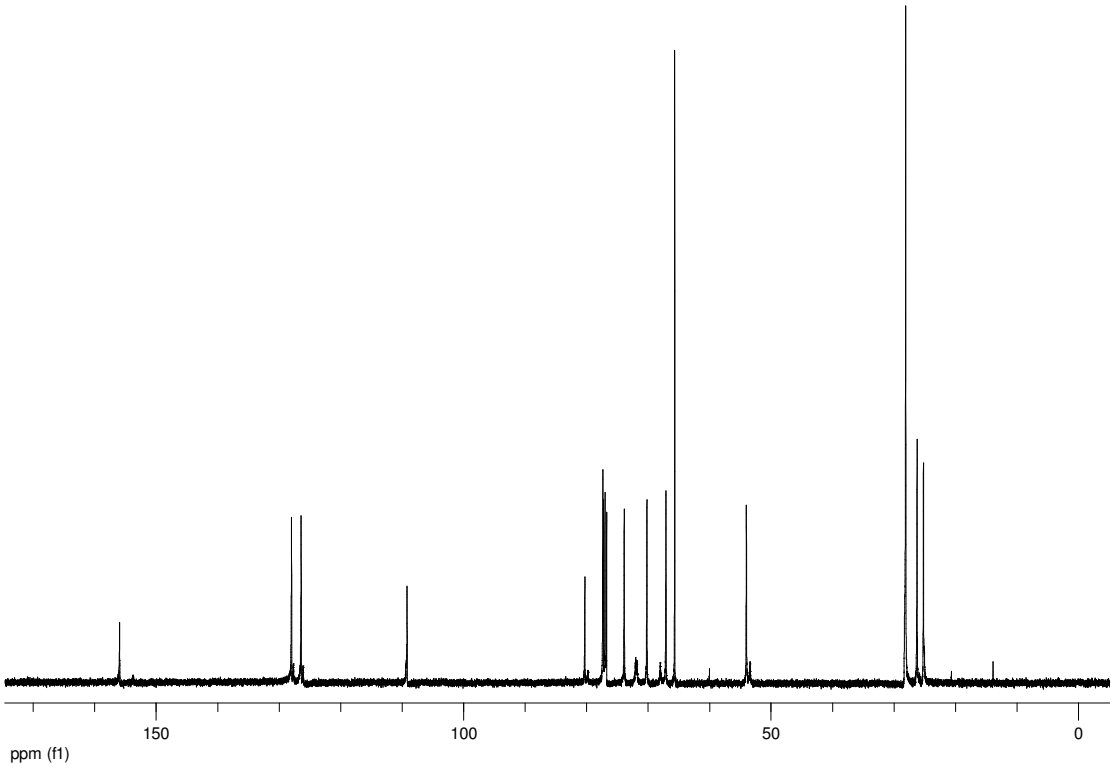
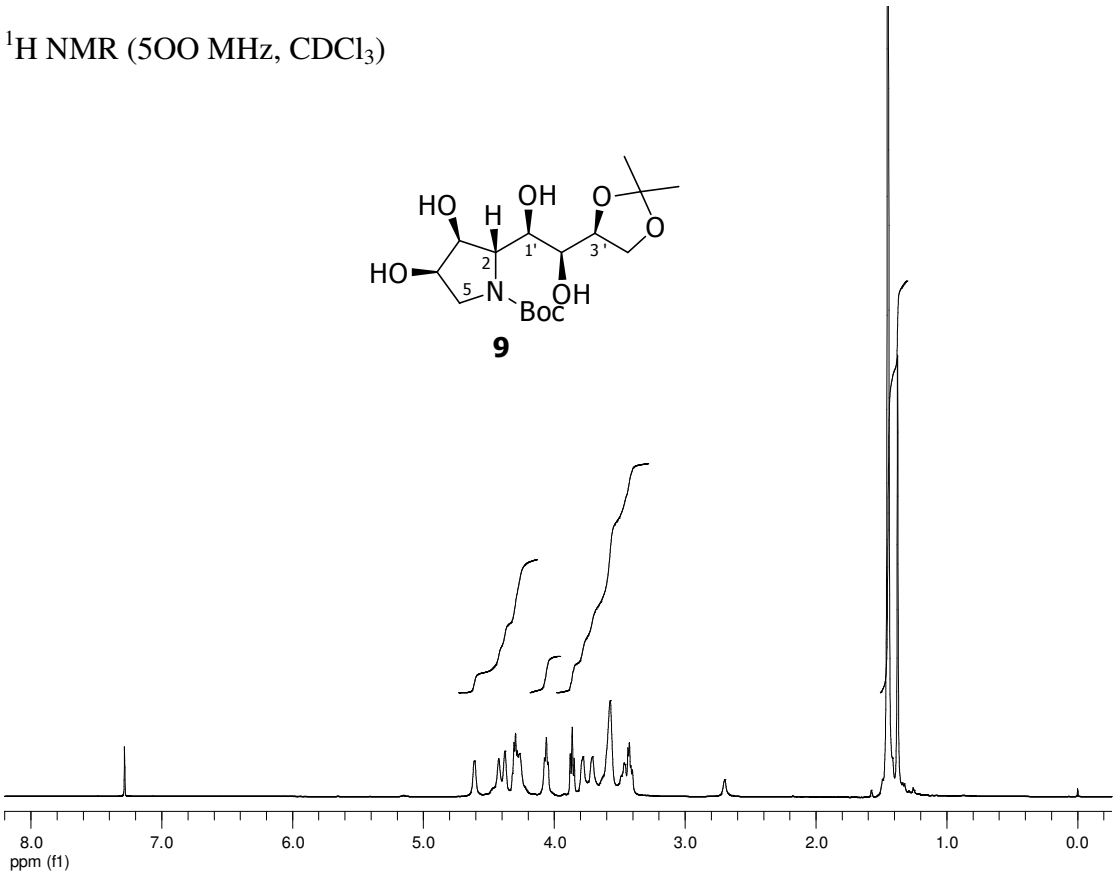
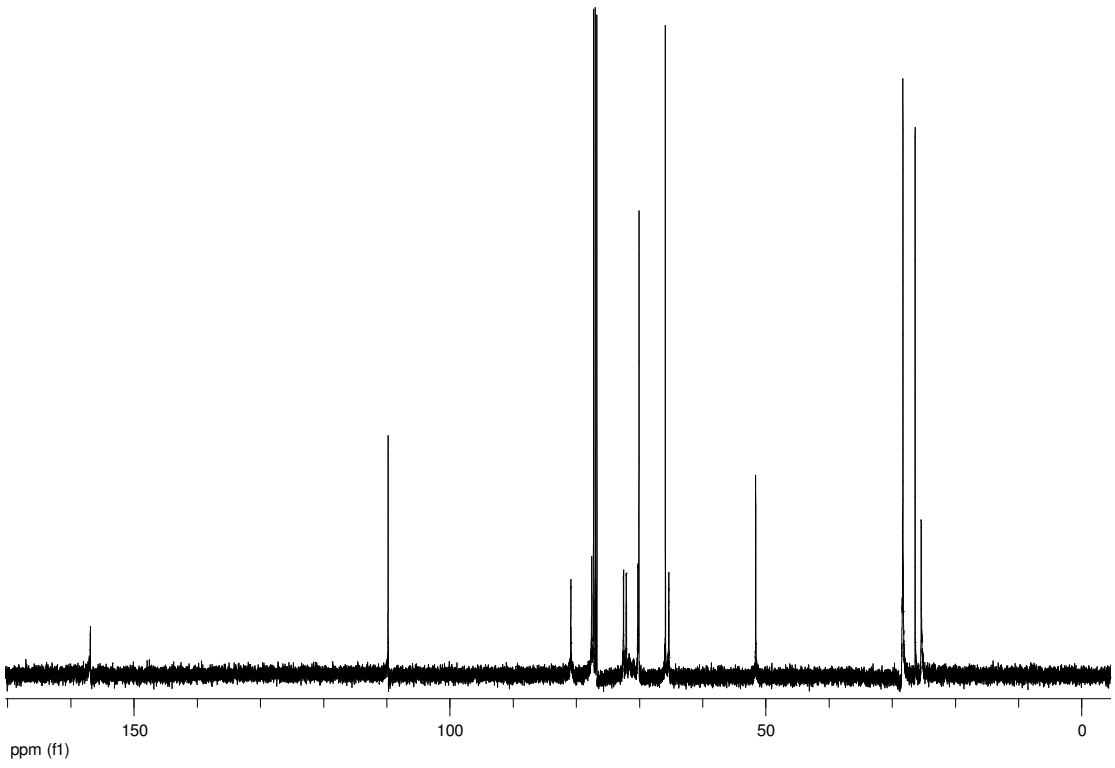
^{13}C NMR (125 MHz, $CDCl_3$)



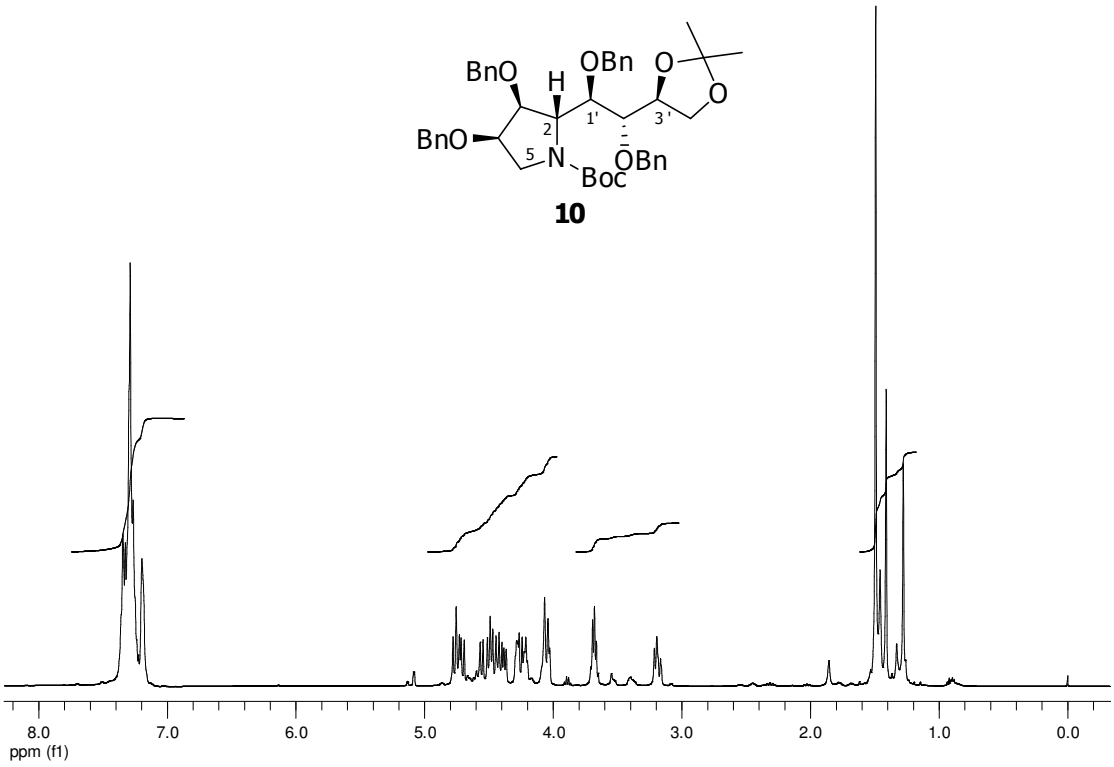
^{1}H NMR (5OO MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (5OO MHz, $CDCl_3$)



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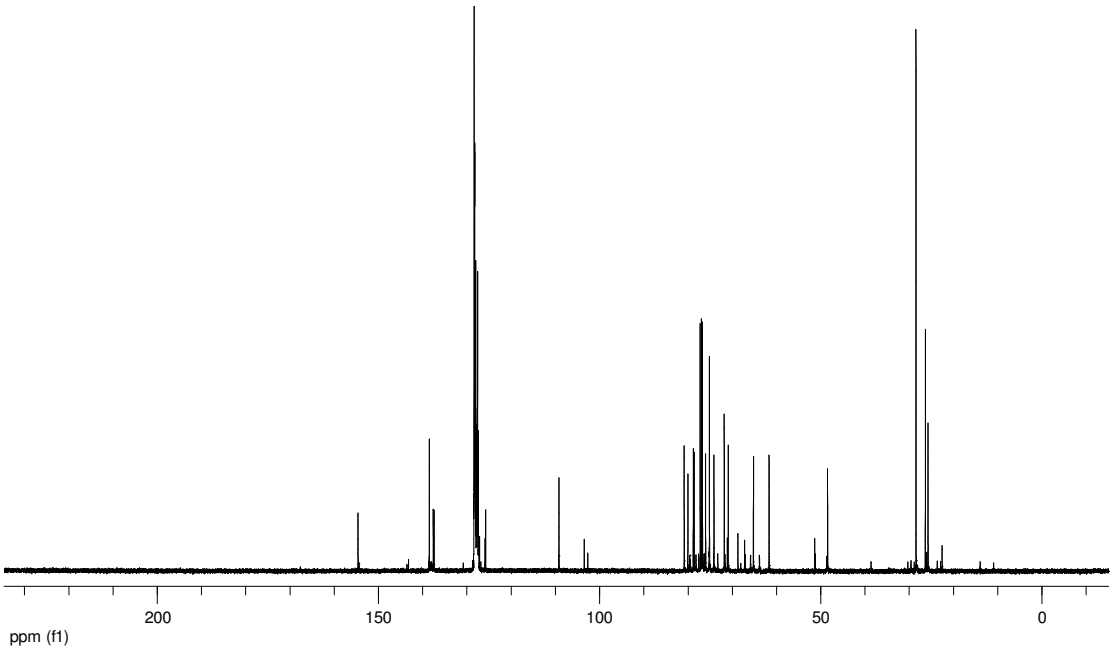
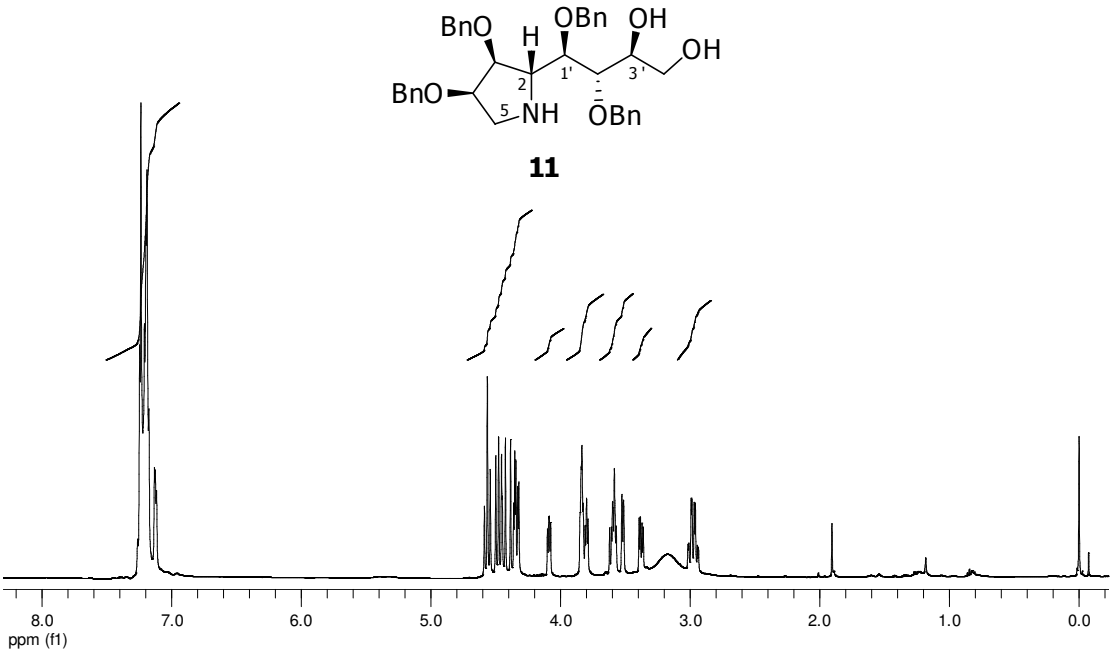
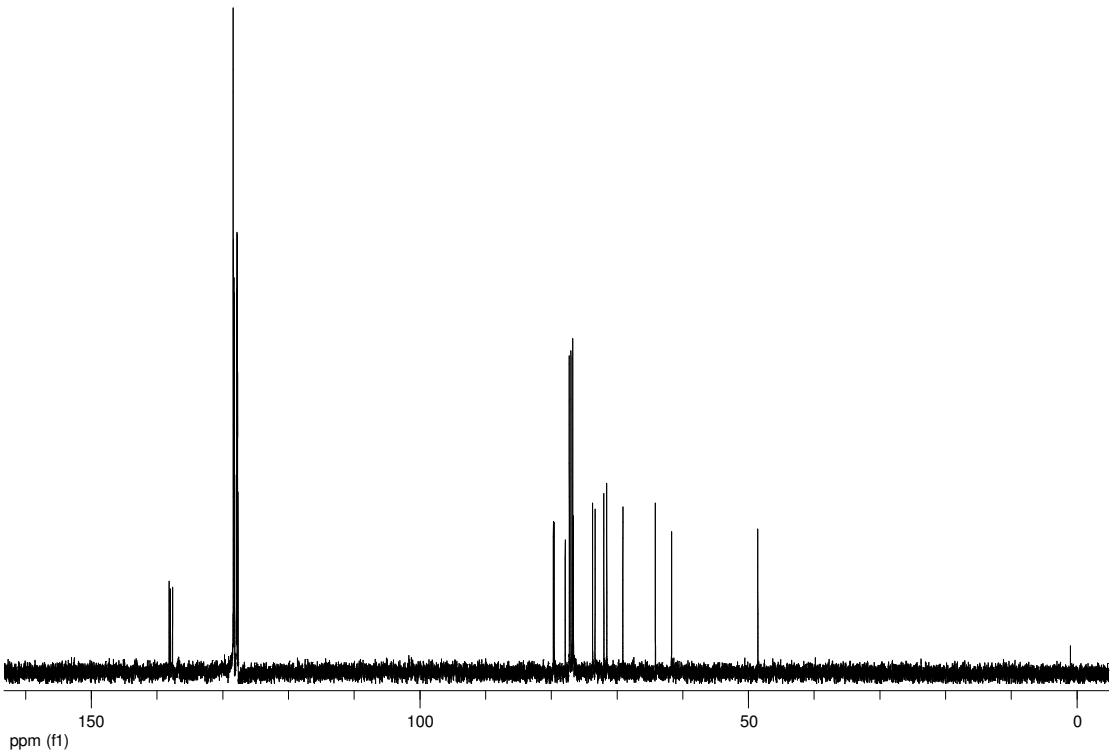
^{13}C NMR (125 MHz, $CDCl_3$)



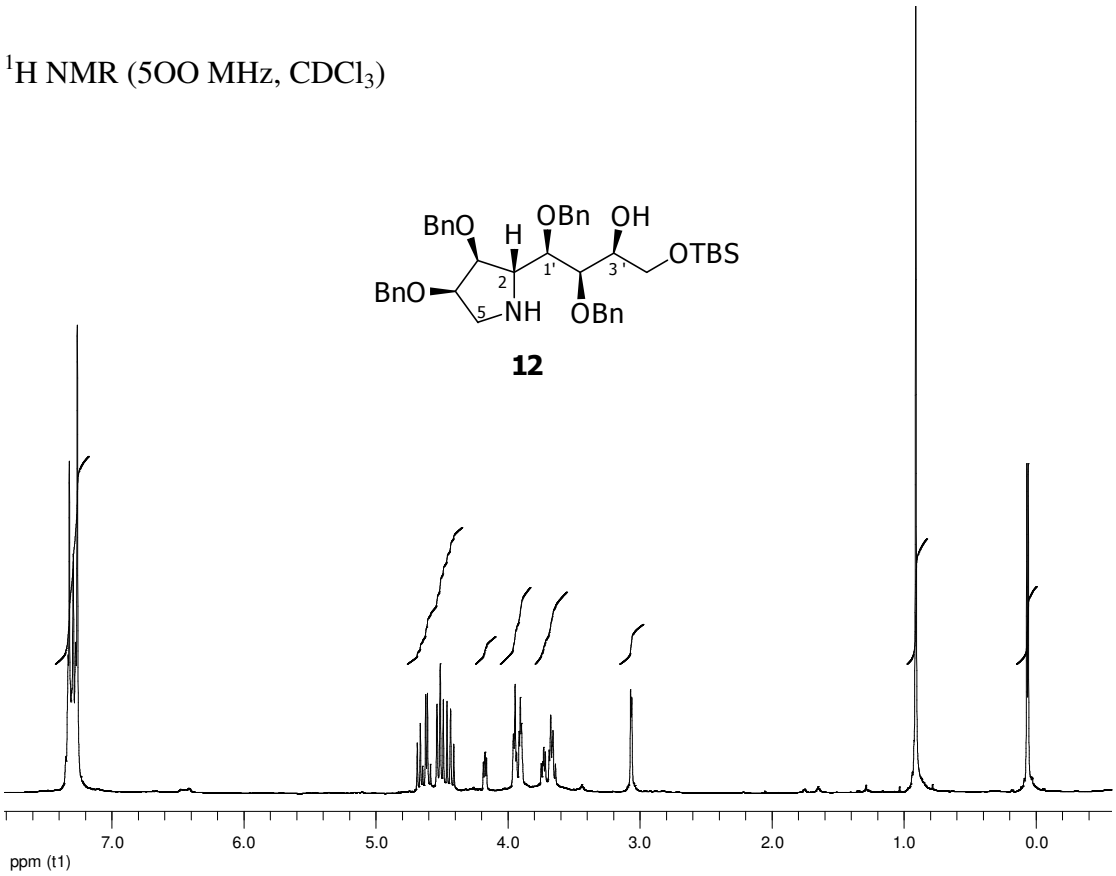
^{1}H NMR (5OO MHz, $CDCl_3$)



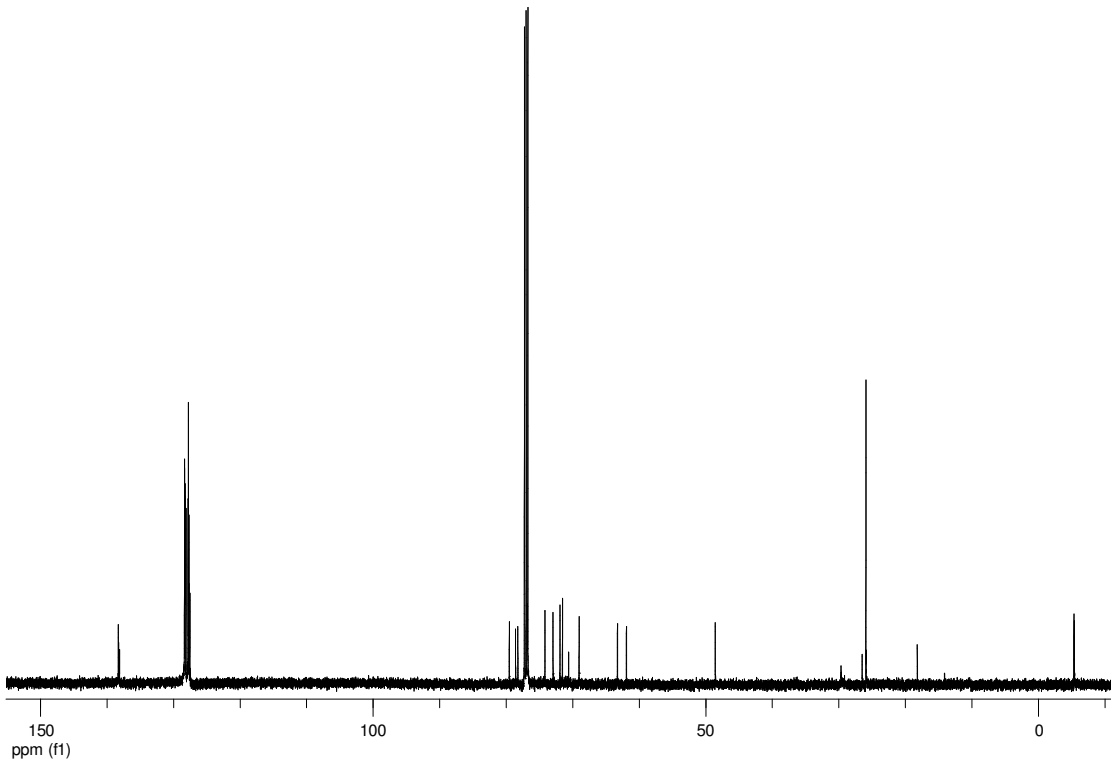
^{13}C NMR (125 MHz, $CDCl_3$)



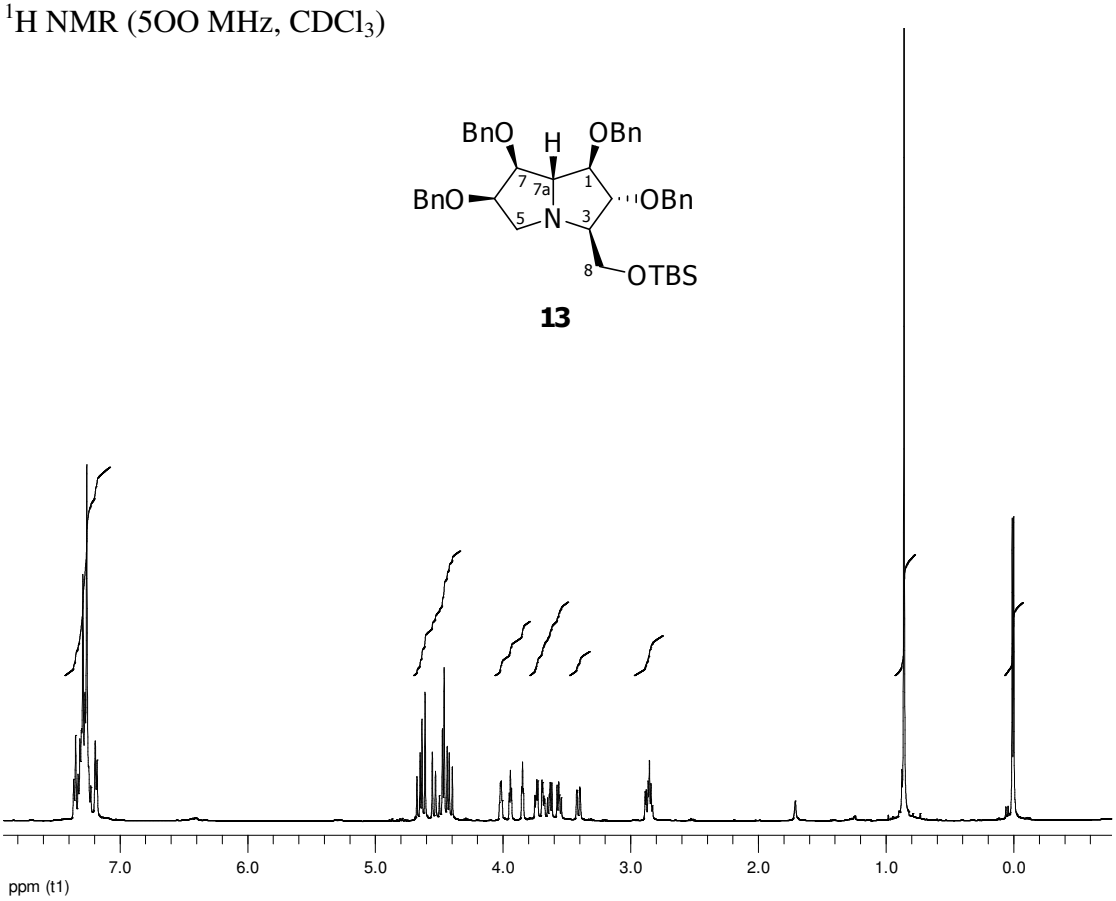
^{1}H NMR (5OO MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)

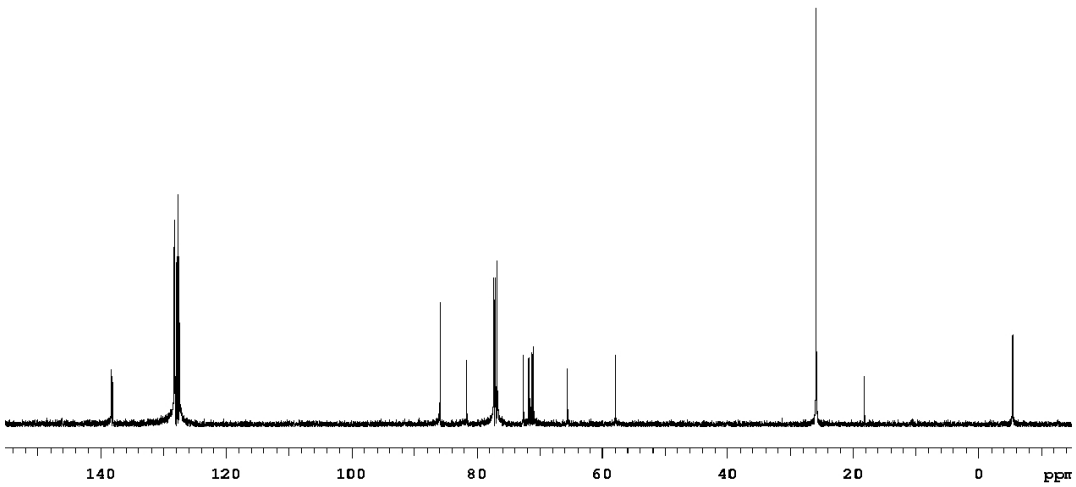


^{1}H NMR (5OO MHz, $CDCl_3$)

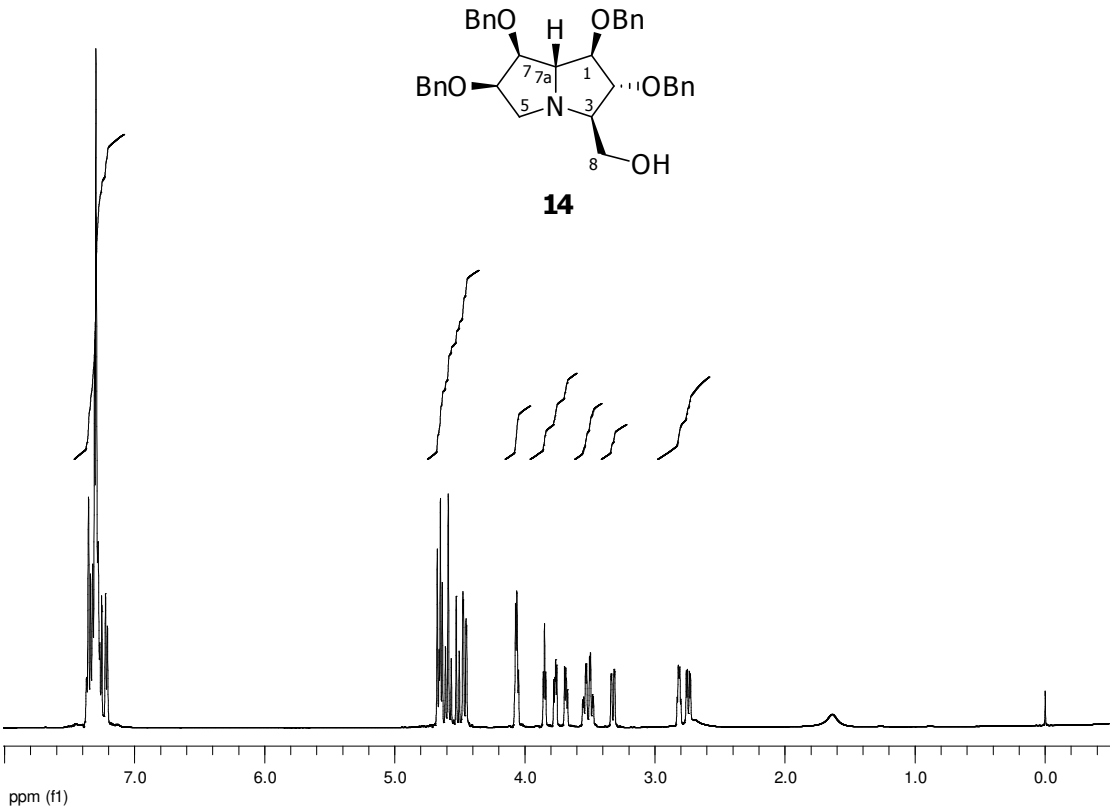


13

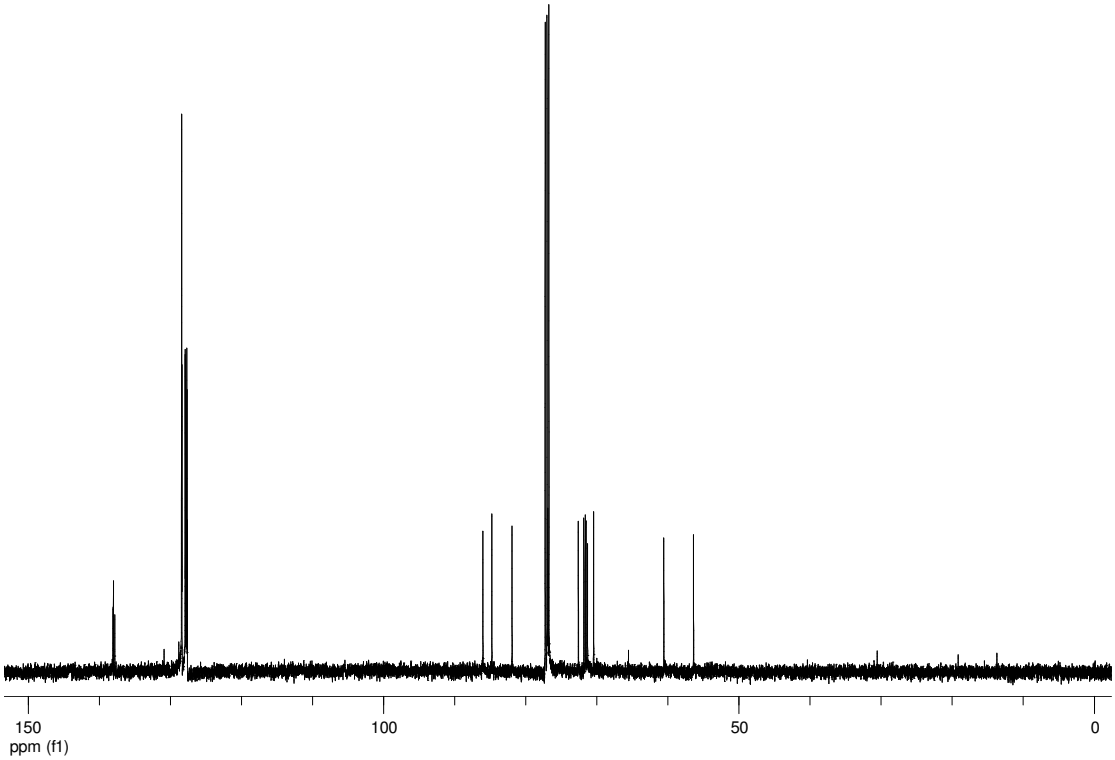
^{13}C NMR (125 MHz, $CDCl_3$)



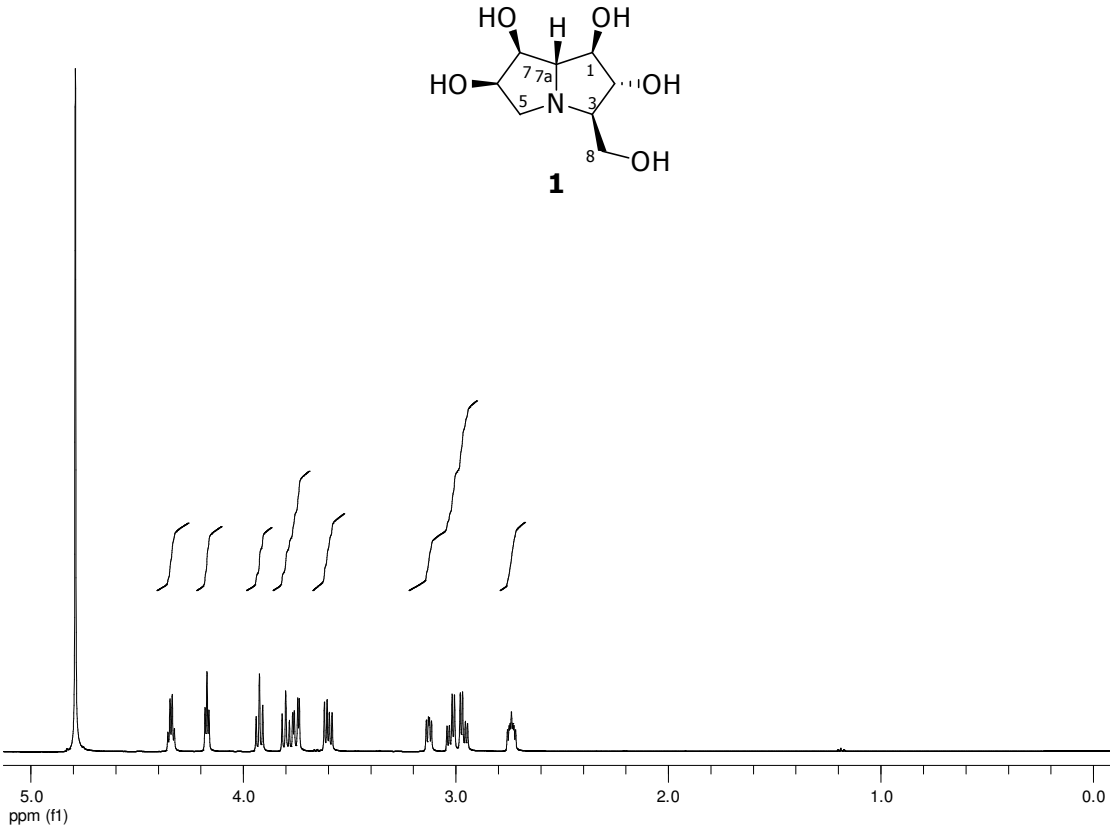
^{1}H NMR (5OO MHz, $CDCl_3$)



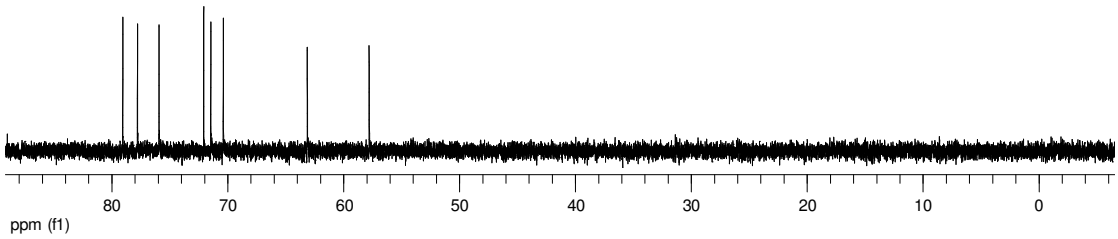
^{13}C NMR (125 MHz, $CDCl_3$)

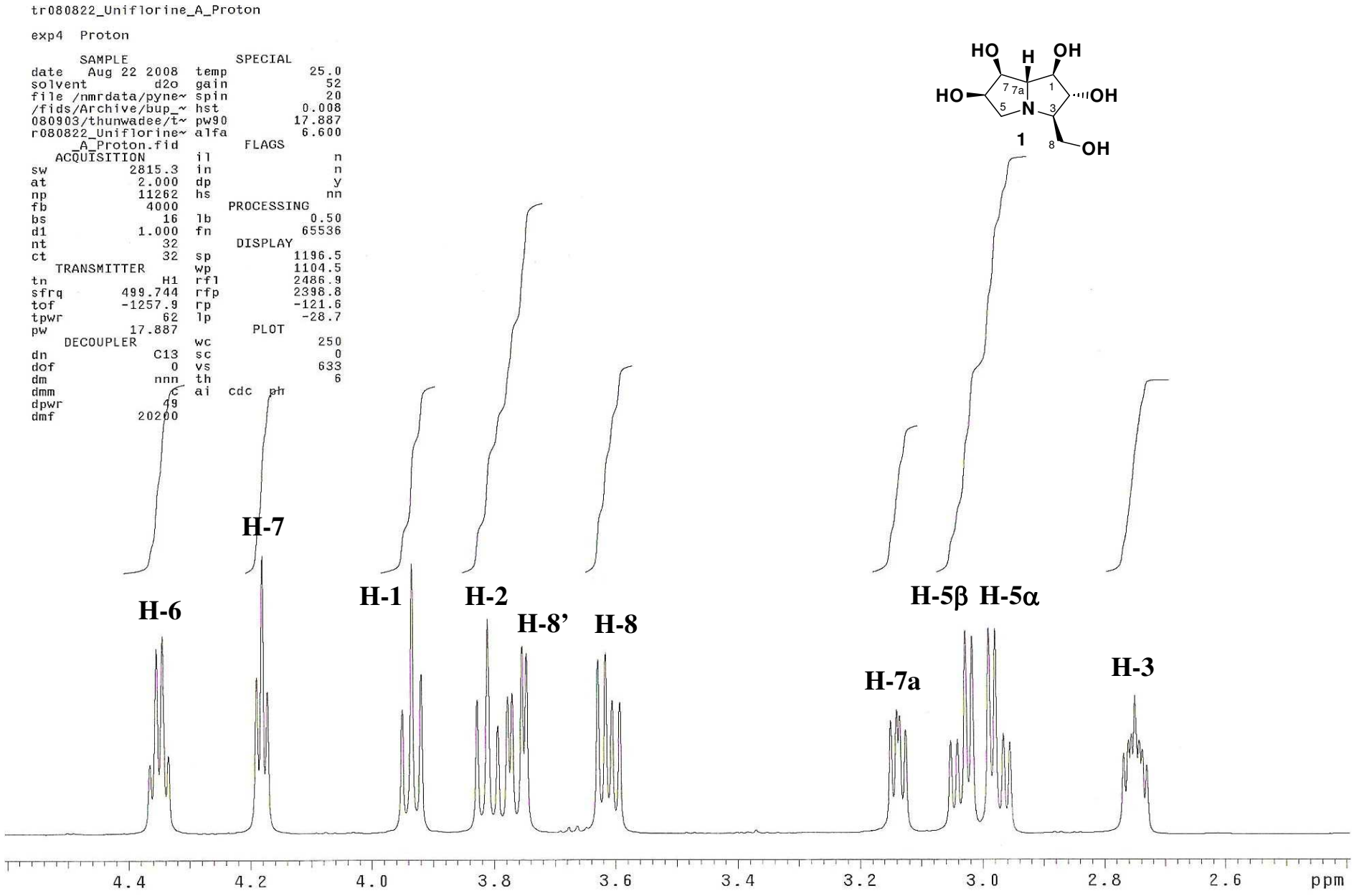


^{1}H NMR (5OO MHz, D_2O)



^{13}C NMR (125 MHz, D_2O)





^{1}H NMR (5OO MHz, D_2O)

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file /nmrdata/pyne~  spin       not used
/fids/Archive/bup_~  hst           0.008
080903/thunwadee/t~  pw90         15.600
r080821_Uniflroine~  alfa          6.600
        _A_13C.fid           FLAGS
   ACQUISITION       il              n
sw          31421.8   in              n
at            1.300   dp              y
np            81726   hs             nn
fb            17000       PROCESSING
bs               64   lb           0.50
d1            1.000   fn       not used
nt              776       DISPLAY
ct              320   sp         5779.7
   TRANSMITTER        wp         5026.7
tn               C13  rfl         9423.4
sfrq        125.716   rfp         7269.4
tof          1884.0   rp          -176.6
tpwr             63   lp          -187.8
pw            7.800         PLOT
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dn                H1  sc              0
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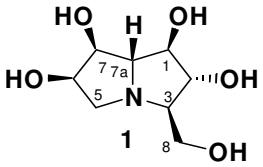
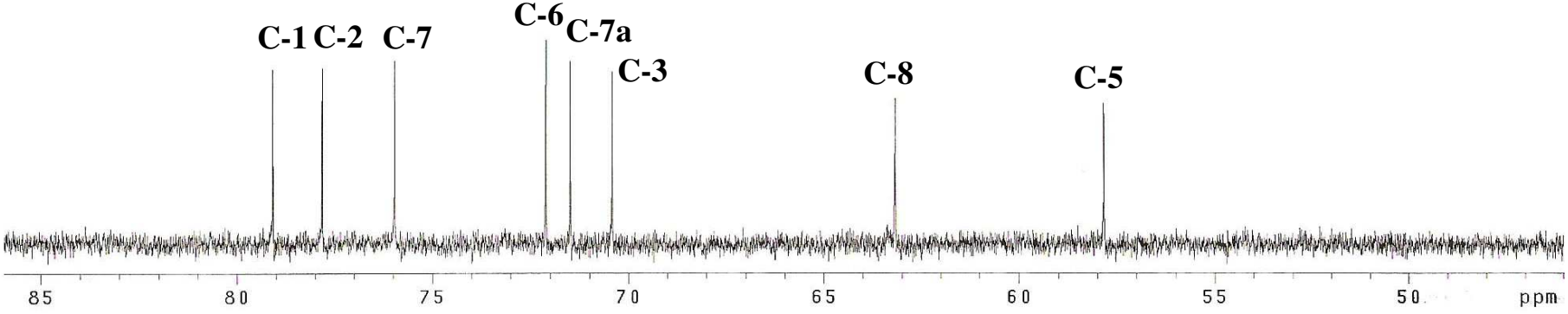
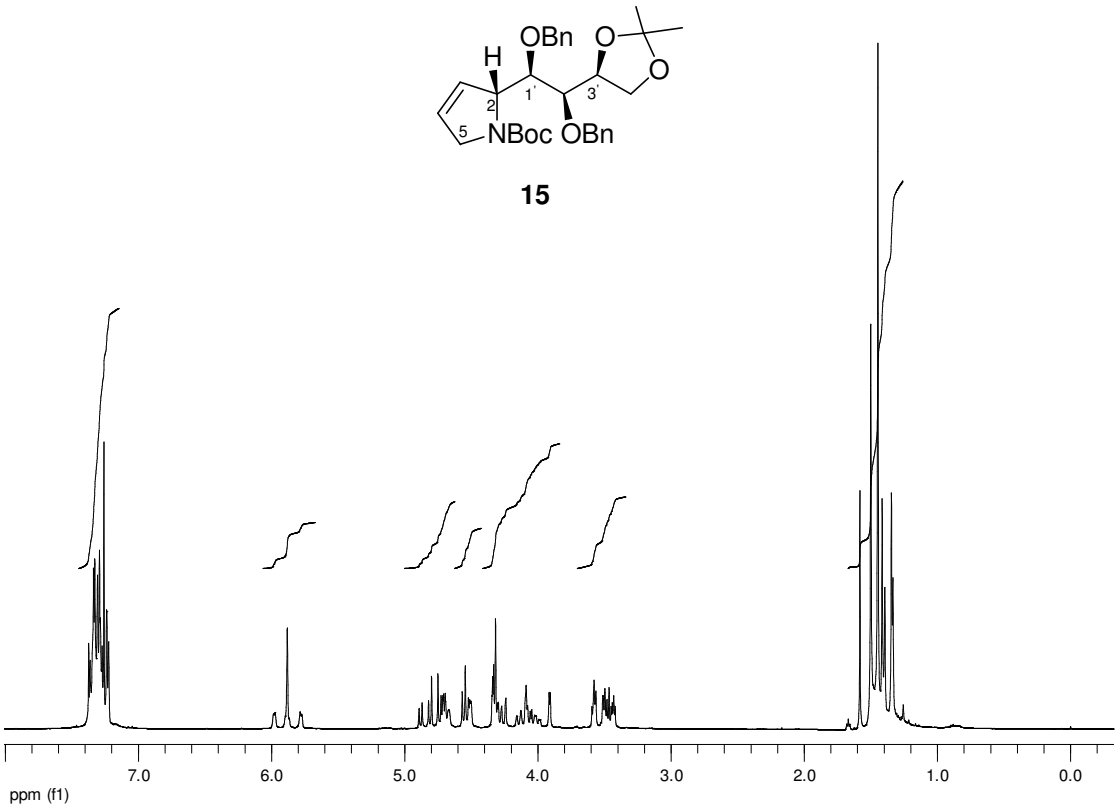




^{13}C NMR (125 MHz, D_2O)

^{1}H NMR (5OO MHz, $CDCl_3$)



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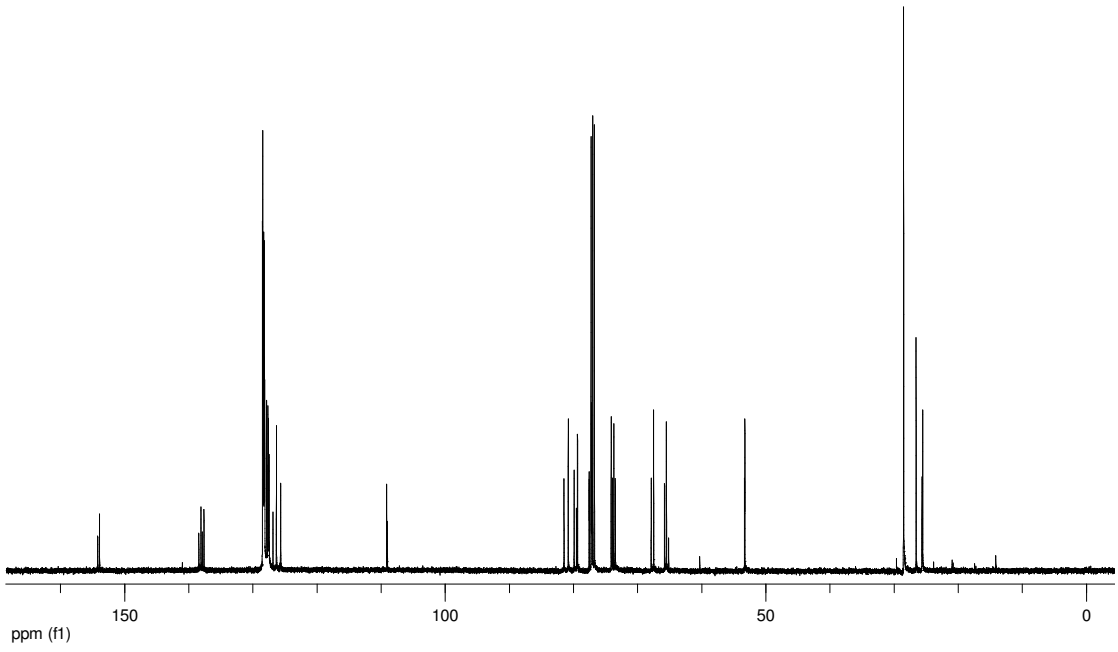
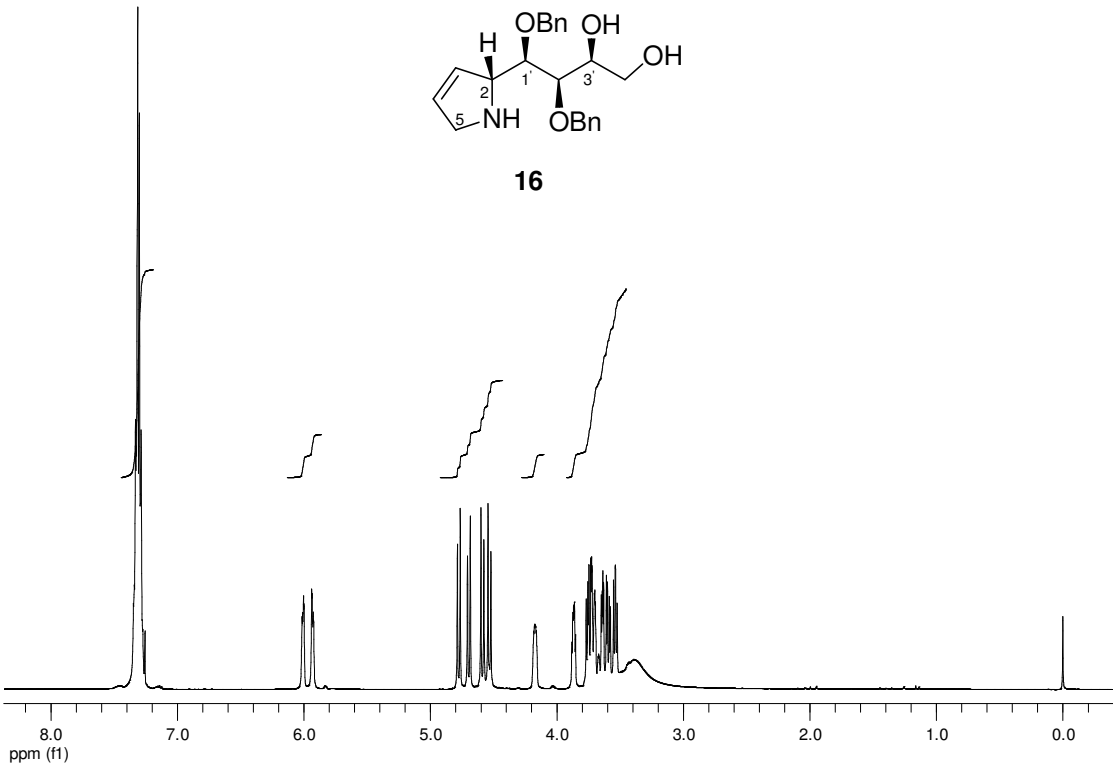
^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (5OO MHz, $CDCl_3$)



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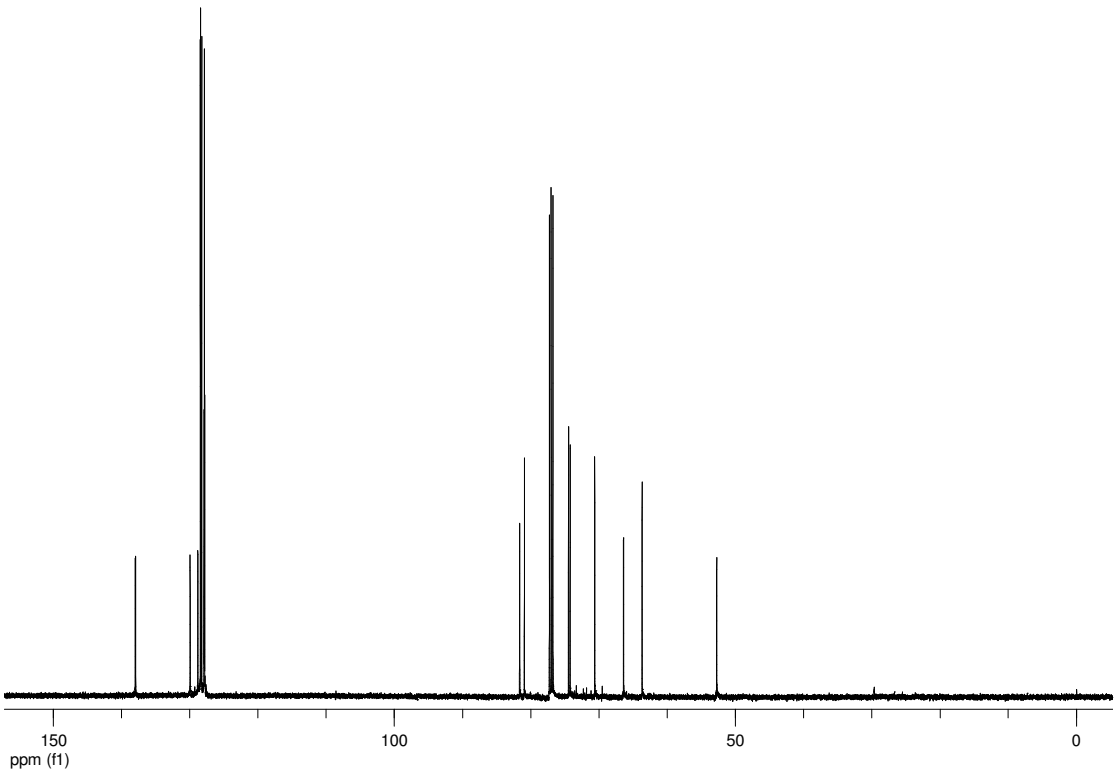
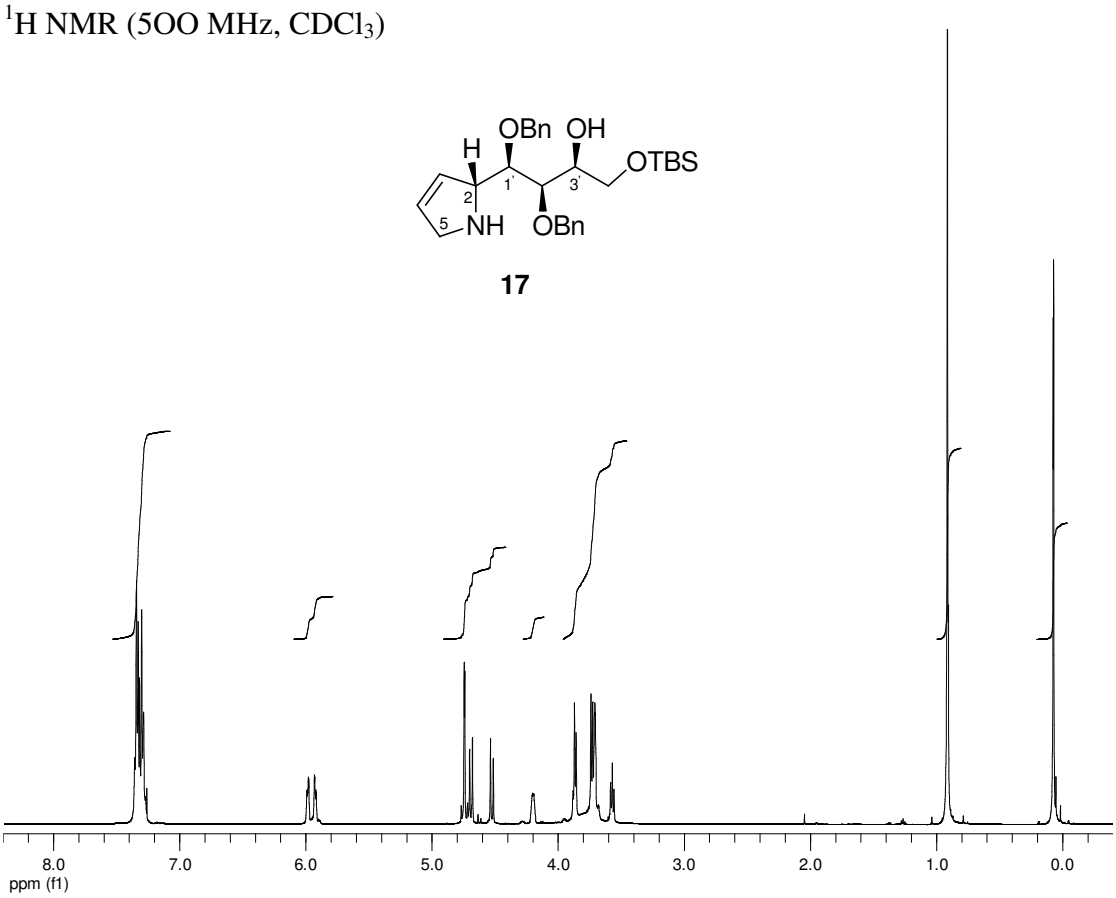
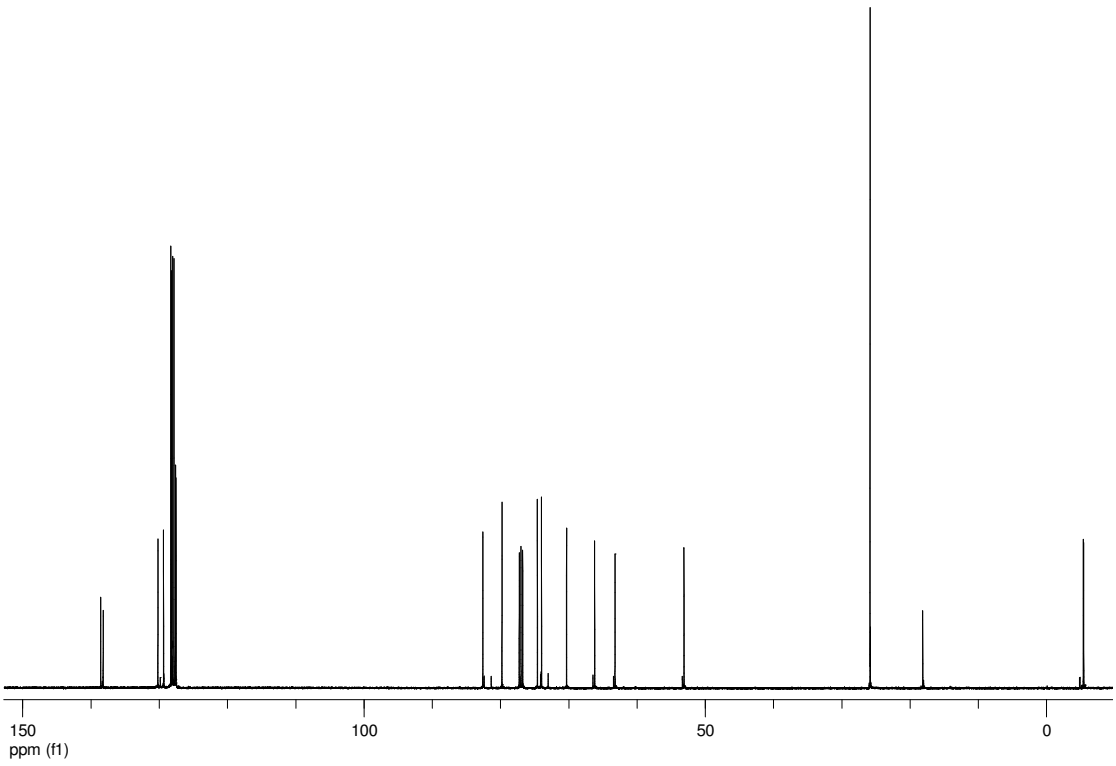


^{1}H NMR (5OO MHz, $CDCl_3$)

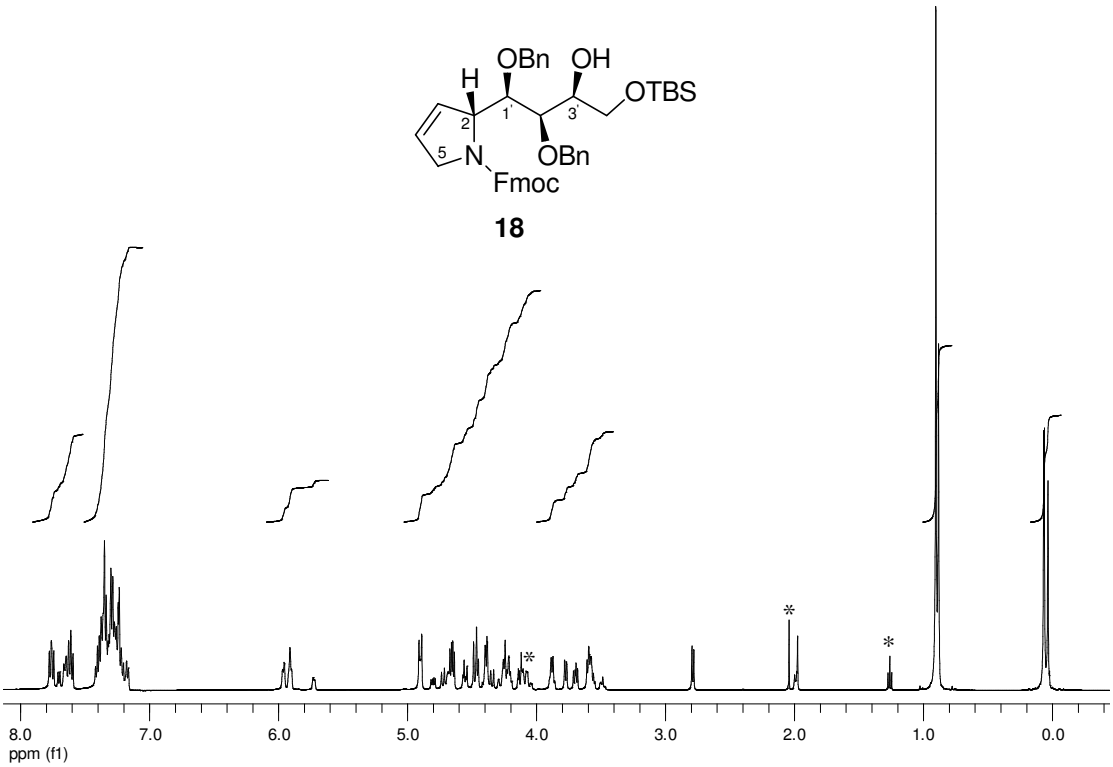


17

^{13}C NMR (125 MHz, $CDCl_3$)

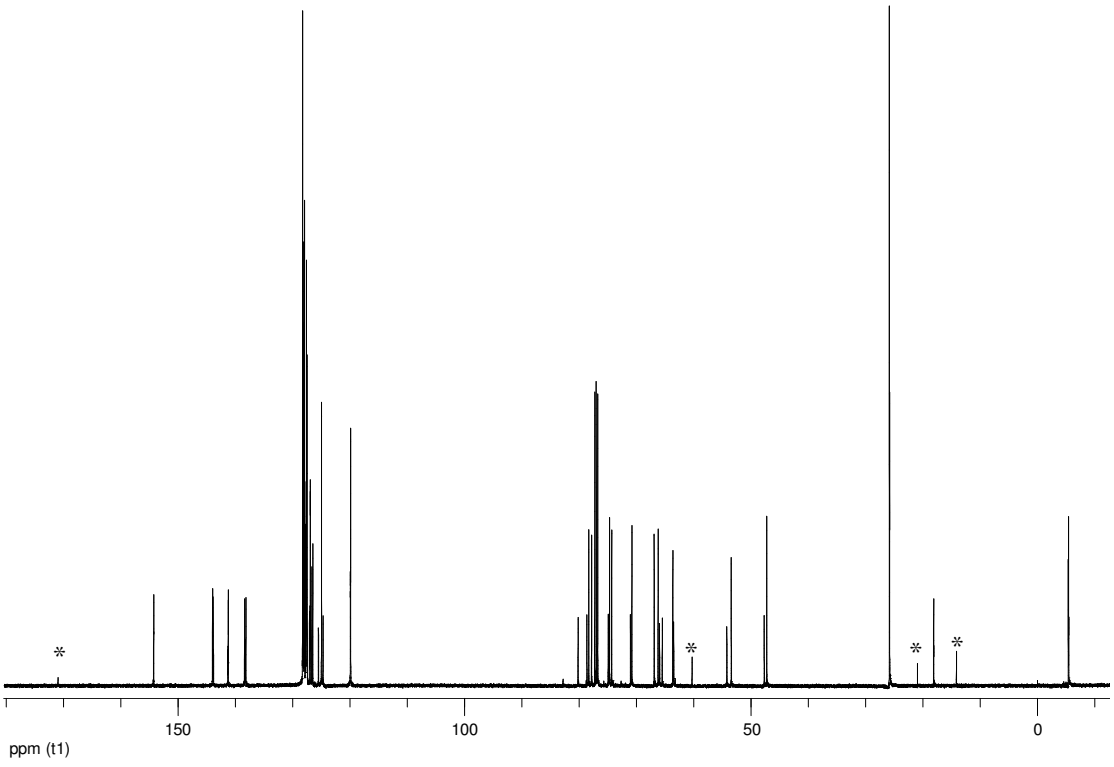


^{1}H NMR (5OO MHz, $CDCl_3$)

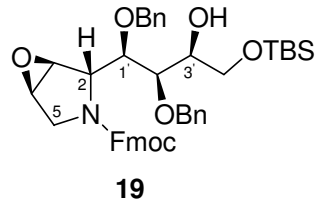


* EtOAc

^{13}C NMR (125 MHz, $CDCl_3$)



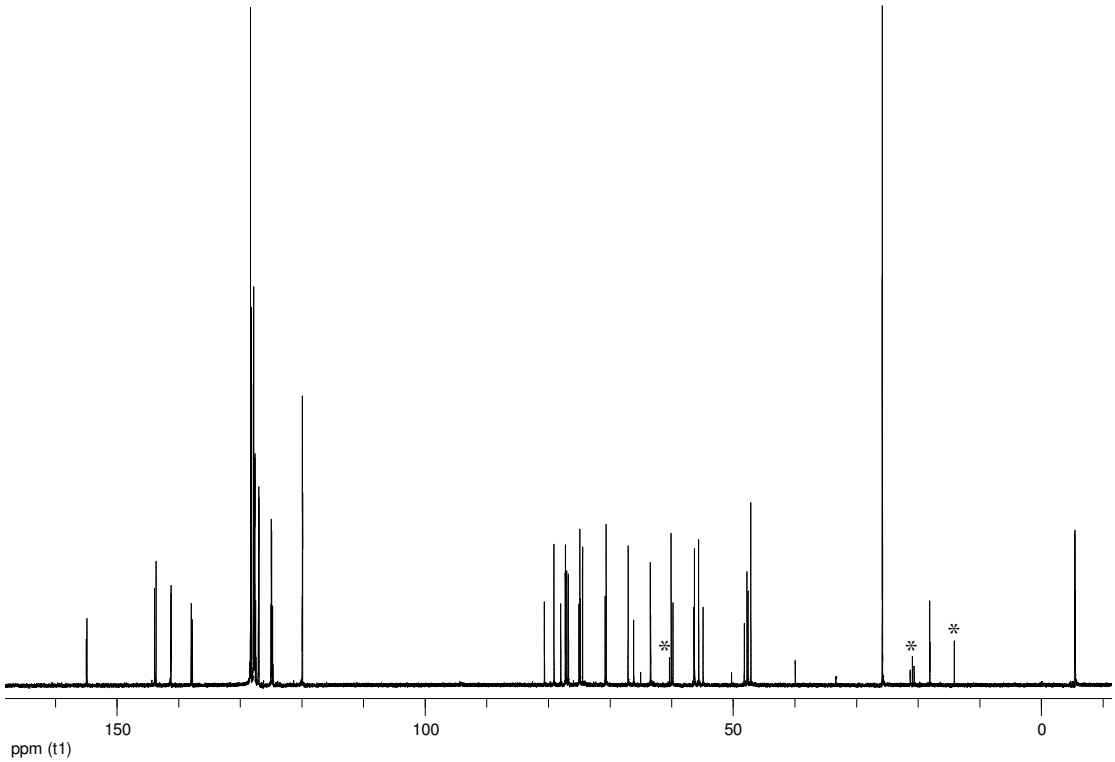
^{1}H NMR (5OO MHz, $CDCl_3$)



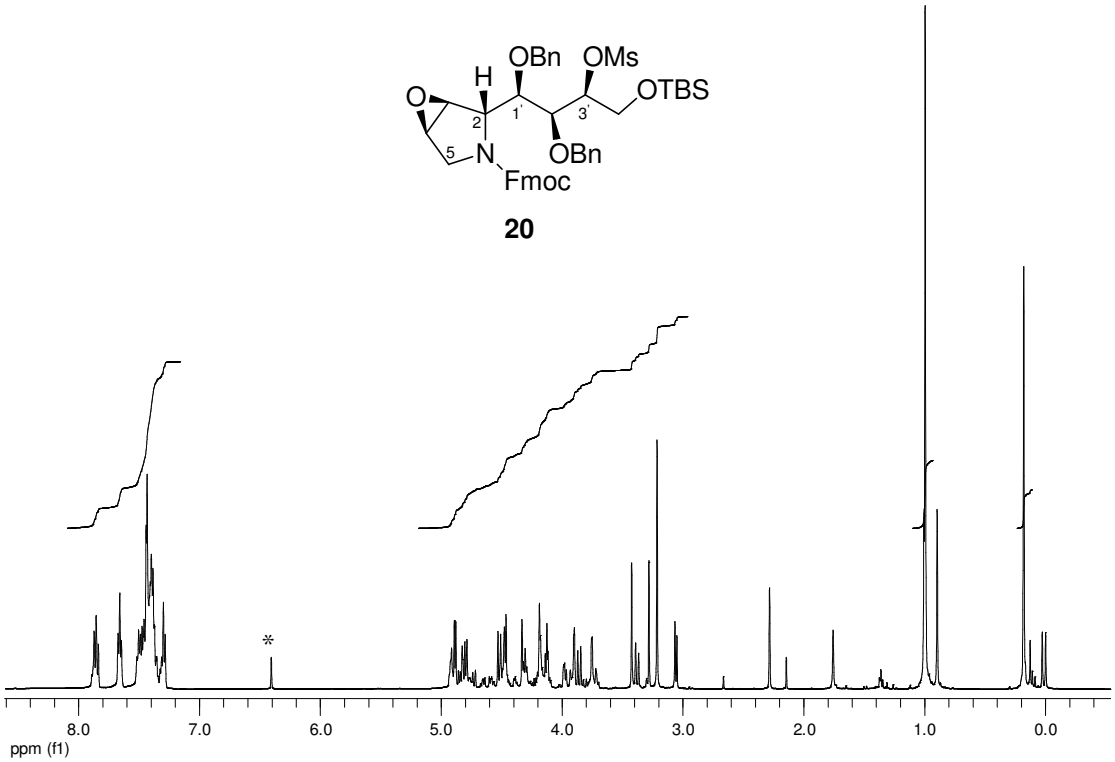
19

* EtOAc

^{13}C NMR (125 MHz, $CDCl_3$)

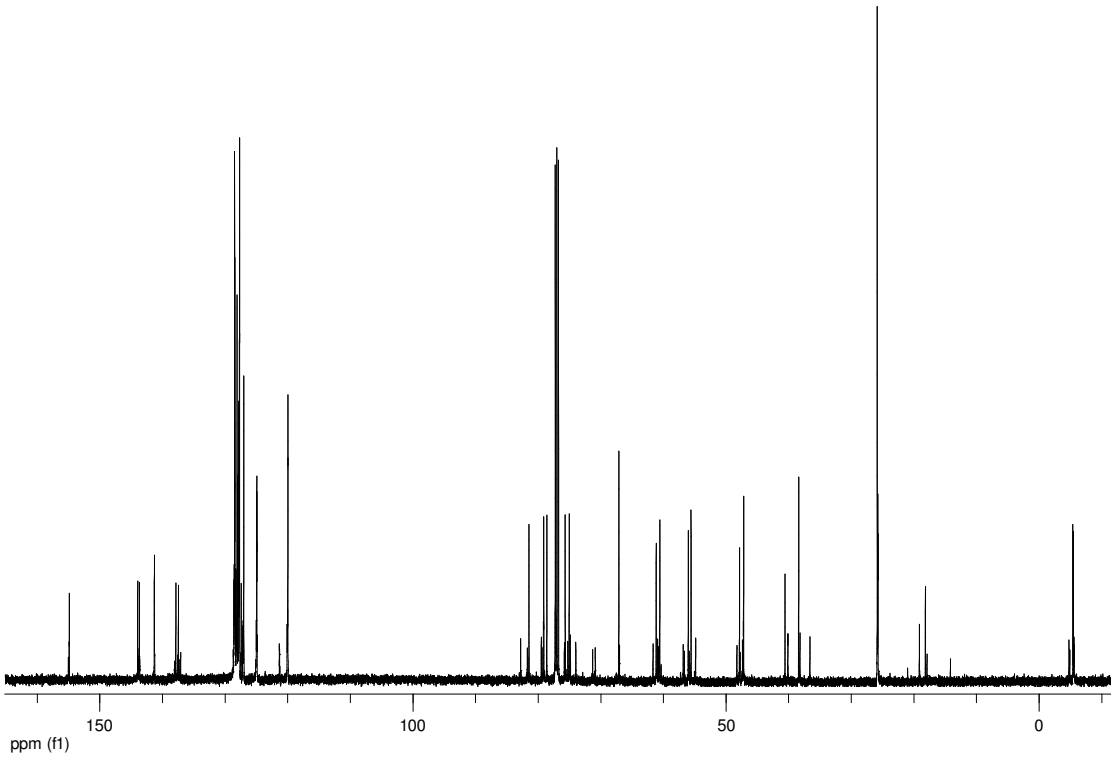


^{1}H NMR (5OO MHz, $CDCl_3$)

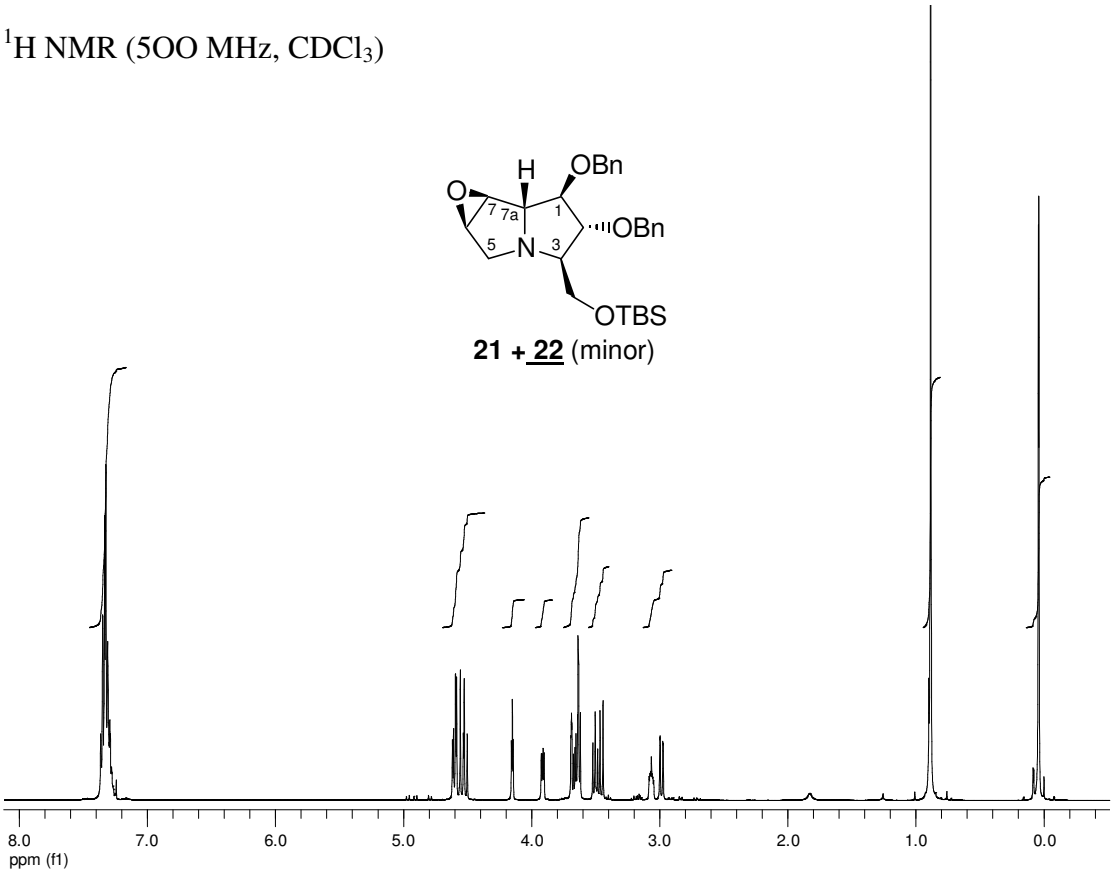


* Impurity

^{13}C NMR (125 MHz, $CDCl_3$)

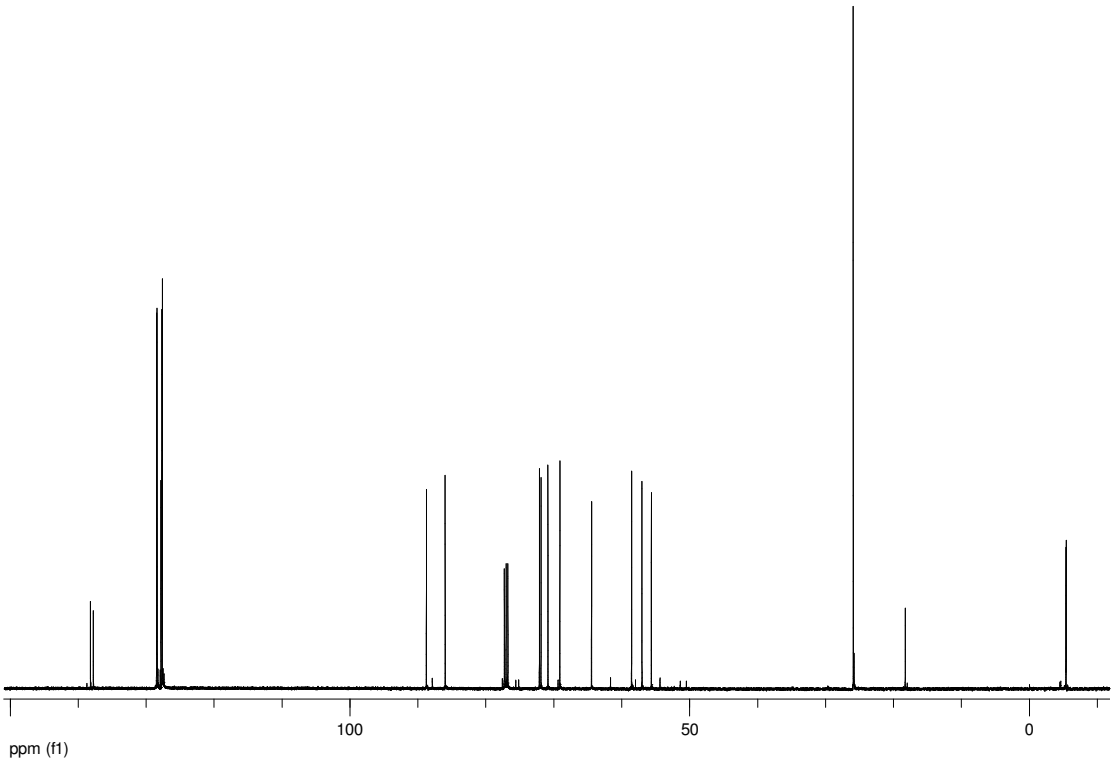


^{1}H NMR (5OO MHz, $CDCl_3$)

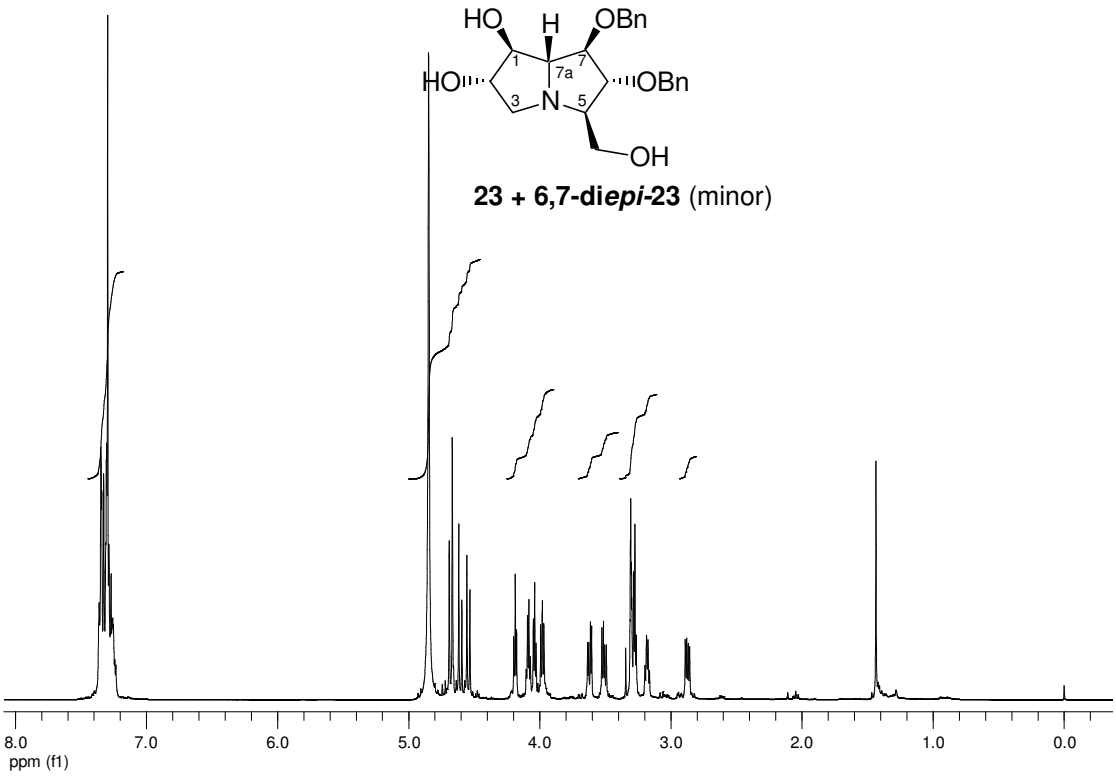


21 + **22** (minor)

^{13}C NMR (125 MHz, $CDCl_3$)

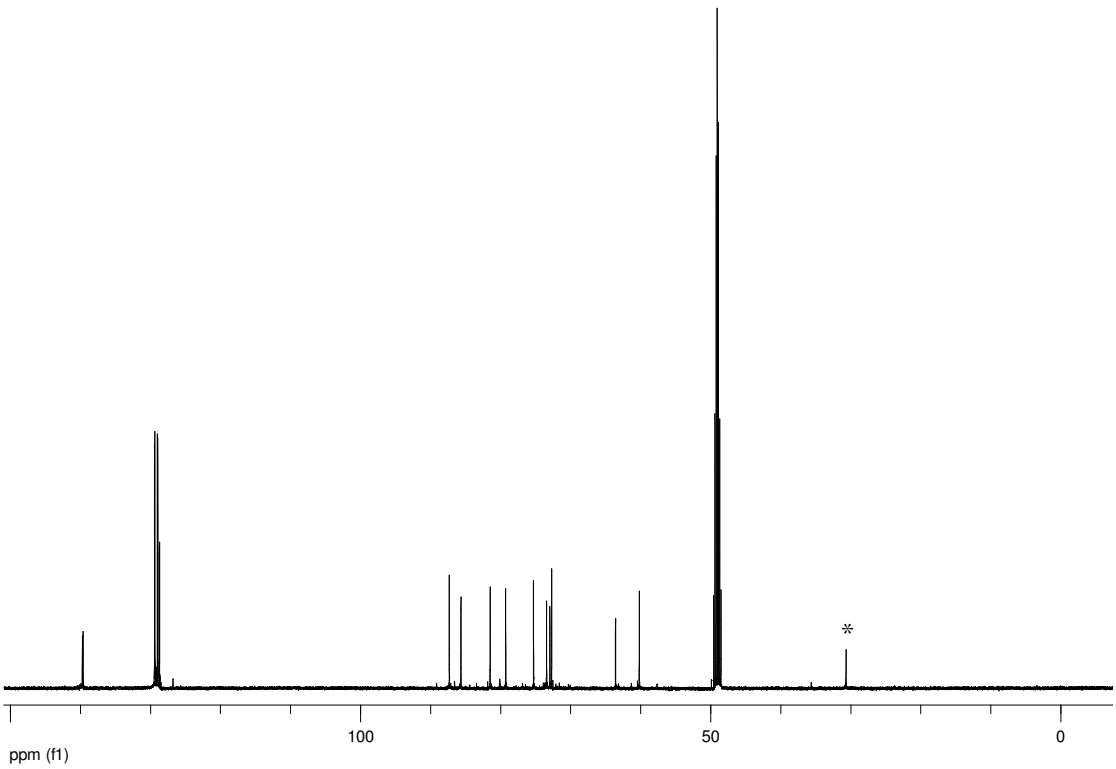


^{1}H NMR (5OO MHz, CD_3OD)



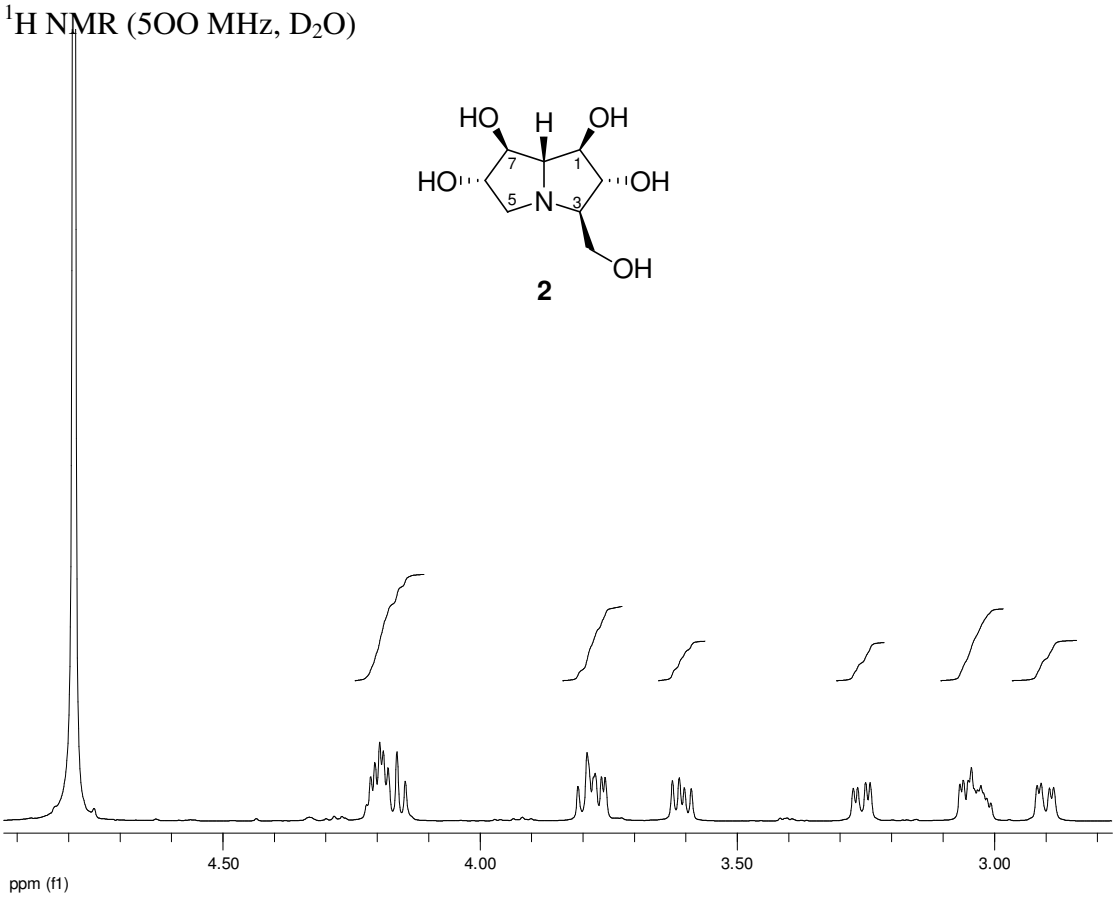
23 + 6,7-di*epi*-23 (minor)

^{13}C NMR (125 MHz, CD_3OD)



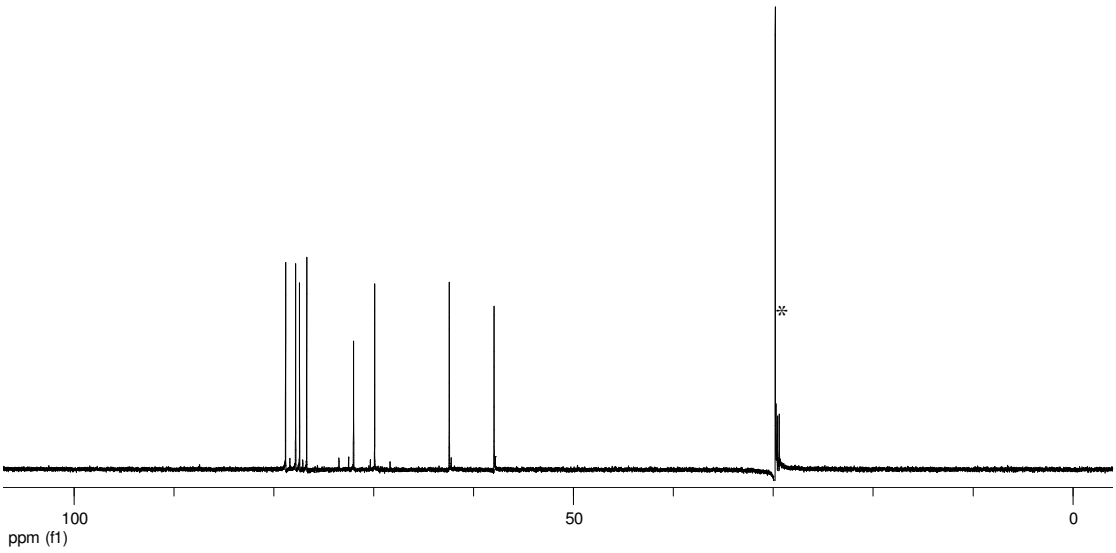
* Acetone

^{1}H NMR (5OO MHz, D_2O)

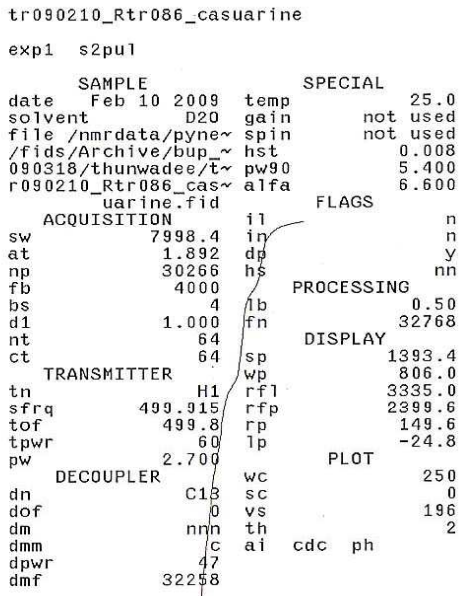


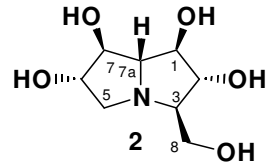
2

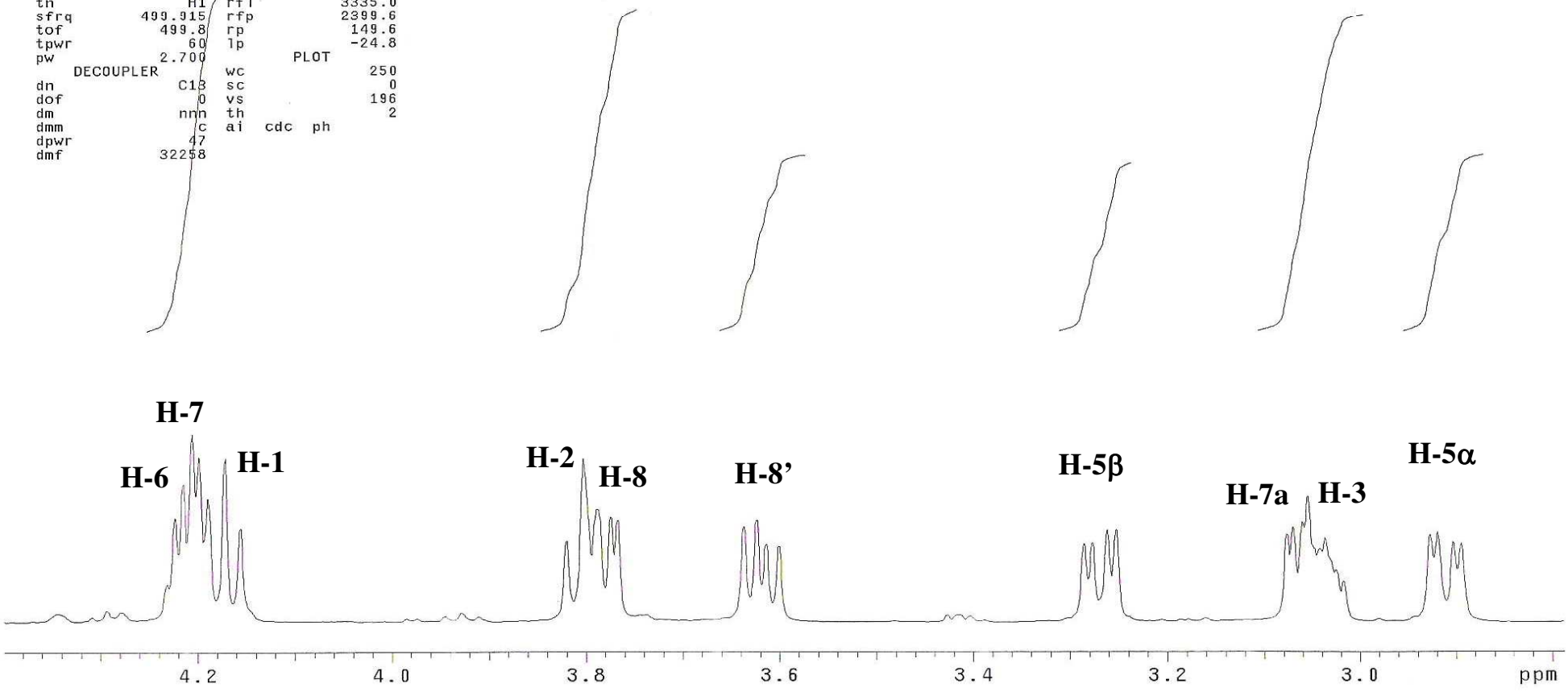
^{13}C NMR (125 MHz, D_2O)



* Acetone







^{1}H NMR (5OO MHz, D_2O)

```
tr090210_Rtr086_casuarine_acetone13C

exp3  s2pul

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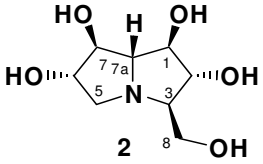
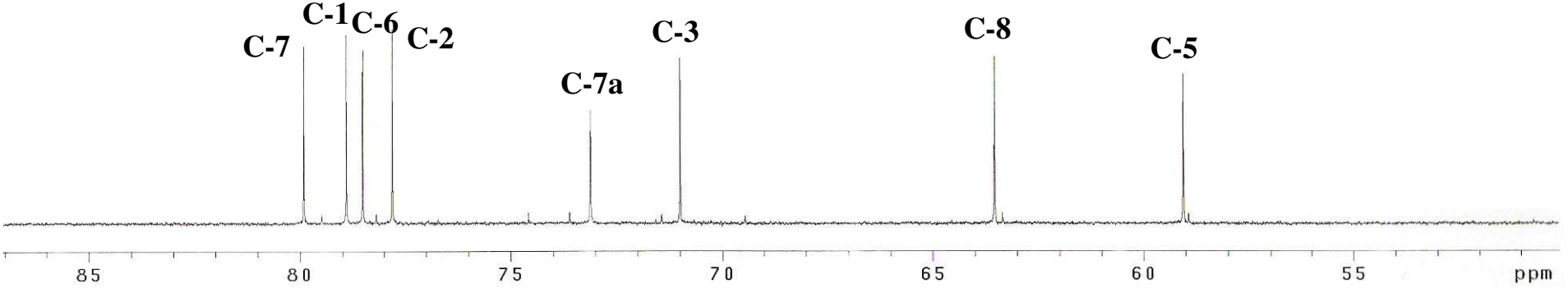
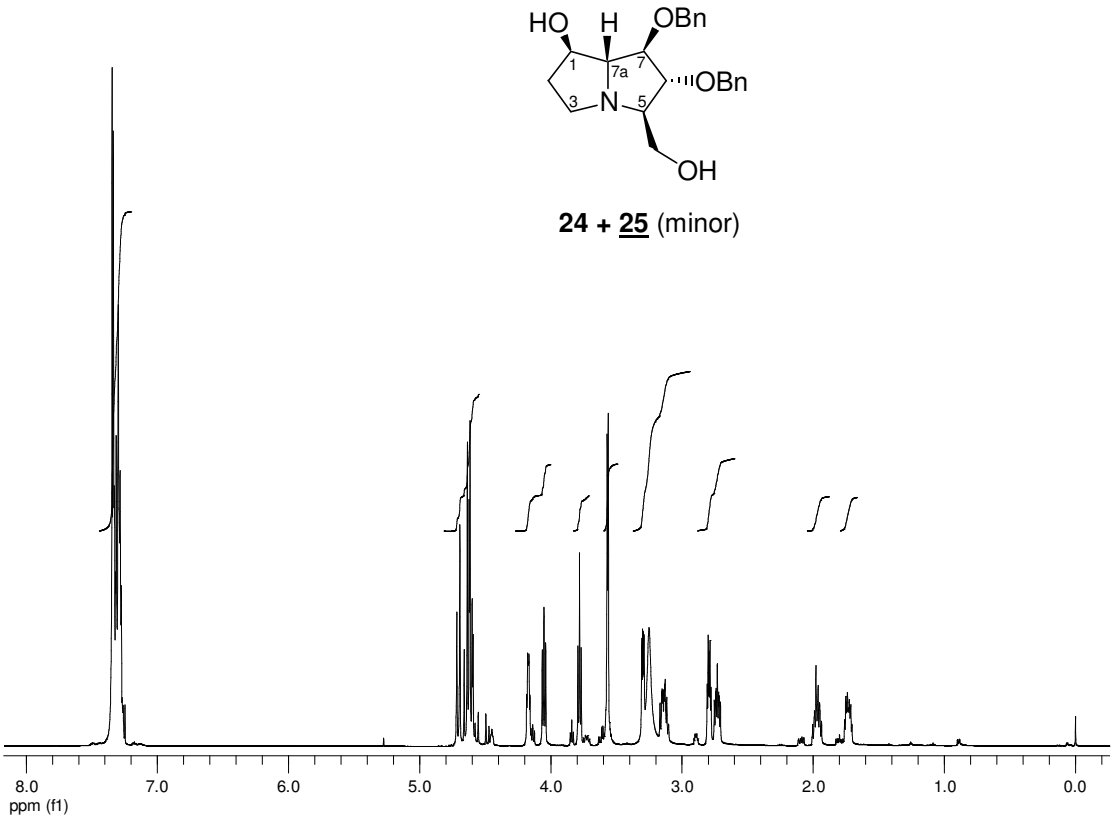
solvent        D2O  gain       not used
file /nmrdata/pyne~ spin       not used
/fids/Archive/bup_~ hst           0.008
090318/thunwadee/t~ pw90         15.800
r090210_Rtr086_cas~ alfa          6.600
uarine_acetone13C.~       FLAGS
                fid  il              n
   ACQUISITION       in              n
sw          31421.8  dp              y
at            1.300  hs             nn
np            81726      PROCESSING
fb            17000  lb           0.50
bs               64  fn       not used
d1            1.000       DISPLAY
nt            14028  sp         6294.7
ct            14028  wp         4647.0
   TRANSMITTER       rfl        5708.5
tn               C13  rfp        3883.0
sfrq        125.717  rp         -174.6
tof          1884.1  lp         -250.1
tpwr             63       PLOT
pw            7.900  wc            250
    DECOUPLER        sc              0
dn               H1  vs            634
dof               0  th              3
dm              yyy  ai  cdc  ph
dmm               w
dpwr             37
dmf           12821
```





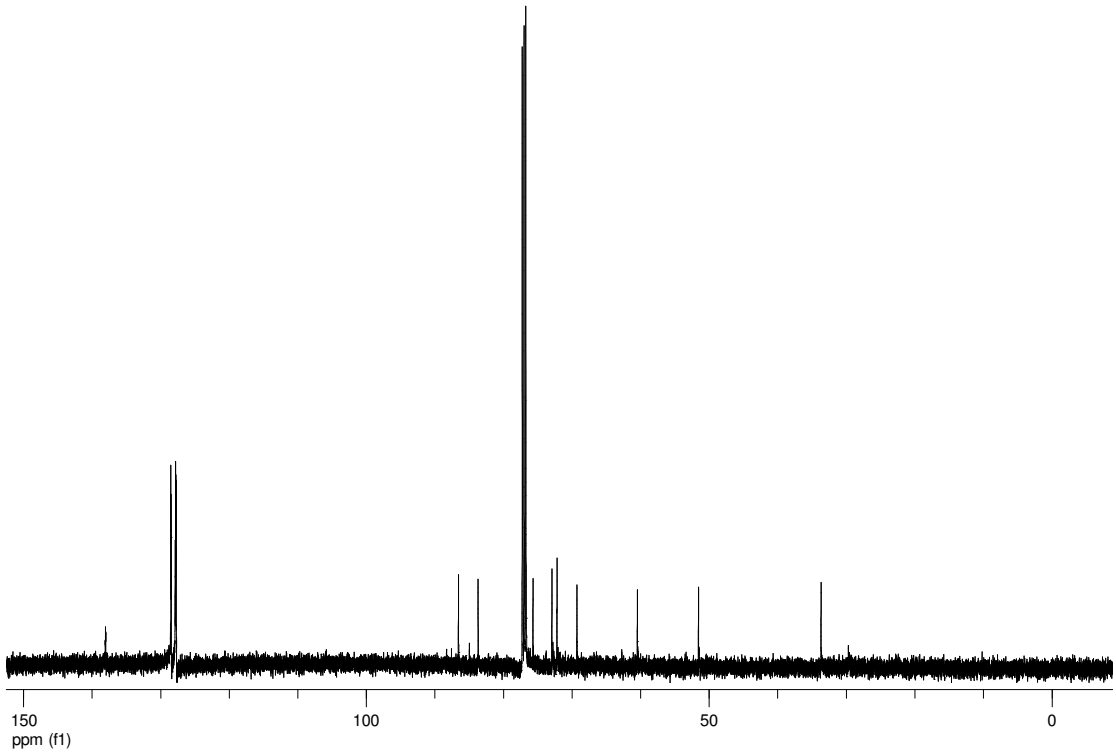
^{13}C NMR (125 MHz, D_2O)

^{1}H NMR (5OO MHz, $CDCl_3$)

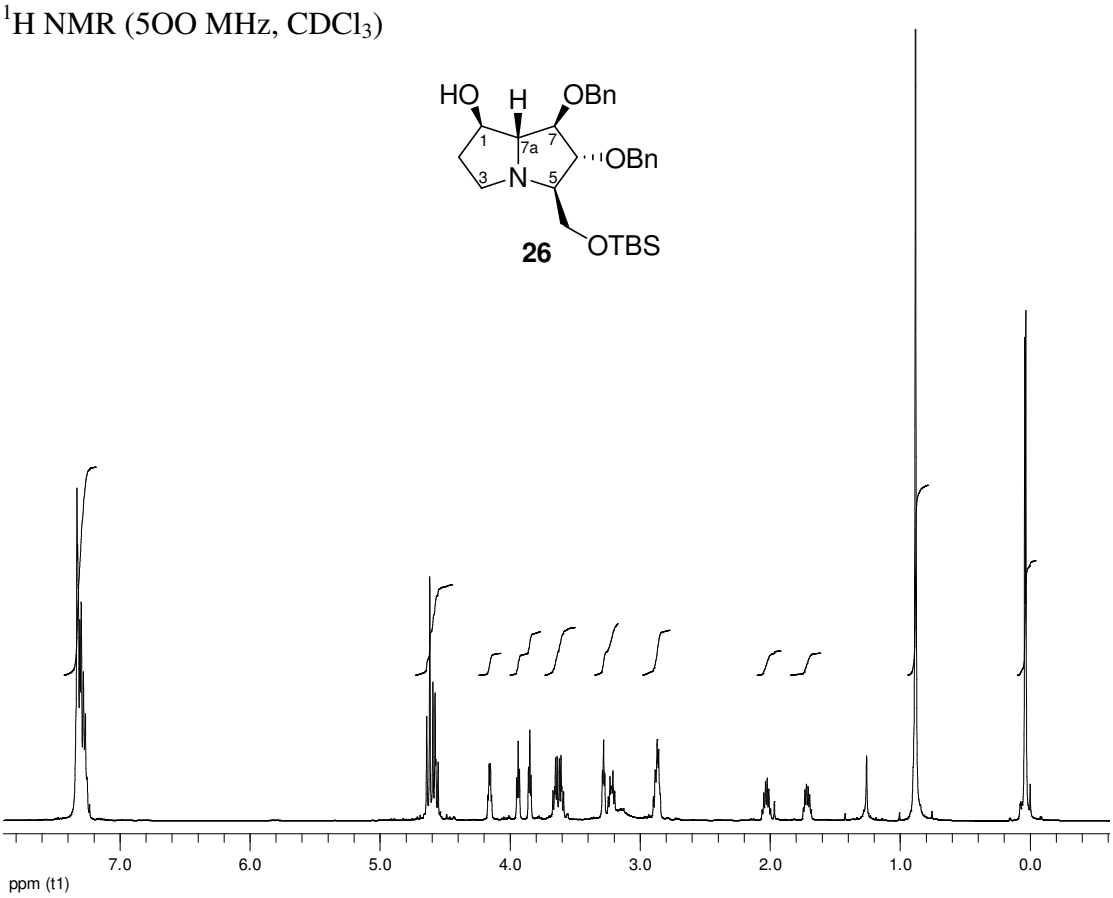


24 + <u>25</u> (minor)

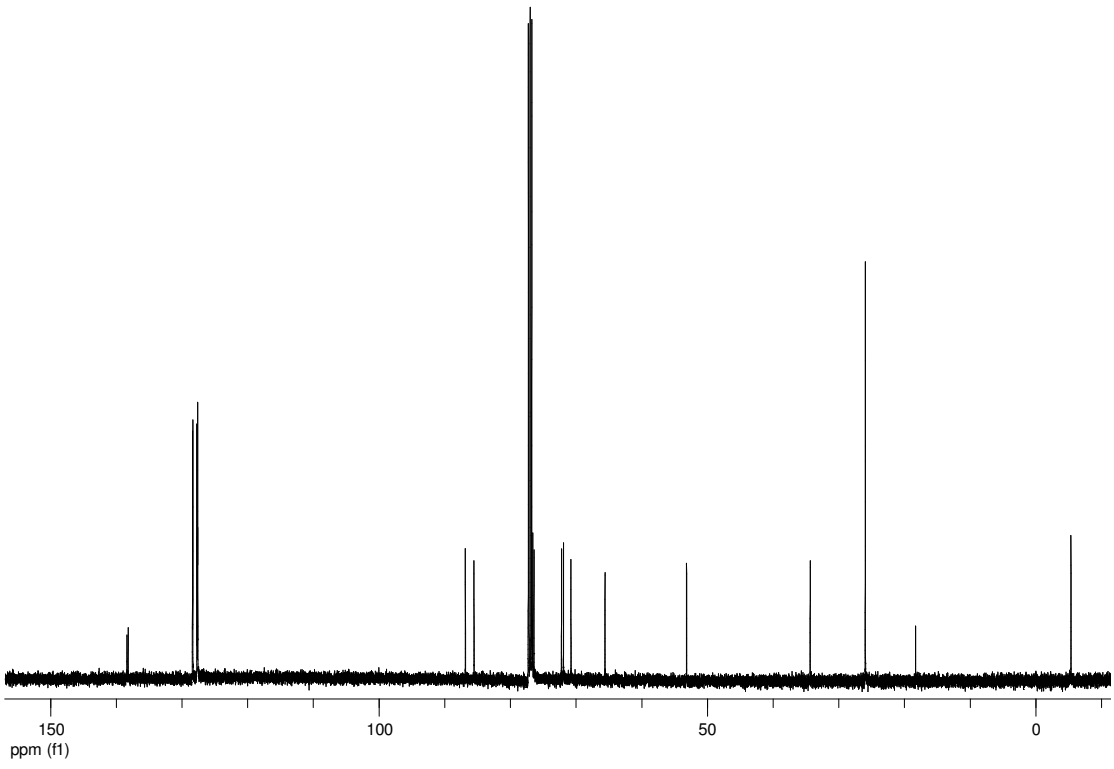
^{13}C NMR (125 MHz, $CDCl_3$)



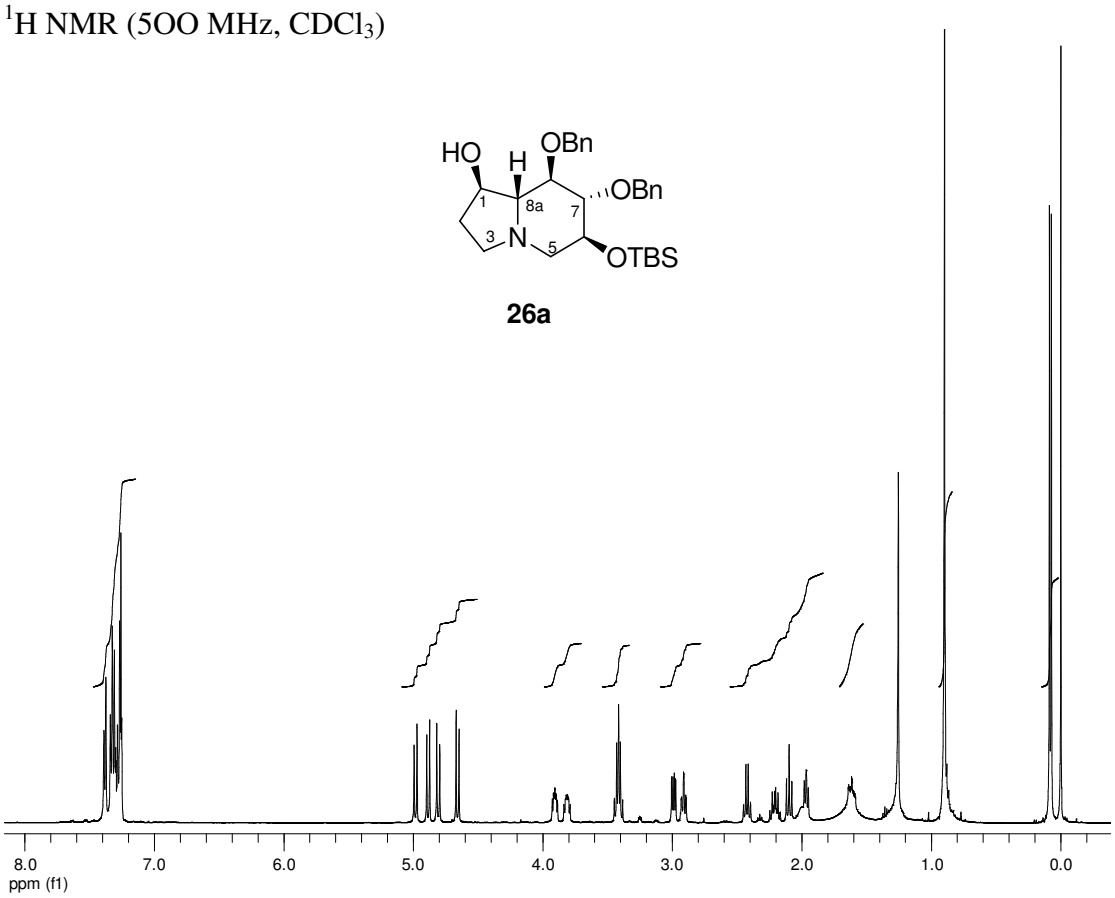
^{1}H NMR (5OO MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)

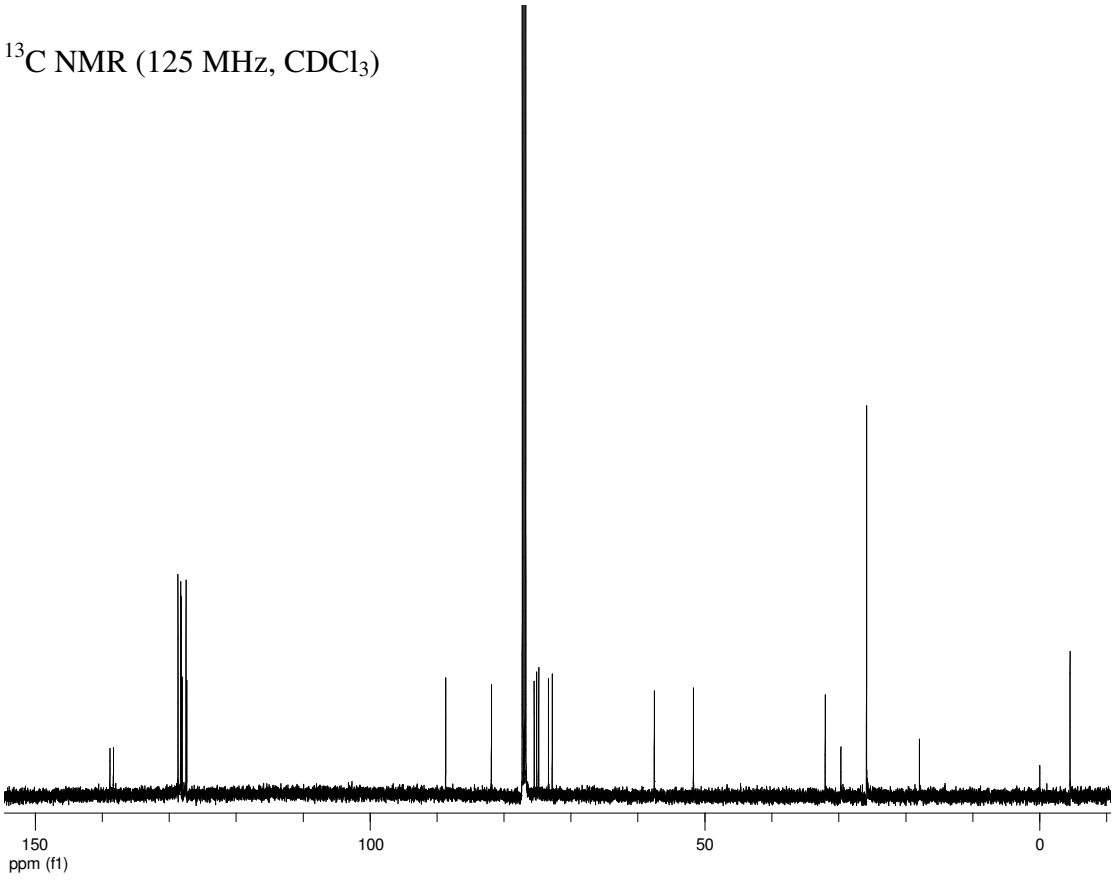


^{1}H NMR (5OO MHz, $CDCl_3$)

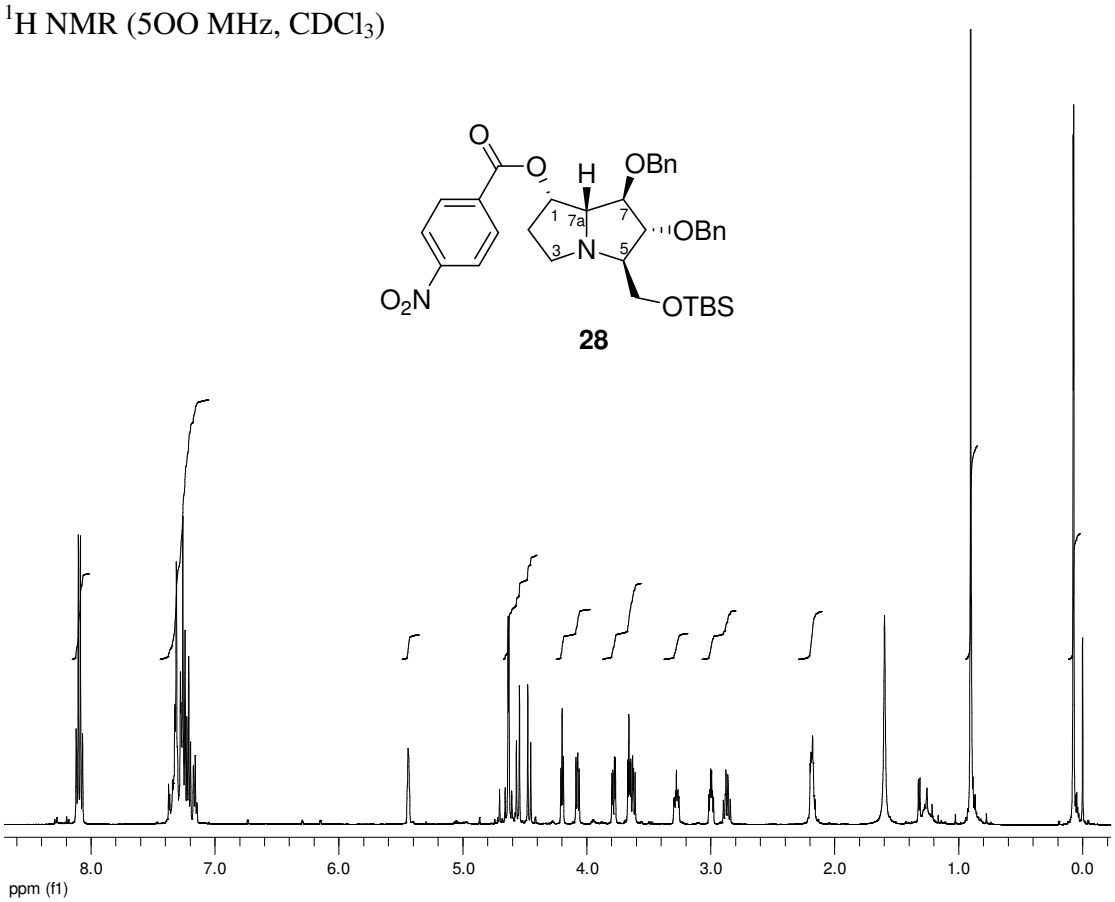


26a

^{13}C NMR (125 MHz, $CDCl_3$)

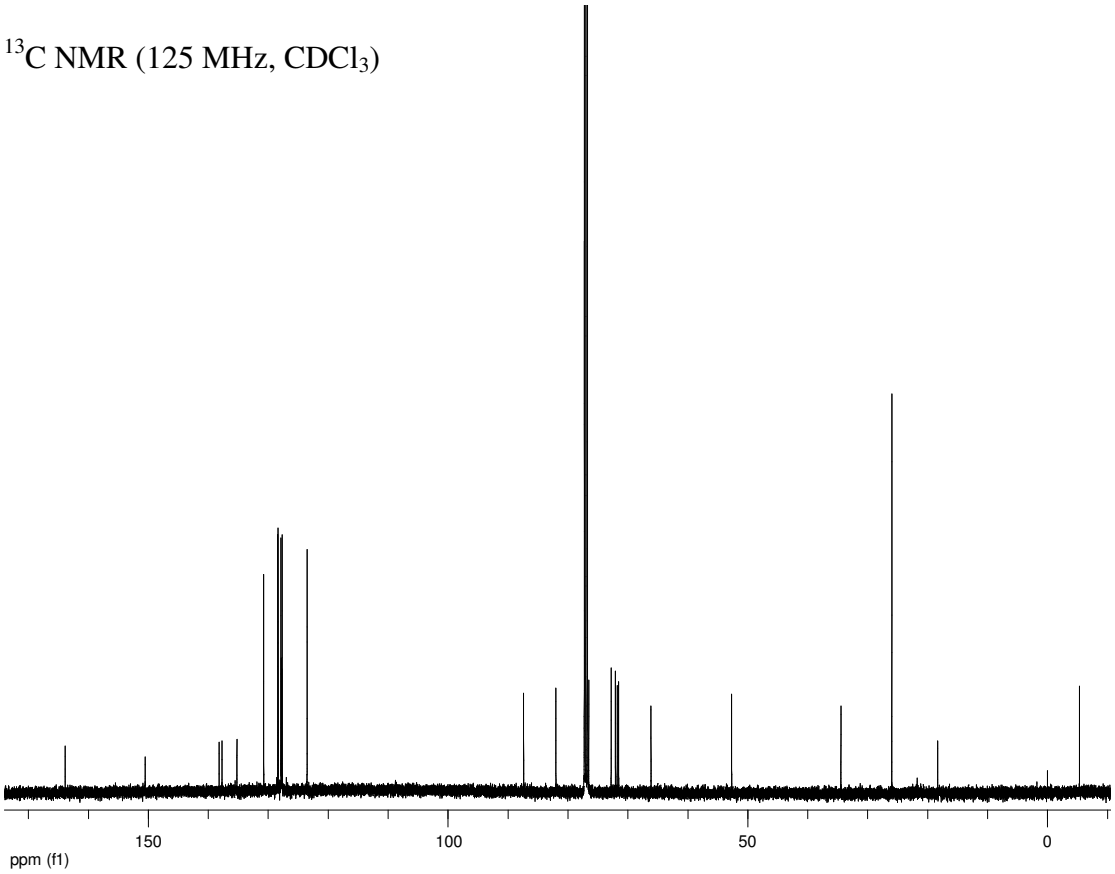


^{1}H NMR (5OO MHz, $CDCl_3$)

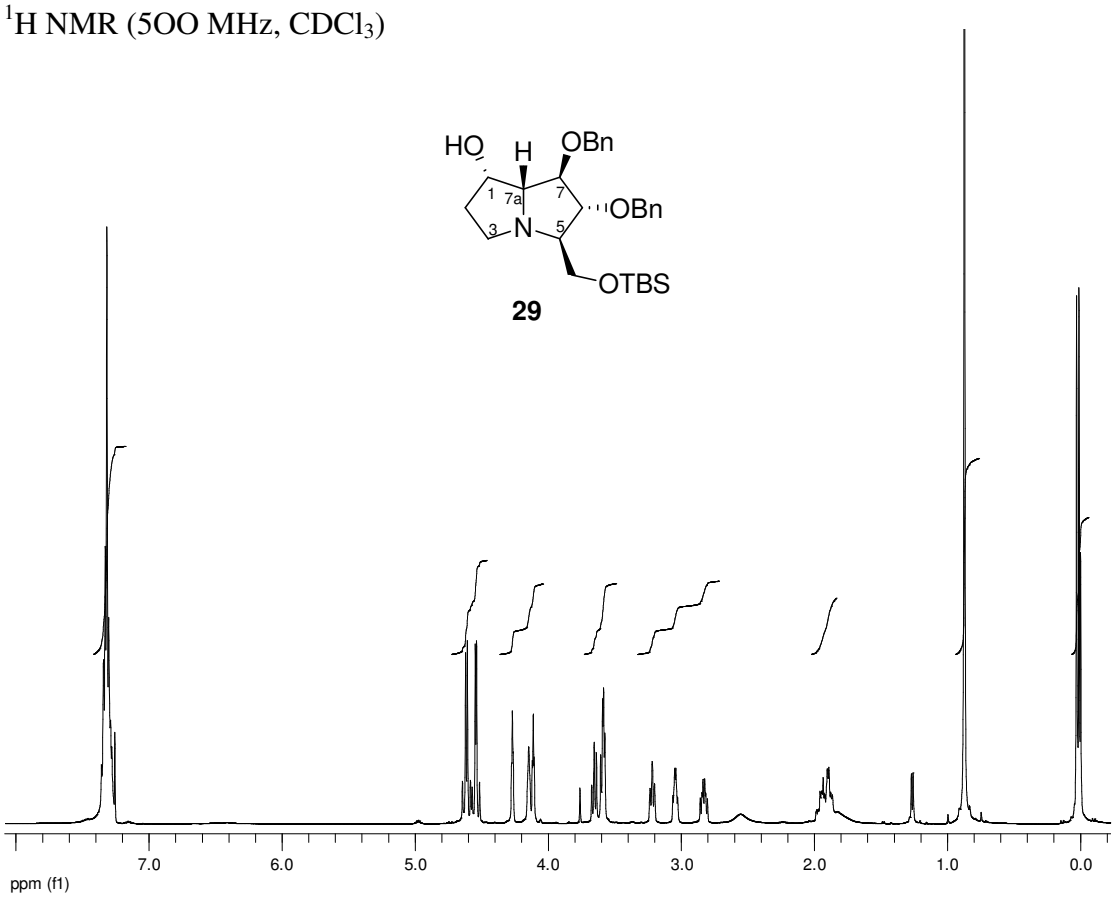


28

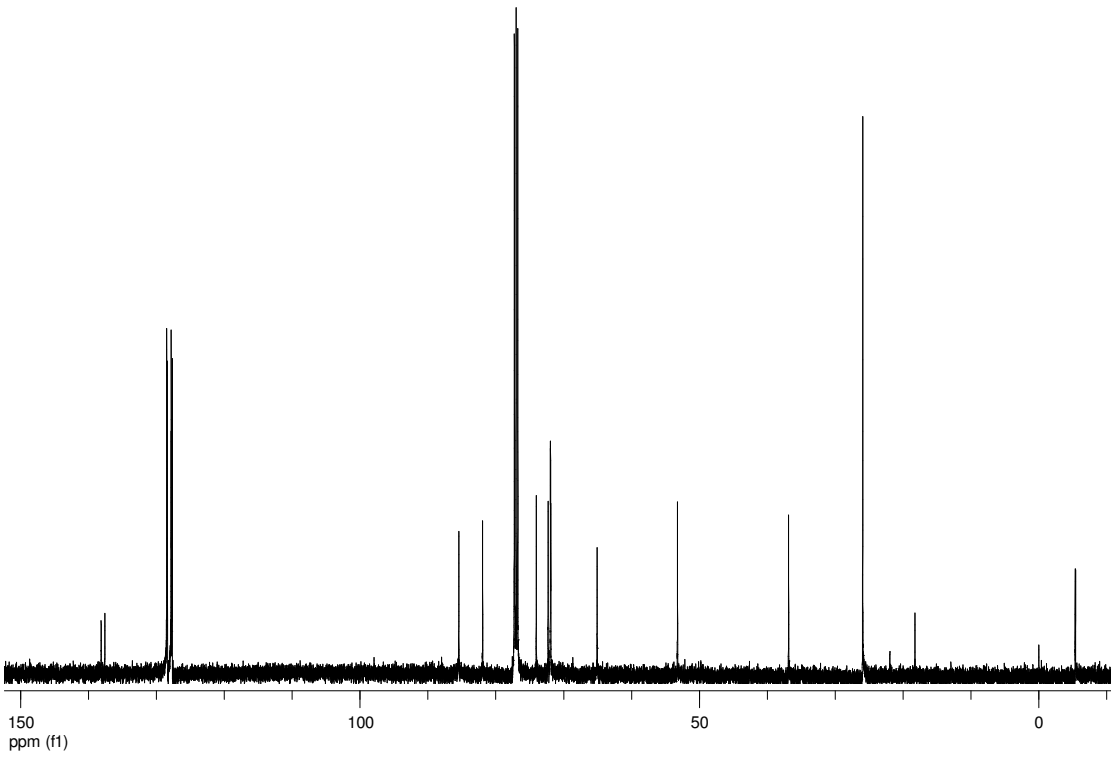
^{13}C NMR (125 MHz, $CDCl_3$)



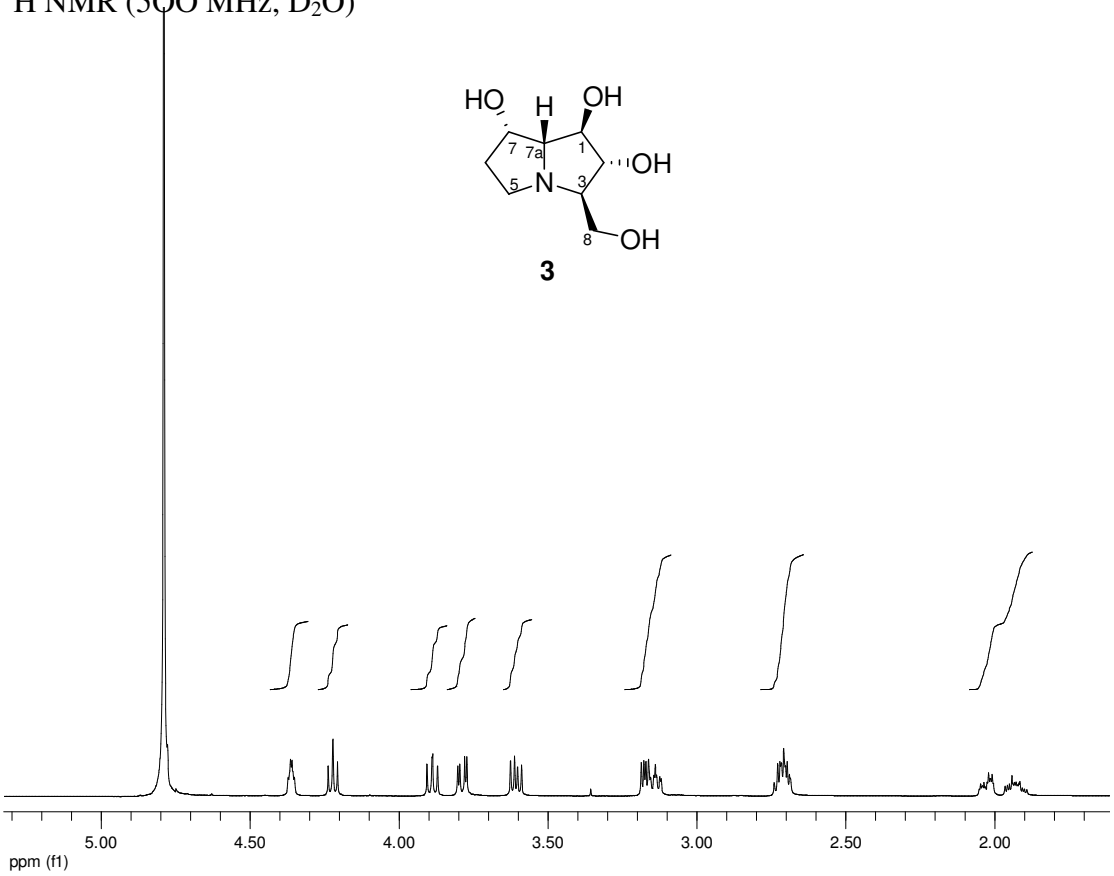
^{1}H NMR (5OO MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)

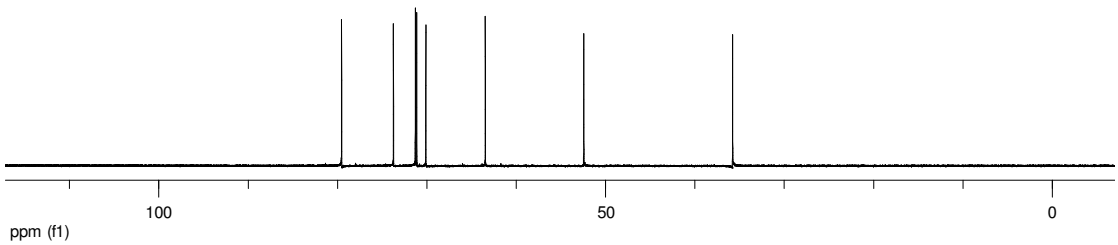


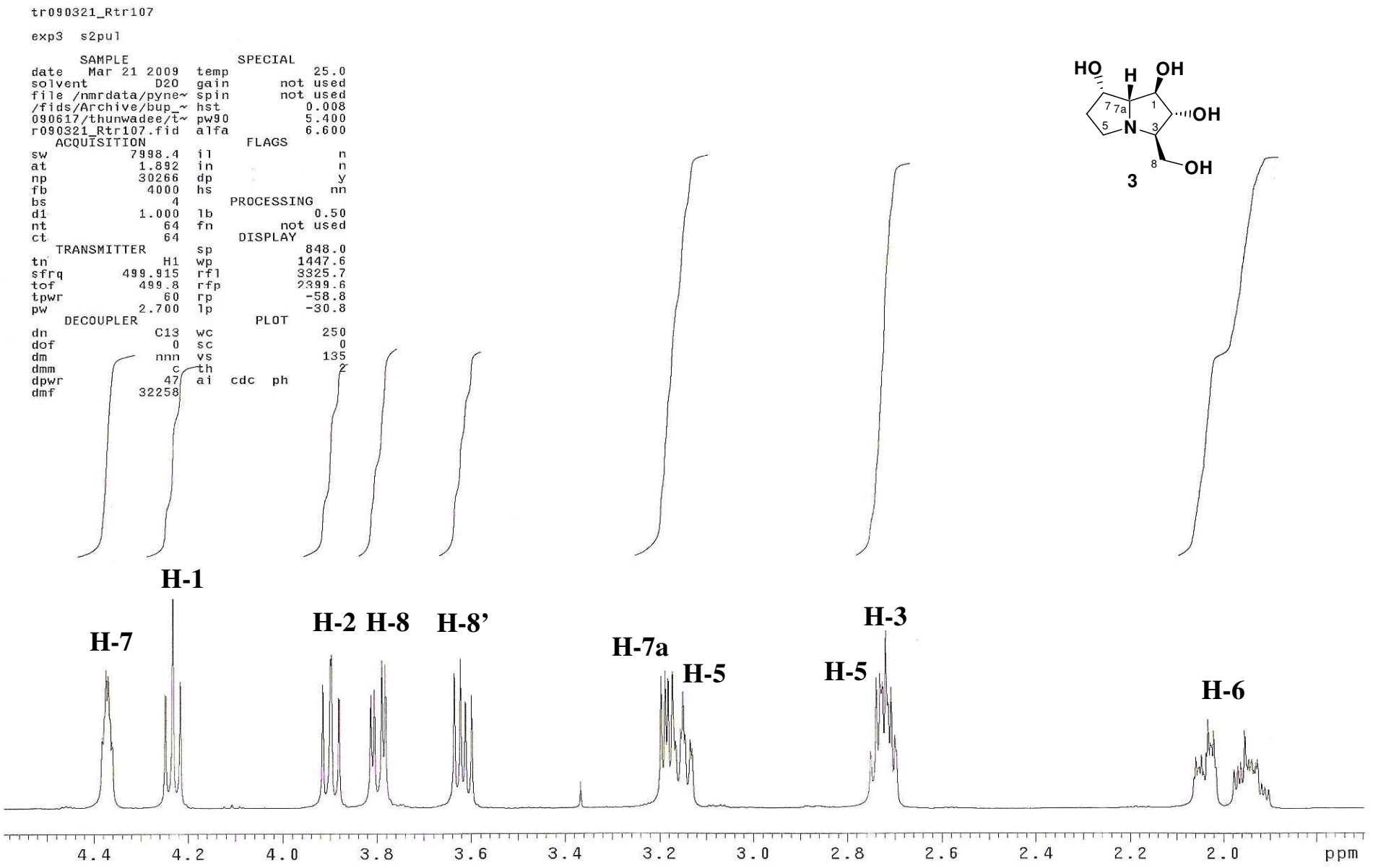
^{1}H NMR (500 MHz, D_2O)



3

^{13}C NMR (125 MHz, D_2O)





^{1}H NMR (5OO MHz, D_2O)

```
tr090327_Rtr107-13C-ACN

exp3  s2pul

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solvent      CDCl3  gain       not used
file /nmrdata/pyne~ spin       not used
/fids/Archive/bup_~ hst           0.008
090617/thunwadee/t~ pw90         15.800
r090327_Rtr107-13C~ alfa          6.600
          -ACN.fid          FLAGS
   ACQUISITION          il              n
sw          31421.8  in              n
at              1.300  dp              y
np            81726  hs             nn
fb            17000       PROCESSING
bs               64  lb           1.00
d1              1.000  fn       not used
nt             1556       DISPLAY
ct             1462  sp          2490.1
   TRANSMITTER          wp          8841.4
tn               C13  rfl         2335.0
sfrq        125.716  rfp          184.8
tof          1884.0  rp           167.7
tpwr             63  lp          -215.0
pw              7.900         PLOT
    DECOUPLER          wc           250
dn                H1  sc             0
dof                0  vs           519
dm               yyy  th             8
dmm                w  ai  cdc  ph
dpwr              37
dmf            12821
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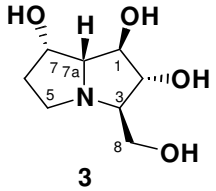
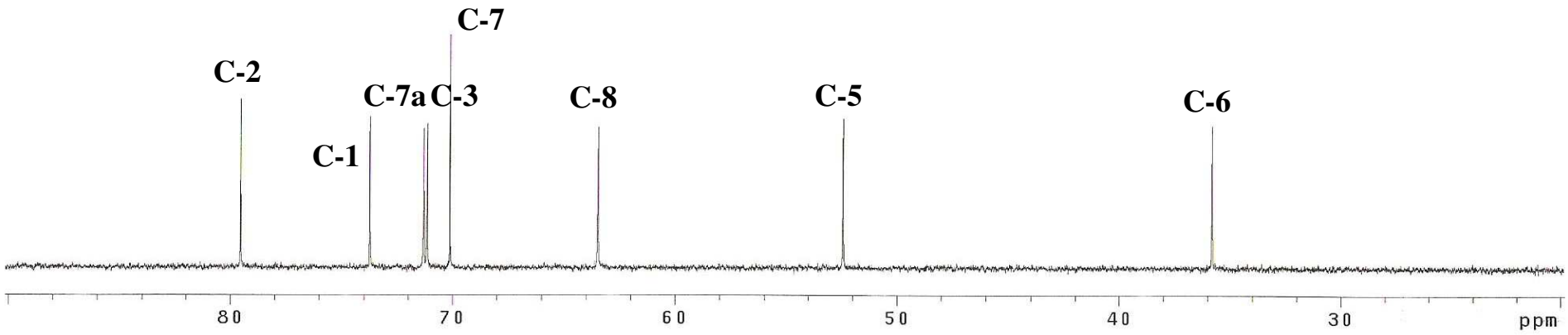


3



^{13}C NMR (125 MHz, D_2O)

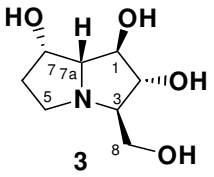
tr090321_Rtr107-gCOSY

Archive directory: /export/home/pyne/vnmrsys/data
Sample directory:

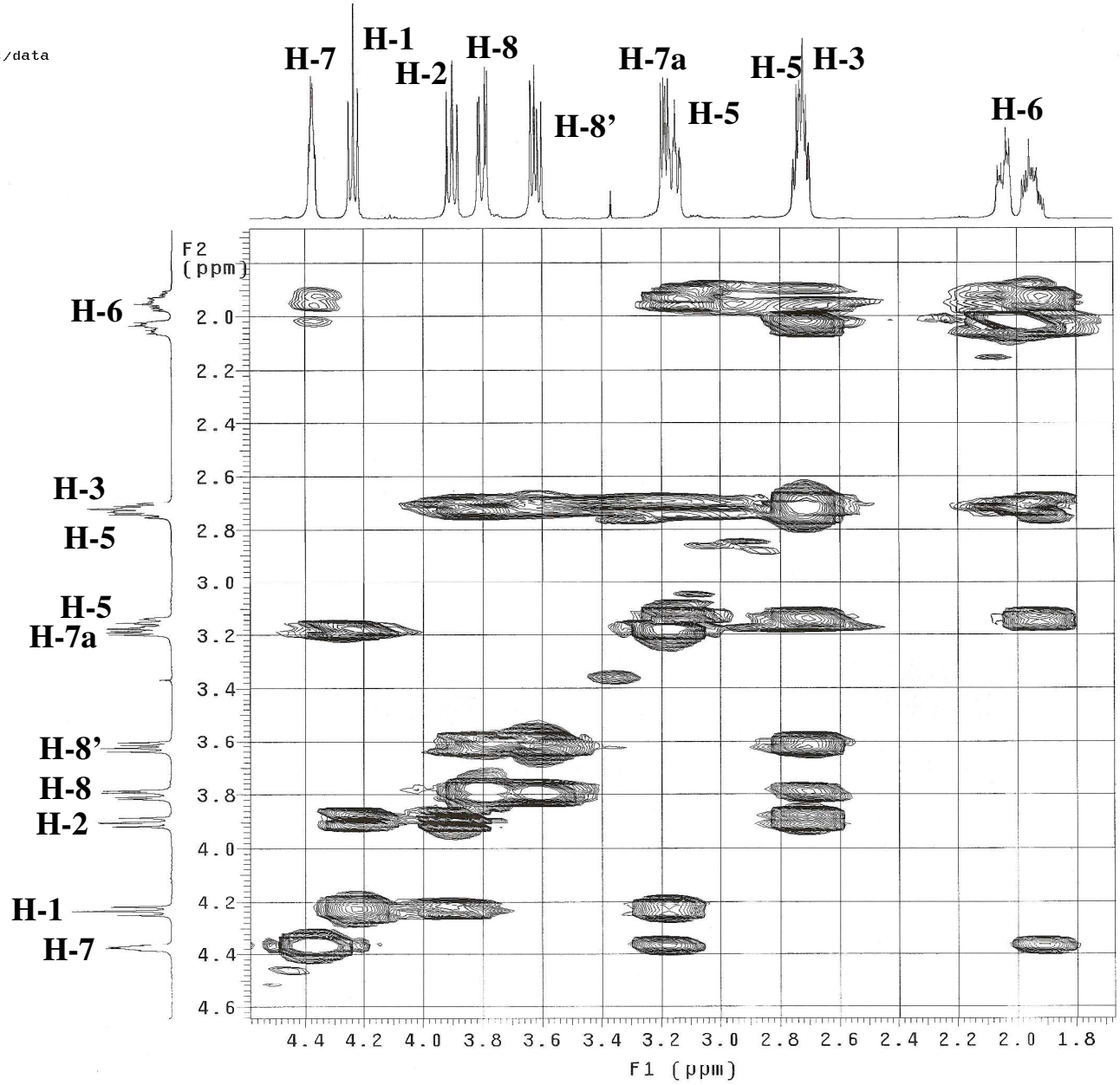
Pulse Sequence: gCOSY

Solvent: D2O
Temp. 25.0 C / 298.1 K
File: tr090321_Rtr107-gCOSY
INOVA-500 "wuthrich"

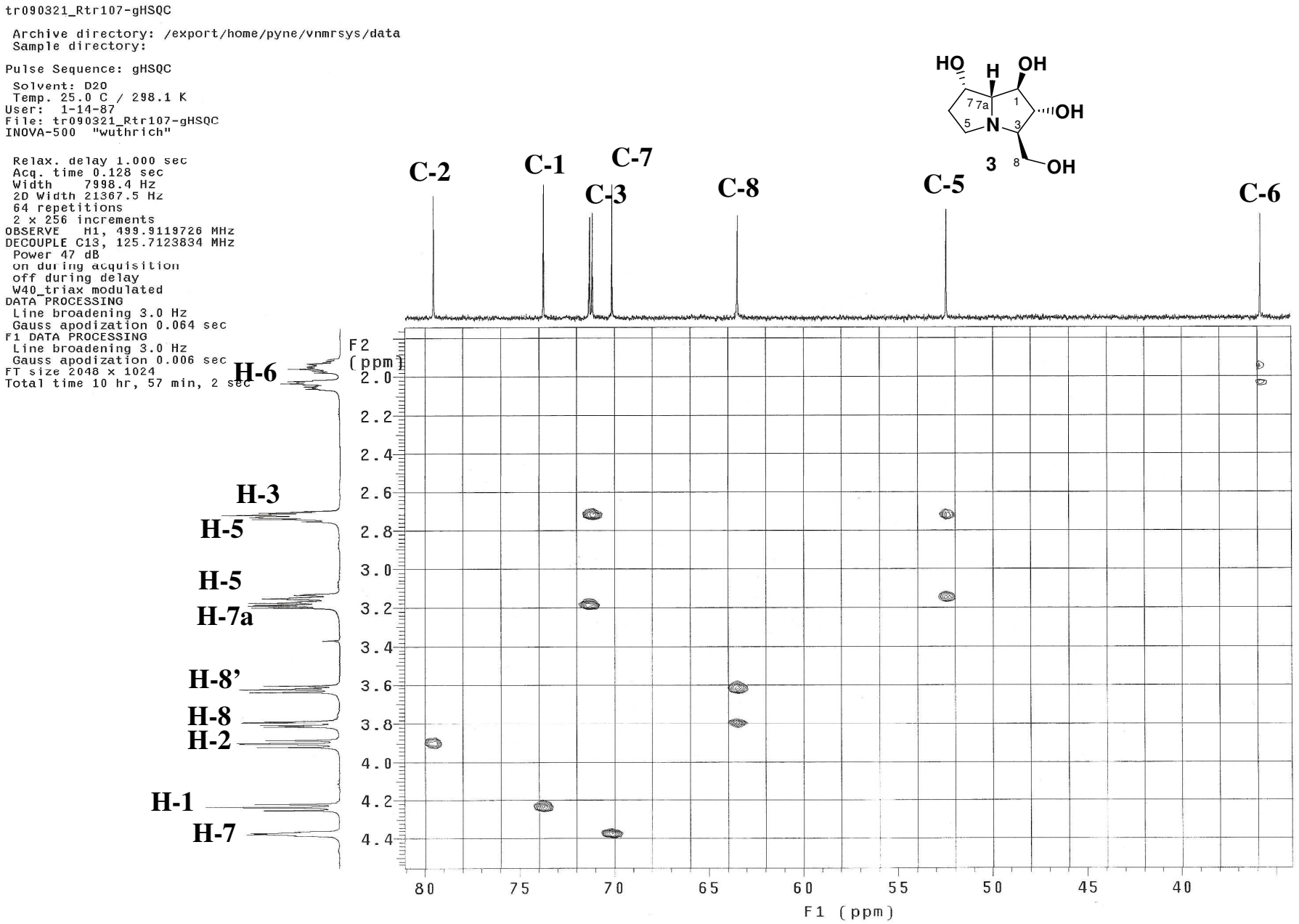
Relax. delay 1.000 sec
Acq. time 0.128 sec
Width 7998.4 Hz
2D Width 7998.4 Hz
32 repetitions
256 increments
OBSERVE H1, 499.9119776 MHz
DATA PROCESSING
Line broadening 3.0 Hz
Sq. sine bell 0.064 sec
F1 DATA PROCESSING
Line broadening 3.0 Hz
Sq. sine bell 0.016 sec
FT size 2048 x 1024
Total time 2 hr, 38 min, 16 sec



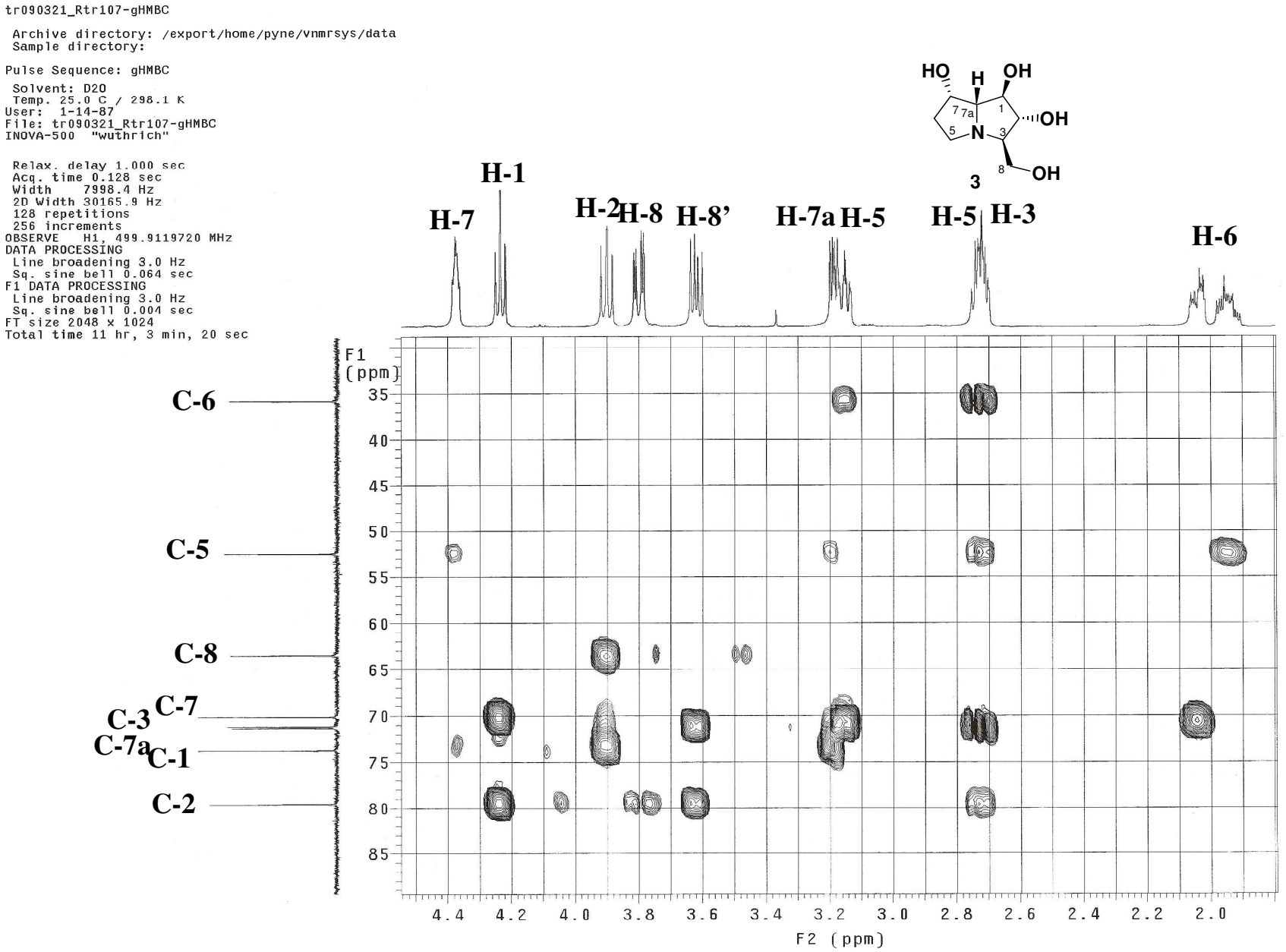
3



COSY (500 MHz, D_2O)

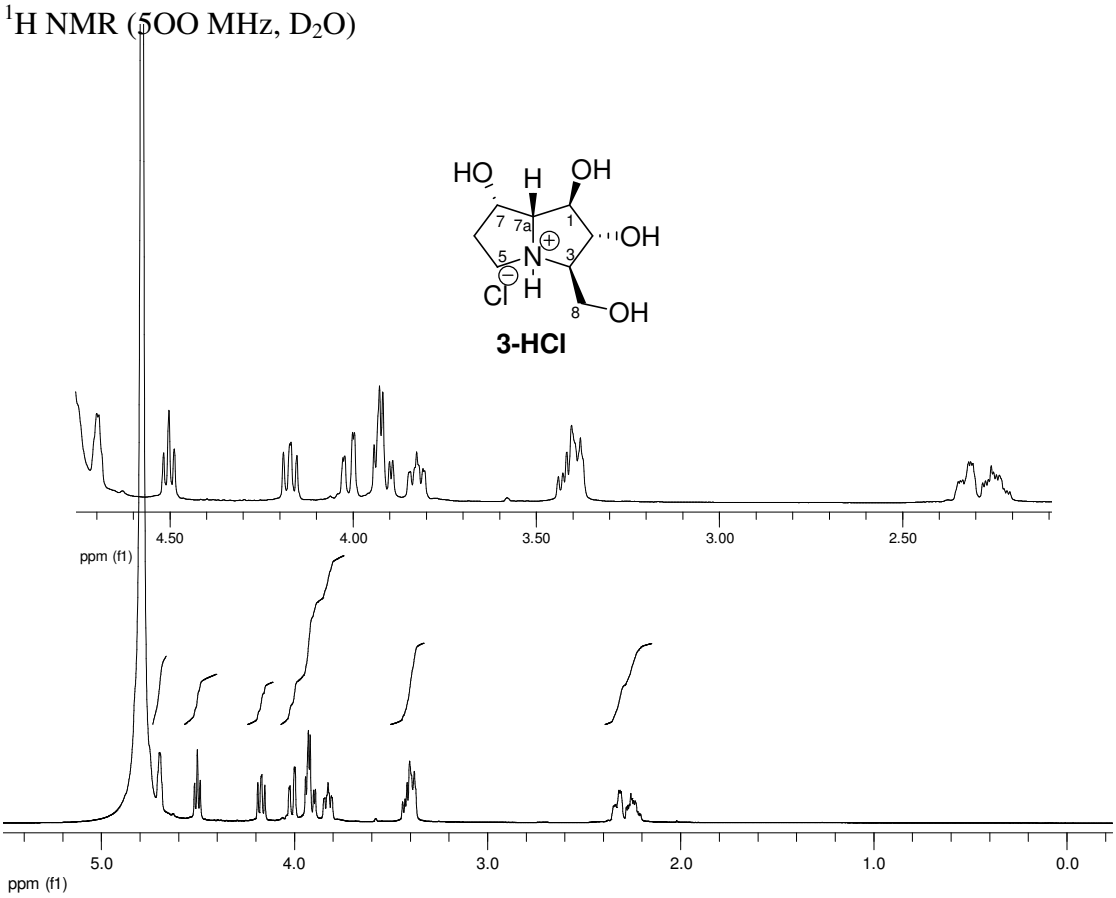


HSQC (500 MHz, D_2O)

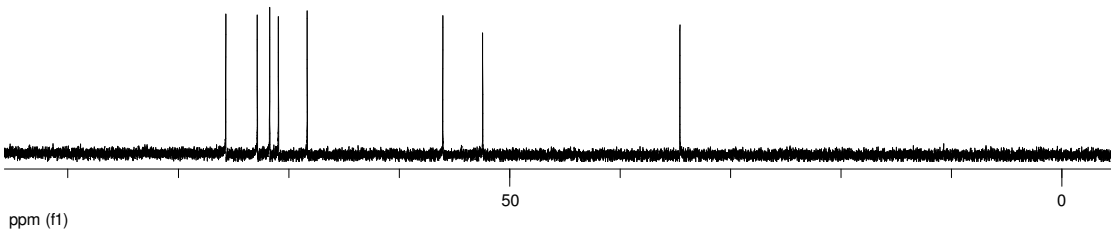


HMBC (500 MHz, D_2O)

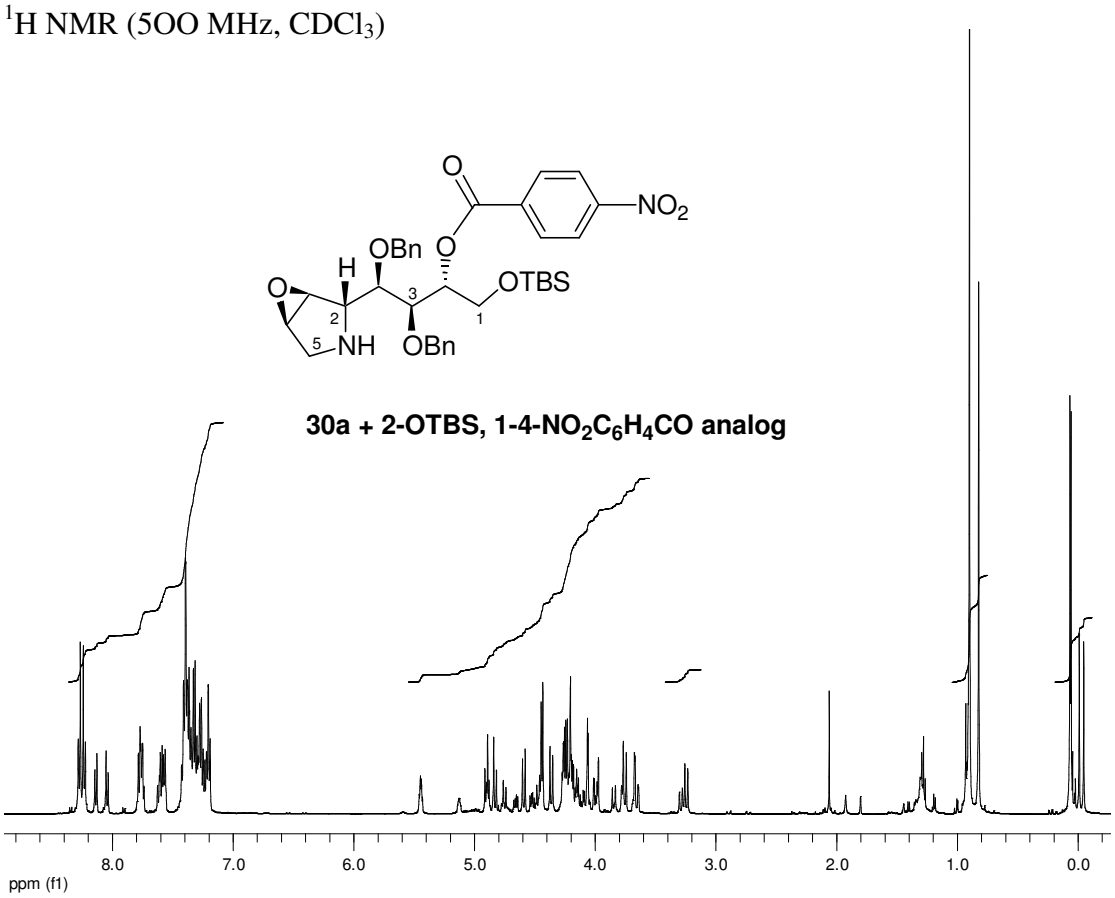
^{1}H NMR (500 MHz, D_2O)



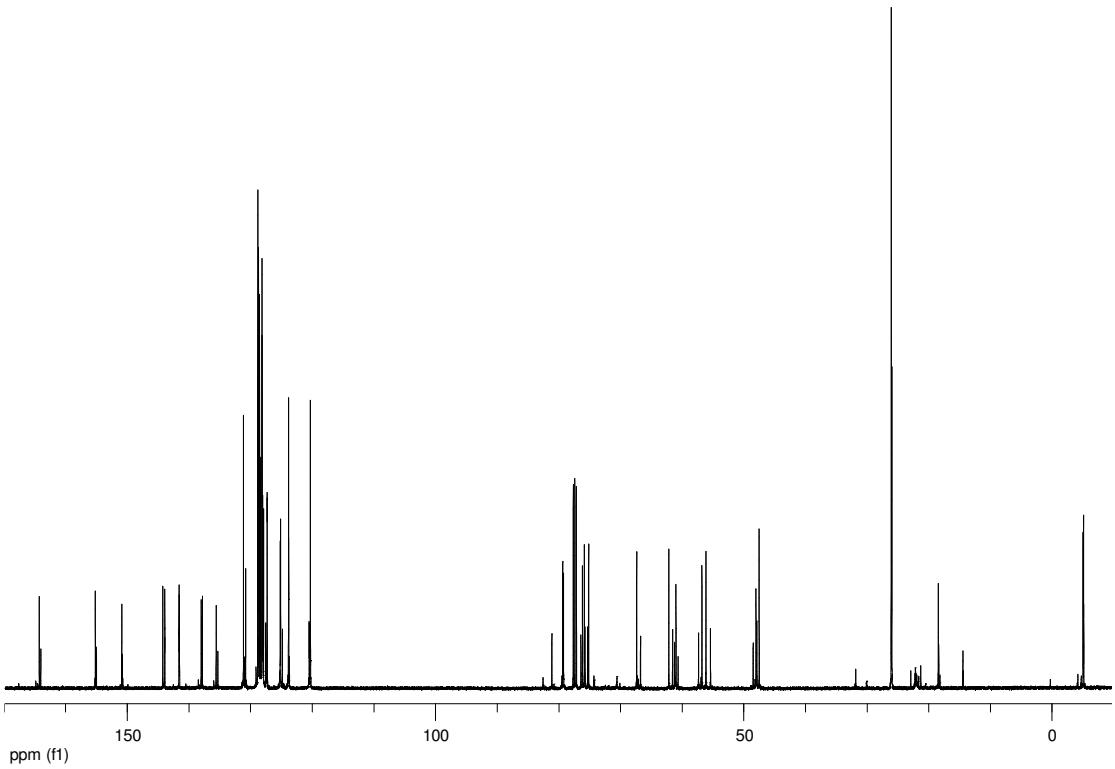
^{13}C NMR (125 MHz, D_2O)



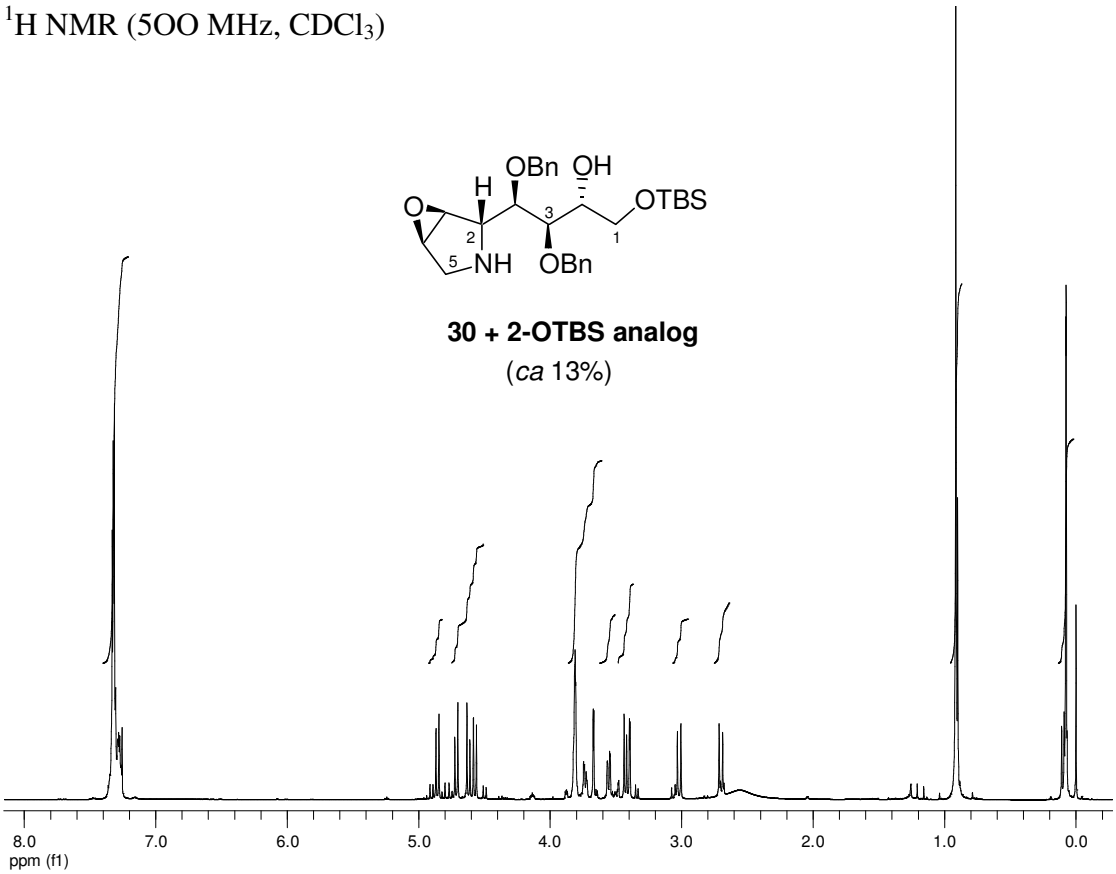
^{1}H NMR (5OO MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)

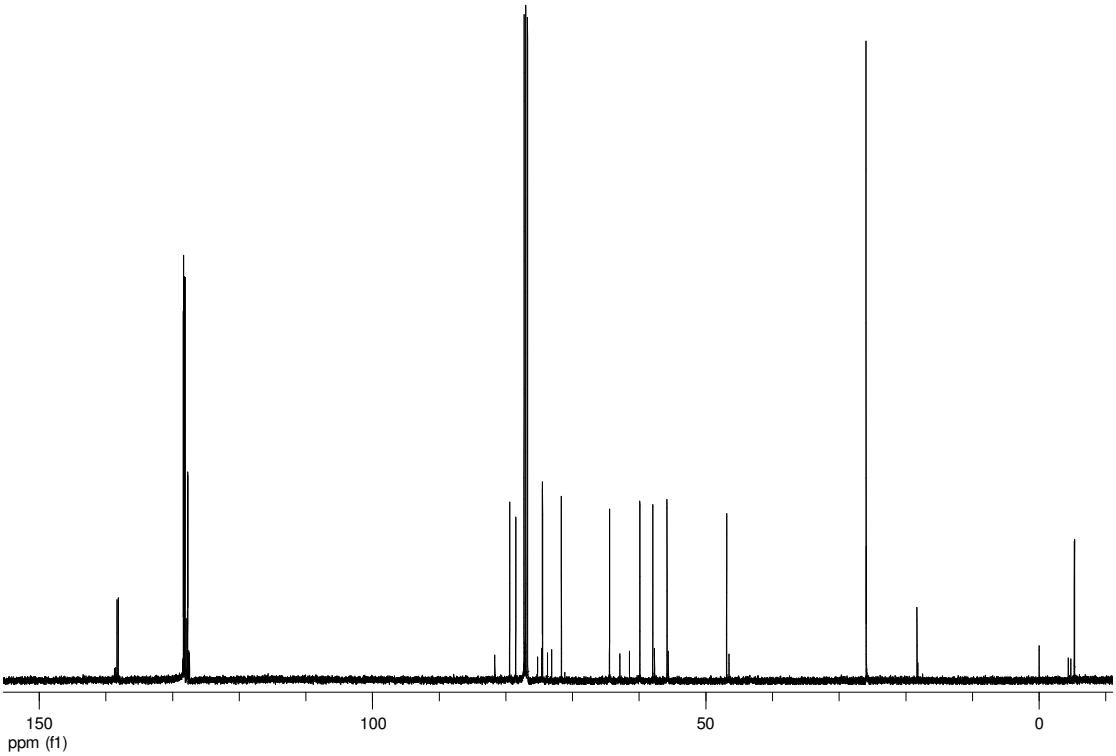


^{1}H NMR (5OO MHz, $CDCl_3$)

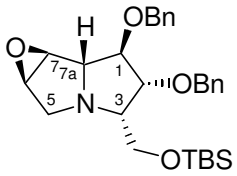


30 + 2-OTBS analog
(*ca* 13%)

^{13}C NMR (125 MHz, $CDCl_3$)

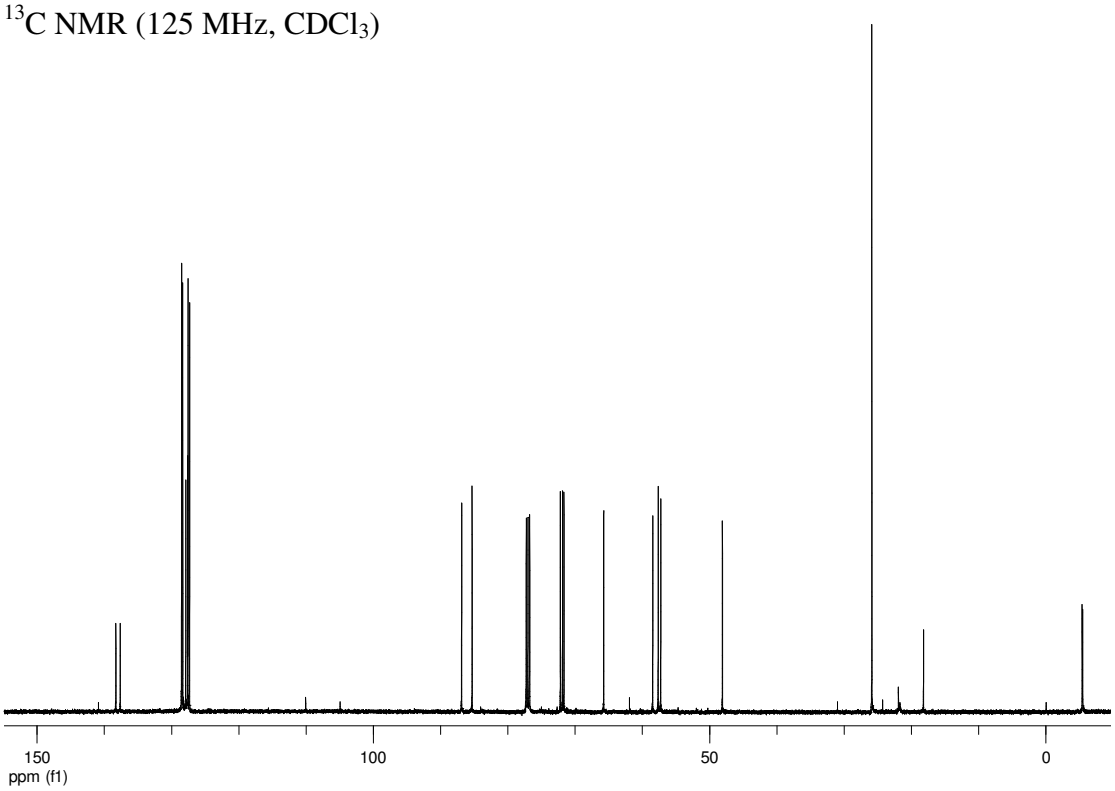


^{1}H NMR (5OO MHz, $CDCl_3$)

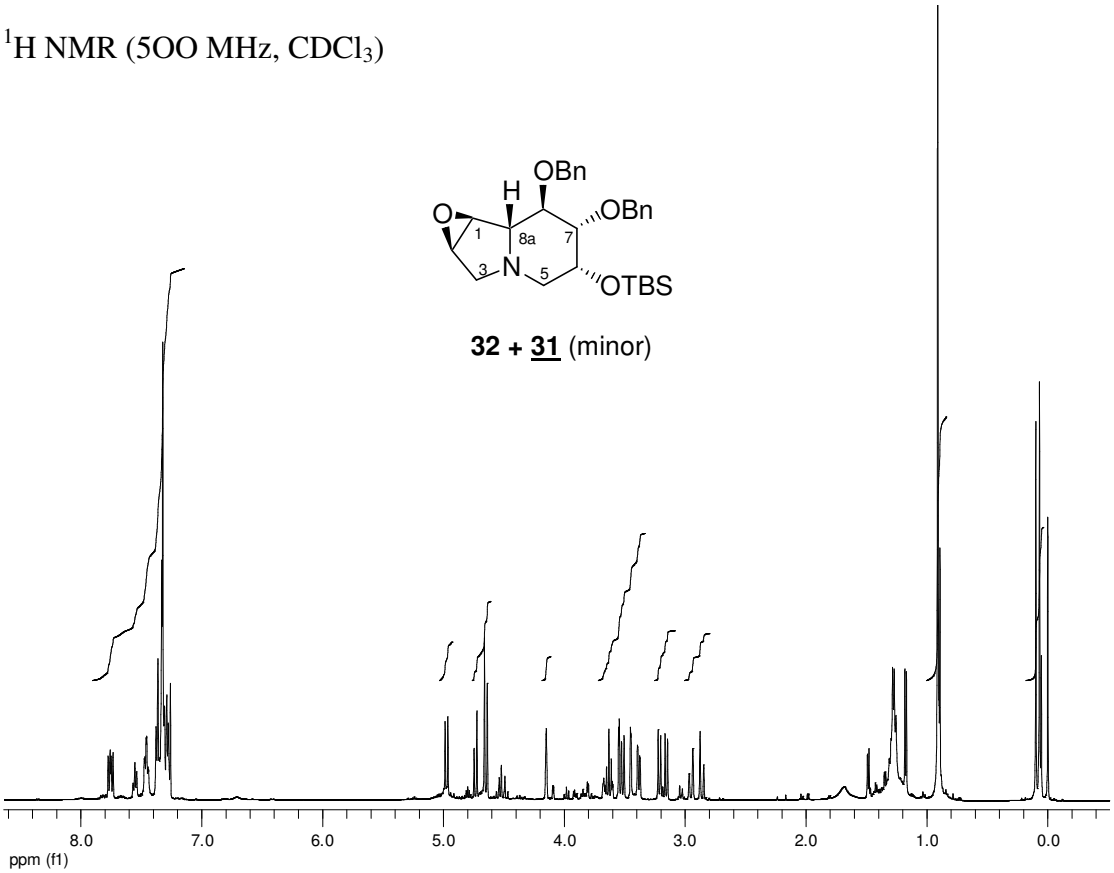


31 + <u>32</u> (minor)

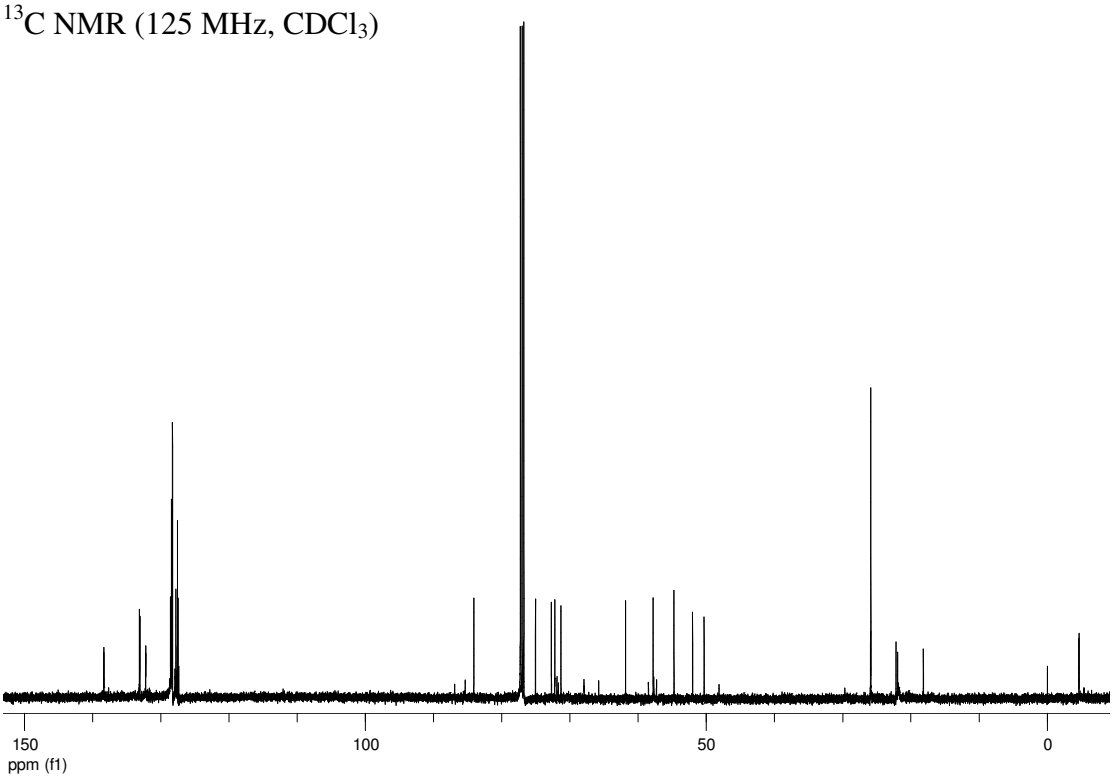
^{13}C NMR (125 MHz, $CDCl_3$)



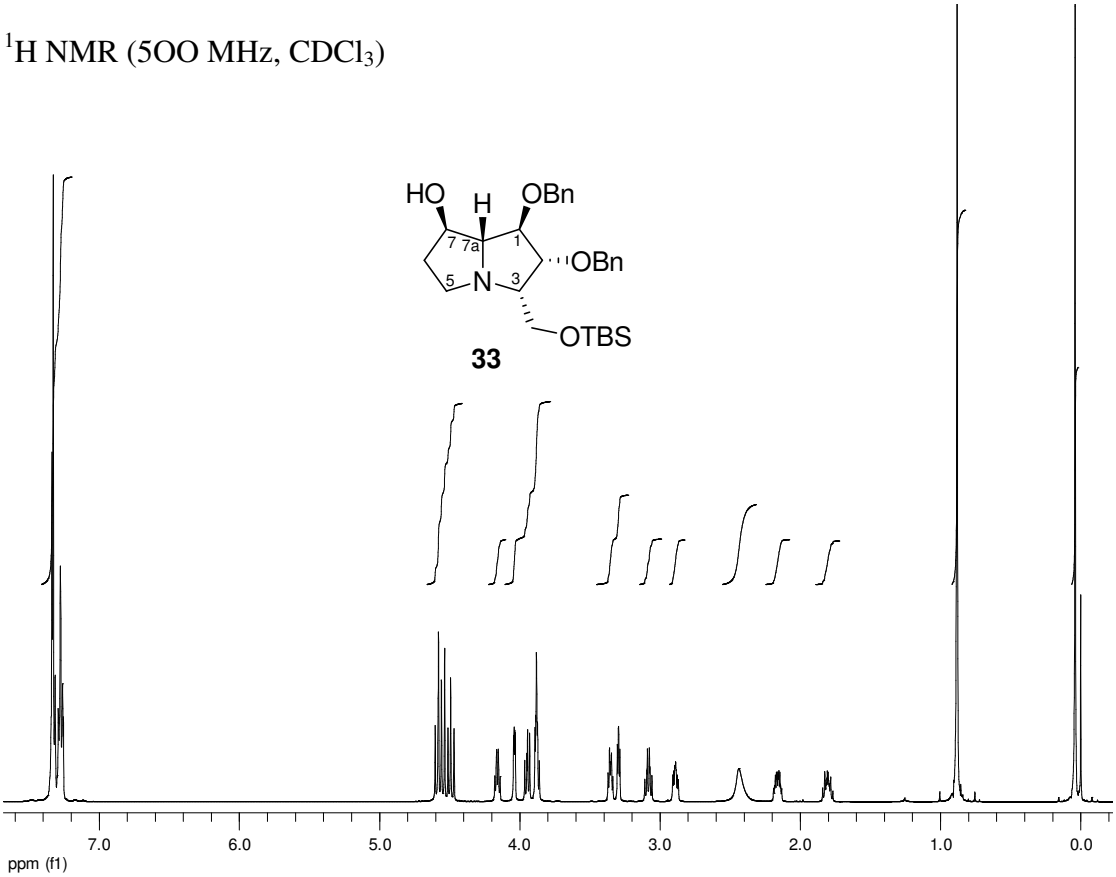
^{1}H NMR (5OO MHz, $CDCl_3$)



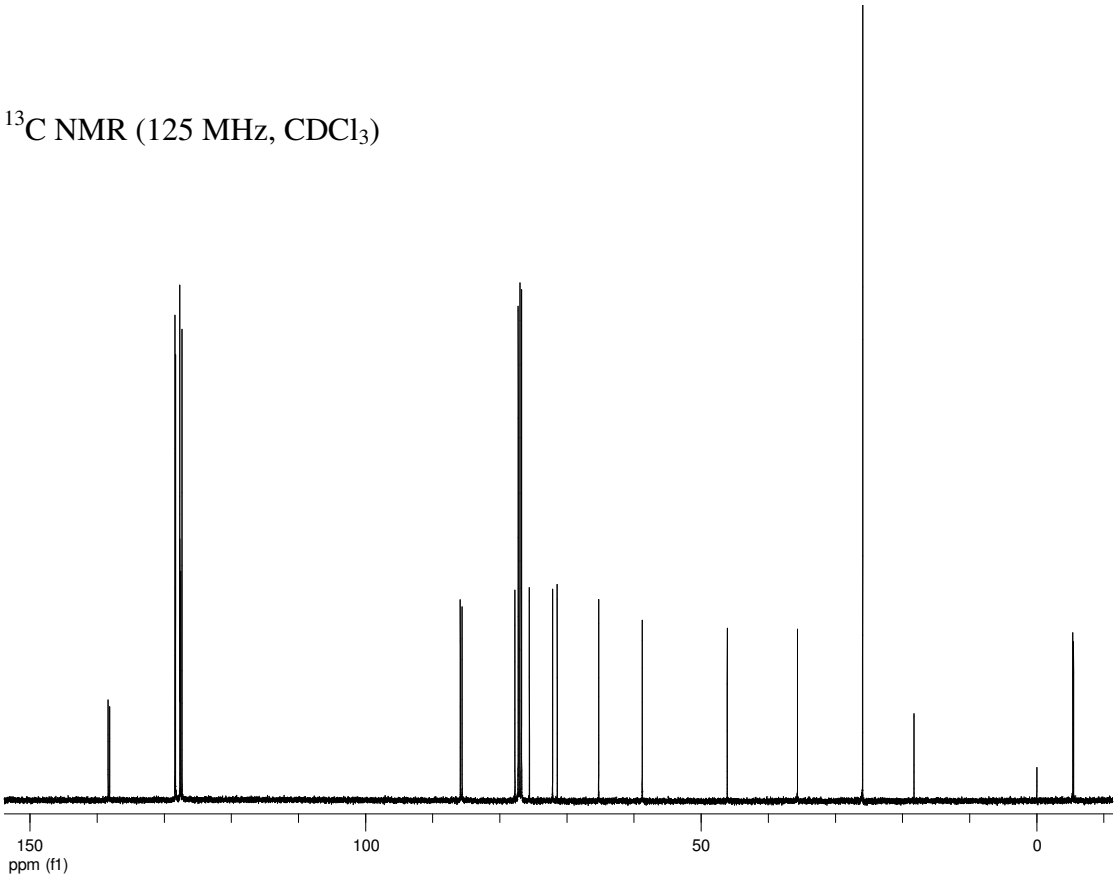
^{13}C NMR (125 MHz, $CDCl_3$)



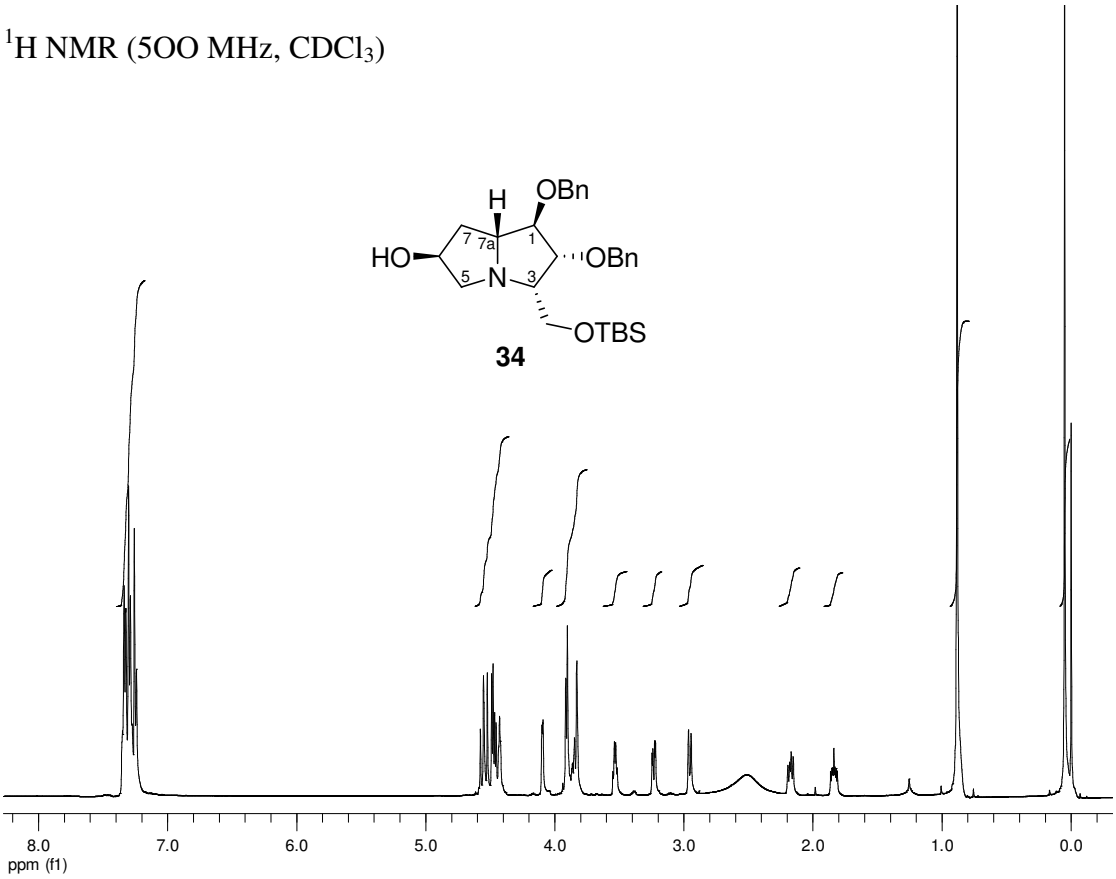
^{1}H NMR (5OO MHz, $CDCl_3$)



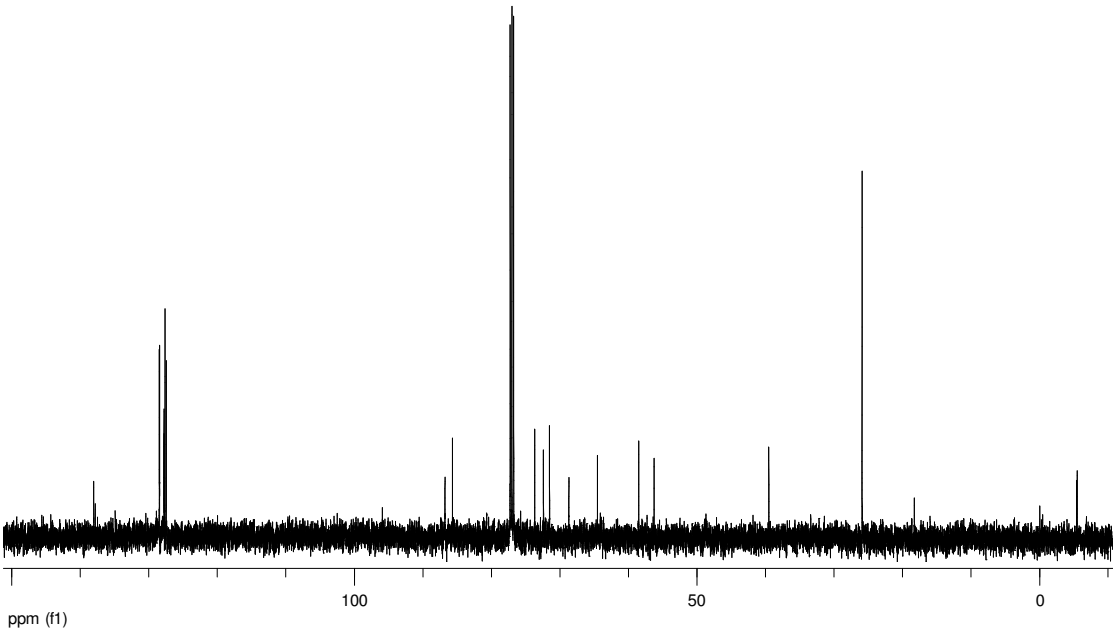
^{13}C NMR (125 MHz, $CDCl_3$)



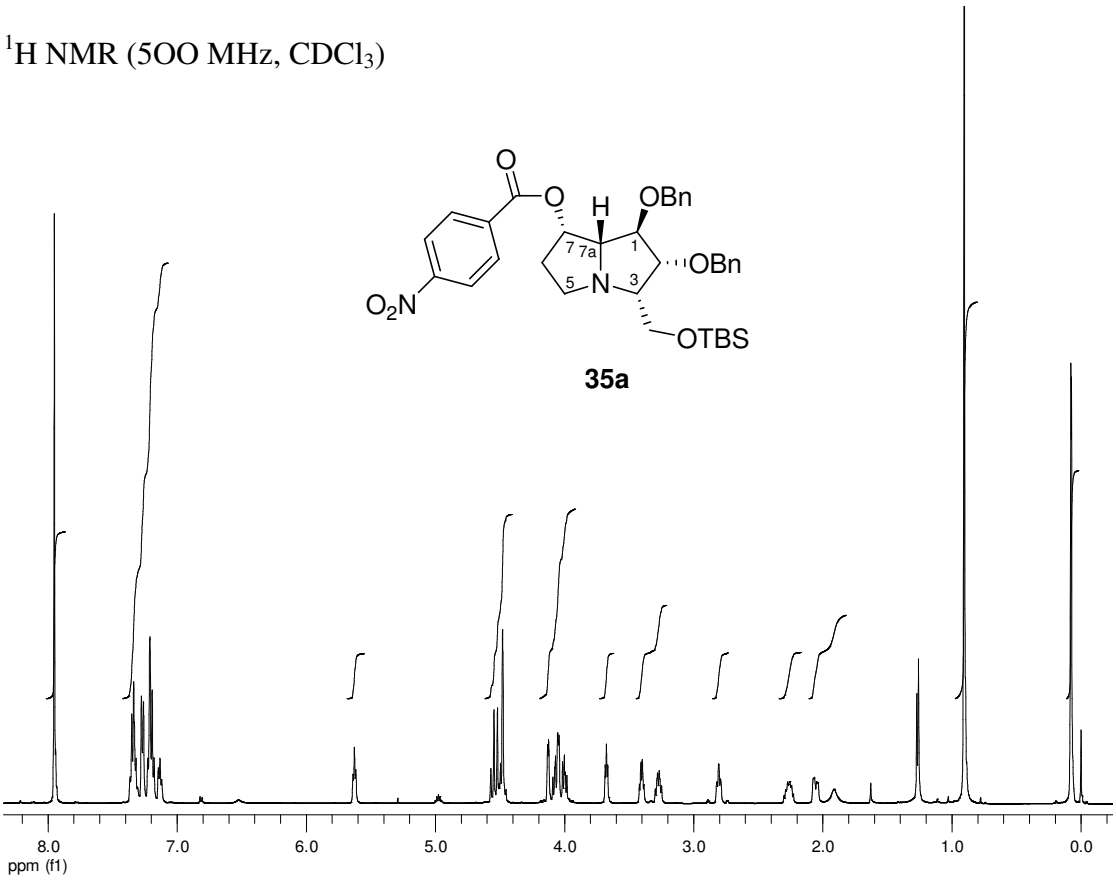
^{1}H NMR (5OO MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)

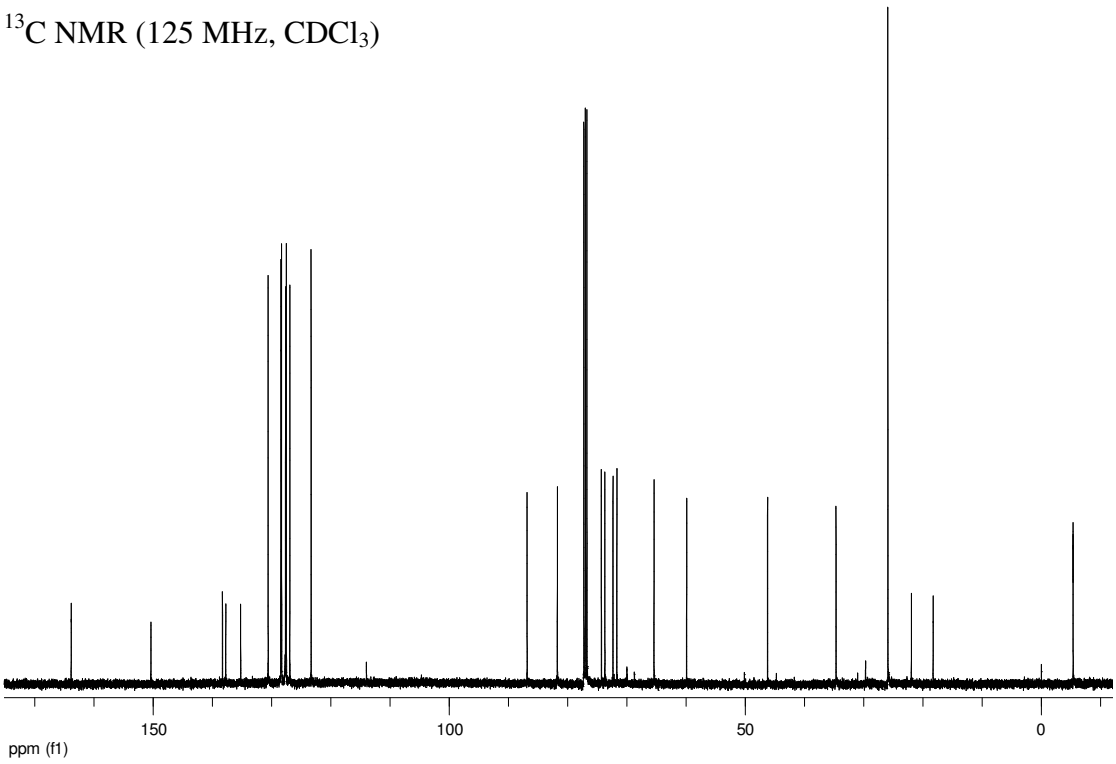


^{1}H NMR (5OO MHz, $CDCl_3$)

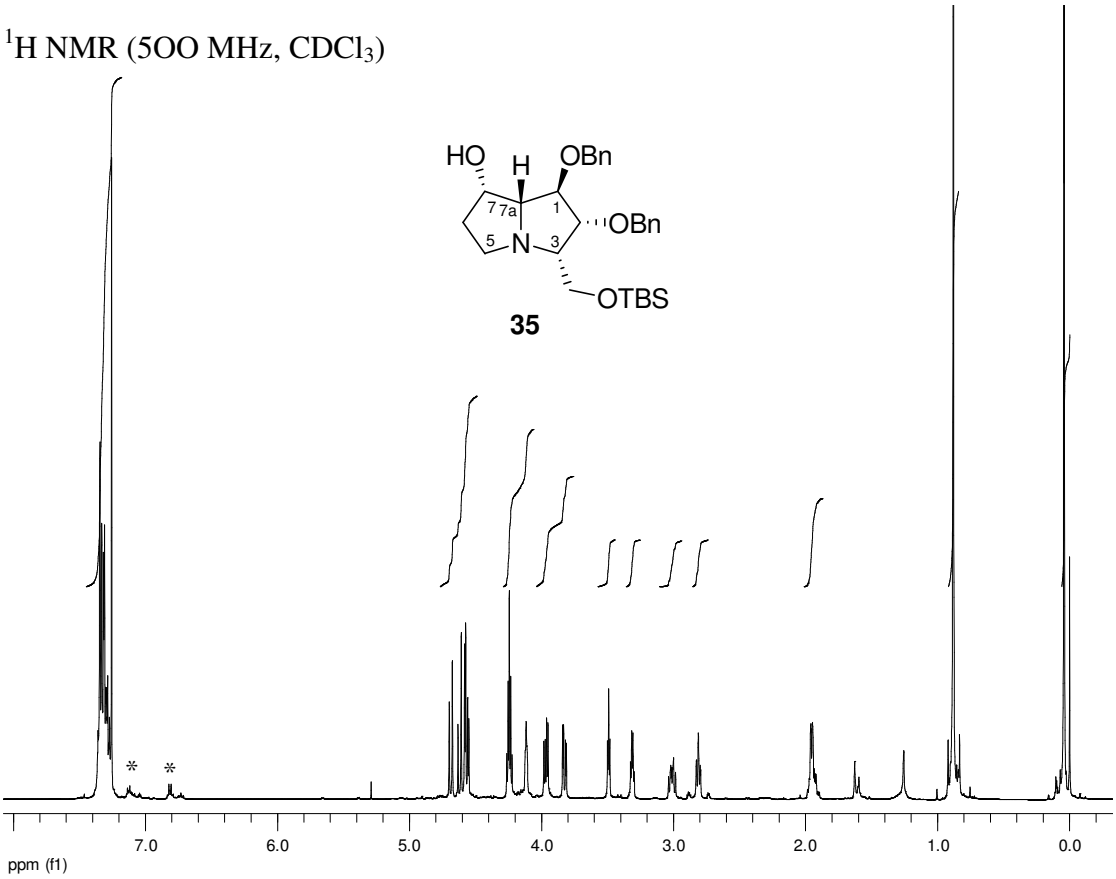


35a

^{13}C NMR (125 MHz, $CDCl_3$)

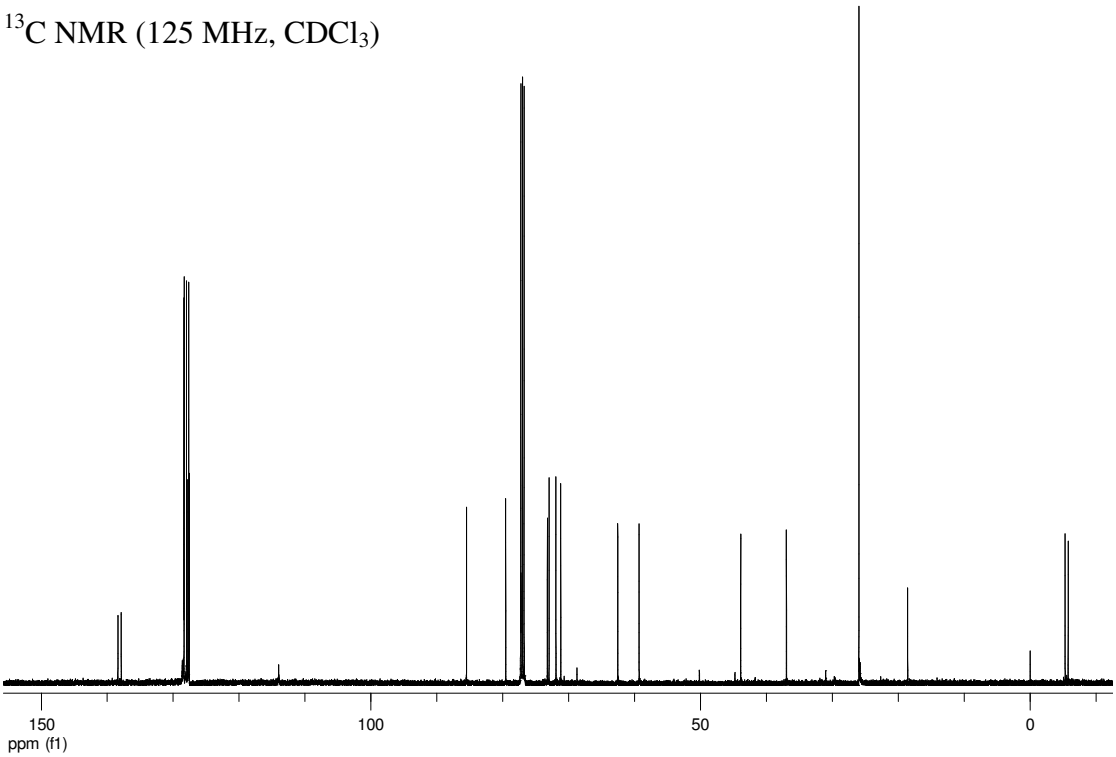


^{1}H NMR (5OO MHz, $CDCl_3$)

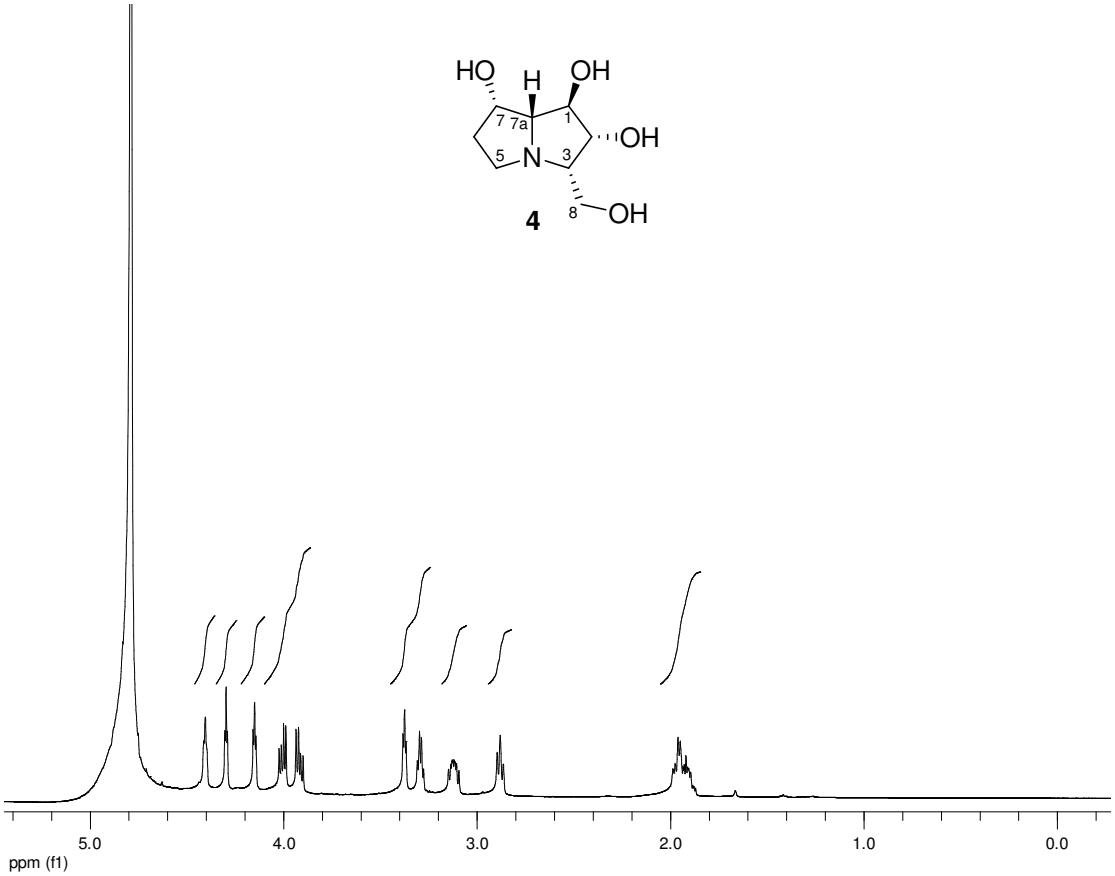


* Impurity

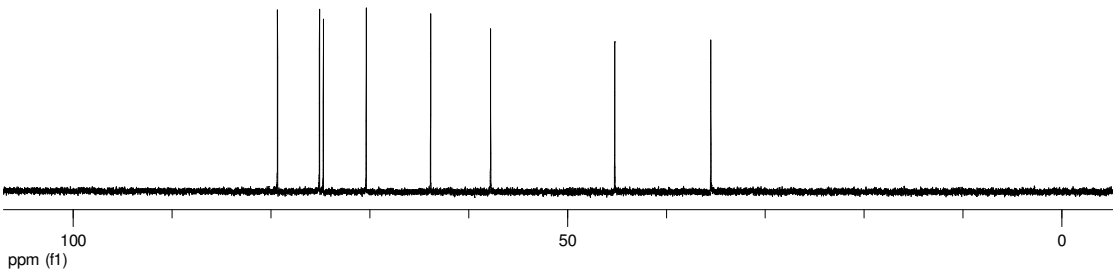
^{13}C NMR (125 MHz, $CDCl_3$)

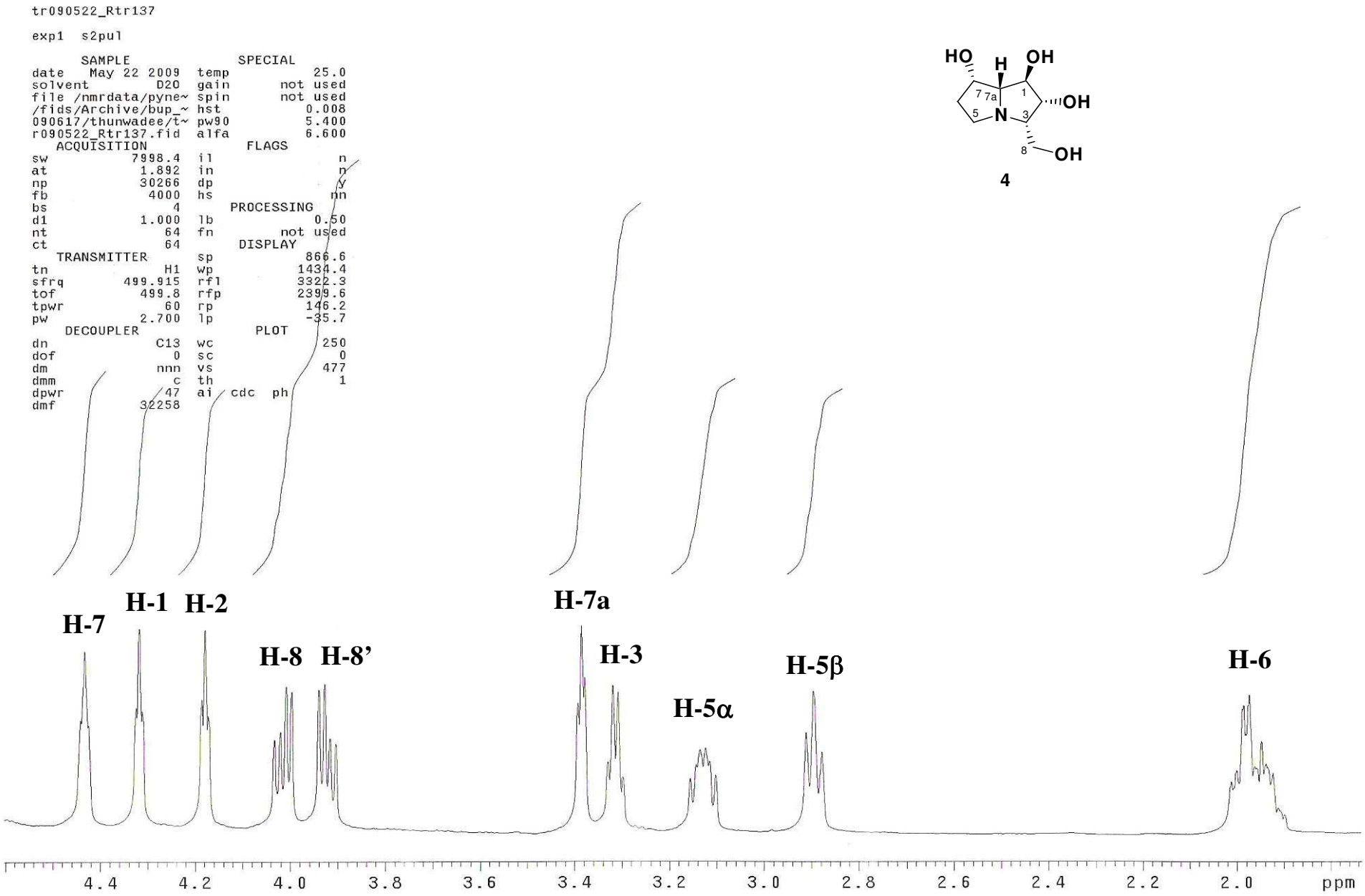


^{1}H NMR (5OO MHz, D_2O)



^{13}C NMR (125 MHz, D_2O)





^{1}H NMR (5OO MHz, D_2O)

tr090522_Rtr137-13C

exp1 s2pul

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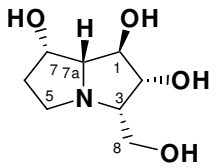
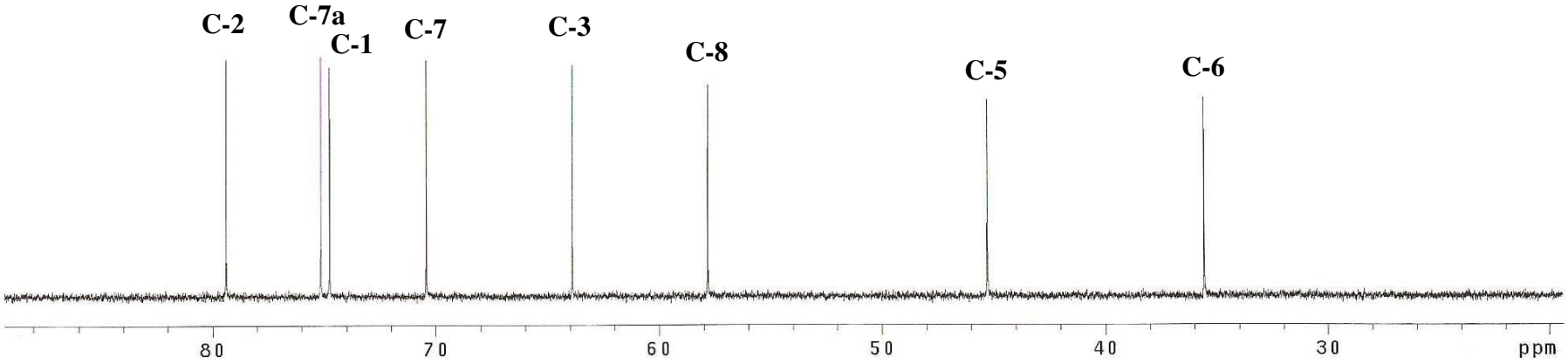
	/fids/Archive/bup_~	hst	0.008
	090617/thunwadee/t~	pw90	15.800
	r090522_Rtr137-13C~	alfa	6.600
	.fid	FLAGS	
ACQUISITION		il	n
sw	31421.8	in	n
at	1.300	dp	y
np	81726	hs	nn
fb	17000	PROCESSING	
bs	64	lb	0.50
d1	1.000	fn	not used
nt	12468	DISPLAY	
ct	12468	sp	2433.0
TRANSMITTER		wp	8794.4
tn	C13	rfl	6619.5
sfrq	125.716	rfp	4469.7
tof	1884.0	rp	150.4
tpwr	63	lp	-169.3
pw	7.900	PLOT	
DECOUPLER		wc	250
dn	H1	sc	0
dof	0	vs	1359
dm	yyy	th	13
dmm	w	ai cdc ph	
dpwr	37		
dmf	12821		

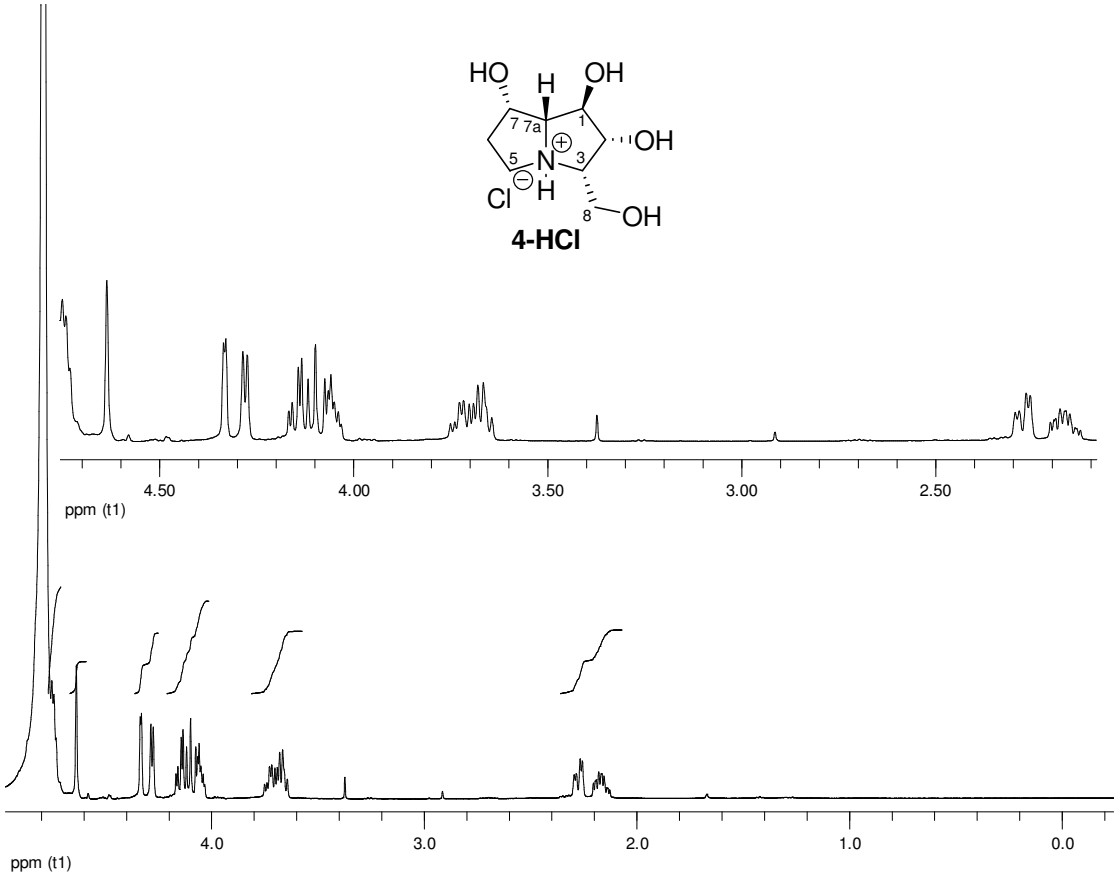


4

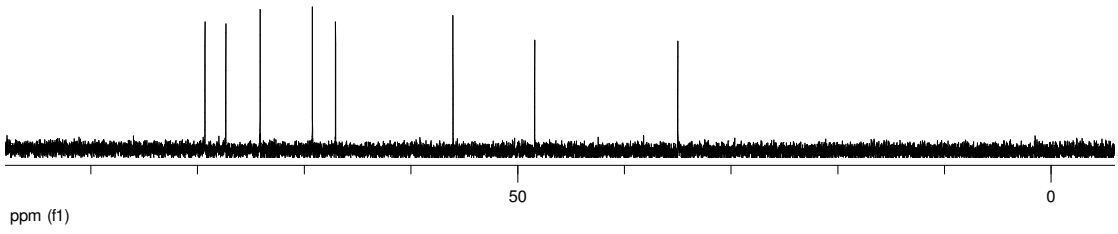


^{13}C NMR (125 MHz, D_2O)

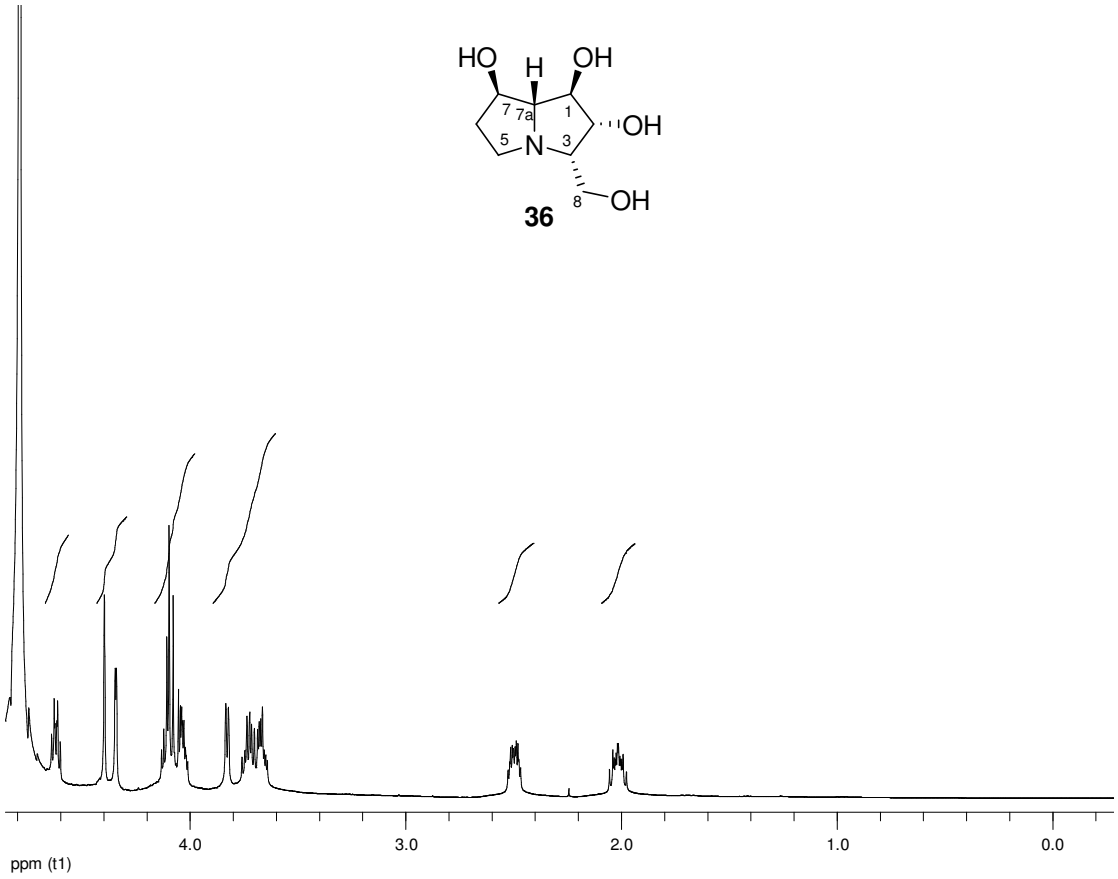
^{1}H NMR (5OO MHz, D_2O)



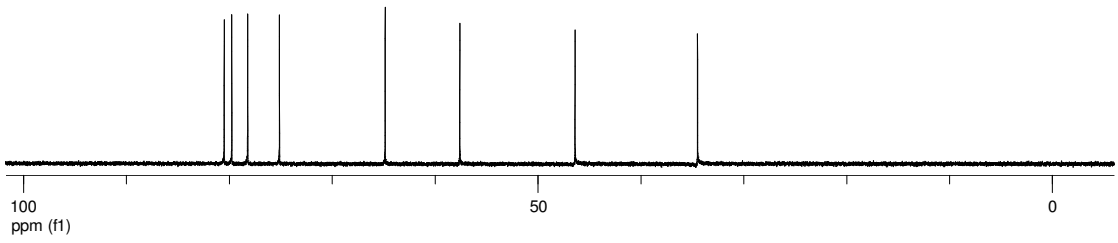
^{13}C NMR (125 MHz, D_2O)

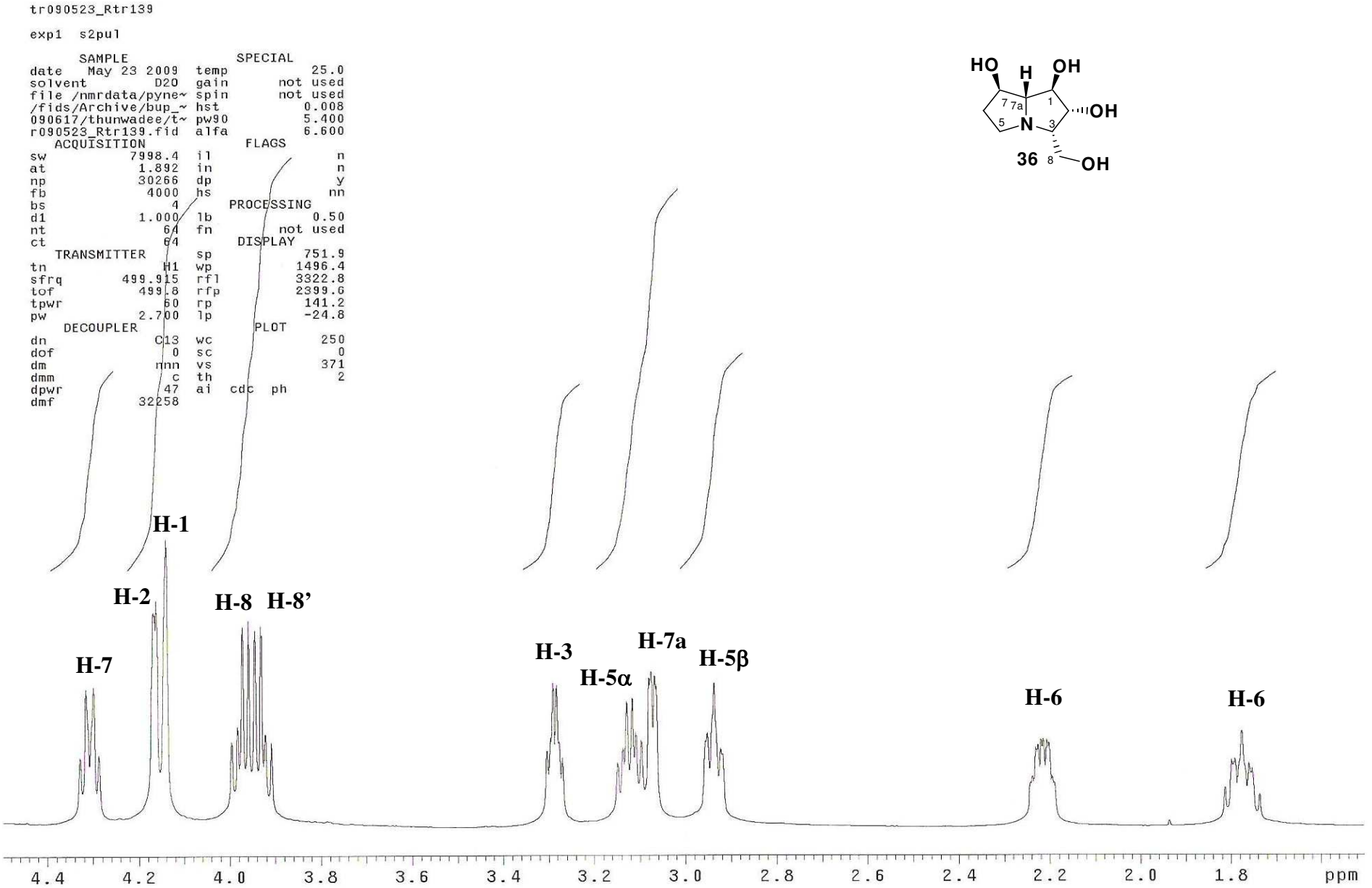


^{1}H NMR (5OO MHz, D_2O)



^{13}C NMR (125 MHz, D_2O)



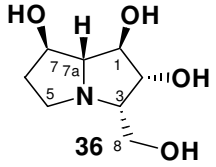


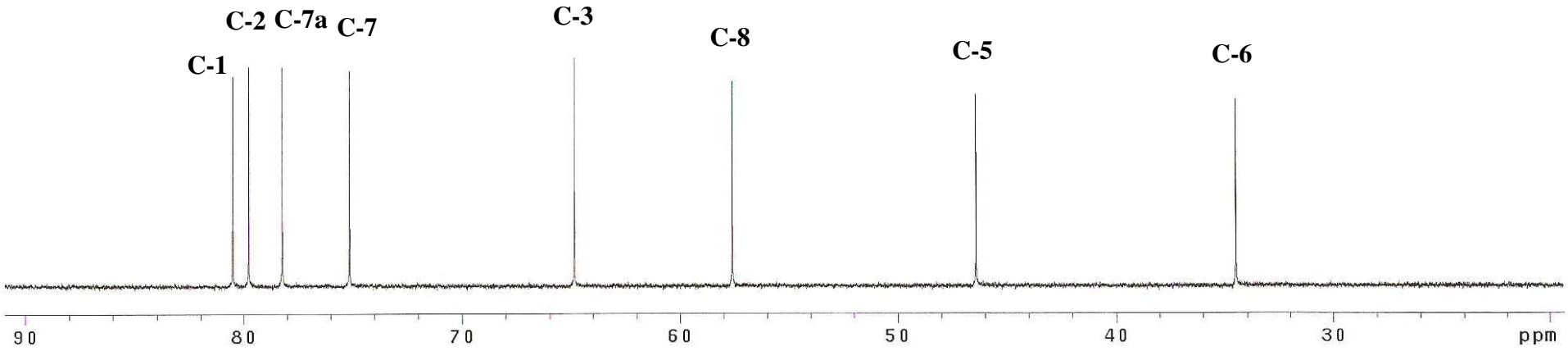
^{1}H NMR (5OO MHz, D_2O)

tr090523_Rtr139-13C

exp1 s2pul

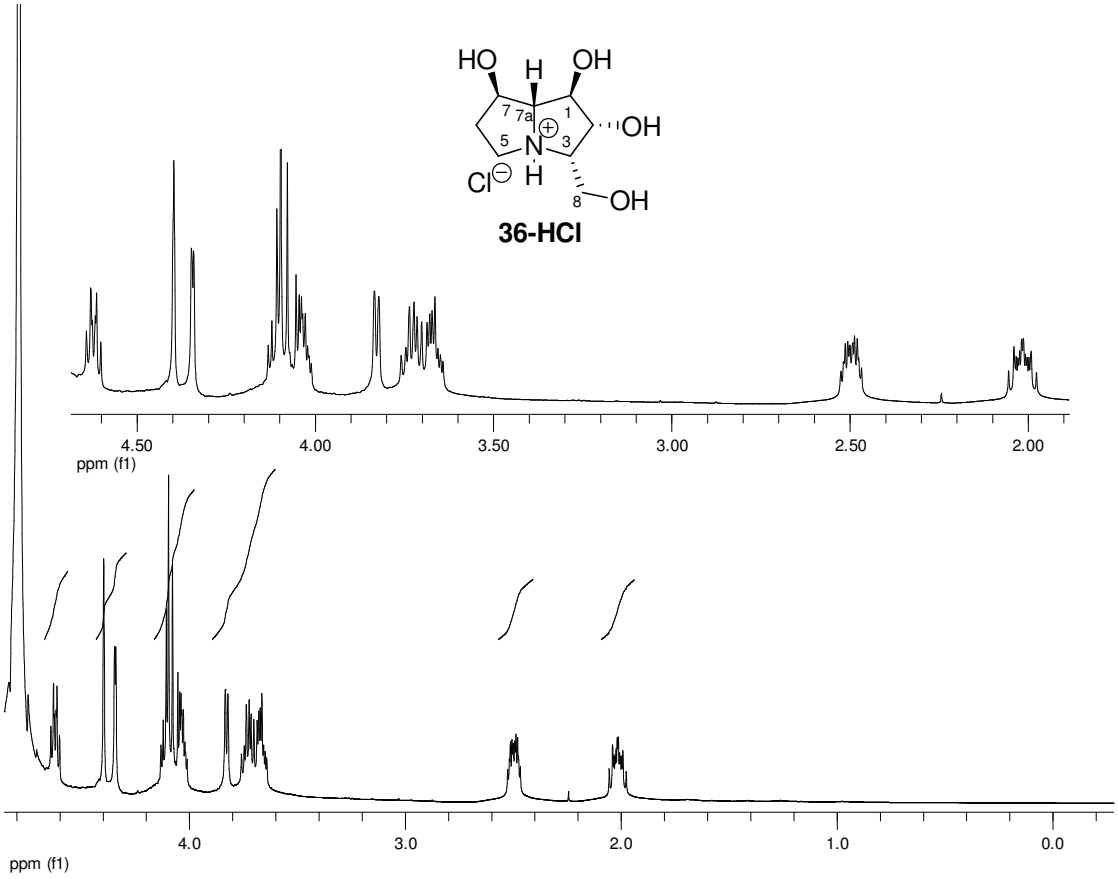
SAMPLE	D_2O	SPECIAL	
date	May 23 2009	temp	25.0
solvent	CDCl3	gain	not used
file	/nmrdata/pyne~	spin	not used
	/fids/Archive/bup_~	hst	0.008
	090617/thunwadee/t~	pw90	15.800
	r090523_Rtr139-13C~	alfa	6.600
	.fid	FLAGS	
ACQUISITION		il	n
sw	31421.8	in	n
at	1.300	dp	y
np	81726	hs	nn
fb	17000	PROCESSING	
bs	64	lb	0.50
d1	1.000	fn	not used
nt	11688	DISPLAY	
ct	11688	sp	2432.5
TRANSMITTER		wp	9001.0
tn	C13	rfl	6486.7
sfrq	125.716	rfp	4336.5
tof	1884.0	rp	160.5
tpwr	63	lp	-199.6
pw	7.900	PLOT	
DECOUPLER		wc	250
dn	H1	sc	0
dof	0	vs	846
dm	yyy	th	8
dmm	w	ai cdc ph	
dpwr	37		
dmf	12821		



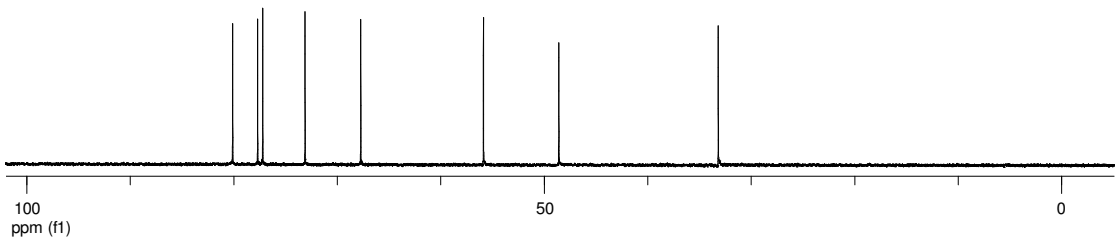


^{13}C NMR (125 MHz, D_2O)

^{1}H NMR (5OO MHz, D_2O)



^{13}C NMR (125 MHz, D_2O)



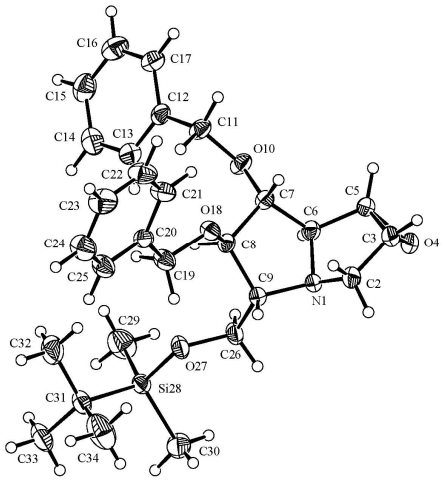


Figure Structure of $C_{28}H_{39}NO_4Si$ **21** with labelling of selected atoms. Anisotropic displacement ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

Crystal/refinement data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 752850).