Supporting information

Chiral indolizinium salts derived from 2-pyridinecarbaldehyde. First diastereoselective syntheses of (–)-1-*epi*-lentiginosine

Hisami Rodriguez-Matsui [1], David M. Aparicio [1], María L. Orea [1], Jorge R. Juárez [1], Victor Gómez-Calvario [1], Dino Gnecco [1], Alan Carrasco-Carballo [2], and Joel L. Terán [1,*]

[1]Centro de Química, Instituto de Ciencias, Benemérita Universidad Autónoma de Puebla, Edif. IC-9 Complejo de Ciencias C.U. 72570 Puebla, México

[2]Laboratorio de Elucidación y Síntesis en Química Orgánica, Benemérita Universidad Autónoma de Puebla, C.U., 72570 Puebla, México

Table of Contents

1. General Information…… …..... .....S2

2. Characterization of Products.… ……S3

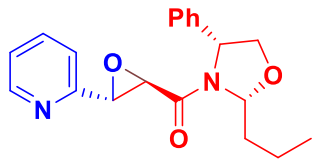
3. ^{1}H and ^{13}C NMR Spectra…….…….....S7

4. X-ray crystallography data S28

General Information

All reagents and solvents were purchased from commercial sources. The ^{1}H and ^{13}C spectra were determined with a Bruker Avance III Spectrometer ($CDCl_3$ or CD_3OD solvents) operating at 500 and 125 MHz, respectively. The chemical shifts were reported in parts per million (ppm), downfield from SiMe4 (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet). Multiplicities were afforded as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); ddd (doublet of doublets of doublets); or m (multiplets). The number of protons for a given resonance is indicated by nH. Coupling constants were reported as a *J* value in Hz. Thin layer chromatography (TLC) was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Optical rotations were determined at room temperature with a Perkin-Elmer 341 polarimeter, using a 1 dm cell with a total volume of 1mL, and are referenced to the D-line of sodium. Mass spectra were recorded with a JEOL Station JMS-700 instrument at a voltage of 70 eV. X-Ray Diffraction analysis was performed on a diffractometer STOE Stadivari using Ag-Kα radiation (λ = 0.56083 Å, AXO micro-source) and equipped with a Dectris Pilatus-100 K detector. Intensities were collected at 295 K, and structures were refined using the current release of SHELXL (2018/3). The products were purified by column chromatography on silica gel 60 (63-200nm).

((2*R*,4*R*)-4-phenyl-2-propyloxazolidin-3-yl)((2*R*,3*S*)-3-(pyridin-2-yl)oxiran-2-yl)methanone, 2a

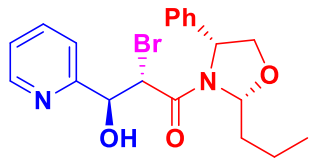


2a

major diastereoisomer

Yellow oil, 85% yield. Major diastereoisomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 4.8 Hz, 1H), 7.45 (m, 1H), 7.13 (m, 2H), 7.07 (dd, *J* = 7.5, 4.9 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 2H), 6.90 (m, 2H), 5.51 (dd, *J* = 9.2, 2.5 Hz, 1H), 5.10 (t, *J* = 6.6 Hz, 1H), 4.33 (dd, *J* = 9.1, 6.9 Hz, 1H), 3.89 (dd, *J* = 9.2, 6.3 Hz, 1H), 3.81 (d, *J* = 1.8 Hz, 1H), 3.59 (d, *J* = 1.9 Hz, 1H), 2.15 (dddd, *J* = 16.3, 9.3, 6.2, 2.5 Hz, 1H), 1.69 (dtd, *J* = 14.2, 9.4, 5.3 Hz, 1H), 1.51 (m, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 149.4, 139.2, 136.2, 128.9, 128.8, 127.8, 126.0, 123.2, 121.0, 91.7, 73.7, 60.4, 57.9, 56.4, 35.2, 18.4, 13.7.. **HRMS(ESI):** Calcd for $C_{20}H_{22}N_2O_3$: 338.1630 Found: 338.1629.

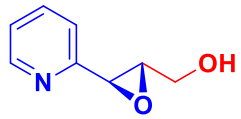
(2*S*,3*S*)-2-bromo-3-hydroxy-1-((2*R*,4*R*)-4-phenyl-2-propyloxazolidin-3-yl)-3-(pyridin-2-yl)propan-1-one, 3



3

White solid, mp = 129 °C, 98% yield. Major rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (dt, *J* = 4.0, 0.8 Hz, 1H), 7.72 (m, 1H), 7.72-7.33 (m, 5H), 7.25 (m, 1H), 6.74 (m, 1H), 5.28 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.08 (dd, *J* = 6.6, 4.6 Hz, 1H), 4.99 (br, 1H), 4.73 (d, *J* = 5.5 Hz, 1H), 4.14 (dd, *J* = 8.9, 6.7 Hz, 1H), 3.98 (dd, *J* = 8.9, 4.6 Hz, 1H), 2.17 (m, 1H), 1.70 (m, 2H), 1.49 (m, 2H), 0.99 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 159.4, 138.3, 137.1, 129.1, 126.6, 125.1, 123.3, 122.0, 91.2, 75.9, 73.8, 61.2, 45.6, 34.9, 18.6, 13.9. HRMS(ESI): Calcd for $C_{20}H_{23}BrN_2O_3$: 418.0892 Found: 418.0890.

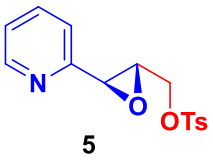
((2*S*,3*S*)-3-(pyridin-2-yl)oxiran-2-yl)methanol.



4

Colorless oil, 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59-8.52 (m, 1H), 7.70 (td, *J* = 7.8, 1.8 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.25 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 4.08 (d, *J* = 2.1 Hz, 1H), 4.05 (dt, *J* = 12.8, 2.4 Hz, 1H), 3.85 (dd, *J* = 12.8, 4.0 Hz, 1H), 3.39 (dq, *J* = 4.2, 2.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 149.4, 137.0, 123.3, 120.3, 61.8, 61.3, 56.0. HRMS(ESI): Calcd for $C_8H_9NO_2$: 151.0633 Found: 151.0630.

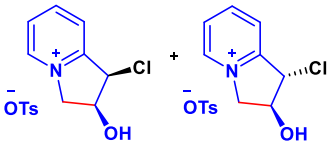
((2*S*,3*S*)-3-(pyridin-2-yl)oxiran-2-yl)methyl 4-methylbenzenesulfonate, 5.



5

Yellow oil, 94% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.77 – 7.70 (m, 2H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.32 – 7.24 (m, 2H), 7.18 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.15 (dt, *J* = 7.9, 1.1 Hz, 1H), 4.33 (dd, *J* = 11.6, 3.2 Hz, 1H), 4.12 – 3.97 (m, 1H), 3.84 (d, *J* = 2.0 Hz, 1H), 3.38 (ddd, *J* = 5.9, 3.1, 1.9 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 148.3, 144.2, 136.1, 131.5, 129.0, 127.0, 122.6, 119.5, 68.2, 56.7, 55.3, 20.7. HRMS(ESI): Calcd for $C_{15}H_{15}NO_4S$: 305.0722 Found: 305.0721.

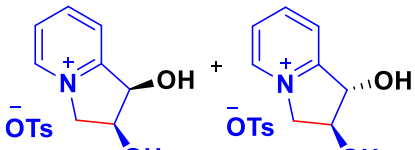
Major diastereoisomer (1*R*,2*S*)-1-chloro-2-hydroxy-2,3-dihydro-1H-indolizin-4-ium 4-methylbenzenesulfonate, 6a.



6a (*dr*= 81:19) 6b

Black oil, quantitative yield. Inseparable diastereomeric mixture. Major diastereoisomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (d, *J* = 6.0 Hz, 1H), 8.66 (td, *J* = 7.9, 1.3 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.14 (t, *J* = 6.9 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 5.94 (d, *J* = 4.8 Hz, 1H), 4.97 (dd, *J* = 13.3, 4.6 Hz, 1H), 4.89 (td, *J* = 4.6, 2.7 Hz, 1H), 4.79 (dd, *J* = 13.4, 2.9 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8, 147.2, 146.0, 143.0, 138.2, 128.6, 128.0, 125.9, 125.4, 69.8, 63.7, 61.2, 21.3. HRMS(ESI): Calcd for $C_{15}H_{16}ClNO_4S$: 341.0488 Found: 341.0486.

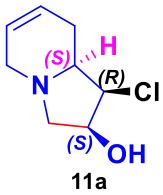
Major diastereoisomer (1*R*,2*S*)-1,2-dihydroxy-2,3-dihydro-1*H*-indolizin-4-ium 4-methylbenzenesulfonate, 10a.



10a (*dr*= 81:19) 10b

Black oil, quantitative yield. Inseparable diastereomeric mixture. Major diastereoisomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, *J* = 5.9 Hz, 1H), 8.46 (t, *J* = 7.7 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.88 (t, *J* = 6.7 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 6.7 Hz, 2H), 5.65 – 5.36 (m, 1H), 4.81 (m, 3H), 2.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 146.3, 142.4, 141.4, 139.5, 129.4, 127.2, 125.3, 124.6, 74.2, 70.4, 63.2, 20.5. HRMS(ESI): Calcd for $C_{15}H_{17}ClNO_5S$: 323.0827 Found: 323.0825.

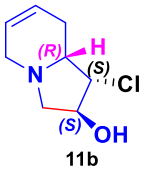
(1*R*,2*S*,8*aS*)-1-chloro-1,2,3,5,8,8a-hexahydroindolizin-2-ol, 11a.



11a

White solid, mp = 140°C, 74% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (ddd, *J* = 10.0, 5.3, 2.4 Hz, 1H), 5.67 (dtd, *J* = 10.1, 2.9, 1.4 Hz, 1H), 4.51 (dt, *J* = 16.9, 5.2 Hz, 2H), 3.48 (dq, *J* = 16.3, 2.3 Hz, 1H), 3.14 (dd, *J* = 10.6, 4.3 Hz, 1H), 2.89 (br, 1H), 2.81 – 2.66 (m, 2H), 2.56 (ddq, *J* = 14.9, 7.8, 2.4 Hz, 1H), 2.46 (br, 1H), 2.10 (dd, *J* = 17.0, 4.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 124.7, 124.5, 70.4, 66.7, 61.3, 60.1, 52.4, 28.0. HRMS(ESI): Calcd for $C_8H_{12}ClNO$: 173.0607 Found: 173.0605.

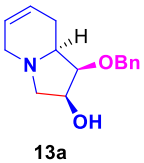
(1*S*,2*S*,8*aR*)-1-chloro-1,2,3,5,8,8a-hexahydroindolizin-2-ol, 11b.



11b

White solid, mp = 136 °C, 14% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (ddd, *J* = 9.9, 5.3, 2.4 Hz, 1H), 5.69 (dddd, *J* = 9.9, 4.4, 2.9, 1.5 Hz, 1H), 4.54 (ddd, *J* = 6.5, 4.6, 1.5 Hz, 1H), 4.16 (dd, *J* = 4.8, 1.5 Hz, 1H), 3.74 (dd, *J* = 10.5, 6.7 Hz, 1H), 3.52 (ddt, *J* = 16.1, 4.4, 2.1 Hz, 1H), 2.93 (ddd, *J* = 15.9, 4.7, 2.1 Hz, 1H), 2.85 (dt, *J* = 9.4, 4.5 Hz, 1H), 2.53 (dddd, *J* = 17.0, 10.1, 4.5, 2.2 Hz, 1H), 2.25 (d, *J* = 4.6 Hz, 1H), 2.16 – 1.96 (m, 1H).^{13}C NMR (125 MHz, $CDCl_3$) δ 124.4, 78.6, 67.6, 61.4, 60.5, 52.6, 27.6. HRMS(ESI): Calcd for $C_8H_{12}ClNO$: 173.0607 Found: 173.0606.

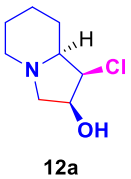
(1*R*,2*S*,8*aS*)-1-(benzyloxy)-1,2,3,5,8,8a-hexahydroindolizin-2-ol, 13a.



13a

Yellow oil, 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.18 (m, 5H), 5.88 – 5.72 (m, 1H), 5.69 – 5.50 (m, 1H), 4.66 (d, *J* = 11.8 Hz, 1H), 4.59 (d, *J* = 11.8 Hz, 1H), 4.13 (dd, *J* = 9.3, 5.6 Hz, 2H), 3.45 (d, *J* = 16.0 Hz, 1H), 3.24 (d, *J* = 10.7 Hz, 1H), 2.93 (br, 1H), 2.71 (d, *J* = 16.0 Hz, 1H), 2.63 – 2.56 (m, 1H), 2.39 (dd, *J* = 10.7, 7.3 Hz, 1H), 2.18 (dd, *J* = 10.0, 4.1 Hz, 1H), 2.12 – 1.94 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.5, 128.5, 127.9, 127.9, 125.4, 124.1, 76.4, 72.5, 70.8, 63.1, 59.2, 52.5, 25.1. HRMS(ESI): Calcd for $C_{15}H_{19}NO_2$: 245.1416 Found: 245.1414.

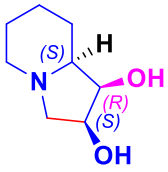
(1*R*,2*S*,8*aS*)-1-chlorooctahydroindolizin-2-ol, 12a.



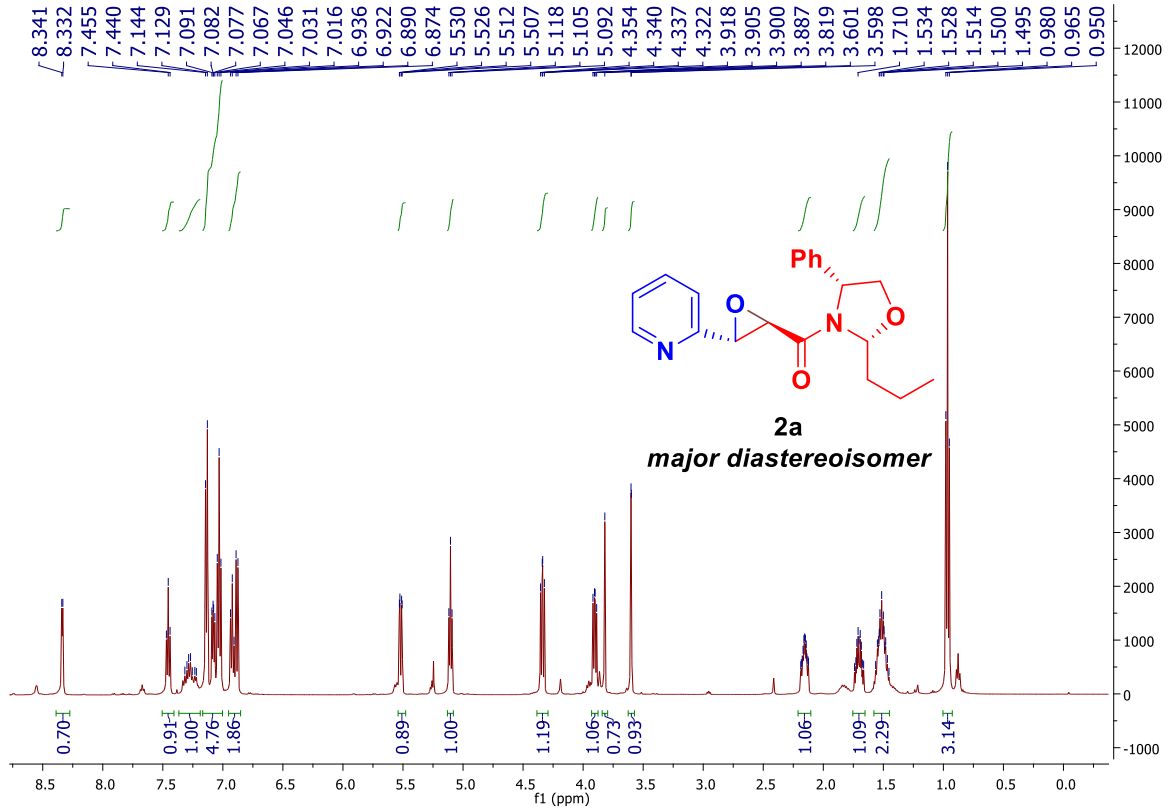
12a

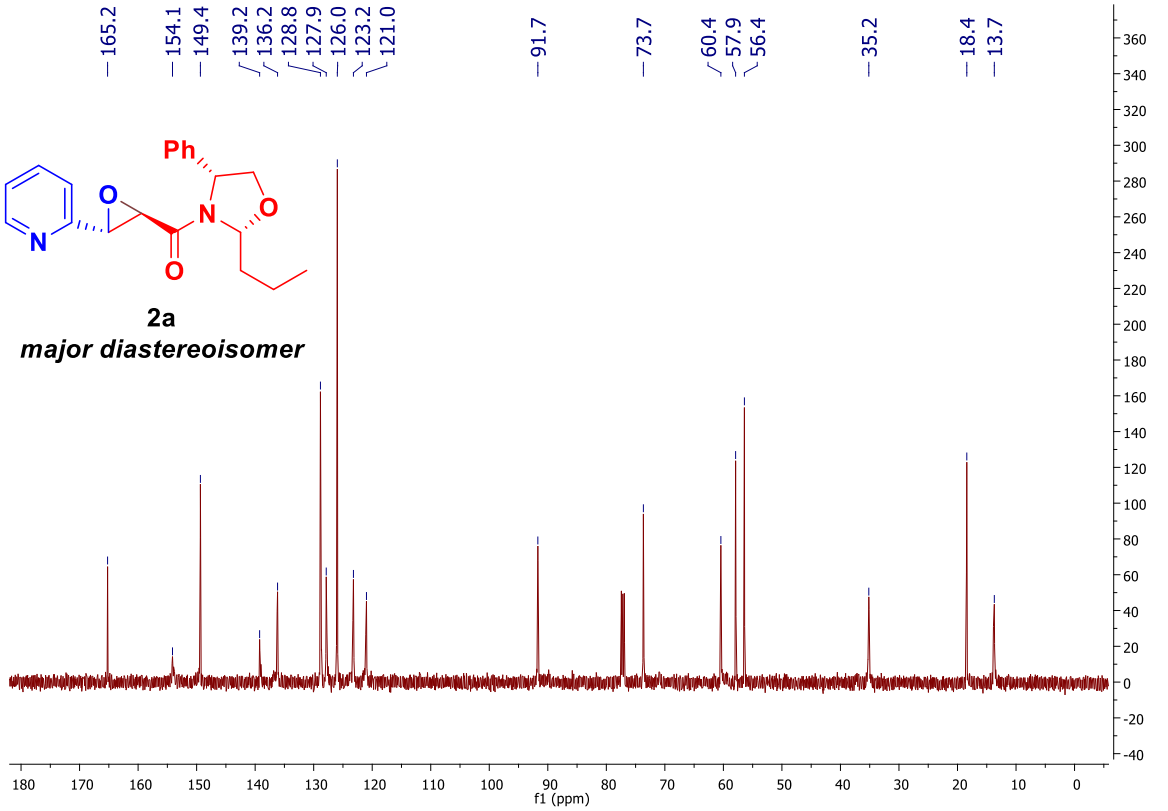
White solid, mp = 148 °C, quantitative yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.42 (dt, *J* = 9.3, 5.2 Hz, 1H), 4.30 (dd, *J* = 5.7, 3.3 Hz, 1H), 2.79 (dt, *J* = 11.3, 3.4 Hz, 1H), 2.65 (dd, *J* = 11.0, 4.7 Hz, 1H), 2.53 (dd, *J* = 11.0, 9.2 Hz, 1H), 2.35 (dt, *J* = 10.8, 3.0 Hz, 1H), 1.98 (td, *J* = 11.9, 3.0 Hz, 1H), 1.63 (dt, *J* = 13.3, 3.4 Hz, 1H), 1.60 – 1.52 (m, 1H), 1.48 – 1.42 (m, 1H), 1.42 – 1.34 (m, 1H), 1.29 (qt, *J* = 13.1, 4.2 Hz, 1H), 1.12 (qt, *J* = 13.1, 4.0 Hz, 1H).^{13}C NMR (125 MHz, $CDCl_3$) δ 69.2, 66.0, 65.7, 57.9, 52.4, 26.1, 24.0, 22.7. HRMS(ESI): Calcd for $C_8H_{14}ClNO$: 175.0764 Found: 175.0763.

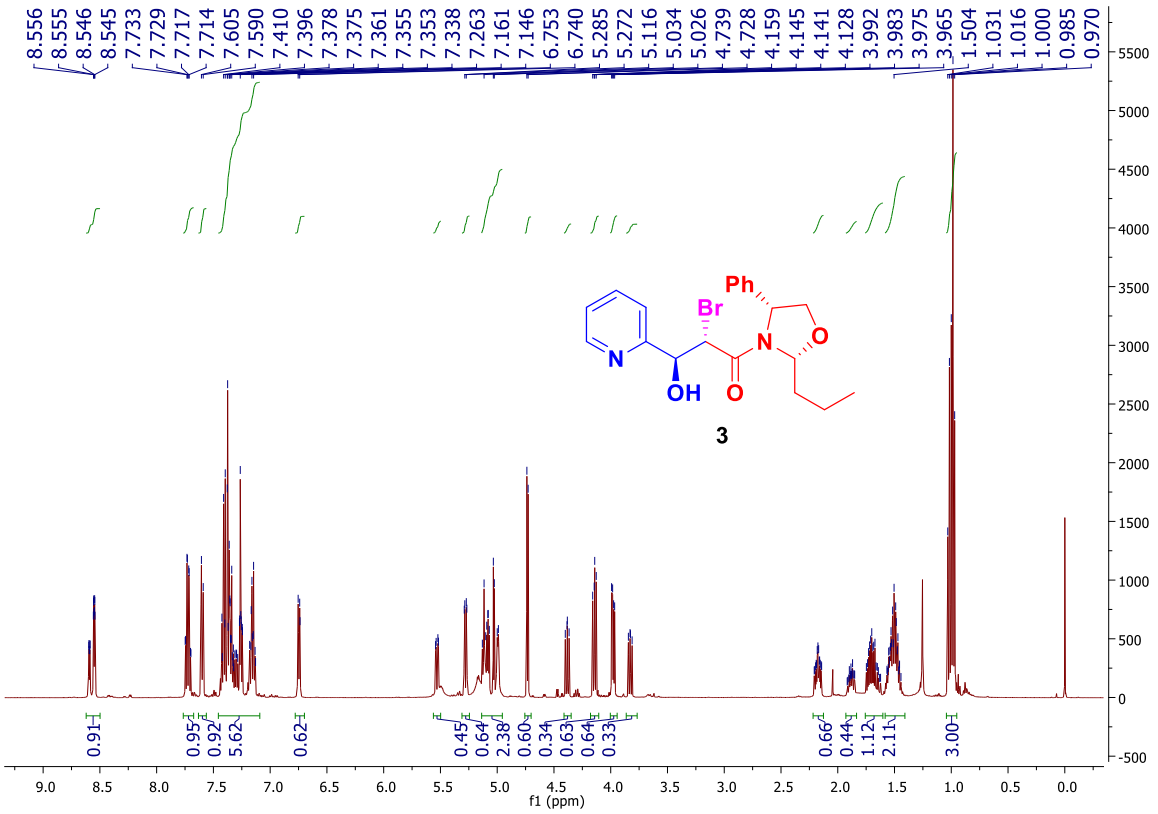
(–)-1-*epi* lentiginosine

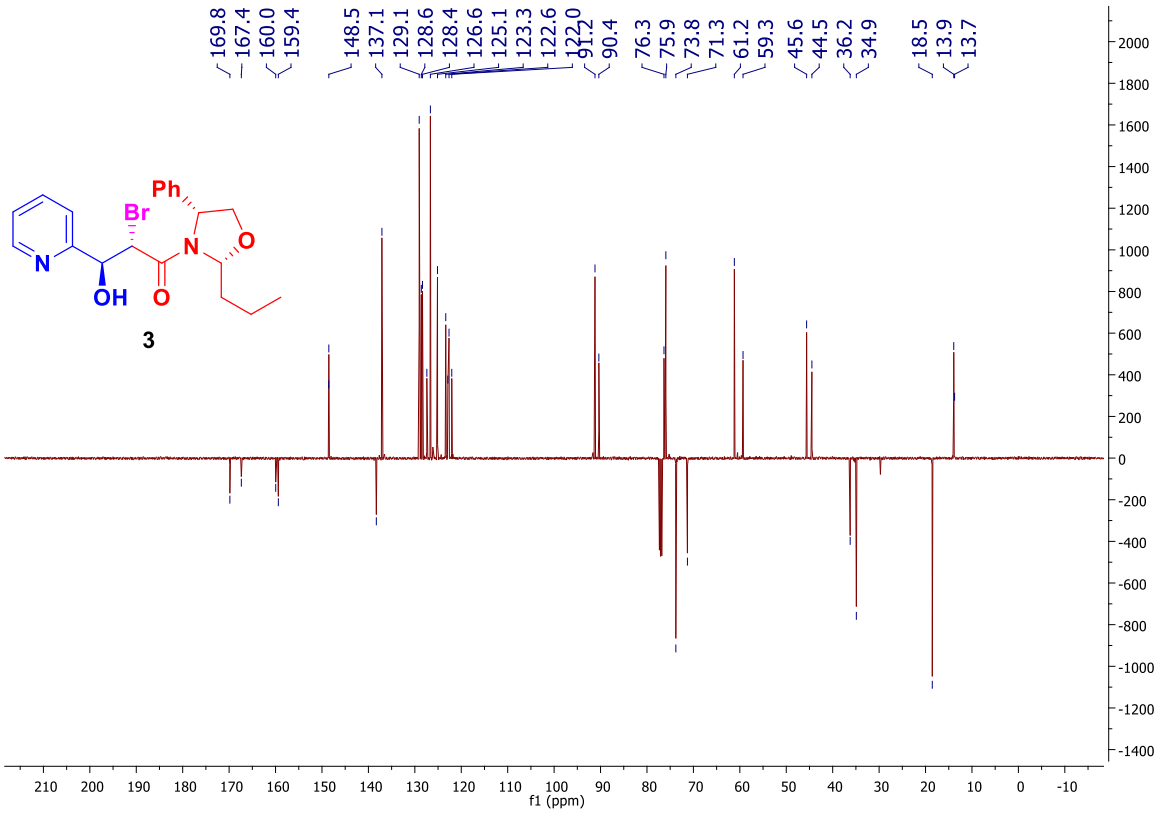


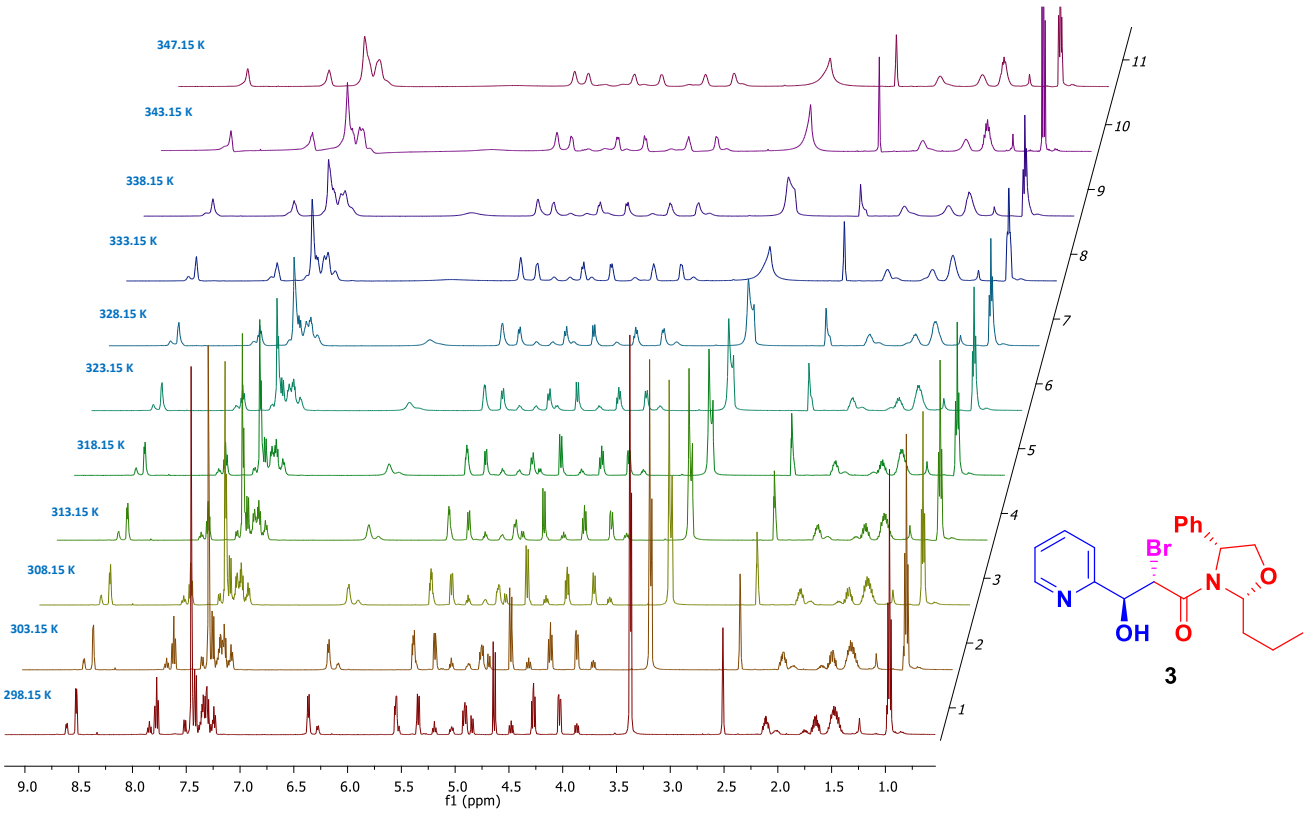
Colorless oil, 87% yield. $[\alpha]_D^{20} = -15.5$ (c 0.3, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22 (ddd, *J* = 7.4, 5.9, 1.8 Hz, 1H), 3.98 (dd, *J* = 6.0, 4.0 Hz, 1H), 3.69 – 3.61 (m, 2H), 3.04 (dd, *J* = 11.1, 3.5 Hz, 1H), 2.94 (dd, *J* = 10.7, 1.7 Hz, 1H), 2.33 (dd, J = 10.7, 7.0 Hz, 1H), 1.97 – 1.88 (m, 1H), 1.88 – 1.81 (m, 2H), 1.78 – 1.68 (m, 1H), 1.67 – 1.49 (m, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 76.6, 69.7, 62.5, 53.1, 29.7, 25.1, 24.9, 23.8. HRMS(ESI): Calcd for $C_8H_{15}NO_2$: 157.1103 Found: 157.1102.


8.341
8.332
7.455
7.440
7.144
7.129
7.091
7.082
7.077
7.067
7.046
7.031
7.016
6.936
6.922
6.890
6.874
5.530
5.526
5.512
5.507
5.118
5.105
5.092
4.354
4.340
4.337
4.322
3.918
3.905
3.900
3.887
3.819
3.601
3.598
1.710
1.534
1.528
1.514
1.500
1.495
0.980
0.965
0.950
Ph
O
N
O
N
O
2a
major diastereoisomer
0.70
0.91
1.00
4.76
1.86
0.89
1.00
1.19
1.06
0.73
0.93
1.06
1.09
2.29
3.14
f1 (ppm)


165.2
154.1
149.4
139.2
136.2
128.8
127.9
126.0
123.2
121.0
91.7
73.7
60.4
57.9
56.4
35.2
18.4
13.7
Ph
O
N
O
N
O
2a
major diastereoisomer
f1 (ppm)

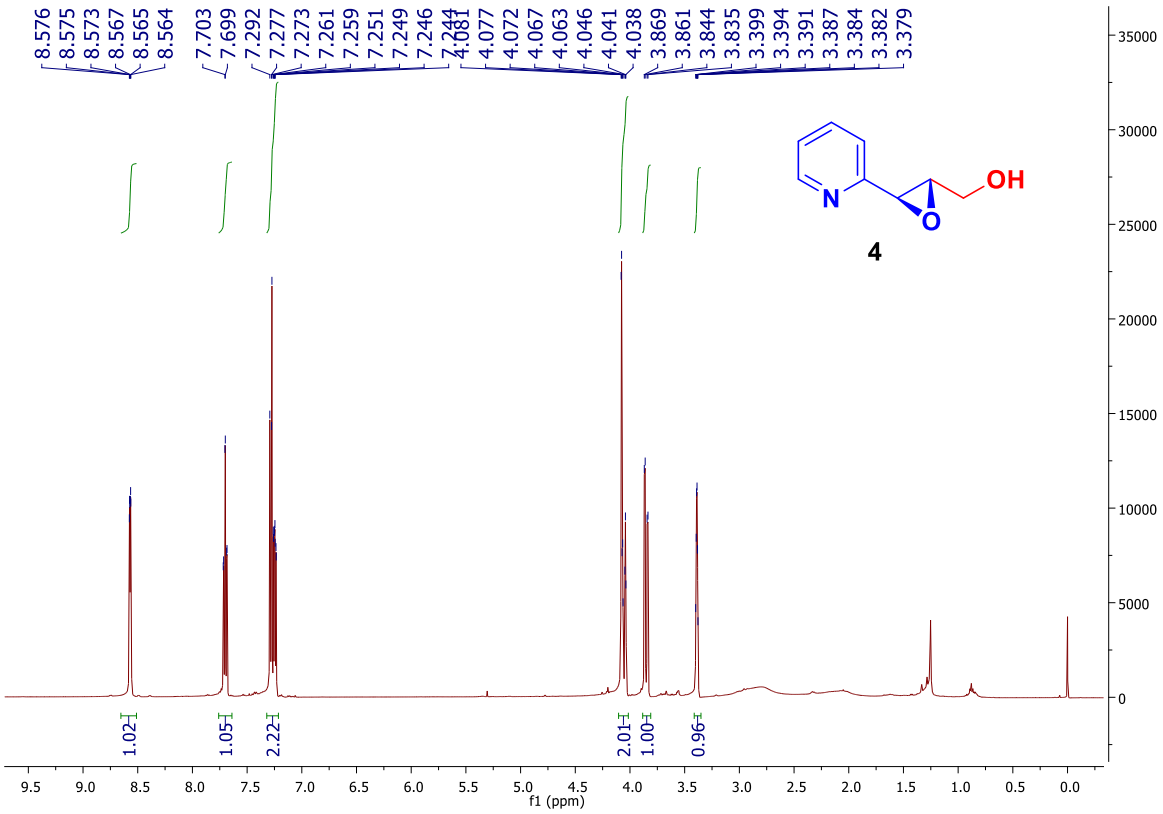

8.556
8.555
8.546
8.545
7.733
7.729
7.717
7.714
7.605
7.590
7.410
7.396
7.378
7.375
7.361
7.355
7.353
7.338
7.263
7.161
7.146
6.753
6.740
5.285
5.272
5.116
5.034
5.026
4.739
4.728
4.159
4.145
4.141
4.128
3.992
3.983
3.975
3.965
1.504
1.031
1.016
1.000
0.985
0.970
Ph
Br
N
O
N
OH
O
3
0.91
0.95
0.92
5.62
0.62
0.45
0.64
2.38
0.60
0.34
0.63
0.64
0.33
0.66
0.44
1.12
2.11
3.00
f1 (ppm)

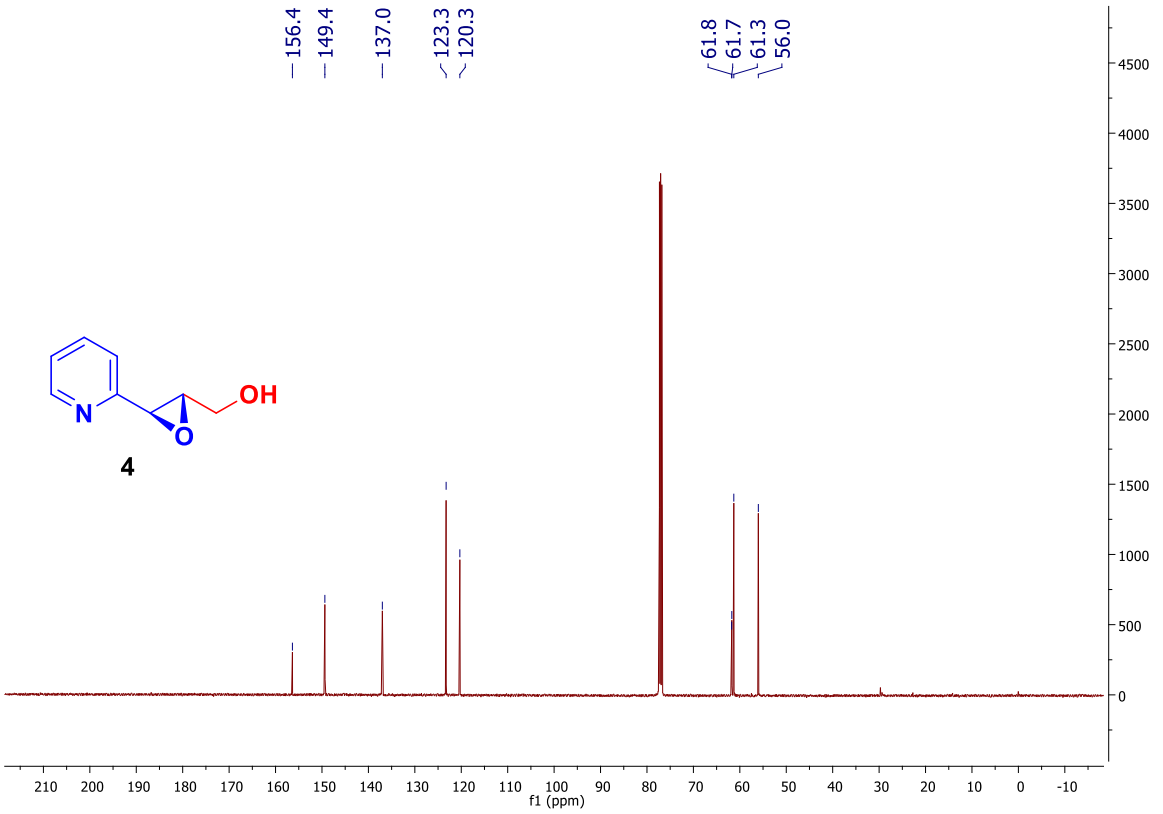

169.8
167.4
160.0
159.4
148.5
137.1
129.1
128.6
128.4
126.6
125.1
123.3
122.6
122.0
91.2
90.4
76.3
75.9
73.8
71.3
61.2
59.3
45.6
44.5
36.2
34.9
18.5
13.9
13.7
Ph
Br
N
O
N
OH
O
3
f1 (ppm)

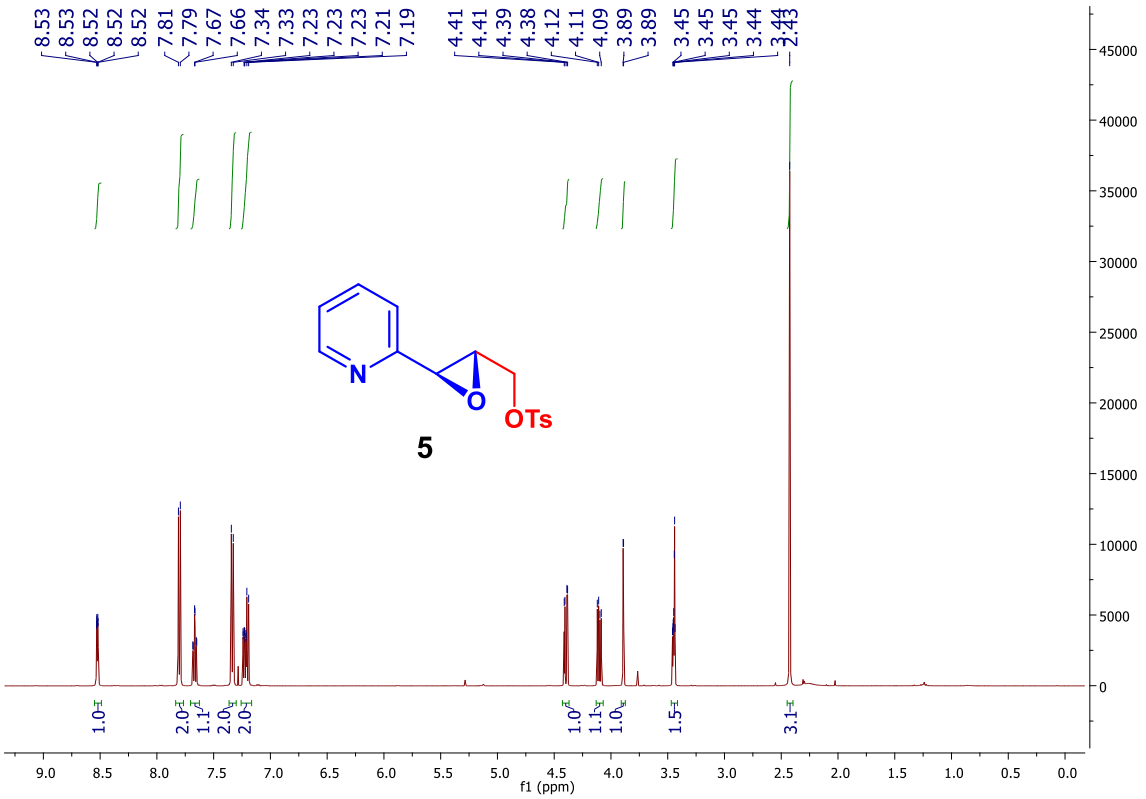


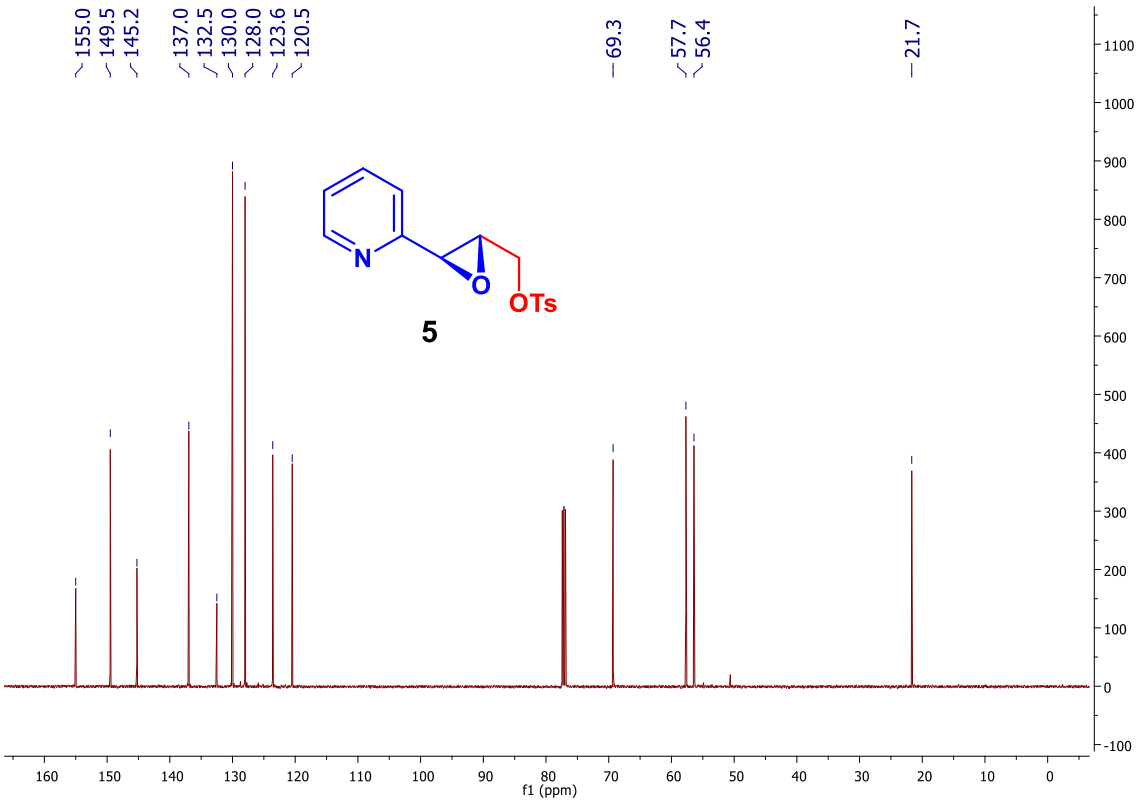
3

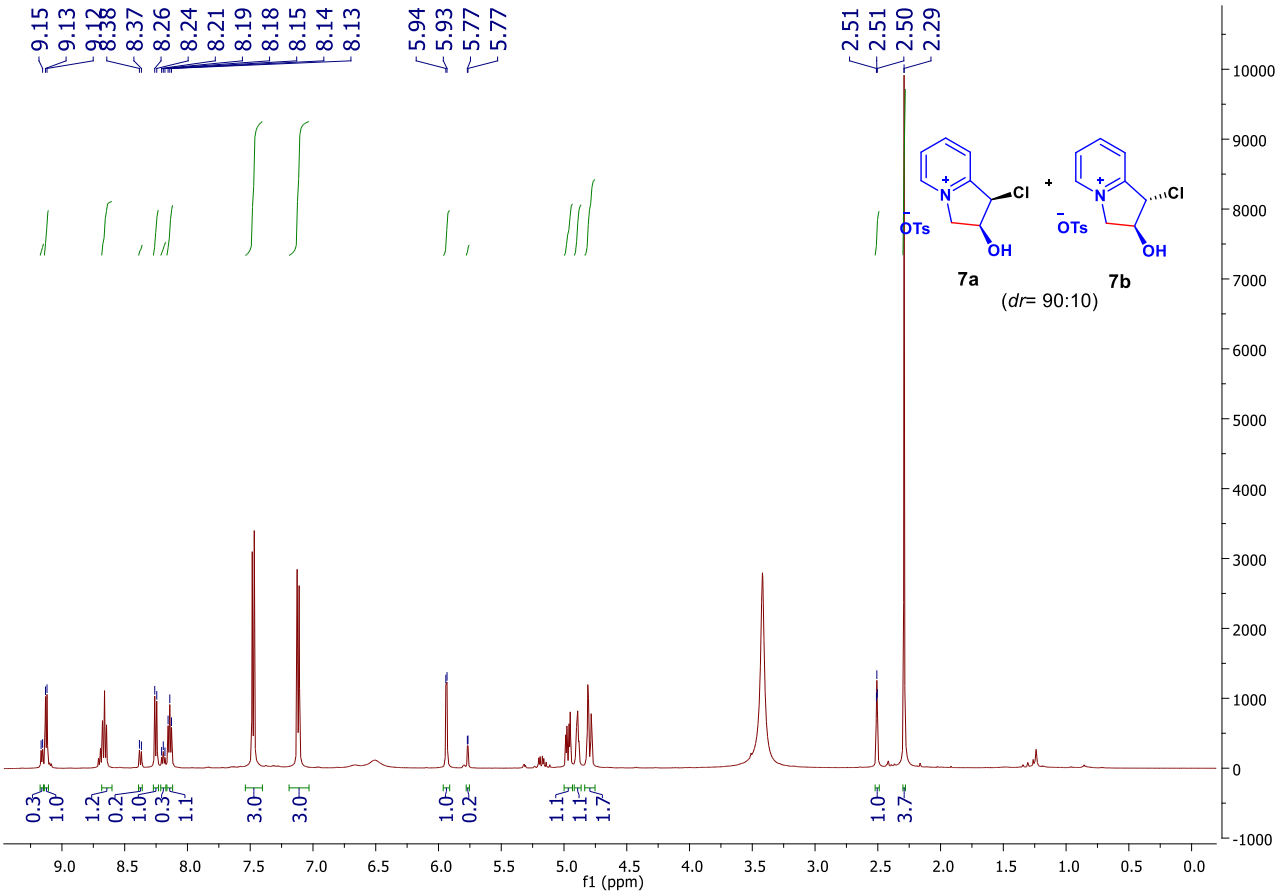
Variable temperatura NMR experiments.

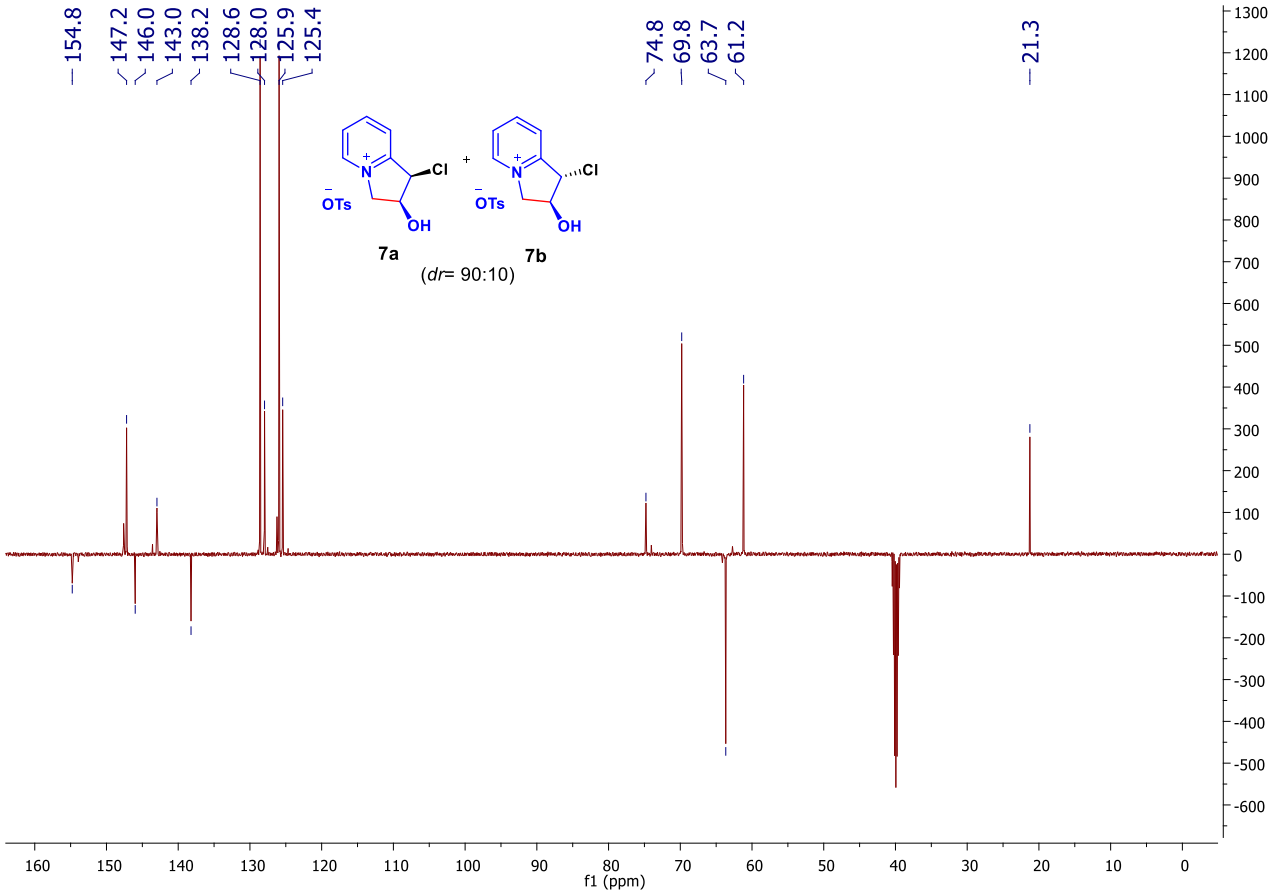

8.576
8.575
8.573
8.567
8.565
8.564
7.703
7.699
7.292
7.277
7.273
7.261
7.259
7.251
7.249
7.246
4.081
4.077
4.072
4.067
4.063
4.046
4.041
4.038
3.869
3.861
3.844
3.835
3.399
3.394
3.391
3.387
3.384
3.382
3.379
OH
N
O
4
1.02
1.05
2.22
2.01
1.00
0.96
f1 (ppm)

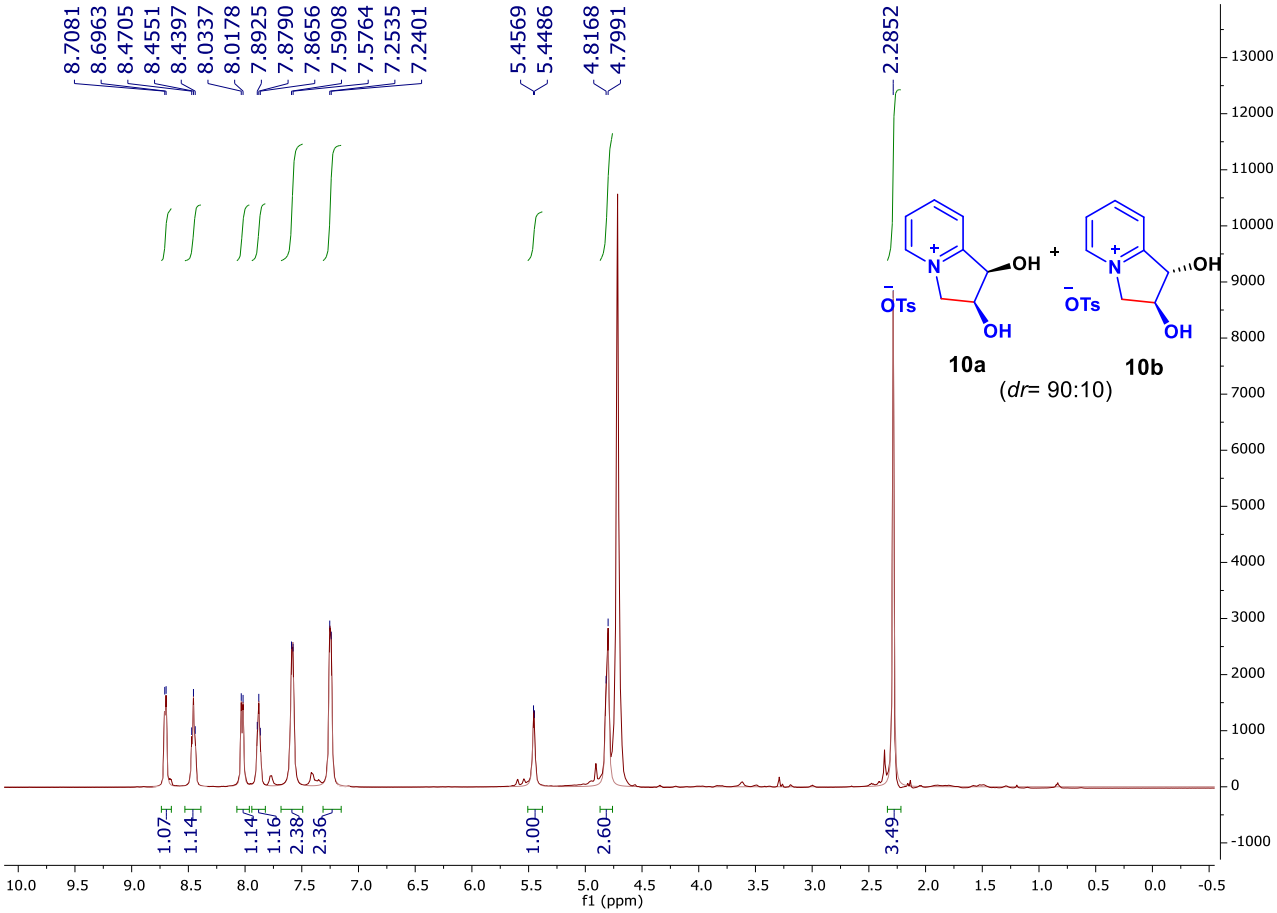

156.4
149.4
137.0
123.3
120.3
61.8
61.7
61.3
56.0
OH
N
O
4
f1 (ppm)

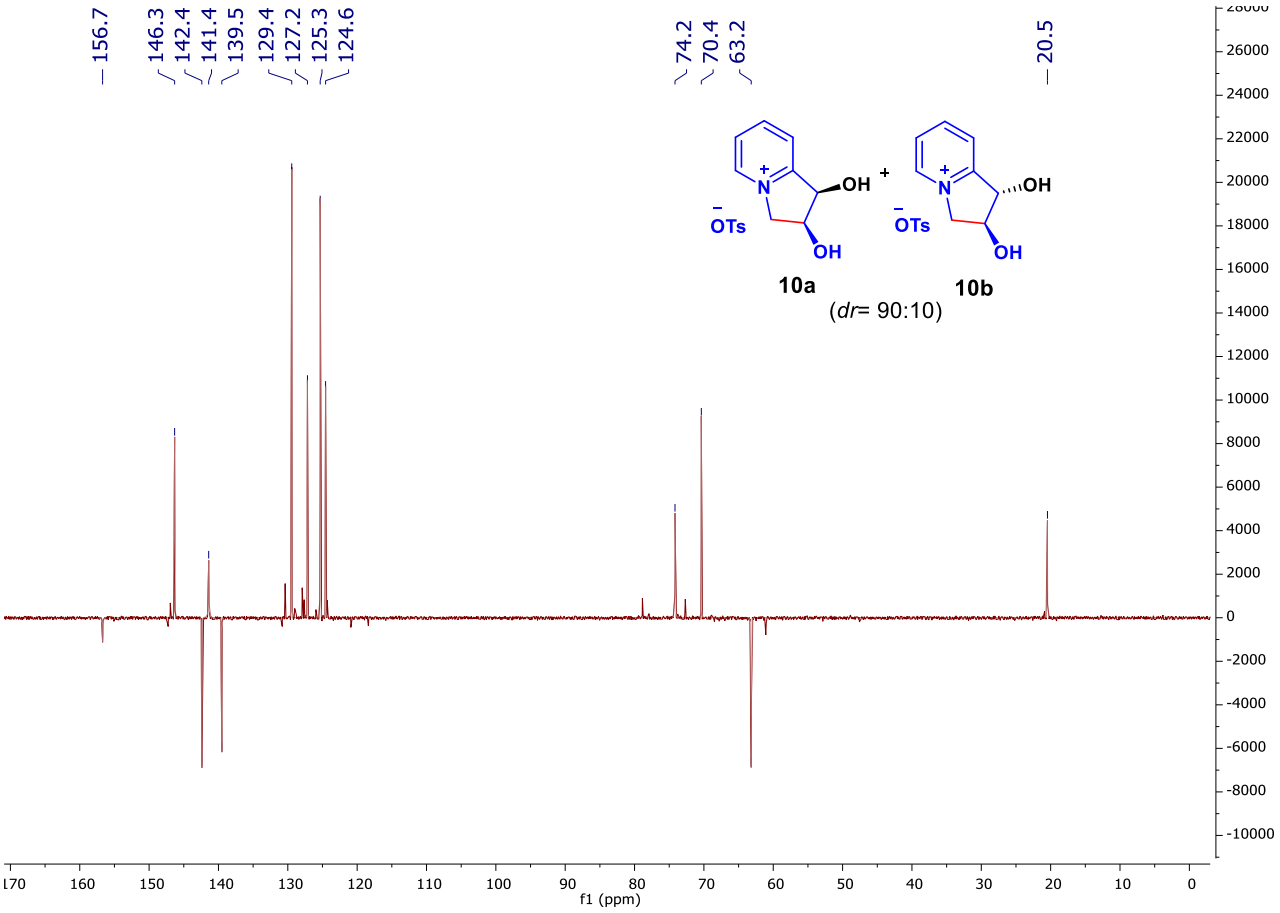

8.53
8.53
8.52
8.52
8.52
7.81
7.79
7.67
7.66
7.34
7.33
7.23
7.23
7.23
7.21
7.19
4.41
4.41
4.39
4.38
4.12
4.11
4.09
3.89
3.89
3.45
3.45
3.45
3.44
3.43
2.43
N
O
OTs
5
1.0
2.0
1.1
2.0
2.0
1.0
1.1
1.0
1.5
3.1
f1 (ppm)

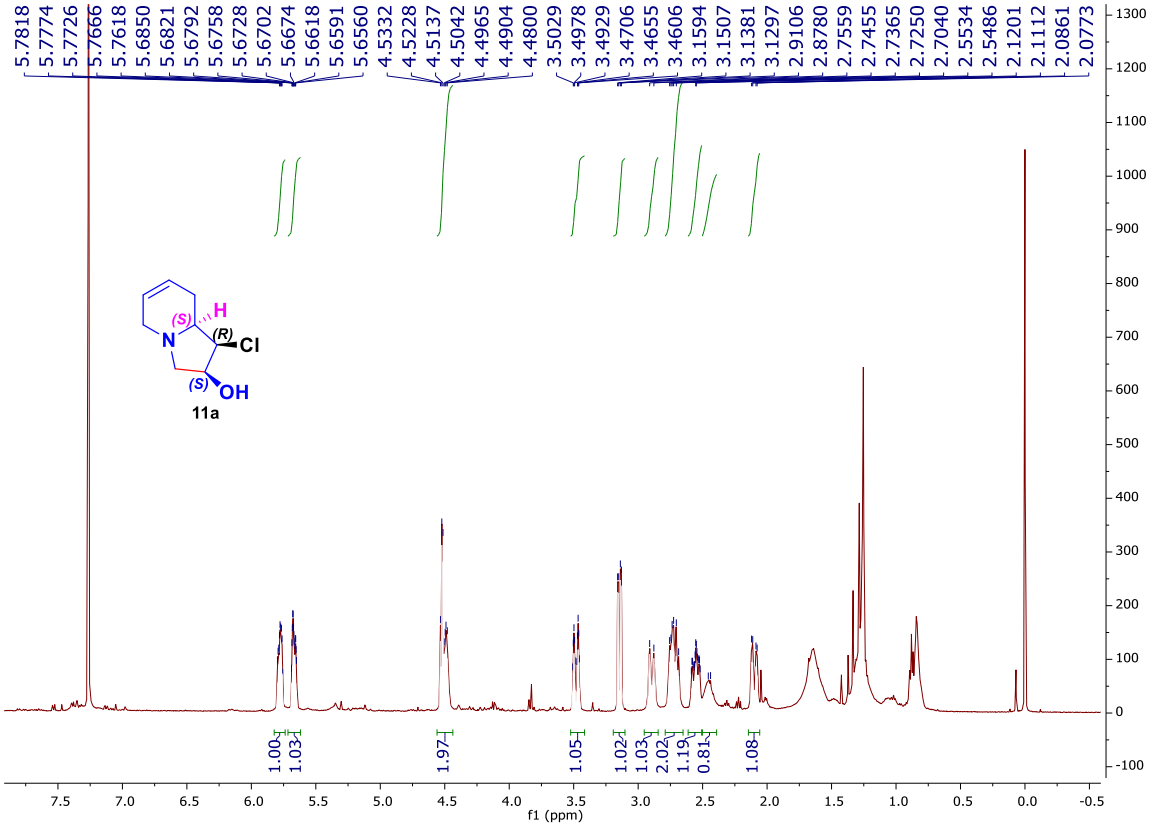

155.0
149.5
145.2
137.0
132.5
130.0
128.0
123.6
120.5
69.3
57.7
56.4
21.7
N
O
OTs
5
f1 (ppm)

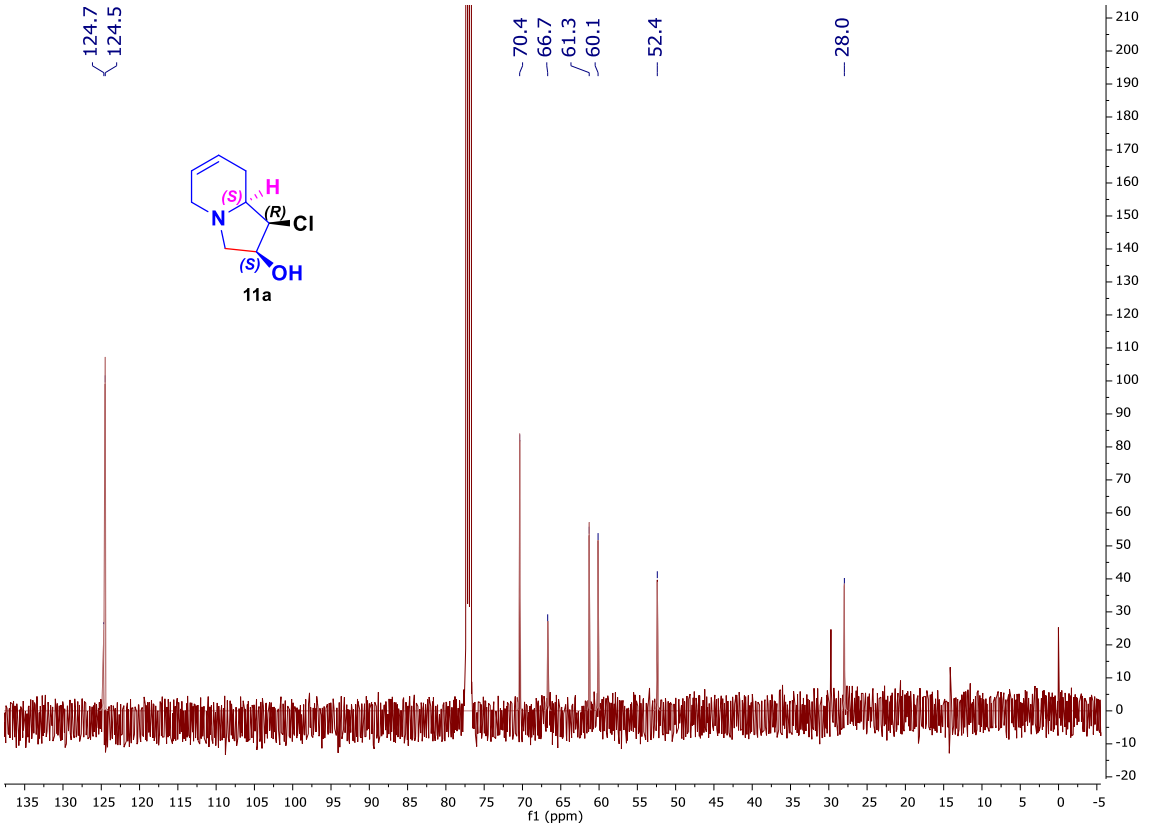

9.15
9.13
8.38
8.37
8.26
8.24
8.21
8.19
8.18
8.15
8.14
8.13
5.94
5.93
5.77
5.77
2.51
2.51
2.50
2.29
Cl
OTs
OH
7a
7b
(dr= 90:10)
f1 (ppm)

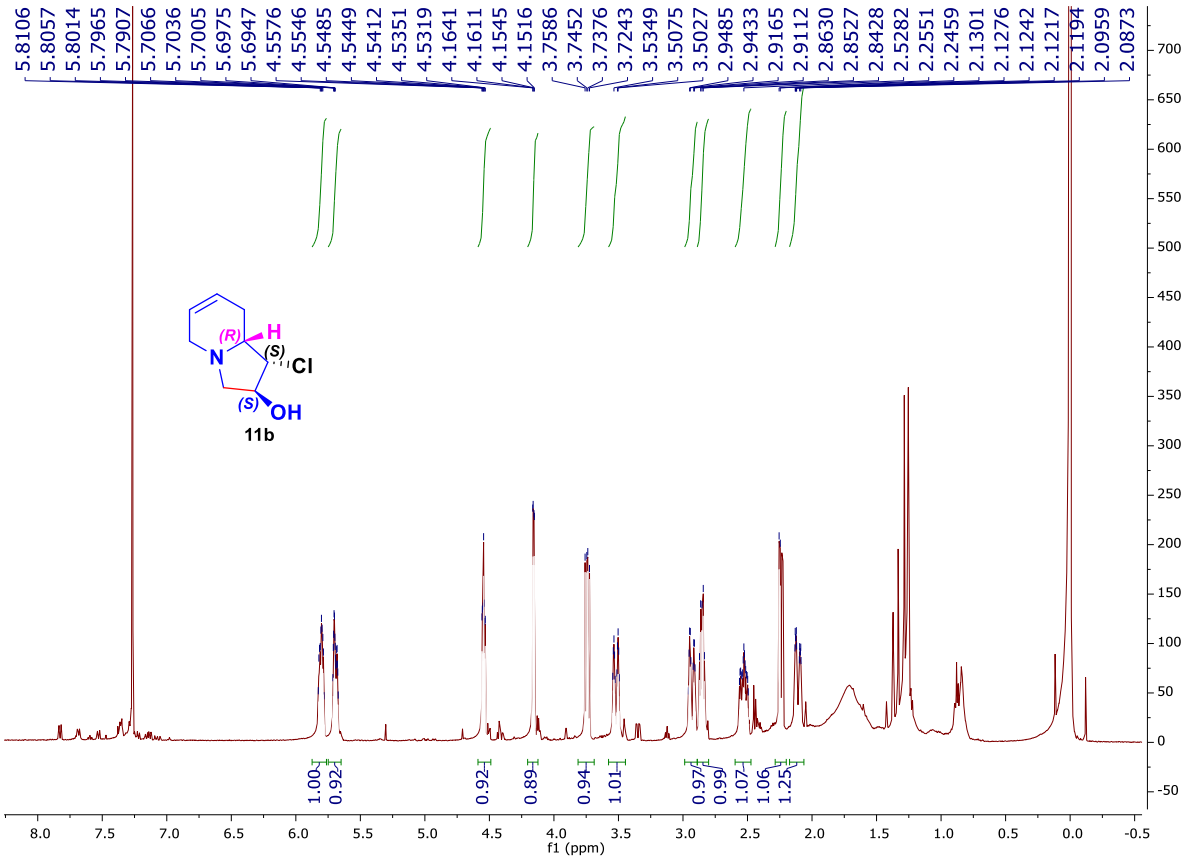

154.8
147.2
146.0
143.0
138.2
128.6
128.0
125.9
125.4
74.8
69.8
63.7
61.2
21.3
Cl
OTs
OH
7a
7b
(dr= 90:10)
f1 (ppm)

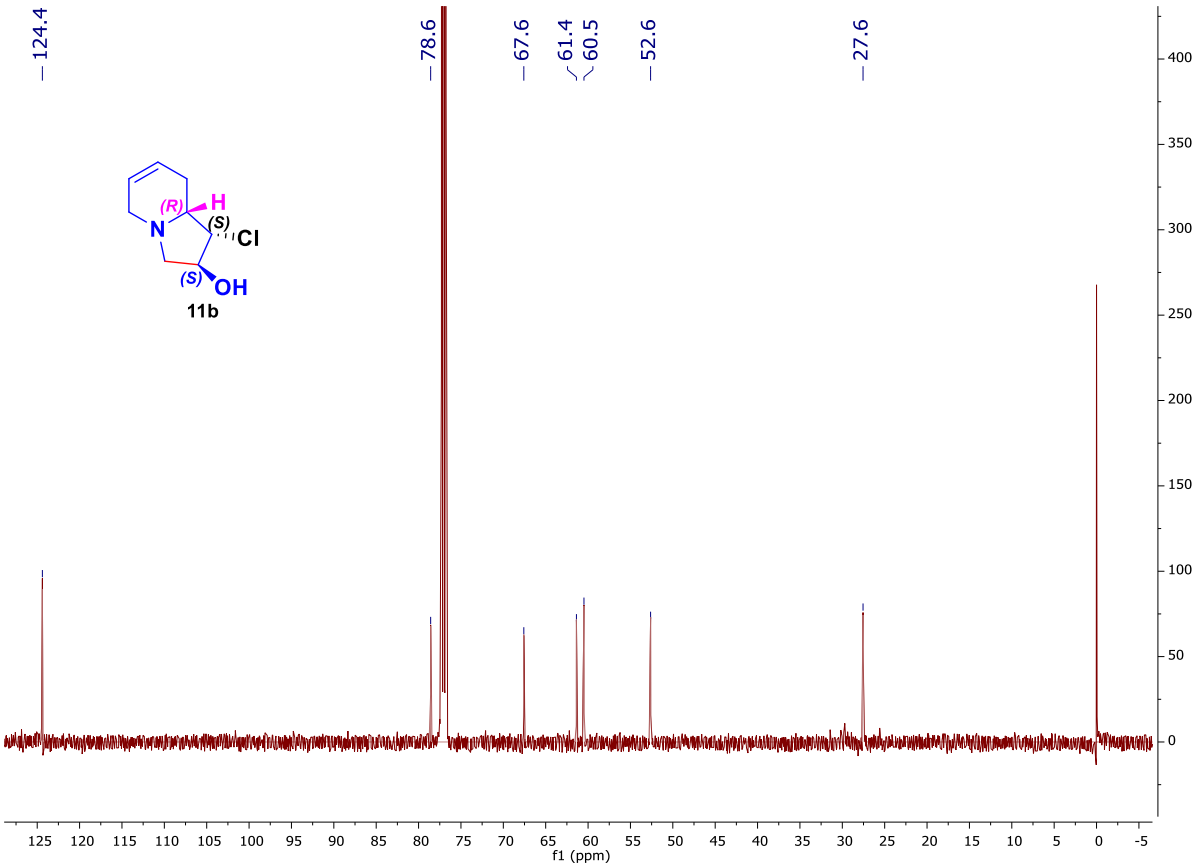

8.7081
8.6963
8.4705
8.4551
8.4397
8.0337
8.0178
7.8925
7.8790
7.8656
7.5908
7.5764
7.2535
7.2401
5.4569
5.4486
4.8168
4.7991
2.2852
1.07
1.14
1.14
1.16
2.38
2.36
1.00
2.60
3.49
f1 (ppm)
OH
OTs
OH
10a
OH
OTs
OH
10b
(dr= 90:10)

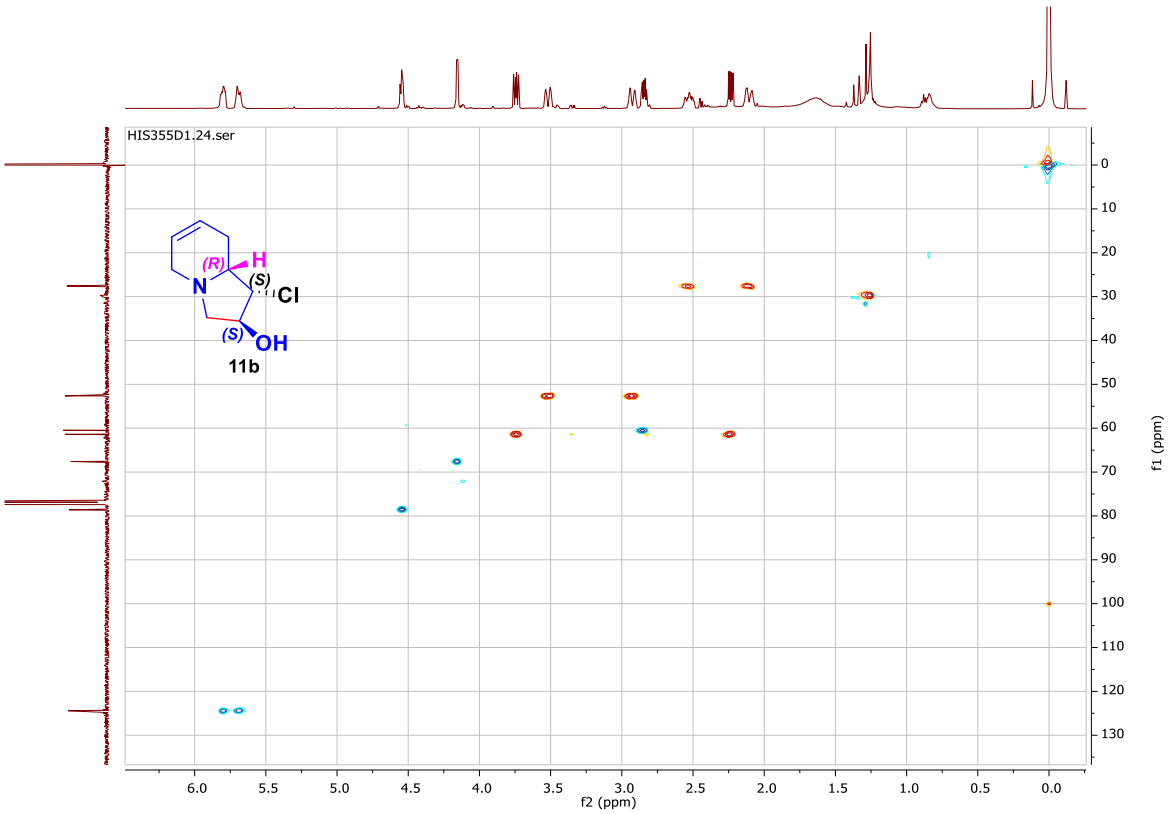

156.7
146.3
142.4
141.4
139.5
129.4
127.2
125.3
124.6
74.2
70.4
63.2
20.5
OH
OTs
OH
10a
OH
OTs
OH
10b
(dr= 90:10)
f1 (ppm)

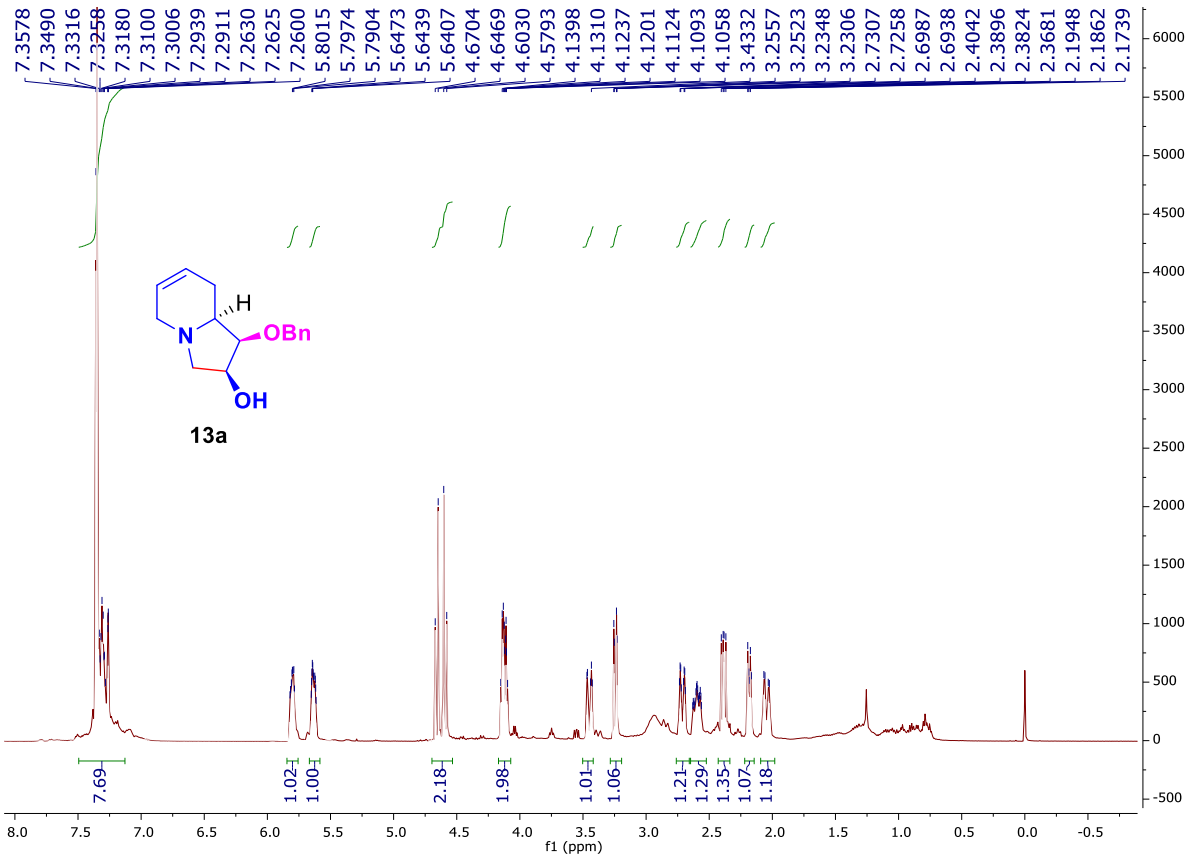

5.7818
5.7774
5.7726
5.7666
5.7618
5.6850
5.6821
5.6792
5.6758
5.6728
5.6702
5.6674
5.6618
5.6591
5.6560
4.5332
4.5228
4.5137
4.5042
4.4965
4.4904
4.4800
3.5029
3.4978
3.4929
3.4706
3.4655
3.4606
3.1594
3.1507
3.1381
3.1297
2.9106
2.8780
2.7559
2.7455
2.7365
2.7250
2.7040
2.5534
2.5486
2.1201
2.1112
2.0861
2.0773
1.00
1.03
1.97
1.05
1.02
1.03
2.02
1.19
0.81
1.08
f1 (ppm)
11a

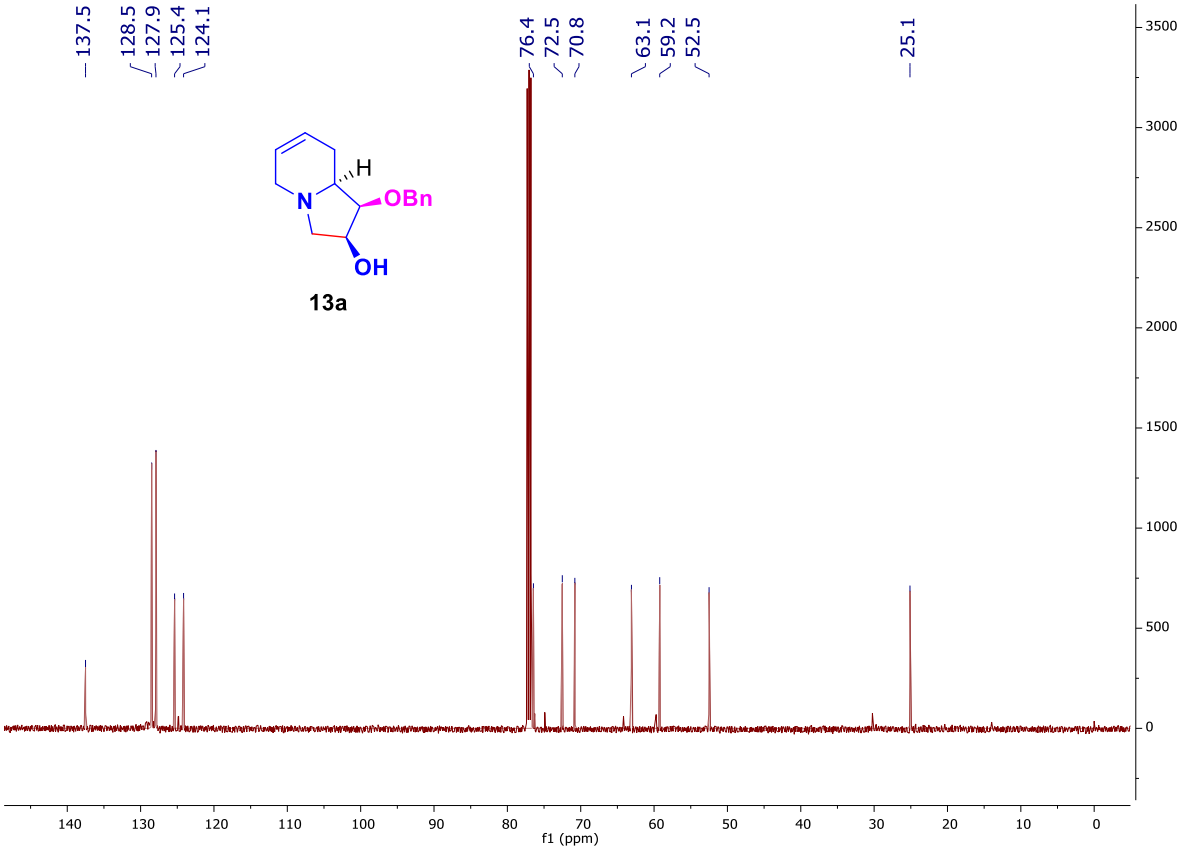

124.7
124.5
70.4
66.7
61.3
60.1
52.4
28.0
f1 (ppm)
11a

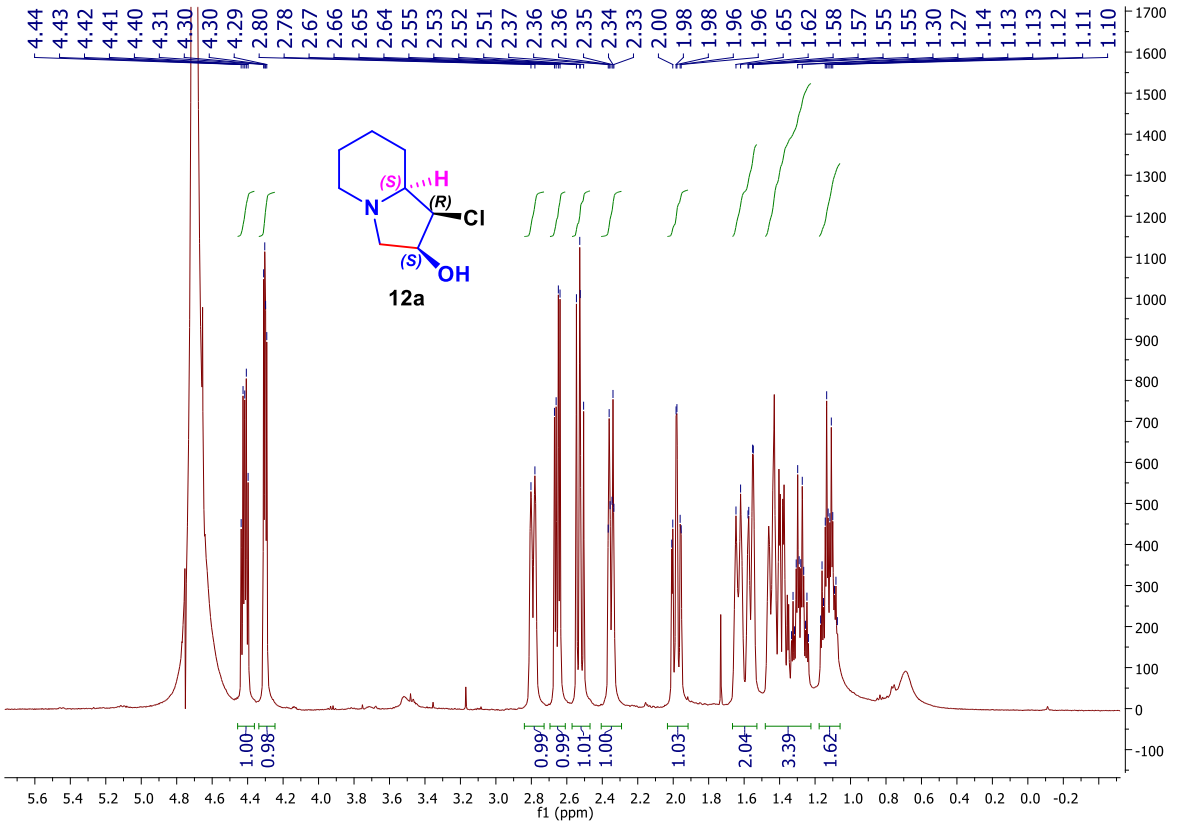

5.8106
5.8057
5.8014
5.7965
5.7907
5.7066
5.7036
5.7005
5.6975
5.6947
4.5576
4.5546
4.5485
4.5449
4.5412
4.5351
4.5319
4.1641
4.1611
4.1545
4.1516
3.7586
3.7452
3.7376
3.7243
3.5349
3.5075
3.5027
2.9485
2.9433
2.9165
2.9112
2.8630
2.8527
2.8428
2.5282
2.2551
2.2459
2.1301
2.1276
2.1242
2.1217
2.1194
2.0959
2.0873
(R)
H
N
(S)
Cl
(S)
OH
11b
1.00
0.92
0.92
0.89
0.94
1.01
0.97
0.99
1.07
1.06
1.25
f1 (ppm)

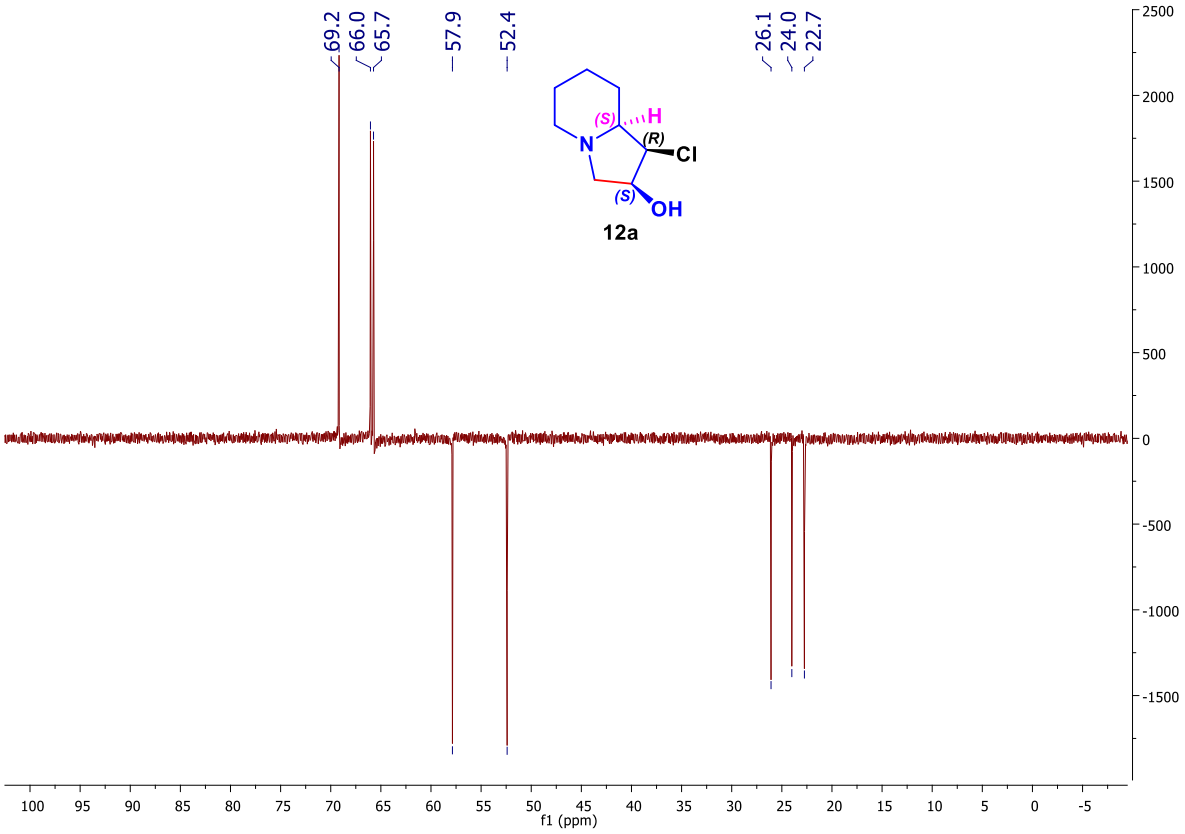

124.4
78.6
67.6
61.4
60.5
52.6
27.6
(R)
H
N
(S)
Cl
(S)
OH
11b
400
350
300
250
200
150
100
50
0
125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5
f1 (ppm)

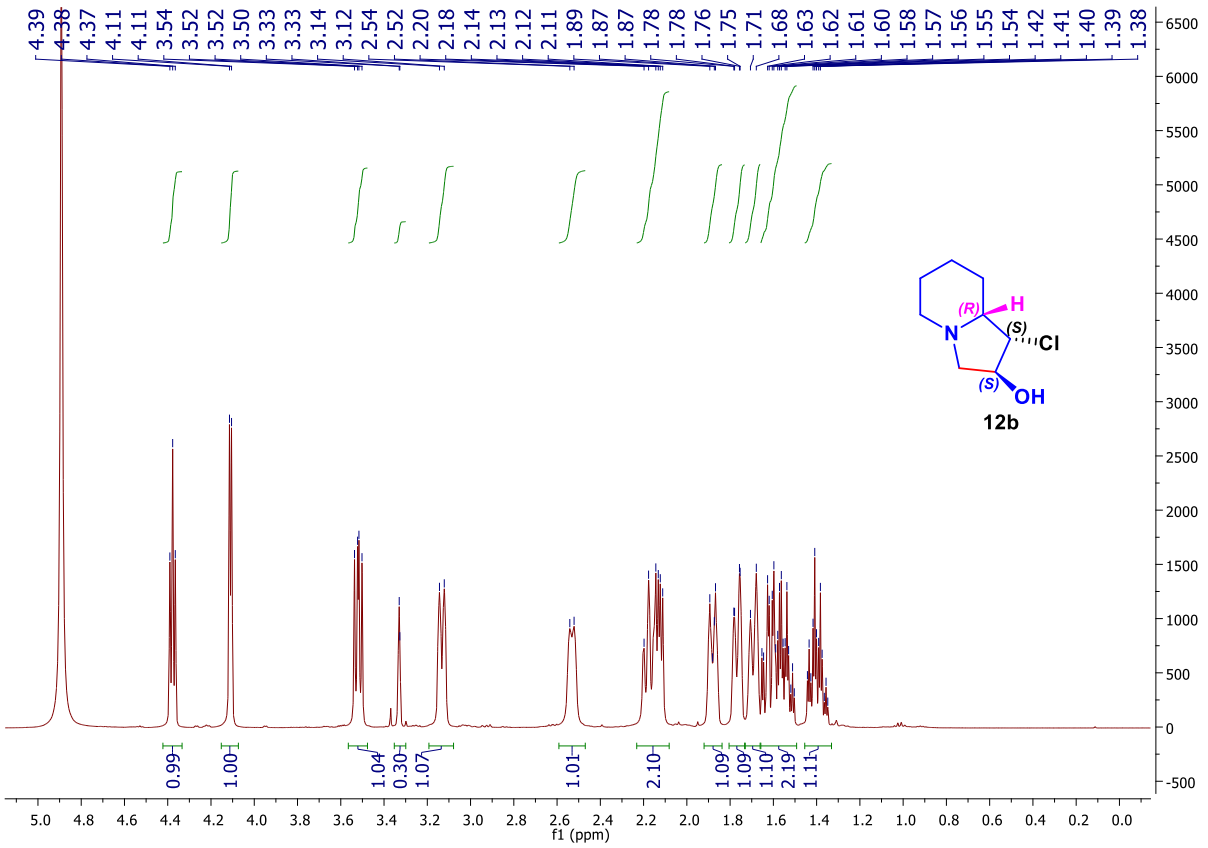

HIS355D1.24.ser
(R)
H
N
(S)
Cl
(S)
OH
11b
f2 (ppm)
f1 (ppm)

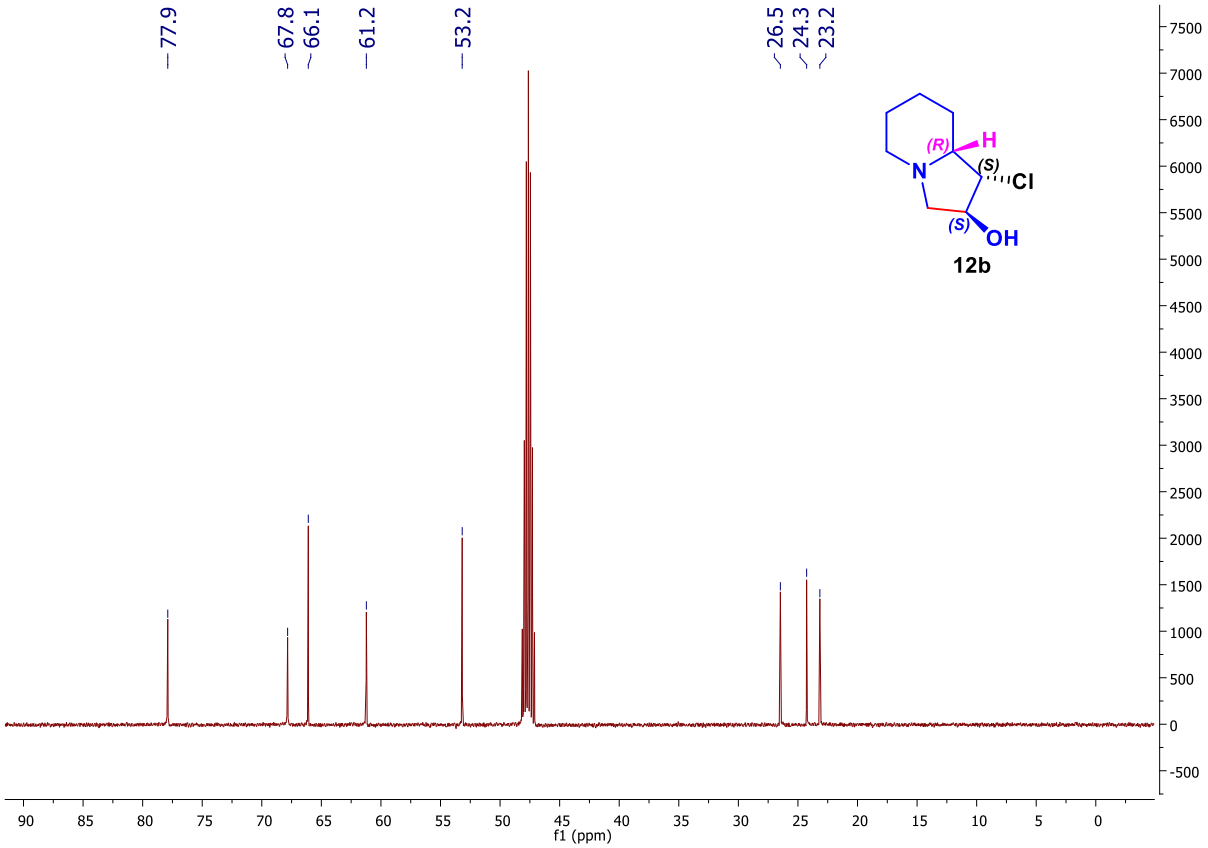

7.3578
7.3490
7.3316
7.3258
7.3180
7.3100
7.3006
7.2939
7.2911
7.2630
7.2625
7.2600
5.8015
5.7974
5.7904
5.6473
5.6439
5.6407
4.6704
4.6469
4.6030
4.5793
4.1398
4.1310
4.1237
4.1201
4.1124
4.1093
4.1058
3.4332
3.2557
3.2523
3.2348
3.2306
2.7307
2.7258
2.6987
2.6938
2.4042
2.3896
2.3824
2.3681
2.1948
2.1862
2.1739
H
N
OBn
OH
13a
7.69
1.02
1.00
2.18
1.98
1.01
1.06
1.21
1.29
1.35
1.07
1.18
f1 (ppm)

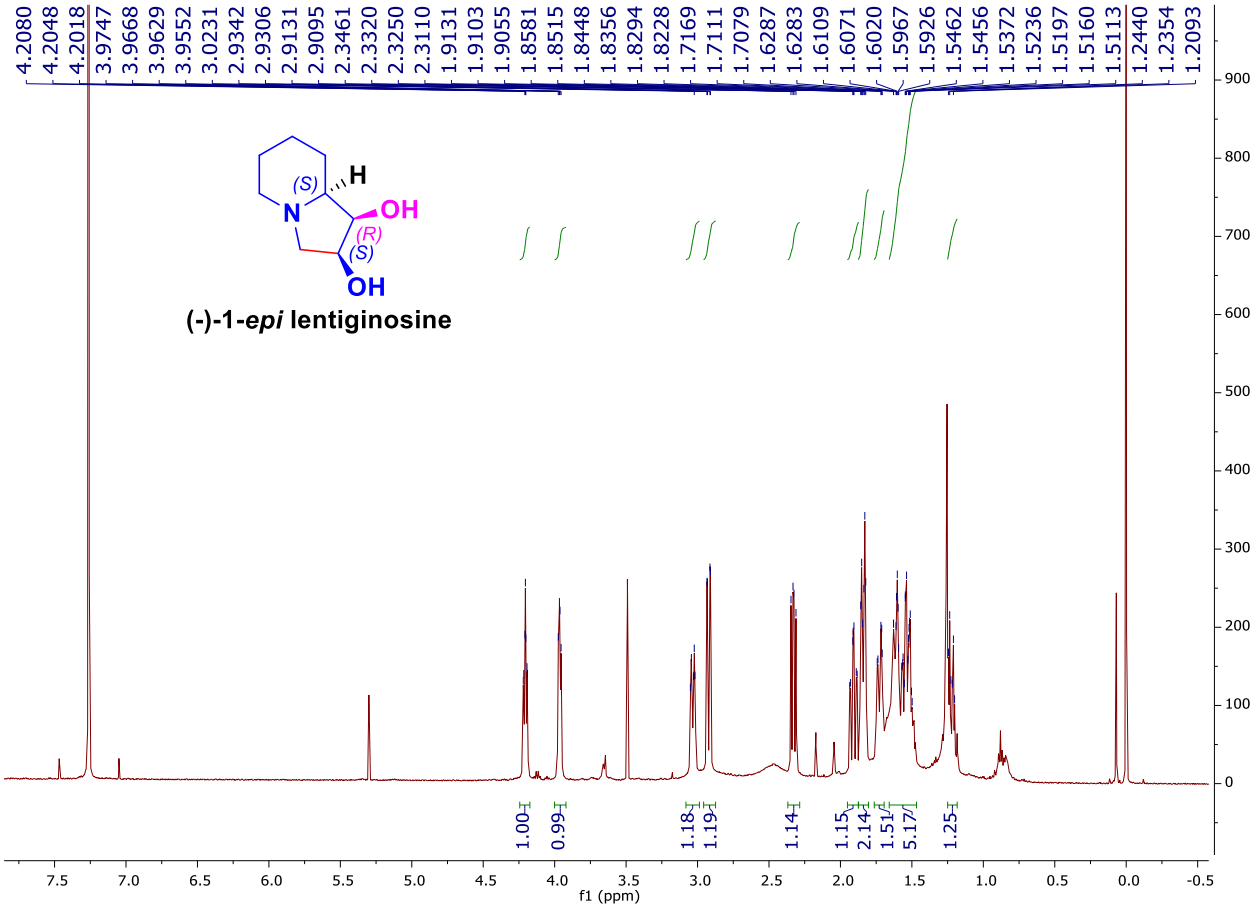

137.5
128.5
127.9
125.4
124.1
76.4
72.5
70.8
63.1
59.2
52.5
25.1
H
N
OBn
OH
13a
3500
3000
2500
2000
1500
1000
500
0
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

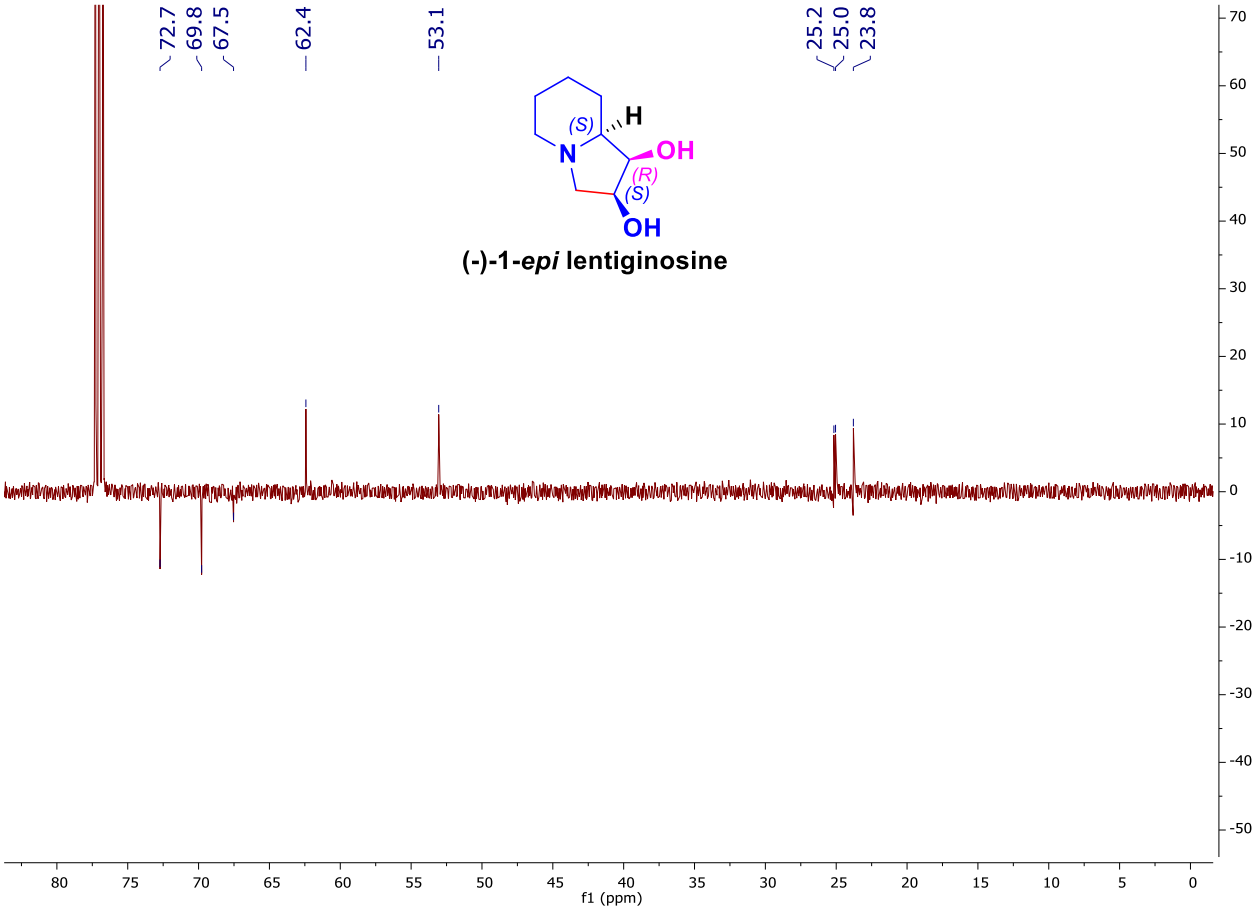

4.44 4.43 4.42 4.41 4.40 4.31 4.30 4.30 4.29 2.80 2.78 2.67 2.66 2.65 2.64 2.55 2.53 2.52 2.51 2.37 2.36 2.36 2.35 2.34 2.33 2.00 1.98 1.98 1.96 1.96 1.65 1.62 1.58 1.57 1.55 1.55 1.30 1.27 1.14 1.13 1.13 1.12 1.11 1.10
(S) H
N
(R) Cl
(S) OH
12a
1.00 0.98 0.99 0.99 1.01 1.00 1.03 2.04 3.39 1.62
f1 (ppm)

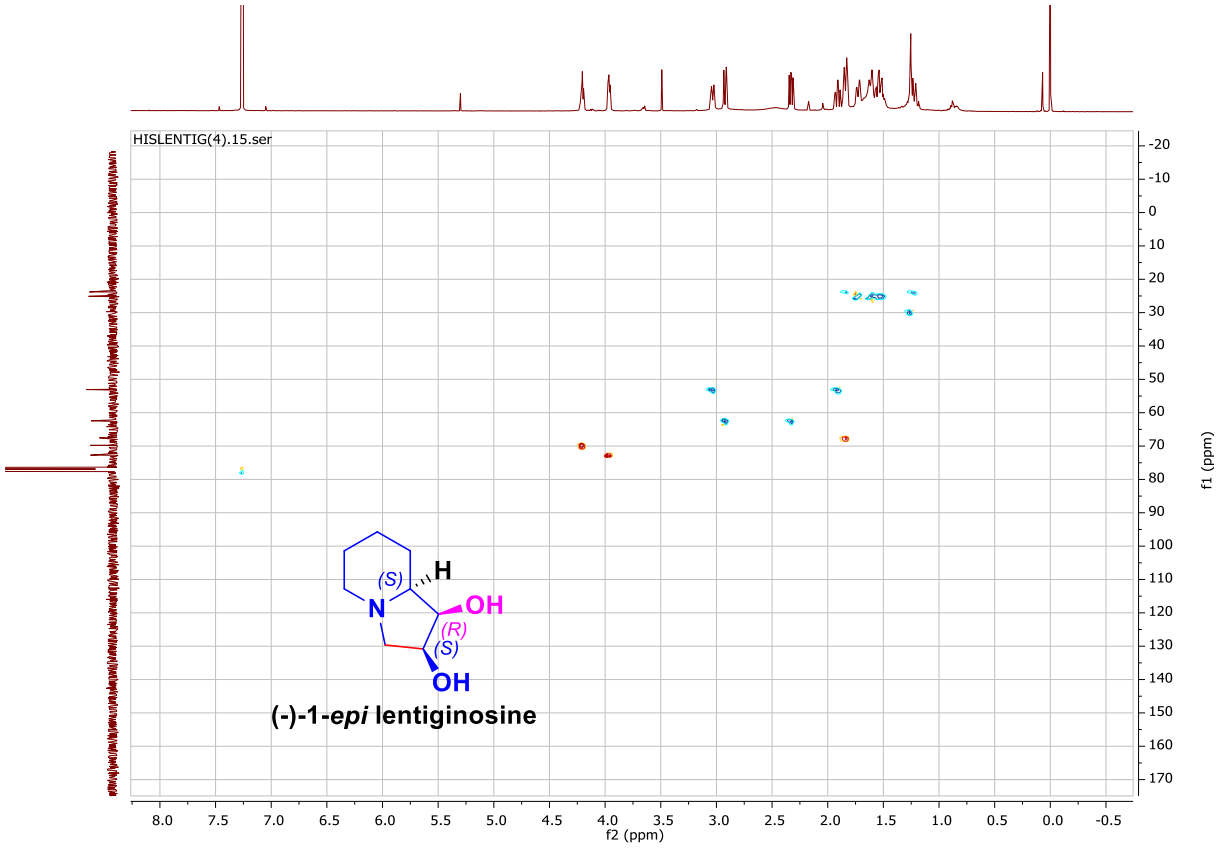

69.2 66.0 65.7 57.9 52.4 26.1 24.0 22.7
(S) H
N
(R) Cl
(S) OH
12a
f1 (ppm)


4.39 4.38 4.37 4.11 4.11 3.54 3.52 3.52 3.50 3.33 3.33 3.14 3.12 2.54 2.52 2.20 2.18 2.14 2.13 2.12 2.11 1.89 1.87 1.87 1.78 1.78 1.76 1.75 1.71 1.68 1.63 1.62 1.61 1.60 1.58 1.57 1.56 1.55 1.54 1.42 1.41 1.40 1.39 1.38
0.99 1.00 1.04 0.30 1.07 1.01 2.10 1.09 1.09 1.10 2.19 1.11
f1 (ppm)
(R) H
N
(S) Cl
(S) OH
12b


77.9 67.8 66.1 61.2 53.2 26.5 24.3 23.2
f1 (ppm)
(R) H
N
(S) Cl
(S) OH
12b


4.2080
4.2048
4.2018
3.9747
3.9668
3.9629
3.9552
3.0231
2.9342
2.9306
2.9131
2.9095
2.3461
2.3320
2.3250
2.3110
1.9131
1.9103
1.9055
1.8581
1.8515
1.8448
1.8356
1.8294
1.8228
1.7169
1.7111
1.7079
1.6287
1.6283
1.6109
1.6071
1.6020
1.5967
1.5926
1.5462
1.5456
1.5372
1.5236
1.5197
1.5160
1.5113
1.2440
1.2354
1.2093
(S)
H
N
OH
(R)
(S)
OH
(-)-1-*epi* lentiginosine
1.00
0.99
1.18
1.19
1.14
1.15
2.14
1.51
5.17
1.25
f1 (ppm)


72.7
69.8
67.5
62.4
53.1
25.2
25.0
23.8
(S)
H
N
OH
(R)
(S)
OH
(-)-1-epi lentiginosine
f1 (ppm)


HISLENTIG(4).15.ser
(S)
H
N
OH
(R)
(S)
OH
(-)-1-epi lentiginosine
f2 (ppm)
f1 (ppm)

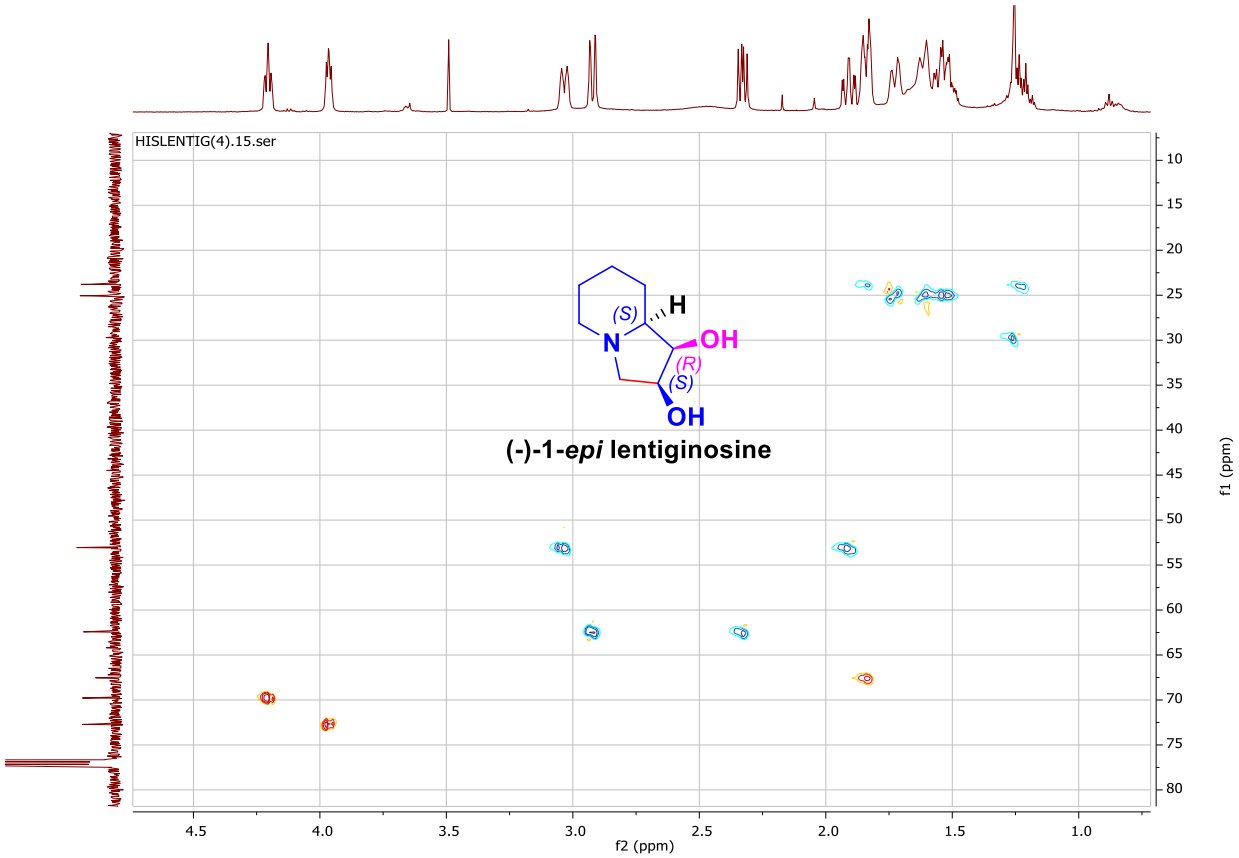

HISLENTIG(4).15.ser
(S)
H
N
OH
(R)
(S)
OH
(-)-1-epi lentiginosine
f2 (ppm)
f1 (ppm)

Table S1. Crystal data for compounds **3**, **10a**, **10b** and **11a**

	3	**10a**	**10b**	**11a**
CCDC deposition	2181510	2181511	2181512	2181513
Formula	$C_{20}H_{23}BrN_2O_3$	$C_8H_{12}ClNO$	$C_8H_{12}ClNO$	$C_8H_{14}ClNO$
fw	419.31	173.64	173.64	175.65
Crystal size (mm^3)	0.34×0.22×0.07	0.50×0.11×0.08	0.30×0.13×0.04	0.61×0.42×0.35
Colour	colourless	colourless	colourless	
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a (Å)	7.1360(3)	7.3321(12)	10.8339(10)	7.4256(2)
b (Å)	8.9300(6)	10.641(2)	6.7230(9)	10.5444(4)
c (Å)	30.3879(14)	11.146(2)	11.3873(10)	11.2574(5)
V ($Å^3$)	1936.45(18)	869.6(3)	829.41(15)	881.44(6)
Z, *Z*'	4, 1	4, 1	4, 1	4, 1
Diffractometer	Stoe Stadivari	Stoe Stadivari	Stoe Stadivari	Stoe Stadivari
Radiation	Ag Kα	Ag Kα	Ag Kα	Ag Kα
T (K)	294(1)	294(1)	294(1)	295(1)
Density ($g.cm^{-3}$)	1.438	1.326	1.391	1.324
Absorption coef. (mm^{-1})	1.155	0.201	0.211	0.198
Transmission factors	0.5253 – 1.0000	0.5177 – 1.0000	0.4573 – 1.0000	0.6181 – 1.0000
Refl. collected (R_{int})	27808 (0.0741)	16944 (0.0715)	20777 (0.0761)	39302 (0.0230)
Refl. independent	4645	2040	1935	2656
(Senθ)/λ ($Å^{-1}$)	0.67	0.65	0.65	0.71
Data / parameters / restraints	4645 / 249 / 0	2040 / 103 / 0	1935 / 103 / 0	2656 / 105 / 0
Flack parameter	*x* = 0.034(13)	*x* = -0.01(7)	*x* = 0.01(6)	*x* = 0.028(15)
R_1, wR_2 [$I > 2\sigma(I)$]	0.0344, 0.0576	0.0311, 0.0528	0.0308, 0.0640	0.0295, 0.0794
R_1, wR_2 [all data]	0.1024, 0.0683	0.0638, 0.0590	0.0479, 0.0674	0.0335, 0.0841
GOF on F^2	0.817	0.784	0.864	1.066

X-ray intensities were collected at room temperature on a Stoe-Stadivari diffractometer equipped with an Axo microfocus source (Ag Kα radiation, λ = 0.56083 Å) and a Dectris Pilatus 100K detector [1]. Structures were refined with SHELXL [2]. For compound **3**, the O atom of the oxazolidine ring is disordered over two positions, O3A and O3B, placed above and below the mean plane of this heterocycle. Occupancies for these sites were refined to 0.37(2) and 0.63(2) for O3A and O3B, respectively. No disordered parts were detected in the other compounds. For all compounds, the refined Flack parameter is consistent with the absolute configuration expected from the synthetic procedure. In all cases, all H atoms bonded to C atoms were placed in calculated positions, while hydroxy H atoms positions were determined from difference maps, and refined with free coordinates. All isotropic displacement parameters for H atoms are calculated from the equivalent displacement parameters of their carrier C/O atoms. Structure factors can be found in the Cif files deposited with the CCDC. Checkcif/PLATON reports are copied below, which do not raise A/B-level issues.

[1] Stoe & Cie (2019). X-AREA and X-RED32. Stoe & Cie, Darmstadt, Germany.
[2] Sheldrick, G. M. (2015). *Acta Cryst*. C**71**, 3-8.

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 10a_Delta4-cis, 10b_Delta4-trans, 11a_Indolizine-cis, 3_Bromohydrin

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 3_Bromohydrin

Bond precision: C-C = 0.0072 A Wavelength=0.56083

Cell:	a=7.1360(3)	b=8.9300(6)	c=30.3879(14)
	alpha=90	beta=90	gamma=90
Temperature:	294 K		

	Calculated	Reported
Volume	1936.45(18)	1936.45(18)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C20 H23 Br N2 O3	C20 H23 Br N2 O3
Sum formula	C20 H23 Br N2 O3	C20 H23 Br N2 O3
Mr	419.30	419.31
Dx,g cm-3	1.438	1.438
Z	4	4
Mu (mm-1)	1.155	1.155
F000	864.0	864.0
F000'	864.82	
h,k,lmax	9,11,40	9,11,40
Nref	4843[2792]	4645
Tmin,Tmax	0.741,0.928	0.525,1.000
Tmin'	0.674	

Correction method= # Reported T Limits: Tmin=0.525 Tmax=1.000AbsCorr = MULTI-SCAN

Data completeness= 1.66/0.96 Theta(max)= 21.999

R(reflections)= 0.0344(2253)

wR2(reflections)= 0.0683(4645)

S = 0.817

Npar= 249

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
PLAT026_ALERT_3_C Ratio Observed / Unique Reflections (too) Low ..        49% Check
PLAT234_ALERT_4_C Large Hirshfeld Difference O3A      --C2       .      0.17 Ang.
PLAT241_ALERT_2_C High   'MainMol' Ueq as Compared to Neighbors of        C4 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of        C9 Check
PLAT331_ALERT_2_C Small Aver Phenyl C-C Dist C12      --C17      .      1.37 Ang.
PLAT341_ALERT_3_C Low Bond Precision on  C-C Bonds ..............   0.00717 Ang.
PLAT910_ALERT_3_C Missing # of FCF Reflection(s) Below Theta(Min).         8 Note
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600        18 Report
```

Alert level G

```
PLAT230_ALERT_2_G Hirshfeld Test Diff for    O3A      --C4       .       6.4 s.u.
PLAT301_ALERT_3_G Main Residue  Disorder ..............(Resd  1  )        4% Note
PLAT398_ALERT_2_G Deviating  C-O-C   Angle From 120 for O3B      .     105.2 Degree
PLAT398_ALERT_2_G Deviating  C-O-C   Angle From 120 for O3A      .     103.5 Degree
PLAT480_ALERT_4_G Long H...A H-Bond Reported H8A      ..O8       .      2.62 Ang.
PLAT791_ALERT_4_G Model has Chirality at C7          (Sohnke SpGr)         S Verify
PLAT791_ALERT_4_G Model has Chirality at C8          (Sohnke SpGr)         S Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         9 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.         0 Info
```

0 **ALERT level A** = Most likely a serious problem - resolve or explain

0 **ALERT level B** = A potentially serious problem, consider carefully

8 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
9 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
7 ALERT type 2 Indicator that the structure model may be wrong or deficient
5 ALERT type 3 Indicator that the structure quality may be low
5 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

Datablock: 10a_Delta4-cis

Bond precision: C-C = 0.0039 A Wavelength=0.56083

Cell:	a=7.3321(12)	b=10.641(2)	c=11.146(2)
	alpha=90	beta=90	gamma=90
Temperature:	294 K		

	Calculated	Reported
Volume	869.6(3)	869.6(3)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C8 H12 Cl N O	C8 H12 Cl N O
Sum formula	C8 H12 Cl N O	C8 H12 Cl N O
Mr	173.64	173.64
Dx,g cm-3	1.326	1.326
Z	4	4
Mu (mm-1)	0.201	0.201
F000	368.0	368.0
F000'	368.43	
h,k,lmax	9,13,14	9,13,14
Nref	2040[1196]	2040
Tmin,Tmax	0.974,0.984	0.518,1.000
Tmin'	0.905	

Correction method= # Reported T Limits: Tmin=0.518 Tmax=1.000AbsCorr = MULTI-SCAN

Data completeness= 1.71/1.00 Theta(max)= 21.498

R(reflections)= 0.0311(1208) wR2(reflections)= 0.0590(2040)

S = 0.784 Npar= 103

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

GOODF01_ALERT_2_C The least squares goodness of fit parameter lies outside the range 0.80 <> 2.00
Goodness of fit given = 0.784

Alert level G

PLAT480_ALERT_4_G	Long H...A H-Bond Reported H1B	..CL1 .	2.95 Ang.
PLAT480_ALERT_4_G	Long H...A H-Bond Reported H2A	..CL1 .	2.90 Ang.
PLAT791_ALERT_4_G	Model has Chirality at C2	(Sohnke SpGr)	S Verify
PLAT791_ALERT_4_G	Model has Chirality at C3	(Sohnke SpGr)	R Verify
PLAT791_ALERT_4_G	Model has Chirality at C4	(Sohnke SpGr)	S Verify
PLAT910_ALERT_3_G	Missing # of FCF Reflection(s) Below Theta(Min).		1 Note
PLAT978_ALERT_2_G	Number C-C Bonds with Positive Residual Density.		0 Info

0 **ALERT level A** = Most likely a serious problem - resolve or explain

0 **ALERT level B** = A potentially serious problem, consider carefully

```
   1 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   7 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   2 ALERT type 2 Indicator that the structure model may be wrong or deficient
   1 ALERT type 3 Indicator that the structure quality may be low
   5 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

Datablock: 10b_Delta4-trans

Bond precision: C-C = 0.0037 A Wavelength=0.56083

Cell:	a=10.8339(10)	b=6.7230(9)	c=11.3873(10)
	alpha=90	beta=90	gamma=90
Temperature:	294 K		

	Calculated	Reported
Volume	829.41(15)	829.41(15)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C8 H12 Cl N O	C8 H12 Cl N O
Sum formula	C8 H12 Cl N O	C8 H12 Cl N O
Mr	173.64	173.64
Dx,g cm-3	1.390	1.391
Z	4	4
Mu (mm-1)	0.211	0.211
F000	368.0	368.0
F000'	368.43	
h,k,lmax	14,8,14	14,8,14
Nref	1936[1140]	1935
Tmin,Tmax	0.967,0.991	0.457,1.000
Tmin'	0.939	

Correction method= # Reported T Limits: Tmin=0.457 Tmax=1.000AbsCorr = MULTI-SCAN

Data completeness= 1.70/1.00 Theta(max)= 21.476

R(reflections)= 0.0308(1399) wR2(reflections)= 0.0674(1935)

S = 0.864 Npar= 103

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level G

```
PLAT791_ALERT_4_G Model has Chirality at C2          (Sohnke SpGr)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C3          (Sohnke SpGr)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C4          (Sohnke SpGr)          R Verify
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          1 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          1 Info
```

0 **ALERT level A** = Most likely a serious problem - resolve or explain

0 **ALERT level B** = A potentially serious problem, consider carefully

0 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
5 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
1 ALERT type 2 Indicator that the structure model may be wrong or deficient
1 ALERT type 3 Indicator that the structure quality may be low
3 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

Datablock: 11a_Indolizine-cis

Bond precision: C-C = 0.0027 A Wavelength=0.56083

Cell:	a=7.4256(2)	b=10.5444(4)	c=11.2574(5)
	alpha=90	beta=90	gamma=90
Temperature:	295 K		

	Calculated	Reported
Volume	881.44(6)	881.44(6)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C8 H14 Cl N O	C8 H14 Cl N O
Sum formula	C8 H14 Cl N O	C8 H14 Cl N O
Mr	175.65	175.65
Dx,g cm-3	1.324	1.324
Z	4	4
Mu (mm-1)	0.199	0.198
F000	376.0	376.0
F000'	376.43	
h,k,lmax	10,14,16	10,14,16
Nref	2655[1538]	2656
Tmin,Tmax	0.905,0.934	0.618,1.000
Tmin'	0.886	

Correction method= # Reported T Limits: Tmin=0.618 Tmax=1.000AbsCorr = MULTI-SCAN

Data completeness= 1.73/1.00 Theta(max)= 23.492

R(reflections)= 0.0295(2478) wR2(reflections)= 0.0841(2656)

S = 1.066 Npar= 105

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT031_ALERT_4_C Refined Extinction Parameter Within Range of ... 2.857 Sigma

---

Alert level G

PLAT063_ALERT_4_G Crystal Size Possibly too Large for Beam Size .. 0.61 mm
PLAT791_ALERT_4_G Model has Chirality at C2 (Sohnke SpGr) S Verify
PLAT791_ALERT_4_G Model has Chirality at C3 (Sohnke SpGr) R Verify
PLAT791_ALERT_4_G Model has Chirality at C4 (Sohnke SpGr) S Verify
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min). 1 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 6 Info
PLAT982_ALERT_1_G The Cl-f'= 0.1009 Deviates from IT-value = 0.0998 Check

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain

0 **ALERT level B** = A potentially serious problem, consider carefully

1 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
7 **ALERT level G** = General information/check it is not something unexpected

```
  1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
  1 ALERT type 2 Indicator that the structure model may be wrong or deficient
  1 ALERT type 3 Indicator that the structure quality may be low
  5 ALERT type 4 Improvement, methodology, query or suggestion
  0 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

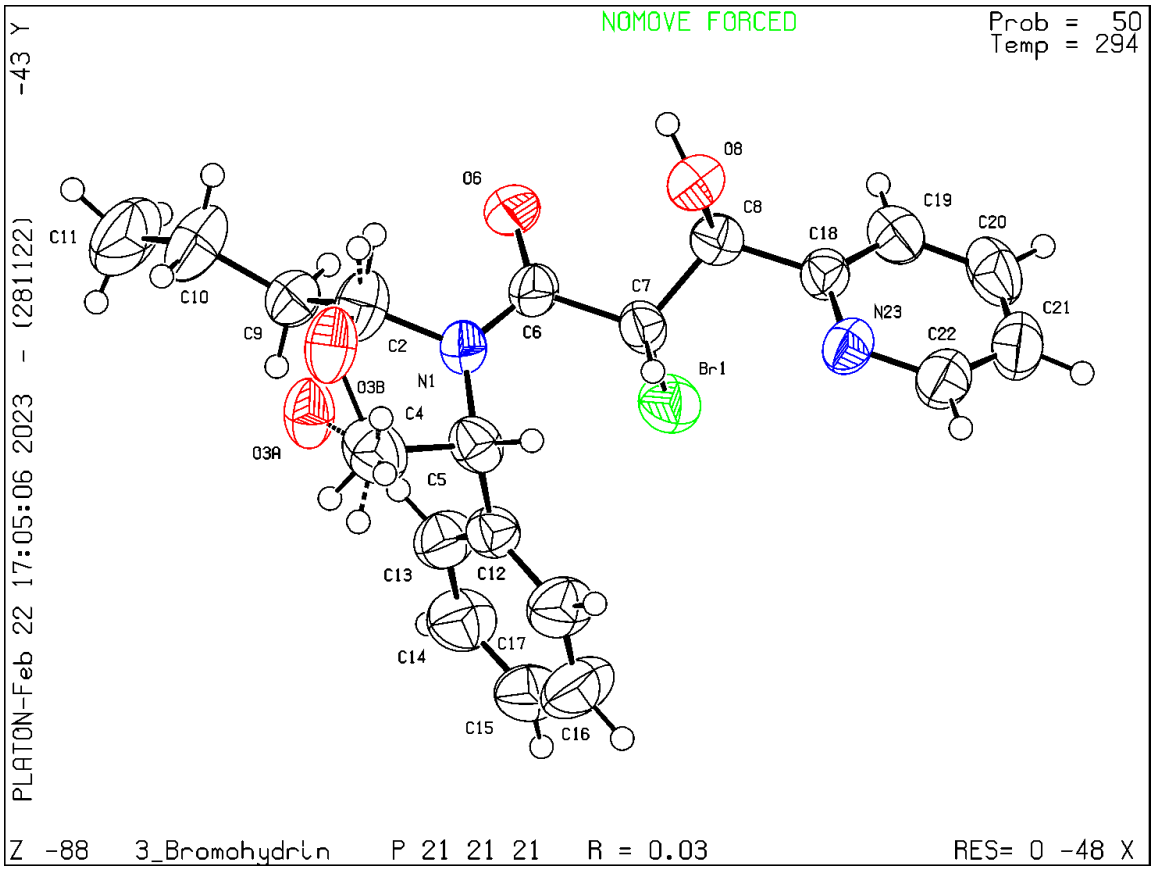
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

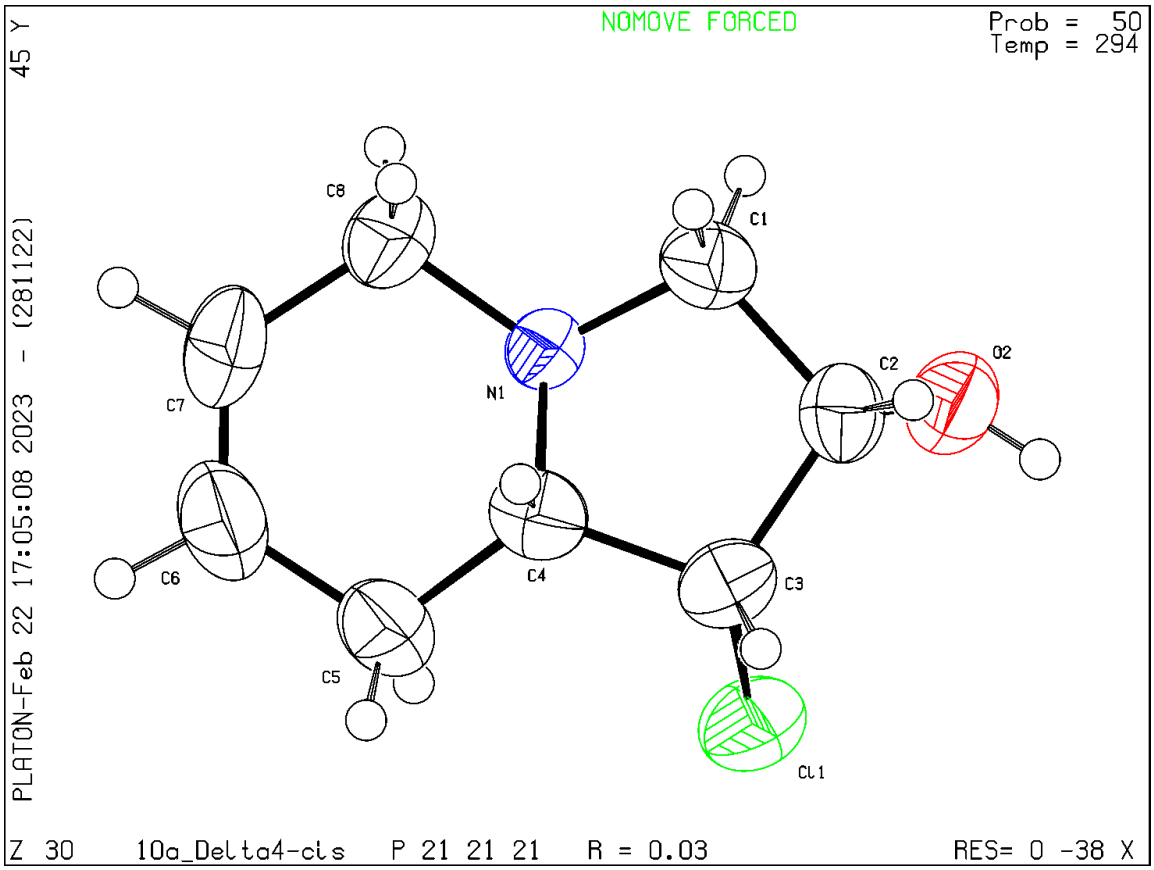
Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 28/11/2022; check.def file version of 28/11/2022

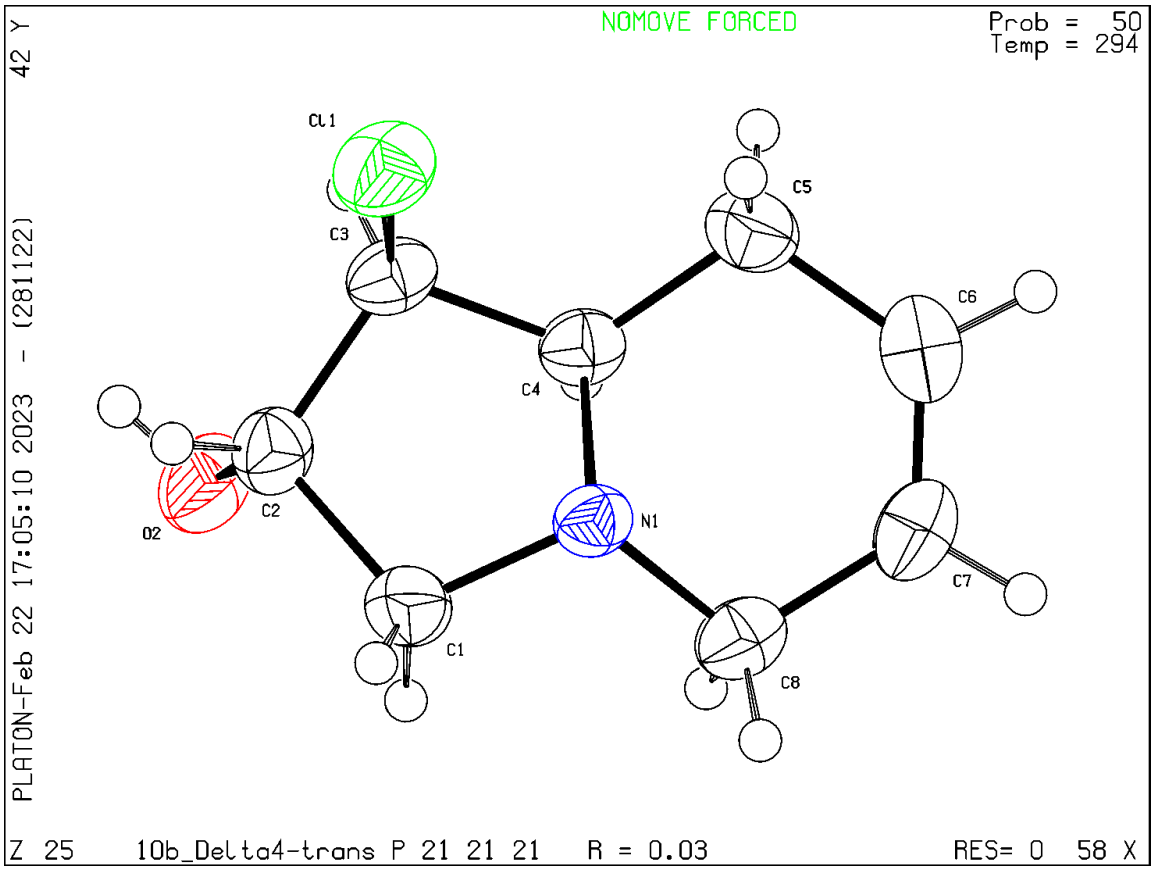
Datablock 3_Bromohydrin - ellipsoid plot



Datablock 10a_Delta4-cis - ellipsoid plot



Datablock 10b_Delta4-trans - ellipsoid plot



Datablock 11a_Indolizine-cis - ellipsoid plot