SUPPORTING INFORMATION

Utilization of pyridoxal acetal salts as water-triggered, slow-release pro-fragrances

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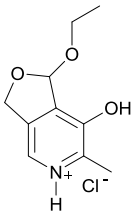
I. General Information. Proton and carbon nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR) were recorded at 400 and 100 MHz, respectively, with solvent resonance as the internal standard (^{1}H NMR: DMSO-d_6 at 2.500 ppm; ^{13}C NMR: DMSO-d_6 at 39.52 ppm). ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. Mass spectra were recorded on a high-resolution electrospray ionization quadrupole mass spectrometer. All reactions were carried out under air with magnetic stirring. Yield refers to isolated yield of analytically pure material. Yields are reported for a specific experiment and as a result may differ slightly from those found in the tables, which are averages of at least two experiments.

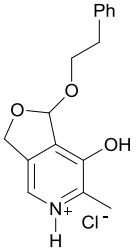
II. General Procedure for the Synthesis of the Pyridoxal Acetal Salts (**3a-3c**). Pyridoxal HCl was added to the appropriate alcohol (0.5 M) and the solution was heated to 60 °C for 2 hours. The solution was then cooled to room temperature and either concentrated *in vacuo* (**3a**, **3c**) or diluted with ether and allowed to crystallize in the freezer before being filtered to provide pure material (**3b, 3d**).

III. Analytical Data for Pyridoxal Acetal Salts (3a-3d)



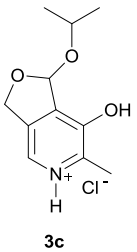
3a

1-ethoxy-7-hydroxy-6-methyl-1,3-dihydrofuro[3,4-c]pyridin-5-ium chloride (***3a***): The title compound was prepared according to the general procedure using pyridoxal HCl **1** (100 mg, 0.491 mmol, 1 equiv) in ethanol (2.5 mL, 0.2 M) affording 115 mg (99%) of the product as a white solid. Analytical Data for **3a**: m.p.: 97-103 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 12.05 (br. s, 1H), 8.28 (s, 1H), 6.58 (s, 1H), 5.14-5.03 (m, 2H), 3.75-3.70 (m, 2H) 2.61 (s, 3H), 1.11 (t, J = 7.0 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 149.5, 143.7, 139.0, 138.8, 125.4, 104.2, 70.0, 64.1, 15.7, 14.9. HRMS (ESI$^+$) calcd for $C_{10}H_{14}N_1O_3$+, 196.0968; found, 196.0923.



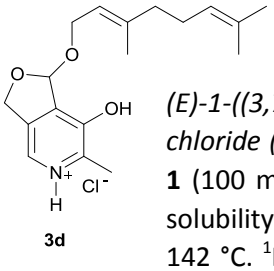
3b

*7-hydroxy-6-methyl-1-phenethoxy-1,3-dihydrofuro[3,4-c]pyridin-5-ium chloride(**3b**)*: The title compound was prepared according to the general procedure using pyridoxal HCl **1** (100 mg, 0.491 mmol, 1 equiv) in 2-phenylethanol (2.5 mL, 0.2 M) affording 139.1 mg (92%) of the product as a white solid. Analytical Data for **3b**: m.p. 168-172 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 12.09 (br. s, 1H), 8.28 (s, 1H), 7.27-7.15 (m, 5H), 6.67 (s, 1H), 5.11-5.06 (m, 2H), 3.96-3.89 (m, 2H), 2.88-2.83 (m, 2H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 149.0, 143.3, 138.6, 138.5, 138.1, 128.8, 128.3, 126.1, 124.97, 103.8, 69.6, 68.7, 35.6, 14.4. HRMS (ESI$^+$) calcd for $C_{16}H_{18}N_1O_3$+, 272.1281; found, 272.1272.



3c

7-hydroxy-1-isopropoxy-6-methyl-1,3-dihydrofuro[3,4-c]pyridin-5-ium chloride (***3c***): The title compound was prepared according to the general procedure using pyridoxal HCl **1** (100 mg, 0.491 mmol, 1 equiv) in isopropanol (2.5 mL, 0.2 M) affording 120 mg (99%) of the product as a white solid. Analytical Data for **3c**: m.p. 116-121 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.92 (br. s, 1H), 8.29 (s, 1H), 6.71 (s, 1H), 5.08, (s, 2H), 4.14-4.08 (m, 1H), 2.62 (s, 3H), 1.16 (d, J =4.0 Hz, 6H) ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 149.3, 143.8, 139.9, 139.0, 125.6, 72.1, 69.6, 24.1, 23.2. HRMS (ESI$^+$) calcd for $C_{11}H_{16}N_1O_3$+, 210.1125; found, 210.1116.

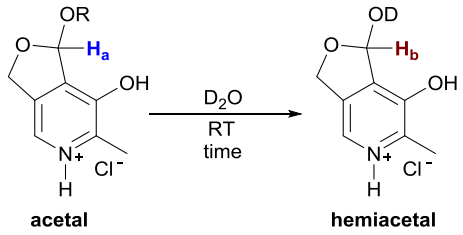


3d

*(E)-1-((3,7-dimethylocta-2,6-dien-1-yl)oxy)-7-hydroxy-6-methyl-1,3-dihydrofuro[3,4-c]pyridin-5-ium chloride (**3d**)*: The title compound was prepared according to the general procedure using pyridoxal HCl **1** (100 mg, 0.491 mmol, 1 equiv) in geraniol (2.5 mL 0.2 M) and in DMSO (0.02 mL, 25 M) to aid in solubility then affording 123 mg (73%) of the product as a white solid. Analytical data for **3d**: m.p. 140-142 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 12.04 (br. s, 1H), 8.28 (s, 1H), 6.63 (s, 1H), 5.30-5.27 (s, 1H), 5.12-5.04 (m, 3H), 4.29-4.19 (m, 2H), 2.62 (s, 3H), 2.03-1.95 (m, 4H), 1.62 (s, 3H), 1.61 (s, 3H), 1.53 (s, 3H) ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 149.0, 143.2, 139.6, 138.5, 138.3, 131.0, 125.0, 123.9, 120.4, 103.3, 69.6, 64.5, 39.0, 25.9, 25.5, 17.6, 16.3, 14.4. HRMS (ESI$^+$) calcd for $C_{18}H_{26}N_1O_3$+, 304.1907; found, 304.1901.

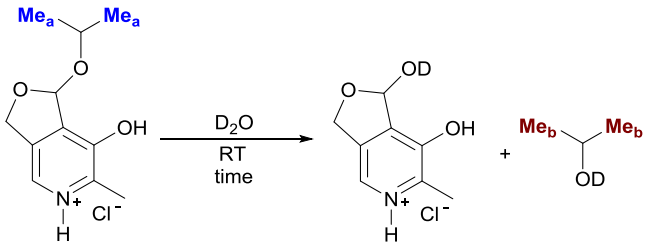
IV. Time-Dependent Stack Plots of Acetal Cleavage

Acetals (**3a-3d**) (0.200 mmol) were dissolved in 1.0 mL of DMSO-d_6/D_2O and the hydrolysis was monitored by ^1H NMR.

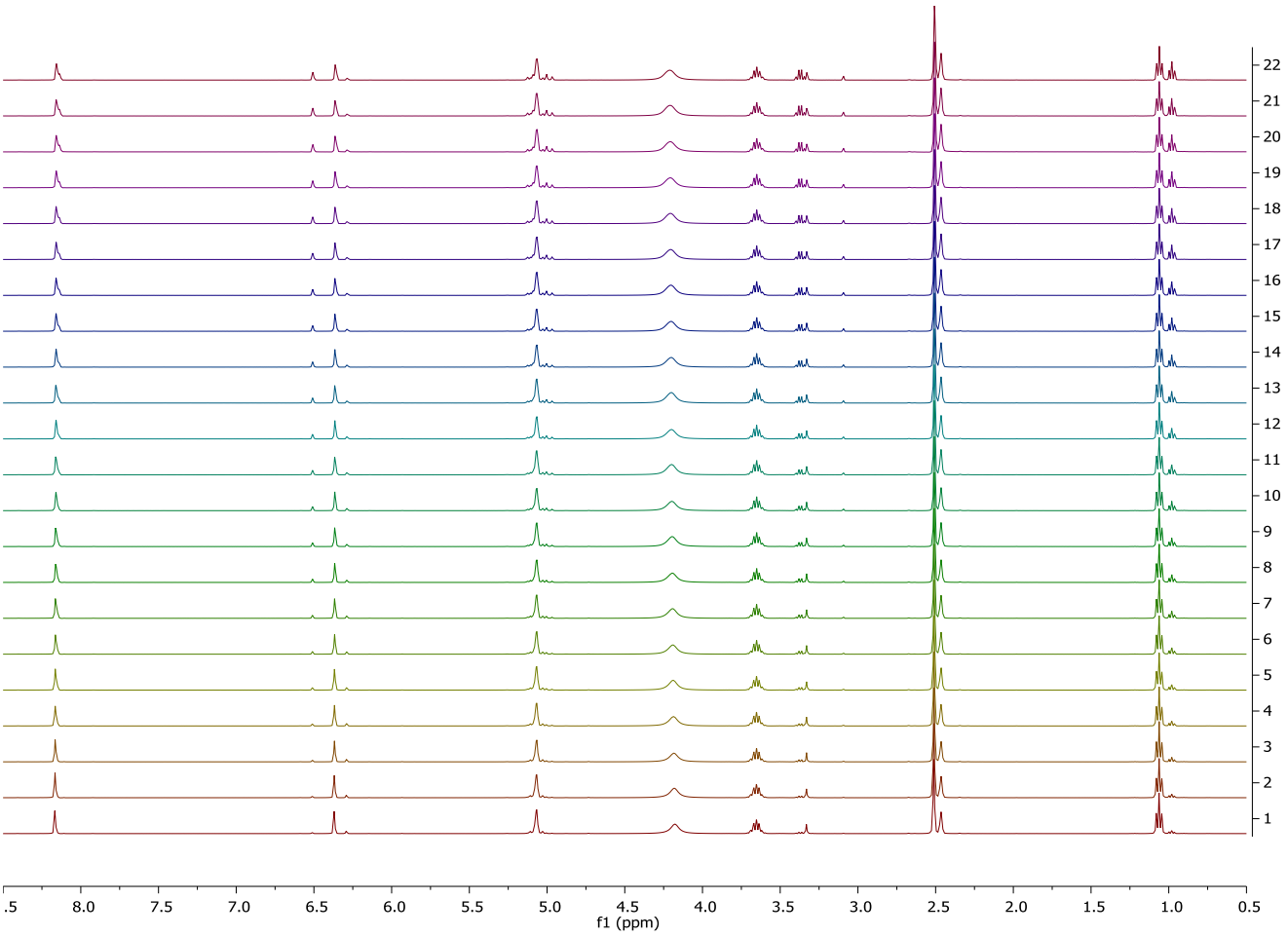


acetal **hemiacetal**

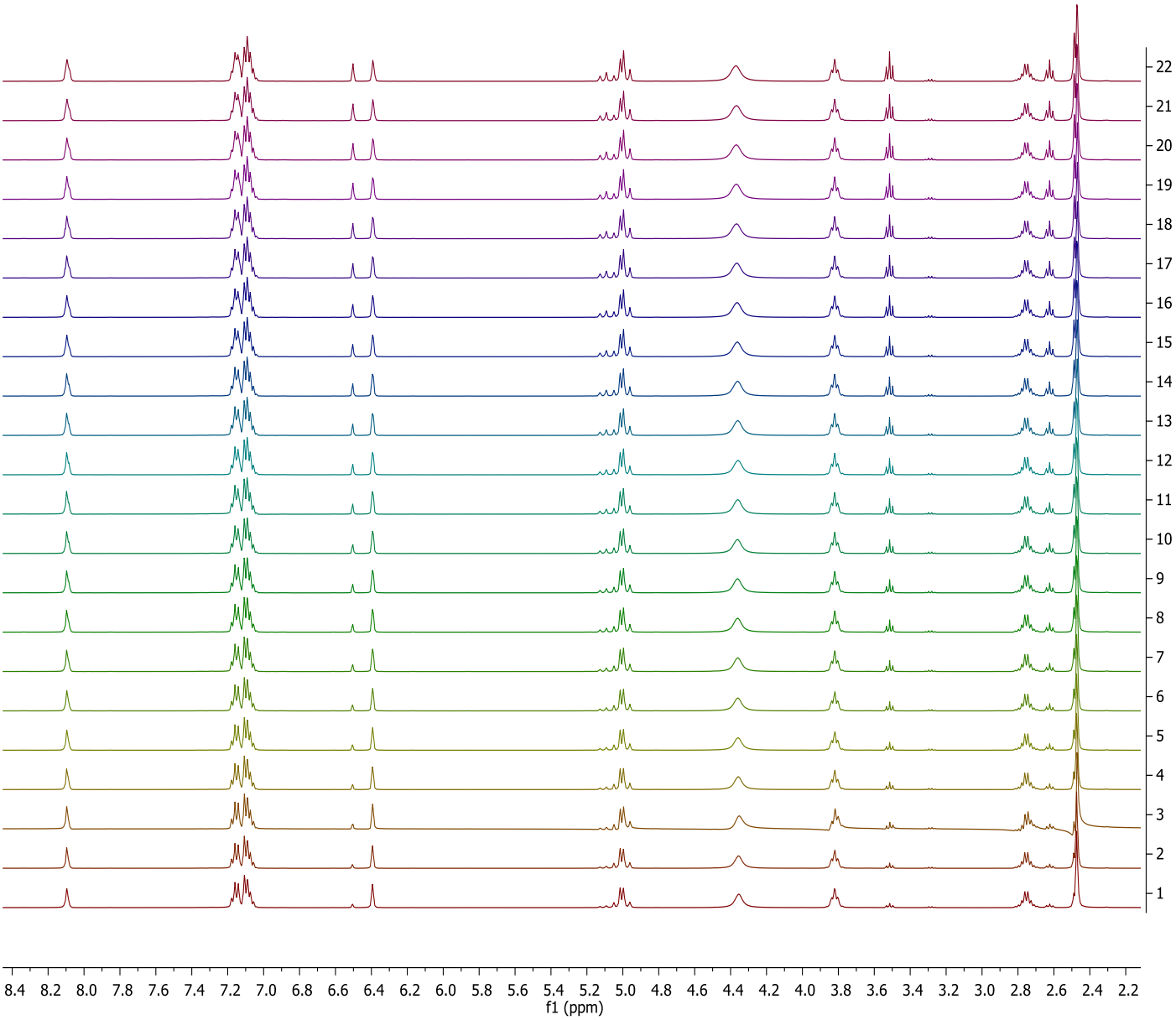
The acetal cleavage was measured by comparing the integration of H_a to H_b whereas $H_b/(H_a+H_b)$ provides the percent completion for the acetal cleavage for **3a** and **3b**. The stack plots below provide a visual counterpart to the graphs in the manuscript. **3c** had some overlap between H_a and H_b so the fully separated methyls of the isopropyl were integrated instead.



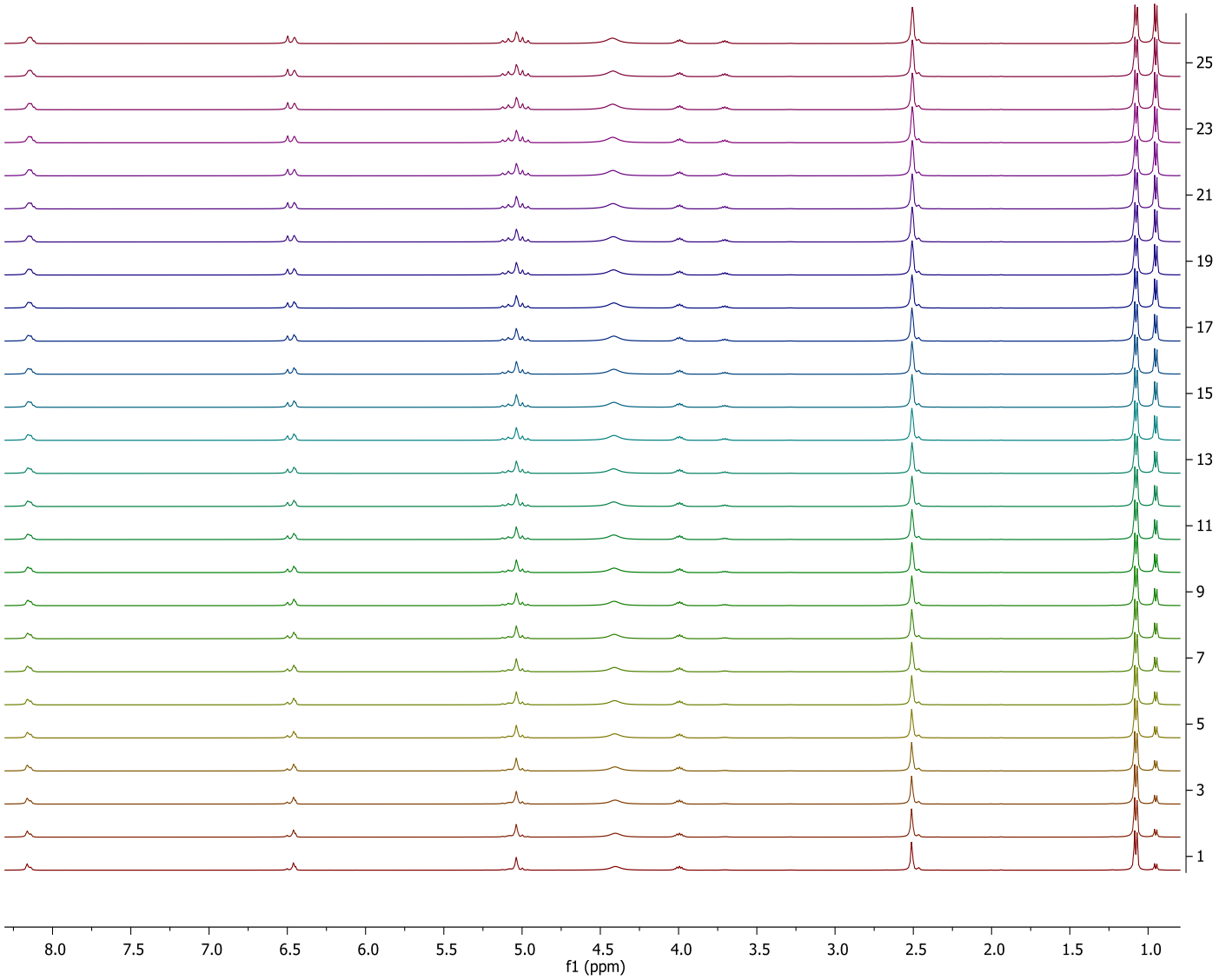
Ethyl Acetal **30% D_2O in DMSO-d_6**



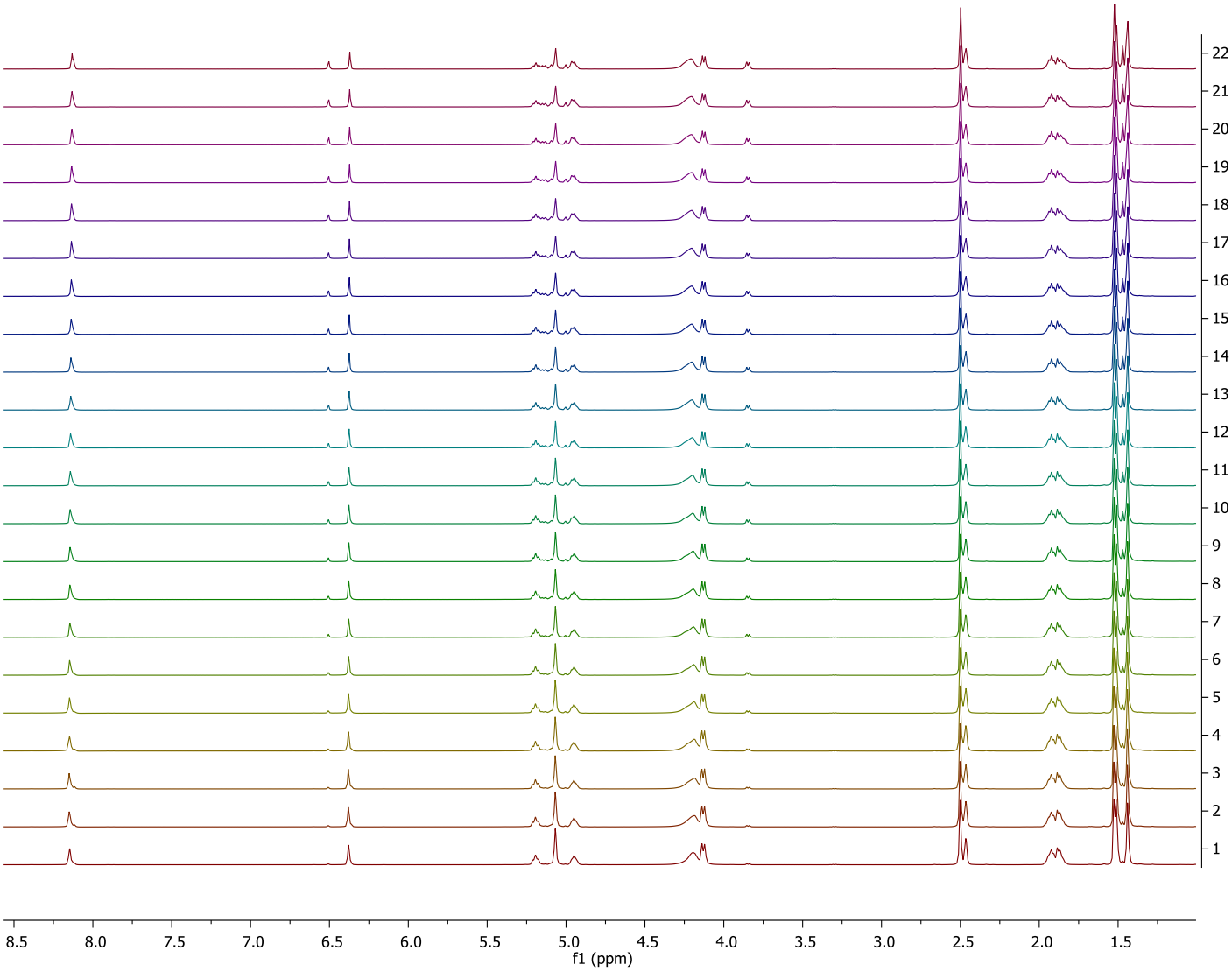
2-Phenylethyl Acetal **30% D_2O in DMSO-d_6**



Isopropyl Acetal **30% D_2O in DMSO-d_6**



Geranyl Acetal **30% D_2O in DMSO-d_6**

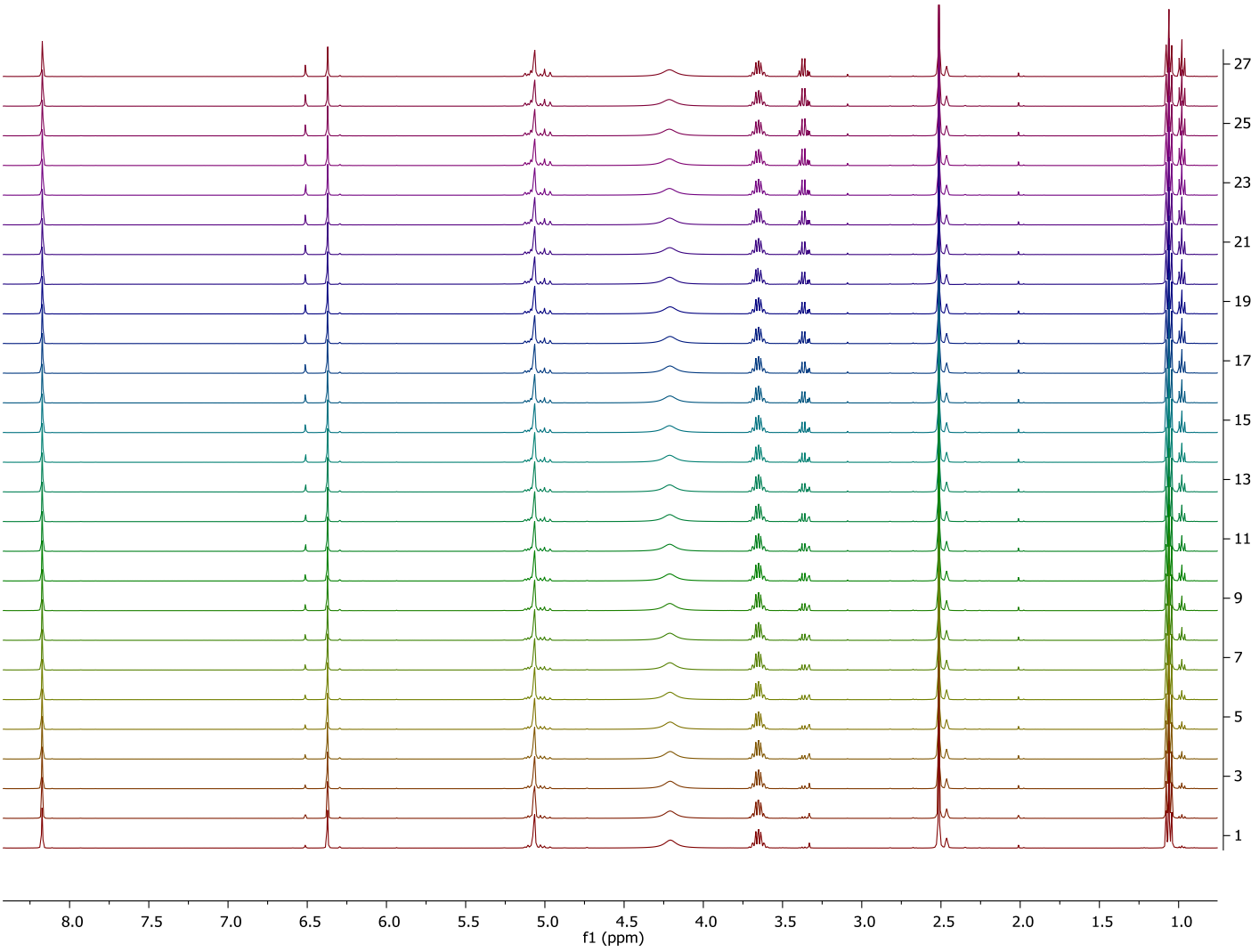


V. Conditions for the Kinetic Reaction Profile for the Release of Ethanol

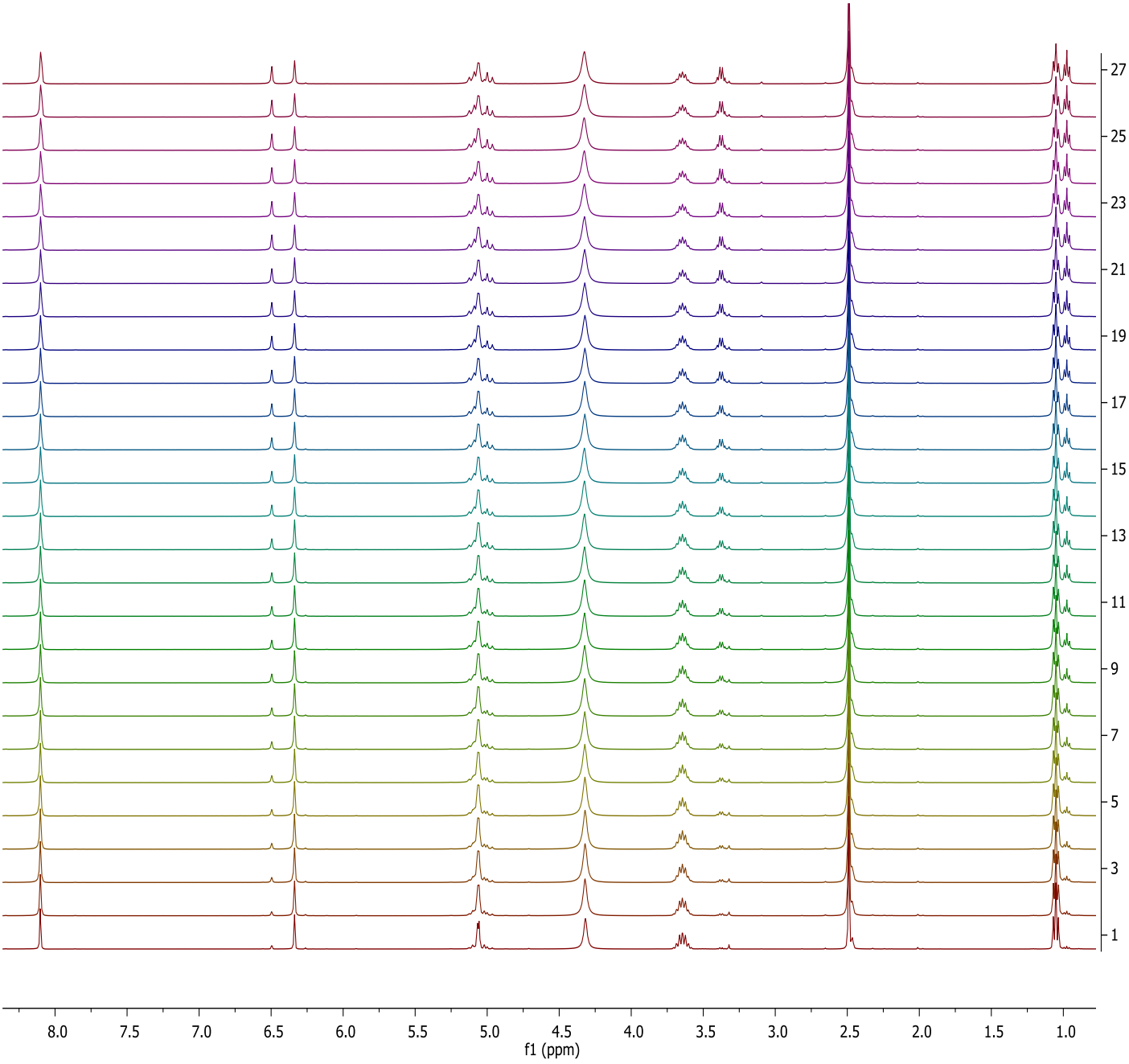
Acetal **3a** (0.1636 mmol) was dissolved in 0.4 mL of DMSO-d_6 (except for 100% D_2O) and varying amounts of D_2O were added as illustrated in the table below.

% D_2O	**100%**	**50%**	**35%**	**20%**
D_2O Added	0.8 mL	0.4 mL	0.23 mL	0.1 mL
Final Molarity	0.2 M	0.2 M	0.25 M	0.3 M

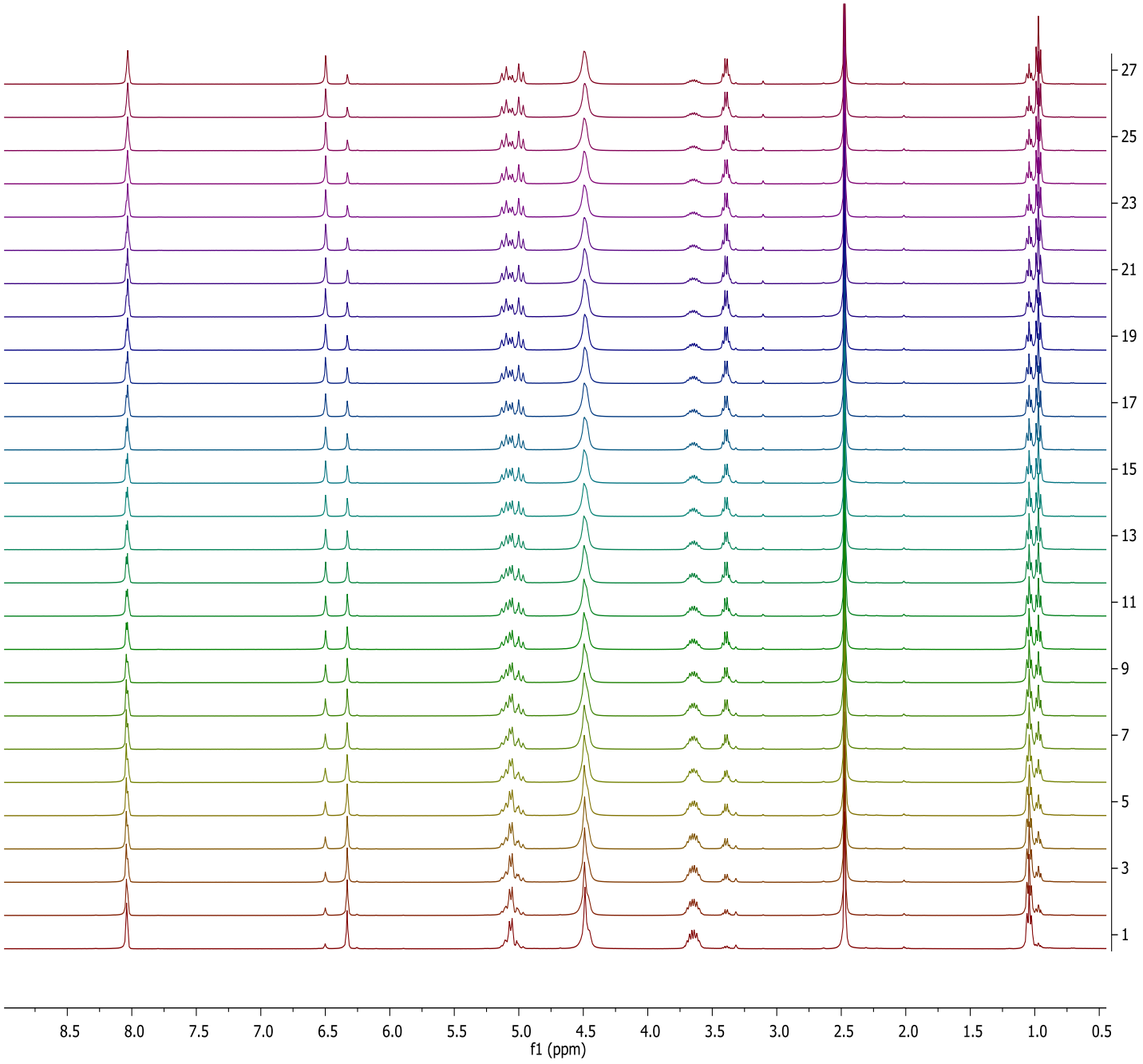
20% D_2O in DMSO-d_6



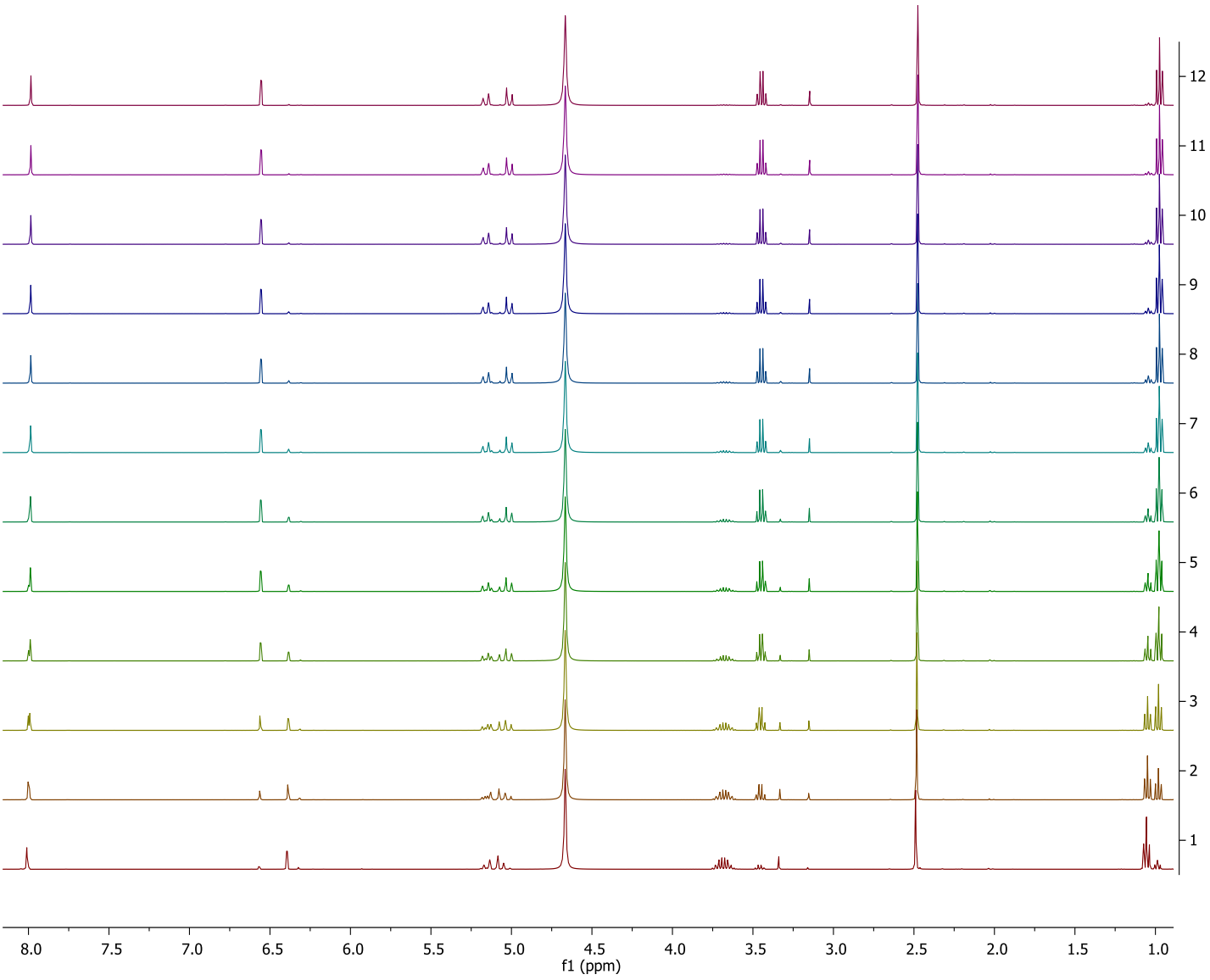
35% D_2O in DMSO-d_6



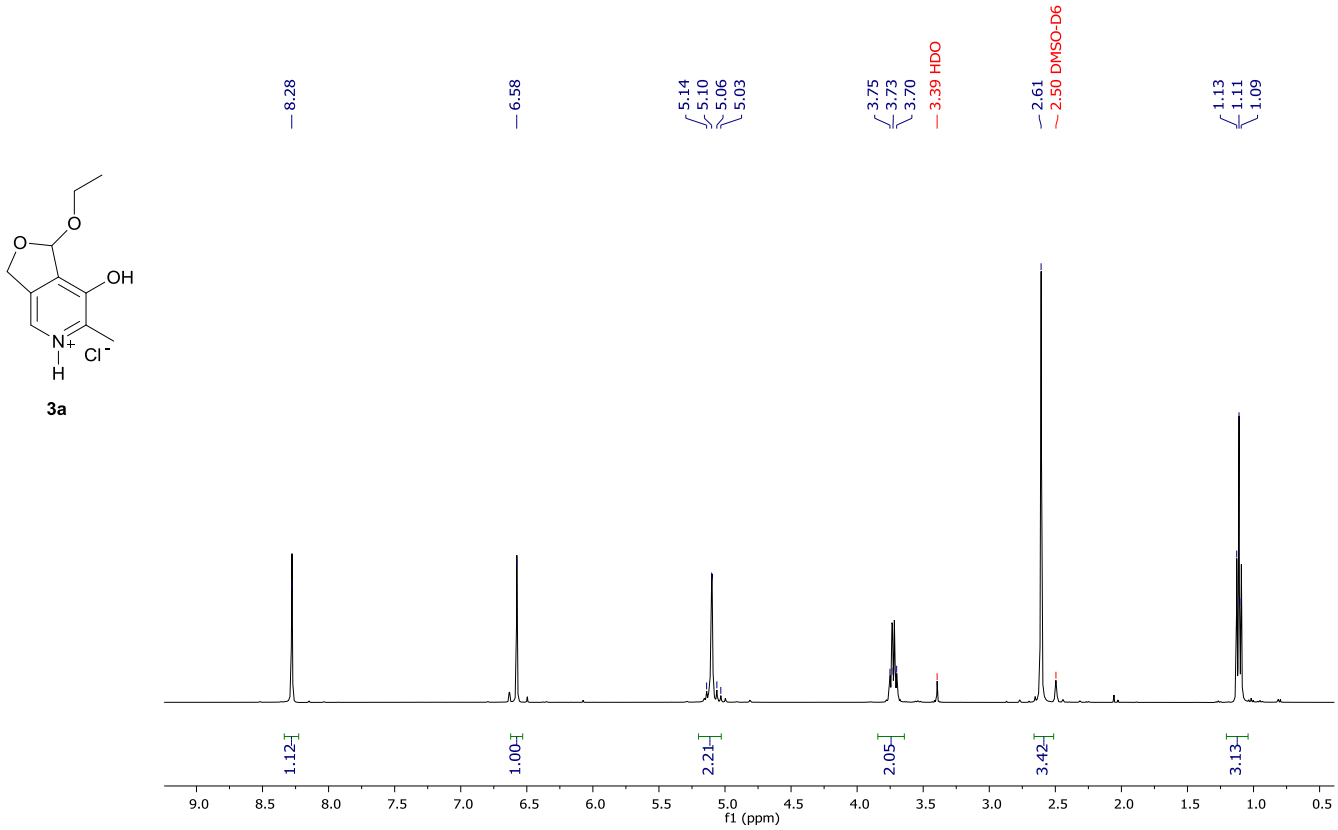
50% D_2O in DMSO-d_6



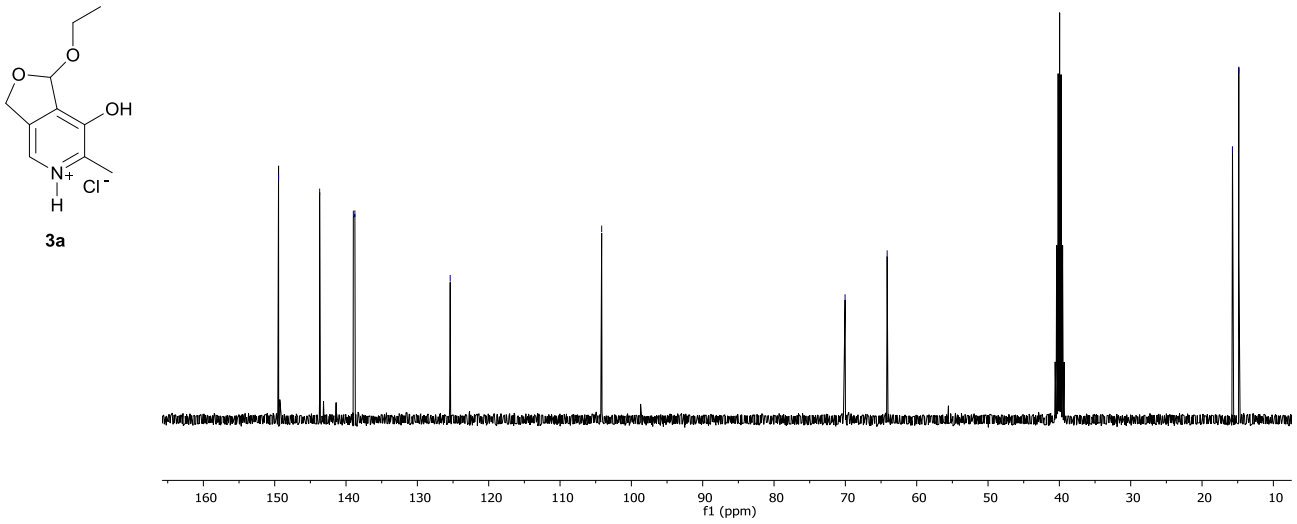
100% D_2O


12
11
10
9
8
7
6
5
4
3
2
1
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

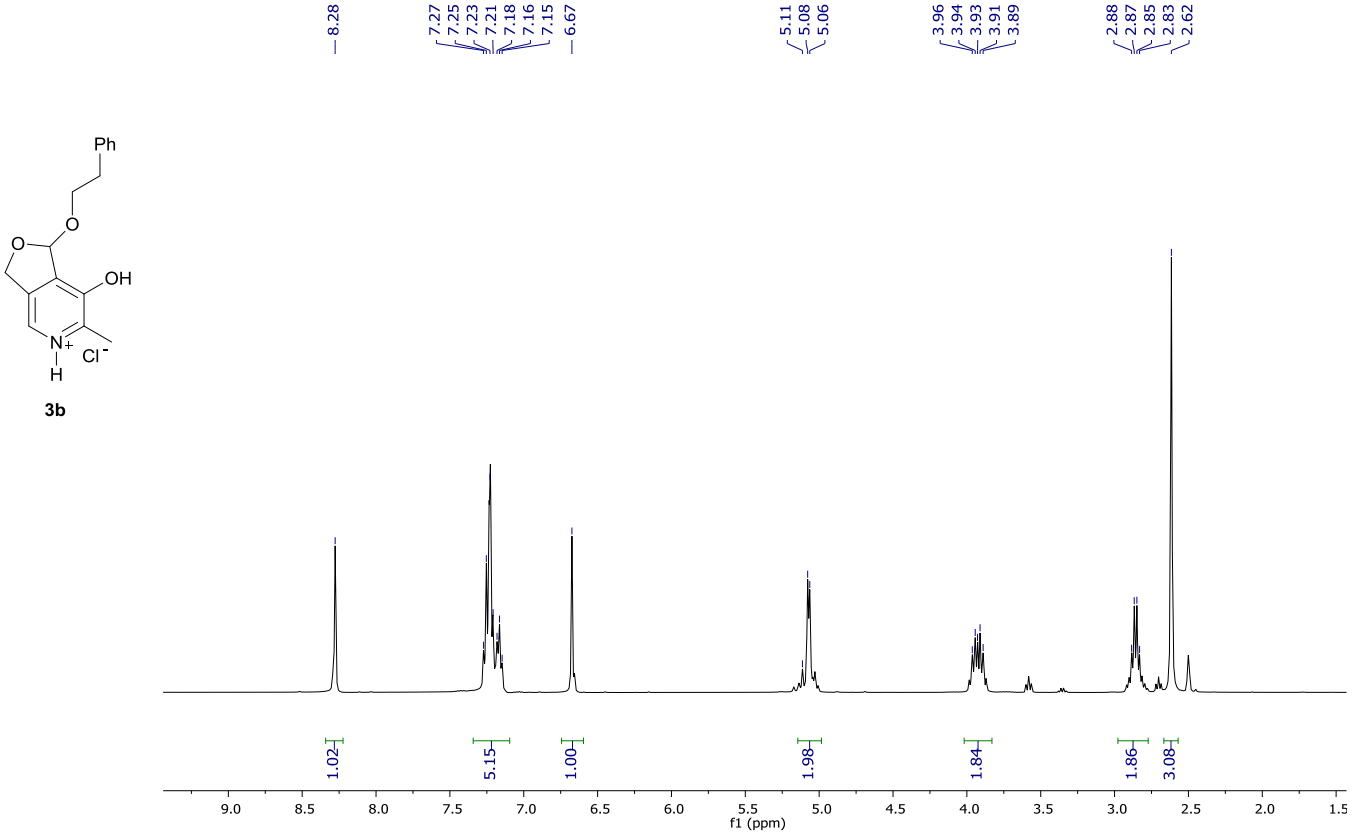
V. ^{1}H and ^{13}C Spectra of Compounds



3a



3a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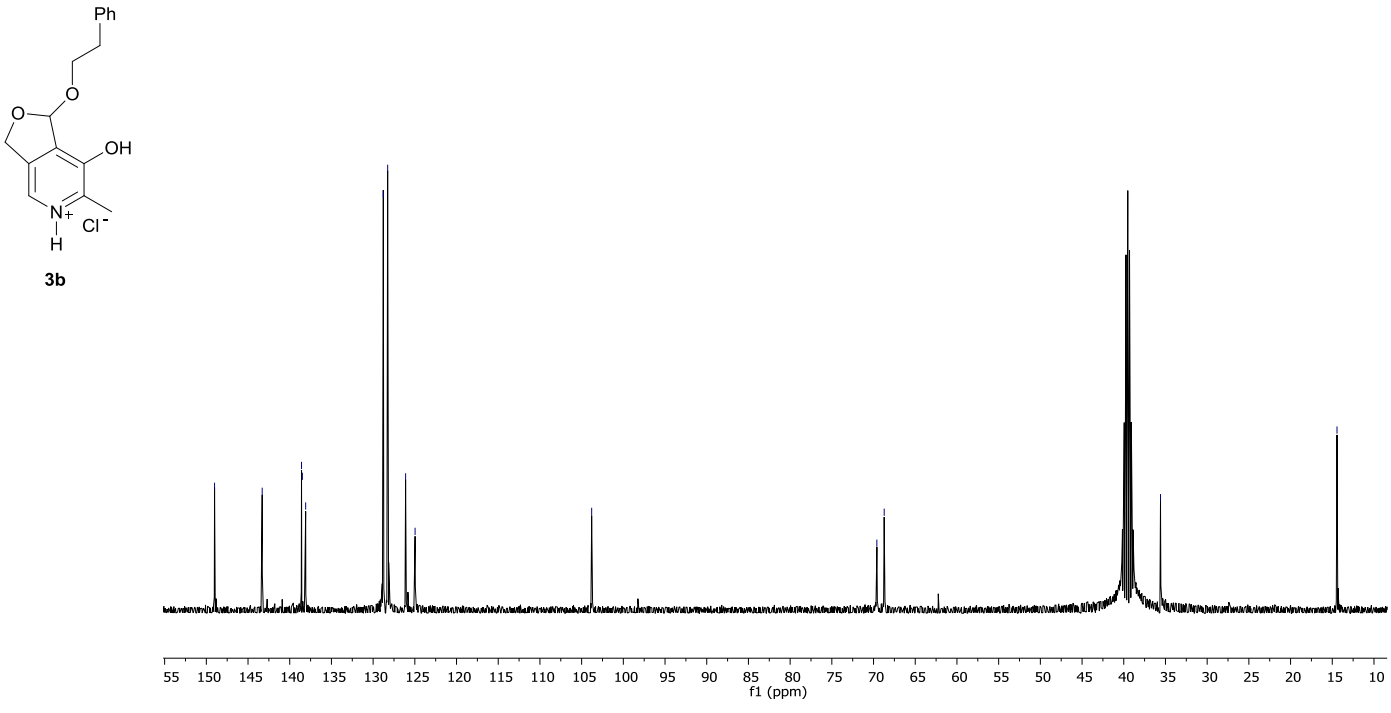
7.27
7.25
7.23
7.21
7.18
7.16
7.15
6.67
5.11
5.08
5.06
3.96
3.94
3.93
3.91
3.89
2.88
2.87
2.85
2.83
2.62
Ph
O
O
OH
N+
H
Cl-
1.02
5.15
1.00
1.98
1.84
1.86
3.08
f1 (ppm)

3b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143.30
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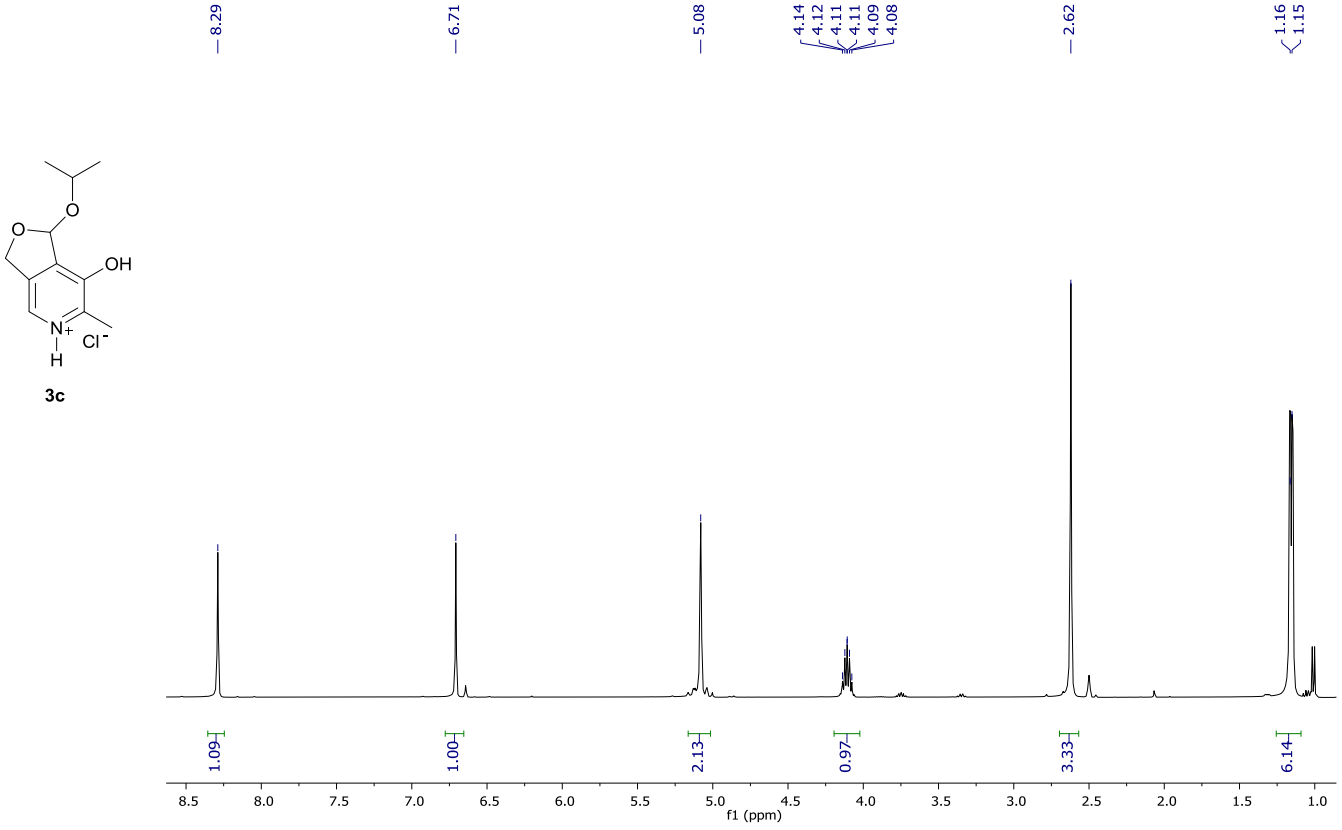
138.49
138.09
128.78
128.26
126.10
124.97
103.80
69.60
68.72
35.59
14.43
Ph
O
O
OH
N+
H
Cl-
f1 (ppm)

3b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4.11
4.11
4.09
4.08
2.62
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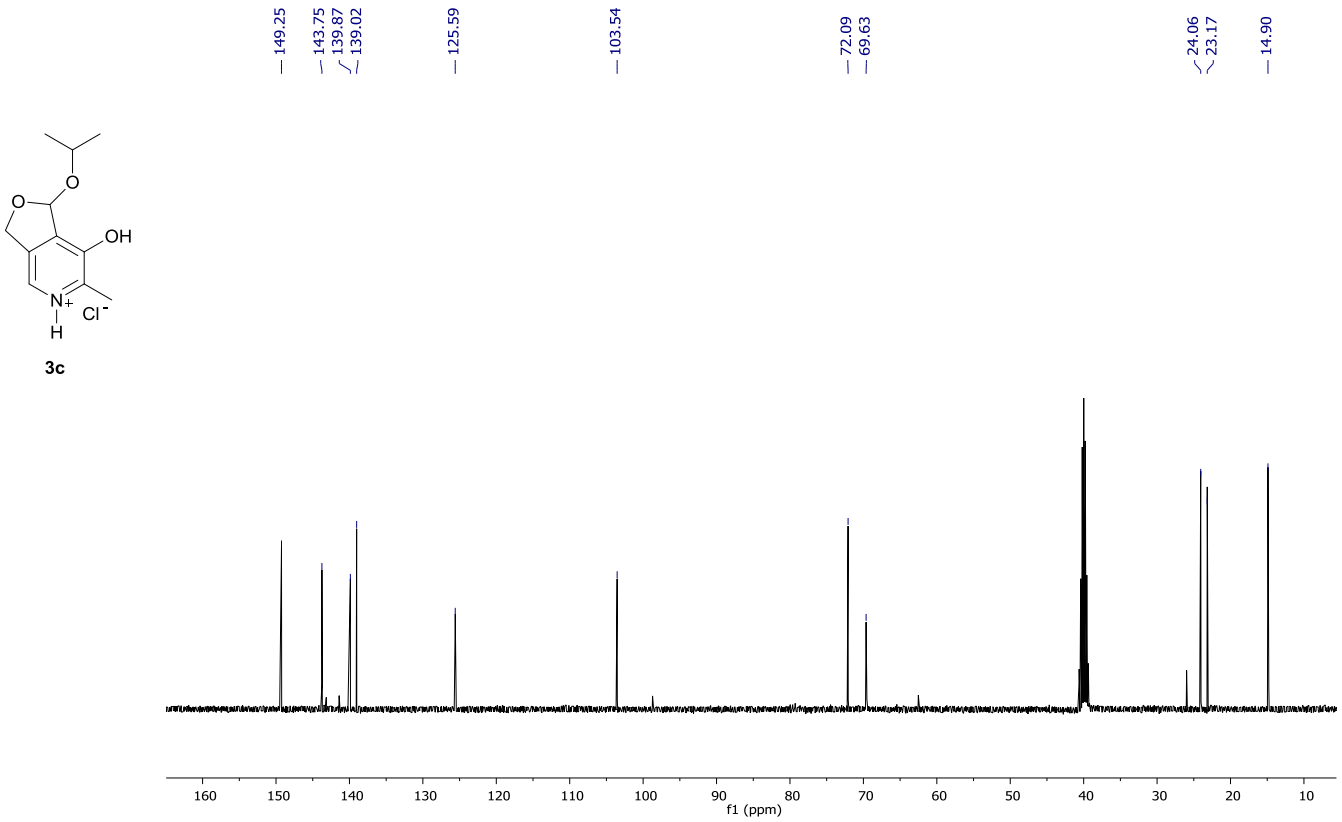
N+
H
Cl-
1.09
1.00
2.13
0.97
3.33
6.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

3c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H
Cl-
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150
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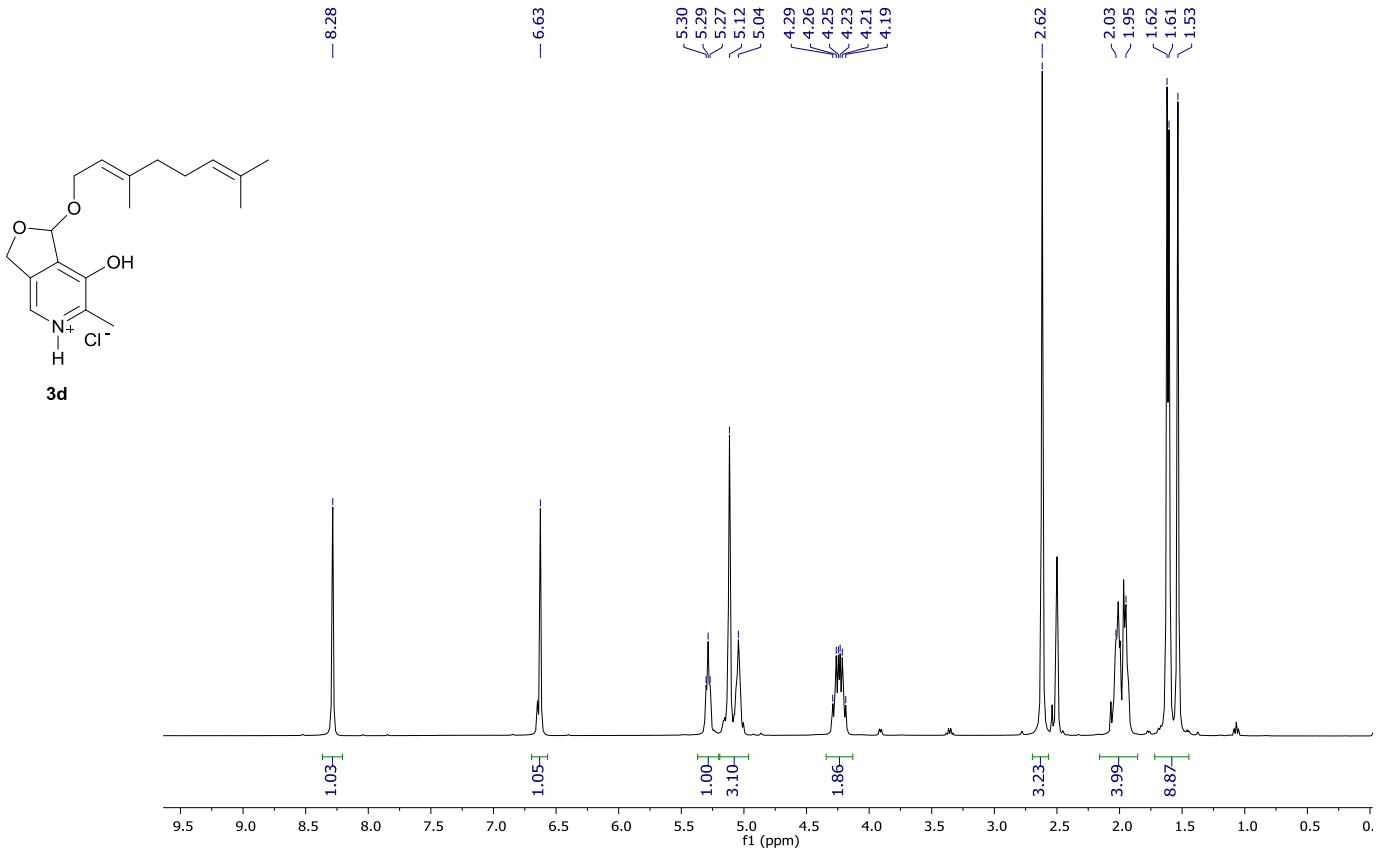
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

3c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6.63
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5.29
5.27
5.12
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2.62
2.03
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1.62
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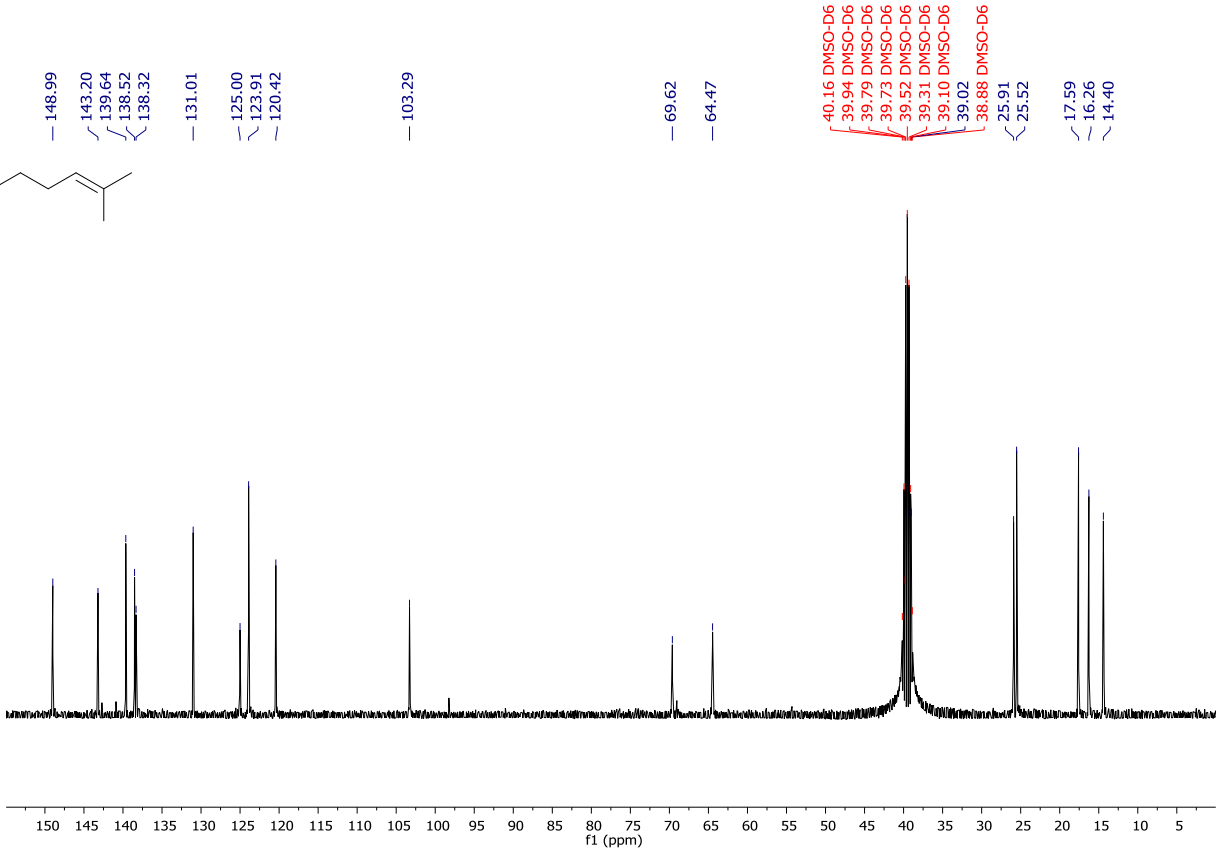
1.53
1.03
1.05
1.00
3.10
1.86
3.23
3.99
8.87
f1 (ppm)

O
O
OH
N+
H
Cl-

3d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139.64
138.52
138.32
131.01
125.00
123.91
120.42
103.29
69.62
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39.94 DMSO-D6
39.79 DMSO-D6
39.73 DMSO-D6
39.52 DMSO-D6
39.31 DMSO-D6
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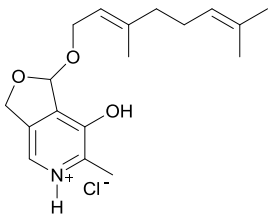
25.52
17.59
16.26
14.40
f1 (ppm)


O
O
OH
N+
H
Cl-

3d