

Supporting Information

**CONFORMATIONAL PROPERTIES AND M1 ANTI  
MUSCARINIC ACTIVITY OF  
4-SUBSTITUTED PIRENZEPINE/TELENZEPINE  
ANALOGUES**

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## 1. Stereochemical stability of ax5 (E/Z-amide) in 1a and 1b.

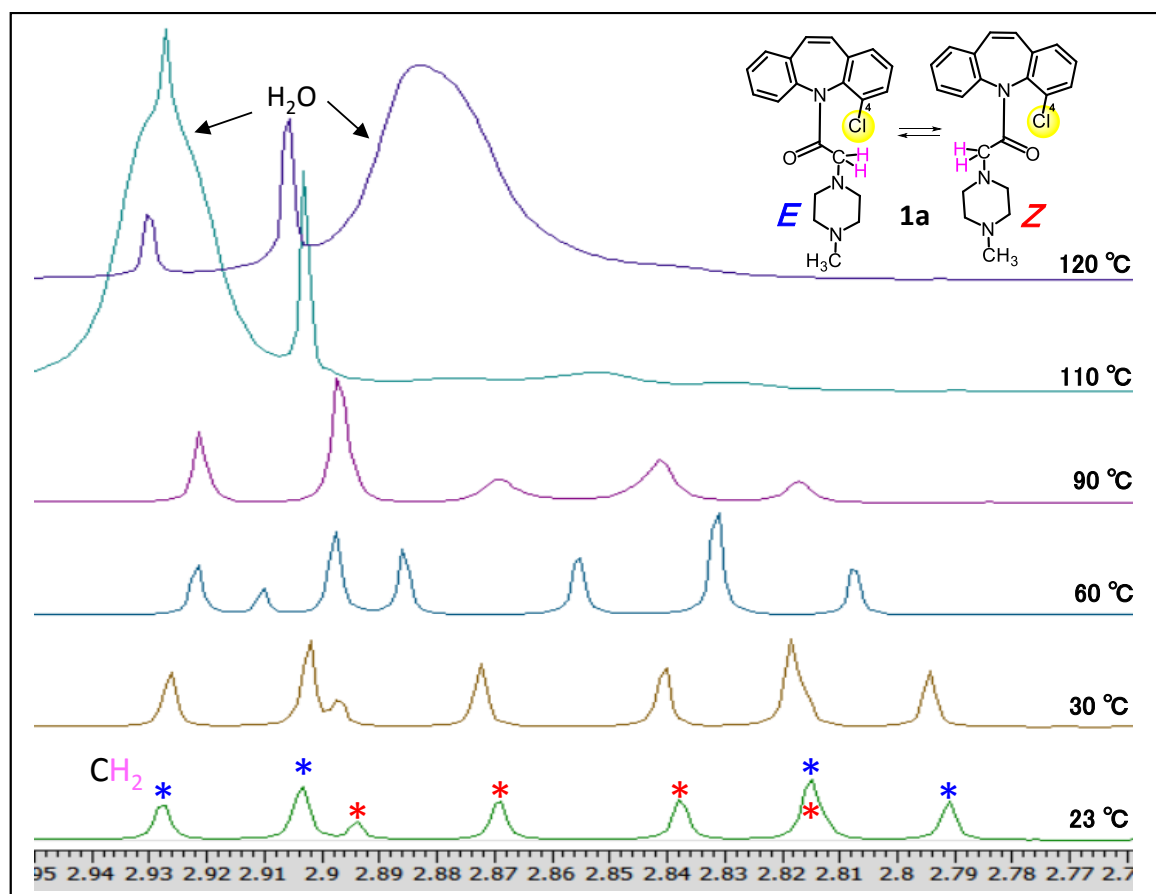
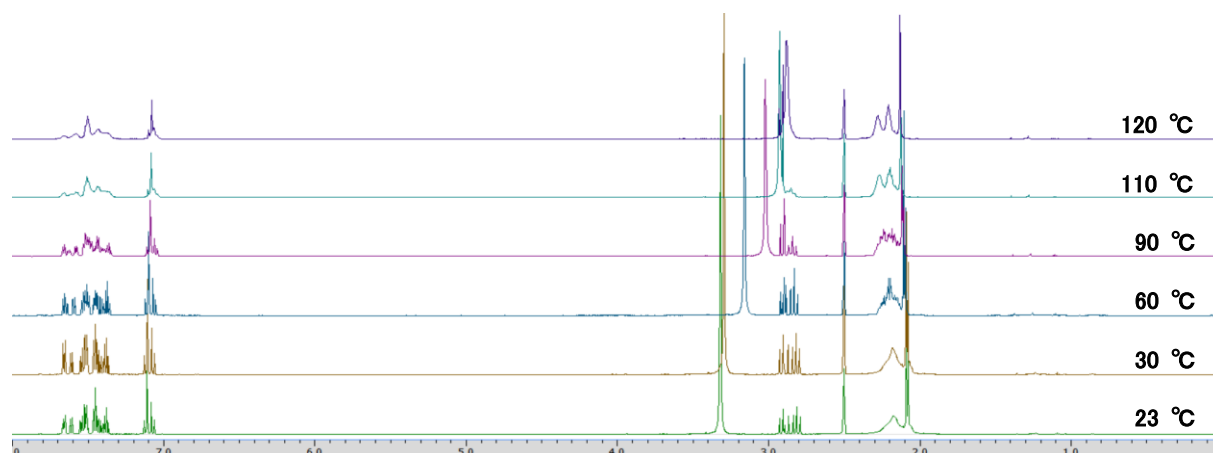
Compound **1a**.

*E* : *Z* = 1.7 : 1 (in *d*-DMSO)

Tc: >110 °C

$\Delta G^\ddagger_{110\text{ }^\circ\text{C}}$  : 86 kJ/mol

VT-NMR spectra



Compound **1b**

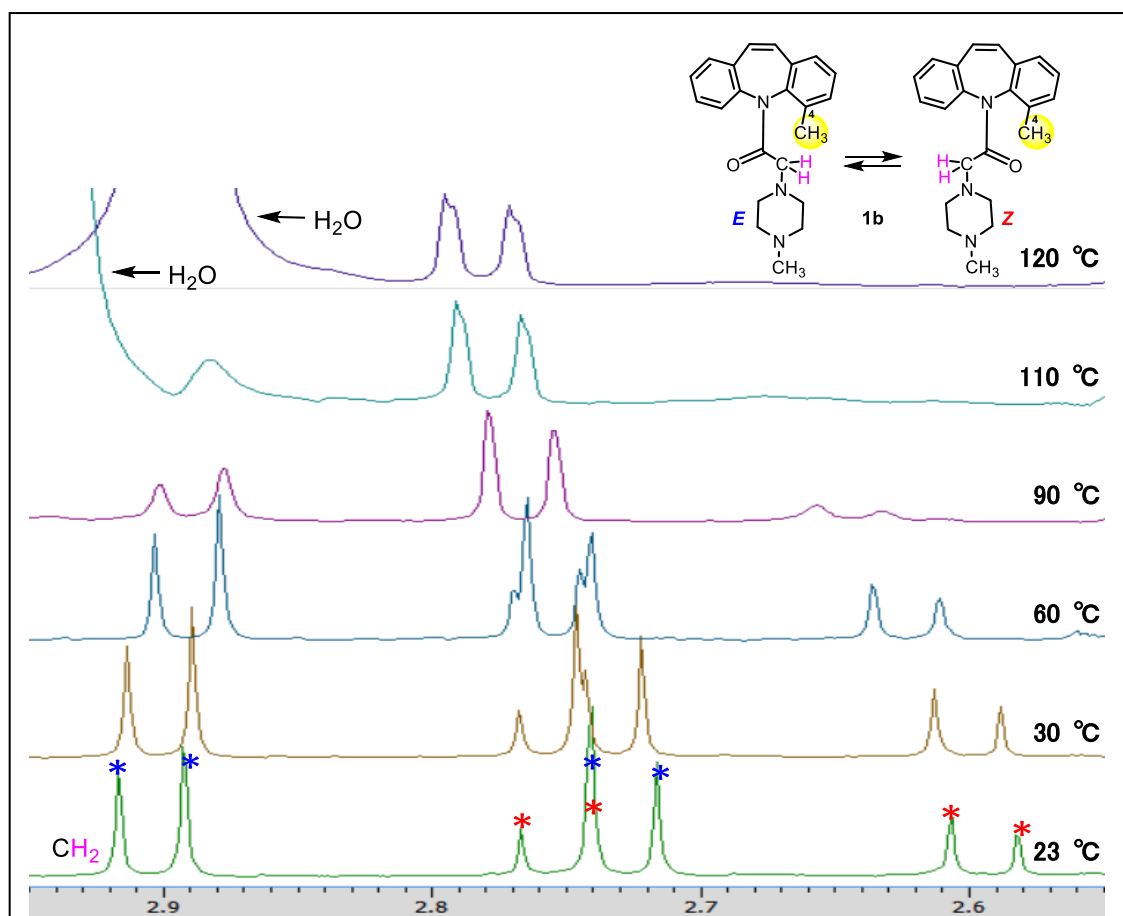
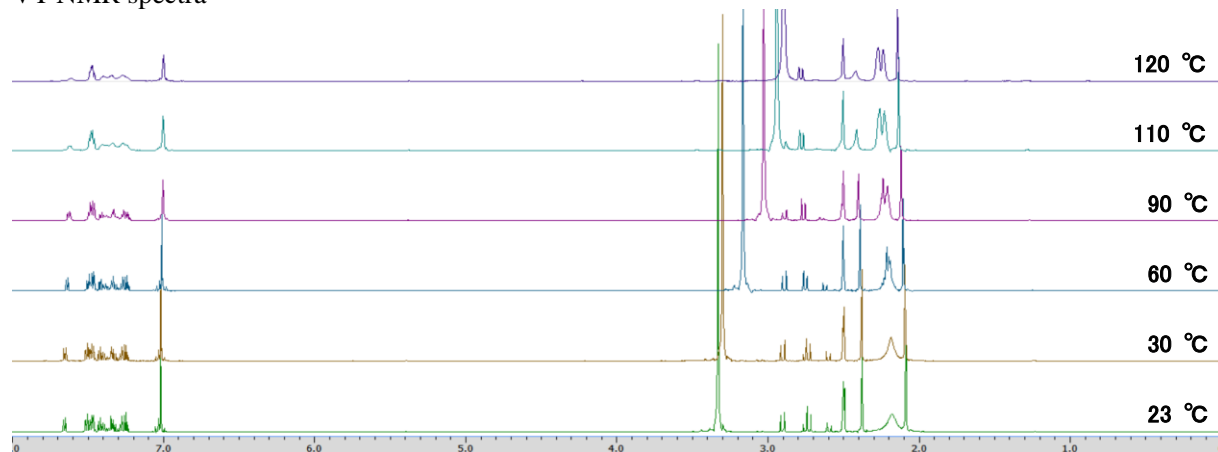
Stability of axis 5

$E : Z = 2.3 : 1$  (in *d*-DMSO)

Tc: 90 °C

$\Delta G^{\ddagger}_{90\text{ °C}} : 84 \text{ kJ/mol}$

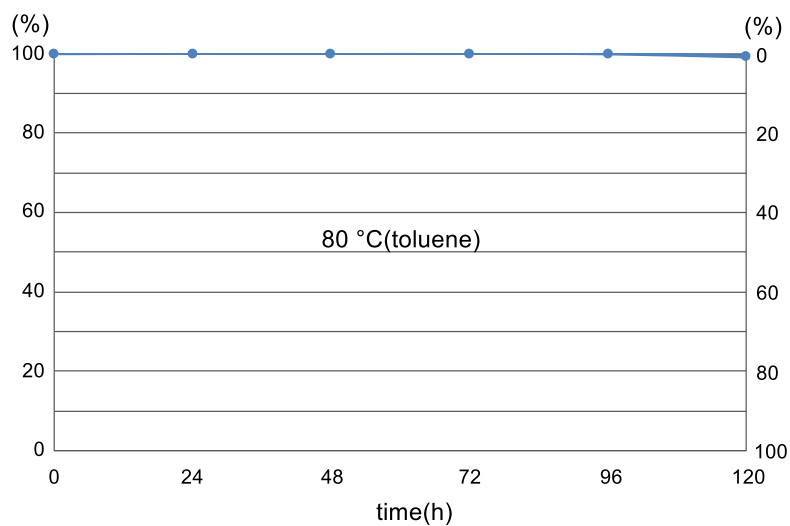
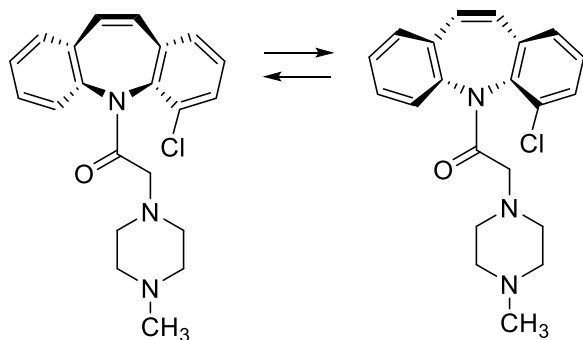
VT-NMR spectra



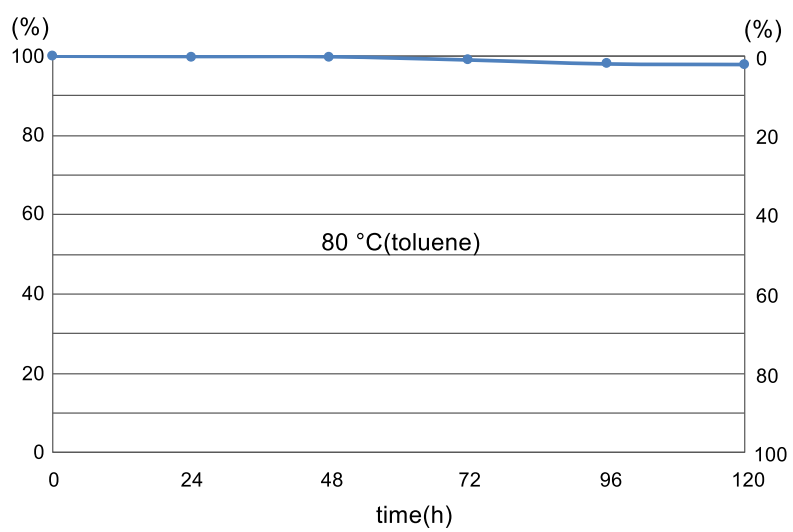
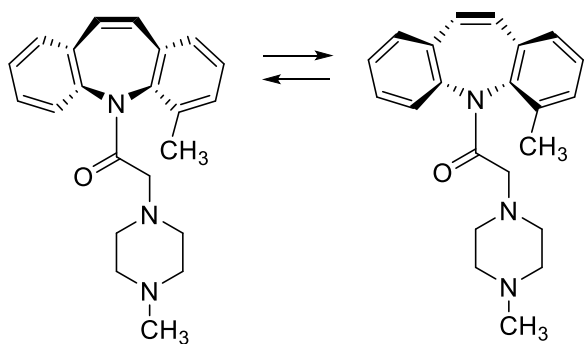
## 2. Physicochemical properties of atropisomers of 1a and 1b.

To examine thermal stability of enantiomers, time-dependent conversion rate (%) was estimated from chiral HPLC analysis of a solution of the enantiomer in toluene after allowing to stand at designated temperatures.

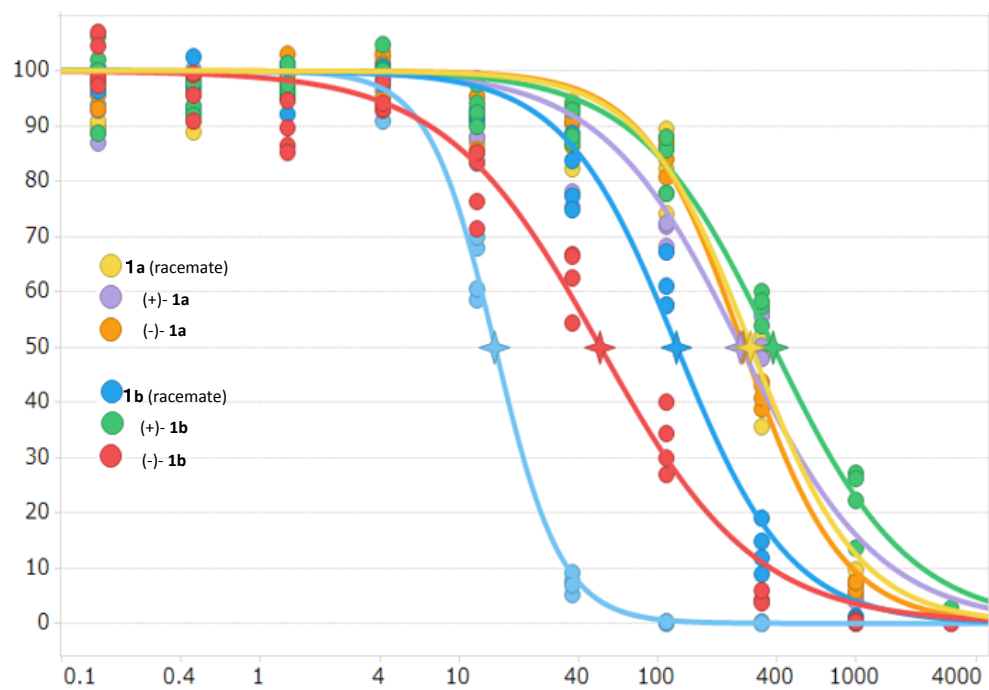
### Conversion of (-)-1a to (+)-1a.



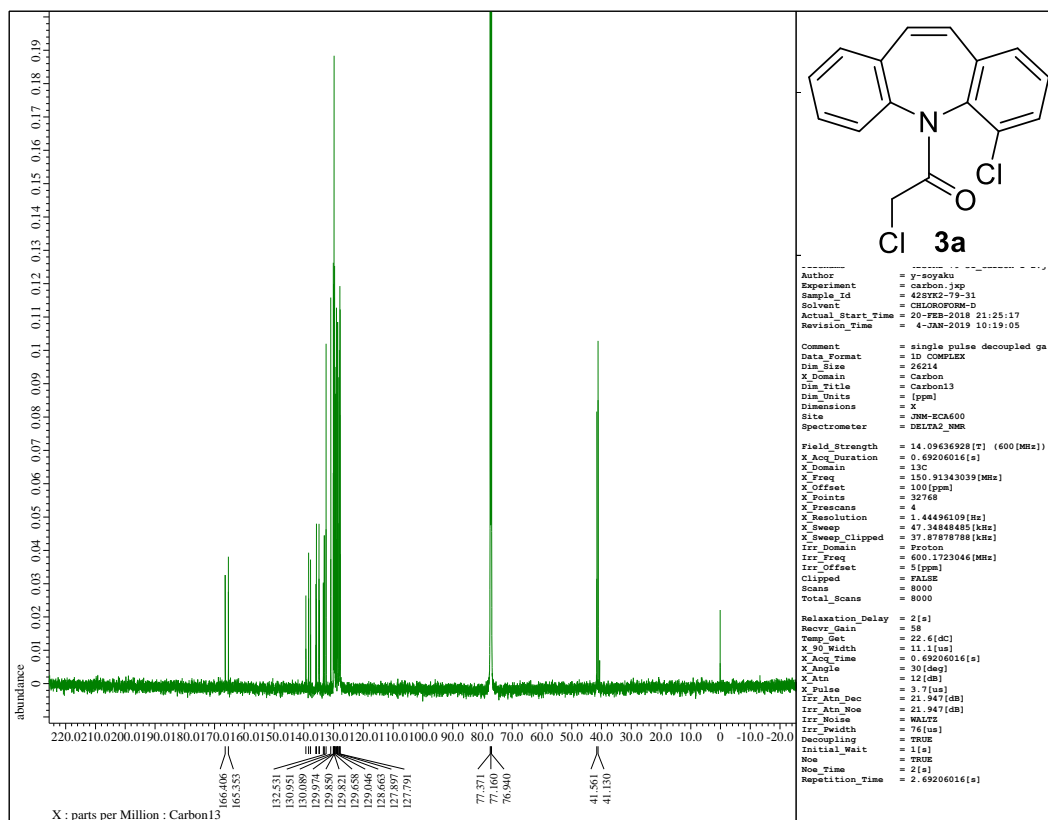
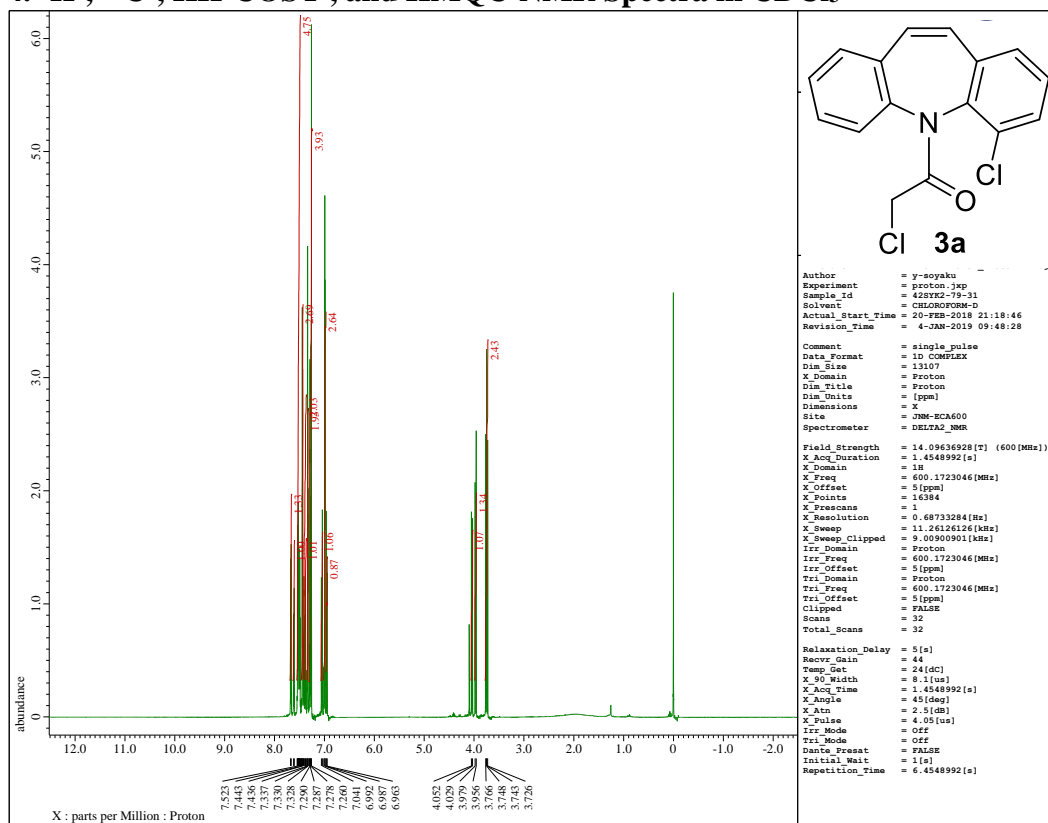
### Conversion of (-)-1b to (+)-1b.

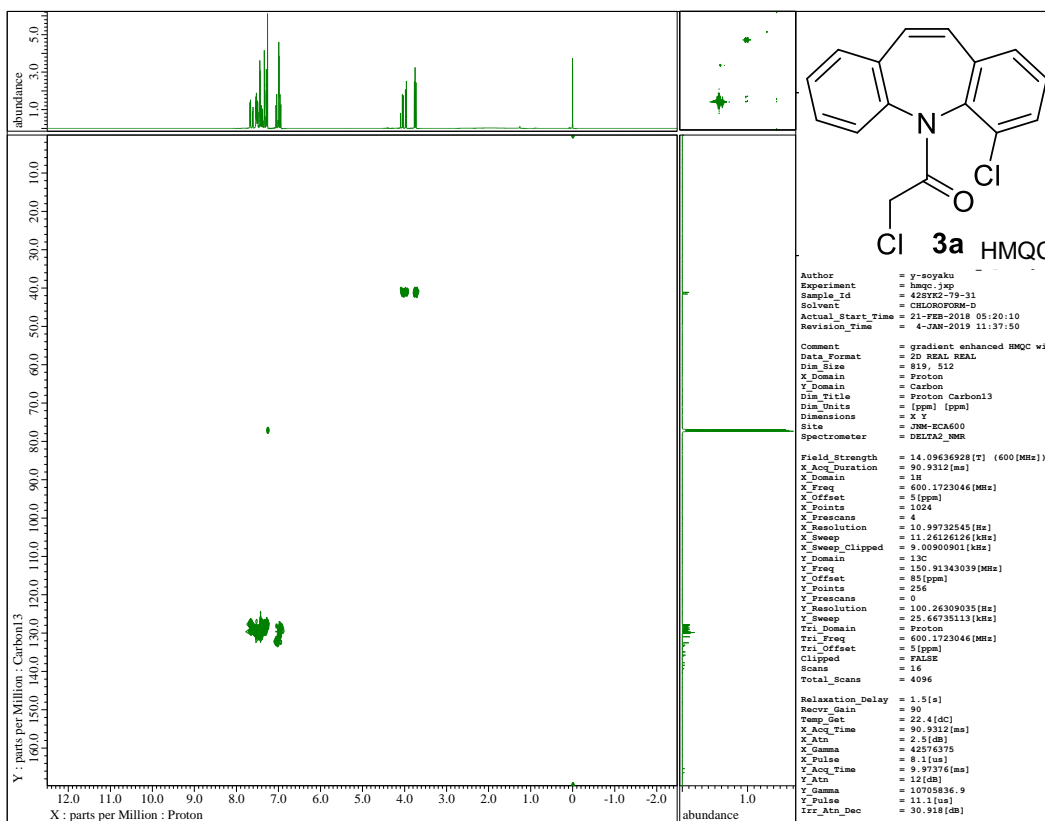
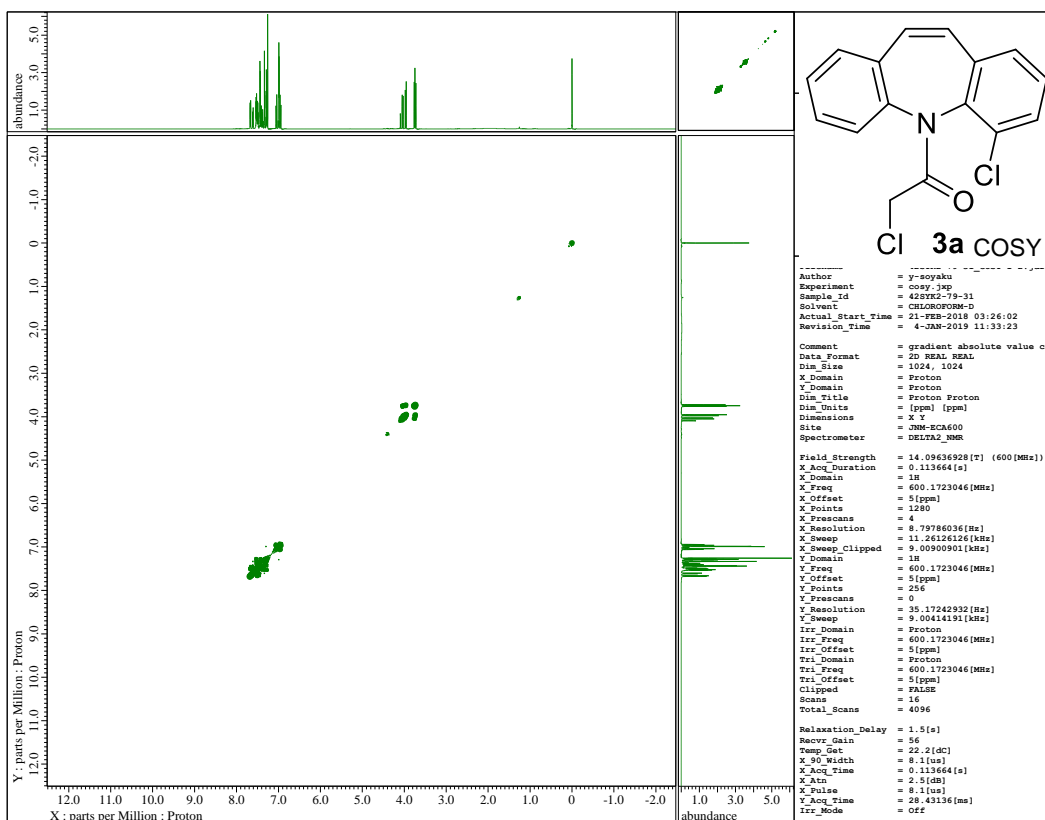


### 3. Ca<sup>2+</sup> assay

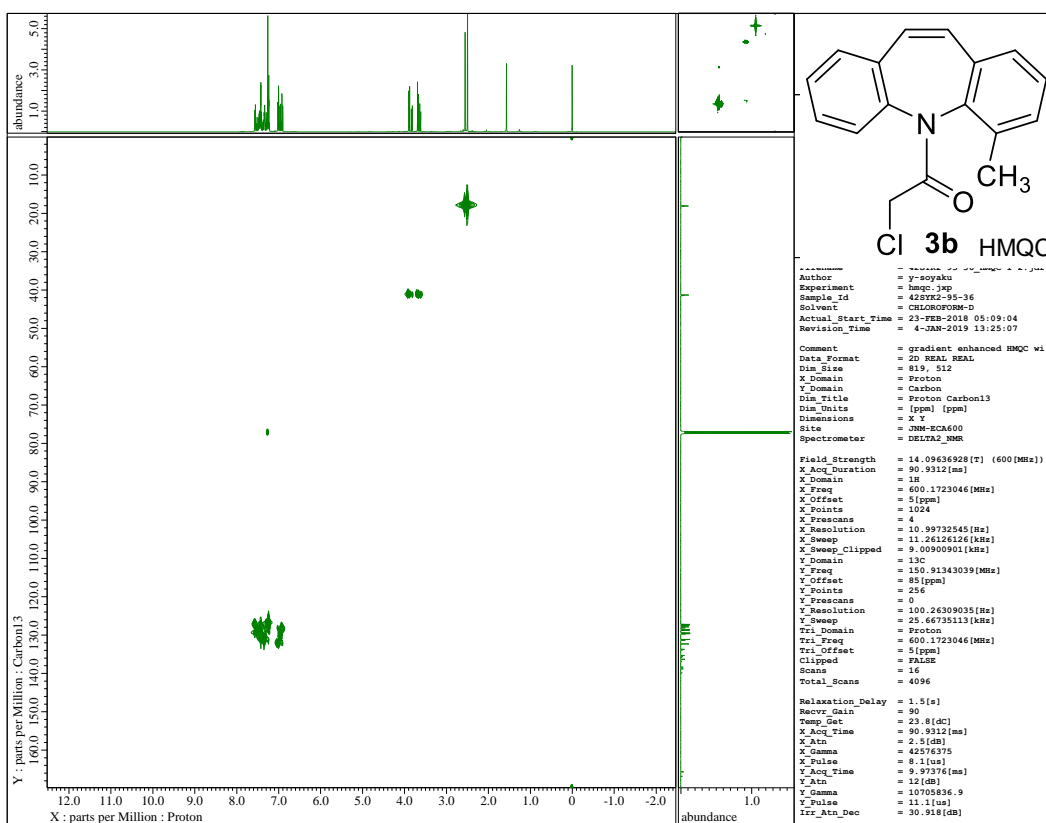
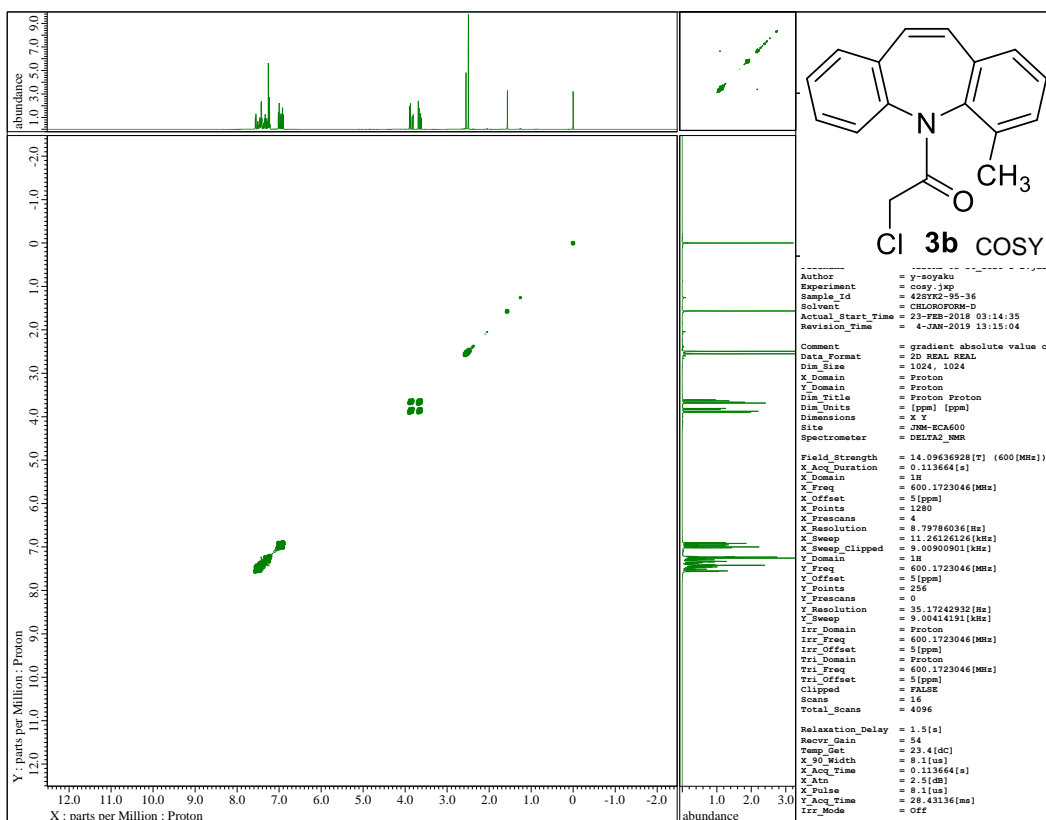


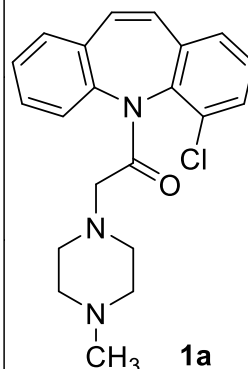
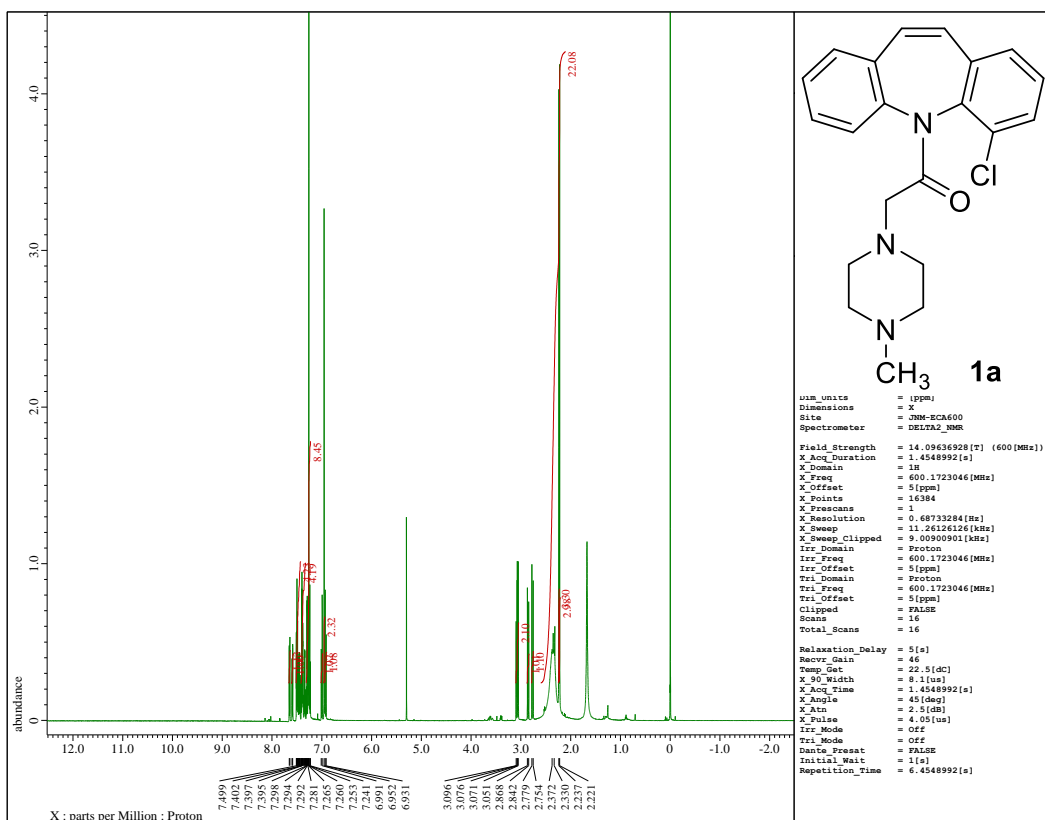
#### 4. <sup>1</sup>H-, <sup>13</sup>C-, HH-COSY-, and HMQC-NMR Spectra in CDCl<sub>3</sub>











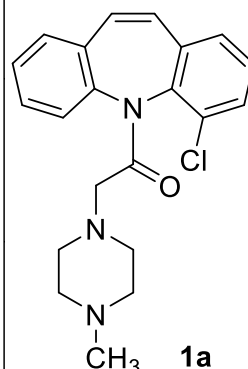
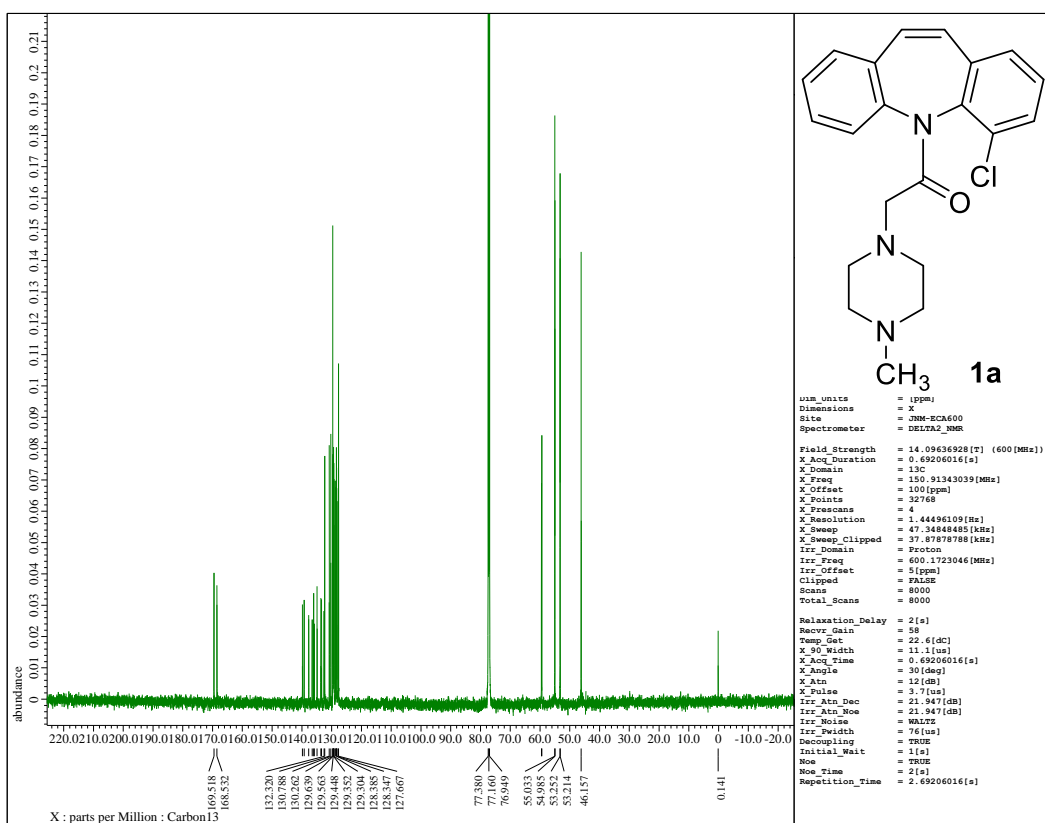
```

um_units      = [ppm]
Dimensions    = X
Site          = NMR-ECA600
Spectrometer  = DELTA2_NMR

Field_Strength = 14.09636928 [T] (600 [MHz])
X_Acq_Duration = 1.4548992 [s]
X_Domain       = 1H
X_Freq         = 600.1723046 [MHz]
X_Offset       = 5 [ppm]
X_Points       = 16394
X_Prescans     = 1
X_Resolution   = 0.68733284 [Hz]
X_Sweep        = 11.2613161 [kHz]
X_Sweep_Clipped = 9.0090901 [kHz]
Irr_Domain     = Proton
Irr_Freq       = 600.1723046 [MHz]
Irr_Offset     = 5 [ppm]
Tri_Domain     = Proton
Tri_Freq       = 600.1723046 [MHz]
Tri_Offset     = 5 [ppm]
Clipped        = FALSE
Scans          = 16
Total_Scans    = 16

Relaxation_Delay = 5 [s]
Recvr_Gain       = 46
Temp_Gst         = 22.5 [dC]
X_90_Width      = 9.1 [us]
X_Acq_Time       = 1.4548992 [s]
X_Angle          = 45 [deg]
X_Atn            = 2.5 [dB]
X_Pulse          = 9 [us]
Irr_Mode         = Off
DanLe_Prasat    = FALSE
Initial_Wait     = 1 [s]
Repetition_Time = 6.4548992 [s]

```



```

um_units      = [ppm]
Dimensions    = X
Site          = NMR-ECA600
Spectrometer  = DELTA2_NMR

Field_Strength = 14.09636928 [T] (600 [MHz])
X_Acq_Duration = 0.69206016 [s]
X_Domain       = 13C
X_Freq         = 150.91343039 [MHz]
X_Offset       = 100 [ppm]
X_Points       = 32768
X_Prescans     = 1
X_Resolution   = 1.44496109 [Hz]
X_Sweep        = 47.34848485 [kHz]
X_Sweep_Clipped = 37.87878788 [kHz]
Irr_Domain     = Proton
Irr_Freq       = 600.1723046 [MHz]
Irr_Offset     = 5 [ppm]
Clipped        = FALSE
Scans          = 8000
Total_Scans    = 8000

Relaxation_Delay = 2 [s]
Recvr_Gain       = 58
Temp_Gst         = 22.6 [dC]
X_90_Width      = 11.1 [us]
X_Acq_Time       = 0.69206016 [s]
X_Angle          = 30 [deg]
X_Atn            = 12 [dB]
X_Pulse          = 3.7 [us]
Irr_Atn_Dec      = 21.947 [dB]
Irr_Atn_Noise   = 21.947 [dB]
Irr_Noise       = FALSE
Irr_Width       = TRUE
Decoupling       = TRUE
Initial_Wait     = 1 [s]
Hoe              = TRUE
Hoe_Time         = 2 [s]
Repetition_Time = 2.69206016 [s]

```

