

Supporting Information

Enantiopure methoxetamine stereoisomers: Chiral resolution, conformational analysis, UV-circular dichroism spectroscopy and electronic circular dichroism

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† Both of Ahmed H.E. Hassan and Kun Won Lee contributed equally to this work and should be first authors.

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Column Description

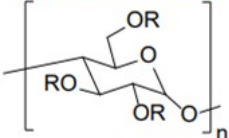
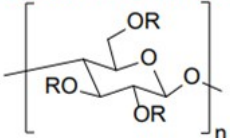
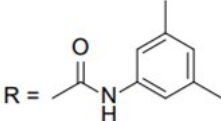
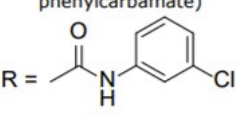
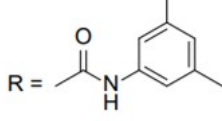
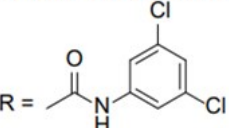
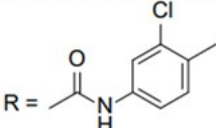
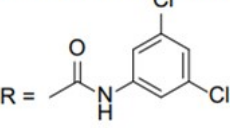
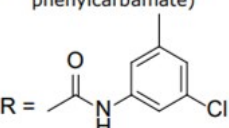
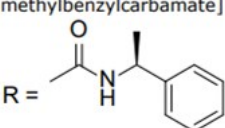
<p>AMYLOSE-BASED</p>  <p>Immobilized on 3 μm silica gel</p>		<p>CELLULOSE-BASED</p>  <p>Immobilized on 3 μm silica gel</p>
<p>CHIRALPAK® IA-3</p> <p>Amylose tris(3,5-dimethylphenylcarbamate)</p>  <p>R =</p>	<p>CHIRALPAK® ID-3</p> <p>Amylose tris(3-chlorophenylcarbamate)</p>  <p>R =</p>	<p>CHIRALPAK® IB-3 CHIRALPAK® IB N-3</p> <p>Cellulose tris(3,5-dimethylphenylcarbamate)</p>  <p>R =</p>
<p>CHIRALPAK® IE-3</p> <p>Amylose tris(3,5-dichlorophenylcarbamate)</p>  <p>R =</p>	<p>CHIRALPAK® IF-3</p> <p>Amylose tris(3-chloro-4-methylphenylcarbamate)</p>  <p>R =</p>	<p>CHIRALPAK® IC-3</p> <p>Cellulose tris(3,5-dichlorophenylcarbamate)</p>  <p>R =</p>
<p>CHIRALPAK® IG-3</p> <p>Amylose tris(3-chloro-5-methylphenylcarbamate)</p>  <p>R =</p>	<p>CHIRALPAK® IH-3</p> <p>Amylose tris[(S)-α-methylbenzylcarbamate]</p>  <p>R =</p>	

Fig S1. Chemical compositions of the stationary phases used to establish chiral chromatographic conditions

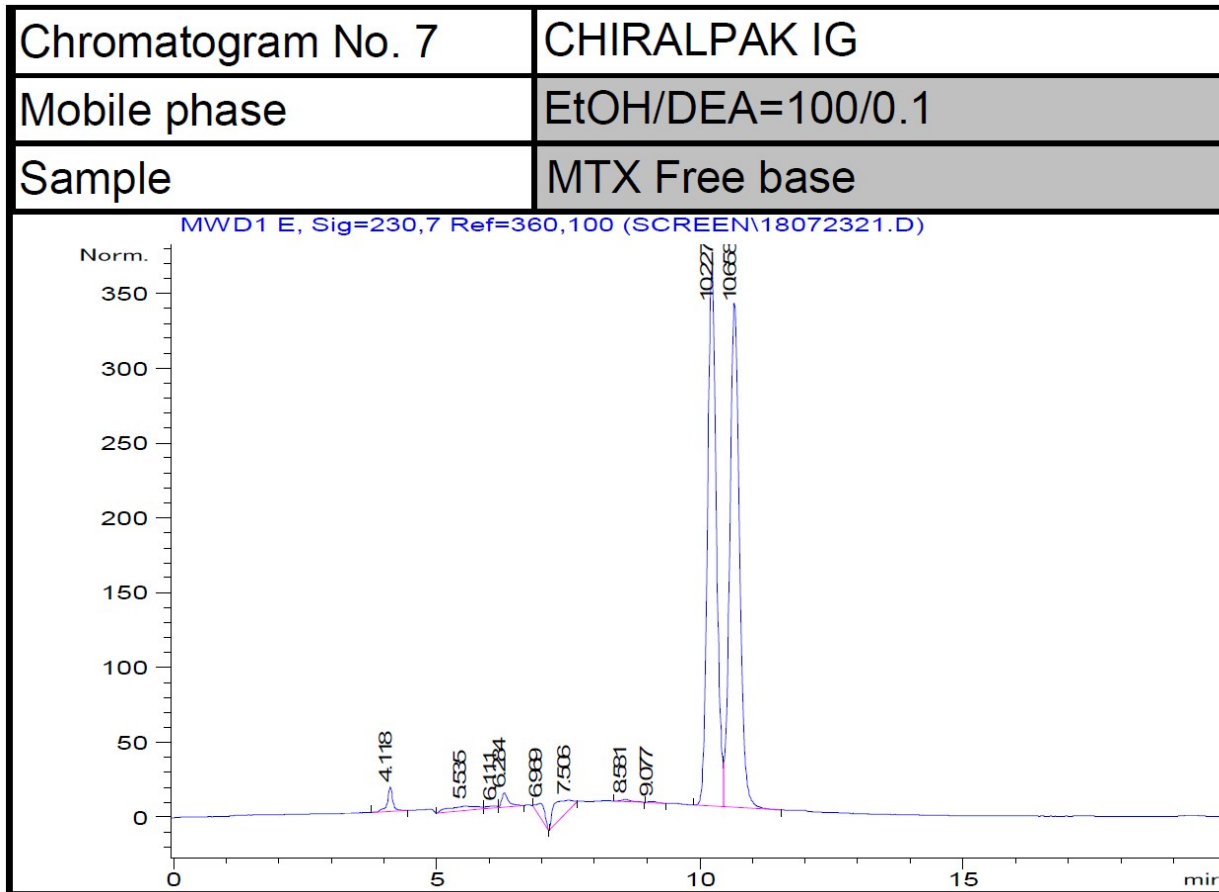


Figure S2. Chromatogram of enantiomers of (*rac*)-MXE free base form resolved on CHIRALPAK® IG-3 stationary phase using ethanol/diethylamine (100/0.1) as a mobile phase

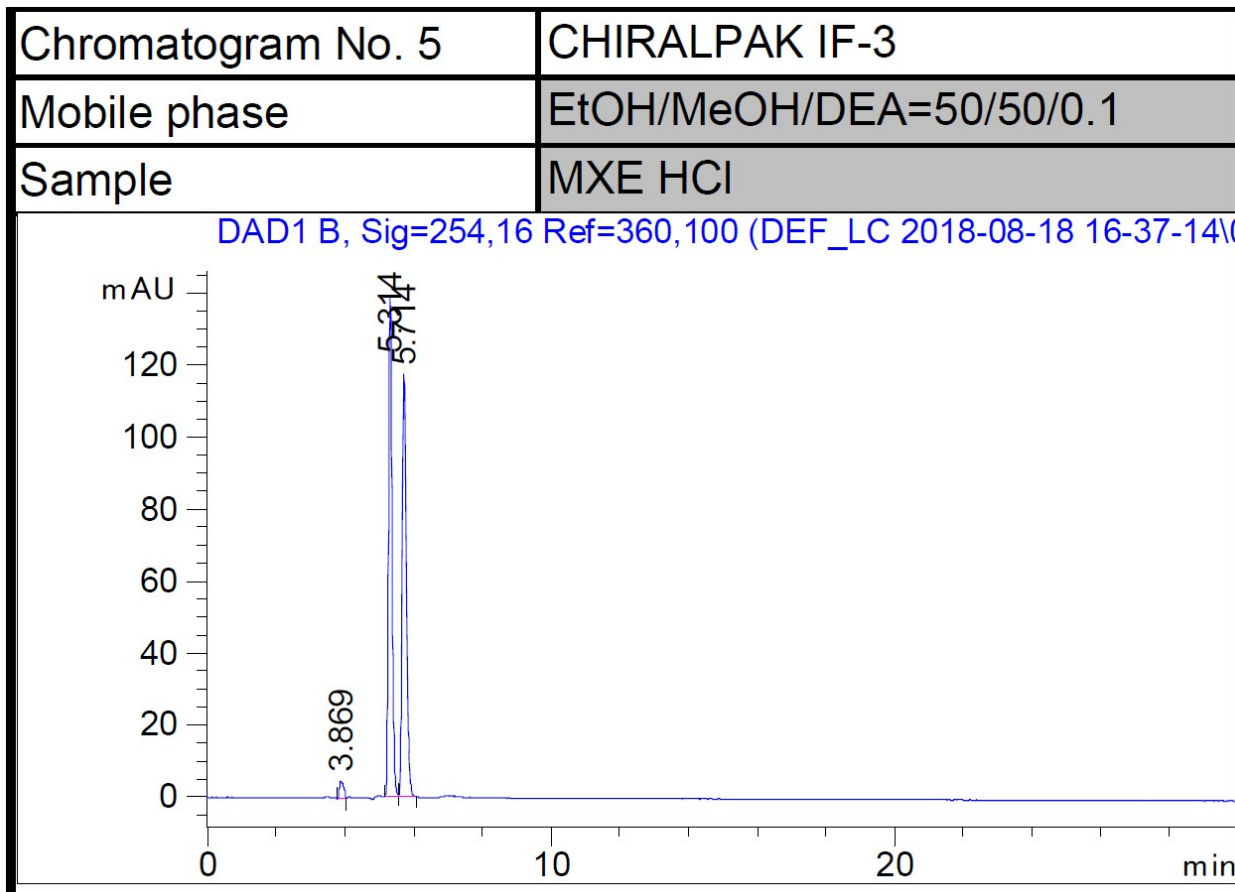


Figure S3. Chromatogram of enantiomers of (*rac*)-MXE HCl salt form resolved on CHIRALPAK® IF-3 stationary phase using ethanol/methanol/diethylamine (50/50/0.1) as a mobile phase.

Sample Info : CHIRALPAK IF-3, 4.6*150 mm
MP: EtOH/MeOH/DEA=50/50/0.1
Flow rate: 0.5ml/min
Sample conc. 1.5~1.8mg/mL in EtOH

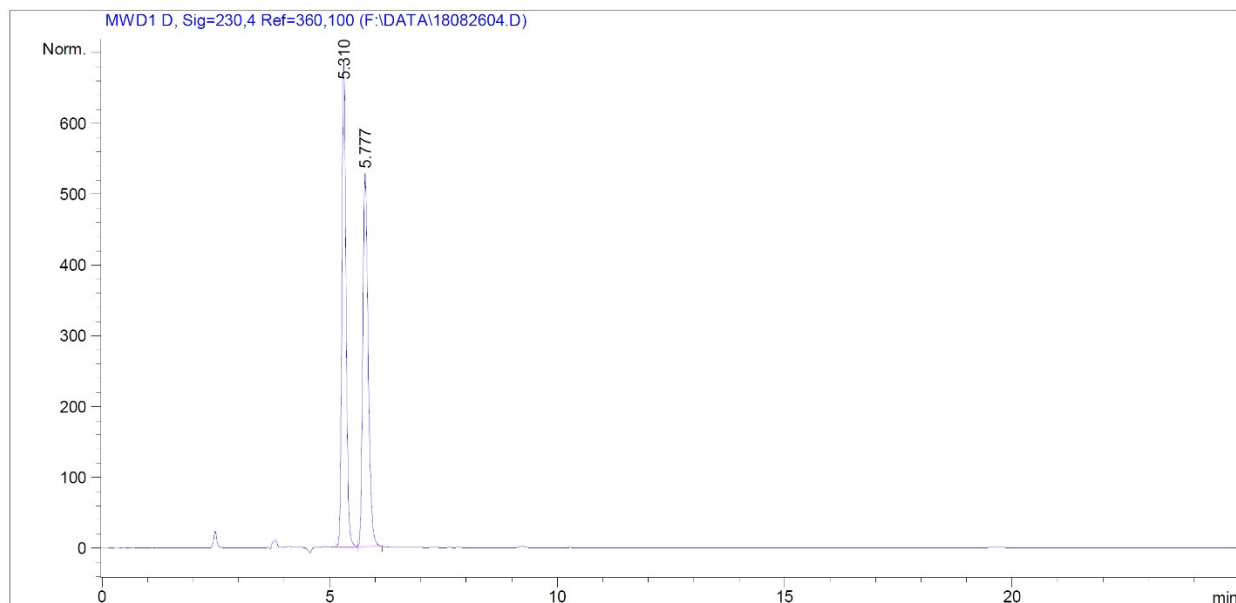
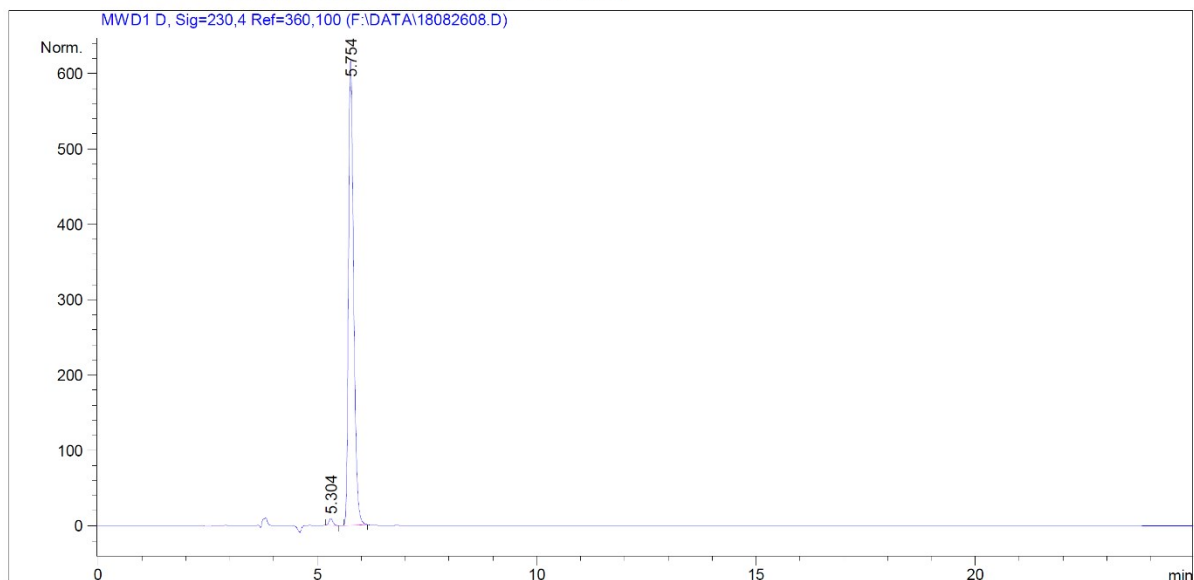


Figure S4. Chromatograms of enantiomers of (*rac*)-MXE free base form resolved on CHIRALPAK® IF-3 stationary phase using ethanol/methanol/diethylamine (50/50/0.1) as a mobile phase.

A

Sample Info : CHIRALPAK IF-3, 4.6*150 mm
MP: EtOH/MeOH/DEA=50/50/0.1
Flow rate: 0.5ml/min
Sample conc. 1.5~1.8mg/mL in EtOH

**B**

Sample Info : CHIRALPAK IF-3, 4.6*150 mm
MP: EtOH/MeOH/DEA=50/50/0.1
Flow rate: 0.5ml/min
Sample conc. 1.5~1.8mg/mL in EtOH

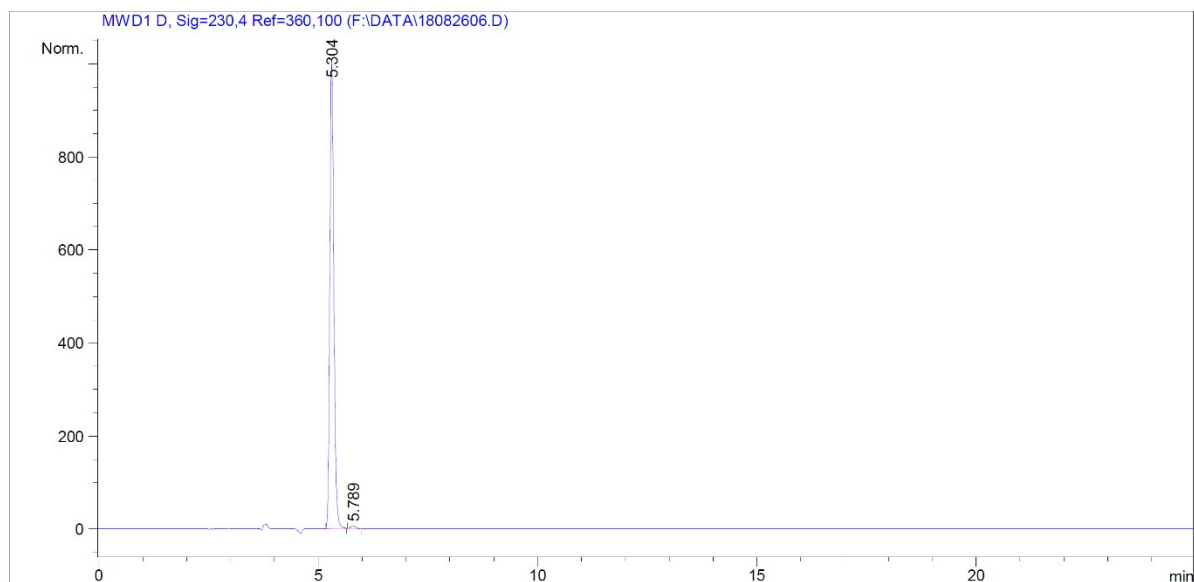


Figure S5. Chromatograms of enantiopure MXE salts with L(-)-DTTA or D-(+)-DTTA showing different retention times on CHIRALPAK® IF-3 stationary phase using ethanol/methanol/diethylamine (50/50/0.1) as a mobile phase: A) L(-)-DTTA MXE salt; B) D-(+)-DTTA MXE salt.

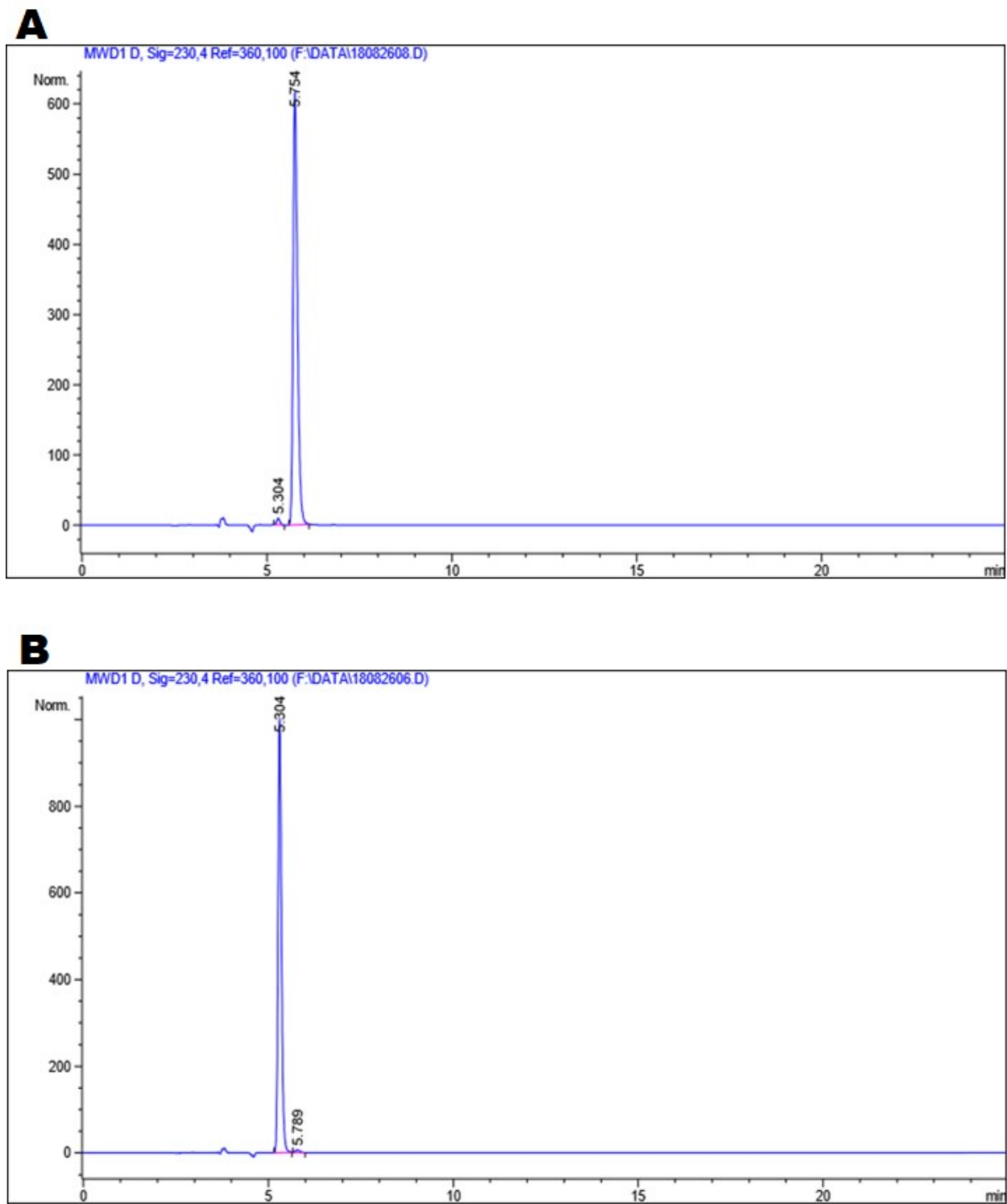


Figure S6. Analytical chiral HPLC chromatograms of the isolated crystals: A) Chromatogram for the obtained enantiopure (*R*)-(-)-MXE HCl; B) Chromatogram for the obtained enantiopure (*S*)-(+)-MXE HCl.

SMD MODEL

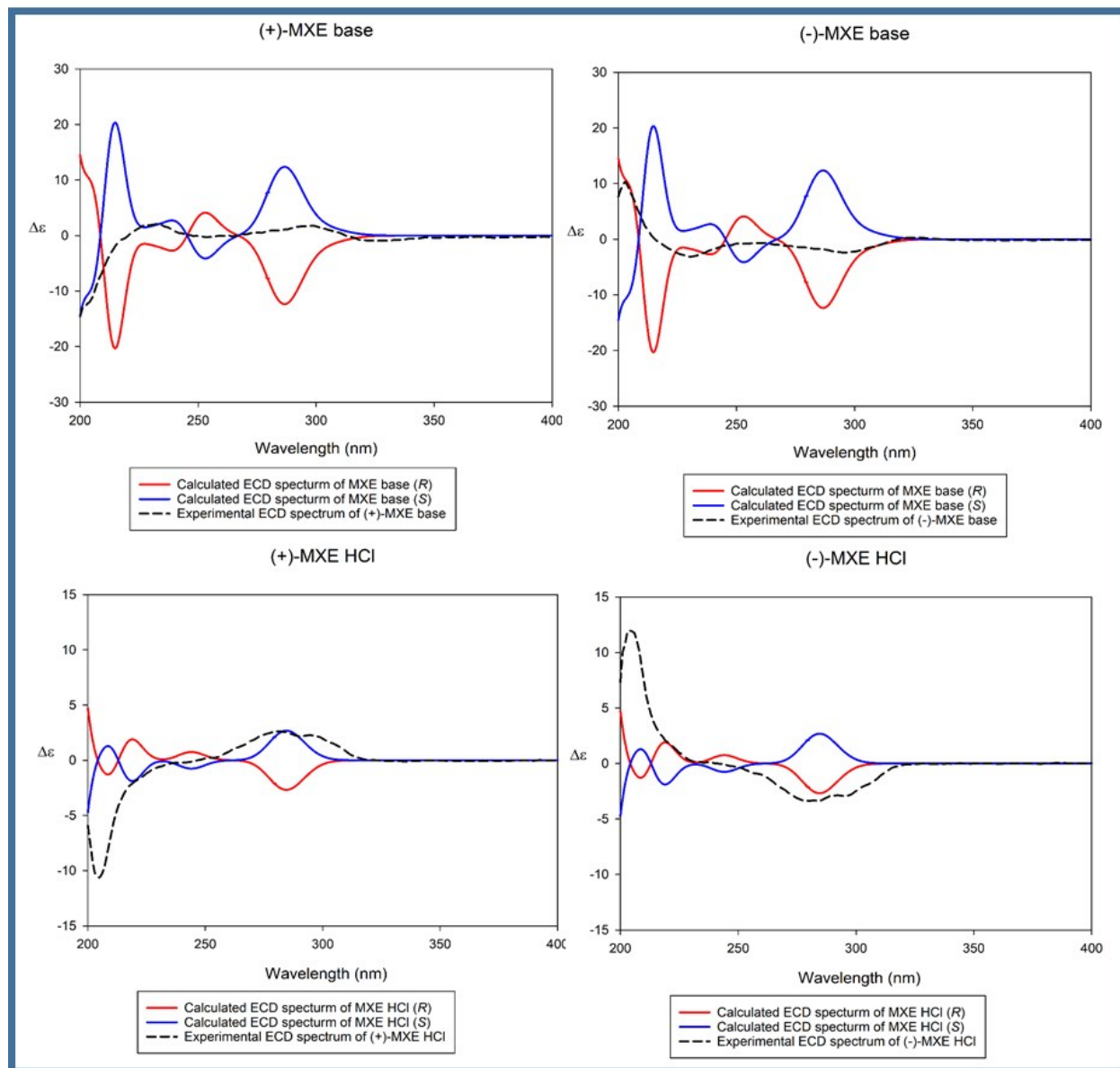
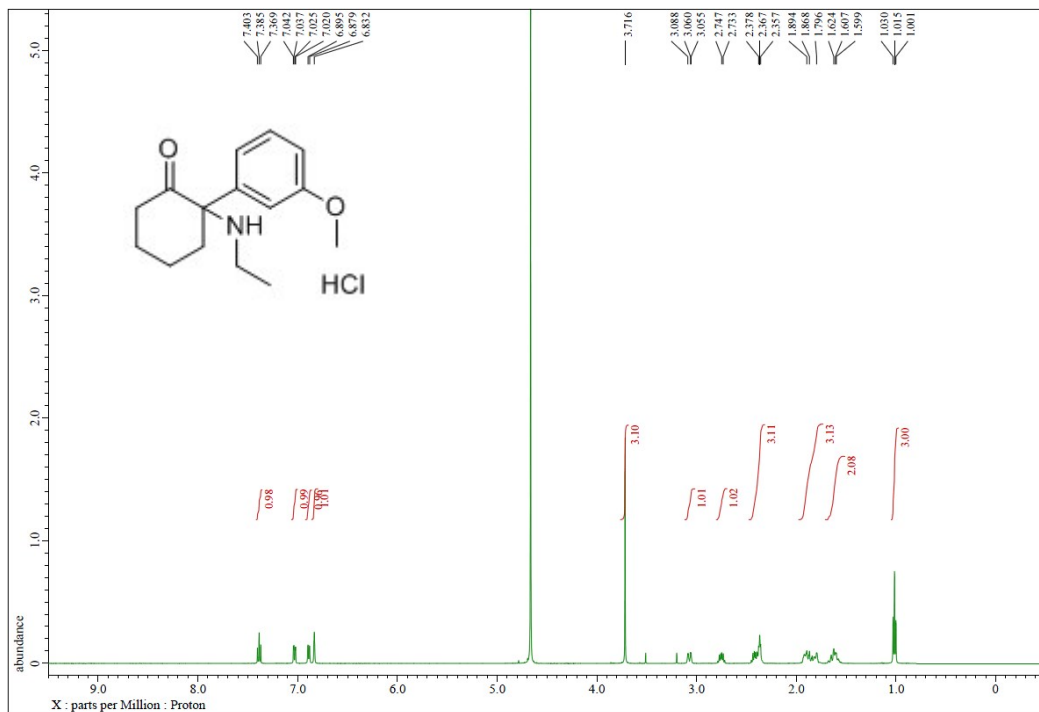
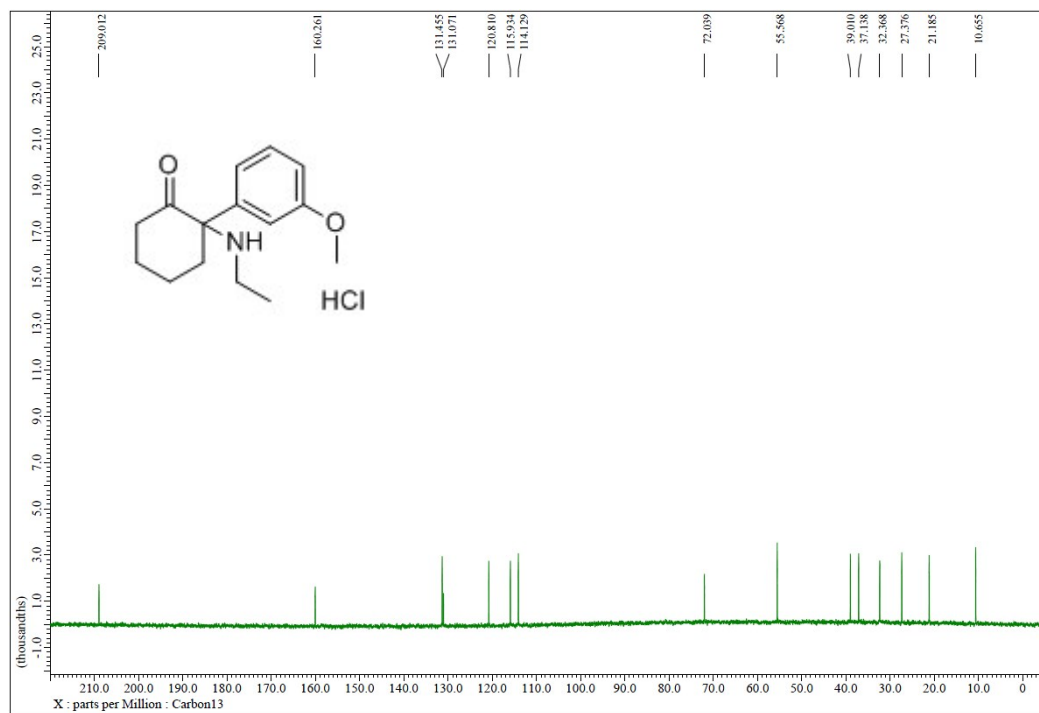


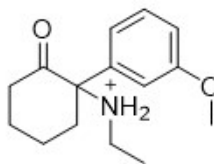
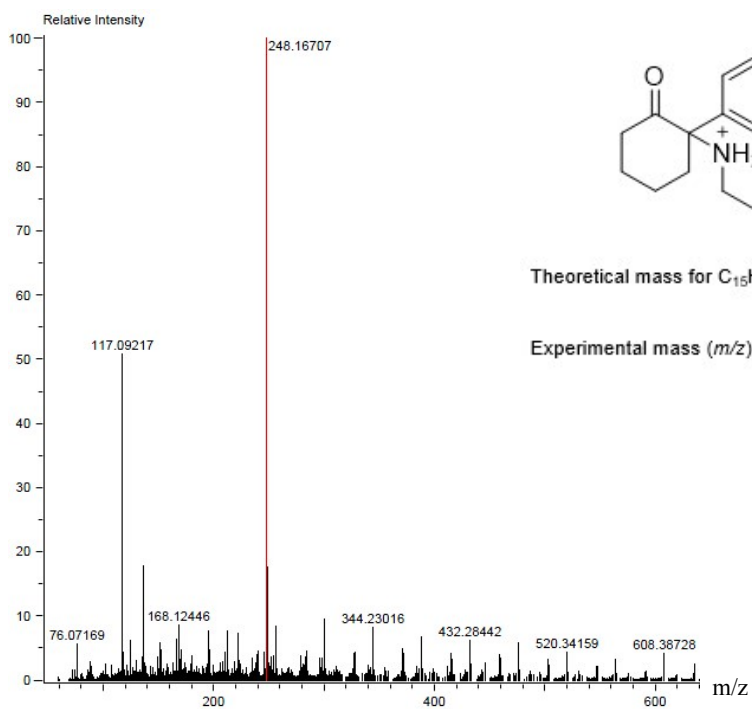
Figure S7. Comparison of experimental and calculated electronic circular dichroism (ECD) spectra of isolated stereoisomers of MXE free base and their HCl forms using solvation model based on density (SMD).



¹H NMR spectrum of (rac)-MXE HCl



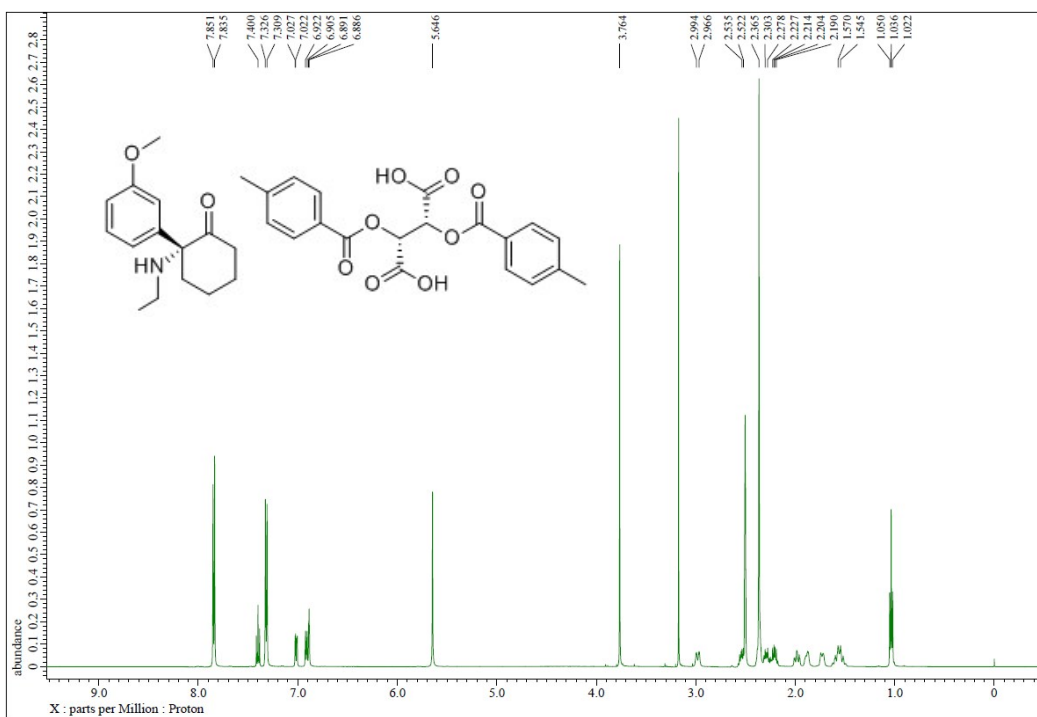
¹³C NMR spectrum of compound (rac)-MXE HCl



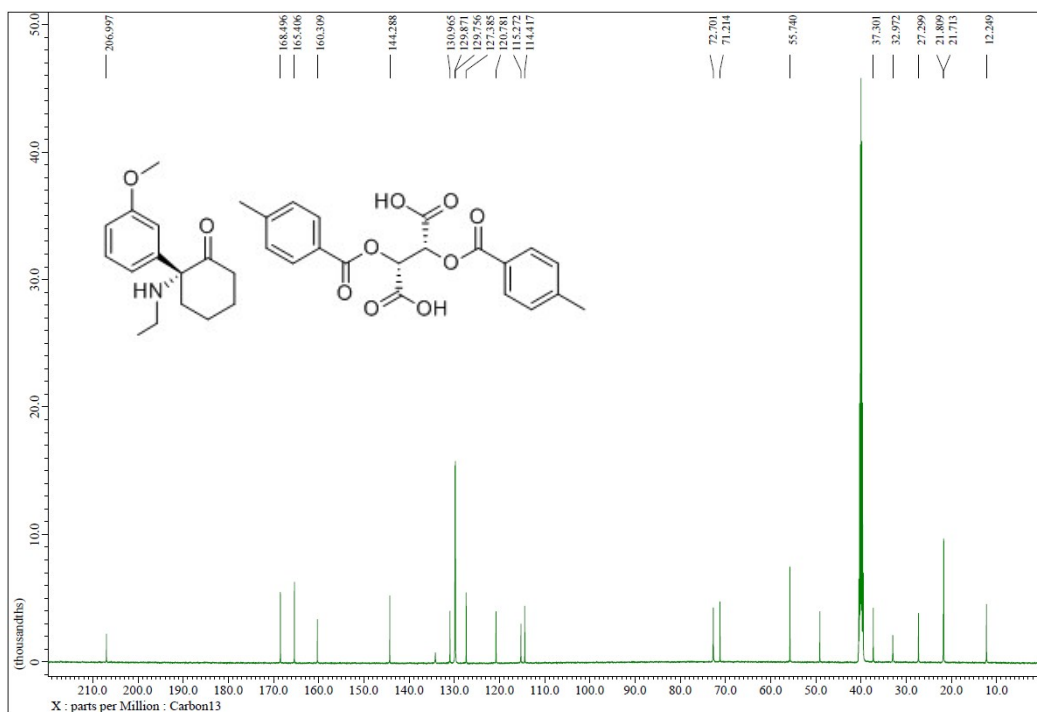
Theoretical mass for $C_{15}H_{22}NO_2^+$ ($[M+H]^+$) : 248.1645

Experimental mass (m/z) : 248.1677

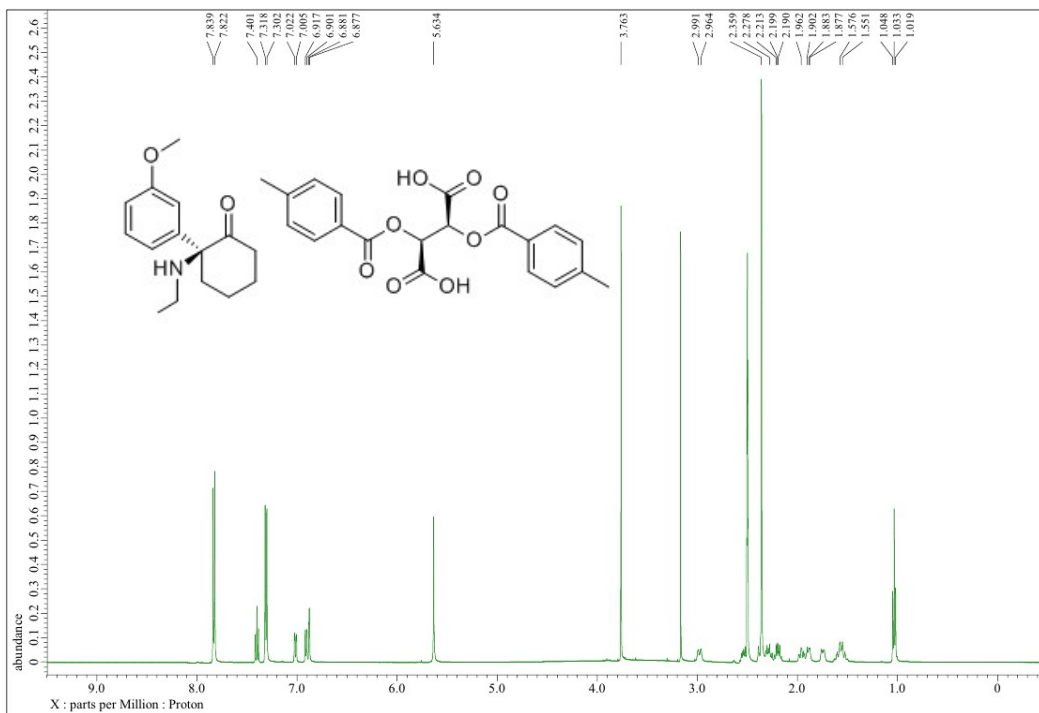
HRMS data of (*rac*)-MXE HCl



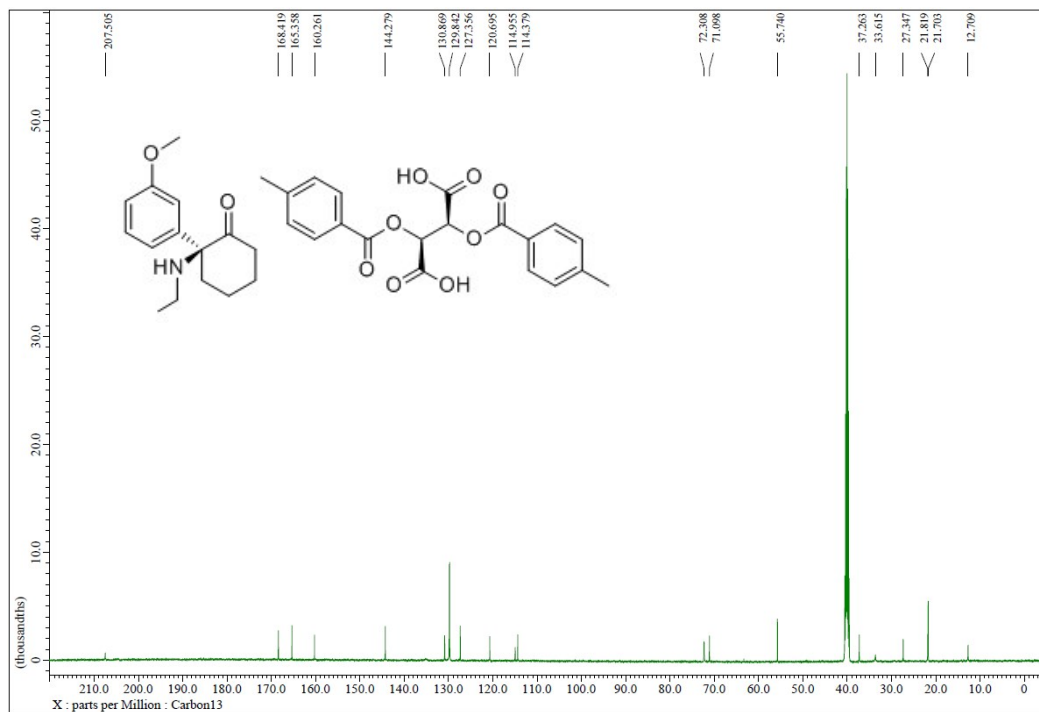
^1H NMR spectrum of (*R*)-MXE L-DTTA salt



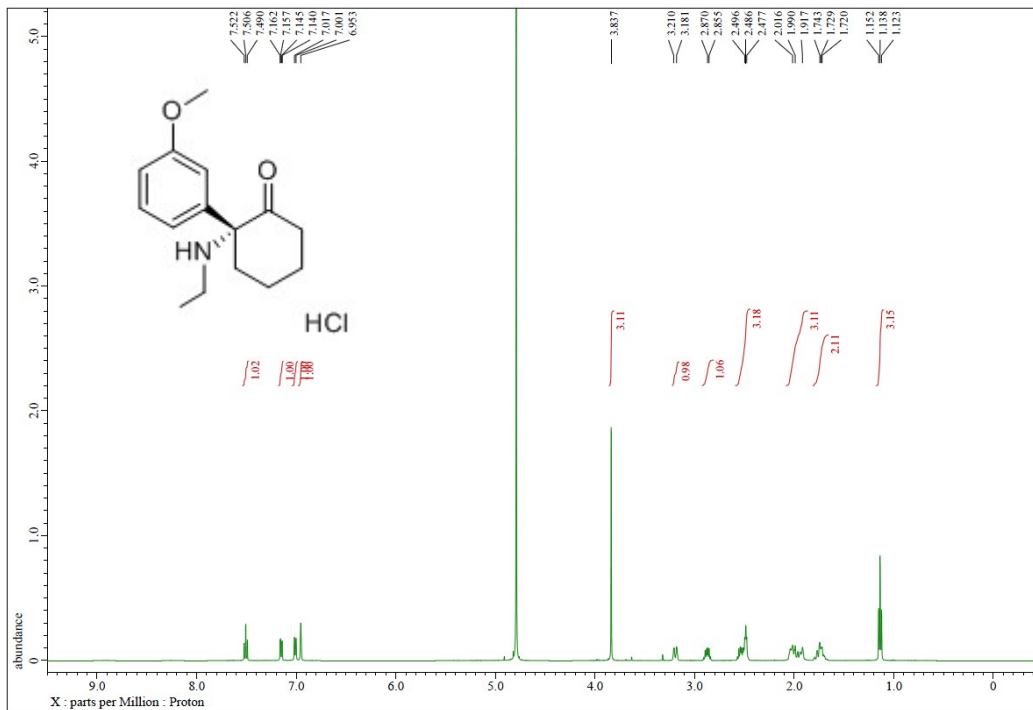
^{13}C NMR spectrum of (*R*)-MXE L-DTTA salt



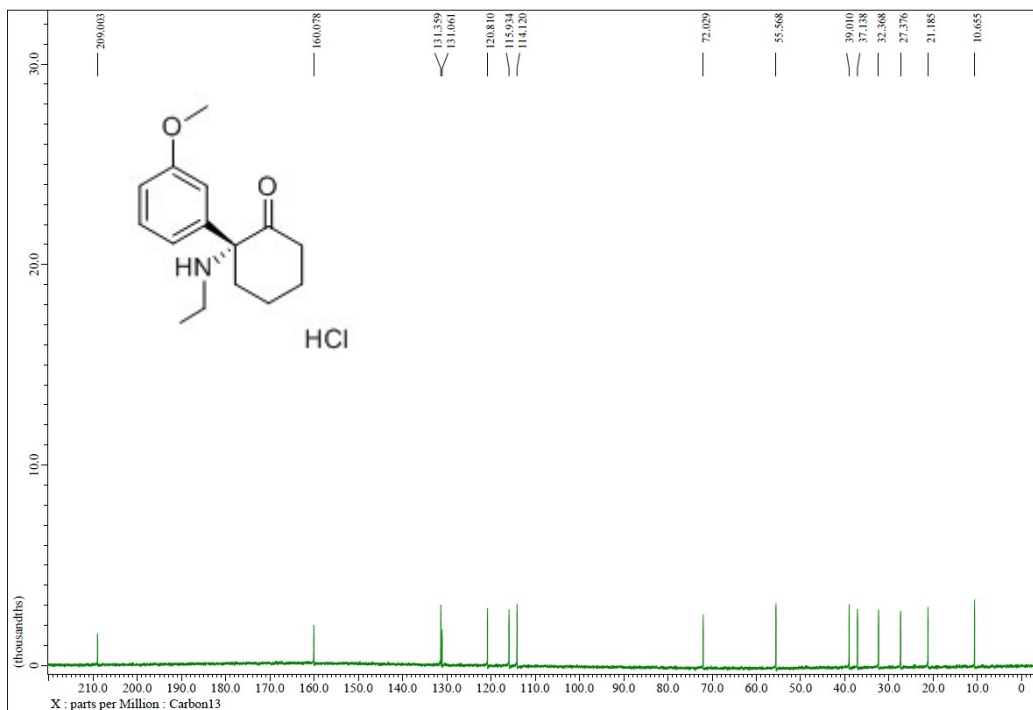
¹H NMR spectrum of (S)-MXE D-DTTA salt



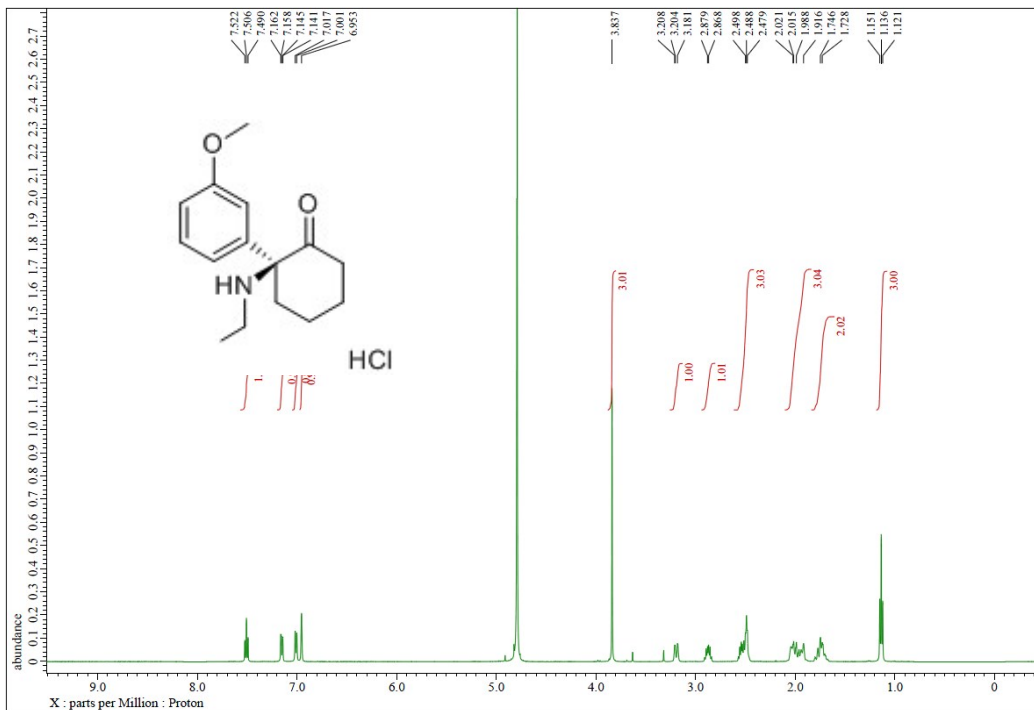
¹³C NMR spectrum of (S)-MXE D-DTTA salt



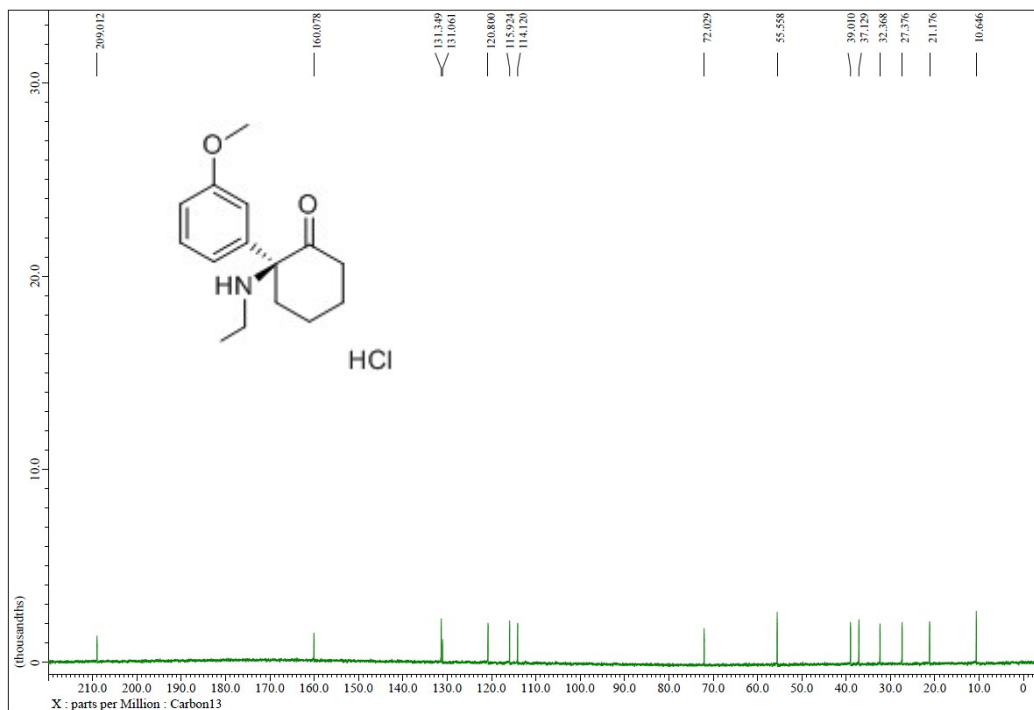
¹H NMR spectrum of compound (R)-MXE HCl



¹³C NMR spectrum of compound (R)-MXE HCl



¹H NMR spectrum of compound (S)-MXE HCl



¹³C NMR spectrum of compound (S)-MXE HCl