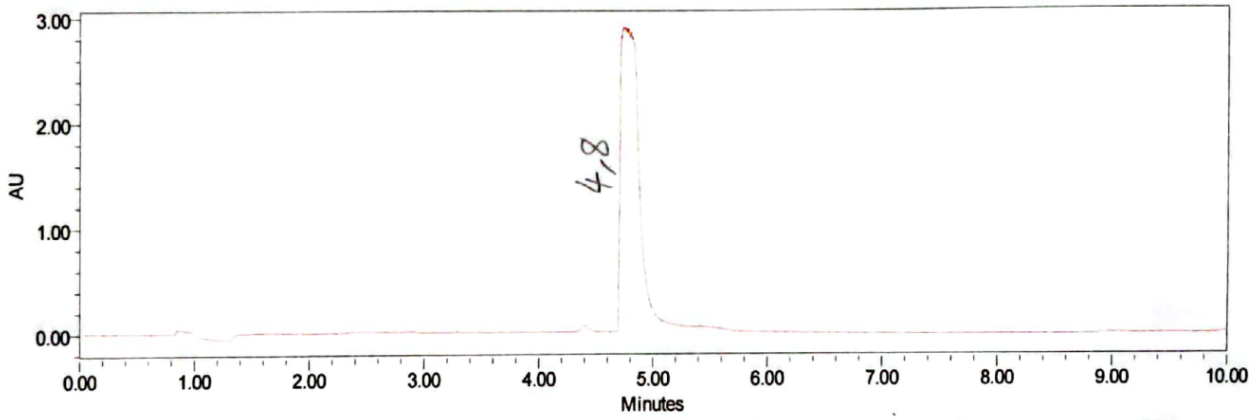
Supporting Information

Table of Contents

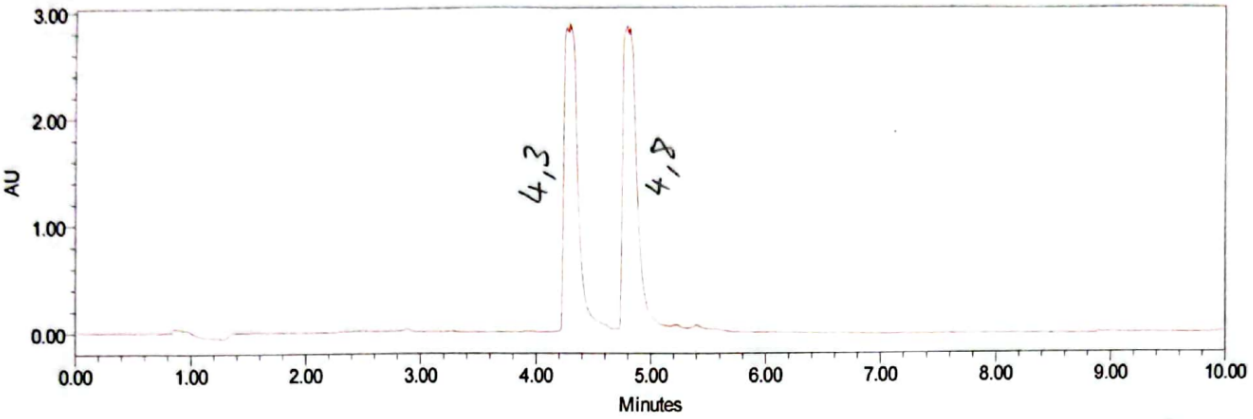
1. Chiral HPLC of (*R*)-norchlorcyclizine and (*R,S*)-norchlorcyclizine

1.1. HPLC of (*R*)-norchlorcyclizine, Rt = 4.8 min.



SampleName: Norchlorcyclizine R; Vial: 1:A,5; Injection: 1; Channel: PDA Spectrum; Date Acquired: 23-Mar-22 13:08:00 CET; Column Name Chiralpak IJ 3um; Acq Method Set 1596psi 2mlmn 40 5 CH3OH DEA

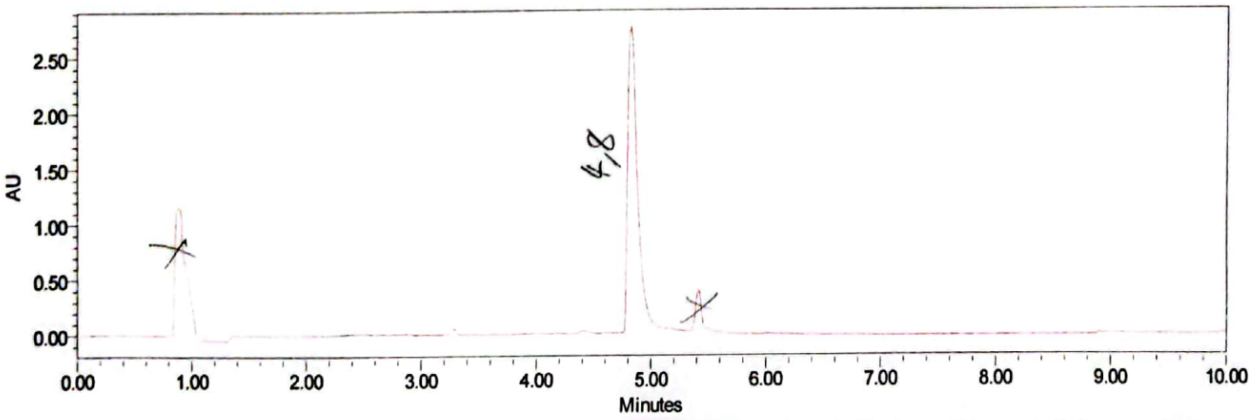
1.2. HPLC of (*R,S*)-norchlorcyclizine, Rt = 4.8 min (*R*) and 4.3 (*S*).



SampleName: Norchlorcyclizine R,S; Vial: 1:A,4; Injection: 1; Channel: PDA Spectrum; Date Acquired: 23-Mar-22 12:56:48 CET; Column Name Chiralpak IJ 3um; Acq Method Set 1596psi 2mlmn 40 5 CH3OH DEA

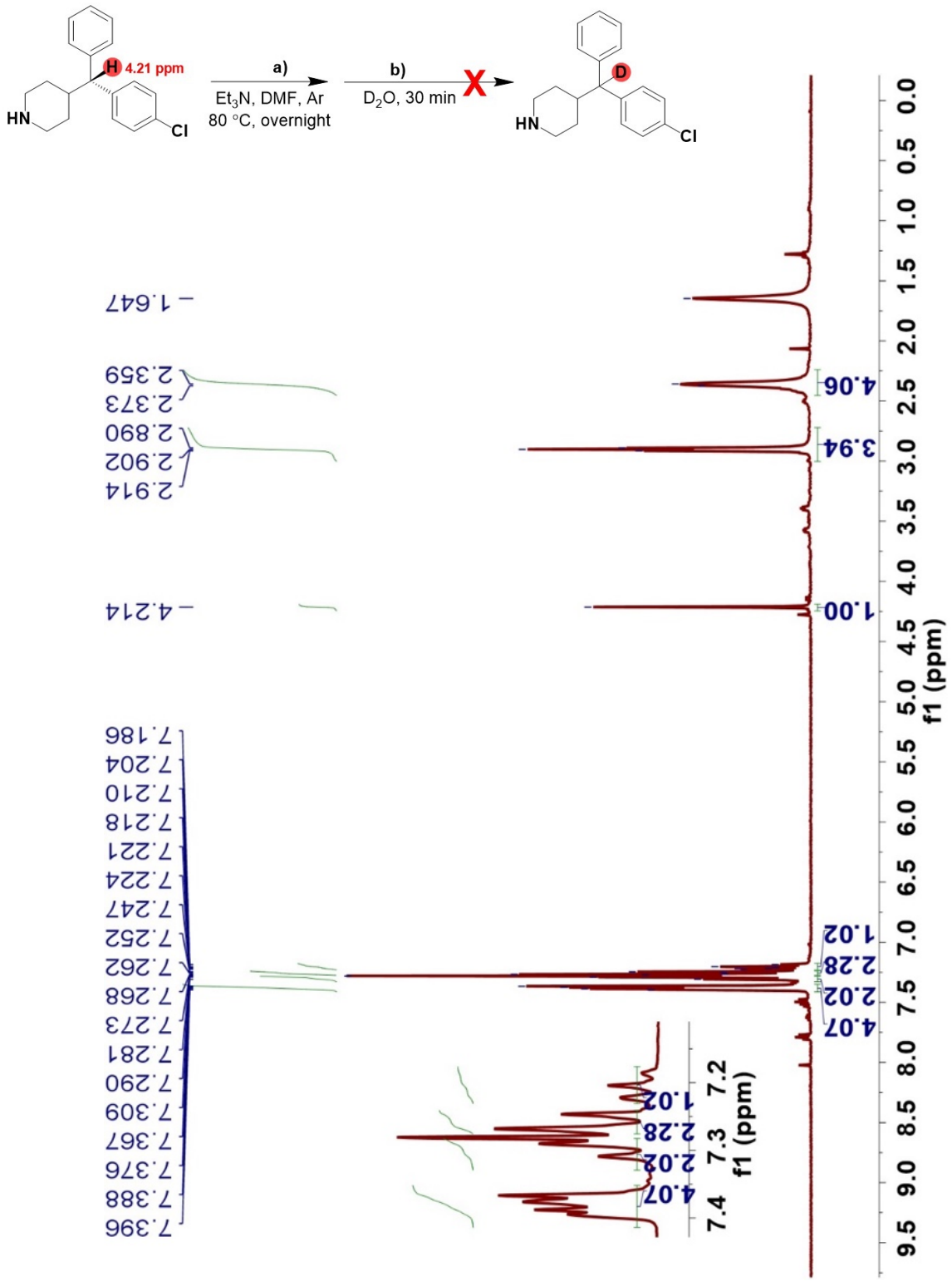
2. Retention of configuration of (*R*)-norchlorcyclizine after reaction in DMF/Et_3N, 80 °C

2.1. Chiral HPLC



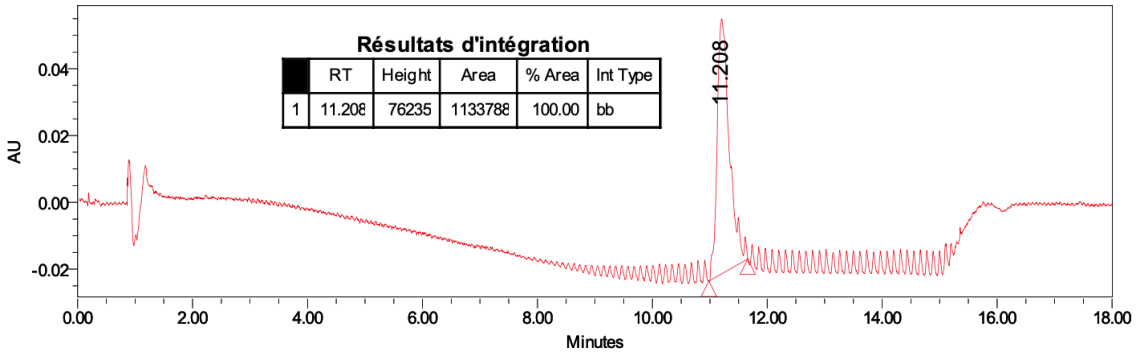
SampleName: Norchlorcyclizine R Et3N DMF; Vial: 1:A,6; Injection: 1; Channel: PDA Spectrum; Date Acquired: 23-Mar-22 13:19:14 CET; Column Name Chiralpak IJ 3um; Acq Method Set 1596psi 2mlmn 40 5 CH3OH DEA

2.2. ^{1}H NMR in $CDCl_3$ (*R*)-norchlorcyclizine after heating overnight at 80 °C in DMF/TEA, and quenching by D_2O.

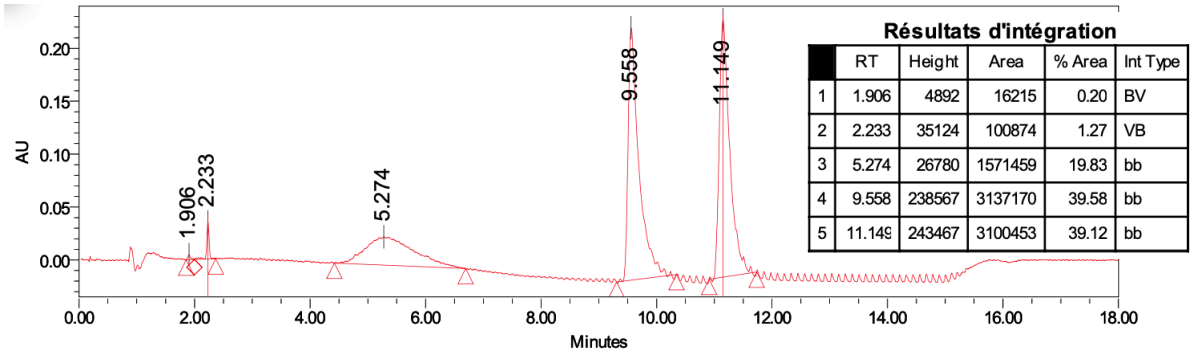


3. Chiral HPLC of (*R*)-emoxyzine-2 and (*R,S*)-emoxyzine-2

3.1. Chiral HPLC of (*R*)-emoxyzine-2 (R_t = 11.2 min)

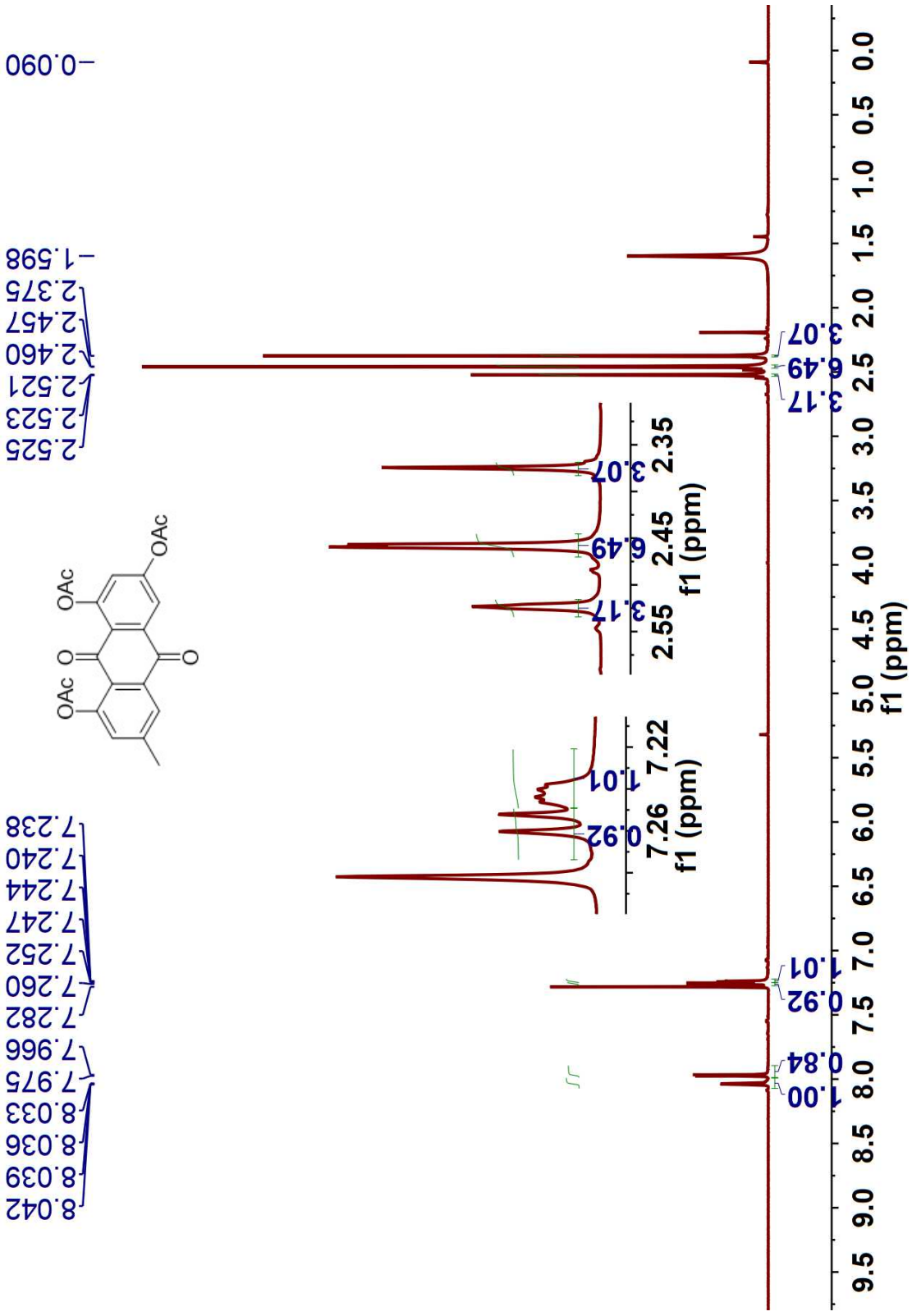


3.2. Chiral HPLC of (*R,S*)-emoxyzine-2. R_t = 9.6 min (*S*, 50%), R_t = 11.1 min (*R*, 50%)

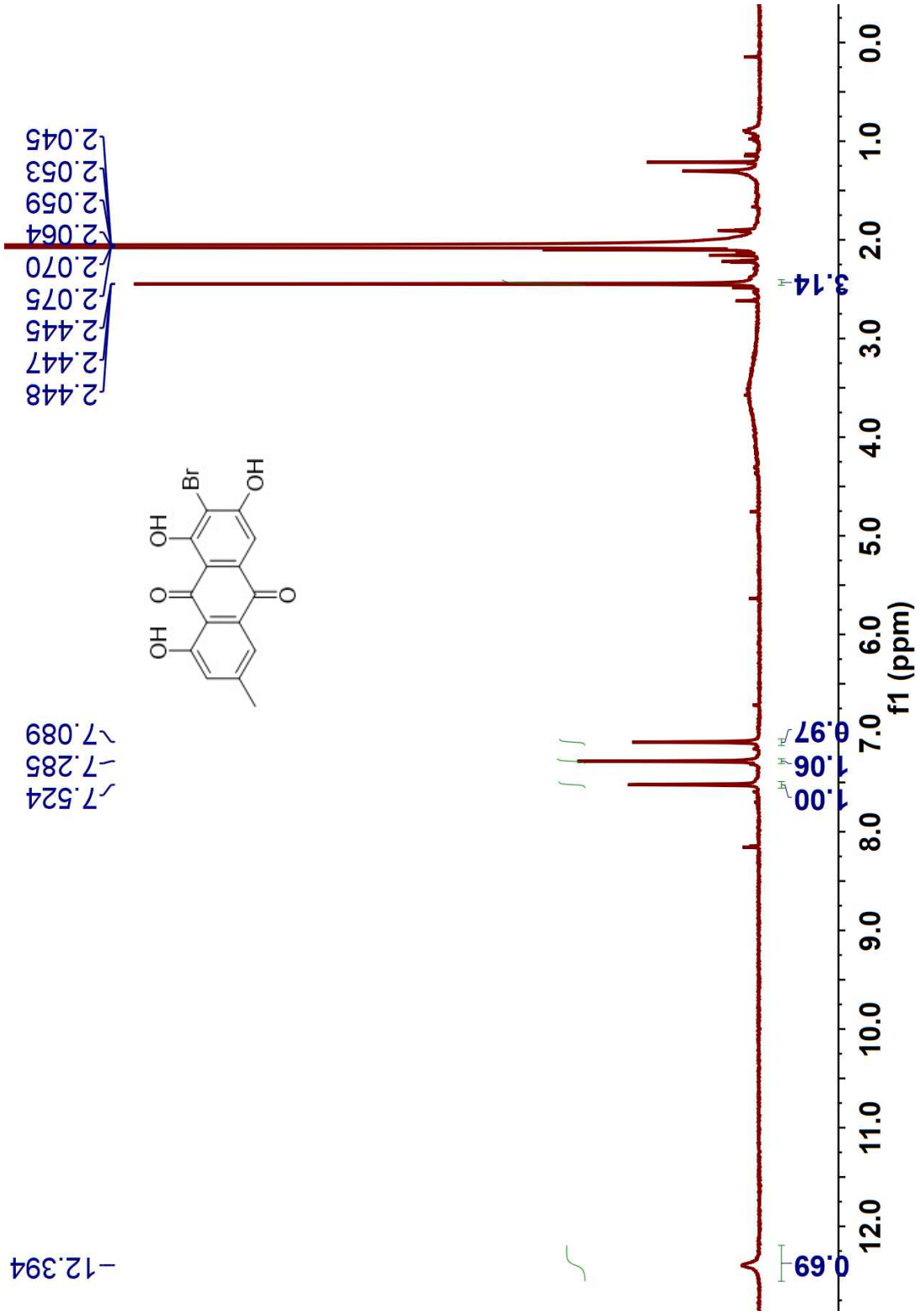


4. ^{1}H-NMR and ^{13}C-NMR of emodin-PA and emoxyzine derivatives, and synthesis intermediates

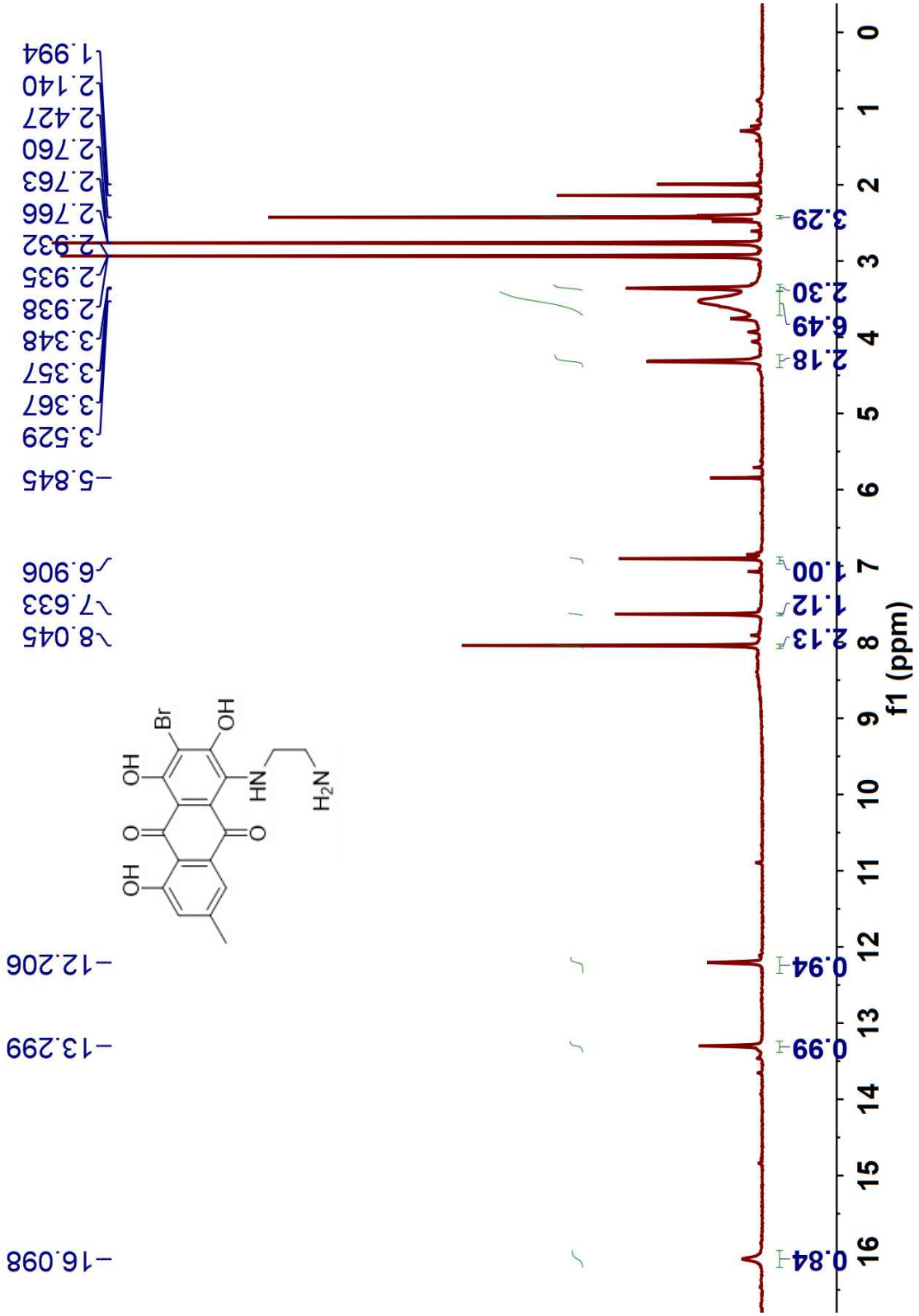
4.1. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 1,3,8-triacetylemodin



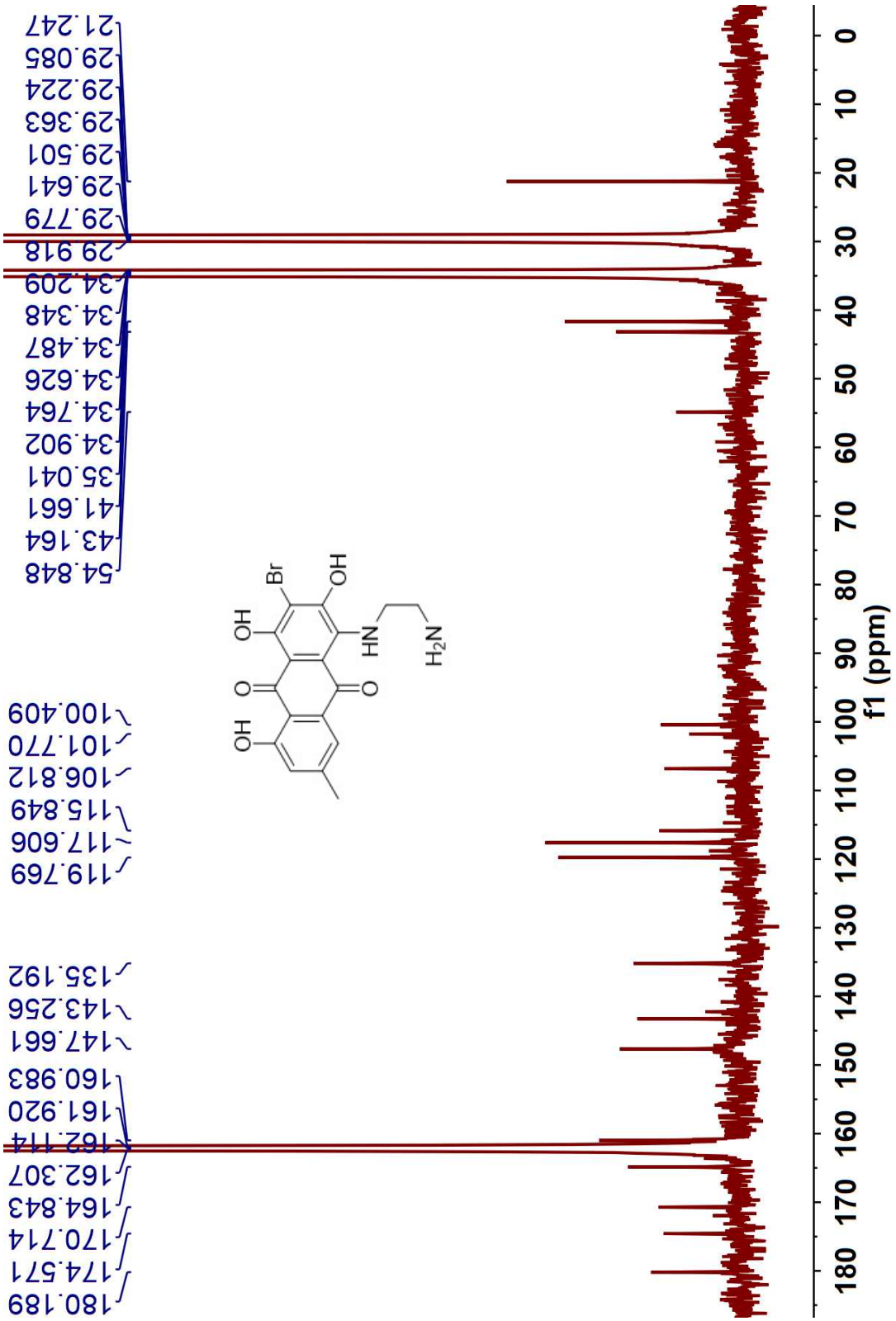
4.2. ^{1}H NMR (400 MHz, acetone-d_6) spectrum of 2-bromoemodin



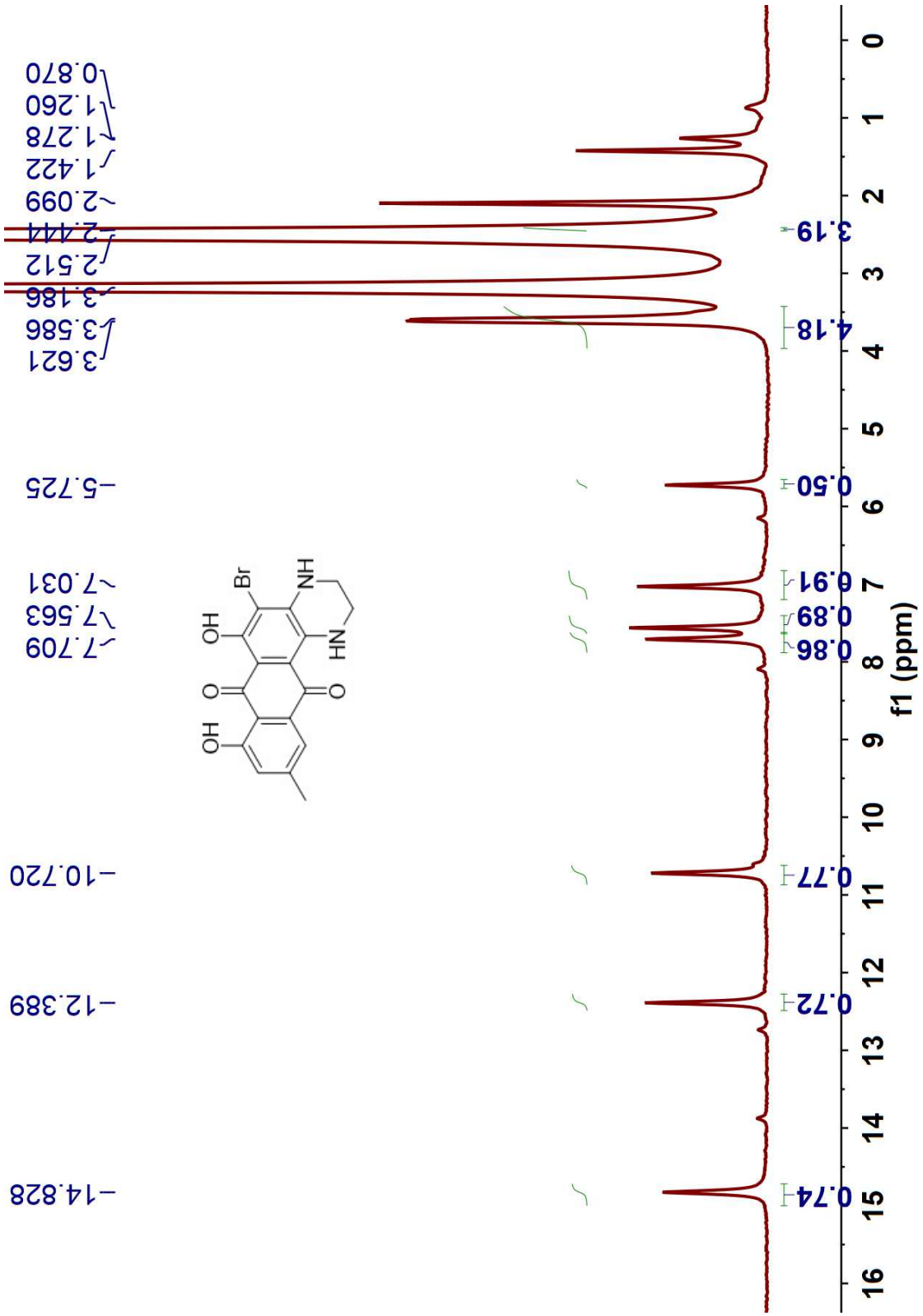
4.3.a. ^{1}H NMR (600 MHz, DMF-d_7) spectrum of emodin-PA-1



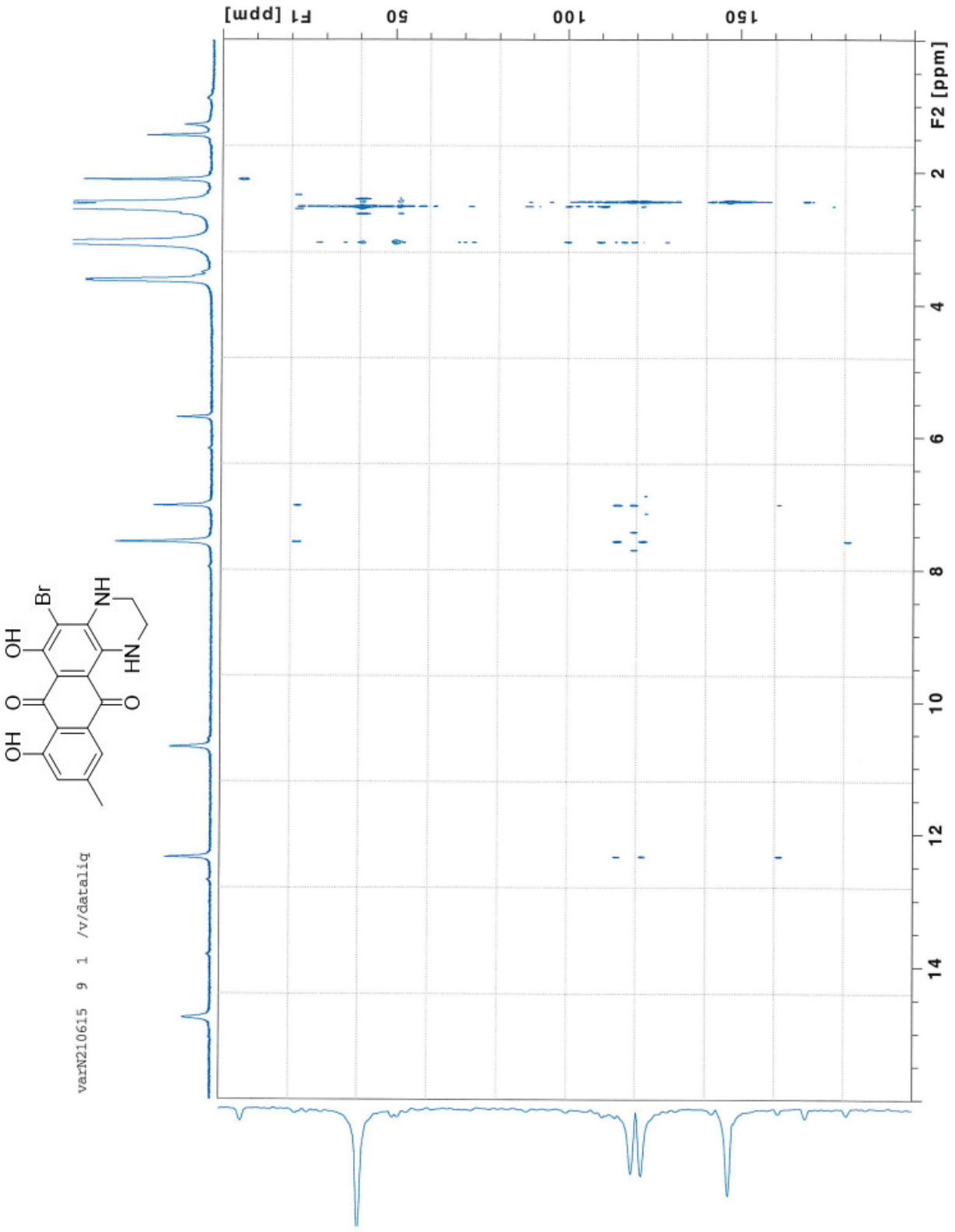
4.3.b. ^{13}C NMR (150 MHz, DMF-d_7) spectrum of emodin-PA-1



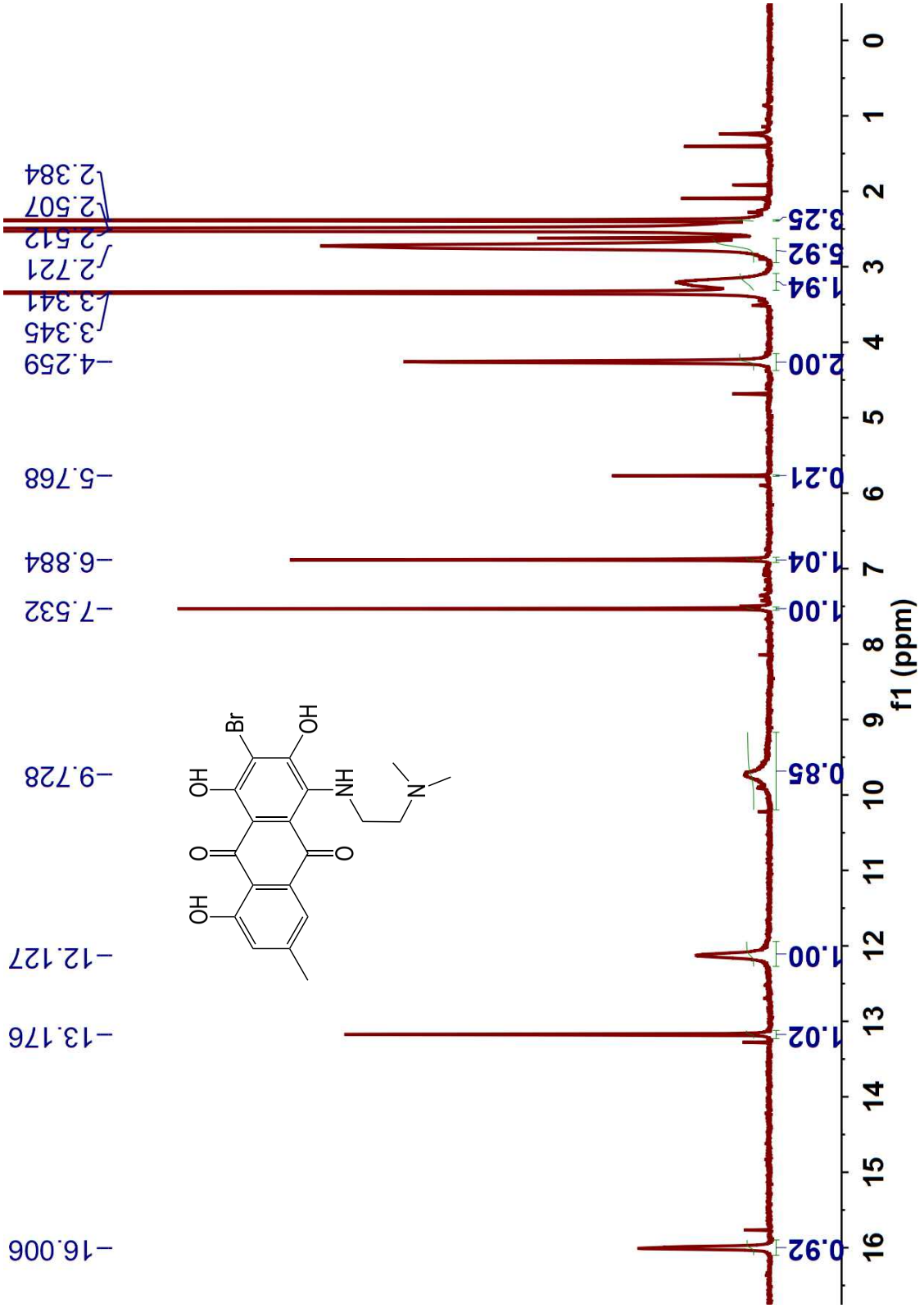
4.4.a. ^{1}H NMR (600 MHz, DMSO-d_6, 373 K) spectrum of emodin-PA-2



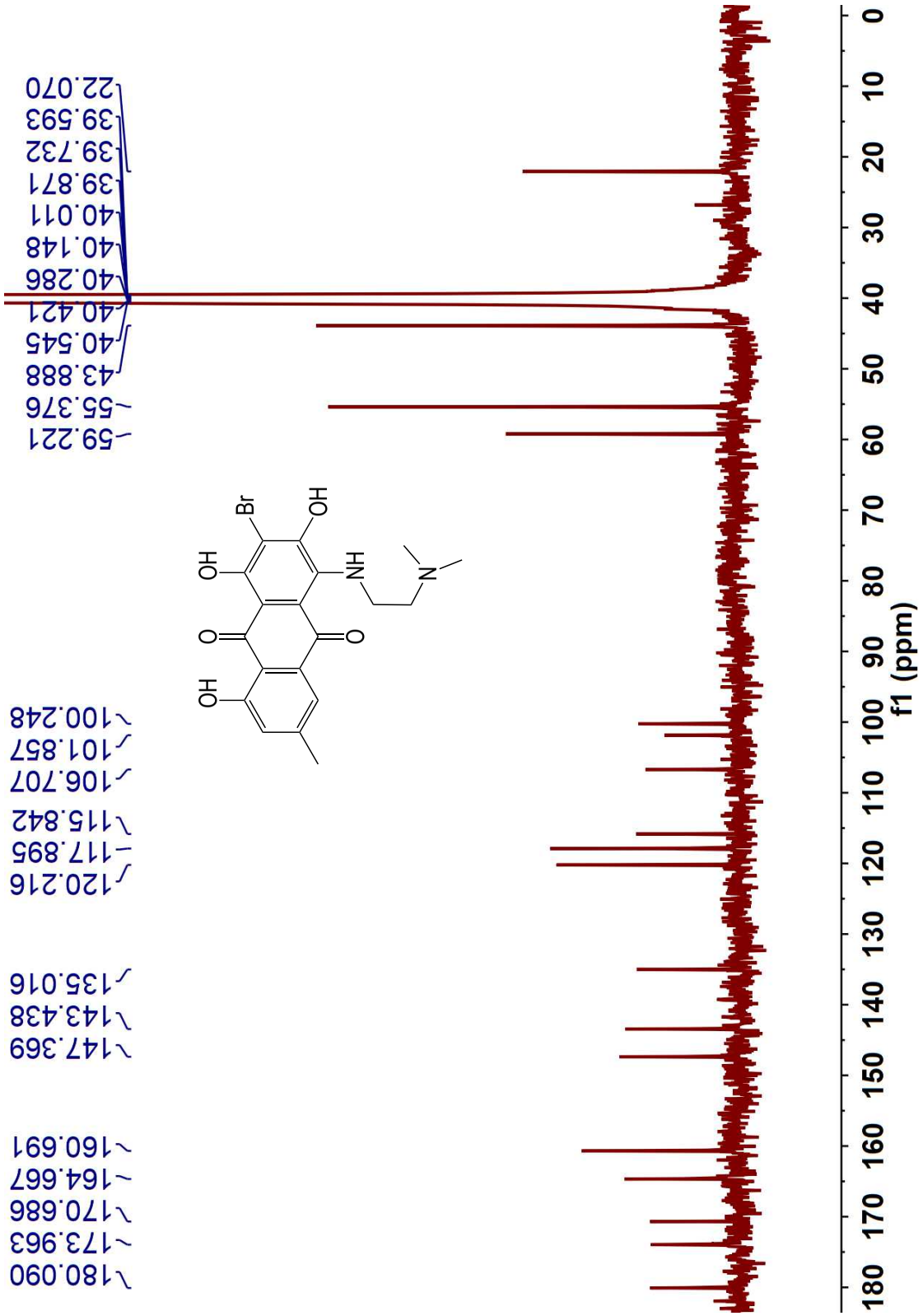
4.4.b. HMBC (600 MHz, DMSO-d_6, 373 K) spectrum of emodin-PA-2



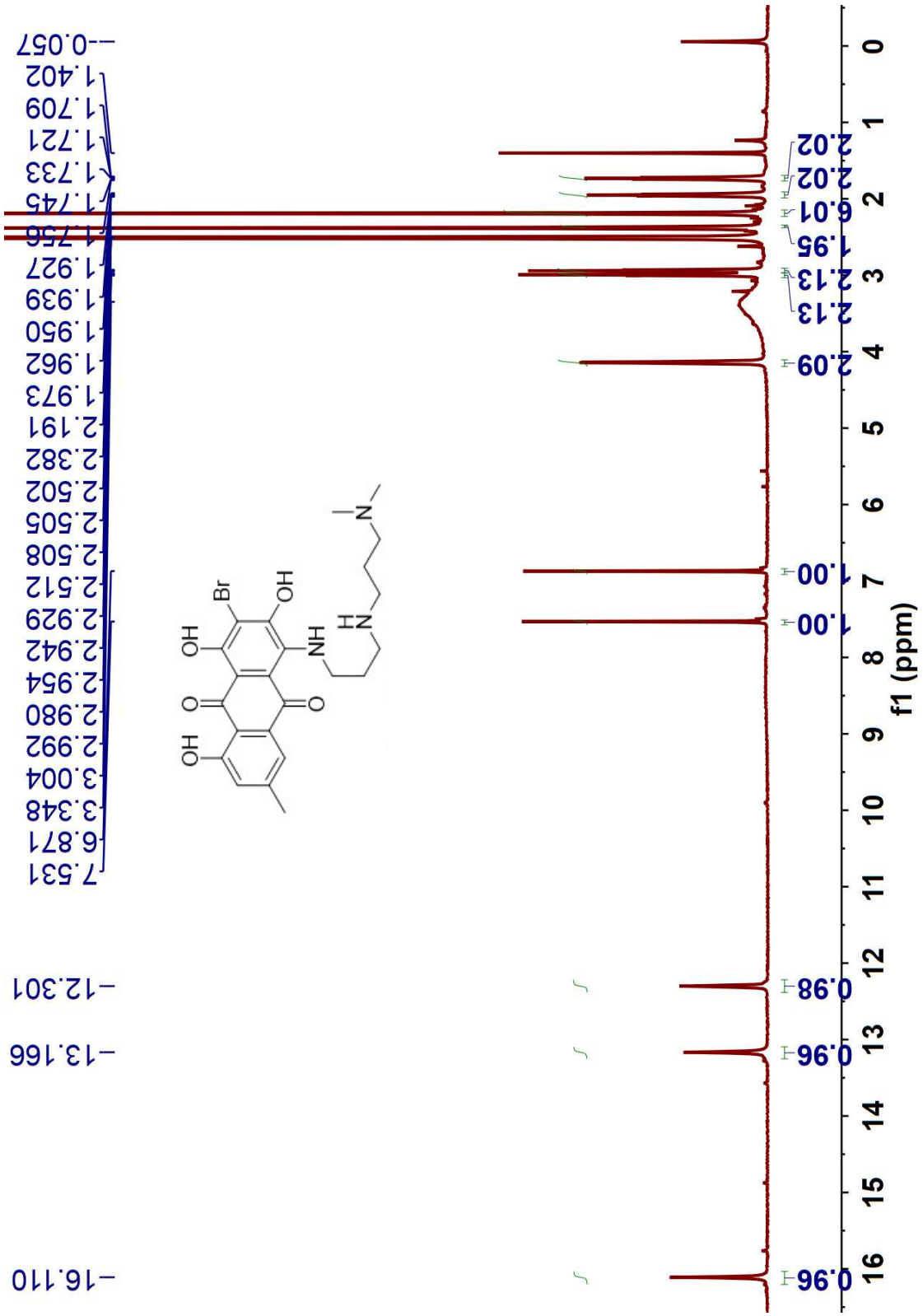
4.5.a. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of emodin-PA-3



4.5.b. ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of emodin-PA-3

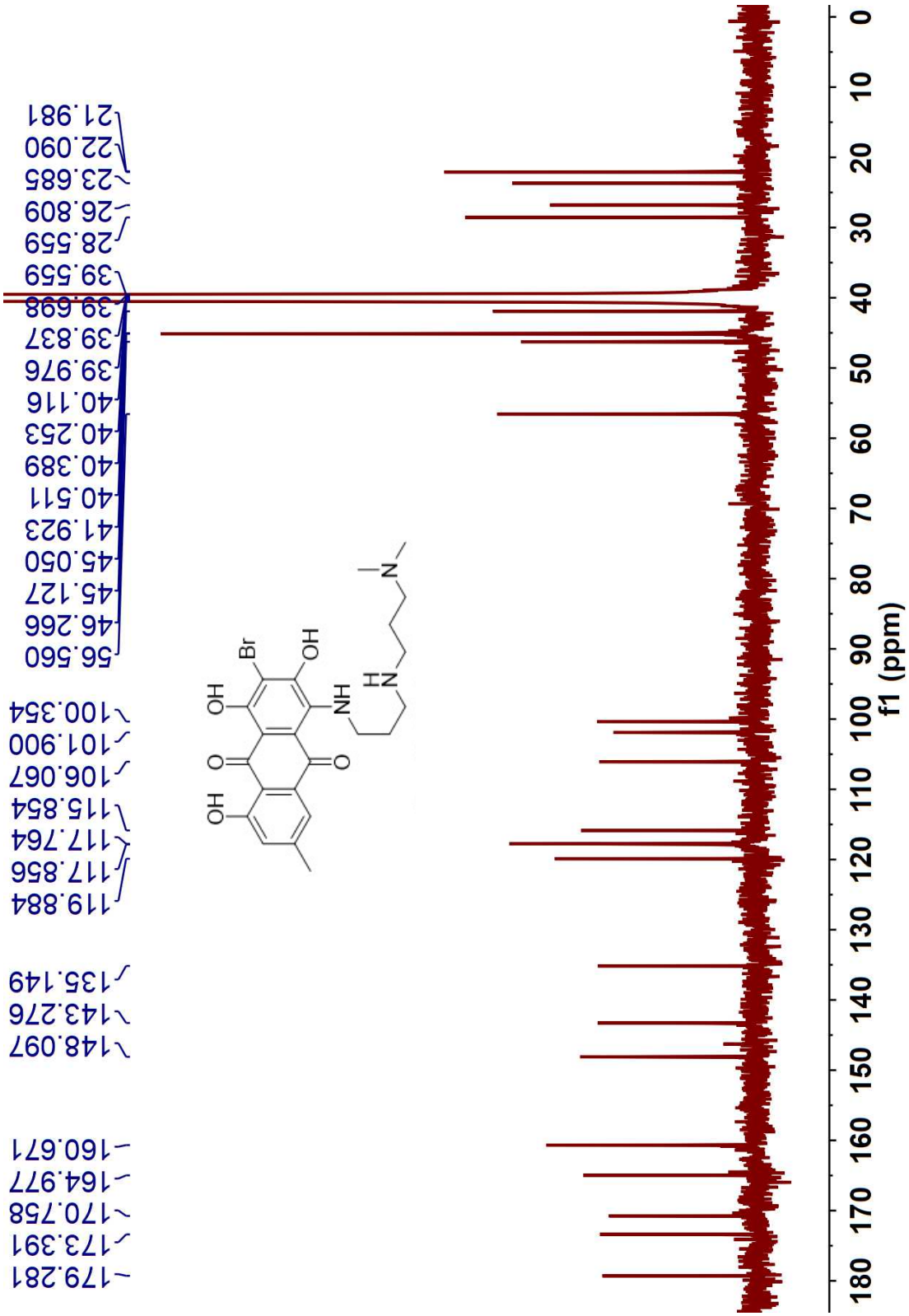


4.6.a. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of emodin-PA-4

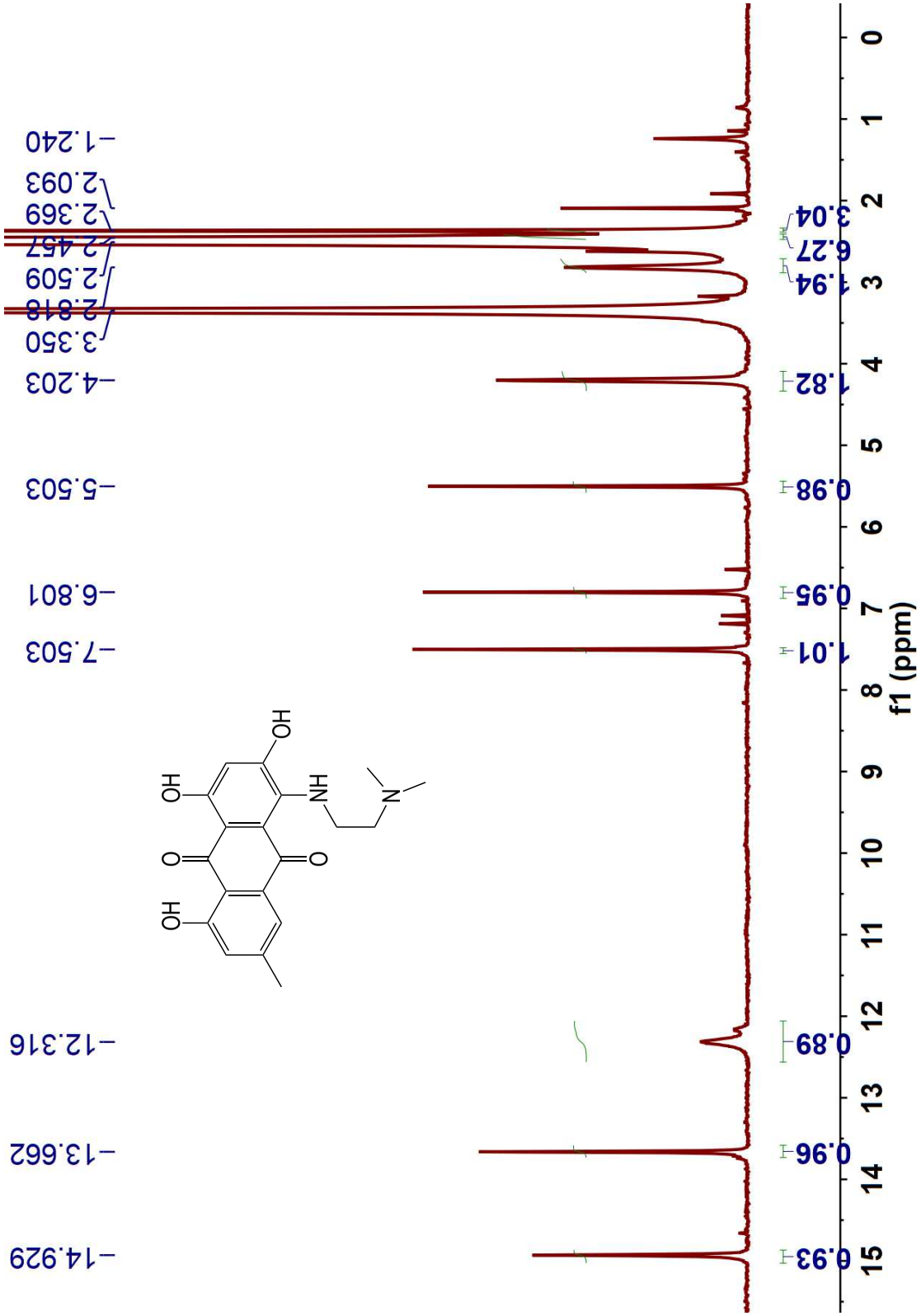


$

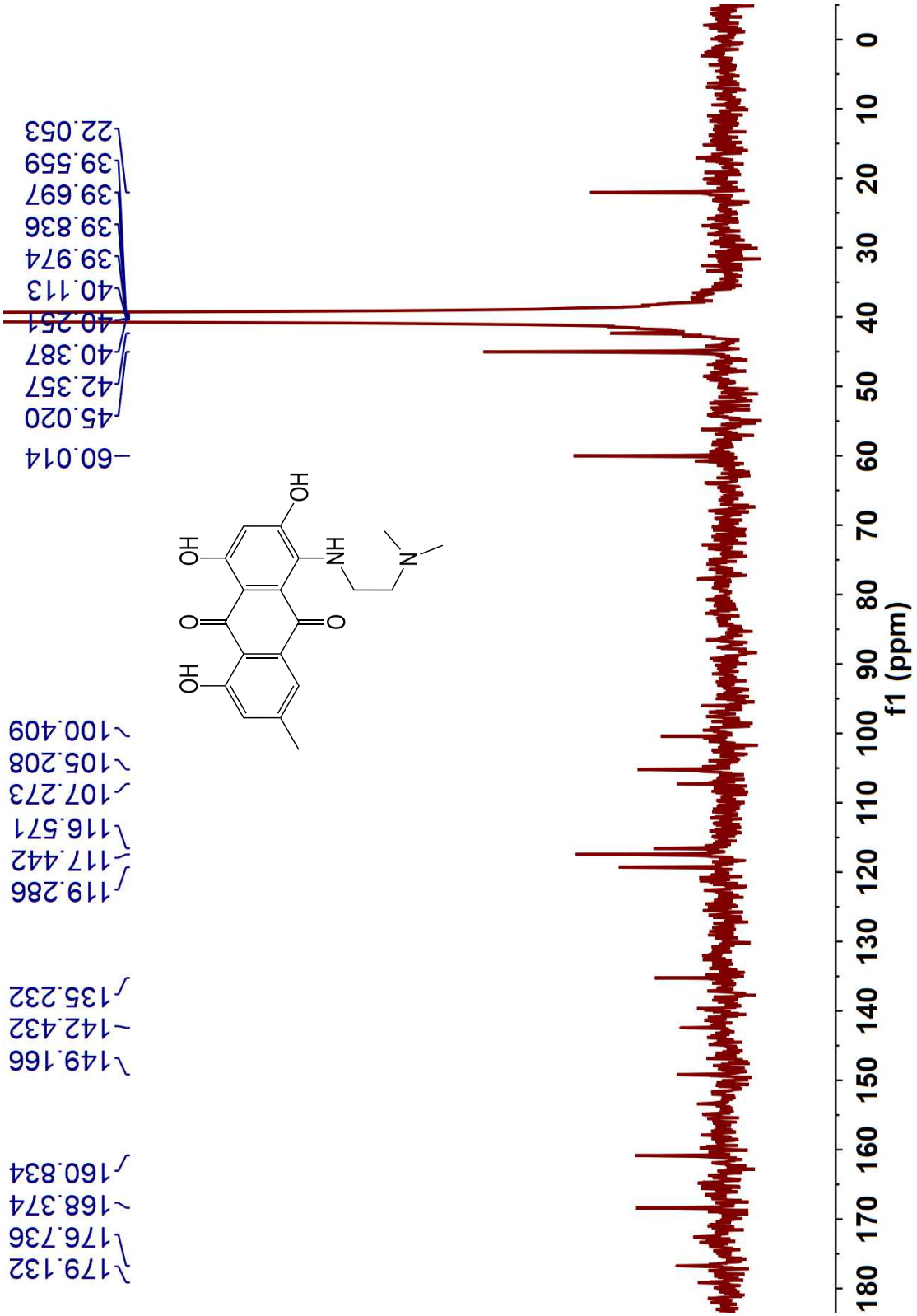
4.6.b. ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of emodin-PA-4



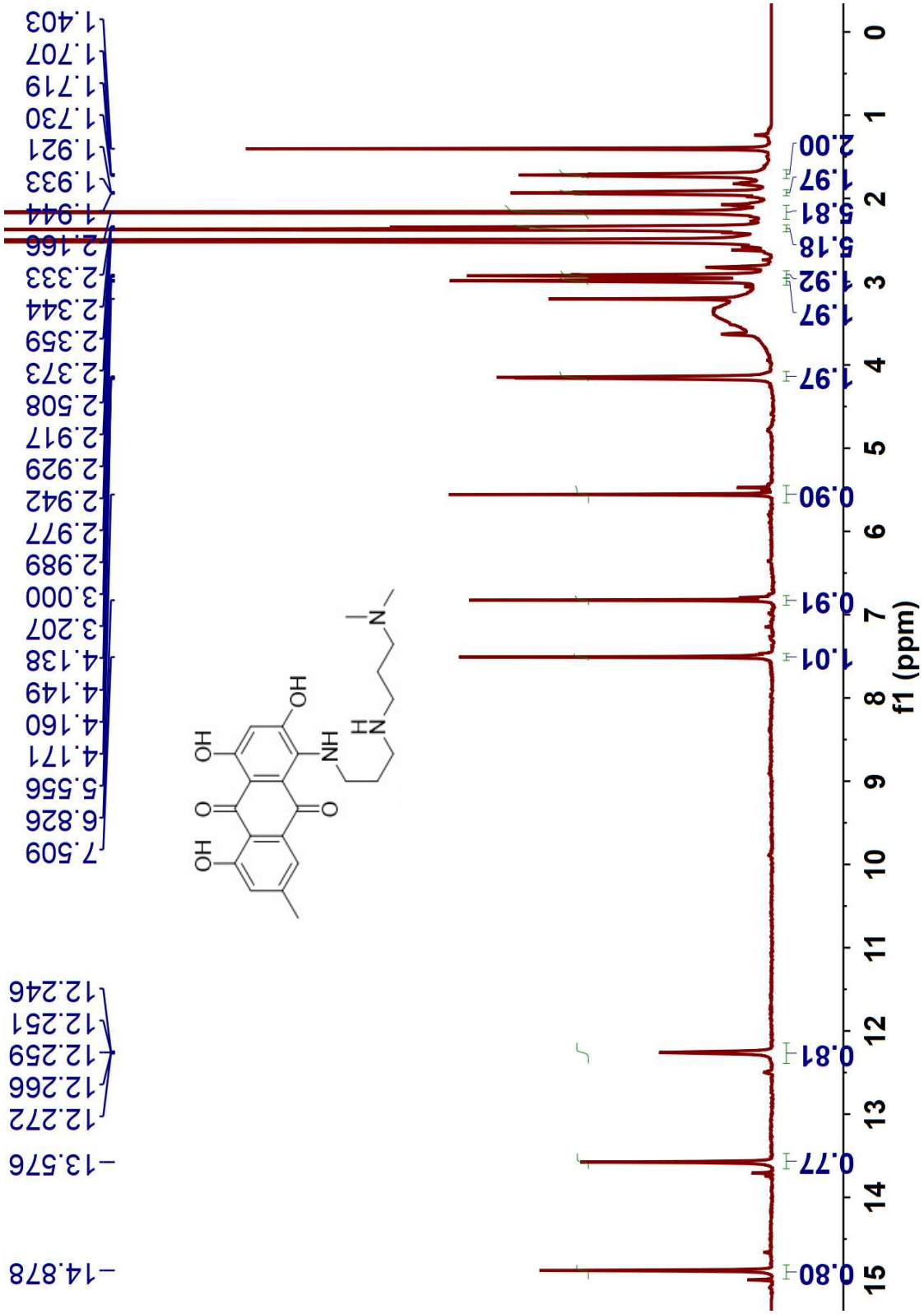
4.7.a. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of emodin-PA-5



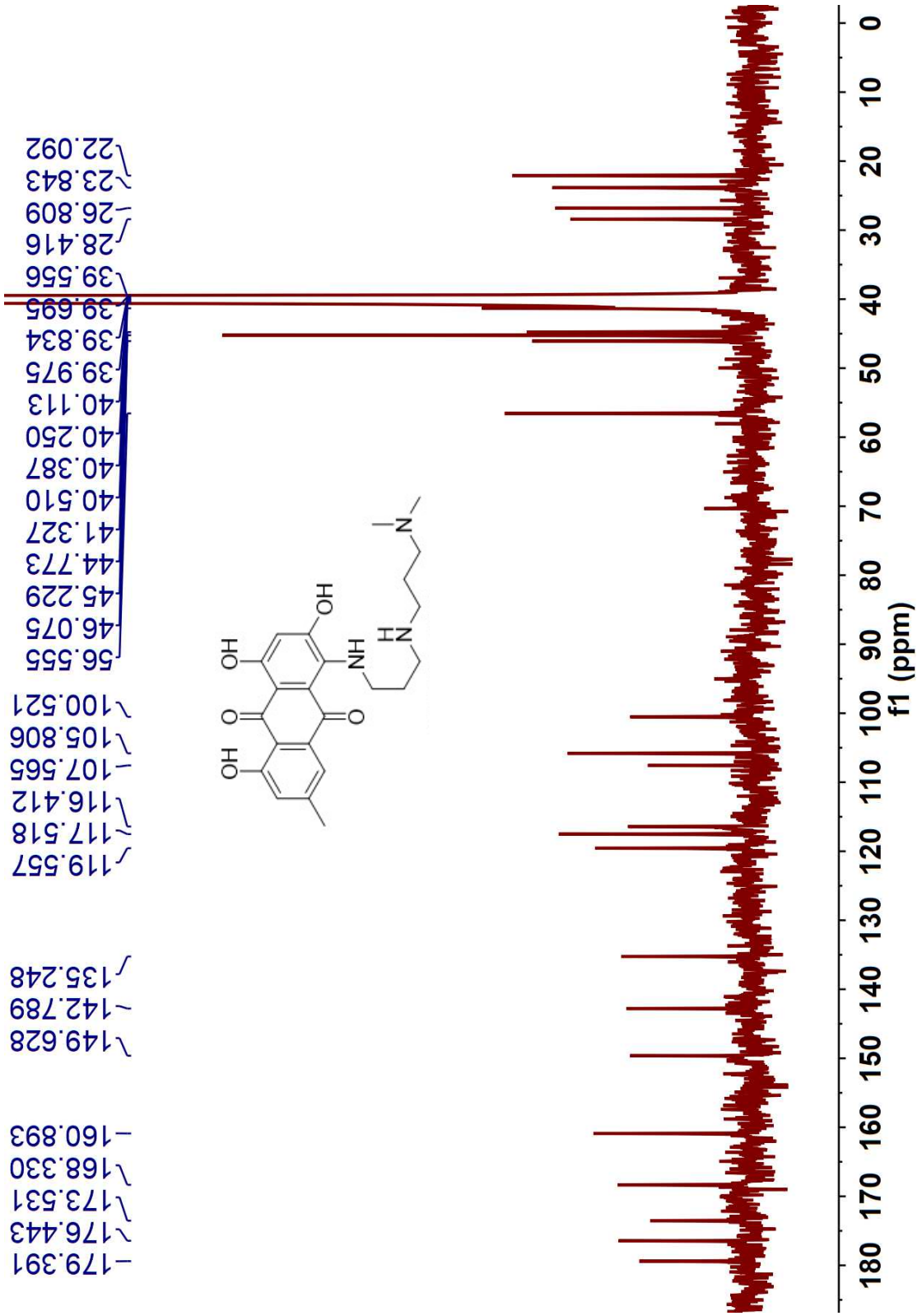
4.7.b. ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of emodin-PA-5



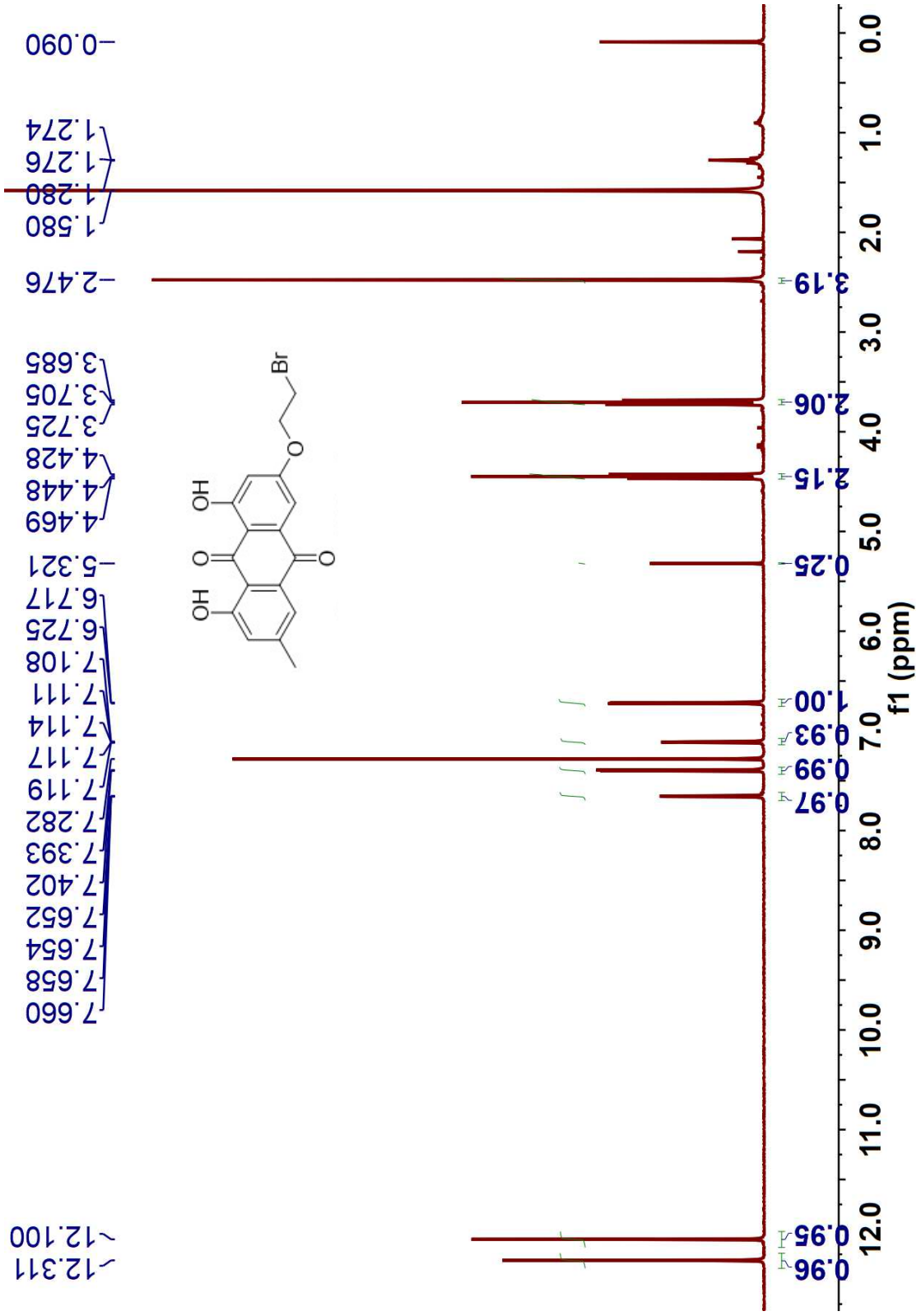
4.8.a. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of emodin-PA-6



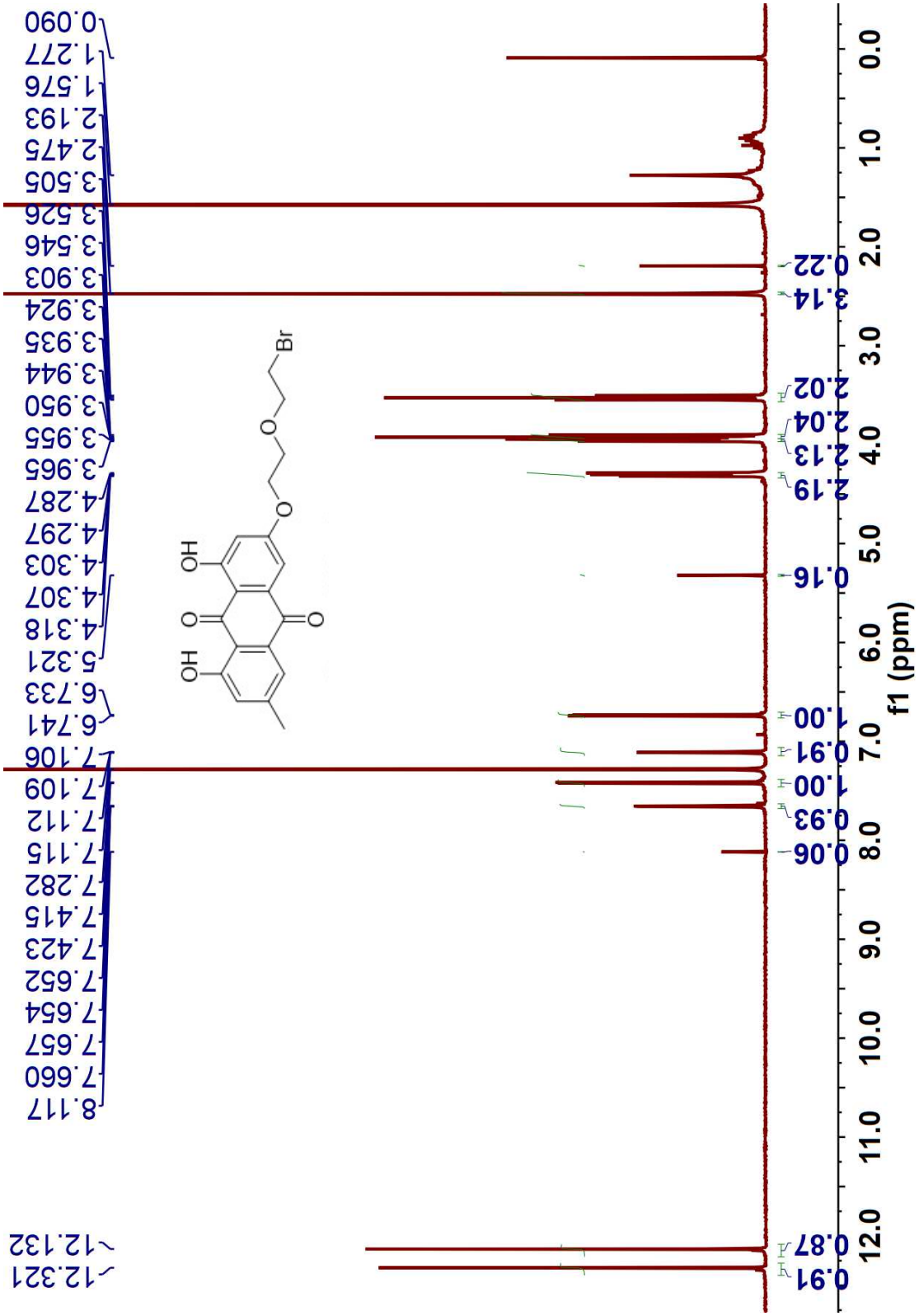
4.8.b. ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of Emodin-PA-6



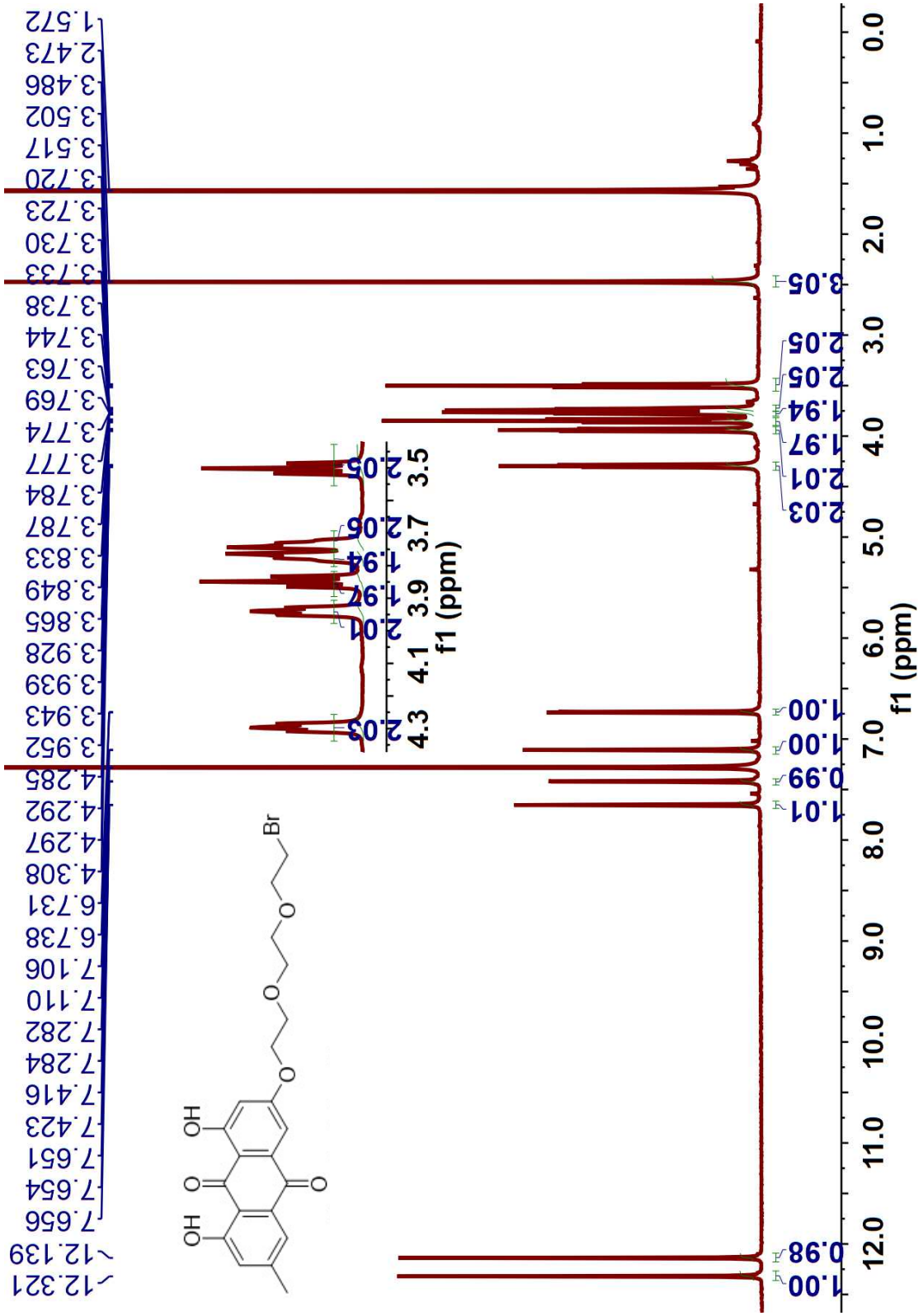
4.9. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of emodin-link-1



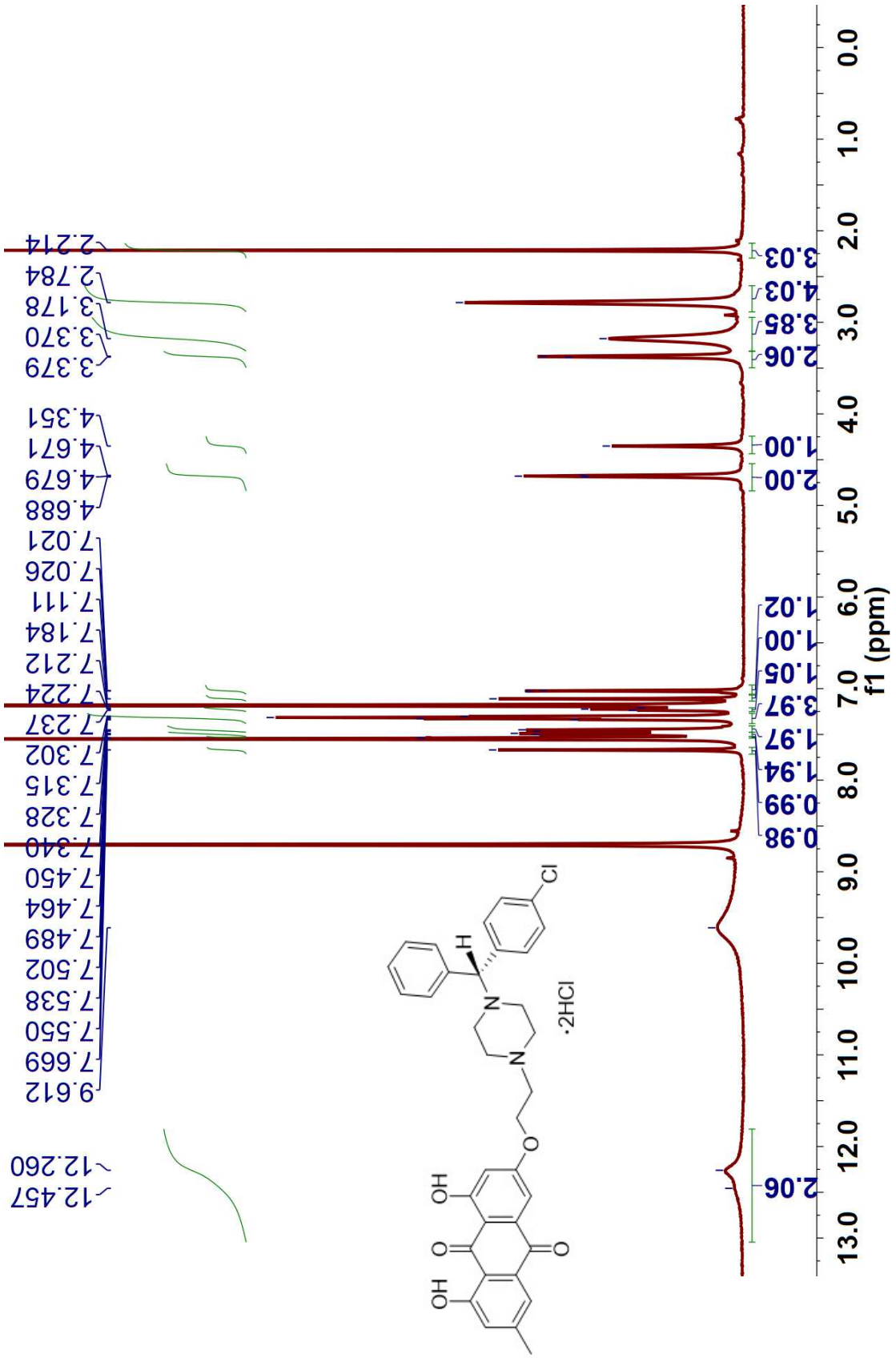
4.10. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of emodin-link-2



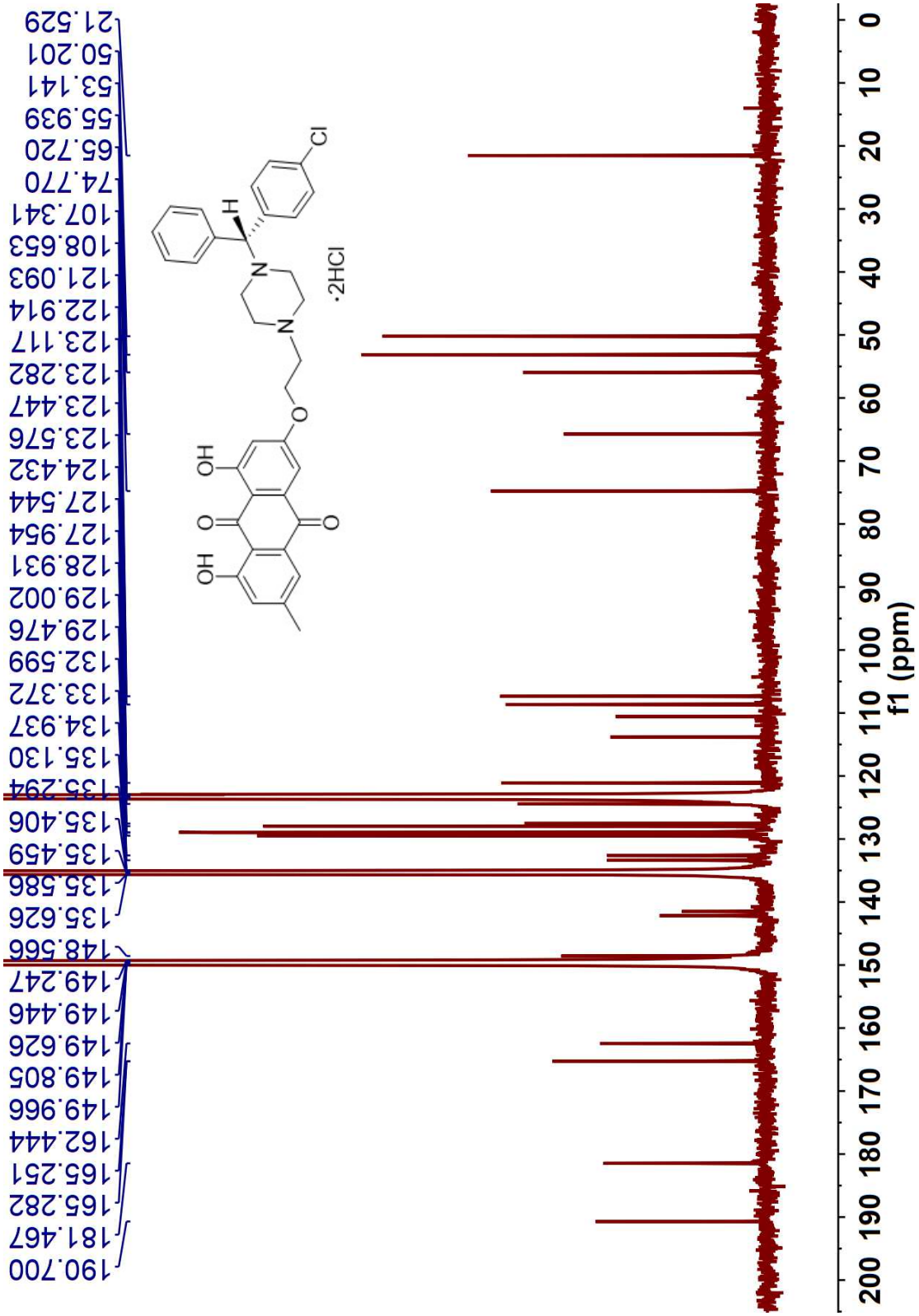
4.11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of emodin-link-3



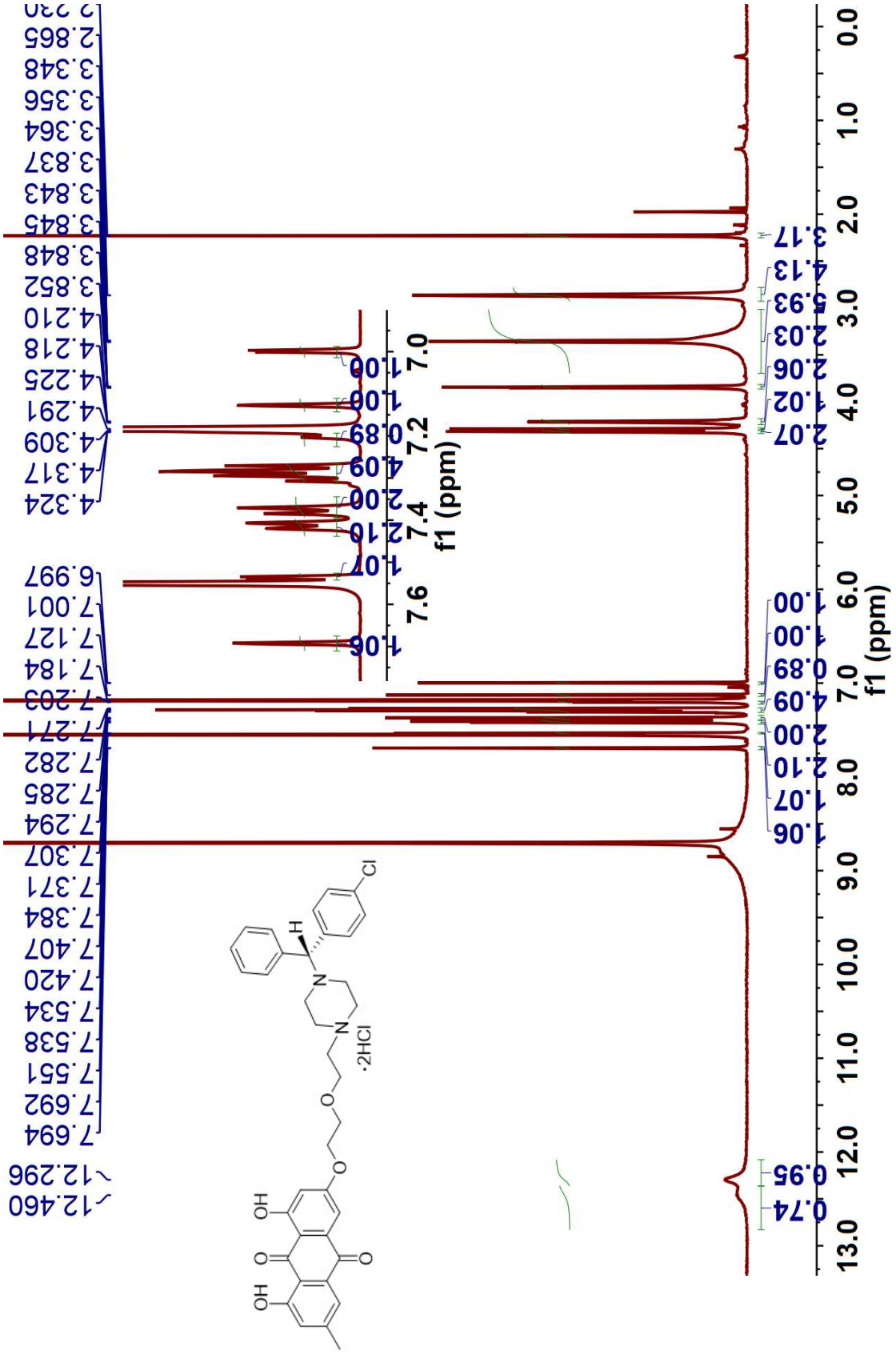
4.12.a. ^{1}H NMR (600 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-1



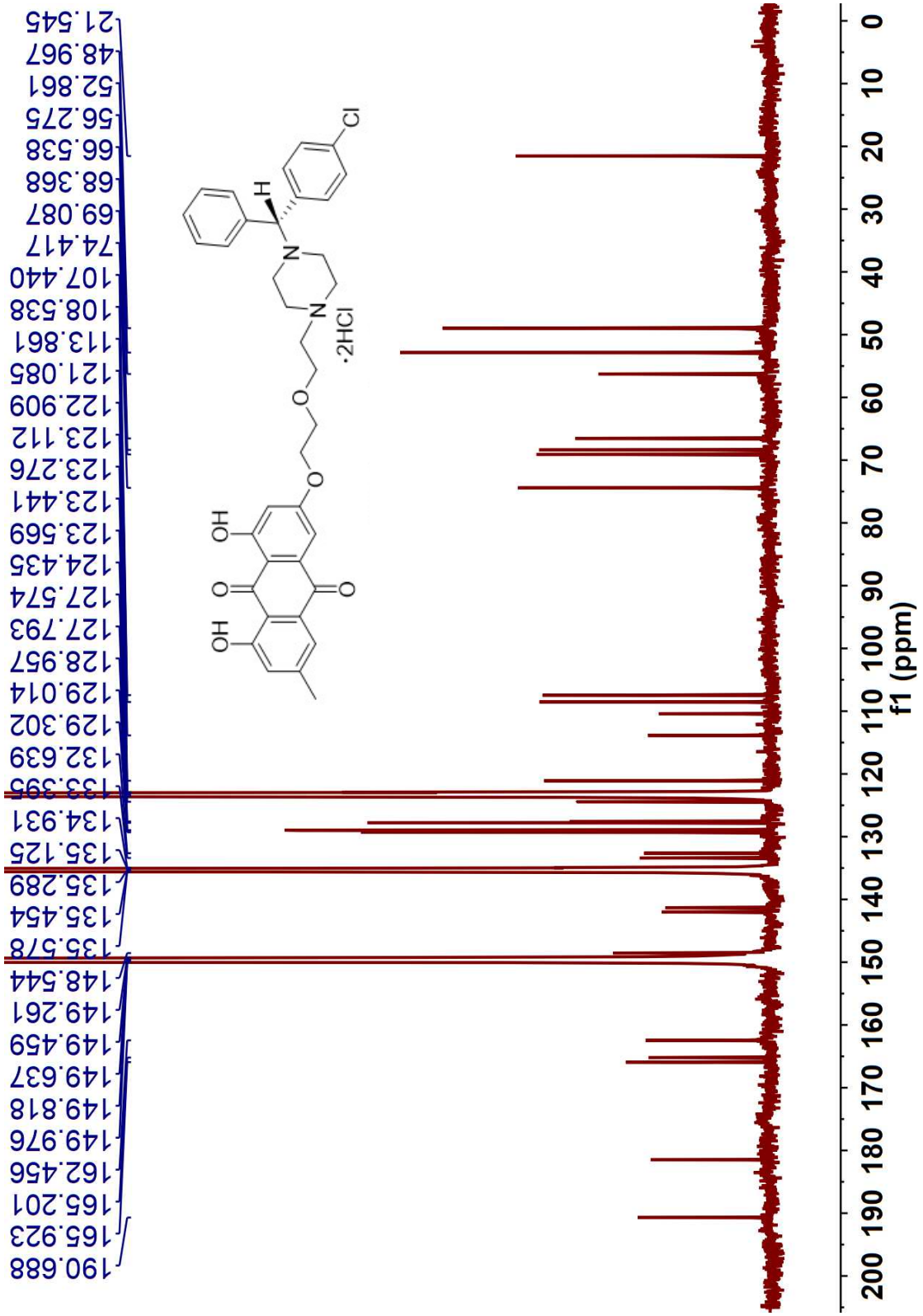
4.12.b. ^{13}C NMR (150 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-1



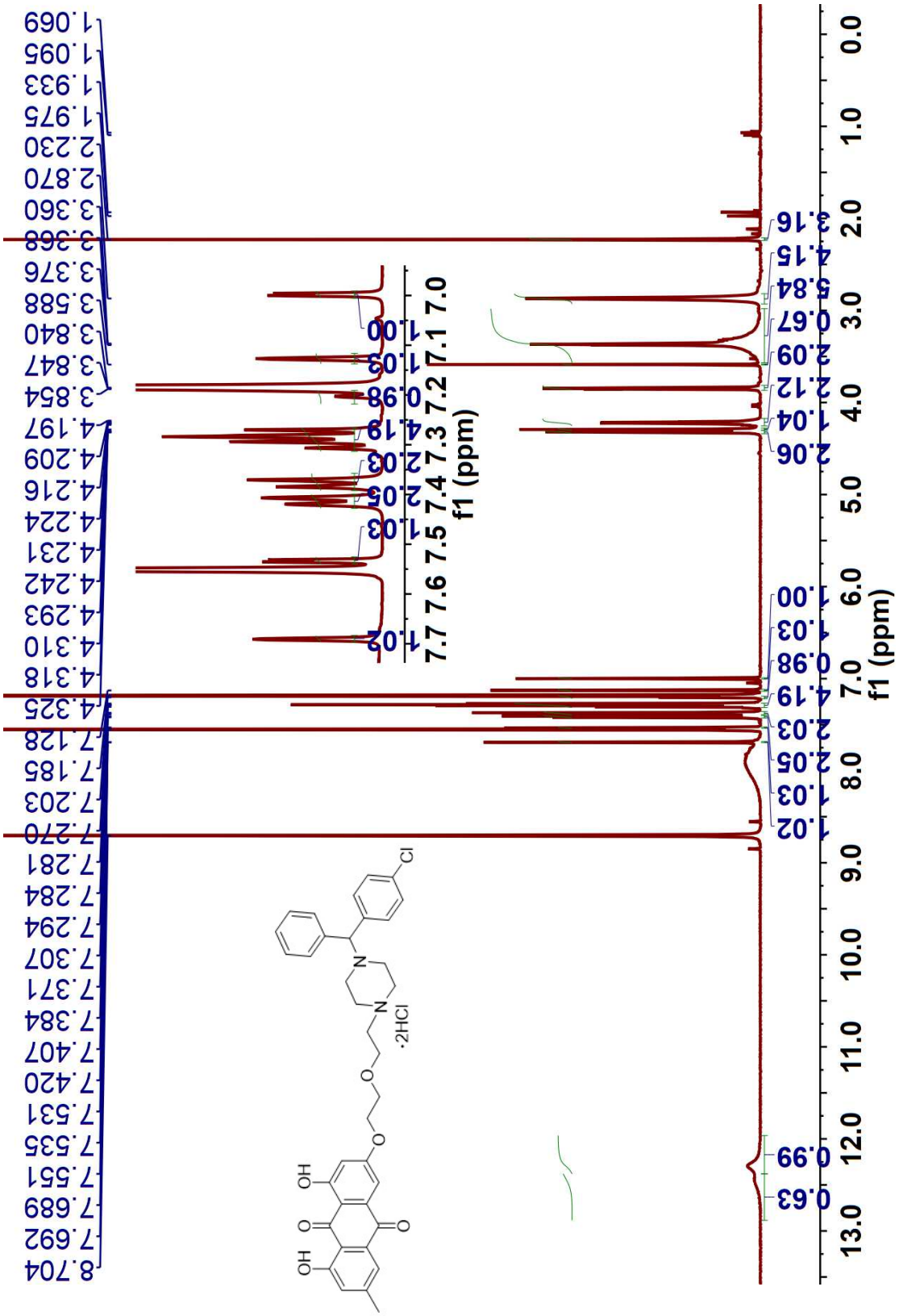
4.13.a. ^{1}H NMR (600 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-2



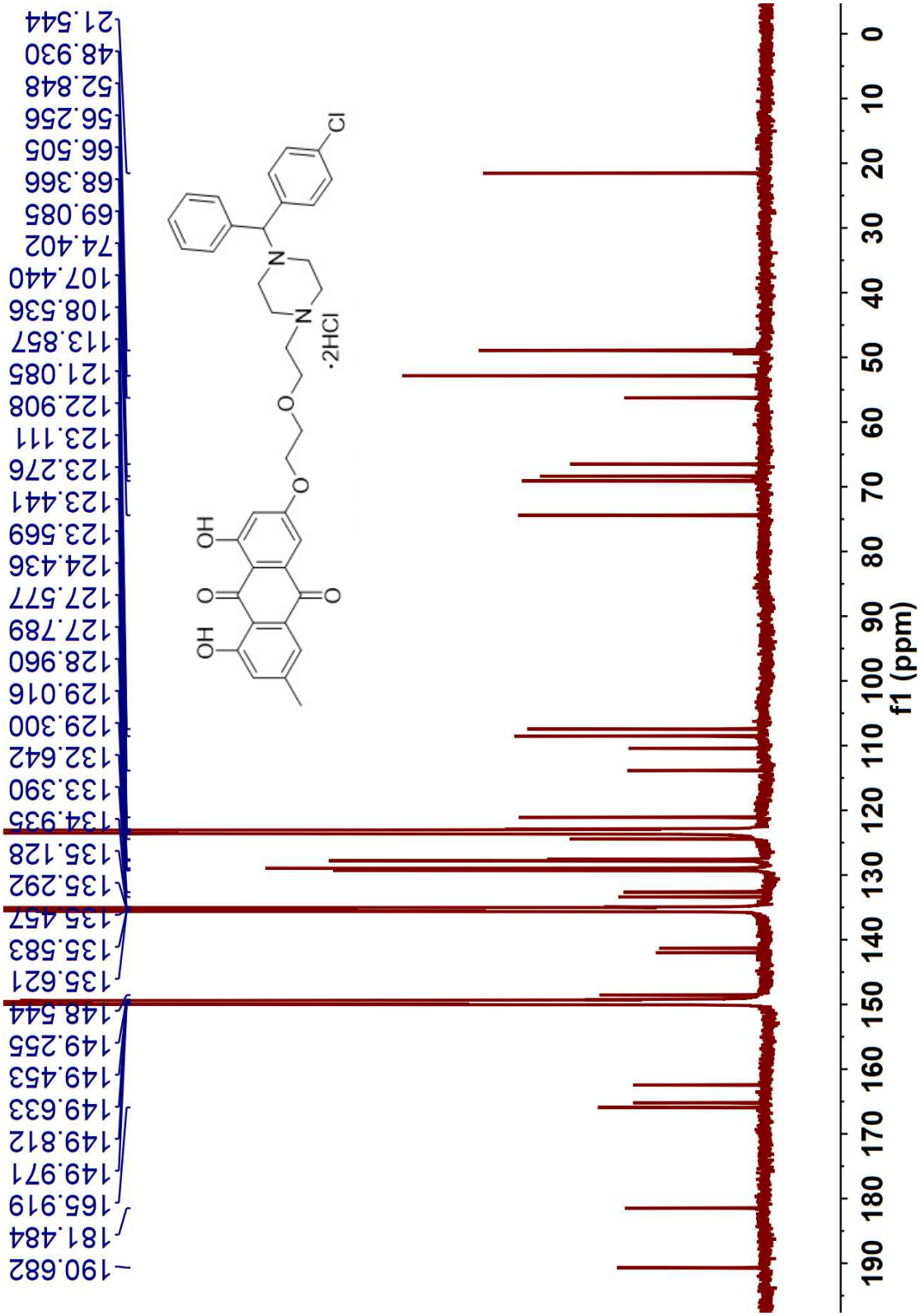
4.13.b. ^{13}C NMR (150 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-2



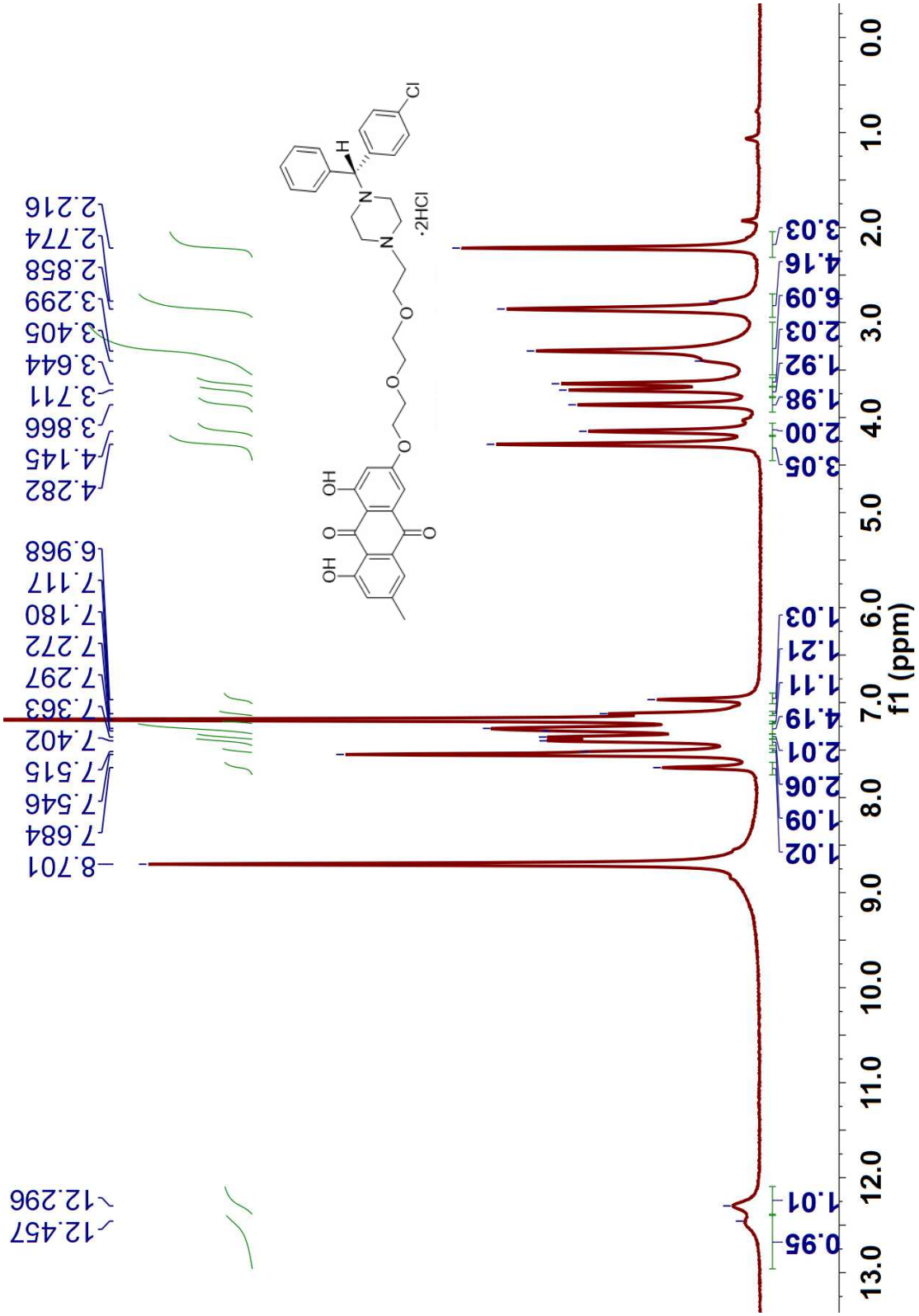
4.14.a. ^{1}H NMR (600 MHz, pyridine-d_5) spectrum of (*R,S*)-emoxyzine-2



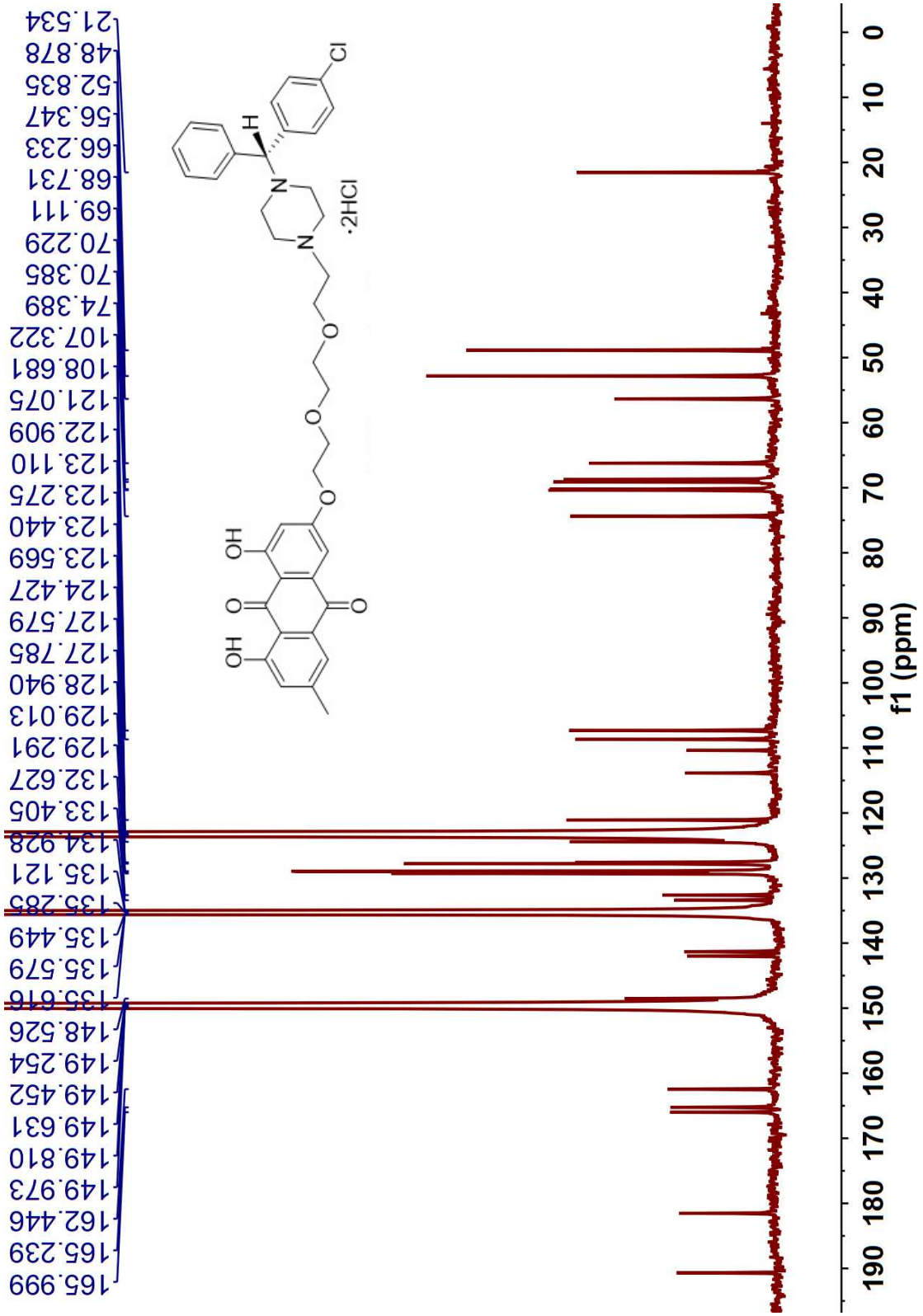
4.14.b. ^{13}C NMR (150 MHz, pyridine-d_5) spectrum of (*R,S*)-emoxyzine-2



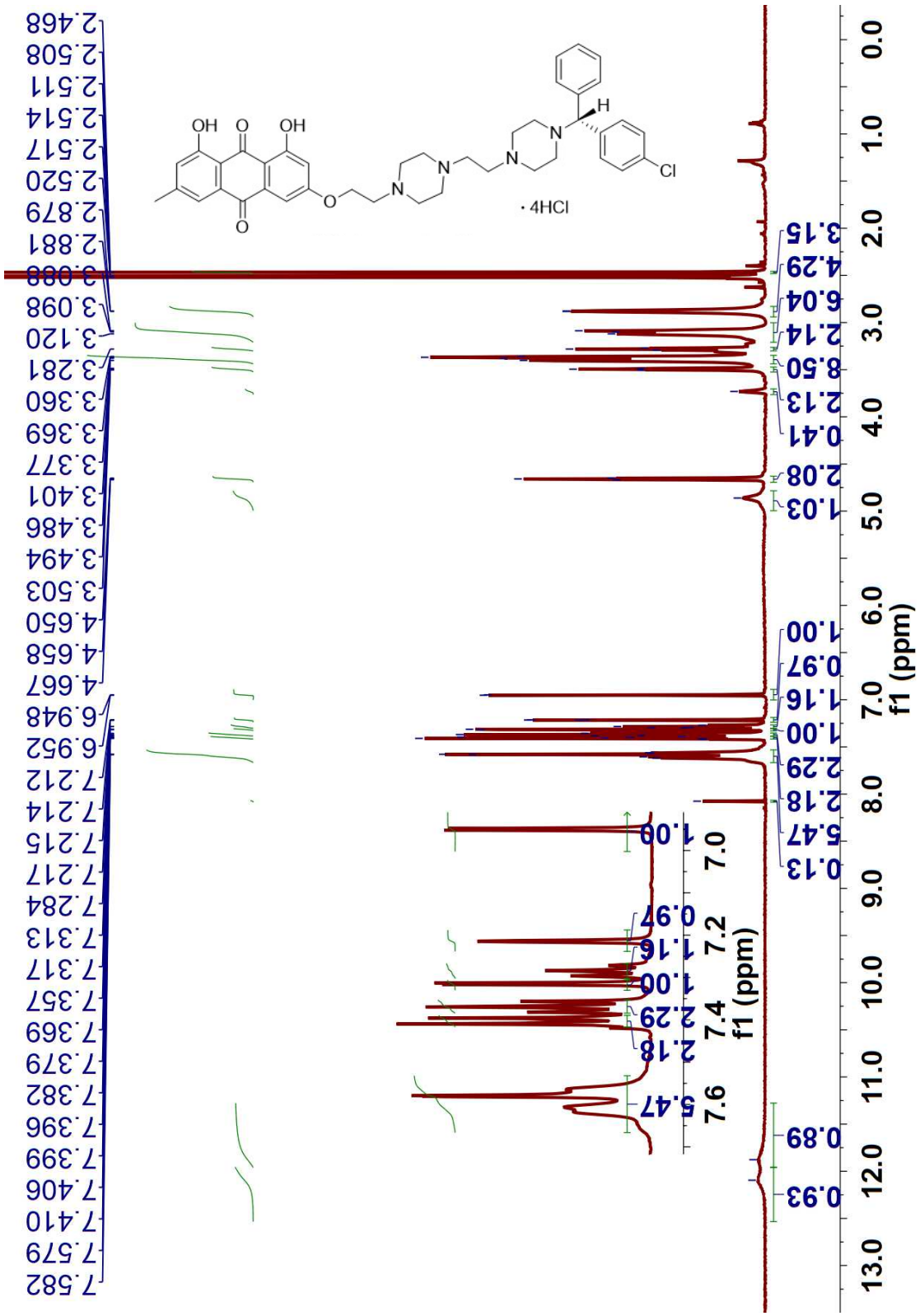
4.15.a. ^{1}H NMR (600 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-3



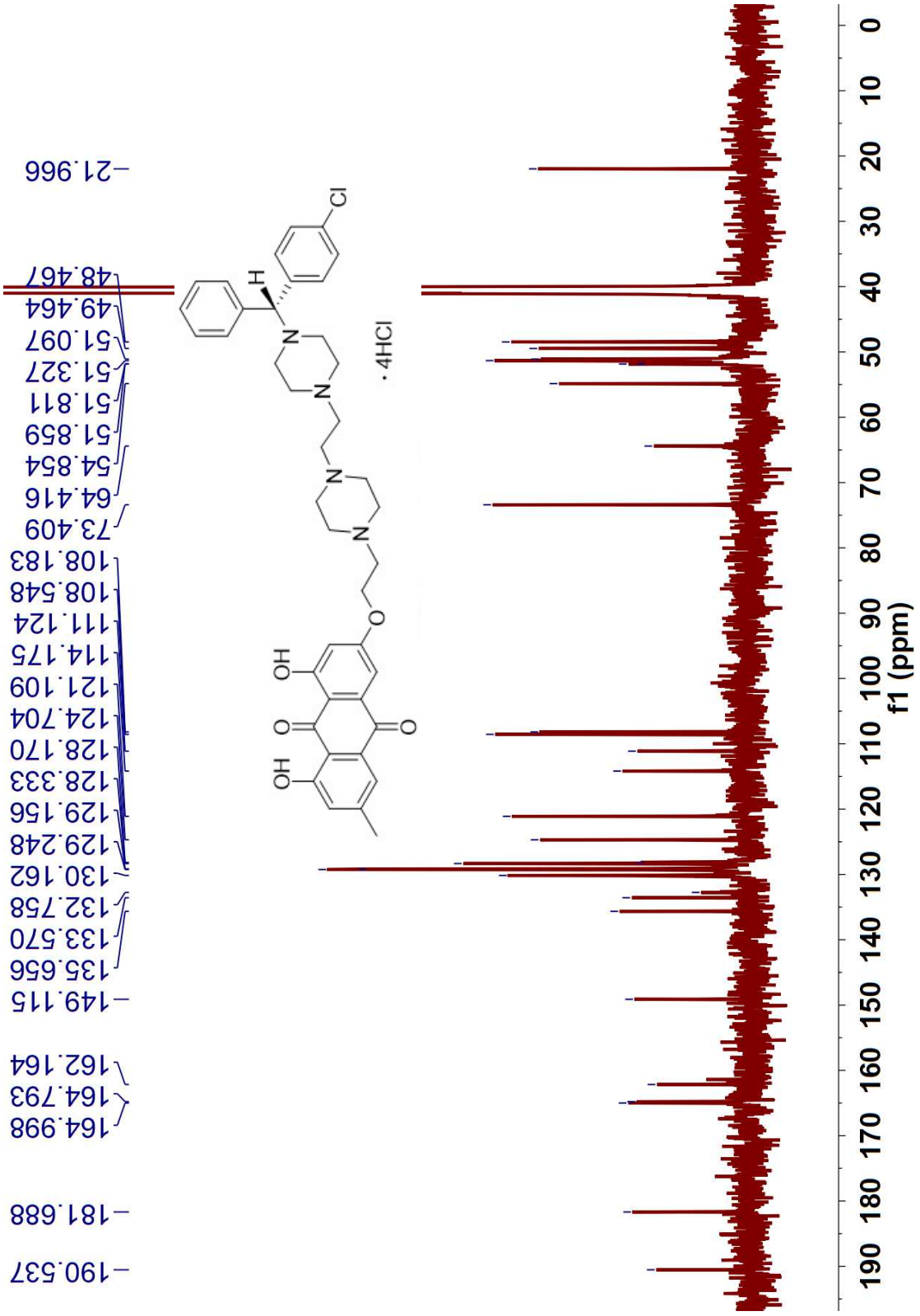
4.15.b. ^{13}C NMR (150 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-3



4.16.a. ^{1}H NMR (600 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-7

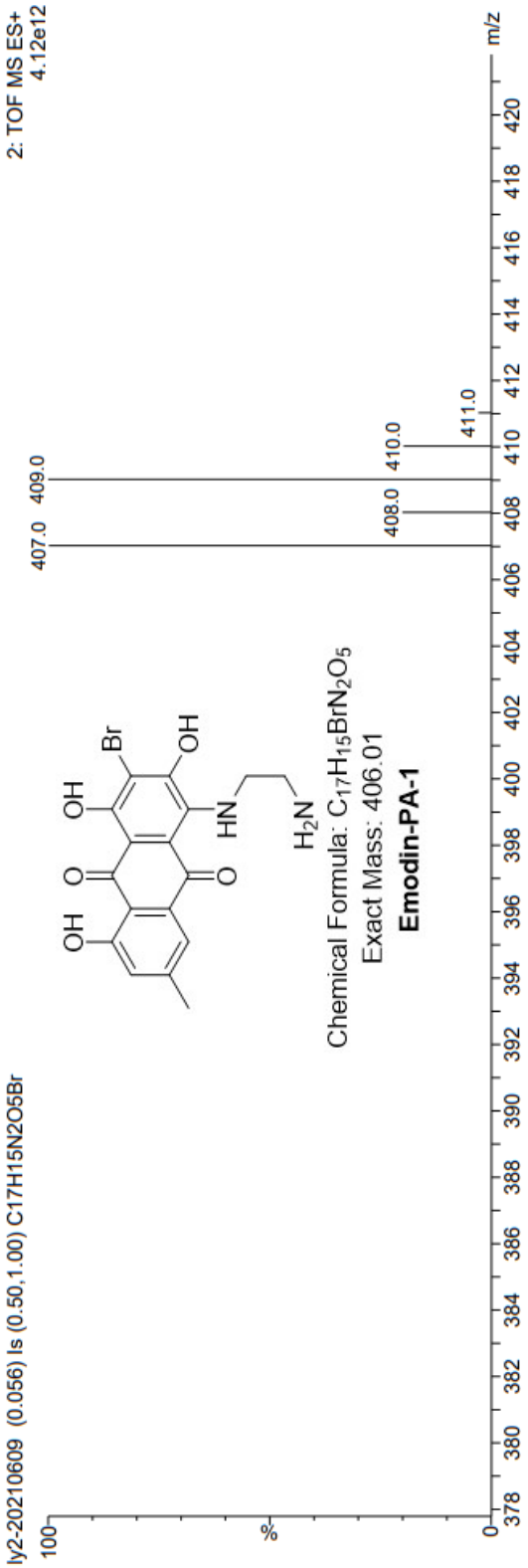


4.16.b. ^{13}C NMR (150 MHz, pyridine-d_5) spectrum of (*R*)-emoxyzine-7

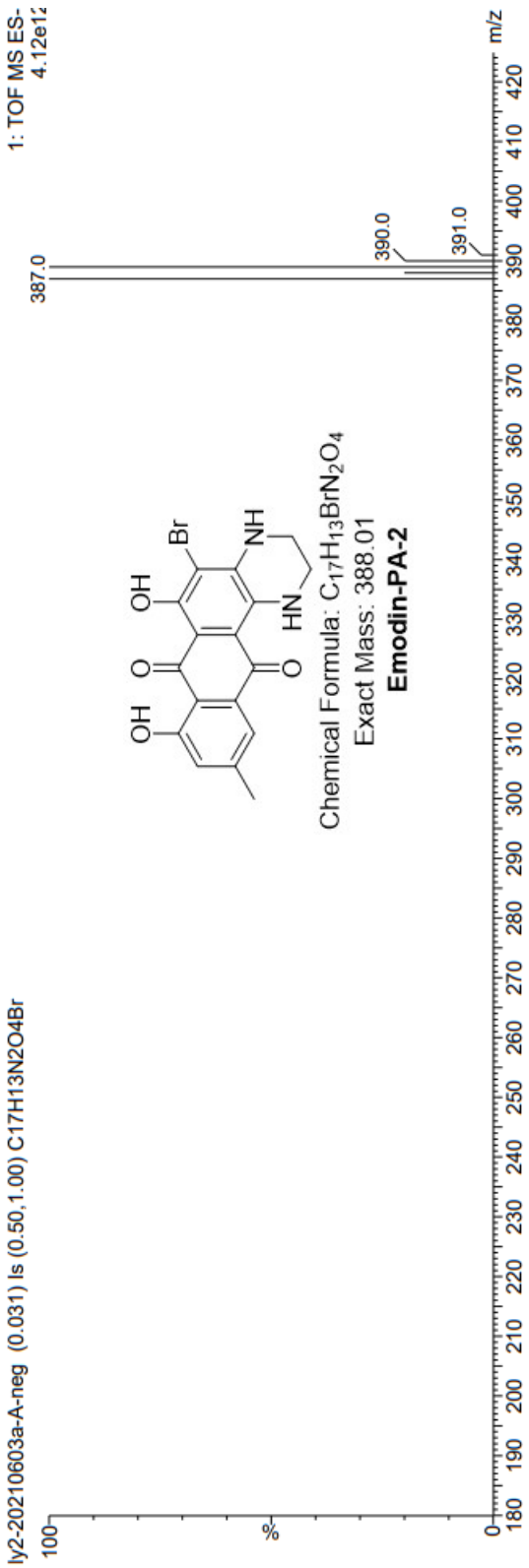


5. Mass spectra of emodin-PA and emoxyzine derivatives

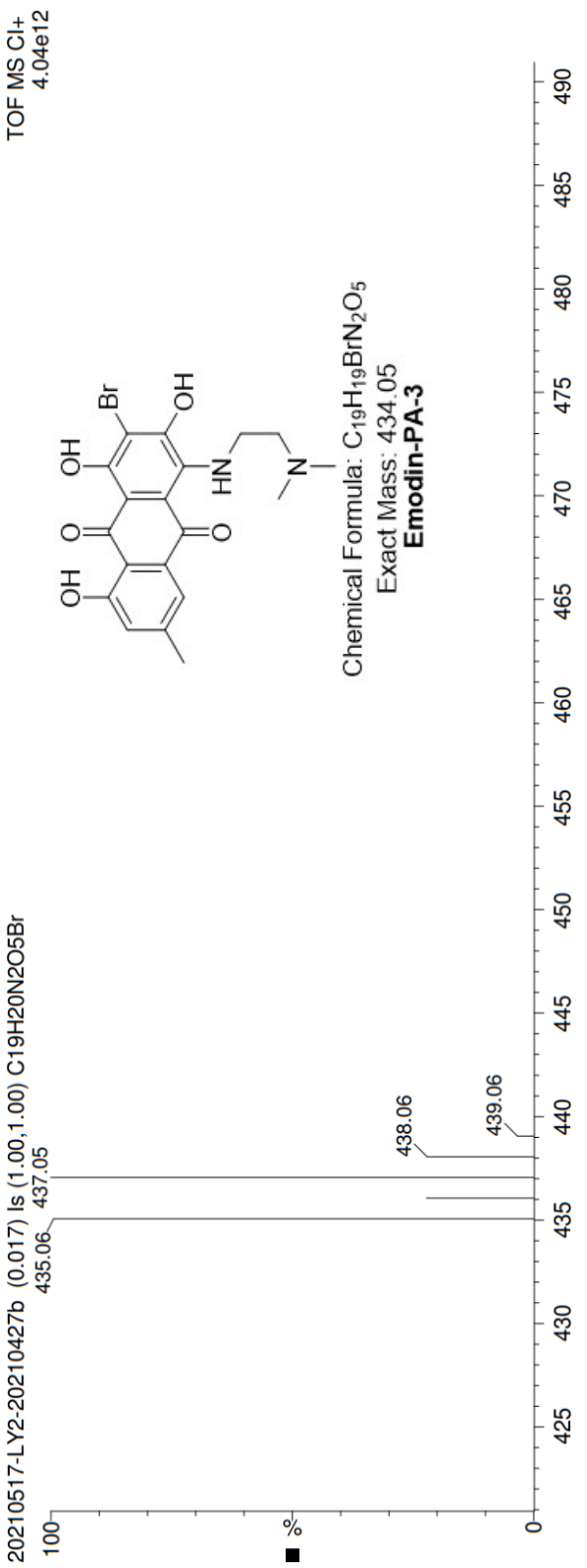
5.1. MS (ESI^+) of emodin-PA-1



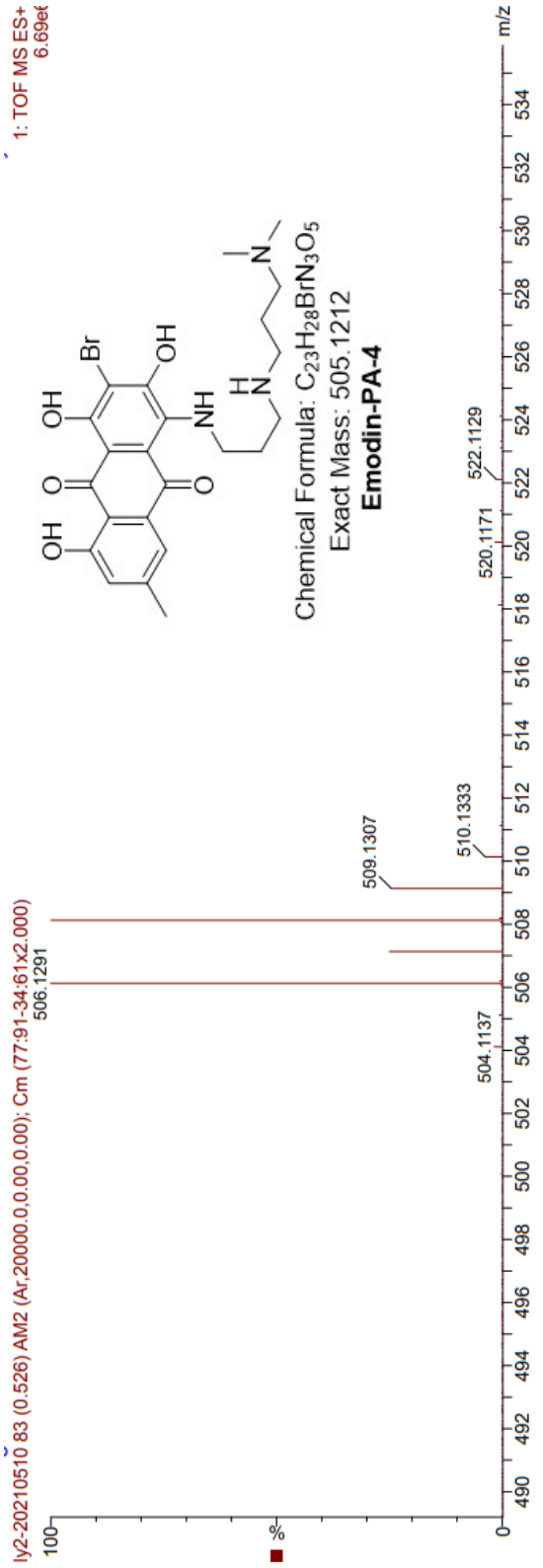
5.2. MS (ESI$^-$) of emodin-PA-2



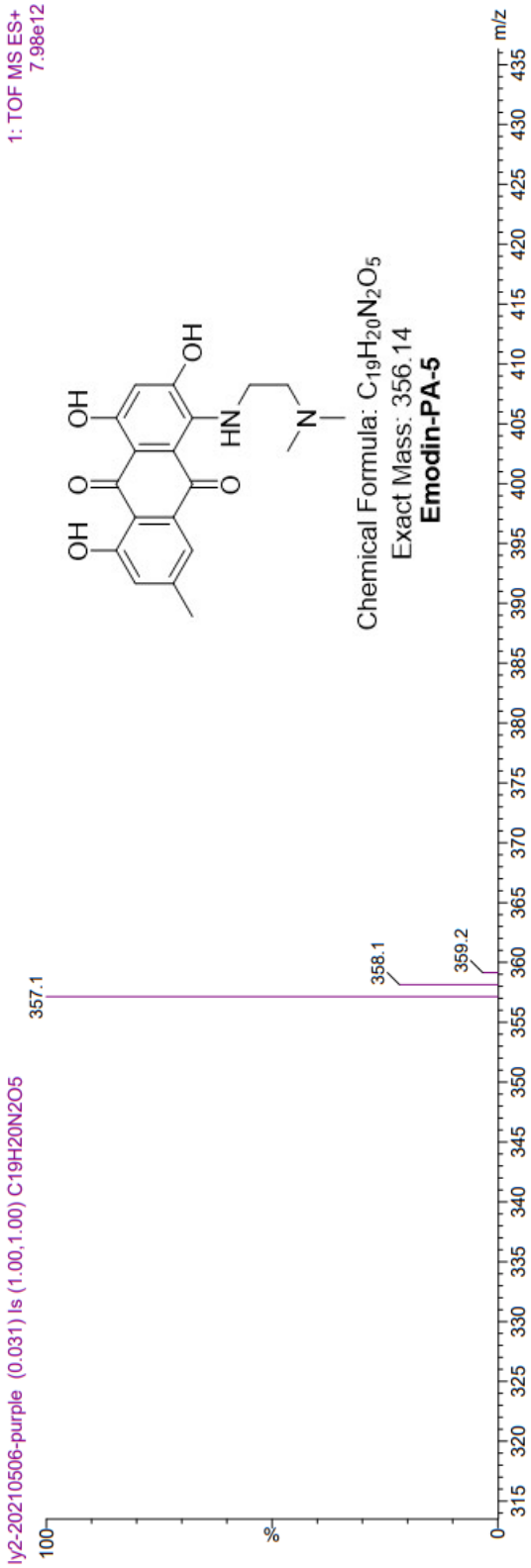
5.3. MS (DCI^+-CH_4) of emodin-PA-3



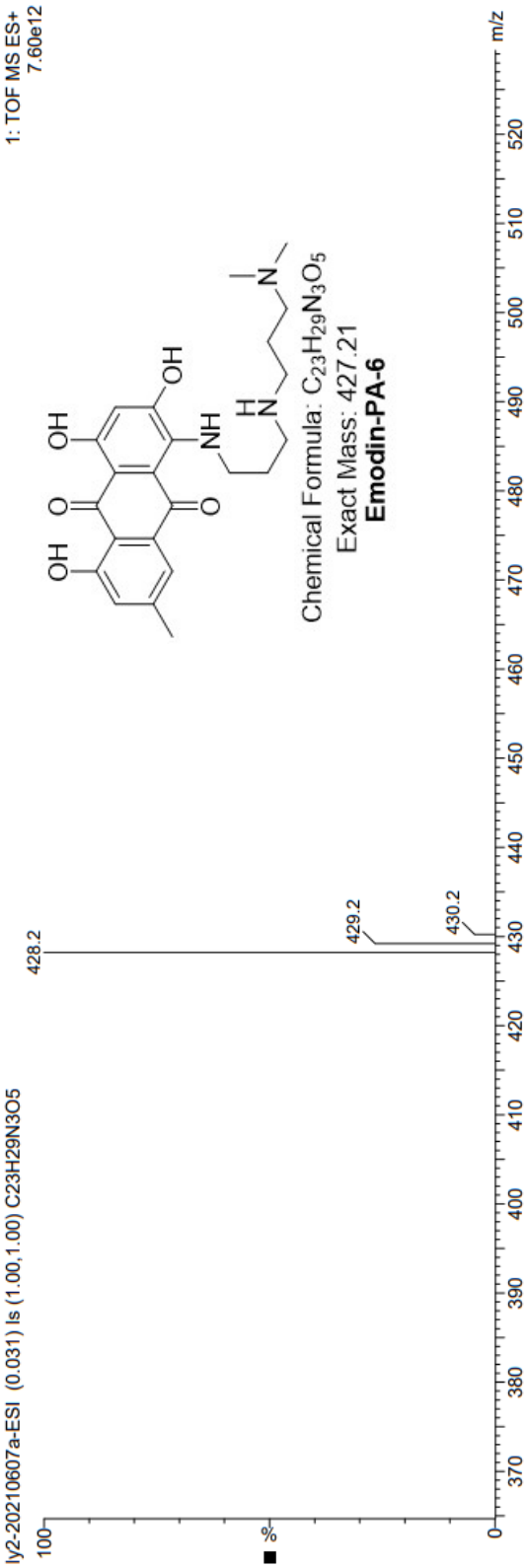
5.4. HRMS (ESI^+) of emodin-PA-4



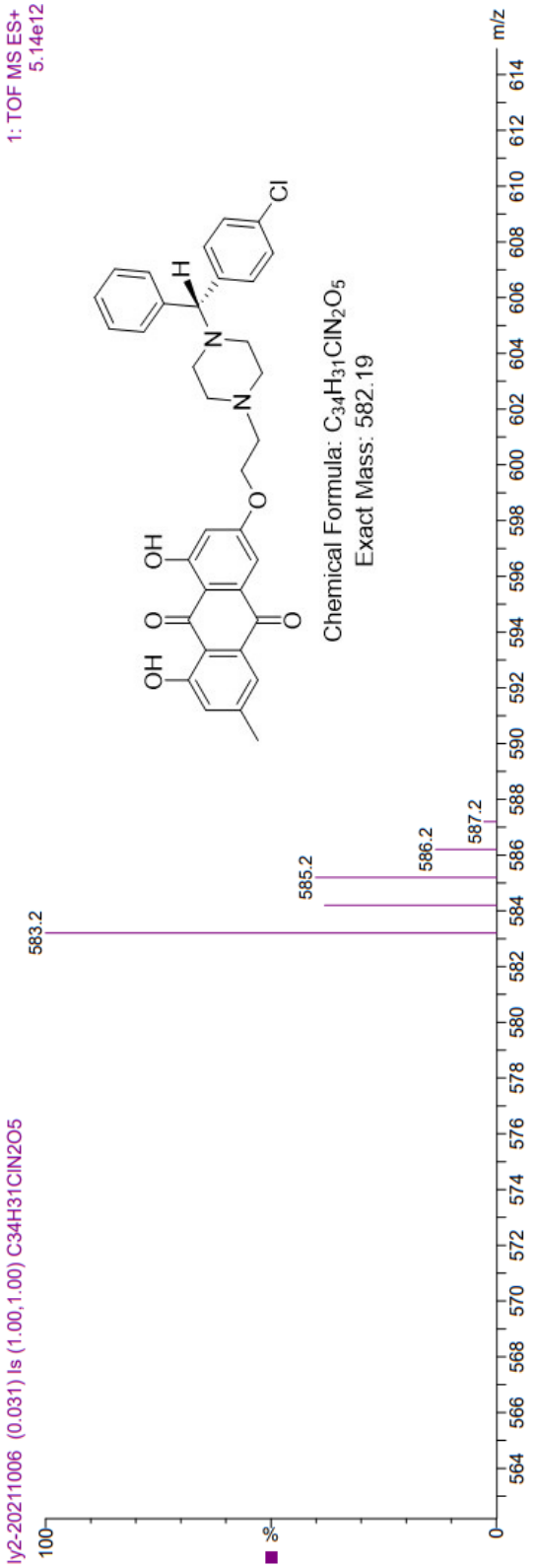
5.5. MS (ESI^+) of emodin-PA-5



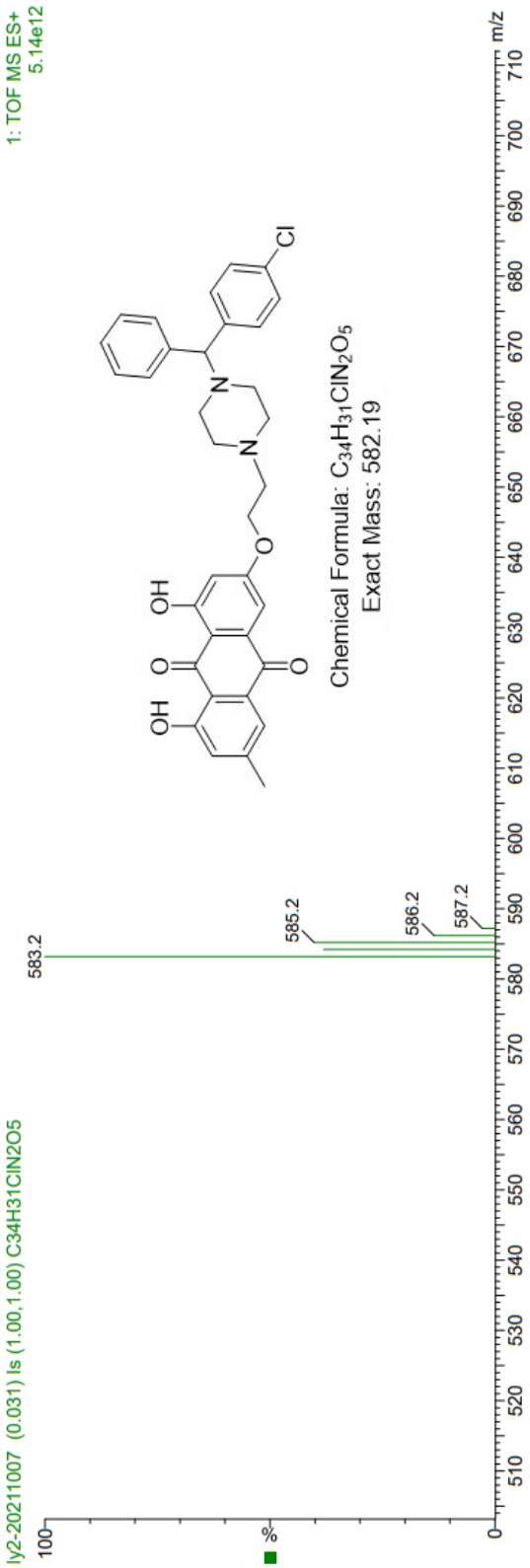
5.6. MS (ESI^+) of emodin-PA-6



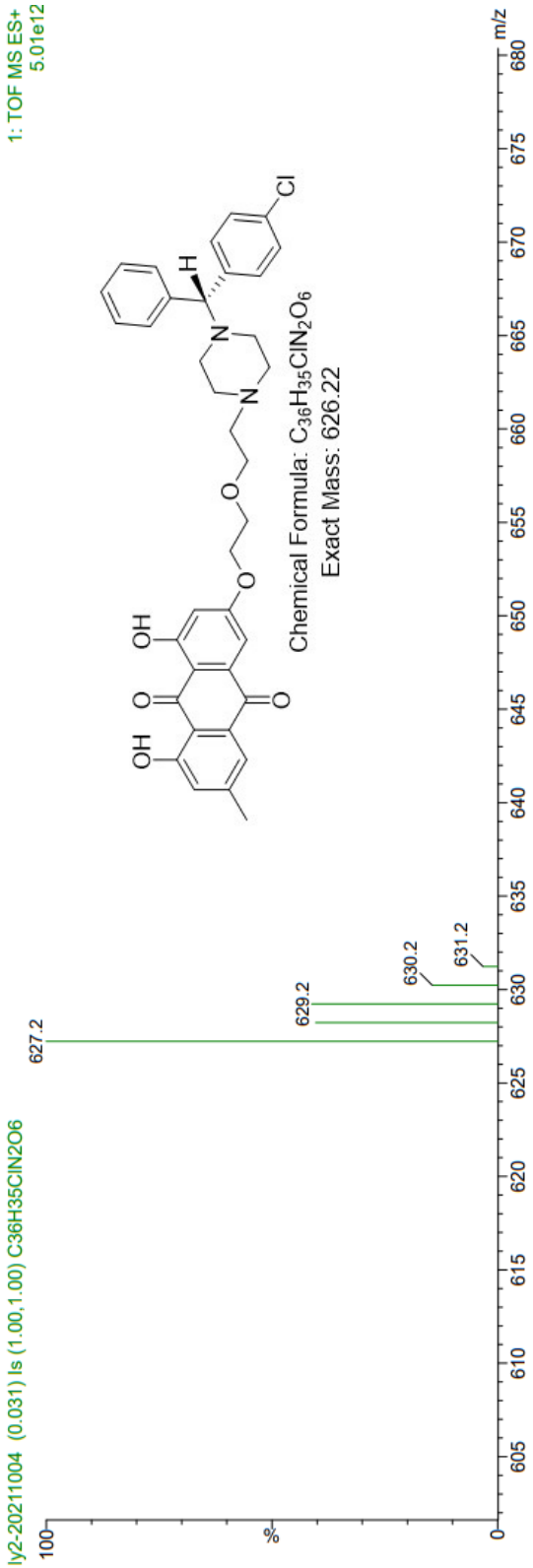
5.7. MS (ESI^+) of (*R*)-emoxyzine-1



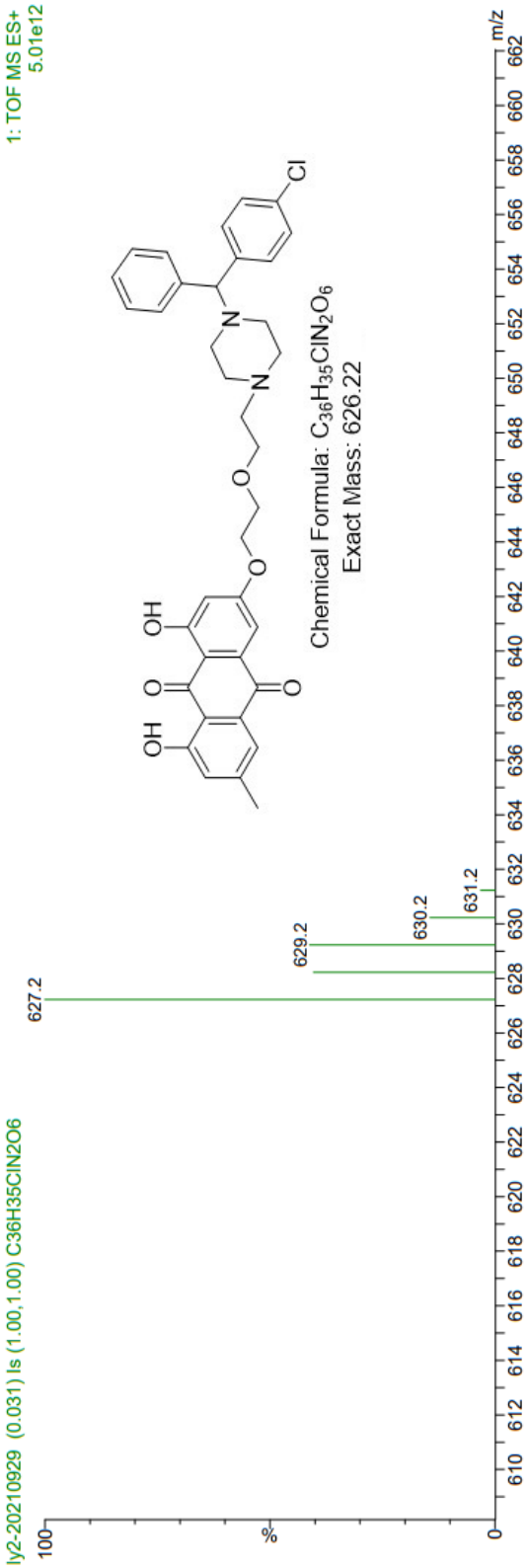
5.8. MS (ESI^+) of (*R,S*)-emoxyzine-1



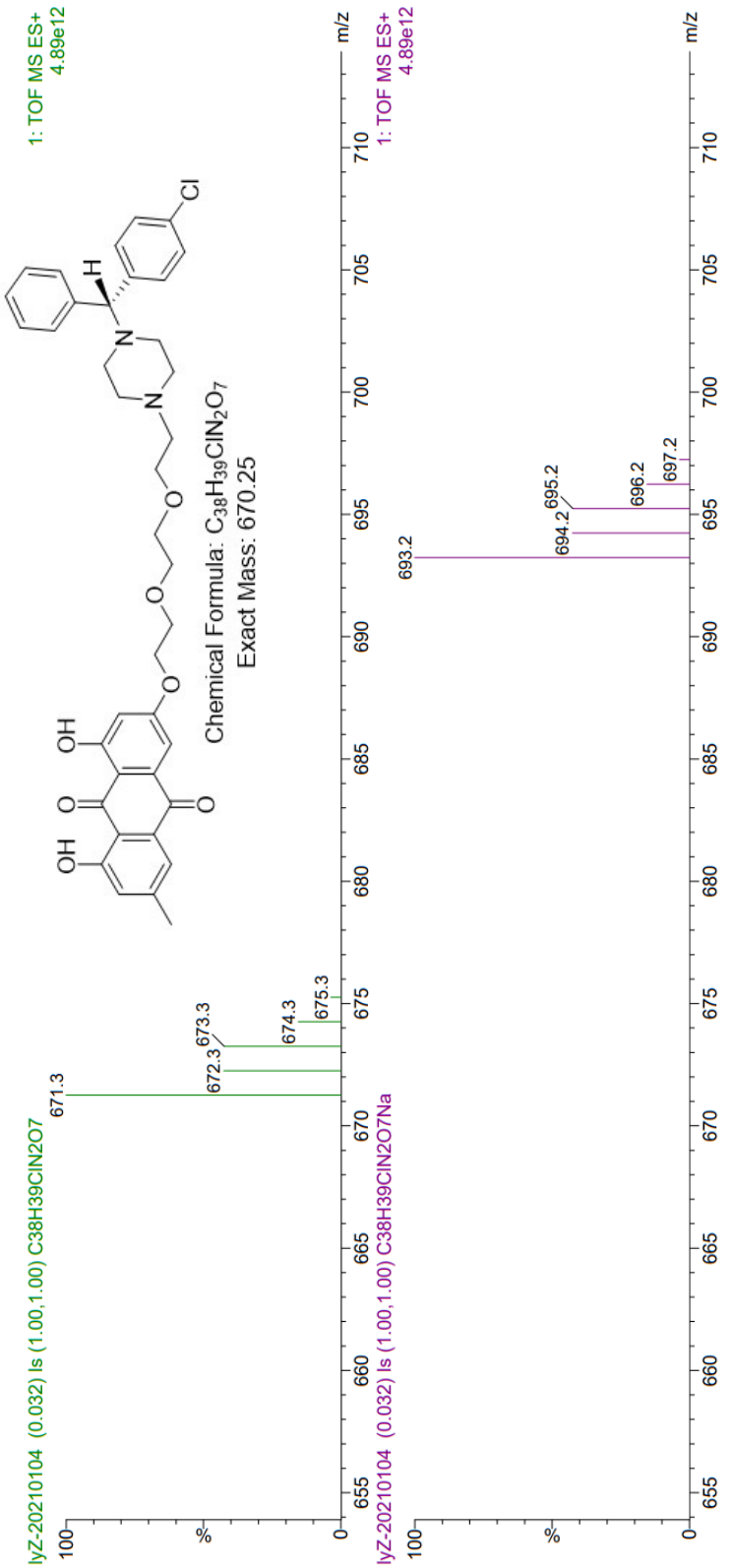
5.9. MS (ESI^+) of (*R*)-emoxyzine-2



5.10. MS (ESI^+) of (*R,S*)-emoxyzine-2



5.11. MS (ESI$^+$) of (*R*)-emoxyzine-3



5.12. MS (ESI^+) of (*R*)-emoxyzine-7