

Supplementary Material

Synthesis of 4-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione derivatives as lead scaffolds for neuroprotective agents

Ayodeji O. Egunlusi, Sarel F. Malan, and Jacques Joubert*

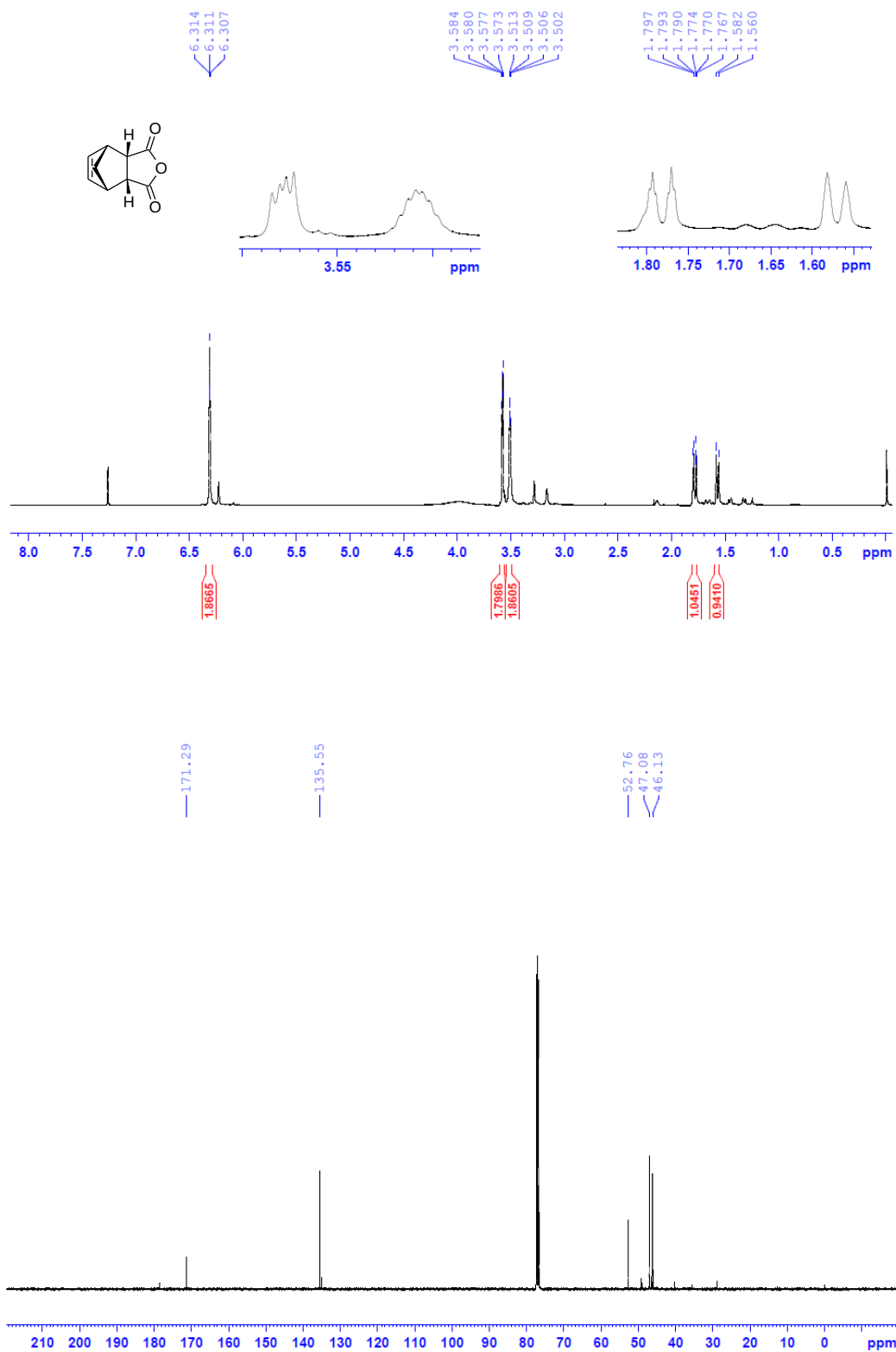
*Pharmaceutical Chemistry, School of Pharmacy, University of the Western Cape,
Private Bag X17, Bellville 7535, South Africa*

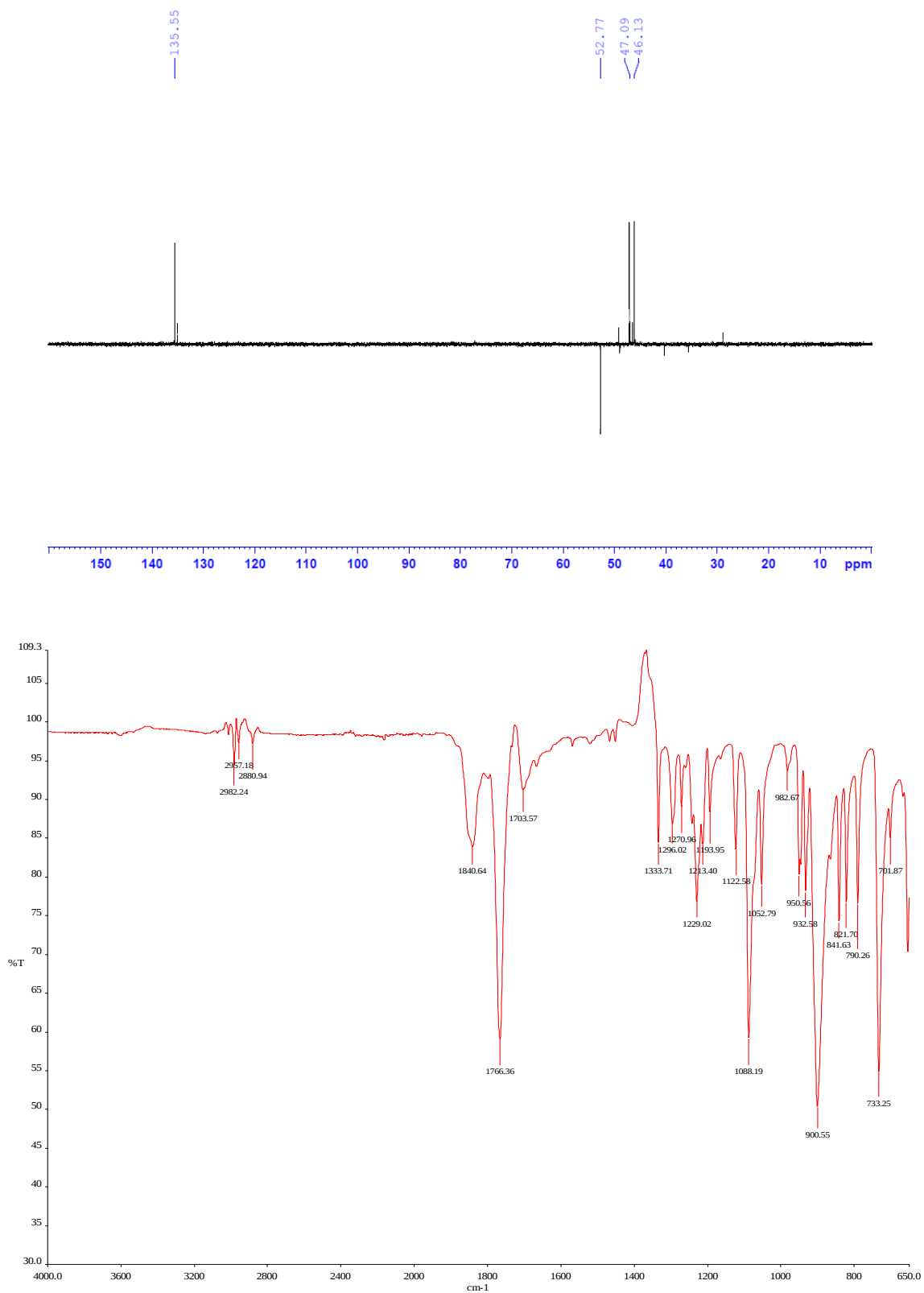
Email: jjoubert@uwc.ac.za

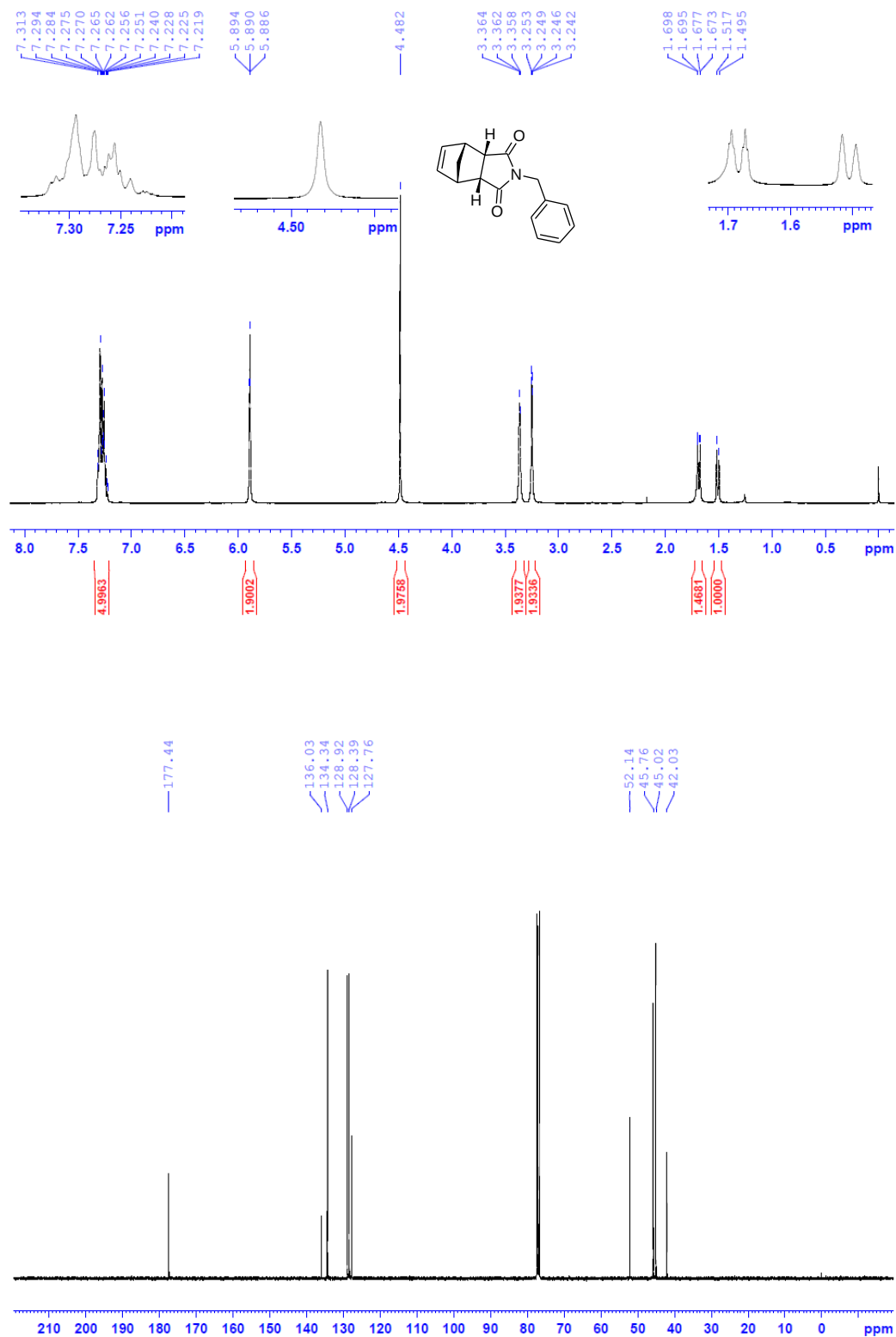
Table of Contents

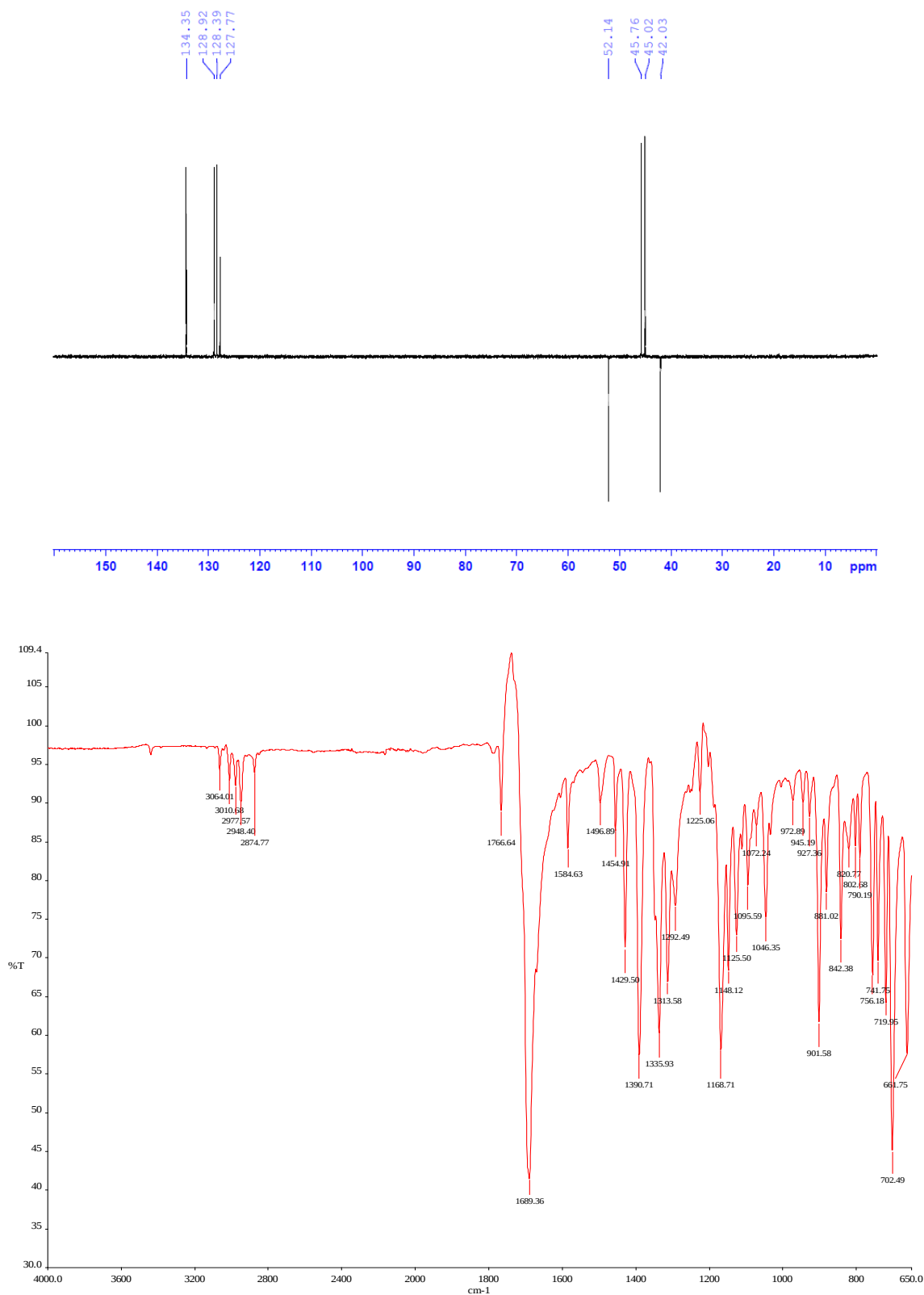
S1.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-oxatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (2).....	S3
S2.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-oxatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (2).....	S4
S3.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-benzyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (3)	S5
S4.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-benzyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (3)	S6
S5.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-benzyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (3)	S7
S6.	¹ H and ¹³ C spectra of <i>N,N'</i> -dibenzylbicyclo[2.2.1]-hept-5-ene-2,3-dicarboxamide (4).....	S8
S7.	DEPT-135 and IR spectra of <i>N,N'</i> -dibenzylbicyclo[2.2.1]-hept-5-ene-2,3-dicarboxamide (4).....	S9
S8.	HRMS spectra of <i>N,N'</i> -dibenzylbicyclo[2.2.1]-hept-5-ene-2,3-dicarboxamide (4).....	S10
S9.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(1-piperidyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (5)....	S11
S10.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(1-piperidyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (5)	S12
S11.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(1-piperidyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (5).....	S13
S12.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-prop-2-ynyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (6)	S14
S13.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-prop-2-ynyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (6)	S15
S14.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-prop-2-ynyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (6)	S16
S15.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-propyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (7)	S17
S16.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-propyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (7) ...	S18
S17.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-propyl-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (7)	S19
S18.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-anilino-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (8).....	S20
S19.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-anilino-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (8)...	S21
S20.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-anilino-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (8)	S22
S21.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(2-aminoethyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (9)	S23
S22.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(2-aminoethyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (9)	S24
S23.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(2-aminoethyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (9)	S25
S24.	¹ H and ¹³ C spectra of 3,5-dioxo-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-en-4-yl]ethyl]-4-azatricyclo[5.2.1.0 ^{2,6}]dec- 8-ene-3,5-dione (10)	S26

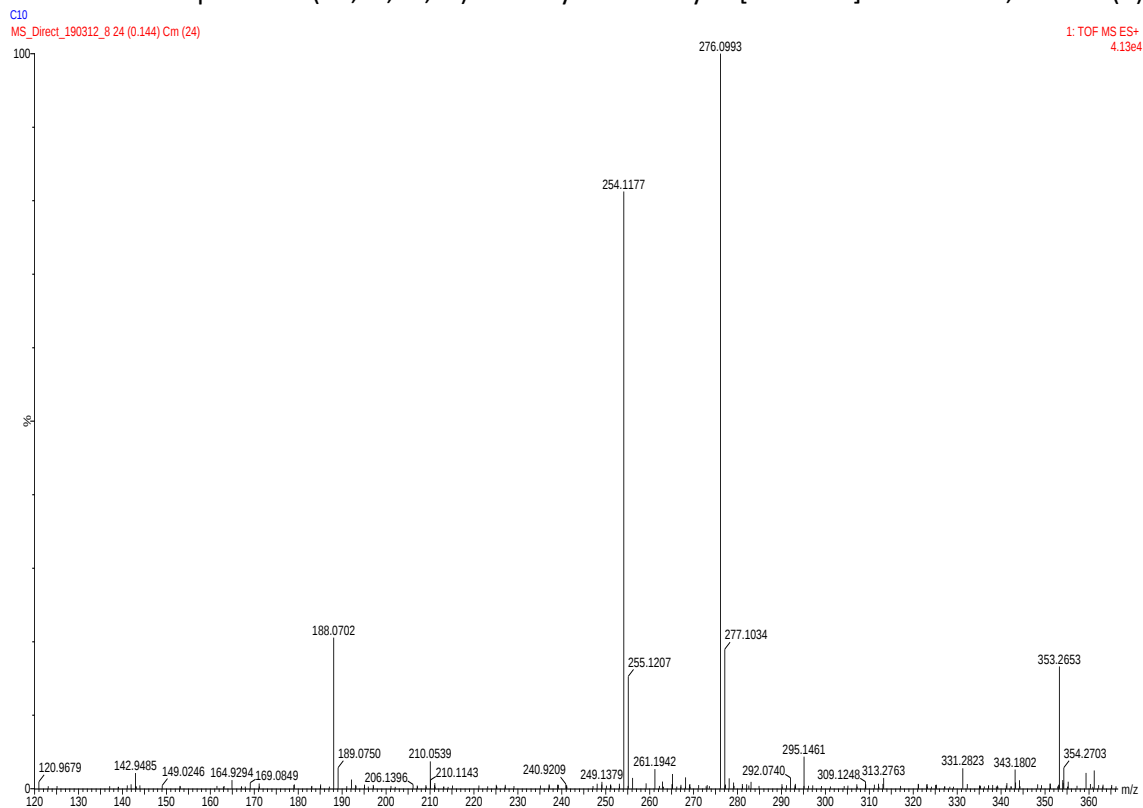
S25.	DEPT-135 and IR spectra of 3,5-dioxo-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-en-4-yl]ethyl]-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (10).....	S27
S26.	HRMS spectra of 3,5-dioxo-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-en-4-yl]ethyl]-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (10)	S28
S27.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(3-aminopropyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (11)	S29
S28.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(3-aminopropyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (11)	S30
S29.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(3-aminopropyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (11) ..	S31
S30.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(4-aminobutyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (12)	S32
S31.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(4-aminobutyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (12)	S33
S32.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-(4-aminobutyl)-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (12)	S34
S33.	¹ H and ¹³ C spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-[2-(dimethylamino)ethyl]-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (13)	S35
S34.	DEPT-135 and IR spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-[2-(dimethylamino)ethyl]-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (13).....	S36
S35.	HRMS spectra of (1 <i>R</i> ,2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i>)-4-[2-(dimethylamino)ethyl]-4-azatricyclo[5.2.1.0 ^{2,6}]dec-8-ene-3,5-dione (13)	S37

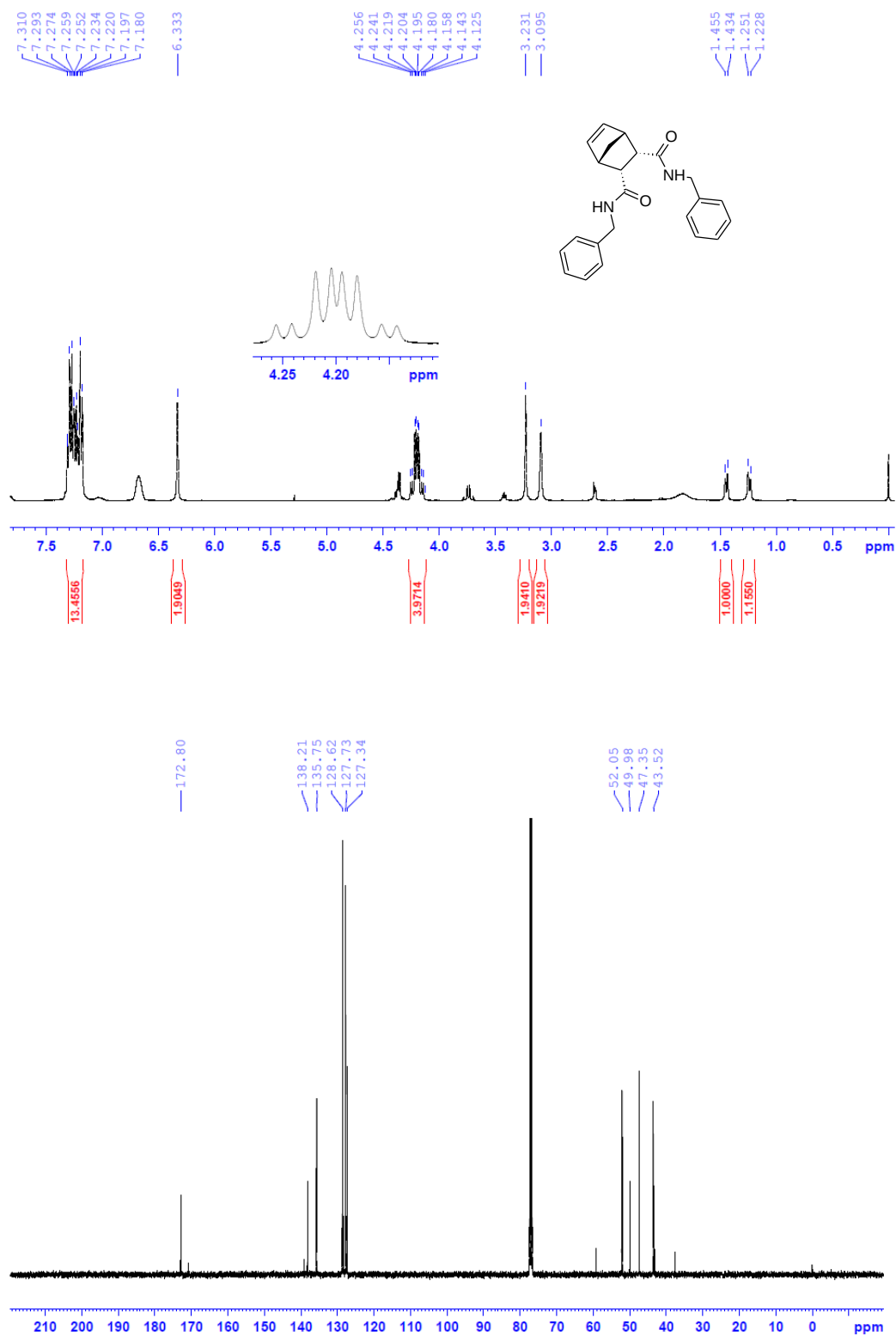
S1. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**2**)

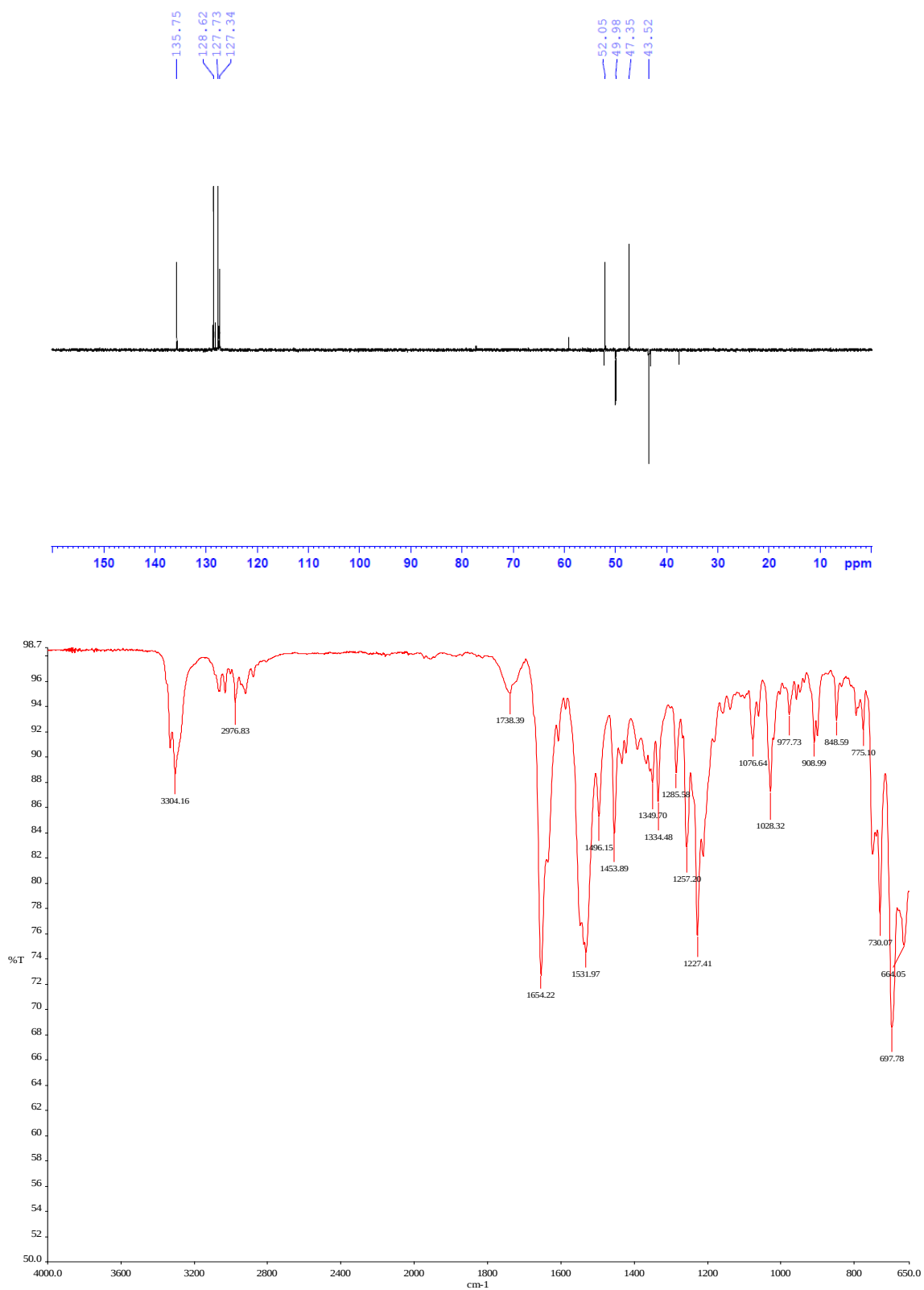
S2. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**2**)

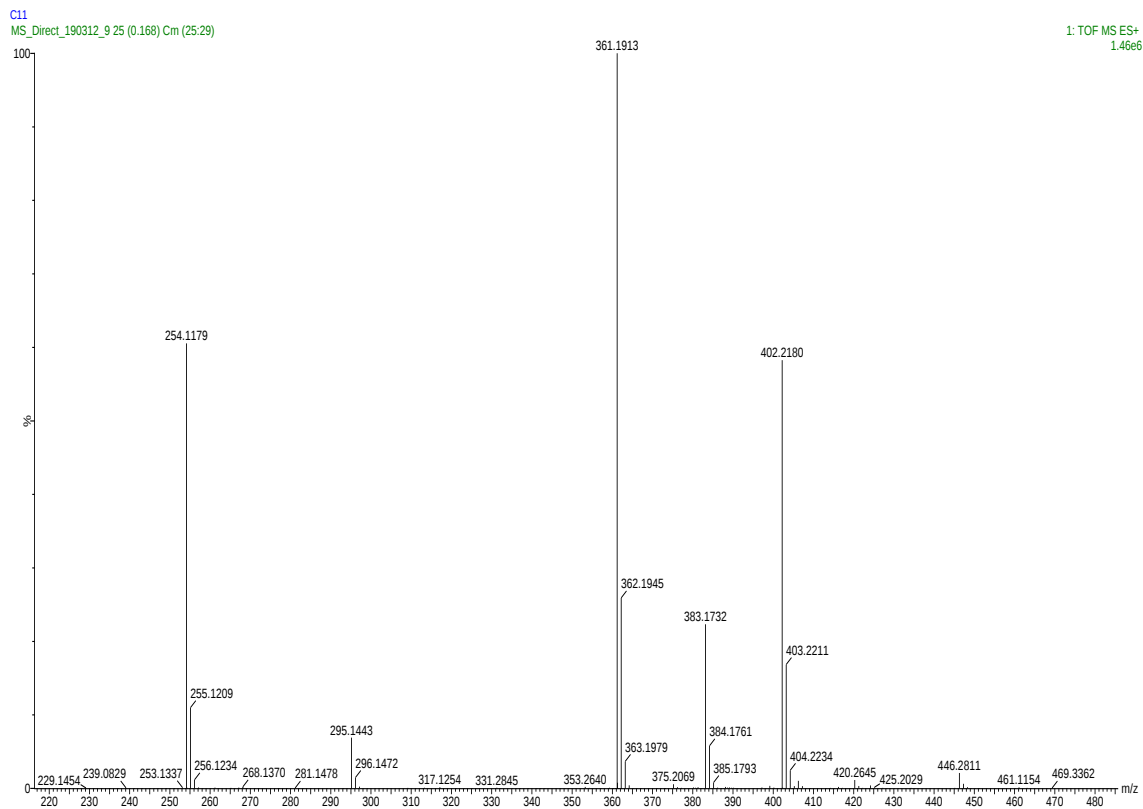
S3. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-benzyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**3**)

S4. DEPT-135 and IR spectra of (1R,2S,6R,7S)-4-benzyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**3**)

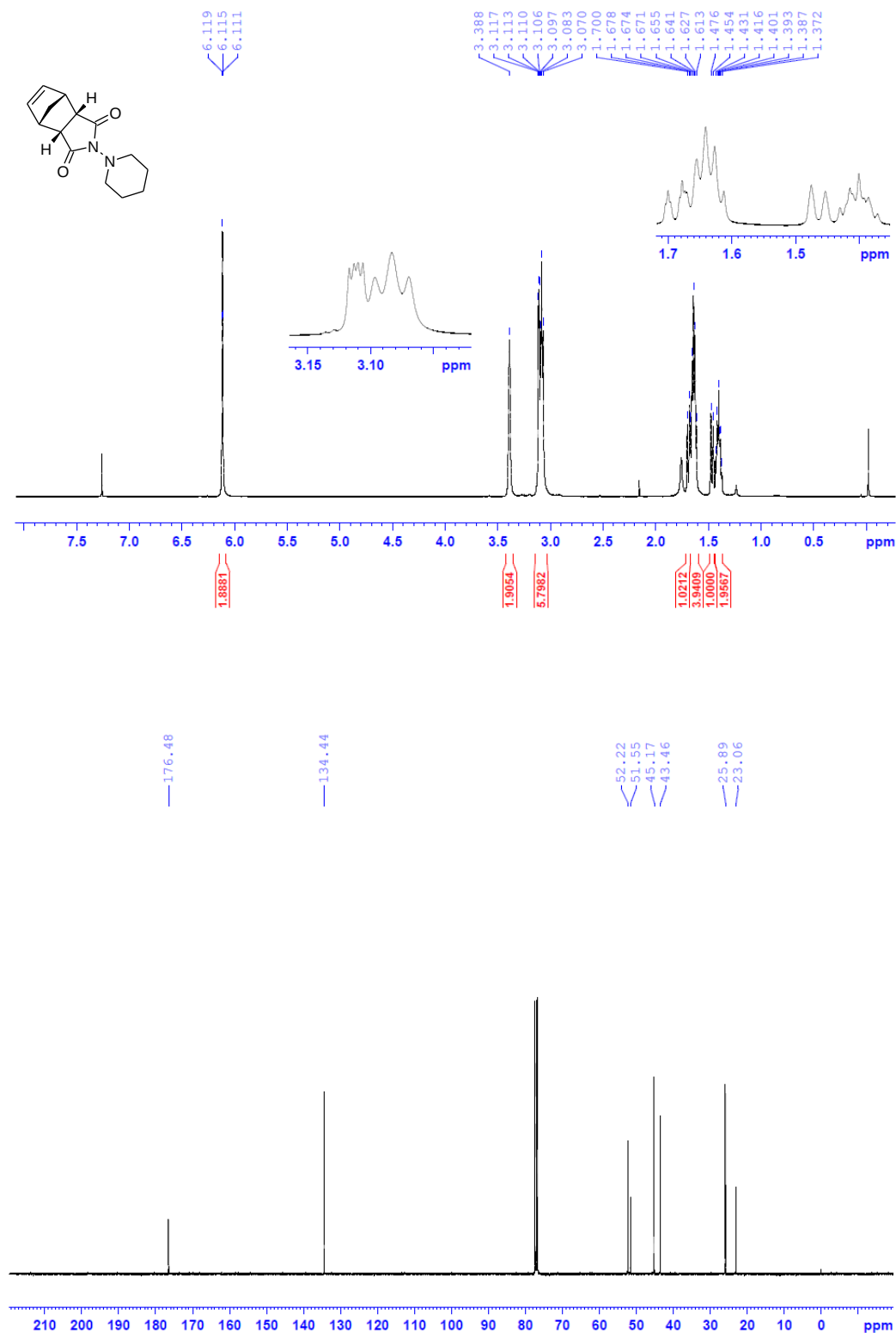
S5. HRMS spectra of (1R,2S,6R,7S)-4-benzyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**3**)

S6. ^1H and ^{13}C spectra of *N,N'*-dibenzylbicyclo[2.2.1]-hept-5-ene-2,3-dicarboxamide (**4**)

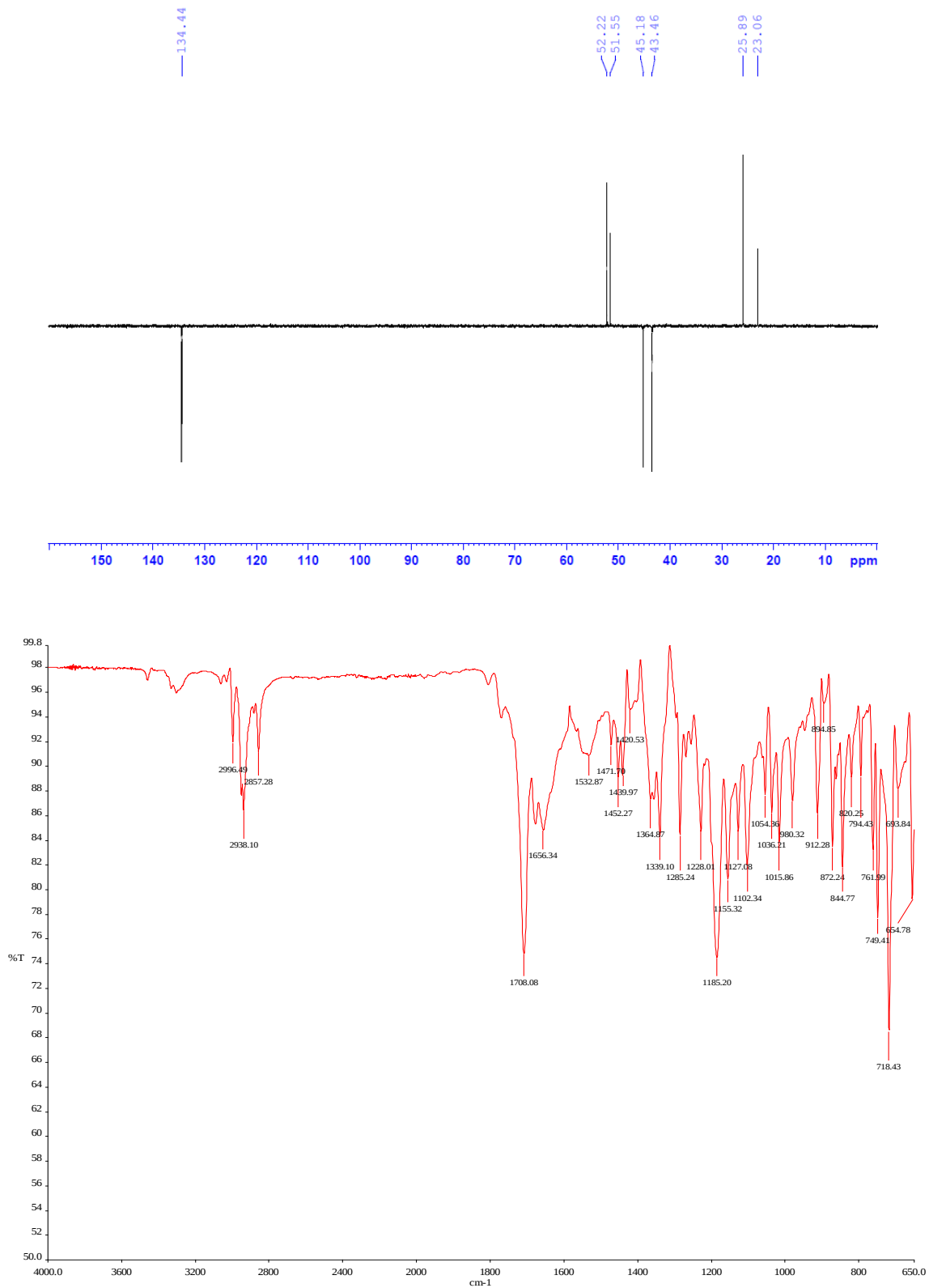
S7. DEPT-135 and IR spectra of *N,N'*-dibenzylbicyclo[2.2.1]-hept-5-ene-2,3-dicarboxamide (4)

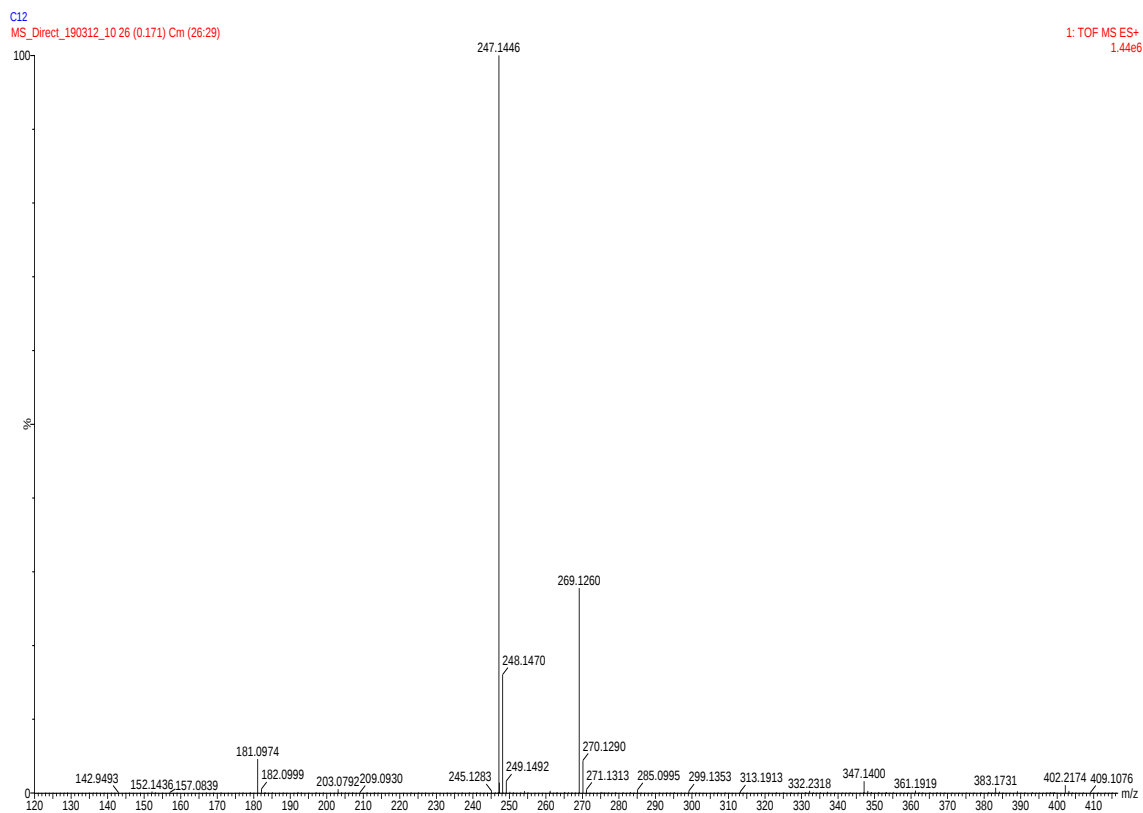
S8. HRMS spectra of *N,N'*-dibenzylbicyclo[2.2.1]-hept-5-ene-2,3-dicarboxamide (**4**)

S9. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-(1-piperidyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (5)

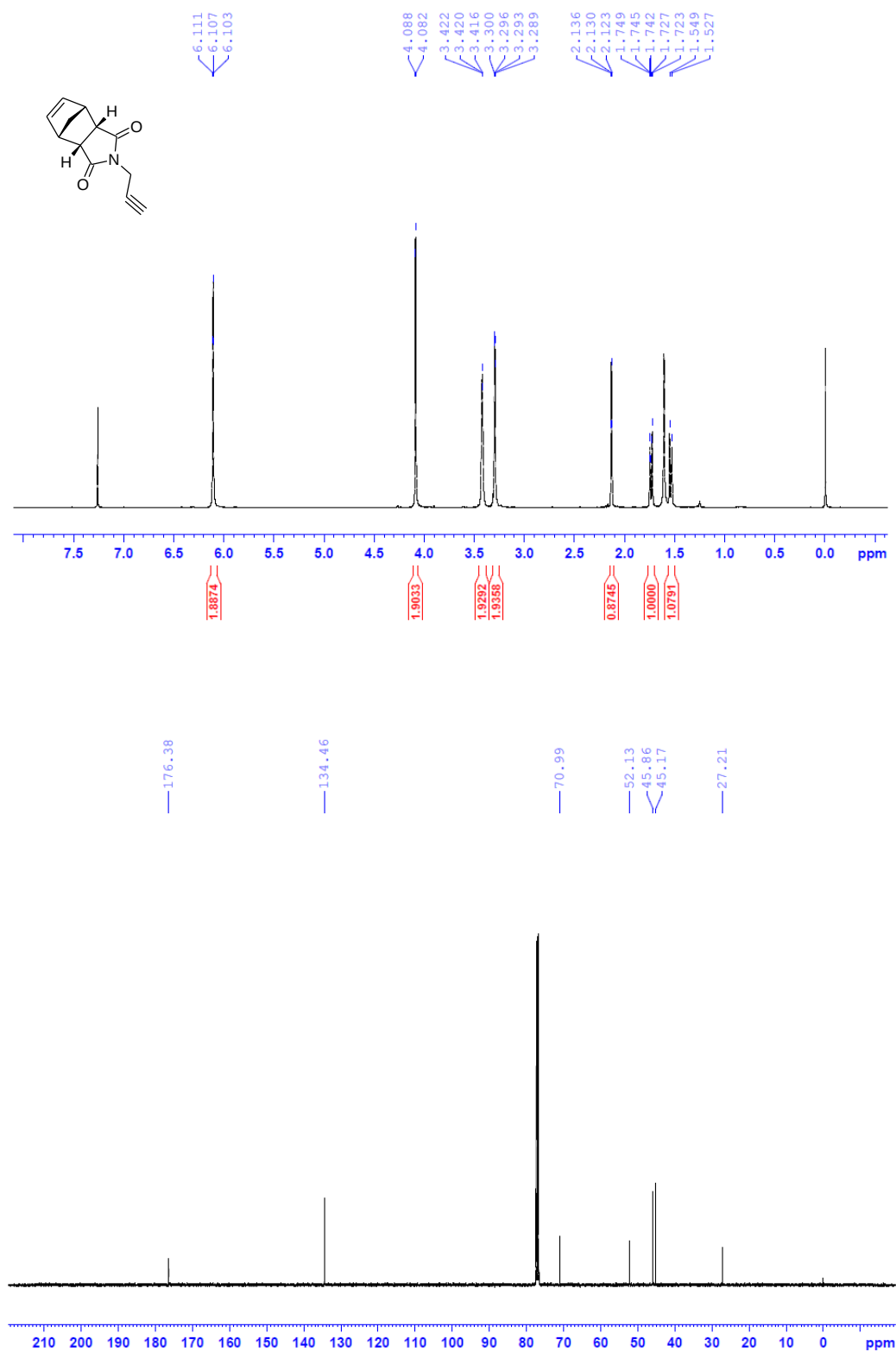


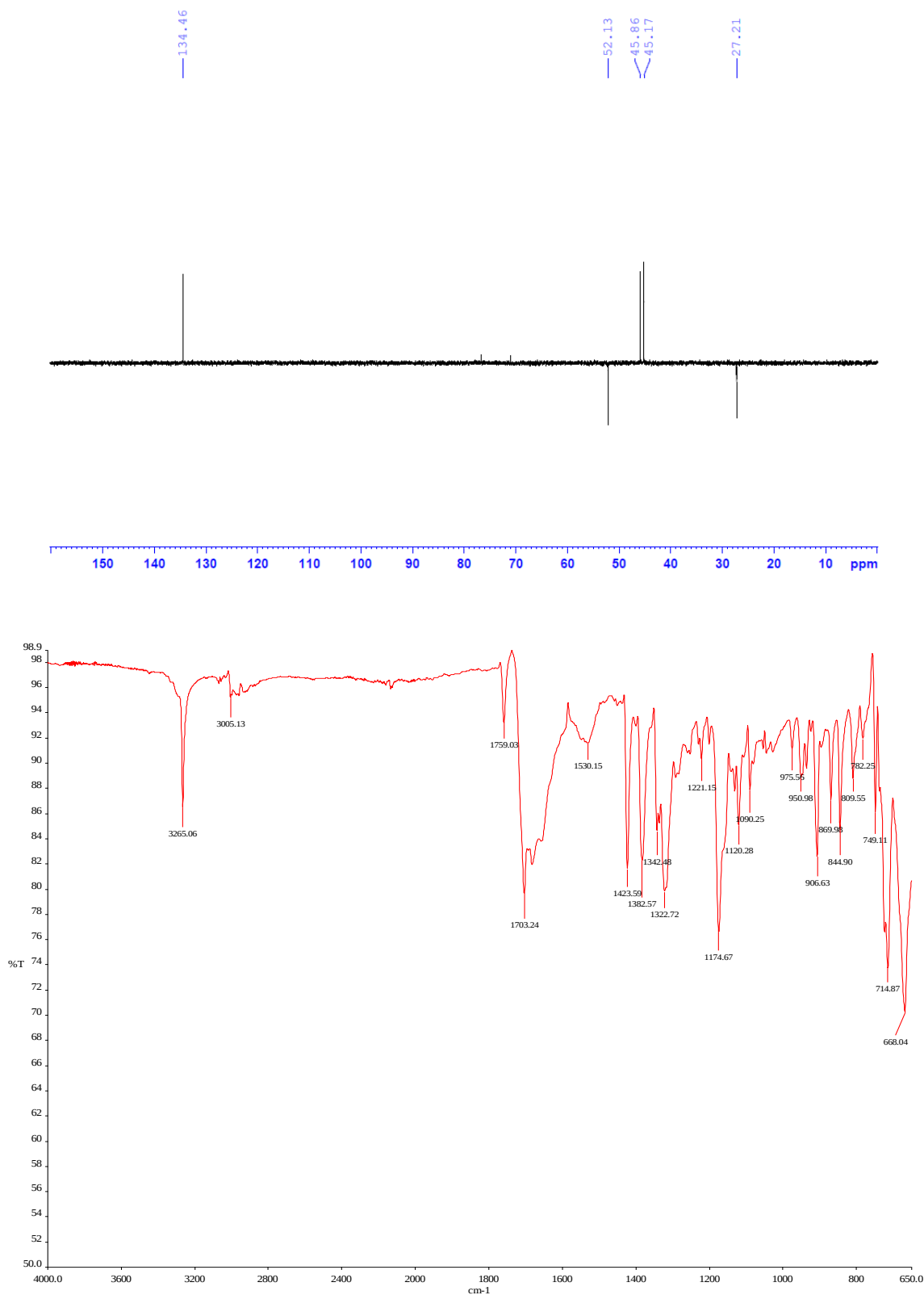
S10. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-(1-piperidyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**5**)

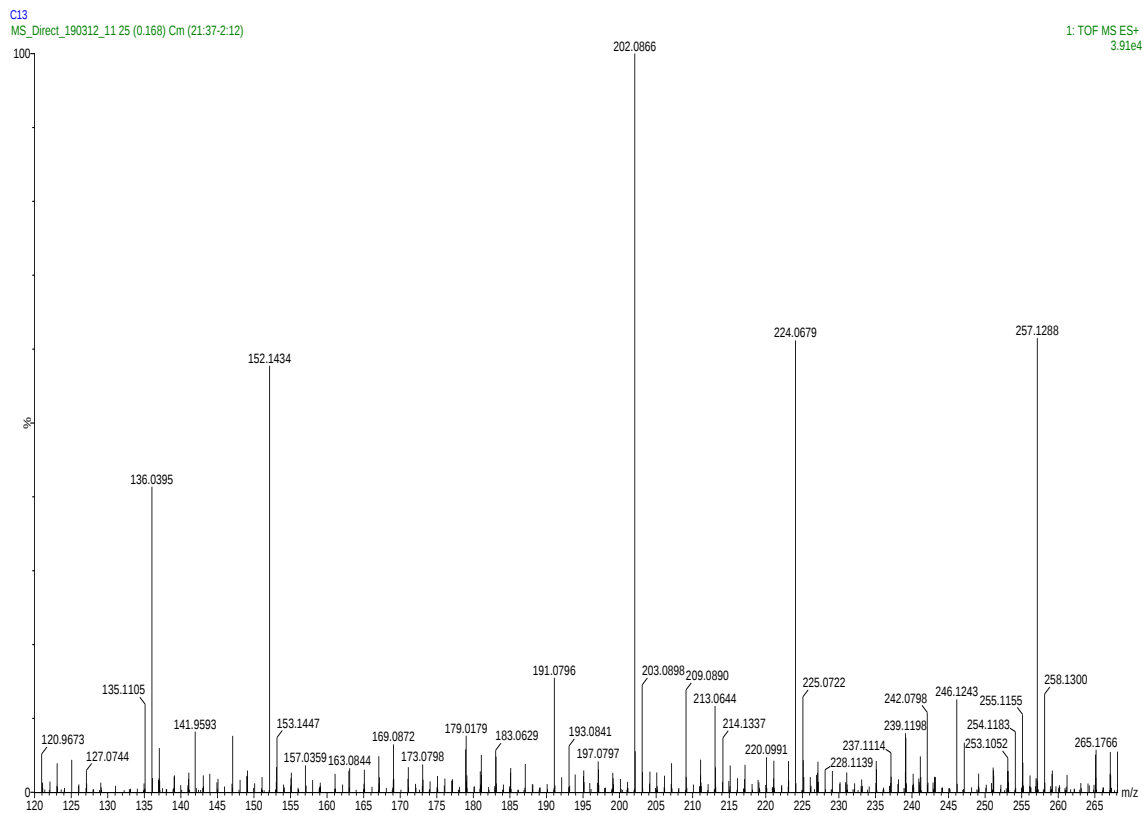


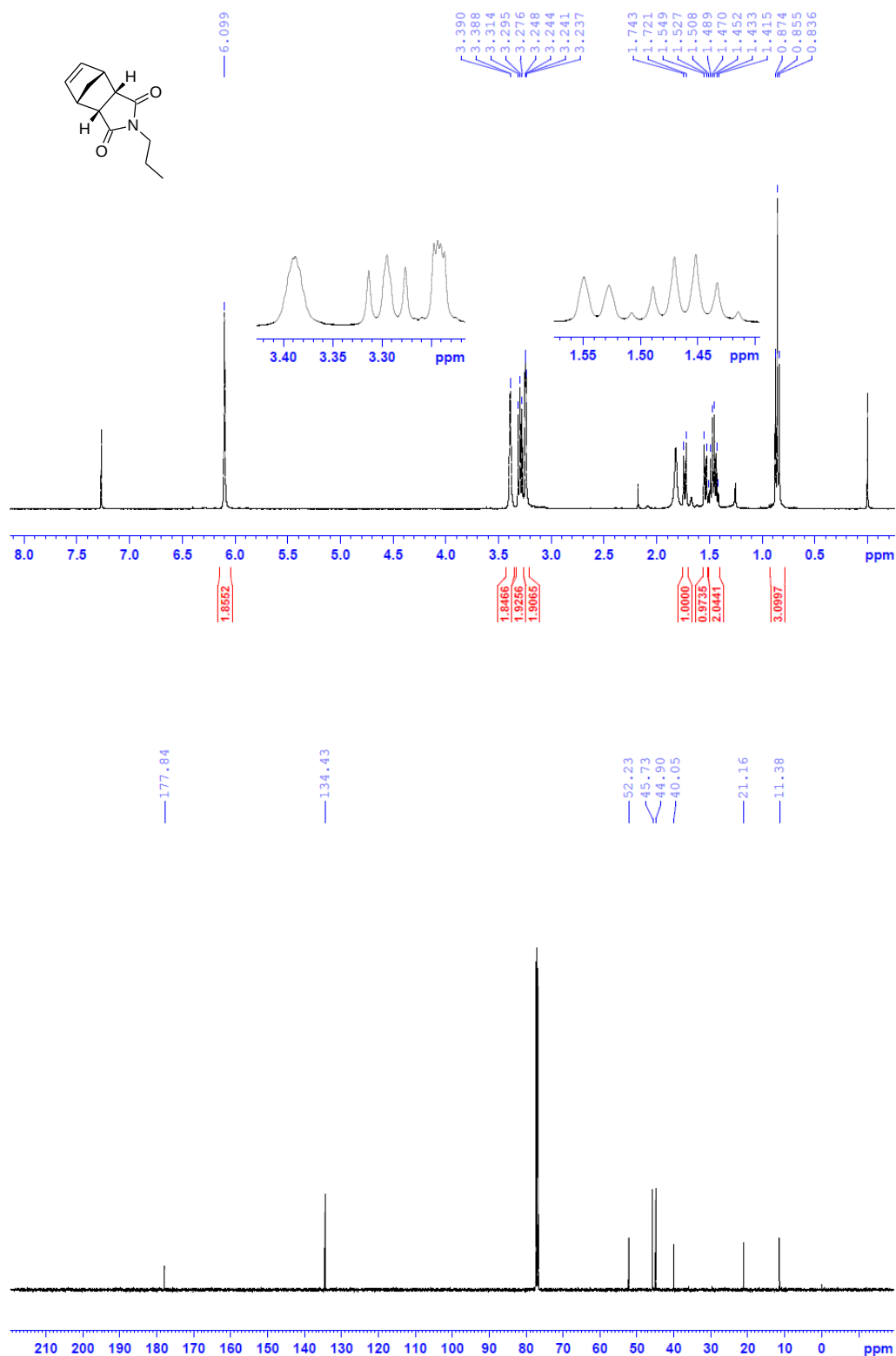
S11. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-(1-piperidyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (5)

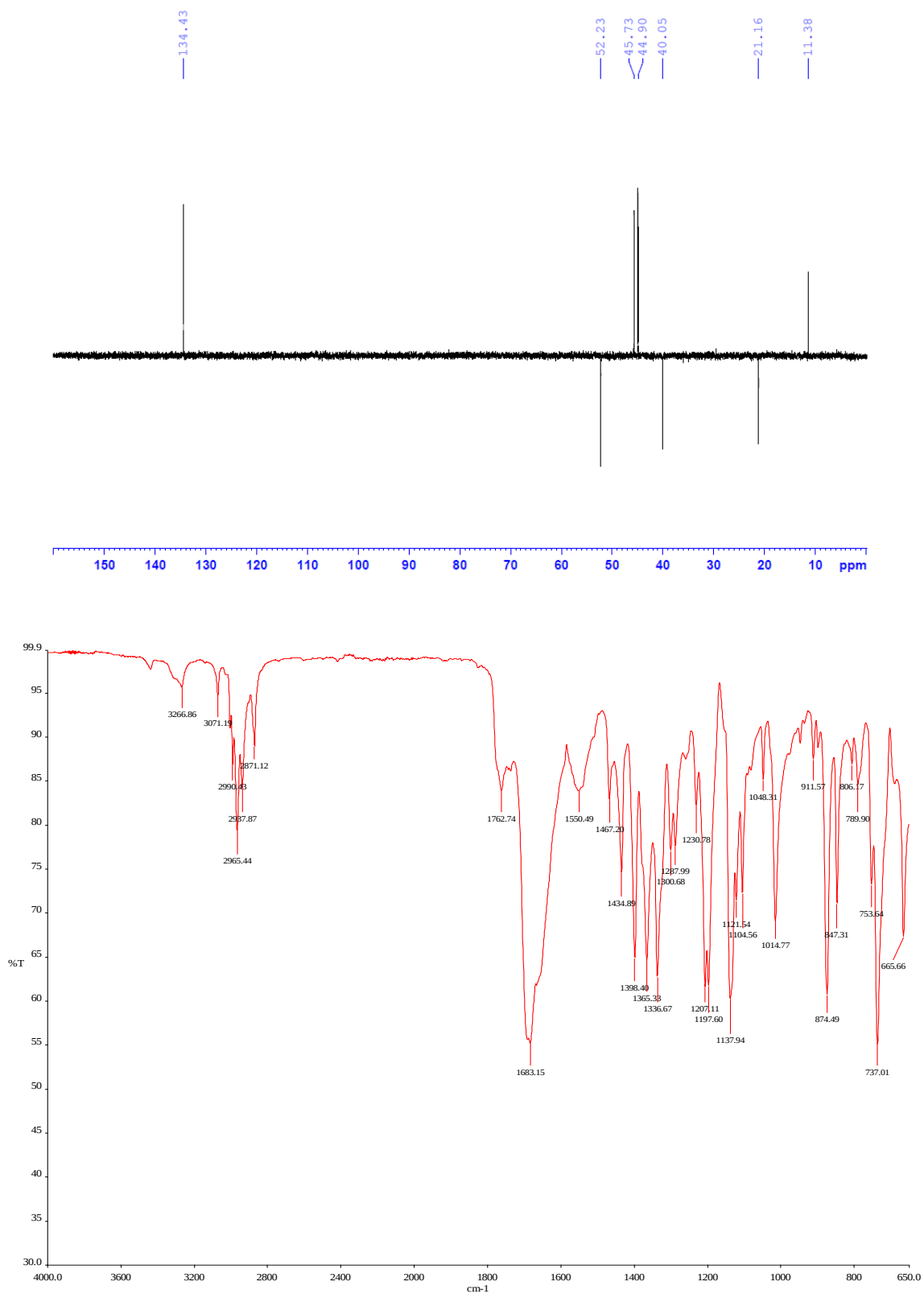
S12. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-prop-2-ynyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**6**)

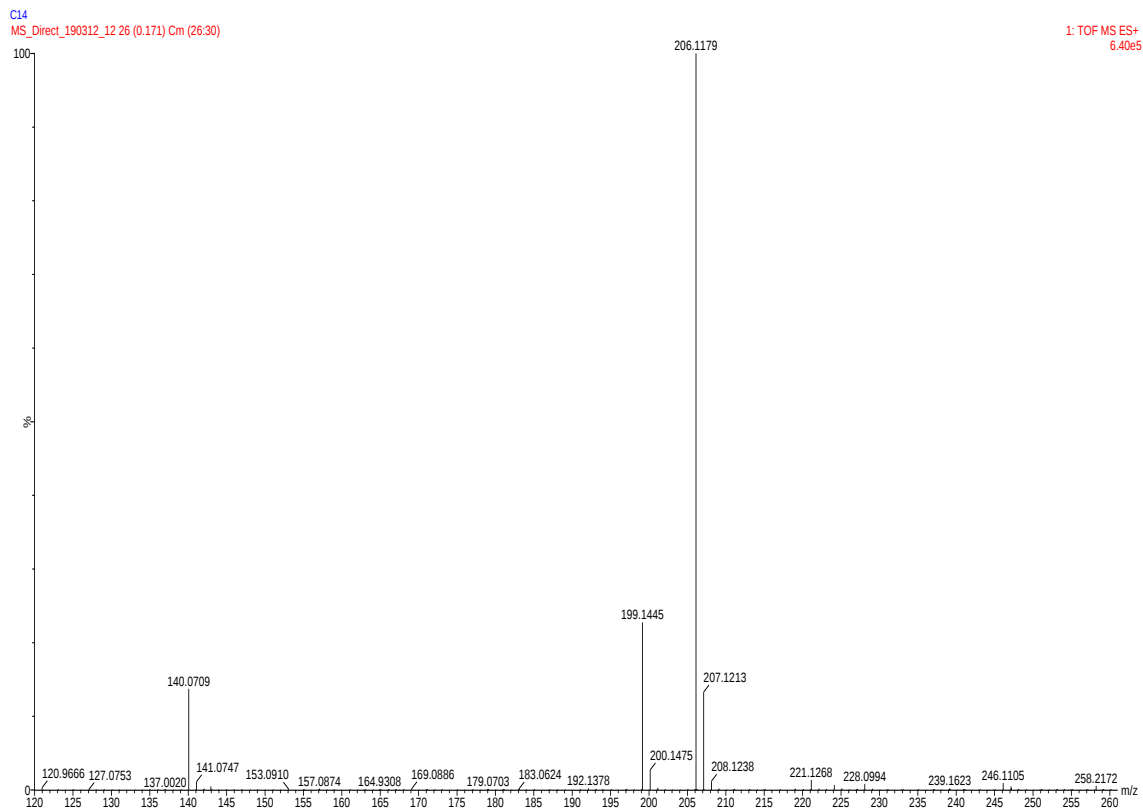


S13. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-prop-2-ynyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (6)

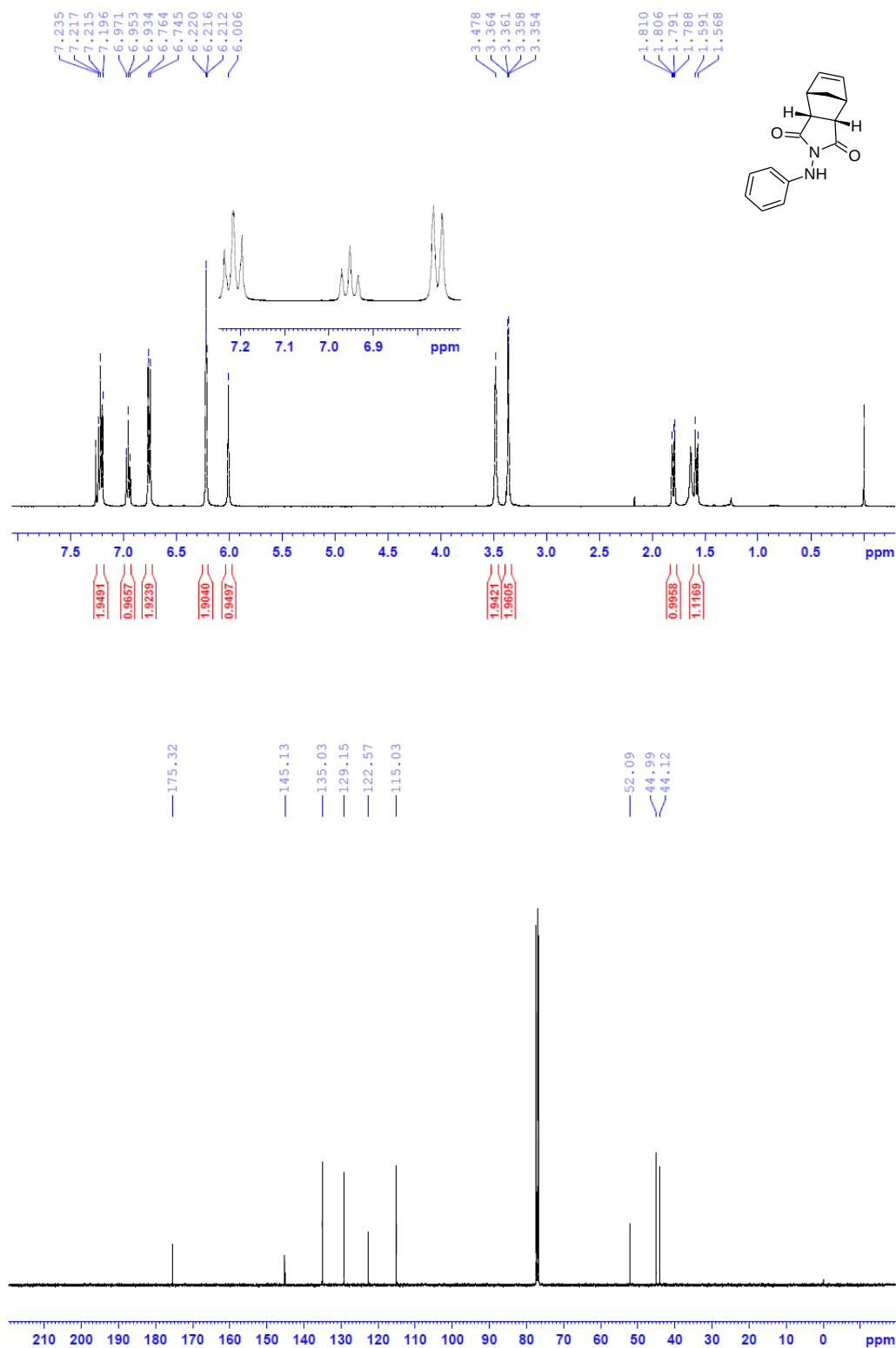
S14. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-prop-2-ynyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**6**)

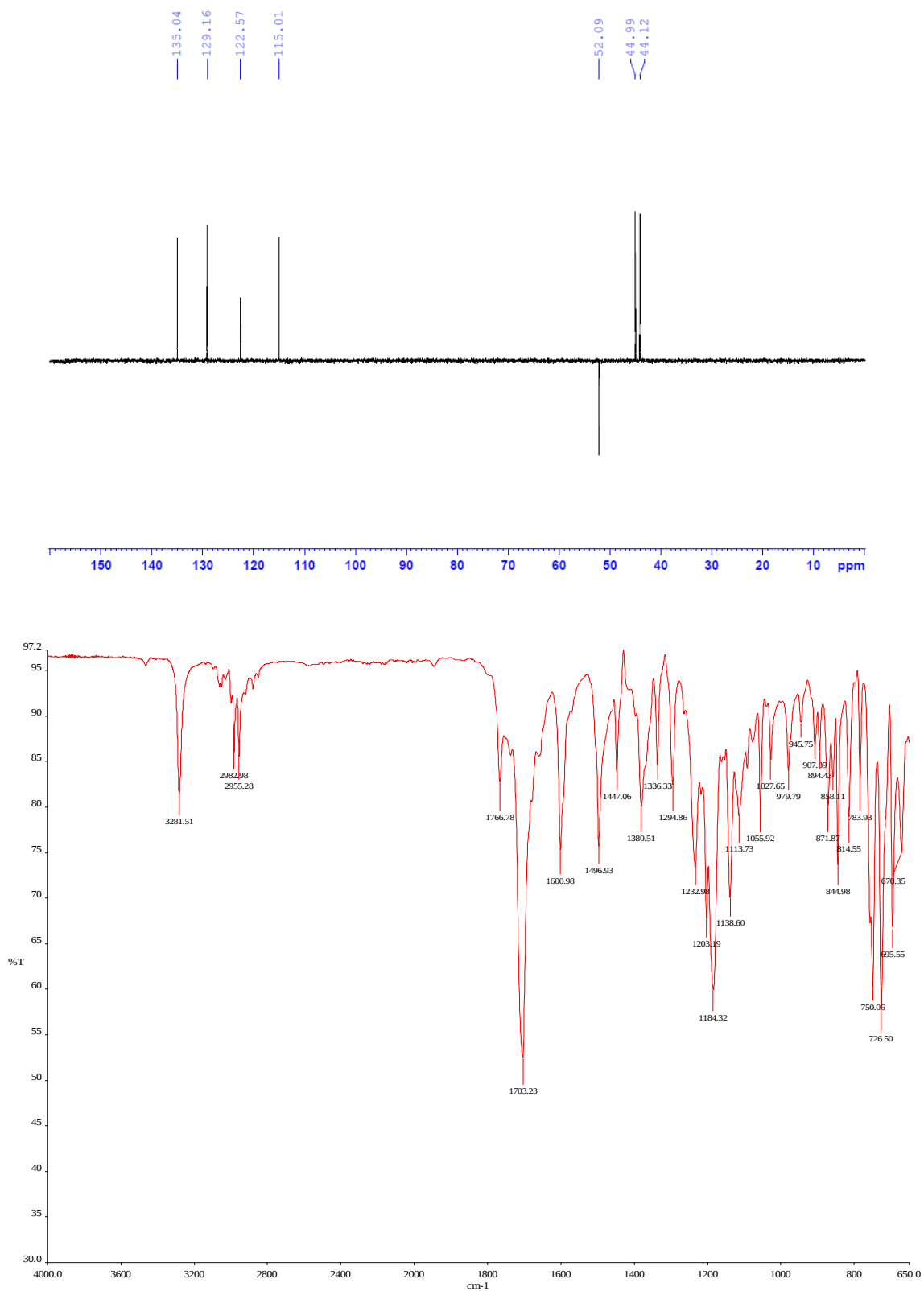
S15. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-propyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (7)

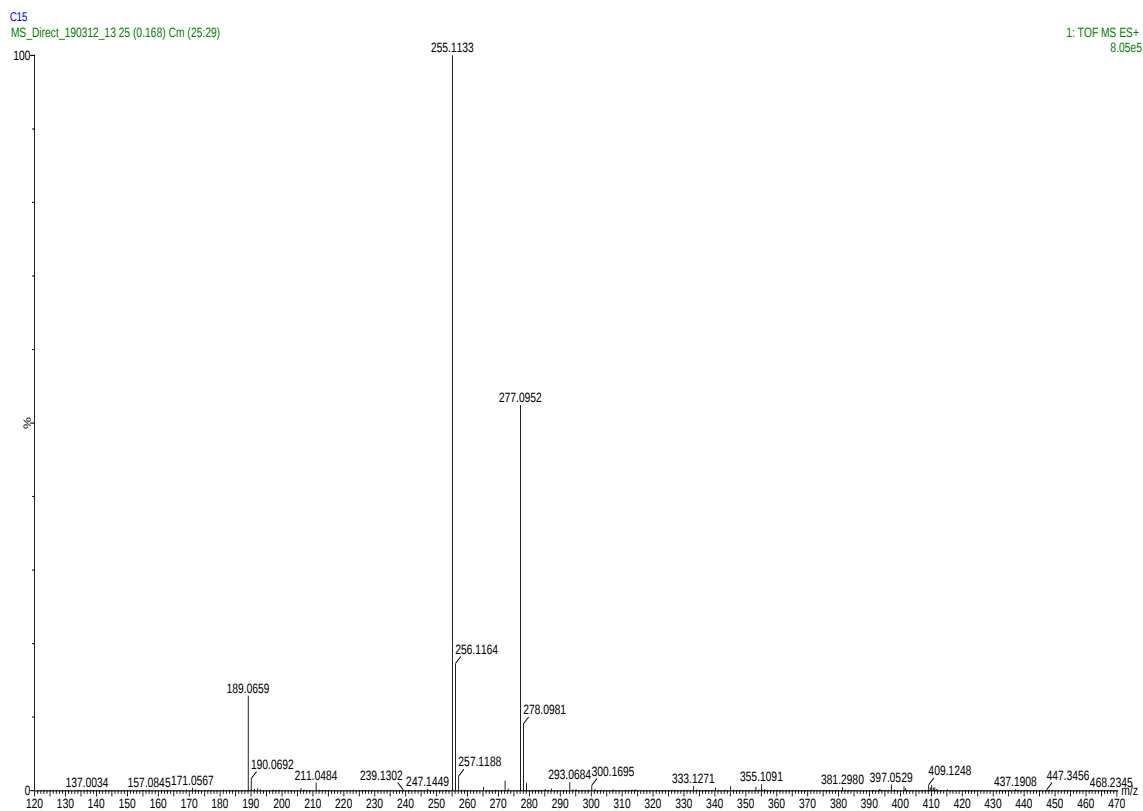
S16. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-propyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**7**)

S17. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-propyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**7**)

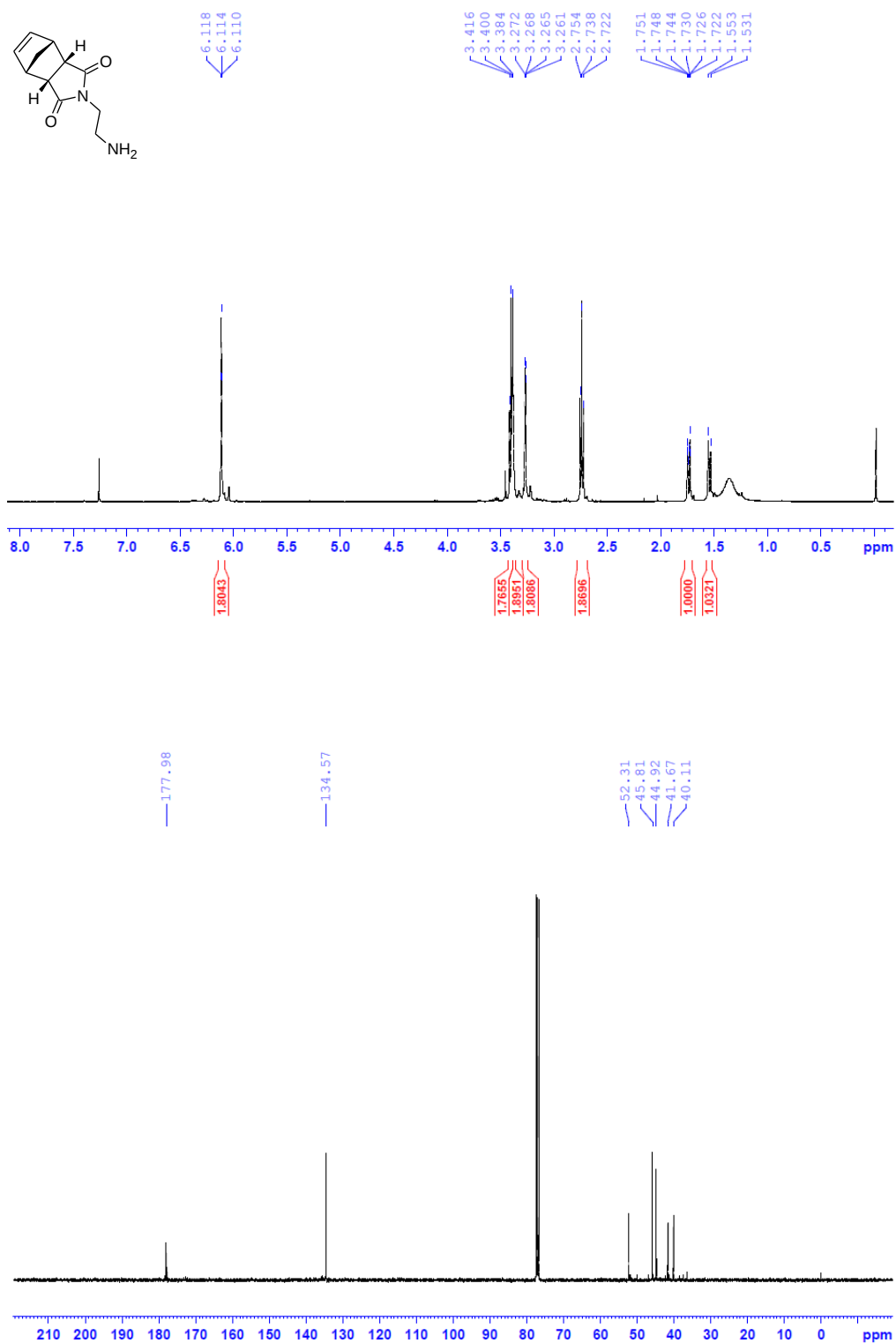
S18. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-anilino-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**8**)



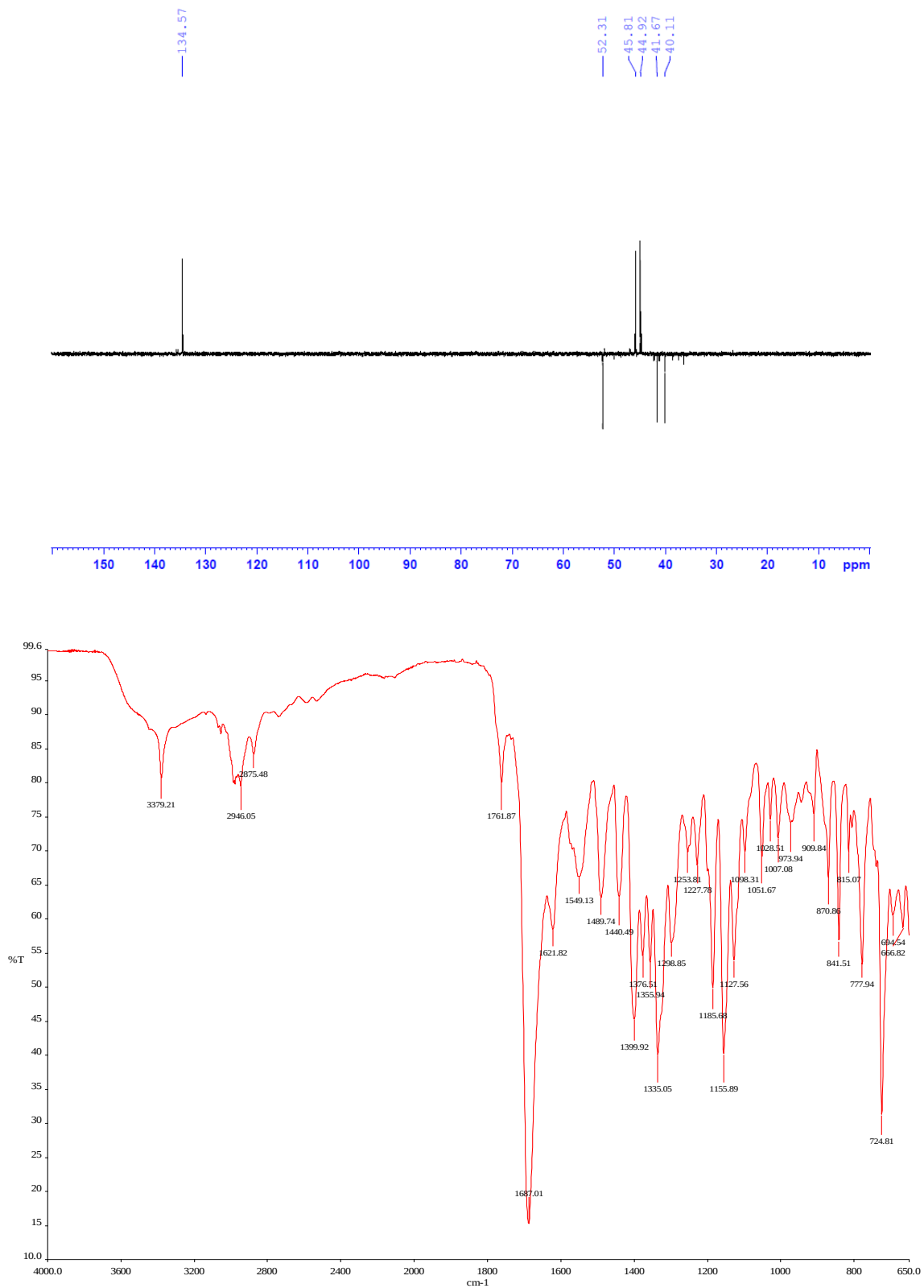
S19. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-anilino-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**8**)

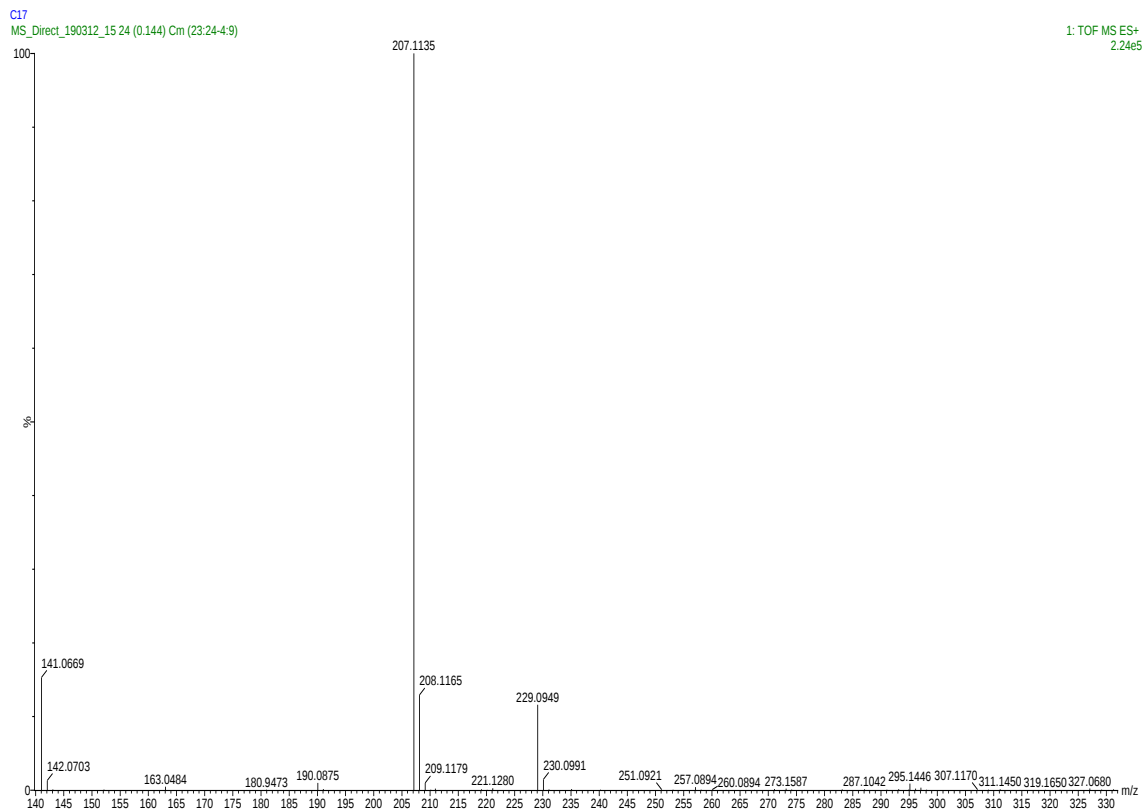
S20. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-anilino-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**8**)

S21. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-(2-aminoethyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (9)

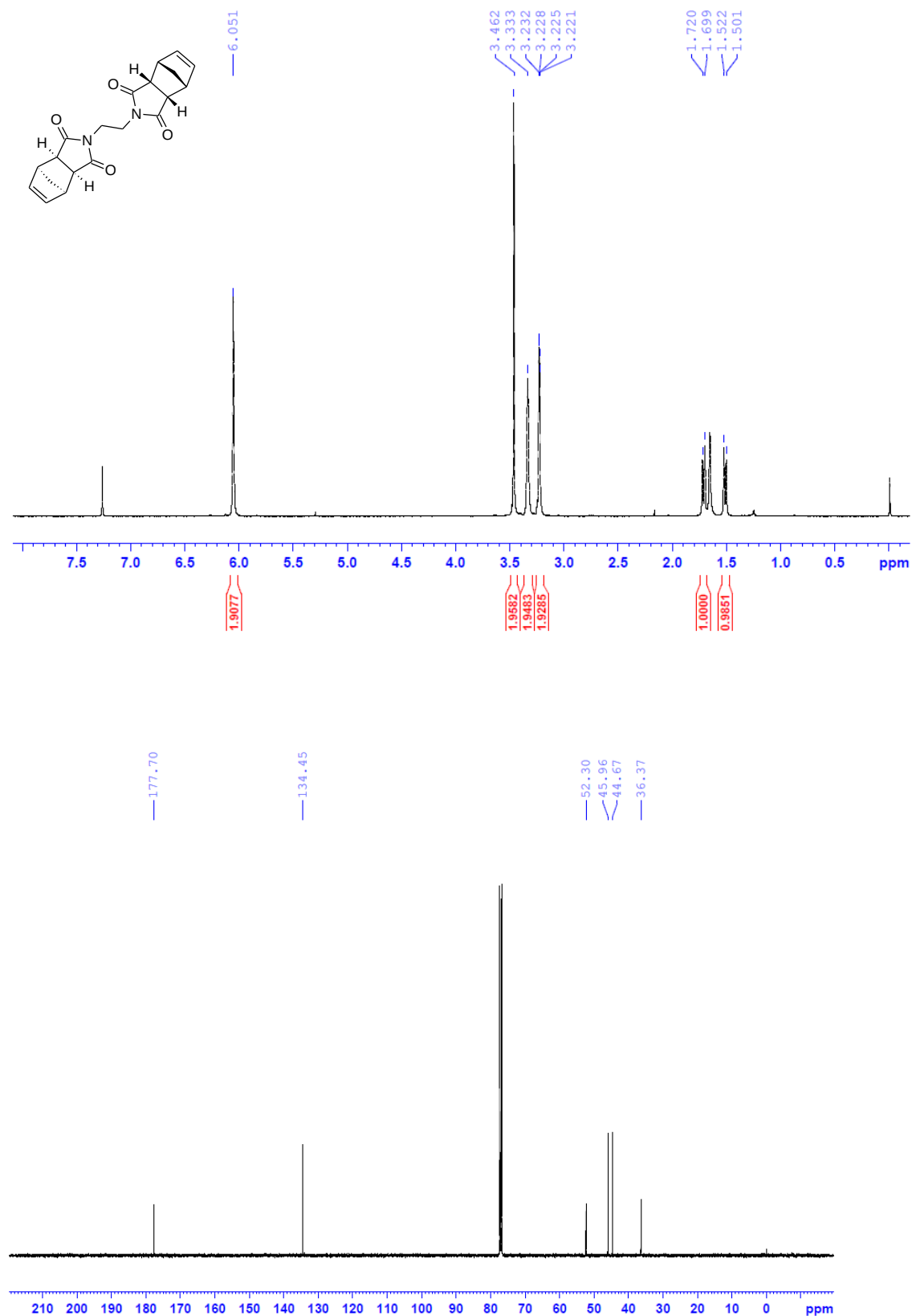


S22. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-(2-aminoethyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**9**)

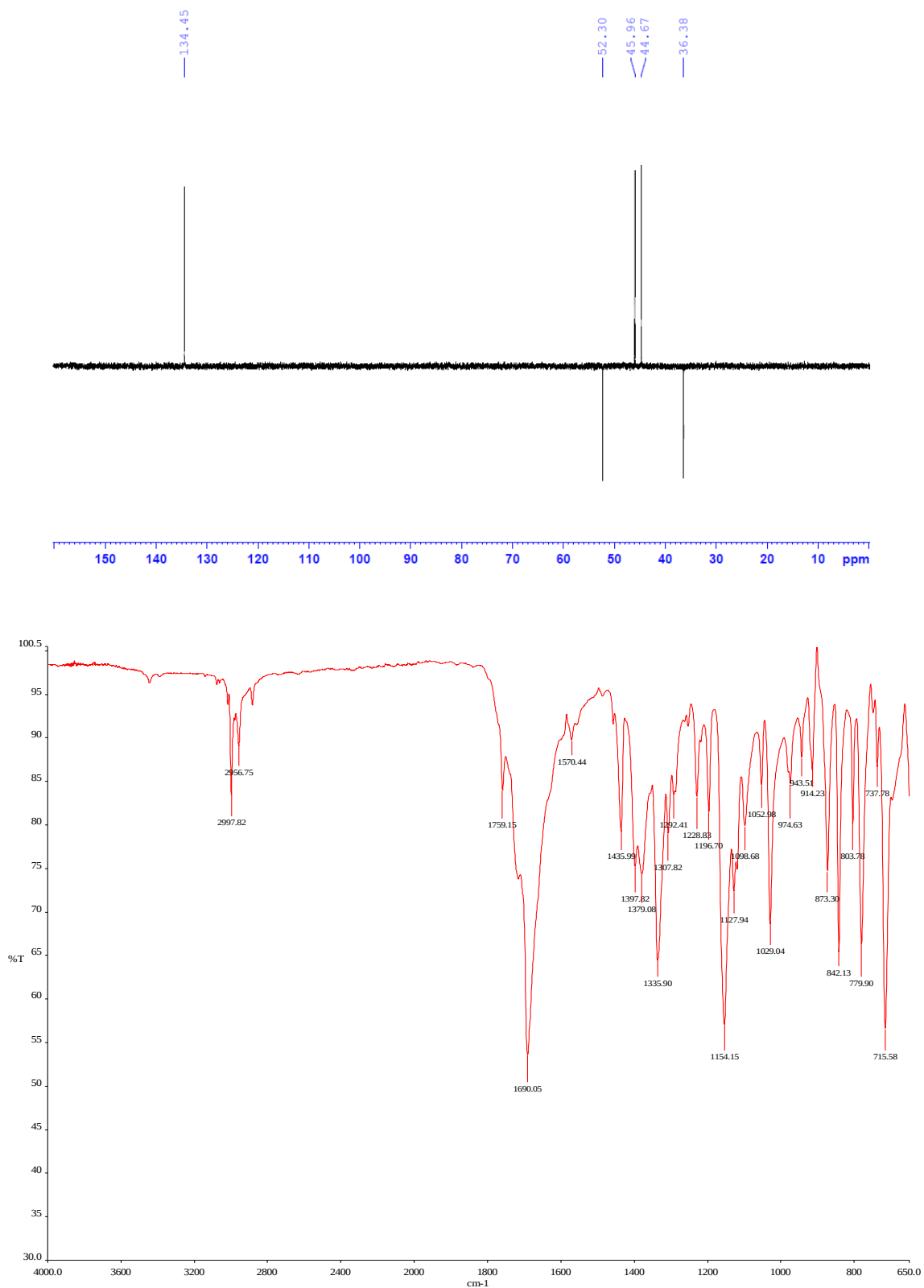


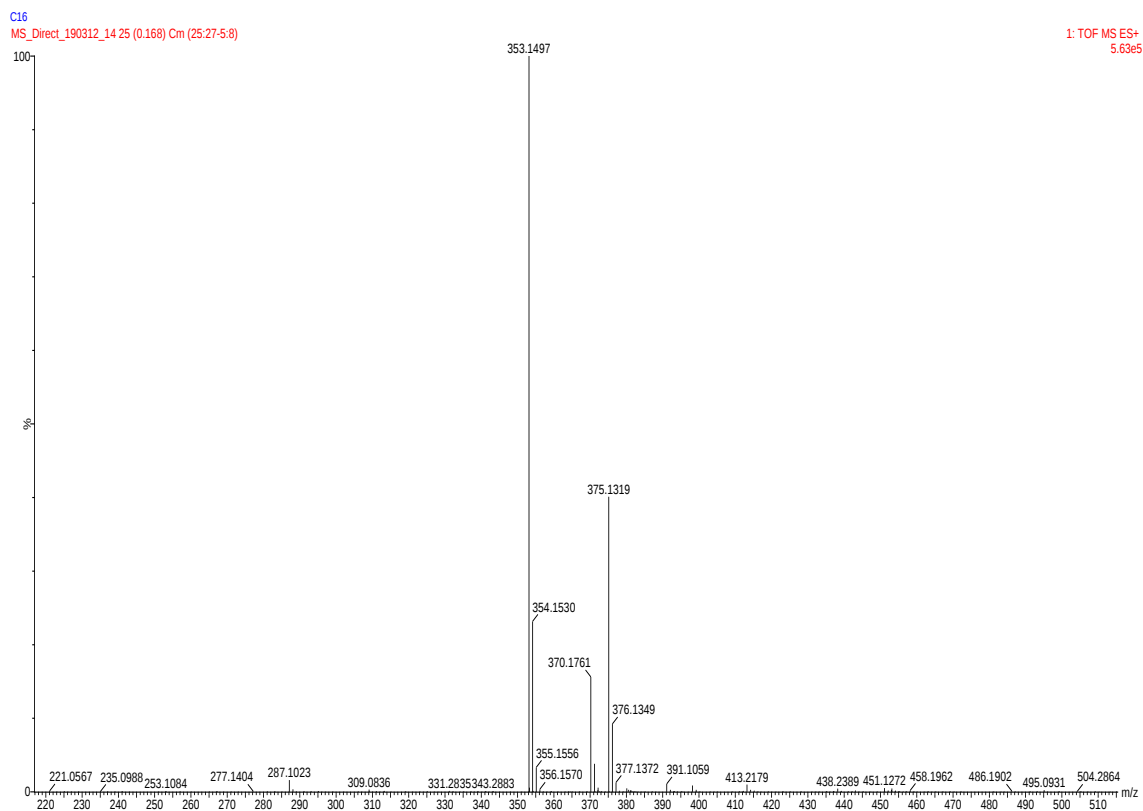
S23. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-(2-aminoethyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**9**)

S24. ^1H and ^{13}C spectra of 3,5-dioxo-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]ethyl]-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**10**)

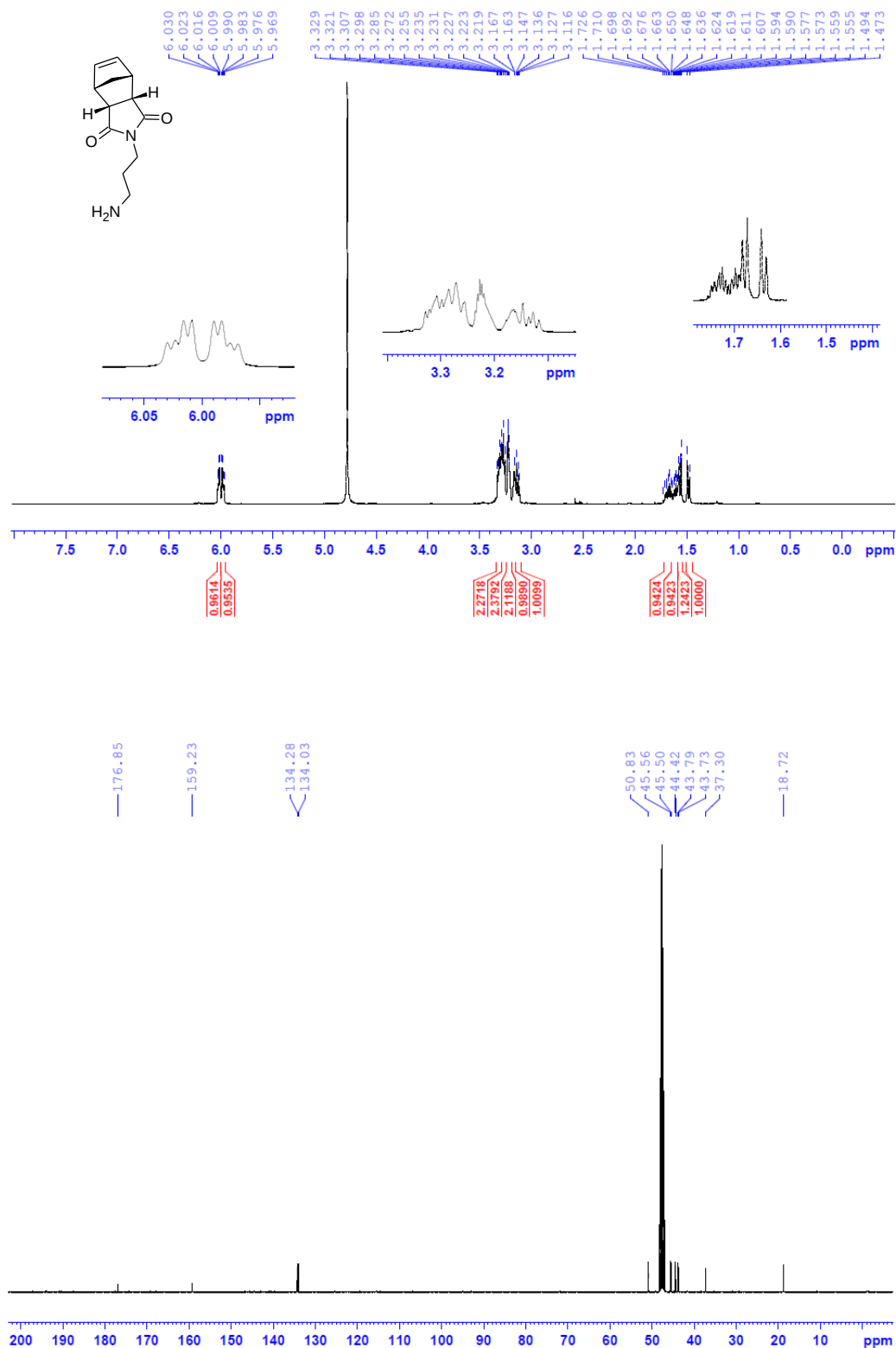


S25. DEPT-135 and IR spectra of 3,5-dioxo-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]ethyl]-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**10**)

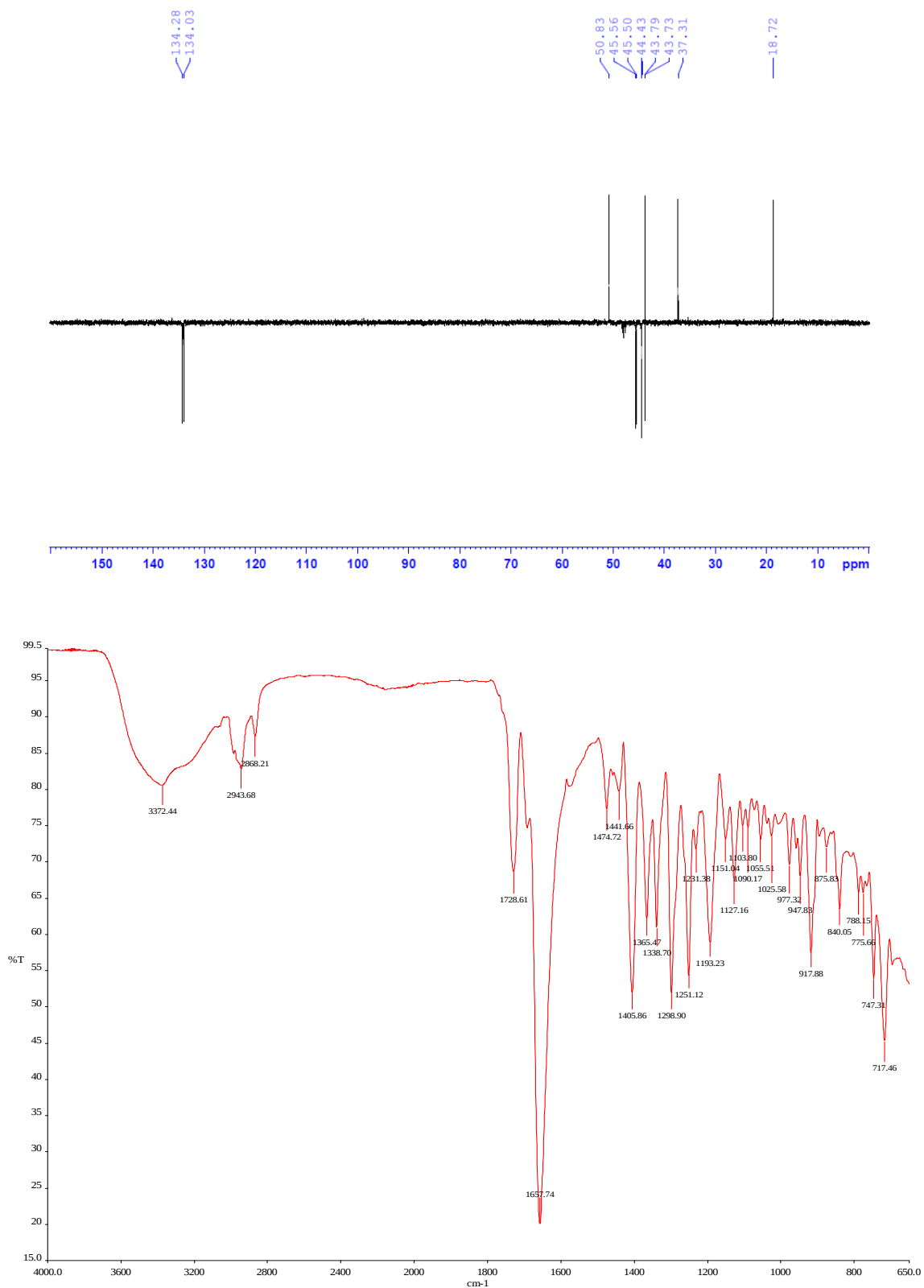


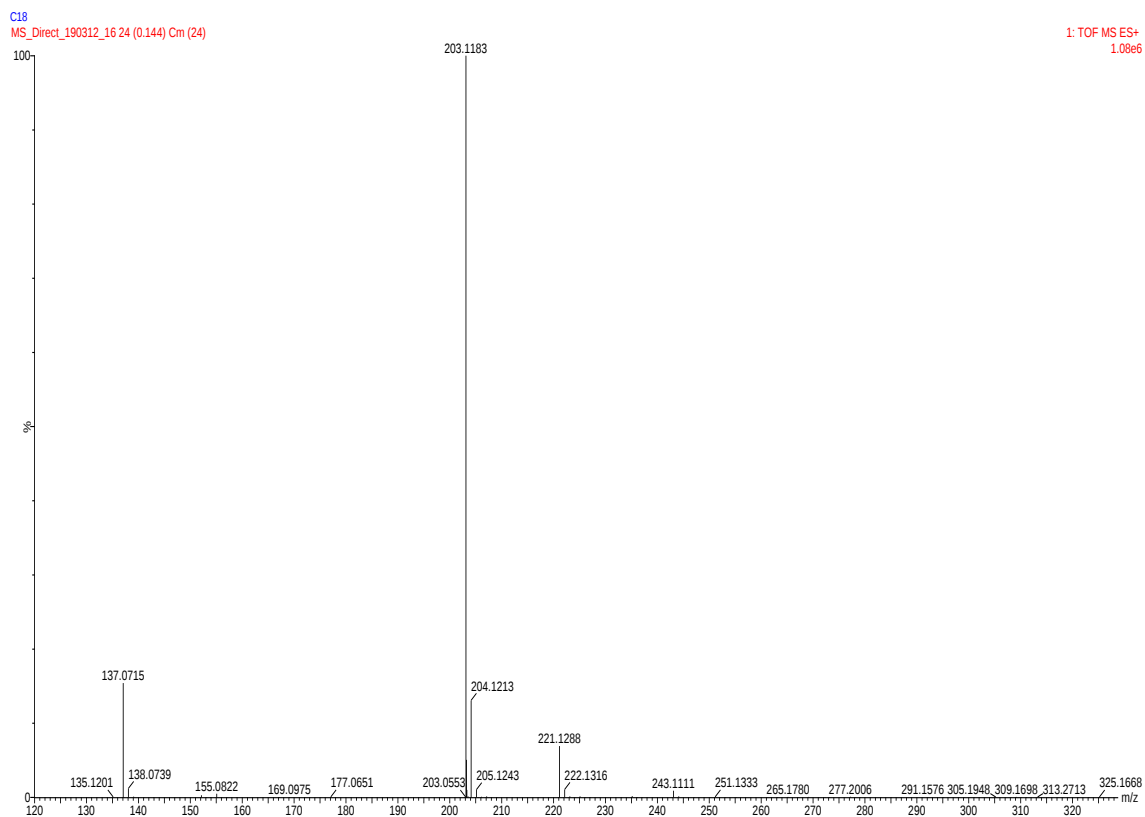
S26. HRMS spectra of 3,5-dioxo-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl]ethyl]-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**10**)

S27. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-(3-aminopropyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**11**)

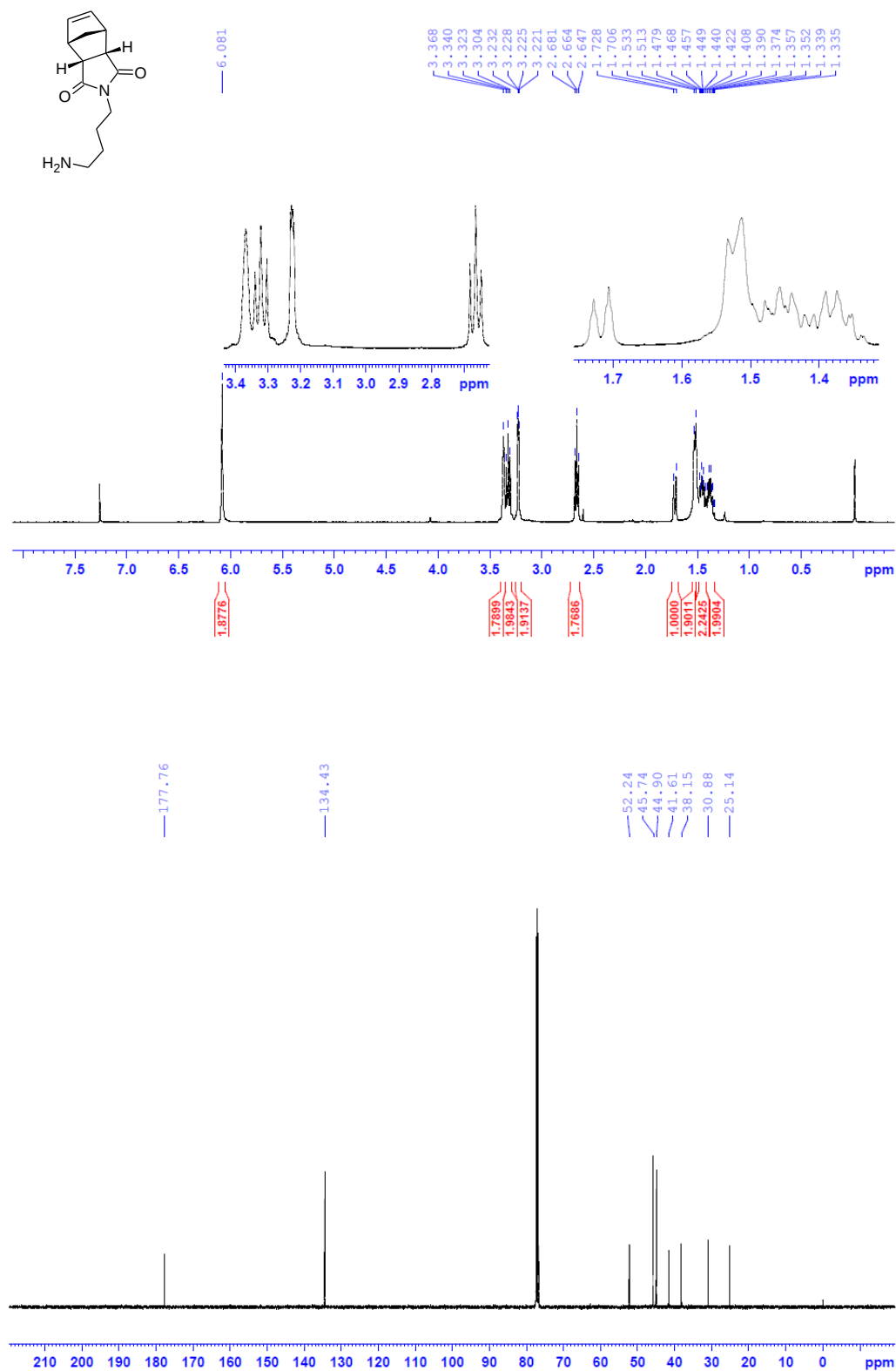


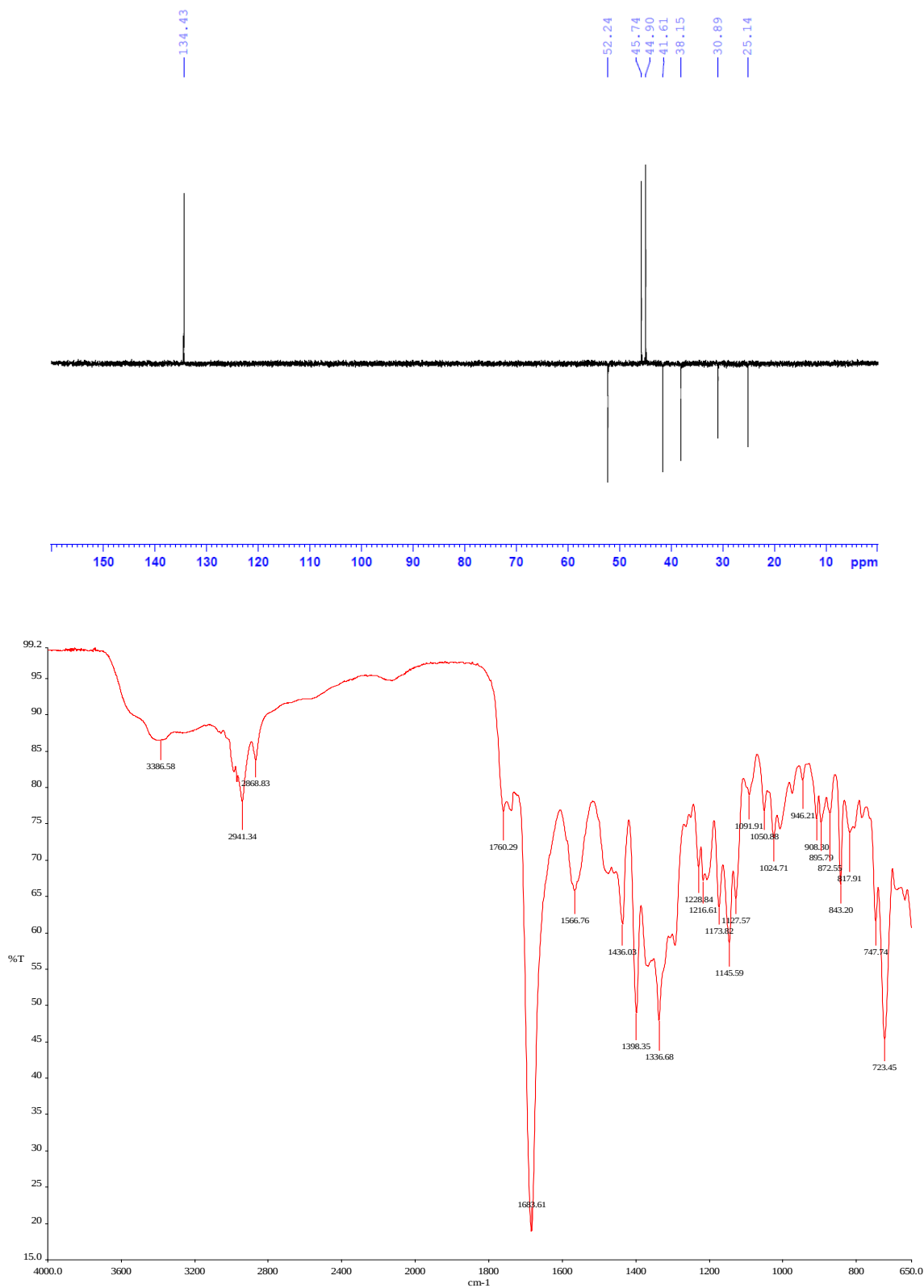
S28. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-(3-aminopropyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**11**)

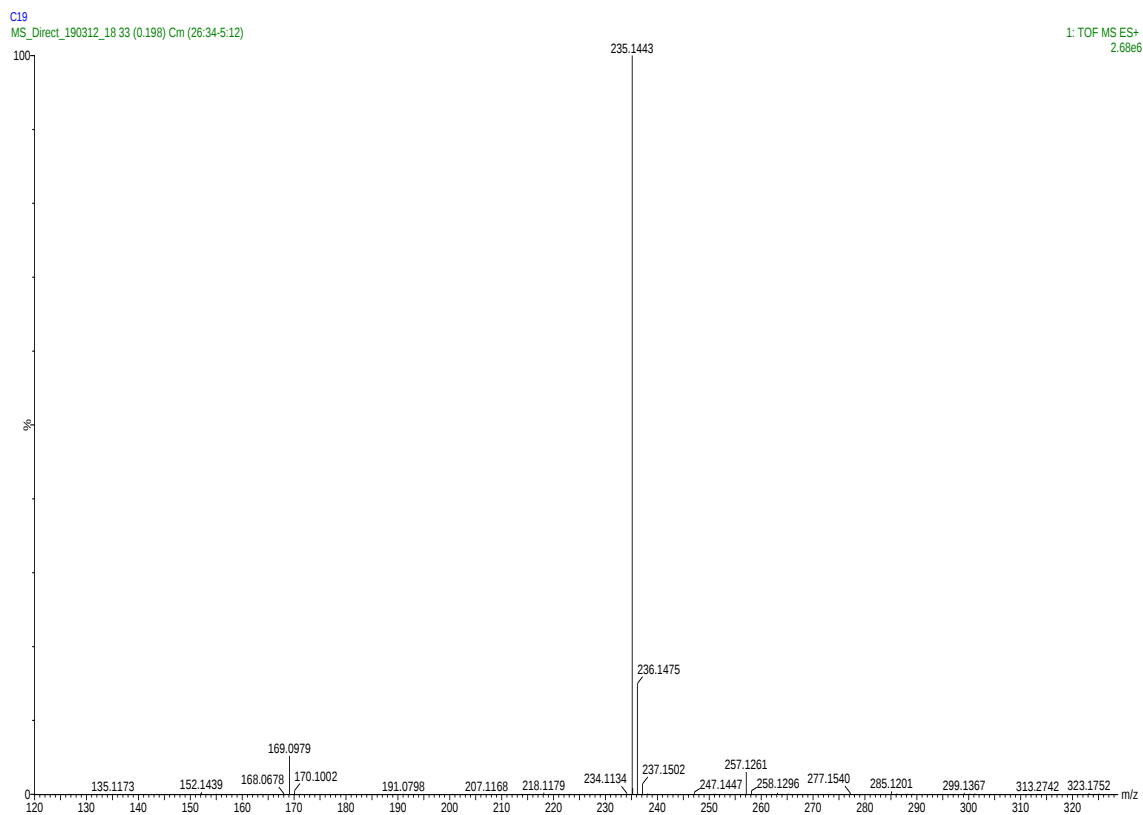


S29. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-(3-aminopropyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**11**)

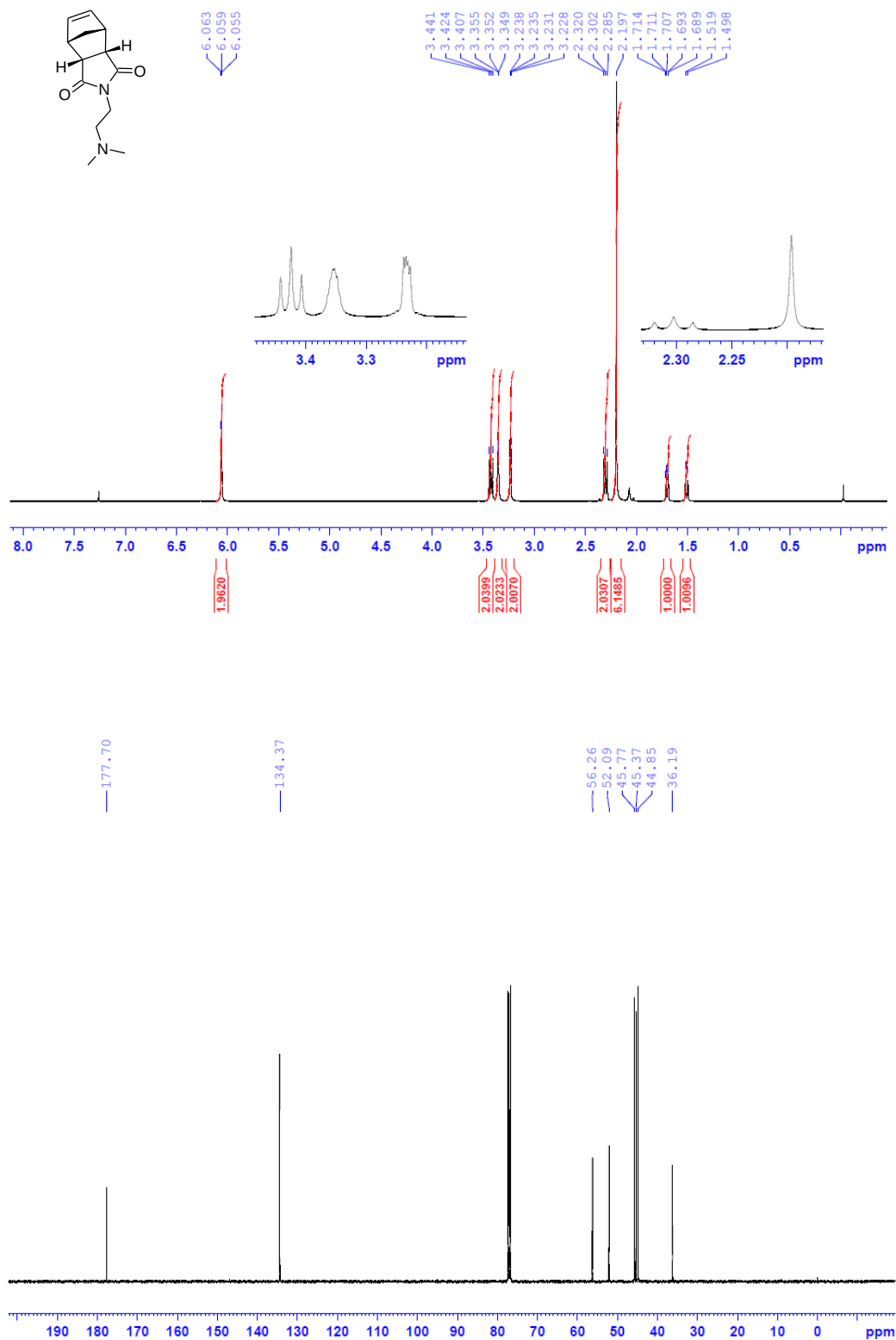
S30. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-(4-aminobutyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**12**)



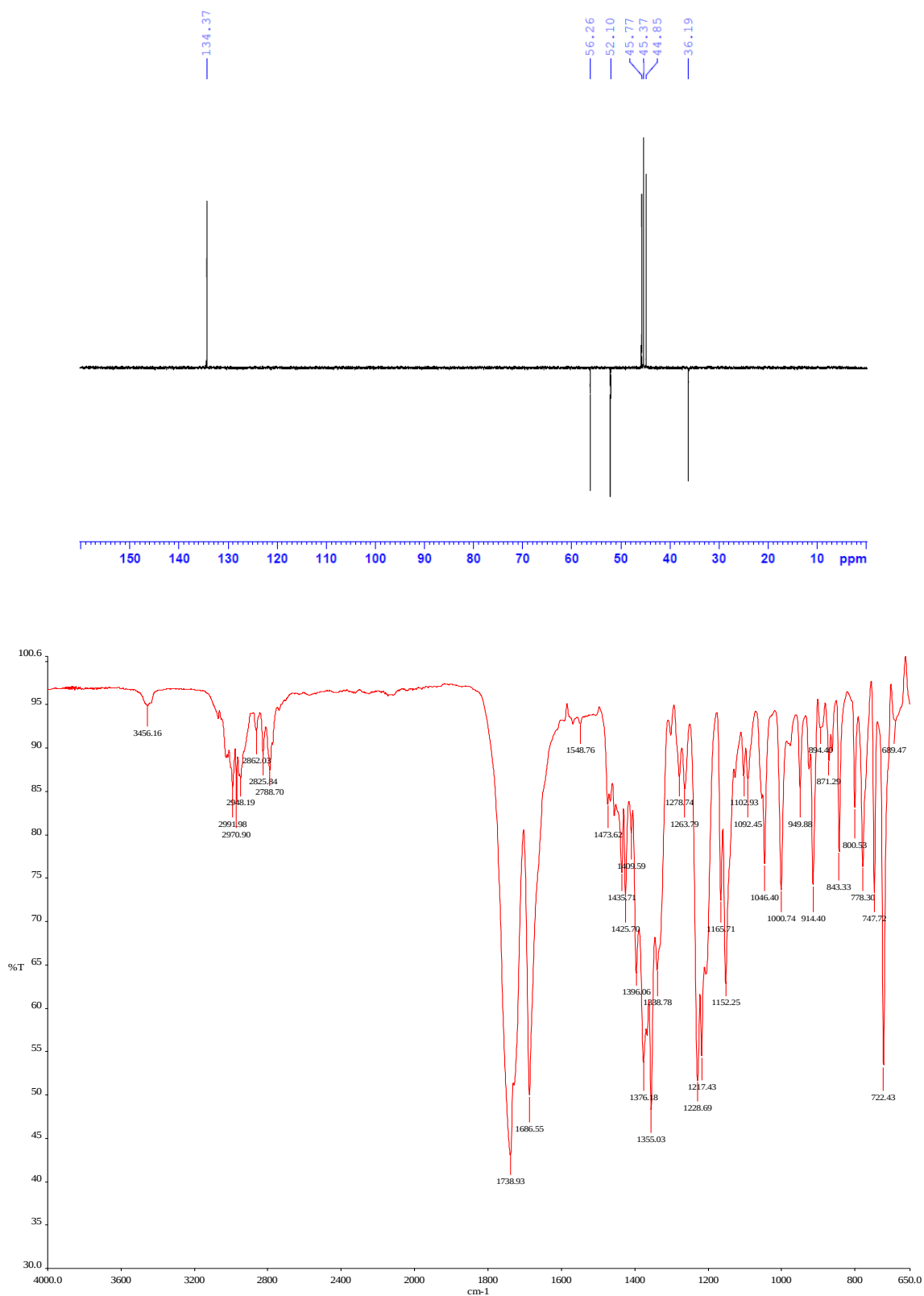
S31. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-(4-aminobutyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**12**)

S32. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-(4-aminobutyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**12**)

S33. ^1H and ^{13}C spectra of (1*R*,2*S*,6*R*,7*S*)-4-[2-(dimethylamino)ethyl]-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**13**)



S34. DEPT-135 and IR spectra of (1*R*,2*S*,6*R*,7*S*)-4-[2-(dimethylamino)ethyl]-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**13**)



S35. HRMS spectra of (1*R*,2*S*,6*R*,7*S*)-4-[2-(dimethylamino)ethyl]-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (**13**)