

Supporting Information

Isocadiolides A-H: Polybrominated Aromatics from a *Synoicum* sp. Ascidian

Jongkyoon Bae,[†] Eunji Cho,[‡] Jae Sung Park,[†] Tae Hyung Won,[†] Su-Yuan Seo,[§] Dong-Chan Oh,[†]
Ki-Bong Oh,^{‡,*} and Jongheon Shin^{†,*}

[†]*Natural Products Research Institute, College of Pharmacy, Seoul National University,
San 56-1, Sillim, Gwanak, Seoul 151-742, Korea*

[‡]*Department of Agricultural Biotechnology, College of Agriculture and Life Science,
Seoul National University, San 56-1, Sillim, Gwanak, Seoul 151-921, Korea*

[§]*Natural History Museum, Ehwa Womans University, 52 Ewhayeodae-gil,
Seodaemun, Seoul 03760, Korea*

*(J. S.) Tel: 82 2 880 2484; Fax: 82 2 762 8322; E-mail: shinj@snu.ac.kr

(K.-B. O.) Tel: 82 2 880 4646; Fax: 82 2 873 3112; E-mail: ohkibong@snu.ac.kr

Contents

Figure S1. The ^1H NMR (800 MHz, acetone- d_6) spectrum of 1	S4
Figure S2. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of 1	S5
Figure S3. The HSQC (800 MHz, acetone- d_6) spectrum of 1	S6
Figure S4. The HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 1	S7
Figure S5. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 1	S8
Figure S6. The ^1H NMR (800 MHz, acetone- d_6) spectrum of 2	S9
Figure S7. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of 2	S10
Figure S8. The HSQC (800 MHz, acetone- d_6) spectrum of 2	S11
Figure S9. The HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 2	S12
Figure S10. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 2	S13
Figure S11. The ^1H NMR (800 MHz, acetone- d_6) spectrum of 3	S14
Figure S12. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of 3	S15
Figure S13. The HSQC (800 MHz, acetone- d_6) spectrum of 3	S16
Figure S14. The HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 3	S17
Figure S15. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 3	S18
Figure S16. The ^1H NMR (600 MHz, acetone- d_6) spectrum of 4	S19
Figure S17. The ^{13}C NMR (150 MHz, acetone- d_6) spectrum of 4	S20
Figure S18. The HSQC (600 MHz, acetone- d_6) spectrum of 4	S21
Figure S19. The HMBC (600 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 4	S22
Figure S20. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 4	S23
Figure S21. The ^1H NMR (800 MHz, acetone- d_6) spectrum of 5	S24
Figure S22. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of 5	S25
Figure S23. The HSQC (800 MHz, acetone- d_6) spectrum of 5	S26
Figure S24. The HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 5	S27
Figure S25. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 5	S28
Figure S26. The ^1H NMR (600 MHz, acetone- d_6) spectrum of 6	S29
Figure S27. The ^{13}C NMR (150 MHz, acetone- d_6) spectrum of 6	S30
Figure S28. The HSQC (600 MHz, acetone- d_6) spectrum of 6	S31
Figure S29. The HMBC (600 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 6	S32
Figure S30. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 6	S33
Figure S31. The NOESY (800 MHz, acetone- d_6) spectrum of 6	S34

Figure S32. The ^1H NMR (400 MHz, acetone- d_6) spectrum of 7	S35
Figure S33. The ^{13}C NMR (100 MHz, acetone- d_6) spectrum of 7	S36
Figure S34. The HSQC (400 MHz, acetone- d_6) spectrum of 7	S37
Figure S35. The HMBC (400 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 7	S38
Figure S36. The NOESY (800 MHz, acetone- d_6) spectrum of 7	S39
Figure S37. The ^1H NMR (800 MHz, acetone- d_6) spectrum of 8	S40
Figure S38. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of 8	S41
Figure S39. The HSQC (800 MHz, acetone- d_6) spectrum of 8	S42
Figure S40. The HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 8	S43
Figure S41. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 8	S44
Figure S42. The NOESY (800 MHz, acetone- d_6) spectrum of 8	S45
Figure S43. The ^1H NMR (800 MHz, acetone- d_6) spectrum of 9	S46
Figure S44. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of 9	S47
Figure S45. The HSQC (800 MHz, acetone- d_6) spectrum of 9	S48
Figure S46. The HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of 9	S49
Figure S47. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of 9	S50
Figure S48. The ^1H NMR (800 MHz, DMSO- d_6) spectrum of 9	S51
Figure S49. The NOESY (800 MHz, DMSO- d_6) spectrum of 9	S52
Figure S50. The 1-D Selective gradient NOESY (800 MHz, DMSO- d_6) spectrum of 9	S53
Figure S51. The varied ratios of 9a and 9b in diverse NMR solvents	S54
Figure S52. Calculated optical rotations of major conformers of 2	S56
Figure S53. Calculated optical rotations of major conformers of 4	S57

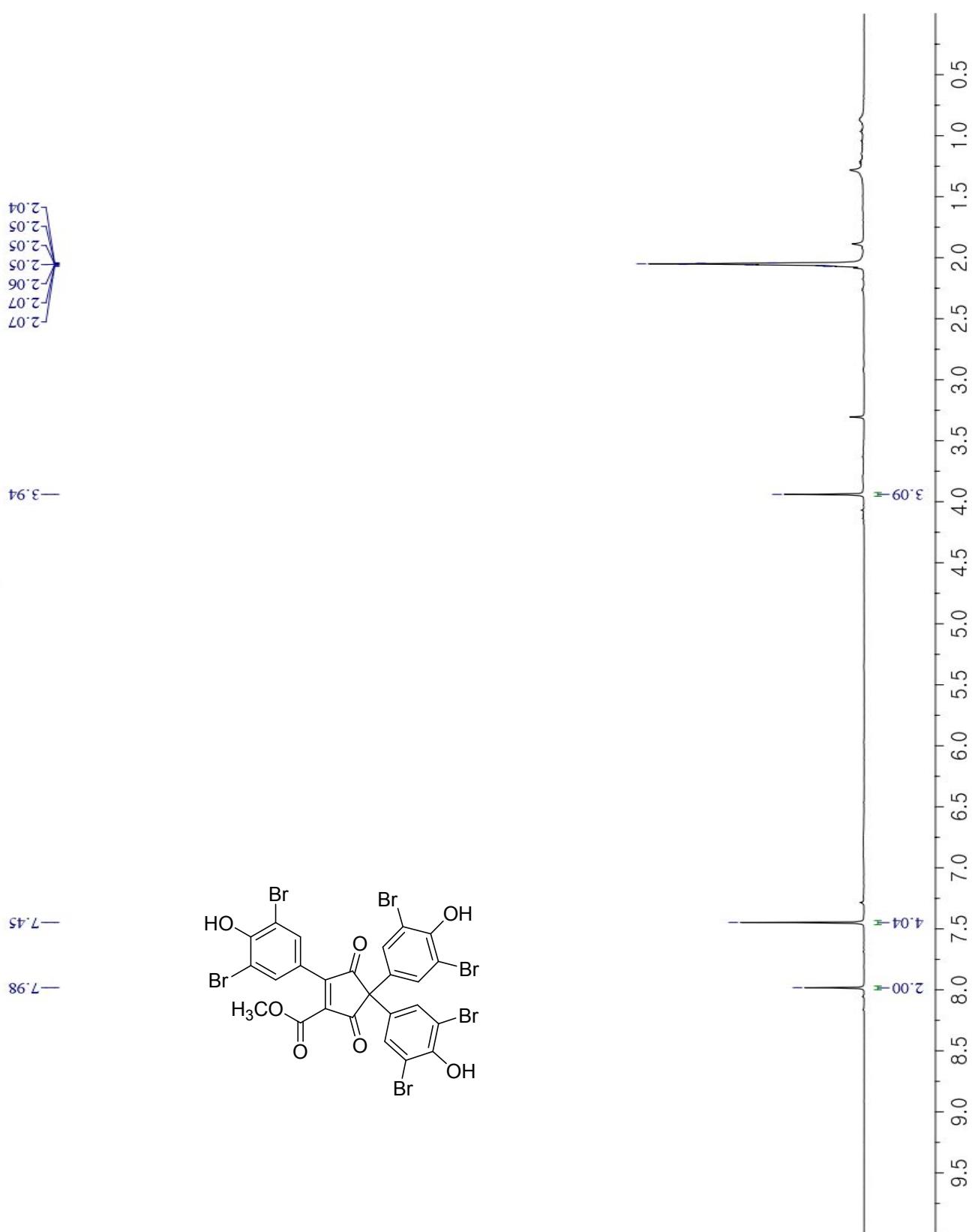


Figure S1. The ^1H NMR (800 MHz, acetone- d_6) spectrum of **1**

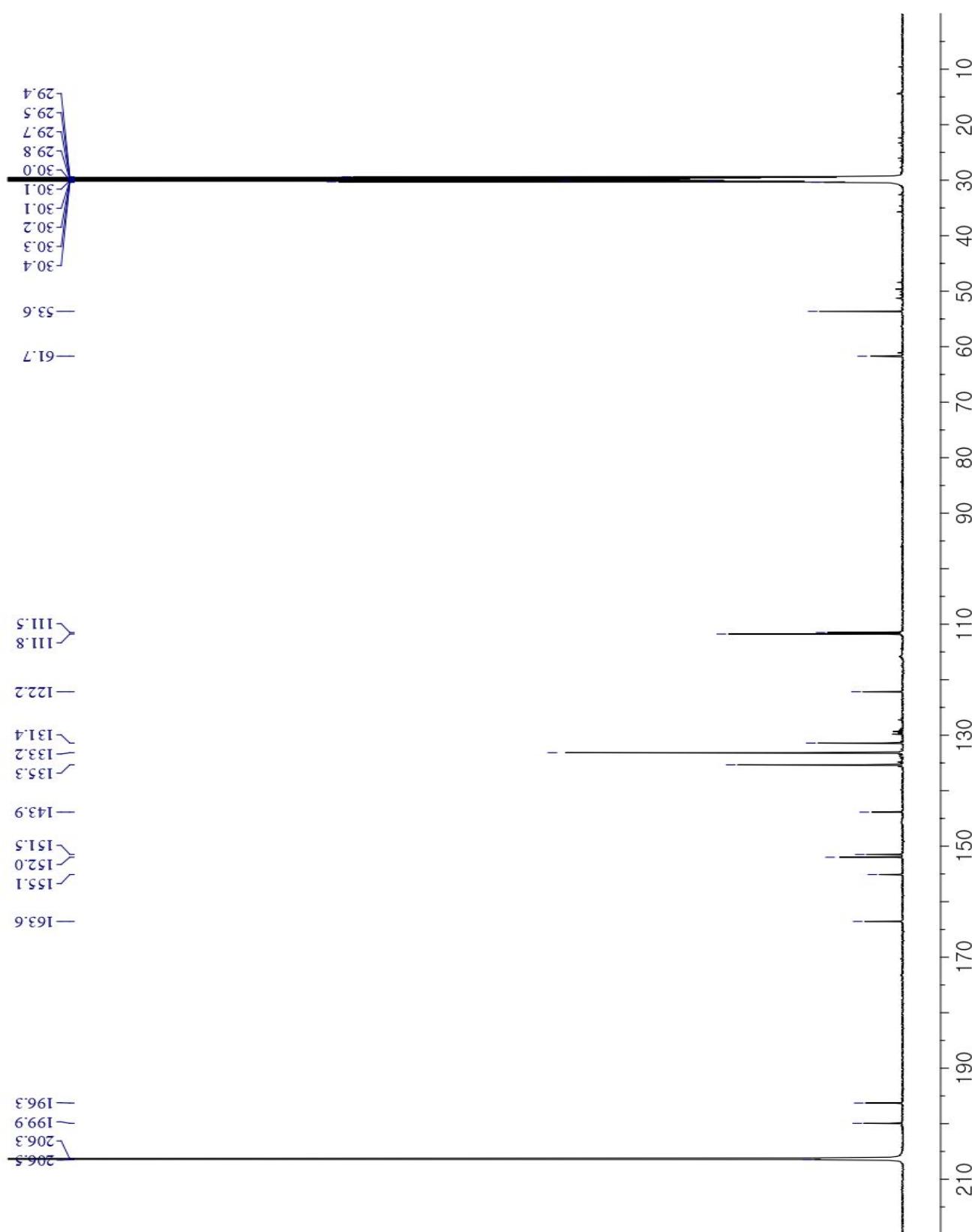


Figure S2. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of **1**

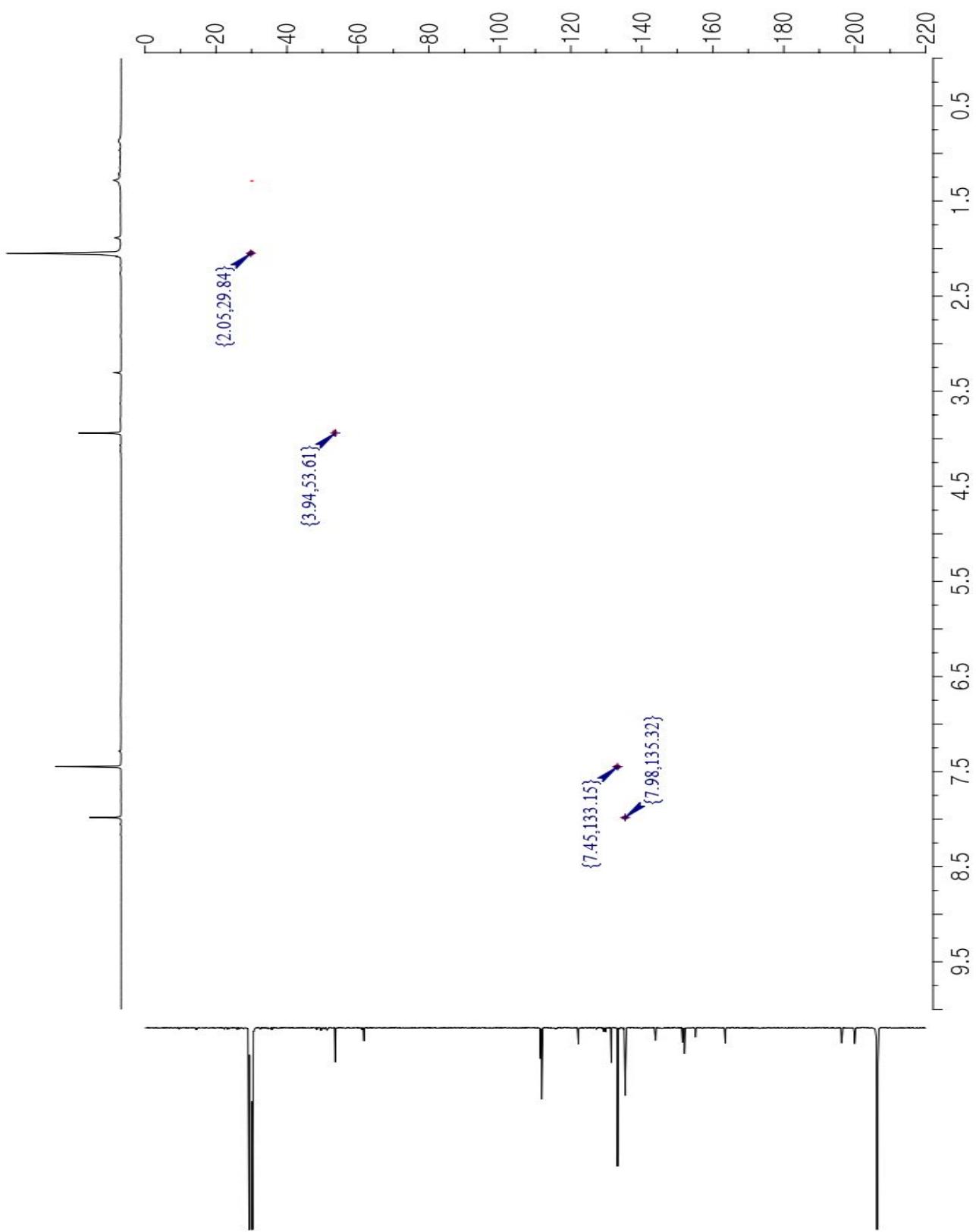


Figure S3. The HSQC (800 MHz, acetone-*d*₆) spectrum of **1**

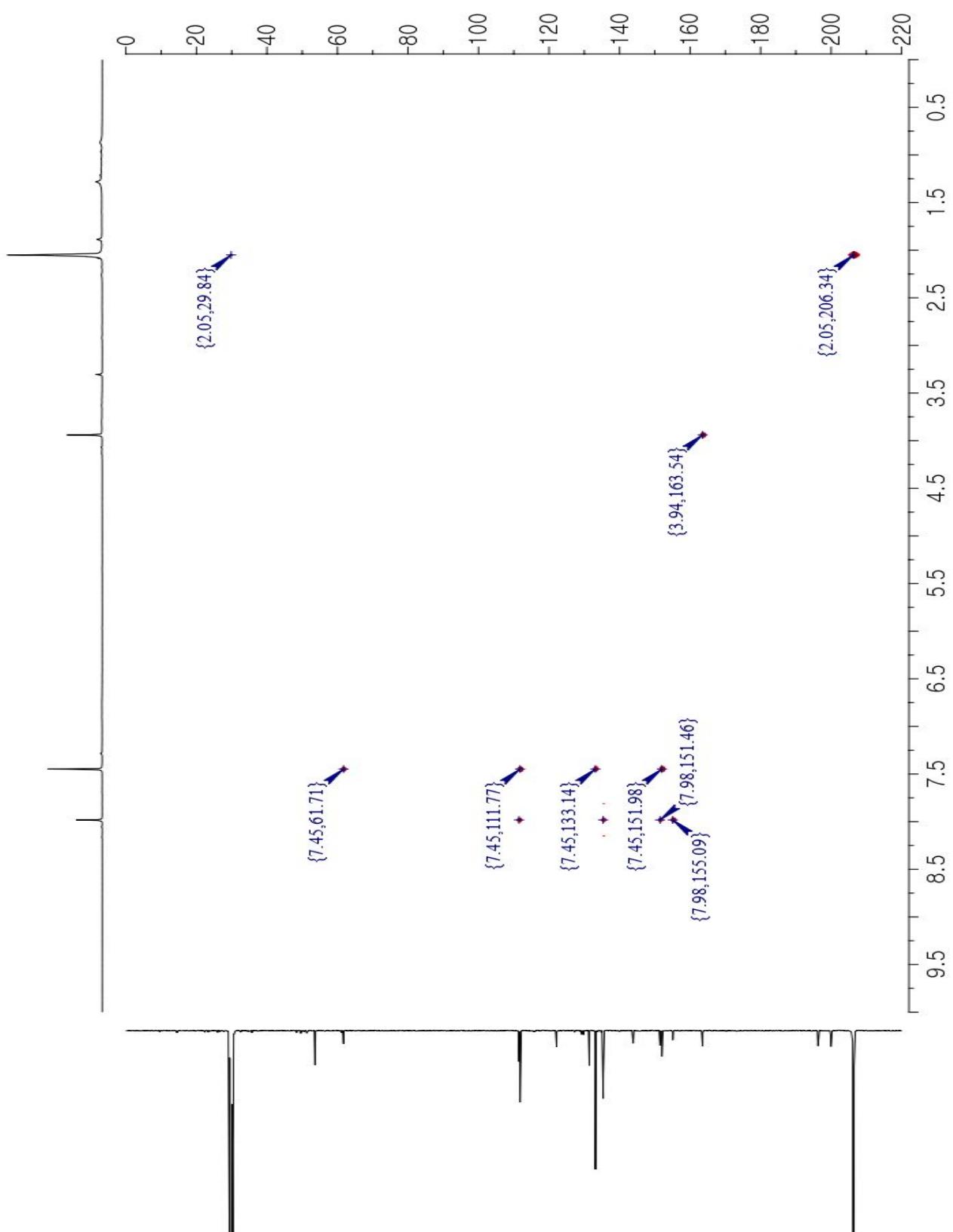


Figure S4. The HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 8 Hz) spectrum of **1**

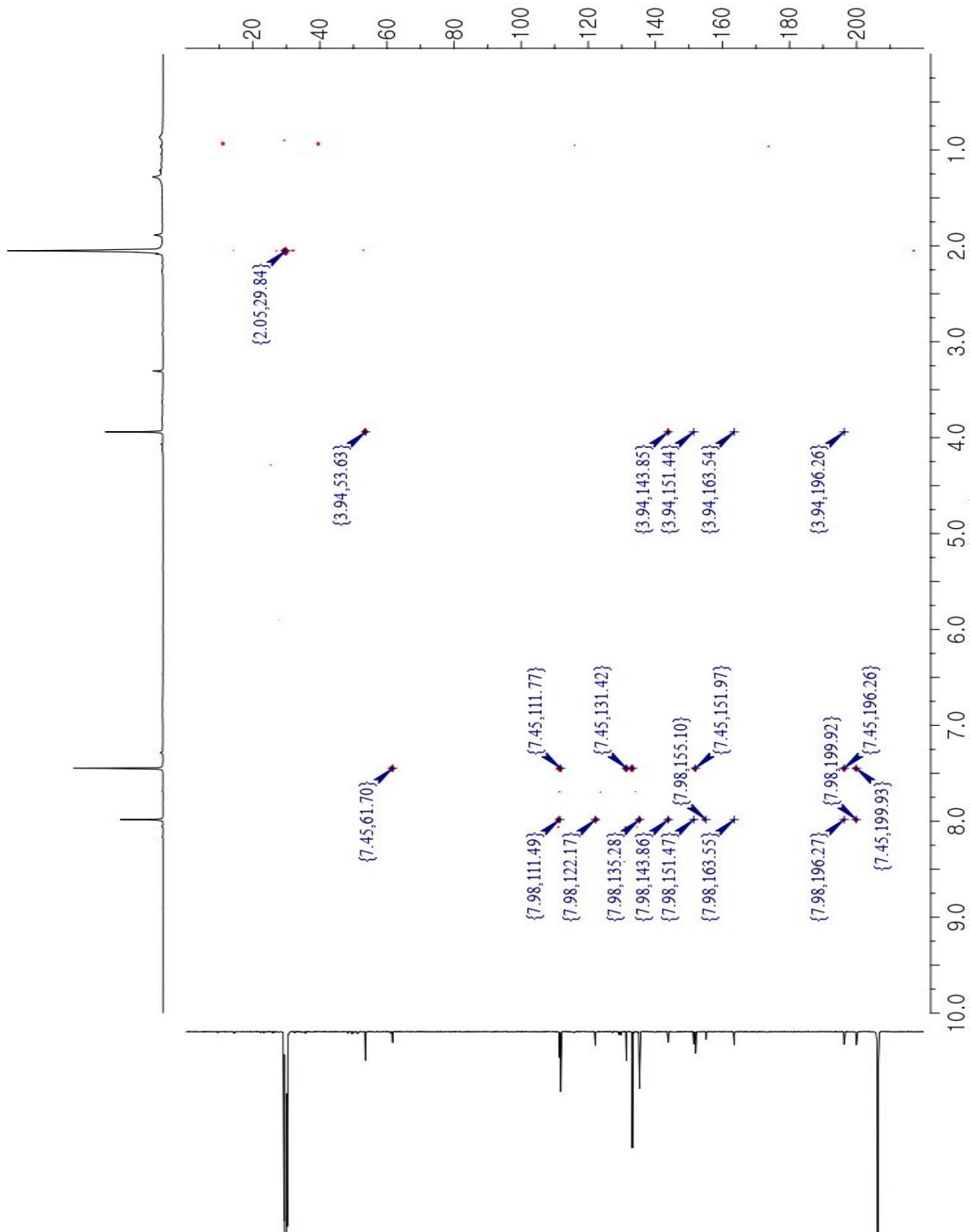


Figure S5. The D-HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 1 Hz) spectrum of **1**

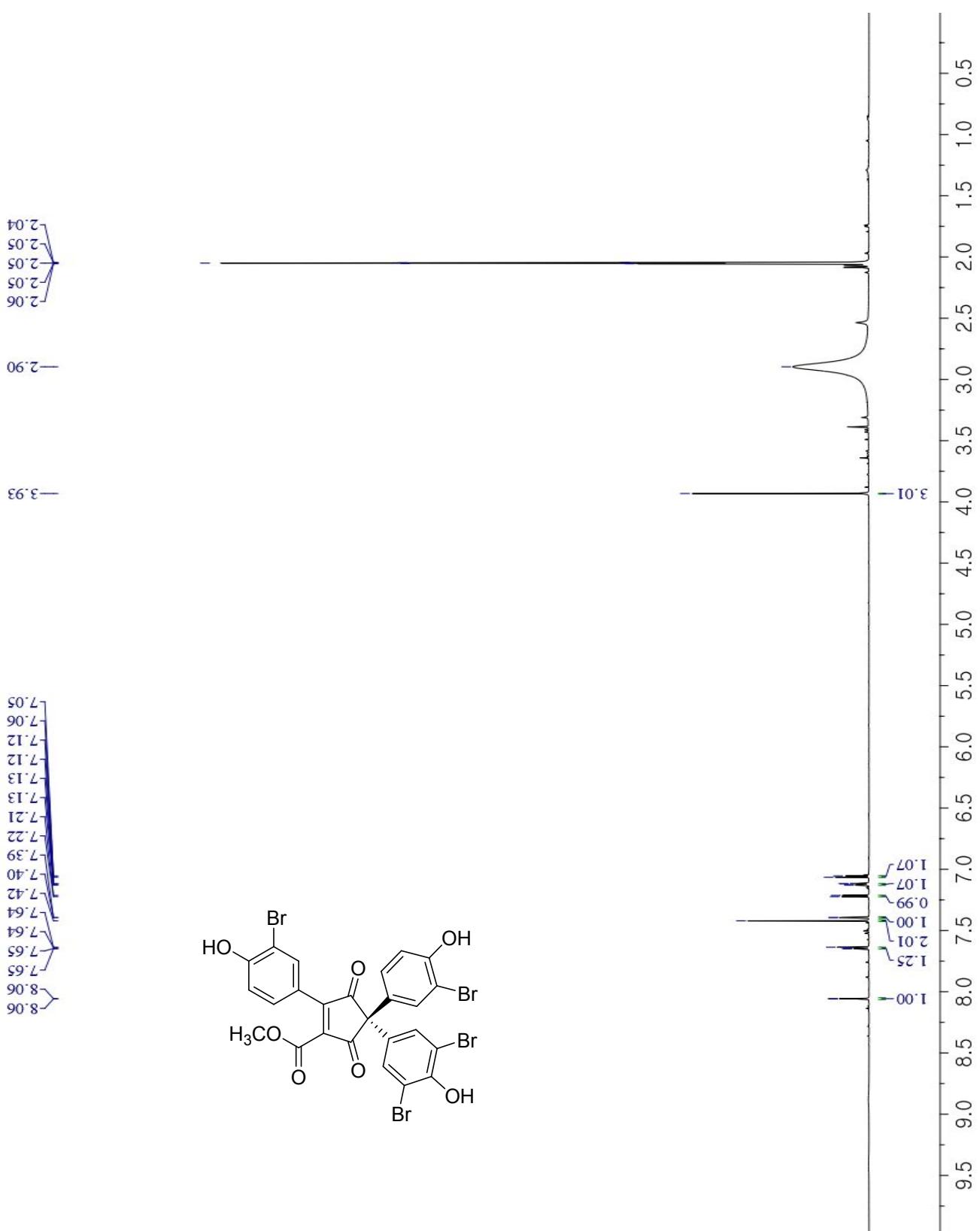


Figure S6. The ^1H NMR (800 MHz, acetone- d_6) spectrum of 2

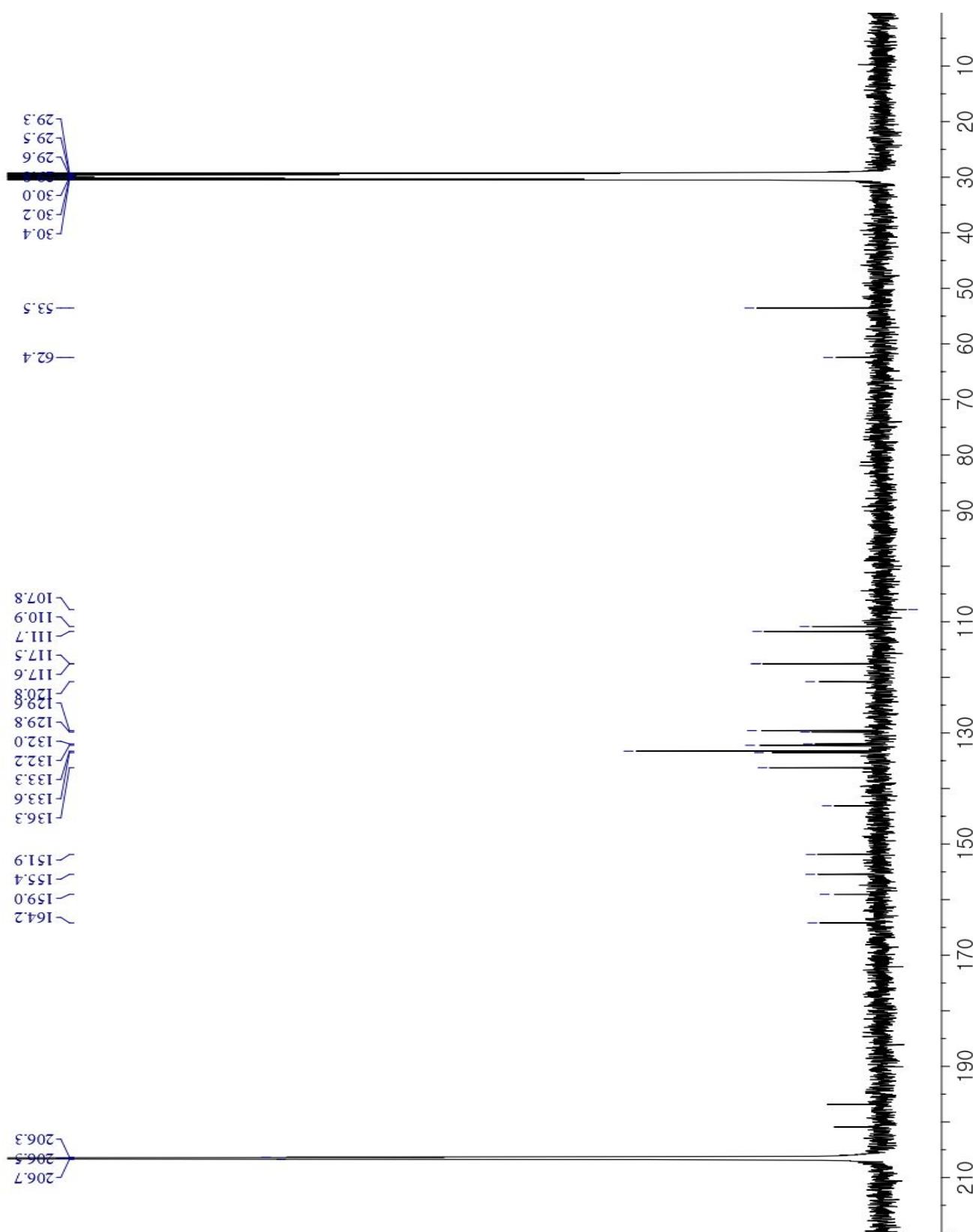


Figure S7. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of **2**

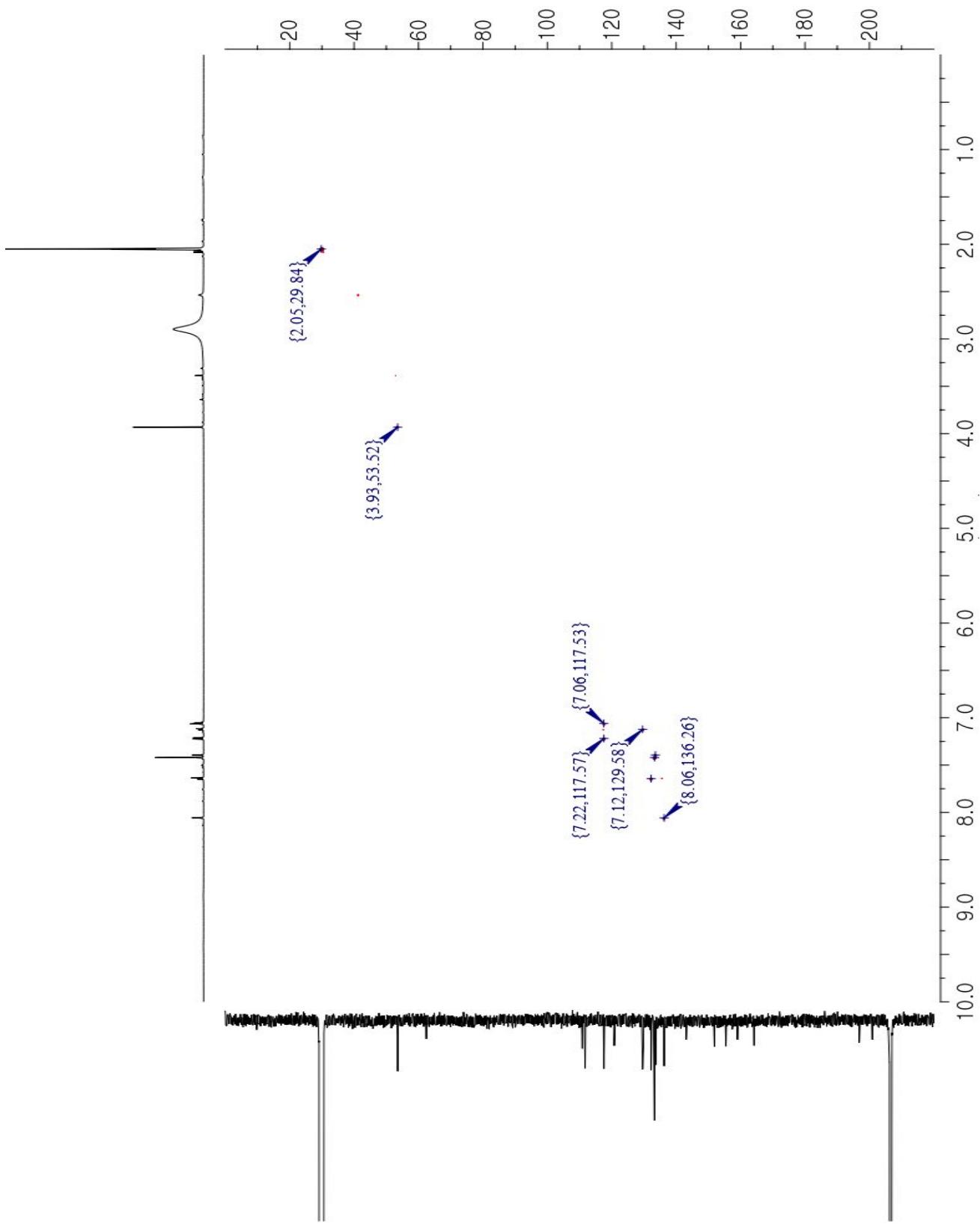


Figure S8. The HSQC (800 MHz, acetone- d_6) spectrum of **2**

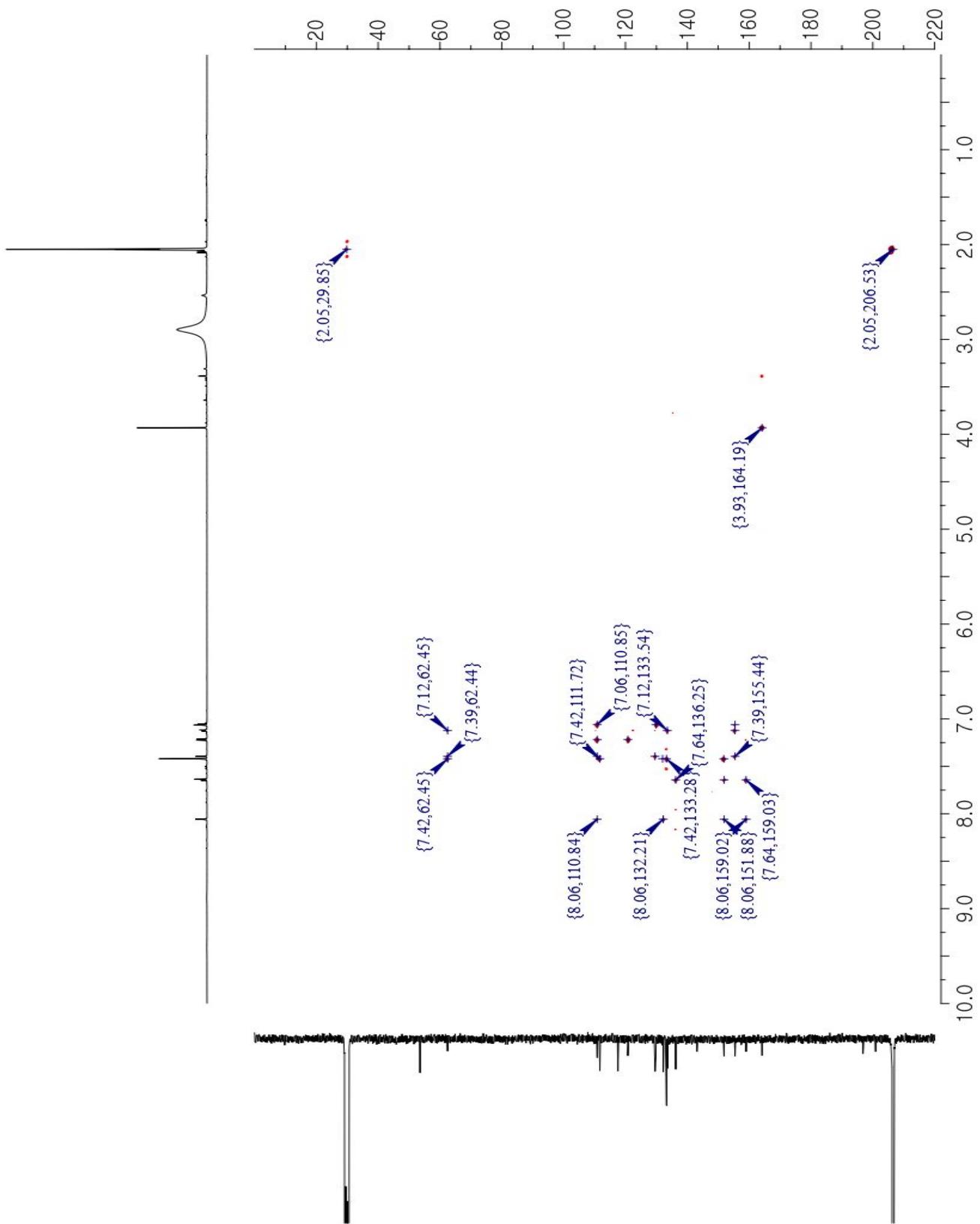


Figure S9. The HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 8 Hz) spectrum of **2**

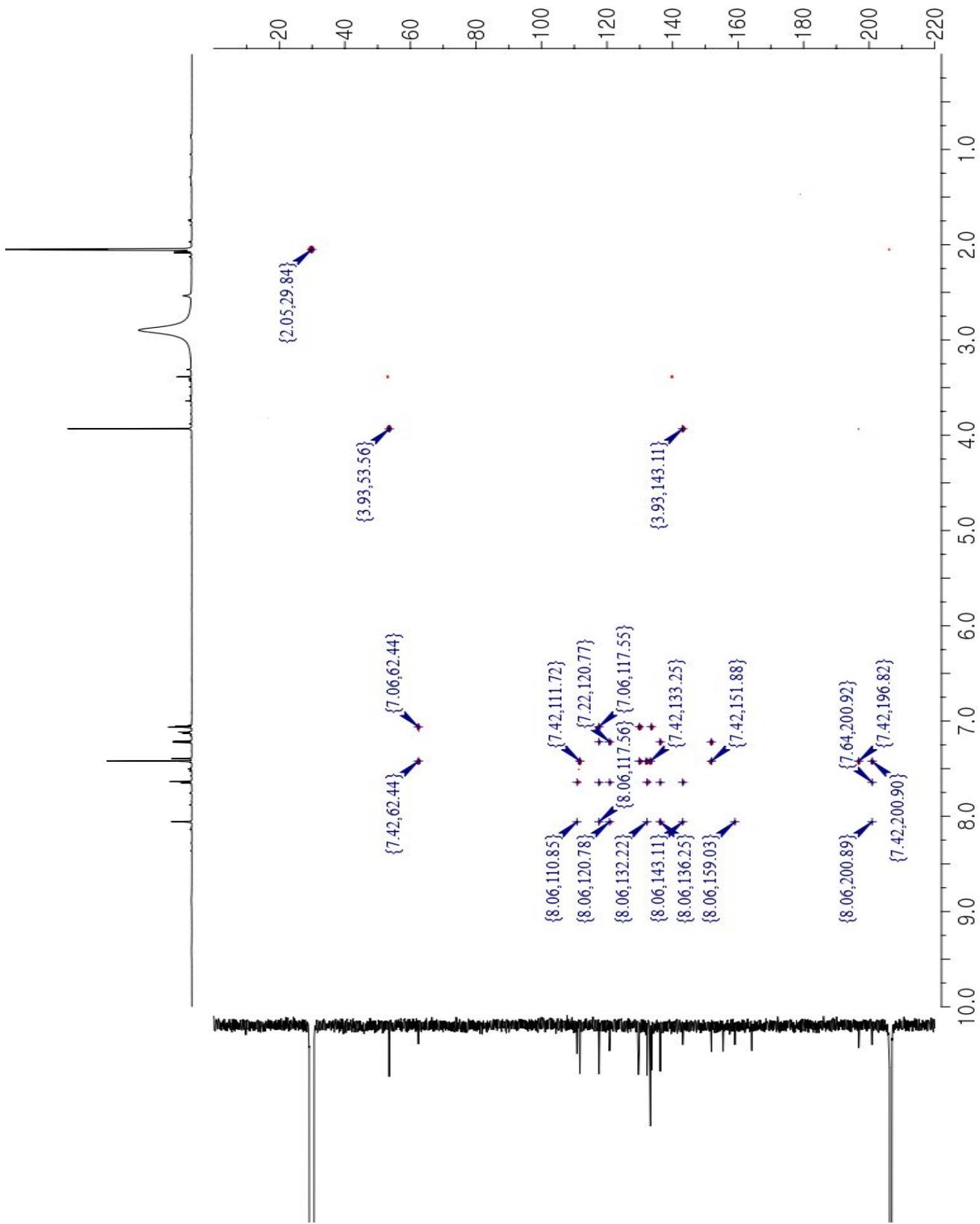


Figure S10. The D-HMBC (800 MHz, Acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of **2**

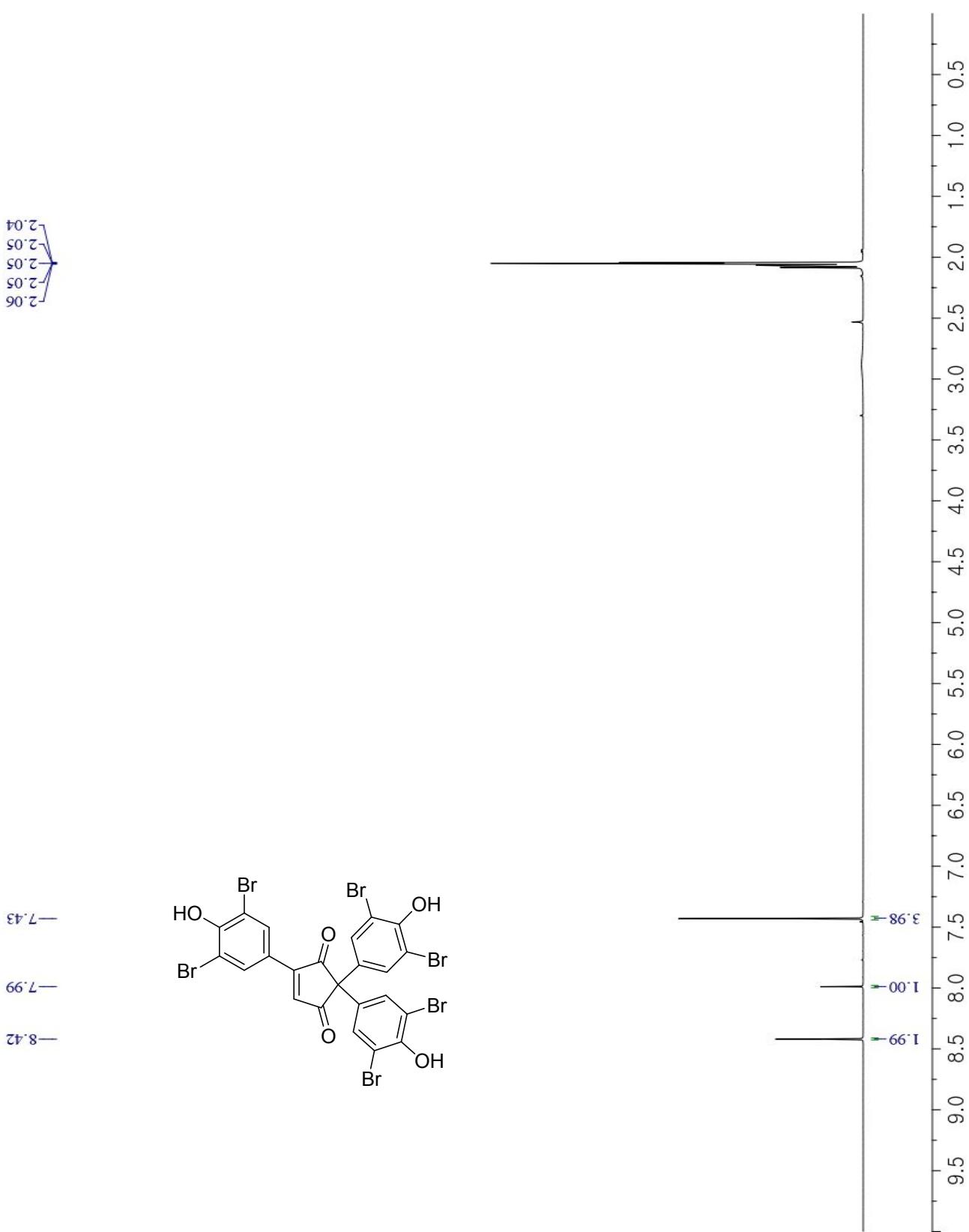


Figure S11. The ^1H NMR (800 MHz, acetone- d_6) spectrum of **3**

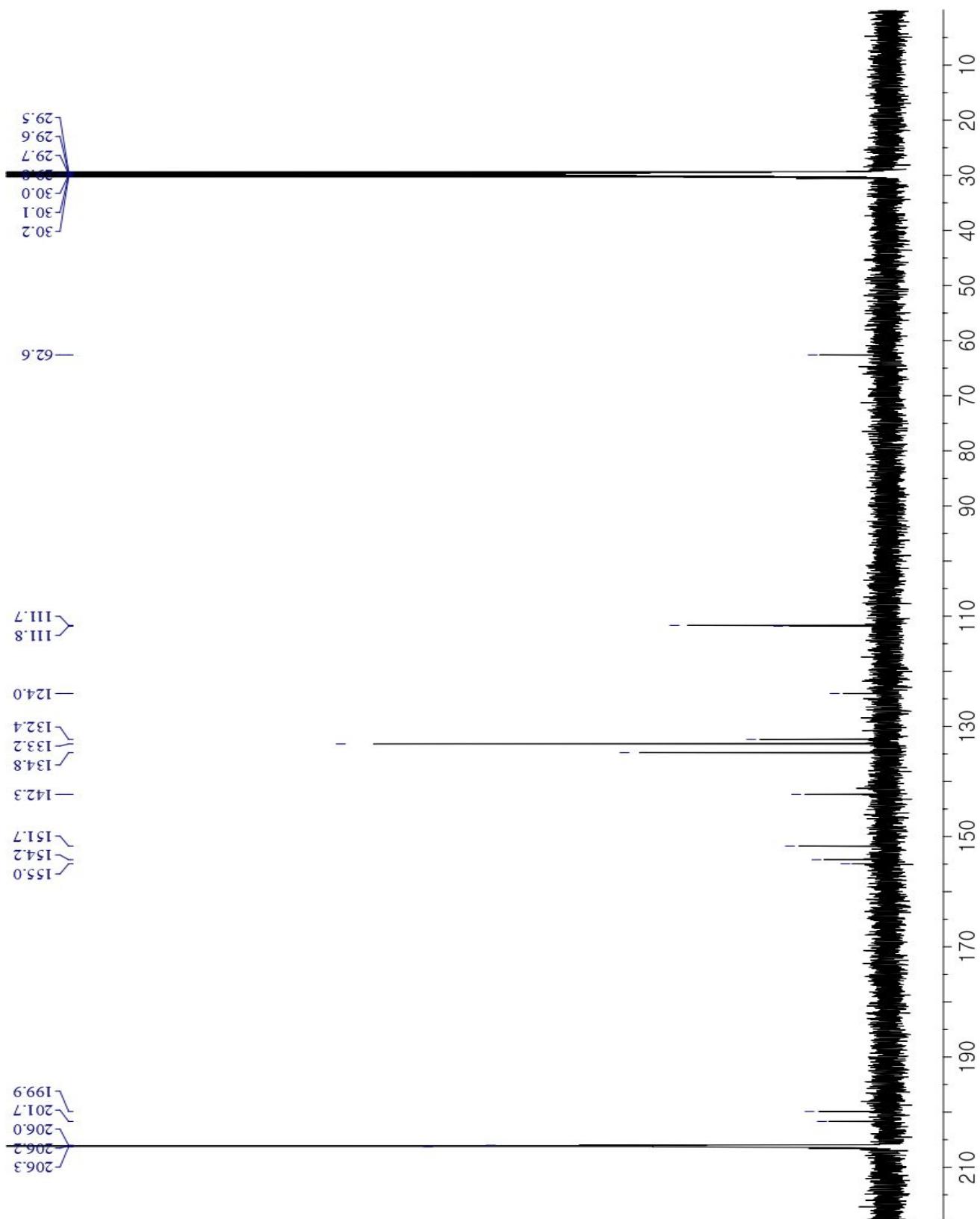


Figure S12. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of **3**

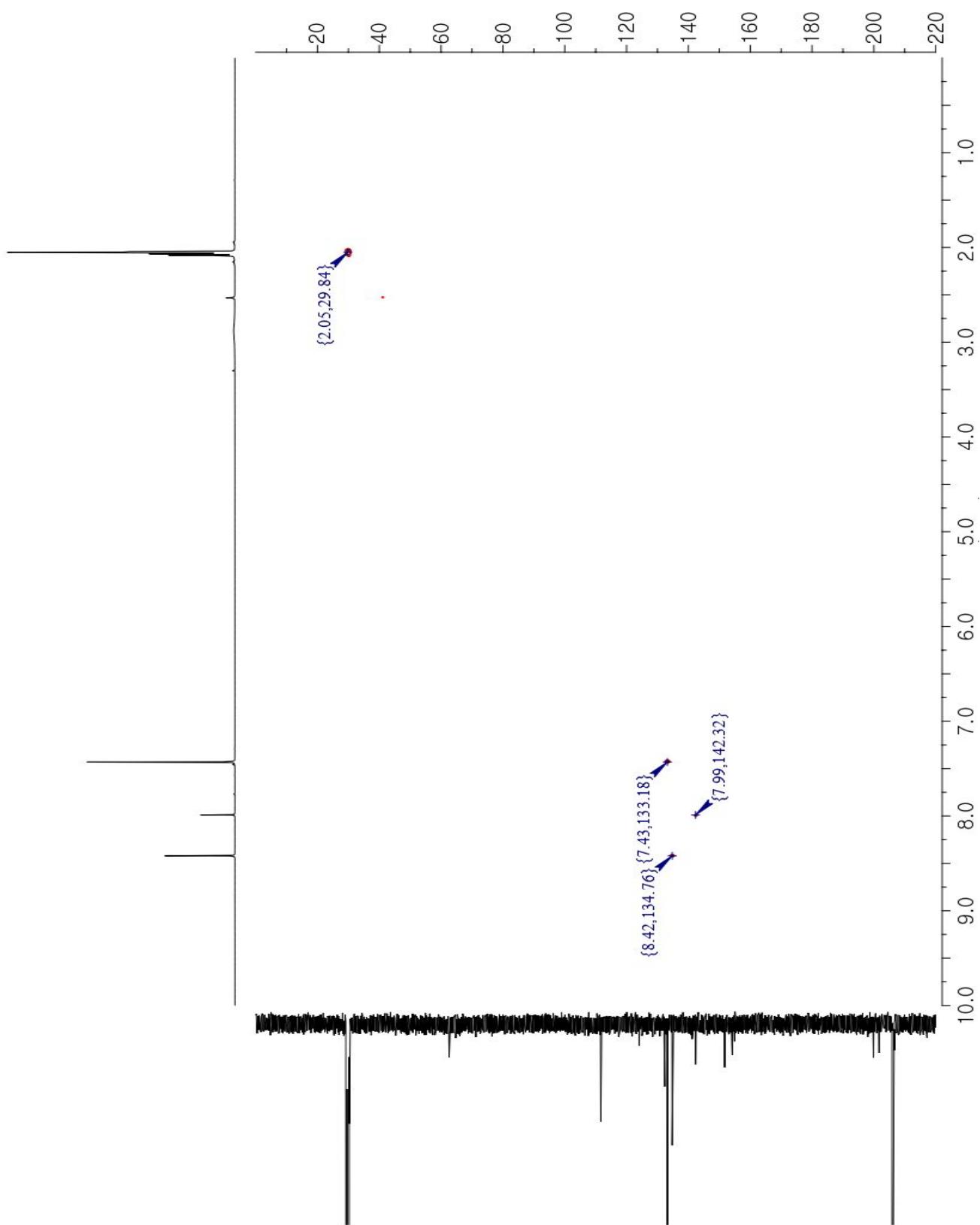


Figure S13. The HSQC (800 MHz, acetone- d_6) spectrum of **3**

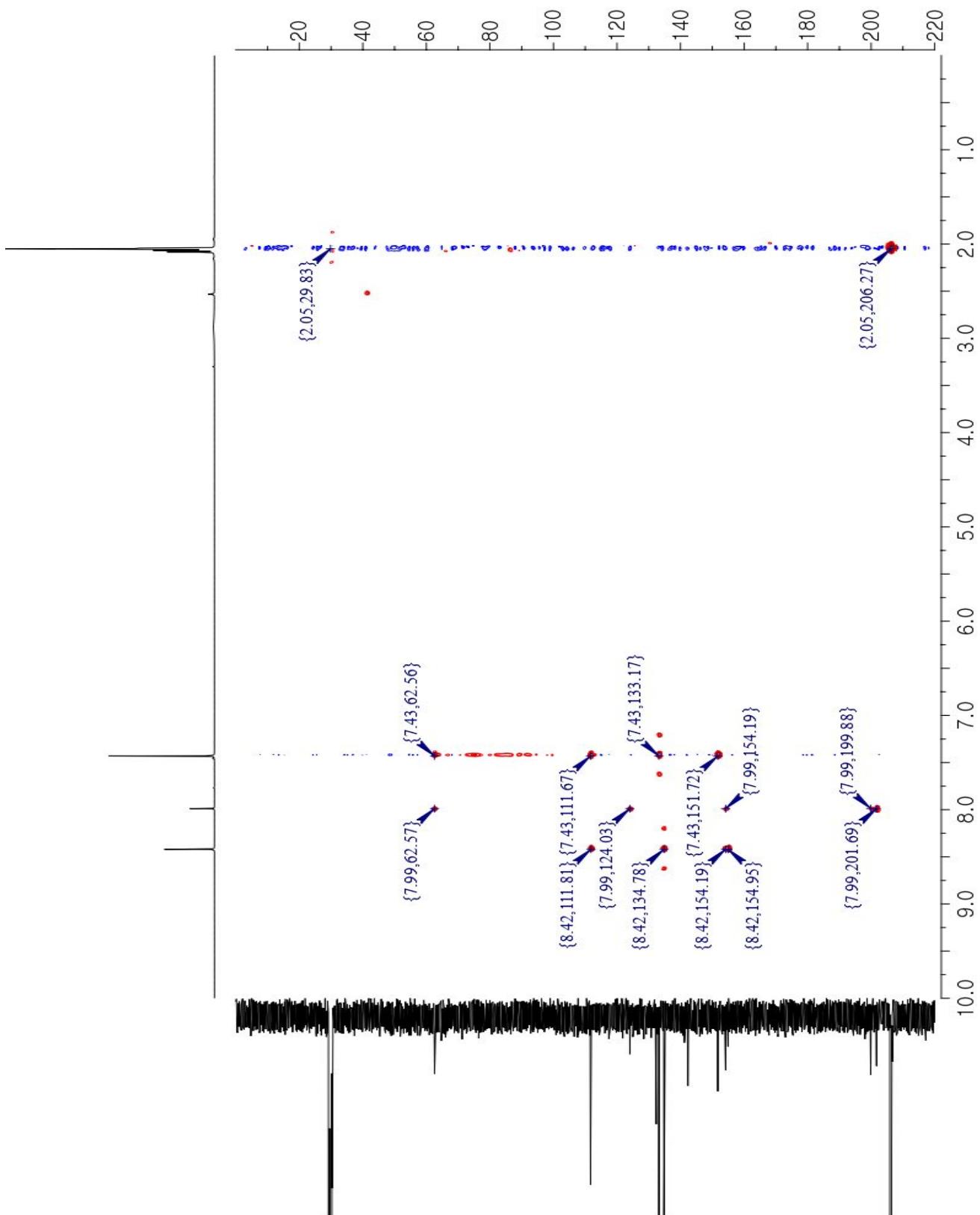


Figure S14. The HMBC (800 MHz, acetone-*d*₆, $J_{\text{CH}} = 8$ Hz) spectrum of **3**

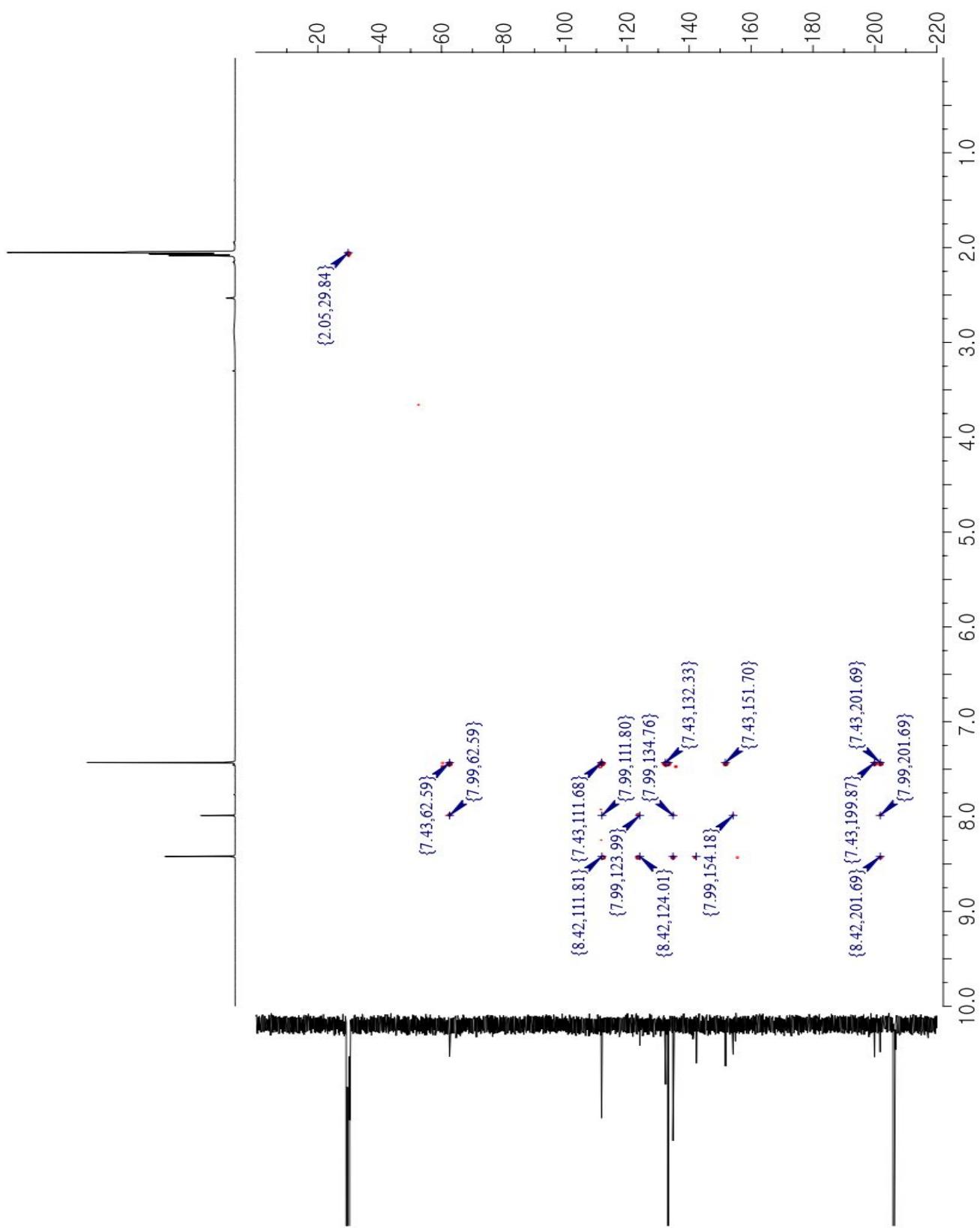


Figure S15. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of **3**

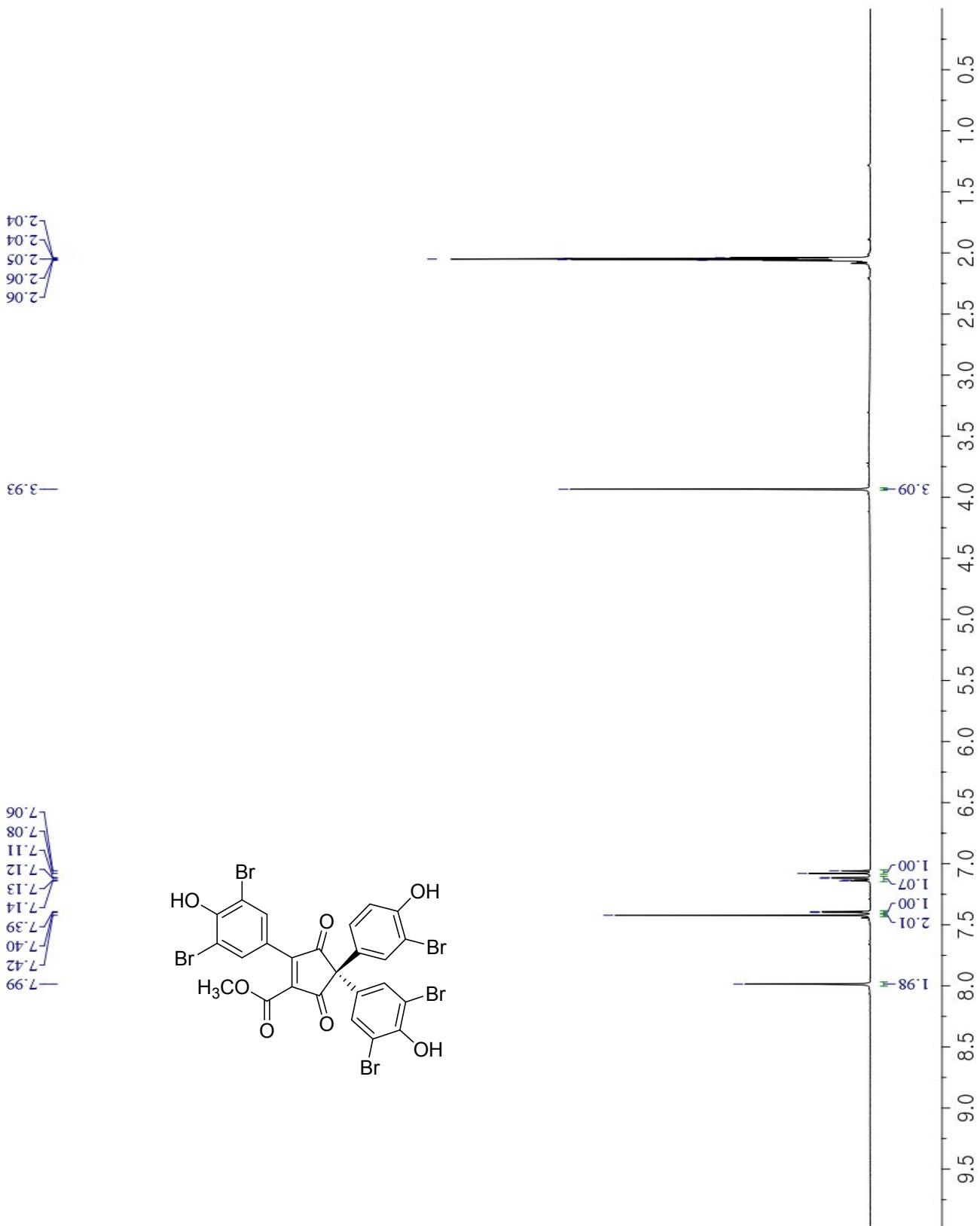


Figure S16. The ^1H NMR (600 MHz, acetone- d_6) spectrum of 4

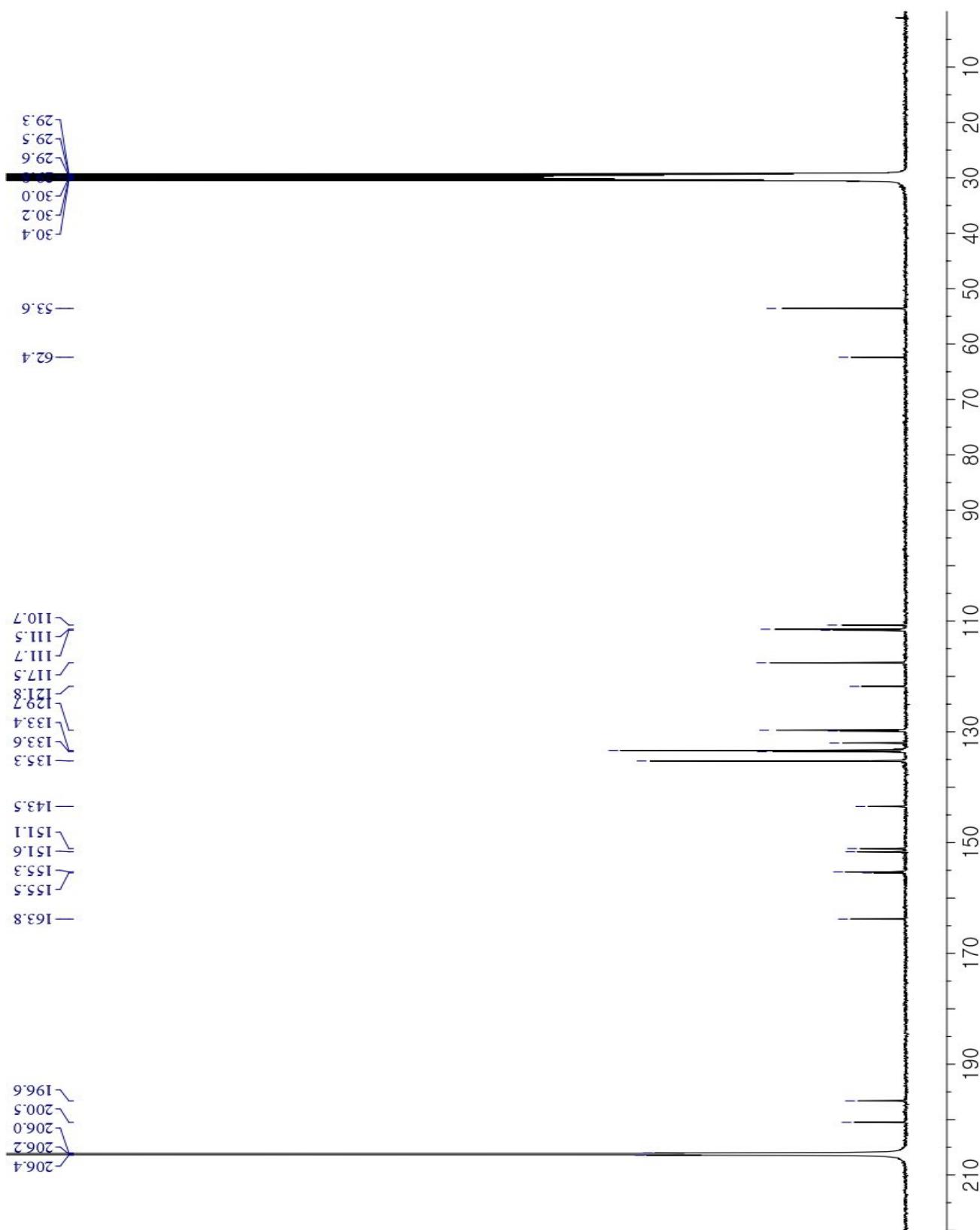


Figure S17. The ^{13}C NMR (150 MHz, acetone- d_6) spectrum of **4**

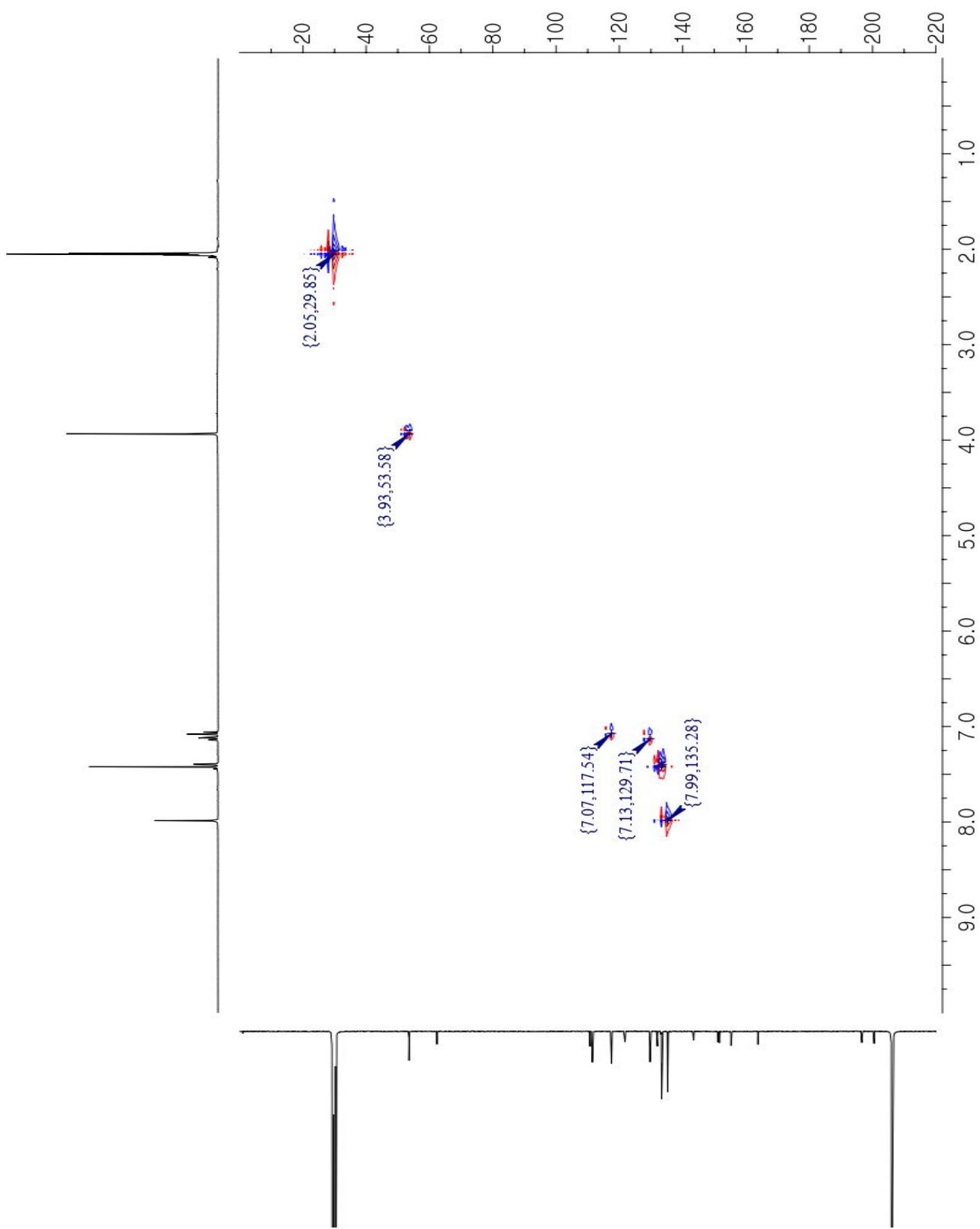


Figure S18. The HSQC (600 MHz, acetone- d_6) spectrum of **4**

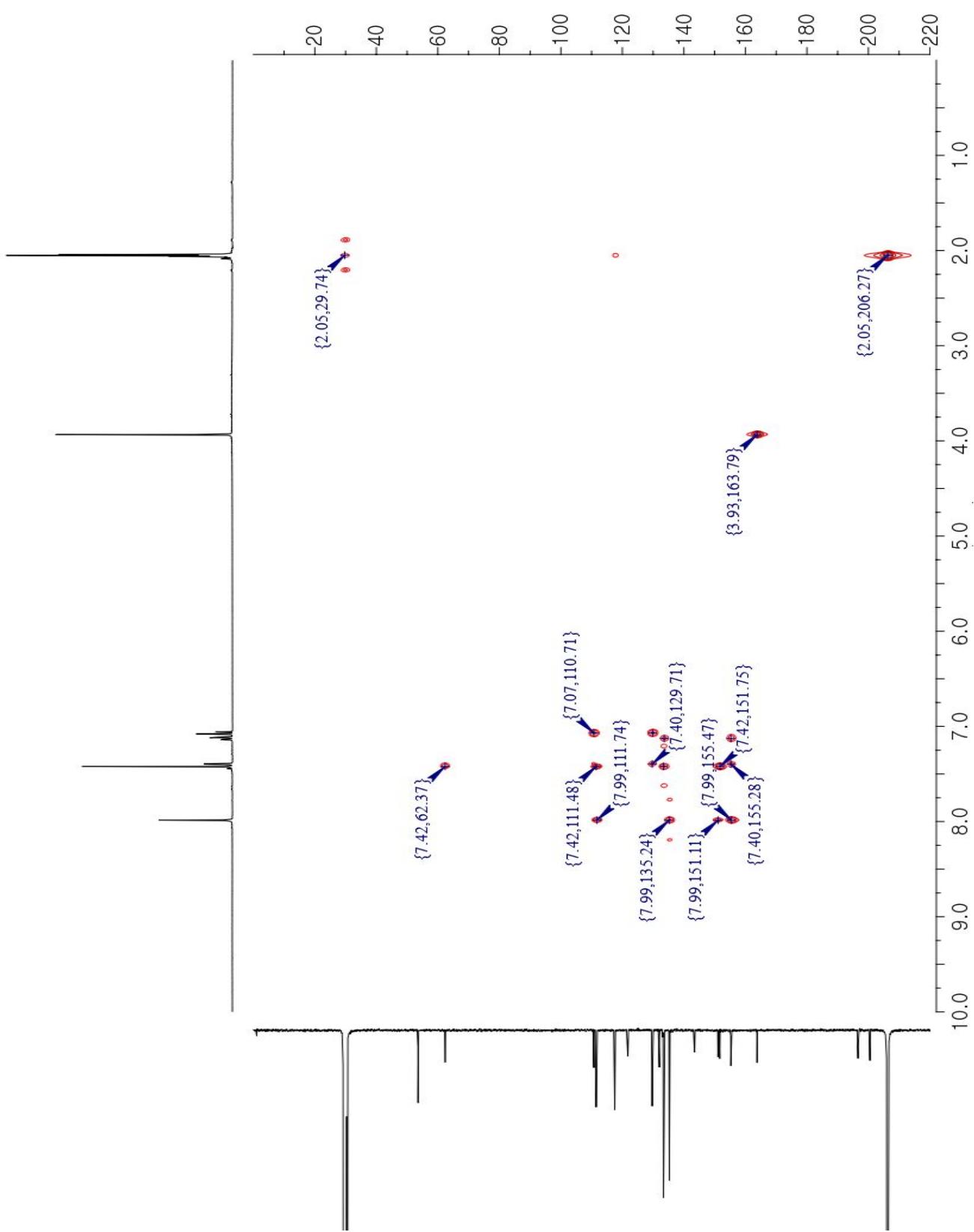


Figure S19. The HMBC (600 MHz, acetone-*d*₆, *J*_{CH} = 8 Hz) spectrum of **4**

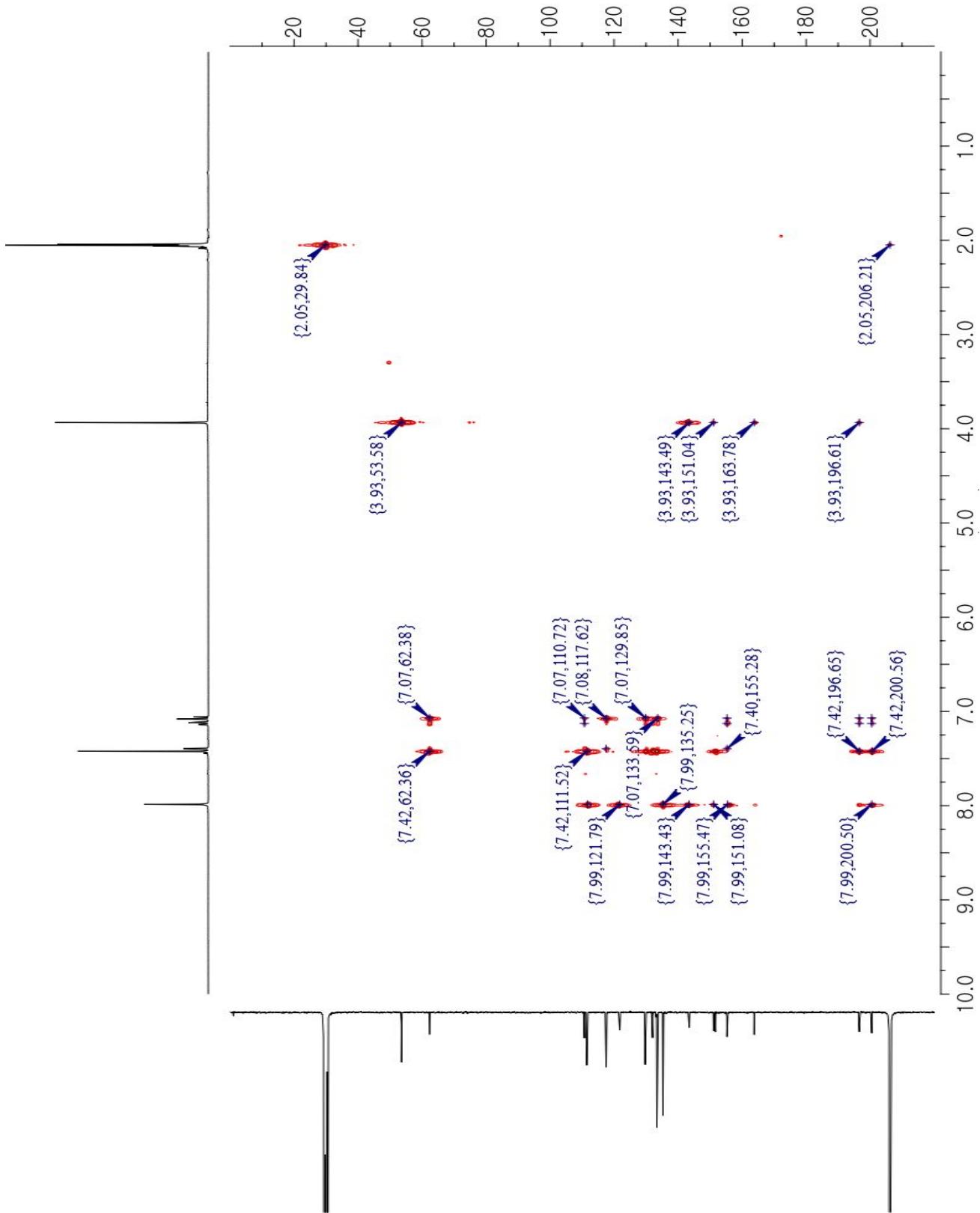


Figure S20. The D-HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 1 Hz) spectrum of **4**

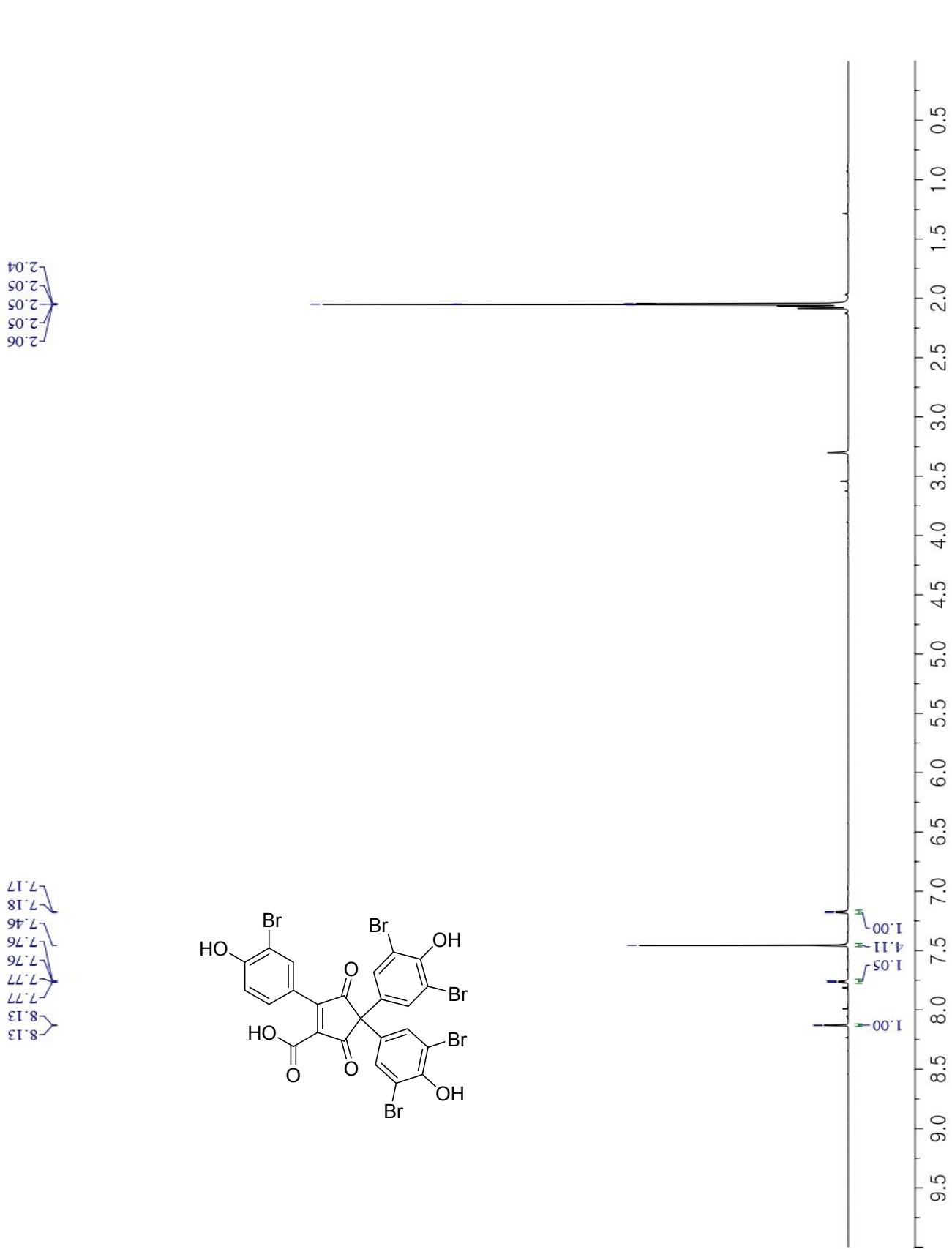


Figure S21. The ^1H NMR (800 MHz, acetone- d_6) spectrum of **5**

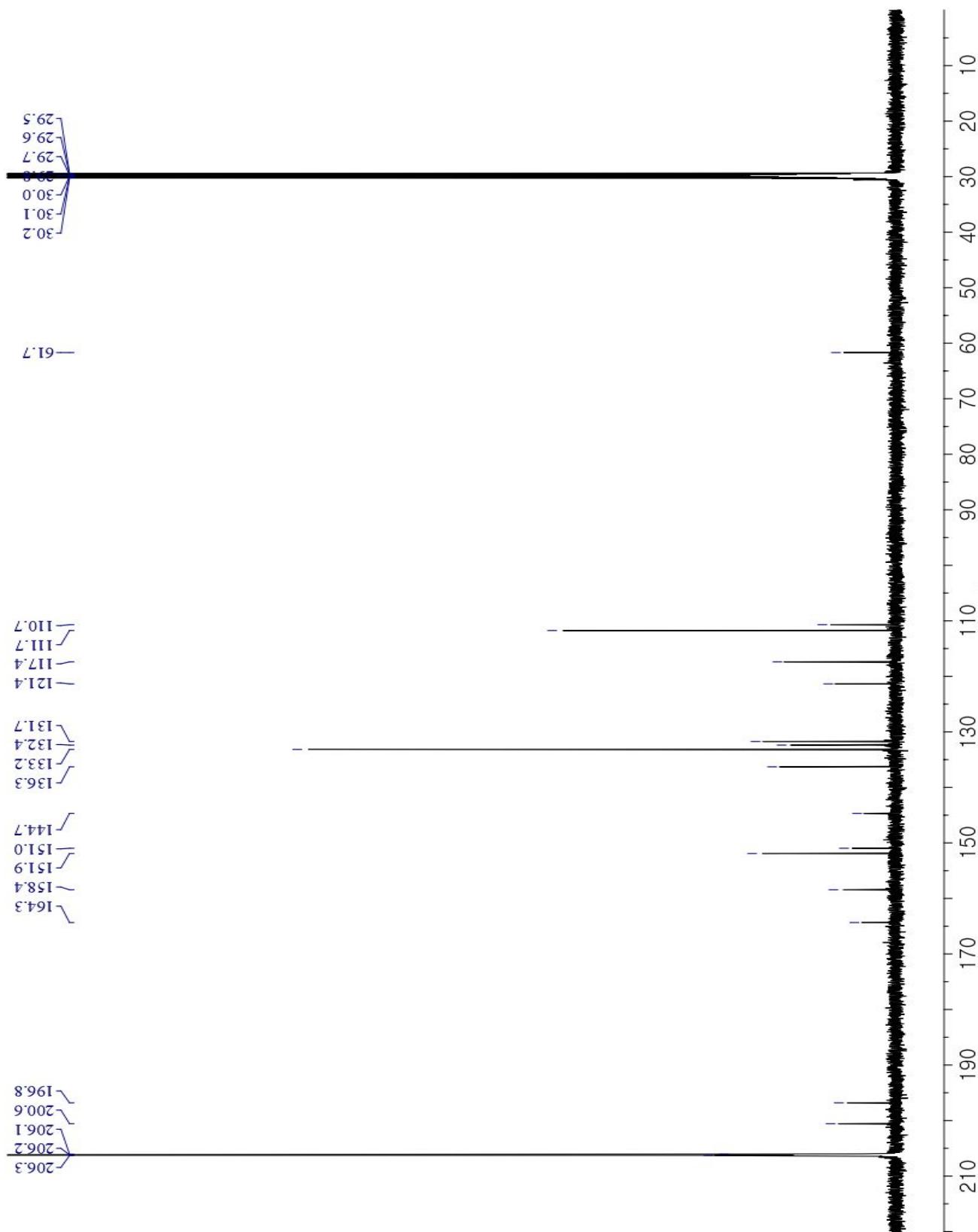


Figure S22. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of **5**

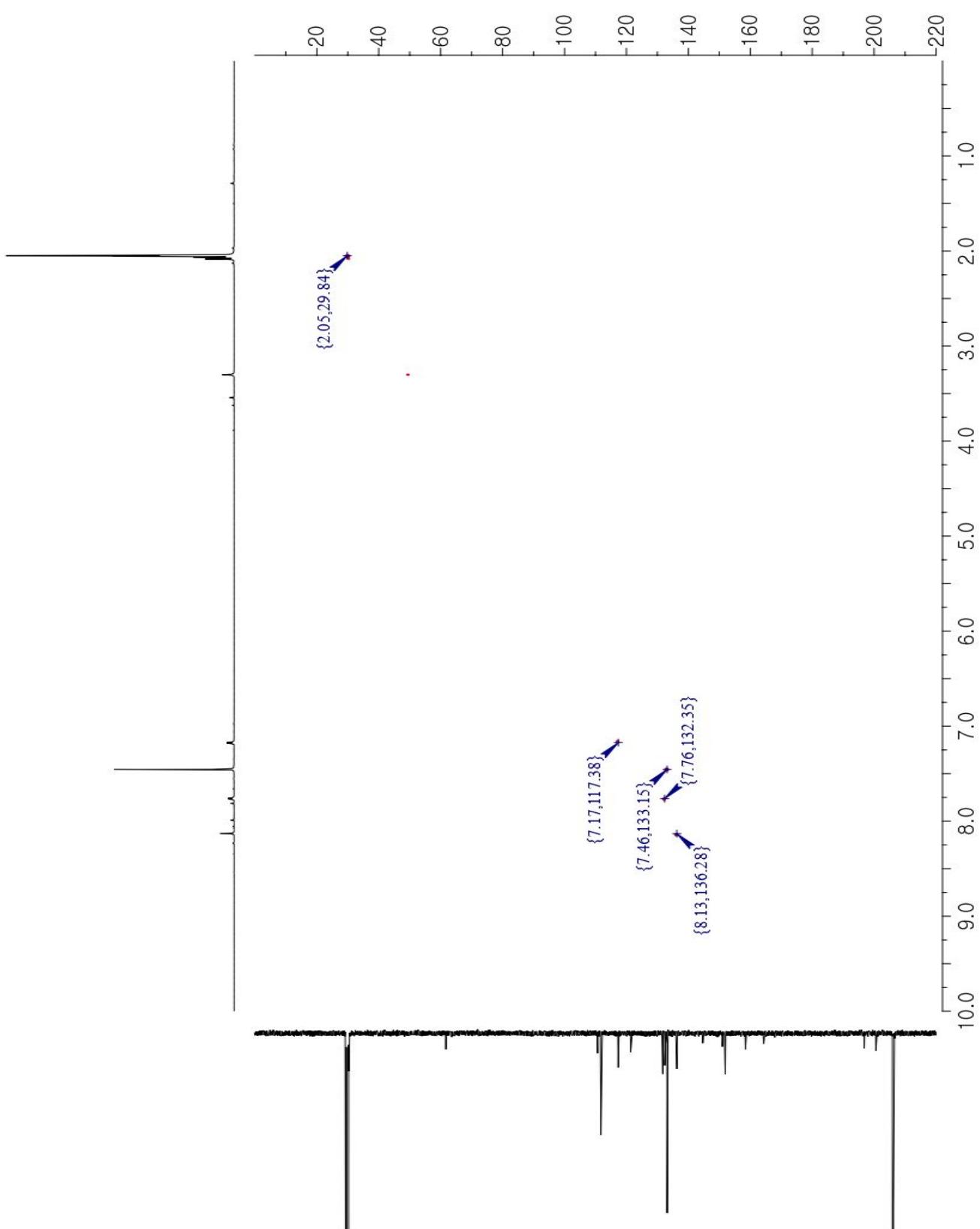


Figure S23. The HSQC (800 MHz, acetone- d_6) spectrum of **5**

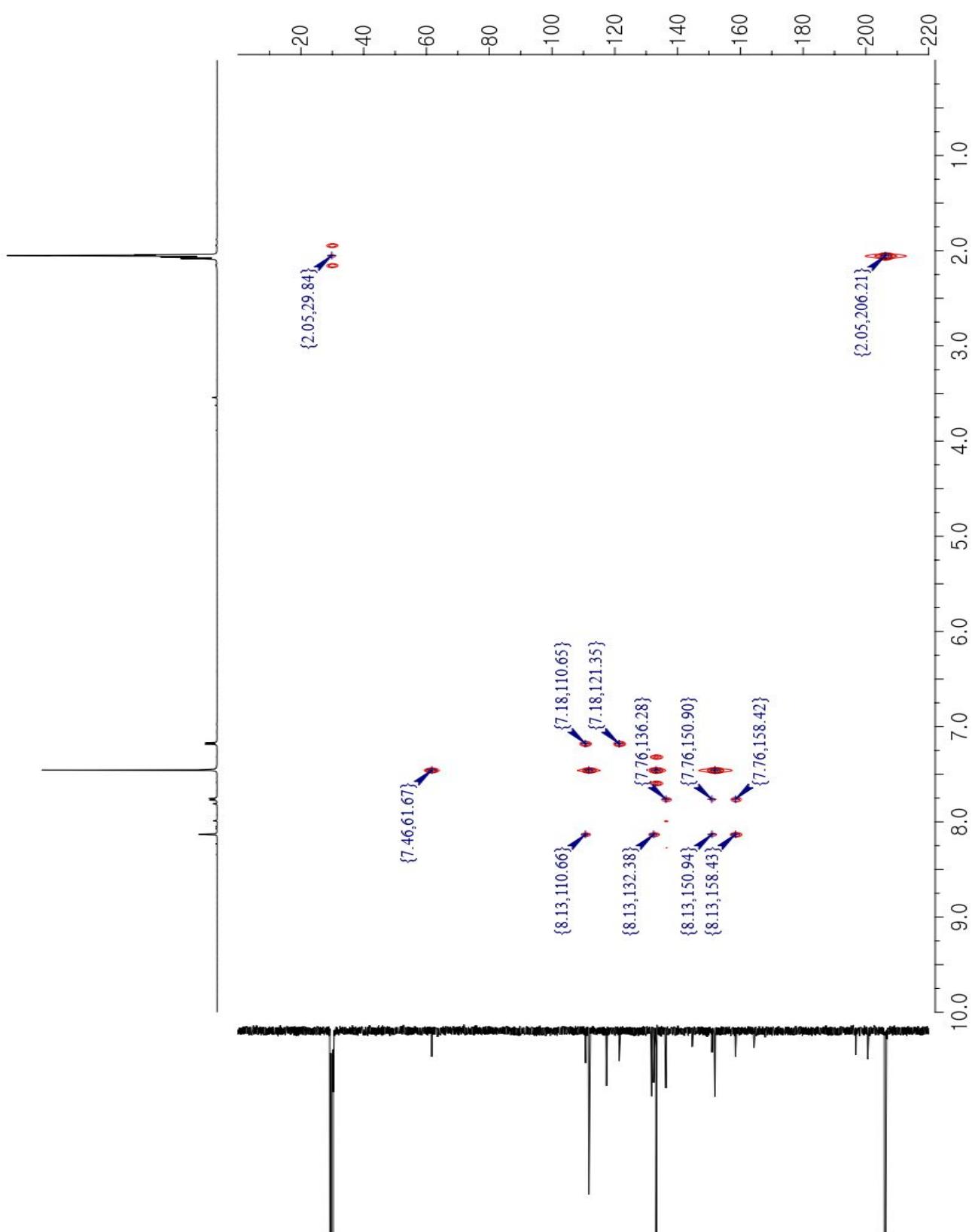


Figure S24. The HMBC (800 MHz, acetone-*d*₆, $J_{\text{CH}} = 8$ Hz) spectrum of **5**

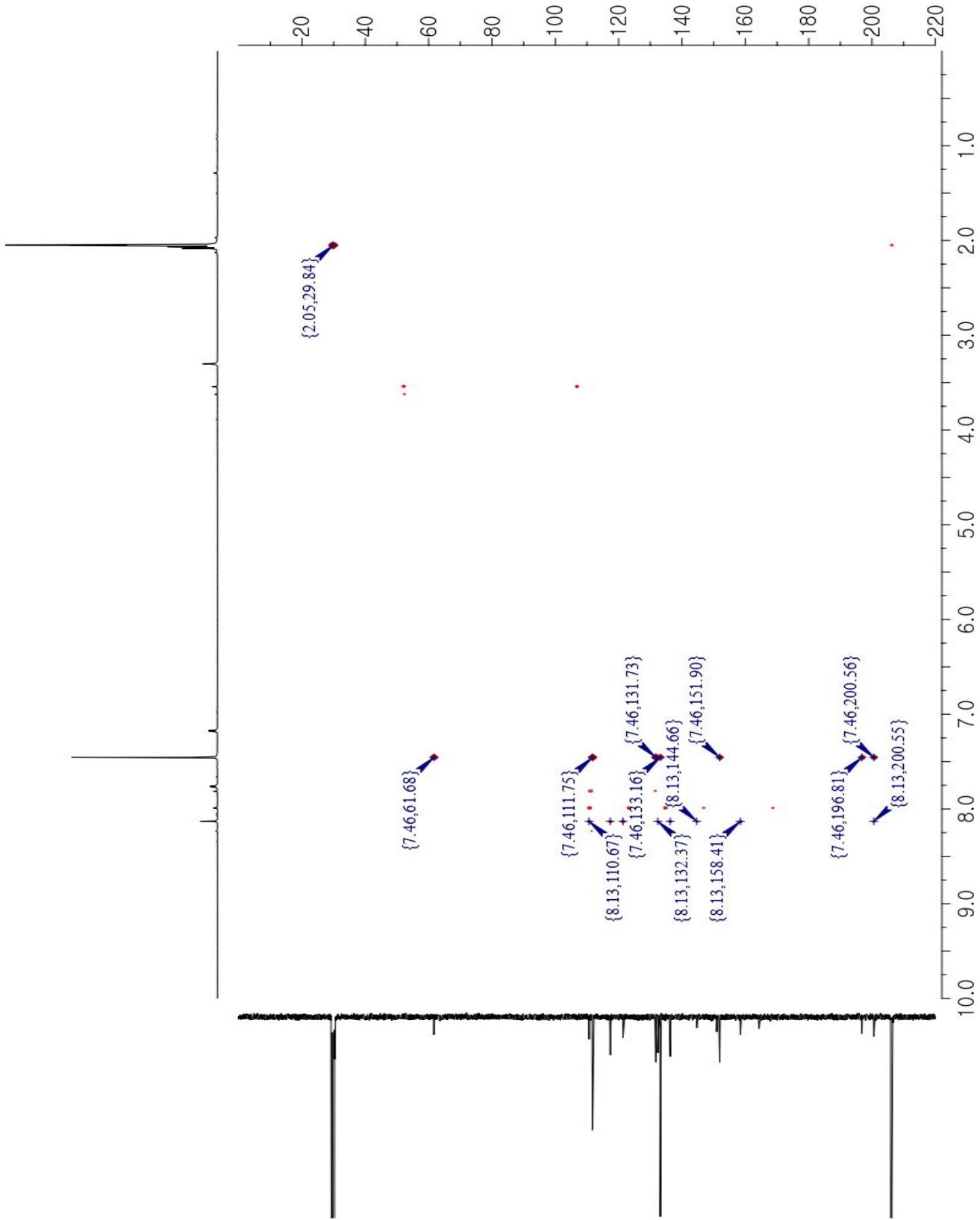


Figure S25. The D-HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 1 Hz) spectrum of **5**

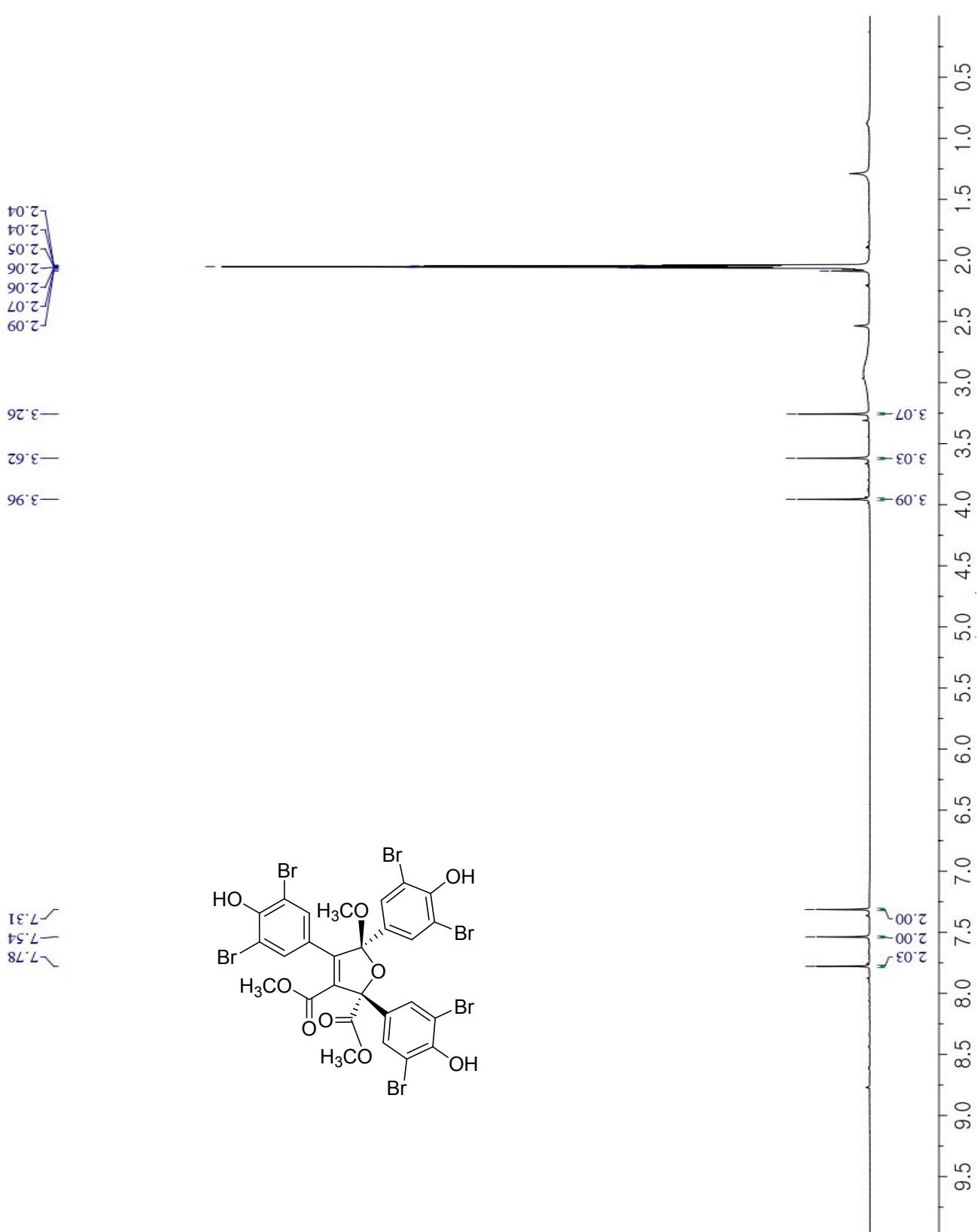


Figure S26. The ^1H NMR (600 MHz, acetone- d_6) spectrum of **6**

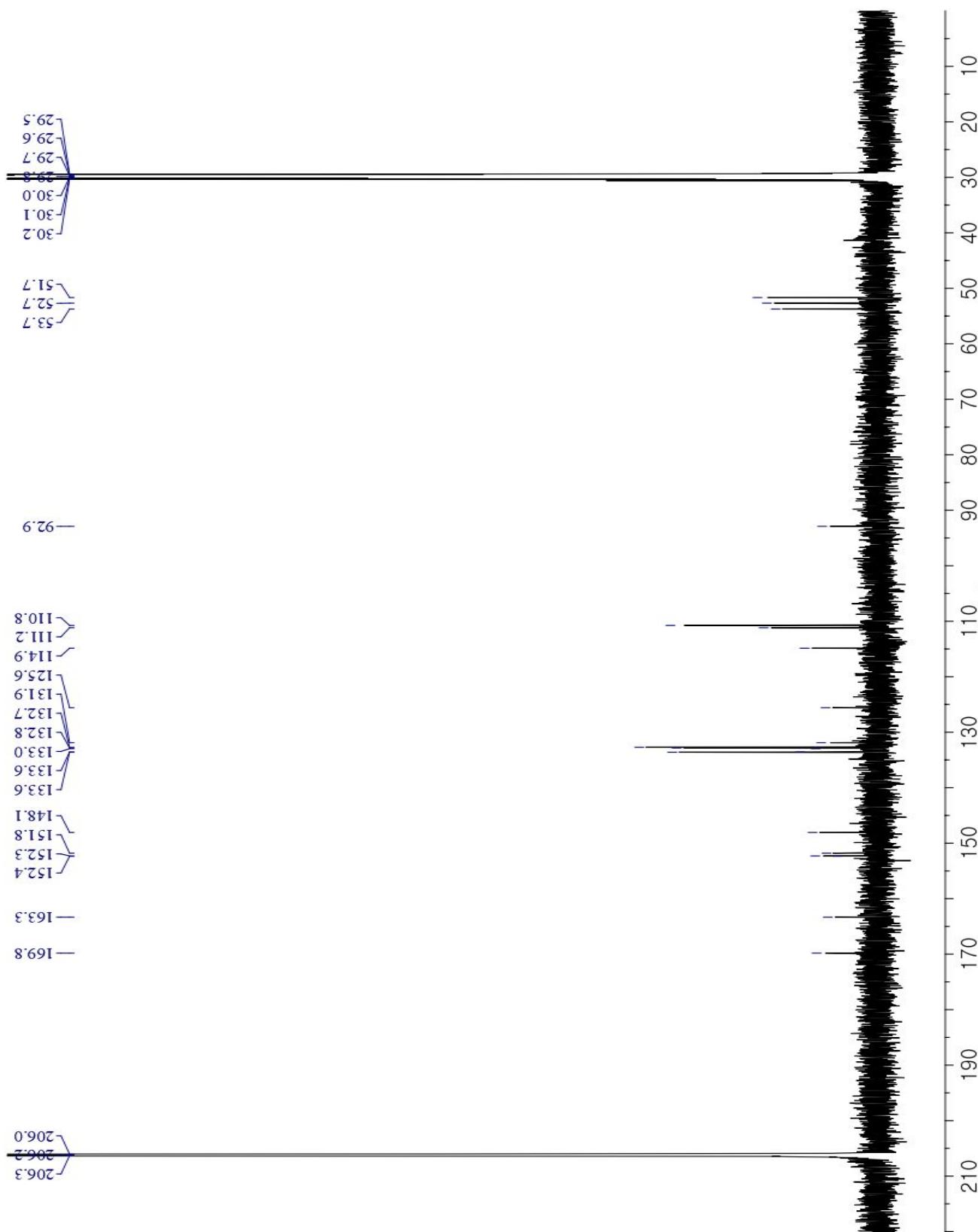


Figure S27. The ^{13}C NMR (150 MHz, acetone- d_6) spectrum of **6**

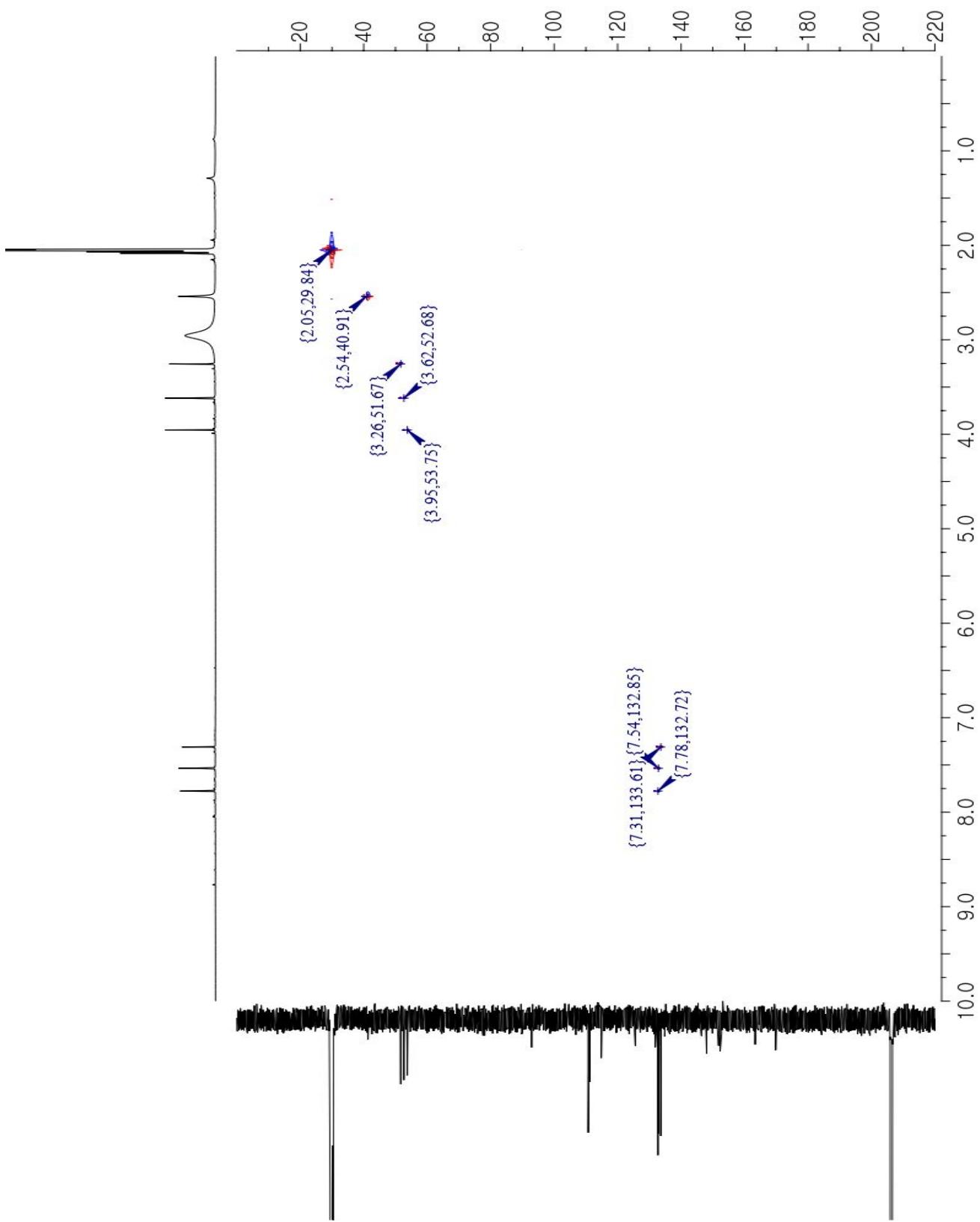


Figure S28. The HSQC (600 MHz, acetone-*d*₆) spectrum of **6**

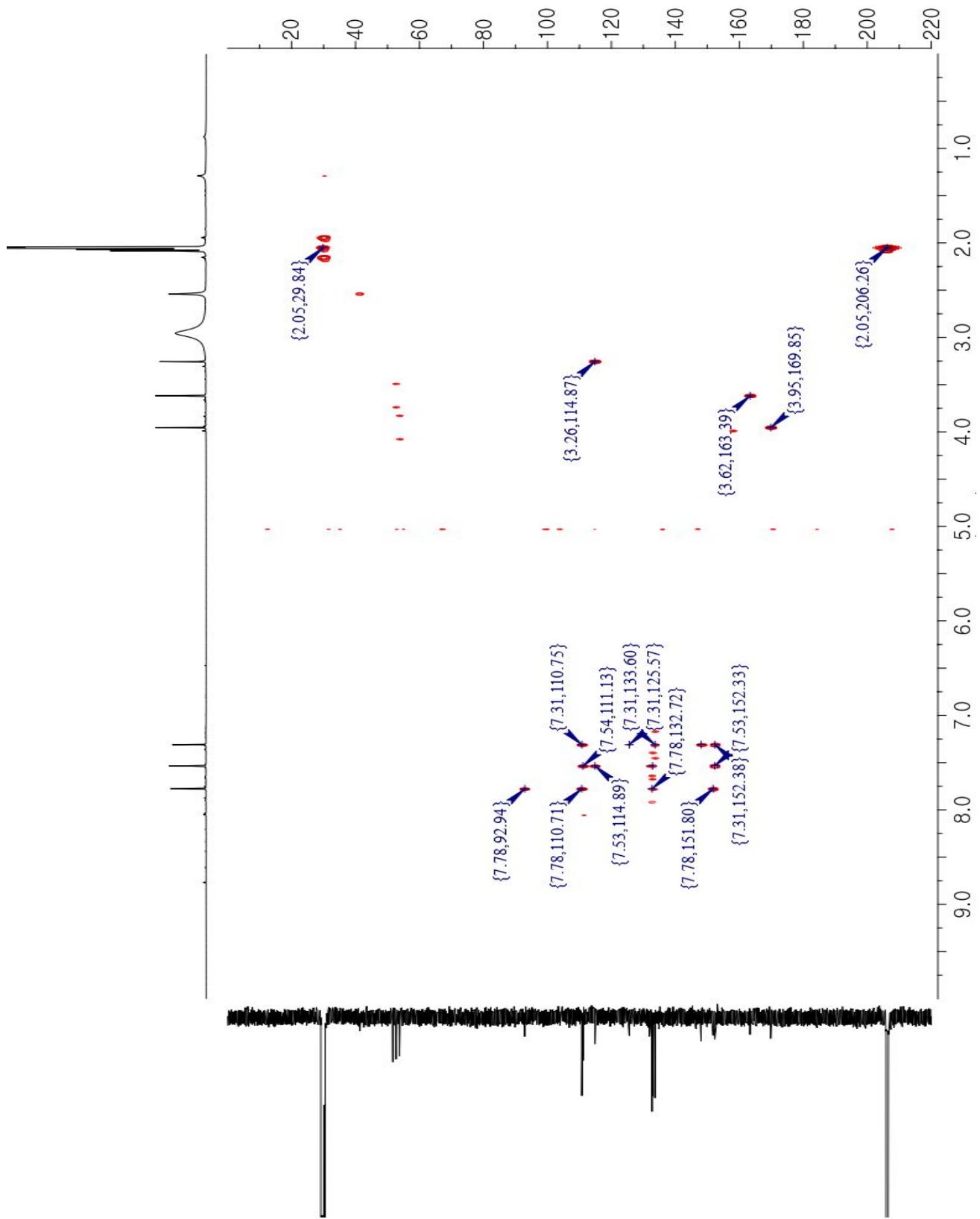


Figure S29. The HMBC (600 MHz, acetone-*d*₆, *J*_{CH} = 8 Hz) spectrum of **6**

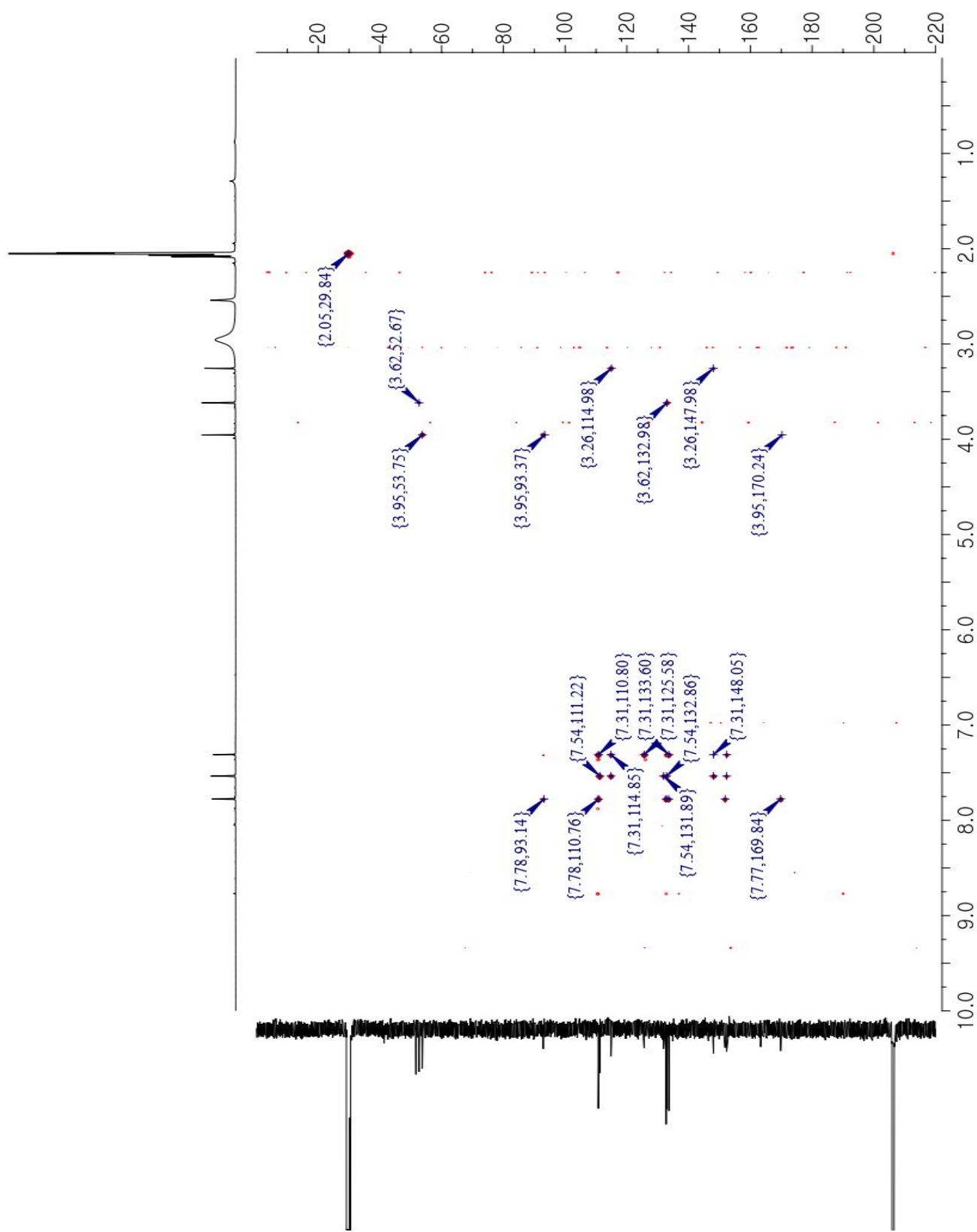


Figure S30. The D-HMBC (800 MHz, acetone- d_6 , $J_{\text{CH}} = 1$ Hz) spectrum of **6**

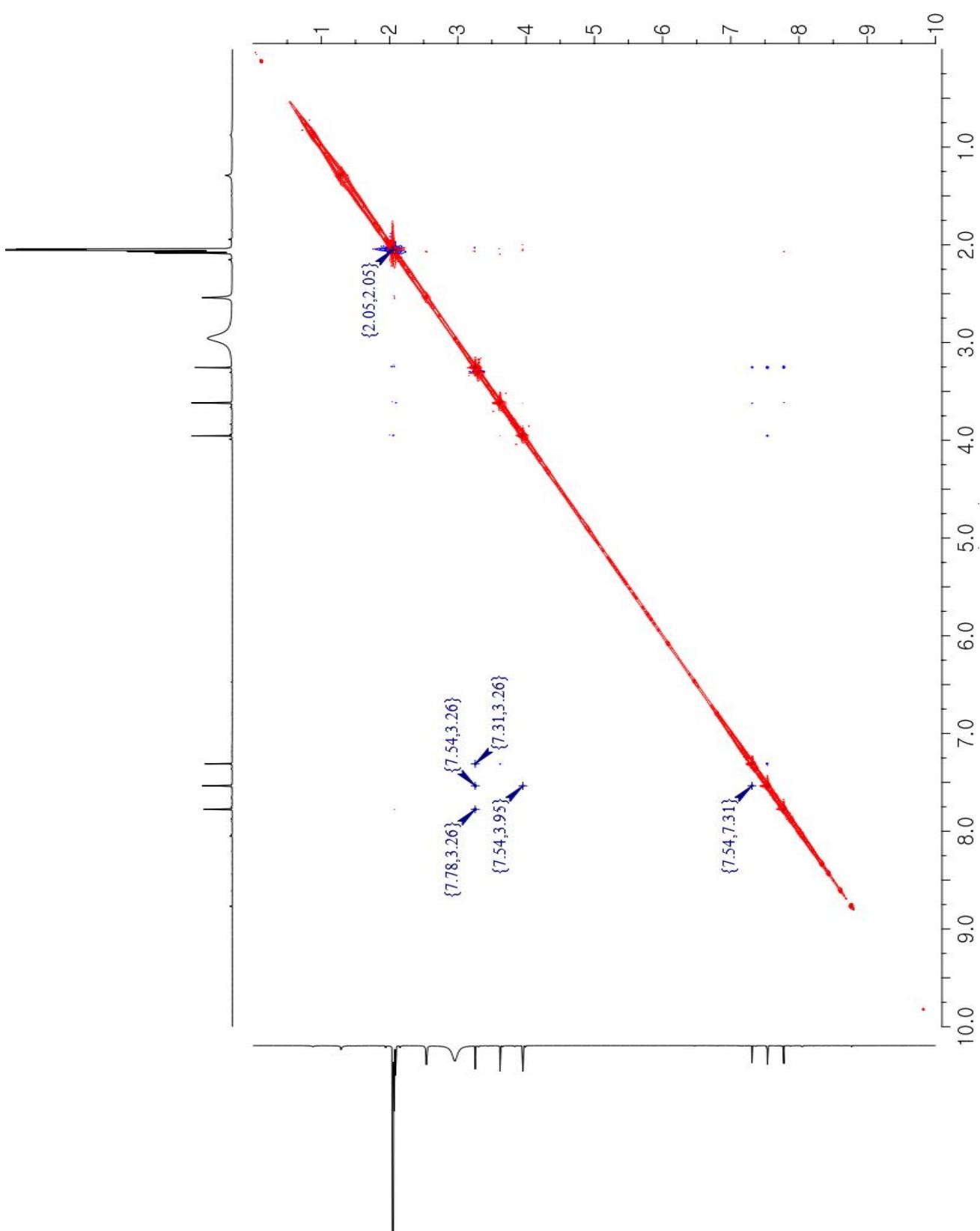


Figure S31. The NOESY (800 MHz, acetone-*d*₆) spectrum of **6**

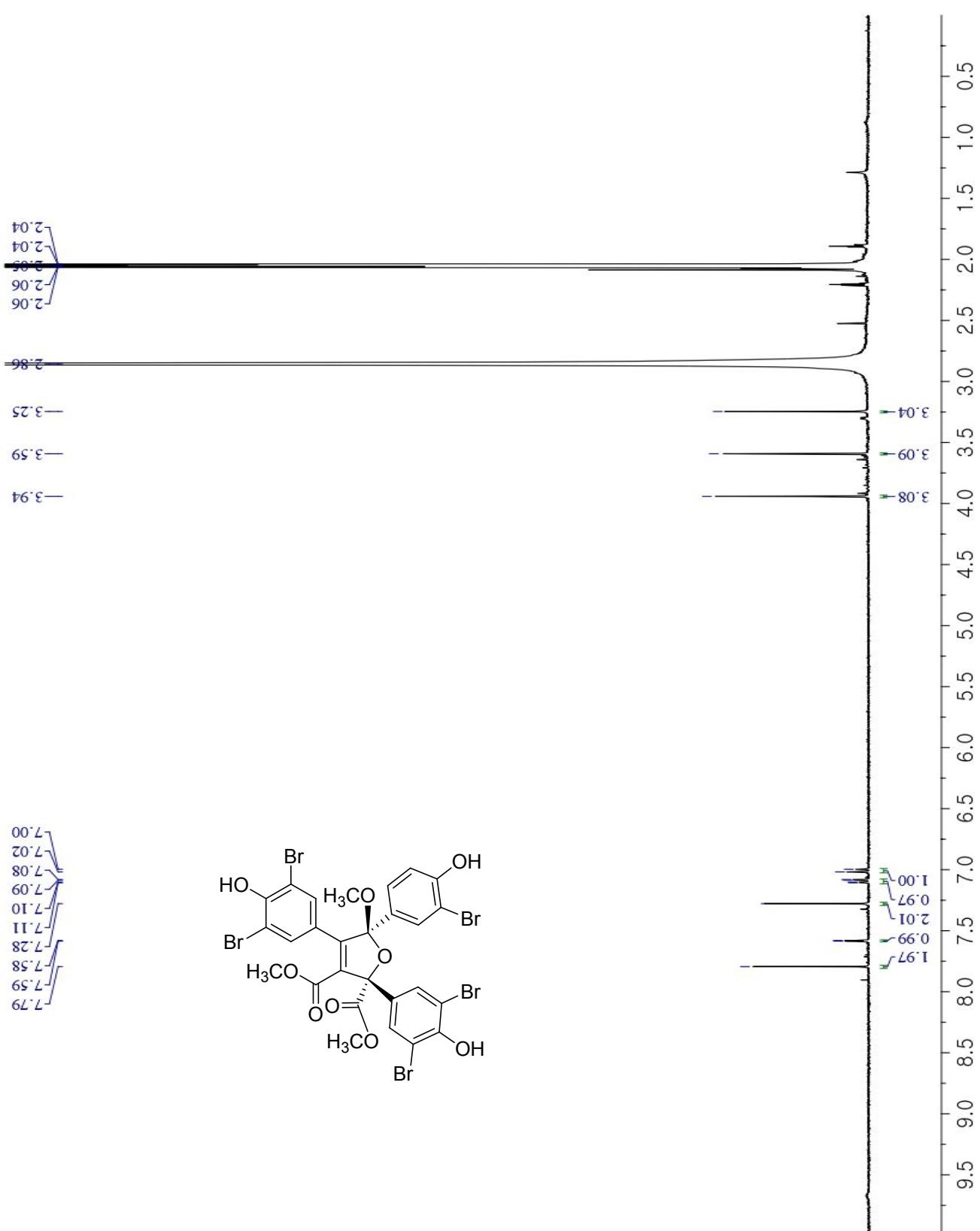


Figure S32. The ^1H NMR (400 MHz, acetone- d_6) spectrum of 7

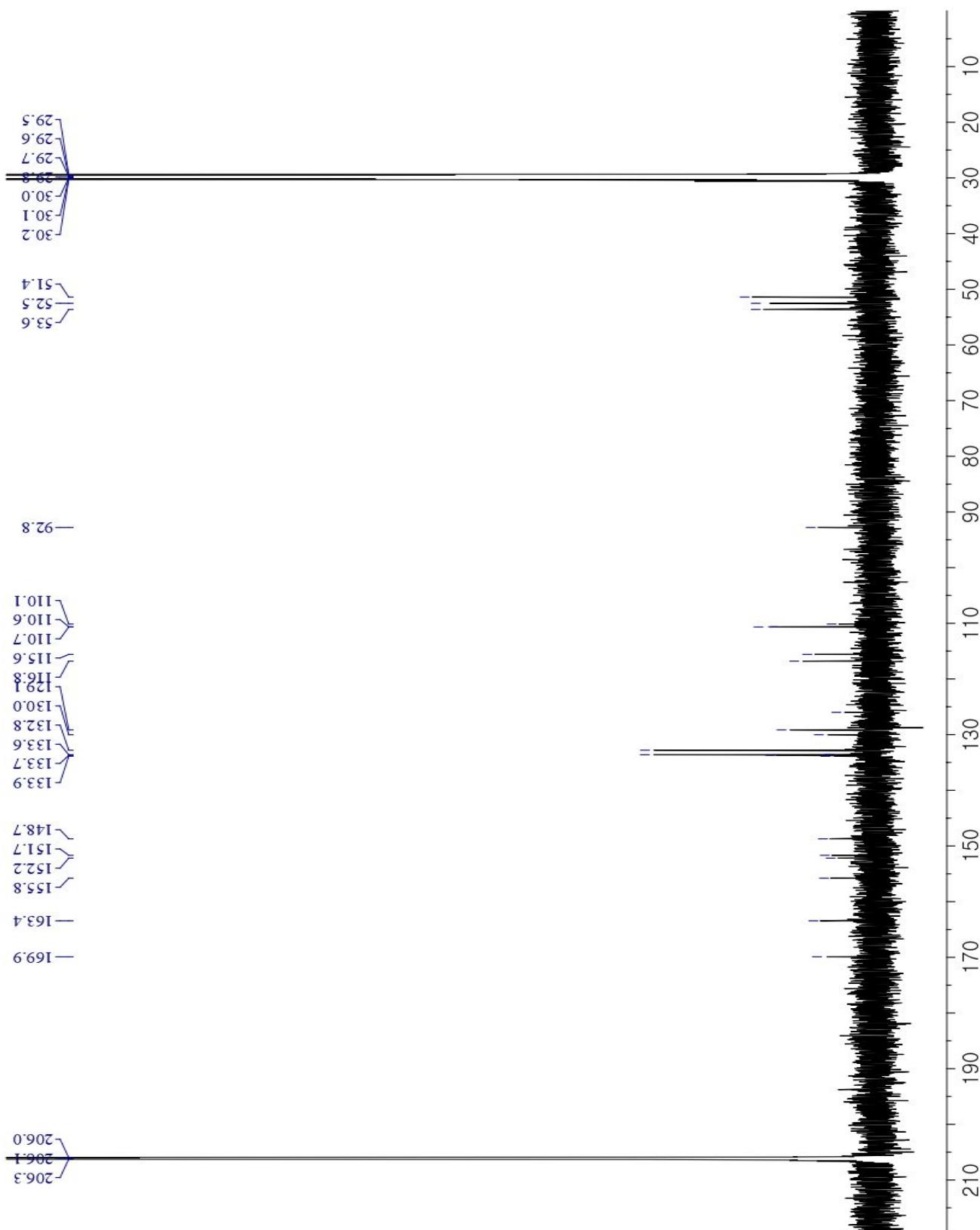


Figure S33. The ^{13}C NMR (100 MHz, acetone- d_6) spectrum of 7

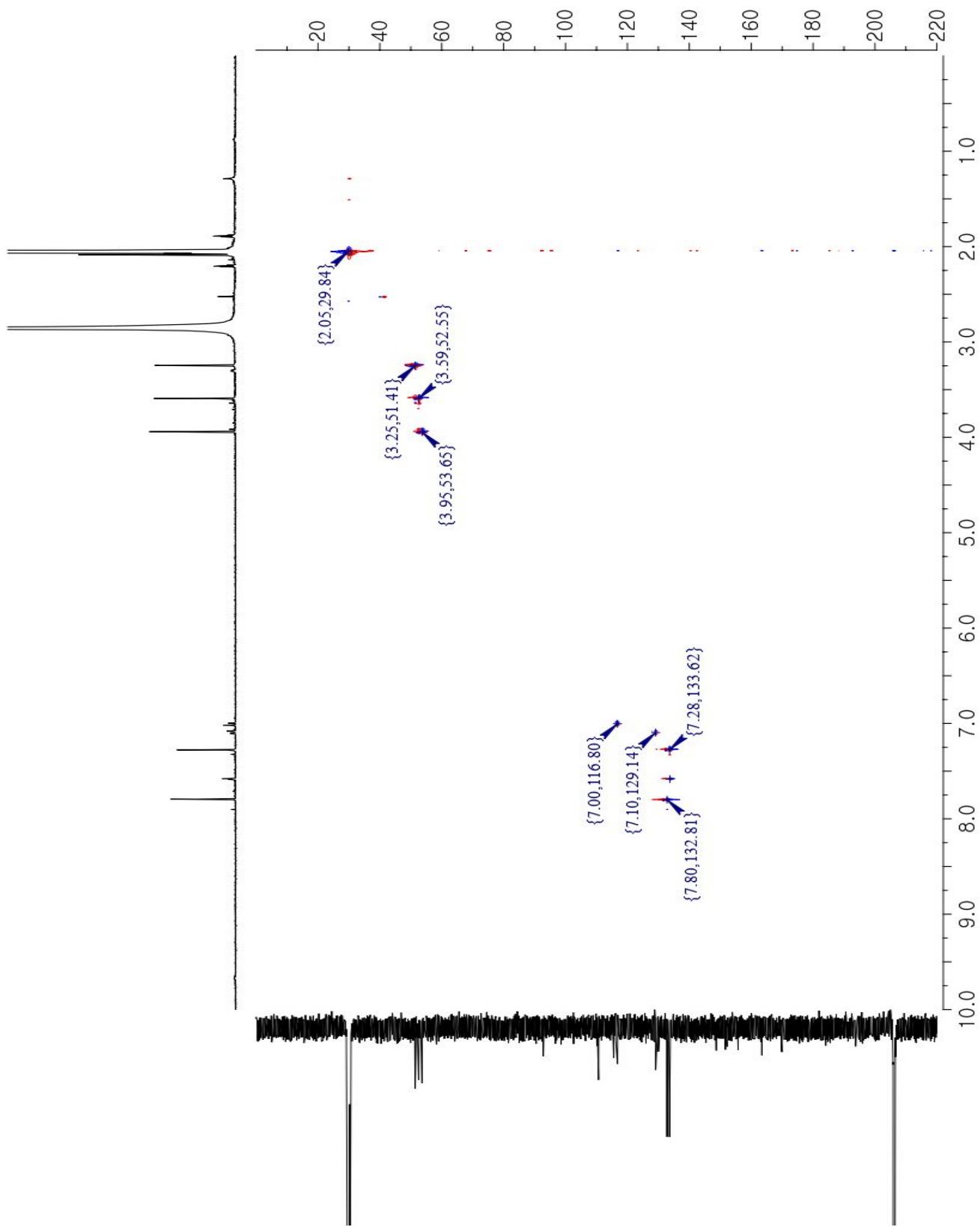


Figure S34. The HSQC (400 MHz, acetone- d_6) spectrum of 7

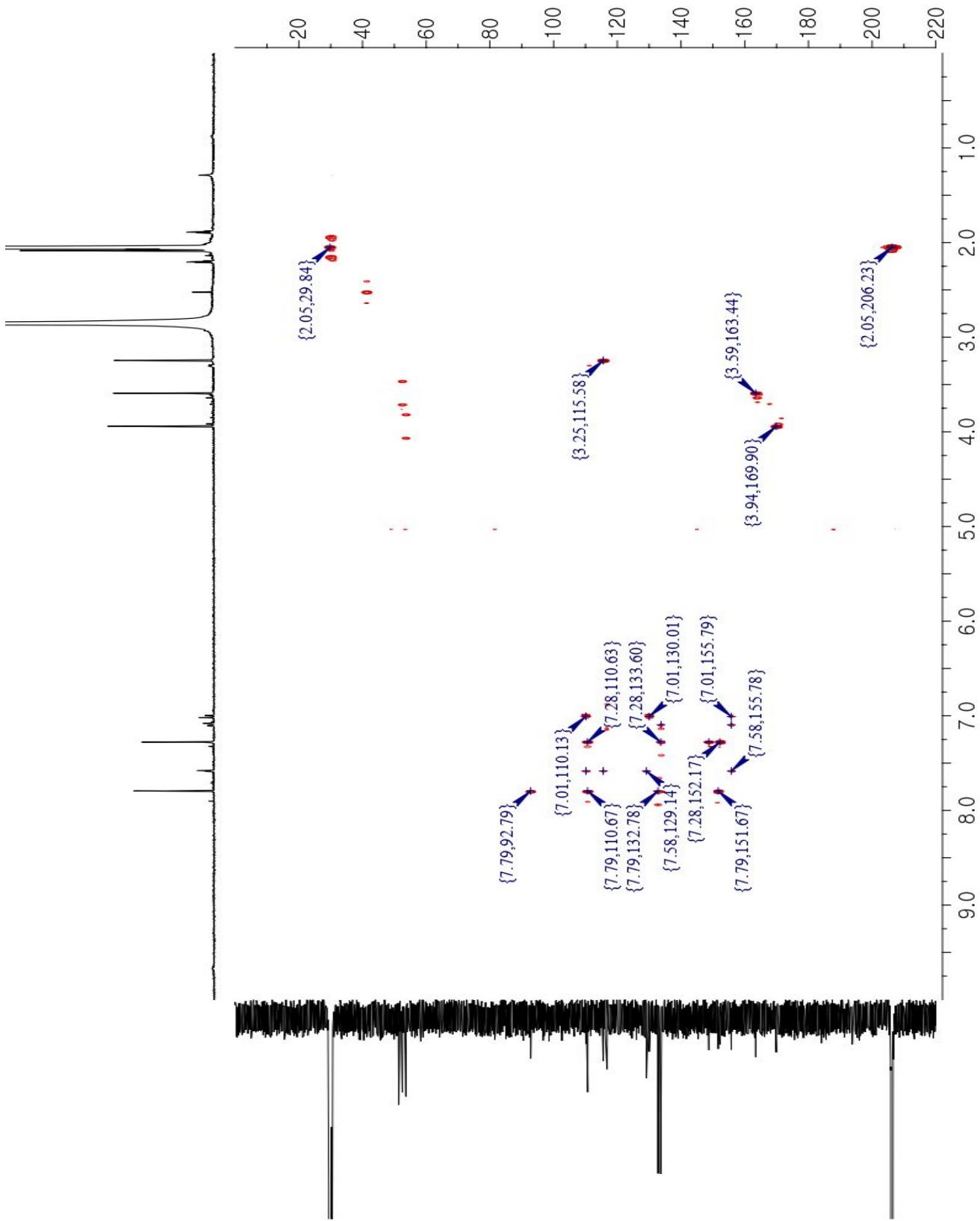


Figure S35. The HMBC (400 MHz, acetone- d_6 , $J_{\text{CH}} = 8$ Hz) spectrum of **7**

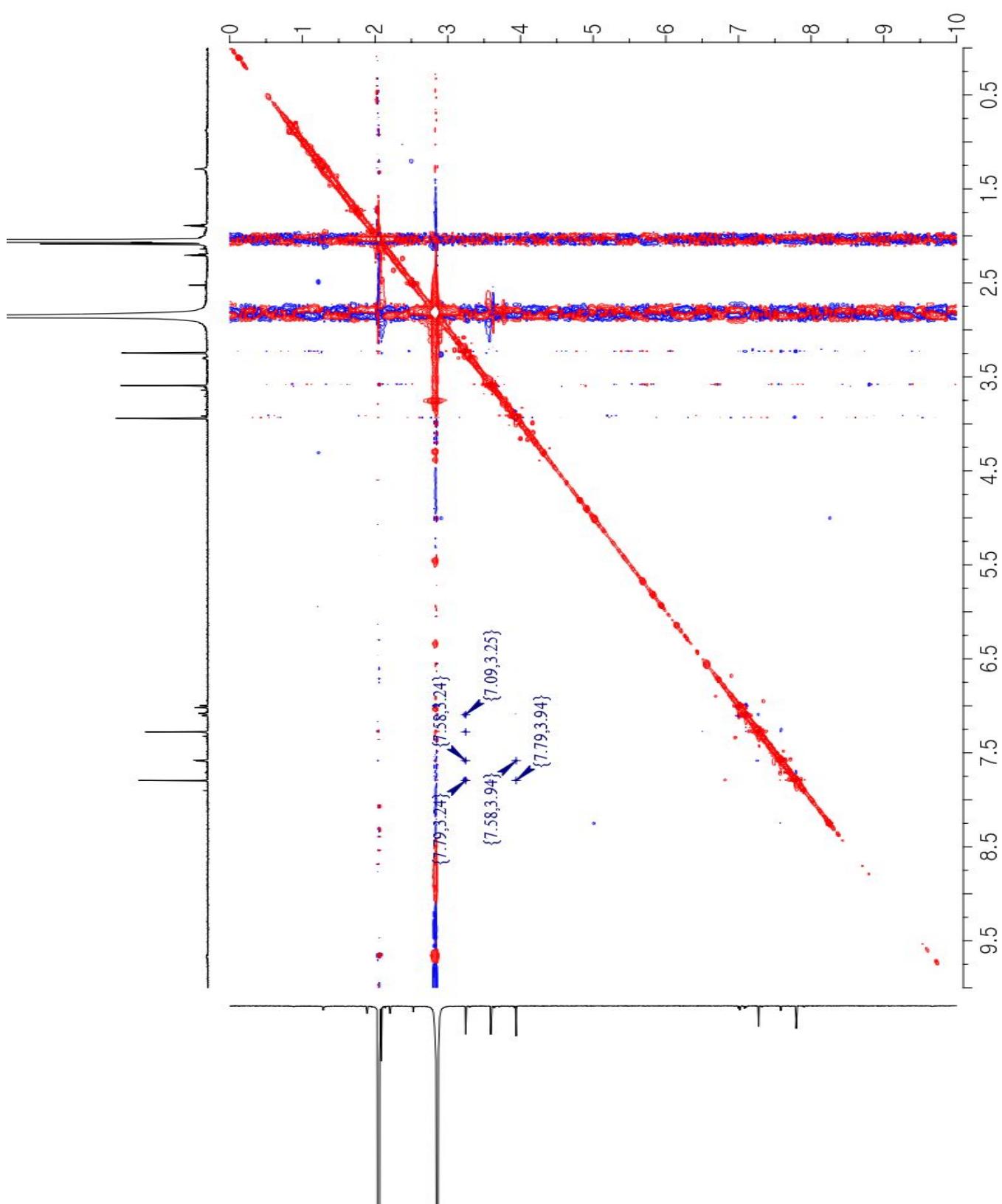


Figure S36. The NOESY (800 MHz, acetone-*d*₆) spectrum of 7

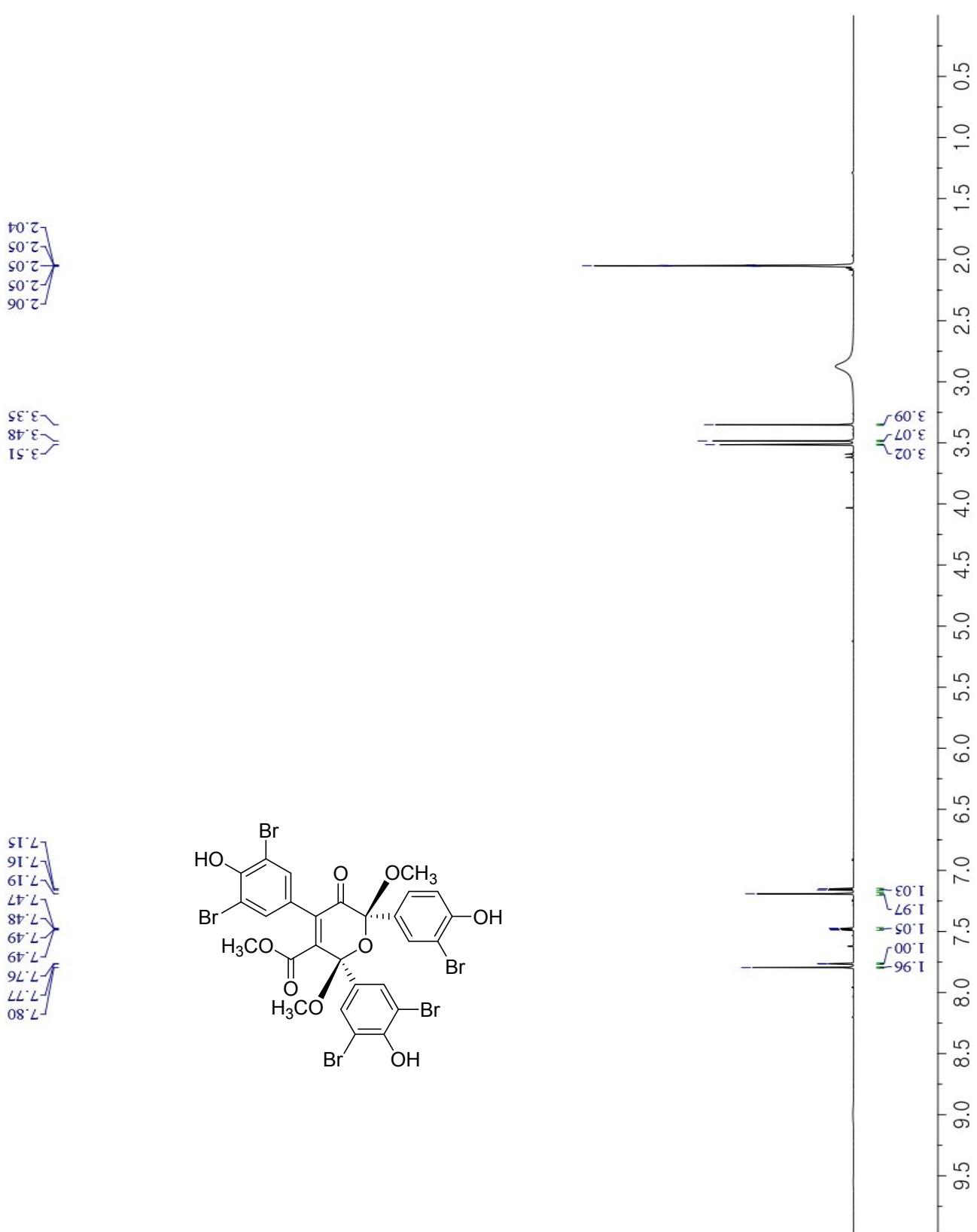


Figure S37. The ^1H NMR (800 MHz, acetone- d_6) spectrum of **8**

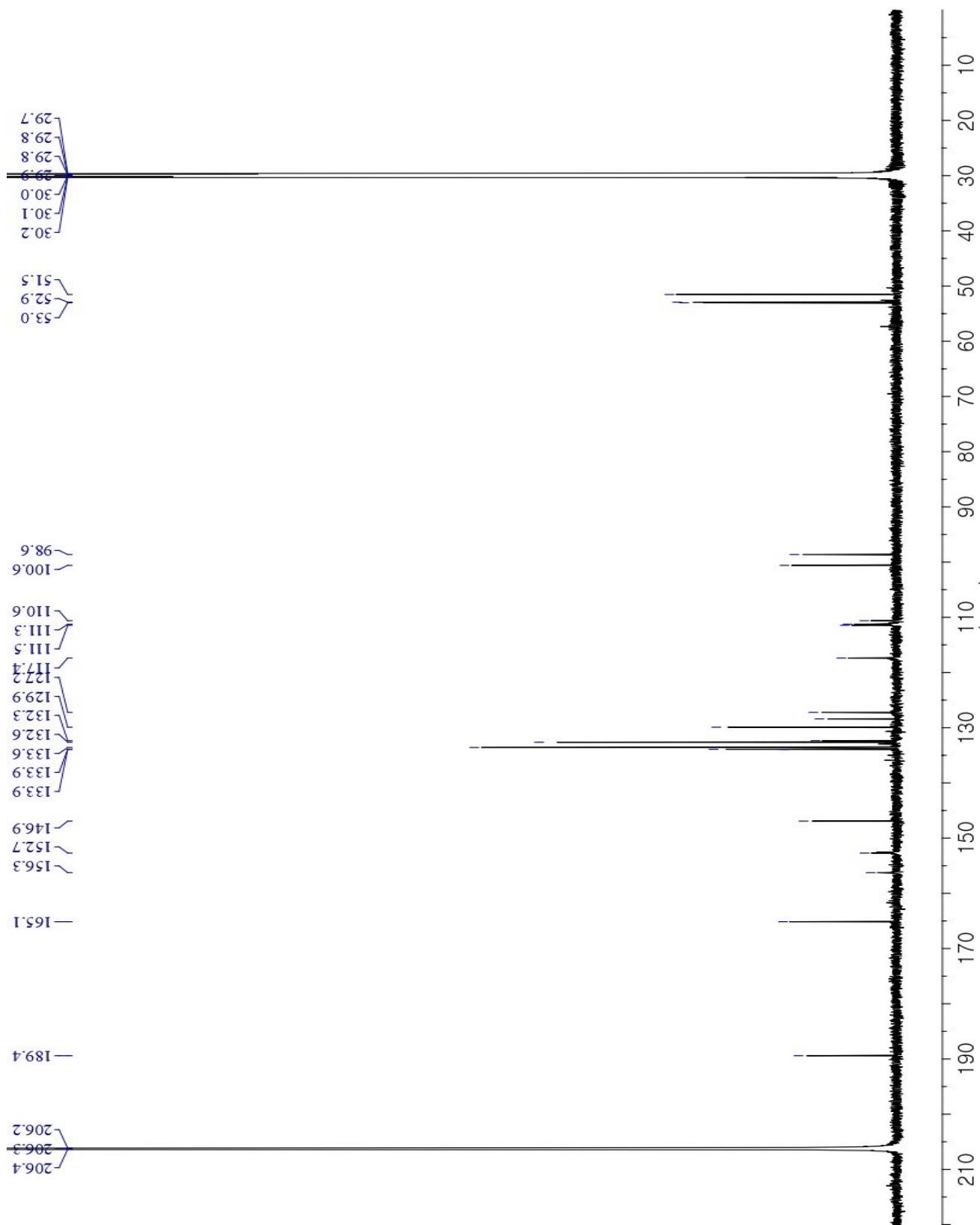


Figure S38. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of **8**

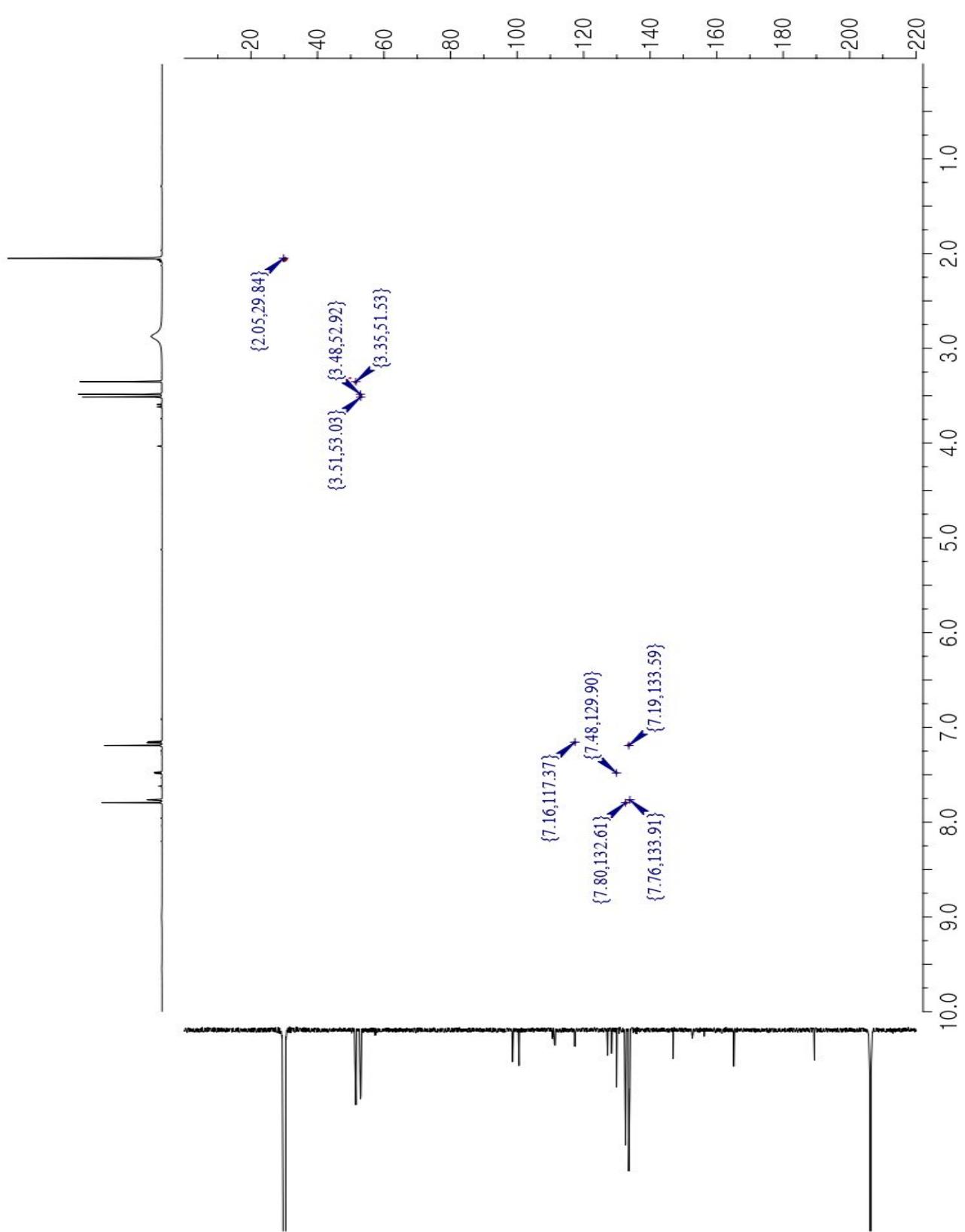


Figure S39. The HSQC (800 MHz, acetone-*d*₆) spectrum of **8**

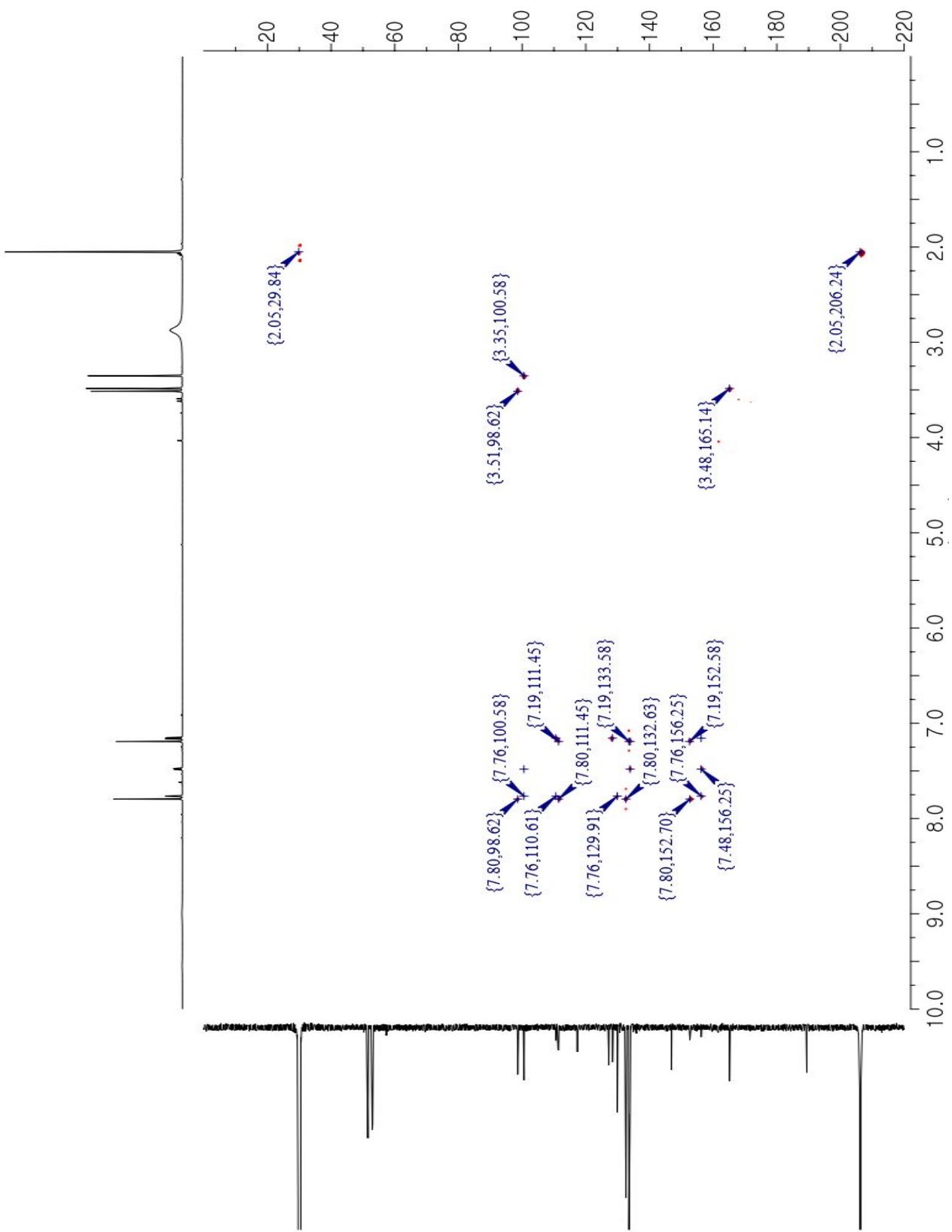


Figure S40. The HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 8 Hz) spectrum of **8**

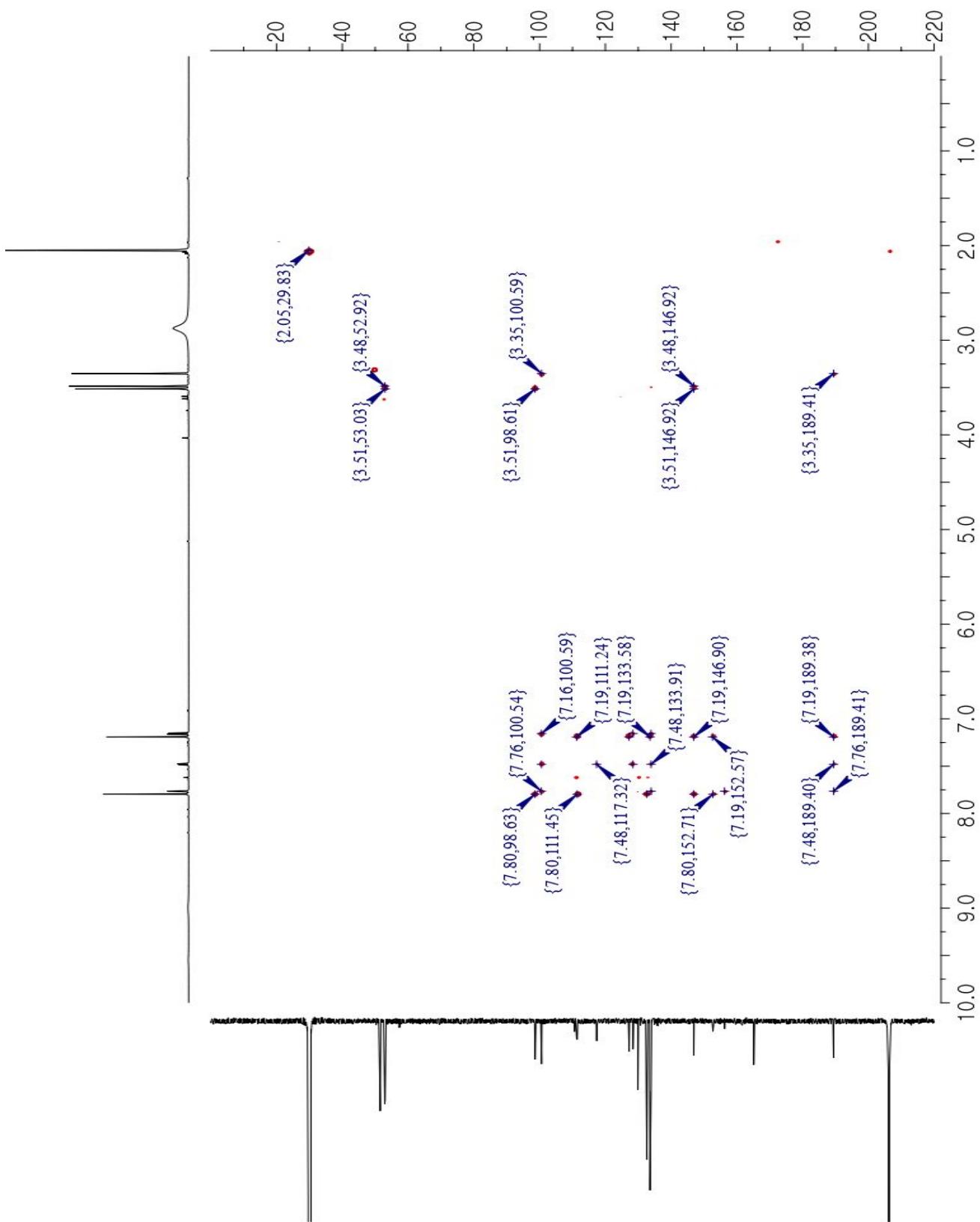


Figure S41. The D-HMBC (800 MHz, acetone-*d*₆, $J_{\text{CH}} = 1$ Hz) spectrum of **8**

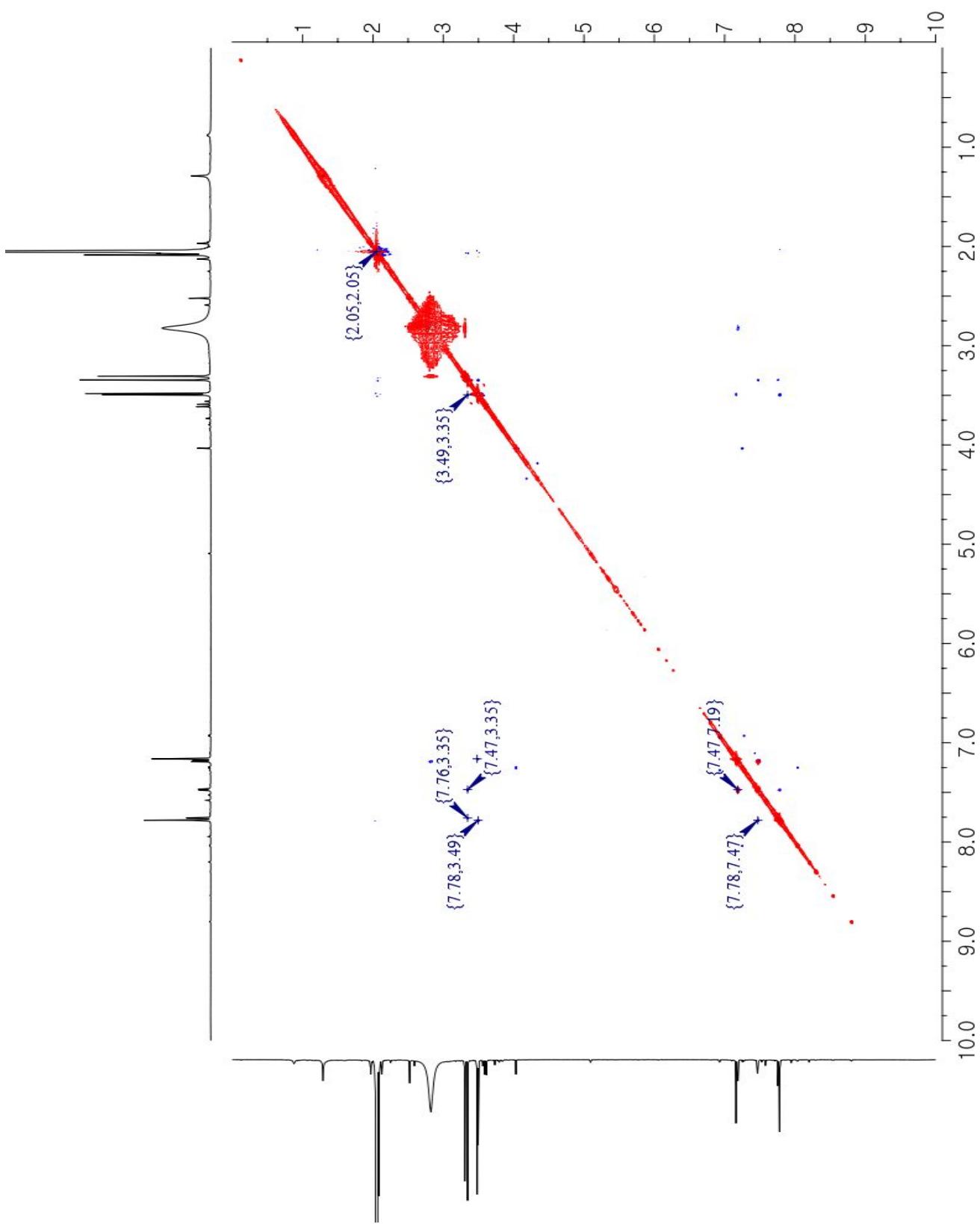


Figure S42. The NOESY (800 MHz, acetone-*d*₆) spectrum of **8**

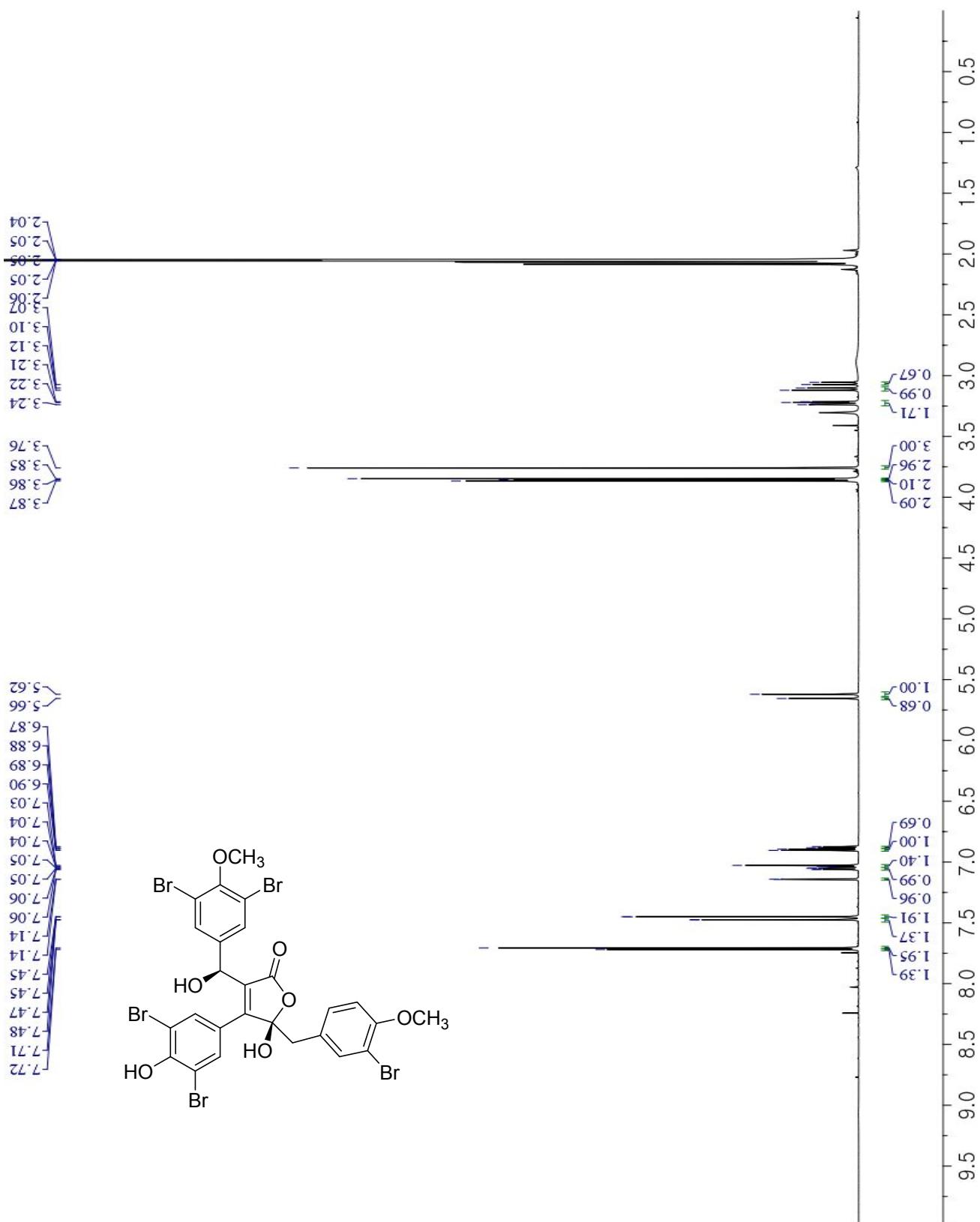


Figure S43. The ^1H NMR (800 MHz, acetone- d_6) spectrum of **9**

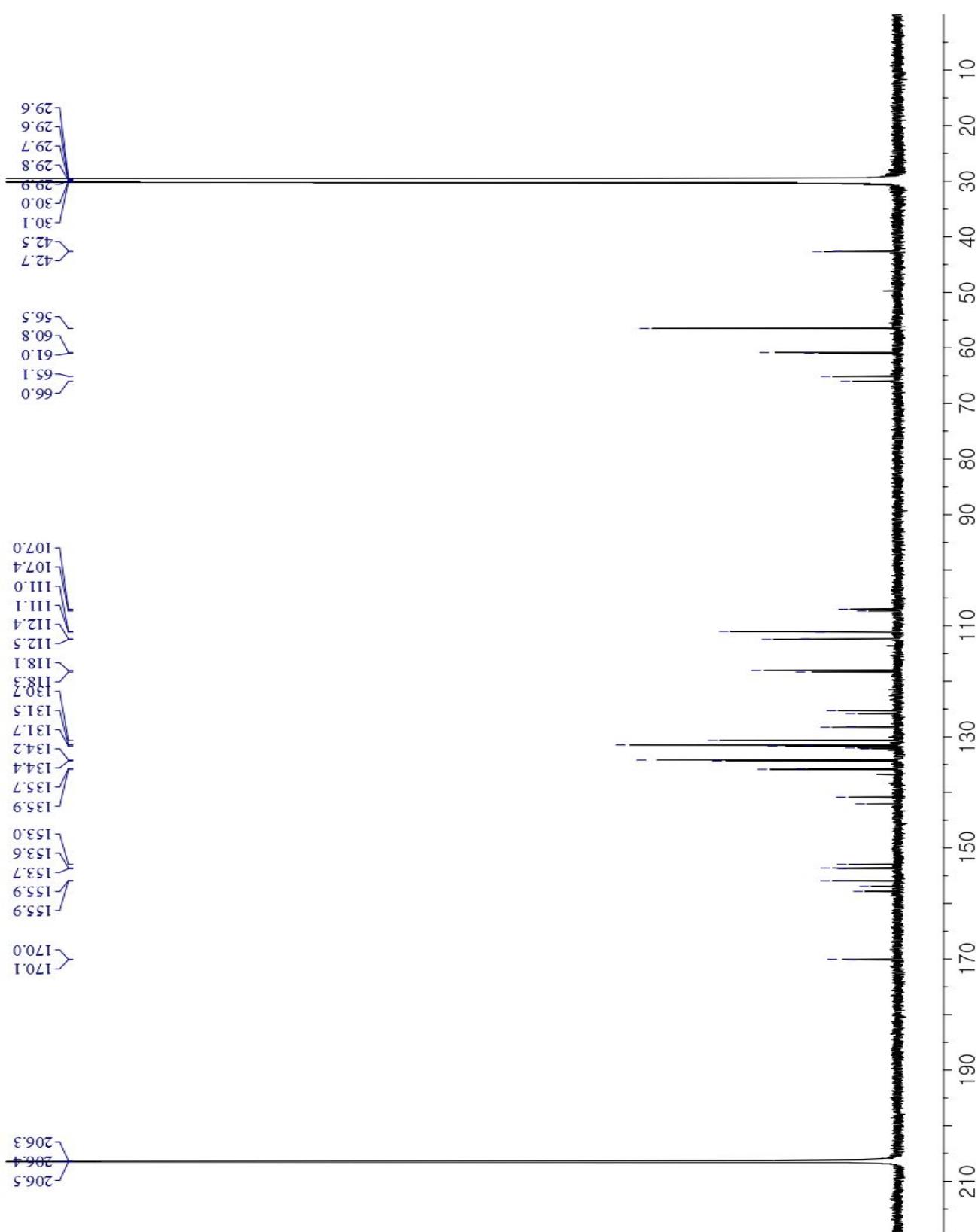


Figure S44. The ^{13}C NMR (200 MHz, acetone- d_6) spectrum of **9**

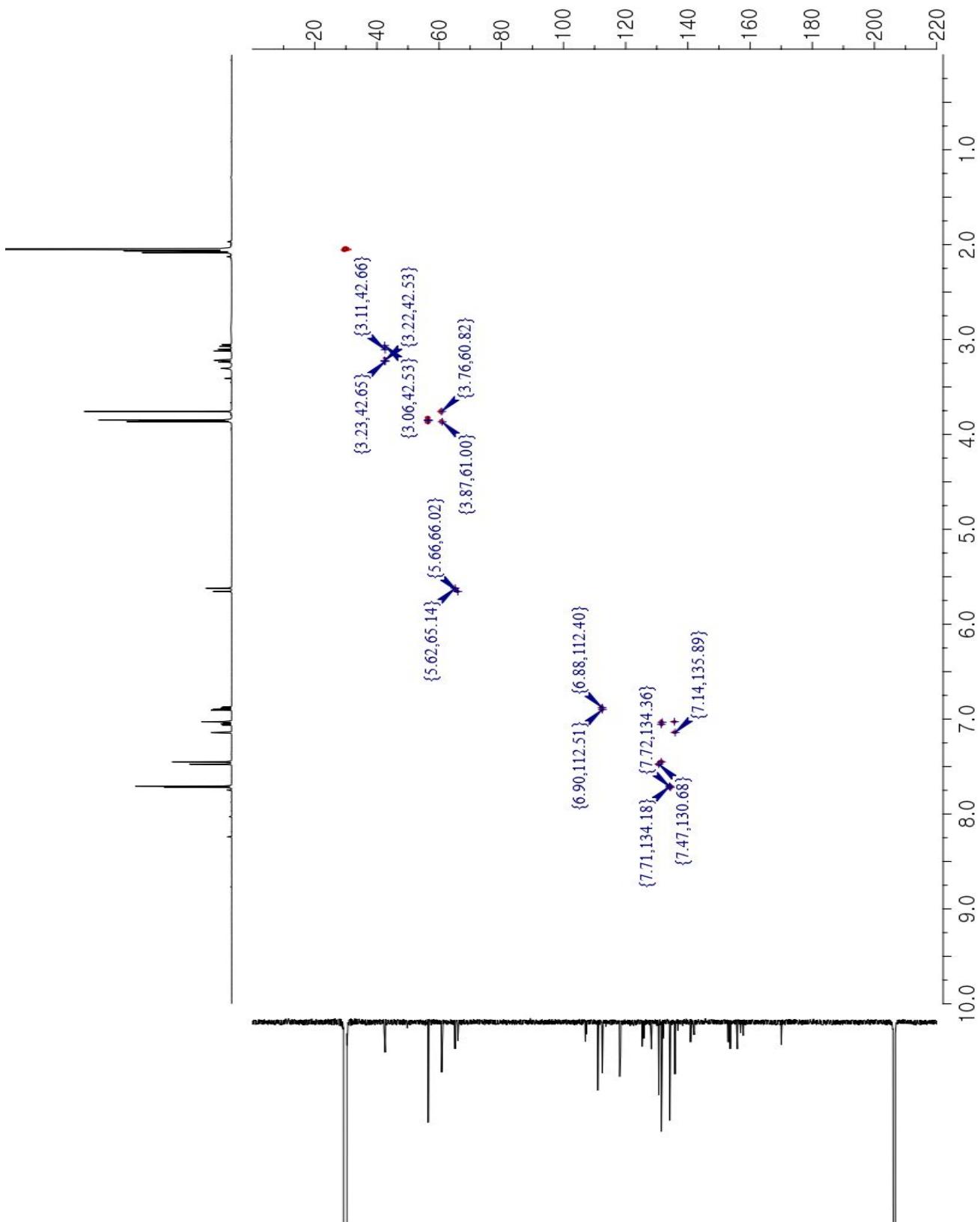


Figure S45. The HSQC (800 MHz, acetone-*d*₆) spectrum of **9**

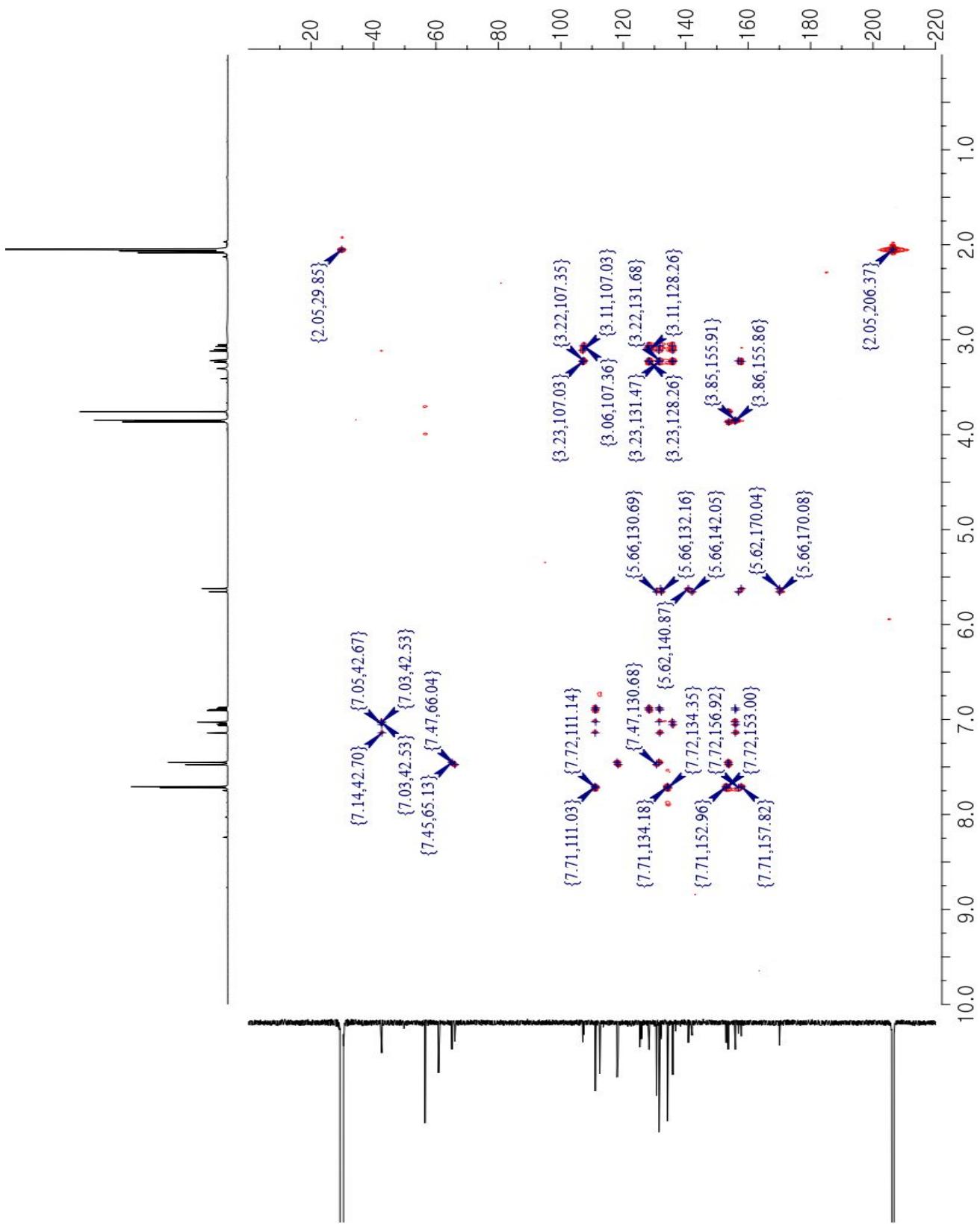


Figure S46. The HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 8 Hz) spectrum of **9**

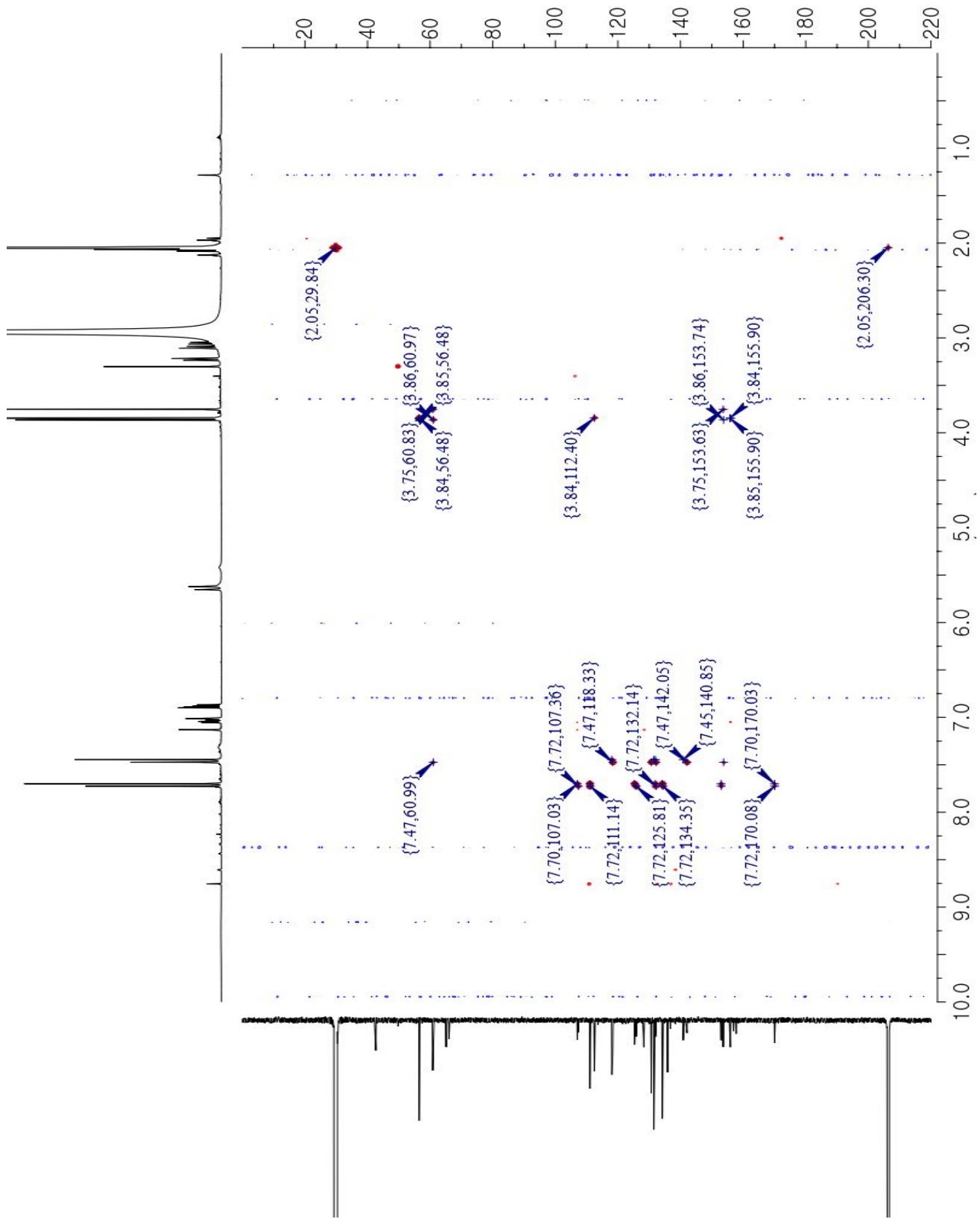


Figure S47. The D-HMBC (800 MHz, acetone-*d*₆, *J*_{CH} = 1 Hz) spectrum of **9**

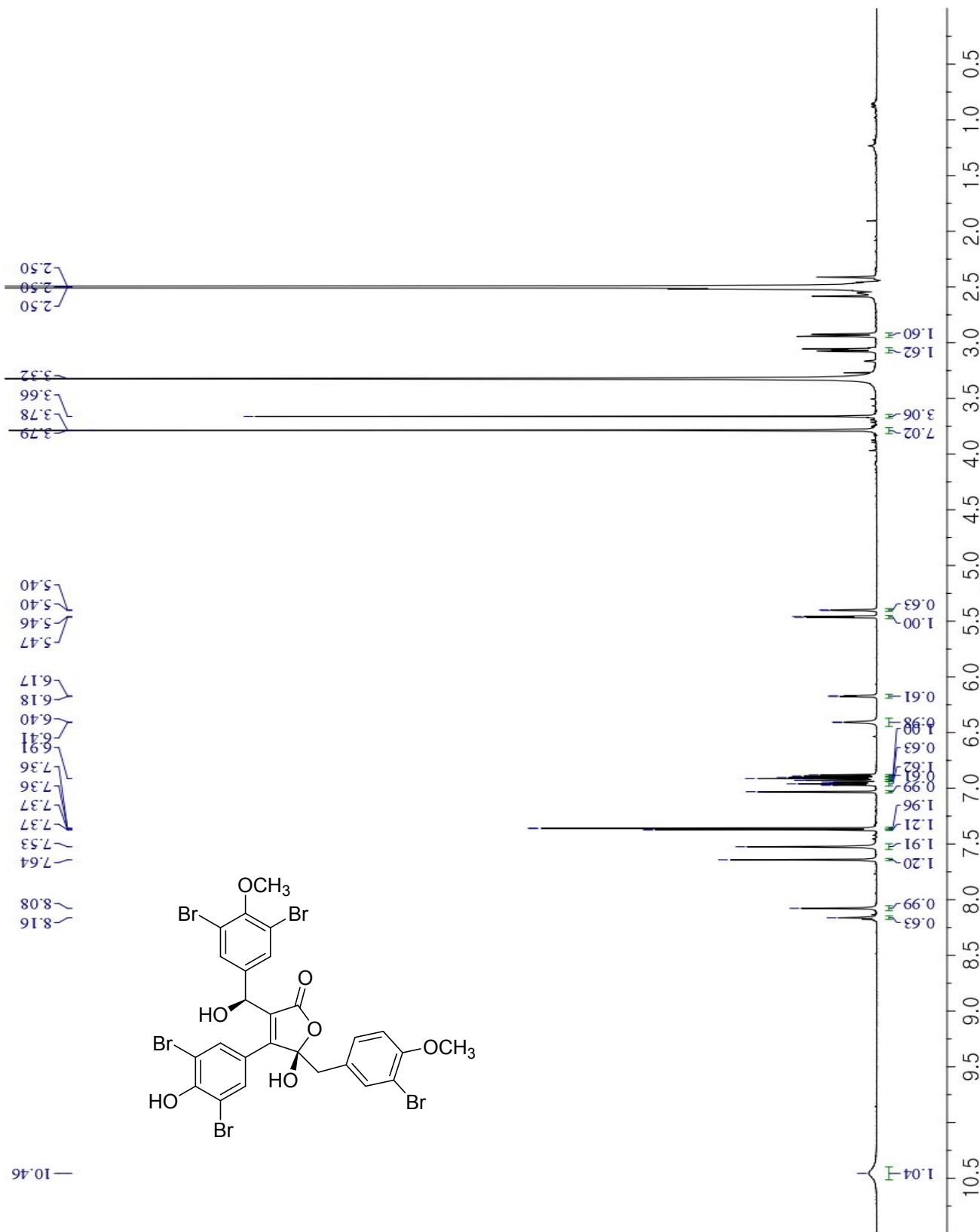


Figure S48. The ^1H NMR (800 MHz, $\text{DMSO}-d_6$) spectrum of **9**

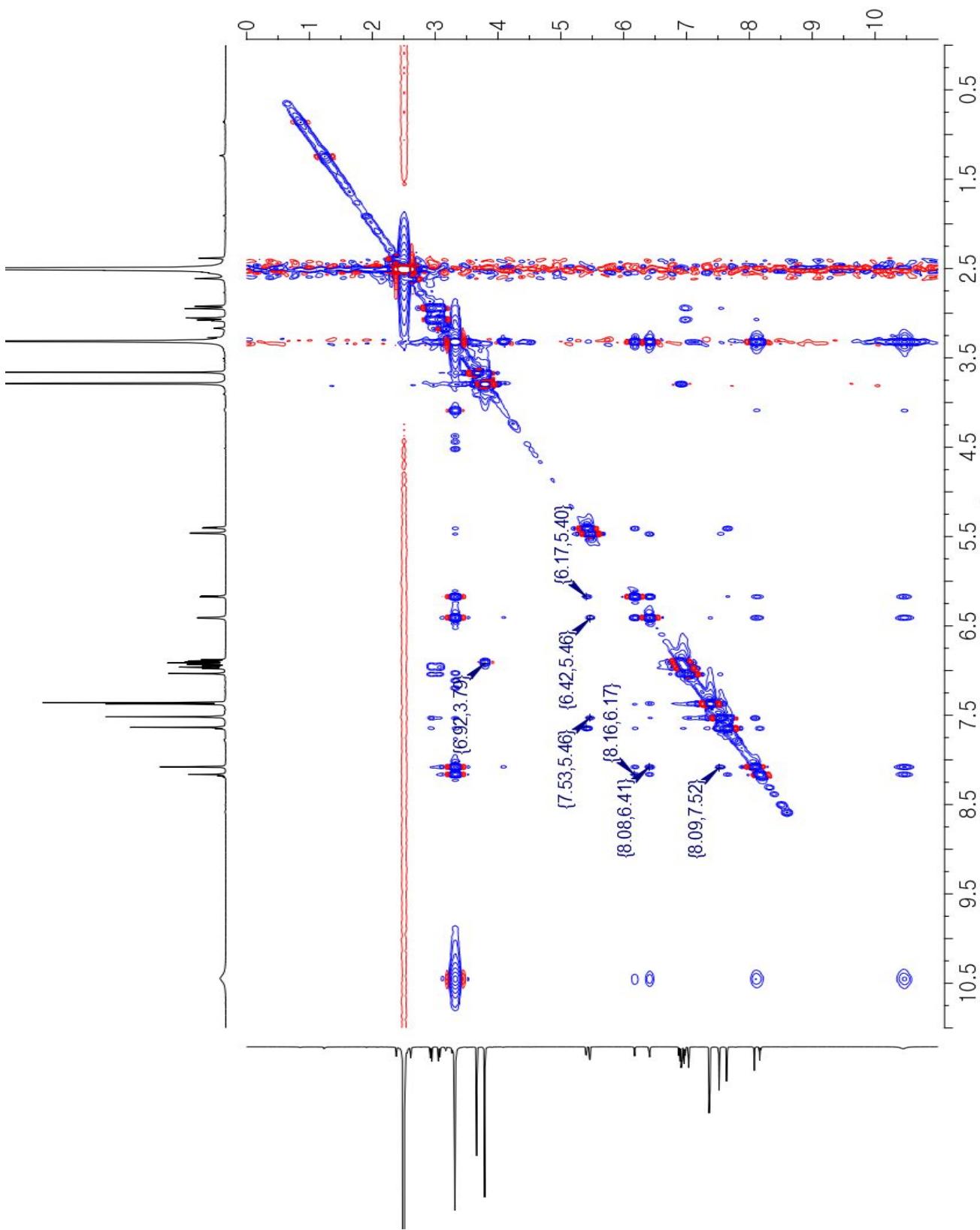


Figure S49. The NOESY (800 MHz, DMSO-*d*₆) spectrum of **9**

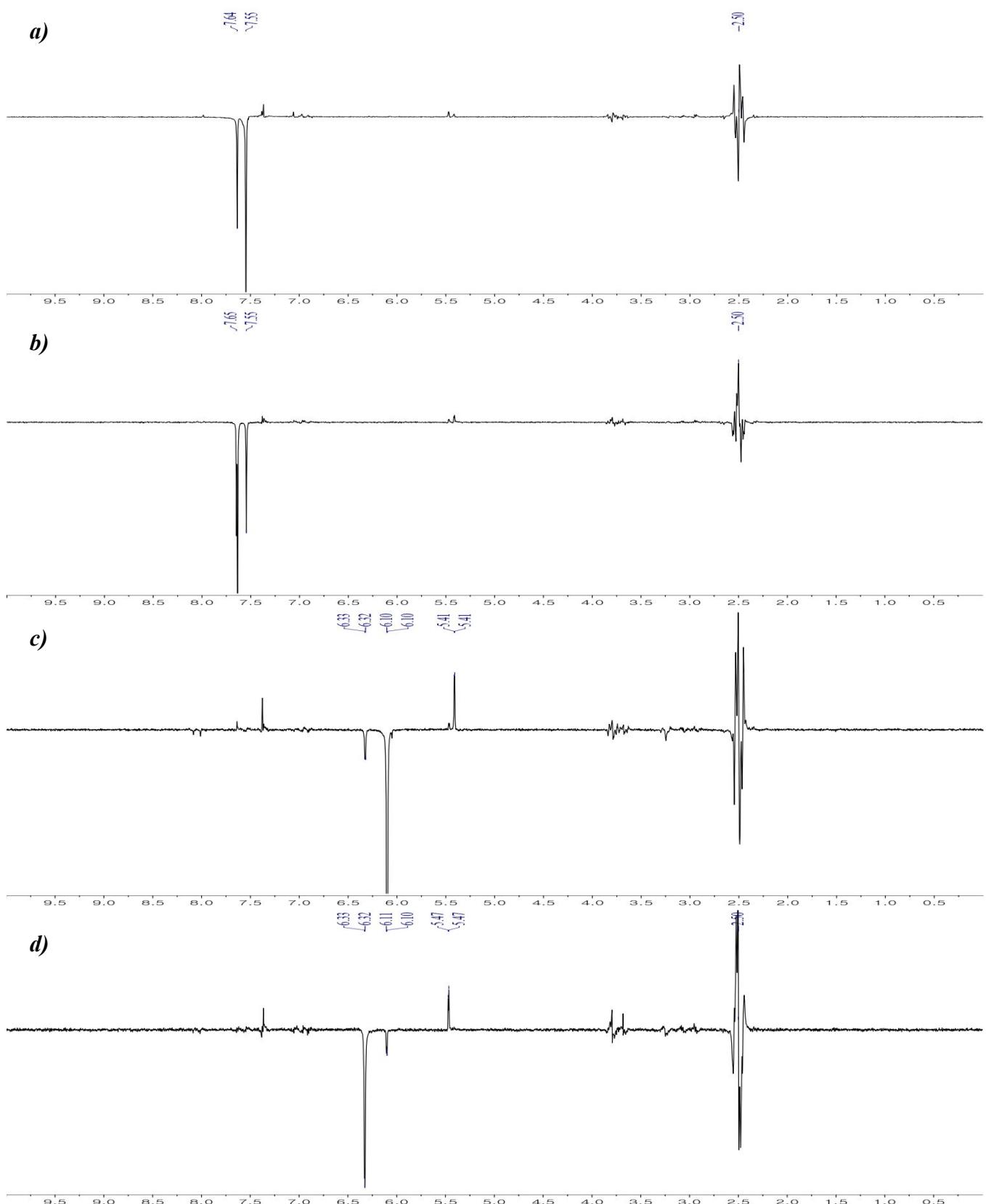
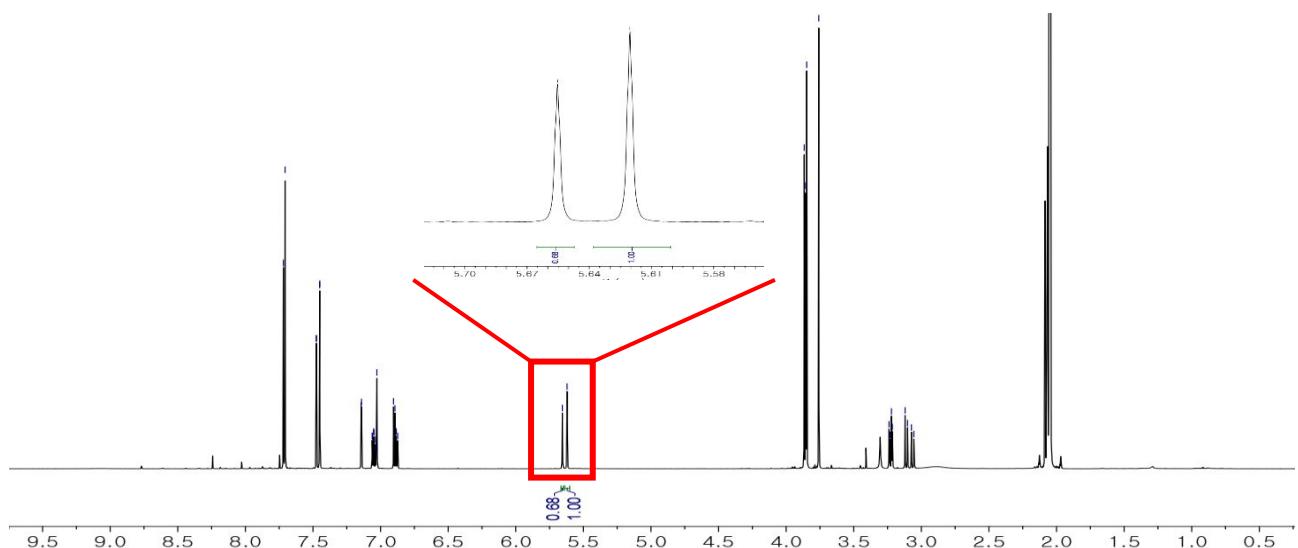
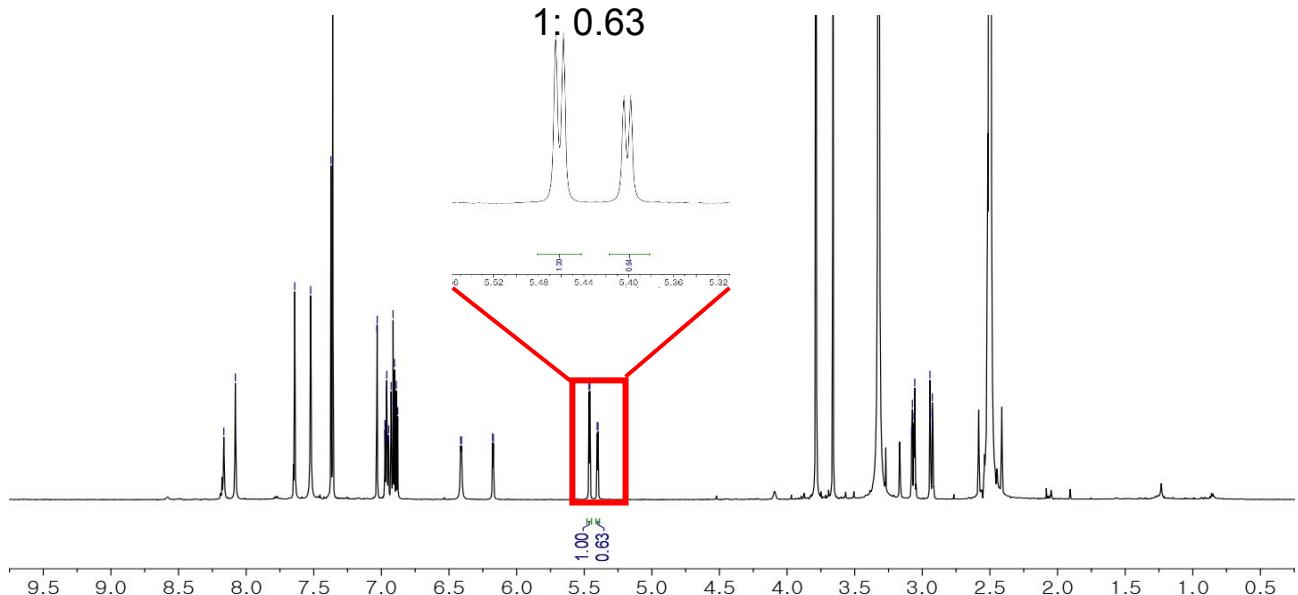


Figure S50. The 1-D Selective gradient NOESY (800 MHz, DMSO-*d*₆) spectrum of **9** (Irradiation at δ_{H} *a*) 7.55 (H-2'/6' of **9a**), *b*) 7.64 (H-2'/6' of **9b**), *c*) 6.10 (6-OH of **9b**), and *d*) 6.32 (6-OH of **9a**)

0.68: 1



1: 0.63



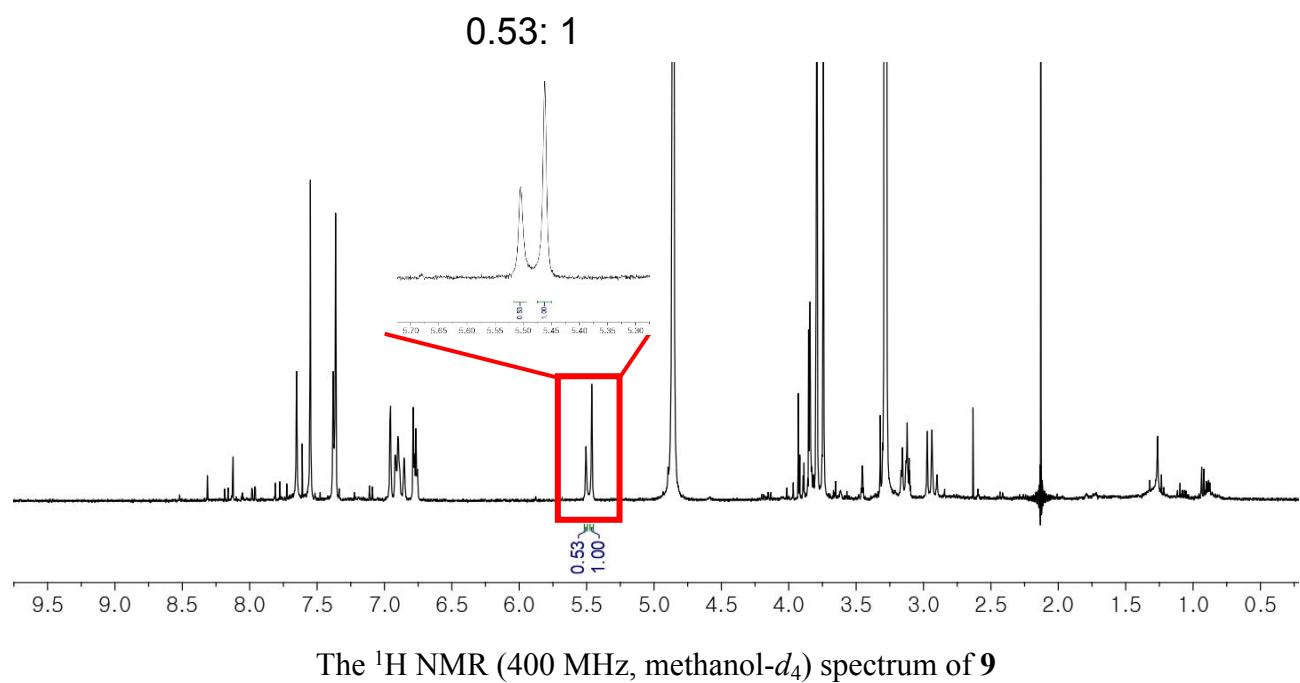


Figure S51. The varied ratios of **9a** and **9b** in diverse NMR solvents

Parameters for calculating specific rotations

Functional: B3-LYP

Basis set: def-SVP

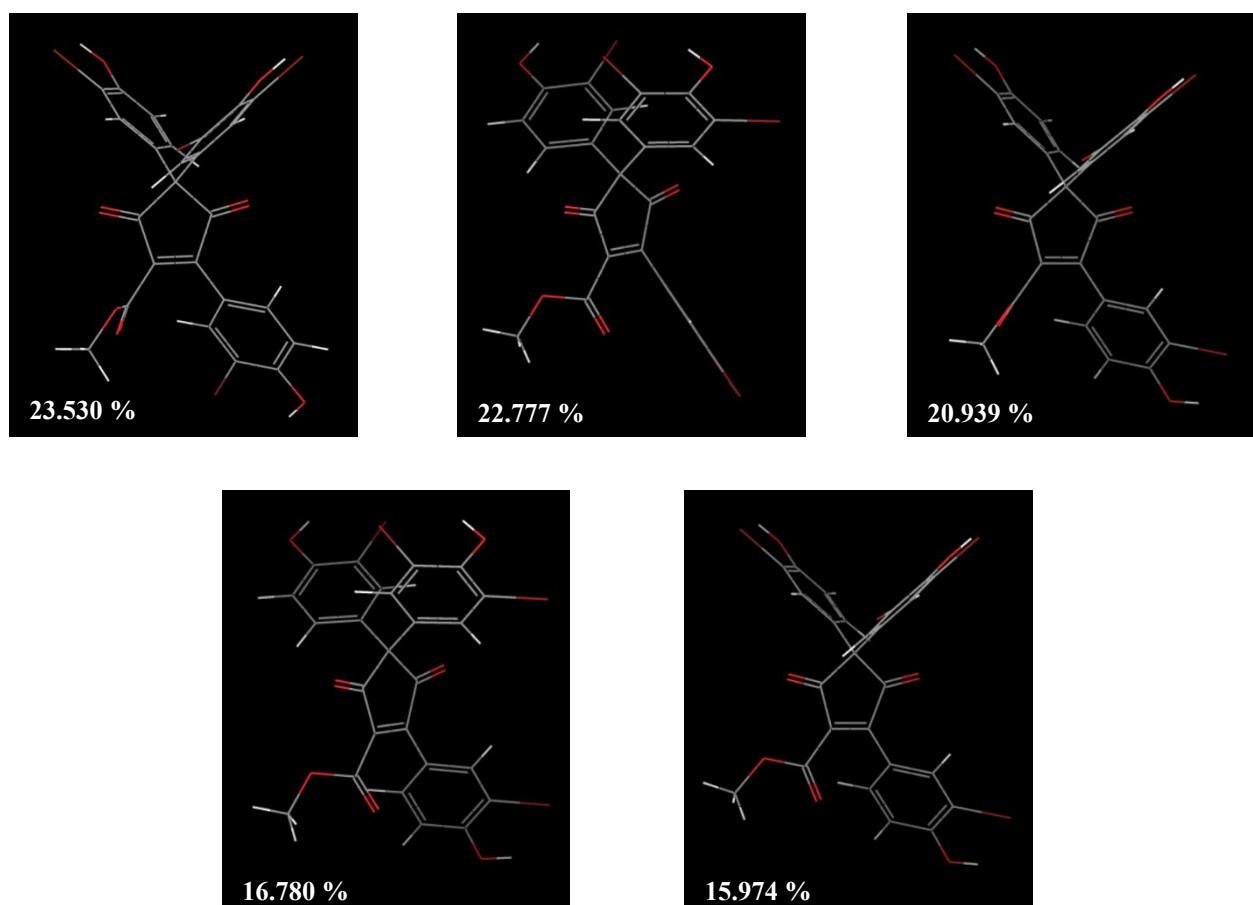
Gridsize: m3

Frequency: 0.7735713524617996E-01

Frequency / eV: 2.104995653760073

Frequency / nm: 589.0000000000000

Frequency / cm⁻¹: 16977.92869016530



Five major conformers (> 15% population) under the relative energy of 1kJ/mol in calculated Boltzmann distribution

Compound 2	1/3*trace (dipole polarizability)	1/3*trace (rotatory dispersion)	Specific rotation $[\alpha]$ in deg*[dm(g/cc)] ⁻¹
23.530 %	397.0	9.9	+513.4
22.777 %	396.5	-10.4	-538.3
20.939 %	397.3	9.7	+501.5
16.780 %	400.8	-19.4	-1009.0
15.974 %	402.5	7.7	+397.5

Figure S52. Calculated optical rotations of major conformers of **2**

Parameters for calculating specific rotations

Functional: B3-LYP

Basis set: def-SVP

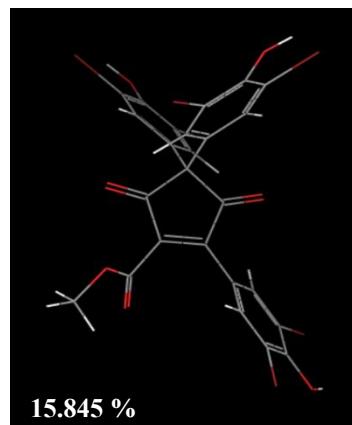
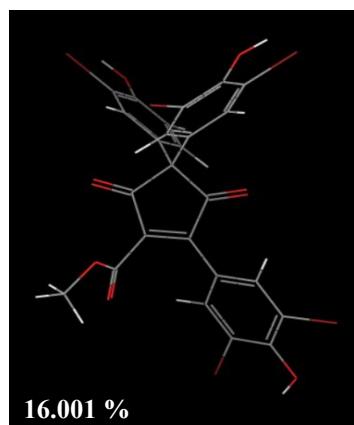
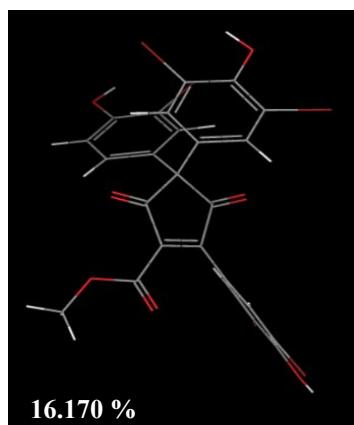
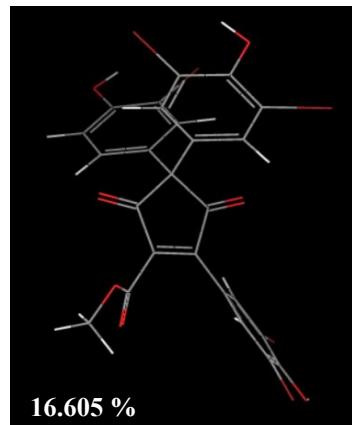
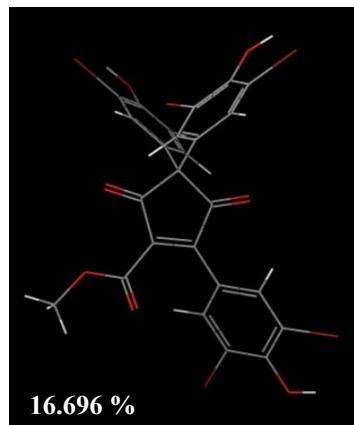
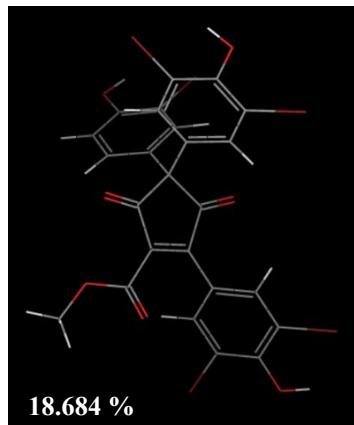
Gridsize: m3

Frequency: 0.7735713524617996E-01

Frequency / eV: 2.104995653760073

Frequency / nm: 589.0000000000000

Frequency / cm⁻¹: 16977.92869016530



Six major conformers (> 15% population) under the relative energy of 1kJ/mol in calculated Boltzmann distribution

Compound 4	1/3*trace (dipole polarizability)	1/3*trace (rotatory dispersion)	Specific rotation [α] in deg*[dm(g/cc)] ⁻¹
18.684 %	420.3	-19.5	-914.6
16.696 %	422.0	8.2	+386.4
16.605 %	421.0	-9.6	-451.2
16.170 %	416.0	-13.4	-627.2
16.001 %	416.6	11.9	+560.1
15.845 %	420.8	17.7	+831.1

Figure S53. Calculated optical rotations of major conformers of 4