

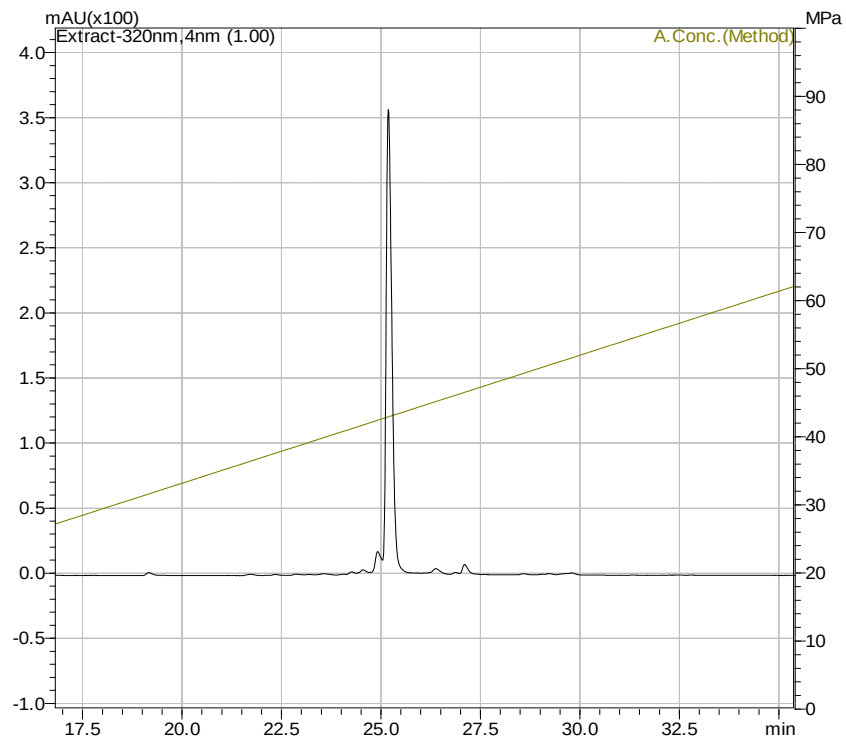


Figure S1. HPLC profile of compounds **1a** and **1b**.

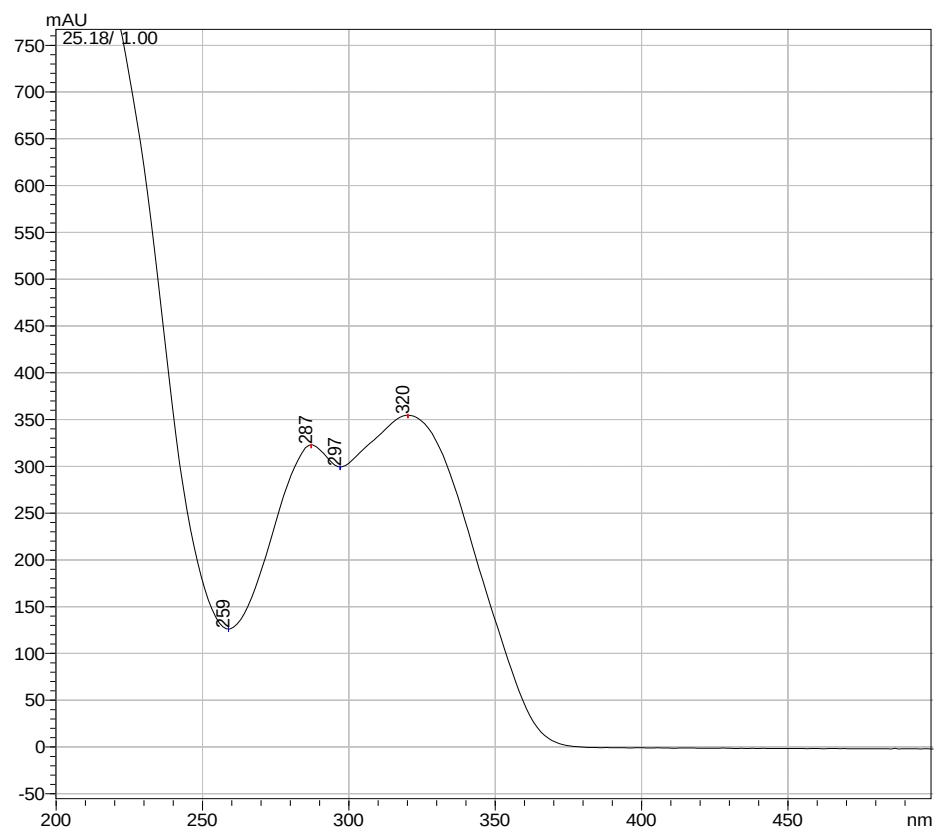


Figure S2. UV spectrum of compounds **1a** and **1b**.

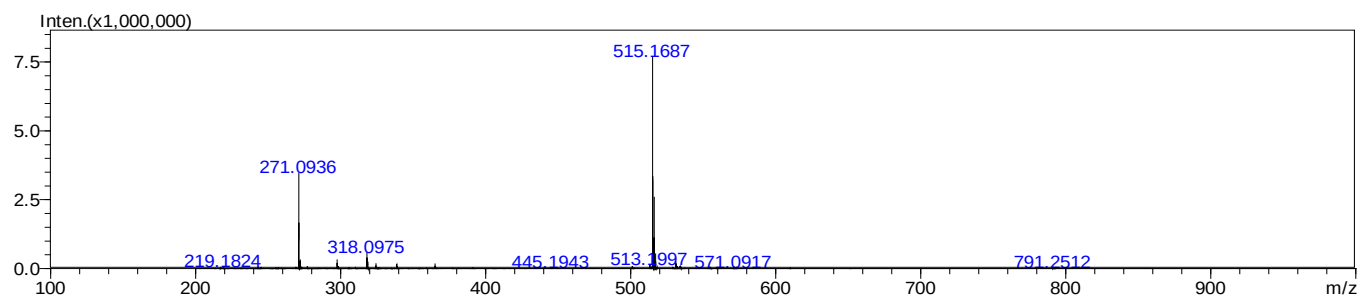


Figure S3. HR-MS spectrum of compounds **1a** and **1b** (positive ion mode).

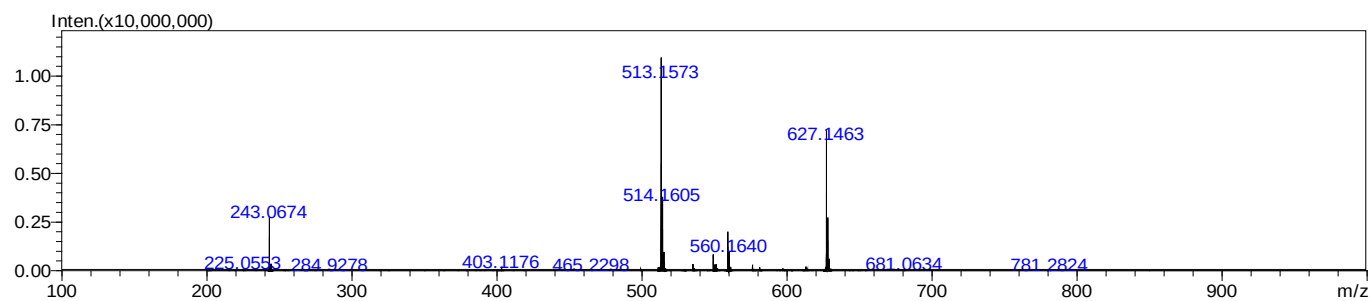


Figure S4. HR-MS spectrum of compounds **1a** and **1b** (negative ion mode).

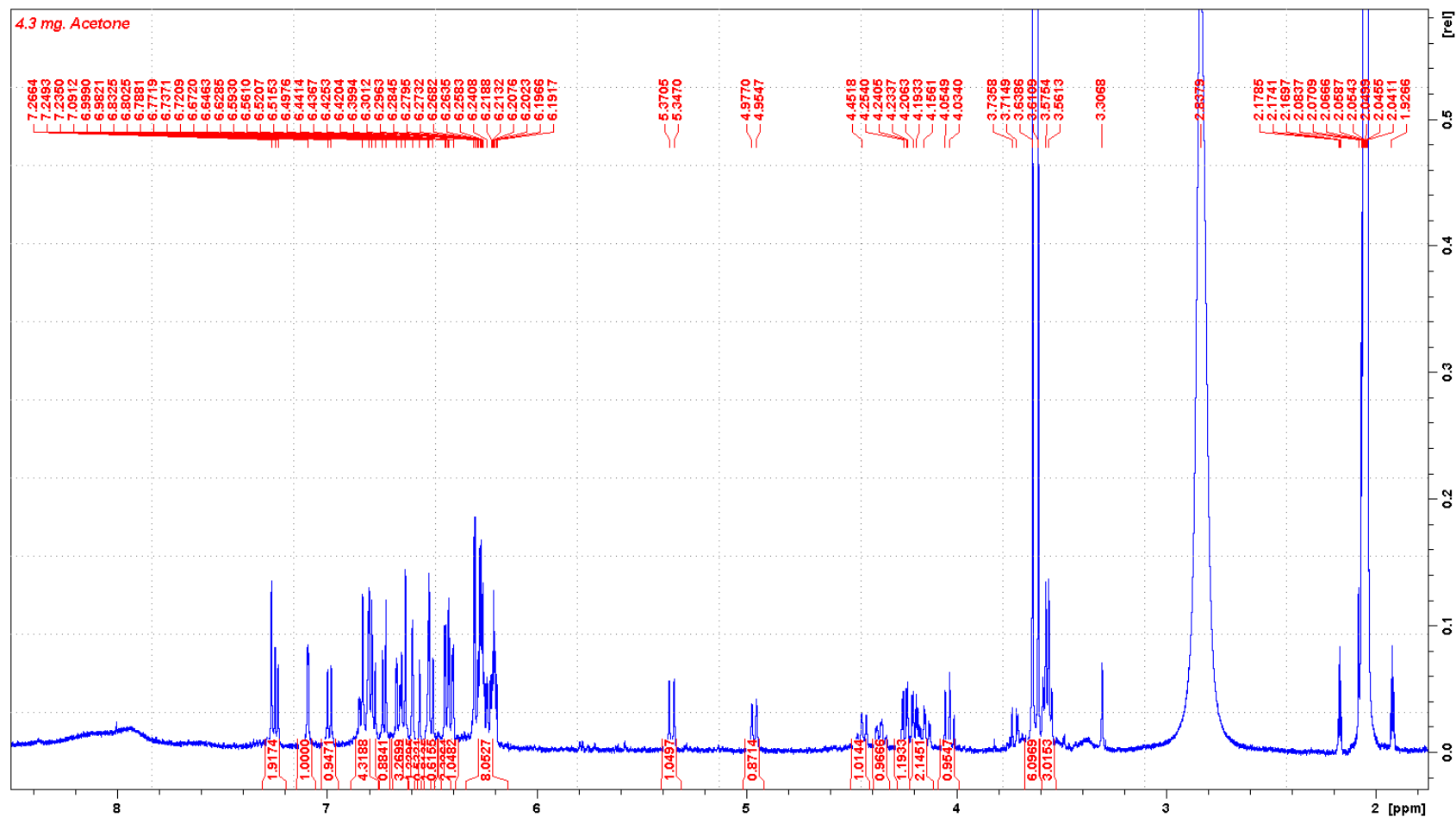


Figure S5. ^1H NMR spectrum of compounds **1a** and **1b**.

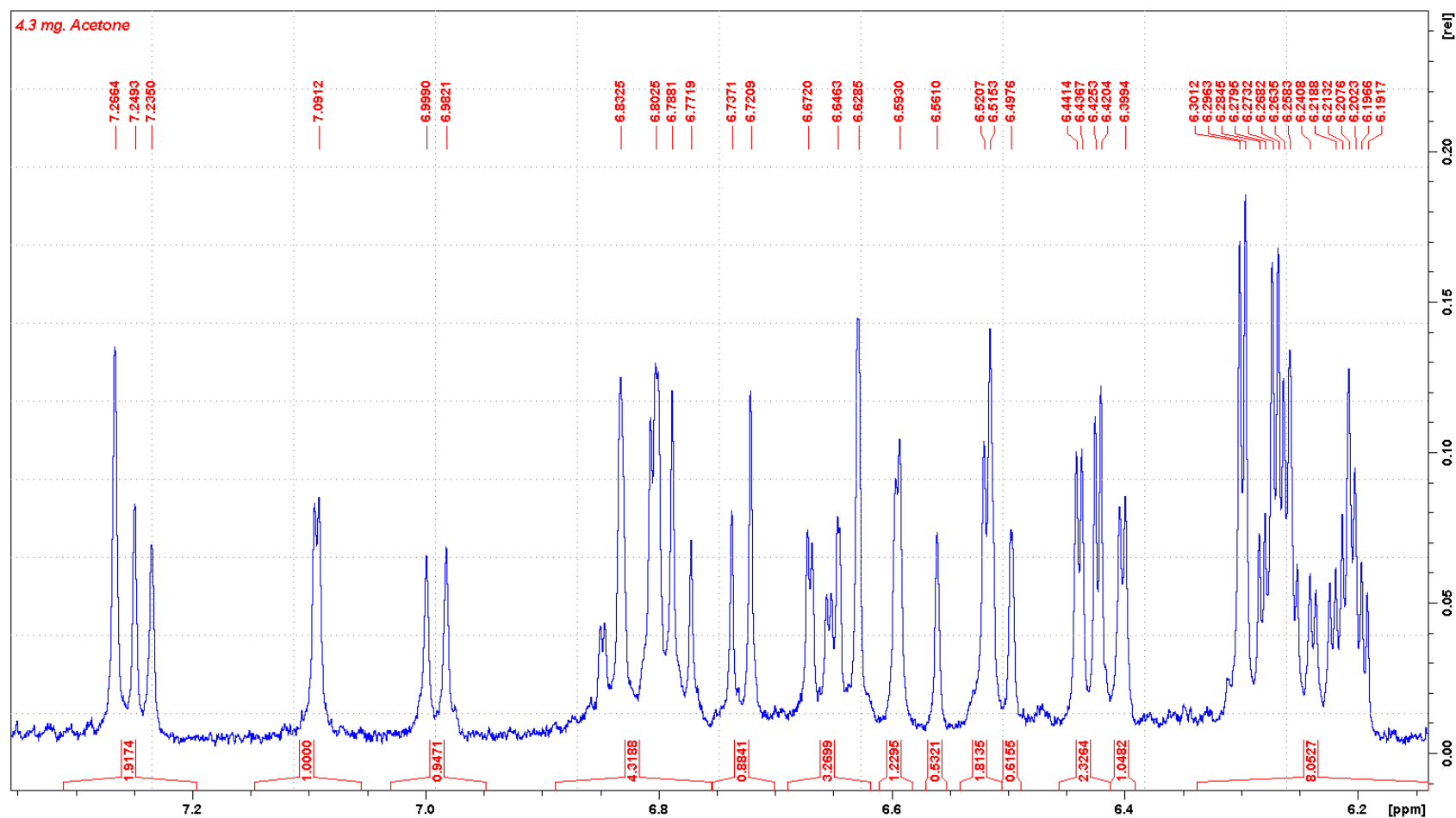


Figure S6. ^1H NMR spectrum of compounds **1a** and **1b** (enlarged).

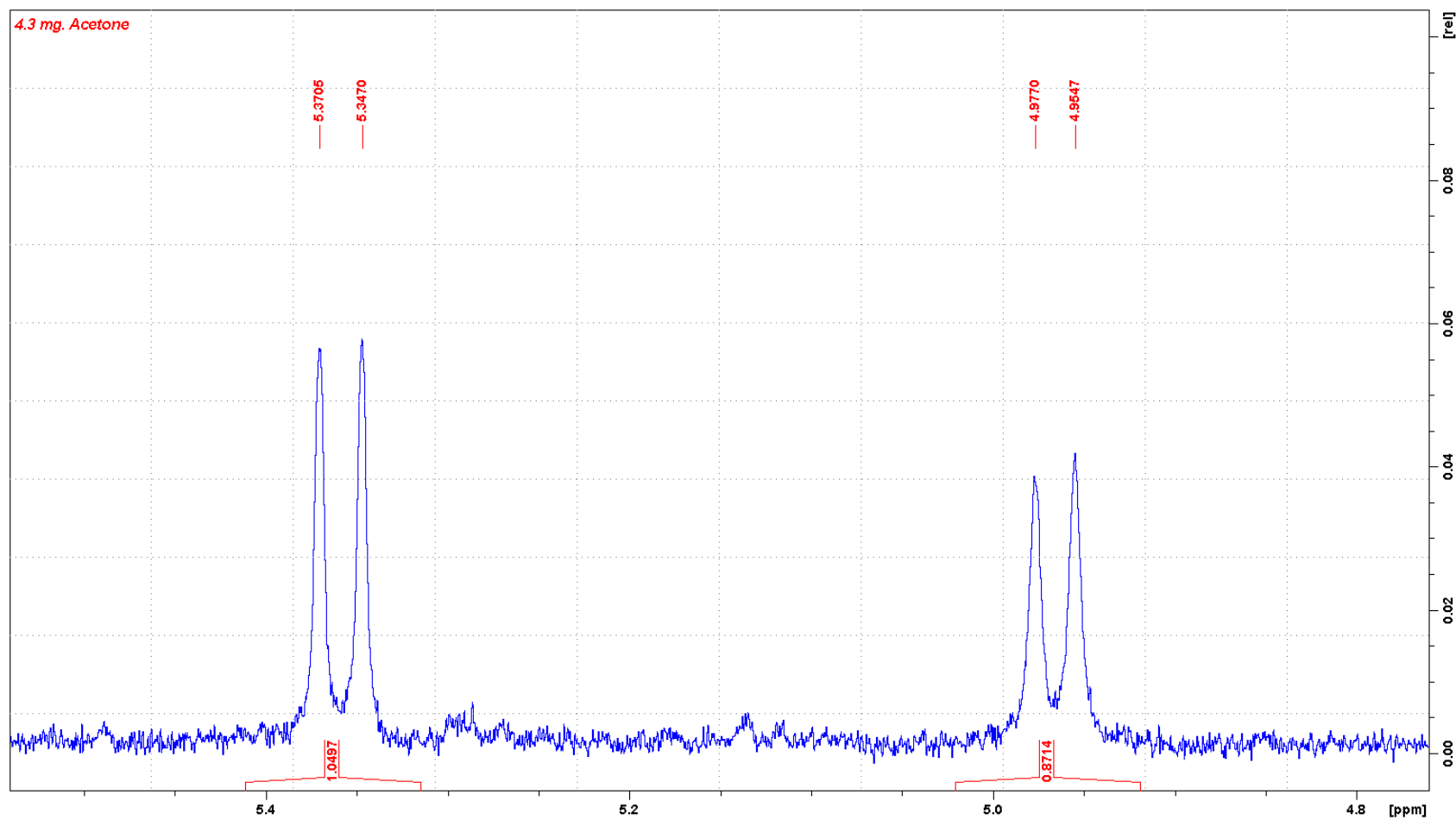


Figure S7. ^1H NMR spectrum of compounds **1a** and **1b** (enlarged).

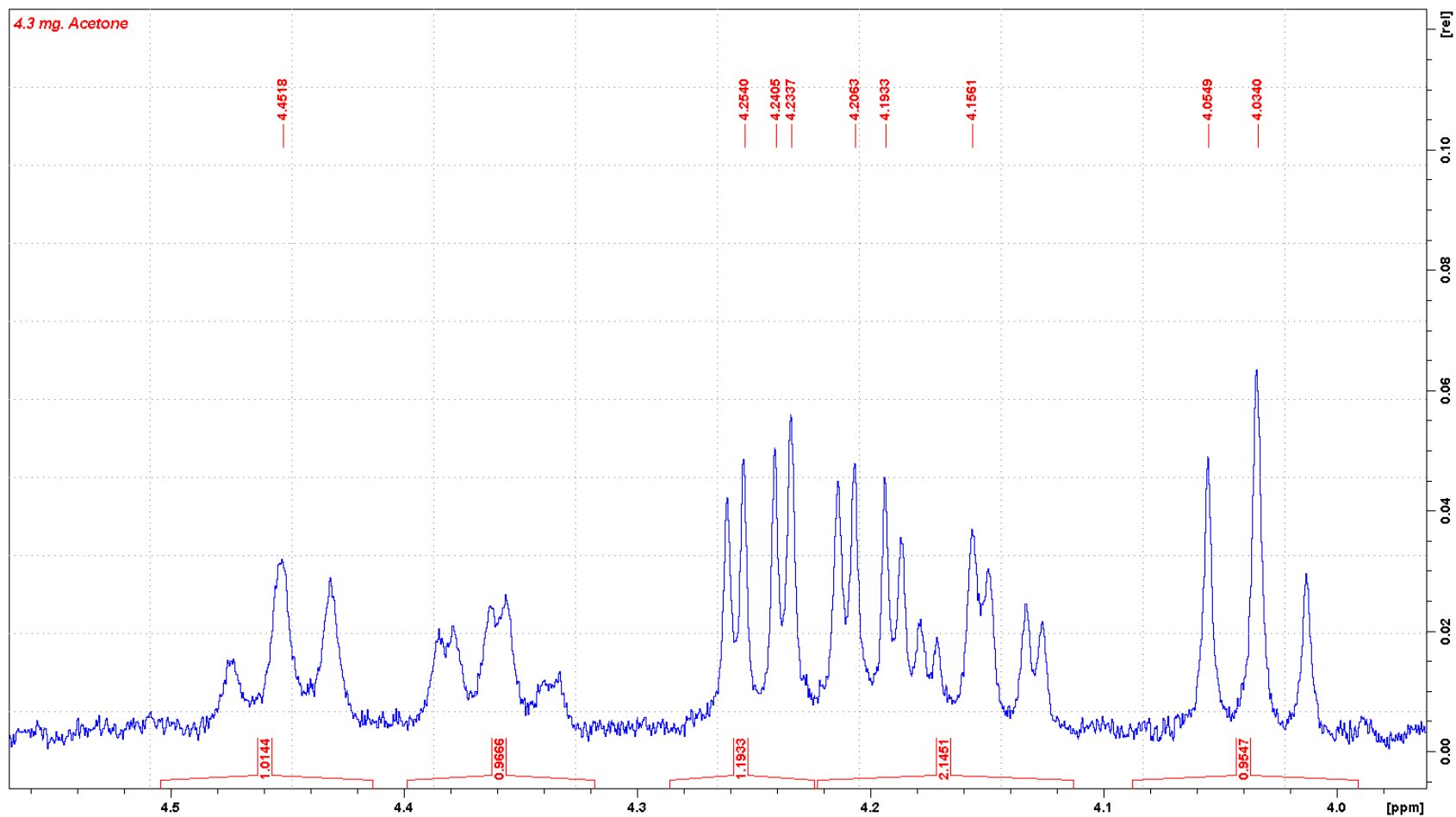


Figure S8. ^1H NMR spectrum of compounds **1a** and **1b** (enlarged).

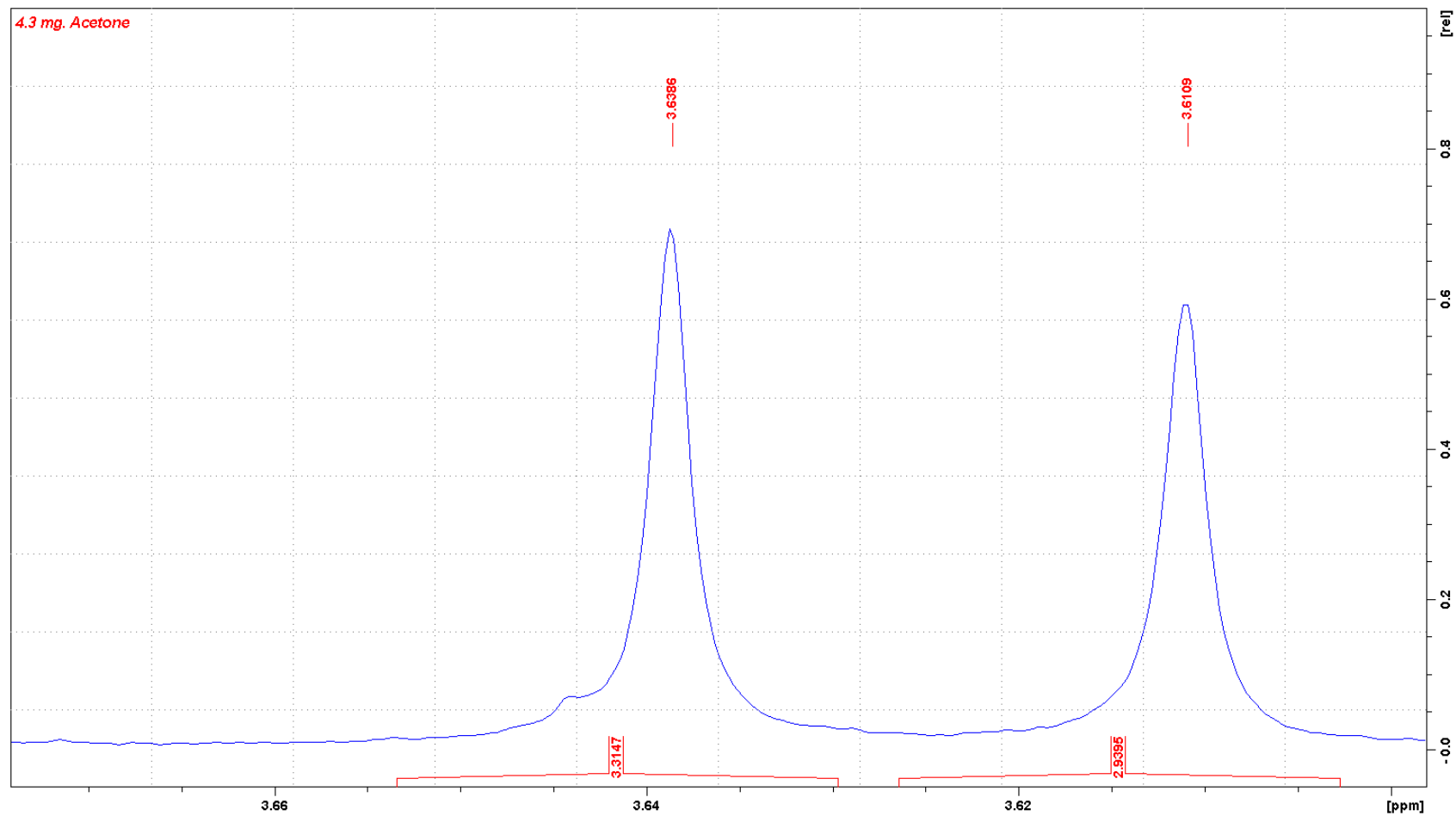


Figure S9. ^1H NMR spectrum of compounds **1a** and **1b** (enlarged).

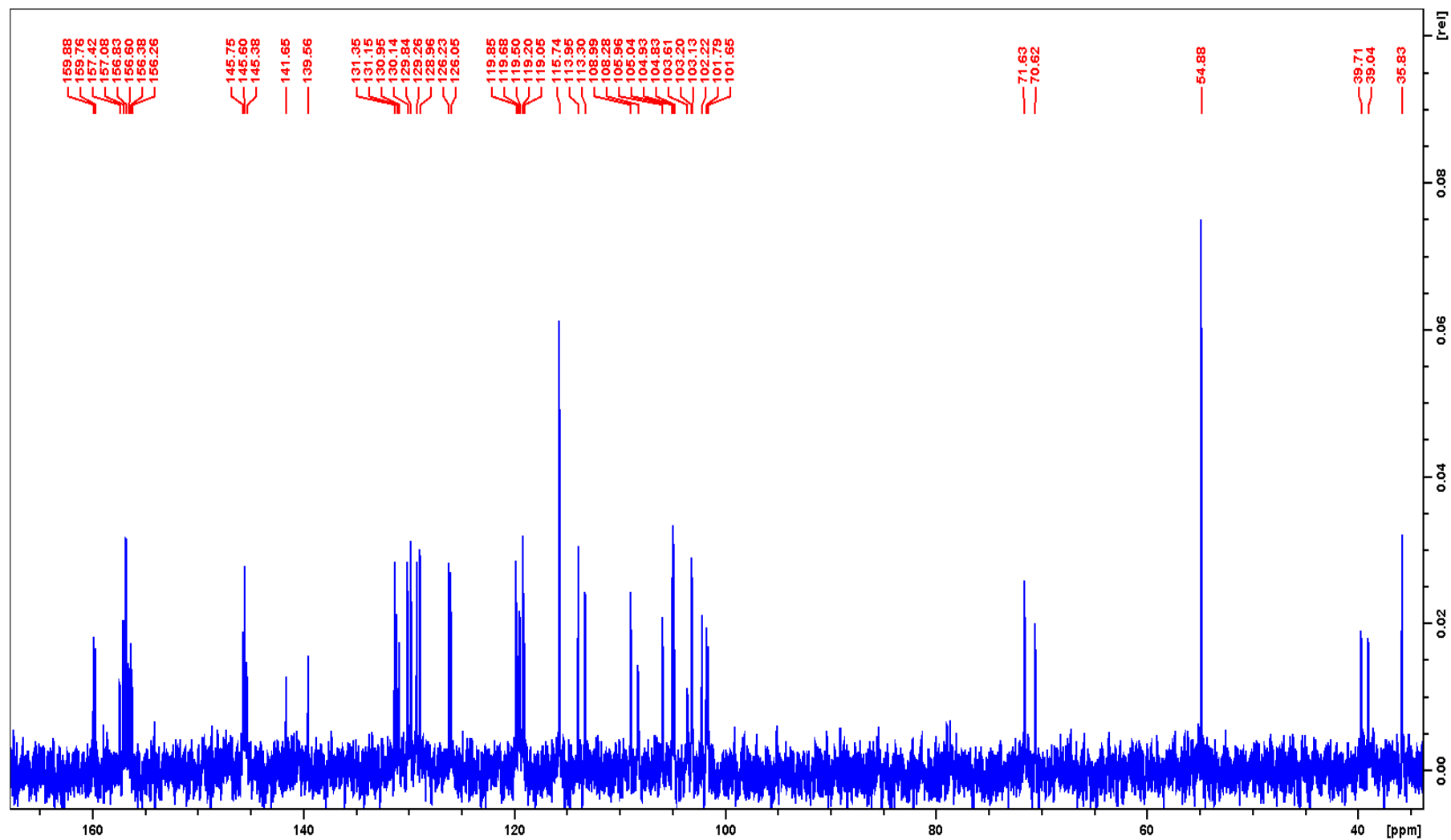


Figure S10. ¹³C NMR spectrum of compounds **1a** and **1b**.

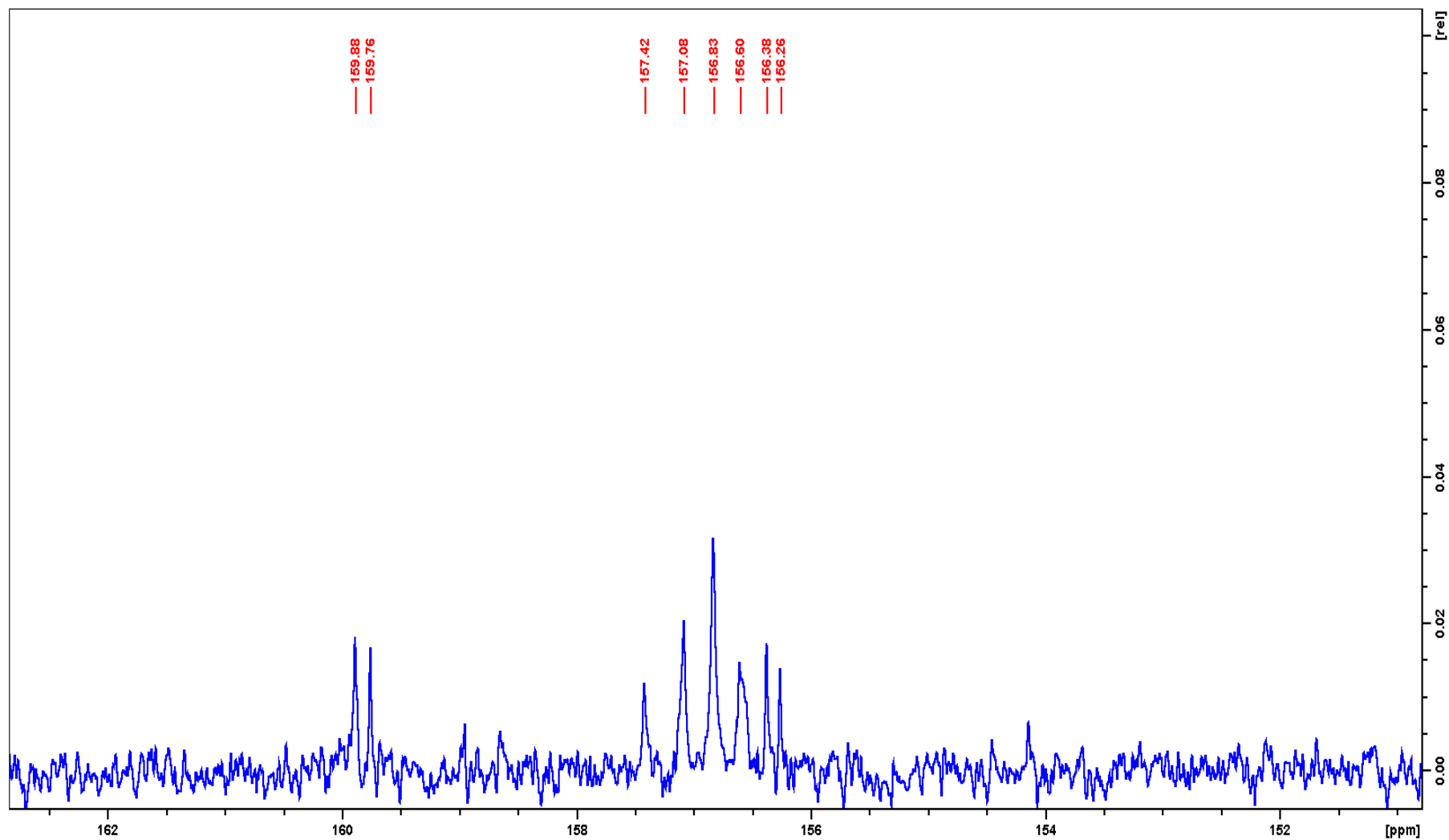


Figure S11. ¹³C NMR spectrum of compounds **1a** and **1b** (enlarged).

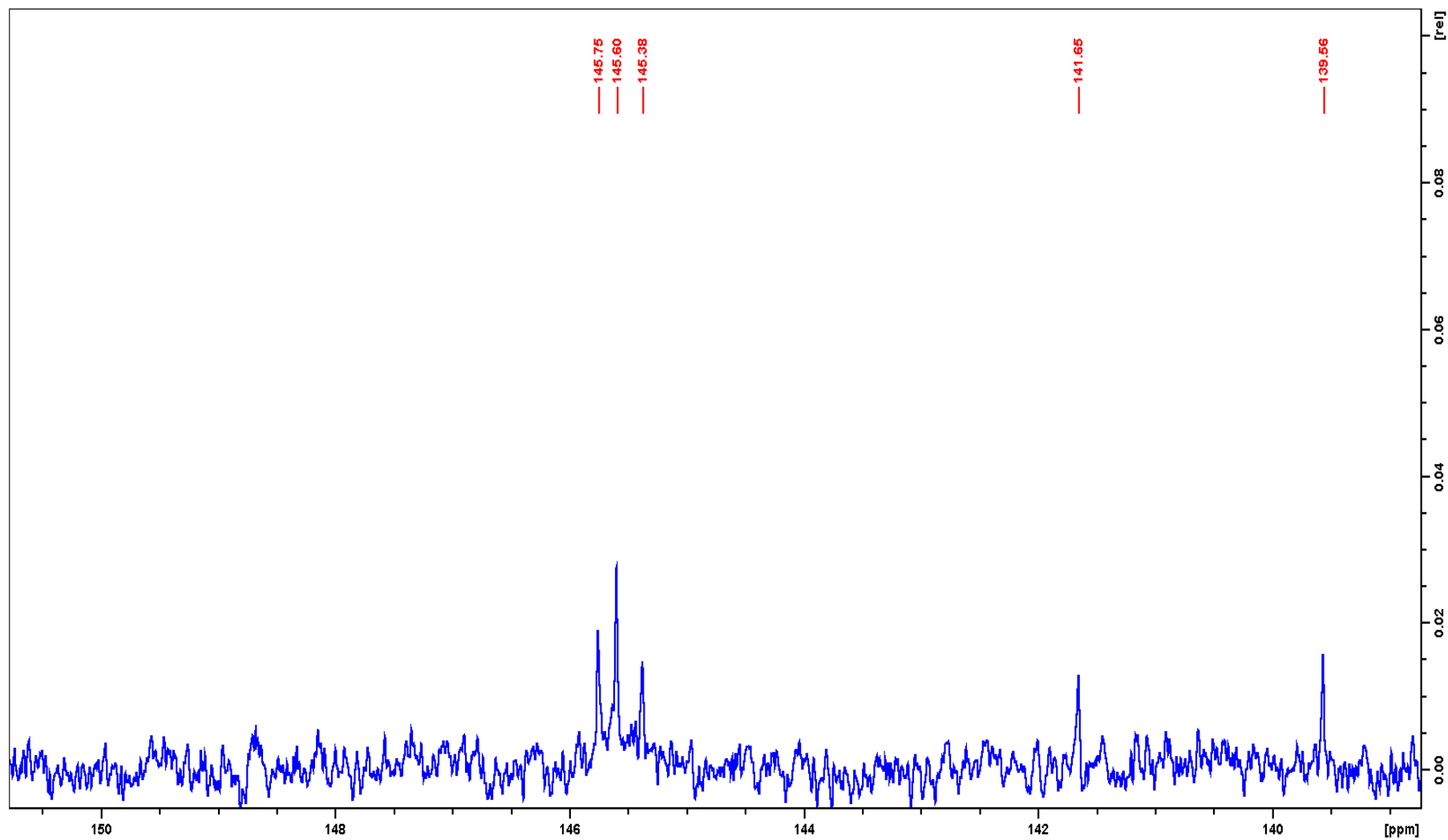


Figure S12. ^{13}C NMR spectrum of compounds **1a** and **1b** (enlarged).

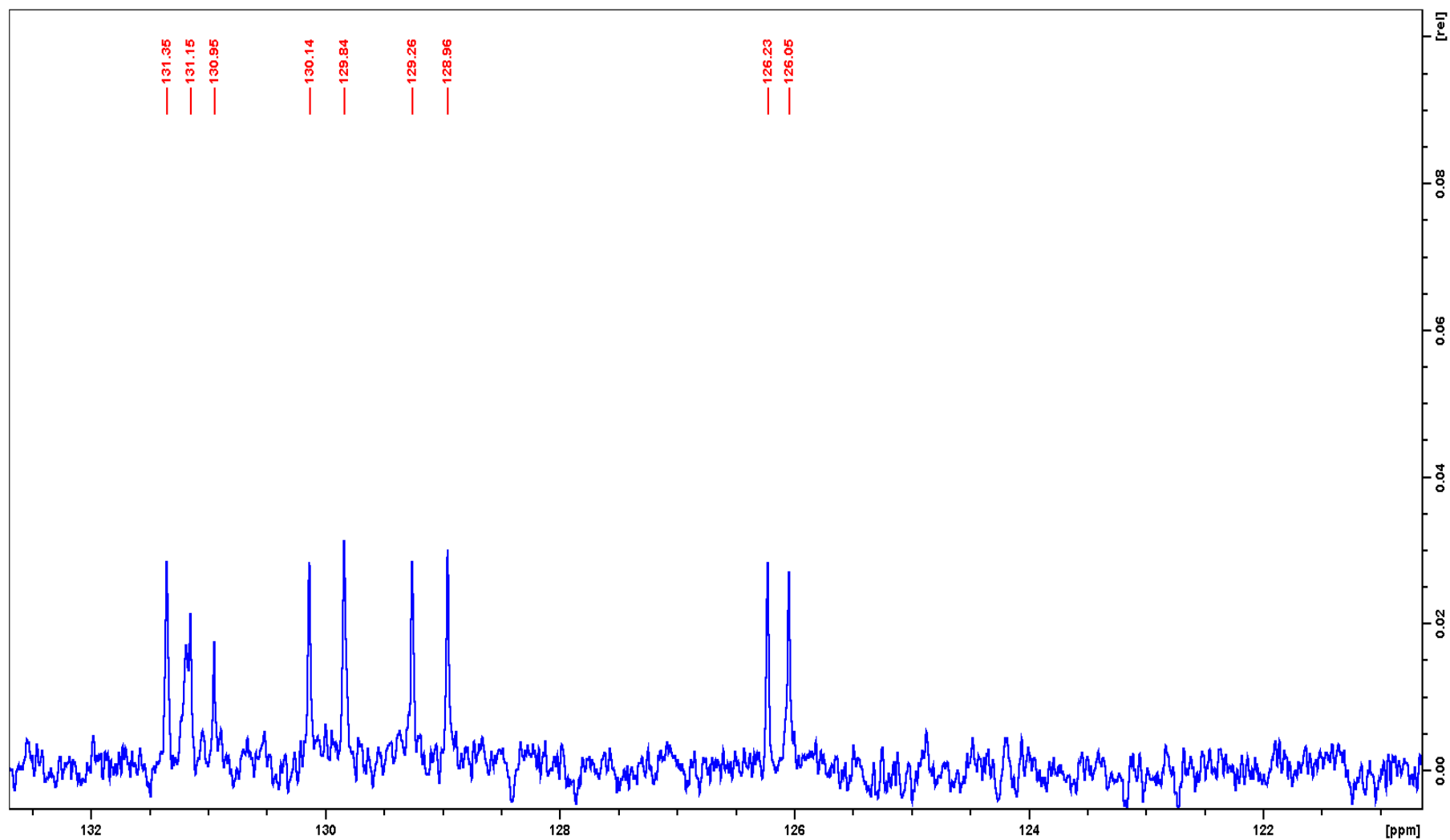


Figure S13. ^{13}C NMR spectrum of compounds **1a** and **1b** (enlarged).

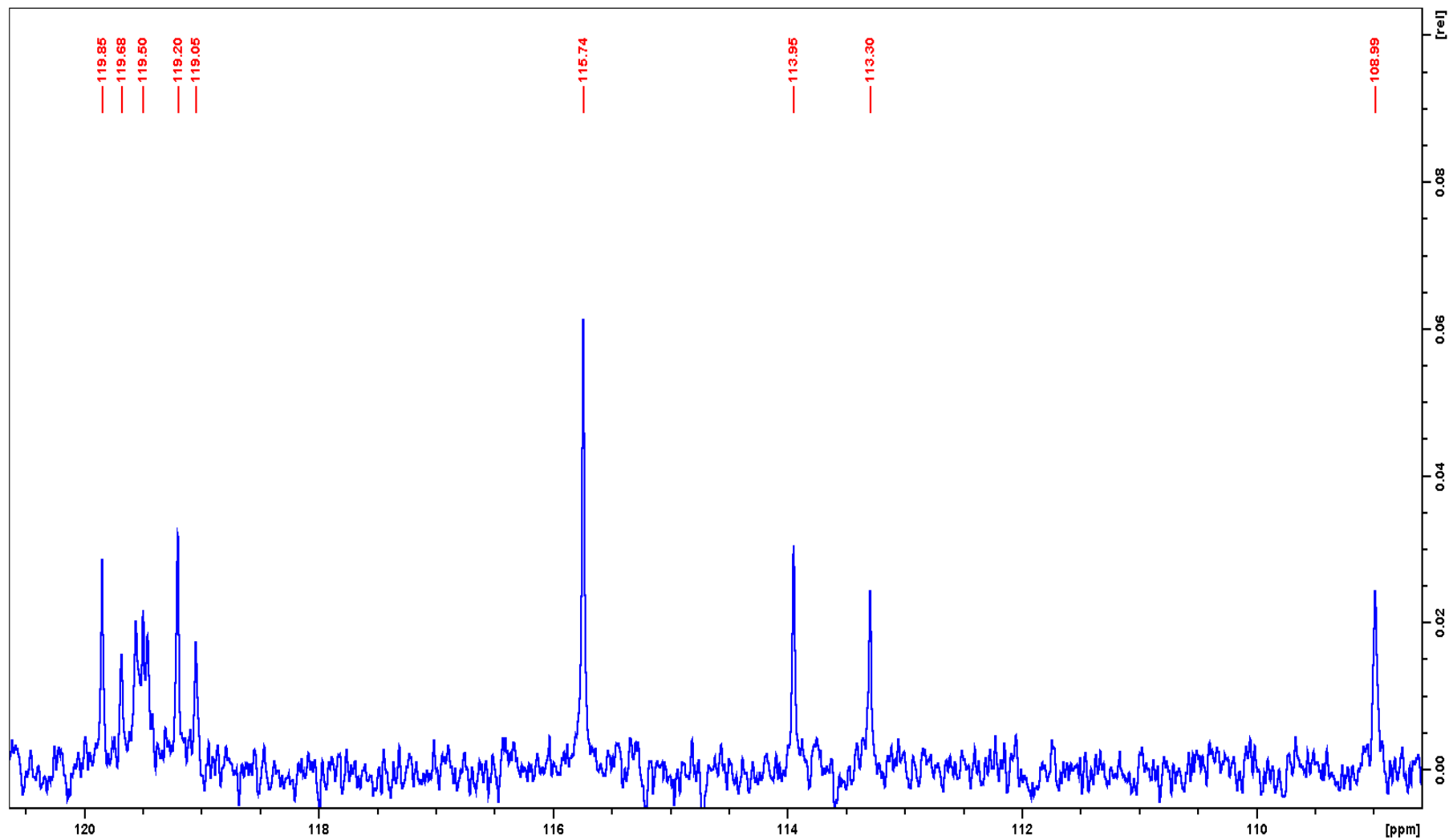


Figure S14. ^{13}C NMR spectrum of compounds **1a** and **1b** (enlarged).

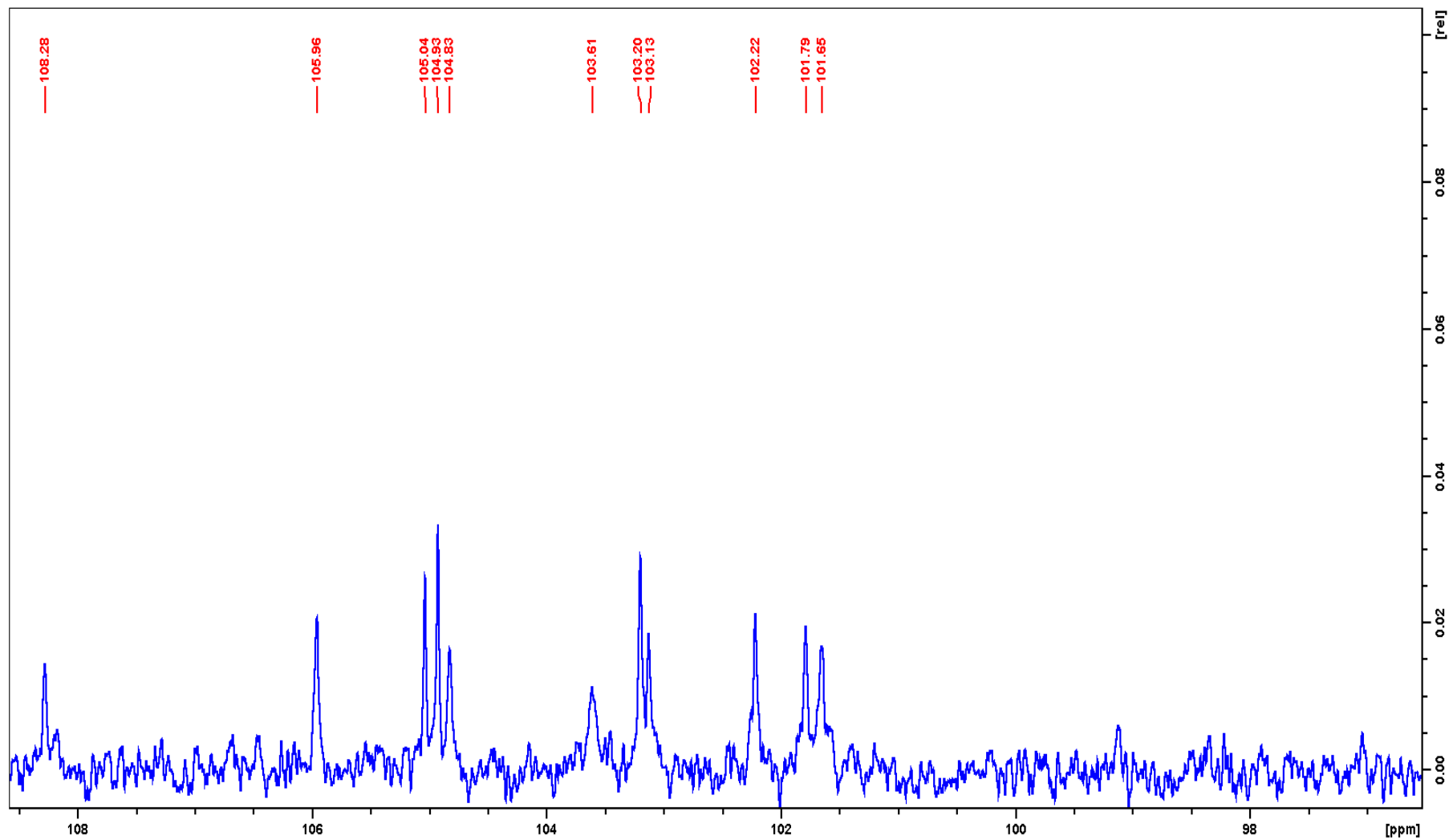


Figure S15. ¹³C NMR spectrum of compounds **1a** and **1b** (enlarged).

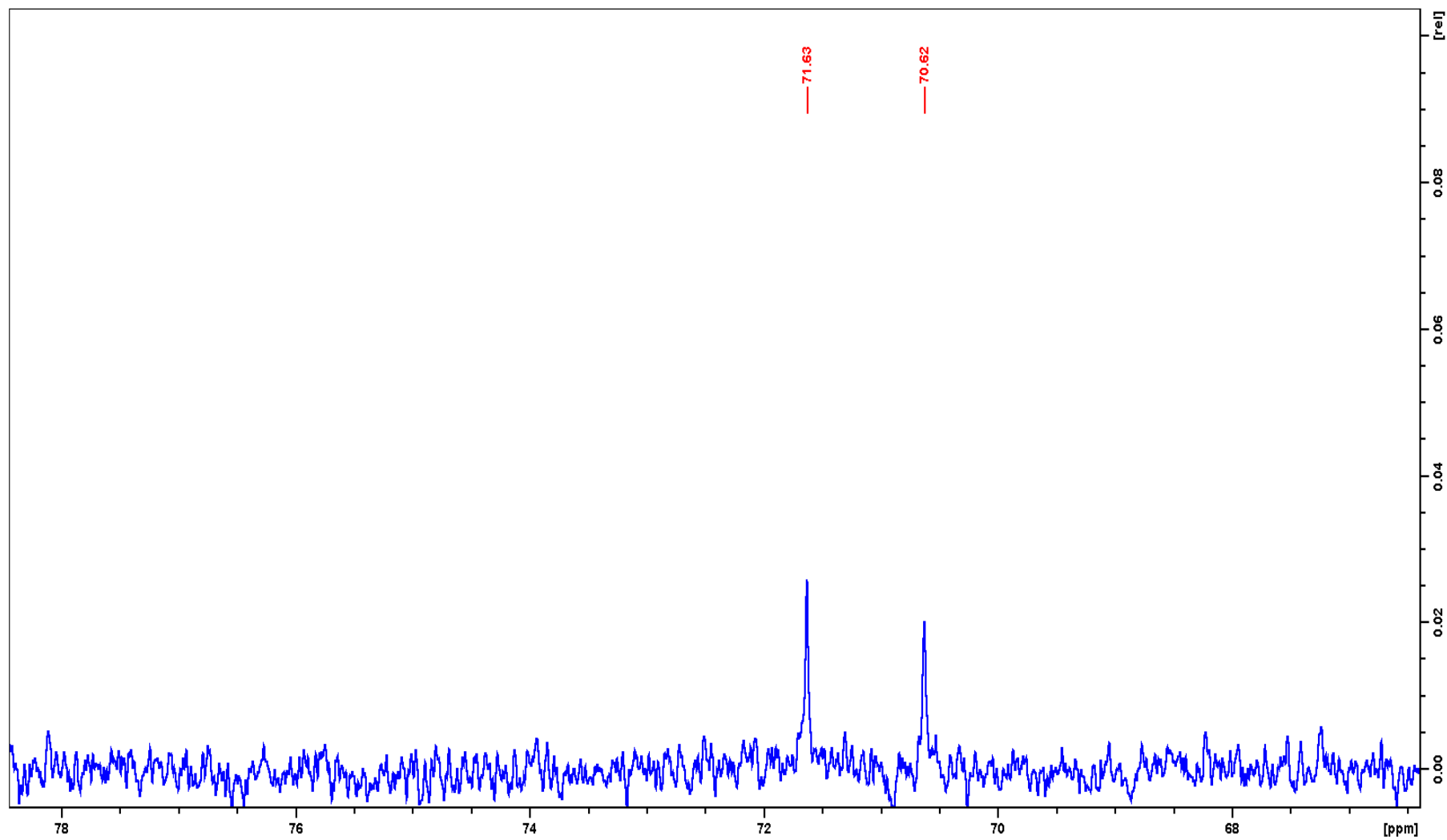


Figure S16. ^{13}C NMR spectrum of compounds **1a** and **1b** (enlarged).

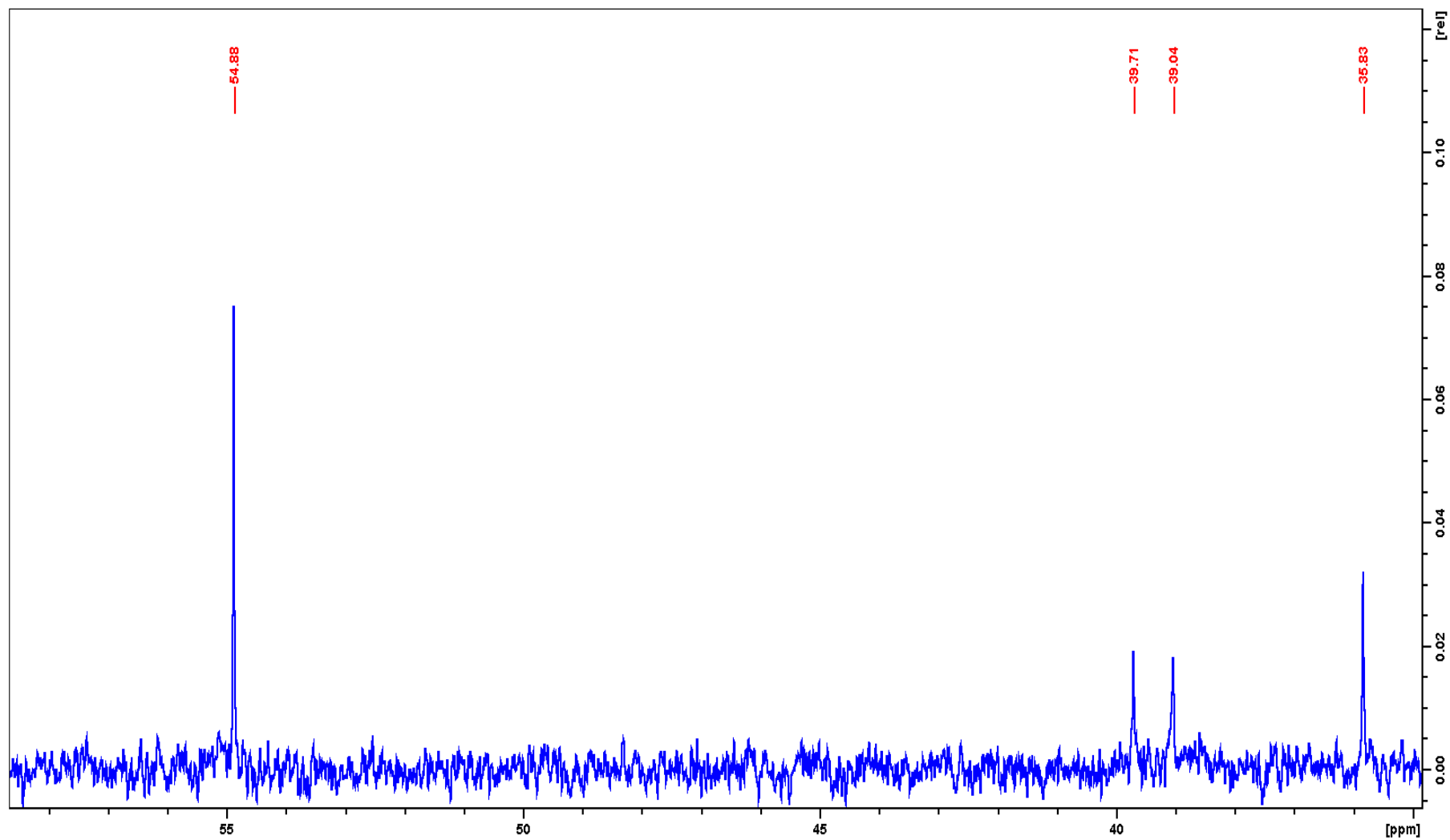


Figure S17. ^{13}C NMR spectrum of compounds **1a** and **1b** (enlarged).

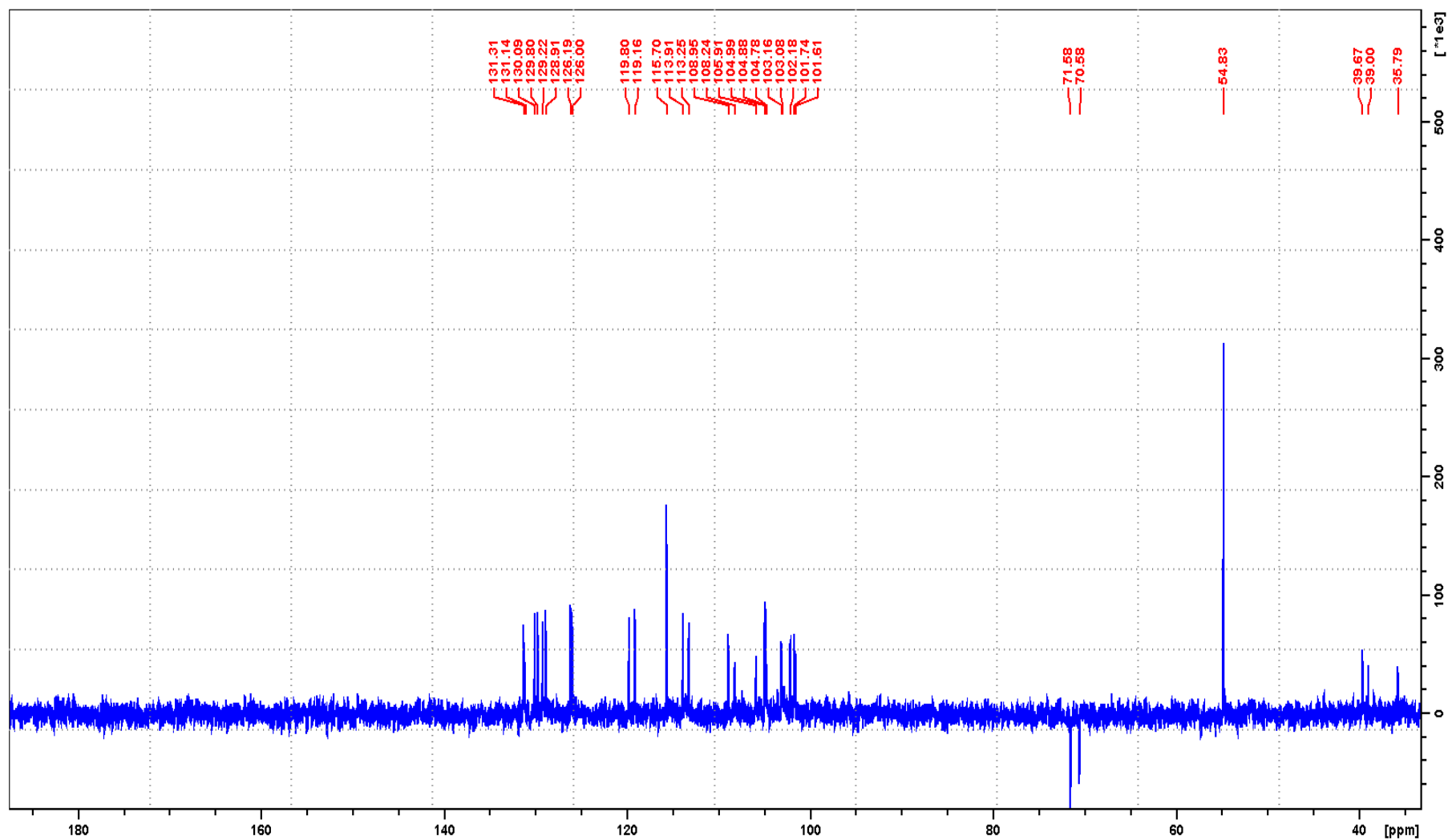


Figure S18. ^{13}C dept135 NMR spectrum of compounds **1a** and **1b**.

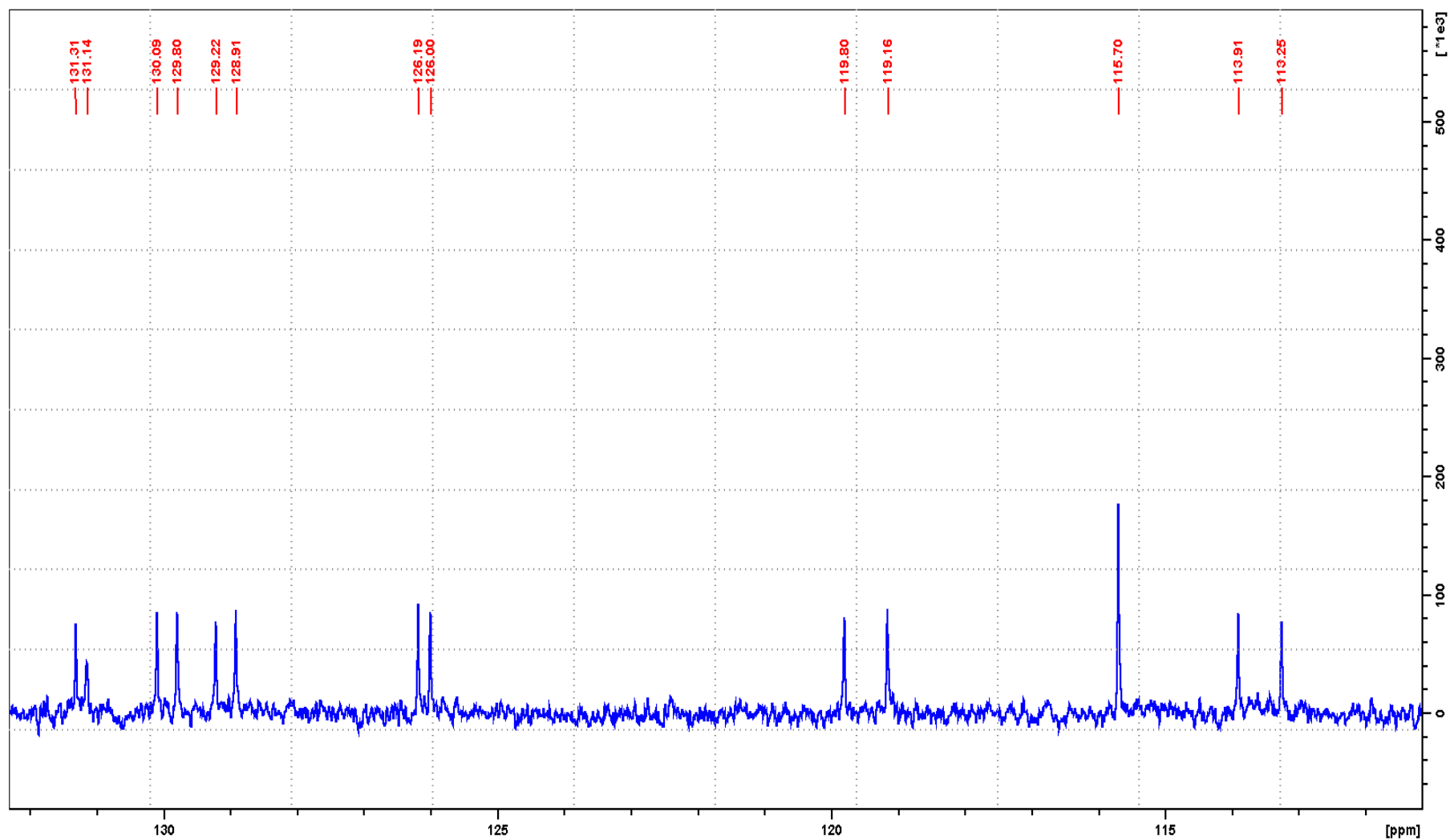


Figure S19. ¹³C dept135 NMR spectrum of compounds **1a** and **1b** (enlarged).

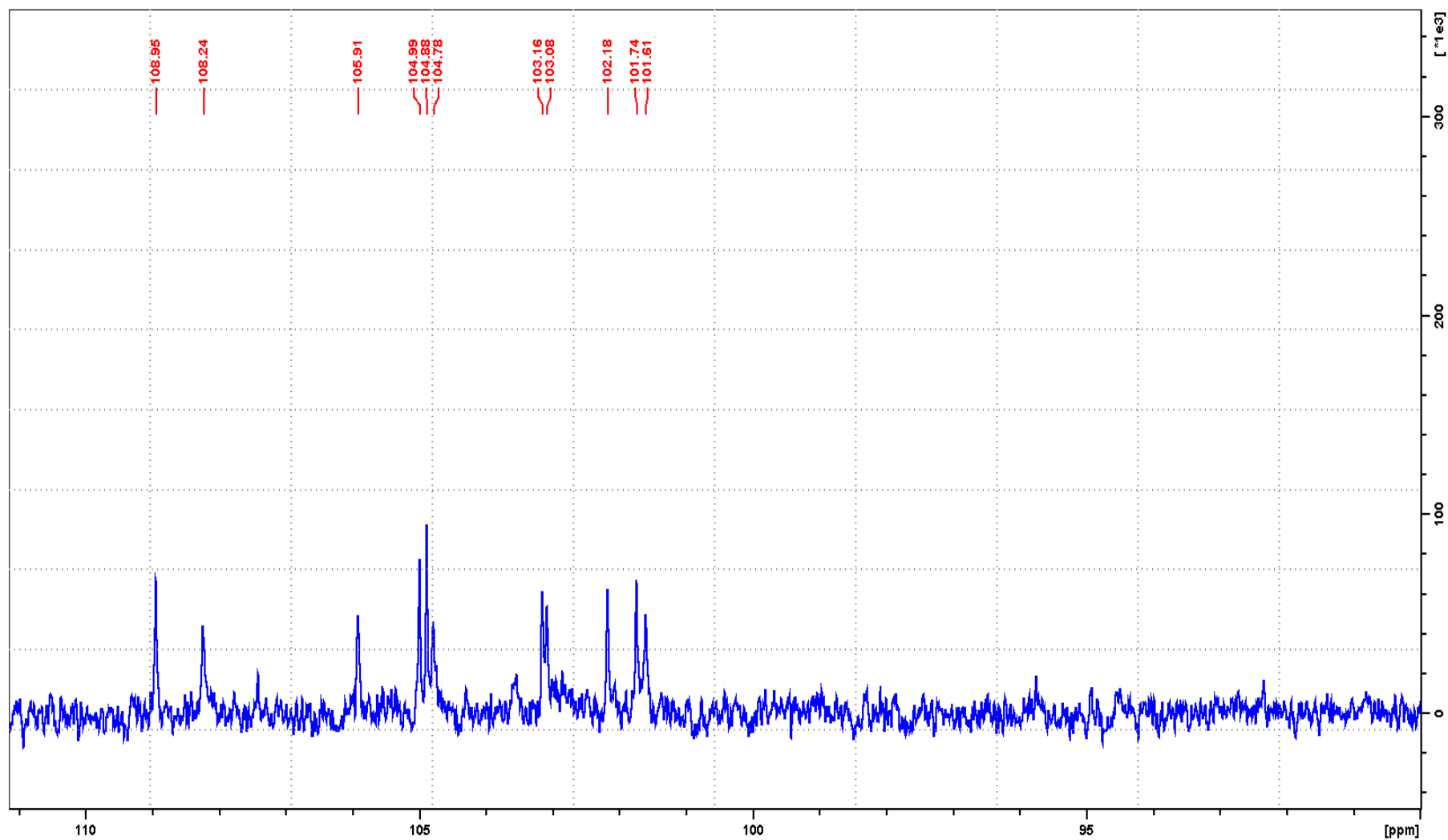


Figure S20. ^{13}C dept135 NMR spectrum of compounds **1a** and **1b** (enlarged).

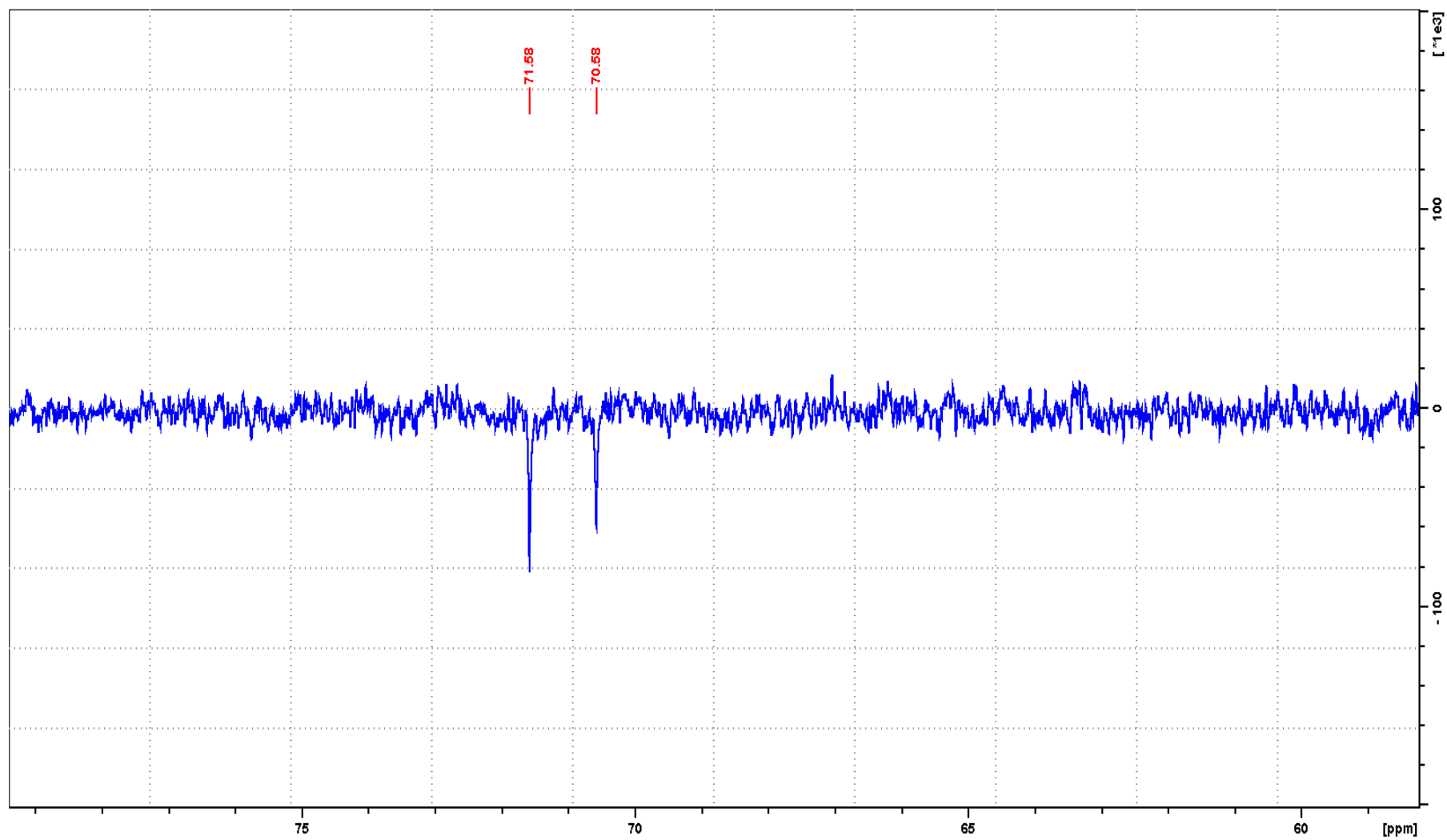


Figure S21. ^{13}C dept135 NMR spectrum of compounds **1a** and **1b** (enlarged).

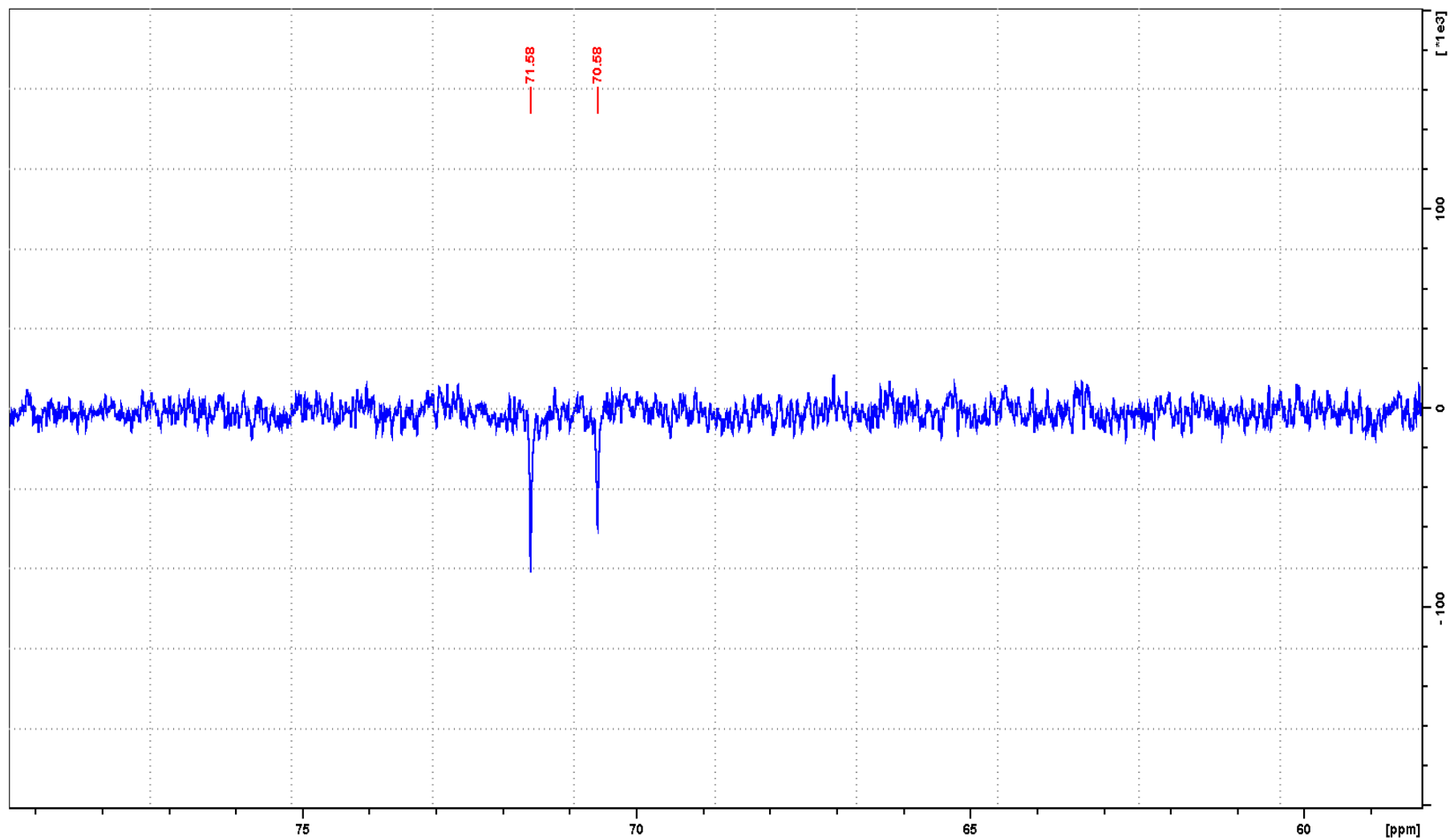


Figure S22. ^{13}C dept135 NMR spectrum of compounds **1a** and **1b** (enlarged).

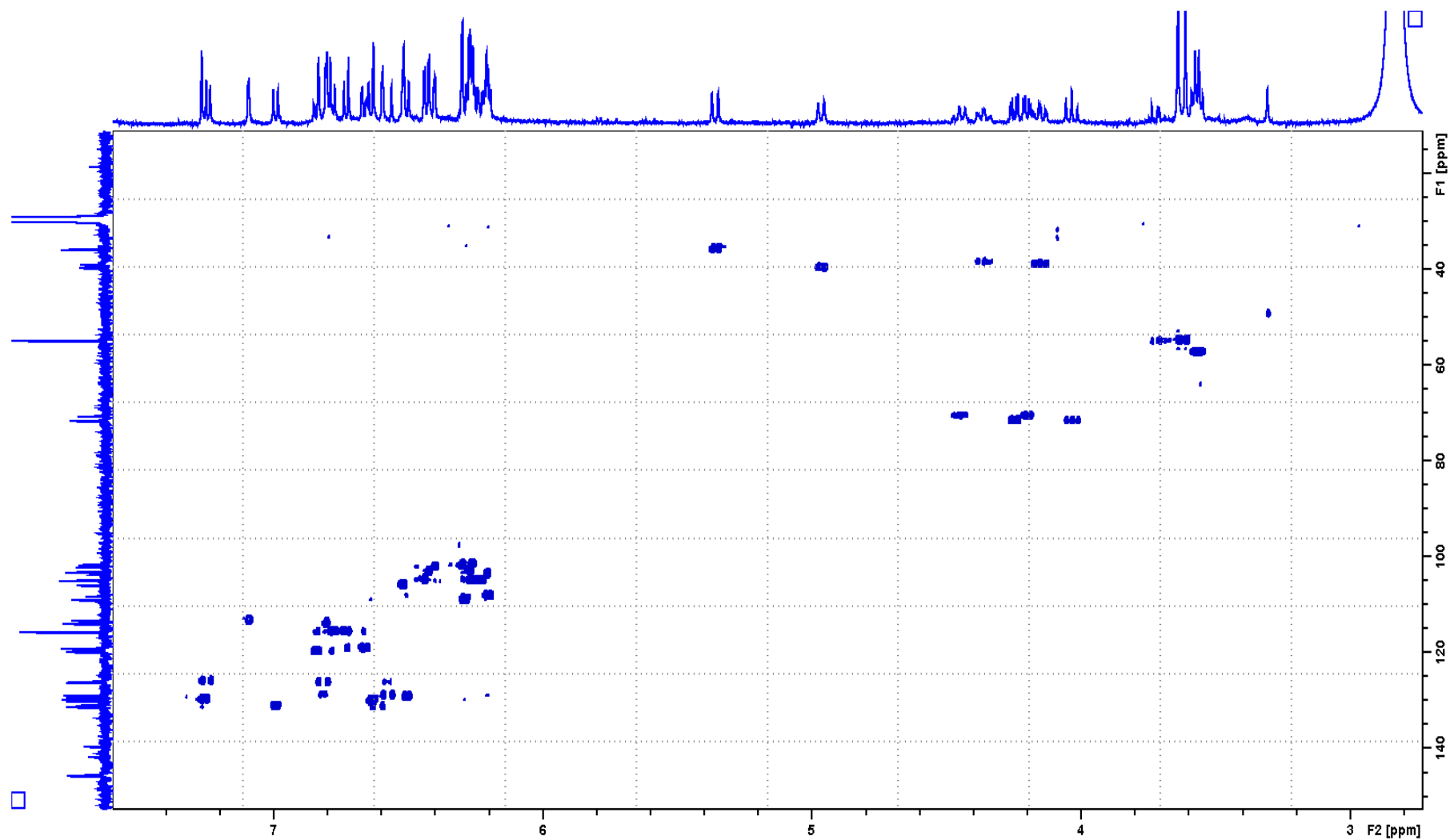


Figure S23. HSQC spectrum of compounds **1a** and **1b**.

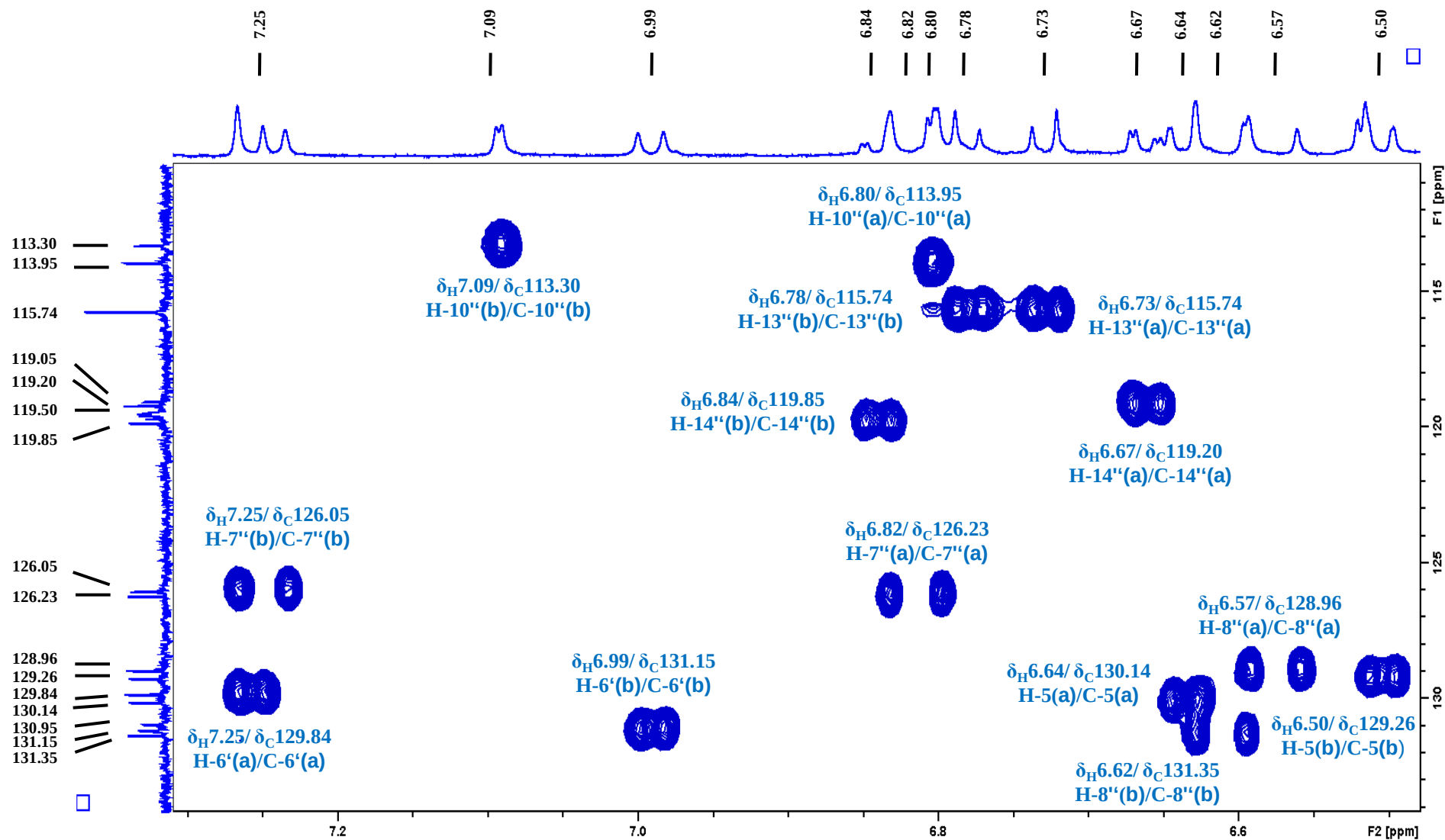


Figure S24. HSQC spectrum of compounds **1a** and **1b** (enlarged).

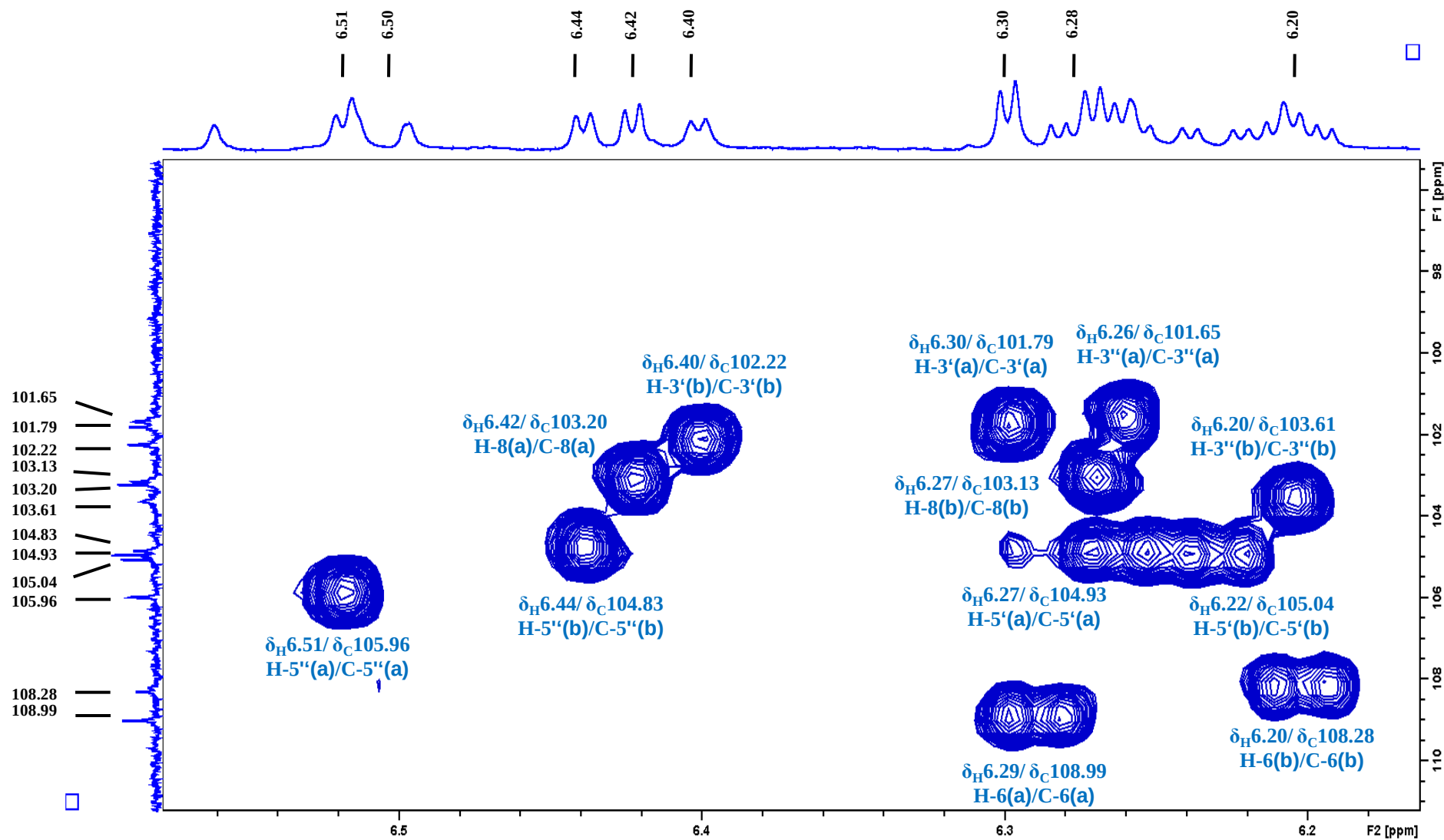


Figure S25. HSQC spectrum of compounds **1a** and **1b** (enlarged).

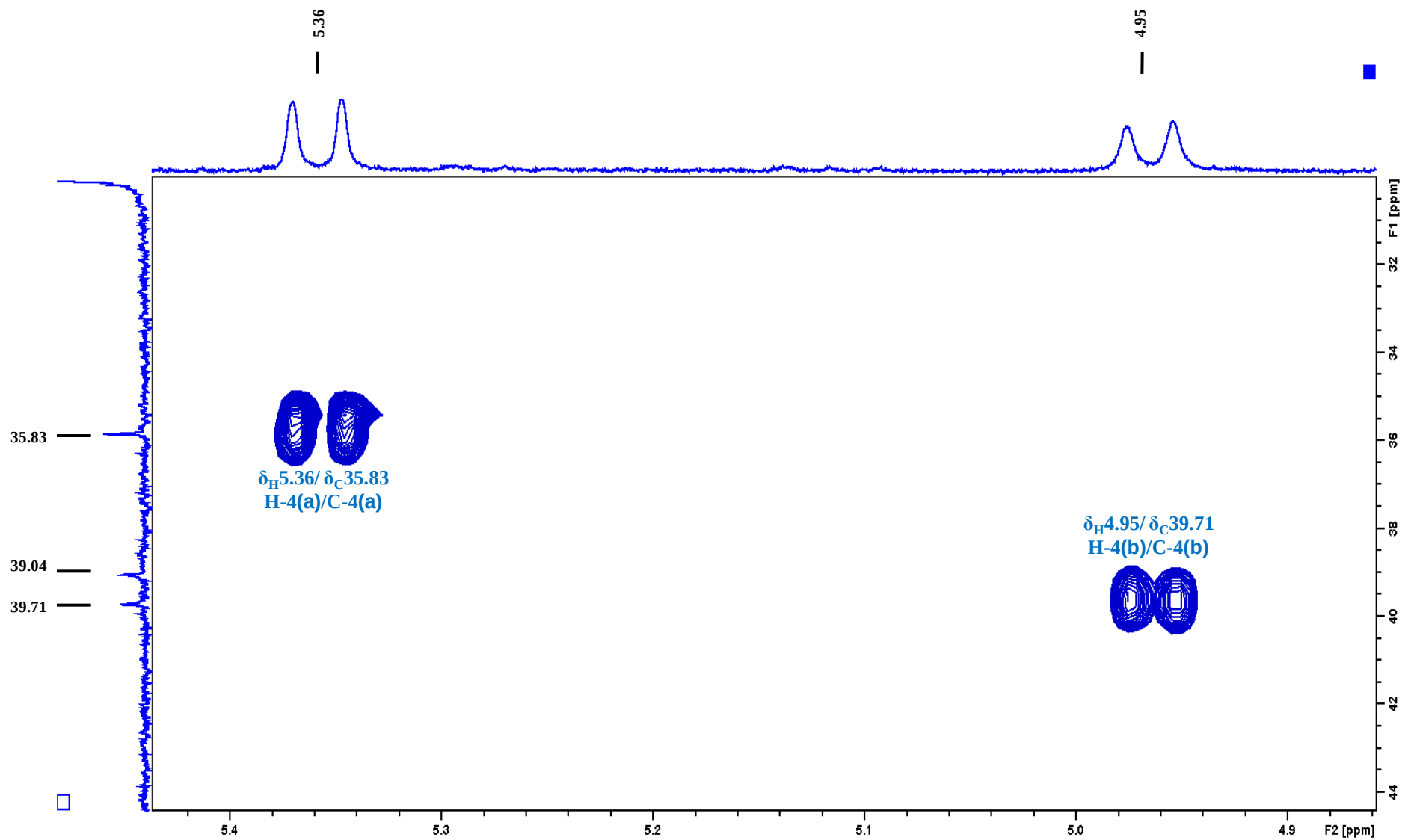


Figure S26. HSQC spectrum of compounds **1a** and **1b** (enlarged).

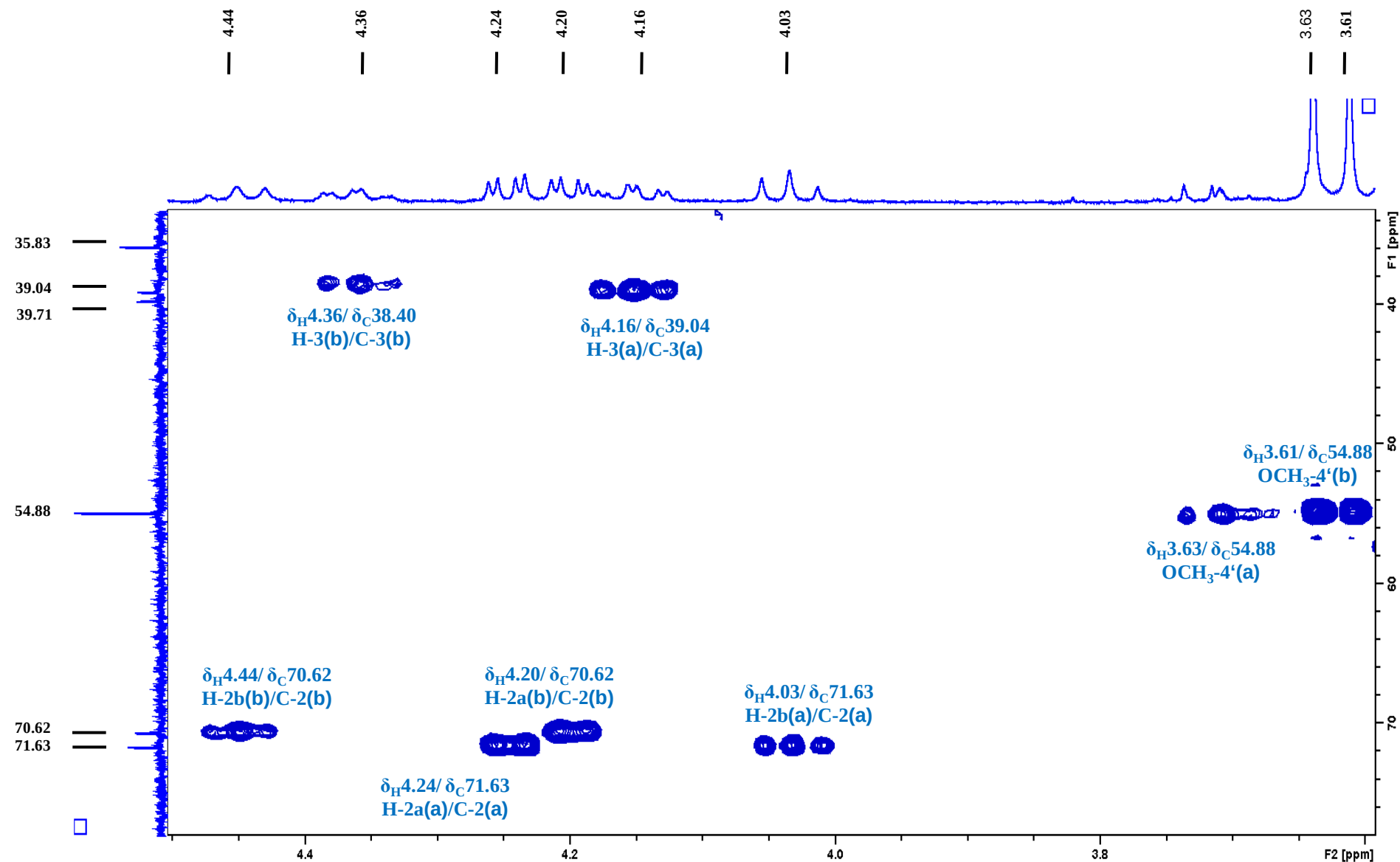


Figure S27. HSQC spectrum of compounds **1a** and **1b** (enlarged).

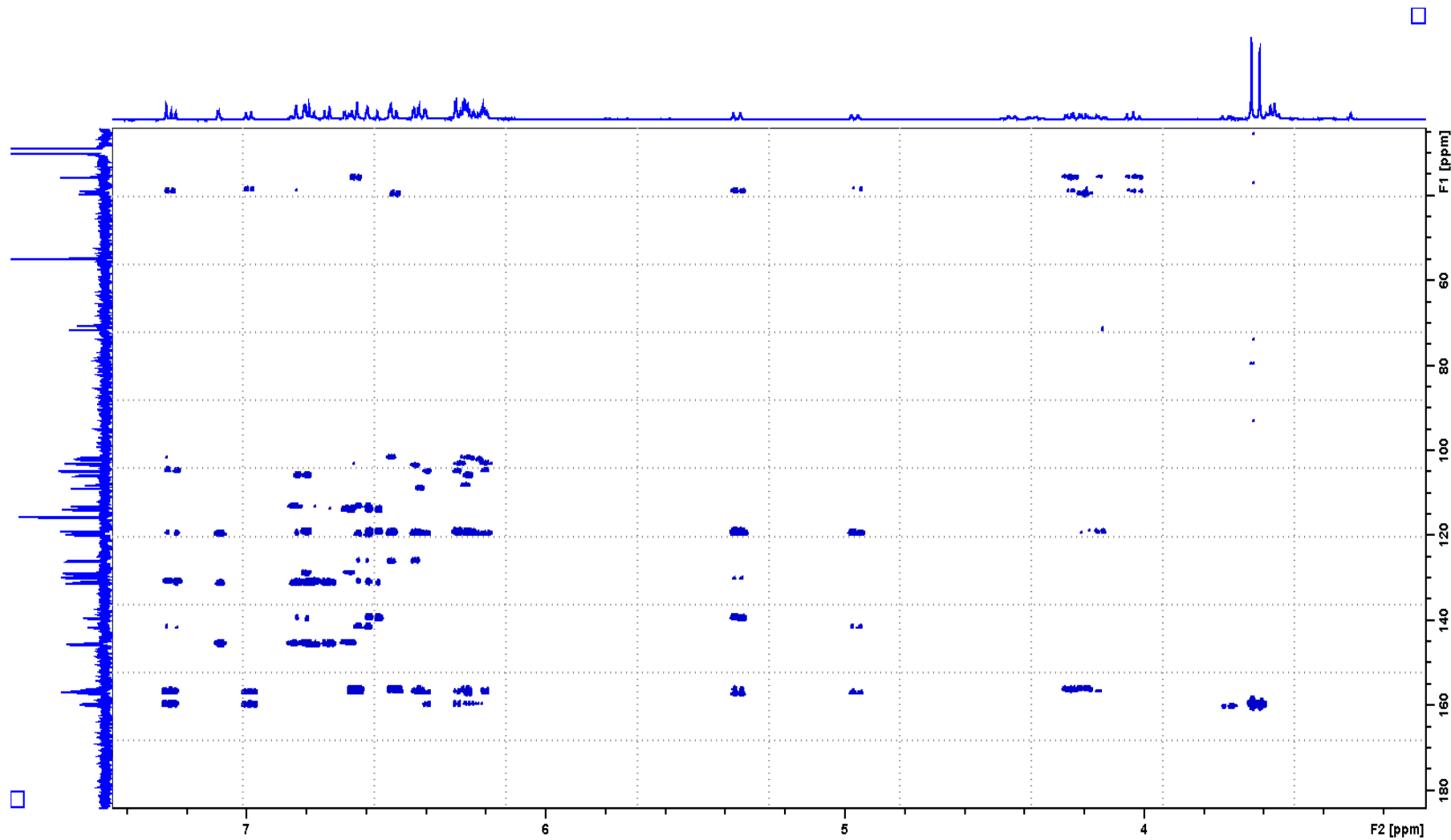


Figure S28. HMBC spectrum of compounds **1a** and **1b**.

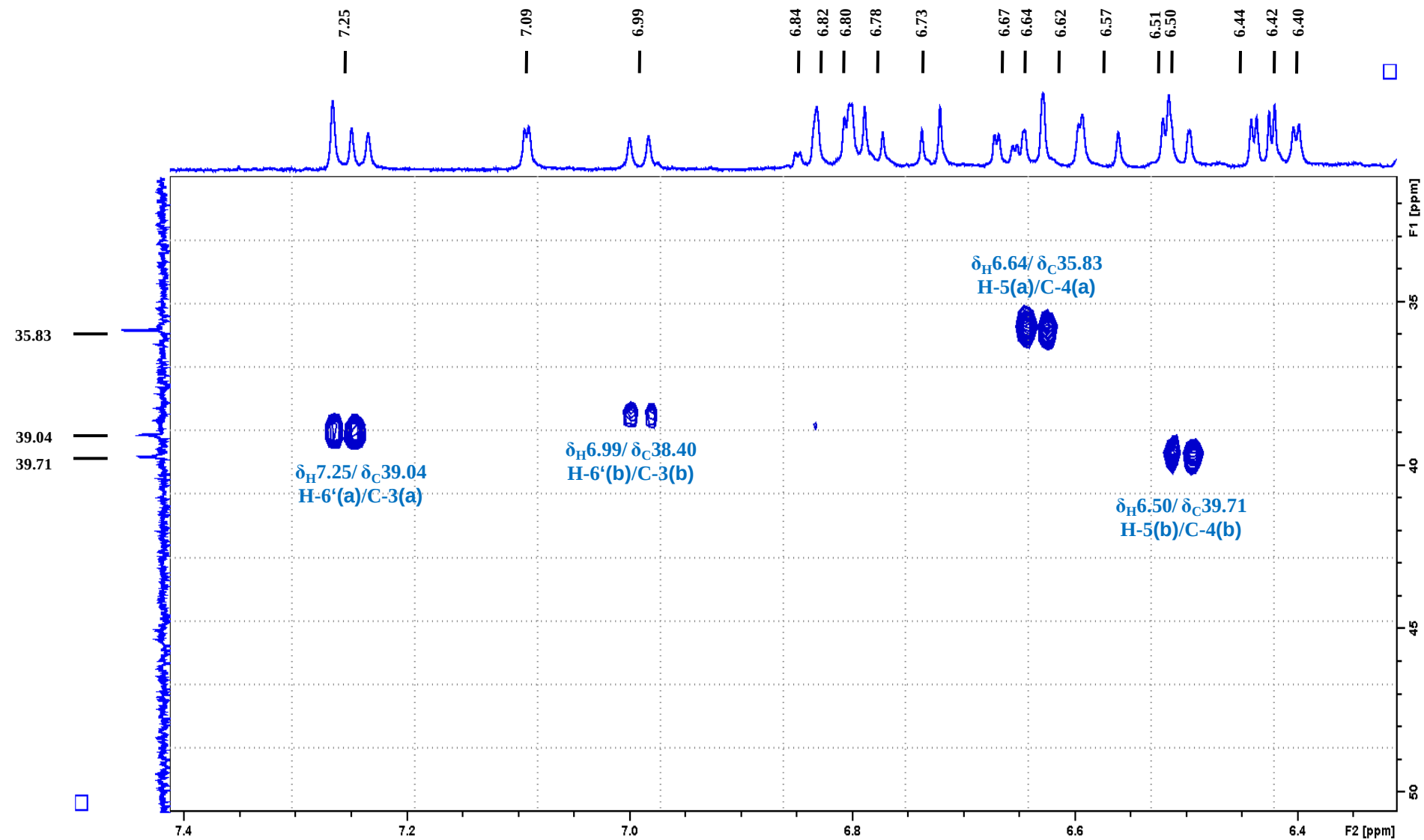


Figure S29. HMBC spectrum of compounds **1a** and **1b** (enlarged).

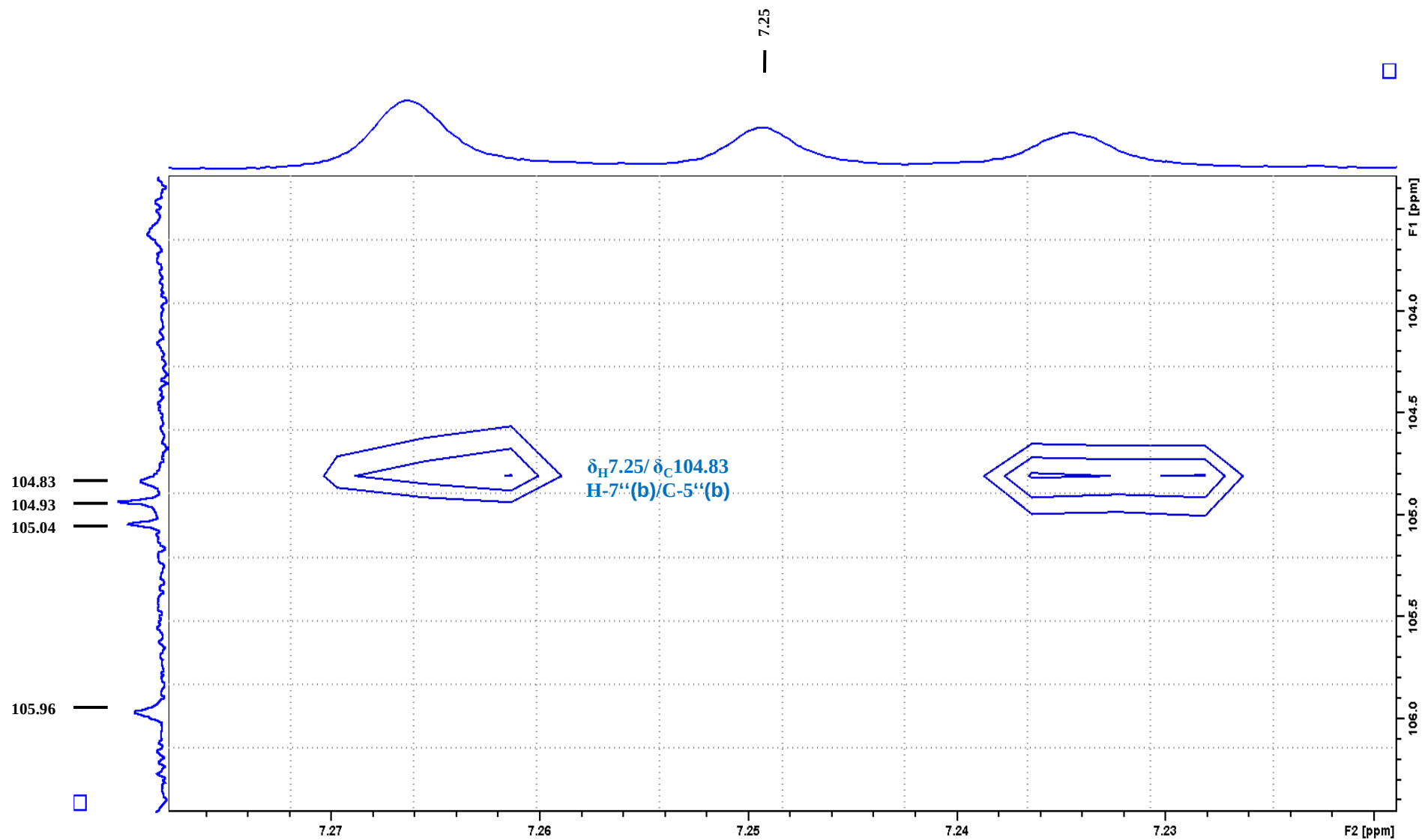


Figure S30. HMBC spectrum of compounds **1a** and **1b** (enlarged).

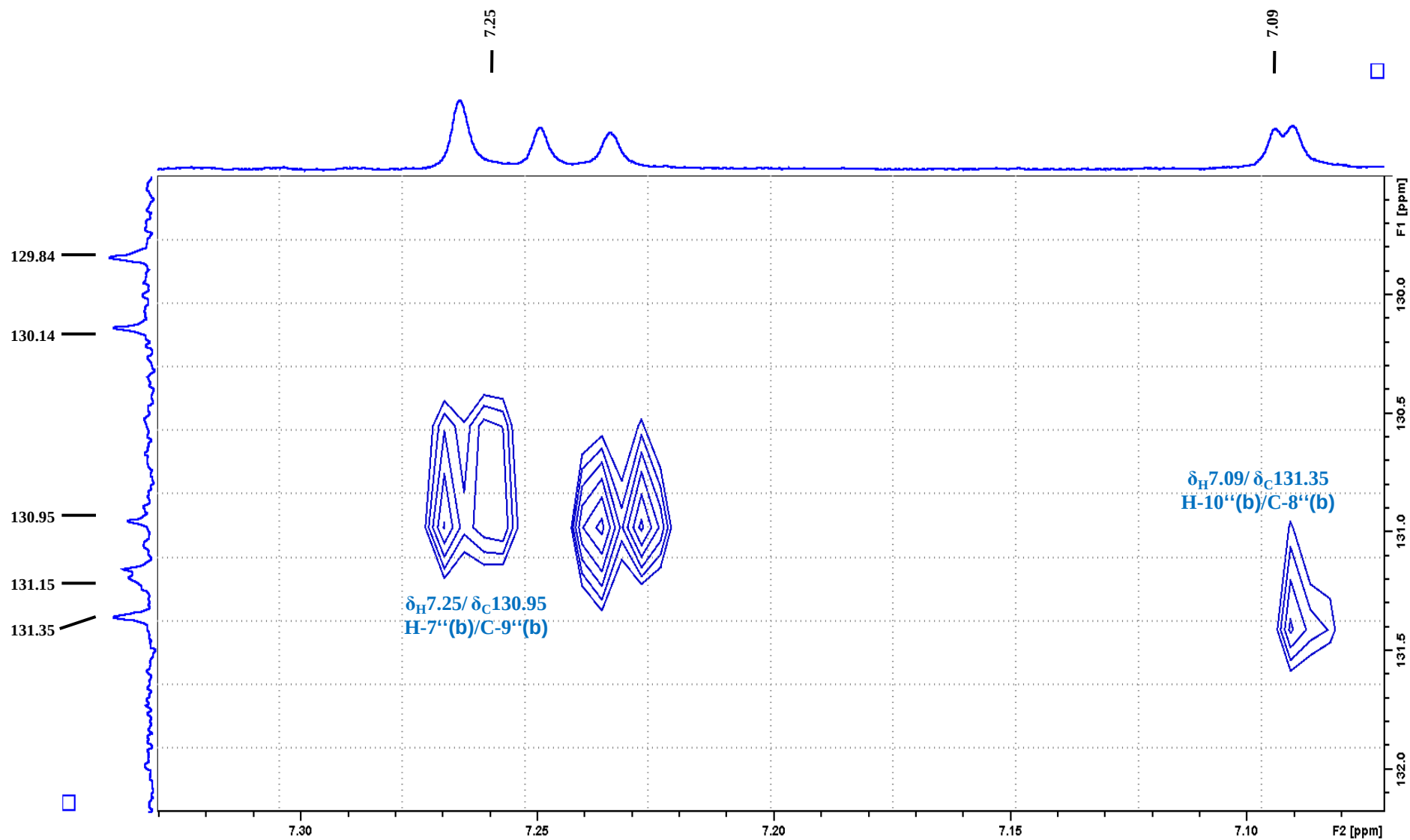


Figure S31. HMBC spectrum of compounds **1a** and **1b** (enlarged).

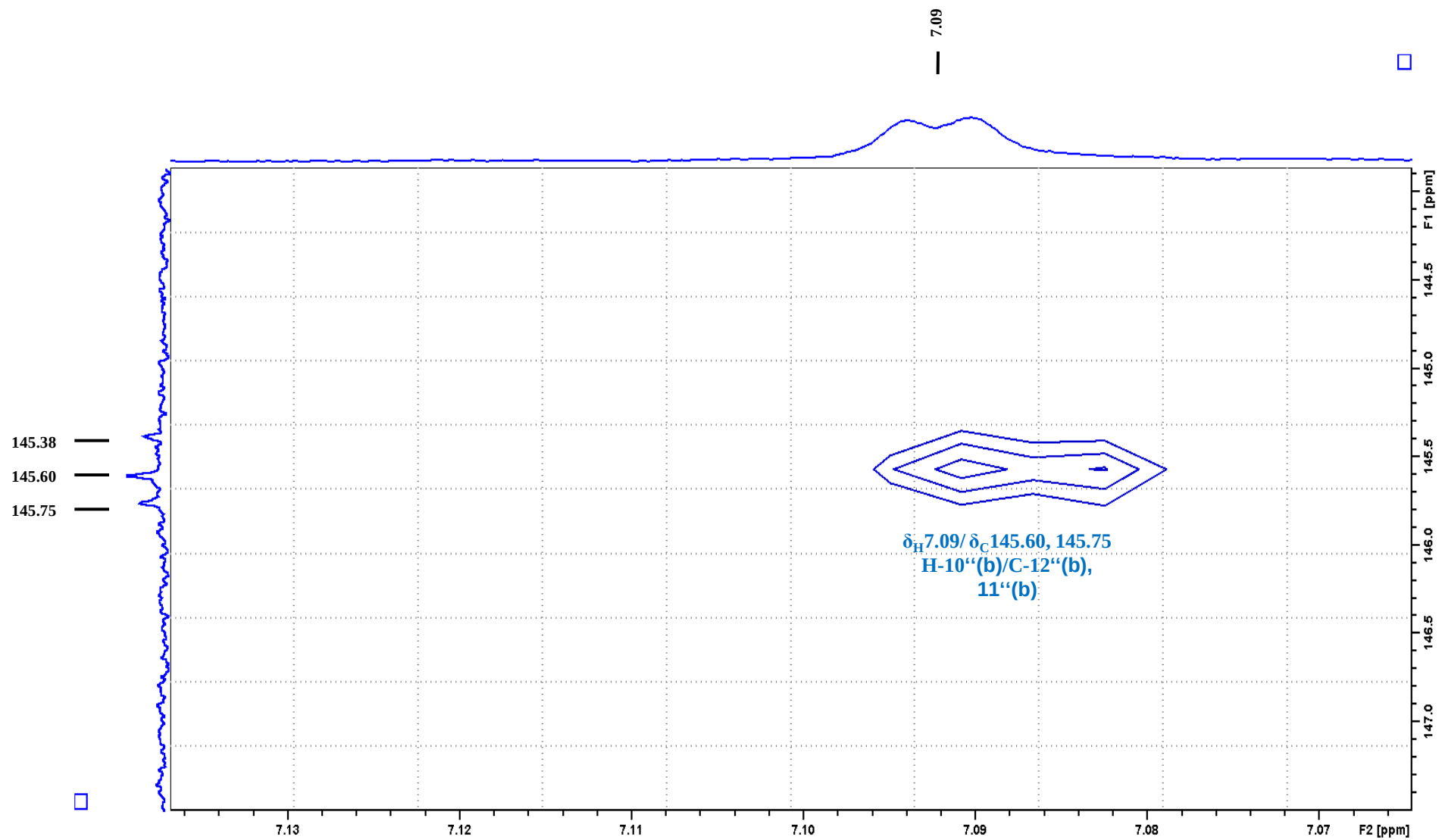


Figure S32. HMBC spectrum of compounds **1a** and **1b** (enlarged).

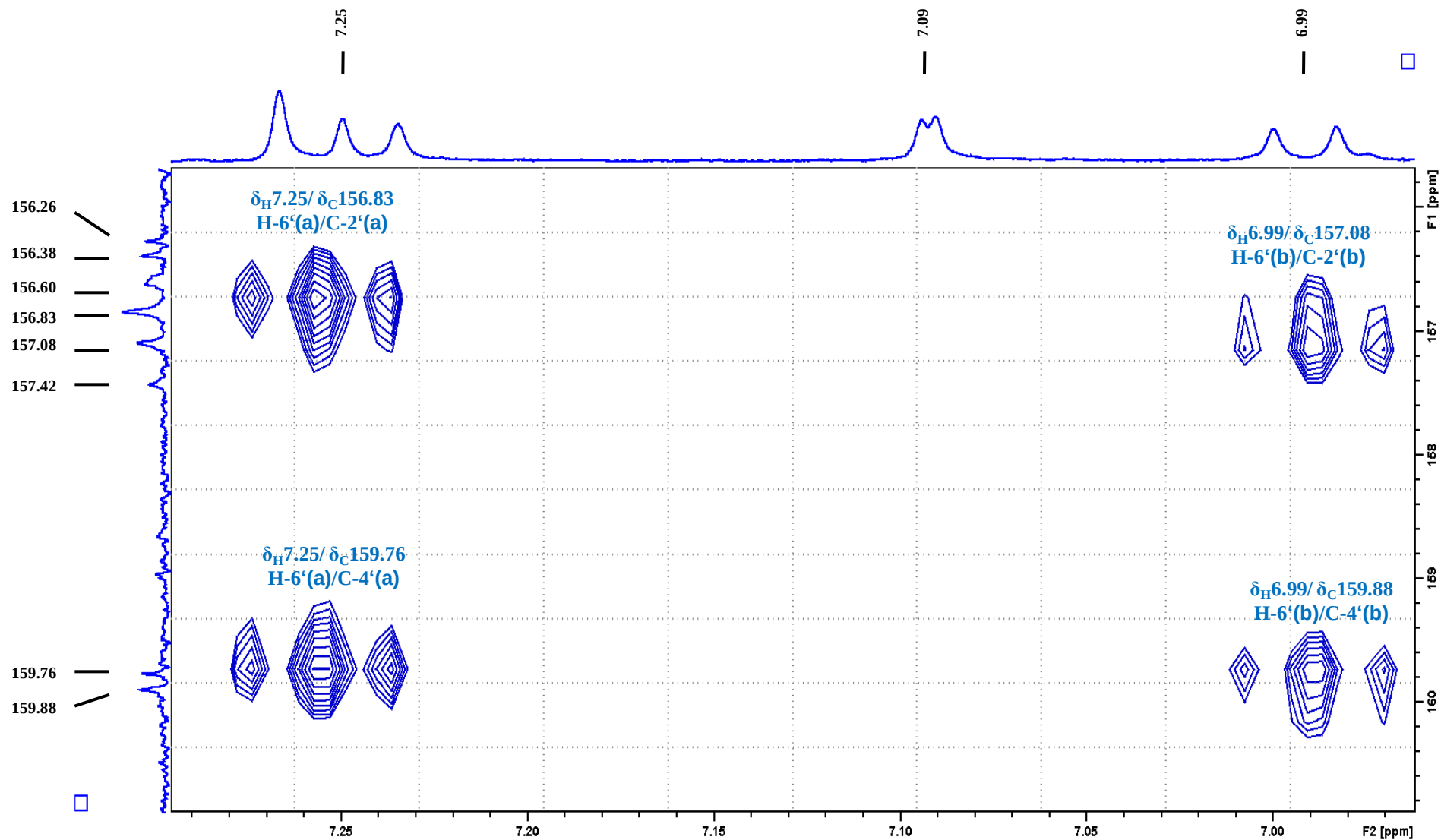


Figure S33. HMBC spectrum of compounds **1a** and **1b** (enlarged).

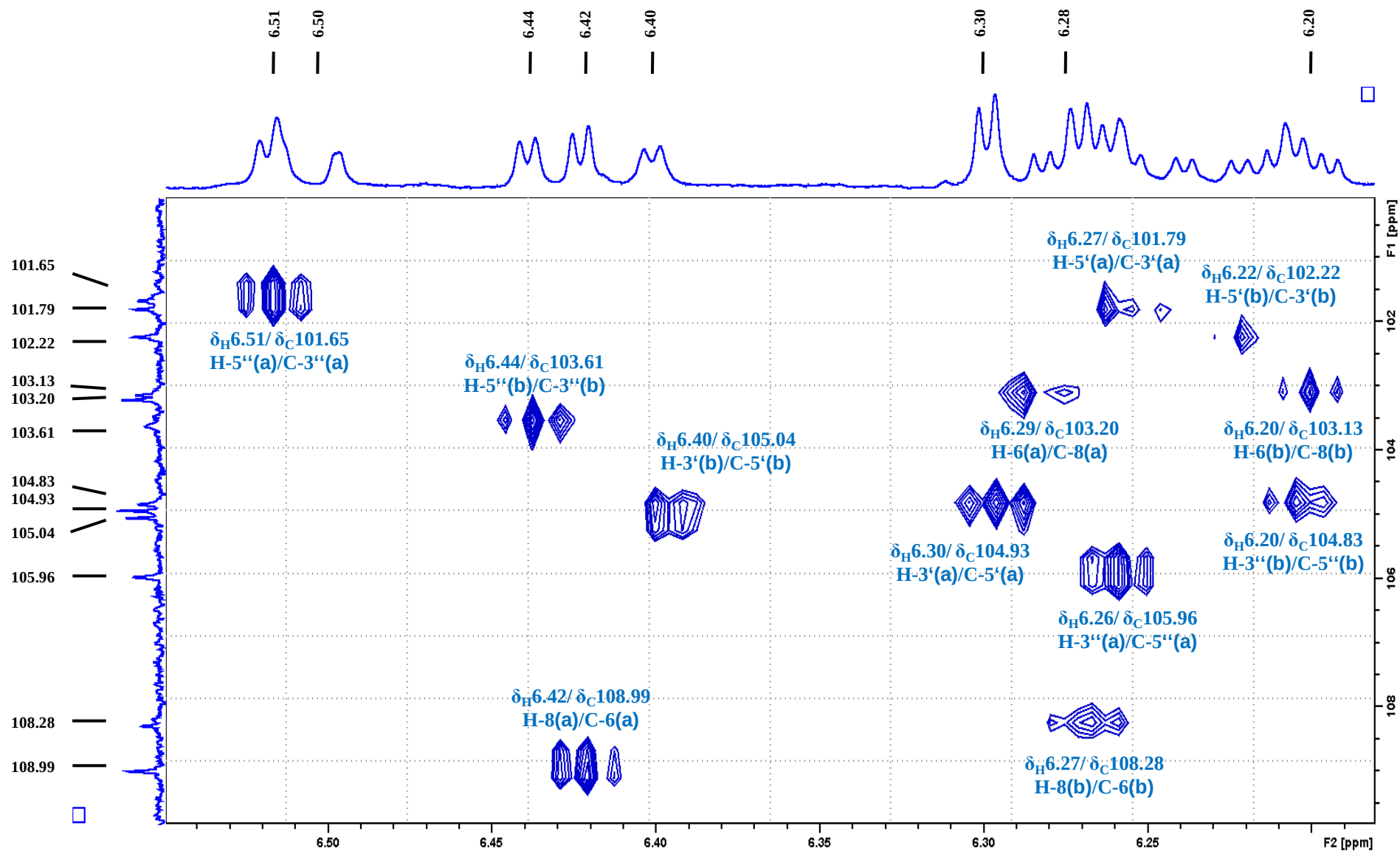


Figure S34. HMBC spectrum of compounds **1a** and **1b** (enlarged).

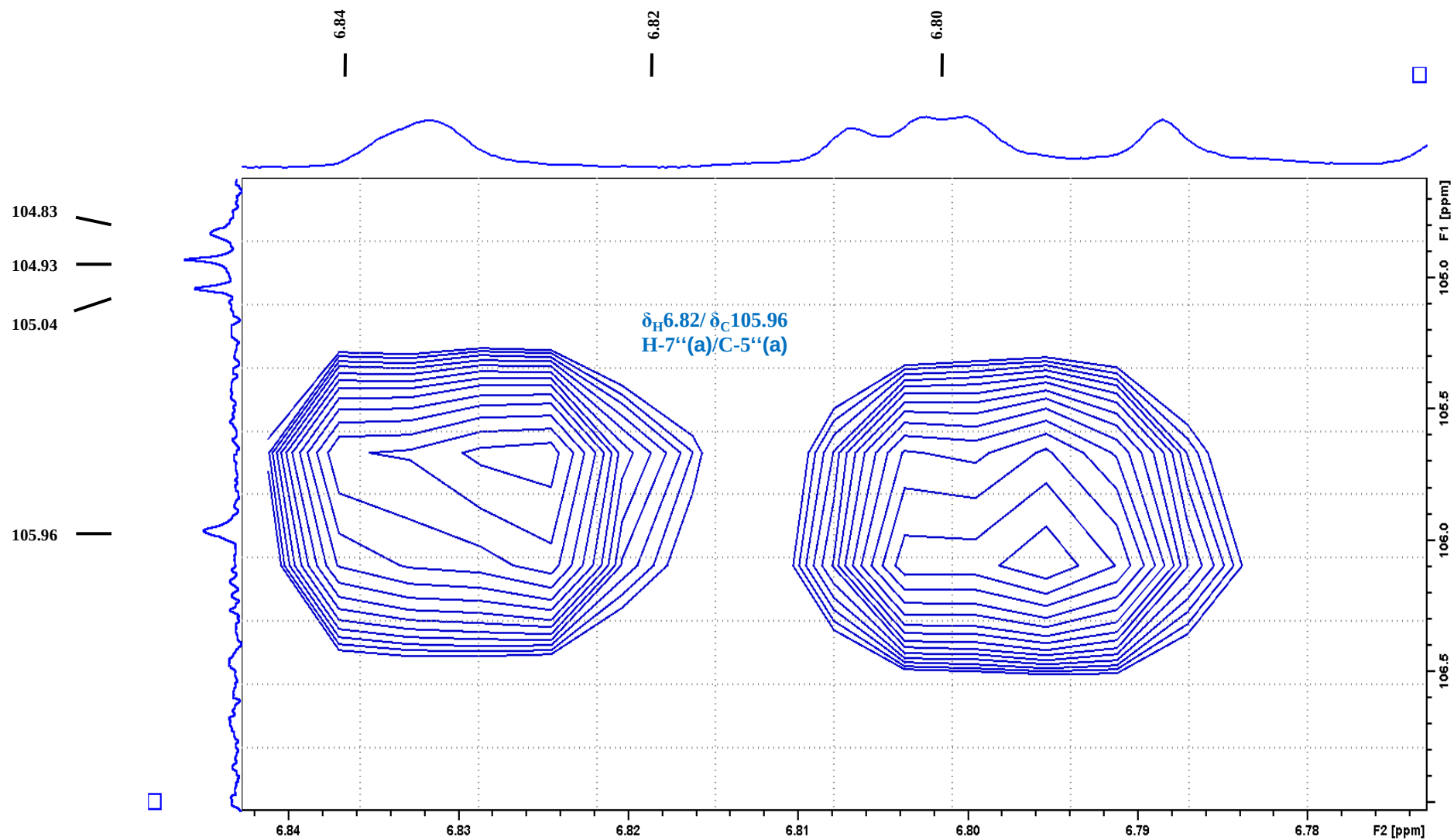


Figure S35. HMBC spectrum of compounds **1a** and **1b** (enlarged).

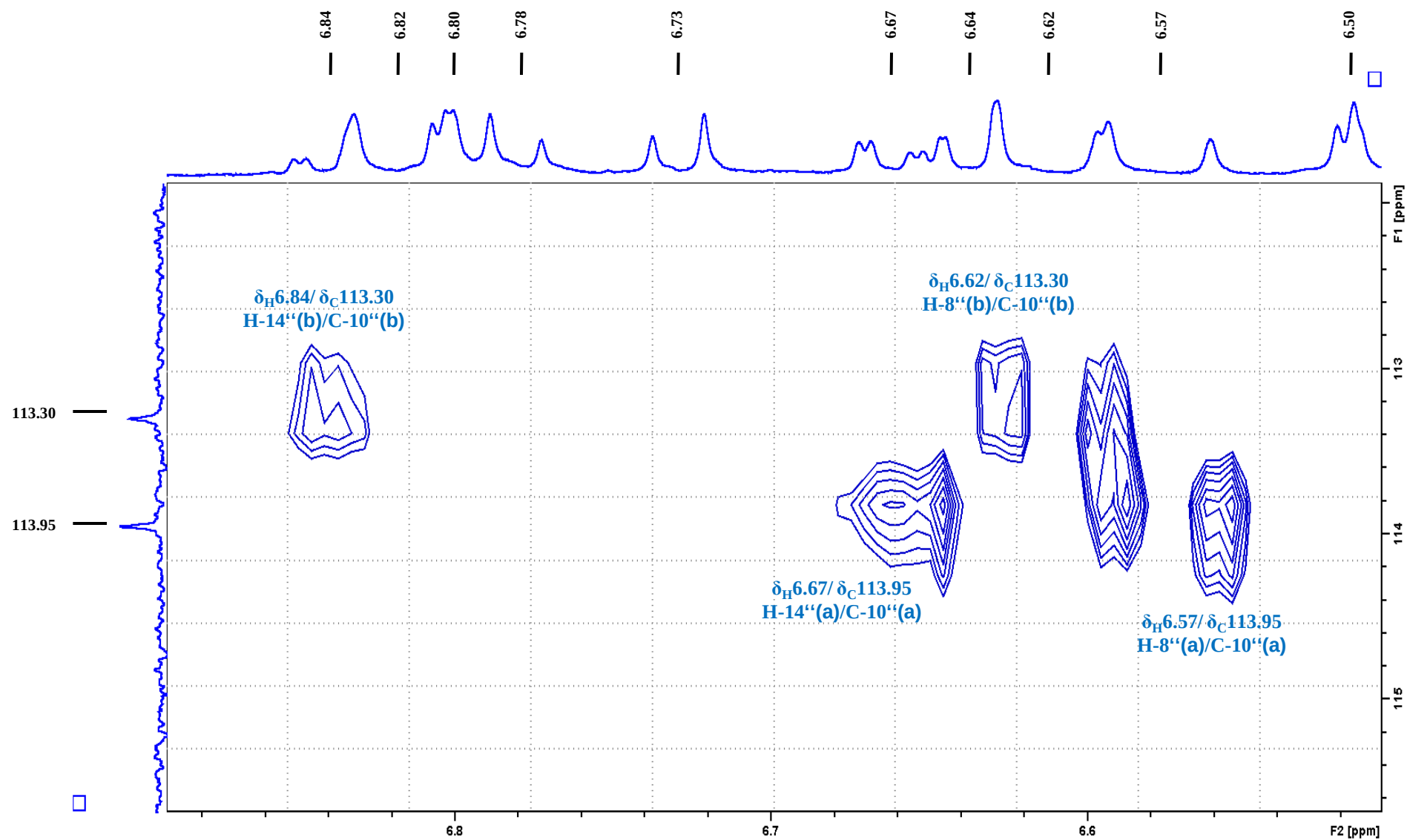


Figure S36. HMBC spectrum of compounds **1a** and **1b** (enlarged).

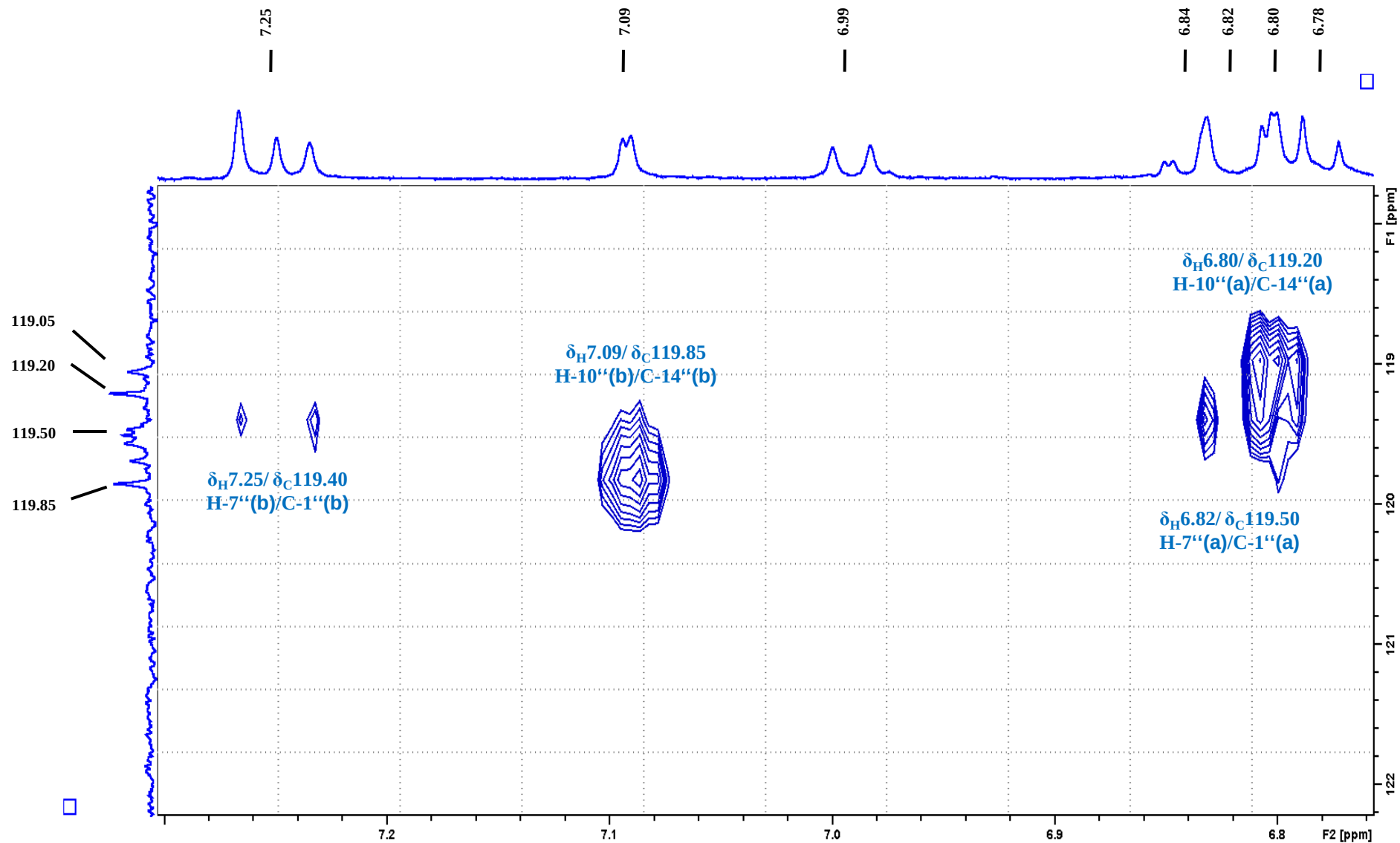


Figure S37. HMBC spectrum of compounds **1a** and **1b** (enlarged).

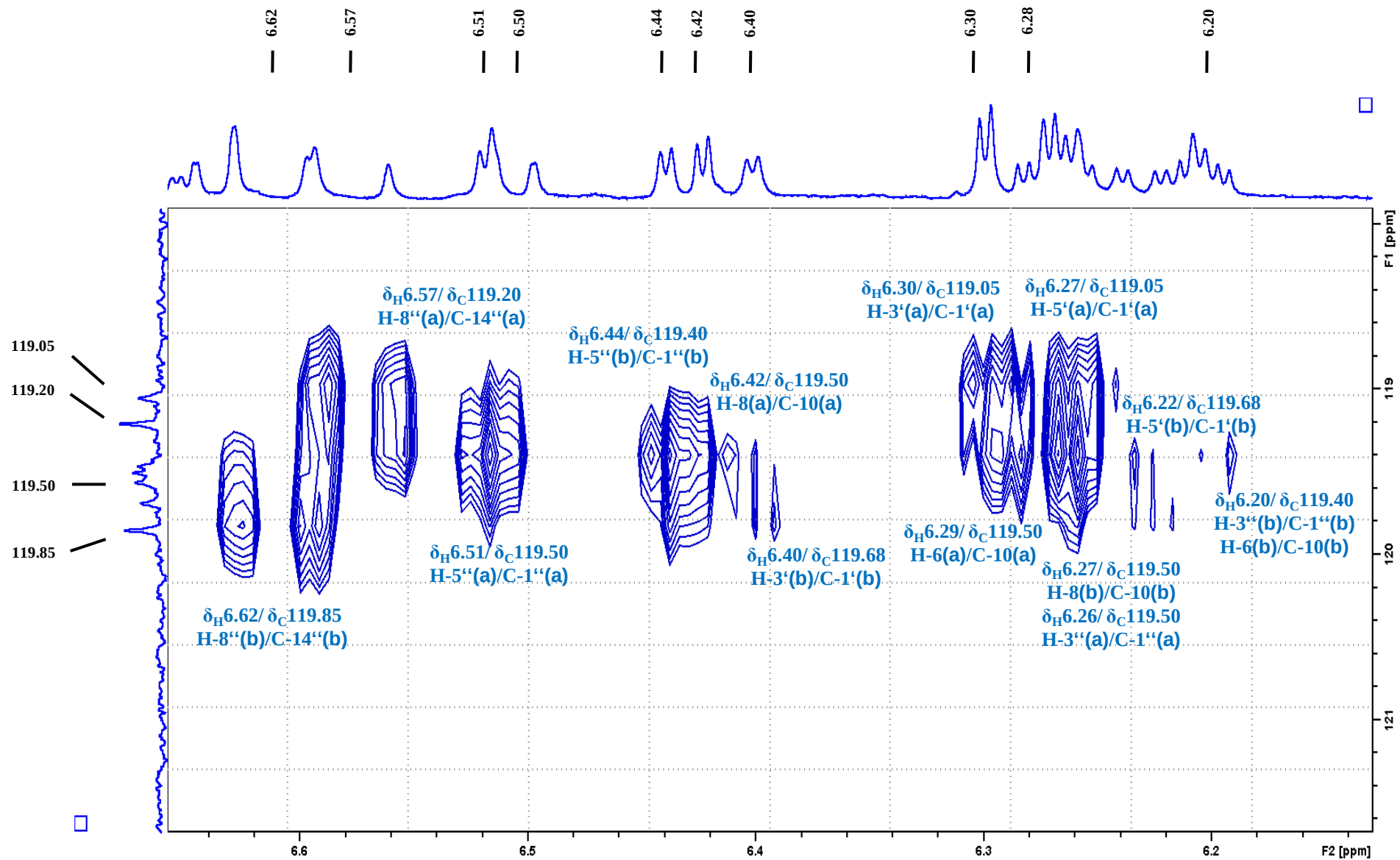


Figure S38. HMBC spectrum of compounds **1a** and **1b** (enlarged).

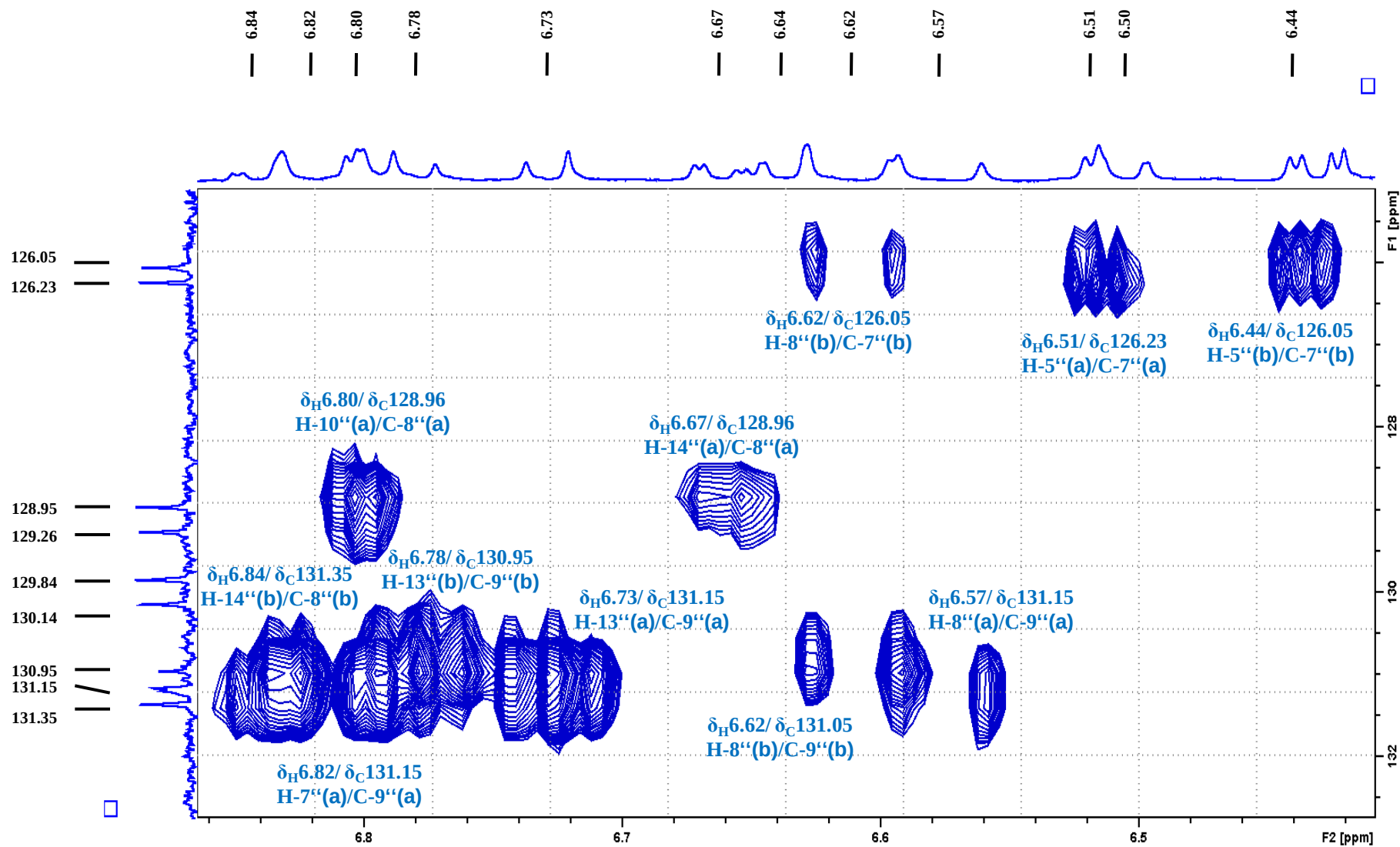


Figure S39. HMBC spectrum of compounds **1a** and **1b** (enlarged).

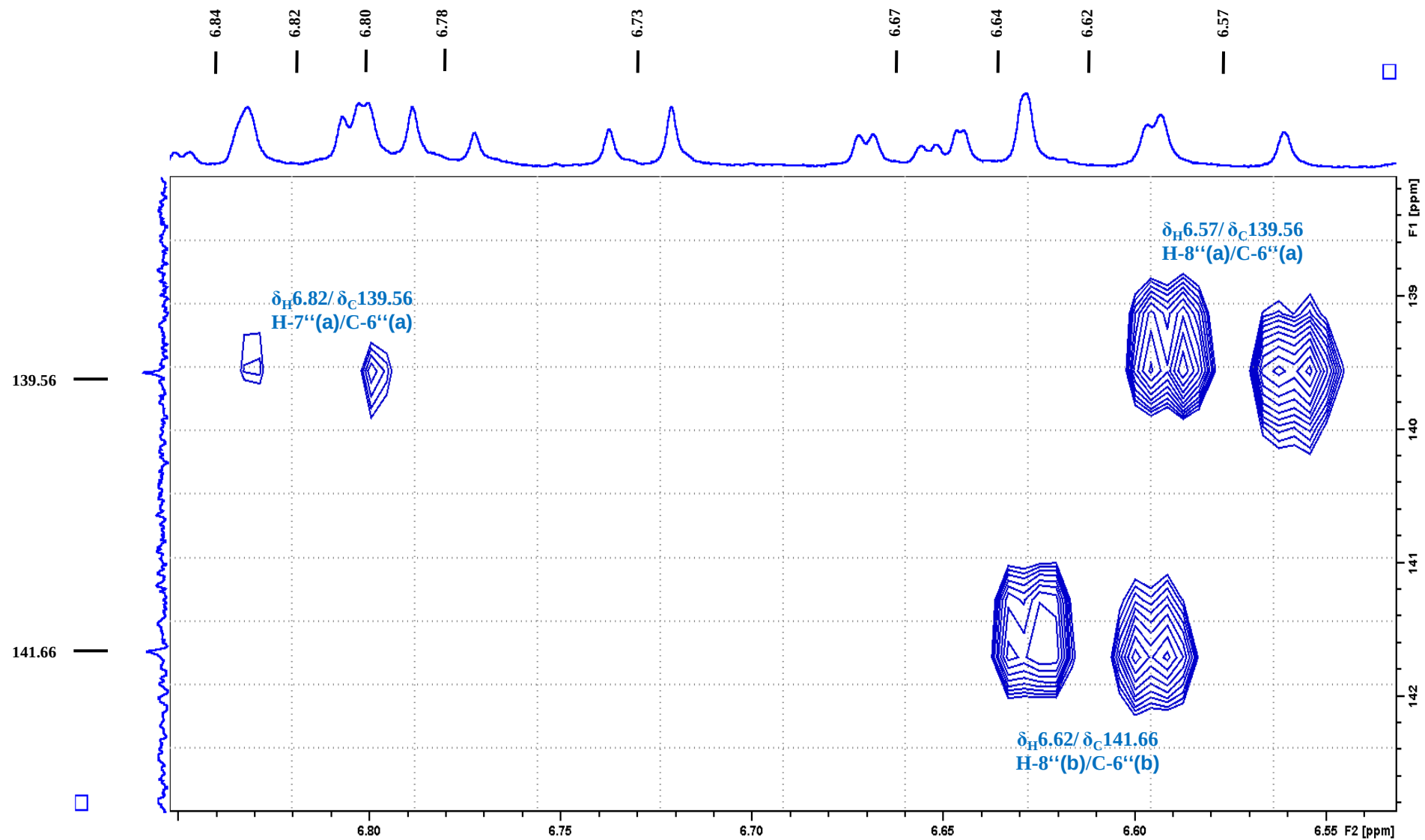


Figure S40. HMBC spectrum of compounds **1a** and **1b** (enlarged).

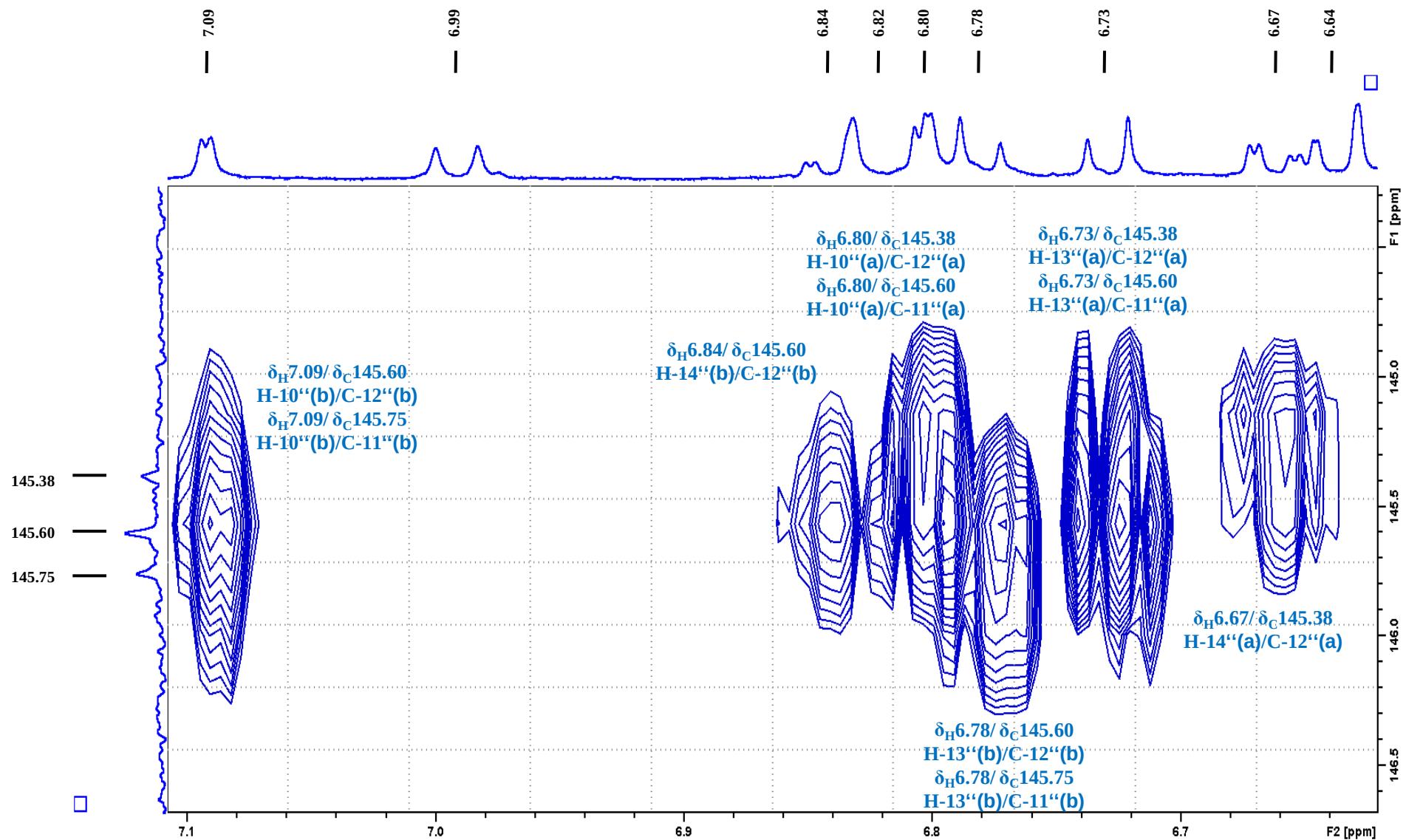


Figure S41. HMBC spectrum of compounds **1a** and **1b** (enlarged).

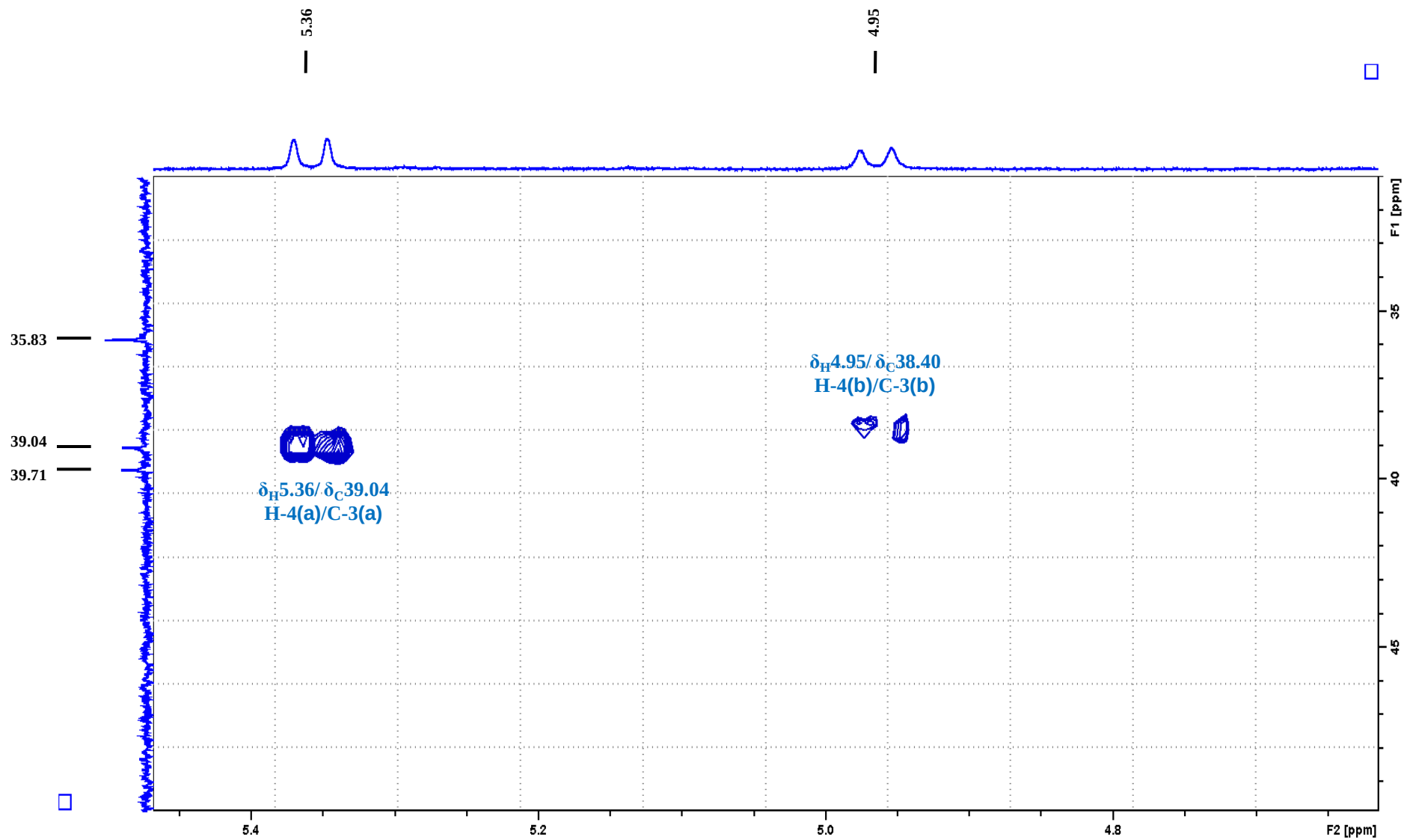


Figure S42. HMBC spectrum of compounds **1a** and **1b** (enlarged).

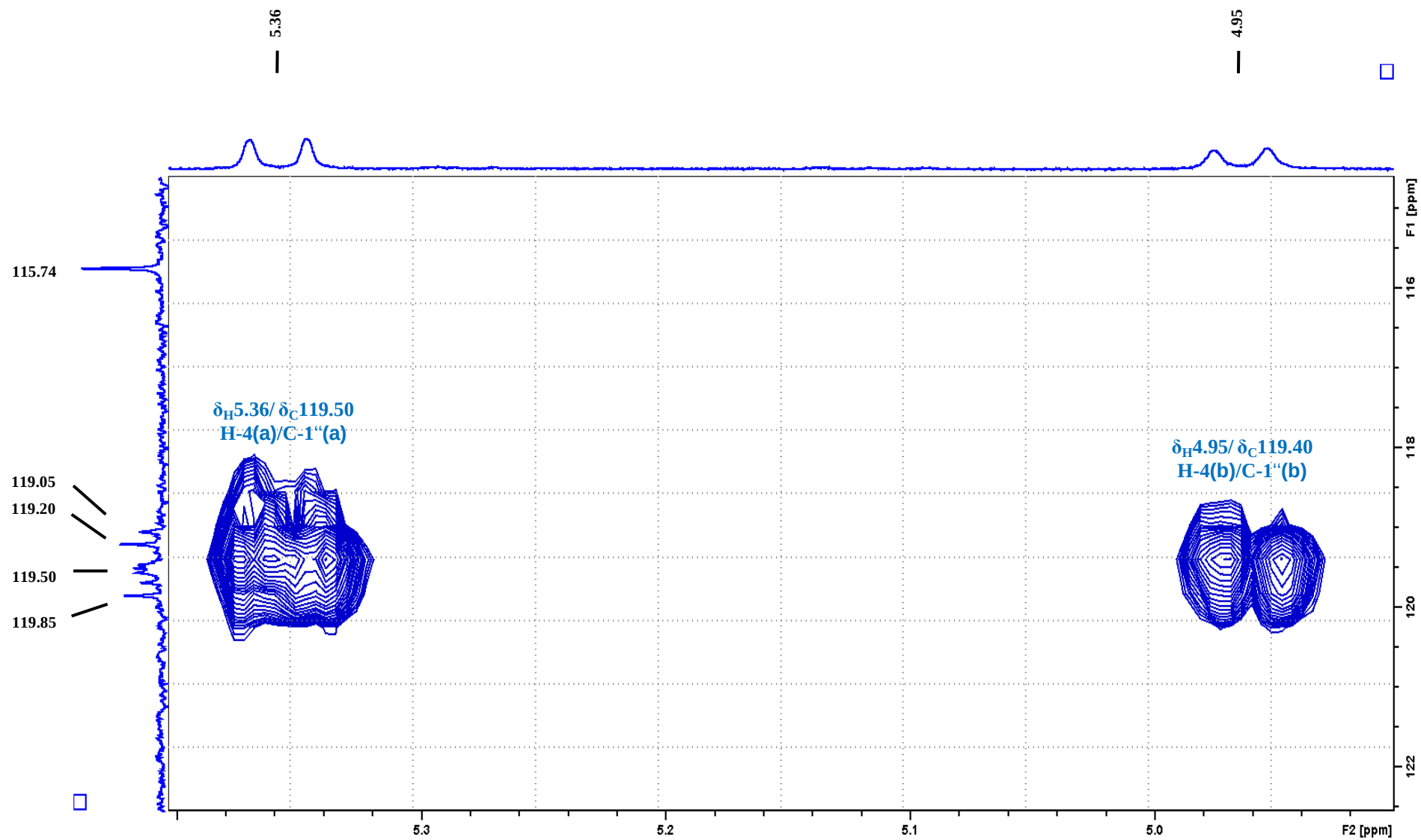


Figure S43. HMBC spectrum of compounds **1a** and **1b** (enlarged).

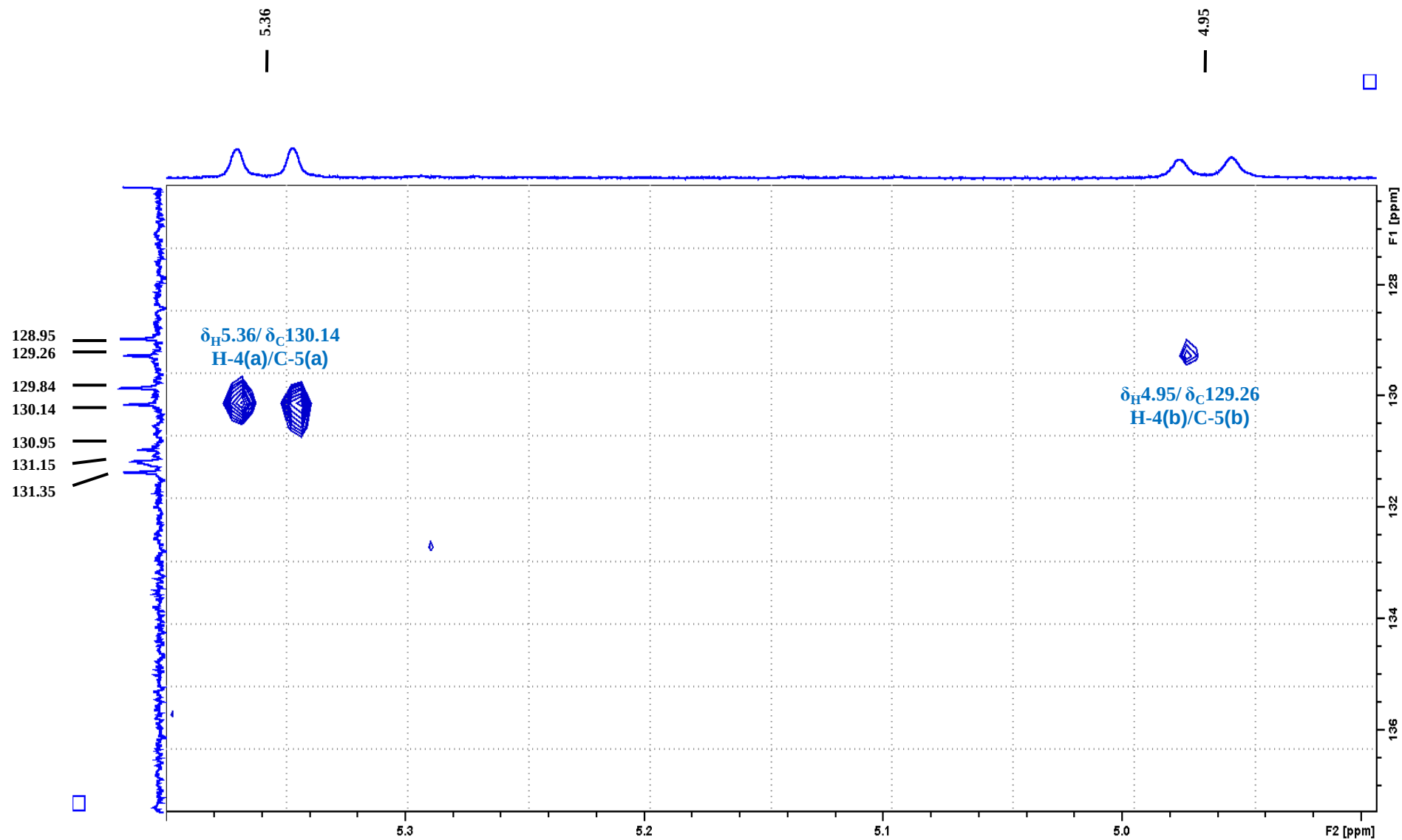


Figure S44. HMBC spectrum of compounds **1a** and **1b** (enlarged).

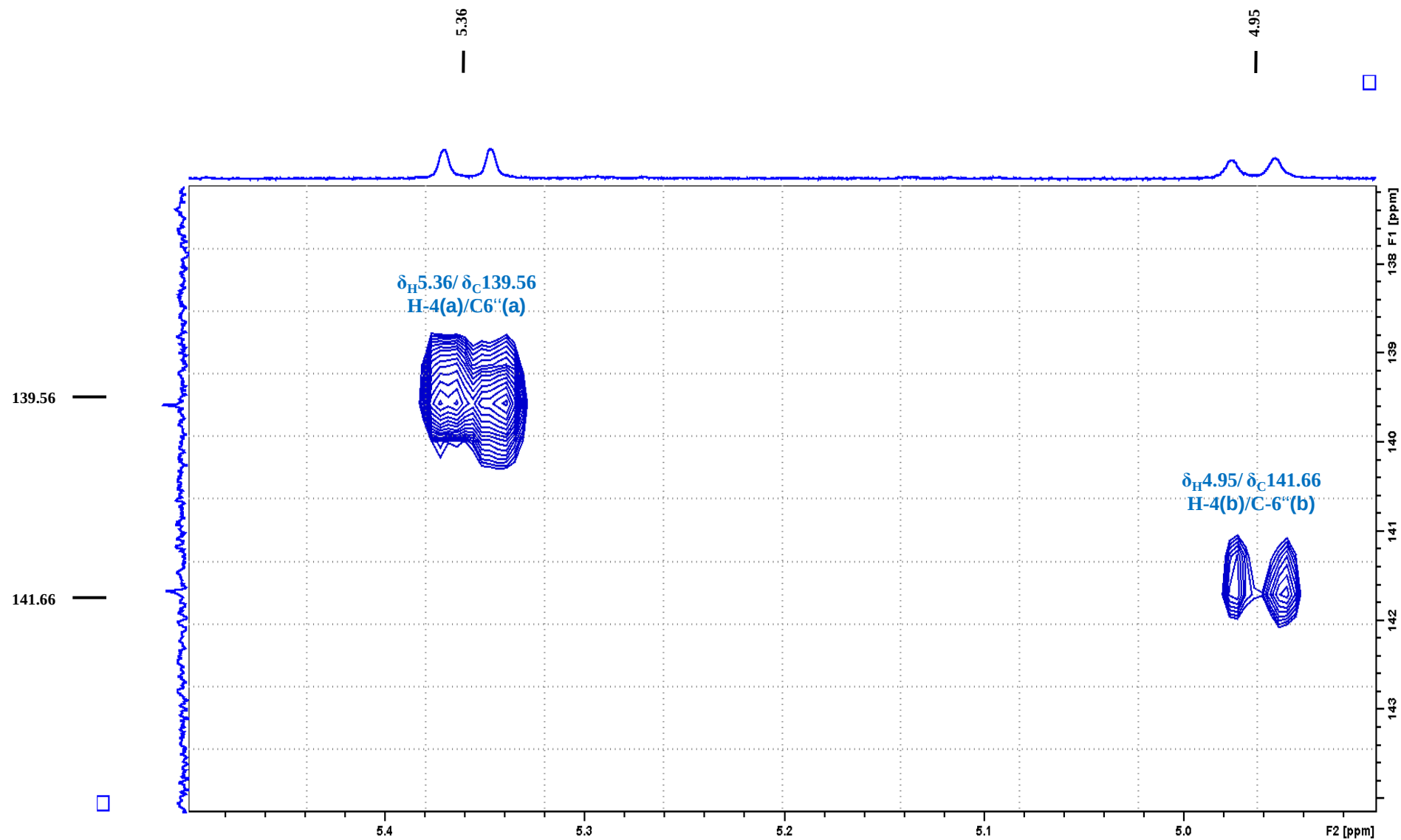


Figure S45. HMBC spectrum of compounds **1a** and **1b** (enlarged).

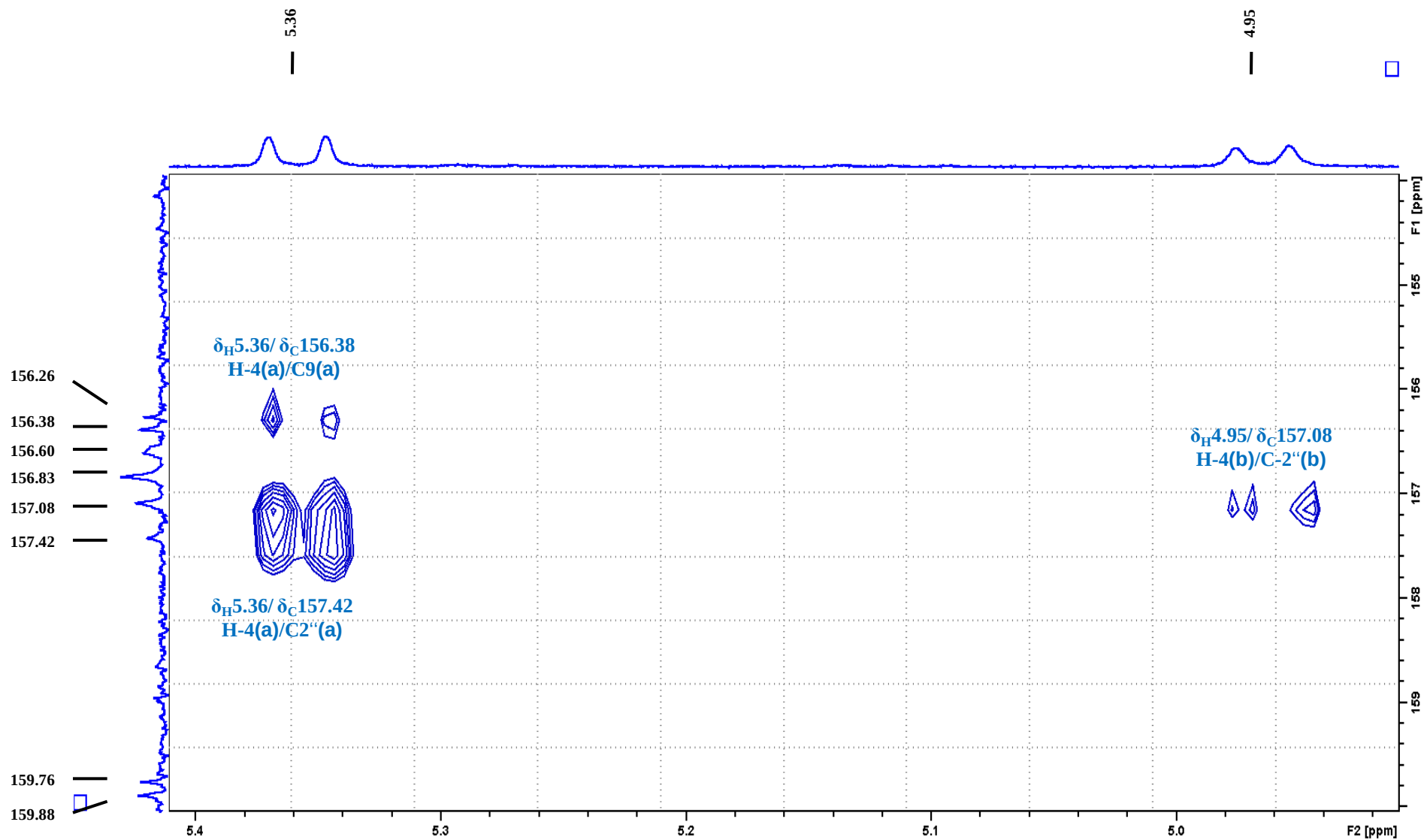


Figure S46. HMBC spectrum of compounds **1a** and **1b** (enlarged).

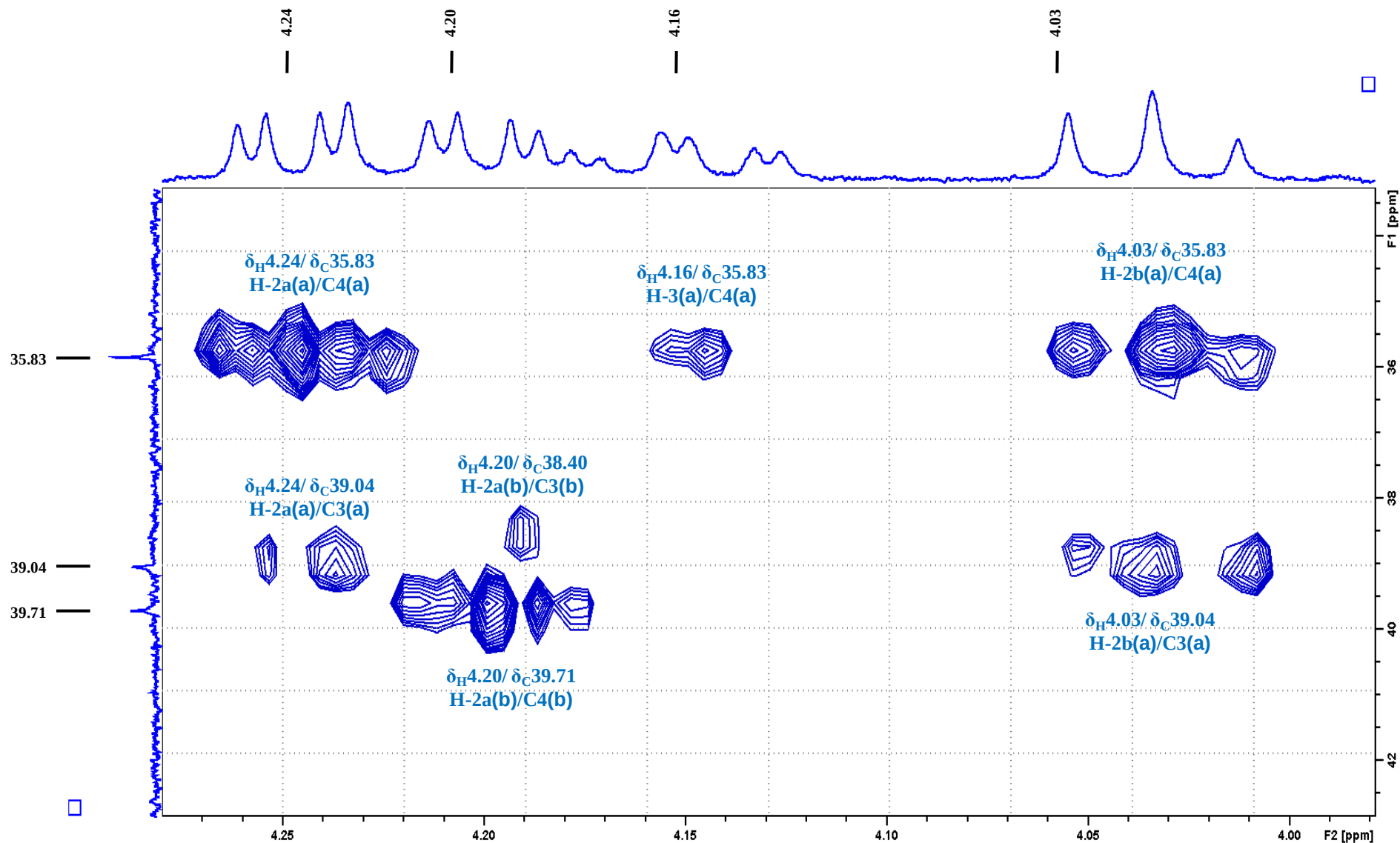


Figure S47. HMBC spectrum of compounds **1a** and **1b** (enlarged).

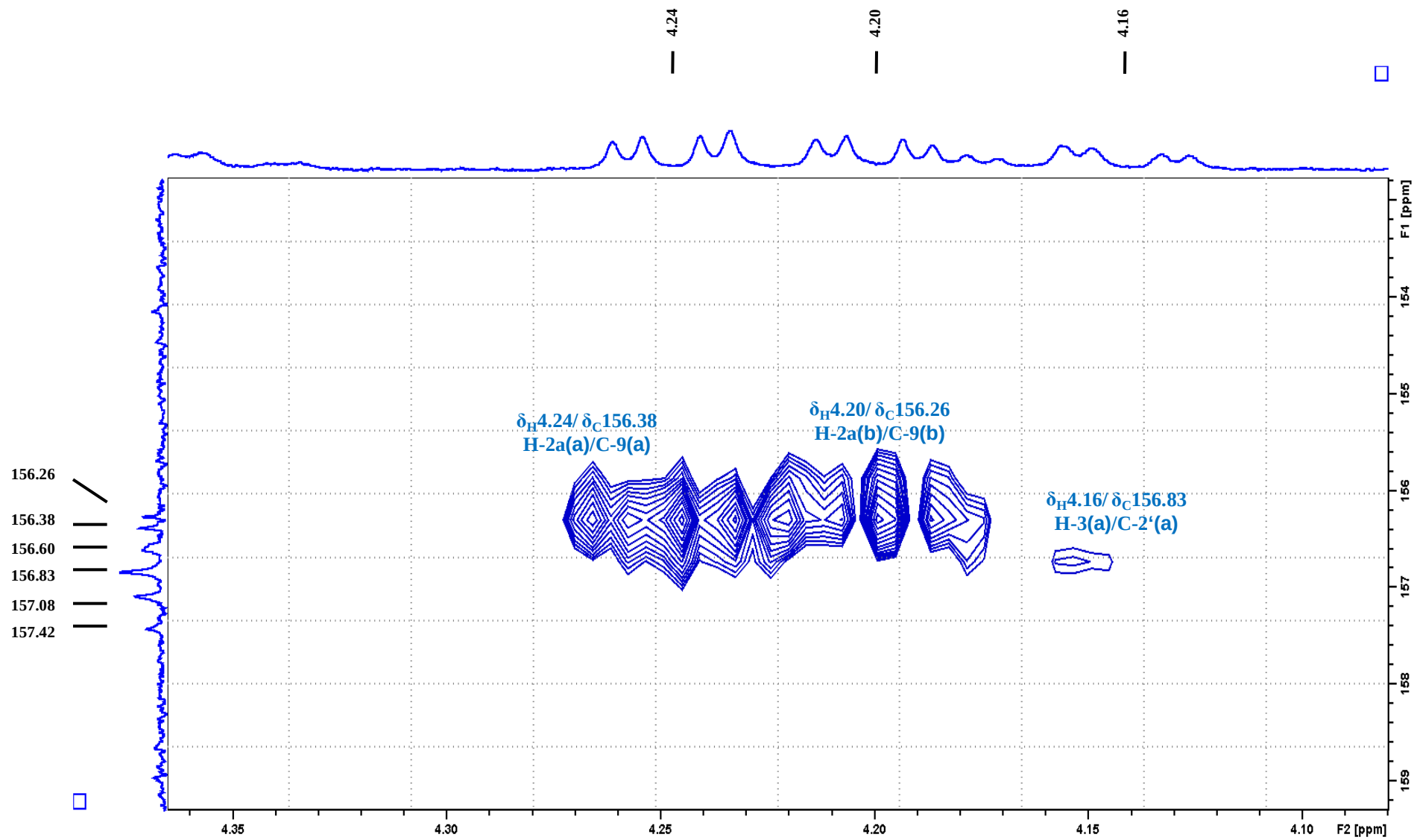


Figure S48. HMBC spectrum of compounds **1a** and **1b** (enlarged).

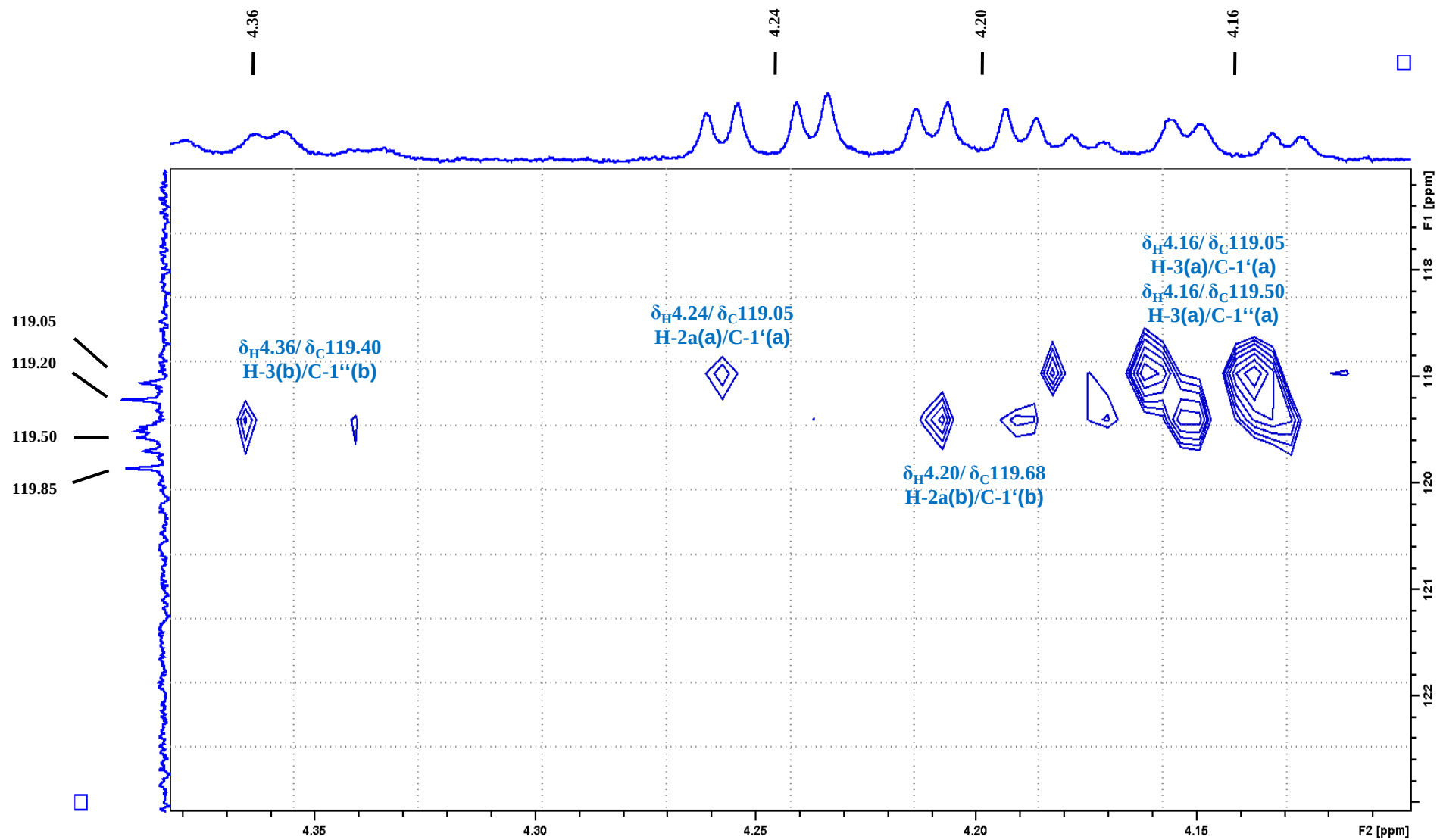


Figure S49. HMBC spectrum of compounds **1a** and **1b** (enlarged).

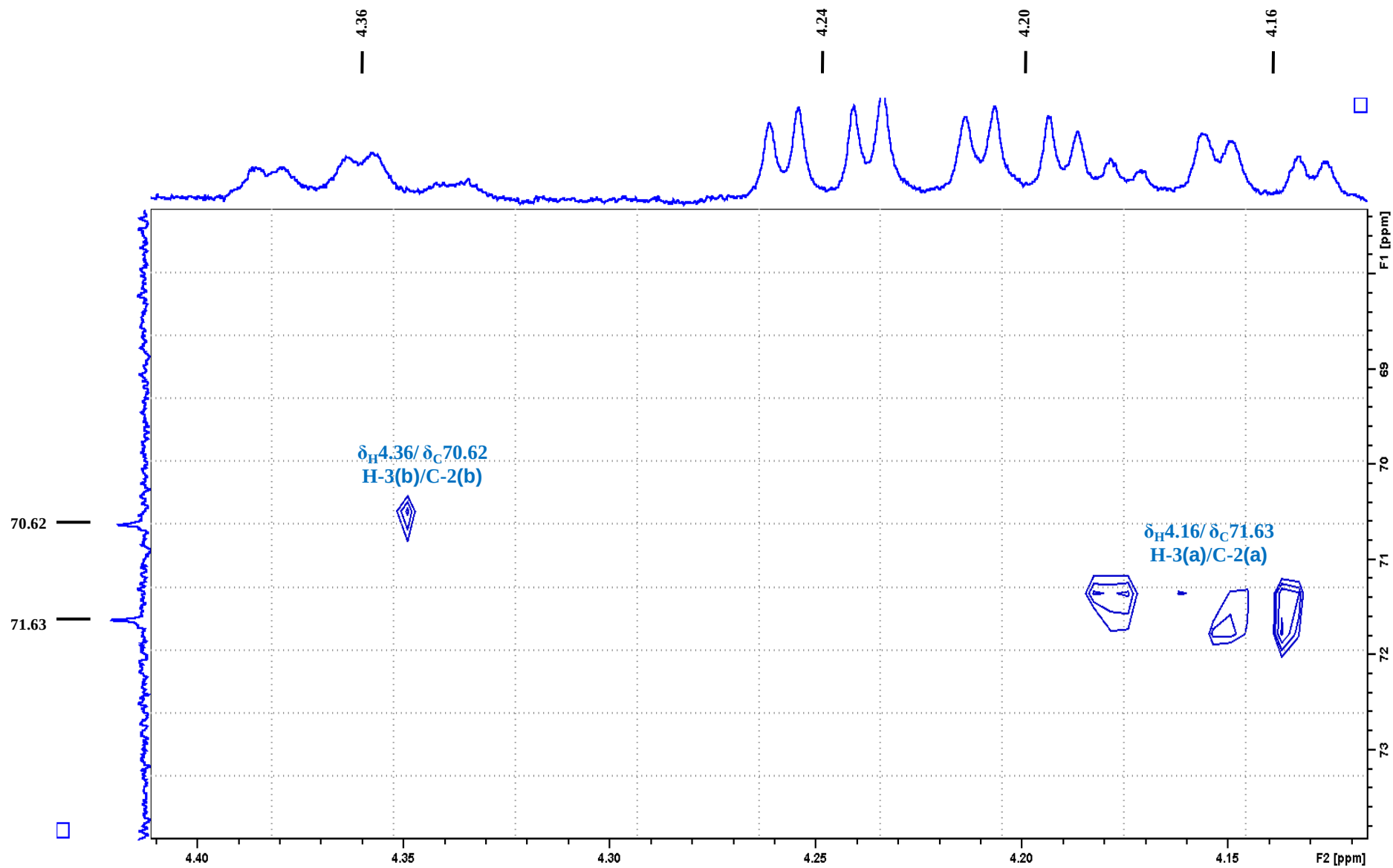


Figure S50. HMBC spectrum of compounds **1a** and **1b** (enlarged).

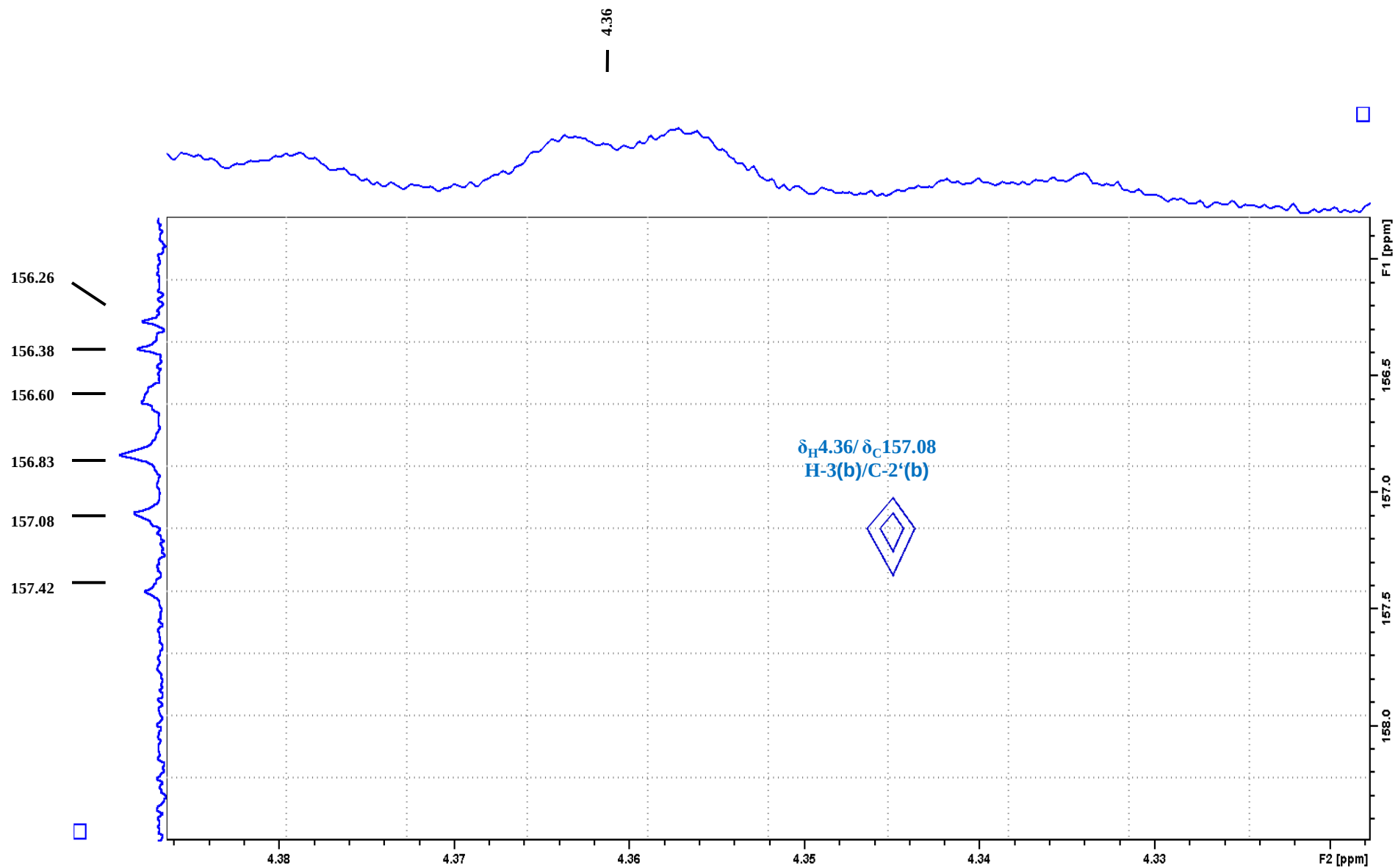


Figure S51. HMBC spectrum of compounds **1a** and **1b** (enlarged).

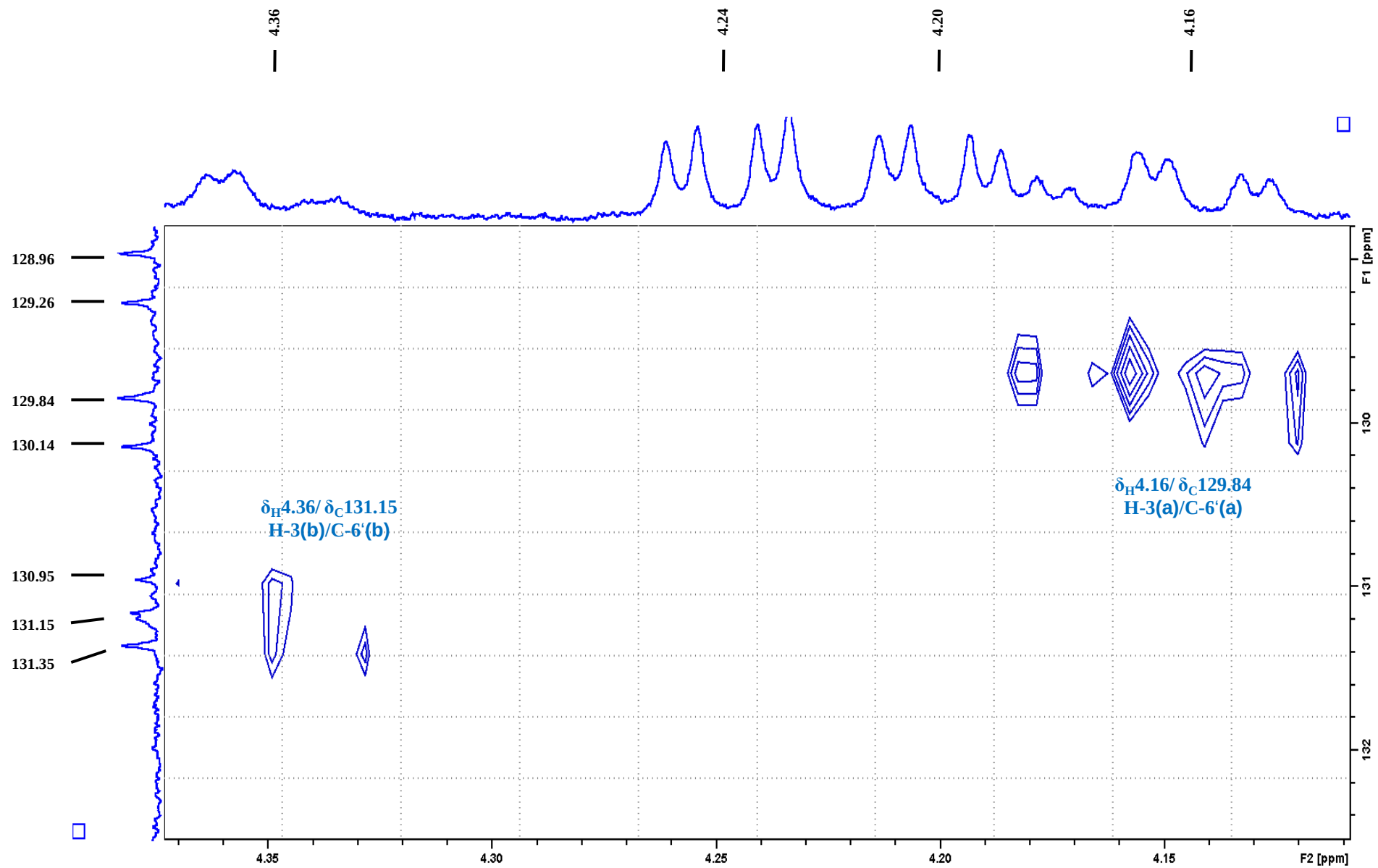


Figure S52. HMBC spectrum of compounds **1a** and **1b** (enlarged).

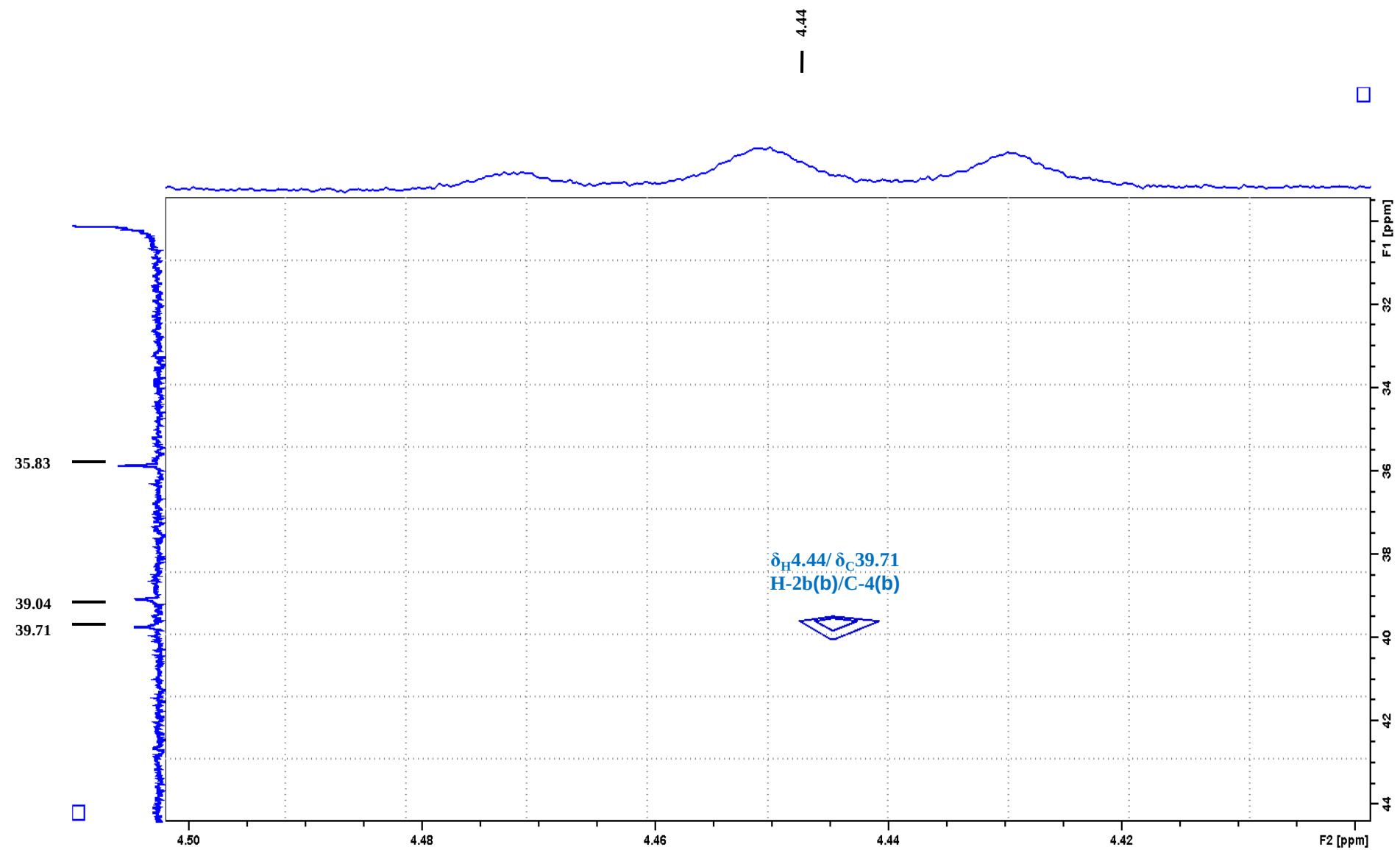


Figure S53. HMBC spectrum of compounds **1a** and **1b** (enlarged).

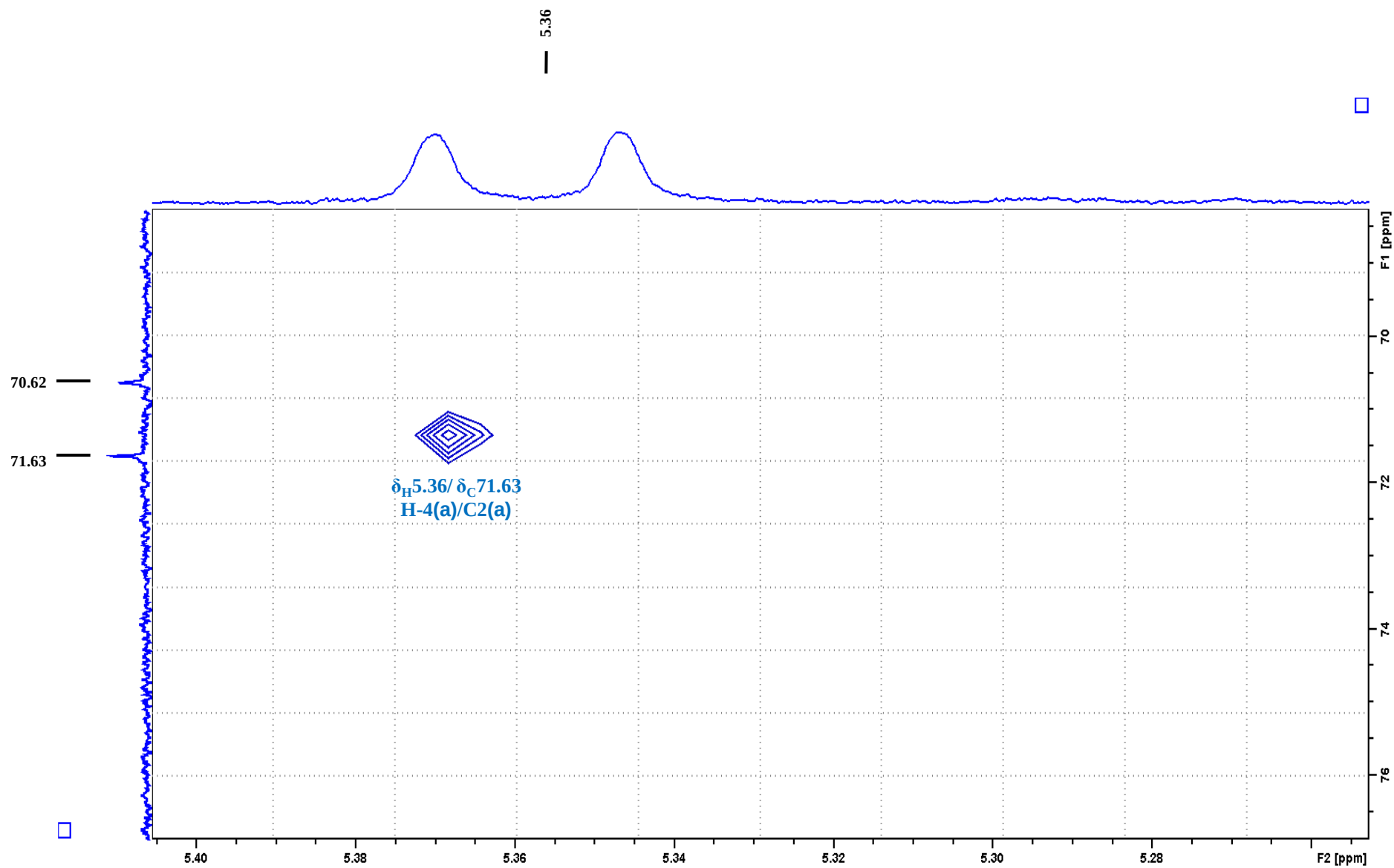


Figure S54. HMBC spectrum of compounds **1a** and **1b** (enlarged).

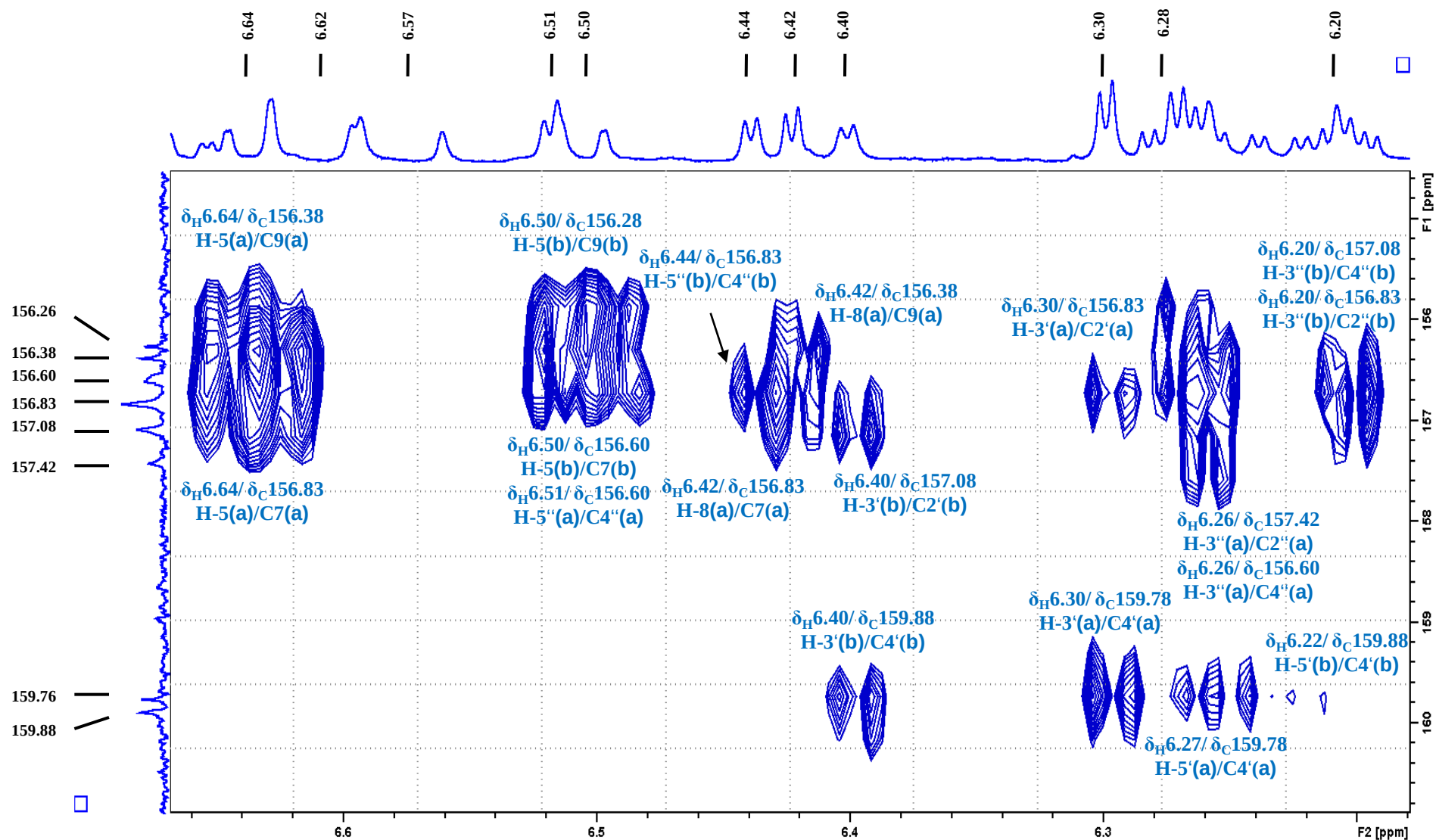


Figure S55. HMBC spectrum of compounds **1a** and **1b** (enlarged).

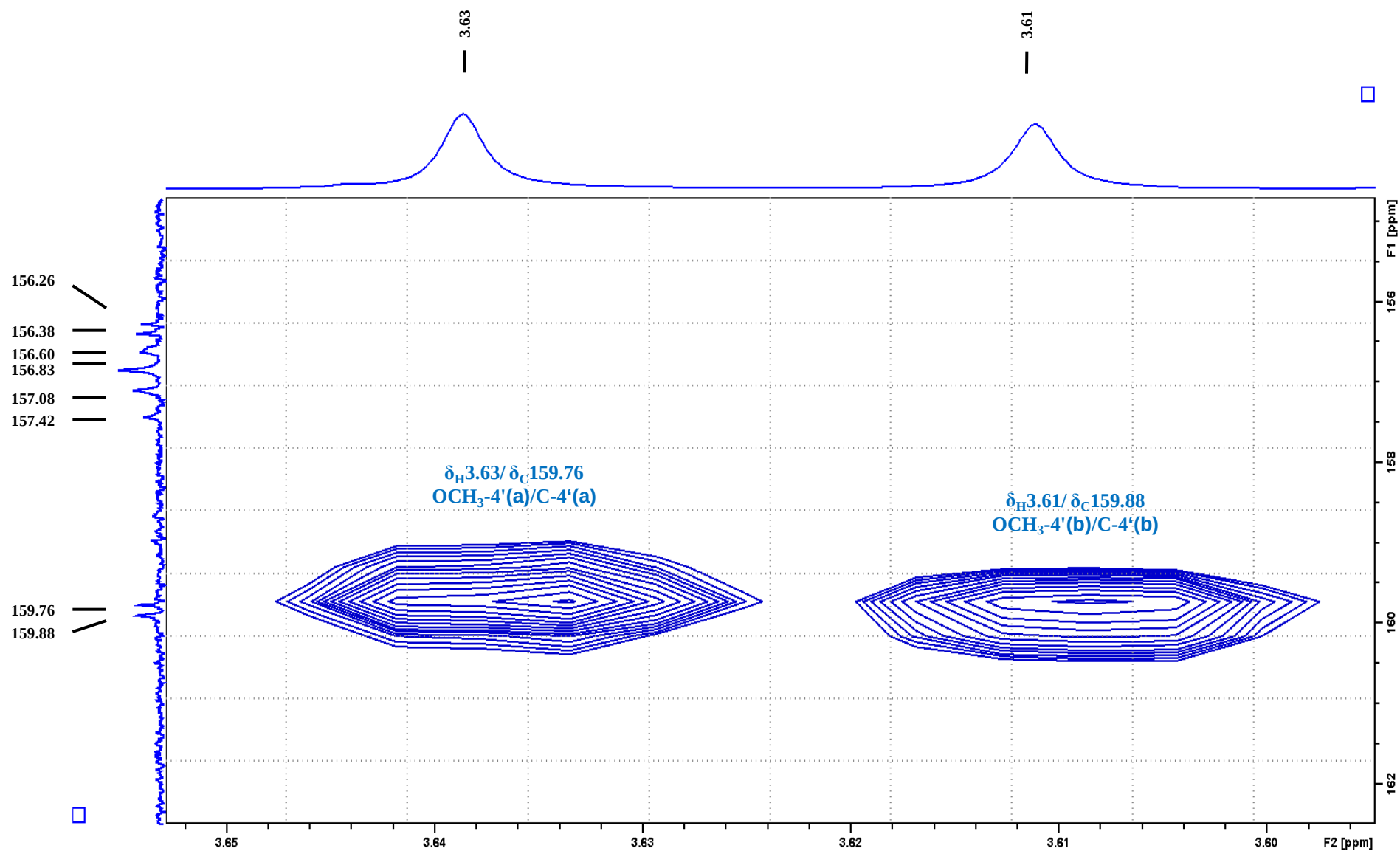


Figure S56. HMBC spectrum of compounds **1a** and **1b** (enlarged).

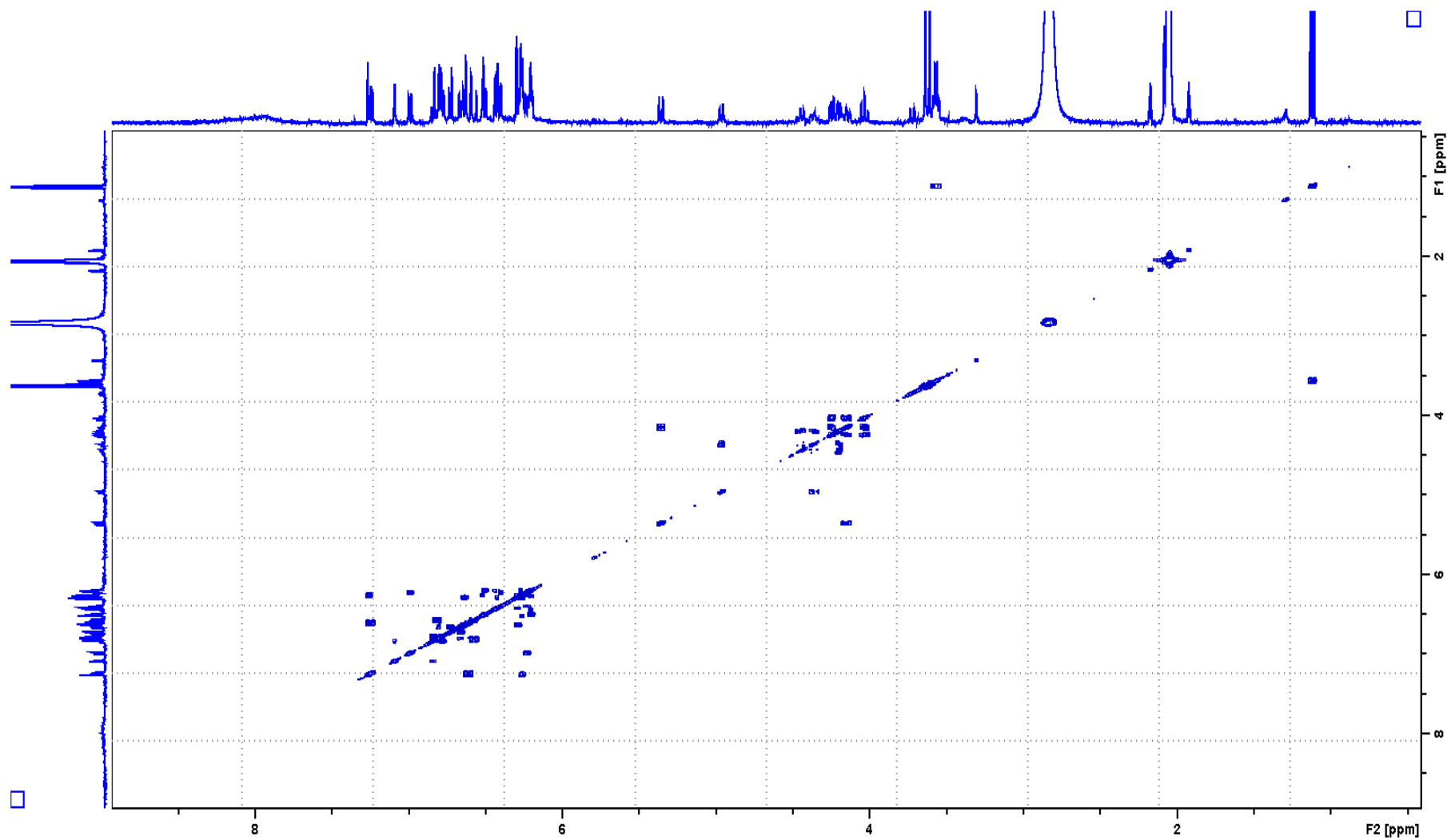


Figure S57. COSY spectrum of compounds **1a** and **1b**.

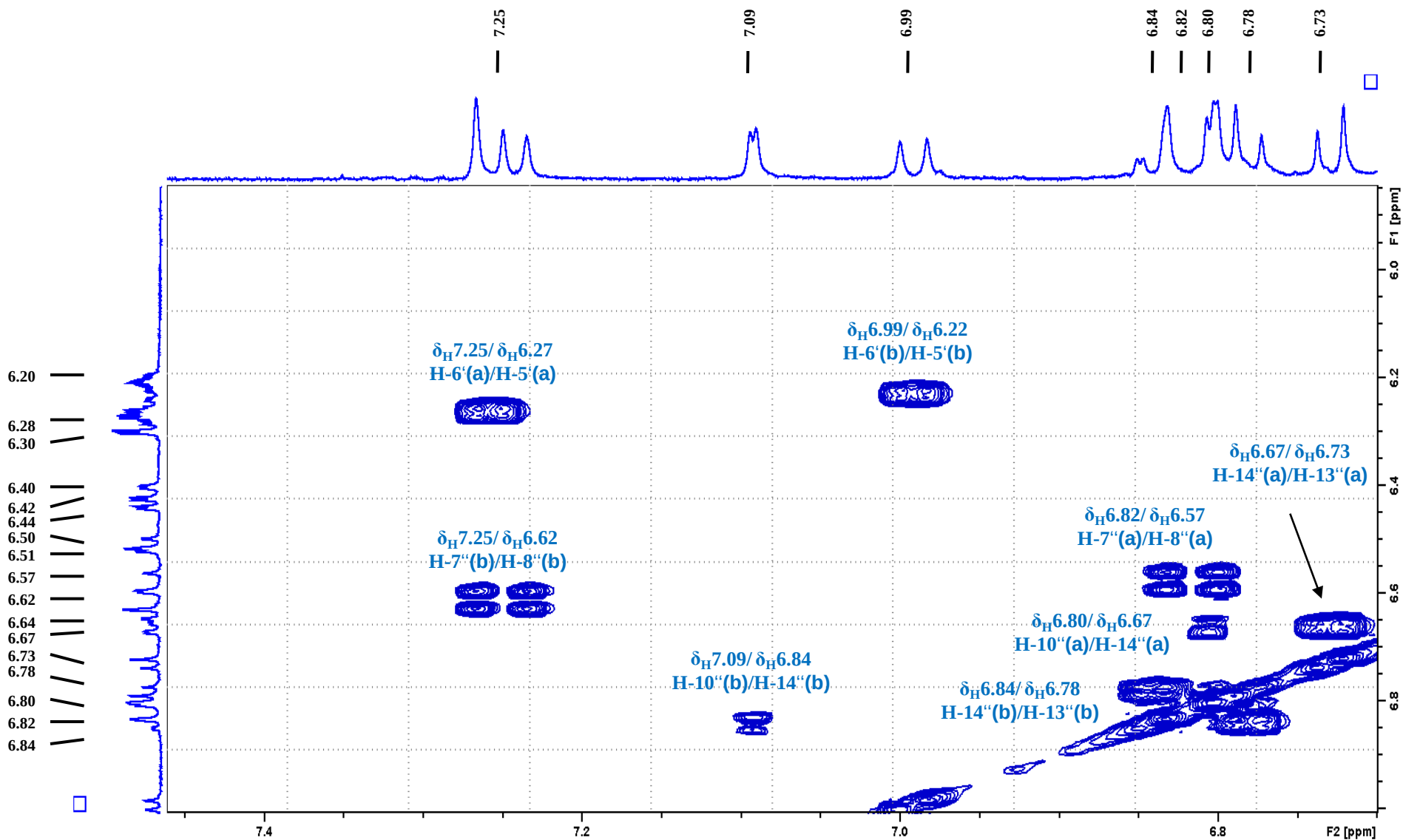


Figure S58. COSY spectrum of compounds **1a** and **1b** (enlarged).

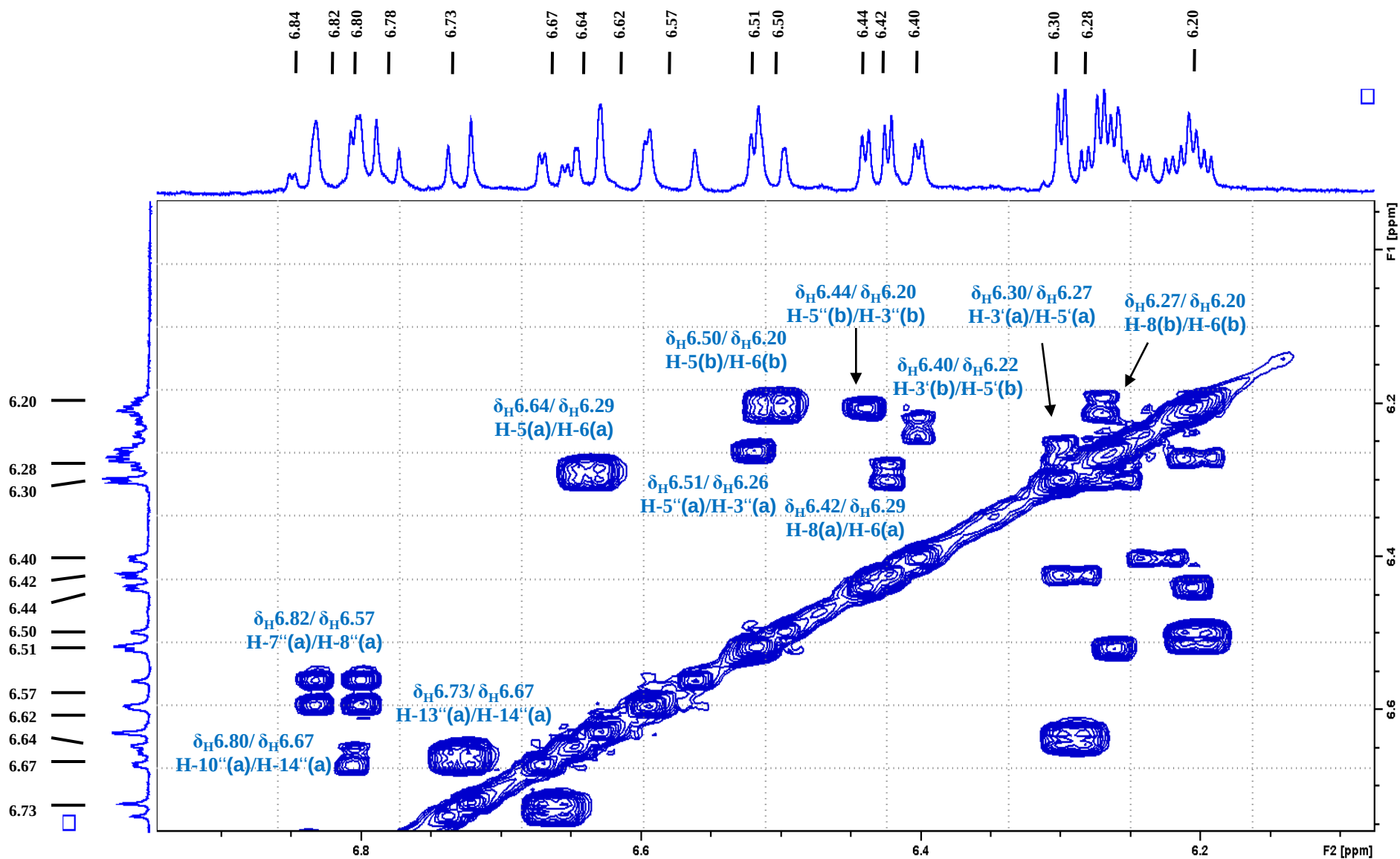


Figure S59. COSY spectrum of compounds **1a** and **1b** (enlarged).

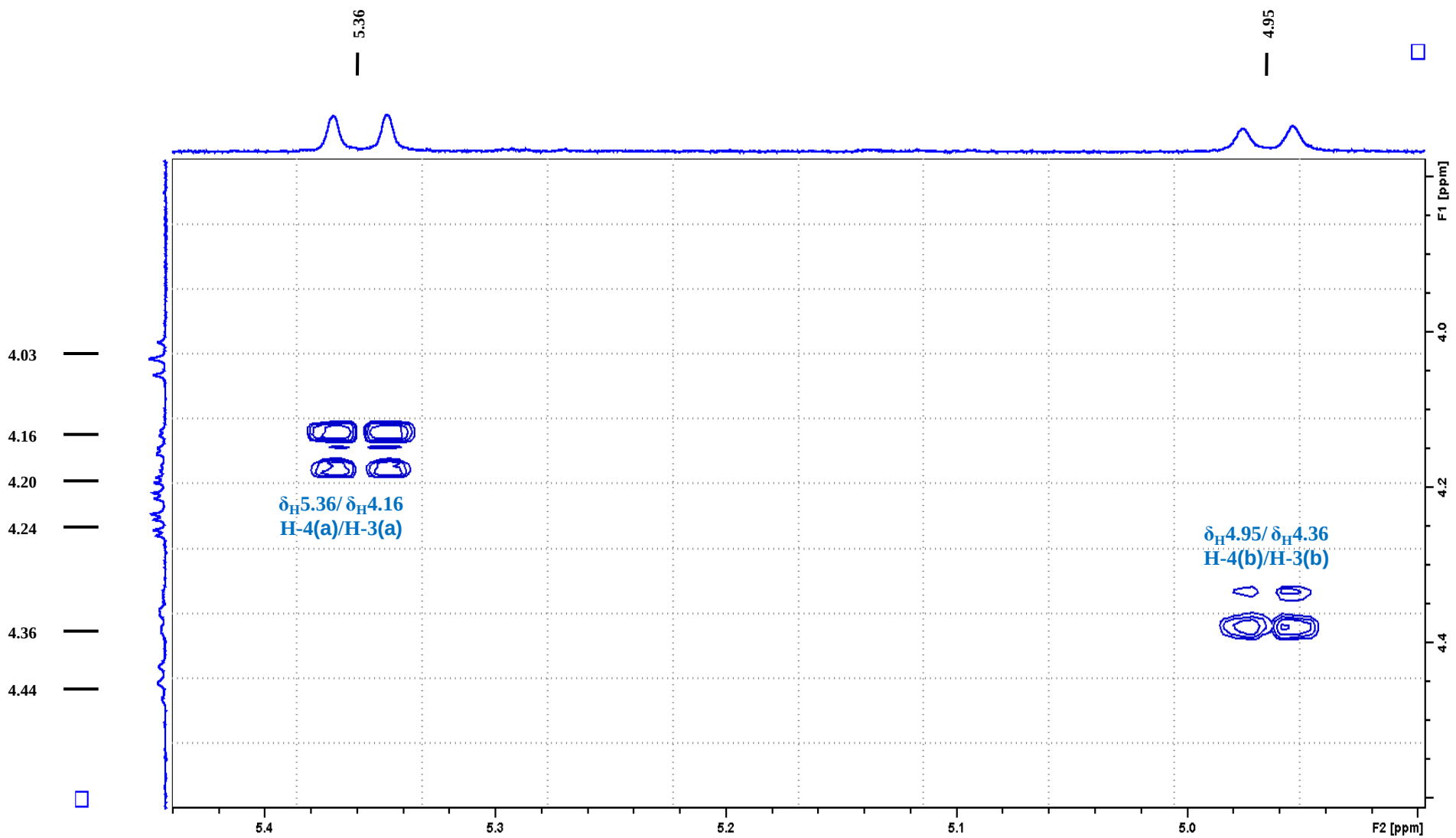


Figure S60. COSY spectrum of compounds **1a** and **1b** (enlarged).

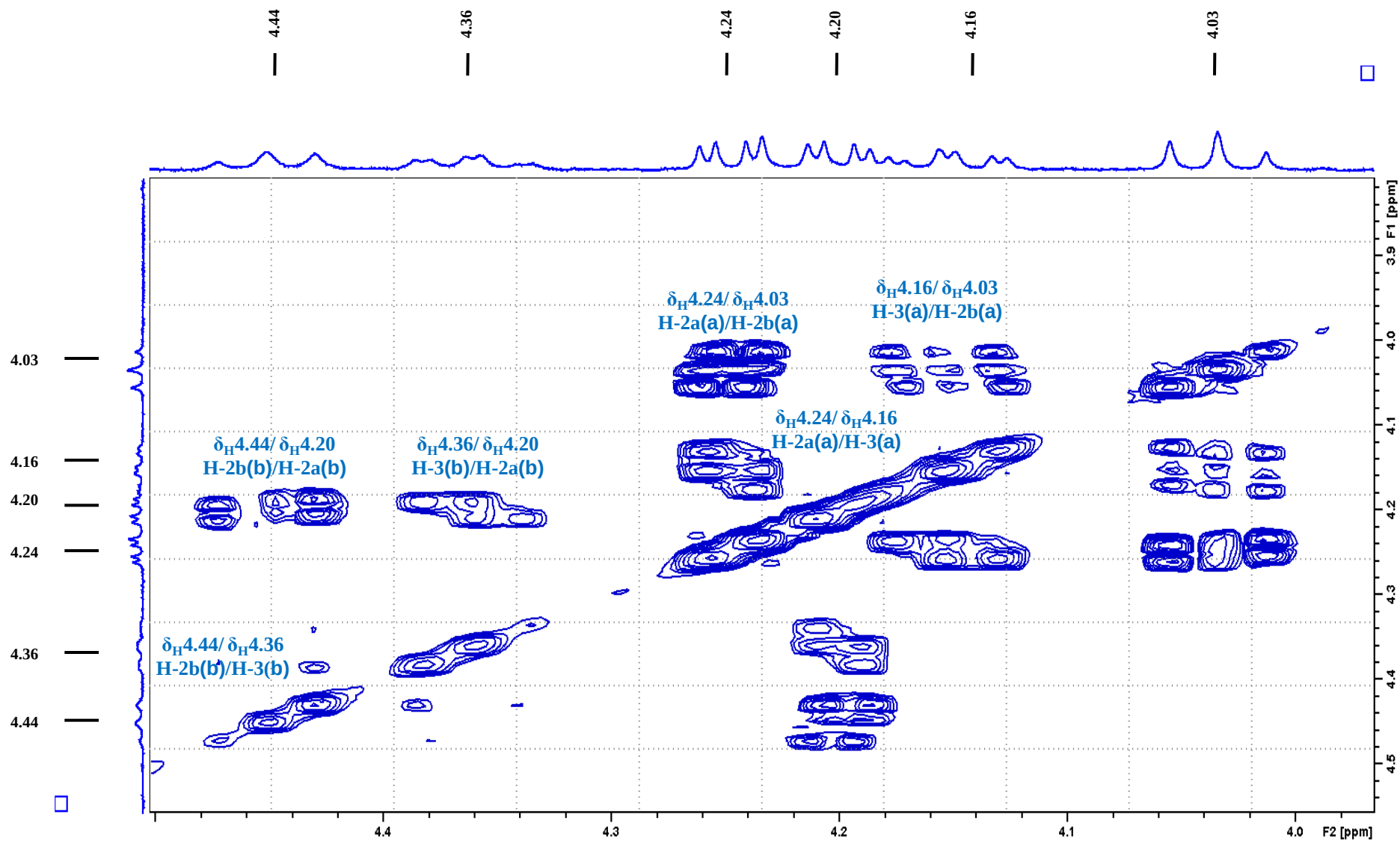


Figure S61. COSY spectrum of compounds **1a** and **1b** (enlarged).

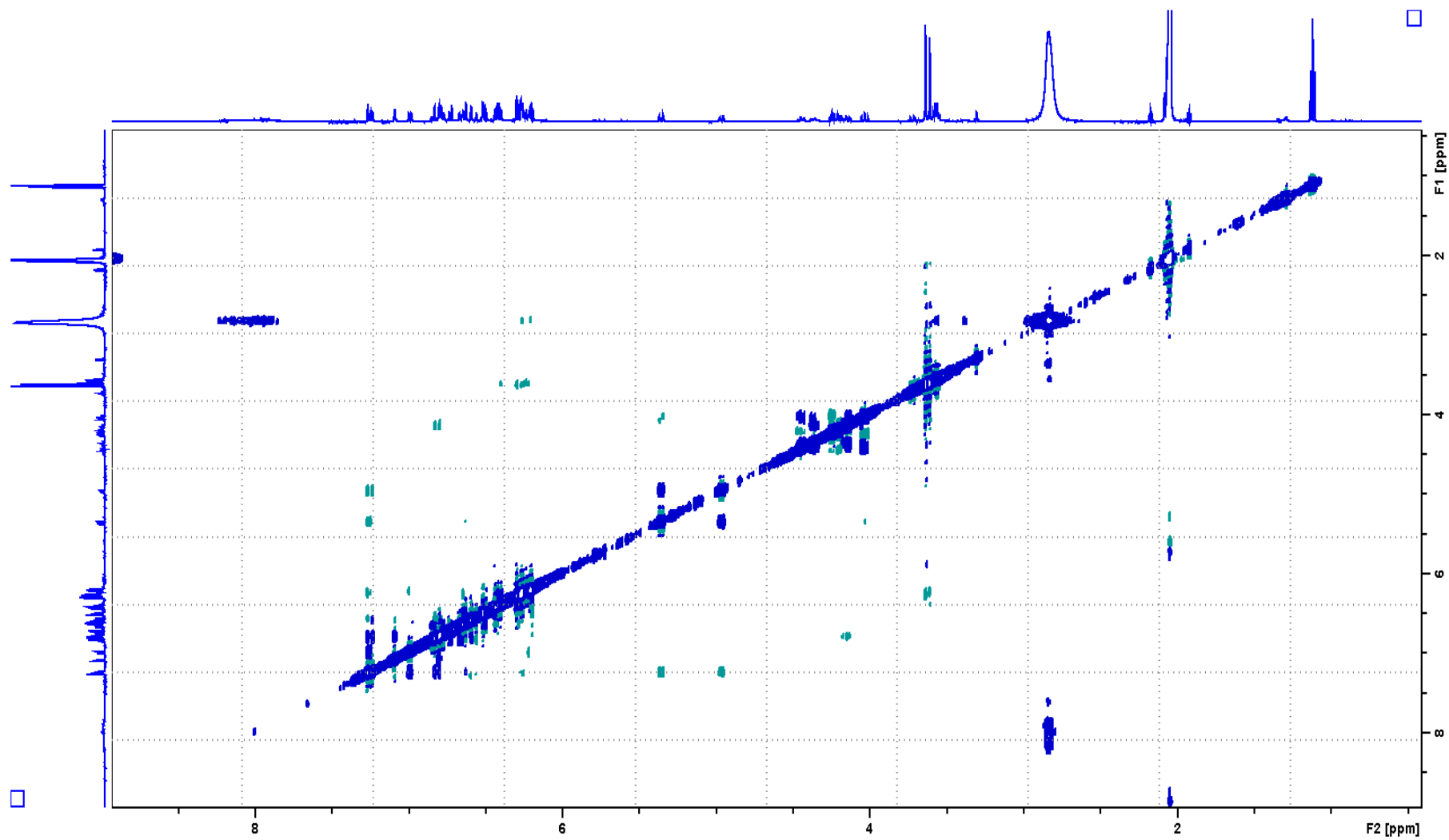


Figure S62. ROESY spectrum of compounds **1a** and **1b**.

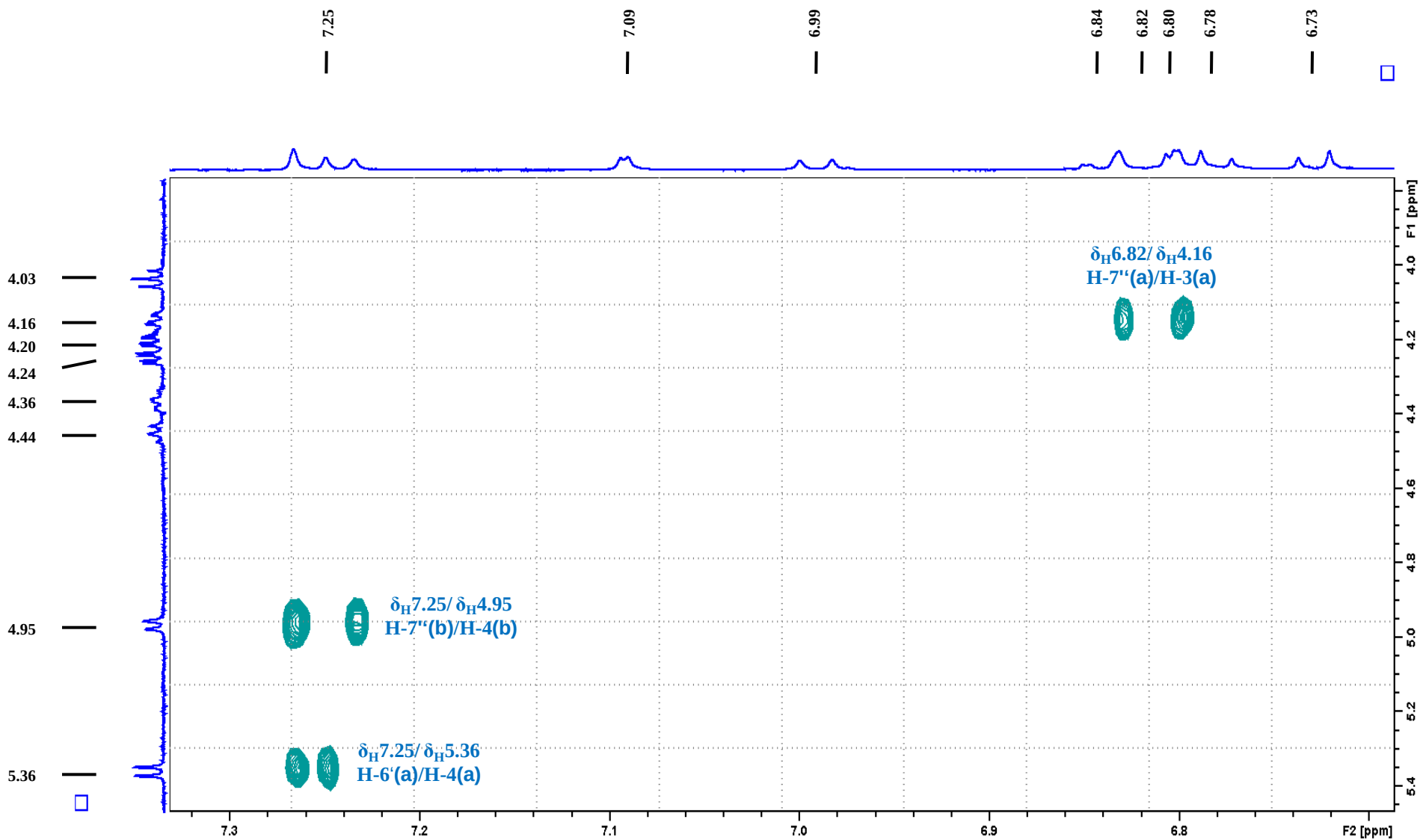


Figure S63. ROESY spectrum of compounds **1a** and **1b** (enlarged).

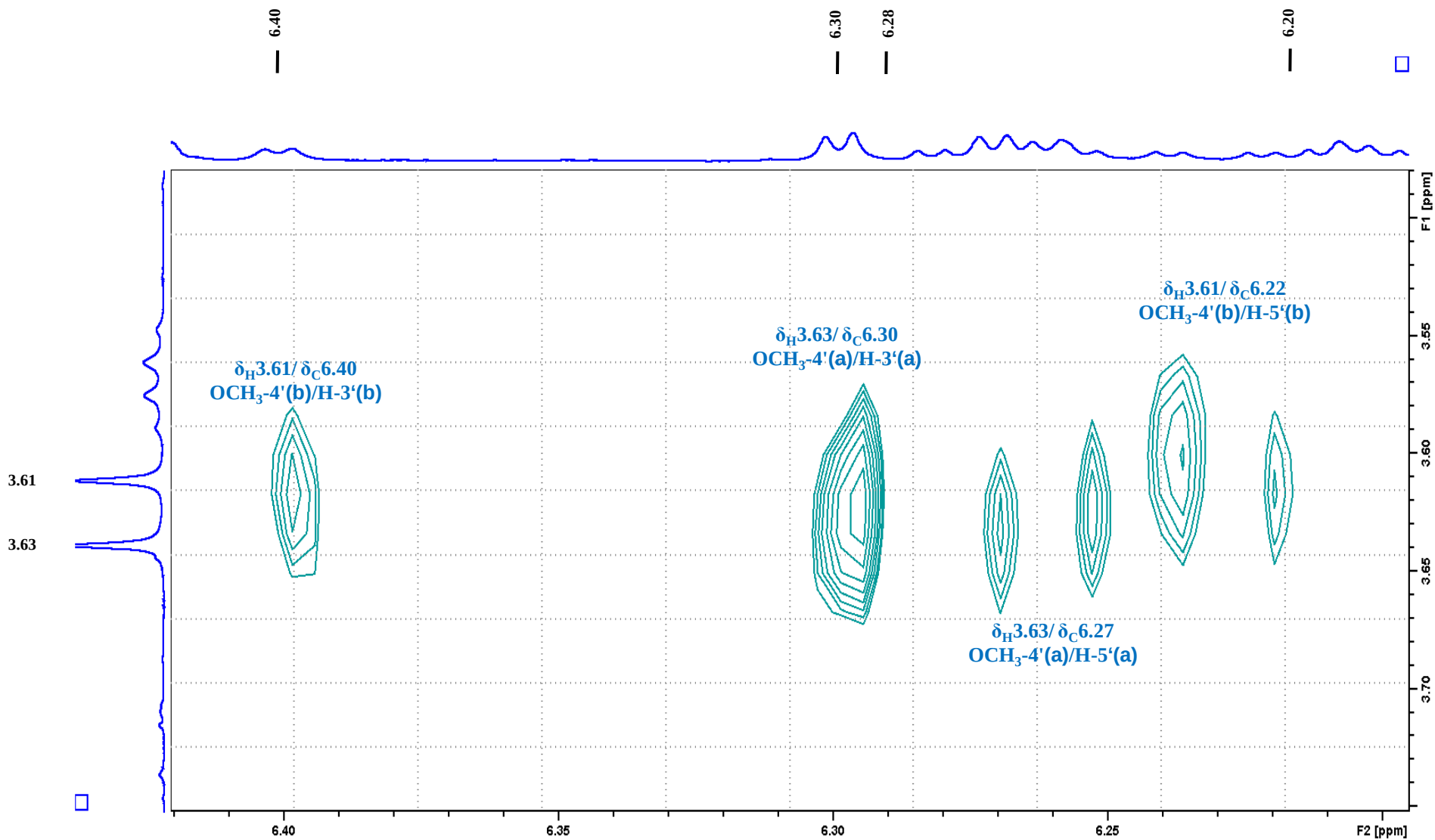


Figure S64. ROESY spectrum of compounds **1a** and **1b** (enlarged).

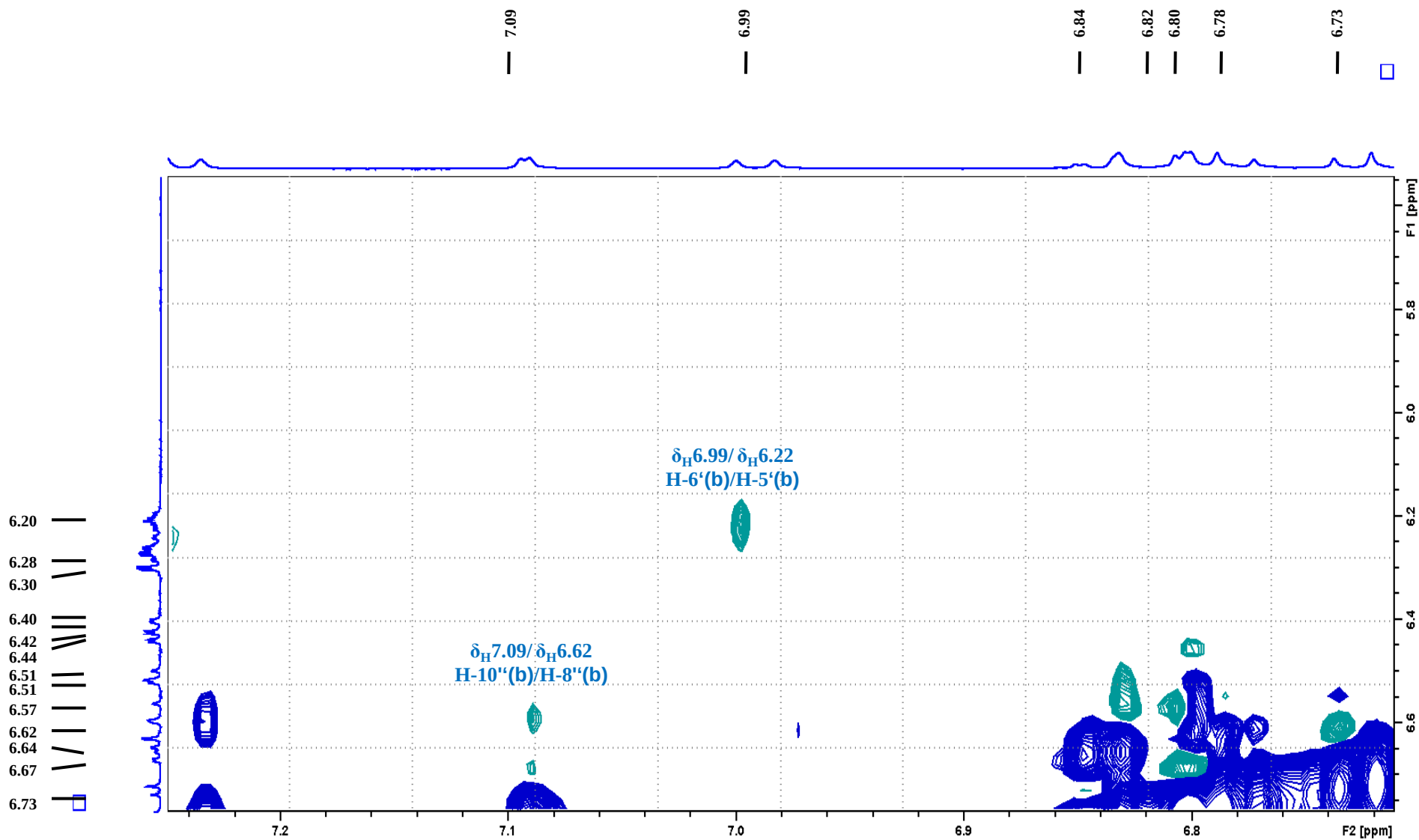


Figure S65. ROESY spectrum of compounds **1a** and **1b** (enlarged).

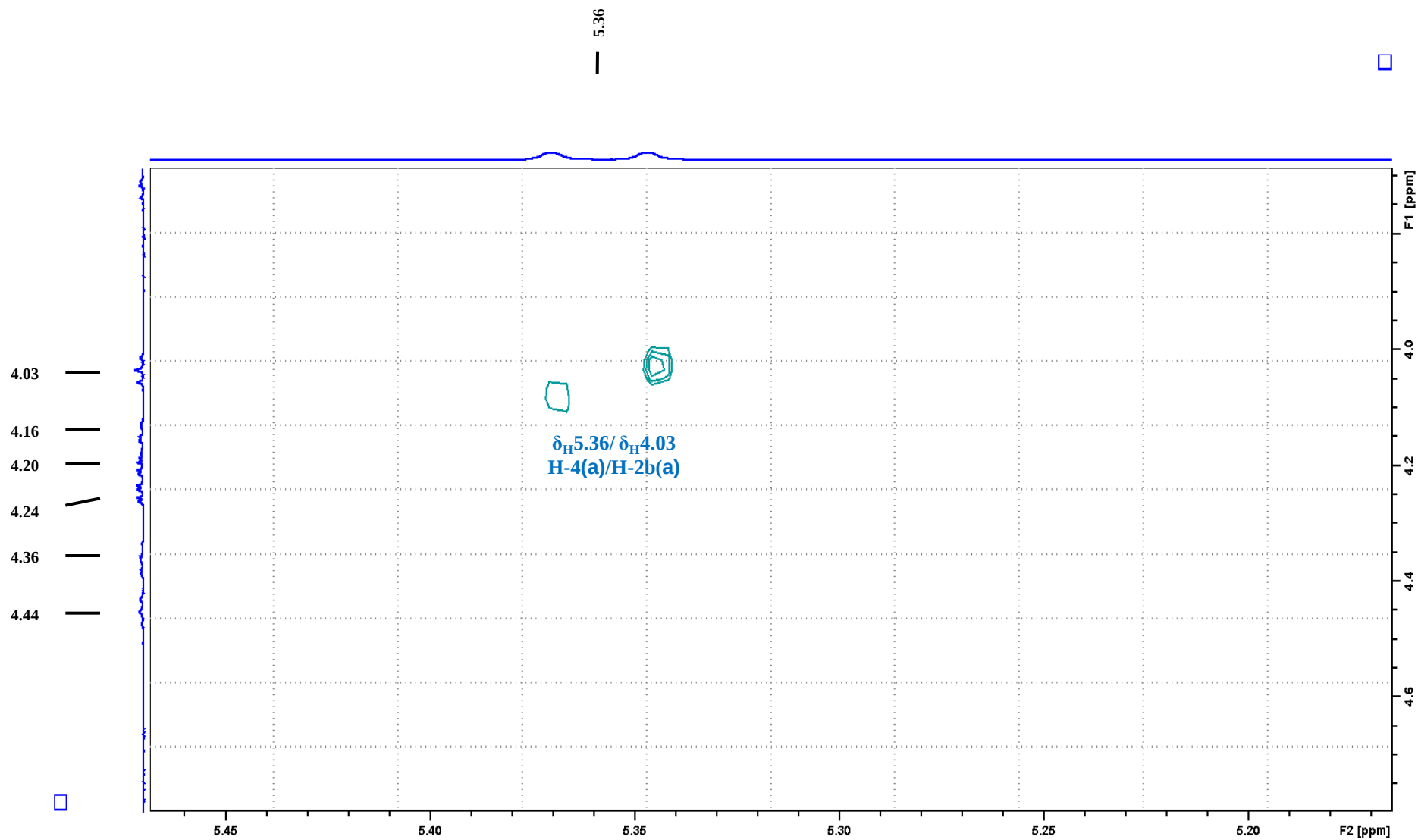


Figure S66. ROESY spectrum of compounds **1a** and **1b** (enlarged).

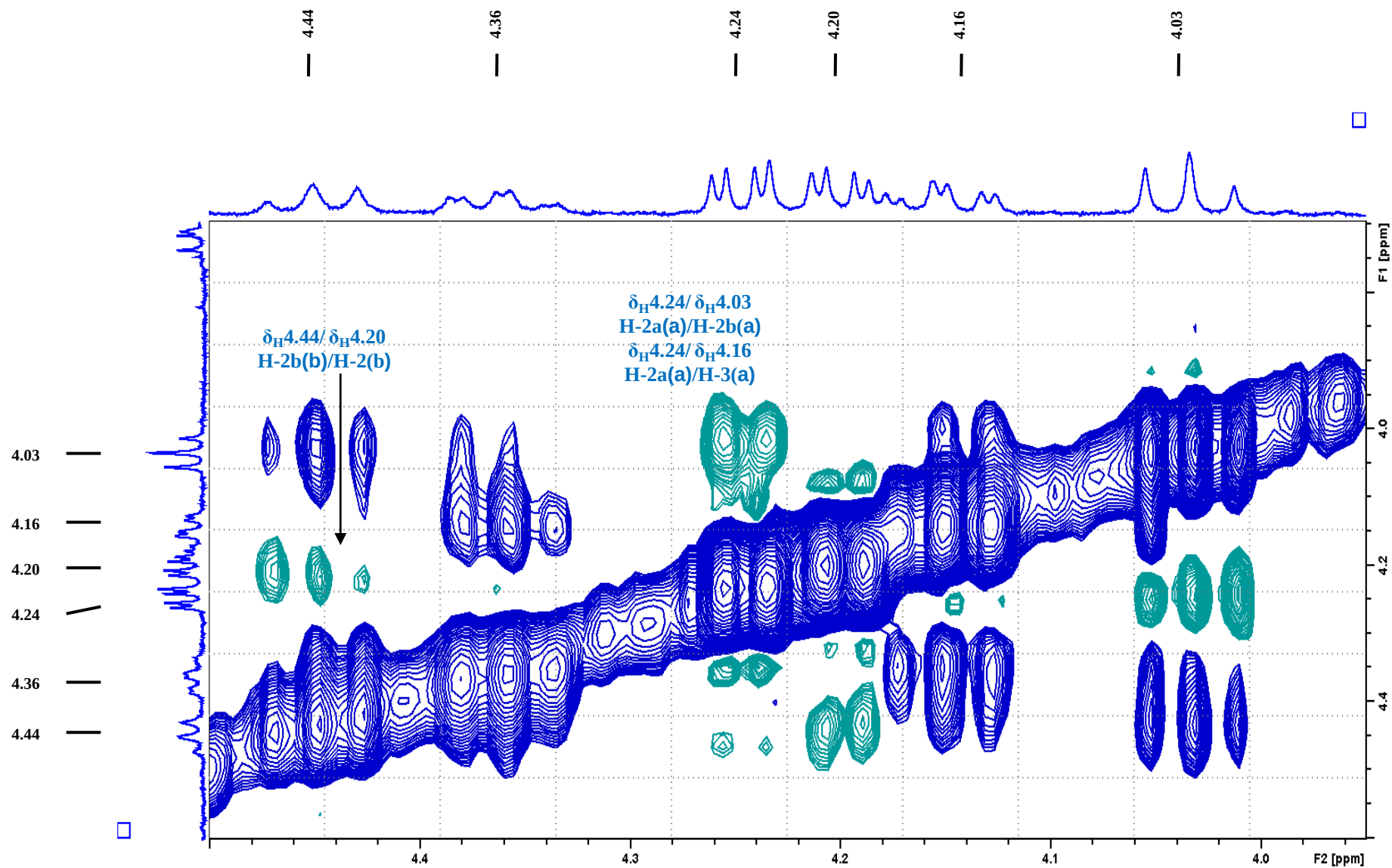


Figure S67. ROESY spectrum of compounds **1a** and **1b** (enlarged).

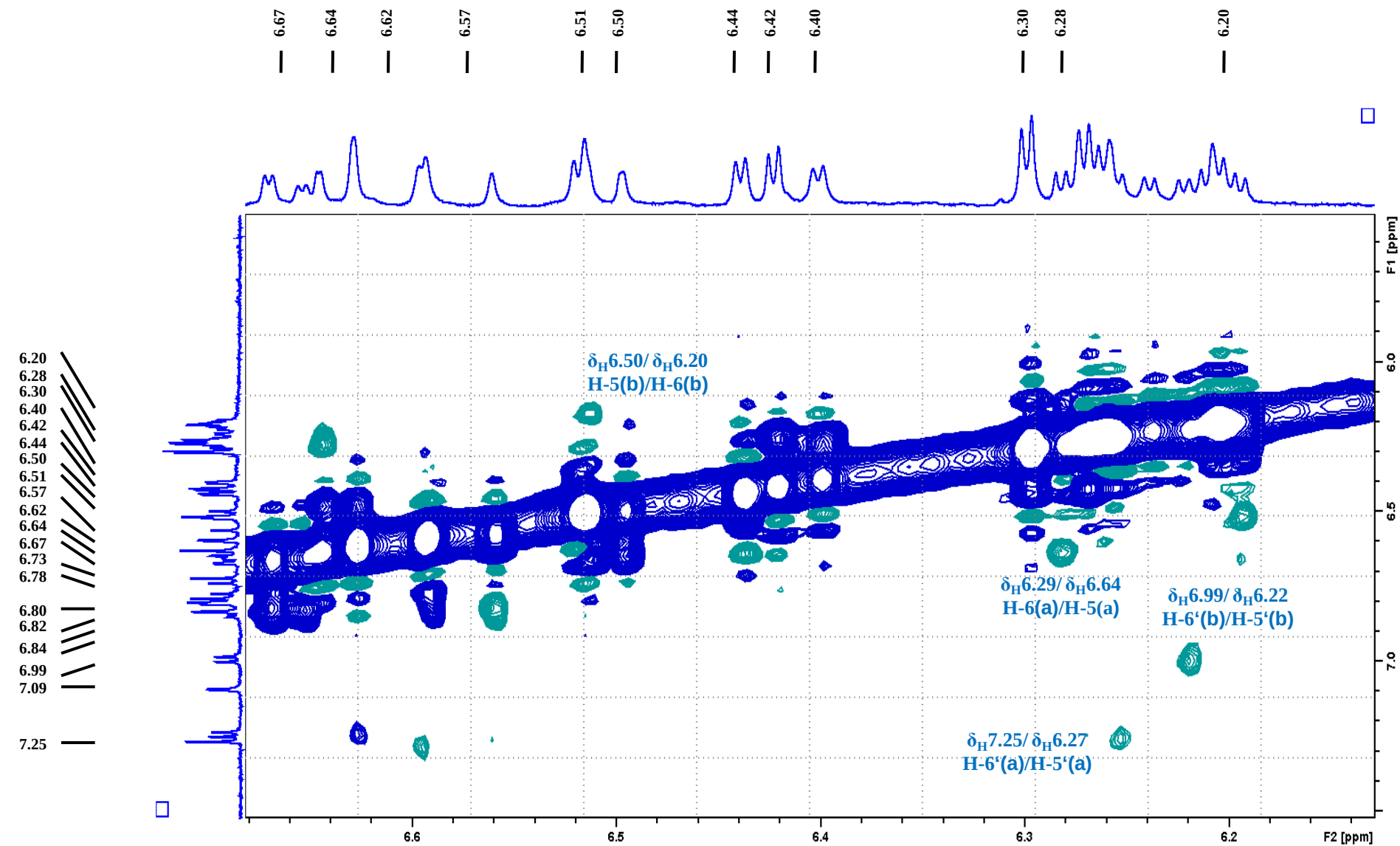


Figure S68. ROESY spectrum of compounds **1a** and **1b** (enlarged).

Compounds	Concentration μg/ml	Ct	-ΔCt	2 ^{-ΔCt}	log ₁₀
Maksar®	50	30,0±3,3	-13,9±1,7	0,0000654	-4,18
	5	20,6±2,5	-4,5±0,5	0,0441942	-1,35
1	50	30,0±3,3	-13,9±1,6	0,0000654	-4,18
	5	20,4±2,4	-4,3±0,5	0,0507657	-1,29
2	50	30,0±3,0	-13,9±1,6	0,0000654	-4,18
	5	19,2±2,3	-3,1±0,4	0,1166300	-0,93
3	50	30,0±3,0	-13,9±1,7	0,0000654	-4,18
	5	19,7±2,4	-3,6±0,4	0,0824692	-1,08
4	50	30,0±3,1	-13,9±1,6	0,0000654	-4,18
	5	20,5±2,4	-4,4±0,5	0,0473661	-1,32
5	50	27,6±3,3	-11,5±1,4	0,0003452	-3,46
	5	18,7±2,2	-2,6±0,3	0,1649384	-0,78
6	50	23,6±2,6	-7,5±0,9	0,0055242	-2,26
	5	19,3±2,1	-3,2±0,4	0,1088188	-0,96
Virus control (DMSO)		16,1±1,9	0	1,0	
Cell control (DMSO)		31,0±3,5			

Table S69. Anti-HSV-1 activity of polyphenolic compounds from *M. amurensis* (RT-PCR).

Ct - cycle threshold in real-time PCR; ΔCt - the difference between Ct value for infected cells treated with polyphenolic compounds and Ct value for the virus control. Values are presented as means ± standard deviations of three independent experiments.

S70. Quantum-chemical modeling

The quantum-chemical calculations for **1** in CH₃OH were performed using density functional theory (DFT) with B3LYP exchange-correlation functional and the polarization continuum model (PCM), implemented in the Gaussian 16 package of programs [35]. The conformational analysis was performed with B3LYP/6-311G(d)_PCM level of theory. The statistical weights (g_{im}) of different conformations were obtained using equation SE1:

$$g_{im} = \frac{e^{-\Delta G_{im} / RT}}{\sum_i e^{-\Delta G_{im} / RT}} \quad (\text{SE1})$$

where the summation was done over stable conformations of **1** with $\Delta G_{im} \leq 5$ kcal/mol; (the subscript “m” denotes conformation with minimal G.

The excitation energies and the rotatory strengths were calculated using time-dependent density functional theory (TDDFT). Each individual transition from electronic ground state to the i -th calculated excited electronic state ($1 \leq i \leq 50$) was simulated as a Gauss-type function. The same values for the bandwidths at $1/e$ peak heights were used.

The total theoretical UV and ECD spectra were obtained after statistical averaging over all selected conformations (equations SE2 and SE3):

$$Absorbance_{calc}(\lambda) = \sum_i g_i \cdot Absorbance_{i,calc}(\lambda) \quad (\text{SE2})$$

$$\Delta\epsilon_{calc}(\lambda) = \sum_i g_i \cdot \Delta\epsilon_{i,calc}(\lambda) \quad (\text{SE3})$$

The scaled theoretical and experimental spectra were obtained using equation SE4:

$$F_{scaled}(\lambda) = \frac{F(\lambda)}{|F(\lambda_{peak})|} \quad (\text{SE4}),$$

where F is absorbance or $\Delta\epsilon$ and the denominator $|F(\lambda_{peak})|$ is a modulo of the peak value for the chosen characteristic band in corresponding spectrum.

The UV shifts $\Delta\lambda$ were obtained while improving the coincidence between calculated and experimental UV spectrum. This UV shift was then taken for simulation of theoretical ECD spectrum.

S71-83. Conformational analysis.

Many Large-Amplitude Motions (LAM) may proceed in compound **1**:

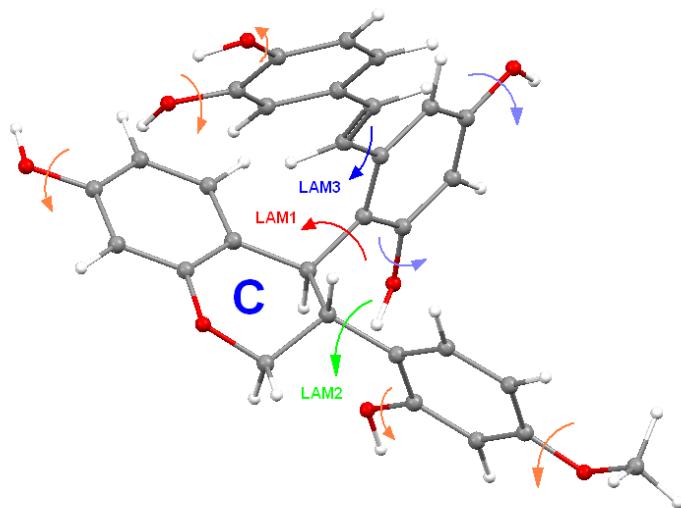


Figure S71. The main LAMs of **1**.

All of the LAMs influenced the UV and ECD spectra of **1**, especially LAM1, LAM2 and LAM3 as well as the inversion of ring C:

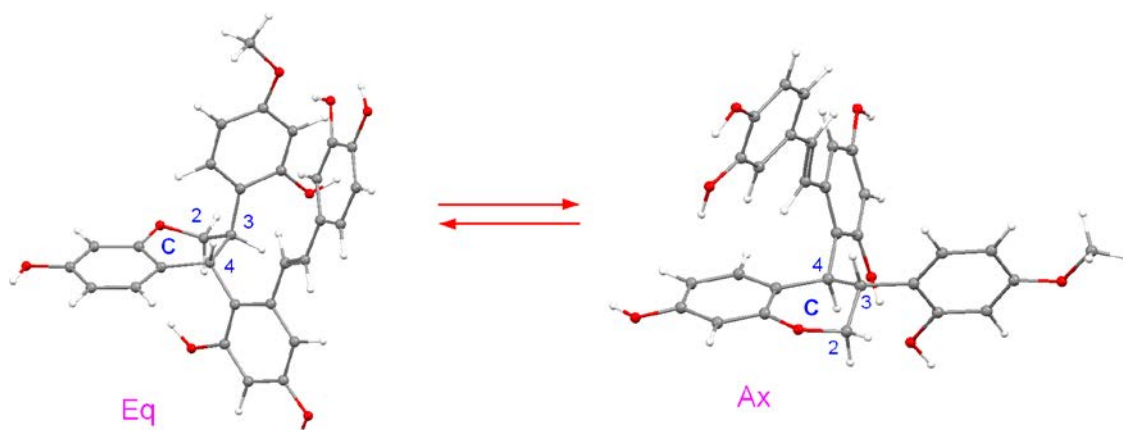


Figure S72. Inversion of ring C.

We used notation “Ax” and “Eq” to distinguish two conformations:

“AX” = axial orientation of H-3;

“Eq” = equatorial orientation of H-3

The inversion of ring C proceeds with overcoming potential barrier $\Delta V^\# \geq 4.1$ kcal/mol. We obtained this value after performing calculations of the potential energy surface (PES) scans along the intrinsic reaction coordinate (IRC) trajectories for several model compounds using B3LYP/6-311G(d) method. First, the transition states (TS) for Ax $\leftrightarrow$ Eq rearrangements were localized and proved by calculations of vibrational spectra (all of them contained one imaginary frequency). After that, the IRC-trajectories were calculated, starting from the TS structure and descending to minima on the potential energy surface. The one-dimensional potential $V(s)$, calculated for these model compounds, is shown in Figure S73:

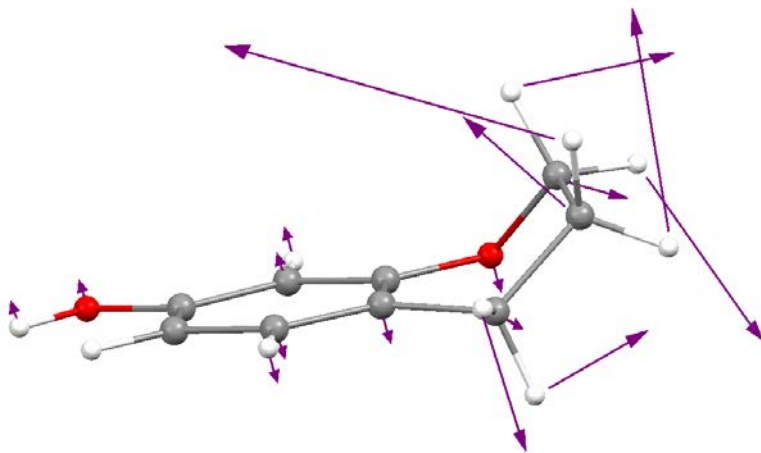


Figure S73. The geometry of the transition state for inversion of pyran ring in chroman-7-ol. The arrows schematically show relative amplitudes of displacements of atoms (for the gradient vector).

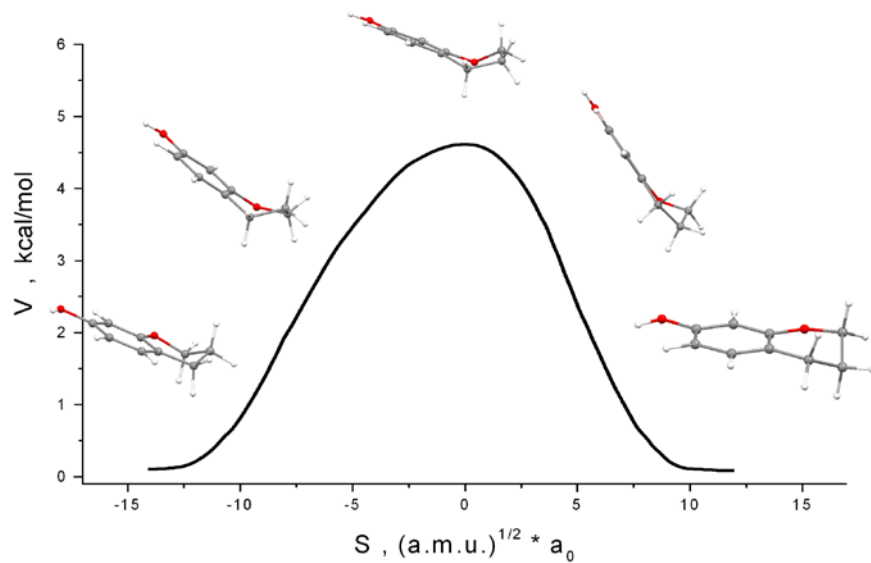


Figure S74. The inversion of chroman-7-ol: the potential energy scan along IRC trajectories.

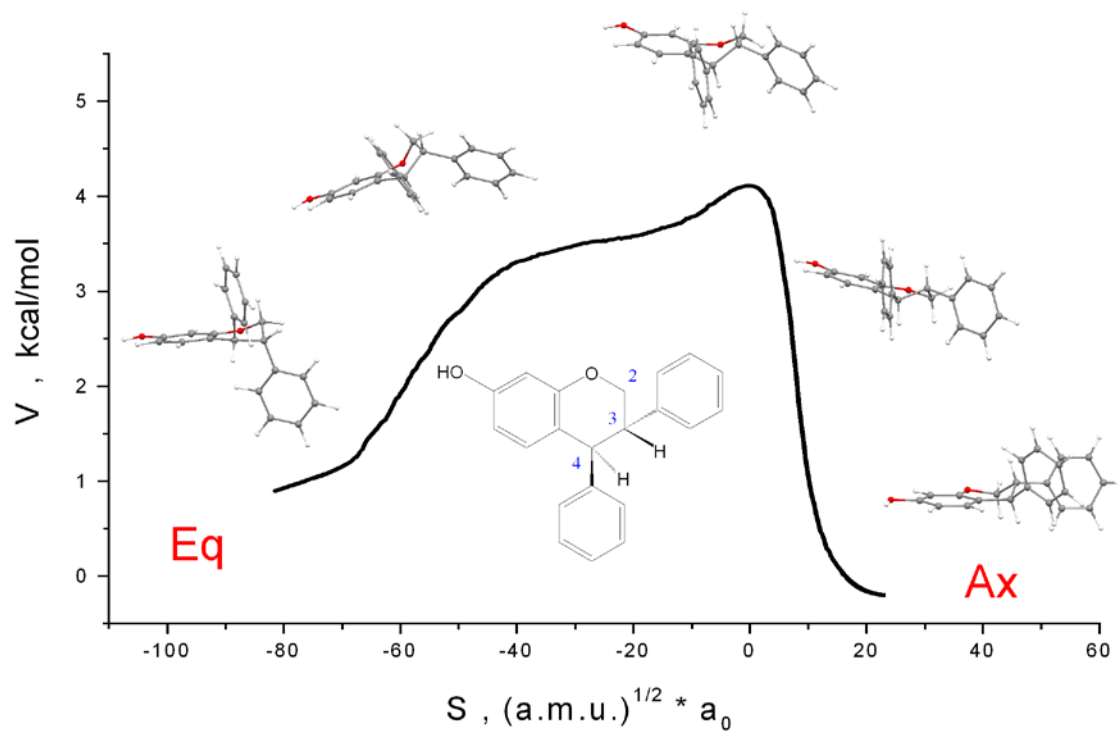


Figure S75. The inversion of (3S,4S)-3,4-diphenylchroman-7-ol: the potential energy scan along IRC trajectories.

One can see, that in the case of (3*S*,4*S*)-3,4-diphenylchroman-7-ol the potential $V(s)$ is very asymmetric and that energies for “Ax” and “Eq” stable conformations differ for about ~ 1 kcal/mol. “Ax” conformation is more stable.

The rotation of 4-vinylbenzene-1,2-diol fragment around C6''–C7'' bond is hindered. There are two (one in the cases, when substituent at C-4 has orientation, “opposite” to substituent at C-3, denoted as “**1a**” conformation, see text) its “stable” orientations (Figure S76):

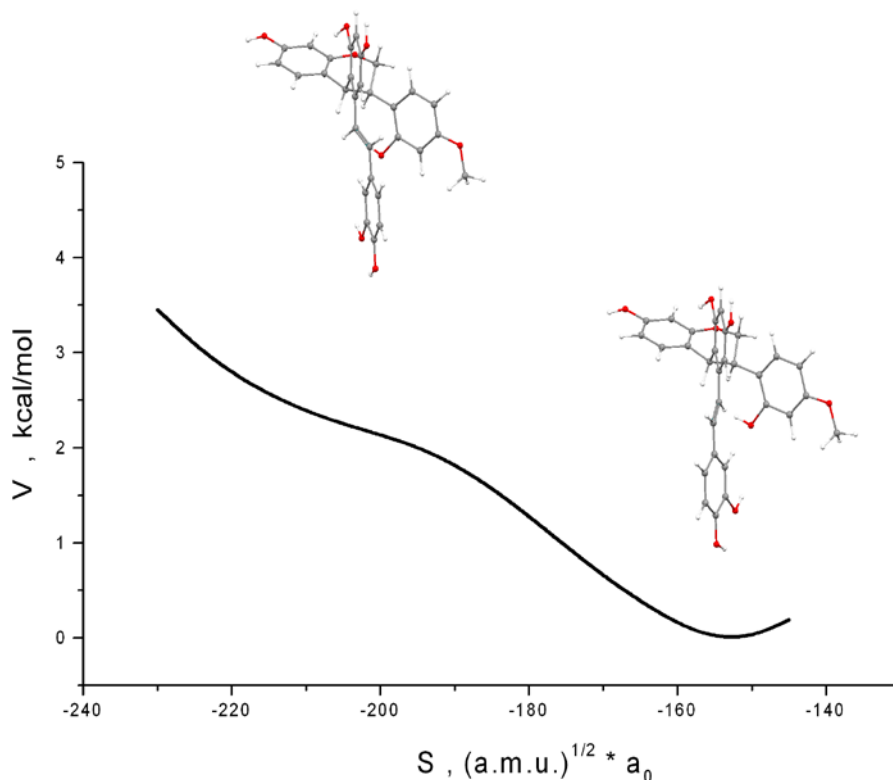


Figure S76. The potential energy as a function of internal rotation of 4-vinylbenzene-1,2-diol fragment around C6''–C7'' bond.

The internal rotation of piceatannol substituent at C4 in diapason $-180^\circ \leq \theta_4 \leq +180^\circ$ may proceed only for “Eq” conformation of cycle C. And even in this case the transfer requires the concerted pronounced transformations of several fragments of molecule:

- 1) the simultaneous internal rotations of 4-vinylbenzene-1,2-diol fragment around C6''–C7'' bond and of the whole piceatannol substituent at C-4;
- 2) the internal rotation of 3,5-dihydroxybenzene substituent at C-3.

The potential energy scan along θ_4 is shown In Figure S77:

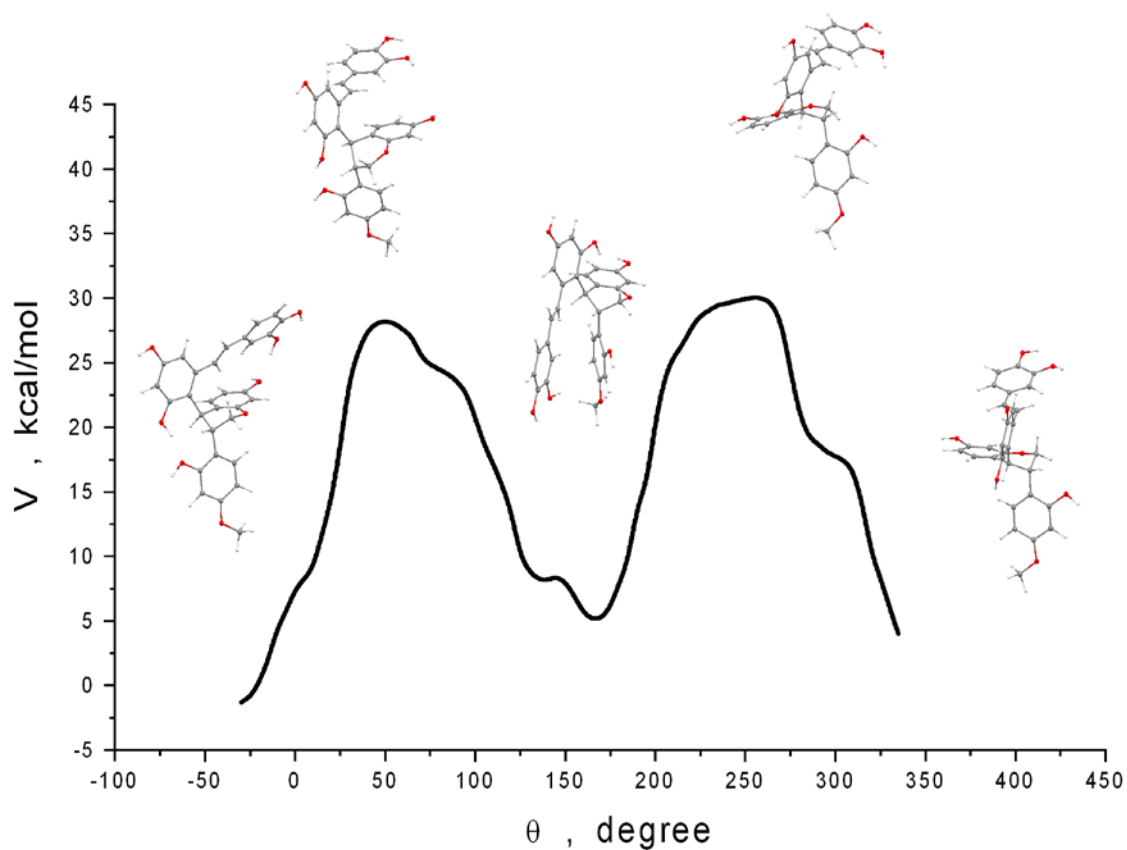


Figure S77. The variation of potential energy during the internal rotation of piceatannol substituent at C-4 around C4–C1'' bond.

We performed the search of the transition state structure (TS) aiming to obtain the lowest possible value for the height of potential energy barrier $\Delta V^\ddagger$ (Figure S78):

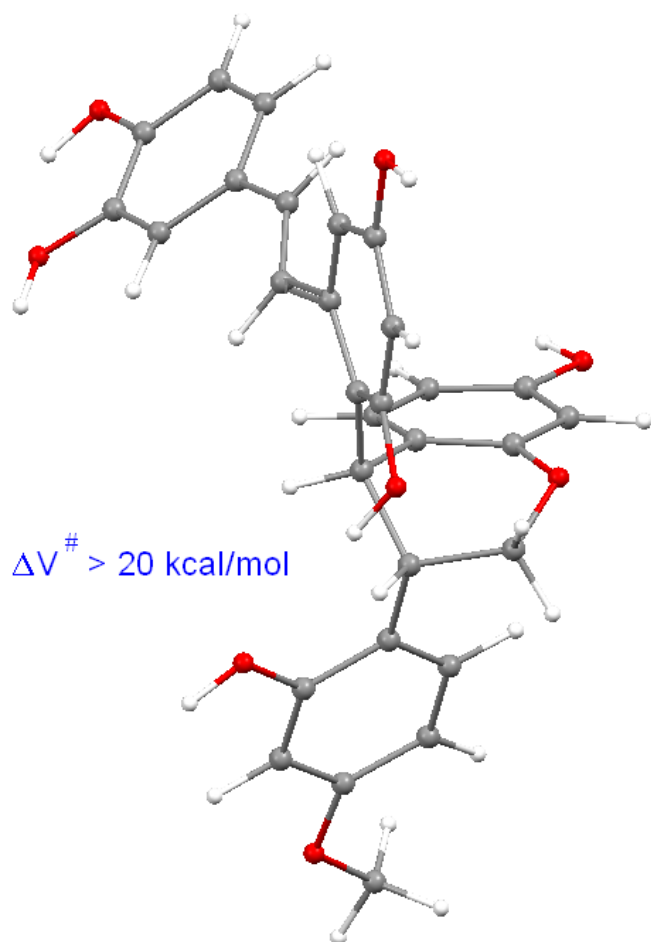
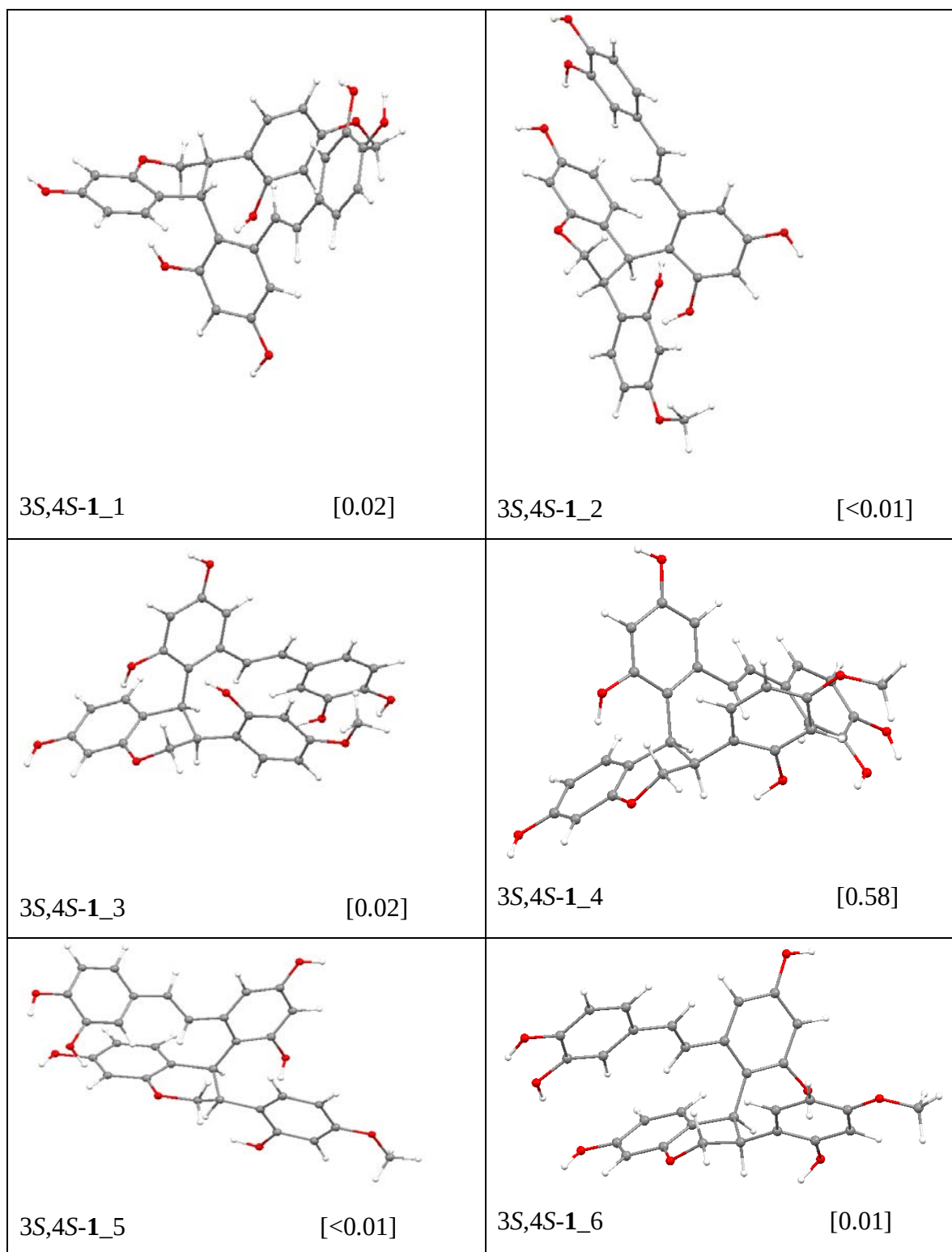
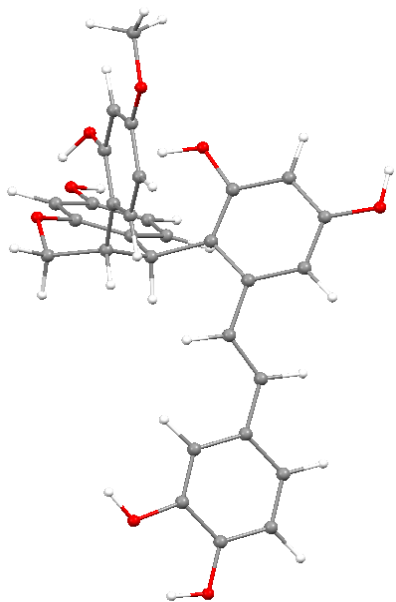


Figure S78. The TS for **3R,4S-1a** $\leftrightarrow$ **3R,4S-1b** rearrangement.

Our estimation gives $\Delta V^\ddagger \geq 20 \text{ kcal/mol}$.

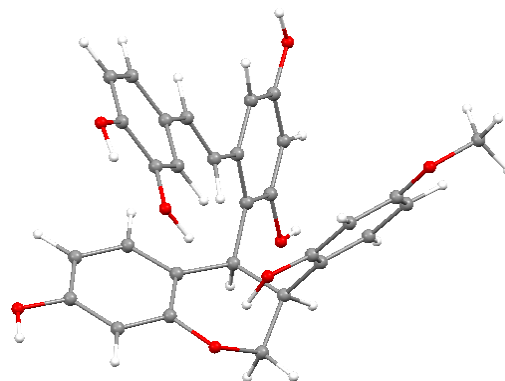
Figure S79. The most stable conformations of 3S,4S-1.





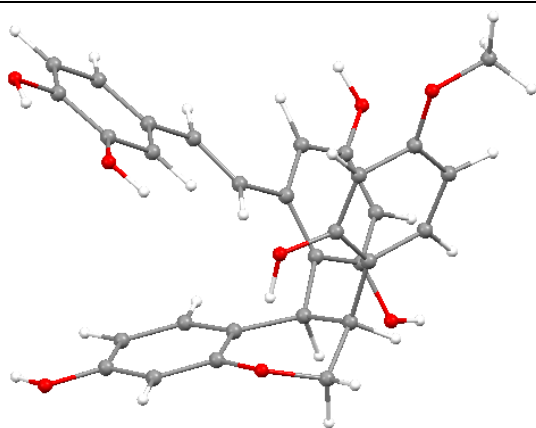
3S,4S-1_7

[0.18]



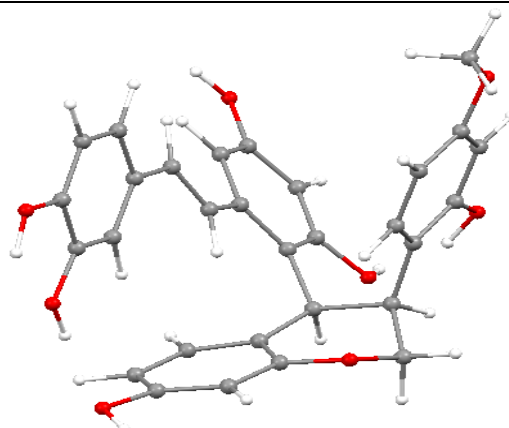
3S,4S-1_8

[0.08]



3S,4S-1_9

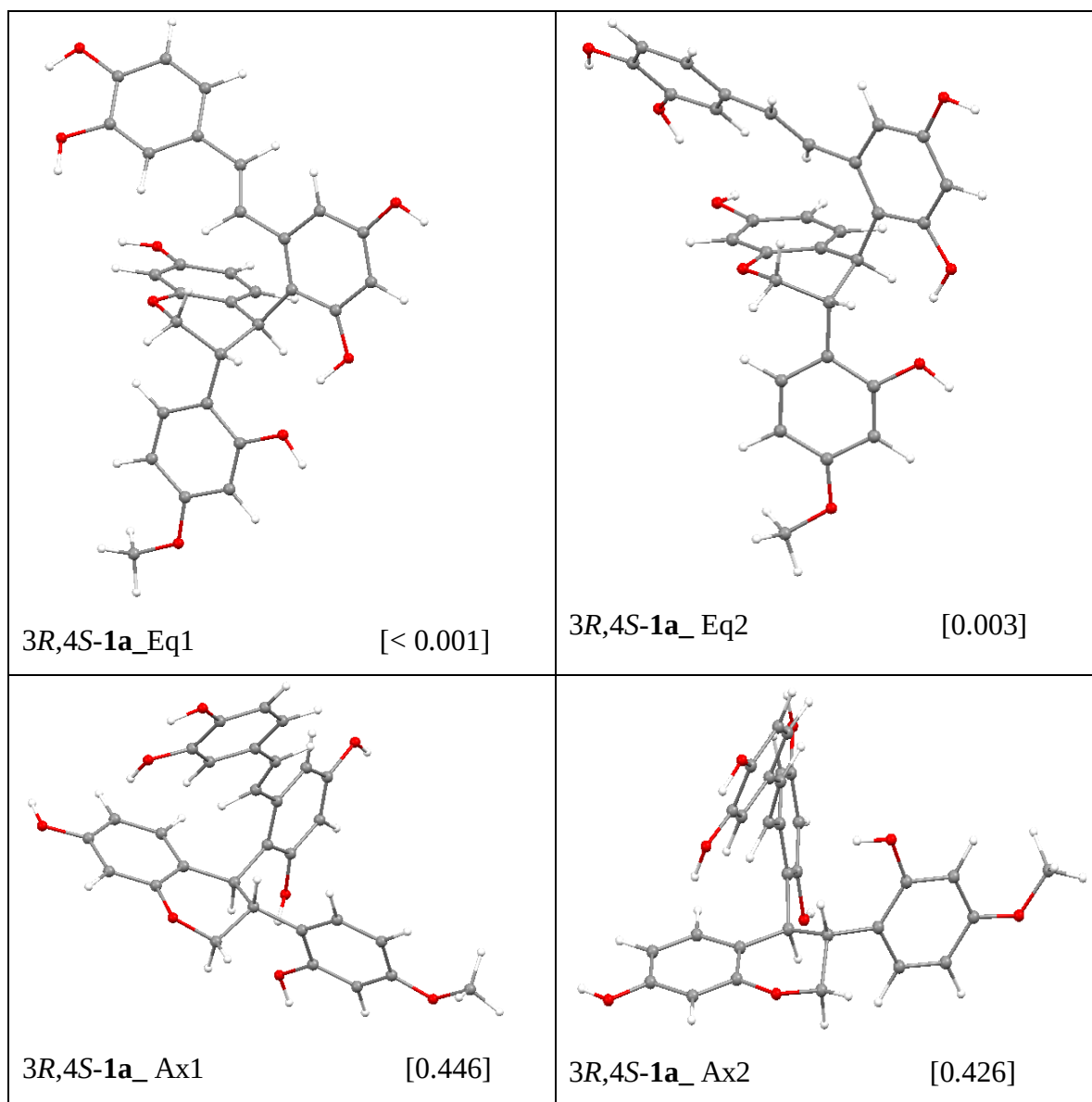
[0.11]

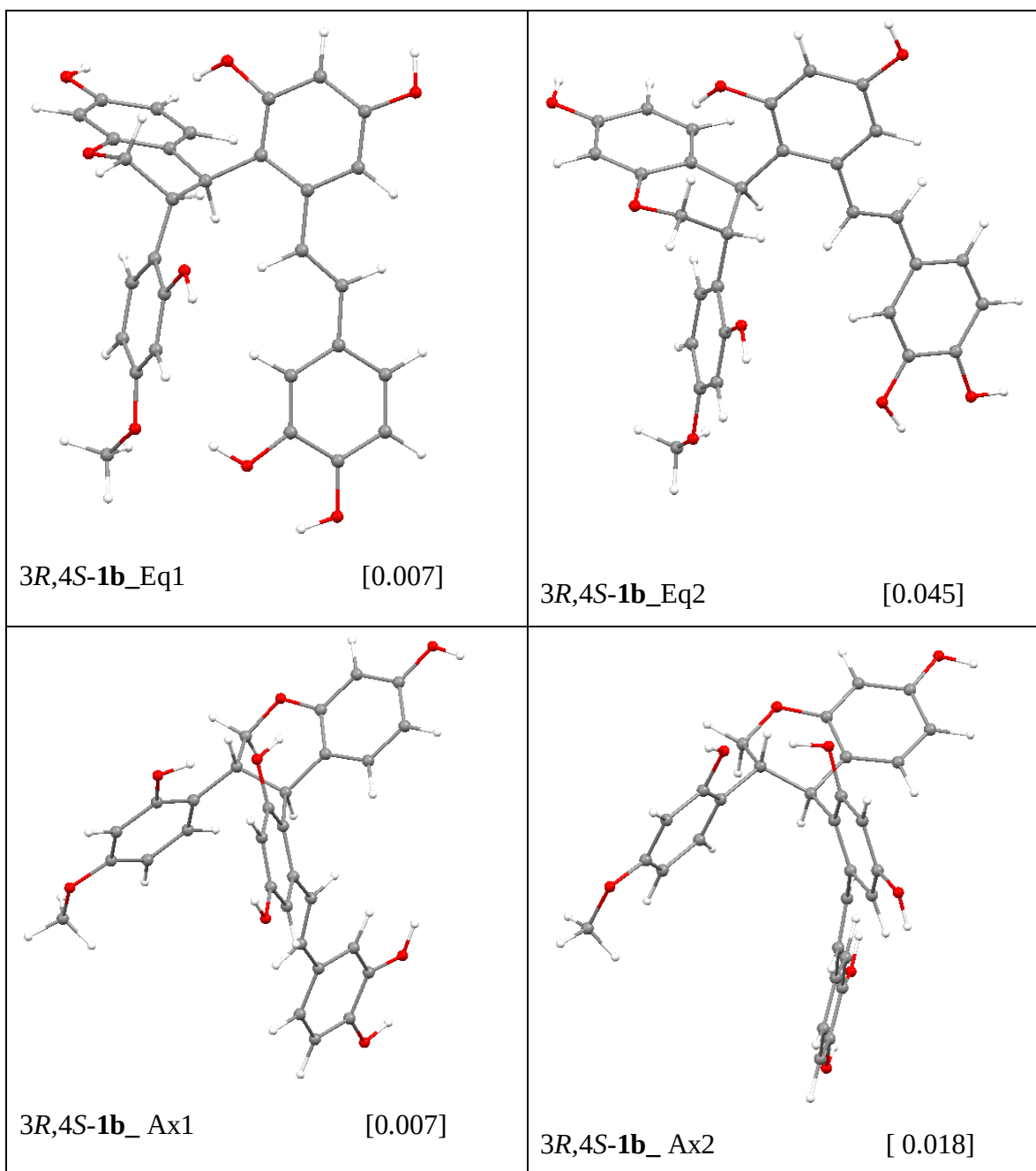


3S,4S-1_10

[< 0.01]

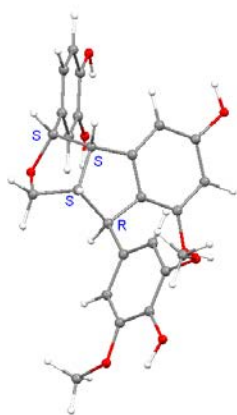
Figure S80 The most stable conformations of 3*R*,4*S* stereoisomer of **1**.



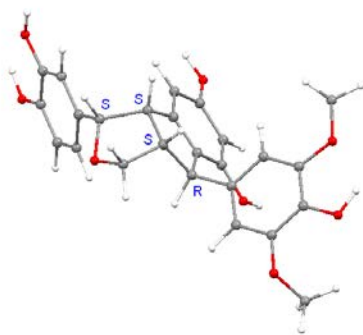


*) the statistical weights are calculated in consideration, that 3R,4S-**1a** and 3R,4S-**1b** conformations form the mono compound 3R,4S-**1**. In the paper these statistical weights were recalculated, according to consideration, that in the NMR time scale 3R,4S-**1a** and 3R,4S-**1b** may be treated as different compounds.

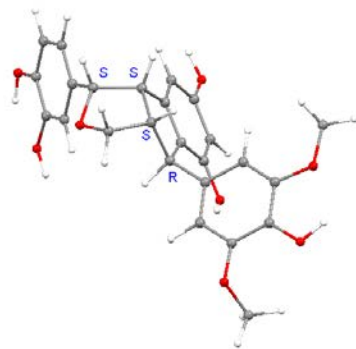
Figure S81 The most stable conformations of 3*S*,4*R* stereoisomer of compound **6**.



6-1
[0.08]



6-2
[0.06]



6-3
[0.86]

Figure S82, The most stable conformations of 3*S*,4*R*-4.

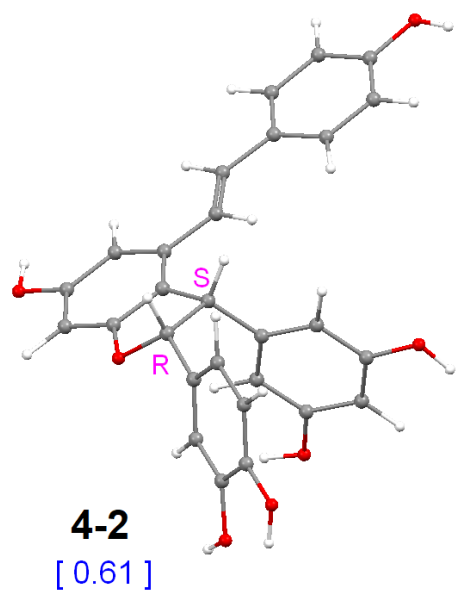
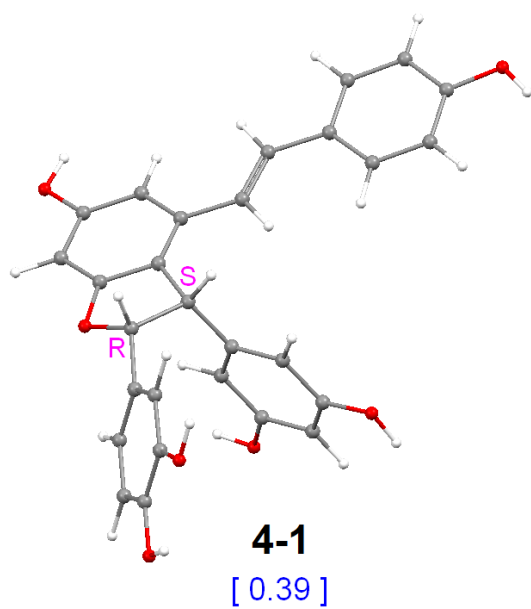
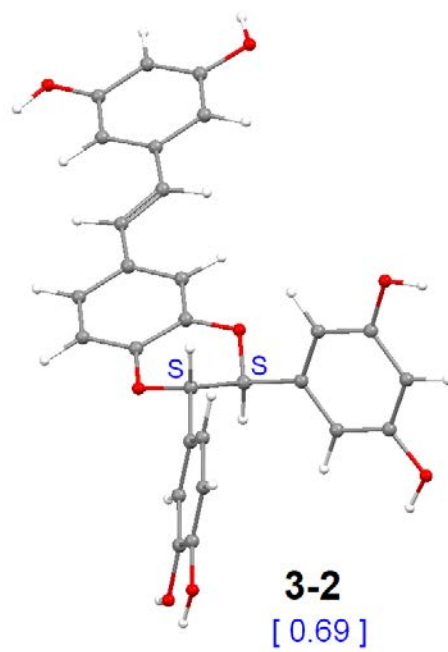
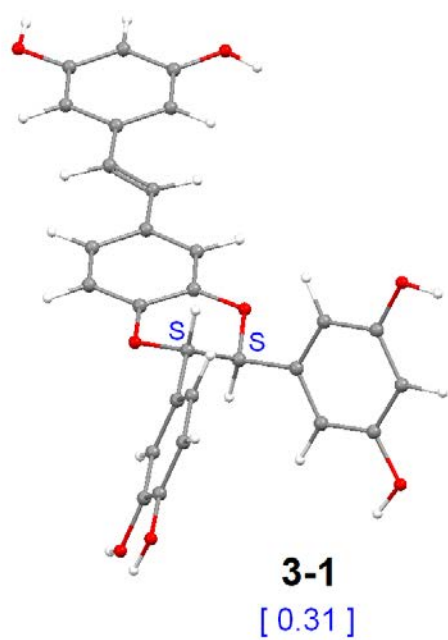


Figure S83. The most stable conformations of 3*S*,4*R*-3.



S84. The modeling of ECD spectra.

The statistically averaged ECD spectra of 3R,4S-**1** were obtained for two limit cases:

1) $\Delta\epsilon_{Ax+Eq}(3R,4S-1) = \Delta\epsilon_{Ax+Eq}(3R,4S-1a_Ax + 3R,4S-1a_EQ + 3R,4S-1b_Ax + 3R,4S-1b_EQ)$ - (red plot);

2) $\Delta\epsilon_{Ax}(3R,4S-1) = +\Delta\epsilon_{Ax}(3R,4S-1a_Ax + 3R,4S-1a_EQ + 3R,4S-1b_Ax)$ - (blue plot).

Thus, in all cases we take into account both conformations for 3R,4S-**1a**, whereas $\Delta\epsilon(3R,4S-1b)$ was calculated in two different manner.

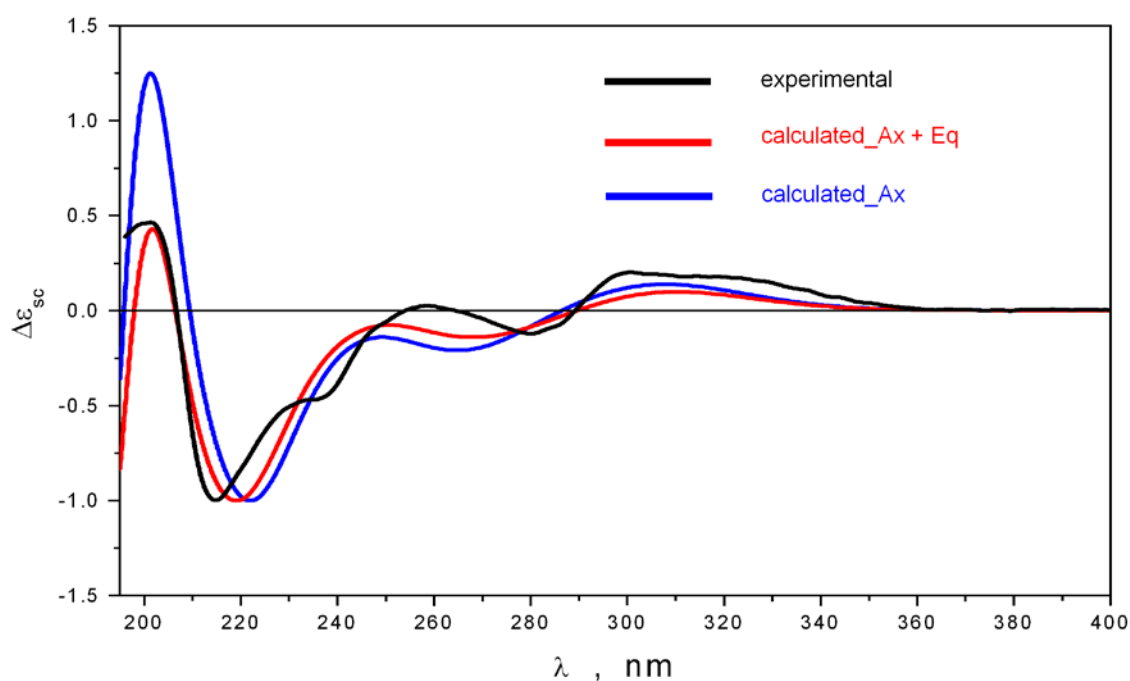


Figure S84. Theoretical ECD spectra of 3R,4S-**1**, compared with experimental ECD spectrum of **1**.

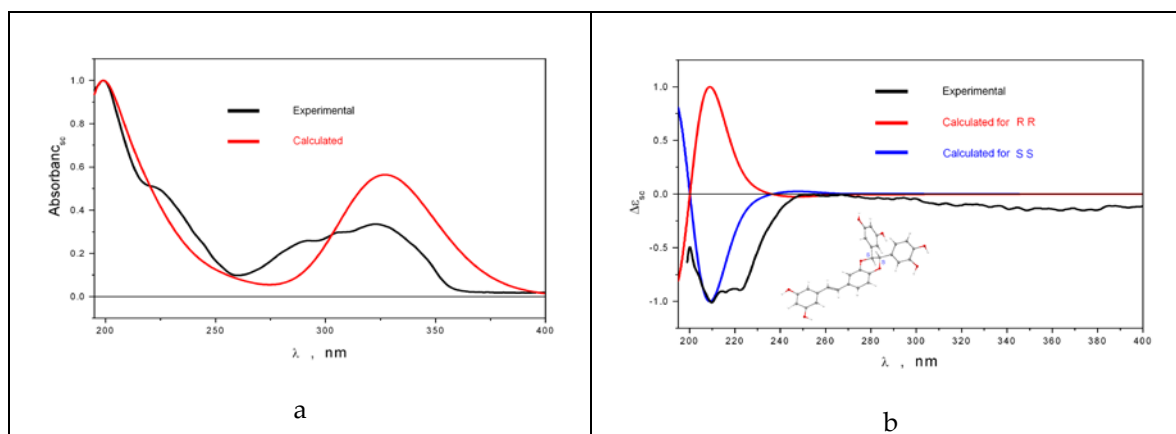


Figure S85. The comparison of experimental and theoretical UV (a) and ECD (b) spectra of **3**.

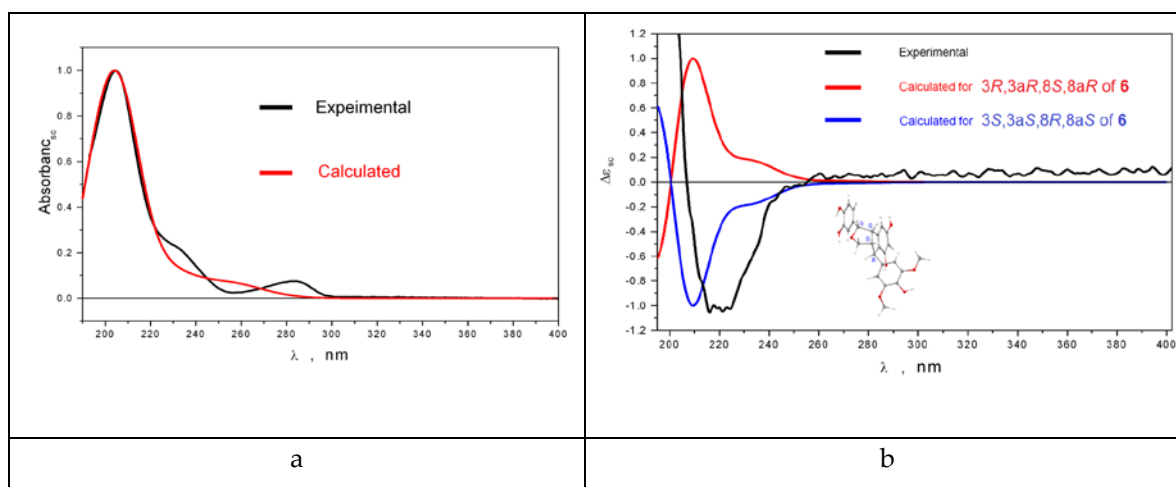


Figure S86. The comparison of experimental and theoretical UV (a) and ECD (b) spectra of **6**.

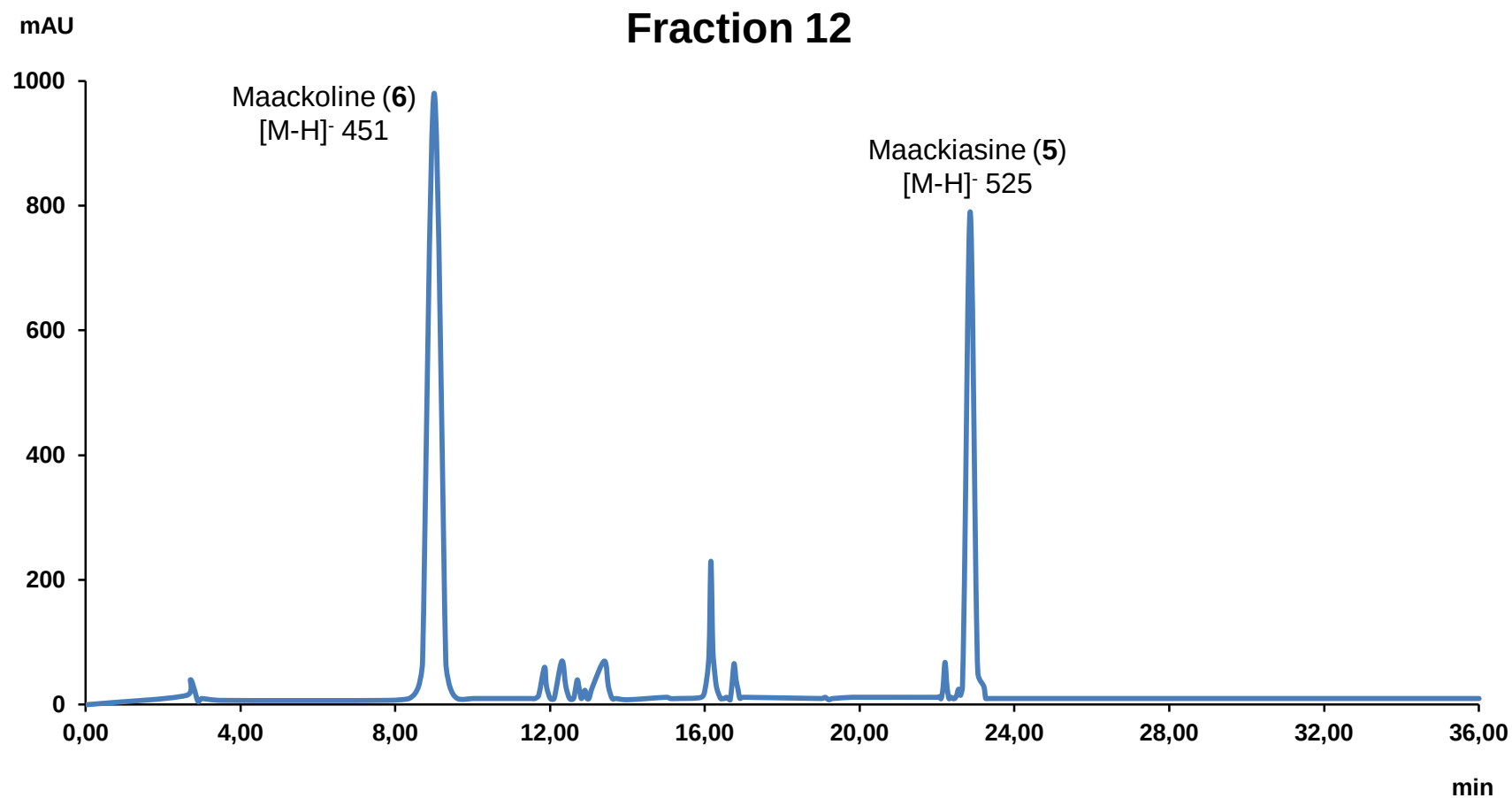


Figure S87. HPLC profile of fraction 12 obtained from *Maackia amurensis* heartwood extract after chromatography on a polyamide column.

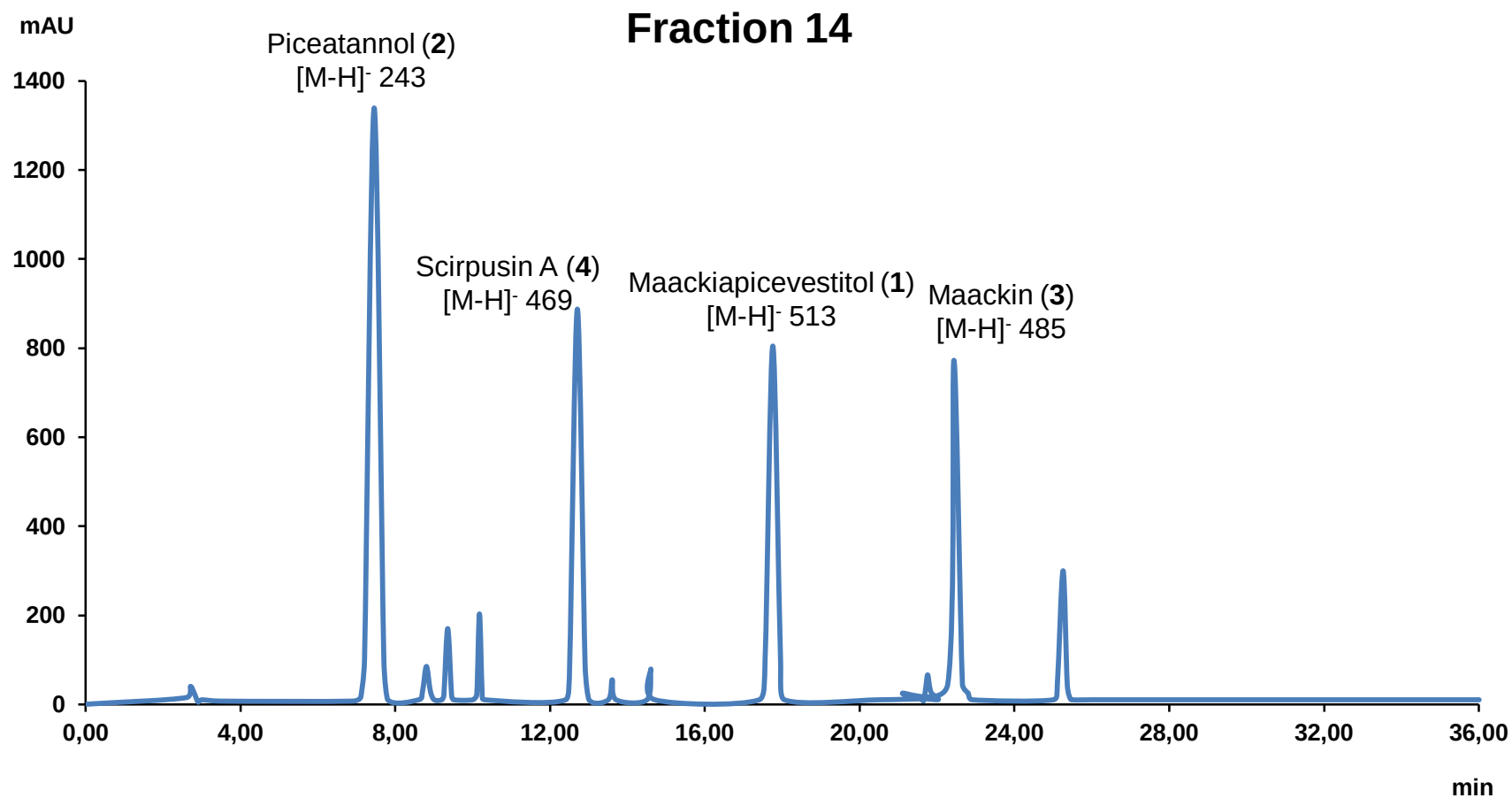


Figure S88. HPLC profile of fraction 1 obtained from *Maackia amurensis* heartwood extract after chromatography on a polyamide column.