Supporting Information

Trimethylsulfoxonium Iodide: A Green Methylating Agent for Site-Selective Methylation of Carbohydrates

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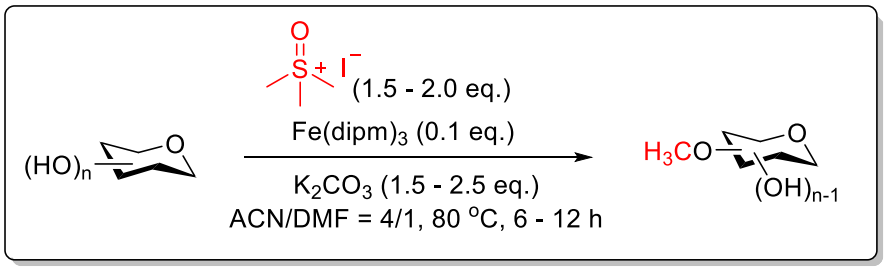
1. General Information

All reagents and solvents were obtained from commercial sources and used without further purifications. The starting materials were synthesized according to literature procedures. Unless otherwise noted, all reactions were carried out under ambient atmosphere in oven-dried tube containing magnetic stir bar and were monitored by thin layer chromatography (TLC) using pre-coated silica gel plates (GF_{254}). TLC plates were visualized by UV light (254 nm) or charred with 10% sulfuric acid in ethanol. Flash column chromatography was performed on silica gel (200-300 mesh) and eluted with petroleum ether/ethyl acetate. All ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded on Brucker spectrometers in $CDCl_3$. Chemical shifts (δ) for NMR were quoted in ppm relative to the solvent peak (δ = 7.26 ppm for ^{1}H NMR and δ = 77.16 ppm for ^{13}C NMR). ^{1}H peak assignments were made by first-order analysis of the spectra, supported by standard ^{13}C-^{1}H heteronuclear singular quantum correlation (C-H HSQC) and ^{1}H-^{1}H correlation spectroscopy (H-H COSY). High resolution mass spectra (HRMS) were reported from the Agilent 1290-6545B QTOF with an ESI source.

2. Experimental Procedure

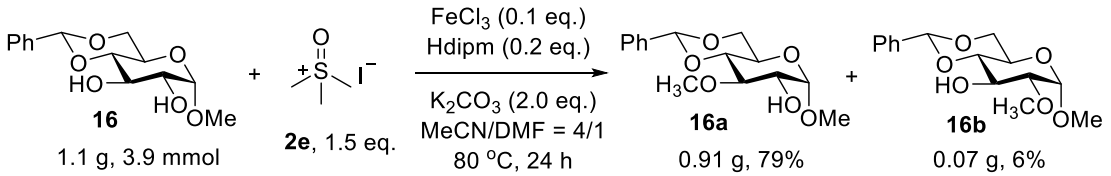
2.1 General procedure



The substrate (0.1 - 0.2 mmol), K_2CO_3 (1.5 - 2.5 equiv.) and $Fe(dipm)_3$ (0.1 equiv.) were dissolved in dry solvent mixture consisting of CH_3CN and DMF in a 4:1 volume ratio. Subsequently, trimethylsulfoxonium iodide (1.5 - 2.0 equiv.) was added, and the mixture was stirred vigorously at 80℃ for the designated hour as evidenced by TLC analysis. Once the reaction was complete, the reaction mixture was concentrated *in vacuo* and the crude residue was purified by column chromatography on silica gel to

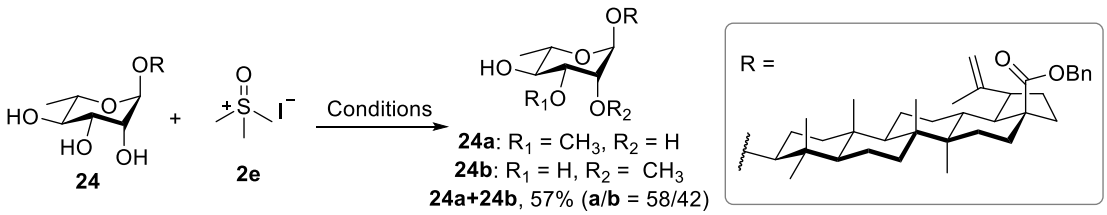
provide the desired products.

2.2 The experimental procedure for the gram-scale synthesis of 16a-b



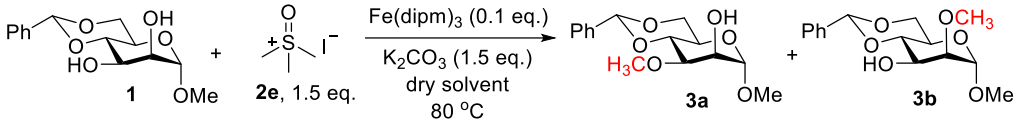
$FeCl_3$ (0.1 equiv., 0.06 g), Hdipm (0.2 equiv., 163.0 μL) and K_2CO_3 (2.0 equiv., 1.08 g) were first pre-stirred in 5.0 mL of dry ACN/DMF (4/1) for 0.5 h at r.t. Subsequently, the **16** (3.9 mmol, 1.10 g) and trimethylsulfoxonium iodide (1.5 equiv., 1.29 g) were added, and the mixture was stirred vigorously at 80℃ for the 24 h. Once the reaction was complete, the reaction mixture was concentrated *in vacuo* and the crude residue was purified by column chromatography on silica gel to provide the desired products, afforded compounds **16a** (0.91 g, 79%) and **16b** (0.07 g, 6%) as white solid.

2.3 The experimental procedure for the synthesis of 24a-b



Compound **24** (0.05 mmol, 34.6 mg), K_2CO_3 (2.5 equiv., 17.3 mg) and $Fe(dipm)_3$ (0.1 equiv., 3.0 mg) were dissolved in 1.0 mL of dry DMF. Subsequently, trimethylsulfoxonium iodide (2.0 equiv., 22.0 mg) was added, and the mixture was stirred vigorously at 80℃ for 10 h. Once the reaction was complete, the reaction mixture was concentrated *in vacuo* and the crude residue was purified by column chromatography on silica gel to provide the desired products, afforded a mixture of compound **24a** and **24b** as white solid (20.0 mg, 56.7%, **24a**/**24b** = 58/42).

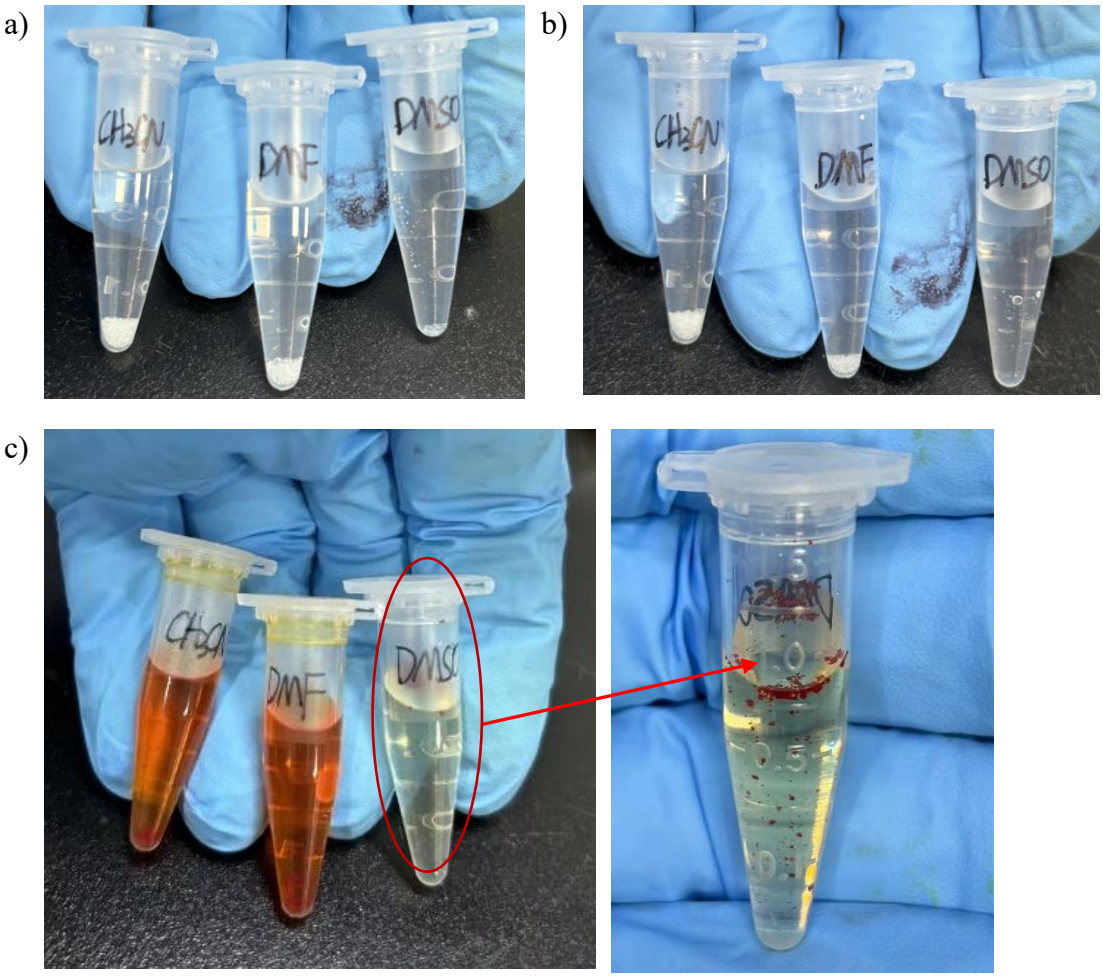
3. Table S1. Evaluation of solvents for selective methylation of substrate **1**[a]



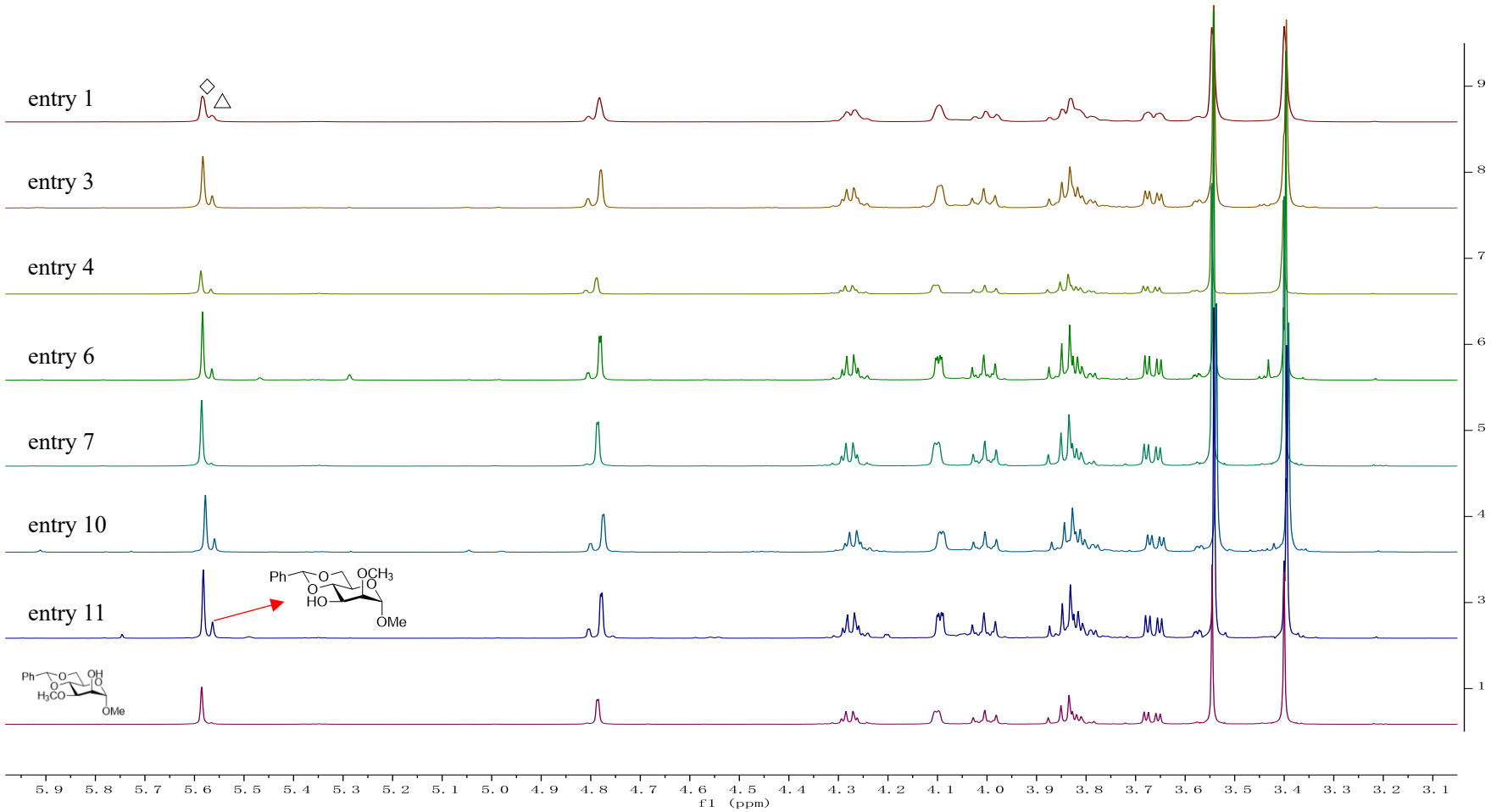
Entry	Solvent	Isolated Yield [b] [%] (**3a/3b**)[c]
1	CH_3CN/DMF (4/1), 6 h	93 (81/19)
2	CH_3CN, 6 h	68 (78/22)
3	DMF, 2 h	91 (83/17)
4	DMSO, 6 h	N. D.[d]
5	CH_3CN/DMSO (4/1), 3 h	92 (80/20)

[a] Reaction conditions: Substrate **1** (0.1 mmol), **2e** (0.15 mmol, 1.5 equiv.), $Fe(dipm)_3$ (0.1 equiv.), K_2CO_3 (1.5 equiv.), solvent (1.0 mL), 80°C. [b] Isolated yield. [c] The ratio was determined by ^1H NMR. [d] No products were detected.

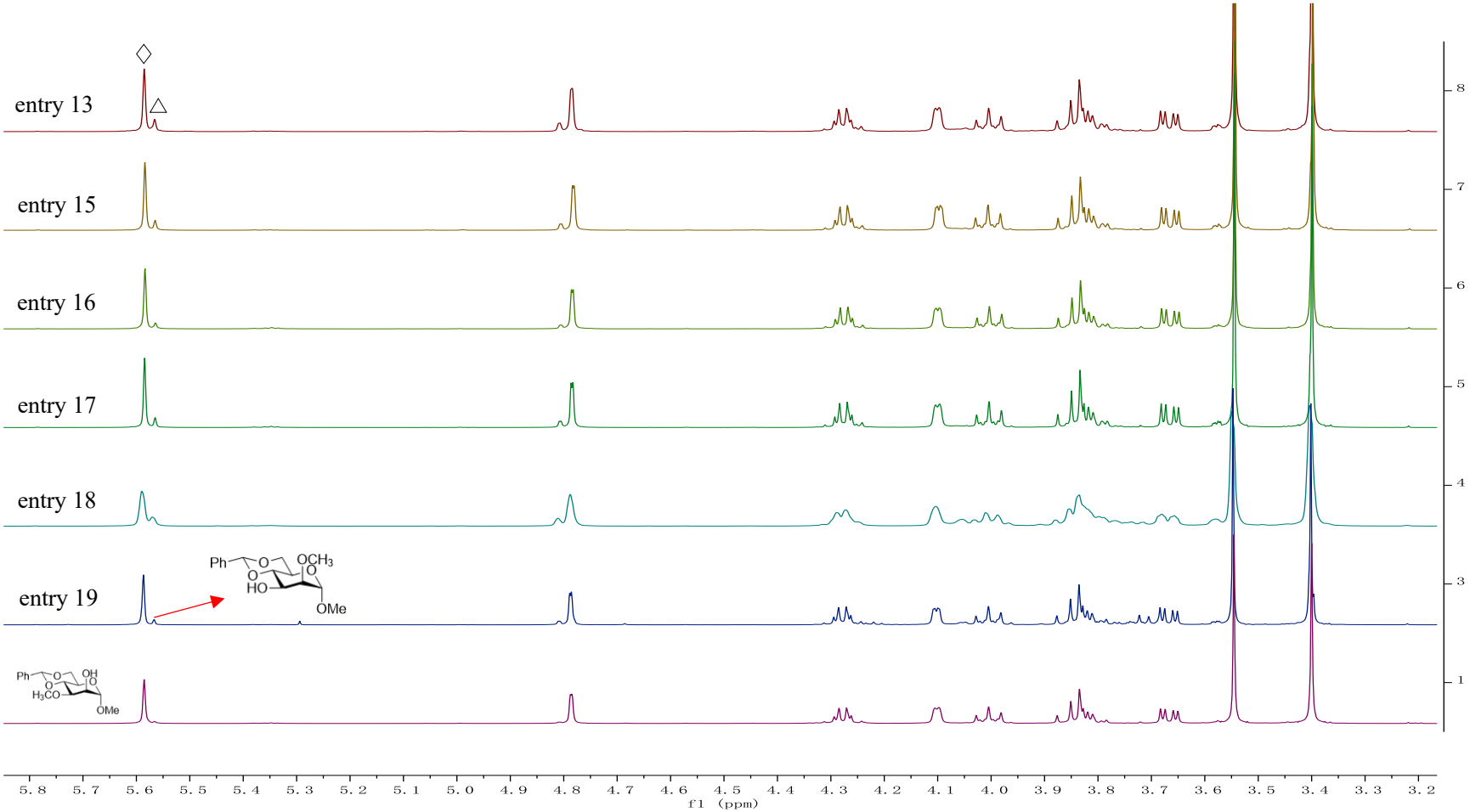
Different solvents were further screened, when pure acetonitrile was employed as the solvent, reaction yield decreased significantly. Conversely, pure DMF exhibited higher reaction efficiency (Table S1, entries 2 and 3). We hypothesized that this discrepancy might be attributed to the differing solubilities of the methylation agent **2e** in these solvents. Indeed, testing confirmed that the agent **2e** dissolved best in DMSO, but was nearly insoluble in acetonitrile regardless of shaking (Figure S1, a and b). This observation also suggests that DMSO maybe as a more suitable solvent for the reaction. However, using pure DMSO resulted in no product formation (Table S1, entry 4). Upon further investigation, the examination revealed poor dispersibility of the catalyst $Fe(dipm)_3$ in DMSO, with most remaining suspended above the solvent, impeding the catalytic reaction (Figure S1, c). In subsequent experiments, upon reusing a mixed solvent of CH_3CN and DMSO, satisfactory reaction results were achieved again (Table S1, entry 5). Thus, from the perspective of reactant solubility, we provided a rational explanation for the suboptimal performance observed with both pure CH_3CN and DMSO. Furthermore, we accounted for the high boiling points of DMF and DMSO, which might complicate the subsequent separation. After comprehensive consideration, we ultimately settled on a mixture of CH_3CN with either DMF or DMSO as the optimal reaction solvent.



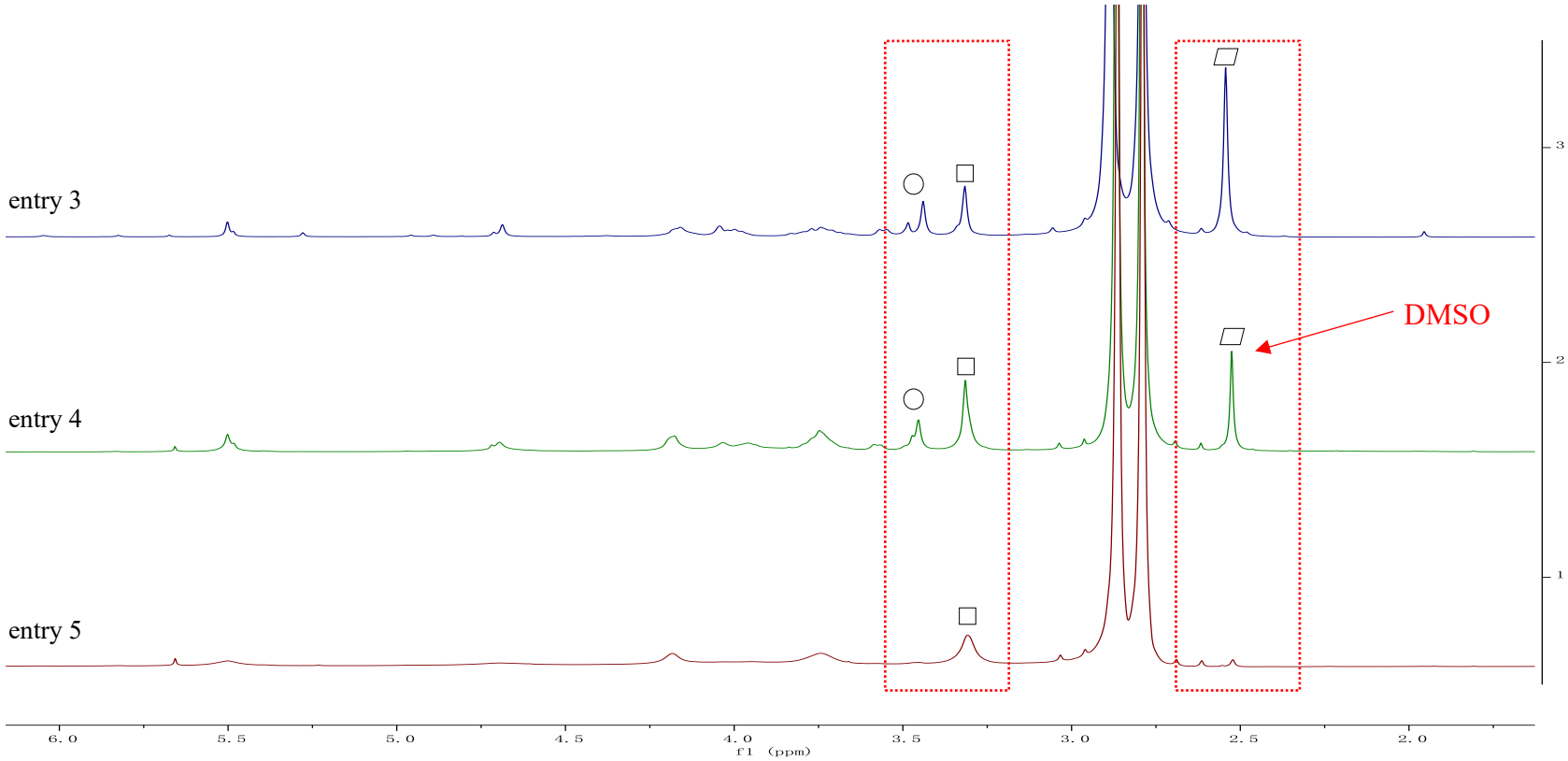
4. Figure S1. a) $(CH_3)_3S(O)I$ (0.15 mmol, 33.0 mg) was mixed in 1.0 mL of pure CH_3CN, DMF, and DMSO, respectively. b) Shake the aforementioned centrifuge tubes for 1 minute. c) $Fe(dipm)_3$ (0.01 mmol, 6.0 mg) was mixed in 1.0 mL of pure CH_3CN, DMF, and DMSO, respectively and then shaken for 1 minute.



5. Figure S2a. ^{1}H-NMR spectra of **3a**/**3b** isolated with various conditions for Table 1.



5. Figure S2b. [1]H-NMR spectra of **3a**/**3b** isolated with various conditions for Table 1.

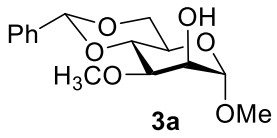


6. Figure S3. ^{1}H-NMR spectra of crude reaction mixtures for entries 3, 4 and 5, Table 1.

The reaction system was monitored using ^{1}H-NMR, which revealed that the quantity of DMSO, derived from trimethylsulfoxonium iodide. Notably, for entry 5, where the substrates exhibited minimal to no reactivity at 40°C, the formation of DMSO was also barely detectable, providing further evidence for the transformation of trimethylsulfoxonium iodide during the methylation process.

7. Characterization Data for the Products

Methyl-3-*O*-4,6-*O*-benzylidene-methyl-*α*-D-mannopyranoside (3a)



3a

General procedure for methylation was followed, the reaction was carried out with methyl-4,6-*O*-benzylidene-*α*-D-mannopyranoside (28.2 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compounds **3a** and **3b** as colorless oil (27.5 mg, 93%, **3a**/**3b** = 81/19).

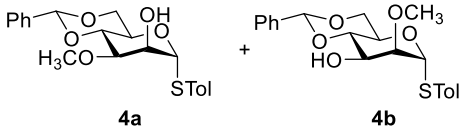
Data for 3a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55-7.44 (m, 2H), 7.44-7.30 (m, 3H), 5.59 (s, 1H), 4.79 (d, *J* = 1.6 Hz, 1H), 4.34-4.21 (m, 1H), 4.14-4.07 (m, 1H), 4.05-3.97 (m, 1H), 3.91-3.75 (m, 2H), 3.67 (dd, *J* = 9.5, 3.5 Hz, 1H), 3.55 (s, 3H), 3.40 (s, 3H), 2.62 (s, 1H). Typical data for **3b**: δ 5.57 (s, 1H), 4.81 (d, *J* = 1.6 Hz, 1H), 3.58 (dd, *J* = 3.8, 1.6 Hz, 3H), 2.45 (d, *J* = 7.9 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.6, 129.1, 128.4, 126.3, 102.0, 101.2, 78.8, 69.2, 69.0, 68.9, 63.3, 58.7, 55.2. Typical data for **3b**: δ 137.5, 129.2.

HRMS (ESI) m/z calcd for $C_{15}H_{20}O_6Na^+$ $[M+Na]^+$ 319.1152, found 319.1158.

***p*-Tolyl-3-*O*-methyl-4,6-*O*-benzylidene-1-thio-*α*-D-mannopyranoside (4a)** and ***p*-Tolyl-2-*O*-methyl-4,6-*O*-benzylidene-1-thio-*α*-D-mannopyranoside (4b)**



4a **4b**

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-4,6-*O*-benzylidene-1-thio-*α*-D-mannopyranoside (37.4 mg, 0.1 mmol),

trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded a mixture of compound **4a** and **4b** as colorless oil (36.5 mg, 94%, **4a**/**4b** = 85/15).

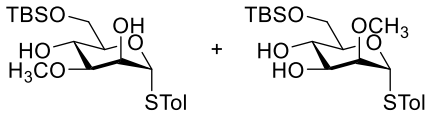
Data for 4a and **4b:**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (dq, *J* = 6.6, 2.9, 2.4 Hz, 2H), 7.44-7.30 (m, 5H), 7.13 (dd, *J* = 7.9, 5.7 Hz, 2H), 5.62-5.49 (m, 2H), 4.43-4.27 (m, 2H), 4.20 (dd, *J* = 10.3, 4.9 Hz, 1H), 4.08 (t, *J* = 9.6 Hz, 1H), 3.92 (t, *J* = 12 Hz, 0.24H), 3.89-3.77 (m, 1.10H), 3.72 (dd, *J* = 9.6, 3.4 Hz, 1H), 3.58 (s, 2.44H, for **4a** 3-OCH_3), 3.52 (s, 0.42H, for **4b** 2-OCH_3), 2.84 (br s, 1H), 2.33 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.2, 137.5, 132.6, 132.4, 130.11, 130.08, 129.6, 129.1, 128.42, 128.37, 126.5, 126.3, 101.9, 88.4, 79.1, 77.7, 70.7, 68.7, 68.6, 64.5, 58.9, 21.2.

HRMS (ESI) m/z calcd for $C_{21}H_{24}O_5SNa^+$ $[M+Na]^+$ 411.1237, found 411.1240.

***p*-Tolyl-3-*O*-methyl-6-(tert-butyldimethylsilyl)-1-thio-*α*-D-mannopyranoside (5a)** and ***p*-Tolyl-2-*O*-methyl-6-*O*-(tert-butyldimethylsilyl)-1-thio-*α*-D-mannopyranoside (5b)**



5a **5b**

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-6-*O*-(tert-butyldimethylsilyl)-1-thio-*α*-D-mannopyranoside (40.0 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/2), afforded a mixture of compound **5a** and **5b** as colorless oil (37.7 mg, 91%, **5a**/**5b** = 64/36).

Data for 5a and **5b:**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34-7.25 (m, 2H), 7.10-6.97 (m, 2H), 5.47 (s, 0.36H, for **5b** H-1), 5.42 (s, 0.64H, for **5a** H-1), 4.21 (dd, *J* = 3.3, 1.6 Hz, 0.65H), 4.13-3.96 (m, 1H), 3.88-3.72 (m, 3H), 3.72-3.58 (m, 1H), 3.45 (s, 1.93H, for **5a** 3-OCH_3), 3.38 (dd, *J* = 9.1, 3.2 Hz, 0.72H), 3.35 (s, 1.01H, for **5b** 2-OCH_3), 3.18 (br s, 1H), 2.24 (s, 3H), 0.82 (d, *J* = 1.4 Hz, 9H), 0.00 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.8, 132.2, 132.1, 129.95, 129.92, 88.0, 84.8, 81.30, 81.26, 72.1, 72.0, 71.7, 71.1, 69.6, 68.5, 64.8, 64.5, 58.1, 57.6, 26.0, 21.2, 18.4, -5.29, -5.33, -5.4.

HRMS (ESI) m/z calcd for $C_{20}H_{34}O_5SSiNa^+$ $[M+Na]^+$ 437.1788, found 437.1796.

Methyl-3-*O*-methyl-6-*O*-(tert-butyldiphenylsilyl)-*α*-D-mannopyranoside (6a) and **Methyl-2-*O*-methyl-6-*O*-(tert-butyldiphenylsilyl)-*α*-D-mannopyranoside (6b)**

6a **6b**

General procedure for methylation was followed, the reaction was carried out with methyl-6-*O*-(tert-butyldiphenylsilyl)-*α*-D-mannopyranoside (43.2 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/2), afforded a mixture of compound **6a** and **6b** as colorless oil (34.1 mg, 77%, **6a**/**6b** = 58/42).

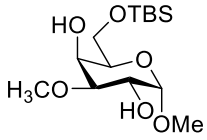
Data for 6a and **6b:**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73-7.65 (m, 4H), 7.46-7.34 (m, 6H), 4.78 (s, 0.42H, for **6b** H-1), 4.75 (s, 0.58H, for **6a** H-1), 4.04 (dt, *J* = 3.5, 1.7 Hz, 0.60H), 3.98-3.83 (m, 2.66H), 3.83-3.74 (m, 0.47H), 3.75-3.56 (m, 2H), 3.50 (s, 1.61H), 3.47 (s, 1.74H), 3.46-3.43 (m, 0.46H), 3.34 (d, *J* = 1.8 Hz, 3H), 2.98 (s, 0.54H), 2.90 (s, 0.39H), 2.49 (d, *J* = 8.0 Hz, 0.41H), 2.37 (s, 0.55H), 1.07 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 134.7, 134.6, 128.81, 128.76, 126.8, 126.7, 99.4, 96.3, 79.9, 78.7, 70.4, 70.2, 69.8, 69.5, 67.7, 65.7, 64.2, 64.0, 56.3, 53.84, 53.75, 25.8, 18.2.

HRMS (ESI) m/z calcd for $C_{24}H_{34}O_6SiNa^+$ $[M+Na]^+$ 469.2017, found 469.2025.

Methyl-3-*O*-methyl-6-*O*-(tert-butyldimethylsilyl)-*α*-D-galactopyranoside (7a)



7a

General procedure for methylation was followed, the reaction was carried out with methyl-6-*O*-(tert-butyldimethylsilyl)-*α*-D-galactopyranoside (30.8 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/2), afforded compound **7a** as colorless oil (21.0 mg, 65%).

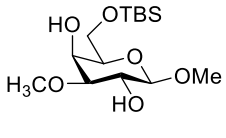
Data for 7a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.81 (d, *J* = 4.0 Hz, 1H), 4.18 (dt, *J* = 3.0, 1.4 Hz, 1H), 3.98-3.86 (m, 2H), 3.83 (dd, *J* = 10.4, 5.5 Hz, 1H), 3.72 (t, *J* = 5.6 Hz, 1H), 3.51 (s, 3H), 3.42 (s, 3H), 3.37 (dd, *J* = 9.7, 3.2 Hz, 1H), 2.68 (s, 1H), 2.18 (d, *J* = 7.8 Hz, 1H), 0.90 (s, 9H), 0.09 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 99.6, 80.5, 70.1, 68.6, 66.1, 63.1, 57.4, 55.4, 26.0, 18.4, -5.3.

HRMS (ESI) m/z calcd for $C_{14}H_{30}O_6SiNa^+$ $[M+Na]^+$ 345.1704, found 345.1713.

Methyl-3-*O*-methyl-6-*O*-(tert-butyldimethylsilyl)-*β*-D-galactopyranoside (8a)



8a

General procedure for methylation was followed, the reaction was carried out with methyl-6-*O*-(tert-butyldimethylsilyl)-*β*-D-galactopyranoside (30.8 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/2), afforded compound **8a** as colorless oil (17.3 mg, 53%).

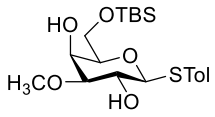
Data for 8a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.18 (d, *J* = 7.7 Hz, 1H), 4.16-4.12 (m, 1H), 3.95 (dd, *J* = 10.3, 6.3 Hz, 1H), 3.86 (dd, *J* = 10.4, 5.4 Hz, 1H), 3.71 (ddd, *J* = 9.5, 7.7, 1.9 Hz, 1H), 3.55 (s, 3H), 3.52 (s, 3H), 3.46 (t, *J* = 4.0 Hz, 1H), 3.20 (dd, *J* = 9.5, 3.3 Hz, 1H), 2.54 (dd, *J* = 2.6, 0.9 Hz, 1H), 2.45 (d, *J* = 2.0 Hz, 1H), 0.90 (s, 9H), 0.09 (d, *J* = 1.6 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 103.9, 82.7, 74.6, 70.8, 65.0, 62.4, 57.3, 56.9, 25.9, 18.3, -5.4.

HRMS (ESI) m/z calcd for $C_{14}H_{30}O_6SiNa^+$ $[M+Na]^+$ 345.1704, found 345.1711.

***p*-Tolyl-3-*O*-methyl-6-*O*-(tert-butyldimethylsilyl)-1-thio-*β*-D-galactopyranoside (9a)**



9a

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-6-*O*-(tert-butyldimethylsilyl)-1-thio-*β*-D-galactopyranoside (40.0 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/2), afforded compound **9a** as colorless oil (27.8 mg, 67%).

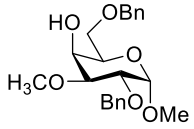
Data for 9a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40-7.32 (m, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 4.35 (d, *J* = 9.7 Hz, 1H), 4.06 (d, *J* = 3.1 Hz, 1H), 3.83 (dd, *J* = 10.4, 5.9 Hz, 1H), 3.77 (dd, *J* = 10.5, 5.1 Hz, 1H), 3.60 (t, *J* = 9.3 Hz, 1H), 3.40 (s, 3H), 3.38-3.33 (m, 1H), 3.09 (dd, *J* = 9.0, 3.2 Hz, 1H), 2.66 (br s, 1H), 2.56 (br s, 1H), 2.32 (s, 3H), 0.90 (s, 9H), 0.09 (d, *J* = 5.1 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.2, 133.1, 129.7, 128.3, 88.8, 83.8, 78.4, 68.5, 65.7, 62.9, 57.4, 25.9, 21.1, 18.3, -5.4.

HRMS (ESI) m/z calcd for $C_{20}H_{34}O_5SSiNa^+$ $[M+Na]^+$ 437.1788, found 437.1794.

Methyl-2,6-di-*O*-benzyl-3-*O*-methyl-*α*-D-galactopyranoside (10a)



10a

General procedure for methylation was followed, the reaction was carried out with methyl-2,6-di-*O*-benzyl-*α*-D-galactopyranoside (37.4 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **10a** as colorless oil (31.3 mg, 81%).

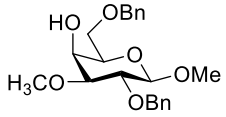
Data for 10a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39-7.23 (m, 10H), 4.80 (d, *J* = 12.2 Hz, 1H), 4.67-4.56 (m, 4H), 4.15-4.10 (m, 1H), 3.94-3.87 (m, 1H), 3.81-3.72 (m, 2H), 3.68 (dd, *J* = 10.0, 6.1 Hz, 1H), 3.59 (dd, *J* = 9.8, 3.3 Hz, 1H), 3.52 (s, 3H), 3.37 (s, 3H), 2.58 (s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.7, 138.1, 128.6, 128.5, 128.1, 127.87, 127.86, 127.83, 98.8, 79.5, 75.7, 73.8, 73.6, 69.9, 68.5, 67.4, 58.2, 55.5.

HRMS (ESI) m/z calcd for $C_{22}H_{28}O_6Na^+$ $[M+Na]^+$ 411.1778, found 411.1784.

Methyl-2,6-di-*O*-benzyl-3-*O*-methyl-*β*-D-galactopyranoside (11a)



11a

General procedure for methylation was followed, the reaction was carried out with methyl-2,6-di-*O*-benzyl-α-D-galactopyranoside (28.2 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **11a** as white solid (32.7 mg, 84%).

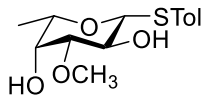
Data for 11a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45-7.16 (m, 10H), 4.85 (d, *J* = 11.2 Hz, 1H), 4.70 (d, *J* = 11.2 Hz, 1H), 4.59 (s, 2H), 4.27 (d, *J* = 7.7 Hz, 1H), 4.07 (d, *J* = 3.4 Hz, 1H), 3.82 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.74 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.55 (s, 3H), 3.50 (s, 3H), 3.24 (dd, *J* = 9.3, 3.4 Hz, 1H), 2.48 (br s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.9, 138.2, 128.6, 128.4, 128.0, 127.9, 127.9, 127.6, 104.8, 83.0, 79.1, 75.1, 73.9, 73.3, 69.4, 66.3, 58.3, 57.0.

HRMS (ESI) m/z calcd for $C_{22}H_{28}O_6Na^+$ $[M+Na]^+$ 411.1778, found 411.1790.

***p*-Tolyl-3-*O*-methyl-1-thio-*β*-L-fucopyranoside (12a)**



12a

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-1-thio-*β*-L-fucopyranoside (27.0 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum

ether: 1/1), afforded compound **12a** as white solid (21.0 mg, 74%).

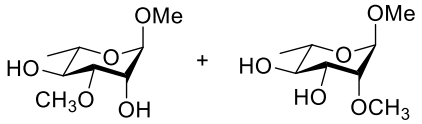
Data for 12a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52-7.41 (m, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 4.42 (d, *J* = 9.7 Hz, 1H), 3.87 (t, *J* = 3.2 Hz, 1H), 3.63-3.58 (m, 2H), 3.51 (s, 3H), 3.22 (dd, *J* = 9.0, 3.3 Hz, 1H), 2.46 (d, *J* = 1.9 Hz, 1H), 2.33 (s, 3H), 2.06 (d, *J* = 3.6 Hz, 1H), 1.38 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.5, 133.5, 129.9, 128.3, 88.7, 84.1, 74.8, 68.5, 68.4, 57.6, 21.3, 16.9.

HRMS (ESI) m/z calcd for $C_{14}H_{20}O_4SNa^+$ $[M+Na]^+$ 307.0975, found 307.0973.

Methyl-3-*O*-methyl-*α*-L-rhamnopyranoside (13a) and **Methyl-2-*O*-methyl-*α*-L-rhamnopyranoside (13b)**



13a **13b**

General procedure for methylation was followed, the reaction was carried out with methyl-α-L-rhamnopyranoside (35.6 mg, 0.2 mmol), trimethylsulfoxonium iodide **2e** (66 mg, 1.5 equiv), and K_2CO_3 (41.4 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (12.0 mg, 0.1 equiv), dissolved in 2.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/1), afforded a mixture of compound **13a** and **13b** as colorless oil (36.0 mg, 94%, **13a**/**13b** = 60/40).

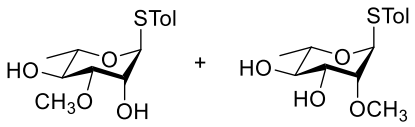
Data for 13a and **13b:**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.72 (s, 0.65H, for **13b** H-1), 4.70 (s, 0.98H, for **13a** H-1), 4.04 (dd, *J* = 3.3, 1.7 Hz, 1H), 3.72-3.59 (m, 2H), 3.59-3.47 (m, 2H), 3.45 (d, *J* = 1.5 Hz, 5.61H), 3.40-3.29 (m, 6.62H), 2.83 (br s, 1.23H), 2.74 (br s, 1.08H), 2.22 (br s, 1.60H), 1.30 (t, *J* = 6.1 Hz, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 100.6, 97.5, 81.5, 80.4, 73.9, 71.6, 71.6, 67.8, 66.9, 59.0, 57.1, 55.0, 54.9, 17.7, 17.6.

HRMS (ESI) m/z calcd for $C_8H_{16}O_5Na^+$ $[M+Na]^+$ 215.0890, found 215.0888.

***p*-Tolyl-3-*O*-methyl-1-thio-*α*-L-rhamnopyranoside (14a)** and ***p*-Tolyl-2-*O*-methyl-1-thio-*α*-L-rhamnopyranoside (14b)**



14a **14b**

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-1-thio-α-L-rhamnopyranoside (27 mg, 0.1 mmol), trimethylsulfoxonium iodide 2e (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/1), afforded a mixture of compound **14a** and **14b** as colorless oil (24.5 mg, 86%, **14a**/**14b** = 66/34).

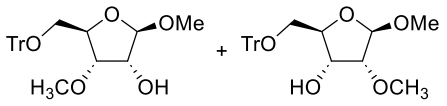
Data for 14a and **14b:**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42-7.29 (m, 2H), 7.19-7.02 (m, 2H), 5.54 (s, 0.34H, for **14b** H-1), 5.48 (s, 0.66H, for **14a** H-1), 4.33 (dd, *J* = 3.3, 1.5 Hz, 0.74H), 4.26-4.04 (m, 1H), 3.83-3.69 (m, 0.77H), 3.59 (t, *J* = 9.3 Hz, 0.81H), 3.50 (s, 1.94H), 3.44 (s, 1.09H), 2.58 (br s, 1.34H), 2.45 (br s, 0.70H), 2.33 (d, *J* = 1.9 Hz, 3H), 1.32 (dd, *J* = 6.2, 2.0 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 136.7, 131.1, 131.0, 129.2, 128.9, 86.8, 83.4, 80.7, 80.6, 73.3, 71.0, 70.9, 67.92, 67.87, 67.5, 57.0, 56.1, 20.1, 16.5, 16.4.

HRMS (ESI) m/z calcd for $C_{14}H_{20}O_4SNH_4^+$ $[M+ NH_4]^+$ 302.1421, found 302.1445.

Methyl-3-*O*-methyl-5-*O*-trityl-*β*-D-ribofuranoside (15a) and **Methyl-2-*O*-methyl-5-*O*-trityl-*β*-D-ribofuranoside (15b)**



15a **15b**

General procedure for methylation was followed, the reaction was carried out with methyl-5-*O*-trityl-β-D-ribofuranoside (40.6 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of

$Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded a mixture of compound **15a** and **15b** as colorless oil (38.4 mg, 91%, **15a**/**15b** =55/45).

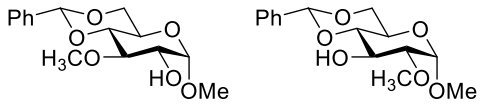
Data for 15a and **15b:**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61-7.41 (m, 6H), 7.39-7.12 (m, 9H), 4.94 (s, 0.45H, for **15b** H-1), 4.88 (s, 0.55H, for **15a** H-1),4.28-4.00 (m, 2H), 4.00-3.84 (m, 0.69H), 3.64 (d, *J* = 4.0 Hz, 0.47H), 3.50 (s, 1.39H), 3.37 (s, 1.34H), 3.34 (d, *J* = 9.8 Hz, 3.59H), 3.29 (dd, *J* = 5.7, 4.1 Hz, 0.77H), 3.19 (dt, *J* = 9.8, 4.8 Hz, 1H), 2.64 (d, *J* = 3.2 Hz, 0.59H), 2.47 (d, *J* = 8.0 Hz, 0.45H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.14, 144.10, 128.8, 128.7, 127.82, 127.79, 127.02, 126.97, 108.4, 105.2, 84.0, 83.4, 81.2, 80.5, 73.1, 71.5, 64.8, 64.5, 58.4, 55.3, 55.2.

HRMS (ESI) m/z calcd for $C_{26}H_{28}O_5Na^+$ $[M+Na]^+$ 443.1829, found 443.1835.

Methyl-3-*O*-methyl-4,6-*O*-benzylidene-α-D-glucopyranoside (16a) and **Methyl-2-*O*-methyl-4,6-*O*-benzylidene-α-D-glucopyranoside (16b)**



16a **16b**

General procedure for methylation was followed, the reaction was carried out with methyl-4,6-*O*-benzylidene-α-D-glucopyranoside (28.2 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **16a** as white solid (24.0 mg, 81%) and **16b** as white solid (2.7 mg, 9%).

Data for 16a:

^{1}H NMR (400 MHz, Chloroform-d) δ 7.56-7.31 (m, 5H), 5.55 (s, 1H), 4.80 (d, *J* = 3.8 Hz, 1H), 4.29 (dd, *J* = 9.9, 4.5 Hz, 1H), 3.82 (dt, *J* = 9.1, 3.6 Hz, 1H), 3.76 (d, *J* = 10.0

Hz, 1H), 3.66 (s, 3H), 3.65-3.60 (m, 1H), 3.61-3.54 (m, 2H), 3.46 (s, 3H), 2.41 (d, *J* = 7.5 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.5, 129.1, 128.4, 126.2, 101.4, 100.0, 82.2, 80.8, 72.4, 69.1, 62.7, 61.2, 55.6.

HRMS (ESI) m/z calcd for $C_{15}H_{20}O_6Na^+$ $[M+Na]^+$ 319.1152, found 319.1155.

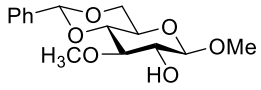
Data for 16b:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55-7.44 (m, 2H), 7.42-7.30 (m, 3H), 5.54 (s, 1H), 4.91 (d, *J* = 3.6 Hz, 1H), 4.29 (dd, *J* = 9.9, 4.5 Hz, 1H), 4.09 (t, *J* = 8.0 Hz, 1H), 3.82 (td, *J* = 9.7, 4.5 Hz, 1H), 3.74 (t, *J* = 10.1 Hz, 1H), 3.54 (s, 3H), 3.51 (d, *J* = 9.3 Hz, 1H), 3.45 (s, 3H), 3.31 (dd, *J* = 9.2, 3.6 Hz, 1H), 2.65 (s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.2, 129.4, 128.4, 126.5, 102.2, 98.0, 81.8, 81.4, 70.4, 69.2, 62.2, 58.9, 55.5.

HRMS (ESI) m/z calcd for $C_{15}H_{20}O_6Na^+$ $[M+Na]^+$ 319.1152, found 319.1154.

Methyl-3-*O*-methyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside 17a



17a

General procedure for methylation was followed, the reaction was carried out with methyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (28.2 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **17a** as white solid (19.2 mg, 65%).

Data for 17a:

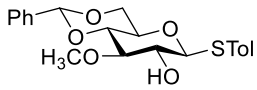
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52-7.46 (m, 2H), 7.40-7.34 (m, 3H), 5.55 (s, 1H), 4.40-4.31 (m, 2H), 3.79 (t, *J* = 10.3 Hz, 1H), 3.67 (s, 3H), 3.62 (dd, *J* = 10.3, 7.8 Hz, 1H), 3.58 (s, 3H), 3.52-3.39 (m, 3H), 2.71 (br s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.3, 129.1, 128.4, 126.2, 104.3, 101.4, 82.4,

81.7, 74.2, 68.8, 66. 5, 61.1, 57.5.

HRMS (ESI) m/z calcd for $C_{15}H_{20}O_6Na^+$ $[M+Na]^+$ 319.1152, found 319.1142.

***p*-Tolyl-3-*O*-methyl-4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (18a)**



18a

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (37.4 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (33.0 mg, 1.5 equiv), and K_2CO_3 (20.7 mg, 1.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 6 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **18a** as white solid (30.3 mg, 78%).

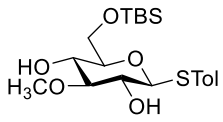
Data for 18a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58-7.41 (m, 4H), 7.40-7.30 (m, 3H), 7.14 (d, *J* = 7.8 Hz, 2H), 5.53 (s, 1H), 4.57 (d, *J* = 8.7 Hz, 1H), 4.37 (dd, *J* = 10.5, 4.8 Hz, 1H), 3.77 (t, *J* = 10.1 Hz, 1H), 3.66 (s, 3H), 3.60-3.31 (m, 4H), 2.70 (s, 1H), 2.35 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.9, 137.3, 133.9, 123.0, 129.1, 128.4, 127.4, 126.2, 101.4, 88.8, 83.7, 81.4, 72.2, 70.8, 68.8, 61.2, 21.3.

HRMS (ESI) m/z calcd for $C_{21}H_{24}O_5SNa^+$ $[M+Na]^+$ 411.1237, found 411.1234.

***p*-Tolyl-3-*O*-methyl-6-*O*-(tert-butyldimethylsilyl)-1-thio-*β*-D-glucopyranoside (19a)**



19a

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-6-*O*-(tert-butyldimethylsilyl)-1-thio-*β*-D-glucopyranoside (40.0 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF

(4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/2), afforded compound **19a** as colorless oil (17.8 mg, 43%).

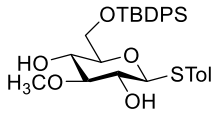
Data for 19a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49-7.34 (m, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 4.45 (d, *J* = 9.5 Hz, 1H), 3.93 (dd, *J* = 10.6, 4.8 Hz, 1H), 3.83 (dd, *J* = 10.5, 5.4 Hz, 1H), 3.67 (s, 3H), 3.55 (t, *J* = 9.1 Hz, 1H), 3.38 (m, 1H), 3.32 (t, *J* = 9.2 Hz, 1H), 3.24-3.11 (m, 2H), 2.50 (br s, 1H), 2.33 (s, 3H), 0.91 (s, 9H), 0.10 (d, *J* = 2.4 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.6, 133.6, 129.9, 127.8, 88.6, 87.0, 78.6, 72.4, 71.9, 64.6, 61.1, 26.0, 21.3, 18.4, -5.3.

HRMS (ESI) m/z calcd for $C_{20}H_{34}O_5SSiNa^+$ $[M+Na]^+$ 437.1788, found 437.1797.

***p*-Tolyl-3-*O*-methyl-6-*O*-(tert-butyldiphenylsilyl)-1-thio-*β*-D-glucopyranoside (20a)**



20a

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-6-*O*-(tert-butyldimethylsilyl)-1-thio-*β*-D-glucopyranoside (52.5 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/2), afforded compound **20a** as pale oil (31.3 mg, 58%).

Data for 20a:

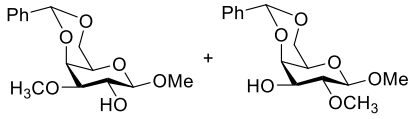
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 7.7 Hz, 4H), 7.54-7.31 (m, 8H), 7.05 (d, *J* = 7.7 Hz, 2H), 4.44 (d, *J* = 9.6 Hz, 1H), 3.94 (d, *J* = 4.4 Hz, 2H), 3.65 (d, *J* = 15.5 Hz, 4H), 3.48-3.40 (m, 1H), 3.35 (t, *J* = 9.2 Hz, 1H), 3.20 (t, *J* = 8.8 Hz, 1H), 2.84 (s, 1H), 2.49 (s, 1H), 2.31 (s, 3H), 1.07 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.6, 135.8, 135.8, 133.6, 133.1, 133.1, 129.97,

129.92, 127.9, 127.6, 88.5, 87.1, 79.3, 72.0, 71.2, 64.5, 61.1, 27.0, 21.3, 19.4.

HRMS (ESI) m/z calcd for $C_{30}H_{38}O_5SSiNa^+$ $[M+Na]^+$ 561.2101, found 561.2100.

Methyl-3-*O*-methyl-4,6-*O*-benzylidene-*β*-D-galactopyranoside (21a) and **Methyl-2-*O*-methyl-4,6-*O*-benzylidene-*β*-D-galactopyranoside (21b)**



21a **21b**

General procedure for methylation was followed, the reaction was carried out with methyl-4,6-*O*-benzylidene-*β*-D-galactopyranoside (28.2 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **21a** as white solid (13.0 mg, 44%) and **21b** as white solid (11.0 mg, 37%,).

Data for 21a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56-7.46 (m, 2H), 7.40-7.29 (m, 3H), 5.55 (s, 1H), 4.41-4.30 (m, 2H), 4.27 (d, *J* = 7.8 Hz, 1H), 4.10 (dd, *J* = 12.4, 1.9 Hz, 1H), 3.93 (dd, *J* = 9.7, 7.7 Hz, 1H), 3.59 (s, 3H), 3.52 (s, 3H), 3.44 (q, *J* = 1.5 Hz, 1H), 3.32 (dd, *J* = 9.7, 3.6 Hz, 1H), 2.50 (s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.8, 129.2, 128.3, 126.6, 104.1, 101.5, 81.4, 72.3, 70.2, 69.6, 66.9, 57.3, 57.2.

HRMS (ESI) m/z calcd for $C_{15}H_{20}O_6Na^+$ $[M+Na]^+$ 319.1152, found 319.1151.

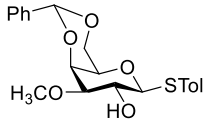
Data for 21b:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59-7.46 (m, 2H), 7.43-7.32 (m, 3H), 5.56 (s, 1H), 4.34 (dd, *J* = 12.4, 1.4 Hz, 1H), 4.26-4.18 (m, 2H), 4.08 (dd, *J* = 12.4, 1.8 Hz, 1H), 3.66 (d, *J* = 3.8 Hz, 1H), 3.63 (s, 3H), 3.58 (s, 3H), 3.49-3.40 (m, 1H), 3.32 (dd, *J* = 9.6, 7.8 Hz, 1H), 2.55 (d, *J* = 7.9 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.7, 129.4, 128.4, 126.6, 104.6, 101.6, 80.9, 75.6, 72.8, 69.3, 66.6, 61.1, 57.1.

HRMS (ESI) m/z calcd for $C_{15}H_{20}O_6Na^+$ $[M+Na]^+$ 319.1152, found 319.1155.

***p*-Tolyl-3-*O*-methyl-4,6-*O*-benzylidene-1-thio-*β*-D-galactopyranoside (22a)**



22a

General procedure for methylation was followed, the reaction was carried out with *p*-tolyl-4,6-*O*-benzylidene-1-thio-*β*-D-galactopyranoside (37.4 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **22a** as white solid (22.9 mg, 59%).

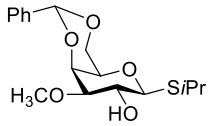
Data for 22a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63-7.54 (m, 2H), 7.44-7.29 (m, 5H), 7.07 (d, *J* = 7.8 Hz, 2H), 5.50 (s, 1H), 4.49 (d, *J* = 9.4 Hz, 1H), 4.38 (dd, *J* = 12.3, 1.6 Hz, 1H), 4.30 (dd, *J* = 3.4, 1.1 Hz, 1H), 4.03 (dd, *J* = 12.4, 1.7 Hz, 1H), 3.80 (t, *J* = 9.4 Hz, 1H), 3.56-3.45 (m, 4H), 3.32 (dd, *J* = 9.3, 3.3 Hz, 1H), 2.50 (s, 1H), 2.34 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.6, 137.9, 134.6, 129.8, 129.2, 128.2, 126.8, 126.6, 101.4, 87.3, 82.5, 72.6, 70.2, 69.6, 67.3, 57.6, 21.4.

HRMS (ESI) m/z calcd for $C_{21}H_{24}O_5SNa^+$ $[M+Na]^+$ 411.1237, found 411.1234.

Isopropyl-3-*O*-methyl-4,6-*O*-benzylidene-1-thio-*β*-D-galactopyranoside (23a)



23a

General procedure for methylation was followed, the reaction was carried out with isopropyl-4,6-*O*-benzylidene-1-thio-*β*-D-galactopyranoside (32.6 mg, 0.1 mmol), trimethylsulfoxonium iodide **2e** (44.0 mg, 2.0 equiv), and K_2CO_3 (34.5 mg, 2.5 equiv) in the presence of $Fe(dipm)_3$ (6.0 mg, 0.1 equiv), dissolved in 1.0 mL of dry ACN/DMF (4/1) at 80°C for 12 h. The reaction mixture was directly purified by flash column chromatography (ethyl acetate/petroleum ether: 1/3), afforded compound **23a** as white

solid (13.6 mg, 40%).

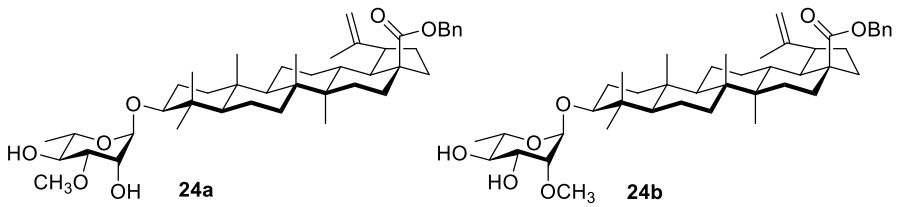
Data for 23a:

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55-7.45 (m, 2H), 7.41-7.29 (m, 3H), 5.53 (s, 1H), 4.44 (d, *J* = 9.6 Hz, 1H), 4.38-4.29 (m, 2H), 4.04 (dd, *J* = 12.4, 1.8 Hz, 1H), 3.97 (t, *J* = 8.0 Hz, 1H), 3.54 (s, 3H), 3.46 (q, *J* = 1.6 Hz, 1H), 3.36-3.25 (m, 2H), 2.57 (s, 1H), 1.39 (d, *J* = 6.7 Hz, 3H), 1.35 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.9, 129.2, 128.3, 126.6, 101.6, 85.8, 82.6, 72.9, 70.3, 69.7, 68.6, 57.5, 34.8, 24.7, 24.2.

HRMS (ESI) m/z calcd for $C_{17}H_{24}O_5SNa^+$ $[M+Na]^+$ 363.1237, found 363.1238.

3-*O*-(3-*O*-Methyl-*α*-L-rhamnopyranosyl)-28-*O*-benzyl Betulinate (24a) and 3-*O*-(2-*O*-Methyl-*α*-L-rhamnopyranosyl)-28-*O*-benzyl Betulinate (24b)



Compound **24** (0.05 mmol, 34.6 mg), K_2CO_3 (2.5 equiv., 17.3 mg) and $Fe(dipm)_3$ (0.1 equiv., 3.0 mg) were dissolved in 1.0 mL of dry DMF. Subsequently, trimethylsulfoxonium iodide (2.0 equiv., 22.0 mg) was added, and the mixture was stirred vigorously at 80℃ for 10 h. Once the reaction was complete, the reaction mixture was concentrated *in vacuo* and the crude residue was purified by column chromatography on silica gel to provide the desired products, afforded a mixture of compound **24a** and **24b** as white solid (20.0 mg, 56.7%, **24a**/**24b** = 58/42).

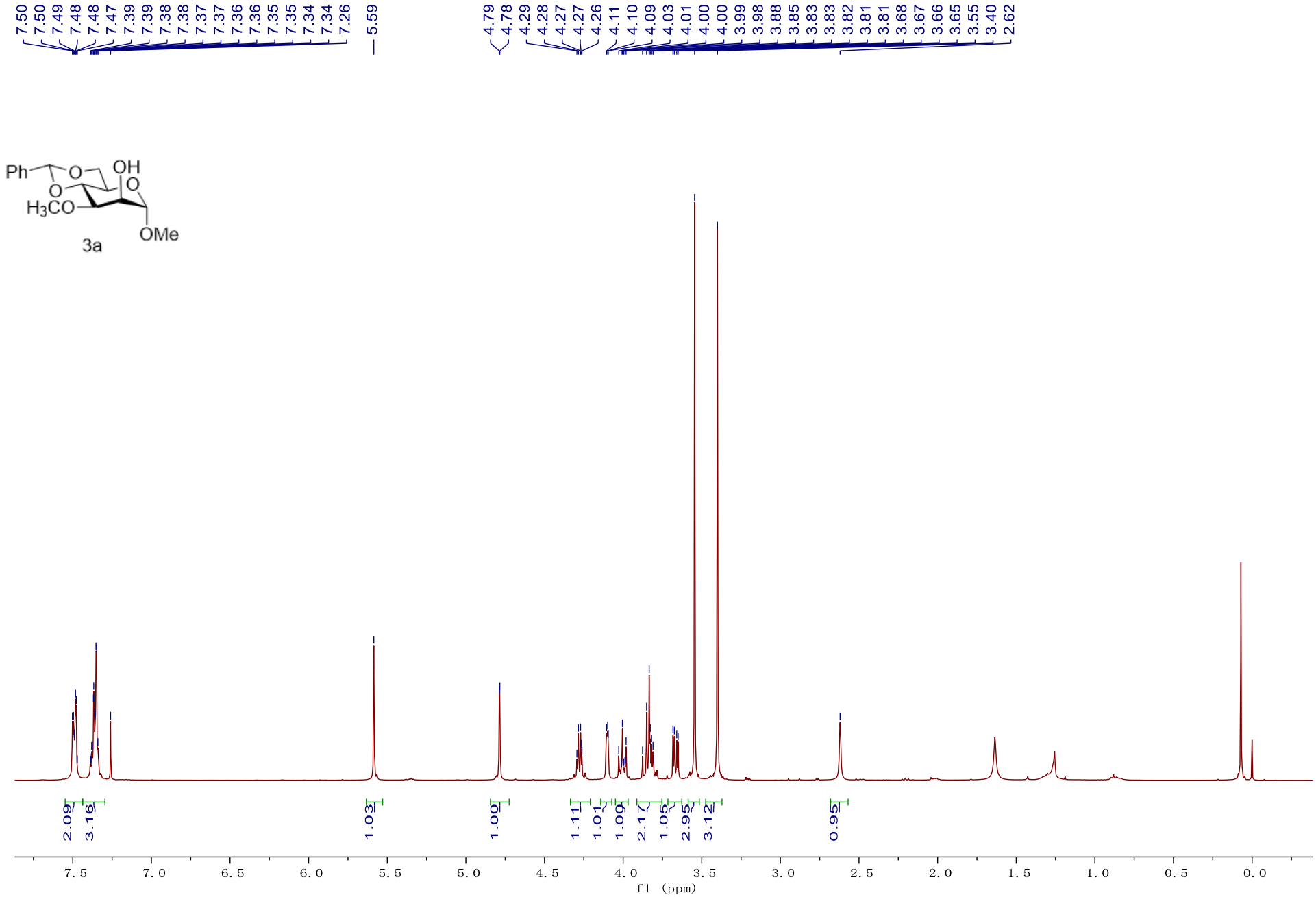
Upon comparison, the NMR data of these compounds is consistent with the reported literature.[1] Additionally, in most instances, the 1H and 13C NMR chemical shifts of the two compounds are listed here. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 4.86 (s, 0.58H, for **24a**), 4.88 (s, 0.42H, for **24b**), 3.47 (s, 1.75H, for **24a**), 3.45 (s, 1.23H, for **24b**). **^{13}C NMR** (101 MHz, Chloroform-*d*) for **24a**: δ 175.97, 89.49, 81.61, 72.01, 28.36, 17.61; for **24b**: δ 175.96, 89.64, 80.70, 71.83, 28.28, 17.52.

8. Reference

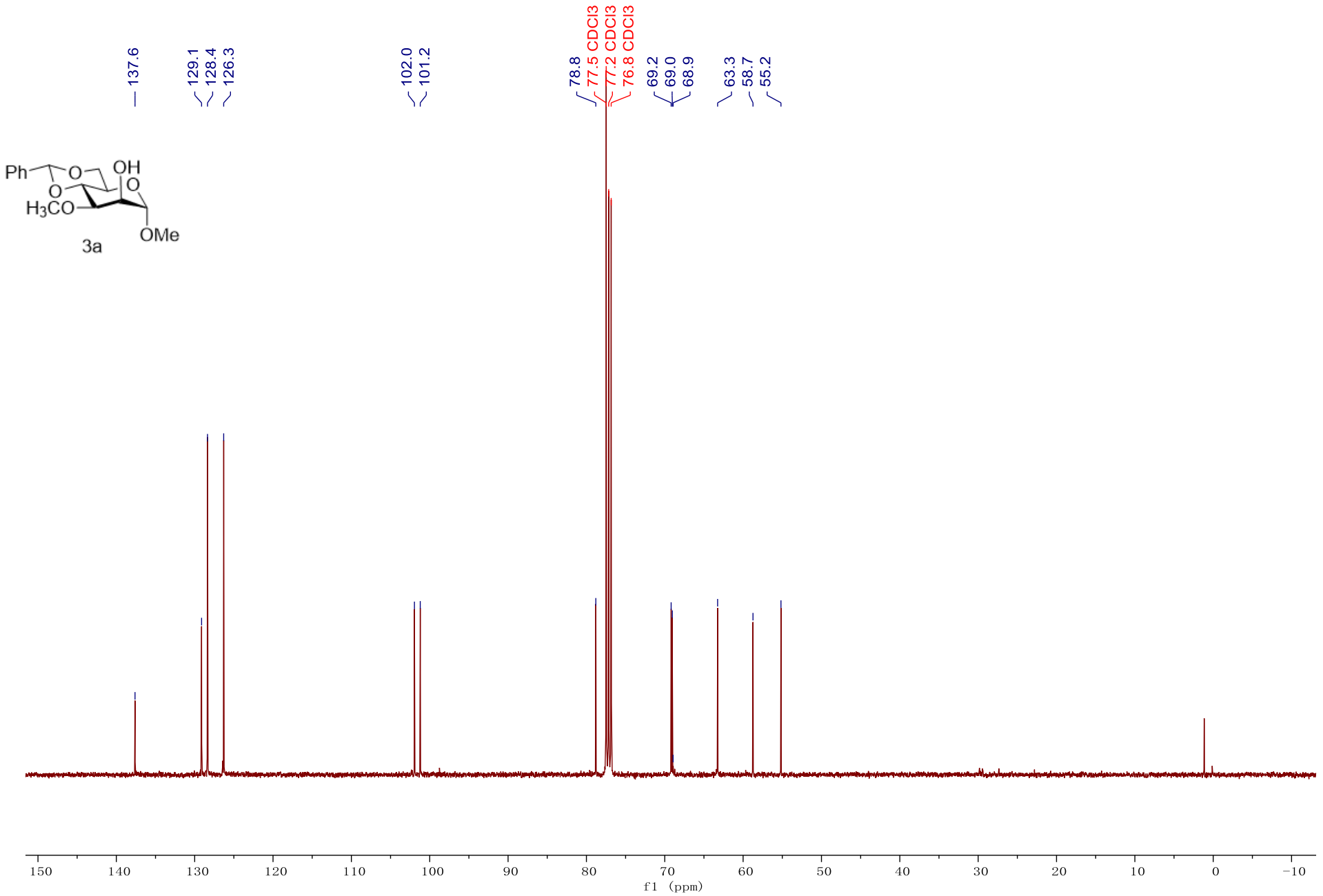
P. Gormand, A. Pichette, J. Legault and J. Alsarraf. *ACS Omega*, 2023, **8**, 36118−36125.

9. Copies of NMR Spectra

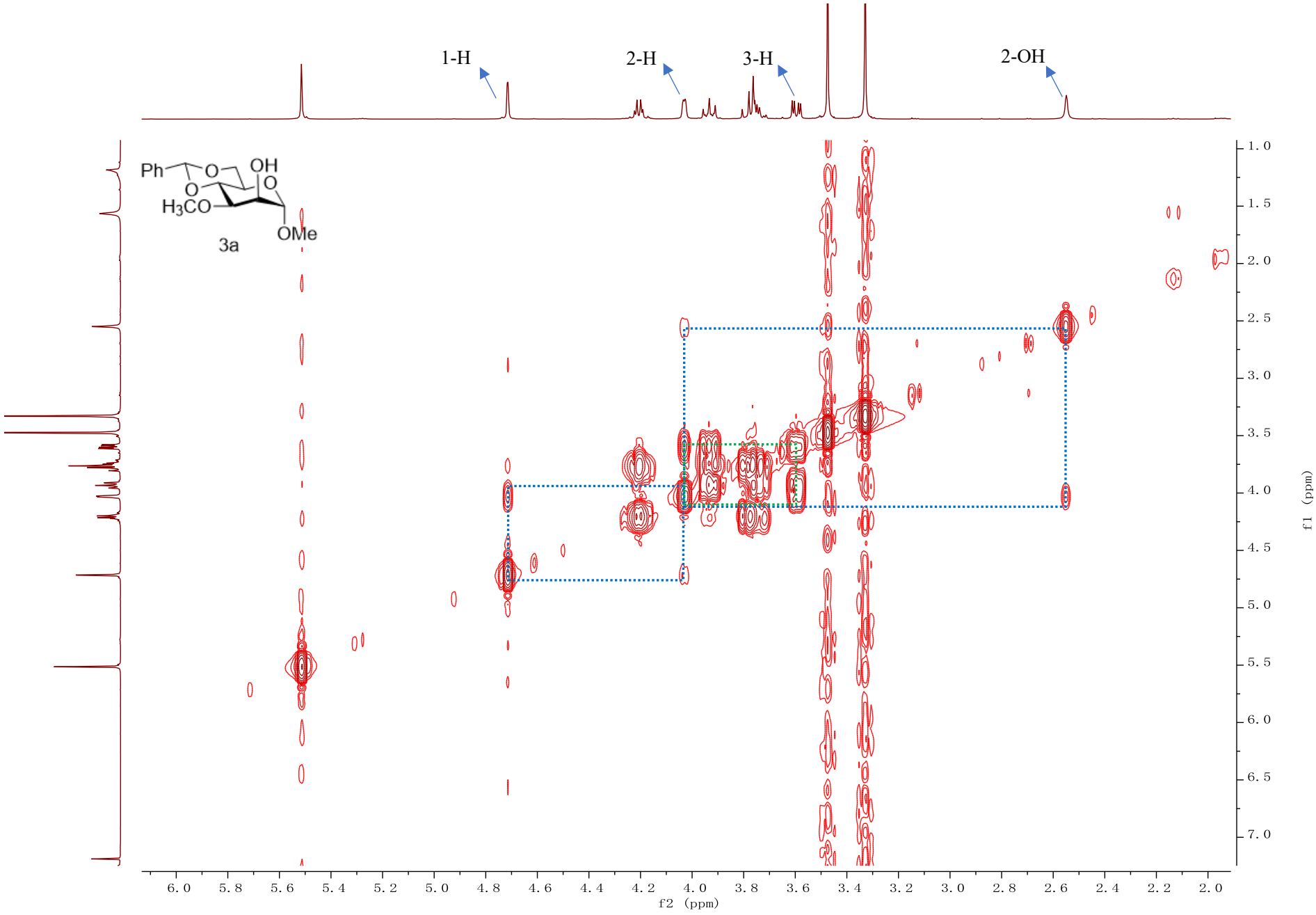
^{1}H-NMR of compound **3a** ($CDCl_3$)



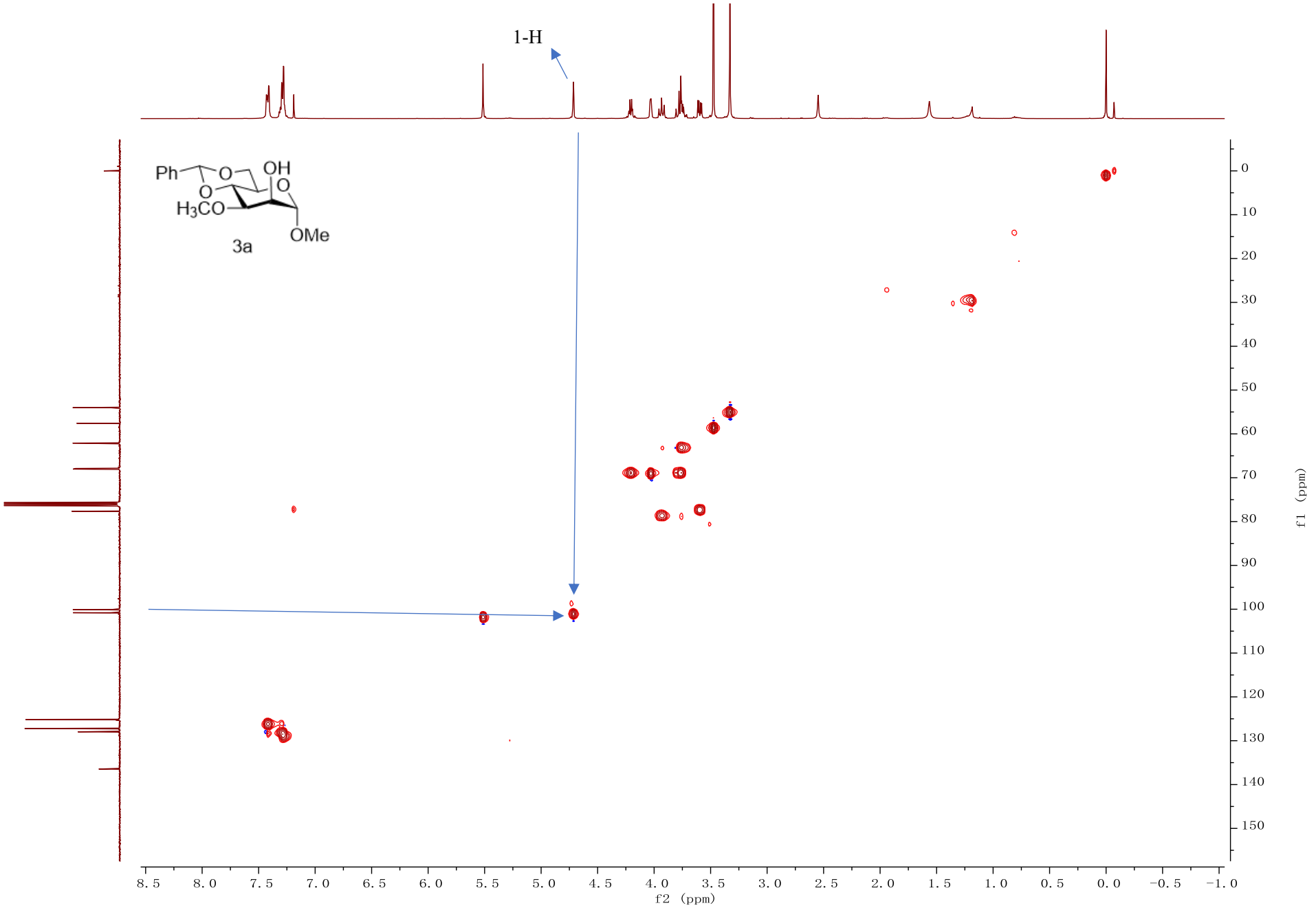
^{13}C-NMR of compound **3a** ($CDCl_3$)



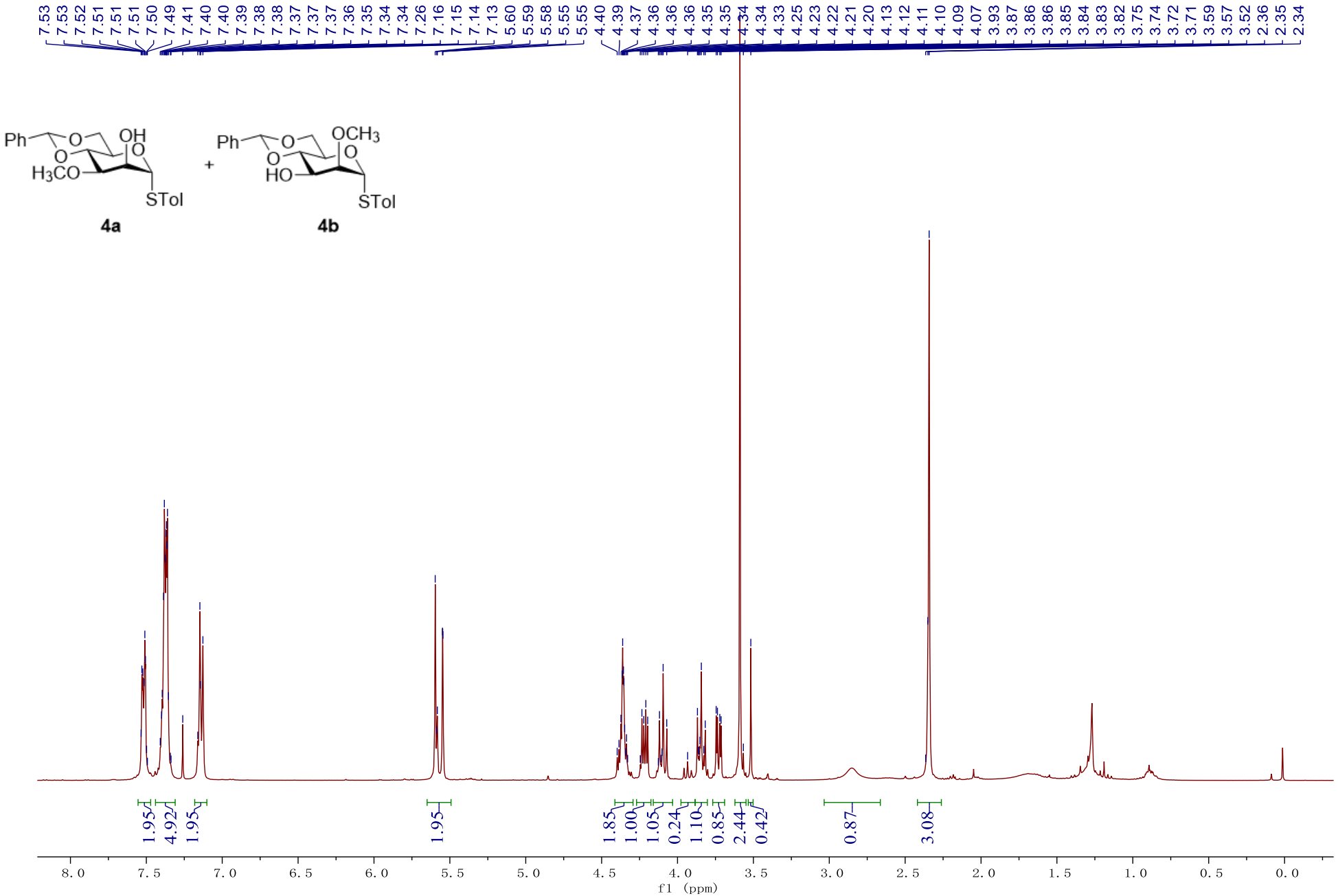
2D-COSY of compound **3a** ($CDCl_3$)



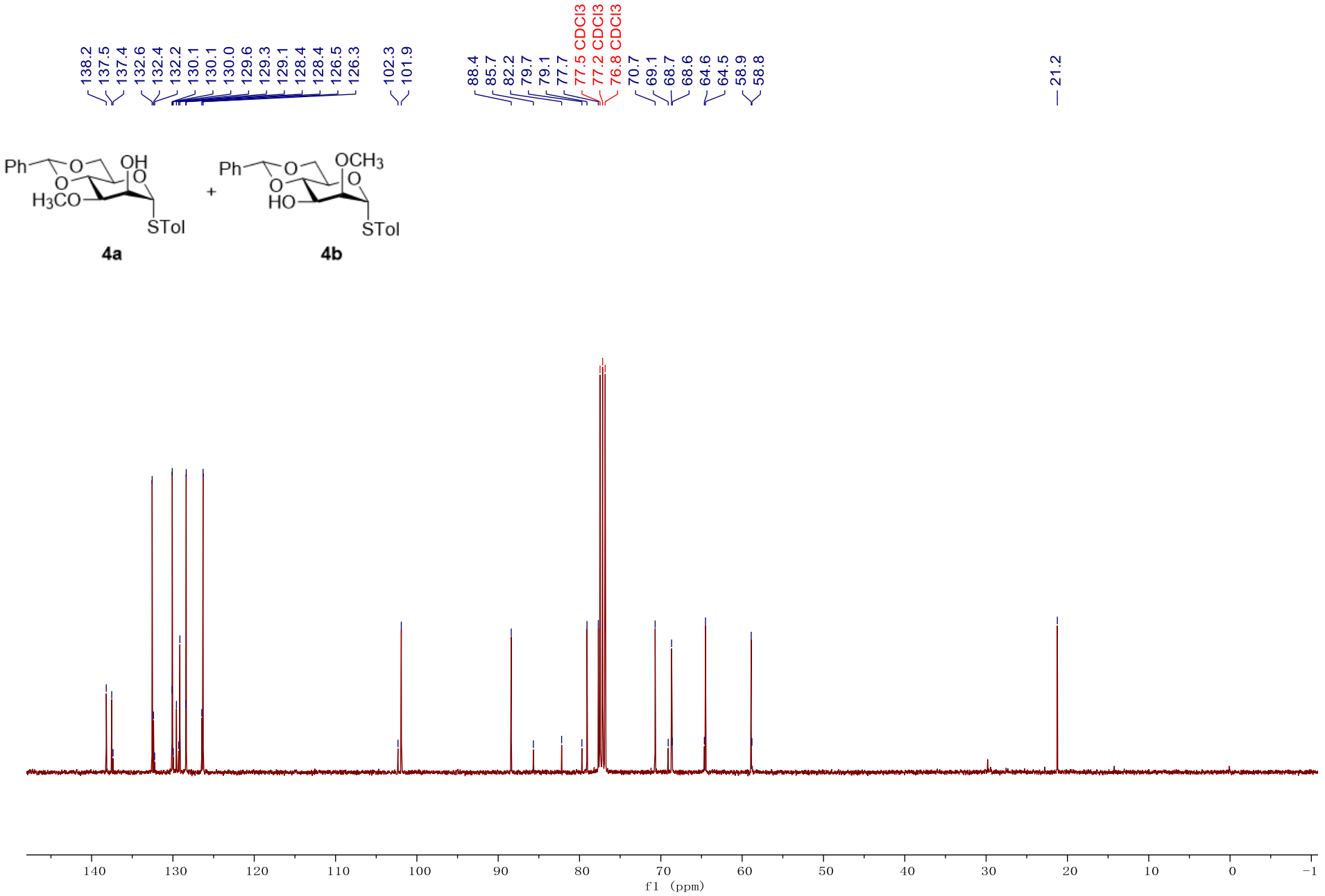
2D-HSQC of compound **3a** ($CDCl_3$)



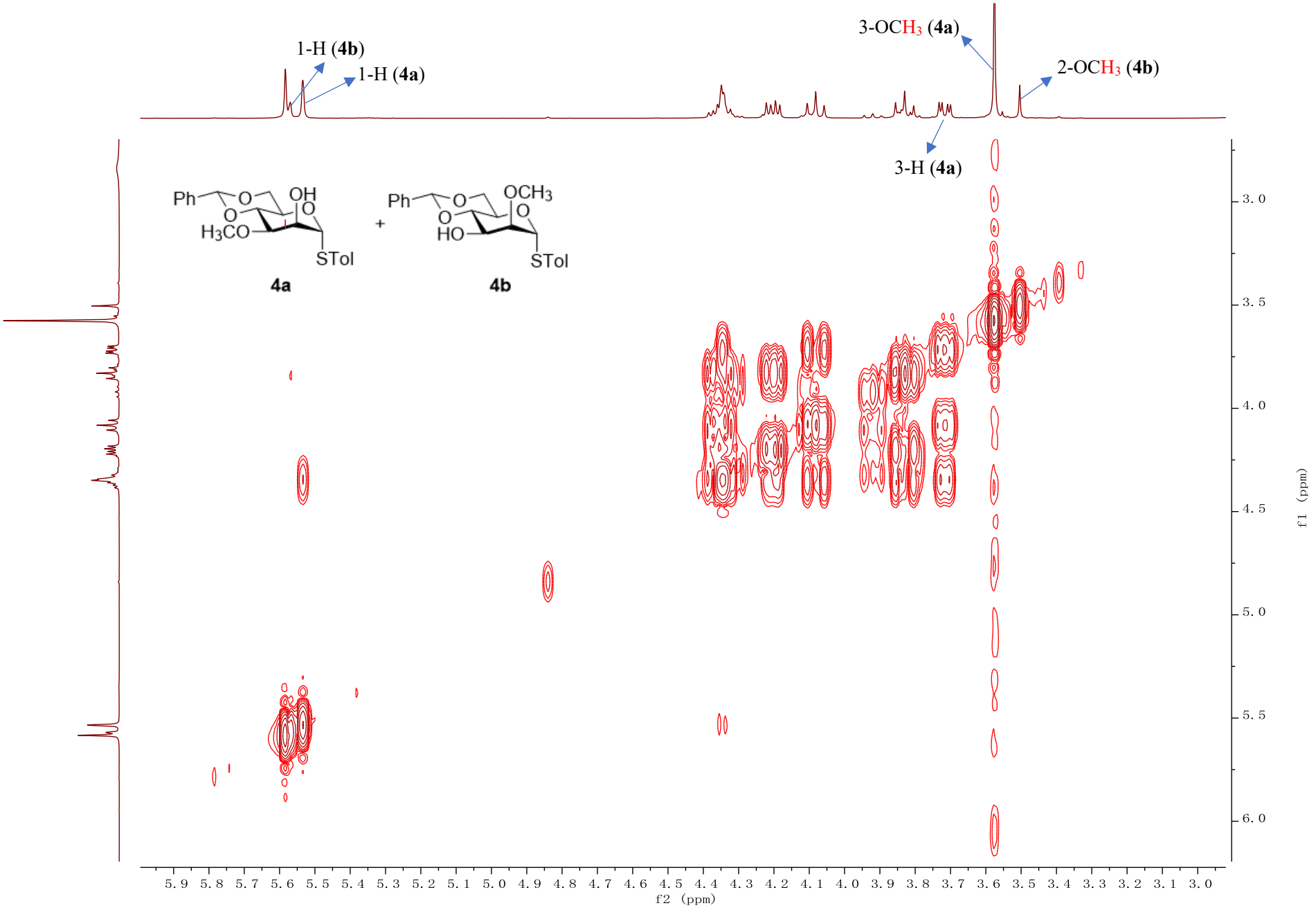
^{1}H-NMR of compound **4a** and **4b** ($CDCl_3$)



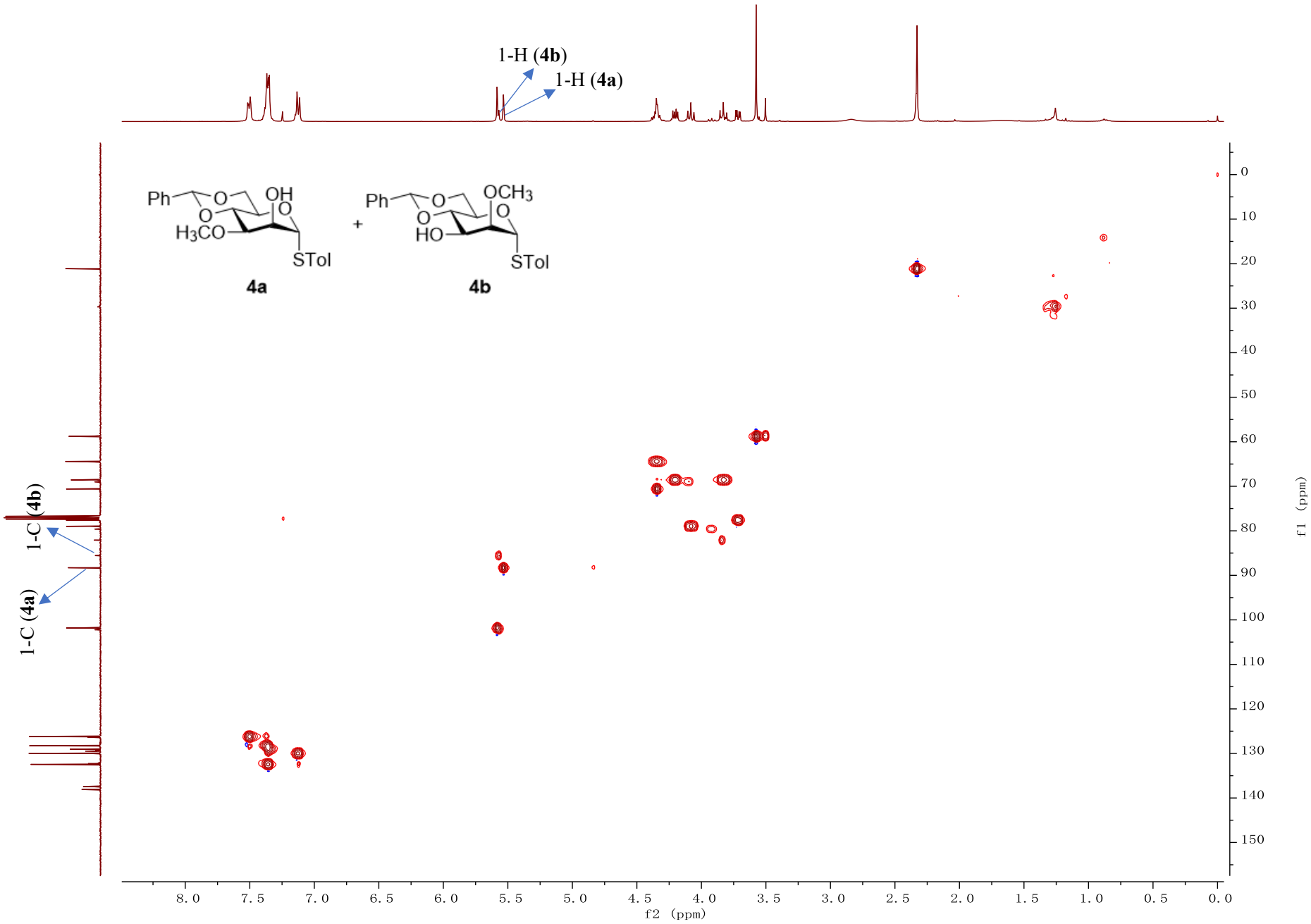
^{13}C-NMR of compound **4a** and **4b** ($CDCl_3$)



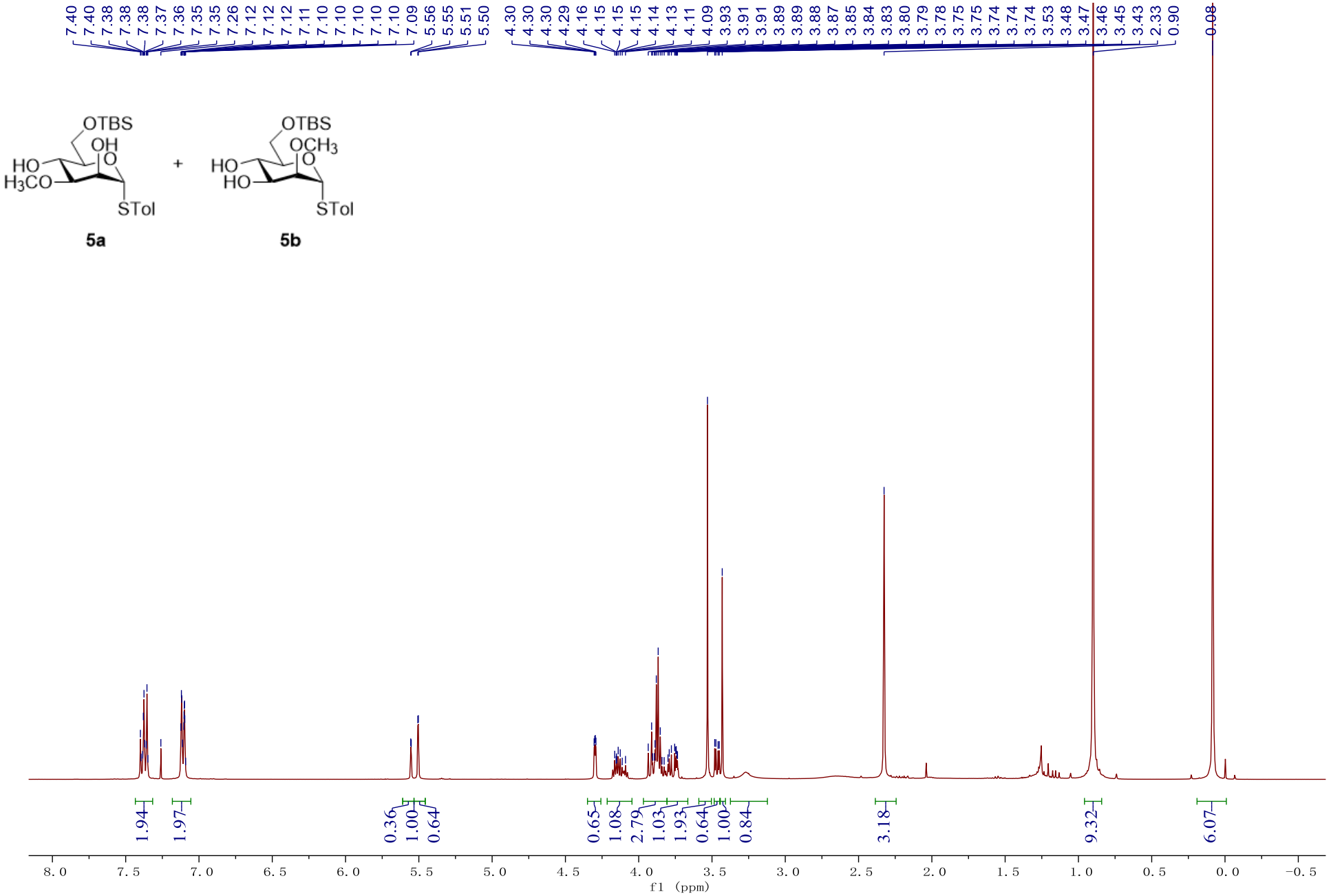
2D-COSY of compound **4a** and **4b** ($CDCl_3$)



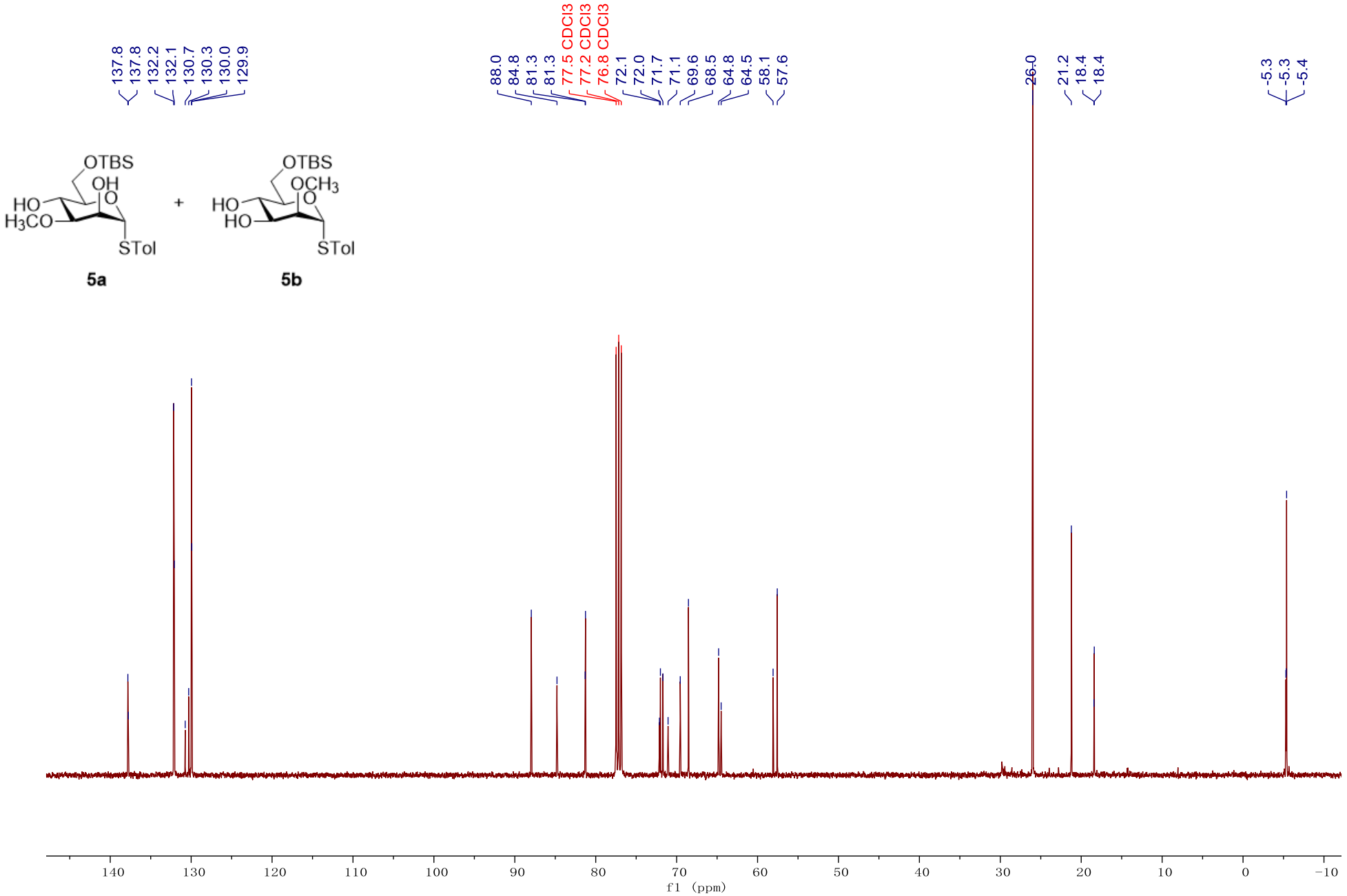
2D-HSQC of compound **4a** and **4b** ($CDCl_3$)



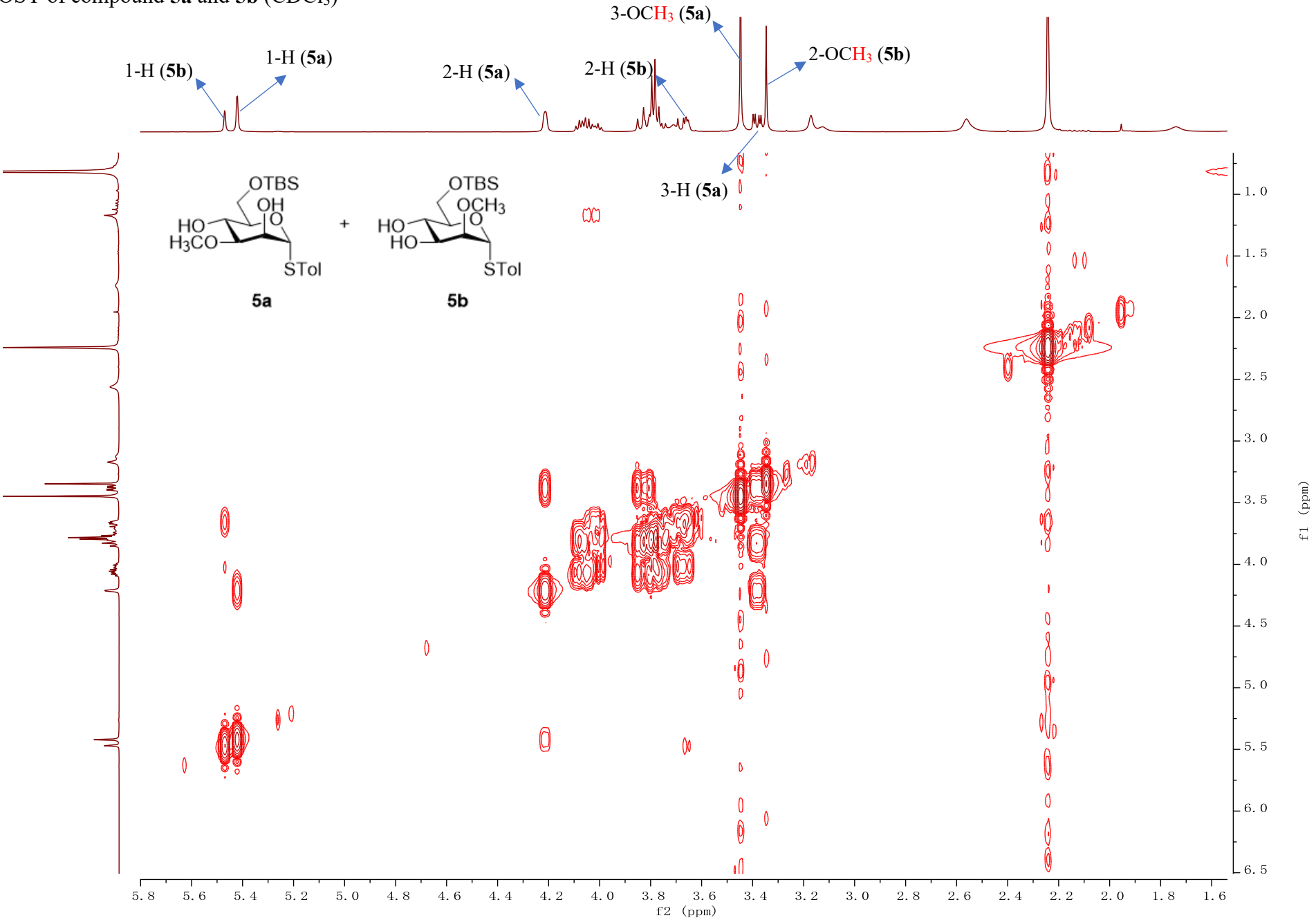
^{1}H-NMR of compound **5a** and **5b** ($CDCl_3$)



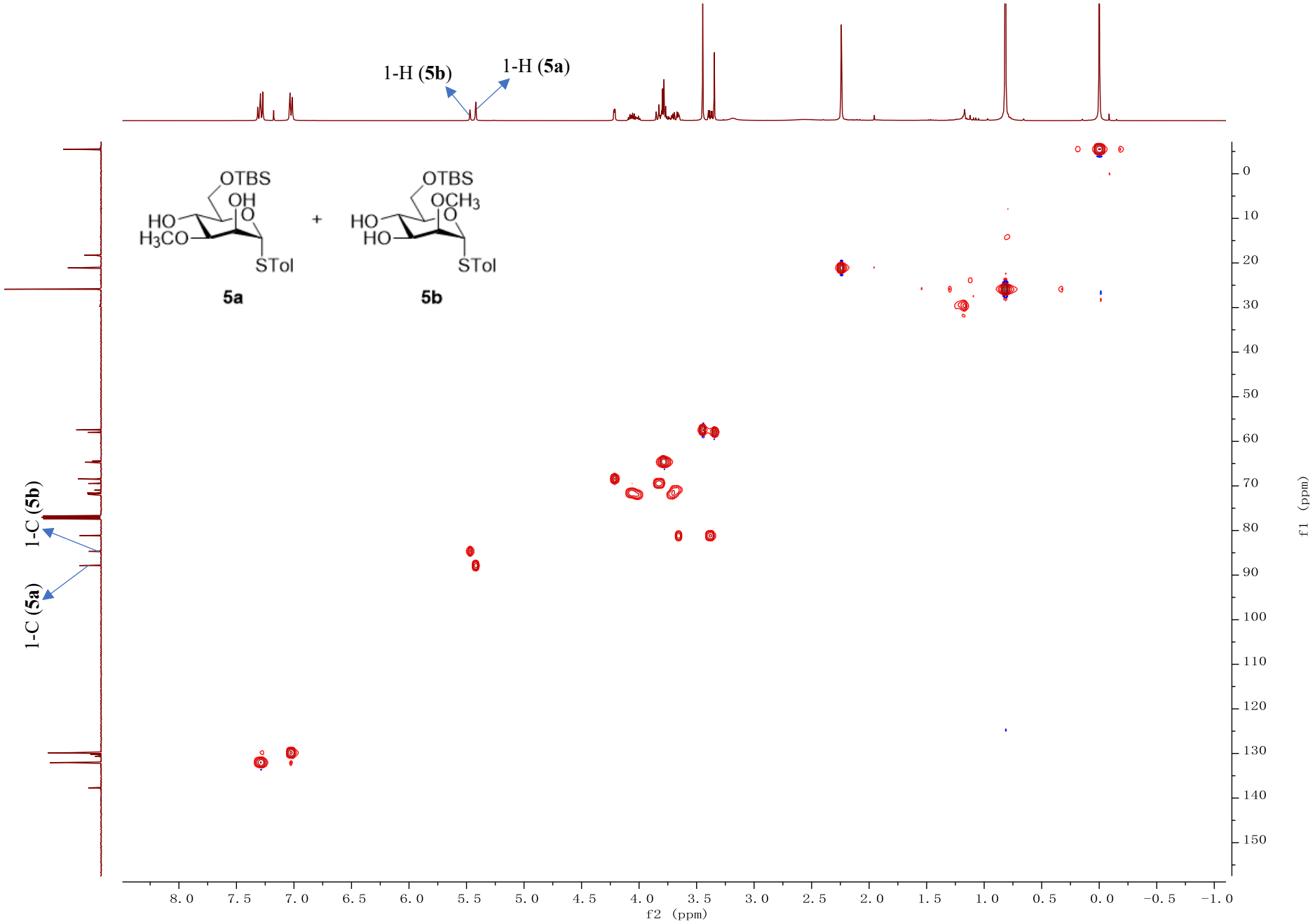
^{13}C-NMR of compound **5a** and **5b** ($CDCl_3$)



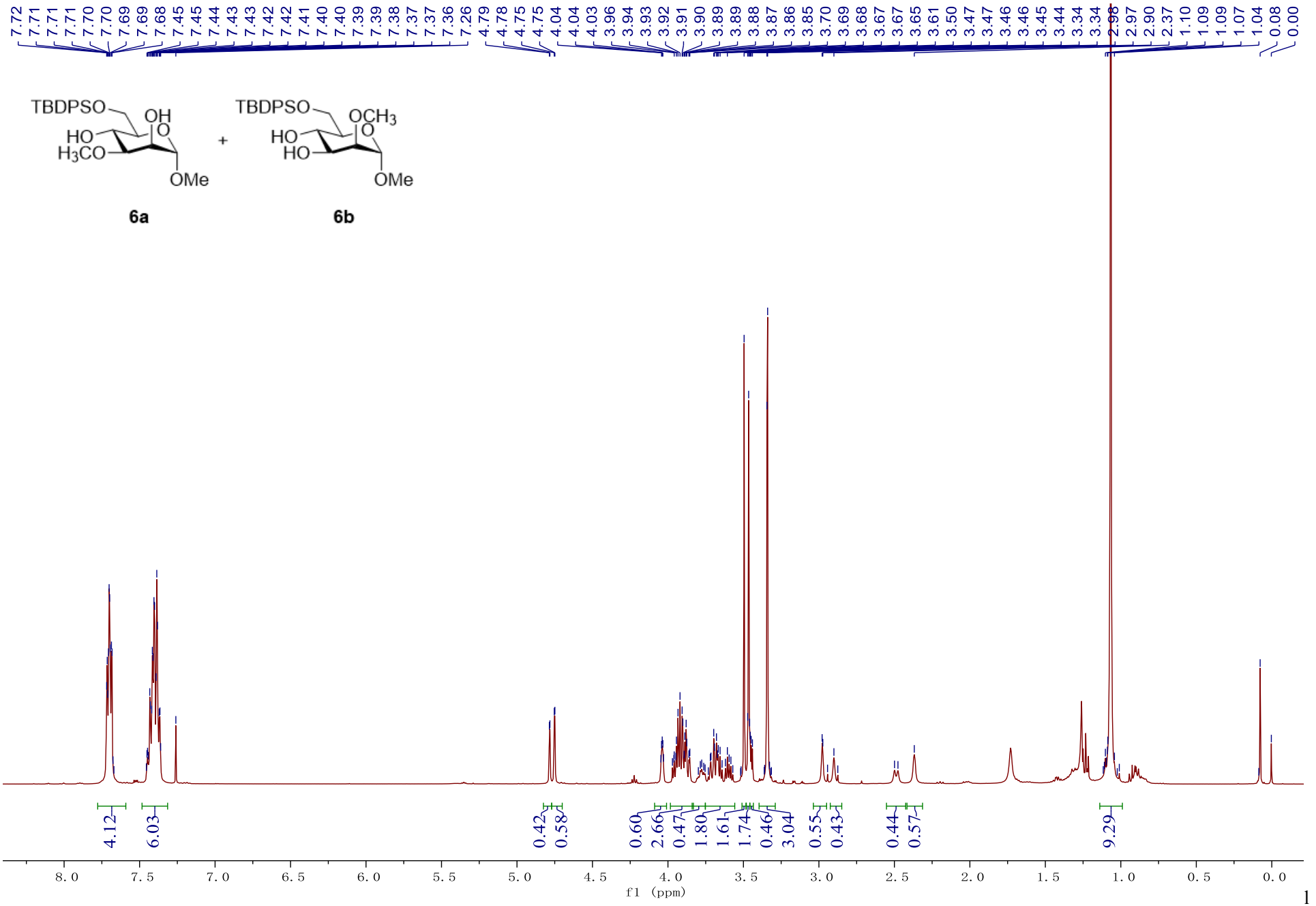
2D-COSY of compound **5a** and **5b** ($CDCl_3$)



2D-HSQC of compound **5a** and **5b** ($CDCl_3$)

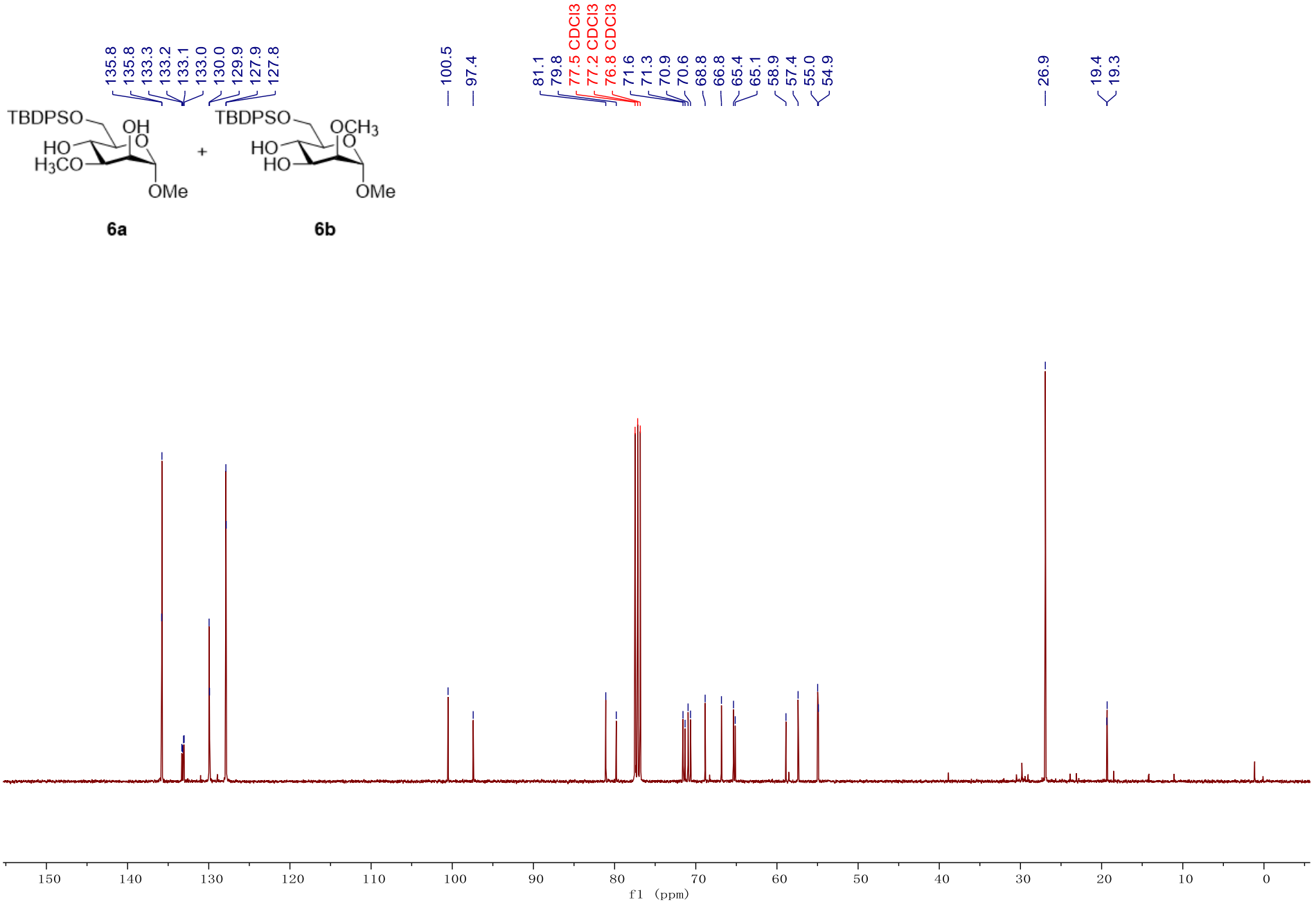


^{1}H-NMR of compound **6a** and **6b** ($CDCl_3$)

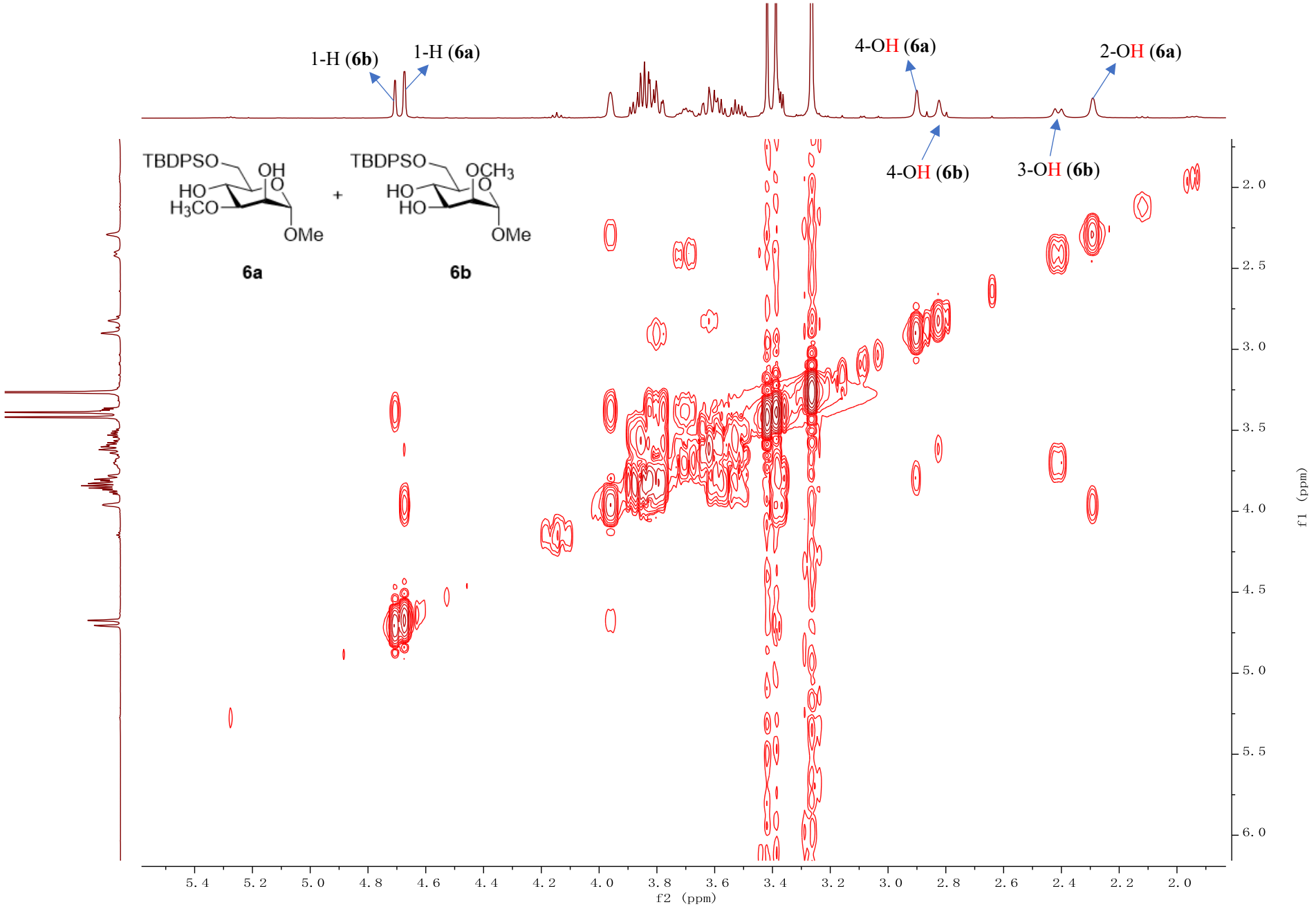


1

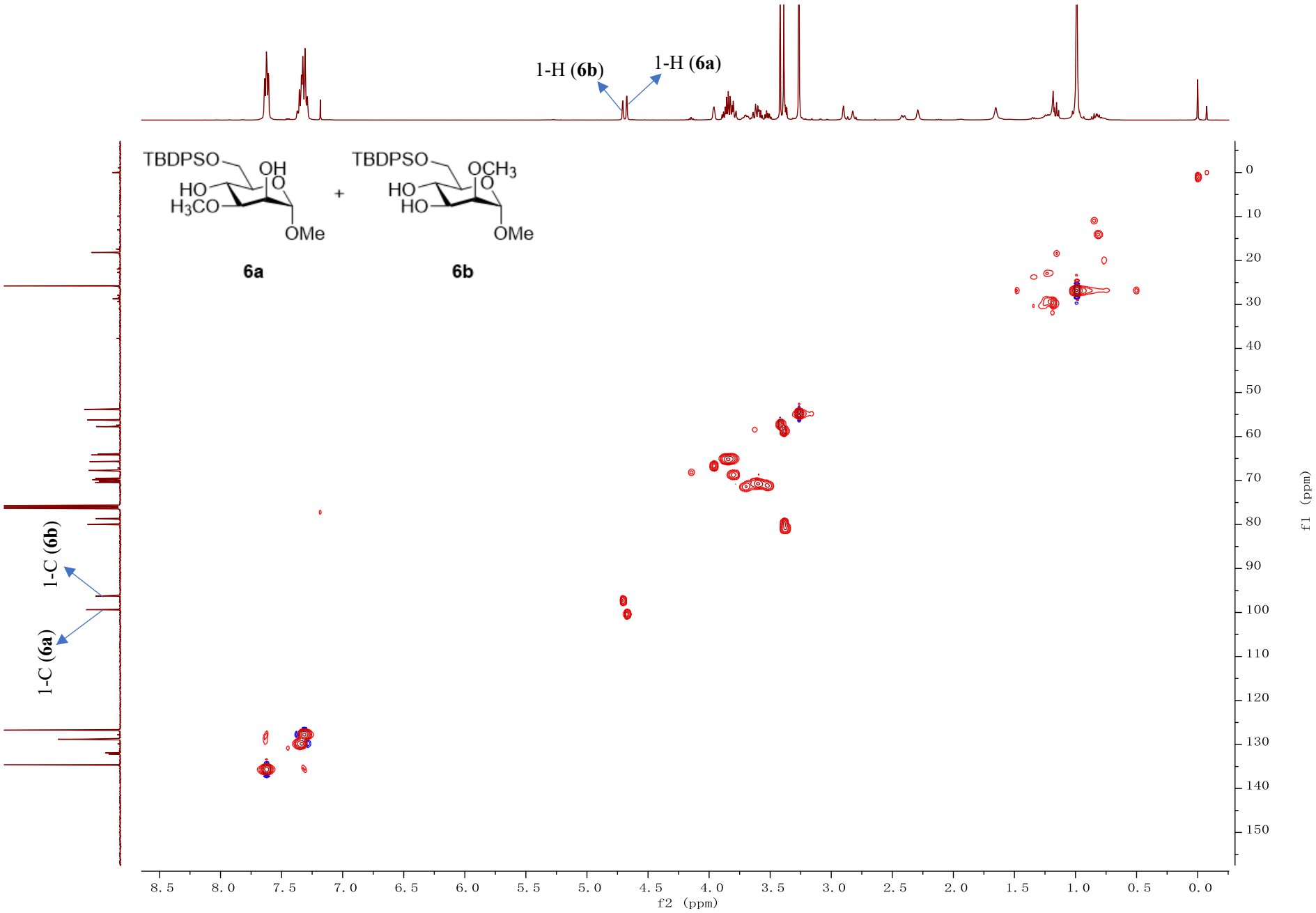
^{13}C-NMR of compound **6a** and **6b** ($CDCl_3$)



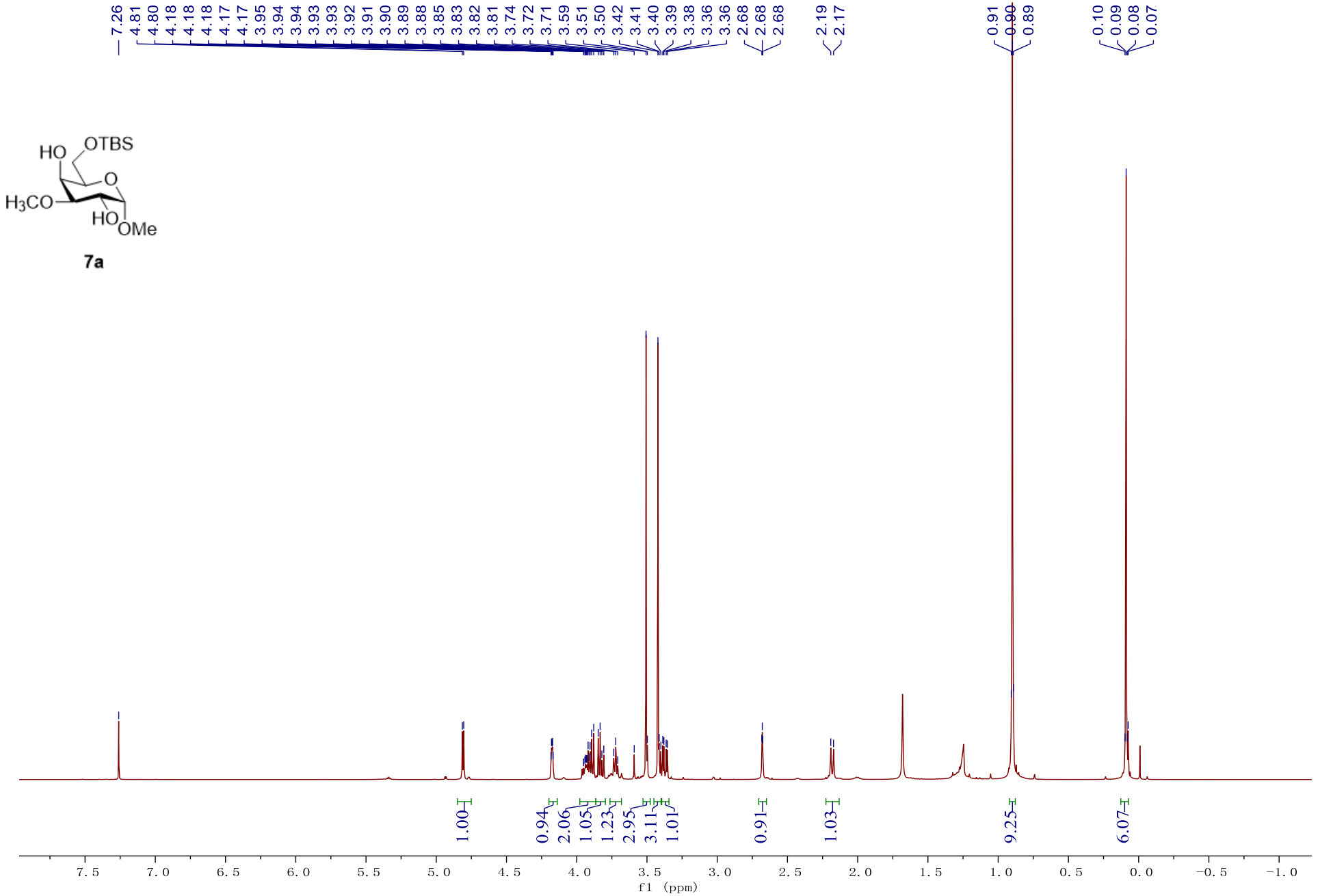
2D-COSY of compound **6a** and **6b** ($CDCl_3$)



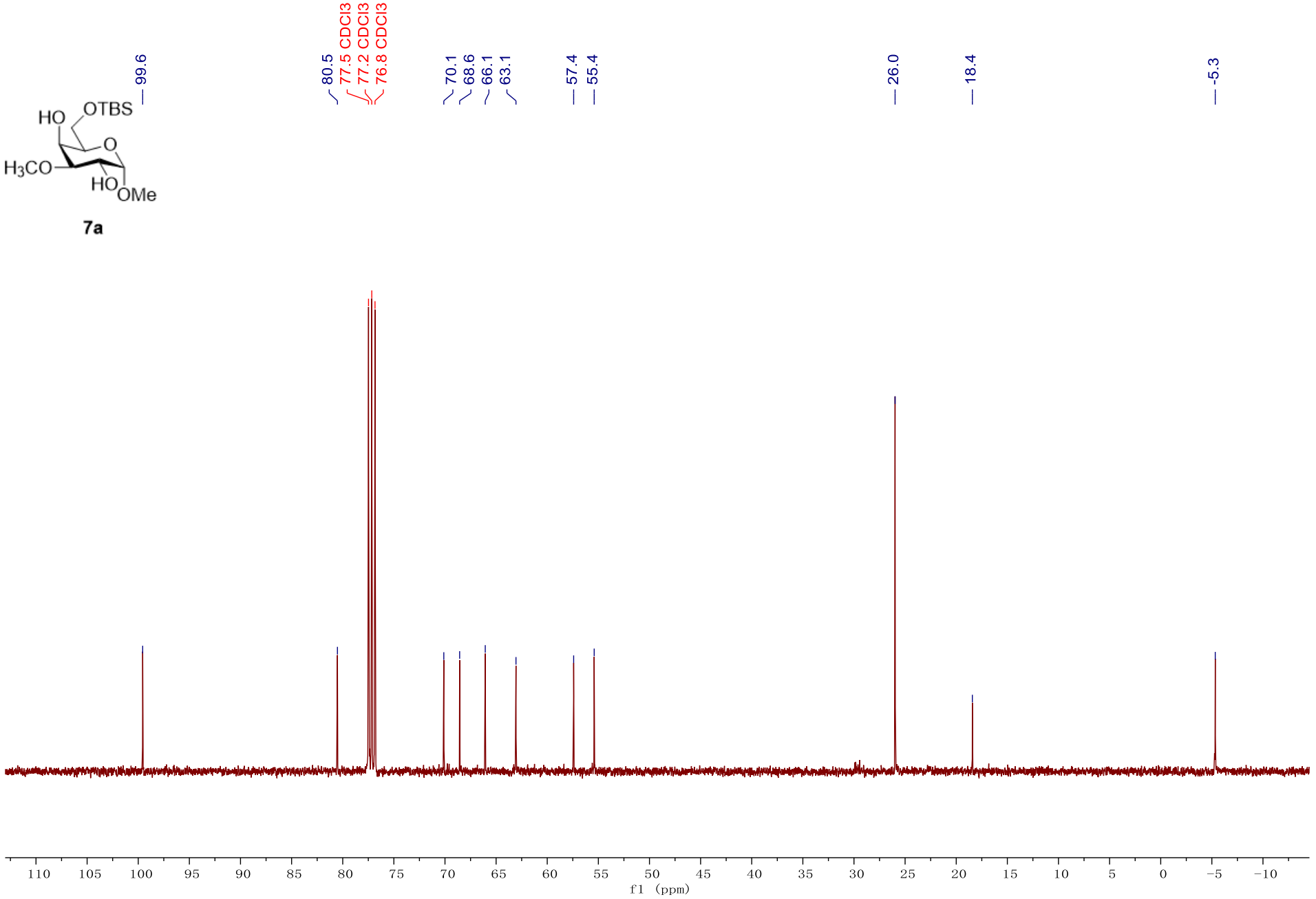
2D-HSQC of compound **6a** and **6b** ($CDCl_3$)



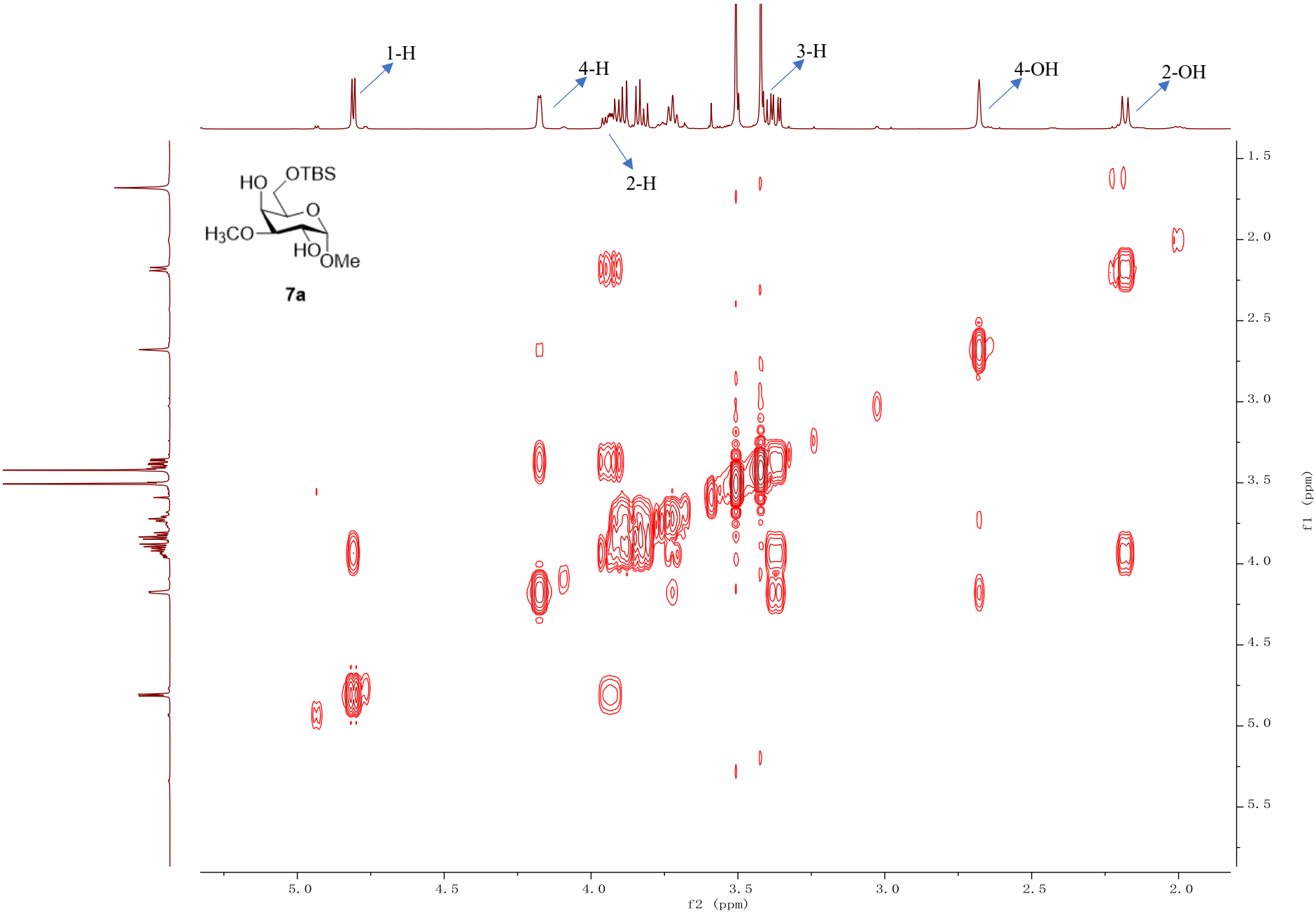
^{1}H-NMR of compound **7a** ($CDCl_3$)



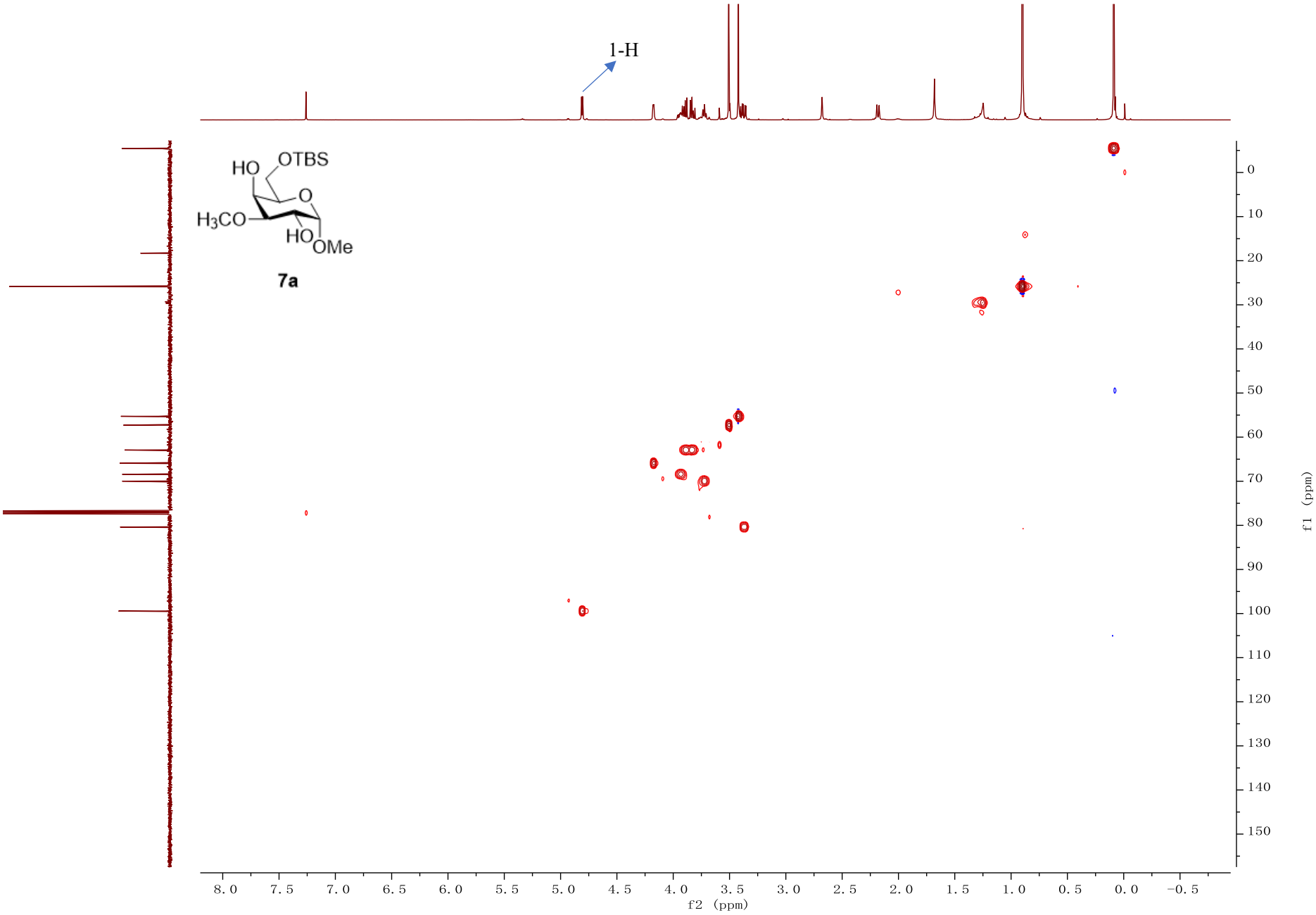
^{13}C-NMR of compound **7a** ($CDCl_3$)



2D-COSY of compound **7a** ($CDCl_3$)



2D-HSQC of compound **7a** ($CDCl_3$)



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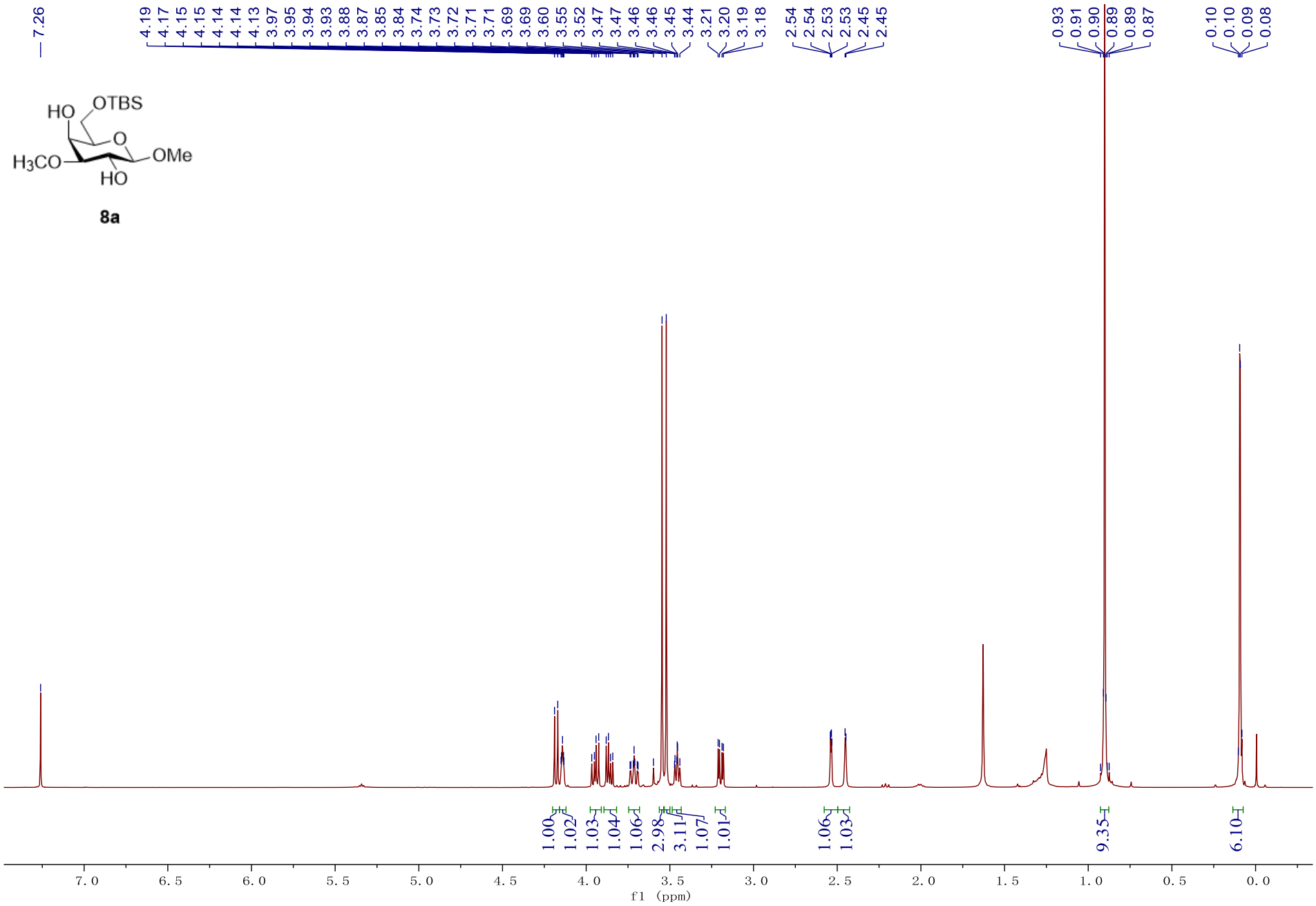
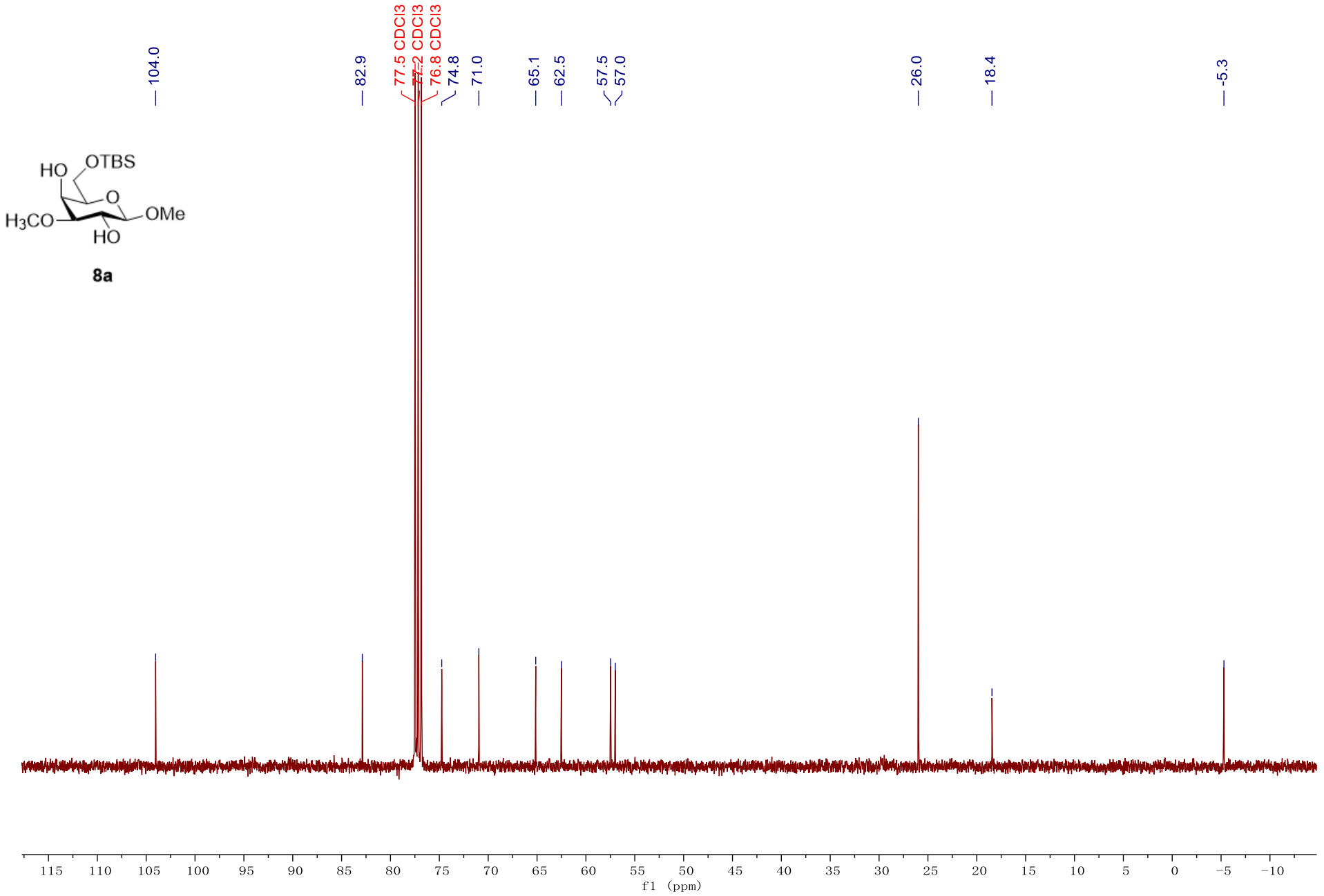
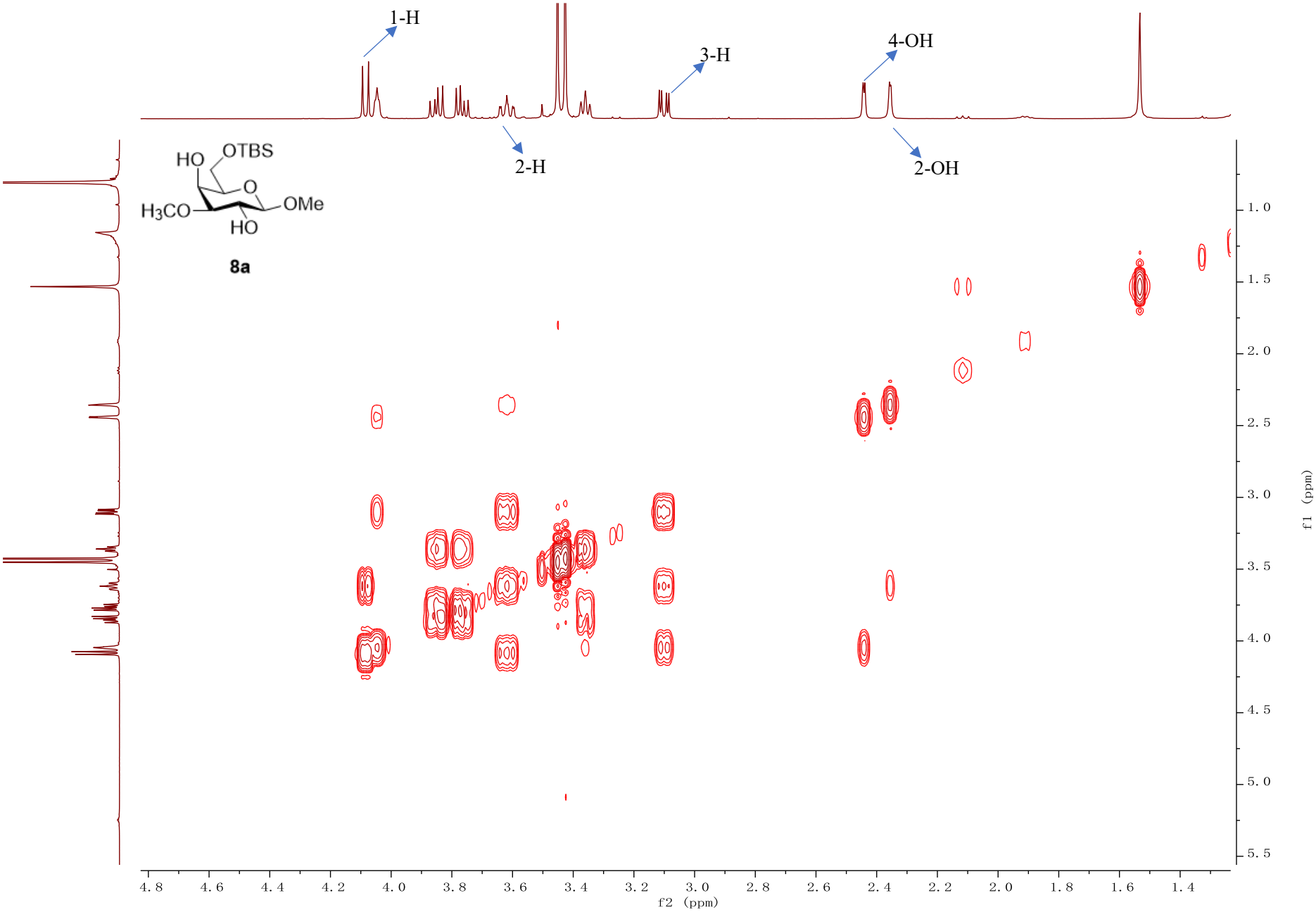


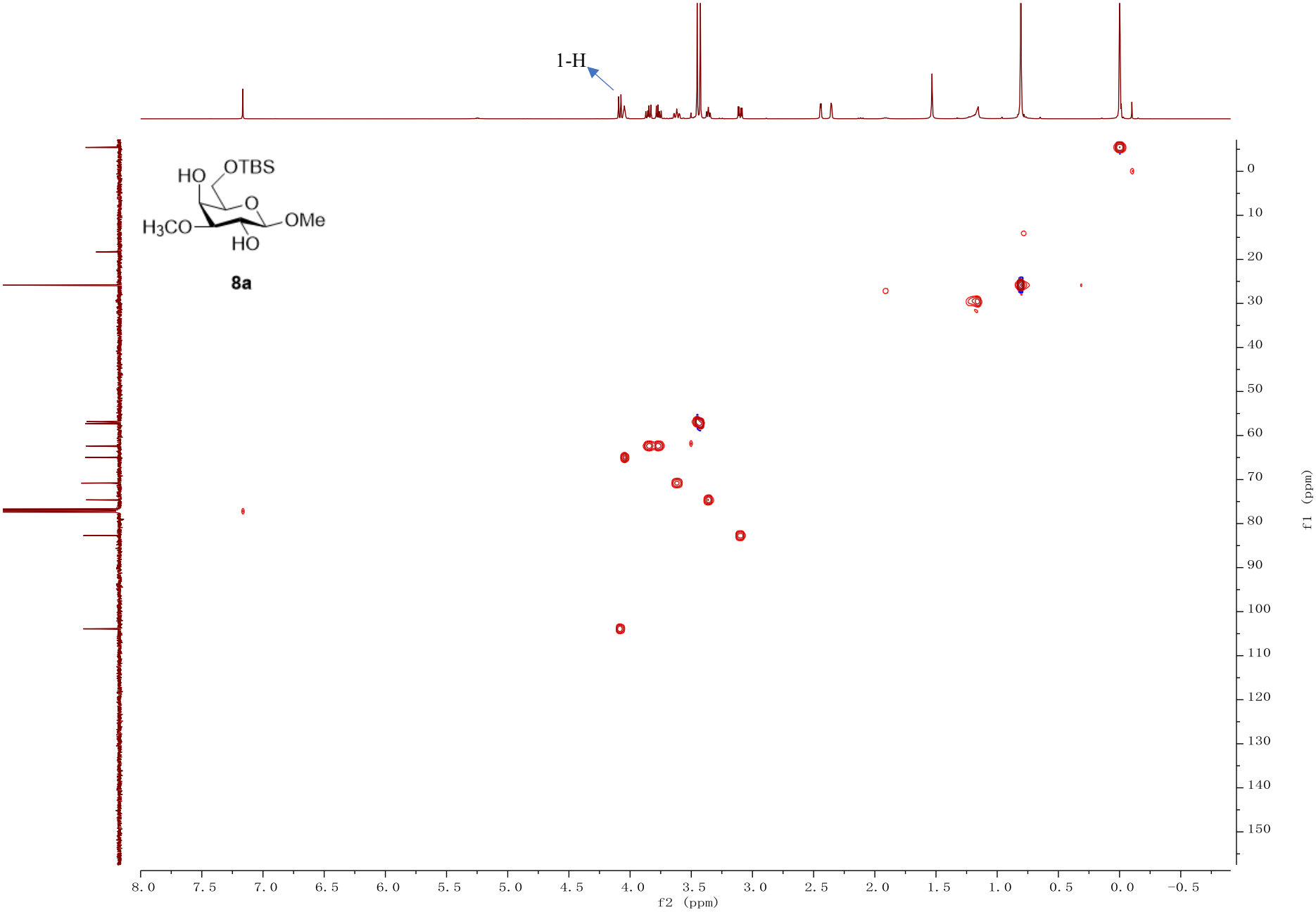
^{13}C-NMR of compound **8a** ($CDCl_3$)



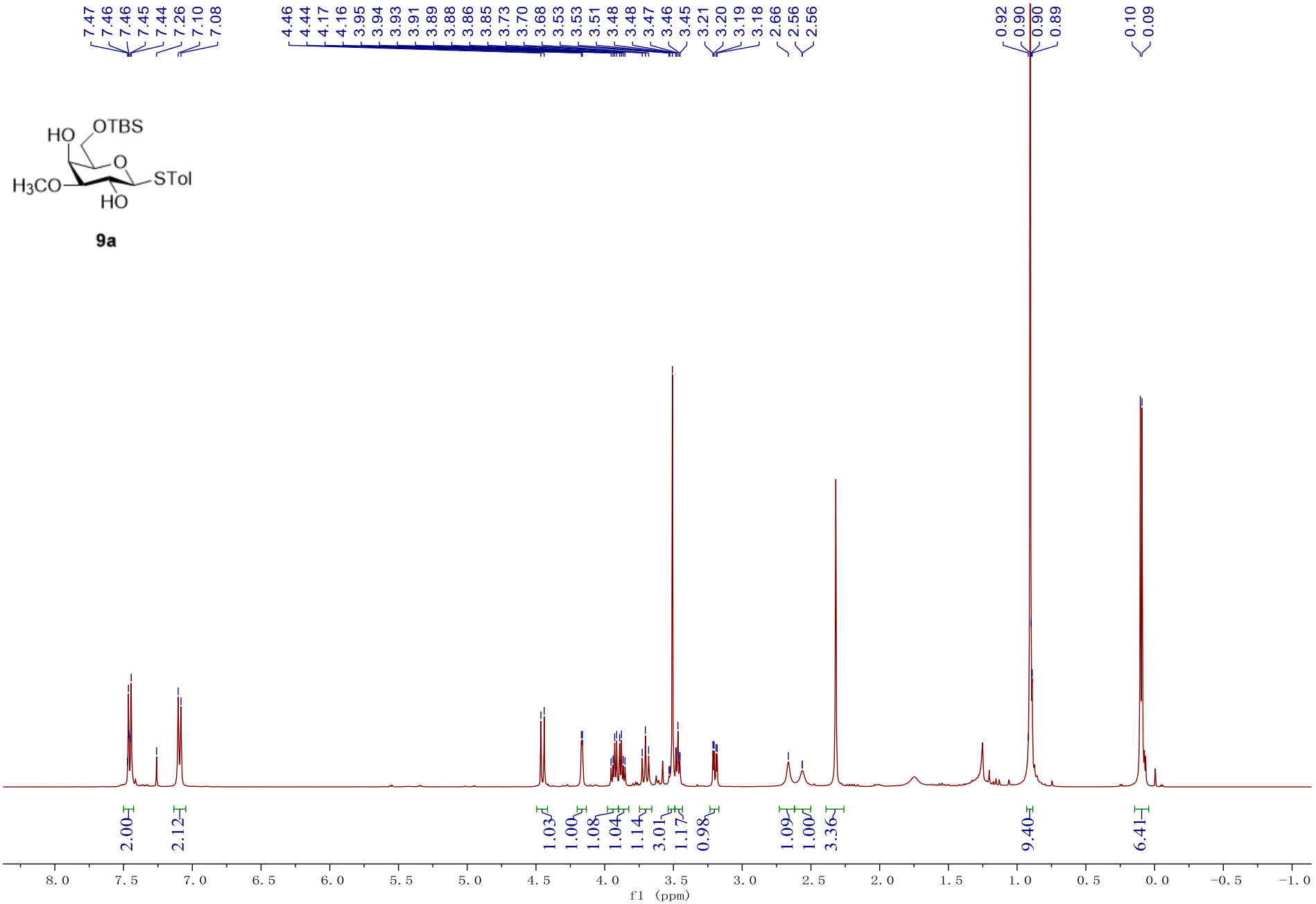
2D-COSY of compound **8a** ($CDCl_3$)



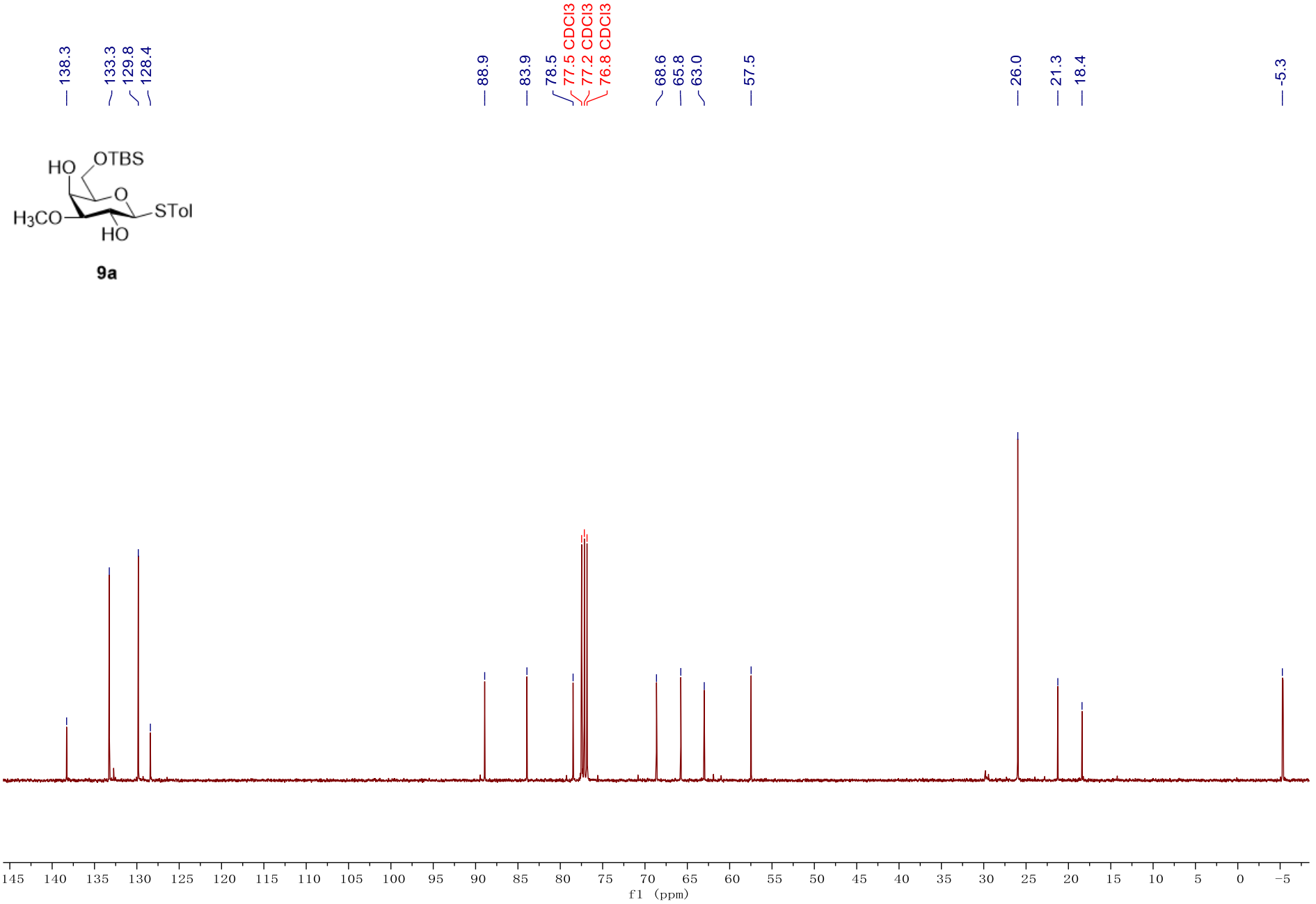
2D-HSQC of compound **8a** ($CDCl_3$)



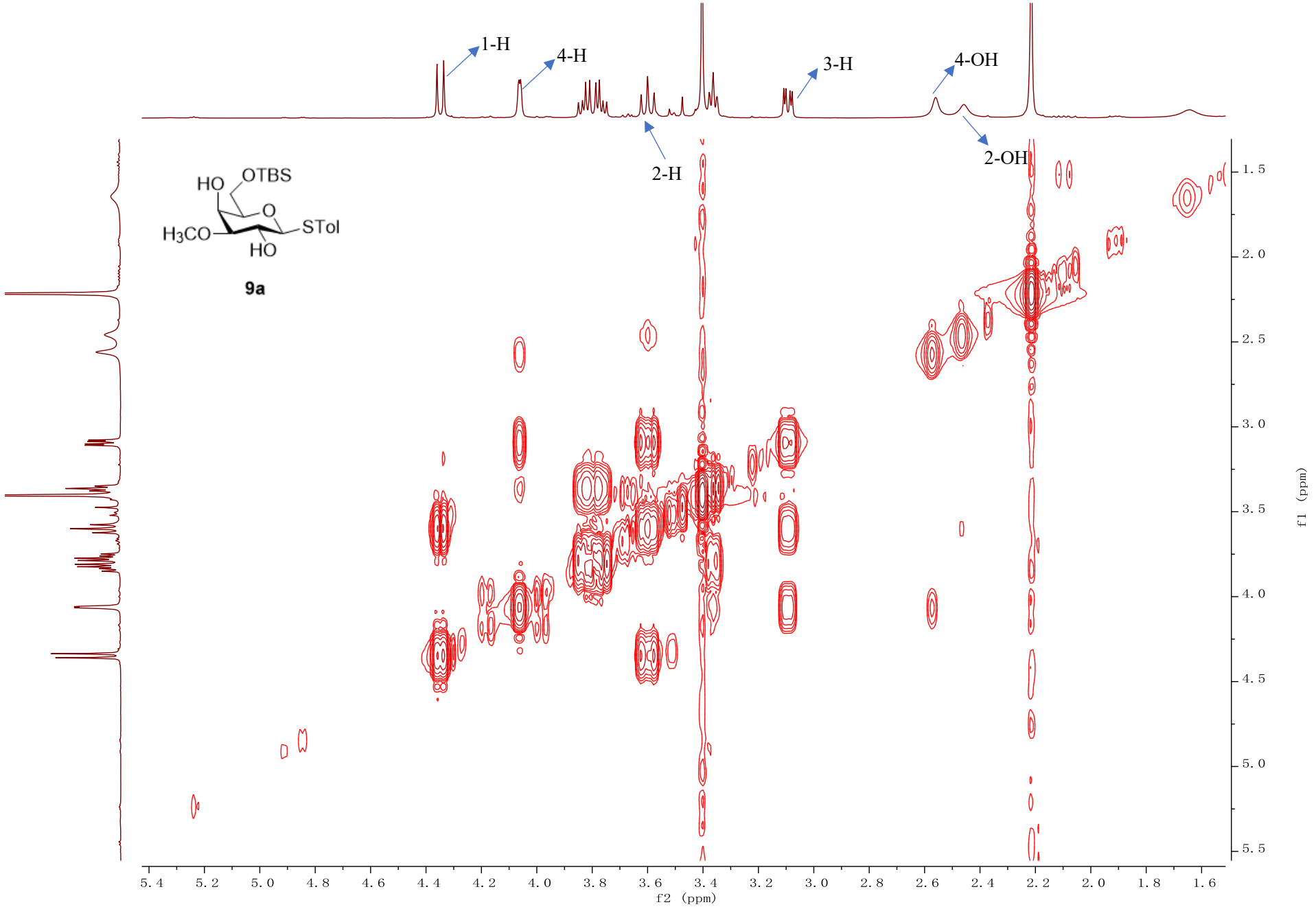
^{1}H-NMR of compound **9a** ($CDCl_3$)



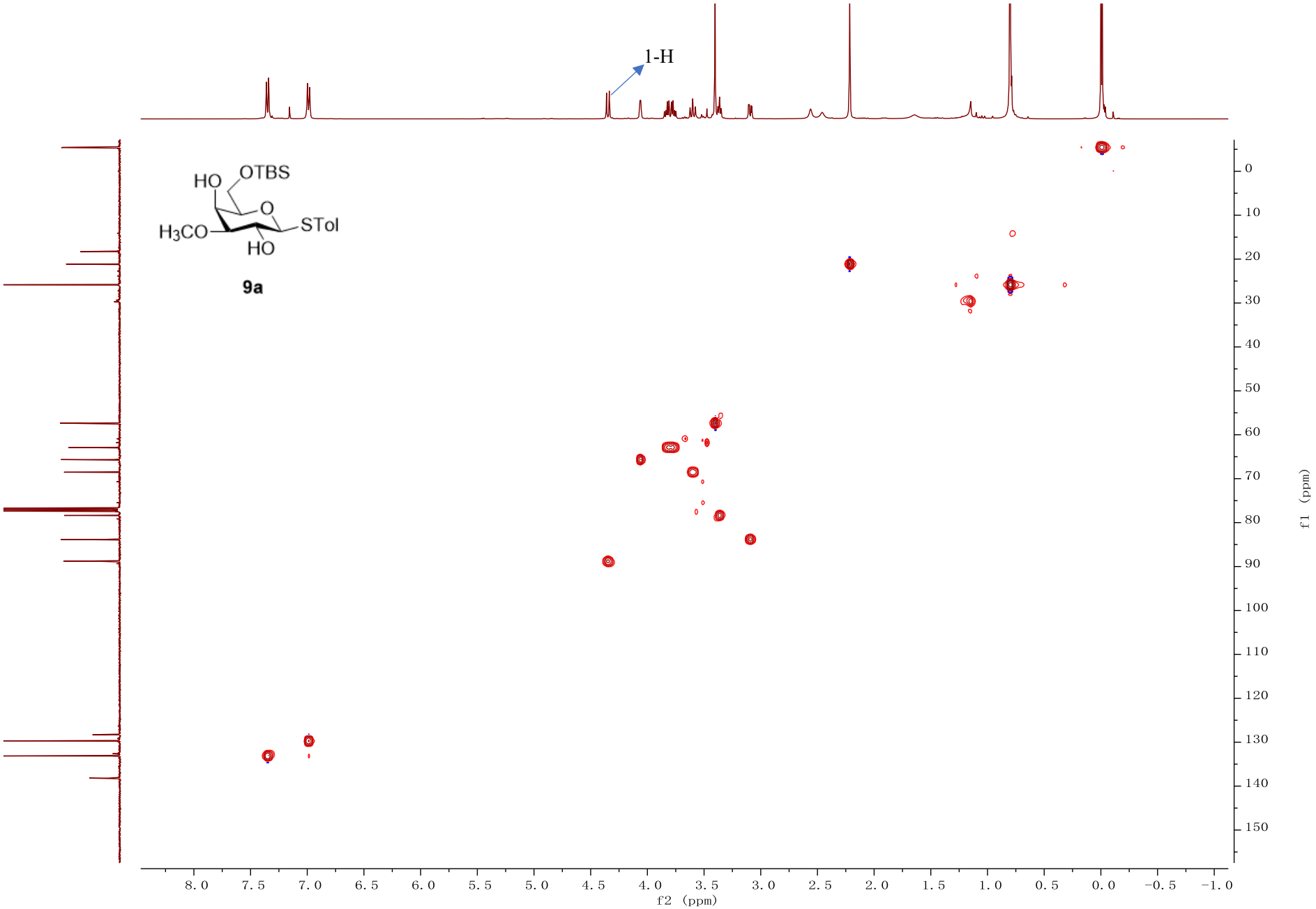
^{13}C-NMR of compound **9a** ($CDCl_3$)



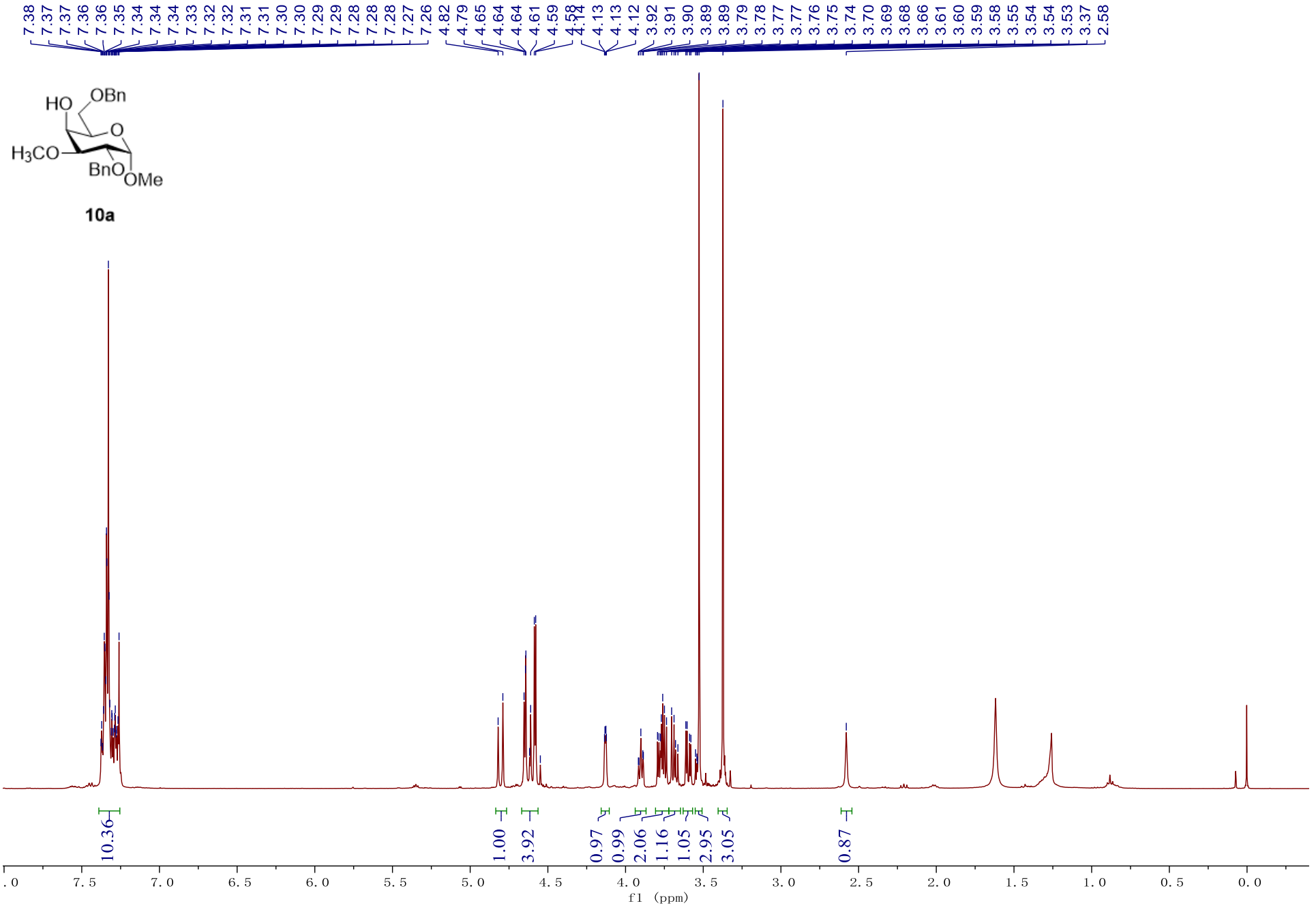
2D-COSY of compound **9a** ($CDCl_3$)



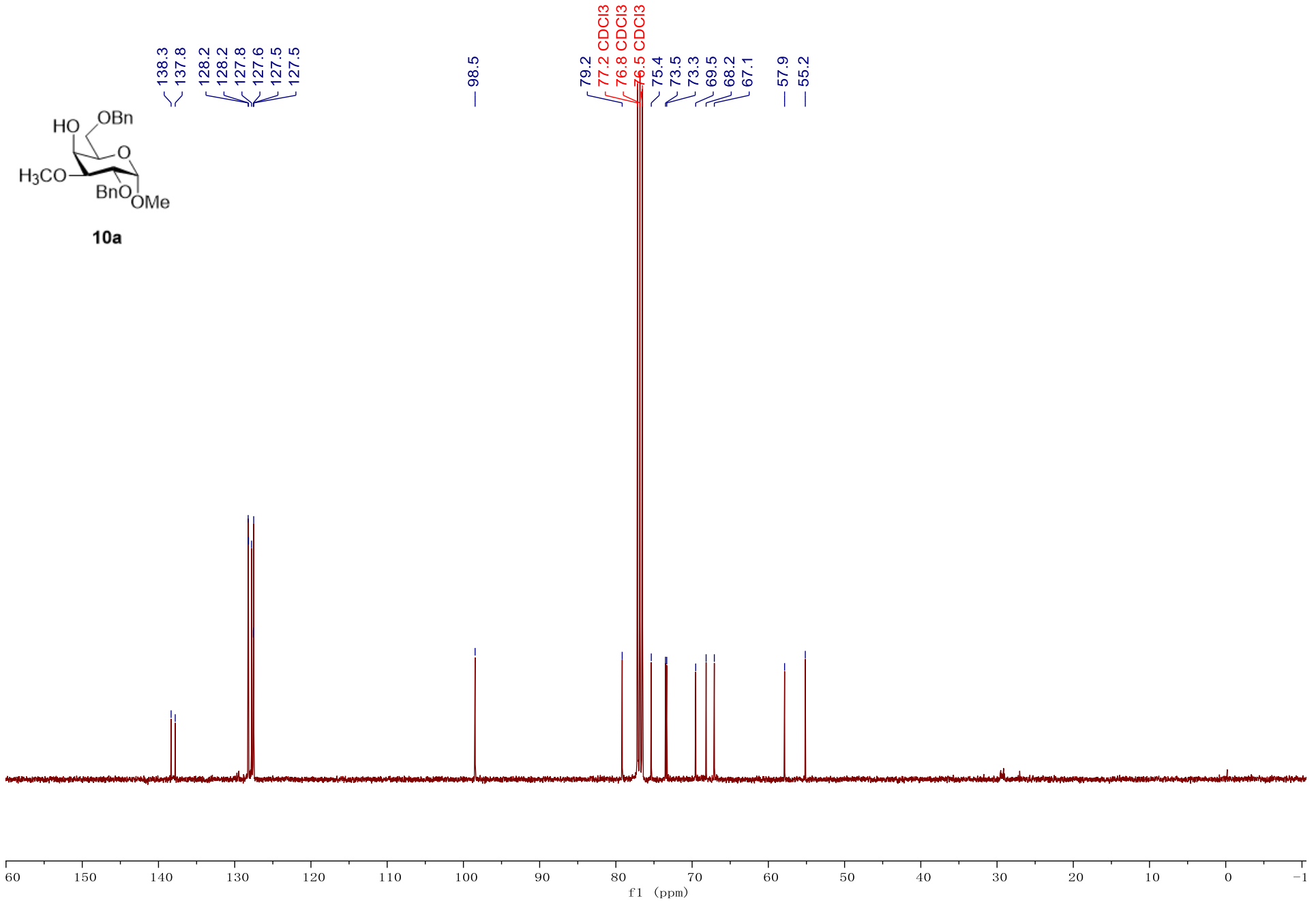
2D-HSQC of compound **9a** ($CDCl_3$)



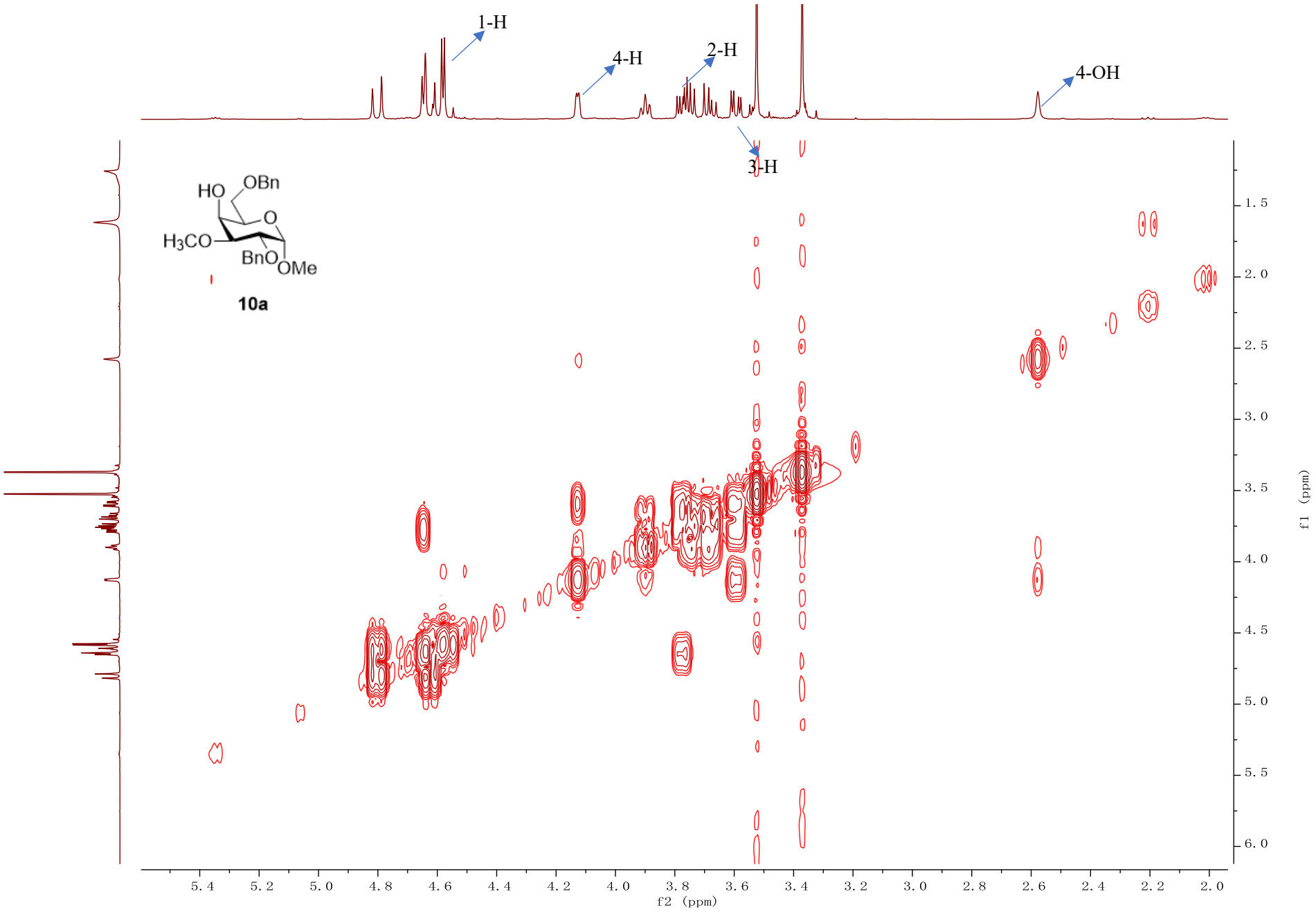
^{1}H-NMR of compound **10a** ($CDCl_3$)



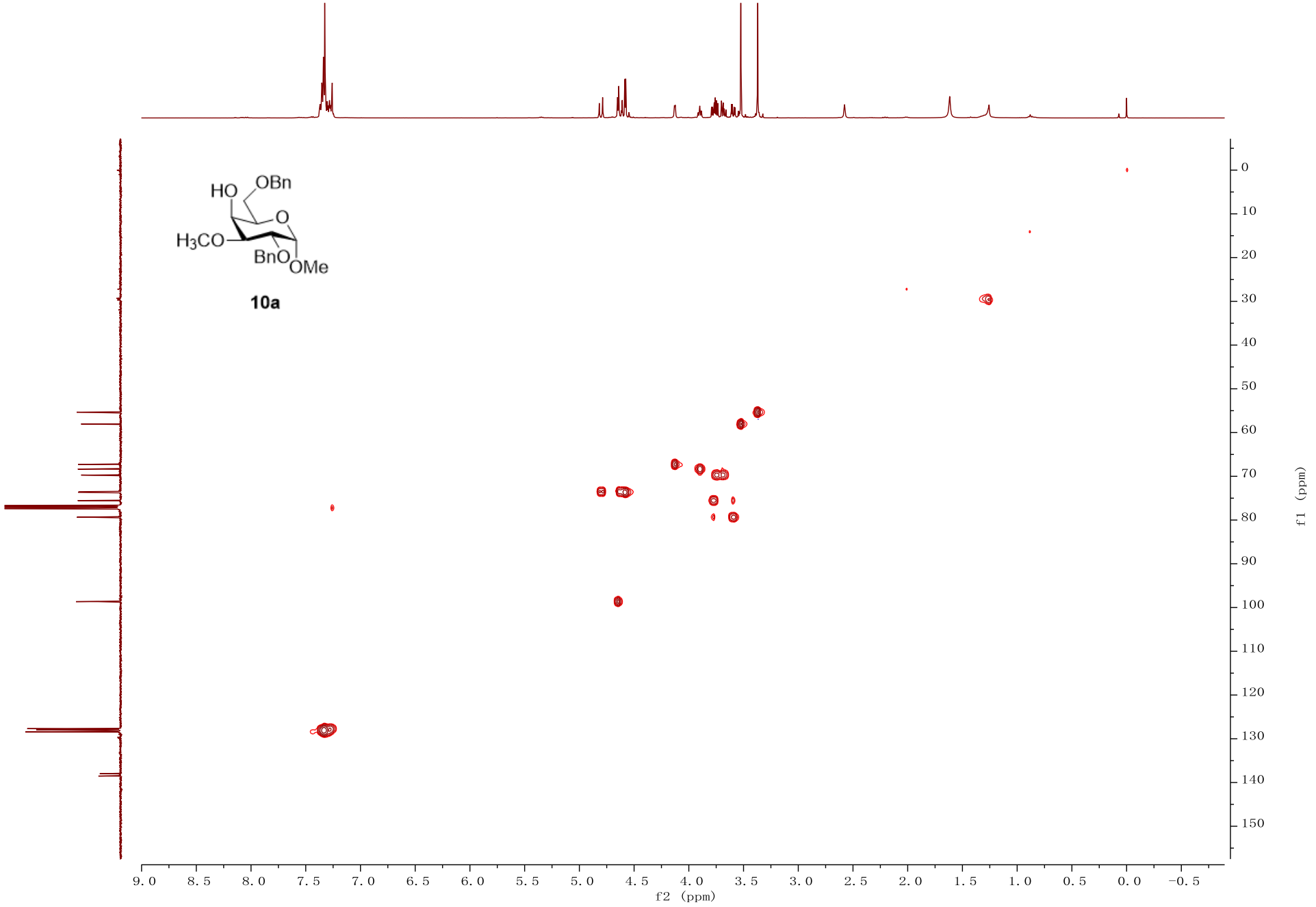
^{13}C-NMR of compound **10a** ($CDCl_3$)



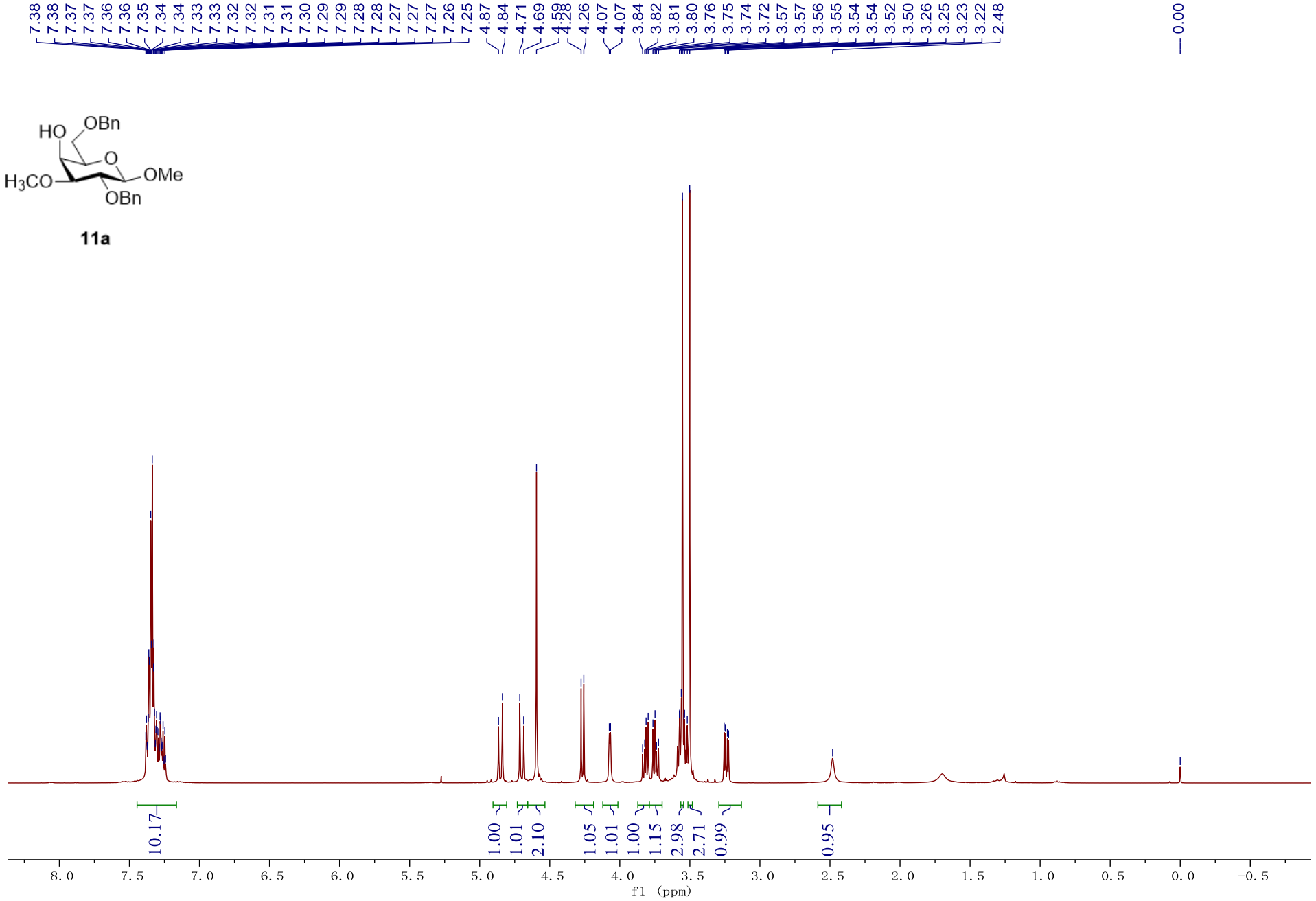
2D-COSY of compound **10a** ($CDCl_3$)



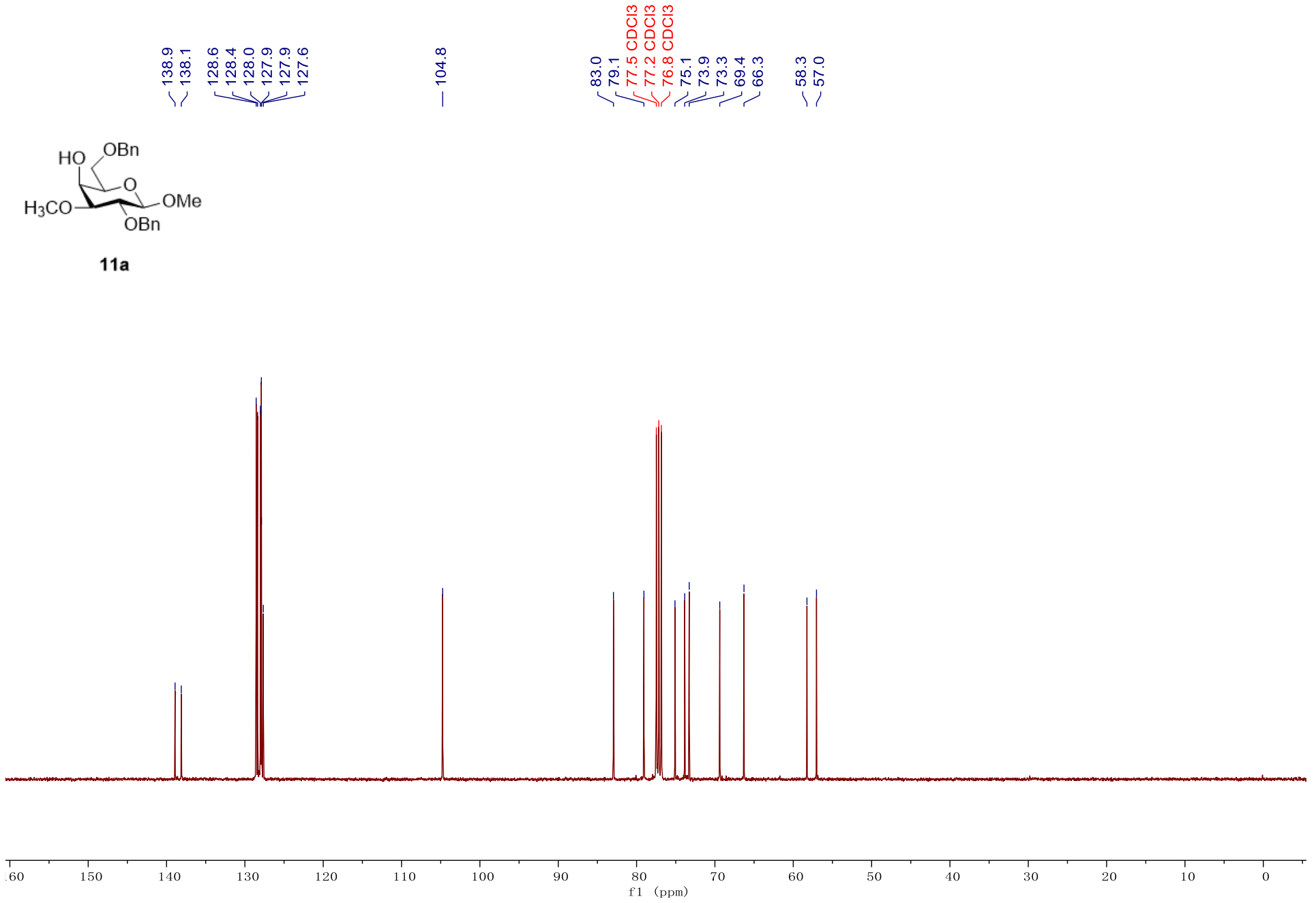
2D-HSQC of compound **10a** ($CDCl_3$)



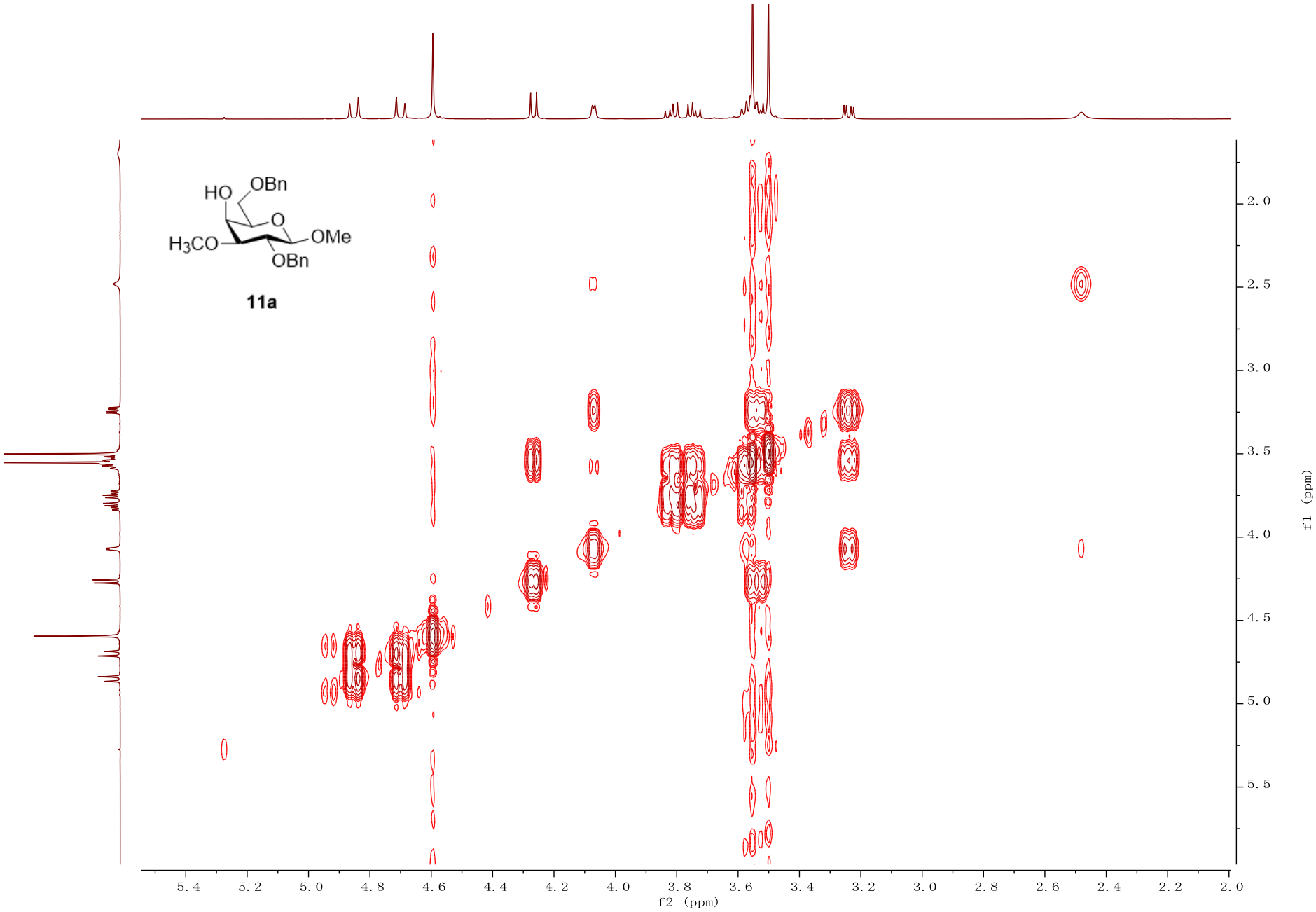
^{1}H-NMR of compound **11a** ($CDCl_3$)



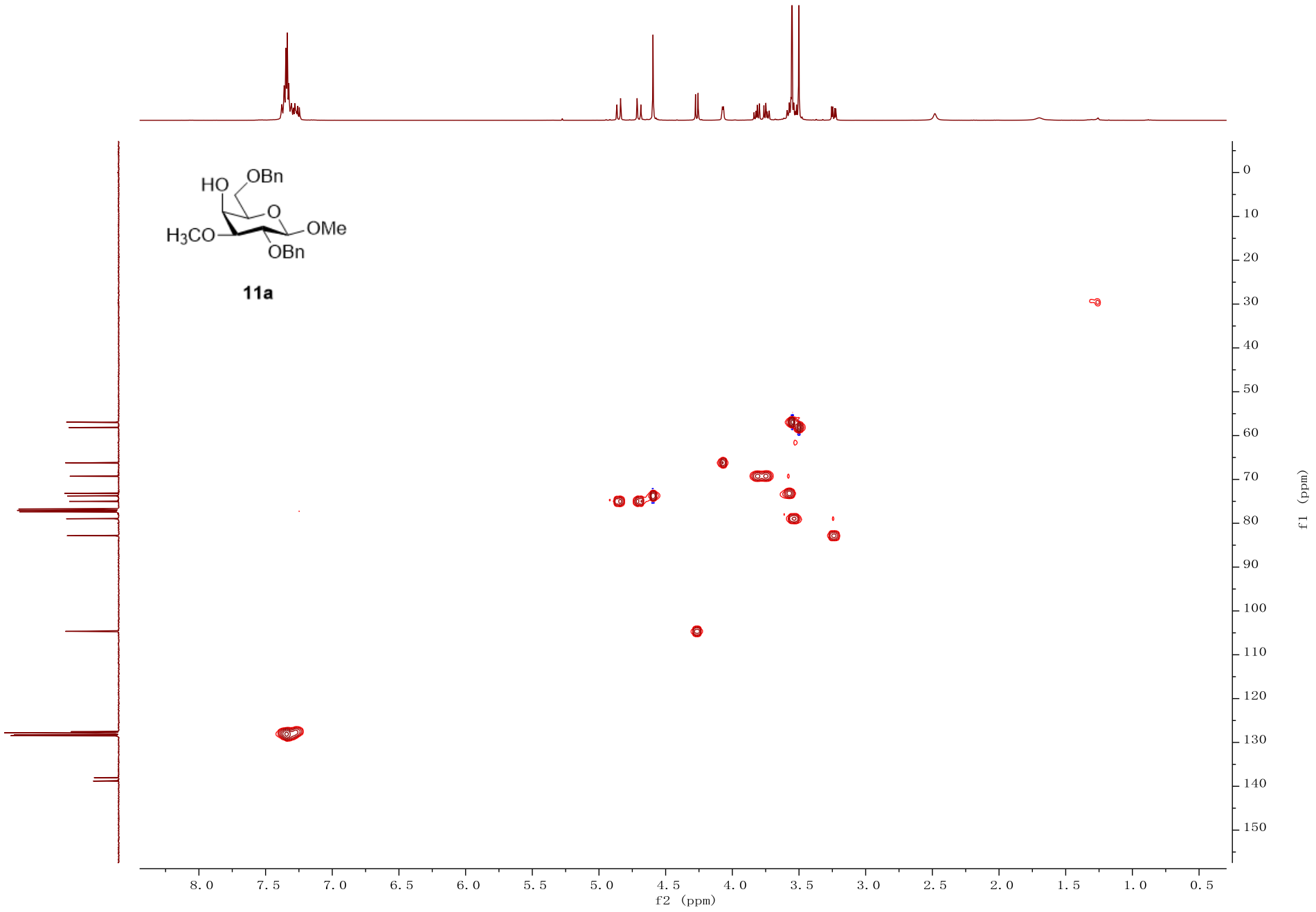
^{13}C-NMR of compound **11a** ($CDCl_3$)



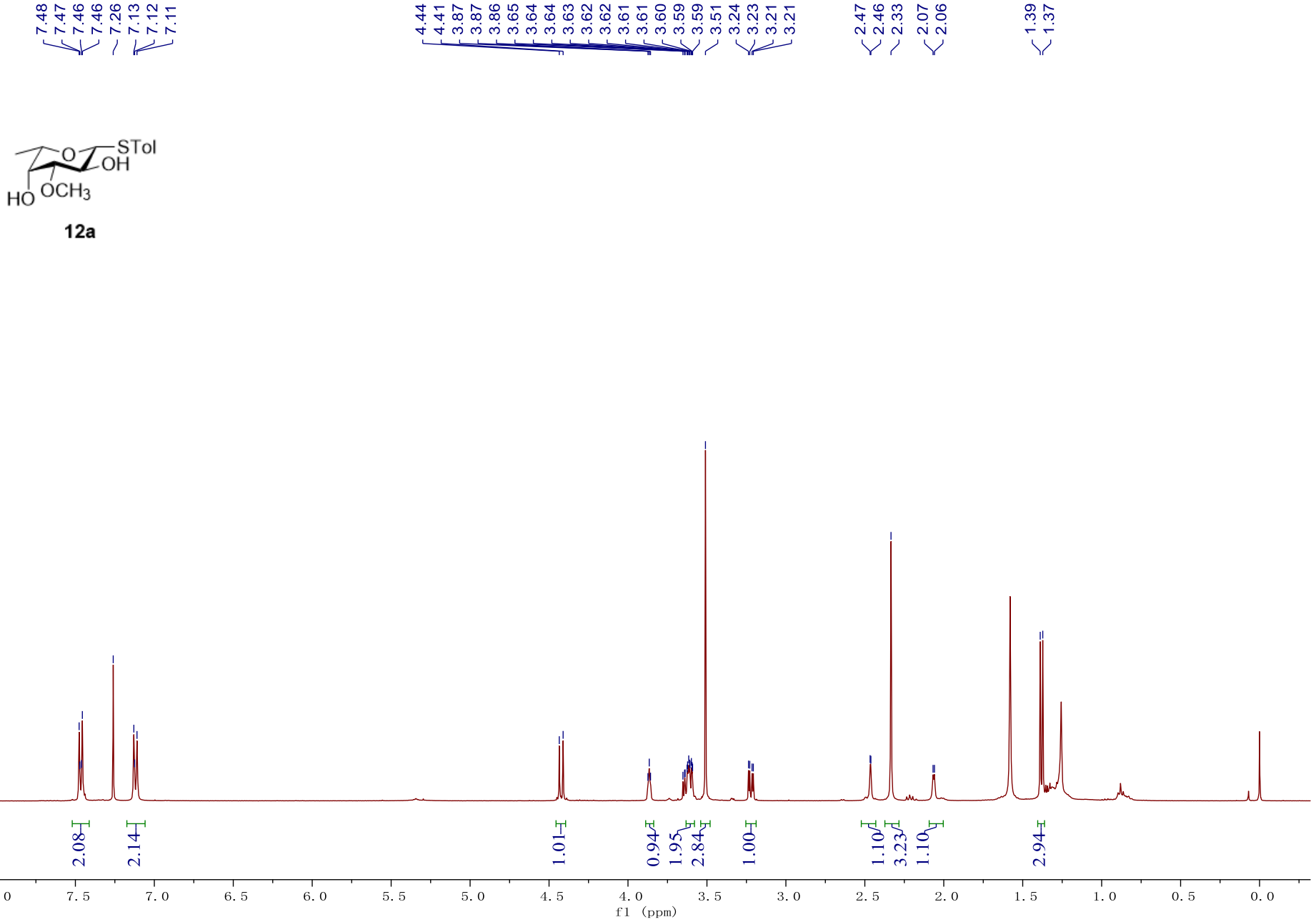
2D-COSY of compound **11a** ($CDCl_3$)



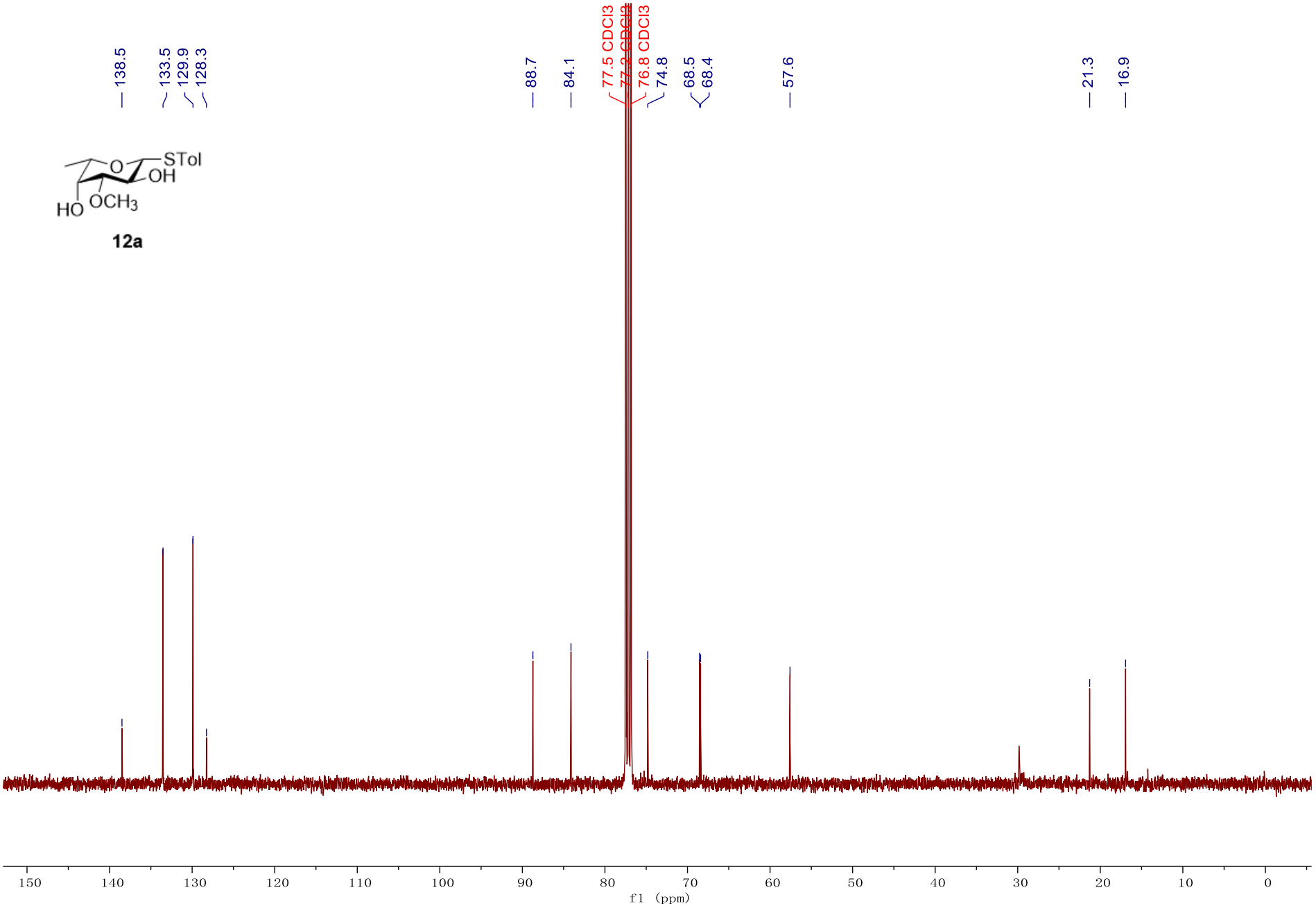
2D-HSQC of compound **11a** ($CDCl_3$)



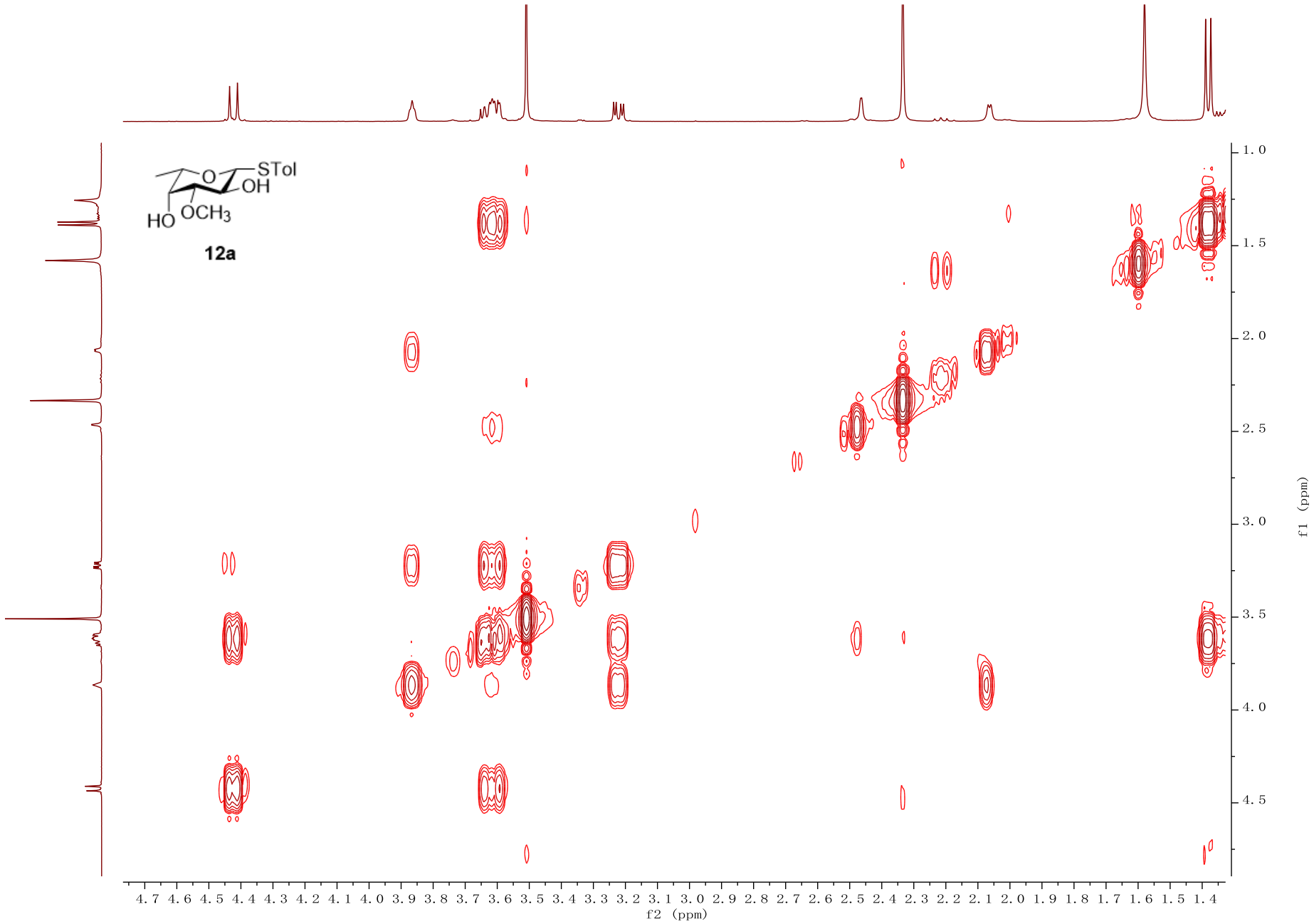
^{1}H-NMR of compound **12a** ($CDCl_3$)



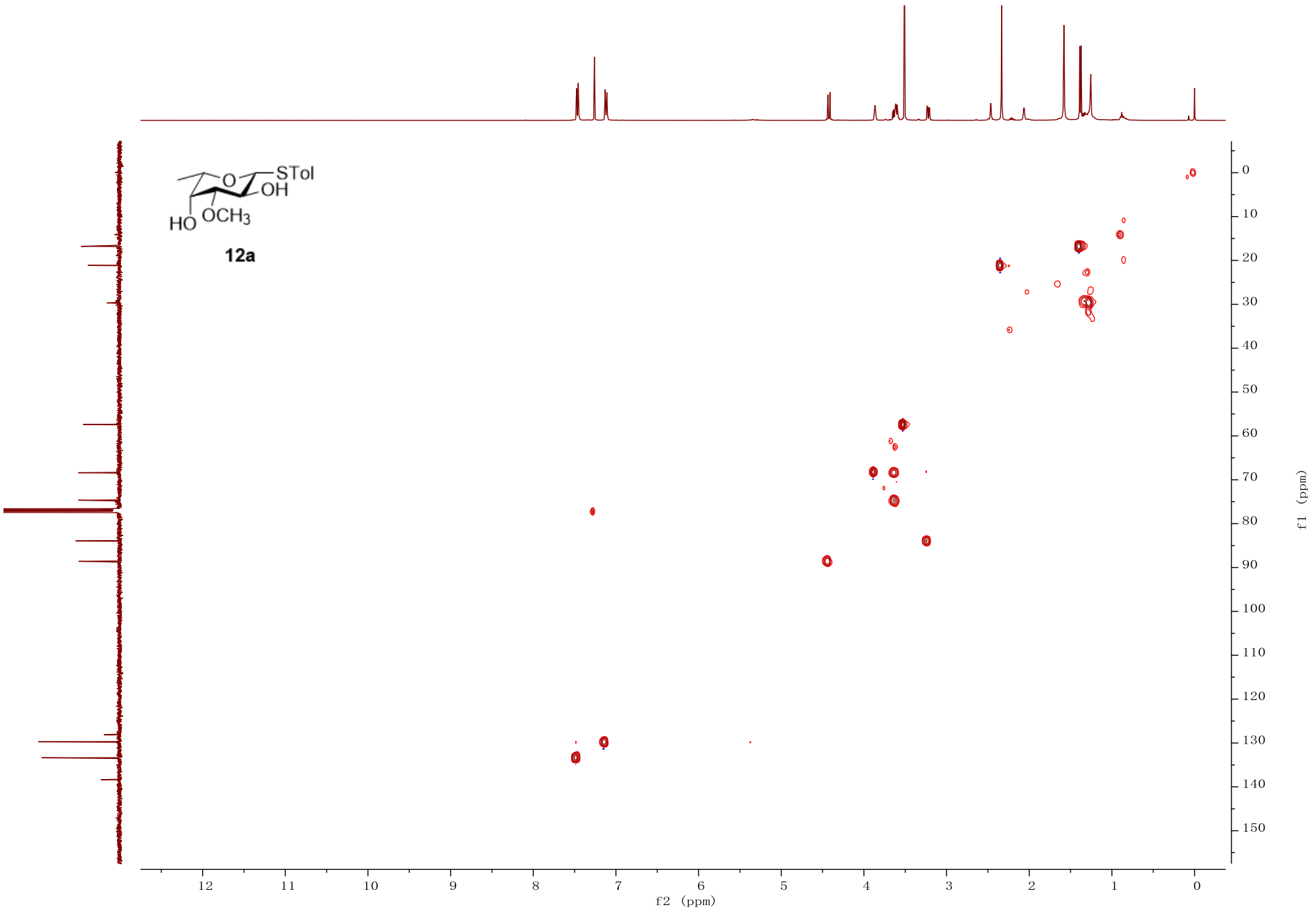
^{13}C-NMR of compound **12a** ($CDCl_3$)



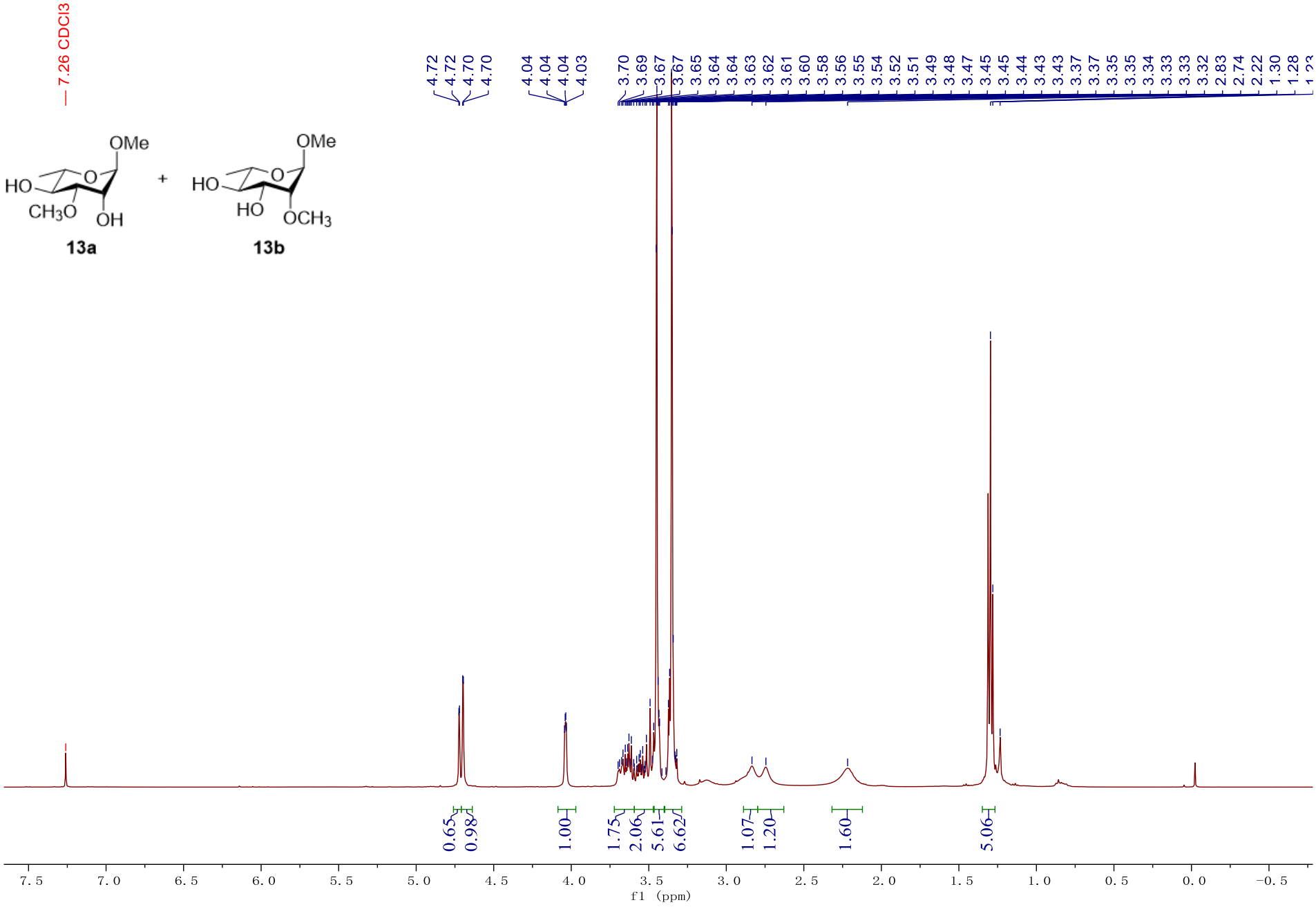
2D-COSY of compound **12a** ($CDCl_3$)



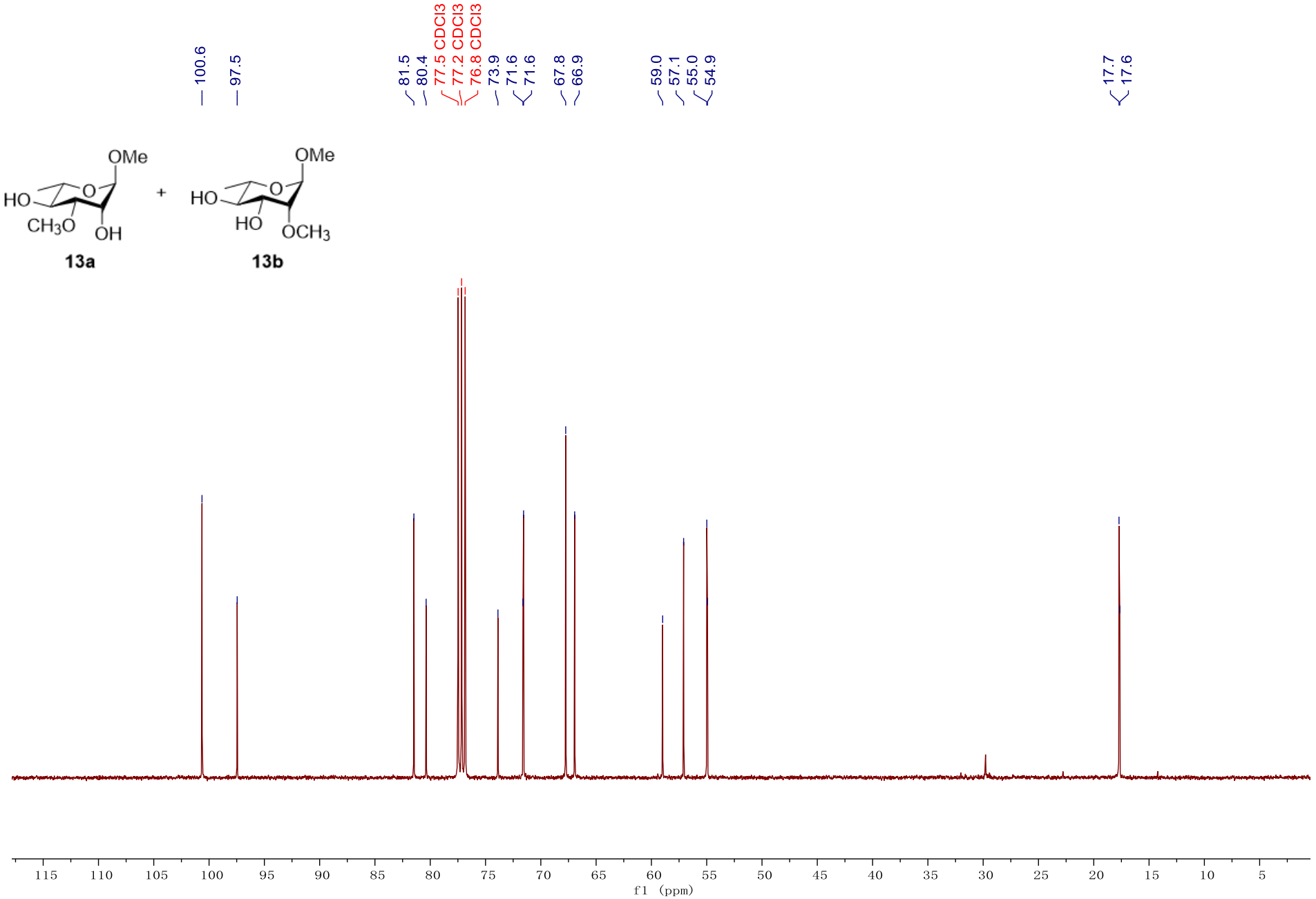
2D-HSQC of compound **12a** ($CDCl_3$)



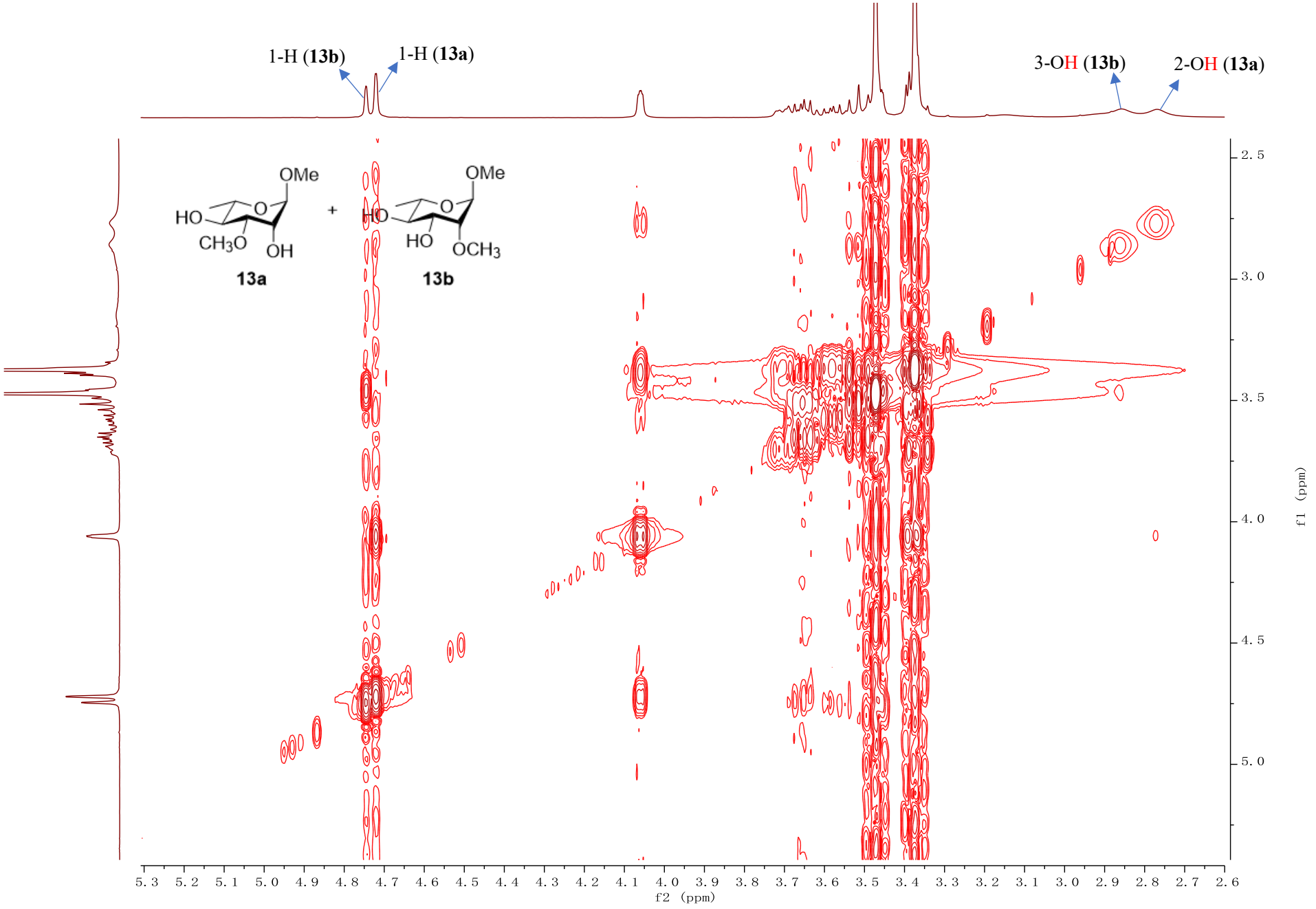
[1]H-NMR of compound **13a** and **13b** ($CDCl_3$)



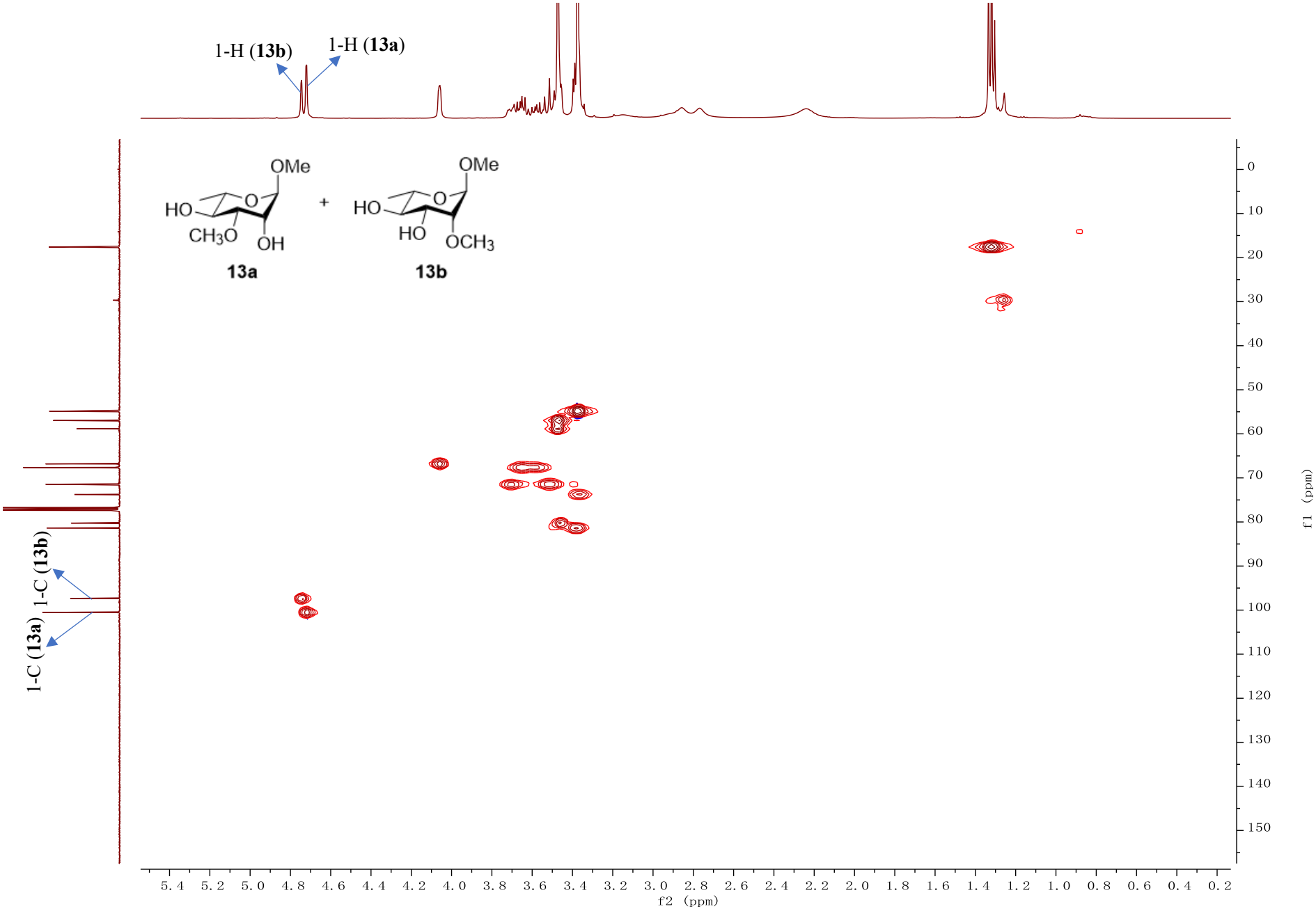
^{13}C-NMR of compound **13a** and **13b** ($CDCl_3$)



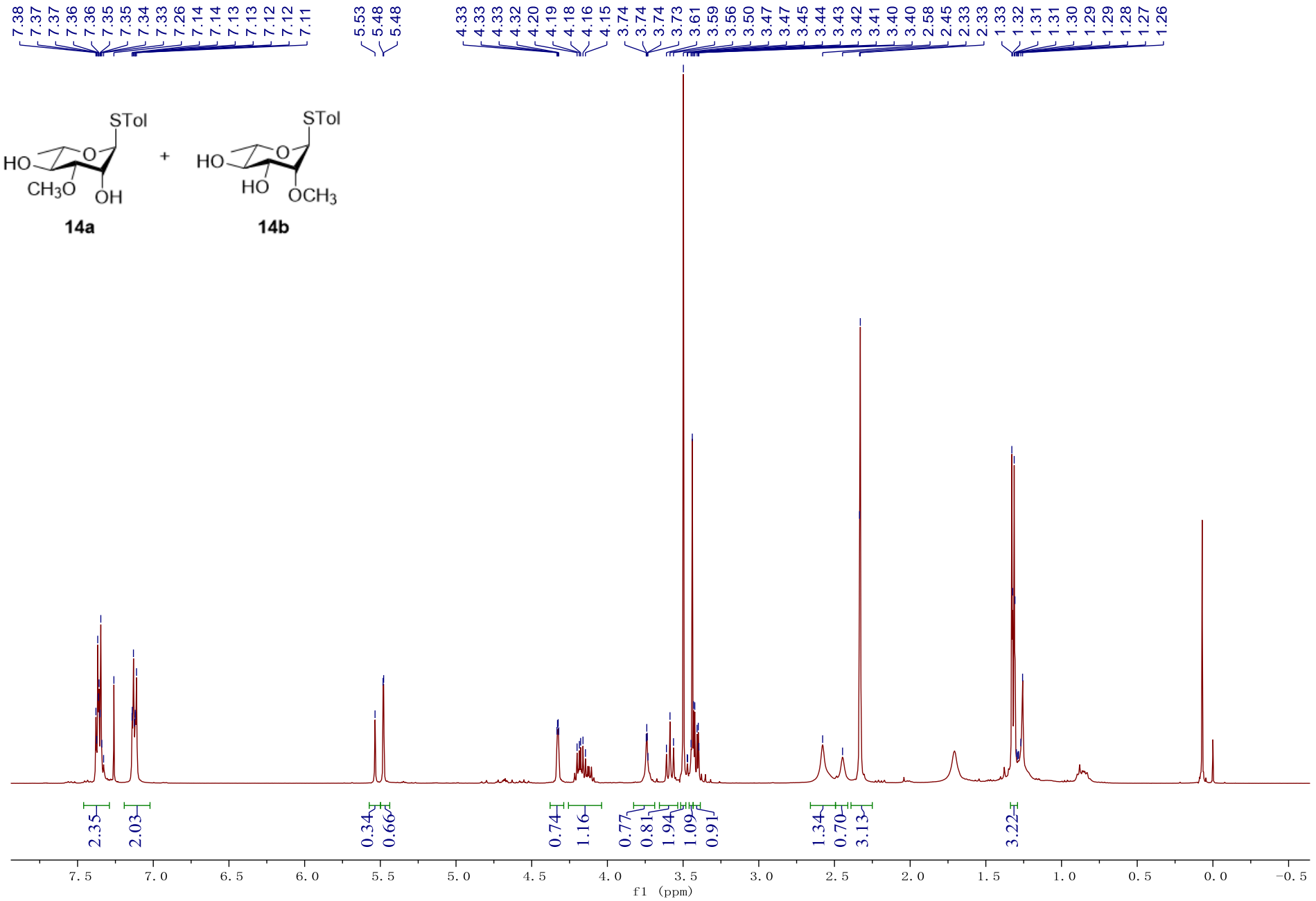
2D-COSY of compound **13a** and **13b** ($CDCl_3$)



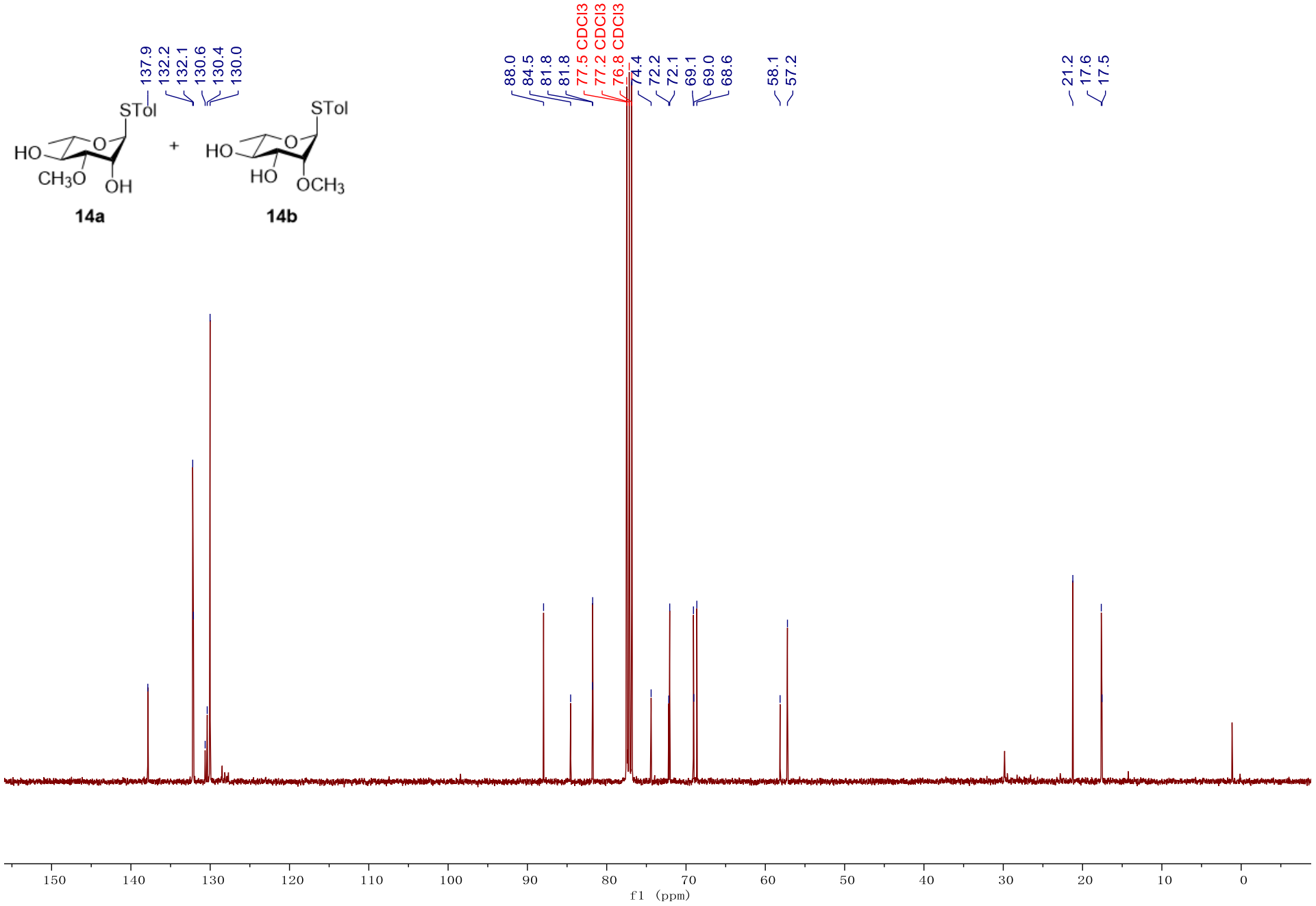
2D-HSQC of compound **13a** and **13b** ($CDCl_3$)



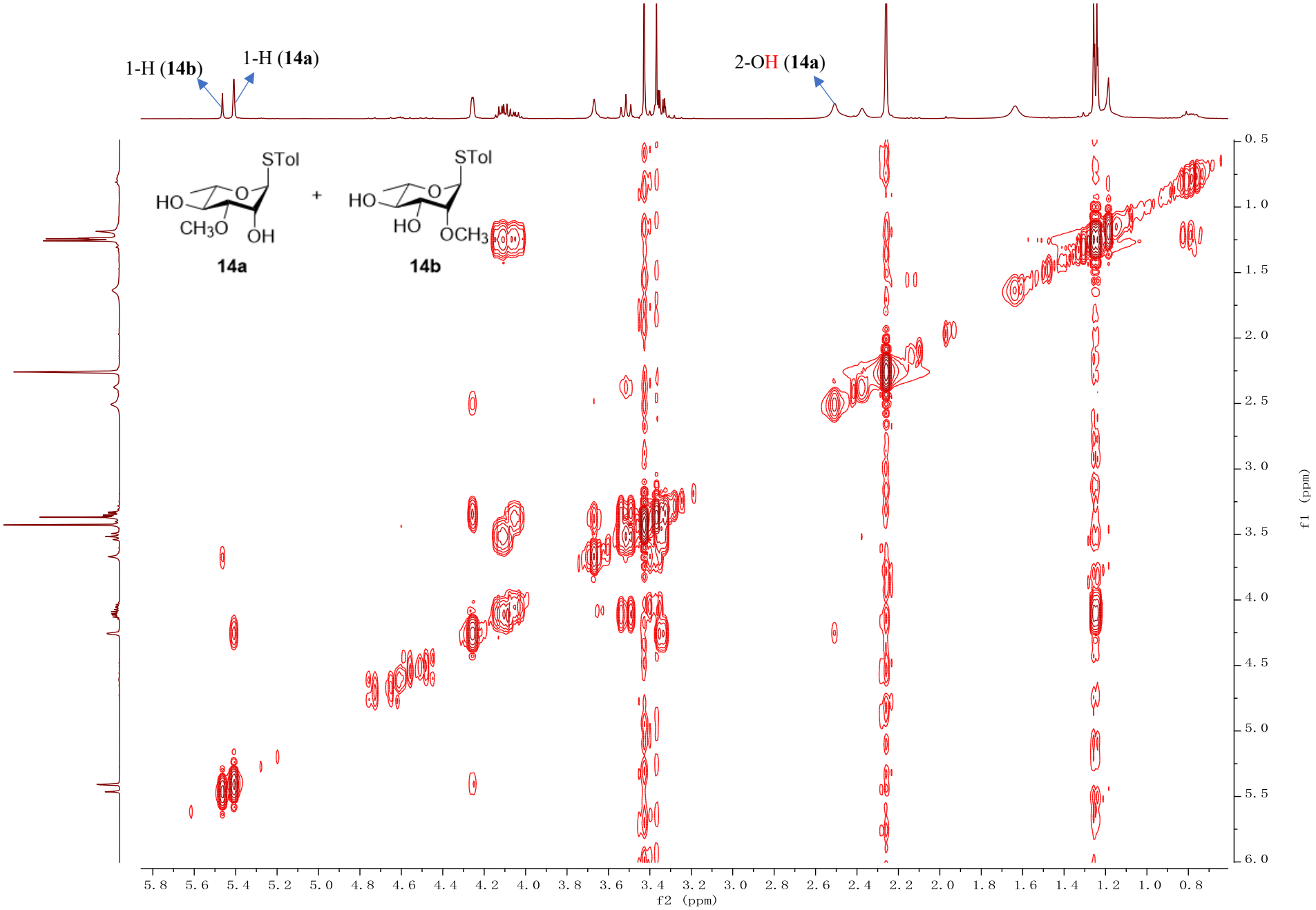
^{1}H-NMR of compound **14a** and **14b** ($CDCl_3$)



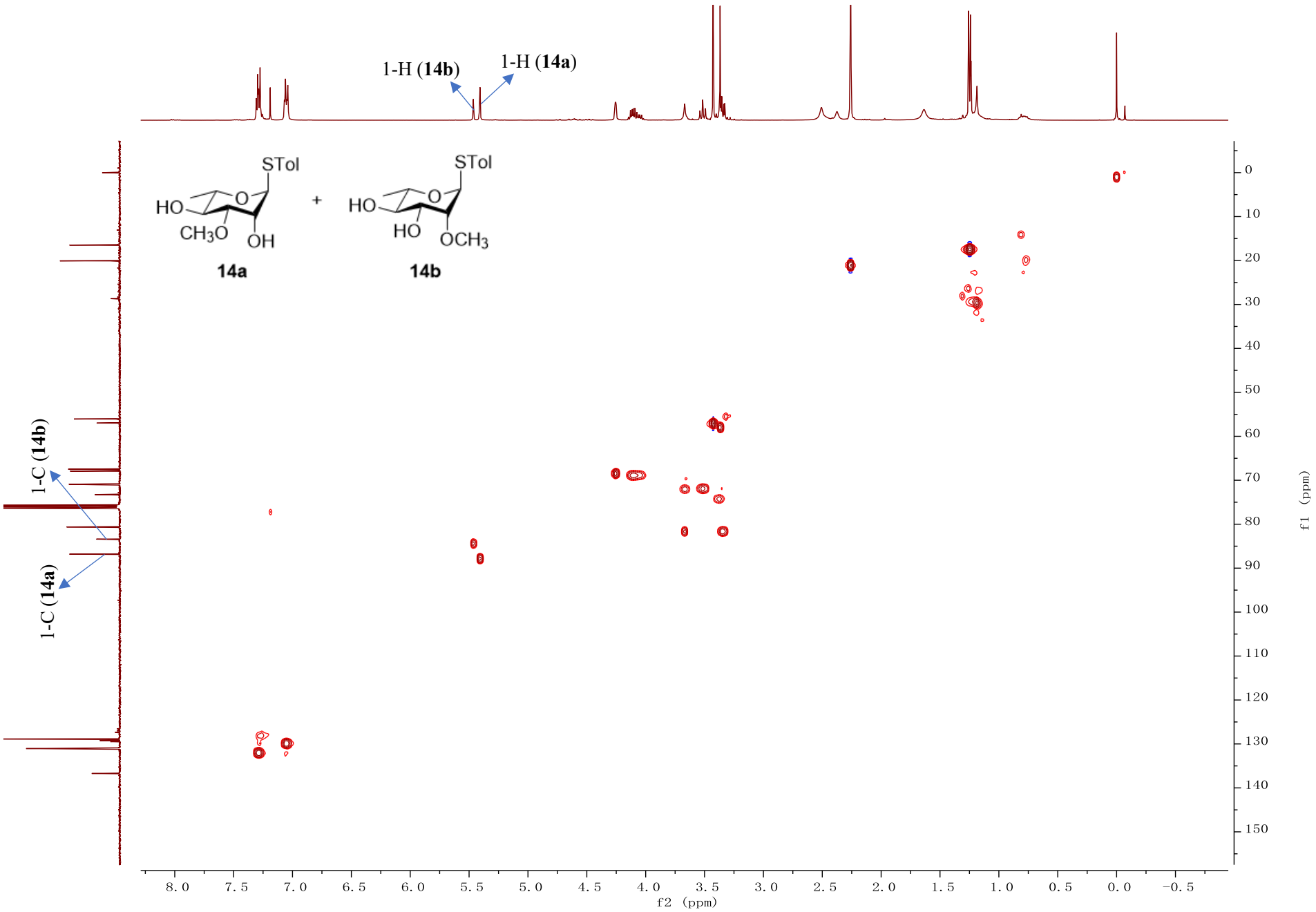
^{13}C-NMR of compound **14a** and **14b** ($CDCl_3$)



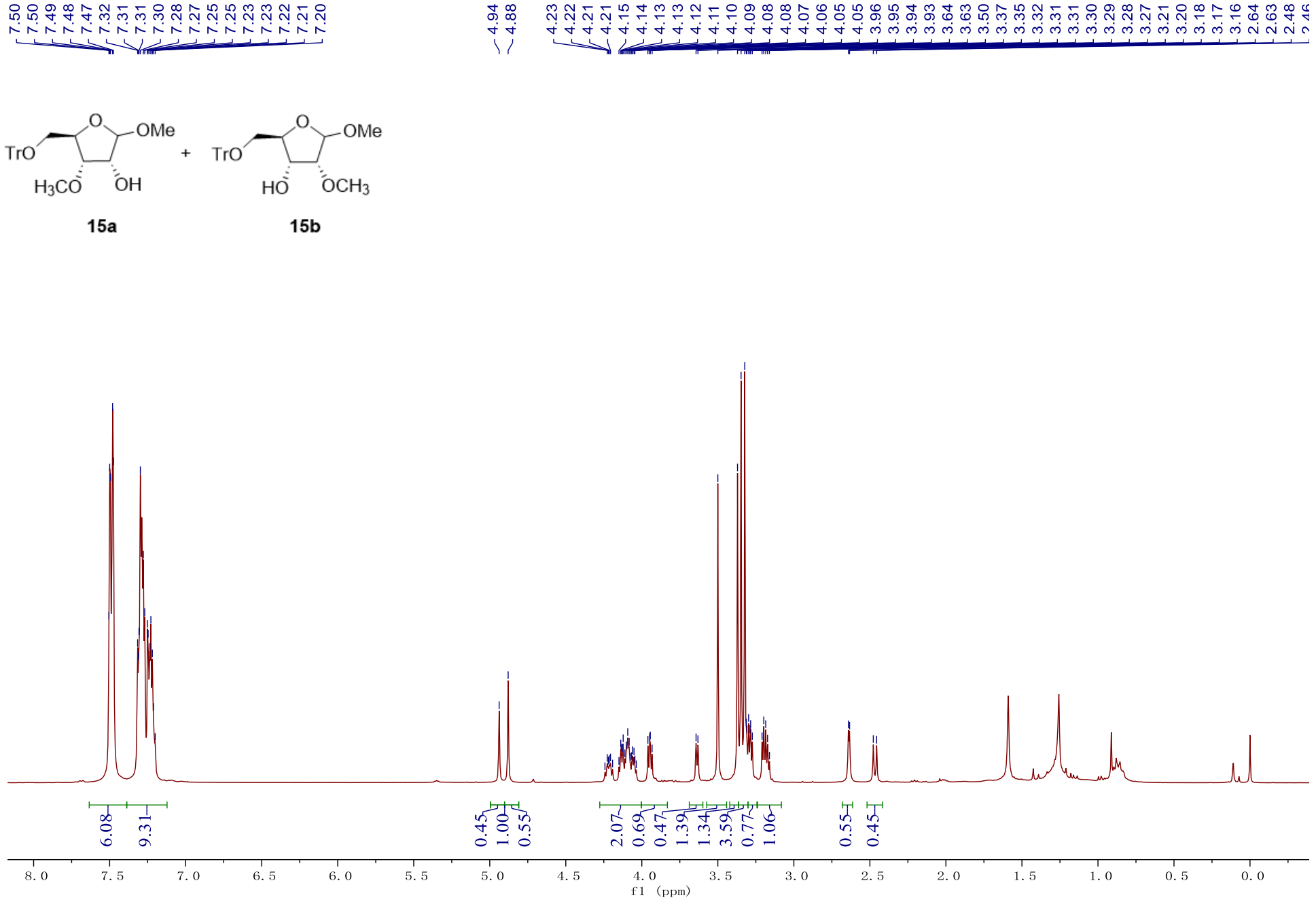
2D-COSY of compound **14a** and **14b** ($CDCl_3$)



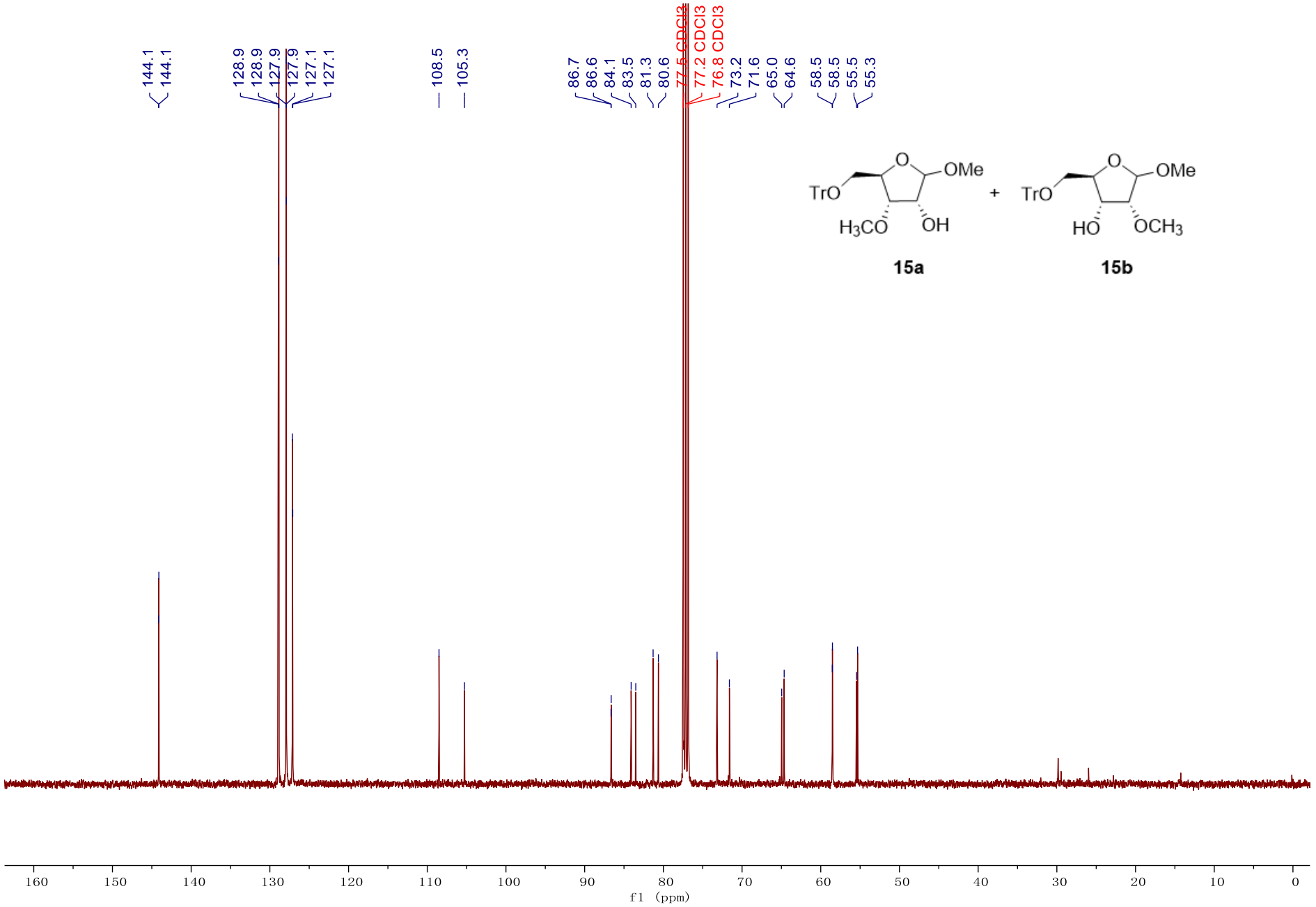
2D-HSQC of compound **14a** and **14b** ($CDCl_3$)



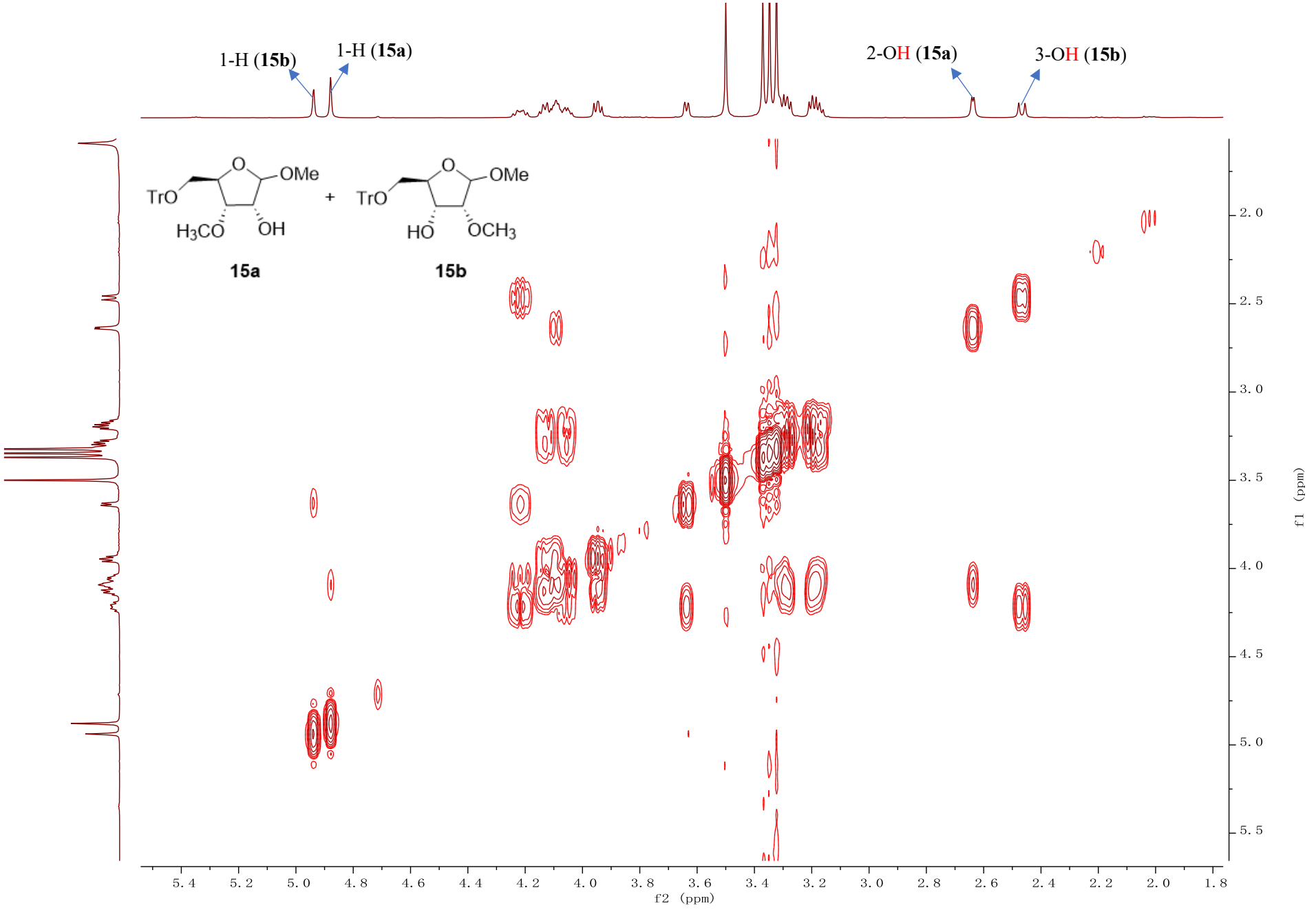
^{1}H-NMR of compound **15a** ($CDCl_3$)



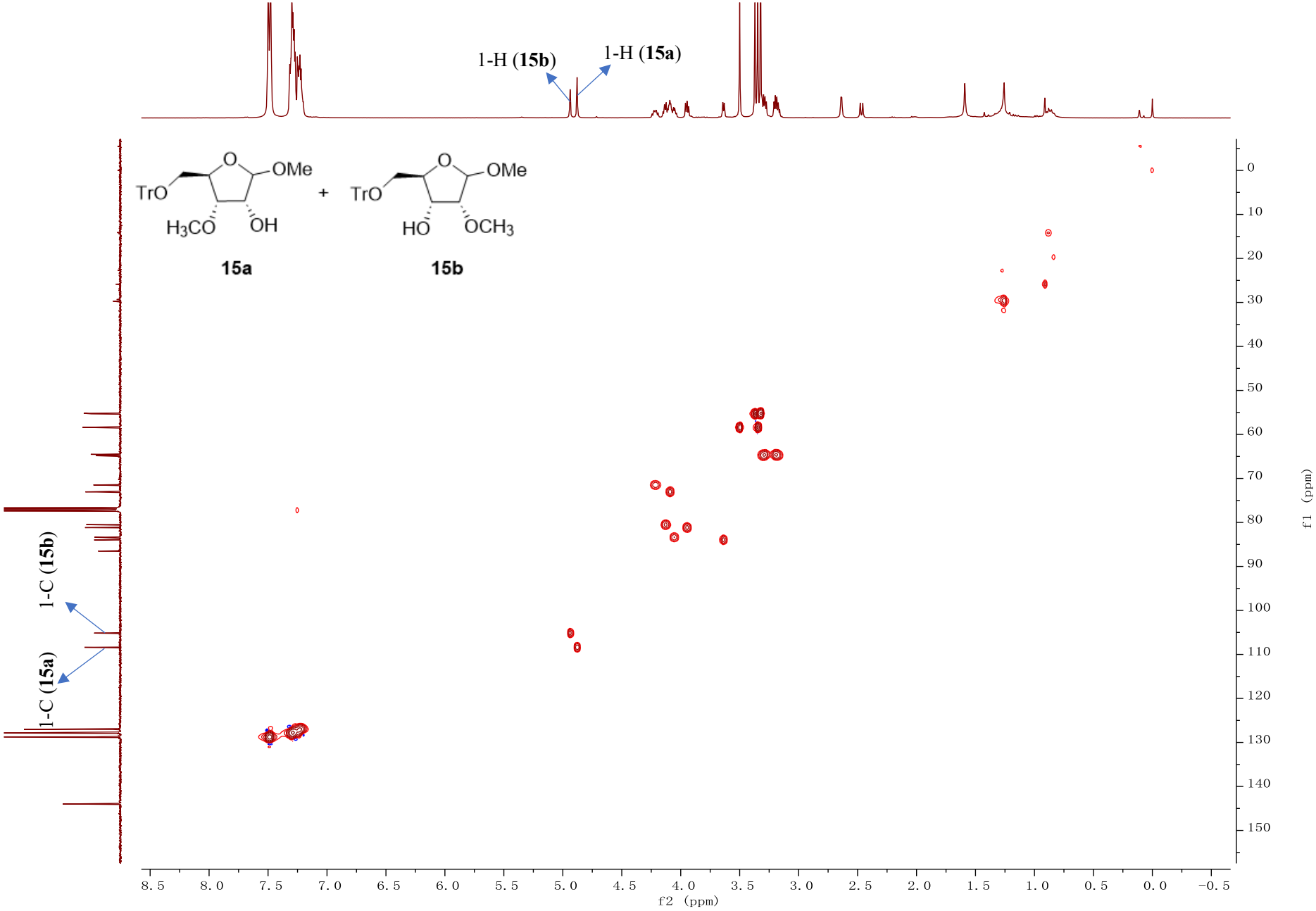
^{13}C-NMR of compound **15a** ($CDCl_3$)



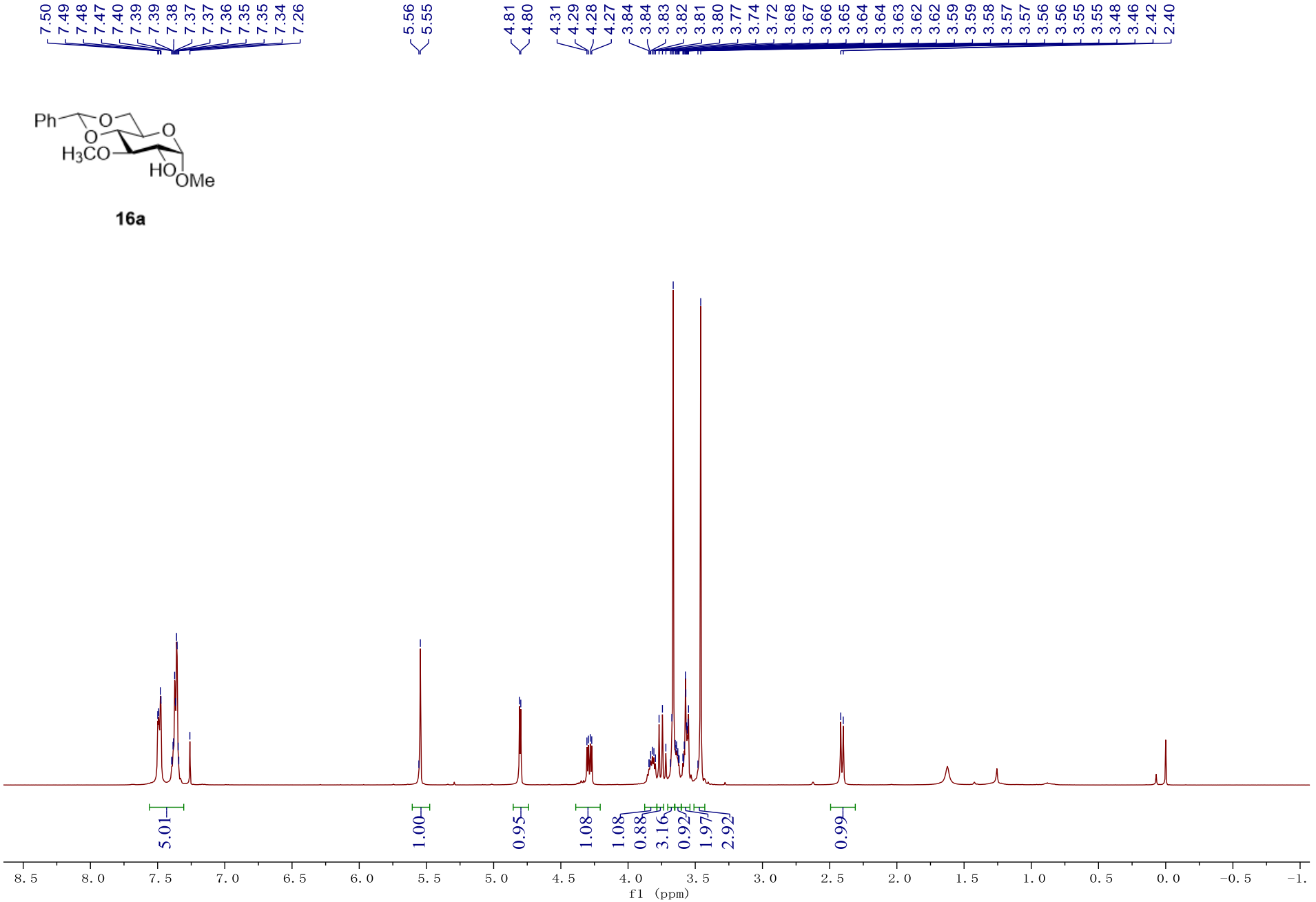
2D-COSY of compound **15a** ($CDCl_3$)



2D-HSQC of compound **15a** ($CDCl_3$)

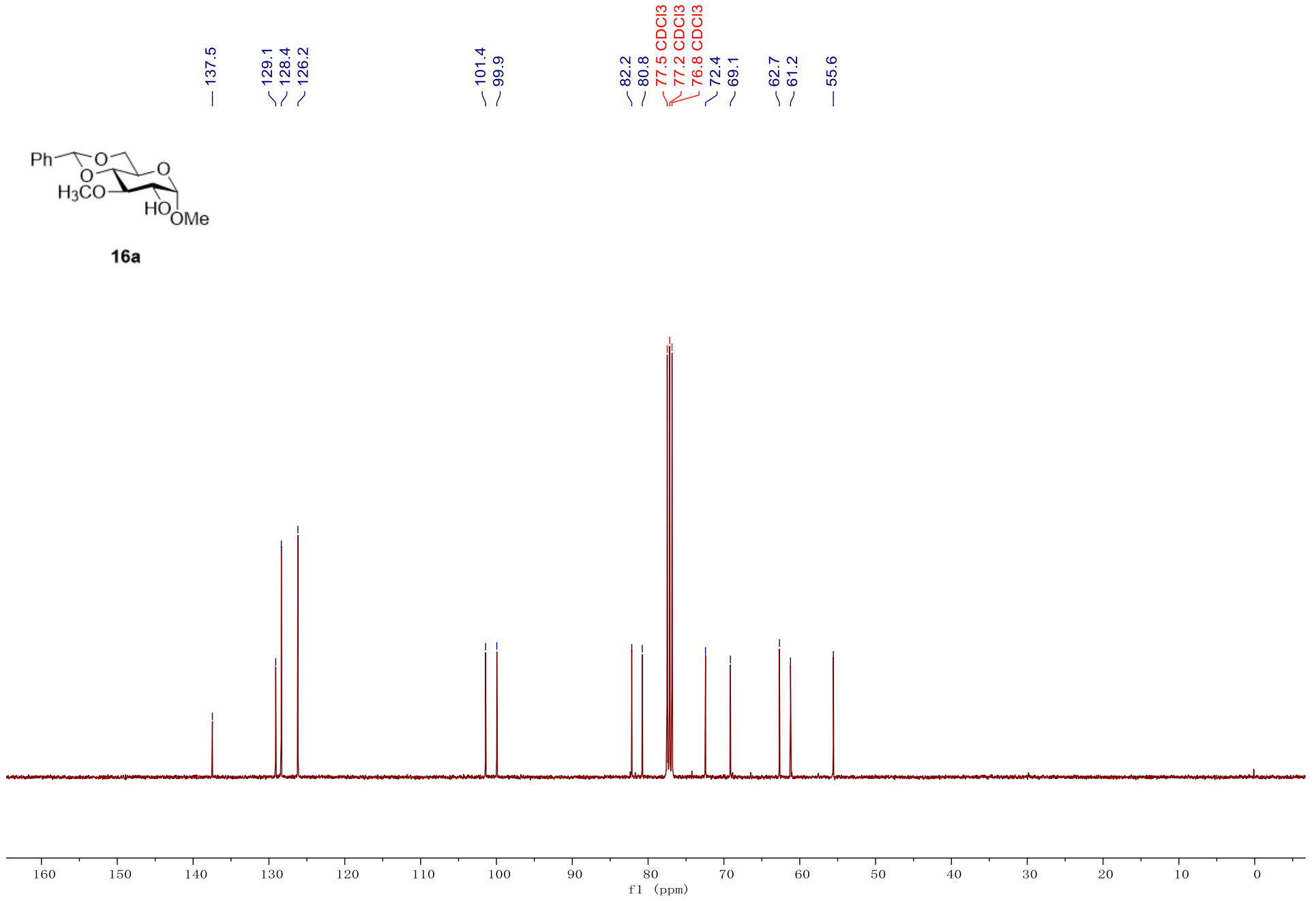


^{1}H-NMR of compound **16a** ($CDCl_3$)



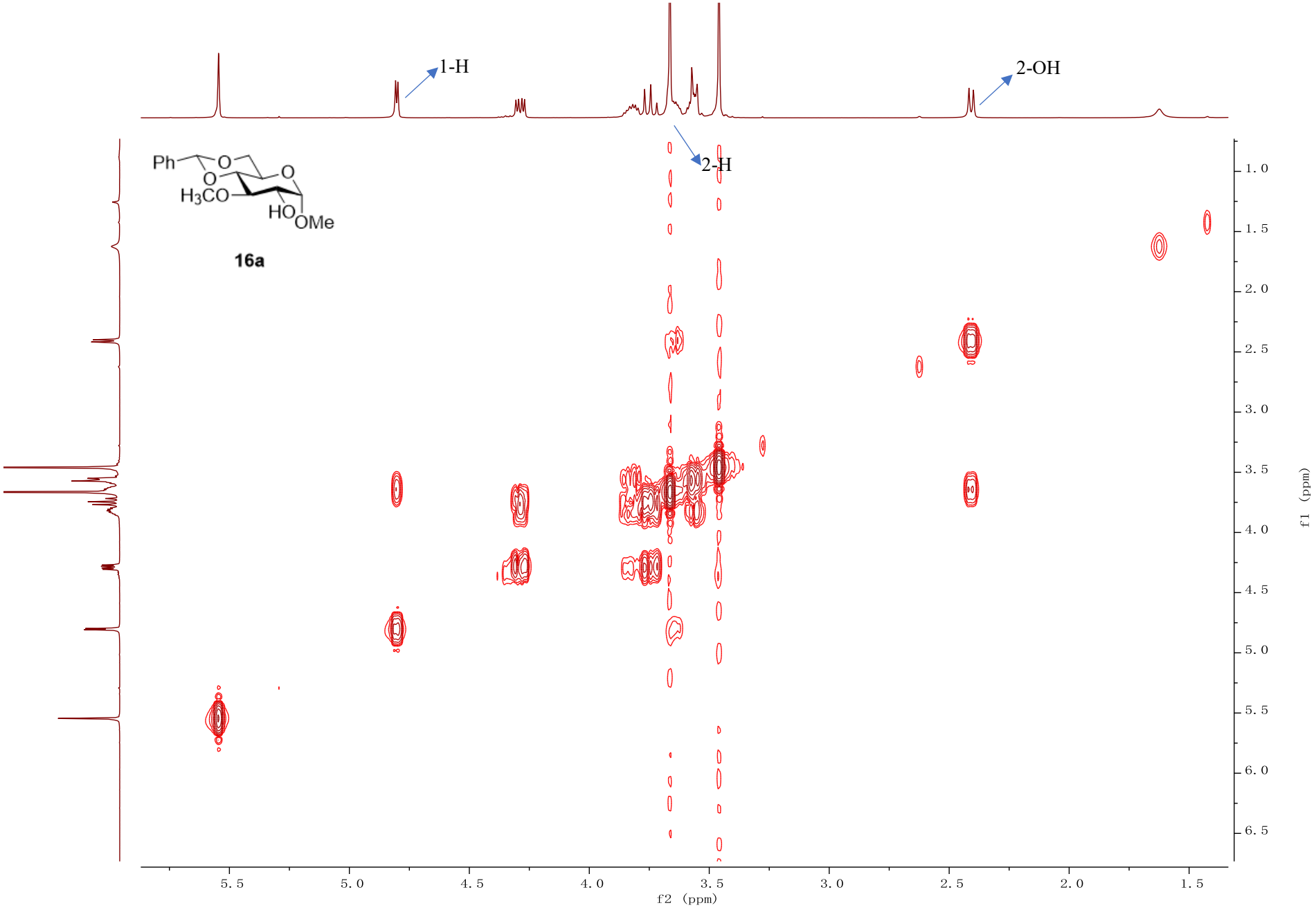
16a

^{13}C-NMR of compound **16a** ($CDCl_3$)

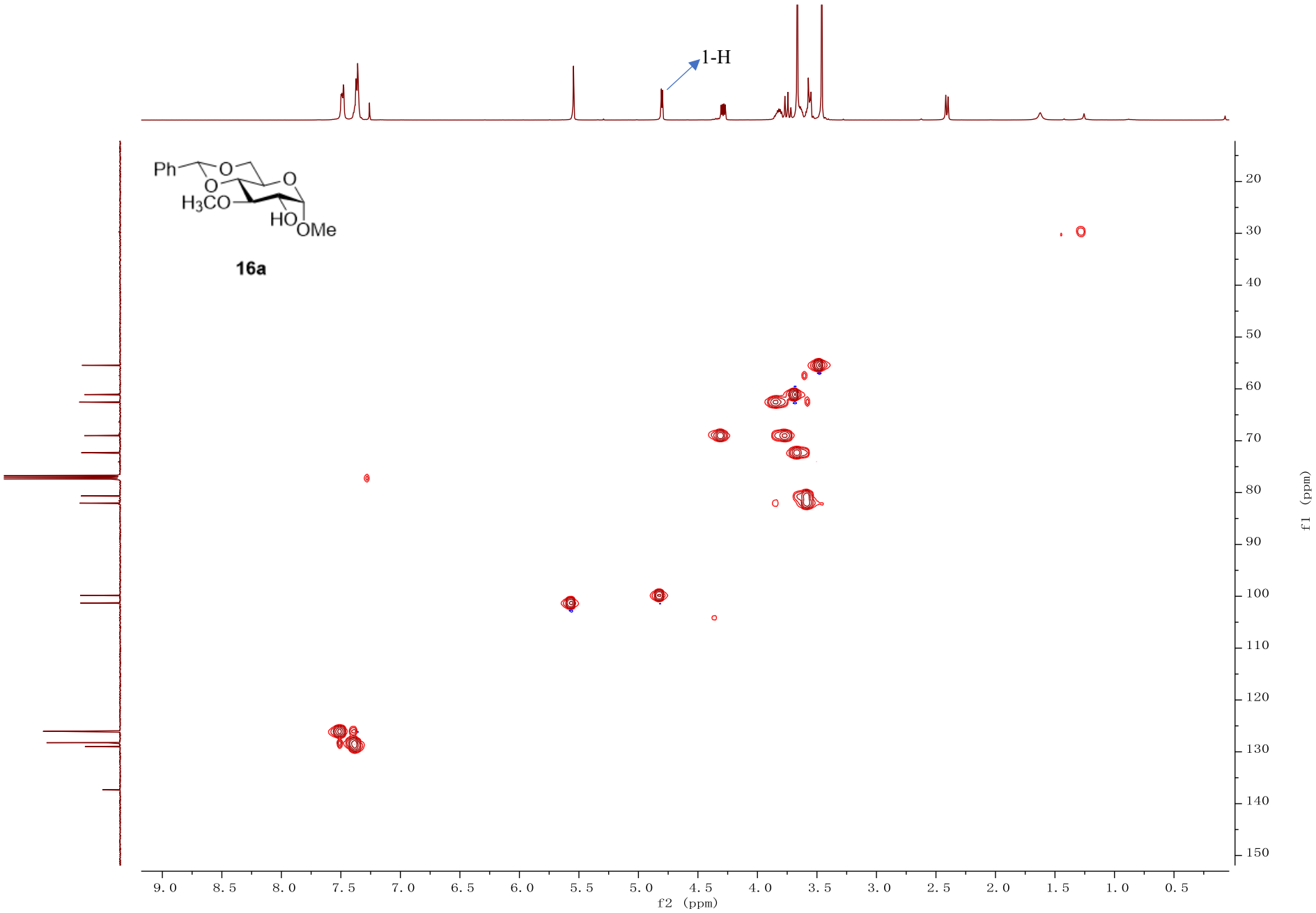


16a

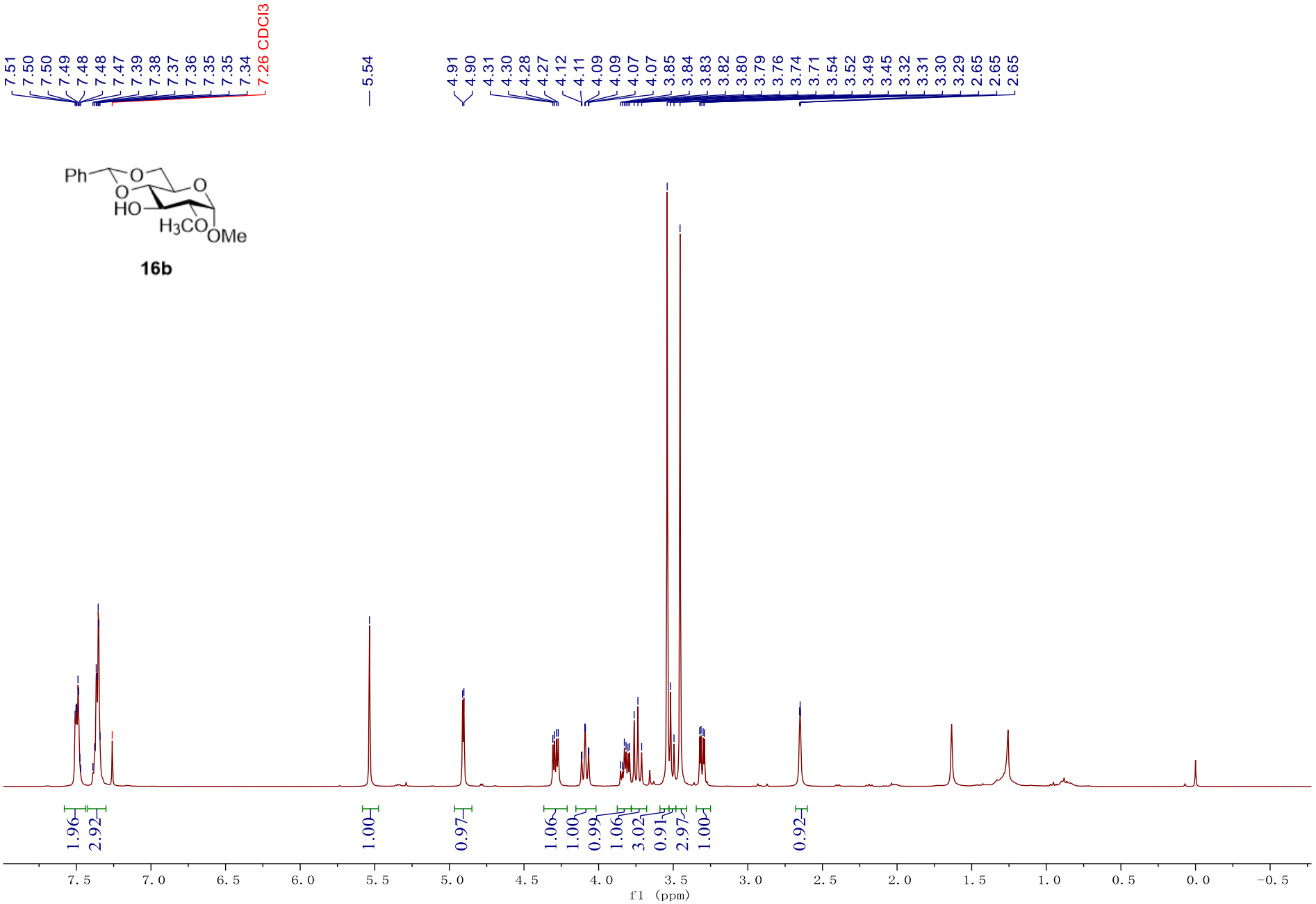
2D-COSY of compound **16a** ($CDCl_3$)



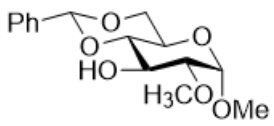
2D-HSQC of compound **16a** ($CDCl_3$)



^{1}H-NMR of compound **16b** ($CDCl_3$)

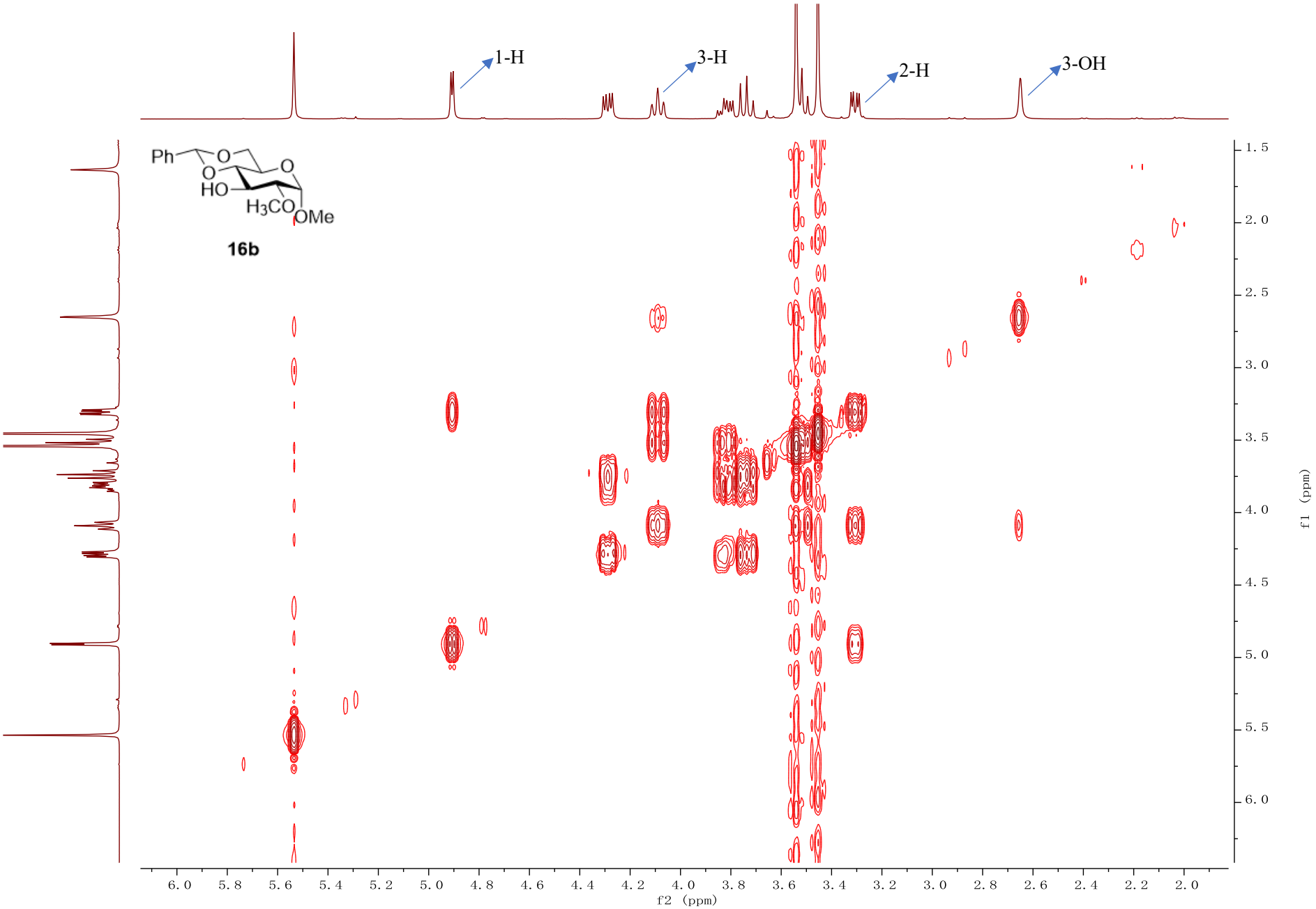


^{13}C-NMR of compound **16b** ($CDCl_3$)

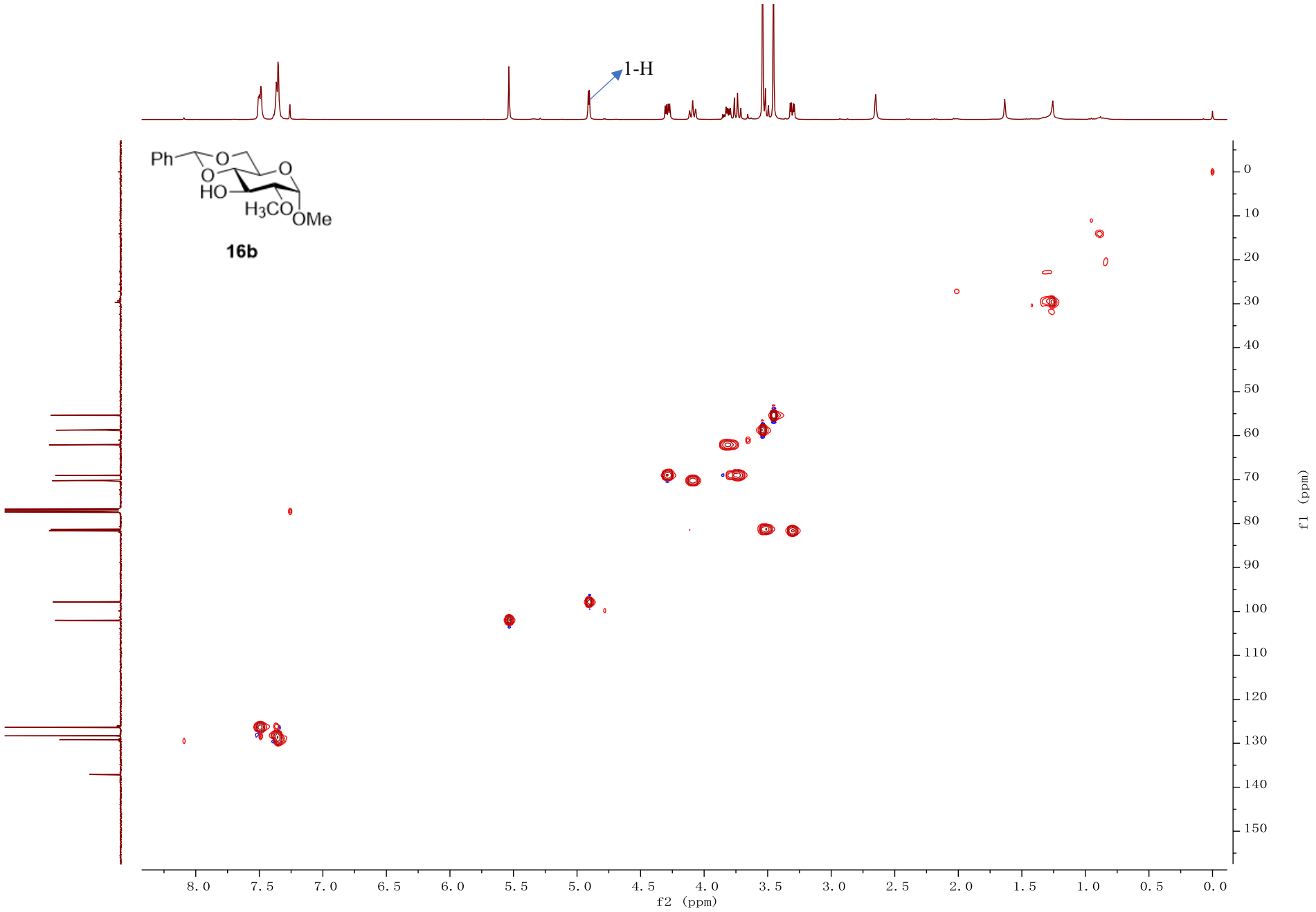


16b

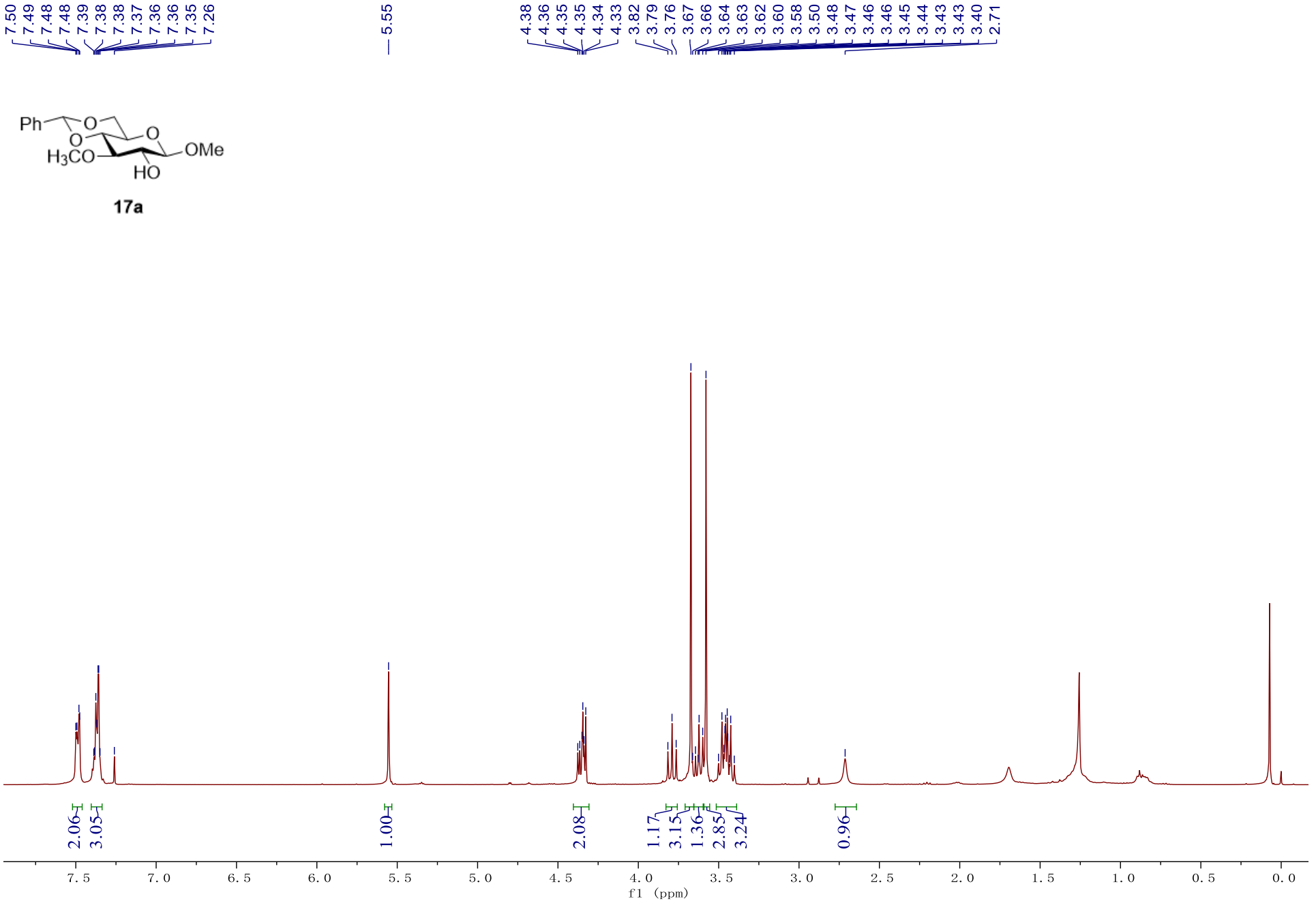
2D-COSY of compound **16b** ($CDCl_3$)



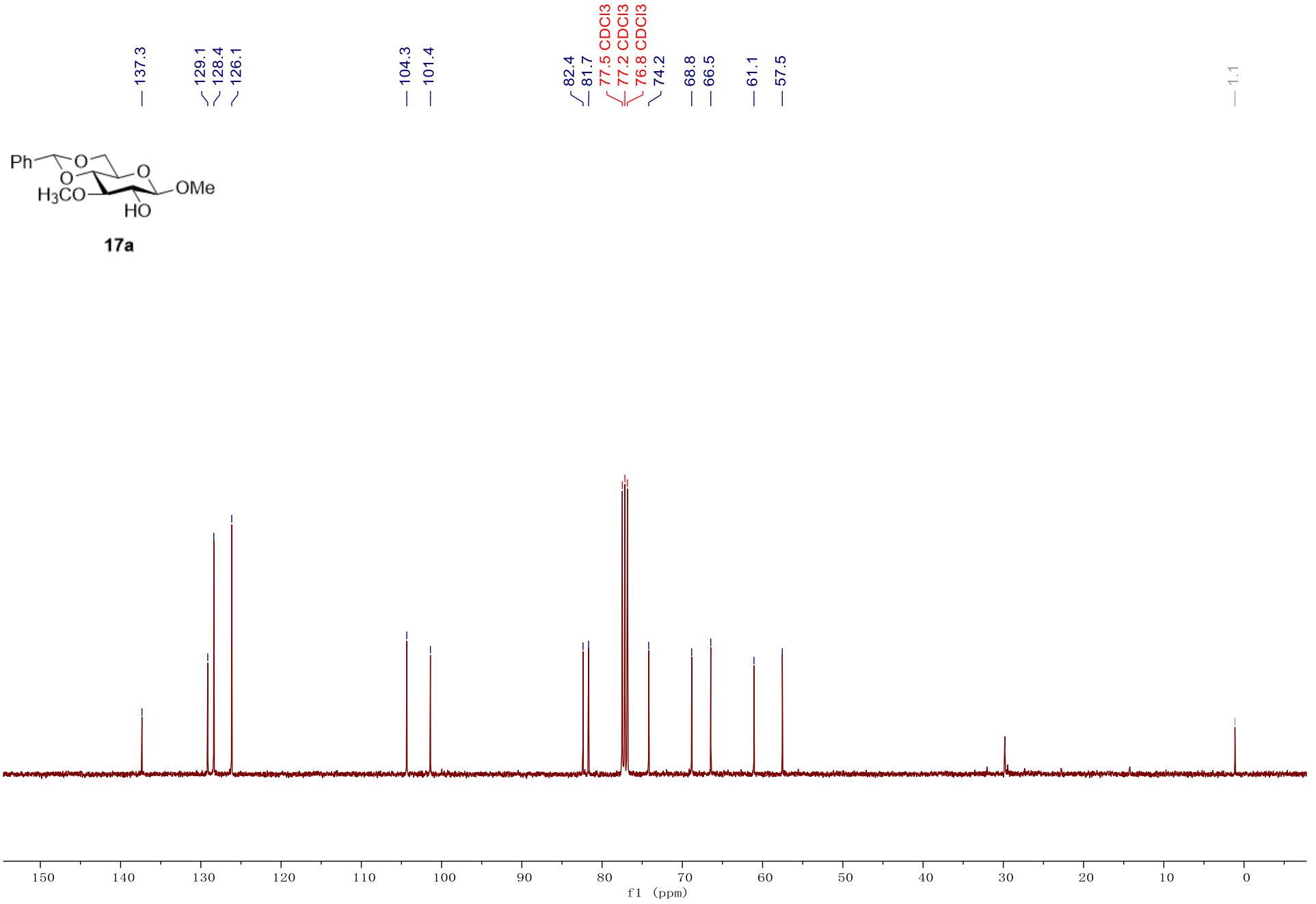
2D-HSQC of compound **16b** ($CDCl_3$)



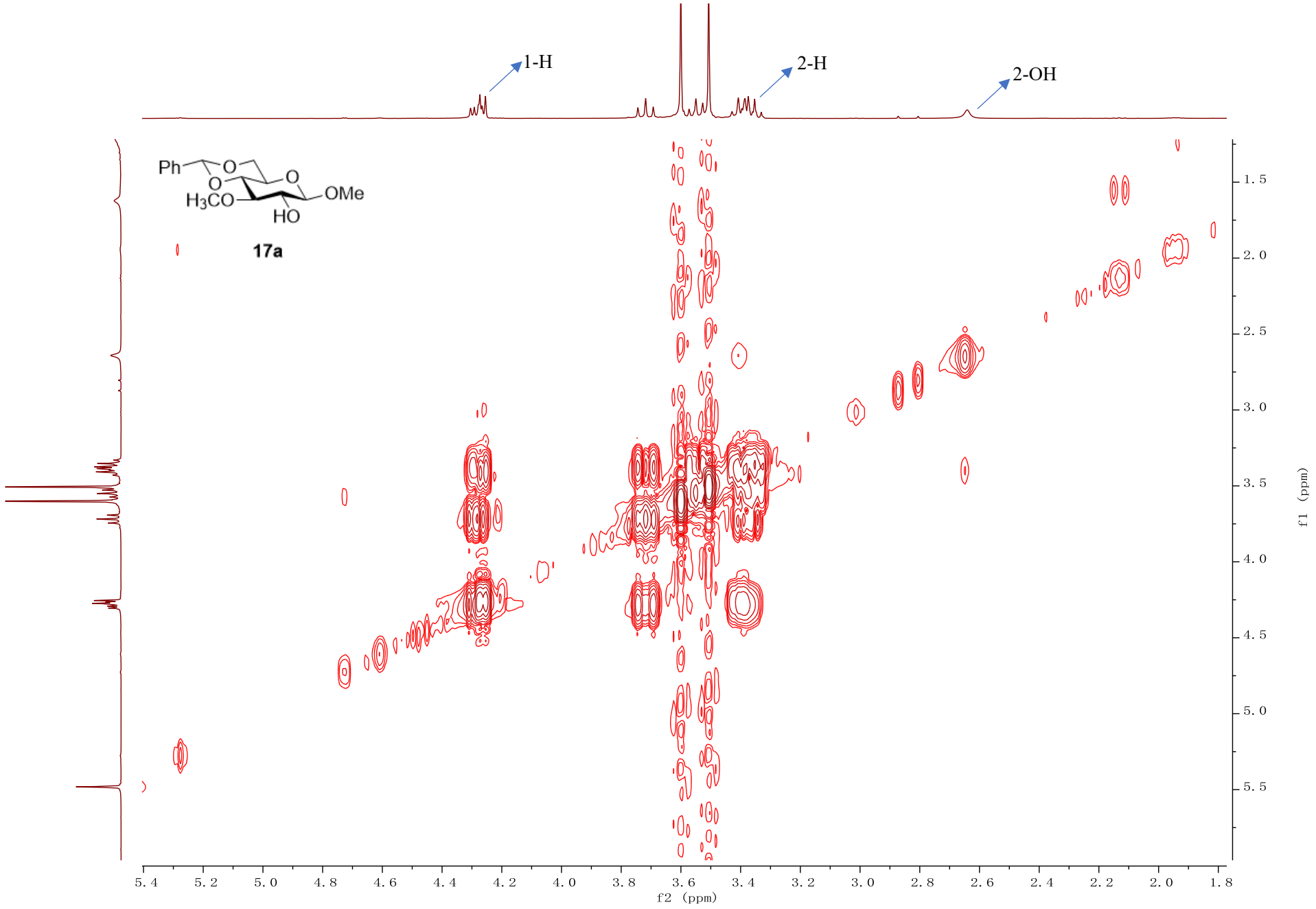
^{1}H-NMR of compound **17a** ($CDCl_3$)



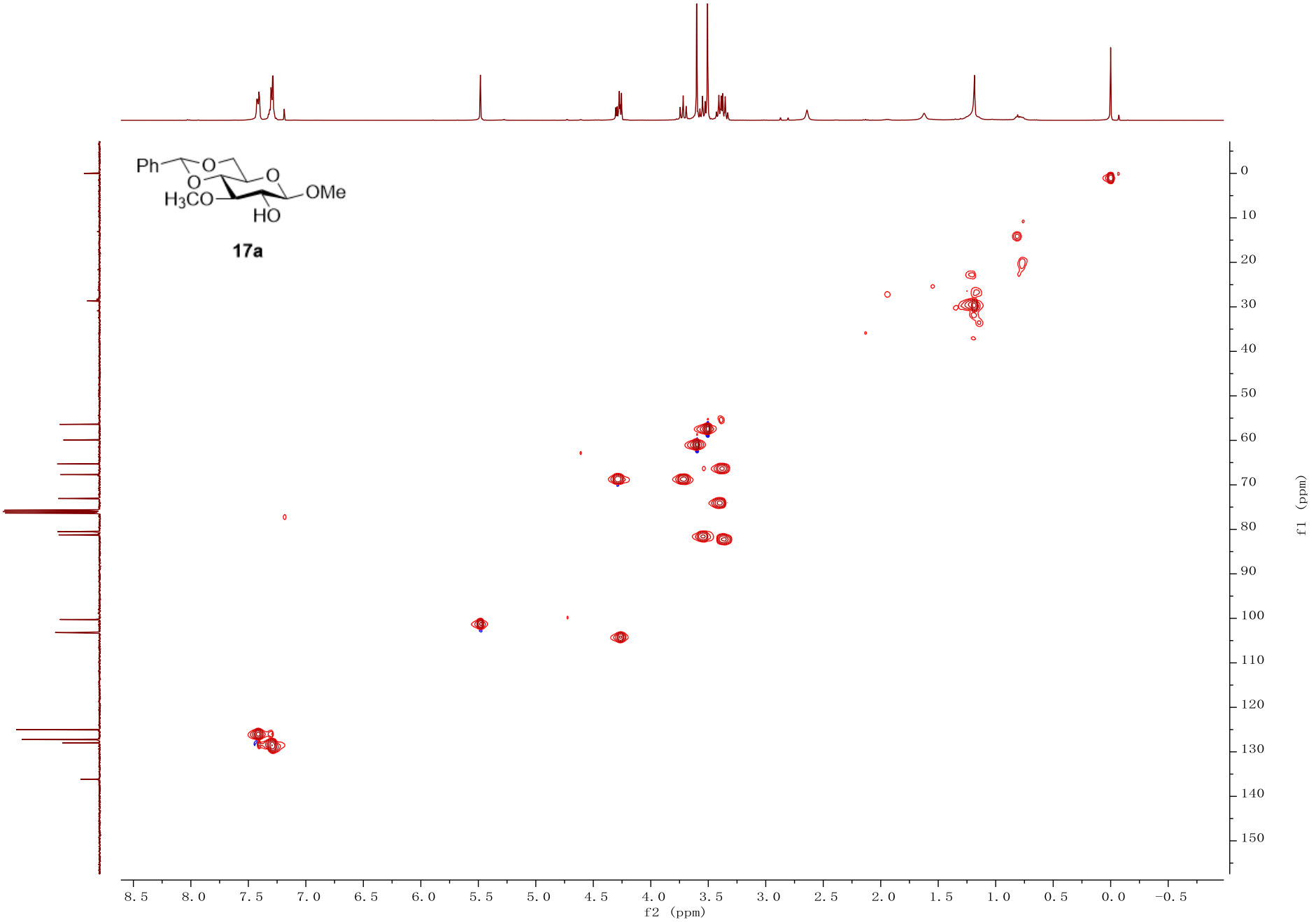
^{13}C-NMR of compound **17a** ($CDCl_3$)



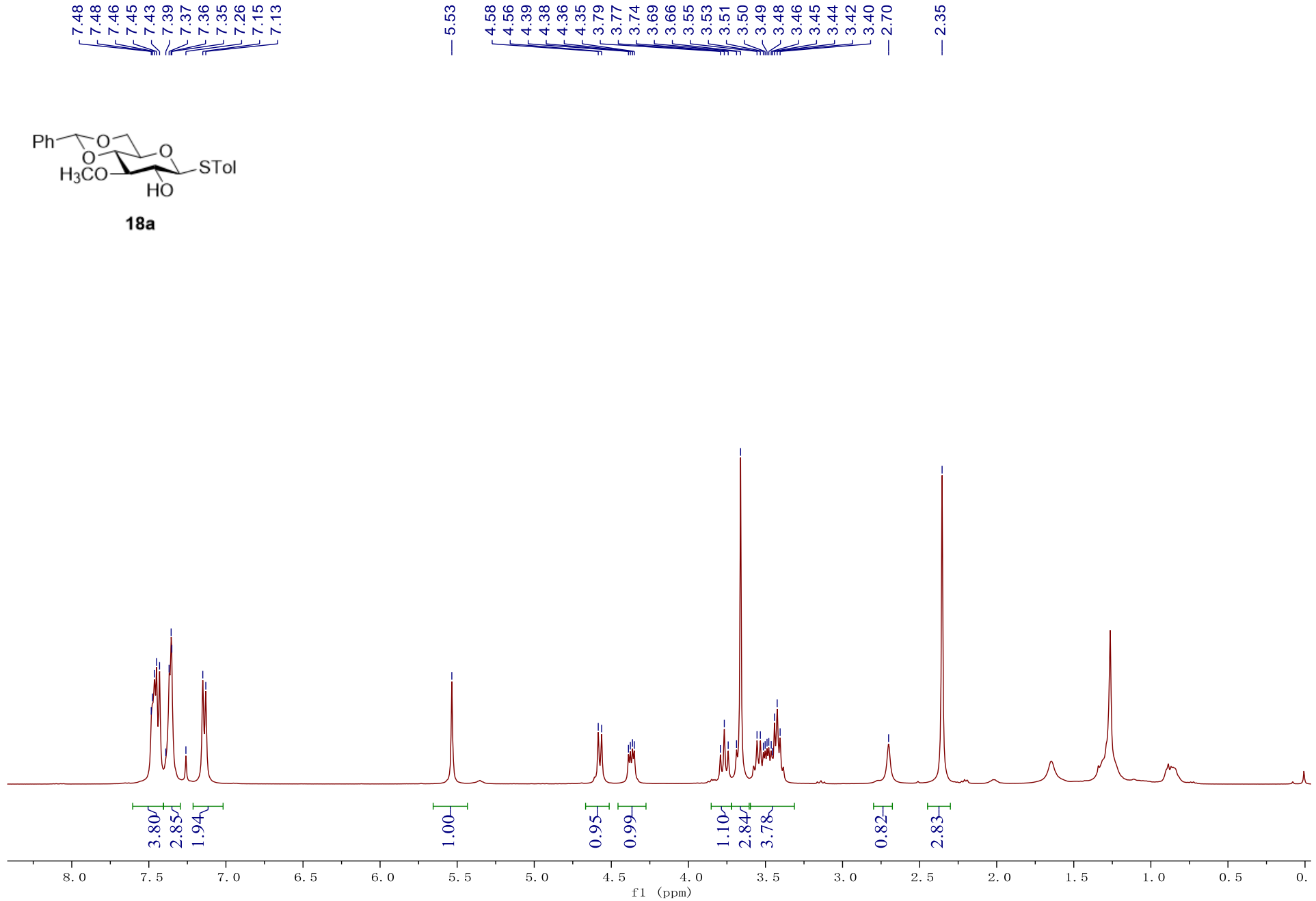
2D-COSY of compound **17a** ($CDCl_3$)



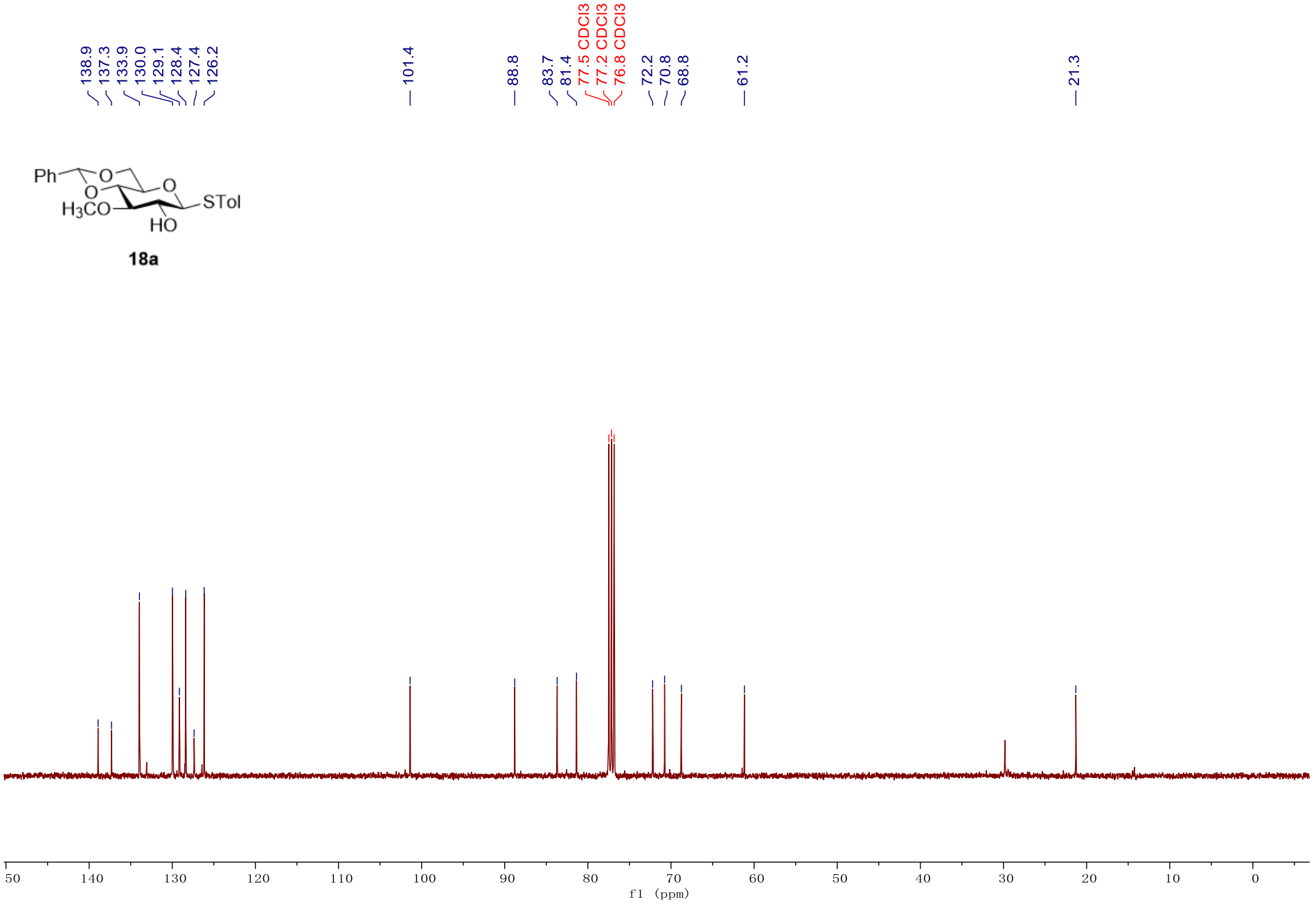
2D-HSQC of compound **17a** ($CDCl_3$)



^{1}H-NMR of compound **18a** ($CDCl_3$)

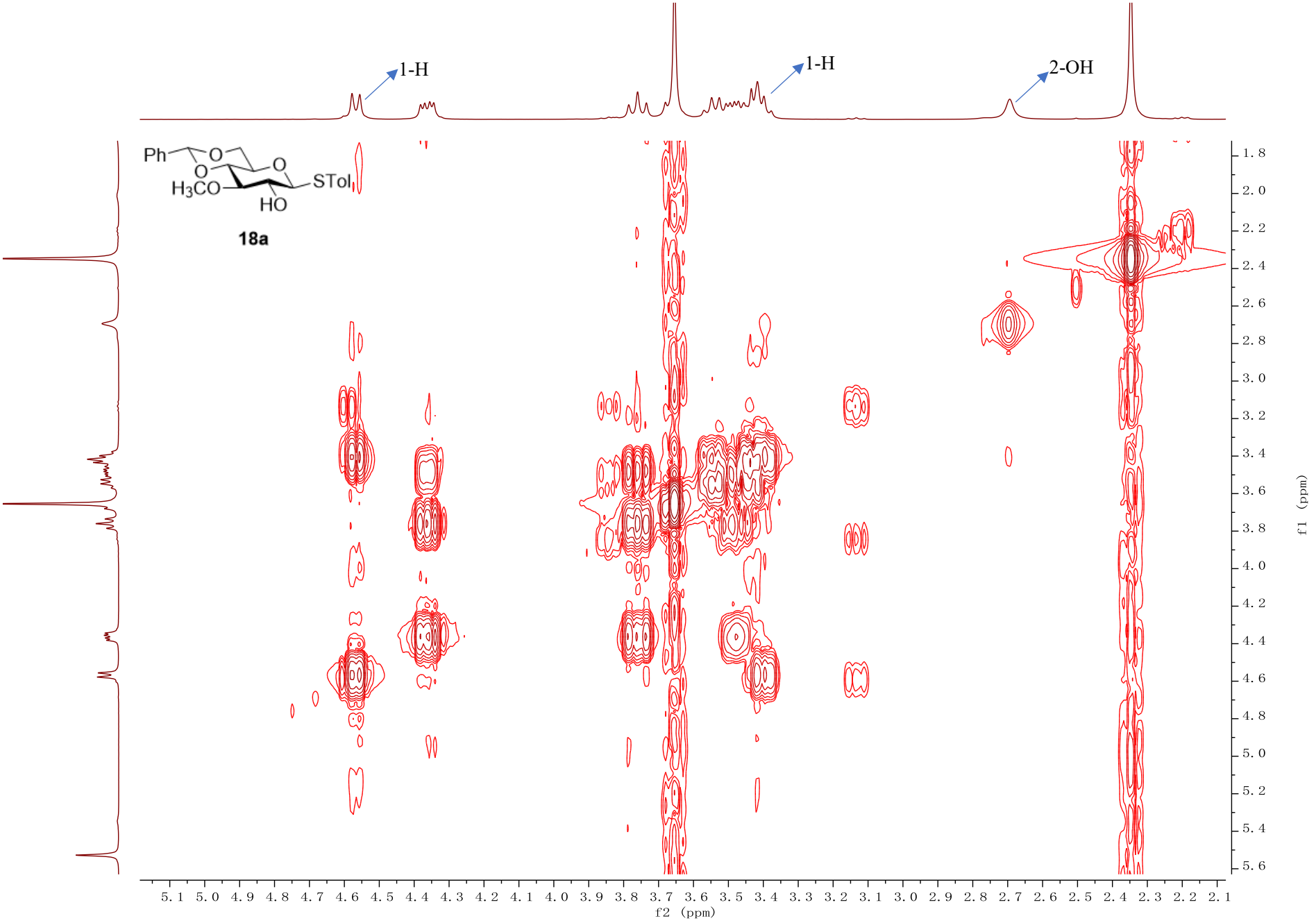


^{13}C-NMR of compound **18a** ($CDCl_3$)

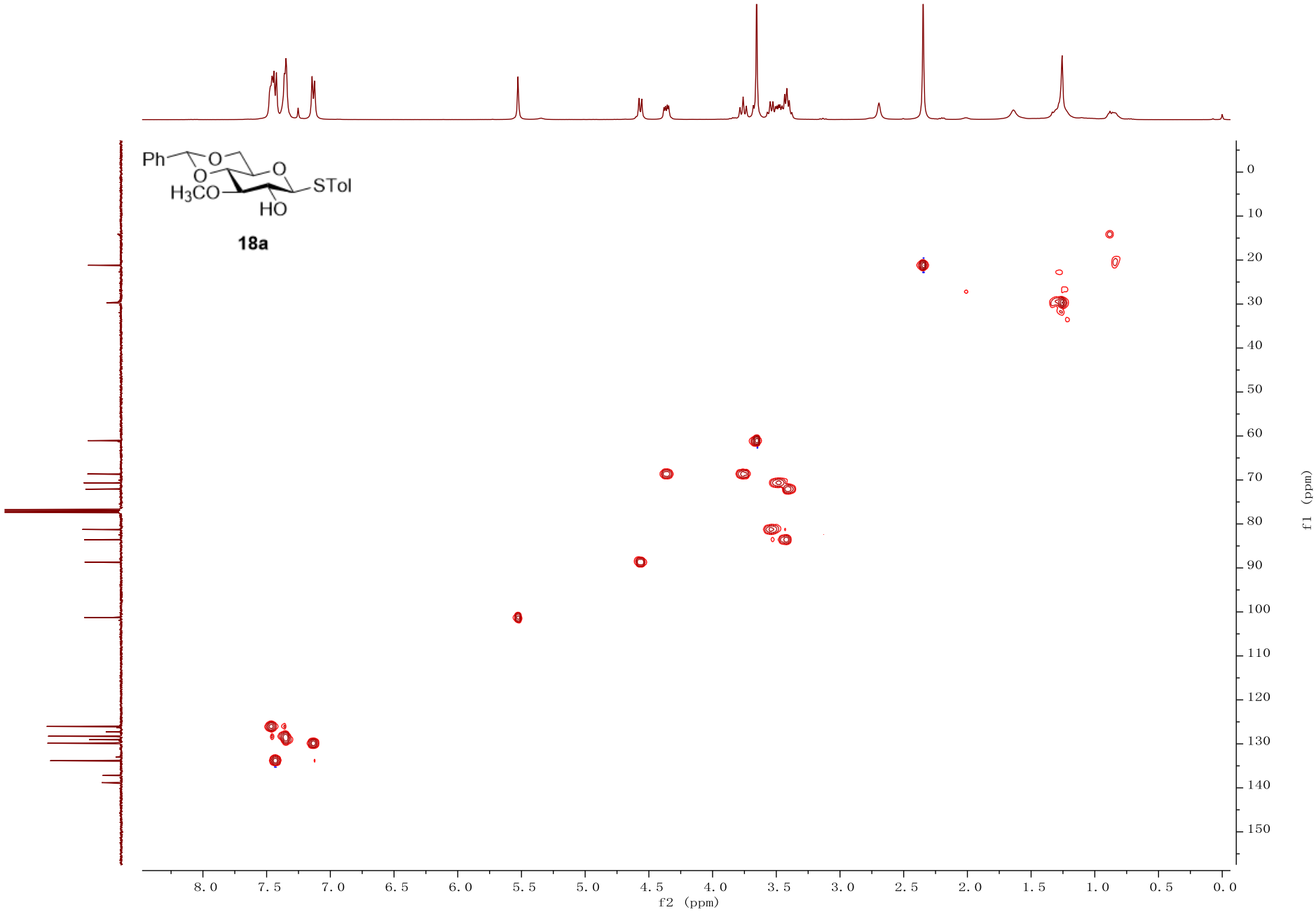


18a

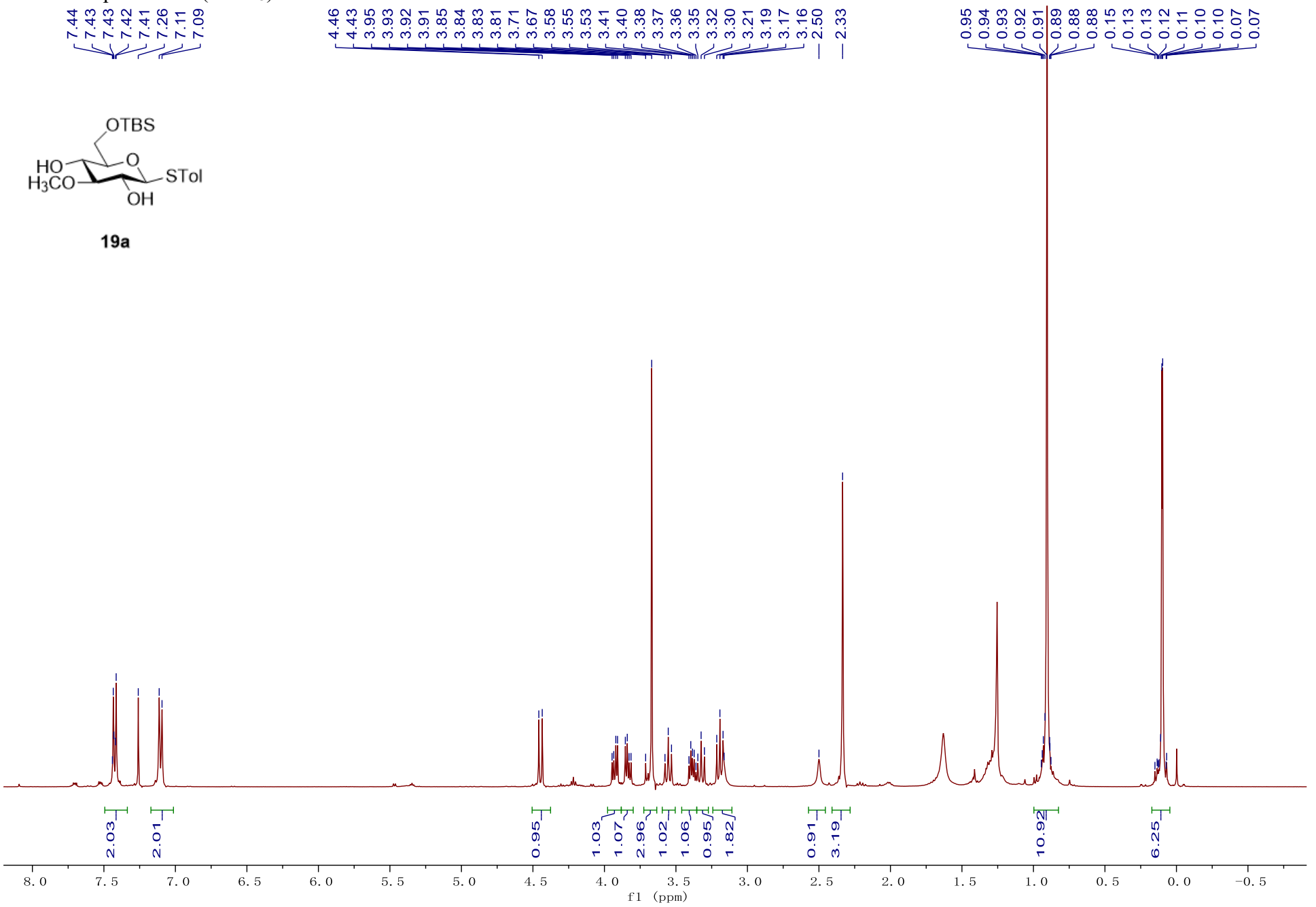
2D-COSY of compound **18a** ($CDCl_3$)



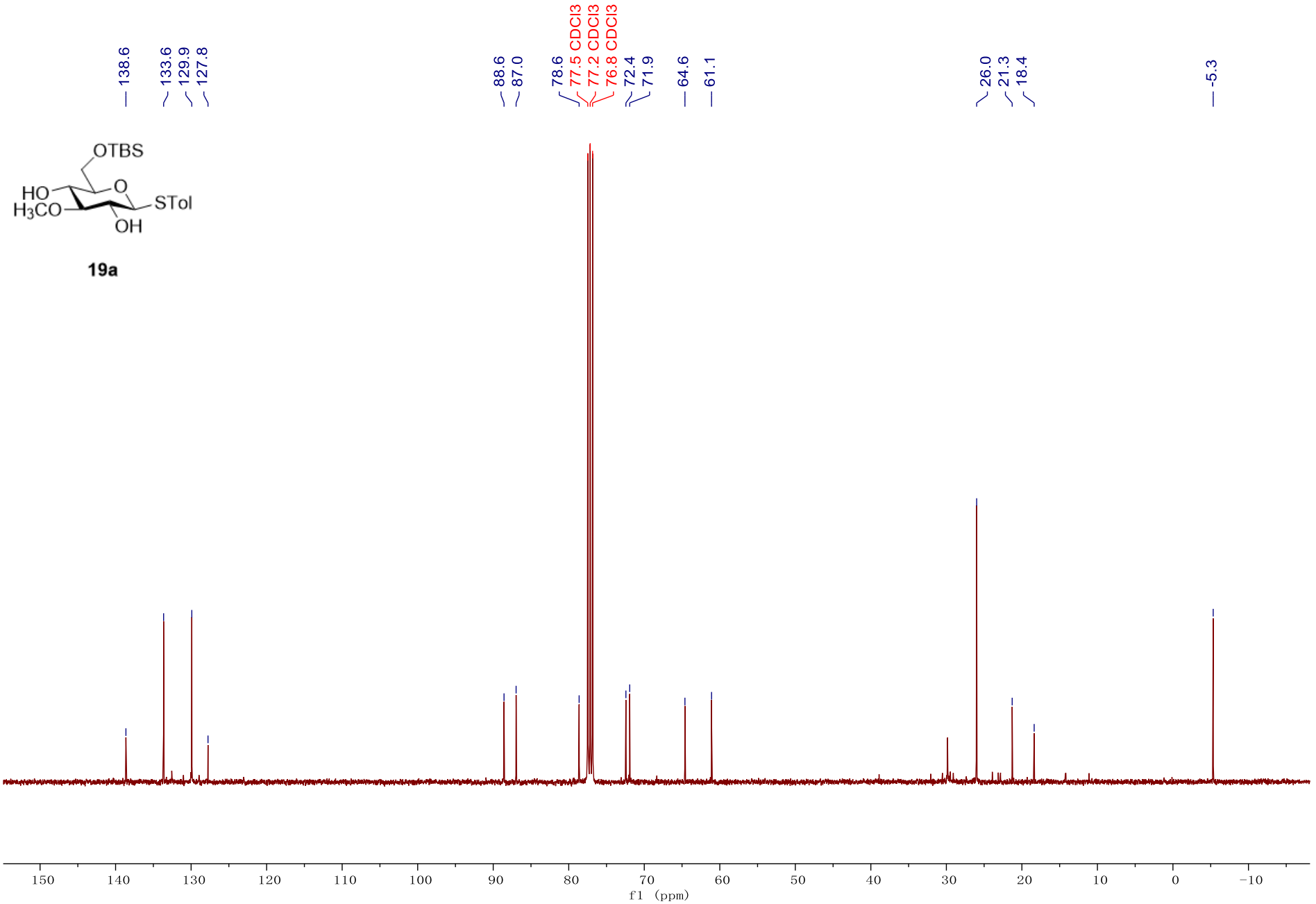
2D-HSQC of compound **18a** ($CDCl_3$)



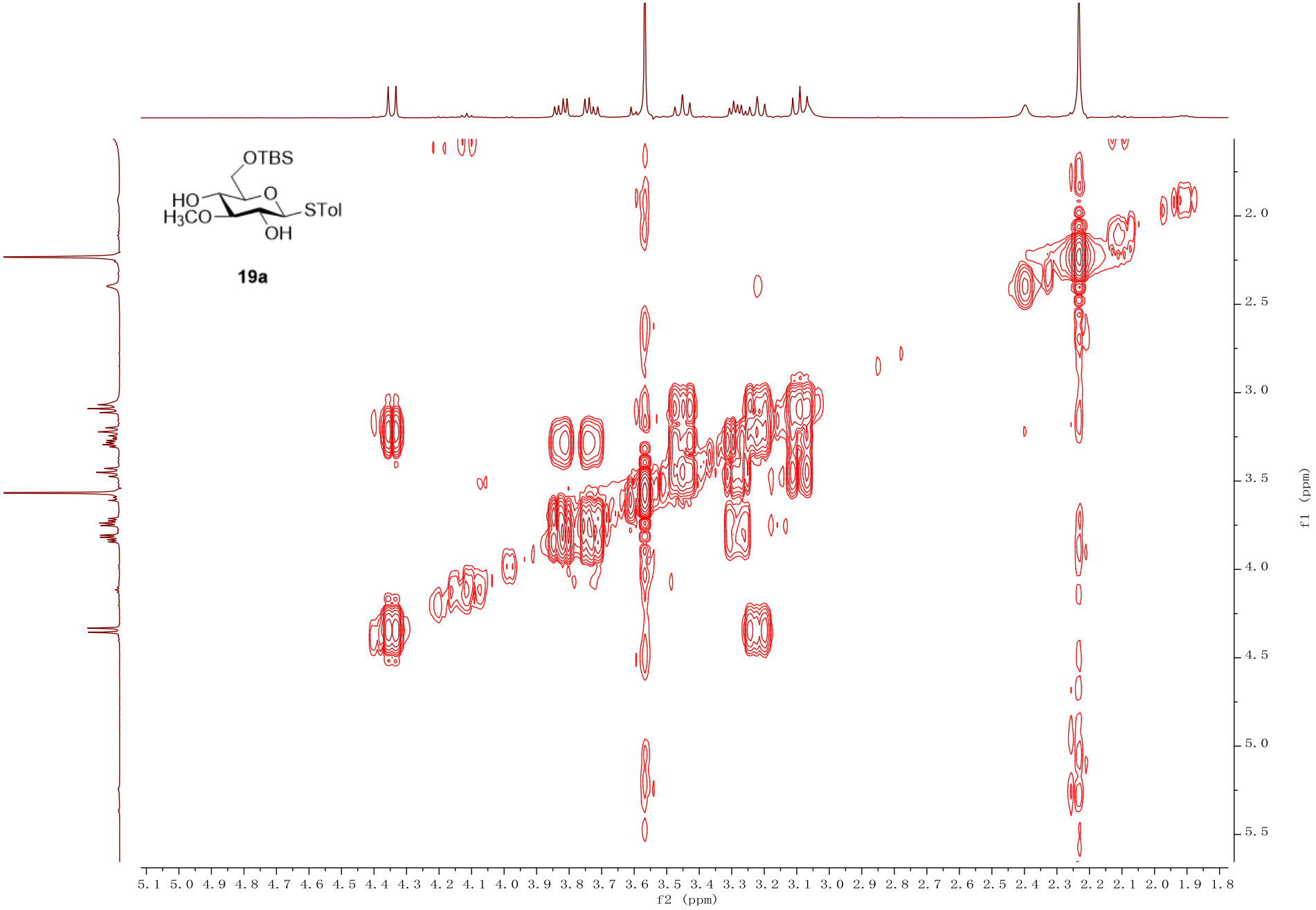
^{1}H-NMR of compound **19a** ($CDCl_3$)



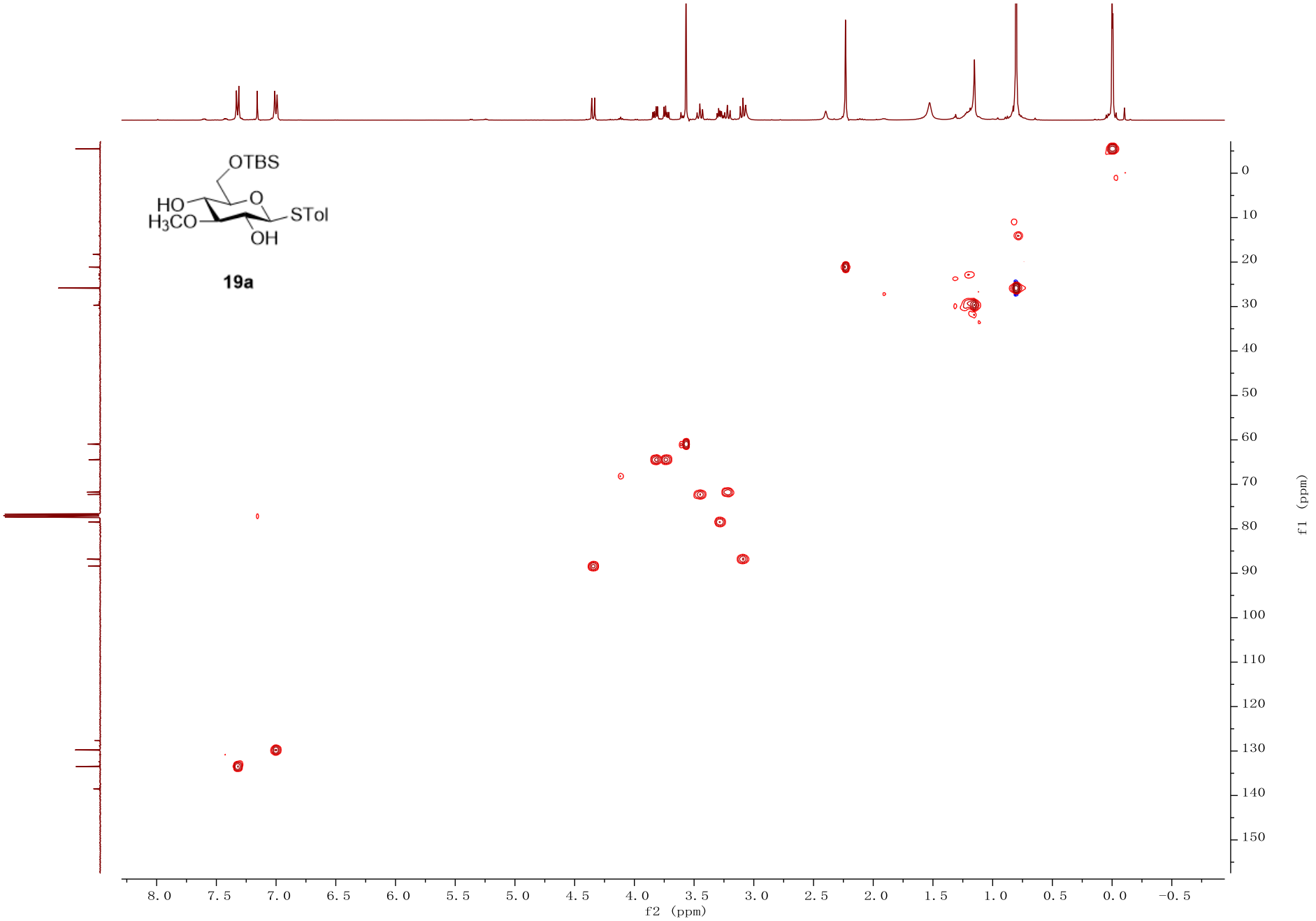
^{13}C-NMR of compound **19a** ($CDCl_3$)



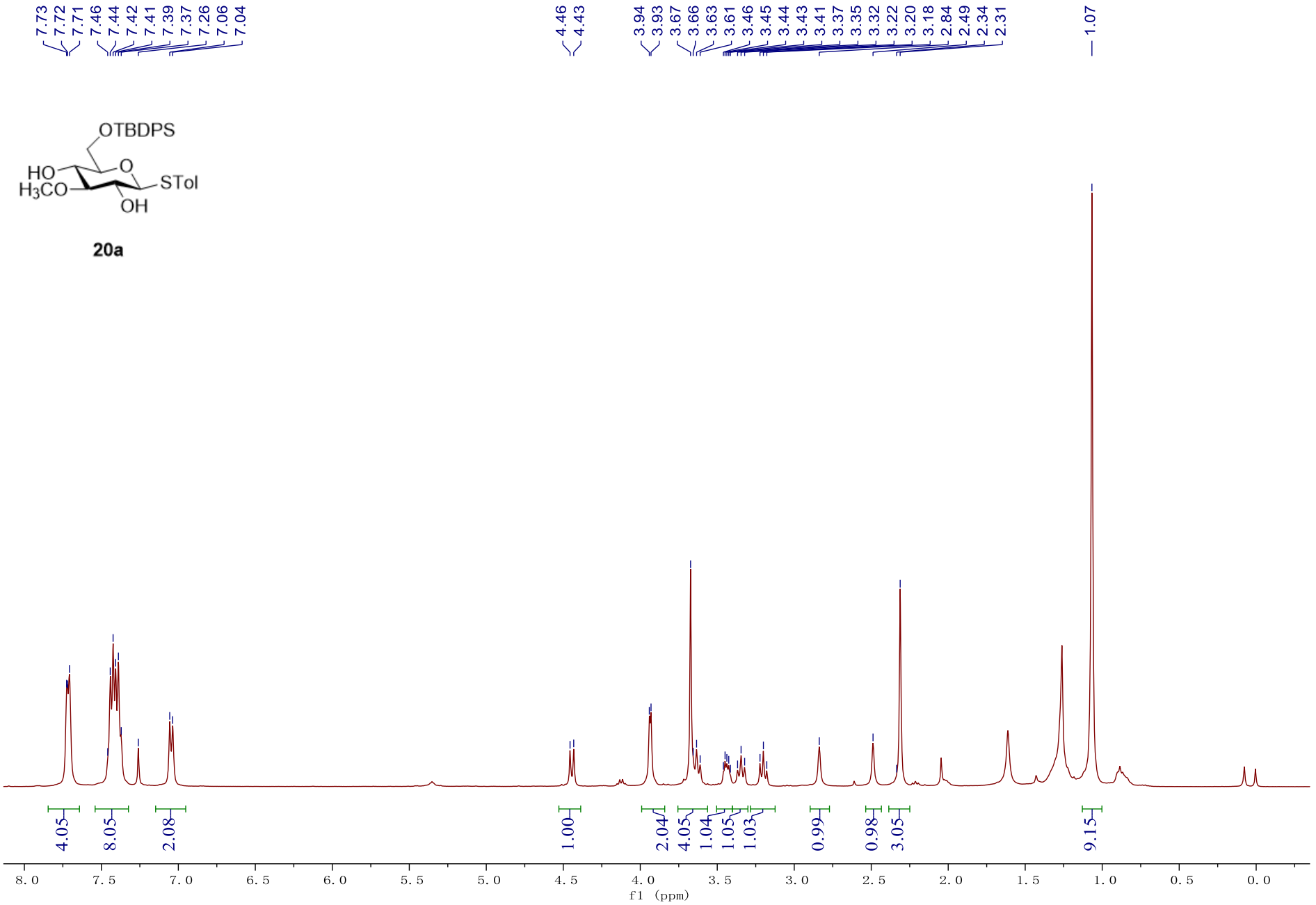
2D-COSY of compound **19a** ($CDCl_3$)



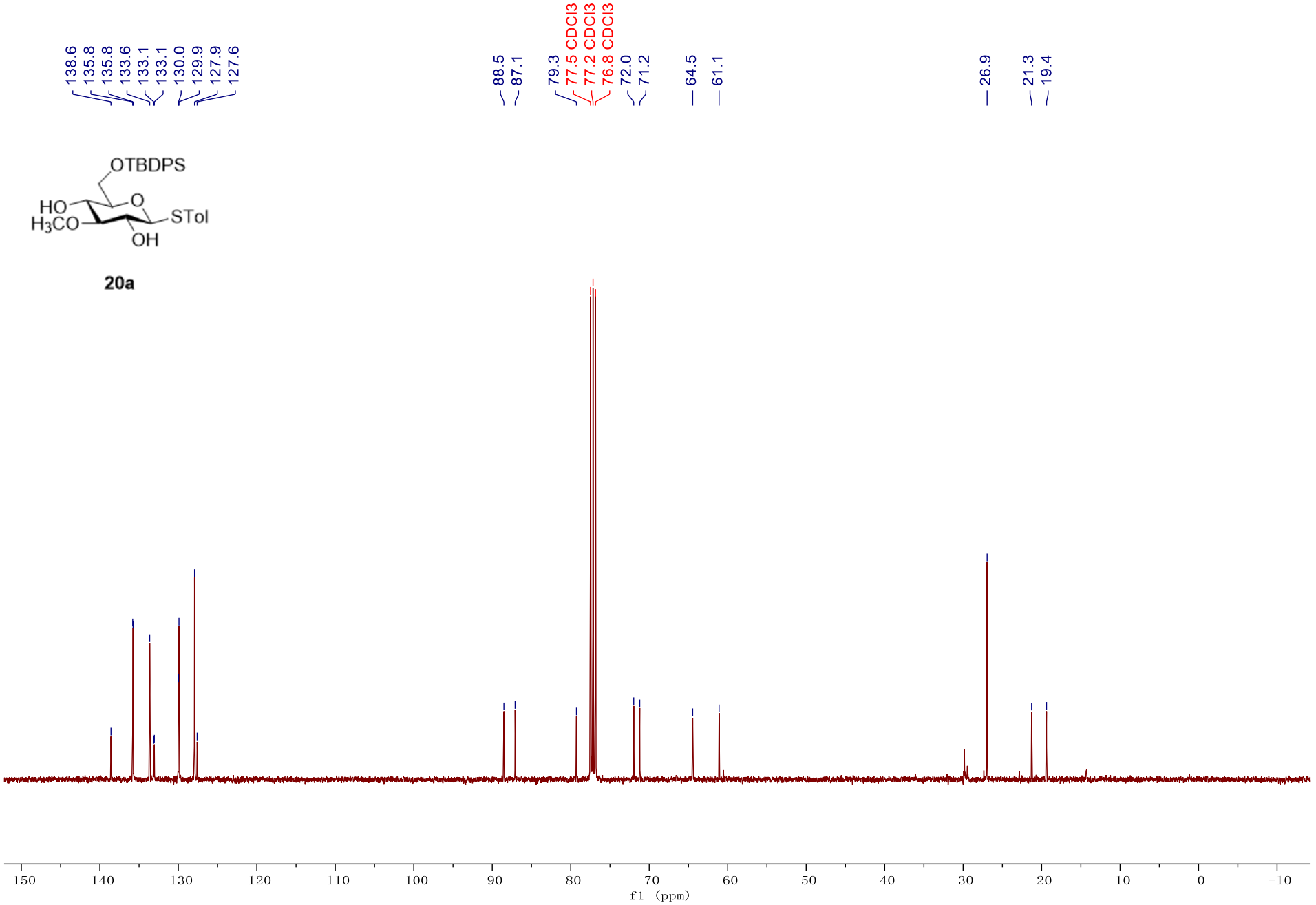
2D-HSQC of compound **19a** ($CDCl_3$)



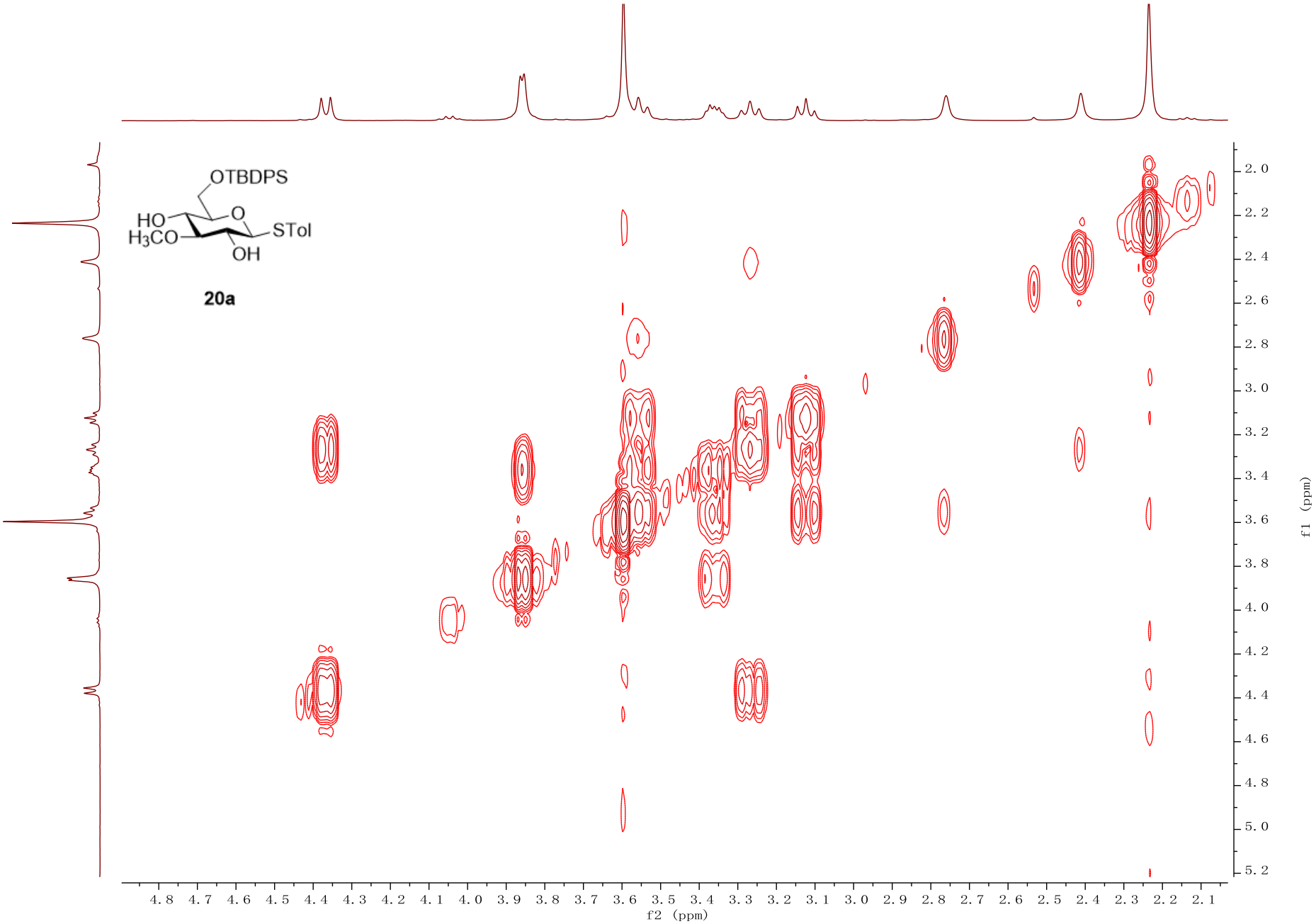
^{1}H-NMR of compound **20a** ($CDCl_3$)



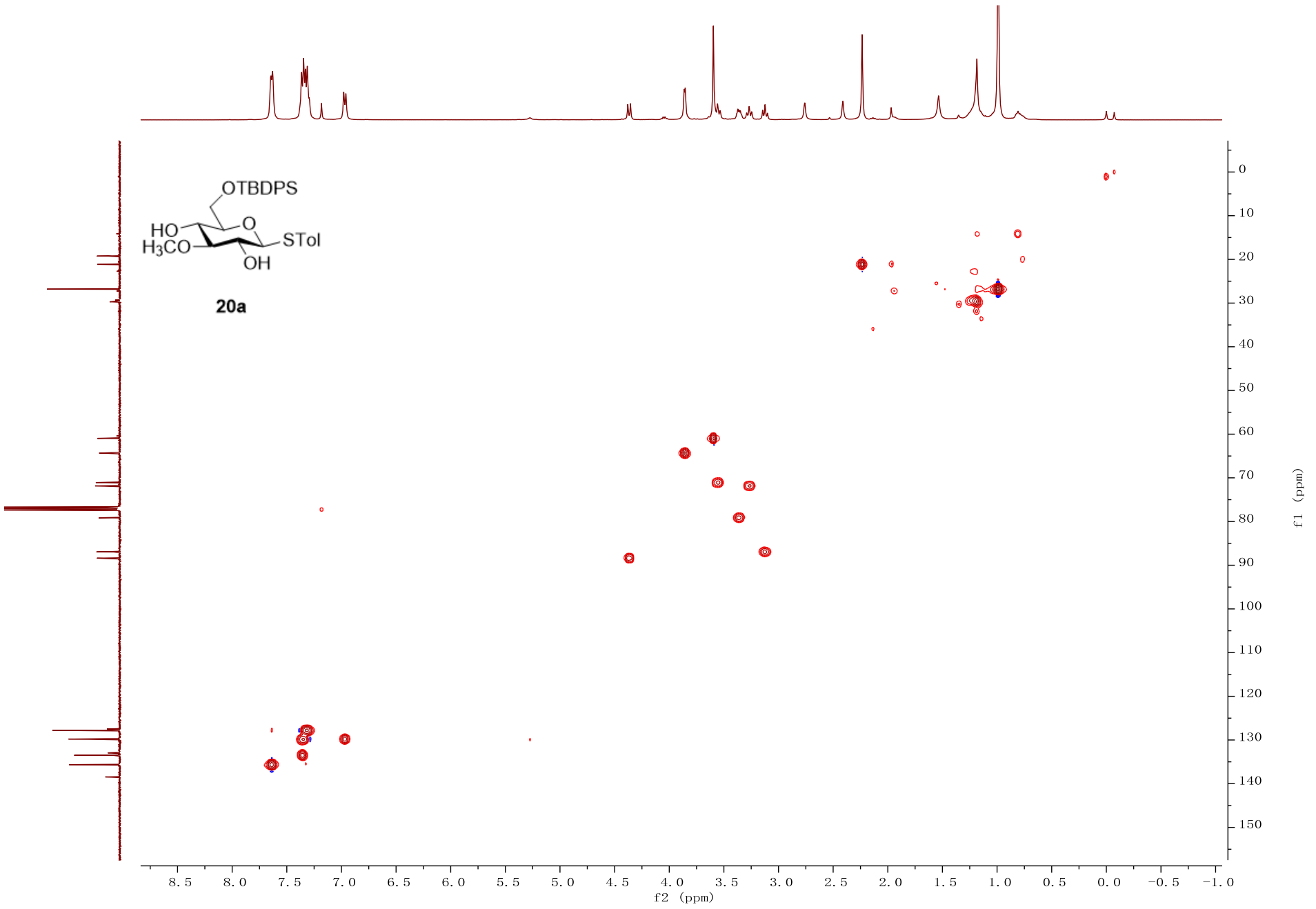
^{13}C-NMR of compound **20a** ($CDCl_3$)



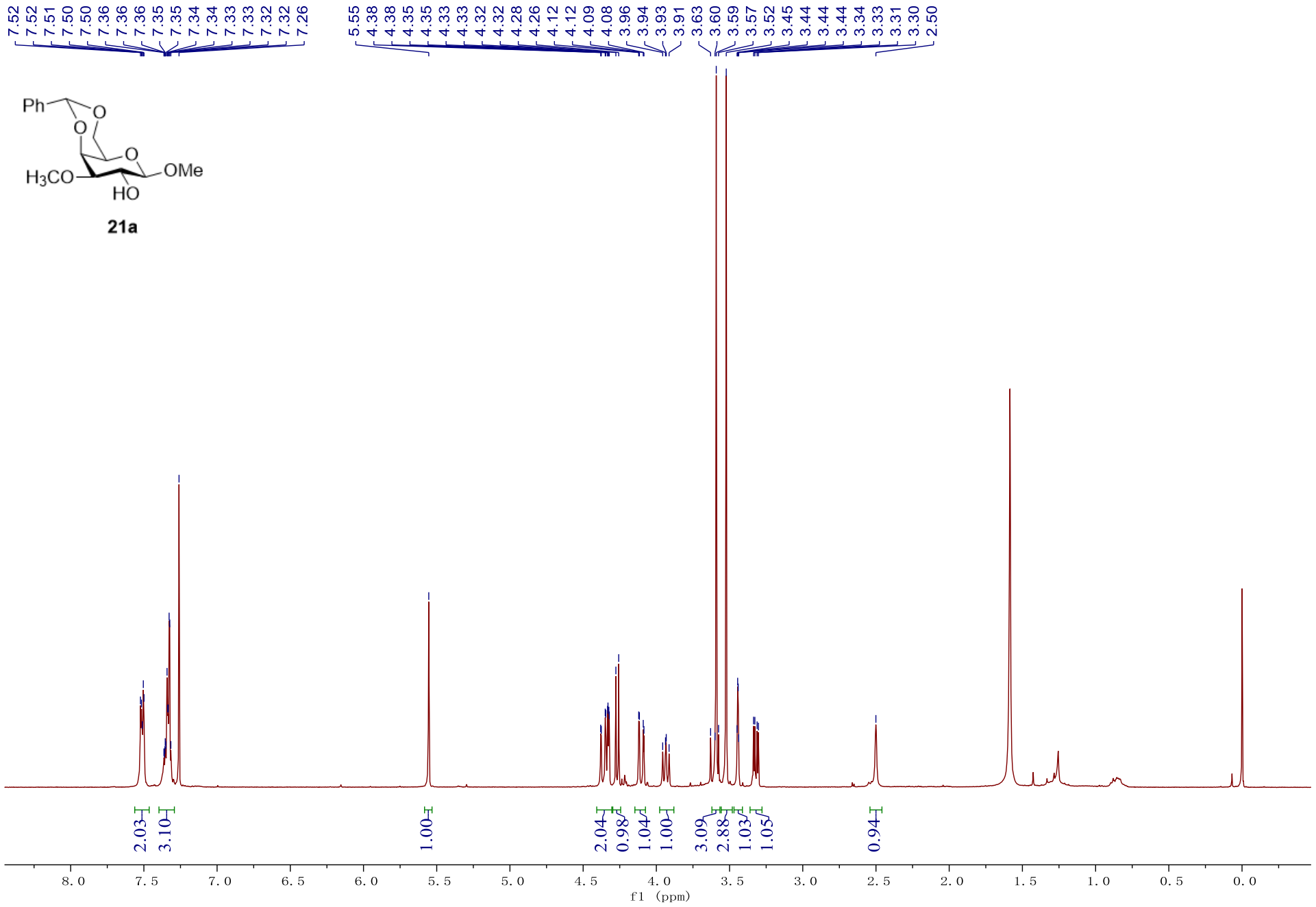
2D-COSY of compound **20a** ($CDCl_3$)



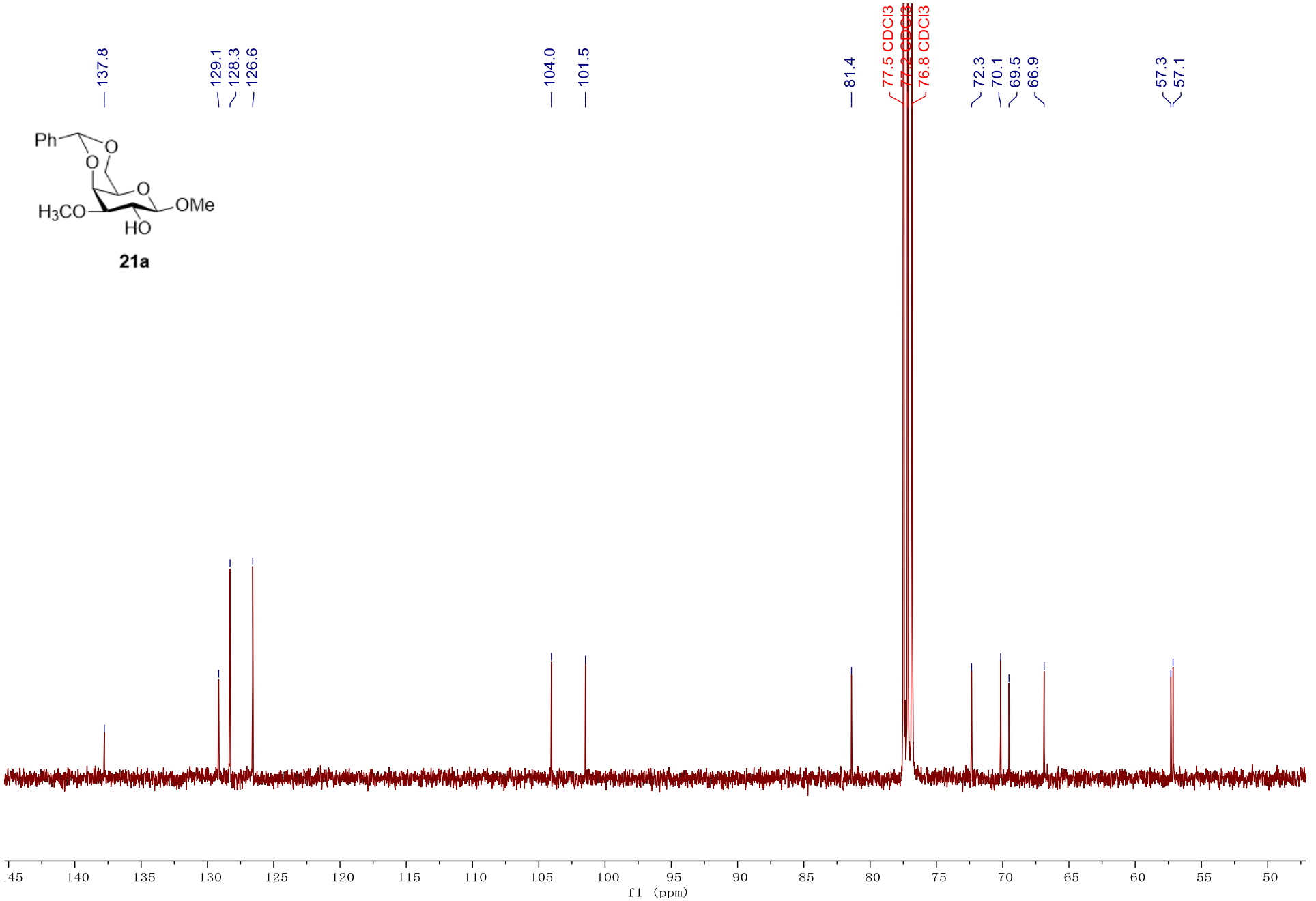
2D-HSQC of compound **20a** ($CDCl_3$)



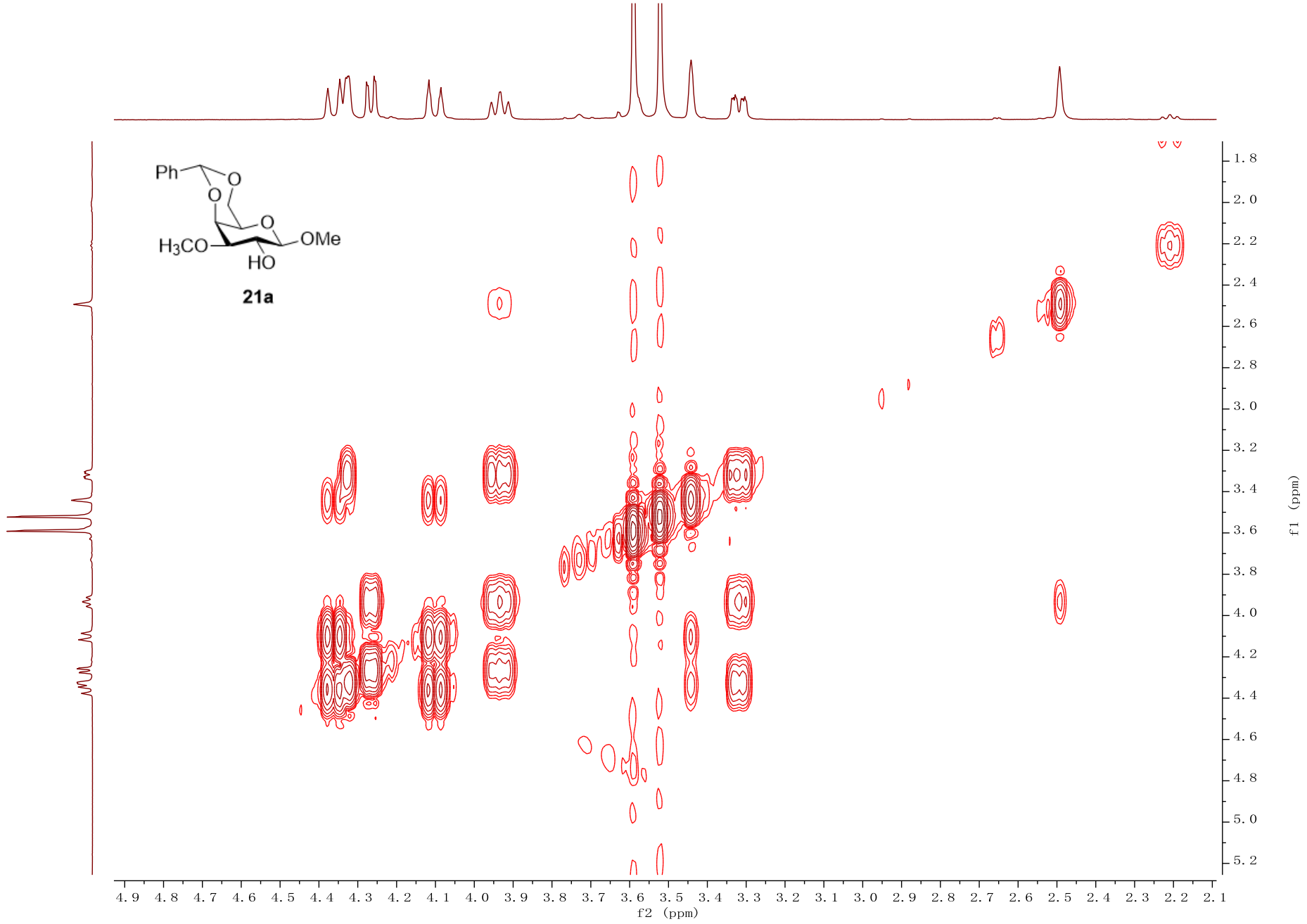
^{1}H-NMR of compound **21a** ($CDCl_3$)



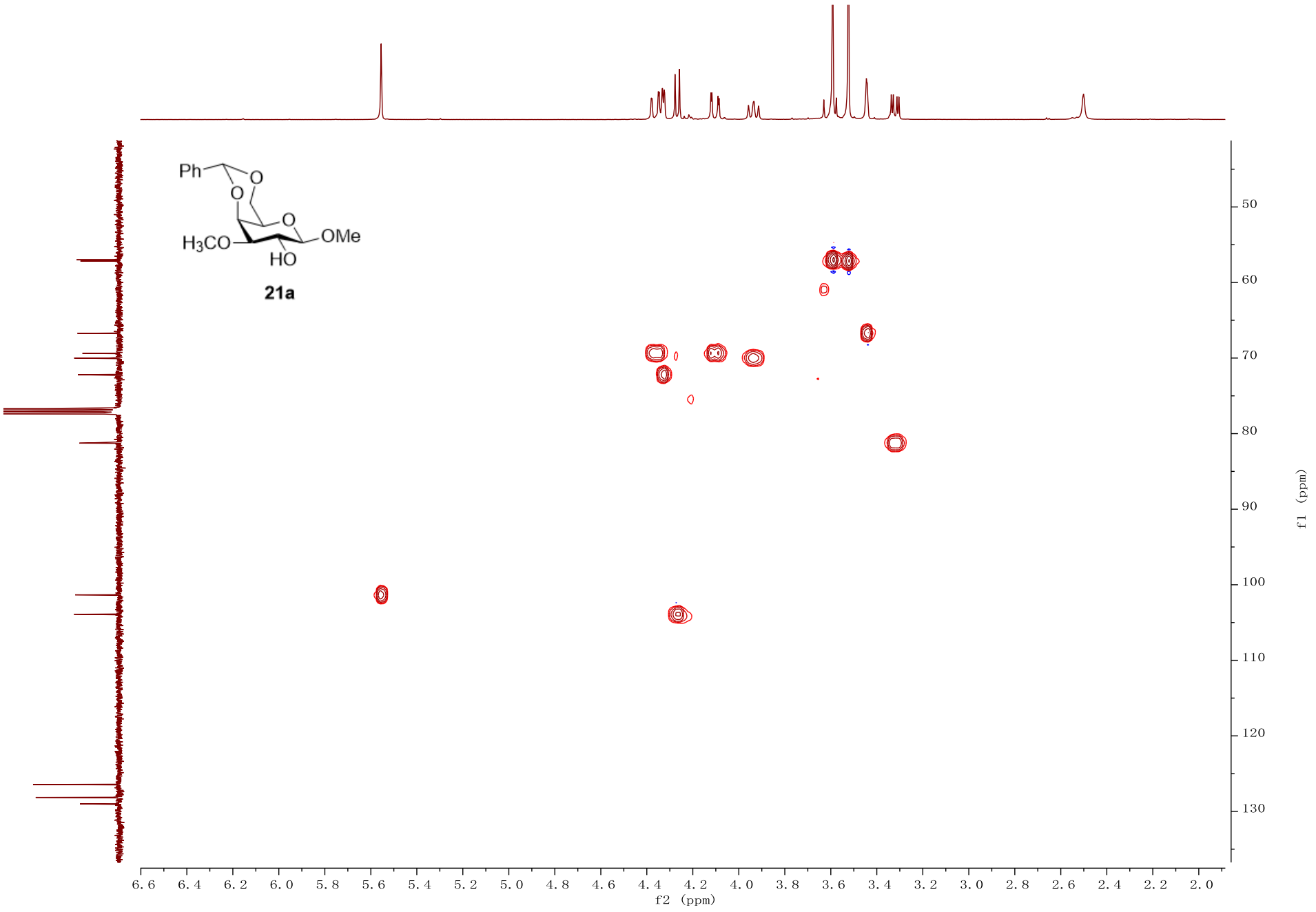
^{13}C-NMR of compound **21a** ($CDCl_3$)



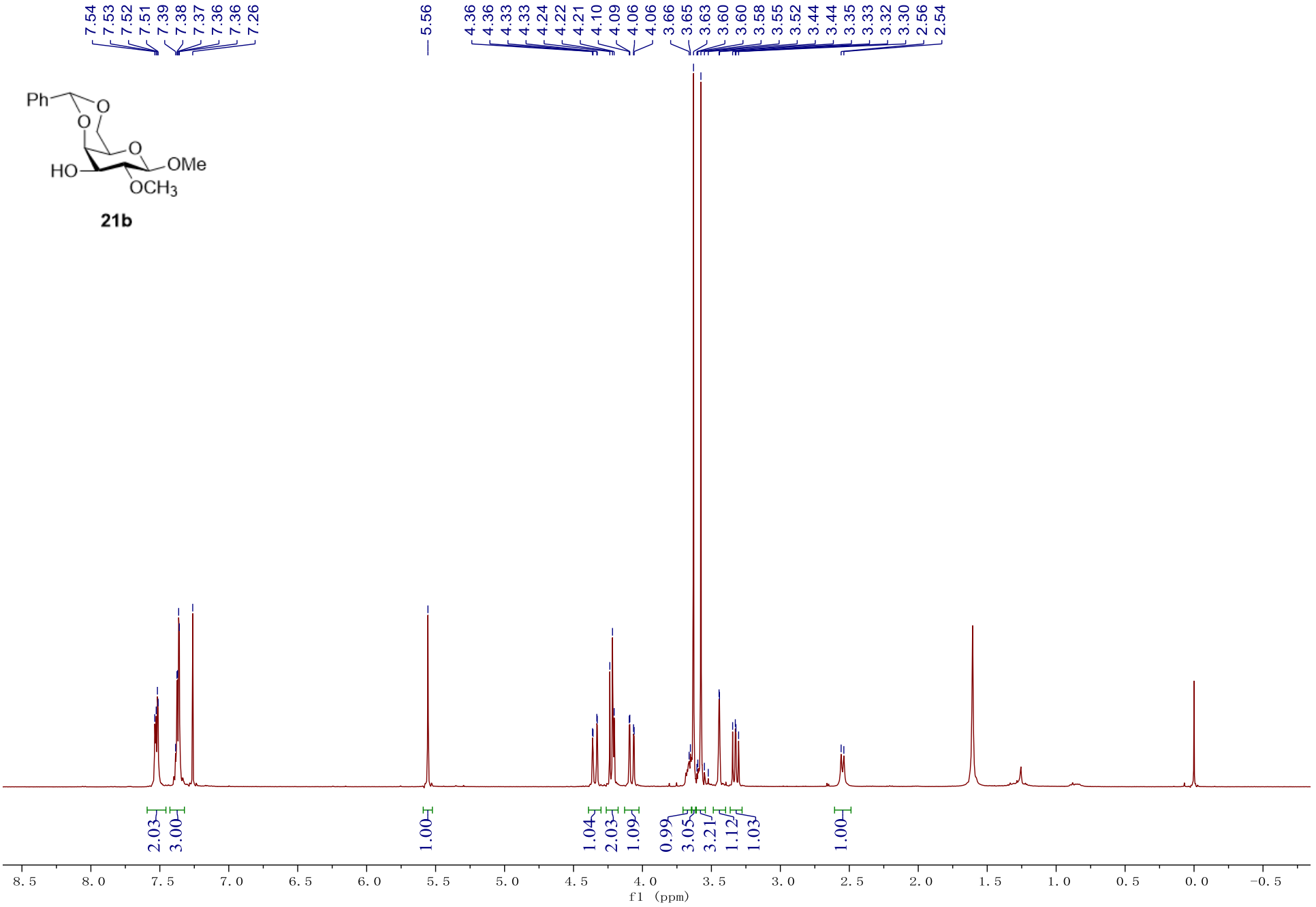
2D-COSY of compound **21a** ($CDCl_3$)



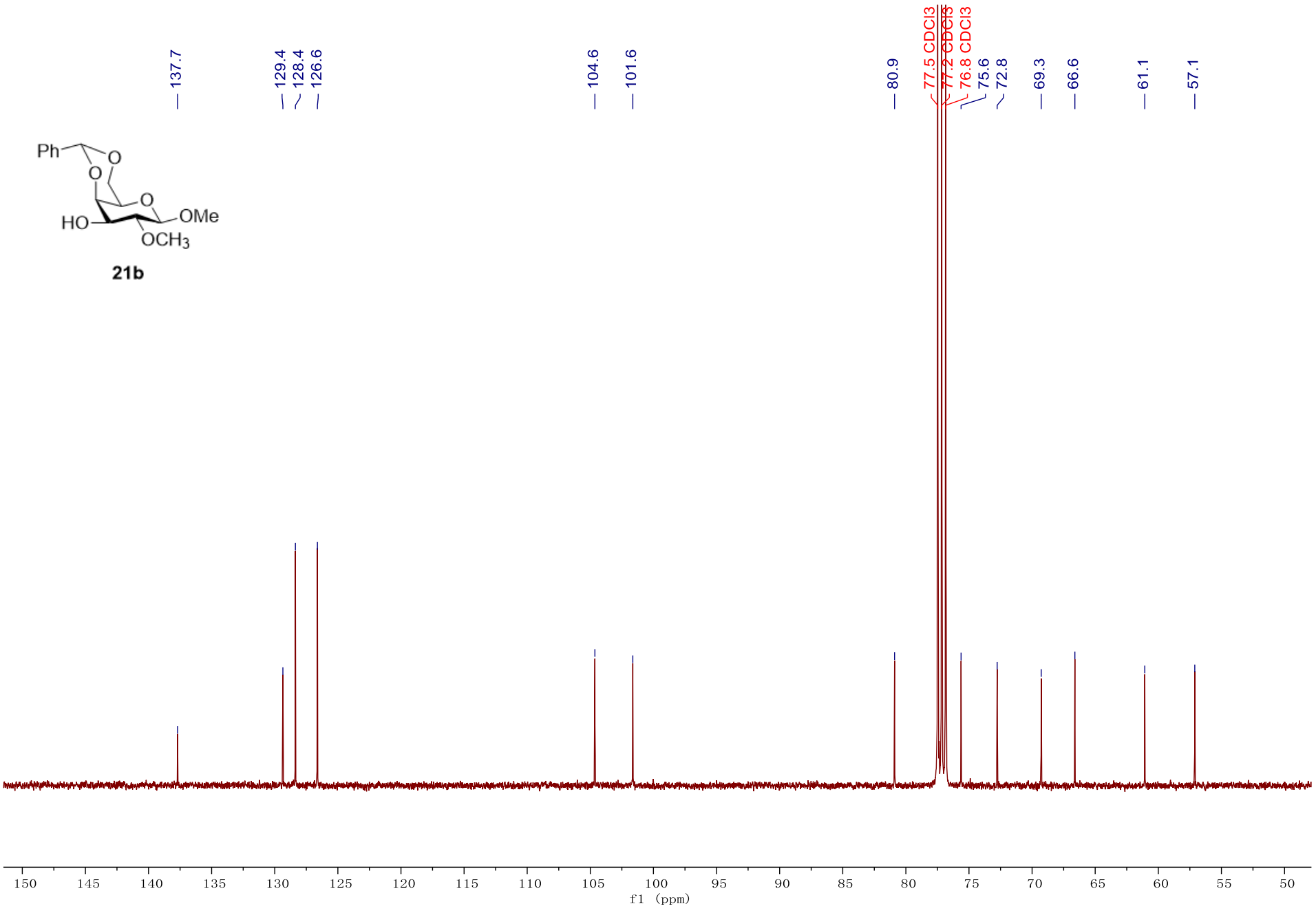
2D-HSQC of compound **21a** ($CDCl_3$)



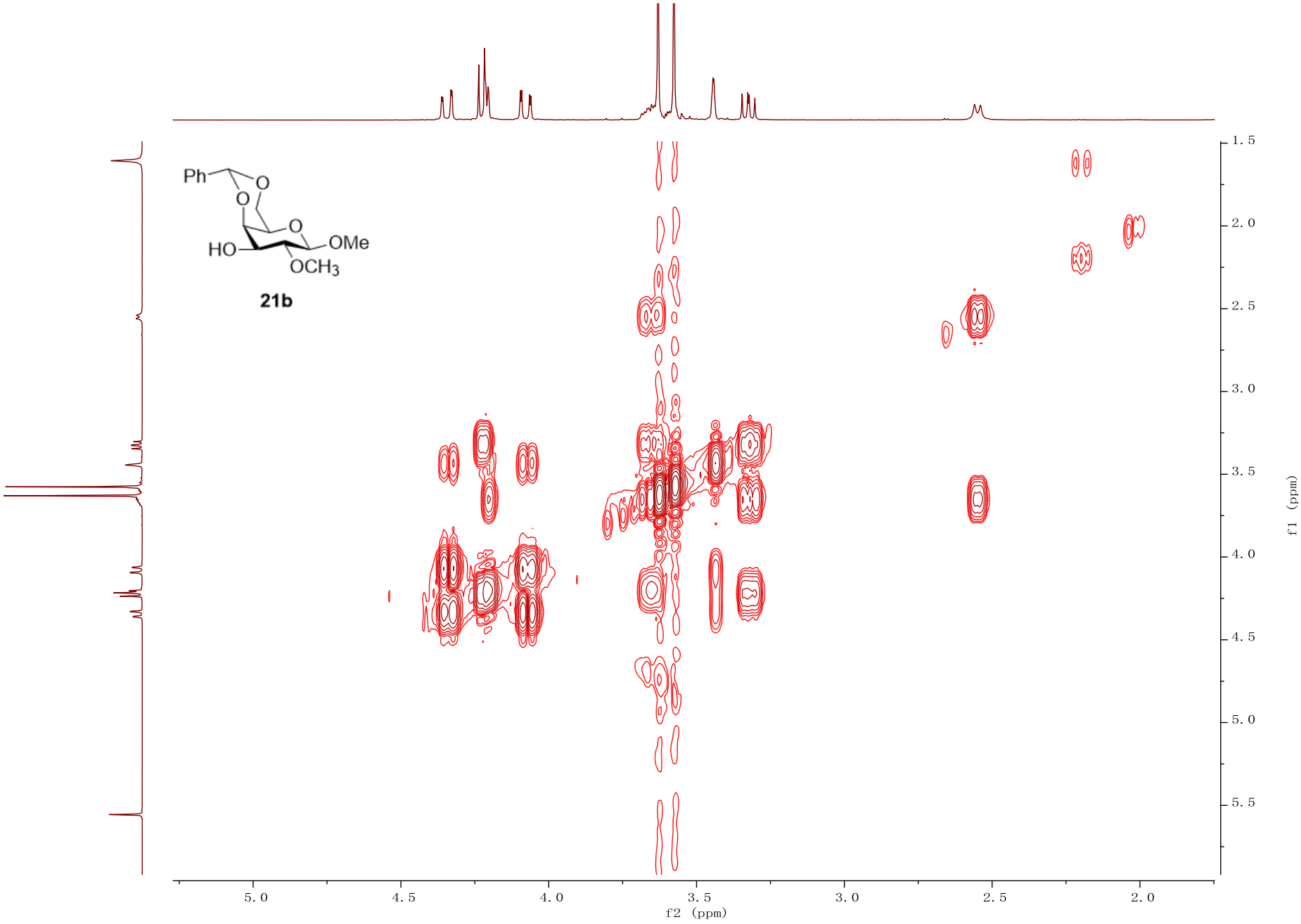
^{1}H-NMR of compound **21b** ($CDCl_3$)



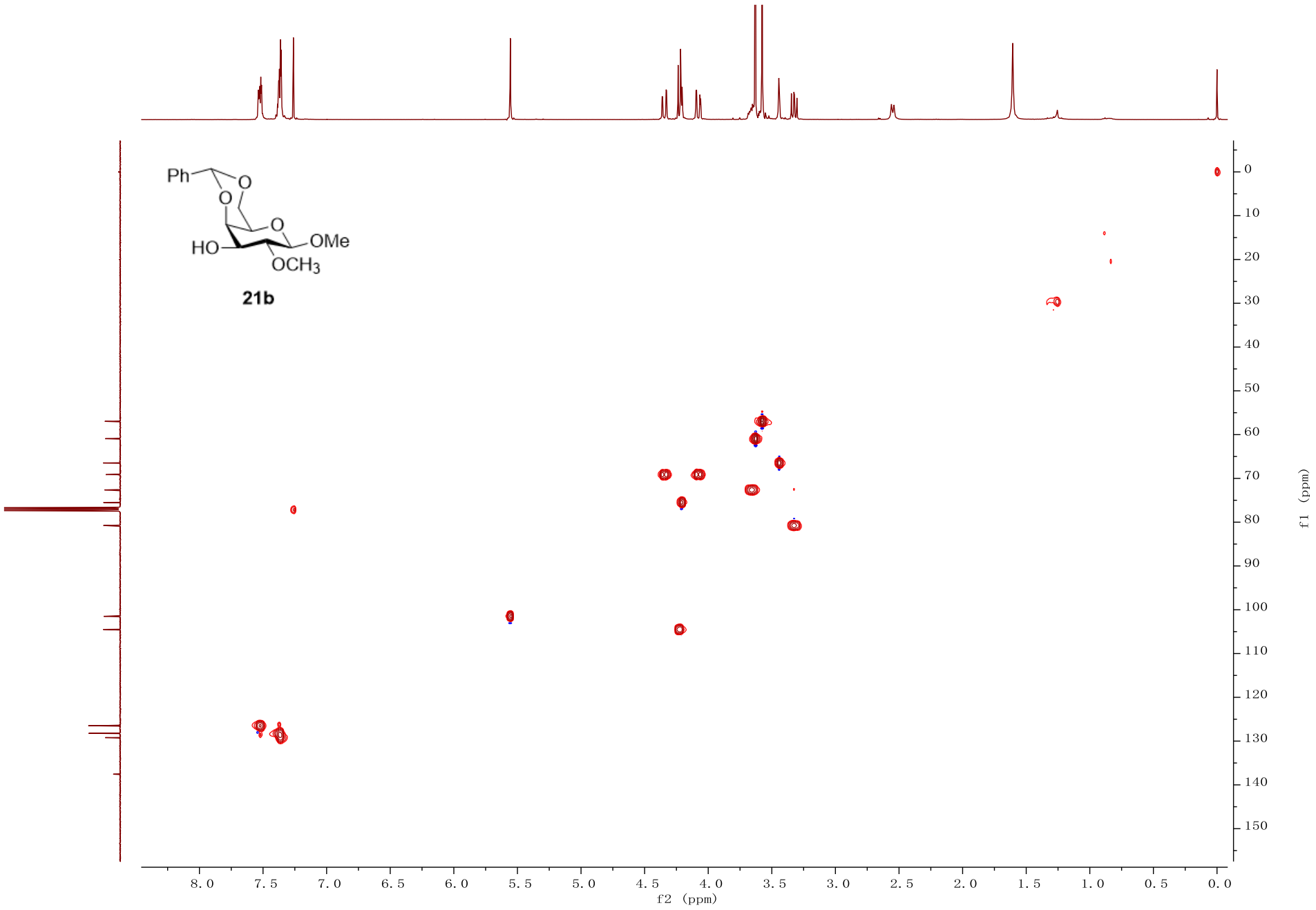
^{13}C-NMR of compound **21b** ($CDCl_3$)



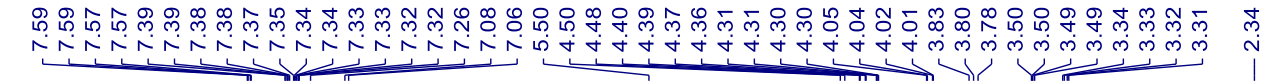
2D-COSY of compound **21b** ($CDCl_3$)

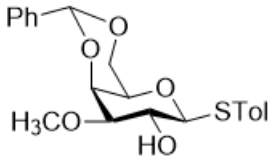


2D-HSQC of compound **21b** ($CDCl_3$)

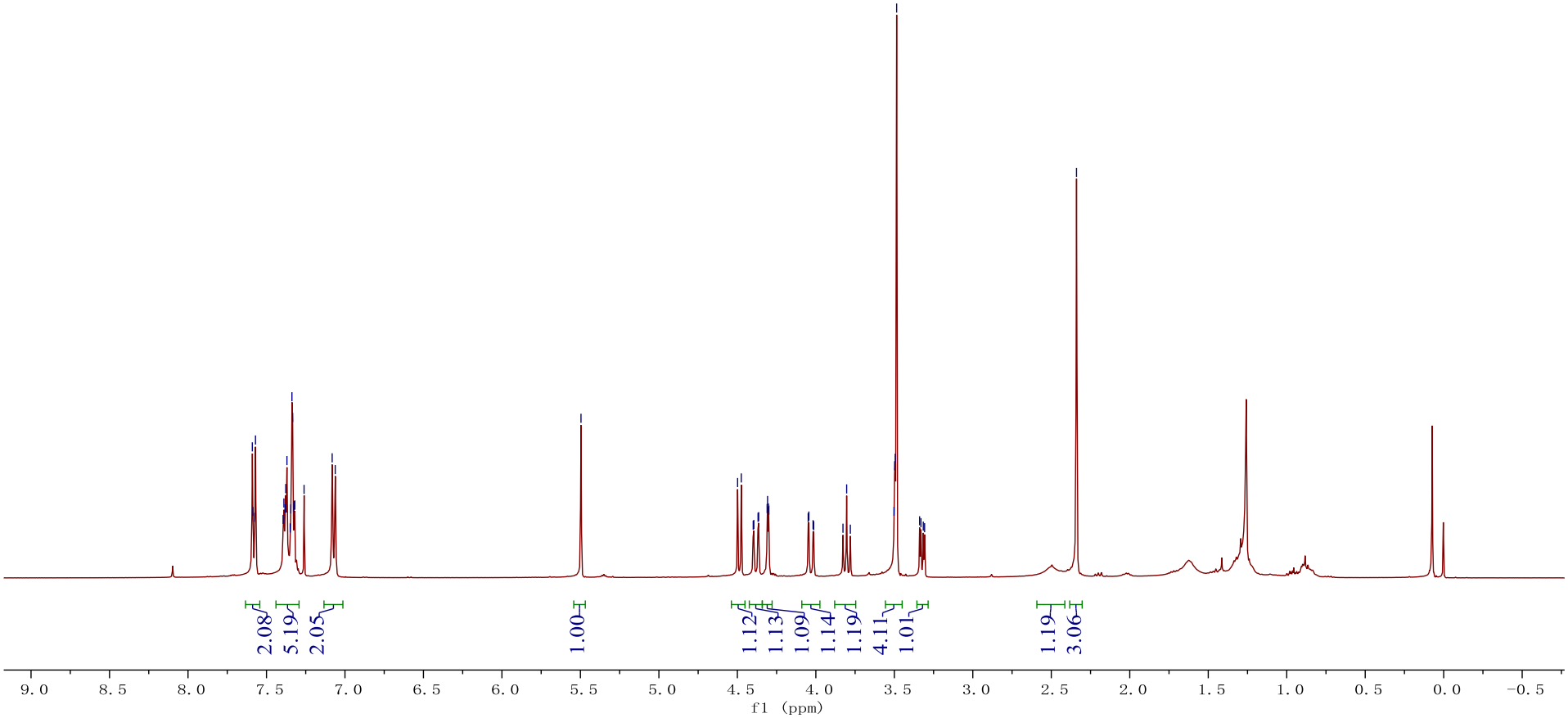


^{1}H-NMR of compound **22a** ($CDCl_3$)

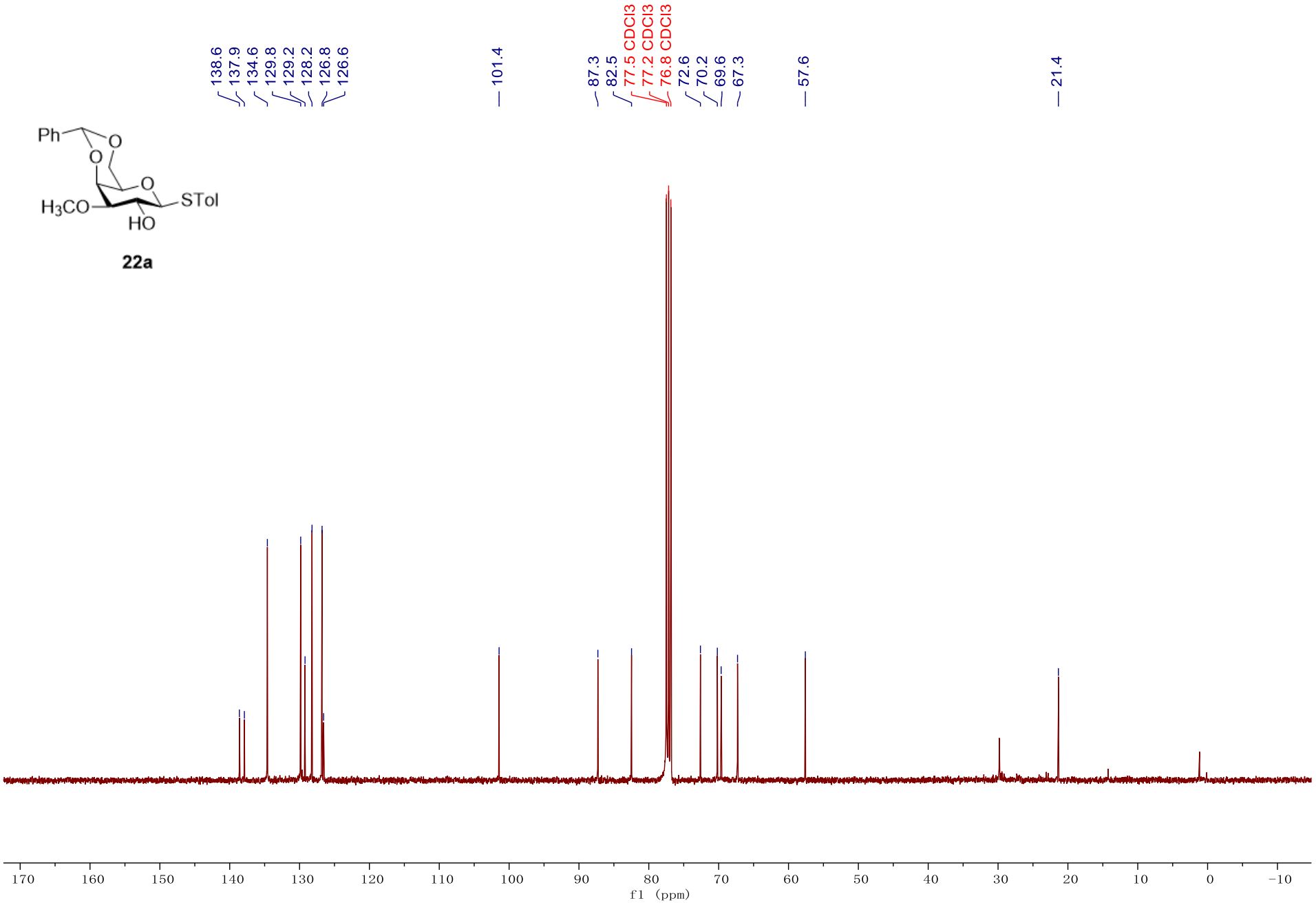




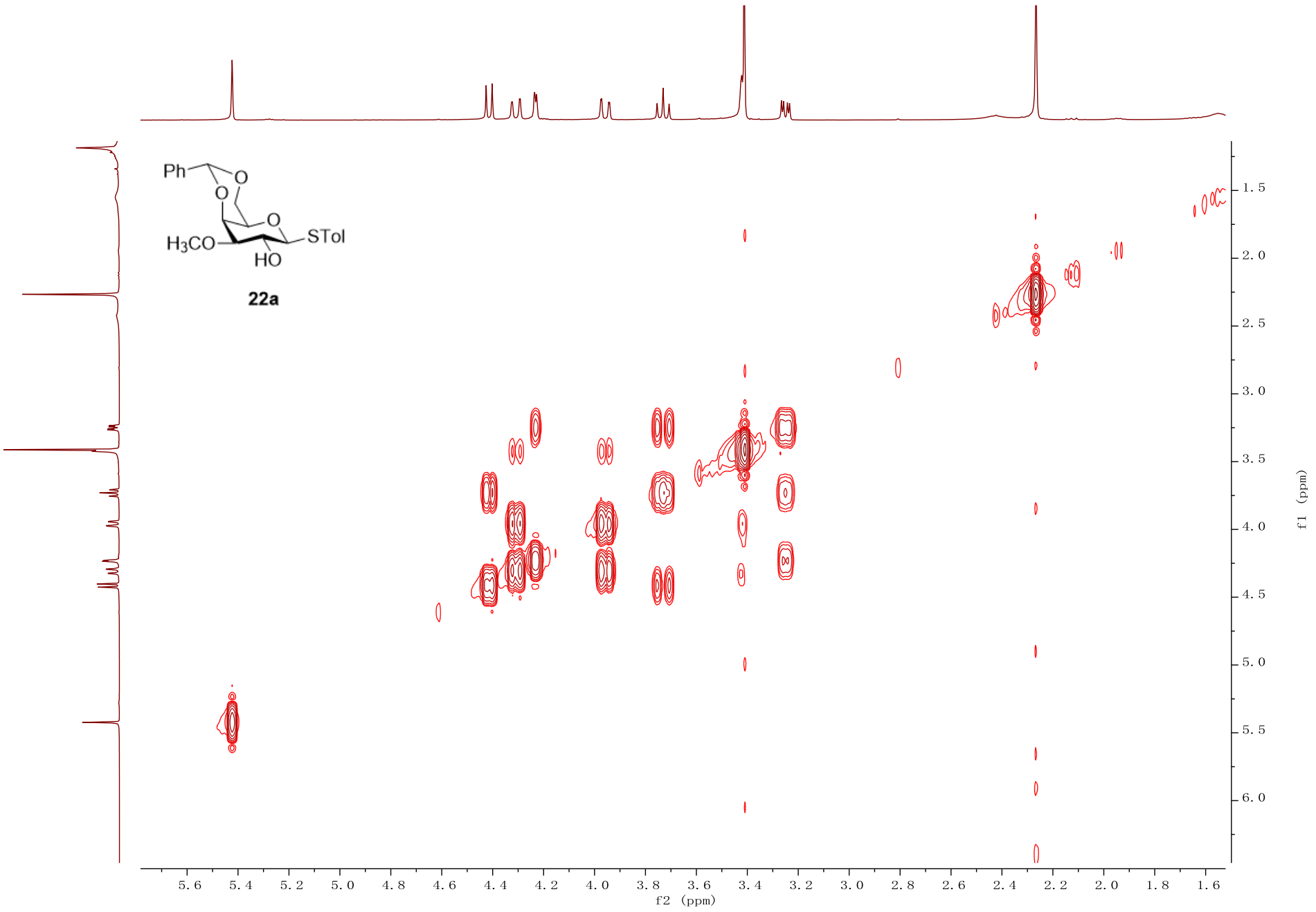
22a



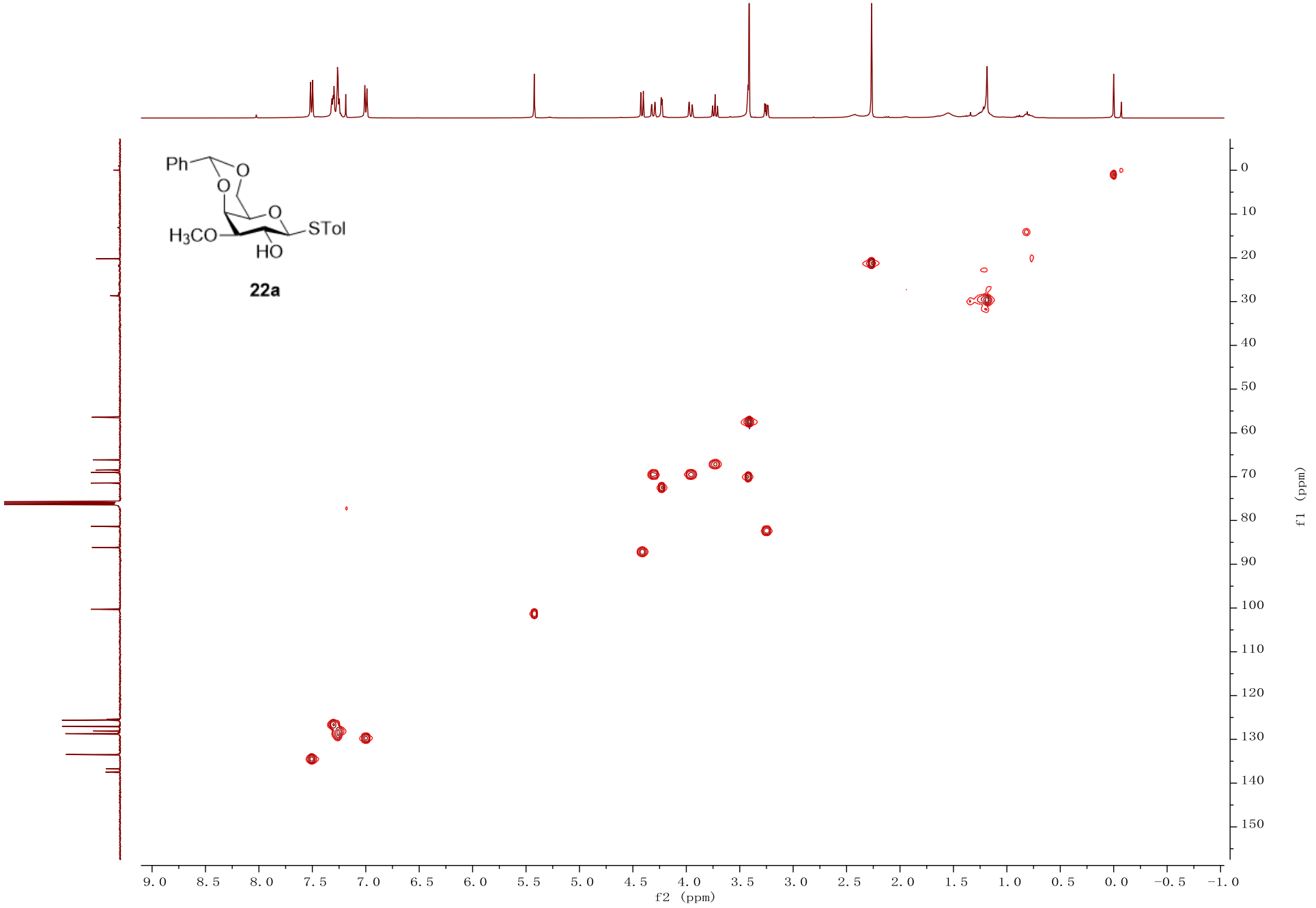
^{13}C-NMR of compound **22a** ($CDCl_3$)



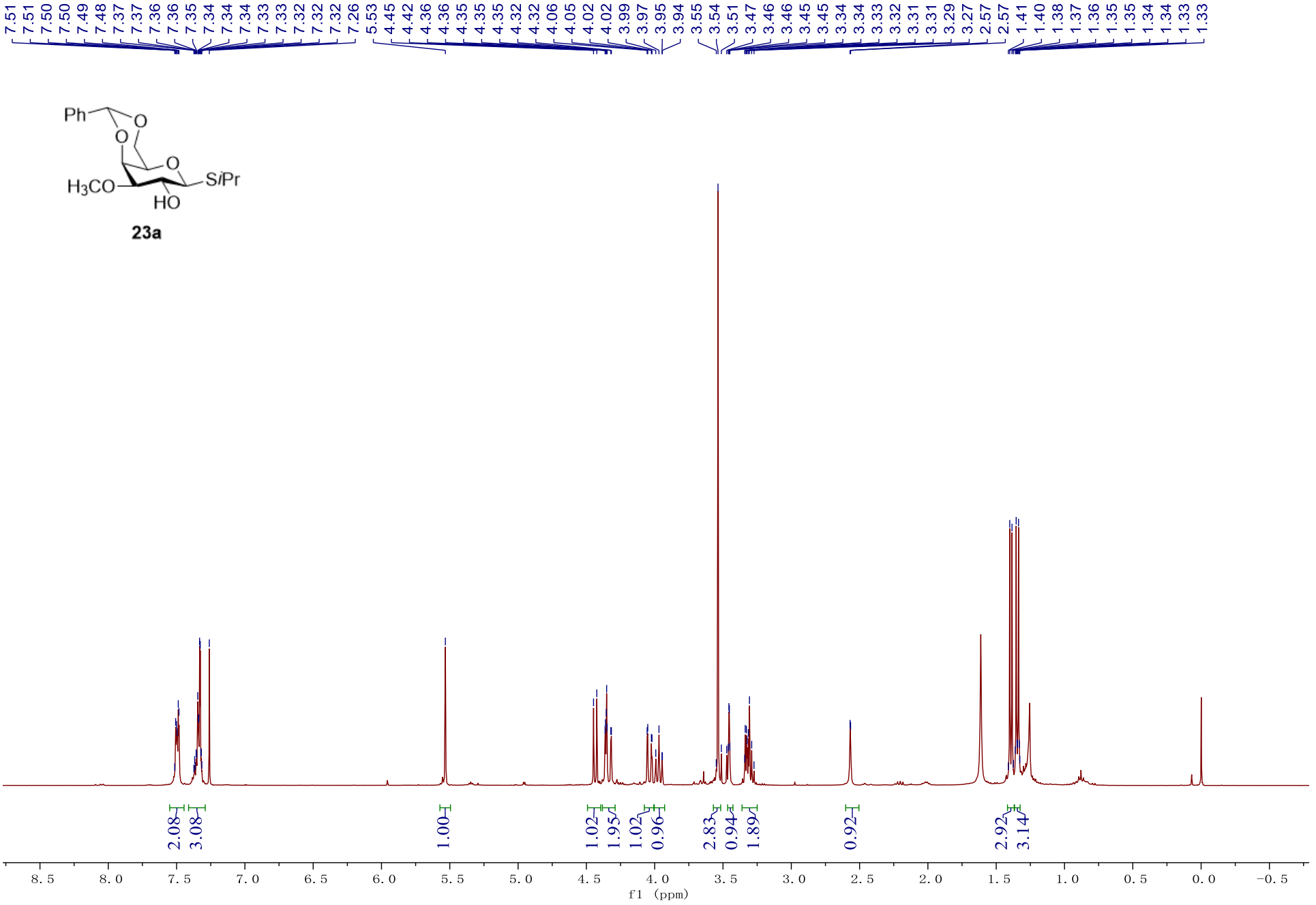
2D-COSY of compound **22a** ($CDCl_3$)



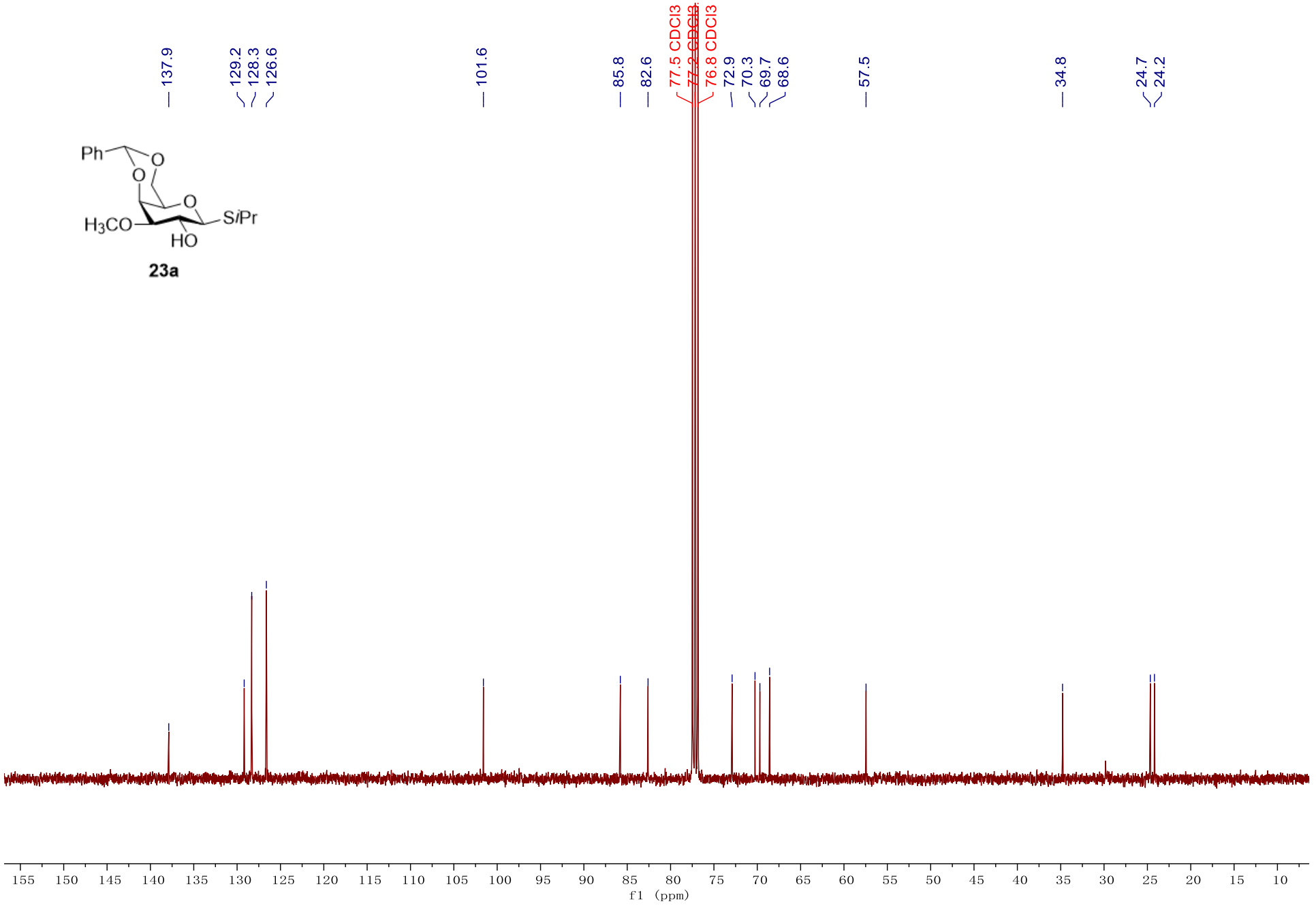
2D-HSQC of compound **22a** ($CDCl_3$)



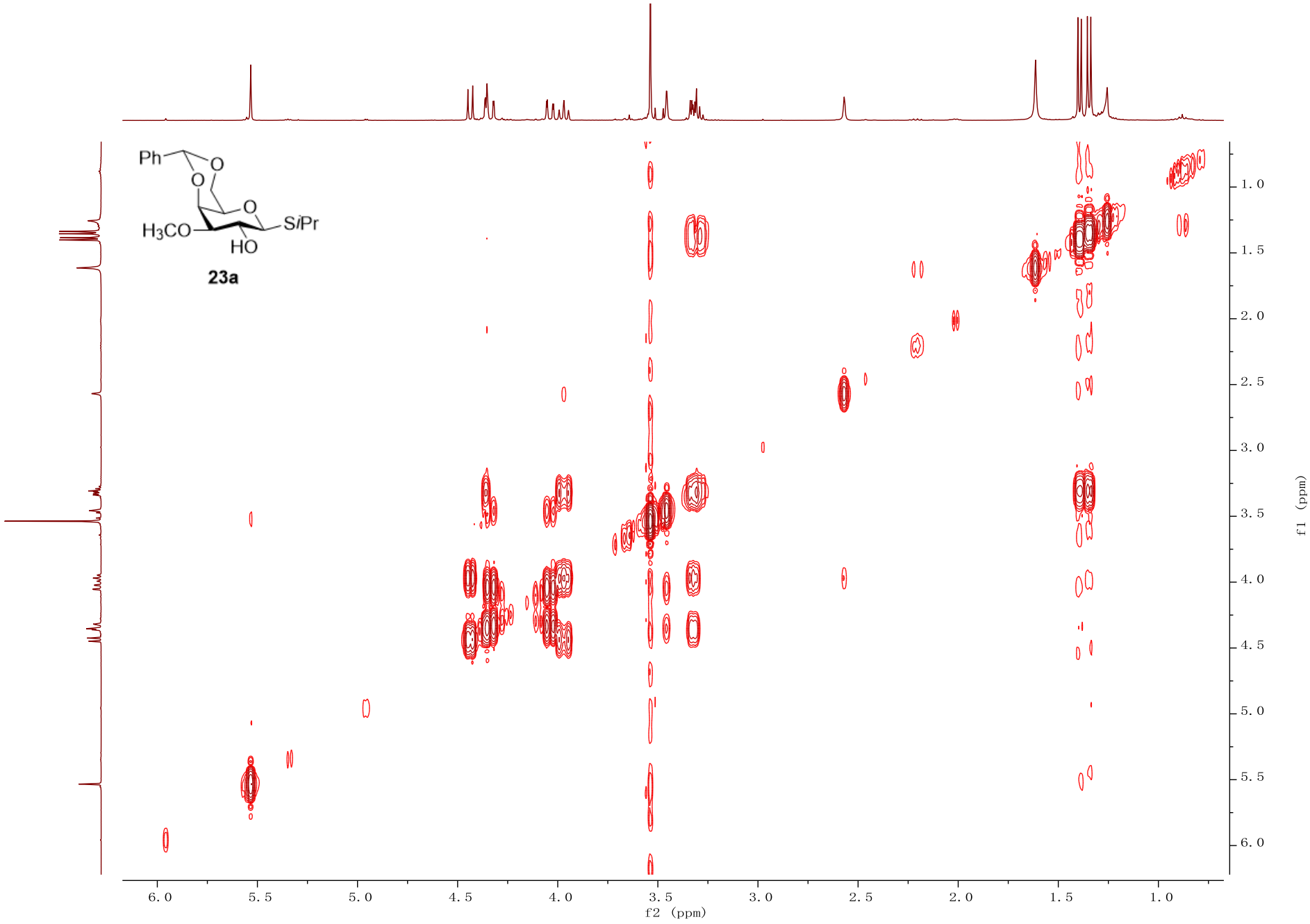
^{1}H-NMR of compound **23a** ($CDCl_3$)



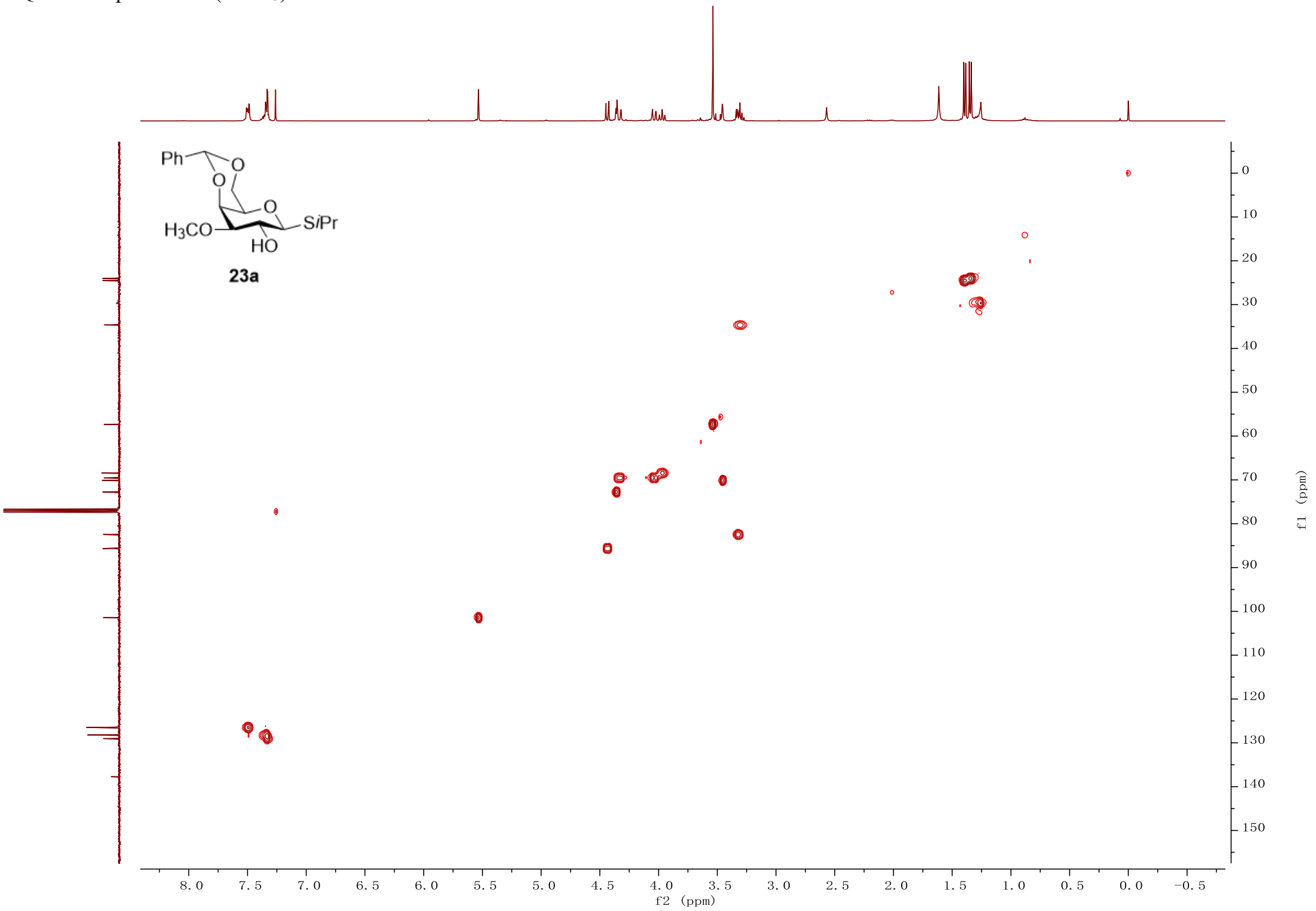
^{13}C-NMR of compound **23a** (CDCl3)



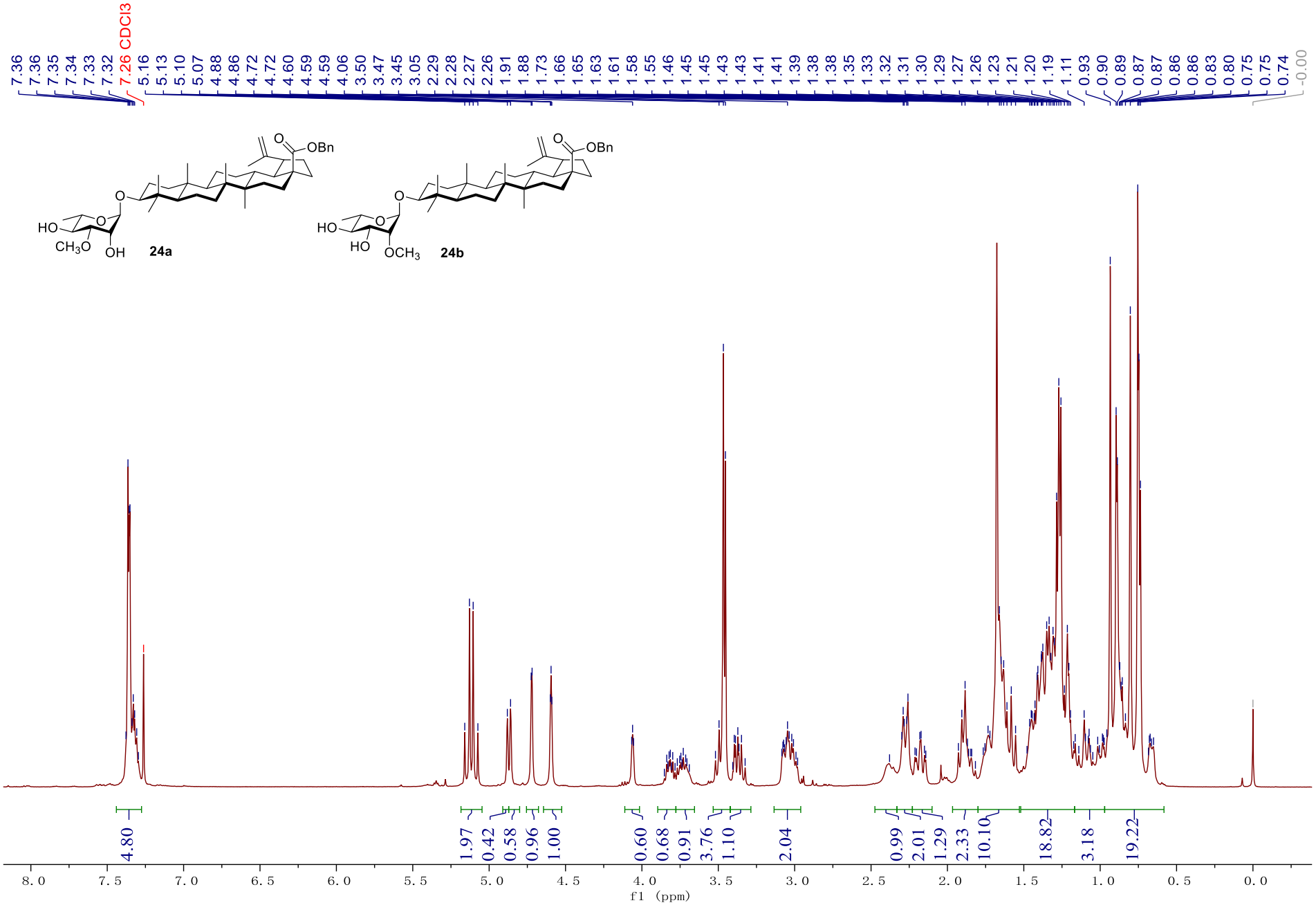
2D-COSY of compound **23a** ($CDCl_3$)



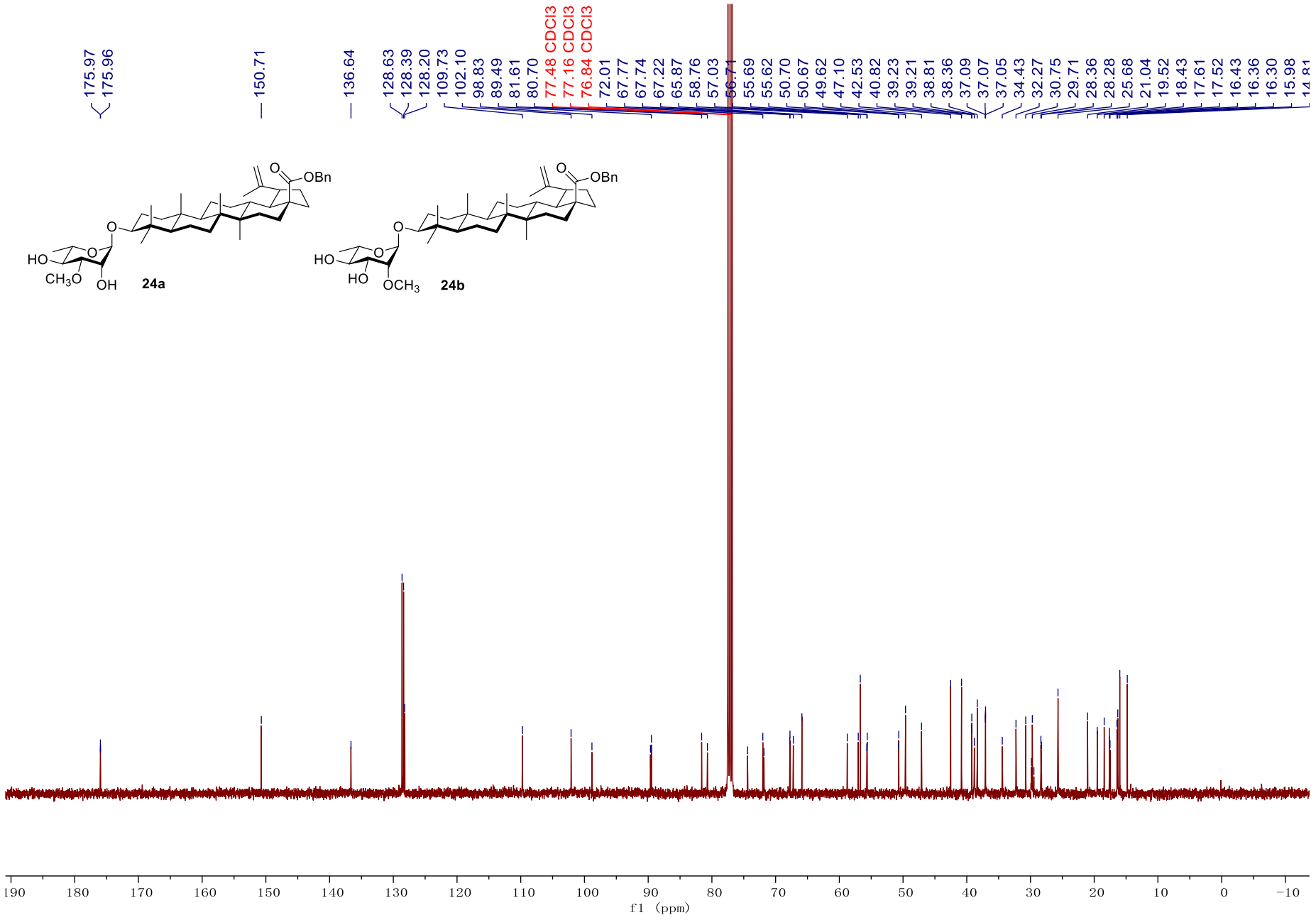
2D-HSQC of compound **23a** ($CDCl_3$)



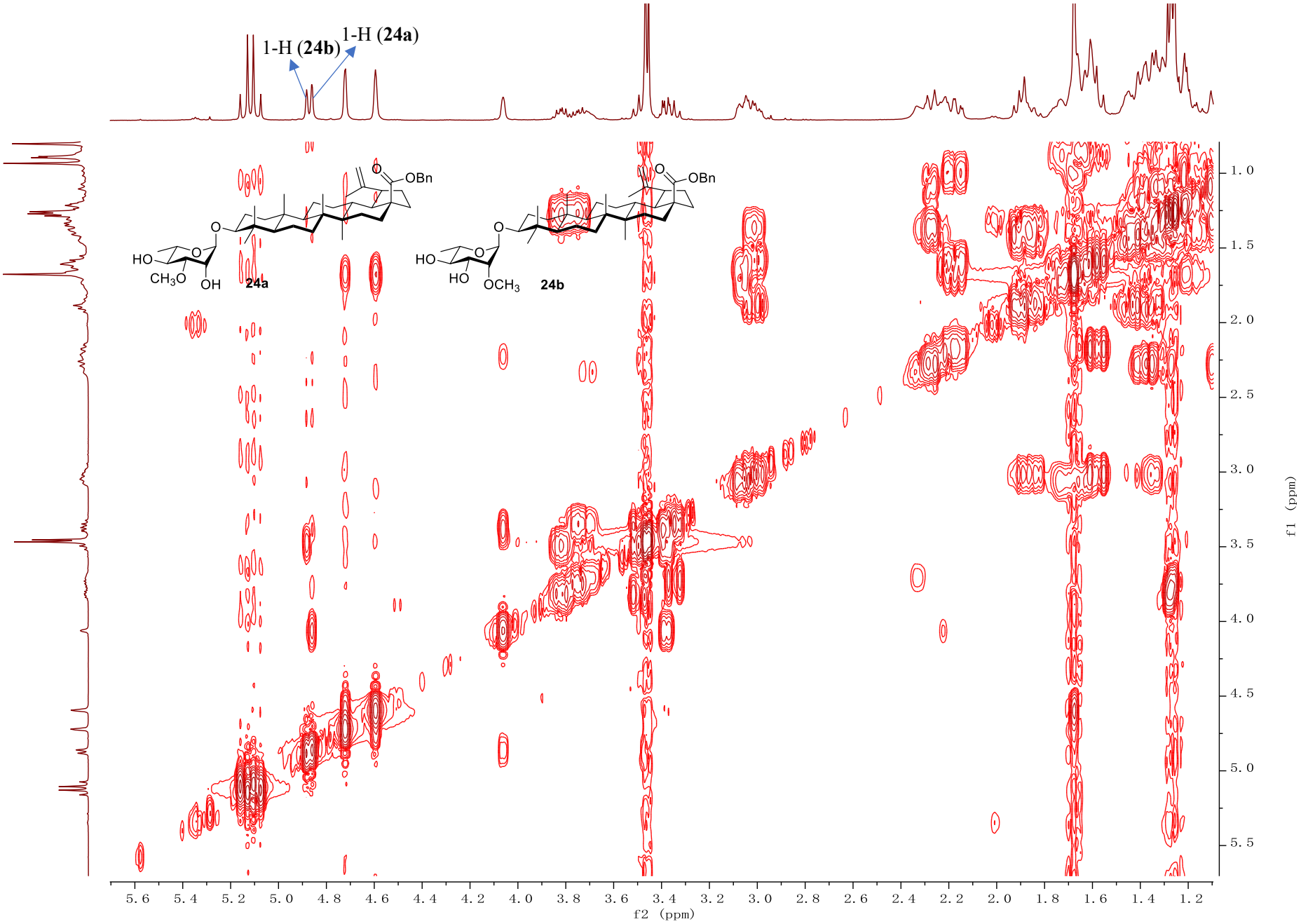
^{1}H-NMR of compound **24a** and **24b** ($CDCl_3$)



^{13}C-NMR of compound **24a** and **24b** ($CDCl_3$)



2D-COSY of compound **24a** and **24b** ($CDCl_3$)



2D-HSQC of compound **24a** and **24b** ($CDCl_3$)