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Supporting Information

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Two-Step Functionalization of Oligosaccharides Using Glycosyl Iodide and Trimethylene Oxide and Its Applications to Multivalent Glycoconjugates

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Supporting Information

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General Information

All reactions were conducted under a dried argon atmosphere. The anhydrous solvents (dichloromethane (DCM) 99.8%, benzene (PhH) 99.8%, Methanol (MeOH) 99.8%, *N*,*N*-dimethylformamide (DMF) 99.8% and pyridine (pyr.) 99.8%) were purchased from commercial sources without further purification. In order to maintain water content of the solvents under 15 ppm, the solvents were dried and stored under 4 Å molecular sieves according to literature procedure.[1] Trimethylsilyl iodide (TMSI, stabilized with copper) was stored at -20 °C under a desiccated Ar atmosphere. TMSI in good condition should be a colorless transparent liquid. All other solvents and reagents were purchased from commercial sources and used without further purification. All glassware utilized was oven-dried or flame-dried before use. Glass-backed TLC plates (Silica Gel 60 with a 254 nm fluorescent indicator) were used without further manipulation and stored with desiccant. TLC plates were visualized using a short-wave UV lamp, stained with an I_2-SiO_2 mixture, and/or by heating TLC plates that were dipped in a solution of ammonium molybdate/cerium (IV) sulfate or anisaldehyde/H_2SO_4/AcOH/EtOH. Flash column chromatography (FCC) was performed using a silica gel (32-63 μm) stationary phase with a variable mobile phase correlated with TLC mobility. NMR experiments were conducted on 400, 800 or 600 MHz instruments using $CDCl_3$ (99.9% D), D_2O (99.9% D) and methanol-d_4 (99.8% D) as the solvent. Chemical shifts were referenced to the appropriate deuterated solvent peak (7.26 ppm for $CDCl_3$; 4.79 ppm for D_2O; 3.31 ppm for methanol-d_4) and were reported in parts per million (ppm). Coupling constants of the coupled protons were averaged to match with each other. High resolution mass spectra were recorded using ESI-Orbitrap LC-MS with internal calibration. The microwave-assisted regioselective silyl exchange

technology (ReSET) reactions were conducted in sealed 10 mL microwave vessels in a commercial microwave reactor (CEM Discover™) which was operated by the Synergy™ software. The reaction temperatures were monitor by the reactor's built-in infrared (IR) detector.

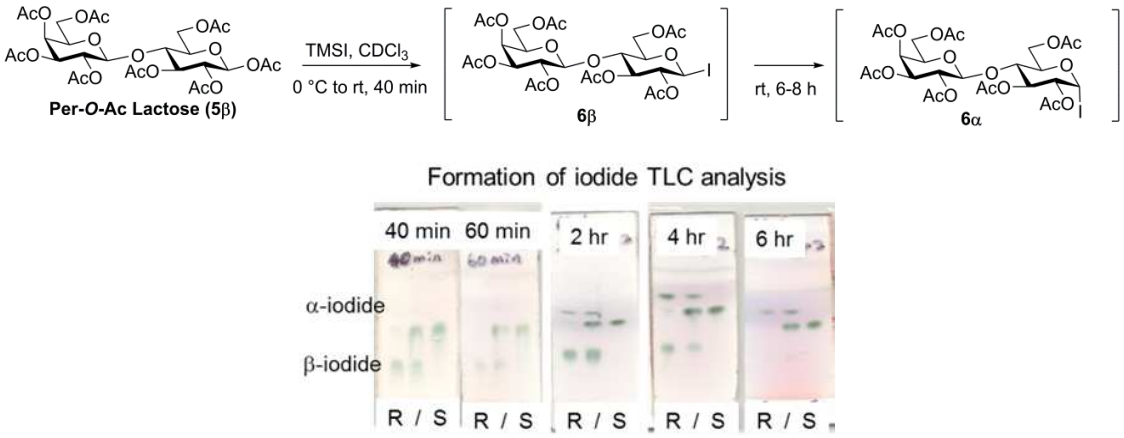


Figure S1. Per-*O*-Ac lactosyl iodide formation was stable enough to monitor by TLC

Synthesis, Purification and Characterization of Compound (25):

Table S1. Reaction mixture composition for synthesis of compound **25**

Compound	MW	Mass (mg)	mmol	Equiv.	Volumn (mL)	Stock conc. (mM)	Final conc. (mM)
Trialkyne-PEG_2-PADRE (**24**)	1827.17	1.4	0.0008	1.0	0.5	1.6	0.33
Globotriaose azide (**20**)	587.53	4.2	0.0072	9.0	1.5	4.8	2.92
$CuSO_4$ pentahydrate	249.53	0.1	0.0004	0.5	0.02	20	0.16
THPTA ligand	434.50	0.9	0.0021	2.6	0.04	50	0.85
Amino-guanidine	110.55	2.3	0.0208	26.0	0.2	100	8.5
Sodium Ascorbate	198.11	4.1	0.0208	26.0	0.2	100	8.5

HPLC condition: HPLC was carried out at 25 ˚C with semi-prep/analytic HPLC system and set detection at 280 nm. Product **25** eluted from column using mobile phase A:

MeCN and B: 0.1% TFA in H_2O. Analytic set-up involves: C_{18}-RP column (250 × 4.6 mm) with a flow rate of 1 mL/min.

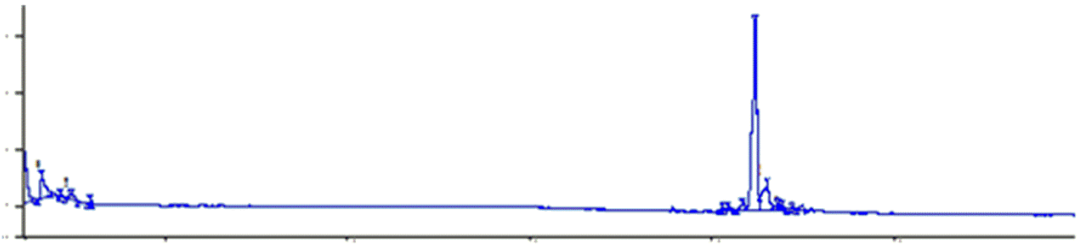


Figure S2. Analytical HPLC profile for compound **25**. T_R = 24.9 min (λ = 280 nm, with gradient of 5% A solution for 10 min, 5-40% A solution for 10 min, 40% A solution for 10 min, and 40-95% A solution for 5 min). A solution: MeCN, B solution: H_2O + 0.1% trifluoroacetic acid.

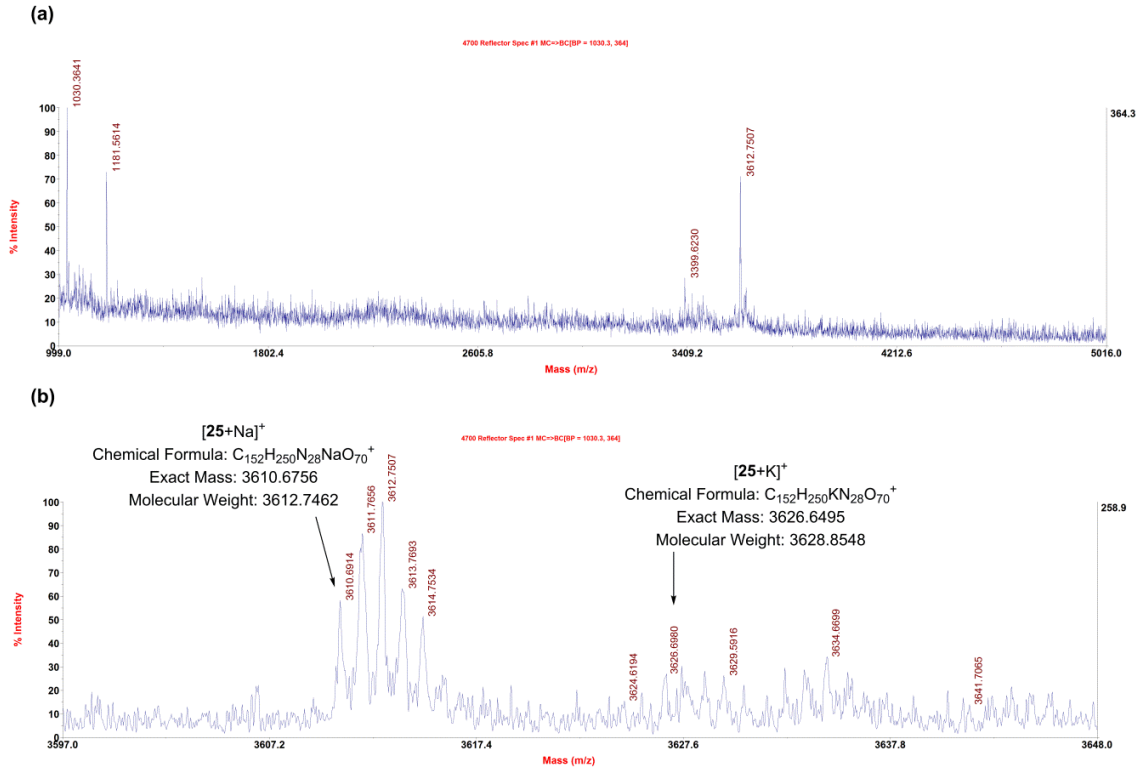
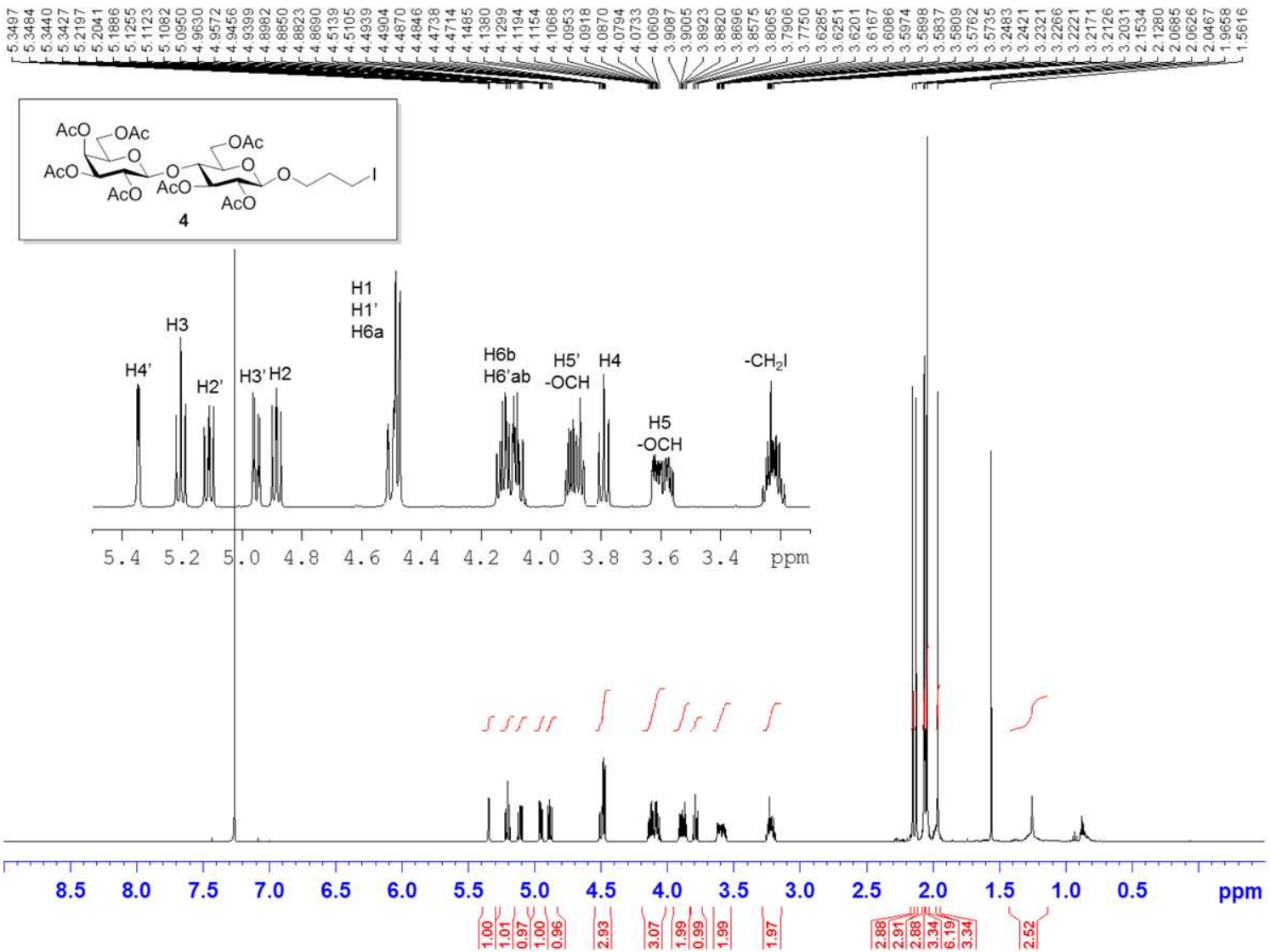
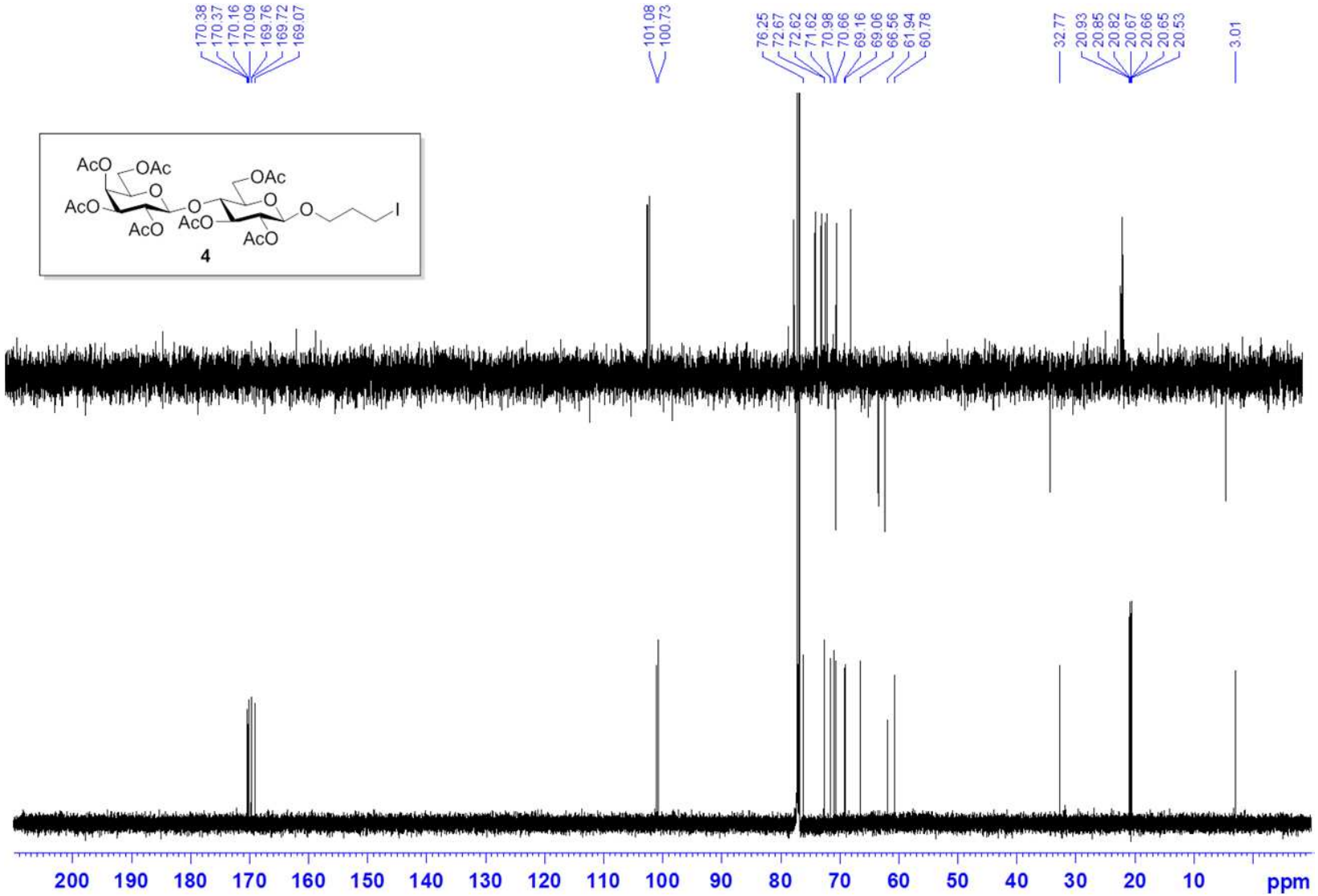


Figure S3. MALDI-TOF HRMS of compound **25.**

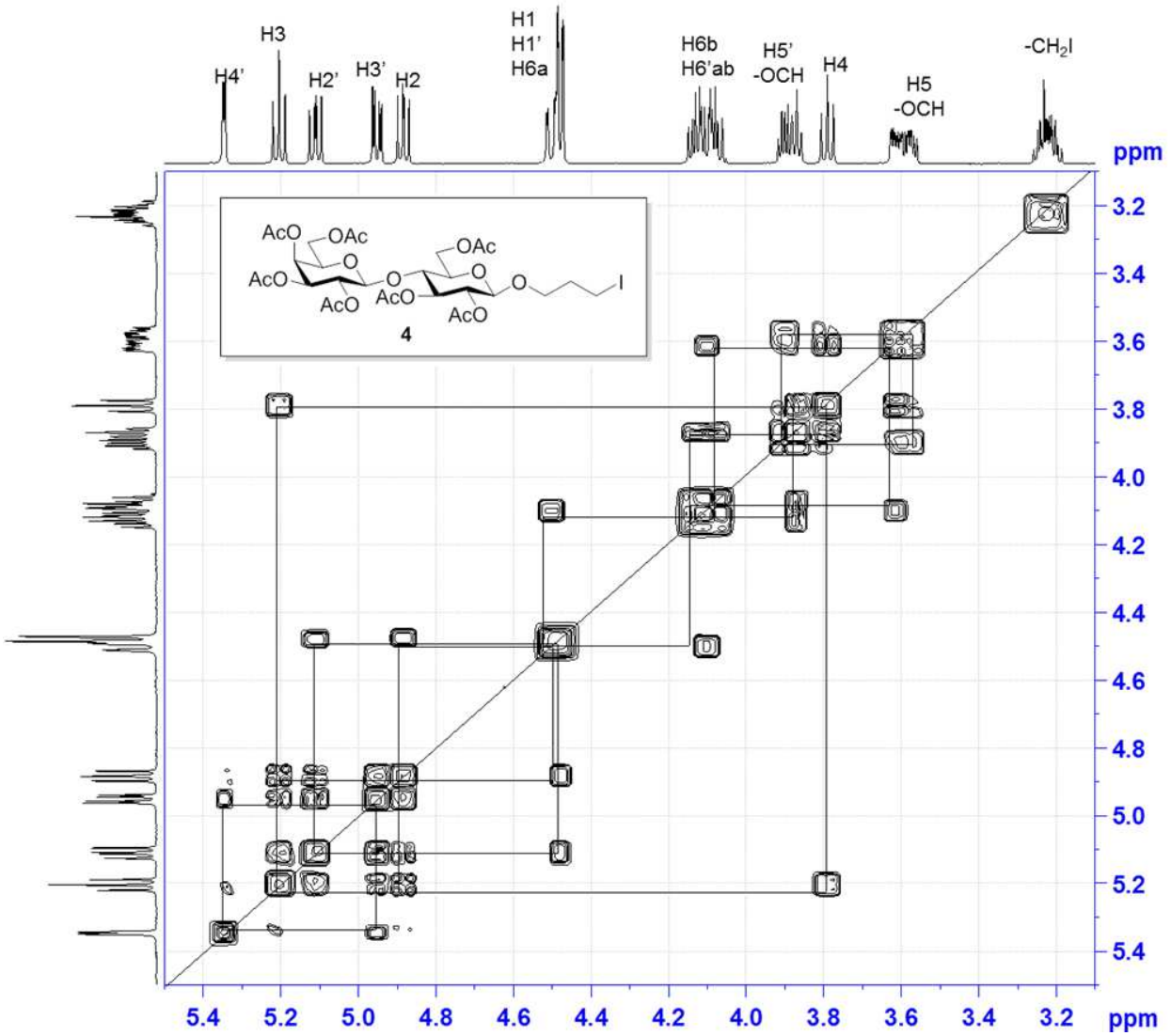
Reference (1) Williams, D. B. G.; Lawton, M. *J. Org. Chem*. **2010**, *75*, 8351-8354.



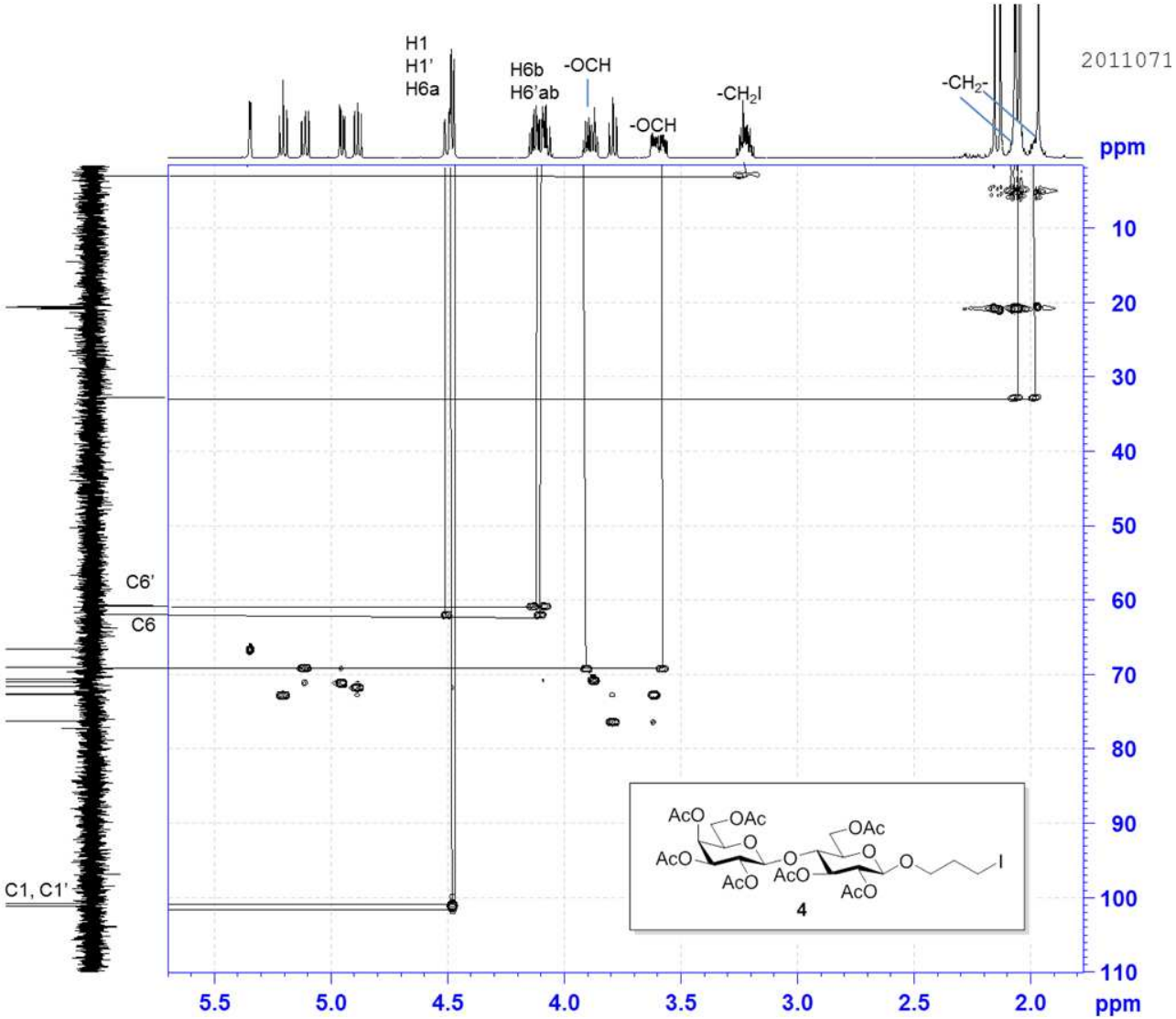
^{1}H NMR spectrum of compound **4** ($CDCl_3$, 600 MHz)



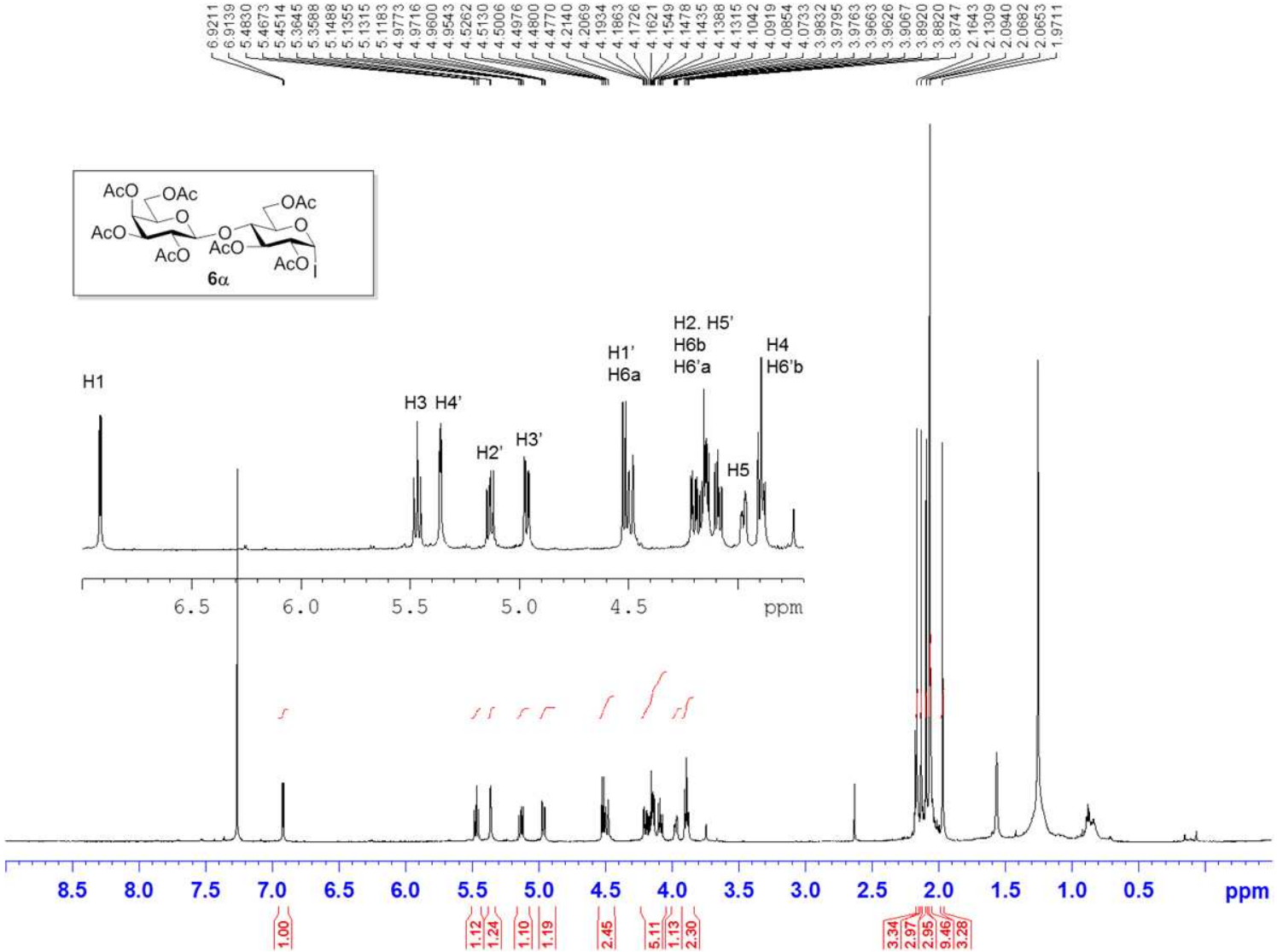
^{13}C and DEPT135 NMR spectrum of compound **4** ($CDCl_3$, 150 MHz)



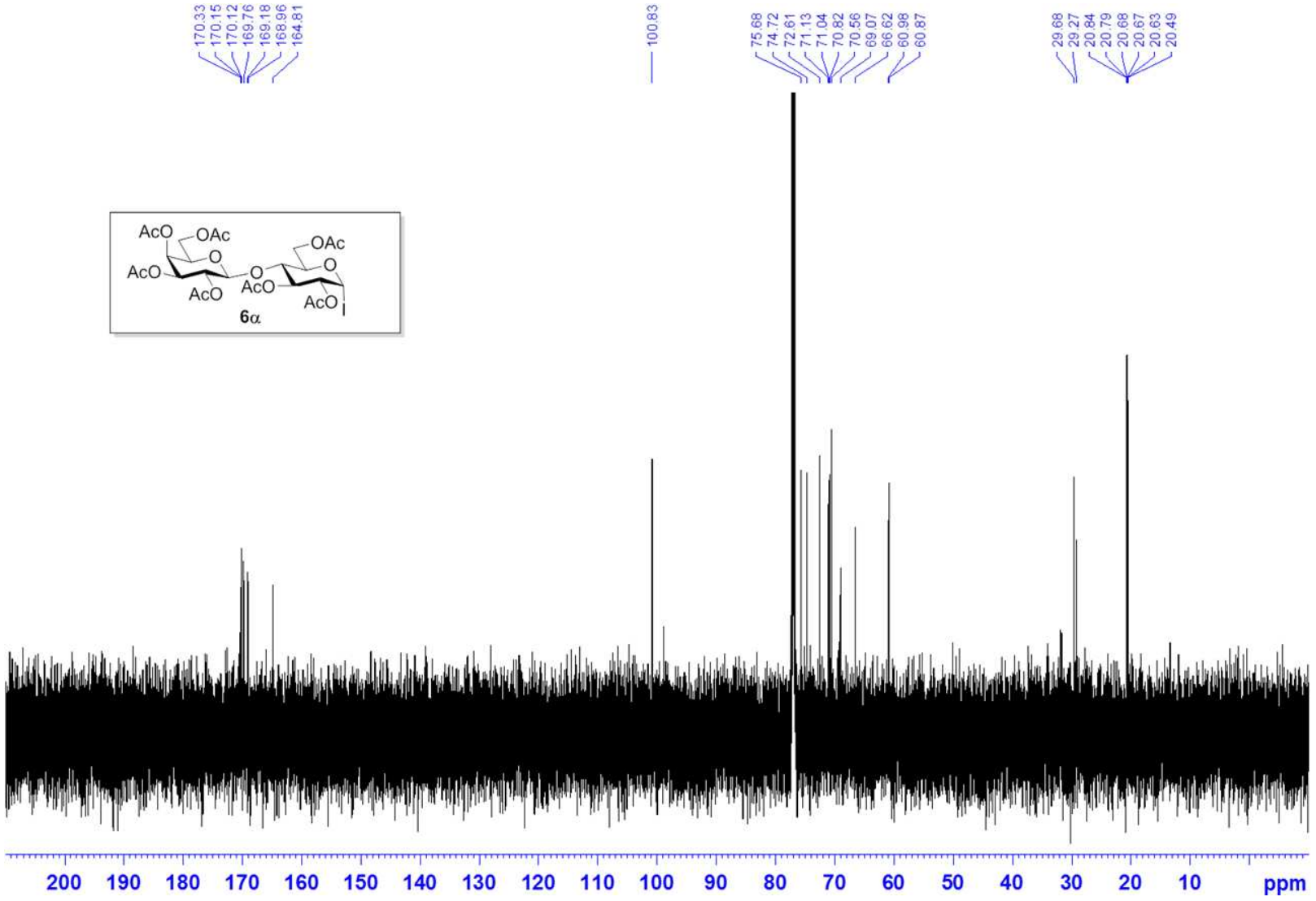
^{1}H-^{1}H COSY spectrum of compound **4** ($CDCl_3$, 600 MHz)



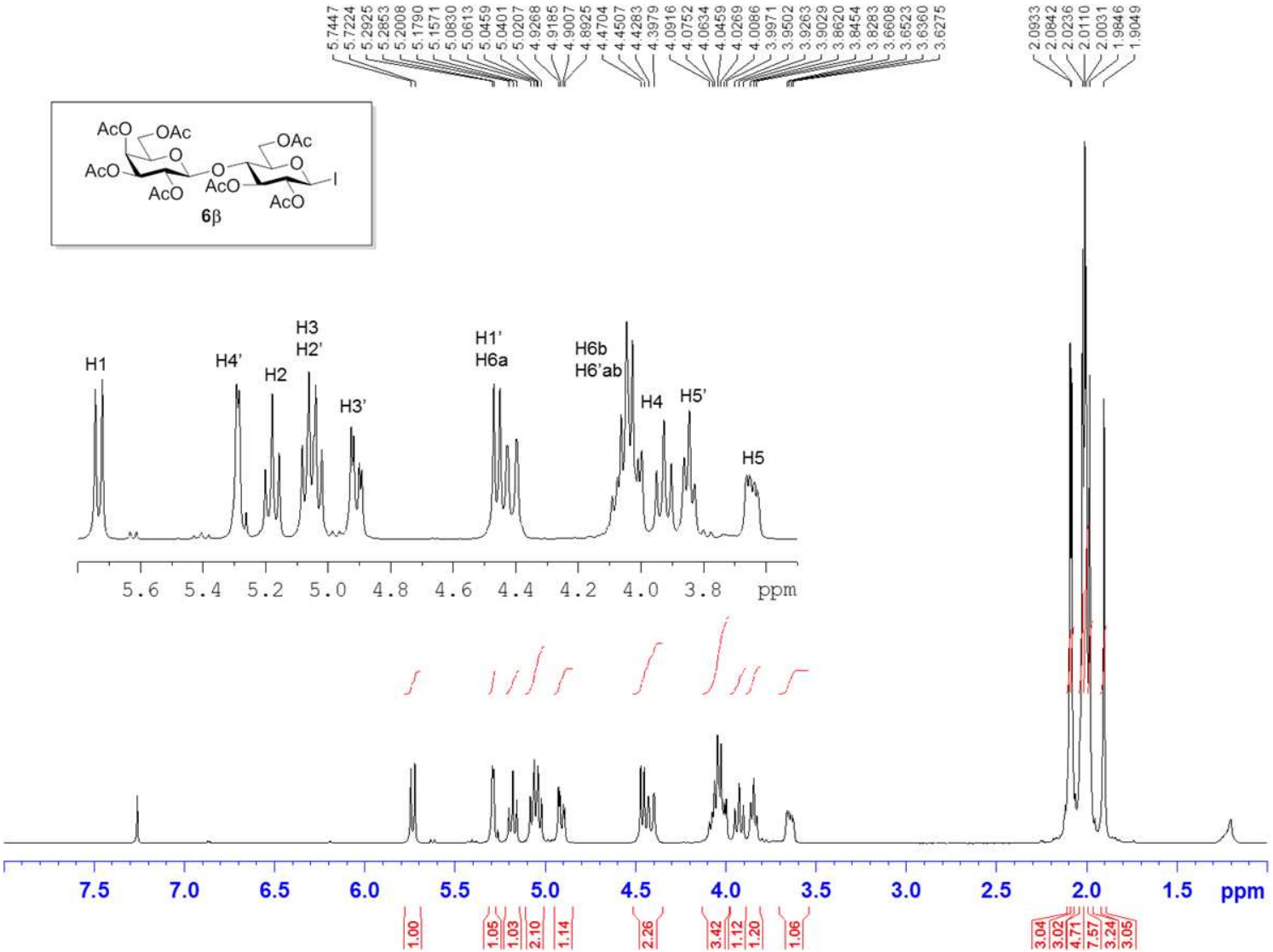
^{1}H-^{13}C HSQC spectrum of compound **4** ($CDCl_3$, 600 MHz)



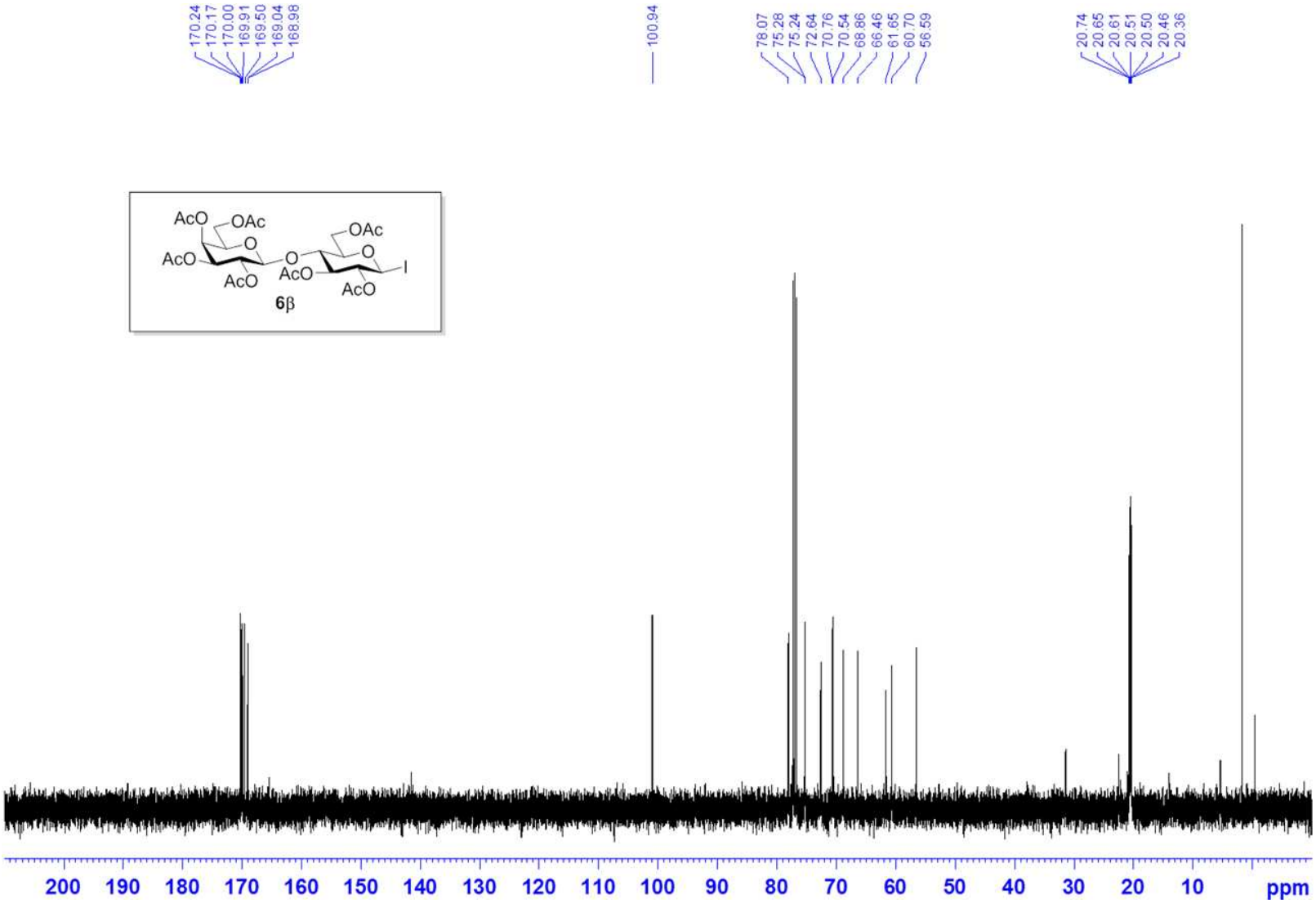
in situ ^{1}H NMR spectrum of compound **6α** ($CDCl_3$, 600 MHz)



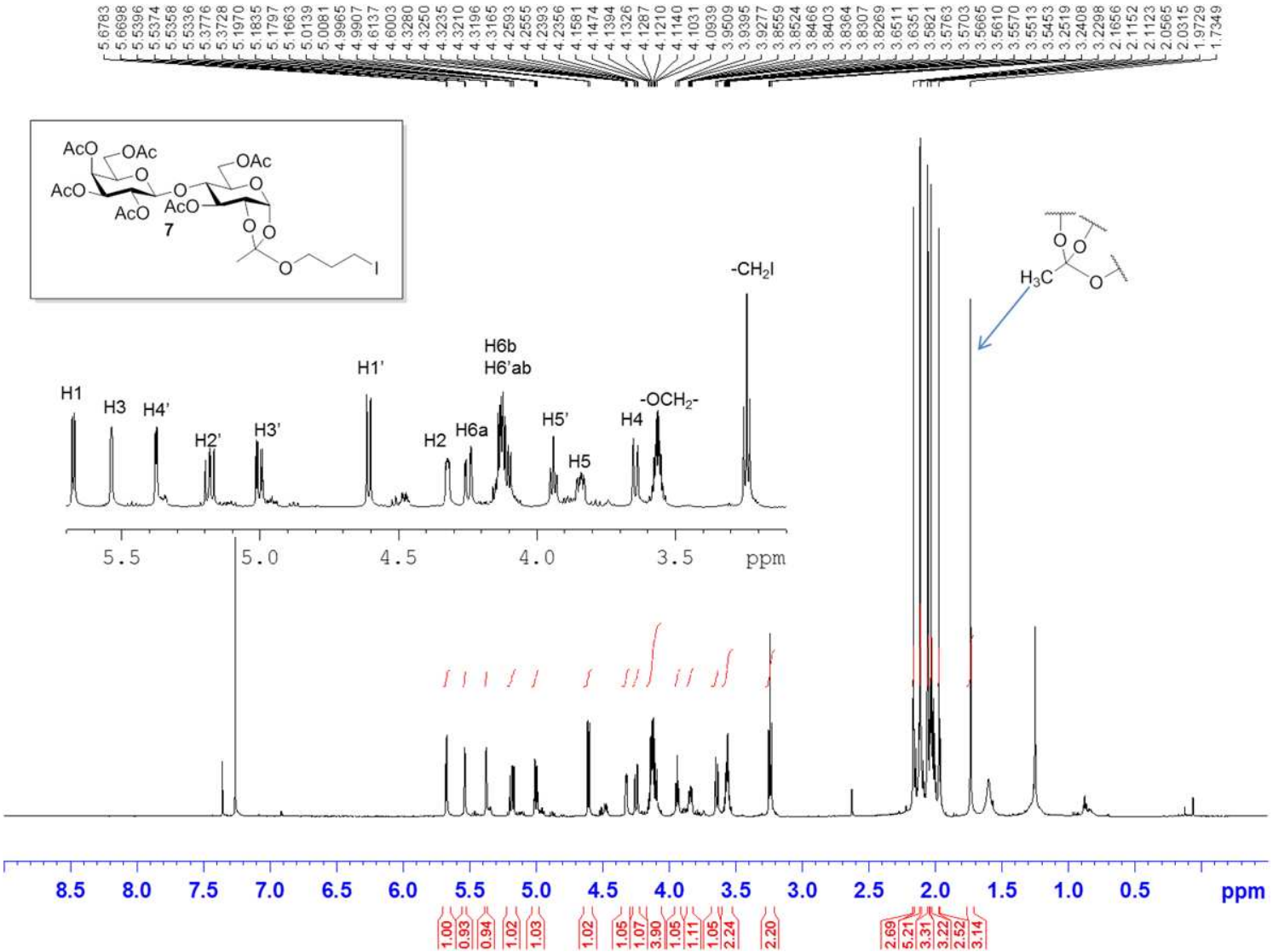
in situ ^{13}C NMR spectrum of compound **6α** ($CDCl_3$, 150 MHz)



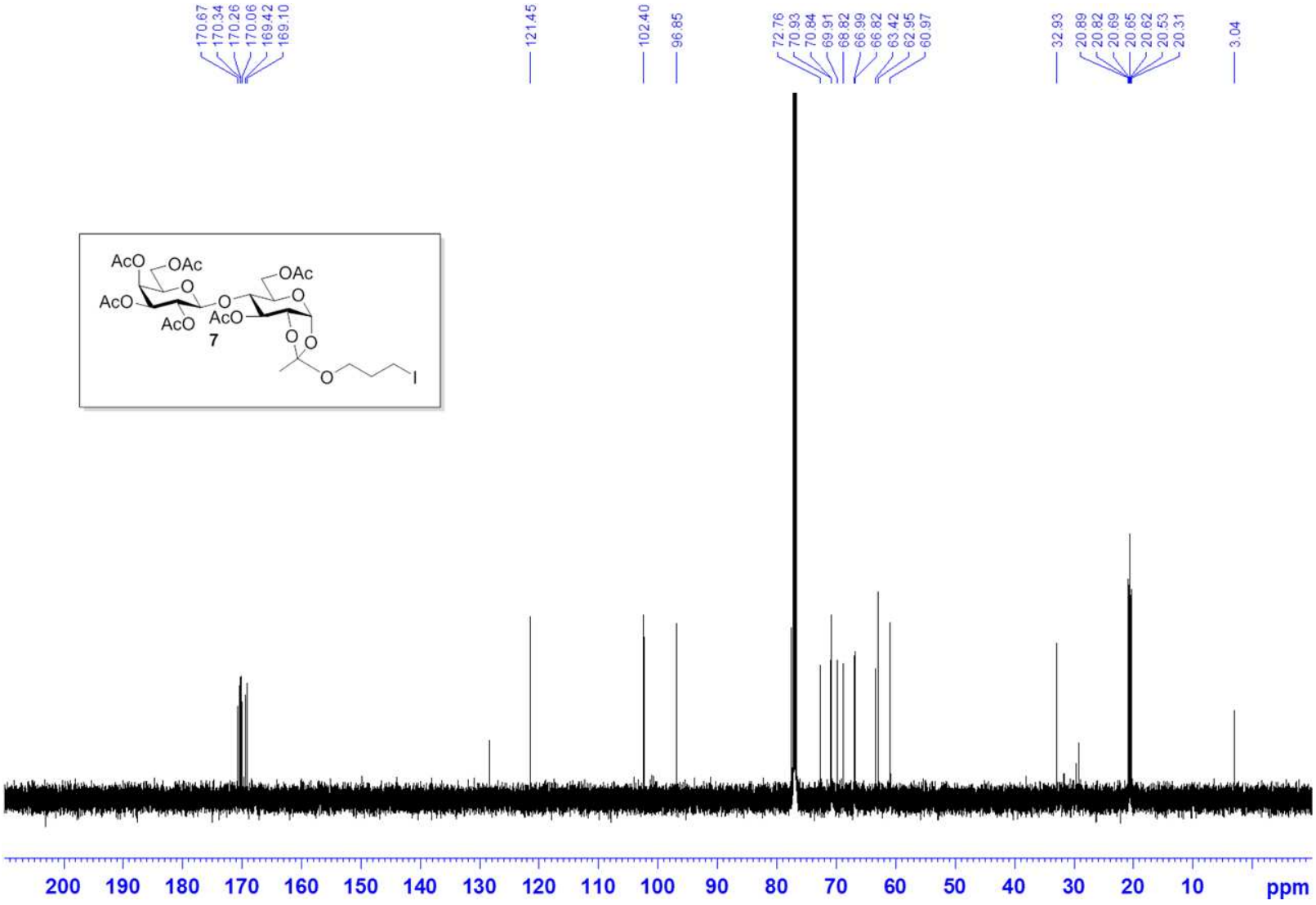
in situ ^{1}H NMR spectrum of compound **6β** ($CDCl_3$, 400 MHz)



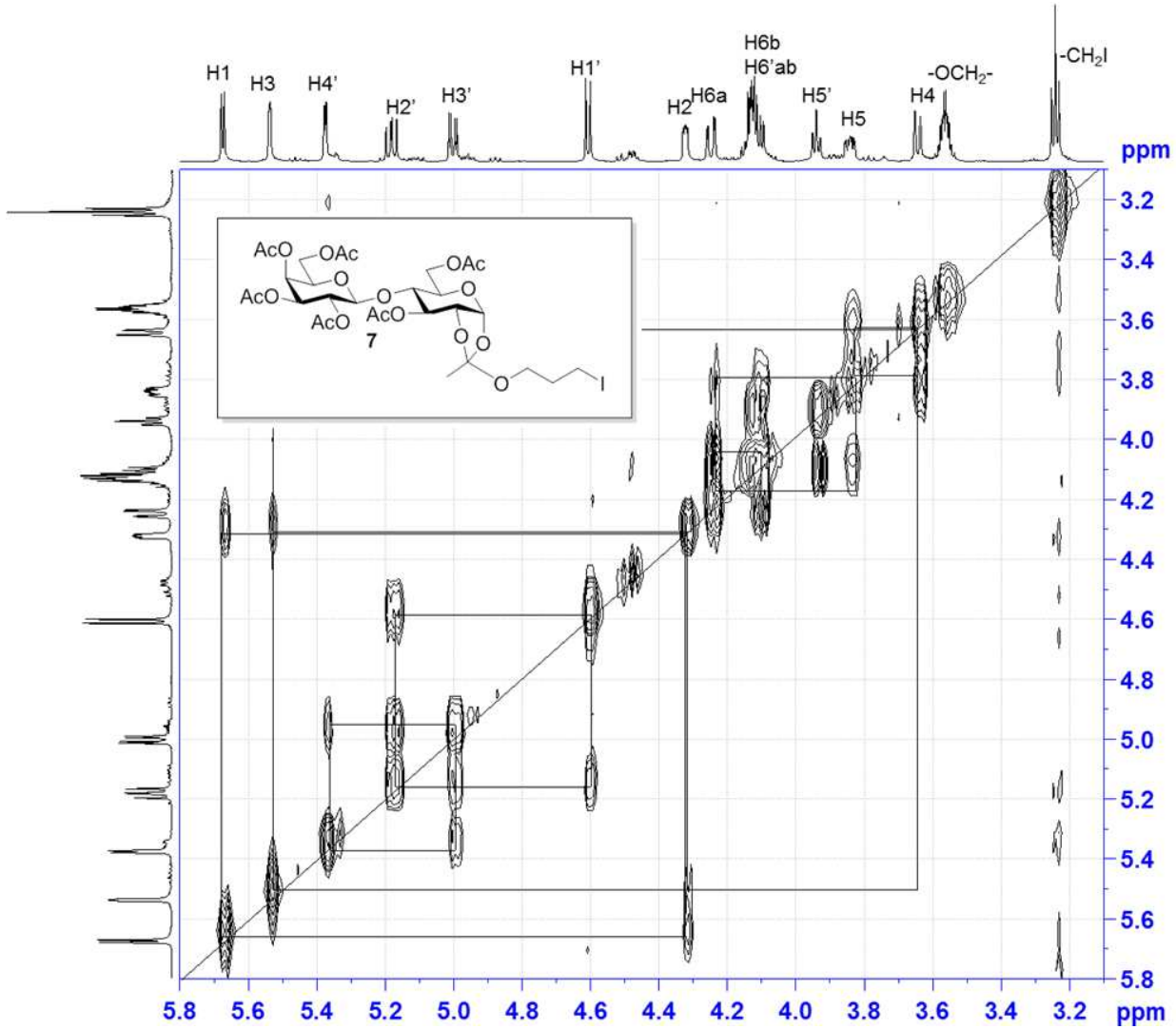
in situ ^{13}C NMR spectrum of compound **6β** ($CDCl_3$, 100 MHz)



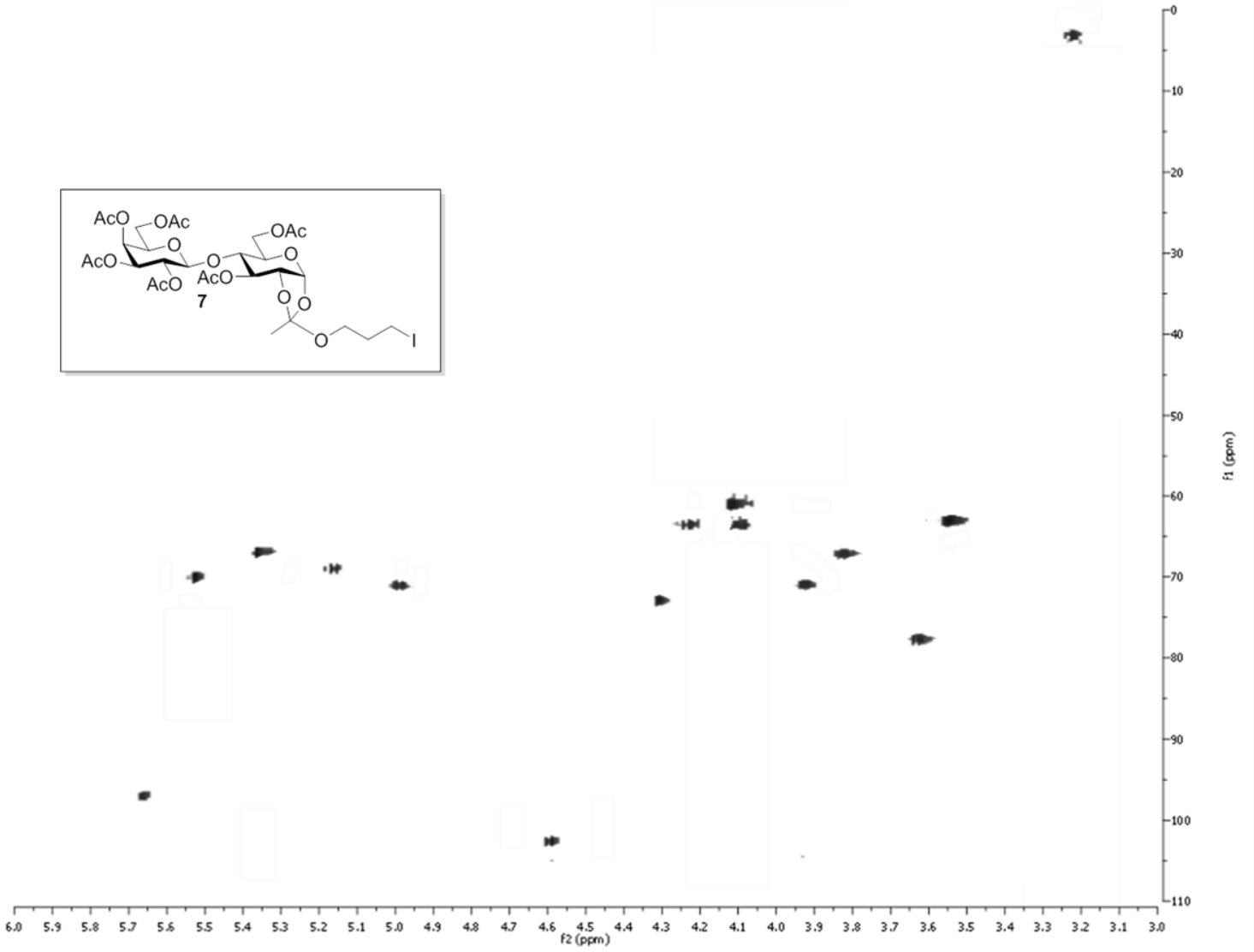
^{1}H NMR spectrum of compound **7** ($CDCl_3$, 600 MHz)



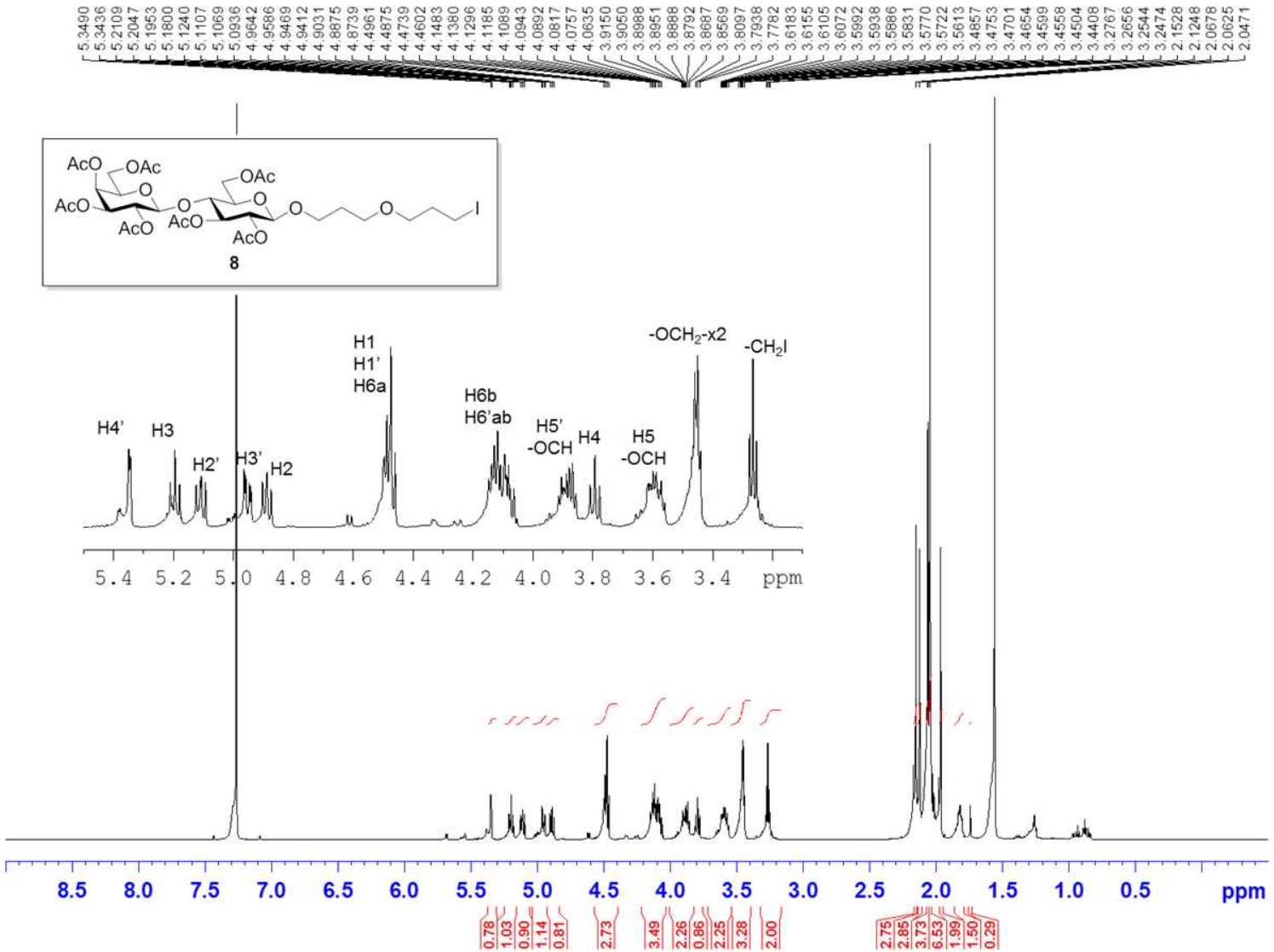
^{13}C NMR spectrum of compound **7** ($CDCl_3$, 150 MHz)



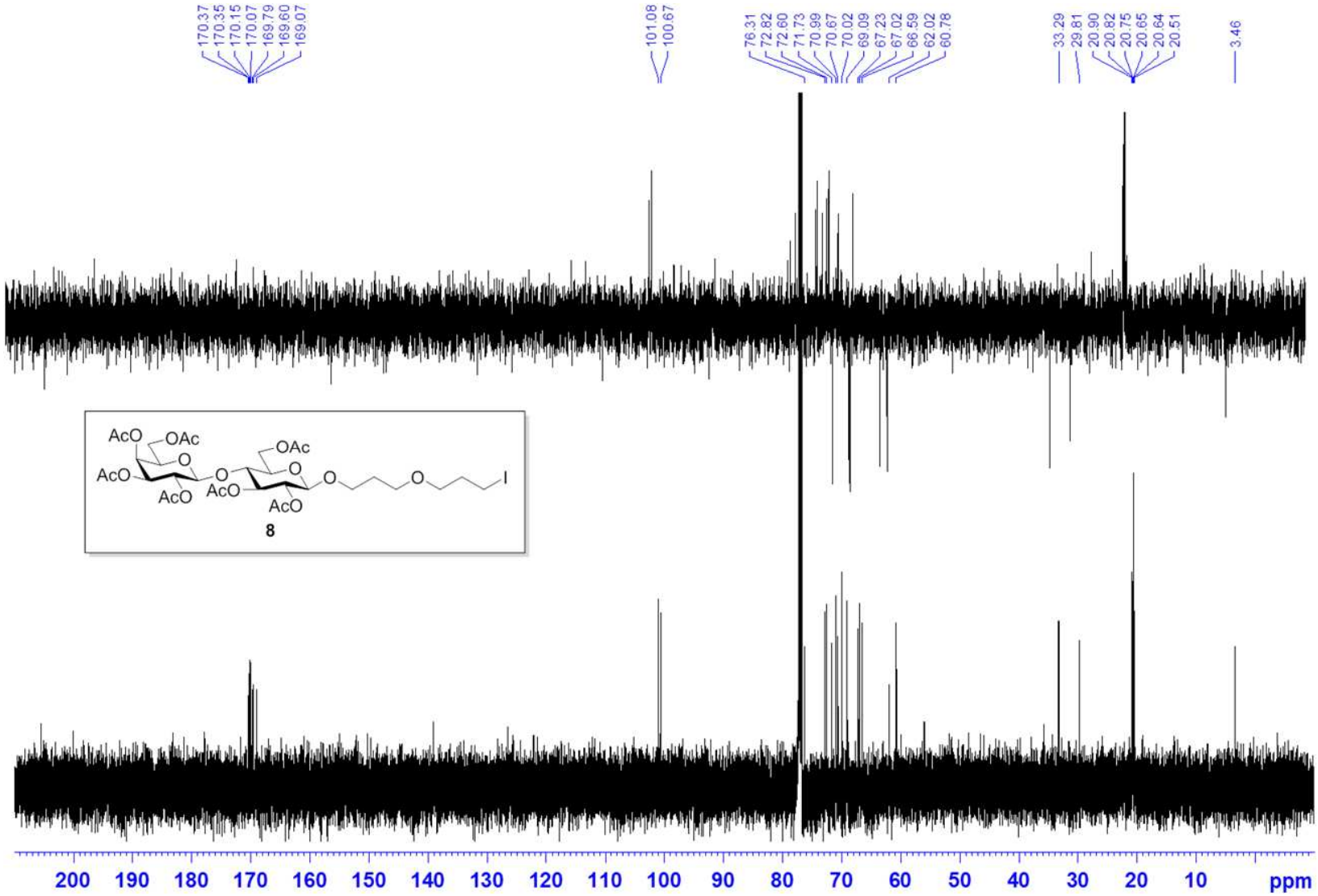
^{1}H-^{1}H COSY spectrum of compound **7** ($CDCl_3$, 600 MHz)



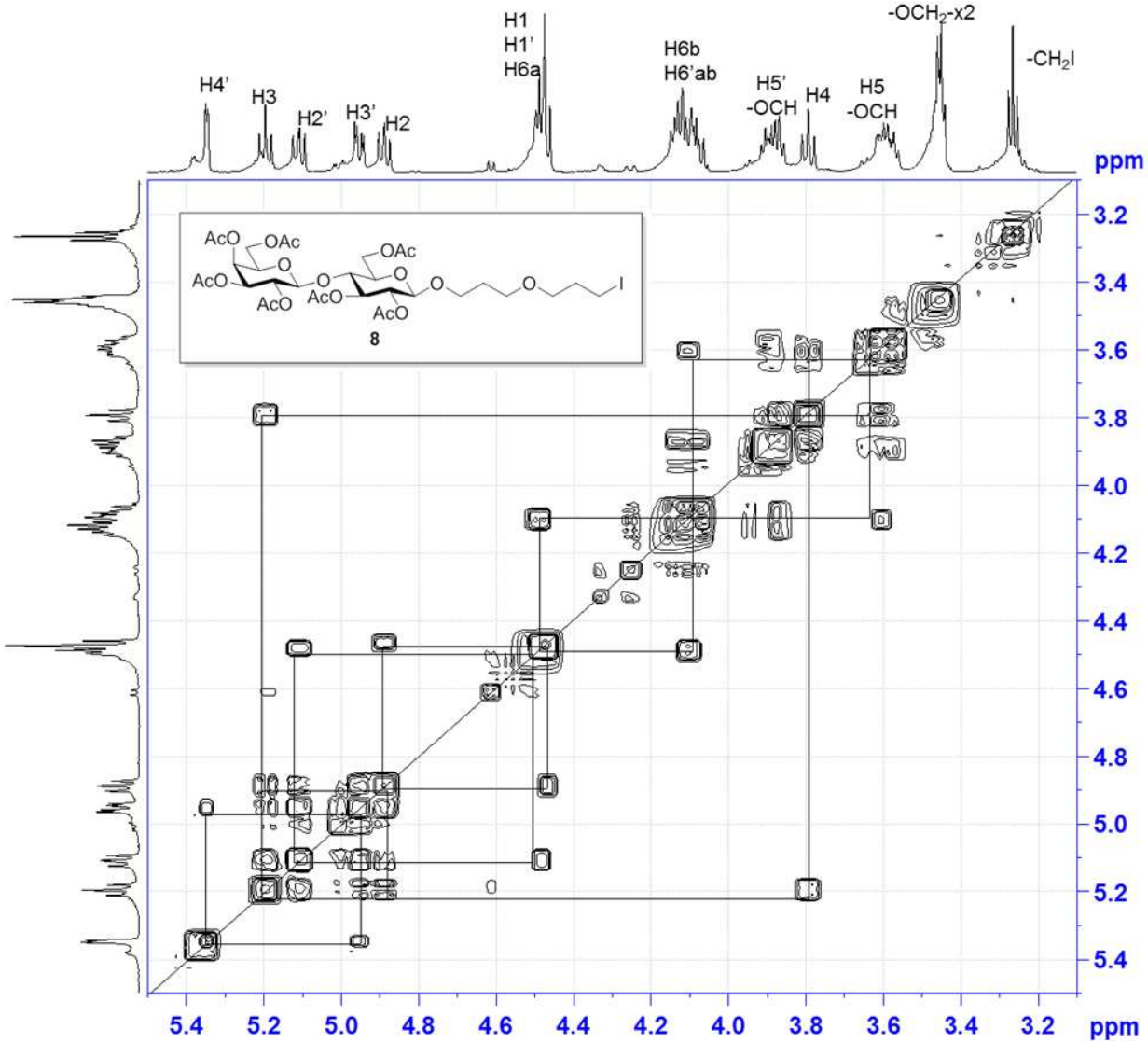
^{1}H-^{13}C HSQC spectrum of compound **7** ($CDCl_3$, 600 MHz)



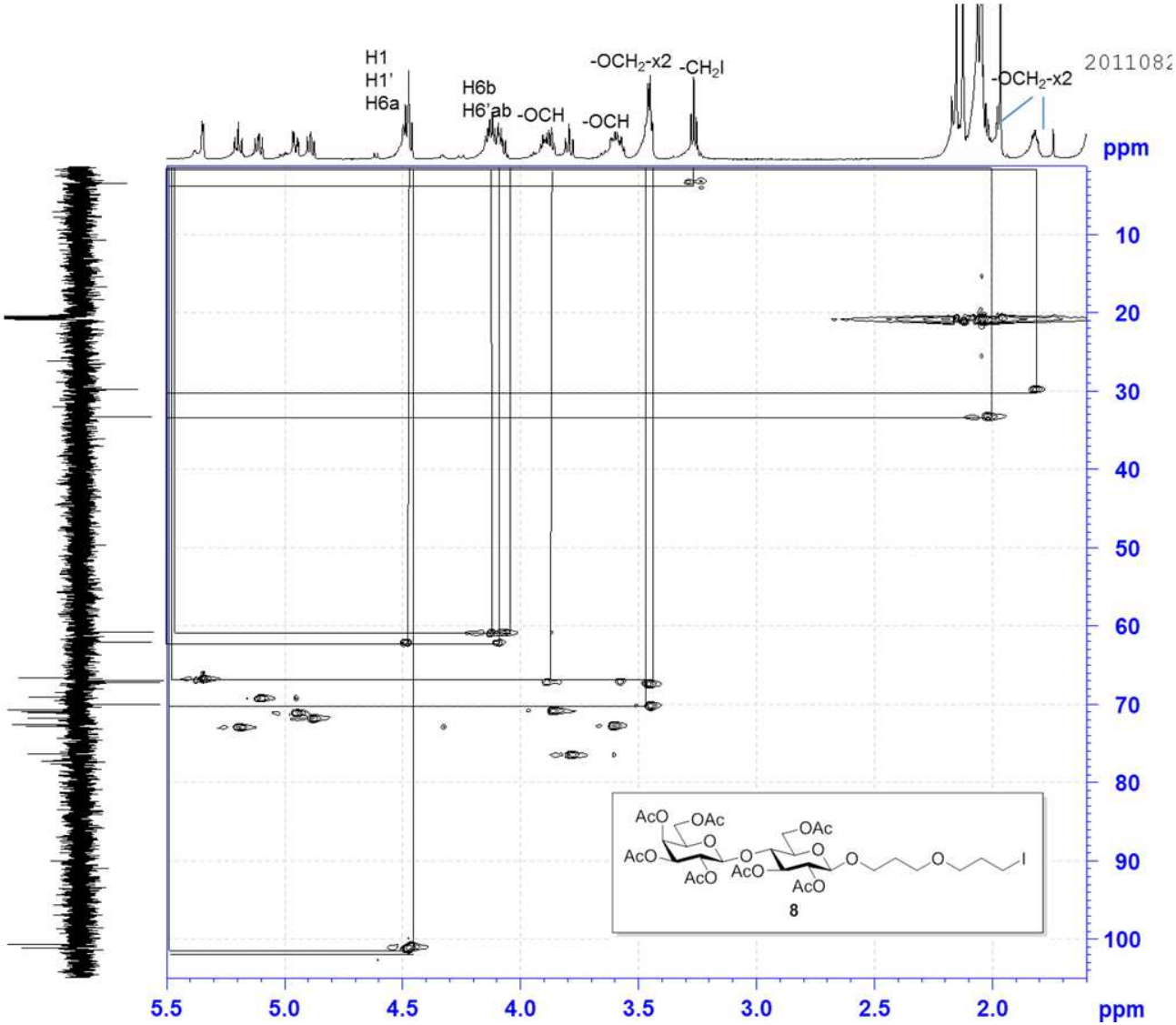
^{1}H NMR spectrum of compound **8** ($CDCl_3$, 600 MHz)



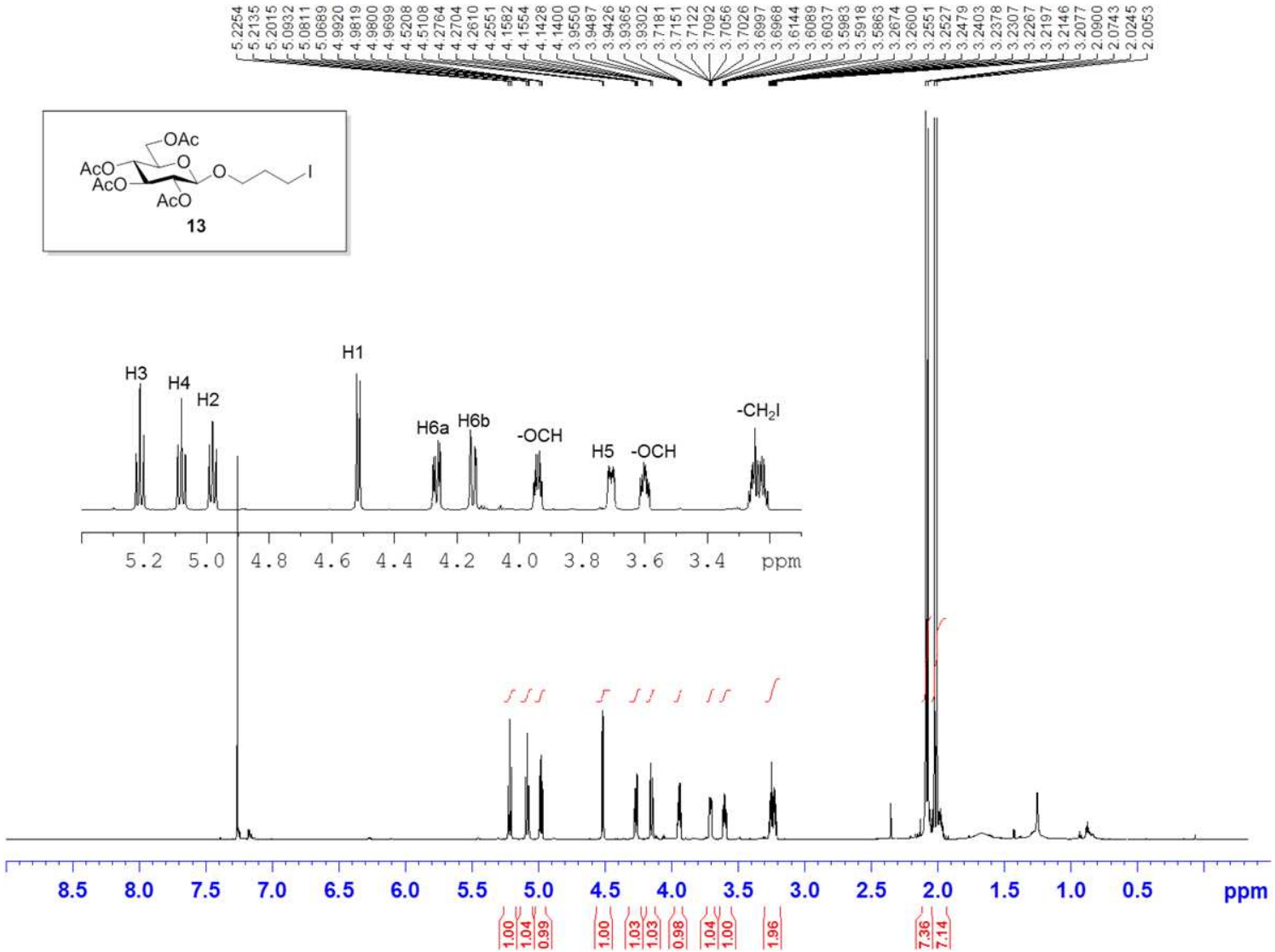
^{13}C and DEPT135 NMR spectrum of compound **8** ($CDCl_3$, 150 MHz)



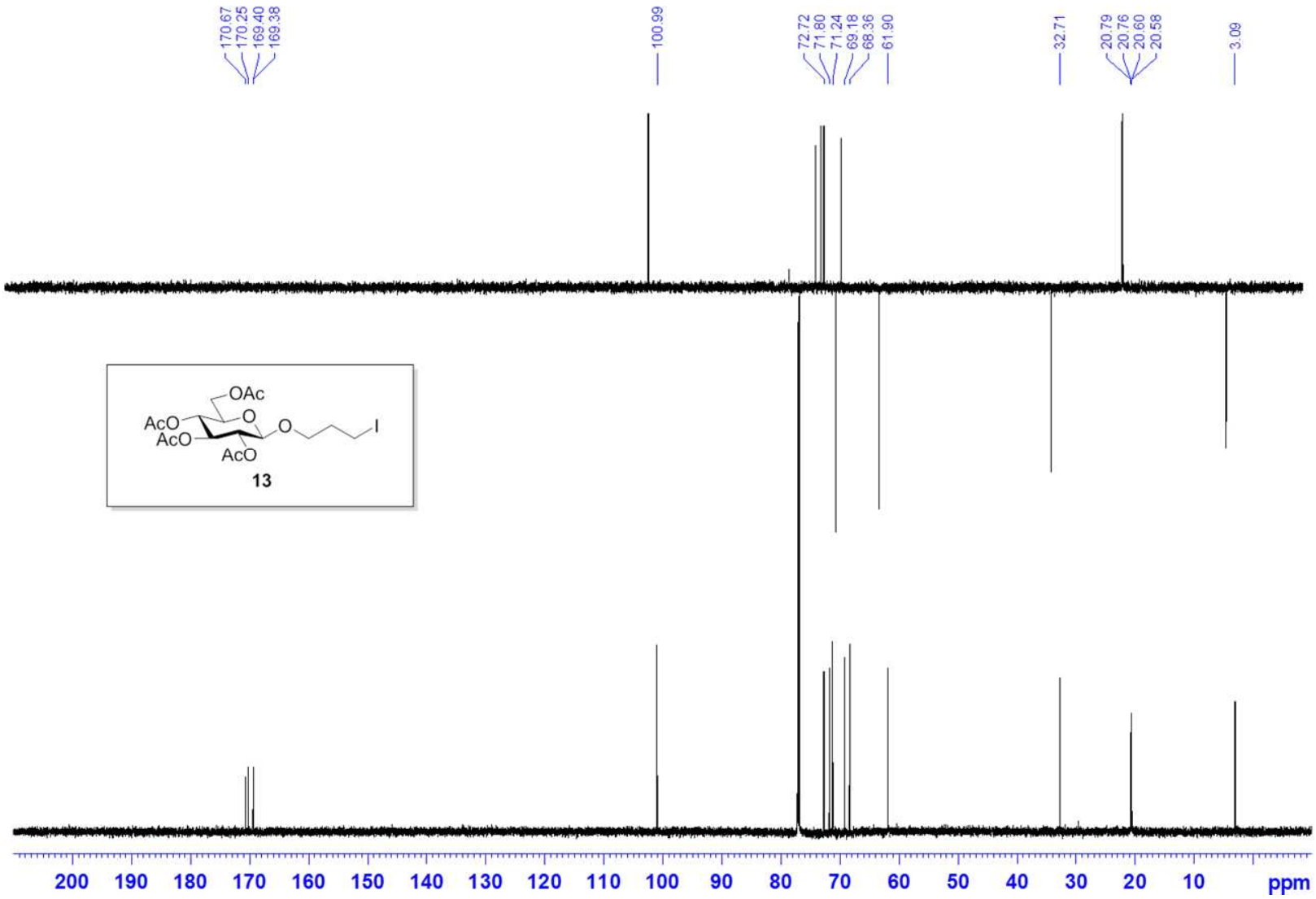
^{1}H-^{1}H COSY spectrum of compound **8** ($CDCl_3$, 600 MHz)



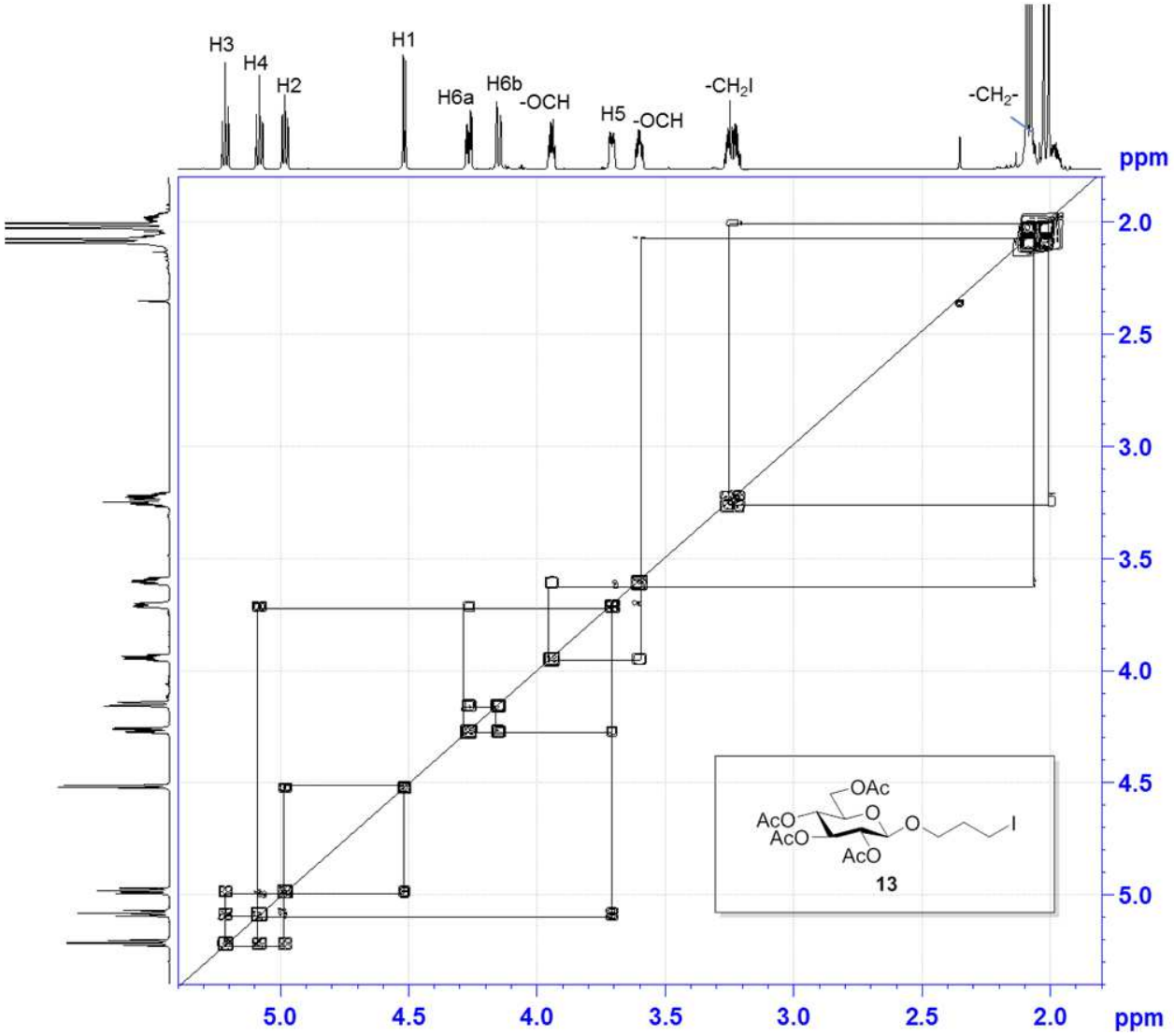
^{1}H-^{13}C HSQC spectrum of compound **8** ($CDCl_3$, 600 MHz)



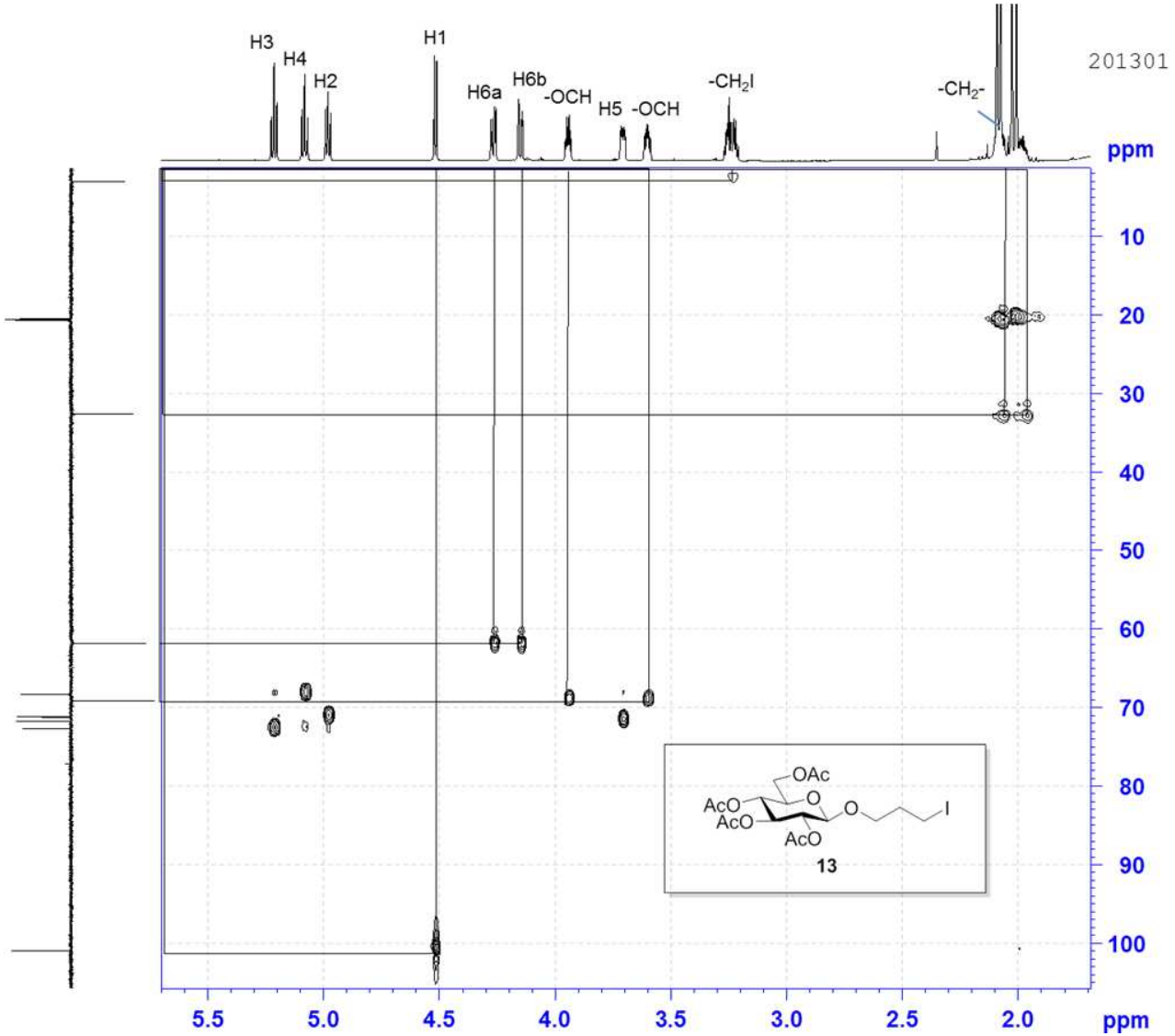
^{1}H NMR spectrum of compound **13** ($CDCl_3$, 800 MHz)



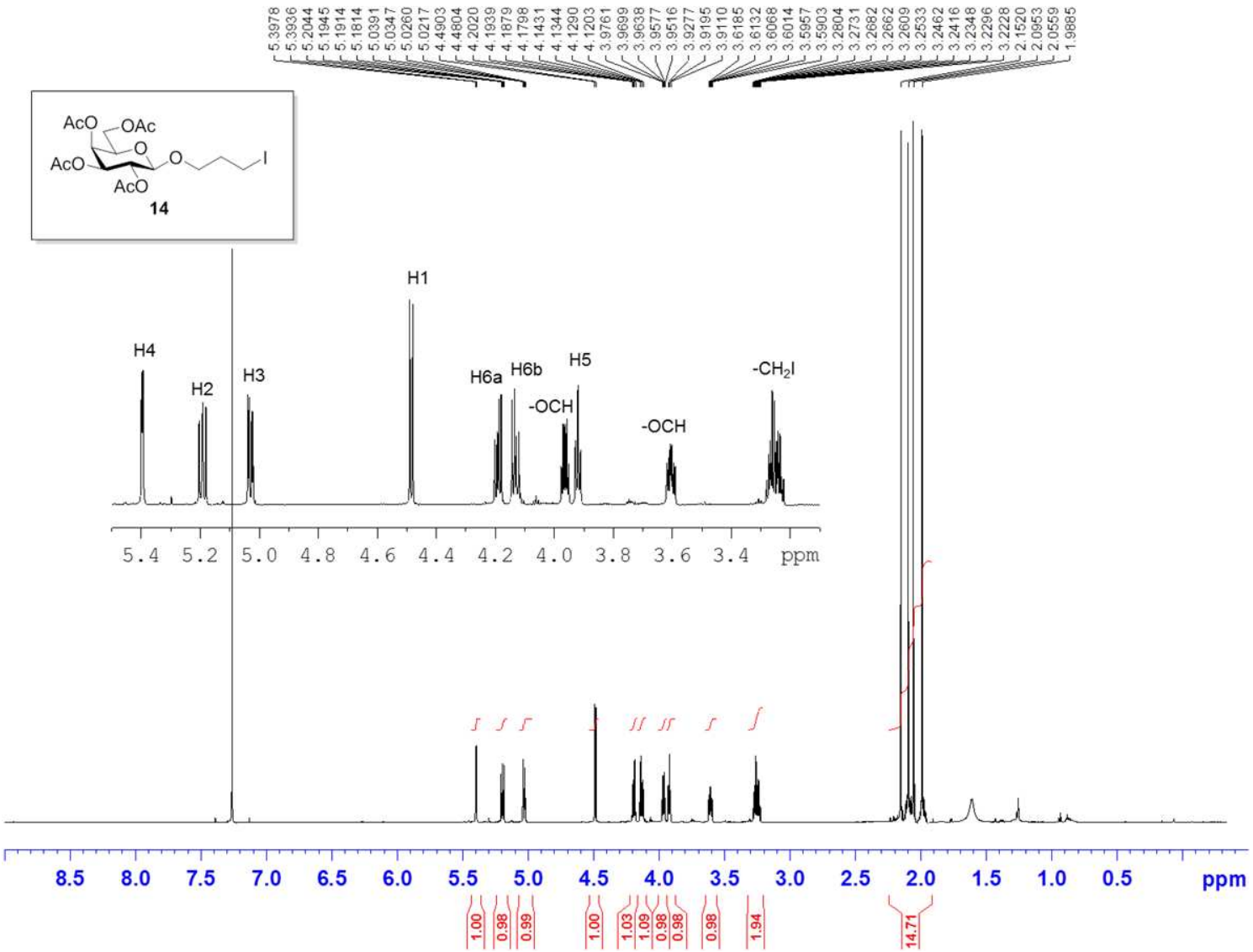
^{13}C and DEPT135 NMR spectrum of compound **13** ($CDCl_3$, 200 MHz)



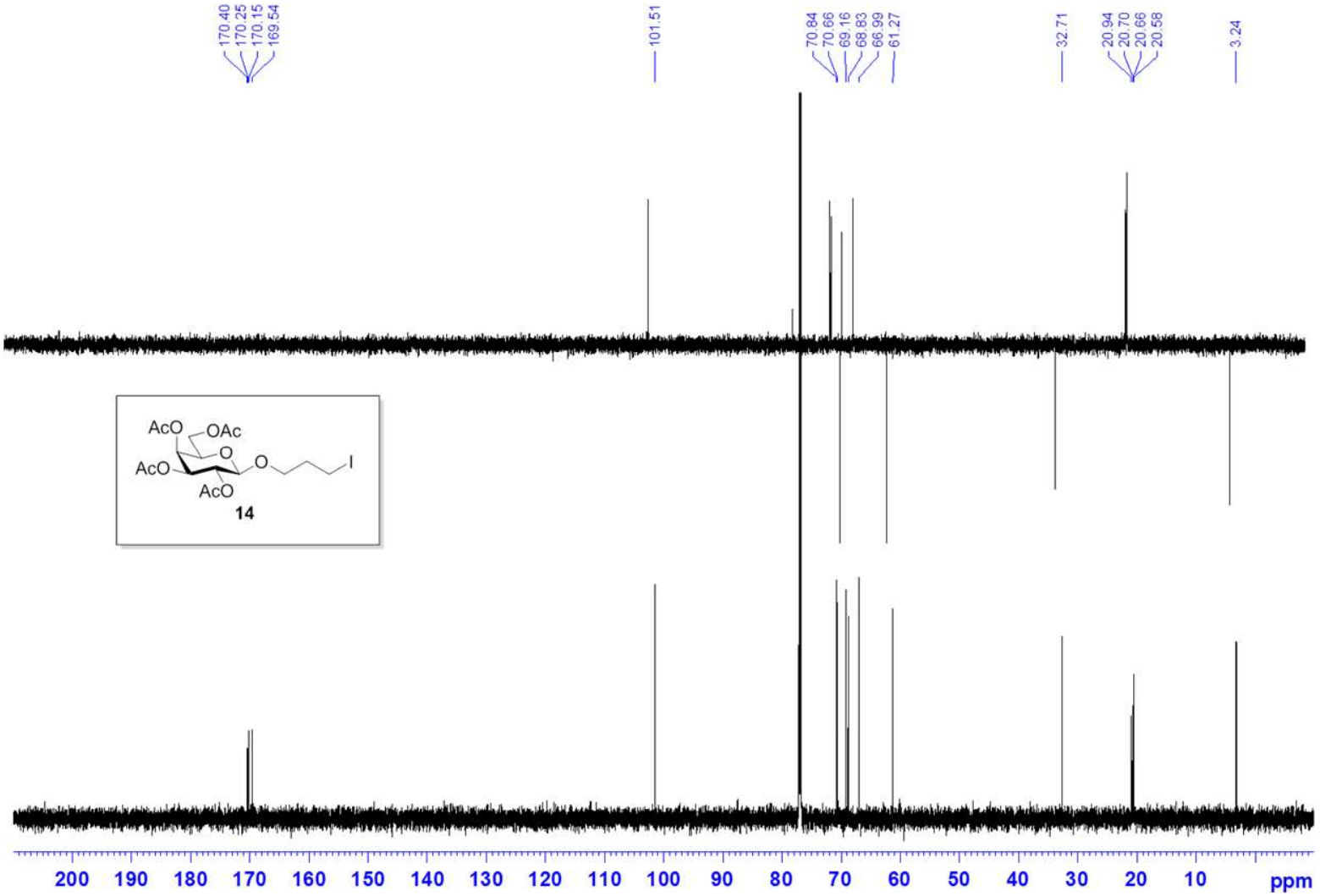
^{1}H-^{1}H COSY spectrum of compound **13** ($CDCl_3$, 800 MHz)



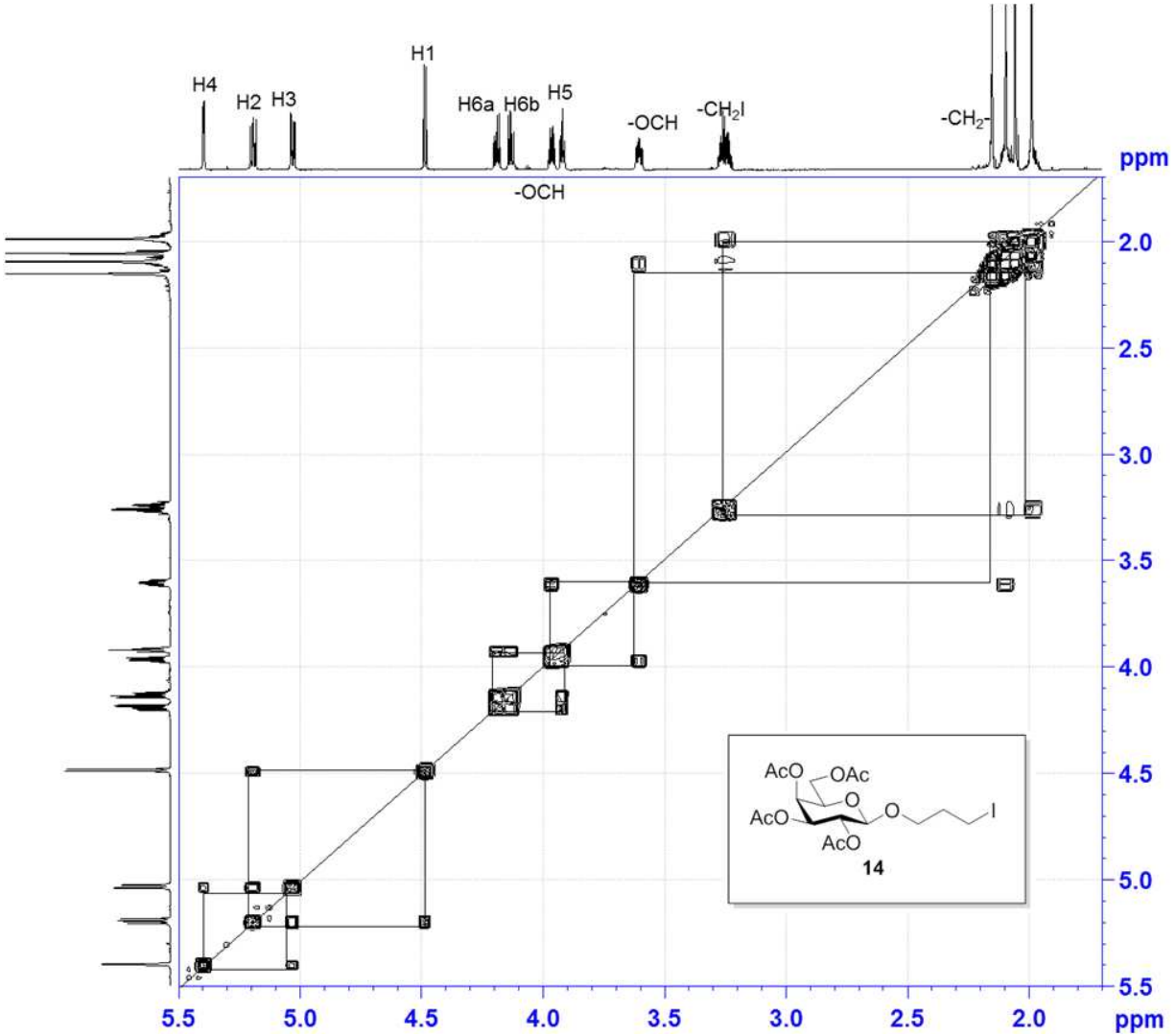
^{1}H-^{13}C HSQC spectrum of compound **13** ($CDCl_3$, 800 MHz)



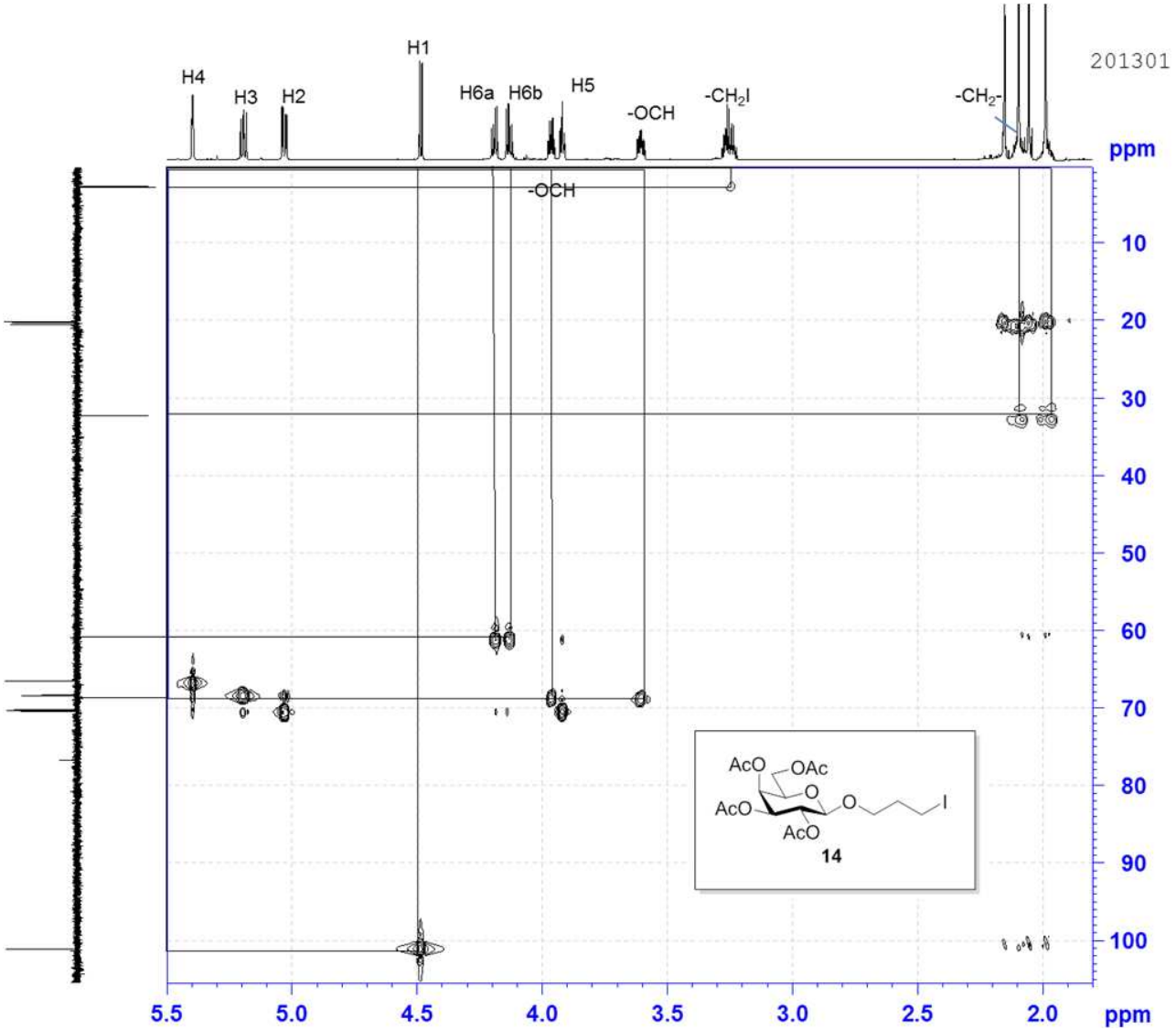
^{1}H NMR spectrum of compound **14** ($CDCl_3$, 800 MHz)



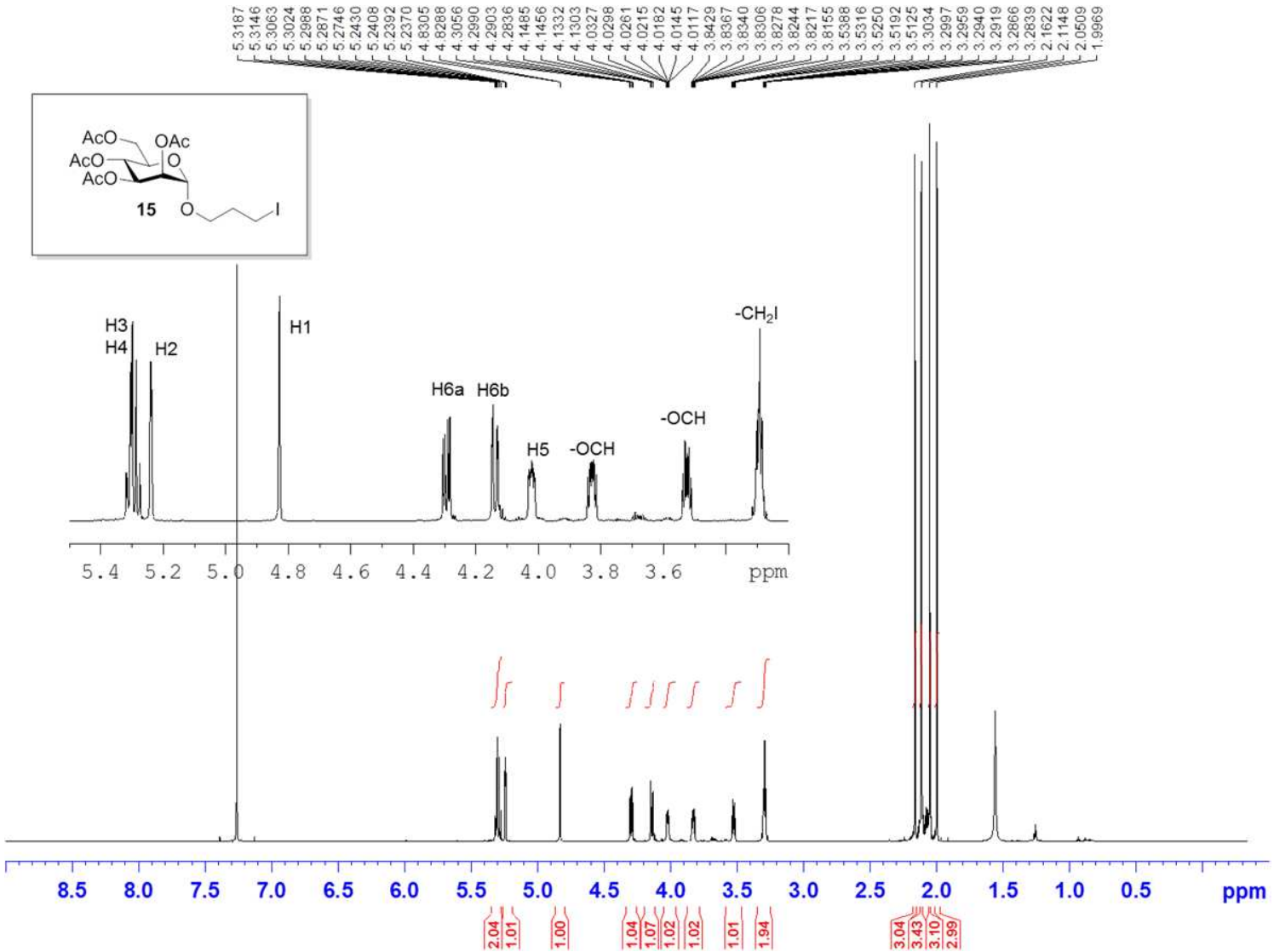
^{13}C and DEPT135 NMR spectrum of compound **14** ($CDCl_3$, 200 MHz)



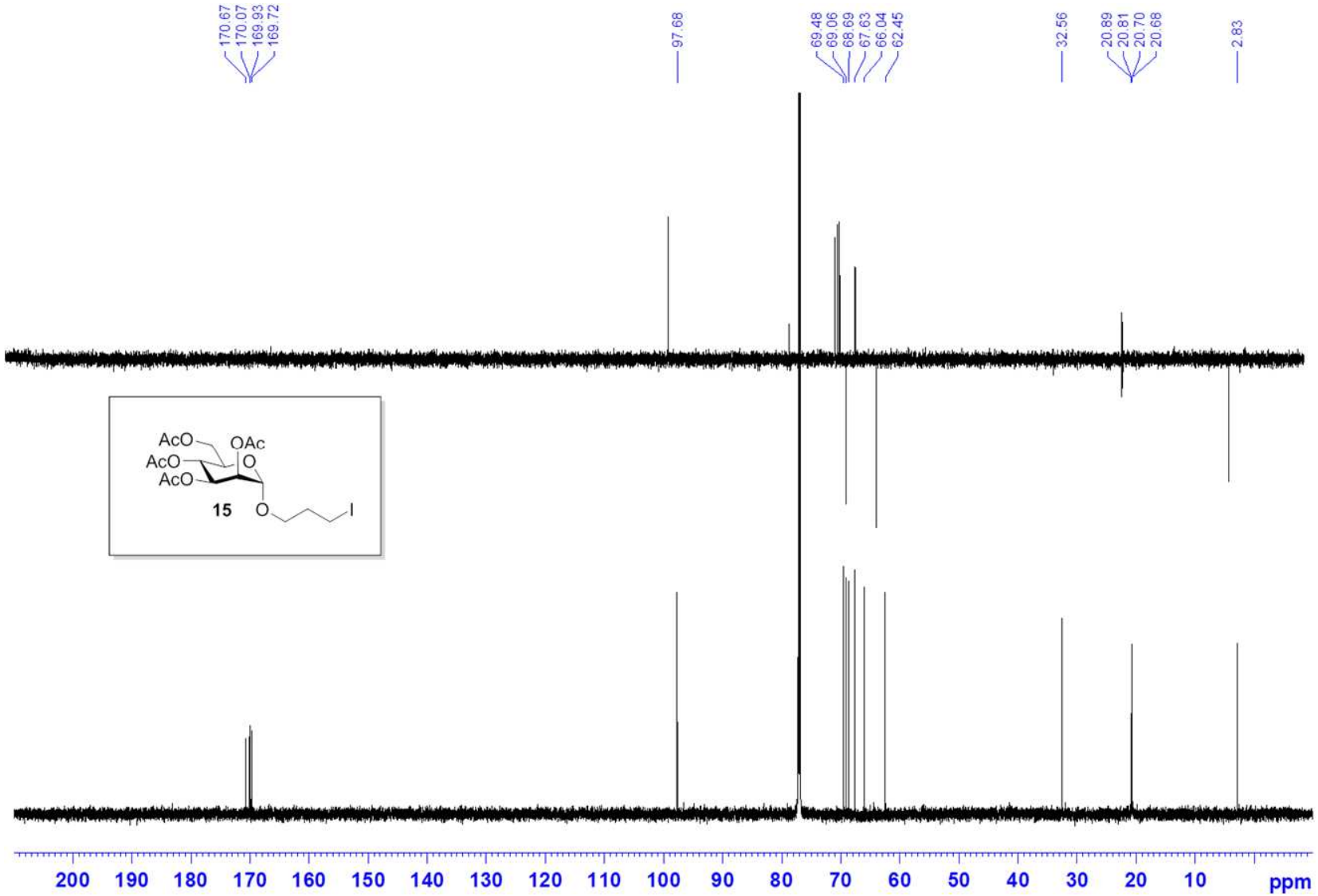
^{1}H-^{1}H COSY spectrum of compound **14** ($CDCl_3$, 800 MHz)



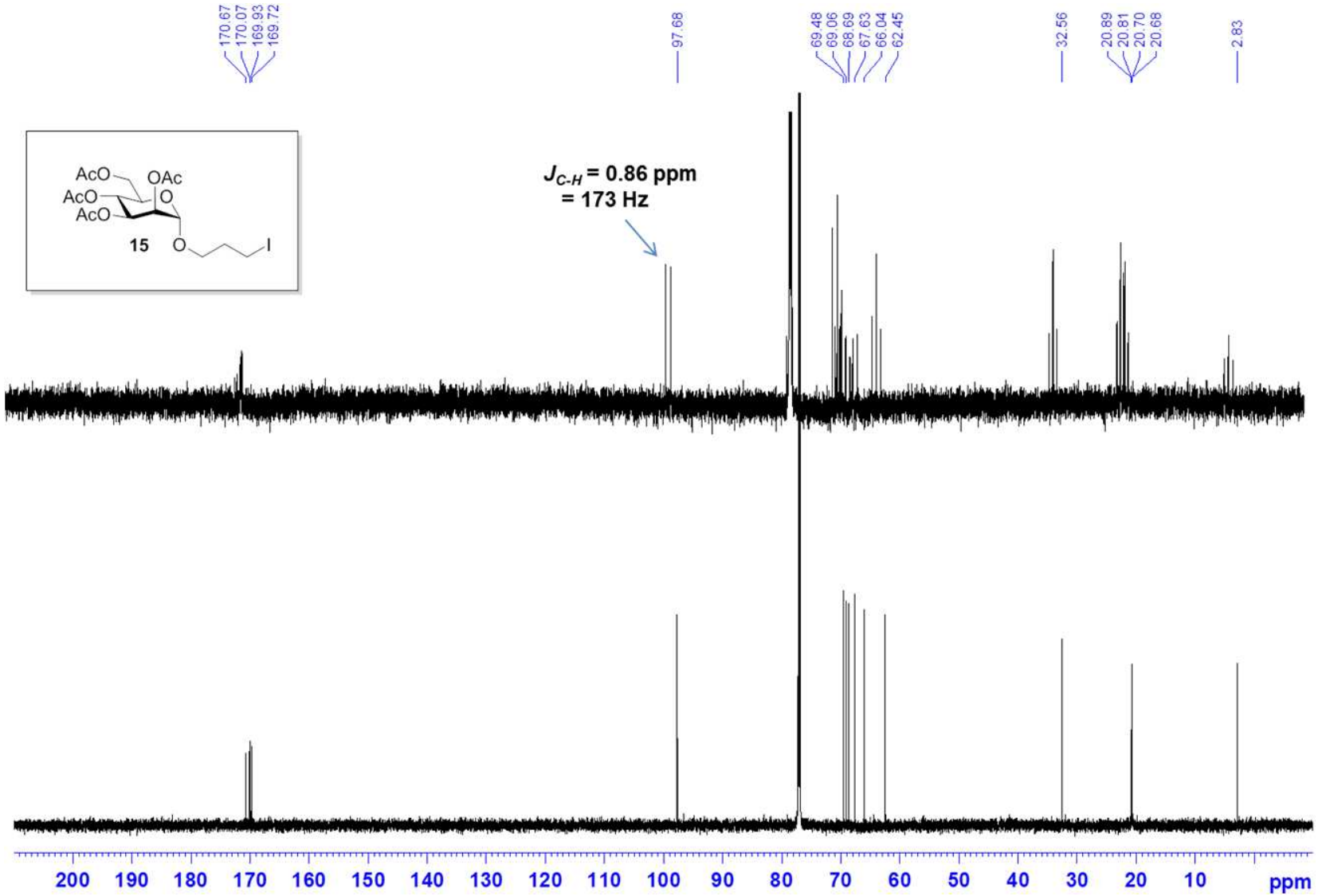
^{1}H-^{13}C HSQC spectrum of compound **14** ($CDCl_3$, 800 MHz)



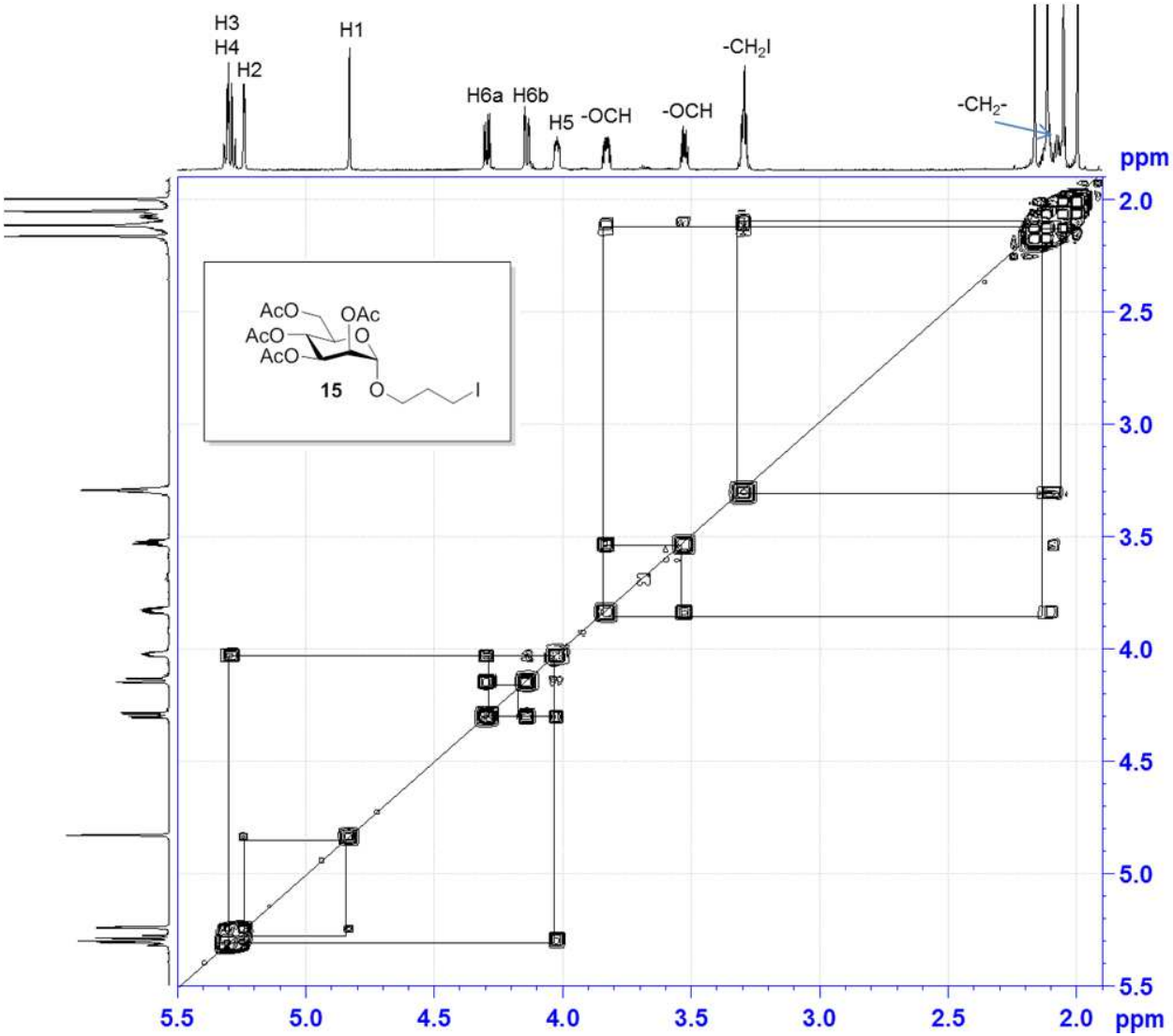
^{1}H NMR spectrum of compound **15** ($CDCl_3$, 800 MHz)



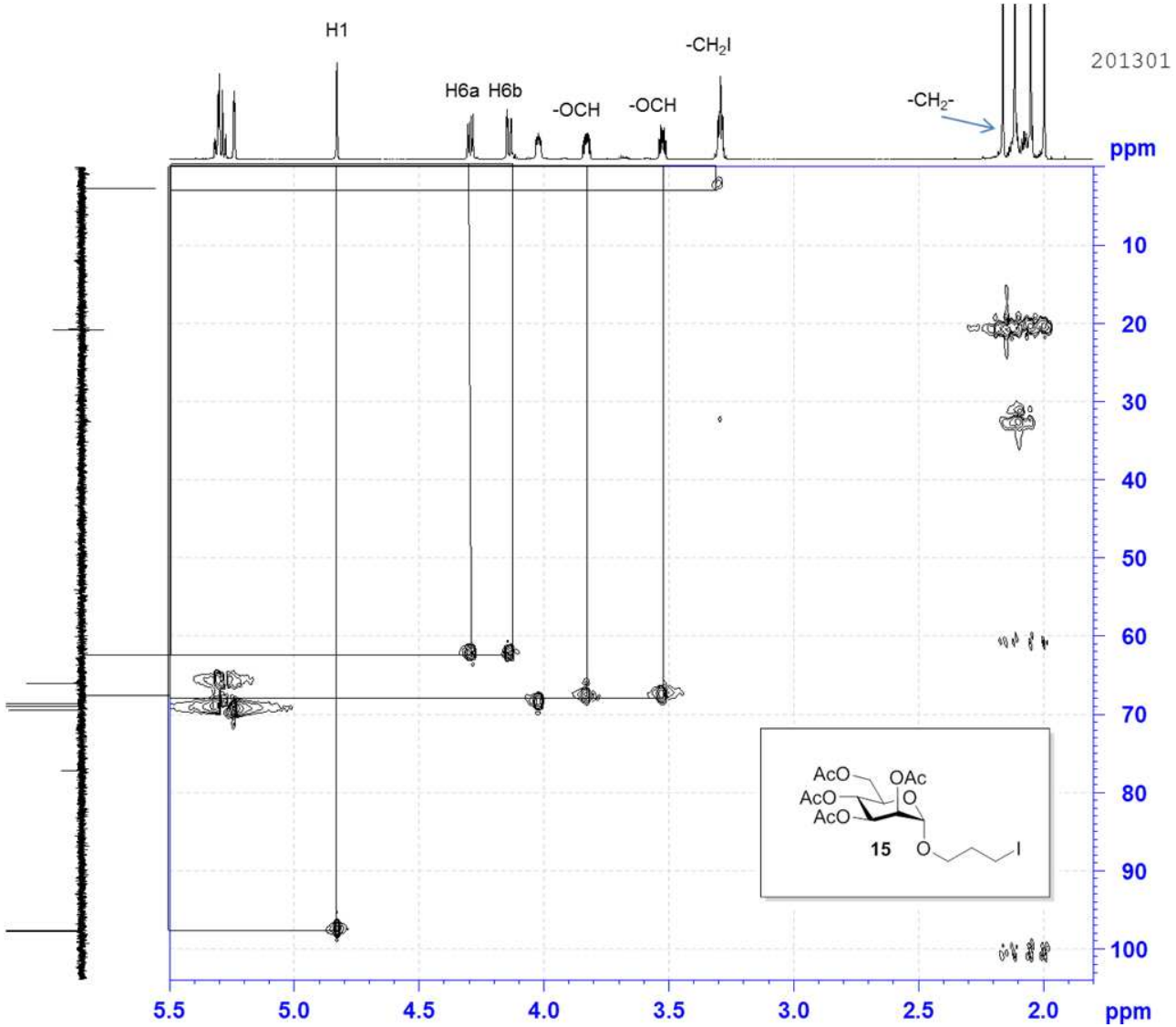
^{13}C and DEPT135 NMR spectrum of compound **15** ($CDCl_3$, 200 MHz)



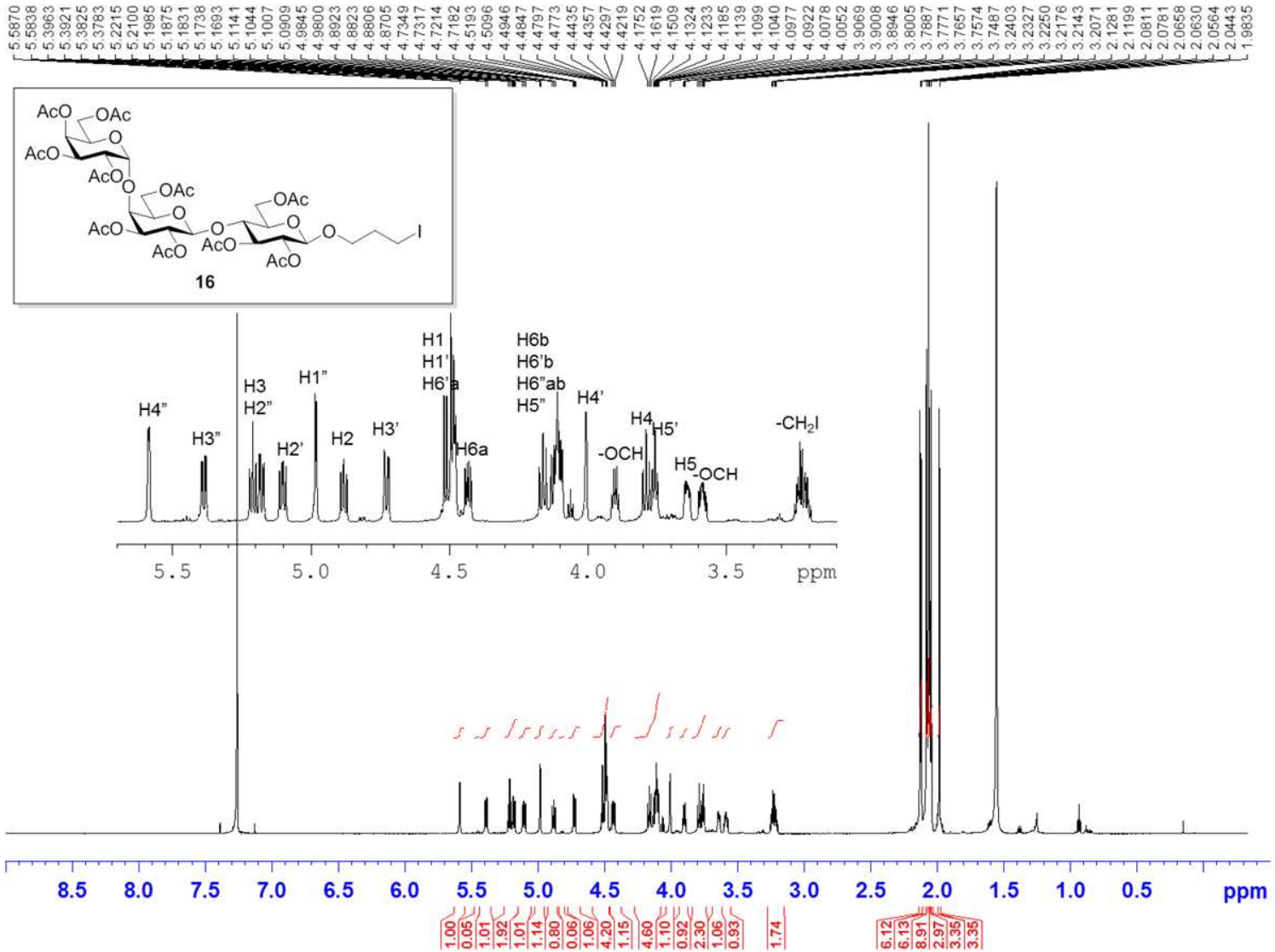
^{13}C and ^{13}C-^{1}H coupled NMR spectrum of compound **15** ($CDCl_3$, 200 MHz)



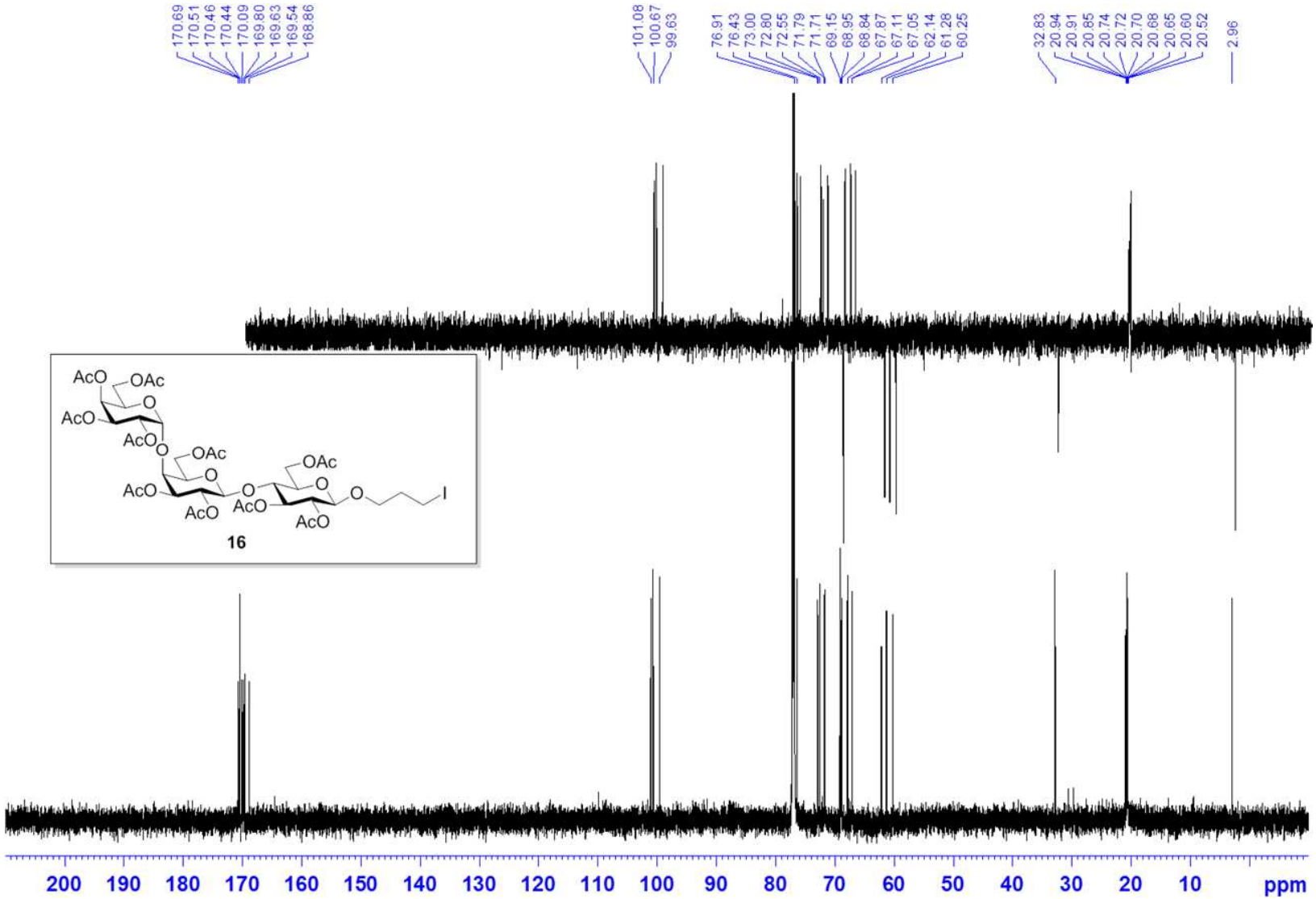
^{1}H-^{1}H COSY spectrum of compound **15** ($CDCl_3$, 800 MHz)



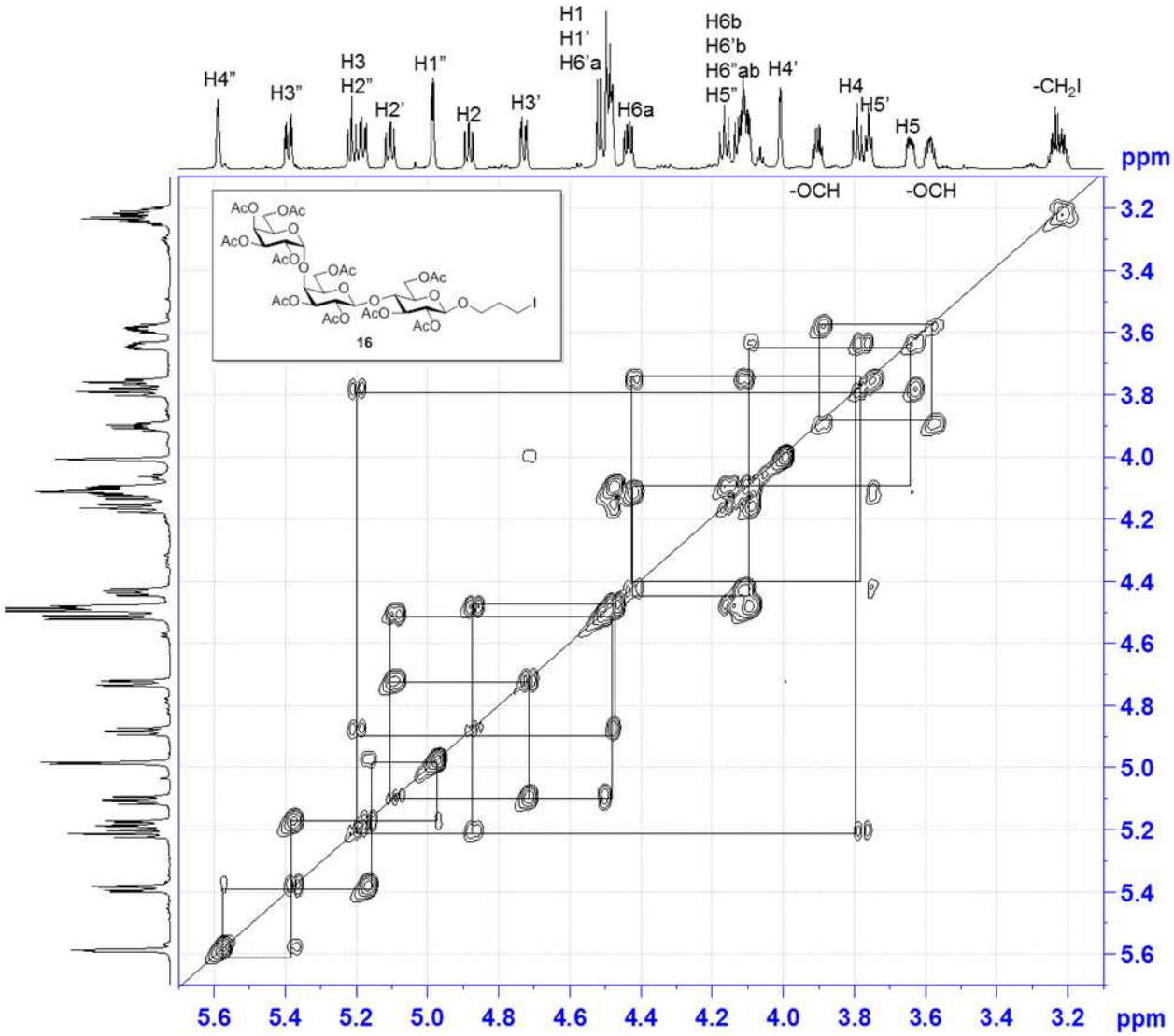
^{1}H-^{13}C HSQC spectrum of compound **15** ($CDCl_3$, 800 MHz)



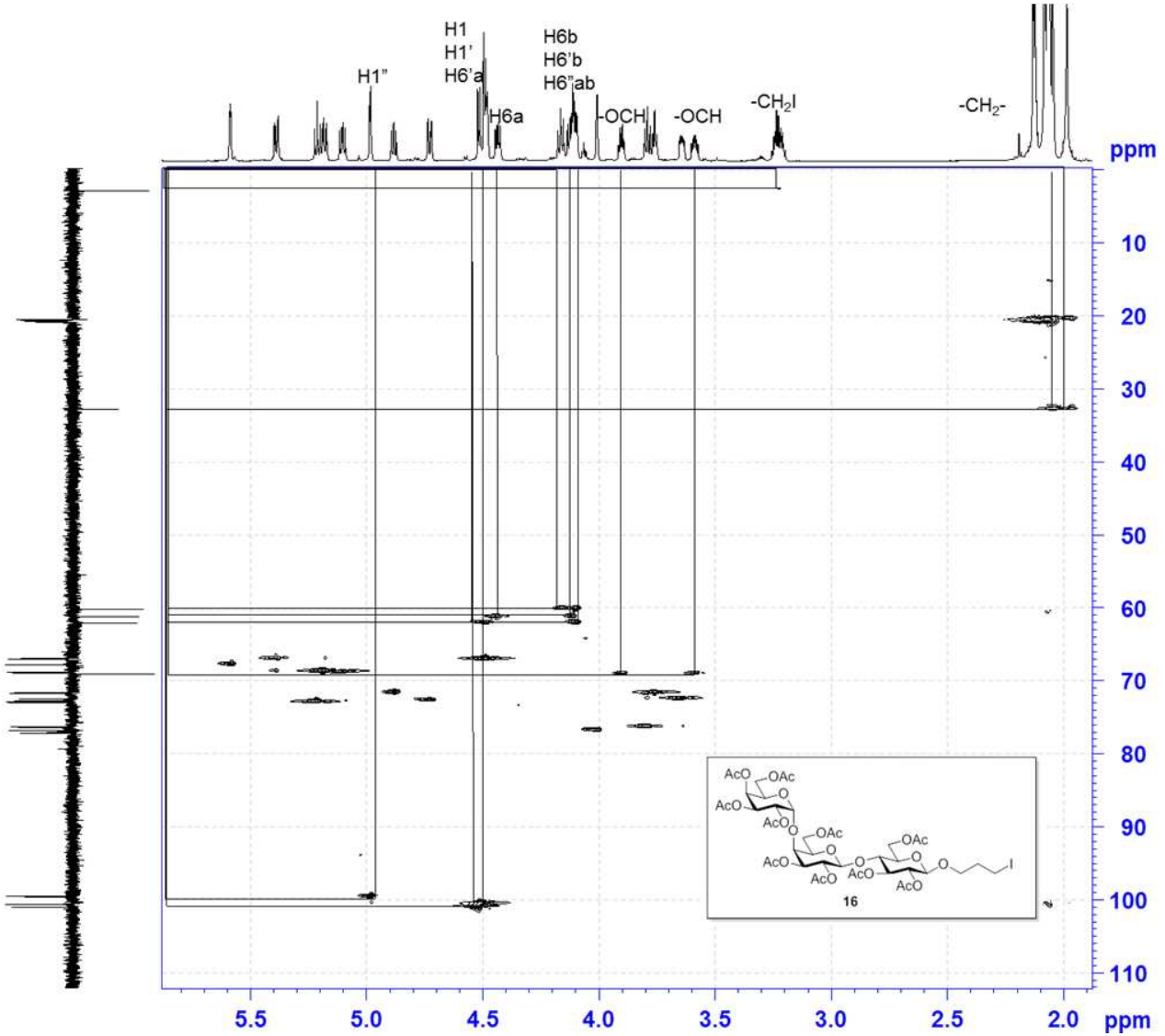
^{1}H NMR spectrum of compound **16** ($CDCl_3$, 800 MHz)



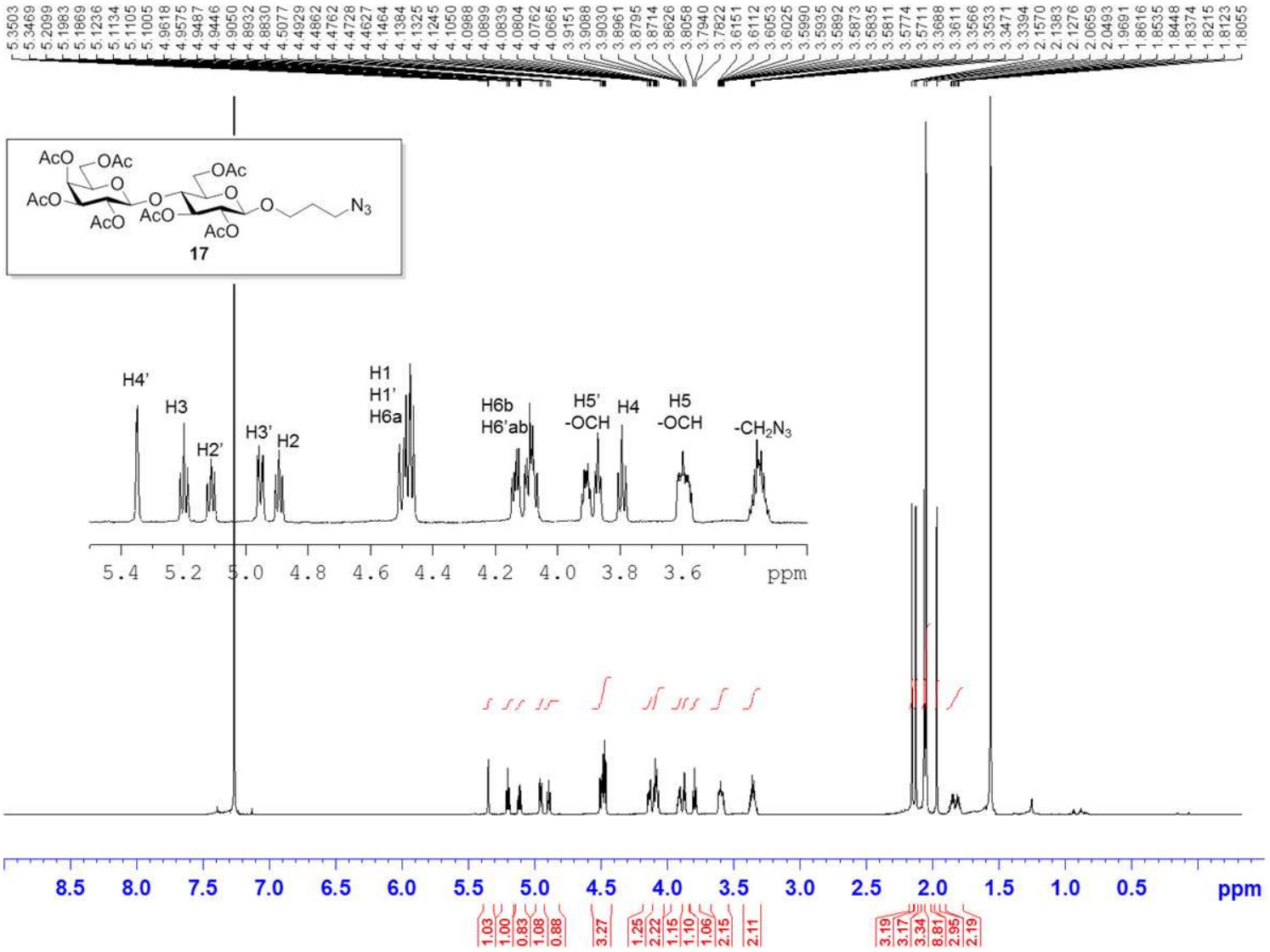
^{13}C and DEPT135 NMR spectrum of compound **16** ($CDCl_3$, 200 MHz)



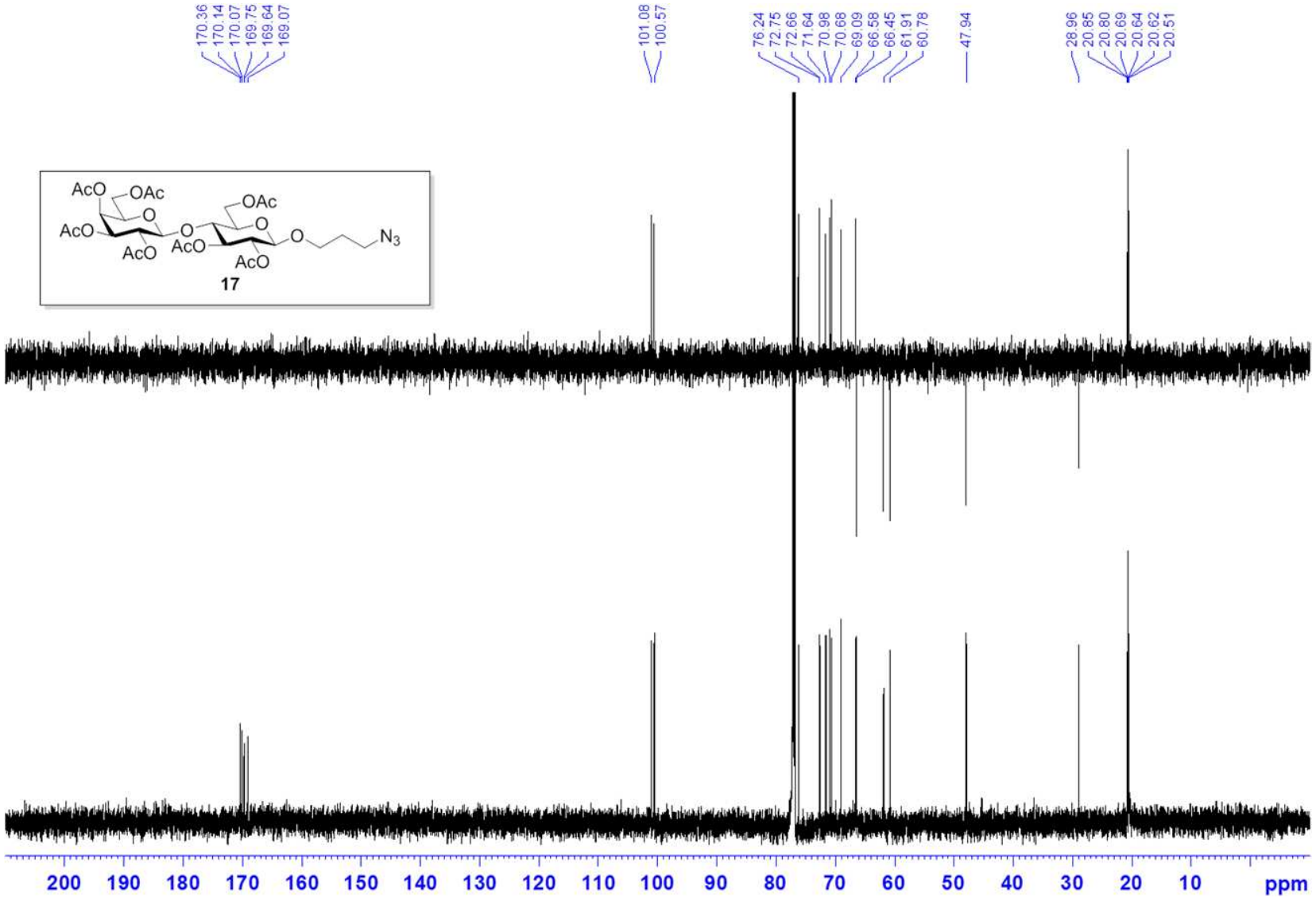
^{1}H-^{1}H COSY spectrum of compound **16** ($CDCl_3$, 800 MHz)



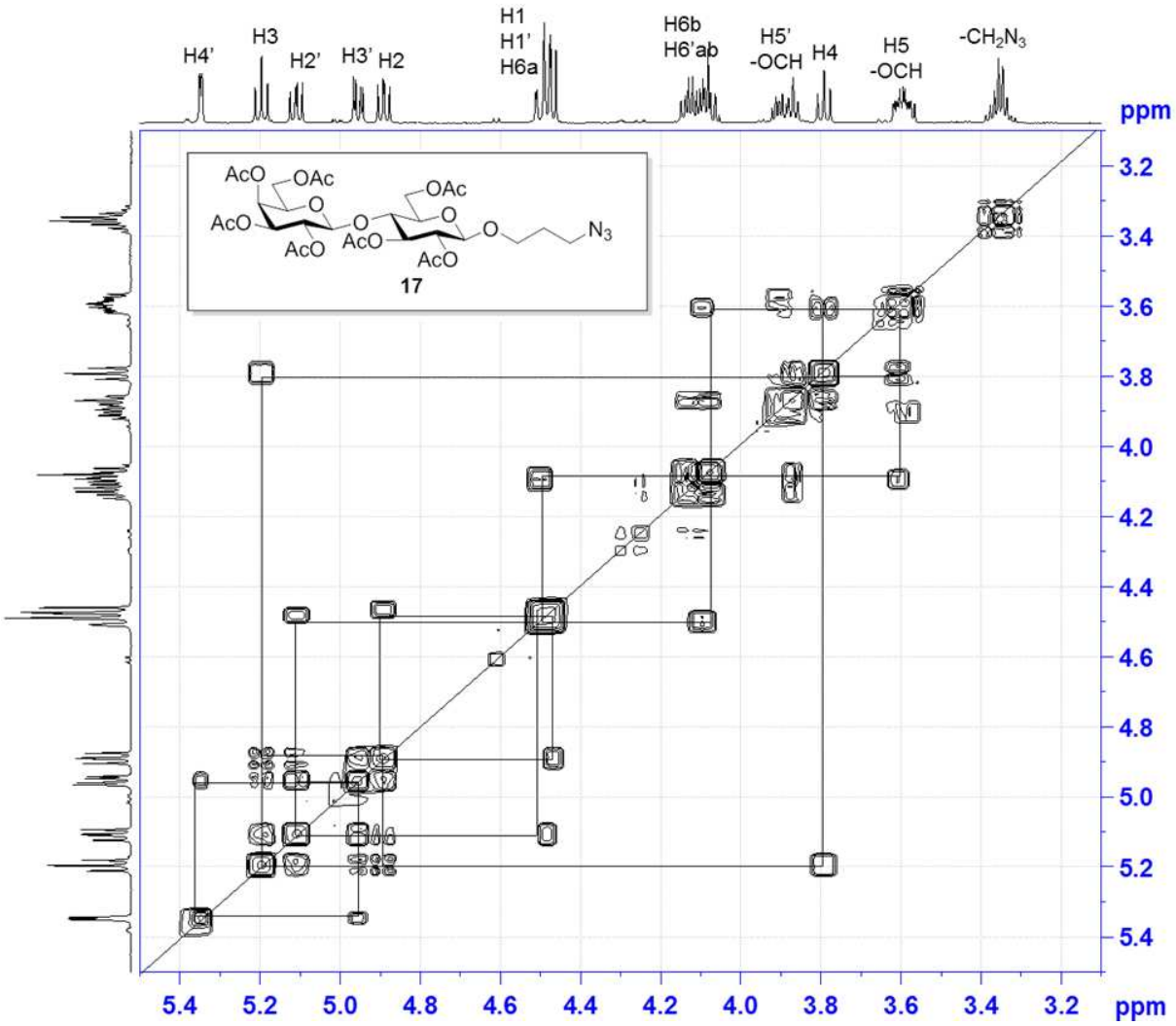
^{1}H-^{13}C HSQC spectrum of compound **16** ($CDCl_3$, 800 MHz)



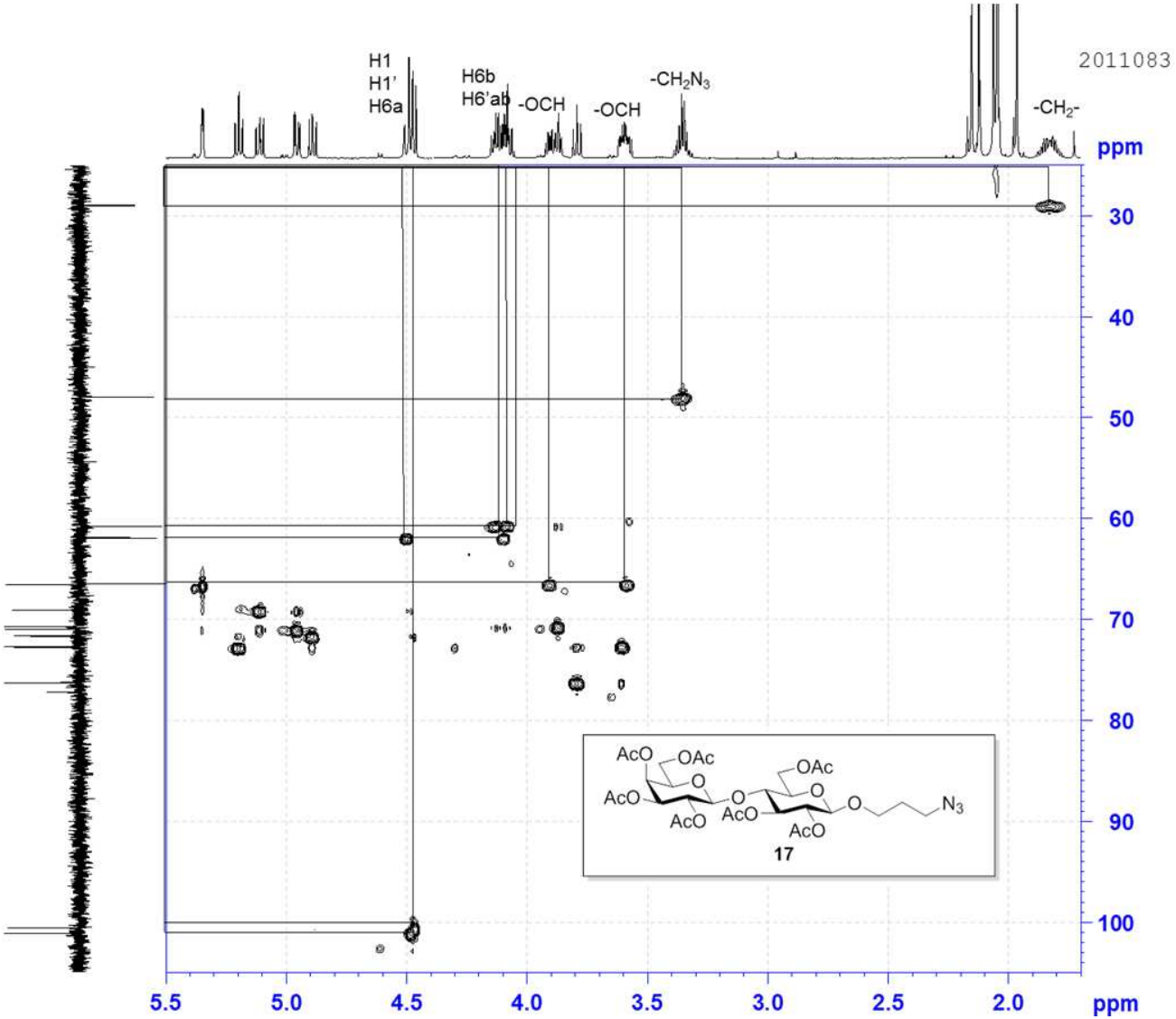
^{1}H NMR spectrum of compound **17** ($CDCl_3$, 600 MHz)



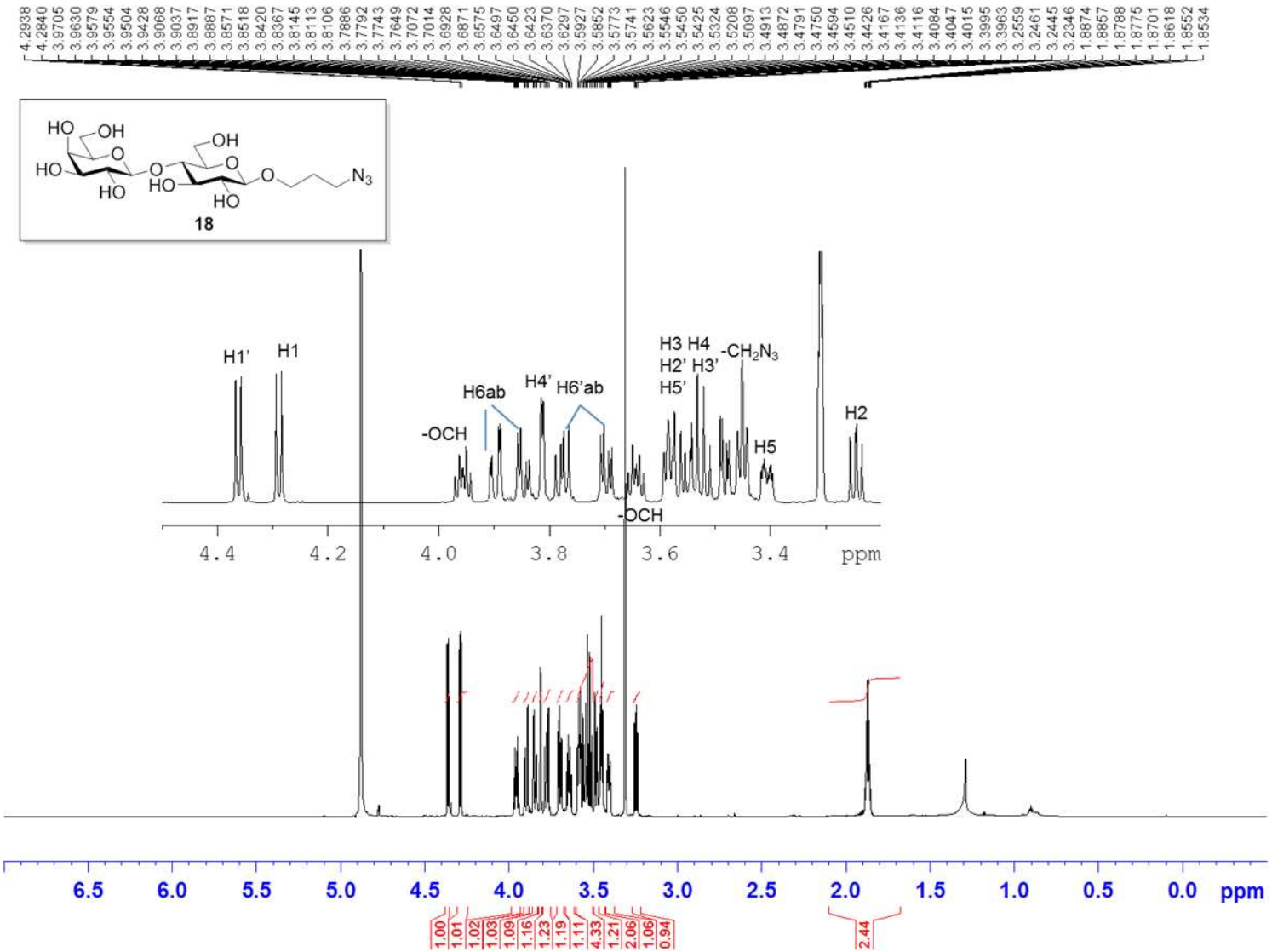
^{13}C and DEPT135 NMR spectrum of compound **17** ($CDCl_3$, 150 MHz)



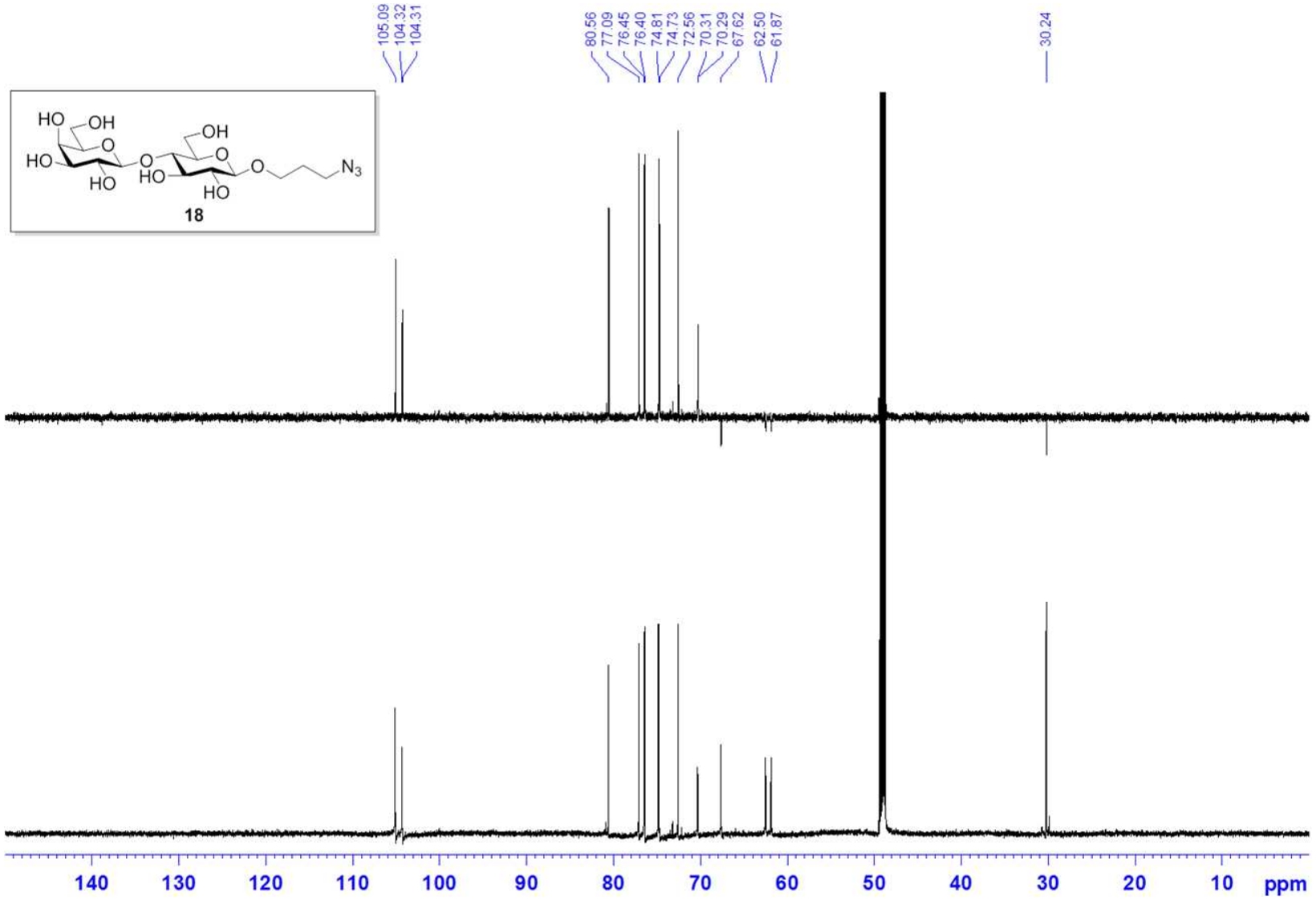
^{1}H-^{1}H COSY spectrum of compound **17** ($CDCl_3$, 600 MHz)



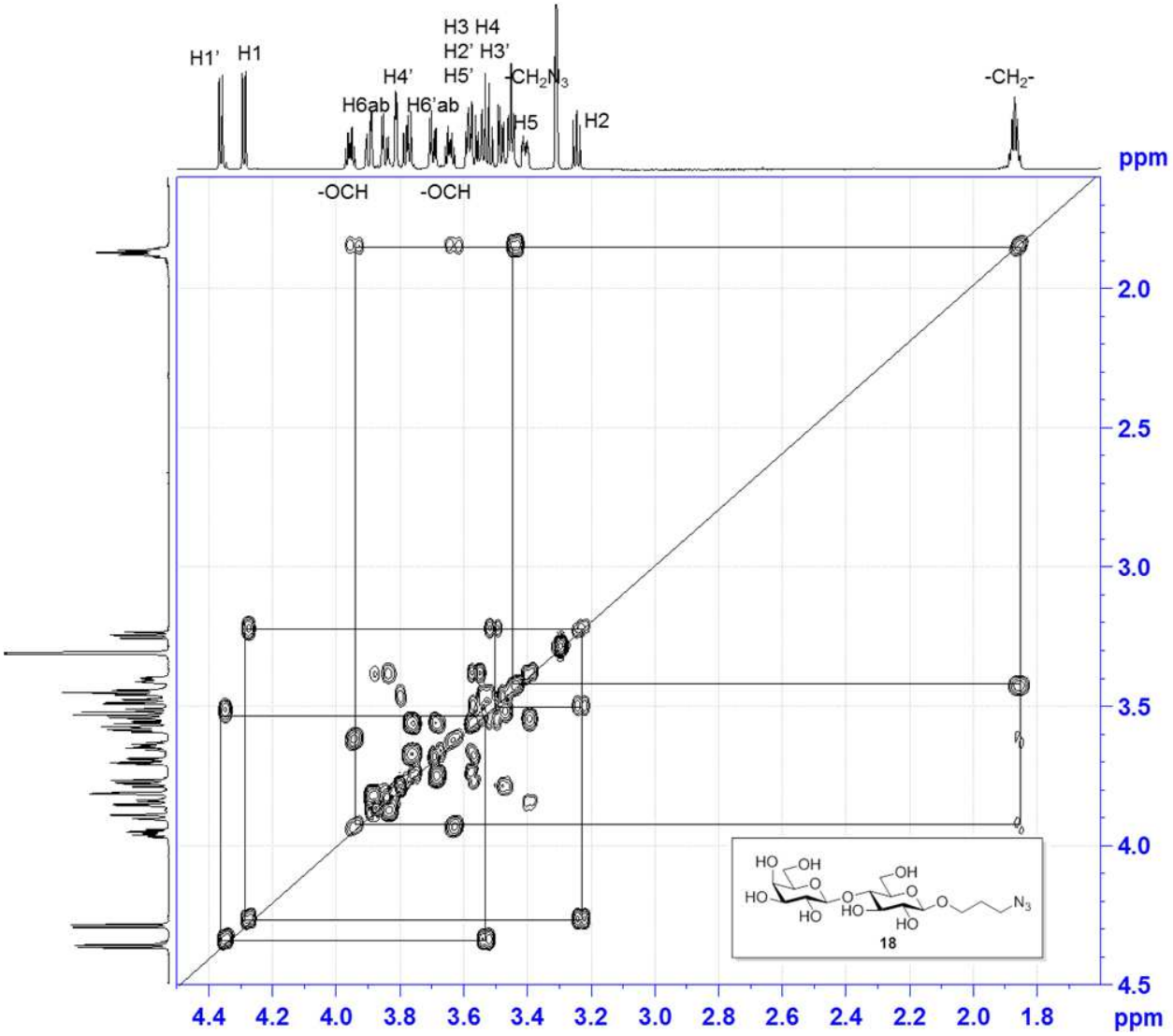
^{1}H-^{13}C HSQC spectrum of compound **17** ($CDCl_3$, 600 MHz)



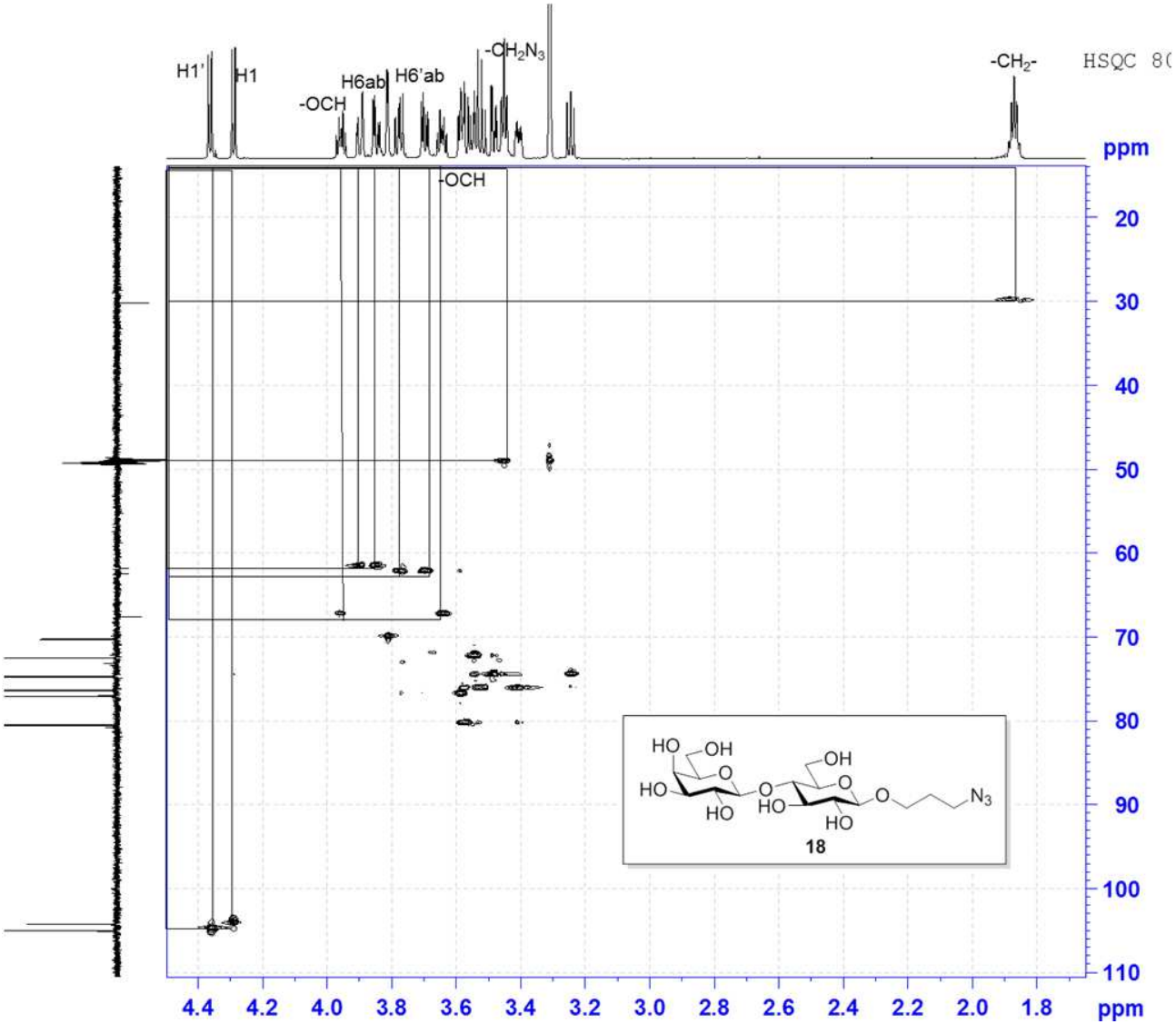
^{1}H NMR spectrum of compound **18** (CD_3OD, 800 MHz)



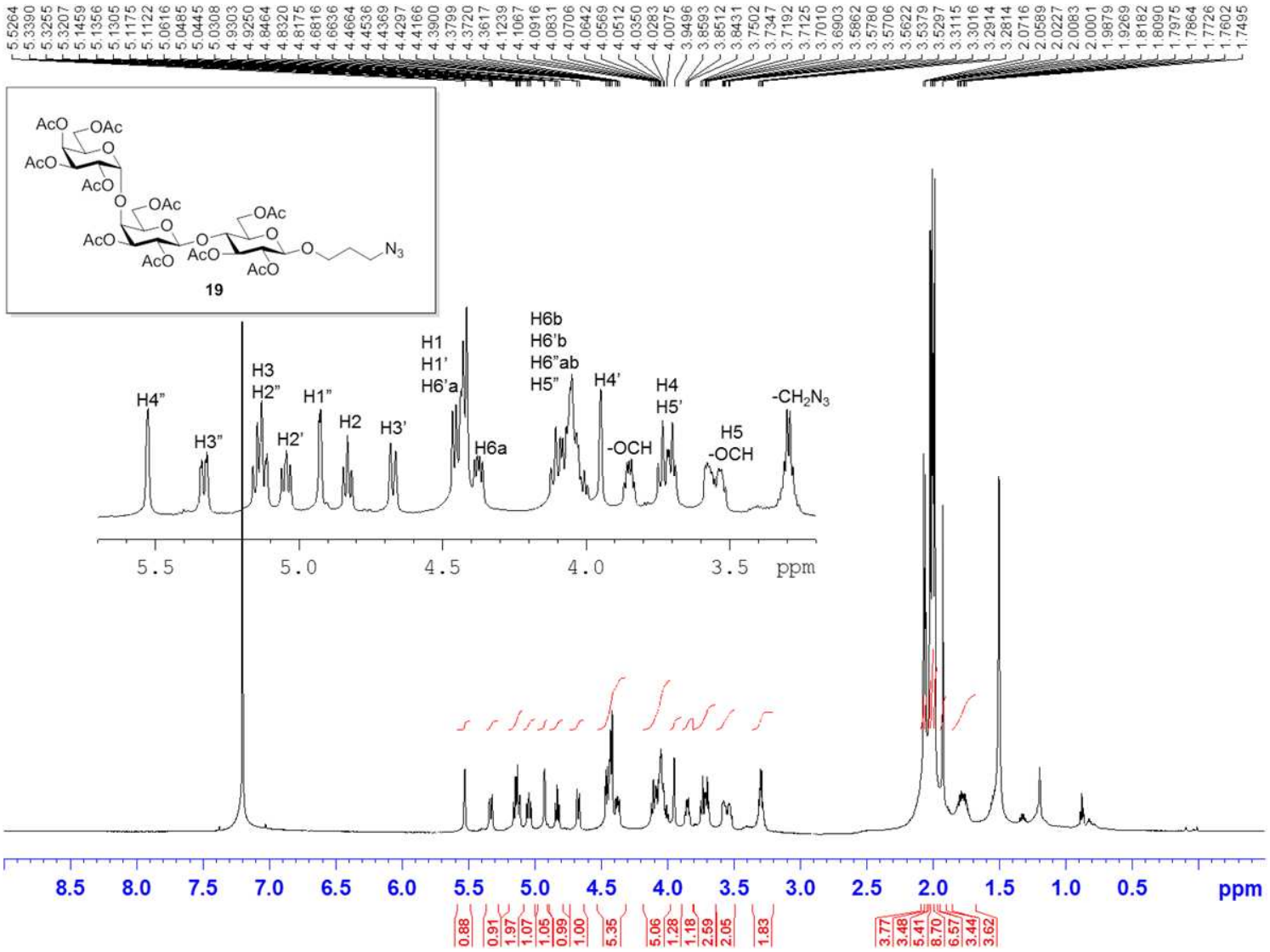
^{13}C and DEPT135 NMR spectrum of compound **18** (CD_3OD, 200 MHz)



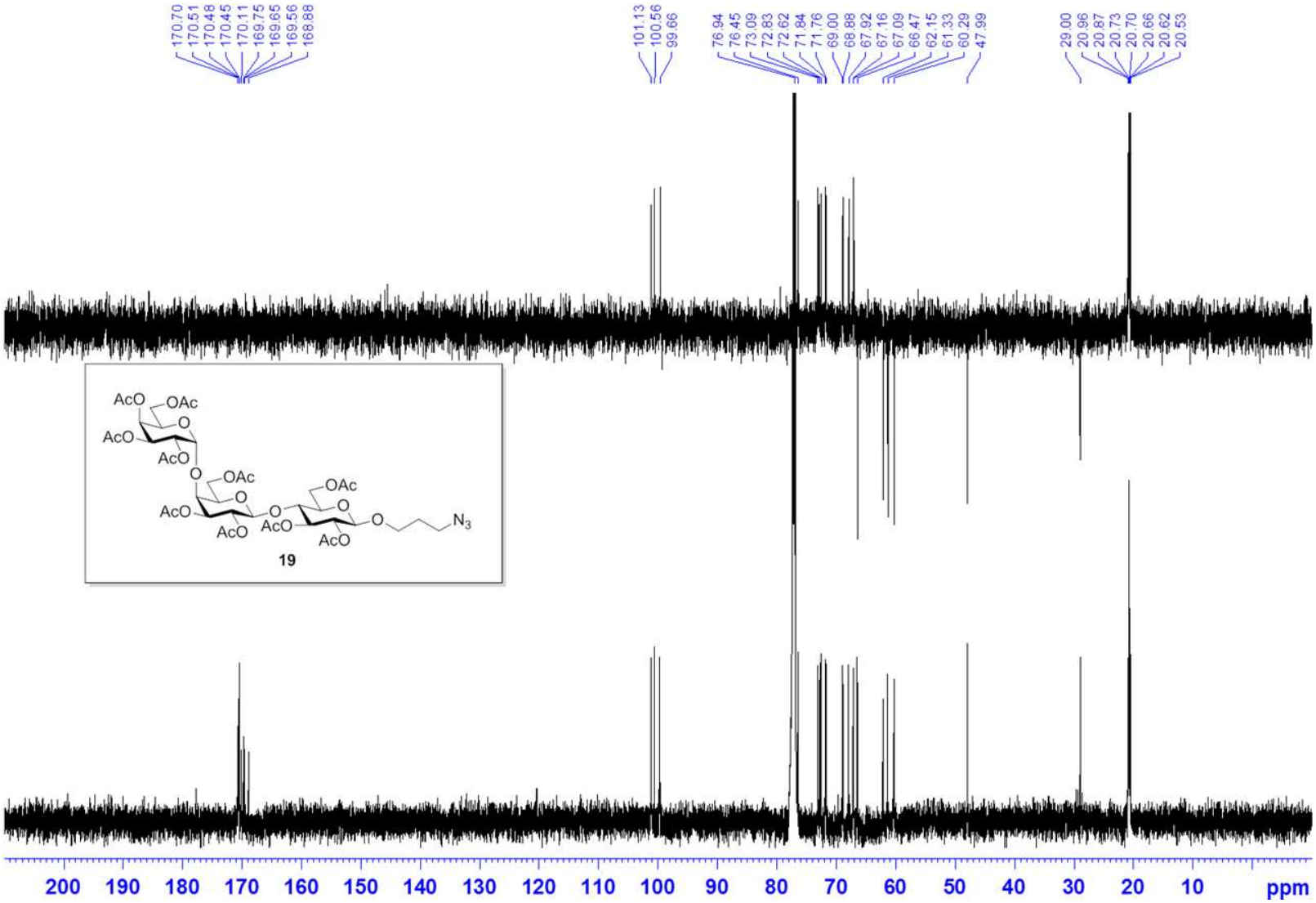
^{1}H-^{1}H COSY spectrum of compound **18** (CD_3OD, 800 MHz)



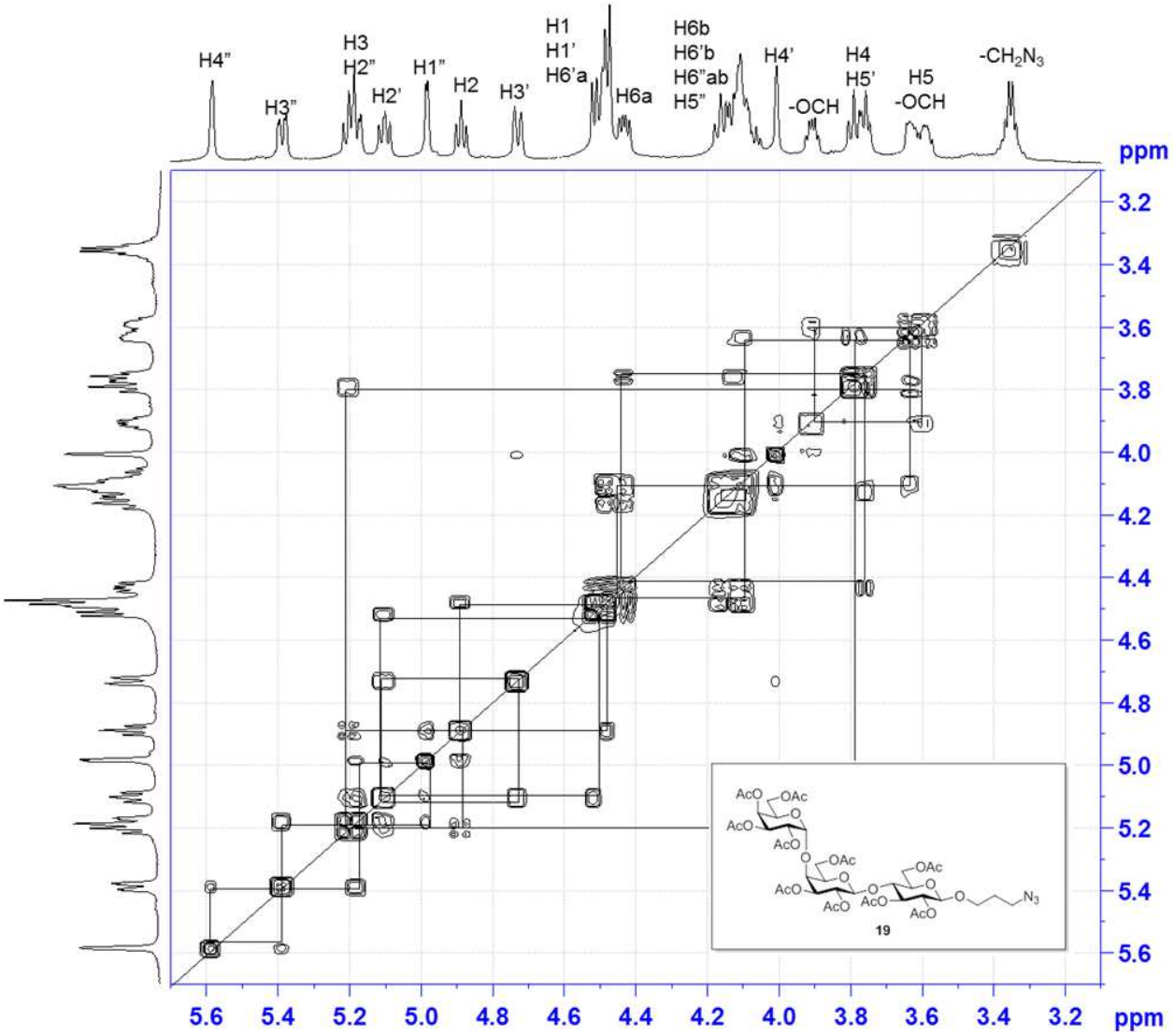
^{1}H-^{13}C HSQC spectrum of compound **18** (CD_3OD, 800 MHz)



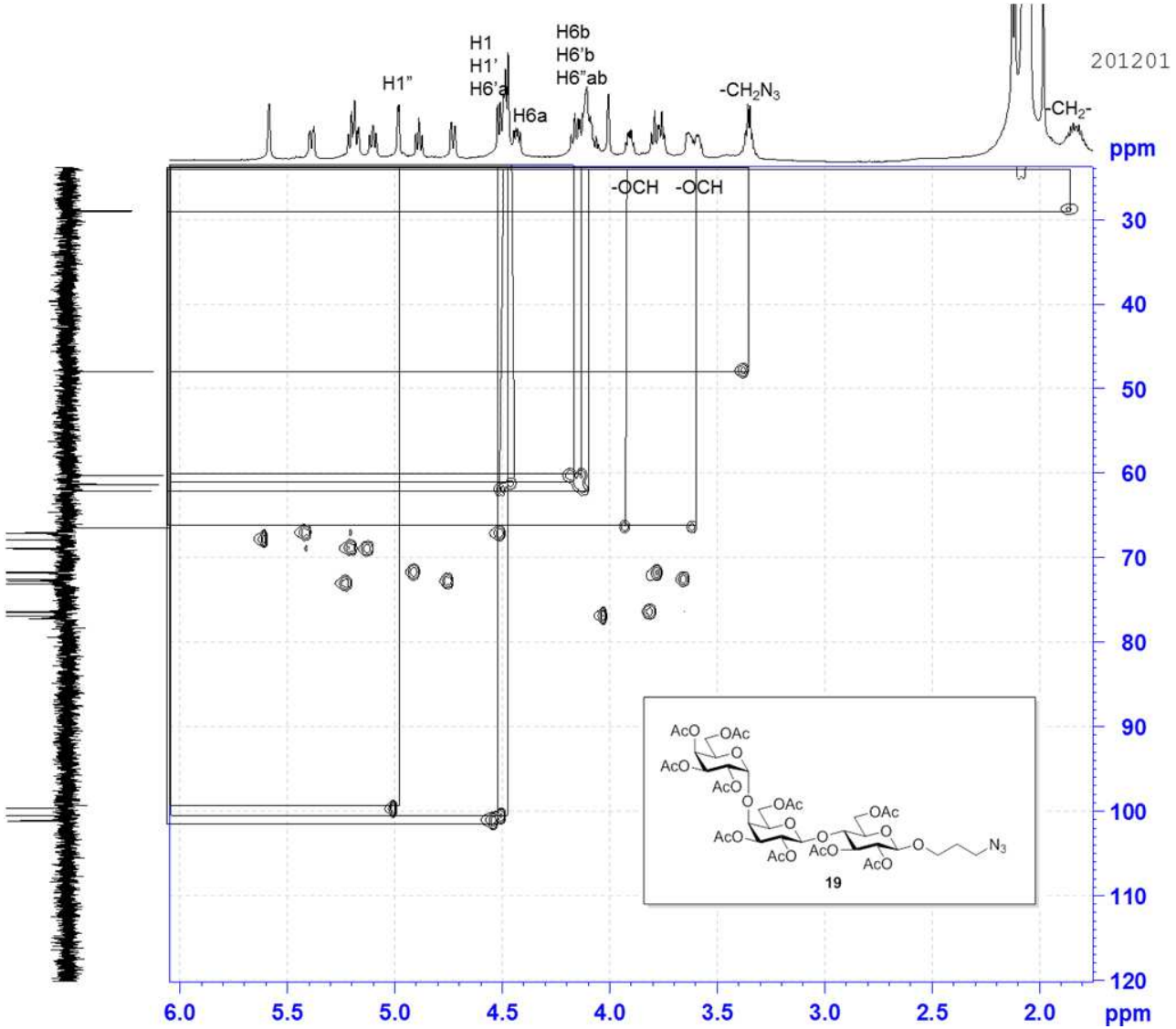
^{1}H NMR spectrum of compound **19** ($CDCl_3$, 600 MHz)



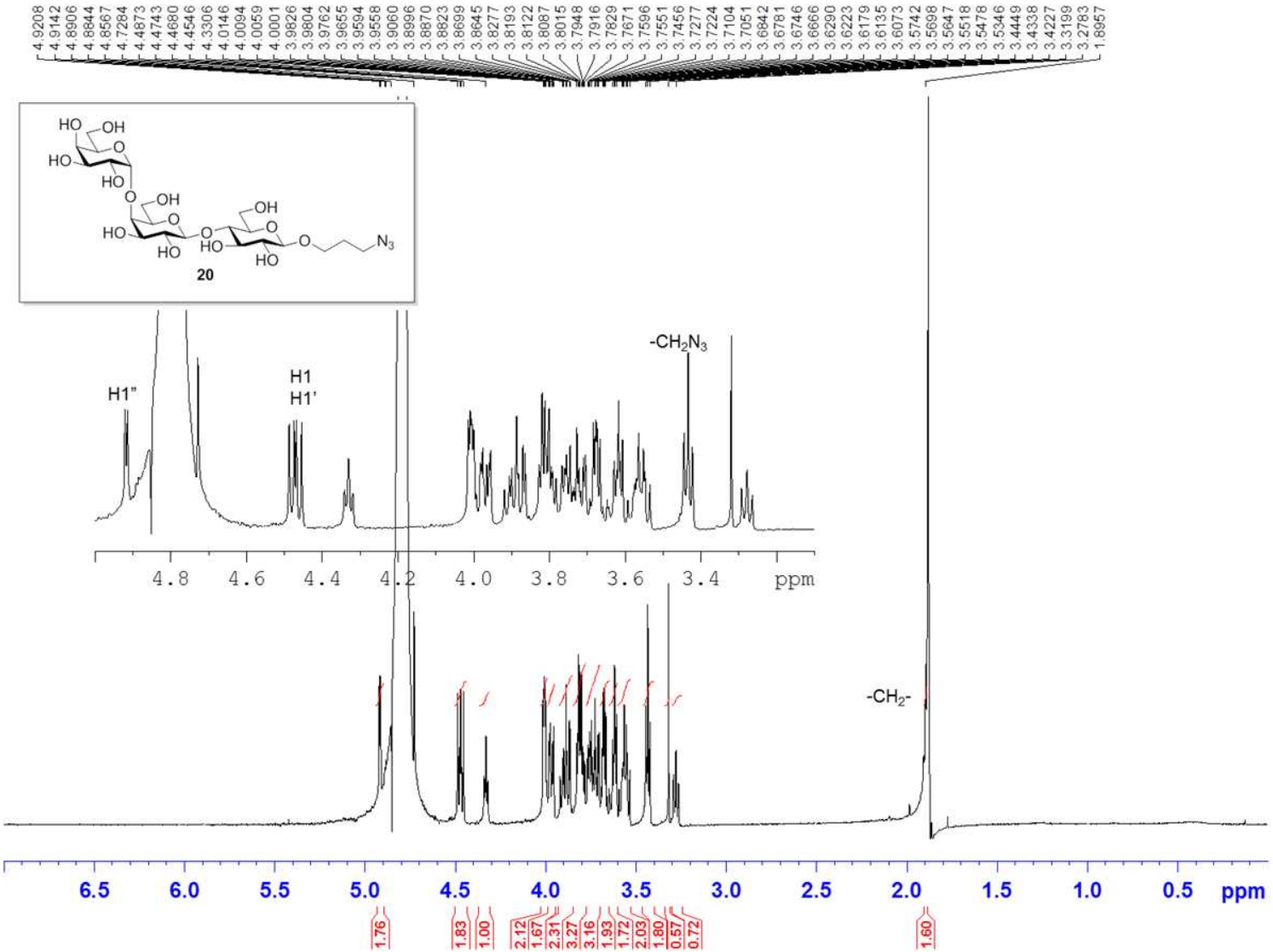
^{13}C and DEPT135 NMR spectrum of compound **19** ($CDCl_3$, 150 MHz)



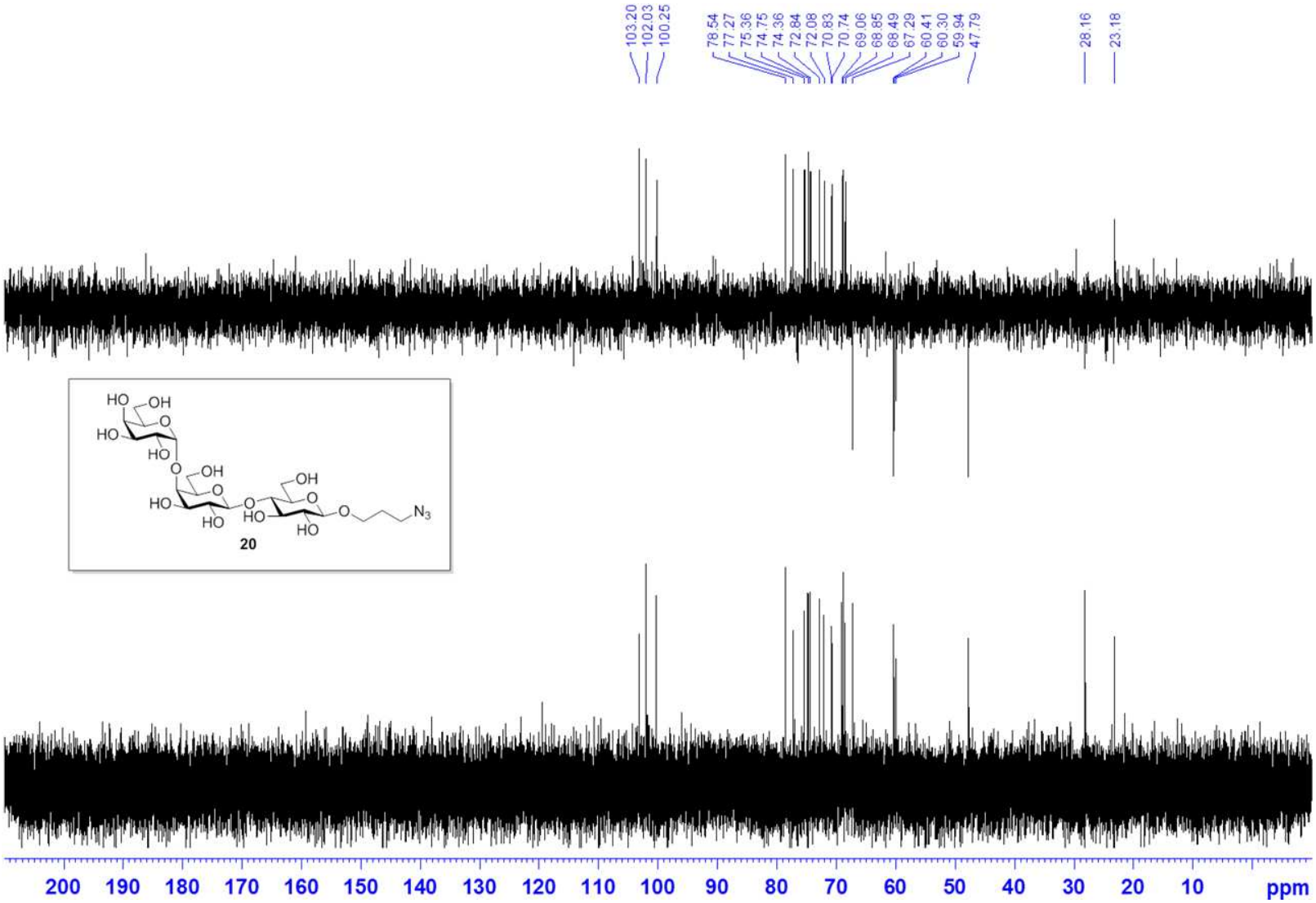
^{1}H-^{1}H COSY spectrum of compound **19** ($CDCl_3$, 600 MHz)



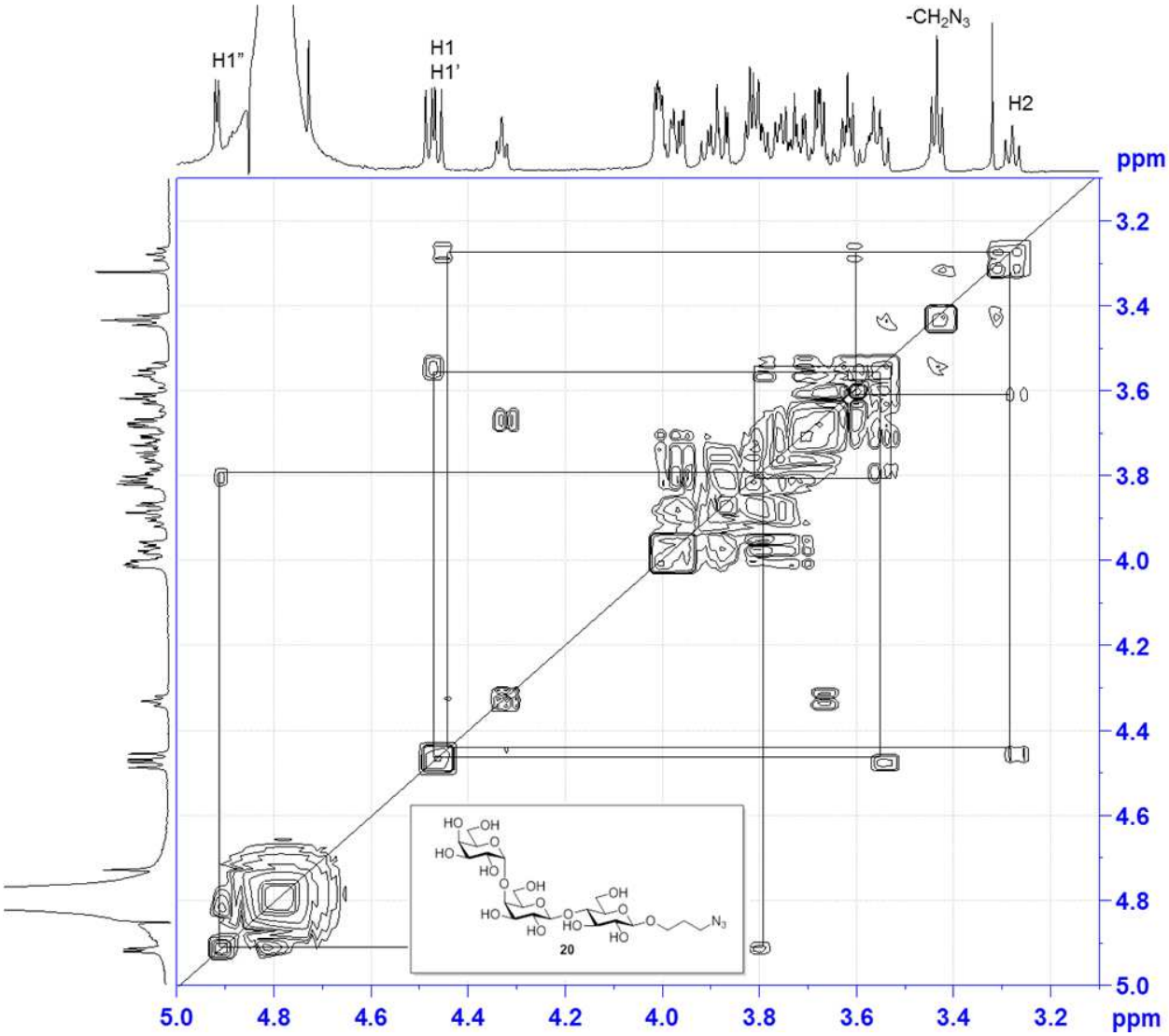
^{1}H-^{13}C HSQC spectrum of compound **19** ($CDCl_3$, 600 MHz)



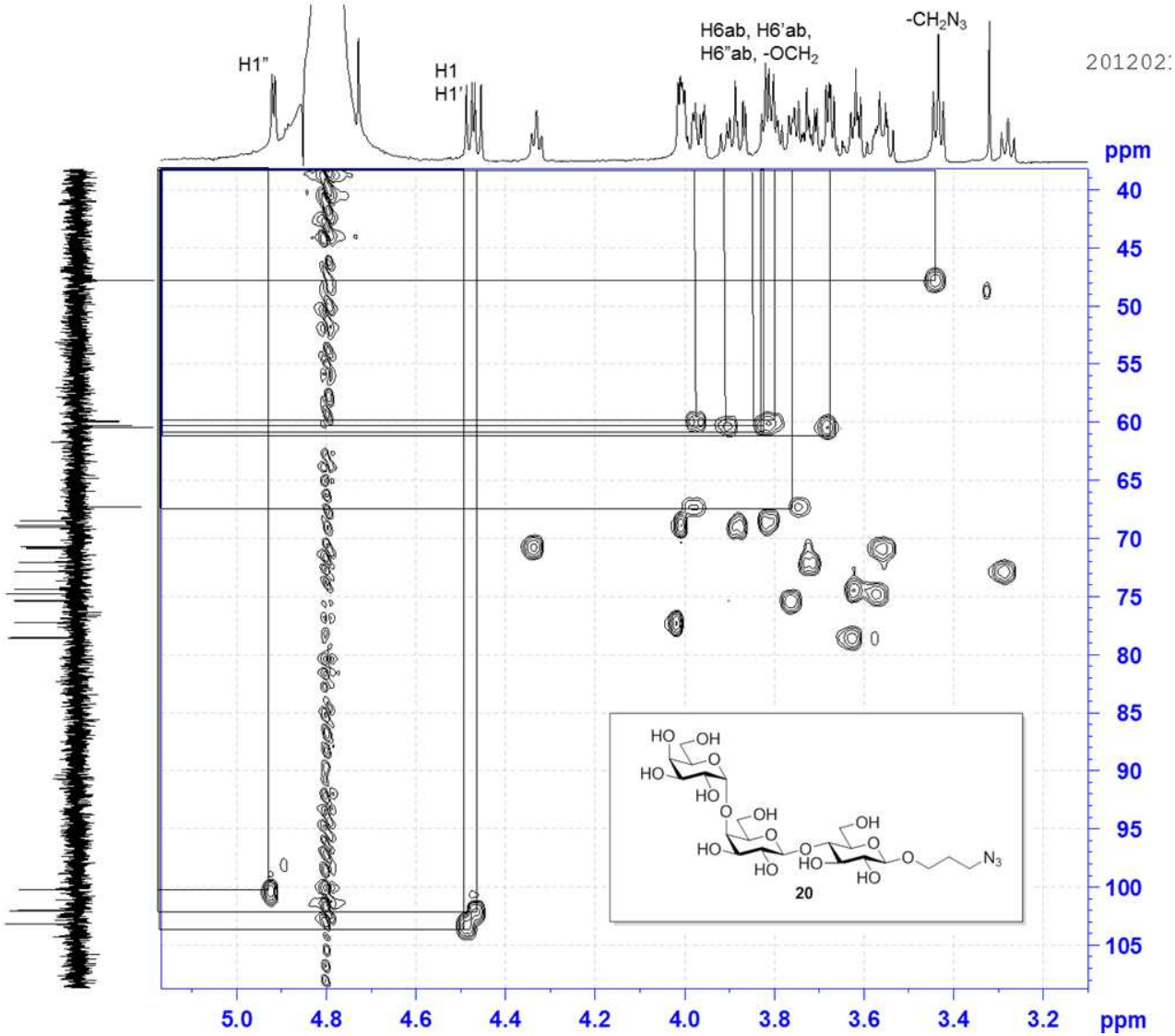
^{1}H NMR spectrum of compound **20** (D_2O, 600 MHz)



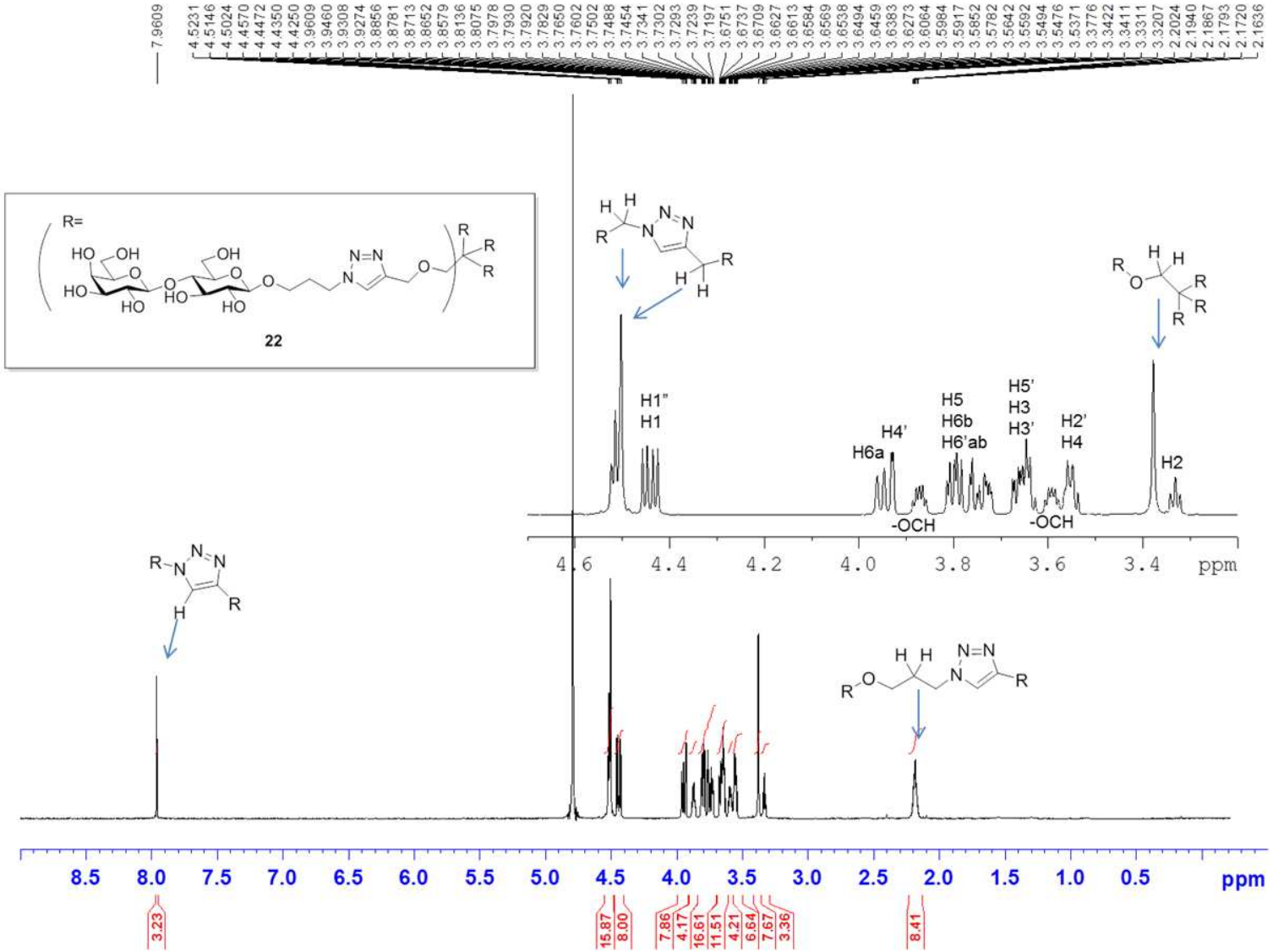
^{13}C and DEPT135 NMR spectrum of compound **20** (D_2O, 200 MHz)



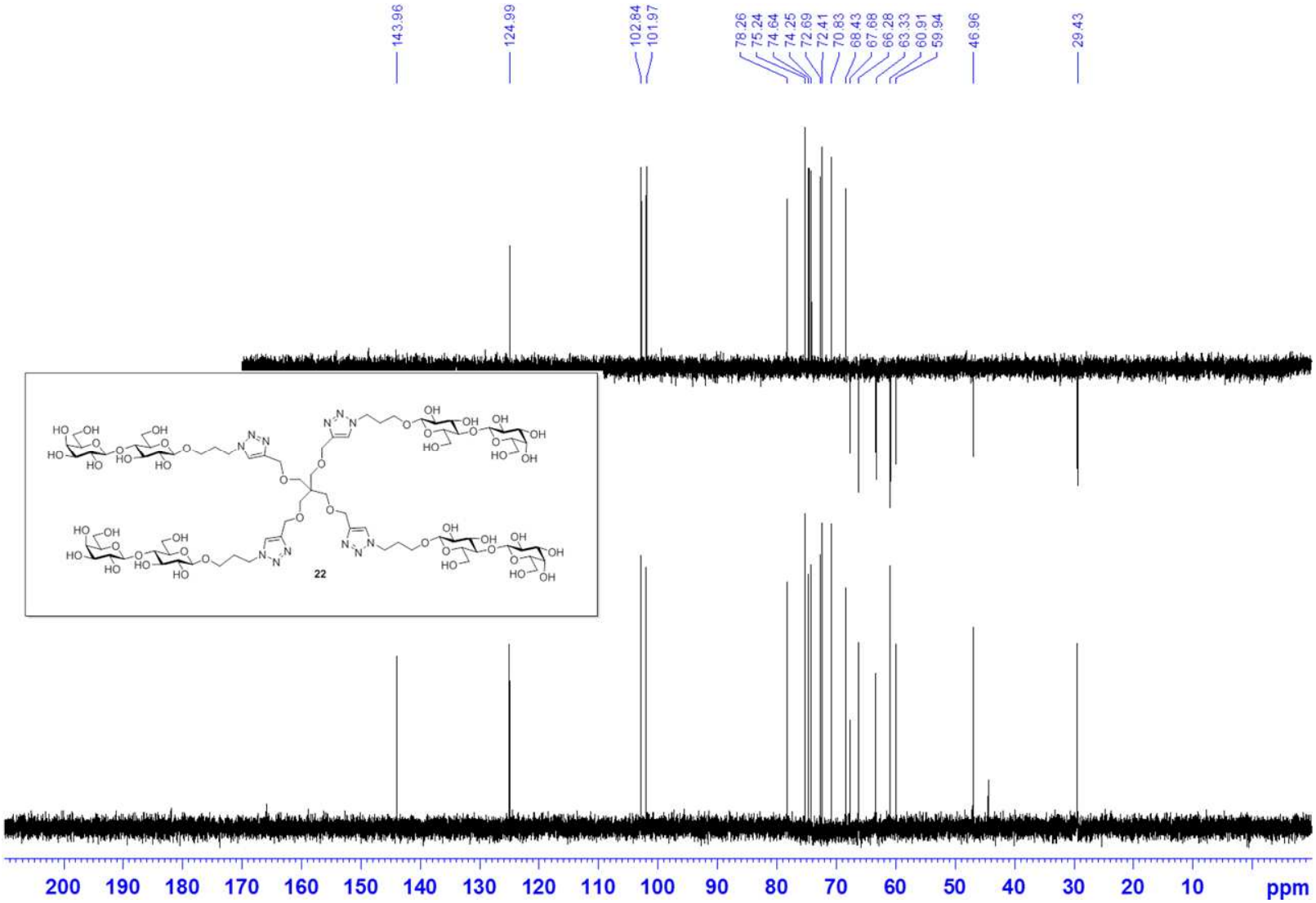
^{1}H-^{1}H COSY spectrum of compound **20** (D_2O, 800 MHz)



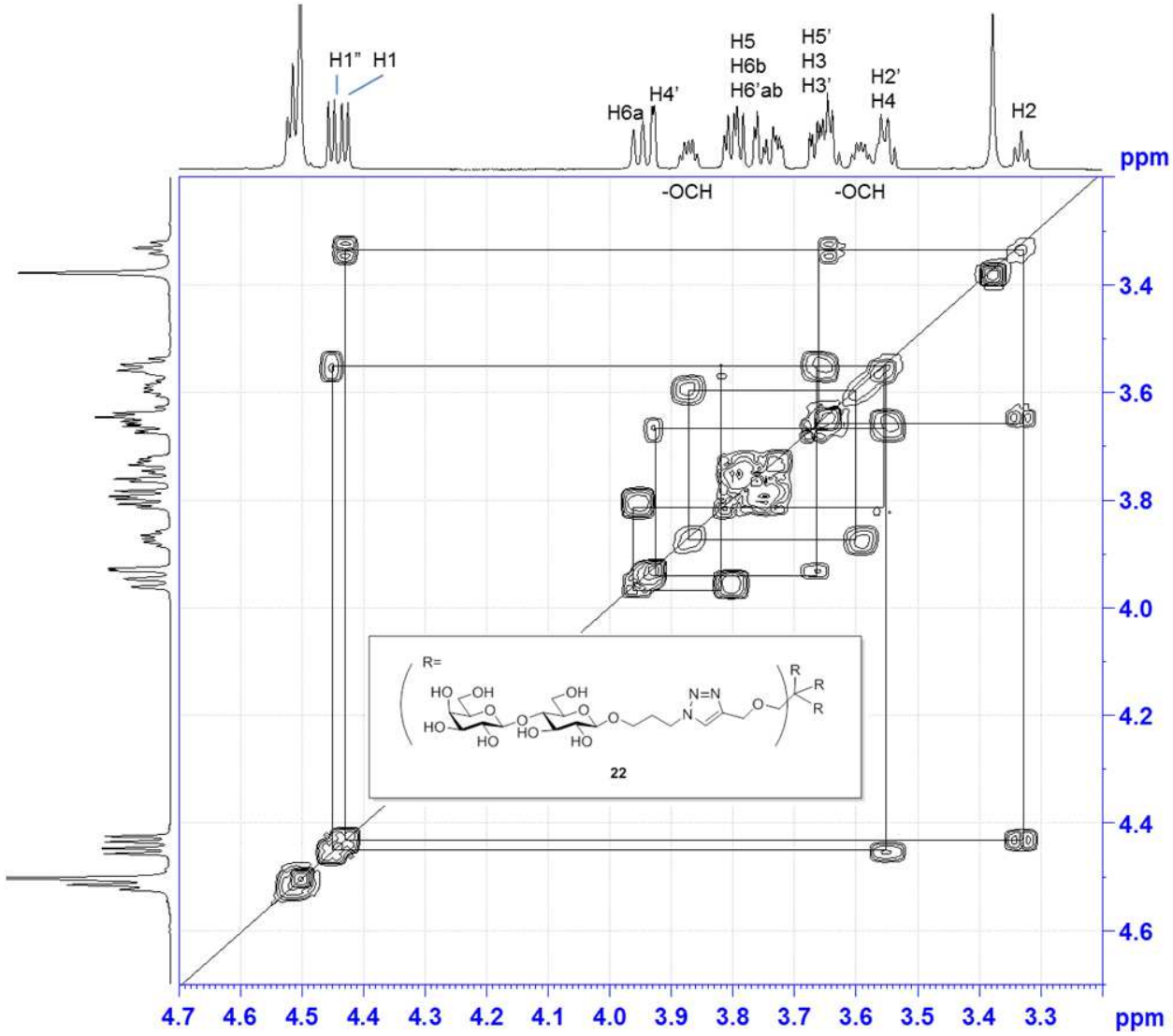
^{1}H-^{13}C HSQC spectrum of compound **20** (D_2O, 800 MHz)



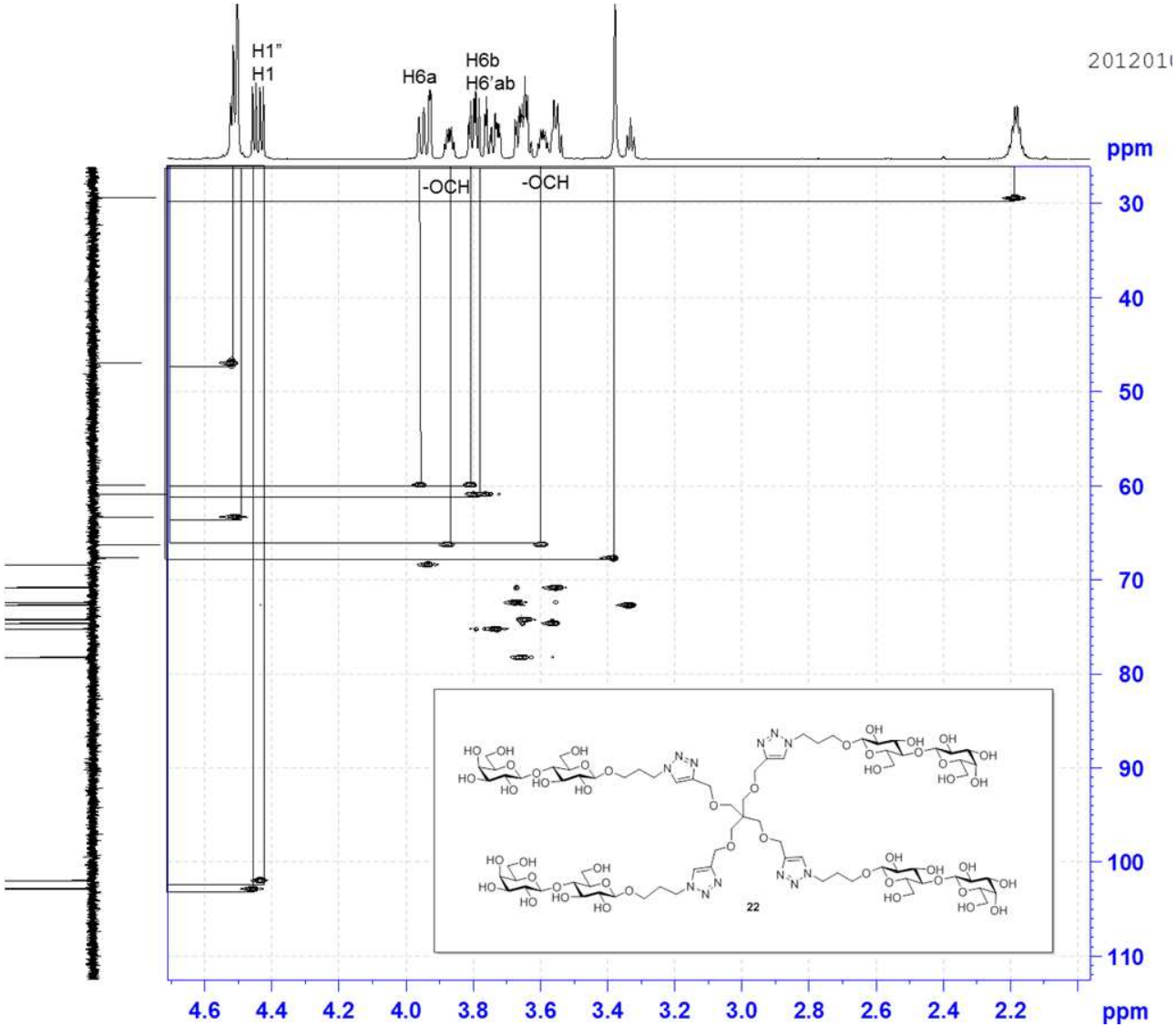
^{1}H NMR spectrum of compound **22** (D_2O, 800 MHz)



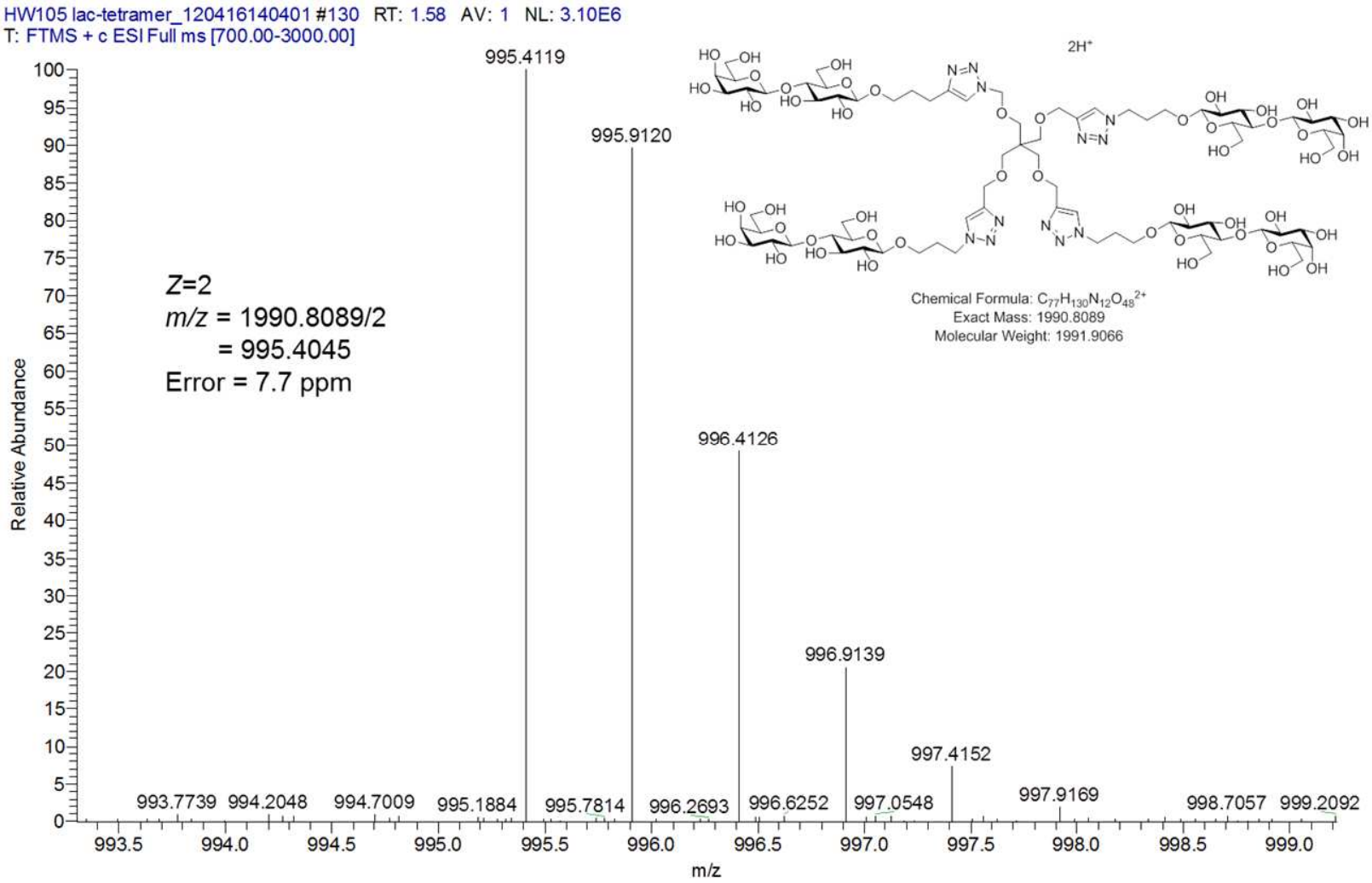
^{13}C and DEPT135 NMR spectrum of compound **22** ($CDCl_3$, 200 MHz)



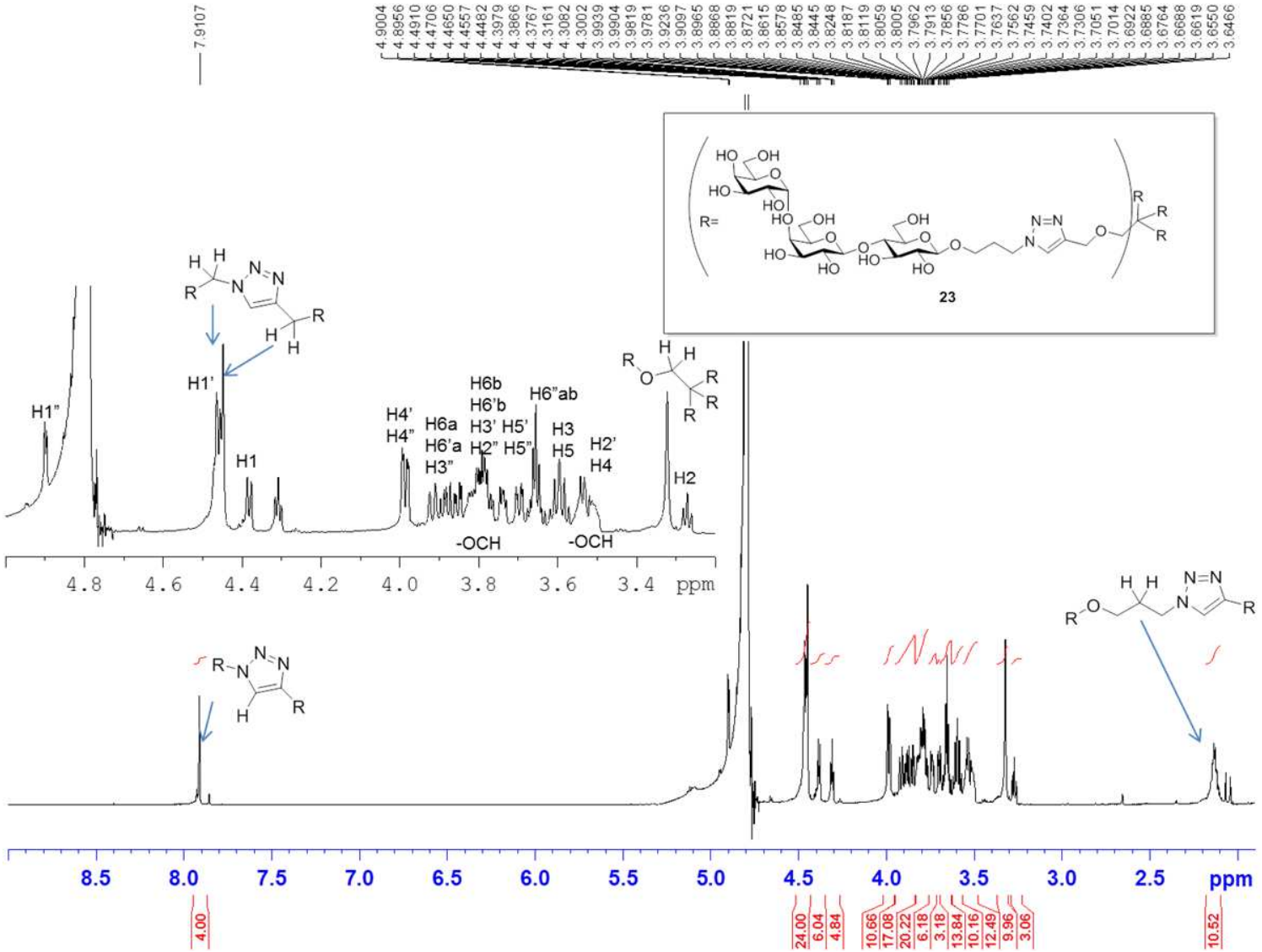
^{1}H-^{1}H COSY spectrum of compound **22** ($CDCl_3$, 800 MHz)



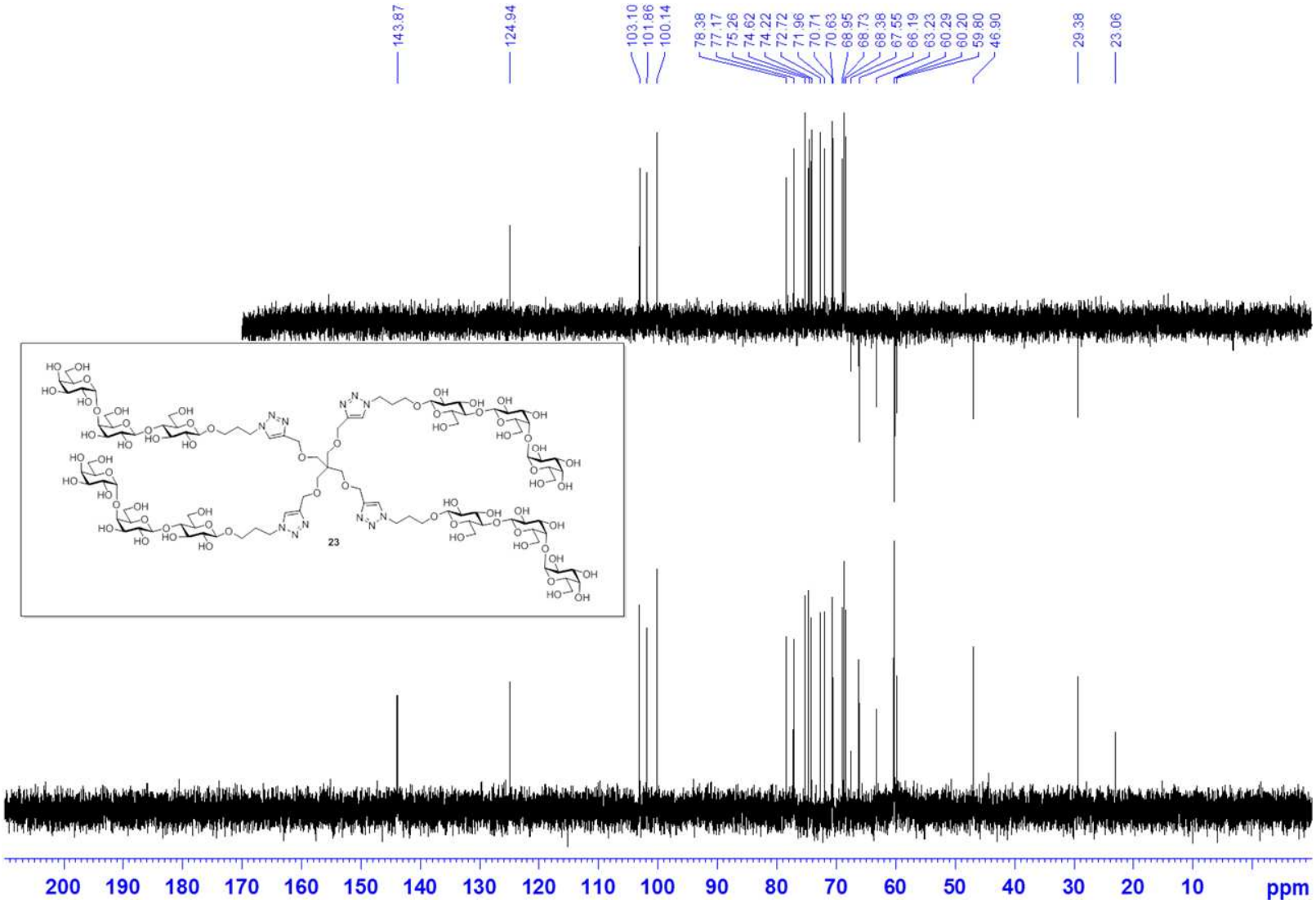
^{1}H-^{13}C HSQC spectrum of compound **22** ($CDCl_3$, 800 MHz)



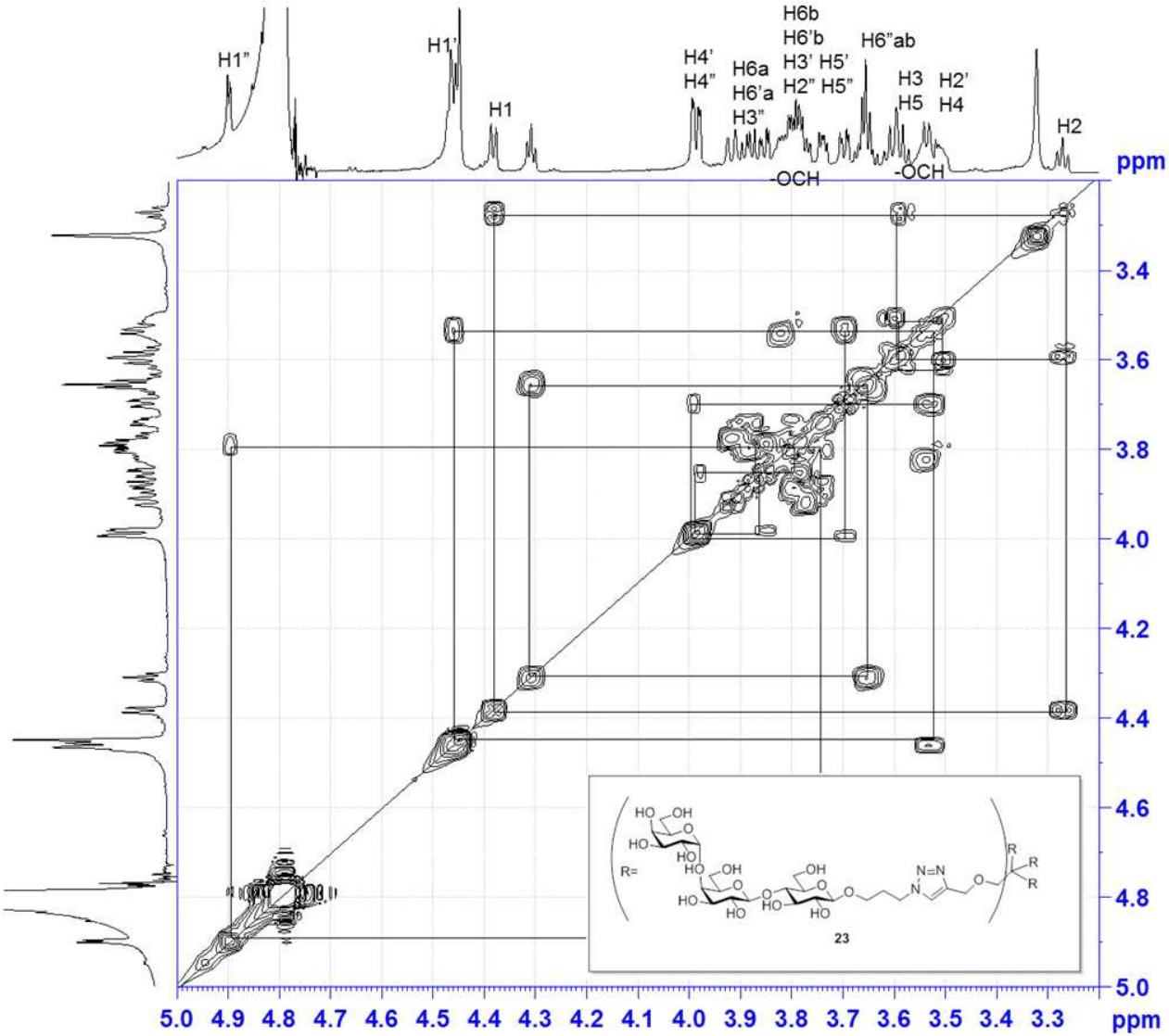
ESI-HRMS of compound **22**



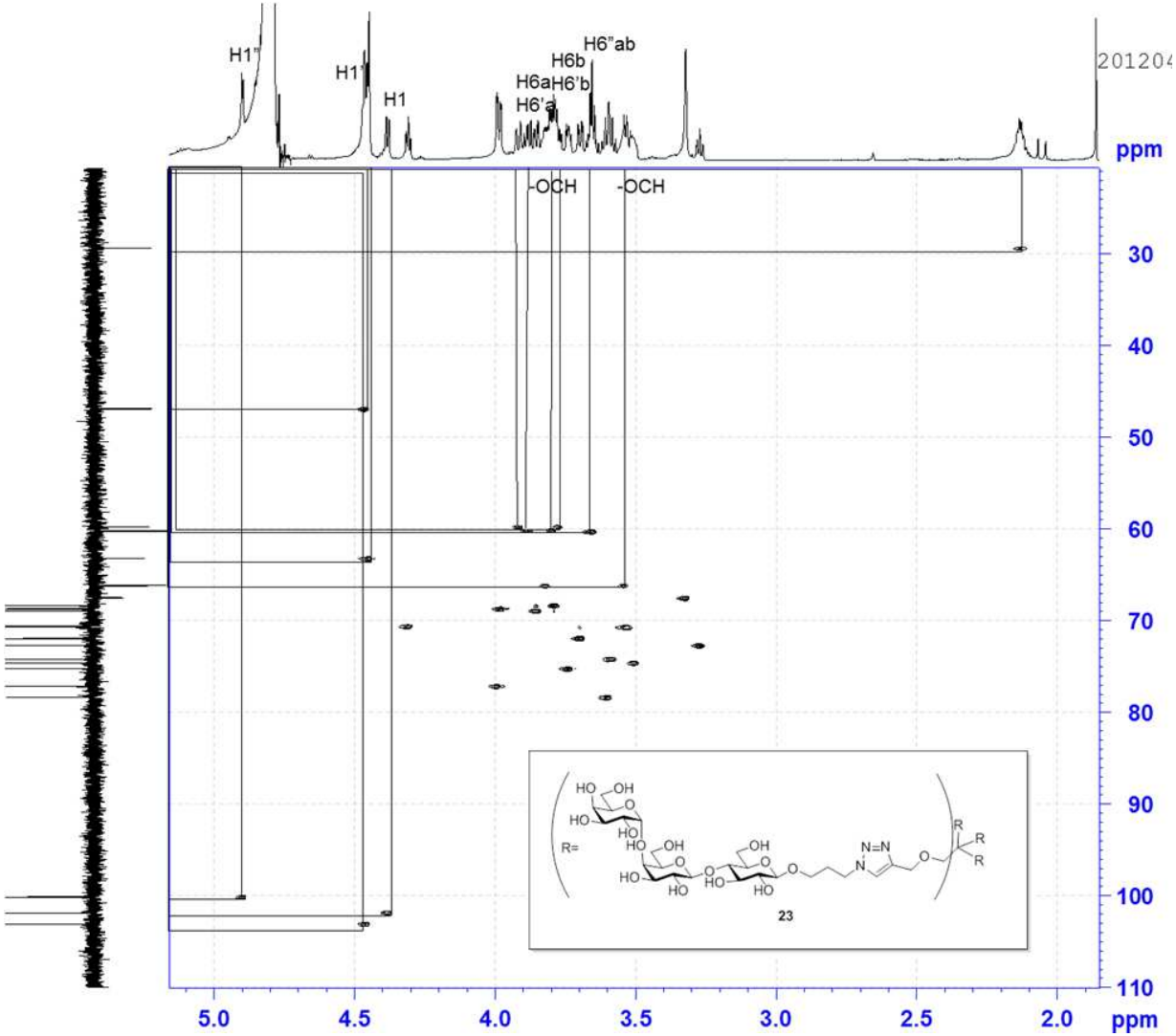
^{1}H NMR spectrum of compound **23** (D_2O, 800 MHz)



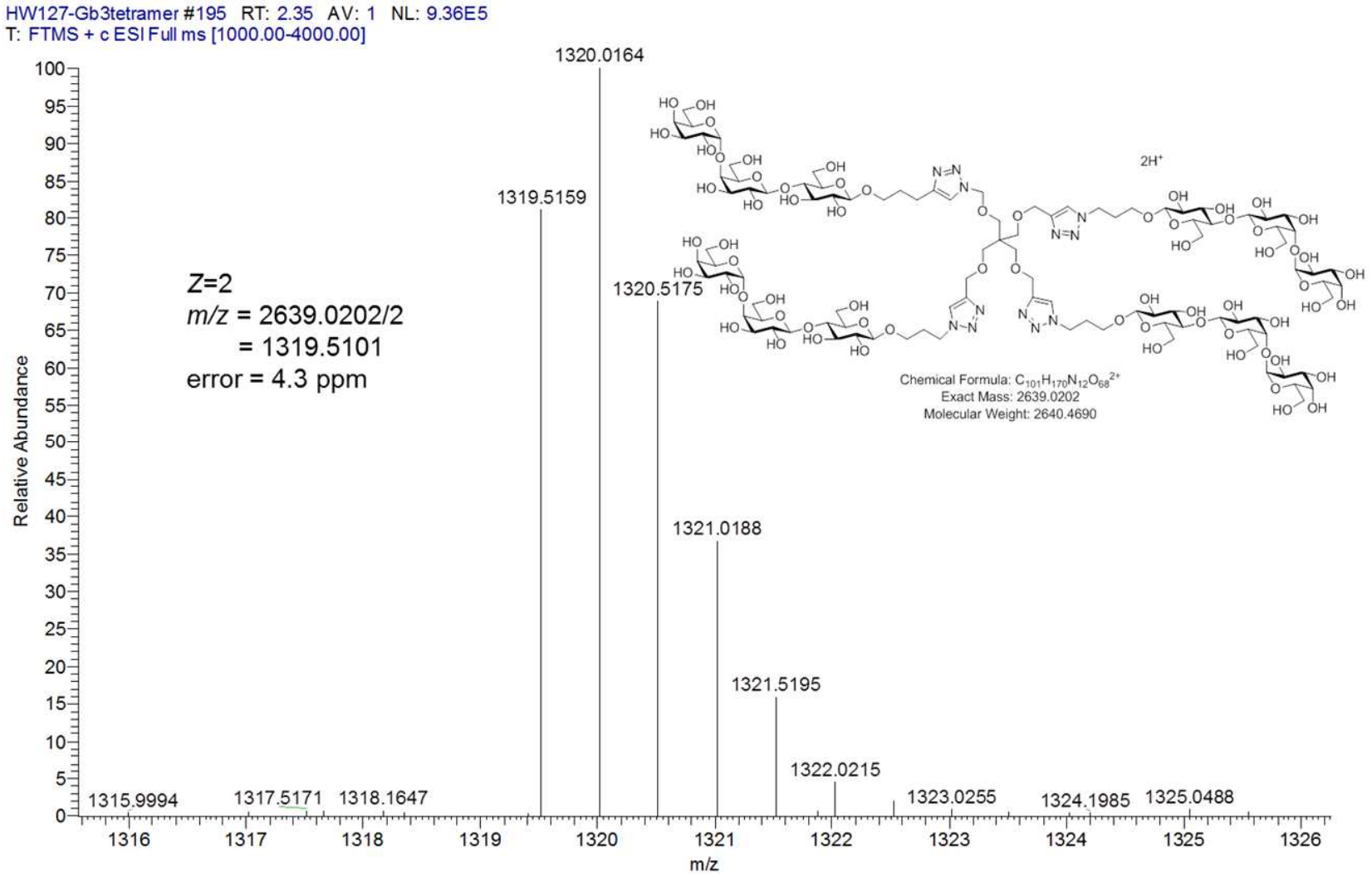
^{13}C and DEPT135 NMR spectrum of compound **23** (D_2O, 200 MHz)



^{1}H-^{1}H COSY spectrum of compound **23** (D_2O, 800 MHz)



^{1}H-^{13}C HSQC spectrum of compound **23** (D_2O, 800 MHz)



ESI-HRMS spectrum of compound **23**