Accepted Manuscript

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PII: S0040-4020(14)00855-2

DOI: 10.1016/j.tet.2014.06.009

Reference: TET 25674

To appear in: *Tetrahedron*

Received Date: 17 February 2014

Revised Date: 22 May 2014

Accepted Date: 2 June 2014

Please cite this article as: Gilmutdinova AA, Gubskaya VP, Fazleeva GM, Latypov SK, Zhelonkina TA, Sharafutdinova DR, Nuretdinov IA, Sinyashin OG, Synthesis and properties of new fullerene c_{60} derivatives, containing acetonide and polyol fragments, *Tetrahedron* (2014), doi: 10.1016/j.tet.2014.06.009.

SYNTHESIS AND PROPERTIES OF NEW FULLERENE C_{60} DERIVATIVES, CONTAINING ACETONIDE AND POLYOL FRAGMENTS.

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New mono- and hexa-methanofullerenes containing different number of acetonide groups are synthesised and characterized. Removing the acetonide protection leads to new chromatographically pure water-soluble polyol methanofullerenes with essentially quantitative yields.

Keywords: hexa-methanofullerenes, acetonide protection, Bingel-Hirsch reaction, water-soluble polyol methanofullerenes

Introduction

Prospects of successful application of fullerene C_{60} derivatives in biology and medicine are substantially defined by possibility of getting their water-soluble forms. A variety of fullerene C_{60} derivatives, possessing satisfactory solubility in polar solvents, including water-soluble ones has been synthesized.[1-3] Solubility of the fullerene functional derivatives in water is defined by the presence of a great number of hydrophilic groups. The overwhelming majority of fullerene water-soluble derivatives are represented by the compounds containing hydroxyl, carboxyl and amino groups.[4,5] One of the most water-soluble derivatives of fullerene C60 (240 mg/ml) is the new malonodiserinolamide polysubstituted methanofullerene obtained by the authors via a new synthetic methodology, which consists of initial protection alcohol groups by ester groups.[4] Subsequent deprotection leads to a non-ionic, highly water-soluble derivative of C60, however it is necessary to notice, that it is not an individual compound, but a mixture of tetra-, penta- and hexa-products in the ratio 15:80:5.

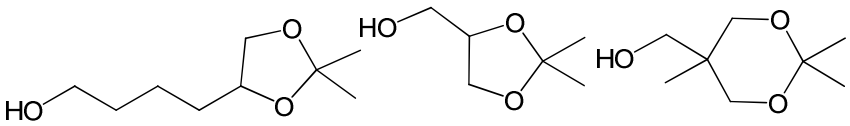
Fullerenols (polyhydroxylated fullerenes) $C_{60}(OH)_n$, being of simple structure and possessing the possibility of further functionalization, also belong to the series of water-soluble fullerene derivatives. For a long time they were considered as the most appropriate representatives of water-soluble fullerenes for the study of biological activity. However, depending on the method of synthesis, fullerenols have various compositions, differing by the number of hydroxyl groups (from 12 to 24), and, respectively, by solubility in water.[5-8] Individually isolated tris-dicarboxymethanofullerenes possess good solubility in water and have antiviral effects.[9-11]

In an alternative approach, high solubility in water (> 200 mg/ml) is achieved at the expense of using the phosphorylated groups on the fullerene sphere, obtained from intermediate pentaphosphonic ethers, with their further hydrolysis.[12]

We believe that the approach, based on obtaining fullerene derivatives with protected hydroxyl groups followed by deprotection seems to be suitable, and suggest to use for these purposes acetonide protection, which can be easily removed in mild conditions. In this work the results of research including the development of the methods of synthesis and the study of the properties of new water-soluble chromatographically-pure fullerene derivatives, containing from 4 to 24 hydroxyl groups per molecule is reported.

Results and discussion

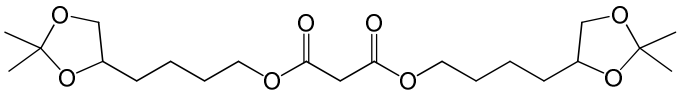
Acetonide derivatives **1, 2, 3** (their yields being 90%, 86%, 61%, respectively) were obtained by reacting triols (1,1,6-hexanetriol, 1,2,3-propanetriol and 1,2,3-tris-oxymethylethane) with acetone at the boiling temperature of the former, with catalytic amounts of para-toluenesulfonic acid, their structures being proved by spectral methods.[13]



1 **2** **3**

The obtained compounds are precursors for the synthesis of malonate derivatives, containing acetonide fragments at different distances from the ester group. Malonate derivative **4-6** were then

obtained by reaction of acetonide derivatives **1-3** with malonyldichloride in the presence of NaH or Et_3N in absolute benzene.



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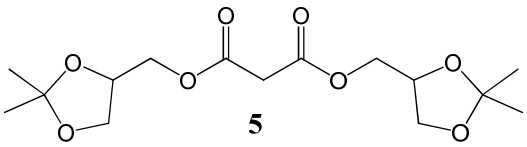

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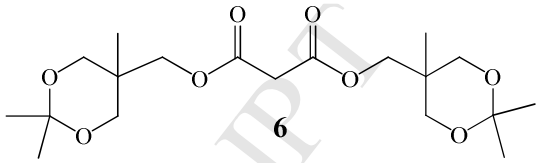

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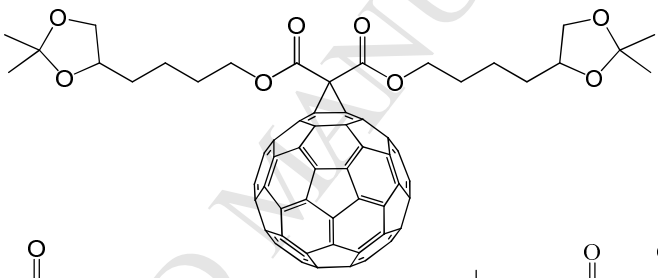
New malonate fullerene derivatives **7-9**, containing acetonide groups, were then synthesized by interaction of fullerene C_{60} with initial precursors **4-6** under Bingel-Hirsch reaction conditions.[14, 15]



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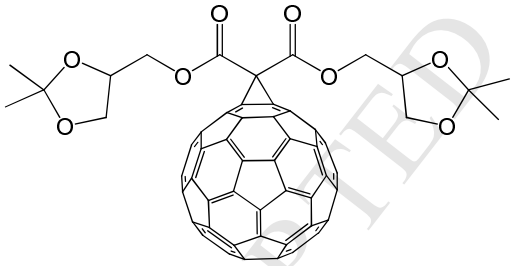

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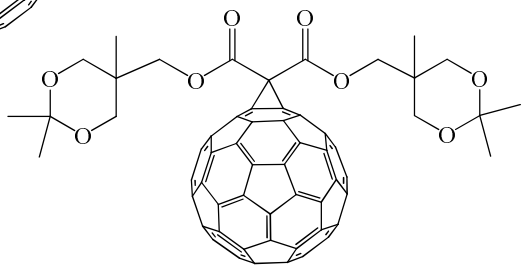


9

The structures and purities of compounds **7-9** were confirmed by the data from spectroscopic methods, mass spectrometry, and HPLC. The UV spectra of compounds **7-9** have absorption bands at 258, 268, 328, and 426 nm typical of virtually all methanofullerenes. The structures of almost all the title compounds were unambiguously established by a variety of NMR correlation methods. Namely, combination of homo- and heteronuclear correlation experiments[16, 17] (see ESI) allows one to get the connection between nuclei starting from the ends of addends up to C_{61} carbons in most of the cases (*vide infra* e.g. for **7**). Then ^{13}C data analysis allows making final conclusion about the structure of fullerene derivatives.

For example, ^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC and HMBC connectivity allows discrimination of addends moiety of **7** (Figure 1) up to C_{61} (52.3 ppm). Most of the fullerene C_{60} cage carbons resonate at low fields but there is also one singlet at sp^3 region (δ = 71.6 ppm) that proves the closed [6,6]-type of the addend linkage. As a whole, the number of peaks observed for compound **7** in the range 138-146 ppm is due to the 58 sp^2-carbons of the C60 sphere, consistent with the C_s symmetry of its molecular structure.

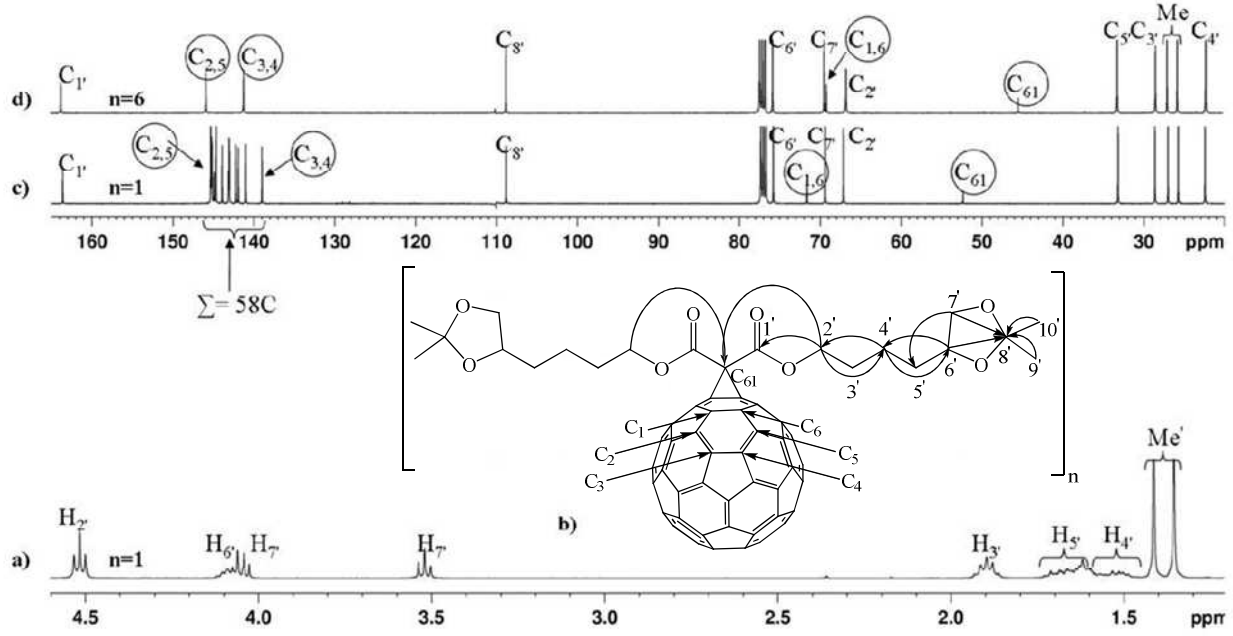


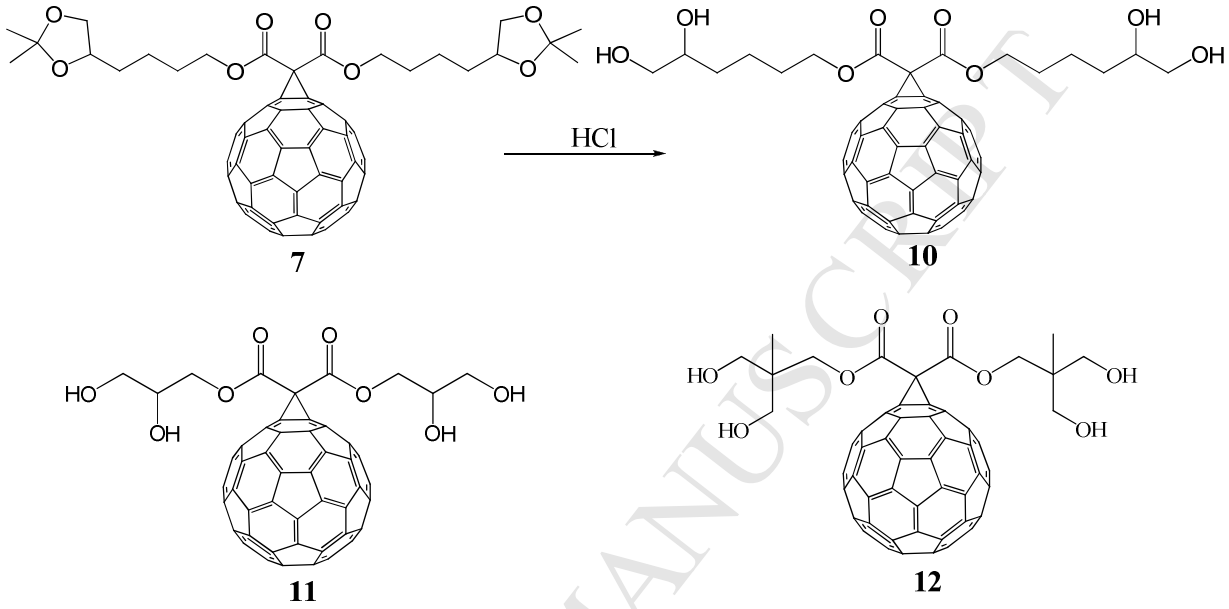
Figure 1. NMR spectra of compounds **7** (a-^{1}H, c-^{13}C) and **13** (d-^{13}C) in $CDCl_3$ at 303K and structure of **7** (**13**) with diagnostic HMBC NMR correlations (b).

Having developed the methods for synthesis of new target fullerene derivatives with protecting groups, we approached the main goal of the present work which is obtaining the fullerene derivatives containing hydroxyl groups by removing the protecting groups.

Acetonide protection in the synthesized compoundds is easily removed by treating them with hydrochloric acid (Scheme 2). In a typical experiment, hydrochloric acid (0.27 mmol) was added to the initial methanofullerene **7** (0.27 mmol), and the reaction mixture was kept in the dark for 24 hours. At the end of the reaction, the initially wine-red toluene solution of compound **7**

became colorless, and compound **10** precipitated, then it was filtered and washed with toluene and acetonitrile. The yield of compound **10** was 80%.

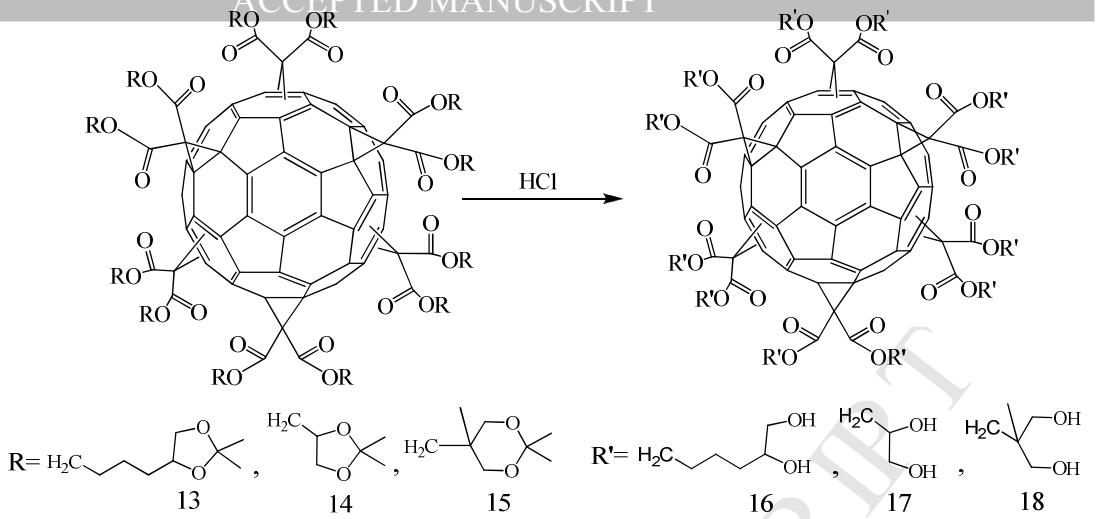
Removal of acenonide protection from compounds **8** and **9** similarly resulted in the formation of compounds **11, 12** (Scheme 1) with yields of 92% and 81%, correspondingly.



Scheme 1.

The solubility of the obtained methanofullerenes **10-12** in polar solvents including water was studied. Monomethanofullerenes C_{60} **10-12** were shown to dissolve well in DMSO/water (1:9) solution, but were insoluble in water with various pH values (5-9).

To increase the solubility of the fullerene derivatives in polar solvents (DMSO, ethanol, water) we synthesized hexa-adducts **13–15** on the basis of malonate precursors **4-6** (Scheme 2) using the methods described in literature.[18-21]



Scheme 2.

For example, to obtain compound **13** we carried out the reaction of fullerene C_{60} (0.3 g, 0.42 mmol), bis(2.2-dimethyl-1.3 –dioxalane-4-O-buthyl) malonate (1.73 g, 4.2 mmol), CBr_4 (13.83 g, 42 mmol) with DBU (1.27 g, 8.3 mmol) in o-DCB. The reaction mixture was stirred at room temperature for 72 hours, and purified by column chromatography to yield pure compound **13** (156 mg, yield 11.7 %).

The structure of compounds **13-15** was proved by spectroscopic methods (IR, UV, NMR), and the composition was proved by MALDI TOF mass-spectrometry. The mass spectrum of compound **13** contains the peak corresponding to the molecular ion $[M]^+$ 3204.34 (calc. 3204).

Results of NMR experiments strongly support the structures of these hexa-adducts of [60]fullerene. First, from variety of NMR correlations the structures of adducts itself up to the C_{61} can be unequivocally determined (e.g. for **13** see Figure 1d). In ^{13}C NMR spectra (Figure 1d) there are only two signals of equal intensity with δ = 141.1 (24C) and δ = 145.7 ppm (24C) corresponding to sp^2 carbons and only one line (ca. two times less in intensity) with δ = 69.1 ppm (12C) attributed to sp^3 carbons of the C_{60} sphere, and as such it can be concluded that the structure of **13** is consistent with high symmetry (T_h).

Finally, deprotected hexa-adducts **16-18** were obtained by removing the acetonide protection from the hexa-adducts **13-15** using the method described earlier for methanofullerenes **10-12.**

The structure of compounds **16-18** was also proved by NMR ^{13}C and ^{1}H spectroscopy, while their composition was confirmed by mass-spectrometry. The mass-spectrum of compound **17** contains the peak corresponding to the $[M+Na]^+$= 2243.3 (Fig. 2). The experimental value of the isotopic distribution $[M+Na]^+$ fully corresponds to the theoretical one (insert on Fig.2). The ^{13}C NMR spectrum of compound **16** does not contain the signals from the carbons of acetonide fragment methyl groups (25 and 27 ppm), as well as the NMR proton spectrum does not contain the signals from the protons of the mentioned groups. Thus compounds **16-18** have the same symmetry (T_h) as the precursors **13-15**.

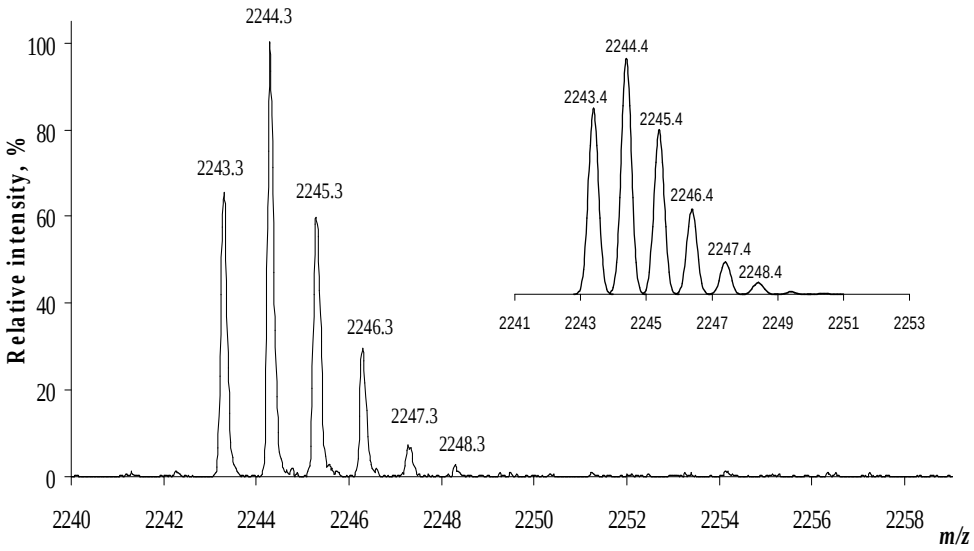


Figure 2. Mass-spectrum for compound **17** $[M+Na]^+$, **insert** –theoretical isotopic distribution $[M+Na]^+$.

The solubility of the obtained polyol methanofullerenes in polar solvents including water was studied. Methanofullerenes containing 24 hydroxy groups dissolved well not only in DMSO-water (1:9) and ethanol, but also in water with pH= 5, 7 and 9. Hexa-adduct **17**, synthesized on the basis of glycerol, demonstrated the best solubility, while increasing the length of the methylene chain in compound **16** resulted in significant decrease of its solubility in polar solvents and water (Table 1).

Table 1. Solubility of compounds **16-18** in water**.**

Compound	Solubility, mg/ml			
	DMSO-water (1:9)	pH=5 ascorbic acid/water (2 mg/ml)	pH=9 Tris(oxy-methyl-amino-methane (1 mg/ml)	pH=7 (physiol. solution) 0,9% NaCl solution
16	100 mg/ml	5 mg/ml	15 mg/ml	-
17	500 mg/ml	10 mg/ml	35 mg/ml	75 mg/ml
18	250 mg/ml	5 mg/ml	30 mg/ml	75 mg/ml

Conclusion

Thus, the target synthesis of new mono- and hexa-methanofullerenes, containing different numbers of acetonide groups (from 2 to 12), was realized by the Bingel-Hirsch reaction, their chemical structures being proved using multiple spectroscopic methods. New chromatographically pure polyol methanofullerenes, containing 4 and 24 hydroxyl groups, were obtained and their structures and properties studied. All the hexa-adducts were shown to be well-soluble in various polar solvents including water. This opens the way to obtaining new derivatives based on fullerenes, containing various functional groups, responsible for manifestation of biological activity, by reacting the free hydroxyl groups.

Experimental

HPLC-analysis was performed using Agilent Technologies 1200 Series using UV-detector with the column with reversed phase C18 (Partisil-5 ODS-3), eluent being toluene/CH_3CN (volume ratio 1:1). Organic solvents were dried and distilled before use. Fullerene C_{60} of 99.9% purity was used (produced by «Fullerene-Center», Nizhny Novgorod). All the chemical reactions were performed in dry argon atmosphere. UV-spectra were recorded on spectrophotometer Specord M-40 in methylene chloride, IR-spectra were recorded on Fourier-spectrometer «Bruker-Vector 22» (tablet with KBr). NMR spectra were registered on NMR spectrometer Avance-600 (Bruker) (600 MHz (^{1}H) and 150 MHz (^{13}C)) at the temperature 30ºC in $CDCl_3$, the residual signal from $CDCl_3$ (δ_H 7.26 ppm and δ_C 77.0 ppm) being used as an internal standard. The structure of compounds was

established on the basis of a series of 1D and 2D NMR correlation experiments (DEPT, ^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC). MALDI mass spectra were recorded on mass-spectrometer ULTRAFLEX III (Bruker Daltonik GmbH, Bremen, Germany) in linear regime, with p-nitroaniline being used as a matrix. Mass-spectra contain the peaks corresponding to the protonated molecular $[M+H]^+$ ion along with frequently present $[M+Na]^+$ and $[M+K]^+$ ions.

4-(2, 2-Dimethyl-1, 3-dioxolane-4-yl)-1-butanol **(1)**

A solution of 1,2,6-hexanetryol (22.2 g) in distilled acetone (100 ml) with a catalytic amount of p-toluenesulfonic acid was boiled for 7 h. Then the reaction mixture was cooled and just calcined potash (100 g) was added. After 12 hours, potash was filtered, and the filtrate was steamed in vacuum using a water-jet pump. The residue was distilled at T=109-110°C (1 mm Hg). Compound **1** (19.5 g) with 68% yield was obtained. [Found:C, 62.02; H, 10.24. $C_9H_{18}O_3$ requires: C, 62.07; H, 10.43%]. IR-spectrum, (liquid film), ν/m^{-1}: 514, 647, 739, 791, 856, 893, 1058, 1157, 1216, 1248, 1325, 1370, 1435, 1457, 3424. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.35 (3H, s, CH_3), 1.40 (3H, s, CH_3), 1.50-1.65 (6H, m, CH_2), 3.51 (1H, dd, *J*= 7.5 Hz, *J*= 7.5 Hz, CH), 3.65 (2H, t, *J*=6.5 Hz, OCH_2), 4.02 (1H, dd, *J*= 7.5 Hz, *J*= 6.0 Hz, CH), 4.03-4.10 (1H, m, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ 108.65, 75.95, 69.36, 62.52, 33.20, 32.47, 26.87, 25.65, 21.98.

(2, 2-Dimethyl-1, 3-dioxolan-4-yl)-1-methanol **(2).**

Compound **2** was synthesized analogously to **1**. The residue was distilled at T=54-55°C (1 mm Hg). As a result compound **2** (12.4 g) was obtained with the yield of 39 %. [Found: C, 54.15; H, 9.64. $C_6H_{13}O_3$ requires: C, 54.3; H, 9.9%]. IR-spectrum, (liquid film), ν/cm^{-1}: 516, 567, 653, 792, 844, 970, 1052, 1074, 1119, 1157, 1214, 1256, 1372, 1457, 3458. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.33 (3H, s, CH_3), 1.40 (3H, s, CH_3), 3.57 (1H, dd, *J*= 5.2 Hz, *J*= 11.9 Hz, CH_2), 3.69 (1H, dd, *J*= 4.1 Hz, *J*= 11.9 Hz, CH_2), 3.76 (1H, dd, *J*= 6.4 Hz, *J*= 8.1 Hz, CH_2), 4.01 (1H, dd, *J*= 6.7 Hz, *J*= 8.1 Hz, CH_2), 4.17.4.24 (1H, m, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ 109.33, 76.12, 65.69, 62.95, 26.61, 25.18.

(2, 2, 5-Trimethyl-1, 3-dioxan-5-yl)methanol **(3).**

Compound **3** was synthesized similarly to **1**. Residue was distilled at T= 80°C (1 mm Hg). Compound **3 (**12.8 g) was obtained with 58 % yield. After the distillation the product crystallized, T_{melt}= 29 °C. [Found:C, 59.65; H, 10.24. $C_8H_{16}O_3$ requires: C, 59.92; H, 10.07 %].IR spectrum, (KBr),ν/cm^{-1}: 521, 562, 679, 731, 790, 829, 912, 933, 989, 1046, 1086, 1153, 1208, 1264, 1349, 1375, 1456, 3441. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.79 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.40 (3H, s,

CH_3), 3.47 (1H, d, *J*= 11.7 Hz, CH_2), 3.61 (1H, s, CH_2), 3.70 (1H, d, *J*= 11.7 Hz, CH_2); ^{13}C NMR (150 MHz, $CDCl_3$): δ98.50, 66.91, 66.22, 35.40, 27.91, 21.14, 18.22.

Bis (2, 2-dimethyl-1, 3-dioxolan 4-O-butyl) malonate **(4).**

To a suspension of NaH (1.38 g, 0.057 mol) in absolute benzene (100 ml) in the flow of dry argon at room temperature 2,2–dimethyl-1,3-dioxolane-4-butanol (10 g, 0.057 mol) was added dropwise. The reaction mixture was stirred at room temperature for 1 h. Having cooled the mixture to a temperature of 5 °C, malonyldichloride (4.05 g, 0.0287 mol) was slowly added dropwise. The mixture was stirred for 8 h and then decanted. The organic layer was evaporated in water-jet pump vacuum. The product was purified by column chromatography (silica gel, eluent: ethylacetate-hexane (3:1)). After column chromatography a viscous light oil was obtained (R_f = 0.54). The yield of pure product was 44% (5.1 g). Mass-spectrum (MALDI): $[M+K]^+$ 455.01 $C_{21}H_{36}O_8$. IR-spectrum (liquid film),ν/cm^{-1}: 514; 607; 739; 791; 856; 1060; 1097; 1158; 1216; 1331; 1370; 1413; 1458; 1733 (C=O); 2869; 2938; 2985. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.29 (6H, s, CH_3), 1.35 (6H, s, CH_3), 1.48-1.73 (12H, m, CH_2), 3.33 (2H, s, CH_2), 3.45 (2H, dd, *J*= 7.3 Hz, *J*= 7.3 Hz, CH_2), 3.98 (2H, dd, *J*= 7.3 Hz, *J*= 5.9 Hz, CH_2), 4.00-4.06 (2H, m, CH), 4.10 (4H, s, OCH_2), ^{13}C NMR (150 MHz, $CDCl_3$): δ166.52, 108.59, 75.64, 69.16, 65.19, 41.37, 32.94, 28.26, 26.75, 25.51, 21.97.

Bis (2, 2-dimethyl-1,3-dioxolane 4-O-methyl) malonate **(5).**

Compound **5** was synthesized from 2,2–dimethyl-1,3-dioxolane-4-methanol and malonyldichloride similarly to **4**. After column chromatography (silica gel, eluent: ethylacetate-hexane-ethanol (2.5:1:0.1)) viscous light oil was obtained with (R_f = 0.51). Pure product yield was 36% (0.9 g). Mass-spectrum (MALDI): $[M]^+$ 332.92 $C_{15}H_{24}O_8$. IR-spectrum (liquid film),ν/cm^{-1}: 511 , 552, 581, 670, 703, 788, 814, 852, 920, 958, 1057, 1096, 1156, 1185, 1205, 1231, 1266, 1316, 1366, 1376, 1427, 1454, 1539, 1644, 1741, 2930. ^{1}H NMR (600 MHz, $CDCl_3$): δ1.36 (6H, s, CH_3), 1.42 (6H, s, CH_3), 3.46 (2H, s, CH_2), 3.75 (2H, dd, *J*= 5.8 Hz, *J*= 8.4 Hz, CH_2), 4.07 (2H, dd, *J*= 6.7 Hz, *J*= 8.4 Hz, CH_2), 4.12-4.28 (4H, m, OCH_2), 4.28-4.36 (2H, m, CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.04, 109.90, 73.27, 66.21, 65.68, 41.08, 26.64, 25.29.

Bis (2, 2, 5-trimethyl-1, 3 –dioxane-5-methyl-O-methyl) malonate (**6).**

To a solution of pentaglyceric semiacetal (1.4 g, 0.0117 mol) and triethylamine (1.18 g, 0.0117 mol) in 50 ml of absolute benzene at 5°C malonyldichloride (0.82 g, 0.0058 mol) was added

dropwise. The reaction mixture was stirred for 8 h. The formed precipitate $Et_3N{\cdot}HCl$ was filtered (its weight being 1.3 g), and filtrate was evaporated in the water-jet pump vacuum. The product was purified by column chromatography on silica gel (eluent was benzene-ethylacetate (5:2)). White crystals with T_{melt} 120^0 C were obtained with the yield 49% (1.1 g). Mass-spectrum (MALDI): $[M+Na]^+$ 411.9, $[M+K]^+$ 427.89. $C_{19}H_{32}O_{8.}$ IR spectrum (KBr),ν/cm^{-1}: 507, 557, 582, 672, 705, 735, 827, 911, 924, 956, 1003, 1062, 1090, 1111, 1186, 1205, 1235, 1266, 1318, 1348, 1372, 1395, 1458, 1536, 1646, 1747, 2861, 2950, 2988. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.85 (6H, s, CH_3), 1.39 (6H, s, CH_3), 1.43 (6H, s, CH_3), 3.44 (2H, s, CH_2), 3.61 (4H, d, *J*= 11.8 Hz, CH_2), 3.65 (4H, d, *J*= 11.8 Hz, CH_2), 4.26 (4H, s, OCH_2). ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.38, 98.11, 67.86, 66.14, 41.43, 33.60, 27.20, 20.08, 17.60.

61-[Bis(2,2-dimethyl-1,3-dioxolane-4-O-butyl) carbonyl]methano[60]fullerene **(7)**

To a solution of fullerene C_{60} (0.3 g, 0.45 mmol) in toluene (200 ml) were sequentially added CBr_4 (0.208 g, 0.63 mmol), bis(2.2-dimethyl-1.3 –dioxolane-4-*O*-butyl)malonate (0.26 g, 0.63 mmol) and DBU (0.095 g, 0.63 mmol). After being stirred for 12 h at room temperature, the reaction mixture was washed with water (2×20 ml) and concentrated. Compound **7** was isolated by column chromatography on silica gel with the yield 49% (0.173 g) using the mixture toluene-acetonitrile (40:1). The purity of **7** was confirmed by HPLC methods. Mass-spectrum (MALDI):$[M+H]^+$ 1134.78 $C_{81}H_{34}O_{8.}$ UV-spectrum (CH_2Cl_2), λ_{max}/nm: 327, 428, 490, 696. IR-spectrum, (KBr),ν/cm^{-1}: 526, 552, 579, 609, 638, 671, 705, 738, 789, 812, 854, 995, 1057, 1096, 1156, 1184, 1206, 1232, 1266, 1369, 1427, 1454, 1538, 1639, 1742, 2327. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.34 (6H, s, CH_3), 1.40 (6H, s, CH_3), 1.53–1.70 (8H, m, CH_2), 1.85-1.94 (4H, m, CH_2), 3.52 (2H, dd, *J*= 7.4 Hz, *J*= 7.4 Hz, CH_2), 4.04 (2H, dd, *J*= 6.0 Hz, *J*= 7.4 Hz, CH_2),, 4.05-4.13 (2H, m, CH), 4.51 (4H, t, *J*= 6.6 Hz, OCH_2). ^{13}C NMR (150 MHz, $CDCl_3$): δ 22.41, 25.75, 27.01, 28.63, 33.20, 52.36, 67.14, 69.41, 71.63, 71.88, 108.82, 138.98, 140.98, 141.90, 142.21, 143.01, 143.05, 143.12, 143.90, 144.64, 144.71, 144.91, 145.14, 145.21, 145.29, 163.60 (C=O).

61-[Bis(2,2–dimethyl-1,3-dioxolane-4-O-methyl)carbonyl] methano[60]fullerene **(8).**

Compound **8** was synthesized with the yield 40% relative to the reacted fullerene similarly to compound **7**. Mass-spectrum (MALDI): $[M+H]^+$ 1050.21 $C_{75}H_{22}O_8$. UV-spectrum (CH_2Cl_2), λ_{max}/nm: 327, 430, 492, 696. IR-spectrum, (KBr), ν/cm^{-1}: 526, 552, 581, 670, 703, 788, 814, 852, 920, 958, 1057, 1096, 1156, 1185, 1205, 1231, 1266, 1316, 1366, 1376, 1427, 1454, 1539, 1644, 1741, 2930, 3460. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.39 (6H, s, CH_3), 1.49 (6H, s, CH_3), 3.91 (2H, dd, *J*= 5.2 Hz, *J*= 8.8 Hz, CH_2), 4.18 (2H, dd, *J*= 6.4 Hz, *J*= 8.8 Hz, CH_2), 4.49-4.56 (2H, m, CH), 4.52 (4H, s, OCH_2). ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.37 (CH_3), 26.84 (CH_3), 51.73 (C61), 66.42, 67.24, 73.14, 73.15, 71.32 (2C-sp^3), 110.12 (2C), 139.15, 141.02, 141.88, 141.89, 142.24, 143.03, 143.07, 143.13, 143.92, 144.63, 144.73, 144.97, 145.00, 145.11, 145.24, 145.33, 163.22 (C=O).

61-[Bis(2.2.5-trimethyl-1.3-dioxane-5-methyl-O-methyl)carbonyl]methano[60]fullerene **(9)**

Compound **9** was synthesized with the yield 60% (0.143 g) relative to the reacted fullerene similarly to compound **7**. Mass-spectrum (MALDI): $[M+H]^+$ 1106.07 $C_{79}H_{30}O_8$. UV-spectrum (CH_2Cl_2), λ_{max}/nm: 326, 429, 491, 697. IR-spectrum, (KBr), ν/cm^{-1}: 526, 557, 582, 672, 705, 735, 827, 911, 924, 956, 1003, 1062, 1090, 1111, 1152, 1186, 1205, 1235, 1266, 1318, 1348, 1372, 1395, 1428, 1458, 1536, 1646, 1747, 2861, 2950, 2988. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.96 (6H, CH_3), 1.43 (6H, s, CH_3), 1.47 (6H, s, CH_3), 3.71 (2H, d, *J*= 12.0 Hz, CH_2), 3.77 (2H, dd, *J*= 12.0 Hz, CH_2), 4.59 (4H, s, OCH_2). ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.84, 19.92, 27.4, 52.57 (C61), 66.16, 71.53 (sp^3-C), 98.26, 125.30, 128.22, 129.03, 137.85, 139.08, 141.04, 141.92, 142.22, 143.04, 143.91, 144.66, 144.69, 144.71, 144.93, 145.08, 145.17, 145.22, 145.30, 163.57 (C=O).

61-[Bis(1,2-hexanediol)carbonyl]methano[60]fullerene **(10)**

To 61-[bis(2,2–dimethyl-1,3-dioxolane-4-*O*-methyl)carbonyl] methano[60]fullerene **7** (0.019 g, 0.167 mmol) in toluene (10 ml) HCl (0.001 ml, 0.167 mmol) was added. The reaction mixture was left in the dark for 24 h. The toluene solution became colourless, sediment precipitated, which was filtered and washed with toluene, the precipitate weight being 0.016 g, (yield 94%). Mass-spectrum

(MALDI): $[M+H]^+$ 1055.94 $C_{75}H_{26}O_8$. IR-spectrum, ν/cm^{-1} (KBr): 420, 526, 703, 997, 1024, 1061, 1096, 1205, 1232, 1267, 1395, 1738, 2855, 2924, 3246, 3384, 3421. ^{1}H NMR (600 MHz, DMSO-d_6) 1.29-1.52 (8H, m, CH_2), 1.77-1.81 (4H, m, CH_2), 3.25 (4H, dd, *J*= 2.1 Hz, *J*= 5.5 Hz, CH_2), 3.33-3.48 (2H, m, CH), 4.46 (4H, t, *J*= 6.6 Hz, OCH_2). ^{13}C NMR (150 MHz, DMSO-d_6) δ 21.91, 27.45, 33.01, 52.87, 66.14, 68.89, 71.02, 71.43, 138.94, 140.95, 141.86, 142.18, 142.99, 143.07, 143.84, 144.52, 144.65, 144.69, 144.79, 145.07, 145.13, 145.21, 145.71, 162.83 (C=O).

61-[Bis(1, 2-propanediol) carbonyl)] methano[60]fullerene **(11)**

Compound **11** was obtained from **8** (0.069g) by the similar method to that of compound **10** with the yield 92% (0.055 g). Mass-spectrum (MALDI): $[M+H]^+$ 970.01 $C_{69}H_{14}O_8$. IR-spectrum, ν/cm^{-1} (KBr): 515, 529, 795, 844, 995, 1033, 1076, 1157, 1214, 1257, 1372, 1455, 1659, 1728, 3457. ^{1}H NMR (600 MHz, DMSO-d_6): δ 3.35 (2H, dd, *J*= 6.0 Hz, *J*= 6.0 Hz,CH_2), 3.84 (2H, br s, CH), 4.34 (2H, br s, OCH_2), 4.49 (2H, br s, OCH_2), 5.04 (4H, br s, OH); ^{13}C NMR (150 MHz, DMSO-d_6) δ 29.65, 52.79, 62.96, 69.11, 69.59, 71.87, 79.74, 139.08, 140.87, 141.86, 142.21, 143.00, 143.06, 143.86, 144.51, 144.65, 144.81, 145.15, 145.23, 145.57, 163.13 (C=O).

61-[Bis(2, 3-diol-1-methyl-propyl) carbonyl)] methano[60]fullerene **(12)**

Compound **12** was obtained from **9** (0.100g) analogously to **10** with the yield 97% (0.09 g). Mass-spectrum (MALDI): $[M+H]^+$ 1026.90 $C_{73}H_{14}O_8$. IR-spectrum, ν/cm^{-1} (KBr): 441, 526, 703, 891, 949, 1000, 1046, 1114, 1207, 1233, 1268, 1390, 1427, 1464, 1636, 1741, 3420. ^{1}H NMR (600 MHz, DMSO-d_6): δ 0.89 (6H, s, CH_3), 3.35 (8H, br s, CH_2), 4.31 (4H, br s, OCH_2). ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.95, 53.23, 63.92, 70.19, 72.08, 79.64, 138.93, 140.95, 141.86, 142.18, 143.00, 142.98, 143.07, 143.84, 144.52, 144.64, 144.68, 145.15, 145.23, 145.57, 163.47 (C=O).

1,2:18,36:22,23:27,45:31,32:55,56-{Hexakis([bis(2,2-dimethyl-1.3-dioxolane-4-O-butyl)carbonyl)]methano}-dodecahydro[60] fullerene **(13)**

To a solution of C_{60} (0.3 g, 0.42 mmol) in O-DCB (20 ml) were added CBr_4 (13.83 g, 42 mmol), bis(2.2-dimethyl-1.3 –dioxolane-4-*O*-butyl) malonate (1.73 g, 4.2 mmol) and DBU (1.27 g, 8.3 mmol) at stirring under an argon atmosphere at room temperature. The colour of the reaction mixture changed immediately from the purple to red. The reaction mixture was stirred for 72 h. The product **13** was purified by column chromatography on silica gel at eluating with the mixture hexane-ethylacetate with the yield 12% (0.156 g). Mass-spectrum (MALDI): $[M+H]^+$: 3204.34 $C_{186}H_{204}O_{48}$. IR spectrum (KBr),ν/cm^{-1}: 529, 540, 673, 856, 995, 1061, 1160, 1219, 1264, 1456, 1644, 1746, 2286, 2868, 2936, 2984, 3468. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.33 (36H, s, CH_3), 1.38 (36H, s, CH_3), 1.40-1.65 (48H, m, CH_2), 1.71-1.75 (24H, m, CH_2) 3.48 (12H, dd, *J*= 6.4 Hz, *J*= 6.8 Hz, CH_2), 4.00 (12H, dd, *J*= 6.4 Hz, *J*= 7.2 Hz, CH_2), 4.02-4.07 (12H, m, CH), 4.26 (24H, t, *J*= 6.4 Hz, OCH_2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.45, 26.02, 27.05, 28.62, 33.21, 45.56, 66.89, 69.95, 75.84 *(sp^3)*, 108.82, 141.05 (sp^2), 146.1 (sp^2), 164.00.

1,2:18,36:22,23:27,45:31,32:55,56-{Hexakis[bis(2,2–dimethyl-1,3-dioxolane-4-O-methyl)carbonyl)]methano}-dodecahydro[60] fullerene **(14)**

Compound **14** was obtained by the method similar to that for compound **13** with the yield 20% (0.181 g). Mass-spectrum (MALDI): $[MH]^+$ 2701.20 $C_{150}H_{132}O_{48.}$ IR spectrum (KBr),ν/cm^{-1}: 523, 665, 715, 795, 841, 936, 998, 1056, 1158, 1213, 1263, 1376, 1455, 1645, 1749, 2986. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.36 (36H, s, CH_3), 1.43 (36H, s, CH_3), 3.76 (12H, dd, *J*= 5.4 Hz, *J*= 5.4 Hz, CH_2), 4.07 (12H, dd, *J*= 6.7 Hz, *J*= 7.2 Hz, CH_2), 4.30 (24H, s, OCH_2), 4.31-4.39 (12H, m, CH); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.24, 26.70, 44.89 (6C, C_{61}), 60.30, 66.38, 66.41, 68.92 *(sp^3)*, 72.91, 109.91, 140.88 (sp^2), 145.84 (sp^2), 163.16 (C=O).

1,2:18,36:22,23:27,45:31,32:55,56-{Hexakis[bis(2.2.5-trimethyl-1.3-dioxane-5-methyl-O-methyl) carbonyl)]methano}-dodecahydro[60] fullerene **(15)**

Compound **15** was obtained by a method similar to that for compound **13** with the yield 28% (0.156 g). Mass-spectrum (MALDI): $[MH]^+$ 3038.3 $C_{174}H_{180}O_{48.}$ IR-spectrum (KBr),ν/cm-1: 523, 673, 714, 828, 913, 935, 1002, 1043, 1090, 1155, 1206, 1264, 1375, 1459, 1748 (C=O), 2960. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.81 (36H, s, CH_3), 1.37 (36H, s, CH_3), 1.41 (36H, s, CH_3), 3.55 (24H, d, J = 12 Hz, CH_2), 3.62 (24H, d, J = 12 Hz, CH_2) 4.35 (24H, s, OCH_2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.63, 20.08, 27.08, 30.79, 33.59, 40.37, 45.44 (6C, C_{61}), 66.00, 69.10 (sp^3), 69.33, 98.00, 141.07 (sp^2), 145.65 (sp^2), 163.47 (C=O).

1,2:18,36:22,23:27,45:31,32:55,56-{Hexakis[(bis(1.2-hexanediol)carbonyl)]methano}-dodecahydro[60]fullerene **(16)**

To a solution of compound **13** (0.022 g, 0.0069 mmol) in toluene (10 ml) HCl (0.002 ml, 0.082 mmol) was added. The reaction mixture was left for 24 h in a dark. The toluene mixture became colorless, the sediment precipitated, which was filtered and washed with toluene. The product yield was 95% (0.018 g). Mass-spectrum (MALDI): $[MH^+]$ 2724.80 $C_{150}H_{156}O_{48.}$ IR spectrum (KBr), ν/cm^{-1}: 533, 672, 715, 924, 972, 1077, 1221, 1265, 1459, 1741 (C=O), 2438, 2783, 2866, 2934, 3369 (OH). ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.15-1.35 (24H, m, CH_2), 1.41 (24H, br s, CH_2), 1.61 (24H, br s, CH_2), 3.22 (24 H, d, J= 5.1 Hz, CH_2, 3.36 (12H, br s, CH), 4.26 (24H, t, J = 5.9 Hz, OCH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 21.19, 28.78, 32.38, 45.52 (6C, C_{61}), 65.80, 66.43, 67.08, 68.95, 70.91 (sp^3), 140.50 (sp^2), 145.01 (sp^2), 162.53 (C=O).

1,2:18,36:22,23:27,45:31,32:55,56-{Hexakis[(bis(1.2-propanediol)carbonyl)]methano}-dodecahydro[60]fullerene **(17).**

Compound **17** was obtained from **14** (0.041g) analogously to **16** with the yield of 94% (0.031g). Mass-spectrum (MALDI): $[MH]^+$ 2220.30 $C_{114}H_{84}O_{48.}$ IR spectrum (KBr), ν/cm^{-1}: 472, 525, 565, 600, 708, 756, 840, 977, 1017, 1050, 1095, 1161, 1187, 1262, 1367, 1436, 1543, 1653, 1742 (C=O), 2926, 3423 (OH). ^{1}H NMR (600 MHz, DMSO-d_6): δ 3.27-3.45 (24H, m, CH_2), 3.73 (12H, br s,

CH), 4.15-4.33 (24H, m, OCH_2); ^{13}C NMR (150 MHz, DMSO-d_6): δ 45.41-45.53 (6C, C_{61}), 59.27, 62.31, 63.04, 68.43, 68.94, 72.42 (sp^3), 140.62 (sp^2), 145.03 (sp^2), 162.72 (C=O).

1,2:18,36:22,23:27,45:31,32:55,56-{Hexakis[(bis(2.3-diol-1-methyl-propyl) carbonyl)] methano}-dodecahydro[60]fullerene **(18)**

Compound **18** was obtained analogously to compound **16** from **15** (0.030 g) with the yield of 99% (0.025 g). Mass-spectrum (MALDI): $[MH]^+$ 2556.30 $C_{138}H_{132}O_{48.}$. IR spectrum (KBr, ν, cm^{-1}): 527, 542, 598, 714, 826, 941, 1040, 1126, 1224, 1372, 1396, 1466, 1736 (C=O), 2880, 2932, 3359 (OH). ^{1}H NMR (600 MHz, DMSO-d_6): δ = 0.75 (36H, br s, CH_3), 3.25 (48H, br s, CH_2), 4. 12 (24H, br s, OCH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 17.63, 30.79, 33.59, 40.37, 45.44 (6C, C_{61}), 66.00, 69.10 (sp^3), 69.33, 98.00, 141.07 (sp^2), 145.65 (sp^2), 163.47 (C=O).

Financial support of the Program for Fundamental research of the Presidium of RAS 24P and RFBR (grant № 12-03-97084 p-Povolzhie-a) is highly appreciated.

The study of the structure of compounds is performed in the department of Federal share spectral-and-analytical centre for physical-chemical research of structure, properties and composition of substances and materials (Joint use centre SAC) and Federal Joint Use centre for physical-chemical research of substances and materials (FJUC PCR) (state contracts of the Ministry of education and science of RF № 02.451.11.7036 u 02.451.11.7019).

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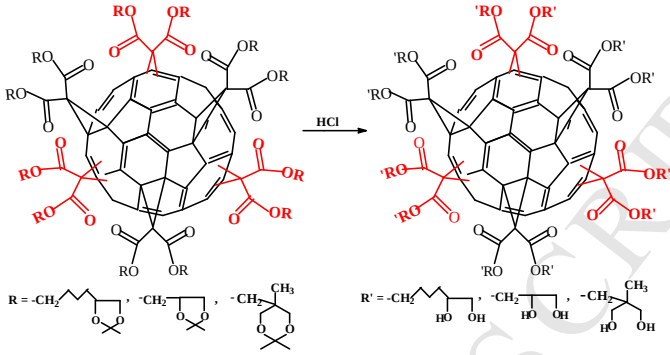
Synthesis and properties of new fullerene C_{60} derivatives, containing acetonide and polyol fragments.

Alina A. Gilmutdinova, Valentina P. Gubskaya, Guzel M. Fazleeva, Shamil K. Latypov, Tatyana A. Zhelonkina, Dilara R. Sharafutdinova, Ildus A. Nuretdinov, Oleg G. Sinyashin

A new approach for synthesis of chromatographically pure water-soluble polyol methanofullerenes with almost quantitative yields has been developed.



Supporting Information

Synthesis and properties of new fullerene C_{60} derivatives, containing acetonide and polyol fragments.

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NMR Spectroscopy. All NMR experiments were performed with a Bruker AVANCE-600 and AVANCE-400 spectrometers. Frequencies are 600.13 MHz in ^{1}H NMR and 150.90 MHz in ^{13}C NMR experiments for AVANCE600; 399.93 MHz in ^{1}H NMR and 100.57 MHz in ^{13}C NMR for AVANCE400. NMR experiments were carried out using standard Bruker pulse programs. The pulse widths were 7 μs (90°) and 12 μs (90°) for ^{1}H and ^{13}C, respectively. Typically 16K and 64K data points were collected for one-dimensional proton and carbon spectra, respectively. 2D experiments parameters were as follows. For ^{1}H–^{1}H correlations (COSY): relaxation delay 1.5 s, data matrix 1K x 2K (256 experiments to 0.5K, zero filling in *F*1, 1K in *F*2), 2 transients in each experiment. For ^{1}H-^{13}C correlations (HSQC): optimized for J = 145 Hz, relaxation delay 2.5 s, data matrix 0.5K x 2K (256 experiments to 0.5K, zero filling in *F*1, 2K in *F*2), 16 transients in each experiment. For ^{1}H-^{13}C long range correlations (HMBC): optimized for J = 8 Hz, relaxation delay 2.5 s, data matrix 0.5K x 2K (256 experiments to 0.5K, zero filling in *F*1, 2K in *F*2), 48 transients in each experiment. All 2D spectra were weighted with sine-bell squared and shifted (π/2 in both dimensions) window functions, and processed with the Bruker software package.

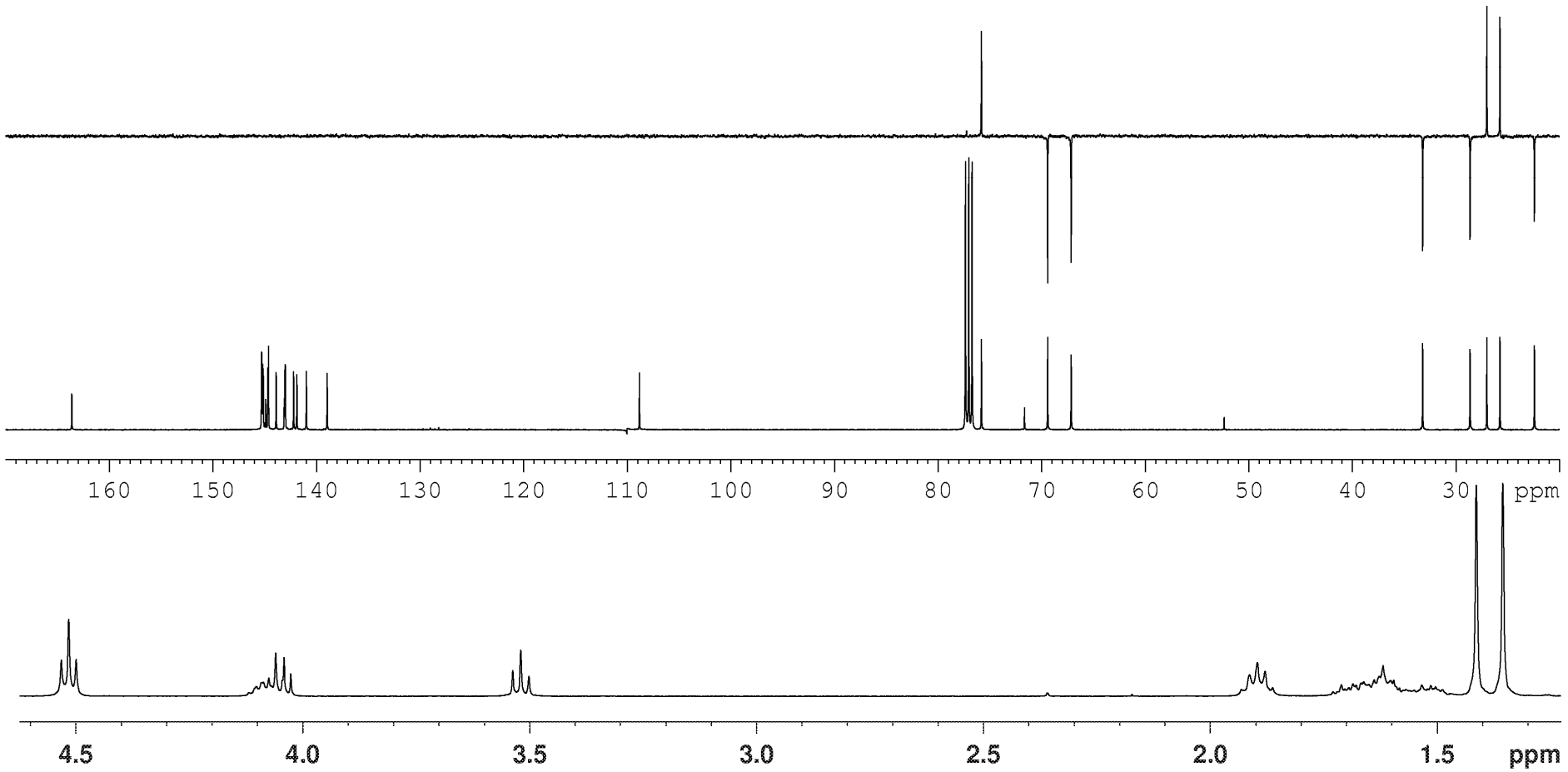

Figure S1. 1D ^{1}H, ^{13}C and DEPT spectra in $CDCl_3$ of **7** (T = 303K).

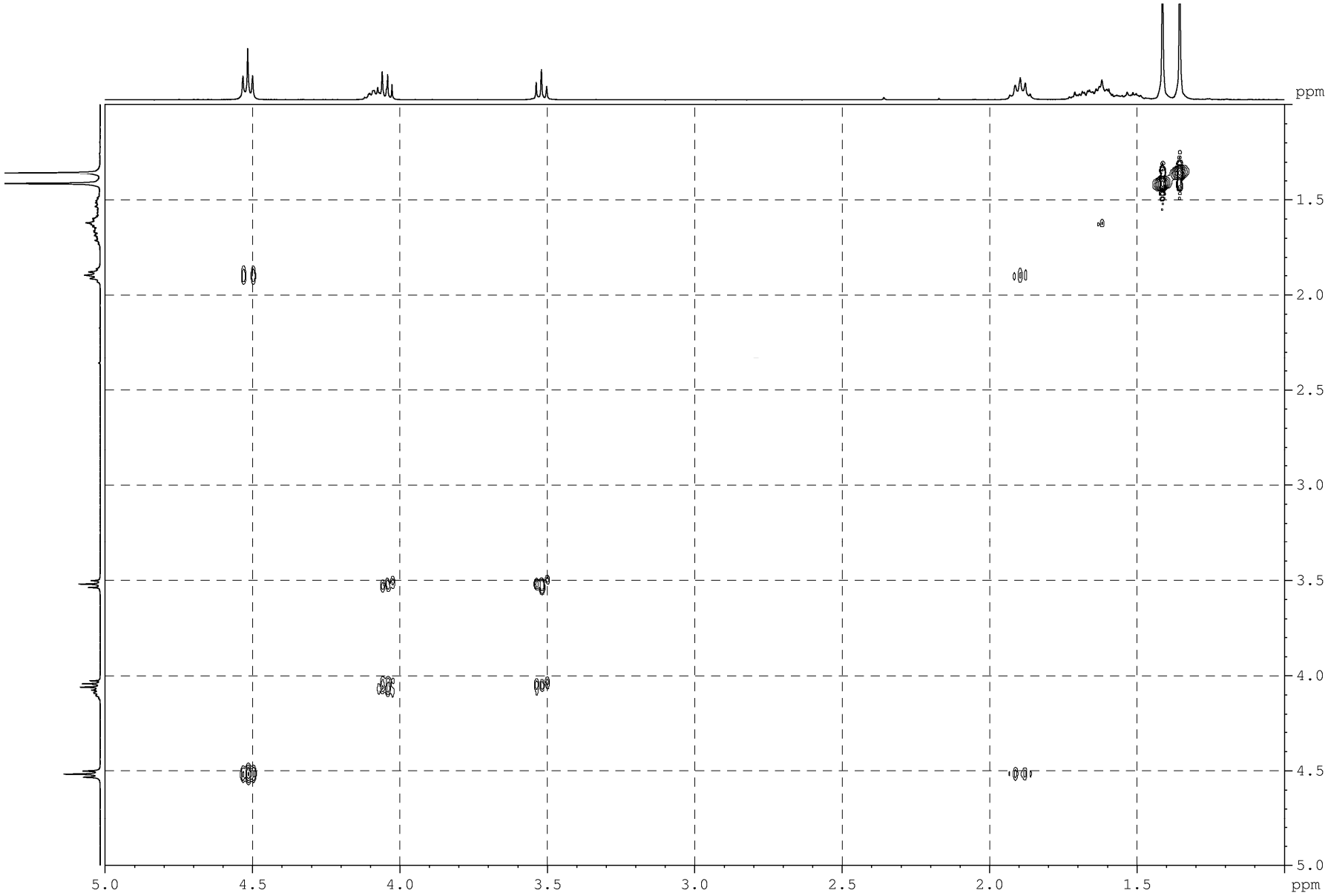

Figure S2. 2D ^{1}H-^{1}H COSY spectrum in CDCl3 of **7** (T = 303K).

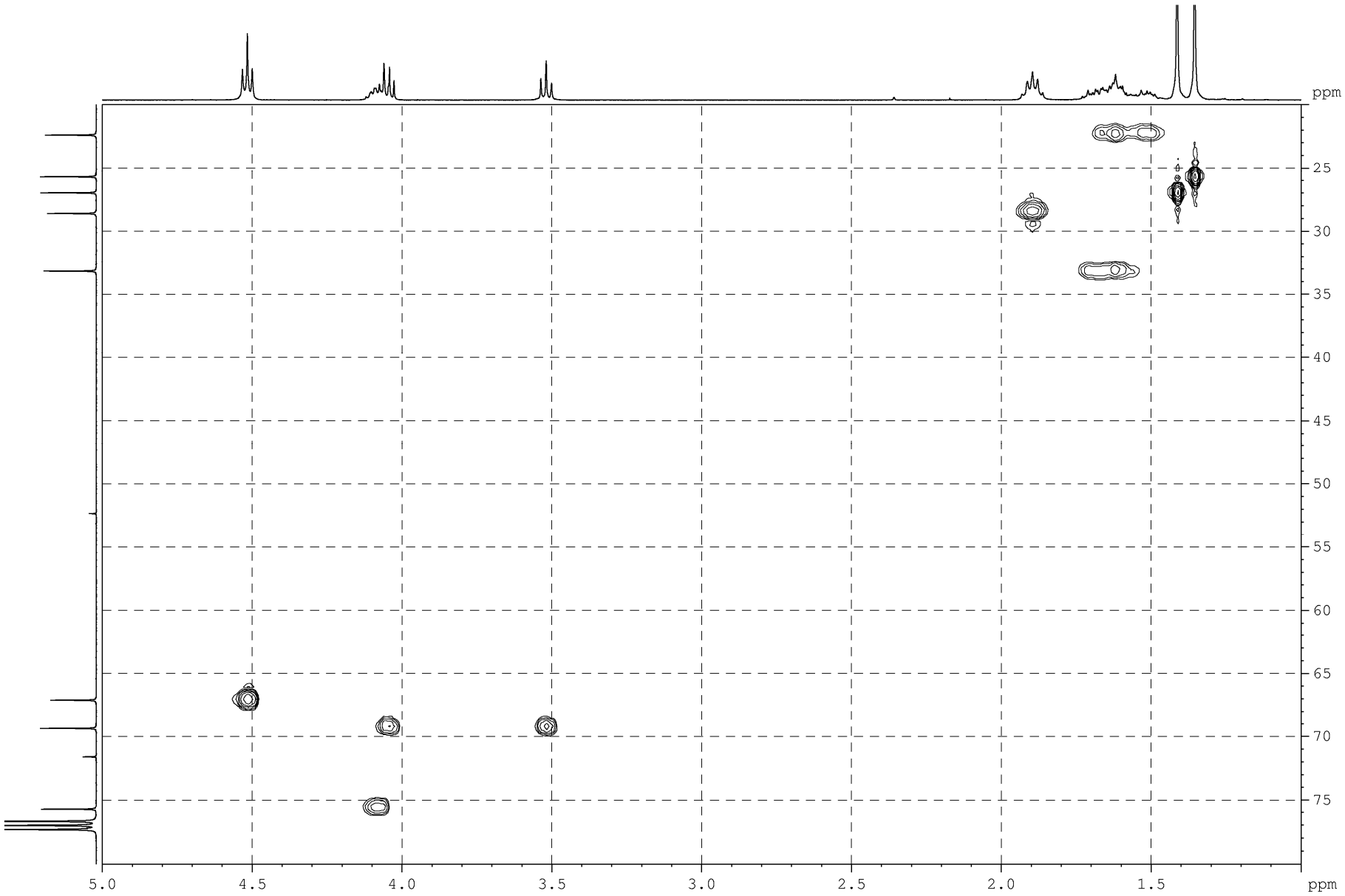

Figure S3. 2D ^{1}H-^{13}C HSQC spectrum in $CDCl_3$ of **7** (T = 303K).

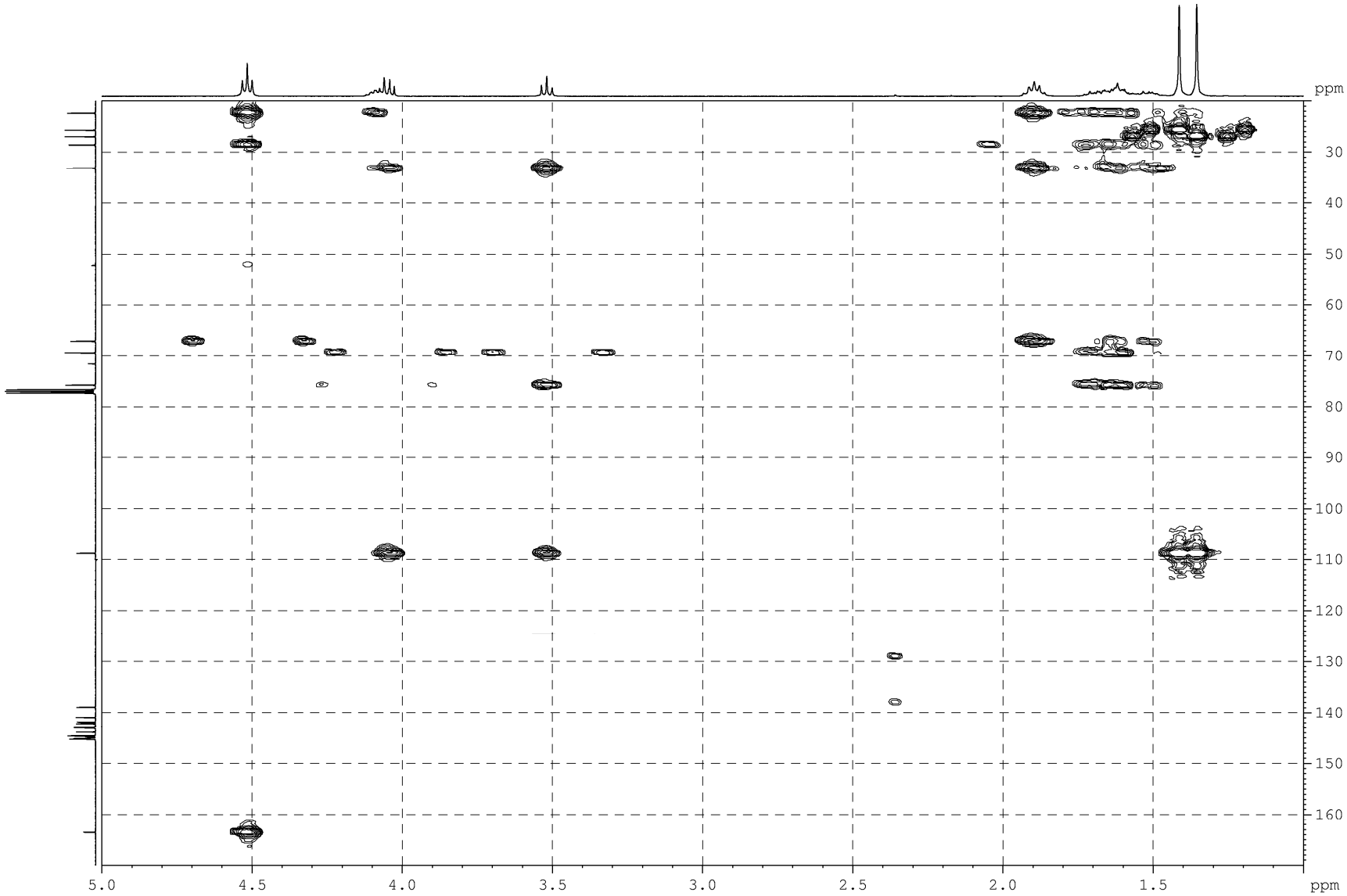

Figure S4. 2D ^{1}H-^{13}C HMBC spectrum in $CDCl_3$ of **7** (T = 303K).

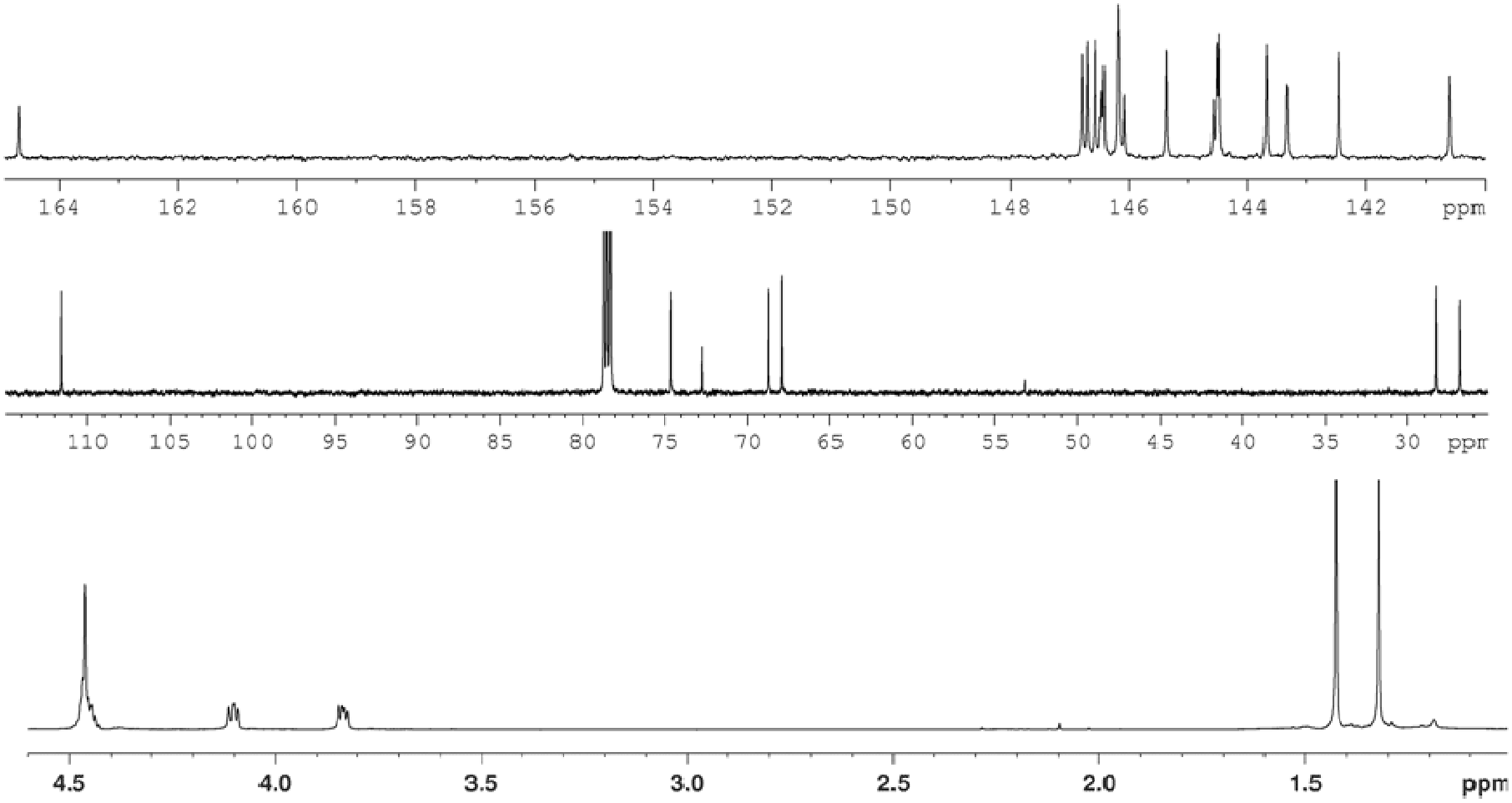

Figure S51D ^{1}H and ^{13}C spectra in $CDCl_3$ of **8** (T = 303K).

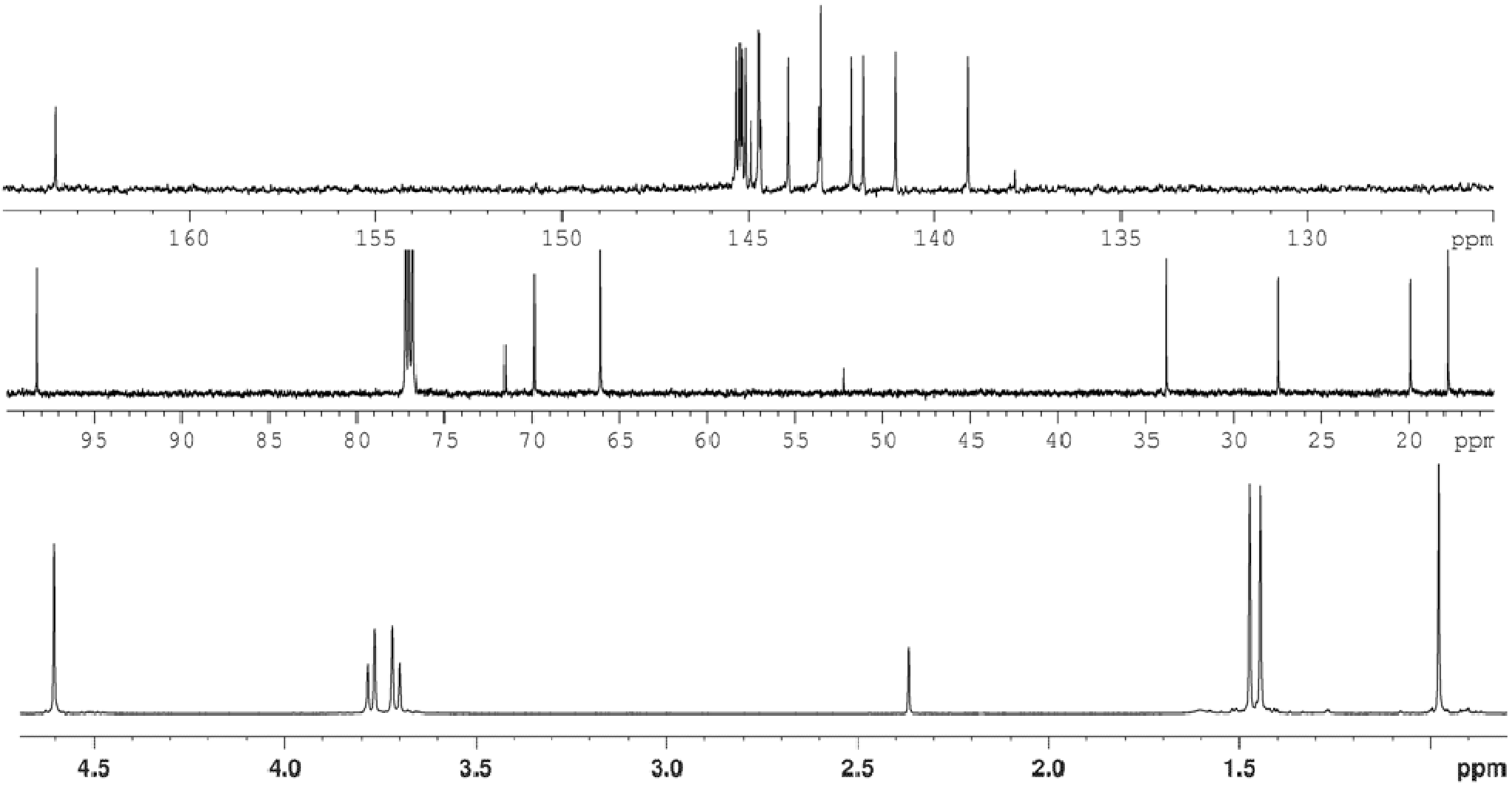

Figure S6. 1D ^{1}H and ^{13}C spectra in $CDCl_3$ of **9** (T = 303K).

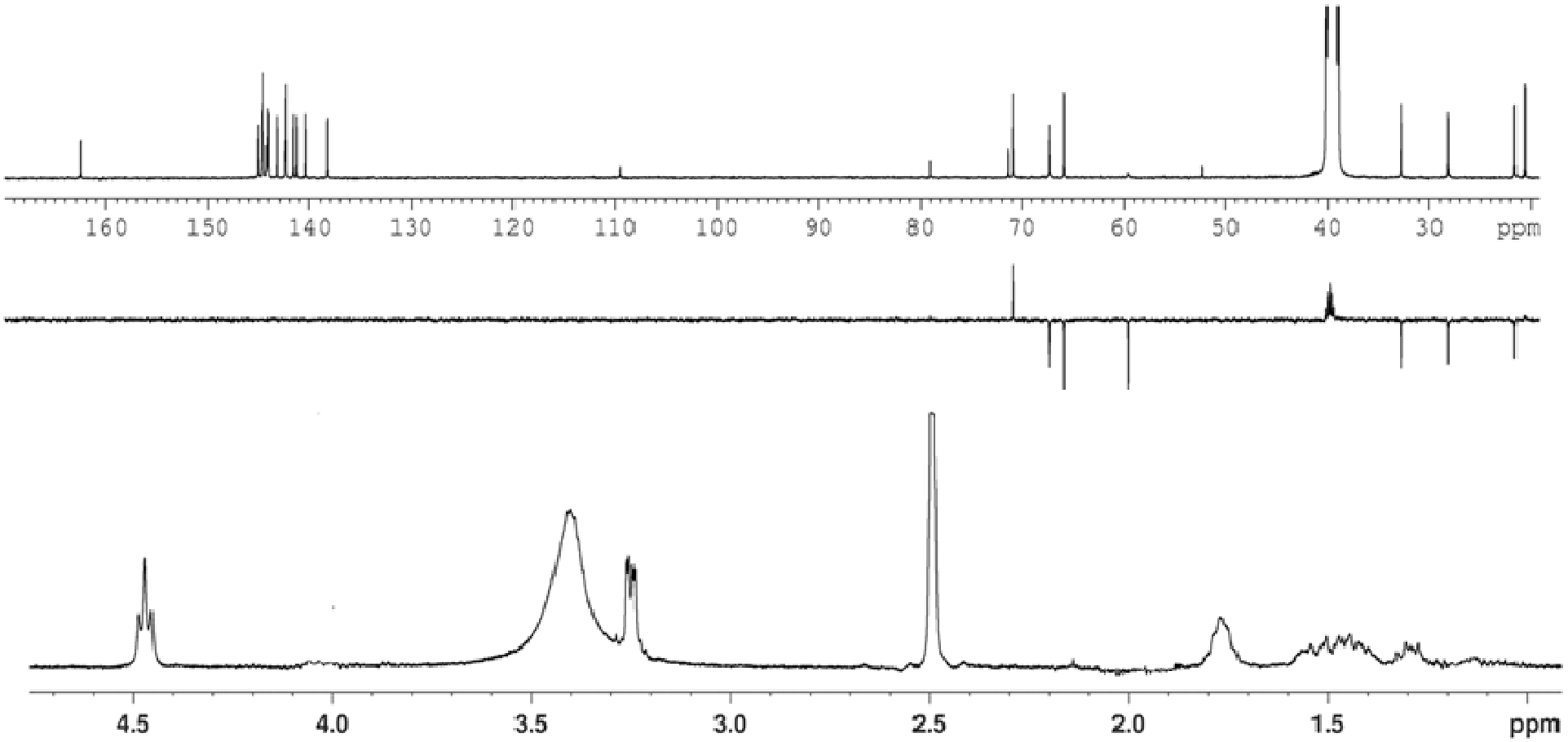

Figure S7. 1D ^{1}H, ^{13}C and DEPT spectra in DMSO of **10** (T = 303K).

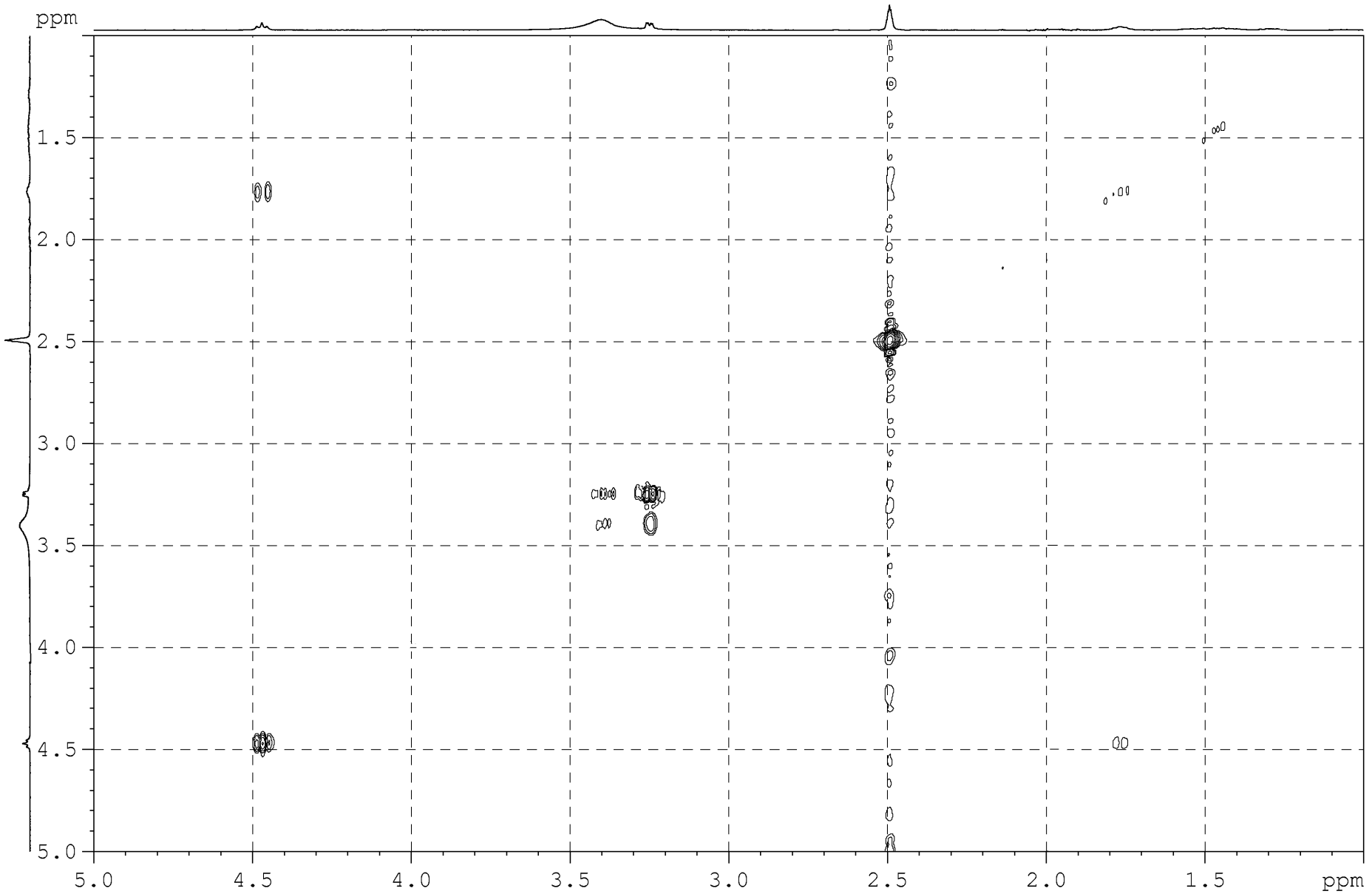

Figure S8. 2D ^{1}H-^{1}H COSY spectrum in DMSO of **10** (T = 303K).

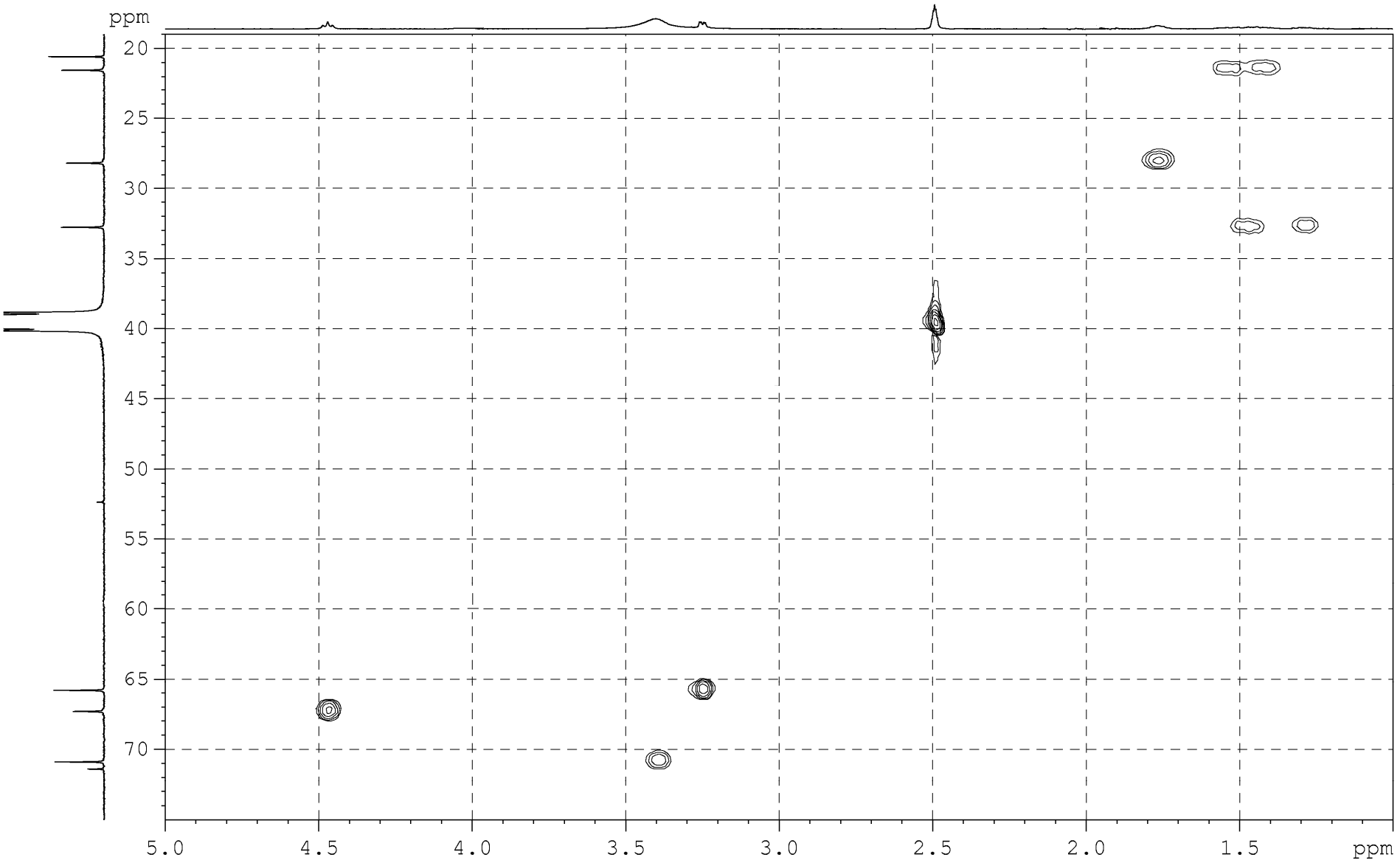

Figure S9. 2D ^{1}H-^{13}C HSQC spectrum in DMSO of **10** (T = 303K).

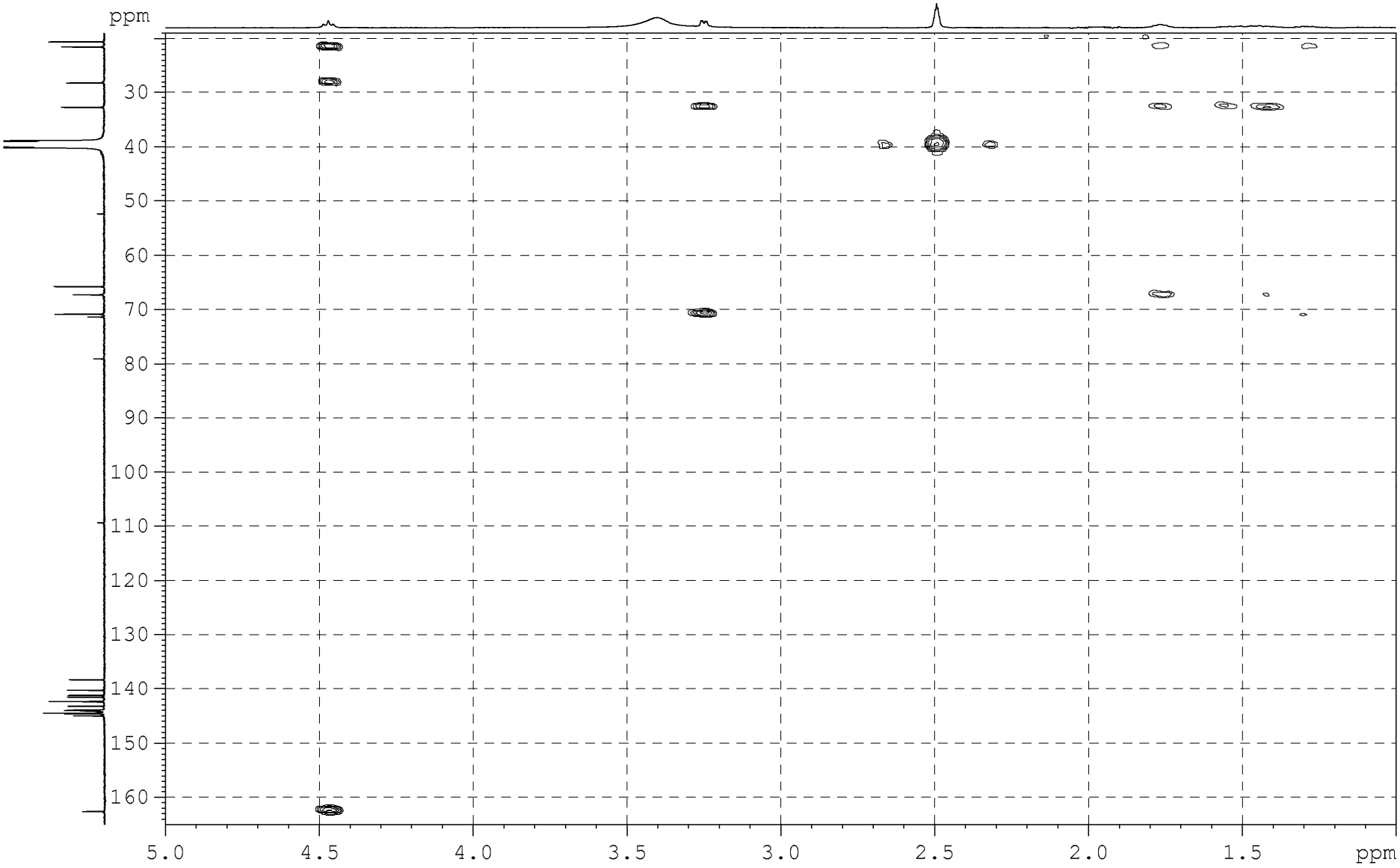

Figure S10. 2D ^{1}H-^{13}C HMBC spectrum in DMSO of **10** (T = 303K).

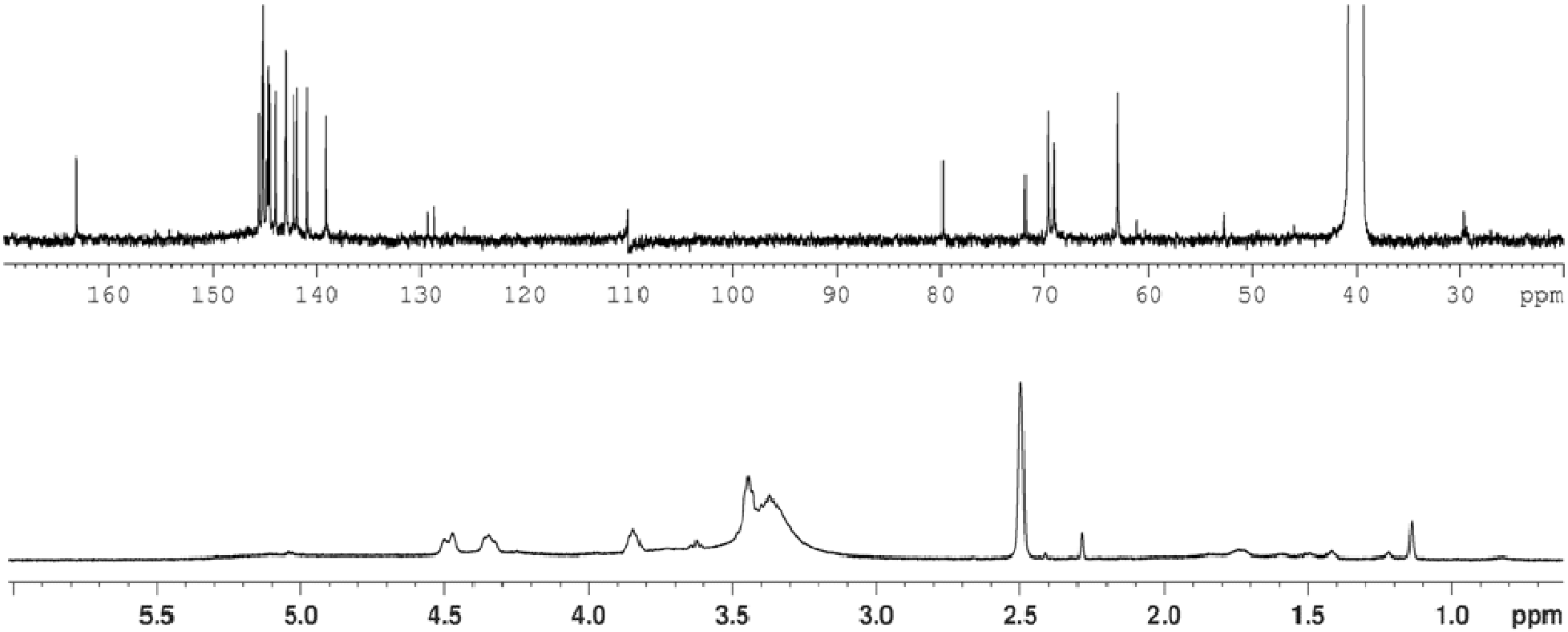

Figure S11. 1D^{1}H and ^{13}C spectra in DMSO of **11** (T = 303K).

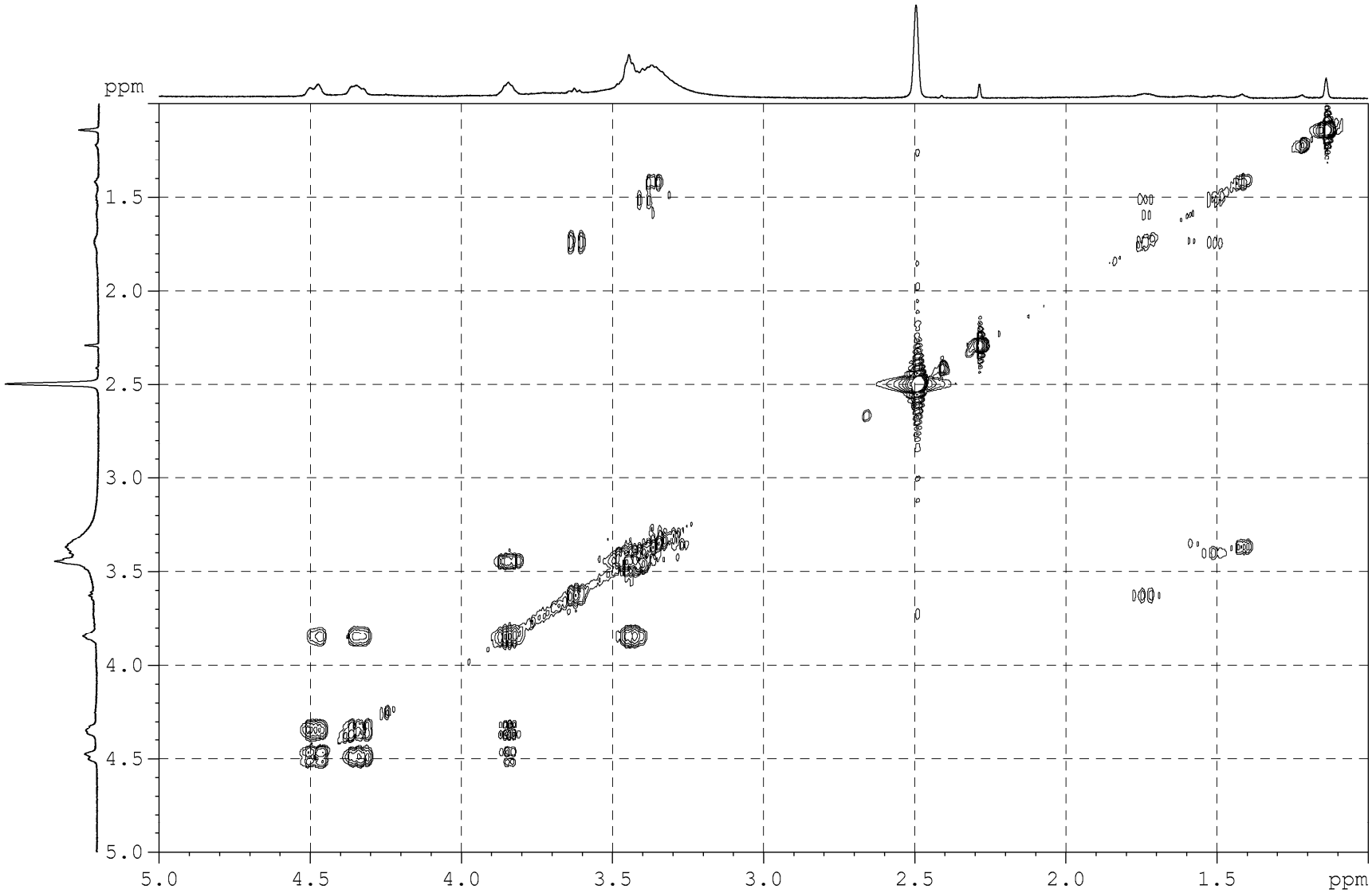

Figure S12. 2D ^{1}H-^{1}H COSY spectrum in DMSO of **11** (T = 303K).

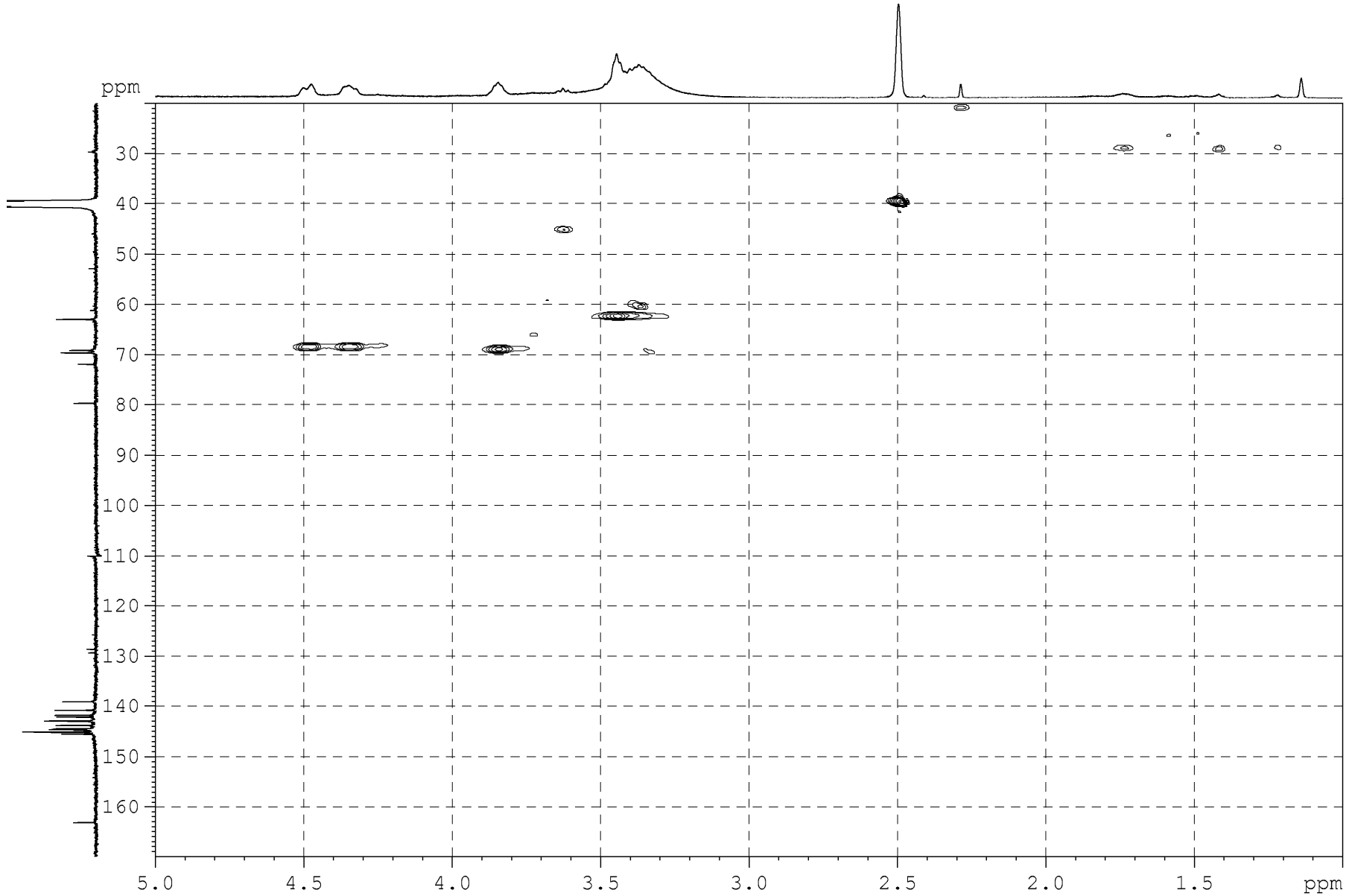

Figure S13. 2D ^{1}H-^{13}C HSQC spectrum in DMSO of **11** (T = 303K)

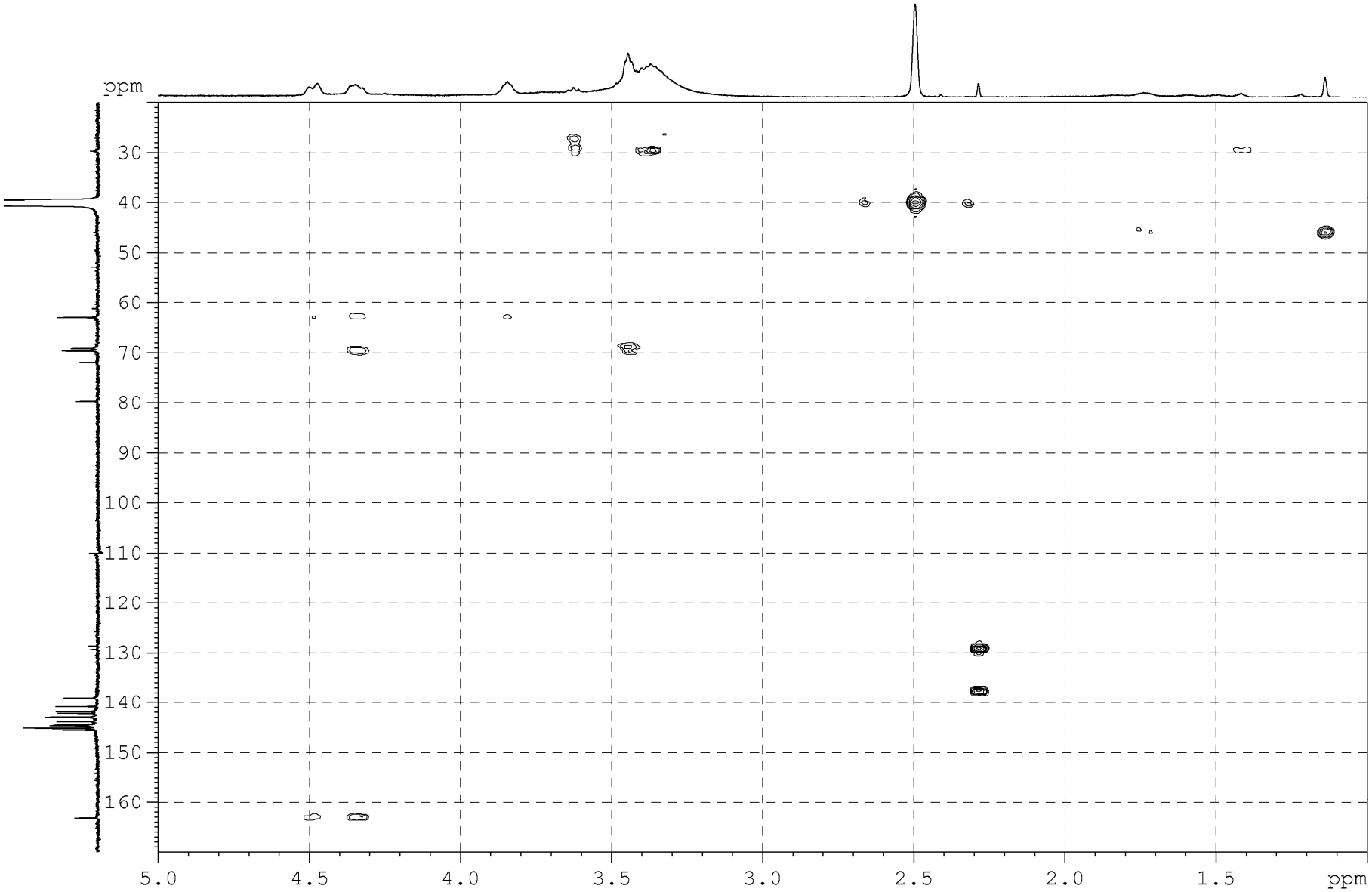

Figure S14. 2D ^{1}H-^{13}C HMBC spectrum in DMSO of **11** (T = 303K).

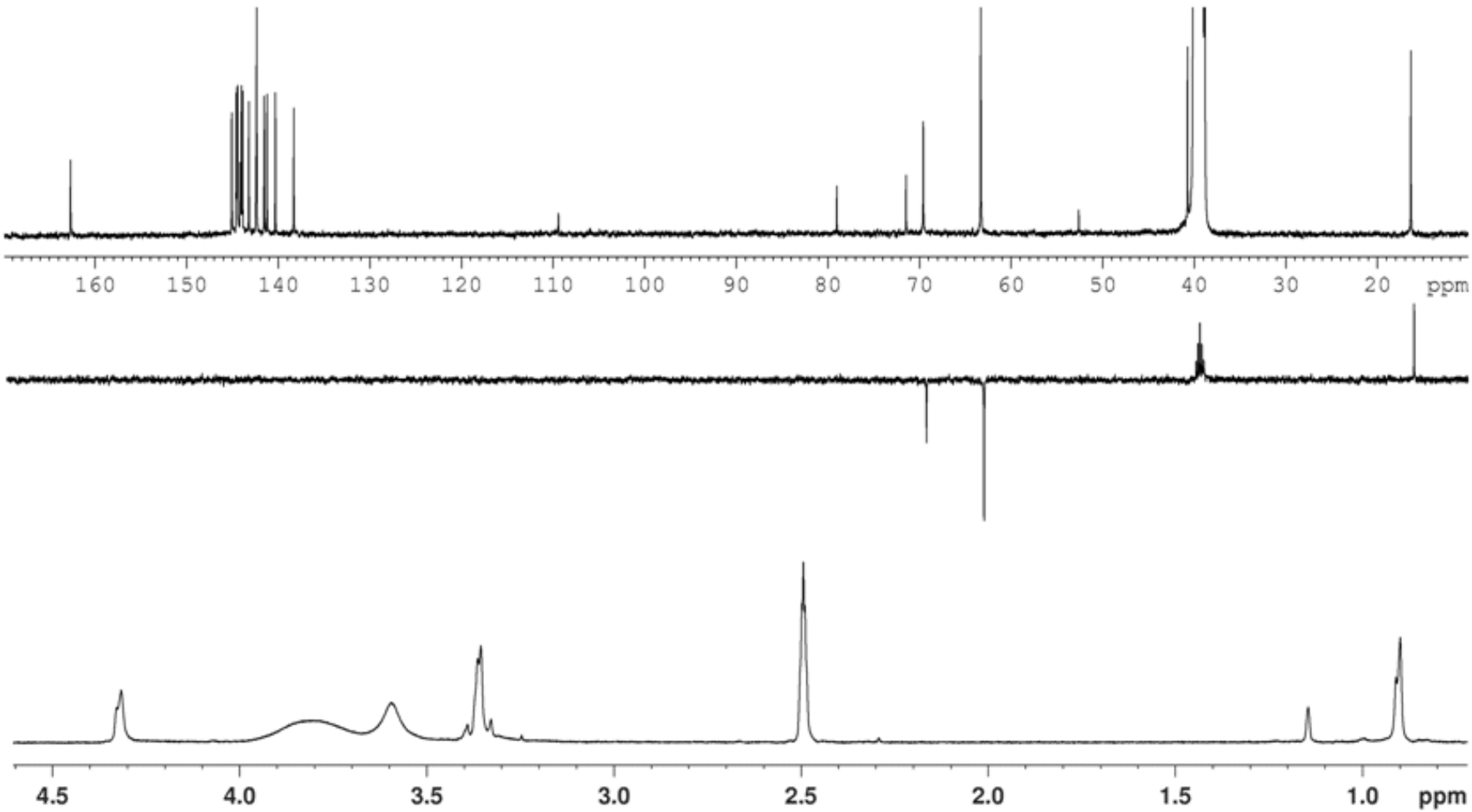

Figure S15. 1D^{1}H, ^{13}C and DEPT spectra in DMSO of **12** (T = 303K).

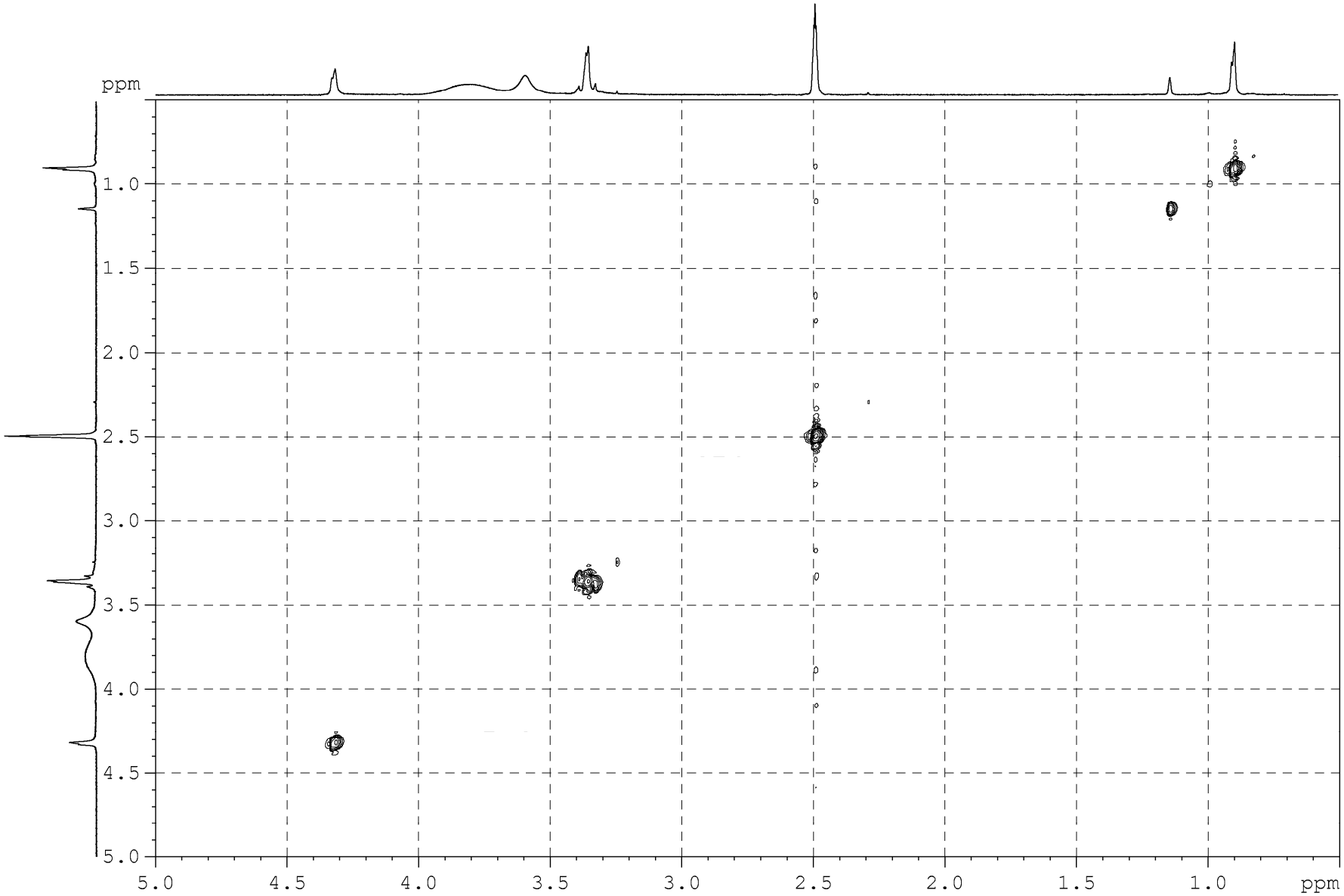

Figure S16. 2D ^{1}H-^{1}H COSY spectrum in DMSO of **12** (T = 303K).

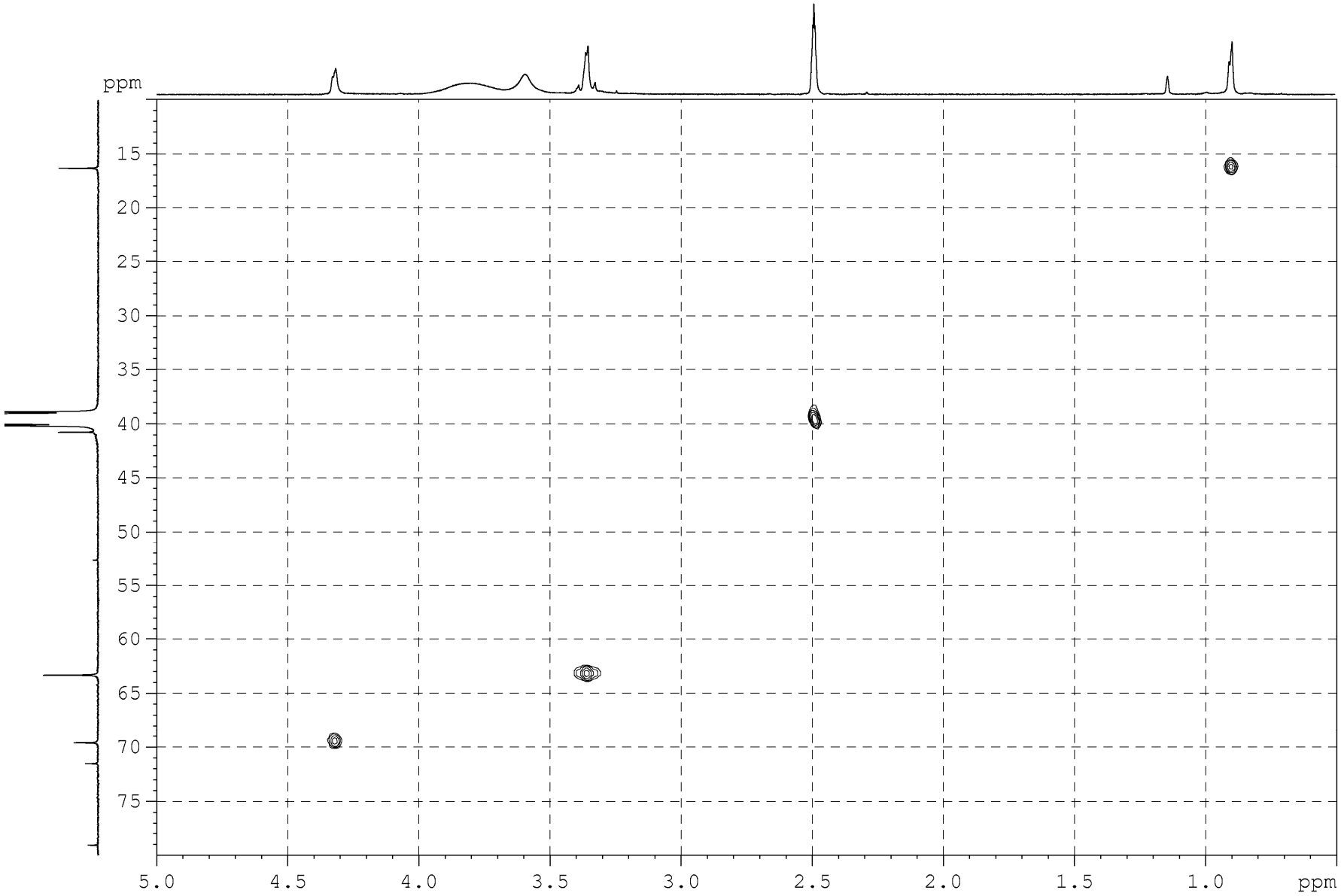

Figure S17. 2D ^{1}H-^{13}C HSQC spectrum in DMSO of **12** (T = 303K)

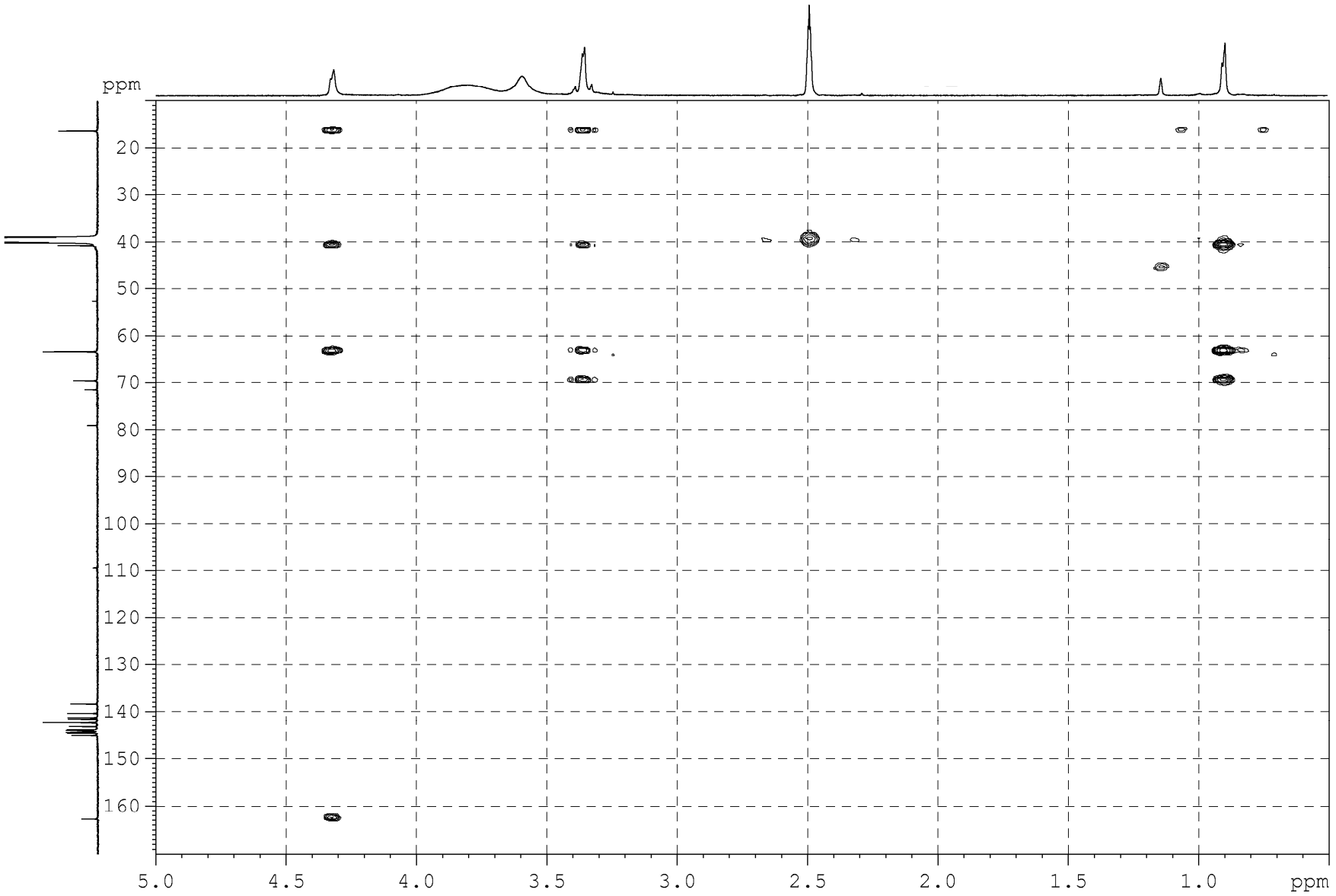

Figure S18. 2D ^{1}H-^{13}C HMBC spectrum in DMSO of **12** (T = 303K).

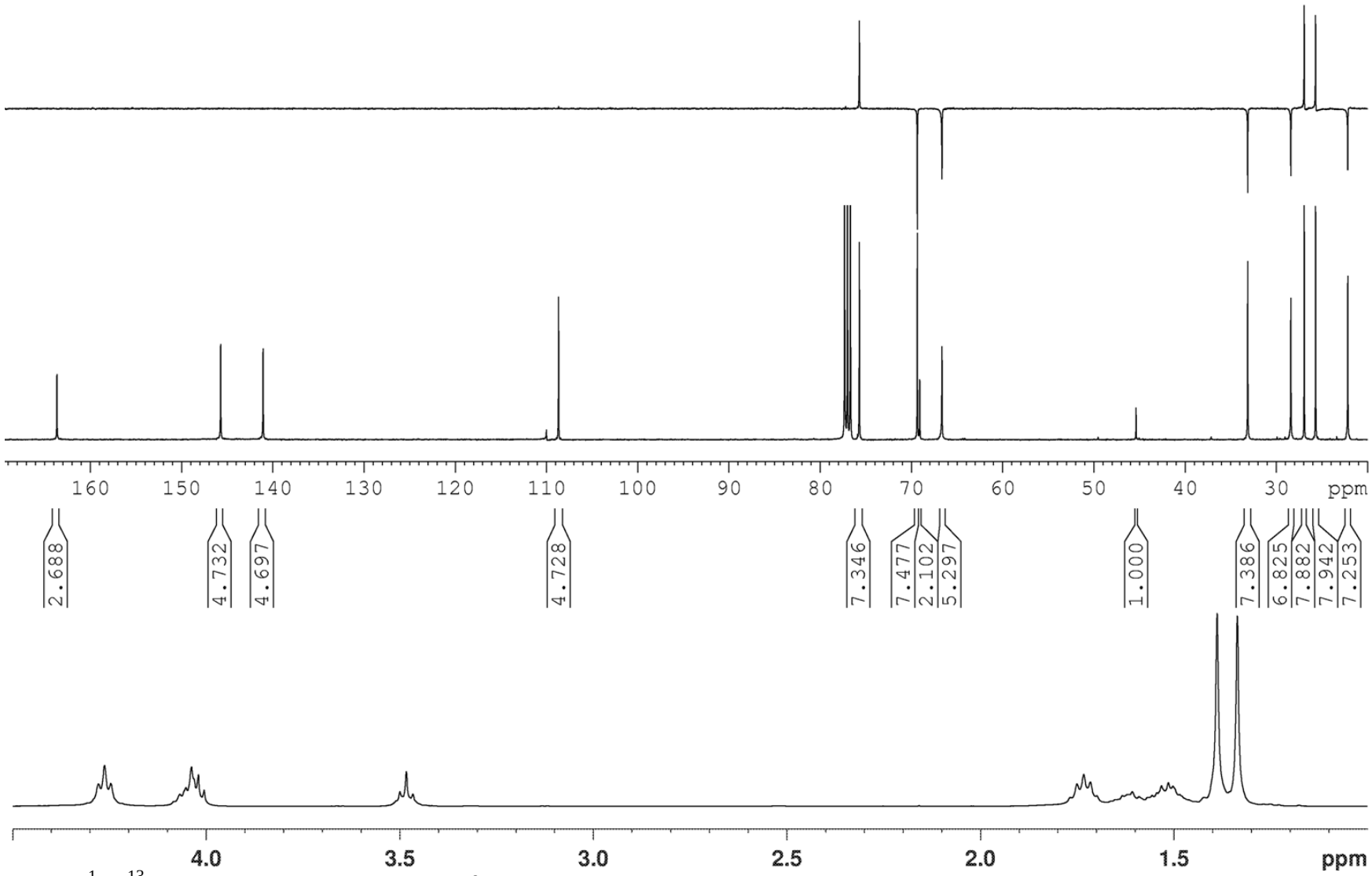

Figure S19. 1D^{1}H, ^{13}C and DEPT spectra in $CDCl_3$ of **13** (T = 303K).

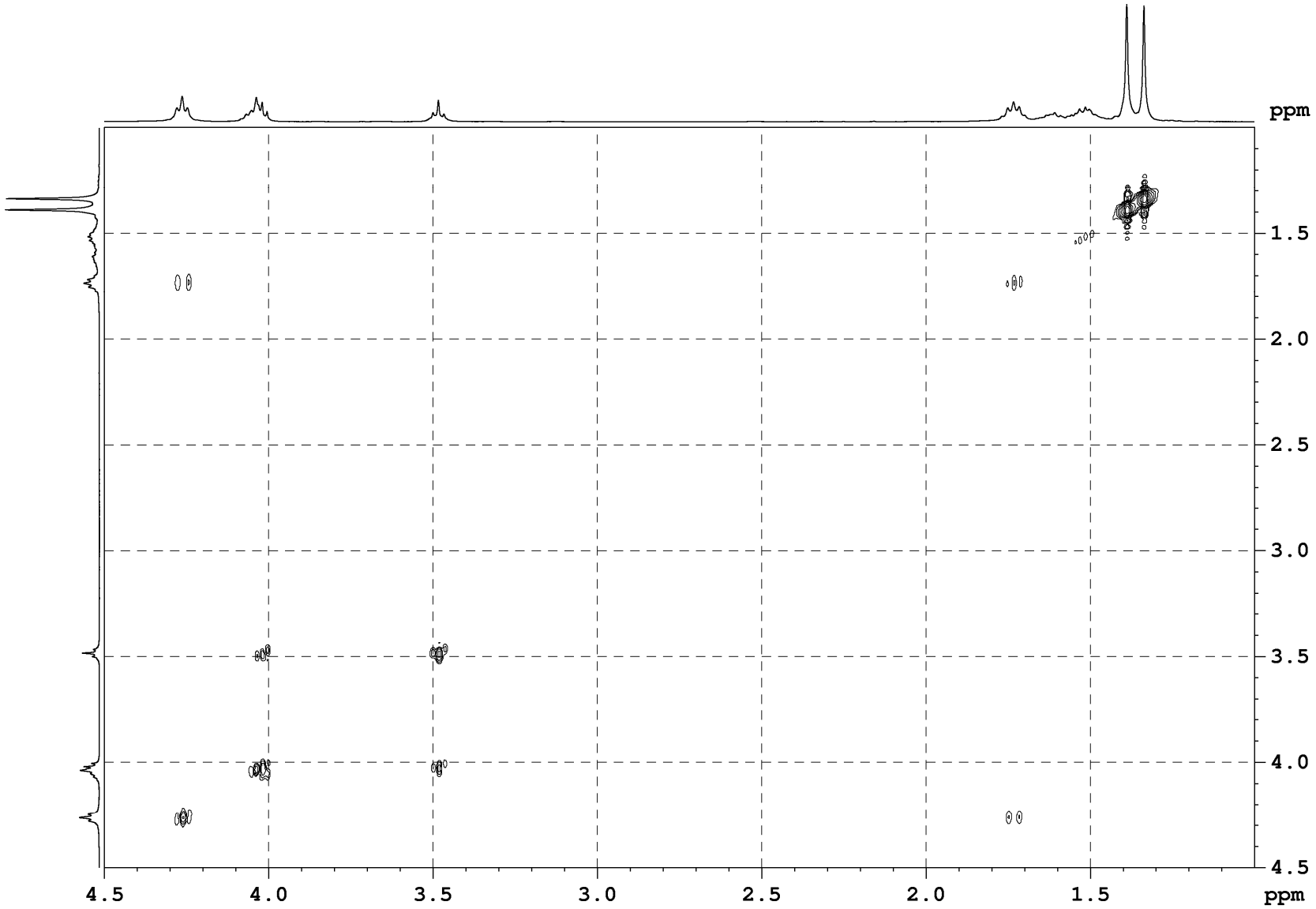

Figure S20. 2D ^{1}H-^{1}H COSY spectrum in $CDCl_3$ of **13** (T = 303K).

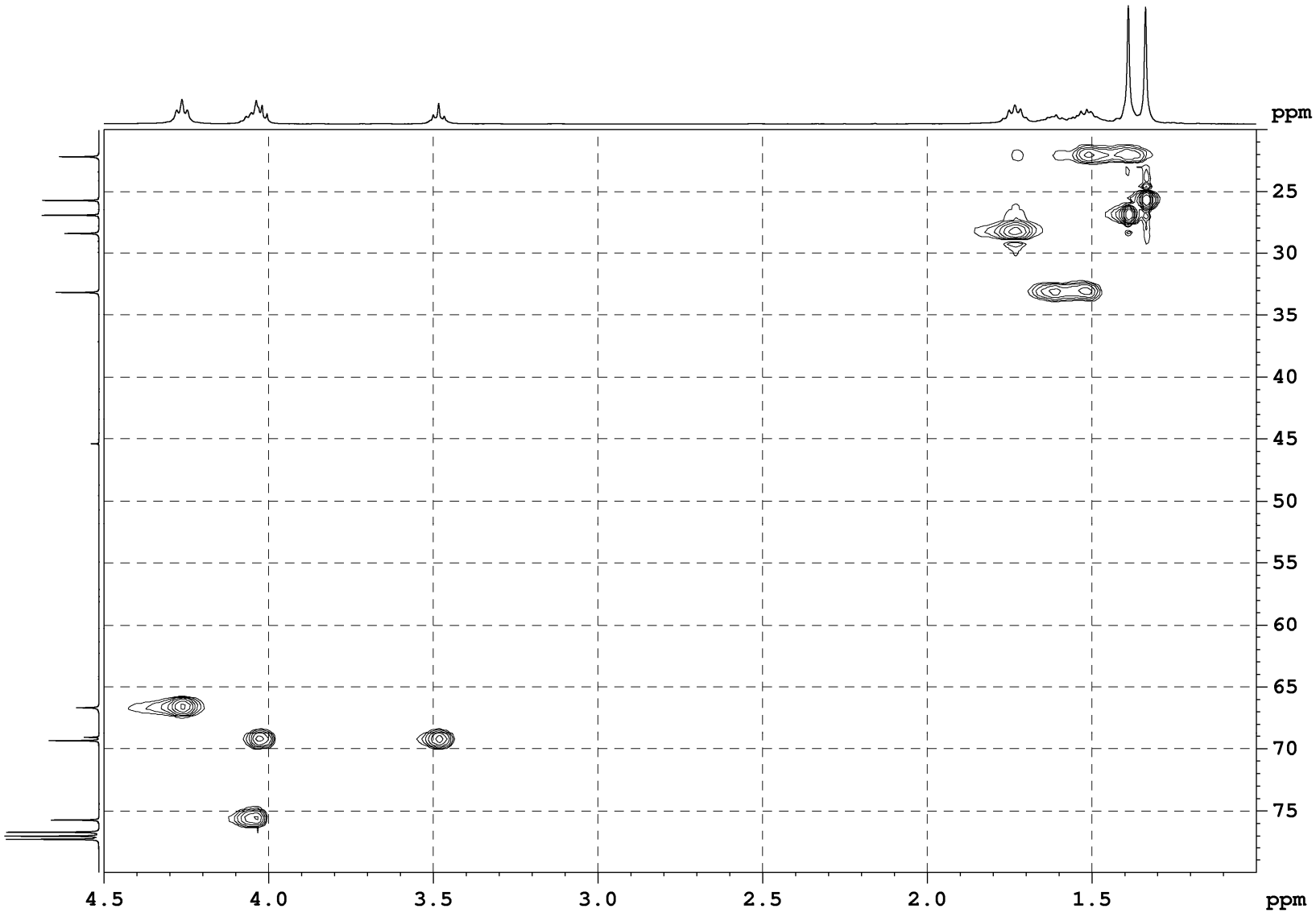

Figure S21. 2D ^{1}H-^{13}C HSQC spectrum in $CDCl_3$ of **13** (T = 303K).

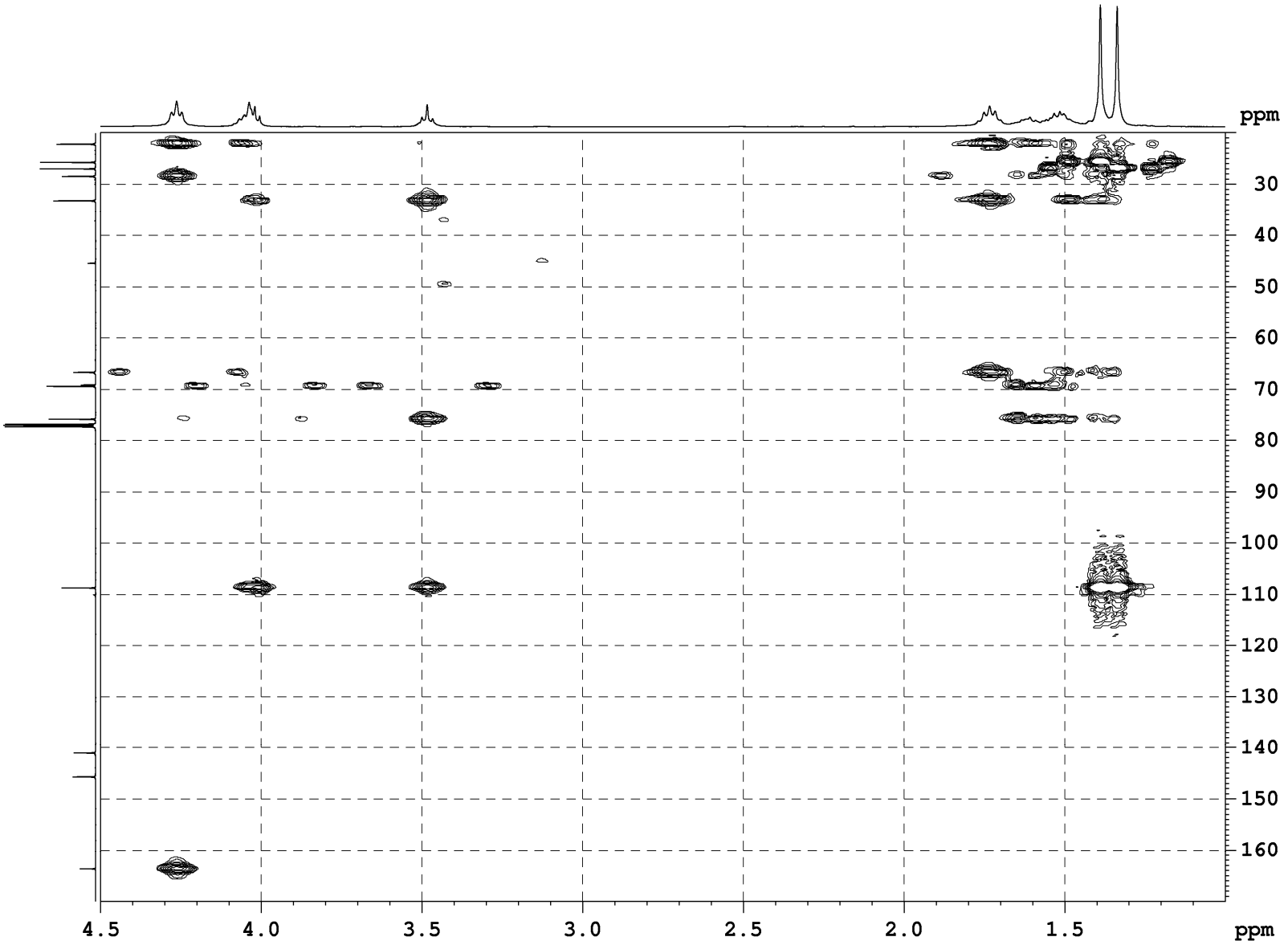

Figure S22. 2D ^{1}H-^{13}C HMBC spectrum in $CDCl_3$ of **13** (T = 303K).

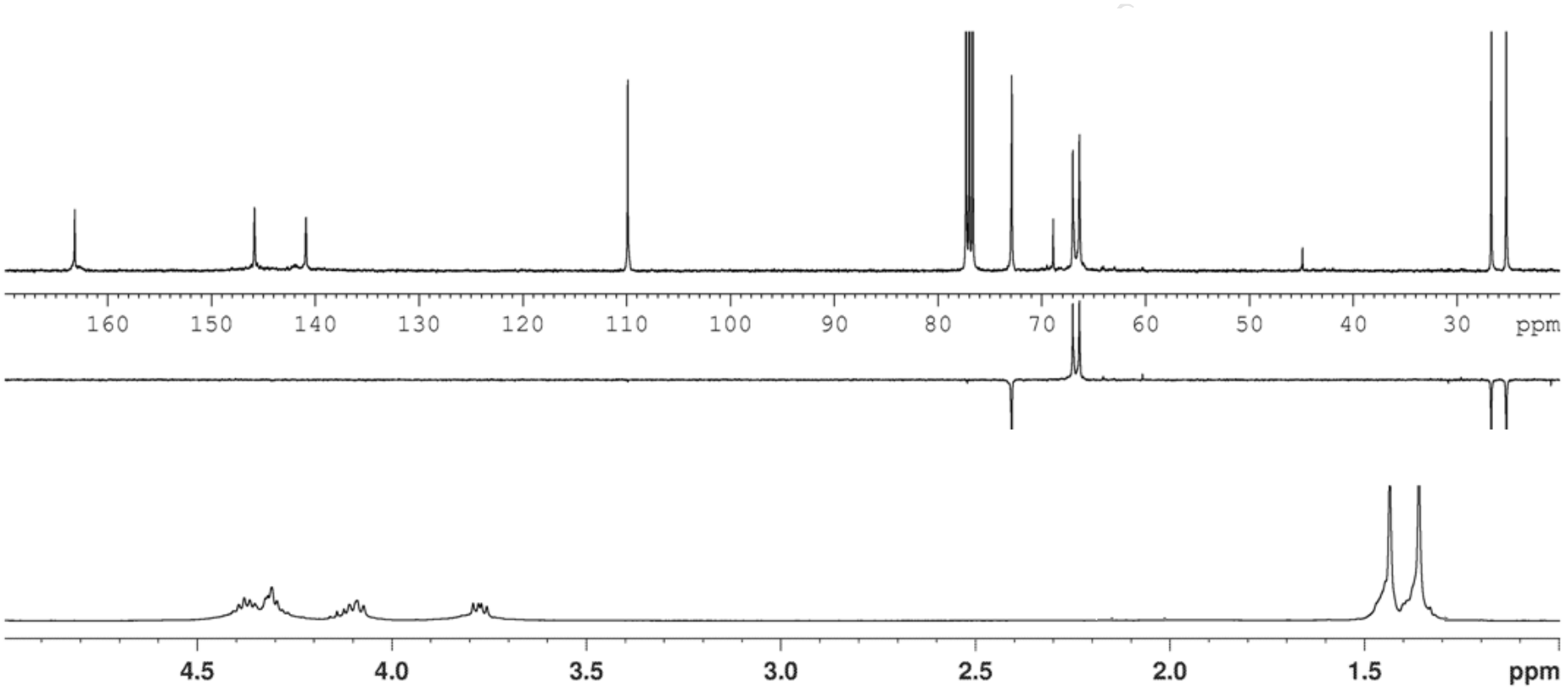

Figure S23. 1D ^{1}H, ^{13}C and DEPT spectra in $CDCl_3$ of **14** (T = 303K).

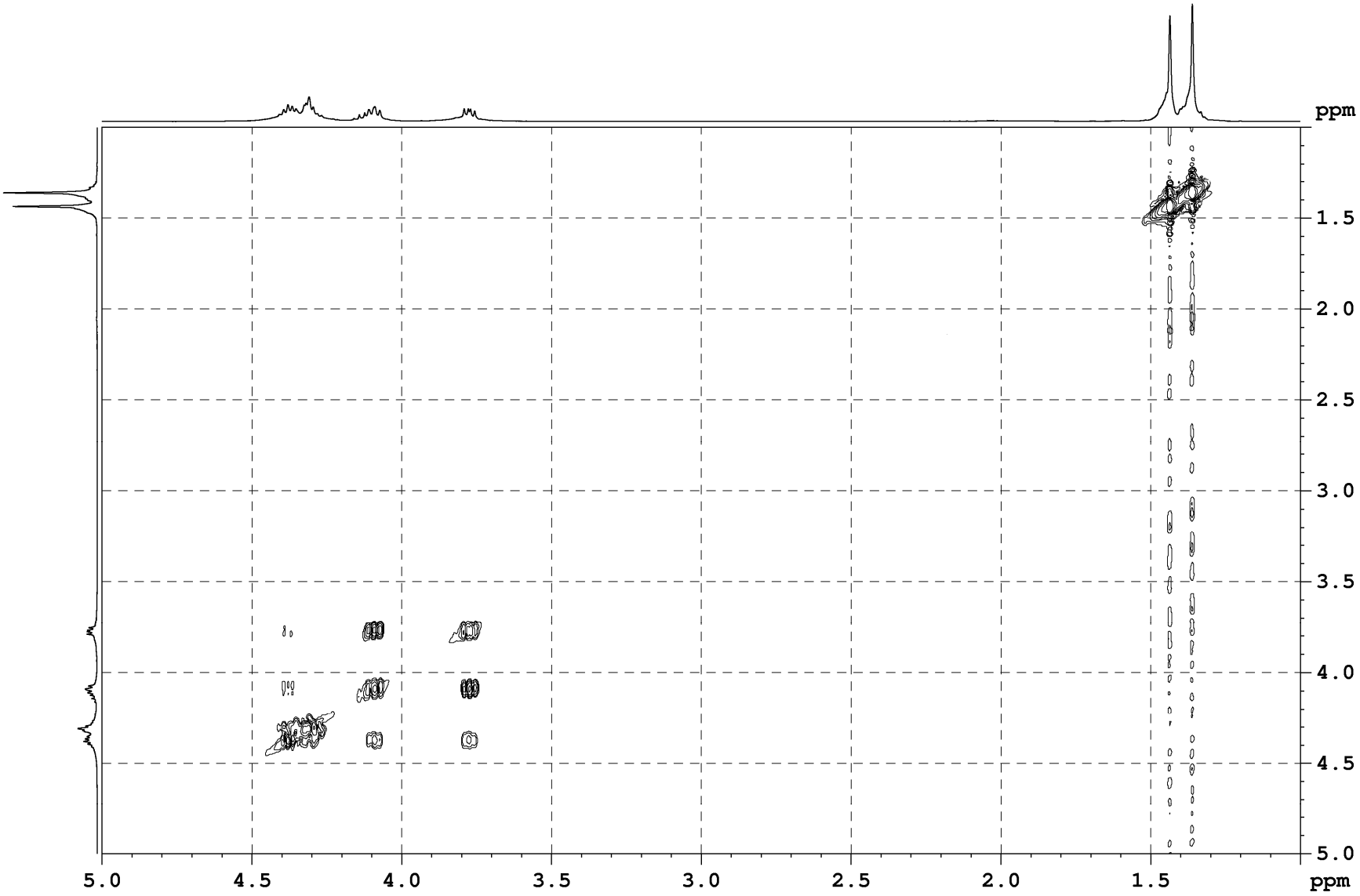

Figure S24. 2D ^{1}H-^{1}H COSY spectrum in $CDCl_3$ of **14** (T = 303K).

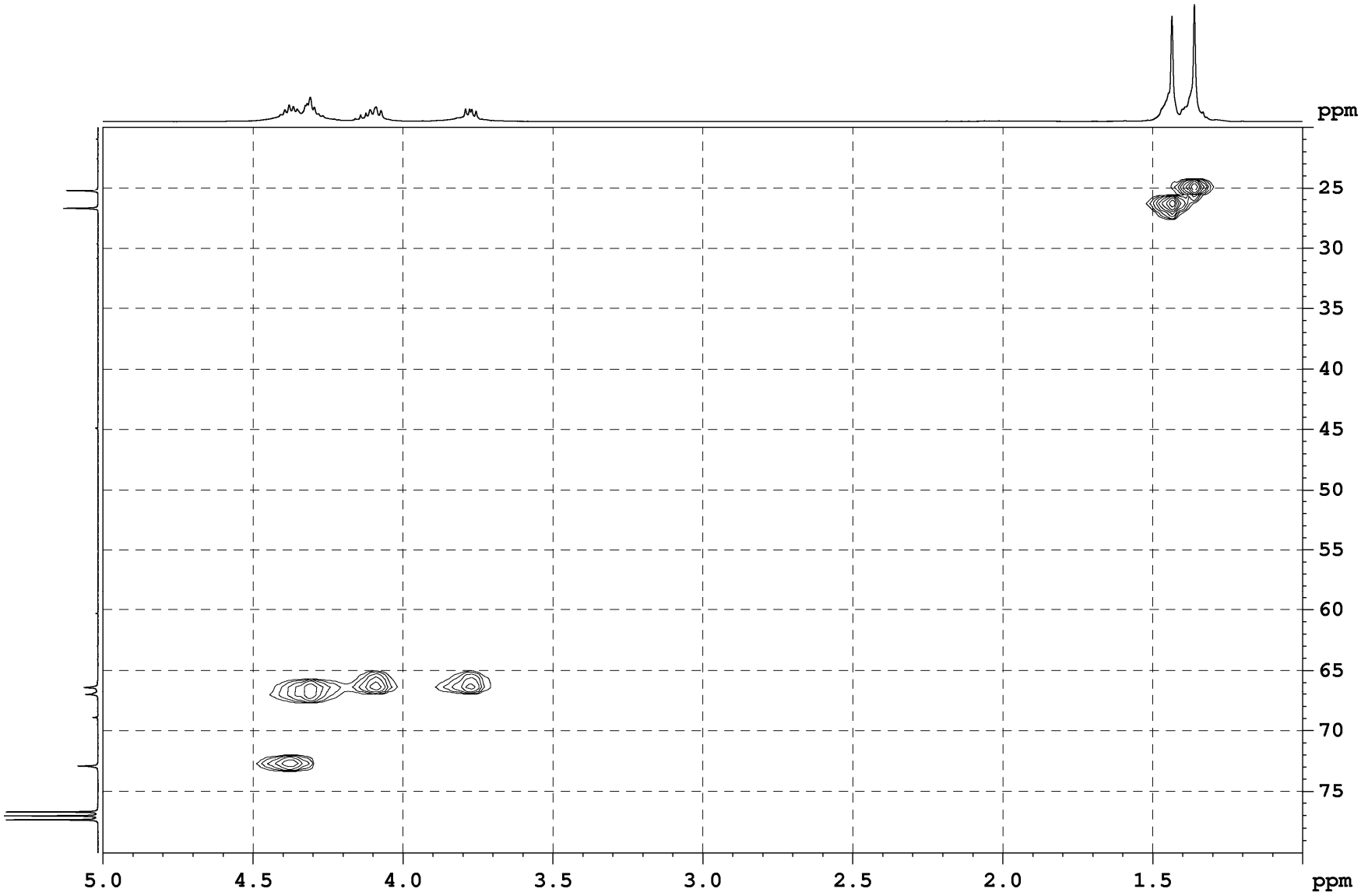

Figure S25. 2D ^{1}H-^{13}C HSQC spectrum in $CDCl_3$ of **14** (T = 303K).

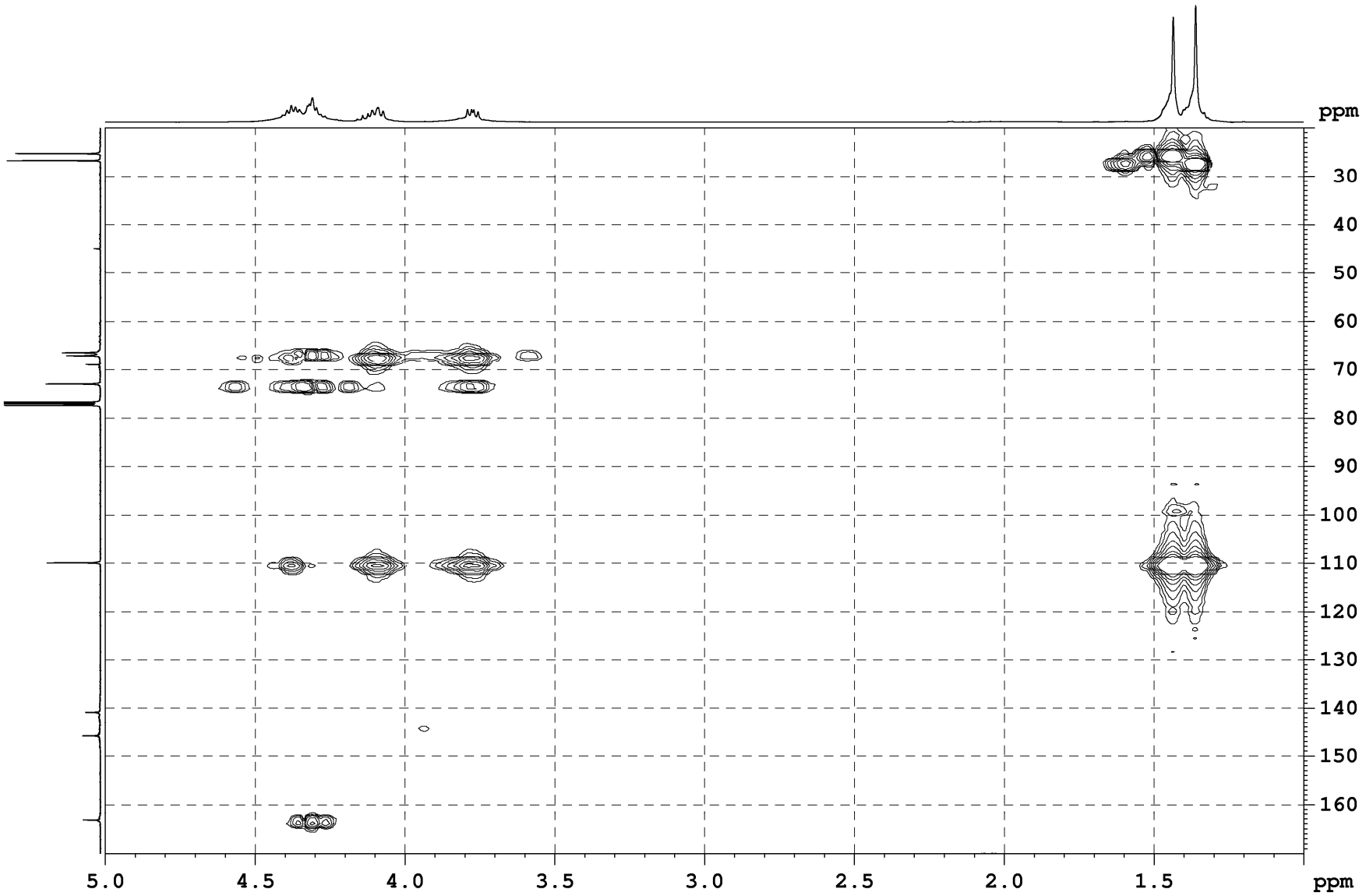

Figure S26. 2D ^{1}H-^{13}C HMBC spectrum in $CDCl_3$ of **14** (T = 303K).

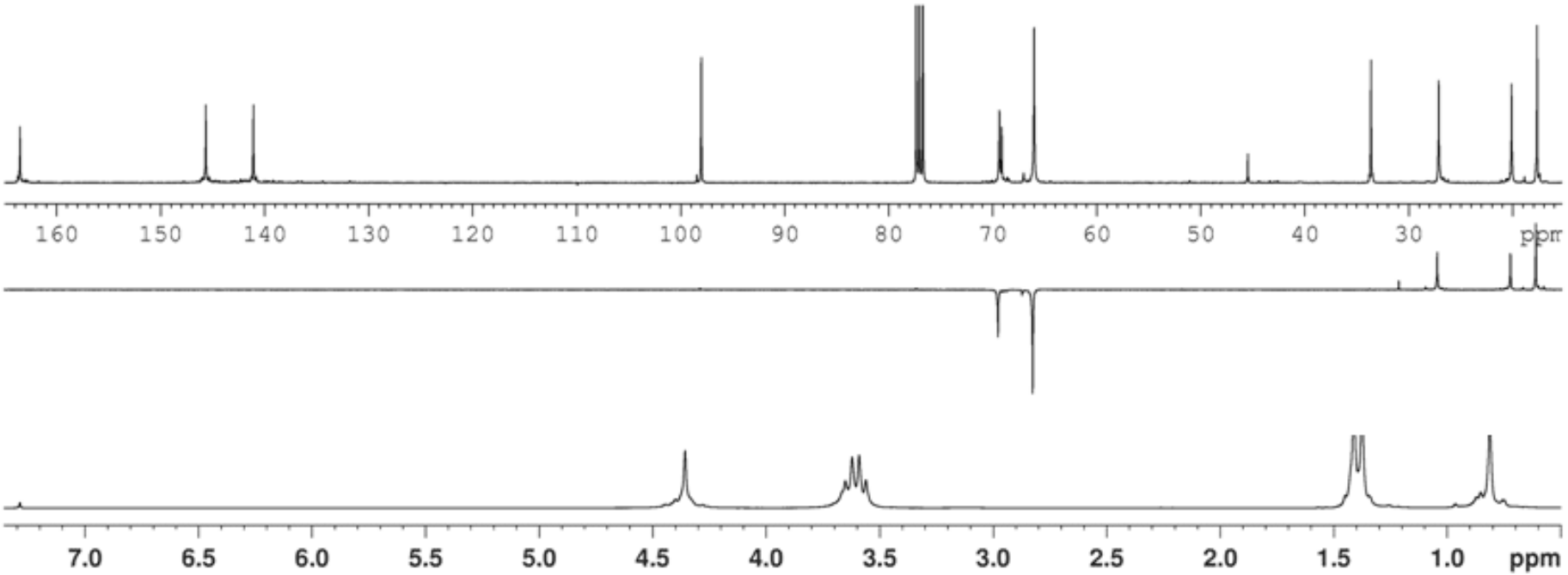

Figure S27. 1D ^{1}H, ^{13}C and DEPT spectra in $CDCl_3$ of **15** (T = 303K).

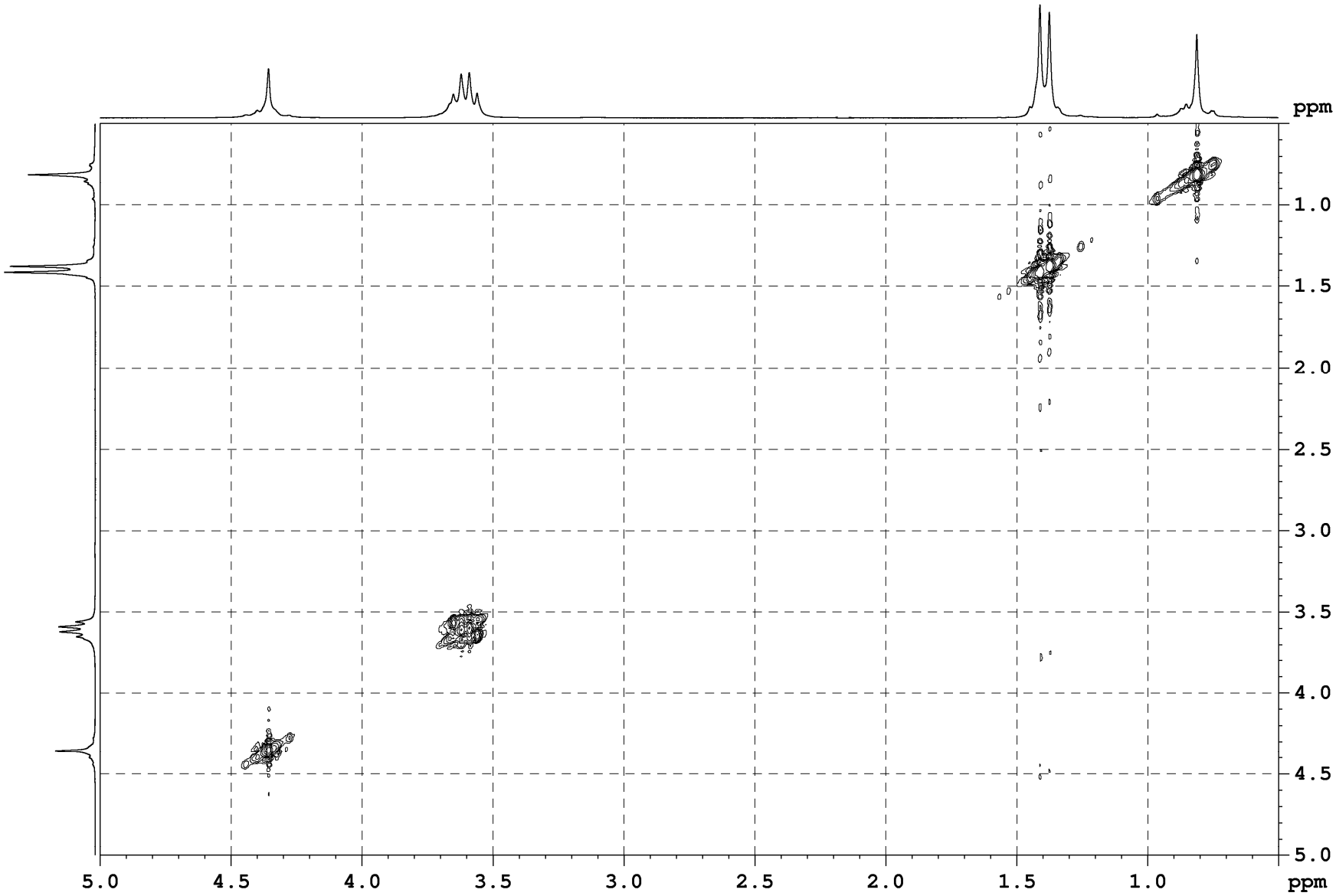

Figure S28. 2D ^{1}H-^{1}H COSY spectrum in $CDCl_3$ of **15** (T = 303K).

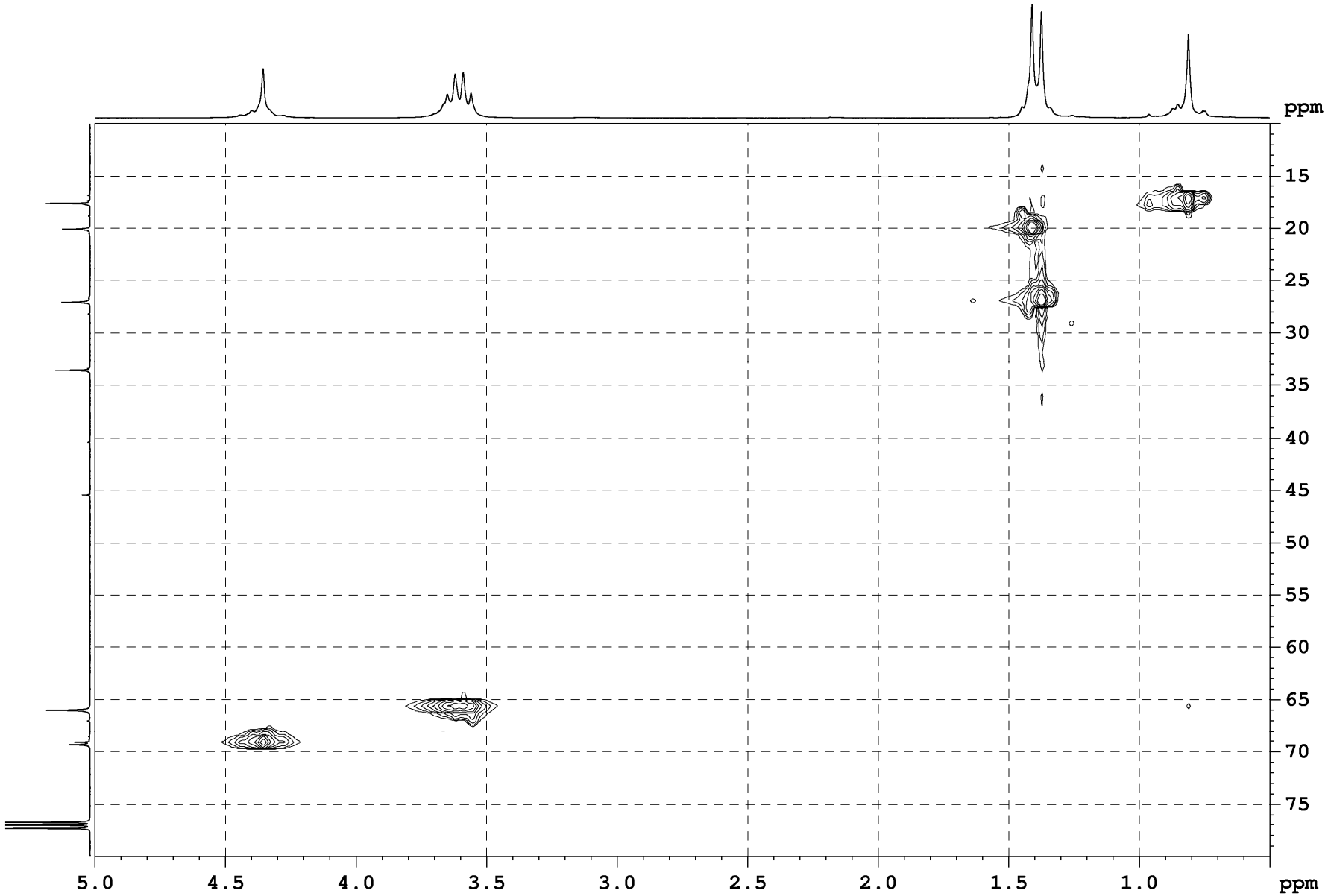

Figure S29. 2D ^{1}H-^{13}C HSQC spectrum in $CDCl_3$ of **15** (T = 303K).

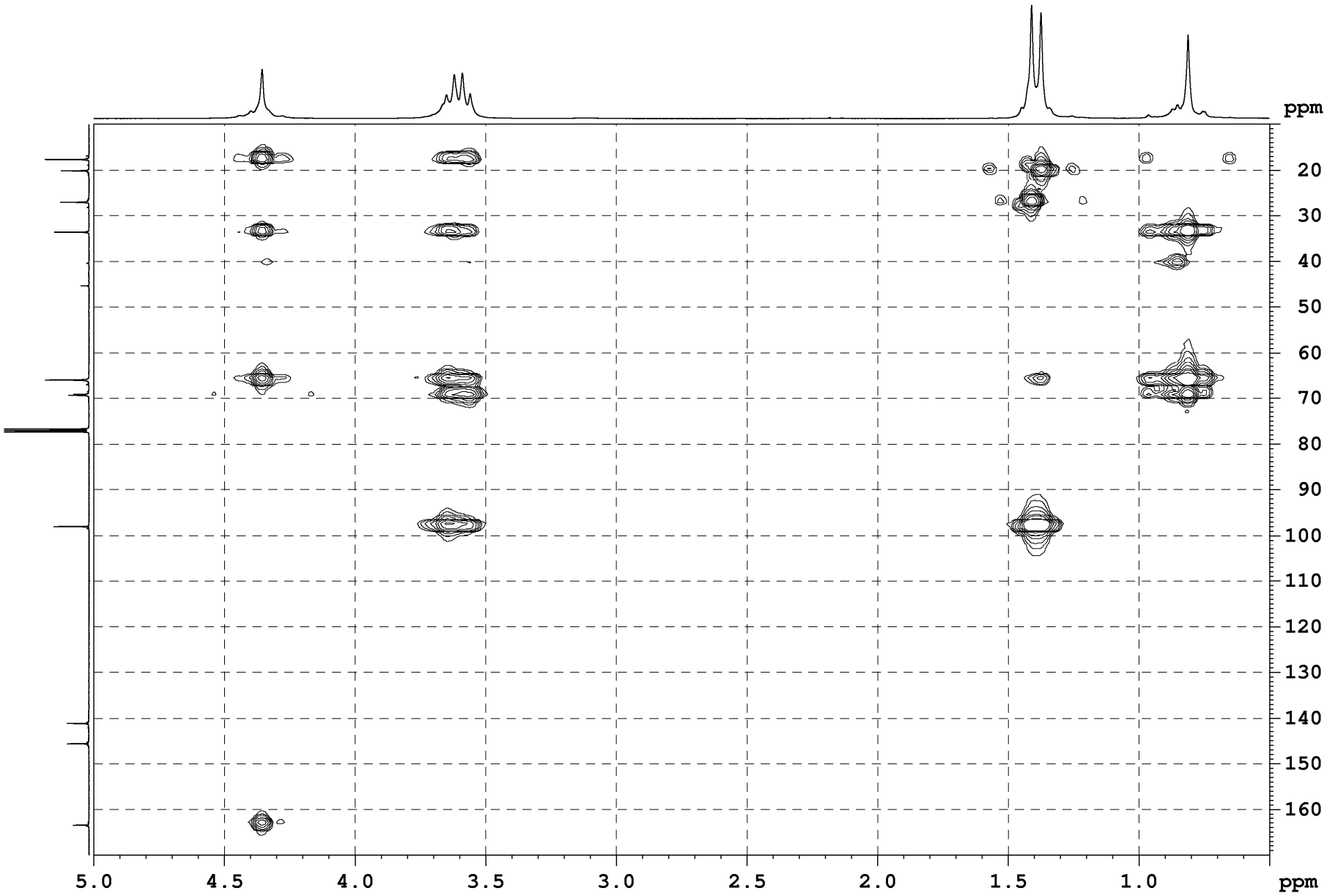

Figure S30. 2D ^{1}H-^{13}C HMBC spectrum in $CDCl_3$ of **15** (T = 303K).

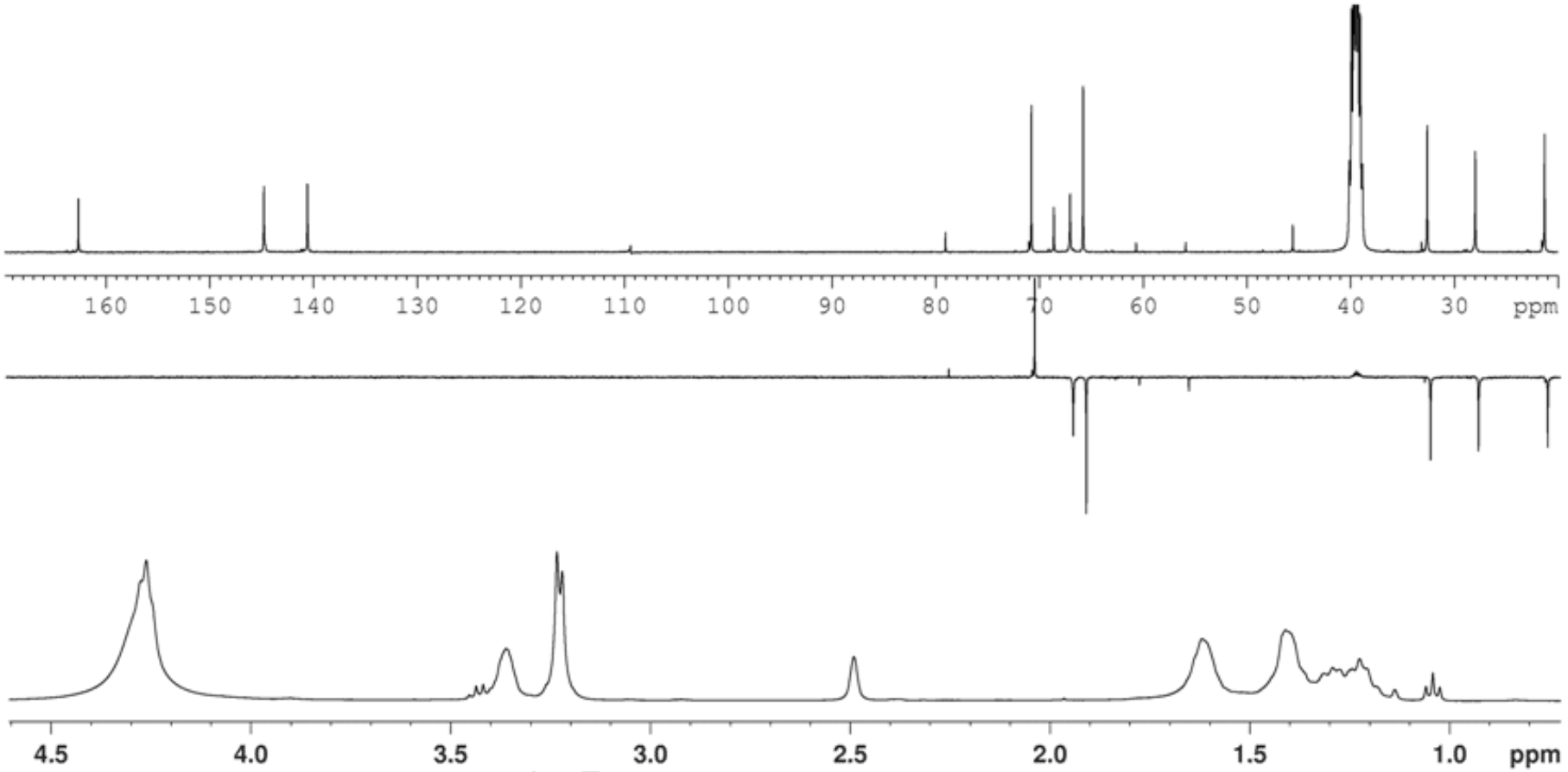

Figure S31. 1D ^{1}H, ^{13}C and DEPT spectra in DMSO of **16** (T = 303K).

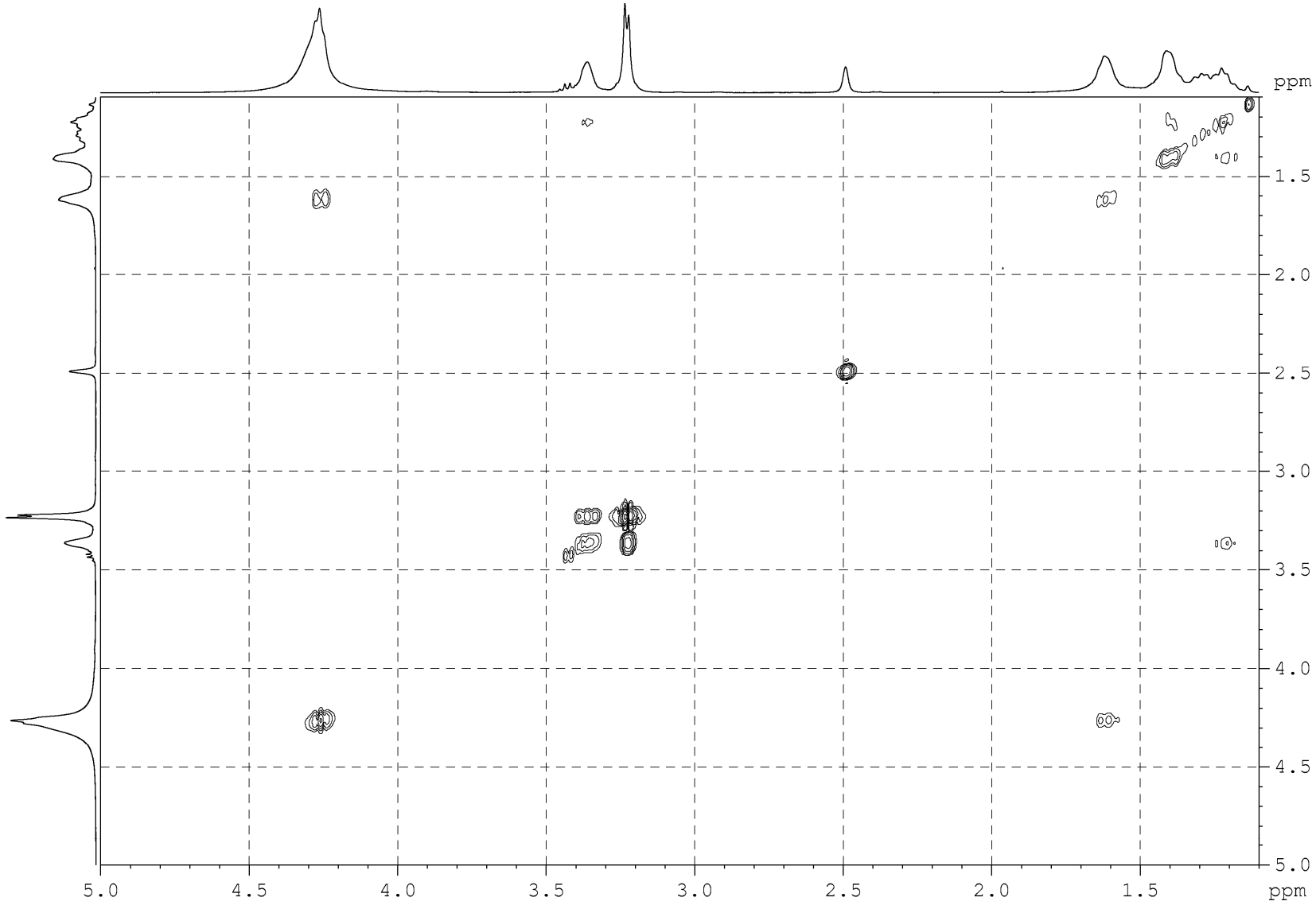

Figure S32. 2D ^{1}H-^{1}H COSY spectrum in DMSO of **16** (T = 303K).

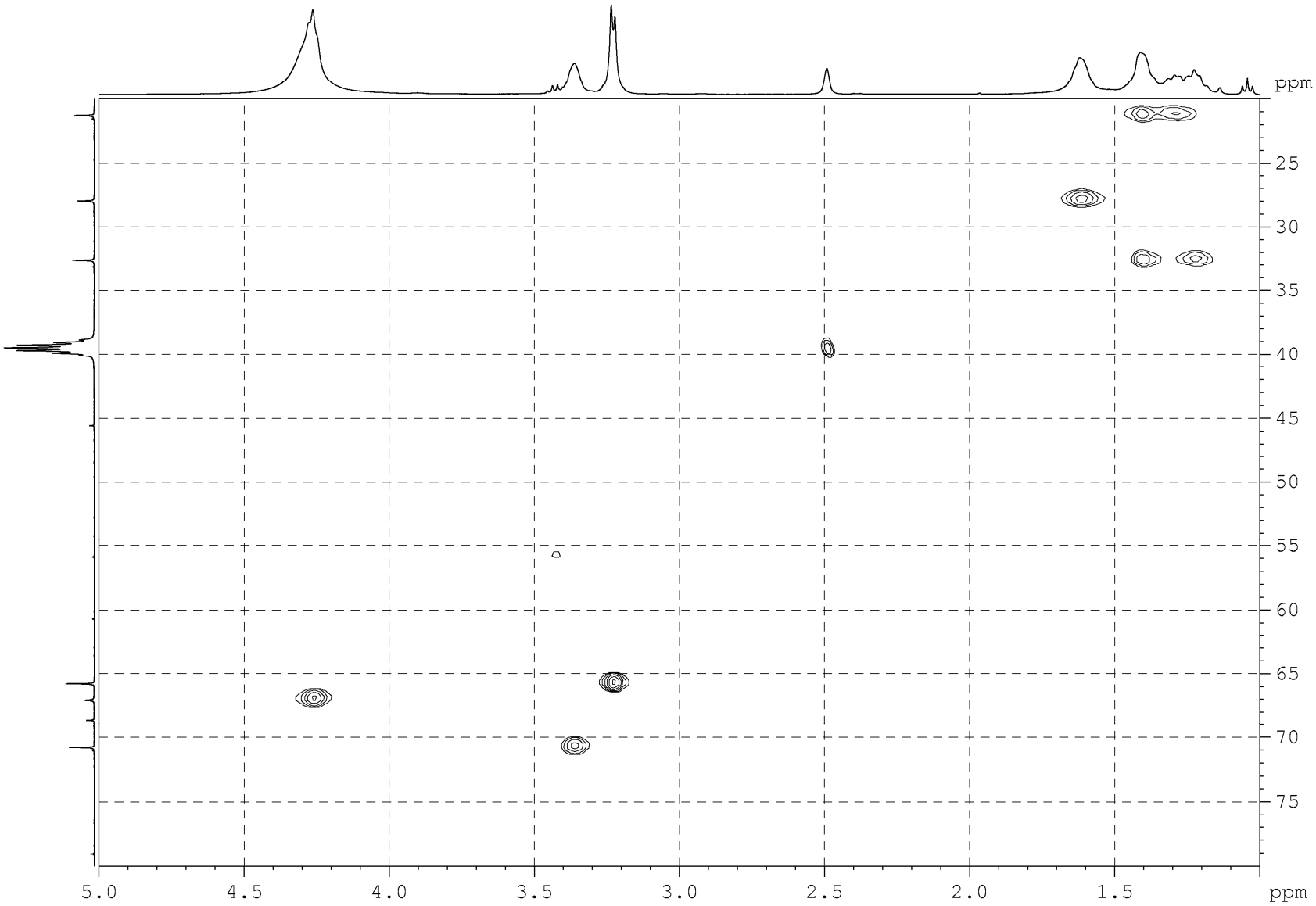

Figure S33. 2D ^{1}H-^{13}C HSQC spectrum in DMSO of **16** (T = 303K).

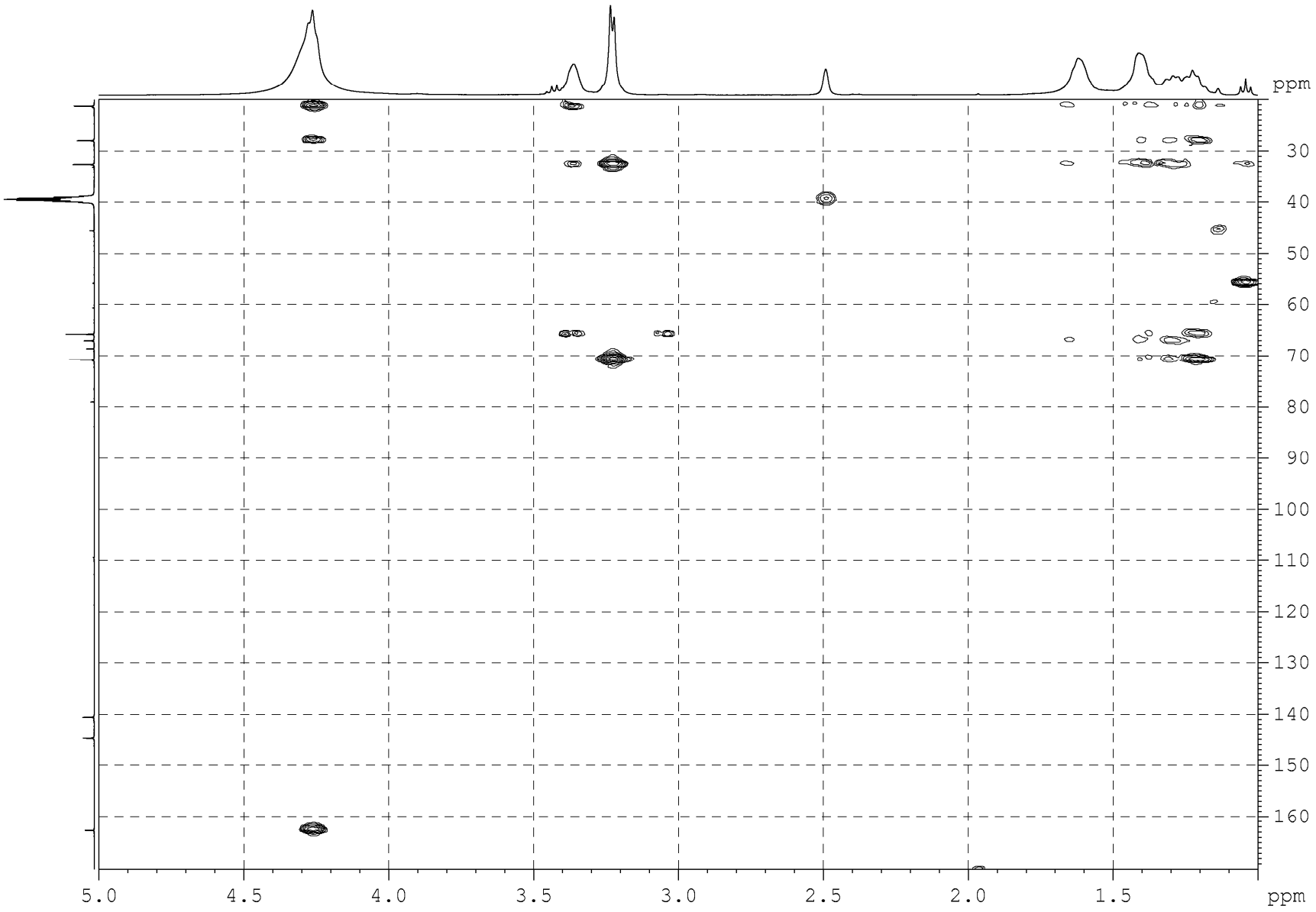

Figure S34. 2D ^{1}H-^{13}C HMBC spectrum in DMSO of **16** (T = 303K).

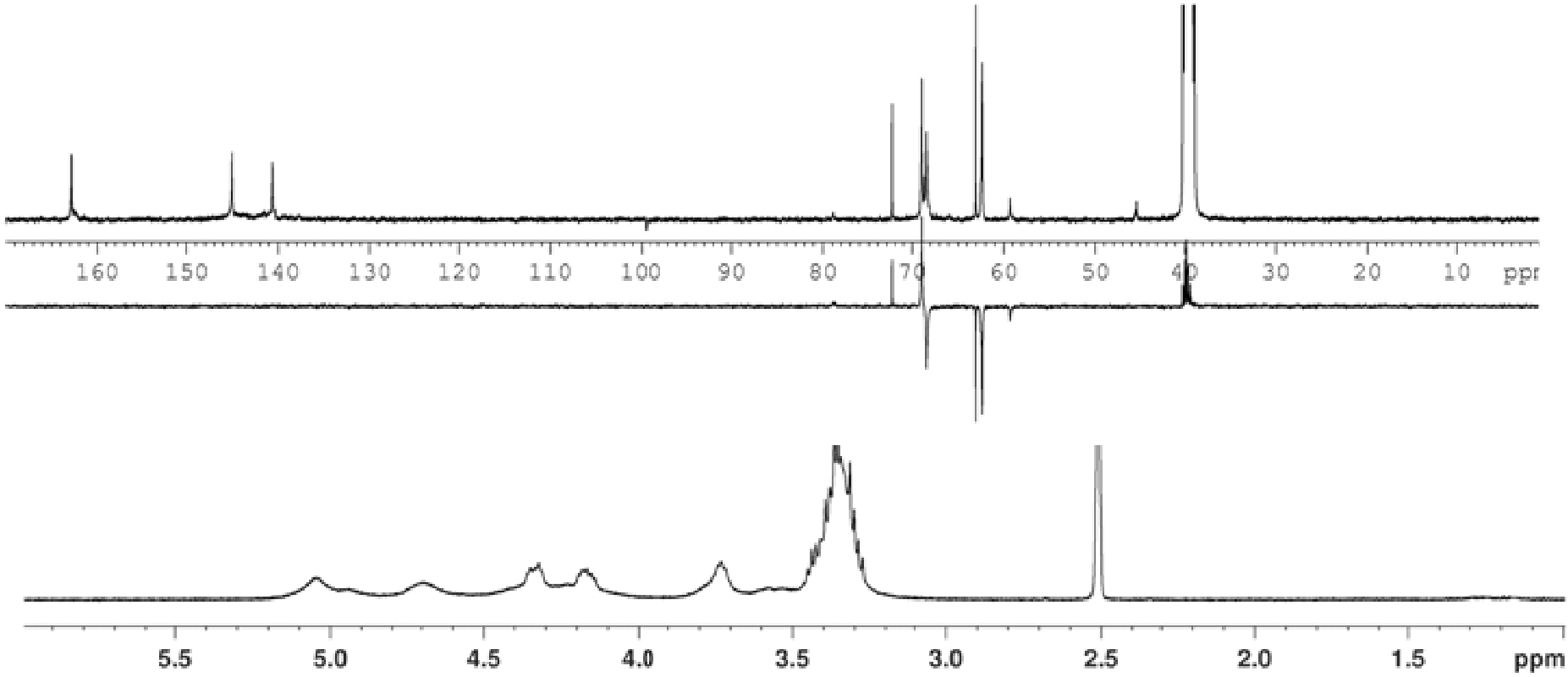

Figure S35. 1D ^{1}H, ^{13}C and DEPT spectra in DMSO of **17** (T = 303K).

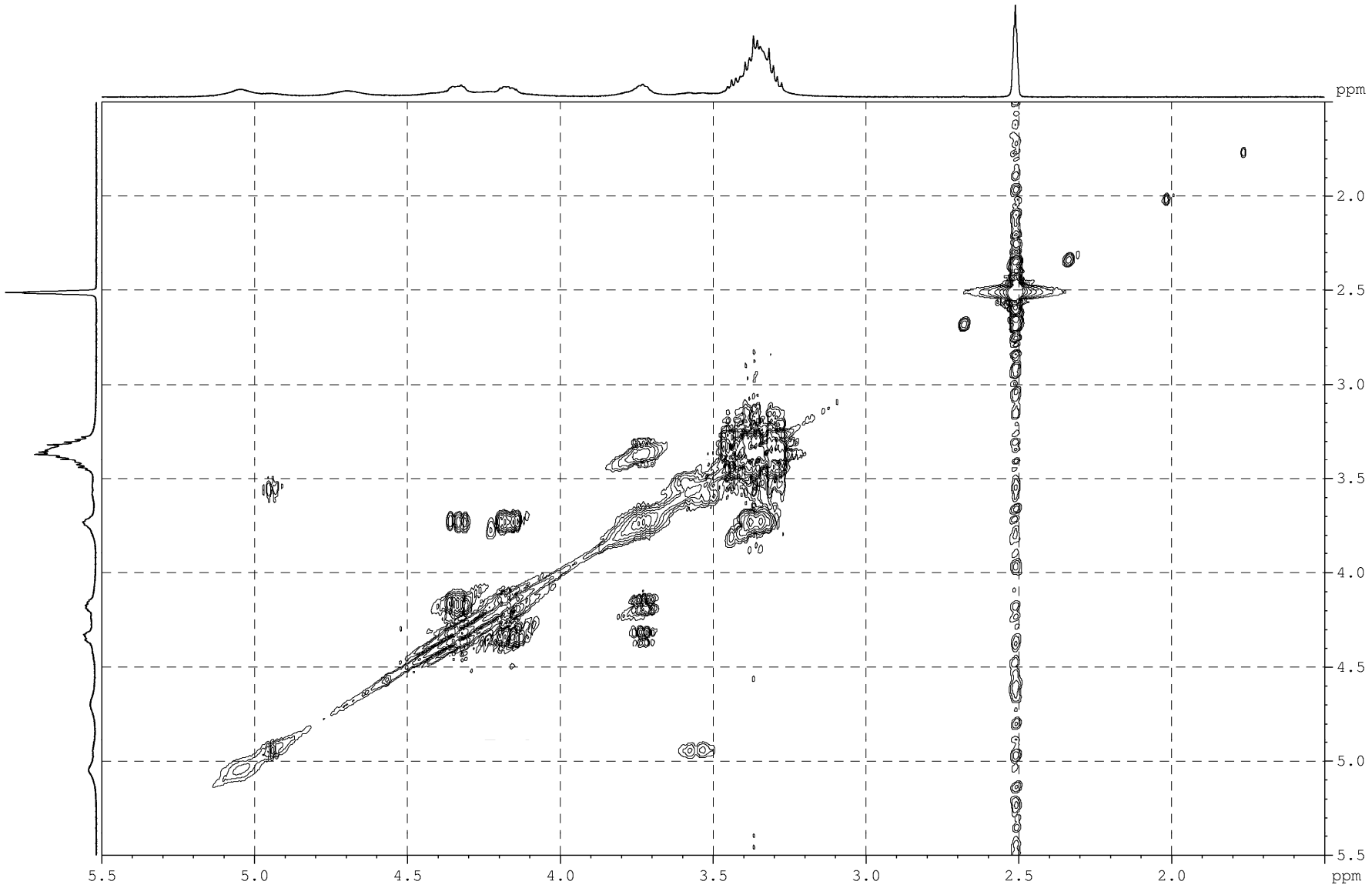

Figure S36. 2D ^{1}H-^{1}H COSY spectrum in DMSO of **17** (T = 303K).

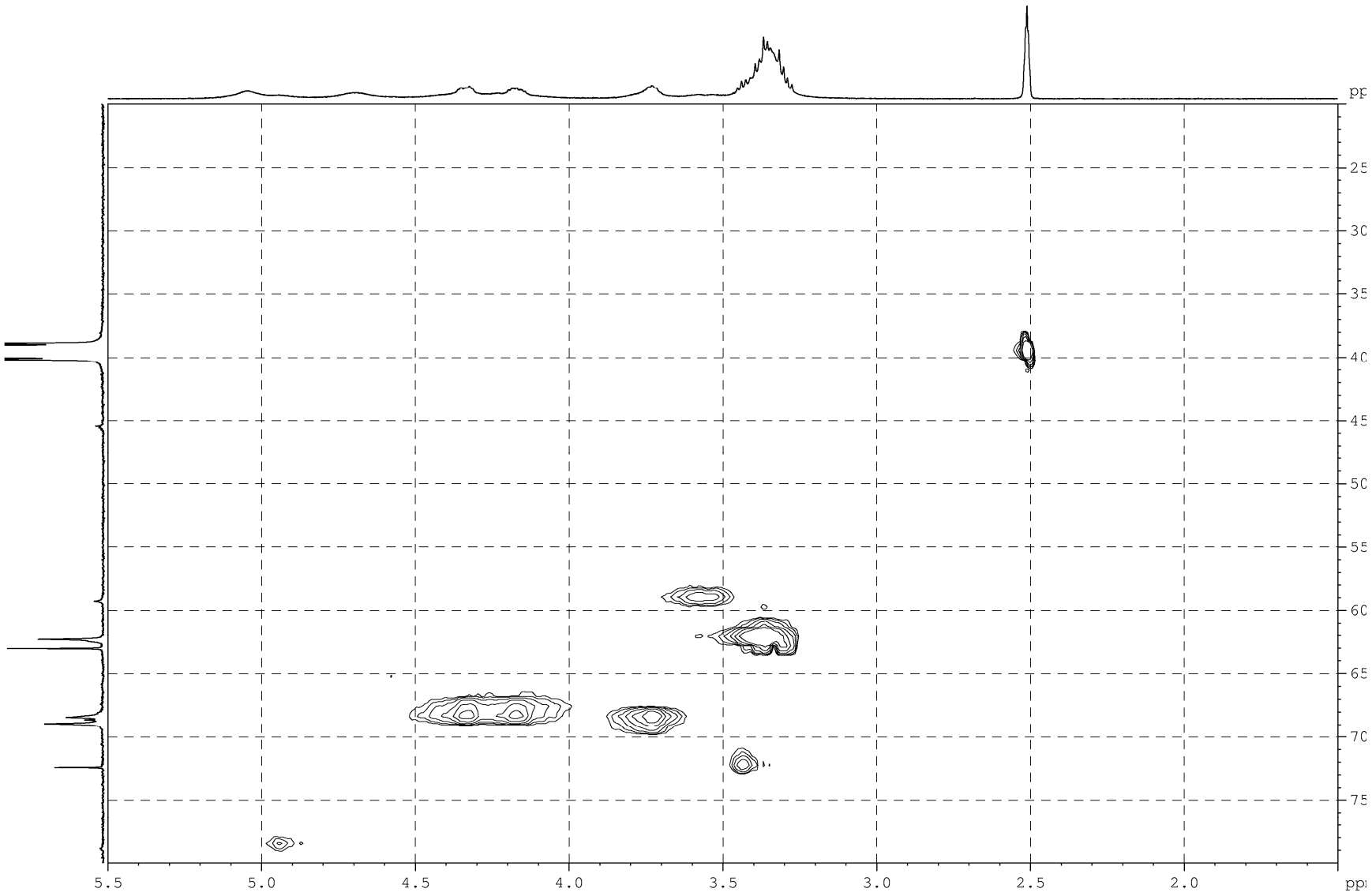

Figure S37. 2D ^{1}H-^{13}C HSQC spectrum in DMSO of **17** (T = 303K).

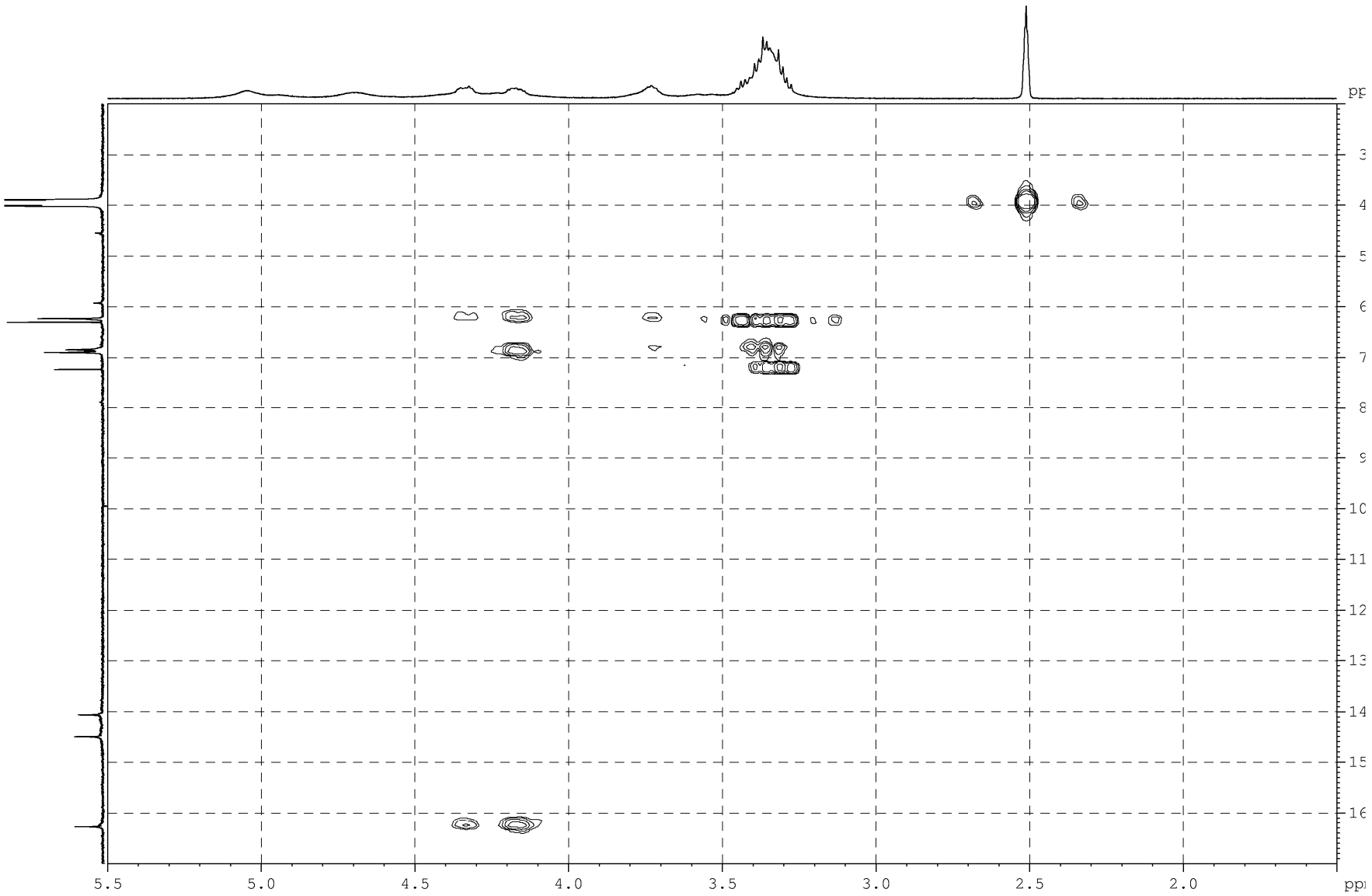

Figure S38. 2D ^{1}H-^{13}C HMBC spectrum in DMSO of **17** (T = 303K).

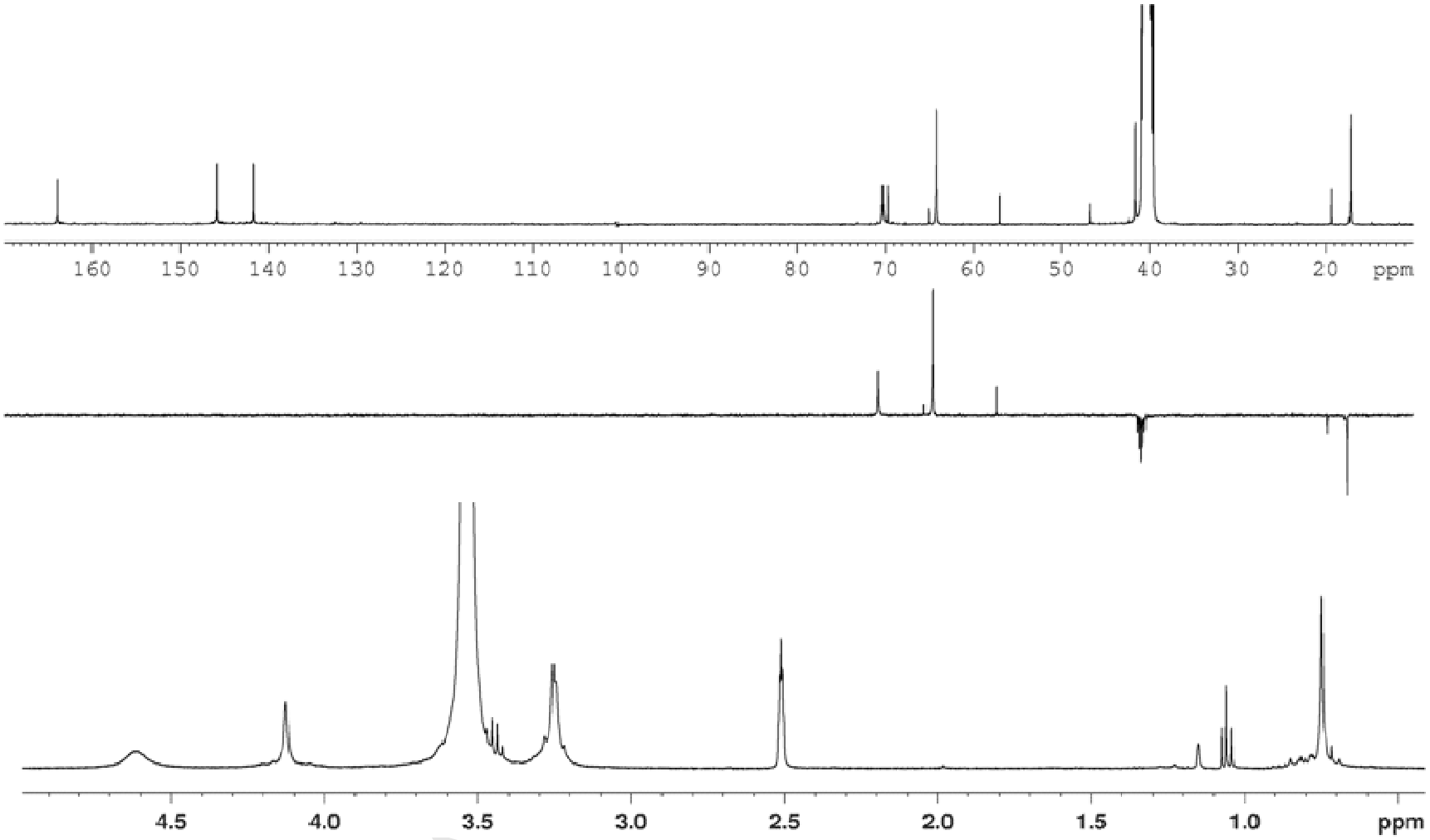

Figure S39. 1D ^{1}H, ^{13}C and DEPT spectra in DMSO of **18** (T = 303K).

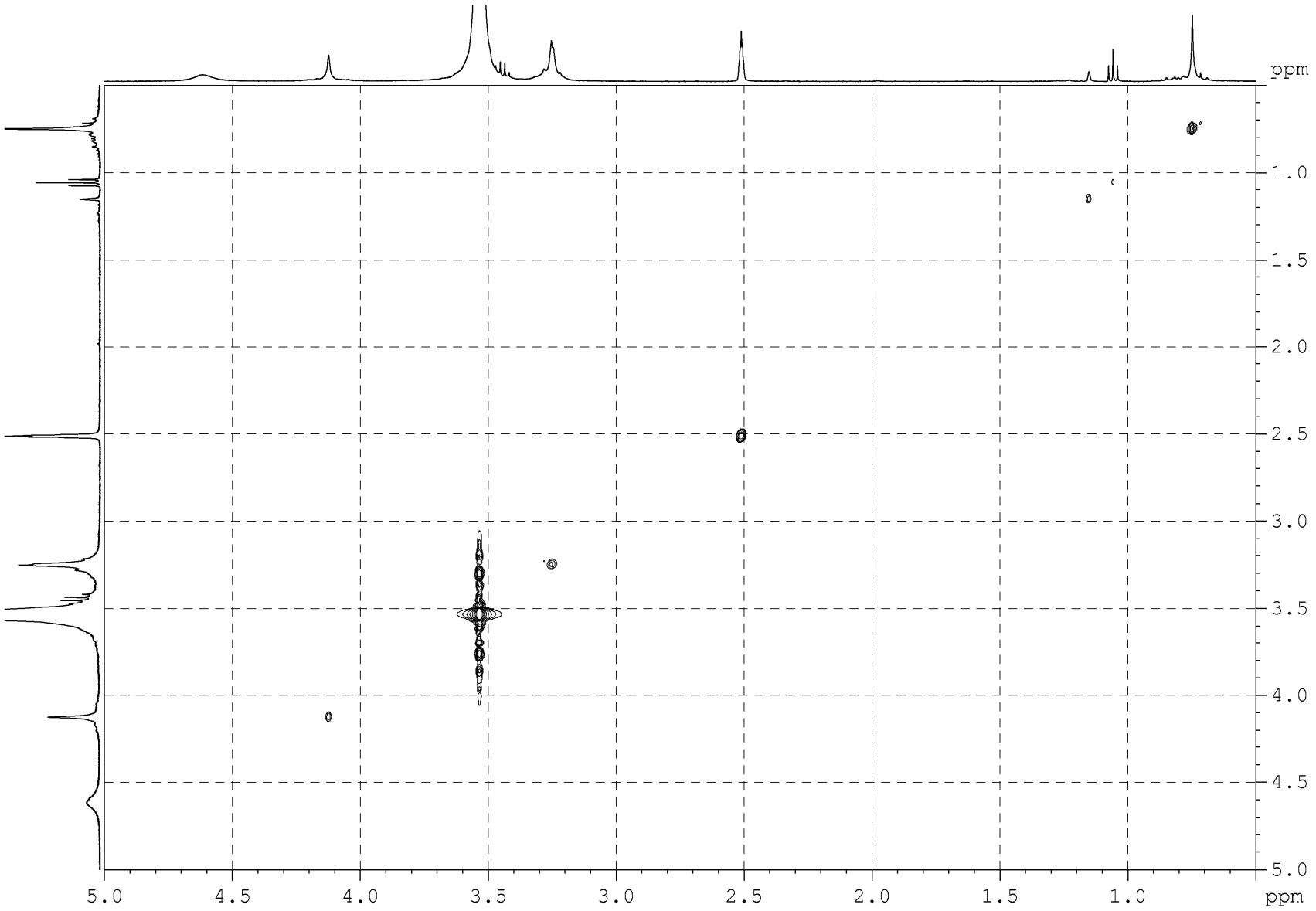

Figure S40. 2D ^{1}H-^{1}H COSY spectrum in DMSO of **18** (T = 303K).

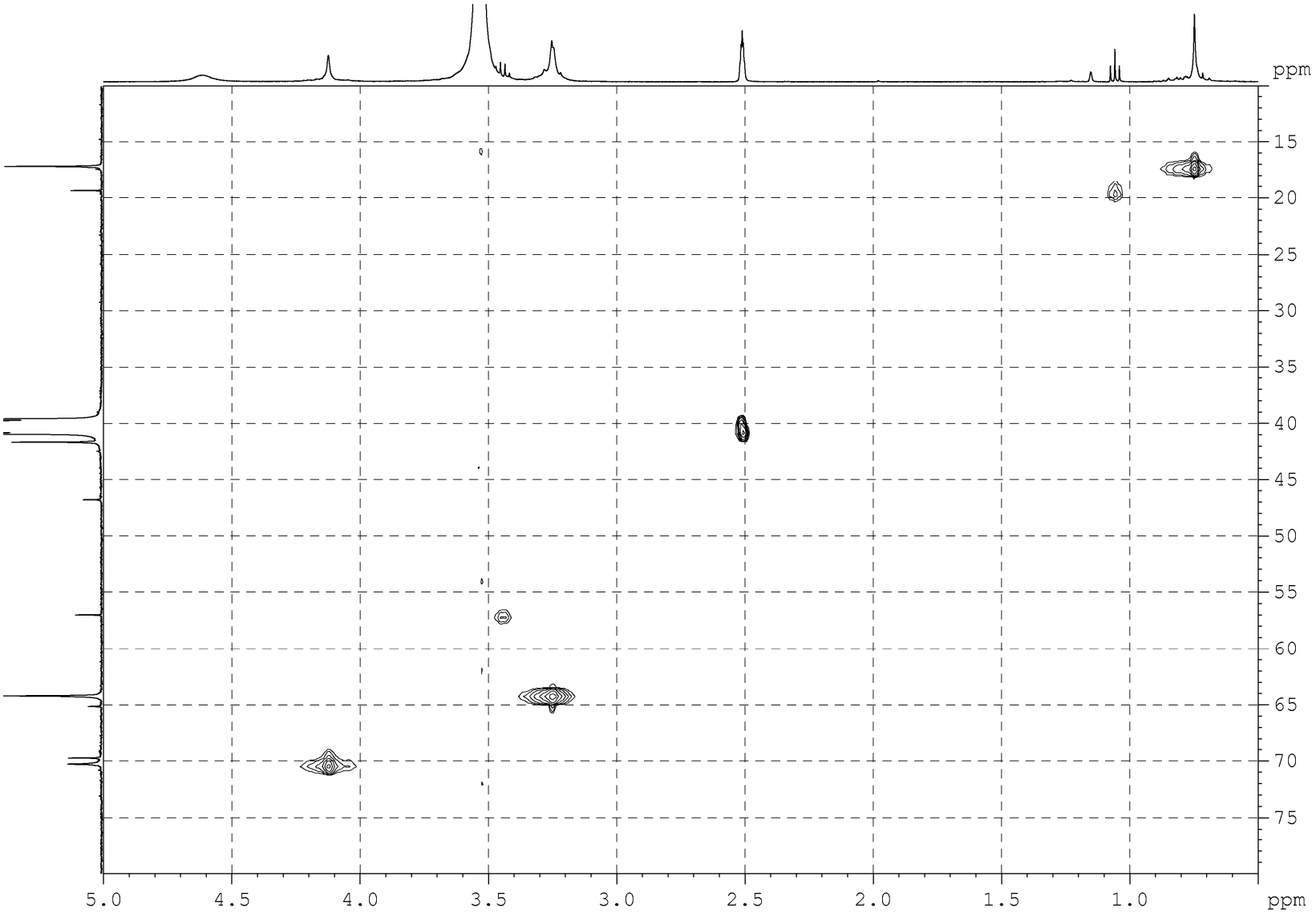

Figure S41. 2D ^{1}H-^{13}C HSQC spectrum in DMSO of **18** (T = 303K).

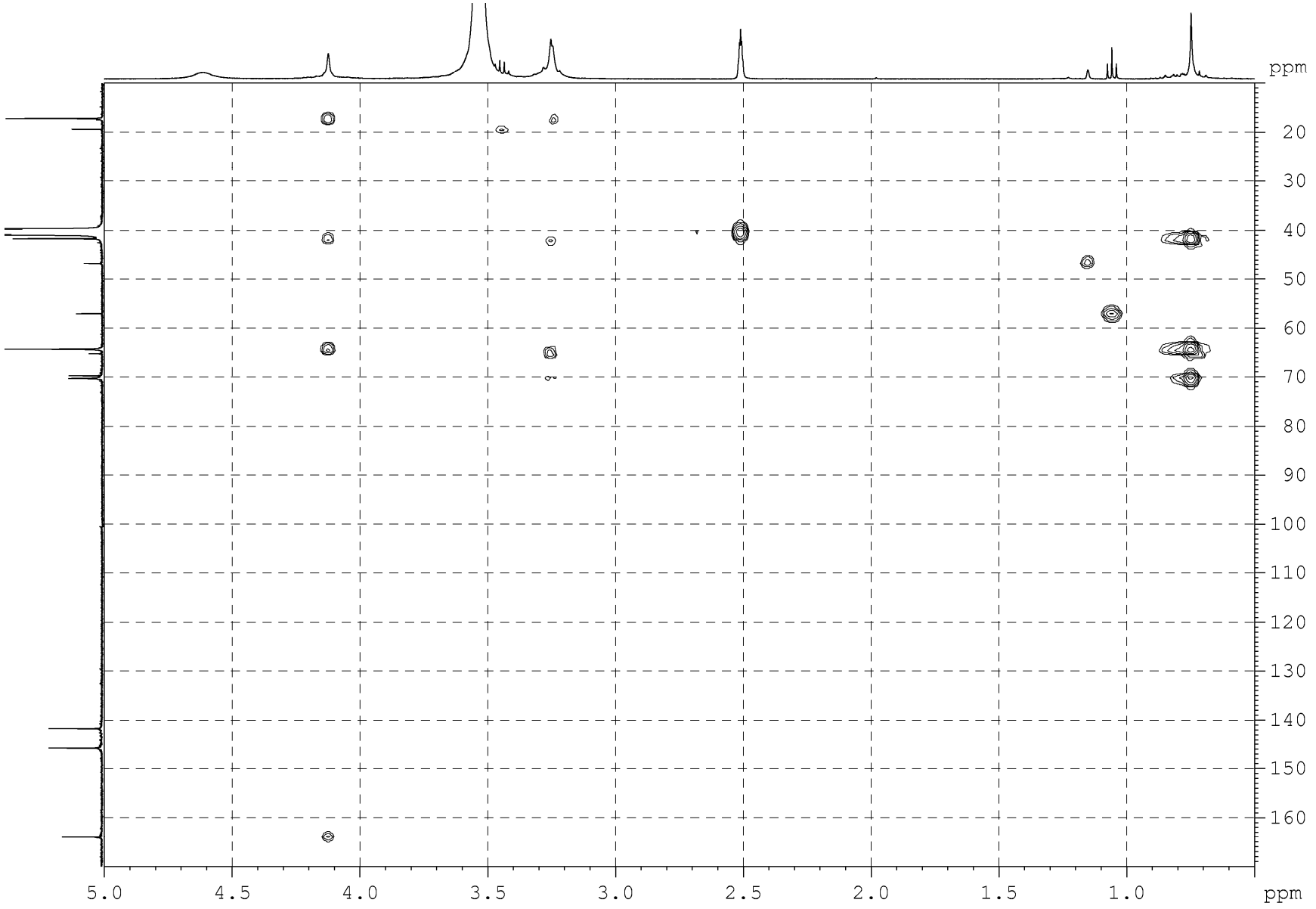

Figure S42. 2D ^{1}H-^{13}C HMBC spectrum in DMSO of **18** (T = 303K).