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Application of Appel reaction to the primary alcohol groups of fructooligosaccharides: Synthesis of 6,6′,6″-trihalogenated 1-kestose derivatives

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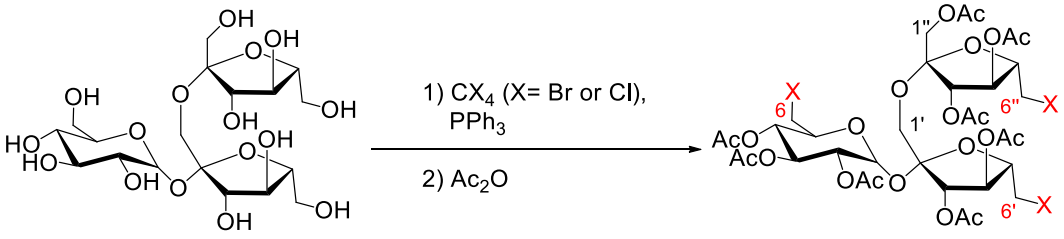
Abstract

1-kestose (*O*-*β*-D-fructofuranosyl-(2→1)-*β*-D-fructofuranosyl-(2→1)-*α*-D-glucopyranoside) is a potential short chain fructooligosaccharide with an inulin-type skeleton. Halogenation of 1-kestose was conducted via the Appel reaction with the use of carbon tetrahalide (CBr_4 or CCl_4) and triphenylphosphine, which was then followed by conventional acetylation. The per-*O*-acetylated form of 6,6′,6′′-trihalogenated derivatives of 1-kestose were conveniently isolated. Further deprotection of the per-*O*-acetylated form resulted in 6-, 6′-, and 6′′-trihalogenated derivatives. The structure elucidation by one- and two-dimensional nuclear magnetic resonance established that halogenations are specific at the 6-, 6′-, and 6′′-position of 1-kestose primary alcohols.



Keywords: Appel reaction; nuclear magnetic resonance (NMR); primary alcohol; regioselective halogenations; 1-kestose; fructooligosaccharides

Introduction

Inulin-type short-chain fructooligosaccharides (FOS) are fructose oligomers that consist of a terminal glucosyl unit and two to five fructosyl units. They are recognized as prebiotic indigestible organosaccharides[1] and due to this property, FOS demand has been increasing in the food industry.[2] 1-Kestose (**1,** Figure 1) is one of FOS that has a *β*-D-fructofuranosyl group on O-1 of the D-fructosyl moiety of sucrose (**2,** Figure 1). 1-Kestose **1** is naturally found in honey and some plants belonging to the Amaryllidaceae family.[3–5] The interest in 1-kestose **1**, as a low-calorie food ingredient, continues to increase due to its sweetening power. FOS syrup enriched by 1-kestose **1** can be used as alternative sweetener for diabetics.[6] To produce 1-kestose **1**, the enzyme derived from the leaves of sugar beets have demonstrated transfructosylation activity in the present of sucrose **2**; thus, the products of transfer were mainly 1-kestose **1** with smaller proportions of other oligosaccharides.[7] Commercial cellulolytic enzymes have also been studied for preparation of FOS with high 1-kestose concentrations.[2]

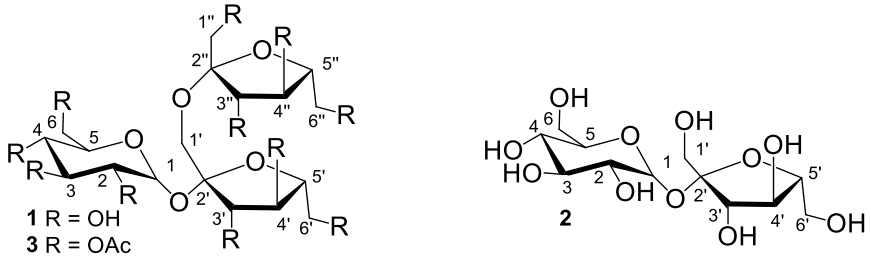


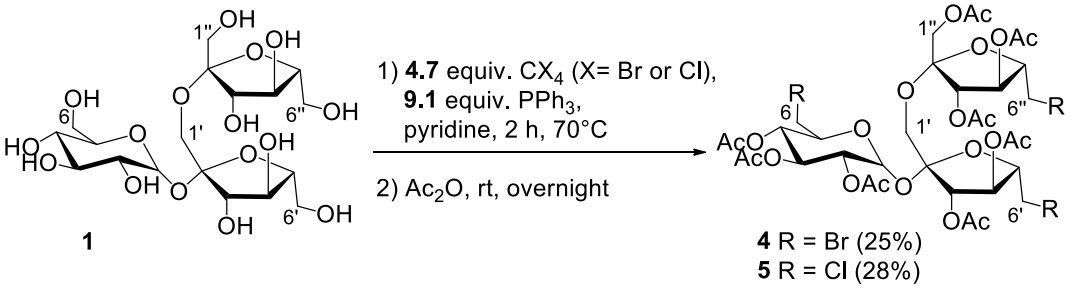
Figure 1. Structure of 1-kestose (**1**), sucrose (**2**), and undecaacetate of 1-kestose (**3**).

Since the specific substitution of sucrose primary hydroxyl groups by chloride enhances the sweetness activity,[8] halogenated carbohydrate derivatives can potentially be used as an alternative sweetener. The direct halogenation of the hydroxyl groups of carbohydrate is a convenient method to achieve the synthesis of halogenated carbohydrate on its primary hydroxyl groups. Thus, selective halogenation for carbohydrate has become an area of interest in organic chemistry. The Appel reaction is one of the most important reactions used to convert the primary hydroxyl group into a halo methylene group in the presence of triphenylphosphine and carbon tetrahalide.[9] This method was used for selective halogenation of primary hydroxyl groups over secondary hydroxyl groups in carbohydrates. Halogenation (particularly for chlorination and bromination) of primary alcohols of sucrose **2**[10]—the main precursor for enzyme-catalyst generation of 1-kestose **1**—has been studied since the 1970s[11], but the reactivity of primary hydroxyl groups attained using the Appel reaction has not been completely identified due to limitation of structure analysis. Recently, we reported that sucrose **2** can be selectively brominated and chlorinated using the Appel reaction at only the 6- and 6'- position with no halogenation at 1'-position supported by one- and two-dimensional (1D and 2D, respectively) NMR analysis.[12] As for trisaccharide modification, halogenation of the primary hydroxyl groups of raffinose (*O*-*α*-D-galactopyranosyl-(1→6)-*α*-D-glucopyranosyl-(1→2)-*β*-D-fructofuranoside) has been reported previously.[13] Raffinose reacted with sulfuryl chloride and the authors found that the chlorinated proportion at the primary position was followed by chlorination at the 4-position of the galactopyranosyl moiety secondary alcohols. To date, no study has been attempted to substitute primary alcohols of FOS using halogens. In midst of FOS, 1-kestose **1** has shown relatively high sweetness activity and is already commercially available. Therefore, its primary alcohol modification would potentially increase the synthesis of alternative sweeteners.

In this study, we aimed to synthesize halogenated 1-kestose **1** at the primary position by using the Appel reaction to comprehensively study the structure elucidation supported by 1D and 2D NMR analysis.

Results and Discussion

Direct substitution of 1-kestose **1** with 4.7 equiv. carbon tetrahalide (bromide or chloride) and 9.1 equiv. triphenylphosphine at 70 °C for two hours (Scheme 1) produced a complex mixture with complicated ^{1}H-NMR analysis due to observation of overlap signals, especially the modified primary centers. The mixture was separated after conventional acetylation. Further purification was conducted using an ether and hexane system as the representative mobile phase to isolate halogenated carbohydrate. The ethyl acetate or dichloromethane system cannot be used for the halogenated proportion.[12] The mixture produced halogenated 1-kestose derivatives in the pre-*O*-acetylated form (bromination **4** and chlorination **5**, Scheme 1).



Scheme 1. Halogenation of 1-kestose (**1**) via Appel reaction with Ph_3P and carbon tetrahalide to produce pre-*O*-acetylated form of halogenated 1-kestose derivatives (bromination **4** and chlorination **5**).

The ^{1}H NMR analysis for peracetylated **4** and **5** showed two regions that contribute to the proton resonance of aliphatic sugar groups in the downfield region and halogenated methylene groups located in the upfield region. Based on ^{13}C NMR, three halogenated methylene in the upfield region were easily determined in the halogenated proportion in the 1-kestose derivatives, but the halogenated position remained unclear. Therefore, 2D NMR (COSY, HETCOR, HMQC, HMBC, NOESY, and TOCSY) was used to determine the halogenated position. For this purpose, $CDCl_3$[12,14] was used as the solvent to increase the visibility of the spin system during the analysis. Undecaacetate 1-kestose[3,15] (**3,** Figure 1, Figures SM-17–24 for detail NMR analysis and Table SM-1 for 1D and 2D NMR and comparison of structure elucidation with the literature) was identified and used to understand the sugar skeleton of halogenated 1-kestose derivatives.

During brominated position investigation of the 1-kestose derivative, ^{1}H-NMR of compound **4** showed eight proton signals in the upfield region. The excess of two protons corresponds to the H-1' glycosidic bond of *O*-*β*-D-fructofuranosyl-(2→1)-*β*-D-fructofuranosyl, which showed considerable geminal coupling with a typical pair of doublets at δ = 3.79 and 3.73 ppm (*J* = 10.3 Hz). The correlation between H-1'a and H-1'b with C-2' in HMBC, supported by HETCOR and HMQC, distinguished this spin system (Figures SM-4–6). The same tendency was also demonstrated by the undecaacetate of 1-kestose **3**, which supported the glycosidic bond signals. The additional six proton signals in the upfield region highlighted the specific brominated proportion of compound **4**. A clear pair of doublets at δ = 3.54 and 3.40 ppm (*J* = 2.3, 11.5 Hz and *J* = 6.3, 11.5 Hz, respectively) were observed by ^{1}H-NMR. The geminal coupling for these spins systems indicated the brominated methylene of the glucose ring at the 6-position, which was easily distinguished by its correlation with H-5 in COSY and with

H-4 and H-5 in TOCSY (Figures SM-3 and SM-8). Moreover, the carbon brominated terminal at the 6-position (δ = 31.1 ppm) was also identified, as supported by HMBC analyses. The observation of the long range correlation of C-6 with H-4 clearly distinguished brominated position which supported by HMQC and HETCOR. The glucose ring's protons and carbons signals were distinguished from fructose rings signals, especially at the C-3, C-4, and C-5 positions, using TOCSY and NOESY (Figures SM-7 and SM-8), which was also, supported by HETCOR, HMQC, and HMBC analyses.

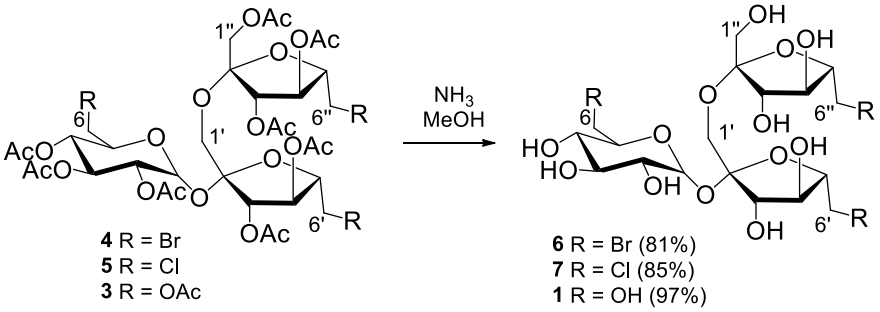
Among 1-kestose's fructose rings, there are three possible primary alcohols at the 6'-, 1'', and 6''-position that are readily brominated. The upfield region of ^{1}H-NMR typically showed two types of doublet at δ = 3.66 ppm (*J* = 6.9 Hz) and 3.69 ppm (*J* = 7.4 Hz), indicating bromination occurred only at the 6'- and 6''-position of compound **4**, respectively. The correlation between H-6' with H-5' in COSY and H-6' with H-4' and H-5' in TOCSY differentiated the bromination at the 6'-position (Figures SM-3 and SM-8). Similarly, brominated 6''-position of compound **4** showed these particular correlations. The brominated terminal of C-6' at δ = 32.0 ppm and C-6''at δ = 32.7 ppm was determined mostly using HMBC with the observation of a cross peak of these carbons at H-4' and H-4'', respectively (Figures SM-6). HETCOR and HMQC coupling between the protons and carbon at the 6'- and/or 6''-position support the identification of bromination position.

The aliphatic sugar groups between the two fructose rings of compound **4** were differentiated using TOCSY and NOESY, which was supported by COSY, HETCOR, HMQC, and HMBC analyses (Figures SM-3–8). Based on ^{1}H- and ^{13}C-NMR, supported by 2D NMR analysis, the 1''-position of compound **4** showed no bromination. The 1''-position of the fructose ring is known to be a neopentyl-like[10,12] terminal having the least reactive proportion. This phenomena also occurred when sucrose was used.[12,16,17] According to these approaches, the bromination product of 1-kestose was determined to be 1'',2,3,3',3'',4,4',4''-octa-*O*-acetyl-6,6',6''-tribromo-6,6',6''-trideoxy-1-kestose (**4**).

For the chlorination product of **5**, the spin system in ^{1}H-NMR showed eight proton signals in the upfield region. Unlike the previous bromination product **4** or undecaacetate 1-kestose **3**, the H-1' of compound **5** exhibited no geminal coupling and presented as a singlet at 3.75 ppm supported by HMBC, HETCOR, and HMQC, (Figures SM-12–14). The chlorinated proportion at the 6-position was shown as a pair of double doublets at δ = 3.68 and 3.57 ppm (*J* = 2.3, 12.0 Hz and *J* = 5.7, 12.0 Hz, respectively). A clear correlation of this chlorinated methylene of the glucose ring with H-5 in COSY and H-4 and H-5 in TOCSY was observed (Figures SM-11 and SM-16). As for the ^{1}H-NMR spin system of 6'- and 6''-chloro of compound **5,** the overlap signals at δ = 3.82–3.78 ppm demonstrated its correlation with H-5' and H-5'' in COSY and H-4', H-5', H-4'', and H-5'' in TOCSY. The brominated terminal of C-6' at δ = 44.4 ppm and C-6'' at δ = 44.6 ppm highlighted the correlated cross peak of these carbons to H-4' and H-4'', respectively. HMBC strongly distinguished the chlorinated 6'- and 6''-position of compound **5** (Figures SM-14). These results support that the chlorination product of 1-kestose is 1'',2,3,3',3'',4,4',4''-octa-*O*-acetyl-6,6',6'-trichloro-6,6',6''-trideoxy-1-kestose (**5**). As with brominated compound **4**, chlorinated compound **5** showed no substitution at the 1''-position. The presence of Br and Cl isotopic peak in ESI-MS of compounds **4** and **5** indicated tri-halogenated proportion of 1-kestose, respectively, which supported our analysis.

To synthesize and elucidate the novel 6,6',6''-trihalogenated 1-kestose derivatives, deacetylation was then conducted. Since suitable deacetylation conditions are generated using saturated ammonium in methanol for sucrose,[12] the undecaacetate of 1-kestose (**3**) was first tested for deacetylation and produced 1-kestose (**1**) within a satisfactory yield (Figures SM-41–48 for NMR analysis). Deacetylation using other methods, such as sodium methoxide, cannot be used for 1-kestose halogenated derivatives. The per-*O*-acetylated trihalogenated derivatives of **4** and **5** were underwent deacetylation, which resulted in compound **6** and **7** (Scheme 2). It was complicated to distinguish the halogenated proportion from the deacetylated

compound **6** and/or **7**, since the halogenated methylene spin system at H-6, H-6′, and H-6′′ overlapped with other signals such as H-3, H-1′, and/or H-1′′ in ^{1}H-NMR. Hence, the HMBC, HMQC, and HETCOR analyses, supported by COSY, TOCSY, and NOESY, are needed to elucidate the complete structure of deacetylated compounds **6** and **7** (Figures SM-27–32 and SM-35–40). However, all the deacetylated trihalogenated 1-kestose derivatives (**6** and **7**) structures and halogenation sites were consistent with those in the corresponding per-*O*-acetylated forms (**4** and **5**).



Scheme 2. Deacetylation of per-*O*-acetylated 1-kestose derivatives (**3**–**5**) to result in 1-kestose (**1**) and deacetylated trihalogenated 1-kestose derivatives (**6** and **7**)

Conclusions

We studied the halogenation of 1-kestose using Appel reactions to synthesize trihalogenated 1-kestose at the 6-, 6′-, and 6′′-position. Isolation and structure elucidation were easily completed using the per-*O*-acetylated form which the 1D and 2D NMR supported the halogenation position. The synthesis and structure elucidation of novel compounds **4** and **5** contribute to the introduction of primary hydroxyl groups into FOS which can potentially be used as low-calorie sweeteners in the future.

Experimental Section

General. All reagents used were of analytical grade. NMR spectra were obtained in $CDCl_3$ or D_2O by JEOL ECA500 (500 and 125 MHz) spectrometer (JEOL, Tokyo, Japan). Optical rotations were measured at 23 ^{o}C on a JASCO DIP370 polarimeter (JASCO, Tokyo, Japan). HRMS spectra were obtained with a Waters UPLC ESI-TOF mass spectrometer (Waters, Milford, CT, USA).

General procedure for Appel reaction: bromination. Solution of 1-kestose (**1**, 0.10 g, 0.198 mmol) in pyridine (2 mL) was cooled in an ice bath and treated with triphenylphosphine (0.47 g, 1.8 mmol, 9.1 equiv), followed by dropwise addition of a solution of carbon tetrabromide (0.30 g, 0.93 mmol, 4.7 equiv) in pyridine (0.93 mL). The reaction mixture was stirred at 70 °C for 2 h. After cooling the mixture in an ice bath, acetic anhydride (3 mL, 32.0 mmol) and pyridine (2 mL) were added, and the mixture was stirred overnight at room temperature. The solvent was evaporated and the residue was partitioned between CH_2Cl_2 and water. The organic layer was washed with 1 M HCl and brine, dried over $MgSO_4$, reduced the solvent under high pressure and then purified by column chromatography on silica gel by elution with hexane/diethyl ether (1:6 and 1:10) to yield

1′′,2,3,3′,3′′,4,4′,4′′-octa-*O*-acetyl-6,6′,6′′-tribromo-6,6′,6′′-trideoxy 1-kestose (**4**; 0.0516 g, 25%) as colorless amorphous mass. $[\alpha]_D$ +22.4 (c = 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.70 (1H, d, $J_{3',4'}$ 8.0 Hz, H-3′), 5.67 (1H, d, $J_{1,2}$ = 4.0 Hz, H-1), 5.50 (1H, d, $J_{3'',4''}$ 6.3 Hz, H-3′′), 5.48–5.42 (2H, m, H-3, H-4′), 5.32 (1H, t, $J_{3'',4''}$ 6.3 Hz, H-4′′), 5.03 (1H, t, $J_{3,4}$ 9.7 Hz, H-4), 4.95 (1H, dd, $J_{1,2}$ 4.0 Hz, $J_{2,3}$ 10.3 Hz, H-2), 4.35–4.28 (2H, m, H-5, H-5′), 4.24 (2H, s, H-1′′), 4.22–4.19 (1H, m, H-5′′), 3.79 (1H, d, $J_{1'a,1'b}$ 10.3 Hz, H-1′a), 3.73 (1H, d, $J_{1'a,1'b}$ 10.3 Hz, H-1′b), 3.69 (2H, d, $J_{5'',6''}$ 7.4 Hz, H-6′′), 3.66 (2H, d, $J_{5',6'}$ 6.9 Hz, H-6′), 3.54 (1H, dd, $J_{5,6a}$ 2.3 Hz, $J_{6a,6b}$ 11.5 Hz, H-6a), 3.40 (1H, dd, $J_{5,6b}$ 6.3 Hz, $J_{6a,6b}$ 11.5 Hz, H-6b), 2.16–2.15 (6H, m, 2 x CH_3), 2.14 (3H, s, CH_3), 2.11 (3H, s, CH_3), 2.09–2.07 (9H, m, 3 x CH_3), 2.02 (3H, s, CH_3) ppm. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 170.2, 170.0, 170.0, 169.8, 169.5 (C=O), 103.8 (C-2′), 103.1 (C-2′′), 90.1 (C-1), 80.7 (C-5′′), 79.8 (C-5′), 78.1 (C-4′′), 77.2 (C-3′′), 76.4 (C-4′), 75.8 (C-3′), 70.8 (C-4), 69.7 (C-2), 69.3 (C-3 & C-5), 62.0 (C-1′′), 61.5 (C-1′), 32.7 (C-6′′), 32.0 (C-6′), 31.1 (C-6), 20.8, 20.8, 20.7, 20.8, 20.6, 20.5, 20.5, 20.5 (CH_3) ppm. HRMS (ESI): calcd. for $C_{34}H_{45}O_{21}Br_3Na$ 1050.9881, 1052.9860 $[M + Na]^+$; found 1050.9899, 1052.9880.

Chlorination. Chlorination was similar to bromination as described above, except carbon tetrabromide in pyridine was replaced with carbon tertrachloride (0.09 mL, 0.93 mmol, 4.7 equiv.) to yield **1′′,2,3,3′,3′′,4,4′,4′′-octa-*O*-acetyl-6,6′,6′′-trichloro-6,6′,6′′-trideoxy-1-kestose** (**5**; 0.0514 g, 28%) as colorless amorphous mass. $[\alpha]_D$ +26.6 (c = 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.70–5.66 (2H, m, H-1, H-3′), 5.50 (1H, d, $J_{3'',4''}$ 6.3 Hz, H-3′′), 5.48–5.41 (2H, m, H-3, H-4′), 5.33 (1H, t, $J_{3'',4''}$ = 6.3 Hz, H-4′′), 5.06 (1H, t, $J_{3,4}$ = 9.7 Hz, H-4), 4.93 (1H, dd, $J_{1,2}$ 3.7 Hz, $J_{2,3}$ 10.6 Hz, H-2), 4.38–4.32 (1H, m, H-5), 4.28–4.22 (3H, m, H-1′′, H-5′), 4.17 (1H, q, $J_{5'',6''}$ 6.5 Hz, H-5′′), 3.82–3.78 (4H, m, H-6′, H-6′′), 3.75 (2H, s, H-1′), 3.68 (1H, dd, $J_{5,6a}$ 2.3 Hz, $J_{6a,6b}$ 12.0 Hz, H-6a), 3.57 (1H, dd, $J_{5,6b}$ 5.7 Hz, $J_{6a,6b}$ 12.0 Hz, H-6b), 2.16 (3H, s, CH_3), 2.15–2.13 (6H, m, 2 x CH_3), 2.11 (3H, s, CH_3), 2.09 (3H, s CH_3), 2.08 (3H, s, CH_3), 2.07 (3H, s, CH_3), 2.02 (3H, s, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 170.2, 170.1, 170.0, 170.0, 169.7, 169.5 (C=O), 103.8 (C-2′), 103.1 (C-2′′), 90.0 (C-1), 80.6 (C-5′′), 79.9 (C-5′), 77.2 (C-4′′), 76.9 (C-3′′), 75.7 C-4′), 75.5 (C-3′), 69.8 (C-5), 69.7 (C-2 & C-4), 69.4 (C-3), 62.2 (C-1′′), 61.6(C-1′), 44.6 (C-6′′), 44.4 (C-6′), 43.2 (C-6), 20.8, 20.7, 20.7, 20.6, 20.5, 20.5 (CH_3) ppm. HRMS (ESI): calcd. for $C_{34}H_{45}O_{21}Cl_3Na$ 919.1387 $[M + Na]^+$; found 919.1395.

1′′,2,3,3′,3′′,4,4′,4′′,6,6′,6′′-Undeca-*O*-acetyl-deoxy-1-kestose (3).[15,18] Solution of 1-kestose (**1**, 0.03 g, 0.06 mmol) in pyridine (15 mL) was treated with acetic anhydride (1 mL, 10.7 mmol), and the mixture was stirred overnight at room temperature. The solvent was removed under reduced pressure and subjected to column chromatography on silica gel by elution with chloroform to yield **3** (0.055 g, 96%) as a colorless liquid. $[\alpha]_D$ + 30.2 (c = 1.0, $CHCl_3$); Ref. [16] $[\alpha]_D$ +31.8 (c = 3.7, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.75 (1H, d, $J_{1,2}$ 3.4 Hz, H-1), 5.69 (1H, d, $J_{3',4'}$ 8.0 Hz, H-3′), 5.48 (1H, d, $J_{3'',4''}$ 6.9 Hz, H-3′′), 5.46 (1H, t, $J_{3',4'}$ 8.0 Hz, H-4′), 5.42 (1H, t, $J_{3,4}$ 9.7 Hz, H-3), 5.34 (1H, t, $J_{3'',4''}$ 6.9 Hz, H-4′′), 5.08 (1H, t, $J_{3,4}$ 9.7 Hz, H-4), 4.91 (1H, dd, $J_{1,2}$ 3.4 Hz, $J_{2,3}$ 10.3 Hz, H-2), 4.39–4.33 (3H, m, H-5, H-6′′), 4.33–4.24 (3H, m, H-6a, H-6′), 4.24–4.20 (3H, m, H-1′′, H-5′), 4.20–4.14 (2H, m, H-6b, H-5′′), 3.69 (1H, d, $J_{1'a,1'b}$ 9.2 Hz, H-1′a), 3.63 (1H, d, $J_{1'a,1'b}$ 9.2 Hz, H-1′b), 2.19–2.14 (3H, m, CH_3), 2.13–2.12 (6H, m, 2 x CH_3), 2.11–2.09 (15H, m, 5 x CH_3), 2.06 (3H, s, CH_3), 2.04 (3H, s, CH_3), 2.01 (3H, s, CH_3) ppm. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 170.7, 170.6, 170.5, 170.1, 169.9, 169.7, 169.6 (C=O), 103.4 (C-2′), 102.9 (C-2′′), 89.2 (C-1), 78.4 (C-5′′), 77.8 (C-5′), 76.5 (C-3′′), 75.5 (C-4′′), 74.9 (C-3′), 73.7 (C-4′), 70.0 (C-2), 69.8 (C-3), 68.2 (C-5), 68.2 (C-4), 63.7 (C-6′′), 63.2 (C-6′), 62.7 (C-1′′), 62.2 (C-1′), 61.7(C-6), 20.8, 20.7, 20.7, 20.6, 20.6, 20.5 (CH_3) ppm. HRMS (ESI): calcd. for $C_{40}H_{54}O_{27}Na$ 989.2750 $[M + Na]^+$; found 989.2797.

General procedure for deacetylation of per-O-acetylated halodeoxy-1-kestose derivatives. Solutions of per-*O*-acetylated halodeoxy-1-kestose derivatives (**3**–**5**, 0.05 g) in 3 mL dry methanol were treated with 1.5 mL saturated ammonia in methanol and stirred overnight at room temperature. The solvent was removed under reduced pressure and subjected to column chromatography on silica gel (pre-washed by methanol) by elution

with methanol/chloroform (3:1). The method produced the corresponding halodeoxy-1-kestose derivatives **1**, **6**, and **7**.

1-Kestose[3] (**1**, 0.034 g, 97%). ^{1}H-NMR (500 MHz, D_2O) δ: 5.37 (1H, d, $J_{1,2}$ 4.0 Hz, H-1), 4.22 (1H, d, $J_{3',4'}$ 8.6 Hz, H-3'), 4.13 (1H, d, $J_{3'',4''}$ 8.6 Hz, H-3''), 4.02 (1H, t, $J_{3'',4''}$ 8.6 Hz, H-4''), 3.98 (1H, t, $J_{3',4'}$ 8.6 Hz, H-4'), 3.83–3.80 (2H, m, H-5', H-5''), 3.79–3.71 (8H, m, H-1'a, H-5, H-6, H-6', H-6''), 3.70–3.60 (4H, m, H-3, H-1'b, H-1''), 3.48 (1H, dd, $J_{1,2}$ 4.0 Hz, $J_{2,3}$ 9.7, H-2), 3.41 (1H, t, $J_{3,4}$ 9.7 Hz, H-4) ppm. ^{13}C-NMR (125 MHz, D_2O) δ: 104.2 (C-2''), 103.7 (C-2'), 92.9 (C-1), 81.6 (C-5'), 81.5 (C-5''), 77.0 (C-3' & C-3''), 74.9 (C-4''), 74.2 (C-4'), 73.0 (C-3), 72.8 (C-5), 71.6 (C-2), 69.6 (C-4), 62.7 (C-6''), 62.6 (C-6'), 61.3 (C-1'), 60.8 (C-1''), 60.5 (C-6) ppm.

6,6',6''-Tribromo-6,6',6''-trideoxy-1-kestose (**6**, 0.030 g, 81%)**.** $[\alpha]_D$ = + 24.8 (c 1.0, MeOH)**.** ^{1}H-NMR (500 MHz, D_2O) δ: 5.36 (1H, d, $J_{1,2}$ 4.0 Hz, H-1), 4.27 (1H, d, $J_{3',4'}$ 8.6 Hz, H-3'), 4.16 (1H, d, $J_{3'',4''}$ 8.6 Hz, H-3''), 4.09–4.05 (2H, m, H-4', H-4''), 4.04–3.98 (3H, m, H-5, H-5', H-5''), 3.87 (1H, d, $J_{1'a,1'b}$ 10.3 Hz, H-1'a), 3.79–3.72 (3H, m, H-6a, H-6''), 3.72–3.65 (5H, m, H-1'b, H-1'', H-6b, H-3), 3.64–3.59 (2H, m, H-6'), 3.52 (1H, dd, $J_{1,2}$ 4.0 Hz, $J_{2,3}$ 10.0, Hz, H-2), 3.43 (1H, t, $J_{3,4}$ 10.0 Hz, H-4) ppm. ^{13}C-NMR (125 MHz, D_2O) δ: 103.9 (C-2''), 103.3 (C-2'), 92.9 (C-1), 80.6 (C-5'), 80.4 (C-5''), 77.4 (C-4''), 76.9 (C-3''), 76.4 (C-3'), 76.3(C-4'), 72.1(C-3), 71.4 (C-4), 71.1(C-5), 71.0 (C-2), 59.9 (C-1', C-1''), 34.2 (C-6), 33.5 (C-6'), 33.5 (C-6'') ppm. HRMS (ESI): calcd. for $C_{18}H_{29}Br_3O_{13}Na$ 714.9035, 716.9015 $[M + Na]^+$; found 714.9053, 716.9034.

6,6',6''-Trichloro-6,6',6''-trideoxy-1-kestose (**7**, 0.032 g, 85%). $[\alpha]_D$ = +26.6 (c 1.0, MeOH). ^{1}H-NMR (500 MHz, D_2O) δ: 5.36 (1H, d, $J_{1,2}$ 4.0 Hz, H-1), 4.26 (1H, d, $J_{3',4'}$ 8.6 Hz, H-3'), 4.16 (1H, d, $J_{3'',4''}$ 8.6 Hz, H-3''), 4.11–4.05 (3H, m, H-4', H-4'', H-5), 4.01–3.94 (2H, m, H-5', H-5''), 3.89–3.73 (7H, m, H-6, H-6', H-6'', H-1'a), 3.71–3.60 (4H, m, H-1'b, H-1'', H-3), 3.52 (1H, dd, $J_{1,2}$ 4.0 Hz, $J_{2,3}$ 9.7 Hz, H-2), 3.47 (1H, t, $J_{3,4}$ 9.7 Hz, H-4) ppm. ^{13}C-NMR (125 MHz, D_2O) δ: 103.9 (C-2''), 103.3 (C-2'), 92.8 (C-1), 80.6 (C-5'), 80.5 (C-5''), 76.6 (C-3''), 76.4 (C-3'), 76.2 (C-4''), 75.3 (C-4'), 72.2 (C-3), 71.6 (C-4), 71.0 (C-5), 70.1 (C-2), 60.2 (C-1'), 60.0 (C-1''), 45.4 (C-6''), 45.2 (C-6'), 44.3 (C-6) ppm. HRMS (ESI): calcd. for $C_{18}H_{29}Cl_3O_{13}Na$ 581.0571, 583.0542 $[M + Na]^+$; found 581.0587, 583.0568.

Acknowledgements

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Supplementary Material

One- and two-dimensional nuclear magnetic resonance (1D and 2D NMR, respectively) figures for all synthetic compounds are available online.

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Supplementary Material

Application of Appel reaction to the primary alcohol groups of fructooligosaccharides: Synthesis of 6,6′,6″-trihalogenated 1-kestose derivatives

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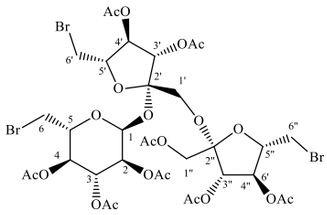
Table of Contents

NMR spectrum

1′′,2,3,3′,3′′,4,4′,4′′-Octa-O-acetyl-6,6′,6′′-tribromo-6,6′,6′′-trideoxy-1-kestose (**4**)



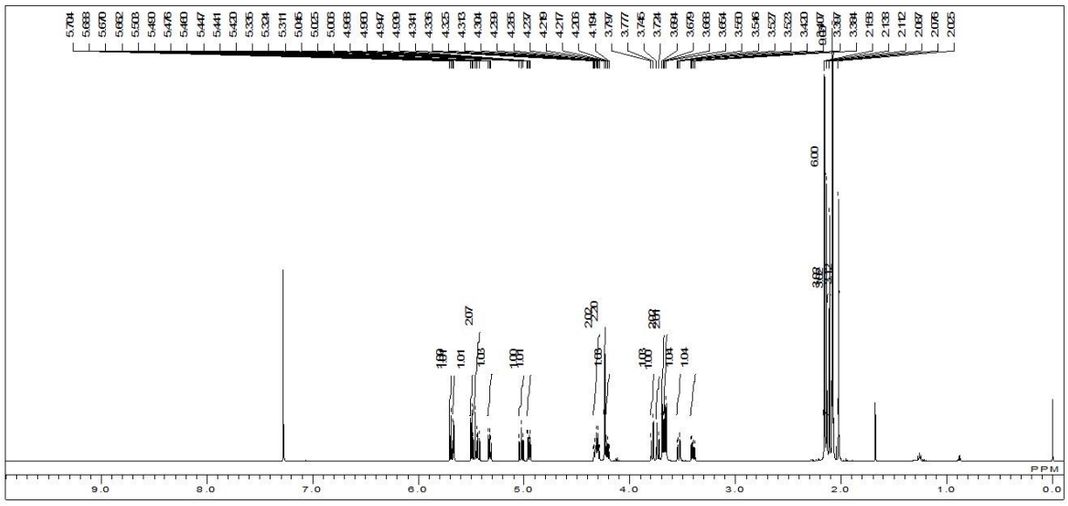


Figure SM-1(a). ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **4**

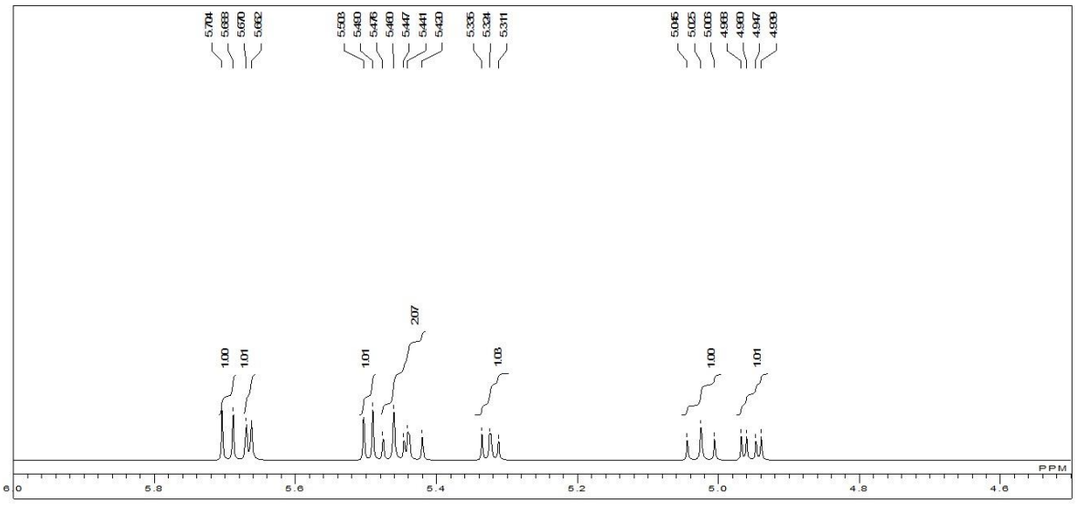


Figure SM-1(b). Selected down field region ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **4**

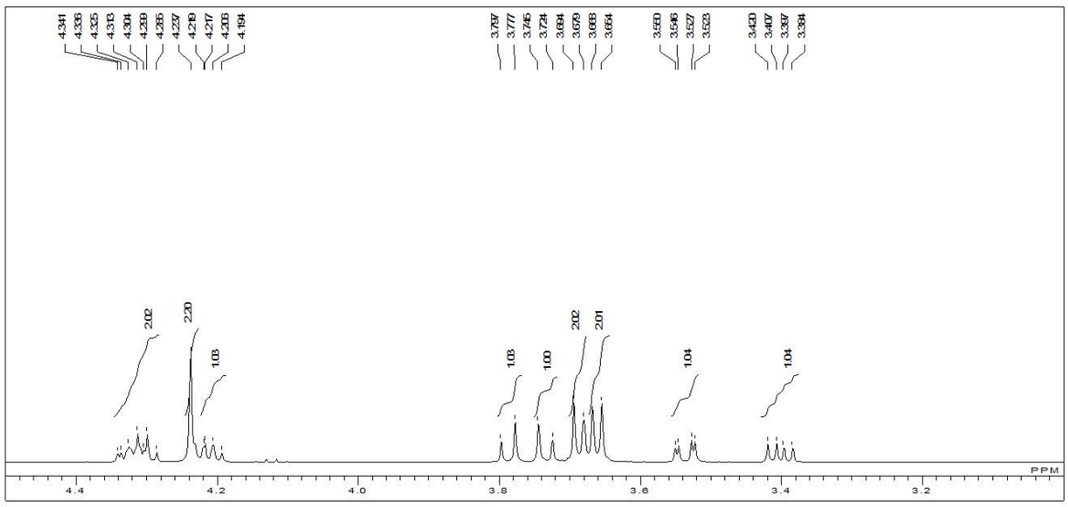


Figure SM-1(c). Selected up field region ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **4**

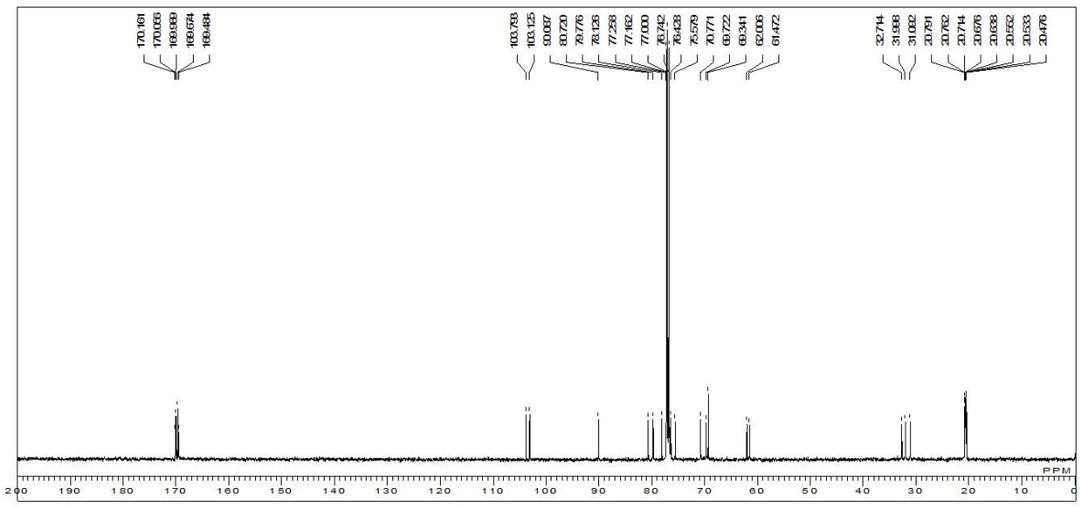


Figure SM-2(a). ^{13}C NMR (125 MHz, $CDCl_3$) of compound **4**

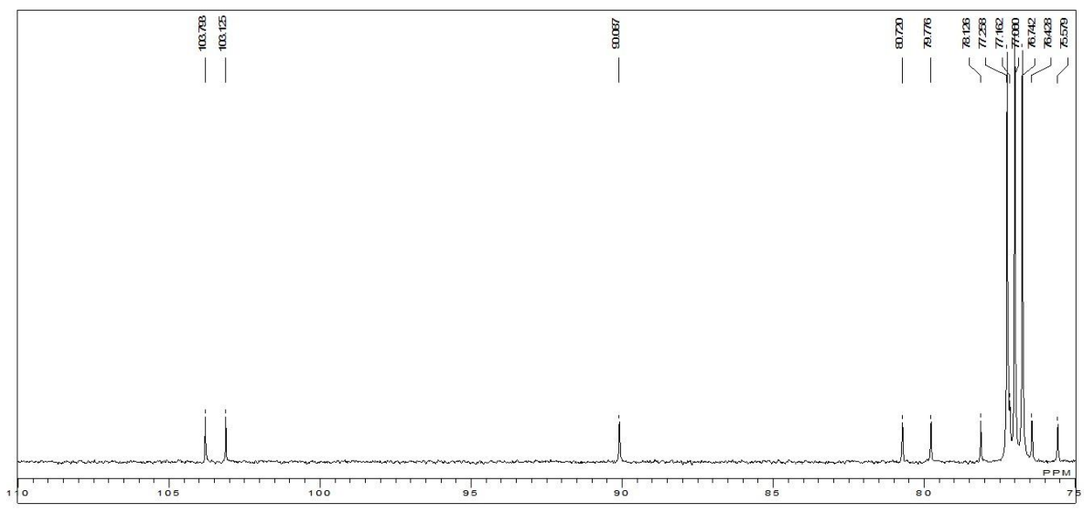


Figure SM-2(b). Selected down field region ^{13}C-NMR (500 MHz, $CDCl_3$) of compound **4**

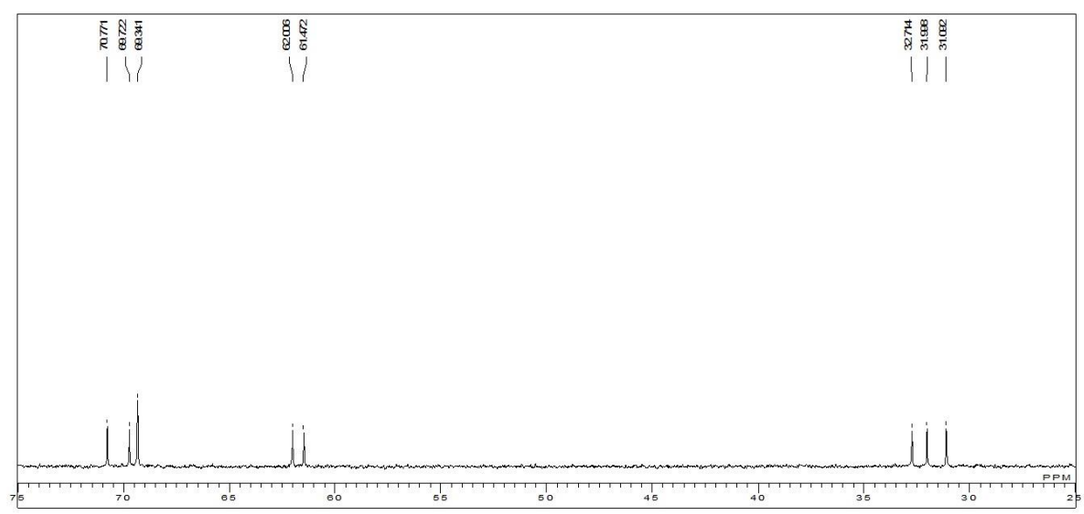


Figure SM-2(c). Selected up field region ^{13}C-NMR (500 MHz, $CDCl_3$) of compound **4**

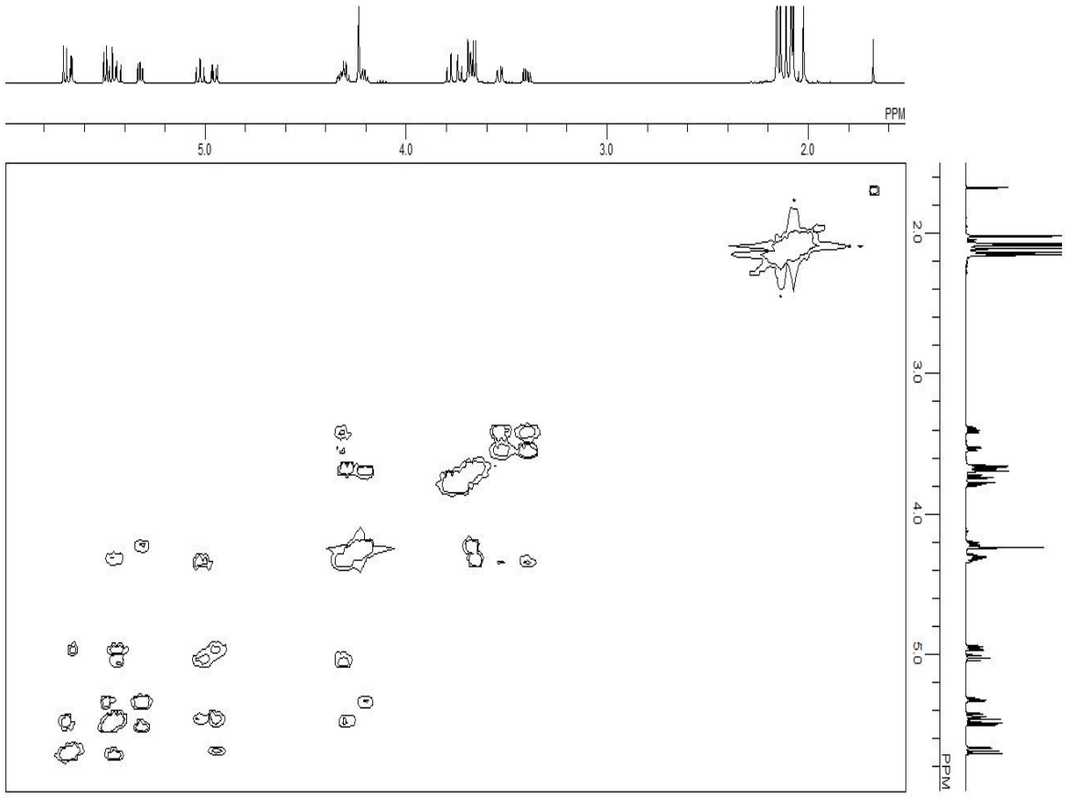


Figure SM-3. ^{1}H-^{1}H COSY 2D-NMR (500 MHz, $CDCl_3$) of compound **4**

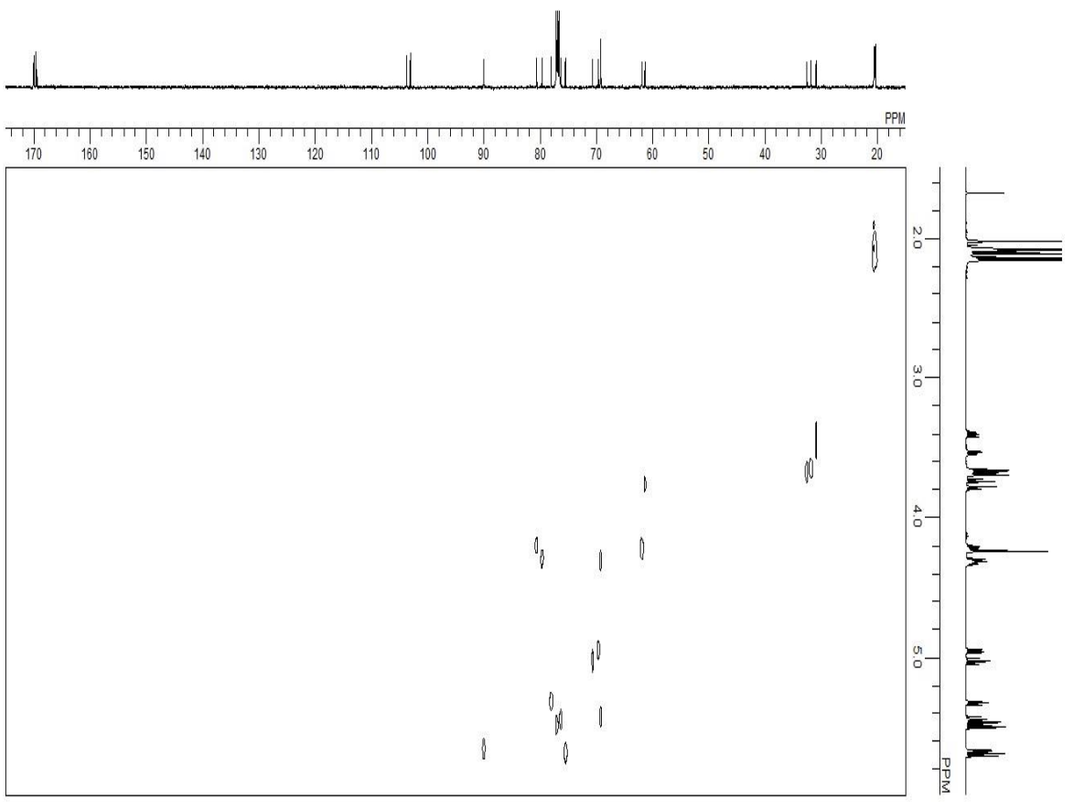


Figure SM-4. ^{13}C-^{1}H HETCOR 2D-NMR (500 MHz, $CDCl_3$) of compound **4**

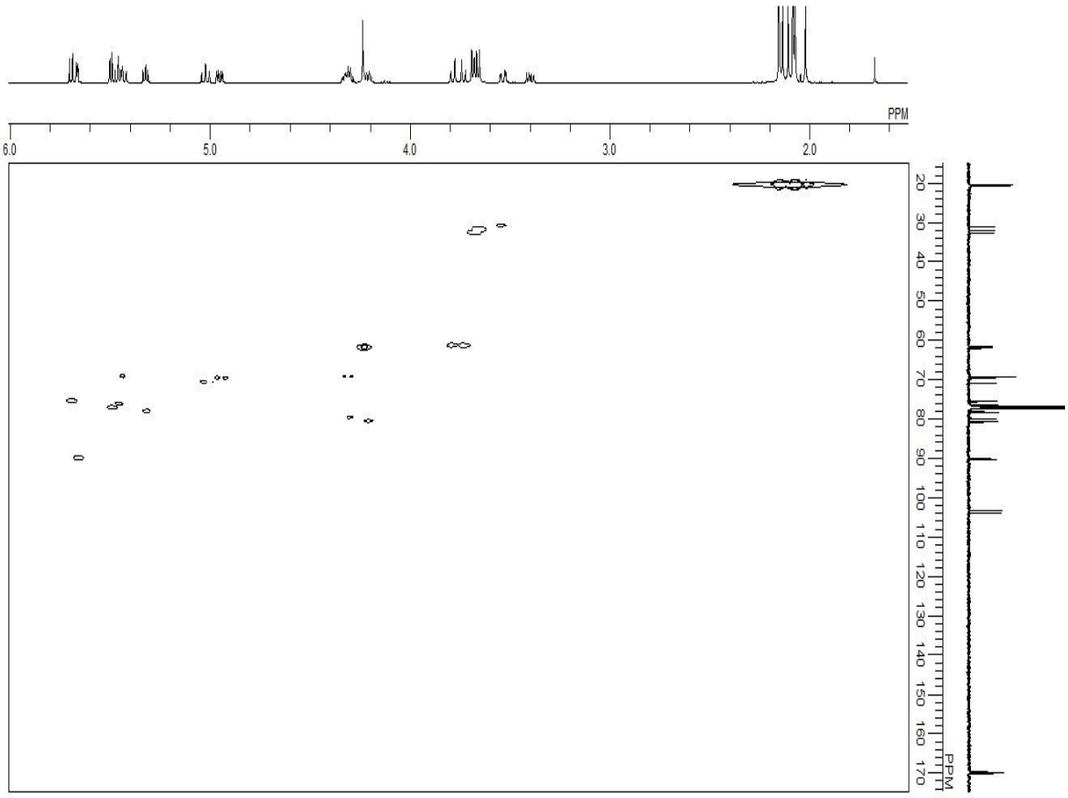


Figure SM-5. ^{1}H-^{13}C HMQC 2D-NMR (500 MHz, $CDCl_3$) of compound **4**

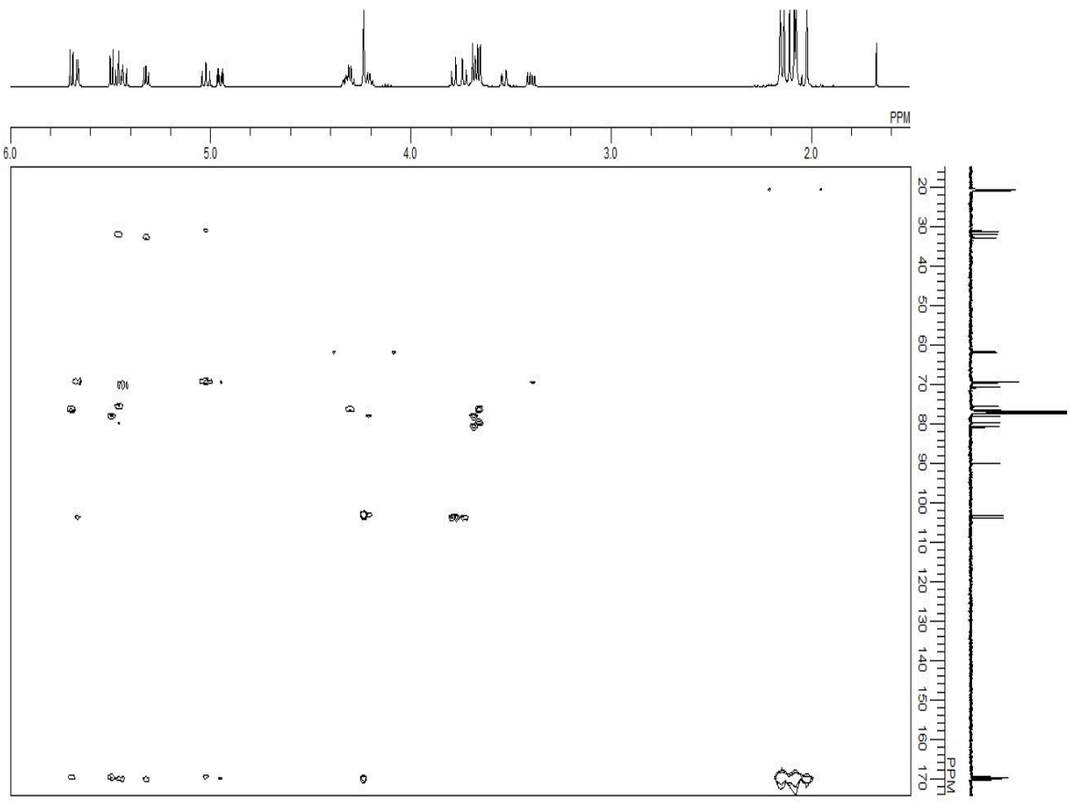


Figure SM-6. ^{1}H-^{13}C HMBC 2D-NMR (500 MHz, $CDCl_3$) of compound **4**

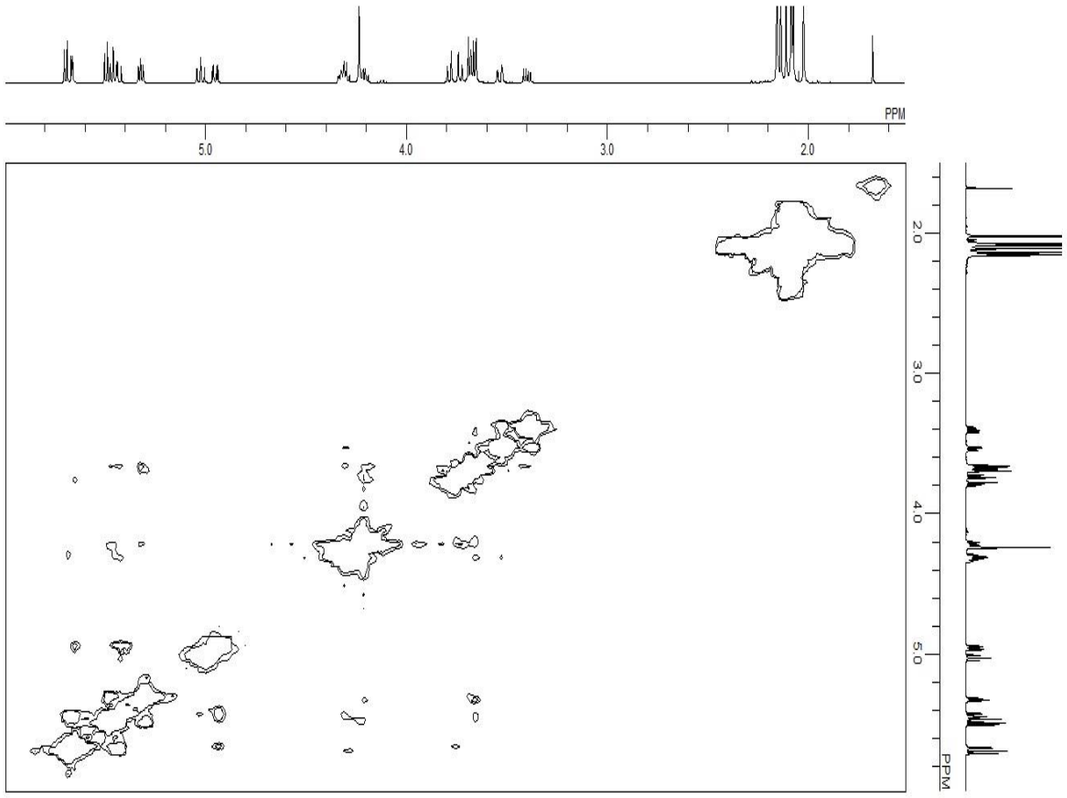


Figure SM-7. ^{1}H-^{1}H NOESY 2D-NMR (500 MHz, $CDCl_3$) of compound **4**

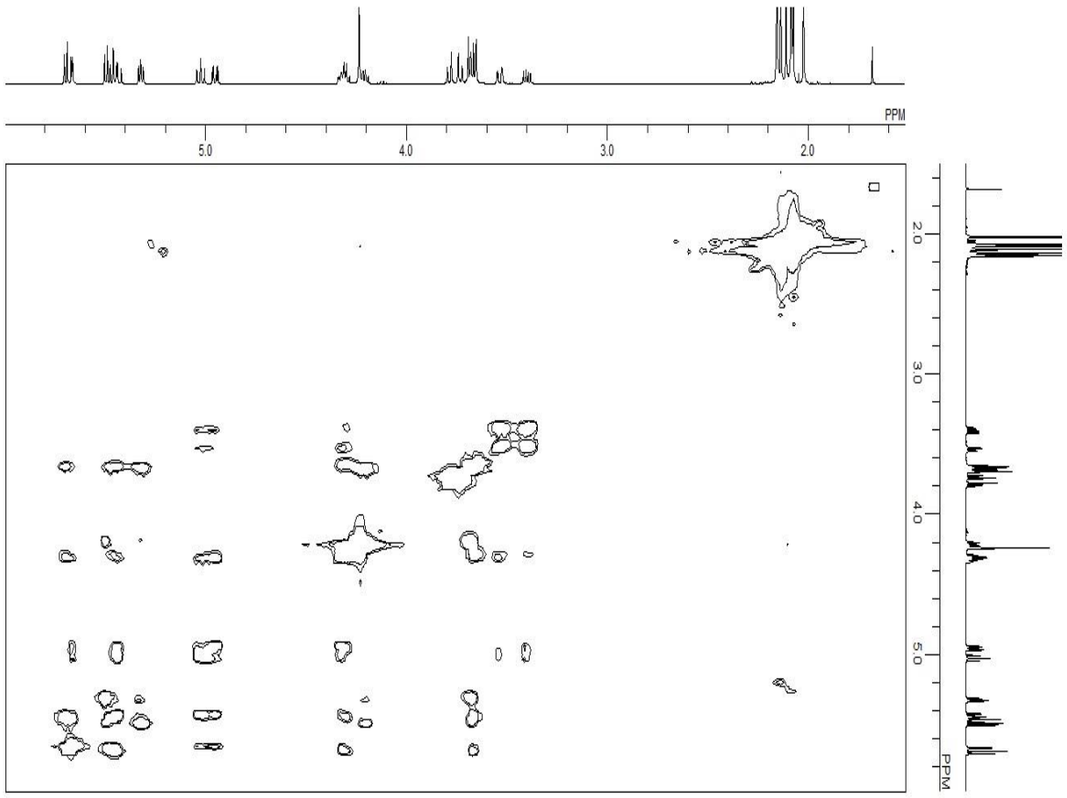
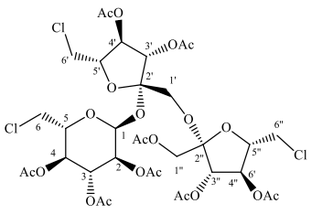


Figure SM-8. ^{1}H-^{1}H TOCSY 2D-NMR (500 MHz, $CDCl_3$) of compound **4**

1′′,2,3,3′,3′′,4,4′,4′′-Octa-O-acetyl-6,6′,6′′-trichloro-6,6′,6′′-trideoxy-1-kestose (**5**)



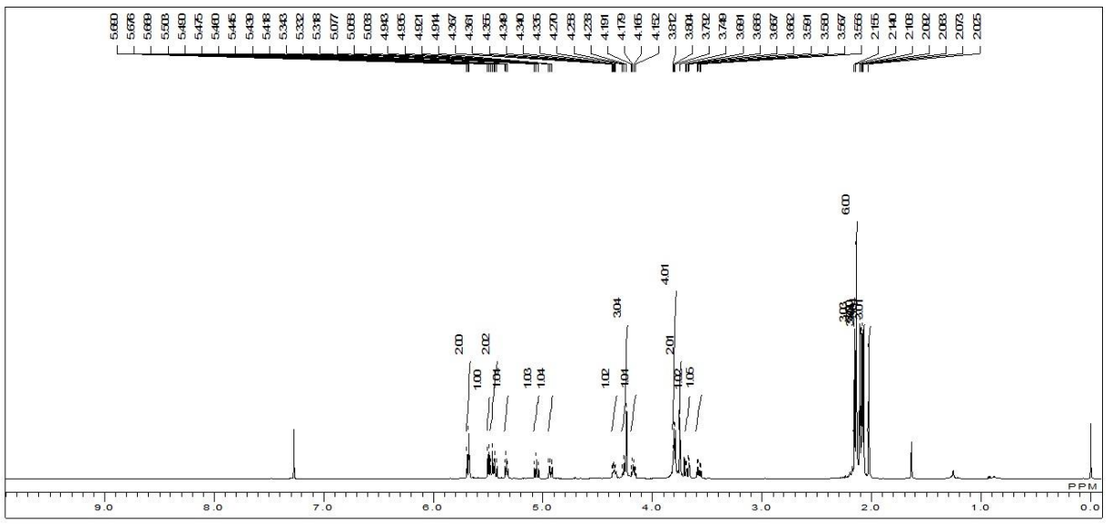


Figure SM-9(a). ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **5**

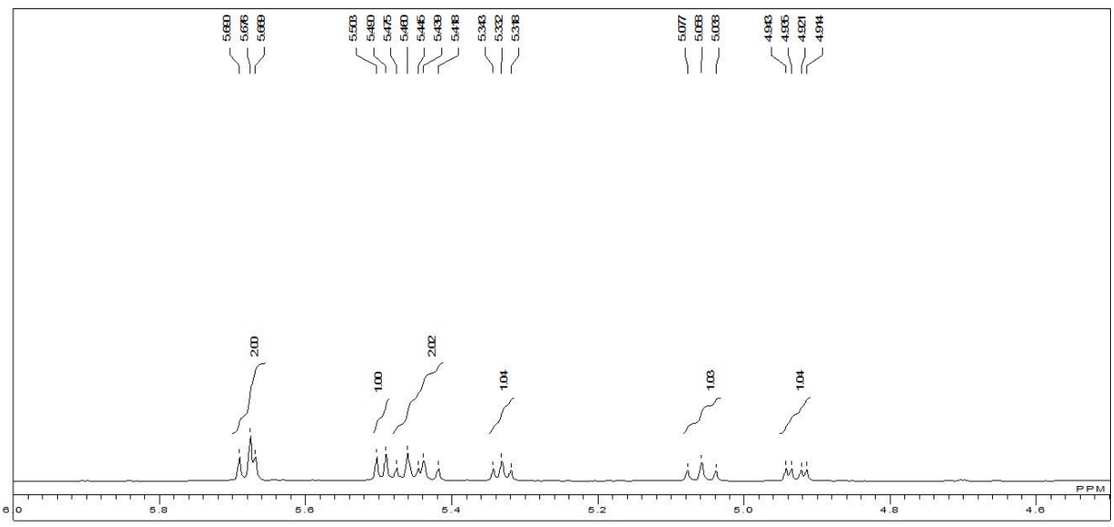


Figure SM-9(b). Selected down field region ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **5**

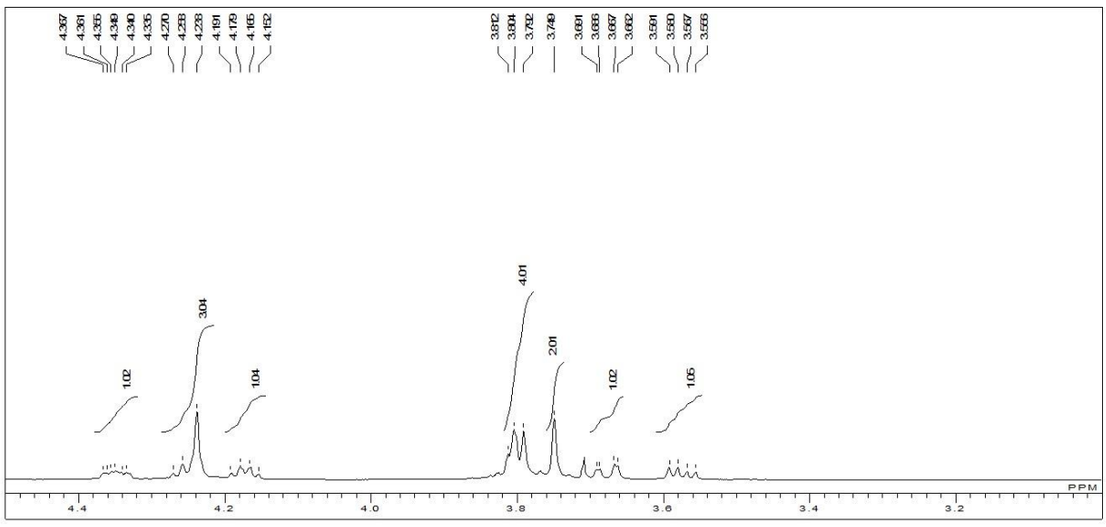


Figure SM-9(c). Selected up field region ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **5**

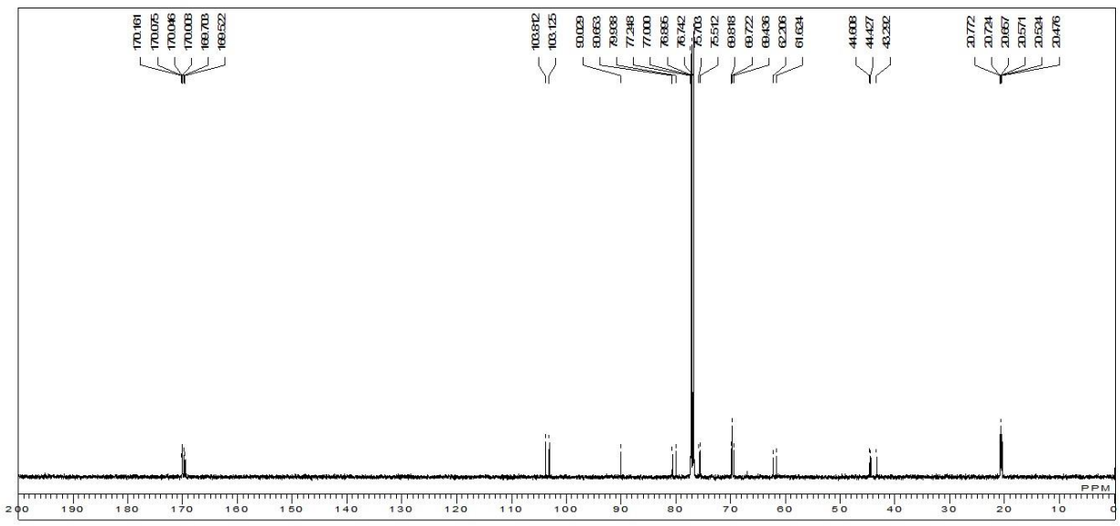


Figure SM-10(a).[13]C NMR (125 MHz, $CDCl_3$) of compound **5**

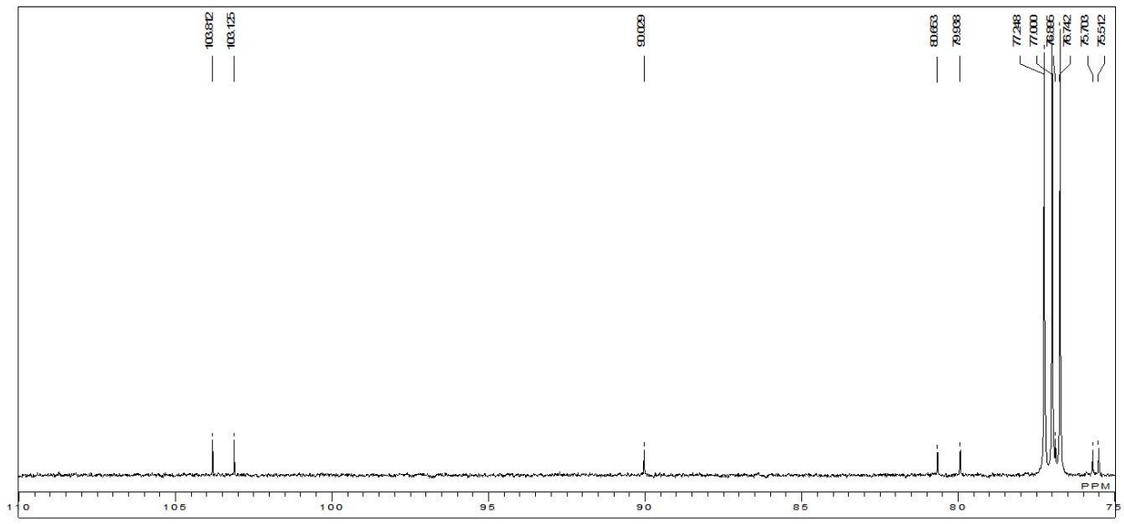


Figure SM-10(b). Selected down field region ^{13}C NMR (125 MHz, $CDCl_3$) of compound **5**

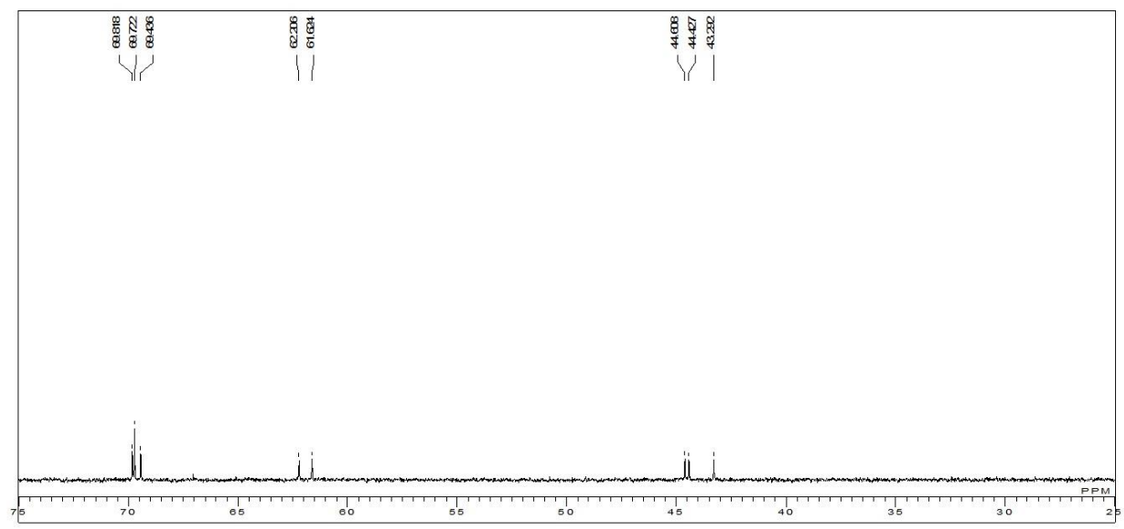


Figure SM-10(c). Selected up field region ^{13}C NMR (125 MHz, $CDCl_3$) of compound **5**

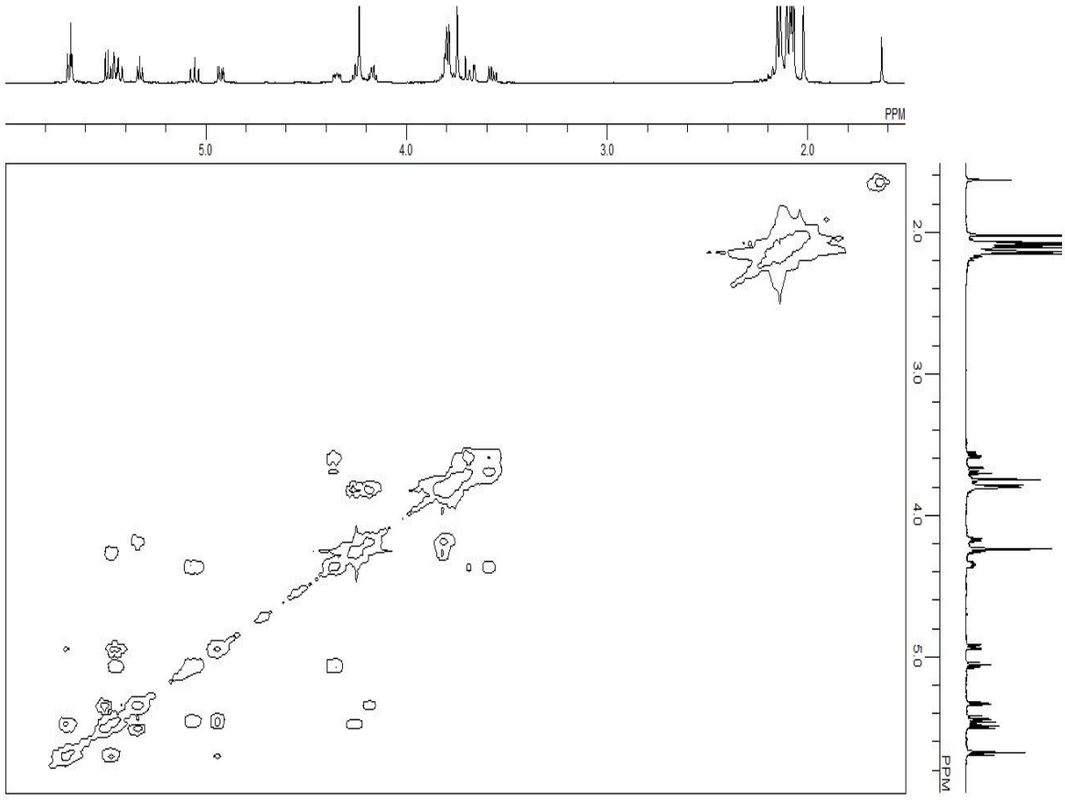


Figure SM-11. ^{1}H-^{1}H COSY 2D-NMR (500 MHz, $CDCl_3$) of compound **5**

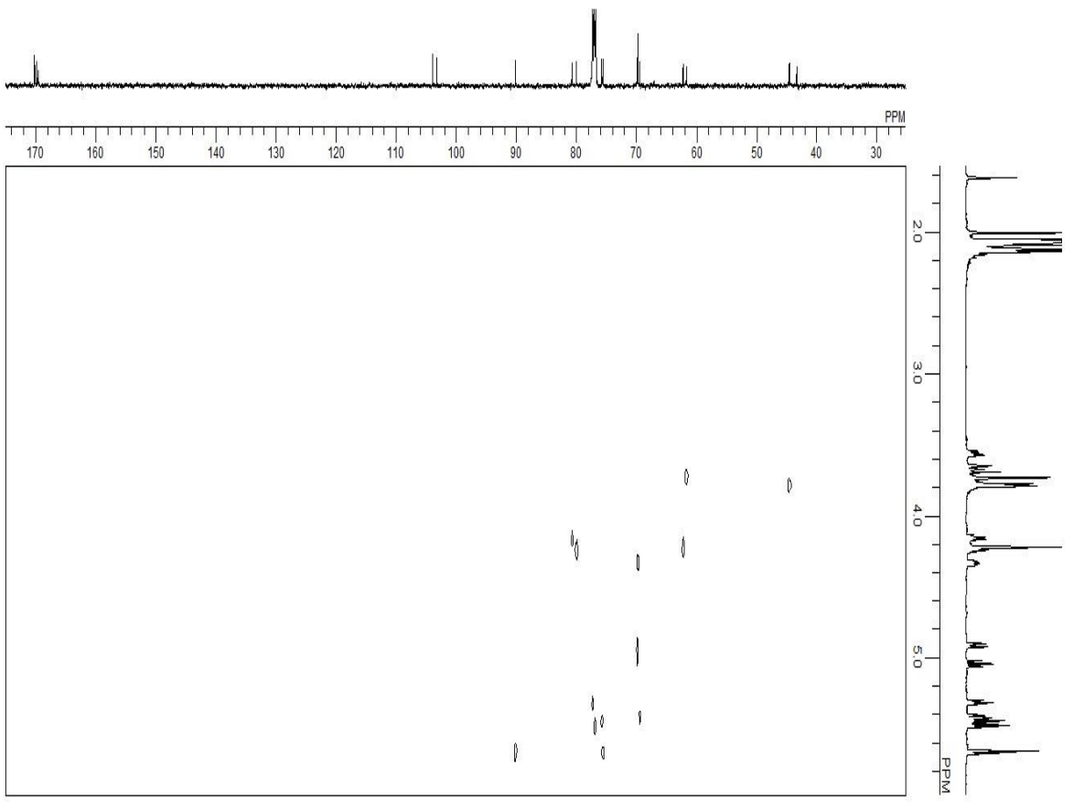


Figure SM-12. ^{13}C-^{1}H HETCOR 2D-NMR (500 MHz, $CDCl_3$) of compound **5**

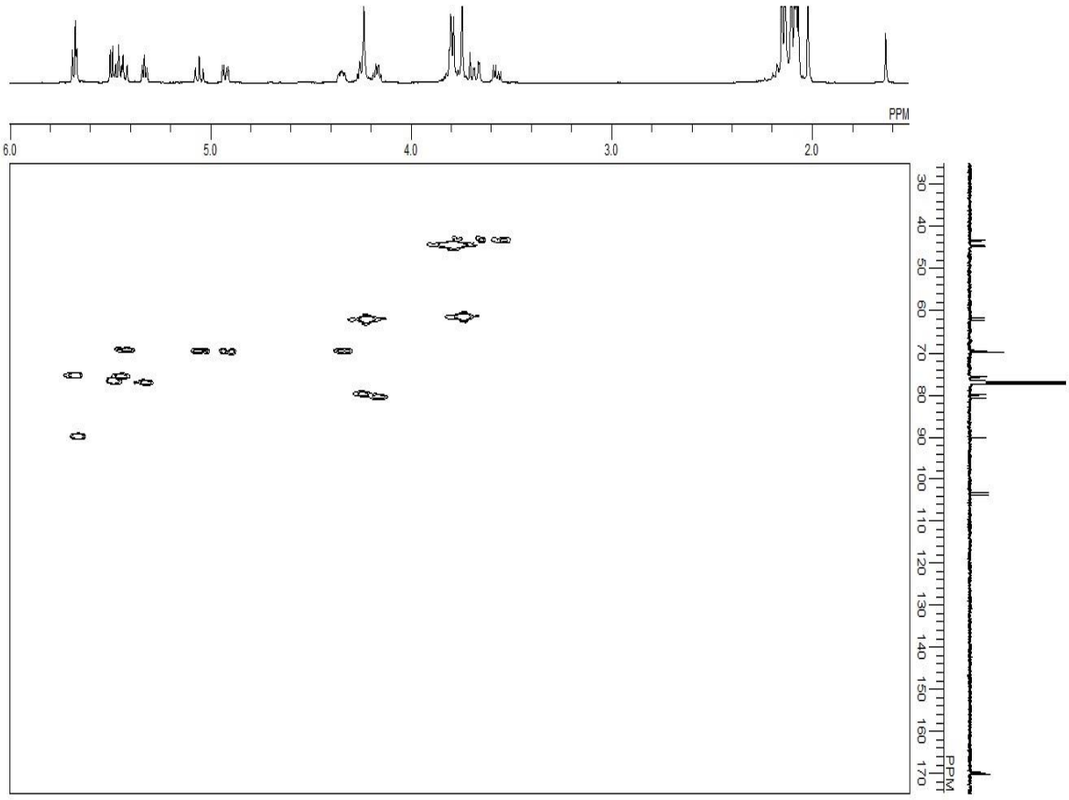


Figure SM-13. ^{1}H-^{13}C HMQC 2D-NMR (500 MHz, $CDCl_3$) of compound **5**

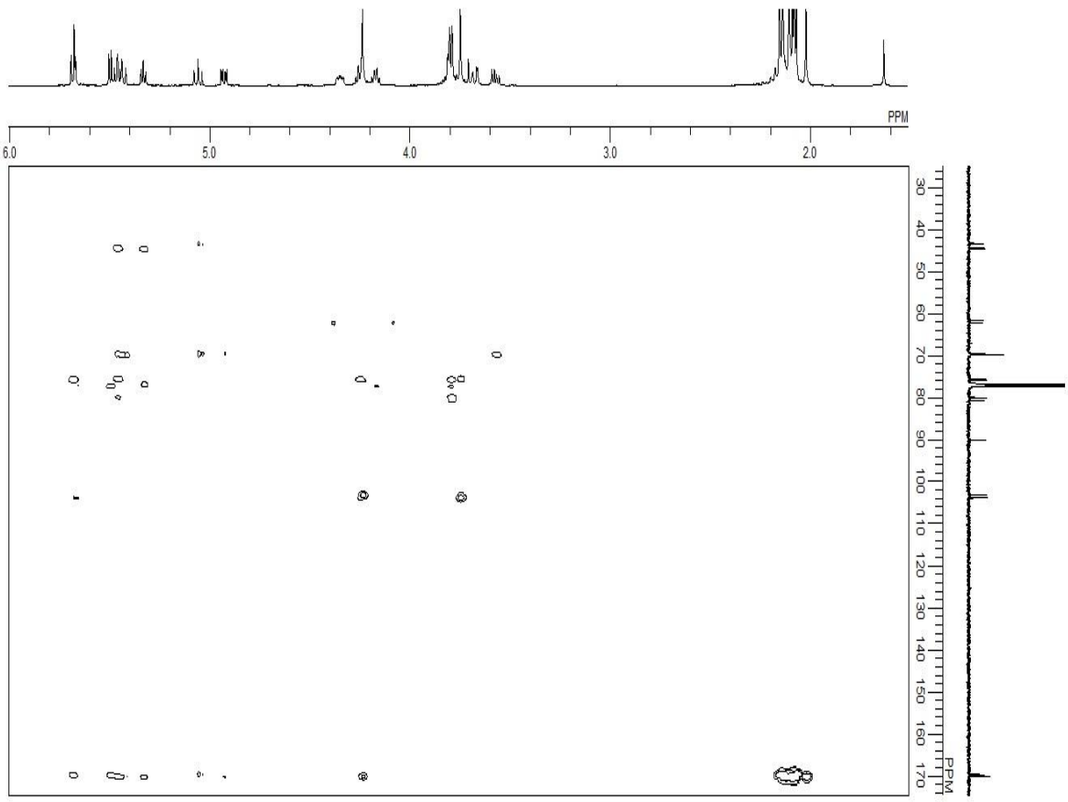


Figure SM-14. ^{1}H-^{13}C HMBC 2D-NMR (500 MHz, $CDCl_3$) of compound **5**

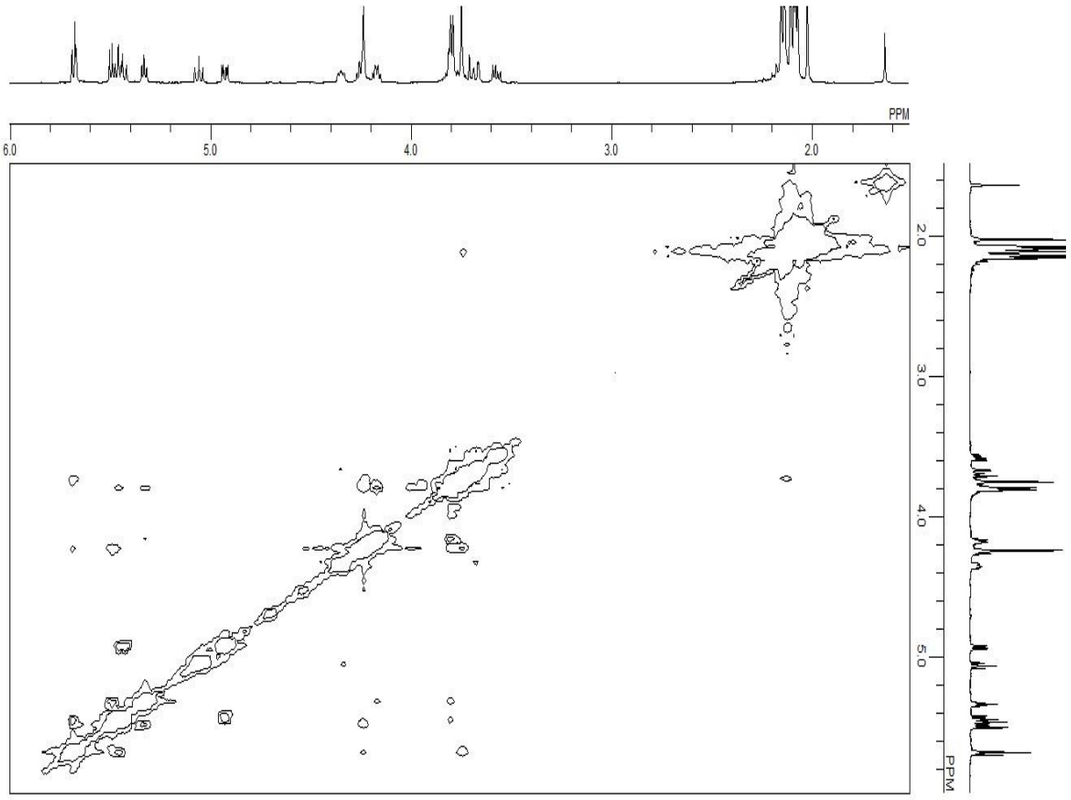


Figure SM-15. ^{1}H-^{1}H NOESY 2D-NMR (500 MHz, $CDCl_3$) of compound **5**

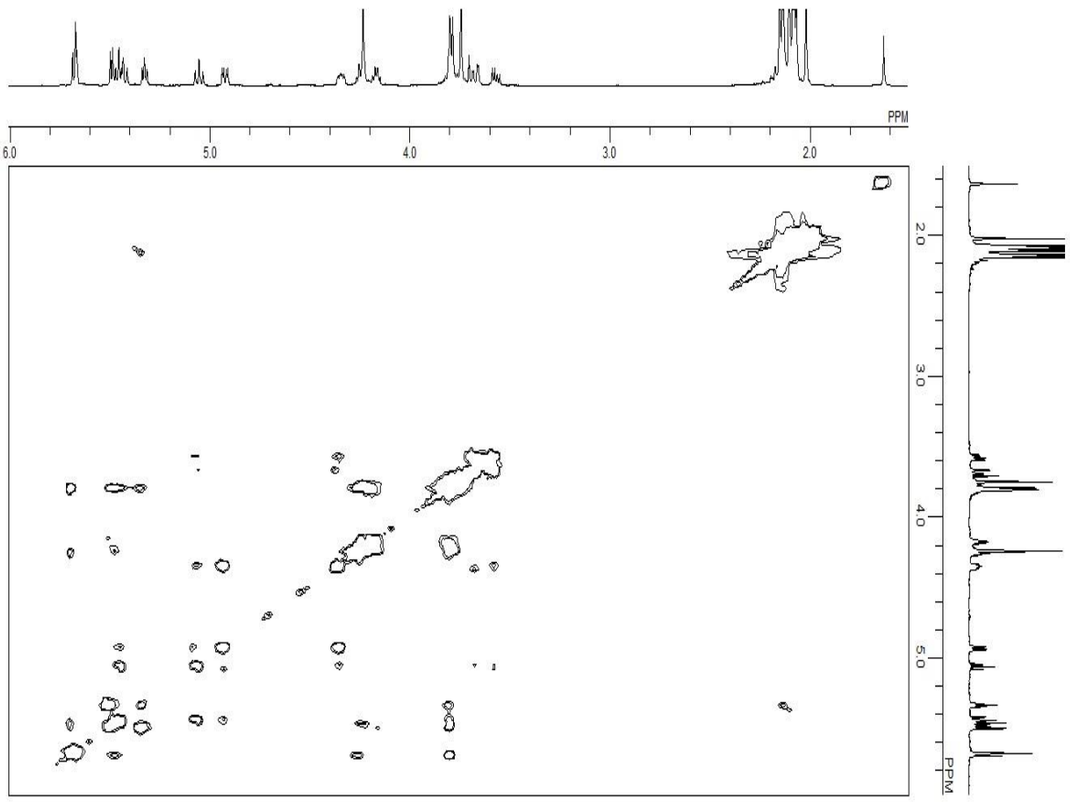
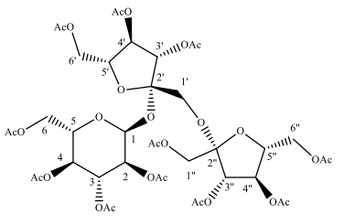


Figure SM-16. ^{1}H-^{1}H TOCSY 2D-NMR (500 MHz, $CDCl_3$) of compound **5**

1′′,2,3,3′,3′′,4,4′,4′′,6,6′,6′′-Undeca-O-acetyl-1-kestose (**3**)



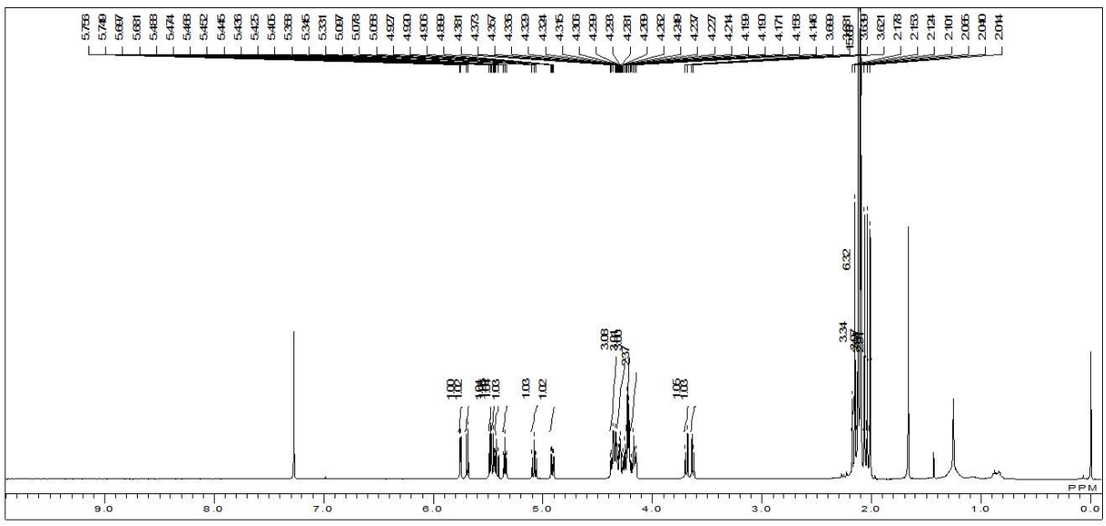


Figure SM-17(a). ^{1}H-NMR (500 MHz, CDCl^{3}) of compound **3**

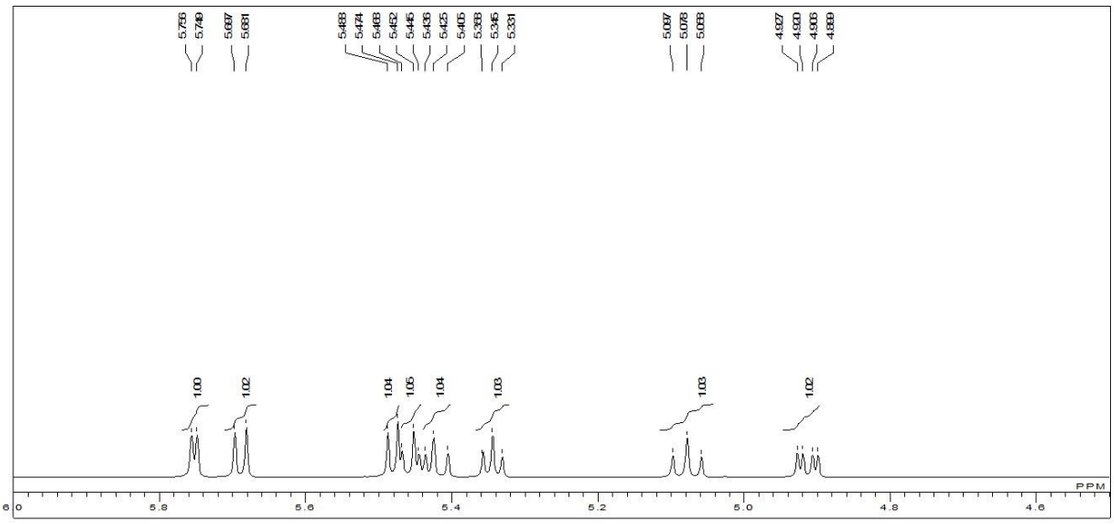


Figure SM-17(b). Selected down field region ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **3**

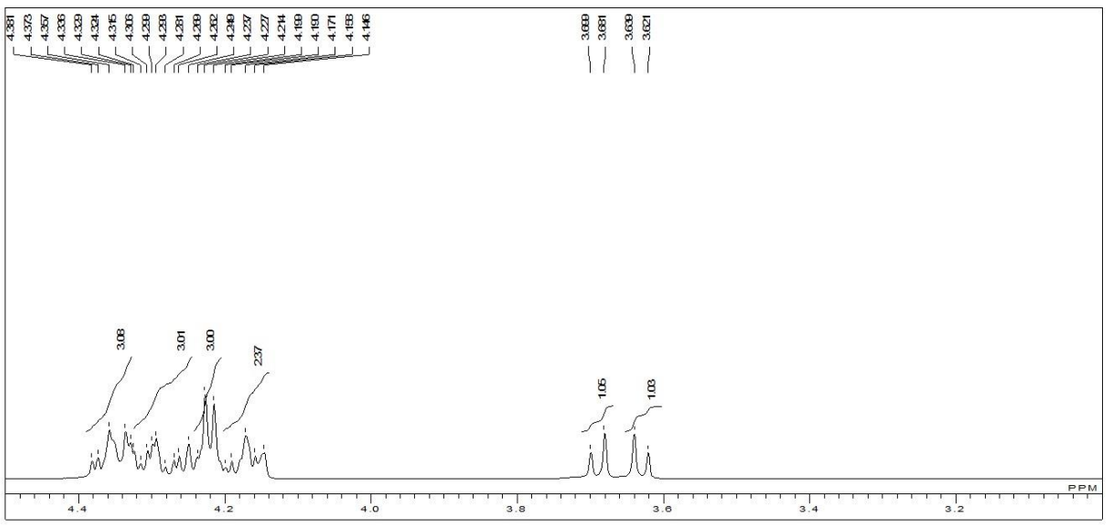


Figure SM-17(c). Selected up filed region ^{1}H-NMR (500 MHz, $CDCl_3$) of compound **3**

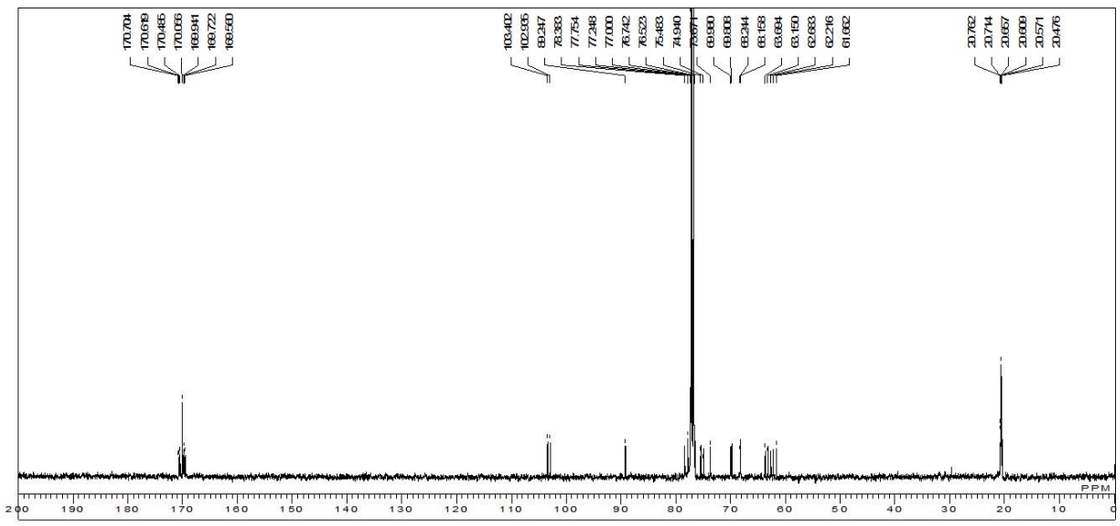


Figure SM-18(a). ^{13}C NMR (125 MHz, $CDCl_3$) of compound **3**

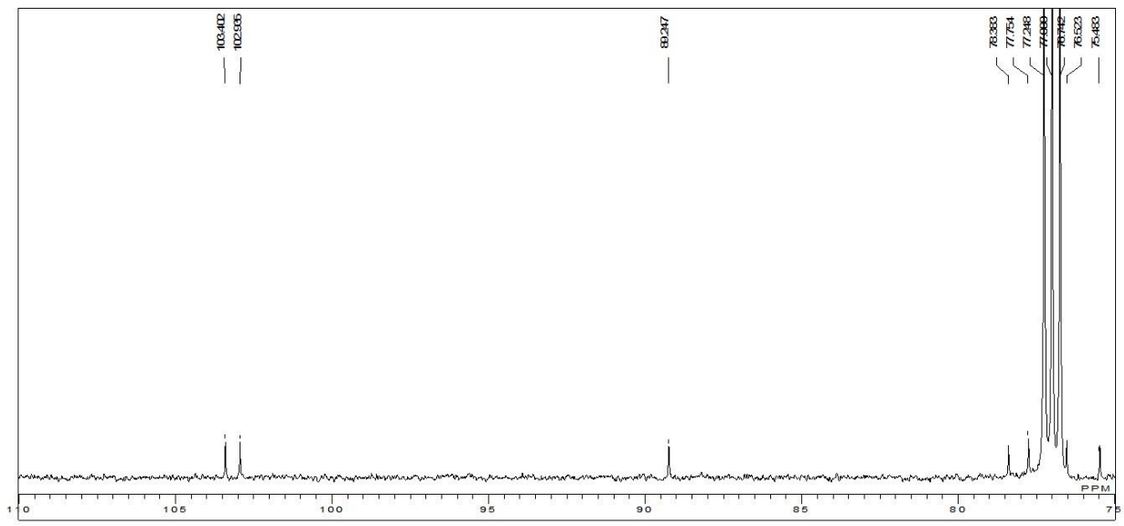


Figure SM-18(b). Selected down field region ^{13}C-NMR (500 MHz, $CDCl_3$) of compound **3**

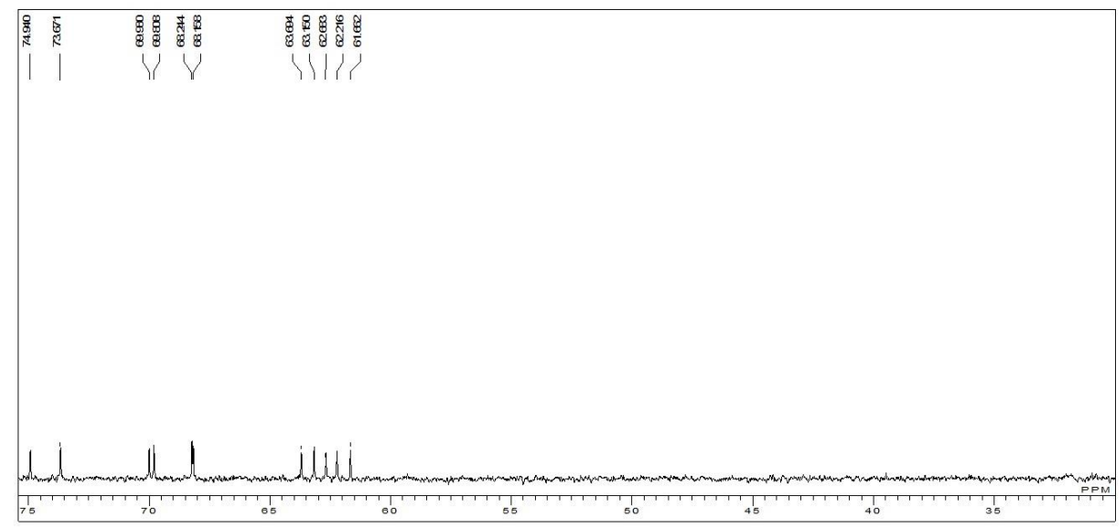


Figure SM-18(c). Selected up filed region ^{13}C-NMR (500 MHz, CDCl3) of compound **3**

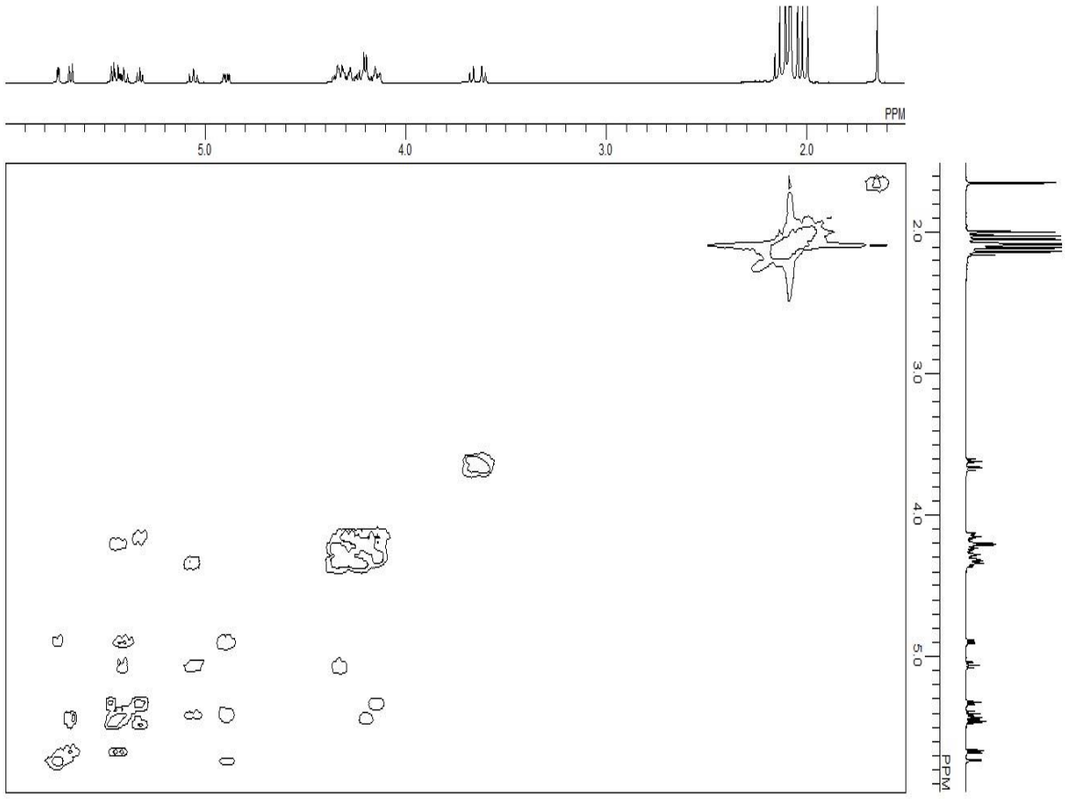


Figure SM-19. ^{1}H-^{1}H COSY 2D-NMR (500 MHz, $CDCl_3$) of compound **3**

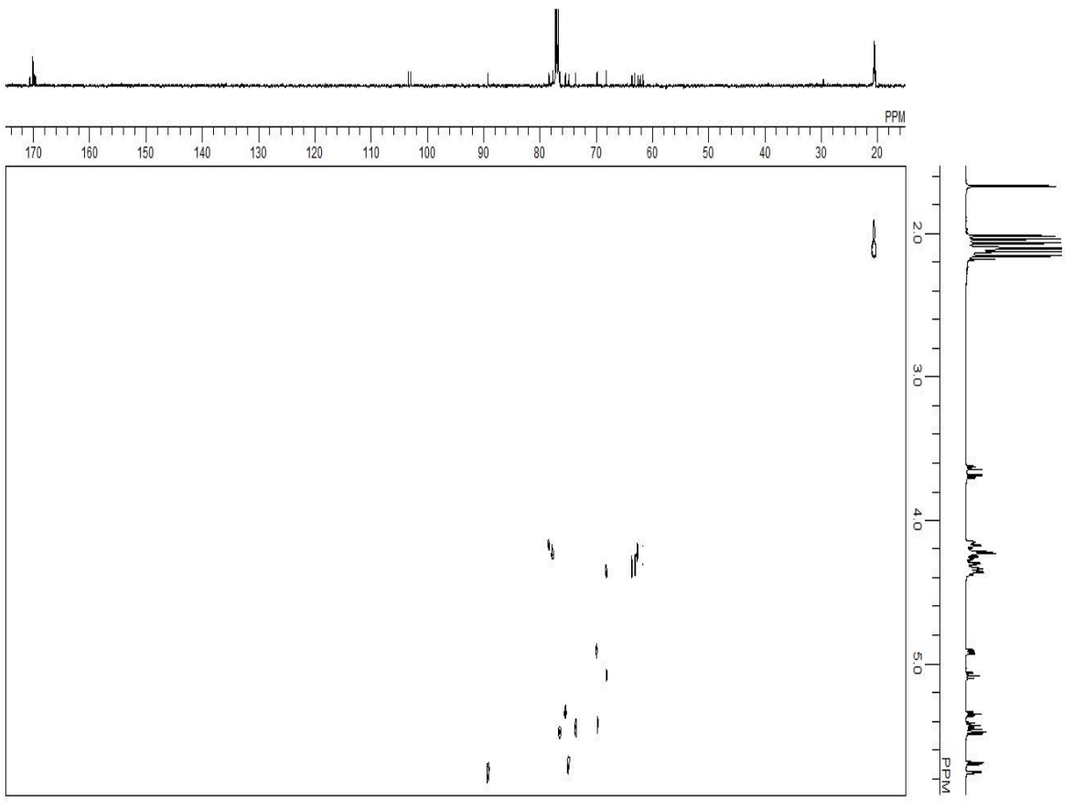


Figure SM-20. ^{13}C-^{1}H HETCOR 2D-NMR (500 MHz, $CDCl_3$) of compound **3**

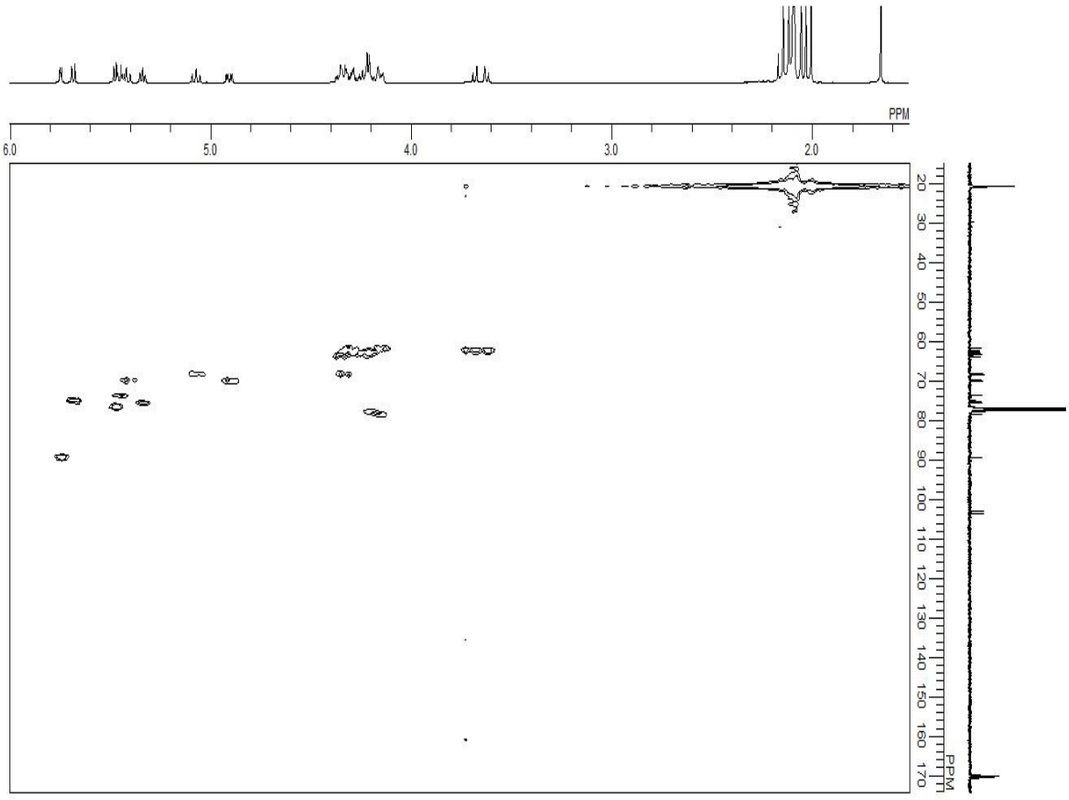


Figure SM-21. ^{1}H-^{13}C HMQC 2D-NMR (500 MHz, $CDCl_3$) of compound **3**

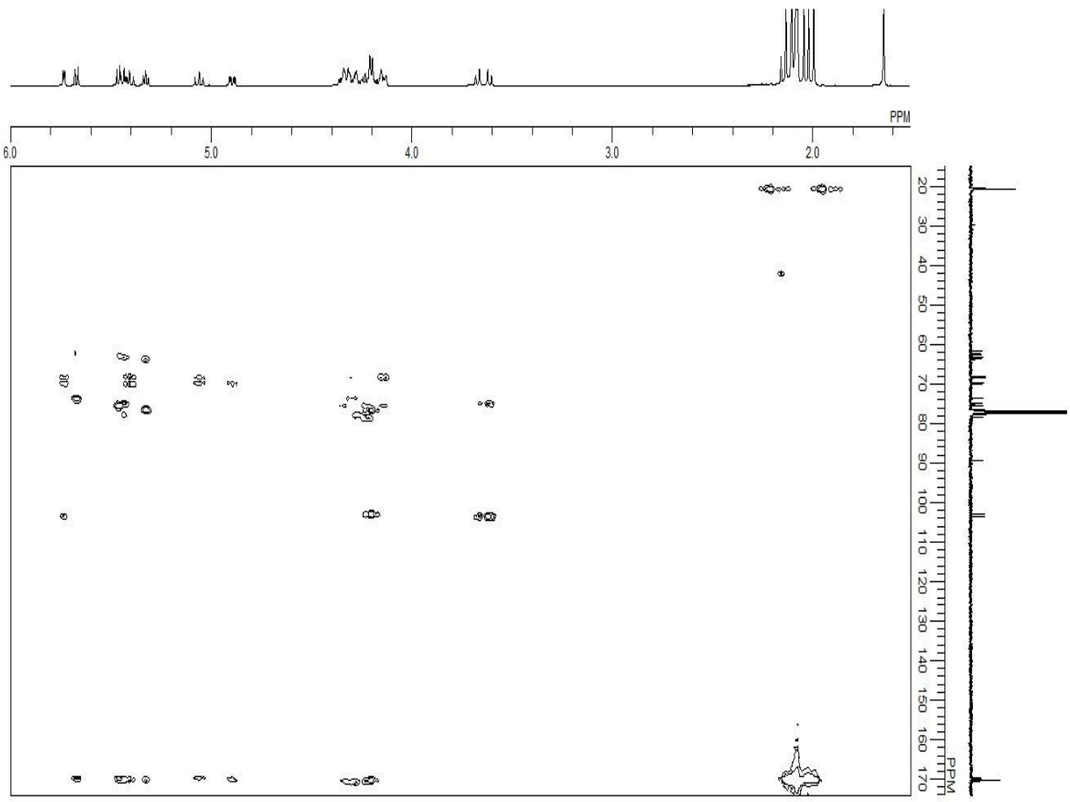


Figure SM-22. ^{1}H-^{13}C HMBC 2D-NMR (500 MHz, $CDCl_3$) of compound **3**

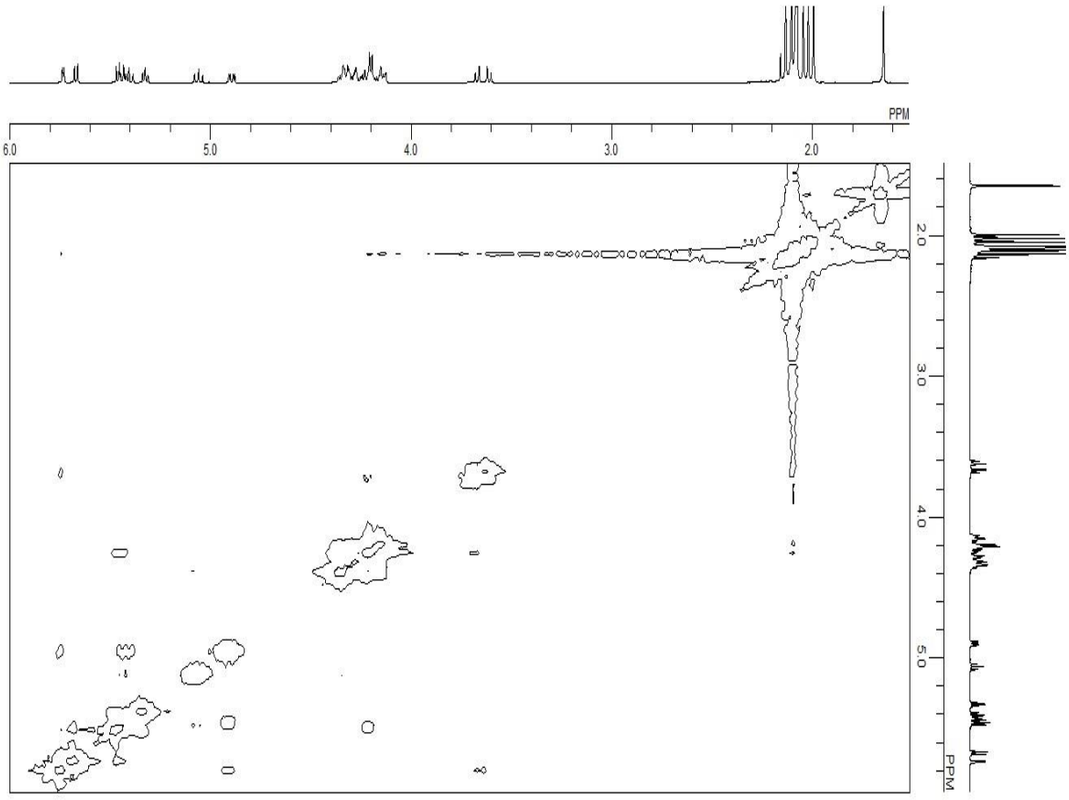


Figure SM-23. ^{1}H-^{1}H NOESY 2D-NMR (500 MHz, $CDCl_3$) of compound **3**

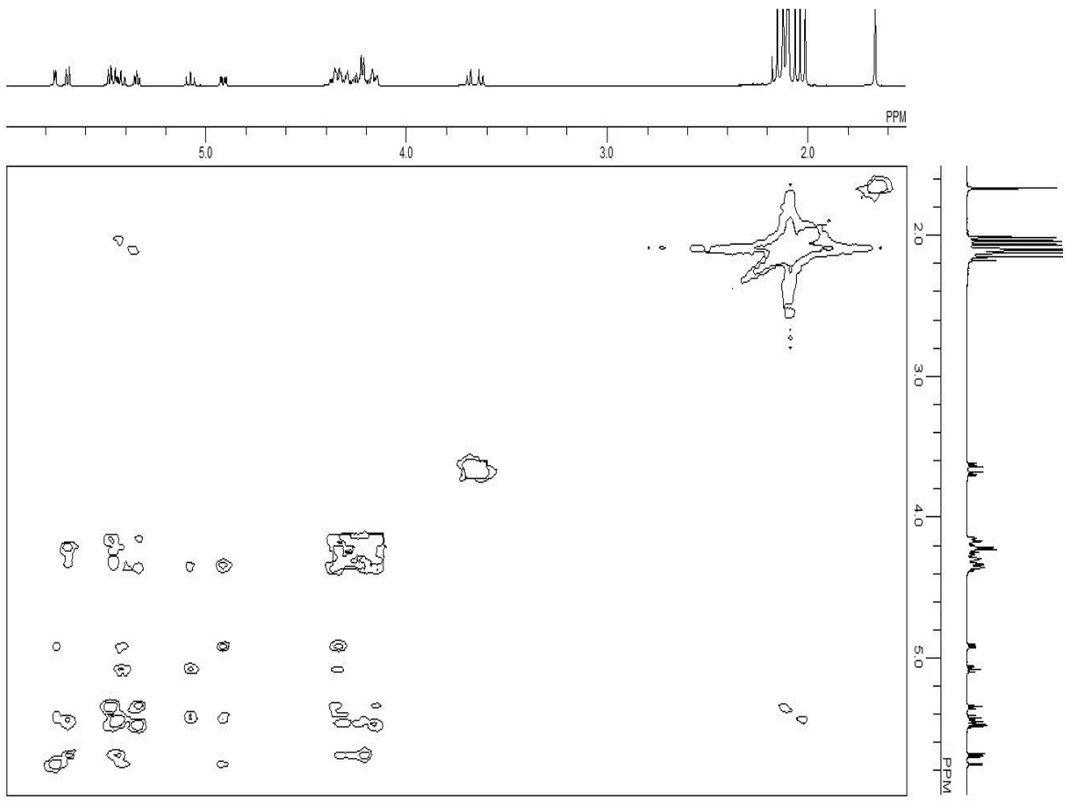
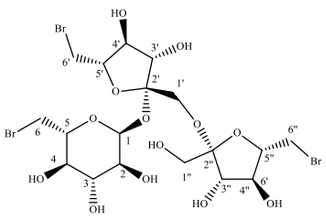


Figure SM-24. ^{1}H-^{1}H TOCSY 2D-NMR (500 MHz, $CDCl_3$) of compound **3**

6,6′,6′′-Tribromo-6,6′,6′′-trideoxy-1-kestose (**6**)



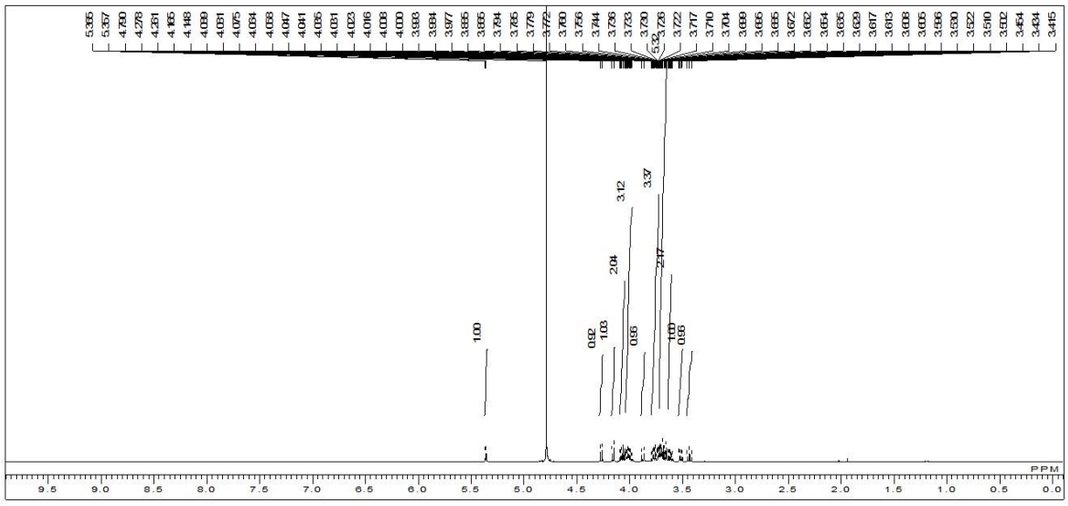


Figure SM-25(a). ^{1}H-NMR (500 MHz, D_2O) of compound **6**

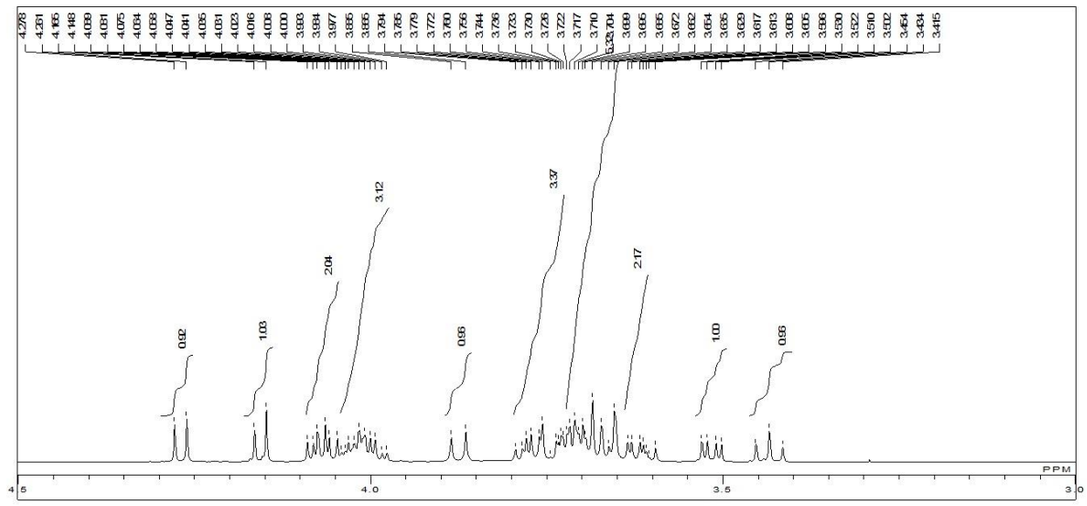


Figure SM-25(b). Selected region ^{1}H-NMR (500 MHz, D_2O) of compound **6**

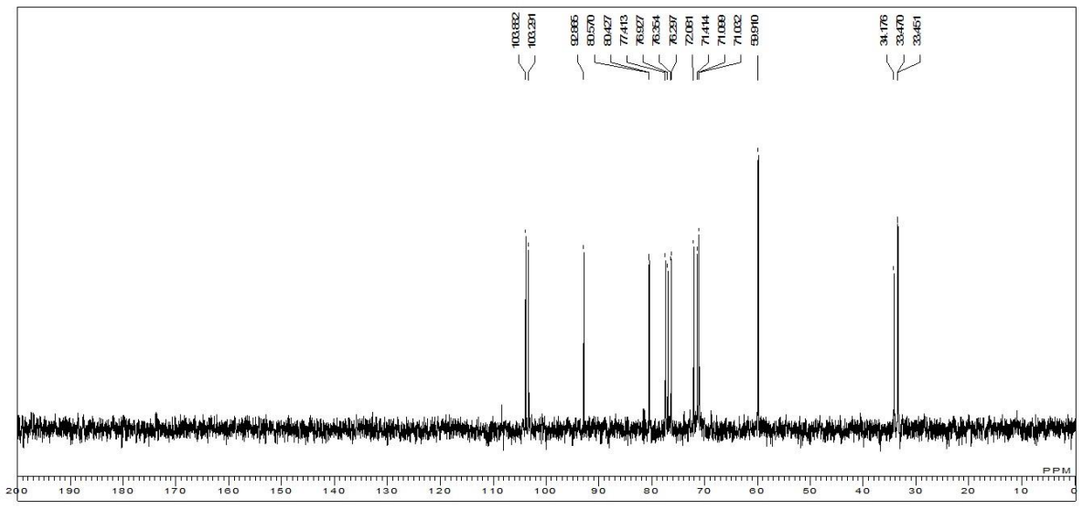


Figure SM-26(a). ^{13}C NMR (125 MHz, D_2O) of compound **6**

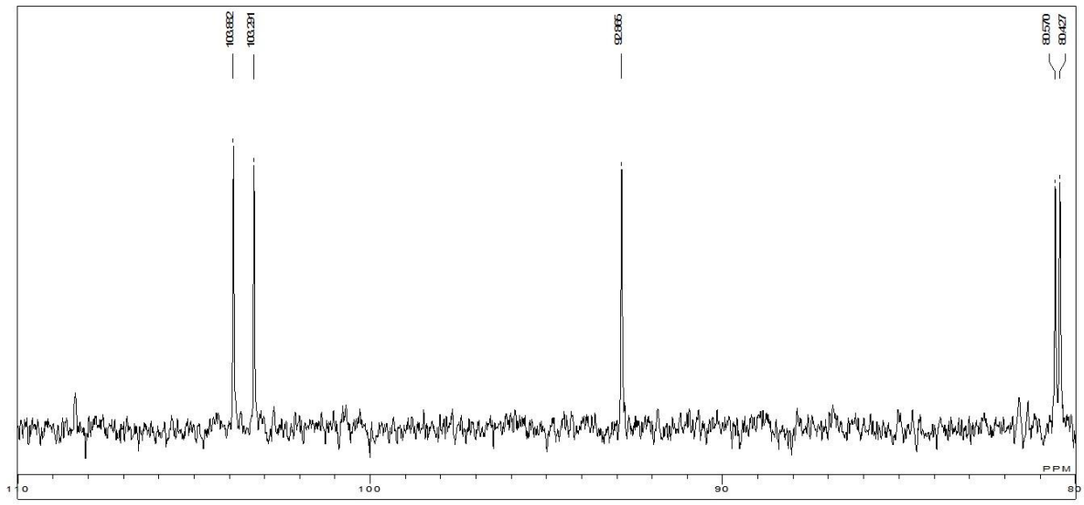


Figure SM-26(b). Selected down field region ^{13}C NMR (125 MHz, D_2O) of compound **6**

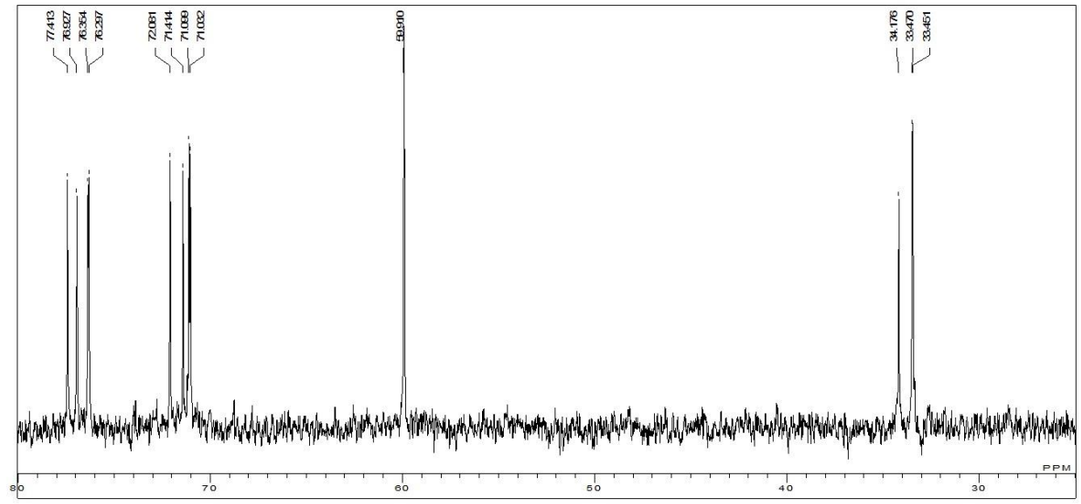


Figure SM-26(c). Selected up field region ^{13}C NMR (125 MHz, D_2O) of compound **6**

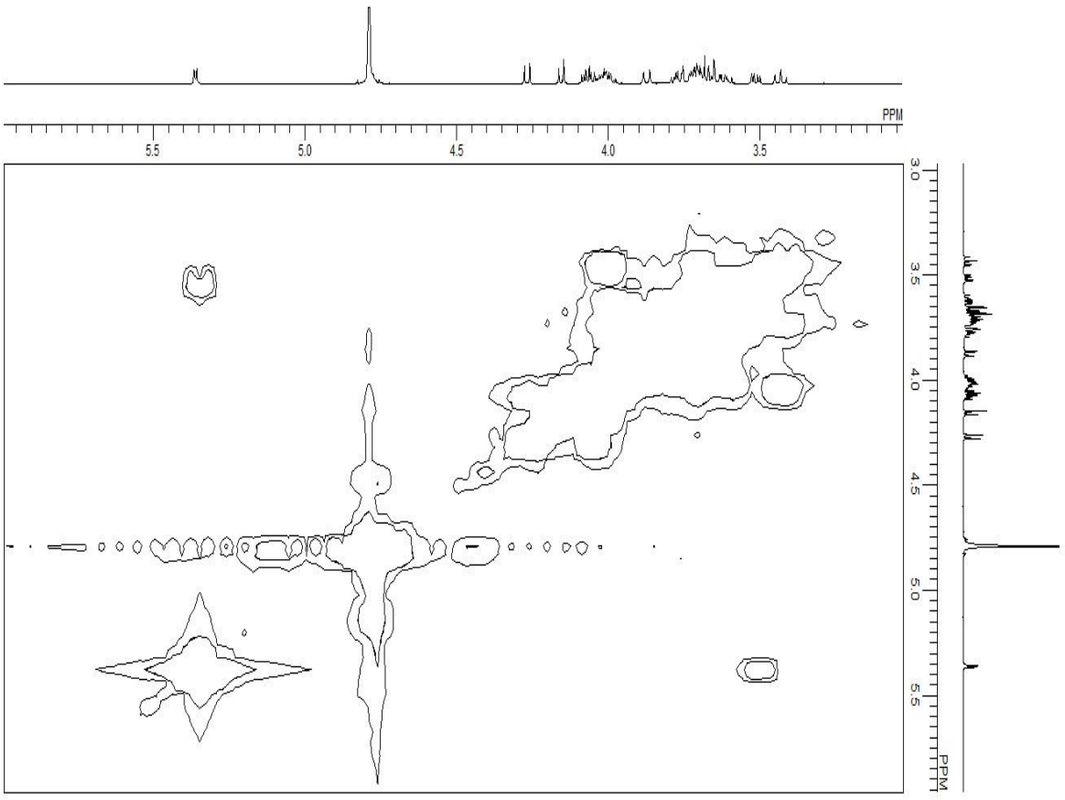


Figure SM-27. ^{1}H-^{1}H COSY 2D-NMR (500 MHz, D_2O) of compound **6**

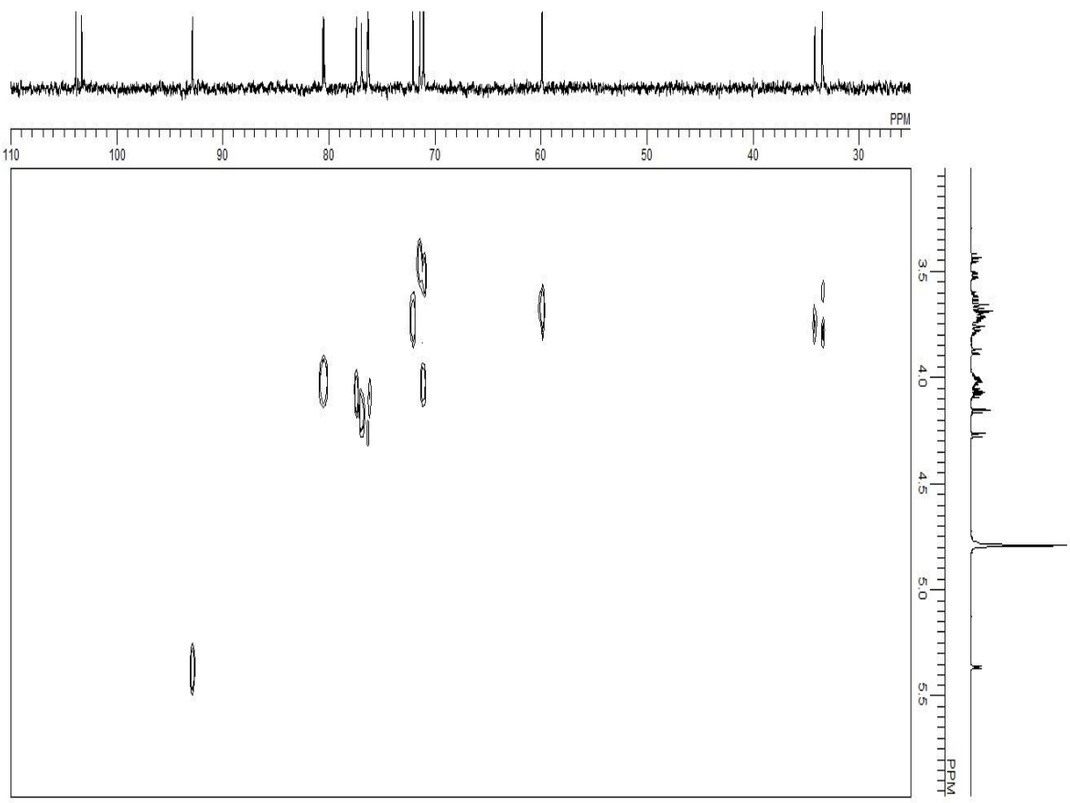


Figure SM-28. ^{13}C-^{1}H HETCOR 2D-NMR (500 MHz, D_2O) of compound **6**

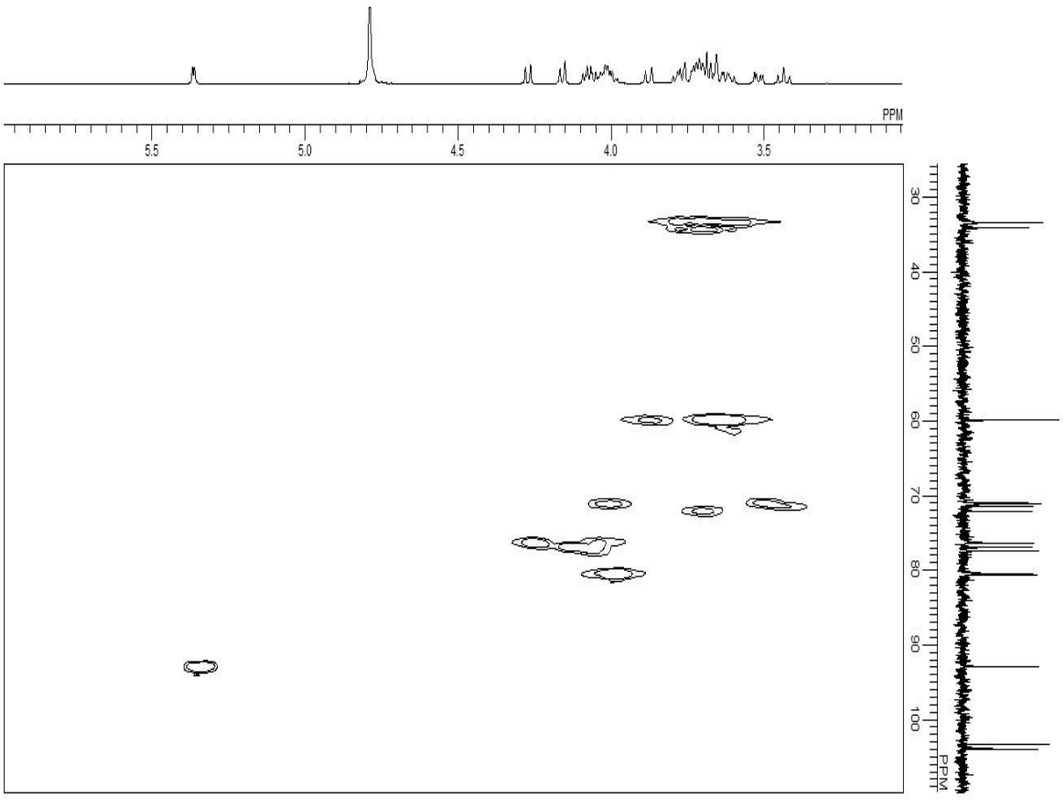


Figure SM-29. ^{1}H-^{13}C HMQC 2D-NMR (500 MHz, D_2O) of compound **6**

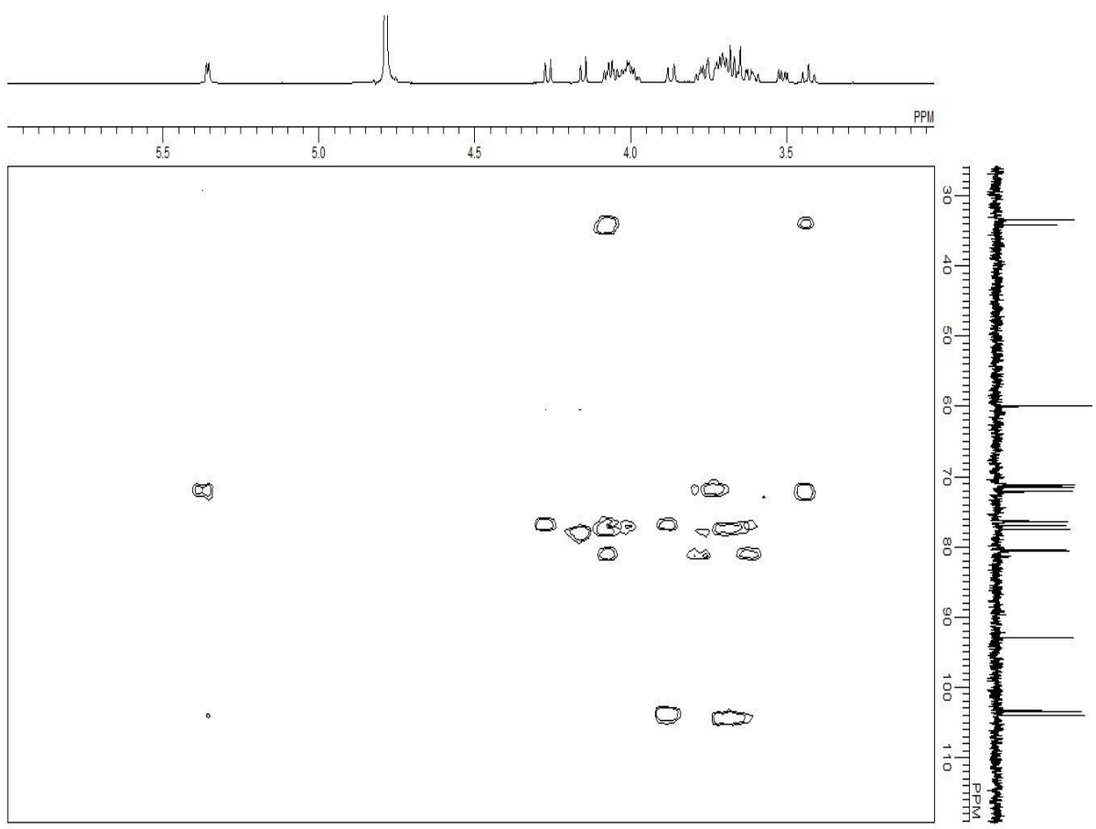


Figure SM-30. ^{1}H-^{13}C HMBC 2D-NMR (500 MHz, D_2O) of compound **6**

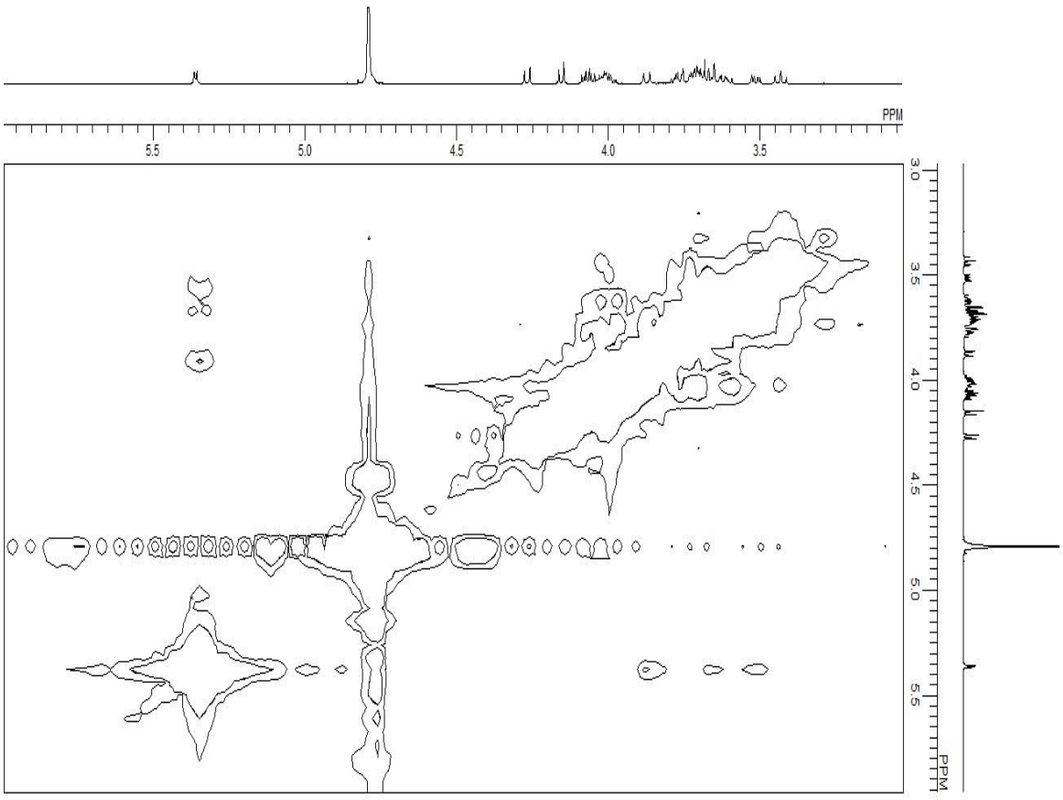


Figure SM-31. ^{1}H-^{1}H NOESY 2D-NMR (500 MHz, D_2O) of compound **6**

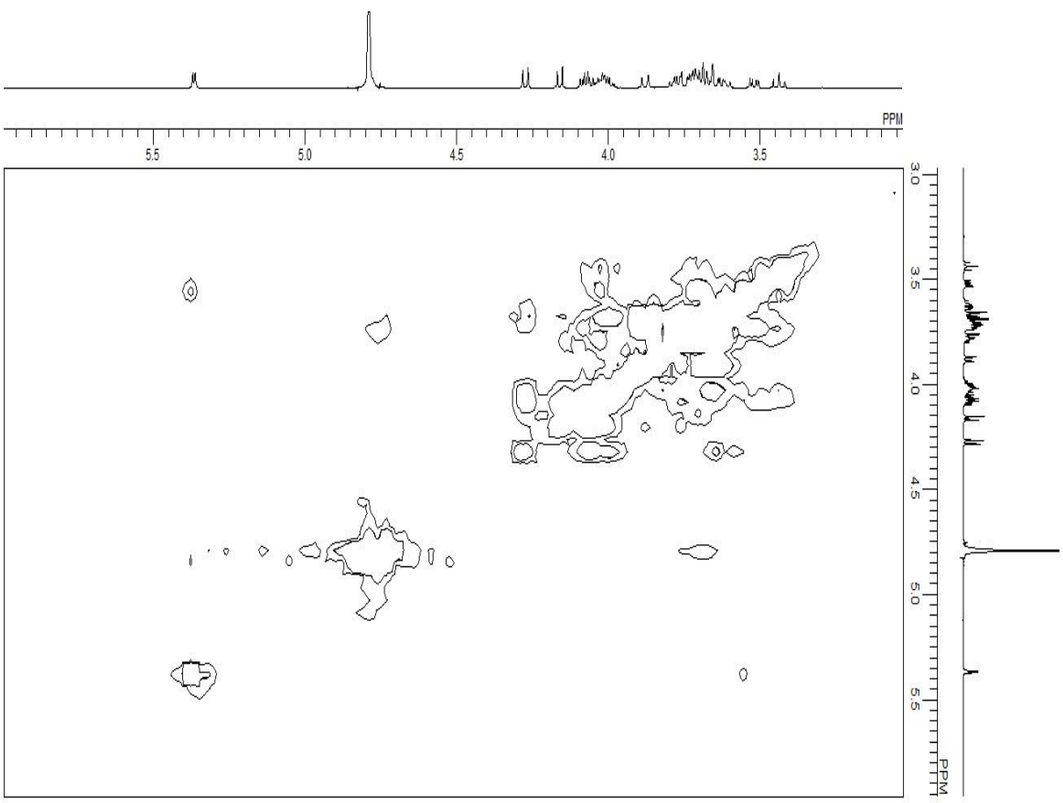
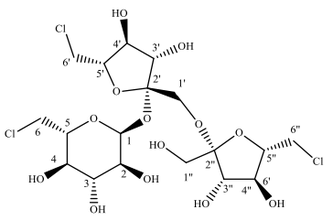


Figure SM-32. ^{1}H-^{1}H TOCSY 2D-NMR (500 MHz, D_2O) of compound **6**

6,6′,6′′-Trichloro-6,6′,6′′-trideoxy-1-kestose (**7**)



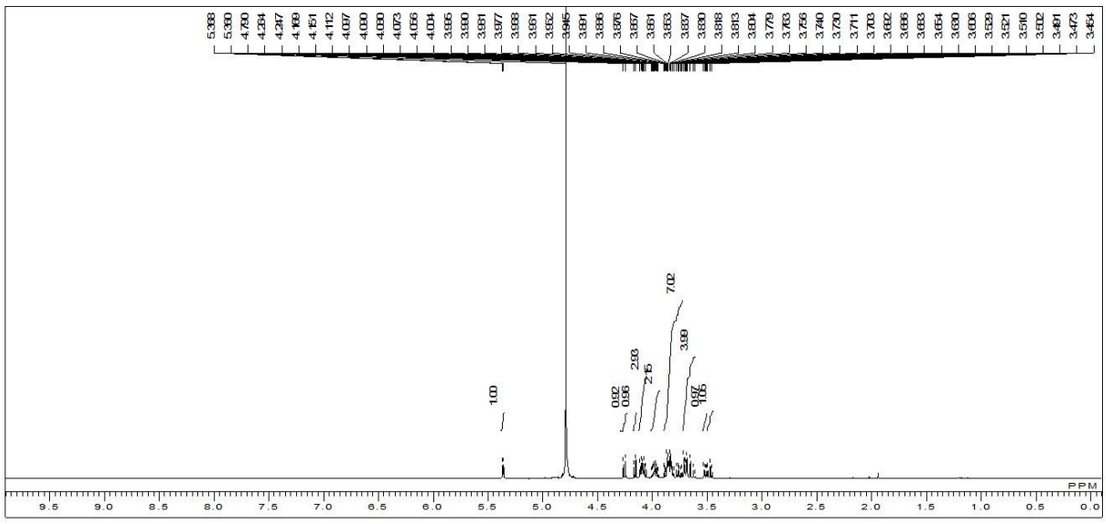


Figure SM-33(a). ^{1}H-NMR (500 MHz, D_2O) of compound **7**

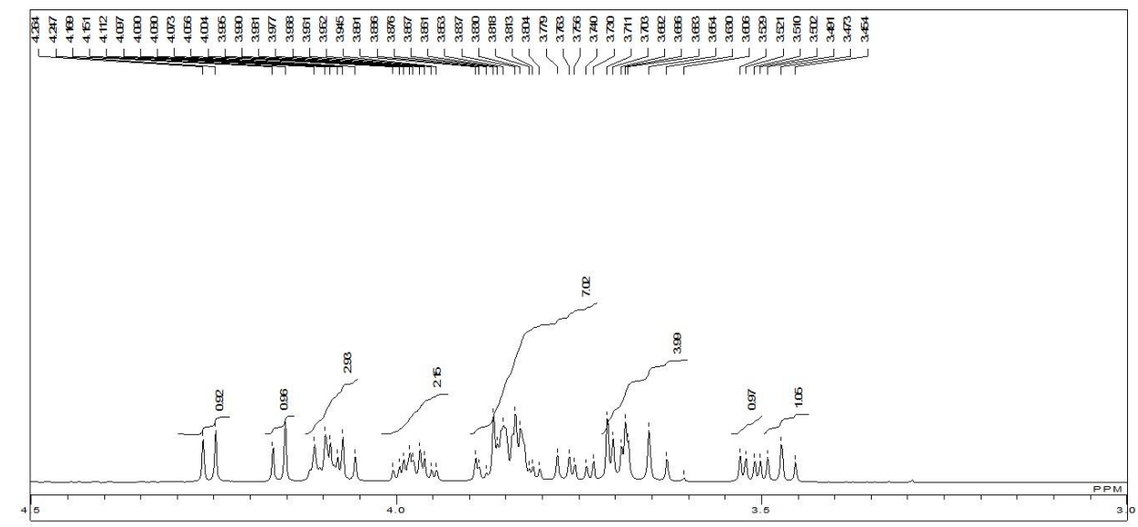


Figure SM-33(b). Selected region ^{1}H-NMR (500 MHz, D_2O) of compound **7**

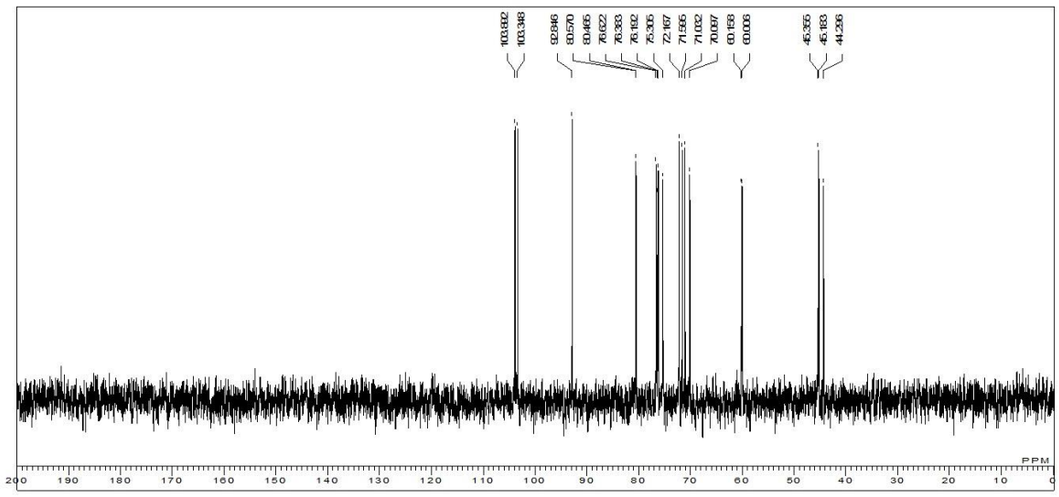


Figure SM-34(a). ^{13}C-NMR (125 MHz, D_2O) of compound **7**

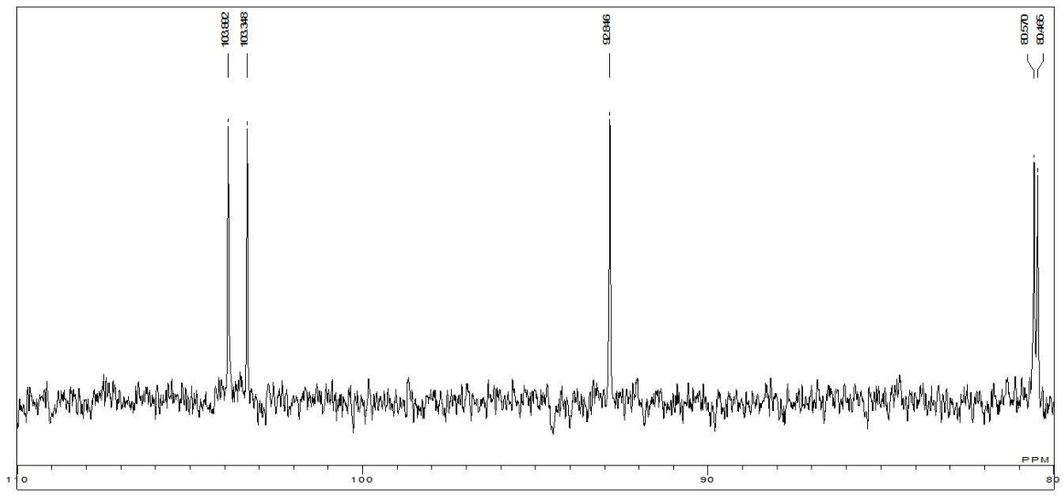


Figure SM-34(b). Selected down field region ^{13}C-NMR (125 MHz, D_2O) of compound **7**

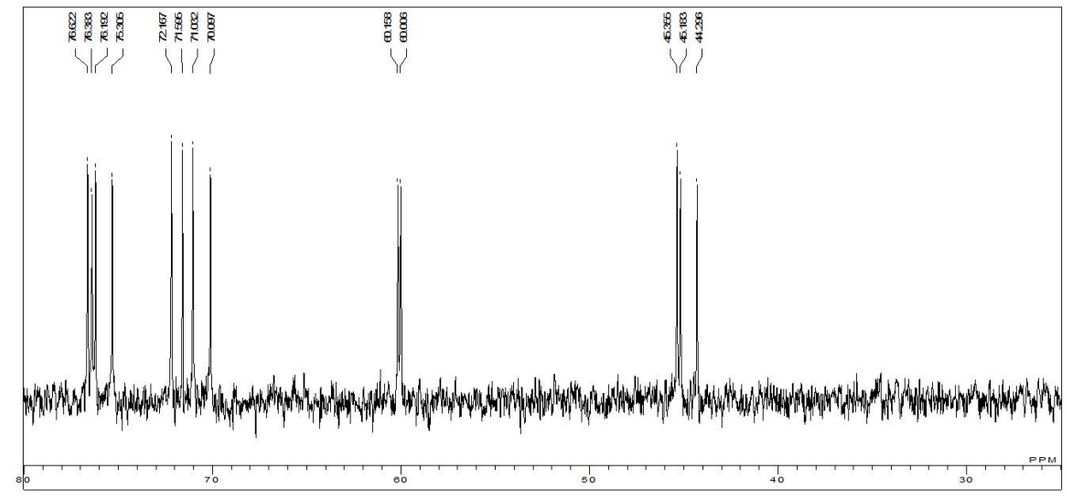


Figure SM-34(c). Selected up field region ^{13}C-NMR (125 MHz, D_2O) of compound **7**

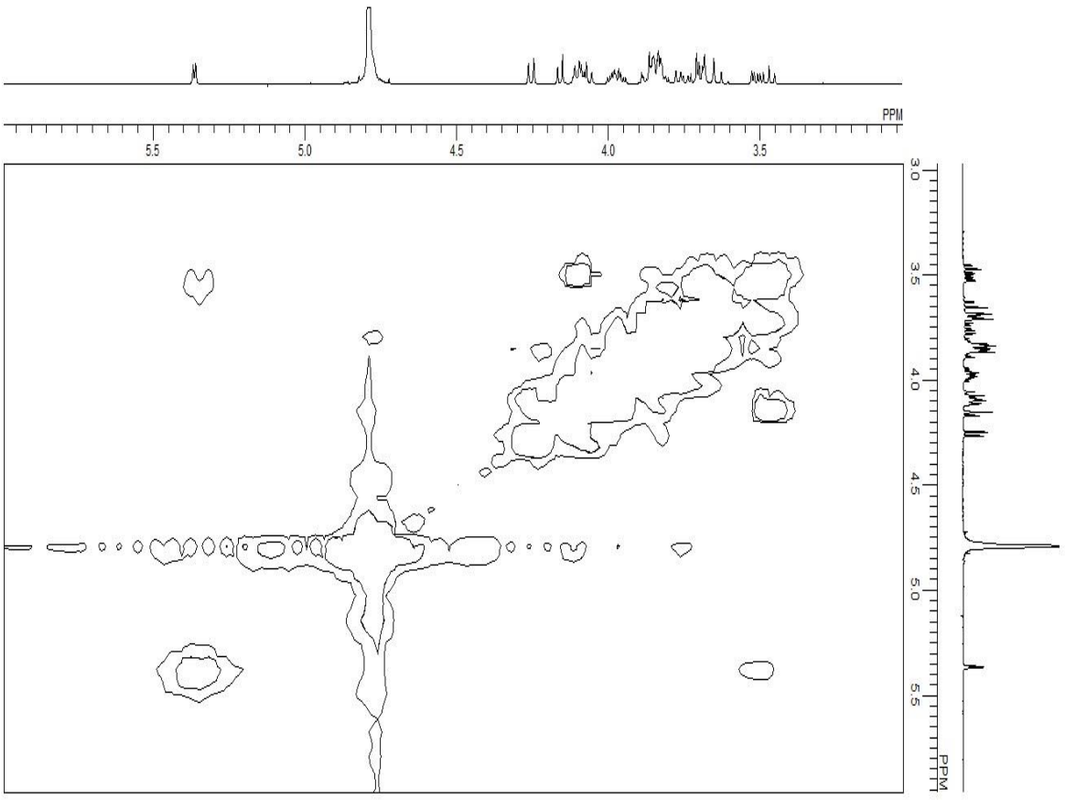


Figure SM-35. ^{1}H-^{1}H COSY 2D-NMR (500 MHz, D_2O) of compound **7**

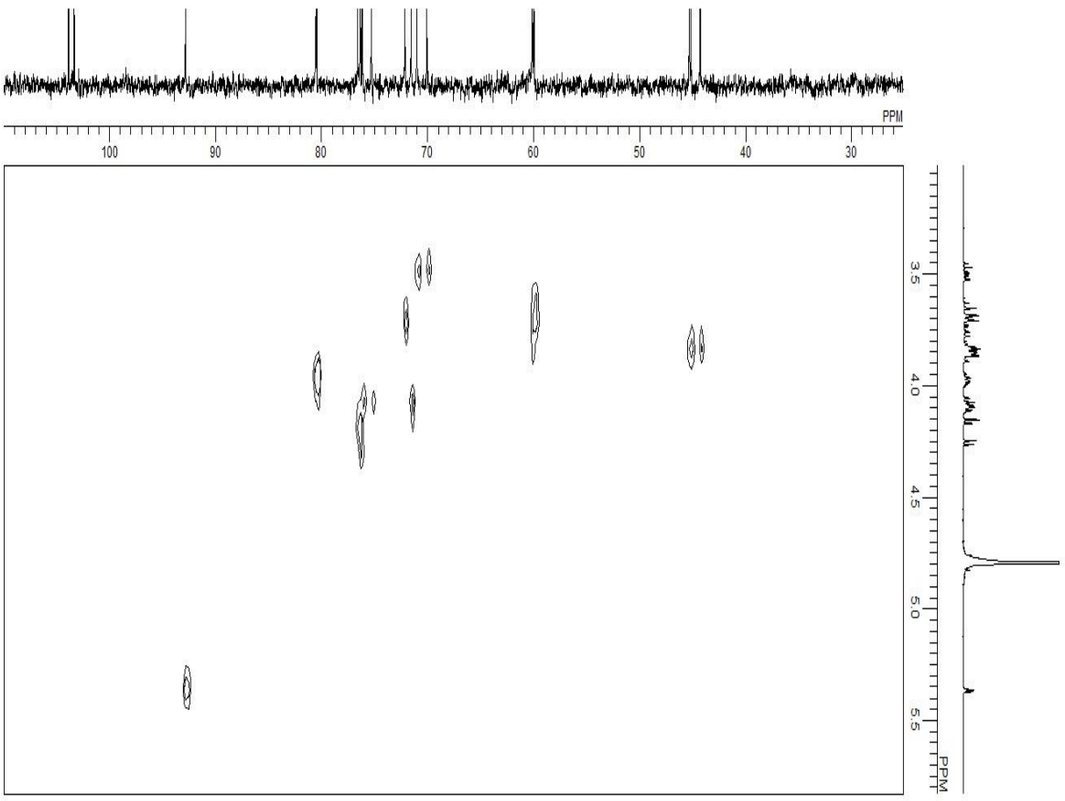


Figure SM-36. ^{13}C-^{1}H HETCOR 2D-NMR (500 MHz, D_2O) of compound **7**

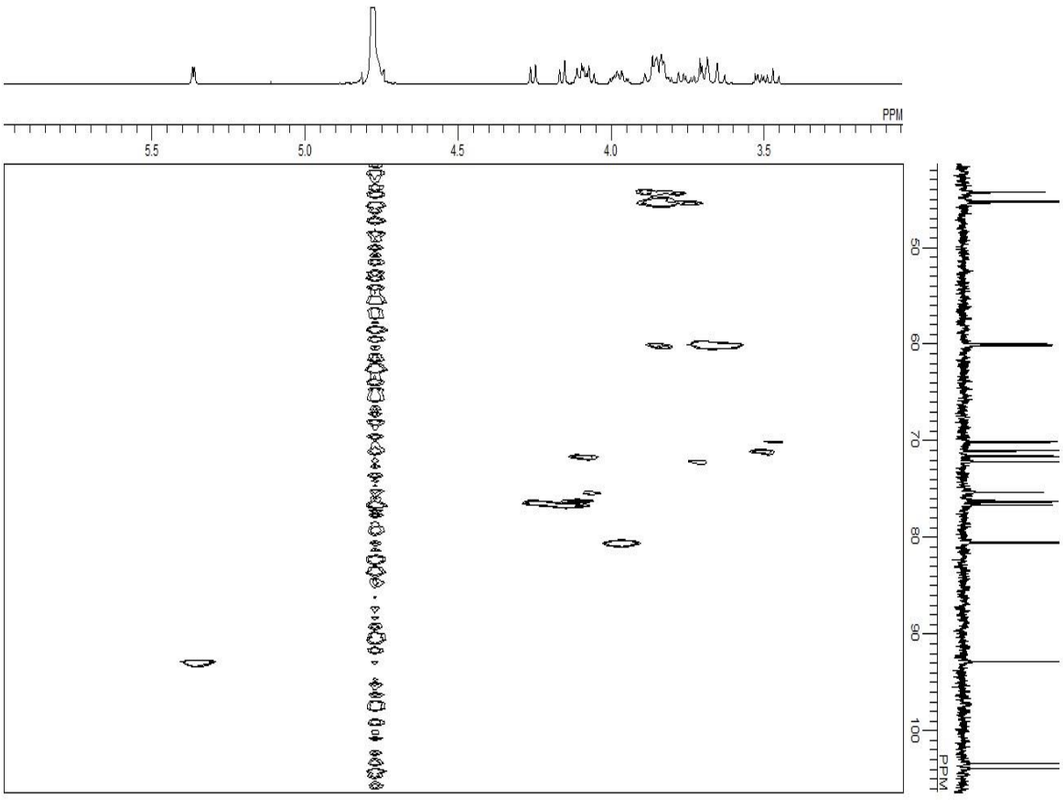


Figure SM-37. ^{1}H-^{13}C HMQC 2D-NMR (500 MHz, D_2O) of compound **7**

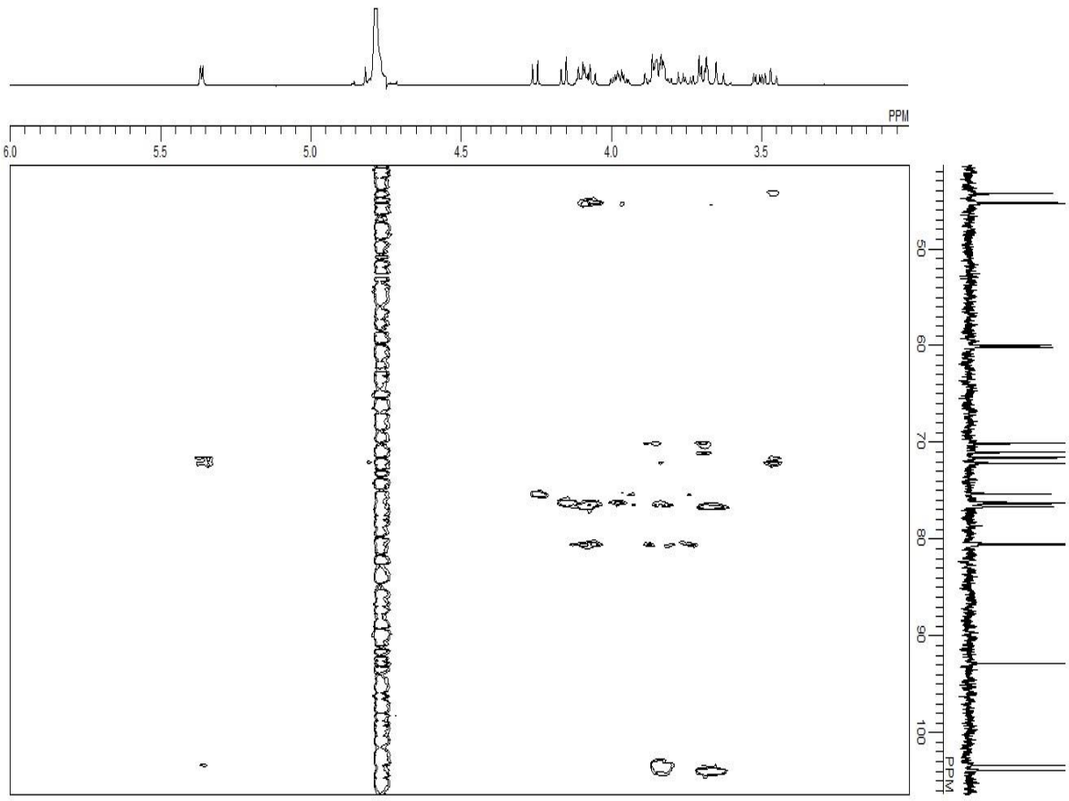


Figure SM-38. ^{1}H-^{13}C HMBC 2D-NMR (500 MHz, D_2O) of compound **7**

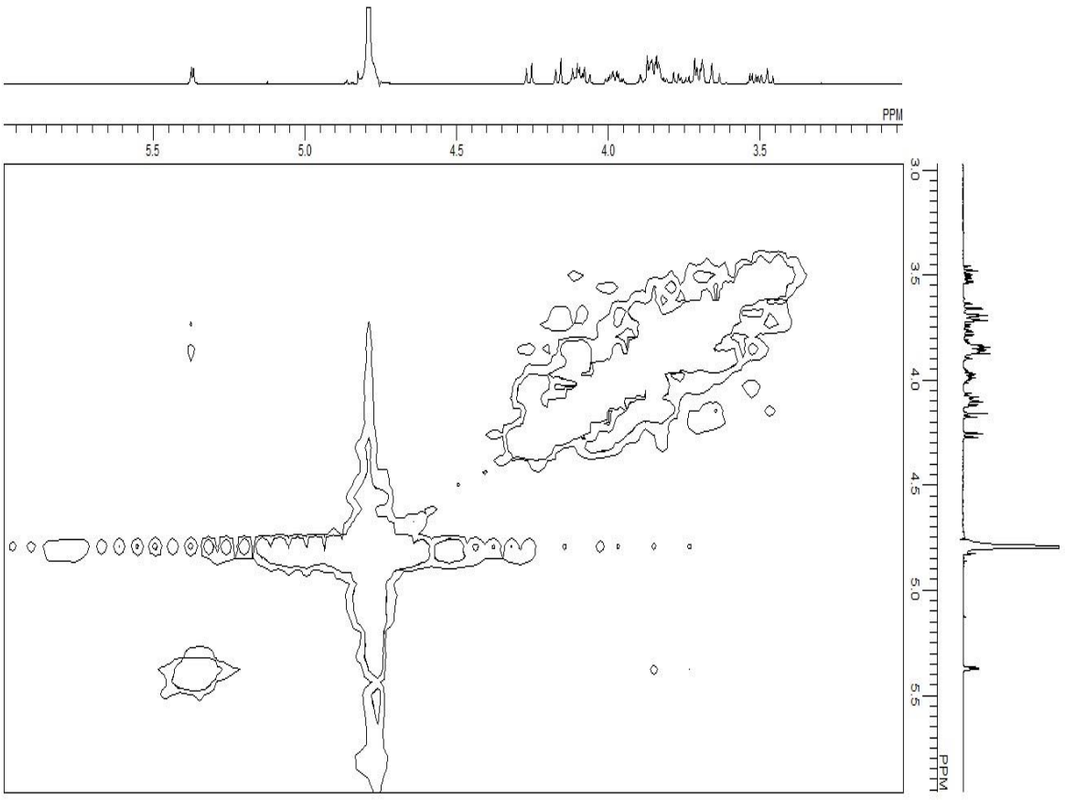


Figure SM-39. ^{1}H-^{1}H NOESY 2D-NMR (500 MHz, D_2O) of compound **7**

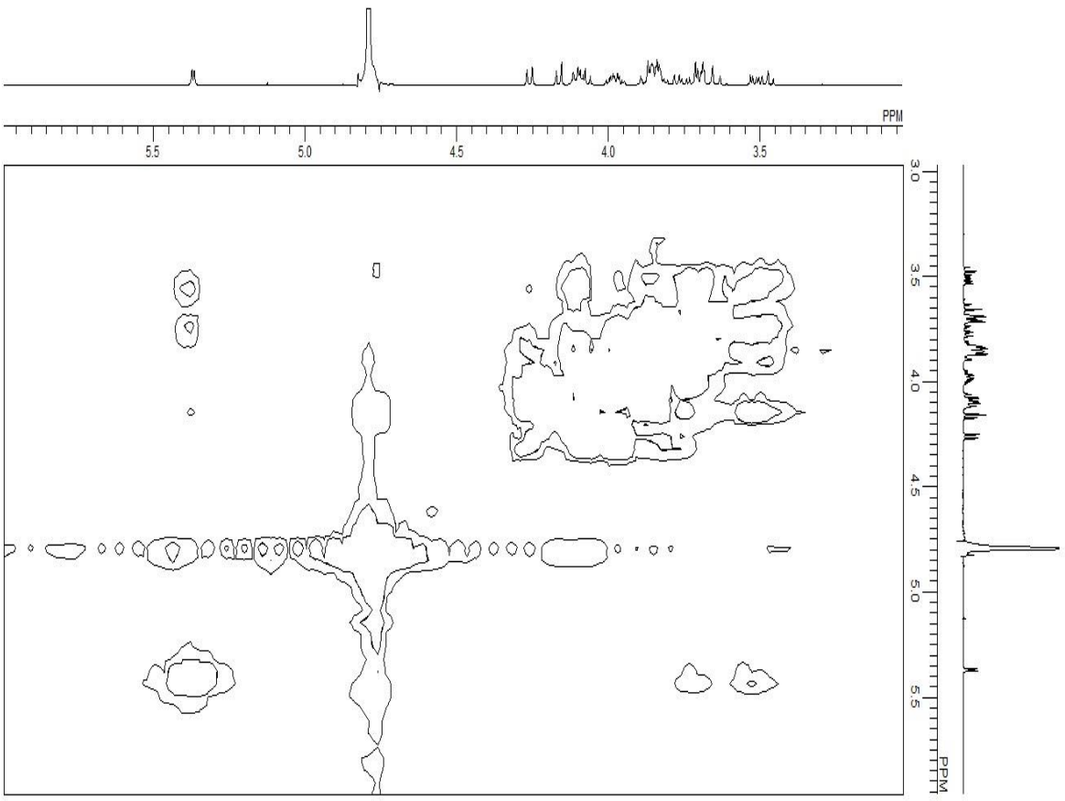
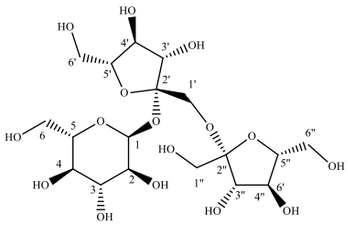


Figure SM-40. ^{1}H-^{1}H TOCSY 2D-NMR (500 MHz, D_2O) of compound **7**

1-kestose (**1**)



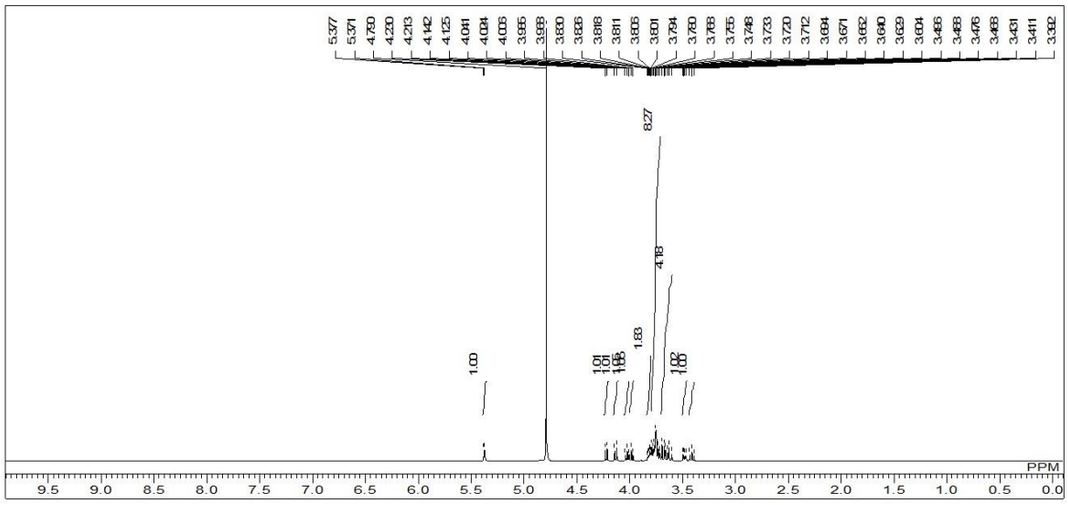


Figure SM-41(a).^{1}H-NMR (500 MHz, D_2O) of compound **1**

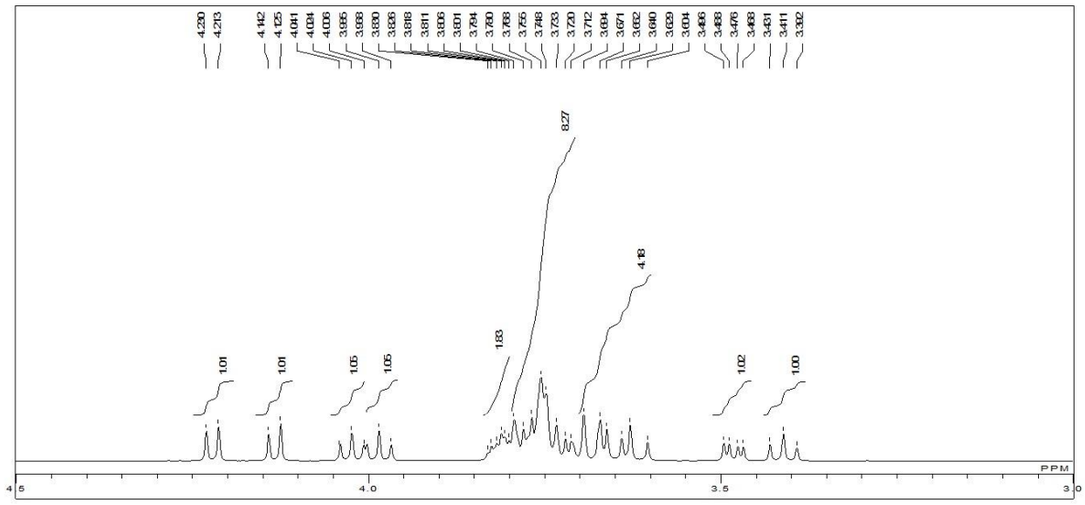


Figure SM-41(b). Selected region ^{1}H-NMR (500 MHz, D_2O) of compound **1**

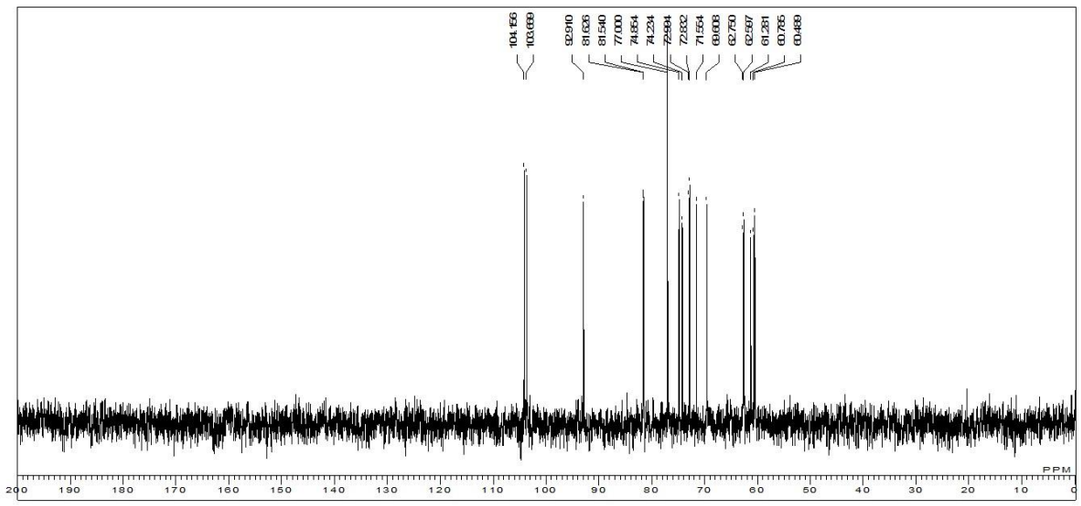


Figure SM-42(a). ^{13}C NMR (125 MHz, D_2O) of compound **1**

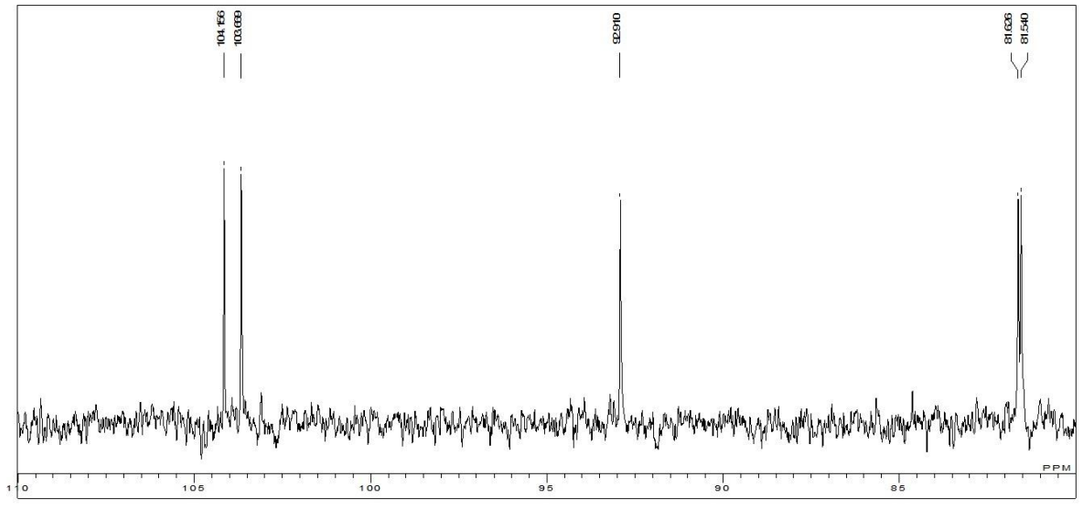


Figure SM-42(b). Selected down field region ^{13}C NMR (125 MHz, D_2O) of compound **1**

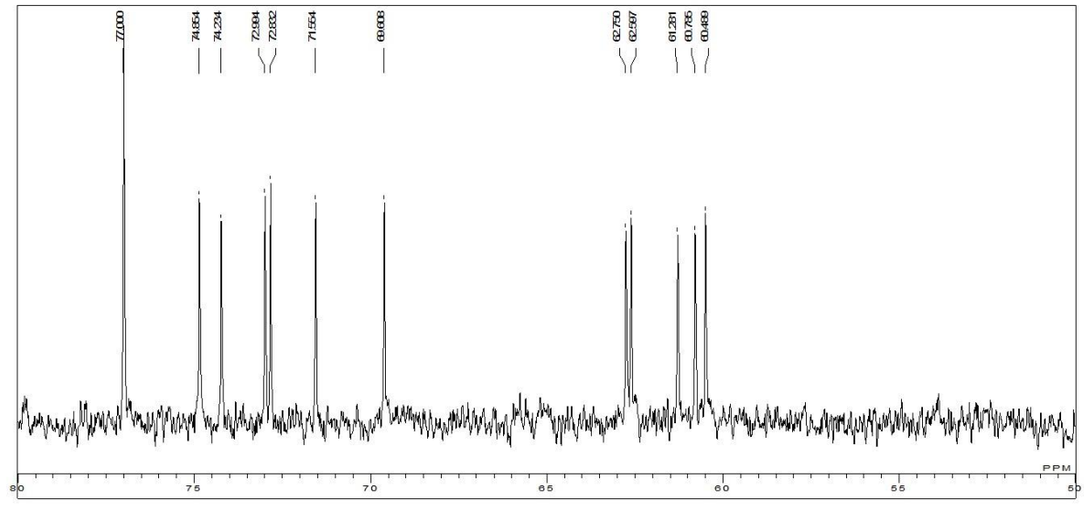


Figure SM-42(c). Selected up field region ^{13}C NMR (125 MHz, D_2O) of compound **1**

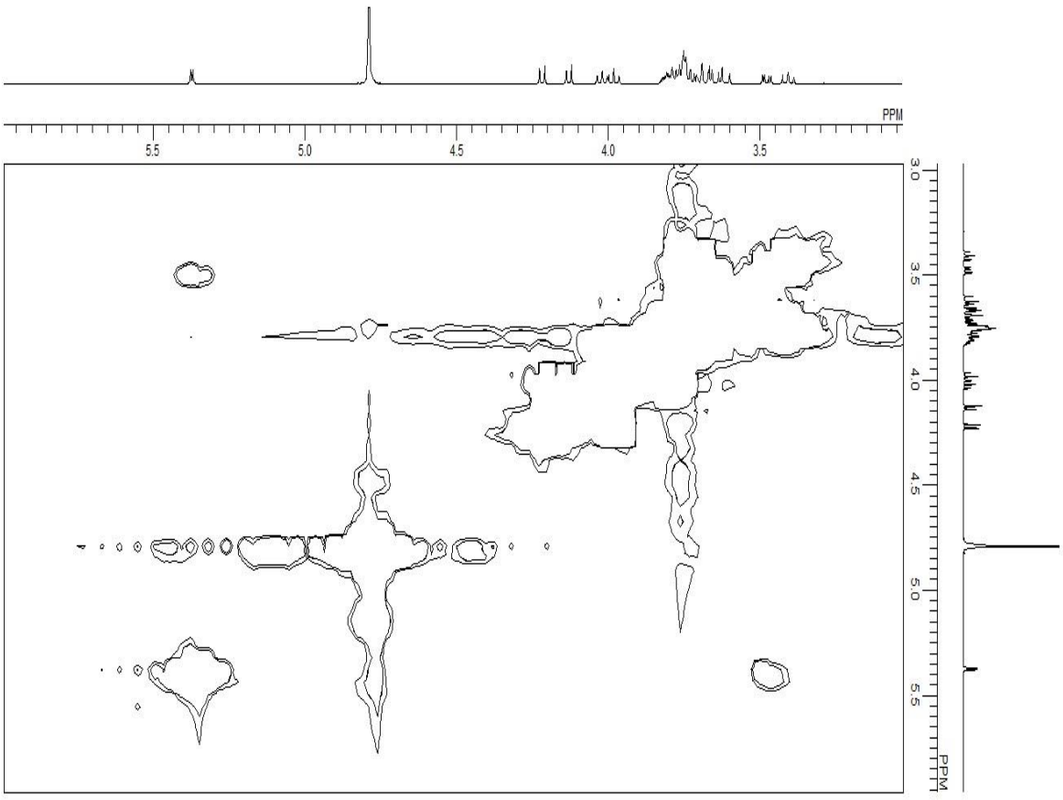


Figure SM-43. ^{1}H-^{1}H COSY 2D-NMR (500 MHz, D_2O) of compound **1**

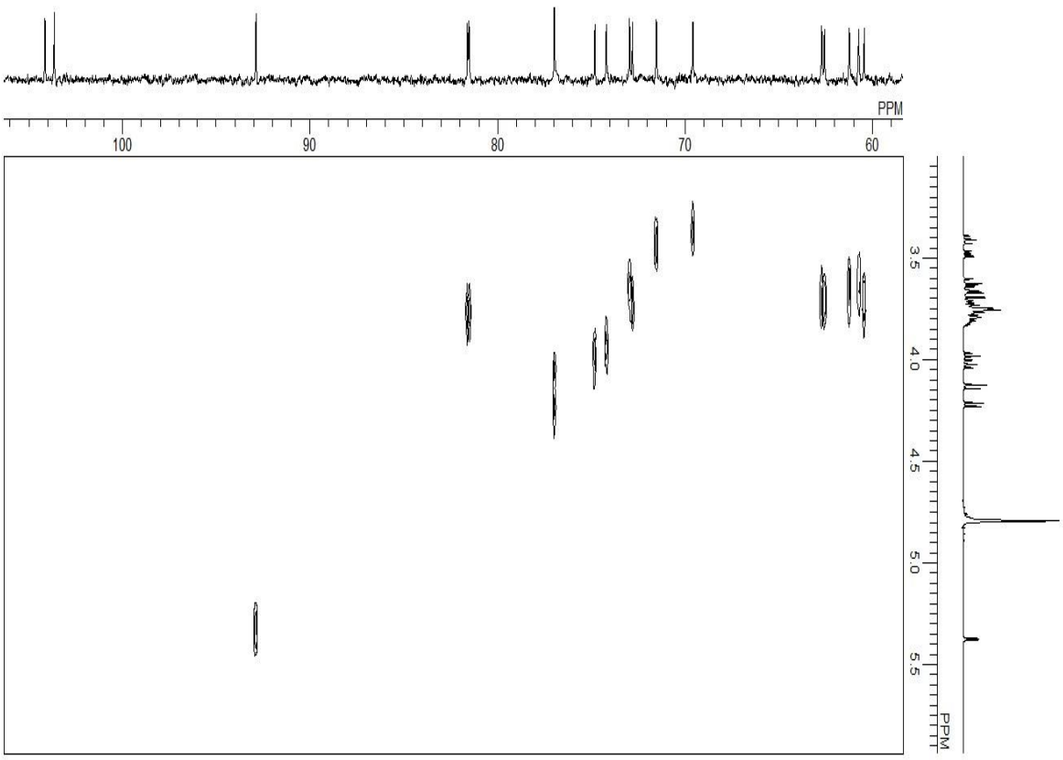


Figure SM-44. ^{13}C-^{1}H HETCOR 2D-NMR (500 MHz, D_2O) of compound **1**

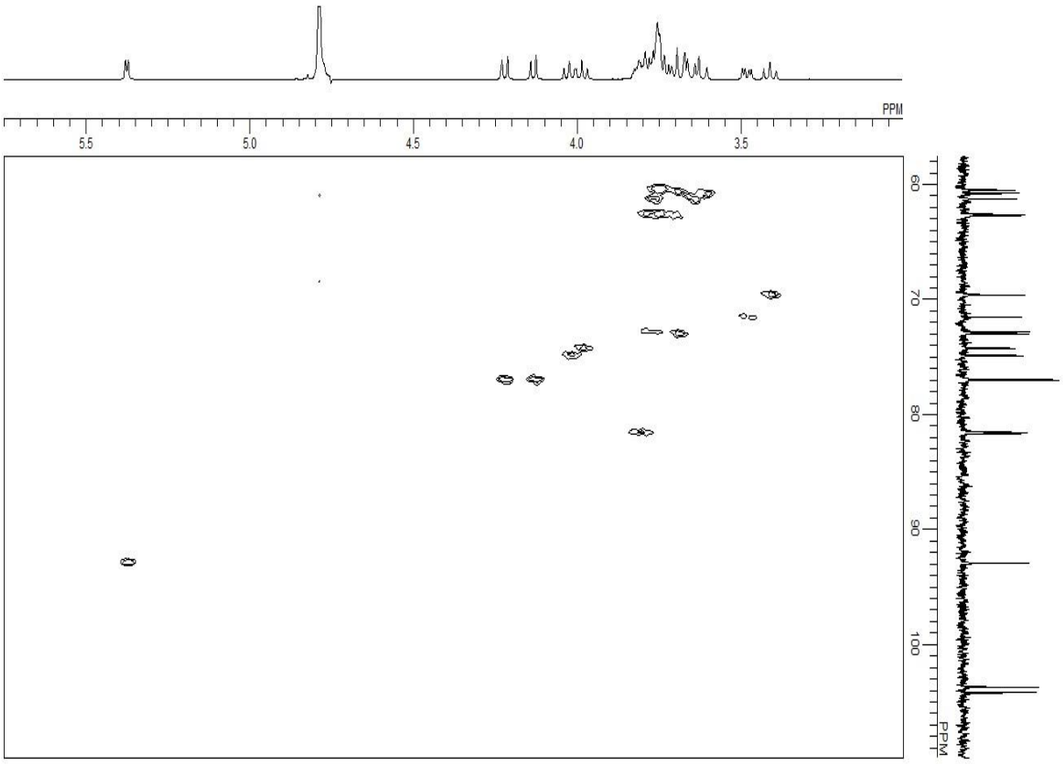


Figure SM-45. ^{1}H-^{13}C HMQC 2D-NMR (500 MHz, D_2O) of compound **1**

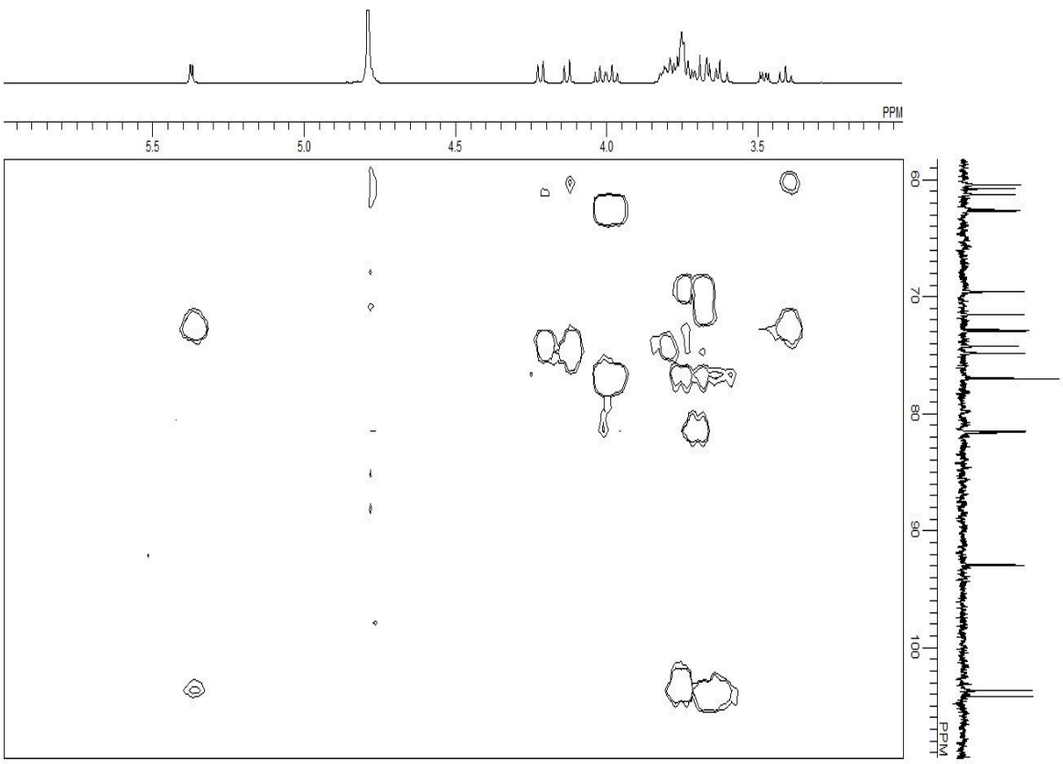


Figure SM-46.^{1}H-^{13}C HMBC 2D-NMR (500 MHz, D_2O) of compound **1**

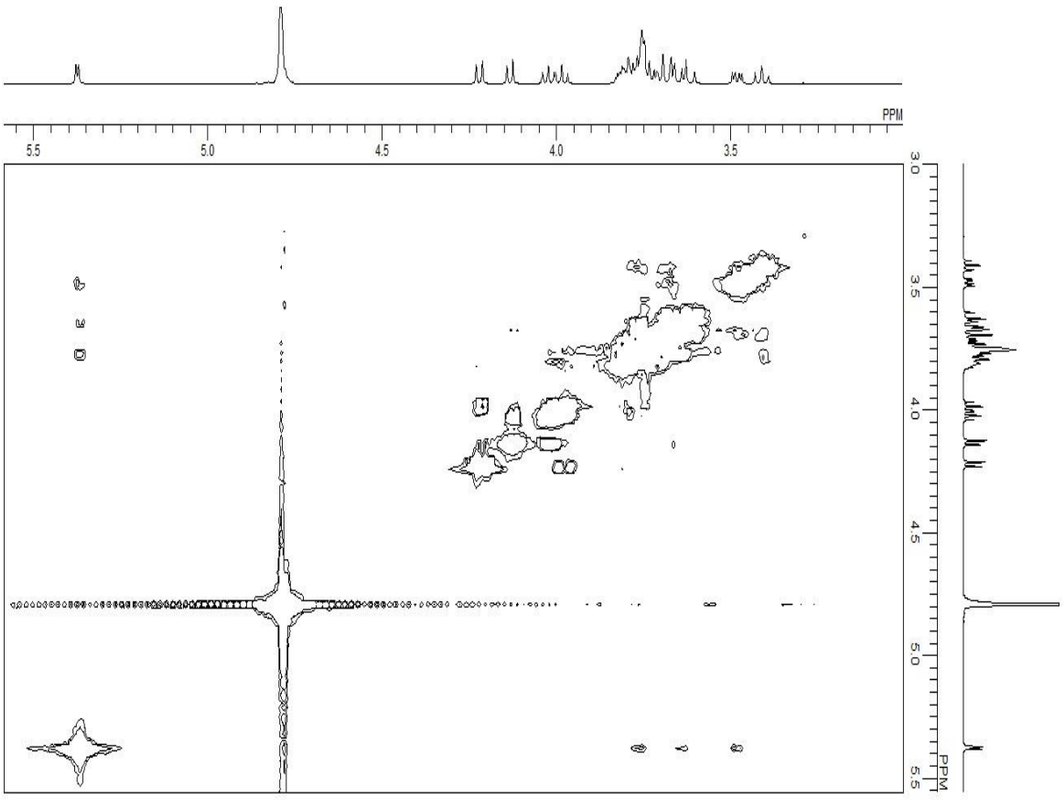


Figure SM-47.^{1}H-^{1}H NOESY 2D-NMR (500 MHz, D_2O) of compound **1**

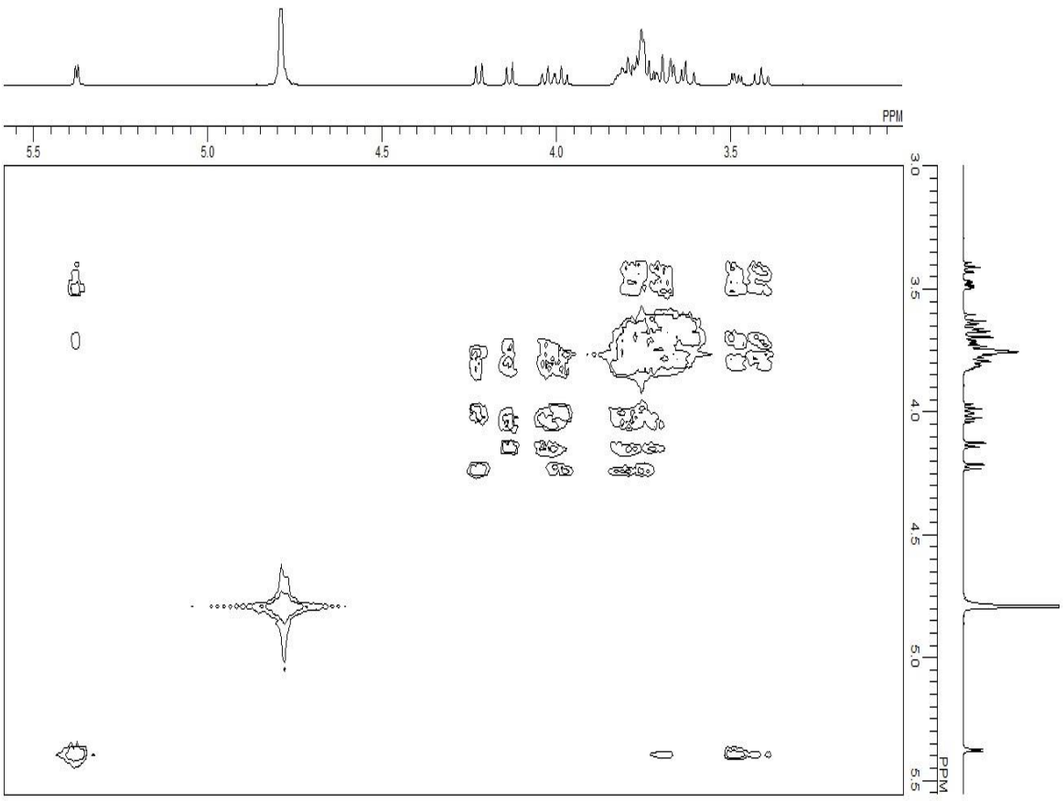


Figure SM-48.^{1}H-^{1}H TOCSY 2D-NMR (500 MHz, D_2O) of compound **1**

^{1}H and 13C NMR literature comparison with observation data

Table SM-1. ^{1}H and ^{13}C NMR literature comparison with observation data of per-O-acetylated 1-kestose and per-O-acetylated halogenated 1-kestose derivatives

Assignment	**1″,2,3,3′,3″,4,4′,4″,6,6′,6″-Undeca-*O*-acetyl-deoxy-1-kestose (3)** CAS: 25101-98-8 (*δ* in ppm and *J* in Hz)						**1″,2,3,3′,3″,4,4′,4″-octa-*O*-acetyl-6,6′,6″-tribromo-6,6′,6′-trideoxy 1-kestose (4)** No CAS (*δ* in ppm and *J* in Hz)		**1″,2,3,3′,3″,4,4′,4″-octa-*O*-acetyl-6,6′,6″-trichloro-6,6′,6″-trideoxy-1-kestose (5)** No CAS (*δ* in ppm and *J* in Hz)	
	Ref [1]		**Ref [2]**		**Observed**		**Observed**		**Observed**	
	δ ^{1}H ($CDCl_3$)	*δ* ^{13}C (100.6 MHz, $CDCl_3$)	*δ* ^{1}H (100 or 220 MHz, $CDCl_3$)	*δ* ^{13}C[a]	*δ* ^{1}H (500 MHz, $CDCl_3$)	*δ* ^{13}C (125 MHz, $CDCl_3$)	*δ* ^{1}H (500 MHz, $CDCl_3$)	*δ* ^{13}C (125 MHz, $CDCl_3$)	*δ* ^{1}H (500 MHz, $CDCl_3$)	*δ* ^{13}C (125 MHz, $CDCl_3$)
1	5.71 (d)	90.3 (d)	5.71		5.75 (d)	89.2	5.67 (d)	90.1	5.70–5.66 (m)	90.0
2	4.88 (dd)	70.3 (d)	4.88		4.91 (dd)	70.0	4.95 (dd)	69.7	4.93 (dd)	69.7
3	5.42 (t)	70.1 (d)	5.42		5.42 (t)	69.8	5.48–5.42 (m)	69.3	5.48–5.41 (m)	69.4
4	5.22 (t)	68.0 (d)	5.04		5.08 (t)	68.2	5.03 (t)	70.8	5.06 (t)	69.7
5	4.40–4.20 (m, overlap 13H signals)	69.0 (d)	4.42–4.07 (11H signals)		4.39–4.33 (m)	68.2	4.35–4.28 (m)	69.3	4.38-4.32 (m)	69.8
6a		59.7 (t)	4.42–4.07 (11H signals)	—	4.33–4.24 (m)	61.7	3.54 (dd)	31.1	3.68 (dd)	43.2
6b			4.42–4.07 (11H signals)		4.20–4.14 (m)		3.40 (dd)		3.57 (dd)	
1′a		63.7 (t)	3.71		3.69 (d)	62.2	3.79 (d)	61.5	3.75 (s)	61.6
1′b			3.62		3.63 (d)		3.73 (d)			
2′	—	104.3 (s)	—		—	103.4	—	103.8	—	103.8
3′	5.37 (d)	76.2 (d)	5.46		5.69 (d)	74.9	5.70 (d)	75.8	5.70–5.66 (m)	75.5
4′	[a]	75.3 (d)	5.32		5.46 (t)	73.7	5.48–5.42 (m)	76.4	5.48–5.41 (m)	75.7

5′	4.40–4.20 (m, overlap 13H signals)	78.1 (d)	4.42–4.07 (11H signals)		4.24–4.20 (m)	77.8	4.35–4.28 (m)	79.8	4.28–4.22 (m)	79.9
6′		62.5 (t)	4.42–4.07 (11H signals)		4.33–4.24 (m)	63.2	3.66 (d)	32.0	3.82–3.78 (m)	44.4
1′′		64.4 (t)	4.42–4.07 (11H signals)		4.24–4.20 (m)	62.7	4.24 (s)	62.0	4.28–4.22 (m)	62.2
2′′	—	103.1 (s)	—		—	102.9	—	103.1	—	103.1
3′′	5.46 (d)	76.6 (d)	5.68		5.48 (d)	76.5	5.50 (d)	77.2	5.50 (d)	76.9
4′′	[a]	76.0 (d)	5.22		5.34 (t)	75.5	5.32 (t)	78.1	5.33 (t)	77.2
5′′	4.40–4.20 (m, overlap 13H signals)	79.1 (d)	4.42–4.07 (11H signals)		4.20–4.14 (m)	78.4	4.22–4.19 (m)	80.7	4.17 (q)	80.6
6′′		62.9 (t)	4.42–4.07 (11H signals)		4.39–4.33 (m)	63.7	3.69 (d)	32.7	3.82–3.78 (m)	44.6
$J_{1,2}$	3.4		3.9		3.4		4.0		3.7	
$J_{2,3}$	10.2		9.0		10.3		10.3		10.6	
$J_{3,4}$	10.2		9.4		9.7		9.7		9.7	
$J_{4,5}$			10.0				2.3		2.3	
$J_{5,6a}$										
$J_{5,6b}$							6.3		5.7	
$J_{6a,6b}$							11.5		12.0	
$J_{1'a,1'b}$					9.2		10.3			
$J_{3',4'}$	8.6		7.0		8.0		8.0			
$J_{4',5'}$			6.0							
$J_{5',6'}$							6.9			
$J_{3'',4''}$	8.6		8.0		6.9		6.3		6.3	
$J_{4'',5''}$			8.0							
$J_{5'',6''}$							7.4		6.5	
CH_3	2.09 (s), 2.12 (s), 2.11 (s), 2.10 (s),	21.5–20.8	2.12 2.09		2.19–2.14 (m), 2.13–2.12 (m),	20.8, 20.7,	2.16–2.15 (m), 2.14 (s),	20.8, 20.8, 20.7, 20.8,	2.16 (s), 2.15–2.13 (m),	20.8, 20.7,

	2.09 (s), 2.08 (s), 2.07 (s), 2.05 (s), 2.02 (s), 2.00 (s)		2.08 2.07 1.99 1.97		2.11–2.09 (m), 2.06 (s), 2.04 (s), 2.01 (s)	20.7, 20.6, 20.6, 20.5	2.11 (s), 2.09-2.07 (m), 2.02 (s)	20.6, 20.5, 20.5, 20.5	2.11 (s), 2.09 (s), 2.08 (s), 2.07 (s), 2.02 (s)	20.7, 20.6, 20.5, 20.5
C=O		170.4–169.7				170.7, 170.6, 170.5, 170.1, 169.9, 169.7, 169.6		170.2, 170.0, 170.0, 169.8, 169.5		170.2, 170.1, 170.0, 170.0, 169.7, 169.5

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[a]Not assign

Table SM-2. ^{1}H and ^{13}C NMR literature comparison with observation data of 1-kestose and halogenated 1-kestose derivatives

Assign-ment	**1-kestose (1)** CAS 562-68-5 (δ in ppm and J in Hz)				**6,6′,6″-Tribromo-6,6′,6″ -trideoxy-1-kestose (6)** No CAS (δ in ppm and J in Hz)		**6,6′,6″-Trichloro-6,6′,6″-trideoxy-1-kestose (7)** No CAS (δ in ppm and J in Hz)	
	Ref [1]		**Observed**		**Observed**		**Observed**	
	^{1}H in ppm (200.13 MHz, D_2O)	^{13}C in ppm (50.32 MHz, D_2O)	^{1}H in ppm (500 MHz, D_2O)	^{13}C in ppm (125 MHz, D_2O)	^{1}H in ppm (500 MHz, D_2O)	^{13}C in ppm (125 MHz, D_2O)	^{1}H in ppm (500 MHz, D_2O)	^{13}C in ppm (125 MHz, D_2O)
1	5.26	93.73	5.37 (d)	92.9	5.36 (d)	92.9	5.36 (d)	92.8
2	3.38	72.39	3.48 (dd)	71.6	3.52 (dd)	71.0	3.52 (dd)	70.1
3	3.59	73.85	3.70–3.60 (m)	73.0	3.72–3.65 (m)	72.1	3.71–3.60 (m)	72.2
4	3.30	70.48	3.41 (t)	69.6	3.43 (t)	71.4	3.47 (t)	71.6
5	3.64 3.68	73.67	3.79–3.71 (m)	72.8	4.04–3.98 (m)	71.1	4.11–4.05 (m)	71.0
6a	3.63	61.40	3.79–3.71 (m)	60.5	3.79–3.72 (m)	34.2	3.89–3.73 (m)	44.3
6b					3.72–3.65 (m)			
1′a	3.54	62.17	3.79–3.71 (m)	61.3	3.87 (d)	59.9	3.89–3.73 (m)	60.2
1′b	3.66		3.70–3.60 (m)		3.72–3.65 (m)		3.71–3.60 (m)	
2′	–	104.50	–	103.7	–	103.3	–	103.3
3′	4.12	77.92	4.22 (d)	77.0	4.27 (d)	76.4	4.26 (d)	76.4
4′	3.88	75.12	3.98 (t)	74.2	4.09–4.05 (m)	76.3	4.11–4.05 (m)	75.3
5′	3.67 3.70	82.46	3.83–3.80 (m)	81.6	4.04–3.98 (m)	80.6	4.01–3.94 (m)	80.6
6′a	3.63	63.44	3.79–3.71 (m)	62.6	3.64–3.59 (m)	33.5	3.89–3.73 (m)	45.2
6′b								
1″a	3.50	61.70	3.70–3.60 (m)	60.8	3.72–3.65 (m)	59.9	3.71–3.60 (m)	60.0
1″b	3.59							

2′′	–	104.96	–	104.2	–	103.9	–	103.9
3′′	4.02	77.94	4.13 (d)	77.0	4.16 (d)	76.9	4.16 (d)	76.6
4′′	3.91	75.74	4.02 (t)	74.9	4.09–4.05 (m)	77.4	4.11–4.05 (m)	76.2
5′′	3.69	82.36	3.83–3.80 (m)	81.5	4.04–3.98 (m)	80.4	4.01–3.94 (m)	80.5
6′′a	3.70	63.59	3.79–3.71 (m)	62.7	3.79–3.72 (m)	33.5	3.89–3.73 (m)	45.4
6′′b	3.64							
$J_{1,2}$			4.0		4.0,		4.0	
$J_{2,3}$			9.7		10.0		9.7	
$J_{3,4}$			9.7		10.0		9.7	
$J_{1'a,1'b}$					10.3			
$J_{3',4'}$			8.6		8.6		8.6	
$J_{3'',4''}$			8.6		8.6		8.6	

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