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The conformation of a tetratritylated α-cyclodextrin with unusual proton NMR

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ABSTRACT

Tetratritylation of α-cyclodextrin (CD) and subsequent peracetylation of the partially tritylated mixture allowed the preparation and isolation of the symmetrical $6^A,6^B,6^D,6^E$-tetratritylated α-CD in pure form. The ^{1}H NMR spectra of the compound showed abnormal behaviour with the anomeric proton of one of the glycopyranosyl systems resonating below 3.0 ppm, which is exceptionally unusual. To understand this anomaly in the ^{1}H NMR data, we performed a complete NMR analysis and using molecular modelling as a tool, we were able to obtain a conformation that can explain the observed NMR phenomenon.

1. Introduction

Cyclodextrins (CDs)[1,2] are rigid, cyclic molecules consisting of six, seven or eight glucopyranosyl units linked together via a series of α-(1→4)-glycosidic linkages; they are called α, β and γ-CD, respectively. By adopting the shape of a truncated cone, all the primary hydroxyl groups at O-6 occupy the narrower end of the cone, while the remaining secondary hydroxyl groups at O-2 and O-3 occupy the other end. Recently, the regioselective substitution of CDs has been a topic of significant interest. Since the discovery of protocols for the regioselective mono- and di-debenzylation of perbenzylated CDs using diisobutyl-aluminium hydride by Sinaÿ's group in 2000,[3] several papers have been published that successfully applied this methodology to synthesize mono- or disubstituted CD derivatives for various applications.[4–9] Parrot-Lopez's group has even extended the methodology to synthesize $6^A,6^B,6^D,6^E$-tetrasubstituted α-CD using an indirect strategy starting from the $6^A,6^D$-diol of perbenzylated α-CD.[10]

Previously, the direct regioselective tetra-substitution of α-CD was investigated by one of us[11,12] via the reaction of anhydrous α-CD with 4.4 equiv of trityl chloride in pyridine at 70 °C for 48 h, and the resulting mixture was methylated. Three tetrasubstituted derivatives including the $6^A,6^B,6^D,6^E$, $6^A,6^B,6^C,6^D$ and $6^A,6^B,6^C,6^E$-tetratritylated α-CDs were obtained in gram quantities and isolated using simple column chromatography on silica gel. The ^{1}H NMR spectra of the anomeric regions of these compounds were reported and for the symmetrical $6^A,6^B,6^D,6^E$-tetratritylated α-CD, which possessed C_2 axial symmetry. The anomeric protons of the three pairs (**AD**, **BE** and **CF**) of glucopyranosyl systems were reported at 5.60, 4.37 and 3.88 ppm; the last two values were quite unusual for alkylated α-O-glycosides. Anomeric protons are generally observed in the region between 4.80 and 5.60 ppm in $CDCl_3$.

These unusual upfield shifts in the ^{1}H NMR spectrum were presumably attributed to the ring anisotropic effects of phenyl rings. Efforts have been spent to understand how the phenyl rings would affect the particular protons using molecular modelling.[12] However, due to the heavy overlapping problems of glucopyranosyl proton signals, the complete assignment of the ^{1}H NMR spectra of tetra-*O*-methyl-$6^A,6^B,6^D,6^E$-tetratrityl-α-CD (**1**, Fig. 1) has never been achieved. Molecular modelling could not give convincing results in explaining the details about which phenyl ring could be causing the shielding and how it affected the proton NMR of a particular glucose pair. Recently, a homologue of **1** using an even larger protecting group, supertrityl [tris(*p*-*tert*-butylphenyl)methyl-], has been reported by Matt's group.[13] Although the authors did not offer any comments about the ^{1}H NMR spectrum of the $6^A,6^B,6^D,6^E$-tetra-supertritylated α-CD, the incompletely assigned NMR data that were reported indeed indicated some anomalies; the anomeric protons were reported to resonate at 5.33, 4.64 and 4.24 ppm in $CDCl_3$.

In an ongoing project, we required multiple substituted α-cyclodextrins as scaffolds. We decided to obtain the desired compounds via multitritylation following a previously published procedure[11] as this method can be easily scaled up. We substituted the methyl protecting group with electron-withdrawing acetyl group to obtain tetratritylated analogues (**2**), from which we observed much more pronounced ^{1}H NMR anomalies, with one of the anomeric protons resonating at 2.88 ppm. This could be the first reported α-*O*-glycopyranoside with an anomeric proton

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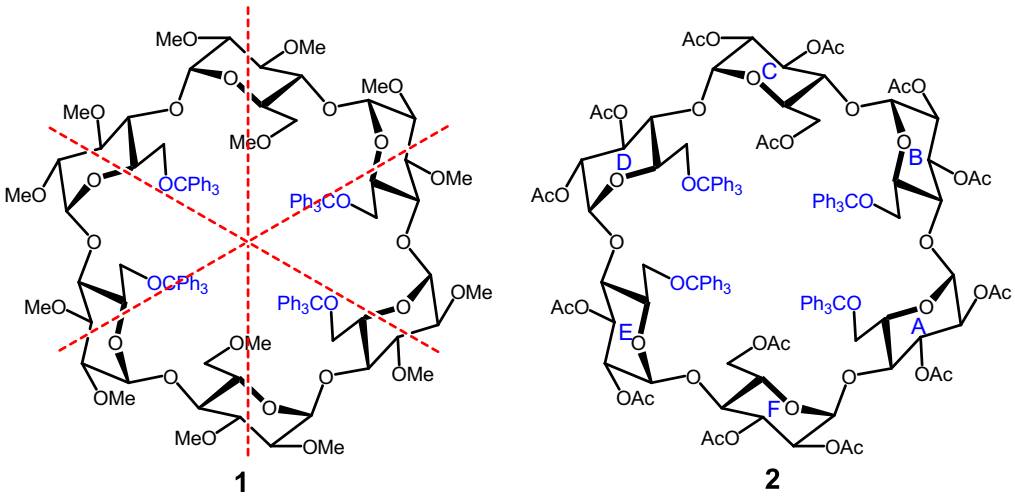


Figure 1. Structure of permethylated and peracetylated $6^A,6^B,6^D,6^E$-tetratrityl-α-CDs.

resonating at a chemical shift below 2.90 ppm. This intriguing NMR phenomenon prompted us to perform complete and unambiguous NMR assignments for all three pairs of glucose units using a series of modern NMR experiments. Combined with molecular modelling, we obtained a molecular model that can offer convincing explanations about the origin of the observed anomalies.

2. Results and discussion

2.1. Synthesis

Among the three common CDs, α-CD has the smallest cone size, which leads to the narrowest primary face. Because trityl is a bulky group, and tritylation is quite selective for primary hydroxyl groups, it has been a real challenge to put more than four trityl groups on the primary face of α-CD. To date, no pentatritylated derivatives of α-CD have been reported. We followed a slightly modified procedure by reacting anhydrous α-CD with 4.5 equiv of trityl chloride in anhydrous pyridine at room temperature for 24 h and then at 70 °C for 18 h. In the original procedure, subsequent permethylation was carried out; however, methyl is not an ideal protecting group because it cannot be easily removed. We decided to use acetyl as protecting groups, because it can be removed by performing a simple Zemplén transesterification. Therefore, a subsequent peracetylation was carried out at 100 °C. The tritylation produced effectively a complex mixture containing some tri- and tetratritylated α-CD. TLC analysis using 20% acetone–toluene as eluent revealed that the first major spot has an R_f of 0.11 along with other major spots below it. After column chromatography, the major spot at R_f 0.11 proved to be a pure compound by ^{1}H NMR (Fig. 2).

2.2. ^{1}H and ^{13}C NMR assignments

To our delight, this compound appeared to be the $6^A,6^B,6^D,6^E$-tetratritylated compound with an axial C_2 symmetry. This assignment was made because only eight sets of acetates were observed, and other protons of the glucose units were also simplified. What puzzled us were the locations of the anomeric protons, which were not easily identified. One anomeric pair (**I**) appears to be at 5.45 ppm, while another pair (**II**) appears to be at 3.62 ppm. The remaining pair could not be identified. What was even more intriguing was that a doublet with a coupling constant of 3.2 Hz was observed at 2.88 ppm. This is very unusual as most α-glucopyranosyl protons resonate in a region between 3.5 and 5.5 ppm.[14–16]

Several 2D experiments including GCOSY, GTOCSY, GHSQC and GHMBC were carried out in order for us to be able to fully assign the spectra. The protons at 5.45 and 3.62 ppm were confirmed to be anomeric protons because in the phase-sensitive GHSQC spectra they both were found to couple to a carbon with chemical shifts at 94.77 and 95.50 ppm, respectively. To our surprise, the doublet at 2.88 pm corresponds in fact to an anomeric proton of the third glucopyranosyl pair (**III**) because it also couples to an anomeric carbon at 95.30 ppm (Fig. 3). This is truly remarkable because, to the best of our knowledge, this could be the first example of O-glycosides with its anomeric proton resonating at such a low frequency. In fact, in this case its chemical shift is the lowest among all the sugar protons. The glucose pair **II** with their anomeric protons resonating at 3.65 ppm was also quite abnormal.

For all the three glucose pairs, the GCOSY experiment did not allow complete assignment of the ^{1}H NMR spectrum. However, this experiment did give some interesting information. For glucose pairs **II** and **III**, the chemical shifts of their neighbouring H-2 resonances are also moved significantly to lower frequencies. Because all the O-2 and O-3 positions have electron-withdrawing acetyl groups attached and the deshielding effect from the π-electrons of the carbonyl would normally place the H-2 and H-3 protons in the 4.8–5.6 ppm region. The H-2 signals of glucose pair **I** resonate in the right region (4.81 ppm); however, the H-2 signals of the glucose pair **II** were observed at 4.25 ppm and the H-2 resonances for the glucose pair **III** were at 4.60 ppm—these values are much lower than expected. The H-3 resonances for all the three pairs were normal, and all of them appeared at a region between 5.1 and 5.5 ppm. Interestingly, the H-3 resonances of the glucose pair **II** (5.13 ppm) did not appear as a 'dd' but as a complex pattern. We attributed this result to higher order coupling. Because the coupling patterns of H-2 signals of the same glucose pair are normal, this indicated that the H-4 and H-5 resonances of glucose pair **II** might resonate at similar frequencies. This was unambiguously confirmed from the GHSQC spectra, where we observed that H-4 and H-5 resonances of the glucose pair **II** appeared at extremely close chemical shifts, 3.88 and 3.91 ppm, respectively. The H-4 signals of all the three pairs resonate in a very close region (3.88 ppm for **I**, 3.92 for **II** and 3.84 for **III**).

All H-5, H-6 and H-6′ protons were observed within a narrow region (3.35–4.00 pm). Due to the complex coupling patterns and high order couplings, the GCOSY did not offer much help in the

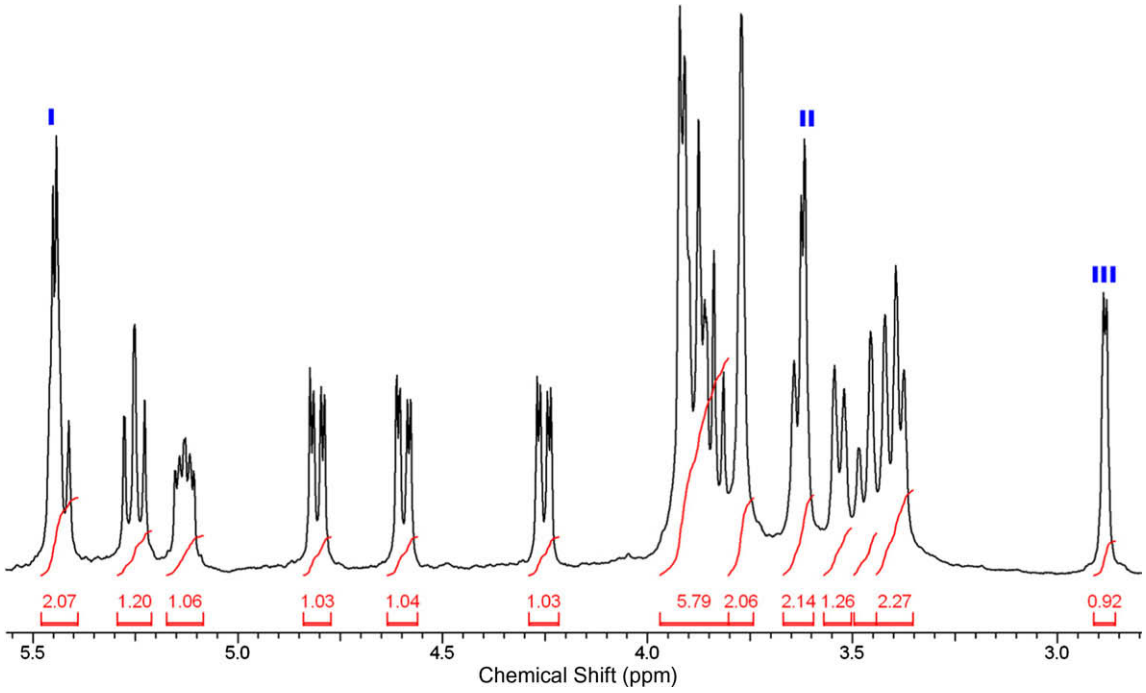


Figure 2. 400 MHz ^{1}H NMR of compound **2** in $CDCl_3$.

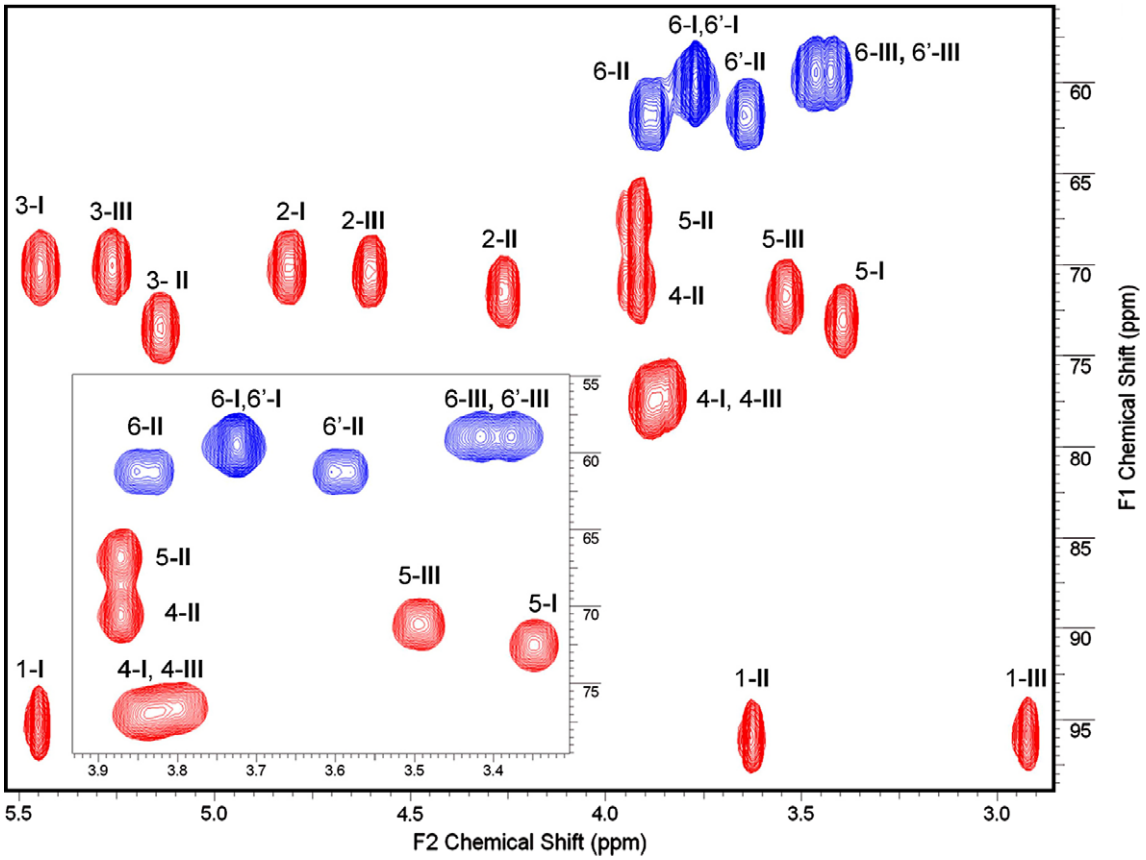


Figure 3. GHSQC NMR spectra of **2** in $CDCl_3$.

assignment but with the help of GTOCSY and GHSQC, the puzzle was clearly solved. Phase-sensitive GHSQC[17] played an instrumental role in this, because it has pulse sequences to place the CH_2 coupling systems into opposite phase from that of CH and CH_3 coupling systems. This differentiates all the protons attached to C-6 from those attached to C-5. In Figure 3, all correlation peaks

Table 1
Chemical shifts of ^{1}H NMR of compound **2** in $CDCl_3$

	H-1($J_{1,2}$)	H-2($J_{2,3}$)	H-3($J_{3,4}$)	H-4($J_{4,5}$)	H-5($J_{5,6}$)	H-6($J_{6,6'}$)	H-6′
Pair I	5.45(3.5)	4.81(10.6)	5.43(8.5)	3.88	3.38	3.77	3.77
Pair II	3.62(3.4)	4.25(10.2)	5.13(8.6)	3.92	3.91	3.86	3.64
Pair III	2.88(3.2)	4.60(10.7)	5.25(9.1)	3.84	3.53	3.47	3.40

Table 2
Chemical shifts of ^{13}C NMR of compound **2** in $CDCl_3$

	C-1	C-2	C-3	C-4	C-5	C-6
Pair I	94.77	69.78	69.86	77.19	72.62	59.56
Pair II	95.50	71.21	73.19	70.84	66.85	61.54
Pair III	95.30	70.26	69.74	76.76	71.41	59.30

in blue are related to the H-6 resonances that correlate with C-6 resonances, and appear in pairs because each proton pair is attached to the same carbon. As there were only three unassigned C–H correlation peaks left at 3.38, 3.53 and 3.91 ppm, we knew those were from the three types of H-5 related to the three pairs. Combined with the GTOCSY experiment, we found that the H-5 at 3.91 ppm belongs to the glucose pair **II,** and it is correlated with two geminal protons at 3.86 ppm (H-6 of **II**) and 3.64 ppm (H-6′ of **II**); the H-5 at 3.53 ppm belongs to glucose pair **III** and correlates with two geminal protons at 3.47 ppm (H-6 of **III**) and 3.40 ppm (H-6′ of **III**). Finally, the H-5 at 3.38 ppm belongs to the glucose pair **I** and it correlates with two protons—both resonating at 3.77 ppm (H-6 and H-6′ of **I**). Tables 1 and 2 summarize results of our assignments for all ^{1}H and ^{13}C signals.

2.3. Correlation NMR assignments with real structure of compound 2

Our next task was to correlate the individual glucose pair (**I–III**) with the **AD**, **BE** and **CF** glucose pairs of the real structure. As can be seen from Figure 1, the O-6 atoms of the **CF** glucopyranosyl units have an acetyl group attached; from the GHMBC spectra, we would expect to see two three-bond correlations peaks from the two H-6 resonances of the **CF** rings to the carbonyl carbon of the attached acetate group. Indeed, the two H-6 signals of glucose pair **II** at 3.86 and 3.64 ppm were found to correlate with a carbonyl group at 169.2 ppm (Fig. 4). We concluded that the glucose pair **II** is related to **CF** units and the anomeric protons of **CF** units are both at 3.62 ppm and their H-4 and C-1 resonances are at 3.92 and 95.50 ppm, respectively (Fig. 5).

Further analysis of the GHMBC revealed that the H-4 resonances of **CF** rings are correlated with an anomeric carbon at 94.77 ppm, which corresponds to the C-1 signals of glucose pair **I**. This signifies that the anomeric C-1 of glucose pair **I** is attached to O-4 of **CF** units, thus glucose pairs **I** are in fact the **BE** units of compound **2**. Additional confirmation of the connection sequence comes from the correlation peak in GHMBC spectra at 95.50 ppm (C-1 resonance of glucose units **CF**), the carbons correlate with protons with chemical shifts of 3.84 (H-4 resonance of glucose pair

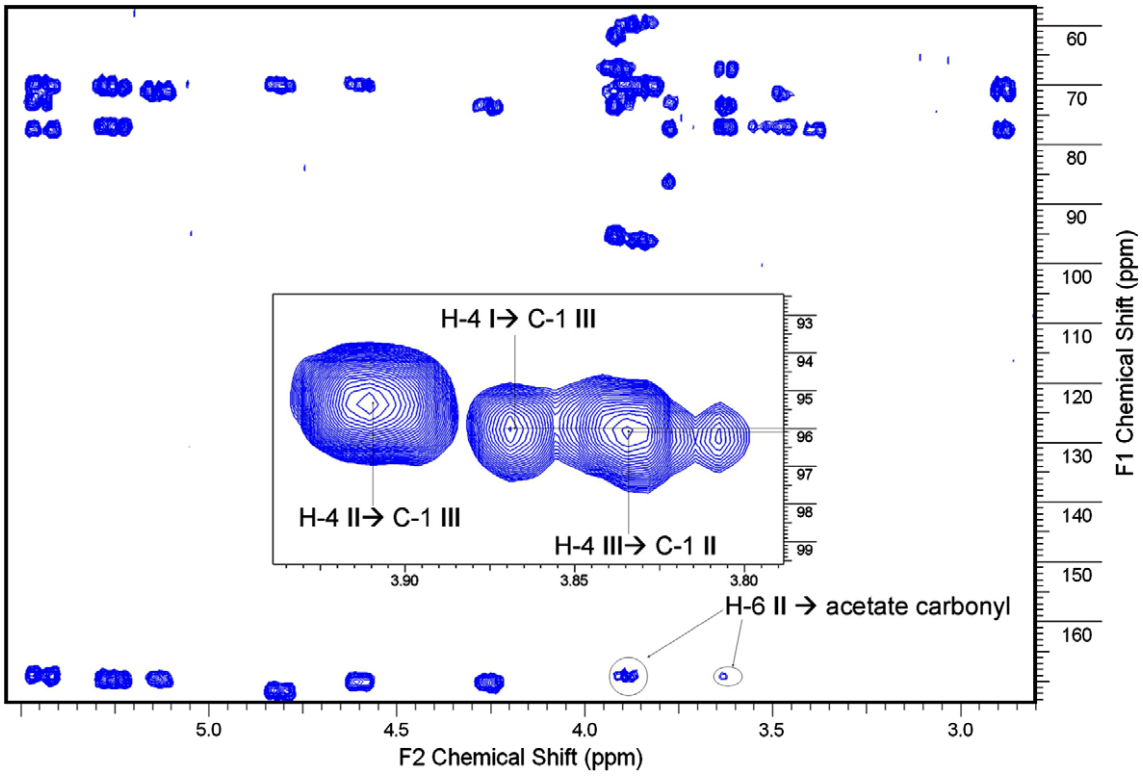


Figure 4. GHMBC NMR spectra of **2** in $CDCl_3$. Glycosidic linkage information is shown in the enlarged inset. From the *F*1-axis, the difference of the anomeric C-1_III and C-1_II was extremely small (95.30 vs 95.50 ppm), but can be clearly seen.

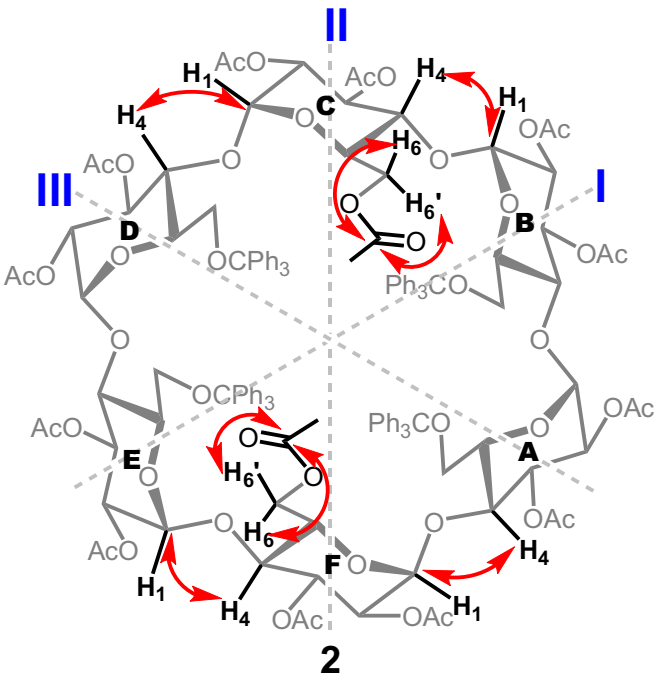


Figure 5. Matching the glucose pairs **I**–**III** from NMR with real structure **2** (arrows indicate the observed correlations in HMBC experiment).

III). This indicates that the anomeric C-1 of glucose units **CF** is linked to the O-4 positions of glucose pair **III**. By examining the connection sequence of the real structure of **2**, we concluded that glucose pair **III** observed in NMR is related to **AD** units of the real structure (Fig. 5).

2.4. Conformation of 2 and origins of the anomalies

Combining information obtained from Table 1 and Figure 5, we can see that the chemical shifts of the H-1 of glucose **AD** and **CF** pairs are the most shifted upfield, together with their respective H-2 resonances, which are also shifted upfield. Comparing the chemical shifts of the anomeric protons of glucose pairs **BE** with **AD**, there is a difference of 2.57 ppm. Previously, Matt and co-workers prepared some $6^{A},6^{B}$-, $6^{A},6^{C}$-, $6^{A},6^{D}$-di-supertritylated α-CD derivatives, they also reported some upfield shifts of NMR signals (to a much less degree than what we observed), and they attributed the changes to steric interactions between the large supertrityl groups.[18] In a later publication[13] on $6^{A},6^{B},6^{D},6^{E}$-tetra-supertritylated α-CD, they reported that for the permethylated compound, the most upfield shifted anomeric pair was at 4.24 ppm, while the other two pairs are at 4.64 and 5.33 ppm. They did not comment on the origins of these shifts.[9]

In our opinion, a conformational change from steric hindrance cannot produce such large changes in chemical shifts. Another possibility might result from the change of pyranosyl ring conformation from the original $^{4}C_{1}$ to others such as $^{1}C_{4}$. However, because the proton ^{3}J coupling constants are normal for all units (Table 1), which corresponds to the regular $^{4}C_{1}$ conformation of α-glucopyranosyl unit, this possibility was excluded. Other effects such as the diamagnetic anisotropic effect of phenyl ring must govern such observed phenomenon. This was also proposed in the previous studies.[12] Diamagnetic anisotropy of phenyl ring results from the ring current of the π-electrons induced by external magnetic fields; the ring current produces additional magnetic field which could add to or subtract from externally applied magnetic field strength. Consequently, when a nucleus is closely facing the phenyl ring, it experiences a reduced magnetic strength (shielding), leading to a resonance with smaller frequency thus smaller chemical shifts. Conversely, when a nucleus is closely located at the vicinity of the edge of the phenyl ring, it experiences an increased magnetic strength (deshielding), leading to a resonance with larger frequency thus higher chemical shifts.

Figure 6 illustrates the observed NMR anomalies regions in compound **2**. In all units, H-1 and H-2 are located at the same face of the α-glucopyranosyl ring. This finding suggests that if the diamagnetic anisotropic effect of a phenyl ring affects the H-1, it most likely will affect H-2 as well. The anomeric regions of **BE** units are unaffected by the ring current effects as the chemical shifts of both H-1 and H-2 resonances are normal. However, the signals for both the H-1 and H-2 of **AD** units resonate at much lower frequencies, and they therefore must be closely facing a phenyl ring from its own or the neighbouring (**BE**) trityl group. The same are true for the **CF** units, their H-1 and H-2 atoms must also be closely facing a phenyl group. Because the **CF** units do not have a trityl group attached, their H-1 and H-2 atoms must experience the diamagnetic anisotropic effects of a phenyl group from the neighbouring trityl groups. As the anomeric protons of the **CF** units are spatially close to **AD** units, we concluded that they must be under the influence of the trityl groups of **AD** pair. This means the trityl group of **D** unit is leaning towards the **C** ring, and the trityl group of **A** unit is leaning towards the **F** unit. The slight upfield shifts of the two H-6 resonances of **C** unit as well as **F** units must also come from trityl groups attached to the **D** and **A** units, respectively, because they are located at the same primary face of α-CD. Consequently, the observed NMR anomalies for **D** unit must come from the trityl group of the **E** unit, and likewise, the trityl group on **B** unit should affect the anomeric region of **A** unit. Overall, the trityl groups in compound **2** shield the anomeric region of the next glucose unit in a clockwise fashion. Because there is no trityl group at either **C** or **F** units, the anomeric regions of the both **B** and **E** units appeared to be normal.

With the above analysis in mind, we used a molecular modelling program to build a model. We performed a systematic rotation

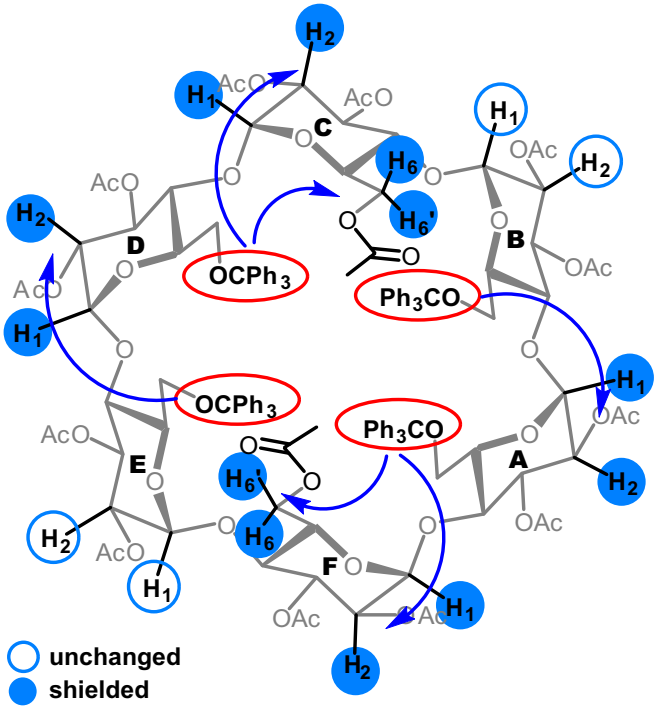
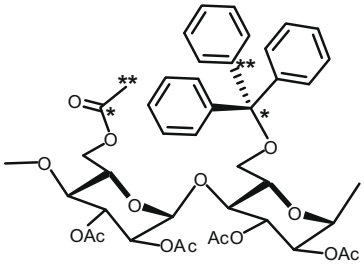


Figure 6. Mapping the diamagnetic anisotropic effect observed in NMR of compound **2**.

along the C5–C6, C6–O6 and O6–C* bonds and examined the relationship of the phenyl rings with respect to the anomeric region, and a model was found that matched the observed properties. The dihedral angles are shown in Table 3.

For **AD**, **BE** and **CF** rings, the C* and C** atoms are defined as follows:



As can be seen from the top view of CPK space filling model (Fig. 7, left), this conformer of the molecule is completely symmetric. The four trityl groups in fact occupy almost all the space available. This explains why it is difficult to introduce a fifth trityl group on α-CD. The eight phenyl groups coloured in green did not contribute to the observed anomalies, but the four phenyl groups coloured in blue are the main cause for the observed upfield shifting of H-1 and H-2 protons. From the right picture, we can clearly see that the blue phenyl (left) of the **A** (or **D**) unit is just located above the H-1 and H-2 of the **F** (or **C**) unit thus magnetically shielding both H-1 and H-2 of the **F** (or **C**) glucose. Similarly, the blue phenyl (right) from **B** (or **E**) unit is situated just above the H-1 and H-2 protons of the **A** (or **D**) glucose, thus it is this phenyl of the **B** (or **E**) units affecting chemical shifts of both H-1 and H-2 of the **A** (or **D**) ring to go upfield. The blue phenyl of the **B** ring is spatially closer to the H-1 and H-2 of the **A** unit; therefore, we saw a more dramatic upfield shifting of the **A** unit.

Table 3
Dihedral angles of the conformer that match the NMR properties

	H5–C5–C6–O6	C5–C6–O6–C*	C6–O6–C*–C**
AD	165	165	180
BE	165	−155	140
CF	170	175	170

From the model, we can also see that because the primary face is very crowded with the presence of four trityl groups, there is very limited space for them to move around. The change of protecting groups at the O-6 of the **CF** rings from acetates to smaller methyl groups will allow slightly improved mobility of the trityl groups of the BE rings, which should result in a slightly reduced shielding effect on the anomeric regions of AD rings. Increased mobility of the trityl groups will make the shielding phenyl groups stay slightly farther from the H-1 and H-2 resonances of the AD rings. This explains why for the previously synthesized *O*-methyl-protected analogue 1, the most upfield shifted anomeric hydrogen resonances are at 3.88 ppm while for the *O*-acetyl protected analogue **2**, the most upfield shifted anomerics are at 2.88 ppm.

3. Conclusions

We have observed a series of anomalies in the chemical shifts of the ^{1}H NMR of a tetratritylated α-CD. Using complementary modern two-dimensional NMR experiments as a tool, we have successfully and unambiguously assigned all the ^{1}H and ^{13}C NMR signals and matched the NMR signals to individual nuclei of the real structure. Using molecular modelling as a tool, we have built a molecular model to help us in understanding the origin of the observed anomalies in NMR spectra. This example clearly demonstrates the truly dramatic effect that the diamagnetic anisotropy of a phenyl ring can have on the spectra of an organic molecule.

4. Experimental

4.1. NMR

All NMR experiments were recorded on a Bruker Advanced DRX instrument with a BBO probe. All ^{1}H experiments were recorded at 400 MHz frequency, and ^{13}C experiments were recorded at

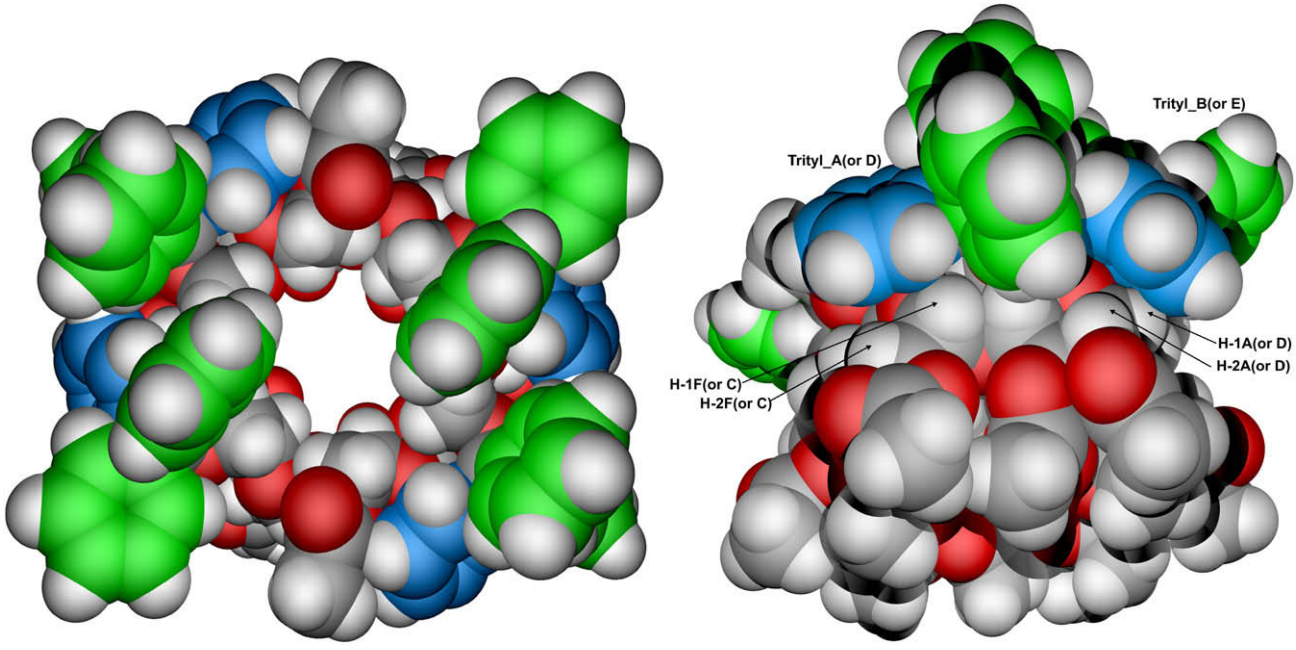


Figure 7. Mapping the diamagnetic anisotropic effect observed in NMR of compound **2**.

100 MHz frequency. All J values are reported in Hertz. Homonuclear experiments such as gradient COSY and TOSCY were recorded using the COSYGPQF and MLEVGPQF sequences, respectively, and heteronuclear experiments such as gradient HSQC and HMBC were recorded using the HSQCEDETGP and HMBCGPLPNDQF sequences, respectively. $CDCl_3$ was used as the solvent in all experiments.

4.2. Synthesis

To a solution of anhydrous α-cyclodextrin (5.70 g, 5.86 mmol) in dry pyridine (30 mL), trityl chloride (7.35 g, 26.37 mmol) was added portion-wise, and the mixture was stirred at room temperature for 24 h. The mixture was heated to 80 °C and stirred for another 18 h. Acetic anhydride (20 mL) was added, and the mixture was heated to 100 °C for another 24 h. The solvent was removed under reduced pressure, and the residue was co-evaporated with toluene (2 × 30 mL). EtOAc (150 mL) was added, and the solution was washed with 10% brine (2 × 100 mL). The organic phase was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel using a mixture of hexane–CH_2Cl_2–acetone (6:2:2) as the eluent to afford the desired compounds as a white solid (2.7 g, yield: 18%). R_f: 0.11 (20% acetone–toluene). $[\alpha]_D^{25}$ +200 (*c* 1.2, $CHCl_3$). Anal. Calcd for $C_{140}H_{144}O_{44}$: C, 66.4; H, 5.7. Found: C, 66.0; H, 6.0. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.56–7.53 (m, 10H, Ar), 7.40–7.31 (m, 30H, Ar), 7.13–7.05 (m, 20H, Ar), 5.50 (dd, $J_{3,4}$ = 8.5, $J_{2,3}$ = 10.5 Hz, 2H, H-3_BE), 5.43 (d, $J_{1,2}$ = 3.5 Hz, 2H, H-1_BE), 5.26 (dd, $J_{3,4}$ = 9.1, $J_{2,3}$ = 10.6 Hz, 2H, H-3_AD), 5.12 (dd, $J_{3,4}$ = 8.6, $J_{2,3}$ = 10.1 Hz, 2H, H-3_CF), 4.81 (dd, $J_{1,2}$ = 3.5, $J_{2,3}$ = 10.6 Hz, 2H, H2-_BE), 4.59 (dd, $J_{1,2}$ = 3.3, $J_{2,3}$ = 10.7 Hz, 2H, H-2_AD), 4.25 (dd, $J_{1,2}$ = 3.3, $J_{2,3}$ = 10.2 Hz, 2H, H-2_CF), 3.92 (dd, $J_{3,4}$ = 8.3, $J_{4,5}$ = 8.3 Hz, 2H, H-4_BE), 3.92–3.70 (m, 14H, H-4_CF, H-5_CF, H-4_BE, H-6_CF, H-4_AD, H-6_BE, H-6′_BE), 3.62 (m, 2H, H-6′_CF), 3.58 (d, $J_{1,2}$ = 3.4 Hz, 2H, H-1_CF), 3.51–3.45 (m, 4H, H-5_AD + H-6_AD), 3.38–3.35 (m, 4H, H-5_BE + H-6′_AD), 2.06 (s, 12H, CH_3 × 4), 2.05 (s, 6H, CH_3 × 2), 2.00 (s, 6H, CH_3 × 2), 1.99 (s, 6H, CH_3 × 2), 1.96 (s, 6H, CH_3 × 2), 1.63 (s, 6H, CH_3 × 2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 171.35, 169.96, 169.78, 169.33, 169.28, 168.88, 168.77 (Ac) 143.72, 143.62 (Ar), 128.86, 128.71, 128.13, 127.63, 127.25, 126.75 (Ar), 95.89 (C-1_CF), 95.79 (C-1_AD), 95.22 (C-1_BE), 86.17 (trityl), 85.80 (trityl), 77.29 (C-4_CF), 76.97 (C-4_AD), 73.45 (C-3_CF), 72.87 (C-5_BE), 71.52 (C-5_AD), 71.38 (C-2_CF), 70.97 (C-4_BE), 70.26 (C-2_AD), 70.06 (C-3_BE), 69.99 (C-2_BE), 69.92 (C-3_AD), 67.18 (C-5_AD), 61.79 (C-6_CF), 59.91 (C-6_BE), 59.38 (C-6_AD), 31.01, 21.05, 20.83, 20.68, 20.58, 20.23 (Ac). ESI MS calcd for $C_{140}H_{144}O_{44}$, 2528.9; found 2551.8 ($M+Na^+$), 2567.9 ($M+K^+$).

4.3. Molecular modelling

The coordinates of α-CD were obtained from the PDB Data Bank (http://www.rcsb.org, ID 1btc[19]). However, the α-CD directly extracted from the crystal structure is unsuitable for use in the current study because it is unsymmetric. Symmetric α-CD was obtained after manual rotations along glycosidic linkages, and the structure was minimized using Accelrys Insight II 2005 molecular modelling package with Amber forcefield. The trityl and acetyl groups were manually added to α-CD, and a systematic rotation was performed (see Table 2 for dihedral angles) to obtain a conformer with C_2 symmetry, and the structure was finally minimized.

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