Triisobutylaluminium and Diisobutylaluminium Hydride as Molecular Scalpels: The Regioselective Stripping of Perbenzylated Sugars and Cyclodextrins

Thomas Lecourt, Alexandre Herault, Alan J. Pearce, Matthieu Sollogoub,* and Pierre Sinaÿ*[a]

Abstract: To explain the remarkable regioselective de-*O*-benzylating properties of diisobutylaluminium hydride (DIBAL-H) and triisobutylaluminium (TIBAL) towards polybenzylated sugars or cyclodextrins, we propose a plausible mechanistic rationale critically involving the kinetic formation of a product-generating 2:1 Al-benzylated sugar complex. For the reaction to occur, one pair of adjacent oxygen atoms should first be able to form a chelation complex with the first equivalent of aluminium reagent, either a highly fluxional complex with tetracoordinate aluminium species or a pentacoordinate one. The second equivalent then induces the regioselectivity of the de-*O*-alkylation by coordinating preferentially to one of the oxygen atoms of the selected pair.

Keywords: carbohydrates · cyclodextrins · diisobutylaluminium hydride · regioselective de-*O*-alkylation · triisobutylaluminium

Introduction

The availability of efficient protecting group introduction and removal strategies is a prerequisite for the harmonious development of carbohydrate chemistry. The benzyl ether function is probably the most widely used protecting group, owing to its stability under a large variety of conditions and its easy removal by mild catalytic hydrogenolysis. In contrast, methyl ethers, for example, are generally regarded as permanent protecting groups, because of the usually harsh conditions required for their removal. As a consequence, numerous benzylation and de-*O*-benzylation reactions have been described.[1] An underdeveloped but attractive route to partially benzylated carbohydrates is provided by controlled de-*O*-benzylation of easily available polybenzylated precursors. This has more particularly been achieved in processes such as catalytic hydrogenolysis,[2] catalytic hydrogen-transfer cleavage,[3] acetolysis,[4] hypoiodite fragmentation,[5] iodine-mediated addition–elimination sequences,[6] or use of Lewis acids such as tin tetrachloride and titanium tetrachloride[7] or a combination of chromium dichloride and lithium iodide.[8]

A few years ago, we serendipitously observed mono-de-*O*-benzylation as a side reaction during our exploration of the scope[9] of the reductive rearrangement of 6-deoxyhex-5-enopyranosides with triisobutylaluminium (TIBAL).[10] By taking advantage of this unplanned finding, we promptly discovered that use of TIBAL led to highly regioselective mono-de-*O*-benzylation of perbenzylated mono- and disaccharide derivatives.[11,12] We found out more recently that diisobutylaluminium hydride (DIBAL-H) promoted a most remarkable regioselective A,D-type bis-de-*O*-benzylation on the primary rim of either α- or β-perbenzylated cyclodextrins,[13] opening the door to further transformations into novel cyclodextrin derivatives.[14–16] Having accumulated these data, we would now like to discuss these results and to propose a mechanism for this unprecedented mode of action of TIBAL and DIBAL-H, acting as so-called "chemical scalpels".[17]

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Results and Discussion

The first step: **formation of a fluxional (or a pentacoordinate?) complex**: As shown in Table 1 (entry 1), when methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (**1**[18]) was treated with a commercial solution of TIBAL in toluene for 3 h at 50 °C, an almost quantitative transformation into **2**[19] was observed. This is in sharp contrast with the robust-

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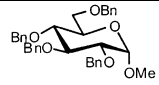
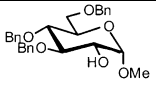
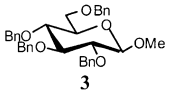
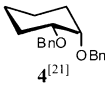
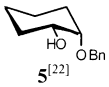
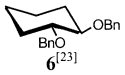
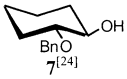
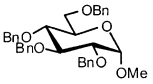
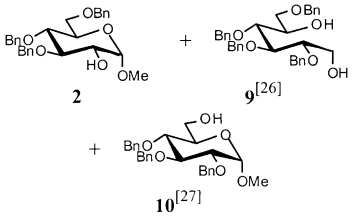
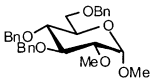
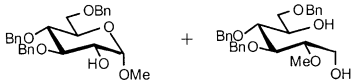
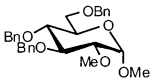
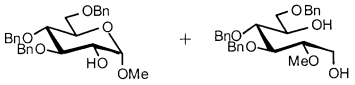
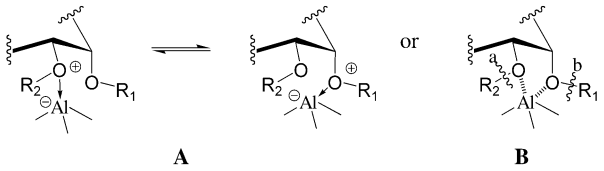
Table 1. Reactions of a variety of benzylated compounds with TIBAL and DIBAL-H.

Entry	Starting material	Reagent [equiv]	Time [h]	Products	Yield [%]
1	 **1**	TIBAL (5)	3	 **2**	98
2	 **3**	TIBAL (10)	48	no reaction	–
3	 **4**[21]	TIBAL (6)	96	 **5**[22]	95
4	 **6**[23]	TIBAL (6)	96	 **7**[24]	15
5	 **8**[25]	TIBAL (3)	72	no reaction	–
6	 **1**	DIBAL-H (10)	6.5	 **2** + **9**[26] + **10**[27]	74 (75/15/10)
7	 **11**	TIBAL (10)	72	 **2** + **12**	36[a] (78/22)
8	 **11**	DIBAL-H (10)	2	 **2** + **12**	83(65/35)

[a] A total of 34 % of starting material was also recovered.

ness of the corresponding β anomer **3**,[20] (entry 2, Table 1) which was recovered unaffected after a prolonged reaction time. Together with the additional results shown in entries 3, 4 and 5 in Table 1, it may be concluded that efficient mono-de-*O*-benzylation with TIBAL requires the presence of a 1,2-*cis* (axial–equatorial) system. Entry 7 in Table 1 demonstrates that TIBAL was similarly able to induce a selective mono-de-*O*-methylation of compound **11** at O-2, although the reaction was slow (less than 30 % yield after 72 h) and some de-*O*-methylation at O-1 was also observed (followed by further reduction to deliver the diol **12**). As now shown in entries 6 and 8 in Table 1, DIBAL-H also preferentially de-*O*-alkylates the 2-position, but with a lower selectivity. A striking feature was the superiority of DIBAL-H over TIBAL for the de-*O*-methylation process (compare entries 6 and 8, Table 1). The competing 6-de-*O*-benzylation observed in entry 6 in Table 1 is discussed, analysed and turned to our advantage later in this discussion

At this stage, we may thus propose that the debenzylation process is initiated by the favourable kinetic formation of a fluxional complex **A**. For convenience, though, we will depict **A** as **B** (Scheme 1). Whether **B** is a real pentacoordinated complex or just a written formalism is not known. The intermediacy of pentacoordinated trialkylaluminium complexes as key intermediates in various organic reactions is now well documented and has especially been scrutinised by Maruoka and Ooi.[28–32] It could also explain selectivities in other reactions.[33–38]

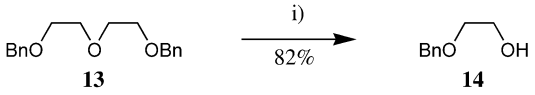


Scheme 1. Formation of a highly fluxional complex **A** or a pentacoordinate complex **B**.

TIBAL and DIBAL-H thus regioselectively select, for geometrical reasons, the two oxygen atoms located at C-1 and C-2. Entries 7 and 8 in Table 1 imply that the regioselectivity of de-*O*-alkylation at position 2 must be explained independently of the nature of the groups located on positions-1 and 2. We therefore now have to understand the next step in terms of regioselectivity: that is, either a or b cleavage (Scheme 1).

Abstract in French: *Afin d'expliquer la remarquable régiosélectivité des réactions de dé-O-benzylation des sucres ou des cyclodextrines perbenzylés effectuées par le DIBAL-H ou le TIBAL, nous proposons un mécanisme plausible mettant en jeu la formation critique d'un complexe actif 2:1 Al-sucre benzylé. Pour que la réaction ait lieu, il est nécessaire qu'une paire d'atomes d'oxygène soit d'abord capable de former un chélate avec un premier équivalent de réactif, se présentant sous la forme soit d'un complexe hautement fluctuant d'espèces tétracoordinées, soit d'un complexe organoaluminique pentacoordiné. Le second équivalent dicte ensuite la régiosélectivité de la dé-O-alkylation en se coordinant préférentiellement à un des deux atomes d'oxygène de la paire initialement choisie.*

A step forward in the analysis: **the informative behaviour of diethyleneglycol dibenzyl ether 13**: An unexpected but illuminating regioselectivity was observed when diethyleneglycol dibenzyl ether **13**[39] was treated with DIBAL-H. As shown in Scheme 2, no de-*O*-benzylation took place. Surprisingly, mono-*O*-benzylated ethyleneglycol **14**[40] was the only isolated reaction product (82% yield).



Scheme 2. Compound **13** does not undergo any de-*O*-benzylation in the presence of DIBAL-H. Reagents and conditions: i) DIBAL-H (5 equiv), toluene (0.5 M), 3 h, 50 °C.

The initial formation of the plausible 1:1 complex **C** (Scheme 3) cannot explain the observed regioselectivity of the reaction, given that DIBAL-H can equally well de-*O*-alkylate or de-*O*-benzylate (see entries 6 and 8 in Table 1). It seems reasonable, as a large excess of aluminium reagent is used, that a second aluminium atom coordinates on another oxygen atom. With those two aluminium atoms, a series of complexes in equilibrium is possible; however, the site between two oxygen atoms once again seems by far the most probable for coordination, because of its electron density and steric availability, leading to the plausible product-generating 2:1 complex **D** (Scheme 3) with two aluminium atoms, as shown in Figure 1.

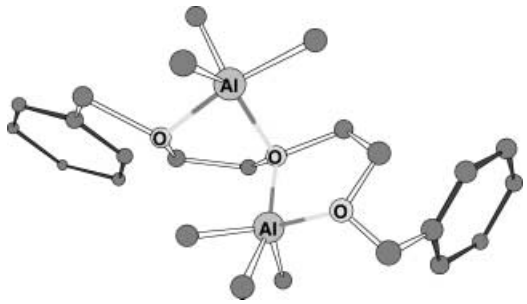
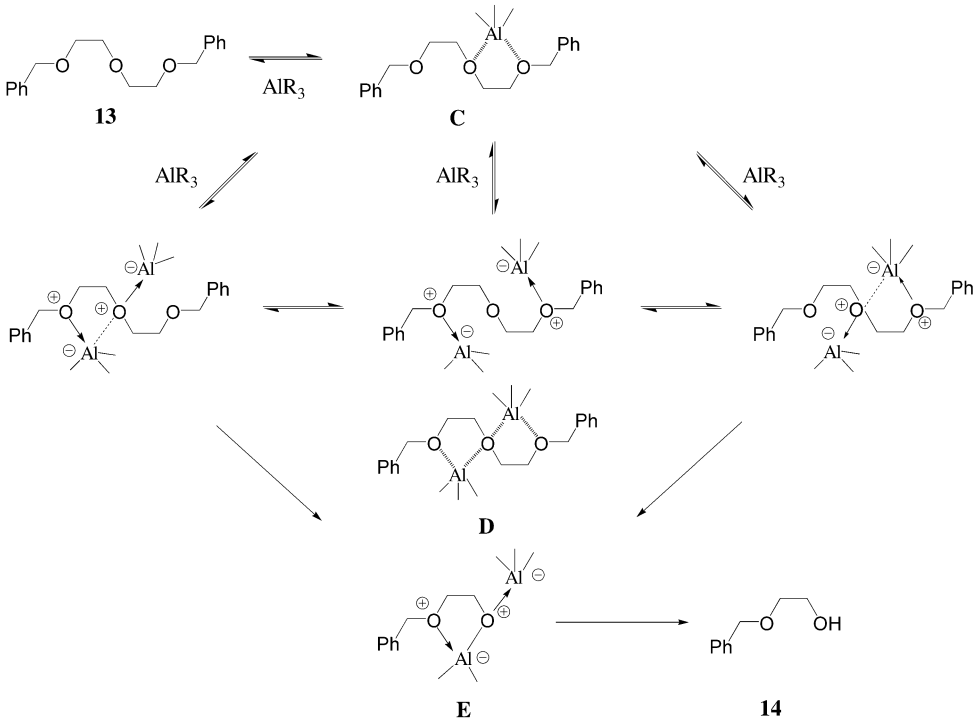


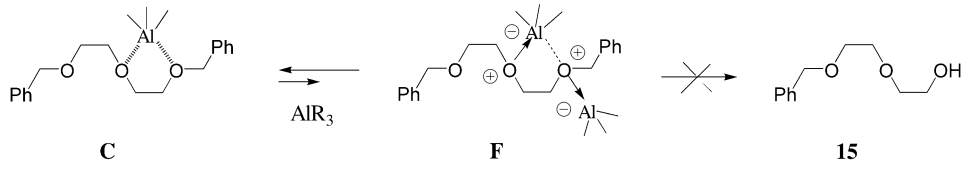
Figure 1. Molecular model for **D**. Hydrogen atoms and isobutyls are omitted for clarity.

The central oxygen atom in **D** is depicted as doubly coordinated. It is notable that the complexation of diethyl ether with two aluminium atoms has already been mentioned.[41] Here again, whether the complex **D** is in fact a double pentacoordinated or a highly fluxional system is not known, but such knowledge is not at all necessary to explain the regiochemical outcome of the mono-de-*O*-benzylation process. To account for the reactivity of such a species, however, it might be clearer to use a more conventional formalism with dative bonds and formal charges. We would therefore depict the reactive form **D** as one in which one aluminium between two oxygen atoms is coordinated by one of them and forms a zwitterionic interaction with the second, which is itself coordinated to a second aluminium atom. This formal di-coordination of the central oxygen weakens its C–O bonds, and the isobutyl aluminium reagent can deliver a hydride to break this bond selectively and produce adduct **E**, which gives alcohol **14** after hydrolysis (Scheme 3).

Complex **F** (Scheme 4) is probably not relevant because it would lead to a de-*O*-benzylated product **15** and involve the



Scheme 3. Proposed mechanism for the formation of alcohol **14**.



Scheme 4. Complex **F**, which would afford compound **15**, is not formed.

location of one aluminium atom in an electronically less favoured position.

In summary, the remarkable regioselectivity of the de-*O*-alkylation of compound **13** could reasonably be explained by the involvement of a second aluminium atom in the process. The two isobutylaluminium molecules would be complexed in the electron-richest sites of the molecule, in this case the two dioxygenated "tweezers" delineated by the ethyleneglycol structure. The symmetry of this species allows each aluminium atom to play the role of Lewis acid or reducing agent indifferently, the reaction always leading to the cleavage of the central C–O bond. Therefore, we propose that the site of cleavage is dictated by the site of complexation with a second aluminium reagent.

Regioselectivity for simple carbohydrates: Adopting the involvement of two molecules of aluminium reagent in the process of de-*O*-alkylation, we can now explain the selectivity of the reaction in the case of sugar derivatives. As previously proposed, the first alane sticks to the most accessible bidentate ligand, or di-oxygenated "tweezers", forming a fluxional or pentacoordinate complex **H** (Scheme 5) requiring the 1,2-*cis*-diol pattern. A second aluminium atom then complexes one of the two oxygen atoms of the "tweezers" to orientate the de-*O*-alkylation by activating the C–O bond. According to the model presented in Figure 2, the orbitals of the two oxygen atoms implicated in the process are not equally accessible: the exocyclic anomeric oxygen atom is axially oriented, and consequently one of its lone pairs is hindered because it is located under the pyranoside ring, whereas both lone pairs of the equatorial 2-oxygen atom are equally available for coordination. Therefore, the second aluminium atom coordinates much more easily to oxygen 2 than to the anomeric oxygen, thereby forming complex **I** and directing the de-*O*-alkylation reaction towards 2-de-*O*-benzylation (Scheme 5). The lower steric demand of DIBAL-H in relation to TIBAL, allowing some approach on O-1, can probably account for the drift in the regioselectivity in the reaction with compound **1**.

Interestingly, a related reaction has been observed in the presence of $AlCl_3$ with disilylated 1,2-cyclohexanediol **16**, through which compound **17** was obtained and characterised by X-ray crystallography (Scheme 6).[42,43] The latter structure led us to envisage an intermediate such as **G** for this reaction, comforting us in our hypothesis of the intermediacy of **I** for de-*O*-alkylation.

In summary, a mechanism involving two molecules of isobutylaluminium reagent, playing two different roles, allows the regioselectivity of the de-*O*-alkylation reactions to be explained. The first molecule of reagent is coordinated in the lone-pair-rich site of the carbohydrate, between two 1,2-*cis* oxygen atoms (the "tweezers"). The second aluminium atom coordinates on the more available oxygen atom to orientate the de-*O*-alkylation by acting as a Lewis acid and therefore weakening a C–O bond; the dealkylation reaction is then achieved by hydride transfer. When a set of dioxygenated "tweezers" is clearly identified and when the remaining orbital of one oxygen atom is clearly more accessible than the other one, then the reaction is regioselective. Compound **1** is a typical example.

Towards DIBAL-H-mediated de-*O*-alkylation at the primary rim of cyclodextrins: As previously alluded to, we would like now to come back to entry 6 (Table 1). As point-

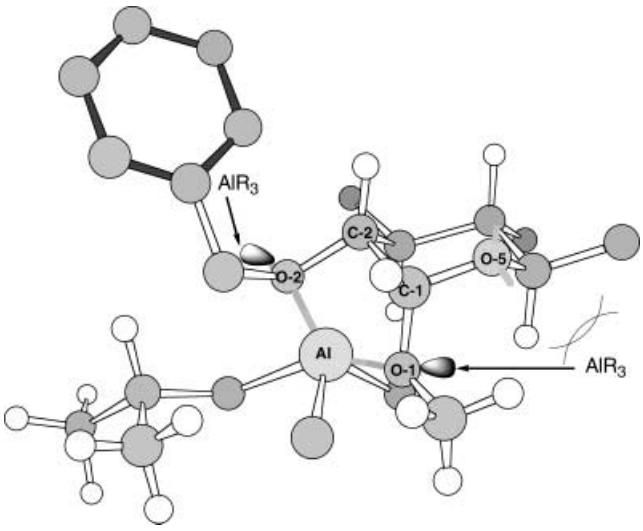
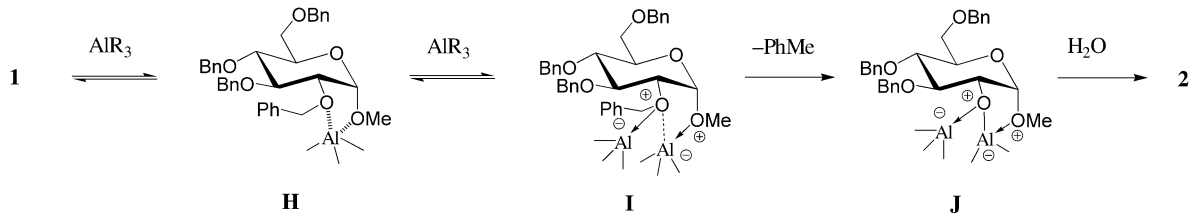
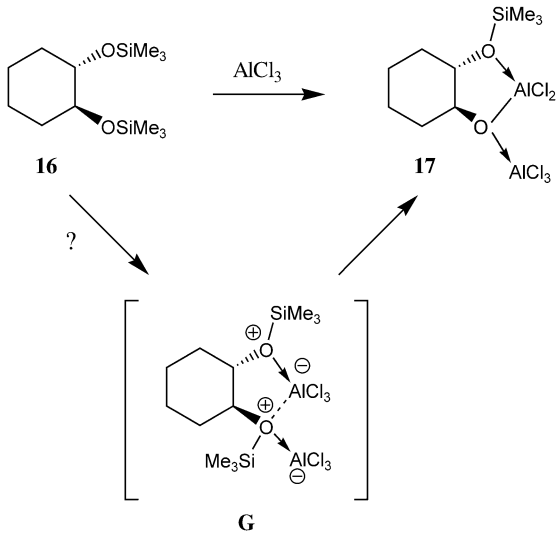


Figure 2. Simplified molecular model for complex **H**, showing the difference in availability of the second lone pair of each oxygen of the tweezers. This model omits non-relevant benzyl and isobutyl groups.



Scheme 5. Proposed mechanism for the TIBAL-mediated de-*O*-benzylation at position 2 of perbenzylated methyl α-D-glucopyranoside.

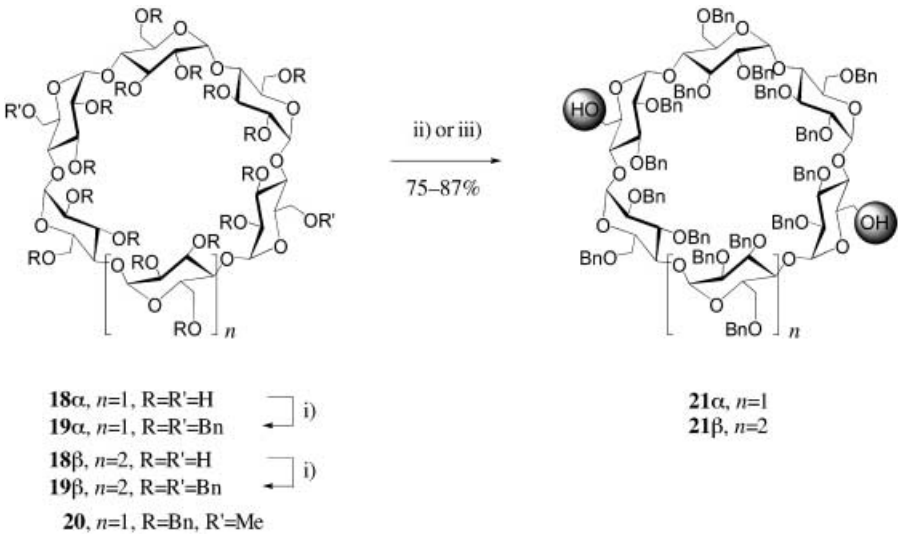


Scheme 6. Proposed intermediate for the known mono-desilylation of **16**.

when DIBAL-H was used; TIBAL was not suitable (entry 3, Table 2). This was further confirmed in entries 4 and 5 in Table 2, in which the possible de-*O*-benzylation at O-2 has been "turned off". We next studied maltose derivatives, which are related to cyclodextrins in structure. Perbenzylated methyl α-D-maltoside **27**[46] gave a complex mixture of products with DIBAL-H (entry 6, Table 2), whereas TIBAL (entry 7, Table 2) performed a selective 2-*O*-debenzylation at the reducing end;[11] no similar reaction was observed at the non-reducing end, probably due to steric hindrance. To focus on the non-reducing end, we subjected the model cyclohexyl derivative **29**[47] to the action of DIBAL-H (entry 8) and isolated the two compounds **30**[48] and **31**, resulting from de-*O*-benzylation at the O-2 and O-6 positions, in 81% yield, as a 1/1 mixture. Therefore, increasing the bulk of the substituent at the anomeric position oriented DIBAL-H de-*O*-benzylation towards position 6.

In summary, DIBAL-H will promote a 6-de-*O*-benzylation on sugars with hindered aglycons (e.g., perbenzylated cyclodextrins **19α/β** or cyclohexyl glucoside **29**) or with no aglycon at all (e.g., deoxy glucose **25**). TIBAL appears to be the reagent of choice for clean de-*O*-benzylation at position 2 of methyl α-D-glucopyranoside, but is inefficient for the deprotection of simple pyranosides at position 6.

ed out, a competitive de-*O*-benzylation occurred at position 6 when DIBAL-H was used as a scalpel. This property of DIBAL-H culminated in the case of perbenzylated cyclodextrins,[13] in which no competitive de-*O*-benzylation at O-2 was observed, in spite of a favourable 1,2-*cis* situation (Scheme 7). We now have to understand the mechanism of this 6-*O*-debenzylation, together with the rules dictating the 2-*O*- versus 6-*O*-regioselectivities, as exquisitely observed in the case of cyclodextrins.



Scheme 7. Synthesis of the $6^A,6^D$ diol from α- and β-cyclodextrins. Reagents and conditions: i) BnCl, NaH, DMSO, 18 h, RT; ii) DIBAL-H (120/140 equiv, 0.5 M), toluene, 2 h, 50 °C; iii) DIBAL-H (15 equiv, 1.5 M), toluene, 2 h, 50 °C.

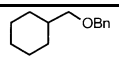
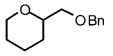
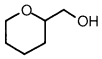
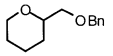
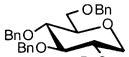
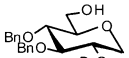
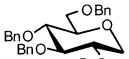
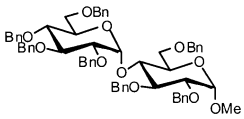
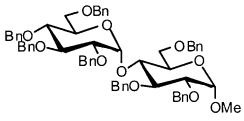
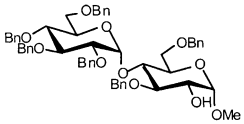
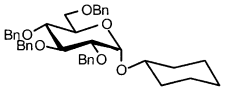
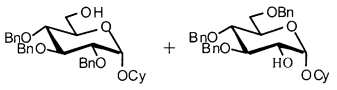
Firstly, we wish to disclose here an improved procedure for the de-*O*-benzylation of perbenzylated α- and β-cyclodextrins **19α** and **19β**.[44] The initially reported reaction conditions involved 120 equivalents of DIBAL-H for the α-CD and admittedly[45] could be considered as unpractical. We have since optimized the reaction conditions and now directly use 15 equivalents of the commercial 1.5 M DIBAL-H solution in toluene, to obtain 87% of the diol **21α**. In order to obtain a practical reaction time (a few hours), the use of an excess of aluminium reagent in the reaction—and generally in all de-*O*-benzylations of fully benzylated sugars—is necessary. This is probably due to numerous non-productive reversible complexations of DIBAL-H or TIBAL on the various oxygen atoms present in the molecule, and also to the existence of aluminium reagents in aggregate forms.

We next performed the experiments presented in Table 2. Entries 1 to 3 in Table 2 showed that the ring oxygen was required (entries 1 and 2, Table 2) for the reaction to occur

The typical entry 4 in Table 2 is again explained through a 2:1 complex. One equivalent of DIBAL-H first forms a complex **K** (Scheme 8), implicating both the ring oxygen atom and the 6-*O*-benzyl group; this is followed by an activation of the less hindered 6-*O*-benzyl by coordination to a second DIBAL-H molecule acting as a Lewis acid. Delivery of a hydride on the benzylic carbon from the so-formed complex **L** gives intermediate **M**.

In this case the kinetically selected dioxygenated tweezers involves the axial ring oxygen lone pair, forming a 1,2-*cis*-fused bicyclic complex (Figure 3). It is predictable that such

Table 2. Model compounds for de-*O*-benzylation at position 6.

Entry	Starting material	Reagent [equiv]	Time [h]	Products	Yield [%]
1	 **22**[49]	DIBAL-H (5)	96	no reaction	–
2	 **23**[50]	DIBAL-H (5)	4	 **24**[51]	89
3	 **23**	TIBAL (5)	18	no reaction	–
4	 **25**[52]	DIBAL-H (10)	5	 **26**[52]	80
5	 **25**	TIBAL (10)	22	89% of starting material	–
6	 **27**	DIBAL-H (10)	12	complex mixture of products	–
7	 **27**	TIBAL (10)	72	 **28**[11]	74
8	 **29**	DIBAL-H (20)	5	 **30** **31**	81 (53/47)

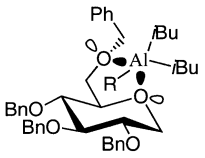


Figure 3. R = *i*Bu, the approach is difficult; R = H, the approach is easier.

an axial approach of the bulky TIBAL reagent will be tempered by steric hindrance, which is apparently less important in the case of DIBAL-H.

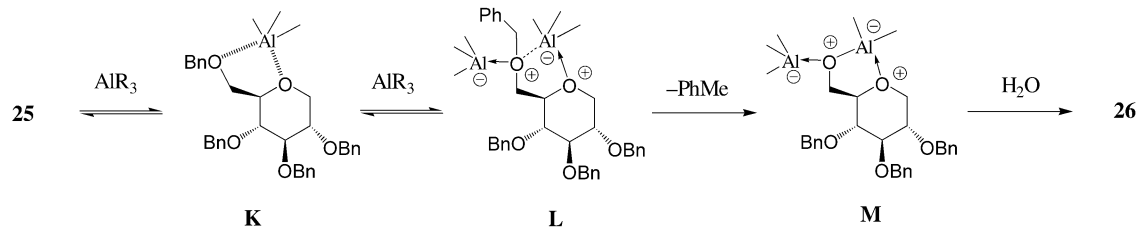
Debenzylation of cyclodextrins

Mechanism of the AD-bis-de-O-benzylation of cyclodextrins: The previous discussion sheds new light on the mechanism of the remarkable bis-de-*O*-benzylation of perbenzylated cyclodextrins. We had initially proposed the involvement of two aluminates on two opposite oxygen atoms of the upper rim of the cyclodextrin[13] (Scheme 9). We now favour a mechanism involving two independent 6-de-*O*-benzylations. This new proposal is supported by further developments in this area in our laboratory.

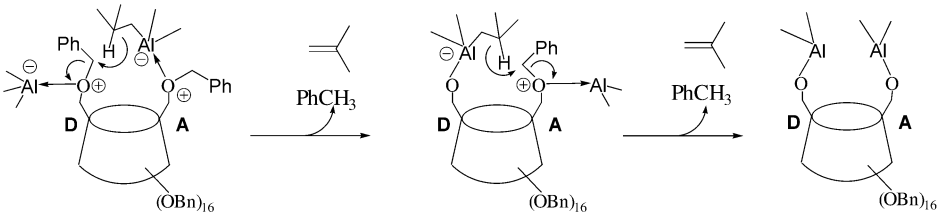
Firstly, we found that the alcohol **32**[13] could also be directly converted into the diol **21α** (Scheme 10).

Another, more convincing indication of the independence of the two de-*O*-benzylation processes emerged when the benzylated 6^A,6^D-capped α-cyclodextrin **33**[13] was bis-de-*O*-benzylated to give the 6^C,6^F-diol **34** *as a single isomer* (Scheme 11). This remarkable result, discussed further in the next paragraph in terms of selectivity, seems to rule out our initial proposal of direct communication between the two opposite debenzylation sites.

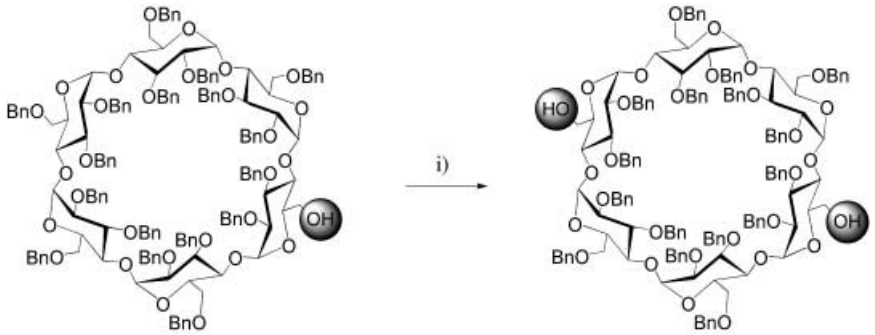
The DIBAL-H mediated bis-de-*O*-benzylation of perbenzylated cyclodextrins may now be explained by the reasonable mechanism illustrated in Scheme 12 in the case of α-CD. The same holds for β-CD. An initial mono-debenzylation of one glucosidic unit occurs on the primary rim via the intermediate **N**, according to previous trends. The high density of benzyl groups on the secondary rim probably precludes the potentially competing debenzylation at O-2. Furthermore, in the case of rather strained CDs, the interglycosidic oxygen lone pairs are no longer properly oriented for a kinetic alumination; this disfavours the efficient formation of O-1,O-2 tweezers, in agreement with previous observations (see Table 2). Steric hindrance caused by the generated aluminium alkoxide **O** directs the approach of a second aluminium pair to the farthest glucosidic tweezers—in the *para* position, we might say—to afford intermediate **P**. This steric effect is probably



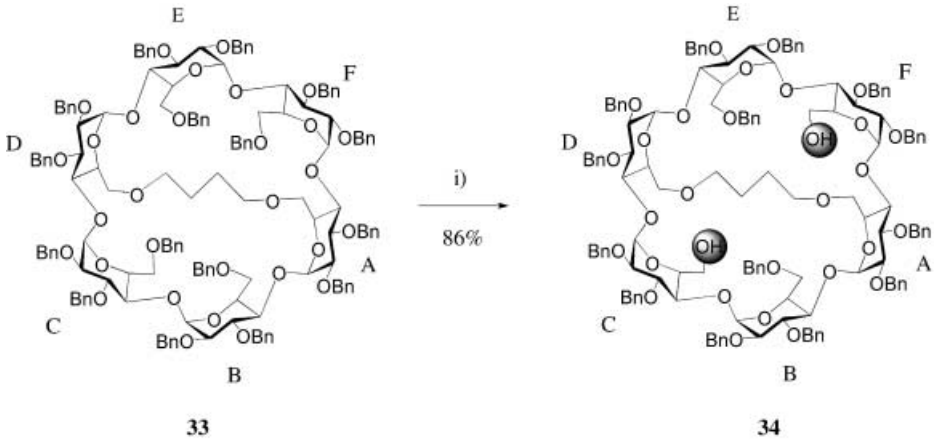
Scheme 8. Proposed mechanism for the DIBAL-H-mediated de-*O*-benzylation of the primary position.



Scheme 9. Originally proposed mechanism for AD-type bis-de-*O*-benzylation of perbenzylated α-cyclodextrin.



Scheme 10. $6^A,6^D$-Bis-de-*O*-alkylation of benzylated α-cyclodextrin. Reagents and conditions: i) DIBAL-H (120 equiv), toluene, 0.5 M, 2 h, 50 °C.



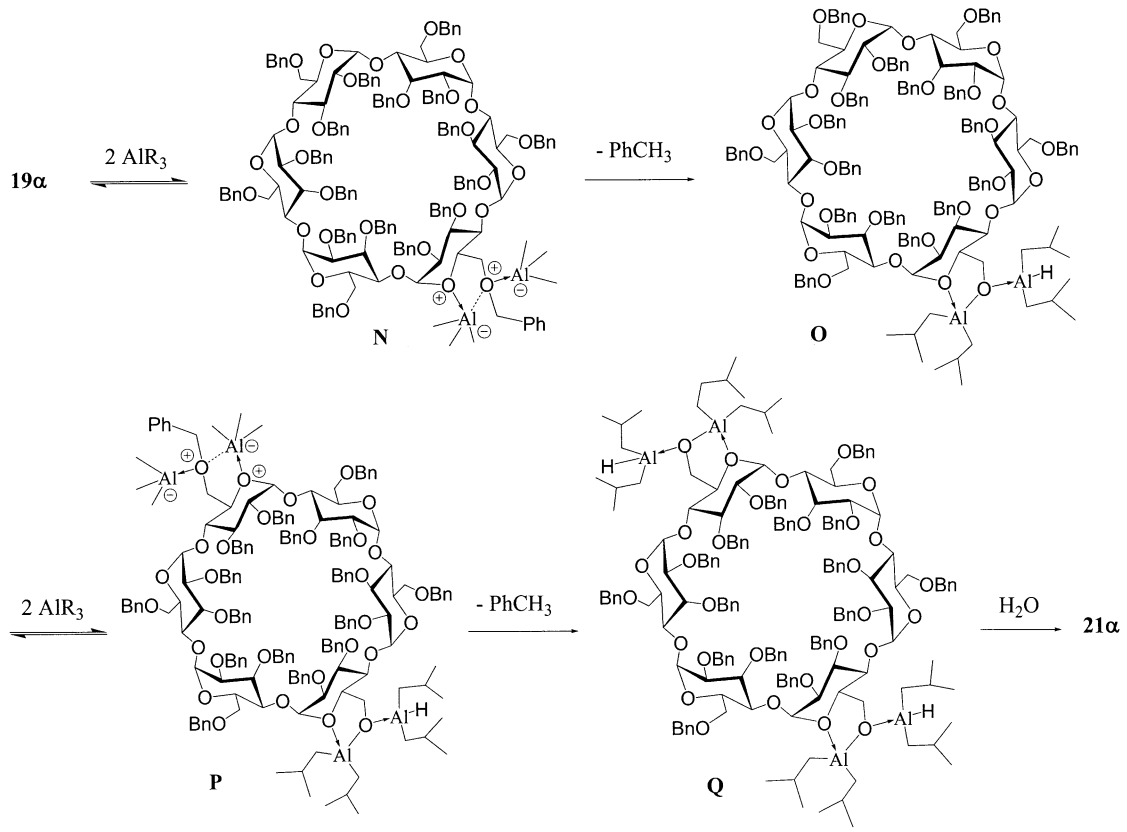
Scheme 11. The bis-de-*O*-benzylation of compound **33** with DIBAL-H gave a single isomer **34**. Reagents and conditions: i) DIBAL-H (30 equiv), toluene, 1 M, 2 h, 50 °C.

reinforced by the presence of the benzyl ethers, resulting in a very remarkable selectivity. Indeed the *para*-de-*O*-methylation of mixed CDs was less selective.[53] In a way, this sterically driven deprotection may be compared well to the similarly sterically directed "*para*-di-protection" of α-cyclodextrin with bulky groups, such as "supertrityl".[54] It is noteworthy that only 30 equivalents of DIBAL-H (0.5 M) are necessary to obtain alcohol **32**, whereas 120 are required to de-*O*-benzylate **32** further into **21α**, giving a token of the steric demand on the benzylated primary rim.

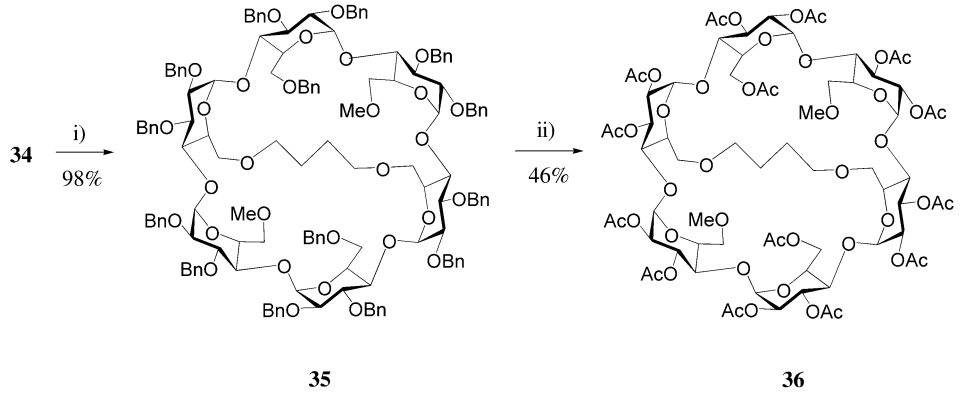
*A step forward: the selectivity in the case of the capped α-cyclodextrin **33***: Finally, we tried to explain the observed formation of a single regioisomer **34** in the de-*O*-benzylation of the $6^A,6^D$-capped α-cyclodextrin **33**. First of all we had to determine the structure of the isomer. For this purpose, the capped α-cyclodextrin **34** was converted in a straightforward manner, as shown in Scheme 13, into the derivative **36**, in which all three pairs of glucosidic units are now chemically differentiated.

The α-CD derivative **36** was then analysed by NMR spectroscopy. The pair of peracetylated sugars was easily characterised by the observed deshielding of the H-6 signals, due to the acetylation of the primary position. The two O-6 methylated units differ from the others in the presence of a NOE signal between the methyl group and one of the two H-6 diastereotopic protons. All signals of each pyranoside ring were attributed by COSY, and finally, the order of the connections between the units was determined by NOE experimentation thanks to cross-peaks between H-1 and H-4 of two successive units (Scheme 14).[55]

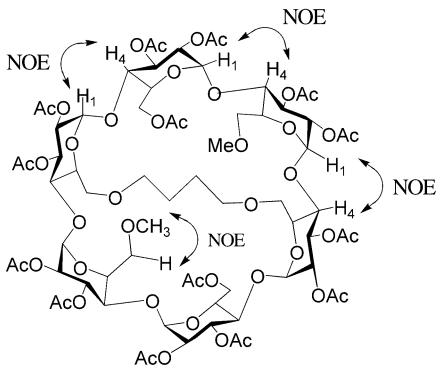
By the previously proposed mechanism, access to a ring oxygen of the glucosidic unit is necessary for the corresponding 6-*O*-debenzylation to occur. Inspection of a molecular model (Figure 4) shows that the (B,E) pair of ring oxygens of the AD-capped α-CD **33** is more hindered, by two benzyl moieties, than the (A,D) and (C,F) pairs. De-*O*-alkylation is next possible on two pairs of units: the one bearing the bridge (A,D) and the one on its left (C,F) (Figure 4, top view). Looking at the lone-pair orbitals of the two remaining O-6 pairs, represented here by $O\text{-}6^A$ and $O\text{-}6^F$ (Figure 4, front view), it appears that $O\text{-}6^A$, as it is bearing the bridge, indeed has one electron pair available for complexation, but the other one is oriented towards the inside of the CD cavity, and thus not kinetically available for complexation by a second aluminium reagent. Given that the two lone pairs of $O\text{-}6^C$ and $O\text{-}6^F$ are the most accessible, the de-*O*-alkylation becomes only possible on the corresponding 6-positions, giving the observed selectivity. In sharp contrast with the methylated derivative **20** (Scheme 7), the capping induces a conformation change around C5–C6, which turns off the critical availability of



Scheme 12. Proposed mechanism for A,D-type bis-de-*O*-benzylation of perbenzylated α-cyclodextrin.



Scheme 13. Synthesis of derivative **36**. Reagents and conditions: i) MeI, NaH, DMF, RT, 3 h; ii) H_2, Pd/C 10%, Pd black, EtOAc/MeOH (1:1), RT, 48 h, then Ac_2O, pyridine, DMAP, RT, 18 h.



Scheme 14. ^{1}H NMR analysis of compound **36**.

one electron lone pair. By our mechanistic hypothesis, the remarkable regioselectivity of this reaction is thus clearly explained.

Conclusion

We have tried in this investigation to explain the rules underlying the regioselective de-*O*-alkylation reactions promoted by the two isobutylaluminium reagents DIBAL-H and TIBAL. The proposed mechanism involves two molecules of aluminium reagent: the first one is trapped by the kinetically most accessible oxygen tweezers to provide a pentacoordinate or a highly fluxional chelate; the second one then directs the mono-de-*O*-alkylation by preferentially coordinating to one of the two oxygen atoms involved in the aluminium complexation. This preference is again dictated by the steric availability of the remaining lone electron pair of the corresponding oxygen atom. These two events should both take place for the regioselective mono-de-*O*-benzylation to occur. Knowledge of the orientation of the lone pairs on each oxygen atom in polybenzylated carbohydrate systems is the key feature for understanding and eventual prediction

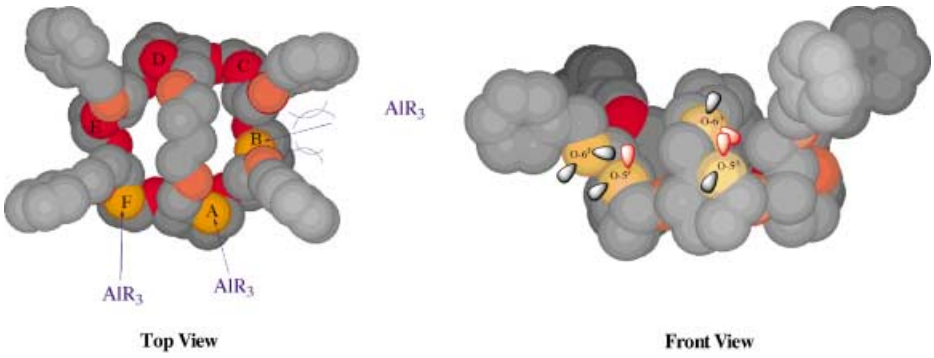


Figure 4. Simplified molecular model of the AD-capped benzylated α-CD **33**. Benzyloxy groups located on the secondary rim of the CD as well as the hydrogen atoms are omitted for the sake of clarity. Top view: Approach of AlR_3 is easier on two pairs of glucosidic units: (A,D) and (C,F). Each pair is represented by its O-5 in orange. Front view: Lone pairs in grey are accessible; lone pairs in red are more hindered; $O\text{-}6^F$ has two available lone pairs; $O\text{-}6^A$ has only one.

of the outcome of this remarkable process. Furthermore, it is possible to tune the selectivity by use either of TIBAL or of DIBAL-H: the first one, being more hindered, allows better selectivities, while the second allows access to more crowded "tweezers" (Scheme 13, Scheme 14, Table 1, and Table 2).

Experimental section

General: Melting points were determined with a Büchi model 535 m.p. apparatus and are uncorrected. Optical rotations were measured at 20 ± 2 °C with a Perkin–Elmer Model 241 digital polarimeter, in a 10 cm, 1 mL cell. Chemical Ionisation Mass Spectra (CI-MS ammonia) and Fast Atom Bombardment Mass Spectra (FAB-MS) were obtained with a JMS-700 spectrometer. Elemental analyses were performed by the Service de Microanalyse de L'Université Pierre et Marie Curie, 4 Place Jussieu, 75005 Paris, France; ^{1}H NMR spectra were recorded with a Bruker DRX 400 instrument for solutions in $CDCl_3$ at ambient temperature. Assignment were aided by COSY experiments. ^{13}C NMR spectra were recorded at 100.6 MHz with a Bruker DRX 400 spectrometer for solutions in $CDCl_3$, with the adoption of 77.00 ppm for the central line of $CDCl_3$. Assignments were aided by the J-mod technique and HMQC. Reactions were monitored by thin-layer chromatography (TLC) on precoated plates of silica gel (60 F_{254}, layer thickness 0.2 mm; E. Merck, Darmstadt, Germany) and detection by charring with sulfuric acid. Flash column chromatography was performed on silica gel 60 (230–400 mesh, E. Merck). DIBAL-H and TIBAL were both purchased from Aldrich as 1.5 and 1 M solutions, respectively, in toluene. Extra dry DMSO is commercially available from Fluka (ref. 41647).

General procedure for de-*O*-alkylation: DIBAL-H (1.5 M solution in toluene) or TIBAL (1 M solution in toluene) was added dropwise to a solution of benzylated compound in freshly distilled toluene, under argon at room temperature, and the mixture was stirred at 50 °C until TLC showed completion of the reaction. After cooling at 0 °C, the mixture was carefully poured onto ice. HCl (1 M) and EtOAc were added, and the mixture was stirred vigorously for 30 min. After extraction with EtOAc, the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was then purified by silica gel flash chromatography.

De-*O*-benzylation of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (1): TIBAL (5.4 mL, 5.4 mmol) was added to a solution of **1** (500 mg, 900 μmol) in toluene (5.4 mL) in the general procedure for de-*O*-alkylation, and the mixture was stirred for 3 h at 50 °C. After purification by silica gel chromatography (Cy/EtOAc 2:1), methyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (**2**, 409 mg, 98 %) was obtained as a white crystalline solid.

Compound 2: M.p. 78 °C (diethyl ether/hexane); $[\alpha]_D^{20} = +95$ ($CHCl_3$, $c = 1.05$) [lit.[20]: m.p. 74–76 °C; $[\alpha]_D^{20} = +97$ ($CHCl_3$, c = 1.0)]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.14 (br s, 1H; OH), 3.41 (s, 3H; OCH_3), 3.38–3.82 (m, 6H; 2-H, 3-H, 4-H, 5-H, 2×6-H), 4.80 (d, $^3J_{1,2}$ = 3.0 Hz, 1H; 1-H), 4.49–4.86 (m, 6H; 3×CH_2Ph), 7.17–7.41 (m, 15H; 15×aromatic-H) ppm; MS (DCI, NH_3): m/z: 482 $[M+NH_3+H]^+$.

Methyl 3,4,6-tri-*O*-benzyl-2-*O*-methyl-α-D-glucopyranoside (11): NaH (60 % w/w, 15 mg, 375 μmol) and iodomethane (28 μL, 375 μmol) were added under argon at rt. to a stirred solution of methyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (**2**, 140 mg, 302 μmol) in THF (1.5 mL). After 2 h, the reaction mixture was hydrolysed with MeOH and concentrated under vacuum. The residue was dissolved in EtOAc (30 mL) and washed with water (2×20 mL) and aq. sat. $Na_2S_2O_3$ (20 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under vacuum. After purification by silica gel chromatography (Cy/EtOAc 3:1), methyl 3,4,6-tri-*O*-benzyl-2-*O*-methyl-α-D-glucopyranoside (**11**, 139 mg, 96 %) was obtained as a colourless oil.

Compound 11: $[\alpha]_D^{20} = +59$ ($CHCl_3$, c = 2.15); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.42 (dd, $^3J_{2,3}$ = 9.5 Hz, $^3J_{2,1}$ = 3.5 Hz, 1H; 2-H), 3.47 (s, 3H; OCH_3), 3.58 (s, 3H; OCH_3), 3.68 (t, $^3J_{4,3} = {}^3J_{4,5}$ = 9.5 Hz, 1H; 4-H), 3.70–3.73 (m, 1H; 6-H), 3.76–3.81 (m, 2H; 6′-H, 5-H), 3.96 (t, $^3J_{3,4} = {}^3J_{3,2}$ = 9.5 Hz, 1H; 3-H), 4.52, 4.87 (AB, J_{AB} = 10.8 Hz, 2H; CH_2Ph), 4.54, 4.67 (AB, J_{AB} = 12.0 Hz, 2H; CH_2Ph), 4.82, 4.96 (AB, J_{AB} = 10.9 Hz, 2H; CH_2Ph), 4.94 (d, $^3J_{1,2}$ = 3.5 Hz, 1H; 1-H), 7.19–7.42 (m, 15H; 15×aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 54.9, 58.9 (2×OCH_3), 68.4 (C-6), 70.1 (C-5), 73.4, 75.0, 75.6 (3×OCH_2Ph), 77.5 (C-4), 82.0 (C-3), 82.2 (C-2), 97.5 (C-1), 126.9–128.7 (15×CH-aromatic), 137.9, 138.2, 138.8 (3×C-arom. quat.) ppm; MS (DCI, NH_3): m/z :496 $[M+NH_3+H]^+$; elemental analysis calcd (%) for $C_{29}H_{34}O_6$ (478.6): C 72.78, H 7.16; found C 72.71, H 7.04.

De-*O*-alkylation of methyl 3,4,6-tri-*O*-benzyl-2-*O*-methyl-α-D-glucopyranoside (11): DIBAL-H (1.3 mL, 1.95 mmol) was added to a solution of **11** (91 mg, 190 μmol) in toluene (2.6 mL), and the mixture was stirred for 2 h at 50 °C in the general procedure for de-*O*-alkylation. After purification by silica gel chromatography (Cy/EtOAc 7:3), **2** (48 mg, 54 %) and 3,4,6-tri-*O*-benzyl-2-*O*-methyl-D-glucitol (**12**, 26 mg, 29 %) were obtained.

Compound 12: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (t, $^3J_{OH,1} = {}^3J_{OH,1'}$ = 5.8 Hz, 1H; OH), 3.15 (d, $^3J_{OH,5}$ = 4.8 Hz, 1H; OH), 3.50 (s, 3H; OCH_3), 3.56–3.63 (m, 2H; 1-H, 2-H), 3.68, 3.72 (AB of ABX, J_{AB} = 9.8 Hz, J_{AX} = 5.0 Hz, J_{BX} = 3.6 Hz, 2H; 6-H, 6′-H), 3.72–3.79 (m, 1H; 1′-H), 3.81 (dd, $^3J_{4,3}$ = 4.0 Hz, $^3J_{4,5}$ = 7.2 Hz, 1H; 4-H), 3.88 (dd, $^3J_{3,4}$ = 4.0 Hz, $^3J_{3,2}$ = 5.2 Hz, 1H; 3-H) 4.06 (dddd, $^3J_{5,4}$ = 7.2 Hz, J_{AX} = 5.0 Hz, $^3J_{5,OH}$ = 4.8 Hz, J_{BX} = 3.6 Hz, 1H; 5-H), 4.57, 4.64 (AB, J_{AB} = 11.4 Hz, 2H; CH_2Ph), 4.58, 4.63 (AB, J_{AB} = 11.9 Hz, 2H; CH_2Ph), 4.70, 4.74 (AB, J_{AB} = 11.4 Hz, 2H; CH_2Ph), 7.26–7.40 (m, 15H; 15×aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.5 (OCH_3), 61.2 (C-1), 70.9 (C-5), 71.1 (C-6), 73.2, 73.5, 74.2 (3×OCH_2Ph), 77.0 (C-4), 78.8 (C-3), 80.9 (C-2), 127.5–128.5 (15×CH-aromatic), 137.8, 137.9, 138.9 (3×C-arom. quat.) ppm; MS (DCI, NH_3): m/z: 484 $[M+NH_3+H]^+$; HRMS (DCI, CH_4): found 467.244; $C_{28}H_{32}O_6$ calcd 467.2434.

Preparation of perbenzylated α-cyclodextrin (19α): α-Cyclodextrin **18α** was dried under vacuum over P_2O_5 until its weight became constant. NaH (60 % w/w, 17.75 g, 443 mmol) was then added to a stirred solution of dried α-cyclodextrin **18α** (12 g, 12.33 mmol) in DMSO (250 mL), under argon at room temperature. Benzyl chloride (51 mL, 443 mmol) was then added dropwise over 1 h. After 18 h, the reaction mixture was then carefully hydrolysed with MeOH (50 mL), diluted with water (500 mL) and extracted with Et_2O (3×500 mL). The combined organic layers were washed with brine (500 mL), dried ($MgSO_4$), filtered and concentrated. After purification by silica gel chromatography (toluene, then toluene/EtOAc 9:1), perbenzylated α-cyclodextrin **19α** was obtained as a white foam (30.4 g, 95 %).

Compound 19α: $[\alpha]_D^{20} = +34$ ($CHCl_3$, c = 1.0); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.50–3.54 (m, ^2J = 11.0 Hz, $^3J_{2,3}$ = 9.5 Hz, $^3J_{2,1}$ = 3.4 Hz, 12H; 2-H, 6-H), 3.92 (br d, $^3J_{5,4}$ = 9.5 Hz, 6H; 5-H), 4.04 (dd, ^2J = 11.0 Hz, $^3J_{6,5}$ = 2.8 Hz, 6H; 6-H), 4.09 (t, $^3J_{4,3} = {}^3J_{4,5}$ = 9.5 Hz, 6H; 4-H), 4.19 (t, $^3J_{3,2} = {}^3J_{3,4}$ = 9.5 Hz, 6H; 4-H), 4.36, 4.44 (AB, J_{AB} = 12.1 Hz, 12H; CH_2Ph), 4.49, 4.54 (AB, J_{AB} = 12.6 Hz, 12H; CH_2Ph), 4.92, 5.24 (AB, J_{AB} = 11.0 Hz, 12H; CH_2Ph), 5.13 (d, $^3J_{1,2}$ = 3.4 Hz, 6H; 1-H), 7.17–7.31 (m, 90H; aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.0 (C-6), 71.5 (C-5), 72.7, 75.6, 73.3 (3×OCH_2Ph), 78.9 (C-2), 79.2 (C-4), 80.9 (C-3), 98.6 (C-1), 126.9–128.3 (CH-aromatic), 138.1, 138.3, 139.3 (3×C-arom. quat.) ppm; MS (FAB): *m/z* (%): 2617.1 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{162}H_{168}O_{30}$ (2595): C 74.98, H 6.52; found C 74.85, H 6.62.

Preparation of perbenzylated β-cyclodextrin (18β): By the same procedure, perbenzylated β-cyclodextrin **19β** was obtained as a white foam (95%).

Compound 19β: $[\alpha]_D^{20} = +34$ ($CHCl_3$, c = 1.0); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.52 (dd, $^3J_{2,3}$ = 9.2 Hz, $^3J_{2,1}$ = 3.3 Hz, 7H; 2-H), 3.58 (d, ^2J = 10.6 Hz, 7H; 6-H), 3.98–4.10 (m, 28H; 3-H, 4-H, 5-H, 6-H), 4.39, 4.43 (AB, J_{AB} = 12.2 Hz, 14H; CH_2Ph), 4.50, 4.54 (AB, J_{AB} = 12.8 Hz, 14H; CH_2Ph), 4.81, 5.11 (AB, J_{AB} = 11.0 Hz, 14H; CH_2Ph), 5.22 (d, $^3J_{1,2}$ = 3.3 Hz, 7H; 1-H), 7,15–7,30 (m, 105H; aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.2 (C-6), 71.4 (C-5), 72.6, 73.2, 75.4 (3×OCH_2Ph), 78.6 (C-4), 78.7 (C-2), 80.8 (C-3), 98.4 (C-1), 126.9–128.3 (CH-aromatic), 138.1, 138.3, 139.2 (3×C-arom. quat.) ppm; MS (FAB): *m/z* (%): 3050.7 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{189}H_{193}O_{35}$ (3027): C 74.98, H 6.52; found C 75.04, H 6.65.

De-*O*-benzylation of perbenzylated α-cyclodextrin (19α): DIBAL-H (1.9 mL, 2.9 mmol) was added dropwise to **19α** (504 mg, 194 μmol), and the mixture was stirred at 50°C The reaction was carefully monitored by TLC (Cy/EtOAc 3:1), and the mixture was hydrolysed after 20 minutes, as usual. After purification by silica gel chromatography (Cy/EtOAc 3:1), **21α** (410 mg, 87%) was obtained as a white foam.

Compound 21α: $[\alpha]_D^{20} = +33$ ($CHCl_3$, c = 1.0); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.35 (br t, $^3J_{OH,6}$ = 5.3 Hz, 2H; OH), 3.44–3.47 (m, 4H; 2×2-H), 3.61 (dd, $^3J_{2,3}$ = 9.6 Hz, $^3J_{2,1}$ = 3.9 Hz, 2H; 2-H), 3.66–3.70 (m, 2H; 6-H), 3.73–4.04 (m, 20H), ; 4.06 (dd, $^3J_{3,2}$ = 9.6 Hz, $^3J_{3,4}$ = 8.5 Hz, 2H; 3-H), 4.14 (br t, $^3J_{3,2} = {}^3J_{3,4}$ = 9.1 Hz, 2H; 3-H), 4.25 (br dd, $^3J_{3,2}$ = 9.7 Hz, $^3J_{3,4}$ = 7.3 Hz, 2H; 3-H), 4.36 (d, ^2J = 12.6 Hz, 2H; CHPh), 4.41 (d, ^2J = 12.6 Hz, 2H; CHPh), 4.51–4.53 (m, 6H; 3×CHPh), 4.54 (d, ^2J = 12.6 Hz, 2H; CHPh), 4.58 (d, ^2J = 12.6 Hz, 2H; CHPh), 4.59 (d, ^2J = 12.4 Hz, 2H; CHPh), 4.60 (d, ^2J = 12.1 Hz, 2H; CHPh), 4.75 (d, $^3J_{1,2}$ = 3.4 Hz, 2H; 1-H), 4.76 (d, $^3J_{1,2}$ = 3.3 Hz, 2H; 1-H), 4.81 (d, ^2J = 11.0 Hz, 4H; 2×CHPh), 4.83 (d, ^2J = 11.8 Hz, 2H; CHPh), 4.93 (d, ^2J = 11.8 Hz, 2H; CHPh), 4.94 (d, ^2J = 10.4 Hz, 2H; CHPh), 5.23 (d, ^2J = 10.7 Hz, 2H; CHPh), 5.49 (d, ^2J = 10.4 Hz, 2H; CHPh), 5.77 (d, $^3J_{1,2}$ = 3.9 Hz, 2H; 1-H), 7.11–7.31 (m, 80H; aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 61.6 (C-6), 69.5, 69.6 (2×C-6), 71.2, 71.6, 72.0 (3×C-5), 72.1, 72.9, 73.2, 73.25, 73.3, 73.9 (6×OCH_2Ph), 74.1 (C-4), 76.1, 76.4 (2×OCH_2Ph), 77.6, 79.0, 79.7 (3×C-2), 80.6, 80.9 (2×C-3), 81.0 (C-4), 81.6 (C-3), 81.7 (C-4), 97.6, 97.7, 98.2 (3×C-1), 126.3–128.3 (CH-aromatic), 137.7, 137.8, 137.9, 138.2, 138.6, 137.7 (6×C-arom. quat.), 139.2 (2×C-arom. quat.) ppm; MS (FAB): *m/z* (%): 2437.0 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{148}H_{156}O_{30}$ (2415): C 73.61, H 6.51; found C 73.46, H 6.62.

De-*O*-benzylation of perbenzylated β-cyclodextrin (19β): DIBAL-H (2.0 mL, 3 mmol) was added dropwise to **19β** (600 mg, 198 μmol), and the system was stirred at 50°C. The reaction was carefully monitored by TLC (Cy/EtOAc 3:1), and the mixture was hydrolysed after 20 minutes, as usual. After purification by silica gel chromatography (Cy/EtOAc 3:1), **21β** (425 mg, 75%) was obtained as a white foam.

Compound 21β: $[\alpha]_D^{20} = +34$ ($CHCl_3$, c = 1.0); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.69 (br s, 1H; OH), 2.78 (br s, 1H; OH), 3.44–3.54 (m, 5H; 5×2-H), 3.60–4.15 (m, 37H; 2×2-H, 7×3-H, 7×4-H, 7×5-H, 14×6-H), 4.44–4.88 (m, 33H; CHPh), 4.89 (d, $^3J_{1,2}$ = 3.3 Hz, 1H; 1-H), 4.98 (d, $^3J_{1,2}$ = 3.7 Hz, 1H; 1-H), 5.00 (d, $^3J_{1,2}$ = 4.0 Hz, 2H; 1-H), 5.02 (d, $^3J_{1,2}$ = 3.4 Hz, 1H; 1-H), 5.04 (d, $^3J_{1,2}$ = 3.5 Hz, 1H; 1-H), 5.06 (d, ^2J = 12.3 Hz 1H; CHPh), 5.21–5.25 (m, 3H; 3×CHPh), 5.30 (d, ^2J = 10.7 Hz 1H; CHPh), 5.56 (d, $^3J_{1,2}$ = 3.8 Hz, 2H; 1-H), 5.67 (d, $^3J_{1,2}$ = 3.7 Hz, 2H; 1-H), 7.12–7.33 (m, 95H; aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 61.4 (2×C-6), 68.7, 68.9, 69.1, 69.2, 69.3 (5×C-6), 71.4 (2×C-5), 71.5 (C-5), 71.6 (2×C-5), 71.7, 71.9 (2×C-5), 72.3, 72.4, 72.5, 72.6 (4×OCH_2Ph), 72.8 (2×OCH_2Ph), 72.9, 73.1, 73.2 (3×OCH_2Ph), 73.3 (2×OCH_2Ph), 73.4 (OCH_2Ph), 74.2 (CH), 74.3, 74.5, 74.7 (3×OCH_2Ph), 75.0 (CH), 74.5, 75.9, 76.0, 76.1 (4×OCH_2Ph), 78.6, 78.7, 78.8, 79.0, 79.4 (5×C-2), 79.5, 79.6, 79.7, 79.8, 80.1, 80.5, 80.6, 80.7 (8×CH), 80.75 (2×CH), 80.8 (2×CH), 81.1, 81.3 (2×CH), 97.4, 97.6, 98.0, 98.2, 98.4, 99.1, 99.2 (7×C-1), 126.7–128.3 (CH-aromatic), 137.7, 137.8 (2×C-arom. quat.), 137.9 (2×C-arom. quat.), 138.0 (2×C-arom. quat.), 138.1 (2×C-arom. quat.), 138.3 (C-arom. quat.), 138.4 (2×C-arom. quat.), 138.5, 138.8 (2×C-arom. quat.), 138.9 (2×C-arom. quat.), 139.0, 139.2, 139.3, 139.4 (4×C-arom. quat.) ppm; MS (FAB): *m/z* (%): 2870.3 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{175}H_{184}O_{35}$ (2847): C 73.82, H 6.51; found C 73.82, H 6.59.

De-*O*-benzylation of α-cyclodextrin monoalcohol (32): DIBAL-H (6.4 mL, 9.6 mmol) was added dropwise to a solution of **32** (200 g, 80 μmol) in toluene (12.8 mL) by the general procedure for de-*O*-alkylation, and the system was stirred at 50°C for 2 h. After purification by silica gel chromatography (Cy/EtOAc 3:1), **21α** (156 mg, 81%) was obtained as a white foam.

1,5-Anhydro-2,3,4,6-tetra-*O*-benzyl-D-glucitol (25): A solution of 1-bromo-2,3,4,6-tetra-*O*-acetyl-α-D-glucose (1.8 g, 4.38 mmol) in Et_2O (5 mL) was slowly added to a stirred suspension of $LiAlH_4$ (1.19 g, 45 mmol) in Et_2O (27 mL) under argon at 0°C. After 1 h at room temperature, the reaction mixture was hydrolysed carefully with water and then filtered through a celite pad.[56] The aqueous layer was neutralised with IR120 H^+, concentrated under vacuum and dried over P_2O_5. The crude residue was dissolved in DMF (20 mL), and NaH (60% w/w, 1.4 g, 35 mmol) and benzyl bromide (4.35 mL, 35 mmol) were carefully added. After 3 h of stirring at room temperature, the reaction mixture was hydrolysed with methanol and concentrated under vacuum. The residue was dissolved in CH_2Cl_2 (100 mL) and washed with aqueous saturated NH_4Cl (2×50 mL) and aqueous saturated NaCl (50 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under vacuum. After purification by silica gel chromatography (Cy/EtOAc 4:1), 1,5-anhydro-2,3,4,6-tetra-*O*-benzyl-D-glucitol **25** (1.473 g, 65%) was obtained as a colourless oil.

Compound 25: $[\alpha]_D^{20} = +28$ ($CHCl_3$, *c* = 1.1) [lit.[52] $[\alpha]_D^{20} = +27$ ($CHCl_3$, *c* = 0.5)]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.22–3.30 (m, 1H; 2-H), 3.42 (ddd, $^3J_{5,4}$ = 9.5 Hz, $^3J_{5,6}$ = 4.2 Hz, $^3J_{5,6'}$ = 2.2 Hz, 1H; 5-H), 3.60 (t, $^3J_{4,3} = {}^3J_{4,5}$ = 9.5 Hz, 1H; 4-H), 3.65–3.70 (m, 3H; 1-H, 3-H, 6-H), 3.72 (dd, $^2J_{6,6'}$ = 10.5 Hz, $^3J_{6,5}$ = 2.2 Hz, 1H; 6′-H), 4.08 (dd, $^3J_{1',1}$ = 11.3 Hz, $^3J_{1',2}$ = 4.7 Hz, 1H; 1′-H), 4.53, 4.87 (AB, J_{AB} = 10.7 Hz, 2H; CH_2Ph), 4.55, 4.63 (AB, J_{AB} = 12.1 Hz, 2H; CH_2Ph), 4.70, 4.76 (AB, J_{AB} = 11.5 Hz, 2H; CH_2Ph), 4.89, 5.01 (AB, J_{AB} = 11.0 Hz, 2H; CH_2Ph), 7.30–7.40 (m, 20H; 20×aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.1 (C-1), 68.9 (C-6), 73.2, 73.5, 75.1, 75.5 (4×OCH_2Ph), 77.7 (C-4), 78.4 (C-2), 79.2 (C-5), 86.3 (C-3), 127.6–128.5 (20×CH-aromatic), 137.8, 138.0, 138.1, 138.7 (4×C-arom. quat.) ppm; MS (DCI, NH_3): *m/z*: 542 (100) $[M+NH_3+H]^+$.

1,5-Anhydro-2,3,4-tri-*O*-benzyl-D-glucitol (26): DIBAL-H (2.9 mL, 4.32 mmol) was added to a solution of 1,5-anhydro-2,3,4,6-tetra-*O*-benzyl-D-glucitol (**25**, 226 mg, 432 μmol) in toluene (5.8 mL) by the general procedure for de-*O*-alkylation, and the system was stirred at 50°C for 5 h. After purification by silica gel chromatography (Cy/EtOAc 2:1), 1,5-anhydro-2,3,4-tri-*O*-benzyl-D-glucitol (**26**, 151 mg, 80%) was obtained as white crystals.

Compound 26: M.p. 79°C [lit.[52] m.p. 76–77°C]; $[\alpha]_D^{20} = +18$ ($CHCl_3$, *c* = 1.0) [lit.[52] $[\alpha]_D^{20} = +17.6$ (CH_2Cl_2, c = 0.2)]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77 (dd, $^3J_{OH,6}$ = 7.1 Hz, $^3J_{OH,6'}$ = 5.9 Hz, 1H; OH), 3.27 (dd, $^2J_{1,1'}$ = 11.0 Hz, $^3J_{1,2}$ = 10.3 Hz, 1H; 1-H), 3.32 (ddd, $^3J_{5,4}$ = 9.7 Hz, $^3J_{5,6}$ = 4.6 Hz, $^3J_{5,6'}$ = 2.7 Hz, 1H; 5-H), 3.52 (t, $^3J_{4,5} = {}^3J_{4,3}$ = 9.1 Hz, 1H; 4-H), 3.64 (dt, $^3J_{2,1} = {}^3J_{2,3}$ = 9.0 Hz, $^3J_{2,1'}$ = 5.2 Hz, 1H; 2-H), 3.65–3.73 (m, 2H; 3-H, 6-H), 3.86 (ddd, $^2J_{6',6}$ = 11.8 Hz, $^3J_{6',OH}$ = 5.9 Hz, $^3J_{6',5}$ = 2.7 Hz, 1H; 5-H), 4.03 (dd, $^2J_{1',1}$ = 11.1 Hz, $^3J_{1',2}$ = 4.9 Hz, 1H; 1′-H), 4.68, 4.77 (AB, J_{AB} = 11.4 Hz, 2H; CH_2Ph), 4.68, 4.92 (AB, J_{AB} = 11.4 Hz, 2H; CH_2Ph), 4.88, 5.28 (AB, J_{AB} = 11.0 Hz, 2H; CH_2Ph), 7.30–7.40 (m, 15H; 15×aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 62.3 (C-1), 67.9 (C-6), 73.3, 75.1, 75.5 (3×OCH_2Ph), 77.6 (C-4), 78.5 (C-2), 79.7 (C-5), 86.2 (C-3), 127.6–128.5 (15×CH-aromatic), 138.0, 138.1, 138.6 (3×C-arom. quat.) ppm; MS (DCI, NH_3): *m/z*: 452 $[M+NH_3+H]^+$.

De-*O*-benzylation of cyclohexyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (29): DIBAL-H (2.3 mL, 3.45 mmol) was added to a solution of **29** (107 mg, 172 μmol) in toluene (4.6 mL) in the general procedure for de-*O*-alkylation, and the system was stirred for 5 h at 50 °C. After purification by silica gel chromatography (Cy/EtOAc 4:1), cyclohexyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (**31**, 35 mg, 39 %) and cyclohexyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**30**, 39 mg, 42 %) were obtained.

Compound 30: $[\alpha]_D^{20} = +60$ ($CHCl_3$, $c = 1.0$) [lit.[48] $[\alpha]_D^{20} = +60$ ($CHCl_3$, c = 0.57)]; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.18$–1.49 (m, 6H; c-H, d-H, e-H), 1.71–1.79, 1.90–1.99 (2 m, 4H; b-H, f-H), 2.09 (d, $^3J_{OH,2} = 9.2$ Hz, 1H; OH), 3.61–3.71 (m, 1H; a-H), 3.66 (t, $^3J_{4,3} = {}^3J_{4,5} = 8.7$ Hz, 1H; 4-H), 3.70 (dd, $^2J_{6,6'} = 10.5$ Hz, $^3J_{6,5} = 2.0$ Hz, 1H; 6-H), 3.74 (dt, $^3J_{2,3} = {}^3J_{2,OH} = 9.2$ Hz, $^3J_{2,1} = 3.8$ Hz, 1H; 2-H), 3.78 (t, $^3J_{3,4} = {}^3J_{3,2} = 8.5$ Hz, 1H; 3-H), 3.81 (dd, $^2J_{6',6} = 10.5$ Hz, $^3J_{6',5} = 3.8$ Hz, 1H; 6′-H), 3.92 (ddd, $^3J_{5,4} = 10.0$ Hz, $^3J_{5,6} = 3.8$ Hz, $^3J_{5,6'} = 2.0$ Hz, 1H; 5-H), 4.52, 4.97 (AB, $J_{AB} = 10.6$ Hz, 2H; CH_2Ph), 4.53, 4.68 (AB, $J_{AB} = 12.1$ Hz, 2H; CH_2Ph), 4.98, 5.02 (AB, $J_{AB} = 11.1$ Hz, 2H; CH_2Ph), 5.07 (d, $^3J_{1,2} = 3.8$ Hz, 1H; 1-H), 7.30–7.40 (m, 15H; 15×aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.9$, 24.1, 25.5, 31.7, 33.4 (C-b, C-c, C-d, C-e, C-f), 68.5 (C-6), 70.5 (C-a), 73.0 (C–H), 73.5, 75.1, 75.3 (3×OCH_2Ph), 76.2 (C–H), 78.7 (C–H), 83.8 (C–H), 96.8 (C-1), 127.6–128.5 (15×CH-aromatic), 138.0, 138.2, 138.8 (3×C-arom. quat.) ppm; MS (DCI, NH_3): m/z: 550 $[M+NH_3+H]^+$.

Compound 31: $[\alpha]_D^{20} = +61$ ($CHCl_3$, $c = 0.9$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.20$–1.52 (m, 6H; c-H, d-H, e-H), 1.66 (br t, $^3J_{OH,6} = {}^3J_{OH,6'} = 5.8$ Hz, 1H; OH), 1.72–1.81, 1.86–1.97 (2 m, 4H; b-H, f-H), 3.53 (dd, $^3J_{2,1} = 3.7$ Hz, $^3J_{2,3} = 9.5$ Hz, 1H; 2-H), 3.57 (t, $^3J_{4,3} = {}^3J_{4,5} = 9.5$ H; 1H; 4-H), 3.52–3.63 (m, 1H; a-H), 3.71–3.86 (m, 3H; 5-H, 6-H, 6′-H), 4.07 (t, $^3J_{3,2} = {}^3J_{3,4} = 9.5$ Hz, 1H; 3-H), 4.68, 4.93 (AB, $J_{AB} = 10.9$ Hz, 2H; CH_2Ph), 4.70, 4.79 (AB, $J_{AB} = 11.9$ Hz, 2H; CH_2Ph), 4.87, 5.05 (AB, $J_{AB} = 10.8$ Hz, 2H; CH_2Ph), 4.94 (d, $^3J_{1,2} = 3.7$ Hz, 1H; 1-H), 7.30–7.40 (m, 15H; 15×aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 24.1$, 24.4, 25.6, 31.4, 33.3 (C-b, C-c, C-d, C-e, C-f), 62.0 (C-6), 70.6 (C-a), 73.0, 75.1 (2×OCH_2Ph), 75.5 (C–H), 75.6 (OCH_2Ph), 77.6 (C–H), 80.1 (C–H), 81.9 (C–H), 94.6 (C-1), 127.5–128.5 (15×C-aromatic), 138.1, 138.2, 138.9 (3×C-arom. quat.) ppm; MS (DCI, NH_3): m/z: 550 $[M+NH_3+H]^+$; elemental analysis calcd (%) for $C_{33}H_{40}O_6$ (532.3): C 74.41, H 7.57; found C 74.14, H 7.86.

6^A,6^D-Butyl-capped α-cyclodextrin (33): PtO_2 was added to a solution of 6^A,6^D-butylene-capped α-cyclodextrin[13] (1 g, 405 μmol) in EtOAc (30 mL). The reaction mixture was stirred under an H_2 atmosphere for 3 h, filtered on a Celite® pad and concentrated under vacuum. After purification by silica gel chromatography (Cy/EtOAc 6:1), **33** (965 mg, 97 %) was obtained as a white foam.

Compound 33: $[\alpha]_D^{20} = +34$ ($CHCl_3$, $c = 1.0$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$–1.20 (m, 2H; O–CH_2–CH_2–), 1.45–1.55 (m, 2H; O–CH_2–CH_2–), 3.04–3.10 (m, 2H; O–CH_2–CH_2–), 3.18–3.25 (m, 2H; O–CH_2–CH_2–), 3.34 (dd, $^2J = 10.3$ Hz, $^3J_{6,5} = 7.3$ Hz, 2H; 6-H), 3.37–3.43 (m, 4H; 2-H, 4-H), 3.48 (dd, $^3J_{2,3} = 10.0$ Hz, $^3J_{2,1} = 3.5$ Hz, 2H; 2-H), 3.50 (d, $^2J = 10.9$ Hz, 2H; 6-H), 3.60 (dd, $^3J_{2,3} = 9.8$ Hz, $^3J_{2,1} = 3.7$ Hz, 2H; 2-H), 3.71 (d, $^2J = 9.8$ Hz, 2H; 6-H), 3.78 (d, $^2J = 10.0$ Hz, 2H; 6-H), 3.92–4.10 (m, 12H; 3-H, 2×4-H, 2×5-H, 6-H), 4.19 (dd, $^3J_{3,2} = 9.8$ Hz, $^3J_{3,4} = 8.6$ Hz, 2H; 3-H), 4.23 (dd, $^3J_{5,4} = 10.0$ Hz, $^3J_{5,6} = 7.8$ Hz, 2H; 5-H), 4.30 (d, $^2J = 12.5$ Hz, 2H; CHPh), 4.31 (t, $^3J_{3,2} = {}^3J_{3,4} = 11.0$ Hz, 2H; 3-H), 4.33 (d, $^2J = 11.0$ Hz, 2H; CHPh), 4.38 (d, $^2J = 10.4$ Hz, 2H; CHPh), 4.44–4.56 (m, 14H; 6×CHPh, 6-H), 4.73 (d, $^2J = 12.5$ Hz, 2H; CHPh), 4.82 (d, $^3J_{1,2} = 3.2$ Hz, 2H; 1-H), 4.86 (d, $^3J_{1,2} = 3.5$ Hz, 2H; 1-H), 4.86 (d, $^2J = 10.4$ Hz, 2H; CHPh), 4.93 (m, 4H; 2×CHPh), 5.07 (d, $^2J = 10.8$ Hz, 2H; CHPh), 5.33 (d, $^3J_{1,2} = 3.7$ Hz, 2H; 1-H), 5.34 (d, $^2J = 10.6$ Hz, 2H; CHPh), 5.58 (d, $^2J = 10.8$ Hz, 2H; CHPh), 7.08–7.36 (m, 80H; aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 26.9$ (O–CH_2–CH_2–), 68.8, 69.0 (2×C-6), 70.4 (O–CH_2–CH_2–), 71.0, 71.5, 71.6 (3×C-5), 71.8 (C-6), 72.3, 72.7, 73.0, 73.1, 73.2, 74.1, 76.1, 76.5 (8(O–CH_2Ph), 77.7, 78.6, 79.8 (3(C-2), 81.0, 80.6, 80.8 (3(C-3), 81.1, 81.4, 82.2 (3(C-4), 98.3, 100.5, 100.6 (3(C-1), 126.1–128.3 (40(CH-aromatic), 138.0, 138.1, 138.2, 138.4, 138.8, 139.4, 139.5, 139.9 (8(C-arom. quat.) ppm; MS (FAB): m/z: 2491.0 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{152}H_{162}O_{30}$ (2468.9): C 73.95, H 6.61; found: C 73.86, H 6.70.

De-*O*-benzylation of 6A,6D-butyl-capped α-cyclodextrin (33): DIBAL-H (2 mL, 3.5 mmol) was added dropwise to a solution of **33** (250 mg, 101 μmol) in toluene (1 mL), and the system was stirred at 50 °C for 2 h by the general procedure for de-*O*-alkylation. After purification by silica gel chromatography (Cy/EtOAc 2:1), **34** (200 mg, 86 %) was obtained as a white foam.

Compound 34: $[\alpha]_D^{20} = +22$ ($CHCl_3$, $c = 1.0$); ^{1}H NMR (400 MHz, $CDCl_3$): $\Delta = 1.36$–1.49 (m, 2H; O–CH_2–CH_2–), 1.55–1.68 (m, 2H; O–CH_2–CH_2–), 2.20 (br s, 2H; OH), 3.26–3.34 (m, 2H; O–CH_2–CH_2–), 3.36–3.45 (m, 4H; 6-H, 4-H), 3.42 (dd, $^3J_{2,3} = 9.3$ Hz, $^3J_{2,1} = 3.2$ Hz, 2H; 2-H), 3.42–3.50 (m, 2H; O–CH_2–CH_2–), 3.53 (dd, $^3J_{2,3} = 9.2$ Hz, $^3J_{2,1} = 3.7$ Hz, 2H; 2-H), 3.54 (dd, $^3J_{2,3} = 9.4$ Hz, $^3J_{2,1} = 3.6$ Hz, 2H; 2-H), 3.59 (d, $^2J = 10.8$ Hz, 2H; 6-H), 3.86–3.96 (m, 8H; 6-H, 2×5-H, 4-H), 4.02 (t, $^3J_{4,3} = {}^3J_{4,5} = 8.8$ Hz, 2H; 4-H), 4.07–4.28 (m, 12H; 3-H, 5-H, 6-H), 4.38 (d, $^2J = 12.6$ Hz, 2H; CHPh), 4.41–4.54 (m, 12H; 5×CHPh, 6-H), 4.57 (d, $^2J = 11.9$ Hz, 2H; CHPh), 4.65 (d, $^2J = 12.5$ Hz, 2H; CHPh), 4.85 (d, $^3J_{1,2} = 3.2$ Hz, 2H; 1-H), 4.91 (d, $^2J = 10.3$ Hz, 2H; CHPh), 4.94 (d, $^2J = 10.3$ Hz, 2H; CHPh), 4.99 (d, $^3J_{1,2} = 3.7$ Hz, 2H; 1-H), 5.00 (d, $^2J = 11.4$ Hz, 4H; 2×CHPh), 5.18 (d, $^3J_{1,2} = 3.6$ Hz, 2H; 1-H), 5.36 (d, $^2J = 10.6$ Hz, 4H; 2×CHPh), 7.10–7.41 (m, 70H; aromatic-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 26.5$ (O–CH_2–CH_2–), 61.5, 69.1 (2×C-6), 70.6 (O–CH_2–CH_2–), 71.6, 71.7, 71.8 (3×C-5), 71.9 (O–CH_2Ph), 72.0 (C-6), 72.8, 72.9, 73.1, 74.6, 75.7, 76.3 (6×O–CH_2Ph), 78.0, 78.1, 79.5 (3×C-2), 80.4, 80.6 (2×C-3), 80.8, 80.8 (2×C-4), 81.2 (C-3), 81.5 (C-4), 97.5, 99.9, 100.3 (3×C-1), 126.4–128.2 (35×CH-aromatic), 138.0 (2×C-arom. quat.), 138.1, 138.6, 139.2, 139.4, 139.6, (5×C-arom. quat.) ppm; MS (FAB): m/z: 2311.0 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{138}H_{150}O_{30}$ (2288.6): C 72.42, H 6.61; found C 72.61, H 6.52.

6^A,6^D-Butyl-capped 6^C,6^F-di-*O*-methyl-α-cyclodextrin (35): NaH (60 % w/w, 45 mg, 428 μmol) and MeI (60 μL, 428 μmol) were added under argon at room temperauture to a stirred solution of **34** (490 mg, 214 μmol) in anhydrous DMF (10 mL). After 3 h stirring, the reaction mixture was hydrolysed with MeOH and concentrated under vacuum. The residue was dissolved in DCM (60 mL) and washed with aqueous saturated NH_4Cl (2×30 mL) and aqueous saturated NaCl (30 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under vacuum. After purification by silica gel chromatography (Cy/EtOAc 3:1), **35** was obtained as a white foam (488 mg, 98 %).

Compound 35: $[\alpha]_D^{20} = +19$ ($CHCl_3$, c = 1.0); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.25$–1.33 (m, 2H; O–CH_2–CH_2–), 1.60–1.70 (m, 2H; O–CH_2–CH_2–), 3.27–3.33 (m, 2H; O–CH_2–CH_2–), 3.34 (s, 6H; OMe), 3.37–3.41 (m, 2H; O–CH_2–CH_2–), 3.43–3.48 (m, 6H; 2-H, 4-H, 6-H), 3.51–3.58 (m, 4H; 2-H, 6-H), 3.61 (dd, $^3J_{2,3} = 9.5$ Hz, $^3J_{2,1} = 3.7$ Hz, 2H; 2-H), 3.66 (d, $^2J = 9.8$ Hz, 2H; 6-H), 3.94–4.05 (m, 8H; 2×4-H, 5-H, 6-H), 3.86 (d, $^2J = 10.0$ Hz, 2H; 6-H), 4.07 (br d, $^3J_{5,4} = 9.7$ Hz, 2H; 5-H), 4.12 (dd, $^3J_{3,2} = 9.6$ Hz, $^3J_{3,4} = 8.0$ Hz, 2H; 3-H), 4.23 (t, $^3J_{3,4} = {}^3J_{3,2} = 9.8$ Hz, 2H; 3-H), 4.28 (dd, $^3J_{5,4} = 10.5$ Hz, $^3J_{5,6} = 7.5$ Hz, 2H; 5-H), 4.36 (d, $^2J = 12.6$ Hz, 2H; CHPh), 4.38 (t, $^3J_{3,4} = {}^3J_{3,2} = 9.5$ Hz, 2H; 3-H), 4.42 (d, $^2J = 13.0$ Hz, 2H; CHPh), 4.43 (d, $^2J = 13.0$ Hz, 2H; CHPh), 4.52 (d, $^2J = 12.1$ Hz, 4H; 2×CHPh), 4.53–4.57 (m, 2H; 6′-H), 4.57 (d, $^2J = 12.5$ Hz, 4H; 2×CHPh), 4.74 (d, $^2J = 12.6$ Hz, 2H; CHPh), 4.81 (d, $^3J_{1,2} = 3.4$ Hz, 2H; 1-H), 4.85 (d, $^3J_{1,2} = 3.2$ Hz, 2H; 1-H), 4.91 (d, $^2J = 10.5$ Hz, 2H; CHPh), 4.98 (d, $^2J = 12.1$ Hz, 2H; CHPh), 5.02 (d, $^2J = 12.2$ Hz, 2H; CHPh), 5.12 (d, $^2J = 10.9$ Hz, 2H; CHPh), 5.33 (d, $^3J_{1,2} = 3.7$ Hz, 2H; 1-H), 5.39 (d, $^2J = 10.4$ Hz, 2H; CHPh), 5.62 (d, $^2J = 10.9$ Hz, 2H; CHPh), 7.11–7.48 (m, 70H; aromatic-H) ppm; ^{13}C NMR (100 MHz): $\delta = 26.8$ (O–CH_2–CH_2–), 58.8 (O*Me*), 68.8 (C-6), 70.3 (O–CH_2–CH_2–), 70.8 (C-6), 71.0, 71.3, 71.4 (3×C-5), 71.8 (O–CH_2Ph), 72.2 (C-6), 72.8, 72.9, 73.0, 74.2, 76.0, 76.5 (6×O–CH_2Ph), 77.5, 78.7, 79.8, (3×C-2), 80.6 (2×C-3), 81.0 (C-3), 81.2, 81.4, 82.2 (3×C-4), 98.3, 100.6, 100.7 (3×C-1), 126.1–128.3 (35×CH-aromatic), 137.9, 138.0, 138.3, 138.8, 139.3, 139.5, 139.7 (7×C-arom. quat.) ppm; MS (FAB): m/z: 2339.0 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{140}H_{156}O_{30}$ (2316.7): C 72.58, H 6.70; found C 72.41, H 6.90.

Preparation of peracetate 36: Pd/C (10 %) and Pd black were added to a solution of **35** (240 mg, 104 mmol) in an EtOAc/MeOH mixture (1:1, 1 mL). The reaction mixture was stirred under an H_2 atmosphere for 48 h, filtrated through a Celite pad, concentrated and dried under vacuum on P_2O_5. Anhydrous pyridine (1 mL) and DMAP (cat.) were added slowly, under argon at 0 °C, to a stirred suspension of the crude residue in Ac_2O (2 mL). The reaction mixture was stirred at room tem-

perature for 18 h. After concentration under vacuum, the residue was purified by silica gel chromatography (acetone/cy 1.5:1) to give **36** (78 mg, 46%) as a colourless oil.

Compound 36: $[\alpha]_D^{20} = +95$ ($CHCl_3$, $c = 0.6$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.52–1.65 (m, 2H; O−CH_2−CH_2−), 1.72–1.82 (m, 2H; O−CH_2−CH_2−), 1.96 (s, 6H; CH_3CO), 2.08 (s, 6H; CH_3CO), 2.09 (s, 6H; CH_3CO), 2.12 (s, 6H; CH_3CO), 2.13 (s, 12H; 2×CH_3CO), 2.16 (s, 6H; CH_3CO), 3.35–3.41 (m, 2H; O−CH_2−CH_2−), 3.43 (s, 6H; OMe), 3.52–3.56 (m, 4H; 6^A-H, 6^D-H, O−CH_2−CH_2−), 3.58 (dd, $^3J_{4,3}$ = 7.5 Hz, $^3J_{4,5}$ = 9.3 Hz, 2H; 4^A-H, 4^D-H), 3.65 (d, ^2J = 10.2 Hz, 2H; 6^C-H, 6^F-H), 3.73 (d, ^2J = 9.9 Hz, 2H; $6'^A$-H, $6'^D$-H), 3.89 (t, $^3J_{4,5} = {}^3J_{4,3}$ = 9.1 Hz, 2H; 4^B-H, 4^E-H), 3.94–3.99 (m, 4H; 4^C-H, 4^F-H, 5^C-H, 5^F-H), 4.01 (br d, ^2J = 9.9 Hz, 2H; $6'^C$-H, $6'^F$-H), 4.25 (br d, $^3J_{5,6}$ = 9.2 Hz, 2H; 5^B-H, 5^E-H), 4.33 (dd, $^3J_{5,6}$ = 7.4 Hz, $^3J_{5,4}$ = 9.3 Hz, 2H; 5^A-H, 5^D-H), 4.52 (d, ^2J = 12.0 Hz, 2H; 6^B-H, 6^E-H), 4.82 (dd, $^3J_{2,1}$ = 3.5 Hz, $^3J_{2,3}$ = 9.7 Hz, 2H; 2^A-H, 2^D-H), 4.82–4.89 (m, 4H; 2^B-H, 2^E-H, $6'^B$-H, $6'^E$-H), 4.93 (dd, $^3J_{2,1}$ = 3.7 Hz, $^3J_{2,3}$ = 10.2 Hz, 2H; 2^C-H, 2^F-H), 4.96 (d, $^3J_{1,2}$ = 3.5 Hz, 2H; 1^A-H, 1^D-H), 5.04 (d, $^3J_{1,2}$ = 3.2 Hz, 2H; 1^B-H, 1^E-H), 5.17 (d, $^3J_{1,2}$ = 3.7 Hz, 2H; 1^C-H, 1^F-H), 5.29 (dd, $^3J_{3,2}$ = 9.7 Hz, $^3J_{3,4}$ = 7.5 Hz, 2H; 3^A-H, 3^D-H), 5.52 (dd, $^3J_{3,2}$ = 10.2 Hz, $^3J_{3,4}$ = 8.8 Hz, 2H; 3^C-H, 3^F-H), 5.57 (dd, $^3J_{3,2}$ = 10.3 Hz, $^3J_{3,4}$ = 9.0 Hz, 2H; 3^B-H, 3^E-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 20.7, 20.8, 20.9 (4×CH_3CO), 20.95 (2×CH_3CO), 21.0 (CH_3CO), 26.5 (O−CH_2−CH_2−), 63.2 (C-6^C), 69.9 (C-3^C), 70.0 (C-2^B), 70.2 (C-5^C), 70.3 (C-6^B), 70.8 (C-5^A), 70.9 (C-3^B), 71.0 (O−CH_2−CH_2−), 71.2 (C-2^C), 71.3 (C-2^A), 71.4 (C-5^B), 71.6 (C-6^A), 72.9 (C-3^A), 77.4 (C-4^A), 78.1 (C-4^B), 78.9 (C-4^C), 97.5 (C-1^A), 97.6 (C-1^B), 97.9 (C-1^C), 169.1, 169.4, 169.5, 170.3, 170.5, 170.6, 170.9 (7×CH_3CO) ppm; MS (FAB): m/z: 1665.9 (100) $[M+Na]^+$.

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