DOI: 10.1002/ejoc.201402588

Synthesis of Cyclophellitol, Cyclophellitol Aziridine, and Their Tagged Derivatives

Kah-Yee Li,[a][‡] Jianbing Jiang,[a][‡] Martin D. Witte,[b] Wouter W. Kallemeijn,[c] Hans van den Elst,[a] Chung-Sing Wong,[a] Sharina D. Chander,[a] Sascha Hoogendoorn,[a] Thomas J. M. Beenakker,[a] Jeroen D. C. Codée,[a] Johannes M. F. G. Aerts,[c] Gijs A. van der Marel,[a] and Herman S. Overkleeft*[a]

Keywords: Cyclitols / Enzyme inhibitors / Aziridines / Azides / Epoxides / Fluorescent probes

Cyclitol epoxides and aziridines are potent and selective irreversible inhibitors of retaining glycosidases. We have previously reported on our studies on the use of activity-based probes derived from cyclophellitol and from its aziridine analogue for activity-based profiling of retaining β-glucosidases in vitro, in situ, and in some examples also in vivo. In this work we disclose full details of the synthesis, purification, and analysis of a comprehensive panel of cyclophellitol analogues, all featuring the β-glucose configuration and designed as tools for selective inhibition and/or imaging of human acid glucosylceramidase (epoxides) or as broad-spectrum probes for retaining β-glucosidases (aziridines).

Introduction

(+)-Cyclophellitol (**1**, Figure 1), isolated and characterized by Umezama and co-workers almost 25 years ago,[1] is a potent and selective mechanism-based inhibitor of retaining β-glucosidases of various biological origins. It is a close analogue of conduritol β-epoxide (CBE), a classical glucosidase inhibitor first described by Günther Legler.[2] (+)-Cyclophellitol (**1**) differs from CBE only in its C5-substituent (cyclophellitol numbering): whereas CBE features a hydroxy group, (+)-cyclophellitol (**1**) possesses a hydroxymethylene moiety, which adds considerably to both potency and specificity towards retaining β-exoglucosidases of this natural product. The absolute stereochemistry of the substituents at C1 to C5 in **1** matches that of a β-glucopyranoside moiety, which explains tight binding of the cyclitol to the active sites of retaining glucosidases. Upon binding, the epoxide is optimally positioned to undergo acid-catalyzed ring-opening by the catalytic diad consisting of two carboxylic acid residues, positioned some 6–7 Å apart. Treatment of retaining β-glucosidases that hydrolyze β-glucosidic linkages through a formal two-step double displacement mechanism, first proposed by Koshland,[3] with (+)-cyclophellitol (**1**) results in the formation of a stable adduct (see Figure 1) and thus in mechanism-based enzyme inactivation.[4]

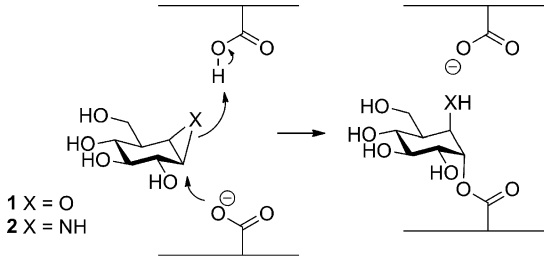


Figure 1. (+)-Cyclophellitol (**1**) and cyclophellitol aziridine (**2**) are mechanism-based inhibitors of retaining β-glucosidases.

Substitution of the epoxide moiety in **1** for an aziridine yields cyclophellitol aziridine (**2**),[5] which inhibits retaining β-glucosidases in a similar fashion.[6]

We have previously reported on our work on activity-based protein profiling of human retaining β-exoglucosidases.[7–9] In those studies we capitalized on the remarkable ability of compounds **1** and **2** to select and inactivate these glycosidases in complex biological samples, ranging from cell extracts to cells and animal models. Grafting a reporter group at C8 of cyclophellitol, through an azide group installed for this purpose at C8 [as in 8-deoxy-8-azido-cyclophellitol (**4**), see Figure 2], allowed us to detect and image human acid glucosylceramidase, or GBA, with high selectivity and efficiency in the context of healthy and

[a] Leiden Institute of Chemistry, Leiden University, Einsteinweg 55, 2300 RA Leiden, The Netherlands
E-mail: h.s.overkleeft@chem.leidenuniv.nl
http://biosyn.lic.leidenuniv.nl
[b] Stratingh Institute of Chemistry, University of Groningen, Nijenborgh 7, 9747 AG Groningen, The Netherlands
[c] Department of Medical Biochemistry, Academic Medical Centre, University of Amsterdam, Meibergdreef 15, 1105 AZ Amsterdam, The Netherlands
[‡] K.-Y. Li and J. Jiang contributed equally to this work
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402588.

(Gaucher) diseased tissue.[7,8] Placing a reporter group on the cyclophellitol aziridine nitrogen, through its acyl congener **5**, enabled us to achieve broad profiling of all human retaining β-glucosidase activities: in addition to GBA, nonlysosomal β-glucosidase (GBA2), cytosolic (broad-specificity) β-glucosidase (GBA3), and the β-glucosidase activity presented by the intestinal lactase-phlorizin hydrolase (LPH).[9]

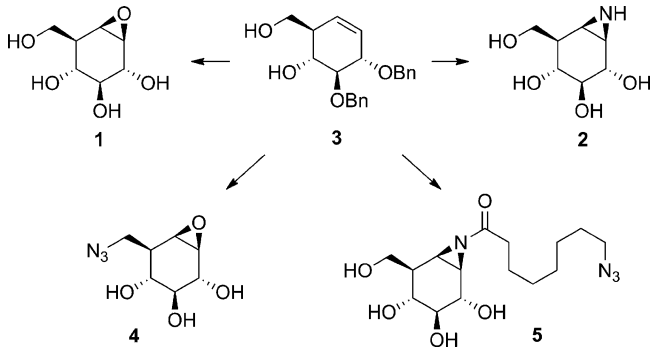


Figure 2. Key intermediate **3**, targets cyclophellitol (**1**) and cyclophellitol aziridine (**2**), and their azide derivatives **4** and **5**, respectively, that are the subjects of the synthetic studies presented here.

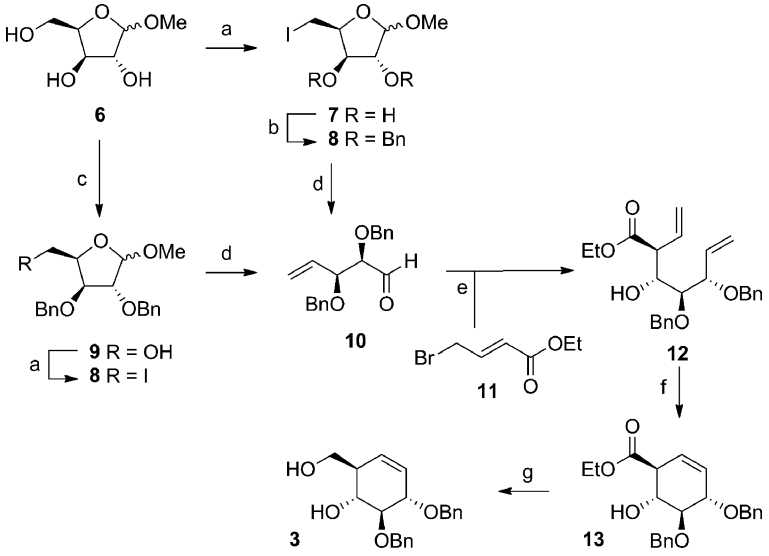
The synthesis of key intermediates **4** and **5** was based on cyclohexene derivative **3** (Figure 2, Scheme 1), previously described by Madsen and co-workers in their paper on the synthesis of (+)-cyclophellitol (**1**).[10] Here we report in detail on the synthesis of compounds **1**–**5**, on the difficulties we encountered, both in the synthesis and in the purification steps, and on the optimized routes that emerged from tackling these. We describe a palette of activity-based probes varying in the reporter moiety (biotin, fluorophore, combination of both) that we derived from azide derivatives **4** and **5**.

Results and Discussion

Access both to epoxides and to aziridines bearing a variety of reporter moieties required easy access to key intermediate **3**. For this purpose we revisited the work of Madsen and co-workers,[10] and this led (see Scheme 1) to a modified, and in places optimized, synthetic route. Consistently with the literature procedure,[11] selective triphenylphosphine-mediated substitution of the primary hydroxy group in methyl xylofuranoside (**6**, α/β mixture, prepared by kinetic Fischer glycosylation of D-xylose in methanolic HCl; see Exp. Sect.) with iodine provided iodides **7**. Ensuing benzylation of the two secondary alcohols in **7** proceeded with complete conversion. However, this transformation was accompanied by rearrangement of the benzylating agent – benzyl trichloroacetimidate (which we needed to add in excess) – to the corresponding benzyl trichloroacetamide, which we found difficult to separate from the desired product **8**. Subsequent reductive Vasella fragmentation of **8** contaminated with this acetamide proved suboptimal (39% yield) and we thus turned to a somewhat more lengthy, but ultimately higher-yielding route.

In this sequence, the primary hydroxy groups in methyl xylofuranosides **6** were temporarily protected as trityl ethers. Next, the secondary hydroxy groups were benzylated under basic conditions (BnBr, NaH, DMF), after which the primary hydroxy groups were liberated and substituted for iodine under the conditions described above. In this vein, iodoxylosides **8** were obtained in high purity in 47% yield over the four steps, with the Vasella fragmentation (zinc dust, sonication) proceeding in 96% yield.

The transformation of aldehyde **10** into key intermediate **3** proceeded by essentially the route published[10] by Madsen and co-workers. The key step in this sequence of events is the lanthanum-triflate-catalyzed Barbier ad-



Scheme 1. Reagents and conditions: (a) I_2, PPh_3, imidazole, THF, 70 °C, **7**:76%, **8**: 88%; (b) $BnOC(=NH)CCl_3$, TfOH, dioxane, 75%; (c) (*i*) TrCl, Et_3N, DMAP, DMF, (*ii*) NaH, BnBr, TBAI, DMF, 0 °C to room temp., (*iii*) *p*-TosOH, MeOH, CH_2Cl_2, 53% over four steps; (d) zinc dust, THF/H_2O (9:1, v/v), ultrasound, 40 °C, 96%; (e) indium powder, $La(OTf)_3$, H_2O, ultrasound, 80%; (f) second-generation Grubbs catalyst, CH_2Cl_2, 40 °C, 89%; (g) (*i*) DIBAL-H, THF, 0 °C to room temperature, (*ii*) $NaBH_4$, H_2O, EtOAc, 94%.

dition[12] of the indium Grignard reagent generated in situ from ethyl 4-bromocrotonate (**11**) to aldehyde **10**. When this reaction was performed on a small scale and the prescribed indium reagent (60 mesh, 99.999% pure) was used, the desired diene **12** was obtained in good yield and stereoselectivity (13:1 diastereomeric ratio with respect to the newly generated chiral center, **12** obtained after purification in 81% yield). The process could be performed on a large scale with equal efficiency (2 mmol vs. 40 mmol), but the cost of expensive 60 mesh indium powder became a significant factor. When the reaction vessel was placed in an ultrasound bath we found that the Barbier addition was complete overnight. Moreover, in this approach we found that the considerably less expensive indium powder containing 1% magnesium as anticaking agent performed equally well, and diene **12** could be prepared in 80% yield on a 44 mmol scale.

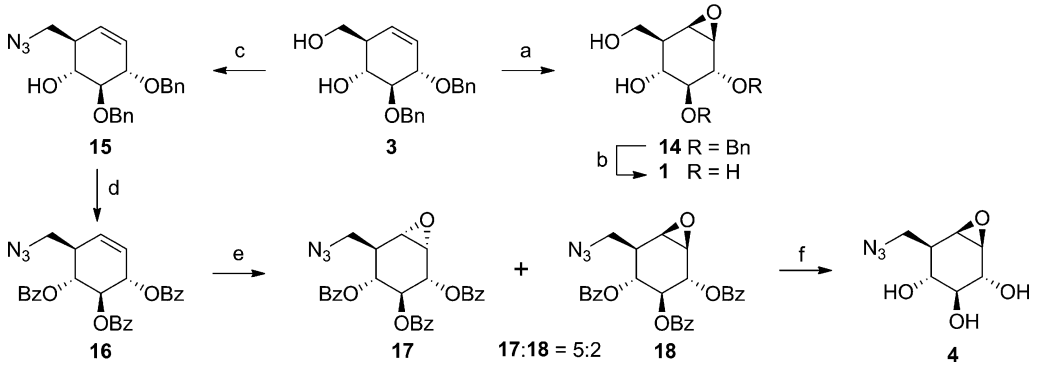
Diene **12** was converted into cyclohexene **13** by treatment with the second-generation Grubbs metathesis catalyst[13] in dichloromethane at 40 °C. Optimal results were obtained when 2–5 mol-% of the catalyst were added. Use of less catalyst or of the first-generation Grubbs catalyst[14] led to lower yields and the formation of an unidentified regioisomer. Reduction of the ethyl ester in **13** was accomplished in two steps by initial transformation into the aldehyde (DIBAL-H) and subsequent reduction to the primary alcohol ($NaBH_4$, H_2O, EtOAc). Overall, key intermediate **3** can be produced on a 30 mmol scale in 30% overall yield over five steps starting from **6**.

Scheme 2 depicts the transformation of cyclohexene **3** into (+)-cyclophellitol (**1**) and 8-deoxy-8-azidocyclophellitol (**4**).

Epoxidation of the homoallylic alcohol in **3** with *meta*-chloroperbenzoic acid went according to the literature procedure in a stereoselective fashion. Optimal results were obtained when the epoxidation was carried out in a buffered biphasic solvent system (1 M aqueous Na_2HPO_4, 1 M aqueous NaH_2PO_4, DCE) at 50 °C. Performing the reaction in a non-buffered solution, with or without an inorganic base ($NaHCO_3$, K_2HPO_4, or Na_2HPO_4) at ambient temperature led to a lower yield and a prolonged reaction time. Hydrogenolysis with Pearlman's catalyst and dihydrogen gas afforded (+)-cyclophellitol (**1**) in good yield and purity.[15]

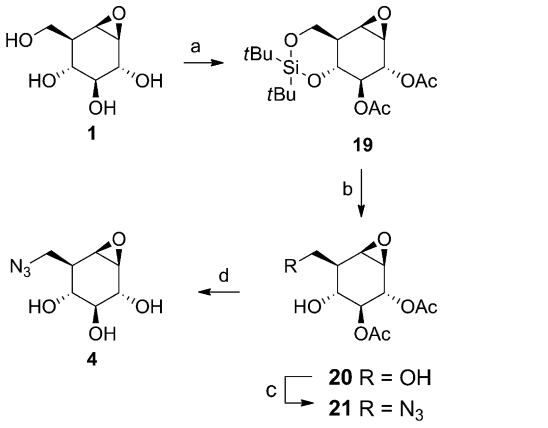
Alternatively, selective tosylation of the primary hydroxy group in **3**, followed by azide substitution, afforded azide derivative **15**. Because the azide functional group, installed for modification with reporter tags as demonstrated below, is not compatible with palladium-catalyzed hydrogenation reactions, we decided to change the protective group pattern at this stage. In a one-pot, two-step procedure, the benzyl ethers in **15** were removed by treatment with anhydrous BCl_3 in dichloromethane. Upon completion of the reaction the mixture was concentrated and co-evaporated from toluene to remove traces of the Lewis acid and the formed benzyl chloride. The crude mixture was then treated with benzoyl chloride and pyridine to afford fully protected cyclohexene derivative **16** in 70% yield over the two steps. Compound **16** lacks a (homo)allylic alcohol to guide the stereoselective epoxidation (as in the transformation of **3** to **14**), and *m*CPBA-mediated epoxidation of **16** proceeded with poor yield and resulted in the predominant formation of 1,6-*epi*-cyclophellitol derivative **17**. The desired protected 8-deoxy-8-azidocyclophellitol isomer **18** could be obtained in 20% yield by use of methyl(trifluoro)-dioxirane (formed in situ from trifluoroacetone and oxone) as the oxidizing agent, though also in this case the 1,6-*epi*-isomer **17** was formed as the major isomer (49%). Removal of the benzoyl esters finally proceeded uneventfully under Zemplén conditions to give target compound **4**. Consistently with the study by Ogawa and co-workers, no methoxide attack on the epoxide functionality was observed.[16]

Scheme 3 depicts an alternative and more efficient synthesis of 8-deoxy-8-azidocyclophellitol (**4**). By starting from (+)-cyclophellitol (**1**), which we could prepare in sufficient quantities by the procedures outlined in Schemes 1 and 2, orthogonally protected derivative **19** was readily prepared in two steps by initial installation of the 4,8-di-*tert*-butylsilylidene protective group and subsequent acetylation of the two remaining secondary alcohol groups. HF/pyridine-mediated removal of the silylidene protective group and selective triflation of the primary alcohol in **20** gave the corresponding triflate, and azide substitution followed by basic methanolysis of the acetate protective groups afforded 8-



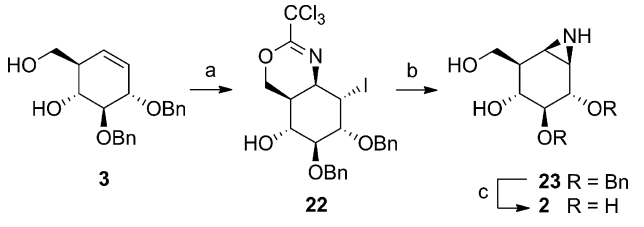
Scheme 2. Reagents and conditions: (a) *m*CPBA, Na_2HPO_4 (aq., 1 M), NaH_2PO_4 (aq., 1 M), dichloroethane, 50 °C, 55%; (b) H_2, $Pd(OH)_2$, MeOH, 88%; (c) (*i*) *p*-TosCl, Et_3N, CH_2Cl_2, (*ii*) NaN_3, DMF, 60 °C, 71%; (d) (*i*) BCl_3, CH_2Cl_2, –78 °C, (*ii*) BzCl, pyridine, 70%; (e) oxone, CF_3OCH_3, $NaHCO_3$, acetonitrile, Na_2EDTA (4 mM), 0 °C, **17**, 49%, **18**, 20%; (f) NaOMe, MeOH, 75%.

deoxy-8-azidocyclophellitol (**4**). In this fashion, target compound **4** was prepared in six steps and 49% overall yield from (+)-cyclophellitol (**1**) with complete stereo- and regiochemical control.



Scheme 3. Reagents and conditions: (a) (*i*) $(t\mathrm{Bu})_2\mathrm{SiOTf}_2$, pyridine, DMF, –40 °C to 0 °C, (*ii*) Ac_2O, pyridine, 60%; (b) HF/pyridine, THF, 0 °C, quant; (c) (*i*) Tf_2O, pyridine, CH_2Cl_2, –25 °C, (*ii*) NaN_3, 15-crown-5, THF, –25 °C to 0 °C, 90%; (d) NaOMe, MeOH, 90%.

Scheme 4 depicts our optimized route towards cyclophellitol aziridine (**2**). Introduction of the trichloroacetimidate functionality at the primary alcohol in **3** set the stage for a stereospecific iodocyclization. Thus, treatment of **3** with trichloroacetonitrile under basic conditions, followed by treatment of the intermediate trichloroacetimidate with iodine, afforded iodide **22** with complete stereocontrol. Acidic hydrolysis of the trichloroacetimidate group in **23** was followed by base-induced intramolecular substitution of the iodine to give partially protected cyclophellitol aziridine derivative **23**. Removal of the two benzyl ether groups in **23** under palladium-catalyzed hydrogenolysis conditions [H_2, $Pd(OH)_2$] resulted in partial reduction of the aziridine moiety. Lewis-acid-mediated debenzylation (BCl_3, CH_2Cl_2) proved abortive as well, and we therefore turned our attention to Birch reduction conditions. Treatment of **23** with lithium in liquid ammonia afforded target compound **2** in 70% yield. Removal of the lithium hydroxide salts formed during the Birch reduction was achieved by cation-exchange chromatography first with an Amberlite H^+ and next with an Amberlite NH_4^+ resin. Overall, cyclophellitol aziridine (**2**) was prepared from cyclohexene **3** in 42% overall yield over the five steps.



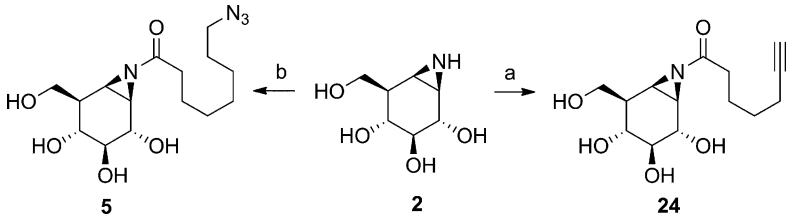
Scheme 4. Reagents and conditions: (a) (*i*) Cl_3CN, DBU, CH_2Cl_2, 0 °C, (*ii*) I_2, $NaHCO_3$, H_2O; (b) (*i*) 37% HCl, dioxane, 60 °C, (*ii*) $NaHCO_3$, MeOH, 60% over four steps; (c) Li, NH_3, THF, –60 °C, 70%.

The procedure presented in Scheme 4 allows for the preparation of sufficient quantities of cyclophellitol aziridine (**2**) for further modification. Acylation of the aziridine nitrogen with a functionalized (azide or alkyne) carboxylic acid, however, proved much more complicated than we had initially foreseen. Condensation of **2** with hept-6-ynoic acid under the agency of *N*,*N*′-diisopropylcarbodiimide (DIC) proved abortive in that no acylated product could be isolated. Treatment of **2** with the acyl chloride of hept-6-ynoic acid did result in *N*-acylation, but the *N*-acylaziridine proved highly susceptible to nucleophilic attack by the chloride ion generated in situ, to yield a mixture of *trans*-chlorocyclitolamine. Attempts to acylate with the *N*-hydroxysuccinimide ester of hept-6-ynoic acid proved abortive and returned the starting material. From these initial studies we identified two complications. To start with, the aziridine nitrogen is less nucleophilic than "normal" aliphatic amines, and, once acylated, the aziridine carbon atoms are rather susceptible to nucleophilic attack.

In view of these factors we turned our attention to the use of 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ), an activating agent that upon reaction yields a non-nucleophilic quinoline derivative as byproduct.[17] In a first experiment, treatment of hept-6-ynoic acid with EEDQ followed by addition of substoichiometric amounts of **2** afforded a mixture of *N*- and *O*-acylated products, with the *N*-acyl aziridine moiety intact and acylation of the primary hydroxy in **2** as the predominant side reaction. This side reaction could be prevented by executing the reaction at 0 °C and quenching by addition of methanol prior to workup.

By the same procedure as described for the synthesis of alkyne **24**, azide-modified aziridine **5** was prepared with equal efficiency (Scheme 5). Both compounds **5** and **24** could be obtained in high purity after preparative HPLC. In order to avoid opening of the acyl aziridine ring at this stage we searched for optimal conditions. It turned out that the standard conditions we normally use for reversed-phase HPLC purification (water/acetonitrile gradient with trifluoroacetic acid or formic acid) are detrimental to the acyl aziridine, which opens either during the HPLC run or during ensuing lyophilization. The acyl aziridine systems in **5** and **24** remained intact when either a neutral water/acetonitrile gradient or a gradient including 25–50 mM aqueous NH_4HCO_3 was used. On concentration of the NH_4HCO_3-containing fractions the pH was kept between 7–8 to prevent liberation of the acyl linker (see the Exp. Sect. for details). At all times after *N*-acylation we found that the major decomposition routes involved chloride attack on the acyl aziridine. These side products arose on HPLC purification even though no chloride salts had been present during the acylation steps. We found that this side reaction can be suppressed when workup after the Birch reduction steps (Scheme 4) was performed with chloride-free milliQ water. In the end, compounds **5** and **24** were obtained in sufficient quantities to allow elaboration to tagged activity-based probes, as demonstrated below.

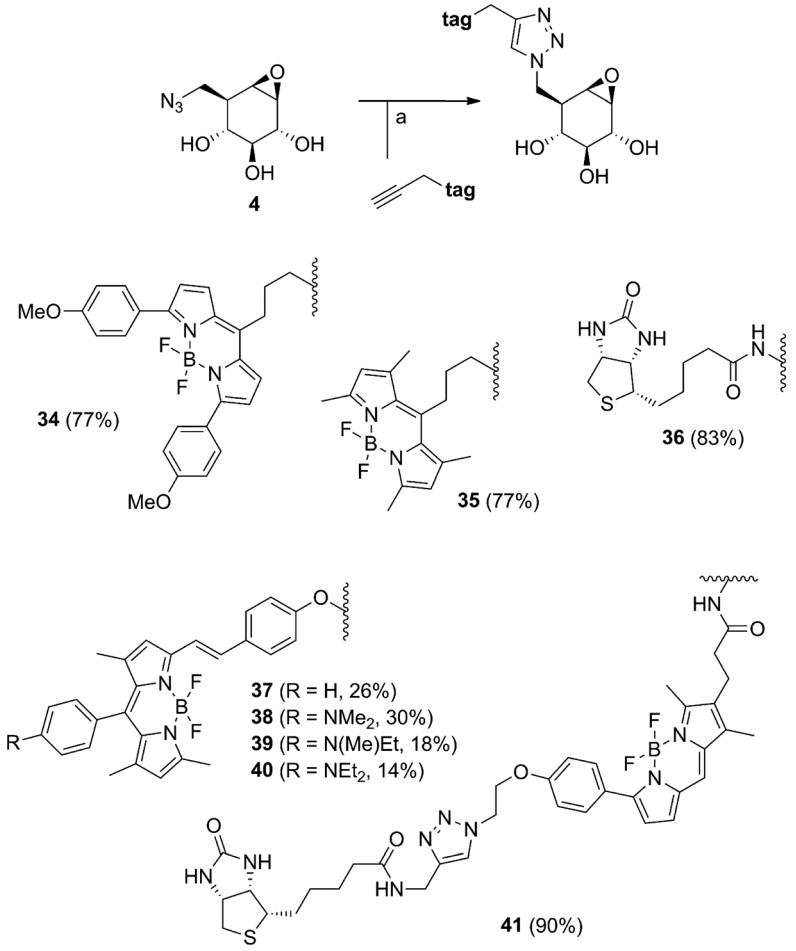
With the azide- and alkyne-modified cyclophellitol and cyclophellitol aziridine derivatives **4**, **5**, and **24** available in



Scheme 5. Reagents and conditions: (a) (*i*) hept-6-ynoic acid, 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ), DMF, 0 °C, (*ii*) HPLC, gradient MeCN/H_2O, 20%; (b) (*i*) 8-azidooctanoic acid, EEDQ, DMF, 0 °C, (*ii*) HPLC gradient MECN/H_2O, 19%.

sufficient quantities, a number of fluorescent and/or biotinylated tags were installed. In each case the conjugation proceeded through copper(I)-catalyzed azide–alkyne Huisgen [3+2] cycloaddition with the appropriate BODIPY/biotin alkyne or azide.[18] The click ligations proceeded uneventfully, with their purification presenting the most important obstacle, especially when dealing with the acylaziridines, which are labile under both acidic and basic conditions as noted before.

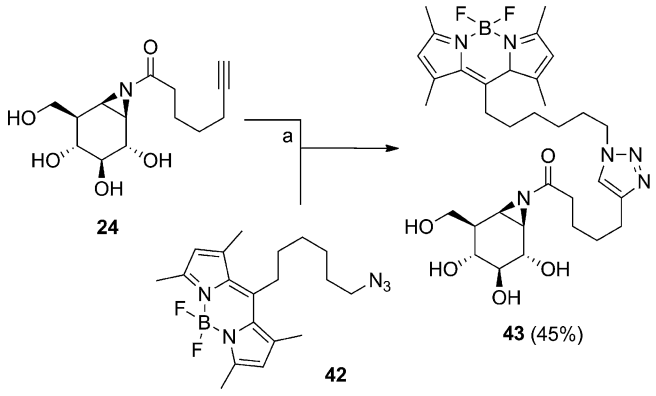
Scheme 6 shows the panel of cyclophellitol-derived activity-based probes that we prepared through copper(I)-catalyzed azide–alkyne click reactions between a number of alkynes **25**–**33** (see Exp. Sect. for their exact structures[19]) and the primary azide group in cyclophellitol derivative **4**. In this fashion, by using symmetrical BODIPY-alkynes that we had reported previously,[19a] we prepared the two red-fluorescent and green-fluorescent cyclophellitol derivatives **34** and **35** that we had used previously for the in situ monitoring of GBA in the context of Gaucher disease. In the same fashion, biotin-cyclophellitol **36** was prepared. To demonstrate the viability of the strategy further we prepared the cyclophellitol-derived activity-based retaining glucosidase probes **37**–**40**, bearing pH-responsive BODIPY dyes,[19c] varying from non-responsive (or permanently fluo-



Scheme 6. Reagents and conditions: (a) alkyne tag **25**–**32** (see Exp. Sect.), $CuSO_4$, sodium ascorbate, toluene/*t*BuOH/H_2O, 80 °C.

rescent, compound **37**) to responsive at various pH values (4.5 to 6, **38**–**40**). As a final example, doubly tagged[19b] cyclophellitol **41**, equipped with both a BODIPY dye for visualization and a biotin for pull-down of potential reactive glucosidases, was prepared.

The synthesis of BODIPY-green-cyclophellitol aziridine **43** starting from alkyne **24** and azide **42** is depicted in Scheme 7 and follows essentially the same conditions as outlined in Scheme 6. As before, HPLC purification of acylaziridine **43** was not straightforward, but use of the optimized conditions based on a neutral gradient readily afforded the target compound after lyophilization.

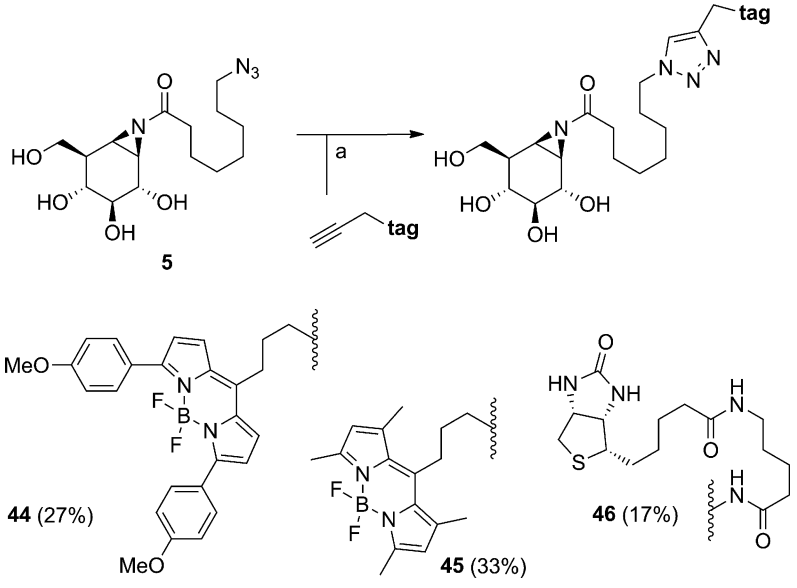


Scheme 7. Reagents and conditions: (a) (*i*) BODIPY-N_3 **42**, $CuSO_4$, sodium ascorbate, DMF, 45%, (*ii*) HPLC (gradient MeCN/H_2O).

By starting from **24** and employing copper(I)-catalyzed azide–alkyne cycloaddition, a diverse series of probes derived from cyclophellitol aziridine can, on paper, be synthesized. However, because we have a number of fluorescent and/or biotinylated alkynes **25**–**26** and **33**[18] (see Exp. Sect.) available, we switched to the use of azide-modified cyclophellitol aziridine **5** (Scheme 8). By the synthesis and purification strategy outlined above for the cyclophellitol derivatives **33**–**35**, the corresponding cyclophellitol aziridine derivatives **44** and **45**, bearing the same BODIPY-green and BODIPY-red tag, respectively, and biotin-Ahx-cyclophellitol aziridine derivative **46** were obtained.

Conclusions

In conclusion, we describe in this paper the full details of the synthesis of a broad panel of inhibitors and activity-based probes for retaining β-glucosidases, based on the known inhibitors (+)-cyclophellitol (**1**) and cyclophellitol aziridine (**2**). The synthetic strategy followed for both compound classes is based on advanced intermediate **3** previously reported by Madsen and co-workers,[10] the synthesis of which we have optimized by following the general route as published and carefully optimizing the individual steps, as well as the order in which some of the transformations are executed. We believe that the collective versatility of these routes of synthesis should allow adaptation directed towards a number of cyclophellitol-type mechanism-based glycosidase inhibitors and activity-based probes. Results from this work provide guidelines for the synthesis of derivatives of 1,6-epicyclophellitol and of 1,6-epicyclophellitol aziridine for the construction of retaining α-glucosidase inhibitors and activity-based probes bearing reporter tags similar to those demonstrated here. Adaptation of the starting materials might lead to cyclophellitol derivatives that emulate other carbohydrates in absolute stereochemistry and that are able, by virtue of this, to target retaining glycosidases that employ a Koshland-type double displacement mechanism and have evolved to recognize other substrate glycosides.

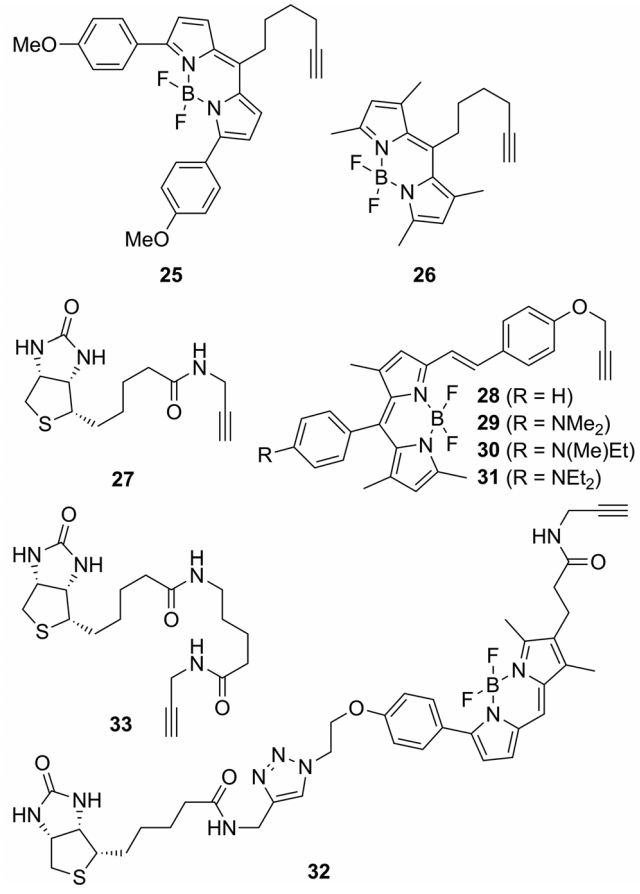


Scheme 8. Reagents and conditions: (a) (*i*) tag alkyne **25**–**26** or **33** (see Exp. Sect.), $CuSO_4$, sodium ascorbate, DMF, (*ii*) HPLC (gradient MeCN/H_2O).

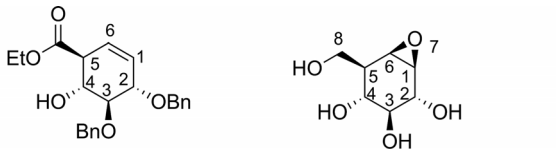
Experimental Section

General Methods and Materials: All reagents and solvents were of commercial grade and used as received unless stated otherwise. THF and dichloromethane were stored over flamed-dried 3 Å molecular sieves. All reactions were performed under inert atmosphere unless stated otherwise. Solvents used for flash chromatography were of pro analysi quality. Reactions were monitored by TLC analysis on aluminum sheets pre-coated with silica gel 60, with detection by UV absorption (254 nm) and by spraying with a solution of $(NH_4)_6Mo_7O_{24}\cdot H_2O$ (25 g L^{-1}) and $(NH_4)_4Ce(SO_4)_4\cdot H_2O$ (10 g L^{-1}) in sulfuric acid (10%), followed by charring at ca. 150 °C, or by spraying with sulfuric acid in ethanol (20%), followed by charring at ca. 150 °C. Column chromatography was performed with Screening Device silica gel in the indicated solvents. High-resolution mass spectra were recorded with a LTQ Orbitrap instrument (Thermo Finnigan). HPLC-MS purifications were performed with an Agilent Technologies 1200 series automated HPLC system and a Quadropole MS 6130 fitted with a semi-preparative Gemini C18 column (Phenomenex, 250 × 10, 5μ, particle size). ^{1}H NMR, ^{13}C NMR, COSY, and HSQC spectra were recorded with a Bruker DMX 400 (400/100 MHz), a Bruker AV 400 (400/100 MHz), and/or a Bruker AV 600 (600/150 MHz) spectrometer in the given solvent. Chemical shifts are reported as δ values in ppm relative to the chloroform residual solvent peak or tetramethylsilane (TMS) as internal standard or the deuterated solvent signal for CD_3OD. Coupling constants are given in Hz. All given ^{13}C spectra are proton-decoupled.

Alkyne Tags 25–33 Used in this Study:



Note: NMR signal assignments and stereochemical descriptors were made according to the atom numbering shown in the formulae below.



General HPLC Purification of Acylated Cyclophellitol Aziridines: Purification of acylated cyclophellitol aziridines **5**, **24**, **42**–**45** by HPLC can be performed either under neutral conditions (water/acetonitrile) as described below or under basic conditions (25–50 mM NH_4HCO_3/acetonitrile). When purifying under basic conditions, the pH during the HPLC run, collection, and lyophilization from *t*BuOH/water/acetonitrile is carefully kept between pH 7–8.

Methyl 2,3-Di-*O*-benzyl-α-D-xylofuranoside (9): D-Xylose (15.0 g, 100 mmol) was added to a solution of acetyl chloride (3 mL, 42 mmol) in MeOH (300 mL). The reaction mixture was stirred for 5 h, after which it was neutralized with $NaHCO_3$. The solution was filtered and concentrated under reduced pressure. The resulting product was taken up in a solution of MeOH/EtOAc (1:4, v/v, 500 mL), filtered, and concentrated again in vacuo in order to remove the remaining salts. The crude methyl xylofuranoside was used without further purification. The crude product was dissolved in DMF (500 mL), and trityl chloride (56 g, 200 mmol), Et_3N (22.3 mL, 160 mmol), and DMAP (610 mg, 0.05 mmol) were added. The reaction mixture was stirred for 18 h and concentrated under reduced pressure. The resulting oil was subsequently redissolved in Et_2O, washed with water, dried with $MgSO_4$, filtered, and concentrated. The resulting oil was again taken up in DMF (500 mL), and BnBr (29.7 mL, 250 mmol) and a catalytic amount of TBAI (1.85 g, 5 mmol) were added, after which the solution was cooled to 0 °C. Sodium hydride (60% dispersion in mineral oil, 17.6 g, 440 mmol) was added, and the reaction mixture was stirred at ambient temperature. After 18 h, when TLC showed full consumption of the starting material, the reaction mixture was cooled to 0 °C and quenched by the addition of MeOH. The solution was further diluted with water and subsequently washed with Et_2O, dried with $MgSO_4$, filtered, and concentrated in vacuo. The resulting product was redissolved in CH_2Cl_2 (250 mL) and MeOH (250 mL), and *p*-toluenesulfonic acid was added until pH 2 was reached. The reaction mixture was stirred at ambient temperature for 18 h, after which it was quenched with saturated $NaHCO_3$. The layers were separated, and the water layer was extracted with EtOAc. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica column chromatography (pentane/EtOAc 70:30→60:40) gave the partly deprotected methyl xylofuranoside (18.1 g, 52.5 mmol, 53%) as an anomeric mixture (α/β ratio 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.21 (m, 20 H, H_{Ar}Bn), 4.89 (d, J = 1.6 Hz, 1 H, H-1α), 4.79 (d, J = 4.4 Hz, H-1β), 4.70 (d, J = 12.0 Hz, 1 H, CH_2Bn), 4.64–4.45 (m, 7 H, CH_2Bn), 4.24 (t, J = 6.8 Hz, 1 H, H-2β), 4.32–4.28 (m, 1 H, H-2α), 4.21–4.19 (m, 1 H, H-4α), 4.15 (dd, J = 3.6, 6.8 Hz, 1 H, H-4β), 4.09–4.07 (m, 1 H, H-3α), 4.04 (dd, J = 4.4, 6.4 Hz, 1 H, H-3β), 3.79–3.73 (m, 1 H, H-5α-β), 3.73 (s, 3 H, OMe-α), 3.36 (s, 3 H, OMe-β) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.4, 137.3, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 107.7, 99.9, 86.8, 84.2, 82.4, 81.9, 80.4, 76.1, 72.4, 72.2, 72.1, 71.9, 62.0, 61.9, 55.4, 54.8 ppm. HRMS calcd. for $[C_{20}H_{24}O_5 + Na]$ $[M + H]^+$ 367.39154; found 367.39162.

Methyl 2,3-Di-*O*-benzyl-5-deoxy-5-iodo-α-D-xylofuranoside (8): Alcohol **9** (18.1 g, 52.5 mmol) was coevaporated with toluene, after which it was dissolved in anhydrous THF (200 mL). Triphenylphosphine (20.7 g, 78.8 mmol) and imidazole (7.15 g, 105 mmol) were added to the solution, which was heated to reflux. A solution of iodine (20.8 g, 78.8 mmol) in anhydrous THF (60 mL) was added, and the reaction mixture was heated at reflux until TLC analysis revealed full conversion of the starting material (3.5 h). The reaction mixture was successively concentrated under reduced pressure, redissolved in EtOAc, and washed with sodium thiosulfate (10%). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Purification by silica column chromatography (pentane/EtOAc 98:2 →80:20) afforded iodine **8** (α/β ratio 4:1, 21.0 g, 46.2 mmol, 88%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 20 H, H_{Ar}Bn), 4.91 (s, 1 H, H-1α), 4.82 (d, J = 3.6 Hz, H-1β), 4.61–4.36 (m, 8 H, H-2α-β, H-4α-β, 2 × CH_2Bn α-β), 4.00–3.96 (m, 2 H, H-3α-β), 3.40–3.30 (m, 7 H, OMe-α-β, H-5α), 3.19–3.15 (m, 1 H, H-5β) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.6, 137.4, 137.3, 137.2, 128.4, 128.3, 128.3, 128.0, 127.8, 127.8, 127.6, 127.6, 108.4, 100.6, 86.5, 83.6, 81.9, 817, 81.5, 77.5, 72.5, 72.4, 72.3, 71.9, 55.8, 55.3, 4.72, 3.11 ppm. HRMS: calcd. for [$C_{20}H_{23}IO_4$ +Na] [M + Na]$^+$ 477.05332; found 477.05332.

(2*R*,3*S*)-2,3-Bis(benzyloxy)pent-4-enal (10): Zinc dust was activated and dried immediately before use: it (54.4 g, 832 mmol) was added slowly to a vigorously stirred HCl solution (3 M, 480 mL). The mixture was stirred for 20 min at ambient temperature, filtered, and subsequently rinsed with water and Et_2O, after which it was dried under high vacuum at elevated temperature. A solution of iodide **8** (21.0 g, 46.2 mmol) in THF/H_2O (9:1, v/v, 520 mL) was sonicated under an argon stream at 40 °C, after which the activated zinc dust (45.3 g, 693 mmol) was added. The reaction mixture was flushed again with argon and sonicated for 2.5 h at 40 °C, followed by filtration through a pad of Celite and removal of THF in vacuo. The resulting mixture was diluted with Et_2O, washed with H_2O, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica column chromatography (pentane/Et_2O 98:2→90:10) afforded the relatively unstable aldehyde **10*** (13.1 g, 44.4 mmol, 96%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.64 (s, 1 H, CHO), 7.30–7.17 (m, 10 H, H_{Ar}Bn), 5.96–5.87 (m, 1 H, CH=), 5.34–5.28 (m, 2 H, CH_2=), 4.70 (d, J = 12.0 Hz, 1 H, CH_2Bn), 4.58 (t, J = 12.4 Hz, 2 H, CH_2Bn), 4.32 (d, J = 12.0 Hz, 1 H, CH_2Bn), 4.14 (dd, J = 4.0, 7.2 Hz, 1 H, C*H*CH=), 3.80 (d, J = 3.2 Hz, 1 H, C*H*CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.4, 137.3, 136.9, 133.7, 128.2, 128.1, 127.9, 127.8, 127.4, 127.5, 119.5, 84.9, 79.6, 73.4, 70.6 ppm. HRMS: calcd. for [$C_{19}H_{20}O_3$] [M + H]$^+$ 297.14852; found 297.14922.

* *Note*: *Aldehyde **10** is stable at –24 °C for up to several months, whereas it decomposes at room temperature after 1 day.*

Alkene 12: Ethyl 4-bromocrotonate (**11**, 26 mL, 142 mmol), La(OTf)$_3$ (54.7 g, 93.2 mmol), and indium powder (11.7 g, 102 mmol) were added to a solution of aldehyde **10** (13.1 g, 44.4 mmol) in H_2O (210 mL). After sonication at 40 °C for 18 h, the reaction mixture was filtered through a plug of celite, extracted with Et_2O, dried with $MgSO_4$, and concentrated under reduced pressure. Purification by silica column chromatography (pentane/EtOAc 94:6→88:12) yielded **12** (14.6 g, 35.5 mmol, 80%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.25 (m, 10 H, H_{Ar}Bn), 5.87–5.78 (m, 1 H, 1-H), 5.71 (dt, J = 9.6, 17.2 Hz, 1 H, 6-H), 5.42 (d, J = 12.0 Hz, 1 H, CH_2=CHCHOBn), 5.38 (d, J = 4.8 Hz, 1 H, CH_2=CHCHOBn), 5.16 (d, J = 10.4 Hz, 1 H, CH_2=CHCHC=O), 5.06 (d, J = 17.2 Hz, 1 H, CH_2=CHCHC=O), 5.01 (d, J = 11.2 Hz, 1 H, CH_2Bn), 4.60 (dd, J = 12.2, 14.4 Hz, 2 H, CH_2Bn), 4.40 (d, J = 11.6 Hz, 1 H, CH_2Bn), 4.19 (t, J = 7.6 Hz, 1 H, 2-H), 4.10 (q, J = 7.0 Hz, 2 H, CH_2 ester), 3.98 (d, J = 9.2 Hz, 1 H, 4-H), 3.54 (d, J = 7.6 Hz, 1 H, 3-H), 3.28 (d, J = 9.6 Hz, 1 H, 5-H), 1.22 (t, J = 7.2 Hz, 3 H, CH_3 ester) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 138.4, 138.3, 134.8, 132.8, 128.3, 128.3, 127.9, 127.8, 127.7, 127.5, 119.9, 119.9, 82.8, 79.3, 74.5, 72.0, 70.7, 60.8, 55.1, 14.0 ppm. HRMS: calcd. for [$C_{25}H_{31}O_5$] [M + H]$^+$ 411.21660; found 411.21653.

Ester 13: The second-generation Grubbs catalyst (753 mg, 0.89 mmol, 2.5 mol-%) was added to a solution of **12** (14.6 g, 35.5 mmol) in dichloromethane (180 mL). The reaction mixture was heated at reflux in the dark for 18 h under a continuous flow of argon at 40 °C, after which an additional quantity of the second-generation Grubbs catalyst (603 mg, 0.71 mmol, 2.0 mol-%) was added. The reaction mixture was again heated at reflux in the dark under a continuous flow of argon until TLC showed complete consumption of the starting material (6 h). The reaction mixture was then concentrated and purified by silica column chromatography (pentane/EtOAc 92:8→84:16) to afford **13** (12.2 g, 32.0 mmol, 89%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.23 (m, 10 H, H_{Ar}Bn), 5.79 (dt, J = 2.4, 10.0 Hz, 1 H, 6-H), 5.66 (dt, J = 2.0, 10.4 Hz, 1 H, 1-H), 4.94 (d, J = 11.2 Hz, 1 H, CH_2Bn), 4.79 (d, J = 11.2 Hz, 1 H, CH_2 Bn), 4.66 (dd, J = 11.6, 15.6 Hz, 2 H, CH_2 Bn), 4.23–4.11 (m, 4 H, 3-H, 4-H, CH_2 ester), 3.64 (dd, J = 7.6, 9.6 Hz, 1 H, 2-H), 3.26–3.23 (m, 1 H, 5-H), 3.04 (br., 1 H, OH), 1.26 (t, J = 8.4 Hz, CH_3 ester) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 138.3, 137.9, 128.4, 128.1, 127.8, 127.8, 127.7, 127.7, 123.9, 82.4, 79.1, 74.7, 71.8, 70.3, 61.2, 50.0, 14.0 ppm. HRMS: calcd. for [$C_{23}H_{27}O_5$] [M + H]$^+$ 383.18530; found 381.18548.

Cyclohexene 3: Ester **13** (12.2 g, 32.0 mmol) was coevaporated with toluene (3 ×), after which it was dissolved in THF (320 mL). DIBAL-H (1 M in hexane, 192 mL, 192 mmol) was added to the solution at 0 °C. The reaction mixture was stirred for 30 min at 0 °C, followed by stirring for 2 h at ambient temperature. It was then quenched with EtOAc (65 mL) at 0 °C, followed by addition of H_2O (75 mL) and sodium borohydride (7.87 g, 208 mmol). The reaction mixture was stirred for 18 h at ambient temperature, after which it was concentrated in vacuo. The crude product was poured into EtOAc and washed with HCl solution (1 M). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Purification by silica column chromatography (pentane/EtOAc 60:40→40:60) yielded diol **3** (10.2 g, 30 mmol, 94%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.20 (m, 10 H, H_{Ar}Bn), 5.73 (dt, J = 2.4, 10.0 Hz, 1 H, 6-H), 5.48 (dt, J = 2.0, 10.0 Hz, 1 H, 1-H), 4.98 (d, J = 11.2 Hz, 1 H, CH_2Bn), 4.73 (d, J = 11.2 Hz, 1 H, CH_2Bn), 4.64 (d, J = 9.2 Hz, 1 H, CH_2Bn), 4.60 (d, J = 11.6 Hz, 1 H, CH_2Bn), 4.17–4.15 (m, 1 H, 2-H), 3.71–3.60 (m, 4 H, 3-H, 4-H, 8-H), 3.28 (br., 1 H, OH), 2.99 (br., 1 H, OH), 2.44–2.43 (m, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3, 137.9, 128.4, 128.3, 127.8, 127.7, 127.7, 127.6, 127.5, 127.2, 83.3, 80.1, 74.7, 72.1, 71.3, 64.6, 45.1 ppm. HRMS: calcd. for [$C_{21}H_{25}IO_4$] [M + H]$^+$ 341.17474; found 341.17501.

2,3-Di-*O*-benzylcyclophellitol (14): A mixture of alkene **3** (3.40 g, 10 mmol) and *m*CPBA (4.44 g, 18 mmol) in DCE (166 mL), NaH_2PO_4 (1 M, 100 mL), and NaH_2PO_4 (1 M, 100 mL) was vigorously stirred at 50 °C for 18 h. The layers were separated, and the water layer was extracted with EtOAc. The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (pentane/Et_2O 12:88→8:92) to provide β-epoxide **14** (1.94 g, 5.45 mmol, 55%) and its epidiastereoisomer (178 mg, 0.5 mmol, 5%) as a white solid.

β-Epoxide 14: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.15 (m, 10 H, H_{Ar}Bn), 4.92 (d, J = 11.6 Hz, 2 H, CH_2Bn), 4.79 (d, J =

11.2 Hz, 2 H, CH_2Bn), 4.65 (d, J = 11.2 Hz, 2 H, CH_2Bn), 3.98 (dd, J = 6.4, 10.8 Hz, 1 H, 8-H), 3.85 (dd, J = 5.6, 10.8 Hz, 1 H, 8-H), 3.79 (d, J = 7.6 Hz, 1 H, 2-H), 3.46 (t, J = 9.2 Hz, 1 H, 4-H), 3.37 (dd, J = 8.0, 10.0 Hz, 1 H, 3-H), 3.26 (d, J = 2.8 Hz, 1 H, 6-H), 3.14 (d, J = 4.0 Hz, 1 H, 1-H), 3.01 (br. s, 1 H, 1 × OH), 2.91 (br. s, 1 H, 1 × OH), 2.15–2.06 (m, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.1 137.3, 128.5, 128.4, 128.0, 127.9, 127.8, 127.6, 83.4, 70.2, 74.8, 72.5, 68.3, 63.6, 54.8, 52.9, 43.3 ppm. HRMS: calcd. for $[C_{21}H_{25}O_5]$ $[M + H]^+$ 357.16965; found 357.16987.

α-Epoxide: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.17 (m, $H_{Ar}Bn$), 4.97 (d, J = 11.2 Hz, CH_2Bn), 4.79 (dd, J = 12.0, 21.2 Hz, 2 H, CH_2Bn), 4.64 (d, J = 11.2 Hz, 1 H, CH_2Bn), 3.86–3.77 (m, 3 H, 3-H, 8-H), 3.56 (t, J = 10.0 Hz, 1 H, 3-H), 3.41 (t, J = 10.0 Hz, 1 H, 4-H), 3.34–3.33 (m, 1 H, 6-H), 3.10 (d, J = 3.6 Hz, 1 H, 1-H), 2.88 (s, 1 H, OH), 2.54 (br., 1 H, OH), 2.15–2.10 (m, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 137.9, 128.5, 128.4, 128.0, 127.9, 127.9, 125.5, 80.8, 79.4, 75.4, 72.5, 70.2, 62.5, 54.4, 54.0, 43.5 ppm. HRMS: calcd. for $[C_{21}H_{25}O_5]$ $[M + H]^+$ 357.16965; found 357.16989.

(+)-Cyclophellitol (1): A catalytic amount of $Pd(OH)_2$ was added to a solution of **14** (71.3 mg, 0.2 mmol) in MeOH (1 mL). The solution was stirred under H_2 for 18 h, after which it was filtered through a small pad of celite. Purification by silica column chromatography (CH_2Cl_2/MeOH 84:16→80:20) afforded (+)-cyclophellitol (**1**, 31 mg, 0.18 mmol, 88%) as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 4.00 (dd, J = 4.4, 10.8 Hz, 1 H, 8-H), 3.68 (dd, J = 9.2, 10.4 Hz, 1 H, 8-H), 3.64 (d, J = 8.0 Hz, 1 H, 2-H), 3.42 (d, J = 2.4 Hz, 1 H, 6-H), 3.21 (dd, J = 8.4, 10.0 Hz, 1 H, 3-H), 3.13–3.08 (m, 2 H, 1-H, 4-H), 1.97 (ddt, J = 1.6, 3.6, 9.4 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 78.5, 72.8, 68.8, 62.5, 57.4, 56.0, 45.9 ppm. HRMS: calcd. for $[C_7H_{13}O_5]$ $[M + H]^+$ 177.07575; found 177.07576.

Azido-cyclohexene 15: *p*-Toluenesulfonyl chloride (1.04 g, 5.48 mmol) and triethylamine (0.90 mL, 6.57 mmol) were added to a solution of **3** (1.24 g, 3.65 mmol) in dichloromethane (26 mL). The solution was stirred at 40 °C for 5 h, after which it was poured into HCl solution (1 M). The mixture was extracted with Et_2O, and the organic layer was dried with $MgSO_4$, after which it was concentrated in vacuo to yield the crude tosylate, which was immediately subjected to azidation. Sodium azide (2.40 g, 36.7 mmol) was added to a solution of the tosylated intermediate (1.75 g, 3.65 mmol) in DMF (35 mL). The solution was stirred for 24 h at 60 °C, after which it was concentrated in vacuo. The crude product was diluted with Et_2O and successively washed with HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. Purification by silica column chromatography (petroleum ether/EtOAc 92:8→84:16) afforded **15** (900 mg, 2.46 mmol, 71%) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.26 (m, 10 H, $H_{Ar}Bn$), 5.79 (dt, J = 2.4, 10.4 Hz, 1 H, 6-H), 5.58 (dt, J = 1.6, 10.4 Hz, 1 H, 1-H), 5.02 (d, J = 11.2 Hz, 1 H, CH_2Bn), 4.72–4.59 (m, 3 H, CH_2 Bn), 4.18–4.16 (m, 1 H, 2-H), 3.61–3.53 (m, 3 H, 3-H, 4-H, 8-H), 3.42 (dd, J = 6.0, 12.0 Hz, 1 H, 8-H), 2.83 (s, 1 H, OH), 2.48 (br., 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3, 137.9, 128.9, 128.4, 128.3, 127.8, 127.7, 127.7, 127.5, 127.4, 83.3, 80.0, 74.7, 71.3, 69.9, 52.5, 43.6 ppm. HRMS: calcd. for $[C_{21}H_{25}NO_3]$ $[M + 3\,H^+ - N_2]$ 340.19072; found 340.19080.

Azido-cyclohexene 16: Boron trichloride (21 mL, 21.1 mmol) was added at –78 °C to a solution of **15** (777 mg, 2.11 mmol) in anhydrous dichloromethane (10 mL). The reaction mixture was kept between –78 °C and –60 °C for 6 h, after which it was quenched with MeOH at –78 °C. The solution was concentrated in vacuo to give the triol intermediate, which was immediately used for benzoylation. The crude product was coevaporated several times with anhydrous toluene, after which it was dissolved in pyridine (10 mL). Benzoyl chloride (2.6 mL, 21.1 mmol) was added at 0 °C, and the reaction mixture was stirred for 18 h at ambient temperature. The mixture was quenched with saturated aqueous $NaHCO_3$, extracted with EtOAc, dried with $MgSO_4$, and concentrated in vacuo. Purification by silica column chromatography (petroleum ether/EtOAc 96:4→94:6) afforded **16** (701.8 mg, 1.46 mmol, 70%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 7.2 Hz, 2 H, $H_{Ar}Bz$), 7.92 (d, J = 7.2 Hz, 2 H, $H_{Ar}Bz$), 7.84 (d, J = 7.2 Hz, 2 H, $H_{Ar}Bz$), 7.53–7.46 (m, 3 H, $H_{Ar}Bz$), 7.40–7.30 (m, 5 H, $H_{Ar}Bz$), 7.26–7.18 (m, 2 H, $H_{Ar}Bz$), 6.00–5.93 (m, 3 H, 2-H, 3-H, 6-H), 5.86 (d, J = 10.0 Hz, 1 H, 1-H), 5.72 (t, J = 9.2 Hz, 1 H, 4-H), 3.64 (dd, J = 4.0, 12.4 Hz, 1 H, 8-H), 3.46 (dd, J = 6.4, 12.4 Hz, 1 H, 8-H), 2.99–2.97 (m, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 165.9, 133.3, 133.2, 133.1, 129.8, 129.7, 129.6, 129.4, 129.0, 128.9, 128.5, 128.4, 128.3, 126.2, 127.0, 72.7, 72.6, 70.3, 52.0, 42.5 ppm. HRMS: calcd. for $[C_{28}H_{25}N_3O_6Na]$ $[M + Na]^+$ 520.14791; found 520.14724.

8-Azido-2,3,4-tri-*O*-benzoyl-8-deoxycyclophellitol (17 and 18): A solution of Na_2EDTA solution in H_2O (0.4 mM, 3.1 mL) and trifluoroacetone (1.34 mL, 15 mmol) were added to **16** (497 mg, 1.0 mmol) in acetonitrile (6.7 mL). A mixture of oxone (3.07 g, 5.0 mmol) and $NaHCO_3$ (588 mg, 7.0 mmol) was added to the solution over a period of 15 min. After the system had been stirred at 4 °C for 4 h, an additional quantity of Na_2EDTA in H_2O (0.4 mM, 1.5 mL), trifluoroacetone (0.7 mL, 7.5 mmol), and a mixture of oxone (1.5 mg, 2.5 mmol) and $NaHCO_3$ (290 mg, 3.5 mmol) were added to the reaction mixture over a period of 15 min. The reaction mixture was stirred at 0 °C for 30 min, after which it was diluted with H_2O. After extraction of the water layer with EtOAc, the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Purification by silica column chromatography (petroleum ether/Et_2O 92:8→90:10 and 84:16→82:16) afforded **17** (254 mg, 0.49 mmol, 49%) and **18** (104 mg, 0.20 mmol, 20%) as white crystals.

Compound 17: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, J = 7.2 Hz, 2 H, $H_{Ar}Bz$), 7.89 (d, J = 7.2 Hz, 2 H, $H_{Ar}Bz$), 7.78 (d, J = 7.2 Hz, 2 H, $H_{Ar}Bz$), 7.53–7.19 (m, 5 H, $H_{Ar}Bz$), 5.96 (t, J = 9.6 Hz, 1 H, 3-H), 5.77 (d, J = 8.8 Hz, 1 H, 2-H), 5.55 (t, J = 9.6 Hz, 1 H, 4-H), 3.77–3.74 (m, 2 H, 6-H, 8-H), 3.64 (dd, J = 4.0, 12.8 Hz, 1 H, 8-H), 3.32 (s, 1 H, 1-H), 2.68 (ddd, J = 3.8, 5.2, 9.2 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 165.9, 165.6, 133.4, 133.0, 129.9, 129.7, 129.5, 129.0, 128.9, 128.6, 128.4, 128.3, 128.1, 72.1, 70.0, 69.9, 54.6, 53.8, 50.8, 40.9 ppm. HRMS: calcd. for $[C_{28}H_{23}N_3O_7]$ $[M + H]^+$ 514.16017; found 514.16088.

Compound 18: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, J = 7.4 Hz, 2 H, $H_{Ar}Bz$), 7.88 (d, J = 7.6 Hz, 2 H, $H_{Ar}Bz$), 7.79 (d, J = 7.6 Hz, 2 H, $H_{Ar}Bz$), 7.56 (t, J = 7.2 Hz, 1 H, $H_{Ar}Bz$), 7.46–7.36 (m, 5 H, $H_{Ar}Bz$), 7.32 (t, J = 7.6 Hz, 2 H, $H_{Ar}Bz$), 7.24 (t, J = 7.2 Hz, 2 H, $H_{Ar}Bz$), 5.84 (t, J = 9.2 Hz, 1 H, 3-H), 5.56 (d, J = 8.4 Hz, 1 H, 2-H), 5.43 (t, J = 10.0 Hz, 1 H, 4-H), 3.67–3.62 (m, 4 H, 6-H, 8-H), 3.44 (s, 1 H, 1-H), 2.72–2.68 (m, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7, 165.6, 165.4, 133.5, 133.3, 133.1, 129.8, 129.6, 129.5, 128.9, 128.7, 128.6, 128.4, 128.3, 128.1, 72.2, 71.4, 67.8, 54.7, 54.2, 50.5, 40.8 ppm. HRMS: calcd. for $[C_{28}H_{23}N_3O_7]$ $[M + H]^+$ 514.16007; found 514.16088.

8-Deoxy-8-azidocyclophellitol (4): A catalytic amount of NaOMe was added to a solution of **18** (104 mg, 0.20 mmol) in MeOH

(1.0 mL), and the mixture was stirred for 1 h at ambient temperature. It was then neutralized with Amberlite IR-120 H^+, filtered, and concentrated in vacuo. Purification by silica column chromatography (dichloromethane/MeOH 94:6→92:8) provided **4** (30.0 mg, 0.15 mmol, 75%) as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 3.84 (dd, J = 3.6, 8.4 Hz, 1 H, 8-H), 3.67 (d, J = 8.0 Hz, 1 H, 2-H), 3.51 (dd, J = 8.8, 12.0 Hz, 1 H, 8-H), 3.36 (d, J = 3.2 Hz, 1 H, 6-H), 3.23 (dd, J = 8.4, 10.0 Hz, 1 H, 3-H), 3.13–3.08 (m, 2 H, 1-H, 4-H), 2.07 (ddt, J = 1.6, 3.6, 9.4 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 78.3, 72.7, 68.6, 57.6, 56.1, 52.4, 43.9 ppm. HRMS: calcd. for $[C_7H_{14}NO_4]$ $[M + 3\,H^+ - N_2]^+$ 176.09173; found 176.09179.

2,3-Di-*O*-acetyl-4,8-*O*-(*tert*-butylsilanediyl)cyclophellitol (19): Pyridine (0.2 mL, 2.5 mmol) was added to a solution of (+)-cyclophellitol (**1**, 47.1 mg, 0.25 mmol) in DMF (2.3 mL), and the solution was cooled to –40 °C. $(t\mathrm{Bu})_2\mathrm{Si(OTf)}_2$ (102 μL, 0.31 mmol) was added to the cooled solution, and the reaction mixture was allowed to warm gradually to 0 °C. At 0 °C the mixture was diluted with EtOAc and washed with H_2O. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with H_2O and brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude product was dissolved in pyridine (2.5 mL) and cooled to 0 °C. Ac_2O (0.25 mL) was added dropwise to the cooled solution, and the reaction mixture was allowed to warm to ambient temperature. After complete conversion the reaction mixture was cooled to 0 °C and quenched with MeOH. The reaction mixture was concentrated in vacuo, and traces of pyridine were removed by co-evaporation with toluene. Purification by column chromatography (pentane/EtOAc 92.5:7.5→90:10) yielded protected cyclophellitol **19** as a colorless oil (57.7 mg, 0.15 mmol, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.06 (m, 2 H, 2-H, 3-H), 4.09–4.01 (m, H, 8-H), 3.99–3.91 (m, 1 H, 8-H), 3.66–3.61 (m, 1 H, 4-H), 3.41 (s, 1 H, 6-H), 3.10 (d, J = 4.8 Hz, 1 H, 1-H), 2.27–2.21 (m, 1 H, 5-H), 2.10 (d, J = 3.6 Hz, 6 H, 2 × CH_3OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 170.1, 74.4, 70.8, 70.3, 66.2, 53.9, 53.0, 42.1, 27.4, 26.9, 22.7, 21.0, 20.9, 19.9 ppm. HRMS: calcd. for $[C_{19}H_{33}O_7Si]$ $[M + H]^+$ 401.19901; found 401.19883.

2,3-Di-*O*-acetylcyclophellitol (20): Pyridine (0.25 mL) was added to a solution of silylene-protected cyclophellitol **19** (38.4 mg, 0.1 mmol) in THF (0.5 mL), and the mixture was cooled to 0 °C. HF·pyridine (1 M, 0.25 mL, 0.25 mmol) was added to the cooled reaction mixture, which was stirred for 1 h at 0 °C. The reaction was quenched with $NaHCO_3$ (s). Excess solids were filtered off over a plug of cotton wool, rinsed with acetone, and the combined filtrate fractions were concentrated in vacuo. Purification by column chromatography (dichloromethane/acetone 75:25) yielded 2,3-*O*-acetylated cyclophellitol **20** as a colorless amorphous solid (27 mg, 0.1 mmol, quant.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.06 (m, 2 H, 2-H, 3-H), 4.09–4.01 (m, H, 8-H), 3.99–3.91 (m, 1 H, 8-H), 3.66–3.61 (m, 1 H, 4-H), 3.36 (t, J = 7.6 Hz, OH), 3.38–3.34 (m, 2 H, 6-H, OH), 3.10 (d, J = 4.8 Hz, 1 H, 1-H), 2.27–2.21 (m, 1 H, 5-H), 2.10 (d, J = 3.6 Hz, 6 H, 2 × CH_3 OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 170.3, 75.1, 71.0, 67.0, 63.0, 55.2, 53.3, 43.7, 21.0, 20.9 ppm. HRMS: calcd. for $[C_{11}H_{16}O_7]$ $[M + H]^+$ 261.09688; found 261.09695.

2,3-Di-*O*-acetyl-8-azido-8-deoxycyclophellitol (21): Pyridine (0.2 mL, 2.5 mmol) was added to a solution of 2,3-acetylated cyclophellitol **20** (65 mg, 0.25 mmol) in CH_2Cl_2 (9.8 mL) and the solution was cooled to –25 °C. Triflic anhydride (52.5 μL, 0.36 mmol) was added, and the reaction mixture was stirred for 1 h at –25 °C. It was then diluted with EtOAc and successively washed with HCl (aq., 0.1 M, 5 mL, pH ≤ 6), satd. $NaHCO_3$ (aq., pH ≥ 6), H_2O, and brine, dried with $MgSO_4$, filtered, and concentrated in vacuo (30 °C, 100 mbar). The triflated intermediate was co-evaporated once with toluene and used in the next step without further purification. The triflated product was dissolved in THF (2.5 mL) and cooled to –25 °C under argon. NaN_3 (53 mg, 0.75 mmol) and 15-crown-5 (46 μL, 0.25 mmol) were added to the cooled solution, and the reaction mixture was allowed to warm gradually to 0 °C. After 20 min the reaction was complete, and the reaction mixture was diluted with Et_2O, silica gel was added, and the solvents were removed under reduced pressure. The silica immobilized product was purified by column chromatography (pentane/EtOAc 80:20→70:30), yielding 2,3-acetylated azidocyclophellitol **21** as a colorless amorphous solid (64 mg, 0.23 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.07 (d, J = 8.4 Hz, 1 H, 2-H), 4.96 (dd, J = 8.4, 10.4 Hz, 1 H, 3-H), 3.88 (dd, J = 4.0, 12.0 Hz, 1 H, 8-H), 3.59 (dd, J = 8.4, 12.0 Hz, 1 H, 8-H), 3.51 (t, J = 10.0 Hz, 1 H, 4-H), 3.41 (d, J = 3.6 Hz, 1 H, 6-H), 3.14 (d, J = 3.6 Hz, 1 H, 1-H), 2.27–2.21 (m, 1 H, 5-H), 2.10 (d, J = 3.6 Hz, 6 H, 2 × CH_3 OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 75.2, 70.7, 66.3, 54.7, 53.9, 50.8, 42.1, 20.9, 20.8 ppm. HRMS: calcd. for $[C_{11}H_{15}N_3O_6]$ $[M + H]^+$ 286.10336; found 286.10344.

8-Azido-8-deoxycyclophellitol (4): NaOMe solution in MeOH (0.02 M, 0.5 mL, 0.01 mmol) was added to a solution of 2,3-acetylated azido cyclophellitol **21** (28.5 mg, 0.1 mmol) in MeOH (0.5 mL) The reaction mixture was stirred overnight at room temperature, and the reaction was quenched with Amberlite IR-120 H^+ until pH-neutral. Amberlite was filtered off over a plug of cotton wool, rinsed with MeOH. Removal of the solvent under reduced pressure yielded azido cyclophellitol **4** without further purification as a colorless amorphous solid (17.9 mg, 0.089 mmol, 89%). Analytical data are in accordance with those described previously (see above).

2,3-Di-*O*-benzylcyclophellitol Aziridine Compound 23: Diol **3** (765 mg, 2.0 mmol) was co-evaporated thrice with toluene and subsequently dissolved in anhydrous CH_2Cl_2 (50 mL). The solution was cooled to 0 °C, and trichloroacetonitrile (200 μL, 2.0 mmol) and 1,8-diazobicyclo[5.4.0]undec-7-ene (14 μL, 0.2 mmol) were added. After the system had been stirred for 2 h at 0 °C, TLC analysis revealed complete conversion to a higher-running product. H_2O (6.2 mL), sodium hydrogencarbonate (1.75 g, 20.8 mmol), and iodine (1.57 g, 6.2 mmol) were added. The resulting mixture was stirred overnight at room temperature, after which it was quenched with $Na_2S_2O_3$ (10%) and extracted with EtOAc. The organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The resulting crude iminal **22** was dissolved in dioxane (18 mL), after which it was cooled to 0 °C. Subsequently, concentrated hydrochloric acid (6.2 mL, 37% in H_2O) was added, and the reaction mixture was stirred at 60 °C for 1 h. The solution was concentrated in vacuo and redissolved in MeOH (49 mL). Sodium hydrogencarbonate (3.36 g, 40 mmol) was added. After stirring at room temperature for 1 d, the reaction mixture was diluted with H_2O and extracted with EtOAc, and the organic fraction was dried with $MgSO_4$ and concentrated in vacuo. Purification by silica gel column chromatography (dichloromethane/MeOH 96:4→90:10) afforded **23** (427 mg, 1.20 mmol, 60%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.26 (m, 10 H, H_{Ar}Bn), 4.96 (d, J = 11.6 Hz, 1 H, CH_2 Bn), 4.78 (d, J = 11.6 Hz, 1 H, CH_2 Bn), 4.65 (d, J = 11.6 Hz, 2 H, CH_2 Bn), 3.97 (dd, J = 5.6, 10.4 Hz, 1 H, 8-H), 3.89 (dd, J = 4.4, 10.8 Hz, 1 H, 8-H), 3.74 (d, J = 8.0 Hz, 1 H, 2-H), 3.52 (t, J = 10.0 Hz, 1 H, 4-H), 3.37 (t, J = 9.6 Hz, 1 H, 3-H), 2.42 (dd, J = 3.2, 6.0 Hz, 1 H, 6-H), 2.27 (d, J = 6.0 Hz, 1 H, 1-H), 2.07 (td, J = 5.1, 8.8 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 137.8, 128.5, 128.5, 127.9, 127.8, 127.8, 84.3,

81.2, 74.7, 72.2, 68.2, 64.5, 42.5, 32.9, 31.4 ppm. HRMS: calcd. for $[C_{21}H_{26}NO_4]$ $[M + H]^+$ 356.18514; found 356.18563.

Cyclophellitol Aziridine Compound 2: Ammonia (20 mL) was condensed at –60 °C. Lithium (200 mg) was added, and the mixture was stirred until the lithium was completely dissolved. A solution of aziridine **23** (427 mg, 1.20 mmol) in THF (27 mL) was added. The reaction mixture was stirred for 30 min at –60 °C and subsequently quenched with milliQ-H_2O (8 mL). The solution was allowed to come to room temperature and stirred until all ammonia had evolved. Next, the solution was concentrated in vacuo, redissolved in milliQ-H_2O, and neutralized with Amberlite IR-120 H^+. Product bound to the resin was washed with water and subsequently eluted with NH_4OH solution (1 M) and evaporated under reduced pressure. The resulting solid was again purified on Amberlite IR-120 NH_4^+ with milliQ-water as eluent until the eluate was neutral. Concentration of the combined eluate under reduced pressure gave the fully deprotected aziridine **3** (147 mg, 0.84 mmol, 70%). ^{1}H NMR (400 MHz, D_2O): δ = 3.61 (dd, J = 4.4, 10.8 Hz, 1 H, 8-H), 3.34–3.25 (m, 2 H, 8-H, 2-H), 2.89 (t, J = 9.6 Hz, 1 H, 3-H), 2.68 (t, J = 9.6 Hz, 1 H, 4-H), 2.22 (dd, J = 3.2, 6.0 Hz, 6-H), 1.93 (d, J = 6.4 Hz, 1 H, 1-H), 1.68–1.64 (m, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 78.8, 73.3, 69.1, 62.9, 44.2, 36.0, 33.4 ppm. HRMS: calcd. for $[C_7H_{14}NO_4]$ $[M + H]^+$ 176.09173; found 176.09170.

Cyclophellitol *N*-(Hept-6-ynoyl)aziridine Compound 24: A preactivated mixed anhydride solution (1 M) was prepared by dissolving EEDQ (209 mg, 0.85 mmol) and hept-6-ynoic acid (0.11 mL, 0.85 mmol) in DMF (0.85 mL), and the reaction mixture was stirred at room temperature for 2 h before use. Cyclophellitol aziridine (**3**, 38 mg, 0.22 mmol) was dissolved in DMF (1.3 mL), and the solution was cooled to 0 °C, after which the preactivated mixed anhydride solution (1 M, 0.11 mL, 0.11 mmol) was added. The reaction mixture was stirred at 0 °C for 30 min, and additional preactivated solution (0.11 mL, 0.11 mmol) was added. After stirring for 45 min at 0 °C, the reaction mixture was quenched with MeOH and concentrated under reduced pressure. Purification by semipreparative reversed-phase HPLC (linear gradient: 13%→16%, 3CV, solutions used: A: H_2O, B: acetonitrile) afforded compound **24** (12.2 mg, 0.04 mmol, 20%) as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 4.06 (dd, J = 4.4, 10.4 Hz, 1 H, 8-H), 3.71–3.66 (m, 2 H, 2-H, 8-H), 3.20 (dd, J = 8.0, 10.0 Hz, 1 H, 3-H), 3.07 (t, J = 10.0 Hz, 1 H, 4-H), 3.02 (dd, J = 3.2, 6.0 Hz, 1 H, 6-H), 2.72 (d, J = 6.0 Hz, 1 H, 1-H), 2.51 (td, J = 1.6, 8.8 Hz, 2 H, CH_2C=O), 2.25–2.15 (m, 3 H, $CH_2C\equiv$, C≡CH), 1.99–1.93 (m, 1 H, 5-H), 1.76–1.70 (m, 2 H, C=OCH_2CH_2), 1.57–1.50 (m, 2 H, $CH_2CH_2C\equiv$) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 188.2, 84.6, 79.1, 73.4, 69.8, 69.3, 63.5, 45.3, 42.5, 41.1, 36.3, 29.1, 25.2, 18.8 ppm. HRMS: calcd. for $[C_{14}H_{22}NO_4]$ $[M + H]^+$ 284.14925; found 284.14952.

Cyclophellitol *N*-(8-Azidooctanoyl)aziridine 5: A preactivated mixed anhydride solution (1 M) was prepared by dissolving EEDQ (74 mg, 0.30 mmol) and 8-azidooctanoic acid (56 mg, 0.30 mmol) in DMF (0.3 mL), and the reaction mixture was stirred at room temperature for 2 h before use. Crude deprotected aziridine (40 mg, 0.23 mmol) was dissolved in DMF (1.3 mL), and the solution was cooled to 0 °C, after which preactivated mixed anhydride solution (1 M, 0.15 mL, 0.15 mmol) was added. The reaction mixture was stirred at 0 °C for 30 min, and additional preactivated solution (0.15 mL, 0.15 mmol) was added. After stirring for 45 min at 0 °C, the reaction mixture was quenched with MeOH and concentrated under reduced pressure. Purification by semipreparative reversed-phase HPLC (linear gradient: 25%→31%, 3CV, solutions used: A: H_2O, B: acetonitrile) afforded **5** (20 mg, 0.058 mmol, 25%) as a white powder. ^{1}H NMR (400 MHz, MeOD): δ = 4.05 (dd, J = 4.4, 10.4 Hz, 1 H, 8-H), 3.69–3.65 (m, 2 H, 2-H, 8-H), 3.30–3.25 (m, 2 H, CH_2N_3 and MeOD solvent signals), 3.19 (dd, J = 8.4, 10.0 Hz, 1 H, 3-H), 3.06 (t, J = 9.6 Hz, 1 H, 4-H), 3.01 (dd, J = 2.8, 6.0 Hz, 1 H, 6-H), 2.72 (d, J = 6.0 Hz, 1 H, 1-H), 2.48 (t, J = 7.2 Hz, 2 H, NC=OCH_2), 1.99–1.93 (m, 1 H, 5-H), 1.63–1.54 (m, 5 H, CH_2 alkyl), 1.36 (s, 7 H, CH_2 alkyl) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 188.5, 79.0, 73.4, 69.3, 63.7, 52.4, 45.2, 42.4, 41.0, 36.8, 30.1, 29.8, 27.6 25.9 ppm. HRMS: calcd. for $[C_{15}H_{27}N_4O_5]$ $[M + H]^+$ 343.19760; found 343.19761.

General Click Procedure for Epoxides 34–36 and 41: Azidocyclophellitol (1 equiv.) and the desired BODIPY-alkyne (1 equiv.) were dissolved in *t*BuOH/toluene/H_2O (1–2 mL, 1:1:1, v/v/v). $CuSO_4$ (0.1 equiv., 100 mM in H_2O) and sodium ascorbate (0.1 equiv., 100 mM in H_2O) were added. Subsequently, the reaction mixture was heated to 80 °C and stirred overnight. The solution was diluted with CH_2Cl_2, washed with H_2O, dried with $MgSO_4$, concentrated under reduced pressure, and purified by silica column chromatography.

BODIPY-Cyclophellitol Derivative 34: Silica column chromatography (dichloromethane/MeOH 100:0→95:5) furnished **34** as a purple powder (14.3 mg, 20.8 mmol, 77%). ^{1}H NMR (400 MHz, MeOD): δ = 7.83 (d, J = 7.2 Hz, 4 H, H_{Ar}Ph), 7.58 (s, 1 H, CH_{trz}), 7.32 (d, J = 4.4 Hz, 2 H, 2 × H_{Ar}), 6.95 (d, J = 8.8 Hz, 4 H, H_{Ar}Ph), 6.63 (d, J = 4.4 Hz, 2 H, 2 × H_{Ar}), 4.80 (dd, J = 3.6, 13.6 Hz, 1 H, 8-H), 4.57 (dd, J = 8.8, 14.0 Hz, 1 H, 8-H), 3.85 (s, 6 H, 2 × CH_3OMe), 3.70 (d, J = 8.0 Hz, 1 H, 2-H), 3.27 (dd, J = 8.4, 10.0 Hz, 1 H, 3-H), 3.17 (t, J = 9.6 Hz, 1 H, 4-H), 3.09 (d, J = 4.0 Hz, 1 H, 6-H), 3.04–3.01 (m, 3 H, 1-H, CH_2 alkyl), 2.80–2.79 (m, 2 H, CH_2 alkyl), 2.41 (td, J = 2.0, 3.6, 8.8 Hz, 1 H, 5-H), 1.89 (br. s, 4 H, 2 × CH_2 alkyl) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 162.2, 158.8, 148.7, 137.5, 132.2, 128.4, 126.5, 124.4, 121.0, 114.6, 78.3, 72.5, 68.6, 57.8, 55.5, 50.7, 49.6, 44.7, 34.2, 31.0, 30.5, 25.8 ppm. HRMS: calcd. for $[C_{36}H_{39}BF_2N_5O_4]$ $[M + H]^+$ 686.29560; found 686.29559.

BODIPY-Cyclophellitol Derivative 35: Silica column chromatography (dichloromethane/MeOH 100:0→95:5) afforded **35** as an orange powder (12.5 mg, 23.6 mmol, 56%). ^{1}H NMR (400 MHz, MeOD): δ = 7.77 (s, 1 H, CH_{trz}), 6.11 (s, 2 H, 2 × H_{Ar}), 4.68 (d, J = 4.0, 14.0 Hz, 1 H, 8-H), 4.60 (dd, J = 7.2, 13.6 Hz, 1 H, 8-H), 3.58 (d, J = 8.0 Hz, 1 H, 2-H), 3.21 (t, J = 10.0 Hz, 1 H, 3-H), 3.12 (t, J = 10.0 Hz, 1 H, 4-H), 3.03–2.99 (m, 2 H, CH_2 alkyl), 2.96 (s, 2 H, 1-H, 6-H), 2.79 (t, J = 6.8 Hz, 2 H, CH_2 alkyl), 2.66 (s, 1 H, CH_2 alkyl), 2.44 (s, 6 H, 2 × CH_3Me), 2.38 (s, 6 H, 2 × CH_3Me), 1.86 (td, J = 7.6, 7.6, 15.0 Hz, 1 H, 5-H), 1.92–1.87 (m, 3 H, CH_2 alkyl), 1.69–1.62 (m, 2 H, CH_2 alkyl) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 154.9, 149.4, 148.5, 147.9, 142.2, 132.6, 124.5, 122.6, 78.3, 72.5, 68.6, 57.4, 55.4, 50.6, 44.7, 32.2, 31.1, 30.8, 29.0, 25.9, 16.5, 14.4 ppm. HRMS: calcd. for $[C_{26}H_{35}BF_2N_5O_4]$ $[M + H]^+$ 530.27447; found 530.27454.

Biotin-Cyclophellitol Derivative 36: Silica column chromatography (dichloromethane/MeOH 100:0→80:20) furnished **36** as a white powder (12.3 mg, 12.6 μmol, 90%). ^{1}H NMR (600 MHz, DMSO): δ = 7.81 (s, 1 H, CH_{trz}), 4.57 (dd, J = 3.6, 13.8 Hz, 1 H, 8-H), 4.36 (dd, J = 10.8, 13.2 Hz, 1 H, 8-H), 4.13–4.23 (m, 3 H, 6-H, CH_2NHC=O), 4.13–4.11 (m, 1 H, 1-H), 3.62 (t, J = 3.0 Hz, 1 H, CH biotin), 3.09–3.09 (m, CH biotin), 2.82 (dd, J = 4.8, 12.6 Hz, 1 H, CH_2 biotin), 2.11–2.05 (m, 3 H, CH_2 alkyl), 1.64–1.58 (m, 1 H, CH_2 alkyl), 1.54–1.37 (m, 3 H, CH_2 alkyl), 1.31–1.29 (m, 3 H, CH_2 alkyl) ppm. ^{13}C NMR (151 MHz, DMSO): δ = 172.0, 162.7, 144.7, 144.6, 123.3, 74.7, 72.2, 70.6, 70.4, 67.7, 61.0, 59.2, 55.4,

47.6, 42.9, 34.9, 34.1, 28.2, 28.0, 25.2, 20.4 ppm. HRMS: calcd. for $[C_{20}H_{30}N_6O_6S]$ $[M + H]^+$ 483.20203; found 483.20170.

General Procedure for the Synthesis of pH-Activatable Cyclophellitol Probes 37–40: Azidocyclophellitol (1 equiv.) and the desired BODIPY-alkyne (1 equiv.) were dissolved in *t*BuOH/toluene/H_2O (1–2 mL, 1:1:1, v/v/v) and sonicated for 30 min under argon. $CuSO_4$ (0.1 equiv., 100 mM in H_2O) and sodium ascorbate (0.1 equiv., 100 mM in H_2O) were added, and the mixture was heated to 80 °C. After 2 h an additional amount of $CuSO_4$ (0.1 equiv.) and sodium ascorbate (0.15 equiv.) were added, and the mixture was stirred at 80 °C for 2 h. The mixture was concentrated under reduced pressure and co-evaporated with toluene. HPLC-MS purification and lyophilization from *t*BuOH/H_2O resulted in **37**–**40** as purple powders.

Phenyl-BODIPY-Cyclophellitol Derivative 37: Yield 2.74 mg, 4.1 μmol, 26%. ^{1}H NMR (600 MHz, MeOD): δ = 8.13 (s, 1 H, CH_{trz}), 7.57 (dd, J = 5.0, 7.4 Hz, 5 H, 5 × H_{Ar}Ph), 7.50 (d, J = 16.2 Hz, 1 H, CH=), 7.30–7.38 (m, 3 H, CH=, 2 × H_{Ar}Ph), 7.07 (d, J = 8.8 Hz, 2 H, 2 × H_{Ar}Ph), 6.75 (s, 1 H, H_{Ar}), 6.08 (s, 1 H, H_{Ar}), 5.24 (s, 1 H, OCH_2), 4.67 (dd, J = 8.6, 13.9 Hz, 2 H, 8-H), 3.62 (d, J = 8.2 Hz, 1 H, 2-H), 3.24 (dd, J = 8.2, 10.0 Hz, 1 H, 3-H), 3.15 (t, J = 9.8 Hz, 1 H, 4-H), 3.00–3.07 (m, 2 H, 1-H, 6-H), 2.53 (s, 3 H, CH_3 Me), 2.42 (td, J = 4.5, 8.5, 9.2 Hz, 1 H, 5-H), 1.46 (s, 3 H, CH_3 Me), 1.42 (s, 3 H, CH_3Me) ppm. ^{13}C NMR (151 MHz, MeOD): δ = 160.7, 155.9, 154.8, 144.8, 144.2, 143.8, 141.8, 137.3, 136.4, 133.9, 132.8, 131.3, 130.4, 130.3, 129.9, 120.9, 126.4, 122.1, 188.7, 118.1, 116.4, 116.3, 78.2, 72.5, 68.7, 62.5, 57.6, 55.4, 51.0, 44.7, 14.8, 14.6, 14.5 ppm. HRMS: calcd. for $[C_{36}H_{37}BF_2N_5O_5]$ $[M + H]^+$ 668.28503; found 668.28553.

Dimethylaminophenyl-BODIPY-Cyclophellitol Derivative 38: Yield 5.44 mg, 7.66 μmol, 30%. ^{1}H NMR (600 MHz, MeOD): δ = 8.15 (s, 1 H, CH_{trz}), 7.56 (d, J = 8.7 Hz, 2 H, 2 × H_{Ar}), 7.49 (d, J = 16.3 Hz, 1 H, CH=), 7.33 (d, J = 16.4 Hz, 1 H, CH=), 7.11 (d, J = 8.6 Hz, 2 H, 2 × H_{Ar} Ph), 7.07 (d, J = 8.7 Hz, 2 H, 2 × H_{Ar} Ph), 6.91 (d, J = 8.6 Hz, 2 H, 2 × H_{Ar} Ph), 6.74 (s, 1 H, H_{Ar}), 6.07 (s, 1 H, H_{Ar}), 5.24 (s, 2 H, OCH_2), 4.87 (dd, J = 3.8, 13.8 Hz, 1 H, 8-H), 4.67 (dd, J = 8.6, 13.9 Hz, 1 H, 8-H), 3.62 (d, J = 8.2 Hz, 1 H, 2-H), 3.20–3.26 (m, 1 H, 3-H), 3.14 (t, J = 9.8 Hz, 1 H, 4-H), 3.03 (d, J = 6.3 Hz, 8 H, 1-H, 6-H, 2 × CH_3 NMe_2), 2.52 (s, 3 H, CH_3 Me), 2.42 (td, J = 2.5, 8.7, 9.2 Hz, 1 H, 5-H), 1.57 (s, 3 H, CH_3 Me), 1.52 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, MeOD): δ = 160.6, 155.3, 154.1, 152.6, 144.9, 144.2, 144.0, 143.4, 136.7, 136.4, 133.6, 131.5, 130.1, 129.8, 126.4, 123.4, 121.8, 118.3, 116.4, 113.7, 78.2, 72.5, 68.7, 62.5, 57.6, 55.5, 51.0, 44.7, 40.6, 15.1, 14.8, 14.6 ppm. HRMS: calcd. for $[C_{38}H_{42}BF_2N_6O_5]$ $[M + H]^+$ 711.32723; found 711.32738.

***N*-Methyl-*N*-Ethylaminophenyl-BODIPY-Cyclophellitol Derivative 39:** Yield 2.43 mg, 4.1 mmol, 18%. ^{1}H NMR (600 MHz, MeOD): δ = 8.15 (s, 1 H, CH_{trz}), 7.56 (d, J = 8.7 Hz, 2 H, 2 × H_{Ar} Ph), 7.49 (d, J = 16.4 Hz, 1 H, CH=), 7.32 (d, J = 16.3 Hz, 1 H, CH=), 7.08 (dd, J = 8.7, 11.3 Hz, 4 H, 4 × H_{Ar} Ph), 6.89 (d, J = 8.7 Hz, 2 H, 2 × H_{Ar} Ph), 6.74 (s, 1 H, H_{Ar}), 6.07 (s, 1 H, H_{Ar}), 5.24 (s, 2 H, OCH_2), 4.87 (dd, J = 3.8, 13.9 Hz, 1 H, 8-H), 4.67 (dd, J = 8.6, 13.9 Hz, 1 H, 8-H), 3.62 (d, J = 8.2 Hz, 1 H, 2-H), 3.51 (q, J = 7.0 Hz, 2 H, CH_2 ethyl), 3.24 (dd, J = 8.2, 9.9 Hz, 1 H, 3-H), 3.14 (t, J = 9.9 Hz, 1 H, 4-H), 3.04 (q, J = 3.8 Hz, 2 H, 1-H, 6-H), 2.99 (s, 3 H, CH_3NMe), 2.52 (s, 3 H, CH_3 Me), 2.42 (td, J = 4.3, 9.8 Hz, 1 H, 5-H), 1.58 (s, 3 H, CH_3 Me), 1.54 (s, 3 H, CH_3 Me), 1.16 (t, J = 7.0 Hz, 3 H, CH_3 ethyl) ppm. ^{13}C NMR (150 MHz, MeOD): δ = 160.6, 155.3, 154.1, 151.1, 144.9, 144.2, 144.0, 143.5, 136.7, 135.7, 133.6, 131.5, 130.2, 129.8, 126.4, 122.9, 121.8, 118.3, 116.4, 113.6, 78.2, 72.5, 68.7, 62.5, 57.6, 55.5, 51.0, 47.6, 44.7, 37.7, 15.1, 14.8, 14.6, 11.2 ppm. HRMS: calcd. for $[C_{39}H_{44}BF_2N_6O_5]$ $[M + H]^+$ 725.34305; found 725.34288.

Diethylaminophenyl-BODIPY-Cyclophellitol Derivative 40: Yield 3.46 mg, 4.1 μmol, 14%. ^{1}H NMR (600 MHz, MeOD): δ = 8.13 (s, 1 H, CH_{trz}), 7.55 (d, J = 8.7 Hz, 2 H, 2 × H_{Ar} Ph), 7.49 (d, J = 16.3 Hz, 1 H, CH=), 7.31 (d, J = 16.3 Hz, 1 H, CH=), 7.06 (dd, J = 3.2, 8.7 Hz, 4 H, 4 × H_{Ar} Ph), 6.85 (d, J = 8.7 Hz, 2 H, 2 × H_{Ar} Ph), 6.72 (s, 1 H, H_{Ar}), 6.06 (s, 1 H, H_{Ar}), 5.23 (s, 2 H, OCH_2), 4.67 (dd, J = 8.6, 13.9 Hz, 2 H, 8-H), 3.62 (d, J = 8.1 Hz, 1 H, 2-H), 3.45 (q, J = 7.0 Hz, 4 H, 2 × CH_2 ethyl), 3.24 (dd, J = 8.2, 9.0 Hz, 1 H, 3-H), 3.15 (t, J = 9.8 Hz, 1 H, 4-H), 3.04 (d, J = 3.7 Hz, 2 H, 1-H, 6-H), 2.52 (s, 3 H, CH_3 Me), 2.42 (td, J = 4.4, 8.6, 9.1 Hz, 1 H, 5-H), 1.60 (s, 3 H, CH_3 Me), 1.56 (s, 3 H, CH_3 Me), 1.20 (t, J = 7.0 Hz, 6 H, 2 × CH_3 ethyl) ppm. ^{13}C NMR (150 MHz, MeOD): δ = 160.5, 155.2, 154.0, 149.8, 144.9, 144.2, 144.0, 143.6, 136.6, 134.7, 133.7, 131.5, 130.3, 129.8, 126.4, 122.3, 121.8, 118.3, 116.4, 113.2, 78.2, 72.5, 68.7, 62.5, 57.6, 55.5, 51.0, 45.4, 44.7, 31.1, 15.1, 14.9, 14.6, 12.7 ppm. HRMS: calcd. for $[C_{40}H_{46}BF_2N_6O_5]$ $[M + H]^+$ 739.35853; found 739.35866.

Biotin-BODIPY-Cyclophellitol Derivative 41: Silica column chromatography (dichloromethane/MeOH 100:0→80:20) furnished **41** as a purple powder (12.3 mg, 12.6 μmol, 90%). ^{1}H NMR (400 MHz, MeOD): δ = 7.84 (d, J = 8.8 Hz, 2 H, H_{Ar}), 7.73 (s, 1 H, CH_{trz}), 7.58 (s, 2 H, H_{Ar} Ph), 7.24 (s, 1 H, CH_{trz}), 7.01 (d, J = 4.0 Hz, 1 H, H_{Ar}), 6.92 (d, J = 8.8 Hz, H_{Ar} Ph), 6.55 (d, J = 4.0 Hz, H_{Ar}), 3.31 (br. s, H_2O solvent peak and 8-H), 4.58 (t, J = 6.8 Hz, 2 H, CH_2O), 4.48–4.38 (m, 6 H, 8-H, 2 × CH_2NHC=O, CH biotin), 4.22 (dd, J = 4.4, 7.6 Hz, CH biotin), 4.02 (t, J = 5.6 Hz, 2 H, CH_2 alkyl), 3.62 (d, J = 8.4 Hz, 1 H, 2-H), 3.21 (dd, J = 8.4, 10.0 Hz, 3-H), 3.12–3.06 (m, 2 H, 4-H, SCH), 3.00 (d, J = 3.6 Hz, 1 H, 6-H), 2.96–2.95 (m, 1 H, 1-H), 2.86 (dd, J = 4.8, 12.8 Hz, 1 H, CH biotin), 2.73 (t, J = 7.2 Hz, 1 H, CH_2 alkyl), 2.67 (d, J = 12.4 Hz, 1 H, CH biotin), 2.48 (s, 3 H, CH_3 Me), 2.42–2.30 (m, 5 H, 5-H, CH_2 alkyl), 2.19–2.16 (m, 5 H, CH_3 Me, CH_2 alkyl), 1.65–1.57 (m, 5 H, CH_2 alkyl), 1.55–1.24 (m, 3 H, CH_2 alkyl) ppm. ^{13}C NMR (150 MHz, MeOD): δ = 175.2, 173.8, 160.2, 160.0, 155.8, 141.2, 135.1, 131.3, 128.8, 126.6, 124.4, 123.9, 118.8, 77.7, 71.7, 68.0, 64.9, 62.6, 57.0, 56.3, 54.9, 50.3, 47.9, 43.8, 40.8, 36.2, 36.1, 35.2, 35.1, 30.3, 29.0, 28.7, 26.0, 13.3, 9.6 ppm. HRMS: calcd. for $[C_{45}H_{56}BF_2N_{12}O_8S]$ $[M + H]^+$ 987.42848; found 987.42855.

BODIPY-Cyclophellitol Aziridine Derivative 43: Alkyne **24** (4.2 mg, 15 μmol) was dissolved in DMF (0.65 mL). BODIPY-azide **42** (6.2 mg, 17 μmol), $CuSO_4$ (12 μL of 1*M* solution in H_2O), and sodium ascorbate (13 μL of a 1 M solution in H_2O) were added, and the solution was stirred for 1 h at ambient temperature. The volatiles were removed under reduced pressure, and compound **43** was purified by semipreparative reversed-phase HPLC (linear gradient: 40%→50%, 3 CV, solutions used: A: H_2O, B: acetonitrile) to yield **43** as an orange powder (4.43 mg, 6.75 μmol, 45%). ^{1}H NMR (400 MHz, MeOD): δ = 7.74 (s, 1 H, CH_{trz}), 6.13 (s, 2 H, H_{Ar}), 4.37 (t, J = 6.8 Hz, 2 H, NCH_2), 4.05 (dd, J = 4.4, 10.0 Hz, 1 H, 8-H), 3.67 (dd, J = 9.2, 10.4 Hz, 1 H, 8-H), 3.65 (d, J = 8.0 Hz, 1 H, 2-H), 3.19 (dd, J = 84, 10.4 Hz, 1 H, 3-H), 3.06 (t, J = 9.6 Hz, 1 H, 4-H), 3.01–2.97 (m, 3 H, 6-H, CH_2C=), 2.72 (t, J = 7.6 Hz, 3 H, 1-H, CH_2-alkyl), 2.54 (t, J = 7.2 Hz, 2 H, NC=OCH_2), 2.43 (d, J = 6.0 Hz, 12 H, 4 × OMe), 1.99–1.93 (m, 3 H, 1-H, CH_2 alkyl), 1.70–1.52 (m, 8 H, CH_2 alkyl), 1.41–1.35 (m, 2 H, CH_2 alkyl) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 188.2, 154.9, 148.8, 148.1, 142.2, 132.6, 123.2, 122.6, 79.1, 73.4, 69.3, 63.5, 51.1, 45.2, 42.5, 41.1, 36.5, 32.9, 31.2, 30.5, 29.9, 29.2, 27.2, 25.9, 25.3, 16.6, 14.4 ppm. HRMS: calcd. for $[C_{33}H_{48}BF_2N_6O_5]$ $[M + H]^+$ 657.37418; found 657.37464.

BODIPY-Cyclophellitol Aziridine Derivative 44: BODIPY-alkyne **25** (9 mg, 26 μmol), $CuSO_4$ (20 μL of 1 *M* solution in H_2O), and sodium ascorbate (23 μL of 1 M solution in H_2O) were added to a solution of **5** (14 mg, 0.03 mmol) in DMF (1 mL). The reaction mixture was stirred at ambient temperature for 2 h, after which it was concentrated under reduced pressure. Purification by semipreparative reversed-phase HPLC [linear gradient: 52→58% B, 3CV (solutions used A: H_2O, B: acetonitrile)] afforded the title compound (5.77 mg, 7.0 μmol, 27%) as a purple powder. ^{1}H NMR (600 MHz, MeOD): δ = 7.83 (d, J = 9.0 Hz, 4 H, H_{Ar} Ph), 7.67 (s, 1 H, CH_{trz}), 7.42 (d, J = 4.2 Hz, 2 H, CH_{Ar}), 6.96 (d, J = 9.0 Hz, 4 H, CH_{Ar}), 6.68 (d, J = 4.2 Hz, 2 H, CH_{Ar}), 4.31 (t, J = 7.2 Hz, 2 H, CH_2N_{trz}), 4.30 (dd, J = 4.2, 10.2 Hz, 1 H, 8-H), 3.84 (s, 6 H, 2 × OMe), 3.68–3.65 (m, 2 H, 2-H, 8-H), 3.18 (dd, J = 8.4, 10.2 Hz, 1 H, 3-H), 3.09–3.03 (m, 3 H, 4-H, =CCH_2), 2.97 (dd, J = 3.0, 6.0 Hz,1 H, 6-H), 2.77 (t, J = 6.6 Hz, 2 H CH_2 alkyl), 2.69 (d, J = 6.0 Hz, 1 H, 1-H), 2.44–2.39 (m, 2 H, CH_2 alkyl), 1.98–1.93 (m, 1 H, 5-H), 1.85–1.81 (m, 6 H, CH_2 alkyl), 1.56–1.51 (m, 2 H, CH_2 alkyl), 1.33–1.20 (m, 6 H, CH_2 alkyl) ppm. ^{13}C NMR (150 MHz, MeOD): δ = 188.5, 162.2, 158.8, 148.6, 146.8, 137.5, 132.2, 132.2, 132.1, 128.4, 126.5, 123.2, 121.0, 114.7, 79.1, 73.4, 69.4, 63.6, 55.8, 51.2, 45.3, 42.4, 41.0, 36.8, 34.1, 31.1, 31.0, 30.3, 30.0, 29.6, 27.2, 25.8, 25.8 ppm. HRMS: calcd. for $[C_{44}H_{54}BF_2N_6O_5]$ $[M + H]^+$ 827.41172; found 827.41207.

BODIPY-Cyclophellitol Aziridine Derivative 45: BODIPY-alkyne **26** (10.4 mg, 0.03 mmol), $CuSO_4$ (20 μL of a 1 M solution in H_2O), and sodium ascorbate (23 μL of a 1 M solution in H_2O) were added to a solution of **5** (10 mg, 0.03 mmol) in DMF (1 mL). The reaction mixture was stirred at ambient temperature for 2 h, after which it was concentrated under reduced pressure. Purification by semipreparative reversed-phase HPLC [linear gradient: 45→48% B, 3CV (solutions used A: H_2O, B: acetonitrile)] afforded the title compound (6.53 mg, 9.7 μmol, 33%) was an orange powder. ^{1}H NMR (600 MHz, MeOD): δ = 7.74 (s, 1 H, CH_{trz}), 6.13 (s, 2 H, H_{Ar}), 4.36 (t, J = 7.2 Hz, 2 H, CH_2N_{trz}), 4.07 (dd, J = 4.2, 10.2 Hz, 1 H, 8-H), 3.71–3.67 (m, 2 H, 2-H, 8-H), 3.22 (dd, J = 8.4, 10.2 Hz, 1 H, 3-H), 3.09 (t, J = 10.2 Hz, 1 H, 4-H), 3.03–3.00 (m, 3 H, 6-H, =CCH_2), 2.79 (t, J = 7.2 Hz, 2 H, CH_2 alkyl), 2.73 (d, J = 6.0 Hz, 1 H, 1-H), 2.48 (dd, J = 1.8, 7.2 Hz, 2 H, CH_2NC=O), 2.45 (s, 6 H, 2 × CH_3), 2.39 (s, 6 H, 2 × CH_3), 2.00–1.97 (m, 1 H, CH_2 alkyl), 1.92–1.86 (m, 4 H, CH_2 alkyl), 1.69–1.64 (m, 2 H, CH_2 alkyl), 1.60–1.56 (m, 2 H, CH_2 alkyl), 1.36–1.25 (m, 7 H, CH_2 alkyl) ppm. ^{13}C NMR (150 MHz, MeOD): δ = 188.5, 154.9, 148.5, 147.9, 142.2, 132.6, 123.4, 122.8, 122.6, 79.1, 73.4, 69.4, 63.6, 51.2, 45.3, 42.4, 41.0, 36.8, 32.2, 31.1, 30.8, 29.9, 29.6, 29.1, 27.2, 25.9, 25.8, 16.5, 14.4 ppm. HRMS: calcd. for $[C_{34}H_{49}BF_2N_6O_5]$ $[M + H]^+$ 671.39044; found 671.39033.

Biotin-Ahx-Cyclophellitol Aziridine Derivative 46: Azide **5** (20 mg, 58 μmol) was dissolved in DMF (2 mL). Biotin-Ahx-alkyne **33** (23 mg, 58 μmol), $CuSO_4$ (0.14 mL of 100 mM solution in H_2O), and sodium ascorbate (0.14 mL of a 100 mM solution in H_2O) were added, and the solution was stirred at 80 °C for 18 h. The solution was concentrated under reduced pressure and purified by semipreparative reversed-phase HPLC (linear gradient: 18%→27%, 3 CV, solutions used: A: H_2O, B: acetonitrile) to yield **46** as a white powder (8.9 mg, 12 μmol, 17%). ^{1}H NMR (400 MHz, MeOD): δ = 7.85 (s, 1 H, CH_{trz}), 4.50 (dd, J = 5.2, 8.0 Hz, 1 H, SCH_2C*H*NH), 4.43 (s, 2 H, C_qCH_2NH), 4.37 (t, J = 6.8 Hz, 2 H, CH_2CH_2NH), 4.31 (dd, J = 4.4, 8.0 Hz, 1 H, CH_2C*H*NH), 4.06 (dd, J = 4.4, 10.0 Hz, 1 H, 8-H), 3.72–3.65 (m, 2 H, 2-H, 8-H), 3.24–3.14 (m, 4 H, 3-H, CH_2N_{trz}, CH biotin), 3.08 (t, J = 9.6 Hz, 1 H, 4-H), 3.03 (dd, J = 3.2, 6.0 Hz, 1 H, 6-H), 2.93 (dd, J = 4.6, 12.8 Hz, 1 H, SCH_2CH), 2.73 (d, J = 5.6 Hz, 1 H, 1-H), 2.71 (d, J = 12.0 Hz, 1 H, SCH_2CH), 2.84 (t, J = 8.0 Hz, 2 H, NC=OCH_2), 2.25–2.18 (m, 4 H, 2 × CH_2CONH), 2.02–1.96 (m, 1 H, 5-H), 1.95–1.86 (m, 2 H, CH_2Ah×), 1.79–1.58 (m, 9 H, CH_2 alkyl, CH_2Ahx, $COCH_2CH_2$), 1.55–1.42 (m, 4 H, CH_2CH_2CHS, CH_2CH_2CHS), 1.38–1.30 (m, 10 H, CH_2 alkyl, CH_2Ahx) ppm. ^{13}C NMR (100 MHz, MeOD): δ = 188.5, 176.0, 175.9, 166.1, 146.3, 124.1, 79.1, 73.4, 69.3, 63.6, 63.4, 61.6, 57.0, 51.3, 49.4, 45.3, 42.4, 41.1, 41.0, 40.2, 36.8, 36.7, 35.7, 31.2, 30.1, 29.9, 29.8, 29.6, 29.5, 27.5, 27.2, 26.9, 26.5, 25.9 ppm. HRMS: calcd. for $[C_{46}H_{57}BF_2N_{12}O_8S]$ $[M + H]^+$ 737.40201; found 737.40146.

BODIPY-cyclophellitol derivatives **34** and **35** have previously been used as activity-based glucosidase probes under the names MDW941 and MDW933, respectively (see ref.[7]). BODIPY-cyclophellitol aziridine **43** and biotin-Ahx-cyclophellitol aziridine **46** have been reported previously under the names BODIPY-aziridine cyclitol and biotin-Ahx-aziridine cyclitol (see ref.[9]).

Supporting Information (see footnote on the first page of this article): ^{1}H NMR and ^{13}C APT NMR spectra for all new compounds.

Acknowledgments

The authors are grateful for financial support from the European Research Council (ERC) (AdG, to H. S. O.), the Netherlands Organization of Scientific Research (NWO-CW) (grant to H. S. O.), and the Chinese Scholarship Council (CSC) (grant to J.-B. J.).

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Received: May 16, 2014
Published Online: August 14, 2014

