CALIFORNIA STATE UNIVERSITY, NORTHRIDGE

TOTAL SYNTHESIS OF ALVARADOINS E & F,
UVEOSIDE, AND 10-EPI-UVEOSIDE

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By

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DEDICATION

I would like to dedicate this work to my parents. It was their unconditional love and support that kept me going in the Masters program. They came to America without being able to speak a word of English to pursue a better life for my sister and I. I'm forever grateful to them and for that reason I strive to succeed and want to make them proud.

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LIST OF ABBREVIATIONS

Ac ₂ O	Acetic anhydride
AcOH	Acetic acid
AgOAc	Silver acetate
AgOBz	Silver benzoate
BF ₃ •OEt ₂	Boron trifluoride etherate
BnBr	Benzyl bromide
BzOH	Benzoic acid
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCM	Dichloromethane
DMF	Dimethylformamide
Et ₃ N	Triethylamine
EtOAc	Ethyl acetate
EtOH	Ethanol
MeOH	Methanol
NaOMe	Sodium methoxide
Pb(OAc) ₄	Lead tetraacetate
TEMPO	2,2,6,6-Tetramethyl-1-piperidinyloxy
THF	Tetrahydrofuran
<i>t</i> -BuLi	<i>tert</i> -butyllithium

ABSTRACT

TOTAL SYNTHESIS OF ALVARADOINS E & F, UVEOSIDE, AND 10-EPI-UVEOSIDE

By

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Master of Science in Chemistry

Alvaradoins E and F, uveoside, and 10-epi-uveoside belong to the anthrone *C*-glycoside family of natural products. They are an intriguing class of natural products which consist of a carbohydrate unit connected to an anthracenone moiety at its *C*-10 position through a glycosidic bond. All four natural products have been shown to exhibit pronounced cytotoxicities toward human oral epidermoid carcinoma (KB) cell lines; furthermore, alvaradoin E was demonstrated to induce apoptosis of cultured LNCaP cells. The first total syntheses of the anthracenone *C*-glycosides alvaradoins E and F, uveoside, and 10-epi-uveoside have been accomplished in eleven steps each from chrysophanic acid and a protected bromogalactose. Key steps in the synthetic pathways include a DBU-induced substitution reaction to stereoselectively produce a β -*C*-glycoside, and a $\text{Pb}(\text{OAc})_4$ -mediated Kochi reaction to introduce the *C*-1' oxygen atom of the natural products.

Chapter 1: Chemical and Biological Significance of Anthrone C-Glycosides

1.1 Introduction

There are a wide variety of compounds produced by nature which exhibit significant biological activities, such as antibacterial, antifungal, and antitumor properties.¹ An example is the anthracycline family, an *O*-glycoside class of chemotherapeutic compounds isolated from *Streptomyces peucetius* var. *caesius*.² Currently, they are among the most effective treatments against a variety of cancer types including the two most predominant types of cancer afflicting the world, lung cancer (with 16% incidence) and breast cancer (with 32% incidence).³ Daunorubicin and valrubicin are examples of the anthracycline family of natural products (Figure 1.1.1). Daunorubicin is used in the treatment of acute myeloid leukemia and valrubicin has medicinal activity against bladder cancer.⁴

Figure 1.1.1 Examples of *O*-glycosides

The examples shown above (daunorubicin and valrubicin) are *O*-glycosides. While natural products containing carbon-oxygen linkages are common, these *O*-aryl linkages are subject to acidic hydrolysis and enzymatic degradation. Replacing the carbon-oxygen bond with a carbon-

carbon bond linkage between the carbohydrate and aromatic moieties affords a new class of structures, the *C*-aryl-glycosides. Examples are kidamycin and galtamycinone, possessing the characteristic glycosidic *C-C* bond and an aromatic aglycone unit (Figure 1.1.2). *C*-glycosides have been important targets for natural product synthesis, since it has been shown that both the aromatic and carbohydrate moieties of these compounds interact with DNA, resulting in intercalation and sequence-specific binding.⁵ Furthermore, the carbon-carbon bond at the anomeric center of *C*-glycosides gives the molecules impressive stability under normal physiological conditions towards most enzymatic degradation pathways and hydrolytic cleavage (Scheme 1.2), resulting in an extended half-life in the cytoplasm.

Figure 1.1.2 Examples of *C*-glycosides

Kidamycin

Galtamycinone

1.2 Enzymatic cleavage of *O*-glycosides

Polysaccharides are polymers of carbohydrates linked by oxygen atoms. Enzymes such as amylase and maltase, both commonly found in nature, are responsible for the conversion of polysaccharides into their simple monomers which are then absorbed into the bloodstream.⁶ Mechanistically, cleavage of an *O*-glycosidic bond can occur with or without retention of configuration at the anomeric center. In the presence of a proton donor from the enzyme, the exocyclic oxygen in *O*-glycosides partakes in hydrogen bonding to create a better leaving group (Scheme 1.2). Once the exocyclic oxygen bond is broken, an oxocarbenium ion is formed and one of two mechanistic pathways takes place, resulting in either stereochemical retention or inversion at the anomeric center.⁷ In the invertive glycosidase pathway, a nucleophile such as water attacks the oxocarbenium ion exclusively from the bottom face, leading to the α - product. In the retention pathway, the departure of the leaving group is assisted by a carboxylate moiety in close proximity to the anomeric carbon atom. The presence of a water molecule hydrolyzes the glycosyl-enzyme bond to form the β - product.⁸ The initial protonation of the exocyclic oxygen plays a crucial role in the hydrolysis of carbohydrates featuring an *O*-glycoside linkage. This reveals why *C*-glycosidic compounds are more stable compared to *O*-glycosidic compounds: the carbon linkage at C-1 cannot be activated as a leaving group by acid, and therefore no hydrolysis can occur.

Scheme 1.2 General enzymatic pathway of a glycosidic cleavage

Inversion pathway:

Retention pathway:

1.3 DNA interaction

Due to their significant biological properties, particularly anticancer activity, C-aryl glycosides have attracted considerable interest in research. Since DNA is responsible for important cellular processes necessary for cell growth and differentiation, it is a desirable target for drugs. Many DNA targeting drugs are responsible for single strand cleavage due to unwinding of the helix.⁹ DNA interaction with C-aryl glycosides occurs by intercalation of the aromatic chromophore into the base pair stack of the helix, and specific base pair binding *via* non-covalent interactions (such as hydrogen bonding and van der Waals interactions) of the carbohydrate moiety in either the minor or major grooves of DNA.¹⁰ The pluramycin family of natural products, including hedamycin, kidamycin, and altromycin, has been well studied and shown to intercalate with DNA through DNA unwinding studies.¹¹ Intercalation by a drug will unwind the double helix of DNA and delay migration on gel electrophoresis, resulting in streaking bands. In addition to intercalation, molecules may also covalently modify DNA through alkylation. For example, kidamycin intercalates duplex DNA *via* a planar aromatic chromophore with the carbohydrate moieties positioning themselves along the minor groove to allow for non-covalent interactions with cytosine and guanine. (Figure 1.3.1) Additionally, kidamycin features a vinyl group that is proposed to alkylate DNA *via* a [2+2] photo-induced cycloaddition. The vinyl group can also be oxidized to an epoxide that can be readily attacked by a nitrogen lone pair of either adenine or guanine.¹² Electrostatic interaction of positively charged ammonium ions (carbohydrate amines protonated at physiological pH) with the negatively charged phosphate backbone of DNA also increases the affinity of C-aryl glycosides for DNA.

Figure 1.3.1 DNA interaction of kidamycin

The pluramycin family of natural products can also alkylate or covalently bind to DNA. Alkylation can occur by the nucleophilic ring opening of the epoxide side chain by a guanine base on DNA. This consequently leads to a DNA lesion as a result of forming a modified base. (Scheme 1.3.2)

Scheme 1.3.2 DNA binding mechanism of pluromycin

1.4 Anthrone C-glycosides

An intriguing class of natural products are the anthrone C-glycosides, which consist of a carbohydrate unit connected to an anthracenone moiety at its C-10 position through a glycosidic bond.¹³ A considerable number of compounds of this family of natural products have been isolated over the past few decades and all of them have shown significant biological activities.¹⁴ For example, cassialoin (Figure 1.4), a representative member of this class, was isolated from plant extracts traditionally used in Ayurvedic and Asian folk medicine, namely a heartwood of *Cassia garrettiana craib* or the roots of *Rheum emodi wall*.¹⁵ This family of compounds, which contains such a unique sugar-anthrone hybridized structure, presents challenges for stereocontrolled synthesis, as well as for structure elucidation.

Figure 1.4 Cassialoin, an anthrone C-glycoside

Chapter 2: Methodology in Anthrone C-Glycoside Synthesis

2.1 Introduction

In the past few decades, there have been numerous studies on the isolation and biological profile of anthrone *C*-glycosides; however, limited investigations in the area of anthrone-*C*-glycoside synthesis have been performed. Cassialoin (Figure 1.4), an anthrone-*C*-glycoside, was the first of this class of natural products to be synthesized by Suzuki et al.¹³

2.2 Alkylation of anthrones

Alkylation of anthrones was demonstrated by the Steiger group in 1986 (Scheme 2.2), who showed that treatment of an anthrone with a base, such as potassium carbonate, and an alkylating agent, such as methyl iodide, results in regioselective alkylation at the C-10 position of the anthrone chromophore.¹⁶ The purpose of this study was to determine whether alkylation at *C*-10 changes the anti-psoriatic properties of anthrones.

Scheme 2.2 Alkylation of anthrone

2.3 In-vitro biosynthesis of the *C*-glycosidic bond in aloin

The available knowledge about the mechanism of *C*-glycoside biosynthesis, and in particular about the formation of C-C linkages of sugars to anthrones, is rather poor. In the different natural compounds with this type of linkage (for example, flavonoids, anthracenone, and xanthrone derivatives), the sugar moiety is always connected to a carbon atom of nucleophilic character, like

the carbon atom *ortho*- or *para*- to a phenolic hydroxyl group. In a study performed by Franz, aloe emodin anthrone (AEA) was mixed with uridine-5'-diphosphate glucose (UDP-Glc) along with a glycosyl transferase enzyme to obtain an anthrone C-glycoside *in vitro* (Figure 2.3).¹⁷ The general reaction mechanism of C-glycosylation may be thought to be similar to O-glycosylation in that an NDP-sugar is transferred to the nucleophilic carbon atom of the anthrone.

Figure 2.3 In-vitro biosynthesis of aloin

2.4 Total synthesis of cassialoin

The first total synthesis of an anthrone C-glycoside natural product was carried out by Suzuki et al. in 2008.¹³ A key step in the synthesis of cassialoin involved the nucleophilic attack of a glycal carbohydrate on an anthraquinone chromophore resulting in the formation of the anthrone-sugar glycosidic bond (Scheme 2.4). A negative aspect of this method is the use of *t*-BuLi as the organometallic reagent for glycal deprotonation; *t*-BuLi is extremely pyrophoric and dangerous to handle. Therefore, we wished to develop a synthesis of this class of natural products which utilizes milder conditions for the formation of the crucial glycosidic carbon-carbon bond.

Scheme 2.4 Synthesis of cassialoin

Chapter 3: Synthesis of alvaradoins E & F, uveoside and 10-epi-uveoside

3.1 Introduction

The anthracenone C-glycosides alvaradoin E (**1**, Figure 3.1) and alvaradoin F (**2**, Figure 3.1) were first isolated from the leaves of the tropical tree *Alvaradoa haitiensis* in 2005 and 2007.^{18,19} Both substances exhibited pronounced cytotoxicities toward human oral epidermoid carcinoma (KB) cell lines ($EC_{50}(\mathbf{1}) = 0.050 \mu\text{M}$; $EC_{50}(\mathbf{2}) = 0.065 \mu\text{M}$) among others; furthermore, alvaradoin E was demonstrated to induce apoptosis of cultured LNCaP cells. These results prompted the investigators to evaluate the *in vivo* activity of **1** and **2** in the P388 murine lymphocytic leukemia model. Alvaradoin E showed antileukemic activity (125% T/C) at a dose of 0.2 mg/kg per injection when administered intraperitoneally.

Uveoside (**3**, Figure 3.1) was isolated in 1998 from the chloroform extract of the roots of *Picramnia antidesma* by Hernandez-Medel and co-workers²⁰; further work on the root bark of *Picramnia antidesma* by the same research group resulted in the isolation (in 2002) of 10-epi-uveoside (**4**, Figure 3.1), a substance also displaying elevated cytotoxicity toward KB cells.²¹

Figure 3.1 Chemical structures of alvaradoins E and F, uveoside, and 10-epi-uveoside

3.2 Objectives and retrosynthetic analysis

Alvaradoins E and F, uveoside, and 10-*epi*-uveoside attracted our attention for three main reasons. First, this family of *C*-glycoside natural products has important biological activities. Second, there has only been a single previous synthesis of a related anthrone *C*-glycoside; therefore, we attempted the synthesis in order to provide an alternative pathway to this family of compounds. Third, we envisioned that the planar structure of the anthrone chromophore would interact with DNA via intercalation, and that the glycoside moiety could selectively bind to different sequences of DNA based on the orientation of the hydroxyl groups.

Based upon our review of the literature, we envisioned that the molecule could be disconnected at the *C*-*C* bond between the anthrone chromophore and the carbohydrate moiety leading to two fragments, compounds **8** and **9a** (Scheme 3.2). Compound **8** could be synthesized from commercially available chrysophanic acid.²² Compound **9a** could be synthesized from commercially available β -D-galactose pentaacetate.²³ A synthetic challenge we anticipated while developing a synthesis for compounds **1–4** was the installation of the acid-labile anomeric C-1' acetate and benzoate esters. We envisioned that with a carboxylic acid precursor, a Hunsdiecker-type reaction^{24,25} could allow us to install the C-1' oxygen atom in the final steps of the synthesis.

Scheme 3.2 Retrosynthetic analysis of alvaradoins E and F, uveoside, and 10-*epi*-uveoside

- 1** Alvaradoin E: X= α -H, Y=OAc
2 Alvaradoin F: X= β -H, Y=OAc
3 Uveoside: X= β -H, Y=OAc
4 10-*epi*-Uveoside: X= α -H, Y=OAc

3.3 Synthesis of fragment 8

The synthesis commenced with the preparation of the chrysothrone chromophore. According to the protocol of Sevenet *et. al.*²², commercially available chrysophanic acid was reduced using SnCl_2 under acidic conditions with AcOH and HCl to furnish chrysothrone **8** in 94% yield. (Scheme 3.3)

Scheme 3.3 Synthesis of fragment 8

3.4 Synthesis of fragment 9a

Following the protocol established by Anderson *et al.*²³, commercially available β -D-galactose pentaacetate was treated with HBr/AcOH to give the C-1 α -bromoglycoside exclusively. The crude product was then treated with trimethyl orthoformate and a catalytic amount of BiCl_3 to furnish **9b** in 99% yield. Deprotection of the acetates under basic conditions, followed by benzyl protection furnished compound **9c** in 76% overall yield. Acetolysis of the methyl glycoside under acidic conditions provided the corresponding diacetate **9a** in 86% yield.

Scheme 3.4 Synthesis of fragment 9a

3.5 Model studies for the formation of anthrone-C-glycoside

With the routes to the anthrone chromophore and glycoside established, we decided to perform model studies toward a direct C-glycoside synthesis by combining anthracenones with C-1 bromosugars under basic conditions. Our initial attempt utilized anthralin²⁶ **5** (prepared by reducing 1,8 dihydroxyanthraquinone with SnCl₂) as the nucleophile and bromoglucoside²⁷ **6b** as the carbohydrate electrophile for the substitution reaction. Treating compound **5** in a solution of CH₂Cl₂ with DBU, followed by addition of compound **6b**, led to the formation of C-glycoside **7**. After flash chromatography, it was found that compound **7** was formed in 42% yield as a 7:1 mixture of β and α stereoisomers at C-5' based on the coupling constants obtained from ¹H NMR. β-stereoisomer: H-5' = 9.6 Hz; α-stereoisomer: H-5' = 3.7 Hz (Scheme 3.5.1). Possible mechanism for the formation of compound **7** and the isomeric product are shown (Scheme 3.5.2 and 3.5.3)

Scheme 3.5.1 Model studies for the formation of the anthrone-C-glycoside **7**

Scheme 3.5.2 Possible mechanism for the formation of anthrone C-glycoside **7**

Scheme 3.5.3 Possible mechanism for the formation of C-5' α -anomer of compound **7**

Motivated by this result, we then prepared bromogalactoside **9d** by treating 1,6-di-*O*-acetyl-2,3,4-tribenzyl-galactose **9a** with HBr/AcOH. Combination of **9d** with **5** in the presence of DBU lead to a 65% yield of C-glycoside **10** as a single β -stereoisomer ($>20:1$ $\beta:\alpha$) at C-5'. (Scheme 3.5.2)

Scheme 3.5.4 Model studies for the formation of the anthrone-C-glycoside **10**

Encouraged by the success of the model systems, we then treated a mixture of **9d** and chrysophanol (**8**) with DBU, which provided a 51% yield of C-glycoside **11**, again with the β stereoisomer in excess ($>20:1$ $\beta:\alpha$ at C-5'); in addition, a 1:1 mixture of diastereomers was formed

at C-10. (Scheme 5.5.3) Accounting for the balance of the materials used in these reactions, TLC also showed the formation of oxidized aromatics (anthraquinones) as well as hydrolyzed carbohydrates (**6** or **9**, R₂ = OH). All attempts to improve the yields by performing the reaction under vigorously anhydrous and anaerobic conditions led to no significant change.

Scheme 3.5.5 Formation of the anthrone-C-glycoside **11**

3.6 Formation of carboxylic acid intermediate

With the formation of the anthrone-glycoside C-C bond established, the next step was to manipulate the C-1' position of the carbohydrate moiety. Prior to the manipulation, we first had to protect the alcohols on the C-1 and C-8 position of the anthrone with a protecting group that is resistant to the hydrolytic conditions necessary for the removal of the C-6' acetate. Initial studies using a pivalate ester protecting group showed promising results; however, late stage removal under nucleophilic, acidic, or basic conditions proved to be problematic, and thus we switched to the less bulky isobutyrate ester. The isobutyrate esters were installed by treating compound **11** with isobutyryl chloride and triethylamine in CH₂Cl₂ (Scheme 3.6). With the protecting groups in place, we were now able to selectively manipulate the C-1' position of the carbohydrate. Hydrolysis of the primary acetate was achieved via the treatment of 5% HCl in methanol, resulting in the formation of the primary alcohol **12** in 77% overall yield. The primary alcohol was then

oxidized to carboxylic acid via a TEMPO-catalyzed oxidation under Zhao's conditions²⁸, to afford compound **13** in 76% yield.

Scheme 3.6 Formation of carboxylic acid intermediate

3.7 Conversion to anomeric acetate

With carboxylic acid **13** in hand, we then explored various reaction conditions for transforming compound **13** into the corresponding glycosyl halide via the Hunsdiecker reaction.^{24,25} It was then discovered that utilizing Kochi's method,²⁹ which involves treatment of carboxylic acid **13** with lead tetraacetate in acetic acid and THF, leads to a clean and stereoselective conversion to α -acetate ester **14**. An explanation for the stereoselective conversion could be due to the neighboring C-2' axial benzyl group hindering attack of the nucleophile from the same face (Scheme 3.7.2). Another reason could be the anomeric effect which is the stabilizing interaction between the lone pair of the oxygen in the ring and the σ^* orbital for the axial (exocyclic) bond leading to the favorable formation of the axial anomer.³⁰ (Scheme 3.7.3) This reaction leads to moderate yields (40%); however, the starting material could be efficiently recovered in good yields (51%) and recycled to increase the overall throughput to compound **14**. (Scheme 3.7.1). Attempts to optimize the reaction by running it for 20 hours compared to 2 hours led to no significant change either in yield or stereochemistry at C-1'. Heat or treatment with strong acid were not performed at this step. Experimental results obtained thus far suggest this reaction is a kinetically-controlled process.

Scheme 3.7.1 Conversion to anomeric acetate

Scheme 3.7.2 Possible mechanism for the stereochemical control

Scheme 3.7.3 Anomeric effect favoring the formation of the axial substituent

3.8 Hydrolysis of isobutyrate and acetate esters

We next attempted hydrolysis of the isobutyrate and acetate esters. Treatment of compound **14** under basic conditions (NaOMe in MeOH; cat. NaCN, MeOH; RNH₂, MeOH) resulted in substrate decomposition and the formation of anthraquinone side products. In addition, the recovered *C*-glycosides were obtained a mixture of stereoisomers at C-5' (Scheme 3.8). Exposure of compound **14** to acidic conditions (5–20% HCl in MeOH) resulted in elimination of the C-1' acetate group and the formation of alkene-containing side products. After considerable amounts of experimentation, we found that solvolysis of the acetate with allyl alcohol could be achieved with BF₃·OEt₂ as the Lewis acid to form the allyl glycoside. Treatment of the allyl glycoside with 20% HCl in MeOH at 40 °C gave diol **15** in 73% overall yield. Compound **15** was then subjected to 10 mol % PdCl₂ in MeOH and THF, which resulted in clean formation of the α -hemiacetal **16** in 86% yield.³¹

Scheme 3.8 Hydrolysis of isobutyrate and acetate esters

3.9 Completion of the Synthesis of Alvaradoins E and F

In order to form alvaradoins E and F, we needed to install an acetate moiety at C-1' position of the carbohydrate. Compound **16** was treated with HBr in acetic acid to form the C-1' glycosyl bromide, which was then immediately combined with silver acetate in acetic acid to give the α -acetate ester^{32,33} **17** in 73% yield (Scheme 3.9). Hydrogenation of compound **17** with Pearlman's catalyst³⁴ then afforded a 1:1 mixture of diastereomers of alvaradoins E and F in 95% yield, which could be separated by careful and repeated column chromatography (SiO₂, 98:2 $\rightarrow$ 94:6 CHCl₃/MeOH). NMR (¹H and ¹³C), high-resolution mass spectrometry (HRMS), and optical rotation data recorded for synthetic alvaradoins E and F matched those reported for the natural compounds.

Scheme 3.9 Completion of the Synthesis of Alvaradoins E and F

3.10 Completion of the Synthesis of Uveoside and 10-epi-Uveoside

To prepare uveoside and 10-epi-uveoside, treatment of compound **16** with HBr in acetic acid gave the expected intermediate glycosyl bromide, which upon treatment with silver benzoate and benzoic acid in CH_2Cl_2 gave the α -benzoate **18** in 76% yield. Hydrogenation with Pearlman's catalyst³⁴ then provided a 1:1 mixture of diastereomers of uveoside and 10-epi-uveoside in 90% yield (Scheme 3.10), which could be separated by radial chromatography.³⁵ Once again, NMR (^1H and ^{13}C), MS, and optical rotation data recorded for synthetic uveoside and 10-epi-uveoside matched with those reported for the natural compounds.

Scheme 3.10 Completion of the Synthesis of Uveoside and 10-epi-Uveoside

Chapter 4: Conclusion

The total synthesis of alvaradoins E and F, uveoside, and 10-epi-uveoside have been achieved in eleven steps each from chrysophanic acid and a benzyl-protected bromogalactoside. Key steps in the synthesis include a base-induced substitution reaction for the stereoselective formation of a β -C-glycoside, and a Kochi reaction to introduce the C-1' oxygen atom of the natural products using $\text{Pb}(\text{OAc})_4$. Preliminary DNA and protein (human serum albumin) binding studies were performed on compounds **1-4** by Minehan research group members, Ryan Shaktah and Laura Vardanyan. It was found that while compounds **1-4** have a poor affinity ($K_a < 10^5 \text{M}^{-1}$) for duplex DNA, compounds 1 and 2 have good affinity ($K_a > 1 \times 10^5 \text{M}^{-1}$) for the plasma protein HSA. Further studies on the biological mode of action of these compounds are underway, but these preliminary results may shed some light on the possible intracellular targets of these compounds.

Chapter 5: Experimental

General Information

Deionized water was used in all of the experiments. Organic extracts were dried over Na_2SO_4 , filtered, and concentrated using a rotary evaporator at water aspirator pressure (20-30 mm Hg). Chromatography refers to flash chromatography and was carried out on SiO_2 ³⁶ (silica gel 60, 230-400 mesh). ^1H and ^{13}C NMR spectra were measured at 400 MHz and 100 MHz, respectively, with a Bruker Avance III 400 NMR spectrometer. Chemical shifts were reported relative to internal CHCl_3 (^1H , $\delta = 7.26$) and CDCl_3 (^{13}C , $\delta = 77.0$). IR spectra were recorded on a Perkin Elmer Spectrum 100 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired from Bruker Daltonics micrOTOF-Q w/Agilent 1200 HPLC. Optical rotations were measured on a Perkin Elmer Model 341 polarimeter using a 100 mm path-length cell at 589 nm.

Compound **6a** (270 mg, 0.50 mmol) was dissolved in CH_2Cl_2 (1.7 mL, 0.3 M) and the solution was cooled to 0 °C. HBr in AcOH (33% solution, 0.18 mL, 2 eq.) was added dropwise and the reaction mixture was stirred at 0 °C for 1 hr. After TLC indicated complete conversion, the reaction mixture was neutralized with saturated NaHCO_3 solution (10 mL) and diluted with CH_2Cl_2 (10 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude oil, **6b**.

To a flask containing anthralin **5** (137 mg, 0.6 mmol, 1.2 eq.), CH_2Cl_2 (2.0 mL, 0.3 M) was added. DBU (83 μL , 0.55 mmol, 1.1 eq.) was added dropwise. The reaction mixture was stirred at rt for 15 minutes. Separately, **6b** was dissolved in CH_2Cl_2 (0.5 mL, 1 M) and was cannulated dropwise into the anthralin reaction mixture flask. The reaction mixture was stirred for 1 hour and was then quenched with saturated NH_4Cl solution (10 mL), diluted with CH_2Cl_2 (10 mL); the phases were separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (9:1 $\rightarrow$ 5:1 hexanes: ethyl acetate) afforded **7** (149 mg, 0.21 mmol, 42%, 7:1 β : α).

¹H NMR (400 MHz, CDCl₃):

11.95 (s, 1H, OH-8); 11.90 (s, 1H, OH-1); 7.50-7.27 (m, 17H, OBn, H-2, H-3); 7.23 (m, 2H, OBn); 6.98 (d, *J*=7.4 Hz, 1H, H-7); 6.91 (dt, *J*=0.7, 8.3 Hz, 1H, H-6); 6.63 (d, *J*=7.3 Hz, 1H, H-4); 5.15 (d, *J*=11.7 Hz, 1H, CH₂,OBn); 4.96 (d, *J*=10.9 Hz, 1H, CH₂, OBn); 4.85-4.73 (m, 3H, CH₂, OBn); 4.52 (d, *J*=11.0 Hz, 2H, CH₂, OBn, H-10); 4.25 (dd, *J*=1.9, 11.7 Hz, 1H, CH₂, OBn); 3.87 (dd, *J*=5.1, 11.6 Hz, 1H, H-6'); 3.72 (t, *J*=8.5 Hz, 1H, H-1'); 3.51 (dd, *J*=1.6, 9.6 Hz, 1H, H-5'); 3.40 (dd, *J*=8.8, 9.5 Hz, 1H, H-2'); 3.26-3.14 (m, 2H, H-3', H-4'); 1.98 (s, 3H, OAc).

¹³C NMR (100 MHz, CDCl₃):

194.1 (C-9), 170.4 (C=O, OAc), 162.1 (C-1), 161.7 (C-8), 144.9, 140.9, 138.2, 137.8, 137.4, 135.8, 134.9, 128.6, 128.5, 128.4, 127.9, 127.8, 127.5, 127.2, 119.2, 118.4, 117.9, 117.3, 116.4, 116.2, 87.6, 84.0, 78.3 (C-5'), 77.1, 76.4, 75.4, 75.0 (C-3'), 73.5 (C-4'), 62.5 (C-2'), 44.6 (C-10), 20.3 (CH₃, OAc).

HRMS–ESI (m/z): calculated for C₄₃H₄₀O₉: 700.2672; found 700.2682 (M)⁺

[α]_D²⁵ = -4.2° (c 0.021, CH₂Cl₂)

IR: 3500-2950 cm⁻¹ (broad), 3328, 3063, 2852, 1741, 1618 (shoulder), 1606, 1604

Compound **9a** (267 mg, 0.50 mmol) was dissolved in CH_2Cl_2 (1.7 mL, 0.3 M) and the solution was cooled to 0 °C. HBr in AcOH (33% solution, 0.18 mL, 2 eq.) was added dropwise and the reaction mixture was stirred at 0 °C for 1 hr. After TLC indicated complete conversion, the reaction mixture was neutralized with saturated NaHCO_3 solution (10 mL) and diluted with CH_2Cl_2 (10 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude oil, **9b**.

To a flask containing anthralin **5** (141 mg, 0.62 mmol, 1.24 eq.), CH_2Cl_2 (2.0 mL, 0.3 M) was added. DBU (83 μL , 0.55 mmol, 1.1 eq.) was then added dropwise. The reaction mixture was stirred at rt for 15 minutes. Separately, **9b** was dissolved in CH_2Cl_2 (0.5 mL, 1 M) and was cannulated dropwise into the anthralin reaction mixture flask. The reaction mixture was stirred for 1 hour and was then quenched with saturated NH_4Cl solution (10 mL), diluted with CH_2Cl_2 (10 mL); the phases were separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (10:1 $\rightarrow$ 4:1 hexanes: ethyl acetate) afforded **10** (231 mg, 0.33 mmol, 65%, >20:1 β : α).

¹H NMR (400 MHz, CDCl₃):

12.01 (s, 1H, OH-8); 11.91 (s, 1H, OH-1); 7.42-7.27 (m, 16H, OBn); 7.04-7.00 (m, 3H); 6.91 (d, $J=4.9$ Hz, 1H); 6.89 (d, $J=4.8$ Hz, 1H); 6.69 (d, $J=7.4$ Hz, 1H); 5.09 (d, $J=11.6$, 1H, CH₂, OBn); 4.82 (d, $J=11.8$ Hz, 1H, CH₂, OBn); 4.73 (d, $J=11.5$, 1H, CH₂, OBn); 4.69 (d, $J=11.6$, 1H, CH₂, OBn); 4.60-4.55 (m, 1H); 4.40 (d, $J=11.9$ Hz, 1H, CH₂, OBn); 3.97-3.86 (m, 2H); 3.77 (t, $J=9.2$ Hz, 1H, H-1'); 3.69 (d, $J=2.0$ Hz, 1H); 3.59 (dd, $J=2.4, 9.0$ Hz, 1H, C-5'); 3.50 (dd, $J=1.6, 9.4$ Hz, 1H, H-4'); 3.34 (dd, $J=5.1, 7.4$ Hz, 1H, H-3'); 1.95 (s, 3H, OAc).

¹³C NMR (100 MHz, CDCl₃):

194.3 (C-9), 170.8 (C=O, OAc), 162.1 (C-1), 161.7 (C-8), 145.0, 141.6, 138.5, 138.4, 137.5, 135.8, 135.0, 128.5, 128.5, 128.1, 127.9, 127.7, 127.6, 127.3, 127.2, 126.6, 119.4, 118.7, 117.8, 117.4, 116.3, 116.0, 85.5, 84.6, 75.4 (C-5'), 74.3, 73.9, 73.3, 72.9 (C-3'), 71.9 (C-4'), 63.4 (C-2'), 45.0 (C-10), 20.6 (CH₃, OAc).

HRMS–ESI (m/z): calculated for C₄₃H₄₀O₉: 700.2672; found 700.2682 (M)⁺

[α]_D²⁵ = +9.5 ° (c 0.006, CH₂Cl₂)

IR: 3500-2950 cm⁻¹ (broad), 3063, 2854, 1741, 1625 (shoulder), 1613, 1610

Compound **9a** (1 g, 1.87 mmol) was dissolved in CH_2Cl_2 (6.2 mL, 0.3 M) and the solution was cooled to 0 °C. HBr in AcOH (33% solution, 0.68 mL, 2 eq.) was added dropwise and the reaction mixture was stirred at 0 °C for 1 hr. After TLC indicated complete conversion, the reaction mixture was neutralized with saturated NaHCO_3 (20 mL) and diluted with CH_2Cl_2 (20 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 15 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude oil, **9b**.

To a flask containing chrysothronone **8** (540 mg, 1.2 eq.), CH_2Cl_2 (7.5 mL, 0.3 M) was added. DBU (0.31 mL, 1.1 eq.) was added dropwise. The reaction mixture was stirred at rt for 15 minutes. Separately, **9b** was dissolved in CH_2Cl_2 (1.9 mL, 1 M) and was cannulated dropwise to the chrysothronone reaction mixture flask. The reaction mixture was stirred for 1 hour. The reaction mixture was then quenched with saturated NH_4Cl solution (20 mL), diluted with CH_2Cl_2 (20 mL), and the phases were separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 15 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (9:1 $\rightarrow$ 5:1 hexanes: ethyl acetate) afforded **11** (682 mg, 0.954 mmol, 51%, >20:1 β : α , as a 1:1 mixture of diastereomers at C.10).

¹H NMR (400 MHz, CDCl₃):

12.17 (s, 1H, OH-8); 12.04 (s, 2H, OH-8, OH-1); 11.93 (s, 1H, OH-1); 7.44-7.29 (m, 31 H, OBn); 7.13-7.05 (m, 5H, OBn); 6.93 (dd, *J*=0.7, 2.7 Hz, 1H); 6.91 (dd, *J*=0.8, 2.7 Hz, 1H); 6.87 (s, 1H, H-2); 6.74 (d, *J*=4.4 Hz, 2H); 6.72 (d, *J*=7.4 Hz, 1H); 6.56 (s, 1H, H-4); 5.13 (d, *J*=11.7 Hz, 1H, CH₂, OBn); 5.12 (d, *J*=11.5 Hz, 1H, CH₂, OBn); 4.89 (d, *J*=11.7, 1H, CH₂, OBn); 4.88 (d, *J*=11.8 Hz, 1H, CH₂, OBn); 4.77 (s, 1H), 4.74 (s, 1H); 4.71-4.60 (m, 4H); 4.54 (s, 1H); 4.53 (s, 1H); 4.47 (d, *J*=11.8 Hz, 1H); 4.46 (d, *J*=11.8 Hz, 1H); 4.06-4.01 (m, 2H); 3.99-3.94 (m, 2H); 3.84-3.77 (m, 2H); 3.75 (s, 2H); 3.64 (d, *J*=1.7, 1H); 3.62 (d, *J*=1.7 Hz, 1H); 3.58-3.54 (m, 2H); 3.41 (t, *J*=6.2 Hz, 2H, H-3'); 2.34 (s, 3H, CH₃); 2.32 (s, 3H, CH₃); 2.01 (s, 3H, OAc); 2.01 (s, 3H, OAc).

¹³C NMR (100 MHz, CDCl₃):

193.6 (C-9), 193.6 (C-9), 170.6 (C=O, OAc), 162.1 (C-1), 162.0 (C-1), 161.7 (C-8), 161.6 (C-8), 147.3, 146.5, 144.6, 144.6, 141.5, 141.5, 138.4, 138.4, 138.4, 138.3, 137.5, 135.4, 134.7, 128.4, 128.4, 128.0, 128.0, 127.8, 127.8, 127.7, 127.6, 127.5, 127.5, 127.2, 127.1, 126.6, 126.5, 120.5, 119.9, 119.2, 118.7, 117.6, 117.1, 116.3, 116.1, 116.0, 115.8, 115.3, 115.0, 85.5, 85.4, 84.8, 84.8, 75.3, 75.2, 74.4, 74.2, 73.8, 73.4, 73.3, 72.9, 71.9, 71.8, 63.3, 44.9 (C-10), 22.1, 22.0, 20.5.

HRMS–ESI (m/z): calculated for C₄₄H₄₂O₉: 714.2829; found 714.2842 (M)⁺

IR: 3500-3000 cm⁻¹ (broad), 3189, 1751, 1678, 1615, 1612

Compound **11** (665 mg, 0.93 mmol) was dissolved in CH₂Cl₂ (3.1 mL, 0.3 M). Isobutyryl chloride (0.20 mL, 2.02 eq.) and Et₃N (0.26 mL, 2.02 eq.) were added dropwise. The reaction mixture was stirred for 30 minutes at rt. After TLC indicated complete conversion, saturated aqueous NH₄Cl (20 mL) and CH₂Cl₂ (20 mL) were added. The phases were separated and the aqueous layer was further extracted with CH₂Cl₂ (2 x 15 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure to give a crude oil.

The crude oil was dissolved in 9:1 MeOH:THF (9.3 mL, 0.1 M). A solution of 5% HCl in MeOH (0.93 mL, 1 M) was added. The reaction mixture was stirred for 1 hr at rt. After TLC indicated complete conversion, the mixture was neutralized with saturated NaHCO₃ (20 mL) and concentrated under reduced pressure to removed MeOH. The residue was diluted with EtOAc (20 mL) and the phases were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (4:1 → 3:1 hexanes: ethyl acetate) afforded **12** (582 mg, 0.716 mmol, 77%, as a 1:1 mixture of diastereomers at C-10).

¹H NMR (400 MHz, CDCl₃):

7.52-7.40 (m, 10H, OBn); 7.40-7.26 (m, 17H, OBn); 7.25-7.20 (m, 4H); 7.11 (s, 1H); 7.05-6.95 (m, 6H, OBn), 6.93 (d, *J*=6.9 Hz, 1H, H-7); 6.85 (s, 1H, H-2); 6.80 (s, 1H); 6.76 (s, 1H, H-4); 5.25 (d, *J*=12.1 Hz, 1H, CH₂, OBn); 5.22 (d, *J*=12.0 Hz, 1H, CH₂, OBn); 4.95 (d, *J*=11.7 Hz, 1H, CH₂, OBn); 4.91 (d, *J*=11.8 Hz, 1H, CH₂, OBn); 4.74-4.64 (m, 4H); 4.61 (d, *J*=11.4 Hz, 1H); 4.60 (d, *J*=11.5 Hz, 1H, CH₂, OBn); 4.54 (t, *J*=1.9 Hz, 2H, H-10); 4.39 (d, *J*=11.9, 1H, CH₂, OBn); 4.38 (d, *J*=12.1, 1H, CH₂, OBn); 3.80-3.73 (m, 2H); 3.68-3.57 (m, 6H); 3.44 (t, *J*= 1.4 Hz, 1H); 3.42 (t, *J*=1.4 Hz, 1H, H-3'); 3.22-3.12 (m, 4H, H-2', H-4'); 2.99-2.84 (m, 4H, H-2'', H-6''); 2.39 (s, 3H, H-11); 2.28 (s, 3H, H-11); 1.43-1.34 (m, 24H, H-3'', H-4'', H-7'', H-8'').

¹³C NMR (100 MHz, CDCl₃):

183.9 (C-9), 183.9 (C-9), 176.0, 175.9, 175.1, 175.0, 149.0, 144.5, 144.4, 143.8, 142.3, 139.7, 139.7, 138.9, 138.8, 138.6, 137.7, 137.7, 132.5, 131.2, 128.6, 128.6, 128.5, 128.5, 128.5, 128.3, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.5, 127.0, 126.9, 126.9, 126.7, 126.5, 125.8, 125.3, 124.5, 122.9, 122.9, 122.3, 85.5, 82.1, 82.0, 79.9, 79.8, 75.0, 74.7, 74.1, 73.4, 73.3, 73.0, 73.0, 71.8, 71.6, 63.2, 45.2 (C-10), 34.0, 34.0, 21.5, 21.4, 18.9, 18.8, 18.6.

HRMS–ESI (m/z): calculated for C₅₀H₅₂O₁₀: 812.3560; found 812.3578 (M)⁺

IR: 3500-2950 cm⁻¹ (broad), 3135, 2971, 1757, 1673, 1617

Compound **12** (560 mg, 0.69 mmol) was dissolved in MeCN (3.45 mL, 0.2 M). Phosphate buffer (2.8 mL, 0.25 M, pH = 6.7) and TEMPO (7.5 mg, 0.07 eq.) were added. The reaction mixture was heated to 35 °C. A solution of NaClO₂ (156 mg, 2 eq.) in H₂O (0.7 mL, 2 M) and a dilute solution of bleach (0.35 mL, 2 mol %) were added dropwise to the reaction mixture. The reaction mixture was stirred at 35 °C for 2 hrs. After TLC indicated complete conversion, saturated aqueous Na₂SO₃ (15 mL) and CH₂Cl₂ (15 mL) were added. The phases were separated and the aqueous layer was further extracted with CH₂Cl₂ (2 x 15 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (1:1 hexanes: ethyl acetate, 1% AcOH) afforded **13** (434 mg, 0.524 mmol, 76%, as a 1:1 mixture of diastereomers at C-10).

¹H NMR (400 MHz, CDCl₃):

7.53-7.41 (m, 10H, OBn); 7.41-7.28 (m, 16H, OBn); 7.25-7.18 (m, 6H, OBn); 7.11 (s, 1H); 7.05-6.97 (m, 6H, OBn); 6.89 (d, $J=7.3$ Hz, 1H, H-7); 6.85 (s, 2H, H-2); 6.70 (s, 1H, H-4); 5.23 (d, $J=11.8$ Hz, 1H, CH₂, OBn); 5.21 (d, $J=11.6$ Hz, 1H, CH₂, OBn); 4.94 (d, $J=11.6$ Hz, 1H, CH₂, OBn); 4.90 (d, $J=11.8$ Hz, 1H, CH₂, OBn); 4.70 (d, $J=11.5$ Hz, 1H, CH₂, OBn); 4.69 (d, $J=11.5$ Hz, 1H, CH₂, OBn); 4.65-4.59 (m, 4H); 4.56-4.48 (m, 4H); 4.25 (s, 2H); 3.82 (dt, $J=3.1, 9.2$ Hz); 3.78 (s, 2H); 3.67 (t, $J=2.2$ Hz, 1H); 3.64 (t, $J=2.2$ Hz, 1H); 3.58 (s, 1H); 3.56 (s, 1H); 2.95-2.85 (m, 4H, H-2'', H-6''); 2.40 (s, 3H, H-11); 2.25 (s, 3H, H-11); 1.42-1.36 (m, 24H, H-3'', H-4'', H-7'', H-8'').

¹³C NMR (100 MHz, CDCl₃):

184.9 (C-9), 184.9 (C-9), 175.4, 175.3, 175.3, 175.2, 168.7, 168.7, 149.4, 149.3, 149.2, 149.1, 144.4, 143.3, 143.3, 143.2, 138.9, 138.9, 138.4, 138.3, 138.1, 138.1, 137.2, 132.9, 132.0, 128.7, 128.7, 128.6, 128.5, 128.5, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 126.9, 126.9, 126.8, 126.7, 126.4, 126.1, 125.8, 125.5, 125.3, 124.7, 123.4, 122.8, 122.7, 84.0, 83.1, 83.0, 76.9, 76.9, 74.1, 73.7, 73.6, 73.5, 73.4, 71.5, 71.4, 44.2, 44.2, 34.0, 21.5, 21.4, 18.8, 18.6.

HRMS–ESI (m/z): calculated for C₅₀H₅₀O₁₁: 826.3353; found 826.3373 (M)⁺

IR: 3477 cm⁻¹ (sharp spike), 2976, 2924, 2874, 1759, 1671, 1617, 1613

Compound **13** (410 mg, 0.50 mmol) was dissolved in THF (5.0 mL, 0.1 M). AcOH (0.09 mL, 3 eq.) and Pb(OAc)₄ (266 mg, 1.2 eq) were added. The reaction mixture was stirred at rt for 2 hrs. The reaction mixture was then filtered through a bed of Celite with EtOAc and the solvent was concentrated *in vacuo* to give an oil. Purification of the residue by flash chromatography (4:1 hexanes: ethyl acetate) afforded **14** (168 mg, 0.20 mmol, 40%, as a 1:1 mixture of diastereomers at C-10), and (1:1 hexanes: ethyl acetate, 1% AcOH) recovered **13** (210 mg, 0.254 mmol, 51%).

¹H NMR (400 MHz, CDCl₃):

7.47-7.37 (m, 7H, OBn); 7.37-7.27 (m, 24H, OBn); 7.20-7.14 (m, 5H, OBn); 7.11 (d, *J*=7.4 Hz, 1H, H-7); 7.03-6.89 (m, 2H); 6.92 (s, 1H, H-2); 6.84 (d, *J*=6.4 Hz, 1H, H-5); 6.82 (d, *J*=6.5, 1H, H-4); 5.98 (d, *J*=2.4 Hz, 2H, H-1'); 4.96 (d, *J*=11.8 Hz, 1H, CH₂, OBn); 4.93 (d, *J*=13.0 Hz, 1H, CH₂, OBn); 4.69 (d, *J*=11.4 Hz, 1H, CH₂, OBn); 4.65 (d, *J*=11.5 Hz, 1H, CH₂, OBn); 4.55-4.41 (m, 10H, CH₂, OBn); 3.96-3.90 (m, 2H); 3.90-3.82 (m, 2H); 3.82-3.76 (m, 2H); 3.63 (t, *J*=2.6 Hz, 2H); 3.01-2.87 (m, 4H, H-2'', H-6''); 2.35 (s, 3H, H-11); 2.33 (s, 3H, H-11); 1.85 (s, 3H, OAc); 1.84 (s, 3H, OAc); 1.45-1.40 (m, 24H, H-3'', H-4'', H-7'', H-8'').

^{13}C NMR (100 MHz, CDCl_3):

181.8 (C-9), 181.8 (C-9), 175.1, 175.0, 174.9, 174.8, 168.6, 149.5, 149.4, 149.4, 143.3, 142.9, 142.9, 142.7, 140.5, 140.4, 138.4, 138.3, 137.6, 137.6, 137.6, 132.1, 131.5, 128.3, 128.3, 128.3, 128.1, 127.9, 127.9, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.0, 126.3, 125.9, 125.4, 125.3, 125.1, 123.2, 123.2, 122.5, 91.8, 78.9, 78.8, 78.6, 78.5, 74.7, 74.5, 73.4, 73.3, 73.0, 72.7, 71.5, 71.4, 71.3, 45.1, 34.0, 34.0, 21.4, 21.3, 20.7, 20.6, 18.8, 18.8, 18.7, 18.7.

HRMS–ESI (m/z): calculated for $\text{C}_{51}\text{H}_{52}\text{O}_{11}$: 840.3510; found 840.3526 (M)⁺

IR: 3500-2950 cm^{-1} (broad), 3227, 2925, 1759, 1673, 1618

Compound **14** (250 mg, 0.30 mmol) was dissolved in CH₂Cl₂ (1.5 mL, 0.2 M) and the solution was cooled to 0 °C. Allyl-OH (0.04 mL, 2 eq.), BF₃·OEt₂ (0.19 mL, 5 eq.), and 4Å molecular sieves were added. The reaction mixture was stirred at rt for 16 hrs. The reaction mixture was then quenched with saturated NaHCO₃ solution (15 mL), diluted with CH₂Cl₂ (15 mL), and the phases were separated. The aqueous layer was then extracted with CH₂Cl₂ (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give a crude oil.

The crude oil was dissolved in THF (1.5 mL, 0.2 M). A solution of 20% HCl in MeOH (1.5 mL, 0.2 M) was added. The reaction mixture was stirred at 40 °C for 16 hrs. The reaction mixture was neutralized with saturated NaHCO₃ solution (15 mL) and diluted with EtOAc (15 mL). The phases were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (10:1 hexanes: ethyl acetate) afforded **15** (153 mg, 0.219 mmol, 73%, as a 1:1 mixture of diastereomers at C-10).

¹H NMR (400 MHz, CDCl₃):

12.16 (s, 1H, OH-8); 12.14 (s, 1H, OH-8); 12.05 (s, 1H, OH-1); 12.01 (s, 1H, OH-1); 7.48-7.39 (m, 10H, OBn); 7.39-7.26 (m, 18H, OBn); 7.07-6.98 (m, 5H, OBn); 6.97 (d, *J*=8.2 Hz, 1H, H-7); 6.91 (d, *J*=8.2 Hz, 1H, H-5); 6.82 (s, 1H, H-2); 6.78 (s, 1H, H-4); 6.75-6.69 (m, 2H); 6.56 (s, 1H); 5.58-5.45 (m, 2H, H-2''); 5.24 (d, *J*=11.7 Hz, 1H); 5.22 (d, *J*=11.6 Hz, 1H); 5.07 (d, *J*=10.3 Hz, 1H); 5.04 (d, *J*=10.3 Hz, 1H); 5.00-4.96 (m, 1H); 4.95-4.91 (m, 1H); 4.85 (d, *J*=11.6 Hz, 1H); 4.81 (d, *J*=11.8, 1H); 4.65-4.52 (m, 10H, CH₂, OBn); 4.41 (d, *J*=5.5 Hz, 1H); 4.38 (d, *J*=5.5 Hz, 1H); 3.99-3.85 (m, 4H); 3.85-3.78 (m, 2H); 3.63 (t, *J*=1.9 Hz, 2H); 3.31-3.16 (m, 4H); 2.36 (s, 3H, H-11); 2.32 (s, 3H, H-11).

¹³C NMR (100 MHz, CDCl₃):

193.8 (C-9), 193.8 (C-9), 162.3 (C-1), 162.3 (C-1), 161.9 (C-8), 161.8 (C-8), 147.5, 146.7, 145.7, 145.7, 141.2, 138.9, 138.8, 138.2, 138.2, 138.0, 137.9, 135.5, 135.0, 133.2, 133.1, 128.5, 128.4, 128.1, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.3, 126.8, 121.0, 119.8, 119.7, 118.6, 117.8, 117.7, 117.5, 117.5, 116.6, 116.4, 116.0, 115.8, 115.6, 115.3, 95.7, 95.6, 81.1, 81.1, 78.0, 77.8, 74.9, 74.8, 74.5, 74.3, 73.9, 72.0, 72.0, 71.7, 71.6, 67.1, 67.1, 43.9 (C-10), 43.8 (C-10), 22.2 (C-11), 22.0 (C-11)

HRMS–ESI (m/z): calculated for C₄₄H₄₂O₈: 698.2880; found 698.2883 (M)⁺

IR: 3500-2880 cm⁻¹ (broad), 3213, 2882, 1622, 1618

Compound **15** (140 mg, 0.20 mmol) was dissolved in 9:1 MeOH:THF (2.9 mL, 0.07 M). PdCl₂ (7.1 mg, 0.2 eq.) was added. The reaction mixture was stirred at rt for 16 hrs. The reaction mixture was then filtered through a bed of Celite with EtOAc and the solvent was concentrated *in vacuo* to give an oil. Purification of the residue by flash chromatography (4:1 hexanes: ethyl acetate) afforded **16** (113 mg, 0.172 mmol, 86%, as a 1:1 mixture of diastereomers at C-10).

¹H NMR (400 MHz, CDCl₃):

12.14 (s, 1H, OH-8); 12.11 (s, 1H, OH-8); 12.01 (s, 1H, OH-1); 11.99 (s, 1H, OH-1); 7.44-7.26 (m, 28H, OBn); 7.06-6.97 (m, 5H, OBn); 6.92 (d, *J*=7.9 Hz, 1H, H-7); 6.85 (d, *J*=8.5, 1H, H-5); 6.82 (s, 1H, H-2); 6.74 (s, 1H, H-4); 6.72 (d, *J*=7.4 Hz, 1H); 6.66 (s, 1H); 6.54 (s, 1H); 5.17 (d, *J*=11.8 Hz, 1H, CH₂, OBn); 5.16 (d, *J*=11.6 Hz, 1H, CH₂, OBn); 4.86 (s, 2H); 4.78 (d, *J*=11.7 Hz, 1H, CH₂, OBn); 4.73 (d, *J*=11.8 Hz, 1H, CH₂, OBn); 4.64-4.53 (m, 8H); 4.36 (d, *J*=4.8 Hz, 1H); 4.32 (d, *J*=4.8 Hz, 1H); 4.08-4.02 (m, 2H); 4.00-3.87 (m, 4H); 3.62 (s, 2H); 2.52 (t, *J*=3.8 Hz, 2H, OH-1'); 2.32 (s, 3H, H-11); 2.30 (s, 3H, H-11).

¹³C NMR (100 MHz, CDCl₃):

193.8 (C-9), 193.7 (C-9), 162.3 (C-1), 162.2 (C-1), 161.7 (C-8), 161.6 (C-8), 147.7, 146.8, 145.4, 145.4, 141.7, 138.8, 138.7, 138.4, 138.3, 137.9, 137.9, 135.7, 135.0, 128.4, 128.4, 128.2, 128.1,

127.9, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 126.8, 126.8, 121.0, 120.0, 119.7, 118.8, 117.6, 117.2, 116.5, 116.2, 116.1, 115.7, 115.4, 115.0, 91.7, 80.2, 80.1, 75.3, 75.2, 74.5, 74.3, 73.7, 73.7, 72.3, 72.2, 71.7, 71.6, 44.0 (C-10), 22.2 (C-11), 22.1 (C-11)

HRMS-ESI (m/z): calculated for $C_{41}H_{38}O_8$: 658.2567; found 658.2574 (M)⁺

IR: 3500-2950 cm^{-1} (broad), 3388, 3032, 1615 (shoulder), 1603

Compound **16** (52 mg, 0.079 mmol) was dissolved in CH₂Cl₂ (0.8 mL, 0.1 M) and the solution was cooled to 0 °C. HBr in AcOH (33% solution, 0.03 mL, 2 eq.) was added dropwise and the reaction mixture was stirred at 0 °C for 1 hr. After TLC indicated complete conversion, the reaction mixture was neutralized with saturated NaHCO₃ solution (10 mL) and diluted with CH₂Cl₂ (10 mL). The phases were separated and the aqueous layer was extracted with CH₂Cl₂ (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give a crude oil.

The crude oil was dissolved in AcOH (1.6 mL, 0.05 M) and AgOAc (16 mg, 1.2 eq.) was added. The reaction mixture was stirred at rt for 16 hrs. The reaction mixture was then filtered through a bed of Celite with EtOAc and the solvent was concentrated *in vacuo* to give an oil. Purification of the residue by flash chromatography (4:1 hexanes: ethyl acetate) afforded **17** (40 mg, 0.057 mmol, 73%, as a 1:1 mixture of diastereomers at C-10).

¹H NMR (400 MHz, CDCl₃):

12.15 (s, 1H, OH-8); 12.09 (s, 1H, OH-8); 12.06 (s, 1H, OH-1); 11.98 (s, 1H, OH-1); 7.42-7.27 (m, 22H, OBn); 7.25-7.11 (m, 12H, OBn); 7.04 (d, *J*=7.5 Hz, 1H, H-7); 6.89 (m, 3H); 6.75 (d, *J*=7.5 Hz, 1H, H-5); 6.71 (s, 2H); 6.55 (s, 1H, H-4); 5.97 (d, *J*=2.0 Hz, 1H, H-5'); 5.95 (d, *J*=2.1 Hz, 1H, H-1'); 4.99 (d, *J*=11.5 Hz, 1H, CH₂, OBn); 4.98 (d, *J*=11.4 Hz, 1H, CH₂, OBn); 4.60-4.40

(m, 14H); 4.00-3.92 (m, 2H); 3.84-3.74 (m, 4H); 3.61-3.56 (m, 2H); 2.31 (s, 3H, H-11); 2.28 (s, 3H, H-11); 1.89 (s, 3H, OAc); 1.87 (s, 3H, OAc).

^{13}C NMR (100 MHz, CDCl_3):

193.5 (C-9), 168.5 (OAc), 162.5 (C-1), 162.4 (C-1), 162.3 (C-8), 162.2 (C-8), 147.5, 147.0, 143.9, 143.7, 141.9, 141.7, 138.3, 138.2, 137.7, 137.7, 137.6, 135.5, 135.2, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.7, 127.7, 127.6, 127.6, 127.4, 127.3, 127.2, 120.8, 120.3, 119.3, 119.0, 117.0, 116.9, 116.6, 116.5, 116.2, 116.2, 114.9, 114.7, 91.4, 91.4, 80.7, 80.6, 79.8, 74.3, 74.2, 73.8, 73.8, 73.6, 73.5, 72.2, 72.1, 71.8, 71.8, 44.4, 22.2, 22.0, 20.7.

HRMS–ESI (m/z): calculated for $\text{C}_{43}\text{H}_{40}\text{O}_9$: 700.2672; found 700.2677 (M)⁺

IR: 3500-2900 cm^{-1} (broad), 3030, 2922, 2859, 1755, 1636 (shoulder), 1616, 1601

Compound **17** (40 mg, 0.057 mmol) was dissolved in EtOAc (1 mL) and EtOH (1 mL). Pearlman's catalyst (7 mg, 20% Pd(OH)₂ on C) was added and the mixture was stirred under a hydrogen atmosphere for 18 hours. The mixture was then filtered through a bed of Celite with 20% MeOH in EtOAc, and the solvent was concentrated in vacuo to give a mixture of **1** and **2** (23 mg, 0.054 mmol, 95%). The mixture was separated via column chromatography (97:3 → 94:6 CHCl₃:MeOH) to afford compound **1**.

Alvaradoin E (**1**), yellow-white solid (m.p. 186-191 °C; lit. 194-196°C):

¹H NMR (400 MHz, CDCl₃):

12.14 (s, 1H, OH-1); 12.02 (s, 1H, OH-8); 7.47 (dd, J=7.6, 8.3 Hz, 1H, H-6); 6.98 (d, J=7.3 Hz, 1H, H-7); 6.93 (d, J= 8.3 Hz, 1H, H-5); 6.83 (s, 1H, H-2); 6.75 (s, 1H, H-4); 5.83 (s, 1H, H-1'); 4.52 (d, J= 2.1 Hz, 1H, H-10); 3.86 (dd, J=2.3, 10.0 Hz, 1H, H-5'); 3.77 (m, 1H, H-2'); 3.73-3.66 (m, 2H, H-3'); 3.46-3.38 (m, 1H, H-4'); 2.40 (s, 3H, CH₃-11); 1.87 (s, 3H, OAc-1')

¹³C NMR (100 MHz, CDCl₃):

193.6 (C-9), 167.9 (C=O, OAc), 162.4 (C-1), 162.2 (C-8), 147.1 (C-3), 143.9 (C-5a), 140.8 (C-4a), 135.5 (C-6), 121.0 (C-4), 118.3 (C-1a), 117.4 (C-5), 116.9 (C-2), 116.3 (C-7), 115.2 (C-8a),

93.2 (C-1'), 79.6 (C-5'), 72.2 (C-3'), 69.5 (C-2'), 68.0 (C-4'), 43.7 (C-10), 22.3 (C-11), 20.5 (CH₃, OAc)

HRMS-ESI (m/z): calculated for C₂₂H₂₂O₉: 430.1264; found 430.1260 (M)⁺

[α]_D²⁰ = -8.9 ° (c 0.0005, CH₃OH); lit. [α]_D²⁰ = -16.8 ° (c 0.07, CH₃OH)

IR: 3381 cm⁻¹ (broad), 2925, 2854, 1744, 1636 (shoulder), 1603

Compound 1 and Compound 2:

¹H NMR (400 MHz, (CD₃)₂CO):

12.02 (s, 1H); 12.00 (s, 1H); 11.91 (s, 2H); 7.56 (m, 2H); 7.18 (d, J=7.5 Hz, 1H); 7.03 (s, 1H); 7.03 (d, J=7.5 Hz, 1H); 6.88 (m, 3H); 6.71 (s, 1H); 6.69 (s, 1H); 5.63 (s, 1H); 5.62 (s, 1H); 4.65 (d, J=2.3 Hz, 2H); 4.54-4.28 (m, 2H); 4.23-3.91 (m, 4H); 3.87-3.84 (m, 2H); 3.70-3.64 (m, 4H); 3.63-3.55 (m, 2H); 2.88 (m, 4H); 2.39 (s, 3H); 2.37 (s, 3H); 1.77 (s, 3H); 1.75 (s, 3H)

¹³C NMR (100 MHz, (CD₃)₂CO):

195.1, 195.0, 168.5, 168.4, 163.3, 163.2, 163.2, 163.0, 148.7, 148.1, 146.7, 142.4, 142.4, 136.8, 136.2, 122.5, 121.3, 120.3, 119.2, 118.3, 117.2, 116.9, 116.7, 116.5, 116.2, 94.5, 81.5, 81.4, 73.2, 70.7, 70.6, 68.4, 68.3, 44.1, 44.0, 22.3, 22.1, 20.5, 20.5

Compound **17** (40 mg, 0.057 mmol) was dissolved in EtOAc (1 mL) and EtOH (1 mL). Pearlman's catalyst (7 mg, 20% Pd(OH)₂ on C) was added and the mixture was stirred under a hydrogen atmosphere for 18 hours. The mixture was then filtered through a bed of Celite with 20% MeOH in EtOAc, and the solvent was concentrated in vacuo to give a mixture of **1** and **2** (23 mg, 0.054 mmol, 95%). The mixture was separated via column chromatography (97:3 → 94:6 CHCl₃:MeOH) to afford compound **2**.

Alvaradoin F (**2**), pale yellow solid (m.p.=203-208 °C; lit. 210-213 °C):

¹H NMR (400 MHz, CDCl₃):

12.14 (s, 1H, OH-8); 12.02 (s, 1H, OH-1); 7.48 (dd, J=7.8, 8.3 Hz, 1H, H-6); 7.02 (d, J=7.5 Hz, 1H, H-5); 6.93 (d, J=8.5 Hz, 1H, H-7); 6.80 (s, 1H, H-2, H-4); 6.74 (s, 1H, H-2); 5.80 (s, 1H, H-1'); 4.53 (s, 1H, H-10); 3.85 (dd, J=3.0, 10.4 Hz, 1H, H-5'); 3.76 (s, 1H, H-2'); 3.72-3.65 (m, 2H, H-3'); 3.48-3.41 (m, 1H, H-4'); 2.37 (s, 3H, CH₃-11); 1.86 (s, 3H, OAc-1')

¹³C NMR (100 MHz, CDCl₃):

193.6 (C-9), 168.1 (C=O, OAc), 162.3 (C-8), 162.2 (C-1), 147.5 (C-3), 144.2 (C-4a), 140.7 (C-5a), 135.2 (C-6), 119.9 (C-5), 119.4 (C-4), 117.4 (C-8a), 116.6 (C-7), 116.4 (C-2), 115.2 (C-1a),

93.3 (C-1'), 79.7 (C-5'), 72.2 (C-3'), 69.4 (C-2'), 67.9 (C-4'), 43.4 (C-10), 22.1 (C-11), 20.4
(CH₃, OAc)

HRMS-ESI (m/z): calculated for C₂₂H₂₂O₉: 430.1264; found 430.1260 (M)⁺

[α]_D²⁰ = -40 ° (c 0.0004, CH₃OH); lit. [α]_D²⁰ = -107.7 ° (c 0.05, CH₃OH)

IR: 3370 cm⁻¹ (broad), 2925, 2854, 1740, 1637 (shoulder), 1618

Compound **16** (52 mg, 0.079 mmol) was dissolved in CH_2Cl_2 (0.8 mL, 0.1 M) and the solution was cooled to 0 °C. HBr in AcOH (33% solution, 0.03 mL, 2 eq.) was added dropwise and the reaction mixture was stirred at 0 °C for 1 hr. After TLC indicated complete conversion, the reaction mixture was neutralized with saturated NaHCO_3 solution (10 mL) and diluted with CH_2Cl_2 (10 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were once washed with 20 mL saturated aqueous NaCl, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude oil.

The crude oil was dissolved in DCM (0.8 mL, 0.1 M). AgOBz (22 mg, 1.2 eq.) and benzoic acid (12 mg, 1.2 eq.) were added. The reaction mixture was stirred at rt for 16 hrs. The reaction mixture was then filtered through a bed of Celite with EtOAc and the solvent was concentrated *in vacuo* to give an oil. Purification of the residue by flash chromatography (6:1 hexanes: ethyl acetate) afforded **18** (46 mg, 0.06 mmol, 76%, as a 1:1 mixture of diastereomers at C-10).

^1H NMR (400 MHz, CDCl_3):

12.15 (s, 1H, OH-8); 12.14 (s, 1H, OH-8); 12.06 (s, 1H, OH-1); 12.01 (s, 1H, OH-1); 7.82-7.77 (m, 4H); 7.59 (t, $J=7.4$ Hz, 2H); 7.46-7.40 (m, 5H); 7.38-7.26 (m, 20H, OBn); 7.24-7.14 (m, 9H, OBn); 7.00 (d, $J=7.4$ Hz, 1H, H-7); 6.89 (d, $J=7.8$ Hz, 1H, H-5); 6.79 (t, $J=3.7$ Hz, 2H, OBz);

6.72-6.68 (m, 2H); 6.60 (s, 1H, H-2); 6.53 (s, 1H, H-4); 6.18 (d, $J=2.2$ Hz, 1H, H-1'); 6.15 (d, $J=2.0$ Hz, 1H); 5.05 (d, $J=11.4$ Hz, 1H, CH₂, OBn); 5.01 (d, $J=11.5$ Hz, 1H, CH₂, OBn); 4.66-4.50 (m, 11H, CH₂, OBn); 4.50-4.42 (m, 2H); 4.08-4.01 (m, 2H); 3.96-3.89 (m, 2H); 3.88-3.81 (m, 2H); 3.75 (t, $J=2.6$ Hz, 2H); 2.25 (s, 3H, H-11); 2.09 (s, 3H, H-11)

¹³C NMR (100 MHz, CDCl₃):

193.5, 193.4, 164.1, 163.9, 162.5, 162.4, 162.3, 162.2, 147.5, 147.0, 143.9, 141.8, 141.5, 138.2, 137.7, 137.7, 137.5, 135.5, 135.2, 133.5, 133.4, 129.7, 129.6, 129.2, 129.2, 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 127.9, 127.9, 127.7, 127.4, 127.4, 127.3, 127.3, 120.7, 119.9, 119.3, 118.9, 117.2, 116.9, 116.6, 116.4, 116.3, 116.2, 114.9, 114.8, 92.1, 92.0, 81.0, 80.0, 79.8, 74.4, 74.2, 73.9, 73.9, 73.8, 72.3, 72.2, 71.9, 71.8, 44.4, 44.2, 22.2, 21.8

HRMS–ESI (m/z): calculated for C₄₈H₄₂O₉: 762.2829; found 762.2860 (M)⁺

IR: 3500-2950 cm⁻¹ (broad), 3360, 2920, 1745, 1650, 1605

Compound **18** (45 mg, 0.059 mmol) was dissolved in EtOAc (1 mL) and EtOH (1 mL). Pearlman's catalyst (8 mg, 20% Pd(OH)₂ on C) was added and the mixture was stirred under a hydrogen atmosphere for 18 hours. The mixture was then filtered through a bed of Celite with 20% MeOH in EtOAc, and the solvent was concentrated in vacuo to give a mixture of **3** and **4** (26 mg, 0.053 mmol, 90%). The mixture was separated via radial chromatography (3:1 EtOAc: hexanes) to afford compound **3**.

Uveoside (**3**), yellow solid (m.p.=224-229 °C; lit. 228-231° C)

¹H NMR (400 MHz, CDCl₃):

12.16 (s, 1H, OH-8); 12.02 (s, 1H, OH-1); 7.80 (d, J=7.3 Hz, 2H, OBz); 7.57 (t, J=7.5, 1H, OBz); 7.43 (m, 3H, OBz, H-6); 7.04 (d, J=7.3 Hz, 1H, H-5); 6.87 (d, J=8.1 Hz, 1H, H-7); 6.62 (s, 1H, H-4); 6.54 (s, 1H, H-2); 5.94 (s, 1H, H-1'); 4.54 (d, J=1.6 Hz, 1H, H-10); 3.95 (m, 2H, H-5', H-2'); 3.87 (m, 1H, H-3'); 3.57 (t, J=9.3 Hz, 1H, H-4'); 1.93 (s, 3H, CH₃-11)

¹³C NMR (100 MHz, CDCl₃):

193.6 (C-9), 166.8 (C=O, OBz), 163.4 (C-8), 162.2 (C-1), 147.7 (C-3), 144.4 (C-5a), 140.4 (C-4a), 135.2 (C-6), 133.5 (C-OBz), 129.6 (C-OBz), 128.9 (C-OBz), 128.5 (C-OBz), 119.9 (C-

OBz), 119.1 (C-5), 117.4 (C-4), 116.5 (C-7), 116.2 (C-2), 115.2 (C-1a), 94.0 (C-1'), 80.2 (C-5'), 72.8 (C-3'), 69.6 (C-2'), 67.9 (C-4'), 43.0 (C-10), 21.6 (C-11)

HRMS-ESI (m/z): calculated for C₂₇H₂₄O₉: 492.1420; found 492.1417 (M)⁺

[α]_D²⁰ = -0.83° (c 0.0024, EtOH); lit. [α]_D²⁰ = -0.20° (EtOH; c 0.60)

IR: 3360 cm⁻¹ (broad), 1925, 2854, 1739, 1603

Compound 3 and Compound 4:

¹H NMR (400 MHz, (CD₃)₂CO):

12.07 (s, 1H); 12.00 (s, 1H); 11.94 (s, 1H); 11.92 (s, 1H); 7.87 (m, 4H); 7.68 (m, 2H); 7.56 (m, 5H); 7.21 (d, J=7.4 Hz, 1H); 7.15 (t, J=7.8 Hz, 1H); 7.05 (s, 1H); 6.90 (d, J=7.6 Hz, 2H); 6.74 (s, 1H); 6.70 (s, 1H); 6.68 (dd, J=0.7, 8.3 Hz, 1H); 6.49 (s, 1H); 5.89 (s, 1H); 5.86 (s, 1H); 4.68 (d, J=3.1 Hz, 2H); 4.53 (m, 2H); 4.20 (s, 2H); 4.03 (dd, J=2.2, 9.9 Hz, 4H); 3.87 (m, 4H); 3.70 (m, 2H); 2.37 (s, 3H); 1.89 (s, 3H)

¹³C NMR (100 MHz, (CD₃)₂CO):

195.0, 194.9, 164.2, 163.9, 163.2, 163.1, 163.1, 162.8, 148.8, 148.0, 146.6, 146.4, 142.3, 142.1, 136.6, 136.2, 134.2, 134.1, 130.4, 130.3, 130.2, 129.4, 129.3, 122.4, 121.2, 119.9, 119.0, 118.2, 118.1, 117.1, 116.9, 116.4, 116.2, 116.1, 116.0, 95.5, 95.2, 81.9, 81.8, 73.5, 73.3, 70.6, 68.4, 68.3, 43.9, 43.6, 22.1, 21.6

Compound **18** (45 mg, 0.059 mmol) was dissolved in EtOAc (1 mL) and EtOH (1 mL). Pearlman's catalyst (8 mg, 20% Pd(OH)₂ on C) was added and the mixture was stirred under a hydrogen atmosphere for 18 hours. The mixture was then filtered through a bed of Celite with 20% MeOH in EtOAc, and the solvent was concentrated in vacuo to give a mixture of **3** and **4** (26 mg, 0.053 mmol, 90%). The mixture was separated via radial chromatography (3:1 EtOAc: hexanes) to afford compound **4**.

10-epi-Uveoside (**4**), yellow solid (m.p.=212-217 °C; lit. 215-217°C):

¹H NMR (400 MHz, CDCl₃):

12.14 (s, 1H, OH-8); 12.04 (s, 1H, OH-1); 7.83 (d, J=7.2 Hz, 2H, OBz); 7.60 (t, J=7.5 Hz, 1H, OBz); 7.43 (t, J=7.7 Hz, 2H, OBz); 7.18 (t, J=7.9, 1H, H-6); 6.89 (d, J=7.5 Hz, 1H, H-5); 6.82 (s, 1H, H-2); 6.80 (d, J=8.3 Hz, 1H, H-7); 6.73 (s, 1H, H-4); 6.06 (s, 1H, H-1'); 4.53 (d, J=1.9 Hz, 1H, H-2); 4.00 (dd, J=2.3, 9.9 Hz, 1H, H-5'); 3.95 (m, 1H, H-2'); 3.85 (m, 1H, H-3'); 3.51 (dd, J=8.0, 9.5 Hz, 1H, H-4'); 2.36 (s, 3H, CH₃)

¹³C NMR (100 MHz, CDCl₃):

193.6 (C-9), 163.6 (C=O, OBz), 162.4 (C-1), 162.2 (C-8), 147.1 (C-3), 143.6 (C-5a), 140.8 (C-4a), 135.5 (C-6), 133.6 (C-OBz), 129.7 (C-OBz), 129.0 (C-OBz), 128.4 (C-OBz), 121.0 (C-5),

118.3 (C-4), 117.2 (C-8a), 116.9 (C-2), 116.2 (C-7), 115.1 (C-1a), 94.0 (C-1'), 80.1 (C-5'), 72.5 (C-3'), 69.6 (C-2'), 68.2 (C-4'), 43.6 (C-10), 22.3 (C-11).

HRMS-ESI (m/z): calculated for $C_{27}H_{24}NaO_9$: 515.1318; found 515.1312 ($M+Na$)⁺

$[\alpha]_D^{20}$ = +28.6 ° (c 0.0014, CH₃OH); lit. $[\alpha]_D^{20}$ = +36 ° (c 0.63, CH₃OH).

IR: 3500-2950 cm⁻¹ (broad), 3148, 1735, 1619

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APPENDIX