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Synthesis of 7-Deoxypancratistatin from Carbohydrates by the Use of Olefin Metathesis

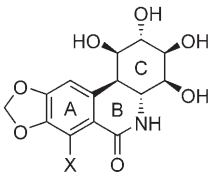
Anders E. Håkansson, Anders Palmelund, Henriette Holm, and Robert Madsen*[a]

Abstract: The stereocontrolled synthesis of (+)-7-deoxypancratistatin is described. The convergent synthesis has been achieved by two different strategies, both of which commence from a pentose and piperonal. The latter is converted into allylic bromide **7**, which is then coupled with a protected methyl 5-deoxy-5-iodo-D-ribofuranoside in the presence of zinc metal. The first strategy involves a total of only 13 steps from D-ribose and piperonal, but suffers from a low yield in the zinc-mediated reaction between ribofuranoside **9**, benzylamine, and bromide **7**. The second strategy involves a total of 18 steps from D-xylose and piperonal. The former is converted into ribofuranoside **28**, which is coupled with bromide **7** in the presence of zinc, and this is followed by ring-closing olefin metathesis. Subsequent Overman rearrangement, dihydroxylation, and deprotection then affords the natural product.

Keywords: antitumour agents · carbohydrates · natural products · olefin metathesis · total synthesis · zinc

Introduction

Pancratistatin (**1**) and the related 7-deoxypancratistatin (**2**) are both hydroxylated phenanthridones isolated from the plant family *Amaryllidaceae*. Pancratistatin was first isolated in 1984 by Pettit and co-workers from the Hawaiian plant



1: Pancratistatin (X = OH)
2: 7-Deoxypancratistatin (X = H)

Hymenocallis littorale[1] and later 7-deoxypancratistatin was isolated from *Haemanthus kalbreyeri* by Ghosal and co-workers.[2] Both compounds possess six contiguous stereogenic centers in the C ring of the phenanthridone skeleton, two of which set up the *trans*-fused BC ring junction. The only difference between the two compounds is the lack of a hydroxy group at the 7-position of **2** compared with that of **1**. The interest in **1** and **2** was greatly intensified by the promising results obtained when the compounds were tested against the NCI human tumour cell line panel. Both compounds showed activities against a variety of different cancer types, with a mean panel GI_{50} value of 91 nM for **1** and with **2** being slightly less active.[3] Their mechanism of action, however, is still not known in any great detail.[4] Potent activities against a set of diverse viruses have also been reported for both compounds.[5] Unfortunately, **1** and **2** are only available in minute quantities by isolation from the natural sources, and the further clinical development of these compounds has been hampered by the lack of material. As a result, it has been an important task to develop short and asymmetric syntheses of both compounds.[6]

The first total synthesis of racemic **1** was reported by Danishefsky and Lee in 1989,[7] and six years later Hudlicky and co-workers described the first enantioselective synthesis.[8] At present, eight different groups have reported synthetic strategies leading to **1**.[7–14] Most remarkable is the synthesis by Trost and Pulley, whereby **1** is prepared in 11% overall yield from conduritol A acetonide after only 12 steps.[9] Racemic **2** was first synthesised by Ohta and Kimoto in 1976 as an advanced intermediate in the total synthesis of another hydroxylated phenanthridone, lycoricidine.[15] A few years later, enantiopure **2** was prepared for the first time by Paulsen and Stubbe as an intermediate in their synthesis of

[a] Dr. A. E. Håkansson, Dr. A. Palmelund, H. Holm, Prof. Dr. R. Madsen
Center for Sustainable and Green Chemistry
Department of Chemistry, Building 201
Technical University of Denmark
2800 Kgs. Lyngby (Denmark)
Fax: (+45) 4593-3968
E-mail: rm@kemi.dtu.dk

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(+)-lycoricidine.[16] Thus, the first two syntheses of **2** were actually achieved before the compound was known to be a natural product. Following its isolation in 1989, the first total synthesis was reported by Keck and co-workers in 1995.[17] At present, six groups have published syntheses of **2**.[15–21] Most notable are the synthesis by Hudlicky's group and the second-generation synthesis by Keck and co-workers. Hudlicky's group used a whole-cell biooxidation of bromobenzene as the first step to afford (1*S*,2*S*)-3-bromocyclohexa-3,5-diene-1,2-diol, which was then converted into **2** by way of a total of ten linear steps in 3.0% overall yield.[18] Keck and co-workers employed a radical cyclisation as the key step in a synthesis that involved a total of 19 steps starting from D-gulono-1,4-lactone and piperonal.[20] The longest linear sequence consisted of 16 steps from piperonal, and afforded **2** in 14% overall yield.

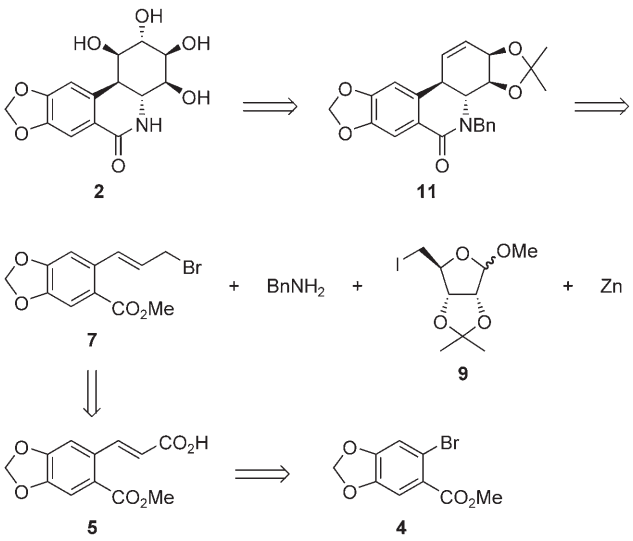
A series of deoxy analogues at the aminocyclitol part (ring C) of **2** have been synthesised and tested against the NCI human tumour cell line panel.[3c,22] The results indicated that at least two hydroxy groups on this ring are essential for the activities of **1** and **2**. Another necessary feature is the *trans*-fused BC ring junction formed by the lactam. These findings have led to the conclusion that enhanced activities in pancratistatin-like compounds are not expected unless they have the fully functionalised aminocyclitol moiety of ring C in **1** and **2**.[3c]

We have recently described a new strategy for the synthesis of enantiopure cyclitols and aminocyclitols.[23] The method is based on three consecutive organometallic reactions starting from a carbohydrate. Firstly, a methyl iodoglycoside is fragmented with zinc metal to produce an unsaturated aldehyde, which is then alkylated with a vinyl or an allyl organometallic reagent in the same pot. The product is a diene, which is subjected to ring-closing olefin metathesis to afford a cyclitol. If an amine is added during the zinc-mediated fragmentation, the intermediate aldehyde is converted into the corresponding imine. In this case, the alkylation reaction generates an aminodiene, which is transformed into an aminocyclitol by ring-closing metathesis.[23] We have applied this method in the synthesis of several cyclitols and aminocyclitols.[24]

Herein, we report the chemical synthesis of 7-deoxypancratistatin (**2**) by using a zinc-mediated tandem reaction followed by ring-closing metathesis as the key steps. The synthesis has been achieved by two different strategies, both of which start from a carbohydrate and a common substituted cinnamyl bromide.

Results and Discussion

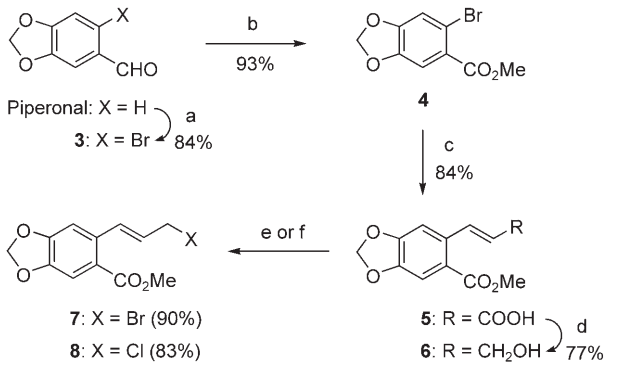
Retrosynthesis: first-generation synthesis: Close inspection of the aminocyclitol moiety revealed that it could be assembled by a metal-mediated fragmentation/allylation reaction followed by ring-closing metathesis (Scheme 1). The *trans*-diol moiety in **2** could be installed from alkene **11** by means of an epoxidation and a *trans*-diaxial ring-opening with an



Scheme 1. Retrosynthesis: first-generation synthesis.

O-nucleophile.[18] Alkene **11** can be prepared by ring-closing metathesis of the corresponding diene, which could be obtained by a zinc-mediated fragmentation of iodofuranoside **9** followed by imine formation with benzylamine and allylation with bromide **7**. The latter could be derived from cinnamic acid **5**, which, in turn, could be formed by a Heck coupling between bromide **4** and acrylic acid. Bromide **4** is a known compound and is easily available from piperonal.

Allylic bromide 7: Treatment of piperonal with bromine and iron filings in glacial acetic acid gave 6-bromopiperonal **3** in 84% yield (Scheme 2).[25] The aldehyde was then oxidised to

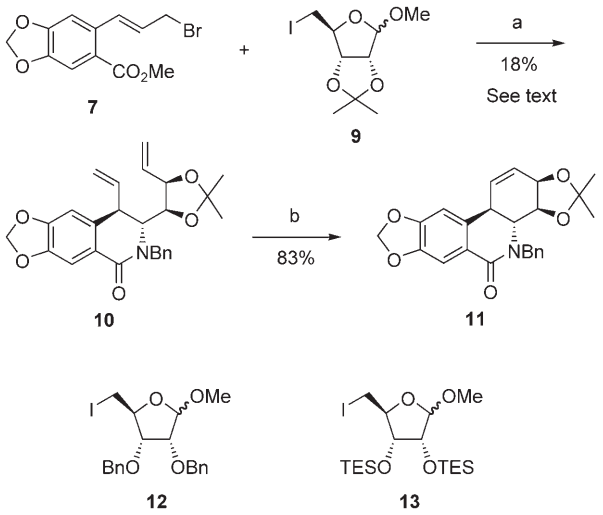


Scheme 2. a) Ref. [25]; b) $NaClO_2$, NaH_2PO_4, acetone, H_2O, then MeOH, H_2SO_4, 65°C; c) acrylic acid, $Pd(OAc)_2$, Ph_3P, Bu_3N, toluene, 110°C; d) $ClCO_2Et$, Et_3N, THF, 0°C, then $NaBH_4$, THF, H_2O, 0°C; e) Ms_2O, Et_3N, LiBr, THF, −40°C → RT; f) MsCl, Et_3N, LiCl, THF, −30°C → RT.

the corresponding carboxylic acid with sodium chlorite, and this was followed by ester formation in acidic methanol. The Heck coupling with acrylic acid was carried out with a catalytic amount of palladium(II) acetate and triphenylphosphine in the presence of tributylamine to afford cinnamic acid **5** in

84% yield. The carboxylic acid was selectively reduced in the presence of the methyl ester by anhydride formation with ethyl chloroformate followed by treatment with sodium borohydride. No reduction of the ester functionality was observed and the allylic alcohol **6** was isolated in 77% yield. At this stage, two different allylic halides, **7** and **8**, were prepared to investigate the influence of the halide in the fragmentation/allylation reaction. Bromide **7** was obtained by mesylating the free hydroxy group with methanesulfonic anhydride in the presence of lithium bromide, while chloride **8** was prepared in a similar manner by treatment with mesyl chloride and lithium chloride.

Zinc-mediated reaction with 9: Methyl iodofuranoside **9** is easily available from D-ribose in two steps[26] and was therefore used as a convenient substrate in our earlier methodology studies.[23,24c] To identify the optimum conditions for the fragmentation/allylation reaction, a series of experiments was performed (Scheme 3). Initial attempts to form **10** by a tandem procedure were inspired by our previous aminocyclitol syntheses.[23] A suspension of **9**, benzylamine, and the appropriate metal in THF was sonicated at 40°C while allylic bromide **7** was added over a period of 3 h. The slow addition was necessary due to the instability of the allylic bromide under the reaction conditions. When this procedure was tested with indium, zinc, and magnesium, only degradation products were observed. One explanation for this discouraging result could be the somewhat slower rate of the reductive fragmentation of **9** in the absence of water.[23,27] To address this problem, the fragmentation/allylation sequence was divided into two separate reactions. Initially, glycoside **9** was fragmented with zinc in a THF/water mixture. Excess zinc was removed by filtration and the aldehyde was isolated by extraction. Without further purification, the aldehyde was taken up in dry THF containing benzylamine and a metal. The mixture was sonicated at 40°C while allylic bromide **7** was added over a period of 3 h. Again, indium, zinc, and magnesium metals were tested in this second reaction. This procedure gave trace amounts of **10** when indium was used as the metal, while none of the desired product was obtained with magnesium. When zinc was employed in the allylation reaction, an encouraging 18% of the desired compound was isolated as a single diastereomer. The product was completely converted into the lactam during the reaction. Under these conditions, the imine is formed in situ in the allylation reaction. Another procedure was also investigated, in which the imine was formed in a separate operation with 3 Å molecular sieves in dry THF. Unfortunately, zinc-mediated allylation of this preformed imine afforded only an 8% yield of lactam **10**. The major by-product in all of these cases seems to arise from a metal-mediated homocoupling of the allylic bromide **7**. To determine the stereochemical outcome, **10** was submitted to metathesis with Grubbs' first-generation catalyst[28] to afford cyclohexene **11** in 83% yield (Scheme 3). The ^{1}H NMR coupling constants in **11** and additional NOE experiments showed that the lactam was formed with the desired stereochemistry at the new stereocenters.

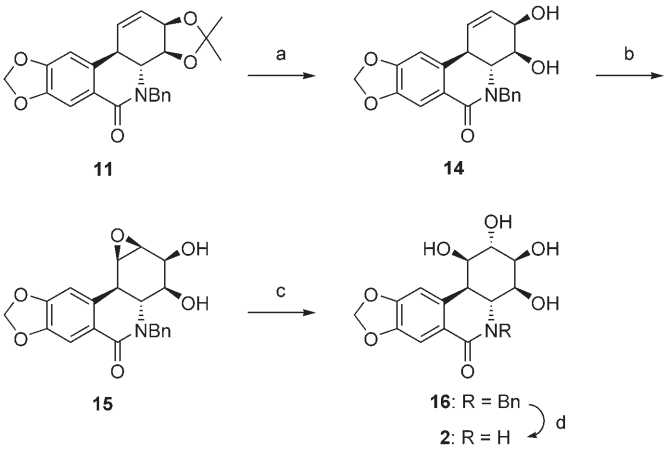


Scheme 3. a) 1) Zn, THF, H_2O, 40°C, ultrasound, 2) Zn, $BnNH_2$, THF, 40°C, ultrasound; b) $[Ru(=CHPh)(PCy_3)_2(Cl)_2]$, CH_2Cl_2. TES = triethylsilyl.

A series of experiments was conducted in an attempt to optimise the yield of lactam **10**. Firstly, the allylic bromide **7** was replaced with chloride **8**. The zinc-mediated allylation with this compound gave lactam **10** in 7% yield as a single diastereomer. Next, the isopropylidene group in **9** was replaced by two benzyl groups and by two triethylsilyl (TES) groups to form **12**[29] and **13**, respectively. In both cases, the allylic bromide **7** was used for the allylation. However, the reaction with **13** gave only a trace amount of the desired product, while the transformation with **12** gave the corresponding lactam in 12% yield as a 3:1 mixture of two diastereomers. Finally, the reaction was performed with *p*-anisidine instead of benzylamine. This afforded the allylation product in 10% yield as a 1:1 mixture of two diastereomers, and the product was found not to undergo lactamisation under the reaction conditions. No further attempts were made to optimise the formation of **10**. These results indicate that the optimum procedure for this transformation involves fragmentation of the iodoglycoside under aqueous conditions followed by transfer of the formed unsaturated aldehyde to an anhydrous solution containing benzylamine and zinc. The allylic bromide is then slowly added to this solution.

Lactam **11** was submitted to acidic conditions to hydrolyse the acetonide and thereby liberate the two hydroxy groups (Scheme 4). An attempt was made to epoxidise alkene **14** by the Sharpless procedure with $[VO(acac)_2]$/*t*BuOOH[30] (acac = acetylacetonate) to give *syn* epoxy alcohol **15**. Unfortunately, this resulted only in a complicated mixture according to TLC. Instead, allylic alcohol **14** was epoxidised with *m*-chloroperbenzoic acid (*m*-CPBA) to give epoxy alcohol **15** as a single diastereomer. When using commercially available *m*-CPBA (50–60% pure), a somewhat sluggish re-

action was observed, but this was circumvented by switching to freshly recrystallised *m*-CPBA.[31] The relative stereochemistry in the epoxy alcohol **15** was not determined since both diastereomers would undergo the *trans*-diaxial ring-opening to produce the desired product. However, it has previously been shown that these *m*-CPBA epoxidations are directed by the allylic alcohol to give the *syn* epoxy alcohol.[32] Epoxide **15** was then refluxed in an aqueous medium containing a catalytic amount of sodium benzoate for three

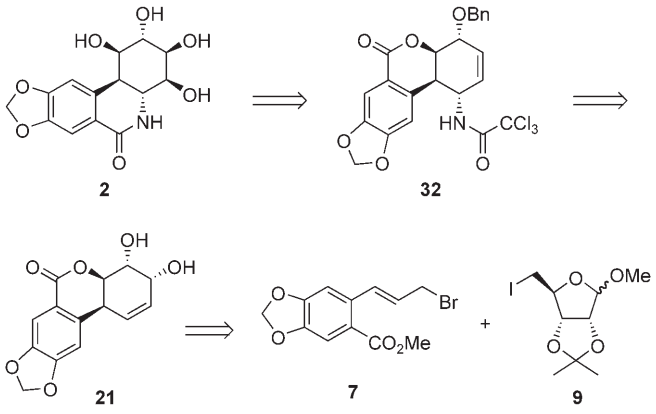


Scheme 4. a) H^+-resin, MeOH, 65 °C; b) *m*-CPBA, CH_2Cl_2; c) BzONa, H_2O, 100 °C; d) H_2, Pd/C, AcOH.

days[18] to afford tetrol **16**. Debenzylation of the benzylamide was achieved by prolonged treatment with hydrogen in the presence of palladium on activated charcoal in glacial acetic acid. 7-Deoxypancratistatin (**2**) was isolated in 22% overall yield from **11**, m.p. 308–309 °C, $[\alpha]_D^{23} = +73.8$ (c = 0.9, DMF), with physical and spectral data in excellent agreement with those reported for the natural substance.[2,17,18] No attempt has been made to optimise the last four reactions in the synthesis.

This first-generation synthesis employs a total of 13 steps starting from D-ribose and piperonal, and thus represents one of the shortest syntheses of (+)-7-deoxypancratistatin from commercially available starting materials. The longest linear sequence is 11 steps from piperonal, but unfortunately the overall yield is only 1.4%. The main reason for the low yield is the difficult tandem reaction between furanoside **9**, benzylamine, and bromide **7**. As a result, it was decided to develop a second-generation synthesis, in which a different zinc-mediated tandem reaction would serve as the key step.

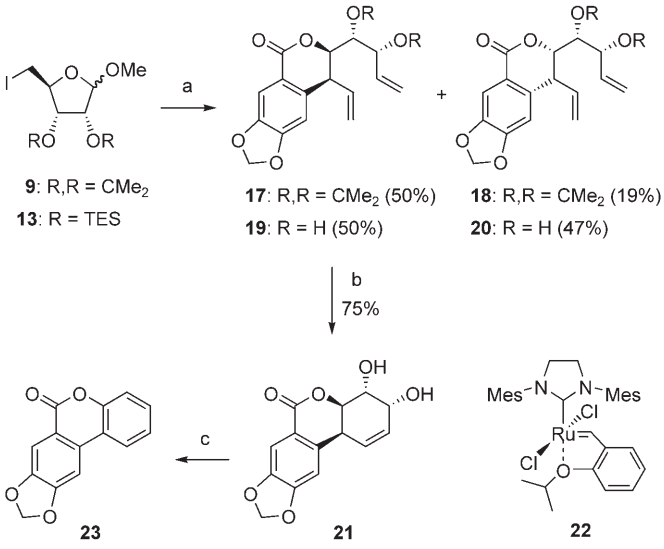
Retrosynthesis: second-generation synthesis: In this case, the target molecule was envisaged as arising from alkene **32** (Scheme 5). Here, the amino group is to be introduced at a late stage in the synthesis, for example, by an Overman rearrangement from diol **21**.[33] This molecule can be prepared by metathesis from the corresponding diene, which, in turn, may be obtained by a zinc-mediated tandem reaction between iodofuranoside **9** and bromide **7**. Thus, the crucial step in the second-generation synthesis may use some of the



Scheme 5. Retrosynthesis: second-generation synthesis.

same starting materials as the first-generation synthesis, the only difference being the presence or absence of benzylamine.

Diol 21: In the first experiment, iodofuranoside **9** was allowed to react with allylic bromide **7** in the presence of zinc (Scheme 6). This afforded a 5:2 mixture of two diastereo-



Scheme 6. a) **7**, Zn, THF, H_2O, ultrasound; b) **22**, CH_2Cl_2, 40 °C; c) (imidazole)$_2$CO, toluene, 50 °C, then phthalimide, [Pd(PPh$_3$)$_4$], THF, 65 °C.

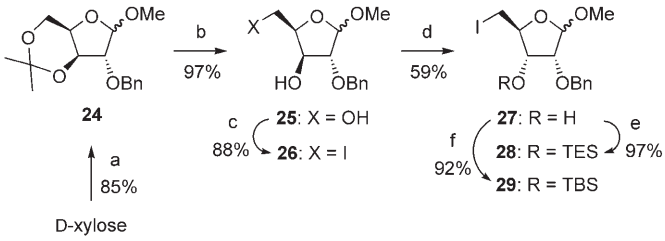
meric coupling products, **17** and **18**, in 69% yield. It was encouraging to observe that the yield of this tandem reaction improved significantly when it was performed in the absence of benzylamine. The stereochemical outcome was established by NMR after the metathesis reaction. Two other iodofuranosides were also investigated. TES-protected furanoside **13** gave a 1:1 mixture of the two diastereomeric dienes **19** and **20** after removal of the TES groups in the work-up. The yield in this case increased to an impressive 97%. Unprotected methyl 5-deoxy-5-iodo-D-ribofuranoside[29] was

also tested and gave a 68% yield of the same two diastereomers in a 3:2 ratio. Diene **19** was converted into the corresponding cyclohexene **21** in 75% yield with Hoveyda's catalyst **22**.[34] The metathesis reaction could also be performed with Grubbs' first-generation[28] and second-generation catalysts,[35] but the conversion was more sluggish in these cases.

Several experiments were then carried out with a view to introducing the nitrogen functionality. Firstly, it was attempted to selectively protect the homoallylic alcohol in diol **21** to make the allylic alcohol available for Overman rearrangement.[36] Unfortunately, silylation with one equivalent of TBSOTf or benzylation with BnBr/Bu_2SnO predominately protected the allylic alcohol. At this point, three protecting group manipulations could be envisaged for blocking of the homoallylic alcohol. However, this approach was not desirable at this stage in the synthesis. Instead, it was attempted to invert the allylic alcohol in **21** by either a Mitsunobu reaction[37] or a selective oxidation/reduction sequence.[38] The nitrogen functionality could then potentially be introduced by epoxidation and ring-opening of the epoxide with an appropriate nitrogen nucleophile. However, none of the experiments aimed at inverting the allylic alcohol were successful. Finally, it was attempted to use a palladium-catalysed allylic substitution reaction with a soft nucleophile. Diol **21** was converted into the corresponding cyclic carbonate, which was then subjected to palladium(0) and phthalimide. Interestingly, but also very disappointingly, this reaction only afforded the arene product **23**. In the light of these results, it was decided not to continue the experiments with diol **21**.

New ribofuranoside: Instead, a slightly modified synthesis was envisaged, employing a ribofuranoside with a benzyl group in the 2-position. After the fragmentation/allylation reaction and ring-closing metathesis, this benzyl group will block the homoallylic alcohol in diol **21**. Hence, this modified strategy will save some protecting group manipulations late in the synthesis at the expense of some additional steps to prepare the ribofuranoside starting material.

To the best of our knowledge, there is no efficient literature method for the preparation of 2-*O*-benzyl ribofuranosides. Kim and co-workers reacted methyl 5-*O*-tosyl-β-D-ribofuranoside with Bu_2SnO and benzyl bromide.[39] This afforded a 1:1 mixture of the 2- and 3-benzylated furanosides in 68% overall yield. We attempted to use this procedure on D-ribono-1,4-lactone, in which the 2-position often displays a higher reactivity than the 3-position.[40] Treatment of 5-bromo-5-deoxy-D-ribono-1,4-lactone[41] with Bu_2SnO and benzyl bromide did indeed afford the 2-benzylated lactone as the major product. Unfortunately, the yield never exceeded 30% and this procedure was therefore abandoned. Instead, it was decided to start from D-xylose, which is also a cheaper carbohydrate than D-ribose, but requires an inversion at C-3. Fischer glycosylation of D-xylose with methanol followed by isopropylidene protection and benzylation gave fully protected **24** in 85% overall yield (Scheme 7).[42] The

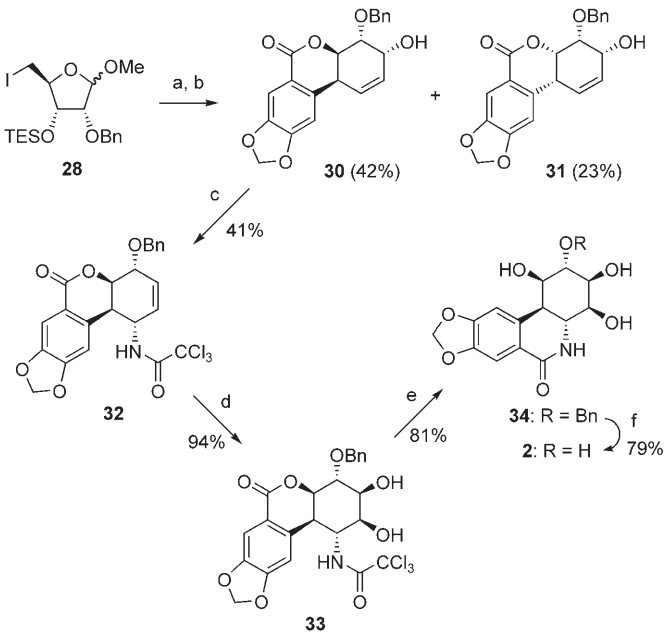


Scheme 7. a) 3 steps, ref. [42]; b) AcOH, H_2O, 60°C; c) I_2, Ph_3P, imidazole, THF, 65°C; d) Tf_2O, pyridine, CH_2Cl_2, −20°C → RT, then $NaNO_2$, DMF; e) TESCl, pyridine; f) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0°C.

isopropylidene group was then removed under acidic conditions to afford diol **25** in 97% yield. Selective iodination at the 5-position was performed with iodine and triphenylphosphine[29] to produce **26** in 88% yield. To invert the configuration at the 3-position, two methods were tested. The free alcohol was converted into the corresponding triflate by treatment with triflic anhydride and reacted with either sodium nitrite[43] or sodium trifluoroacetate.[44] Both reactions gave a clean displacement of the triflate while leaving the primary iodide unaffected. In the latter case, the formed trifluoroacetate was hydrolysed in the work-up by treatment with a 3:1 mixture of acetic acid and methanol. Ribofuranoside **27** was isolated in 59% yield from **26** by using sodium nitrite and in 47% yield by using sodium trifluoroacetate. Finally, a silyl group was introduced at the 3-position to form **28** and **29**, respectively.

Ribofuranosides **27**–**29** were submitted to the zinc-mediated tandem reaction to investigate the influence of a bulky substituent in the 3-position. The dienes were then subjected to ring-closing metathesis and converted into the corresponding cyclohexenes. After these reactions, furanoside **27** furnished a 37% yield of **30**:**31** in a 1:3 ratio in favour of the undesired isomer (Scheme 8). Introducing a bulky protecting group at the 3-position changed the ratio of **30** and **31** to 2:1 in favour of the desired compound. The silyl groups were removed in the work-up following the fragmentation/allylation reaction. TES-protected furanoside **28** gave **30**:**31** in 65% overall yield, while the yield with TBS-protected **29** was 61%. In all cases, traces of the last two isomers were also observed in isolated yields below 10%. The yields and the selectivities were not improved by using allylic chloride **8** in the tandem reaction. Catalyst **22**[34] was chosen for the metathesis reaction since it gave a better yield than the Grubbs' first- and second-generation catalysts.[28,35] The stereochemical outcome of the tandem reaction is the same as that observed in our earlier methodology studies with iodofuranoside **9** and cinnamyl bromide.[23]

Completion of the synthesis: With allylic alcohol **30** in hand, the focus then turned to the Overman rearrangement to introduce the nitrogen functionality.[33] Initially, it was attempted to install the trichloroacetimidate by treating **30** with trichloroacetonitrile in the presence of a catalytic amount of sodium hydride. This reaction proceeded very



Scheme 8. a) **7**, Zn, THF, H_2O, 40 °C, ultrasound, then H^+-resin, MeOH, 50 °C; b) **22**, CH_2Cl_2, 40 °C; c) CCl_3CN, DBU, CH_2Cl_2, −45 °C → −20 °C, then 1 mmHg, neat, 120 °C; d) OsO_4, NMO, THF; e) K_2CO_3, MeOH, 65 °C; f) H_2, $Pd(OH)_2$/C, EtOAc.

slowly and so a different approach with DBU as the base was chosen. Under these conditions, the desired imidate was produced very cleanly. To facilitate the Overman rearrangement, heat is normally applied, but a number of additives have also proven beneficial for the [3,3]-sigmatropic rearrangement. Mercury(II) and palladium(II) have been shown to catalyse the rearrangement at or slightly above room temperature.[33] Other authors have seen great improvements by adding potassium carbonate.[45] Danishefsky and Lee performed a closely related reaction in their total synthesis of pancratistatin, whereby an allylic trichloroacetimidate was rearranged under pyrolysis conditions.[7] Applying these conditions to our system gave the desired trichloroacetamide **32** in an overall yield of 41 % from the allylic alcohol **30**. Further heating of the reaction mixture led to decomposition. Several experiments were carried out with the aim of improving the yield, such as by adding palladium(II) complexes or potassium carbonate, but only decomposition was observed. The use of a trifluoroacetimidate instead of the chloro compound was investigated in a final attempt to improve the yield. This modification has been shown to give an improved yield in the allylic rearrangement in some cases.[46] The trifluoroacetimidate of **30** was generated at −78 °C with butyllithium as the base and then rearranged in refluxing toluene to afford the corresponding trifluoroacetamide in 30 % yield. No attempt was made to further optimise this result due to the precautions necessary when handling trifluoroacetonitrile, which is a highly toxic gas.

With a feasible route to trichloroacetamide **32** at hand, attention was then turned to the introduction of the *cis*-diol at the cyclohexane moiety. This was achieved by a diastereoselective dihydroxylation with osmium tetroxide/NMO[47] to give the desired diol **33** in 94 % yield. Treatment of diol **33** with potassium carbonate in refluxing methanol promoted methanolysis of the trichloroacetamide and a lactone-to-lactam transformation yielding 2-*O*-benzyl-7-deoxypancratistatin (**34**) in 81 % yield. Finally, the benzyl group was removed by hydrogenolysis over Pearlman's catalyst to afford 7-deoxypancratistatin (**2**) in 79 % yield, m.p. 308–310 °C, $[\alpha]_D^{23} = +72.7$ ($c = 2.3$, DMF), with the same spectral data as those of the previous product.

Conclusion

In summary, we have described two synthetic strategies for the preparation of 7-deoxypancratistatin. Both strategies are based on a zinc-mediated tandem reaction between a ribofuranoside and allylic bromide **7**, followed by ring-closing olefin metathesis. The first strategy requires only a total of 13 steps from commercially available starting materials, but unfortunately it suffers from a low yield in the zinc-mediated reaction. The second strategy requires a total of 18 steps, and the longest linear sequence involves 13 steps from D-xylose giving an overall yield of 4.3 %. The two syntheses are relatively short compared to previous syntheses of 7-deoxypancratistatin. They highlight the utility of the zinc-mediated tandem reaction combined with ring-closing metathesis for converting carbohydrates into important carbocyclic structures in relatively few steps.

Experimental Section

General: Thin-layer chromatography was performed on aluminium plates precoated with silica gel 60. Compounds were visualised by heating after dipping in a solution of $Ce(SO_4)_2$ (2.5 g) and $(NH_4)_6Mo_7O_{24}$ (6.25 g) in 10 % aqueous H_2SO_4 (250 mL). Flash column chromatography was performed on silica gel 60 (0.035–0.063 mm), while dry column chromatography[48] was carried out with silica gel 60 (0.015–0.040 mm). Optical rotations were measured with a Perkin Elmer 241 polarimeter. IR spectra were recorded on a Perkin Elmer 1720 Infrared Fourier Transform spectrometer. NMR spectra were recorded on a Varian Unity Inova 500 or a Varian Mercury 300 spectrometer. Mass spectrometry was carried out at the Department of Chemistry, University of Copenhagen. Microanalyses were conducted at the Department of Chemistry, University of Copenhagen or at the Institute of Physical Chemistry, University of Vienna.

6-Bromo-5-methoxycarbonyl-benzo[1,3]dioxole (4): A solution of $NaClO_2$ (59.4 g, 0.657 mol) and $NaH_2PO_4 \cdot H_2O$ (160 g, 1.16 mol) in H_2O (1000 mL) was added dropwise to a suspension of **3**[25] (44.83 g, 0.196 mol) in acetone (1000 mL) containing 2-methyl-2-butene (250 mL, 2.36 mol), keeping the temperature below 30 °C. The mixture was stirred vigorously for 2 h, then adjusted to pH 1 with concentrated aqueous HCl and extracted with EtOAc (3 × 250 mL). The combined organic layers were concentrated in vacuo and the residue was taken up in MeOH (400 mL) containing concentrated H_2SO_4 (3 mL). The mixture was stirred under reflux for 2 days. After the mixture had been cooled to room temperature, H_2O (100 mL) was added, which led to the deposition of a precipitate. This precipitate was collected by filtration and the mother liquor was partly concentrated in vacuo to produce a second crop of precipitate, which was also collected by filtration. The combined solids were dissolved in CH_2Cl_2 (300 mL), and this solution was washed with H_2O (250 mL) and saturated aqueous $NaHCO_3$ solution (250 mL), dried

($MgSO_4$), and concentrated in vacuo to afford **4** (47.09 g, 93%) as off-white crystals. R_f = 0.81 (heptane/EtOAc, 1:1); m.p. 89.0–90.0°C (MeOH) (lit.:[49] 88–88.5°C); IR (KBr): $\tilde{\nu}$ = 3056, 2956, 1718, 1615, 1485, 1244, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.33 (s, 1H), 7.10 (s, 1H), 6.05 (s, 2H), 3.90 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 151.0, 147.2, 124.7, 115.0, 114.5, 111.1, 102.6, 52.4 ppm; elemental analysis calcd (%) for $C_9H_7BrO_4$: C 41.73, H 2.72, Br 30.84; found: C 41.67, H 2.65, Br 30.85.

6-((*E*)-2-Carboxyvinyl)-5-methoxycarbonyl-benzo[1,3]dioxole (5): A degassed solution of Bu_3N (46 mL, 0.19 mol), acrylic acid (5.5 mL, 0.080 mol), and Ph_3P (629 mg, 2.40 mmol) in toluene (35 mL) under N_2 atmosphere was heated to reflux and then $Pd(OAc)_2$ (229 mg, 1.02 mmol) and a solution of **4** (10.03 g, 0.0387 mol) in toluene (20 mL) were added sequentially. The reaction mixture was stirred under reflux overnight and then cooled to room temperature, whereupon 2M HCl (200 mL) was added. The resulting mixture was added to refluxing EtOAc (2000 mL), which was stirred until all the solids had dissolved. The solution obtained was washed with brine (200 mL) and dried ($MgSO_4$). Most of the solvent was removed in vacuo to leave an off-white solid, which was collected by filtration. The solid was washed with ice-cooled diethyl ether (2× 100 mL) to give **5** (8.09 g, 84%) as a white powder. R_f = 0.31 (hexane/EtOAc/AcOH, 1:1:0.01); m.p. 262–264°C (EtOAc); IR (KBr): $\tilde{\nu}$ = 2962, 2568, 1731, 1681, 1506, 1237, 1121, 1037 cm^{-1}; ^1H NMR (300 MHz, [D$_6$]DMSO): δ = 12.36 (br s, 1H), 8.22 (d, J = 15.8 Hz, 1H), 7.45 (s, 1H), 7.34 (s, 1H), 6.40 (d, J = 16.2 Hz, 1H), 6.17 (s, 2H), 3.82 ppm (s, 3H); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.7, 167.2, 152.0, 149.7, 142.6, 132.2, 125.5, 121.8, 110.6, 108.2, 103.7, 53.5 ppm; elemental analysis calcd (%) for $C_{12}H_{10}O_6$: C 57.60, H 4.03; found: C 57.46, H 3.97.

6-((*E*)-3-Hydroxy-1-propenyl)-5-methoxycarbonyl-benzo[1,3]dioxole (6): A suspension of **5** (29.37 g, 0.124 mol) in THF (400 mL) at 0°C under N_2 was first treated with Et_3N (22 mL, 0.158 mol) and then ethyl chloroformate (14.0 mL, 0.146 mol) was added dropwise. The mixture was stirred at 0°C for 1.5 h and then filtered into ice-cold H_2O (75 mL). $NaBH_4$ (12.0 g, 0.317 mol) was added in small portions to the resulting solution, keeping the temperature at 0°C. The mixture was stirred for 3 h at 0°C and then the reaction was quenched by slowly adding 2M HCl (250 mL). The resulting mixture was extracted with EtOAc (3×200 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (2×200 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was recrystallised from heptane/EtOAc and the mother liquor was concentrated in vacuo and purified by flash column chromatography (heptane/EtOAc, 9:1) to give a combined yield of **6** of 22.45 g (77%) as a white solid. R_f = 0.41 (hexane/EtOAc, 1:1); m.p. 105.0–106.0°C (hexane/EtOAc); IR (KBr): $\tilde{\nu}$ = 3524, 3434, 2900, 1713, 1610, 1488, 1260, 1120, 1038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39 (dt, J = 15.7, 1.3 Hz, 1H), 7.35 (s, 1H), 6.99 (s, 1H), 6.15 (dt, J = 15.9, 5.8 Hz, 1H), 6.02 (s, 2H), 4.32 (dd, J = 5.7, 1.4 Hz, 2H), 3.85 (s, 3H), 1.93 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1, 151.1, 147.0, 135.6, 130.6, 130.0, 122.0, 110.1, 107.3, 102.0, 63.9, 52.2 ppm; elemental analysis calcd (%) for $C_{12}H_{12}O_5$: C 61.01, H 5.12; found: C 60.88, H 5.11.

6-((*E*)-3-Bromo-1-propenyl)-5-methoxycarbonyl-benzo[1,3]dioxole (7): A solution of **6** (4.34 g, 18.4 mmol) in THF (70 mL) at −40°C under Ar was treated first with Et_3N (4.0 mL, 28.3 mmol) and then LiBr (5.15 g, 59.3 mmol) was added. Ms_2O (4.82 g, 27.7 mmol) was added in small portions and the reaction mixture was allowed to warm slowly to room temperature. After the reaction mixture had been stirred for 4 h, the reaction had gone to completion and the mixture was quenched by adding 1M HBr (50 mL). The resulting mixture was extracted with EtOAc (3× 50 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc, 9:1) to afford **7** (4.94 g, 90%) as a white solid. R_f = 0.40 (heptane/EtOAc, 3:1); m.p. 65.5–66.0°C (heptane); IR (KBr): $\tilde{\nu}$ = 2954, 1711, 1608, 1500, 1486, 1230, 1115, 1034 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.51 (br d, J = 15.6 Hz, 1H), 7.38 (s, 1H), 7.01 (s, 1H), 6.18 (dt, J = 15.5, 7.8 Hz, 1H), 6.04 (s, 2H), 4.17 (dd, J = 7.6, 0.9 Hz, 2H), 3.87 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8, 151.1, 147.5, 134.4, 133.1, 127.0, 122.4, 110.3, 107.2, 102.1, 52.3, 33.6 ppm; elemental analysis calcd (%) for $C_{12}H_{11}BrO_4$: C 48.18, H 3.71, Br 26.71; found: C 48.24, H 3.78, Br 26.56; HRMS (FAB) calcd for $C_{12}H_{12}BrO_4$: 298.9919 $[M+H]^+$; found: 298.9899.

6-((*E*)-3-Chloro-1-propenyl)-5-methoxycarbonyl-benzo[1,3]dioxole (8): A solution of **6** (4.01 g, 17.0 mmol) in THF (45 mL) at −30°C under N_2 was treated first with Et_3N (3.6 mL, 25.9 mmol) and then LiCl (2.16 g, 51.1 mmol) was added. MsCl (1.5 mL, 19.4 mmol) was added dropwise over a period of 10 min and the reaction mixture was allowed to warm slowly to room temperature. After 3 h, the reaction had reached completion and the mixture was quenched by adding 1M HCl (25 mL). The resulting mixture was extracted with EtOAc (3×40 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated to dryness under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc, 9:1) to afford **8** (3.60 g, 83%) as a white solid. R_f = 0.53 (hexane/EtOAc, 3:1); m.p. 76.0–76.5°C (hexane/EtOAc); IR (KBr): $\tilde{\nu}$ = 2953, 1714, 1505, 1237, 1117, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.53 (dt, J = 15.5, 0.9 Hz, 1H), 7.37 (s, 1H), 7.00 (s, 1H), 6.09 (dt, J = 15.5, 7.2 Hz, 1H), 6.03 (s, 2H), 4.25 (dd, J = 7.2, 0.9 Hz, 2H), 3.87 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8, 151.2, 147.5, 134.6, 133.0, 126.8, 122.5, 110.4, 107.4, 102.2, 52.3, 45.6 ppm; elemental analysis calcd (%) for $C_{12}H_{11}ClO_4$: C 56.60, H 4.35; found: C 56.53, H 4.29.

(7*R*,8*R*)-6-Benzyl-7-((4*S*,5*R*)-2,2-dimethyl-5-vinyl-[1,3]dioxolan-4-yl)-8-vinyl-7,8-dihydro-6*H*-[1,3]dioxolo[4,5-*g*]isoquinolin-5-one (10): Freshly activated Zn[23] (2.06 g, 31.5 mmol) was added to a solution of **9** (1.40 g, 4.46 mmol) in THF/H_2O (3:1, 60 mL) and the mixture was sonicated at 40°C until complete conversion of the starting material, as monitored by TLC. The mixture was then filtered through a pad of Celite, which was successively rinsed with CH_2Cl_2 and H_2O. The combined filtrate was extracted with CH_2Cl_2 (3×100 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product was redissolved in THF (40 mL) and then $BnNH_2$ (0.58 mL, 5.31 mmol) and freshly activated Zn (3.30 g, 50.5 mmol) were added under N_2. Bromide **7** (3.36 g, 11.2 mmol) was dissolved in THF (7 mL) and this solution was added in small portions to the mixture over 1 h with sonication at 40°C. The mixture was sonicated for an additional 4.5 h at 40°C and then left overnight at room temperature. It was then quenched with H_2O and filtered through a pad of Celite, and the pad was successively rinsed with CH_2Cl_2 and H_2O. The organic phase was washed with H_2O (2×100 mL) and saturated aqueous $NaHCO_3$ solution (100 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified twice by column chromatography (hexane/EtOAc, 5:1, followed by CH_2Cl_2/EtOAc, 19:1) to afford **10** (350 mg, 18%) as a clear oil that solidified on standing. R_f = 0.38 (hexane/EtOAc, 3:1); m.p. 46.5–48.0°C (hexane); $[\alpha]_D^{23}$ = −131.2 (c = 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.54 (s, 1H), 7.24–7.21 (m, 5H), 6.41 (s, 1H), 5.95–5.93 (m, 2H), 5.78–5.66 (m, 1H), 5.66 (d, J = 14.4 Hz, 1H), 5.30–5.19 (m, 3H), 4.71 (dt, J = 10.3, 1.2 Hz, 1H), 4.50 (dt, J = 17.0, 1.3 Hz, 1H), 4.29 (dd, J = 8.9, 6.0 Hz, 1H), 4.15 (dd, J = 10.0, 5.9 Hz, 1H), 4.03 (d, J = 14.5 Hz, 1H), 3.39 (dd, J = 10.2, 1.3 Hz, 1H), 3.01 (dd, J = 6.2, 1.2 Hz, 1H), 1.48 (s, 3H), 1.18 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.8, 150.9, 147.6, 138.1, 137.4, 133.8, 132.3, 129.7, 128.4, 127.5, 123.2, 120.2, 116.8, 109.5, 108.8, 107.9, 101.8, 79.5, 79.4, 58.3, 50.5, 42.9, 28.4, 25.6 ppm; elemental analysis calcd (%) for $C_{26}H_{27}NO_5$: C 72.04, H 6.28, N 3.23; found: C 71.81, H 6.23, N 3.19.

(3*R*,4*S*,4a*R*,11b*R*)-5-Benzyl-3,4-isopropylidenedioxy-3,4a,5,11b-tetrahydro-4*H*-[1,3]dioxolo[4,5-*j*]phenanthridin-6-one (11): $[Ru(=CHPh)(PCy_3)_2(Cl)_2]$[28] (34 mg, 0.041 mmol) was added to a degassed solution of **10** (149 mg, 0.344 mmol) in CH_2Cl_2 (40 mL) under N_2 and then the system was degassed once more with N_2. The mixture was protected from light and was left to stir for 3 days at room temperature. Thereafter, a 1.5M solution of $P(CH_2OH)_3$ in 2-propanol (1 mL) was added and the mixture was stirred overnight at 40°C. It was then cooled and washed with H_2O (3×20 mL) and the organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by dry column chromatography (EtOAc/hexane, 0:1 → 1:0) to give **11** (116 mg, 83%) as white crystals. R_f = 0.51 (hexane/EtOAc, 2:1); m.p. 213.0–214.5°C (hexane/EtOAc); $[\alpha]_D^{23}$ = +24.5 (c = 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.59 (s, 1H), 7.21–7.10 (m, 5H), 6.84 (s, 1H), 6.27 (dt, J = 10.0, 1.7 Hz, 1H), 6.02 (dt, J = 9.8, 3.1 Hz, 1H), 5.96 (s, 2H), 5.35 (d, J =

15.8 Hz, 1H), 5.01 (d, J = 15.9 Hz, 1H), 4.55–4.51 (m, 1H), 4.27 (dd, J = 9.2, 6.9 Hz, 1H), 3.59 (dd, J = 12.0, 9.2 Hz, 1H), 3.44 (dd, J = 11.9, 1.7 Hz, 1H), 1.26 (s, 3H), 1.21 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 151.2, 147.0, 140.3, 133.8, 128.4, 128.1, 126.9, 126.6, 126.1, 123.7, 109.4, 109.3, 103.9, 101.8, 75.0, 71.9, 60.8, 46.6, 38.7, 27.6, 25.4 ppm; elemental analysis calcd (%) for $C_{24}H_{23}NO_5$: C 71.10, H 5.72, N 3.45; found: C 70.79, H 5.67, N 3.40.

Methyl 5-deoxy-5-iodo-2,3-bis-*O*-triethylsilyl-D-ribofuranoside (13): TESCl (2.7 mL, 16.1 mmol) was added to a solution of methyl 5-deoxy-5-iodo-D-ribofuranoside[29] (1.464 g, 5.34 mmol) in pyridine (40 mL) under N_2 and the mixture was stirred at room temperature for 3 h. It was then diluted with hexane (50 mL), washed with H_2O (3×30 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc/Et_3N, 99:0:1 → 97:2:1) to give a 4:1 anomeric mixture of **13** (2.236 g, 83%) as a colourless oil. R_f = 0.93 (hexane/EtOAc, 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.82 (d, J = 3.8 Hz, 0.2H), 4.69 (s, 0.8H), 4.06–3.92 (m, 1.8H), 3.89–3.72 (m, 1.2H), 3.51–3.20 (m, 2H), 3.41 (s, 0.6H), 3.39 (s, 2.4H), 0.97 (t, J = 8.1 Hz, 9H), 0.96 (d, J = 8.1 Hz, 9H), 0.70–0.57 ppm (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, β-isomer): δ = 108.2, 80.6, 77.2, 75.9, 55.6, 9.6, 7.0, 6.9, 5.0 ppm (2×); elemental analysis calcd (%) for $C_{18}H_{39}IO_4Si_2$: C 43.02, H 7.82; found: C 42.61, H 7.46.

(7*R*,8*S*)-7-((1*R*,2*R*)-1,2-Dihydroxy-but-3-enyl)-8-vinyl-7,8-dihydro-1,3-dioxolo[4,5-*g*,2]benzopyran-5-one (19): Freshly activated Zn[23] (140 mg, 2.14 mmol) was added to a solution of **13** (102 mg, 0.203 mmol) in THF/H_2O (4:1, 4 mL) under N_2. The slurry was sonicated at 40 °C while a solution of **7** (201 mg, 0.672 mmol) in THF (2 mL) was added by means of a syringe pump over a period of 4 h. After an additional 2 h at 40 °C under sonication, the reaction mixture was filtered through a pad of Celite, which was subsequently rinsed with EtOAc and H_2O. The filtrate was extracted with EtOAc (3×25 mL) and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was redissolved in MeOH (10 mL) and heated at 40 °C for 2 h in the presence of an acidic ion-exchange resin (Amberlite IR-120, 4 mL). The mixture was then filtered and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc, 3:2) to give **19** (31 mg, 50%) as a white solid. R_f = 0.59 (heptane/EtOAc, 2:1); m.p. 50–52 °C (CH_2Cl_2); $[\alpha]_D^{23}$ = +214.3 (c = 1.7, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3414, 2912, 1708, 1618, 1482, 1270, 1035 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (s, 1H), 6.62 (s, 1H), 6.10–5.90 (m, 4H), 5.41 (dt, J = 17.4, 0.9 Hz, 1H), 5.30 (dt, J = 10.2, 0.9 Hz, 1H), 5.20 (br d, J = 10.5 Hz, 1H), 5.10 (br d, J = 17.1 Hz, 1H), 4.55 (dd, J = 6.9, 3.0 Hz, 1H), 4.29 (br t, J = 5.1 Hz, 1H), 3.98 (dd, J = 6.9, 4.5 Hz, 1H), 3.48 (dd, J = 8.4, 3.0 Hz, 1H), 3.05 (br s, 1H), 2.70 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.5, 153.1, 148.0, 138.5, 136.2, 133.8, 119.3, 118.4, 118.0, 109.5, 107.4, 102.4, 80.2, 73.4, 72.6, 44.9 ppm; elemental analysis calcd (%) for $C_{16}H_{16}O_6$: C 63.15, H 5.30; found: C 62.84, H 5.32.

(3*R*,4*R*,4a*R*,11b*S*)-3,4-Dihydroxy-3,4,4a,11b-tetrahydro-6*H*-[1,3]benzodioxolo[5,6-*c*,1]benzopyran-6-one (21): Catalyst **22**[34] (71 mg, 0.113 mmol) was added to a solution of **19** (690 mg, 2.28 mmol) in CH_2Cl_2 (12 mL) under Ar and the mixture was stirred under reflux for 5 h. The solvent was then removed in vacuo and the residue was crystallised from absolute EtOH to give **21** (473 mg, 75%) as a white solid. R_f = 0.40 (hexane/EtOAc, 1:4); m.p. 231.5–233.0 °C (EtOH); $[\alpha]_D^{23}$ = −20.0 (c = 0.7, DMSO); IR (KBr): $\tilde{\nu}$ = 3448, 2908, 1707, 1615, 1484, 1285, 1034 cm^{-1}; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.30 (s, 1H), 7.14 (s, 1H), 6.15 (s, 1H), 6.13 (s, 1H), 5.57 (dd, J = 10.2, 0.8 Hz, 1H), 5.43 (dd, J = 10.2, 1.7 Hz, 1H), 5.20 (dd, J = 3.8, 0.9 Hz, 1H), 4.83 (t, J = 4.0 Hz, 1H), 4.80 (d, J = 7.7 Hz, 1H), 4.21–4.15 (m, 1H), 4.02 (dd, J = 8.5, 3.8 Hz, 1H), 3.71–3.66 ppm (m, 1H); ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 162.9, 152.3, 147.1, 138.3, 129.6, 125.9, 117.4, 107.8, 107.7, 102.1, 77.0, 66.8, 64.1, 33.5 ppm; elemental analysis calcd (%) for $C_{14}H_{12}O_6$: C 60.87, H 4.38; found: C 60.68, H 4.24.

Methyl 2-*O*-benzyl-D-xylofuranoside (25): Furanoside **24**[42] (17.0 g, 57.8 mmol) was dissolved in 70% aqueous AcOH (75 mL) and the solution was heated at 60 °C for 1 h. It was then concentrated in vacuo and the remaining volatiles were coevaporated with absolute EtOH (2× 50 mL) and toluene (50 mL) to give **25** (14.25 g, 97%) as a syrup. A limited amount of **25** was purified by flash column chromatography (heptane/EtOAc, 1:1 → 7:10) in order to obtain full characterisation data for the two anomers. **α-25**: The analytical data are in accordance with literature values.[50] **β-25**: R_f = 0.16 (heptane/EtOAc, 1:1); $[\alpha]_D^{23}$ = −39.1 (c = 1.4, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3435, 2930, 1641, 1455, 1195, 1103, 1039 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 5H), 4.92 (s, 1H), 4.66 (d, J = 12.0 Hz, 1H), 4.60 (d, J = 11.9 Hz, 1H), 4.43–4.31 (m, 2H), 3.96 (d, J = 1.7 Hz, 1H), 3.88 (d, J = 4.1 Hz, 2H), 3.41 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.4, 128.7, 128.1, 127.9, 107.3, 88.4, 82.4, 76.1, 72.1, 62.4, 55.6 ppm; HRMS (FAB) calcd for $C_{13}H_{18}O_5Na$: 277.1052 [M+Na]$^+$; found: 277.1047.

Methyl 2-*O*-benzyl-5-deoxy-5-iodo-D-xylofuranoside (26): A solution of **25** (9.115 g, 35.8 mmol), Ph_3P (14.17 g, 54.0 mmol), and imidazole (4.942 g, 72.6 mmol) in THF (150 mL) was heated to reflux and a solution of I_2 (13.72 g, 54.1 mmol) in THF (40 mL) was added slowly. The solution was refluxed for 45 min, then cooled to room temperature, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (heptane/EtOAc, 3:1 → 2:1) to give a combined yield of **α-26** and **β-26** of 11.50 g (88%) as colourless oils. Pure samples of both anomers were isolated. **α-26**: R_f = 0.50 (heptane/EtOAc, 1:1); $[\alpha]_D^{23}$ = +75.7 (c = 3.4, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3470, 2910, 1198, 1118, 1033, 992 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.29 (m, 5H), 4.84 (d, J = 4.4 Hz, 1H), 4.70 (d, J = 12.0 Hz, 1H), 4.64 (d, J = 11.9 Hz, 1H), 4.47 (dd, J = 6.5, 5.3 Hz, 1H), 4.37 (q, J = 6.6 Hz, 1H), 3.92 (dd, J = 5.0, 4.5 Hz, 1H), 3.41 (s, 3H), 3.30 (dd, J = 10.0, 7.1 Hz, 1H), 3.19 (dd, J = 10.0, 6.2 Hz, 1H), 1.97 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.7, 128.8, 128.5, 128.3, 100.8, 85.3, 77.6, 75.3, 73.2, 55.7, 3.0 ppm; HRMS (FAB) calcd for $C_{13}H_{17}IO_4$: 364.0172 [M]$^+$; found: 364.0168. **β-26**: R_f = 0.64 (heptane/EtOAc, 1:1); $[\alpha]_D^{23}$ = −56.8 (c = 4.3, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3496, 2927, 1455, 1367, 1103, 1025, 930 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.30 (m, 5H), 5.01 (s, 1H), 4.61 (s, 2H), 4.55 (dt, J = 7.6, 3.8 Hz, 1H), 4.25 (br d, J = 3.2 Hz, 1H), 4.01 (s, 1H), 3.38 (s, 3H), 3.32 (d, J = 7.7 Hz, 2H), 2.74 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 128.7, 128.2, 127.8, 107.2, 86.2, 83.9, 73.7, 72.1, 55.4, 1.9 ppm; HRMS (FAB) calcd for $C_{13}H_{17}IO_4$: 364.0172 [M]$^+$; found: 364.0175.

Methyl 2-*O*-benzyl-5-deoxy-5-iodo-D-ribofuranoside (27): A solution of **26** (501 mg, 1.38 mmol) in CH_2Cl_2 (10 mL) was cooled to −20 °C under Ar. Pyridine (0.50 mL, 6.21 mmol) was added, and then Tf_2O (0.45 mL, 2.73 mmol) was added dropwise. The mixture was stirred for 2.5 h at room temperature and then the reaction was quenched with ice-cold 2 M HCl (20 mL). The mixture was extracted with CH_2Cl_2 (2×30 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (40 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was redissolved in DMF (5 mL) under Ar and $NaNO_2$ (392 mg, 5.68 mmol) was added. The resulting mixture was stirred for 4 h at room temperature, then quenched with H_2O (50 mL) and extracted with diethyl ether (5×30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (heptane/EtOAc, 4:1) to give a combined yield of **α-27** and **β-27** of 298 mg (59%) as a colourless oil. Pure samples of both isomers were isolated. **α-27**: R_f = 0.18 (heptane/EtOAc, 2:1); $[\alpha]_D^{23}$ = +24.4 (c = 1.5, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3526, 2930, 1454, 1197, 1127, 1088, 1027, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.30 (m, 5H), 4.93 (d, J = 4.2 Hz, 1H), 4.74 (d, J = 11.7 Hz, 1H), 4.64 (d, J = 11.8 Hz, 1H), 4.07 (dt, J = 5.0, 2.3 Hz, 1H), 3.93 (dd, J = 6.0, 4.0 Hz, 1H), 3.90 (dd, J = 6.4, 2.1 Hz, 1H), 3.43 (s, 3H), 3.31 (d, J = 5.0 Hz, 2H), 2.96 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.0, 128.7, 128.4 (2×), 102.9, 84.3, 77.3, 72.7 (2×), 55.3, 7.6 ppm; HRMS (FAB) calcd for $C_{13}H_{16}IO_4$: 363.0093 [M−H]$^+$; found: 363.0107. **β-27**: R_f = 0.41 (heptane/EtOAc, 2:1); $[\alpha]_D^{23}$ = +0.2 (c = 4.1, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3420, 2954, 2906, 1455, 1243, 1125, 1076, 953, 736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.31 (m, 5H), 4.91 (s, 1H), 4.74 (d, J = 11.8 Hz, 1H), 4.63 (d, J = 11.8 Hz, 1H), 4.17–4.11 (m, 1H), 3.99 (br q, J = 5.8 Hz, 1H), 3.93 (d, J = 5.4 Hz, 1H), 3.38 (s, 3H), 3.37 (dd, J = 10.6, 5.6 Hz, 1H), 3.28 (dd, J = 10.6, 6.6 Hz, 1H), 2.65 ppm (br d, J = 8.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.7, 128.6, 128.3, 128.0, 105.6, 83.7, 82.4, 74.7, 73.0, 55.3, 7.7 ppm; HRMS (FAB) calcd for $C_{13}H_{16}IO_4$: 363.0093 [M−H]$^+$; found: 363.0106.

Methyl 2-*O*-benzyl-5-deoxy-5-iodo-3-*O*-triethylsilyl-D-ribofuranoside (28): TESCl (0.80 mL, 4.77 mmol) was added to a solution of **27** (719 mg, 1.97 mmol) in pyridine (10 mL) under Ar. The reaction mixture was stirred at room temperature for 2 h, and was then diluted with hexane (30 mL) and washed with H_2O (30 mL) and brine (30 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo, and the residue was purified by flash column chromatography (hexane/EtOAc, 15:1) to give a combined yield of **α-28** and **β-28** of 916 mg (97%) as a colourless oil. Pure samples of both isomers were isolated. **α-28**: R_f = 0.49 (heptane/EtOAc, 3:1); $[\alpha]_D^{23}$ = +76.8 (c = 1.4, $CHCl_3$); IR (film): $\tilde{\nu}$ = 2953, 2875, 1455, 1240, 1175, 1018, 842 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.26 (m, 5H), 4.91 (d, J = 4.0 Hz, 1H), 4.69 (d, J = 11.9 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 3.93 (dd, J = 6.5, 5.3 Hz, 1H), 3.80–3.75 (m, 2H), 3.49–3.43 (m, 1H), 3.45 (s, 3H), 3.30 (dd, J = 11.0, 4.1 Hz, 1H), 0.96 (t, J = 7.9 Hz, 9H), 0.69–0.60 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.0, 128.4, 128.3, 127.9, 103.2, 81.1, 77.9, 74.3, 73.0, 55.9, 9.2, 7.0, 5.0 ppm; HRMS (FAB) calcd for $C_{19}H_{30}IO_4Si$: 477.0958 $[M-H]^+$; found: 477.0973. **β-28**: R_f = 0.53 (heptane/EtOAc, 3:1); $[\alpha]_D^{23}$ = +11.2 (c = 2.1, $CHCl_3$); IR (film): $\tilde{\nu}$ = 2954, 2875, 1455, 1241, 1147, 1039, 846 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.27 (m, 5H), 4.87 (s, 1H), 4.72 (d, J = 11.8 Hz, 1H), 4.64 (d, J = 11.8 Hz, 1H), 4.16 (dd, J = 7.4, 4.5 Hz, 1H), 3.94–3.87 (m, 1H), 3.76 (d, J = 4.7 Hz, 1H), 3.49 (dd, J = 10.9, 3.7 Hz, 1H), 3.39 (s, 3H), 3.28 (dd, J = 11.0, 5.2 Hz, 1H), 0.97 (t, J = 7.9 Hz, 9H), 0.66 ppm (d, J = 7.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.9, 128.5, 128.0, 127.9, 105.8, 82.8, 81.0, 75.7, 72.7, 55.5, 9.4, 6.9, 4.9 ppm; HRMS (FAB) calcd for $C_{19}H_{30}IO_4Si$: 477.0958 $[M-H]^+$; found: 477.0956.

Methyl 2-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-5-deoxy-5-iodo-D-ribofuranoside (29): A solution of **27** (190 mg, 0.52 mmol) in CH_2Cl_2 (2 mL) under Ar at 0°C was treated with 2,6-lutidine (0.15 mL, 1.30 mmol) and then TBSOTf (0.18 mL, 0.78 mmol) was added. The reaction mixture was stirred at 0°C for 1 h, then diluted with hexane (10 mL) and washed with H_2O (10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo, and the residue was purified by flash column chromatography (heptane/EtOAc, 9:1) to give a combined yield of **α-29** and **β-29** of 230 mg (92%) as a colourless oil. Pure samples of both isomers were isolated. **α-29**: R_f = 0.61 (heptane/EtOAc, 3:1); $[\alpha]_D^{23}$ = +76.8 (c = 3.2, $CHCl_3$); IR (film): $\tilde{\nu}$ = 2927, 2856, 1471, 1251, 1172, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.27 (m, 5H), 4.94 (d, J = 4.3 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.64 (d, J = 12.1 Hz, 1H), 3.93 (dd, J = 6.4, 5.6 Hz, 1H), 3.81–3.76 (m, 2H), 3.46 (dd, J = 10.8, 3.8 Hz, 1H), 3.45 (s, 3H), 3.29 (dd, J = 11.0, 4.3 Hz, 1H), 0.90 (s, 9H), 0.11 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.0, 128.4, 128.3, 127.9, 103.3, 80.9, 77.8, 74.4, 73.0, 55.9, 26.0, 18.3, 9.1, −4.2, −4.5 ppm; MS (FAB) calcd for $C_{19}H_{30}IO_4Si$: 477.10 $[M-H]^+$; found: 477.10. **β-29**: R_f = 0.65 (heptane/EtOAc, 3:1); $[\alpha]_D^{23}$ = +11.8 (c = 2.9, $CHCl_3$); IR (film): $\tilde{\nu}$ = 2928, 2857, 1471, 1254, 1151, 1040 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 5H), 4.88 (s, 1H), 4.71 (d, J = 11.6 Hz, 1H), 4.63 (d, J = 11.8 Hz, 1H), 4.16 (dd, J = 7.3, 4.3 Hz, 1H), 3.94–3.90 (m, 1H), 3.77 (d, J = 4.3 Hz, 1H), 3.47 (dd, J = 10.7, 4.7 Hz, 1H), 3.39 (s, 3H), 3.26 (dd, J = 10.8, 5.4 Hz, 1H), 0.91 (s, 9H), 0.13 (s, 3H), 0.10 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.9, 128.5, 127.9, 127.9, 106.0, 82.6, 81.1, 75.8, 72.7, 55.5, 25.9, 18.2, 9.2, −4.3, −4.5 ppm; HRMS (FAB) calcd for $C_{19}H_{30}IO_4Si$: 477.0958 $[M-H]^+$; found: 477.0959.

(3*R*,4*R*,4a*R*,11b*S*)-4-Benzyloxy-3-hydroxy-3,4,4a,11b-tetrahydro-6*H*-[1,3]benzodioxolo[5,6-*c*,1]benzopyran-6-one (30): Freshly activated Zn[23] (1.43 g, 21.8 mmol) was added to a solution of **28** (1.03 g, 2.15 mmol) in THF/H_2O (3:1, 40 mL) under Ar. The slurry was sonicated at 40°C while a solution of **7** (1.991 g, 6.66 mmol) in THF (10 mL) was added by means of a syringe pump over a period of 4 h. After an additional 3 h at 40°C under sonication, the reaction was quenched by the addition of H_2O (30 mL). The mixture was filtered through a pad of Celite, which was subsequently rinsed first with EtOAc and then with H_2O. The filtrate was extracted with EtOAc (3×30 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was redissolved in MeOH (60 mL) and this solution was heated at 50°C for 3 h in the presence of an acidic ion-exchange resin (Amberlite IR-120). The mixture was then filtered and concentrated in vacuo to give a residue that was purified by flash column chromatography (heptane/EtOAc, 4:1) to give a clear oil (538 mg, R_f = 0.08 (heptane/EtOAc, 3:1)). This oil was dissolved in CH_2Cl_2 (20 mL) and the solution was degassed under Ar. Catalyst **22**[34] (41 mg, 0.065 mmol) was added and the mixture was stirred under reflux for 3.5 h. The solvent was then removed in vacuo and the residue was purified by flash column chromatography (heptane/EtOAc, 2:1) to give **30** (330 mg, 42%) and **31** (184 mg, 23%), both as white foams. **30**: R_f = 0.43 (hexane/EtOAc, 1:1); m.p. 70–72°C (CH_2Cl_2); $[\alpha]_D^{23}$ = −140.9 (c = 1.5, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3419, 2911, 1713, 1617, 1481, 1402, 1280, 1117, 1035 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.47 (s, 1H), 7.39–7.30 (m, 5H), 6.73 (s, 1H), 6.06 (d, J = 1.0 Hz, 1H), 6.05 (d, J = 1.0 Hz, 1H), 5.73 (brd, J = 10.5 Hz, 1H), 5.47 (ddd, J = 10.3, 3.9, 2.0 Hz, 1H), 4.85 (brt, J = 4.2 Hz, 1H), 4.76 (d, J = 11.6 Hz, 1H), 4.72 (d, J = 11.6 Hz, 1H), 4.53–4.49 (m, 1H), 4.14 (brt, J = 4.4 Hz, 1H), 3.61–3.58 (m, 1H), 2.42 ppm (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.6, 153.0, 147.9, 137.7, 137.3, 129.7, 128.9, 128.6, 128.2, 126.3, 118.0, 109.6, 107.2, 102.2, 75.1, 75.0, 74.4, 64.7, 34.6 ppm; HRMS (FAB) calcd for $C_{21}H_{19}O_6$: 367.1181 $[M+H]^+$; found: 367.1191. **31**: R_f = 0.20 (hexane/EtOAc, 1:1); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.48 (s, 1H), 7.40–7.29 (m, 5H), 6.70 (s, 1H), 6.06 (d, J = 1.0 Hz, 1H), 6.05 (d, J = 1.0 Hz, 1H), 6.04–6.01 (m, 1H), 5.49 (brd, J = 9.9 Hz, 1H), 4.97 (m, 1H), 4.89 (d, J = 12.0 Hz, 1H), 4.69 (d, J = 12.0 Hz, 1H), 4.44–4.38 (m, 1H), 3.72 (dd, J = 5.1, 1.8 Hz, 1H), 3.45–3.42 (m, 1H), 2.82 ppm (brd, J = 9.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 153.0, 147.9, 137.5, 136.9, 129.5, 128.7, 128.1 (2×), 125.4, 118.2, 109.8, 106.6, 102.3, 76.7, 74.5, 70.5, 63.5, 39.0 ppm.

(1*S*,4*R*,4a*R*,11b*R*)-4-Benzyloxy-1,4,4a,11b-tetrahydro-1-(2,2,2-trichloroacetylamino)-6*H*-[1,3]benzodioxolo[5,6-*c*,1]benzopyran-6-one (32): DBU (0.46 mL, 3.07 mmol) and CCl_3CN (0.31 mL, 3.09 mmol) were successively added to a solution of **30** (780 mg, 2.13 mmol) in CH_2Cl_2 (50 mL) under Ar at −45°C. The mixture was stirred for 7 h at −20°C, and then the reaction was quenched with saturated aqueous NH_4Cl solution (35 mL). The resulting mixture was extracted with CH_2Cl_2 (3×25 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was passed through a short pad of silica gel, eluting with heptane/EtOAc (4:1). After concentration of the eluate and co-evaporation of the volatiles with toluene (3×5 mL), the residue was heated to 120°C under reduced pressure (~1 mmHg) for 40 h. It was then purified by flash column chromatography (heptane/EtOAc, 3:1 → 2:1) to give **32** (442 mg, 41%) as a white solid. R_f = 0.55 (heptane/EtOAc, 1:1); m.p. 234–236°C (EtOAc/heptane); $[\alpha]_D^{23}$ = −33.5 (c = 1.1, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3421, 1712, 1505, 1482, 1263, 1059, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.54 (s, 1H), 7.40–7.30 (m, 5H), 6.80 (d, J = 9.5 Hz, 1H), 6.68 (s, 1H), 6.10–6.02 (m, 1H), 6.06 (s, 1H), 6.04 (s, 1H), 5.89 (dd, J = 10.5, 1.4 Hz, 1H), 4.82 (brs, 1H), 4.69 (d, J = 11.6 Hz, 1H), 4.64 (d, J = 11.4 Hz, 1H), 4.48 (brt, J = 9.3 Hz, 1H), 4.16–4.09 (m, 1H), 3.03 ppm (dd, J = 10.0, 2.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2, 161.5, 152.5, 148.4, 137.3, 137.2, 130.9, 128.8, 128.4, 128.1, 128.1, 126.9, 118.0, 110.7, 107.6, 102.4, 76.6, 72.5, 71.0, 50.7, 38.4 ppm; HRMS (FAB) calcd for $C_{23}H_{19}Cl_3NO_6$: 510.0278 $[M+H]^+$; found: 510.0260.

(1*R*,2*S*,3*S*,4*R*,4a*R*,11b*R*)-4-Benzyloxy-2,3-dihydroxy-1,2,3,4,4a,11b-hexahydro-1-(2,2,2-trichloroacetylamino)-6*H*-[1,3]benzodioxolo[5,6-*c*,1]benzopyran-6-one (33): *N*-Methylmorpholine *N*-oxide monohydrate (25 mg, 0.185 mmol) and OsO_4 (4% in H_2O, 0.1 mL, 0.016 mmol) were successively added to a solution of **32** (45 mg, 0.088 mmol) in THF (2 mL) under Ar. The mixture was stirred for 5 days under Ar and then the reaction was quenched by the addition of 10% aqueous $NaHSO_3$ (20 mL). The resulting mixture was extracted with EtOAc (3×15 mL) and the combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc, 1:1) to give **33** (45 mg, 94%) as a white solid. R_f = 0.12 (heptane/EtOAc, 1:1); m.p. 213–214°C (hexane/EtOAc); $[\alpha]_D^{23}$ = +8.9 (c = 0.6, DMSO); IR (KBr): $\tilde{\nu}$ = 3423, 2905, 1708, 1483, 1259, 1075, 1036 cm^{-1}; ^1H NMR (300 MHz, [D$_6$]DMSO): δ = 8.81 (d, J = 9.7 Hz, 1H), 7.40–7.30 (m, 6H), 6.84 (s, 1H), 6.09 (s, 1H), 6.08 (s, 1H), 5.00 (d, J = 3.6 Hz, 1H), 4.89–4.85 (m, 1H), 4.68 (d, J = 11.9 Hz, 1H), 4.67 (d, J = 7.5 Hz, 1H), 4.63 (d, J = 11.7 Hz, 1H), 4.13–4.01 (m, 1H), 3.93–3.84 (m, 1H), 3.35–3.29 ppm (m, 1H); ^{13}C NMR (75 Hz, [D$_6$]DMSO): δ = 163.4, 161.1, 151.3, 147.2, 138.1, 136.4, 128.4,

127.8 (2×), 117.8, 109.0, 108.3, 102.2, 93.1, 76.8, 75.9, 71.7, 70.8, 69.2, 51.5, 38.0 ppm; HRMS (FAB) calcd for $C_{23}H_{21}Cl_3NO_8$: 544.0333 $[M+H]^+$; found: 544.0350.

(1*R*,2*S*,3*S*,4*S*,4a*R*,11b*R*)-2-Benzyloxy-1,3,4-trihydroxy-1,3,4,4a,5,11b-hexahydro-2*H*-[1,3]dioxolo[4,5-*j*]phenanthridin-6-one (34): K_2CO_3 (1.12 g, 8.10 mmol) was added to a suspension of **33** (399 mg, 0.732 mmol) in MeOH (50 mL) under Ar and the mixture was refluxed for 18 h. It was then cooled, neutralised with an acidic ion-exchange resin (Amberlite IR-120), and concentrated in vacuo. The residue was purified by flash column chromatography (CH_2Cl_2/MeOH, 100:0 → 96:4) to give **34** (236 mg, 81%) as a white solid. R_f = 0.48 ($CHCl_3$/MeOH, 17:3); m.p. 164.0–165.0 °C (MeOH); $[\alpha]_D^{23}$ = +31.0 (c = 1.5, DMSO); IR (KBr): $\tilde{\nu}$ = 3392, 2905, 1656, 1464, 1261, 1074, 1038 cm^{-1}; ^1H NMR (300 MHz, [D$_6$]DMSO): δ = 7.40–7.26 (m, 6H), 6.98 (s, 1H), 6.92 (s, 1H), 6.08 (s, 2H), 5.27 (brs, 1H), 5.17 (brs, 1H), 4.85 (m, 1H), 4.67 (d, J = 12.0 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.60 (brs, 1H), 4.03 (brs, 1H), 3.86–3.82 (m, 1H), 3.78–3.65 (m, 2H), 2.95 ppm (brd, J = 10.3 Hz, 1H); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 164.0, 150.5, 145.9, 138.3, 135.1, 128.4, 127.6, 127.6, 123.8, 106.8, 105.8, 101.6, 77.5, 71.1, 71.0, 70.6, 66.0, 50.2, 40.7 ppm; HRMS (FAB) calcd for $C_{21}H_{22}NO_7$: 400.1396 $[M+H]^+$; found: 400.1400.

7-Deoxypancratistatin (2): From **11**: Acidic ion-exchange resin (Amberlite IR-120, 2 mL) was added to a solution of **11** (418 mg, 1.03 mmol) in MeOH (5 mL) and the mixture was refluxed for 53 h. It was then filtered and concentrated in vacuo, and the concentrate was passed through a pad of silica gel to give a crude yield of **14** (405 mg, R_f = 0.08 (hexane/EtOAc, 2:1)). This was taken up in CH_2Cl_2 (25 mL) under Ar and *m*-CPBA (890 mg, 5.16 mmol) was added. The mixture was stirred for 24 h at room temperature, and then the reaction was quenched by the addition of 10% aqueous Na_2SO_3 (50 mL). The resulting mixture was stirred for 1.5 h, then extracted with CH_2Cl_2 (2×35 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to give a crude yield of **15** (325 mg, R_f = 0.24 (hexane/EtOAc, 1:2)). An aqueous solution of sodium benzoate (5.2 mg in 20 mL) was added to the residue and the slurry was refluxed for 3 days. The mixture was then cooled and concentrated in vacuo. The residue of **16** (R_f = 0.19 (hexane/EtOAc, 1:4)) was redissolved in AcOH (7 mL) and the solution was degassed. Pd/C (90 mg) was added and the system was evacuated twice by the application of high vacuum and filled with H_2. The system was fitted with a balloon filled with H_2 and the reaction mixture was stirred at room temperature. Additional H_2 was introduced as needed. After one week, the mixture was filtered through a pad of Celite and concentrated in vacuo. The residue was purified by flash column chromatography (CH_2Cl_2/MeOH, 9:1) to give **2** (70 mg, 22%) as a white solid. R_f = 0.61 ($CHCl_3$/MeOH, 5:1); m.p. 308–309 °C (MeOH) (lit.:[18] 306–309 °C); $[\alpha]_D^{23}$ = +73.8 (c = 0.9, DMF) (lit.:[17b] +74.6, c = 0.85, DMF).

From **34**: Pd(OH)$_2$/C (432 mg) was added to a solution of **34** (225 mg, 0.563 mmol) in EtOAc (30 mL). The system was twice evacuated by the application of high vacuum and filled with H_2. The system was fitted with a balloon filled with H_2 and the reaction mixture was stirred for 20 h at room temperature. The mixture was then filtered through a pad of Celite, which was subsequently rinsed with MeOH (100 mL). The combined organic phases were concentrated in vacuo and the residue was purified by flash column chromatography (CH_2Cl_2/MeOH, 9:1) to give **2** (138 mg, 79%) as a white solid. R_f = 0.13 ($CHCl_3$/MeOH, 17:1); m.p. 308–310 °C (MeOH) (lit.:[18] 306–309 °C); $[\alpha]_D^{23}$ = +72.7 (c = 2.3, DMF) (lit.:[17b] +74.6, c = 0.85, DMF); IR (KBr): $\tilde{\nu}$ = 3401, 2902, 1656, 1610, 1466, 1264, 1039 cm^{-1}; ^1H NMR (300 MHz, [D$_6$]DMSO): δ = 7.31 (s, 1H), 6.91 (s, 1H), 6.87 (brs, 1H), 6.08 (s, 2H), 5.38 (d, J = 4.0 Hz, 1H), 5.10 (d, J = 5.7 Hz, 1H), 5.08 (d, J = 6.4 Hz, 1H), 4.80 (d, J = 7.6 Hz, 1H), 4.36–4.29 (m, 1H), 3.97 (dd, J = 6.8, 3.5 Hz, 1H), 3.88–3.82 (m, 1H), 3.77–3.64 (m, 2H), 2.98 ppm (brd, J = 10.0 Hz, 1H); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 164.0, 150.5, 145.9, 135.4, 123.8, 106.8, 105.5, 101.6, 73.4, 70.3, 70.2, 68.7, 50.4, 40.1 ppm; HRMS (FAB) calcd for $C_{14}H_{16}NO_7$: 310.0927 $[M+H]^+$; found: 310.0926.

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