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A concise synthetic route to the conduritols from pentoses

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A short synthetic strategy for preparation of the conduritols is described. The key step employs a zinc-mediated fragmentation of protected methyl 5-deoxy-5-iodo-D-pentofuranosides followed by an allylation of the intermediate aldehyde in the same pot. The allylation is performed with 3-bromopropenyl benzoate and occurs with good diastereoselectivity. An amino group can be introduced in the product by trapping the intermediate aldehyde as the imine prior to the allylation. The functionalised 1,7-octadienes, thus obtained, are converted into protected conduritols by ring-closing olefin metathesis.

Introduction

The synthesis of conduritols (cyclohex-5-ene-1,2,3,4-tetrols) has attracted considerable attention in the past twenty years.[1] The conduritols consist of six diastereomers which are labeled A to F. Two of these are *meso* compounds while the remaining four are optically active. Conduritols A and F are naturally occurring,[2] while the epoxide of conduritol B is an irreversible β-glucosidase inhibitor.[3] The conduritols have been used as key intermediates in the preparation of natural products and other biologically important molecules.[4]

A number of strategies have been developed for the synthesis of enantiopure conduritols. Usually, the starting material is either *p*-benzoquinone,[5] cyclohexa-3,5-diene-1,2-diol,[6] an inositol,[7] or a carbohydrate.[8–12] In the latter case, the carbocyclisation step has been performed by either a Ferrier reaction,[8] a Ramberg–Bäcklund reaction,[9] a pinacol coupling,[10] or a ring-closing olefin metathesis reaction.[11] We have recently described a zinc-mediated tandem reaction for converting carbohydrates into acyclic dienes that can be cyclised by metathesis.[12] In this reaction, methyl 6-iodohexopyranosides are subjected to a reductive fragmentation to produce unsaturated aldehydes, which are then alkylated by a vinyl organometallic reagent in the same pot (Fig. 1a). By using this procedure, (−)-conduritols B and C have been prepared from D-glucose and D-mannose, respectively.[12,13]

We envisaged that this strategy could be further developed by employing the recently published reactions with 3-bromopropenyl acetate (**A**) and 3-bromopropenyl benzoate (**B**).[14] These reagents are known to perform α-acyloxyallylations of aldehydes in the presence of zinc and indium. Consequently, we speculated that these allylic bromides could be used in the zinc-mediated tandem reaction with a methyl 5-iodopentofuranoside as the carbohydrate substrate (Fig. 1b). The product would then be the same eight-carbon diene as obtained earlier, but with the possibility of generating different stereogenic centers.

Herein, we report a short synthetic route to the conduritols where a zinc-mediated reaction between a pentofuranoside and an acyloxyallyl bromide serve as the key step.

Results and discussion

Methyl iodofuranoside **1** is easily available from D-ribose[15] and has been used as a convenient test substrate in the development of our earlier methods.[12,16] In these methodology studies, iodofuranoside **1** was treated with zinc in the presence of allyl or propargyl bromide to afford a 1,7-diene or a 1,7-enyne, respectively. The tandem reactions were performed in a THF–H_2O mixture under sonication at 40 °C. The addition of water as a co-solvent enhanced the rate of the reactions.

Thus, for the initial experiment, furanoside **1** and acetate **A** were treated with zinc under these conditions (Scheme 1). This resulted in one major product **3a**, which was isolated in 72% yield as a 4 : 1 mixture of two isomers. A minor product (9%) containing several other isomers was also isolated. Some of these isomers may result from migration of the acetyl group, which has been observed earlier.[14] The major product mixture was therefore deacetylated and protected with an additional isopropylidene group, which gave one single symmetrical product. This experiment shows that migration of the acetyl groups does in fact occur under the reaction conditions.

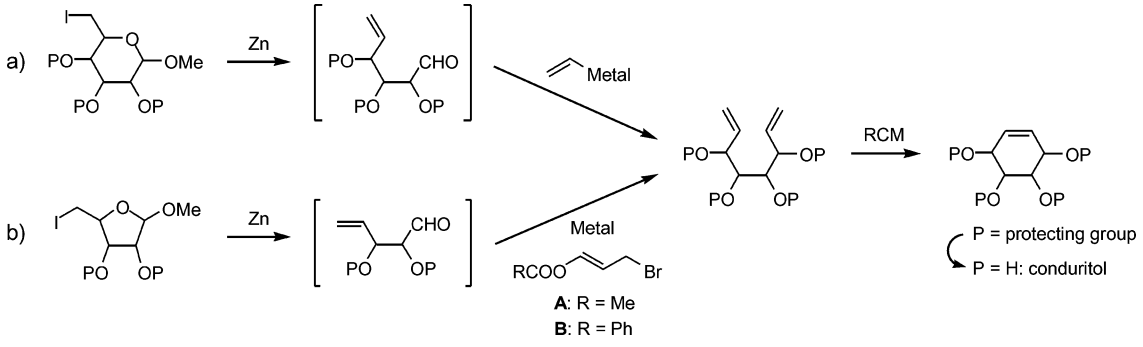

Fig. 1 Strategies for synthesis of the conduritols.

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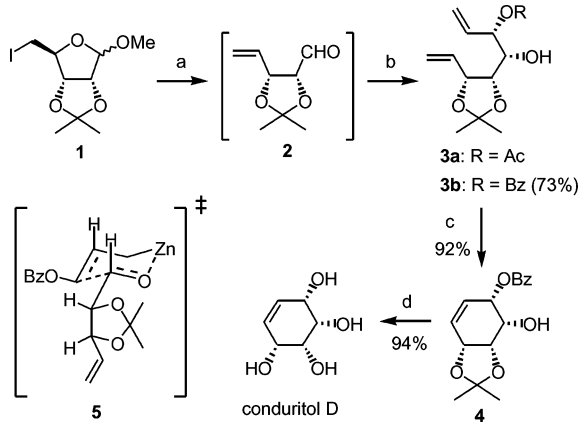


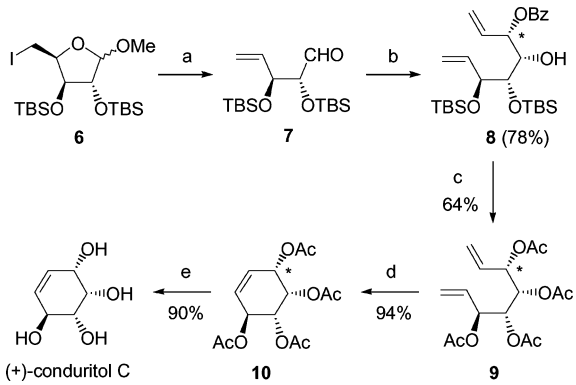
Scheme 1 *Reagents and conditions*: (a) Zn, THF, H_2O, ultrasound, 40 °C; (b) Zn, **A** or **B**, THF, H_2O, ultrasound, 40 °C; (c) $(PCy_3)(C_3H_4N_2Mes_2)Cl_2Ru{=}CHPh$, CH_2Cl_2, 40 °C; (d) AcOH, H_2O, 80 °C, then MeOH, H_2O, NaOH, rt.

The tandem reaction between **1** and **A** was also studied in the presence of indium, which has previously been shown to change the stereochemical outcome in some cases.[12] However, the reaction was quite sluggish under these conditions and gave rise to a more complex product mixture in addition to a considerable amount of unreacted **1**. Apparently, indium is not sufficiently reactive to affect the reductive fragmentation of **1**. Instead, this fragmentation was carried out with zinc to give aldehyde **2**, which was separated from the zinc salts by extraction.[16] The indium-mediated coupling with **A** was subsequently repeated by using this aldehyde as the substrate. In this experiment, diene **3a** was isolated in 42% yield with no sign of acetyl migration. It should be noted that diene **3a** is the major diastereomer regardless of the metal used in the allylation. A small amount (5%) of several other diastereomers was also obtained from the reaction with indium. Although this two-step sequence with zinc and indium does seem to solve the problem with ester migration, the overall yield is lower than when the reaction is performed with zinc in a one-pot sequence. As a result, it was decided to use the one-pot conditions with zinc and to avoid the ester migration by employing a more stable ester group. Gratifyingly, when furanoside **1** was treated with zinc and benzoate **B**, the reaction furnished diene **3b** in 73% yield as a single isomer.

Compound **3b** was then converted into cyclohexene **4** in 92% yield by ring-closing olefin metathesis with Grubbs' 2nd-generation catalyst.[17] The highly coloured ruthenium catalyst was removed in the workup by treating the reaction mixture with tris(hydroxymethyl)phosphine.[18] Cyclohexene **4** is an interesting chiral building block that can be prepared from D-ribose in only four steps. Deprotection of **4** under acidic conditions to hydrolyse the isopropylidene group followed by basic conditions to remove the ester group then afforded conduritol D in 94% yield, with spectral data in agreement with literature values. Conduritol D was also obtained from diene **3a** when this compound was subjected to metathesis followed by deprotection. These results confirm the stereochemistry of the major products in the allylation reactions. The stereochemical outcome is in accordance with earlier observations in similar systems[12,14] and can be rationalised by the Felkin–Anh transition state **5**.[19]

To further explore the use of benzoate **B** as an allylating reagent, the zinc-mediated tandem reaction was also investigated on a methyl iodofuranoside with *xylo*-configuration. As the hydroxy groups in the 2- and 3-position are *trans*, an isopropylidene group cannot be used in this case to protect the diol. Instead, the TBS (*tert*-butyldimethylsilyl) group was chosen, since it is very stable, easy to introduce, and can be selectively removed using a fluoride reagent. It is necessary to protect the 2- and 3-positions in the furanoside in order to obtain a high yield and a good diastereoselectivity in the tandem reaction.[12]

Thus, methyl iodofuranoside **6** (Scheme 2) was synthesised in three steps from D-xylose.[20] The fragmentation–allylation reaction was initially carried out under the same conditions as described for furanoside **1**. This gave compound **8** as a 7 : 2 mixture of diastereomers in about 80% yield. Unfortunately, the isolated product was contaminated with a byproduct, which could not be removed by column chromatography. The byproduct seems to arise from a zinc-mediated homocoupling of allylic bromide **B**. As a consequence, the conditions were changed to avoid this homocoupling. Iodofuranoside **6** was first sonicated with zinc and converted into aldehyde **7**. Excess zinc was removed by filtration, but the aldehyde was not further purified. Instead, indium and benzoate **B** were added and the mixture was sonicated again to give diene **8** in 78% yield with no sign of the byproduct from the zinc experiment. Diene **8** was isolated as the same 7 : 2 mixture of diastereomers as observed with zinc. The diastereomeric mixture could not be separated by flash chromatography and was therefore used in the next step.

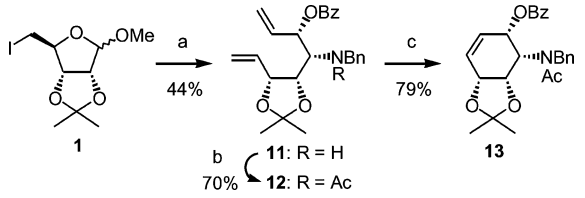


Scheme 2 *Reagents and conditions*: (a) Zn, THF, H_2O, ultrasound, 40 °C; (b) In, **B**, THF, H_2O, ultrasound, 40 °C; (c) MeOH, NaOH, rt, then TBAF, THF, rt, then Ac_2O, Et_3N, DMAP, THF, rt; (d) $(PCy_3)(C_3H_4N_2Mes_2)Cl_2Ru{=}CHPh$, CH_2Cl_2, 40 °C; (e) MeOH, K_2CO_3, rt. (* = 7 : 2 mixture).

Ring-closing metathesis of diene **8** was attempted with Grubbs' 2nd-generation catalyst[17] and Hoveyda–Grubbs' 2nd-generation catalyst.[21] In both cases, only partial conversion was observed, presumably due to steric hindrance from the bulky TBS groups. To overcome this problem, the TBS groups were removed and replaced by another protecting group. Several attempts to cleave the TBS groups without migration of the benzoyl group failed, and it was decided to remove both protecting groups and then peracetylate the resulting tetrol. We have previously shown that the tetraacetylated dienes are good substrates for ring-closing metathesis while the corresponding tetrols are not compatible with the ruthenium catalysts.[12] The benzoyl group was deprotected with sodium hydroxide in methanol and the crude product was treated with TBAF to afford the fully deprotected tetrol. Subsequent acetylation gave tetraacetate **9** in 64% overall yield as a 7 : 2 mixture of diastereomers, which co-eluted by flash chromatography. The diene mixture was subjected to ring-closing metathesis to afford the corresponding cyclohexenes in 94% yield. In this case, the ruthenium catalyst was removed in the workup by treatment with activated carbon.[22] Again, it was not possible to separate the two isomers by column chromatography, but the major isomer could be isolated in pure form by crystallisation. The structure of the major isomer was assigned as (+)-conduritol C tetraacetate by comparison with literature data. Accordingly, the stereochemical outcome of the allylation is the same as observed above in the ribose experiment.

The zinc-mediated fragmentation–allylation reaction can also be used for introducing an amino group. If benzylamine is added

to the reaction mixture, the intermediate aldehyde will form an *N*-benzylimine, and allylation of this imine will then occur to form an *N*-benzyl aminodiene.[12] We decided to investigate this possibility with benzoate **B**, since this strategy would give rise to aminoconduritols. Contrary to the aldehyde experiments above, the imine reactions must occur under strictly anhydrous conditions. To explore the formation and allylation of this imine, aldehyde **2** was treated with benzylamine and 3 Å molecular sieves in dry THF. The molecular sieves were removed after 2 h followed by addition of zinc and benzoate **B**. The resulting mixture was sonicated at 40 °C which gave aminodiene **11** in 41% yield as a single diastereomer (Scheme 3).



Scheme 3 *Reagents and conditions*: (a) Zn, TMSCl, THF, ultrasound, 40 °C, then $BnNH_2$, 3 Å MS, THF, rt, then Zn, **B**, THF, ultrasound, 40 °C; (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 40 °C; (c) $(C_3H_4N_2Mes_2)Cl_2Ru{=}CHC_6H_4OC_3H_7$, toluene, 80 °C.

The next step was to develop a one-pot procedure where the fragmentation of iodofuranoside **1** was followed by imine formation and then allylation of the imine. The zinc-mediated fragmentation of **1** proceeds considerably slower in pure THF compared to the THF–H_2O mixture, but the rate can be enhanced by the addition of TMSCl.[16] Using these conditions, full conversion of iodofuranoside **1** was achieved in about 2 h. The reaction mixture was filtered and the filtrate was stirred with benzylamine and 3 Å molecular sieves followed by sonication with zinc and benzoate **B**. These one-pot conditions resulted in 44% yield of diene **11** as a single isomer. A few minor byproducts were also isolated, but not further identified.

Carbohydrate-derived amines are incompatible with ring-closing metathesis when ruthenium catalysts are used.[12,16] Thus, the amine functionality in **11** had to be blocked prior to the metathesis reaction. Somewhat surprisingly, this amino group was not very reactive and sterically demanding protecting groups like Boc and Fmoc could not be introduced. Instead, it was found that amine **11** could be acetylated to give amide **12** in 70% yield. Reflux for two days was required before complete conversion was observed, which reflects the lack of reactivity of the amine functionality in **11**.

Ring-closing metathesis of diene **12** proceeded slowly in refluxing dichloromethane, but in toluene at 80 °C **12** was converted smoothly into cyclohexene **13**. Both Grubbs' 2nd-generation catalyst[17] and Hoveyda–Grubbs' 2nd-generation catalysts[21] were able to catalyse the conversion, but the Hoveyda–Grubbs' catalyst gave a cleaner and a slightly faster reaction, to afford the product **13** in 79% yield. The stereochemistry in **13** was established by NMR. The double bond was saturated with hydrogen over Pearlman's catalyst followed by hydrolysis of the isopropylidene group. The resulting cyclohexanediol exists in a chair conformation, and the ^1H NMR coupling constants confirmed the all-*syn* stereochemistry as shown in **13**. Hence, the imine allylation with benzoate **B** gave the same major diastereomer as the allylation of the aldehydes.

In conclusion, we have described a short synthetic method for preparation of enantiopure conduritols. The key steps are three organometallic reactions: zinc-mediated fragmentation of a protected pentose, zinc- or indium-mediated allylation with 3-bromopropenyl benzoate, and ruthenium-catalysed ring-closing metathesis. This procedure complements our previously developed protocol where a protected hexose served as the starting material.

Experimental

For general experimental methods, see our earlier work.[13] All sonications were performed in a Branson 1210 sonic bath. Zinc dust was activated by stirring with 1 M HCl for 5 min followed by filtration and wash with water, acetone and Et_2O, and then drying under high vacuum with a heatgun. Flash column chromatography was performed with silica gel 60 (0.035–0.070 mm) while dry column chromatography[27] was carried out with silica gel 60 (0.015–0.040 mm).

1,2,7,8-Tetradeoxy-3-benzoyl-5,6-*O*-isopropylidene-D-*allo*-octa-1,7-dienitol (3b)

Zinc (1.04 g, 15.9 mmol) was added to a deoxygenated solution of methyl furanoside **1** (500 mg, 1.59 mmol) in THF–H_2O (4 : 1, 15 mL). The mixture was sonicated at 40 °C under N_2 for 1 h, at which point TLC revealed full conversion into aldehyde **2**. Benzoate **B** (287 mg, 1.19 mmol) was then added and the sonication continued at 40 °C. After 1 h another portion of benzoate **B** (287 mg, 1.19 mmol) was added and the mixture was sonicated for an additional 1 h. The mixture was filtered through Celite, which was then rinsed with Et_2O (50 mL). The filtrate was washed with 0.1 M HCl (50 mL), saturated $NaHCO_3$ (2 × 50 mL) and H_2O (50 mL). The combined aqueous phases were extracted with Et_2O (50 mL). The combined organic phases were dried with $MgSO_4$ and absorbed on Celite. Purification by dry column chromatography (hexane–EtOAc, 19 : 1 → 17 : 3) gave 371 mg (73%) of **3b** as a clear oil. R_f 0.28 (heptane–EtOAc, 3 : 1); $[\alpha]_D$ −27 (*c* 2.2, $CHCl_3$); ν_{max}(neat)/cm^{-1}: 3498, 2987, 1718, 1272; δ_H (300 MHz, $CDCl_3$): 8.02–7.99 (m, 2H), 7.50 (m, 1H), 7.41–7.35 (m, 2H), 6.07–5.88 (m, 2H), 5.72 (m, 1H), 5.47–5.33 (m, 3H), 5.22 (ddd, J = 1.2, 1.5, 10.5 Hz, 1H), 4.63 (m, 1H), 3.97–3.96 (m, 2H), 1.46 (s, 3H), 1.30 (s, 3H); δ_C (75 MHz, $CDCl_3$): 165.5, 133.7, 133.3, 131.2, 130.2, 129.8, 128.5, 120.2, 118.3, 109.3, 78.7, 77.4, 76.5, 70.9, 28.0, 25.6; Anal. calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 68.04; H, 6.73%.

(1*S*,2*S*,3*S*,6*R*)-3-Benzoyloxy-8,8-dimethyl-2-hydroxy-7,9-dioxabicyclo[4.3.0]non-4-ene (4)

Diene **3b** (154 mg, 0.48 mmol) was dissolved in deoxygenated CH_2Cl_2 (10 mL) and Grubbs' 2nd-generation catalyst (41 mg, 0.05 mmol) was added. The solution was stirred under N_2 for 90 min at 40 °C. A 1.5 M solution of $P(CH_2OH)_3$ in 2-propanol (1.2 mL) was then added and the reaction was stirred for an additional 18 h at 40 °C. The mixture was washed with H_2O (2 × 15 mL), dried and absorbed on Celite. Purification by dry column chromatography (CH_2Cl_2–MeOH, 50 : 0 → 49 : 1) gave 129 mg (92%) of **4** as a solid. R_f 0.36 (heptane–EtOAc, 1 : 1); $[\alpha]_D$ +52 (*c* 1.6, $CHCl_3$); ν_{max}(KBr)/cm^{-1}: 1720, 1698, 1274; δ_H (300 MHz, $CDCl_3$): 8.12–8.08 (m, 2H), 7.58 (m, 1H), 7.47–7.42 (m, 2H), 6.04 (ddd, J = 1.2, 2.9, 10.2 Hz, 1H), 5.94 (ddt, J = 0.5, 3.2, 10.3 Hz, 1H), 5.53 (m, 1H), 4.66 (m, 1H), 4.50 (dd, J = 3.2, 6.3 Hz, 1H), 4.16 (dt, J = 3.6, 7.2 Hz, 1H), 2.52 (d, J = 7.2 Hz, OH), 1.54 (s, 3H), 1.45 (s, 3H); δ_C (75 MHz, $CDCl_3$): 166.4, 133.4, 130.0 (2C), 128.6 (2C), 126.3, 111.0, 74.4, 71.7, 69.1, 66.3, 27.3, 25.9; Anal. calcd. for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.33; H, 6.23%.

Conduritol D

Cyclohexene **4** (81 mg, 0.28 mmol) was dissolved in 80% AcOH (5 mL) and stirred for 1 h at 80 °C. The solvent was removed *in vacuo* and the crude product was dissolved in MeOH–H_2O (5 : 1, 5 mL). NaOH (100 mg) was added and the resulting solution was stirred for 1 h at room temperature. Saturated NH_4Cl (1 mL) was added and the reaction mixture was absorbed on Celite. Purification by dry column chromatography (EtOAc–MeOH, 10 : 0 → 9 : 1) gave 39 mg (94%) of the target compound as a clear oil. R_f 0.06 (CH_2Cl_2–MeOH, 5 : 1); δ_H (300 MHz, CD_3OD):

5.79 (d, $J = 1.5$ Hz, 2H), 4.10 (d, $J = 2.8$ Hz, 2H), 3.80 (d, $J = 4.7$ Hz, 2H); δ_C (75 MHz, CD_3OD): 130.3 (2C), 72.0 (2C), 69.1 (2C). NMR data are in accordance with literature values.[23]

1,2,7,8-Tetradeoxy-3-benzoyl-5,6-di-*O*-(*tert*-butyldimethylsilyl)-L-*talo*-octa-1,7-dienitol (8)

Zinc (234 mg, 3.58 mmol) was added to a deoxygenated solution of methyl furanoside **6** (180 mg, 0.358 mmol) in THF–H_2O (4 : 1, 3 mL). The mixture was sonicated at 40 °C for 1 h, at which point TLC revealed full conversion into aldehyde **7**. The reaction mixture was filtered through Celite, which was then rinsed with THF–H_2O (4 : 1, 2 mL). Benzoate **B** (129 mg, 0.537 mmol) and indium (205 mg, 1.79 mmol) were added and the reaction was sonicated under argon at 40 °C for 1 h. The mixture was filtered through Celite, which was then washed with Et_2O (30 mL). The organic phase was washed with 1 M HCl (20 mL), saturated $NaHCO_3$ (2 × 20 mL) and H_2O (20 mL), dried and absorbed on Celite. Purification by flash column chromatography (heptane–EtOAc, 25 : 0 → 24 : 1) gave the target compound (140 mg, 78%) as a clear oil (7 : 2 mixture of diastereomers). R_f 0.48 (heptane–EtOAc, 3 : 1); ν_{max}(KBr)/cm^{-1}: 3498, 2956, 1723, 1260. For the major isomer **8**: δ_H (500 MHz, $CDCl_3$): 8.09–8.01 (m, 2H), 7.59 (m, 1H), 7.45–7.39 (m, 2H), 6.20–6.07 (m, 2H), 5.74 (d, $J = 7.2$ Hz, 1H), 5.48 (d, $J = 17.3$ Hz, 1H), 5.49–5.21 (m, 3H), 4.42 (m, 1H), 4.04 (d, $J = 8.6$ Hz, 1H), 3.67 (dd, $J = 4.2$, 8.9 Hz, 1H), 0.98–0.88 (m, 18H), 0.18–0.02 (m, 12H); δ_C (75 MHz, $CDCl_3$): 165.9, 134.8, 132.9, 131.7, 130.6, 129.9, 128.4, 120.6, 116.8, 76.3, 75.6, 74.8, 72.0, 26.0, 25.9, 18.2, 18.2, −3.4, −4.4, −4.7, −5.0. Anal. calcd. for $C_{27}H_{46}O_5Si_2$: C, 63.98; H, 9.15. Found: C, 63.73; H, 8.90%.

1,2,7,8-Tetradeoxy-3,4,5,6-tetra-*O*-acetyl-L-*talo*-octa-1,7-dienitol (9)

Compound **8** (424 mg, 0.84 mmol) and NaOH (134 mg, 3.35 mmol) were dissolved in dry MeOH (10 mL) and stirred under argon for 1.5 h. CH_2Cl_2 (40 mL) was added and the solution was washed with saturated NH_4Cl (2 × 20 mL) and H_2O (2 × 20 mL). The combined aqueous phases were extracted with CH_2Cl_2 (10 mL) and the combined organic phases were dried and concentrated under reduced pressure. The residue was dissolved in THF (10 mL), and a 0.5 M solution of TBAF in THF (4.0 mL) was added. The solution was stirred under argon for 30 min, after which Ac_2O (0.79 mL, 8.4 mmol), Et_3N (1.40 mL, 10.1 mmol) and DMAP (catalytic) were added. After stirring for another 1.5 h, the reaction mixture was diluted with Et_2O (40 mL) and washed with saturated $NaHCO_3$ (2 × 20 mL) and H_2O (2 × 20 mL). The combined aqueous phases were extracted with CH_2Cl_2 (10 mL) and the combined organic phases were dried and absorbed on Celite. Purification by flash column chromatography (heptane–EtOAc, 9 : 1 → 8 : 2) gave the target compound (184 mg, 64%) as a solid (7 : 2 mixture of diastereomers). R_f 0.18 (heptane–EtOAc, 3 : 1); ν_{max}(KBr)/cm^{-1}: 1746, 1372, 1215. For the major isomer **9**: δ_H (500 MHz, $CDCl_3$): 5.82 (ddd, $J = 6.5$, 10.6, 17.2 Hz, 1H), 5.69 (ddd, $J = 5.1$, 10.4, 17.5 Hz, 1H), 5.52 (m, 1H), 5.40 (m, 1H), 5.33–5.21 (m, 6H), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H); δ_C (75 MHz, $CDCl_3$): 170.1, 169.9, 169.8, 169.7, 132.0, 130.8, 119.9, 118.2, 73.2, 71.4, 70.1, 70.1, 21.1, 21.0, 20.9, 20.9. Anal. calcd. for $C_{16}H_{22}O_8$: C, 56.14; H, 6.48. Found: C, 56.36; H, 6.48%. NMR data are in accordance with literature data.[12]

(+)-Conduritol C tetraacetate (10)

Compound **8** (81 mg, 0.24 mmol) was dissolved in deoxygenated CH_2Cl_2 (5 mL) and Grubbs' 2nd-generation catalyst (10 mg, 0.012 mmol) was added. The solution was stirred under N_2 for 1.5 h at 40 °C. Activated carbon (200 mg) was then added and the reaction was stirred for an additional 18 h at room temperature. The mixture was filtered through Celite, dried and concentrated under reduced pressure. Purification by flash column chromatography (heptane–EtOAc, 9 : 1 → 8 : 2) gave 70 mg (94%) of the target compound as a solid (7 : 2 mixture of diastereomers). It was not possible to separate the two isomers by chromatography, but pure (+)-conduritol C tetraacetate (40 mg) could be obtained by recrystallisation from MeOH. R_f 0.23 (heptane–EtOAc, 1 : 1); ν_{max}(KBr)/cm^{-1}: 1756, 1372, 1229. For the major isomer **10**: mp 100–101 °C (MeOH) (lit.[24] mp 96–97.5 °C); $[a]_D$ + 200.7 (*c* 1.5, $CHCl_3$) (lit.[25] $[a]_D^{24}$ +194 (*c* 1.1, $CHCl_3$)); δ_H (300 MHz, $CDCl_3$): 5.78 (m, 1H), 5.68–5.62 (m, 4H), 5.18 (dd, $J = 1.4$, 8.4 Hz, 1H), 2.12 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H); δ_C (75 MHz, $CDCl_3$): 170.6, 170.4, 170.1, 169.9, 127.6, 127.2, 70.6, 69.9, 69.6, 67.7, 21.1, 21.0, 20.9, 20.8. Anal. calcd. for $C_{14}H_{18}O_8$: C, 53.50; H, 5.77. Found: C, 53.74; H, 5.82%. NMR data are in agreement with literature values.[12] For the minor isomer: δ_H (300 MHz, $CDCl_3$): 5.86 (d, $J = 1.5$ Hz, 2H), 5.40 (dd, $J = 1.0$, 5.6 Hz, 2H), 5.32 (d, $J = 5.1$ Hz, 2H), 2.09 (s, 6H), 2.06 (s, 6H). δ_C (75 MHz, $CDCl_3$): 170.2 (2C), 170.0 (2C), 127.8 (2C), 69.4 (2C), 68.3 (2C), 21.1 (2C), 21.0 (2C). NMR data are in accordance with the reported spectra for conduritol A tetraacetate.[26]

Deacetylation of **10** (102 mg) with K_2CO_3 in MeOH followed by purification by flash chromatography (CH_2Cl_2–MeOH, 9 : 1 → 8 : 2) afforded 43 mg (90%) of (+)-conduritol C. R_f 0.20 ($CHCl_3$–MeOH, 3 : 1); ν_{max}(KBr)/cm^{-1}: 3367, 1054, 1022. δ_H (500 MHz, CD_3OD): 5.65 (dt, $J = 2.2$, 10.3 Hz, 1H), 5.56 (m, 1H), 4.27–4.22 (m, 2H), 4.02 (m, 1H), 3.53 (dd, $J = 2.1$, 7.5 Hz, 1H); δ_C (50 MHz, CD_3OD): 130.9, 130.1, 76.2, 74.1, 70.7, 69.6. NMR data are in accordance with the literature values.[24]

1,2,4,7,8-Pentadeoxy-3-benzoyl-4-benzylamino-5,6-*O*-isopropylidene-D-*allo*-octa-1,7-dienitol (11)

Zinc (1.7 g, 26.0 mmol) and TMSCl (0.20 mL, 1.63 mmol) were added to a deoxygenated solution of methyl furanoside **1** (1.0 g, 3.18 mmol) in anhydrous THF (15 mL). The mixture was sonicated at 40 °C under N_2 for 2 h, at which point TLC revealed full conversion into aldehyde **2**. The reaction mixture was filtered through Celite, and the Celite pad was washed with anhydrous THF (2 mL). Benzylamine (1.0 mL, 14.2 mmol) and 3 Å molecular sieves (10 g) were added and the reaction was stirred for 2 h at ambient temperature and then filtered. Zinc (1.5 g, 22.3 mmol) and benzoate **B** (1.15 g, 4.77 mmol) were added and the reaction mixture was sonicated at 40 °C under N_2. After 4 h the mixture was filtered through Celite, which was then rinsed with Et_2O (150 mL). The filtrate was washed with saturated $NaHCO_3$ (4 × 100 mL), saturated NaCl (2 × 50 mL) and H_2O (2 × 50 mL), and the organic phase dried and absorbed onto Celite. Purification by dry column chromatography (hexane–EtOAc, 9 : 1 → 8 : 2) gave 568 mg (44%) of **11** as a clear oil. R_f 0.42 (hexane–EtOAc, 3 : 1); $[a]_D$ −25 (*c* 1.9, $CHCl_3$); ν_{max}(neat)/cm^{-1}: 2986, 1723, 1271; δ_H (300 MHz, $CDCl_3$): 8.08–8.01 (m, 2H), 7.57–7.52 (m, 1H), 7.46–7.39 (m, 2H), 7.28–7.21 (m, 5H), 6.04–5.88 (m, 3H), 5.45–5.28 (m, 3H), 5.20 (ddd, $J = 1.1$, 1.8, 10.3 Hz, 1H), 4.63 (m, 1H), 4.14 (d, $J = 12.3$ Hz, 1H), 3.88 (dd, $J = 6.1$, 10.1 Hz, 1H), 3.65 (d, $J = 12.6$ Hz, 1H), 3.14 (dd, $J = 2.5$, 10.2 Hz, 1H), 1.48 (s, 3H), 1.31 (s, 3H); δ_C (75 MHz, $CDCl_3$): 165.6, 140.7, 134.6, 133.2, 132.6, 130.4, 129.8, 128.6, 128.5, 128.2, 127.2, 118.5, 117.7, 108.9, 79.4, 78.5, 77.2, 59.7, 53.2, 28.2, 25.7. Anal. calcd. for $C_{25}H_{29}NO_4$: C, 73.68; H, 7.17; N, 3.44. Found: C, 73.26; H, 7.14; N, 3.25%.

1,2,4,7,8-Pentadeoxy-3-benzoyl-4-(*N*-benzyl)acetamido-5,6-*O*-isopropylidene-D-*allo*-octa-1,7-dienitol (12)

Aminodiene **11** (446 mg, 1.10 mmol) was dissolved in CH_2Cl_2 (20 mL), and Ac_2O (0.41 mL, 4.38 mmol), Et_3N (0.92 mL, 6.57 mmol) and DMAP (13 mg, 0.11 mmol) were added. The solution was stirred at 40 °C for 2 days. The resulting orange solution was diluted with CH_2Cl_2 (30 mL), washed with 1 M AcOH (2 × 10 mL) and H_2O (10 mL), dried, and absorbed onto

Celite. Purification by dry column chromatography (hexane–EtOAc, 9 : 1 → 8 : 2) gave **12** (284 mg, 70%) as a white solid (two rotamers by NMR). R_f 0.20 (hexane–EtOAc, 3 : 1); ν_{max}(KBr)/cm^{-1}: 1723, 1638, 1272; δ_H (300 MHz, $CDCl_3$, major rotamer): 8.06 (d, $J = 7.2$ Hz, 2H), 7.60–7.21 (m, 8H), 6.06–5.89 (m, 2H), 5.74 (ddd, $J = 7.2$, 10.3, 17.2 Hz, 1H), 5.50–5.15 (m, 5H), 4.59–4.19 (m, 3H), 3.63 (dd, $J = 6.2$, 7.7 Hz, 1H), 2.15 (s, 3H), 1.41 (s, 3H), 1.23 (s, 3H); δ_C (50 MHz, $CDCl_3$, major rotamer): 172.7, 166.3, 134.5, 133.9, 133.6, 132.9, 129.8, 128.7, 128.4, 128.2, 127.6, 126.4, 119.1, 118.9, 108.9, 79.8, 78.9, 74.8, 59.6, 47.4, 27.9, 25.2, 22.7.

(1*S*,2*S*,3*S*,6*R*)-3-Benzoyloxy-2-(*N*-benzyl)acetamido-8,8-dimethyl-7,9-dioxabicyclo[4.3.0]non-4-ene (13)

Diene **12** (275 mg, 0.61 mmol) and Hoveyda–Grubbs' 2nd-generation catalyst (38 mg, 0.06 mmol) were dissolved in deoxygenated toluene (10 mL) and stirred at 80 °C under N_2 for 2 h. A 1.5 M solution of $P(CH_2OH)_3$ in 2-propanol (2 mL) was added and the reaction was stirred for an additional 18 h at 80 °C. The mixture was washed with H_2O (2 × 10 mL), dried and absorbed onto Celite. Purification by dry column chromatography (CH_2Cl_2–MeOH, 100 : 0 → 97 : 3) gave 204 mg (79%) of **13** as a solid. R_f 0.34 (heptane–EtOAc, 1 : 1); $[\alpha]_D$ +138.7 (*c* 1.7, $CHCl_3$); ν_{max}(KBr)/cm^{-1}: 2983, 1718, 1651, 1272; δ_H (500 MHz, $CDCl_3$): 8.25 (d, $J = 7.2$ Hz, 2H), 7.57 (t, $J = 7.4$ Hz, 1H), 7.44 (t, $J = 7.8$ Hz, 2H), 7.26–7.11 (m, 5H), 5.99 (dd, $J = 5.4$, 10.1 Hz, 1H), 5.98–5.79 (m, 2H), 5.53 (dd, $J = 1.6$, 4.0 Hz, 1H), 5.22 (d, $J = 18.0$ Hz, 1H), 4.74 (d, $J = 17.9$ Hz, 1H), 4.61 (m, 1H), 4.31 (d, $J = 4.7$ Hz, 1H), 2.06 (s, 3H), 1.43 (s, 3H), 0.99 (s, 3H); δ_C (75 MHz, $CDCl_3$): 172.9, 166.1, 139.0, 133.1, 131.0, 130.3, 129.7, 128.5, 128.5, 126.9, 125.4, 124.4, 110.9, 74.4, 73.5, 66.7, 50.8, 50.5, 28.1, 26.2, 21.9; Anal. calcd. for $C_{25}H_{27}NO_5$: C, 71.24; H, 6.46; N, 3.32. Found: C, 70.96; H, 6.62; N, 3.27%.

Cyclohexene **13** and $Pd(OH)_2$/C were suspended in THF and stirred under H_2 at room temperature for 24 h. The mixture was filtered and concentrated. The residue was dissolved in 80% AcOH, and stirred at 80 °C for 1.5 h. Concentration and purification by flash chromatography (EtOAc) gave (1*S*,2*S*,3*S*,4*R*)-1-benzoyloxy-2-(*N*-benzyl)acetamido-3,4-dihydroxycyclohexane. δ_H (300 MHz, $CDCl_3$): 7.97–7.93 (m, 2H), 7.56 (m, 1H), 7.45–7.39 (m, 2H), 7.26–7.17 (m, 3H), 7.05 (d, $J = 7.0$ Hz, 2H), 5.44 (br s, 1H), 5.06 (d, $J = 17.8$ Hz, 1H), 4.87 (d, $J = 18.0$ Hz, 1H), 4.41 (br s, 1H), 4.21 (br s, 1H), 3.72 (m, 1H), 2.06 (s, 3H), 1.70–1.67 (m, 2H), 1.28–1.26 (m, 2H).

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