Efficient Synthesis of Enantiopure Conduritols by Ring-Closing Metathesis

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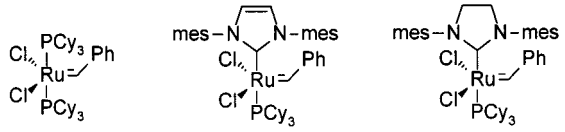
Two short synthetic approaches to enantiopure conduritols are described starting from the chiral pool. In both cases, the cyclohexene ring is assembled via ring-closing olefin metathesis. The terminal diene precursers for the metathesis reaction are prepared either from octitols or from tartaric acids. The former route involves a new method for selective bromination of the primary positions in long-chain carbohydrate polyols. Subsequent reductive elimination with zinc then generates the diene. The latter route uses a highly diastereoselective addition of divinylzinc to tartaric dialdehydes for preparation of the dienes.

Introduction

Cyclohex-5-ene-1,2,3,4-tetrols are an important class of cyclitols known as the conduritols. A total of 10 different stereoisomers exist of which six are diastereomers (conduritols A−F).[1] They display diverse biological activities, e.g., as insulin modulators[2] and glycosidase inhibitors.[3] In addition, many synthetic analogues of the conduritols have attracted significant attention.[4] Due to the carbocyclic structure, the conduritols are also valuable starting materials for synthesis of natural products.[5]

Only conduritol A[6] and (+)-conduritol F[7] have been found in nature and only in small amounts. All 10 stereoisomers have been prepared in nonracemic form by chemical synthesis.[1,8] However, many of the previous synthetic approaches require a significant number of steps, particularly for manipulation of protecting groups, e.g., benzyl groups. Recently, the method of ring-closing olefin metathesis (RCM) was introduced as a powerful technique for formation of the cyclohexene ring in the conduritols.[9] Since the pioneering catalyst developments by Schrock and Grubbs, the area of olefin metathesis has emerged as a very effective new tool for C−C bond formation.[10] The area of carbohydrate chemistry has also taken advantage of olefin metathesis mainly by the use of catalyst **1**.[11] However, carbohydrate derivatives are generally not very reactive toward metathesis due to the electron-withdrawing oxygen substituents. This problem has very recently been circumvented by the use of newly developed N-heterocyclic carbene catalysts **2**[12] and **3**,[13] which are more reactive than **1** for metathesis of carbohydrates.[9a,b] In particular, complex **3** appears to be the catalyst of choice as it is more reactive than **2** and very recently has become commercially available.[14]



1 **2** **3**

Herein, we report convenient routes to conduritols from higher carbon sugars and tartaric acids by the use of ring-closing metathesis catalyst **3**. We also demonstate a new reaction for selective bromination of the terminal positions in carbohydrate polyols.

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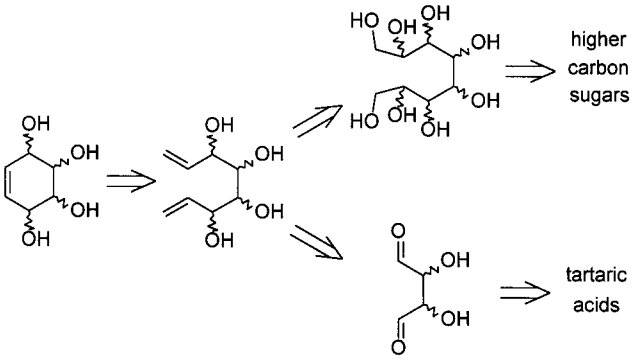
Scheme 1



Results and Discussion

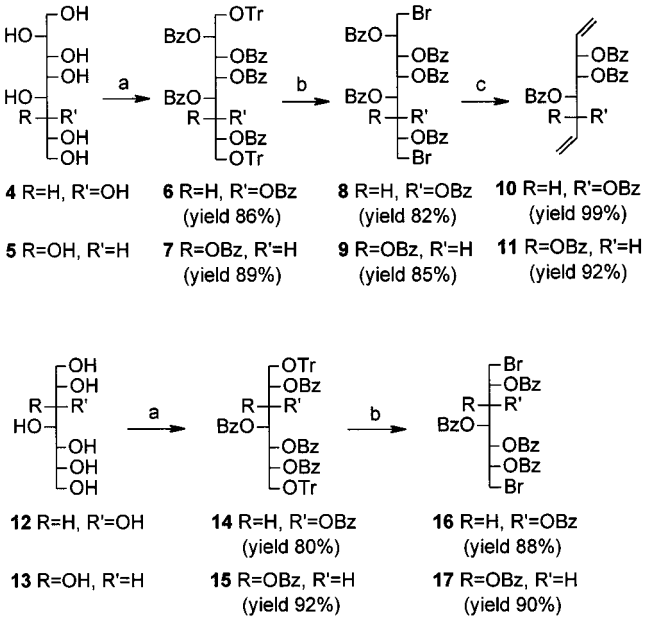
Retrosynthesis. Inspection of the carbon skeleton in the conduritols gives rise to the retrosynthetic analysis outlined in Scheme 1. A major task is to find short and efficient methods for preparation of the diene precursers for the RCM reaction. These eight-carbon dienes can originate either from the corresponding octitols by elimination or from four-carbon dialdehydes by addition of two vinyl groups. The octitols can be prepared from higher carbon sugars while the dialdehydes are available from tartaric acids. The higher carbon sugar route is a new approach to conduritols while the tartaric acid route has previously been explored for preparation of a (+)-conduritol E derivative.[9d]

Dienes from Higher Carbon Sugars. The one-pot Wittig/dihydroxylation transformation gives easy access to several higher carbon sugars from simple aldoses.[15] Subjecting the reaction to D-glucose gives D-*erythro*-L-*galacto*-octonolactone, which on reduction with sodium borohydride gives octitol **4** (Scheme 2). The same elongation on D-galactose gives D-*threo*-L-*galacto*-octonolactone, which on reduction provides octitol **5**.

It was decided to introduce bromine at the primary positions that would then set the stage for a reductive elimination in the presence of zinc. However, regioselective bromination of the terminal positions in these unprotected polyols is not trivial. Simple reaction with triphenylphosphine and carbontetrabromide[16] caused cyclization to derivatives of tetrahydrofuran. Acetyl bromide, which has been developed for bromination of smaller polyols,[17] was not suitable either due to competing cyclization and epimerization reactions. Tosylation was not sufficiently regioselective to be synthetically useful. To circumvent the problem of an intramolecular cyclization when the primary position is activated, it was decided to tritylate these positions. This was easily achieved in a hot pyridine solution with 2.5 equiv of trityl chloride. The same reaction mixture could be used for a subsequent benzoylation of the remaining six secondary hydroxy groups after cooling to room temperature. By pouring the reaction mixture into ethanol−ice, protected octitols **6** and **7** crystallized in high yields.

A saturated solution of hydrogen bromide in acetic acid is a frequently applied brominating agent in carbohydrate chemistry.[18] Indeed, direct treatment of **6** and **7** with this highly acidic mixture affected bromination of the primary positions to give **8** and **9**. Under these conditions, the trityl groups are cleaved immediately and yellow trityl bromide precipitates. Presumably, 1,2-benzoxonium ions are then formed which undergo ring-opening at the least sterically hindered position. Minor byproducts were also isolated containing bromine at a secondary position or acetate at the primary position. The best results were obtained when the reaction was allowed to proceed for 7 days apparently because some primary acetate is slowly converted into bromide. This bromination procedure constitutes a new method for the selective introduction of bromine in longer chain alditols. It has the additional advantage that the products are set up directly for a reductive elimination with zinc to give dienes **10** and **11** in high yields.

Scheme 2[a]



[a] Key: (a) TrCl, pyridine, 90 °C; then BzCl, rt; (b) HBr in AcOH, rt; (c) Zn, AcOH/EtOAc/H_2O (6:3:1), ultrasound.

To further explore the versatility of this bromination reaction, heptitols **12**[19] and **13** were also prepared (Scheme 2). Tritylation and benzoylation of these proceeded as described above to give crystalline **14** and **15**, which on bromination with hydrogen bromide in acetic acid gave dibromides **16** and **17**. Treatment of these with zinc and deprotection give dienes that we have previously cyclized to trihydroxycyclopentenes by RCM.[9a] On the other hand, the corresponding acetylated α,ω-ditrityl heptitols and octitols did not undergo clean bromination at the primary positions with hydrogen bromide in acetic acid. Fairly complex mixtures of epimers were obtained in these cases, presumably due to migration of the 1,2-acetoxonium ions.[20]

Dienes from Tartaric Acids. Preparation of conduritols from tartaric acids is a particularly short and efficient strategy. In a recent synthesis of a (+)-conduritol E derivative from protected L-tartaric acid, the first step involved reduction with Dibal-H to the corresponding

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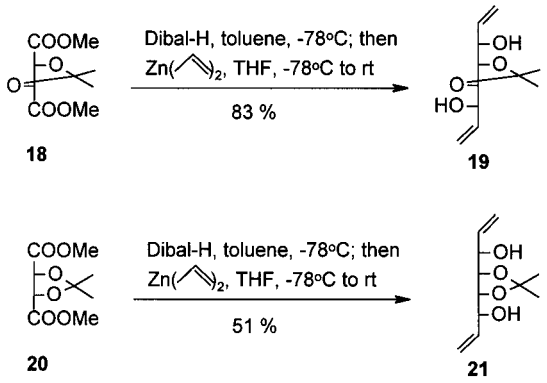
Scheme 3

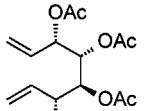
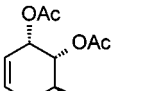
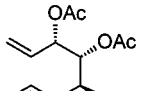
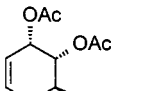
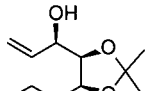
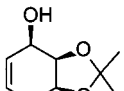


dialdehyde followed by vinyl Grignard addition.[9d] The major diastereomer **19** was obtained in this case in a ratio of 3:1 (**19**/other two diastereomers).[9d] However, we observed that by using divinylzinc this ratio could be improved to greater than 10:1 (Scheme 3). This is in accordance with addition reactions in similar systems where divinylzinc gives significantly better diastereoselectivity than vinyl Grignard.[9a,21] Furthermore, vinyl Grignard can act as a reducing agent, and more reduction of the intermediate dialdehyde to alcohol was observed with this reagent than when using divinylzinc. It is important for the chemoselectivity in the Dibal-H reduction that this reaction is carried out at −78 °C. This could only be performed with Dibal-H in toluene as severe precipitation occurred when Dibal-H in hexane was used. The reactions could also be performed on meso tartaric acid **20** where the diastereoselectivity with divinylzinc was about 3:1. In this case, the vinyl Grignard reagent was rather unselective and gave a quite complex mixture. The structures of **19** and **21** were verified after the RCM reaction. The formation of these as the major products with divinylzinc is in accordance with the predictions from the Felkin−Anh model.[22]

Ring-Closing Olefin Metathesis. The obtained dienes were then converted into the conduritols by RCM. Initial experiments revealed that benzoylated diene **10** or the corresponding unprotected tetrol gave low yields and significant decomposition in the metathesis reaction. Therefore, the benzoyl groups were replaced with acetyl groups to give diene **22**, which was well suited for metathesis in accordance with our previous experience.[9a] As anticipated,[9a,10] complex **3** was the best catalyst for the ring-closure giving a near-quantitative yield of the natural (+)-conduritol F tetraacetate **23** (Table 1, entries 1 and 2). A similar result was obtained for (+)-conduritol E tetraacetate **25** (entry 3). Diene tetraacetate **24** is available either from D-galactose (Scheme 2) or from L-tartaric acid (Scheme 3), the latter route being the shortest. Meso diene **21** could be cyclized directly to conduritol D acetonide **26** without changing the protecting group (entry 4) presumably aided by the Thorpe−Ingold effect from the isopropylidene group.[23]

In conclusion, we have developed a convenient synthesis of conduritols D−F starting from either higher carbon sugars or tartaric acids. These syntheses complement our previously developed preparation of conduritol B and C using a zinc-mediated tandem reaction.[9a] In all cases, the cyclohexene ring has been prepared by RCM with catalyst **3**. Hereby, we have now prepared five of the six diastereomeric conduritols in few steps from the chiral pool. These strategies should also be promising for synthesis of analogues and other natural products.

Table 1. Formation of Conduritols by RCM[a]

Entry	Diene	Catalyst	Conduritol	Yield
1	 **22**	10% **1**	 **23**	81%[b]
2		7.5% **3**		95%
3	 **24**	7.5% **3**	 **25**	96%
4	 **21**	5% **3**	 **26**	72%

[a] All reactions were carried out in CH_2Cl_2 at 40 °C. [b] 18% of **22** was recovered.

Experimental Section

For general procedures, see the preceding paper in this issue.[15]

D-*erythro*-L-*galacto*-Octitol (4). D-*erythro*-L-*galacto*-Octonolactone[15] (5.36 g, 22.5 mmol) was dissolved in H_2O (100 mL), and acidic ion-exchange resin (12 mL, Amberlite IR-120-H^+) was added. The mixture was cooled in ice and stirred while $NaBH_4$ (1.15 g, 30.4 mmol) was added at such a rate that the pH was maintained around 5. An additional amount of $NaBH_4$ (1.40 g, 37.0 mmol) was then added, increasing the pH to about 9. After the mixture was stirred at 0 °C for 1 h, more ion-exchange resin (125 mL, Amberlite IR-120-H^+) was added decreasing the pH to 3. The mixture was stirred overnight. The resin was removed by filtration and washed with H_2O. The filtrate was concentrated and co-concentrated with MeOH (4 × 100 mL) to give a white solid. Recrystallization from EtOH/H_2O yielded 4.01 g (74%) of **4**. Mp: 148−150 °C (lit.[24] mp 153−154 °C). ^{13}C NMR (D_2O, 75 MHz): δ 74.4, 72.7, 72.0, 70.8, 70.4, 68.9, 64.0, 63.3.

D-*threo*-L-*galacto*-Octitol (5). D-*threo*-L-*galacto*-Octonolactone[15] (25.0 g) was reduced with $NaBH_4$ as described above to give after recrystallization from H_2O 20.8 g (82%) of **5**. Mp: 216−218 °C (lit.[25] mp 230 °C). ^{13}C NMR (D_2O, 75 MHz): δ 70.5 (2C), 69.6 (2C), 68.5 (2C), 63.5 (2C).

D-*glycero*-D-*galacto*-Heptitol (13). D-*glycero*-D-*galacto*-Heptonolactone[15] (17.8 g) was reduced with $NaBH_4$ as described above to give after recrystallization from MeOH/H_2O 15.8 g (87%) of **13**. Mp: 178−182 °C (lit.[26] mp 187−188 °C). ^{13}C NMR (D_2O, 75 MHz): δ 73.1, 72.4, 71.4, 71.3, 70.4, 65.4 (2C).

General Procedure for Tritylation/Benzoylation (Scheme 2). Trityl chloride (7.0 g, 25.0 mmol) was added in

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portions to a slurry of the polyol (10.0 mmol) in redistilled pyridine (35 mL) at 90 °C over 2−5 h. The solution was then cooled to 0 °C before benzoyl chloride (10.5 mL, 90.0 mmol) was added. After the solution was stirred for 48 h at room temperature, the crude product was poured into a mixture of EtOH (60 mL) and ice (30 mL) and stirred for 2 h to provide a solid that was filtered off.

2,3,4,5,6,7-Hexa-*O*-benzoyl-1,8-di-*O*-triphenylmethyl-D-*erythro*-L-*galacto*-octitol (6). R_f = 0.47 (hexane/EtOAc = 2:1). Mp: 98−100 °C ($CHCl_3$/EtOH). $[\alpha]_D$: +3.5 (*c* 2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.25−6.85 (m, 60H), 6.16 (dd, *J* = 8.2, 4.1 Hz, 1H), 6.09 (dd, *J* = 6.6, 3.9 Hz, 1H), 6.05 (dd, *J* = 6.4, 3.0 Hz, 1H), 5.99 (t, *J* = 4.0 Hz, 1H), 5.81 (ddd, *J* = 8.8, 5.8, 3.2 Hz, 1H), 5.58 (ddd, *J* = 7.7, 4.3, 2.7 Hz, 1H), 3.40−3.05 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.1, 165.0 (2C), 164.8 (2C), 164.6, 143.2 (6C), 132.7−132.5 (6C), 129.8−126.6 (60C), 86.8, 86.5, 71.6, 70.9, 70.8, 70.0 (2C), 69.2, 62.1, 61.9. Anal. Calcd for $C_{88}H_{70}O_{14}$: C, 78.21; H, 5.22. Found: C, 77.99; H, 5.24.

2,3,4,5,6,7-Hexa-*O*-benzoyl-1,8-di-*O*-triphenylmethyl-D-*threo*-L-*galacto*-octitol (7). R_f = 0.51 (hexane/EtOAc = 2:1). Mp: 118−120 °C ($CHCl_3$/EtOH). $[\alpha]_D$: −12.5 (*c* 2.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.89 (d, *J* = 7.6 Hz, 4H), 7.82 (d, *J* = 7.5 Hz, 4H), 7.68 (d, *J* = 7.4 Hz, 4H), 7.49−7.35 (m, 6H), 7.30−7.17 (m, 24H), 7.03−6.98 (m, 18H), 6.04 (d, *J* = 5.2 Hz, 2H), 5.98 (dd, *J* = 5.2, 2.6 Hz, 2H), 5.78 (ddd, *J* = 6.4, 6.1, 2.6 Hz, 2H), 3.27 (dd, *J* = 9.4, 6.4 Hz, 2H), 3.12 (dd, *J* = 9.4, 6.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.0 (4C), 164.7 (2C), 143.2 (6C), 132.8 (2C), 132.6 (2C), 132.5 (2C), 129.9−126.6 (60C), 86.7 (2C), 70.8 (2C), 70.7 (2C), 70.4 (2C), 61.6 (2C). Anal. Calcd for $C_{88}H_{70}O_{14}$: C, 78.21; H, 5.22. Found: C, 77.98; H, 5.22.

General Procedure for Bromination (Scheme 2). The dityrityl compound (1.5 mmol) was treated with 32% HBr in AcOH (20 mL) in a closed flask for 7 days. The mixture was diluted with CH_2Cl_2 (50 mL) and washed with H_2O (200 mL) and 5% aqueous $NaHCO_3$ (3 × 200 mL). The organic phase was dried and concentrated and the residue purified by flash chromatography.

2,3,4,5,6,7-Hexa-*O*-benzoyl-1,8-dibromo-1,8-dideoxy-D-*erythro*-L-*galacto*-octitol (8). R_f = 0.46 (hexane/EtOAc = 2:1). $[\alpha]_D$: +5.58 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 8.21−7.10 (m, 30H), 6.20−6.00 (m, 4H), 5.68 (dt, *J* = 6.4, 2.3 Hz, 1H), 5.59 (ddd, *J* = 6.9, 4.4, 4.1 Hz, 1H), 3.71 (dd, *J* = 11.5, 4.1 Hz, 1H), 3.65−3.38 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.1, 165.0 (4C), 164.8, 133.5, 133.2 (2C), 133.0 (3C), 130.1−127.8 (30C), 71.0, 70.8 (2C), 70.6, 69.0, 68.7, 30.1, 29.0. Anal. Calcd for $C_{50}H_{40}O_{12}Br_2$: C, 60.50; H, 4.06; Br, 16.10. Found: C, 60.95; H, 4.20; Br, 15.94.

2,3,4,5,6,7-Hexa-*O*-benzoyl-1,8-dibromo-1,8-dideoxy-D-*threo*-L-*galacto*-octitol (9). R_f = 0.53 (hexane/EtOAc = 3:1). Mp: 152−155 °C (hexane/EtOAc). $[\alpha]_D$: +12.7 (*c* 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.96−7.83 (m, 12H), 7.54−7.41 (m, 6H), 7.36−7.22 (m, 12H), 6.07 (d, *J* = 6.6 Hz, 2H), 6.03 (dd, *J* = 6.6, 2.6 Hz, 2H), 5.67 (ddd, *J* = 6.6, 6.2, 2.6 Hz, 2H), 3.56 (dd, *J* = 10.8, 6.2 Hz, 2H), 3.50 (dd, *J* = 10.8, 6.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.1 (2C), 164.9 (4C), 133.2 (4C), 133.0 (2C), 129.8−128.1 (30C), 71.2 (2C), 70.7 (2C), 69.5 (2C), 28.9 (2C). Anal. Calcd for $C_{50}H_{40}O_{12}Br_2$: C, 60.50; H, 4.06; Br, 16.10. Found: C, 60.18; H, 4.13; Br, 16.05.

3,4,5,6-Tetra-*O*-benzoyl-1,2,7,8-tetradeoxy-D-*gulo*-octa-1,7-dienitol (10). Dibromide **8** (0.33 g, 0.33 mmol) was dissolved in a mixture of EtOAc (3 mL), H_2O (1 mL), and AcOH (6 mL). Activated zinc[9a] (1.00 g, 15.3 mmol) was added and the mixture sonicated for 3 h. The precipitate was filtered off and washed with H_2O and CH_2Cl_2. The filtrate was diluted with CH_2Cl_2 (60 mL) and washed with H_2O (25 mL) and 5% aqueous $NaHCO_3$ (50 mL). The organic layer was dried and concentrated and the residue purified by flash chromatography (hexane/EtOAc = 3:1) to provide 0.20 g (99%) of **10** as a foam. R_f = 0.35. $[\alpha]_D$: −27.2 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.15−7.88 (m, 8H), 7.66−7.27 (m, 12H), 6.09−5.81 (m, 6H), 5.53−5.27 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.3, 165.2, 165.1, 164.9, 133.3, 133.1, 132.9 (2C), 131.5, 131.2, 129.7−128.2 (20C), 120.9, 120.8, 73.6, 73.4, 71.4, 71.2. Anal. Calcd for $C_{36}H_{30}O_8$: C, 73.21; H, 5.12. Found: C, 73.36; H, 5.47.

3,4,5,6-Tetra-*O*-benzoyl-1,2,7,8-tetradeoxy-L-*manno*-octa-1,7-dienitol (11). Prepared from dibromide **9** as described above for **10**. R_f = 0.50 (hexane/EtOAc = 3:1). $[\alpha]_D$: −80.0 (*c* 2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.08 (dd, *J* = 7.4, 0.6 Hz, 4H), 7.96 (dd, *J* = 7.3, 1.5 Hz, 4H), 7.55 (dt, *J* = 7.6, 1.5 Hz, 2H), 7.50 (dd, *J* = 8.0, 0.6 Hz, 2H), 7.41 (dd, *J* = 7.6, 7.4 Hz, 4H), 7.32 (dd, *J* = 8.0, 7.3 Hz, 4H), 6.06 (ddd, *J* = 17.3, 10.4, 6.9 Hz, 2H), 5.96 (d, *J* = 5.2 Hz, 2H), 5.87 (m, 2H), 5.55 (d, *J* = 17.4 Hz, 2H), 5.38 (d, *J* = 10.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.2 (2C), 165.0 (2C), 133.1 (2C), 132.9 (2C), 131.3 (2C), 129.7 (4C), 129.6 (6C), 129.5 (2C), 128.3-(4C), 128.2 (4C), 121.0 (2C), 73.5 (2C), 70.9 (2C). Anal. Calcd for $C_{36}H_{30}O_8$: C, 73.21; H, 5.12. Found: C, 72.86; H, 5.00.

2,3,4,5,6-Penta-*O*-benzoyl-1,7-di-*O*-triphenylmethyl-D-*glycero*-D-*gulo*-heptitol (14). R_f = 0.42 (hexane/EtOAc = 7:2). Mp: 111−112 °C ($CHCl_3$/EtOH). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 7.87−6.96 (m, 55H), 6.33 (dd, *J* = 7.6, 4.4 Hz, 2H), 5.96 (t, *J* = 4.4 Hz, 1H), 5.56 (ddd, *J* = 7.6, 4.7, 3.4 Hz, 2H), 3.45 (dd, *J* = 10.5, 4.7 Hz, 2H), 3.29 (dd, *J* = 10.5, 3.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.0, 164.9 (2C), 164.8 (2C), 143.2 (6C), 132.8−126.6 (60C), 86.6 (2C), 71.4 (2C), 69.6 (2C), 69.5, 61.9 (2C). Anal. Calcd for $C_{80}H_{64}O_{12}$: C, 78.93; H, 5.30. Found: C, 78.79; H, 5.45.

2,3,4,5,6-Penta-*O*-benzoyl-1,7-di-*O*-triphenylmethyl-D-*glycero*-D-*galacto*-heptitol (15). R_f = 0.62 (hexane/EtOAc = 2:1). Mp: 173−176 °C ($CHCl_3$/EtOH). $[\alpha]_D$: +21.4 (*c* 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.91−7.82 (m, 10H), 7.55−7.42 (m, 5H), 7.35−7.24 (m, 22H), 7.05−6.95 (m, 18H), 6.20 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.04 (dd, *J* = 6.9, 1.8 Hz, 1H), 5.94 (dd, *J* = 6.9, 2.9 Hz, 1H), 5.79 (m, 1H), 5.53 (m, 1H), 3.40 (dd, *J* = 10.8, 3.2 Hz, 1H), 3.36 (dd, *J* = 9.8, 6.9 Hz, 1H), 3.24 (dd, *J* = 9.9, 5.5 Hz, 1H), 3.21 (dd, *J* = 10.9, 5.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.1 (2C), 165.0, 164.7, 164.5, 143.3 (6C), 132.9, 132.8 (2C), 132.7, 132.6, 129.8−126.6 (55C), 86.8, 86.6, 71.1, 70.7, 70.1, 69.2, 69.1, 62.0 (2C). Anal. Calcd for $C_{80}H_{64}O_{12}$: C, 78.93; H, 5.30. Found: C, 78.67; H, 5.42.

2,3,4,5,6-Penta-*O*-benzoyl-1,7-dibromo-1,7-dideoxy-D-*glycero*-D-*gulo*-heptitol (16). R_f = 0.64 (hexane/EtOAc = 2:1). Mp: 158−160 °C (Et_2O). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.96−7.82 (m, 10H), 7.56−7.38 (m, 5H), 7.37−7.22 (m, 10H), 6.16−6.04 (m, 3H), 5.68 (dd, *J* = 10.9, 5.1 Hz, 2H), 3.79 (dd, *J* = 11.4, 4.4 Hz, 2H), 3.63 (dd, *J* = 11.4, 5.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.1, 164.9 (4C), 133.2 (5C), 129.8 (4C), 129.7, 128.3−128.0 (20C), 70.9 (4C), 68.5, 30.0 (2C). Anal. Calcd for $C_{42}H_{34}O_{10}Br_2$: C, 58.76; H, 3.99. Found: C, 58.80; H, 3.86.

2,3,4,5,6-Penta-*O*-benzoyl-1,7-dibromo-1,7-dideoxy-D-*glycero*-D-*galacto*-heptitol (17). R_f = 0.60 (hexane/EtOAc = 2:1). Mp: 138−142 °C (EtOH). $[\alpha]_D$: +3.3 (*c* 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.08−7.79 (m, 10H), 7.59−7.19 (m, 15H), 6.08−6.02 (m, 3H), 5.71 (dt, *J* = 6.3, 2.1 Hz, 1H), 5.64 (dt, *J* = 6.1, 4.9 Hz, 1H), 3.79 (dd, *J* = 11.4, 4.5 Hz, 1H), 3.62−3.53 (m, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 165.1−164.9 (5C), 133.5, 133.4 (2C), 133.2, 133.1, 130.0−128.1 (25C), 71.1, 70.8, 70.2, 70.0, 68.6, 29.8, 28.9. Anal. Calcd for $C_{42}H_{34}O_{10}Br_2$: C, 58.76; H, 3.99; Br, 18.61. Found: C, 59.02; H, 3.83; Br, 18.39.

4,5-*O*-Isopropylidene-1,2,7,8-tetradeoxy-L-*manno*-octa-1,7-dienitol (19). To a solution of L-tartrate **18** (2.5 g, 11.5 mmol) in toluene (20 mL) at −78 °C was added a 1.2 M solution of Dibal-H in toluene (22 mL, 26.4 mmol) over 5 min. The mixture was stirred at −78 °C for 2 h followed by dropwise addition of a 0.5 M solution of divinylzinc[9a] in THF (92 mL, 46 mmol) over 20 min. The stirring was continued for 1 h at −78 °C, and the solution was then allowed to warm to room temperature. The mixture was carefully quenched with H_2O (10 mL) followed by addition of a saturated aqueous solution of Rochelle salt (100 mL) and EtOAc (100 mL). After the mixture was stirred for 30 min, the phases were separated and the aqueous phase was extracted with EtOAc (3 × 100 mL). The combined organic phases were dried and concentrated. The residue was purified by flash chromatography (hexane/EtOAc = 2:1) to afford 2.03 g (83%) of **19** as a syrup.

$R_f = 0.50$. $[\alpha]_D$: −44.9 (*c* 2.1, $CHCl_3$). ^1H and ^{13}C NMR are in accordance with literature data.[9b]

4,5-*O*-Isopropylidene-1,2,7,8-tetradeoxy-*allo*-octa-1,7-dienitol (21). Prepared from *meso*-tartrate **20** as described above for **19**. $R_f = 0.50$ (hexane/EtOAc = 2:1). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.04 (ddd, J = 17.4, 10.6, 5.7 Hz, 2H), 5.39 (dt, J = 17.4, 1.6 Hz, 2H), 5.28 (dt, J = 10.6, 1.4 Hz, 2H), 4.36 (ddd, J = 7.1, 5.7, 1.5 Hz, 2H), 4.03 (dd, J = 7.2, 1.5 Hz, 2H), 1.41 (s, 3H), 1.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.8 (2C), 117.0 (2C), 109.1, 80.4 (2C), 70.7 (2C), 28.1, 25.7. Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.07; H, 8.67.

3,4,5,6-Tetra-*O*-acetyl-1,2,7,8-tetradeoxy-D-*gulo*-octa-1,7-dienitol (22). Diene **10** (1.00 g, 1.69 mmol) was dissolved in a mixture of MeOH (10 mL) and CH_2Cl_2 (1 mL). Sodium (25 mg) was added and the solution stirred at room temperature for 20 h. The solvent was removed in vacuo and the residue purified by flash chromatography ($Et_2O \rightarrow$ acetone) to give 261 mg of a syrup. To a solution of this in CH_2Cl_2 (25 mL) were added Ac_2O (0.85 mL, 9.0 mmol), Et_3N (1.6 mL, 11.5 mmol), and a crystal of DMAP. The mixture was stirred at room temperature for 20 h and then concentrated and purified by flash chromatography (hexane/EtOAc = 2:1) to afford 438 mg (76%) of **22** as a syrup. $R_f = 0.55$. $[\alpha]_D$: −16.0 (*c* 2.2, $CHCl_3$). ^1H NMR (CD_3OD, 300 MHz): δ 5.80 (ddd, J = 16.5, 10.6, 5.1 Hz, 1H), 5.78 (ddd, J = 15.4, 10.6, 5.1 Hz, 1H), 5.42−5.20 (m, 8H), 2.06 (s, 3H), 2.06, (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (CD_3OD, 75 MHz): δ 171.4, 171.3 (2C), 171.2, 133.1, 132.9, 121.4, 120.3, 74.0, 73.7, 71.9 (2C), 20.9, 20.8, 20.7, 20.6. Anal. Calcd for $C_{16}H_{22}O_8$: C, 56.14; H, 6.48. Found: C, 56.19; H, 6.47.

General Procedure for Ring-Closing Olefin Metathesis (Table 1). The catalyst was added to a deoxygenated solution of the diene (100 mg) in CH_2Cl_2 (5 mL) under a nitrogen atmosphere. The solution was stirred at 40 °C until TLC revealed full conversion (about 4 h). The mixture was concentrated and the residue purified by flash chromatography.

(+)-Conduritol F Tetraacetate (23). $R_f = 0.27$ (hexane/EtOAc = 2:1). $[\alpha]_D$: +47.1 (*c* 1, $CHCl_3$) (lit.[27] $[\alpha]^{25}_D$ +45.6 (*c* 1.12, $CHCl_3$)). ^1H and ^{13}C NMR are in accordance with literature data.[27]

3,4,5,6-Tetra-*O*-acetyl-1,2,7,8-tetradeoxy-L-*manno*-octa-1,7-dienitol (24). A solution of diene **19** (2.03 g, 11.4 mmol) in 80% aqueous AcOH (50 mL) was stirred at 50 °C for 22 h. The solvent was removed in vacuo to leave a solid. This was treated with Ac_2O (7.2 mL, 76.3 mmol), Et_3N (10.7 mL, 76.8 mmol), and a crystal of DMAP in CH_2Cl_2 (75 mL) at room temperature for 20 h. The mixture was washed with H_2O (50 mL) and the aqueous layer extracted with CH_2Cl_2 (20 mL). The combined organic phases were dried and concentrated, and the residue was purified by flash chromatography (hexane/EtOAc = 2:1) to give 2.73 g (83%) of **24** as a syrup. $R_f = 0.63$. $[\alpha]_D$: −27.0 (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.71 (ddd, J = 17.0, 10.1, 7.5 Hz, 2H), 5.38 (dd, J = 17.0, 0.2 Hz, 2H), 5.34 (dd, J = 10.1, 0.2 Hz, 2H), 5.32−5.20 (m, 4H), 2.06 (s, 6H), 2.04 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.7 (2C), 169.4 (2C), 132.3 (2C), 120.7 (2C), 71.6 (2C), 69.5 (2C), 20.9 (2C), 20.7 (2C). Anal. Calcd for $C_{16}H_{22}O_8$: C, 56.14; H, 6.48. Found: C, 56.20; H, 6.43.

(+)-Conduritol E Tetraacetate (25). $R_f = 0.26$ (hexane/EtOAc = 2:1). $[\alpha]_D$: +199.3 (*c* 1, MeOH). ^1H and ^{13}C NMR are in accordance with literature data.[28]

Conduritol D Acetonide (26). R_f = 0.49 (EtOAc). Mp: 123−124 °C (hexane/EtOAc). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.76 (s, 2H), 4.53 (m, 2H), 4.04 (bs, 2H), 1.41 (s, 3H), 1.38 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 131.4 (2C), 75.4 (2C), 66.3 (2C), 26.0, 25.0. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.09; H, 7.71. Removal of the isopropylidene group with 80% aqueous AcOH gave conduritol D as a syrup with ^1H and ^{13}C NMR in accordance with literature data.[29]

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