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Synthesis of Both Enantiomers of Conduritol C Tetraacetate and of *meso*-Conduritol D Tetraacetate by Oxidation of Benzoquinone Bis(ethylene acetal)

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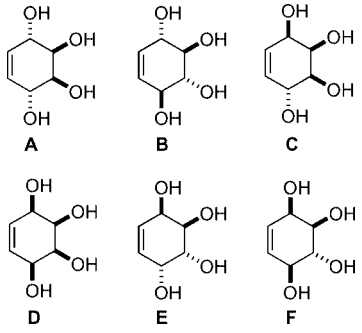
Epoxidation of *p*-benzoquinone bis(ethylene acetal) (**1**) with *m*-chloroperbenzoic acid or hydrogen peroxide/benzonitrile afforded corresponding monoepoxide **2**, which was converted into *p*-benzoquinone mono(ethylene acetal) monoepoxide **5** with perchloric acid. Dihydroxylation of **1** with osmium tetroxide or ruthenium trichloride/sodium periodate afforded corresponding *cis*-diol **6**, which was subsequently acetylated to give diacetate **7**. One ethyleneacetal moiety in **7** could be selectively hydrolyzed with silica gel/ferric chloride under solvent-free conditions to give ketone **8**, which, upon reduction with sodium borohydride and subsequent acetylation of the formed alcohol group, afforded two diastereomeric triacetates **10**. Hydrolysis of the remaining acetal functions in the two diastereomers **10**, followed by reduction of the second carbonyl group as described above, afforded racemic conduritol C and *meso*-conduritol D tetraacetates **12** and **13**, respectively. Enzymatic resolution of the racemic *arabino*-configured triacetate **10** with Lipozym failed, while the *ribo*-configured counterpart reacted smoothly to give enantiomerically pure D-*ribo*- and L-*ribo*-configured triacetates **10**. The latter pair of enantiomerically pure triacetates were converted into both enantiomers of conduritol C tetraacetate **13** as described for the racemic compounds.

Introduction

Conduritols are tetrahydroxy-substituted cyclohexenes, commonly denoted as conduritols A through F following the order of their discovery or first chemical synthesis. Six diastereomeric forms of conduritols exist: the two *meso* forms A and D and the four enantiomeric pairs B, C, E, and F (Scheme 1).[1] The only diastereomers so far found in nature are the achiral conduritol A and (+)-conduritol F: conduritol A was first isolated from Eagle vine (*Marsdenia condurango*)[2] and is found in several other tropical plants, whereas (+)-conduritol F is widespread in green plants.[3]

Conduritols and their derivatives display some interesting biological activities, which make their chemical synthesis attractive. Conduritol A derivatives, for example, exhibit insulin-modulating activity,[4] while conduritol epoxides and aminoconduritols are potent glycosidase inhibitors and have been shown to inhibit human immunodeficiency virus (HIV).[5] Furthermore, conduritols are important precursors for the synthesis of a wide variety of inositol derivatives,[6] cyclophellitol,[7] and pseudosugars.[8]

All stereoisomers of conduritols A–F have been chemically synthesized by various methods in recent years; the published syntheses have been reviewed.[9] Addition of bromine to benzoquinone, followed by reduction of the carbonyl groups and nucleophilic substitution of the bromine



Scheme 1. Conduritols A–F.

groups, has been widely used for syntheses of various conduritols.[6d,10] None of these methods, however, has aimed at the use of a direct epoxidation or dihydroxylation of benzoquinone or simple derivatives thereof for the synthesis of conduritols, although this would appear to be the most straightforward route (Scheme 2). Despite the fact that direct hydroxylation of substituted benzoquinones generated in situ from the corresponding phenols has been reported to proceed smoothly with dimethyl dioxirane,[11] the reaction had never been performed on *p*-benzoquinone itself, while osmium tetroxide hydroxylations had also only been performed on substituted phenols and quinones.[12] A product obtained from osmium tetroxide hydroxylation of *p*-benzoquinone had been assumed to be dihydroxydihydro-1,4-benzoquinone, but the final verification was never adduced.[13] Similarly, monoepoxidation of *p*-benzoquinone

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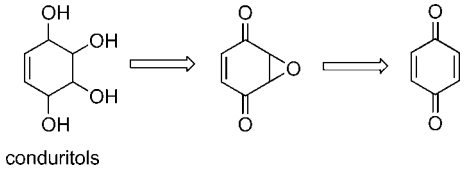
had only been possible after temporary "blocking" of one double bond through the formation of a Diels–Alder adduct,[14] while epoxidation of *p*-benzoquinone with hydrogen peroxide had resulted in a mixture of the monoepoxide and several hydroxylated byproducts.[15] However, diepoxidation with hydrogen peroxide in alkaline solution has been described to proceed smoothly with *p*-benzoquinone ethylenemonoacetal. This process is also used on an industrial scale and on *p*-benzoquinone mono(diphenylethyleneacetal), but does not yield the monoepoxide.[16] For a successful monoepoxidation we anticipated that *p*-benzoquinone bis(ethylene acetal) (**1**) should be a suitable starting material, since diepoxidation would be expected to proceed slowly for steric reasons.



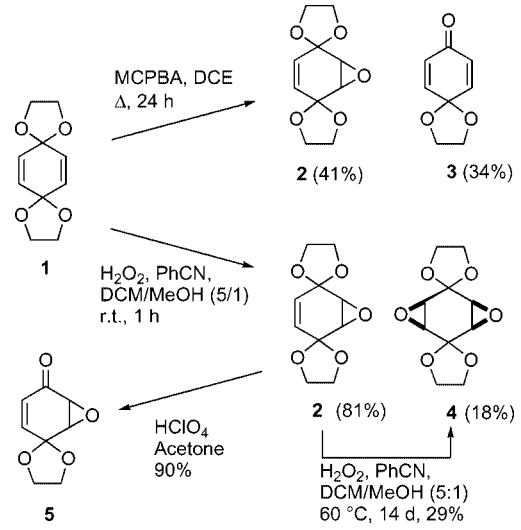
Scheme 2. Conduritols by epoxidation of benzoquinone.

Results and Discussion

p-Benzoquinone bis(ethylene acetal) (**1**) can easily be prepared on a large scale from the corresponding tetramethylacetal.[17] Unfortunately, the tetramethylacetal is not commercially available and is difficult to prepare by electrochemical means[18] or by strenuous Pd-catalyzed dimerization of cyclopropenes.[19] In our hands, diacetal **1** was best prepared by Heller's method,[20] starting from the inexpensive 1,4-cyclohexanedione, which was first acetalized with ethyleneglycol and then subjected to dibromination and dehydrobromination. Direct acetalization of *p*-benzoquinone with ethyleneglycol is not possible though, as had already been reported previously.[21]

Epoxidation of Benzoquinone Bis(ethylene acetal)

Because epoxidation of diacetal **1** had not so far been described in the literature, we first treated **1** with 3-chloroperbenzoic acid in dichloromethane at ambient temperature (Scheme 3). Inspection of the reaction mixture by TLC revealed the very slow formation of two products. After 7 d, the reaction appeared to be complete, and work up yielded crystalline monoepoxide **2** (26%) and *p*-benzoquinone mono(ethylene acetal) **3** (20%). Under more drastic conditions (dichloroethane, 24 h reflux), monoepoxide **2** and monoacetal **3** were isolated in 41% and 34% yields, respectively. We next tested several other epoxidation methods and reagents, but neither hydrogen peroxide under basic conditions nor dimethyl dioxirane gave any reaction with **1**. This result is surprising as *p*-benzoquinone mono(ethylene acetal) affords diepoxides under those conditions.[16] Finally, we found that the classical H_2O_2/PhCN reagent (peroxybenzimidic acid)[22] would react smoothly with **1** at room temperature to afford monoepoxide **2** in 81% yield, together with the crystalline, *cis*-configured diepoxide **4** in 18% yield. Although compound **2** can be converted into **4** under harsher conditions (H_2O_2/PhCN, 14 d, 60 °C), the epoxidation of **2** is still sluggish and only affords **4** in a poor 29% yield. We attribute the difficult epoxidation of **2** to steric and stereoelectronic factors. It has been shown from measurements and calculations of the dipole moment and the Kerr constant that *p*-benzoquinone monoepoxide adopts a boat conformation with the epoxide ring in a *syn* orientation,[23] and we assume a similar conformation for monoepoxide **2**, whereas diepoxide **4** and starting material **1** had each been shown by X-ray to adopt an almost flat conformation in the six-membered ring (Figure 1).[24] Thus, in a boat conformation, the dioxolane rings of monoepoxide **2** would force the epoxidation reagent to attack from the same side as where the first epoxide ring lies, which, in turn, should be sterically disfavored, causing the second epoxidation to proceed slowly. Obviously, this is not the case for monoepoxide **5** since this derivative is known to be epoxidized rapidly [*p*-benzoquinone mono(ethylene acetal) yields only the corresponding diepoxide upon treatment with hydrogen peroxide[16]]. On the other hand, monoepoxide **5** can easily be prepared in 90% yield from **2** by selective hydrolysis of one ethyleneacetal functional group with aqueous $HClO_4$ in acetone (Scheme 3).



Scheme 3. Epoxidation and dihydroxylation of compound **1**.

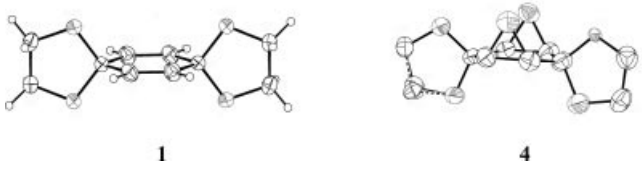


Figure 1. X-ray structures of compounds **1** and **4**.[24]

Attempts to open the epoxide rings in **2** or **5** in order to obtain the corresponding dihydroxy derivatives, which should be suitable precursors for the synthesis of conduritols, have so far failed: under various sets of acidic or basic aqueous conditions, extensive decomposition of the starting material was observed, and we have attributed this failure to "overcrowding" of functional groups around the six-membered rings, which make these epoxides prone to several side reactions. Nevertheless, compound **5** must be regarded as quite a versatile building block since it contains a reactive epoxide group that should open regioselectively upon treatment with strong nucleophiles, an enone group that should be usable for further modifications by selective nucleophilic 1,2- or 1,4-additions or stereoselective reductions, and a second masked carbonyl group allowing for additional derivatizations in subsequent steps. The use of compound **5** as a versatile building block for the synthesis of conduritol derivatives is currently under investigation and will be published elsewhere.

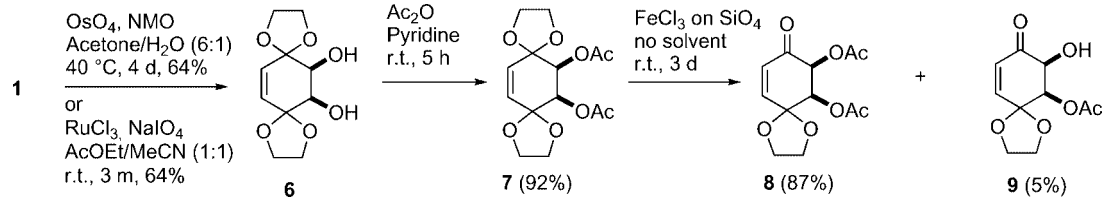
Dihydroxylation of Benzoquinone Bis(ethylene acetal)

We next turned our efforts to the examination of the *cis*-selective dihydroxylation of **1**. Surprisingly, neither the dihydroxylation of this compound nor that of any related benzoquinone diacetals has yet been described in the literature, so we first tested various reagents and sets of conditions for *cis*-selective dihydroxylation of olefins. $KMnO_4$[25] or I_2/wet AgOAc[26] gave the dihydroxylated product in very poor yield or not at all, respectively, but better results were obtained with the OsO_4/NMO[27] or $RuCl_3/NaIO_4$[28] reagents. Under carefully optimized conditions (Scheme 4), *syn*-diol **6** could be obtained in 64% yield. It is noteworthy that dihydroxylation of **1** is rather difficult, due to the strongly electron-withdrawing effects of the two acetal functional groups. Furthermore, in all hydroxylation reactions with OsO_4 and $RuCl_3$ we observed that the reactions never proceeded to completion: unchanged starting material could even be reisolated when molar amounts of the more reactive $RuCl_3/NaIO_4$ reagent were applied.

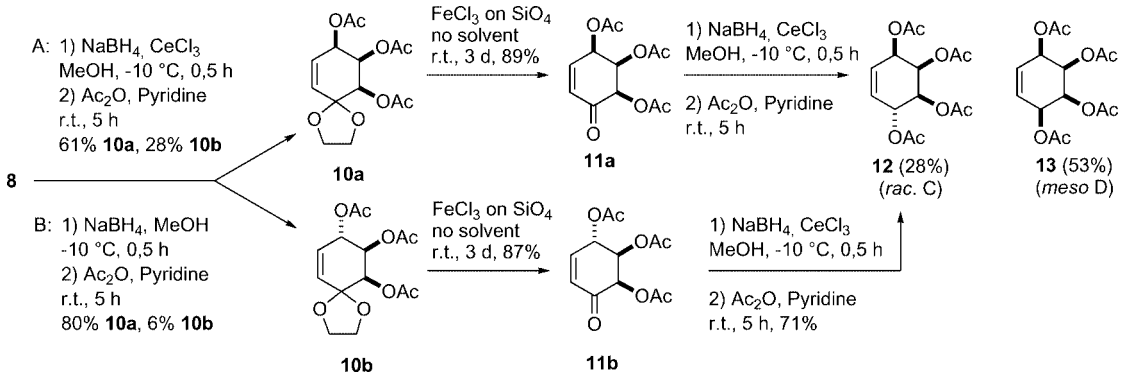
Acetylation of diol **6** gave compound **7** in 92% yield (Scheme 4). It was originally planned to subject this to a selective hydrolysis of one acetal group to afford enone **8** for generation of the third hydroxy group through diastereoselective reduction of the carbonyl function, as it is reported in the literature that one acetal group in a *p*-benzoquinone diacetal can be selectively hydrolyzed under acidic conditions,[29] but bis(ethylene acetal) **7** resisted all attempts to hydrolyze it under acid conditions. Neither aqueous HCl solution (0.1–1.0 M), nor concentrated aqueous HCl solution, nor $HClO_4$ (70%) affected diacetal **7**. Similarly, other reagents known to cleave acetals efficiently[30] were unable to hydrolyze compound **7**. Only treatment with ferric chloride on silica gel under solvent-free conditions[31] finally resulted in the selective cleavage of only one acetal functional group, so diacetal **7** was finely ground in a mortar, mixed with commercially available silica gel loaded with $FeCl_3$, and stirred in the absence of any solvent in a flask, whereupon TLC revealed the slow formation of a more slowly moving product. After stirring for 3 d at ambient temperature, the initially yellow mixture had turned white and all starting material has disappeared, as shown by TLC. After chromatographic workup of the mixture, the crystalline monoacetals **8** and **9** were isolated in 61% and 5% yields, respectively. It should be noted that compound **8** was prone to deacetylation during chromatography on silica gel, a fact that might be responsible for the final isolation of small amounts of monoacetylated byproduct **9**, which had not been detectable by TLC prior to workup. Since the products were crystalline, however, enone **8** could be directly crystallized from the crude reaction mixture in 87% yield, so the solvent-free selective monodeacetalation of *p*-benzoquinone diacetals with $FeCl_3$ on silica gel proved to be the method of choice here.

Next, enone **8** was reduced to afford racemic diastereomers **10a** and **10b** (Scheme 5). Because the initial diastereomeric reduction products (monoalcohols) were rather difficult to separate, due to their similar mobilities during chromatography on silica gel, the intermediate crude alcohols were directly acetylated, after which chromatographic separation could be achieved nicely. On treatment with the $NaBH_4/CeCl_3$ reagent (Luche's reagent),[32] chosen in order to avoid 1,4-reduction of the enone moiety in **8**, and after subsequent acetylation of the crude reduction products, an approximately 2:1 mixture of diastereomers **10a** and **10b** was obtained in 89% overall yield. In its proton NMR spectrum, compound **10a**, isolated in 61% yield, showed a vicinal coupling constant of 4.7 Hz between the proton at the newly formed asymmetric center and its adjacent proton and so was assigned the *ribo* configuration. Similarly, diastereomer **10b**, isolated in 28% yield, showed a vicinal coupling constant of 8.4 Hz and was assigned the *arabino* configuration. The structure assigned to diastereomer **10a** was additionally confirmed by X-ray structure determination.[24]

With $NaBH_4$ alone, no 1,4-reduction of enone **8** was observed and the diastereomeric selectivity of the reduction was increased to approximately 13:1. After acetylation of



Scheme 4.



Scheme 5.

the crude reaction products, compounds **10a** and **10b** were thus isolated in 80% and 6% yields, respectively. Similar observations of increased diastereoselectivity during reduction of enones have been documented.[32c,d] Removal of the ethyleneacetal moieties in **10a** and **10b** was again achieved by application of ferric chloride on silica gel under solvent-free conditions to afford the crystalline enone tetraacetates **11a** and **11b** in 89% and 87% yields, respectively. It is noteworthy that under aqueous hydrolytic conditions (70% aqueous $HClO_4$, ambient temp.), no hydrolysis of the ethyleneacetals occurred at all (c.f. conversion of compound **8** to **9**). The nonoccurrence of any possible rearrangement or acetyl group migration during deprotection of **10** was unambiguously verified by X-ray structure analysis of **11a** (Figure 2)[24] and comparison of the NMR spectroscopic data for both diastereomers, which showed that the relative configuration had been preserved.

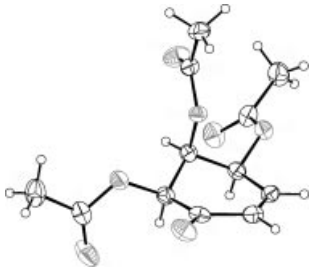


Figure 2. X-ray structure of compound **11a**.

Reduction of **11a** with the $NaBH_4/CeCl_3$ reagent in methanol, followed by acetylation of the intermediate alcohol, gave racemic conduritol tetraacetate **12** (conduritol C) and *meso*-conduritol tetraacetate **13** (conduritol D) in a ratio of approximately 1:2. In contrast, reduction and acetylation of **11b** resulted exclusively in diastereomer **12**. Similar findings had previously been described by Vogel et al.,[33] who also found a rather unselective reduction of **11a**. By deduction from the X-ray data for compound **11a**[24] we explain the reduction of **11a** in terms of a preferential attack of the hydride nucleophile at the less hindered *Si* face of the enone to give **13** as the main product (Figure 3), whereas attack at the *Re* face to give **12** as the minor byproduct is still possible. In contrast, **11b** displays two axially oriented acetoxy groups, which steer reduction so that it occurs only at the *Si* face of the carbonyl group through complexation with the pseudoaxial 4-acetoxy group to give **12** exclusively. Compounds **12** and **13** showed analytical data identical to those published elsewhere.[33,34]

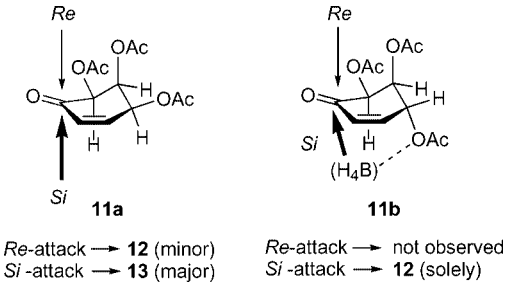
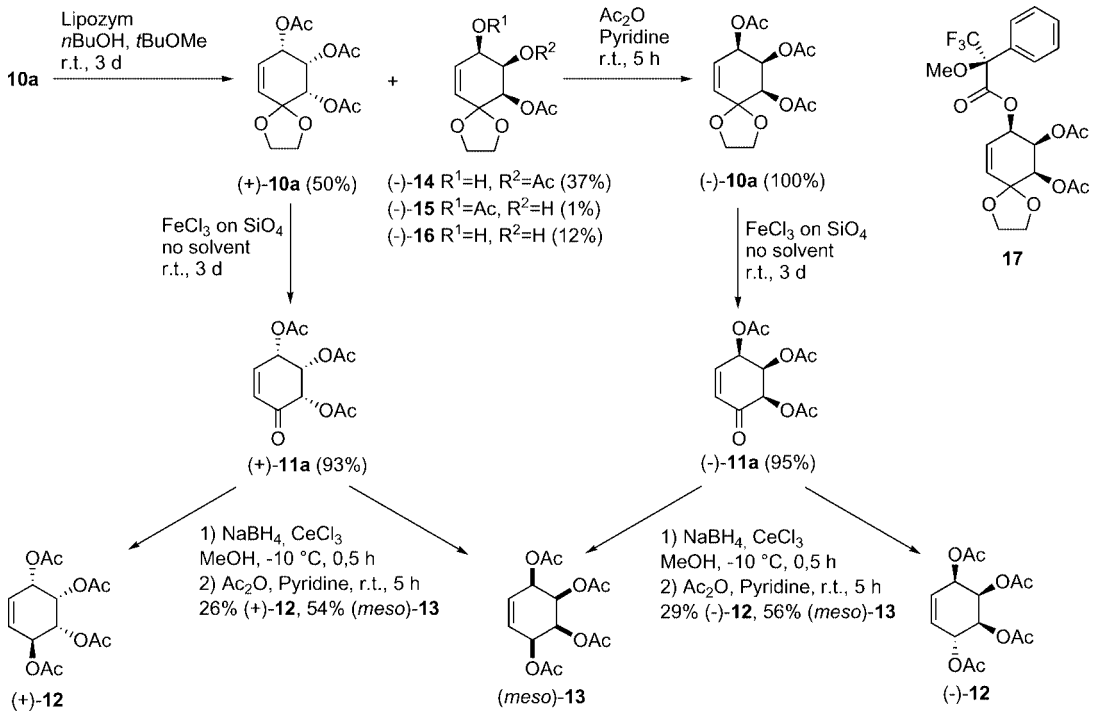


Figure 3. Reduction of diastereomers **11a** and **11b**.

Enzymatic Resolution

For the preparation of enantiomerically pure conduritols we used an approach based on kinetic resolution of racemic compounds **10** with lipases, since enzymatic resolutions have proved to be very efficient for the preparation of enantiomerically pure coduritols and their precursors.[34a,35] Here we used Lipozym exclusively. While compound **10a** was a good substrate for Lipozym, its diastereomer **10b** did not show any sign of enzymatic saponification even after a month: obviously, only the *ribo* configuration of **10a** is recognized by Lipozym, whereas the *arabino* configuration of **10b** is not, although the Kazlauskas rule predicts that **10b** should also be a substrate for Lipozym.[36] Subjection of racemic **10a** to transesterification catalyzed by Lipozym in a mixture of *n*-butanol and *tert*-butyl methyl ether left L-*ribo* enantiomer (+)-**10a** untouched and afforded the partially deacetylated crystalline D-*ribo* enantiomers (–)-**14**, (–)-**15**, and (–)-**16**. After chromatographic separation, alcohol (–)-**14** was subsequently reacetylated to provide (–)-**10a**, and the enzymatic resolution of **10a** thus appeared to be virtually quantitative, giving both enantiomers of **10a** in better than 99.5% *ee*. The absolute configuration of (–)-**10a** was unambiguously assigned by acylation with (+)-Mosher's acid chloride and determination of the configura-



Scheme 6.

tion from the X-ray structure of Mosher's ester **17** (details not shown here).

Finally, both enantiomers were deacetalated with the ferric chloride/silica gel reagent as described above to afford crystalline ketones (+)-**11a** and (–)-**11a** in 93% and 95% yields, respectively. The following reduction-reacetylation sequence as outlined above for racemic **11a** gave both enantiomers of conduritol C tetraacetate (+)-**12** and (–)-**12** and *meso*-conduritol tetraacetate **13**. The diastereoselectivity of the reduction step was of the same magnitude as described above for racemic **11a** (Scheme 6).

Experimental Section

General Remarks: NMR spectra were recorded with a Bruker Avance 400 spectrometer at 400 MHz for ^{1}H and 100.6 MHz for ^{13}C NMR spectra, respectively. Chemical shifts in $CDCl_3$ are reported in δ (ppm) relative to tetramethylsilane (TMS) as internal standard. Coupling constants *J* are reported in Hz. Assignment of signals was achieved by first-order inspection of the spectra and by ^{1}H,^{1}H-, ^{13}C,^{1}H-COSY, HMQC, or NOESY experiments performed with a Bruker DRX 600 spectrometer. MS spectra were recorded with Finnigan TSQ 70 MAT (EI) and Bruker Apex II FT-ICR (FAB) instruments. Specific optical rotations [*α*] were recorded with a Perkin–Elmer polarimeter Model 341 at 589 nm (Na-D) for solutions in $CHCl_3$ at 20 °C if not stated otherwise. Elemental analyses were performed with a Hekatech CHNS analyzer Euro EA 300. Melting points were determined with a Büchi SMP-20 instrument. GC was performed with Varian/Chrompack CP 9000 and CP 9001 instruments with the use of Chirasil-β-cyclodextrin columns. TLC was performed on Macherey & Nagel silica gel (SIL G/UV254) plates. Spots were detected by visual inspection of the plates under UV light, by charring with H_2SO_4 (5% in EtOH), with $KMnO_4$ (5% in H_2O), and with I_2. Preparative column chromatography was performed by eluting compounds with various mixtures of solvents from glass columns of various size filled with Macherey & Nagel silica gel S (0.032–0.063 mm). X-ray structures were recorded with a Enraf Nonius CAD4 or a Stoe IPDS diffractometer. Enzymatic reactions were performed by shaking the reactions mixtures on an orbital shaker. All solvents were dried and purified by distillation prior to use. Solutions in organic solvents were dried with Na_2SO_4, filtered, and concentrated on a rotary evaporator.

6,7-Epoxy-1,4,9,12-tetraoxadispiro[4.2.4.2]tetradec-13-ene (2), 1,4-Dioxaspiro[4.5]deca-6,9-dien-8-one (3) and *cis*-6,7,13,14-Diepoxy-1,4,9,12-tetraoxadispiro[4.2.4.2]tetradecane (4)

Method a: A solution of *p*-benzoquinone bis(ethylene actal) (**1**,[20] 1.36 g, 6.94 mmol) and *m*-chloroperbenzoic acid (3.54 g, 20.83 mmol) in $C_2H_4Cl_2$ (80 mL) was heated at reflux for 22 h, washed with ice-cold aqueous NaOH solution (20%), dried, and the solvents were evaporated. Chromatography of the residue with toluene/acetone (10:1) first afforded impure compound **3**, which was further purified by microdistillation to give pure **3** (359 mg, 34%), showing physical data identical to those published previously.[37] Eluted next was crystalline **2** (604 mg, 41%). M.p. 162 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 5.62 (s, 2 H, 13-H, 14-H), 4.11 (m, 8 H, 2-H, 2-H′, 3-H, 3-H′, 10-H, 10-H′, 11-H, 11-H′), 3.31 (s, 2 H, 6-H, 7-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 128.4 (2 C, C-13, C-14), 103.4 (2 C, C-5, C-8), 65.7[a] (2 C, C-2, C-10), 65.6[a] (2 C, C-3, C-11), 52.3 (2 C, C-6, C-7) ppm ([a] assignment may be exchanged). FAB-MS: *m/z* = 235 $[M + Na]^+$, 213 $[M + H]^+$. $C_{10}H_{12}O_5$ (212.20): calcd. C 56.60, H 5.70; found C 56.75, H 5.61.

Method b: A mixture of compound **1** (2.00 g, 10.19 mmol), $NaHCO_3$ (2 g), and aqueous H_2O_2 solution (30%, 50 mL) in benzonitrile (40 mL), CH_2Cl_2 (40 mL), and MeOH (200 mL) was vigorously stirred at ambient temp. for 24 h, washed with ice-cold aqueous $NaHCO_3$ solution, dried, and concentrated. Chromatography of the residue first afforded **2** (1.75 g, 81%). Eluted next was **4** (418 mg, 18%). M.p. 162–163 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 4.22[a] (m, 4 H, 2-H, 2-H′, 10-H, 10-H′), 4.12[a] (m, 4 H, 3-H, 3-

H′, 11-H, 11-H′), 3.17 (s, 4 H, 6-H, 7-H, 13-H, 14-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 102.1[a] (C-5), 101.4[a] (C-8), 66.5[b] (2 C, C-2, C-10), 65.9[b] (2 C, C-3, C-11), 55.0 (4 C, C-6, C-7, C-13, C-14) ppm ([a,b] assignment may be exchanged). FAB-MS: *m*/*z* = 251 $[M + Na]^+$, 229 $[M + H]^+$, 211 $[M + H - H_2O]^+$. $C_{10}H_{12}O_6$ (228.20): calcd. C 52.63, H 5.30; found C 52.47, H 5.32.

Method c: Treatment of compound **2** (1.07 g, 5.03 mmol) at 60 °C for 14 d as described under method b) afforded **4** (333 mg, 29%), together with unchanged **2** (757 mg, 71%).

***rac*-6,7-Epoxy-1,4-dioxaspiro[4.5]deca-9-en-8-one (5):** A solution of compound **2** (2.56 g, 12.06 mmol) and $HClO_4$ (70%, 0.1 mL) in acetone (300 mL) was stirred at ambient temp. for 1 h, diluted with CH_2Cl_2 (200 mL), washed with aqueous $NaHCO_3$ solution, dried, and concentrated. The oily residue was triturated with boiling diisopropyl ether and the solvent was decanted while warm from a sticky brown residue. Evaporation of the solvent and recrystallization of the residue from EtOH gave **5** (1.82 g, 90%). M.p. 58–59 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 6.32 (dd, $J_{9,10}$ = 10.6 Hz, $J_{6,10}$ = 2.8 Hz, 1 H, 10-H), 5.98 (dd, $J_{9,10}$ = 10.6 Hz, $J_{7,9}$ = 2.0 Hz, 1 H, 9-H), 4.19 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 3.59 (dd, $J_{6,7}$ = 3.5 Hz, $J_{6,10}$ = 3.0 Hz, 1 H, 6-H), 3.48 (dd, $J_{6,7}$ = 3.7 Hz, $J_{7,9}$ = 2.0 Hz, 1 H, 7-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 192.5 (C-8), 141.8 (C-10), 127.6 (C-9), 101.3 (C-5), 66.2[a] (C-2), 66.0[a] (C-3), 55.1 (C-6), 52.1 (C-7) ppm ([a] assignment may be exchanged). FAB-MS : *m*/*z* = 169 $[M + H]^+$, 154 $[M - O + H_2]^+$, 136 $[m/z\ 154 - H_2O]^+$. $C_8H_8O_4$ (168.15): calcd. C 57.14, H 4.80; found C 57.43, H 4.87.

***cis*-1,4,9,12-Tetraoxadispiro[4.2.4.2]tetradec-13-ene-6,7-diol (6)**

Method a: A mixture of compound **1** (1.00 g, 5.10 mmol), NMO monohydrate (1.10 g, 8.10 mmol), and an aqueous solution of OsO_4 (4%, 5 mL) in acetone (60 mL) and H_2O (10 mL) was stirred at 40 °C for 4 d. After addition of a small amount of Na_2SO_3 the mixture was concentrated. Chromatography of the residue with toluene/acetone 1:1 and crystallization from toluene afforded **6** (751 mg, 64%). M.p. 124 °C (toluene). ^{1}H NMR ([D$_4$]-MeOH): δ = 5.71 (s, 2 H, 13-H, 14-H), 4.06 (m, 8 H, 2-H, 2-H′, 3-H, 3-H′, 10-H, 10-H′, 11-H, 11-H′), 3.91 (s, 2 H, 6-H, 7-H) ppm. ^{13}C NMR ([D$_4$]MeOH): δ = 131.2 (2 C, C-13, C-14), 106.6 (2 C, C-5, C-8), 73.9 (2 C, C-6, C-7), 67.3[a] (2 C, C-2, C-10), 66.4[a] (2 C, C-3, C-11) ppm ([a] assignment may be exchanged). FAB-MS for $C_{10}H_{14}O_6$ (*m*/*z* 230): 253 $[M + Na]^+$, 231 $[M + H]^+$, 213 $[M + H - H_2O]^+$. $C_{10}H_{14}O_6$ (230.22): calcd. C 52.17, H 6.13; found: C 52.46, H 6.13.

Method b: A mixture of compound **1** (712 mg, 3.63 mmol), $NaIO_4$ (1.16 g, 5.44 mmol), and $RuCl_3 \cdot 3H_2O$ (122 mg, 0.47 mmol) in ethyl acetate (15 mL), MeCN (15 mL), and H_2O (5 mL) was vigorously shaken at ambient temp. for 3 min, poured into saturated aqueous Na_2SO_3 solution, and extracted with CH_2Cl_2. Concentration of the extracts and chromatography of the residue with toluene/acetone 1:1 first afforded reisolated **1** (71 mg, 10%). Eluted next was **6** (535 mg, 64%).

***cis*-6,7-Diacetoxy-1,4,9,12-tetraoxadispiro[4.2.4.2]tetradec-13-ene (7):** A solution of compound **6** (2.04 g, 8.87 mmol) in a mixture of acetic anhydride (25 mL) and pyridine (25 mL) was stirred at ambient temp. for 5 h, diluted with CH_2Cl_2 (200 mL), washed with ice-cold aqueous HCl solution and saturated aqueous $NaHCO_3$ solution, dried, and concentrated. Crystallization of the residue from EtOH afforded **7** (2.566 g, 92%). M.p. 164 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 5.74 (s, 2 H, 13-H, 14-H), 5.38 (s, 2 H, 6-H, 7-H), 4.02 (m, 8 H, 2-H, 2-H′, 3-H, 3-H′, 10-H, 10-H′, 11-H, 11-H′), 2.12 [s, 6 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 170.3 [2 C, *C*{O}CH_3], 130.2 (2 C, C-13, C-14), 103.4 (2 C, C-5, C-8), 70.8 (2 C, C-6, C-7), 66.2[a] (2 C, C-2, C-10), 65.2[a] (2 C, C-3, C-11), 21.0 [2 C, C{O}*C*H$_3$] ppm ([a] assignment may be exchanged). FAB-MS: *m*/*z* = 337 $[M + Na]^+$, 315 $[M + H]^+$. $C_{14}H_{18}O_8$ (314.29): calcd. C 53.50, H 5.77; found C 53.65, H 5.77.

***cis*-6,7-Diacetoxy-8-oxo-1,4-dioxaspiro[4.5]dec-9-ene (8) and *cis*-6-Acetoxy-7-hydroxy-8-oxo-1,4-dioxaspiro[4.5]dec-9-ene (9)**

Method a: Finely ground compound **7** (3.20 g, 10.17 mmol) was mixed with silica gel/$FeCl_3$ (30 g, containing 0.4 mmol $FeCl_3$/g silica gel), the mixture was stirred at ambient temp. for 3 d until the initial yellow color had disappeared, and the silica gel was then extracted several times with diethyl ether. The combined extracts were washed with saturated aqueous $NaHCO_3$ solution, dried, and concentrated, and chromatography of the residue with toluene/acetone 5:1 first afforded **8** (1.676 g, 61%). M.p. 110–111 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 6.52 (dd, $J_{9,10}$ = 10.4 Hz, $J_{6,10}$ = 2.3 Hz, 1 H, 10-H), 6.20 (d, $J_{9,10}$ = 10.4 Hz, 1 H, 9-H), 5.81 (d, $J_{6,7}$ = 2.8 Hz, 1 H, 7-H), 5.51 (t, $J_{6,7}$ = 2.5 Hz, 1 H, 6-H), 4.14 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 2.18, 2.09 [2 × s, 6 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 190.2 (C-8), 170.1, 169.5 [2 C, *C*{O}CH_3], 143.8 (C-10), 130.0 (C-9), 103.3 (C-5), 72.7 (C-6), 72.5 (C-7), 66.0[a] (C-2), 65.9[a] (C-3), 20.8, 20.5 [2 C, C{O}*C*H$_3$] ppm ([a] assignment may be exchanged). FAB-MS: *m*/*z* = 293 $[M + Na]^+$, 271 $[M + H]^+$. $C_{12}H_{14}O_7$ (270.24): calcd. C 53.33, H 5.22; found C 53.05, H 5.19. Eluted next was **9** (116 mg, 5%). M.p. 126–127 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 6.53 (dd, $J_{9,10}$ = 10.2 Hz, $J_{6,10}$ = 2.5 Hz, 1 H, 10-H), 6.26 (d, $J_{9,10}$ = 10.4 Hz, 1 H, 9-H), 5.55 (t, $J_{6,7}$ = 3.0 Hz, 1 H, 6-H), 4.66 (t, $J_{6,7}$ = 3.3 Hz, 1 H, 7-H), 4.14 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 3.41 (d, $J_{7,OH}$ = 3.3 Hz, 1 H, 7-OH), 2.05 [s, 3 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 196.6 (C-8), 170.1 [*C*{O}CH_3], 145.1 (C-10), 128.7 (C-9), 103.3 (C-5), 73.9 (C-6), 72.3 (C-7), 66.0[a] (C-2), 65.9[a] (C-3), 20.7 [C{O}*C*H$_3$] ppm ([a] assignment may be exchanged). FAB-MS: *m*/*z* = 251 $[M + Na]^+$, 229 $[M + H]^+$, 211 $[M + H - H_2O]^+$. $C_{10}H_{12}O_6$ (228.20): calcd. C 52.63, H 5.20; found C 52.34, H 5.30.

Method b: Treatment of compound **7** (1.95 g, 6.21 mmol) with silica gel/$FeCl_3$ (20 g) as described above, without chromatography but with direct crystallization from EtOH, instead afforded **8** (1.46 g, 87%).

***rac*-(8*RS*,9*RS*,10*RS*)- (10a) and *rac*-(8*RS*,9*SR*,10*SR*)-8,9,10-Triacetoxy-1,4-dioxaspiro[4.5]dec-6-ene (10b)**

Method a: $NaBH_4$ (193 mg, 5.09 mmol) was added in small portions at –10 °C to a solution of compound **8** (917 mg, 3.39 mmol) and $CeCl_3 \cdot 7H_2O$ (0.4 M in MeOH, 30 mL) in CH_2Cl_2 (30 mL), and the mixture was stirred for 30 min at –10 °C, allowed to warm to ambient temp. over 30 min, diluted with H_2O (20 mL), and poured into saturated aqueous NaCl solution (50 mL). The resulting mixture was extracted with ethyl acetate (3 × 50 mL), the combined extracts were dried and concentrated, the residue was dissolved in pyridine (20 mL), and acetic anhydride (20 mL) was added with cooling with an ice bath. The mixture was stirred at ambient temp. for 5 h and worked up as described for the preparation of compound **7**, and chromatography of the residue with toluene/acetone 10:1 and crystallization from EtOH first afforded **10b** (299 mg, 28%). M.p. 87–88 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 5.86 (dd, $J_{6,7}$ = 10.2 Hz, $J_{6,10}$ = 2.3 Hz, 1 H, 6-H), 5.64 (m, $J_{8,9}$ = 8.3 Hz, 2 H, 7-H, 8-H), 5.37 (dd, $J_{8,9}$ = 8.5 Hz, $J_{9,10}$ = 2.3 Hz, 1 H, 9-H), 5.30 (t, $J_{9,10}$ = 2.0 Hz, 1 H, 10-H), 4.05 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 2.13, 2.08, 2.04 [3 × s, 9 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 170.5, 170.4, 169.9 [3 C, *C*{O}CH_3], 130.1 (C-6), 128.2 (C-7), 103.8 (C-5), 70.9 (C-8), 70.7 (C-10), 68.8 (C-9), 65.6[a] (C-2), 65.5[a] (C-3), 20.9, 20.8, 20.7 [3 C, C{O}*C*H$_3$] ppm ([a] assignment may be exchanged). FAB-MS: *m*/*z* = 337 $[M + Na]^+$, 315 $[M + H]^+$, 255

$[M + H - HOAc]^+$. $C_{14}H_{18}O_8$ (314.29): calcd. C 53.50, H 5.77; found C 53.56, H 5.84. Eluted next and crystallized from EtOH was **10a** (651 mg, 61%). M.p. 95–96 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 5.93 (dd, $J_{9,10}$ = 10.2 Hz, $J_{6,10}$ = 3.9 Hz, 1 H, 10-H), 5.79 (d, $J_{9,10}$ = 10.1 Hz, 1 H, 9-H), 5.61 (m, $J_{7,8}$ = 4.7 Hz, 1 H, 7-H), 5.47 (dd, $J_{6,7}$ = 2.3 Hz, $J_{7,8}$ = 4.7 Hz, 1 H, 8-H), 5.22 (d, $J_{6,7}$ = 1.8 Hz, 1 H, 6-H), 4.04 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 2.12, 2.08, 2.07 [3 s, 9 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 170.1, 170.0, 169.9 [3 C, *C*{O}CH_3], 130.5 (C-9), 127.7 (C-10), 103.7 (C-5), 69.9 (C-6), 67.8 (C-8), 66.2[a] (C-2), 65.2[a] (C-3), 64.8 (C-7), 20.9, 20.8, 20.7 [3 C, C{O}*C*H_3] ppm ([a] assignment may be exchanged). FAB-MS: *m*/*z* = 337 $[M + Na]^+$, 315 $[M + H]^+$, 255 $[M + H - HOAc]^+$. $C_{14}H_{18}O_8$ (314.29): calcd. C 53.50, H 5.77; found C 53.70, H 5.73.

Method b: Treatment of compound **8** (923 mg, 3.42 mmol) in CH_2Cl_2 (30 mL) with $NaBH_4$ (195 mg, 5.12 mmol), followed by workup, acetylation, and chromatography as described under method a first afforded **10b** (64 mg, 6%). Eluted next was **10a** (859 mg, 80%).

***rac*-(1*RS*,5*RS*,6*RS*)-1,5,6-Triacetoxy-4-oxocyclohex-2-ene (11a):** Treatment of compound **10a** (908 mg, 2.89 mmol) with silica gel/$FeCl_3$ (12 g, containing 0.4 mmol $FeCl_3$/g silica gel) at ambient temp. for 3 d and crystallization of the crude product as described for the preparation of compound **9** gave **11a** (695 mg, 89%). M.p. 110–111 °C (dec.) (EtOH). ^{1}H NMR ($CDCl_3$): δ = 6.67 (dt, $J_{2,3}$ = 10.6 Hz, 1 H, 2-H), 6.24 (dd, $J_{2,3}$ = 10.5 Hz, 1 H, 3-H), 5.96 (m, 1 H, 1-H), 5.87 (m, 1 H, 6-H), 5.61 (d, 1 H, 5-H), 2.19, 2.09, 2.08 [3 × s, 9 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 189.8 (C-4), 170.0, 169.4, 169.3 [3 C, *C*{O}CH_3], 144.3 (C-2), 128.9 (C-3), 72.6 (C-5), 72.5 (C-6), 68.1 (C-1), 20.6, 20.4, 20.3 [3 C, C{O}*C*H_3] ppm. FAB-MS: *m*/*z* = 293 $[M + Na]^+$, 271 $[M + H]^+$. $C_{12}H_{14}O_7$ (270.24): calcd. C 53.33, H 5.22; found C 53.34, H 5.23.

***rac*-(1*SR*,5*RS*,6*RS*)-1,5,6-Triacetoxy-4-oxocyclohex-2-ene (11b):** Treatment of compound **10b** (445 mg, 1.42 mmol) with silica gel/$FeCl_3$ (8 g, containing 0.4 mmol $FeCl_3$/g silica gel) at ambient temp. for 3 d and crystallization of the crude product as described for the preparation of compound **9** gave **11b** (333 mg, 87%). M.p. 106–107 °C dec. (EtOH). ^{1}H NMR ($CDCl_3$): δ = 6.56 (dd, $J_{3,4}$ = 10.3 Hz, 1 H, 4-H), 6.28 (d, $J_{3,4}$ = 10.3 Hz, 1 H, 3-H), 6.01 (m, 1 H, 2-H), 5.87 (m, 1 H, 1-H), 5.72 (d, 1 H, 6-H), 2.12, 2.10, 2.07 [3 s, 9 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 190.4 (C-5), 170.5, 170.4, 169.9 [3 C, *C*{O}CH_3], 141.3 (C-4), 129.8 (C-3), 72.7 (C-2), 72.1 (C-6), 69.9 (C-1), 20.6, 20.5, 20.2 [3 C, C{O}*C*H_3] ppm. FAB-MS: *m*/*z* = 293 $[M + Na]^+$, 271 $[M + H]^+$. $C_{12}H_{14}O_7$ (270.24): calcd. C 53.33, H 5.22; found C 53.44, H 5.15.

***rac*-Conduritol C Tetraacetate (12) and *meso*-Conduritol D Tetraacetate (13)**

Method a: Treatment of compound **11a** (717 mg, 2.28 mmol) and $CeCl_3 \cdot 7H_2O$ (30 mL, 0.4 M in MeOH) in CH_2Cl_2 (20 mL) with $NaBH_4$ (132 mg, 3.42 mmol), followed by acetylation of the crude product and chromatography as described for the preparation of **10** under method a, first afforded **12** (201 mg, 28%) as a colorless oil. Physical data were identical to those published previously.[6d] Eluted next was crystalline **13** (380 mg, 53%). M.p. 105 °C (EtOH); M.p.[38] 105 °C (EtOH). Spectroscopic data were identical to those published previously.[33,34b]

Method b: Treatment of compound **11b** (333 mg, 1.23 mmol) and $CeCl_3 \cdot 7H_2O$ (0.4 M in MeOH, 15 mL) in CH_2Cl_2 (15 mL) with $NaBH_4$ (70 mg, 1.85 mmol), followed by acetylation of the crude product and chromatography as described for the preparation of **10** under method a, first afforded **12** (275 mg, 71%).

(+)-(8*S*,9*S*,10*S*)-8,9,10-Triacetoxy-1,4-dioxaspiro[4.5]dec-6-ene [(+)-10a], (–)-(6*R*,7*R*,8*R*)-6,7-Diacetoxy-8-hydroxy-1,4-dioxaspiro[4.5]dec-9-ene [(–)-14], (–)-(8*R*,9*R*,10*R*)-8,10-Diacetoxy-9-hydroxy-1,4-dioxaspiro[4.5]dec-6-ene [(–)-15], and (–)-(6*R*,7*R*,8*R*)-6-Acetoxy-7,8-dihydroxy-1,4-dioxaspiro[4.5]dec-9-ene [(–)-16]: A mixture of racemic **10a** (1.42 g, 4.52 mmol), Lipozym (4 g), and *n*-butanol (4 mL) in *tert*-butyl methyl ether (150 mL) was shaken at ambient temp. for 3 d on an orbital shaker, filtered through a layer of Celite, and concentrated. Chromatography of the residue with toluene/acetone 5:1 and crystallization from EtOH first afforded (+)-**10a** (710 mg, 50%). M.p. 95–96 °C (EtOH). *ee* > 99.5%. $[\alpha]_D$ = +109.6 (*c* = 1.0, $CHCl_3$). ^{1}H and ^{13}C NMR data were identical to those of racemic **10a**. FAB-MS: *m*/*z* = 337 $[M + Na]^+$, 315 $[M + H]^+$, 255 $[M + H - HOAc]^+$. $C_{14}H_{18}O_8$ (314.29): calcd. C 53.50, H 5.77; found C 53.55, H 5.76. Eluted next and crystallized from EtOH was (–)-**14** (455 mg, 37%). M.p. 91–92 °C (EtOH). $[\alpha]_D$ = –130.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 5.87 (dd, $J_{9,10}$ = 10.4 Hz, 1 H, 10-H), 5.74 (dd, $J_{9,10}$ = 10.4 Hz, 1 H, 9-H), 5.43 (m, 1 H, 6-H), 5.18 (d, 1 H, 8-H), 4.34 (m, 1 H, 7-H), 4.04 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 3.00 (d, 1 H, 8-OH), 2.15, 2.14 [2 × s, 6 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 170.3, 170.2 [2 C, *C*{O}CH_3], 129.7 (C-9), 128.0 (C-10), 104.1 (C-5), 71.9 (C-8), 69.1 (C-6), 68.6 (C-7), 66.5[a] (C-2), 65.3[a] (C-3), 21.0, 20.9 [2 C, C{O}*C*H_3] ppm ([a] assignment may be exchanged). FAB-MS: *m*/*z* = 295 $[M + Na]^+$. $C_{12}H_{16}O_7$ (272.26): calcd. C 52.94, H 5.92; found C 52.85, H 5.87. Eluted next was (–)-**15** (12 mg, 1%). ^{1}H NMR ($CDCl_3$): δ = 5.80 (m, 2 H, 6-H, 7-H), 5.57 (d, 1 H, 10-H), 5.47 (m, 1 H, 8-H), 4.09 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 3.96 (d, 1 H, 9-H), 1.81 (d, 1 H, 9-OH), 2.13, 2.08 [2 × s, 6 H, C{O}CH_3] ppm. ^{13}C NMR ($CDCl_3$): δ = 170.9, 170.0 [2 C, *C*{O}CH_3], 129.4[a] (C-6), 127.5[a] (C-7), 104.5 (C-5), 71.7 (C-8), 70.8 (C-9), 66.9 (C-10), 66.5[b] (C-2), 65.3[b] (C-3), 21.0, 20.9 [2 C, C{O}*C*H_3] ppm ([a,b] assignment may be exchanged). Eluted next and crystallized from EtOH was (–)-**16** (125 mg, 12%). M.p. 102–103 °C (EtOH). $[\alpha]_D$ = –120.8 (*c* = 1.0, MeOH). ^{1}H NMR ([D$_6$]acetone): δ = 5.98 (dd, $J_{9,10}$ = 10.1 Hz, 1 H, 10-H), 5.57 (d, $J_{9,10}$ = 10.1 Hz, 1 H, 9-H), 5.10 (d, 1 H, 6-H), 4.12 (m, 1 H, 7-H), 4.03 (m, 4 H, 2-H, 2-H′, 3-H, 3-H′), 3.94 (m, 1 H, 8-H), 3.79 (d, 1 H, 8-OH), 3.30 (d, 1 H, 7-OH), 2.06 [s, 3 H, C{O}CH_3] ppm. ^{13}C NMR ([D$_6$]acetone): δ = 171.3 [*C*{O}CH_3], 134.3 (C-10), 129.4 (C-9), 106.0 (C-5), 74.3 (C-6), 69.7 (C-8), 67.6 (C-7), 67.4[a] (C-2), 66.7[a] (C-3), 21.8 [C{O}*C*H_3] ppm ([a] assignment may be exchanged). FAB-MS: *m*/*z* = 253 $[M + Na]^+$, 231 $[M + H]^+$. $C_{10}H_{14}O_6$ (230.22): calcd. C 52.17, H 6.13; found C 52.25, H 6.15.

(6*R*,7*R*,8*R*)-6,7-Diacetoxy-8-[(*S*)-(methoxy)(phenyl)(trifluoromethyl)acetoxy]-1,4-dioxaspiro[4.5]dec-9-ene (17): A solution of (–)-**14** (39 mg, 0.14 mmol) and (*S*)-methoxyphenyltrifluoromethylacetyl chloride (77 mg, 0.16 mmol) in pyridine (5 mL) was stirred at ambient temp. for 12 h, concentrated, and crystallized from EtOH to afford **17** (70 mg, 100%). M.p. 100–101 °C (EtOH). $[\alpha]_D$ = –70.0 (*c* = 1.0, $CHCl_3$). A suitable crystal was selected for determination of the X-ray structure.[24]

(–)-(8*R*,9*R*,10*R*)-8,9,10-Triacetoxy-1,4-dioxaspiro[4.5]dec-6-ene [(–)-10a]: Treatment of compound (–)-**14** (100 mg, 0.37 mmol) with acetic anhydride (5 mL) in pyridine (5 mL) at ambient temp. for 2 h, followed by work up as described for the preparation of compound **7**, afforded (–)-**10a** (115 mg, 100%). M.p. 95–96 °C (EtOH). *ee* > 99.5%. $[\alpha]_D$ = –110.7 (*c* = 1.0, $CHCl_3$). ^{1}H and ^{13}C NMR data were identical to those of racemic **10a**. FAB-MS: *m*/*z* = 337 $[M + Na]^+$, 315 $[M + H]^+$, 255 $[M + H - HOAc]^+$. $C_{14}H_{18}O_8$ (314.29): calcd. C 53.50, H 5.77; found C 53.73, H 5.80.

(+)-(1*S*,5*S*,6*S*)-1,5,6-Triacetoxy-4-oxocyclohex-2-ene [(+)-11a]: Treatment of compound (+)-**10a** (301 mg, 0.96 mmol) with silica gel/$FeCl_3$ (8 g, containing 0.4 mmol $FeCl_3$/g silica gel) as described

for the preparation of compound **9** under method b afforded (+)-**11a** (240 mg, 93%). M.p. 110–111 °C (dec.) (EtOH). $[\alpha]_D$ = +116.4 (c = 1.0, $CHCl_3$). ^1H and ^{13}C NMR data were identical to those of racemic **11a**. FAB-MS: m/z = 293 $[M + Na]^+$, 271 $[M + H]^+$. $C_{12}H_{14}O_7$ (270.24): calcd. C 53.33, H 5.22; found C 53.39, H 5.27.

(–)-(1*R*,5*R*,6*R*)-1,5,6-Triacetoxy-4-oxocyclohex-2-ene [(–)-11a]: Treatment of compound (–)-**10a** (246 mg, 0.78 mmol) with silica gel/$FeCl_3$ (8 g, containing 0.4 mmol $FeCl_3$/g silica gel) as described for the preparation of compound **9** under method b afforded (–)-**11a** (201 mg, 95%). M.p. 110–111 °C (dec.) (EtOH). $[\alpha]_D$ = –116.5 (c = 1.0, $CHCl_3$). ^1H and ^{13}C NMR data were identical to those of racemic **11a**. FAB-MS: m/z = 293 $[M + Na]^+$, 271 $[M + H]^+$. $C_{12}H_{14}O_7$ (270.24): calcd. C 53.33, H 5.22; found C 53.56, H 5.14.

(+)-Conduritol C Tetraacetate [(+)-12], (–)-Conduritol C Tetraacetate [(–)-12], and *meso*-Conduritol D Tetraacetate (13)

Method a: Treatment of compound (+)-**11a** (190 mg, 0.70 mmol) and $CeCl_3 \cdot 7H_2O$ (0.4 M in MeOH, 5 mL) in CH_2Cl_2 (20 mL) with $NaBH_4$ (40 mg, 1.06 mmol), followed by acetylation of the crude product and chromatography as described for the preparation of **10** under method a, first afforded (+)-**12** (57 mg, 26%) as a colorless oil. $[\alpha]_D$ = +194.8 (c = 1.0, $CHCl_3$); ref.[39] $[\alpha]_D$ = +194.0 (c = 1.1, $CHCl_3$). ^1H and ^{13}C NMR data were identical to those published previously.[6d,33,40] Eluted next was crystalline **13** (119 mg, 54%).

Method b: Treatment of compound (–)-**11a** (170 mg, 0.63 mmol) and $CeCl_3 \cdot 7H_2O$ (0.4 M in MeOH, 5 mL) in CH_2Cl_2 (5 mL) with $NaBH_4$ (36 mg, 0.94 mmol), followed by acetylation of the crude product and chromatography as described for the preparation of **10** under method a, first afforded (–)-**12** (57 mg, 29%) as a colorless oil. $[\alpha]_D$ = –194.3 (c = 1.0, $CHCl_3$); ref.[33] $[\alpha]_D^{25}$ = –186.0 (c = 2.0, $CHCl_3$). ^1H and ^{13}C NMR data were identical to those published previously.[6d,33,40] Eluted next was crystalline **13** (111 mg, 56%).

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[1] a) G. E. McCasland, E. C. Horswill, *J. Am. Chem. Soc.* **1953**, *75*, 4020–4026; b) G. E. McCasland, J. M. Reeves, *J. Am. Chem. Soc.* **1955**, *77*, 18121814.
[2] K. Kübler, *Arch. Pharm.* **1908**, *346*, 620.
[3] H. Kindl, O. Hoffmann-Ostenhof, *Fortschr. Chem. Org. Naturst.* **1966**, *24*, 149–205.
[4] D. C. Billington, F. Perron-Sierra, J. Duhault, J. Espinal, S. Challal, *Bioorg. Med. Chem. Lett.* **1994**, *4*, 2307–2312.
[5] a) G. Legler, *Mol. Cell. Biochem.* **1973**, *2*, 31–38; b) G. Legler, *Adv. Carbohydr. Chem. Biochem* **1990**, *48*, 319–384; c) Y. Kameda, N. Asano, M. Yoshikawa, K. Matsui, *J. Antibiot.* **1980**, *33*, 1575–1576; d) E. Truscheit, W. Frommer, L. Müller, B. Junge, D. D. Schmidt, W. Wingender, *Angew. Chem.* **1981**, *93*, 738–755; *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 774–776; e) N. S. Radin, R. R. Vunnam, *Meth. Enzymol.* **1981**, *72*, 673–684; f) C. Ziegler, G. Mersmann, *Biochim. Biophys. Acta* **1984**, *799*, 203–208; g) R. A. Aleksejczyk, G. A. Berchtold, A. G. Braun, *J. Am. Chem. Soc.* **1985**, *107*, 2554–2555; h) M. V. Ganey, R. E. Padykula, G. A. Berchtold, A. G. Braun, *J. Org. Chem.* **1989**, *54*, 2787–2793; i) D. H. R. Barton, J. Camara, P. Dalko, S. D. Géro, B. Quidet-Sire, P. Stütz, *J. Org. Chem.* **1989**, *54*, 3764–3766.
[6] a) L. E. Brammer, T. Hudlicky, *Tetrahedron: Asymmetry* **1998**, *9*, 2011–2014; b) S. Saito, R. Shimazawa, R. Shirai, *Chem. Pharm. Bull.* **2004**, *52*, 727–732; c) M. E. L. Podeschwa, O. Plettenburg, H.-J. Altenbach, *Eur. J. Org. Chem.* **2005**, *14*, 3116–3127; d) M. Podeschewa, O. Plettenburg, J. von Brocke, O. Block, S. Adelt, H.-J. Altenbach, *Eur. J. Org. Chem.* **2003**, *10*, 1958–1972.
[7] B. M. Trost, E. J. Hembre, *Tetrahedron Lett.* **1999**, *40*, 219–222.
[8] a) D. A. Entwistle, T. Hudlicky, *Tetrahedron Lett.* **1995**, *36*, 2591–2594; b) L. Pingli, M. Vandewalle, *Tetrahedron* **1994**, *50*, 7061–7074.
[9] a) M. Balci, *Pure Appl. Chem.* **1997**, *69*, 97–104; b) M. S. Gültekin, M. Celik, M. Balci, *Curr. Org. Chem.* **2004**, *8*, 1159–1186.
[10] a) T. Hudlicky, D. A. Entwistle, K. K. Pitzer, A. J. Thorpe, *Chem. Rev.* **1996**, *96*, 1195–1220; b) D. C. Billington in *Carbohydrate Mimics* (Ed.: Y. Chapleur), Wiley-VCH, Weinheim, **1998**, pp. 433–441; c) H.-J. Altenbach, H. Stegelmeier, E. Vogel, *Tetrahedron Lett.* **1978**, *19*, 3333–3336; d) A. E. Gal, J. P. Voorstad, *J. Labelled Compd. Radiopharm.* **1987**, *24*, 397–407; e) Z.-X. Guo, A. H. Haines, S. M. Pyke, S. G. Pyke, R. J. K. Taylor, *Carbohydr. Res.* **1994**, *264*, 147–153.
[11] a) J. K. Crandall, M. Zucco, R. S. Kirsch, D. M. Coppert, *Tetrahedron Lett.* **1991**, *32*, 5441–5442; b) A. Altamura, C. Fusco, L. D′Accolti, R. Mello, T. Prencipe, R. Curci, *Tetrahedron Lett.* **1991**, *32*, 5445–5448; c) W. Adam, A. Schönberger, *Tetrahedron Lett.* **1992**, *33*, 53–56; d) W. Adam, L. Hadjiarapoglou, K. Mielke, A. Treiber, *Tetrahedron Lett.* **1994**, *35*, 5625–5628.
[12] J. Y. Savoie, P. Brassard, *Can. J. Chem.* **1971**, *49*, 3515–3523.
[13] To our surprise this work has never been cited before: E. M. Terry, N. A. Milas, *J. Am. Chem. Soc.* **1926**, *48*, 2647–2652.
[14] a) K. Alder, F. H. Flock, H. Beumling, *Chem. Ber.* **1960**, *93*, 1896–1899; b) A. Ichihara, M. Kobayashi, K. Oda, S. Sakamura, *Tetrahedron* **1979**, *35*, 2861–2866.
[15] A. Brunmark, *J. Biolumin. Chemilumin.* **1989**, *4*, 219–225.
[16] a) R. Keller, Hoechst AG, Ger. Offen, DE 3045680, **1982** *Chem. Abstr.* 98:34904; b) F. Busque, P. de March, M. Figueredo, J. Font, S. Rodriguez, *Tetrahedron: Asymmetry* **2001**, *12*, 3077–3080; c) F. Busque, M. Canto, P. de March, M. Figueredo, J. Font, S. Rodriguez, *Tetrahedron: Asymmetry* **2003**, *14*, 2021–2032.
[17] R. Keller, E. Konz, Hoechst AG, Ger. Offen, DE 3017393, **1981** *Chem. Abstr.* 96:51988.
[18] a) P. Margaretha, P. Tissot, *Helv. Chim. Acta* **1975**, *58*, 933–936; b) A. Nilsson, U. Palmquist, T. Pettersson, A. Ronian, *J. Chem. Soc., Perkin Trans. 1* **1978**, 708–715; c) D. R. Henton, B. L. Chenard, J. S. Swenton, *J. Chem. Soc., Chem. Commun.* **1979**, 326–327.
[19] P. Binger, B. Biedenbach, *Chem. Ber.* **1987**, *120*, 601–605.
[20] a) J. E. Heller, A. S. Dreiding, B. R. O′Connor, H. E. Simmons, G. L. Buchanan, R. A. Raphael, R. Taylor, *Helv. Chim. Acta* **1973**, *56*, 272–280; b) B. R. O'Connor, du Pont and Co., US 3636054 19720118, **1972** *Chem. Abstr.* 76:99637.
[21] P. de March, M. Escoda, M. Figuredo, J. Font, A. Alvarez-Larena, J. F. Piniella, *J. Org. Chem.* **1995**, *60*, 3895–3897.
[22] R. D. Bach in *Enzyclopedia of Reagents for Organic Synthesis* (Ed.: Leo A. Paquette), John Wiley, **1995**, pp. 3944–3945 and references cited therein.
[23] B. A. Arbuzov, A. N. Vereshchagin, S. G. Vul′fson, A. A. Solov′ev, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1972**, 1291–1294 *Chem. Abstr.* 77:88030.
[24] CCDC-619356 for compound **1**, -619357 for compound **4**, and -619358 for compound **11a** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[25] a) K. B. Wiberg, K. A. Saegebarth, *J. Am. Chem. Soc.* **1957**, *79*, 2822–2824; b) V. Bushan, R. Rathore, S. Chandrasekaran, *Synthesis* **1984**, 431–433.
[26] R. B. Woodward, F. V. Brutcher, *J. Am. Chem. Soc.* **1958**, *80*, 209–211.
[27] a) V. Vanrheenen, D. Y. Cha, W. M. Hartley, *Org. Synthesis Coll. Vol.* **1988**, *6*, 342–348.
[28] a) P. H. J. Carlsen, T. Katsuki, V. S. Martin, K. B. Sharpless, *J. Org. Chem.* **1981**, *46*, 3936–3938.
[29] a) R. K. Chaturvedi, J. Adams, E. H. Cordes, *J. Org. Chem.* **1968**, *33*, 1652–1653; b) A. J. Stern, J. S. Swenton, *J. Org. Chem.* **1989**, *54*, 2953–2958.
[30] a) I. E. Markó, A. Ates, A. Gautier, B. Leroy, J.-M. Plancher, Y. Quesnel, J.-C. Vanherck, *Angew. Chem.* **1999**, *111*, 3411–3413; *Angew. Chem. Int. Ed.* **1999**, *38*, 3207–3209; b) S. E. Sen, S. C. Roach, J. K. Boggs, G. J. Ewing, J. Magrath, *J. Org. Chem.* **1997**, *62*, 6684–6686; c) E. Markó, A. Ates, A. Gautier, B. Leroy, J.-M. Plancher, Y. Quesnel, J.-C. Vanherck, *Angew. Chem.* **1999**, *111*, 3411–3413; *Angew. Chem. Int. Ed.* **1999**, *38*, 3207–3209; d) G. Barone, E. Bedini, A. Iadonisi, E. Manzo, M. Parrilli, *Synlett* **2002**, *10*, 1645–1648; e) N. R. Swamy, Y. Venkateswarlu, *Tetrahedron Lett.* **2002**, *43*, 7549–7552; f) X. Xia, D. Bai, *Synlett* **2001**, *4*, 535–537; g) M. D. Carrigan, D. Sarapa, R. C. Smith, L. C. Wieland, R. S. Mohan, *J. Org. Chem.* **2002**, *67*, 1027–1030; h) C. Johnstone, W. J. Kerr, J. S. Scott, *Chem. Commun.* **1996**, *3*, 341–432; i) M.-Y. Chen, L. N. Patkar, Mi.-D. Jan, A. S.-Y. Lee, C.-C. Lin, *Tetrahedron Lett.* **2004**, *45*, 635–639; j) J. G. Fernandez, C. O. Mallet, A. M. Marin, J. Fuentes, *Carbohydr. Res.* **1995**, *274*, 263–268.
[31] A. Fadel, R. Yefsah, J. Salaün, *Synthesis* **1987**, 37–40.
[32] a) J.-L. Luche, *J. Am. Chem. Soc.* **1978**, *100*, 2226–2227; b) J.-L. Luche, L. Rodriguez, P. Crabbé, *J. Chem. Soc., Chem. Commun.* **1978**, 601–602; c) A. L. Gemal, J.-L. Luche, *J. Am. Chem. Soc.* **1981**, *103*, 5454–5459; d) A. Krief, D. Surleraux, *Synlett* **1991**, 273–275.
[33] C. Le Drain, E. Vieira, P. Vogel, *Helv. Chim. Acta* **1989**, *72*, 338–347.
[34] a) M. Podeschwa, O. Plettenburg, J. vom Brocke, O. Block, S. Adelt, J.-J. Altenbach, *Eur. J. Org. Chem.* **2003**, 1958–1972; b) J. Bange, A. F. Haughan, J. R. Knight, J. Sweeney, *J. Chem. Soc., Perkin Trans. 1* **1998**, 1039–1046.
[35] a) C. R. Johnson, P. A. Plé, J. P. Adams, *J. Chem. Soc., Chem. Commun.* **1991**, 1006–1007; b) L. Dumortier, P. Liu, S. Dobbelaere, J. van der Eycken, M. Vandewalle, *Synlett* **1992**, 243–245; c) A. Patti, C. Sanfilippo, M. Piatelli, G. Nicolosi, *Tetrahedron: Asymmetry* **1996**, *7*, 2665–2670; d) A. Patti, C. Sanfilippo, M. Piatelli, G. Nicolosi, *Tetrahedron: Asymmetry* **1997**, *8*, 2083–2084; e) A. Patti, C. Sanfilippo, M. Piatelli, G. Nicolosi, *Tetrahedron: Asymmetry* **1997**, *8*, 1569–1573; f) A. Patti, C. Sanfilippo, M. Piatelli, G. Nicolosi, *Tetrahedron: Asymmetry* **1998**, *9*, 2809–2817; g) A. Patti, C. Sanfilippo, G. Nicolosi, *Tetrahedron: Asymmetry* **1999**, *10*, 3273–3276; h) S.-K. Chung, Y.-U. Kwon, *Org. Lett.* **2001**, *3*, 3013–3016; i) Y.-U. Kwon, C. Lee, S.-K. Chung, *J. Org. Chem.* **2002**, *67*, 3327–3338; j) M. W. Miller, C. R. Johnson, *J. Org. Chem.* **1997**, *62*, 1582–1583; k) C. R. Johnson, M. W. Miller, *J. Org. Chem.* **1995**, *60*, 6674–6675; l) A. Patti, C. Sanfilippo, M. Piatelli, G. Nicolosi, *J. Org. Chem.* **1996**, *61*, 6458–6461; m) J. T. Kohrt, J.-X. Gu, C. R. Johnson, *J. Org. Chem.* **1998**, *63*, 5088–5093; n) H. Yoshizaki, J.-E. Bäckvall, *J. Org. Chem.* **1998**, *63*, 9339–9341.
[36] a) R. J. Kazlauskas, A. N. E. Weissfloch, A. T. Rappaport, L. A. Cuccia, *J. Org. Chem.* **1991**, *56*, 2656–2665; b) P. Grochulski, F. Bouthillier, R. Kazlauskas, A. N. Serreqi, J. D. Schrag, E. Ziomek, M. Cygler, *Biochemistry* **1994**, *33*, 3494–3500.
[37] D. R. Henton, B. L. Chenard, J. S. Swenton, *J. Chem. Soc., Chem. Commun.* **1979**, 326–327.
[38] R. Criegee, P. Becher, *Chem. Ber.* **1959**, *90*, 2516–2521.
[39] H. A. J. Carless, O. Z. Oak, *J. Chem. Soc., Chem. Commun.* **1991**, *2*, 61–62.
[40] L. Hyldtoft, R. Madsen, *J. Am. Chem. Soc.* **2000**, *122*, 8444–8452.

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