81. Catalytic One-Pot Osmylation of Cyclohexadienes: Stereochemical and Conformational Studies of the Resulting Polyols

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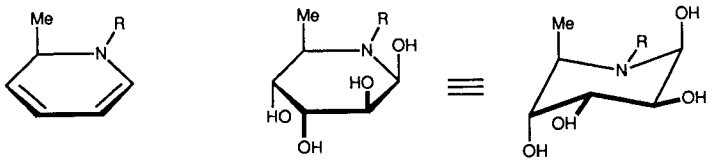
Catalytic double osmylation is described for a series of cyclohexadienes in acetone/H_2O in the presence of the co-oxidant *N*-methylmorpholine *N*-oxide (NMO). The formation of polyols occurred stereospecifically with cyclohexadienes **3**, **7**, and **11a**, leading thereby to tetrols **5a**, and **9a** and to *allo*-inositol (**14a**), respectively. To the contrary, *trans*-cyclohexadiene-diol **15a** gave a mixture of the stereoisomeric inositols **18a** (*epi*), **19a** (*neo*), and **20a** (*chiro*). High-field NMR let to clearcut conformational analyses of the polyhydroxylated derivatives.

Introduction. – In a preliminary communication, we described the one-pot double catalytic osmylation of dihydropyridine **1** which led stereospecifically to the aminodideoxyaltrose derivative **2** [1]. The stereospecific '*cis/trans/cis/trans*' outcome of this multistep reaction – which led in good yield to 5 asymmetric centres – is most probably due to minimization of steric interactions during each osmylation step. Due to the strong anomeric effect, which is more pronounced in piperidinoses than in pyranoses, compound **2** occurred exclusively in the chair conformation [1].



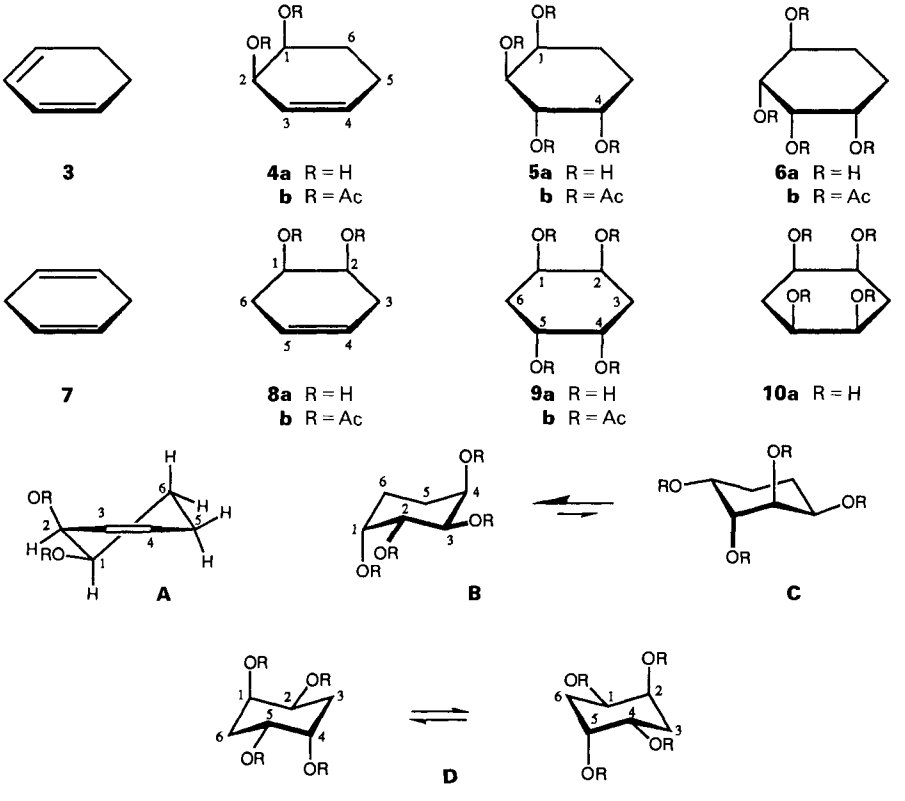
1 R = CO_2Bn **2**

In the meantime, *Sharpless, Park,* and *Moon Kim* reported a similar catalytic osmylation methodology with open-chain conjugated (*E,E*)-dienes, and found stereoselectivities which were strongly in favour of the '*cis/trans/cis*' stereoisomeric tetrols [2]. Besides these two preliminary studies [1] [2], osmylation of 1,3-dienes has received but little attention, despite its obvious utility in the synthesis of polyhydroxylated compounds, $KMnO_4$ being used more frequently than OsO_4, leading usually with poor stereoselectivity to a mixture of tetrols [3–9].

We describe herein catalytic single and double osmylation of cyclohexadienes **3**, **7**, **11a**, and **15a** with *N*-methylmorpholine *N*-oxide (NMO) as the co-oxidant, the experi-

mental conditions being similar to those used for the synthesis of aminodideoxyaltrose **2**, and to those described by *Sharpless* and coworkers [2] (see below).

Catalytic Osmylation of Cyclohexa-1,3-diene (3) and Cyclohexa-1,4-diene (7). – Catalytic osmylation of **3** in the presence of an excess of NMO (more than 2 equiv.) at room temperature in acetone/H_2O led exclusively to tetrol **5a** which was characterised as its tetraacetate **5b** (overall yield 86%). The same procedure applied to cyclohexadiene **7** gave tetrol **9a** and thence the corresponding tetraacetate **9b** (81% overall yield). Since **5a** and **9a** are the less hindered tetrols, it is most likely that they were formed under steric control. Incomplete osmylation of **3** in the presence of 1 equiv. of NMO, followed by acetylation gave **4b** (79%) and **5b** (5%). Diene **7**, treated likewise, led to a mixture of **8b** (32%) and **9b** (27%). These results indicate that diol **8a** is more reactive (less hindered) than diol **4a**.

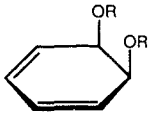


While *Pasternak* and *Friedli* could show that catalytic osmylation of enediol **4a** in the presence of an excess of $AgClO_3$ led stereospecifically to tetrol **5a** in good yield [3], *Zelinski et al.* found that hydroxylation of diene **3** with $KMnO_4$ gave **6a** in poor yield only [4]. The stereochemical outcome of this latter reaction was explained by assuming a '*cis*-complexation' of both double bonds by $KMnO_4$ followed by an '*anti*'-hydrolysis of the so-formed 'manganic ester' [5]. As to the double hydroxylation of diene **7** with

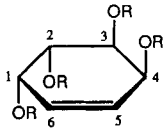
$KMnO_4$, it gave a mixture **8a**/**9a**, both in poor yield [6]. Eventually, *McCasland et al.* described the catalytic osmylation of **7** in the presence of $AgClO_3$ which led to **9a**/**10a**, the former being the major product [10].

It appears, therefore, that the OsO_4/NMO hydroxylation is the method of choice, since it leads to higher yields; furthermore, it is stereospecific, at least with dienes **3** and **7**.

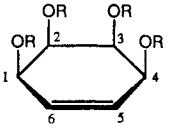
Catalytic Osmylation of Cyclohexa-3,5-diene-1,2-diols 11a (*cis*) and 15a (*trans*). – Catalytic mono- and bis-osmylation of cyclohexadiene-diols **11a** and **15a** in the presence of NMO led to conduritols and to cyclitols. Thus, osmylation of **11a** for 15 h in the presence of 2 equiv. of NMO followed by acetylation led to conduritol E tetraacetate (**12b**; 48%) and *allo*-inositol hexaacetate (**14b**; 31%), whereas conduritol D tetraacetate (**13b**) could not be isolated. This indicates that steric crowding in **12a** is such that the second osmylation step occurs with difficulty. According to *Nakajima et al.*, catalytic osmylation of **11a** in the presence of $AgClO_3$ gave mostly phenol (48%) and small amounts of conduritol E (4% **12b** after acetylation) [7]. Furthermore, when bis-acetate



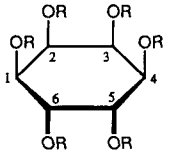
11a R = H
b R = Ac



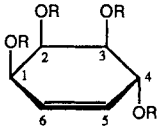
12a R = H, conduritol E
b R = Ac



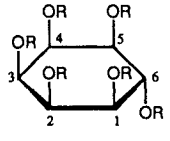
13a R = H, conduritol D
b R = Ac



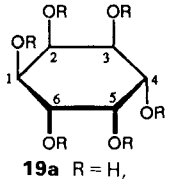
14a R = H, *allo*-inositol
b R = Ac



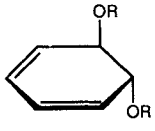
16a R = H, conduritol C
b R = Ac



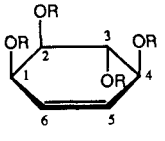
18a R = H, *epi*-inositol
b R = Ac



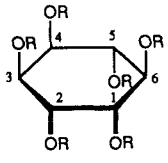
19a R = H, *neo*-inositol
b R = Ac



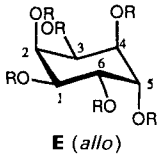
15a R = H
b R = Ac



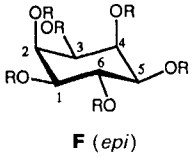
17a R = H, conduritol F
b R = Ac



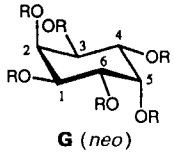
20a R = H, *chiro*-inositol
b R = Ac



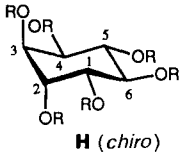
E (*allo*)



F (*epi*)



G (*neo*)



H (*chiro*)

11b was hydroxylated with $KMnO_4$ in neutral medium, these authors isolated **12b** only (61%) [8], whereas catalytic osmylation of **11a** in the presence of 1 equiv. of NMO led to a mixture **12b**/**13b** after acetylation (see below). When **12b** was hydroxylated with $KMnO_4$, *allo*-inositol was isolated as its acetate **14b** (45%) [8].

Catalytic osmylation of **11a** in the presence of 1 equiv. only of NMO followed by acetylation gave **12b**/**13b** (overall yield 88%), **12b** being the major product; under these conditions, **11a** was entirely consumed after 2 h and *allo*-inositol (**14a**) did not form.

From these two experiments, *i.e.* catalytic osmylation of **11a** in the presence of 1 or 2 equiv. of NMO, one concludes that conduritol D (**13a**) is transformed into *allo*-inositol (**14a**) at a faster rate than its stereoisomer conduritol E (**12a**). This is clearly due to a steric interaction between OsO_4 and the OH functions which is more pronounced in **12a** than in **13a**, a conclusion which had also reached *Angyal* and *Gilham* [11]. Furthermore, since **13a** and **12a** gave the same inositol **14a**, bis-osmylation of **11a** is stereospecific overall.

Diol **15a**, which was prepared according to *Platt* and *Oesch*'s procedure [12], was osmylated in the presence of a 2-fold excess of NMO (more than 2 equiv.) for 5 d and the reaction mixture acetylated to give **18b** (*epi*)/**19b** (*neo*)/**20b** (*chiro*) in a 42:11:47 ratio (overall yield 60%). The same experimental conditions applied to diacetate **15b** for 3 d led, after acetylation, to **16b**/**18b**/**19b**/**20b** in a 50:9:13:28 ratio.

Mono-osmylation of **15a** or of **15b** in the presence of 1 equiv. of NMO, followed by peracetylation, led to **16b**/**17b**/**19b**/**20b** in a 66:25:2:7 ratio (as determined by ^{1}H-NMR).

These results indicate that conduritol F (**17a**) is more reactive (towards OsO_4) then its stereoisomer conduritol C (**16a**). This again is best explained by steric crowding (in the transition states) which is more severe in **16** than in **17**. Nevertheless, it is rather surprising that the seemingly more crowded conduritol C (**16a**) was formed at a faster rate than conduritol F (**17a**).

Structural Analyses of the Polyols. – The above described conduritols and cyclitols all are known compounds. Their relative configurations were established decades ago, in most cases by applying low-field NMR techniques. We used 250- and 400-MHz ^{1}H-NMR spectroscopy to analyze unequivocally their conformations.

Cyclohexene-diols and Diacetates **4** *and* **8**. Compounds **4** are asymmetric; a large coupling constant (J(1,6ax) = 10.2 Hz) clearly demonstrates that diol **4a** occurs essentially in its pseudo-chair conformation **A**[1]). As a consequence, all C*H* atoms of **4** appear with well differentiated chemical shifts (8 *m*, see *Table 1*). Compounds **8** also belong to the C_1 point group; nevertheless a fast equilibrium between the two enantiomeric pseudo-chair conformations leads to a simplification of the ^{1}H-NMR spectrum at room temperature with only 3 differentiated chemical shifts (see *Table 1*).

Table 1. *Selected ^{1}H-NMR Data of Diols* **4a** *and* **8a**, *and of Their Acetates* **4b** *and* **8b**. 250 MHz, 300 K. δ in ppm, J in Hz, internal standard TMS.

	Solvent	H–C(1)	H–C(2)	H–C(3)	H–C(4)	H–C(5)	H_{ax}–C(6)	H_{eq}–C(6)
4a	CD_3OD	3.73	4.04	5.69	5.81	2.05[a]), 2.21[b])	1.82	1.68
b	$CDCl_3$	5.10	5.42	5.67	5.99	2.25[c])	1.95	1.78
8a	CD_3OD	3.86	3.86	2.24[d])	5.53	5.53	2.24[d])	
b	$CDCl_3$	5.18	5.18	2.35[d])	5.62	5.62	2.35[d])	

[1]) The pseudo-chair conformation **A** is also corroborated by the J(1,2), J(2,3), and J(2,4) coupling constants (see *Table 1*). For similar half-chair conformations, see [13–15].

Tab. 1 (cont.)

		$J(1,2)$	$J(1,6a)$	$J(1,6e)$	$J(2,3)$	$J(2,4)$	$J(2,6e)$	$J(3,4)$	$J(3,5)$[d])	$J(4,5)$[d])	$J(4,6e)$	$J(5a,5e)$	$J(5,6a)$[d])	$J(5,6e)$[e])	$J(6a,6e)$
4b	$CDCl_3$	3.9	10.2	3.3	4.3	1.0	1.0	9.9	2.1	3.6	0.3	18.2	7.0	5.5	12.6

[a]) H_{ax}–C(5).
[b]) H_{eq}–C(5).
[c]) *AB* pattern for H_{eq}–C(5) and H_{ax}–C(5).
[d]) Mean values for H_{eq}–C(3)/H_{eq}–C(6) and for H_{ax}–C(3)/H_{ax}–C(6).
[e]) These data represent mean values of coupling constants with H_{ax}–C(5) and H_{eq}–C(5).

Cyclohexane-tetrols and Tetraacetates **5** *and* **9**. Tetrol **5a** is C_2-symmetric, so that only 3 peaks appear in the ^{13}C-NMR spectrum at room temperature (and 4 peaks in the ^{1}H-NMR), the interconversion between the chair conformations **B** and **C** being fast (see *Table 2*). According to the coupling constant $J(2,3)$, measured from the ^{13}C-satellites of the H–C(2), H–C(3) signal, **B** is the major conformation (60%) at equilibrium. At – 60°, both chair conformations **B** and **C** appear as well separated C_2-symmetric entities, the **B**/**C** ratio being 56:44 for **5a**, and 90:10 for **5b** (see *Table 2*).

Tetrol **9a** and its tetraacetate **9b** have C_i symmetry, so that 3 peaks should appear in the ^{13}C-NMR spectrum for the ring *C*-atoms, and 4 peaks in the ^{1}H-NMR spectrum for the cyclohexane H-atoms; this is indeed observed at high field and at low temperature (– 30°), with $J(2ax,3ax) = J(5ax,6ax) = 12$ Hz (these are the only *J* values which can be determined) for **9b**. At room temperature though, the fast conformational inversion between the 2 identical chair conformations **D** leads to 2 peaks in the ^{13}C- and to 2 peaks in ^{1}H-NMR, the fast inverting molecule having statistical C_{2h} symmetry. Such a conformational analysis could not be achieved at 60 MHz [10].

Conduritols E–F and Tetraacetates **12**, **13**, **16**, *and* **17**. Structure and conformation of conduritols C, D, E, and F were already studied by *Abraham et al.* at high-field ^{1}H-NMR [16]. *Vogel* and coworkers undertook a higher-resolution ^{1}H- and ^{13}C-NMR study of conduritols C, D, and F and confirmed *Abraham*'s conformational analyses [17] [18]. Our own highfield ^{1}H- and, in part, ^{13}C-NMR investigations led to similar conclusions in terms of conformational analysis (see *Exper. Part*). Conduritol D (**13a**) undergoes a fast conformational equilibrium between the 2 enantiomeric half-chairs (3 peaks in ^{1}H- and 3 in ^{13}C-NMR at room temperature). Conduritol E (**12a**) is C_2-symmetric and its ^{1}H-NMR shows 3 peaks both at – 30° and at room temperature Conduritol F (**17a**) being asymmetric (C_1 point group) appears with 6 peaks in the ^{1}H-NMR at room temperature.

Inositols and Hexaacetates **14** (*allo*), **18** (*epi*), **19** (*neo*), *and* **20** (*chiro*). *allo*-Inositol hexaacetate (**14b**) is asymmetric and leads to 6 peaks both in the ^{1}H- and in the ^{13}C-NMR for the ring H- and C-atoms at low temperature (see *Table 3*), the absorption bands having been attributed *via* double-irradiation techniques. At – 30°, $J(1,6) = 11$ Hz can be determined which demonstrates the *trans*-diaxial configuration of these 2 protons as indicated in **E** (the other *J* values are smaller than 3 Hz). At 45°, a fast equilibrium occurs between the two enantiomeric chair conformations as demonstrated by the simplified spectrum, the molecule having now a statistical C_s symmetry (3 peaks in the ^{1}H- and 3 in the ^{13}C-NMR).

epi-Inositol hexaacetate (**18b**) having C_s symmetry shows 4 peaks in the ^{1}H- and in the ^{13}C-NMR, as expected (see *Table 3*). Only one chair conformation is present, *i.e.* **F**, with 4 equatorial AcO groups ($J(1,6) = J(5,6) = 10.4$ Hz).

Table 2. *Selected ^{1}H-NMR* (400 MHz) *and ^{13}C-NMR* (100.6 MHz) *Data of Tetrols* **5a** *and* **9a** *and of Their Tetraacetates* **5b** *and* **9b**. δ in ppm, internal standard TMS (^{1}H) and $CDCl_3$ (δ ($CDCl_3$) = 77 ppm; ^{13}C)[a]).

	Solvent, temp.	H–C(1)	H–C(2)	H–C(3)	H–C(4)	H–C(5)	H–C(6)	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)
5a	CD_3OD, 25°	3.93	3.73	3.73	3.93	1.76, 1.63	1.63, 1.76	70.23	73.29	73.29	70.23	26.59	26.59
	CD_3OD, −60° **B**	3.98	3.64	3.64	3.98	1.82, 1.58	1.58, 1.82	71.22	72.01	72.01	71.22	26.22	26.22
	C	3.82	3.84	3.84	3.82	1.70, 1.58	1.58, 1.70	68.30	74.12	74.12	68.30	27.00	27.00
5b	$CDCl_3$, −25°	5.32	5.13	5.13	5.32	1.86, 1.71	1.71, 1.86	68.96	69.21	69.21	68.96	23.29	23.29
	$CDCl_3$, −60° **B**	5.34	5.03	5.03	5.34	*ca.* 1.75	*ca.* 1.75	69.16	69.59	69.59	69.16	23.39	23.39
	C	4.97	5.19	5.19	4.97	[b])	[b])	68.54	68.62	68.62	68.54	23.54	23.54
9a	D_2O, 25°	4.00	4.00	1.87	4.00	4.00	1.87	70.30	70.30	34.88	70.30	70.30	34.89
9b	$CDCl_3$, 25°	5.30	5.30	2.05	5.30	5.30	2.05	67.85	67.85	29.06	67.85	67.85	29.06
	$CDCl_3$, −30°	5.44	5.08, 1.95	2.10	5.44	5.08, 1.95	2.10	67.93	67.07	28.58	67.93	67.07	28.58

[a]) Assignment of the ^{1}H- and ^{13}C-NMR signals by selective decoupling experiments.

[b]) Not determined.

Table 3. *Selected ^{1}H- and ^{13}C-NMR Data of Inositol Hexaacetates* **14b**, **18b**, **19b**, *and* **20b**. δ in ppm, internal standard TMS (^{1}H) and $CDCl_3$ (δ ($CDCl_3$) = 77 ppm; ^{13}C).

	Frequency, solvent, temp.	H–C(1)	H–C(2)	H–C(3)	H–C(4)	H–C(5)	H–C(6)	Frequency, solvent, temp.	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)
14b	400 MHz, $CDCl_3$, −30°	5.28[a])	5.63	5.24	5.29[a])	5.42	5.46	100.6 MHz, $CDCl_3$, −30°	66.58	68.46	65.22	67.59	67.22	66.09
	400 MHz, $CDCl_3$, 45°	5.32	5.45	5.45	5.32	5.47	5.47	100.6 MHz, $CDCl_3$, 45°	67.72	67.50	67.50	67.72	67.34	67.34
18b	250 MHz, C_6D_6, 27°	5.02	5.82	4.66	5.82	5.02	6.04	62.9 MHz, $CDCl_3$, 27°	68.9	68.6	67.4	68.6	68.9	65.9
19b	250 MHz, $CDCl_3$, 27°	5.35	5.66	5.35	5.35	5.66	5.35	62.9 MHz, $CDCl_3$, 27°	67.5	68.1	67.5	67.5	68.1	67.5
20b	250 MHz, $CDCl_3$, 27°	5.32	5.40	5.40	5.32	5.43	5.43	62.9 MHz, $CDCl_3$, 27°	68.9	69.8	69.8	68.9	67.3	67.3

[a]) Can be inverted.

neo-Inositol hexaacetate (**19b**) is C_{2h}-symmetric so that only 2 peaks appear in the ^{1}H- and ^{13}C-NMR (see *Table 3*). The coupling constants ($J(1,6) = J(3,4) = 11.1$ Hz and $J(1,2) = J(2,3) = J(4,5) = J(5,6) = 2.5$ Hz) can be calculated by simulation *via* the LAOCOON-III (PANIC) iteration program [19], showing thereby that conformation **G** is the predominant one for **19b**.

chiro-Inositol hexaacetate **20b** is C_2-symmetric and leads to 3 peaks in the ^{1}H- and ^{13}C-NMR (see *Table 3*), as expected. The coupling constants are calculated as above *via* the LAOCOON-III program [19] and permit to state that **H** is the dominant chair conformation, as expected ($J(2,3) = 2.5$ Hz; $J(1,2) = J(3,4) = 1.4$ Hz; $J(1,6) = J(5,6) = J(4,5) = 10.3$ Hz).

Conclusion. – Double catalytic osmylation in the presence of 2 equiv. of NMO in acetone/H_2O proved to be '*cis*/*trans*/*cis*'-stereospecific with (*Z*,*Z*)-cyclohexadienes **3**, **7**, and **11a**, leading thereby to tetrol **5a**, to tetrol **9a**, and to *allo*-inositol (**14a**), respectively. The C_2-symmetric *trans*-cyclohexadiene-diol **15a** gave a mixture of the three stereoisomeric inositols **18a–20a**, *via* conduritol C (**16a**) and conduritol F (**17a**), the overall yield being moderate. The absence of stereoselection in this latter instance is reminiscent of the non-stereoselective osmylation as described recently by *Campbell et al.* for a 1,5-disubstituted cyclohexa-1,3-diene [20].

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Experimental Part

General. Flash chromatography (FC): silica gel (*Merck 60*, 230–400 mesh). TLC: Al roll silica gel (*Merck 60*, F_{254}). M.p.: *Kofler* hot bench or *Büchi-SMP-20* apparatus; corrected. IR Spectra (cm^{-1}): *Perkin-Elmer 157-G*. ^{1}H- and ^{13}C-NMR Spectra: *Bruker AC-F-250*, and *AM-400* using double-irradiation techniques; tetramethylsilane (TMS; ^{1}H) and $CDCl_3$ or C_6D_6 (δ ($CDCl_3$) = 77.0 or δ (C_6D_6) = 128.0 ppm rel. to TMS; ^{13}C) as internal references; δ in ppm and J in Hz. High-resolution (HR) MS were measured on a *MAT-311* spectrometer at the University of Rennes. Microanalyses were carried out by the 'Service Central de Microanalyses' of the CNRS, at Vernaison.

Reagents. The catalyst was prepared according to [21] from OsO_4 (1 g) and 1 ml of 70% *t*-BuOOH in 200 ml of *t*-BuOH, a soln. which is *ca.* 0.02 mmol per ml. *Amberlyst A-26* (OH^- form) was prepared starting from its chloride percursor *A-26* (Cl^- form; 10 g) by adding 1N aq. NaOH and letting the ion exchange occur for 1 h. The *Amberlyst A-26* (OH^- form) beads were then rinsed several times with H_2O and MeOH and could be kept for several weeks in the cold.

Cyclohexane-r-*1*,c-*2*,t-*3*,t-*4*-*tetrayl Tetraacetate* (**5b**). To a stirred soln. of cyclohexa-1,3-diene (**3**; 3.12 g, 38.9 mmol) in acetone/H_2O 9:1 (30 ml) were added NMO (16.02 g, 118 mmol, *ca.* 3 equiv.) and cat. OsO_4 soln. (5 ml). After 2 h at r.t., the soln. was evaporated and the crude residue taken up in Ac_2O (25 ml) and pyridine (50 ml) and left to react at r.t. for 15 h. Some AcOEt was added and the soln. washed sequentially with 10% aq. Na_2SO_3 soln., 10% aq. $NaHCO_3$ soln., and brine. The combined org. soln. was dried ($MgSO_4$) and evaporated and the residue separated by column chromatography (AcOEt): **5b** (10.58 g, 86%). Colourless crystals. M.p. 163–164° (AcOEt). IR (KBr): 1740, 1375, 1365, 1240, 1220, 1200. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 2*. Anal. calc. for $C_{14}H_{20}O_8$ (316.30): C 53.16, H 6.37; found: C 53.2, H 6.3.

Cyclohexane-r-*1*,c-*2*,t-*3*,t-*4*-*tetrol* (**5a**). To a stirred soln. of **5b** (1.88 g, 5.94 mmol) in MeOH (20 ml) was added *Amberlyst A-26* (OH^-). After 1 h at r.t., the suspension was filtered, the resin washed with hot MeOH, and the org. soln. evaporated: **5a** (867 mg, 100%). Colourless crystals. M.p. 214–215° (MeOH; [22]: 216°). IR (KBr): 3350 (br.), 2950, 2935, 2895, 1450, 1250. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 2*. Anal. calc. for $C_6H_{12}O_4$ (148.16): C 48.64, H 8.16; found: C 48.6, H 8.3.

cis-*Cyclohex-3-ene-1,2-diyl Diacetate* (**4b**). As described for **5b**, with **3** (1.87 g, 23.4 mmol), acetone/H_2O 9:1 (15 ml), NMO (3.21 g, 23.7 mmol, 1 equiv.), cat. OsO_4 soln. (5 ml), Ac_2O (10 ml), and pyridine (20 ml). FC of the crude (AcOEt/cyclohexane 3:7) gave **4b** as an oil (3.64 g, 79%) and **5b** (360 mg, 5%). **4b**: IR (KBr): 1735, 1365, 1245, 1225. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 2*. HR-MS: 138.0685 ($C_8H_{10}O_2$, $[M - CH_3CO_2H]^+$, calc. 138.06807).

cis-*Cyclohex-3-ene-1,2-diol* (**4a**). As described for **5a**, with **4b** (742 mg, 3.74 mmol), THF (6 ml), MeOH (15 ml), and *Amberlyst A-26* (OH^-): **4a** (426 mg, 100%). Oil. IR (KBr): 3395 (br.), 2920, 1075. ^{1}H-NMR: *Table 1*.

Cyclohexane-r-*1*,c-*2*,t-*4*,t-*5-tetrayl Tetraacetate* (**9b**). As described for **5b**, with cyclohexa-1,4-diene (**7**; 925 mg, 11.9 mmol), acetone/H_2O 9:1 (14 ml), NMO (4.19 g, 31.0 mmol, 2.6 equiv.), cat. OsO_4 soln. (5 ml), Ac_2O (6 ml)/pyridine (12 ml; 40° for 15 h): **9b** (3.05 g, 81%). Colourless crystals. M.p. 170–171° (CH_2Cl_2/hexane; [23]: 170°). IR (KBr): 1540, 1525, 1380, 1365, 1245, 1235. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 2*. Anal. calc. for $C_{14}H_{20}O_8$ (316.30): C 53.16, H 6.37; found: C 53.1, H 6.4.

Cyclohexane-r-*1*,c-*2*,t-*4*,t-*5-tetrol* (**9a**). As described for **5a**, with **9b** (727 mg, 2.3 mmol), MeOH (10 ml), and *Amberlyst A-26* (OH^-): **9a** (339 mg, 100%). Colourless crystals. M.p. 246° (MeOH; [23]: 241°). IR (KBr): 3370, 3260, 2940, 1390, 1350, 1225. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: *Table 2*. Anal. calc. for $C_6H_{12}O_4$ (148.16): C 48.64, H 8.16; found: C 48.6, H 8.3.

cis-*Cyclohex-4-ene-1,2-diyl Diacetate* (**8b**). As described for **5b**, with **7** (905 mg, 11.3 mmol), acetone/H_2O 9:1 (10 ml), NMO (1.54 g, 11.4 mmol, 1 equiv.), cat. OsO_4 soln. (5 ml), Ac_2O (6 ml), and pyridine (12 ml). FC (AcOEt/cyclohexane 3:7) gave **8b** (825 mg, 37%) as an oil and **9b** (973 mg, 27%). **8b**: IR (KBr): 1740, 1365, 1250, 1220. ^{1}H-NMR: *Table 1*. HR-MS: 138.0685 ($C_8H_{10}O_2$ $[M - CH_3CO_2H]^+$, calc. 138.06807).

cis-*Cyclohex-4-ene-1,2-diol* (**8a**). As described for **5a**, with **8b** (685 mg, 3.45 mmol), THF (2 ml), MeOH (5 ml), and *Amberlyst A-26* (OH^-): **8a** (371 mg, 94%), colourless crystals after FC (AcOEt) of the crude. M.p. 79° (crystal washed with Et_2O; [6] [24]: 74–78.5°). IR (KBr): 3260 (br.), 2890. ^{1}H-NMR: *Table 1*. Anal. calc. for $C_6H_{10}O_2$ (114.14): C 63.13, H 8.83; found: C 63.0, H 8.9.

Conduritol E Tetraacetate (**12b**) *and* allo-*Inositol Hexaacetate* (**14b**). As described for **5b**, with *cis*-cyclohexa-3,5-diene-1,2-diol (**11a**; 685 mg, 6.10 mmol), acetone/H_2O 9:1 (14 ml), NMO (1.74 g, 12.7 mmol, 2.1 equiv.), cat. OsO_4 soln. (5 ml; 15 h at r.t.), and Ac_2O (5 ml)/pyridine (10 ml; 40° for 15 h). FC (AcOEt/cyclohexane 4:6) of the crude gave **14b** (830 mg, 31%) and **12b** (920 mg, 48%), both as colourless crystals.

12b: M.p. 156° (AcOEt/hexane; [7]: 153°). IR (KBr): 1745 (br.), 1370, 1245, 1215. ^{1}H-NMR (400 MHz, $CDCl_3$, 25°): 5.68 (H–C(1), H–C(4)); 5.44 (H–C(2), H–C(3)); 5.91 (H–C(5), H–C(6)); 2.08 (Ac); 2.02 (Ac); $|J(1,6) + J(4,5)| \approx 4$, $|J(1,2) + J(3,4)| \approx 3.5$, $J(2,3) \approx 10$, $J(5,6) \approx 10$. ^{1}H-NMR (400 MHz, $CDCl_3$, −30°): 5.68; 5.41; 5.92; 2.10; 2.04. ^{13}C-NMR (100.6 MHz, $CDCl_3$, 25°): 170.2 (C=O); 169.9 (C=O); 128.2 (C(5), C(6)); 66.6 (C(2), C(3)); 66.1 (C(1), C(4)); 20.8 (Me); 20.6 (Me). Anal. calc. for $C_{14}H_{18}O_8$ (314.28): C 53.50, H 5.77; found: C 53.7, H 5.7.

14b: M.p. 141–143° (CH_2Cl_2/hexane; [25]: 144°). IR (KBr): 1745 (br.), 1435, 1370, 1225. ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 3*. Anal. calc. for $C_{18}H_{24}O_{12}$ (432.37): C 50.00, H 5.60; found: C 49.8, H 5.5.

Conduritol E (**12a**). As described for **5a**, with **12b** (290 mg, 0.92 mmol), THF (2 ml), MeOH (5 ml), and *Amberlyst A-26* (OH^-): **12a** (126 mg, 94%). Colourless crystals. M.p. 183° (MeOH; [7]: 180°). IR (KBr): 3365 (br.), 1105, 1095. ^{1}H-NMR (400 MHz, CD_3OD, 25°): 4.23 (H–C(1), H–C(4)); 3.90 (H–C(2), H–C(3)); 5.75 (H–C(5), H–C(6)). ^{13}C-NMR (100.6 MHz, CD_3OD): 130.8 (C(5), C(6)); 71.2 (C(2), C(3)); 67.7 (C(1), C(4)). Anal. calc. for $C_6H_{10}O_4$ (146.16): C 49.31, H 6.90; found: C 49.4, H 7.1.

allo-*Inositol* (**14a**). As described for **5a**, with **14b** (334 mg, 0.77 mmol): **14a** (132 mg, 95%). Colourless crystals. M.p. 310° (dec.; [25]: 320° (dec.)). IR (KBr): 3480–3180, 2920, 1440, 1420, 1110. Anal. calc. for $C_6H_{12}O_6$ (180.16): C 40.00, H 6.71; found: C 39.9, H 6.8.

Conduritol E Tetraacetate (**12b**) *and Conduritol D Tetraacetate* (**13b**). As described for **5b**, with **11a** (218 mg, 1.94 mmol), acetone/H_2O 9:1 (4 ml), NMO (269 mg, 1.99 mmol, 1 equiv.), cat. OsO_4 (2 ml), Ac_2O (3 ml)/pyridine (6 ml; 5 h at 40°). FC (AcOEt/cyclohexane 4:6) of the crude residue gave **12b** (343 mg, 56%; see above) and **13b** (195 mg, 32%), both as colourless crystals. **13b**: M.p. 107–108° (AcOEt/hexane; [7]: 102–104°). IR (KBr): 1745, 1730, 1365, 1230, 1215. ^{1}H-NMR (250 MHz, $CDCl_3$, 25°): 5.58 (*m*, H–C(1), H–C(4)); 5.37 (*m*, H–C(2), H–C(3)); 5.90 (*m*, H–C(5), H–C(6)); 2.01 (Ac).

Conduritol C Tetraacetate (**16b**), epi-*Inositol Hexaacetate* (**18b**), neo-*Inositol Hexaacetate* (**19b**), *and* chiro-*Inositol Hexaacetate* **20b**. To a stirred soln. of diacetate **15b** (303 mg, 1.54 mmol, 2.15 equiv.) in acetone/H_2O 9:1 (8 ml) were added NMO (446 mg, 3.29 mmol) and cat. OsO_4 soln. (1.5 ml). After 24 h at r.t., the soln. was evaporated, the residue taken up in Ac_2O (3.5 ml) and pyridine (7 ml), and the resulting soln. heated overnight to 45°. Et_3N (5 ml) was added and the soln. kept for 24 h at 45°. After addition of toluene and MeOH, the soln. was

evaporated and the crude residue separated into several fractions by column chromatography. Each fraction was partly resolved by FC (AcOEt/cyclohexane 4:6) whereby **16b**, **18b**, **19b**, and **20b** could be isolated.

16b: M.p. 93° (AcOEt/cyclohexane; [7]: 92°). IR (KBr): 1740, 1360, 1225. ^{1}H-NMR (C_6D_6, 250 MHz, 25°): 5.48 (H–C(1)); 5.90 (H–C(2)); 5.33 (H–C(3)); 5.96 (H–C(4)); 5.58 (H–C(5)); 5.40 (H–C(6)); 1.68 (Ac); 1.66 (Ac); 1.63 (Ac). ^{13}C-NMR (62.9 MHz, C_6D_6, 25°): 170.0 (CO); 169.6 (CO); 169.1 (CO); 128.4 (C(6)); 127.6 (C(5)); 71.2 (C(3)); 70.3 (C(2)); 69.9 (C(4)); 68.2 (C(1)); 20.5 (Me); 20.3 (Me); 20.3 (Me); 20.2 (Me).

18b: M.p. 183–184° (CH_2Cl_2/hexane; [9]: 186°). ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 3*.

19b: M.p. 257–259° (MeOH; [9]: 250–252°). ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 3*.

20b: M.p. 113–114° (Et_2O/hexane; [26]: 111–112°). ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 3*.

Conduritol C Tetraacetate (**16b**) *and Conduritol F Tetraacetate* (**17b**). As described for **5b**, with *trans*-cyclohexa-3,5-diene-1,2-diol (**15a**; 200 mg, 1.8 mmol), acetone/H_2O 9:1 (5 ml), NMO (241 mg, 1.8 mmol, 1 equiv.), cat. OsO_4 soln. (2 ml; 20 h at r.t.), Ac_2O (2.5 ml)/Et_3N (5 ml; 15 h at 40°). ^{1}H-NMR (250 MHz): **16b**/**17b** (*ca.* 70%) 3:1, **18b**/**19b**/**20b** (< 20%). Compound **17b** could not be isolated in pure form, but its ^{1}H-NMR was identical with the one of a pure sample of **17b** as synthetized by *Le Drian et al.* [18]. ^{1}H-NMR (non-purified **17b**; 250 MHz, C_6D_6): 5.90 (*dd*, J = 11.0, 7.5, H–C(3)); 5.65 (*m*, H–C(1)); 5.55 (*ddd*, J = 7.5, 1.7, 1.2, H–C(4)); 5.39 (*m*, H–C(5), H–C(6)); 5.23 (*dd*, J = 11.0, 3.9, H–C(2)); 1.71, 1.69, 1.63, 1.56 (4*s*, AcO).

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