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Stable spiro-endoperoxides by sunlight-mediated photooxygenation of 1,2-*O*-alkylidene-5(*E*)-eno-5,6,8-trideoxy-α-D-*xylo*-oct-1,4-furano-7-uloses

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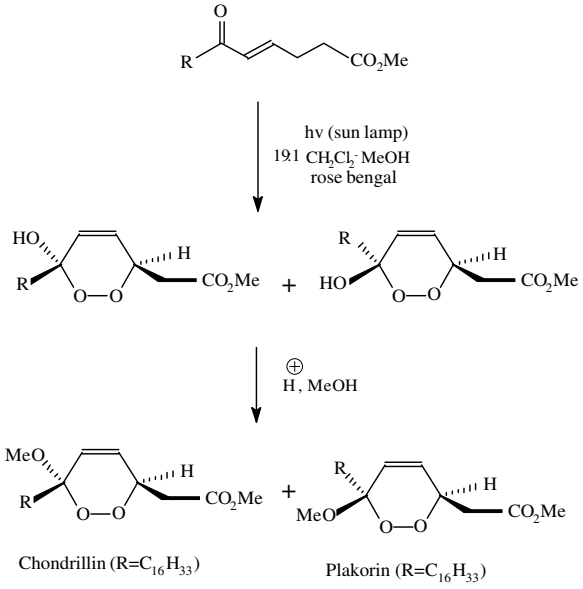
Abstract—Sunlight-mediated photooxygenation of 3-*O*-acetyl and 3-*O*-methyl derivatives of 1,2-*O*-alkylidene-5(*E*)-eno-5,6,8-trideoxy-α-D-*xylo*-oct-1,4-furano-7-uloses (**1a**–**e**) in carbon tetrachloride solution gave stable 4,7-epidioxy derivatives in 4*R* (**2a**–**e**) and 4*S* (**3a**–**e**) configurations. The presence of an *endo* alkyl, on the 1,2-*O*-alkylidene group and its size, resulted in an increase of the yield of the 4*S* isomers. 3-*O*-Acetyl derivatives yielded products as a mixture of C-7 anomers, whereas 3-*O*-methyl derivatives gave pure single stereoisomers.

Keywords: Endoperoxides; Spiroketals; Furano sugars; Antimalarial drugs; Antibiotics

1. Introduction

The importance of endoperoxides is well known as they possess significant biological properties.[1,2] Certain natural compounds, which possess endoperoxide groups such as Artemisinin and Artellene, represent a promising new class of antimalarial drugs.[1,3] Several biologically active cyclic peroxyketals have been isolated from marine sponges, some of which have antitumour activities (e.g., Xestin A and B).[4–6] Snider and Shi first realized the total synthesis of antitumour cyclic peroxyketals related to xestin A and B[7] and chondrillin, and plakorin[8] by using rose bengal as a sensitizer and a sun lamp (Scheme 1). A similar procedure has been used for the asymmetric total synthesis of chondrillin and plakorin using singlet oxygenation/radical rearrangements,[9,10] and for the preparation of an antimalarially active cyclic peroxyketal.[11] During the total synthesis of chondrillin and plakorin, the hemiketal hydroxyl group was easily methylated using the glycosylation conditions (catalytic amount of TsOH in MeOH for



Scheme 1.

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40 h at room temperature), which indicated that chemical behaviour of this group is similar to the anomeric hydroxyl of free sugars (Scheme 1).[8]

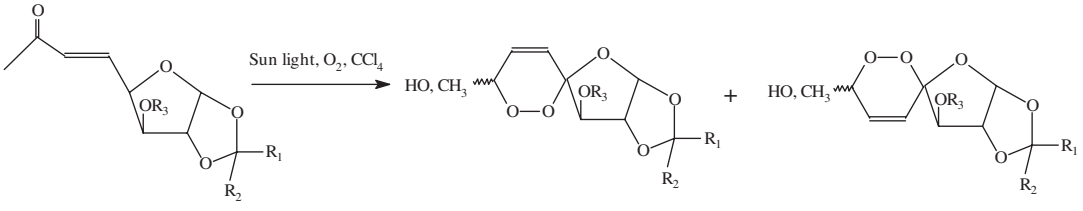
Useful reviews on photooxidations and the formation of endoperoxides have recently been published.[12,13]

Compounds with spiroketal groups are also important, since they are found in some biologically active molecules. For example, polyether antibiotics such as salinomycin and narasin contain spiroketal rings.[14,15]

2. Results and discussion

In the light of the foregoing results, we were prompted to prepare carbohydrate based compounds having such peroxyhemiketal groups, with a view to obtain biologically active substances. The furanose ring substituted enones (compounds **1a**–**e**) were considered to be suitable compounds for light-mediated oxygenations to prepare new spiro-endoperoxides (compounds **2a**–**e** and **3a**–**e**) (Scheme 2). The targeted compounds would have the benefits of possessing both endoperoxide and spiroketal moieties, and thus they might show some biological activities. Further, they could also be converted to new sugar derivatives, which otherwise would be difficult to synthesize. For example, deoxygenation of the peroxide group could lead to new spirodifuranose derivatives. During the preparation of the starting compounds **1a**–**e**,[16] we noticed some minor chemical changes in their solutions under day light. We therefore decided to investigate the photochemical behaviour of these compounds in the absence of sensitizers. Sunlight-mediated oxygenation of **1a**–**e** was carried out by exposing dilute (0.1%) carbon tetrachloride solutions to sunlight (receiving a direct sunshine for approximately 4 h a day) for about 20–40 days, with occasional shaking of the flask to dissolve some air (continuous introduction of air produced similar results). Irradiation of the solutions with a sodium light (400 W) gave similar results but at a slower rate. Preliminary experiments were carried out using several different solvents, and carbon tetrachloride being a good solvent for oxygen was found to be the most suitable. Our search is continuing for suitable sensitizers and less toxic solvents. Use of rose bengal as a sensitizer in carbon tetrachloride did not increase the reaction rate significantly. Acetone as a triplet sensitizer[13] was a good candidate and indeed gave a similar reaction but with additional products. Progress of the reactions was monitored by TLC (8.5:1.5 light petroleum–butanol and/or 2:1:1 toluene–AcOEt–hexane). ^{1}H NMR spectrum of the crude photo-oxygenation product from **1a** indicated the presence of four stereoisomers, which were fractionated on a silica gel column to give two fractions of 4*R* (**2a**) and 4*S* (**3a**) (eluted first) isomers. Both isomers were isolated as a mixture of C-7 anomers. Several attempts for efficient separation of C-7 anomers failed. However, a pure component of the 4*R* isomer (**2a)** was crystallized (11%) from ethyl acetate–petroleum ether as the major stereoisomer. NOESY spectra correlations were used for the differentiation of the 4*R* and 4*S* configurations. Monitoring the above reaction by TLC clearly indicated formation of an intermediate product during the early stages of the reaction, which had similar R_f value as the cis isomer of the starting compound. A similar intermediate product was actually isolated in the reaction of **1e** and shown to be the cis isomer. Starting compounds and their cis isomers almost disappeared at the end of the reaction and only the isolated 4,7-epidioxy derivatives were observed (TLC).

The structural evidence for the endoperoxides was obtained by ^{1}H and ^{13}C NMR, NOESY, EI-MS, APCI-MS and C, H analysis. Most of the signals of the major and minor stereoisomers are well resolved in their ^{1}H and ^{13}C NMR spectra. The ^{1}H signals of the diastereo-



1a $R_1 = R_2 = CH_3$; R_3 = Ac
1b $R_1 = CCl_3$; R_2 = H; R_3 = Ac
1c $R_1 = CCl_3$; R_2 = H; R_3 = Me
1d R_1 = H; $R_2 = CCl_3$; R_3 = Ac
1e R_1 = H; $R_2 = CCl_3$; R_3 = Me

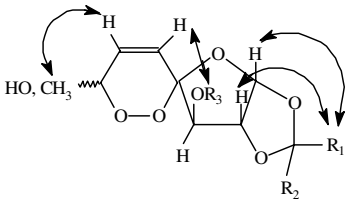
2a (40%)
2b (64%)
2c (69%)**
2d *
2e *

3a (30%)
3b*
3c *
3d (55%)
3e (80%)**

* Not isolated in a reasonable purity
** Single diastereoisomer

Scheme 2.

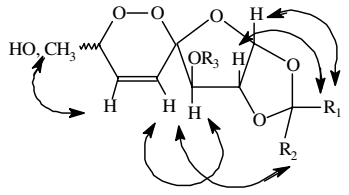
isomeric pairs (epimeric at C-7) were almost identical in respect of the coupling constants but only the ratio of the signals and the chemical shift values was different. There were a few overlapping signals, but this did not mask the general pattern of the signals of the major anomers. Similarities of the spectra of the C-7 anomers did not permit differentiation of the configurations of C-7.



Characteristic NOESY correlations of the 4*R* isomers

In the NOESY spectra of the 4*S* isomer (**3a**), and its acetyl derivative, correlations between H-3, H-5 and the *endo* isopropylidene methyl group were observed. Cross-peaks were observed for both the major and the minor C-7 anomers. The NOESY spectra of the 4*R* isomer (**2a**) and its acetyl derivative did not show a correlation between H-3 and H-5, indicating that these protons are not in a cis arrangement.

A NOESY correlation was observed between H-5 and the acetyl group on C-3 for the acetyl derivative of **2a** (4*R* configuration); however, this was not present in the NOESY spectrum of the acetyl derivative of **3a** (4*S* configuration).



Characteristic NOESY correlations of the 4*S* isomers

The coupling constants for the double bond protons ($J_{5,6}$) were ~10.0 Hz for all the epidioxy derivatives, indicating that the double bond is part of a six membered ring.[4] The observed coupling constants, $J_{1,2} \sim 4$ Hz, $J_{2,3} \sim 2$ Hz for **3a** and $J_{1,2} \sim 4$ Hz, $J_{2,3} \sim 0$ Hz for **2a**, are typical for furanose rings. ^{13}C NMR (DEPT) spectra provided further evidence for the structures of the products and indicated the presence of tertiary carbons (Table 1).

Further corroborating evidence was provided by the mass spectra. EI-mass spectra of **2a** and **3a** were almost identical except for the intensities of the peaks. The mass spectra: *m*/*z* (fragment, % (**3a**), % (**2a**)): *m*/*z* 287 (M^+-CH_3, 15, 50), 271 [(M^++1)$-O_2$, 3, 6], 270 (M^+-O_2, 12, 18), 269 [(M^+-CH_3)$-H_2O$] or [(M^+-O_2)−H, 15, 50], 245 [(M^++1)−acetone, 10, 25], 210 (270-AcOH, 75, 39), 185 (15, 10), 181 (45, 18), 167 (10, 10), 153 (20, 15), 141 (30, 12), 129 (60, 27), 113 (43, 21), 85 (100, 57), 59 (80, 100). When the intensity of the peak at *m*/*z* 287 was increased to 100%, a small M^++1 peak at *m*/*z* 303 was detected. In the mass spectra of the acetyl derivative of **2a** and **3a**, characteristic peaks at *m*/*z* 329 (M^+-CH_3), 311 [(M^+-O_2)−H, 6%], 312 (M^+-O_2, 6%), 269 (312-acetyl, 58%), 286 (M^+−acetone), 227 ($M^+-CH_3-Ac-OAc$, 12%) 226 (269-Ac, 12%), 210 (312-OAc−Ac, 15%), 184 (42%), 167 (12%), 142 (37%), 112 (62%), 97 (90%), 43 (100%) were found with similar intensities.

Photooxygenation of the compound **1b** also gave a diastereoisomeric mixture of the corresponding 4,7-epidioxy derivatives, differing at the configurations on C-4 and C-7. ^1H NMR spectrum of the crude reaction mixture indicated a mixture of three stereoisomers, in a ratio of 70:22:8. The fourth isomer was only vaguely detectable. The diastereoisomers were fractionated on a silica gel column as for the isopropylidene derivatives, to give two fractions. The first fraction contained a mixture of minor isomers and the second one contained the syrupy 4*R* isomer (**2b**). This product was crystallized from carbon tetrachloride (mp 121–126 °C) to give the main diastereoisomer, which still contained approximately 10% of C-7 epimer. Further crystallizations did not improve the purity.

No correlation between H-3 and H-5 was observed in the NOESY spectrum of the 4*R* isomer confirming the assigned configuration.

EI-MS spectrum of **2b** showed a small M^++1 peak at *m*/*z* 391 and a small M^+-H_2O at *m*/*z* 373. Major peaks were: M^+-O_2 at *m*/*z* 358–360–362 (a three chlorine isotopic pattern) 60%, [(M^+−1)]$-O_2$ or [(M^+-H_2O)$-CH_3$] at *m*/*z* 357–359–361 (a three chlorine isotopic pattern) 60%, [(M^+-O_2)−AcOH] at *m*/*z* 298–300–302 (a three chlorine isotopic pattern) 35%, {[(M^+−1)]$-O_2$}−AcOH at *m*/*z* 297–299–301 (a three chlorine isotopic pattern) 35%, and a base peak at *m*/*z* 167.

Photooxygenations of both **1d** and **1e** under similar conditions gave the 4*S* isomers (**3d**) and (**3e**), respectively, as the main products. Compound **3d** contained approximately 10% of its C-7 epimer (NMR), whereas **3e** was obtained as pure single stereoisomer in 80% yield. NOESY spectra of **3d** and **3e** indicated cross-peaks between H-3 and H-5, which show that the double bond is *endo* to the condensed ring system. In all other 4,7-epidioxy derivatives, the main diastereoisomers contain the peroxide groups at the *endo* position (4*R* configuration). Dipolar repulsions between the *endo* trichloromethyl group and the *endo* peroxide group may cause instability and hence the stereoisomer with the *endo* peroxide group does not form as the main product in this case. Models indicate that this assumption may be possible when the furanose ring has the $^3T_2$ conformation.

Table 1. ^{1}H NMR (400 MHz) chemical shifts (δ ppm) and $J_{H,H}$ values (Hz) in $CDCl_3$, for epidioxy derivatives

Compd	H-1	$J_{1,2}$	H-2	$J_{2,3}$	H-3	H-5	$J_{5,6}$	H-6	H-CCl_3	OAc	Me C-7	CH_3 isopropyl *endo–exo*	OMe
3a	6.03d	3.6	4.73dd	1.7	5.18d	5.89d	9.90	6.06d		2.10	1.42	1.55–1.38	
3a[a]	5.98d	3.7	4.76dd	2.2	5.30d	5.84d	10.0	6.00d		2.08	1.38	1.55–1.46	
2a	6.06d	4.0	4.60d	0.0	5.16s	5.72d	10.0	6.12d		2.14	1.47	1.65–1.31	
2a[a]	6.07d	4.1	4.64d	0.0	5.67s	5.76d	10.0	6.01d		2.07	1.42	1.62–1.30	
3a(Ac)	6.05d	4.0	4.80dd	2.9	5.30d	5.99d	9.90	6.51d		2.11–2.04	1.70	1.59–1.43	
3a(Ac)[a]	6.05d	4.0	4.66dd	2.2	5.39d	5.95d	10.0	6.52d		2.15–2.10	1.59	1.55–1.34	
2a(Ac)	6.07d	4.0	4.80d	0.0	5.17s	5.88d	9.90	6.47d		2.12–2.08	1.71	1.68–1.42	
2a(Ac)[a]	6.11d	4.0	4.55d	0.0	5.76s	5.81d	10.0	6.61d		2.15–2.08	1.68	1.66–1.33	
2b	6.18d	4.2	4.76d	0.0	5.33s	5.56d	10.0	6.06d	5.66s	2.00	1.35		
2b[a]	6.19d	4.2	4.80d	0.0	5.65s	5.93d	10.0		5.64s	2.19	1.53		
3d	6.14d	4.0	5.05dd	2.3	5.40d	5.92d	9.90	6.03d	5.55s	2.09	1.38		
2c	6.27d	4.3	4.90d	0.0	3.73s	6.00d	9.80	6.16d	5.73s		1.51		3.49
3e	6.14d	4.7	4.98dd	3.9	4.20d	5.83d	9.80	6.15d	5.62s		1.48		3.47

(Ac): 7-*O*-Acetyl derivatives.
[a] Minor C-7 anomers.

Table 2. ^{13}C NMR chemical shifts (δ ppm) for the 1,2-*O*-isopropylidene protected epidioxy derivatives

	C-1	C-2, C-3	C-5, C-6	Tertiary carbons $C_{isopropylidene}$, C-4, C-7	C=O (Ac)	Me groups
3a	104.9	84.6, 80.6	125.2, 131.7	115.3, 102.0, 95.8	171.2	28.2, 27.5, 23.0, 20.9
3a[a]	105.1	84.7, 79.6	126.4, 133.3	115.5, 103.9, 97.1	170.1	28.2, 27.7, 23.1, 20.8
2a	107.2	83.9, 79.5	124.9, 133.9	115.1, 106.4, 95.7	169.5	27.6, 26.7, 23.1, 20.9
2a[a]	109.1	84.2, 78.7	125.2, 134.2	115.1, 107.7, 96.7	169.1	27.3, 26.8, 23.1, 21.1
3a(Ac)	104.6	84.6, 80.3	125.2, 129.1	115.7, 102.1, 100.4	169.5 (2C)	28.4, 27.9, 21.8, 21.6, 20.7
3a(Ac)[a]	105.6	84.8, 79.3	127.4, 129.4	115.7, 104.4, 101.0	169.5	28.3, 27.7, 22.1, 21.6, 21.0
2a(Ac)	107.3	83.8, 79.4	122.0, 130.4	115.3, 106.5, 100.6	169.1, 168.9	27.5, 26.8, 22.3, 21.5, 21.0
2a(Ac)[a]	108.0	84.2, 78.7	125.8, 130.7	115.3, 109.0, 101.6	—	27.3, 26.9, 22.2, 21.8, 20.3

(Ac): 7-*O*-Acetyl derivatives.
[a] Minor C-7 anomers.

Table 3. ^{13}C NMR chemical shifts (δ ppm) for the 1,2-*O*-trichloroethylidene protected epidioxy derivatives

	C-1, C_{HCCCl_3}	C-2, C-3	C-5, C-6	Tertiary carbons C-4, CCl_3, C-7	Ac (C=O)	OMe	Me groups
2b	107.6, 110.0	85.8, 78.4	120.4, 134.8	105.8, 99.4, 96.1	169.2		23.1, 20.9
2b[a]	105.3, 108.1	86.1, 79.9	123.7, 135.1	104.8, 99.3, 97.4	168.9		22.9, 20.9
3d	104.5, 111.5	87.1, 79.9	124.3, 131.8	103.5, 97.1, 95.7	170.9		22.8, 20.7
2c	107.7, 109.6	87.0, 84.3	121.8, 133.1	106.3, 99.3, 95.9		59.1	23.3
3e	104.3, 112.7	89.0, 87.2	123.4, 134.3	104.8; 97.8, 95.6		59.2	23.2

[a] Minor C-7 epimer.

The ^{1}H and ^{13}C spectra are consistent with the proposed structures and a negative polarity APCI MS spectra in methanol–chloroform produced ($M+Cl^-$) peaks at *m/z* 425, 427 (100%), 429, 431 (a four chlorine isotopic pattern), as the base peak group for **3d** and at *m/z* 397, 399 (100%), 401, 403 for **3e** (Tables 1–3).

Photooxygenation of the compound **1c** under similar conditions gave a crude product, which was directly crystallized from ethyl acetate–petroleum ether to give the pure 4,7-epidioxy derivative (69%) as a single stereoisomer. The ^{1}H and ^{13}C spectra were consistent with the structure (**2c**). The supernatant solution contained a mixture of C-7 anomers of **2c** in small amounts. Negative polarity APCI MS spectrum in methanol–chloroform produced ($M+Cl^-$) peaks at *m/z* 397, 399 (100%), 401, 403 (a four chlorine isotopic pattern), as the base peak group. The NOESY spectrum of this compound did not show any correlation between H-3 and H-5 but instead cross-peaks were observed between H-5 and the methoxyl group, which indicates that the pure stereoisomer has the peroxide group at the *endo* position and the double bond occupying the *exo* position (4*R* configuration).

3. Experimental

3.1. General methods

^{1}H (400 MHz) and ^{13}C NMR (100 MHz) and NOESY spectra were recorded on a Varian AS 400 instrument. Mass spectra were recorded on Micromass UK Plat-

form-II and on HP 6890 GC/MS. APCI mass spectra were recorded on Agilent 1100 (LS-MSD). Optical rotation measurements were carried out on a Schmidt–Haensch Polartronic E polarimeter. TLC and column chromatography were performed on precoated aluminium plates (Merck 5554) and silica gel G-60 (Merck 7734), respectively. All solvent removals were carried out under reduced pressure. Light petroleum refers to the fraction with bp 40–70 °C.

3.2. 3-*O*-Acetyl-5-(*E*)-eno-1,2-*O*-isopropylidene-5,6,8-trideoxy-α-D-*xylo*-1,4-furano-7-ulose (1a)

A solution of 1,2-*O*-isopropylidene-α-D-glucofuranose (10.0 g, 45.4 mmol) in methanol (150 mL) was mixed with a solution of sodium metaperiodate (12 g, 56.1 mmol) in water at room temperature. Crystallized salts were filtered after 3 h. Solution was neutralized with dilute $NaHCO_3$, and the solvent was removed at 50 °C. Solid residue (6.8 g) was dissolved in DMF (150 mL) and mixed with $PPh_3{=}CHCOCH_3$ (14.4 g, 45.3 mmol). The mixture was heated at 100 °C for 3 h. After removal of the solvent, the residue was dissolved in pyridine (75 mL) and Ac_2O (4.1 mL, 43.5 mmol) was added. The mixture was kept at room temperature for 24 h. Pyridine was removed and the remaining syrup was purified on a silica gel column (light petroleum–ethyl acetate, 10:1) to give as a first fraction a mixture of cis and trans isomers (1.5 g, 13%) and then pure trans isomer (5.0 g, 52%). The latter was crystallized from light petroleum, mp 74–75 °C, $[\alpha]_D^{25}$ 8.0 (*c* 0.77, CH_2Cl_2), ^1H NMR ($CDCl_3$): δ 6.63 (dd, 1H, $J_{5,6} = 16.0$, $J_{4,5} = 4.6$ Hz, H-5), 6.39 (dd, 1H, $J_{4,6} = 1.7$ Hz, H-6), 5.98 (d, $J_{1,2} = 3.7$ Hz, H-1), 5.28 (d, 1H, $J_{2,3} = 0$, $J_{3,4} = 3.1$ Hz, H-3), 4.95 (ddd, 1H, H-4), 4.59 (d, 1H, H-2), 2.24 (s, 3H, $COCH_3$), 2.01 (s, 3H, OAc), 1.51 and 1.33 (2 × s, CH_3-isopropylidene).

Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.95; H, 6.91.

3.3. (4*S*)-3-*O*-Acetyl-5-eno-4,7-epidioxy-1,2-*O*-isopropylidene-5,6,8-trideoxy-α-D-*threo*-1,4-furano-4,7-diulo-octose (3a)

Compound **1a** (1.0 g, 3.70 mmol) was dissolved in carbon tetrachloride (1 L) in a glass flask with a stopper. The solution was shaken vigorously and exposed to day light (receiving direct sunlight approximately 4 h a day) with occasional shaking to dissolve some air. Average room temperature was 30–35 °C. There was practically no unreacted material after 40 days. Two slower moving products were observed (TLC). The solvent was then removed and the syrupy residue was redissolved in chloroform. Some resinous material remained undissolved. The chloroform solution was concentrated and applied to a silica gel column, eluting with light petroleum–butanol (85:15). First fractions containing the faster moving (TLC) product were combined. The solvent was removed to obtain the title product as a syrup (0.35 g, 31%).

Anal. Calcd for $C_{13}H_{18}O_8$: C, 51.65; H, 6.00. Found: C, 51.47; H, 5.91.

This compound (0.1 g) was acetylated in pyridine with Ac_2O according to the usual procedure. The acetylated syrupy product was not further purified but its NMR spectra indicated complete acetylation.

3.4. (4*R*)-3-*O*-Acetyl-5-eno-4,7-epidioxy-1,2-*O*-isopropylidene-5,6,8-trideoxy-α-D-*threo*-1,4-furano-4,7-diulo-octose (2a)

Further fractions from the previous experiment contained the slower moving product (TLC). Removal of the solvent gave **2a** as a syrup (0.45 g, 40%). Crystallization of which gave one of the diastereoisomer of **2a** (11%), mp 139–140 °C, $[\alpha]_D^{19}$ −130.0 (*c* 0.06, $CHCl_3$).

Anal. Calcd for $C_{13}H_{18}O_8$: C, 51.65; H, 6.00. Found: C, 51.50; H, 5.94.

The syrupy **2a** (0.1 g) was acetylated in pyridine with Ac_2O according to the usual procedure. The acetylated syrupy product was not further purified but its NMR spectra indicated complete acetylation.

3.5. (4*R*)-3-*O*-Acetyl-5-eno-4,7-epidioxy-1,2-*O*-(*S*)-trichloroethylidene-5,6,8-trideoxy-α-D-*threo*-1,4-furano-4,7-diulo-octose (2b)

A solution of compound **1b** (1.0 g, 2.78 mmol) in carbon tetrachloride (1 L) was exposed to sunlight and isolated as described in the first experiment. After column chromatography, fractions containing mainly the faster moving product (TLC) combined to give the mixture of isomers (0.1 g). Fractions containing the slower moving main product gave the title compound (0.7 g, 64%) as a syrup after the removal of the solvent.

Anal. Calcd for $C_{12}H_{13}Cl_3O_8$: C, 36.81; H, 3.35. Found: C, 36.78; H, 3.45.

A portion of the above syrupy product was crystallized from carbon tetrachloride yielding the main stereoisomer contaminated with a small amount of C-7 epimer. Mp 121–126 °C.

3.6. (4*S*)-3-*O*-Acetyl-5-eno-4,7-epidioxy-1,2-*O*-(*R*)-trichloroethylidene-5,6,8-trideoxy-α-D-*threo*-1,4-furano-4,7-diulo-octose (3d)

Compound **1d** (1.0 g, 2.78 mmol) in carbon tetrachloride solution (1 L) was exposed to sunlight and isolated as described in the first experiment. TLC indicated practically a single product. (A very small amount of a slower moving product was detectable.) The title product was

obtained as a syrup (0.6 g, 55%) after column chromatography.

Anal. Calcd for $C_{12}H_{13}Cl_3O_8$: C, 36.81; H, 3.35. Found: C, 36.75; H, 3.30.

3.7. 5,6-*O*-Isopropylidene-1,2-*O*-(*S*)-trichloroethylidene-α-D-glucofuranose

A solution of 1,2-*O*-(*S*)-trichloroethylidene-α-D-glucofuranose (β-chloralose) (5 g, 16.2 mmol), 2,2-dimethoxypropane (4 mL, 32.4 mmol) and PTSA (5 mg) in DMF (50 mL) was stirred for 24 h at room temperature. The mixture was neutralized with 5% solution of $NaHCO_3$ and the solvent was removed. The syrupy residue was crystallized from methanol (4.5 g, 80%), mp 188–189 °C, $[\alpha]_D^{19}$ −12.0 (*c* 0.96, MeOH). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 6.20 (d, 1H, $J_{1,2} = 3.9$ Hz, H-1), 5.87 (s, 1H, $HCCCl_3$), 5.53 (br s, 1H, OH), 4.70 (d, 1H, H-2), 4.23 (ddd, 1H, H-5), 4.08 (br d, 1H, $J_{3,4} = 6.6$ Hz, H-3), 4.04 (dd, 1H, $J_{4,5} = 2.7$ Hz, H-4), 3.98 (dd, 1H, $J_{6a,6b} = 9.5$, $J_{5,6a} = 6.5$ Hz, H-6a), 3.82 (dd, 1H, $J_{5,6b} = 5.9$ Hz, H-6b), 1.33 (s, 3H, CH_3-isopropylidene), 1.2 (s, 3H, CH_3-isopropylidene).

Anal. Calcd for $C_{11}H_{15}Cl_3O_6$: C, 37.79; H, 4.32. Found: C, 37.82; H, 4.05.

3.8. 5,6-*O*-Isopropylidene-3-*O*-methyl-1,2-*O*-(*S*)-trichloroethylidene-α-D-glucofuranose

To a solution of 5,6-*O*-isopropylidene-1,2-*O*-(*S*)-trichloroethylidene-α-D-glucofuranose (5 g, 14.3 mmol) in DMF (50 mL) were added methyl iodide (1.78 mL, 28.6 mmol) and BaO (4.4 g). The mixture was stirred for 24 h at room temperature. The salts were filtered and washed with dichloromethane and the filtrate and the washings were combined and evaporated at 50 °C. The residue was taken into dichloromethane, decolourized with sodium thiosulfate solution, washed with water and then dried. The removal of the solvent gave a white cystalline solid (4.8 g, 92%), mp 130–132 °C, $[\alpha]_D^{19}$ −37.3 (*c* 1.00, chloroform). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.15 (d, 1H, $J_{1,2} = 3.9$ Hz, H-1), 5.58 (s, 1H, $HCCCl_3$), 4.89 (d, 1H, H-2), 4.27 (ddd, 1H, H-5), 4.07 (dd, 1H, $J_{6a,6b} = 9.0$, $J_{5,6a} = 6.2$ Hz, H-6a), 4.01–3.97 (m, 2H, H-4 and H-6b), 3.84 (d, $J_{3,4} = 2.7$ Hz, H-3), 3.48 (s, 3H, OCH_3), 1.43 (s, 3H, CH_3-isopropylidene), 1.34 (s, 3H, CH_3-isopropylidene).

Anal. Calcd for $C_{12}H_{17}Cl_3O_6$: C, 39.64; H, 4.71. Found: C, 39.50, H, 4.65.

3.9. 3-*O*-Methyl-1,2-*O*-(*S*)-trichloroethylidene-α-D-glucofuranose (3-*O*-Methyl-β-chloralose)

5,6-*O*-Isopropylidene-3-*O*-methyl derivative from the previous experiment (5 g, 13.8 mmol) was mixed with methanol (200 mL), water (20 mL) and concd HCl (three drops). Complete dissolution occurred as the hydrolysis progressed. Hydrolysis was monitored by TLC (toluene–methanol, 9:1). Most of the methanol was removed after neutralization with $NaHCO_3$ and the aqueous residue was extracted with dichloromethane (4 × 25 mL). Dried solution was concentrated and light petroleum was added until slight cloudiness affording white crystals (4 g, 90%), mp 121–122 °C, $[\alpha]_D^{19}$ −40.7 (*c* 0.5, $CHCl_3$).

Anal. Calcd for $C_9H_{13}Cl_3O_6$: C, 33.41; H, 4.05. Found: C, 33.45; H, 4.20.

3.10. 3-*O*-Methyl-1,2-*O*-(*S*)-trichloroethylidene-α-D-*xylo*-1,4-furanodialdose

A solution of the 3-*O*-methyl ether (5 g, 15.4 mmol) from the previous experiment in methanol (50 mL) was mixed with a solution of sodium metaperiodate (3.97 g, 18.5 mmol) and kept at room temperature for three hours. Usual working up procedure gave the crude title product (3.15 g) (NMR). Crystallization from chloroform–petroleum ether gave a crystalline product in the free aldehyde form (2 g, 44%), mp 76–78 °C, $[\alpha]_D^{19}$ −34.0 (*c* 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.60 (d, H-5), 6.39 (d, 1H, $J_{1,2} = 3.5$ Hz, H-1), 5.57 (s, 1H, $HCCCl_3$), 4.97 (d, 1H, $J_{2,3} = 0.0$ Hz H-2), 4.45 (dd, 1H, $J_{4,5} = 1.5$ Hz, H-4) 4.17 (d, $J_{3,4} = 3.9$ Hz, H-3).

3.11. 5-(*E*)-Eno-3-*O*-methyl-1,2-*O*-(*S*)-trichloroethylidene-5,6,8-trideoxy-α-D-*xylo*-1,4-furano-7-ulose (1c)

A solution of aldehyde (from the previous experiment) (5 g, 17.2 mmol) in THF (125 mL) was mixed with $PPh_3{=}CHCOCH_3$ (8.2 g, 25.7 mmol) and the mixture was refluxed for 4 h. The mixture was filtered and the solvent was removed. The remaining syrup was purified on a silica gel column, eluting with light petroleum–ethyl acetate (10:1). A mixture of cis and trans isomers was first collected. Later fractions contained the pure trans isomer which crystallized from the eluting solvent. Recrystallization from the same solvent gave pure **4** (3.7 g, 65%), mp 103–105 °C, $[\alpha]_D^{24}$ −57.7 (*c* 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.74 (dd, 1H, $J_{5,6} = 16.0$, $J_{4,5} = 5.5$ Hz, H-5), 6.39 (dd, 1H, $J_{4,6} = 1.5$ Hz, H-6), 6.28 (d, 1H, $J_{1,2} = 3.9$ Hz, H-1), 5.63 (s, 1H, $HCCCl_3$), 4.99 (d, 1H, H-2), 4.75 (ddd, 1H, H-4), 3.88 (d, 1H, $J_{3,4} = 3.5$ Hz, H-3), 3.41 (s, 3H, OMe).

Anal. Calcd for $C_{11}H_{13}Cl_3O_5$: C, 39.85; H, 3.95. Found: C, 39.78; H, 3.53.

3.12. (4*R*)-5-Eno-4,7-epidioxy-3-*O*-methyl-1,2-*O*-(*S*)-trichloroethylidene-5,6,8-trideoxy-α-D-*threo*-1,4-furano-4,7-diulo-octose (2c)

A solution of compound **1c** (1.0 g, 3.02 mmol) in carbon tetrachloride (1.0 L) was exposed to sunlight as de-

scribed in the first experiment. Carbon tetrachloride was removed. The syrupy residue was dissolved in light petroleum and ethyl acetate was added until cloudiness and kept in the refrigerator to give the crystals of the title compound (0.76 g, 69%), mp 127–130 °C. $[\alpha]_D^{19}$ −115.0 (*c* 0.64, $CHCl_3$).

Anal. Calcd for $C_{11}H_{13}Cl_3O_7$: C, 36.34; H, 3.60. Found: C, 36.31; H, 3.53.

3.13. 5-(*E*)-Eno-3-*O*-methyl-1,2-*O*-(*R*)-trichloroethylidene-5,6,8-trideoxy-α-D-*xylo*-1,4-furano-7-ulose (1e)

3-*O*-Methyl-1,2-*O*-(*R*)-trichloroethylidene-α-D-*xylo*-pentadialdose[17] (5 g, 17.2 mmol) was reacted with PPh_3=CH-$COCH_3$ (8.2 g, 25.7 mmol) as in Experiment 3.11 (except the reflux time was 6 h). Compound **1e** was obtained in crystalline form (3.7 g, 65%), mp 111–113 °C, $[\alpha]_D^{19}$ −22.5 (*c* 0.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 6.74 (dd, 1H, $J_{5,6} = 16.0$, $J_{4,5} = 5.0$ Hz, H-5), 6.39 (dd, 1H, $J_{4,6} = 1.5$ Hz, H-6), 6.15 (d, 1H, $J_{1,2} = 3.9$ Hz, H-1), 5.32 (s, 1H, $HCCCl_3$), 4.79 (d, 1H, H-2), 5.20 (ddd, 1H, H-4), 3.99 (d, 1H, $J_{3,4} = 3.1$ Hz, H-3), 3.40 (s, 3H, OMe), 2.27 (s, 3H, $COCH_3$).

Anal. Calcd for $C_{11}H_{13}Cl_3O_5$: C, 39.85; H, 3.95. Found: C, 40.11; H, 3.88.

3.14. (4*S*)-5-Eno-4,7-epidioxy-3-*O*-methyl-1,2-*O*-(*R*)-trichloroethylidene-5,6,8-trideoxy-α-D-*threo*-1,4-furano-4,7-diulo-octose (3e)

A solution of compound **1e** (1.0 g, 3.02 mmol) in carbon tetrachloride (1.0 L) was exposed to sunlight as described in the first experiment. Carbon tetrachloride was removed to give a syrup (0.88 g, 80%). NMR spectrum of which indicated the presence of almost pure title compound as a single stereoisomer. This was crystallized from chloroform solution added hexane until cloudiness, mp 105–106 °C, $[\alpha]_D^{19}$ (*c* 0.64, $CHCl_3$).

Anal. Calcd for $C_{11}H_{13}Cl_3O_7$: C, 36.34; H, 3.60. Found: C, 36,08; H, 3.48.

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