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SYNTHESIS AND THERMAL CHEMISTRY OF ISOLEVOGLUCOSENONE

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ABSTRACT

Isolevoglucosenone (1,6-anhydro-2,3-dideoxy-β-D-*glycero*-hex-2-enopyranos-4-ulose, **3**) has been synthesized from levoglucosenone (**2**) in six steps. Thus, 1,6-anhydro-4-*O*-benzyl-3-deoxy-β-D-*erythro*-hexopyranos-2-ulose, obtained by Michael addition of benzyl alcohol to **2**, was reduced with sodium borohydride to yield a separable mixture of the C-2 epimeric alcohols 1,6-anhydro-4-*O*-benzyl-3-deoxy-β-D-*arabino*- and -*ribo*-hexopyranose, both of which displayed intramolecular hydrogen-bonding. Acetylation, hydrogenolytic debenzylation, and pyridinium chlorochromate oxidation then led to the 2-*O*-acetyl-1,6-anhydro-hexos-4-uloses, from which **3** was obtained by tetraethylammonium acetate-catalyzed β-elimination of acetic acid. On sealed-tube thermolysis in the range of 210–260°, **3** generated 3-oxidopyrylium by loss of formaldehyde; this ylide was efficiently trapped by unreacted **3**, to yield the $[4_\pi + 2_\pi]$-1,3-dipolar cycloadducts **14** and **15**. The structure of **14** was fully elucidated by an X-ray crystallographic study. Neither **3** was, nor the adducts **14** and **15** were, detected among the products from acid-catalyzed pyrolysis of cellulose.

INTRODUCTION

Controlled pyrolysis of biomass is a method of considerable potential for the production of useful chemical compounds. For this reason, the pyrolysis of cellulose has been extensively investigated[1]. In the absence of a catalyst, cellulose depolymerizes by intramolecular transglycosylation, to give levoglucosan (1,6-anhydro-β-D-glucopyranose, **1**) as the major product in up to 60% yield[2]. In the presence of such protonic acid catalysts as phosphoric acid, however, there is an increased production of char, water, and non-condensing gases, and, at atmo-

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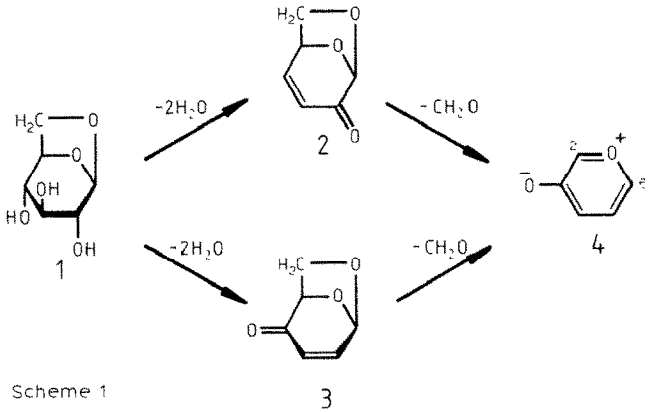
spheric pressure, the major component of the tarry pyrolyzate is[3–5] levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose, **2**); it is obtained from cellulose in yields of 2–12%, depending upon the scale of operation, and arises, at least formally, by double dehydration of levoglucosan (**1**) (see Scheme 1).



Scheme 1

An alternative double dehydration of **1**, involving loss of the 2-hydroxyl group, should lead to the isomeric 1,6-anhydro-2,3-dideoxy-β-D-*glycero*-hex-2-enopyranos-4-ulose (**3**), for which the trivial name "isolevoglucosenone" has been proposed[6].

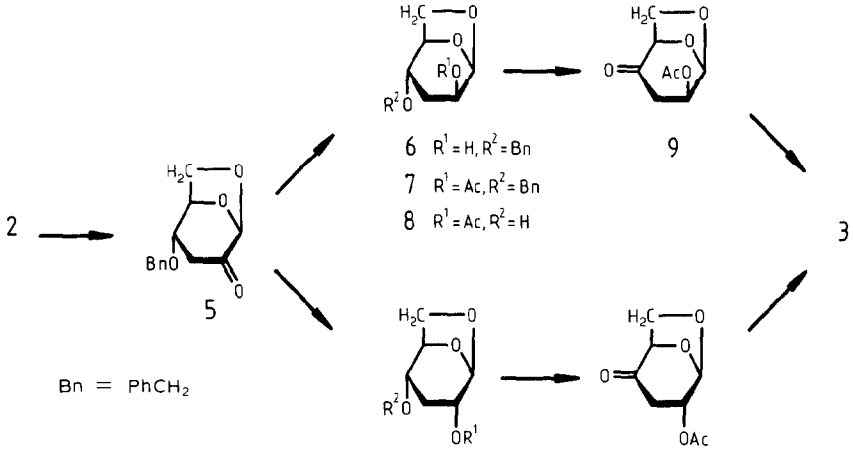
Köll and co-workers[7] reported two six-step, chemical syntheses of **3**, from **1** and from 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose, respectively, and Achmatowicz and co-workers[8] encountered the racemic analog of **3** as a byproduct in the glycosidation of the furan-derived 2,3-dideoxy-DL-hex-2-enopyranos-4-ulose. The German workers[7], with authentic material in hand, examined, by t.l.c. and ^{1}H-n.m.r. spectroscopy, the dichloromethane extract of a tar obtained by vacuum pyrolysis of a cellulose–sodium dihydrogenphosphate mixture for the presence of **3**, but could not detect any.

For several reasons, we chose to re-examine the possible pyrolytic production of isolevoglucosenone **3** from cellulose. We had shown[4] that higher yields of **2** can be obtained by phosphoric acid-catalyzed pyrolysis of cellulose under a flow of nitrogen at atmospheric pressure, rather than under vacuum. Also, we had shown[9] that **2** undergoes pyrolytic loss of formaldehyde under the conditions of its synthesis, to generate 3-oxidopyrylium (**4**) (see Scheme 1), and we isolated a variety of dimers and adducts resulting from the *in situ* condensation of ylide **4** with itself and with **2**, respectively. Hence, it is possible that, even if **3** is formed, it may not survive under pyrolytic conditions, but may undergo subsequent transformations into other compounds having structures characteristic of their origin.

To examine these possibilities further, we therefore synthesized **3** by a new route, examined acid-catalyzed cellulose pyrolyzates for its presence, and determined its thermal chemistry.

RESULTS AND DISCUSSION

Synthesis of isolevoglucosenone (**3**). — The route outlined in Scheme 2 was used, starting from levoglucosenone (**2**), which was readily available from the acid-catalyzed pyrolysis of waste paper[3].



Scheme 2

1,6-Anhydro-4-*O*-benzyl-3-deoxy-D-*erythro*-hexopyranos-2-ulose (**5**) was formed essentially quantitatively (t.l.c. evidence) by Michael addition of benzyl alcohol to **2**, using potassium benzoxide in benzyl alcohol, and it was isolated in 79% yield. Its ^{1}H- (Tables I and II) and ^{13}C-n.m.r. chemical-shifts were similar to those of the analogous products resulting[3,10] from addition of water or methanol to **2**. In particular, the configuration at C-4 in **5** could be determined from its ^{1}H-n.m.r. spectrum, in which 3,4-couplings of 5.6 and 1.2 Hz were observed, consistent with vicinal *ea* and *ee*-coupling, respectively, on a 1,6-anhydro-hexopyranose ring[11]. Addition of the benzyloxy group to **2** had thus occurred from "below" the plane of the pyranose ring, *i.e.*, on the side opposite to the 1,6-anhydro bridge, to yield the *erythro* product **5**.

When the preparation of **5** was conducted in relatively less benzyl alcohol, for a longer period of time, or in the presence of a greater concentration of potassium benzoxide, products resulting from the base-catalyzed oligomerization[10] of **2** were detected by t.l.c., and, in one case, the dimer described in ref. 10 was isolated, and characterized by ^{1}H-n.m.r. spectroscopy. It is interesting, however, that in no such experiment was there any evidence for the formation of the C-4 epimer of compound **5**.

TABLE I

^{1}H-N M R DATA[a] FOR COMPOUNDS **5–8** AND **10–12**

Compound	Chemical shift (δ) and multiplicity								
	H-1	*H-2*	*H-3a*	*H-3e*	*H-4*	*H-5*	*H-6*$_{endo}$	*H-6*$_{exo}$	*Other*
5[b]	5 07 br s	—	2 63 dd	2 44 dddd	3 78 ddd[d]	4 64 dddd	3 71 dd[d]	3 77 dd[d]	7 2–7 4 m, Ph, 4 47 s, PhCH_2
6	5 35 s	3 5–3 9 m[d]	1 51 ddd	2 21 br dd	3 4–3 5 m	4 5–4 6 m[e]	—3 5–3 9 m[d]—		7 2–7 4 m, Ph, 4 5–4 6 m, PhCH_2[e], 2 28 d, OH
7	5 44 br s	4 99 ddd	1 72 ddd	2 1–2 4 m	3 4–3 6 m	4 5–4 65 m[d]	—3 7–3 9 m—		7 2–7 4 m, Ph, 4 5–4 65 m, PhCH_2[d], 2 06 s, OAc
8	5 44 br s	5 00 ddd	1 83 ddd	2 0–2 3 m	3 8–4 0 m[d]	4 53 m	—3 8–4 0 m[d]—		3 54 br s, OH, 2 08 s, OAc
10[f]	5 40 d	3 56 dq	—1 98 m—		3 46 q	4 6–4 7 m[d]	3 75 dd	3 83 dd	7 3–7 4 m, Ph, 4 6–4 7 m[d], PhCH_2, 3 02 d, OH
11	5 44 br s	4 4–4 7 m[d]	—1 95–2 1 m—		3 33 m	4 4–4 7 m[d]	—3 65–3 9 m—		7 2–7 4 m, Ph, 4 4–4 7 m, PhCH_2[d], 2 12 s, OAc
12	5 43 br s	4 69 m	2 05–2 35 m	1 83 dm	3 64 m	4 55 m	—3.75–3 95 m—		2 91 br s, OH, 2 13 s, OAc

[a]At 90 MHz, unless specified otherwise. [b]At 200 MHz [c]$W_{1/2}$ = 1.2 Hz. [d,e]Denotes spectral overlap. [f]At 360 MHz.

TABLE II

^{1}H-N M R COUPLING-CONSTANTS[a] FOR COMPOUNDS **5–8** AND **10–12**

Compound	Coupling constants (Hz)										
	$J_{1,2}$	$J_{2,3a}$	$J_{2,3e}$	$J_{3a,4}$	$J_{3e,4}$	$J_{3a,3e}$	$J_{4,5}$	$J_{5,6endo}$	$J_{5,6exo}$	$J_{6,6}$	*Other*
5[b]				5.6	1.2	17.1	1 8	1 7	5.1	8.0	$J_{1,3e}$ ~1.0, $J_{3e,5}$ 2.2
6	0	10.3	6.1	4.4	small	14.2					$J_{2,OH}$ 9.1
7	1.3	10 6	6 1	4.2	small	13.9					
8	1.7	10.5	3.2	~4	small	14					
10[c]	2.4	5.9	<1.5	~4.5	<1.5	[d]	2.8	0.8	5.4	7.7	$J_{2,OH}$ 12.1
11	small										
12	small					16.0					

[a]90 MHz [b]200 MHz. [c]360 MHz [d]A value of 17 Hz was assumed for the computer-simulation.

Ketone **5** could be reduced with sodium borohydride *in situ, i.e.,* in benzyl alcohol solution without prior isolation, or in aqueous solution after isolation. By either treatment, a mixture of the D-*arabino*- and D-*ribo*-alcohols **6** and **10** was obtained in high yield, in the ratio of 11:9 (as judged by ^{1}H-n.m.r. spectroscopy). Samples of each epimer were isolated crystalline following chromatographic separation, and they were acetylated to give the crystalline monoacetates **7** and **11** respectively.

The D-*arabino* configuration was readily assigned to compounds **6** and **7** on the basis of their ^{1}H-n.m.r. data (see Tables I and II); they displayed 2,3-coupling constants of >10 and 6 Hz, consistent with *aa*- and *ae*-coupling, respectively[11]. These contrast with the 3,4-coupling constants of ≤4.4 Hz and near zero for the same molecules, attributable to *ae*- and *ee*-coupling, respectively.

Whereas the configuration in **10** and **11** could be assumed to be D-*ribo* by elimination, few supportive data could be extracted from a first-order analysis of their ^{1}H-n.m.r. spectra owing to the overlap of signals, especially the two H-3 resonances. Computer simulation of the 360-MHz, ^{1}H-n.m.r. spectrum of **10**, however, provided the coupling data shown in Table II. Compound **10** was thus confirmed to have the D-*ribo* configuration, as the 2,3- and 3,4-couplings obtained were consistent with *ae*- and *ee*-aligned protons; the pyranose conformation was seen to be $^1C_4$ from the absence of vicinal ring-proton coupling >6 Hz (larger coupling would be predicted for a boat conformation considered to be present in certain 2,4-disubstituted derivatives of levoglucosan[11]).

The 2-hydroxyl groups in both epimers **6** and **10** were involved in intramolecular hydrogen-bonding. The i.r. spectra of **6** and **10** in dilute carbon tetrachloride solution respectively displayed hydroxyl absorptions of 3590 and 3560 cm^{-1} that were shifted to lower frequency by ~35 and 65 cm^{-1}, respectively, relative to the position characteristic of a free hydroxyl group, and the ^{1}H-n.m.r. H-2,OH-couplings of 9.1 and 12.1 Hz, respectively, indicated dihedral angles approaching[12] 180°. The 2-hydroxyl group in **6** is thus bonded to the oxygen atom of the 1,6-anhydro bridge, whereas that in **10** is involved in a stronger, bifurcated hydrogen-bond with both O-4 and O-5, analogous to that proposed for the 2-hydroxyl group in 1,6-anhydro-4-*O*-benzyl-β-D-glucopyranose[13]. Stronger intramolecular hydrogen-bonding in **10** than in its C-2 epimer **6** is consistent with the considerably lessened polarity of **10**, and hence, the ease with which these two compounds could be separated chromatographically.

The selectivity found here in the borohydride reduction of the 4-*O*-benzyl-2-ulose **5**, to give the D-*arabino* (**6**) and D-*ribo* (**10**) compounds in the ratio of 11:9, is much lower than that observed in the reduction of its 4-hydroxy analog, where the D-*arabino* and D-*ribo* products were isolated[3], after acetylation, in yields of 71 and 15%, respectively.

Debenzylation of **7** by hydrogenolysis in the presence of palladium-on-charcoal proceeded satisfactorily to give **8**, but the analogous debenzylation of the epimer **11**, to give **12**, was slower, and there was occasionally a lag time of 10–40

min before hydrogen uptake began. We did not discover an explanation for this lag. These epimeric alcohols display intramolecular hydrogen-bonding, having i.r. stretching absorptions, in dilute carbon tetrachloride solution, for hydroxyl at 3595 (for **8**) and 3590 cm^{-1} (for **12**).

Oxidation of the alcohols **8** and **12** with the basic, dimethyl sulfoxide–pyridine–sulfur trioxide complex–triethylamine reagent[14] was expected to yield isolevoglucosenone (**3**) directly, by *in situ* β-elimination of acetic acid from the first-formed 4-uloses **9** and **13**. Although t.l.c. and n.m.r. evidence suggested that **3** was, in fact, formed as the sole product, we were able to isolate this volatile product from the reaction mixture in only low yields, despite our applying a variety of extraction, distillation, crystallization, and chromatography techniques in attempts to separate it from the accompanying dimethyl sulfoxide. A two-step, oxidation–elimination procedure proved more satisfactory. Thus, oxidation of **8** and of **12** with pyridinium chlorochromate[15] provided, in good yield, colorless syrups whose ^{1}H-n.m.r. spectra indicated that β-elimination had not taken place, and that were presumed to be **9** and **13**, respectively. The 4-ulose **13**, in its expected $^1C_4$(D) conformation, has *trans*-diaxially related OAc-2 and H-3 substituents, and it readily eliminated acetic acid during chromatography on silica gel, to give **3**, thus isolated in 61% yield (from **12**). The 4-ulose **9**, by contrast, has an equatorially aligned 2-acetoxyl group in its expected $^1C_4$(D) conformation, and eliminates acetic acid less readily. Several alkaline reagents were tested without much success, but treatment of **9** in boiling acetonitrile solution under reflux with a catalytic amount of tetraethylammonium acetate* proved most effective. After chromatography on a short column of silica gel, **3** was isolated in 71% yield (from **8**).

Isolevoglucosenone (**3**) was identified by its known ^{1}H-n.m.r. spectrum[8] and optical rotation[7] (it is highly dextrorotatory, making its trivial name somewhat incongruous), and from its high-resolution mass spectrum. Its synthesis from **2** was also achieved without separation or purification of the intermediates; the reduction of **6** + **10** was performed in benzyl alcohol, and the β-elimination of acetic acid (*i.e.*, **9** + **13**→**3**) was effected by using tetraethylammonium acetate catalysis; in this case, **3** was obtained in ~25% yield (nonoptimized) from **2**.

Isolevoglucosenone (**3**) decomposes on storage during several months at −25°, and hence is not so stable in this respect as levoglucosenone (**2**).

Thermal chemistry of isolevoglucosenone (**3**). — Phosphoric acid-catalyzed pyrolyzates[9] of cellulose were examined by g.l.c., but no component appeared that had the retention time found for authentic **3**, in agreement with the findings of Köll and co-workers[7]. Thus, if **3** is formed, it must also be rapidly degraded during pyrolysis. We therefore examined the behavior of **3** under conditions of thermolysis.

*We thank Prof. F. W. Lichtenthaler for suggesting this reagent. Tetrabutylammonium acetate has been used for elimination of TsOH from cyclohexyl tosylate[16] and that of BrOAc from a complex 4-acetoxy-3-bromo-3-cyano-hexahydropyridine derivative[17], but no other reports on the utility of tetraalkylammonium acetates for effecting elimination reactions have been encountered.

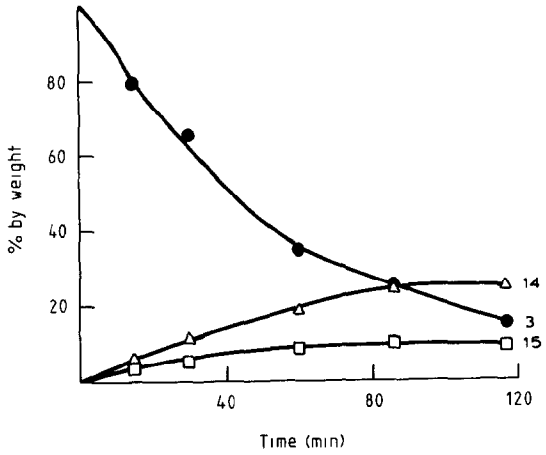
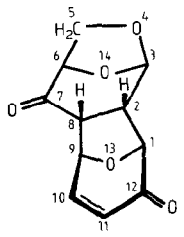


Fig. 1. Thermolysis of isolevoglucosenone (**3**; 10% w/w) in diphenyl ether at 210°.

Aliquots of a mixture of **3**, dibenzofuran (as an internal standard), and diphenyl ether (as diluent) were heated at 210° in sealed, quartz capillary-tubes. The progress of the reaction was monitored by g.l.c. analysis, and the results are shown in Fig. 1. As the starting material **3** was consumed, two products (**14** and **15**) were formed, in the ratio of 3:1, in an estimated, maximum combined-yield of



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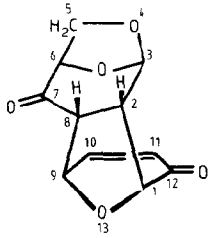

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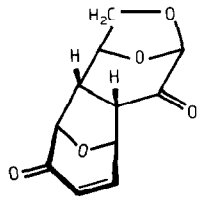

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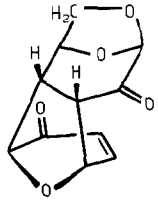

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TABLE III

^{1}H- AND ^{13}C-N M R DATA[a] FOR ADDUCTS **14** AND **15**

Compound	*Chemical shift (δ)*										
	C-1	*C-2*	*C-3*	*C-5*	*C-6*	*C-7*	*C-8*	*C-9*	*C-10*	*C-11*	*C-12*
14	84.2[b]	45 1	103.0	66.4	78.8[b]	188.1	50 0	78.1[b]	150.3	126.3	180.6
15	83.4[b]	45.5	98.5	66.4	78.7[b]	—[c]	50.7	74.0[b]	150 1	129.7	—[c]
	H-1	*H-2*	*H-3*	*H-5,5'*	*H-6*	*H-8*	*H-9*	*H-10*	*H-11*		
14	4 5–4.7 m[d]	2.60 dm	5 92 br s[e]	3 8–4 1 m	4.5–4.7 m[d]	2.96 d	5 14 d	7.28 dd	6.01 dd[e]		
15	4.70 d	3 20 dd	5 64 s	3.7–4 2 m	4.39 t	3.50 dd	5.11 dd	7 23 dd	6.16 dd		
	Coupling constants (Hz)[f]										
	$J_{1,2}$	$J_{1,11}$[g]	$J_{2,3}$	$J_{2,8}$	$J_{8,9}$	$J_{9,10}$	$J_{10,11}$				
14	small (98°)	1.3	small (75°)	8.2 (1.2°)	~0 (101°)	4 5	9.9				
15	7.8	1.1	~0	9.8	7.7	4 7	9.8				

[a]At 80 and 20 MHz, respectively, ^{13}C-signals assigned with the aid of GASPE experiments[18]. [b]Assignments interchangeable. [c]Carbonyl signals were not sufficiently intense to be detected. [d]-[e]Signals overlap [f]Corresponding dihedral angles involved, from the crystal-structure data on adduct **14**, are shown in parentheses [g]Assignments tentative, because this coupling is only clearly resolved in the H-11 resonance.

34%. In similar experiments conducted at 210 and 260° in the absence of the diluent, **3** was converted more rapidly into the same products in similar maximum yields, but subsequent degradation of these products, and accompanying production of char, was then clearly observed.

In order to characterize the products **14** and **15**, the thermolysis of **3** in diphenyl ether at 210° was repeated on a larger scale, and the reaction mixture was separated chromatographically. The major adduct **14** was obtained crystalline, whereas the minor adduct **15** was obtained pure, in low yield, only as a syrup. Their ^{13}C- and ^{1}H-n.m.r. data are listed in Table III. From their ^{13}C-n.m.r. spectra, it was clear that these products are isomers resulting from $[4_\pi + 2_\pi]$-1,3-dipolar cycloadditions between isolevoglucosenone (**3**) and its pyrolysis product, 3-oxidopyrylium (**4**).

3-Oxidopyrylium (**4**) acts as the dipolar, 4π component in such reactions, adding the ene across C-2 and C-6 of **4**. Two adducts resulting from the analogous $[4_\pi + 2_\pi]$-1,3-dipolar cycloadditions of levoglucosenone (**2**) and ylide **4**, have been isolated from the thermolysis of **2**, and shown[9] to have structures **16** and **17**.

There are eight isomers that might result from such cycloadditions of **3** with **4**. The structures assigned to adducts **14** and **15** were largely determined from an examination of their ^{1}H-n.m.r.-spectral coupling-patterns (assigned with the aid of decoupling experiments), and by inspection of molecular models. The near-zero 2,3-couplings in the spectra of **14** and **15** established that ylide **4** had approached from the less-hindered side of **3** in both cases, *i.e.*, from "below" the plane of its pyranose ring, and thus opposite the 1,6-anhydro bridge; adducts resulting from the alternative addition of **4** from "above" this plane should have $J_{2,3}$ values of ~5 Hz. The 1,2- and 8,9-couplings in the spectrum of **14** were near zero, but, in that of **15** they were 7.8 and 7.7 Hz, respectively. The relationship of the pyranose ring to the 1,9-oxa bridge is thus *syn* in **14**, but *anti* in **15**. The relative orientation of the enone functionality with respect to the C-7 ketone in the minor adduct **15** was evident from the proton–proton coupling-pattern, when the resonance at highest field had been assigned to H-2. This approach could not be used to assign the orientation of the enone in the major adduct **14**, owing to a lack of discernible 1,2- and 8,9-couplings. For this reason, a single-crystal, X-ray structure analysis of **14** was undertaken.

The crystal structure of adduct **14**. — A stereochemical depiction of **14**, produced from the X-ray data, is shown in Fig. 2, and the atomic co-ordinates are listed* in Table IV. The four sequential C–O bonds in the C-5–O-4–C-3–O-14–C-6 atom-sequence have the characteristic, long–short–short–long pattern of bond lengths found in most 1,6-anhydropyranose systems[19].

*Supplementary data: Lists of the observed and calculated structure factors, anisotropic thermal parameters, principal torsion-angles, bond lengths, bond angles, selected mean-plane data, and ring-puckering parameters have been deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/327/*Carbohydr. Res.*, 146 (1986) 113–128.

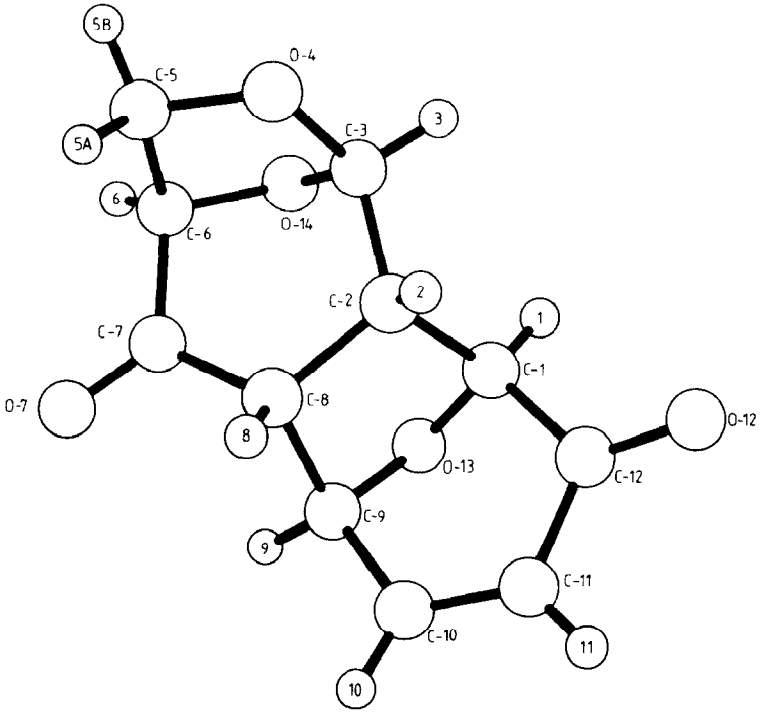

Fig. 2. Stereochemical drawing of **14** from the X-ray data.

Calculation of ring-puckering parameters[20,21] and mean-plane data revealed that the two six-membered rings in **14** have $sofa_O$ conformations, with their five ring-carbon atoms almost coplanar and their ring-oxygen atoms (O-13 and O-14) out-of-plane by ~80 pm. The enone functionality is not coplanar, being twisted out of planarity by ~10°, as shown by a C-10–C-11–C-12–O-12 torsion-angle of 170.4°, and O-12 being 12.0 pm above the mean plane defined by carbon atoms 1, 9, 10, 11, and 12 (see Fig. 2). The conformations of the two five-membered rings in **14** are very similar, lying midway between envelope and twist conformations, despite the fact that they contain alternately one and two oxygen atoms. The conformation of the anhydro ring lies midway between $E_{O\text{-}14}$ (ϕ = 36°) and ${}^{C\text{-}6}T_{O\text{-}14}$ (ϕ = 54°), while that of the furanoid ring lies midway between the $E_{O\text{-}13}$ (ϕ = 180°) and ${}^{C\text{-}9}T_{O\text{-}13}$ (ϕ = 198°) conformations.

The vicinal 1,2-, 2,3-, 2,8-, and 8,9-proton couplings in the ^{1}H-n.m.r. spectrum of **14** in solution correlate well with those predicted from the Karplus equation and the dihedral angles found in the solid state (see Table III). Thus, near-zero coupling corresponded with dihedral angles in the range of 75–101°, and an 8.2-Hz coupling, with a 1° dihedral angle.

With the two isolevoglucosenone–3-oxidopyrylium adducts **14** and **15** now characterized, structural similarities between them and the two levoglucosenone–3-

TABLE IV

FINAL POSITIONAL AND EQUIVALENT THERMAL PARAMETERS FOR ADDUCTS **14**[a]

Atom	*x*	*y*	*z*	$10^2 \times U_{eq}$[b] *or* U_{iso} ($Å^2$)
C-1	0.8052(5)	0.3043(3)	0.3021(7)	4.8(5)
C-2	0.8712(5)	0.3972(3)	0.2632(5)	4.2(5)
C-3	1.0385(5)	0.4029(3)	0.3092(6)	4.6(5)
O-4	1.0895(3)	0.4928(2)	0.2971(4)	6.2(4)
C-5	1.1595(7)	0.5032(4)	0.1196(7)	6.1(6)
C-6	1.1272(5)	0.4151(3)	0.0264(6)	4.9(5)
C-7	0.9766(5)	0.4158(3)	−0.0661(6)	5.5(5)
O-7	0.9632(4)	0.4229(3)	−0.2297(4)	9.8(5)
C-8	0.8397(5)	0.4096(3)	0.0563(6)	4.7(5)
C-9	0.7435(6)	0.3259(4)	0.0100(7)	5.7(6)
C-10	0.5806(6)	0.3410(4)	0.0575(8)	6.9(7)
C-11	0.5352(6)	0.3304(4)	0.2277(8)	6.6(7)
C-12	0.6438(5)	0.3137(3)	0.3728(7)	5.9(6)
O-12	0.6137(4)	0.3142(3)	0.5340(5)	9.9(5)
O-13	0.8045(3)	0.2599(2)	0.1298(4)	5.5(3)
O-14	1.1233(3)	0.3551(2)	0.1794(4)	5.1(3)
H-1	0.857(4)	0.268(2)	0.386(5)	5(1)
H-2	0.823(4)	0.441(2)	0.333(5)	4(1)
H-3	1.061(4)	0.377(2)	0.434(5)	4(1)
H-5A	1.101(5)	0.566(3)	0.065(6)	7(1)
H-5B	1.266(7)	0.520(4)	0.133(8)	12(2)
H-6	1.205(4)	0.393(2)	−0.055(5)	5(1)
H-8	0.774(4)	0.460(2)	0.040(5)	4(1)
H-9	0.769(4)	0.301(2)	−0.130(6)	7(1)
H-10	0.517(6)	0.361(4)	−0.038(7)	11(2)
H-11	0.443(5)	0.329(3)	0.264(6)	8(2)

[a]Estimated standard deviations in parentheses. [b]For non-hydrogen atoms, $U_{eq} = {}^1/_3 \Sigma_i \Sigma_j U_{ij} a_i^* a_j^* a_i a_j$.

oxidopyrylium adducts **16** and **17** may be seen, and a general conclusion as to their mode of formation drawn. All four adducts result from approach of ylide **4** from "below" the plane of the pyranose ring in enones **2** and **3** (*i.e.*, on the side opposite the sterically hindering 1,6-anhydro bridge) and from an *anti* alignment of the carbonyl entities in the combining units.

Is isolevoglucosenone (**3**) *a primary, cellulose-pyrolysis product?* — In a recent examination[9] of the pyrolysis of phosphoric acid-doped cellulose, conditions were optimized for the production of several components having molecular weights greater than that of the major product, namely, levoglucosenone (**2**). These components were shown to be the result of pyrolytic loss of formaldehyde from **2**, to give 3-oxidopyrylium (**4**), which subsequently dimerized, or underwent cycloaddition with **2**. The same pyrolyzates were examined by g.l.c. analysis for the presence of the products (**14** and **15**) of thermolysis of isolevoglucosenone (**3**), as their detection would provide evidence for the production of **3**. Adducts **14** and **15** were, however, not detected.

In conclusion, no evidence for the pyrolytic synthesis of isolevoglucosenone (**3**) was obtained in this study.

EXPERIMENTAL

General methods. — T.l.c. was performed on Baker-flex IB2-F silica plates, eluted with 3:2 ethyl acetate–1,2-dichloroethane and developed with 1:2:37 anisaldehyde–sulfuric acid-ethanol spray-reagent, followed by heating at 110°. Carbon and hydrogen analyses were performed by Galbraith Laboratories, Inc. Levoglucosenone (**2**) was prepared as reported[3]. Optical rotations were measured at ~20° for chloroform solutions within the concentration range of 0.83 to 4.74 g/100 mL of solution. N.m.r. spectra were recorded, with Varian FT-80A, JEOL FX-90Q, Varian XL-200, and Bruker 360-MHz spectrometers, for solutions in $CDCl_3$, using tetramethylsilane as an internal standard. High-resolution mass spectra were recorded with a Kratos MS 30 instrument. I.r. spectra were recorded with a Perkin–Elmer 580 spectrometer for 5mM solutions in CCl_4 in cells having a 1-mm path-length.

*1,6-Anhydro-4-O-benzyl-3-deoxy-β-*D-erythro-*hexopyranos-2-ulose* (**5**). — A stock solution of potassium benzoxide in benzyl alcohol was prepared by adding potassium hydride (~0.13 g, containing a small amount of oil) to benzyl alcohol (2.5 mL). A portion of this solution (0.05 mL) was then added to a solution of **2** (0.145 g) in benzyl alcohol (5 mL), causing the mixture to darken slightly. After 5 min, this solution was diluted with chloroform, successively washed with M aqueous hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and distilled water, the chloroform evaporated *in vacuo*, and the benzyl alcohol removed by distillation at 26.6 Pa, and, finally, by azeotropic distillation with water (× 2) and absolute ethanol. This yielded **5** as a yellow oil (0.20 g, 79%); a single component by t.l.c. (blue, u.v.-absorbing, R_F 0.67). Purification by vacuum distillation gave a colorless oil, $[\alpha]_D$ −143°; ν_{max}^{film} 1740 cm^{-1} (C=O); ^{13}C-n.m.r. (signals assigned with the aid of a GASPE experiment[18]): δ 198.3 (C-2), 137.4 (Ph, q), 128.6, 128.0, and 127.7 (Ph), 101.4 (C-1), 76.2 and 74.9 (C-4,5), 70.8 and 65.2 (C-6 and Ph*C*H_2), and 37.4 (C-3); it subsequently crystallized from ether–hexane; m.p. 57–58°, $[\alpha]_D$ −146°.

Anal. Calc. for $C_{13}H_{13}O_4$: C, 66.7; H, 6.0. Found: C, 66.5; H, 6.1.

Borohydride reduction of **5**. — (*a*) *In aqueous methanol.* A solution of sodium borohydride (0.29 g) in water (5 mL) was added to a solution of **5** (0.291 g) in methanol (5 mL). The solution was stirred for 10 min and then processed in the usual way[22] to afford a colorless oil (0.249 g, 85%) shown by t.l.c. to contain largely two compounds, **6** (brown, u.v.-absorbing, R_F 0.32) and **10** (brown, u.v.-absorbing, R_F 0.51), together with three less-mobile, minor impurities.

(*b*) *In benzyl alcohol.* A solution of **5** in benzyl alcohol was prepared, as just described, from **2** (0.088 g), except that, 5 min after the addition of potassium benzoxide, a suspension of sodium borohydride (0.073 g) in ethanol (4 mL) was added to the mixture, which was then stirred for 0.5 h at room temperature, made neutral with acetic acid, evaporated under vacuum, and the resulting white residue transferred to a short column of silica, which was eluted with a gradient of ethyl

acetate–hexane (from 1:2 to 2:1). The fractions found by t.l.c. to contain **6** and **10** were combined and evaporated, to give material that spontaneously crystallized (0.106 g, 64% from **2**). ^{1}H-N.m.r. spectroscopy of this material showed it to be an 11:9 mixture of **6** and **10** (determined from the relative intensities of their H-3 resonances).

Column-chromatographic separation (eluant: gradient of ethyl acetate–hexane from 1:2 to 2:1) provided crystalline samples of both isomers. 1,6-Anhydro-4-*O*-benzyl-3-deoxy-β-D-*arabino*-hexopyranose (**6**) was twice recrystallized from ethyl acetate–hexane to give white needles, m.p. 117.5–119°, $[\alpha]_D$ −91°; $\nu_{max}^{CCl_4}$ 3590 cm^{-1}.

Anal. Calc. for $C_{13}H_{16}O_4$: C, 66.1; H, 6.8. Found: C, 66.3; H, 7.0.

Syrupy 1,6-anhydro-4-*O*-benzyl-3-deoxy-β-D-*ribo*-hexopyranose (**10**) crystallized spontaneously from diethyl ether at −20°, and had m.p. 36–37°. On recrystallization from diethyl ether at −20° and then from ethyl acetate–hexane, a second, higher-melting form was obtained as white needles, m.p. 56–57°, $[\alpha]_D$ −60° $\nu_{max}^{CCl_4}$ 3560 cm^{-1}.

Anal. Calc. for $C_{13}H_{16}O_4$: C, 66.1; H, 6.8. Found: C, 66.1; H, 6.7.

*2-O-Acetyl-1,6-anhydro-4-O-benzyl-3-deoxy-β-*D-arabino-*hexopyranose* (**7**). — A solution of **6** (0.551 g) in pyridine was acetylated with acetic anhydride in the usual way[22], to yield a viscous oil (0.651 g, 100%) that was shown by t.l.c. to be one product (black, u.v.-absorbing, R_F 0.58). Following vacuum distillation, it had $[\alpha]_D$ −76°.

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.7; H, 6.5. Found: C, 64.5; H, 6.4.

*2-O-Acetyl-1,6-anhydro-4-O-benzyl-3-deoxy-β-*D-ribo-*hexopyranose* (**11**). — Acetylation of **10** (0.582 g) was conducted in the usual way[22], to yield **11** (0.670 g, 98%) which crystallized spontaneously upon removal of the solvent. Recrystallization (× 2) from ethyl acetate–hexane gave white needles having m.p. 85–87°, $[\alpha]_D$ −38°; R_F 0.60.

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.7; H, 6.5. Found: C, 64.8; H, 6.6.

*2-O-Acetyl-1,6-anhydro-3-deoxy-β-*D-arabino-*hexopyranose* (**8**). — Compound **7** (0.482 g) in ethanol (35 mL) was hydrogenolyzed at atmospheric pressure in the presence of 10% palladium-on-charcoal (0.41 g). After 2 h, 1 equiv. of hydrogen had been absorbed. The catalyst and solvent were removed, to give a colorless oil (0.311 g, 95%) shown by t.l.c. (brown, R_F 0.29) to be one component. Purification by flash chromatography[23] gave **8** as an oil; $[\alpha]_D$ −148°; $\nu_{max}^{CCl_4}$ 3595 cm^{-1}.

Anal. Calc. for $C_8H_{12}O_5$: C, 51.1; H, 6.4. Found: C, 50.9; H, 6.4.

*2-O-Acetyl-1,6-anhydro-3-deoxy-β-*D-ribo-*hexopyranose* (**12**). — Compound **11** (0.428 g) was hydrogenolyzed overnight in the presence of 10% palladium-on-charcoal (0.45 g) in ethanol (35 mL) at atmospheric pressure. T.l.c. indicated the presence of a single product (dark green, R_F 0.23). The catalyst and solvent were removed, to yield **12** as a syrup (0.280 g, 97%) which crystallized upon storage at −20°. Recrystallization from ethyl acetate–hexane gave white plates; m.p. 63–64°, $[\alpha]_D$ −51°; $\nu_{max}^{CCl_4}$ 3590 cm^{-1}.

Anal. Calc. for $C_8H_{12}O_5$: C, 51.1; H, 6.4. Found: C, 51.3; H, 6.6.

*1,6-Anhydro-2,3-dideoxy-β-*D-glycero-*hex-2-enopyranos-4-ulose* (**3**). — (*a*) *From* **8**. Pyridinium chlorochromate (0.71 g) was suspended in dichloromethane (3 mL, dried over molecular sieve), and a solution of **8** (0.167 g) in dichloromethane (3 mL, dried) was added. The mixture was rapidly stirred in a stoppered flask for 27 h at room temperature; t.l.c. then showed the presence of a single, non-u.v.-absorbing product (blue, R_F 0.55). Diethyl ether (18 mL) was added, and the supernatant liquor was decanted from the insoluble residue, which was extracted twice with diethyl ether, the extracts and solution combined, filtered through a short plug of silica gel, and the filtrate evaporated, to give an oil; the ^{1}H-n.m.r. spectrum of this product was consistent with its being the 4-ulose **9**.

The entire sample was dissolved in acetonitrile (9.2 mL, dried over molecular sieve) and a solution of tetraethylammonium acetate in dry acetonitrile (0.8 mL) was added, to give a final concentration of catalyst of 0.01M. This solution was boiled under reflux for 0.5 h, to give a single product (t.l.c., blue, u.v.-absorbing, R_F 0.60). After the solution had been cooled, most of the solvent was evaporated *in vacuo*, and the mixture was transferred to a short column of silica gel and eluted with 1:1 ethyl acetate–hexane. Fractions containing the product were combined, and evaporated, to yield **3** (0.080 g, 71%). Purification by vacuum distillation gave a pale-yellow oil having $[\alpha]_D$ +331° (lit.[7] +318°; and[24] −327° for the L isomer); ν_{max}^{film} 2967, 2898, 1739, 1715, 1694, and 892; *m/z* 127 (5%), 126.032 (M^+, 76%; calc. for $C_6H_6O_3$: 126.032), 98 (M − CO, 4), 97 (M − CHO, 4), 96 (M − CH_2O, 8), 85 (M − C_2HO, 16), 83 ($C_4H_3O_2$, 100), 68 (C_4H_4O, 58), 55 (32), and 39 (50%). The ^{1}H-n.m.r. spectrum of **3** was consistent with that previously reported[8].

(*b*) *From* **12**. Compound **12** (0.444 g) was oxidized as just described, by using pyridinium chlorochromate (2.85 g) in dichloromethane (24 mL) for 26 h at room temperature. The presence of a single component was observed by t.l.c., and, although it had R_F and visual characteristics identical to those of **3**, the ^{1}H-n.m.r. spectrum was consistent with its being the 4-ulose **13**. Acetic acid was readily eliminated from this product, however, by column chromatography on silica gel with 1:3 ethyl acetate–hexane as the eluant. This yielded enone **3** as a pale-yellow oil (0.181 g, 61%) having a ^{1}H-n.m.r. spectrum identical to that of the afore-described compound.

Thermolysis of isolevoglucosenone (**3**). — (*a*) *Preliminary experiments.* A stock solution of isolevoglucosenone (**3**, 70 mg) in diphenyl ether (0.7 g, purified according to ref. 25) containing dibenzofuran (7 mg) as an internal standard, was prepared. Aliquots (15 μL) were sealed in quartz capillary-tubes. Several of these tubes were placed in a furnace preheated to 210°, and were then taken out individually after the elapse of various time-intervals. The contents of each tube were washed out with acetone (200 μL) and analyzed by g.l.c. on a glass column (1.5 m × 2 mm i.d.) packed with 5% of Pluronic F-68 (BASF)[26] on Gas-Chrom Q (100–120 mesh), programmed from 90 to 210° at 8°/min, with nitrogen as the carrier gas (22 mL·min^{-1}), and flame-ionization detection. The relative peak-areas for **3** (R_T 5.0

min) and the adducts **14** (R_T 21.5 min) and **15** (R_T 20.1 min) were normalized with respect to the peak area of dibenzofuran (R_T 10.3 min), and the results are shown in Fig. 1; diphenyl ether was eluted at 7.6 min. Similar experiments were conducted at 230°, at 260° using neat **3**, and at 210° using a 1:9 (w/w) mixture of **3** and diphenyl ether. In all cases, the adducts **14** and **15** were the preponderant products, although minor proportions of later-eluting compounds were also detected.

(*b*) *Preparative experiment.* Half of a mixture of isolevoglucosenone (**3**, 0.224 g) and diphenyl ether (1.84 g) was placed in each of two quartz tubes. These were sealed, and heated in a furnace for 2 h at 210°. Examination of the product by g.l.c. indicated a 17:25:8 mixture (by weight) of **3, 14,** and **15**, and t.l.c. (eluted twice with 2:1 ethyl acetate–light petroleum ether) revealed **3** (R_F 0.57), **14** (major, R_F 0.20), and **15** (secondary, R_F 0.27), and unidentified, lesser components at R_F 0.13, 0.03, and the baseline. The product was fractionated by flash chromatography[23] on silica gel eluted with 1:1 ethyl acetate–hexane. Only a small, syrupy sample (~2 mg) of the minor adduct **15** was obtained pure (t.l.c. and g.l.c. evidence), but this was sufficient to permit obtaining the n.m.r.-spectral data listed in Table III. Fractions containing the major adduct **14** were combined, and evaporated to afford a crystalline residue (31 mg, 16%). Recrystallized from ethyl acetate–hexane, it had m.p. 189–194° (with sublimation) and the n.m.r.-spectral data listed in Table III; it was subjected to X-ray crystal structure analysis.

X-Ray crystal analysis of adduct **14**. — Weissenberg and precession photographs showed the crystals to be orthorhombic, with the unique space-group $P2_12_12_1$. The crystal data were as follows: $C_{11}H_{10}O_5$, a = 887.07(17), b = 1504.1(3), c = 727.88(17) pm, Z = 4, ρ (calculated) 1.52 g·cm^{-3}, μ(MoKα) = 1.31 cm^{-1}. The structure was solved by direct methods using the SOLV program[27] and subsequent difference-Fourier syntheses (for the hydrogen atoms). The final R, R_w values were 0.036, 0.025 for the 657 independent reflections, with $I > 3\,\sigma(I)$, where $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$. Full details of the structure determination are included in the supplementary material.

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