Carbohydrate Research, 226 (1992) 337–343
Elsevier Science Publishers B.V., Amsterdam

Note

Ethylenic acetals of sucrose and their copolymerization with vinyl monomers

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(Received August 5th, 1991; accepted November 8th, 1991)

Structural modifications of natural products to give them new physical, chemical, or biological properties have been considered for a long time. Sugars are specially interesting substrates as they are generally available in large quantities and are renewable resources. Among them, sucrose is one of the most accessible for industrial uses, and its potential has not been completely explored, even though its chemistry has received much attention[1]. Notable efforts have been directed towards possible applications of sucrose derivatives in areas other than classical food markets. The idea that interesting properties could be found for water-soluble and, possibly, biodegradable polymers like polyvinylsugars has recently received growing attention (see, for instance, chapter 15 in ref. 1d). To the best of our knowledge no attempt of preparing ethylenic monomers such as sucrose acetals with a double bond in the acetal substituent has been published.

The acetal function, well-known for a long time in carbohydrate chemistry as a protecting group[2], has more recently also been recognized as a functional group with its own reactivity[3]. Due to the necessity of having a monofunctionality for the monomer to be engaged in free-radical chain polymerization, our objective has been the selective preparation of 4,6-*O*-acetals with a unique double bond as a reactive side group. Such a compound is necessary in order to obtain (Scheme 1) a polyvinylic backbone that is substituted by sucrose side chains (through the acetal linkage) in a comb-like arrangement by polymerisation or copolymerisation with various vinylic monomers.

Generally speaking, the preparation of cyclic acetals of sucrose has been studied, but this work has met with limited success[1a,b]. The exception is more recent work concerning isopropylidene acetals[4]. Since acidic conditions are required for these

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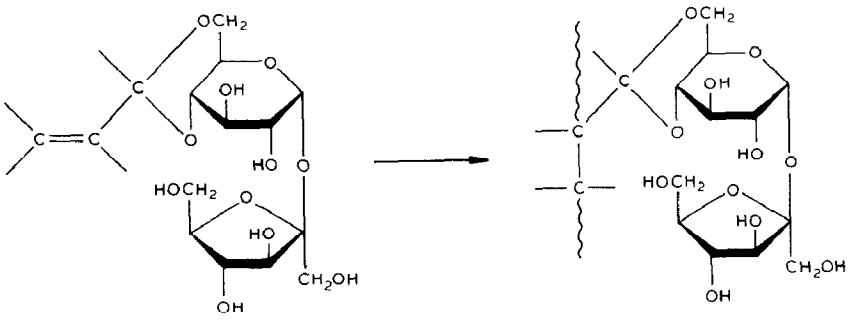
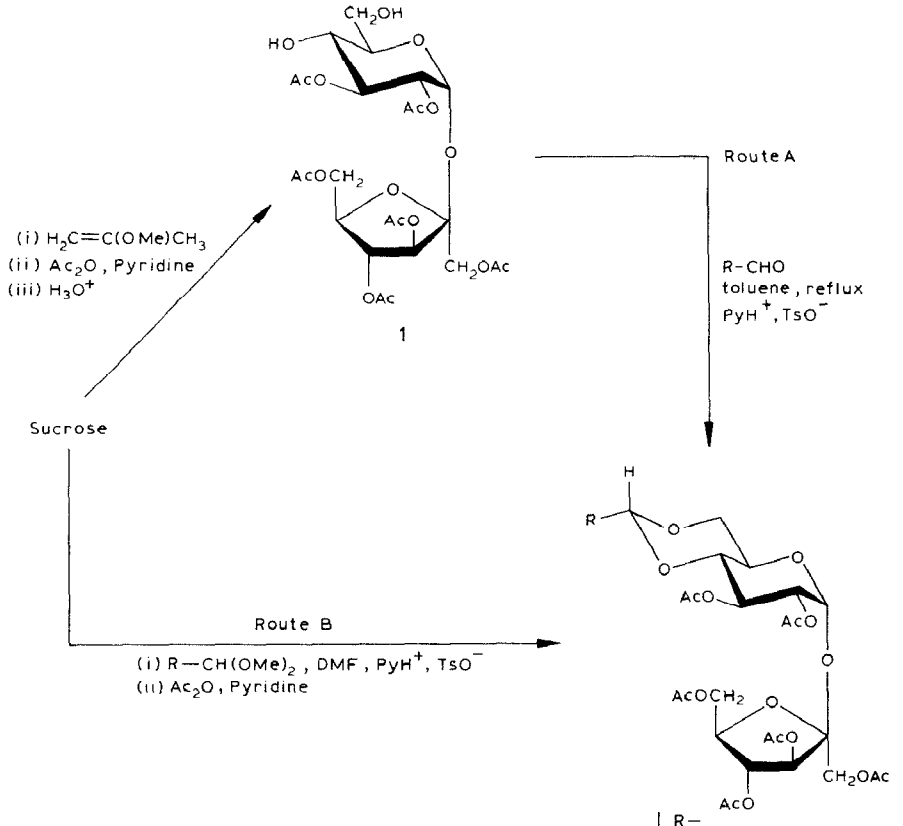
0008-6215/92/$ 05.00



Scheme 1



	R–
2	$PhCH{=}CH{-}$
3	$H_2C{=}CH{-}$
4	$H_2C{=}C(Me){-}$
5	$H_2C{=}CH{-}C_6H_4{-}$
6	H–
7a	$H_2C{=}CH{-}CH_2{-}$
7b	$MeCH{=}CH{-}$

Scheme 2

syntheses, most of the acetalation catalysts often cause rupture of the sucrose glycosidic linkage and degradation reactions.

On the other hand, the preparation of cyclic acetals of monosaccharides has been well developed[3]. Among different procedures, it should be noted that Jedlińsky *et al.* have described a convenient method for the preparation of ethylenic acetals of both methyl α-D-gluco- and α-D-manno-pyranosides[5]. Transacetalation is also a well-known route to prepare acetals[6].

This paper deals with the reaction of sucrose or its corresponding semi-protected diol **1** with ethylenic aldehydes or ethylenic dimethyl acetals (Scheme 2). Reaction of sugars with unsaturated carbonyl compounds requires anhydrous experimental conditions. For this purpose azeotropic removal of water with toluene in a Dean–Stark trap can be applied to the synthesis of sucrose acetals. If sucrose is used in the protected form **1**, the glycosidic linkage is preserved in spite of the reaction temperature and acidity of the reaction medium. A convenient catalyst is pyridinium *p*-toluenesulfonate. Under these conditions, several new ethylenic acetals of sucrose have been obtained in good yields (Table I). The yield of products depends on the structure of the aldehyde. It is noteworthy that the reactivity of aldehydes containing benzene units is higher, thus corroborating the observations of Jedlińsky and coworkers[5].

Such a preparation would be more attractive for industrial purposes if it could be carried out with unprotected sucrose, but these reaction conditions are no more suitable as the glycosidic linkage is then cleaved. However, it has been found that a transacetalation carried out in *N,N*-dimethylformamide, under acidic conditions, at room temperature with the appropriate aldehyde dimethyl acetal as reagent, was a quite convenient procedure (Scheme 2). The reagents can easily be prepared or are commercially available. Results are described in Table I. Yields are calculated after classic acetylation of the crude reaction mixture and further purification by column chromatography. This reaction is highly regioselective, and only the 4,6-monoacetal is obtained under these conditions.

All of these compounds have been identified on the basis of their ^{1}H- and ^{13}C-n.m.r. spectra. In general, the ^{1}H-n.m.r. spectra clearly show signals corresponding to ethylenic protons (5–7 p.p.m.), and the ^{13}C-n.m.r. spectra show characteristic signals for both the ethylenic and the three acetalic carbon atoms. In all cases, the presence of only one of the two possible diastereomers with the new acetal carbon atom is observed. The R-group appear in the equatorial position, the axial isomer being less stable because of its interaction with *syn* axial protons.

TABLE I

Yield of ethylenic acetals of sucrose

Compound	**2**	**3**	**4**	**5**	**6**	**7**
Yield (%)	65[a] 35[b]	20[a] 20[b]	20[a]	65[a]	25[a]	80[a]

[a] Route A: yields are calculated with respect to diol **1**. [b] Route B: yields are calculated with respect to sucrose.

The fact that the reaction with 3-butenal dimethyl acetal takes place with concomitant isomerisation of the double bound of the lateral chain from the terminal position to the 2-position is noteworthy. (This phenomenon has also been observed with reagents such as vinyl ethers[7].)

Lastly, we have also obtained by the same procedure and in moderate yield the 4,6-*O*-methylidene derivative **6**. Several syntheses of methylene acetal of monosaccharides have been reported in the literature[2,8a]; however, either complex reagents are needed, or low yields are obtained, except for a method using phase-transfer catalysis[8b].

The polymerizability of some of these monomers was then examined in a series of copolymerization experiments with styrene, using a free-radical initiator. Compounds **2**, **3**, and **5** were evaluated.

Copolymers were only obtained with monomer **5**. Results of copolymerization are given in Table II. The copolymer was insoluble in common organic solvents such as dichloromethane, acetone, and methanol. However, it exhibited good solubility in polar solvents such as *N,N*-dimethylformamide, dimethyl sulfoxide, and *N,N*-dimethylacetamide. The copolymer composition was determined by ^{1}H-n.m.r. spectroscopy by comparing the peak areas of aromatic protons (6.2–7.4 p.p.m.) with those of the acetate protons of sucrose groups as well as with both the methylene and methine protons of the polymer chain (0.8–2.2 p.p.m.). As can be seen, the copolymer composition is the same as that of the co-monomer used in the reaction. This indicates that the reactivity of the styrene group is not significantly affected by the attached sucrose moieties.

However, no copolymer was obtained with monomers **2** and **3**. According to n.m.r. spectroscopy, the products formed were mixtures of **2** and polystyrene or **3** and polystyrene. This result may be due either to the extremely low reactivity of the polymerizable groups towards free-radical polymerization or to the occurrence of termination reactions.

The glass transition temperature (T_g) of the copolymer was determined by differential scanning calorimetry (d.s.c.). The copolymer having blocked hydroxyl groups, has a lower glass transition temperature than polystyrene. This fact indicates a

TABLE II

Copolymerisation of styrene and **5** in the presence of a free-radical initiator[a]

Molar percentage composition		*Yield (%)*	M_n[b]	T_g(°)
Monomers	*Copolymer*			
Styrene:**5** 83:17	Styrene:**5** 83:17	55	9500	92

[a] Conditions were as follows: solvent, toluene; temperature, 70°; 1 mol.% AIBN; reaction time, 12 h. [b] The rather low molecular weight could be due either to chain-transfer or to termination reactions. No evidence for such processes could be obtained by ^{1}H-n.m.r. spectroscopy owing to the low proportion of end groups with respect to comonomer units (d.p.$_n$ 46). However, the partial conversion might indicate the occurrence of a termination process.

higher chain mobility which is very likely due to a decrease of intermolecular forces resulting from the bulkiness of the sucrose groups.

EXPERIMENTAL

General methods. — Melting points were determined on a Büchi apparatus. Evaporations were performed under diminished pressure. Optical rotations were measured on a Perkin–Elmer 141 polarimeter in 1-dm tubes. Column chromatography was performed with Silica Gel 60 (E. Merck 70–230 mesh), and t.l.c. was carried out on precoated plates (E. Merck 5724), with detection by charring with H_2SO_4. ^{1}H-n.m.r. spectra (60 or 250 MHz) were recorded on a Varian T-60 spectrometer or on a Bruker AC 250 spectrometer. Peak multiplicities are given by: s, singlet; d, doublet; t, triplet; m, multiplet. Chemical shift data are given in δ-units (p.p.m.) measured downfield from internal Me_4Si, and spin-spin coupling data are in Hz. ^{13}C-n.m.r. spectra were recorded on a JEOL FX 60 spectrometer. Number-average molecular weight (M_n) of the copolymer was obtained by gel-permeation chromatography (g.p.c.) in tetrahydrofuran, using polystyrene samples as standards for calibration. Glass transition temperature (T_g) was determined by differential scanning calorimetry (d.s.c.) using a Mettler TA 3000 apparatus. Elemental analyses for C, H, and O were carried out by the Service Central d'Analyses du CNRS in Lyon, France.

Typical procedure for synthesis of the ethylenic acetals of sucrose **2**, **3**, **4**, *and* **5**. — A solution of the diol **1** and ethylenic aldehyde (3 mol. equiv.) in toluene, with a catalytic amount of pyridinium *p*-toluenesulfonate was refluxed in a flask fitted with a Dean-Stark trap and a reflux condenser. The reaction was monitored by t.l.c. (1:1 EtOAc–hexane). After 5 h the starting material had disappeared; the solution was then neutralised with Na_2CO_3 and filtered, and the solvent was evaporated under reduced pressure to give a syrup. The crude material was separated by column chromatography (1:1 EtOAc–hexane) to give the pure monoacetal of sucrose.

1′,2,3,3′,4′,6′-Hexa-O-*acetyl-4,6*-O-*cinnamylidenesucrose* (**2**). — Yield 65%; m.p. 65–67°; $[\alpha]_D^{20}$ +42° (*c* 0.1, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): δ 7.3 (s, 5 H, C_6H_5), 6.8 (d, 1 H, H-9), 6.1 (dd, 1 H $J_{7,8}$ 4.0 Hz, H-8), 5.64 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.45 (m, 3 H, H-3, H-3′, H-4′), 5.15 (d, 1 H, $J_{7,8}$ 4.0 Hz, H-7), 4.82 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 2.15 (m, 18 H, OAc); ^{13}C-n.m.r. ($CDCl_3$): δ 170.2, 170.3, 169.9, 169.8 (4 × Me*C*O), 135.5, 133.7 (C-8, C-9), 128.3, 126.6, 123.9 (C_6H_4), 103.8 (C-2′), 100.8 (C-7), 90.2 (C-1), 20.2 (*Me*CO).

Anal. Calc. for $C_{33}H_{40}O_{17}$: C, 56.01; H, 5.66; O, 38.47. Found: C, 55.97; H, 5.67; O, 38.08.

1′,2,3,3′,4′,6′-Hexa-O-*acetyl-4,6*-O-*acrylidenesucrose* (**3**). — Yield 20%; m.p. 46–47°; $[\alpha]_D^{20}$ +23° (*c* 0.1, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): δ 5.64 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 6.0 (m, 1 H, H-8), 5.4 (m, 4 H, H-3, H-3′, H-4′, H-7), 4.8 (m, 3 H, H-2, H-9, H-9′), 2.15 (m, 18 H, OAc); ^{13}C-n.m.r. ($CDCl_3$): δ 170.5, 170.1, 170.0, 169.7 (Me*C*O), 133.2 (C-8), 119.0 (C-9), 103.9 (C-2′), 100.7 (C-7), 90.4 (C-1), 20.5 (*Me*CO).

Anal. Calc. for $C_{27}H_{36}O_{17}$: C, 51.26; H, 5.69; O, 43.03; Found: C, 51.46; H, 5.76; O, 42.18.

1′,2,3,3′,4′,6′-Hexa-O-acetyl-4,6-O-methacrylidenesucrose (**4**). — Yield 25%; ^{1}H-n.m.r. ($CDCl_3$): δ 5.7 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.5 (m, 3 H, H-3, H-3′, H-4′), 5.2 (s, 1 H, H-7), 4.9 (m, 3 H, H-2, H-9, H-9′), 2.2 (2s, 18 H, OAc); 1.9 (s, 3 H, Me).

1′,2,3,3′,4′,6′-Hexa-O-acetyl-4,6-O-vinylbenzylidenesucrose (**5**). — Yield 65%; m.p. 125–126°; $[\alpha]_D^{20}$ + 36° (*c* 0.1, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): δ 5.65 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.8 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 5.1 (s, 1 H, H-7), 5.4 (m, 5 H, H-3, H-3′, H-4′, H-9, H-9′), 6.65 (m, 1 H, $J_{8,9}$ 10.0 Hz, H-8), 7.3 (s, 4 H, C_6H_4); ^{13}C-n.m.r. ($CDCl_3$): δ 170.7, 170.4, 170.2, 169.8 (4 × Me*C*O), 138.4, 136.4 (C-8, C-9), 126.4, 126.1 (C_6H_4).

Anal. Calc. for $C_{33}H_{40}O_{17}$: C, 56.01; H, 5.66; O, 38.47. Found: C, 55.48; H, 5.58; O, 37.43.

Typical procedure for synthesis of ethylenic acetals of sucrose **2** *and* **3**. — To a suspension of sucrose in anhydrous *N,N*-dimethylformamide stirred at room temperature were added the appropriate ethylenic aldehyde dimethyl acetal (1.5 mol. equiv.) and a catalytic amount of *p*-toluenesulfonic acid. The reaction was monitored by t.l.c. (1:1 EtOAc–acetone). After 20 h, the solution was neutralised with Na_2CO_3, filtered, and *N,N*-dimethylformamide was evaporated under reduced pressure. The crude material was dissolved in pyridine and treated at 0° with acetic anhydride. After 24 h the solution was poured onto ice–water mixed with Na_2CO_3, and the mixture was extracted with CH_2Cl_2. The extracts were washed with a sat. aq. solution of $NaHCO_3$ and dried. The solvent was codistilled with toluene to give a syrup which sometimes crystallised. The crude product was separated by column chromatography (1:1 EtOAc–hexane) to give the pure monoacetal.

Preparation of 1′,2,3,3′,4′,6′-hexa-O-acetyl-4,6-O-methylidenesucrose (**6**). — Formaldehyde dimethyl acetal (2.5 mol. equiv.) and a catalytic amount of pyridinium *p*-toluenesulfonate were added to a solution of diol **1** in anhydrous toluene. The solution was refluxed and the reaction was monitored by t.l.c. After 20 h the solution was neutralised with Na_2CO_3 and filtered, and the solvent was evaporated. Column chromatography of the residue gave **6** in 25% yield. ^{1}H-N.m.r. ($CDCl_3$): δ 5.64 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.45 (m, 3 H, H-3, H-3′, H-4′), 5.15 (dd, H-7, H-7′), 4.8 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 2.15 (s, 18 H, OAc); ^{13}C-n.m.r. ($CDCl_3$): δ 170.4, 170.0, 169.9, 169.8, 169.6 (5 × Me*C*O), 103.8 (C-2′), 93.5 (C-7), 90.2 (C-1), 20.2 (*Me*CO).

Anal. Calc. for $C_{25}H_{34}O_{17}$: C, 49.50; H, 5.61; O, 44.88. Found: C, 49.51; H, 5.54; O, 43.88.

Preparation of 1′,2,3,3′,4′,6′-hexa-O-acetyl-4,6-O-butenylidenesucrose **7a** *and* **7b**. — The preparation was carried out according to the procedure described for compound **6**, with 3-butenal dimethyl acetal as reagent. After 3 h, the reaction mixture was neutralised, filtered, and evaporated. The crude material was examined by t.l.c. which showed the presence of two compounds that were partially separated on a chromatography column (1:1 ethyl acetate–hexane); total yield: 80%.

7a: m.p. 95–98°; $[\alpha]_D^{20}$ + 53° (*c* 0.1, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): δ 5.65 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1); 5.45 (m, 3 H, H-3, H-3′, H-4′); 5.25 (m, 1 H, H-7), 4.8 (dd, 1 H $J_{2,3}$ 10.0 Hz, H-2), 2.15 (m, 20 H, H-8,8′, OAc); ^{13}C-n.m.r. ($CDCl_3$): δ 170.4, 170.1, 169.6, 169.9 (4 × Me*C*O), 132.1, 117.6 (C-9, C-10), 103.9 (C-2′); 101.9 (C-7); 90.4 (C-1); 38.6 (C-8); 20.6 (OAc).

7b: m.p. 115–117°; $[\alpha]_D^{20}$ + 62° (*c* 0.1, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): δ 5.65 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.8 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 2.15 (m, 18 H, OAc), 1.75 (d, 3 H, H-10,10′,10″); ^{13}C-n.m.r. ($CDCl_3$): δ 170.4, 170.1, 169.9, 169.6 (4 × Me*C*O), 133.2, 126.7 (C-8, C-9), 103.9 (C-2′), 101.9 (C-7), 90.4 (C-1), 20.6 (OAC), 17.6 (C-10).

Preparation of cinnamaldehyde dimethyl acetal. — To a solution of cinnamaldehyde (10 g; 0.075 mol) in anhydrous MeOH (80 mL), were added trimethylorthoacetate (17.5 g; 0.1 mol) and a catalytic amount of *p*-toluenesulfonic acid. After stirring for 24 h at room temperature, the solution was neutralised (Na_2CO_3), filtered, and evaporated. The crude material thus obtained was used directly without further purification.

Preparation of p-*vinylbenzaldehyde.* — This preparation was realised in two steps, according to Leebrick and Rambden[9] for the first part, and Dale et al.[10] for the second part. Vinylbenzaldehyde was obtained in 60% yield in 95% purity, and was used without any further purification.

Copolymerization. — Sucrose monomer and styrene were introduced into a Schlenk apparatus and dissolved in toluene. Azobisisobutyronitrile (AIBN, 1 mol.%) was used as initiator. Oxygen was removed by a stream of nitrogen. Copolymerization was carried out for 12 h at 70°. The polymerization was stopped by pouring the reaction mixture into MeOH. The copolymer was then filtered, washed several times with MeOH, and dried *in vacuo* at 60°. The absence of residual monomer was confirmed by s.e.c. analysis of the copolymer.

ACKNOWLEDGMENTS

This work was carried out with the financial support of Béghin-Say and the Centre National de la Recherche Scientifique within the framework of the Groupement Scientifique "Sucrochemistry".

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