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Sucrose tricarboxylate by sonocatalysed TEMPO-mediated oxidation

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Abstract

Oxidation of sucrose by the NaOCl/TEMPO system provided sucrose tricarboxylate without the addition of sodium bromide as co-catalyst when high-frequency (500 kHz) ultrasound was applied, in contrast to very limited conversion without sonication. In the presence of sodium bromide, sonication also caused acceleration of the oxidation. The rate increase due to sonication of the oxidant system prior to sucrose addition suggests that ultrasound acts at the level of the formation of the nitrosonium ion, the active oxidising species in the catalytic cycle.

Keywords: Sucrose; Oxidation; Ultrasound; TEMPO; Uronic acids

1. Introduction

Polyhydroxy–polycarboxylates are interesting targets for carbohydrates as organic raw materials, due to their possible applications as cation-sequestering agents [1–3]. These polycarboxylates can be obtained by various methods, which can either involve cleavage of carbon–carbon bonds by glycol oxidation [4,5], or by selective oxidation of the primary alcohol functionality keeping intact the carbohydrate backbone. In this latter case, the oxidation of carbohydrates to uronic acids can be achieved by heterogeneous catalysis over platinum [6–11], electrocatalysis [12,13], or bioconversion [14]. An increasingly popular method is the use of the NaOCl/TEMPO system [15–20]. Its efficiency was demonstrated by Davis and Flitsch [21] and van Bekkum and co-workers [22–24], either for partially protected or unprotected monosaccharides, or with oligo- or polysaccharides, as well as more recently by Schnatbaum and Schäfer using electrochemical regeneration of the TEMPO reagent [25]. In the 'classical' method, sodium bromide is needed to catalyse the formation of the $C_9H_{18}N^+{=}O$ ion, which is the active oxidising species. The exact role of the halide ions has been related to steric factors or dissociation constants of ClOH or BrOH [16,23,26]. Rychnovsky and co-workers recently reported some mechanistic studies on the role of added salts in the case of *m*-CPBA-promoted oxidations using TEMPO [27] as well as on the influence of the redox potential of the nitroxyl radicals [28]. New clues on the mechanism could also be obtained from our recent work on the sonocatalysis of the reac-

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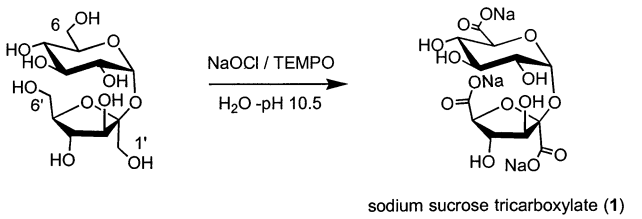


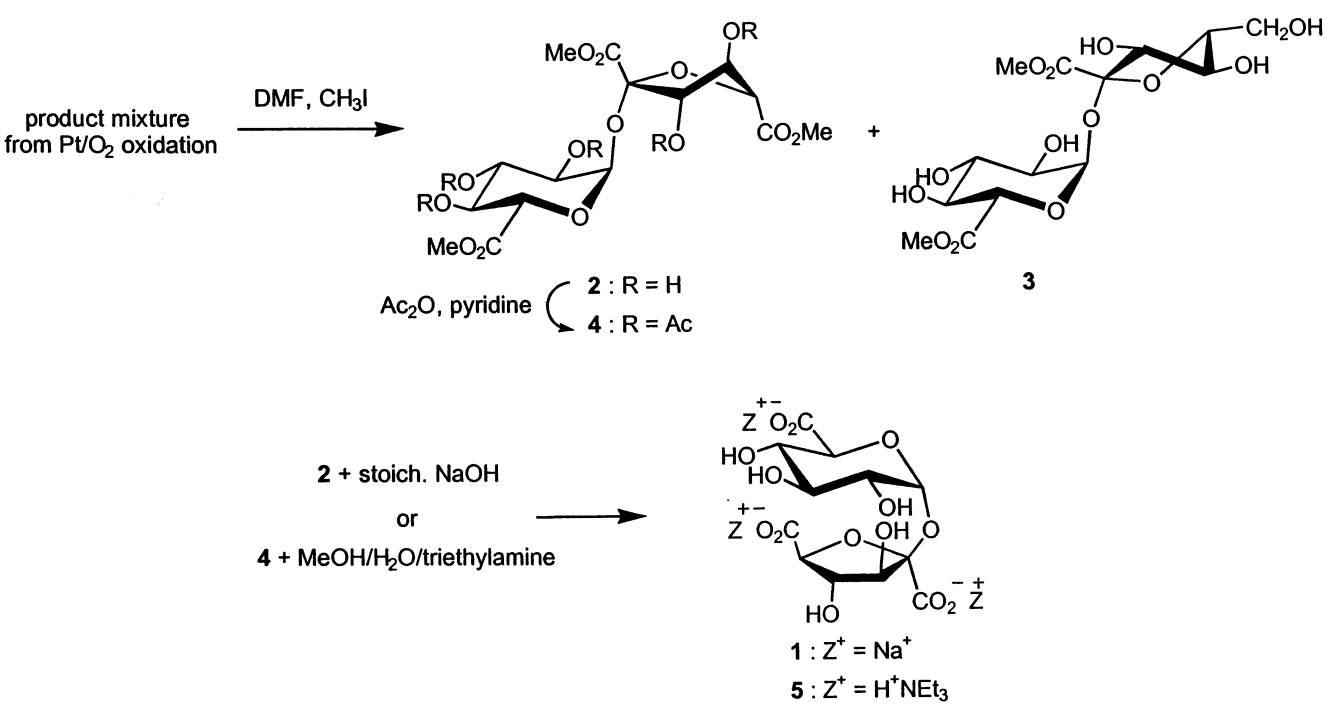
Scheme 1.

tion [29] using methyl α-D-glucopyranoside as model substrate, showing that the reaction can proceed without sodium bromide, as well as from the results reported in a patent claiming that upon heating, sodium bromide was not essential [30]. When high-frequency ultrasound (500 kHz) was applied to the system, we observed an acceleration of the process. We now report our results in the bleach-TEMPO oxidation of sucrose for which little is available in the literature [23,31], with a focus on the effect of ultrasonic waves [32–34].

2. Results and discussion

An aqueous solution of sucrose was treated with sodium hypochlorite (2.2 equivalents), in the presence of sodium bromide and TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy, 0.4 mol equivalents and 0.0065 molar equivalents, respectively, per primary hydroxyl group), maintained at pH 10.5 by addition of sodium hydroxide (pH-stat) and at ca. 5 °C, the typical conditions optimised by van Bekkum and co-workers [23] (Scheme 1).

Preparation of an authentic sample of sodium or triethylammonium sucrose tricarboxylates.—For identification and quantification purposes, authentic samples of **1** and **5** were prepared from a mixture of carboxylates, obtained by the Pt/O_2 method [6], which was subjected to an esterification–saponification sequence as shown in Scheme 2. Treatment with methyl iodide in DMF afforded a complicated mixture of products, from which the trimethyl ester of the triacid **2** could be isolated, and further transformed (Ac_2O–pyridine) into its penta-*O*-acetyl derivative **4**, which was fully characterised. Comparison of the ^1H NMR spectrum with that of sucrose octaacetate showed the disappearance of the signals corresponding to the protons at positions 6, 1′ and 6′. As observed in the case of the dicarboxy analogues for which NMR data are available [7], H-5 and H-5′ are shifted downfield, as well as H-4′. Also based on the study of NMR spectra (especially δ and J



Scheme 2.

values for H-4′ of the dimethyl ester of the 6,1′-diacid **3** that was isolated as side product, in comparison with the triester **2**), it was possible to establish the conformation of the fructosyl moiety, with an inversion of the twist envelope placing the glucosyl moiety in a pseudo-equatorial orientation for the triester **2** with a pseudo-equatorial H-4′ ($\Delta\delta = +0.43$ ppm, $\Delta J_{3',4'} = -1.9$ Hz), whereas it is in a pseudo-axial orientation for the diester **3**.

Careful alkaline treatment (triethylamine in methanol–water) of the protected triester **4**, followed by co-evaporation with water, led to the tris-(triethylammonium) salt of the triacid **5** free from any other salt. Alternatively, treatment of the triester **2** with stoichiometric amounts of sodium hydroxide led to the sodium tricarboxylate **1**. The structure of the triethylammonium salt **5** was deduced from 2D carbon–proton NMR spectroscopy measurements, allowing the full assignment of all hydrogen and carbon atoms. Carbon atoms at C-5–C-5′, and C-6–C-6′ provide broad signals, resulting probably from an exchange between the salt and protons of the solvent. Similar observations were made in the case of the trisodium salt **1** obtained by semi-preparative size-exclusion chromatography from a mixture prepared by the Pt/O_2 method. This fact was not observed in the case of the crude reaction samples, in which large amounts of salts (e.g., NaCl, NaBr) are present, displacing largely the equilibrium towards the carboxylate species, unlike in pure water.

Effects of ultrasonic waves.—The rate of sodium hydroxide addition is directly related to the oxidation reaction rate, because of the production of one H^+ per catalytic cycle at the TEMPO regeneration step by symproportionation of N–OH and N^+=O. The oxidation of sucrose could thus be analysed through the determination of the rate of addition of base, the volume of added base, the analytical yield (Dionex chromatography), and the ^{13}C NMR spectrum of the crude products. Effects of sucrose concentration, amount of sodium hypochlorite, of sodium bromide, of TEMPO, and the activation conditions on the reaction outcome are reported in Table 1.

Using an excess of sodium hypochlorite led to lower yields. The volume of added base was larger (8.6–13.8 mL) than the stoichiometric amount (7.7 mL), indicating the formation of derivatives containing more than three carboxylic acid functions. In these cases, new peaks in the carboxyl region as well as new anomeric carbons (δ 99.7 and 93.2) were observed in the ^{13}C NMR spectrum corresponding to a pentacarboxylate, which could be isolated in trace amount upon multiple precipitation from water–methanol mixtures. The largest change was for C-2′, which indicates some cleavage of the C-3′–C-4′ bond. Furthermore, the signals corresponding to C-3′ and C-4′ in the tricarboxysucrose salts are absent. This is consistent with a larger sensitivity of the secondary alcohol functions towards oxidation in a furanosyl ring compared with a pyranosyl one [22,23]. If sodium hypochlorite is added stepwise, the side oxidations are less favoured, leading to improved yields [3].

In the preliminary report, we mentioned the possibility of performing the reaction without sodium bromide [29]. We first checked this in the simpler case of the oxidation of methyl α-D-glucopyranoside to sodium (methyl α-D-glucopyranosid)uronate. Without sonication, the reaction was very sluggish, with only 21% conversion after 3 h. Ultrasound appeared to be necessary to complete the reaction, with increased yields based on the conversion of the glucoside, but with a slower reaction rate compared with the reaction in the presence of sodium bromide (Table 2).

The decrease of the reaction rate in the presence of oxygen (in brackets in Table 2) can be attributed to the trapping by O_2 of some of the species that might be involved in the catalysis [35].

It was checked that no reaction occurred under ultrasound either without NaOCl or without TEMPO. This, along with the effect of presonication of the oxidant system (vide infra), might suggest that ultrasound promotes the formation of other species able to participate in the oxidation cycle, increasing the rate of formation of N^+=O cations, as could be the reason for a more efficient reaction in the presence of bromides compared with chlorides.

In the case of sucrose, as for methyl α-D-glucopyranoside, the sonocatalysis permits a

Table 1
Reaction of sucrose at 5 ± 2 °C using 0.4 equivalents of NaBr [a]

Sucrose concentration (mM)	NaOCl (equivalents) [a]	TEMPO (equivalents) [a]	Conditions	Rate [b] (mL of NaOH/min)	**1** [c] (%)
40	2.2	0.0065	[d]	0.8	54
40	2.2	0.0065	20 kHz	1.0	55
40	2.2	0.0065	500 kHz	1.9	74
20	2.2	0.0065	[d]	0.22	68
20	2.2	0.0065	500 kHz	0.39	71
20	2.2	0.025	[d]	0.65	66
20	2.2	0.025	500 kHz	1.37	67
20	2.2	0.06	[d]	0.79	74
20	2.2	0.06	500 kHz	1.41	58
20	2.2	0.125	[d]	1.35	70
20	2.2	0.125	500 kHz	1.45	55
20	2.2	0.20	[d]	2.5	63
20	2.2	0.20	500 kHz	3.4	53
20	3.2	0.0065	[d]	0.27	57
20	3.2	0.0065	500 MHz	0.34	64
20	3.2	0.0065	[d,e]	0.18	16
20	3.2	0.0065	500 MHz [e]	0.36	63
20	3.2	0.125	[d]	2.1	21 [f]
20	3.2	0.125	500 MHz	2.8	46 [f]
20	2.2 Fraction [g]	0.0065	[d]	0.13	78
20	2.2 Fraction [g]	0.0065	500 MHz	0.20	80

[a] Per primary hydroxyl groups.
[b] Maximum slope of the base addition versus time.
[c] Analytical yield (ion exchange chromatography).
[d] Without sonication.
[e] Reaction stopped after the stoechiometric amount of base added.
[f] 175% base addition indicating overoxidation.
[g] NaOCl added in 10 portions.

Table 2
Oxidation of methyl α-D-glucopyranoside to sodium (methyl α-D-glucopyranosid)uronate: influence of the presence of sodium bromide (reactions stopped after 3 h) [a]

Conditions	NaOH addition rate [b] (mL/min)		Glucoside conversion [c] (%)		Yield [d] (%)		Yield/conversion	
	no Br^-	Br^-	no Br^-	Br^-	no Br^-	Br^-	no Br^-	Br^-
Without sonication		0.7	21	97	19	74	90	76
	(–)		(29)		(12)		(41)	
20 kHz, 0.26 W/mL, 13 mm probe	0.1	0.9	69	98	59	74	86	77
500 kHz, 0.22 W/mL, 35 mm probe	0.3	1.9	84	96	82	63	98	64
	(0.2)		(71)		(69)		(98)	

[a] Same conditions as in Table 1 except for sodium bromide; in brackets are given the results for the reaction in the presence of oxygen.
[b] Maximum slope of the base addition versus time.
[c] Measured by HPLC on NH_2-grafted column.
[d] Analytical yields (anion exchange chromatography).

reaction in the absence of sodium bromide (Fig. 1), although with a smaller conversion rate when only 0.65 mol% of TEMPO was used. This is due to the relative rates of the oxidation and to the decomposition of sodium hypochlorite, potentially affected by ultra-

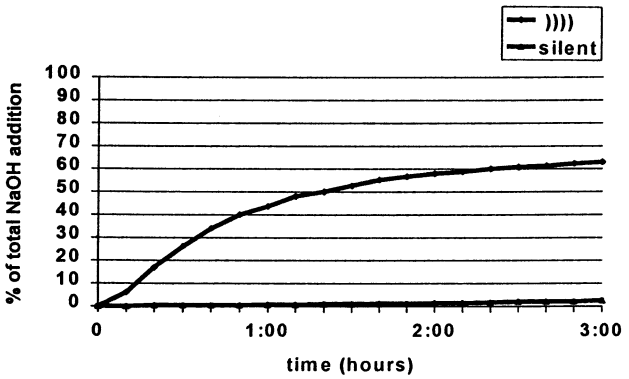


Fig. 1. Addition of base as a function of time for the oxidation of sucrose (2.2 equivalents of NaOCl, 0.0065 equivalents of TEMPO, no NaBr) with or without sonication (500 kHz).

sound [36], preventing the completion of the reaction even when sodium hypochlorite was added stepwise. Since excess of sodium hypochlorite led to overoxidation, the alternative was to increase the rate of the reaction by using larger amounts of TEMPO, but keeping it well below the stoichiometric amount (Table 3). The optimised conditions in the absence of sodium bromide are the use of 0.06 equivalents of TEMPO, providing a 79% analytical yield of sodium sucrose tricarboxylate in less than 2 h at 5 °C.

In a final set of experiments, we investigated the effect of the presonication of the oxidant mixture (30 min at 5 °C) in the absence of sucrose. Compared with the classical reaction, this procedure led to a much faster reaction: using 0.65 mol% of TEMPO and in the presence of NaBr, reaction rates were 0.94 and 0.33 mL/min (for reactions with or without continued sonication after sucrose addition, respectively), compared with 0.39 and 0.22 mL/min for the corresponding reactions without presonication (Table 1). The yield of the reaction combining ultrasound before and during the sucrose oxidation was increased to 86% compared with 71%, whereas the 'presonicated' reaction further conducted without sonication, provided a 56% instead of 68% yield. Using 6 mol% of TEMPO and in the absence of NaBr, rates were also increased (3.0 and 0.74 mL/min, respectively, compared with 0.6 and 0.13 mL/min), showing an acceleration ratio larger than the regular classical sonochemical one. These observations are consistent with a faster $N–O^{\bullet} \rightarrow N^{+}=O$ oxidation step mediated by ultrasound.

Table 3
Reaction of sucrose at 5 ± 2 °C without NaBr

Sucrose concentration (mM)	NaOCl (equivalents) [a]	TEMPO (equivalents) [a]	Conditions	Rate [b] (mL of NaOH/min)	**1** [c] (%)
40	2.2	0.0065	[d]		
40	2.2	0.0065	20 kHz	0.16	23
40	2.2	0.0065	500 kHz	0.17	18
40	4.4	0.0065	500 kHz	0.26	9
40	2.2	0.06	[d]	0.13	16
40	2.2	0.06	500 kHz	0.6	79
40	2.2	0.125	[d]	0.25	16
40	2.2	0.125	500 kHz	0.86	71
40	2.2	0.20	[d]	2.2	41
40	2.2	0.20	500 kHz	4.8	63
40	3.2	0.06	[d]	0.35	29
40	3.2	0.06	500 kHz	1.18	48
40	2.2 Fraction [e]	0.06	[d]	0.09	26
40	2.2 Fraction [e]	0.06	500 kHz	0.18	48
80	2.2	0.06	[d]	0.5	50
80	2.2	0.06	500 MHz	3.4	72

[a] Per primary hydroxyl groups.
[b] Maximum slope of the base addition versus time.
[c] Analytical yield (ion exchange chromatography).
[d] Without sonication.
[e] NaOCl added in 10 portions.

3. Conclusions

The sonocatalysis of the TEMPO-mediated oxidation is confirmed in the case of sucrose. Ultrasound could act at the level of the formation of the nitrosonium (N^+=O) salt through an easier formation of oxidant species, potentially via homolytic cleavage of chlorine or bromine or their hypohalous acids. Sucrose tricarboxylate can thus be obtained in good yields without the usually necessary sodium bromide. These observations provide new elements on the role of the bromide ions in the catalytic process even under conventional conditions.

4. Experimental

General.—Methyl α-D-glucopyranoside was purchased from Sigma, whereas all other chemicals were purchased from Aldrich. Sucrose was obtained from Béghin-Say S.A. Reactions were monitored by thin-layer chromatography (TLC) using aluminium Silica Gel plates (60 F254). Flash-chromatography separations were performed using E. Merck Silica Gel 60H (40–63 μ) under 1 bar pressure. Chromatography solvents were purchased from Carlo–Erba S.A. Nuclear magnetic resonance spectra were recorded on Bruker spectrometers at frequencies from 200 to 500 MHz for ^{1}H and from 50 to 125 MHz for ^{13}C. FAB mass spectra were recorded with Zab2-Seq VG Micromass (for compound **5**) and ZabSpec TOF Micromass (for compound **1**) instruments. Semi-preparative size-exclusion chromatography was performed on Biogel P2 (Bio–Rad) and elution with water with RI detection. Analytical ion-exchange chromatography was performed on a DIONEX DX-500 chromatograph using a Carbopac PA1 column (4 × 250 mm) with electrochemical detection (PED) in pulse amperometric mode (Au and Ag/AgCl electrodes, with a + 0.1, + 0.6, − 0.8 V pulsation cycle) and elution with NaOH and NaOAc mixtures (0–3 min: 40% 200 mM NaOH–10% 1 M NaOAc in 100 mM NaOH–50% water; 3–10 min: linear gradient, 30% 200 mM NaOH–40% 1 M NaOAc in 100 mM NaOH–30% water; 10–25 min: 30% 200 mM NaOH–40% 1 M NaOAc in 100 mM NaOH–30% water; flow rate 1 mL/min). Accuracy was 2–6% over the 15–80% yield range, as estimated from different assays. Results given in the Tables are mean values over two or three measurements.

Ultrasound equipment.—For the experiments at 20 kHz, the ultrasound generator was a 300 W (electric power) Vibra-Cell apparatus, coupled with titanium horns having a 13, 25 or 35 mm diameter (0.1 to 0.6 W/mL acoustic power). Acoustic power was evaluated by calorimetric measurement. For the 500 MHz experiments, the transductor is a lead titanate–zirconate ceramic pasted together with a stainless steel plate (35 mm diameter, 0.08 to 0.22 W/mL acoustic power).

Hydrogen peroxide titration.—The hydrogen peroxide formation rate was evaluated by the iodometric method (I_3^- ions are quantified at 352 nm). The starting soln (pH 2, aq H_2SO_4) was degassed by bubbling argon for 15 min before the ultrasonic irradiation at 15 °C. Samples (250 μL) were taken at intervals of 10 min for 1 h. Potassium iodide (0.1 M) and ammonium molybdate $(NH_4)_6Mo_6O_{24}\cdot 4H_2O$ (0.1 mM) were kept refrigerated and in the dark before use. Absorbance at 352 nm was measured after a 10 min delay and compared with a calibration curve.

General procedure for the oxidation reactions.—The same systems were used for both the classical and the sonochemical reaction. A connection to a second flask allowed the permanent presence of the electrode of the pH-stat without any risk of deterioration due to ultrasound. Temperature was maintained by fluid circulation and measured using a thermocouple. The reaction volume was 200 mL. To a solution of the carbohydrate substrate (8 mmol based on primary hydroxyl group, i.e., 1.55 g of methyl α-D-glucopyranoside or 0.91 g of sucrose) was added NaBr (0.32 g, 0.4 equiv per primary hydroxyl group) and TEMPO (8 mg for 0.65 mol% per primary hydroxyl group). This mixture was cooled at 5 °C. An approx 12% NaOCl soln (typically 8.5 mL, 2.2 equiv based on primary hydroxyl groups) adjusted at pH 10 by addition of 4 M HCl and also cooled at 5 °C was added to the

reaction mixture, and the pH was adjusted to 10.5 by addition of 0.5 M NaOH. The reaction temperature was maintained at 5 ± 2 °C and the pH was kept constant by addition of 0.5 M NaOH. The reaction was stopped (most often after that a stoichiometric amount of base was added) by quenching excess oxidant with EtOH (10 mL) and the mixture was neutralised by addition of 4 M HCl. The resulting solution was then concentrated, freeze-dried and identified by ion exchange chromatography and NMR spectroscopy in comparison with authentic standards prepared as described in the following section. In the case of overoxidation of sucrose, a pentacarboxylate was detected in the reaction mixture [^{13}C NMR (D_2O, 50 MHz): δ 71.6, 72.7, 73.3, 73.6, 78.7 (C-2,3,4,5,5′), 93.2 (C-1), 99.7 (C-2′), 173.1, 173.8, 174.3, 175.4, 177.6 (5 COONa)].

An analytical sample of sodium (methyl α-D-glucopyranosid)uronate was prepared by precipitation of a concd aq soln with EtOH. The solid was washed with a 7:3 EtOH–water mixture and the structure was confirmed by ^{13}C NMR (50.32 MHz, D_2O): δ (ppm) 55.4 (OMe), 71.5 (C-2), 72.5 (C-4,5), 73.4 (C-3), 99.8 (C-1), 177.2 (C-6) [17]. The amount of sodium ions (chloride and bromide) was quantified by analytical ion chromatography using an AS11 (4×250 mm) column on the Dionex DX-500 system (30% 5 mM NaOH–70% water, flow rate 2 mL/min).

Preparation of a calibration sample of triethylammonium sucrose tricarboxylate.—A 10 g crude sample of sodium sucrose tricarboxylate, prepared by the Pt/O_2 method [6] (possibly containing small amounts of corresponding mono- or dicarboxylates), was mixed with anhyd DMF (20 mL) and methyl iodide (20 mL). The mixture was stirred at room temperature (rt) in the dark for 15 days. The solvents were evaporated and the residue was purified by flash-chromatography (30:10:9:1 CH_2Cl_2–MeOH–acetone–water). Among fractions containing the desired product (R_f 0.4), the purest was evaporated providing the trimethyl ester **2** as an oil (1.7 g, 18%). ^{1}H NMR (CD_3OD, 300 MHz): δ 5.43 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.47 (d, 1 H, $J_{4,5}$ 9.9 Hz, H-5), 4.45 (dd, 1 H, $J_{3',4'}$ 6.3, $J_{4',5'}$ 7.0 Hz, H-4′), 4.37 (d, 1 H, H-3′), 4.29 (d, 1 H, H-5′), 3.77, 3.81, 3.84 (3s, 9 H, 3 OMe), 3.75 (t, 1 H, $J_{2,3}$ 9.6, $J_{3,4}$ 9.2 Hz, H-3), 3.51 (dd, 1 H, H-2), 3.47 (dd, 1 H, H-4) 3. ^{13}C NMR (CD_3OD, 75 MHz): δ 172.5, 171.6, 169.9 (C-6,1′,6′), 104.6 (C-2′), 96.3 (C-1), 82.0, 80.7, 77.3, 74.5, 74.0, 73.7, 73.2 (C-2,3,4,5,3′,4′,5′), 53.9, 53.1, 53.0 (OMe). Partial separation led to the isolation of a small amount of the dimethyl ester **3** (R_f 0.33). ^{1}H NMR (CD_3OD, 300 MHz): δ 5.51 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.41 (d, 1 H, $J_{4,5}$ 9.2 Hz, H-5), 4.29 (d, 1 H, $J_{3',4'}$ 8.2 Hz, H-3′), 4.02 (t, 1 H, $J_{4',5'}$ 8.2 Hz, H-4′), 3.93 (m, 1 H, H-5′), 3.81, 3.84 (2s, 6 H, 2 OMe), 3.76 (m, 3 H, H-3,6′ab), 3.60 (t, 1 H, $J_{3,4}$ 9.2 Hz, H-4), 3.55 (dd, 1 H, $J_{2,3}$ 9.2 Hz, H-2); ^{13}C NMR (CD_3OD, 75 MHz): δ 172.0, 171.0 (C-6,1′), 103.1 (C-2′), 95.7 (C-1), 84.8, 81.1, 75.2, 74.4, 74.0, 73.0, 72.9 (C-2,3,4,5,3′,4′,5′), 63.4 (C-6′), 54.0, 53.3 (OMe).

Preparation of the peracetylated triester **4**.—Triester **2** (0.2 g, 0.47 mmol) was treated in 10 mL of a 1:1 pyridine–Ac_2O mixture for 12 h at rt. After evaporation of the solvent (co-evaporation with toluene), silica gel chromatography of the residue (1:1 EtOAc–hexane) provided the peracetylated triester **4**, as a white solid (80 mg, 27%); $[\alpha]_D^{21}$ +38 (*c* 1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.91 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.62 (t, 1 H, $J_{3',4'} = J_{4',5'}$ 6.6 Hz, H-4′), 5.52 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 9.6 Hz, H-3), 5.49 (d, 1 H, H-3′), 5.12 (dd, 1 H, $J_{4,5}$ 10.6 Hz, H-4), 4.88 (dd, H-2), 4.61 (d, 1 H, H-5), 4.52 (d, 1 H, H-5′), 3.78, 3.74, 3.72 (3 s, 9 H, 3 CO_2Me), 2.18, 2.09, 2.05, 2.02, 2.01 (5 s, 15 H, 5 Ac); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.2, 169.8, 169.7, 169.6, 169.5 (5 Ac), 168.2, 167.9, 166.1 (C-6,1′,6′), 101.1 (C-2′), 92.1 (C-1), 78.7, 78.3, 75.4, 69.7, 69.2, 69.0, 68.4 (C-2,3,4,5,3′,4′,5′), 53.2, 52.8, 52.6 (3 OMe), 20.6, 20.5, 20.4, 20.0 (5 Ac). Anal. Calcd for $C_{25}O_{19}H_{32}$: C, 47.18; H, 5.07. Found: C, 47.08; H, 5.09.

Deacetylation and saponification of **4** was achieved by careful treatment with a 8:1:1 MeOH–NEt_3–water mixture at rt. Slow deprotection of the three methyl ester functions was followed over a 21 day period by TLC (7:32 propan-2-ol–water). The mixture was then co-evaporated several times with water in order to eliminate all the triethylammonium

acetate formed, thus producing the pure triethylammonium sucrose tricarboxylate **5** in quantitative yield. 2D C–H NMR spectroscopy at 300 and 500 MHz allowed full assignment of all patterns: ^{1}H NMR (D_2O, 300 MHz): δ 5.52 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.17 (t, 1 H, $J_{3',4'}$ 7.8, $J_{4',5'}$ 7.0 Hz, H-4′), 4.09 (d, 1 H, H-5′), 4.08 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-5), 4.07 (d, 1 H, H-3′), 3.73 (t, 1 H, $J_{3,4}$ 9.5, $J_{2,3}$ 9.8 Hz, H-3), 3.44 (dd, 1 H, H-2), 3.34 (t, 1 H, H-4), 3.20 (q, 8 H, $J = 7$ Hz, 3 Et), 1.30 (t, 9 H, 3 Et); ^{13}C NMR (D_2O, 125 MHz): δ 176.9, 175.9 (C-6,6′), 174.7 (C-1′), 103.5 (C-2′), 93.9 (C-1), 80.1 (C-5′), 79.7 (C-3′), 75.7 (C-4′), 73.7 (C-5), 73.3 (C-3), 72.2 (C-4), 71.5 (C-2), 46.6 (Et), 8.3 (Et). High-resolution FABMS (thioglycerol matrix): calcd for $C_{24}H_{47}O_{14}N_2$: m/z 587.3027; found 587.3010 $[(M - HNEt_3 + 2H)]^+$. Treatment of the triester **2** (30 mg) in MeOH (4.3 mL) with NaOH (0.1 N, 1 equiv) at rt led to the corresponding sodium salt **1** which could be further purified by size-exclusion chromatography using Biogel P6 and elution with water. ^{1}H NMR (D_2O, 300 MHz): δ 5.44 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.24 (t, 1 H, $J_{3',4'} = J_{4',5'}$ 7.7 Hz, H-4′), 4.17 (d, 1 H, $J_{4,5}$ 9.8 Hz, H-5), 4.17,4.15 (2 d, 2 H, H-3′, H-5′), 3.84 (t, 1 H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 3.55 (dd, 1 H, H-2), 3.41 (t, 1 H, H-4), ^{13}C NMR (D_2O, 75 MHz): δ 177.3, 176.9 (C-6,6′), 174.9 (C-1′), 104.1 (C-2′), 94.6 (C-1), 80.6 (C-5′), 79.9 (C-3′), 76.2 (C-4′), 73.5 (C-5), 73.3 (C-3), 72.4 (C-4), 71.7 (C-2). High-resolution FABMS for **1** (glycerol matrix): calcd for $C_{12}H_{14}O_{14}Na_3$: m/z 451.0077; found 451.0097 $[M + H]^+$.

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