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PREPARATION OF TRIHYDROXYCARBOXYLATES BEARING A LONG-CHAIN ALKYL ACETAL GROUP FROM GLUCONO-1,5-LACTONE

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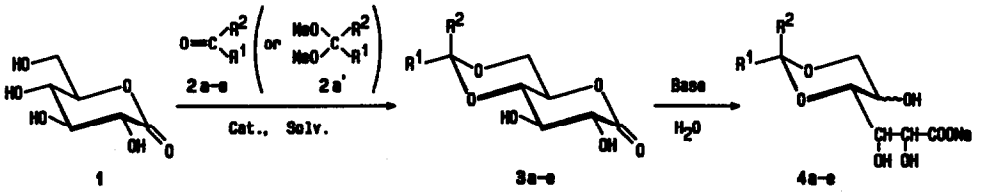
Summary: Title compounds could be easily prepared by the acetalization of glucono-1,5-lactone with long-chain alkyl carbonyl compounds followed by alkaline hydrolysis. These carboxylates can be utilized as a new type of cleavable surfactant.

Sucrose fatty acid esters[1] and alkylglycosides[2] are representative amphipathic compounds derived from saccharides. Recently, they have been produced on an industrial scale and widely utilized as surfactants for food, cosmetics, drugs, or in the biochemical field.[3] Such saccharide-derived materials have become a focus of great interest again because they not only have excellent surface active properties but also saccharides are vast natural resources and they are safe for human use.

Glucono-1,5-lactone (**1**) is an oxidation product of glucose and an easily accessible commercial material. In this work, we found that new saccharide derivatives (**4**) could be obtained by a one-pot reaction of the acetalization of **1** with long-chain alkyl aldehydes or ketones (**2**), followed by alkaline hydrolysis (SCHEME). The protection of hydroxyl groups in saccharides with an isopropylidene or a benzylidene group is a well-known operation,[4] but to our knowledge there has been no systematic study from the synthetic standpoint on the saccharide derivatives bearing a long-chain alkyl acetal group. It is well known there is some difference in reactivity, reaction conditions, or work-up procedures between long-chain aliphatic compounds and short-chain aliphatic or aromatic compounds.

Newly obtained carboxylates **4** are amphipathic compounds. It is expected that they will be stable and will show surface active properties under neutral and basic conditions, but they will be decomposed into non-surface active species under acidic conditions. Thus compounds **4** can be utilized as a new natural-origin type of cleavable surfactant.[5]



SCHEME

TABLE Preparation of Carboxylates 4.

Run No.	2,3,4	R^1	R^2	Reaction Conditions[a] TsOH(mol ratio)	Solv.[b]	(mmHg)	(h)	Yield[c] (%)
1	**a**	$C_{11}H_{23}$	H	0.2	DMF	≈40	12	58
2	**a**	"	"	"	DMSO	"	"	24
3	**a**	"	"	0.1	DMAc	"	"	37
4	**a**	"	"	0.2	"	"	"	46
5	**a**	"	"	0.6	"	"	"	70
6	**a**	"	"	1.0	"	"	"	59
7	**a**	("	")[d]	0.1	DMF	"	10	40
8	**a**	("	")[d]	"	"	≈760	24	42
9	**b**	C_8H_{17}	CH_3	0.2	"	≈40	12	32
10	**c**	C_9H_{19}	"	"	"	"	"	29
11	**d**	$C_{11}H_{23}$	"	"	"	"	"	49
12	**e**	(geranyl)[e]	"	"	"	"	"	21

a. Reaction temp. at 80°C, **1**:**2** = 1.2:1.0 (molar ratio).
b. DMF: dimethylformamide, DMSO: dimethylsulfoxide, DMAc: dimethylacetamide.
c. Isolated yield of **4** based on **2**.
d. $C_{11}H_{23}CH(OCH_3)_2$ (**2a'**) was used instead of **2a**.
e. geranyl: $(CH_3)_2C{=}CH(CH_2)_2(CH_3)C{=}CH(CH_2)_2$-.

Typical synthetic procedures for carboxylate **4** are as follows (in the case of **4a**): A 100-mL round-bottom flask containing 2.14 g of **1** (12 mmol), 1.84 g of dodecanal (**2a**; 10 mmol), 0.40 g of p-toluenesulfonic acid monohydrate (TsOH; 2 mmol), and 30 mL of dry DMF was attached to a rotary evaporator. The reaction mixture became homogeneous immediately. The flask was rotated for 12 h in a water bath adjusted at about 80°C under reduced pressure (≈40 mmHg). After DMF was evaporated off at about 80°C/1 mmHg, a 50 mL aqueous solution of sodium bicarbonate (4.20 g, 50 mmol) was added to the residue. This mixture was stirred and heated under atmospheric pressure until the

reaction mixture became homogeneous. White solids precipitated from the solution when the flask was allowed to cool. Following filtration, the insoluble solids were washed with cold water and ethanol several times. After drying under reduced pressure, 2.22 g of **4a** was obtained as a white powder[6] (58 % yield). The intermediate compound, 4,6-O-dodecylideneglucono-1,5-lactone (**3a**),[7] could be isolated as a white solid by extraction of the acetalized products with a water/ether solvent system followed by recrystallization from chloroform (21 % yield).

The preparation results of carboxylates **4a-e** under various acetalization conditions are summarized in the table. The acetalization reaction was carried out under reduced pressure at about 80°C to eliminate water liberated during the reaction (except run 8). A satisfactory result was obtained when the molar ratio of **1** to **2** was 1.2. A large excess of **1** over **2** was not so effective because some elaborate work-up procedures such as column chromatography were required to separate **4** from sodium gluconate derived from unreacted **1**.

The acetalization process could be monitored by measuring the amount of unreacted **1** in the silanized reaction mixture with GLC (column: 3 % silicone SE-30 on Celite 545, 1 m glass). Three solvents[8] which dissolved **1** and didn't evaporate during the reaction under reduced pressure using water-jet aspirator were chosen. DMF (bp 150°C/760 mmHg) and DMAc (bp 165°C) afforded similar results (runs 1 and 4). In the case of DMSO (bp 189°C), however, the isolated yield of **4** was not so good in spite of the completion of the acetalization (run 2), probably because a small amount of residual DMSO in the hydrolysis reaction mixture might prevent **4** precipitating from the solution. When 0.1 molar equiv of TsOH was used, the isolated yield was relatively low (runs 3, 9, and 10). In these cases, unreacted **1** still remained even after 12 h. The isolated yield was improved by using more than 0.2 molar equiv TsOH (runs 4-6). The reaction time required at least more than 8 h to achieve complete acetalization. It is surmised that the lower yields of **4b-e** from ketones compared to **4a** may be attributed mainly to the moderate water solubility of these compounds (runs 9-12). Especially, because **4e** derived from geranylacetone has good water solubility, the investigation of other solvents for recrystallization is desirable. A similar result was obtained by using dodecanal dimethyl acetal (**2a'**) instead of **2a** (run 7). In the case of **2a'**, the acetalization reaction could be carried out under atmospheric pressure because methanol instead of water was liberated during the reaction (run 8).

The alkaline hydrolysis of crude **3** was very easy as described in the typical procedures. The probable structure of carboxylates **4** is illustrated in SCHEME,[9] which is expected based on their NMR data[6,7] and some previous reports about the acetalization of saccharides.[4]

Aqueous solutions of these carboxylates **4** under basic conditions (pH 11) have surface active properties. Especially, **4a** and **4d** showed clear cmc values as follows: **4a**; 1.5×10^{-3} M (at 50°C, γ_{cmc} = 29.0 mN/m), **4d**; 3.0×10^{-3} M (at 40°C, γ_{cmc} =

38.0 mN/m), which were measured with a Wilhelmy tensiometer.

Detailed investigations of their surface active properties and their acid-decomposition profiles are now in progress.

References and Notes

1. For example: T.Yamada, N.Kawase, and K.Ogimoto, Yukagaku, **29**, 543(1980). (Chem. Abstr. **93**:151979x)
2. For example: D.E.Koeltzow and A.Urfer, JAOCS, J.Am.Oil Chem.Soc., **61**, 1651(1984); T.Böcker and J.Thiem, Tenside, Surfactants, Deterg., **26**, 318(1989).
3. P.A.Egan, CHEMTECH, 758(1989).
4. For example: A.N.de Belder, Adv.Carbohydr.Chem., **20**, 220(1965); R.F.Brady,Jr., ibid., **26**, 197(1971); D.M.Clode, Chem.Rev., **79**, 491(1979).
5. For example: D.A.Jaeger and M.R.Frey, J.Org.Chem., **47**, 311(1982); D.A.Jaeger, J.Jamrozik, T.G.Golich, M.W.Clennan, and J.Mohebalian, J.Am.Chem.Soc., **111**, 3001 (1989); D.Ono, A.Masuyama, and M.Okahara, J.Org.Chem., in press.
6. Physical data of **4a**: white solid, mp 212-214°C(dec). IR(Hitachi 260, KBr): 3490, 3220, 2920, 2850, 1620, 1460, 1400, 1260, 1140, 1050, 950 cm^{-1}. FAB-MS[JEOL JMS-DX303, m/e, rel.int.]: 407[$(M+Na)^+$,78], 385[$(M+H)^+$,10], 118[100]. ^1H NMR[Bruker AM-600(600 MHz), $(CD_3)_2SO$, DSS as an internal standard, 70°C]: δ 0.88(t,3H), 1.27-1.37(m,18H), 1.53(m,2H), 3.54-3.64(m,2H), 3.66(dd,1H), 3.75(m,1H), 3.92(dd,1H), 4.01 (m,1H), 4.77(t,0.5H), 4.87(t,0.5H), excluded DMSO overlapping region (from 2.7 to 3.5 ppm). ^{13}C NMR: δ 15.27, 23.49, 25.04, 25.09, 30.12, 32.76, 35.27, 35.33, (41.1-42.6: DMSO overlapped), 68.21, 73.06, 73.39, 77.00, 77.42, 105.19, 176.92. Anal. Found(calcd for $C_{18}H_{33}O_7Na$): C, 56.24(56.17); H, 8.65(8.65). Probable structures of all other compounds (**4b-e**) were similarly ascertained by their spectral data and elemental analyses.
7. Physical data of **3a**: white solid, mp 104-106°C. IR(KBr): 3450, 3300, 2960, 2940, 2850, 1760, 1470, 1420, 1240, 1220, 1100, 1050, 960 cm^{-1}. FAB-MS(m/e, rel.int.): 367[$(M+Na)^+$,5], 345[$(M+H)^+$,49], 154[100]. ^1H NMR[$(CD_3)_2CO$, TMS as an internal standard, 27°C]: δ 0.88(t,3H), 1.30-1.45(m,18H), 1.60(m,2H), 3.85-4.00(m,1.5H), 4.15(m,1.5H), 4.35-4.45(m,2H), 4.60-5.05(m,2H+1H, the 1H disappeared on addition of D_2O), 5.43(d,1H,disappeared on addition of D_2O). ^{13}C NMR: δ 14.35, 23.33, 24.72, (29.00-30.72: acetone overlapped), 32.64, 34.76, 67.45, 73.85, 74.90, 75.13, 82.37, 105.39, 175.30. Anal. Found(calcd for $C_{18}H_{32}O_6$): C, 62.33(62.77); H, 9.27(9.36).
8. There is a previous report that DMF was used as a solvent in the preparation of 4,6-O-benzylidene-methyl-α-D-glucopyranoside under reduced pressure; M.E.Evans, Carbohydr.Res., **21**, 473(1972).
9. Because the ^1H NMR peaks of **4a-e** in the range from 3.5 to 4.4 ppm show complex coupling manners, the presence of some stereoisomers is suggested.

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