

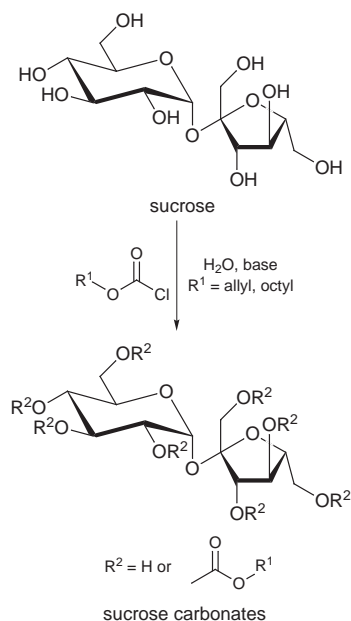
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Mono-*O*-allyloxycarbonyl sucrose derivatives have been prepared by reaction of unprotected sucrose with allyl chloroformate in pure water, whereas the presence of a co-solvent is necessary in the case of the reaction with octyl chloroformate, for which polysubstitution is favoured because of hydrophobic interactions.

## Introduction

The most attractive targets for the chemical utilization of sucrose as a raw material are tensioactive derivatives and polymerizable compounds, and often, the applications necessitate the synthesis of mono- or di-substituted derivatives.<sup>1</sup> Economically, the direct transformation of sucrose without any protection step is the most important requirement. However the chemistry of unprotected sucrose is limited by the choice of solvents which are either expensive, or difficult to remove. Among the few solvents able to solubilize unprotected sucrose, water, with the highest sucrose solubility (2.6 M, 67% w/w at 20 °C) and with its non-toxicity and cheapness, has always been an attractive medium for sucrochemistry. We report herein the first preparation of allyl- and octyl-oxycarbonyl derivatives of sucrose by reaction with chloroformates using unprotected sucrose in aqueous medium (Scheme 1).



Scheme 1

## Results and discussion

Chloroformates are widely used in synthetic organic chemistry since they lead, by reaction with amines or alcohols, respectively to carbamates and carbonates which are useful protecting

**Table 1** Influence of the pH on the yield of monocarbonate obtained from the reaction of sucrose (40% w/w solution in water) with allyl chloroformate 0.25 equiv.)

pH <sup>a</sup>	DMAP (mol%) <sup>b</sup>	T/°C	t/min <sup>c</sup>	Yield <sup>d</sup> (%)
7		10	330	49
7		23	110	55
7	1	19	75	24
7	10	2	72	47
8		2	170	68
8	1	2	60	62
9		2	35	65
10		2	120	57
10		2	40	74
10		2	20 <sup>e</sup>	77
10		2	18 <sup>f</sup>	44
11		3	34	46

<sup>a</sup> NaOH, pH-Stat. <sup>b</sup> DMAP, based on chloroformate. <sup>c</sup> Chloroformate is added dropwise over 30 min. <sup>d</sup> Isolated yields after silica gel chromatography. <sup>e</sup> Addition in 15 min. <sup>f</sup> Addition in one portion.

groups. The reaction medium is often an organic solvent, except for amines which are sufficiently nucleophilic to react much faster than water.<sup>2</sup> Bis(alkyl carbonates) can also be prepared, as well as cyclic carbonates in the case of glycols, although a *cis* relationship is generally required. For unprotected polyols, group migrations usually occur as in the case of esters of alkanic acids. We first examined the reaction of unprotected sucrose with allyl chloroformate using water as the solvent.<sup>3</sup>

Dropwise addition of allyl chloroformate to an aqueous sucrose solution (4-fold excess) provided mainly monosubstituted allyloxycarbonylated sucrose derivatives in moderate to good yields depending on the reaction conditions (Table 1).<sup>4</sup> More substituted derivatives were also obtained and identified as being mostly dicarbonates although they were not fully characterized. First, the influence of the pH on the yield and the reaction rate was studied. As a result of the competition between the esterification rate and the hydrolysis either of the chloroformate or the products, the best balance between the reaction time and the yield was obtained for pH 10 at 2 °C, although good yields were also obtained at lower pH (8) but in a sluggish reaction. Sucrose carbonates were also obtained under neutral conditions, although in lower yields. Low reaction rates led to extensive competitive chloroformate hydrolysis in this case. When adding DMAP as catalyst in order to speed up the reaction, satisfactory yields were not observed below pH 8. On the other hand under more basic conditions (pH 11), the hydrolysis of the products led to lower yields. In this case, the more substituted products were present in much smaller amounts, indicating a faster hydrolysis compared to the monocarbonates.

As the sucrose–water interactions are known to influence the outcome of some chemical transformations,<sup>5</sup> we studied the effects of increasing the concentration of the starting sucrose solution in water. Faster reaction rates were observed when the reaction was conducted at pH 10 without any other catalyst or

**Table 2** Reaction of sucrose (10% solution, w/w) with octyl chloroformate (0.25 equiv., 15–40 min addition time) in various basic conditions

Solvent	pH <sup>b</sup>	DMAP <sup>c</sup> (equiv.)	T/°C	t/h	Monosubstituted carbonates (%) <sup>d,e</sup>
Water	10	—	rt	18	— <sup>e</sup>
Water	10	0.1	rt	0.3	8 <sup>e</sup>
Water	10	—	0	4.5	—
Water	10	0.01	0	3	9 <sup>e</sup>
Water	9	0.01	0	1.5	13 <sup>e</sup>
Water	10.5 to 11.7 <sup>f</sup>	2	0	0.3	14 <sup>e,g</sup>
9:1 Water–THF	10	—	0	4.5	—
9:1 Water–THF	10	0.01	1	1.5	18 <sup>e</sup>
9:1 Water–THF	10	0.1	3	0.7	16 <sup>e</sup>
1:1 Water–THF	10	0.1	1	0.8	72 <sup>e</sup>
1:1 Water– propan-2-ol	10	0.1	1	0.8	76 <sup>e</sup>

<sup>a</sup> w/w. <sup>b</sup> pH-stat, NaOH. <sup>c</sup> Based on chloroformate. <sup>d</sup> Isolated yield after flash chromatography. <sup>e</sup> Polysubstituted carbonates detected by TLC and found in the faster moving fractions of the flash chromatography. <sup>f</sup> No NaOH. <sup>g</sup> Analytical yield (HPLC) after extraction with butan-2-ol.

at pH 8 in the presence of 1 mol% of DMAP, but the yields of mono-*O*-allyloxycarbonyl sucrose derivatives were only slightly increased. The selectivity (in terms of degree of substitution) was not influenced by the water–sucrose ratio. In order to compare this behaviour with that of other esters,<sup>6,7</sup> we turned to the case of a more lipophilic chloroformate. The reaction of unprotected sucrose with octyl chloroformate<sup>3</sup> was conducted under the conditions used for the allyl derivative (40% w/w sucrose in water), but no trace of monosubstituted products could be detected in the highly heterogeneous reaction mixture. Thin layer chromatography indicated the presence of poly-*O*-allyloxycarbonyl sucrose derivatives, which could also be isolated by flash chromatography but were not identified further because of the complexity of the mixture. This propensity towards polysubstitution can be explained by the effect of water which forces hydrophobic molecules to aggregate. Moreover, it has been shown that the presence of sucrose increases this phenomenon.<sup>5</sup>

Since changing the pH or temperature conditions did not provide any improvement in the formation of monosubstituted products, we then used dilute sucrose solutions (10% w/w). As shown in Table 2, the reaction provided monosubstituted carbonates only in the presence of DMAP, even though the yields were not satisfactory. Increasing the reaction temperature and/or the amount of catalyst did not improve the reactant mixing but led to the production of more polysubstituted sucrose derivatives.<sup>8</sup> Using DMAP as the sole base (2 equiv.) led to similar results. In order to counteract the strong tendency towards polysubstitution, we then used a 9:1 (w/w) THF–water mixture as the solvent. In this case some monosubstituted products were formed. In a 1:1 mixture (THF–water or propan-2-ol–water) satisfactory results were obtained, with yields reaching those observed in the allyl case (over 70%).<sup>9</sup> It has been shown that adding a co-solvent to water makes it possible to direct a chemical process towards the less hydrophobic-effect sensitive pathway when two or more routes are possible.<sup>10</sup> In the present example, the polysubstitution is limited because the aggregation of octyl chloroformate with the initially formed amphiphilic monocarbonates is disfavoured in the aquo-organic solvent compared to pure water.

## Conclusion

This study shows that the reaction of sucrose with hydrophobic electrophilic species leads mostly to polysubstituted products

when water is used as solvent. However, as the preparation of monosubstituted derivatives without the utilization of solvents like DMF or DMSO is attractive from the industrial viewpoint, we have shown that mixtures of simple organic solvents with water are suitable media for such chemical transformations. In contrast, when substrates having a shorter chain are involved, pure water can be used provided that the reaction is fast enough in order to circumvent the competitive hydrolyses.

After the control of the degree of substitution, we are now focusing on the other key selectivity issue in the chemistry of unprotected sucrose in aqueous medium which is the regioselectivity. Work on the influence of the reaction conditions (pH, catalyst, co-solvent, temperature) on the relative reactivity of all hydroxy groups in the sucrose molecule is currently in progress in our laboratory.

## Acknowledgements

Financial support from the CNRS and Beghin-Say is gratefully acknowledged. We thank the CNRS for a grant to S. B. (on leave to the Polish Academy of Sciences, Warsaw) and A. W. We also thank M. Hervé Martin for his participation in the allyl chloroformate synthetic as well as analytical work.

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- 3 General methods and typical procedure used for the preparation of sucrose carbonates. To a stirred aqueous solution of sucrose (28 mmol, 9.6 g in different solvents) adjusted with a pH-Stat (METROHM 736 GP Titrino) and cooled to about 0 °C (ice–salt bath) was added allyl or octyl chloroformate (7 mmol) within 15 to 40 minutes (automatic syringe). The reaction was considered finished when the pH value (addition of base) was measured constant over 10 minutes. The solution was neutralized with 5% (w/w) aqueous acetic acid. The crude mixture was either extracted with butan-2-ol and analysed by analytical HPLC or evaporated to dryness and submitted to silica gel chromatography (as a solid mixture adsorbed on silica gel). Two fractions were isolated: polysubstituted products ( $R_f = 0.60–0.80$  for allyl and  $0.90–1.00$  for octyl); monosubstituted products ( $R_f = 0.40–0.50$  for allyl and  $0.60–0.75$  for octyl). Sucrose did not elute in this solvent. Eluent for the TLC and flash chromatography: chloroform–methanol–acetone–water (56:20:20:4). HPLC: Nucleosil NH<sub>2</sub> column with CH<sub>3</sub>CN–water (90:10), flow: 0.8 ml min<sup>-1</sup>, RI detection.
- 4 Data for mono-*O*-allyloxycarbonyl sucrose derivatives. Elemental analysis for C<sub>16</sub>H<sub>26</sub>O<sub>13</sub>·0.7H<sub>2</sub>O: Calc.: C, 43.8; H, 6.3. Found: C, 43.8; H, 6.1. *m/z* (FAB+) 427 (M + H<sup>+</sup>). Carbon NMR ( [<sup>2</sup>H<sub>6</sub>]DMSO, 75 MHz) and analytical HPLC allowed the identification of some isomers after partial separation by flash chromatography. Consistent effects on chemical shifts were observed (*ca.* +7 ppm for the carbon directly connected to the carbonate function, and *ca.* –2 ppm for the neighbouring carbon atoms). 3-*O*-Allyloxycarbonyl sucrose:  $\delta$  154.7 (C=O), 132.6, 118.3 (C=C), 104.3 (C-2'), 91.7 (C-1), 82.9 (C-5'), 80.5 (C-3), 77.0 (C-3'), 74.4 (C-4'), 72.7 (C-5), 69.7 (C-2), 67.7 (CH<sub>2</sub>-allyl), 67.5 (C-4), 63.0, 62.3, 60.1 (C-6, 1', 6'); 4'-*O*-allyloxycarbonyl sucrose:  $\delta$  154.2 (C=O), 132.3, 118.8 (C=C), 104.7 (C-2'), 92.5 (C-1), 81.6 (C-4'), 80.2 (C-5'), 75.1 (C-3'), 73.0 (C-3,5), 71.9 (C-2), 69.9 (C-4), 68.4 (CH<sub>2</sub>-allyl), 62.6, 61.6, 60.5 (C-6, 1', 6'); mixture of 6, 1' and 6'-*O*-allyloxycarbonyl sucrose:  $\delta$  154.6, 154.5, 154.3 (C=O), 132.4, 132.3, 118.8, 118.6 (C=C), 104.5, 104.2, 102.0 (C-2'), 92.3, 92.0, 91.9 (C-1), 83.1, 83.0, 79.2 (C-5'), 77.2, 76.6, 76.5 (C-3'), 74.9, 74.7, 73.5 (C-4'), 72.9–73.1 (C-3,5), 71.8, 71.7, 71.6 (C-2), 70.3, 70.0, 69.9 (C-4), 69.6, 68.2, 68.1, 67.1, 65.9 (carbonated primary carbons of sucrose and CH<sub>2</sub>-allyl), 63.0, 62.7, 62.3, 61.8, 61.0, 60.7 (non-carbonated C-6, 1', 6').
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- 7 S. Thévenet, G. Descotes, A. Bouchu and Y. Queneau, *J. Carbohydr. Chem.*, 1997, **16**, 691.
- 8 The polysubstituted sucrose octylcarbonates, when formed rapidly, tend to separate out of the reaction mixture, and often cover the glassware as well as the pH-stat electrode, preventing an accurate measure and control of the basic conditions.
- 9 Data for mono-*O*-octyloxycarbonyl sucrose derivatives. Elemental analysis for  $C_{21}H_{38}O_{13} \cdot 0.8H_2O$ : Calc.: C, 49.2; H, 7.8. Found: C, 49.1; H, 7.5%.  $\delta_H$ (300 MHz,  $[^2H_6]DMSO$ ) 0.95 (t, 3 H, Me), 1.25 (m, 10 H, CH<sub>2</sub>), 1.70 (m, 2 H, CH<sub>2</sub>), 3.45 (s, 2 H, O-CH<sub>2</sub>), 3.10–5.65 (m, 21 H, sucrose);  $\nu_{max}(KBr)/cm^{-1}$  999.9, 1047.8, 1266.8, 1401.9, 1748.8, 2855.0, 2926.7, 3341.1;  $m/z$  ( $M^+ + NH_3$ ) 516.
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Paper 8/00096D

Received 5th January 1998

Accepted 13th February 1998