Selective Esterification of Sucrose using Pivaloyl Chloride

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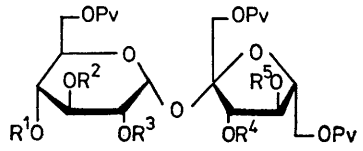
Summary Crystalline 1′,3,3′,4′,6,6′-hexa-*O*-pivaloylsucrose (**2**), a 2,4-diol, has been isolated directly in 45% yield from the reaction of sucrose with pivaloyl chloride in pyridine; by variation of the reaction conditions, a variety of penta- [(**1**) and (**4**)], hexa- [(**5**) and (**7**)], and hepta-pivalates [(**3**),(**6**), and (**8**)] have been isolated after column chromatography.

SELECTIVE esterification has found general application in carbohydrate chemistry[1] as a convenient method for the preparation of certain synthetic intermediates, but with the notable exception of sucrose. Since sterically hindered sulphonyl halides have shown increased selectivity in their reactions with sucrose,[2,3] we have investigated the use of pivaloyl chloride (2,2-dimethylpropionyl chloride), a reagent that has been exploited for the synthesis of 5′-esters of nucleosides.[4] When sucrose was treated in pyridine with pivaloyl chloride (20 equiv.) for 6 h at −40 °C and then for 24 h at room temperature, it afforded four products after chromatography: two major components, the octapivalate (40%), m.p. 135—136 °C, $[\alpha]_D$ +61° (MeOH), and the 4-ol or 1′,2,3,3′,4′,6,6′-hepta-pivalate (**6**) (50%), m.p. 106—108 °C, $[\alpha]_D$ +51·6° (MeOH) and two minor components, the 2-ol (**3**) and the 3-ol (**8**).† On repeating the esterification as above but for 1 h only at −40 °C, the reaction mixture contained

† Satisfactory analyses were obtained for all compounds reported herein.

at least six products which, after chromatographic fractionation, afforded (**6**) followed by the 2,4-diol (**2**) (33%), m.p. 155 °C, $[\alpha]_D$ + 54·5° (MeOH) and two other hexapivalates, namely the 3,3′-diol (**7**) (10%) and the 3′,4-diol (**5**), and then two penta-pivalates, identified as the 2,4,4′-triol (**1**) and the 3,3′,4-triol (**4**) (11%), m.p. 128—129 °C, $[\alpha]_D$ + 61° (MeOH). Each compound was identified by ^{1}H n.m.r. spectroscopy at 220 MHz, before and after the addition of trichloroacetyl isocyanate,[5] and by mass spectrometry. The information derived from carbamate formation was two-fold, in that the methine hydrogen adjacent to the carbamate was deshielded markedly (1—2 p.p.m.) and for each carbamate group a singlet N–H resonance appeared at low field. Consequently, it was possible to assign both the number and positions of the free hydroxy groups in the products.



(**1**); $R^1 = R^3 = R^5 = H$, $R^2 = R^4 = Pv$
(**2**); $R^1 = R^3 = H$; $R^2 = R^4 = R^5 = Pv$
(**3**); $R^1 = R^2 = R^4 = R^5 = Pv$, $R^3 = H$
(**4**); $R^1 = R^2 = R^4 = H$, $R^3 = R^5 = Pv$
(**5**); $R^1 = R^4 = H$; $R^2 = R^3 = R^5 = Pv$
(**6**); $R^1 = H$, $R^2 = R^3 = R^4 = R^5 = Pv$
(**7**); $R^1 = R^3 = R^5 = Pv$, $R^2 = R^4 = H$
(**8**); $R^1 = R^3 = R^4 = R^5 = Pv$, $R^2 = H$
Pv = $COCMe_3$

The 2,4-diol (**2**) was obtained in improved yield (45%) without the need for chromatography by modification of the reaction conditions (7 equiv. of reagent, −40 °C, 8 h) and crystallisation from light petroleum; the petroleum liquors also afforded the 3,3′-diol (**7**) in higher yield (35%). The synthetic utility of these new derivatives of sucrose is illustrated by the conversion of the 4-ol (**6**) into *galacto*-sucrose[6] *via* the 4-mesylate, and into the 4-chloro-4-deoxy-*galacto*-sucrose,[7] by use of sulphuryl chloride,[8] and thence by reductive dehalogenation to 4-deoxy-sucrose. As anticipated from previous studies,[9] the ^{13}C n.m.r. spectrum of the latter showed that the C-4 resonance had shifted 35 p.p.m. upfield.

The reaction of sucrose with pivaloyl chloride is a novel and potentially valuable route to specifically blocked sucrose esters of synthetic utility that otherwise would be accessible with difficulty and we are currently applying this reaction to other carbohydrate derivatives.

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