One-Step Conversion of Primary Alcohols in the Carbohydrate Series to the Corresponding Carboxylic *tert*-Butyl Esters

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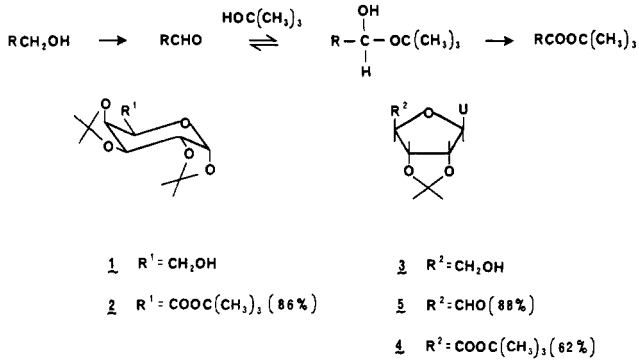
We have developed a simple and convenient method for accomplishing the conversion $RCH_2OH \rightarrow RCOO\ t\text{-Bu}$ which can be carried out in a single flask. The primary alcohol is first allowed to react with 4 molar equiv of 2:1 chromium trioxide–pyridine complex generated from the components in 4:1 methylene chloride–dimethylformamide (DMF) at room temperature. After 15 min, ca. 10 equiv



of acetic anhydride[1] and 20 equiv of *tert*-butyl alcohol are added, and the subsequent reaction is allowed to proceed until all the aldehyde has been consumed (ca. 16 h). Upon isolation good yields of *tert*-butyl carboxylic ester are obtained. This process, demonstrated in the present work with suitably protected carbohydrates,[2] clearly depends on the interaction of aldehyde and *tert*-butyl alcohol to form the corresponding *tert*-butyl hemiacetal which is undoubtedly the slow step in the formation of the ester. Unreactive aromatic aldehydes such as piperonal are not converted to *tert*-butyl esters under the conditions outlined above, doubtless because hemiacetal formation is unfavorable. Apart from this limitation and the usual question of interfering functionality in the substrate, this one-step synthesis of *tert*-butyl esters from primary alcohols should be of some generality.[3] The initial part of the process can also be used for the rapid and efficient transformation of carbohydrate primary alcohols to aldehydes.[4,5]

Experimental Section

General Methods. Analytical thin-layer chromatography (TLC) was carried out on 0.25 mm Merck silica gel 60 F-254 plates. Eluents were (a) water–saturated ethyl acetate and (b) toluene–ethyl acetate (2:1). Compounds were visualized by charring plates sprayed with sulfuric acid in ethanol (10%, v/v). NMR spectra were recorded on a JEOL 270 spectrometer with chemical shifts reported in parts per million relative to Me_4Si as internal standard. Optical rotations were obtained on a Perkin-Elmer 241 polarimeter and melting points were determined with a Fischer-Johns melting point apparatus. Commerical chromium(VI) oxide Fluka AG was used.

***tert*-Butyl (1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranos)uronate (2).** Chromium(VI) oxide (0.40 g, 4.0 mmol) and pyridine (0.645 mL, 8.0 mmol) in dichloromethane–DMF (4:1), v/v, 10 mL) was stirred for 15 min at 23 °C. 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (1, 0.26 g, 1.0 mmol) in dichloromethane–DMF (4:1, v/v, 2 mL) was added followed by acetic anhydride (0.75 mL, 8.0 mmol) and *tert*-butyl alcohol (1.88 mL, 20.0 mmol). The mixture was stirred at 23 °C for 16 h. Ethanol (0.5 mL) was added, and the mixture was stirred for an additional 10 min and diluted with ethyl acetate (50 mL). The resulting mixture was filtered with gentle suction through a sintered glass funnel and packed as a column with silica in ethyl acetate (3 cm), with a layer of anhydrous sodium sulfate on top. Elution with ethyl acetate (ca. 200 mL), removal of solvent in vacuo, and column chromatography on silica gel using 1:1 toluene–ethyl acetate as eluent yielded pure **2** as an oil which solidified on standing (0.284 g, 86%): $[\alpha]^{22}_D$ – 96.3° (*c* 1.00, chloroform). Anal. Calcd for $C_{16}H_{26}O_7$: C, 58.2; H, 7.93; O, 33.9. Found: C, 58.4; H, 8.00; O, 33.7. ^1H NMR ($CDCl_3$) δ 1.33, 1.44, 1.49, 1.53 (4s, *t*-Bu, 4 CH_3), 4.28 (d, 1 H, H-5), 4.36 (dd, 1 H, H-2), 4.52 (dd, 1 H, H-4), 4.63 (dd, 1 H, H-3), 5.63 (d, 1 H, H-1); $J_{1,2}$ = 5.3, $J_{2,3}$ = 2.4, $J_{3,4}$ = 7.6, $J_{4,5}$ = 2.3 Hz.

***tert*-Butyl 2′,3′-*O*-Isopropylideneuridine-5′-carboxylate (4).** 2′,3′-*O*-Isopropylideneuridine (**3**, 0.284 g, 1.0 mmol) was oxidized as described for the preparation of **2**. Column chromatography was performed on a small column of silica with water–saturated ethyl acetate as eluent yielding **4** (0.221 g, 62%): mp 161 °C (crystallized from chloroform–diethyl ether), $[\alpha]^{22}_D$ +13.0° (*c* 1.00, chloroform). Anal. Calcd for $C_{16}H_{22}N_2O_7$: C, 54.2; H, 6.26; N, 7.90; O, 31.6. Found: C, 54.2; H, 6.37; N, 7.75; O, 31.8. ^1H NMR ($CDCl_3$) δ 1.37, 1.54 (2 s, each 3 H), 1.46 (s, 9 H, *t*-Bu), 4.61 (d, 1 H, H-4′), 5.19 (d, 1 H, H-2′), 5.28 (dd, 1 H, H-3′), 5.61 (s, 1 H, H-1′), 5.74 (d, 1-H, H-5), 7.45 (d, 1 H, H-6), $J_{1',2'}$ = ~0, $J_{2',3'}$ = 5.9, $J_{3',4'}$ = 1.6, $J_{5,6}$ = 7.9 Hz; ^{13}C NMR ($CDCl_3$) δ 25.15; 26.72 [$(RO)_2C(CH_3)_2$], 28.04 [$R'OC(CH_3)_3$], 82.67, 84.35, 84.56, 87.91, 97.32 [C-1′, C-2′, C-3′, C-4′, $R'OC(CH_3)_3$], 102.75 (C-5), 113.51 [$(RO)_2C(CH_3)_2$], 143.86 (C-6), 150.89 (C-2), 163.86 (C-4), 168.58 (C-5′).

1-(2′,3′-*O*-Isopropylidene-β-D-*ribo*-pentadialdo-1,4-furanosyl)uracil (5).[4a] Chromium(VI) oxide (0.40 g, 4.0 mmol) and pyridine (0.645 mL, 8.0 mmol) were stirred in dichloromethane–DMF (4 : 1, v/v, 5 mL) for 15 min at room temperature. 2′,3′-*O*-Isopropylideneuridine (**3**, 0.284 g, 1.0 mmol) in dichloromethane–DMF (4 : 1, v/v, 4 mL) was added followed by acetic anhydride (0.378 mL, 4.0 mmol). The mixture was stirred for 5 min, quenched with ethanol (0.5 mL) and poured into ethyl acetate (50 mL). The resulting mixture was worked up as described for **2**. The product was precipitated from toluene (10 mL) with petroleum ether to give **5**, 0.249 g (88%): ^1H NMR ($CDCl_3$) δ 1.37, 1.54 (2 s, each 3 H), 4.56 (d, 1 H, H-4′), 5.11 (d, 1 H, H-2′), 5.22 (dd, 1 H, H-3′), 5.49 (s, 1 H, H-1′), 5.78 (d, 1 H, H-5), 7.25 (d, 1 H, H-6), 9.44 (s, 1 H, H-5′), $J_{1',2'}$ = ~0; $J_{2',3'}$ = 6.3, $J_{3',4'}$ = 1.6, $J_{4',5'}$ = ~0, $J_{5,6}$ = 7.9 Hz. ^{13}C NMR ($CDCl_3$) δ 24.88, 26.55 (2 CH_3), 83.81, 84.97, 94.17, 100.18 (C-1′, C-2′, C-3′, C-4′), 102.96 (C-5), 113.75 [$(RO)_2C(CH_3)_2$], 144.30 (C-6), 150.72 (C-2), 163.61 (C-4), 199.31 (C-5′).

Registry No. 1, 4064-06-6; 2, 92985-13-2; 3, 362-43-6; 4, 92985-14-3; 5, 27999-65-1; *tert*-butyl alcohol, 75-65-0.

(1) For the use of acetic anhydride in chromium trioxide oxidations; see: Garegg, P. J.; Samuelsson, B. *Carbohydr. Res.* **1978**, *67*, 267.

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(3) For another conversion of primary alcohols to esters, see: Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. *Tetrahedron Lett.* **1979**, 165.

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