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Note

A convenient synthesis of 1,2,3,4-tetra-*O*-acetyl-α-D-fucopyranose from D-galactose

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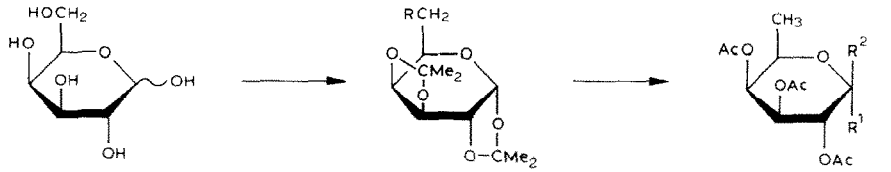
It is known that acetylation of D-fucose under acid-catalyzed conditions affords 1,2,3,4-tetra-*O*-acetyl-α-D-fucopyranose (**5**) in 65% yield[1]. In the present work, it was found that, under base-catalyzed conditions similar to those used to prepare the L-form[2], the yield of product **5** increased to 75%. The synthesis of D-fucose involves acetonation of D-galactose (**1**) to 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**2**), conversion of **2** to the 6-*O*-tosyl derivative **3**, and substitution of an iodide residue to form 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[3,4]. This compound is then subjected to catalytic hydrogenation to give 1,2:3,4-di-*O*-isopropylidene-α-D-fucopyranose (**4**), which upon acid hydrolysis affords D-fucose. Several new reactions have become available in the last two decades for direct reduction of sulfonates to alkyl groups[5–9], making it unnecessary to convert the tosyl derivative **3** to the iodo derivative. Furthermore, the preparation of the desired acetyl derivative **5** (or the β anomer **6**) by hydrolysis of **4** could be skipped entirely since acetolysis conditions[10] could be used to prepare the tetraacetates **5** and **6** directly in one step from **4**.

The experimental section gives details of the preparation starting from the tosyl derivative **3**. The choice of reducing agent was the $NaBH_4$–Me_2SO reagent first applied to carbohydrate chemistry by Weidmann et al.[5], and later applied to a number of other sulfonates in this laboratory as well, for example, the reduction of methyl 2,3-*O*-isopropylidene-5-*O*-(4-toluenesulfonyl)-β-D-ribofuranoside to methyl 5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside[11]. The acetolysis conditions[12,13] used afforded a mixture of the α and β anomers, from which the α anomer **5** crystallized in 39% yield. The acetolysis reagent has also been used as an isomerization reagent to catalyze the formation of α anomers of hexopyranoses from the β anomers[12]. Therefore, the syrupy material remaining after crystallization of **5** was recycled through acetolysis and additional crystalline **5** was obtained.

Attempts to prepare large quantities of **2** by acetonation of **1** using either anhydrous ferric chloride[14] or iodine[15] as catalysts only afforded trace amounts of



1

2 R = OH
3 R = OTs
4 R = H

5 R^1 = OAc, R^2 = H
6 R^1 = H, R^2 = OAc

Scheme 1.

the product, which was the reason for using the classical anhydrous $CuSO_4$–concd H_2SO_4 method[16] to prepare this derivative.

EXPERIMENTAL

General methods.—Melting points were obtained with a Kofler hot-stage. A Perkin–Elmer model 141 polarimeter equipped with 1-dm tubes was used to determine optical rotations. IR spectra were recorded as KBr pellets on a Perkin–Elmer Model 21 spectrophotometer. Organic solutions were dried over anhyd Na_2SO_4. Evaporations were performed on a rotary evaporator at the temperatures stated.

1,2 : 3,4-Di-O-isopropylidene-6-O-(4-toluenesulfonyl)-α-D-galactopyranose (**3**).—1,2 : 3,4-Di-*O*-isopropylidene-α-D-galactopyranose (**2**) was prepared by acetonation of D-galactose (**1**)[16], and this was converted to **3** by tosylation[4]; mp 90–91°C; $[\alpha]_D^{24}$ −64°(*c* 4.06, $CHCl_3$); lit.[17] mp 89–91°C; $[\alpha]_D$ −63°($CHCl_3$).

1,2 : 3,4-Di-O-isopropylidene-α-D-fucopyranose (**4**).—Into a 500-mL reaction flask were placed **3** (47 g, 113 mmol), Me_2SO (300 mL), and $NaBH_4$ (17 g), and the mixture was stirred for 24 h in an oil bath at 85–90°C. The mixture was chilled and added in small portions to a stirred solution of 1% AcOH (1 L) kept ice-cold by addition of ice and by external chilling of the flask in an ice bath. After stirring for 30 min, $CHCl_3$ (200 mL) was added, and the mixture was stirred vigorously for ~ 15 min. The contents of the flask were transferred to a large separating funnel with a powder funnel plugged with glass wool to remove a sticky white solid. The $CHCl_3$ layer was separated and the aqueous layer was extracted further with $CHCl_3$ (4 × 150 mL). Each time fresh $CHCl_3$ was added, it was first passed over the sticky white substance on the glass wool, and this was in turn simultaneously rubbed and pressed with a glass rod. The $CHCl_3$ extracts were combined, washed with water (4 × 80 mL), and dried. The filtered solution was evaporated (30°C) to give a colorless oil, which was distilled to afford a clear, colorless liquid (**4**) (19.5 g, 70% yield); bp 56–58°C (6.65 Pa); $[\alpha]_D^{30}$ −55° (*c* 4.24, $CHCl_3$); lit.[18] $[\alpha]_D^{19}$ −52°; bp 83–84°C (60 Pa).

1,2,3,4-*Tetra*-O-*acetyl*-α-D-*fucopyranose* (**5**).—A solution of **4** (19 g, 78 mmol) in Ac_2O (140 mL) was chilled to −12°C, glacial AcOH (60 mL) was added dropwise,

followed after 10 min by concd H_2SO_4 (4 mL), which was also added dropwise. The mixture was stirred at the same temperature for 1 h, during which time it turned quite dark, and then it was stored in a refrigerator for 3 days. The brown mixture was poured into ice–water (500 mL) and stirred until the ice melted (~ 30 min). The mixture was extracted with $CHCl_3$ (200 mL), the $CHCl_3$ layer was separated, dried, filtered, and evaporated. This process was repeated three more times. The combined $CHCl_3$ extracts were evaporated (30°C) and then coevaporated (40°C) with toluene. The syrupy residue was dissolved in EtOAc (200 mL) and washed with satd aq NaCl (200 mL), satd aq $NaHCO_3$ (2 × 200 mL), again with satd aq NaCl, and dried. Each aqueous layer, except the final one, was back-washed with a small volume of EtOAc. The dried EtOAc solution was filtered, evaporated (30°C), and coevaporated (40°C) with toluene (2 × 100 mL), and finally spun for 2 h at 40°C in vacuo. The syrup weighed 24.33 g (94% yield). It was dissolved in a minimum quantity of Et_2O, chilled for ~ 10 min, seeded[1], and placed in the freezer overnight. The crystalline mass was broken up, filtered (suction), washed with ice-cold Et_2O, and dried in a desiccator in vacuo. Several additional crops of crystals were obtained from the mother liquors for a total of 10.14 g (39%) of the α anomer **5**. These crystals were slightly tan in color; therefore, they were dissolved in a minimal amount of $CHCl_3$ and passed through a small column of silica gel (Baker No. 3404, 40–140 mesh) with only $CHCl_3$ to wash the gel. This filtration removed the colored contaminants, and product **5** was recrystallized in several crops as described above to yield 8.29 g; mp 93°C; mmp 93–94°C; $[\alpha]_D^{28}$ +116° (*c* 1.33, $CHCl_3$); lit.[1] mp 94°C; $[\alpha]_D^{25}$ +122° (*c* 1.04, $CHCl_3$). For the L form[2]: mp 93°C; $[\alpha]_D^{20}$ −116° (*c* 1, $CHCl_3$).

After most of the α anomer **5** had been crystallized, 11.35 g of a hard gum remained, presumably containing mainly the β anomer **6**; $[\alpha]_D^{24}$ +62.4° (*c* 2.23, $CHCl_3$). This was treated with Ac_2O (61 mL)–glacial AcOH (27 mL)–concd H_2SO_4 (1.8 mL) as described above, and the mixture was worked up in the same way. The syrup obtained weighed 6.73 g, and crystallization, passage through a small silica gel column to remove colored impurities, and recrystallization were performed as described above to give an additional 3.24 g of the α anomer **5** in two crops; mp 93–94°C.

The IR spectra of **5** obtained here were identical to that of the previous preparation[1] and to the preparation described hereafter.

1,2,3,4-*Tetra*-O-*acetyl*-α-D-*fucopyranose* (**5**) *by acetylation of* D-*fucose*—D-Fucose (Pfanstiehl Laboratories, Inc., 10 g) was added to an ice-cold mixture of Ac_2O (56 mL) and dry pyridine (88 mL), and the mixture was stirred at 0°C for 2 h. The sugar dissolved in ~ 45 min. After being kept at room temperature for 21 h, the mixture was poured on ice chips (250 mL) and stirred for 2 h, and then $CHCl_3$ (100 mL) was added. The mixture was stirred for 10 min, and transferred to a separating funnel, and the $CHCl_3$ layer was isolated. The aqueous layer was extracted further with $CHCl_3$ (3 × 40 mL), all extracts were combined and washed with water (150 mL), satd $NaHCO_3$ carbonate solution (2 × 150 mL), water (200

mL), and dried. The solution was filtered, $CHCl_3$ removed by evaporation (40°C), and the syrup was coevaporated (45°C) three times with toluene to remove traces of pyridine. The thick syrup was placed in a desiccator under vacuum for 5 days, at which time crystals began appearing. The product was isolated by crystallization from Et_2O in the freezer as described previously. Three crops of **5** were obtained for a total of 15.19 g (75%); mp 93–93.5°C. The remaining syrup (5.93 g) appeared to be mainly the β anomer **6**, and after being stored in vacuo for 2 weeks it had $[\alpha]_D^{24}$ +49° (*c* 2.10, $CHCl_3$); lit.[1] $[\alpha]_D^{24}$ +47° (*c* 2.1, $CHCl_3$). Specific rotations for the L form range[2] from −39 to −56°.

REFERENCES

1 L.M. Lerner, *Carbohydr. Res.*, 19 (1971) 255–258.
2 D.H. Leaback, E.C. Heath, and S. Roseman, *Biochemistry*, 8 (1969) 1351–1359.
3 K. Freudenberg and K. Raschig, *Ber. Dtsch. Chem. Ges.*, 60 (1927) 1633–1636.
4 O.T. Schmidt, *Methods Carbohydr. Chem.*, 1 (1962) 191–194.
5 H. Weidmann, N. Wolf, and W. Tempe, *Carbohydr. Res.*, 24 (1972) 184–187.
6 M.E. Evans and F.W. Parrish, *Methods Carbohydr. Chem.*, 6 (1972) 177–179.
7 V.K. Srivastava and L.M. Lerner, *Carbohydr. Res.*, 64 (1978) 263–265.
8 H.H. Baer and H.R. Hanna, *Carbohydr. Res.*, 110 (1982) 19–41.
9 E.-P. Barrette and L. Goodman, *J. Org. Chem.*, 49 (1984) 176–178.
10 R.D. Guthrie and J.F. McCarthy, *Adv. Carbohydr. Chem. Biochem.*, 22 (1967) 11–23.
11 L.M. Lerner, *J. Org. Chem.*, 43 (1978) 161–163.
12 E. Montgomery and C.S. Hudson, *J. Am. Chem. Soc.*, 56 (1934) 2463–2464.
13 M.L. Wolfrom and R. Montgomery, *J. Am. Chem. Soc.*, 72 (1950) 2859–2861.
14 P.P. Singh, M.M. Gharia, F. Dasgupta, and H.C. Srivastava, *Tetrahedron Lett.*, (1977) 439–440.
15 K.P.R. Kartha, *Tetrahedron Lett.*, 27 (1986) 3415–3416.
16 O.T. Schmidt, *Methods Carbohydr. Chem.*, 2 (1963) 318–325.
17 A.B. Foster, W.G. Overend, M. Stacey, and L.F. Wiggins, *J. Chem. Soc.*, (1949) 2542–2546.
18 K. Gătzi and T. Reichstein, *Helv. Chim. Acta*, 21 (1938) 914–925.