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Preliminary communication

Reactions of glycals with furan and thiophene

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We recently reported a facile *C*-glycosylation *via* a Lewis acid-catalyzed addition–rearrangement reaction of enol esters and silyl enol ethers with glycals[1]. Growing interest in the formation of a carbon–carbon bond at the anomeric center, and the development of selective procedures for alkylation of glycals in reactions catalyzed by Lewis acids[2,3] and metal complexes[4,5], prompts us to describe our linking of five-membered heterocycles to unsaturated pyranoid compounds. We consider that the linking of furan to a pyranoid ring through a carbon–carbon bond at the anomeric center particularly significant, because of its synthetic versatility. For example, furan derivatives have been transformed into sugars in three different ways: (*a*) 2,5-dialkoxylation followed by acid-catalyzed hydrolysis[6], (*b*) Diels–Alder cyclo-addition of 3-nitro-2-propenoic esters[7] or cyclic vinylene carbonate[8], and (*c*) 2,5-cyclo coupling with polyhalo ketones[9].

3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol(**1**),2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (**2**), and 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**3**) reacted with a large excess of furan (20–50 molar excess) in dichloromethane at 20–25° in the presence of 5–10 mol% of one of the following catalysts: aluminum chloride, titanium tetrachloride, stannic chloride, stannous chloride, ferric chloride, zinc chloride, or boron trifluoride etherate. Examination of the reaction mixtures by t.l.c. in 2:1 (v/v) hexane–ethyl acetate revealed that the sugar substrate was completely consumed in 5–30 min when the reaction was conducted in the presence of stannic chloride or boron trifluoride. Reactions were terminated by diluting with dichloromethane and shaking with aqueous sodium hydrogencarbonate. Products were isolated in 40–60% yield by chromatography, on a column of silica gel (230–400 mesh, Merck) with 9:1 (v/v) light petroleum–ethyl acetate, of the syrupy residue obtained after evaporation of the organic solvent. Infrared and ^{1}H-n.m.r. (200 MHz) spectroscopy, the latter permitting unequivocal assignment of the configuration of unsaturated pyranoid derivatives provided that the geometry of one of the allylic centers is known [10–12], were used for structural analysis.

Two oily products were obtained in approximately equal amounts from the reaction of furan with glycal **1**. The less polar compound ($[\alpha]_D$ + 245°) was identified as 4,6-di-*O*-acetyl-1,5-anhydro-2,3-dideoxy-3-*C*-(2-furyl)-D-*ribo*-hex-1-enitol (**4**). The more

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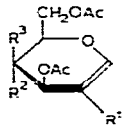
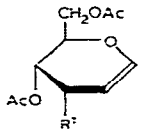
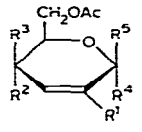


1 R^1 = H, R^2 = OAc, R^3 = H
2 R^1 = OAc, R^2 = OAc, R^3 = H
3 R^1 = OAc, R^2 = H, R^3 = OAc



4 R^1 = 2-furyl
5 R^1 = 2-thienyl



6 R^1 = H, R^2 = OAc, R^3 = H, R^4 = 2-furyl, R^5 = H
7 R^1 = OAc, R^2 = OAc, R^3 = H, R^4 = 2-furyl, R^5 = H
8 R^1 = OAc, R^2 = OAc, R^3 = H, R^4 = H, R^5 = 2-furyl
9 R^1 = OAc, R^2 = H, R^3 = OAc, R^4 = 2-furyl, R^5 = H
10 R^1 = H, R^2 = OAc, R^3 = H, R^4 = 2-thienyl, R^5 = H
11 R^1 = H, R^2 = OAc, R^3 = H, R^4 = OEt, R^5 = H

polar compound ($[\alpha]_D$ + 54°) was identified as 2-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)furan (**6**).

On reaction with furan, compound **2** gave a product (homogeneous in t.l.c.) which was a 3:2 mixture of 2-(2,4,6-tri-*O*-acetyl-3-deoxy-α- and -β-D-*erythro*-hex-2-enopyranosyl)furan (**7** and **8** respectively). Glycal **3** gave a single, crystalline compound (m.p. 97°, $[\alpha]_D$ −190°) which was identified as 2-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*threo*-hex-2-enopyranosyl)furan (**9**).

Isolation of the 3-substituted glycal from the reaction of **1** with furan was somewhat unexpected, because other *C*-nucleophiles seem to react with glycals exclusively[1,2,10] at C-1; and so, in order to investigate this reaction further, we treated **1** with thiophene. Again, two products were obtained in equimolar amounts. The less polar product was identified as 4,6-di-*O*-acetyl-1,5-anhydro-2,3-dideoxy-3-*C*-(2-thienyl)-D-*ribo*-hex-1-enitol (**5**); an oil, $[\alpha]_D$ +280° (*c* 1, dichloromethane). The more polar product was identified as 2-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)thiophene (**10**); an oil, $[\alpha]_D$ + 132° (*c* 1, dichloromethane).

Because kinetically controlled products were obtained in the three reactions described, we reasoned that another source of the allylic-cation intermediate might result in a different distribution of products. Accordingly, ethyl 4,6-di-*O*-acetyl-α-D-*erythro*-hex-2-enopyranoside (**11**) was used instead of **1**, under identical reaction-conditions. The reaction was slower, but no significant difference in distribution of products was observed.

Correct elemental analyses were obtained for compounds **4**–**10** (distilled at 150–160°/0.5 torr; product **9** crystallized, and was recrystallized from hexane). ^{1}H-N.m.r. signals (see Table I) in the aromatic region agreed with reported data[13].

From the results herein described, the following conclusions may be drawn. (*a*) 2-Unsaturated pyranosyl compounds, versatile synthons, can be obtained from glycals in good yield by simple Friedel–Crafts alkylation. (*b*) Formation of a carbon–carbon bond in addition–rearrangement reactions of glycals is not necessarily a regiospecific process. (*c*) Substituents on the glycal ring play a significant role in directing the incoming nucleophile. The configuration of C-4 can apparently influence the anomeric ratio; a substituent on C-2 appears to make the reaction completely regioselective, allowing reaction only at C-1.

TABLE I

^{1}H CHEMICAL-SHIFTS AND COUPLING CONSTANTS (IN Hz)

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6,6'*	*AcO*	*Aromatic*
4	6.53, p.d., 1 H, $J_{1,2}$ 6.0, $J_{1,3}$ 1.7	4.81, t, 1 H, $J_{1,2}$ 6.0, $J_{2,3}$ 6.0	4.03, p.t., 1 H, $J_{2,3} \simeq J_{3,4}$ = ~6.0, $J_{1,3}$ 1.7	5.05, p.d., 1 H, $J_{3,4}$ 6.2, $J_{4,5}$ 10.0	4.15, m, 1 H	4.31, m, 2 H	1.99, 2.10, 2 s, 9 H	7.38, m, 1 H; 6.34, p.d., 1 H, *J* 3.0, 1.7; 6.14, d, 1 H, *J* 3.0
5	6.54, p.d., 1 H, $J_{1,2}$ 6.0, $J_{1,3}$ 1.0	4.94, t, 1 H, $J_{1,2} \simeq J_{2,3}$ = ~6.0	4.1, m, 2 H (H-3, 5)	5.11, p.d., 1 H, $J_{3,4}$ 6.0, $J_{4,5}$ 9.5	4.1, m, 2 H	4.3, m, 2 H	1.95, 2.10, 2 s, 6 H	7.26, m, 1 H; 7.00, m, 1 H; 6.86, m, 1 H
6	5.3–5.4, m, 2 H	6.02, m, 2 H, $J_{2,3}$ 10.0		5.3–5.4, m, 2 H	3.85, m, 1 H	4.16, m, 2 H	2.06, 2.09, 2 s, 6 H	7.46, d, 1 H, *J* 1.7; 6.36, m, 2 H
7	5.37, b.s., 1 H		5.84, p.d., 1 H, $J_{1,3}$ 1.3, $J_{3,4}$ 2.5	5.50, m, 1 H	3.89–4.08, m, 1 H	4.1–4.3, m, 2 H	2.05–2.10, 3 s, 9H	7.48, d, 1 H, *J* 1.3; 6.34–6.46, m, 2 H
8	5.37, b.s., 1 H		5.73, t, 1 H, $J_{1,3} \simeq J_{3,4}$ = ~2.0	5.50, m, 1 H	3.89–4.08, m, 1 H	4.1–4.3, m, 2 H	2.05–2.10, 3 s, 9 H	7.43, d, 1 H, *J* 1.5; 6.34–6.46, m, 2 H
9	5.42, d, 1 H, $J_{1,3}$ 1.7		6.02, p.d., 1 H, $J_{1,3}$ 1.7, $J_{3,4}$ 5.8	5.34, p.d., 1 H, $J_{3,4}$ 5.8, $J_{4,5}$ 2.0	4.08–4.31, m, 3 H		2.00, 2.10, 2.12, 3 s, 9 H	7.47, m, 1 H; 6.38, b.s., 2 H
10	5.51, b.s., 1 H	5.92, m, 2 H, $J_{2,3}$ 10.0		5.38, m, 1 H, $J_{4,5}$ ~9	3.93, m, 1 H	4.24, m, 2 H	2.05, 2.07, 2 s, 6 H	7.28, m, 1 H; 7.00, m, 2 H

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