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Note

Regioselectivity in the reactivity of dibutylstannylene derivatives of glycals*

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Regioselective acylations of D-glucal (**1**) have been studied intensively[1] due to their utility in synthesis. Conventional methods of acylation of **1** yield all possible esters[1]. Hindered reagents ($TsCl$[2], Ph_3CCl[3], $^tBuMe_2SiCl$[4–6]) selectively acylate at O-6. Regioselective acylations[7] and silylations[6] of L-rhamnal (**14**) gave 3- or 4-acyl (40–60%) and 3-monosilylated (70–95%) derivatives, respectively. Cyclic tin derivatives of vicinal diols show selectivity in various reactions[8]. Thus, regioselective acetylations[8–10], alkylations[11–13], and oxidations[14–16] of stannylene derivatives of carbohydrates and the monosubstitution of 2′,3′-*O*-(dibutylstannylene)-nucleosides[8] have been reported.

In a search for improved selectivity, the acylation of cyclic dibutylstannylene derivatives of some glycals has been investigated. It was anticipated that the flexible dihydropyran ring would permit the formation of a cyclic dibutylstannylene derivative, and we now report a practical method for 3-acylation of the dibutylstannylene derivatives **7** and **15**.

Reaction of **1** with 1.1 mol. equiv. of dibutyltin oxide in hot methanol resulted in dissolution, usually within 40 min. Since acylations using this solution did not go to completion even after the addition of a large excess of the acylating agents[8], the methanol was removed and the resulting white solid (**3/4**) was acylated. The dibutylstannylene derivatives (**7** and **15**, respectively) of 6-*O*-trityl-D-glucal[3] (**2**) and L-rhamnal[17] (**14**) were prepared similarly. The 3-acylated products (**6, 8, 11, 16,** and **19**) obtained in these reactions were purified by column chromatography and their structures established on the basis of the ^1H- and ^{13}C-n.m.r. spectra and by comparison with the data of known compounds[6,7].

The reaction of **3/4** with Ac_2O/NEt_3 (1 mol. equiv. of each), either in *N,N*-dimethylformamide or dichloromethane for 6 h at room temperature, gave 53% of a 7:2 mixture (n.m.r. data) of 6- (**5**) and 3-*O*-acetyl-D-glucal (**6**) which could not be

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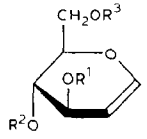
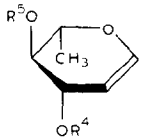
fractionated. Similar mixtures were obtained on reaction of **3/4** with AcCl or BzCl/NEt_3. The reaction of **1** with Ac_2O/pyridine for 6 h at room temperature yielded a 2.5:1 mixture of **5** and **6**. Thus, it appears that a mixture of 4,6- (**3**) and 3,4-di-*O*-(dibutylstannylene)-D-glucal (**4**) is probably involved in these reactions, so that selective acylation of **1** was not possible and, therefore, 6-*O*-trityl-D-glucal (**2**) was investigated.

Reaction of the 2,3-*O*-dibutylstannylene derivative (**7**) of **2** with Ac_2O or BzCl/NEt_3 (1.5 mol. equiv.) in *N,N*-dimethylformamide or dichloromethane for 3 h at room temperature gave mainly the 3-*O*-acetyl (**8**, 88%) and 3-*O*-benzoyl (**11**, 85%) derivatives, respectively. Likewise, treatment of the L-rhamnal derivative **15** with Ac_2O or BzCl/NEt_3 for 4 h gave the 3-*O*-acetyl[7] (**16**, 81%) and 3-*O*-benzoyl[7] (**19**, 78%) derivatives, respectively. The absence of 4-*O*-acyl derivatives (**9**, **17**[7], and **20**[7]) in these reactions was confirmed by t.l.c., using reference compounds prepared by non-selective methods. Partial acylation[7] of **2** gave **8–11** and **13** (**12** was not formed). Compounds **17** and **20** were obtained in a similar manner[7]. Acylation at O-3 and O-4 resulted in a downfield shift (1.0–1.2 p.p.m.) of the signals for H-3 (ddd) and H-4 (dd), respectively, in the ^{1}H-n.m.r. spectra. Likewise, there were shifts[7] in the resonances for C-1 (downfield by 1.3–2.0 p.p.m.) and C-2 (upfield by 4.0–5.0 p.p.m.) in the ^{13}C-n.m.r. spectra on acylation at O-3. Only small shifts occurred on 4-acylation. The dibutylstannylene derivatives **3/4**, **7**, and **15** did not react under alkylating conditions (MeI or $PhCH_2Br$ in *N,N*-dimethylformamide at 30–80°), and higher temperature and longer reaction time caused decomposition of the enol ethers.





1 $R^1 = R^2 = R^3 = H$
2 $R^1 = R^2 = H, R^3 = Tr$
3 $R^1 = H, R^2, R^3 = SnBu_2$
4 $R^1, R^2 = SnBu_2, R^3 = H$
5 $R^1 = R^2 = H, R^3 = Ac$
6 $R^1 = Ac, R^2 = R^3 = H$
7 $R^1, R^2 = SnBu_2, R^3 = Tr$
8 $R^1 = Ac, R^2 = H, R^3 = Tr$
9 $R^1 = H, R^2 = Ac, R^3 = Tr$
10 $R^1 = R^2 = Ac, R^3 = Tr$
11 $R^1 = Bz, R^2 = H, R^3 = Tr$
12 $R^1 = H, R^2 = Bz, R^3 = Tr$
13 $R^1 = R^2 = Bz, R^3 = Tr$

14 $R^4 = R^5 = H$
15 $R^4, R^5 = SnBu_2$
16 $R^4 = Ac, R^5 = H$
17 $R^4 = H, R^5 = Ac$
18 $R^4 = R^5 = Ac$
19 $R^4 = Bz, R^5 = H$
20 $R^4 = H, R^5 = Bz$
21 $R^4 = R^5 = Bz$

EXPERIMENTAL

General methods. — N.m.r. spectra (^1H, 90 MHz; ^{13}C, 22.63 MHz) were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Bruker WH-90-FT spectrometer. Optical rotations were measured on a JASCO-DIP-181 polarimeter. Silica Gel 60 (230–400 mesh ASTM) (Merck) was used for flash-column chromatography. T.l.c. was performed on Silica Gel G (Acme). Compounds were purified by column chromatography.

Preparation of the dibutylstannylene derivatives. — To a solution of **1, 2,** or **14** (5 mmol) in methanol (50 mL) was added dibutyltin oxide (5.5 mmol), and the solution was heated to reflux until it became homogeneous (40 min). The solvent was evaporated and the resulting dibutylstannylene derivative (**3/4, 7,** or **15**) was dried under high vacuum (60° for 1 h) before use.

3- (**6**) *and 6-O-acetyl-*D*-glucal* (**5**). — A suspension of **3/4** (0.3 g, 0.8 mmol) in dry *N,N*-dimethylformamide was treated with Et_3N (0.15 mL, 1 mmol) and Ac_2O (0.1 mL, 1 mmol) for 6 h at room temperature. Solvent was removed from the resulting solution under high vacuum. Column chromatography of the residue on silica gel (60–120 mesh, 10 g), using light petroleum–ethyl acetate (9:1), gave a 7:2 mixture (78 mg, 52%) of **5** and **6**. ^1H-N.m.r. data: δ 2.08, 2.15 (2 s, 6 H, 2 OAc), 2.30–2.95 (m, 3 H, HO-3,4,6), 3.44–4.10 (m, 8 H, H-4,5,6,6'), 4.28, 5.29 (ddd, 2 H, $J_{2,3}$ 2, $J_{3,4}$ 7, $J_{1,3}$ 1.7 Hz, H-3), 4.67, 4.75 (dd, 2 H, $J_{1,2}$ 6, $J_{2,3}$ 2 Hz, H-2), 6.32, 6.44 (dd, 2 H, H-1).

3- (**8**) *and 4-O-acetyl-* (**9**), *3,4-di-O-acetyl-* (**10**), *3-O-benzoyl-* (**11**), *and 3,4-di-O-benzoyl-6-O-trityl-*D*-glucal* (**13**). — To a solution of **2**[3] (1.18 g, 3 mmol) in *N,N*-dimethylformamide (8 mL) and pyridine (1 mL, 12.5 mmol) at 0° was slowly added Ac_2O (0.32 mL, 3 mmol) or BzCl (0.35 mL, 3 mmol). The solution was then stirred for 4 h at room temperature, diluted with water, and extracted with dichloromethane, the combined extracts were concentrated, and the residue was subjected to flash chromatography (light petroleum–ethyl acetate, 3:1) to yield **10** (282 mg, 19.7%), **8** (143 mg, 11%), **9** (286 mg, 22%), **13** (700 mg, 39%), and **11** (675 mg, 45%).

A suspension of **7** (1.24 g, 2 mmol) in *N,N*-dimethylformamide (3 mL; or CH_2Cl_2, 5 mL) was treated with Et_3N (0.45 mL, 3.2 mmol) and Ac_2O (0.3 mL, 3 mmol) or BzCl (0.35 mL, 3 mmol) for 2 h at room temperature. Solvent was removed and the residue was subjected to column chromatography (light petroleum–ethyl acetate, 20:1) to give **8** (0.84 g, 85%) and **11** (0.76 g, 88%) as syrups.

Compound **2** had $[\alpha]_D$ +20° (*c* 1, methanol). N.m.r. data: ^1H, δ 2.15 (bs, 2 H, HO-3,4), 3.31 (dd, 1 H, $J_{6,6'}$ 10, $J_{5,6}$ 4 Hz, H-6), 3.51 (dd, 1 H, $J_{5,6'}$ 2.5 Hz, H-6'), 3.70–3.93 (m, 2 H, H-4,5), 4.11–4.33 (m, 1 H, H-3), 4.73 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 2 Hz, H-2), 6.40 (dd, 1 H, H-1), 7.10–7.66 (m, 15 H, 3 Ph); ^{13}C, δ 63.2 (t, C-6), 69.8, 71.3, 77.1 (3 d, C-3,4,5), 87.2 (s, CPh_3), 102.8 (d, C-2), 127.4, 128.1, 128.9 (aromatic), 143.9 (s, aromatic), 144.6 (d, C-1).

Compound **8** had $[\alpha]_D$ +2° (*c* 0.26, methanol). N.m.r. data: ^1H, δ 2.08 (s, 3

H, OAc), 2.84 (d, 1 H, *J* 5 Hz, HO-4), 3.28–3.66 (m, 2 H, H-6,6′), 3.77–4.22 (m, 2 H, H-4,5), 4.73 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 2 Hz, H-2), 5.26 (ddd, 1 H, $J_{1,3}$ 1.7, $J_{3,4}$ 8 Hz, H-3), 6.51 (dd, 1 H, H-1), 7.11–7.66 (m, 15 H, 3 Ph); ^{13}C, δ 21.3 (q, $OCOCH_3$), 63.1 (t, C-6), 68.6, 72.9, 77.3 (3 d, C-3,4,5), 87.3 (s, CPh_3), 99.2 (d, C-2), 127.4, 128.2, 129.0 (3 d, aromatic), 144.2 (s, aromatic), 146.5 (d, C-1), 171.9 (s, $OCOCH_3$).

Anal. Calc. for $C_{27}H_{26}O_5$: C, 75.33; H, 6.09. Found: C, 75.09; H, 6.18.

Compound **9** had $[\alpha]_D$ +51° (*c* 1.25, methanol). N.m.r. data: ^{1}H, δ 1.88 (s, 3 H, OAc), 2.82 (bs, 1 H, HO-3), 3.17 (dd, 1 H, $J_{6,6'}$ 10, $J_{5,6}$ 4 Hz, H-6), 3.48 (dd, 1 H, $J_{5,6'}$ 3 Hz, H-6′), 4.08 (ddd, 1 H, $J_{4,5}$ 8 Hz, H-5), 4.13–4.35 (m, 1 H, H-3), 4.88 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 1.8 Hz, H-2), 5.13 (dd, 1 H, $J_{3,4}$ 6 Hz, H-4), 6.55 (dd, 1 H, H-1); ^{13}C, δ 20.9 (q, $OCOCH_3$), 62.4 (t, C-6), 67.3, 72.9, 75.6 (3 d, C-3,4,5), 87.2 (s, CPh_3), 102.7 (d, C-2), 127.4, 128.1, 129.1 (3 d, aromatic), 143.9 (s, aromatic), 144.9 (d, C-1), 171.1 (s, $OCOCH_3$).

Anal. Found: C, 75.22; H, 6.19.

Compound **10** had $[\alpha]_D$ +60° (*c* 1.2, methanol). N.m.r. data: ^{1}H, δ 1.80, 1.86 (2 s, 6 H, 2 OAc), 3.0–3.4 (m, 2 H, H-6,6′), 4.0–4.33 (m, 1 H, H-5), 4.71 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 3.0 Hz, H-2), 5.0–5.38 (m, 2 H, H-3,4), 6.44 (d, 1 H, H-1), 7.0–7.7 (m, 15 H, 3 Ph); ^{13}C, δ 20.9, 21.1 (2 q, $OCOCH_3$), 62.1 (t, C-6), 67.8, 68.2, 76.0 (3 d, C-3,4,5), 87.2 (s, CPh_3), 98.8 (d, C-2), 127.4, 128.1, 129.1 (3 d, aromatic), 144.1 (s, aromatic), 146.4 (d, C-1), 171.8, 172.1 (2 s, $OCOCH_3$).

Anal. Calc. for $C_{29}H_{28}O_6$: C, 73.71; H, 5.97. Found: C, 73.63; H, 5.99.

Compound **11** had $[\alpha]_D$ −88° (*c* 0.14, methanol). N.m.r. data: ^{1}H, δ 2.75 (bs, HO-4), 3.33–3.66 (m, 2 H, H-6,6′), 3.88–4.33 (m, 2 H, H-4,5), 4.88 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 2.5 Hz, H-2), 5.55 (ddd, 1 H, $J_{1,3}$ 1.8, $J_{3,4}$ 8 Hz, H-3), 6.55 (dd, 1 H, H-1), 7.11–7.77 (m, 15 H, 3 Ph); ^{13}C, δ 63.0 (t, C-6), 68.6, 73.4, 77.9 (3 d, C-3,4,5), 87.5 (s, CPh_3), 99.2 (d, C-2), 127.4, 128.2, 128.7, 129.1, 130.5, 133.4, 144.2 (aromatic), 146.7 (d, C-1), 168.1 (s, OCOPh).

Anal. Calc. for $C_{32}H_{28}O_5$: C, 78.03; H, 5.73. Found: C, 78.08; H, 5.81.

Compound **13** had $[\alpha]_D$ −11° (*c* 2.7, methanol). N.m.r. data: ^{1}H, δ 3.31–3.57 (m, 2 H, H-6,6′), 4.26–4.55 (m, 1 H, H-5), 5.02 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 3 Hz, H-2), 5.60 (ddd, 1 H, $J_{3,4}$ 6, $J_{1,3}$ 1.8 Hz, H-3), 5.73 (t, 1 H, $J_{4,5}$ 6 Hz, H-4), 6.62 (dd, 1 H, H-1), 7.05–8.35 (m, 25 H, 5 Ph); ^{13}C, δ 62.1 (t, C-6), 68.3, 68.4, 76.1 (3 d, C-3,4,5), 87.1 (s, CPh_3), 98.7 (d, C-2), 127.0, 127.3, 127.9, 128.9, 130.6, 133.1, 134.5, 143.9 (aromatic), 146.4 (d, C-1), 162.5, 168.2 (2 s, OCOPh).

Anal. Calc. for $C_{39}H_{32}O_6$: C, 78.50; H, 5.41. Found: C, 78.29; H, 5.48.

3-O-Acetyl- (**16**) *and 3-O-benzoyl-*L*-rhamnal* (**19**). — To a suspension of **15** (0.73 g, 2 mmol) in *N*,*N*-dimethylformamide (1.5 mL; or CH_2Cl_2, 3 mL) was added Et_3N (0.45 mL, 3.2 mmol) and Ac_2O (0.3 mL, 3 mmol) or BzCl (0.35 mL, 3 mmol) at room temperature, and the mixture was stirred for 2 h. The solvent was removed and the residue was subjected to column chromatography (light petroleum–ethyl acetate, 20:1) to give syrupy **16** (0.28 g, 81%) and crystalline **19** (0.37 g, 78%).

Compound **16** had $[\alpha]_D$ +21° (*c* 2.1, chloroform); lit.[7] $[\alpha]_D^{25}$ +21° (chloro-

form). N.m.r. data: ^{1}H, δ 1.35 (d, 3 H, $J_{5,6}$ 6 Hz, H-6,6,6), 2.11 (s, 3 H, OAc), 3.22 (bs, 1 H, HO-4), 3.57 (dd, $J_{3,4}$ 7, $J_{4,5}$ 9 Hz, H-4), 3.86 (dq, 1 H, H-5), 4.66 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 2 Hz, H-2), 5.22 (ddd, 1 H, $J_{1,3}$ 1.8 Hz, H-3), 6.44 (dd, 1 H, H-1).

Compound **19** had m.p. 63–64° (from dichloromethane–hexane), $[\alpha]_D$ +121° (*c* 1, chloroform), lit.[7] m.p. 64–65°, $[\alpha]_D^{25}$ +120° (chloroform). N.m.r. data: ^{1}H, δ 1.44 (d, 3 H, $J_{5,6}$ 6 Hz, H-6,6,6), 3.33–4.22 (m, 3 H, H-4,5 and HO-4), 4.80 (dd, 1 H, $J_{1,2}$ 7, $J_{2,3}$ 3 Hz, H-2), 5.44 (ddd, 1 H, $J_{1,3}$ 1.7, $J_{3,4}$ 8 Hz, H-3), 6.48 (dd, 1 H, H-1), 7.20–8.33 (m, 5 H, Ph).

4-*O*-Acetyl-L-rhamnal (**17**) had $[\alpha]_D$ −40° (*c* 1.5, chloroform); lit.[7] $[\alpha]_D^{25}$ −41° (chloroform). N.m.r. data: ^{1}H, δ 1.28 (d, 3 H, $J_{5,6}$ 6 Hz, H-6,6,6), 1.33 (bs, 1 H, HO-3), 2.13 (s, 3 H, OAc), 3.75–4.07 (m, 1 H, H-5), 4.10–4.37 (m, 1 H, H-3), 4.75 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9 Hz, H-4), 4.79 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 2 Hz, H-2), 6.37 (dd, 1 H, H-1).

4-*O*-Benzoyl-L-rhamnal (**20**) had m.p. 75–76° (from dichloromethane–hexane), $[\alpha]_D$ −78° (*c* 1.1, chloroform); lit.[7] m.p. 76°, $[\alpha]_D^{25}$ −79° (chloroform). N.m.r. data: ^{1}H, δ 1.42 (d, 3 H, $J_{5,6}$ 6 Hz, H-6,6,6), 3.94 (dq, $J_{4,5}$ 8 Hz, H-5), 4.91 (dd, 1 H, $J_{1,2}$ 7, $J_{2,3}$ 3 Hz, H-2), 4.95 (m, 1 H, H-3), 5.48 (t, $J_{3,4}$ 8 Hz, H-4), 6.48 (dd, 1 H, H-1), 7.22–8.25 (m, 5 H, Ph).

3,4-Di-*O*-benzoyl-L-rhamnal (**21**) had $[\alpha]_D$ +231° (*c* 1.3, chloroform); lit.[7] $[\alpha]_D^{25}$ +229° (chloroform). N.m.r. data: ^{1}H, δ 1.44 (d, 3 H, $J_{5,6}$ 6 Hz, H-6,6,6), 4.32 (dq, 1 H, $J_{4,5}$ 3 Hz, H-5), 4.94 (dd, 1 H, $J_{1,2}$ 7, $J_{2,3}$ 3 Hz, H-2), 5.41 (t, $J_{3,4}$ 8 Hz, H-4), 5.65 (ddd, 1 H, $J_{1,3}$ 1.7 Hz, H-3), 6.50 (dd, 1 H, H-1), 7.10–8.45 (m, 10 H, 2 Ph).

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