Acta Chemica Scandinavica, 1993: 47: 826–828
Printed in Belgium – all rights reserved

ACTA
CHEMICA SCANDINAVICA
ISSN 0904-213X

2-(Trimethylsilyl)ethyl Glycosides.† Transformation into the Corresponding 1-*O*-Acyl Sugars

Ulf Ellervik and Göran Magnusson*

Organic Chemistry 2, Chemical Center, The Lund Institute of Technology, University of Lund, Box 124, 221 00 Lund, Sweden

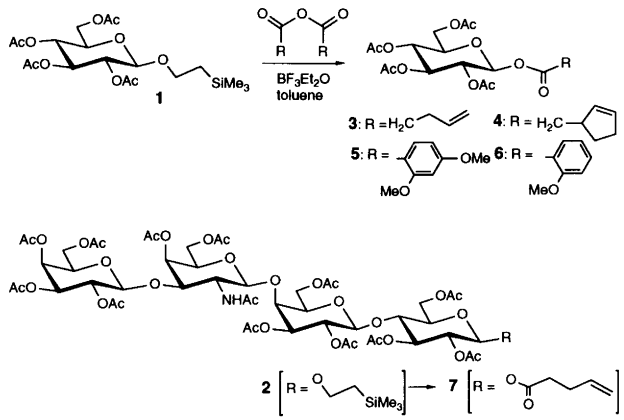
Ellervik, U. and Magnusson, G., 1993. 2-(Trimethylsilyl)ethyl Glycosides. Transformation into the Corresponding 1-*O*-Acyl Sugars. – Acta Chem. Scand. 47: 822–828.

(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside and (trimethylsilyl)ethyl 2,3,6-tri-*O*-acetyl-4-*O*-{2,3,6-tri-*O*-acetyl-4-*O*-[2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-galactopyranosyl]-β-D-galactopyranosyl}-β-D-glucopyranoside have been transformed in high yield into the corresponding 1-*O*-β-acyl saccharides by treatment with various carboxylic anhydrides in the presence of boron trifluoride–diethyl ether in toluene. The carboxylic anhydrides (4-pentenoic, 2-cyclopentenylacetic, 2,4-dimethoxybenzoic, and 2-methoxybenzoic anhydride) were synthesized from the corresponding carboxylic acids by treatment with *N,N*-bis[2-oxo-3-oxazolidinyl]-phosphorodiamidic chloride.

1-*O*-Acyl pyranosides having the 1,2-*trans* configuration, are useful as glycosyl donors.[1] For practical synthetic reasons, the 1-*O*-acyl group is, in most cases, the same as the remaining acyl protecting groups (normally acetyl or benzoyl), which may sometimes limit the usefulness of these compounds. We have developed methods for the one-step high-yield transformation of 2-(trimethylsilyl)-ethyl (TMSEt) glycosides into the corresponding hemiacetal-, 1-chloro-, and 1-*O*-acyl pyranosides.[2] The nature of the 1-*O*-acyl group can be chosen at will and the starting 1,2-*trans* configuration is largely maintained in the product.

We now report the transformation of the TMSEt glycosides **1** and **2** into the 1-*O*-acyl pyranosides **3**–**7**, having potential for selective activation by various electrophiles during a glycosylation process. The synthesis of 1-*O*-pentenoyl esters, via less direct routes, has been reported by others,[3] and used as glycosyl donors. A highly efficient 1-*O*-acylation reaction is especially important with large and sensitive oligosaccharide donors (such as **7**) since these are normally highly valuable, being secured late in multistep synthetic sequences.

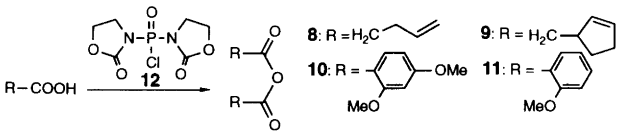
Treatment of the TMSEt glycosides **1** and **2** with a carboxylic anhydride and boron trifluoride–diethyl ether,[2a] according to Scheme 1, gave the corresponding 1-*O*-acyl pyranosides **3**–**7** in good yields and with high stereoselectivity. The expected β-1-*O*-acyl pyranoside was always formed as the major product. In fact, the crude reaction products from the synthesis of **5**–**7** contained no



Scheme 1.

α-anomer and in the least efficient case (**4**), the β/α-ratio was 97:3. The use of **3**–**7** in glycoside synthesis will be reported elsewhere.

The carboxylic anhydrides **8**–**11** were prepared by the excellent method developed by Cabré-Castellvi *et al.*[4] Thus, treatment of the corresponding, commercially available, carboxylic acids with *N,N*-bis[2-oxo-3-oxazolidinyl]phosphorodiamidic chloride (**12**) gave **8**–**11** in good yields (Scheme 2). The reagent **12** was prepared on a 30 g scale according to the published procedure.[4]



Scheme 2.

* To whom correspondence should be addressed.
† Part 9. For part 8, see Ekberg, T. and Magnusson, G. *Acta Chem. Scand. 47* (1993). *In press.*

Experimental

Melting points are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. ^1H and ^{13}C NMR spectra were recorded with a Varian XL-300 instrument. Chemical shifts are given in ppm downfield from the signal for Me_4Si, with reference to internal $CHCl_3$ (7.26 ppm). Thin layer chromatography was performed on Kieselgel 60 F254 plates (Merck). Column chromatography was performed on SiO_2 (Matrex LC-gel; 60A, 35-70 My, Grace). The TMSEt glycosides **1**[2a] and **2**[2c] were synthesized as reported.

1-O-(4-Pentenoyl)-2,3,4,6-tetra-O-acetyl-u-D-glucopyranose (**3**). 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**1**, 1.12 g, 2.5 mmol) was dissolved in toluene (12.5 ml, dried by passage through a bed of Al_2O_3), 4-pentenoic anhydride (**8**, 0.69 g, 3.75 mmol) and boron trifluoride–diethyl ether (250 µl, 2 mmol) were added, and the mixture was stirred at 55 °C. The reaction was monitored by TLC (EtOAc–heptane 1:1). When the reaction was complete (~30 min) dichloromethane (60 ml) was added. The organic phase was washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4) and concentrated. The residue was chromatographed (SiO_2; EtOAc–heptane 1:1) to give **3** (1.07 g, 99%). Recrystallization from methanol gave 0.85 g of **3** (80%). $[\alpha]_D^{20}$ 0° (*c* 1.0, $CHCl_3$), m.p. 73–74 °C. ^1H NMR ($CDCl_3$): δ (protons marked with an asterisk are assigned to the 1-*O*-acyl group) 5.70–5.90 (m, 1 H, H-4*), 5.74 (d, 1 H, *J* 8.2 Hz, H-1), 5.0–5.3 (5 H, H-2,3,4,5*), 4.30, 4.10 (d, AB system, 2 H, *J* 12.6, 4.6, 2.0 Hz, H-6), 3.84 (dd, 1 H, *J* 10.0, 4.4, 2.1 Hz, H-5), 2.3–2.5 (m, 4 H, H-2,3*), 2.09, 2.03, 2.02, 2.01 (s, 3 H each, OAc). Anal. C, H.

1-O-(2-Cyclopentenylacetyl)-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**4**). 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**1**, 1.12 g, 2.5 mmol) was treated with **9** (878.6 mg, 3.75 mmol) as in the synthesis of **3** to give **4** (963 mg, 85%). Recrystallization (methanol) gave 595 mg of **4** (52%, β/α 97:3). $[\alpha]_D^{20}$ −6° (*c* 0.9, $CHCl_3$), m.p. 90–92 °C. ^1H NMR ($CDCl_3$): δ 5.78, 5.62 (d, AB system, 2 H, *J* 2.2, 5.6 Hz, CH=CH), 5.74 (d, 1 H, *J* 8.3 Hz, H-1), 5.10–5.30 (m, 3 H, H-2,3,4), 4.30, 4.10 d, AB system, 2 H, *J* 12.5, 4.6, 2.4 Hz, H-6), 3.80–3.90 (m, 1 H, H-5), 3.08 (m, 1 H), 2.30–2.50 (m, 5 H), 2.10–2.20 (m, 1 H), 2.09, 2.05, 2.04, 2.03 (s, 3 H each, OAc). Anal. C, H.

1-O-(2,4-Dimethoxybenzoyl)-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5**). 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**1**, 1.12 g, 2.5 mmol) was treated with **10** (1.30 g, 3.75 mmol) as in the synthesis of **3** to give **5** (741 mg, 58%). Recrystallization (EtOAc–heptane) gave 572 mg of **5** (45%). $[\alpha]_D^{20}$ −27.1° (*c* 1.0, $CHCl_3$), m.p. 121–123 °C. ^1H NMR ($CDCl_3$): δ 7.90 (d, 1 H, *J* 8.8 Hz, ArH), 6.50 (dd, 1 H, *J* 2.5, 8.8 Hz, ArH), 6.40 (d, 1 H, *J* 2.1 Hz, ArH), 5.90 (d, 1 H, *J* 8.0 Hz, H-1), 5.1–5.4 (m, 3 H, H-2,3,4), 4.33, 4.13 (d, AB system, 2 H, *J* 12.6, 4.6, 2.4 Hz, H-6), 3.93 (m, 1 H, H-5), 3.89, 3.86 (s, 3 H each, OCH_3), 2.07, 2.05, 2.04, 2.00 (s, 3 H each, OAc). Anal. C, H.

1-O-(2-Methoxybenzoyl)-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**6**). 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**1**, 1.12 g, 2.5 mmol) was treated with **11** (1.07 g, 3.75 mmol) as in the synthesis of **3** to give **6** (1.020 g, 85%). Recrystallization (EtOAc–heptane) gave 666 mg of **6** (55%). $[\alpha]_D^{20}$ −26° (*c* 0.9, $CHCl_3$), m.p. 100–102 °C. ^1H NMR ($CDCl_3$): δ 7.86 (dd, 1 H, *J* 1.9, 8.0 Hz, ArH), 7.52 (dt, 1 H, *J* 1.8, 9.0 Hz, ArH), 7.00 (m, 2 H, ArH), 5.96 (d, 1 H, *J* 8.3 Hz, H-1), 5.10–5.40 (m, 3 H, H-2,3,4), 4.32, 4.13 (d, AB system, 1 H, *J* 12.4, 4.4, 2.3 Hz, H-6), 3.91 (s, 3 H, OCH_3), 3.85–3.95 (m, 1 H, H-5), 2.07, 2.05, 2.04, 2.00 (s, 3 H each, OAc). Anal. C, H.

1-O-(4-Pentenoyl)-2,3,6-tri-O-acetyl-4-O-{2,3,6-tri-O-acetyl-4-O-[2-acetamido-4,6-di-O-acetyl-2-deoxy-3-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-galactopyranosyl]-β-D-galactopyranosyl}-β-D-glucopyranose (**7**). 2-(Trimethylsilyl)ethyl 2,3,6-tri-*O*-acetyl-4-*O*-{2,3,6-tri-*O*-acetyl-4-*O*-[2-acetamido-4,6-di-*O*-acetyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-galactopyranosyl]-β-D-galactopyranosyl}-β-D-glucopyranoside (**2**, 29 mg, 0.022 mmol) was dissolved in dry toluene (200 µl). 4-Pentenoic anhydride (**8**, 62 mg, 0.34 mmol) and boron trifluoride–diethyl ether (15 µl, 0.12 mmol) were added and the mixture was stirred for 4 h. Triethylamine (1 ml) was added and the mixture was concentrated. The residue was chromatographed (SiO_2; EtOAc–heptane 5:1 → 1:10) to give **9** (26 mg, 89%). $[\alpha]_D^{20}$ 10° (*c* 1.8, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 6.77 (d, 1 H, *J* 6.5 Hz, NH), 5.7–5.9 (m, 1 H, C*H*=CH_2), 5.67 (d, 1 H, *J* 8.2 Hz, H-1), 5.37, 5.32 (2 d, 1 H each, *J* 3.2, 3.2 Hz, H-4″, H-4‴), 5.10 (d, 1 H, *J* 8.0 Hz, H-2‴), 4.84 (dd, 1 H, *J* 2.7, 10.3 Hz, H-3′), 4.57 (d, 1 H, *J* 8.0 Hz, H-1‴), 4.39 (d, 1 H, *J* 7.6 Hz, H-1′), 3.05 (br d, 1 H, H-2″), 2.25–2.50 (m, 4 H, OCOCH_2CH_2–), 1.95–2.20 (9 s, 39 H, 13 OAc).

4-Pentenoic anhydride (**8**). 4-Pentenoic acid (2.54 g, 25.2 mmol) was dissolved in dichloromethane (22 ml), and triethylamine (3.5 ml, 25 mmol) and *N*,*N*-bis[2-oxo-3-oxazolidinyl]phosphorodiamidic chloride (3.25 g, 12.7 mmol) were added. The mixture was stirred at room temperature for 30 min. The solvent was evaporated off, the residue extracted with diethyl ether, and the ethereal solution was concentrated. The residue was distilled at 105 °C (18 mmHg) to give **8** (1.96 g, 84%). ^1H NMR ($CDCl_3$): δ 5.82 (ddt, 2 H, *J* 6.5, 10.2, 17.2 Hz, H-4,4′), 5.08 (dd, 2 H, *J* 1.6, 17.1 Hz, H-5,5′), 5.05 (d, 2 H, *J* 8.9 Hz, H-5,5′), 2.56 (dt, 4 H, *J* 7.0, 1.2 Hz, H-2,2′), 2.41 (q, 4 H, *J* 7.1 Hz, H-3,3′). ^{13}C NMR ($CDCl_3$): δ 168.7, 135.7, 116.2, 34.5, 28.1.

2-Cyclopentenylacetic anhydride (**9**). 2-Cyclopentenylacetic acid (2.55 g, 20.0 mmol) was dissolved in dichloro-

methane (20 ml), and triethylamine (3.0 ml, 20 mmol) and *N,N*-bis[2-oxo-3-oxazolidinyl]phosphorodiamidic chloride (2.55 g, 10.0 mmol) were added. The mixture was treated as in the synthesis of **8** to give crude **9**. Short-path distillation gave **9** (2.03 g, 86%; diastereomeric mixture). ^{1}H NMR ($CDCl_3$): δ 5.79, 5.69 (d, AB system, 4 H, *J* 2.2, 5.7 Hz, CH=CH), 3.11 (m, 2 H), 2.65, 2.32 (d, AB system, 4 H, *J* 7.0, 16.0 Hz, CH_2CO), 2.34 (m, 4 H), 2.18 (m, 2 H), 1.49 (m, 2 H).

2,4-Dimethoxybenzoic anhydride (**10**). 2,4-Dimethoxybenzoic acid (3.62 g, 20 mmol) was dissolved in dichloromethane (20 ml), and *N*-methylpiperidine (2.4 ml, 20 mmol) and *N,N*-bis[2-oxo-3-oxazolidinyl]-phosphorodiamidic chloride (2.55 g, 10.0 mmol) were added. The mixture was stirred for 40 min at room temperature, then cooled to 0 °C and cold saturated sodium hydrogen carbonate solution (7 ml) was added. The organic phase was washed with saturated sodium hydrogen carbonate solution and the combined water phases were extracted with dichloromethane. The organic extract was dried (Na_2SO_4) and concentrated and the residue recrystallized (EtOAc–heptane) to give **10** (1.82 g, 52%). M.p. 69–71 °C. ^{1}H NMR ($CDCl_3$): δ 8.01 (d, 2 H, *J* 8.8 Hz, ArH), 6.55 (2 H, ArH), 6.47 (d, 2 H, *J* 2.3 Hz, ArH), 3.88 (s, 6 H, OMe), 3.84 (s, 6 H, OMe).

2-Methoxybenzoic anhydride (**11**). 2-Methoxybenzoic acid (3.04 g, 20 mmol) was dissolved in dichloromethane (20 ml), and *N*-methylpiperidine (2.4 ml, 20 mmol) and *N,N*-bis[2-oxo-3-oxazolidinyl]phosphorodiamidic chloride (2.55 g, 10.0 mmol) were added. The mixture was treated as in the synthesis of **10** to give crude **11**. Recrystallization (EtOAc) gave **11** (1.93 g, 68%). M.p. 66–68 °C. ^{1}H NMR ($CDCl_3$): δ 8.02 (dd, 2 H, *J* 1.9, 7.8 Hz, ArH), 7.56 (dt, 2 H, *J* 1.8, 7.4 Hz, ArH), 7.03 (q, 4 H, *J* 7.8 Hz, ArH), 3.86 (s, 6 H, OCH_3).

Acknowledgments. This work was supported by the Swedish Natural Science Research Council.

References

1. Paulsen, H. and Paal, M. *Carbohydr. Res. 135* (1984) 53.
2. (a) Jansson, K., Ahlfors, S., Frejd, T., Kihlberg, J., Magnusson, G., Dahmén, J., Noori, G. and Stenvall, K. *J. Org. Chem. 53* (1988) 5629; (b) Jansson, K., Noori, G. and Magnusson, G. *J. Org. Chem. 55* (1990) 3181; (c) Ray, A. K. and Magnusson, G. *Acta Chem. Scand. 46* (1992) 487; (d) Magnusson, G. *Trends Glycosci. Glycotechnol. 4* (1992) 358.
3. (a) Kunz, H., Wernig, P. and Schults, M. *Synlett* (1990) 631; (b) Lopez, J. C. and Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* (1991) 159.
4. Cabré-Castellvi, J., Palomo-Coll, A., Palomo-Coll, A. L. *Synthesis* (1981) 616.

Received October 21, 1992.