Carbohydrate Research
Elsevier Publishing Company, Amsterdam
Printed in Belgium

Note

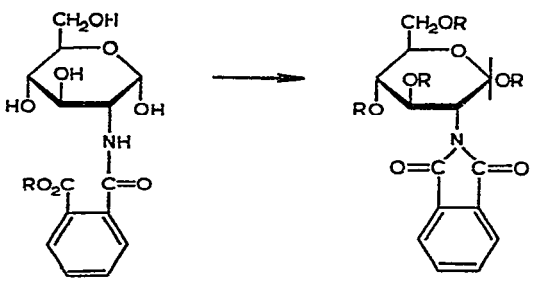
Some phthaloyl derivatives of 2-amino-2-deoxy-D-glucopyranose

SHIGEHIRO HIRANO

Department of Chemistry, Belfer Graduate School of Science, Yeshiva University, New York, N. Y. 10033 (U. S. A.) and Department of Agricultural Chemistry, Kyoto University, Kyoto (Japan)*

(Received April 9th, 1970)

A selective *N*-acetylation of amino sugars with carboxylic anhydrides in methanol was previously reported[1,2], and the procedure has been used for preparative *N*-acylation of amino sugars[3]. In the present work, the procedure is applied to the preparation of some phthaloyl derivatives of 2-amino-2-deoxy-D-glucopyranose. The reaction of 2-amino-2-deoxy-D-glucopyranose with phthalic anhydride in methanol gave 2-(2-carboxybenzamido)-2-deoxy-α-D-glucopyranose (**1**). Under acetylation conditions, **1** gave 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-α-D-glucopyranose (**3**). Treatment of **3** in methanol containing hydrochloric acid at reflux gave 2-deoxy-2-phthalimido-β-D-glucopyranose (**4**), whereas **1** in methanol in the precense of dry Amberlite IR 120(H^+) at reflux gave methyl 2-deoxy-2-[2-(methoxycarbonyl)-benzamido]-α-D-glucopyranoside (**2**). Treatment of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose with phthalic anhydride in methanol gave 1,3,4,6-tetra-



1 R = H
2 R = Me

3 R = Ac
4 R = H

O-acetyl-2-(2-carboxybenzamido)-2-deoxy-β-D-glucopyranose (**5**). Phthalic anhydride did not react with 2-amino-2-deoxy-D-glucopyranose in water[4] and with 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-D-glucopyranose in the fusion reaction at elevated temperature[5].

*All correspondence with regard to the present work should be addressed to the Yeshiva University, New York.

EXPERIMENTAL

General methods. — Melting points are uncorrected. N.m.r. spectra were measured with a Varian A-60 spectrometer with tetramethylsilane as internal standard in chloroform-*d*, and 2,2-dimethyl-2-silapentane-5-sulfonate in D_2O. I.r. spectra were recorded with a Perkin–Elmer 257 spectrometer or a Shimadzu AR-7 spectrometer. Specific rotations were measured with a Bendix automatic polarimeter or a Yanagimoto direct-reading polarimeter.

2-(2-Carboxybenzamido)-2-deoxy-α-D-glucopyranose (**1**). — To a solution of 2-amino-2-deoxy-D-glucopyranose, prepared from 2-amino-2-deoxy-D-glucopyranose hydrochloride (10.0 g) in methanol (70 ml) and metallic sodium (1.0 g) according to a previous paper[1], was added phthalic anhydride (7.0 g) under shaking at room temperature. The solution was heated at reflux in a water bath for 10 min, and then cooled to room temperature. The precipitate produced was filtered off and washed with a small volume of cold methanol. Recrystallization from methanol–water (4:1, v/v) gave 15 g (96%), m.p. 186–187°, $[\alpha]_D^{17}$ +114→ +84° (*c* 0.5, water); i.r. data: ν_{max}^{Nujol} 1710 (C=O), 750 cm^{-1} (*o*-disubstituted Ph); n.m.r. data (D_2O): δ 7.63 (m, 4 protons, Ph).

Anal. Calc. for $C_{14}H_{17}NO_8$: C, 51.37; H, 5.24; N, 4.28. Found: C, 51.37; H, 5.20; N, 4.31.

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-phthalimido-α-D-glucopyranose (**3**). — A mixture of acetic anhydride (15 ml) and dried pyridine (27 ml) was added to **1** (5.0 g) under cooling. The mixture was kept for 24 h at room temperature, and then poured into ice–water. The emulsion was extracted with chloroform (3 × 50 ml). The extract was dried (sodium sulfate) and concentrated *in vacuo* to give a syrup, which was dissolved in a small volume of methanol. Ether was added, and the solution kept in a refrigerator overnight gave crystals, which were recrystallized from hot methanol, 3.6–5.3 g (50–70%), m.p. 131°, $[\alpha]_D^{16}$ +98° (*c* 0.5, chloroform); i.r. data: ν_{max}^{Nujol} 1760 and 1710 (=O), 740 cm^{-1} (*o*-disubstituted Ph), no OH absorption at 3600–3000 cm^{-1}; n.m.r. data: (chloroform-*d*): δ 7.79 (m, 4 protons, Ph), 6.55 (q, 1 proton, H-3, $J_{3,4}$ 11.5 Hz); 2.28 (d, 1 proton, H-1, $J_{1,2}$ 3.5 Hz), 4.70 (q, 1 proton, H-2, $J_{2,3}$ 11,5 Hz), 5.15 (m, 1 proton, H-5), 4.1–4.5 (m, 3 protons, H-4, H-6_a and H-6_b), 2.12, 2.08, 2.05, 1.86 (s, 12 protons, OAc). The properties of the β-D isomer have been reported[6].

Anal. Calc. for $C_{22}H_{23}NO_{11}$: C, 55.34; H, 4.86; N, 2.93. Found: C, 55.26, H, 4.79; N, 2.83.

Methyl 2-deoxy-2-[2-(methoxycarbonyl)benzamido]-α-D-glucopyranoside (**2**). — A mixture of **1** (5.0 g) and dried Amberlite IR-120 (H^+, 10.0 g) was heated for 5 h at reflux in methanol (200 ml). The suspension cooled to room temperature was filtered. The filtrate was concentrated to a syrup, which was dissolved in a minimum volume of ethanol. After addition of ether and petroleum ether (b.p. 39–49°), the mixture was kept for 5 days in a refrigerator. The crystals were recrystallized from ethanol–ether–petroleum ether, yield 4.3 g (79%), m.p. 192–193°, $[\alpha]_D^{17}$ +21° (*c* 0.5, water); i.r. data: ν_{max}^{KBr} 1710 and 1640 (C=O), 740 cm^{-1} (*o*-disubstituted Ph); n.m.r. data (D_2O):

δ 7.63 (m, 4 protons, Ph), 4.92 (d, 1 proton, H-1 $J_{1,2}$ 3.0 Hz), 3.92 (s, 3 protons, COMe), 3.43 (s, 3 protons, OMe).

Anal. Calc. for $C_{16}H_{21}NO_8$: C, 54.08; H, 5.96; N, 3.94. Found: C, 54.03; H, 5.94; N, 4.07.

2-Deoxy-2-phthalimido-β-D-glucopyranose (**4**). — A solution of **3** (1.0 g) in methanol (20 ml) containing conc. hydrochloric acid (1.4 ml), was heated for 4 h at reflux. An excess of silver carbonate was added and the mixture was filtered off. The filtrate was concentrated to a syrup. Crystallization and recrystallization from acetone gave 0.4 g (62%), m.p. 187–188°, $[\alpha]_D^{17}$ +29° (*c* 1.0, water); i.r. data: ν_{max}^{KBr} 1725 (C=O), 725 cm^{-1} (*o*-disubstituted Ph); n.m.r. data (D_2O): δ 7.84 (m, 4 protons, Ph), 5.50 (d, 1 proton, H-1, $J_{1,2}$ 8.0 Hz), 3.30–4.50 (m, 6 protons, pyranose ring protons), no Ac–Me signals and no OMe signals.

Anal. Calc. for $C_{14}H_{15}NO_7$: C, 54.37; H, 4.89; N, 4.53. Found: C, 54.05; H, 5.00; N, 4.28.

1,3,4,6-Tetra-O-acetyl-2-(2-carboxybenzamido)-2-deoxy-β-D-glucopyranose (**5**). — A solution of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose[7] (1.3 g) and phthalic anhydride (0.5 g) in methanol (20 ml) was kept overnight at room temperature and then concentrated to a syrup. Crystallization and recrystallization from ethanol–ether–petroleum ether gave 1.5 g (93%), m.p. 180–181° (lit.[6]: m.p. 181–182°); i.r. data: ν_{max}^{KBr} 1750 and 1710 (C=O), 750 cm^{-1} (*o*-substituted Ph); n.m.r. data (chloroform-*d*): δ 7.45–7.92 (m, 4 protons, Ph), 5.87 (d, 1 proton, H-1, $J_{1,2}$ 8.0 Hz), 4.0–5.5 (m, 6 protons, pyranose ring protons), 2.17 (s, 3 protons, OAc), 2.09 (s, 6 protons, OAc), 2.05 (s, 3 protons, OAc).

ACKNOWLEDGEMENT

Part of this work carried out at the Department of Chemistry, Belfer Graduate School of Science, Yeshiva University was supported by a grant HD-02646 of the National Institute of Health to Dr. Karl Meyer.

REFERENCES

1 Y. Inouye, K. Onodera, S. Kitaoka, and S. Hirano, *J. Amer. Chem. Soc*, 78 (1956) 4722.
2 Y. Inouye, K. Onodera, S. Kitaoka, and S. Hirano, *J. Org. Chem.*, 25 (1960) 1265.
3 D. Horton and H. Mayer, *Biochem. Prep.*, 11 (1964) 1.
4 S. Takanashi, T. Kawaguchi, and T. Kawada, *Chem. Pharm. Bull.* (Tokyo), 14 (1966) 1433.
5 M. Fling, F. B. Minard. and S. W. Fox, *J. Amer. Chem. Soc.*, 69 (1947) 2466.
6 B. R. Baker, J. P. Joseph, R. E. Schaub, and J. H. Williams, *J. Org. Chem.*, 19 (1954) 1786.
7 M. Bergman and L. Zervas, *Ber.*, 64 (1931) 975.