Carbohydrate Research, 26 (1973) 431–434

Note

β-Elimination in aldonolactones. The formation of an unsaturated derivative on benzoylation of D-*glycero*-D-*gulo*-heptono-1,4-lactone*

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(Received April 18th, 1972; accepted in revised form, June 2nd, 1972)

Elimination reactions have been described for 2-acetamido-2-deoxy-aldono-1,4-lactones[1,2]. Dijong and Wittkötter[3] have found that acetylation of 4-*O*-benzyl-D-*glycero*-D-*gulo*-heptono-1,5-lactone with pyridine–acetic anhydride caused the formation of an unsaturated 1,5-lactone derivative as a result of β-elimination. In a previous paper[4] we reported that the reaction of D-galactono-1,4-lactone with an excess of benzoyl chloride and pyridine for 16 h afforded a di-unsaturated lactone derivative. We now report on the reaction of D-*glycero*-D-*gulo*-heptono-1,4-lactone under similar conditions.

Benzoylation of D-*glycero*-D-*gulo*-heptono-1,4-lactone (**1**) with benzoyl chloride in pyridine for 2 h at room temperature afforded crystalline penta-*O*-benzoyl-D-*glycero*-D-*gulo*-heptono-1,4-lactone[5] (**2**). The i.r. absorption spectrum showed a carbonyl band at 1790 cm^{-1} as expected for a 1,4-lactone. When the benzoylation reaction was conducted for 16 h with an excess of benzoyl chloride and pyridine, 2,5,6,7-tetra-*O*-benzoyl-2,3-dideoxy-D-*arabino*-hept-2-enono-1,4-lactone (**3**) was obtained as the main product in 24% yield. Two other unsaturated compounds, which are under investigation, were isolated from the mother liquors. The u.v. absorption spectrum, the shift of the lactone carbonyl band to a lower frequency in the i.r. spectrum, which corresponds to α,β unsaturation, as well as the n.m.r. spectrum are in agreement with the structure assigned to **3**. Reductive ozonolysis of **3** gave oxalic acid and partially benzoylated arabinose, which was characterized after saponification as the *N*-(4-nitrophenyl)-D-arabinosylamine. Catalytic hydrogenation of **3** was stereoselective, apparently attack from below the pentaatomic ring being hindered by the bulky exocyclic group. The resulting crystalline 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptono-1,4-lactone (**4**) was treated with saturated methanolic ammonia to give 3-deoxy-D-*gluco*-heptonamide (**5**) which had the same i.r. spectrum as a sample prepared by Sprinson *et al.*[6] by a Kiliani synthesis starting with 2-deoxy-D-*arabino*-hexose. This conclusively proves the configuration of the deoxy lactone **4**.

*Dedicated to Professor V. Deulofeu, in honor of his 70th birthday.

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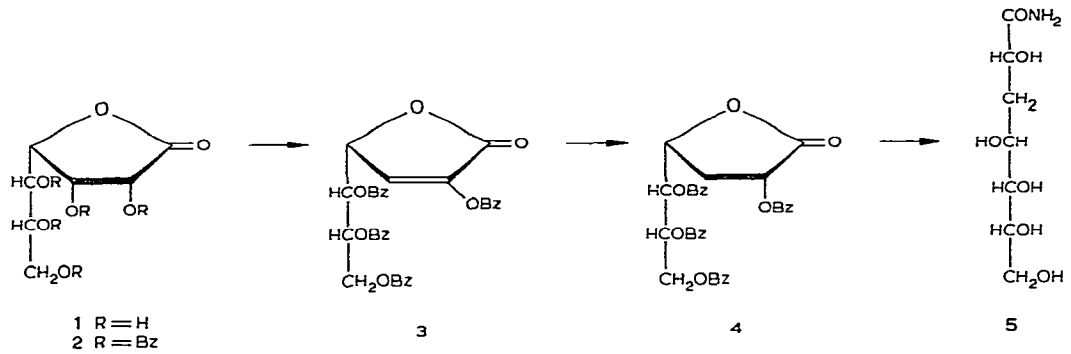

1 R=H
2 R=Bz

Facile elimination reactions due to the acidic nature of the proton which is in position α to the carbonyl group have been found in both aldono-1,4-lactone derivatives[1,2,4] and 1,5-acylated lactones[3,7]. The fact that an elimination is equally possible for D-galactono-1,4-lactone[4] with a *cis*-orientation of leaving groups and D-*glycero*-D-*gulo*-heptono-1,4-lactone with *trans*-leaving groups would suggest an E_1 mechanism for this elimination reaction. The ease of formation of acylated deoxy lactones by reduction of the unsaturated derivatives suggests their use as intermediates for the synthesis of deoxy aldofuranose derivatives[8].

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. I.r. spectra were recorded with a Perkin–Elmer infracord spectrophotometer. N.m.r. spectra were determined with a Varian A-60 spectrometer in chloroform-*d* with tetramethylsilane as the internal reference. T.l.c. was performed on Silica Gel G (E. Merck, Darmstadt, Germany), with 49:1 benzene–ethyl acetate as the mobil phase; the spots were detected with iodine vapors.

2,5,6,7-Tetra-O-*benzoyl-2,3-dideoxy*-D-arabino-*hept-2-enono-1,4-lactone* (3). — D-*glycero*-D-*gulo*-Heptono-1,4-lactone (2 g) was suspended in anhyd. pyridine (40 ml), and benzoyl chloride (20 ml) was slowly added. The mixture was shaken for 16 h at room temperature and then poured with stirring into ice–water (100 ml). After 3 h, the product was extracted with chloroform, and the extract was washed successively with saturated sodium hydrogen carbonate solution and water, dried (sodium sulfate), and evaporated *in vacuo* with the aid of toluene to remove the pyridine. The syrup crystallized from ether (0.730 g). From the mother liquors an additional amount (0.660 g) was obtained (total yield 24%). Pure 3 was obtained by recrystallization from benzene, m.p. 181–182°, $[\alpha]_D^{16}$ +24.8° (*c* 0.9, chloroform); u.v. datum: λ_{max}^{MeOH} 232 nm (ε 37,500); i.r. data: ν_{max}^{Nujol} 1775 (α,β-unsaturated 1,4-lactone), 1750 (benzoate carbonyl), 1700 (s) and 1650 (w) cm^{-1} (C=C–C=O); n.m.r. data: τ 1.7–2.7 (21-proton multiplets, 4 Bz and H-3), 4.0 (2-proton, broad signal, H-5,6), 4.45 (1-proton non resolved signal, H-4) and 4.85–5.7 (2-proton multiplets, H-7,7′).

Anal. Calc. for $C_{35}H_{26}O_{10}$: C, 69.30; H, 4.29. Found: C, 69.18; H, 4.45.

*Ozonolysis of 2,5,6,7-tetra-*O*-benzoyl-2,3-dideoxy-*D-arabino*-hept-2-enono-1,4-lactone.* — To a solution of **3** (600 mg) in ethyl acetate (40 ml) chilled in a dry ice–acetone bath, ozone was passed through for 90 min. The reaction solution was hydrogenated over 10% palladium-on-calcium carbonate at atmospheric pressure and room temperature. The catalyst was removed by filtration and the solution evaporated under reduced pressure to a syrup that was dissolved in chloroform. This solution was extracted three times with water. The aqueous layer gave a positive test for oxalic acid (reduction to glyoxylic acid detected colorimetrically[9]), and calcium oxalate was precipitated by addition of a calcium chloride solution. The chloroform solution was evaporated to dryness and the residue treated with sodium methoxide in methanol for 1 h. Paper chromatography of the solution with 5:2:2 butanol–ethanol–water as developer and silver nitrate–sodium hydroxide or aniline phthalate as indicator showed the presence of arabinose. The sugar was characterized by preparation of the *N*-(4-nitrophenyl)-D-arabinosylamine which was identical with an authentic sample prepared from D-arabinose, m.p. and mixed m.p. 200–202°, lit.[10]: m.p. 206°.

*Catalytic hydrogenation of 2,5,6,7-tetra-*O*-benzoyl-2,3-dideoxy-*D-arabino*-hept-2-enono-1,4-lactone* (**3**). *Preparation of 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-*D-gluco*-heptono-1,4-lactone* (**4**). — A solution of **3** (600 mg) in ethyl acetate (70 ml) was hydrogenated over 5% palladium-on-charcoal (300 mg) at atmospheric pressure and room temperature. The catalyst was filtered off, the filtrate evaporated under reduced pressure, and the residue crystallized from ethanol (580 mg, 97%), m.p. 203–204° after recrystallization from benzene; $[\alpha]_D^{20}$ +14.0° (*c* 0.9, chloroform); i.r. data: ν_{max}^{Nujol} 1790 (1,4-lactone), 1720 cm^{-1} (benzoate carbonyl); n.m.r. data: τ 1.75–2.8 (20-proton multiplets, 4 Bz), 4–4.5 (3-proton multiplet, H-2,5,6), 4.75–5.65 (3-proton multiplet, H-4,7,7′) and 6.75–8.0 (2-proton multiplet, H-3,3′).

Anal. Calc. for $C_{35}H_{28}O_{10}$: C, 69.08; H, 4.62. Found: C, 69.02; H, 4.71.

*3-Deoxy-*D-gluco*-heptonamide.* — 2,5,6,7-Tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptono-1,4-lactone (500 mg) was suspended in 16% methanolic ammonia (100 ml) and shaken to dissolution. After 24 h at room temperature the solution was evaporated under diminished pressure and the residue crystallized from ethanol (150 mg, 90%), m.p. 163–167° raised to 166–167° by recrystallization from 1:1 methanol–ethanol; $[\alpha]_D^{20}$ +34.5° (*c* 0.7, water); (lit.[6]: m.p. 163–164°, $[\alpha]_D^{24}$ +20.2°); i.r. data: ν_{max}^{Nujol} 3400 (OH), 3100 (NH_2), and 1630 and 1580 cm^{-1} (amide carbonyl). The i.r. spectrum was identical with that of an authentic sample[6] and the mixed melting point was not depressed.

ACKNOWLEDGMENTS

The authors thank Dr. Sprinson for a sample of 3-deoxy-D-*gluco*-heptonamide and a tracing of its i.r. spectrum, Dr. B. B. de Deferrari for the microanalyses, Mr. J. J. Ferrer for the measurement of n.m.r. spectra, and the Consejo Nacional de Investigaciones Científicas y Técnicas (Buenos Aires) for financial support.

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