Note

Acyl migration in 1-amino-2,3,4-tri-*O*-benzoyl-1-deoxy-D-erythritol

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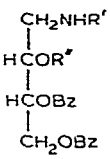
(Received June 23rd, 1970; accepted for publication in revised form, August 4th, 1970)

The acid-catalysed isomerisation of 2,3-diacetamido-4-hydroxypentane to form 2-acetamido-4-acetoxy-3-aminopentane has shown that 1,2-migration of an acetyl group from nitrogen to oxygen atoms is preferred to 1,3-migration[1]. During the ammonolysis of 2,3,4,5,6-penta-*O*-benzoyl-*aldehydo*-D-glucose, the *N*-benzoyl groups of the 1,1-dibenzamido-1-deoxy-D-glucitol produced are contributed largely by O-2, and it has been proposed[2] that, in a 1-amino-D-glucitol intermediate, benzoyl groups migrate to N-1 from O-2 and O-3. The present report describes O→N transbenzoylation in 1-amino-2,3,4-tri-*O*-benzoyl-1-deoxy-D-erythritol (**1**), which leads to 1-benzamido-3,4-di-*O*-benzoyl-1-deoxy-D-erythritol (**2**).



1 R′ = H; R″ = Bz
2 R′ = Bz; R″ = H
3 R′ = R″ = Bz

Evaporation of a chloroform solution of **1** (obtained by treatment of the hydrobromide[3] with sodium hydrogen carbonate) gave the benzamide isomer **2**. The same result was obtained after storage overnight of a chloroform solution of **1**. The structure of **2** as a 1-benzamido-1-deoxy-D-erythritol dibenzoate was demonstrated by elemental and i.r. spectral analyses, by its lack of reaction with ninhydrin or nitrous acid, and by its benzoylation to 1-benzamido-2,3,4-tri-*O*-benzoyl-1-deoxy-D-erythritol (**3**), which was also synthesised directly from 1-amino-1-deoxy-D-erythritol *p*-toluenesulphonic acid salt[4].

The position of the hydroxyl group in **2** was determined by p.m.r. analysis. After removal of the OH signal at δ 4.86 by deuterium exchange, the spectrum contained single-proton signals at δ 3.33 and 5.42, which were assigned to methine protons geminal to the hydroxyl and benzoate groups, respectively. The two-proton absorptions at δ 4.02 and 4.70 were attributed respectively to H-1,1′ and H-4,4′. These assignments are based on correlation tables[5] and are also predicted from the

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electronegativity of the various substituents. Decoupling experiments showed that the H-4,4′ signal was coupled exclusively to the signal at 5.42, and the H-1,1′ signal to that at 3.33, from which it follows that C-2 bears the hydroxyl group, so that **2** is the 3,4-dibenzoate.

The seven-line signal for H-4,4′ at δ 4.70 represents the partly overlapping AB octet of an ABX pattern with fourfold repetition of $J_{4,4'}$ 12.5 Hz. The quartet for the corresponding X pattern due to H-3 is further split by coupling to H-2, yielding the symmetrical seven-line signal at δ 5.42 with fourfold repetition of $J_{2,3}$ 8 Hz. Graphical analysis of these two lower-field signals yielded the coupling constants $J_{3,4}$ 9 Hz and $J_{3,4'}$ −6.5 Hz, as well as $\Delta\nu_{4,4'}$ 7.8 Hz. The symmetrical H-2 signal at δ 3.33 is an octet due to the X portion of an ABX pattern (AB = H-1,1′) that is further split by coupling to H-3 with $J_{2,3}$ 8 Hz; adjacent lines of the X quartet itself are separated by 5.5 Hz. The H-1,1′ absorption at δ 4.02 is a twelve-line signal, which represents the AB octet of an ABX pattern (X = H-2) that is further complicated by coupling to the amido group. This constitutes additional evidence for the assignments given to the two methylene signals.

The transbenzoylation probably occurs directly from O-2 to N-1, although the possibility of migration from, say, O-3 to N-1 followed by migration from O-2 to O-3 could only be eliminated by evidence from isotopically labelled compounds. A preference for 1,2- over 1,3-migration would require a lower free energy of activation for the formation of the 1,3-oxazolidine ring intermediate than for the perhydro-1,3-oxazine ring intermediate. This requirement may perhaps be inferred from the analogous[2] reaction of alditols to form cyclic acetals, where the kinetic product is often a 1,3-dioxolane ring that isomerises to a 1,3-dioxane ring in the thermodynamic product[6]. In the cyclisation of a homologous series of aminoalkyl bromides too, the rate of formation of a five-membered ring is greater than that of rings of other sizes[7].

EXPERIMENTAL

Evaporations were conducted under diminished pressure. Melting points were determined in a Buchi oil-bath apparatus. Optical rotations were measured in a Bellingham polarimeter Model A for 1% solutions in chloroform in 1-dm cells. I.r. spectra were obtained with a Perkin–Elmer grating spectrophotometer, Model 257. P.m.r. spectra were determined with a Varian HA-100 spectrometer in chloroform-*d* at 32° with frequency sweep and TMS lock signal; chemical shifts are reported in δ units.

*1-Benzamido-3,4-di-*O*-benzoyl-1-deoxy-*D*-erythritol* (**2**). — A solution of the hydrobromide[3] (1.6 g, 31 mmoles) of **1** in chloroform (50 ml) was shaken with a solution of sodium hydrogen carbonate (11.7 g, 140 mmoles) in water (84 ml). The chloroform layer was washed with water until free of alkali (litmus paper) and bromide (silver nitrate), and dried (sodium sulphate). This solution gave a violet colour with ninhydrin, and its i.r. spectrum contained a weak amine band at 3400 cm^{-1} and benzoic ester bands at 1720 (C=O), 1600 (ring), 1584 (ring), 1260 (C—O), 1109

(O—CH_2), 1070 (ring) and 1027 cm^{-1} (ring). After removal of the chloroform, the residue was crystallised from benzene–light petroleum (b.p. 60–80°) to give a product (855 mg, 64%), m.p. 118.5–119°, which did not react with ninhydrin and did not evolve nitrogen gas on treatment with nitrous acid. Recrystallisation raised the m.p. to 119–120°, $[\alpha]_D^{29}$ −104°, R_F 0.37 (t.l.c., Camag Silica Gel D-5, ethyl acetate–cyclohexane 1:1, iodine detection); i.r. data (film): 3370 (NH and OH), 3060 (NH), 1720 (benzoate C=O), 1635 (amide I), 1600 (ring), 1577 (ring), 1530 (amide II), 1488, 1450, 1314, 1218 and 1260 (benzoate C-O), 1176, 1112 (benzoate O-CH_2), 1070 (ring), 1026 (ring) and 710 cm^{-1} (ring); p.m.r. data: see Discussion.

Anal. Calc. for $C_{25}H_{23}NO_6$ (433): C, 69.27; H, 5.35; N, 3.23. Found: C, 69.17; H, 5.23; N, 3.39.

A solution of **2** (433 mg, 1 mmole) in pyridine (5 ml) was treated with benzoyl chloride (0.23 ml, 2 mmoles). The reaction mixture was poured into excess water the next day. A benzene solution of the deposit obtained was washed, dried (magnesium sulphate), and concentrated to a solid, which was crystallised from benzene–light petroleum (b.p. 60–80°) to give a product (338 mg, 63%), m.p. 139°, mixture m.p. with **3** 140°.

*1-Benzamido-2,3,4-tri-*O*-benzoyl-1-deoxy-*D*-erythritol* (**3**). — Benzoyl chloride (14.5 ml, 120 mmoles) was added dropwise to a magnetically stirred solution of 1-amino-1-deoxy-D-erythritol *p*-toluenesulphonic acid salt[4] (5.86 g., 20 mmoles) in pyridine (70 ml). After 18 h, water (3 ml) was added, and most of the pyridine was evaporated. A solution of the concentrate in benzene was washed and dried (magnesium sulphate). Addition of light petroleum (b.p. 60–80°) produced crystals (8.7 g, 81%), m.p. 135–137°. A benzene solution of the crystals was treated with Norit three times. Four recrystallisations from benzene, followed by one recrystallisation from ethanol, yielded the pure product, m.p. 139.5°, $[\alpha]_D^{28}$ −19°.

Anal. Calc. for $C_{32}H_{27}NO_7$ (538): C, 71.50; H, 5.06; N, 2.61. Found: C, 71.59; H, 5.19; N, 2.56.

ACKNOWLEDGMENTS

The author thanks Prof. E. Dimant of the Hebrew University of Jerusalem for his guidance and help, and Dr. Y. Shvo of the University of Tel Aviv for the p.m.r. spectra.

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