[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, BETHESDA 14, MD.]

# 2-Deoxy-D-ribose. V.[1] Synthesis of the Two Anomeric 9-(2-Deoxy-D-ribofuranosyl)-adenines through 5-Benzoyl-2-deoxy-D-ribose Diisopropyl Dithioacetal

BY CHRISTIAN PEDERSEN[2] AND HEWITT G. FLETCHER, JR.

RECEIVED MARCH 31, 1960

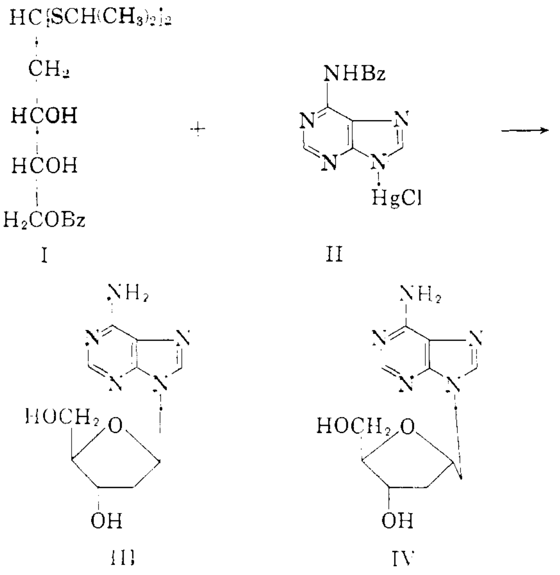
Condensation of 5-*O*-benzoyl-2-deoxy-D-ribose diisopropyl dithioacetal with chloromercuri-6-benzamidopurine, followed by removal of the acyl groups, gives 2′-deoxyadenosine and its anomer.

Nucleosides are normally synthesized through condensation of acylated glycosyl halides with suitably substituted purines and pyrimidines. Representatives of this class of substance, containing 2-deoxy-D-ribofuranosyl moieties, have recently been obtained by the use of this type of reaction[1,3,4]; in earlier work, preformed pentofuranosylpurines[5] and pyrimidines[6,7] were reduced at C2′ by various means to obtain 2′-deoxynucleosides.

In two recent communications[8,9] we have shown that aldose dithioacetals and alkyl 1-thioaldosides condense with the silver salts of carboxylic acids to give 1-*O*-acyl-aldoses. In extending this general investigation we have now found that the reaction may be used for the synthesis of two anomeric purine nucleosides.

Preliminary experiments afforded chromatographic evidence that ethyl 1-thio-β-D-glucopyranoside condensed (in boiling acetonitrile) with chloromercuri-6-benzamidopurine (II) to give (after removal of the N-benzoyl group) a glucosyladenine. 5-*O*-Benzoyl-2-deoxy-D-ribose diisopropyl dithioacetal (I)[10] was therefore condensed under similar conditions with the same purine derivative (II). After removal of the protecting groups the product was chromatographed on a cellulose column and the two anomeric 9-(2-deoxy-D-ribofuranosyl)-adenines (III and IV) isolated in crystalline form. The β-anomer was identical with natural 2′-deoxyadenosine while the α-anomer has been obtained earlier in this Laboratory.[1]

While the yields obtained in this procedure were quite low (6.3% for the β-anomer, 8.1% for the α-anomer), earlier experience in the D-glucose series[8] suggests that an alkyl 5-*O*-benzoyl-2-deoxy-1-thio-D-ribofuranoside would have given more satisfactory results.[11,12] Attempts to make such a compound have, however, as yet met with no success.



## Experimental

**2′-Deoxyadenosine (III) and 9-(2-Deoxy-α-D-ribofuranosyl)-adenine (IV).**—One gram of 5-*O*-benzoyl-2-deoxy-D-ribose diisopropyl dithioacetal[10] was dissolved in 50 ml. of acetonitrile and 5.07 g. (4 molar equivalents) of chloromercuri-6-benzamidopurine[13] added. The mixture was stirred and refluxed for 4 hr.[14] The solvent was then removed *in vacuo* and the residue extracted several times with dichloromethane. Concentrated *in vacuo*, the combined extracts afforded a solid; this was dissolved in 20 ml. of methanol, barium methoxide (6 ml., 1 *N*) added, and the solution refluxed for 4 hr. The mixture was neutralized with carbon dioxide, evaporated to dryness and the residue treated with 20 ml. of water. After filtration the solution was concentrated to dryness and the residue extracted with methanol (3 × 25 ml.). Evaporation of the methanolic extracts left a residue of 0.70 g. Chromatography of this material on paper, using isopropyl ether–ethanol–water (16:4.5:1, v./v.), showed strong ultraviolet-absorbing spots corresponding to adenine, 2′-deoxyadenosine and 9-(2-deoxy-α-D-ribofuranosyl)-adenine; two weaker, unidentified spots of lower $R_f$ were also observed. A similar chromatography of the methanol-insoluble material (0.45 g.) showed that it contained adenine but only a trace of 2′-deoxyadenosine.

The methanol-soluble product (0.7 g.) was dissolved in 20 ml. of methanol and 2 ml. of water and put on a column containing 700 g. of powdered cellulose. Elution was

---

[1] 2-Deoxy-D-ribose. IV, R. K. Ness and H. G. Fletcher, Jr., THIS JOURNAL, **82**, 3434 (1960).

[2] Chemical Foundation Fellow 1958–1960.

[3] M. Hoffer, R. Duschinsky, J. J. Fox and N. Jung, THIS JOURNAL, **80**, 4112 (1959).

[4] H. Venner, *Chem. Ber.*, **93**, 140 (1960).

[5] C. D. Anderson, L. Goodman and B. R. Baker, THIS JOURNAL, **81**, 3967 (1959).

[6] D. M. Brown, D. B. Parihar, C. B. Reese and A. Todd, *J. Chem. Soc.*, 3035 (1958).

[7] G. Shaw and R. N. Warrener, *ibid.*, 50 (1959).

[8] C. Pedersen and H. G. Fletcher, Jr., THIS JOURNAL, **82**, 3215 (1960).

[9] C. Pedersen, H. W. Diehl and H. G. Fletcher, Jr., *ibid.*, **82**, 3425 (1960).

[10] H. Zinner and H. Nimz, *Chem. Ber.*, **91**, 1657 (1958).

[11] Since isopropyl dithioacetals are somewhat more reactive than unbranched alkyl dithioacetals, a di-*t*-butyl dithioacetal or a *t*-butyl 5-*O*-benzoyl-2-deoxy-1-thio-D-ribofuranoside should undergo condensations with heavy metal salts under relatively mild conditions.

[12] Whether masking at C5 is necessary to prevent ring enlargement during these condensations remains to be proved.

[13] Reference 1, footnote 15.

[14] In other runs the refluxing was extended to 20 hr. or the mixture was simply stirred at room temperature for 24 hr. As estimated from paper chromatograms, the yields of glycoside thus obtained were lower than when refluxing was halted after 4 hr. A single experiment, in dimethyl sulfoxide at 90° for 5 hr., appeared to give a yield comparable to that with acetonitrile described here.

carried out with isopropyl ether–ethanol–water (16:4.5:1, v./v.) and 20-ml. fractions of eluate collected. Fractions 190 to 272 contained adenine. Fractions 360 to 475 were pooled and evaporated to dryness. The residue was extracted with hot methanol (3 × 100 ml.) and the combined extracts were freed of solvent *in vacuo*. The product (150 mg.) was dissolved in *ca.* 5 ml. of water, treated with a small amount of decolorizing carbon, filtered and concentrated to a volume of 2 ml. When seeded and kept at 5° overnight the solution deposited 42.4 mg. (6.3%) of 2′-deoxyadenosine as colorless crystals melting partially *ca.* 165° and finally at 190–192° (cor.).[15] Admixture with authentic natural nucleoside gave no depression. In water ($c$ 0.40) it rotated $[\alpha]^{20}D$ −27.0°. Like the natural nucleoside it showed an absorption minimum at 225 mμ and a maximum at 260 mμ, the $A_M$ at this latter wave length being 15,220.

Fractions 500 to 630 contained a component with the chromatographic characteristics of 9-(2-deoxy-α-D-ribofuranosyl)-adenine. They were pooled and evaporated to dryness. The residue was dissolved in 40 ml. of hot absolute alcohol and, after filtration, the solution concentrated to a volume of *ca.* 10 ml. After cooling at −5° overnight there was obtained 55.0 mg. (8.1%) of 9-(2-deoxy-α-D-ribofuranosyl)-adenine, melting at 201–205° (cor.). Two recrystallizations from absolute alcohol gave 35.5 mg. of pure nucleoside melting at 208–210° (cor.) and rotating $[\alpha]^{20}D$ +69° in water ($c$ 0.32). At 260 mμ it showed an absorption maximum: $A_M$ 16.290. A minimum was shown at 228 mμ. Ness and Fletcher[1] reported for 9-(2-deoxy-α-D-ribofuranosyl)-adenine m.p. 209–211° (cor.), $[\alpha]^{20}D$ +71° and $A_M$ 15,900 at 260 mμ. A mixed melting point of the samples from the two sources was undepressed. No evidence was found for the presence of a 7-(2-deoxy-D-ribofuranosyl)-adenine in any of the fractions of this chromatography.

---

(15) This behavior on melting is highly characteristic of the substance; see refs. 1 and 4.

---

[CONTRIBUTION FROM THE PULP AND PAPER RESEARCH INSTITUTE OF CANADA AND THE DEPARTMENT OF CHEMISTRY, MCGILL UNIVERSITY, MONTREAL, CANADA]

# Isolation and Properties of an *O*-Acetyl-4-*O*-methylglucurono-xyloglycan from the Wood of White Birch (*Betula papyrifera*)[1]

BY T. E. TIMELL

RECEIVED JANUARY 20, 1960

Extraction with dimethyl sulfoxide of a chlorine holocellulose from the wood of white birch has yielded a water-soluble *O*-acetyl-4-*O*-methylglucurono-xyloglycan containing one α-(1 → 2)-linked 4-*O*-methyl-D-glucuronic acid residue and 3.6 *O*-acetyl groups per 10 xylose residues. Hydrolysis of the methylated and reduced polysaccharide gave D-yxlose, 2-*O*-methyl-D-xylose, 3-*O*-methyl-D-xylose, 2,3-di-*O*-methyl-D-xylose and 2,3,4-tri-*O*-methyl-D-glucose in a mole ratio of 1:4.8:3.0:15.6:2.7. The hemicellulose consumed 6.6 moles of periodate per average repeating unit, giving D-xylose as the only reducing sugar after reduction and hydrolysis. It is tentatively concluded that the *O*-acetyl groups were located in the xylan framework and probably mostly attached to $C_3$, and that the carboxyl groups were neither lactonized nor ionized. The number- and weight-average degrees of polymerization of the polysaccharide as determined by osmometry and light scattering were 180 and 470, respectively.

In an earlier investigation[2] it was shown that untreated wood contains few, if any, formyl ester groups, and that the formyl groups previously found probably had been formed during the analysis by alkaline or acid decomposition of wood polysaccharides. It was concluded that all acyl groups in wood are acetyl groups. Ritter and co-workers[3–6] were the first to show that the acyl groups in wood are associated with the holocellulose portion. This observation was confirmed by later investigators,[7,8] and it was found[9] that the acyl groups are probably attached to the acidic xylans present in both hardwoods and softwoods.

In a previous study[10] it was shown that the polysaccharide obtained on alkaline extraction of wood or holocellulose from white birch contains a linear framework of about 200 (1 → 4)-linked β-D-xylopyranose residues,[11] every tenth of which, on the average, carries a 4-*O*-methyl-D-glucuronic acid residue as a terminal side chain, attached through $C_2$. In this hemicellulose all acyl groups originally present had, of course, been removed by the alkali. A polysaccharide still containing *O*-acetyl groups has now been isolated from the wood of the same species. This paper is concerned with the isolation and molecular properties of this *O*-acetyl-4-*O*-methylglucurono-xyloglycan and also attempts to establish tentatively the location of its *O*-acetyl groups and the nature of the carboxyl groups.

The extractive-free wood meal contained 5.07% *O*-acetyl groups, identified through two crystalline acetates. Treatment of the wood with chlorine and alcoholic ethanolamine[12] gave a holocellulose which contained almost all of the original *O*-acetyl groups. The holocellulose was exhaustively extracted with dimethyl sulfoxide[9] to give an *O*-acetyl-4-*O*-methylglucurono-xyloglycan containing 9.33% *O*-acetyl groups and representing 50% of the total amount of this polysaccharide present in the wood. *O*-Acetylated sugars, when treated similarly, were recovered unchanged, and variation in experimental conditions did not alter the yield or *O*-acetyl content of the hemicellulose. The partly acetylated polysaccharide was a fluffy powder, easily soluble in water, dimethyl sulfoxide, dimethylformamide, formamide and aqueous alkali.

---

(1) Paper presented at the Symposium on Wood Hemicelluloses before the Division of Cellulose Chemistry at the 136th Meeting of the American Chemical Society, Atlantic City, N. J., September, 1959.

(2) T. E. Timell, *Svensk Papperstidn.*, **60**, 762 (1957).

(3) G. J. Ritter and E. F. Kurth, *Ind. Eng. Chem.*, **25**, 1250 (1933).

(4) E. F. Kurth and G. J. Ritter, THIS JOURNAL, **56**, 2720 (1934).

(5) C. D. Bird and G. J. Ritter, *ibid.*, **59**, 802 (1937).

(6) R. L. Mitchell, S. C. Rogers and G. J. Ritter, *Ind. Eng. Chem.*, **40**, 1528 (1948).

(7) F. W. Klingstedt, *Paperi ja Puu*, **19**, 613, 648 (1937); **20**, 104 (1938).

(8) W. Klauditz, *Holzforsch.*, **11**, 47 (1957).

(9) E. Hägglund, B. Lindberg and J. McPherson, *Acta Chem. Scand.*, **10**, 1160 (1956).

(10) C. P. J. Glaudemans and T. E. Timell, THIS JOURNAL, **80**, 941, 1209 (1958).

(11) C. P. J. Glaudemans and T. E. Timell, *Svensk Papperstidn.*, **61**, 1 (1958).

(12) T. E. Timell and E. C. Jahn, *ibid.*, **54**, 831 (1951).