[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

# The Preparation of Alpha Aldose Acetates from Acetylated Glycosides[1]

BY RAYMOND M. HANN AND C. S. HUDSON

Montgomery and Hudson[2] have employed the catalytic action of sulfuric acid upon solutions of aldose-β-acetates in mixtures of acetic acid and acetic anhydride to bring about a transformation to the isomeric alpha form of the acetate, a procedure which is preferable to the usual use of zinc chloride as catalyst of this change. Recently we have attempted to employ various modifications of this procedure in an effort to utilize it for the preparation of the alpha form of certain glycoside acetates, and have found in many cases that hydrolysis followed by acetylation occurs to give alpha aldose acetates in large yield. While such a reaction may be anticipated, its application as a preparative method has not been reported; because of its simplicity and convenience we desire to record it and therefore describe its application to several glycoside acetates.

## Experimental

**α-Mannose Pentaacetate from Tetraacetyl-α-methylmannoside.**—A solution of 5.2037 g. of finely powdered tetraacetyl-α-methylmannoside at 20° in 25 cc. of a transforming mixture (previously prepared by adding 2 cc. of concd. sulfuric acid dropwise to an ice cold mixture of 70 cc. of acetic anhydride (95%) and 30 cc. of glacial acetic acid (99.5%)) was transferred to a glass polariscope tube with sealed glass end plates and the changes in rotation observed. The data are summarized in Table I.

The optical change during the first twenty minutes is very small but thereafter it follows a unimolecular course. After the solution had reached constant rotation it was poured into an excess of ice-cold sodium bicarbonate solution and extracted with carbon tetrachloride. The extract was dried, concentrated to a dry sirup, and brought to crystallization by solution in ether and treatment with petroleum ether. The alpha pentaacetate crystallized in large colorless prisms showing a specific rotation[3] of +55.4° in chloroform in agreement with the known value.[4] The yield of recrystallized material was 2.4 g. (44%). From a larger preparation 12.8 g. (59%) of alpha acetate was obtained from 20 g. of acetylated glycoside. This method of preparing the alpha acetate is advantageous because the tetraacetate of α-methylmannoside is easily available since the glycoside can be prepared readily in large yield from vegetable ivory.[5]

TABLE I

ROTATIONAL DATA ON THE TRANSFORMATION OF TETRAACETYL-α-METHYLMANNOSIDE

| Time after soln., min. | Time | $[\alpha]^{20}_D$ | $k$ |
|---|---|---|---|
| 4 | ... | +46.7 | .. |
| 5 | ... | 46.6 | .. |
| 10 | ... | 46.2 | .. |
| 15 | ... | 46.2 | .. |
| 20 | 0 | 46.2 | .. |
| 30 | 10 | 46.6 | 0.021 |
| 40 | 20 | 46.8 | .019 |
| 50 | 30 | 47.2 | .022 |
| 60 | 40 | 47.6 | .023 |
| 80 | 60 | 48.2 | .024 |
| 100 | 80 | 48.9 | .026 |
| 120 | 100 | 49.4 | .026 |
| 150 | 130 | 49.9 | .025 |
| 180 | 160 | 50.4 | .025 |
| 240 | 220 | 51.2 | .025 |
| 300 | 280 | 52.0 | .027 |
| 360 | 340 | 52.4 | .027 |
| ∞ (24 hrs.) | ∞ | 53.2 | .. |
| | | | Average .024 |

**α-Glucose Pentaacetate from Tetraacetyl-β-methylglucoside.**—A solution of 25 g. of the acetylated glycoside in 204 cc. of the transforming mixture previously described, showed at 20° rapid upward change in specific rotation reaching an equilibrium value of +89.0° after forty-eight hours. The neutralizing solution was extracted with carbon tetrachloride, the extract concd. to a dry sirup and brought to crystallization by solution in 75 cc. of absolute alcohol. The first fraction (14.3 g., 53%) rotated +100.2° in chloroform and two subsequent fractions (6.1 g. +70.7°; 3.4 g. +24.7°) brought the recovered yield to 92% of total pentaacetate, the latter fractions doubtless containing beta glucose pentaacetate.

**α-Glucose Pentaacetate from Tetraacetyl-β-thiophenol Glucoside.**—A pilot experiment containing 0.8546 g. of the thioglycoside acetate in 25 cc. of transforming mixture showed an original specific rotation of −20.2°, which increased gradually at 20° to an equilibrium value of +76.0°. A parallel experiment with 3.7 g. of starting material yielded 2.0 g. (61%) of α-glucose pentaacetate melting at 113° and showing the correct specific rotation of 101.4°.

**α-Glucose Pentaacetate from Tetraacetylthio-β-naphthol β-Glucoside.**—A solution of 2.0191 g. of tetraacetylthio-β-naphthol β-glucoside in 25 cc. transforming mixture changed at 20° in specific rotation from −20.4 to +15.4° in six hours, but upon standing overnight a considerable separation of β-naphthol disulfide had occurred, preventing further readings. The solution was treated in the usual manner and α-glucose pentaacetate obtained in 50% yield (0.8 g.) by treatment of the dried sirup with ether.

**Other Acetylated Methylglycosides.**—While products were not isolated in all cases, tests were conducted on

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Montgomery and Hudson, THIS JOURNAL, **56**, 2463 (1934).

(3) Throughout the article specific rotation refers to the $[\alpha]^{20}_D$ value.

(4) Hudson and Dale, THIS JOURNAL, **37**, 1282 (1915).

(5) Hudson, "Organic Syntheses," Vol. VII, p. 64.

several glycoside acetates by observing rotation changes. Pentaacetyl-β-methyl-[β-*d*-galaheptoside] (2.1207 g. in 25 cc. of reagent) changed in specific rotation from +43.5 to −63.3° in forty-eight hours, and triacetyl-β-thiophenol *d*-xyloside very slowly changed in the expected positive direction.

**Conversion of Tetraacetyl-α-methyl-γ-*d*-mannoside to a New Pentaacetate of *d*-Mannose.**—The previously mentioned glycoside acetates and the α-aldose acetates resulting from their transformation are all of the normal stable ring type. It seemed possible that glycoside acetates of the gamma ring type might lead to the synthesis of acetates of the corresponding ring type, most of which are at present unknown, and experiments were conducted with tetraacetyl-γ-methylmannoside to test this hypothesis. Preliminary observation showed that the reagent employed for the normal glycoside acetates caused very rapid conversion and some attendant decomposition, so a solution containing only 0.02 cc. of sulfuric acid in 100 cc. of a 2:1 acetic anhydride–acetic acid mixture was employed. A solution of 5.0876 g. of tetraacetyl-γ-methylmannoside[6] (m. p. 63°, specific rotation +106.3° in chloroform) in 26 cc. of the transforming solution changed in specific rotation from +108.7 to +70.2° during the course of five days at 20°. The solution was treated in the usual manner and the sirup obtained from the carbon tetrachloride crystallized from a small amount of 50% alcohol; yield 2.2 g. (41%). Recrystallized successively from 5 parts of 50% alcohol it showed specific rotations of +89.6 and 89.3° (0.3177 g. in 25 cc. of chloroform in a 2-dm. tube rotated 2.27° to the right). The new pentaacetate of mannose crystallized in brilliant prisms and melted to a clear colorless oil at 76° (corr.).

*Anal.* Calcd. for $C_{16}H_{22}O_{11}$: C, 49.2; H, 5.7. Found: C, 49.3; H, 5.8. Acetyl determination: 0.1130 g. consumed 14.4 cc. of 0.1 *N* NaOH. Calcd., 14.5 cc.

At the time of its preparation (Dec., 1932) it was thought likely that the substance was an acetate of the gamma type, possessing a ring structure, but the recent conversion of an acetylated methylmannoheptoside of the gamma type to an aldehydo acetate (see the accompanying article by Montgomery and Hudson) by the transforming solution makes further investigation of the new mannose pentaacetate necessary before a structure can be assigned to it.

We are indebted to Dr. F. H. Goldman for carrying out the carbon and hydrogen determinations, and to Professor W. N. Haworth for seed crystals of γ-methylmannoside.

## Summary

A convenient procedure for the preparation of α-aldose acetates from acetylated glycosides is described. This is an alternative method to the usual acetylation of sugars and in some cases (*e. g.*, the mannose series) it is a preferable one. Acetates of glycosides of the stable ring type yield acetates of this type. One acetylated glycoside of the gamma ring type (tetraacetyl-γ-methylmannoside) has been tested; it is transformed in large yield to a new crystalline pentaacetate of mannose.

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(6) Haworth, Hirst and Webb, *J. Chem. Soc.*, 656 (1930); Harris, Hirst and Wood, *ibid.*, 2119 (1932).

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# Reduction Studies in the Morphine Series. IV. Allopseudocodeine[1]

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The catalytic reduction of allopseudocodeine I in dilute acetic acid with a colloidal palladium catalyst proceeds exclusively in the "abnormal" sense, with saturation of the alicyclic double bond and reductive rupture of the ether linkage, giving tetrahydroallopseudocodeine III.[2] When the hydrogenation is carried out in ethanol in the presence of palladium on calcium carbonate, nearly equal amounts of tetrahydroallopseudocodeine and the new non-phenolic dihydroallopseudocodeine II are formed. Under similar conditions pseudocodeine, the diastereomer of allopseudocodeine, and γ-isomorphine give predominantly tetrahydro derivatives.[3] Under those special conditions which we have found to favor "normal" saturation of the double bond alone,[3] allopseudocodeine is converted in 80% yield to its dihydro derivative II; as by-products, small amounts of tetrahydroallopseudocodeine and tetrahydrodesoxycodeine IV are obtained.

Reduction of allopseudocodeine with sodium and alcohol gives as the principal products the previously-described[4] mixture of dihydrodesoxycodeines-B and -C VI and a phenolic dihydroallopseudocodeine V. The latter is converted to

(1) The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia and the University of Michigan.

(2) Speyer and Krauss, *Ann.*, **432**, 233 (1932).

(3) Lutz and Small, THIS JOURNAL, **54**, 4415 (1932); Small and Lutz, *ibid.*, **56**, 1928 (1934).

(4) Small and Lutz, *ibid.*, **56**, 1738 (1934).