## **Preliminary communication**

The oxidation of 2-acetamido-2-deoxyaldoses. Two unsaturated lactones from 2-acetamido-2-deoxy-D-glucose, -D-mannose, and -D-galactose

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Although aqueous bromine has long been used for the conversion of simple aldoses into aldonic acids, the action of this oxidant on 2-acylamido-2-deoxyaldoses does not appear to have been investigated. We now report some aspects of the behavior of the three most readily accessible 2-acetamido-2-deoxyaldoses (1, 2, and 3) with this convenient reagent, and describe the transformation that occurs when the products thus obtained are treated with alkali.

Each of the sugars (1-3) was subjected to the action of unbuffered bromine-water, and the reaction mixture was processed as described by von Euw and Reichstein<sup>1</sup>. The product from 2-acetamido-2-deoxy-D-glucose (1) was obtained as a hygroscopic foam:  $\nu_{\text{max}}^{\text{KBr}}$  1750 (C=O), 1660, and 1560 cm<sup>-1</sup> (amide); paper chromatography showed the crude oxidation product (4) to be heterogeneous. Hydrolysis of a sample of 4 with hot 4 M hydrochloric acid gave material chromatographically indistinguishable from 2-amino-2deoxy-D-gluconic acid<sup>2</sup>. With dicyclohexylamine, the oxidation product gave a crystalline salt: C<sub>20</sub>H<sub>38</sub>N<sub>2</sub>O<sub>7</sub>\*, m.p. 191-194°,  $[\alpha]_D$  -2.9° (c 0.95, water);  $\nu_{\text{max}}^{\text{KBr}}$  3200 (NH), 1780 (C=O), and 1630 and 1560 cm<sup>-1</sup> (amide), indicating that 2-acetamido-2-deoxy-D-gluconic acid is one of the oxidation products obtained from 1.

The oxidation of 2-acetamido-2-deoxy-D-mannose (2) with bromine-water led to the isolation in 51% yield of a product having m.p. 172-173° and  $[\alpha]_D$  +87.4° (c 1.0, water);  $v_{max}^{\text{KBr}}$  3400 (OH), 3300 (NH), 1770 (C=O), and 1660 and 1550 cm<sup>-1</sup> (amide); n.m.r. data (methyl sulfoxide- $d_6$ )  $\tau$  1.92 (doublet, J 9.0 Hz, removed by D<sub>2</sub> O exchange; NH), 4.40 (doublet, removed by D<sub>2</sub>O exchange; OH), 5.02 (quartet,  $J_{2,\text{NH}}$  9.0,  $J_{2,3}$  4.5 Hz; H-2), 5.20 (doublet, OH), unresolved multiplets at 5.40-6.60, and 8.04 (NAc). The elemental analysis corresponded to C<sub>8</sub>H<sub>13</sub>NO<sub>6</sub>, and the compound is assigned structure 5, namely, 2-acetamido-2-deoxy-D-mannono-1,4-lactone.

With aqueous bromine, 2-acetamido-2-deoxy-D-galactose (3) gave the known<sup>3,4</sup>

<sup>\*</sup>Acceptable elemental analyses were obtained for all compounds reported. Melting points are corrected values.



2-acetamido-2-deoxy-D-galactono-1,4-lactone (6): m.p.  $162-166^{\circ}$ ,  $[\alpha]_{D} -21.6^{\circ}$  (c 1.09, water);  $\nu_{max}^{KBr}$  3350 (OH), 3250 (NH), 1780 (C=O), and 1650 and 1550 cm<sup>-1</sup> (amide).

Treatment of 4 with methanolic potassium hydroxide at room temperature afforded a mixture of two crystalline products (A and B) in approximately equal proportions; similar treatment of the lactones 5 and 6 gave essentially the same mixture of products. By careful recrystallization of the mixture from methanol solution, one of the components (A) could be obtained in pure form: m.p. 186–188°,  $[\alpha]_D$  +41.1° (c 1.04, water);  $\nu_{\text{Max}}^{\text{KBr}}$  3350 (OH), 3200 (NH), 1750 (C=O), 1680 (C=C), 1630 and 1540 (amide), and 960 cm<sup>-1</sup>. The elemental composition of the substance corresponded to C<sub>8</sub>H<sub>11</sub>NO<sub>5</sub>; its n.m.r. spectrum (methyl sulfoxide- $d_6$ ) included signals at  $\tau$  0.05 (broad singlet, disappearing after D<sub>2</sub>O exchange; NH), 2.50 (doublet,  $J_{3,4}$  2.0 Hz, vinyl proton; H-3), 4.75–5.0 (2H multiplet collapsing on D<sub>2</sub>O exchange to a 1H quartet centered at 4.82,  $J_{3,4}$  2.0 Hz,  $J_{4,5}$  4.5 Hz; H-4), 5.27 (triplet, J 5.5 Hz, disappearing after D<sub>2</sub>O exchange; primary OH), and 7.92 (NAc). The Legal test for unsaturated lactones was positive. Acetylation with acetic anhydride-pyridine gave a di-O-acetyl derivative which was obtained as a chromatographically homogeneous syrup having  $[\alpha]_D$  +58.1° (c 0.86, chloroform) and an elemental composition corresponding to C<sub>12</sub>H<sub>15</sub>NO<sub>7</sub>. I.r. absorption (neat) was observed at 3280 (NH), 1750 (C=O),

1720 (OAc), 1660 (C=C), and 1630 and 1540  $\text{cm}^{-1}$  (amide); the n.m.r. spectrum (chloroform-*a*) included signals at  $\tau$  1.82 (broad singlet, NH), 2.51 (doublet, *J* 1.5 Hz; H-3), 4.65-4.90 (multiplet, 2H), 5.40-5.90 (multiplet, 2H), 7.77 (NAc), and 7.88 and 7.92 (OAc).

Although crystalline, the second component (B) of the mixture could not be obtained in pure form. The i.r. spectrum of this component very closely resembled that of A, except that it showed an absorption band at 915 cm<sup>-1</sup> (not at 960 cm<sup>-1</sup>). The n.m.r. spectrum of component B was also very similar to that of A, except that its low-field doublet of 2.0 Hz appeared at  $\tau$  2.58 (not at  $\tau$  2.50). These spectral characteristics clearly revealed the composition of the mixtures of the two components; in addition, the component B proved to be levorotatory, and mixtures rich in it were found to give values as low as  $[\alpha]_D -97^{\circ}$  (c 0.40, water).

The spectral data, as well as the fact that these two compounds are formed from both the D-gluco (4) and the D-manno compound (5), clearly indicate that they are diastereoisomeric 2-acetamido-2,3-dideoxyhex-2-enono-1,4-lactones; that they are also formed from the D-galacto lactone (6) suggests that they are epimeric at C-4. Such a proposal implies that the two components may be interconvertible in the presence of alkali and, indeed, this proved to be the case. Treatment of component A (available in pure form) with methanolic potassium hydroxide at room temperature caused a levomutarotation and the formation of a mixture such as had been separately obtained from 4, 5, and 6; treated similarly, a fraction rich in component B showed a dextro-mutarotation.

As there is no reason to suppose that the configuration of C-5 has been affected, structures 8 and 9 may be assigned to the two products. Although optical rotatory considerations suggest that the pure isomer A,  $[\alpha]_{D}$  +41.1°, is 8, and the levorotatory isomer B is 9, other evidence bearing on this point was sought. The saturated lactone 5 readily gave an isopropylidene acetal when treated with acetone and anhydrous copper(II) sulfate: m.p. 161–164°,  $[\alpha]_D$  +75.8° (c 1.04, methanol);  $\nu_{max}^{KBr}$  3300 (OH), 3200 (NH), 1750 (C=O), 1650 and 1540 (amide), and 1380 and 1370 cm<sup>-1</sup> (Me<sub>2</sub>C); n.m.r. signals (acetone- $d_6$ ) at  $\tau$  7.05 (deleted by D<sub>2</sub>O exchange; OH), 7.97 (NAc), and 8.61 and 8.68 (Me<sub>2</sub>C); the elemental composition corresponded to  $C_{11}H_{17}NO_6$ . It is reasonable to assume that the isopropylidene group spans O-5-O-6 as in 7; an analogous derivative of 6 was described by Karrer and Meyer<sup>3</sup>. An attempt was made to p-toluenesulfonylate the remaining hydroxyl group (at C-3) in 7 through the use of p-toluenesulfonyl chloride in pyridine solution. However, no trace of the expected derivative was detected, and the material isolated proved to be a sulfur-free, unsaturated compound having a composition corresponding to  $C_{11}H_{15}NO_5$ : m.p. 124–125°,  $[\alpha]_D$  –29.1° (c 1.01, chloroform);  $\nu_{max}^{KBr}$  3300 (NH), 1780 (C=O), 1710 (C=C), 1660 and 1550 (amide), and 1385 and 1380 cm<sup>-1</sup>  $(Me_2C)$ ; n.m.r. signals (chloroform-d) at  $\tau$  2.15 (broad singlet, NH), 2.41 (doublet, J 2.0 Hz; H-3), 5.06 (quartet, J 2.0 and 7.1 Hz; H-4), 5.85-6.10 (multiplet, 3H), 7.80 (NAc), and 8.55 and 8.67 (Me<sub>2</sub> C).

The unsaturated lactone A (available in pure form) was condensed with acetone in the presence of anhydrous copper(II) sulfate to give a crystalline product 10, identical in all respects with that obtained through the attempted sulfonylation of 7. It is, therefore, evident that the dextrorotatory lactone is 2-acetamido-2,3-dideoxy-D-*erythro*-hex-2-enono-1,4-lactone (8), and that the levorotatory isomer is the corresponding D-*threo* compound

(9). In passing, it may be noted that 10 appeared to be unaccompanied by isomeric materials, regardless of whether it was prepared from 7 or 8.

The investigation outlined here is being extended; further details, together with a discussion of the mechanistic features of some of the reactions involved, will be provided elsewhere.

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