906. 5-*Acetamido*-5-*deoxy*-L-*arabinose: A Sugar Derivative containing Nitrogen as the Hetero-atom in the Ring.*

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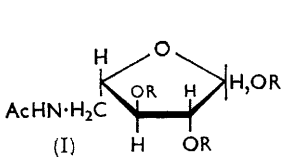
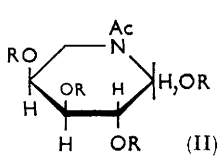
5-Acetamido-5-deoxy-L-arabinose has been synthesized and found to exist in two forms which differ in the position of ring-closure of the terminal aldehyde group. One form probably has a normal five-membered furanose ring, and the other a six-membered ring in which the hetero-atom is nitrogen instead of oxygen.

5-Acetamido-5-deoxy-L-arabinose was required as a reference compound in connection with studies on the oxidation of polyhydric acetamido-deoxy-alcohols by *Acetobacter suboxydans*.[1] 1,2-*O*-Isopropylidene-5-*O*-toluene-*p*-sulphonyl-L-arabinose was prepared[2] and reaction with methanolic ammonia, followed by *N*-acetylation, gave 5-acetamido-5-deoxy-1,2-*O*-isopropylidene-L-arabinose which was hydrolyzed to give 5-acetamido-5-deoxy-L-arabinose. This compound was found to exist in two forms (I and II; R = H).



(I)



(II)

The two forms, which were chemically and physically distinct, were separated by cellulose-column chromatography and were obtained pure. They gave the same crystalline phenylosazone which was identical with that obtained from 5-acetamido-5-deoxy-*keto*-L-*erythro*-pentulose.[1] The same crystalline 1-acetamido-1-deoxy-L-lyxitol was obtained from the two compounds on reduction by sodium borohydride.

[1] Jones, Perry, and Turner, *Canad. J. Chem.*, 1962, **40**, 503.
[2] Hirst, Jones, and Williams, *J.*, 1947, 1062.

It was concluded, on this evidence, that the two compounds were both 5-acetamido-5-deoxy-L-arabinose and that the difference between them was in the position of ring-closure of the terminal aldehyde group. The possibility of a four-membered ring was discounted and it was assumed that one compound possessed a normal five-membered furanose ring; it was therefore probably 5-acetamido-5-deoxy-L-arabinofuranose (I; R = H). The other compound possessed a six-membered ring formed by ring-closure on to the nitrogen atom of the amide group as in (II; R = H); it may be named 1-acetyl-L-*gluco*(*manno*)-2,3,4,5-tetrahydroxypiperidine.

5-Acetamido-5-deoxy-L-arabinofuranose (I; R = H) gave infrared absorption bands consistent with the assigned structure. The results of periodate oxidation in unbuffered aqueous solution indicated that the compound contained a furanose ring.

1-Acetyl-L-*gluco*(*manno*)-2,3,4,5-tetrahydroxypiperidine (II; R = H) gave different infrared absorption bands consistent with its assigned structure. Again the results of periodate oxidation in unbuffered aqueous solution were in agreement with the proposed six-membered ring.

Both compounds (I and II; R = H) were stable in neutral aqueous solution at room temperature. However, addition of a drop of ammonia solution resulted in the rapid formation of an equilibrium mixture of the two. Equilibration was also catalyzed by acetic acid, but much less effectively. The equilibrium mixture was also formed when an aqueous solution of either compound was heated. The furanose (I; R = H) formed the major portion of the equilibrium mixture in all cases.

The furanose gave a syrupy tri-*O*-acetyl derivative (I; R = Ac), and the piperidine derivative gave a crystalline tetra-*O*-acetyl derivative (II; R = Ac), both acetates having infrared absorption consistent with the structures assigned. The piperidine derivative also gave a crystalline tetrabenzoate (II; R = Bz), with appropriate infrared absorption.

The formation of the tetra-*O*-acyl derivatives was strong evidence for the presence of a six-membered ring. The absence of absorptions due to NH in the infrared spectra showed that ring-closure of the aldehyde group had occurred on to the nitrogen atom, with the elimination of the hydrogen atom of the amide group.

5-Acetamido-5-deoxy-L-arabinofuranose (I; R = H), on reaction with methanolic hydrogen chloride at room temperature, became dark after several hours and the several products were not investigated. 1-Acetyl-L-*gluco*(*manno*)-2,3,4,5-tetrahydroxypiperidine (II; R = H), on reaction with methanolic hydrogen chloride at room temperature, immediately formed a syrupy methyl glycoside. After the initial change, the optical rotation of the reaction mixture remained constant. On periodate oxidation in unbuffered aqueous solution the syrupy methyl glycoside consumed 1·8 mol. of periodate and released 0·8 mol. of formic acid, which showed that the compound possessed a six-membered ring.

Experimental

M. p.s were determined on a Fisher–Johns m. p. apparatus. Optical rotations were measured at 23° ± 3° for aqueous solutions, unless otherwise stated. Infrared spectra were measured on a Perkin-Elmer model 21 spectrophotometer. Solutions were concentrated under reduced pressure, in a rotary-film evaporator. Paper chromatography was carried out by the descending method at room temperature on Whatman No. 1 filter paper for qualitative purposes or on Whatman 3MM filter paper for preparative purposes, with the following mobile phases: (A) butan-1-ol–ethanol–water (3 : 1 : 1 v/v); (B) butan-1-ol–pyridine–water (5 : 3 : 2 v/v); (C) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4 v/v). The compounds were detected with (i) alkaline silver nitrate [3] or (ii) *p*-anisidine hydrochloride [4] spray reagents and rates of movement are quoted relative to that of rhamnose (R_{Rh}).

1,2-O-*Isopropylidene*-5-O-*toluene*-p-*sulphonyl*-L-*arabinose*.—This compound was prepared from methyl α-L-arabinofuranoside (120 g.) by Hirst, Jones, and Williams's method.[2] Recrystallization from methanol gave needles (55 g., 23%), m. p. 125—127° (lit.,[2] 131°).

[3] Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.
[4] Hough, Jones, and Wadman, *J.*, 1950, 1702.

5-*Acetamido*-5-*deoxy*-1,2-O-*isopropylidene*-L-*arabinose*.—1,2-*O*-Isopropylidene-5-*O*-toluene-*p*-sulphonyl-L-arabinose (35 g.) was dissolved in dry methanol (750 ml.), and the solution was cooled to 0°, saturated with dry ammonia, and then heated in an autoclave at 120° for 16 hr. After cooling, the dark mixture was boiled with charcoal, then filtered and passed through Amberlite IRA-400 (OH^-) anion-exchange resin (400 ml.). The eluate was evaporated to dryness and the residue was *N*-acetylated with aqueous acetic anhydride,[5] to yield 5-*acetamido*-5-*deoxy*-1,2-O-*isopropylidene*-L-*arabinose*. The product was recrystallized three times from methanol–ether, to give needles (10 g., 43%), m. p. 143—144°, $[\alpha]_D$ −45° (*c* 2·0 in MeOH) (Found: C, 51·8; H, 7·6; N, 5·8. $C_{10}H_{17}NO_5$ requires C, 52·0; H, 7·4; N, 6·1%), $\nu_{max.}$ (0·8% in KBr) 3250s and 1570s (NH), 1640s (*N*-Ac), 1380s (CH of isopropylidene group) $cm.^{-1}$.

5-*Acetamido*-5-*deoxy*-L-*arabinose*.—5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-L-arabinose (8·6 g.) was heated in 50% aqueous acetic acid (40 ml.) at 95° for 1·5 hr. The dark solution was evaporated, yielding 5-acetamido-5-deoxy-L-arabinose as a clear brown syrup (7 g., 99%) which was examined on paper chromatograms. Both sprays i and ii showed two spots R_{Rh} 0·51 and 1·13 (solvent A), 0·57 and 1·02 (solvent B), and 0·83 and 1·09 (solvent C). The two components were separated on a cellulose column (54 × 4·5 cm.) with butan-1-ol half-saturated with water as the irrigant and were obtained in a pure state.

5-*Acetamido*-5-*deoxy*-L-*arabinofuranose* (I; R = H) was obtained from the eluate as a pale yellow syrup (3·5 g.), $[\alpha]_D$ 0° (*c* 3·0), R_{Rh} 1·13 (solvent A), 1·02 (solvent B), and 1·09 (solvent C), $\nu_{max.}$ (smear on KBr pellet) 3300s (OH and NH), 1715w (CHO), 1630s (*N*-Ac), 1555s (NH) $cm.^{-1}$ (Found: C, 45·2; H, 7·5; N, 7·1. $C_7H_{13}NO_5$ requires C, 44·0; H, 6·8; N, 7·3%).

1-*Acetyl*-L-gluco(manno)-2,3,4,5-*tetrahydroxypiperidine* (II; R = H) was obtained from the eluate as a syrup (2·27 g.). This was dissolved in ethanol and ether was added. The syrup was reprecipitated but it changed to a white amorphous powder (1·9 g.) at room temperature in 48 hr., then having m. p. 135—138°, $[\alpha]_D$ +19·4° (*c* 2·65) (Found: C, 43·7; H, 7·0; N, 7·3%), R_{Rh} 0·51 (solvent A), 0·57 (solvent B), and 0·83 (solvent C), $\nu_{max.}$ (0·8% in KBr) 3380s (OH), 1615s and 1595s (*N*-Ac) $cm.^{-1}$. No absorption due to NH was detected.

5-*Acetamido*-5-*deoxy*-L-erythro-*pentose Phenylosazone*.—(*a*) *From* 5-*acetamido*-5-*deoxy*-L-*arabinofuranose* (I; R = H). The phenylosazone was prepared by using glacial acetic acid and phenylhydrazine, as yellow needles, m. p. 179—181° (decomp.), mixed m. p. with the phenylosazone [1] prepared from 5-acetamido-5-deoxy-*keto*-L-*erythro*-pentulose 175—178° (decomp.). (*b*) *From* 1-*acetyl*-L-gluco(manno)-2,3,4,5-*tetrahydroxypiperidine* (II; R = H). The phenylosazone was prepared as above and obtained as bright yellow needles, m. p. 175—176° (decomp.), mixed m. p. (as above) 173—177° (decomp.). The three preparations of the phenylosazone moved at identical rates on paper chromatograms and gave indistinguishable infrared spectra over the range 4000—600 $cm.^{-1}$.

1-*Acetamido*-1-*deoxy*-L-*lyxitol*.—(*a*) *From* 5-*acetamido*-5-*deoxy*-L-*arabinofuranose* (I; R = H). 5-Acetamido-5-deoxy-L-arabinofuranose (200 mg.) was reduced with sodium borohydride (200 mg.) in aqueous solution at 0° for 3 hr. After removal of sodium borate and boric acid, the product was obtained as a yellow syrup (182 mg.). This crystallized from ethanol–ether and two recrystallizations from ethanol–ether gave 1-*acetamido*-1-*deoxy*-L-*lyxitol* as needles (110 mg., 55%), m. p. 126—127°, $[\alpha]_D$ −10·5° (*c* 1·05). (*b*) *From* 1-*acetyl*-L-gluco(manno)-2,3,4,5-*tetrahydroxypiperidine* (II; R = H). This piperidine (200 mg.) was reduced with sodium borohydride (200 mg.) as described above. However, reduction was slower in this case and required 48 hr. for completion. The 1-acetamido-1-deoxy-L-lyxitol that was obtained recrystallized twice from ethanol–ether as needles (120 mg., 60%), m. p. 126·5—127·5°, mixed m. p. with the preceding product 126—127·5°, $[\alpha]_D$ −11° (*c* 1·2) (Found: C, 43·75; H, 7·9; N, 7·4. $C_7H_{15}NO_5$ requires C, 43·5; H, 7·8; N, 7·25%). The two preparations of 1-acetamido-1-deoxy-L-lyxitol moved at identical rates on paper chromatograms, R_{Rh} 0·84 (solvent A), 0·80 (solvent B), and 1·07 (solvent C), and had identical infrared spectra over the range 4000—600 $cm.^{-1}$, $\nu_{max.}$ (0·8% in KBr) 3380s (OH), 3300s and 1560m (NH), 1625s (*N*-Ac) $cm.^{-1}$.

The Equilibrium between 1-*Acetyl*-L-gluco(manno)-2,3,4,5-*tetrahydroxypiperidine* (II; R = H) *and* 5-*Acetamido*-5-*deoxy*-L-*arabinofuranose* (I; R = H).—(*a*) *Influence of heat*. 2% Aqueous solutions of each compound were heated in a water-bath at 90°. Samples were removed at intervals, from each solution, and examined on paper chromatograms run in solvent A. The same equilibrium mixture of the two compounds was formed from each

[5] Levvy and McAllan, *Biochem. J.*, 1959, **73**, 127.

compound after 1—2 hr. The equilibrium mixture from each compound had $[\alpha]_D$ +4°, which indicated a 4 : 1 ratio of (I) : (II). Aqueous solutions were stable at room temperature for 24 hr. since no changes in optical rotation were noted and no interconversion was detectable by paper chromatography. (*b*) *Influence of ammonia.* One drop of concentrated ammonia solution was added to a 2% aqueous solution (0·5 ml.) of each compound which was then left at room temperature and examined as above. Equilibrium was reached after 5 min. and both equilibrium mixtures had $[\alpha]_D$ +6·7°, which indicated a 2 : 1 mixture of (I) : (II). (*c*) *Influence of acetic acid.* One drop of glacial acetic acid was added to a 2% aqueous solution (0·5 ml.) of each compound. The solutions were left at room temperature and examined as above. Some interconversion occurred but equilibrium was not reached in 24 hr.

*5-Acetamido-*1,2,3-*tri*-O-*acetyl*-5-*deoxy*-L-*arabinofuranose* (I; R = Ac).—5-Acetamido-5-deoxy-L-arabinofuranose (100 mg.) was treated with acetic anhydride in pyridine solution at room temperature for 20 hr., giving the 1,2,3-*triacetate* as a syrup (131 mg., 82%), $[\alpha]_D$ +5° (*c* 2·62 in $CHCl_3$) (Found: *O*-Ac + *N*-Ac, 53·4. $C_{13}H_{19}NO_8$ requires *O*-Ac + *N*-Ac, 54·4%), $\nu_{max.}$ (6% in $CHCl_3$) 3450w and 1520m (NH), 1745s (*O*-Ac), 1670s (*N*-Ac) cm.$^{-1}$. The acetate was chromatographically pure, R_{Rh} 2·54 (solvent A, spray i).

1-*Acetyl*-L-gluco(manno)-2,3,4,5-*tetra-acetoxypiperidine* (II; R = Ac).—1-Acetyl-L-*gluco*-(*manno*)-2,3,4,5-tetrahydroxypiperidine (100 mg.) was acetylated similarly; it gave a 2,3,4,5-*tetra-acetate* that recrystallized from methanol as prisms (140 mg., 75%), m. p. 181—182°, $[\alpha]_D$ +87° (*c* 1·85 in $CHCl_3$) (Found: C, 50·35; H, 5·85; N, 4·1; *O*-Ac + *N*-Ac, 59·6. $C_{15}H_{21}NO_9$ requires C, 50·1; H, 5·85; N, 3·9; *O*-Ac + *N*-Ac, 59·9%), $\nu_{max.}$ (0·8% in KBr) 1750s (*O*-Ac), 1670s (*N*-Ac) cm.$^{-1}$. No absorption due to NH was detected.

1-*Acetyl*-L-gluco(manno)-2,3,4,5-*tetrabenzoyloxypiperidine* (II; R = Bz).—1-Acetyl-L-*gluco*(*manno*)-2,3,4,5-tetrahydroxypiperidine (100 mg.) with benzoyl chloride in pyridine at 5° for 18 hr. gave the 2,3,4,5-*tetrabenzoate* as a microcrystalline powder (200 mg., 63%), m. p. 178—179°, $[\alpha]_D$ +219° (*c* 1·0 in $CHCl_3$) (Found: C, 69·4; H, 4·5; N, 2·5. $C_{35}H_{29}NO_9$ requires C, 69·2; H, 4·8; N, 2·3%), $\nu_{max.}$ (0·8% in KBr) 1725s (*O*-Bz), 1680m (*N*-Ac) cm.$^{-1}$. No absorption due to NH was detected.

Reaction of 5-*Acetamido*-5-*deoxy*-L-*arabinofuranose* (I; R = H) *with Methanolic Hydrogen Chloride.*—5-Acetamido-5-deoxy-L-arabinofuranose (200 mg.) was dissolved in 1% methanolic hydrogen chloride (10 ml.) and set aside at room temperature. The optical rotation, measured at intervals, increased to a maximum positive value (+14·7°) after 0·4 hr. and then fell steadily (to −22·9° after 5 hr.). The solution became deep yellow and the rotation could not be measured after 5 hr. In a duplicate experiment, the mixture was neutralized with silver carbonate after 0·4 hr., filtered, and evaporated to a brown syrup (190 mg.) that was weakly reducing towards Fehling's solution and contained at least two components (paper chromatography in solvent A, R_{Rh} 1·02 and 1·14, spray ii). The syrup could not be satisfactorily separated into its components.

Reaction of 1-*Acetyl*-L-gluco(manno)-2,3,4,5-*tetrahydroxypiperidine* (II; R = H) *with Methanolic Hydrogen Chloride.*—(*a*) The compound {20 mg.; $[\alpha]_D$ +35·7° (*c* 2·0 in MeOH)} was dissolved in 1% methanolic hydrogen chloride (2 ml.) and left at room temperature and the optical rotation was measured at intervals:

Time (hr.)	0·08	0·33	1·0	2·0	4·0
$[\alpha]_D$	+56·0°	+56·3°	+56·3°	+56·5°	+56·7°

The solution remained clear and colourless and after the initial change the optical rotation remained essentially constant. (*b*) The compound (150 mg.) was left in 1% methanolic hydrogen chloride (15 ml.) at room temperature for 10 min. The solution was then neutralized with silver carbonate, filtered, and concentrated to a clear colourless syrup (150 mg.) which was examined on paper chromatograms run in solvent A. Spray i showed one faint spot, R_{Rh} 1·36, and spray ii showed a very strong spot, R_{Rh} 1·13, and a faint spot, R_{Rh} 1·36. The component having R_{Rh} 1·13 was separated by chromatography in solvent A and obtained as a clear colourless syrup (120 mg., 75%) which was non-reducing towards Fehling's solution. This syrup, 1-*acetyl*-L-gluco(manno)-3,4,5-*trihydroxy*-2-*methoxypiperidine*, had $[\alpha]_D$ +52° (*c* 2·28 in MeOH), $\nu_{max.}$ (smear between " IR tran 2 " plates) 3400s (OH), 1625s (*N*-Ac) cm.$^{-1}$ (no absorption due to NH) (Found: OMe, 14·95; N, 6·6. $C_8H_{15}NO_5$ requires OMe, 15·1; N, 6·8%).

Periodate Oxidation.—The compound (100 mg.) was dissolved in water, a two-fold molar excess of sodium metaperiodate solution was added, and the volume was made up to 100 ml.

with water. The uptake of periodate was determined by the neutral thiosulphate method.[6] Acid released was estimated by addition of ethylene glycol (2 ml.) to an aliquot part (5 ml.), followed by titration after 15 min. with 0·01N-sodium hydroxide to 1% w/v Methyl Red (screened with Methylene Blue). Results are given in moles of either oxidant or product per mole of carbohydrate at various times (hr.).

(1) 5-Acetamido-5-deoxy-L-arabinofuranose.

Time	0·08	1·17	2·3	5·5	9·5	22·5
Uptake	1·75	2·13	2·18	2·31	2·38	2·44
Acid	1·26	1·73	1·87	2·10	2·20	2·30

(2) 1-Acetyl-L-(*gluco*(*manno*)-2,3,4,5-tetrahydroxypiperidine.

Time	0·08	1·0	2·7	4·5	7·5	21·5	32
Uptake	2·10	2·57	2·64	2·73	2·80	2·96	2·94
Acid	1·16	1·86	2·08	2·21	2·36	2·70	2·81

No formaldehyde was detected by the chromotropic acid method [7] in either (1) or (2).

(3) 1-Acetyl-L-*gluco*(*manno*)-3,4,5-trihydroxy-2-methoxypiperidine.

Time	0·12	0·83	2·17	4·75	7·5
Uptake	1·23	1·48	1·59	1·74	1·80
Acid	0·29	0·53	0·67	0·79	0·80

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[6] Neumuller and Vasseur, *Arkiv Kemi*, 1953, **5**, 235.
[7] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.