NOTES

$Ethyl \ Benzyloxy carbonyl glycyl glycinate$

A solution of 1.25 g (0.005 mole) of benzyloxycarbonylglycylguanidine in 5 ml of dimethylformamide was added to an aqueous solution of 0.7 g (0.005 mole) of ethyl glycinate hydrochloride, the pH of which was adjusted to 8 with alkali. The resultant clear solution was stirred at room temperature overnight and then evaporated on a water bath (40°) under reduced pressure (0.4 mm Hg). The residue was treated with water until crystallization occurred, then filtered, and air dried to yield 1.35 g (90%) of white solid which was recrystallized from ethyl acetate and melted at 80° (lit. m.p. 80° (4)).

Anal. Calcd. for C14H18N2O5: C, 57.1; H, 6.1. Found: C, 57.0; H, 6.2.

Similarly prepared were the following.

Ethyl Hippurylglycinate

This was obtained in 76% yield. It was recrystallized from water and melted at 117° (lit. m.p. 117° (5)). Anal. Calcd. for $C_{13}H_{16}N_2O_4$: C, 59.1; H, 6.1. Found: C, 59.0; H, 6.2.

Ethyl Benzyloxycarbonyl-DL-alanylglycylglycinate

This was obtained in 50% yield. It was recrystallized from ethanol-water and melted at 110° (lit. m.p. 113° (6)).

Anal. Calcd. for C17H23N3O6: C, 55.9; H, 6.3. Found: C, 56.0; H, 6.4.

Ethyl Formyl-L-valylglycinate

This was obtained in 71% yield. It was recrystallized from ethyl acetate - petroleum ether and melted at 155° (lit. m.p. 156-157° (7)).

Anal. Calcd. for C10H18N2O4: C, 52.2; H, 7.8; N, 12.2. Found: C, 52.1; H, 7.9; N, 12.4.

Ethyl Formyl-L-phenylalanylglycinate

This was obtained in 82% yield. It was recrystallized from water and melted at 132° ; $[\alpha]_D^{25} + 4.6^{\circ}$ (c, 1.6 in absolute ethanol) (lit. m.p. $131-132^{\circ}$; $[\alpha]_{D^{26}} + 4.4^{\circ}$ (7))

Anal. Caled. for C14H18N2O4: C, 60.5; H, 6.5; N, 10.1. Found: C, 60.3; H, 6.6; N, 10.6.

Ethyl Tosyl-L-prolylglycinate

This was obtained in 68% yield. It was recrystallized from hexane - ethyl acetate (2:1) and melted at 84-86°; $[\alpha]_{D^{25}} - 115.8^{\circ}$ (c, 4.5 in absolute ethanol).

Anal. Calcd. for C16H22N2O5S: C, 54.3; H, 6.2; N, 7.9. Found: C, 54.4; H, 6.1; N, 8.0.

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SYNTHESIS OF 5-BENZAMIDO-5-DEOXY-D-XYLOPYRANOSE

M. S. PATEL AND J. K. N. JONES

The synthesis of the N-acetyl (1, 2) $(I, R = COCH_3)$ and the N-benzyl (3) (I, R = CH_2Ph) derivatives of 5-amino-5-deoxy-D-xylopyranose (4) (I, R = H) and of the corresponding furanose compounds has been described (1-4). Recently we attempted the preparation by reported procedures of the acetobromo derivative of 5-acetamido-5deoxy-p-xylopyranose (I, $R = COCH_3$) but were unsuccessful. The synthesis of the benzamido derivative of 5-amino-5-deoxy-D-xylopyranose (I, R = COPh) was therefore undertaken in the hope that this would yield, after O-benzoylation, a benzoylbromo sugar.

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Also, it was of interest to compare the effect of the presence of a N-benzoyl group in 5-amino-5-deoxy-D-xylopyranose on the ratio of the pyranose and furanose forms of I, R = COPh.

5-Amino-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (II) was prepared from D-xylose by an improved procedure (5). On treatment with an excess of benzoyl chloride in 10% aqueous sodium hydroxide it readily yielded crystalline 5-benzamido-3-O-benzoyl-5deoxy-1,2-O-isopropylidene-D-xylofuranose (III) in 92% yield. The latter, on treatment with a catalytic amount of sodium methoxide in methanol, yielded 5-benzamido-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (IV) in 82.5% yield (based on compound II). On treatment with benzoyl chloride (1.1 moles) in pyridine, compound IV gave III in 25% yield. Hydrolysis of IV with an acidic ion-exchange resin yielded 5-benzamido-5-deoxy-Dxylopyranose (I, R = COPh) (51% yield) as the major product in equilibrium with 5-benzamido-5-deoxy-D-xylofuranose (V). No other product was detected by chromatography (8).



Cellulose column chromatography of the above mixture gave compounds V and I, R = COPh. One of these (I, R = COPh) was obtained in a crystalline form, and the other was obtained as a pale yellow chromatographically uniform syrup which could not be crystallized. The infrared spectrum of this syrup showed characteristic absorption caused by the presence of OH, NH, and an aromatic ring. The results of periodate oxidation in unbuffered aqueous solution also indicated that the compound possessed the structure V. The compound was, therefore, 5-benzamido-5-deoxy-D-xylofuranose. The crystalline compound (I, R = COPh) showed no NH band in its infrared spectrum and the results of periodate oxidation in unbuffered aqueous solution were consistent with the pyranose structure.

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EXPERIMENTAL

Apparatus, Methods, and Material

Solutions were concentrated under reduced pressure below 40° with a rotatory vacuum-type evaporator. Melting points were determined on a Fisher-Johns melting point apparatus. Optical rotations were measured at $20 \pm 3^{\circ}$ with a Hilger standard polarimeter. Infrared spectra were measured with a Perkin-Elmer model 21 spectrophotometer. Paper chromatography was performed by the descending method at room temperature on Whatman No. 1 filter paper in the following solvent system (v/v/v): 1-butanol – ethanol – water (3:1:1). Sugars were detected on paper chromatograms by the following spray reagents: (*i*) alkaline silver nitrate (6); (*ii*) *p*-anisidine hydrochloride (7); (*iii*) modified ceric ammonium nitrate reagent (8); (*iv*) orcinol – trichloroacetic acid (ketose spray) (9).

Rates of movement of the sugars on paper chromatograms are given relative to that of L-rhamnose. Thin-layer chromatography was carried out on silica gel G supplied by Research Specialities Company, Richmond, California. Benzene-isopropanol (2:1) was used as eluent. The developed plates were dried in air, sprayed with concentrated sulfuric acid, and then heated in an oven at about 150°. Organic microanalyses were performed by Dr. C. Daessle, Montreal.

Periodate Oxidation

The compound under examination (10-15 mg) was dissolved in water containing 0.3 *M* sodium metaperiodate solution (1 ml). The total volume was made up to 25 ml with additional water. A blank was prepared with 0.3 *M* sodium metaperiodate (1 ml), which was made up to 25 ml with water. The solutions were stored in the dark at room temperature. Aliquots (2 ml) were removed at intervals from each of the two solutions for the determination of periodate uptake (11). Formic acid production was determined by addition of ethylene glycol (3 ml) to an aliquot portion (2 ml), followed by titration after 10 min with 0.01 *N* sodium hydroxide, with phenolphthalein as indicator. The results are summarized in Table I. (No formaldehyde was detected in either *a* or *b* by the chromotropic acid method (12).)

TABLE I

48.00
1.88
1.53

5-Amino-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (II) (Modified Procedure of Szarek and Jones (5))

Raney nickel (10) (10 g) was added to a solution of 5-azido-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (10.0 g) (3) in methanol (250 ml) and the mixture was shaken overnight. Fresh catalyst (15 g) was then introduced, and after being shaken for an additional 6.0 h the solution was filtered and concentrated to give a crystalline product (5.0 g). This material could be recrystallized readily from ether, yielding crystals of m.p. 102–110°. The substance is highly hygroscopic, and satisfactory analytical results were not obtained. The infrared spectrum in chloroform showed absorption at 3 350 cm⁻¹ (OH and NH) and absorption at 1 382 and 1 392 cm⁻¹ (the isopropylidene group), but was devoid of azide absorption.

5-Benzamido-3-O-benzoyl-5-deoxy-1,2-O-isopropylidene-D-xylofuranose

To a solution of 5-amino-5-deoxy-1,2-O-isopropylidene-b-xylofuranose (3.5 g) in 10% aqueous sodium hydroxide (50 ml) was added excess benzoyl chloride (7 ml). After a few minutes of vigorous shaking a solid product separated; this was dissolved in chloroform (25 ml) and the solution was washed successively with aqueous sodium hydrogen carbonate and with water, and then dried (MgSO₄). Concentration of the filtered solution gave a solid (6.8 g, 92%), which was crystallized from benzene-petrol (b.p. 40-60°) as fine needles of m.p. 148-149° and $[\alpha]_{\rm D}$ -64° (c, 1.2 in chloroform). The infrared spectrum in chloroform showed absorptions at 1 665 cm⁻¹ (the amide-I band) and 1 730 cm⁻¹ (ester carbonyl stretching), absorptions at 1 460 and 1 495 cm⁻¹, 1 590 and 1 610 cm⁻¹ attributable to the aromatic ring, and a doublet at 1 382 and 1 390 cm⁻¹ (the isopropylidene group), but was devoid of OH absorption.

Anal. Calcd. for C₂₂H₂₃NO₆: C, 66.5; H, 5.8; N, 3.5. Found: C, 66.8; H, 6.0; N, 3.45.

5-Benzamido-5-deoxy-1,2-O-isopropylidene-D-xylose (IV)

To a solution of 5-benzamido-3-O-benzoyl-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (0.33 g) in absolute methanol (15 ml) was added a catalytic amount of metallic sodium. The reaction solution was allowed to stand at room temperature for 2 h with occasional shaking. It was then poured onto ice, and after the ice had melted the solution was concentrated to one-half the initial volume and then extracted

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with chloroform. The combined chloroform extracts were washed with water, dried (MgSO₄), and filtered, and the filtrate was concentrated to a syrup (0.255 g) which crystallized immediately. Recrystallization from benzene-petrol (b.p. 40-60°) gave needles (0.225 g, 98.4%) of m.p. 163-163.5° and $[\alpha]_{\rm p} + 15^{\circ}$ (c, 1.23 in CH₃OH). The infrared spectrum in chloroform showed absorptions at 3 485 cm⁻¹ attributable to OH, at 3 400 cm⁻¹ attributable to NH, at 1 650 cm⁻¹ (the amide-I band), at 1 530 cm⁻¹ (the amide-II band). aromatic absorption at 1 610, 1 585, 1 495, and 1 460 cm⁻¹, a doublet at 1 380 and 1 385 cm⁻¹ (isopropylidene group, and showed the absence of an ester.

Anal. Calcd. for C15H19NO5: C, 61.4; H, 6.5; N, 4.8. Found: C, 61.4; H, 6.4; N, 5.0.

Benzoylation of IV

5-Benzamido-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (3.4 g) in pyridine (10 ml) was treated with benzoyl chloride (1.1 moles) and the mixture was left at room temperature overnight. Water was then added to the solution and the mixture was extracted with chloroform (3 \times 30 ml). The solution was washed successively with dilute sulfuric acid, with sodium bicarbonate solution, and with water. The dried chloroform solution was evaporated and the product recrystallized from benzene-petrol (40-60°). The yield of purified product was 1.95 g. It had m.p. 148°, identical with the product (III) described above.

Hydrolysis of 5-Benzamido-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (IV)

To an aqueous suspension (100 ml) of 5-benzamido-5-deoxy-1,2-O-isopropylidene-D-xylofuranose (1.345 g) was added Rexyn 50 (H form) (Fisher Scientific Company) (ca. 5.0 g). The reaction mixture was stirred at 75° until all the solid had dissolved (ca. 3 h). Rexyn 50 was removed by filtration and the filtrate was stirred with a small quantity of Duolite A-4 (OH form) to remove acidity. The filtered solution was concentrated to yield a colorless syrup (1.109 g) which was examined on paper chromatograms as well as by thin-layer chromatography. Sprays i and ii both showed the presence of components on paper chromatograms at $R_{\rm rh}$ 1.4 (I, R = COPh) and 2.0 (V). No unchanged starting material was detected either on paper chromatograms (spray iii) or by thin-layer chromatography. The syrup was placed on a cellulose column (54 \times 2.5 cm) and irrigated with pure 1-butanol. Fractions (3 ml) were collected automatically. Chromatographic examination of the fractions showed that a partial separation of the two components (0.14 g of V and 0.20 g of I, R = COPh) had been achieved. The unresolved mixture was refractionated using the same experimental conditions. Complete separation was then obtained. The two components (I, R = COPh and V) of the hydrolysate were obtained in a chromatographically pure state.

(a) 5-Benzamido-5-deoxy-D-xylofuranose (V)

This component was obtained from the eluate as a yellow syrup (0.218 g) which could not be crystallized. The compound had $[\alpha]_{D^{20}} + 19.2^{\circ}$ (c, 0.8 in methanol) and $R_{\rm th}$ 2.0. The infrared spectrum (thin film on KBr) showed characteristic absorption caused by OH at 3310 cm^{-1} , by NH at 1557 cm^{-1} , and by the aromatic ring at 1 460, 1 495, 1 590, and 1 610 cm⁻¹.

(b) 5-Benzamido-5-deoxy-D-xylopyranose (I, R = COPh)

This component was obtained from the eluent above as a white crystalline solid (0.6 g, 51.7%). It crystallized from methanol-ether with 1 molecule of methanol as a solvent of crystallization and had an indefinite melting point (m.p. 94-102°), $[\alpha]_D^{20} - 11.5^\circ$ (c, 0.69 in methanol), and R_{rh} 1.4. The infrared spectrum of this material (0.8% in KBr) showed strong absorption at $3 310 \text{ cm}^{-1}$ attributable to OH, strong absorption at 1 625 cm⁻¹ caused by N-benzoyl (amide-I), aromatic absorption at 1 475, 1 495, and 1 590 cm⁻¹, but no absorption caused by NH.

Anal. Calcd. for C12H15NO5 CH3OH: C, 55.7; H, 1.9; N, 5.0. Found: C, 55.6; H, 7.1; N, 5.1.

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