oxalacetate (21.0 g, 100 mmol) in 100 ml of ethanol was heated at reflux with stirring until solution was complete (about 30 min). The reaction mixture was then added to 1l. of water and the pH adjusted to 2 with dilute phosphoric acid to precipitate 20.0 g (76.7%) of crude product melting at 162–165°. Two recrystallizations from ethanol provided the pure pyrroline, **6**: mp 164–165°; ir 3430 cm^{-1} (OH), 1710 (lactam C=O), 1680 (ester C=O); uv 272 mμ shoulder (ϵ 10,900), 242 (ϵ 25,100); (10^{-3} *N* ethanolic NaOH) 307 mμ (ϵ 23,900), 229 (ϵ 20,900); nmr δ 1.11 ppm t (J = 7 Hz, CH_2CH_3), 2.82 s (NCH_3), 4.17 q (J = 7, OCH_2CH_3), 5.06 s ($NCHC_6H_5$), 7.32 m (C_6H_5), 8.50 b (OH, exchanges with D_2O).

Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.53; H, 5.64; N, 5.59.

1-Methyl-2,3-diacetoxy-4-ethoxycarbonyl-5-phenylpyrrole (10).—The hydroxypyrrolinone, **6** (13.1 g, 50 mmol), was stirred overnight at room temperature in 40 ml of acetic anhydride containing anhydrous pyridine (4.0 g, 50 mmol). The reaction mixture was concentrated and the residue dissolved in chloroform which was then washed twice with water. After drying ($MgSO_4$) and removing the solvent, a solid was obtained which was crystallized from benzene to give 12.0 g (70%) of the pyrrole, **10**: mp 122–124°; ir 1780 cm^{-1} (acetoxy C=O), 1710 (ester C=O), uv 273 mμ (ϵ 7000), 220 mμ shoulder (ϵ 16,400); nmr δ 1.00 ppm t (J = 6 Hz, CH_2CH_3), 2.40 s and 2.42 s ($COCH_3$), 3.97 q (J = 7, OCH_2CH_3), 7.30 s (C_6H_5).

Anal. Calcd for $C_{18}H_{19}NO_6$: C, 62.60; H, 5.55; N, 4.06. Found: C, 61.84, 62.89; H, 5.56, 5.91; N, 4.12.

1-Methyl-3-acetoxy-4-ethoxycarbonyl-5-phenyl-3-pyrrolin-2-one (9).—Following the above procedure, only limiting the acetylation period to 20 min, the hydroxypyrrolinone, **6** (13.1 g, 50 mmol), was monoacetylated. The solid obtained after removing the chloroform was washed with ether to yield 14.7 g (97.5%) of crude enol acetate, **9**. Sublimation at 90° (0.05 mm) provided an analytical sample: mp 101–102°; ir 1790 cm^{-1} (acetoxy C=O), 1710 (ester C=O), 1670 (lactam C=O); uv, end absorption; nmr δ 1.10 ppm t (J = 7 Hz, CH_2CH_3), 2.32 s ($COCH_3$), 2.73 s (NCH_3), 4.08 m (OCH_2CH_3), 5.13 s ($NCHC_6H_5$), 7.30 m (C_6H_5).

Anal. Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.15; H, 5.99; N, 4.87.

***cis*-1-Methyl-4-ethoxycarbonyl-5-phenyl-2-pyrrolidone (11b).**—Enol acetate **9** (7.5 g, 25 mmol) in 50 ml of glacial acetic acid was hydrogenated at atmospheric pressure over 50 mg of PtO_2 for 15 hr. An additional 50 mg of catalyst was added and hydrogenation continued for 10 hr. The total hydrogen uptake was 40 mmol. Filtration and removal of the solvent gave, after washing with ether, 4.0 g (65%) of crude ester **11b**. Sublimation at 80° (0.05 mm) provided the analytical sample: mp 80–81°; ir 1750 cm^{-1} (ester C=O), 1700 (lactam C=O); nmr δ 0.90 ppm t (J = 7 Hz, CH_2CH_3), 2.52 q (J = 9, C_3H), 3.11 q (J = 9, C_3H), 3.68 m (H_b + OCH_2CH_3), 4.81 d (J = 9, H_a), 7.20 m (C_6H_5).

Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.02; H, 6.78; N, 5.64.

The above ester (2.0 g, 8.1 mmol) was heated at reflux in 25 ml of 5 *N* HCl containing 10 ml of dioxane. Removal of the solvent and crystallization of the residue from acetone gave 1.6 g (90%) of a solid identical in all respects with the *cis* acid **4b**.

***trans*-1,5-Diphenyl-4-carboxy-2-pyrrolidinone (14a).**—Following the procedure describing the preparation of **4**, benzylidineaniline (18.1 g, 100 mmol) and succinic anhydride (11.0 g, 100 mmol) were heated at reflux in 200 ml of benzene for 36 hr. Cooling and scratching induced crystallization and yielded 20.0 g (71.5%) of crude product melting at 120–158°. Three crystallizations from acetone gave the pure *trans* acid **14a**: mp 179–180° with softening at 166°; ir (Nujol) 2800–2500 cm^{-1} (OH), 1740 (carboxyl C=O), 1670 (lactam C=O); nmr δ 3.07 ppm m (CH_2 + H_b), 5.55 d (J = 4 Hz, H_a), 7.25 m (2 C_6H_5).

Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.63; H, 5.02; N, 4.91.

Registry No.—Succinic anhydride, 108-30-5; **2**, 622-29-7; **4a**, 20-178-20-5; **4b**, 20-178-21-6; **6**, 20-178-22-7; **9**, 20-178-23-8; **10**, 20-178-24-9; **11a**, 20-178-25-0; **11b**, 20-178-26-1; **14a**, 20-178-27-2.

N-Acylenamines from Oxazolines. A New Route to 2-Acetamidoglycals

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When acetylated with isopropenyl acetate in the presence of a trace of *p*-toluenesulfonic acid, the two epimeric aldoses, 2-acetamido-2-deoxy-D-glucose and 2-acetamido-2-deoxy-D-mannose, show sharply divergent behavior. The former gives a mixture of the anomeric 1,3,4,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-D-glucopyranoses, together with 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose.[2] The latter, on the other hand, gives at least five products[3,4] and among these is 3,4,6-tri-*O*-acetyl-2-(*N*-acetylacetamido)-1,2-dideoxy-D-*arabino*-hex-1-enopyranose, obtained in 14% yield; partial deacetylation of this di-*N*-acylenamine gives 2-acetamido-D-glucal (**4**, 2-acetamido-1,2-dideoxy-D-*arabino*-hex-1-enopyranose), the first amino sugar related glycal to be encountered. It was unfortunate that a substance of such potential interest should be available in such low yield from a comparatively expensive aldose, and we now wish to report an alternative and novel synthesis of **4** which makes this unsaturated amino sugar much more readily accessible.

Ozazolines that are derived from 2-acylamino-2-deoxyaldoses, and in which C-1 and C-2 of the sugar moiety are part of the oxazoline ring, have been made by a variety of methods[5-9] and an investigation in this laboratory has recently shown that acetylated oxazolines (such as **1** and **3**) may be prepared quite conveniently by treatment of 2-acylamino-2-deoxyaldoses with a mixture of acetic anhydride and anhydrous zinc chloride.[10] We have now found that the acetylated oxazoline, **1**,[9,11] from 2-acetamido-2-deoxy-D-glucose, readily isomerizes when heated at 100° in tetramethylurea solution containing a trace of *p*-toluenesulfonic acid. Thin layer chromatography of the amorphous product revealed a compound which was unsaturated; on de-*O*-acetylation with sodium methoxide, it gave a crystalline product which proved to be 2-acetamido-D-glucal (**4**). That the immediate product of the isomerization, **2**, had not crystallized was not surprising, since an earlier attempt[3] to obtain this substance in crystalline form had failed. (See Scheme I.)

The acetylated oxazoline derived from 2-acetamido-2-deoxy-D-mannose (**3**)[9,10] also gave **2** and, after de-*O*-

(1) Staff Fellow, National Institutes of Health, 1967–1969.

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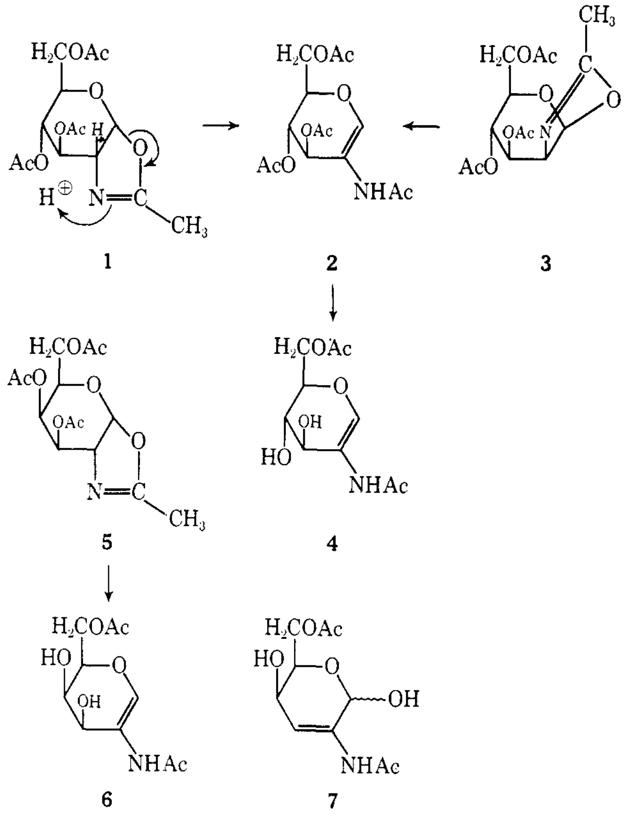
SCHEME I



acetylation, 4.[12] The facile rearrangement of these two oxazolines in which a proton is lost from the 4 position of the heterocycle and the C-5–oxygen bond cleaves to give an *N*-acylenamine is, as far as we are aware, unique. However, owing to the special character of C-5 (which is also C-1 of an aldose) in oxazolines such as **1** and **3**, these heterocycles may be expected to differ considerably in their properties from those oxazolines in which C-5 of the heterocycle is attached to only one oxygen atom. It may be relevant to note that the proton at the 4 position of an aldofuranose-derived 2-phenyloxazoline has been found to be labile under alkaline conditions, the oxazoline undergoing an elimination to give an oxazole.[13] Mechanistic considerations aside, the rearrangement described here affords a practicable synthetic pathway for the preparation of 2-acetamido-D-glucal (**4**) from the relatively accessible 2-acetamido-2-deoxy-D-glucose. In addition, if the process is a general one, it should serve to make available isomeric 2-acetamidoglycals. To explore this possibility, we have heated 2-methyl(3′,4′,6′-tri-*O*-acetyl-1,2-dideoxy-α-D-galactopyrano)[2′,1′:4,5]-2-oxazoline[10] (**5**) in tetramethylurea solution containing *p*-toluenesulfonic acid. De-*O*-acetylation of the initial product from the reaction gave a crystalline substance which proved to be identical with an unsaturated compound prepared earlier in this laboratory[14] through de-*O*-acetylation of one of the products from the action of isopropenyl acetate–*p*-toluenesulfonic acid on 2-acetamido-2-deoxy-D-galactose. Evidence obtained in the course of the earlier investigation was interpreted as indicating that this compound was 2-acetamido-2,3-dideoxy-D-*threo*-hex-2-enose (**7**). However, formation of the material from the oxazoline, **5**, strongly suggests that it is not **7** but the analog of **4**, namely, 2-acetamido-D-galactal (**6**). Independent evidence confirming this suggestion will be presented in a separate communication.[15]

Experimental Section[16]

2-Acetamido-1,2-dideoxy-D-*arabino*-hex-1-enopyranose (4, 2-Acetamido-D-glucal). A. From 2-Methyl(3′,4′,6′-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2′,1′:4,5]-2-oxazoline (1).—The oxazoline (**1**) was prepared in 65% yield from 2-acetamido-2-deoxy-D-glucose by a modification[17] of the procedure describe earlier:[10] $[\alpha]^{20}$D 7.0° (*c* 0.99, chloroform), 0.45° (*c* 1.79, acetone); Khorlin and his coworkers[9] recorded $[\alpha]^{20}$D 10° (chloroform). Although the material was syrupy, it was homogeneous when chromatographed on a thin layer of silica gel G_{254} (E. Merck, Darmstadt) using benzene–ether–methanol (14:14:1). One gram of **1** was dissolved in tetramethylurea (5 ml) which had been dried over molecular sieve, type 4-A (Fisher Scientific Co.), and the solution was passed through a column (3 × 5 cm) of molecular sieve, type 4-A, and directly into a dry flask containing a saturated solution of anhydrous *p*-toluenesulfonic acid in benzene (67 μl). The column was washed with an additional 28 ml of dry tetramethylurea which was allowed to run into the reaction mixture. The solution was heated at 100° (oil bath) and samples were removed periodically for examination. Each sample was freed of tetramethylurea *in vacuo* and then subjected to tlc on silica gel G_{254} using benzene–ether–methanol (14:14:1). The acetylated glycal was detected by fluorescein–bromine[3] or by spraying with 10% sulfuric acid, the latter reagent reacting with **2** to give a brick-red color. After 21 hr, virtually all of the **1** had disappeared and the reaction mixture then consisted of **2** and of another component whose chromatographic behavior suggested that it might be 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyranose, the normal hydrolytic product of **1**. The reaction mixture was cooled and then concentrated *in vacuo* (*ca.* 1-mm pressure) at 35° (bath) to give an amber-colored oil which was chromatographed on a column of silica gel (2.9 × 25 cm, no. 7734 of E. Merck) using benzene–ether–methanol (14:14:1) to yield **2**: 521 mg, 52% yield. A portion of the syrupy **2** was de-*O*-acetylated in conventional fashion with sodium methoxide to yield crystalline **4**, mp 124–125°; a mixture melting point with material prepared earlier from 2-acetamido-2-deoxy-D-mannose[3] was undepressed.

B. From 2-Methyl(3′,4′,6′-tri-*O*-acetyl-1,2-dideoxy-β-D-mannopyrano)[2,′1′:4,5]-2-oxazoline (3).—Crystalline **3** (470 mg), prepared in 11% yield from 2-acetamido-2-deoxy-D-mannose by a modification[17] of the method described earlier,[10] was treated exactly as described above for its D-*gluco* analog. After 6 hr, only a trace of **3** remained; removal of solvent and chromatography of the crude product gave **2**: 286 mg, 61%. De-*O*-acetylation afforded **4**, mp and mmp 124.5–125°.

2-Acetamido-1,2-dideoxy-D-*lyxo*-hex-1-enopyranose (6, 2-Acetamido-D-galactal) from 2-Methyl(3′,4′,6′-tri-*O*-acetyl-1,2-dideoxy-α-D-galactopyrano)[2′,1′:4,5]-2-oxazoline (5).—The oxazoline, **5** (1 g), prepared as described by Pravdić, Inch, and Fletcher,[10] was treated exactly as described for the other two oxazolines (**1** and **3**) to yield a chromatographically homogeneous syrup (330 mg) which gave a red color when sprayed (tlc) with 10% sulfuric acid[12] and also gave a positive fluorescein–bromine test for unsaturation. De-*O*-acetylation of a sample of the syrup with sodium methoxide yielded, from 2-propanol, a crystalline compound of mp 152–153.5° and $[\alpha]^{20}$D 83.2° (*c* 0.53, water). The nmr spectrum of this product was identical with that of a substance previously designated as 2-acetamido-2,3-dideoxy-D-*threo*-hex-2-enose (**7**)[14] and reported as having mp 152–153° and

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[12] A transient brick-red color is formed when 2-acetamidoglycal derivatives on thin layer silica gel or paper are sprayed with 10% sulfuric acid. Dr. G. G. Ashwell of this institute informs us that thin layer chromatography of the crude product obtained through the action of acetic anhydride and zinc chloride on 2-acetamido-2-deoxy-D-mannose, followed by sulfuric acid spray, reveals a component which gives this red color. It is likely, therefore, that a derivative of **2** is formed as a by-product in the preparation of **3** by the method of ref 10.

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[16] Melting points correspond to corrected values.

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$[\alpha]^{20}_{D}$ 76.1° (c 1.0, water); a mixture melting point was undepressed.

Registry No.—4, 10293-59-1; 7, 17327-17-2.

2-Cyclopropylpyridine

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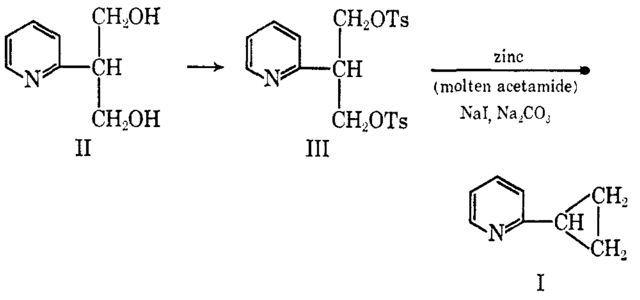
The synthesis of 2-cyclopropylpyridine (I) has previously been reported by one of us.[1] It had been prepared in small quantity in a six-step synthesis. The ultraviolet spectrum had been reported [λ_{max} 2690 Å (log ϵ 3.58)] in absolute alcohol. Although derivatives had been prepared, no analysis had been reported on I itself.[2]

In a recent publication,[3] Gray and Kraus cast doubt as to whether I had been obtained. Although they[3] did not actually prepare I, they did prepare 4-cyclopropylpyridine. Other data[4,5] seem to confirm the earlier report of Gray and Kraus.

It was felt that the unequivocal synthesis of I itself would be necessary to solve the dilemma. A new synthesis of I was achieved and is reported here. Commercially available II[6] was converted into III by standard procedures. Using a modification of the method of Dolbier,[7] III was readily converted into I in 80% yield of crude material. The product, I, was purified by preparative gc and was free from all detectable contamination.



Pure I had a λ_{max} of 2685 Å (log ϵ 3.60) in absolute alcohol. The ir spectrum (neat) and nmr spectrum were consistent with the structure assigned to I; the methinyl proton of the cyclopropyl ring appeared as the expected triplet of triplets at τ 7.8–8.3. A comparison of the spectra of I and cyclopropylbenzene[8] shows the close relation of the two compounds.

From the properties of this product, I, it is clear that the product reported previously was indeed impure. It is not possible to say what percentage of I was in the original product,[1] if indeed there was any, but the uv spectrum of I is essentially identical with that previously reported.

Attempts to prepare I from 2-vinylpyridine and methylene *via* the Simmons–Smith reaction[9] were uniformly unsuccessful.

Experimental Section

All melting points are corrected and were determined on a Fisher-Johns apparatus. Ir spectra were taken on a Beckman IR-4 spectrophotometer. Nmr spectra were taken on a Varian A-60-A instrument. Uv spectra were taken on a Cary 14 spectrophotometer. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Preparation of the Ditosylate of 2-(2-Pyridyl)-1,3-Propanediol (III).—2-(2-Pyridyl)-1,3-propanediol,[6] II (7.65 g, 0.05 mol), was dissolved in dry pyridine (125 ml) and cooled to 0–5°. *p*-Toluenesulfonyl chloride (38 g, 0.02 mol) was slowly added. The mixture was placed in a refrigerator overnight and then poured onto ice–water (700 ml) with stirring. The solid which came out of solution was crystallized from methyl alcohol, giving 15.0 g (65%) of white crystals: mp 106–107°; ir (KBr) 1175 cm^{-1} (tosylate);[10] nmr ($CDCl_3$) τ 1.50–2.67 (m, 12), 5.60 (d, 4), 7.00 (quintet, 1), 7.53 (s, 6).

Anal. Calcd for $C_{22}H_{23}NO_6S_2$: C, 57.23; H, 5.02; N, 3.04. Found: C, 57.22; H, 5.02; N, 3.09.

2-Cyclopropylpyridine (I).—A mixture of dry acetamide (40 g), sodium iodide (1 g), and sodium carbonate (3 g) was heated to 150° in a three-neck flask fitted with magnetic stirrer, thermometer, solid addition device,[11] and a Liebig condenser connected by tubing to a solution of calcium hydroxide. Powdered zinc (AR grade) (8 g, 0.06 mol) was added and the temperature was maintained at 150°. The ditosylate II (9.24 g, 0.02 mol) was slowly added (10 min) through the solid addition flask. Carbon dioxide, as expected, was evolved and formed calcium carbonate in the calcium hydroxide trap.[12] After 10 min, the condenser was removed and the apparatus was set up for distillation. The pot temperature was raised to 220° and a liquid began to distil at a head temperature of 150–180°. No cold water was used in the distilling condenser since acetamide (bp 222°, mp 82°) was distilling over with the product. The distillation was continued for 40 min. Water (50 ml) was added to the distillate, followed by ether (50 ml). The layers were separated and the ether layer was washed with water (three 25-ml portions), dried ($MgSO_4$), concentrated, and distilled, giving 2.0 g (83%) of crude 2-cyclopropylpyridine. The crude liquid was then purified by preparative gc on a dinonylphthalate column. The preparative gc gave a clear, colorless liquid (characteristic alkyl pyridine odor) free from all detectable contamination: bp 184–185° (758 mm), 31° (0.25 mm); n^{25}_{D} 1.5380; uv λ_{max} (100% ethanol) 268.5 mμ (log ϵ 3.60); ir (neat) 1030 and 1040 cm^{-1}; nmr (CCl_4) τ 2.70 (m, 4), 7.80–8.30 (3 triplets, 1), and 9.15 (m, 4).

Anal. Calcd for C_8H_9N: C, 80.67; H, 7.74; N, 11.76. Found: C, 80.75; H, 7.59; N, 11.69.

The picrate had mp 133–134°.

Anal. Calcd for $C_{14}H_{12}N_4O_7$: C, 48.28; H, 3.47. Found: C, 48.18; H, 3.50).

Registry No.—I, 20797-87-9; I (picrate), 20797-88-0; III, 20797-89-1.

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