ENAMINES DERIVED FROM 2-AMINO-2-DEOXY-D-GLUCOSE AND ACETOACETIC ESTERS

A. GÓMEZ SÁNCHEZ, A. CERT VENTULÁ,

Departamento de Química Orgánica, Universidad de Sevilla, and Instituto de Química Orgánica General, Patronato "Juan de la Cierva", C.S.I.C., Seville (Spain)

AND U. SCHEIDEGGER

Research Laboratory, Varian AG, Zürich (Switzerland)

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ABSTRACT

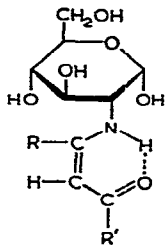
Reactions of 2-amino-2-deoxy-β-D-glucopyranose with acetoacetic esters in methanol–triethylamine produced 2-[2-(1-alkoxycarbonyl-1-propenyl)amino]-2-deoxy-α-D-glucopyranoses (**4–6**). Acetylation of **4–6** gave the tetraacetates **4a–6a**, and the acetylated β-D anomers of **4–6** were obtained directly by reaction of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose with the appropiate β-ketoester. Acid hydrolysis of the tetra-*O*-acetylated methyl enamino ester (**4a**) gave 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride.

When the reactions of 2-amino-2-deoxy-D-glucose with acetoacetic esters were carried out in methanol–triethylamine under more drastic conditions, 5-(D-*arabino*-tetrahydroxybutyl)-2-methyl-3-pyrrolecarboxylic esters (**7**) were obtained; in aqueous conditions, 2-methyl-3-pyrrolecarboxylic esters (**8**) and D-erythrose were also formed.

Conversion of the enamino esters **4–6** into the corresponding (tetrahydroxybutyl)pyrroles (**7**) and 2-methyl-3-pyrrolecarboxylic esters (**8**) occurred very easily under a variety of conditions. These results add support to the point of view that enamines are intermediates in the formation of pyrroles from 2-amino sugars and β-dicarbonyl compounds.

INTRODUCTION

2-Amino-2-deoxy-D-glucose reacts[1] readily with β-diketones (2,4-pentanedione and 1-phenyl-1,3-butanedione) and with benzoylacetaldehyde yielding enamino ketones (**1**). These substances can be converted into 4-acyl-2-(D-*arabino*-tetrahydroxybutyl)pyrroles (**2**). On this basis, it has been considered[1,2] that enamines of formula **1**, or a tautomeric form, are intermediates in the more-general reaction of amino sugars and β-dicarbonyl compounds which results in the formation of (tetrahydroxybutyl)-pyrroles. However, previous attempts[1a] to obtain an enamino ester from ethyl acetoacetate and 2-amino-2-deoxy-D-glucose were unsuccessful, in spite of the fact that the two substances readily condense[2] to form ethyl 5-(D-*arabino*-tetrahydroxy-



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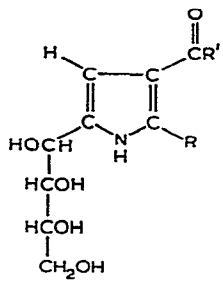

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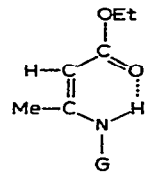


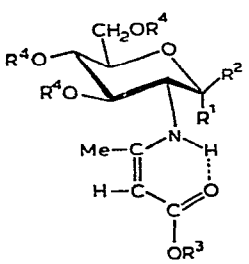
G=glycosyl group

3

butyl)-2-methyl-3-pyrrolecarboxylate. We now describe conditions under which the reactions of 2-amino-2-deoxy-D-glucose with acetoacetic esters can be stopped at the enamine stage, and the further transformations of these enamines into 5-(D-*arabino*-tetrahydroxybutyl)-2-methyl-3-pyrrolecarboxylic esters. The formation of ethyl 3-(glycosylamino)crotonates (**3**) in the reactions of glycosylamines with ethyl acetoacetate has been previously described[3].

RESULTS AND DISCUSSION

Treatment of 2-amino-2-deoxy-β-D-glucopyranose with β-ketoesters (methyl acetoacetate, ethyl acetoacetate, and *tert*-butyl acetoacetate) in methanol containing catalytic amounts of triethylamine, at room temperature, afforded 3-aminocrotonic esters (**4–6**) in high yields. No reaction was observed when triethylamine was omitted. The physical constants and yields of the products are indicated in Table I. The evidence that provides the basis for the assignment of structures **4–6** is as follows.



	R^1	R^2	R^3	R^4
4	OH	H	Me	H
4*a*	OAc	H	Me	Ac
4*b*	H	OAc	Me	Ac
5	OH	H	Et	H
5*a*	OAc	H	Et	Ac
5*b*	H	OAc	Et	Ac
6	OH	H	CMe_3	H
6*a*	OAc	H	CMe_3	Ac
6*b*	H	OAc	CMe_3	Ac

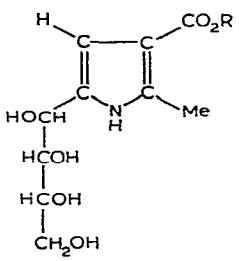
Like the similarly constituted ketoenamines **1**, compounds **4–6** showed high, positive, optical rotations (Table I) suggestive of α-D anomeric configurations, and gave positive Fehling's and ferric chloride tests. Their u.v. and i.r. spectra (Table II) were those typical of intramolecularly bonded, *N*-monosubstituted 3-aminocrotonic esters[4,5]. With acetic anhydride and pyridine at 0°, **4–6** gave the α-D tetraacetates **4a–6a**. The corresponding β-D anomers (**4b–6b**) were obtained directly by treatment of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose with the appropiate acetoacetate in *p*-dioxane–triethylamine. The physical properties (Table I) and light

absorptions (Table II) of these acetates were also in accordance with their formulations.

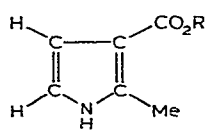
The p.m.r. spectra (Table III) of the anomeric methyl esters (**4a** and **4b**) provided further confirmation of these structures. The chemical shifts of H-1 and the $J_{1,2}$ values indicated the anomeric configurations. The signal appearing at δ 2.25 p.p.m. in the spectrum of the α-D anomer was assigned as the axial acetoxyl group on C-1. The signals given by the protons of the substituents on the nitrogen had δ values corresponding to an *N*-monosubstituted 3-aminocrotonic ester having the methoxycarbonyl and amino groups in *cis* disposition[6]. No traces of the corresponding *trans* isomers, which can be easily detected by the i.r.[5] and p.m.r. spectra[6], were observed. These derivatives, similarly to the ethyl 3-(glycosylamino)crotonic esters (**3**), seem to be more stable in the chelated *cis* form than the simple 3-(alkylamino)crotonic esters which, under similar conditions, are mixtures of the *cis* and *trans* isomers[5,6].

Treatment of the α-D methyl ester **4a** with hydrochloric acid in acetone gave an almost quantitative yield of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride. Therefore, this derivative can be easily prepared in high yield by using the readily accessible enamino esters (**4** and **5**) as intermediates.

When the reactions of 2-amino-2-deoxy-D-glucose hydrochloride with acetoacetic esters were carried out in methanol–triethylamine with heating, 5-(D-*arabino*-tetrahydroxybutyl)-2-methyl-3-pyrrolecarboxylic esters (**7**) were obtained in yields of approximately 35%. The same products were obtained when the amino sugar hydrochloride and the equivalent amount of sodium carbonate were allowed to react with the β-ketoesters in acetone–water or methanol–water at room temperature; under these conditions, trace amounts of 2-methyl-3-pyrrolecarboxylic esters (**8**) were



7a R = Me
7b R = Et
7c R = CMe_3



8a R = Me
8b R = Et
8c R = CMe_3

chromatographically detected in the reaction mixtures. The yields of these simple pyrroles were increased when the reactions were performed in aqueous basic solutions. For instance, in the reaction with *tert*-butyl acetoacetate at pH 9–10, *tert*-butyl 2-methyl-3-pyrrolecarboxylate (**8c**) was isolated in a yield of 8%. Similar observations had already been made in the reactions using ethyl acetoacetate[1a].

Conversion of enamino esters **4–6** into the corresponding (tetrahydroxybutyl)-pyrroles (**7**) and 2-methyl-3-pyrrolecarboxylic esters (**8**) occurred much more easily than the similar transformation of the ketoenamines **1**. The reaction was studied in detail for the *tert*-butyl enamino ester **6**, which gave rise to very insoluble, crystalline, pyrrole derivatives. Heating a suspension of **6** in water gave *tert*-butyl 2-methyl-

TABLE I

2-[2-(1-ALKOXYCARBONYL-1-PROPENYL)AMINO]-2-DEOXY-α-D-GLUCOPYRANOSES AND THEIR *O*-ACETYL DERIVATIVES

Substance	*M.p.*[a] *(degrees)*	$[\alpha]_{5461}$ *(degrees)*	*Yield (%)*	*Formula*	*Calc.*			*Found*		
					C	*H*	*N*	*C*	*H*	*N*
4	102–104 (EtOH)	+221 (EtOH)	60	$C_{11}H_{19}NO_7$	47.65	6.9	5.05	47.3	7.3	4.7
4a	160–162 (EtOH)	+222 (Cf)[b]	42	$C_{19}H_{27}NO_{11}$	51.2	6.1	3.15	51.06	6.4	2.9
4b	140–141 (EtOH–H_2O)	+125 (Cf)	49	$C_{19}H_{27}NO_{11}$	51.2	6.1	3.15	51.6	5.8	2.9
5	100–101 (EtOH)	+231 (EtOH)	65	$C_{12}H_{21}NO_7$	49.5	7.3	4.8	49.3	7.1	4.5
5a	144–146 (EtOH)	+215 (Cf)	57	$C_{20}H_{29}NO_{11}$	52.3	6.4	3.05	52.5	6.2	3.1
5b	108–109 (EtOH–H_2O)	+126 (Cf)	59	$C_{20}H_{29}NO_{11}$	52.3	6.4	3.05	52.5	6.4	3.0
6	145–146 (AcOEt)	+221 (EtOH)	56	$C_{14}H_{23}NO_7$	52.65	7.9	4.4	52.8	7.6	4.2
6a	166–167 (MeOH)	+187 (Cf)	61	$C_{22}H_{33}NO_{11}$	54.2	6.8	2.9	54.5	7.1	3.0
6b	109–110 (EtOH–H_2O)	+134 (Cf)	58	$C_{22}H_{33}NO_{11}$	54.2	6.8	2.9	54.35	6.8	3.2

[a]In parentheses crystallization solvent. [b]Cf, chloroform solution.

3-pyrrolecarboxylate (17%) and (tetrahydroxybutyl)pyrrole (**7c**, 35%). The mother liquor showed the presence of D-erythrose and 2-amino-2-deoxy-D-glucose, and the

TABLE II

U.V. AND I.R. ABSORPTIONS[a] OF COMPOUNDS **4–6** AND THEIR *O*-ACETYL DERIVATIVES **4a–6a** AND **4b–6b**

Substance	*U.v. absorption*[b]		*I.r. absorption* (cm^{-1})					
	λ_{max} (*nm*)	*log ε*	*Phase*	*OH and/or NH*	*AcO*	*C=O*	*C=C*	*NH*
4	287	4.29	N	3260b		1635	1585	1505m
4a	280	4.33	Cf	3260w	1762	1665	1620	1500m
4b			Cf	3253w	1758	1666	1620	1499m
5	287	4.27	N	3280b		1653m	1595	1503m
						1633	1580	
5a	281	4.23	Cf	3260w	1760	1658	1619	1497w
5b			Cf	3258w	1760	1660	1621	1492m
6	287	4.37	N	3442m,b		1648	1600	1493m
				3255m,b				
6a	280	4.14	C	3255w	1763	1655	1619	1493
6b			Cf	3260w	1762	1658	1623	1493m

[a]Abbreviations: N, solid in Nujol mull; C, solution in carbon tetrachloride; Cf, solution in chloroform; m, medium; w, weak; b, broad. When no indication is given, it is implied that a strong band was observed. [b]In ethanol.

latter compound is considered to arise from partial hydrolysis of **6**. When the reaction was performed in a buffer of pH 9–10, the yield of the (tetrahydroxybutyl)pyrrole (**7c**) was increased considerably (87%). A high yield (73%) of *tert*-butyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)pyrrolecarboxylate (**7c**) was also obtained when the cyclization reaction was performed by heating in an anhydrous methanol–triethylamine mixture. Similar observations were made for the two other crotonic esters **4** and **5**.

The physical and chemical properties of the (tetrahydroxybutyl)pyrrole esters **7a** and **7c**, and those of the corresponding tetraacetates were similar to those of the already known[7] ethyl ester **7b** and its tetraacetate. Oxidations of **7a** or **7c** with three moles of sodium periodate per mole gave high yields of the corresponding alkyl 5-formyl-2-methyl-3-pyrrolecarboxylate (**9a** and **9c**). The u.v. and i.r. spectra of these new pyrrolealdehydes were similar to those of known[8,9] ethyl 5-formyl-2-methyl-3-pyrrolecarboxylate (**9b**). Also, the spectroscopic properties of the new *tert*-butyl 2-methyl-3-pyrrolecarboxylate (**8c**) were very similar to those[1a] of the corresponding ethyl ester (**8b**).

The isolation of enamino esters **4–6** and their easy transformation into pyrrole derivatives add further support to the view[1,2] that enamines **10** (*i.e.* tautomeric forms of enamino ketones **1** and enamino esters **4-6**) are intermediates in the formation of pyrroles from amino sugars and β-dicarbonyl compounds. The internal aldehyde–enamine condensation of these intermediates would yield the two diastereoisomeric pyrroline derivatives **11a** and **11b**. *trans*-Elimination of the elements of water from **11a** would yield (tetrahydroxybutyl)pyrroles (**2**). The fission of the sugar chain, which

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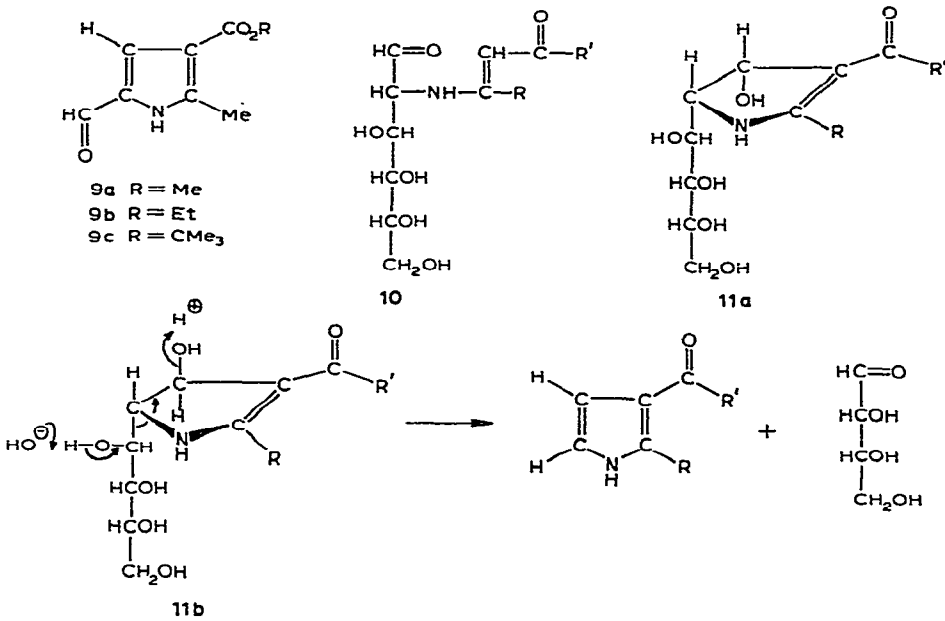
TABLE III

CHEMICAL SHIFTS (δ, p.p.m.) AND COUPLING CONSTANTS (Hz) OF 1,3,4,6-TETRA-*O*-ACETYL-2-[2(1-METHOXYCARBONYL-1-PROPENYL)AMINO]-2-DEOXY-α- AND -β-D-GLUCOPYRANOSE (*4a* AND *4b*) AT 100 MHz IN CHLOROFORM-*d*[a]

Substance	*NH*	*:CH*	*CMe*	*OAc*	*OMe*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*
4a	8.55d[b] $J_{NH,2}$ 10.6	4.50	1.93	1.99, 2.02 2.07, 2.25	3.58	6.14d $J_{1,2}$ 3.9	3.84sx $J_{2,3}$ 9.9	5.30t $J_{3,4}$ 9.1	5.10t $J_{4,5}$ 9.4	4.05m $J_{5,6'}$ 2.0	4.35q	4.05m
4b	8.46d $J_{NH,2}$ 10.8	4.51	1.97	1.99, 2.02 2.08, 2.09	3.60	5.63d $J_{1,2}$ 8.5	3.69sx $J_{2,3}$ 9.0	5.20t $J_{3,4}$ 9.0	5.08t $J_{4,5}$ 9.0	3.87m $J_{5,6}$ 4.2 $J_{5,6'}$ 2.1	4.36q $J_{6,6'}$ −12.3	4.10q

[a]The spectrometer was locked on the signal of the tetramethylsilane internal reference. [b]Signal multiplicities are indicated as following: d, doublet; t, triplet; q, quartet; sx, sextet; m, multiplet; the absence of any indication implies that a singlet was observed.

produces the symple pyrroles (**8**), can occur in diastereoisomer **11b**, and might be envisaged as a concerted *trans*-elimination catalyzed by both the hydroxyl and hydrogen ions, as indicated.



EXPERIMENTAL

General. — Melting points are uncorrected. Solutions were dried with $MgSO_4$ and were evaporated *in vacuo* below 40°. Light petroleum refers to the fraction of b.p. 50–70°. Identification of compounds was based on mixed melting points and comparison of i.r. spectra and chromatographic mobilities. Paper chromatography was performed on Whatman No. 1 paper, with butyl alcohol–ethanol–water–ammonia (40:10:49:1, organic phase) as the developer and detection with the following reagents: (*a*) alkaline silver nitrate, for polyhydroxylic compounds; (*b*) Ehrlich reagent[1a], for pyrroles; (*c*) aniline acid phthalate, for reducing sugars. Thin-layer chromatography (t.l.c.) was performed on Silica gel G (Merck) with detection by (*d*) sulphuric acid–water (1:1) or with reagent (*b*). Optical rotations at 5461 Å were determined with a Bendix–Ericsson Type 143C polarimeter. The u.v. spectra were obtained on a Beckman DU spectrometer, and i.r. spectra on a Perkin–Elmer 621 instrument. The p.m.r. spectra were recorded for solutions in chloroform-*d* (internal tetramethylsilane) on a Varian HA-100 spectrometer. Acetylation reactions were carried out by dissolving the sample (one part) in ice-cooled pyridine (six parts), and adding, dropwise and with stirring, acetic anhydride (three parts). After being stored in the refrigerator for 48 h, the mixture was poured on to ice, and the material that separated was washed thoroughly with water, scratched until crystallization, and recrystallized.

Formation of enamino esters **4–6**. — A suspension of 2-amino-2-deoxy-β-D-glucopyranose (3.58 g, 20 mmoles) in a mixture of methanol (40 ml), the appropiate ketoester (26 mmoles), and triethylamine (0.1 ml) was shaken at room temperature for a period of 10 h, after which the sugar had dissolved. In the reactions with methyl acetoacetate and ethyl acetoacetate, crystallization of the almost pure, enamino esters occurred shortly afterwards. After filtration of the crystalline mass, the mother liquors were evaporated to yield a second crop. Recrystallizations were effected from the solvents indicated in Table I. In the reaction with *tert*-butyl acetoacetate, the solution was evaporated to leave a crystalline residue which was thoroughly washed with light petroleum, and recrystallized from ethyl acetate. Physical constants, yields, and analytical data of the products are given in Tables I and II.

*1,3,4,6-Tetra-*O*-acetyl-2-[2-(1-alkoxycarbonyl-1-propenyl)amino]-2-deoxy-α-D-glucopyranoses* (**4a–6a**). — Acetylation of the enamino esters **4–6** by the standard procedure gave the corresponding tetraacetates (**4a–6a**). Recrystallization solvents, yields of pure products, and analytical data are indicated in Table I; physical constants are given in Tables I, II, and III.

*1,3,4,6-Tetra-*O*-acetyl-2-[2-(1-alkoxycarbonyl-1-propenyl)amino]-2-deoxy-β-D-glucopyranoses* (**4b–6b**). — A suspension of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride (3.8 g, 10 mmoles) in a mixture of *p*-dioxane (40 ml), the appropiate β-ketoester (11 mmoles), and triethylamine (2 ml, *ca.* 20 mmoles) was shaken for 24 h at room temperature. The remaining solid (triethylamine hydrochloride) was filtered off, and the filtrate was evaporated to a syrup which was dissolved in a small volume of warm ethanol. The cold solution was poured on to ice, and the crystalline solid that separated was filtered off and recrystallized from the solvent indicated in Table I. Yields of recrystallized products and analytical data are indicated in Table I; physical constants are given in Tables I, II, and III.

The methyl ester **4b** was also prepared in the following way. 1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (8.9 g, 25 mmoles) was added to a solution of methyl acetoacetate (3.5 g, 30 mmoles) in *p*-dioxane (35 ml), and the suspension shaken until dissolution was complete. After 24 h, the solution was evaporated to yield a syrup which crystallized upon treatment with a hot mixture of ethanol–water (1:2). This material (7.3 g, m.p. 120–125°), recrystallized from ethanol–water (1:1), gave compound **4b** (6.7 g, 60%), m.p. 136–138°, identical with a sample prepared by the procedure described previously.

Acid hydrolysis of compound **4a**. — Treatment of a solution of compound **4a** (1 g) in boiling acetone (10 ml) with 5M hydrochloric acid (0.7 ml) produced a thick mass of crystals. After cooling, this suspension was diluted with ether and filtered, affording 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride (0.8 g, 94%), m.p. 183–184° (dec.), identical with an authentic specimen.

*Methyl 2-methyl-5-(*D-arabino-*tetrahydroxybutyl)-3-pyrrolecarboxylate* (**7a**). — (*a*) A mixture of 2-amino-2-deoxy-D-glucose hydrochloride (2.16 g, 10 mmoles) and sodium carbonate (0.53 g, 5 mmoles) was dissolved in the minimum volume of water (*ca.* 7 ml). Methyl acetoacetate (1.27 g, 11 mmoles) was added, and then acetone to

give a solution which was allowed to stand for 24 h at room temperature. Refrigeration then afforded crystalline **7a** which was filtered off; evaporation of the mother liquor yielded a second crop. The combined products were washed with water, and with ethanol–ether (1:4). Two recrystallizations from ethanol yielded **7a** (0.91 g, 35%), m.p. 133–134°, $[\alpha]_{5461}^{20}$ −25° (*c* 0.5, water); λ_{max} (water) 220 (sh) and 262 nm (ε 8,860, 6,220); ν_{max} (Nujol) 3450s and 3290b-s (OH, NH), 1730s and 1674s (CO_2Me), 1593w and 1507sh-w cm^{-1} (pyrrole ring).

(*b*) A mixture of 2-amino-2-deoxy-D-glucose hydrochloride (1.08 g, 5 mmoles), methyl acetoacetate (1.16 g, 10 mmoles), triethylamine (1,3 ml), and methanol (20 ml) was heated gently until dissolution was complete (20 min), and then under reflux for a further 5 min. Evaporation of the solution (to one-third volume) and refrigeration afforded compound **7a**. After crystallization from ethanol, the product (0.86 g, 33%) had m.p. 133–134°, and was identical with a sample prepared according to procedure (*a*).

Anal. Calc. for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.91; N, 5.40. Found: C, 50.68; H, 7.15; N, 5.23.

This compound consumed 3.03 mol. of sodium metaperiodate in an analytical oxidation (calc.: 3.0 mol.).

Acetylation of **7a** gave the corresponding tetra-acetate, m.p. 102–105° (from ether–light petroleum, 2:1), $[\alpha]_{5461}^{21}$ −90° (*c* 1, chloroform); ν_{max} (C_2Cl_4) 3420w (NH), 3293w (associated NH), 1755s (AcO), 1715s (CO_2Me), 1595w and 1525w cm^{-1} (pyrrole ring).

Anal. Calc. for $C_{19}H_{25}NO_{10}$: C, 53.39; H, 5.90; N, 3.28. Found: C, 53.50; H, 5.65; N, 3.43.

Methyl 5-formyl-2-methyl-3-pyrrolecarboxylate (**8**, *R = Me*). — A solution of methyl 5-(D-*arabino*-tetrahydroxybutyl)-2-methyl-3-pyrrolecarboxylate (2.42 g, 9.3 mmoles) in water (50 ml at 40°) was treated with 35 ml of a saturated solution of sodium metaperiodate heated at 40°. Compound **8** (R = Me) crystallized rapidly. After cooling, the solid was filtered off, washed thoroughly with water, and recrystallized from acetone–water (1:1). The product (1.25 g, 80%) had m.p. 153–155°, λ_{max} (ethanol) 212, 224, 248, 292 nm (ε, 13,308, 12,635, 5,040, 18,830); ν_{max} ($CHCl_3$) 3425m (NH), 3255b-m (associated NH), 1709s (CO_2Me), 1651s (HC=O), 1569m and 1506sh-m cm^{-1} (pyrrole ring).

Anal. Calc. for $C_8H_9NO_3$: C, 57.48; H, 5.42; N, 8.38. Found: C, 57.15; H, 5.61; N, 8.22.

tert-*Butyl 2-methyl-5-(*D-arabino-*tetrahydroxybutyl)-3-pyrrolecarboxylate* (**7c**). — (*a*) The reaction between 2-amino-2-deoxy-D-glucose hydrochloride, sodium carbonate, and *tert*-butyl acetoacetate was carried out in methanol–water at room temperature, as described above for the methyl ester. After 3 days, the solution was evaporated to one-third volume, and refrigerated to yield compound **7c**. The product was washed with water and water–ethanol (4:1), and recrystallized from water to give **7c** (32%), m.p. 141–142°, $[\alpha]_{5461}^{20}$ −28° (*c* 1, ethanol); λ_{max} (water) 225 sh, 262 nm, (ε, 9,000, 6,940); ν_{max} (Nujol) 3523m, 3400sh-m, and 3300b-s (OH, NH), 1700s and 1667b-m (CO_2CMe_3), 1591m and 1524w cm^{-1} (pyrrole ring).

(*b*) The reaction of the amino sugar and *tert*-butyl acetoacetate in methanol–triethylamine was carried out as indicated under (*b*) for the methyl ester. The reaction mixture was evaporated to a syrup which was washed with light petroleum, and dissolved in warm water. Refrigeration of the solution gave 35% of **7c**, m.p. 138–140°, identical to a sample obtained by procedure (*a*).

Anal. Calc. for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.65. Found: C, 56.10; H, 7.56; N, 4.53.

This compound consumed 2.97 mol. of sodium metaperiodate (calc.: 3.0 mol.).

*Reaction between 2-amino-2-deoxy-*D*-glucose hydrochloride and* tert*-butyl acetoacetate at pH 9–10.* — *tert*-Butyl acetoacetate (4.74 g, 30 mmoles) was added to a solution of 2-amino-2-deoxy-D-glucose hydrochloride (3.22 g, 15 mmoles) in 100 ml of a sodium carbonate–sodium hydrogen carbonate buffer (pH 9–10), and the mixture was heated for 3 h at 70°. The cooled solution was extracted with ether (4 × 50 ml) and brought to pH 7.2 by addition of Amberlite IR-120 (H^+) resin. T.l.c. (benzene–ethanol, 4:1) of the concentrated aqueous layer did not show the presence of any compound detectable with Ehrlich reagent. The dried ethereal extract was evaporated to yield a syrup which was extracted with light petroleum (6 × 20 ml). The combined extracts were evaporated to afford a crystalline solid which was recrystallized from light petroleum. *tert*-Butyl 2-methyl-3-pyrrolecarboxylate (0.22 g, 8.2%) had m.p. 111–112°; λ_{max} (ethanol) 224, 257 nm (ε 8,040, 7,460); ν_{max} (CCl_4) 3472s (NH), 3340w (associated NH), 1701s (CO_2CMe_3), 1575m and 1490m cm^{-1} (pyrrole ring).

Anal. Calc. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.33; H, 8.35; N, 7.92.

T.l.c. (benzene–ethanol, 4:1, with a few drops of triethylamine) of the fraction insoluble in light petroleum showed the presence of compound **7c** (R_F 0.37), *tert*-butyl 2-methyl-3-pyrrolecarboxylate (R_F 0.79), and two unidentified, Ehrlich-positive, substances (R_F 0.46 and 0.40). Treatment with warm water gave **7c** (0.16 g), m.p. 136–139°, identical with the preparation described above.

tert*-Butyl 5-formyl-2-methyl-3-pyrrolecarboxylate* (**8**, $R = CMe_3$). — Sodium metaperiodate (8.5 g, 40 mmoles) was added portionwise to a vigorously stirred suspension of compound **7c** (3.0 g, 10 mmoles) in a mixture of water (100 ml) and ether (100 ml). After 0.5 h, the pH was brought to 7.0 by addition of 2M sodium hydroxide. The aqueous layer was extracted with ether (50 ml), and the ethereal fractions were combined and dried. Evaporation left a solid which was recrystallized twice from acetone–water. The product (1.32 g, 63%) had m.p. 97–98°; λ_{max} (ethanol) 212, 227, 254sh, 294 nm (ε 15,680, 15,300, 7,000, 22,840); ν_{max} ($CHCl_3$) 3427m (NH), 3255b-m (associated NH), 1698s (CO_2CMe_3), 1651s (HC=O), 1566w and 1507sh-m cm^{-1} (pyrrole ring).

Conversion of enamino esters **4–6** *into pyrrole derivatives.* — (*a*) *tert*-Butyl enamino ester (**6**) (1.59 g, 5 mmoles) was heated for 2 h in a mixture of anhydrous methanol (20 ml) and triethylamine (1 ml). T.l.c. (ethyl acetate–ethanol 4:1), then showed that all of the starting material had disappeared, and had been replaced by two Ehrlich-positive products of the same mobilities as (tetrahydroxybutyl)pyrrole

(**7c**, major component) and *tert*-butyl 2-methyl-3-pyrrolecarboxylate, respectively. Evaporation of the solvent left a residue which crystallized upon treatment with warm light petroleum. The solid fraction (1.35 g, m.p. 137–140°), recrystallized from water, gave compound **7c** (1.1 g, 73%), m.p. 140–142°, identical with the sample described above.

Similar experiments with methyl and ethyl enamino esters **4** and **5** afforded the corresponding (tetrahydroxybutyl)pyrroles **7a** and **7b** in yields of 72% and 89%, respectively.

(*b*) A suspension of *tert*-butyl enamino ester **6** (2.4 g, 7.5 mmoles) in water (50 ml) was heated until dissolution. Crystallization of *tert*-butyl 2-methyl-3-pyrrolecarboxylate began shortly afterwards, and was completed by cooling at room temperature. After recrystallization from light petroleum, the product (0.23 g, 17%) had m.p. 111–112°, and was identified with the sample previously described.

Paper chromatography of the aqueous mother liquor showed the presence of (tetrahydroxybutyl)pyrrole (**7c**) (R_F 0.85), D-erythrose (R_F 0.43), and 2-amino-2-deoxy-D-glucose (R_F 0.26). The solution was concentrated to 5 ml and refrigerated to afford *tert*-butyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-pyrrolecarboxylate (**7c**) (0.8 g, 35%), identical with the preparation described above.

(*c*) A solution of ethyl enamino ester **5** (4.0 g) in water (100 ml) was allowed to stand at room temperature until the optical rotation remained constant (*ca.* 30 h). Ethyl 2-methyl-3-pyrrolecarboxylate (0.16 g) crystallized and had m.p. 79–80°; λ_{max} (ethanol) 226, 257 nm (ε 6,647, 5,923); ν_{max} ($CHCl_3$) 3483 m (NH), 3310 w (associated NH), 1690 s (CO_2Et), 1576 m and 1492 m cm^{-1} (pyrrole ring), in agreement with the values previously recorded[1a]. The mother liquor was extracted with ether (3 × 25 ml), and the combined extracts were dried and evaporated. Crystallization of the oily residue from ethanol–water gave an additional amount (90 mg) of ethyl 2-methyl-3-pyrrolecarboxylate, m.p. 76–79°, identical with the sample described above.

Concentration and refrigeration of the aqueous layer gave ethyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-pyrrolecarboxylate (**7b**, 0.76 g, 20%), m.p. 139–140°, identified with an authentical sample.

(*d*) *tert*-Butyl enamino ester (**6**) (1.0 g) was dissolved in 20 ml of a warm (50°) sodium carbonate–sodium hydrogen carbonate buffer (pH 9–10), and the solution was maintained at 50° for 0.5 h. The solid (0.85 g) that crystallized was filtered off, air dried, and extracted with ether (3 × 10 ml). The residual solid (0.83 g, 87%), m.p. 137–139°, was chromatographically homogeneous *tert*-butyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-pyrrolecarboxylate (**7c**); after recrystallization from water, the product (0.74 g) had m.p. 139–141°, and was identical with the sample described above.

The dried ether extracts were evaporated to leave an oily residue (29 mg) which was crystallized from light petroleum to yield *tert*-butyl 2-methyl-3-pyrrolecarboxylate (15 mg), m.p. 110–112°, identified with the sample previously described.

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