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ENAMINE AND PYRROLE FORMATION FROM 2-AMINO-2-DEOXY-D-GLUCOSE AND DIMETHYL ACETYLENEDICARBOXYLATE*

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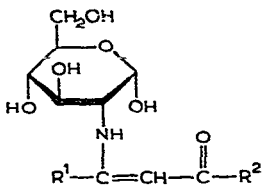
ABSTRACT

Addition of 2-amino-2-deoxy-β-D-glucopyranose to dimethyl acetylenedicarboxylate afforded an almost quantitative yield of amorphous 2-deoxy-2-(1,2-dimethoxycarbonylvinyl)amino-D-glucose (**5**). Acetylation of this adduct gave crystalline 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-[(*Z*)-1,2-dimethoxycarbonylvinyl]amino-α-D-glucopyranose (**6a**); the corresponding β-D anomer (**6b**) was obtained by addition of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose to dimethyl acetylenedicarboxylate. *O*-Deacetylation of tetra-acetate **6a** with barium methoxide in methanol occurred selectively at C-1, yielding enamine **6c** derived from 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose. Conversion of the crude adduct **5** into 3-methoxycarbonyl-5-(D-*arabino*-tetrahydroxybutyl)-2-pyrrolecarboxylic acid (**7**) took place by heating in water or in slightly basic media in yields up to 83%. Acetylation of **7** gave the tricyclic derivative **8**, and its periodate oxidation afforded 5-formyl-3-methoxycarbonyl-2-pyrrolecarboxylic acid (**9**). Oxidation of **9** with alkaline silver oxide yielded 3-methoxycarbonyl-2,5-pyrroledicarboxylic acid (**10**).

INTRODUCTION

2-Amino-2-deoxy-D-glucose reacts[1] with β-dicarbonyl compounds, yielding enamino ketones or esters (**1**) that can be easily transformed into 2-(D-*arabino*-tetrahydroxybutyl)pyrroles (**2**) in good yields. On this basis, it might be anticipated that other reactions of the amino sugar that yield enamines similar to **1** would ultimately result in the formation of pyrroles. With this idea in mind, we have investigated the addition of the amino group of 2-amino-2-deoxy-D-glucose to acetylenic esters, and the further cyclization of the resulting enamines into pyrroles. It is known[2] that the reaction of α-amino ketones with dimethyl acetylenedicarboxylate produces pyrrole derivatives, presumably *via* enamine intermediates **3** that undergo an internal aldehyde–enamine condensation, yielding the pyrroline derivatives **4**. The latter compounds were isolated in some instances and converted into the corresponding pyrroles.

*Dedicated to Dr. Horace S. Isbell, in honour of his 75th birthday.



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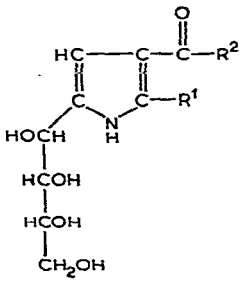

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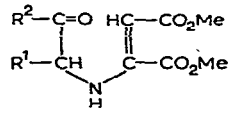

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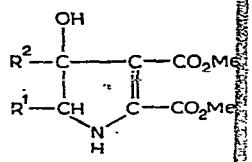

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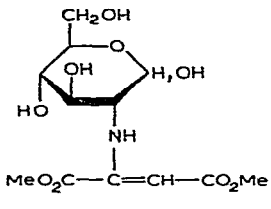
RESULTS AND DISCUSSION

Treatment of 2-amino-2-deoxy-β-D-glucopyranose with dimethyl acetylenedicarboxylate in methanol at room temperature afforded an almost quantitative yield of a non-crystalline product that is considered to have the gross structure **5** on the basis of the following evidence.

Adduct **5** gave positive Fehling's and ferric chloride tests, presumably because of its hydrolysis to dimethyl oxalacetate and the parent amino sugar. Paper chromatography showed the presence of a substance of R_F 0.73, in addition to 2-amino-2-deoxy-D-glucose. Acetylation of **5** with acetic anhydride in pyridine gave (>90% yield) chromatographically homogeneous, crystalline tetra-acetate **6a**, which had



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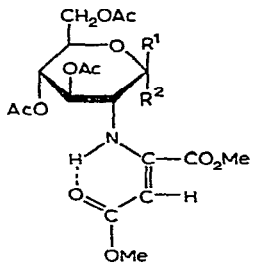


6a $R^1 = H$, $R^2 = OAc$
6b $R^1 = OAc$, $R^2 = H$
6c $R^1 = H$, $R^2 = OH$

λ_{max} 302 nm, in the range expected[3] for a 3-aminofumarate. Its i.r. spectrum showed bands at 3258 (chelated NH group), 1676 (conjugated, intramolecularly bonded, ester group), and 1610 cm^{-1} (skeletal vibration[3,4] of –C=C–NH). The band of medium intensity at 787 cm^{-1}, also observed in simple 3-alkylaminofumarates[3] and in the (Z)-form of 3-alkylaminocrotonates[4], is assigned as the out-of-plane =C–H vibration. The second, non-bonded, carbonyl ester band of the 3-aminofumarate portion of the molecule was expected[3] to appear at 1740 cm^{-1} and was considered to be overlapped by the strong acetate absorption. The band at 860 cm^{-1} and the high value (+200°) of $[\alpha]_{5461}$ suggested the α-D anomeric configuration. The p.m.r. spectrum of **6a**

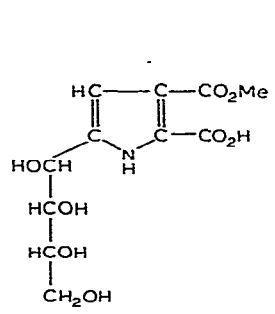
showed the NH as a doublet at τ 2.01, and the vinyl proton at τ 4.66, in accordance with the data reported[3] for simple 3-aminofumarates having a secondary amino group. The anomeric proton appeared as a doublet ($J_{1,2}$ 3.9 Hz) at τ 3.68, thus confirming the α-D anomeric configuration. The rest of the spectrum was fully consistent with the assigned structure (see Experimental section).

For purposes of comparison, the β-D anomer (**6b**) of **6a** was prepared by addition of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose to dimethyl acetylenedicarboxylate. This substance had $[\alpha]_{5461}$ +94°, and showed the anomeric doublet ($J_{1,2}$ 8.6 Hz) at τ 4.34. Other properties of both isomers were very similar (see Experimental section).

Attempts to transform tetra-acetate **6a** into the fully *O*-deacetylated parent substance were unsuccessful. As observed[5] for related enamines, treatment of **6a** with catalytic amounts of barium methylate in methanol at 0° brought about *O*-deacetylation at C-1 and gave the tri-*O*-acetylated enamino ester **6c** which was isolated in 62% yield. This substance had λ_{max} 298 nm (ε 11,400) typical of a 3-aminofumarate[3], and showed a strong i.r. hydroxyl band at 3440 cm^{-1}; other features of its i.r. spectrum were very similar to those observed for the tetra-acetate **6a**. The p.m.r. spectrum of **6c** showed three *O*-acetyl singlets at τ 7.92, 8.00, and 8.06, at the same positions as the three non-anomeric acetoxyl groups of compound **6a**; the signal at τ 7.75 due to the axial, anomeric acetoxyl group of the latter substance disappeared during the *O*-deacetylation reaction. The anomeric configuration of compound **6c** was deduced from the high value (+240°) of $[\alpha]_{5461}$ and the $J_{1,2}$ coupling (3.45 Hz). In contrast to similarly constituted tri-*O*-acetylated enamino esters[5], H-1 and the OH proton of compound **6c** were not coupled with each other, appearing as a doublet and a broad singlet, respectively. The location of the OH group on C-1 was proved by degradation of **6c** into known[5] 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride by hydrolysis with 5M hydrochloric acid in acetone.

Heating of the crude adduct **5** with water or with slightly basic, aqueous solutions afforded 3-methoxycarbonyl-5-(D-*arabino*-tetrahydroxybutyl)-2-pyrrolecarboxylic acid (**7**); the best yields (83%) were obtained by using a borate buffer of pH 8, followed by acidification. Evidence for the structure of this pyrrole derivative is as follows.

Compound **7** gave a positive Ehrlich test for pyrrole, and consumed one equivalent of sodium hydroxide per mole. The u.v. spectrum (λ_{max} 212, 248, and 291 nm; ε 21,600, 7,400, and 8,300) was very close to those of other derivatives of 2,3-pyrroledicarboxylic acid[6] and esters[7]. The strong i.r. bands at 1723 and 1620 cm^{-1} indicated the presence of two different carbonyl groups; in accordance with the literature[6], the band at the lower frequency may be assigned to the carbonyl of the ester group strongly chelated to the carboxyl group, but an alternative, more probable, explanation of the large difference between the two frequencies is that there exists a strong, mechanical coupling between the vibrations of the two co-planar carbonyl groups that results in symmetric and asymmetric vibration modes. The bands of strong or medium intensity at 1590 and 1510 cm^{-1} are assigned as stretching vibrations[8] of the



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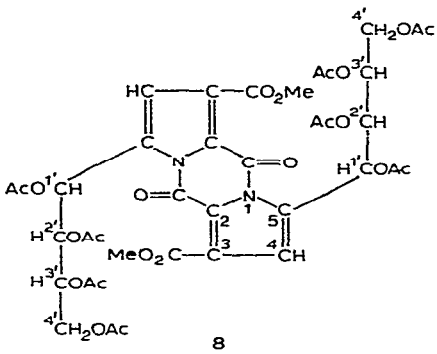

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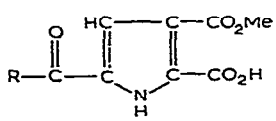
pyrrole ring. The rest of the spectrum and other physical properties (see Experimental section) of compound **7** were consistent with the assigned structure, and were very similar to those observed for other 2-(D-*arabino*-tetrahydroxybutyl)pyrroles[1,9].

The location of the carboxyl group at the α position of the pyrrole ring in **7** was established when acetylation gave the tricyclic derivative **8**. The formation of this type of bimolecular anhydride, the so-called[10] "pyrocoles", is a property of 2-pyrrolecarboxylic acids[10]. Structure **8** was consistent with the microanalytical data and the molecular mass of the product, and with the i.r. spectrum which showed carbonyl bands at 1740 (*O*-acetyl), 1705 (pyrrolecarboxylic ester), and 1592 cm^{-1} (unsaturated, mesomeric, 2,5-dioxopiperazine ring), but no absorptions for NH or CO_2H. The p.m.r. spectrum showed neither NH nor CO_2H signals, and fully confirmed the assigned structure.

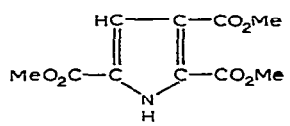
During the formation of a pyrrole, the easy hydrolysis of an ester group that would appear at the α position of the ring is well documented[11]; for instance, condensation of diethyl oxalacetate with amino acetone hydrochloride in alkaline, aqueous solution produces 4-methyl-3-ethoxycarbonyl-2-pyrrolecarboxylic acid[12].

The (tetrahydroxybutyl)pyrrole **7** consumed three moles of periodate per mole and afforded a high yield of 5-formyl-3-methoxycarbonyl-2-pyrrolecarboxylic acid (**9**), which was further characterized as its phenylhydrazone. Oxidation of the pyrrolealdehyde **9** with alkaline silver oxide gave 3-methoxycarbonyl-2,5-pyrroledicarboxylic acid (**10**) that could be transformed into known[13] trimethyl 2,3,5-pyrroletricarboxylate (**11**) by esterification with methanol–hydrogen chloride.

Attempts to obtain compounds similar to **5** and **6b** by the addition of 2-amino-2-deoxy-β-D-glucopyranose, and its tetra-*O*-acetyl derivative, to methyl propiolate were unsuccessful.



9 R = H
10 R = OH



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EXPERIMENTAL

General methods. — Melting points are uncorrected. Solutions were dried with magnesium sulphate and evaporated under diminished pressure below 40°. Light petroleum refers to the fraction of b.p. 50–70°. Identification of products was based on mixture melting points and comparison of i.r. spectra. Paper chromatography (p.c.) was performed on Whatman No. 1 paper by the descending technique with butyl alcohol–ethanol–water–ammonia (40:10:49:1, organic phase), and detection with alkaline silver nitrate. Thin-layer chromatography (t.l.c.) was performed on 0.25-mm layers of Silica Gel HF_{254} (Merck), and detection was effected with 50% sulfuric acid and heating, or with u.v. light of 254 nm. Optical rotations at 5461 Å were determined with a Bendix-NPL 143C polarimeter. U.v. spectra were obtained with a Unicam SP-800 spectrometer, and i.r. spectra with a Perkin–Elmer 621 instrument. P.m.r. spectra at 100 MHz were recorded for solutions in chloroform-*d* on a JNM-PS-100 spectrometer; tetramethylsilane was used as the internal standard, and signal assignments were verified by spin decoupling.

*2-Deoxy-2-(1,2-dimethoxycarbonylvinyl)amino-*D*-glucose* (**5**). — A suspension of 2-amino-2-deoxy-β-D-glucopyranose (5.4 g, 30 mmoles) in methanol (10 ml) containing dimethyl acetylenedicarboxylate (4.4 g, 30 mmoles) was shaken at room temperature for 20 h. The resulting turbid solution was filtered and evaporated. The syrupy residue was treated repeatedly with ether, yielding **5** (9.2 g, 95%) as a yellow, amorphous solid, which was deliquescent on exposure to air. Attempts to crystallize this product were unsuccessful.

P.c. of this material showed the presence of a spot of R_F 0.73 in addition to 2-amino-2-deoxy-D-glucose (R_F 0.30). It gave positive Fehling's and ferric chloride tests.

*1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[(Z)-1,2-dimethoxycarbonylvinyl]amino-α-*D*-glucopyranose* (**6a**). — A solution of the crude adduct **5** (3.0 g) in pyridine (13 ml) was treated with acetic anhydride (10 ml) at 0°. After being stored in the refrigerator for 48 h, the reaction mixture was poured on to ice, and the precipitate was washed several times with ice-cooled water. The resulting crystalline solid (6.25 g, 93%), m.p. 141–144°, was recrystallized from ethanol to yield chromatographically pure **6a**, m.p. 144–146°, $[\alpha]_{5461}^{20}$ +200° (*c* 0.8, chloroform), R_F 0.55 (t.l.c.; ether–light petroleum, 4:1); λ_{max} (ethanol) 302 nm (ε 11,300), ν_{max} (carbon tetrachloride) 3258 w (chelated NH), 1756 b-s (OAc and non-chelated CO_2Me), 1671 s (chelated CO_2Me), and 1610 s cm^{-1} (C=C–NH); ν_{max} (Nujol) 860 w (α-D-glucopyranose), and 770 m cm^{-1} (=CH). P.m.r. data: τ 2.01 (1-proton doublet, $J_{NH,2}$ 10.75 Hz, NH), 3.68 (1-proton doublet, $J_{1,2}$ 3.9 Hz, H-1), 4.66 (1-proton singlet, =CH), 4.70 (1-proton triplet, $J_{2,3} \simeq J_{3,4}$ 9.6 Hz, H-3), 4.94 (1-proton triplet, $J_{4,5}$ 9.5 Hz, H-4), 5.52 (4-proton multiplet, H-2, 5,6,6'), 6.12 and 6.31 (3-proton singlets, 2 CO_2Me), 7.71 (3-proton singlet, AcO-1), 7.92, 7.99, and 8.04 (3-proton singlets, 3 OAc).

Anal. Calc. for $C_{20}H_{27}NO_{13}$: C, 49.08; H, 5.56; N, 2.86. Found: C, 49.23; H, 5.65; N, 2.86.

*1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[(Z)-1,2-dimethoxycarbonylvinyl]amino-β-*D*-glucopyranose* (**6b**). — A solution of dimethyl acetylenedicarboxylate (1.5 g, 10 mmoles) and 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (3.4 g, 10 mmoles) in *p*-dioxane (20 ml) was heated at 40° for 5 min. T.l.c. (ether–light petroleum, 4:1) showed the formation of a single product of R_F 0.48. After being stored for 48 h at room temperature, the reaction mixture was evaporated to a syrup that was extracted with ether. The extract was filtered and evaporated, and the syrupy residue was dissolved in a small volume of ethanol. The solution was poured on to ice, and the resulting crystalline solid was filtered off and recrystallized from ethanol–water. The product **6b** (2.6 g, 53%) had m.p. 98–100°, $[\alpha]_{5461}^{20}$ +94° (*c* 1, chloroform), λ_{max} (ethanol) 300 nm (ε 12,200); ν_{max} (carbon tetrachloride) 3255 w (chelated NH), 1756 b-s (OAc and non-chelated CO_2Me), 1676 s (chelated CO_2Me), and 1610 b-s cm^{-1} (C=C–NH); ν_{max} (Nujol) 898 m (β-D-glucopyranose) and 782 m cm^{-1} (=CH). P.m.r. data: τ 2.11 (1-proton doublet, $J_{NH,2}$ 10.65 Hz, NH), 4.34 (1-proton doublet, $J_{1,2}$ 8.6 Hz, H-1), 4.71 (1-proton singlet, =CH), 4.83 (2-proton multiplet, H-3,4), 5.68 (1-proton double doublet, $J_{5,6}$ 4.6, $J_{6,6'}$ −12.5 Hz, H-6), 5.93 (1-proton double doublet, $J_{5,6'}$ 2.5 Hz, H-6′), 6.1 (2-proton multiplet, H-2,5), 6.12 and 6.31 (3-proton singlets, 2 CO_2Me), 7.92 (6-proton singlet, 2 OAc), and 7.97 (6-proton singlet, 2 OAc).

Anal. Calc. for $C_{20}H_{27}NO_{13}$: C, 49.08; H, 5.56; N, 2.86. Found: 49.43; H, 5.82; N, 2.93.

*3,4,6-Tri-*O*-acetyl-2-deoxy-2-[(Z)-1,2-dimethoxycarbonylvinyl]amino-α-*D*-glucopyranose* (**6c**). — A solution of tetra-acetate **6a** (2.93 g, 6 mmoles) in warm, dry methanol (50 ml) was cooled in an ice-salt bath. The solute partly crystallized, and to the suspension was added 0.5M methanolic barium methoxide (1.5 ml). Upon shaking, all the solid dissolved, and the solution was kept at 0° for 45 min. T.l.c. (ether) then showed that all of the starting material had reacted. The reaction mixture (pH 7–8) was concentrated to half volume and diluted with water, yielding the product (1.54 g), m.p. 67–71°. Further dilution of the mother liquor with water and refrigeration afforded a second crop (0.17 g, total yield 62%), m.p. 70–74°. The combined fractions were recrystallized from ethanol to afford pure **6c**, m.p. 74–75°, $[\alpha]_{5461}^{20}$ +240° (*c* 1, chloroform), R_F 0.53 (t.l.c.; ether–light petroleum, 4:1), λ_{max} (ethanol) 298 nm (ε 11,400); ν_{max} (KBr) 3440 b-m (OH and NH), 1745 b-s (OAc and non-chelated CO_2Me), 1675 s (chelated CO_2Me), 1600 s (C=C–NH), 853 m (α-D-glucopyranose), 779 m cm^{-1} (=CH). P.m.r. data: τ 1.87 (1-proton doublet, $J_{NH,2}$ 10.5 Hz, NH), 4.59 (1-proton doublet, $J_{1,2}$ 3.4 Hz, H-1), 4.68 (1-proton triplet, $J_{2,3} \simeq J_{3,4}$ 8.9 Hz, H-3), 4.78 (1-proton singlet, =CH), 5.1 (broad, 1-proton singlet, OH), 5.03 (1-proton triplet, $J_{4,5}$ 9.3 Hz, H-4), 5.8 (4-proton multiplet, H-2,5,6,6′), 6.13 and 6.30 (3-proton singlets, 2 CO_2Me), 7.92, 8.00, and 8.06 (3-proton singlets, 3 OAc).

Anal. Calc. for $C_{18}H_{25}NO_{12}$: C, 48.32; H, 5.63; N, 3.13. Found: C, 47.97; H, 5.69; N, 2.85.

Acid hydrolysis of enamine **6c**. — A boiling solution of enamine **6c** (447 mg, 1 mmole) in acetone (30 ml) was treated with 5M hydrochloric acid (0.25 ml, 1.2 mmoles). The cooled reaction mixture was diluted with ether (30 ml) and refrigerated,

yielding 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride (275 mg, 80%), m.p. 195–200° (dec.), $[\alpha]_{5461}^{16}$ +135° (*c* 1, water); lit.[5] m.p. 193–196° (dec.), $[\alpha]_{5461}^{20}$ +144°. The i.r. spectrum was identical with that previously described[5].

3-Methoxycarbonyl-5-(D-arabino-*tetrahydroxybutyl*)*-2-pyrrolecarboxylic acid* (7). — (*a*) A solution of crude adduct **5** (0.96 g, 3 mmoles) in 20 ml of borate buffer (pH 7–8) was kept at room temperature for 24 h, and then heated at 100° for 0.5 h. The cooled mixture was brought to pH 1 by addition of conc. hydrochloric acid, and was refrigerated for 48 h. The product (**7**, 340 mg) that crystallized had m.p. 176–180° (dec.); concentration of the mother liquor afforded a second crop (375 mg; total yield, 83.5%), m.p. 183–185° (dec.). After several recrystallizations from water, the analytical sample had m.p. 199–201° (dec.), $[\alpha]_{5461}^{21}$ −27° (*c* 0.5, water); λ_{max} (water) 212, 248, and 291 nm (ε 21,600, 7,400, and 8,300); ν_{max} (KBr) 3515 m, 3465 s, 3370 b-s, and 3282 b-m (OH and NH), 3100 m (pyrrole CH), 2840 w and 2580 b-w (CO_2H), 1723 s and 1620 b-s (CO_2Me and CO_2H), 1590 sh-m and 1510 s cm^{-1} (pyrrole ring).

Anal. Calc. for $C_{11}H_{15}NO_8$: C, 45.67; H, 5.23; N, 4.84; neutralization equivalent, 289.2. Found: C, 45.76; H, 5.27; N, 4.75; neutralization equivalent, 291.6.

This compound consumed 3.03 mol. of periodic acid in an analytical oxidation.

(*b*) A solution of crude compound **5** (0.96 g, 3 mmoles) in M sodium hydroxide (10 ml) was heated at 100° for 0.5 h. The cooled mixture was worked up as described above. The product (270 mg, 31%) had m.p. 186–190° (dec.), and was identical with the sample described above.

(*c*) A solution of compound **5** (0.48 g, 1.5 mmoles) in 10 ml of sodium carbonate–sodium hydrogen carbonate buffer (pH 9–10) was heated at 100° for 0.5 h. The reaction mixture was neutralized with Amberlite IR-120(H^+) resin, and then brought to pH 1 by addition of conc. hydrochloric acid. Working up as indicated above gave the product (219 mg, 50.5%), m.p. 186–190° (dec.), identical to the sample prepared in (*a*).

(*d*) A suspension of compound **5** (9.6 g, 30 mmoles) in water (25 ml) was heated at 100° until dissolution (*ca.* 0.5 h). The reaction mixture was refrigerated for 24 h, yielding the product (0.75 g, 8.5%), m.p. 198–202° (dec.), identical with the preparations described above.

Acetylation of compound **7**. — To an ice-cooled suspension of pyrrolecarboxylic acid **7** (0.15 g) in dry pyridine (15 ml) was added dropwise acetic anhydride (0.75 ml). The suspension was kept in the refrigerator and shaken occasionally until dissolution was complete (2.5 days). The reaction mixture was then poured on to ice, and the resulting crystalline solid (0.21 g, 93%), m.p. 144–150°, was washed with water. Two recrystallizations from ethanol–water (2:1) gave pure "pyrocole" **8**, m.p. 154–156°, $[\alpha]_{5461}^{26}$ −170° (*c* 2, chloroform), λ_{max} (ethanol) 248, 280, and 323 nm (ε 8,400, 5,900, and 6,300); ν_{max} (KBr) 1740 b-s (OAc), 1705 sh-m (CO_2Me), and 1592 m cm^{-1} (C=O of the unsaturated, mesomeric, 2,5-dioxopiperazine ring). P.m.r. data: τ 3.20 (2-proton double doublet, $J_{1',4}$ 0.8 Hz, $J_{1',2'}$ 2.0 Hz, 2 H-1'*), 3.30 (2-proton doublet,

*The numbering system used for this compound is given in formula **8**.

2 H-4), 4.30 (2-proton double doublet, $J_{2',3'}$ 10.0 Hz, 2 H-2'), 4.65 (2-proton multiplet, 2 H-3'), 5.68 (2-proton double doublet, $J_{3',4'a}$ 5.0 Hz, $J_{4'a,4'b}$ −12.5 Hz, 2 H-4'a), 5.88 (2-proton double doublet, $J_{3',4'b}$ 3.0 Hz, 2 H-4'b), 6.08 (6-proton singlet, 2 CO_2Me), 7.84, 7.88, 7.96, and 8.04 (6-proton singlets, 8 OAc).

Anal. Calc. for $C_{38}H_{42}N_2O_{22}$: C, 51.94; H, 4.82; N, 3.19; molecular mass, 878. Found: C, 51.92; H, 4.86; N, 3.17; molecular mass (Rast), 962.

5-Formyl-3-methoxycarbonyl-2-pyrrolecarboxylic acid (**9**). — To a stirred suspension of pyrrolecarboxylic acid **8** (0.87 g, 3 mmoles) in water (10 ml) was added M sodium hydroxide (3.1 ml), and the resulting solution was treated with a slight excess of a saturated, aqueous solution of sodium metaperiodate. Pyrrolealdehyde **9** (0.37 g, 63%), m.p. 178–186°, crystallized rapidly and was recrystallized from water. The pure product had m.p. 186–187°, λ_{max} (water) 232 and 293 nm (ε 12,500 and 16,800), ν_{max} (KBr) 3472 w (NH), 2730 m, 2705 m, and 2680 m (HC=O), 1745 s, 1692 s, and 1650 b-s (CO_2Me, CO_2H, and HC=O), 1565 s and 1498 s cm^{-1} (pyrrole ring).

Anal. Calc. for $C_8H_7NO_5$: C, 48.73; H, 3.58; N, 7.11. Found: C, 48.64; H, 3.50, N, 6.94.

The corresponding phenylhydrazone, prepared in the usual way, had m.p. 208–210° (from ethanol–water, 1:1).

Anal. Calc. for $C_{14}H_{13}N_3O_4$: C, 58.53; H, 4.67; N, 14.63. Found: C, 58.55; H, 4.74; N, 14.40.

3-Methoxylcarbonyl-2,5-pyrroledicarboxylic acid (**10**). — A suspension of silver oxide in water was prepared by adding M sodium hydroxide (3.2 ml) to a solution of silver nitrate (0.37 g, 2.2 mmoles) in water (0.6 ml). Pyrrolealdehyde **9** (0.20 g, 1 mmole) was added, the mixture was heated for 1 h at 100°, cooled, and filtered, and the solid residue was washed several times with hot water. The combined filtrate and washings were acidified (Congo red) with dilute nitric acid. The resulting precipitate (68 mg, 32%) was washed with water and recrystallized from ethanol–water to give **10**, m.p. 220° (dec.), λ_{max} (water) 227, 259, and 275 nm (ε 20,200, 9,100, and 8,900); ν_{max} (KBr) 3225 s (NH), 2600 b-m (CO_2H), 1747 s, 1694 s, and 1633 b-s (CO_2Me and CO_2H), 1568 m and 1505 m cm^{-1} (pyrrole ring).

Anal. Calc. for $C_8H_7NO_6$: C, 45.08; H, 3.31; N, 6.57. Found: C, 45.26; H, 3.21; N, 6.60.

Treatment of **10** with methanol containing hydrogen chloride in the usual way gave the corresponding trimethyl ester **11**, m.p. 131–132°, λ_{max} (ethanol) 226 and 271 nm (ε 23,700 and 17,300); ν_{max} (Nujol) 3280 m (NH), 1740 s and 1700 m cm^{-1} (CO_2Me); lit.[13] m.p. 130–131°; λ_{max} (ethanol) 224 and 270 nm (ε 25,720 and 16,990); ν_{max} (Nujol) 3281, 1739 and 1700 cm^{-1}.

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