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# AMADORI COMPOUNDS: VACUUM THERMOLYSIS OF 1-DEOXY-1-L-PROLINO-D-FRUCTOSE

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ABSTRACT

Amadori compounds are important precursors of color and aromas in foods, and proline–sugar reactions produce bready aromas in roasted cereals and baked goods. To produce the volatile aroma-compounds, 1-deoxy-1-L-prolino-D-fructose was heated under vacuum, first at 140°, and then at 240°. The distillates were condensed at −70°, and from them 22 compounds were identified by g.l.c.–m.s., p.m.r., i.r. spectroscopy, g.l.c. and synthesis. At 140°, there were major proportions of 6-carbon dehydration products (dihydrofurans, dihydropyrones, pyrones, and a methylcyclopentenolone), lesser proportions of scission compounds (acetic acid and the pyrrolidine amides of formic, acetic, and propionic acids), substituted furfurylamines, a diazepine, proline, and pyrrolidines derived from proline. At 240°, the title compound yields more of the pyrrolidine derivatives, maltol, pyrrolidine amides of formic, acetic, and propionic acids, a γ-lactone, and 2-pyrrolino-substituted furans. Product aromas were determined and degradation schemes, based on the isolated products, were formulated.

## INTRODUCTION

Amadori compounds form in the Maillard reaction and are precursors of aroma and flavor in processed foods[1]. Evidence from model studies shows the reaction of L-proline or L-hydroxyproline with 1,3-dihydroxy-2-propanone or glyceraldehyde produces bread- and cracker-like aromas[2,3]. The reaction of D-glucose with L-hydroxyproline produces acetonylpyrrole, which has a bread-like aroma[4]. When D-glucose and L-proline are heated together, further products having roasted aromas, derivatives of 1(*H*)-pyrrolizines, and a tetrahydroindolizinone are produced[5].

The established importance of Maillard browning-reactions for food acceptance led us to investigate the thermal decomposition of an Amadori compound containing

*Mention of firm names or trade products does not imply that they are endorsed or recommended by the U.S. Department of Agriculture over other firms or similar products not mentioned.

TABLE I

PYROLYSIS PRODUCTS FROM 1-DEOXY-1-L-PROLINO-D-FRUCTOSE

| *Compounds* | *Presence at* | | *Low temperature*[a] *relative peak area (%)* | *Derivation from hexose carbon atoms* | $R_t$ (*min*)[b] a/1 | a/2 | f/2 | *Aroma* |
|---|---|---|---|---|---|---|---|---|
| | *140°* | *240°* | | | | | | |
| *Amides* | | | | | | | | |
| 1 *N*-Formylpyrrolidine | + | + | 0.8 | 1 | 9.6 | | | Minty |
| 2 *N*-Acetylpyrrolidine | + | + | 1.5 | 2 | 11.7 | | | Minty |
| 3 *N*-Propionylpyrrolidine | | + | | 3 | 12.3 | | | |
| 4 *N*-Butyrylpyrrole | + | | 1.9 | 4 | 14.6 | | | Burnt nut |
| *Cyclic enolones* | | | | | | | | |
| 5 2,5-Dimethyl-2,4-dihydroxy-3(2*H*)-furanone | + | | 5.8 | 6 | 14.7 | | | Burnt sugar |
| 6 2-Hydroxy-1-methylcyclopenten-3-one | + | | 1.2 | 6 | 14.9 | | | Maple |
| 7 2,5-Dimethyl-4-hydroxy-3(2*H*)-furanone | + | | 2.0 | 6 | 15.0 | | | Burnt sugar |
| 8 2,3-Dihydro-3,5-dihydroxy-6-methyl-4(*H*)-pyran-4-one | + | | 50.0 | 6 | 17.6 | | | None |
| 9 3-Hydroxy-2-methyl-4(*H*)-pyran-4-one | | + | Trace | 6 | 21.5 | | | Maple-burnt sugar |
| 10 3,5-Dihydroxy-2-methyl-4(*H*)-pyran-4-one | + | | 1.0 | 6 | 26.3 (17.9) | | | Trace maple |

TABLE I (*continued*)

| *Compounds* | *Presence at* | | *Low temperature*[a] *relative peak area (%)* | *Derivation from hexose carbon atoms* | $R_t$ (*min*)[b] | | | *Aroma* |
|---|---|---|---|---|---|---|---|---|
| | *140°* | *240°* | | | a/1 | a/2 | f/2 | |
| ***Proline derivatives*** | | | | | | | | |
| **11** 1-Pyrroline | + | | 1.6 | | | 3.9 | | Fresh corn |
| **12** 2-(Hydroxymethyl)pyrrolidine | + | | 1.1 | | | | 2.8 | Amine-cornlike |
| **13** *Octa*hydro-5(*H*),10(*H*)-dipyrrolo(1,2-*a*:-1′,2′-*d*)pyrazine-5,10-dione | + | + | 6.2 | | 35.0 | | | Nutlike |
| **14** Proline | + | +[c] | | | | | | |
| **15** Pyrrolidine-2-carboxaldehyde | | + | | | | | | |
| ***Furfuryl derivatives*** | | | | | | | | |
| **16** *N*-(5-Methyl-2-furfuryl)pyrrolidine | | + | | 6 | 18.3 | | | Nutlike |
| **17** *N*-(5-Methyl-2-furfuryl)-2-pyrroline | + | + | 2.3 | 6 | 21.8 | | | Trace nutlike |
| **18** *N*-(5-Hydroxymethyl-2-furfuryl)-2-pyrroline | + | + | 1.6 | 6 | 27.9 | | | Trace nutlike |
| **19** *N*-(5-Hydroxymethyl-2-furfuryl)pyrrolidine | | + | | 6 | 31.5 | | | Nutlike |
| ***Lactones*** | | | | | | | | |
| **20** 4-Butanolide | + | | Trace | 4 | 4.0 | | | |
| **21** 4-Methylbutanolide | | + | | 5 | 5.0 | | | |
| ***Acid*** | | | | | | | | |
| **22** Acetic acid | + | | 22.5 | 2 | 15.8 | | | |

[a]Calculated from the ratio of individual peak areas to the total area for peaks tested. [b]$R_t$ = retention time; *a*/1 = column *a*/program 1, and so on. [c]Isolated from pyrolysis residue.

an amino acid substituent, in order to augment our earlier study on the thermolysis of 1-deoxy-1-piperidino-D-fructose[6]. In doing so, the effect of changing the amine moiety on products, aroma, and degradation pathways would be evident.

## RESULTS AND DISCUSSION

The title compound was decomposed in two stages, first *in vacuo* at 140° and then at 240°. The distillates were collected separately and fractionated by either preparative g.l.c. or t.l.c., or both. All structures were determined spectrometrically and most were verified by comparison of either g.l.c., p.m.r., i.r., or m.s. data, or all of them, with synthetic compounds. The products identified (Table I) were all isolated from the distillate, except for proline. In the 140° distillate, $C_6$ products of hexose dehydration preponderated, together with the proline self-condensation product **13**. Small proportions of hexose fragmentation-products (**1**, **2**, **4**, and **20**) were also present, and the fragment produced in greatest quantity (22.5%) was acetic acid. The 6-carbon, cyclic enolones (**5–10**) were responsible for the strong burnt-sugar-to-burnt-marshmallow aroma of this fraction. The corn- to nut-like aromas of the proline-derived components (**11–13**) and the 2-furfuryl derivatives (**17** and **18**) were only subtly apparent. The 240° distillate, which consisted in part of the 2-furfurylpyrrolidines (**16–19**) and the proline-derived **13** and **15**, had a pronounced roasted-to-burned nut aroma. Because all of the components in this fraction were not identified, the compounds responsible for odor are uncertain. One enolone (**9**) was found in the high-temperature distillate, but only in trace amounts. In comparison with the earlier thermolysis of an Amadori product[6], these findings were not unexpected as, from $K_b$ studies on the free amines[7], the title compound should be more weakly basic than

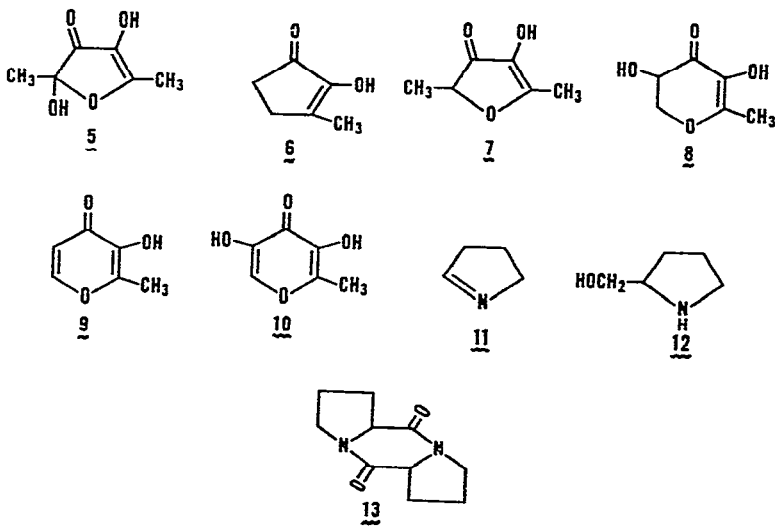


Fig. 1. Structures of pyrolysis products 5–13 formed from 1-deoxy-1-L-prolino-D-fructose.

1-deoxy-1-piperidino-D-fructose. Also, the product composition and relative amounts differed.

Five previously identified Maillard-browning, nonnitrogenous hexose-dehydration products from the 2,3-enolization pathway are present: dihydrofurans **5** and **7**, and pyrones **8**, **9**, and **10**. Earlier, **5** and **7** were not found in significant amounts, and **8**, **9**, and **10** were absent[6]. The major products of the previous thermolysis were aminated $C_4$ reductones, which have also been found in other Maillard-browning studies[8–10]. Our latest findings imply that the more-weakly basic amino acid (such as proline) produces lesser amounts of fragmentation products. Consequently, an Amadori compound substituted with a less basic amine will yield more $C_6$ enolones, which, in general, are more fragrant than the 4-carbon reductones, and have a stronger caramel, or burnt-sugar aroma. Of the products having an enolone structure, only **8** is odorless. Compound **8** has been produced by acid- and base-catalyzed degradations of D-fructose[11,12], deterioration of orange-juice powder[13], and browning of an L-lysine–lactose system[14]. Two g.l.c. peaks corresponded to compound **10**, a phenomenon, previously noted[14], that indicates that a portion of this pyrone is formed during the chromatography. Hence, in the pyrolysis, pyrone **10** is most probably formed by dehydrogenation of **8**. Products **8** and **10** are not observed in pyrolysis mixtures when the amine is strongly basic, as with piperidine[6]. Furthermore, when D-glucose and L-proline are heated for 6 min at 200°, compounds **6**, **7**, **8**, and **10** are formed and no $C_4$ reductones are produced[5].

Isolation of methylcyclopentenolone (**6**) and maltol (**9**) is a first instance for their detection in a pyrolyzate from Amadori compounds; **6** is formed at the lower temperature and **9** at the higher. Usually, they appear together in browning reactions that are carried out under low-pH or high-temperature conditions. However, we cannot demonstrate whether the change in the amine or the temperature is significant as an explanation for their formation, as **6** may originate from the less-basic Amadori compound at the lower temperature. Their formation is important because both contribute to a pleasant burnt-sugar aroma. Of the remaining carbohydrate-derived components, **20** and **21**, only **20** has been previously found in the earlier pyrolysis work[6].

Residues of both low- and high-temperature pyrolysis show that 1-deoxy-1-L-prolino-D-fructose cleaves to yield the free amino acid, which, in turn, may react

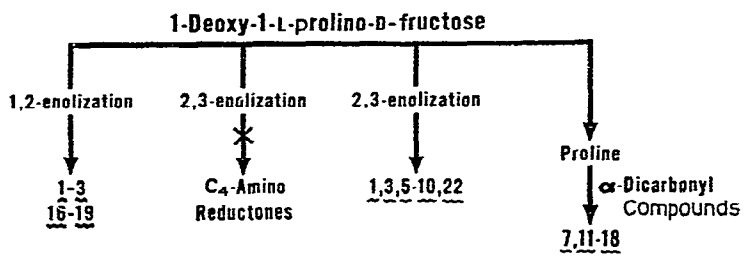


Fig. 2. Decomposition paths of 1-deoxy-1-L-prolino-D-fructose.

further and produce additional products. Continued heating at the lower temperature leads to the four proline-derived compounds and two amides via routes indicated in Fig. 2. However, when L-proline is heated at 185° in ethylene glycol, only the anhydride **13** is formed. As a consequence, other routes to the free amines (Fig. 2) must exist; they result from redox reactions between the amino acid and several reactive intermediates (Fig. 2) produced from the carbohydrate portion of 1-deoxy-1-L-prolino-D-fructose. It was demonstrated earlier that, during pyrolysis of Amadori compounds, the 1-amino moiety is freed and substitutes onto reactive intermediates, such as unsaturated ketones[6]. The pyrrolidine amides **1**, **2**, and **3** are probably further examples of this process. Because thermolysis of the free amino acid did not yield any pyrrolidine, compounds **16–19** and, perhaps, **1**, **2**, and **3** may be formed by an alternative path involving sugar participation.

After 1,2-enolization (Fig. 3) and while still attached to the saccharide, the amino acid undergoes decarboxylation. The resulting products are the 2-furfurylamines

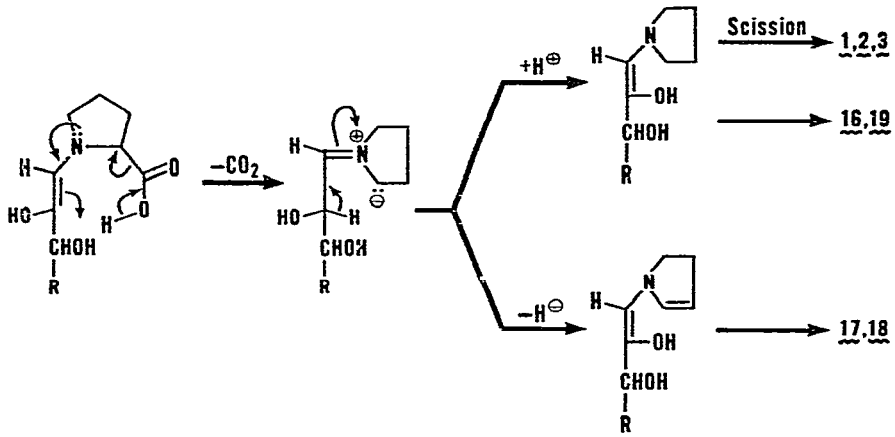


Fig. 3. Mechanism for the decarboxylation of 1-deoxy-1-L-prolino-D-fructose.

**16–19** and amides **1–3**. Decarboxylation would be facilitated by enolization in the sugar[15], and the remainder of the dehydration route would be similar to the mechanism proposed for the acid catalyzed-elimination reaction of D-fructose that leads to substituted furfuraldehydes[16,17]. This mechanism is favored, because the decarboxylating species is locked into a 1,2-enolization, which then directs the dehydration in the generation of 2-furaldehydes. Retention of the 1-amino substituent during enolizations of sugars, to yield substituted furan derivatives, was demonstrated previously with the isolation of *N*-(furoylmethyl)-amines or -amino acids from the acidic treatment of appropriate Amadori compounds[18,19].

The pyrrolidines **1** and **2**, and pyrrolines **17** and **18**, are formed at both experimental temperatures. The relative amounts of 1- and 2-carbon fragments are far smaller than those found in the decomposition of an Amadori compound sub-

stituted with the more basic amine; the yield of 3-carbon amide is nearly the same[6]. The furfuryl amines are newly identified products in these pyrolyzates and various amounts can be found under both experimental conditions.

Synthetic **16** and **19** were prepared from the reaction of the appropriate aldehyde with *N*-formylpyrrolidine (Fig. 4); compound **17** was obtained in 3–5% yield by the acid-catalyzed ring expansion of the amine formed from the reaction of cyclopropanecarboxaldehyde and 5-methyl-2-furfurylamine. Spectral data established the structure of **18**. As the fragmentation pattern of **18** closely parallels that of **17**, and **19** that of **16**, we consider that the assignment for **18** is correct.

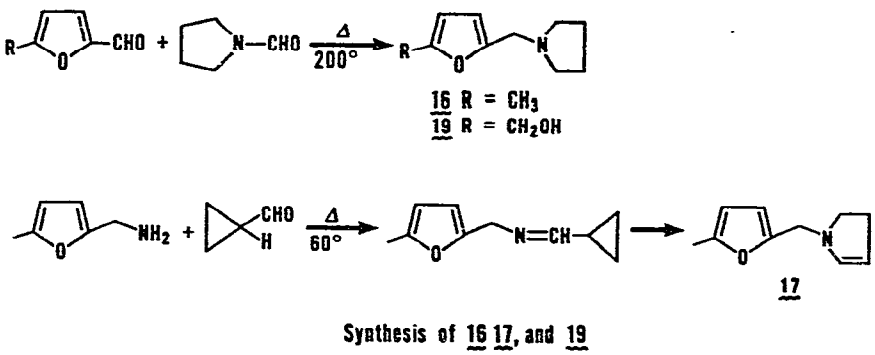


Fig. 4. Synthesis of compounds **16**, **17**, and **19**.

TABLE II

MASS SPECTRA OF SELECTED PYROLYSIS PRODUCTS[a]

| *Component* | m/e (*relative* %)[b] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **1** | 99(100) | 71(28) | 70(68) | 43(50) | 42(32) | | | |
| **3** | 127(93) | 99(21) | 98(48) | 71(27) | 70(100) | 57(25) | 55(32) | 43(41) |
| **4** | 137(100) | 122(18) | 109(6) | 108(6) | 94(72) | 85(15) | 78(8) | 67(22) |
| | 57(32) | 43(68) | | | | | | |
| **11** | 69(95) | 68(45) | 54(6) | 44(15) | 42(47) | 41(100) | | |
| **12** | 101(2) | 100(2) | 82(2) | 71(5) | 70(100) | 55(5) | 43(8) | |
| **15** | 99(24) | 87(6) | 71(37) | 57(100) | 56(43) | 44(25) | 43(80) | 42(5) |
| **16** | 165(28) | 164(13) | 150(4) | 122(7) | 95(100) | 84(3) | 83(7) | 70(8) |
| | 55(3) | | | | | | | |
| **17** | 163(72) | 162(100) | 161(18) | 148(25) | 134(20) | 133(38) | 120(42) | 95(20) |
| | 81(20) | 68(19) | 65(30) | 64(19) | | | | |
| **18** | 179(33) | 178(10) | 162(27) | 152(22) | 148(55) | 142(10) | 126(15) | 111(100) |
| | 108(32) | 70(18) | 68(17) | 55(22) | | | | |
| **19** | 181(100) | 150(46) | 136(8) | 111(93) | 84(20) | 83(42) | 70(23) | 55(22) |
| **20** | 86(13) | 74(13) | 73(8) | 43(100) | | | | |
| **21** | 100(11) | 85(43) | 56(93) | 55(23) | 43(70) | 42(35) | 41(100) | |

[a]Column *a*/program *1* (g.l.c.–m.s.). [b]Relative % = % of base peak.

The only observed pyrrole (**4**) is a component of the low-temperature distillate. Other aromatized, nitrogen-containing compounds have been found when primary amines were treated with reducing sugars[20–22]. More recently, a number of heterocyclic aromatic compounds have been isolated from the reaction of D-glucose with L-proline[5]. As no pyrrolizine or indolizinone derivatives were found in our study, they evidently arise by a different pathway.

To obtain additional information on the origin of substituted amines, synthetic **8**, and L-proline were treated at 140° in ethylene glycol (Table III and Fig. 5). This reaction not only delineates another path for the decarboxylation of the amino acid, but also shows that **8** can undergo ring contraction and form a dihydrofuran. Finally, it also suggests that **7**, **16**, **17**, and **18** would be formed in higher amounts in pyrolysis

TABLE III

BROWNING PRODUCTS FROM **8** AND **14**

| *Component* | $R_t$ (*min*)[a] | *Yield*[b] (%) |
|---|---|---|
| **7** | 15 | 17 |
| **10** | 26.3 | 1 |
| **13** | 35.2 | 4 |
| **16** | 18.3 | 37 |
| **17** | 21.9 | 31 |
| **18** | 27.7 | 8 |

[a]Column *a*/program *1*. [b]Calculated from the ratio of individual peak areas to the total area for the peaks listed.

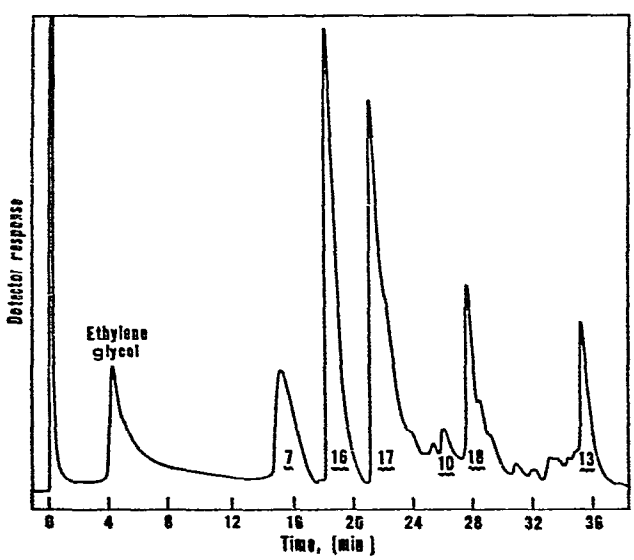


Fig. 5. G.l.c. of reaction products from heating 2,3-dihydro-3,5-dihydroxy-6-methyl-4(*H*)-pyran-4-one with L-proline; column *a*/program *1* of Table I.

of the Amadori compound if **8** had not been removed by distillation. Other products are formed in the reaction of **8** with L-proline, but have not thus been far identified.

The results from the pyrolysis of 1-deoxy-1-L-prolino-D-fructose and the condensation of L-proline with **8** suggest modified pathways for the decomposition of Amadori compounds substituted with a secondary amino acid. Substitution of proline for piperidine did alter the decomposition products, their relative amounts, and produced several types not observed in our earlier study. Several pyrolysis components were isolated that have not been reported in previous L-proline–hexose reactions. Individual product aromas varied from caramel to amine or nutlike. Finally, the decomposition path was changed from one of abundant scission to one of significant hexose dehydration.

## EXPERIMENTAL

*General methods.* — A Model 1848 Varian Aerograph gas chromatograph, equipped with dual-flame detectors, was used; one detector was fitted with a variable effluent-splitter. Samples were on-column injected, and stainless-steel columns were used for either analytical or preparative chromatography, or both: (*a*) 3% 8 BP on 80–100 Chromosorb W, 4 ft × 0.125 in; (*b*) 3% SE-30 on 100–120 Varaport, 5 ft × 0.125 in; (*c*) 3% SP-1000 on 80–100 Sup T, 4 ft × 0.125 in; (*d*) 10% Versamide 900 on 60–80 Chromosorb W, 8 ft × 0.125 in; (*e*) 3% OV-17 on 80–100 Chromosorb Q, 6 ft × 0.125 in; and (*f*) 10% 8 BP on 80–100 Chromosorb W, 4 ft × 0.25 in. Temperature programs were (*1*) 70° for 4 min, 4°/min to 225° and then isothermal until elution was completed; (*2*) 100°, 4°/min to 225°; (*3*) 130°, 4°/min to 225°; (*4*) 90° for 4° min, 4°/min to 210°; and (*5*) 110°, 6°/min to 220°. Flow rates were 35 ml/min for the 0.125-in. columns and 50 ml/min for the 0.25-in. columns. Selected effluents were collected in Teflon tubing, which was cooled by Dry Ice.

*Spectrometric methods.* — The i.r. spectra were recorded by a Perkin–Elmer Model 621 spectrometer from solutions in chloroform. The mass spectra were determined as either individual samples on a Nuclide 12-90G-DF mass spectrometer at 70 eV or as resolved components from g.l.c.–m.s. analysis on a Packard gas chromatograph, Model 846, coupled to the Nuclide 12-90G-DF spectrometer. The p.m.r. spectra of chloroform-*d* solutions were recorded with a Varian HA-100 instrument, and tetramethylsilane served as the internal standard.

*Pyrolysis.* — The Amadori compound (15 g) was placed in a thick-walled flask connected to a receiver by a wide-bore tube. The receiver was cooled with a Dry Ice–ethanol bath. After the system had been evacuated to 0.1 torr, the sample was heated for 3.5 h at 140°. The receiver was allowed to warm to room temperature, and the initial distillate was extracted with chloroform. The extract was dried over anhydrous sodium sulfate and evaporated at 0°; yield 0.50 g. The receiver was reconnected, and the pyrolysis residue was then heated for 3 h at 250° under 0.1 torr; however, chloroform–methanol was used to extract the distillate; yield 0.30 g.

The distillate at 140° was examined by g.l.c.–m.s., and columns *a* and *c*,

programs *1* and *2* (Table I), were employed to resolve the products. When needed, individual components were isolated on column *c* following program *2*. In comparisons of isolated compounds with those prepared by synthesis, identical retention time on at least two columns was one criterion for identity.

*Fractionation of the 240° distillate.* — The total distillate at 240° was applied to three, 2-mm thick, preparative Silica Gel SF-254, t.l.c. plates (Brinkmann). Each plate was developed with ethyl acetate and viewed with a u.v. lamp. The plates were divided into three zones, and each zone was extracted with ethyl acetate: (*1*) (0–35 mm, 116 mg), (*2*) (35–60 mm, 85 mg), and (*3*) (60–90 mm, 119 mg). A sample from each fraction was analyzed by g.l.c.–m.s. on column *a* with program *1*. When needed, fractions were further resolved on columns *a* and *c* according to respective programs *1* and *2*.

Zone 1 contained **1**, **13**, **15**, and **16**; zone 2, **2**, **3**, and **17**; zone 3, **9**, **18**, **19**, and **21**. Of the 25 products in this mixture, 11 were identified. All of the identified products were correlated by g.l.c. with synthetic compounds whenever possible, on columns *a*, *b*, *c*, or *d*, and at least one of them was used.

*1-Deoxy-1-*L*-prolino-*D*-fructose.* — D-Glucose (26.25 g) was dissolved in 200 ml of anhydrous methanol, L-proline (18.75 g) was added, and the solution was refluxed for 40 min. Malonic acid (3.75 g) was then added, and the solution was refluxed for an additional 2 h. The mixture was cooled, and concentrated to one-half its original volume. Further cooling produced 13 g of crystalline product. Reconcentration of the mother liquor and recooling yielded an additional 15 g. Both crops were combined and recrystallized from the minimum amount of methanol; m.p. 111–114°, lit.[23] 112–113°.

*Anal.* Calc. for $C_{11}H_{19}O_7 \cdot CH_3OH$: C, 46.57; H, 7.49; N, 4.52. Found: C, 46.55; H, 7.61; N, 4.65.

The following compounds were prepared by published procedures: **5** (ref. 24), **7** (ref. 25), **8** (ref. 26), **10** (ref. 27), **11** (ref. 28), (±)-5-carboxy-2-pyrrolidinone[29], and (±)-5-ethoxycarbonyl-2-pyrrolidinone[30]. Compounds **6** and **9** were purchased from Dow Chemical Corporation and Aldrich, respectively.

*2-(Hydroxymethyl)pyrrolidine* (**12**). — A lithium aluminum hydride–ether mixture (100 ml of ether containing 1.15 g of lithium aluminum hydride) was brought to reflux in a Soxhlet apparatus, which contained a cup charged with (±)-2-ethoxycarbonyl-5-pyrrolidinone (1.45 g). After 6 h, the starting material had completely dissolved, and the solution was refluxed further for 4 h. Care was taken to remove the heater at the point when vigorous evolution of hydrogen occurred. The mixture was cooled and, after addition of 3 ml of water, filtered. The precipitate was washed several times with ether. All ether extracts were combined, dried (sodium sulfate), and evaporated *in vacuo* at 30°. The residue contained the product, as well as some starting material (as shown by g.l.c.). Final purification was completed by preparative g.l.c. on column *e*; p.m.r. $\delta$(H): 1.41 (1 H, multiplet), 1.76 (3 H, multiplet), 2.88 (2 H, hydroxymethyl methylene triplet), and 3.35 (1 H, $\beta$-methylene

multiplet); *m/e* (relative %): 101 (2), 100 (2), 82 (2), 71 (5), 70 (100), 55 (5), and 43 (8).

*Octahydro-5H,10H-dipyrrolo(1,2:1',2'-d)pyrazine-5,10-dione (proline anhydride,* **13**). — L-Proline (2 g) was added to 10 ml of ethylene glycol, and the mixture was heated for 2 h at 145–150°. The solution was cooled, diluted with an equal volume of water, brought to saturation with salt, and then extracted twice with chloroform. The combined organic phase was dried (sodium sulfate), and evaporated. The residue was sublimed at 120°/0.1 torr; $\nu_{max}$ 3000, 2980, 1665 (vs), and 1465 (s) $cm^{-1}$; p.m.r. $\delta$(H): 1.13 (2H, methine doublet), 352 (4H, methylene quartet), and 2.12 (10H, methylene multiplet); *m/e* (relative %): 194 (38), 166 (3), 138 (5), 124 (6), 115 (5), 115 (5), 70 (100), 69 (6), and 55 (5).

N-(*5-Methyl-2-furfuryl)pyrrolidine* (**16**). — 5-Methyl-2-furaldehyde (6.5 g) was added to 24 g of *N*-formylpyrrolidine during a 20-min period. The solution was then refluxed for 7 h. Water (50 ml) was added to the cooled solution and the mixture was acidified with dilute hydrochloric acid. The solution was extracted three times with ether. The aqueous phase was made alkaline (pH 11) with 3M potassium hydroxide, sodium chloride was added to saturation, and the solution was extracted three times with ether (400 ml total volume) to yield 10 g of a colorless oil. G.l.c. analysis on column *a*/program *4* showed the product to be 95% pure. Preparative g.l.c. was used to obtain a sample of spectral purity; p.m.r. $\delta$(H): 6.01 (1H, vinyl, doublet, $J_{AB}$ 2 Hz), 5.82 (1 H, vinyl, finely split doublet), 3.54 (2H, singlet), 2.52 (4H, $\alpha$-methylene), 2.24 (3H, *C*-methyl), and 1.78 (4H, $\beta$-methylene). Mass-spectral data are listed in Table II.

N-(*5-Hydroxymethyl-2-furfuryl)pyrrolidine* (**19**). — 5-(Hydroxymethyl)-2-furaldehyde (0.378 g) was added during 15 min to 2.97 g of *N*-formylpyrrolidine. The resulting solution was refluxed for 12 h. The product (0.360 g) was isolated as already described. G.l.c. on column *f*/program *5* showed four components present. A portion of the product was subjected to g.l.c.–m.s. analysis, and the compound corresponding to the product ($M^+$ 181) was separated by preparative g.l.c. (yield, based on g.l.c. areas, 26%); $\nu_{max}$ 3600, 2960, 2920, 2800, 1650 (w), 1560 (w) $cm^{-1}$; p.m.r. $\delta$(H): 6.15 (1H, vinyl, $J_{AB}$ 2 Hz), 6.07 (1H, vinyl), 4.51 (2 H, hydroxymethylene), 3.58 (2 H, methylamino), 2.52 (4H, $\alpha$-methylene), 2.35 (1H, hydroxyl), and 1.80 (4H, $\beta$-methylene). Mass-spectral data are listed in Table II.

N-(*Cyclopropylcarbonyl)imidazole.* — Imidazole (6.8 g) and triethylamine (10.1 g) were added to 75 ml of ether. The mixture was cooled to 5°, and then cyclopropylcarbonyl chloride (10.3 g) in 20 ml of ether was added dropwise to the stirred mixture. After 2.5 h, the mixture was filtered, and the ether phase was washed with 30 ml of 10% sodium carbonate. The dried (sodium sulfate) ether phase was evaporated; yield, 13.1 g; $\nu_{max}$ 1720 $cm^{-1}$; *m/e* (relative %): 136 (19), 86 (5), 85 (18), 69 (81), 68 (100), 67 (7), 58 (8), 41 (63), 40 (20), and 39 (22).

*Cyclopropyl carboxaldehyde.* — The preceding amide (9.0 g) was dissolved in 80 ml of anhydrous ether at 3°. Small portions of lithium aluminum hydride (0.95 g) were added during 30 min to the stirred solution. After 1 h, the mixture was acidified

with 2.5M sulfuric acid and the ether phase was removed. The aqueous solution was extracted twice with ether and the combined ether phase was washed once with 10% sodium carbonate and once with water. Evaporation of the dried ether phase gave 4.0 g of product. The material was identical to that previously obtained[31].

*5-Methyl-2-furfurylamine.* — 5-Methyl-2-furaldehyde (5.0 g), 2.5 g of Raney nickel[32], and 20 ml of methanol saturated with ammonia were mixed and then hydrogenated for 4 h at 100° and 120 lb.in.$^{-2}$.

The mixture was filtered and the solvent removed *in vacuo*. The residue was distilled at 40 torr and the fraction boiling at 100–120° isolated; yield, 1.5 g; *m/e* (relative %): 111 (96), 110 (61), 96 (100), 95 (98), 94 (65), 83 (38), 82 (4), 81 (7), 78 (25), 69 (7), 68 (42), 67 (12); 65 (5), 55 (15), and 53 (20).

N-(*5-Methyl-2-furfuryl*)*cyclopropylcarbaldimine.* — An equimolar amount (0.1 mole) of cyclopropylcarboxaldehyde was added in four portions to 5-methyl-2-furfurylamine while stirring with several potassium hydroxide pellets at 4°. The mixture was brought to room temperature and stirred for an additional 2 h. The product was removed by filtration. G.l.c. showed the mixture to contain starting material and product. The reactants were removed by evaporation at 80°/40 torr. The residue was further distilled in a Kügelrohr at 0.1 torr; yield 9.0 g; p.m.r. $\delta$(H): 5.95 (1 H, vinyl doublet); 5.78 (1H, vinyl doublet), 4.35 (1H, finely split carbaldimino doublet), 2.25 (5H, methyl and methylene protons), 1.66 (1H, methine multiplet), and 0.78 (4H, cyclopropane methylene multiplet); *m/e* (relative %): 163 (20), 96 (5), 95 (100), 94 (4), 81 (0.5), 70 (6), 68 (7), 55 (11), and 43 (8).

N-(*5-Methyl-2-furfuryl*)-*2-pyrroline* (**17**). — A portion of the carbaldimine and sufficient ammonium chloride to absorb the liquid were heated in a sealed glass tube for 20 h at 110–120°. Upon cooling, the mixture was extracted with chloroform, and the solution was examined by g.l.c. with column *a*/program *1*. The peak corresponding to the previously detected 2-pyrroline (**17**) was isolated by using column *f*/program *5*. Analytical g.l.c. indicated product yields of 3 to 5% (based on component peak-area divided by the total area for all volatile products); p.m.r. $\delta$(H): 6.03 (1H, vinyl proton), 5.87 (1H, vinyl proton), 5.31 (1H, $\alpha$ pyrroline vinyl proton, quartet), 4.10 (1H, $\beta$ pyrroline vinyl proton), 3.54 (2H, furfuryl methylene protons, singlet), 2.90 (2H, $\alpha$-methylene protons, quartet), 2.24 (3 H, methyl protons), and 2.15 (2H, $\beta$-methylene protons, quartet); *m/e* (relative %): 163 (72), 162 (100), 148 (25), 134 (17), 133 (34), 120 (35), 95 (31), 81 (15), 68 (19), 65 (29), and 64 (11).

*Reaction of* **8** *and* **14**. — Synthetic **8** (144 mg) and L-proline (115 mg) were added to 20 ml of ethylene glycol. The resulting mixture was stirred and heated for 3 h at 185°. After cooling, the solution was poured into 40 ml of water. The final aqueous solution was extracted with three 25-ml portions of chloroform. The combined chloroform phase was dried (sodium sulfate) and evaporated at 0° to give a brown oil. This product was then examined by g.l.c.–m.s. with column *a*/program *1*.

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