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3-Hydroxypyrroles. III.[1] Synthesis and Tautomerism of N-Alkyl-3-hydroxypyrroles[2]

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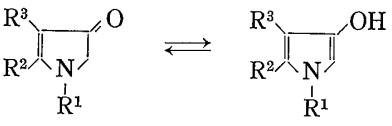
Syntheses of 3-hydroxypyrroles (4-oxo-2-pyrrolines) (**1b**—**1d**) bearing no substituents on the ring carbon and of 3-hydroxypyrrole-4-carboxylates (**2**—**4**) with no substituents at C-5 were accomplished; the former by hydrogenolysis of the benzyl esters (**6b** and **6c**) or by acid cleavage of the *tert*-butyl ester (**7**), and the latter by acid cleavage of the diesters (**15** and **16**) or of the pyrrolinone (**17**). On the basis of spectral evidence, compounds **1c** and **1d** exist in the keto form while compounds **2**—**4** exist in the enol form. Only **1b** was shown to be at equilibrium between the two tautomers. New information concerning the factors governing the tautomerism of 3-hydroxypyrroles was obtained.

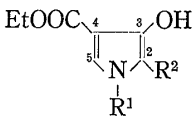
Keywords——3-hydroxypyrrole; N-alkyl-4-oxo-2-pyrroline; 3-hydroxypyrrole-4-carboxylate; 2- and 3-methyl-4-oxo-2-pyrroline; hydrogenolysis of benzyl esters; tautomerism; intramolecular hydrogen bonding

It has been reported that nonsubstituted 3-hydroxyfuran exists in the keto form,[4] and that nonsubstituted 3-hydroxythiophen exists in a keto-enol equilibrium.[5] However, nonsubstituted 3-hydroxypyrrole has not been synthesized to date, and there is no direct evidence to show whether form **1a** or **1'a** is preferred. The factors or the types of substitution affecting the preferred form of its derivatives are also unclear. We have examined the syntheses of N-alkyl-4-oxo-2-pyrrolines (**1b**—**1d**) bearing no substituents on the ring carbon and of 2,5- and 5-unsubstituted 3-hydroxypyrrole-4-carboxylates (**2**—**4**), and obtained new information on the tautomerism of 3-hydroxypyrroles.



1 ⇌ **1'**

	R^1	R^2	R^3
a :	H	H	H
b :	Me	H	H
c :	CH_2Ph	H	H
d :	Ph	H	H
e :	H	Me	H
f :	H	H	Me
g :	H	Me	Me



2: R^1=Me, R^2=H
3: R^1=CH_2Ph, R^2=H
4: R^1=CH_2Ph, R^2=CH_2CH_2COOEt

Chart 1

1) Part II: T. Momose, T. Tanaka, T. Yokota, N. Nagamoto, and K. Yamada, *Chem. Pharm. Bull.* (Tokyo), **26**, 3521 (1978).
2) A preliminary report of this work has appeared: T. Momose, T. Tanaka, and T. Yokota, *Heterocycles*, **6**, 1827 (1977).
3) Location: *133-1, Yamada-kami, Suita, Osaka 565, Japan.*
4) A. Hofmann, W.v. Philipsborn, and C.H. Eugster, *Helv. Chim. Acta*, **48**, 1322 (1965).
5) M.C. Ford and D. Mackay, *J. Chem. Soc.*, **1956**, 4985.

1. Synthesis and Structure of N-Alkyl-3-hydroxypyrroles

Bauer[6] has reported the synthesis of 2,3-dimethyl-4-oxo-2-pyrroline (**1g**) *via* the hydrogenolysis of 4-benzyloxy-2,3-dimethylpyrrole, and Pfeiffer and Bauer[7] later reported the synthesis of **1g** from the 3-hydroxypyrrole-2-carboxylate (**5g**) by treatment with 6 N hydrochloric acid.

We attempted the synthesis of **1a** and **1c** based on their methods, but could not obtain them either by the hydrogenolysis of 3-benzyloxypyrroles (**9a** and **9c**) obtained from the hydroxypyrrolecarboxylate (**5a**)[8] *via* the 3-benzyloxypyrrolecarboxylates (**8a** and **8c**) or by the treatment of **5a** and **5c** with 6 N hydrochloric acid. However, we obtained **1b**—**1d** by the following reaction sequences. Attempts to obtain **1a** by analogous procedures were again unsuccessful.

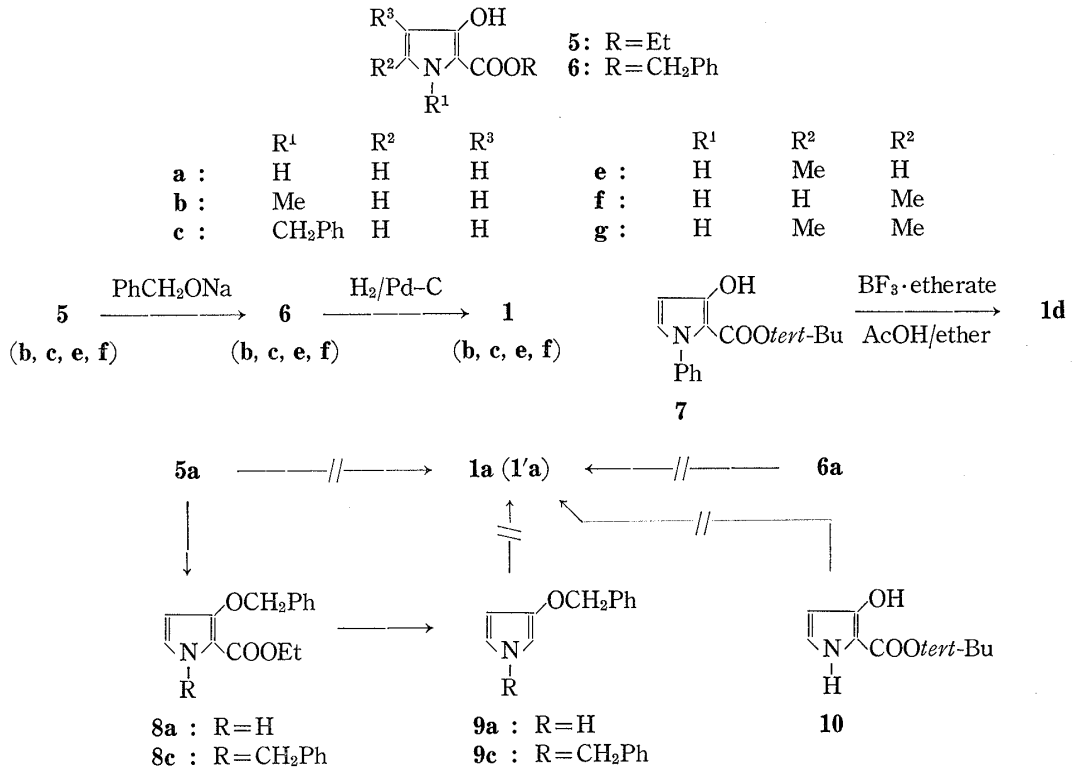


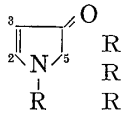
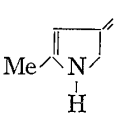
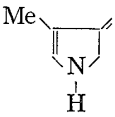
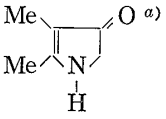
Chart 2

The benzyl esters (**6b** and **6c**) obtained from the ethyl esters (**5b** and **5c**)[8] by ester exchange with sodium benzyl alcoholate[9] gave N-methyl- and N-benzylpyrrolinone (**1b** and **1c**) *via* hydrogenolysis over 5% palladium on charcoal (Pd–C). The *tert*-butyl ester (**7**)[8] gave N-phenylpyrrolinone (**1d**) on treatment with boron trifluoride etherate (BF_3·etherate)/acetic acid in ether. Compound **1b** is at equilibrium between the keto and enol forms, with a predominance of the former, judging from its proton magnetic resonance (PMR) spectra measured in deuteriochloroform (keto: enol=14: 3) and in methanol-d_4 (keto: enol=9: 4).

6) H. Bauer, *Ann.*, **736**, 1 (1970).
7) G. Pfeiffer and H. Bauer, *Ann.*, **1976**, 383.
8) T. Momose, T. Tanaka, T. Yokota, N. Nagamoto, and K. Yamada, *Chem. Pharm. Bull.* (Tokyo), **26**, 2224 (1978).
9) Though Chong and Clezy reported that the base-catalyzed ester exchange reaction of 3-hydroxypyrrole-2-carboxylates proceeded to only a slight extent, we were able to carry out the exchange reaction in good yield by using 2 equivalents of benzyl alcoholate; see R. Chong and P.S. Clezy, *Aust. J. Chem.*, **20**, 935 (1967).

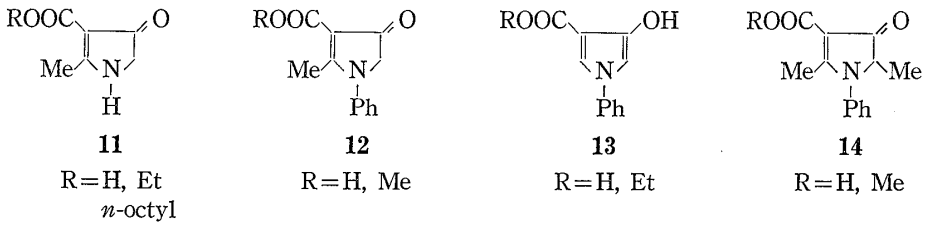
The compounds **1c** and **1d** apparently exist in the keto form in both chloroform and methanol. However, the ready disappearance of the PMR signals due to C-5 methylene protons in methanol-d_4 solution is probably due to deuterium exchange, and suggests the participation of the enol form. The compounds **1b**—**1d** are extremely unstable and resinify within several hours.

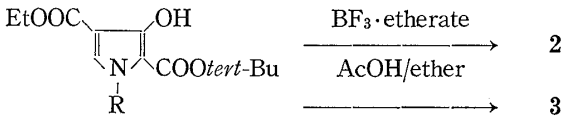
Table I. PMR and UV Data for the Pyrrolinones (**1b**—**1g**)

	PMR ($CDCl_3$) δ: C_2–H	C_3–H	C_5–H	UV (EtOH) nm:
 R=Me	7.75(d, J=3.0)	5.07(d, J=3.0)	3.72(s)	328
R=CH_2Ph	7.84(d, J=3.6)	5.10(d, J=3.6)	3.58(s)	327
R=Ph	8.39(d, J=3.7)	5.46(d, J=3.7)	4.10(s)	243, 354
	—	5.05(s-like)	3.90(s-like)	305
	—	—	—	325
 [a]	—	—	3.58[b]	315[c]

a) H. Bauer, *Ann.*, **736**, 1 (1970). b) In DMSO-d_6. c) In MeOH.

The nonsubstituted 3-hydroxypyrrole (**1a** or **1'a**) could not be isolated after hydrogenolysis of the benzyl ester (**6a**) nor on cleavage of the *tert*-butyl ester (**10**)[8] by treatment with BF_3·etherate. Compound **1g** is reasonably stable, but **1a** was not isolable. We therefore sought to synthesize monomethylpyrrolinones (**1e** and **1f**) *via* hydrogenolysis of the benzyl esters (**6e** and **6f**) which were obtained from the corresponding ethyl esters (**5e** and **5f**).[9]





15: R=Me
16: R=CH_2Ph

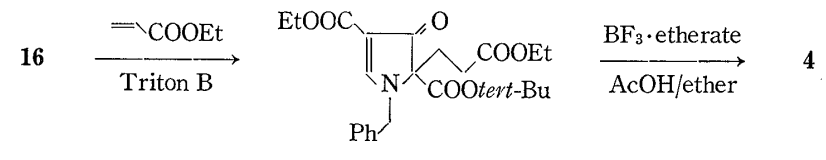


Chart 3

We obtained **1e** in fairly pure form, though it was unstable, but **1f** could be detected only by the ultraviolet (UV) spectrum measurements of the reaction mixture.

2. Synthesis and Structure of 3-Hydroxypyrrole-4-carboxylates

Though 3-hydroxypyrrole-4-carboxylates (**11**, **12**, **13**, and **14**) are known, the only known compound unsubstituted at C-5 is **13**.[10] We synthesized 2,5- and 5-unsubstituted N-alkyl-3-hydroxypyrrole-4-carboxylates (**2**—**4**) as follows.

The *tert*-butyl esters (**15** and **16**)[8] gave the N-methyl- and N-benzylpyrroles (**2** and **3**) on treatment with BF_3·etherate/AcOH in ether. These compounds show an absorption at *ca.* 3300 cm^{-1} due to a hydroxyl group in their infrared (IR) spectra, and show one maximum at 242 or 243 nm in their UV spectra.[11] The signals of the ring protons appear as doublets (J=2.8—3.0 Hz) in the PMR spectra, the feature suggesting that compounds **2** and **3** exist in the enol form.

The 5-unsubstituted, 2-substituted 3-hydroxypyrrole-4-carboxylate (**4**) was obtained *via* acid cleavage of the pyrrolinone (**17**) prepared[1] by the Michael reaction of the diester (**16**)[8] with ethyl acrylate. This compound shows a hydroxyl absorption in its IR spectrum and a maximum only at 242 nm in its UV spectrum. It is clear that **4** exists in the enol form.

Although the compounds **2**—**4** exist exclusively in the enol form even in methanol, it is noteworthy that the C-2 proton of **2** was not observed in PMR measurement of the methanol-d_4 solution owing probably to deuterium exchange, and accordingly the C-5 proton appeared as a singlet.

3. Tautomeric Structure of 3-Hydroxypyrroles

From the data for the newly prepared compounds (**1b**—**1f**, **2**, **3**, and **4**) and known compounds (**1g**, **5**, and **11**—**14**), the following conclusions were reached. i) In 3-hydroxypyrroles lacking polar functionalities on the ring, the keto form is more stable than the enol one[13] judging from the properties of the compounds (**1b**—**1d**) bearing no substituents on the ring carbon and of the 2,3-dimethyl derivative.[6] ii) The compounds having a carbonyl, phenyl[14] or cyano[15] functionality at the 2-position exist in the enol form owing to conjugation between the enol and the substituents. As mentioned by Chong and Clezy,[9] the intramolecular hydrogen bonding between the hydroxyl group at the 3-position and the carbonyl group at the 2-position is important for stabilization of the enol. iii) Intramolecular hydrogen bonding would be possible in 3-hydroxypyrrole-4-carboxylates, and the enol form forms a longer conjugated system[16] than does the keto form. Therefore the compounds (**2**—**4** and **13**) should exist in the enol form. On the other hand, in the ketonic compounds (**11**, **12**, and **14**), the conformation required for intramolecular hydrogen bonding between the hydroxyl and the neighboring carboxyl group would be eliminated as a result of the steric repulsion between the ring methyl and the carboxyl groups, and consequently the conjugation between the ring and the carboxyl group would become weak. As for the com-

10) *a*) J. Davoll, *J. Chem. Soc.*, **1953**, 3802; *b*) R.S. Atkinson and E. Bullock, *Can. J. Chem.*, **41**, 625 (1963). The nomenclature for the pyrrole-3-carboxylates in this paper is tentatively based on the 3-hydroxypyrrole system.

11) The N-phenyl derivative (**13**)[12] was reported by Davoll[10a] to show maxima at 246 and 255 nm in its UV spectrum. We synthesized it from *tert*-butyl 4-ethoxycarbonyl-1-phenyl-3-hydroxypyrrole-2-carboxylate[8] by the method used for **2** and **3**.

12) E. Benary and R. Konrad, *Ber.*, **56B**, 44 (1923).

13) Bodor *et al.* have reported that the keto form is more stable than the enol form based on calculation of the heats of atomization; see N. Bodor, M.J.S. Dewar, and A.J. Harget, *J. Am. Chem. Soc.*, **92**, 2929 (1970).

14) S.K. Gupta, *Synthesis*, **1975**, 726.

15) T. Murata, T. Sugawara, and K. Ukawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 2571 (1973).

16) The preference for the enol form of 4-hydroxypyrrole-2-carboxylic acid reported by Kuhn and Osswald is probably due to this conjugation. R. Kuhn and G. Osswald, *Chem. Ber.*, **89**, 1423 (1956).

pounds (**2**—**4** and **13**) bearing no substituents at the 5-position, the enol form is preferable owing to stabilization by both intramolecular hydrogen bonding and a longer conjugated system. Though Davoll[10a] reported that the existence of the enol form for **13** was due to interannular conjugation between the pyrrole and benzene ring, the finding that the N-phenyl compound (**1d**) exists in the keto form suggests that this conjugation is not important.

Experimental[17]

General Procedure for the Ester Exchange Reaction with Sodium Benzyl Alcoholate——Metallic sodium (2 mol) was dissolved in dry benzyl alcohol, and the ethyl esters (**5**)[8] (1 mol) were added. The mixture was heated at 130—140° under N_2 for 7 hr. After the addition of cold water, the mixture was acidified with 10% H_2SO_4, and extracted with benzene. The extract was washed with satd. $NaHCO_3$. After removal of the benzene and benzyl alcohol *in vacuo* (5—10 mmHg), the residue was distilled under reduced pressure (the distillates crystallized immediately).

Benzyl 3-Hydroxypyrrole-2-carboxylate (**6a**)——bp 170° (1 mmHg), mp 79.0—80.0°. Colorless needles (from ether–petr. ether). Yield: 37.3%. IR ν_{max}^{KCl} cm^{-1}: 3320, 1660, 1580. MS *m/e*: 217 (M^+, 7.8%), 91 (100%). UV λ_{max}^{EtOH} nm (ε): 265 (19500). PMR ($CDCl_3$) δ: 5.29 (2H, s, CH_2Ph), 5.85 (1H, t, J=2.6, C_4–H), 6.68 (1H, t, J=2.6, C_5–H), 7.37 (5H, s), 7.7 (1H, br, OH), 8.2 (1H, br, NH). *Anal.* Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.22; H, 5.04; N, 6.63.

Benzyl 3-Hydroxy-1-methylpyrrole-2-carboxylate (**6b**)——bp 160° (1 mmHg), mp 57.5—58.5°. Colorless plates (from *n*-hexane). Yield: 57.3%. IR ν_{max}^{KCl} cm^{-1}: 3380, 1650. MS *m/e*: 231 (M^+, 14.4%), 91 (100%). UV λ_{max}^{EtOH} nm (ε): 265 (21100). PMR (CCl_4) δ: 3.68 (3H, s), 5.26 (2H, s, CH_2Ph), 5.58 (1H, d, J=3.0, C_4–H), 6.40 (1H, d, J=3.0, C_5–H), 7.30 (5H, s), 7.88 (1H, br, OH). *Anal.* Calcd. for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.42; H, 5.66; N, 6.27.

Benzyl 1-Benzyl-3-hydroxypyrrole-2-carboxylate (**6c**)——bp 185° (0.006 mmHg), mp 78.5—79.5°. Colorless needles (from *n*-hexane). Yield: 63.8%. IR ν_{max}^{KCl} cm^{-1}: 3430, 3415, 1705, 1605. MS *m/e*: 307 (M^+, 7.0%), 91 (100%). UV λ_{max}^{EtOH} nm (ε): 266 (18600). PMR (CCl_4) δ: 5.16, 5.21 (each 2H, s, $CH_2Ph\times2$), 5.72 (1H, d, J=3.0, C_4–H), 6.56 (1H, d, J=3.0, C_5–H), 6.75—7.35 (10H, m), 8.05 (1H, br, OH). *Anal.* Calcd. for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.26; H, 5.58; N, 4.73.

Benzyl 3-Hydroxy-5-methylpyrrole-2-carboxylate (**6e**)——bp 160° (0.009 mmHg), mp 124.0—125.0°. Colorless plates (from EtOH). Yield: 46.5%. IR ν_{max}^{KCl} cm^{-1}: 3290, 1645. MS *m/e*: 231 (M^+, 13.3%), 91 (100%). UV λ_{max}^{EtOH} nm (ε): 274 (21300). PMR ($CDCl_3$) δ: 2.17 (3H, s), 5.25 (2H, s, CH_2Ph), 5.57 (1H, d, $J_{1,4}$=3.0, C_4–H), 7.32 (5H, s), 7.4—8.1 (br, NH and OH). *Anal.* Calcd. for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.32; H, 5.72; N, 6.10.

Benzyl 3-Hydroxy-4-methylpyrrole-2-carboxylate (**6f**)——bp 150° (0.001 mmHg), mp 102.0—103.0°. Colorless leaflets (from 80% EtOH). Yield: 65.7%. IR ν_{max}^{KCl} cm^{-1}: 3330, 1635. MS *m/e*: 231 (M^+, 12.7%), 91 (100%). UV λ_{max}^{EtOH} nm (ε): 269 (16000). PMR ($CDCl_3$) δ: 1.98 (3H, s), 5.27 (2H, s, CH_2Ph), 6.50 (1H, d, $J_{1,5}$=3.0, C_5–H), 7.33 (5H, s), 7.4—8.2 (br, NH and OH). *Anal.* Calcd. for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.54; H, 5.71; N, 6.18.

Ethyl 3-Benzyloxypyrrole-2-carboxylate (**8a**)——A suspension consisting of ethyl 3-hydroxypyrrole-2-carboxylate (**5a**) (0.6 g), benzyl chloride (1.02 g), anhydrous K_2CO_3 (1.66 g) and dry acetone (50 ml) was refluxed for 10 hr. After filtration of the suspension, the filtrate was evaporated down, and purified by column chromatography on silica gel in $CHCl_3$ to give **8a** (0.42 g, 44.3%) as a fraction of lower *Rf* value and ethyl 1-benzyl-3-benzyloxypyrrole-2-carboxylate (**8c**) (0.36 g, 27.8%) as a higher *Rf* fraction, with recovery of the starting material (0.13 g). Compound **8a**: Colorless plates (from cyclohexane and next from MeOH–H_2O), mp 94.0—95.0°. IR ν_{max}^{KBr} cm^{-1}: 3230, 1656. MS *m/e*: 245 (M^+, 11.0%), 91 (100%). UV λ_{max}^{EtOH} nm (ε): 266 (19200). PMR ($CDCl_3$) δ: 1.38 (3H, t, J=7.0), 4.35 (2H, q, J=7.0), 5.12 (2H, s, CH_2Ph), 5.92 (1H, t, J=3.0, C_4–H), 6.73 (1H, t, J=3.0, C_5–H), 7.25—7.55 (5H, m), 8.90 (1H, br, NH). *Anal.* Calcd. for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.14; N, 5.71. Found: C, 68.65; H, 6.20; N,5.87. Compound **8c**: Colorless plates (from diisopropyl ether), mp 60.0—61.0°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1685, 1655. MS *m/e*: 335 (M^+, 2.4%), 91 (100%). UV λ_{max}^{EtOH} nm(ε): 266 (19600). PMR (CCl_4) δ: 1.29 (3H, t, J=7.6), 4.25 (2H, q, J=7.6), 5.04 (2H, s, OCH_2Ph), 5.48 (2H,s, NCH_2Ph), 5.83 (1H, d, J=3.0, C_4–H), 6.65 (1H, d, J=3.0, C_5–H), 7.00—7.60 (10H, m). *Anal.* Calcd. for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.37; H, 6.49; N, 4.36.

17) All melting points and boiling points are uncorrected. IR spectra were measured on a Hitachi EPI-G3 or Hitachi 215 infrared grating spectrophotometer. Mass (MS), UV and PMR spectra were recorded on Hitachi RMU-6E, Hitachi 124 and Hitachi R-20A (60 MHz) spectrometers, respectively. Tetramethylsilane was used as an internal standard in the PMR spectra. All the organic extracts were washed with satd. NaCl solution and dried over anhydrous magnesium sulfate before concentration. Column chromatography was performed on Mallinckrodt silicic acid, and thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 HF_{254}.

3-Benzyloxypyrrole (9a)——A solution of LiOH (0.2 g) in H_2O (20 ml) was added to a solution of **8a** (0.42 g) in EtOH (20 ml), and the mixture was refluxed under N_2 for 4 hr. The mixture was acidified (as determined with Congo red) with c. HCl, and the resulting precipitate (3-benzyloxypyrrole-2-carboxylic acid) was collected, washed and dried *in vacuo* (0.32 g). The carboxylic acid (0.32 g) was sublimed at 160°/20 mmHg to give **9a** (0.24 g, 80.9%) as unstable crystals, mp 95.0—96.0°. IR ν_{max}^{KBr} cm^{-1}: 3310, 1565. MS *m/e*: 173 (M^+, 21.9%), 91 (100%). PMR ($CDCl_3$) δ: 4.90 (2H, s, OCH_2Ph), 5.98 (1H, q-like, C_4–H), 6.35 (1H, q-like, C_2–H), 6.55 (1H, q-like, C_5–H), 7.36 (5H, s-like), 7.75 (1H, br, NH).

1-Benzyl-3-benzyloxypyrrole (9c)——A solution of LiOH (1.34 g) in H_2O (30 ml) was added to a solution of **8c** (2.34 g) in EtOH (30 ml), and the mixture was refluxed under N_2 for 5 hr. After removal of EtOH, the mixture was extracted with $CHCl_3$. The extract was concentrated and passed through a silica gel column (10 g) to give **9c** (1.13 g, 61.5%) as unstable crystals, mp 75—76°. Evolution of a gas observed in the column is probably due to silica gel-catalyzed decarboxylation of lithium 1-benzyl-3-benzyloxypyrrole-2-carboxylate concomitantly extracted. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1620. MS *m/e*: 263 (M^+, 19.4%), 91 (100%). PMR (CCl_4) δ: 4.78, 4.82 (each 2H, s, $CH_2Ph\times2$), 5.75 (1H, q-like, C_4–H), 6.08 (1H, t-like, C_2–H), 6.32 (1H, t-like, C_5–H), 6.87—7.45 (10H, m).

Hydrogenolysis of **9c** (0.4 g) in EtOH (20 ml) with 5% Pd–C (0.4 g) gave only a complex mixture, probably of decomposition products.

1-Methyl-4-oxo-2-pyrroline (1b)——Compound **6b** (0.35 g) was hydrogenated over 5% Pd–C (0.3 g) in EtOH (20 ml) at atomspheric pressure until the starting material had disappeared on TLC. After filtration, the filtrate was evaporated under reduced pressure to give **1b** as an unstable oil. IR ν_{max}^{film} cm^{-1}: 1625, 1545. MS *m/e*: 97 (M^+, 100%). UV λ_{max}^{EtOH} nm: 328; $\lambda_{max}^{n\text{-hexane}}$ nm: 322. PMR analysis of this material gave an tautomer (keto: enol) composition of *ca.* 14: 3 in $CDCl_3$ and of 9: 4 in CD_3OD. PMR ($CDCl_3$) δ: 3.13 (s, N–CH_3 for pyrrolinone), 3.48 (s, N–CH_3 for pyrrole), 3.72 (s, C_5–H for pyrrolinone), 5.07 (d, J=3.0, C_3–H for pyrrolinone), 5.67 and 6.16 (m, three ring H for pyrrole), 7.75 (d, J=3.0, C_2–H for pyrrolinone); (CD_3OD) δ: 3.16 (s, N–CH_3 for pyrrolinone), 3.47 (s, N–CH_3 for pyrrole), 4.99 (d, J=3.2, C_3–H for pyrrolinone), 5.55 (d, J=3.0, C_4–H for pyrrole), 6.20 (d, J=3.0, C_5–H for pyrrole), 7.97 (d, J=3.2, C_2–H for pyrrolinone).

1-Benzyl-4-oxo-2-pyrroline (1c)——Compound **1c** was obtained from **6c** in a manner similar to that for **1b**, as an unstable oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630, 1530. MS *m/e*: 173 (M^+, 43.5%), 91 (100%). UV λ_{max}^{EtOH} nm: 327; $\lambda_{max}^{n\text{-hexane}}$ nm: 332 PMR ($CDCl_3$) δ: 3.58 (2H, s, C_5–H), 4.43 (2H, s, CH_2Ph), 5.10 (1H, d, J=3.6, C_3–H), 7.36 (5H, m, benzene ring H), 7.84 (1H, d, J=3.6, C_2–H); (CD_3OD) δ: 4.51 (2H, s, CH_2Ph), 5.02 (1H, d, J=3.0, C_3–H), 7.22 (5H, m), 8.12 (1H, d, J=3.0, C_2–H).

2-Methyl-4-oxo-2-pyrroline (1e)——Compound **1e** was prepared from **6e** in a manner similar to that for **1b**, as an unstable solid. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1642. MS *m/e*: 97 (100%). UV λ_{max}^{EtOH} nm: 305; $\lambda_{max}^{n\text{-hexane}}$ nm: 293. PMR ($CDCl_3$) δ: 2.19 (3H, s-like, C_2–CH_3), 3.90 (2H, s-like, C_5–H), 5.05 (1H, s-like, C_3–H), 7.2 (1H, br, NH); (CD_3OD) δ: 2.19 (3H, s), 4.98 (1H, s, C_3–H).

1-Phenyl-4-oxo-2-pyrroline (1d)——A mixture of *tert*-butyl 1-phenyl-3-hydroxypyrrole-2-carboxylate (**7**)[8] (0.1 g), boron trifluoride etherate (1.0 ml), AcOH (1.2 ml) and dry ether (10 ml) was stirred at room temperature for 48 hr. After the addition of ether (10 ml) and H_2O (10 ml), $NaHCO_3$ powder was added to the mixture until foaming ceased. After separation of the ethereal layer, the aqueous layer was extracted with ether. The combined ethereal layer was washed, dried and evaporated to give **1d** as an unstable oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1655, 1596, 1530. MS *m/e*: 159 (M^+, 100%). UV λ_{max}^{EtOH} nm: 243, 354; $\lambda_{max}^{n\text{-hexane}}$ nm: 250, 342. PMR ($CDCl_3$) δ: 4.10 (2H, s, C_5–H), 5.46 (1H, d, J=3.7, C_3–H), 6.88—7.56 (5H, m, benzene ring H), 8.39 (1H, d, J=3.7, C_2–H); (CD_3OD) δ: 5.38 (1H, d, J=3.2, C_3–H), 7.2 (5H, m, benzene ring H), 8.72 (1H, d, J=3.2).

Ethyl 1-Methyl-3-hydroxypyrrole-4-carboxylate (2)——Compound **2** was prepared from *tert*-butyl 4-ethoxycarbonyl-1-methyl-3-hydroxypyrrole-2-carboxylate (**15**)[8] in a manner similar to that for **1d**, as an unstable oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3325, 1715, 1655. MS *m/e*: 169 (M^+, 30.6%), 123 (100%). UV λ_{max}^{EtOH} nm: 243; $\lambda_{max}^{n\text{-hexane}}$ nm: 239. PMR (CCl_4) δ: 1.35 (3H, t, J=7.0), 3.57 (3H, s), 4.25 (2H, q, J=7.0), 6.00 (1H, d, J=3.0, C_2–H), 6.71 (1H, d, J=3.0, C_5–H), 6.93 (1H, br, OH); (CD_3OD) δ: 1.30 (3H, t, J=7.5), 3.52 (3H, s), 4.21 (2H, q, J=7.0), 6.85 (1H, s, C_5–H).

Ethyl 1-Benzyl-3-hydroxypyrrole-4-carboxylate (3)——Compound **3** was prepared from *tert*-butyl 1-benzyl-4-ethoxycarbonyl-3-hydroxypyrrole-2-carboxylate (**16**)[8] in a manner similar to that for **1d**, as an unstable oil. IR ν_{max}^{film} cm^{-1}: 3350, 1705, 1640. MS *m/e*: 245 (M^+, 14.9%), 91 (100%). UV λ_{max}^{EtOH} nm: 242; $\lambda_{max}^{n\text{-hexane}}$ nm: 239. PMR (CCl_4) δ: 1.32 (3H, t, J=6.5), 4.23 (2H, q, J=6.5), 4.85 (2H, s, CH_2Ph), 6.13 (1H, d, J=2.8, C_2–H), 6.81 (1H, d, J=2.8, C_5–H), 7.2 (5H, m); (CD_3OD) δ: 1.30 (3H, t, J=7.5), 4.22 (2H, q, J=7.5), 4.92 (2H, s, CH_2Ph), 6.14 (1H, d, J=2.8, C_2–H), 6.98 (1H, d, J=2.8, C_5–H), 7.20 (5H, m).

Ethyl 1-Benzyl-4-ethoxycarbonyl-3-hydroxypyrrole-2-propionate (4)——Compound **4** was prepared from ethyl 1-benzyl-5-*tert*-butoxycarbonyl-3-ethoxycarbonyl-4-oxo-2-pyrroline-5-propionate (**17**)[1] in a manner similar to that for **1d**, as an unstable oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3400, 1720, 1675. MS *m/e*: 345 (M^+, 12.0%), 91 (100%). UV λ_{max}^{EtOH} nm: 242; $\lambda_{max}^{n\text{-hexane}}$ nm: 238. PMR (CCl_4) δ: 1.19 (3H, t, J=7.5), 1.31 (3H, t, J=7.5), 1.8—2.8 (4H, m, CH_2CH_2COO), 4.03 (2H, q, J=7.5), 4.24 (2H, q, J=7.5), 5.03 (2H, s, CH_2Ph), 6.73 (1H, s, C_5–H), 6.9—7.4 (5H, m); (CD_3OD) δ: 1.20 (3H, t, J=7.0), 1.31 (3H, t, J=7.0), 2.10—2.75 (4H, m), 4.03 (2H, q, J=7.0), 4.11 (2H, q, J=7.0), 5.04 (2H, s, CH_2Ph), 6.97 (1H, s, C_5–H), 6.9—7.4 (5H, m).